SYNTHETIC STRATEGIES FOR THE TOTAL SYNTHESIS OF ACUTUMINE ALKALOIDS AND THE DEVELOPMENT OF RADICAL DEOXYCHLORINATION REACTIONS

Thesis by

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Für mini Fründe und Familie

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ABSTRACT

The acutumine alkaloids are a family of architecturally complex propellane natural products with promising medicinal properties. Herein, we disclose the continued development of a synthetic strategy toward the asymmetric total synthesis of acutumine alkaloids. The spirocyclic scaffold was synthesized in two new series, which follow our successful access to the dechloroacutumine core in 2013. Central to the synthetic design is the retro-aldol/Dieckmann cyclization of a cyclobutyl lactone to install the spirocycle. The key cyclobutane intermediate is obtained via a photo-mediated [2+2]-cycloaddition of a furanyl dihydroindolone, which is accessible via a stereoselective 1,2-addition/reductive cyclization sequence of a benzoquinone-derived imine. Installation of the dimethoxyenone motif is accomplished via a late-stage elimination of a dimethoxyketal, which furnished the requisite vinylogous ester after methylation. Overall, these efforts have culminated in the synthesis of the complete carbocyclic core and oxidation pattern of the natural product (–)-acutuminine, with a C10 neopentyl alcohol in place of the neopentyl chloride.

Ten of the known acutumine alkaloids contain a neopentyl chloride; this motif provided underlying motivation for the development of novel radical deoxychlorination reactions, including the chlorination of cesium oxalates. This reaction allows access to hindered 2° and 3° alkyl chlorides, provides complementary reactivity to standard heterolytic conditions, and is performed under mild conditions using visible light and ethyl trichloroacetate as a $Cl^{\bullet}$ source. Application to deoxybromination and deoxyfluorination is also demonstrated, showcasing the versatility of the discovered halogenation. This method should find broad utility in the deoxyhalogenation of hindered alcohols, particularly in the pharmaceutical industry where selective installation of fluorides is a common challenge.

PUBLISHED CONTENT AND CONTRIBUTIONS

Portions of the work described herein were disclosed in the following communication:

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D.C.G. contributed to the reaction development, conducted experiments, and participated in preparation of the supporting data and writing the manuscript.

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LIST OF ABBREVIATIONS

$[\alpha]_D$	angle of optical rotation of plane-polarized light
Å	angstrom(s)
ABNO	9-azabicyclo[3.3.1]nonane *N*-oxyl
Ac	acetyl
acac	acetylacetonate
AIBN	azobisisobutyronitrile
APCI	atmospheric-pressure chemical ionization
aq	aqueous
atm	atmosphere(s)
BDE	bond dissociation energy
bipy	2,2'-bipyridine
BMEA	bis(2-methoxyethyl)amine
Bn	benzyl
Boc	*tert*-butoxycarbonyl
bp	boiling point
br	broad
brsm	based on recovered starting material
Bu	butyl
^{i}Bu	*iso*-butyl
^{n}Bu	butyl or *norm*-butyl
^{t}Bu	*tert*-butyl

c	concentration of sample for measurement of optical rotation
^{13}C	carbon-13 isotope
/C	supported on activated carbon charcoal
°C	degrees Celcius
calc'd	calculated
CAN	ceric ammonium nitrate
Cbz	benzyloxycarbonyl
CDI	1,1'-carbonyldiimidazole
cf.	consult or compare to (Latin: *confer*)
cis	on the same side
cm^{-1}	wavenumber(s)
conv.	conversion
COSY	homonuclear correlation spectroscopy
CSA	camphor sulfonic acid
Δ	heat or difference
δ	chemical shift in ppm
d	doublet
d	deutero or dextrorotatory
D	deuterium
DABCO	1,4-diazabicyclo[2.2.2]octane
dba	dibenzylideneacetone
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCE	1,2-dichloroethane

de novo	starting from the beginning; anew
DIAD	diisopropyl azodicarboxylate
DIBAL	diisobutylaluminum hydride
DIPEA	*N*,*N*-diisopropylethylamine
DMAP	4-(dimethylamino)pyridine
DMDO	dimethyldioxirane
DME	1,2-dimethoxyethane
DMF	*N*,*N*-dimethylformamide
DMPU	1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone
DMSO	dimethylsulfoxide
dr	diastereomeric ratio
ee	enantiomeric excess
E^+	electrophile
E	*trans* (entgegen) olefin geometry
e.g.	for example (Latin: *exempli gratia*)
EI	electron impact
ent	enantiomer of
epi	epimeric
equiv	equivalent(s)
ESI	electrospray ionization
Et	ethyl
et al.	and others (Latin: *et alii*)
ETCA	ethyl 2,2,2-trichloroacetate

FAB	fast atom bombardment
FTIR	fourier transform infrared spectroscopy
g	gram(s)
GC	gas chromatography
h	hour(s)
^{1}H	proton
[H]	reduction
HCA	1,1,1,3,3,3-hexachloroacetone
hfc	tris[3-(heptafluoropropylhydroxymethylene)-*d*-camphorate]
HFIP	hexafluoroisopropanol
HMBC	heteronuclear multiple-bond correlation spectroscopy
HMDS	hexamethyldisilazide
HMPA	hexamethylphosphoramide
$h\upsilon$	irradiation with light
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectrometry
HSQC	heteronuclear single quantum coherence spectroscopy
Hz	hertz
IC_{50}	half maximal inhibitory concentration (50%)
i.e.	that is (Latin: *id est*)
iso	isomeric
in situ	in the reaction mixture
J	coupling constant in Hz

k	rate constant
kcal	kilocalorie(s)
kg	kilogram(s)
L	liter
l	levorotatory
LAH	lithium aluminum hydride
L-Selectride	lithium tri-*sec*-butylborohydride
LC/MS	liquid chromatography–mass spectrometry
LDA	lithium diisopropylamide
LED	light emitting diode
m	multiplet or meter(s)
M	molar or molecular ion
m	*meta*
μ	micro
m-CPBA	*meta*-chloroperbenzoic acid
Me	methyl
^{MeO}bpy	4,4’-dimethoxy-2,2’-bipyridine
MeOH	methanol
MeCN	acetonitrile
mg	milligram(s)
MHz	megahertz
min	minute(s)
mL	milliliter(s)

MM	mixed method
mol	mole(s)
Ms	methanesulfonyl (mesyl)
MS	molecular sieves
m/z	mass-to-charge ratio
N	normality
NBS	*N*-bromosuccinimide
NCS	*N*-chlorosuccinimide
ND	not determined
nm	nanometer(s)
nM	nanomolar
NMI	1-methylimidazole
NMO	*N*-methylmorpholine *N*-oxide
NMR	nuclear magnetic resonance
nOe	nuclear Overhauser effect
NOESY	nuclear Overhauser enhancement spectroscopy
Nu^{-}	nucleophile
o	*ortho*
[O]	oxidation
p	*para*
PCC	pyridinium chlorochromate
Ph	phenyl
pH	hydrogen ion concentration in aqueous solution

PhH	benzene
PhMe	toluene
PIDA	[bis(acetoxy)iodo]benzene
PIFA	[bis(trifluoroacetoxy)iodo]benzene
Pin	pinacol
pK_a	acid dissociation constant
pm	picometer(s)
PMB	*para*-methoxybenzyl
ppm	parts per million
PPTS	pyridinium *para*-toluenesulfonate
Pr	propyl
^{i}Pr	isopropyl
^{n}Pr	propyl or *norm*-propyl
p-OMeTPT	2,4,6-tris(4-methoxyphenyl)pyrylium tetrafluoroborate
psi	pounds per square inch
p-TSA	*para*-toluenesulfonic acid
Pyr	pyridine
q	quartet
quant.	quantitative
R	generic (alkyl) group
R_L	large group
R	rectus
RCM	ring-closing metathesis

recry.	recrystallization
Red-Al	sodium bis(2-methoxyethoxy)aluminium hydride
ref	reference
R_f	retention factor
RF	response factor
rgt.	Reagent
rr	regioisomeric ratio
rt	room temperature
s	singlet or seconds
S	sinister
SAR	structure-activity relationship
sat.	saturated
SEM	2-(trimethylsilyl)ethoxymethyl
SFC	supercritical fluid chromatography
SPhos	2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl
t	triplet
TASF	tris(dimethylamino)sulfonium difluorotrimethylsilicate
TBABr	tetra-*n*-butylammonium bromide
TBACl	tetra-*n*-butylammonium chloride
TBAF	tetra-*n*-butylammonium fluoride
TBAI	tetra-*n*-butylammonium iodide
TBHP	*tert*-butyl hydroperoxide
TBS	*tert*-butyldimethylsilyl

TCDP	1,1’-thiocarbonyldi-2(1*H*)-pyridone
temp	temperature
TEMPO	2,2,6,6-tetramethylpiperidine 1-oxyl
TES	triethylsilyl
Tf	trifluoromethanesulfonyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
TMEDA	*N,N,N′,N′*-tetramethylethylenediamine
TMS	trimethylsilyl
TOF	time-of-flight
Tol	tolyl
trans	on the opposite side
Ts	*para*-toluenesulfonyl (tosyl)
UV	ultraviolet
UVA	ultraviolet A (315–400 nm)
UVC	ultraviolet C (100–280 nm)
vide infra	see below
w/v	weight per volume
X	anionic ligand or halide
xs	excess
Z	*cis* (zusammen) olefin geometry

Chapter 1

An Introduction to Acutumine Alkaloids

1.1 INTRODUCTION

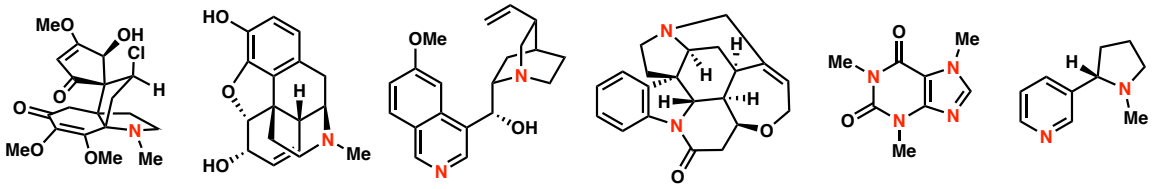
Natural products are a rich source of pharmaceutically active molecules with applications ranging from traditional folk medicine to large-scale development of drugs in the modern pharmaceutical industry.[1] Biologists and chemists alike have often looked to natural products to discover novel bioactive agents; currently, approximately one third of marketed drugs are derived from natural products.[2] With the advent of chemical proteomics, the study of naturally occurring small molecules has received renewed interest because it can lead to the elucidation of new mode of actions and the discovery of new druggable biological targets (*target based drug discovery*).[1,3,4] Within the realm of synthetic organic chemistry, natural products also take on an inspirational role due to their highly complex architectures that stimulate the creative minds of total synthesis chemists. Along these lines, natural products are often the underlying motivation for the development

of novel chemical transformations,[5] as well as clever, modular, and scalable synthetic routes that permit access to relevant analogues for structure-activity relationship (SAR) studies.[6] From serving as inspiration for reaction design to providing lead molecules for drug development, natural products remain of significant interest to chemists around the globe.

1.2 ALKALOIDS — A BRIEF INTRODUCTION

Alkaloids, such as (–)-acutumine (**1**, Figure 1.1),[7–9] are naturally occurring molecules that contain at least one basic nitrogen atom. Among this class of natural products, morphine (**2**) was the first to be isolated in 1805 from the poppy plant *Papaver somniferum*.[10] Quinine (**3**) – another famous alkaloid used in the treatment of malaria – was isolated from the bark of the *cinchona* tree shortly thereafter in 1920.[11] Aside from plant sources, alkaloids are also widely found in a variety of organisms, including bacteria and fungi. Due to their breadth of pharmaceutical properties, alkaloids have found widespread use as medicines, toxins, stimulants, and psychotropic substances. In particular, caffeine (**5**) and nicotine (**6**) are heavily present in our day-to-day lives.

Figure 1.1 *A selection of biologically active alkaloids.*



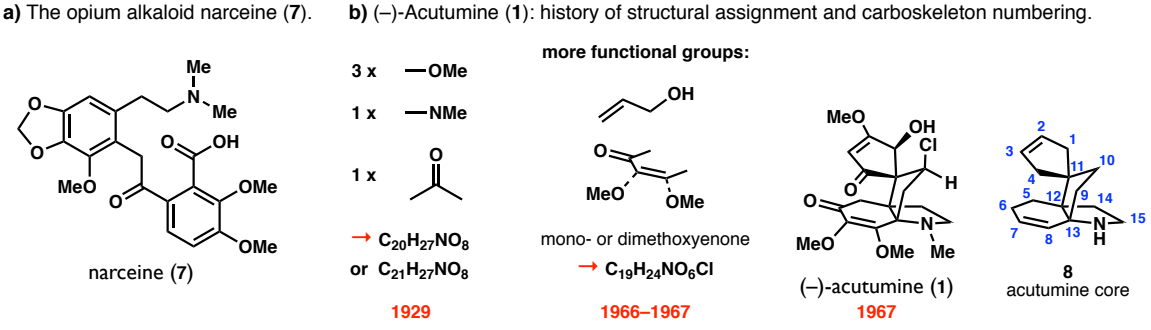
acutumine (**1**) morphine (**2**) quinine (**3**) strychnine (**4**) caffeine (**5**) nicotine (**6**)

1.3 (–)-ACUTUMINE AND RELATED NATURAL PRODUCTS

1.3.1 Isolation and Structural Assignment

The alkaloid (–)-acutumine (**1**, Figure 1.2b) was first isolated by Goto and Sudzuki from the leaves of the Chinese moonseed plant (*Sinomenium acutum*) in 1929.[7] The structure of this highly complex natural product posed a significant assignment challenge, and the authors proposed possible molecular formulas of $C_{20}H_{27}NO_8$ or $C_{21}H_{27}NO_8$. Their conclusions were based on the observations that 1) its absorption spectrum resembled that of narceine (**7**, Figure 1.2a), an opium alkaloid from *Papaver somniferum*, and 2) various functional group tests indicated the presence of three methoxy groups, one ketone, and an N–Me group (Figure 1.2b).

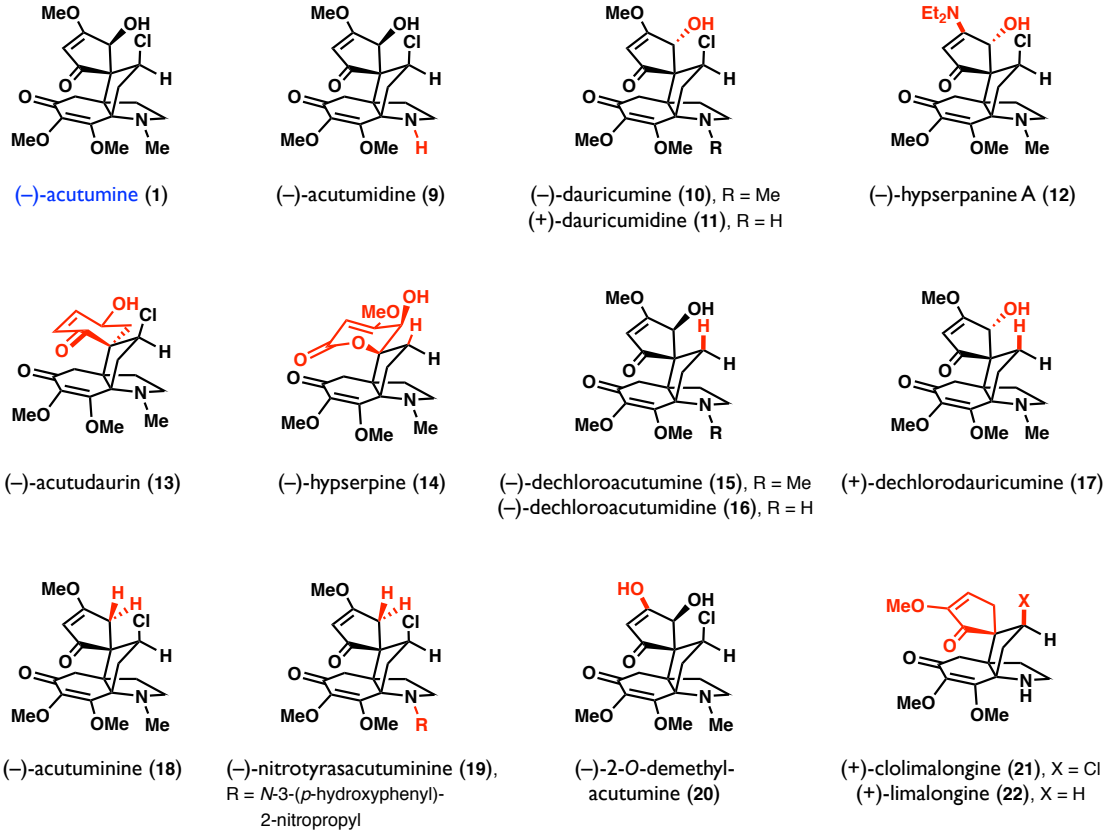
Figure 1.2 *The structures of narceine (**7**) and (–)-acutumine (**1**).*



The complete structure of (–)-acutumine (**1**) remained obscure for almost 40 years, until the Goto group disclosed further analyses in 1966 and 1967.[12,13] The molecular formula was revised to $C_{19}H_{24}NO_6Cl$ based on mass spectrometric and combustion analysis, which indicated the presence of a chlorine atom. With the advent of NMR spectrometry, further functional groups could be identified, such as the allylic alcohol and methoxyenone (Figure 1.2b). The extensive efforts to assign the structure of (–)-acutumine

(**1**) ultimately culminated in the 1967 publication of the X-ray crystal structure of this highly complex alkaloid and its acetate derivative,[14,15] revealing that (–)-acutumine (**1**) contains a [4.3.3] propellane core with a spirocyclic cyclopentenone. The X-ray crystal structure also established that (–)-acutumine (**1**) contains a neopentyl chloride at C10, as well as five contiguous stereocenters, two of which are all carbon quaternary centers.

Figure 1.3 *Acutumine natural product family.*



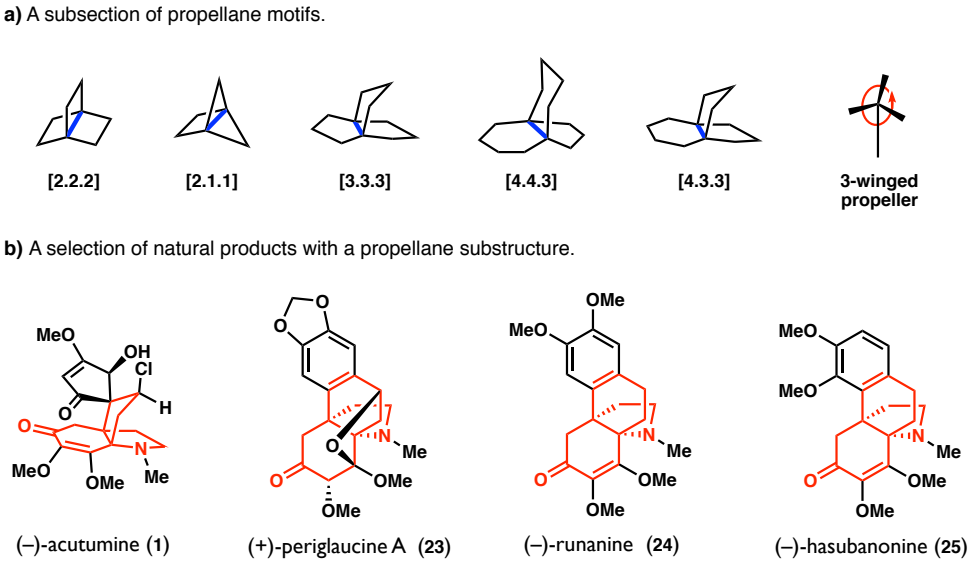
Since the landmark publication in 1929, fifteen related acutumine natural products have been isolated to date (Figure 1.3).[7–9,16–28] Mostly, these alkaloids differ in the functionalization and oxidation of the key spirocyclic cyclopentenone (highlighted in red), although variants with larger spirocycles such as (–)-acutudaurin (**13**)[22] and (–)-hypserpine

(**14**)[21] are known as well. A number of dehalogenated and N-demethylated variants have been disclosed also, including (–)-dechloroacutumine (**15**)[20] and (–)-acutumidine (**9**).[13,29]

1.3.2 Propellane Core: Related Natural Product Families

Natural products are often classified by the architecture of their carboskeleton or other substructures, such as complex heterocycles. One commonly encountered substructure is a propellane core (Figure 1.4a).[30] Most propellanes are classified via the 3 bridging rings that surround a common C–C bond (highlighted in blue). For instance, a [2.2.2] propellane contains three bridging rings with two carbons each, and the [4.3.3] propellane contains three bridging rings with four, three, and three carbons respectively.

Figure 1.4 *A selection of propellane motifs and natural products.*



The terminology "propellane" derives from the structural similarity of three bridging rings to a three-winged propeller. There are over 10,000 molecules that have been identified with a propellane core, amongst which are various natural products and

alkaloids.[30] One such example is (–)-acutumine (**1**, Figure 1.4b), which contains a [4.3.3] propellane core, as well as the related hasubanan alkaloids (+)-periglaucine A (**23**),[31] (–)-runaine (**24**),[32] and (–)-hasubanonine (**25**),[33] each of which are [4.4.3] propellanes.

The structural assignment of (–)-acutumine (**1**) in 1967 (see section 1.3.1) was key in hinting toward a biosynthetic link between the acutumine and hasubanan alkaloids.[34] Both natural product families contain a propellane core (highlighted in red, Figure 1.4b), which consists of a dihydroindolone bicycle that is bridged with a 5- or 6-membered ring. This architectural commonality is one of the chief foundations for our laboratories interest in the synthesis of both hasubanan and acutumine alkaloids since we imagined that these complex natural products could be accessed via a unified synthetic strategy.

1.3.3 Biological Activity and Medicinal Properties

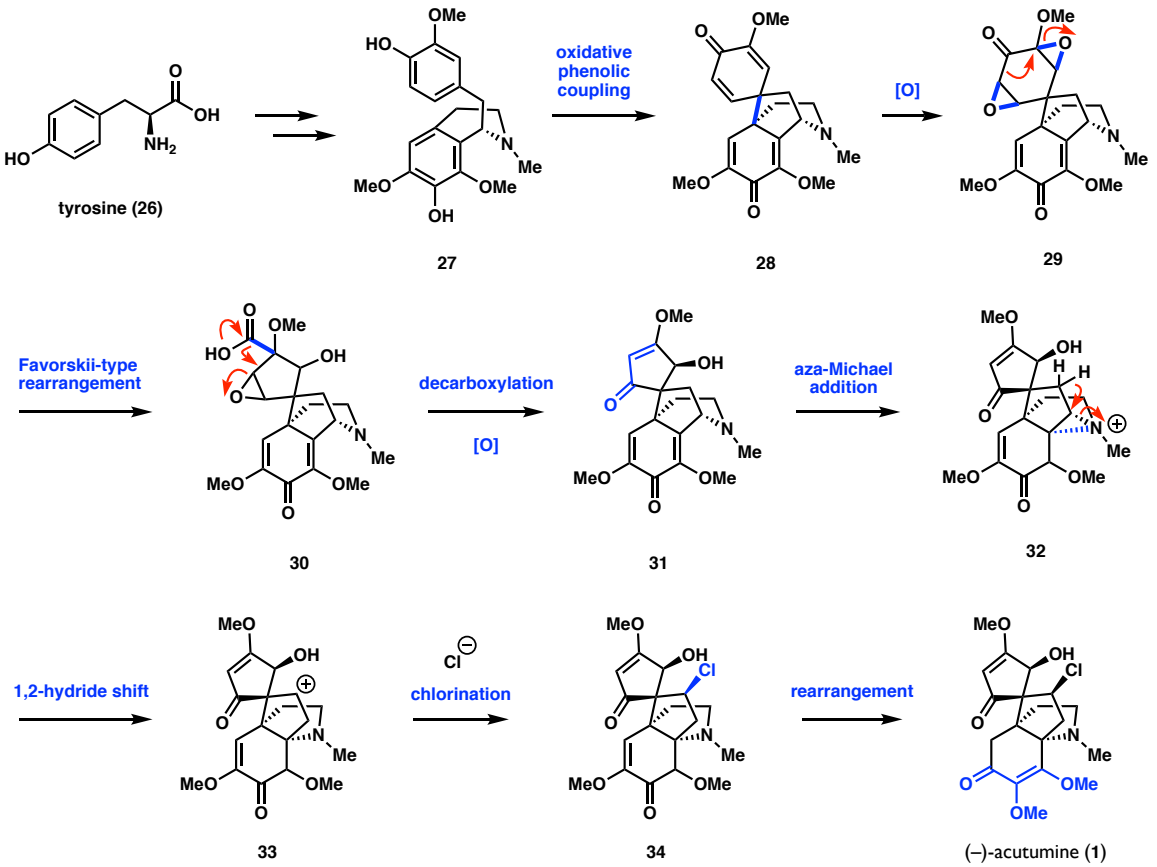
(–)-Acutumine (**1**) has shown promising biological activity related to neurological disorders, cancer, and inflammation.[24,35,36] In particular, this complex alkaloid and structural analogues were patented in 2004 as they showed promising antiamnesic activity in mice, which were subjected to a Morrison water maze model.[36] (–)-Acutumine (**1**) has also demonstrated selective T-cell cytotoxicity in MOLT4 and HUT78 cell lines, albeit in moderate inhibitory concentrations (IC_{50} = 13.2 μM).[24] Finally, in 2016 (–)-acutumine (**1**) was subjected to an anti-inflammatory assay, in which it was shown to inhibit the formation of prostaglandin D2 in RAW264.7 cells (49% inhibition at 2 μM).[35] Despite the breadth of interesting biological activity, the biological target and the essential pharmacophore of (–)-acutumine (**1**) are unknown. This uncertainty lends importance to the further study of

the biological activity of acutumine natural products, as well as underlines the need for SAR (structure-activity relationship) studies to locate its possible warheads and medicinally relevant, potent analogues.

1.3.4 Biosynthesis

One year after the structure of (–)-acutumine (**1**) had been determined via X-Ray crystallography, Barton proposed a biosynthetic pathway for this complex alkaloid (Scheme 1.1).[34] In his work, Barton postulated that (–)-acutumine (**1**) is derived from two

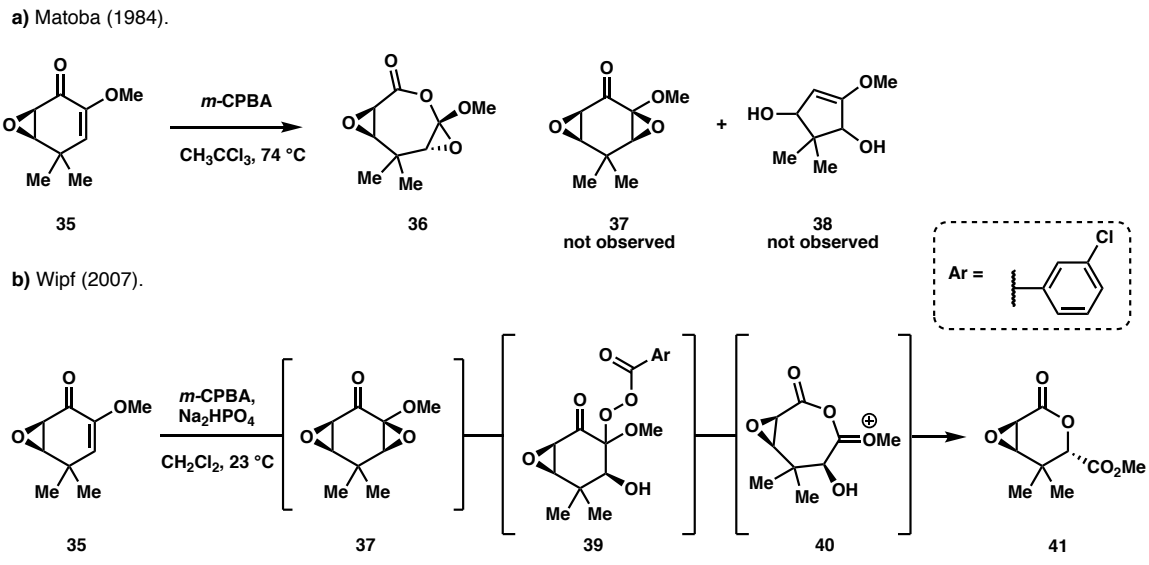
Scheme 1.1 *Barton's biosynthetic proposal (1968).*



molecules of tyrosine (**26**), which in analogy to the benzoisoquinoline pathway may be advanced to bisphenol **27**.[37] A key oxidative phenolic coupling may then install the spirocycle found in the natural product. After bis-epoxidation of dienone **28**, a Favorskii-type rearrangement may reveal the cyclopentane found in the natural product, which after decarboxylation, epoxide-opening, and oxidation affords cyclopentenone **31**. A subsequent aza-Michael addition was then thought to form aziridine-type intermediate **32**, which induces a key hydride shift to reveal cation **33** which is trapped with chloride to afford the key neopentyl chloride found in the natural product. Following final rearrangement on the 6-membered ring, (–)-acutumine (**1**) is formed.

In 1984, Matoba investigated the feasibility of the intermediacy of a bis-epoxy-dienone and Favorskii-type rearrangement in the biosynthesis of (–)-acutumine (**1**).[38] The authors found that exposing mono-epoxide **35** (Scheme 1.2a) to *m*-CPBA resulted in formation of lactone **36**; bis-epxoide **37** and Favorskii-rearrangement product **38** were not

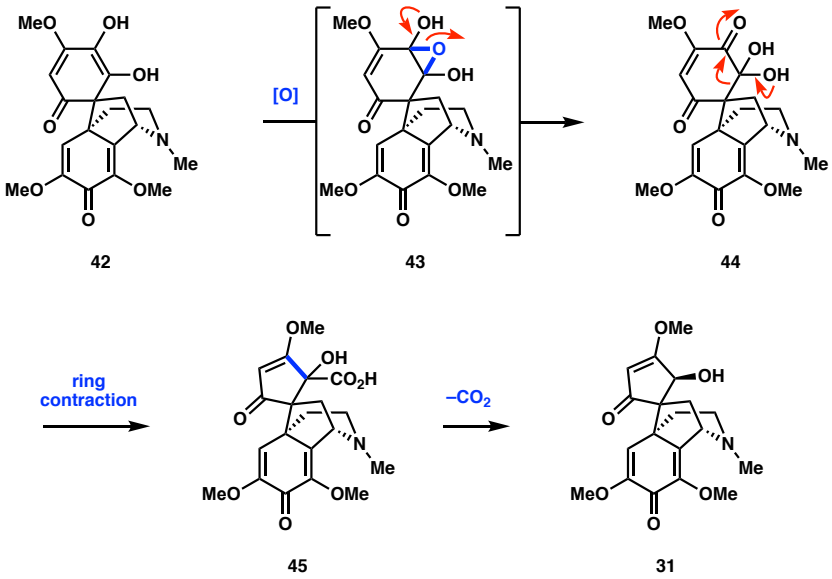
Scheme 1.2 *Matoba and Wipf's investigations into the biosynthesis of (–)-acutumine.*



observed. In 2007, Wipf and coworkers followed up on Matoba's investigations, and discovered that epoxidation of enone **35** induced lactone-formation and rearrangement to ring-contracted lactone **41**.[39] Again, Favorskii-products were not observed. At this point in time, Wipf proposed a correction to the structural assignment of Matoba's oxidation product **36**, which the authors believed would rearrange to 6-membered lactone **41** via the intermediacy of oxonium **40**.

Overall, both investigations into the rearrangements of bis-epoxy-dienones could not verify the feasibility of a Favorskii-type ring-contraction in the biosynthesis of (–)-acutumine (**1**, Scheme 1.1). Wipf thus put forth an alternative mechanism for the formation of cyclopentenone **31** (Scheme 1.3),[39] which was partly based on the disclosure of a novel acutumine alkaloid in 2001, (–)-acutudaurin (**13**, Figure 1.3), which contains a spirocyclic

Scheme 1.3 *Wipf's alternate mechanism for the formation of spirocyclic cyclopentenone* ***31*** *found in (–)-acutumine (****1****).*



cyclohexenone.[22] It was imagined that a similar enone **42** related to acutudaurin may undergo epoxidation in nature (Scheme 1.3), thus leading to α-hydroxylated quinone **44**. This highly oxidized quinone could then undergo a ring contraction event and form the requisite cyclopentenone **31** upon final decarboxylation. Despite the lack of evidence for a Favorskii-rearrangement process on model-systems in a chemistry laboratory, the authors conclude their investigations with the thought that an enzymatic process may still render Barton's original proposed reactivity feasible in nature. Thus, the precise process by which the spirocyclic cyclopentenone is formed in the biosynthesis of (–)-acutumine (**1**) still remains elusive.

1.3.5 Biochemical Investigations into the Biosynthesis

Since its original isolation in 1929 from *Sinomenium acutum*, (–)-acutumine (**1**) has been isolated from plants of the Menispermacae family as well. A number of enlightening feeding studies have been conducted with both species in order to elucidate some of the biosynthetic pathways involved in the synthesis of (–)-acutumine (**1**), as well as to investigate interconversion of some of the natural product family members. One of the key elements in Barton's biosynthetic proposal is that the synthesis of (–)-acutumine (**1**) begins with tyrosine, which is elaborated to a benzylisoquinoline motif (see **27**, Scheme 1.1, Section 1.3.4). The biosynthesis of benzylisoquinoline derivatives from tyrosine has been well established in the literature,[40] so Sugimoto *et al.* set out to investigate whether tyrosine is indeed a precursor to (–)-acutumine (**1**). In the late 1990s, the authors fed ^{14}C-labeled tyrosine to the *Menispermum dauricum* root culture.[41,42] ^{14}C-labeled acutumine was

subsequently isolated, indicating that the alkaloid is indeed derived from two molecules of tyrosine. Thus, the intermediacy of a benzylisoquinoline core in the biosynthesis is feasible.

Upon formation of the benzylisoquinoline core, Barton proposed that an oxidative phenolic coupling may install the vicinal all-carbon quaternary stereocenters. Similar intra- and intermolecular phenolic couplings have been shown to be operative in the biosynthesis of related molecules, and it occurs through cytochrome P450 enzymes (CYPs).[43–46] In order to investigate the potential involvement of CYP enzymes in the biosynthesis of (–)-acutumine (**1**), the *Menispermum dauricum* root culture was treated with ketoconazole, a known CYP inhibitor.[46] The various alkaloid constituents were subsequently analyzed, and it was found that there was an increased content of tyramine, an early precursor of the benzylisoquinoline core, and that there was a decreased amount of (–)-acutumine (**1**). These results are indirect evidence that CYP enzymes are involved in the biosynthesis of (–)-acutumine (**1**) during an phenolic oxidation process.

A number of feeding studies were also conducted to investigate the Cl-substituent found in (–)-acutumine (**1**).[29,14,13,37,34,41,42,47] In particular, there was a concern that the chlorine atom may have been introduced during the isolation process since chlorinated natural products from terrestrial and higher order plants are very rare.[48–50] In order to investigate this question, Barton *et al.* utilized hydrochloric acid containing ^{36}Cl to isolate acutumine (**1**) from *Sinomenium acutum*.[34] The isotopically labeled acid was used to macerate the plant, and after isolation and separation of (–)-acutumine (**1**), it was determined that the natural product was not isotopically labeled. This indicated that the chlorine atom was present in the natural product before the isolation process had begun.

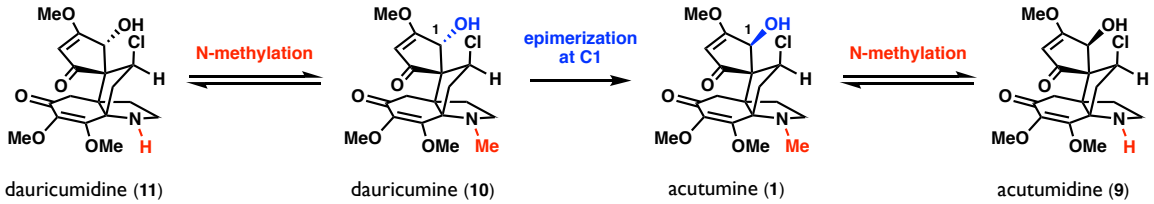
There have also been a number of studies on the respective quantities of (–)-dechloroacutumine (**15**) and (–)-acutumine (**1**) that are formed in media with differing Cl-concentrations. Cl-deficient media were rich in (–)-dechloroacutumine (**15**), and ranged to isolations without detectable quantities of (–)-acutumine (**1**). Highly chlorinated media, on the other hand, showed a distribution of both natural products, indicating that the concentration of chloride in the environment and the plant is crucial in the biosynthesis of (–)-acutumine (**1**).

One of the key questions that has remained unanswered over the years is how the chloride is installed in (–)-acutumine (**1**). It was hypothesized that (–)-dechloroacutumine (**15**) may be a biosynthetic precursor to (–)-acutumine (**1**), considering that they share a biosynthetic pathway from tyrosine.[42] In order to investigate this hypothesis, ^{3}H-labeled dechloroacutumine was fed to the *Menispermum dauricum* root culture, and it was found that 28% was taken up by the plant.[42] Small quantities (5%) of ^{3}H-labeled acutumine were then isolated, indicating that (–)-dechloroactumine (**15**) is a precursor to (–)-acutumine (**1**). However, the fact that only 5% out of 28% was converted to (–)-acutumine (**1**) has two possible meanings: 1) (–)-dechloroacutumine (**15**) is not a direct precursor to (–)-acutumine (**1**) and other biosynthetic processes are involved in between, or 2) the plant cells may be accumulating (–)-dechloroacutumine (**15**) or compartmentalizing enzymes are involved in the biosynthesis. This type of compartmentalizing or regulation has been described in natural product biosynthesis in the past.

In 2001, Sugimoto *et al.* disclosed novel labeling experiments which shed light on other biosynthetic interconversions between a number of acutumine alkaloids.[23] First, ^{36}Cl-

labeled alkaloids **1** and **9**–**11** (Figure 1.5) were generated by growing the *Menispermum dauricum* root culture in ^{36}Cl-labeled medium. The chromatographically separated, ^{36}Cl-labeled alkaloids were then independently fed to the *Menispermum dauricum* root culture in a Cl-deficient medium. The root culture metabolized each isotopically labeled alkaloid, and the acutumine alkaloids that were produced with ^{36}Cl were subsequently analyzed. The results of the four feeding experiments were that 1) dauricumine (**10**) is epimerized to acutumine (**1**), 2) dauricumine (**10**) and dauricumidine (**11**) interconvert by an N-methylation/demethylation process, and 3) that acutumine (**1**) and acutumidine (**9**) interconvert via a similar N-methylation/demethylation. The epimerization between dauricumidine (**11**) and acutumidine (**9**) and vice versa was not observed, nor the epimerization of acutumine (**1**) to dauricumine (**10**).

Figure 1.5 *Proposed biosynthetic interconversion between acutumine alkaloids.*



Overall, the results of these interconversion studies suggest that dauricumine (**10**) is the biogenetic precursor to acutumine (**1**), and that it is likely the first chlorinated alkaloid produced in the root culture. It is these conclusions that have further cemented the hypothesis that acutumine (**1**) is not a direct product of dechloroacutumine (**15**, Figure 1.3, Section 1.3.1). Instead, it is envisioned that dechlorodauricumine (**17**) may be the substrate for biochlorination, leading to dauricumine (**10**, Figure 1.5), which is then epimerized to acutumine (**1**). Despite the extensive studies summarized in this section, to our knowledge,

feeding studies of dechlorodauricumine (**15**) have not been disclosed to date. Thus, the chlorination process and the identity of the halogenation substrate remain elusive.

1.4 PREVIOUS SYNTHETIC STUDIES OF ACUTUMINE

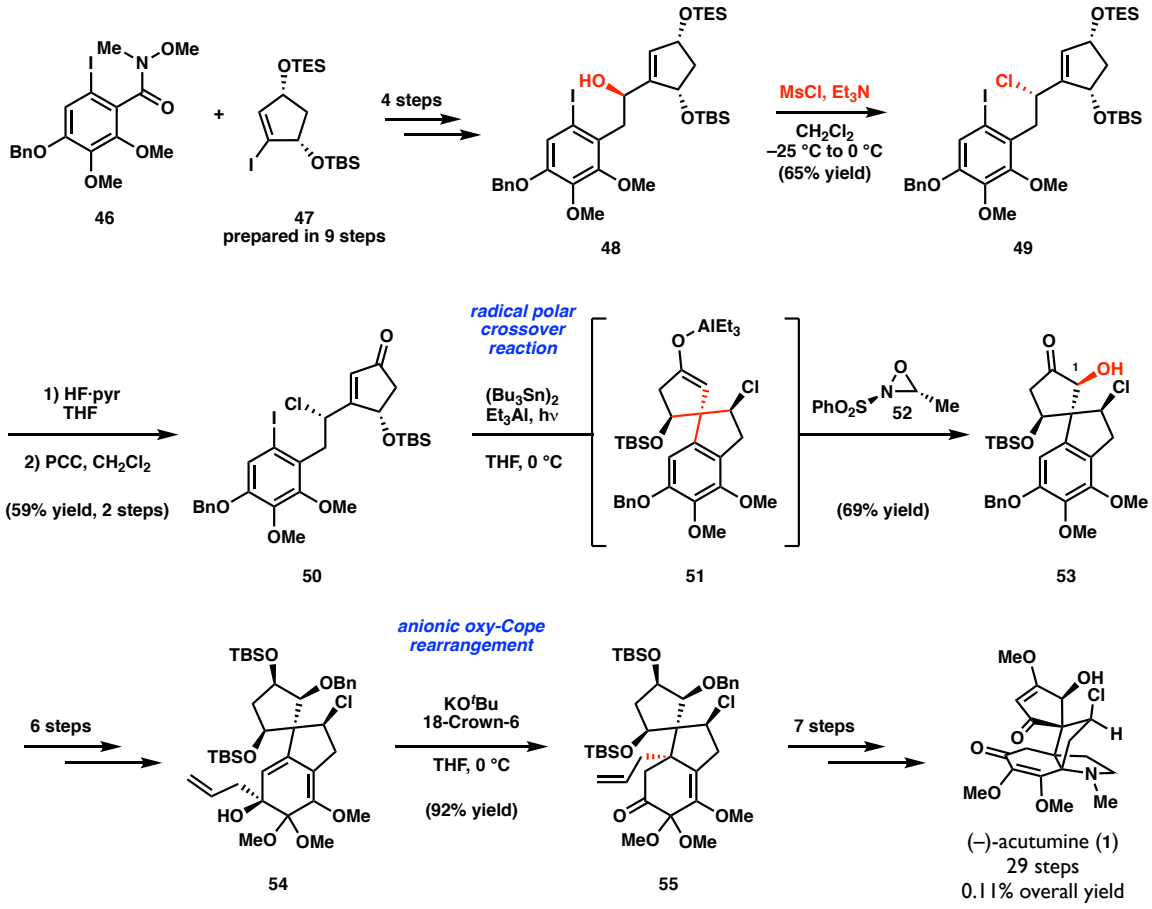
Between the years of 2005–2007,[51–53] Castle and Sorensen disclosed their core synthetic strategies toward the acutumine framework, highlighting the increasing synthetic interest in this complex alkaloid scaffold. Both laboratories continued their synthetic efforts on this natural product for several years, culminating in the first asymmetric total synthesis by Castle in 2009.[54–56] Our own synthetic efforts toward (–)-acutumine (**1**) began in 2011,[57,58] and the second total synthesis was disclosed by Herzon in 2013.[59–61] There have also been a number of synthetic efforts toward the acutumine scaffold that are exclusively published in dissertations, including work from the laboratories of Kobayashi,[62] Martin,[63] and Raney/Livinghouse.[64] Advanced efforts toward a total synthes of (–)-acutumine (**1**) in the Sorensen laboratory are also disclosed in two dissertations.[65,66]

1.4.1 Castle's Total Synthesis

After disclosing their key steps to the acutumine core in 2005 and 2007,[51,52] Castle completed the first total synthesis of (–)-acutumine (**1**) in 2009.[54,55] Their strategy leveraged a beautiful radical-polar crossover reaction to install the spirocyclic framework (Scheme 1.4). First, secondary alcohol **48** — obtained in 4 steps from vinyl iodide **46** and Weinreb amide **47** —was chlorinated early on in the synthesis, and the resulting secondary chloride **49** was carried through the remaining steps. Upon revealing enone **50**, the authors

induced the key radical-polar crossover reaction by generating the aryl radical in the presence of hexabutylditin and a flood lamp. Following 1,4-addition into the enone and crossing over to the polar mechanism, aluminum enolate **51** was oxidized with oxaziridine **52** in one-pot to afford α-hydroxyketone **53**. With three of the necessary four rings in hand, the authors advance ketone **53** six steps to homoallylic alcohol **54**, which was subjected to an anionic oxy-Cope rearrangement to install the final quaternary carbon. The allyl handle **55** was subsequently leveraged to install the pyrrolidine ring, and final oxidation to the spirocyclic cyclopentenone afforded (–)-acutumine (**1**) after a total 29-step sequence.

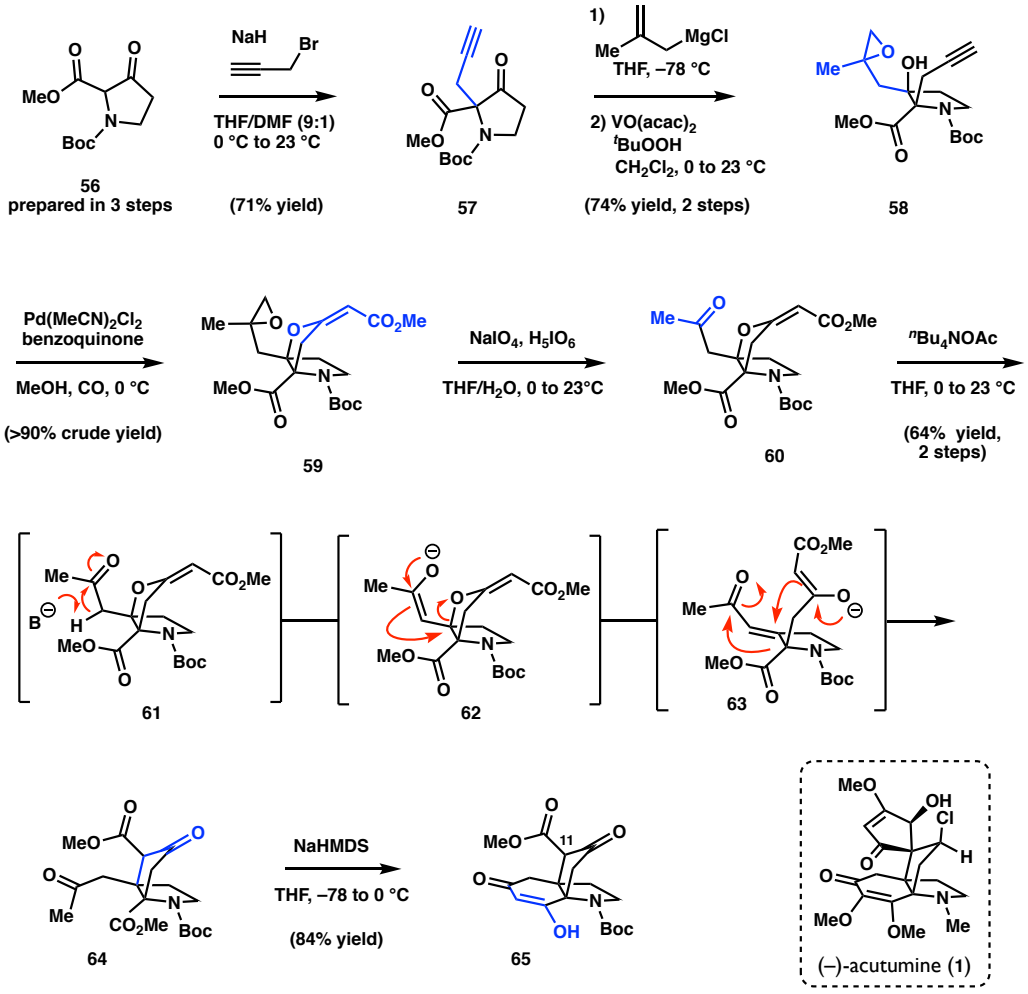
Scheme 1.4 *Castle's synthesis of (–)-acutumine (**1**) (2009).*



1.4.2 Sorensen's Strategy

In 2007, Sorensen and Moreau disclosed their key strategy to access the propellane framework of acutumine, harnessing classical carbonyl chemistry (Scheme 1.5).[53] Pyrrolidinone **56** — available in three steps from N-Boc-β-alanine[67] — was first functionalized via an alkylation/Grignard addition sequence, affording epoxide **58** after treatment with ^{t}BuOOH and VO(acac)$_2$. Utilizing the neopentyl alcohol found in **58**, a Pd-

Scheme 1.5 *Sorensen's initial access to the propellane core of (–)-acutumine (**1**).*

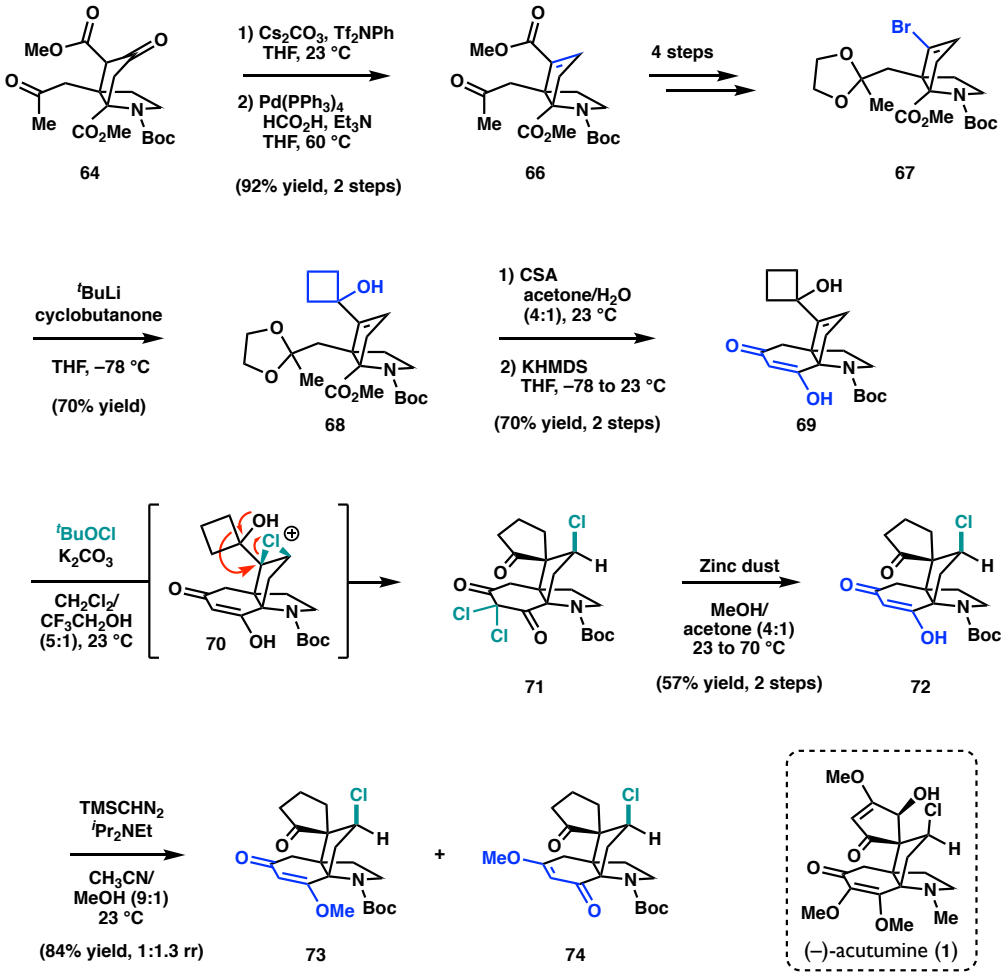


mediated carbonylative cyclization afforded vinylogous ester **59**, which provided key cyclization precursor **60** upon periodiate mediated epoxide-cleavage to the ketone. Treatment of ketone **60** with mild base induced E1cb elimination of masked enolate **62**, which subsequently underwent a Michael addition to afford bicycle **64**. A subsequent Dieckmann cyclization with NaHMDS afforded the propellane core **65** after a total of 10 steps. Subsequent efforts were directed at functionalizing C11 and installing the spirocycle through carbonyl condensation chemistry. Unfortunately, the ring closure to the spirocycle proved challenging, culminating in a revised synthetic strategy.

In an effort to address the spirocycle formation, the Sorensen group developed a novel strategy involving a chloronium-induced semipinacol rearrangement of cyclobutanol **69** (Scheme 1.6),[65,66] which would not only address the spirocycle formation, but also the very challenging installation of the neopentyl chloride found in (–)-acutumine (**1**). The Sorensen group found that treatment of cyclopentanone **64** — an intermediate from their prior synthetic efforts — could be converted to cyclopentene **66** via enol-triflate formation and Pd-mediated reduction. The ester functional group handle could subsequently be converted to vinyl bromide **67** in four steps, which allowed for a vinyllithium addition into cyclobutanone to afford cyclobutanol **68**. After much experimentation, it was found that dioxolane-deprotection and Dieckmann cyclization to vinylogous acid **69** was required first for a subsequent successful semipinacol. The key chloronium-induced semipinacol rearrangement was then accomplished by subjecting cyclobutanol **69** to ^{t}BuOCl and K_2CO_3, affording a single isomer of the desired spirocycle **71**. Unfortunately, the chloronium-formation was accompanied by overoxidation on the 6-membered ring,

leading to the dichloro-malonate motif found in product **71**. Nevertheless, the authors were able to subject chloride **71** to Zn dust and afford the desired vinylogous acid **72** in good yield over two steps. Finally, methylation of the vinylogous acid with $TMSCHN_2$ afforded a 1:1.3 mixture of the desired and undesired vinylogous ester isomers **73** and **74**, culminating in a 21-step synthesis of the acutumine core starting from N-Boc-β-alanine.

Scheme 1.6 *Chloronium-induced semipinacol rearrangement strategy: Sorensen's synthesis of the spirocyclic core.*

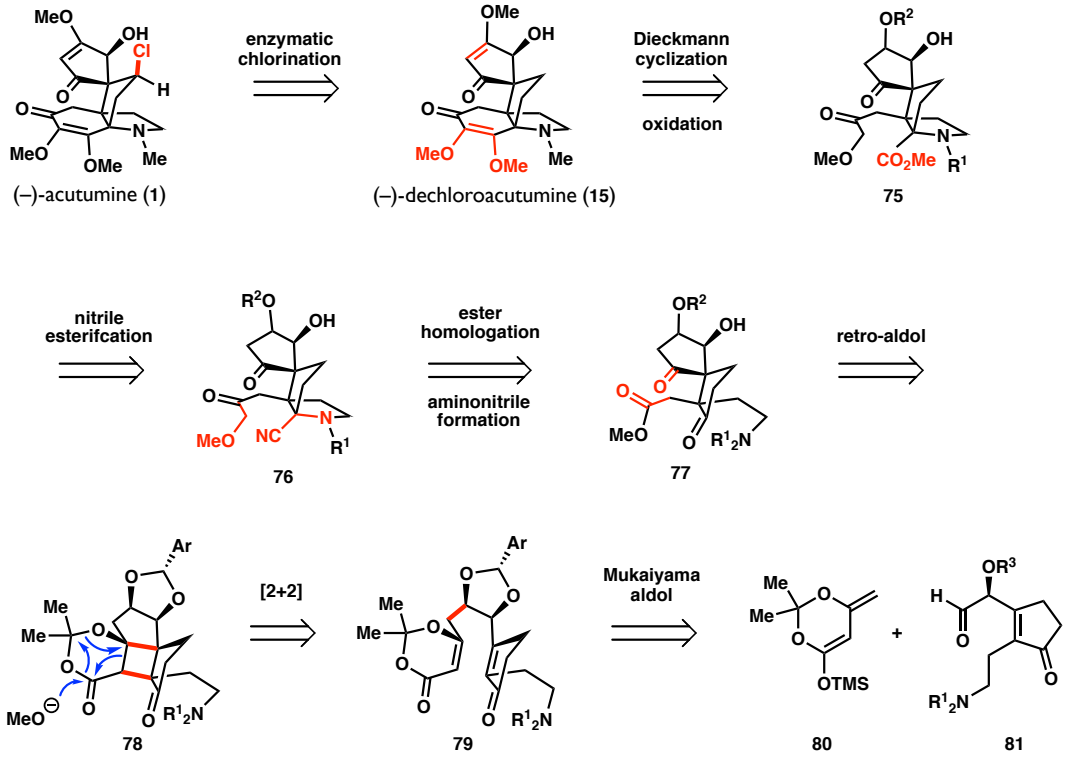


Having successfully formed the spirocyclic core of acutumine on the model substrate (Scheme 1.6), the Sorensen laboratory began investigating the advancement of a more functionalized system (not shown) so as to bring in the oxidation state needed for the spirocyclic cyclopentenone.[66] To the best of our knowledge, those efforts have proven unfruitful to date.

1.4.3 Kobayashi's Strategy

In 2009, Kobayashi and Ngyuen disclosed their synthetic strategy toward acutumine (**1**).[62] Their retrosynthetic analysis envisioned a late-stage enzymatic chlorination of dechloroacutumine (**15**), which may be arise from a Dieckmann cyclization

Scheme 1.7 *Kobayashi's retrosynthetic analysis.*

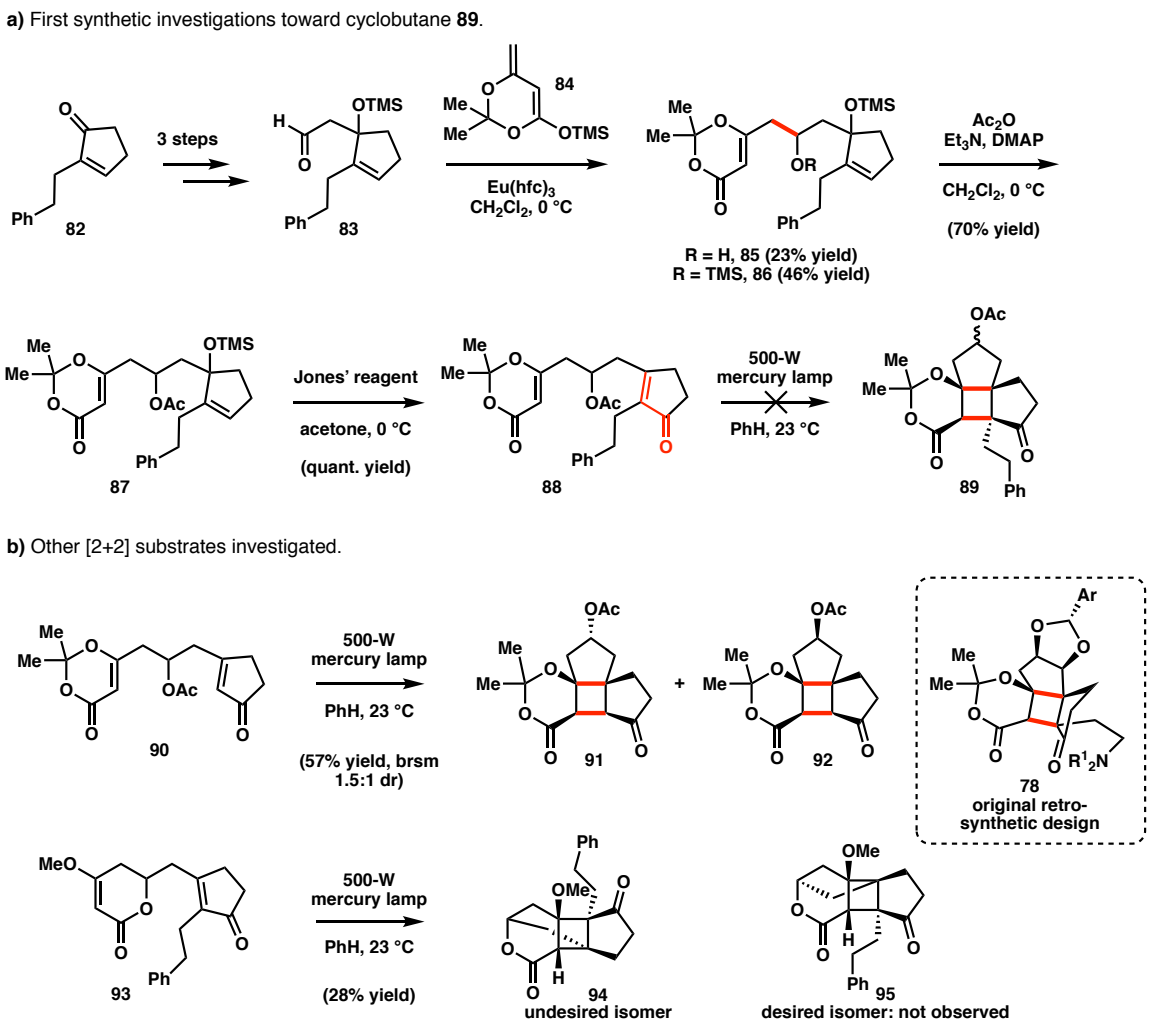


of α-methoxyketone **75**. The ester in **75** was envisioned to derive from nitrile **76**, the product of a key aminonitrile formation of cyclopentanone **77** that could forge the pyrrolidine ring. It was further imagined that tricarbonyl intermediate **77**, which contains the spirocyclic core, could be obtained through a [2+2]-cycloaddition/retro-aldol sequence of cyclopentenone **79**. This key intermediate was further simplified to silyl enol ether **80** and aldehyde **81**, which were envisioned to couple in a Mukaiyama aldol event to afford the [2+2]-precursor **79**.

Initial synthetic efforts were directed at accessing the key cyclobutane through the photo-mediated [2+2]-cycloaddition. Toward this end, cyclopentenone — accessed in four steps from 3-phenylpropanal — was advanced three steps to aldehyde **83** (Scheme 1.8a). Subsequent coupling with silyl enol ether **84** afforded the desired product as a mixture of free and silylated alcohols **85** and **86** in a combined 69% yield. Subsequent acetylation and Jones' oxidation to the requisite enone **88** was accomplished in good yield. Unfortunately, when the key bis-enone **88** was subjected to UV light (500W Hg lamp), no desired product was observed. The authors attributed the lack of reactivity to the congested nature of the cyclobutane product **89**, and set out to investigate more simplified cycloaddition precursors. The authors thus accessed bis-enone **90** (Scheme 1.8b), which indeed underwent the desired [2+2]-cycloaddition to cyclobutanes **91** and **92** in 57% yield (brsm), as an inconsequential mixture of diastereomers at the acetate-protected alcohol. However, the product did not contain the crucial handle for pyrrolidine installation, and a more direct access to the oxidation state of the spirocyclic cyclopentanone was desired as well. Thus, a more functionalized enone **93** was synthesized and subjected to the same [2+2]-

conditions; unfortunately, the authors found exclusive formation of the undesired cycloaddition isomer **94** in a modest 28% yield after six days of UV irradiation. To the best of our knowledge, these [2+2]-cycloaddition studies conclude the disclosed chemistry performed to realize the Kobayashi strategy; retro-aldol trials of cyclobutane **91** were not discussed.

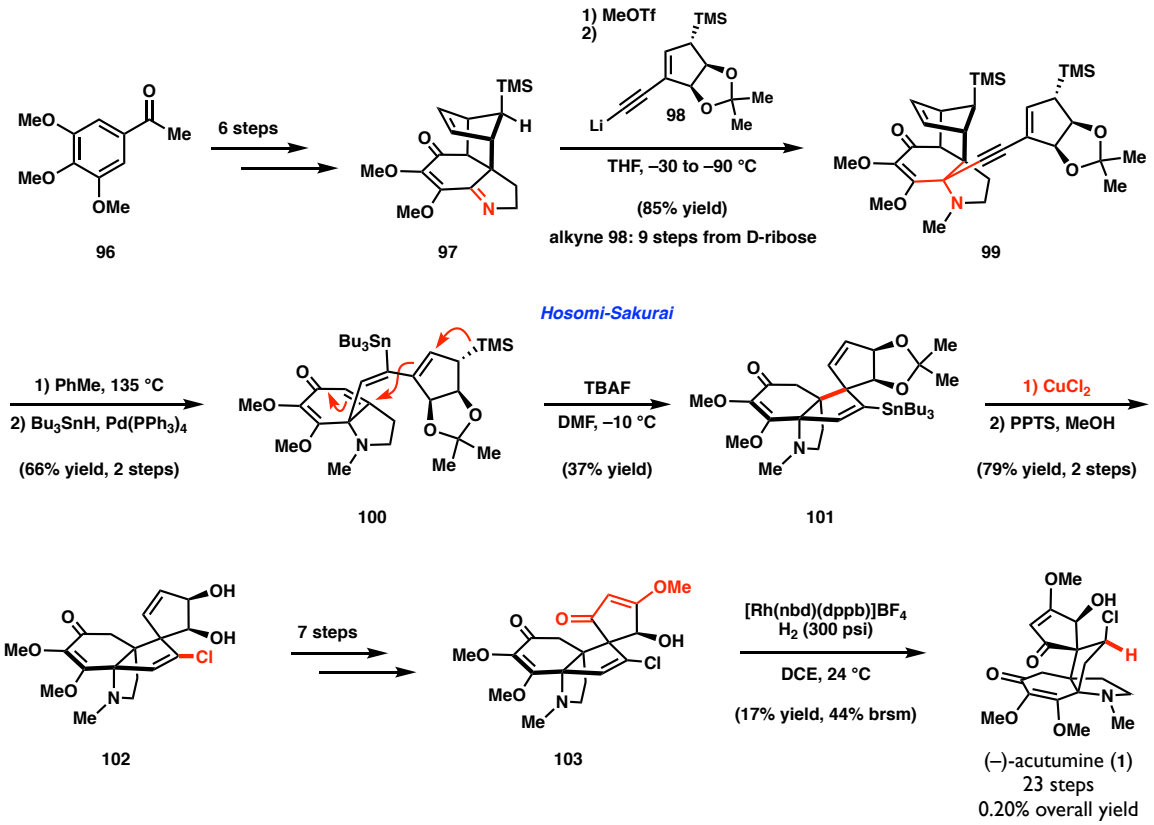
Scheme 1.8 *Synthetic progress toward key cyclobutane motif.*



1.4.4 Herzon's Total Synthesis

In 2013, Herzon disclosed the second total synthesis of (–)-acutumine (**1**, Scheme 1.9).[59,60] Central to the authors' strategy was benzoquinone-derived imine **97**, which could be prepared in six steps from commercially available benzophenone **96**. Imine **97** contained a cyclopentadiene-adduct, which allowed for the stereocontrolled 1,2-addition of alkyne **98** after activation with methyl triflate. After removal of the chiral auxiliary and installation

Scheme 1.9 *Herzon's synthesis of (–)-acutumine (**1**) (2013).*



of a vinyl tin functional group handle, allyl silane **100** was subjected to a key Hosomi-Sakurai cyclization to afford the spirocyclic core of the natural product in a single step. The vinyl tin handle **101** was subsequently exchanged for the chloride found in the natural

product, and diol **102** was oxidized to cyclopentenone **103** in an additional seven steps. Finally, (–)-acutumine (**1**) was obtained in 17% yield after a total of 23 steps via a difficult, late-stage vinyl chloride reduction, which was accomplished with a homogenous rhodium catalyst and 300 psi of H_2 gas. Extensive experimentation was necessary for this final step to avoid hydrodehalogenation.[61,68] In fact, hydrodehalogenation with Pd/C and H_2 was readily accomplished, affording the natural product (–)-dechloroacutumine (**15**) as well.

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Chapter 2

The Reisman Strategy Toward (–)-Acutumine

2.1 INTRODUCTION

The Reisman group initiated studies toward a total synthesis of (–)-acutumine in 2011. At this time, Dr. Raul Navarro and Dr. Kangway Chuang had developed an efficient, asymmetric synthetic strategy toward the dihydroindolone core of the hasubanan alkaloids, a motif that is common to the acutumine framework as well. Their pioneering work and their syntheses of four hasubanan and one erythrina alkaloids laid the foundation for our work on (–)-acutumine. This chapter details: 1) a brief background on the hasubanan chemistry,[†] 2) the Reisman 1st generation approach to (–)-acutumine, as pioneered by Dr.

[†] Portions of this chapter were adapted from the following communications: a) Chuang, K. V.; Navarro, R.; Reisman, S. E. *Chem. Comm.* **2011**, *2*, 1086, DOI: 10.1039/c1sc00095k, copyright 2011 The Royal Society of Chemistry. b) K. V.; Navarro, R.; Reisman, S. E. *Angew. Chem., Int. Ed.* **2011**, *50*, 9447, DOI: 10.1002/anie.201104487, copyright 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim. These studies were conducted by Dr. Kangway V. Chuang and Dr. Raul Navarro, graduate students in the Reisman group.

Raul Navarro and Dr. John Butler,[‡] and 3) the culmination of this work toward a 2nd generation synthesis of (–)-acutumine.[§]

2.2 SYNTHESIS OF HASUBANAN ALKALOIDS — THE FOUNDATION OF THE ACUTUMINE STRATEGY

The Reisman laboratory has a long-standing interest in the synthesis of biologically active, complex alkaloid natural products. Under this purview was a growing interest in the hasubanan,[1,2] erythrina,[3] cepharatine,[4,5] and acutumine alkaloids (Figure 2.1).[1,2] These polycyclic alkaloids are isolated from plants used in traditional Chinese medicine, and have shown interesting medicinal properties. For instance, hasubanan alkaloids, as constituents of *Stephania* plants, have been used to treat asthma, dysentery, fever, and malaria.[2] Furthermore, due to the structural similarity between the hasubanan alkaloids and morphine, it has been suggested that the unnatural enantiomers of hasubanan natural products may exhibit analgesic properties.[6] As such, these molecules have sparked the interest of synthetic chemists for over 40 years. Racemic syntheses of the hasubanan

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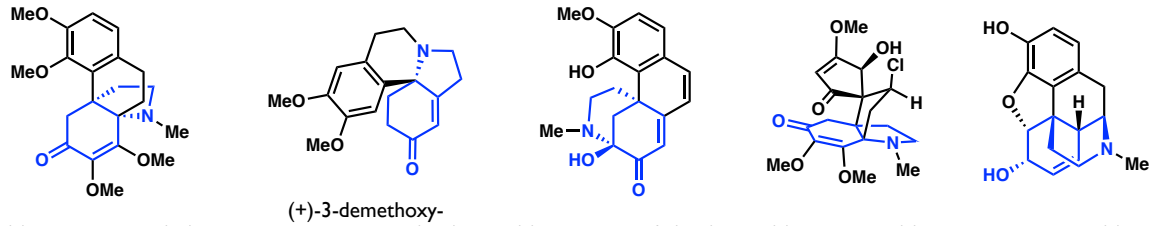
[‡] Portions of this chapter were adapted from the following communication and dissertation: a) Navarro, R.; Reisman, S. E. *Org. Lett.* **2012**, *14*, 4354, DOI: 10.1021/ol3017964, copyright 2012 American Chemical Society; b) Navarro, R. New Strategies for the Total Synthesis of Aza-Propellane Natural Products. Ph.D. Dissertation, California Institute of Technology: Pasadena, California, 2013. These studies were conducted by Dr. Raul Navarro, a graduate student in the Reisman group.

[§] Dr. Raul Navarro and Dr. John Butler initiated the studies on the 2nd generation synthesis, which Dr. Haoxuan Wang and Denise Grünenfelder carried forward upon their departure from the Reisman group.

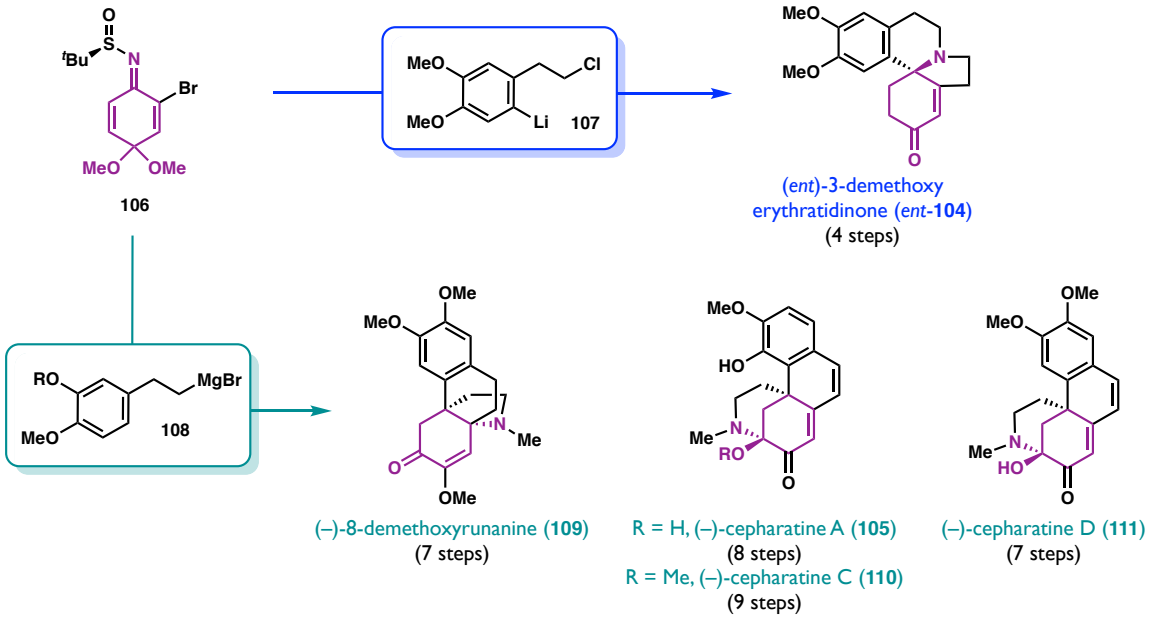
alkaloids commenced in the 1970s,[7,8] while later studies, such as the 21-step synthesis of cepharamine by Schultz and Wang in 1998,[6] rendered access in optically pure form.[9,10]

Figure 2.1 *Selection of hasubanan, erythrina, cepharatine, and acutumine alkaloids.*



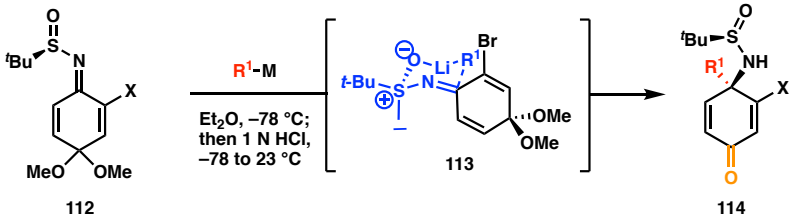
In considering the architecture of this collection of natural products, we realized that an enantioenriched 4-aminocyclohexadienone motif, such as imine **106** (Scheme 2.1), could serve as a common intermediate to these natural products. Furthermore, accessing **106** may enable a divergent synthesis of hasubanan, erythrina, and cepharatine alkaloids, while also laying a foundation for the structurally more divergent acutumine alkaloids.

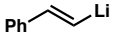
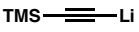
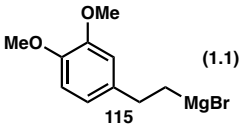
Scheme 2.1 *Strategy toward the synthesis of hasubanan and erythrina alkaloids.*



With this in mind, the stereoselective 1,2-addition of organometallic species to benzoquinone-derived imines,[11,12] such as **112** (Table 2.1), was developed.[13] This 1,2-addition strategy leverages Ellman's chiral auxiliary and a bulky halogen substituent in the α-position to enable access to adducts **114** in good yield and excellent dr.[14–17] The diastereoselectivity is dictated by the chelation of the organometallic species to the sulfinyl

Table 2.1. *Stereoselective 1,2-addition of organometallic nucleophiles to benzoquinone-derived imines* ***112*** *to access chiral 4-aminocyclohexadienones* ***114****.*



entry	X	R^1–M (equiv)	dr[a]	Yield[b] (%)
1	Cl	^{n}BuLi (1.1)	97:3	90
2	Br	^{n}BuLi (1.1)	98:2	88
3	Br	 (2.0)	98:2	68[c]
4	Br	 (2.0)	> 98:2	99[c,d,e]
5	Br	 (1.1)	96:4	82[c]

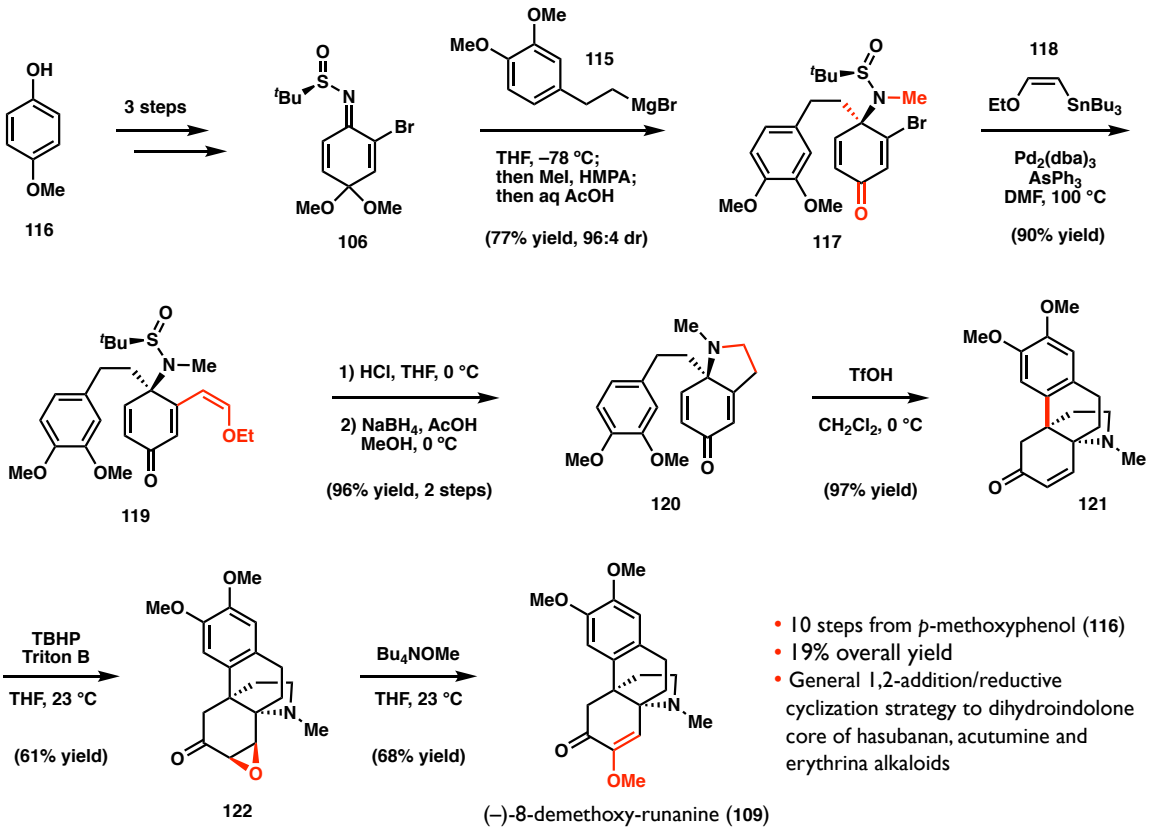
[a] Determined by HPLC. [b] Isolated yields of major isomer.
[c] Reaction conducted in THF. [d] Isolated as a mixture of diastereomers. [e] Reaction conducted at 0 °C.

imine in a chair-like transition state **113**,[17] where the bulky halogen substituent is pointing away from the sulfoxide substituent and its lone-pair. It was found that a number of organolithium and Grignard reagents were suitable nucleophiles in this chemistry, including sp-, sp^2-, and sp^3-nucleophiles. We were also pleased to see that Grignard **115**

performed well, affording the resulting 1,2-addition product in 82% yield and 96:4 dr. This paved the way for our subsequent syntheses of a number of hasubanan alkaloids.

Leveraging this stereoselective 1,2-addition of Grignard **115** to sulfinyl imine **112** (Table 2.1), Dr. Kangway Chuang and Dr. Raul Navarro synthesized a number of hasubanan alkaloids; below is a brief description of one of these syntheses, as a number of its key steps directly influenced our strategy toward (–)-acutumine (**1**).

Scheme 2.2 *Synthesis of the hasubanan alkaloid (–)-8-demethoxyrunanine (**109**).*



In the forward sense, (–)-8-demethoxyrunanine (**109**)[18] could be accessed in 10 steps from *p*-methoxyphenol (**116**) in 19% overall yield utilizing this strategy (Scheme 2.2).[9] Stereoselective 1,2-addition to imine **106** (derived from *p*-methoxyphenol in three

steps) was followed by *in situ* methylation of the sulfinyl amine and acid-mediated cleavage of the ketal protecting group to afford dienone **117**. Subsequently, the vinyl bromide was leveraged as a handle for a Stille cross-coupling with Z-ethoxy-vinyl-tributylstannane (**118**)[19] to furnish vinyl ether **119**, effectively a masked aldehyde. This substrate could be subjected to a two-step reductive cyclization sequence to install pyrrolidine **120**, first via HCl-mediated deprotection of the chiral sulfinyl amine, followed by a reductive amination with $NaBH_4$ in AcOH. Tetracycle **121** was then accessed by subjecting enone **120** to triflic acid,[20] which induced an intramolecular Michael-addition of the electron-rich aromatic ring, installing the vicinal quaternary centers. Finally, epoxidation, epoxide-opening with methoxide, and elimination of H_2O afforded (–)-8-demethoxyrunanine (**109**).

This general synthetic strategy consisting of a stereoselective 1,2-addition/reductive cyclization was leveraged in the synthesis of four hasubanan alkaloids and one erythrina alkaloid in total, demonstrating its versatility in alkaloid total synthesis. With this chemistry developed in our group, we set out to expand its use to that in the synthesis of the structurally related acutumine alkaloids.

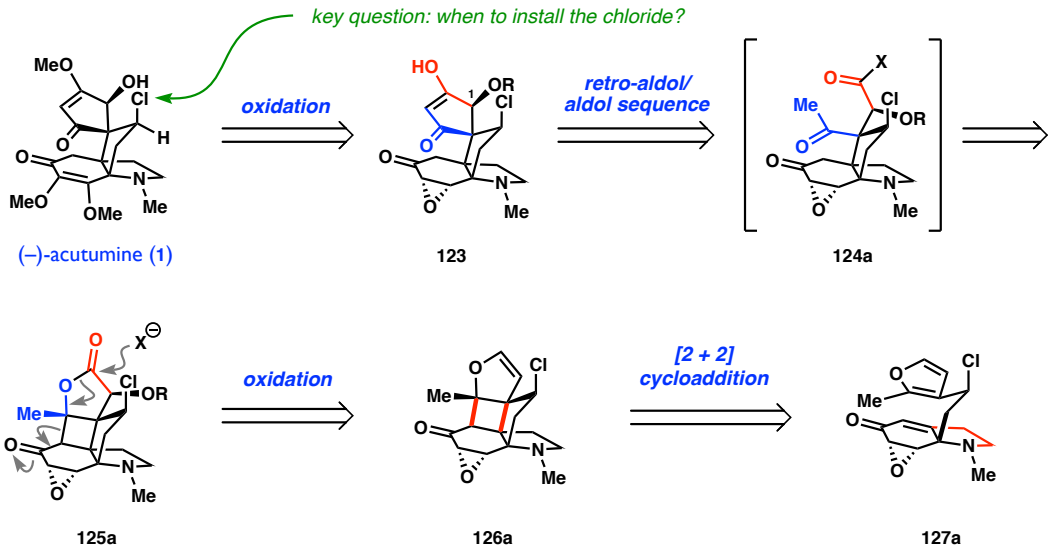
2.3 (–)-ACUTUMINE — RETROSYNTHETIC ANALYSIS AND FIRST GENERATION SYNTHESIS

2.3.1 Original Retrosynthesis

Our synthetic strategy toward (–)-acutumine (**1**) is centered on the use of a [2+2]-cycloaddition/retro-aldol/aldol sequence to install the spirocyclic core (Figure 2.2).[21]

Retrosynthetically, it was envisioned that (–)-acutumine (**1**) could be simplified to vinylogous acid **123**, a synthon that can be readily fragmented through an aldol-like cyclization to ketone **124a**. In the forward sense, it was imagined that cyclobutyl lactone **125a** could undergo a retro-aldol fragmentation with an external nucleophile X^-, and that the resulting ketone **124a** might undergo the desired aldol cyclization to form the spirocycle when subjected to base. Cyclobutyl lacone **125a** could be derived from oxidation of furan **126a**, which may be accessed through a key [2+2]-cycloaddition of dihydroindolone **127a**.

Figure 2.2 *Original retrosynthetic analysis of (–)-acutumine (**1**).*

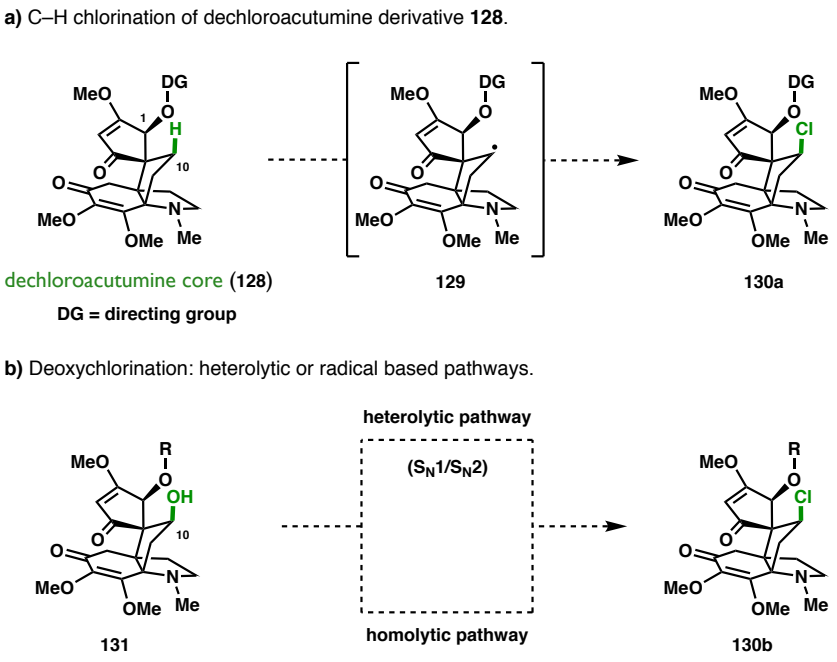


This retrosynthetic analysis reveals a familiar core from our work on the hasubanan and erythrina alkaloids, and we were confident we could access this fragment through the chemistry developed in our laboratory. However, one of the key questions in our retrosynthetic strategy remained — namely, the installation of the neopentyl chloride. Two possibilities were envisioned: 1) installing the chloride early on and carrying it through the synthesis, which may be challenging given the photochemistry we hoped to perform, or 2)

install the chloride at a late-stage. The second strategy — a late-stage chlorination — was thought to be rather challenging, as it would entail chlorinating a highly complex alkaloid at a sterically encumbered position. However, this approach was particularly attractive to us since it opened up avenues for the development of new chemistry.

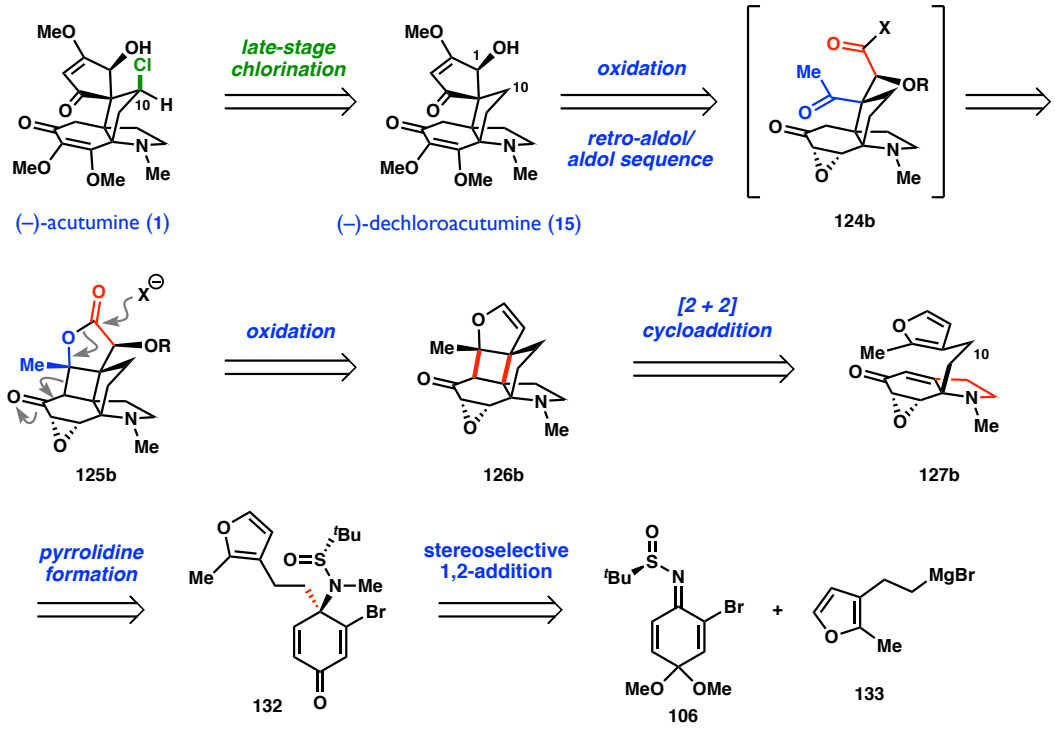
Two possible strategies were envisioned to perform this late-stage chlorination: 1) leveraging the oxidation state at C1 to conduct a directed C–H chlorination of dechloroacutumine (Scheme 2.3a), and 2) a deoxychlorination of neopentyl alcohol **131**, which could occur either through a heterolytic or homolytic fashion (Scheme 2.3b). While both strategies had unique challenges and advantages, a C–H chlorination route was pursued in our 1st generation synthesis, as this simplified the core structure of the molecule to that of dechloroactumine, and avoided the necessity for the installation of a neopentyl alcohol.

Scheme 2.3 *Two chlorination strategies to install the neopentyl chloride.*



Thus, initial efforts targeted dihydroindolone **127b**, which now lacks the C10 chloride (Figure 2.3). Inspired by our work on the hasubanan alkaloids,[9,22] synthetic access to the dihydroindolone core was planned via pyrrolidine formation of vinyl bromide **132**, which may be accessed via a stereoselective 1,2-addition of furanyl Grignard **133** to sulfinyl imine **106**. With this retrosynthetic plan, outlined in Figure 2.3, preparation of cyclobutyl lactone **125b**, the precursor to the key retro-aldol/aldol sequence, was commenced.

Figure 2.3 *Retrosynthesis of dechloroacutumine core – the C10-deoxy strategy.*



2.3.2 Carbamate-Enabled Retro-Aldol/Aldol: the C10-Deoxy-Route

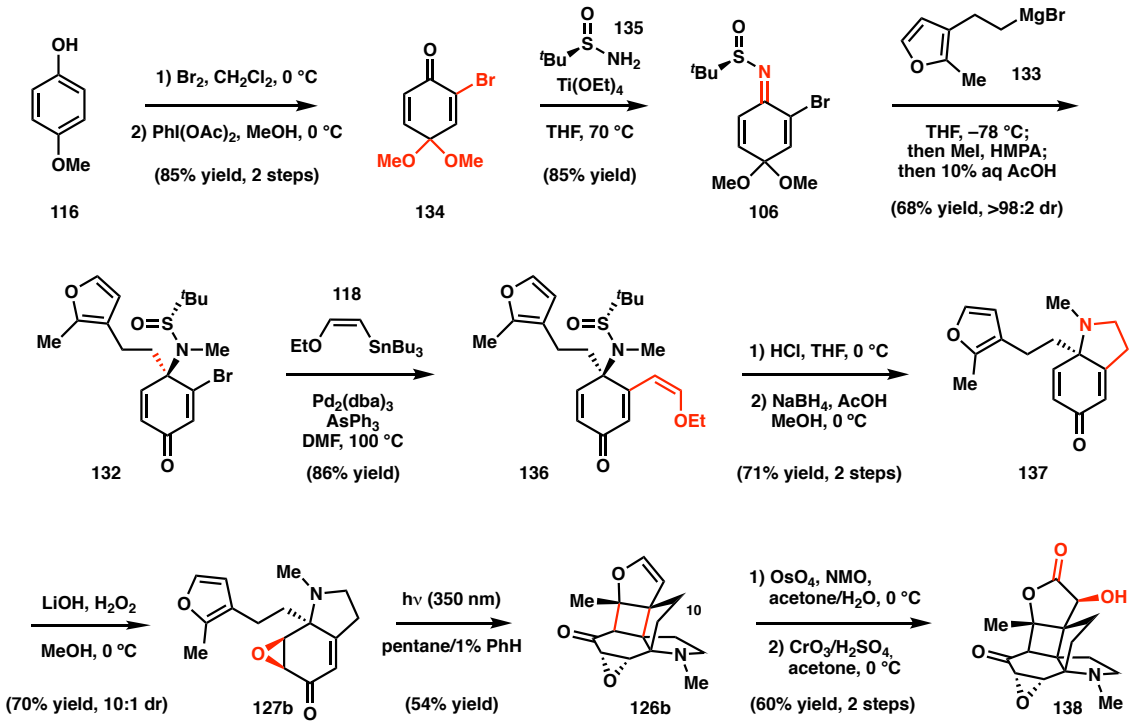
Sulfinyl imine **106** was first prepared from commercially available *p*-methoxyphenol (**116**) via a bromination, oxidative dearomatization, and imine formation sequence (Scheme 2.4a).[21] Subsequent highly stereoselective 1,2-addition of Grignard **133**[23] was followed by *in situ* methylation of the sulfonamide, and subsequent ketal deprotection upon workup with AcOH afforded enone **132**. With electron-deficient vinyl bromide **132** in hand, masked aldehyde **136** was accessed via a Stille cross-coupling utilizing $Pd_2(dba)_3$ and Ph_3As. A subsequent reductive cyclization sequence afforded the desired pyrrolidine ring **137**. Early investigations into the photo-mediated [2+2]-cycloaddition revealed that an undesired dienone rearrangement occurred when enone **137** was subjected to UVA light (Scheme 2.4b).[21,22] However, this was circumvented by initial C8–C9 epoxidation of the dienone to give epoxyenone **127b** in good yield (Scheme 2.4a). Subjecting this particular substrate to UVA light in pentane was now met with success, affording the desired cyclobutane **126b** in moderate yield. Subsequent dihydroxylation and Jones' oxidation readily afforded the α-hydroxylactone **138**,[22] which could be tested in the key retro-aldol/aldol sequence.

With cyclobutyl lactone **138** in hand, lactone-opening and retro-aldol fragmentation was induced by subjection to K_2CO_3 in MeOH (Scheme 2.5a). Surprisingly, the desired ketone **142** was not obtained; instead, the retro-aldol event was followed by a rapid ketalization cascade to afford the tentatively assigned caged ketal **143**.[22] After much experimentation, it was found that carbamate **144** could undergo a controlled retro- aldol event in which the carbamate functionality served as an internal nucleophile (Scheme

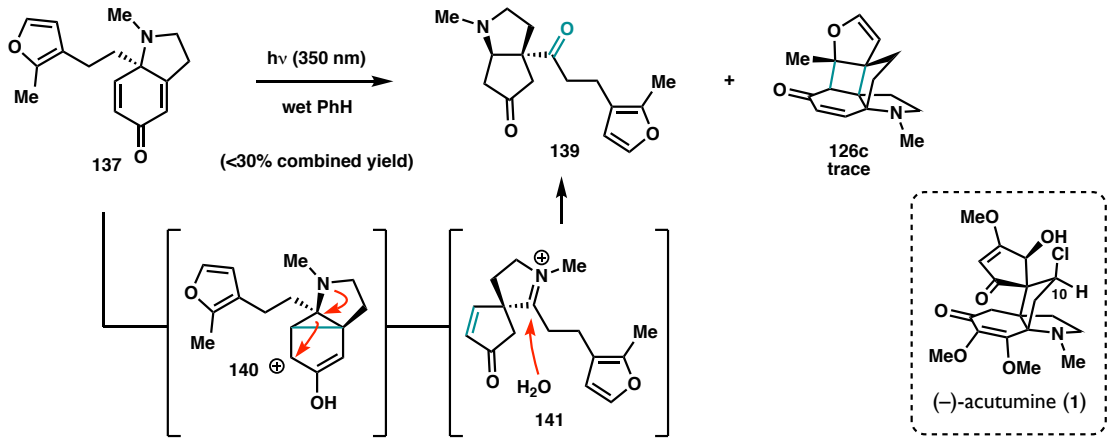
2.5b). When subjected to LiHMDS, oxazolidinedione **145** was formed and the resulting enolate could be trapped with TBSOTf to afford silyl ether **146**. This ketone could now be

Scheme 2.4 *Synthesis of key cyclobutane **138** in the C10-deoxy series.*

a) Synthesis of α-hydroxylactone **138** from *p*-methoxyphenol (**116**).

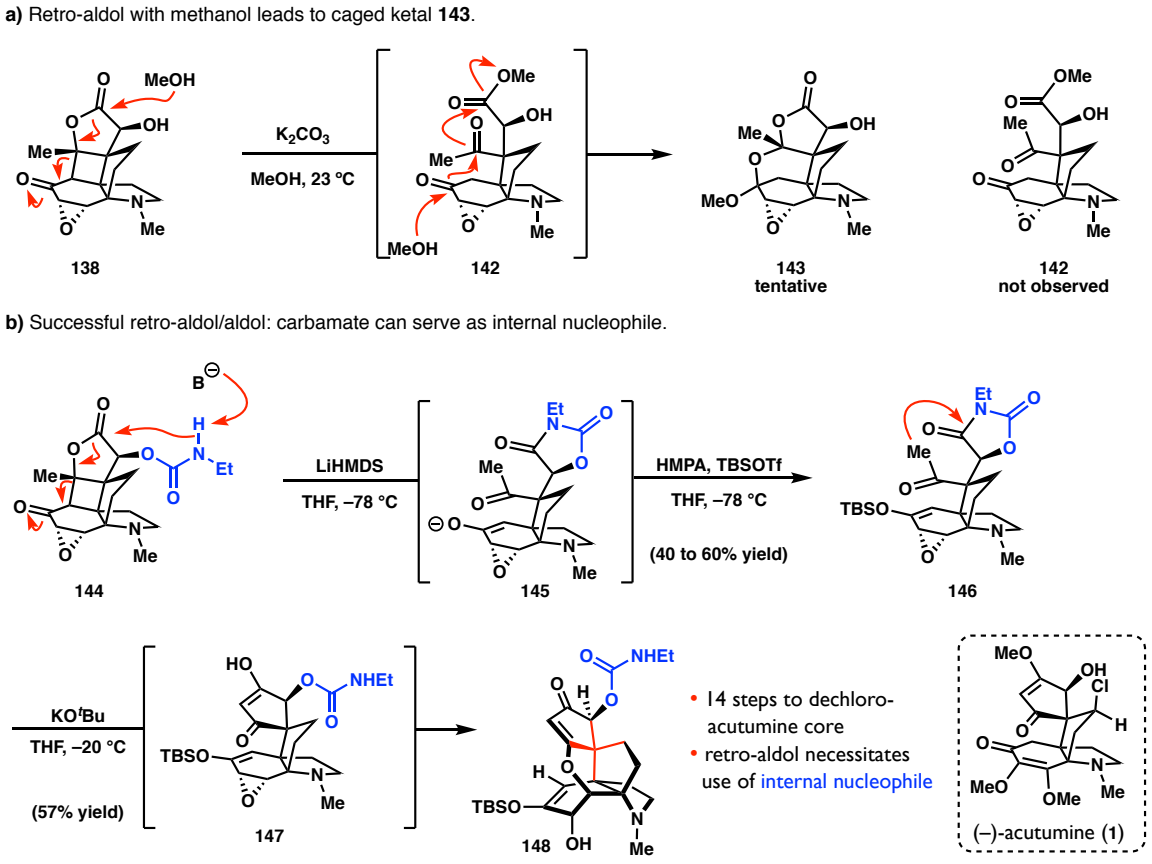


b) Photolytic oxa-di-π-methane rearrangement to ketone **139**.



subjected to KO^{t}Bu at –20 °C to construct the spirocyclic core of dechloroactumine **148**. Interestingly, vinylogous acid **147** was not isolated; instead, analysis by 2D-NMR indicated that epoxide-opened, caged ether **148** was obtained. This culminated in the synthesis of the spirocyclic core of dechloroacutumine in 14 steps from *p*-methoxyphenol (**116**). One important note here is that performing the retro-aldol reaction with the carbamate nucleophile, and trapping the resulting enolate was important to subsequently tame the carbonyl chemistry necessary to perform the aldol reaction. Subsequent work on our total synthesis (*vide infra*) has shown that this carbonyl chemistry can be extremely challenging in these systems with multiple enolizable positions.

Scheme 2.5 *Retro-aldol reactivity and successful spirocycle formation.*



2.3.3 A Challenging C–H Chlorination — Transition to C10-OR Route

During the initial efforts to access the dechloroacutumine core, a post-doc in our laboratory, Dr. John Butler, began investigating the feasibility of a late-stage C–H chlorination. Unfortunately, trials on cyclobutyl lactone **138** (Scheme 2.5a) and model systems proved very challenging given the state-of-the-art in 2012/2013. These included efforts to perform a Hoffman-Löffler-Freytag (HLF) reaction,[24,25] which would leverage the carbamate moiety installed to control the retro-aldol/aldol sequence. In this case, installing the N–chloro carbamate motif on the acutumine core was unsuccessful. Unsurprisingly, chlorination of the carbamate moiety was rendered very challenging in the presence of the tertiary, basic pyrrolidine motif. Further investigations involved C(sp^3)–H activation methods with Pd[26] or Ir[27] to enable subsequent chlorination with an electrophilic chlorine source, as well as radical atom-transfer reactions.[28,29] Again, chlorination products were never observed. Given the challenges we faced, we set out to access the same spirocyclic core with oxidation state at C10 so that the deoxychlorination pathway outlined in Scheme 2.3b could be investigated.

2.4 SERIES WITH OXYGEN FUNCTIONAL GROUP HANDLE AT C10

2.4.1 Accessing the C10-Oxidized [2+2]-Precursor

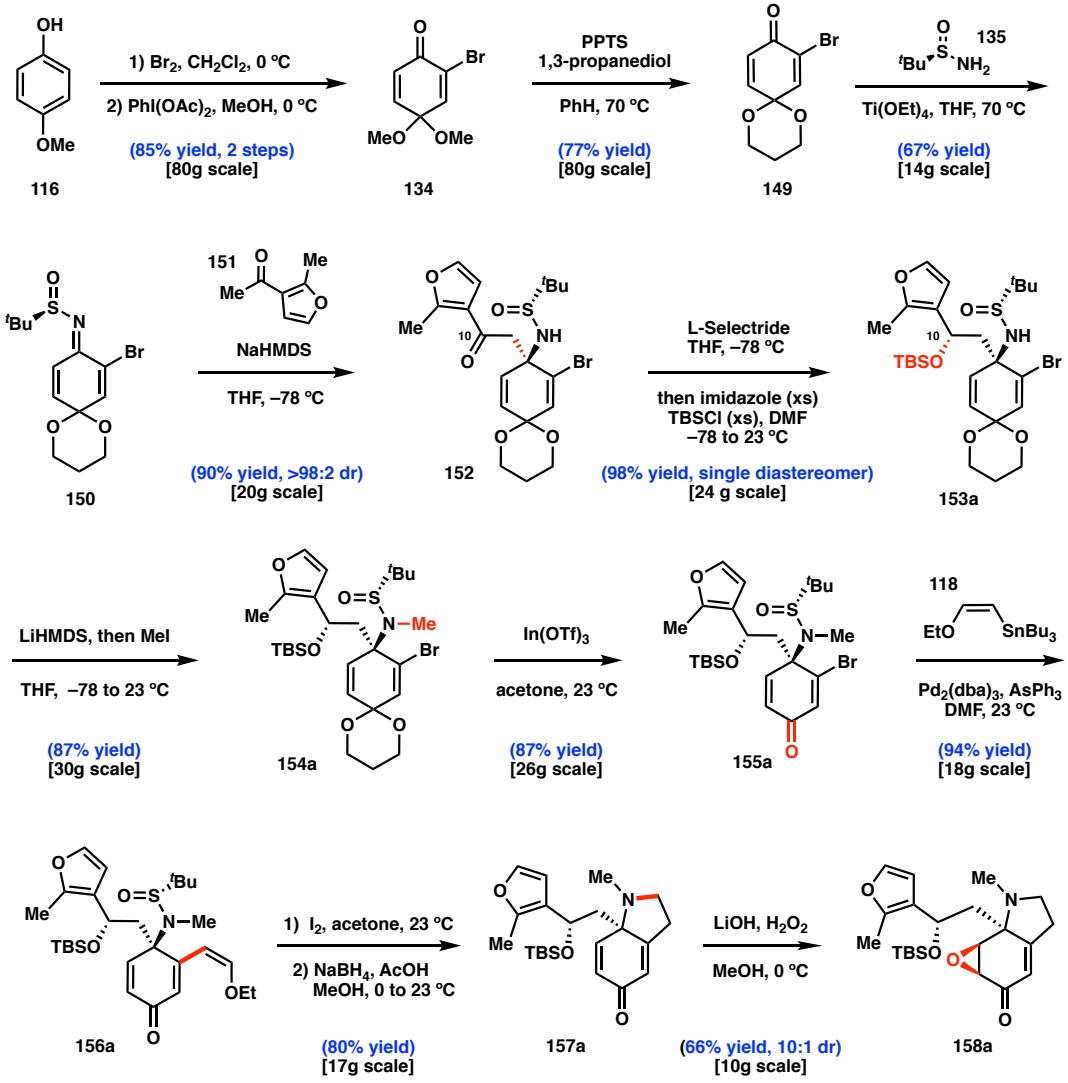
With the path toward the spirocyclic core of the acutumine alkaloids laid out in the "deoxy"-route, the parallel route was investigated in which an oxygen functional group handle at C10 would be installed and carried through the synthesis. As is often the case with making changes to a synthesis fairly early on, a number of challenges had to be

addressed: many reaction conditions had to be tweaked to enable synthetically useful yields. Some protecting group strategy had to be altered, for instance in the case of the dimethoxyketal in the first five steps of the synthesis.

Analogous to our previous route, dimethoxyketal **134** was accessed from *p*-methoxyphenol (**116**) via bromination and oxidative-dearomatization (Scheme 2.6). This process proved to be very scaleable: the synthesis was commenced with 100g of *p*-methoxyphenol, which was split into two batches of 80g, following bromination, for the oxidative dearomatization step. This large scale sequence was performed with no change in yield from previous campaigns. The 1st generation synthesis involved subsequent imine formation, followed by 1,2-addition/N-methylation/ketal deprotection in a single pot; however, it was found that the analogous dienone to **132** (Scheme 2.4) in the C10–OTBS series was highly sensitive, necessitating an early transketalization to a dioxane ketal prior to the imine formation and 1,2-addition. Specifically, transketalization to dioxane **149** was performed in excellent yield with 1,3-propanediol and catalytic PPTS in PhH at 70 °C (Scheme 2.6). Subsequent sulfinyl imine formation proceeded smoothly, giving access to ample quantities of our 1,2-addition substrate **150**. We were delighted to find that the sodium enolate derived from ketofuran **151**[30] was a suitable nucleophile in this chemistry, giving access to ketone **152** with excellent dr. This substrate now contains the oxidation at C10 necessary for subsequent chlorination. One important feature to note about this 1,2-addition is that it initially led to irreproducible yields of the desired product. Ultimately, it proved crucial to add the imine to the preformed enolate via syringe pump (translating to three syringe pumps with 50 mL syringes each on a >20g scale), so that the temperature of

the reaction could be maintained at –78 °C. Monitoring the reaction by TLC showed that even warming the reaction in the capillary could be detrimental, leading to a blackened mixture with numerous product spots.

Scheme 2.6 *Accessing [2+2]-precursor* ***158a***.



With ketone **152** in hand, subsequent highly selective reduction with L-selectride and *in situ* protection with TBSCl afforded silyl ether **153a**, which was deemed a suitably stable oxygen functional group handle that could be retained throughout the synthesis. Silyl

ether **153a** was now advanced to the dihydroindolone core. Nitrogen methylation was followed by ketal deprotection, which proceeded in the highest yield with $In(OTf)_3$ in acetone.[31] With the electron-deficient vinyl bromide **155a** in hand, subsequent Stille cross-coupling with Z-ethoxy-vinyl-tributylstannane (**118**)[19] proceeded smoothly at room temperature, to afford consistent 94% yield of the desired masked aldehyde **156a** on over 20g scale. We were now poised to install the pyrrolidine ring; however, it was found that the conditions from our 1st generation synthesis, which utilized HCl to deprotect the sulfinyl imine, were too harsh in this system, which wasn't surprising given the TBS-ether present in the substrate. Ultimately, milder deprotection conditions using iodine in acetone proved fruitful;[32] this reaction proceeded quite rapidly, in 30–45 minutes, at room temperature on large scale. Subsequent reductive amination afforded dihydroindolone **157a**. Initially, a dramatic loss in yield was observed upon scale-up of this reductive cyclization, dropping from a 70–80% yield to about 50% while moving from a 1 g to > 5 g scale. There were a number of items that proved crucial in this reaction to enable consistent 80% yield on large scale. First, it was important to filter the crude material from the iodine-mediated sulfinyl deprotection through a Celite plug before commencing the second step. It was observed that very fine solids, derived from the sodium sulfite quench, would carry over in the reductive amination step and so cause a drop in yield. Second, it proved crucial to add the $NaBH_4$/AcOH mixture slowly, dropwise via cannula to the substrate at 0 °C in the reductive amination step. Initially, this reaction presented with poor conversion, and upon warming to room temperature, and addition of more reductant, would commonly result in over-reduction at the enone and a drop in yield. However, if the rate of

reductant addition was slowed down and the substrate maintained at 0 °C, no need was found to increase reductant equivalents and the yield was consistently 80% (this reaction has been performed three times on 16–17 g scale to date). Epoxidation of enone **157a** proceeded uneventfully with H_2O_2 and LiOH to provide the C10-oxidized [2+2]-precursor **158a**, even on large scale.

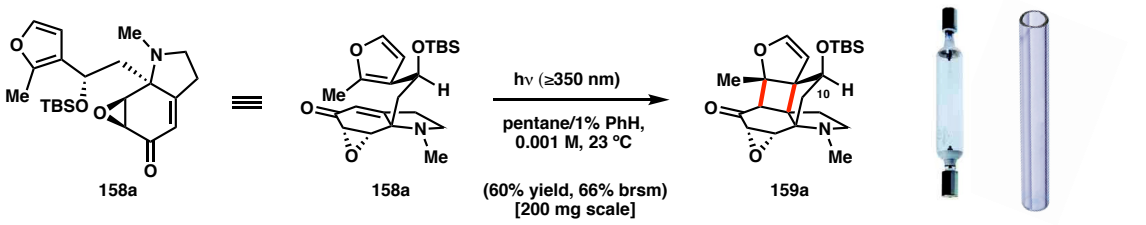
2.4.2 [2+2]-Cycloaddition with C10-Oxidation – a Scale-Up Challenge

With key epoxyenone **158a** in hand, the [2+2]-cycloaddition in the presence of UVA light was investigated. It is important here to address the evolution of our [2+2]-cycloaddition over the years, as moving from initial reactions on 5–20 mg scale toward scale-up campaigns that required pushing through 10–15 g of enone necessitated various modifications. When this reaction was originally developed by Dr. Raul Navarro on the C10-deoxy series (Scheme 2.4, Section 2.3.2), a Luzchem photoreactor with a carousel apparatus was utilized that could fit several 13 x 100 mm borosilicate test tubes.[21] When slightly larger scales were required, a medium-pressure mercury lamp (Hanovia PC451050) was employed, which necessitated the use of a Uranium-glass filter to remove wavelengths below 300 nm (Scheme 2.7a). This setup was suitable for single batch runs up to circa 200 mg scale. In pursuit of larger-scale, single batches, the effects of concentration on the reaction were briefly investigated; however, it was found that increasing the concentration two-fold to 0.002 M caused a drop in conversion (Scheme 2.7b, entry 2). Using this photo-setup was also met with a safety hazard on occasion; while the mercury lamp was cooled by sitting in a jacketed water condenser, the environment in

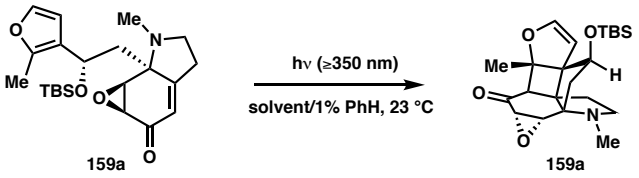
the photobox could reach temperatures that were too high for pentane and caused over-pressurization. Thus, the use of hexanes as a reaction solvent was investigated instead (Scheme 2.7b, entry 3). Although it was feasible, the amounts of unidentified precipitate that formed during the course of the reaction were much larger in hexanes than had been observed in pentane, thus affecting the absorption of UV light by the substrate. This caused drop in conversion and yield. Overall, the single-batch limitation of this chemistry needed to be addressed, so the use of flow conditions using a syringe pump were investigated.

Scheme 2.7 *[2+2]-cycloaddition with medium-pressure Hg lamp and Uranium filter.*

a) [2+2]-cycloaddition utilizing medium-pressure mercury lamp.



b) Comparison of concentration and solvent choice.



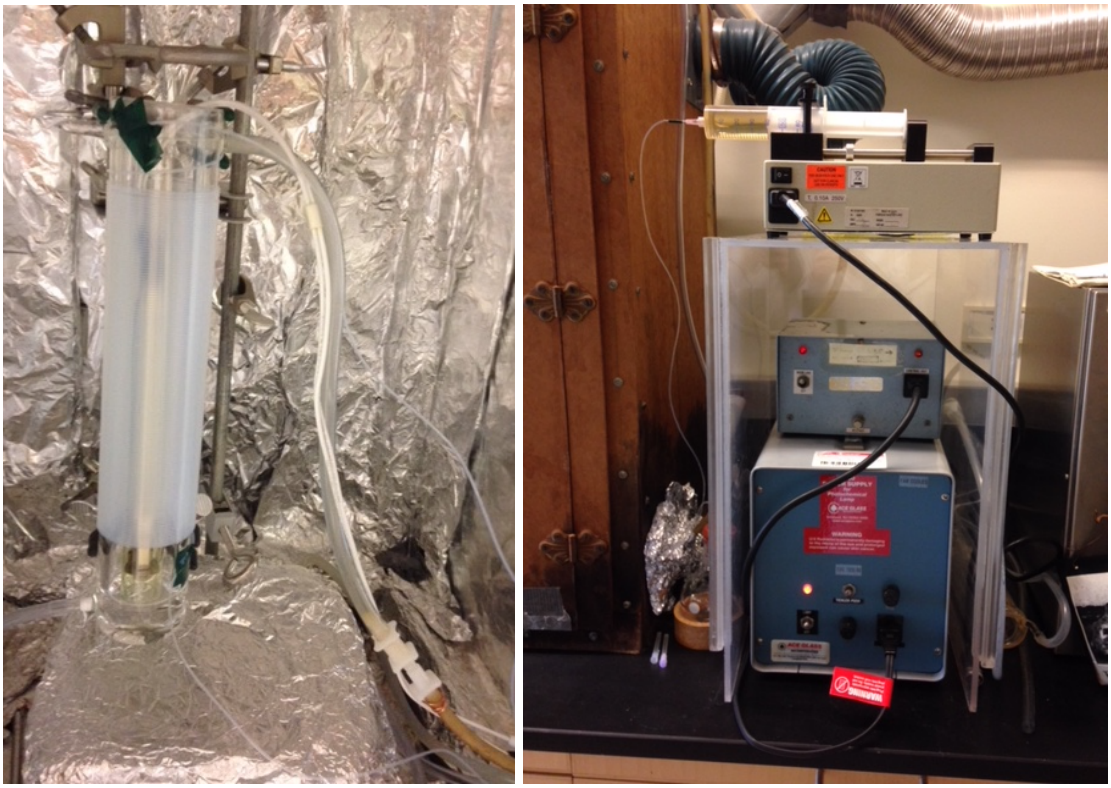
entry	solvent	concentration	scale	estimated conversion	isolated yield
1	pentane	0.001 M	200 mg	complete[a]	60% yield (66% brsm)
2	pentane	0.002 M	400 mg	~70%	61% (37% SM)
3	hexanes	0.002 M	400 mg	~60%	41% (63% brsm)

[a] Complete conversion means only trace peak of XX observed by LC/MS (158a is always re-isolated).

Flow chemistry has proven particularly useful in the scale-up of photo-mediated transformations.[33–35] Without a dedicated flow-chemistry setup, a few trials were run simply using a syringe pump. The reaction mixture – outside the photobox — was slowly pumped through cannula tubing that was led into the photobox and wrapped around the

cooling condenser containing the mercury lamp (Figure 2.4).[36,37] The cannula tubing then led back out of the photobox and into a collection flask. After preliminary trials in flow, it was found that the precipitate that forms in our cycloaddition reaction is detrimental to flow-chemistry, as it gradually coats the cannula tubing and thus obstructs effective UV-light absorption of the substrate. Based on ^{1}H NMR, it was found that the precipitate consists of both the desired product and larger quantities of an unidentified polymerized side-product that has very limited solubility in apolar organic solvents.

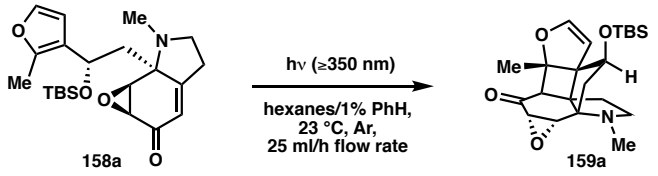
Figure 2.4 *Images of reaction setup for photochemistry trials in flow. Left: cannula wrapped around water condensor/Hg lamp. Right: syringe pump setup outside photobox.*



When the flow-trial was set up with PTFE cannula under argon, full conversion of the starting enone **158a** could be accomplished with a 25 mL/h flow-rate (Scheme 2.8a). Unfortunately, the isolated yield of the product cyclobutane **159a** was only 15% and no starting material was re-isolated, indicating that large amounts of decomposition had occurred. In particular, this reaction also showed a novel side product that had not been observed before. LC/MS mass analysis indicated it was an oxidized product (+O_2), but it could never be successfully isolated. Another observation in this first flow chemistry trial was the discoloration of the cannula tubing after only 4 h of irradiation. This concern led us to investigate the use of FEP cannula due to its reported higher resistance to discoloration in the presence of UV light.[36] Our experience thus far was that the polymeric

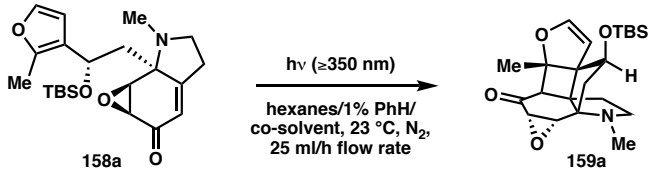
Scheme 2.8 *Investigating [2+2]-cycloaddition in flow.*

a) Trial in flow with PTFE cannula.



(15% yield, 35 mg scale)

b) Trials in flow with FEP cannula.



[35 mg scale]

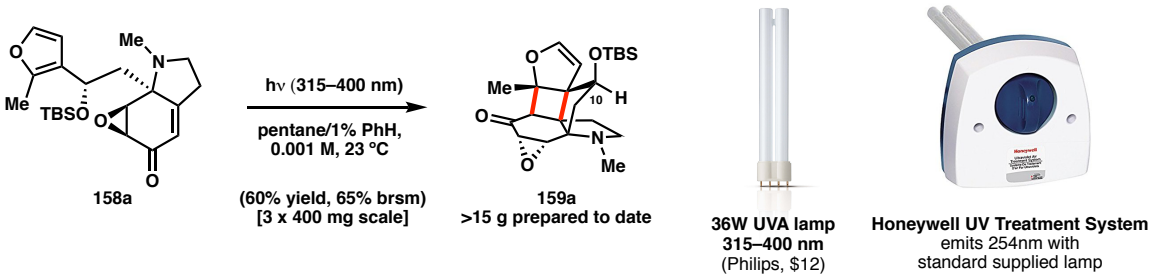
entry	solvent	ratio	yield (brsm)	comment
1	hexanes/EtCN	9:1	27% (44%)	cloudy/solid
2	hexanes/EtCN	5:1	19% (41%)	more solid than entry 1

precipitate was solely soluble in highly polar solvents, such as acetone and acetonitrile. In order to mitigate the precipitate formation, the use of propionitrile as a co-solvent was investigated (Scheme 2.8b). While initial trials indicated that slightly higher yields of cyclobutane **159a** could be obtained utilizing the FEP tubing (27% and 19%, entries 1–2), there was still significant amount of precipitate and tubing discoloration after 3 h, and the precipitate appeared to increase with the increase of polar co-solvent. Overall, our investigations into flow chemistry did not afford acceptable yields compared to the single-batch reaction (60%, 66% brsm), which let us pursue a path in which we could render our batch-chemistry more efficient for material throughput.

With little success in conducting the [2+2]-cycloaddition in flow for scale-up purposes, an alternative was sought to address the single-batch limitation. Other total synthesis efforts in our laboratory also utilized photo-mediated transformations, for which we had purchased several Honeywell lamps (UV100A1059). This Honeywell system is commercially used for curing airducts, but it has proven effective in our total syntheses that required irradiation at 254 nm. It is important to note, however, that these low-pressure lamps emit solely at a narrow range around 254 nm (~250–260 nm), unlike a medium-pressure mercury lamp that emits a range up to visible light. Thus, a suitable light bulb was required that emits at 350 nm for our [2+2]-cycloaddition. Gratifyingly, a Hollywood lighting supplier was located which provided bulbs that emit between 315–400 nm (Philips 232934), which are used medically in the treatment of psoriasis. These bulbs had the correct connectivity and voltage to fit into the Honeywell system, and we were extremely pleased to find that our chemistry worked comparably well in this setup with identical

yields (Scheme 2.9), albeit with somewhat longer reaction times. As our photochemistry efforts expanded, three of these reactions could be run simultaneously in the three separate photoboxes, each at a 400 mg scale. Although not an ideal scale for our needs, we were successful in moving from 200 mg single batches to the ability of pushing through 1.2 g of material on any given run.

Scheme 2.9 *[2+2]-cycloaddition with Honeywell/Philips setup.*

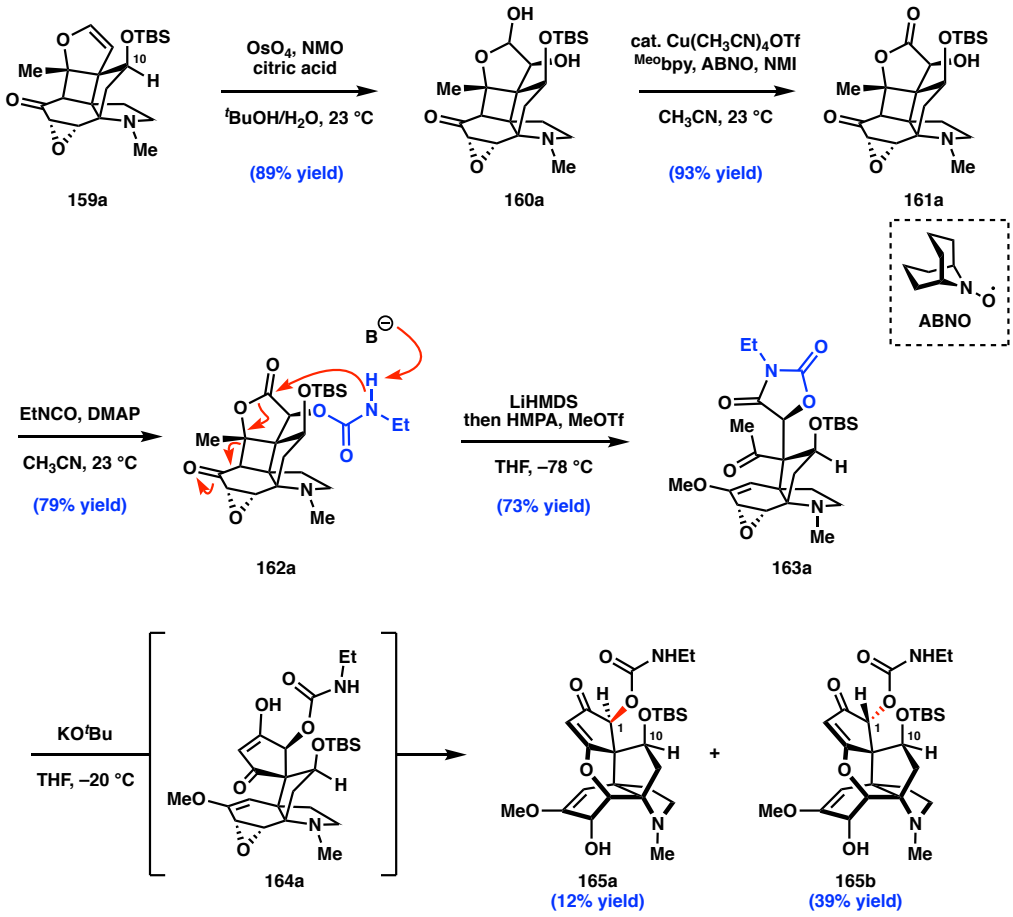


2.4.3 Accessing the Spirocyclic Core with Oxidation at C10

With access to significant amounts of cyclobutane **159a**, elaboration to the spirocyclic core of (–)-acutumine was investigated, utilizing the chemistry previously developed in our 1st generation synthesis. Indeed, α-hydroxylactone **161a** (Scheme 2.10) was obtained, albeit with some changes in reaction conditions: first, dihydroxylation of **159a** with OsO_4 resulted in much slower conversion and poor mass balance compared to the C10-deoxy series. It was then found, however, that the addition of 4.0 equivalents of citric acid aided this reaction considerably. In this case, citric acid may protonate and mask the basic amine, thus preventing undesired N-oxide formation. Furthermore, literature reports have indicated that citric acid may also prevent the formation of Os(VIII) and

Os(IV) species by binding to and stabilizing the Os(VI) in solution.[38] Interestingly, applying conditions from our 1st generation synthesis to form lactone **138** (Scheme 2.4a), it was found that oxidation of the intermediate lactol under Jones' conditions resulted in large amounts of overoxidation to the diketone product (not shown). In search for a milder

Scheme 2.10 *Accessing spirocyclic core with oxidation at C10.*



oxidation reaction, we were pleased to find that the copper-based conditions reported by Stahl performed beautifully,[39,40] allowing us to access lactone **161a** in 83% yield over two steps. Subsequent carbamate formation with ethyl isocyanate performed well, affording our retro-aldol precursor **162a**. We were gratified to find that the retro-aldol reactivity

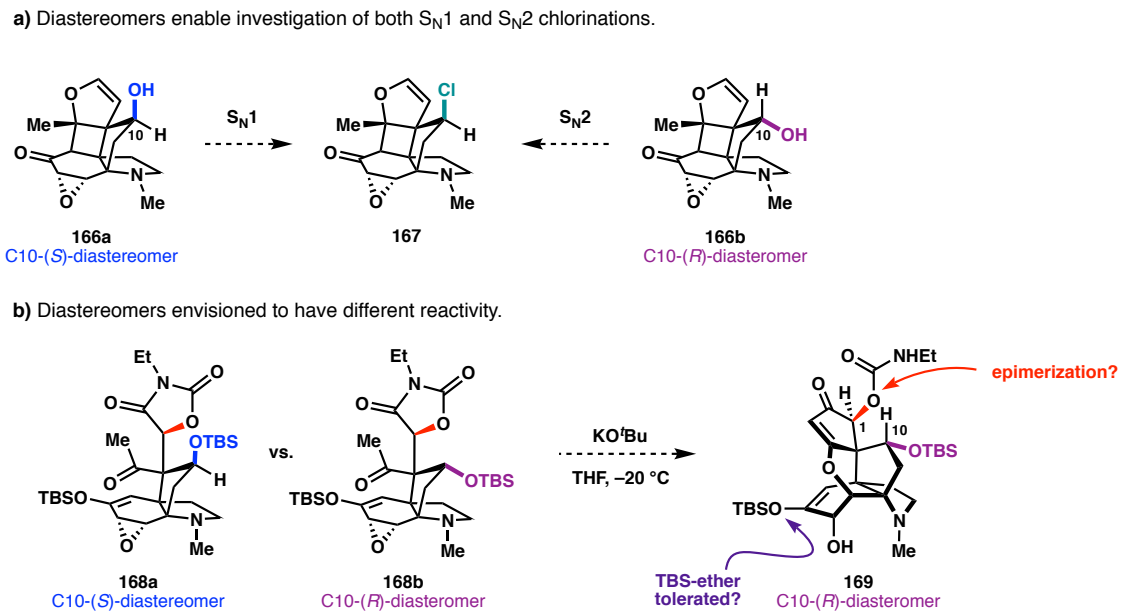
translated to this new system, affording methyl enol ether **163a** after trapping with MeOTf. Ultimately, while subjecting ketone **163a** to KO^{t}Bu afforded caged ether **165a**, it was accompanied by large amounts of epimerization at C1, likely due to the non-bonding, steric interaction between the bulky C10-OTBS group and carbamate moiety. It is also noteworthy that a switch from TBSOTf to MeOTf in the retro-aldol step (compare to the C10-deoxy series, Scheme 2.5b, Section 2.3.2) was required for subsequent aldol cyclization to proceed. It was hypothesized that the presence of the bulky –OTBS groups at both C10 and C6 were sterically prohibitive to this cyclization.

2.4.4 Investigations of the (R)-Diastereomer at C10

At the outset of our pursuit of a neopentyl alcohol at C10 as a chlorination handle, it was viewed of paramount interest to investigate a wide variety of both heterolytic and radical chlorination reaction conditions. In considering S_N2-type deoxychlorinations, it was evident that accessing the (*R*)-diastereomer at C10 would be beneficial (Scheme 2.11a). Furthermore, the challenge we had faced in the C10-(*S*)-series involving epimerization at C1 during aldol cyclization might be eliminated through using the C10-(*R*)-series, as the TBS-ether would now be further removed from the C1–carbamate (Scheme 2.11b). Finally, it was also of interest whether the aldol-cyclization would now proceed as it had in the C10-deoxy-series with the silyl enol ether on the 6-membered ring. Previously, we were not able to cyclize the bis-TBS-ether **168a**, again likely due to steric congestion. While we were able to mitigate this challenge and restore activity by making the methyl enol ether

instead (**163a**, Scheme 2.10, Section 2.4.3), it was still of interest to us to see if the (*R*)-diastereomer at C10 would succeed here.

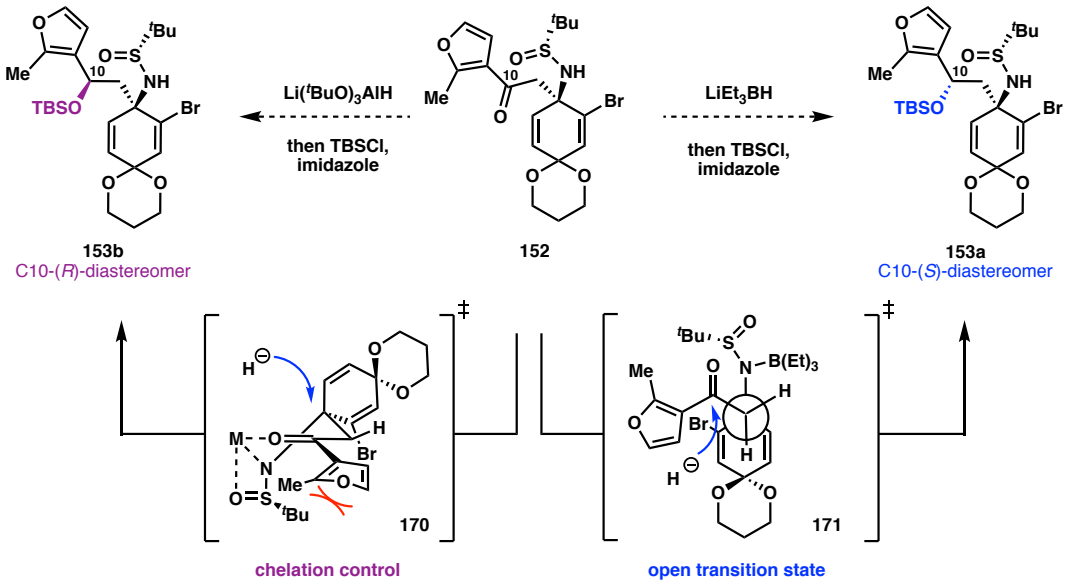
Scheme 2.11 *Rationale for accessing C10-(R)-diastereomeric series.*



In 2008, Davis and coworkers reported on the reduction of N-sulfinyl β-amino ketones,[41] and demonstrated that resulting diastereomers could be obtained selectively depending on the reductant employed. The authors proposed that the selectivity was a result of either a chelation-controlled or an open transition state; Scheme 2.12 shows their reduction selectivity model as applied to our ketone **152**.

With this selectivity model in mind, a variety of reduction conditions were tested that would increase chelation control and reduce hydride source size, which should allow to access the C10-(*R*)-diasetereomer **153b** (Scheme 2.12). As exemplified in entry 1, Table 2.2, the use of chelation controlled reduction conditions in our case resulted in the *in situ* cyclization of the formed alkoxide onto the enone moiety, affording cyclic ether **172**. These

Scheme 2.12 *Reduction selectivity model for ketone* ***152***.

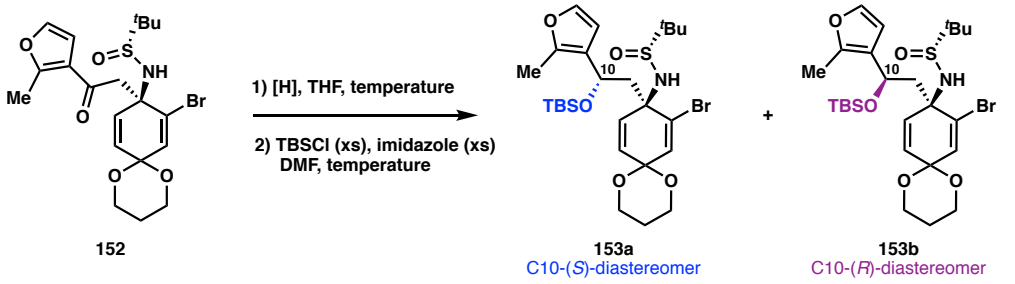


results are in line with our previous observations that the alkoxide moiety requires trapping as a TBS-ether *in situ* after reduction with L-selectride. Lithium tri-*tert*-butoxyaluminum hydride ($Li(O^tBu)_3AlH$) was slow to reduce our ketone (Table 1, entry 5). Unfortunately, upon more forcing conditions (either warming up the reaction mixture or using LiCl additive to increase chelation), loss of both the furan and the chiral sulfinyl auxiliary were observed. Investigation of another chelation controlled reductant, zinc borohydride, surprisingly still favored major isomer **153a** (dr >10:1, entry 4). After little success with chelation controlled reductions, smaller reductants were investigated as well; however, the use of sodium borohydride (entry 2), borane (entry 8), and Red-Al (entry 10) still favored (*S*)-isomer **153a**, and in some cases resulted in incomplete reduction or a messy reaction profile. Similar observations were also made using DIBAL-H (entry 9). Only upon the use of $LiBH_4$ or LAH could the formation of the (*R*)-diastereomer be improved, with both reagents resulting in a 2:1 ratio, still favoring the (*S*)-isomer **153a** (entries 3 and 7). Since

the change of reductant size was met with only moderate success, we turned our attention to solvent effects.

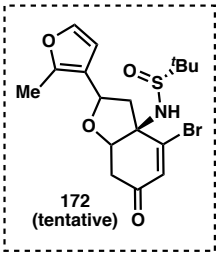
It was anticipated that changing the solvent of the reaction from THF to the non-coordinating CH_2Cl_2 might increase chelation control. However, in the case of both the zinc borohydride and LAH reductions, this solvent change resulted in *in situ* cyclization of the substrate (Table 2.2, entries 11 and 12), whereas the L-Selectride reduction remained unchanged (entry 13). These results further confirmed that effective chelation control was

Table 2.2. *Reductant screen to access C10-(R)-TBS-ether* ***153b****.*



entry	reductant	temperature (°C)	dr (153a:153b)	conversion/product
1	$Me_4N(OAc)_3BH$	23	-	cyclized (172)
2	$NaBH_4$	0	5:1	full conv.
3	$LiBH_4$	0	2:1	full conv.
4	$Zn(BH_4)_2$	23	>10:1	full conv.
5	$Li(O^tBu)_3AlH$, LiCl	–78 to 23	-	loss of furan & ^{t}Bu-group
6	L-Selectride	–78	>20:1	full conv.
7	LAH	–78	2:1	full conv.
8	BH_3•THF	–78 to 23	-	messy
9	DIBAL	–78	-	50% conv.; very messy
10	Red-Al	–78	5:1	incomplete conv.

entry	reductant	solvent	dr (153a:153b)	conversion/product
11	$Zn(BH_4)_2$	CH_2Cl_2	-	cyclized (172)
12	LAH	CH_2Cl_2	-	cyclized (172)
13	L-Selectride	CH_2Cl_2	>20:1	incomplete TBS-protection
14	LAH	THF/CH_2Cl_2 (1:1)	2.4:1	incomplete TBS-protection



challenging in our system, since those conditions also facilitated cyclization of the product alcohol onto the enone.

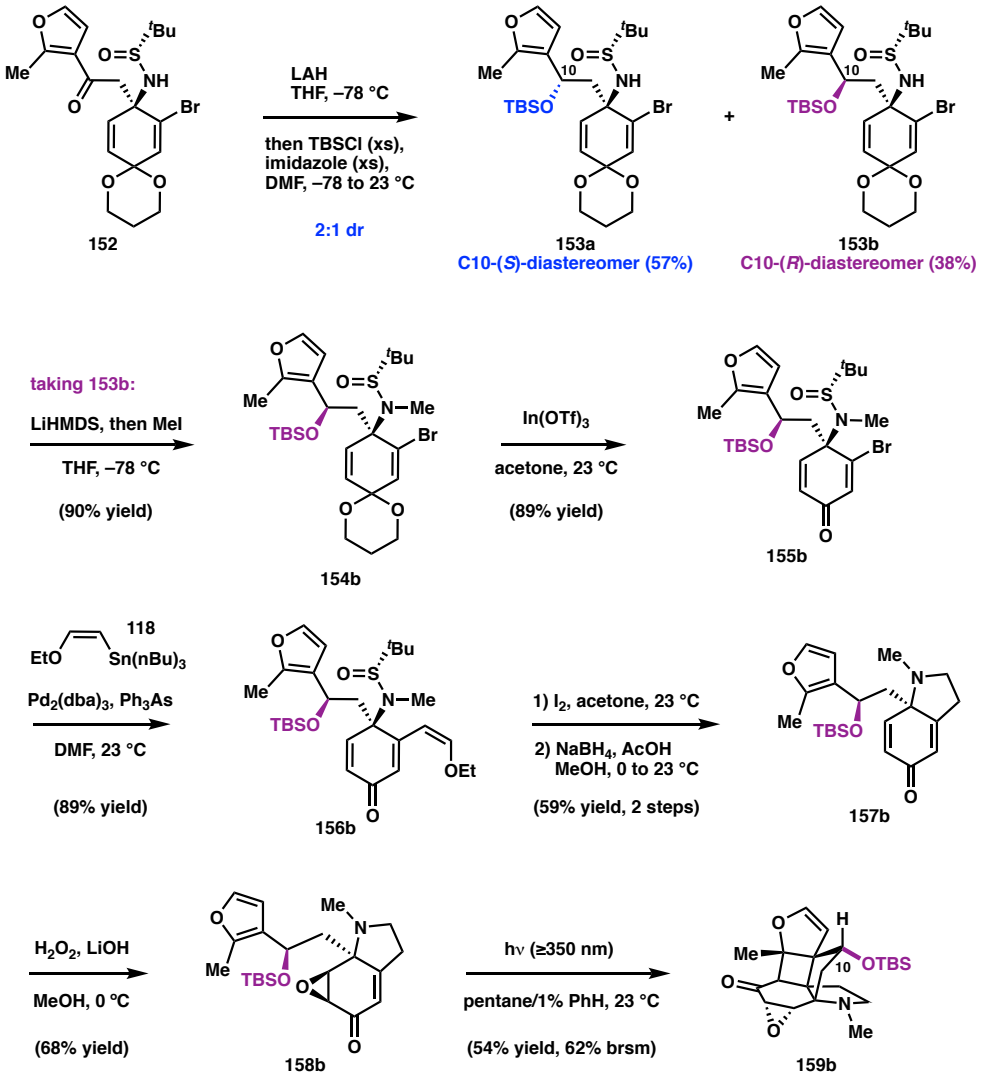
In considering the transition states of ketone **152** (Scheme 2.12), it was hypothesized that the difficulties in affording a chelation-controlled reduction may be due to the presence of the furan-group, causing a steric clash with the *tert*-butyl group of the sulfone as depicted in **170** (Scheme 2.12). This would then favor open-transition state **171**, leading to the undesired C10-(*S*)-isomer **153a**. It was hypothesized that early methylation of the nitrogen may influence this transition state, effecting a change in the diastereoselectivity. However, methylation of amine **152** proved to be unsuccessful under a variety of conditions (not shown), likely due to facile enolization of the ketone moiety. N-Boc-protection and LAH reduction were envisioned to afford the same methylated and reduced product; however, N-Boc-**152** could not be prepared, since strong bases such as *n*-BuLi are required for Boc-protection of secondary N-sulfonamides,[42] which are not compatible with the base-sensitive ketone.

At this time, the optimal reduction/protection conditions were performed on a large scale so that the remaining steps of the synthesis could be investigated in the C10-(*R*)-diastereomeric series. Lithium borohydride and LAH were compared, as they had both provided a 2:1 dr (**153a** : **153b**, Table 2.2). However, lithium borohydride afforded varying yields upon scale-up, so the LAH conditions described (Table 2.2, entry 7) were applied to scale-up ether **153b** on a 6 g scale (Scheme 2.13).

With synthetically useful quantities of TBS-ether **153b** in hand, the subsequent sequence to cyclobutane **159b** proceeded fairly uneventfully (Scheme 2.13). First,

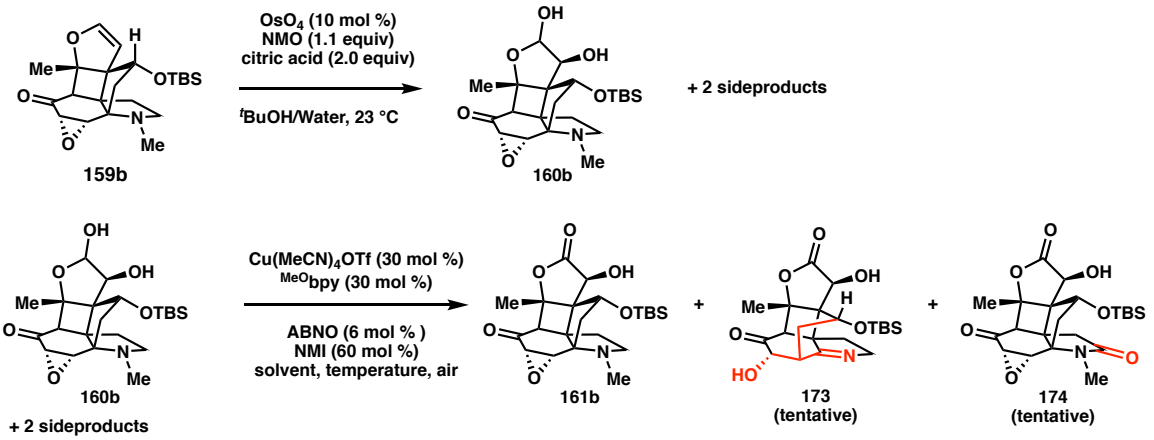
methylation of the sulfonamide and subsequent dioxane deprotection afforded enone **155b**. Stille cross-coupling then afforded the analogous masked aldehyde **156b**, which could be subjected to the reductive cyclization sequence developed for the (*S*)-isomer in order to provide pyrrolidine **157b**. Finally, epoxidation and [2+2]-cycloaddition furnished cyclobutane **159b**.

Scheme 2.13 *Synthesis of C10-(R)-cyclobutane* ***159b***.



With sufficient cyclobutane **159b** in hand, we were staged to investigate the subsequent steps in the synthesis. Unfortunately, both oxidation and the carbamate formation steps proved to be much more difficult using the (*R*)-diastereomer at C10. Subjecting cyclobutane **159b** to Upjohn dihydroxylation resulted in a much slower reaction (17 h instead of 30 min), as well as the formation of two initially unidentified side products (Scheme 2.14). This mixture was subjected to the Stahl oxidation conditions,[17a] and by LC/MS it was found that the side products were oxidized as well. After chromatographic separation, and based on LC/MS and NMR analysis, these two side products were then tentatively identified as rearranged imine **173** and lactam **174**. Overall, the lactone formation from diol **160b** proved very slow due to the diol's insolubility in CH_3CN. A brief solvent and temperature screen revealed that performing the oxidation in a 1:1 mixture of

Scheme 2.14 *Dihydroxylation and Stahl oxidation screen to lactone* ***161b***.



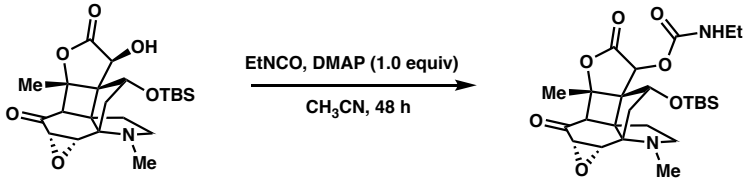
entry	solvent	temperature	result/conversion[a]
1	CH_3CN	23 °C	slow conversion[b]
2	CH_3CN	50 °C	slow conversion, 35% yield
3	CH_3CN/^{t}BuOH (1:1)	23 °C	48% yield
4	CH_3CN/^{t}BuOH (1:1)	50 °C	slow conversion, 60% yield

[a] Isolated yield reported over 2 steps. [b] Comparable yields to entry 4 upon several resubmissions.

CH_3CN and ^tBuOH at 50 °C could afford the lactone **161b** in 60% yield over the two steps (Scheme 2.14, entry 4), although a long reaction time (48 h) was required along with increased equivalents of reagents. Upon the third addition of additional reagents (see Experimental Section 2.7), the starting material finally went into solution, giving a homogenous green solution.

At this stage, sufficient lactone **161b** had been obtained in order to test the carbamate formation and key retro-aldol/aldol sequence. Unfortunately, formation of carbamate **162b** proved challenging, as the reaction conversion was much slower compared to the (*S*)-diastereomer (Table 2.3). Initially, increasing the amount of isocyanate over a period of 48 h provided carbamate **162b** in 55% yield (Table 2.3, entry 1). However, this result proved irreproducible, so a variety of conditions were surveyed to improve the carbamate formation. Starting with an excess of isocyanate (entry 2), heating the reaction (entry 3), and using pyridine as a base (entry 4) did not improve the carbamate formation.

Table 2.3. *Reaction conditions screened to access carbamate* ***162b****.*



161b **162b**

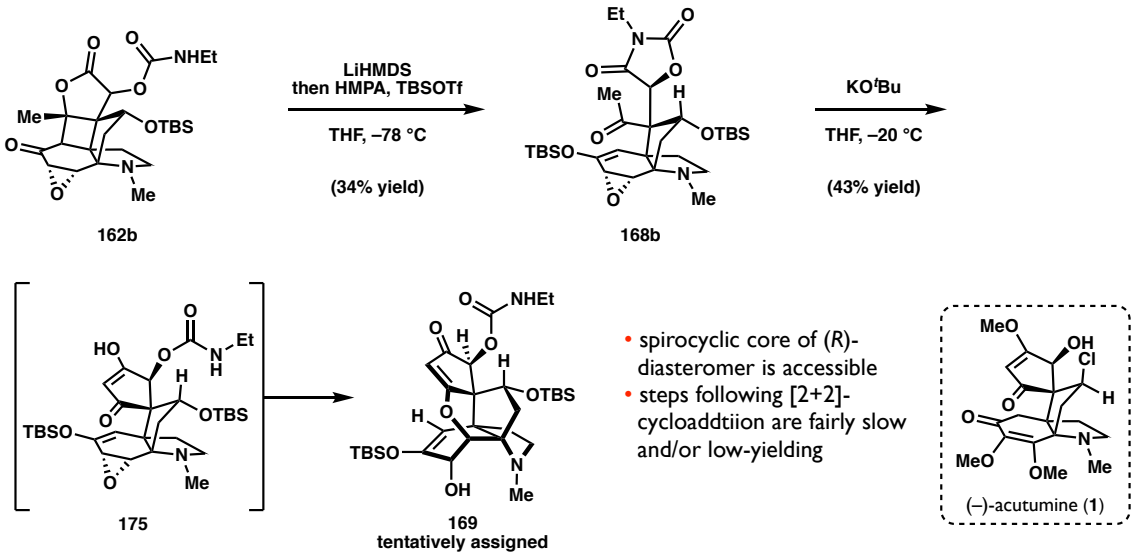
entry	isocyanate (equiv)	temperature	additive/conditions	result
1	2.2 to xs	23 °C	-	55% yield[a]
2	10	23 °C	-	no product, mess upon addition of more isocyanate
3	2.2	50 to 90 °C	-	mostly SM; trace product at 90°C
4	2.2	23 °C	2.0 equiv Pyr	mostly SM; trace product
5	2.2	0 to 23 °C	0.1 equiv $BF_3{\cdot}Et_2O$	decomposition
6	2.2	–78 to 23 °C	1.2 equiv LiHMDS	decomposition

[a] Slow conversion and not reproducible.

Resorting to more forcing conditions, using Lewis acid activation (entry 5) and discrete deprotonation of the alcohol with LiHMDS (entry 6), resulted in decomposition. Nevertheless, the first trial (entry 1) had afforded 5 mg of carbamate **162b**, which was subjected to the retro-aldol/aldol sequence.

We were pleased to find that deprotonation of carbamate **162b** with LiHMDS, followed by trapping of the enolate with TBSOTf, in the presence of HMPA, afforded the retro-aldol product **168b** in moderate yield (Scheme 2.15). Subseqeuent aldol reaction in the presence of potassium *tert*-butoxide proceeded smoothly, confirming our original hypothesis that the more remote secondary –OTBS group in **168b** would relieve the steric congestion observed in the opposite diastereomeric series (see Scheme 2.11b, Section 2.4.4). The isolated aldol product is tentatively assigned as bridged ether **169** (Scheme 2.15), based on our previous observations (see **165a** and **165b**, Scheme 2.10, Section 2.4.3). However, more material is required to confirm the structure of **169** via 2D-NMR analysis.

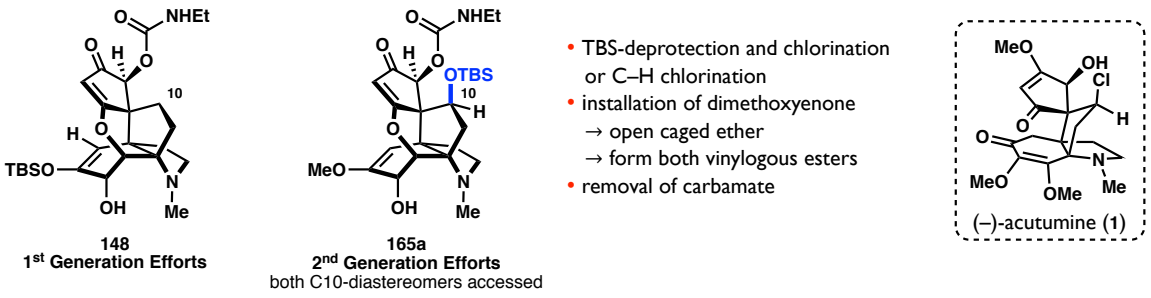
Scheme 2.15 *Retro-aldol/aldol to spirocyclic core with C10-(R)-OTBS group.*



2.5 OVERVIEW OF THE REMAINING CHALLENGES

At this stage of the project, we had successfully accessed the spirocyclic core of the acutumine alkaloids with and without an oxidation handle at C10 for chloride installation (Figure 2.5, spirocycles **148** and **165a**). Despite this achievement, there were a number of significant challenges remaining on this project. In particular, these challenges included 1) chlorination at C10 either through TBS-deprotection and deoxychlorination of **165a** or C–H chlorination of **148**, 2) installation of the dimethoxyenone, which would require oxidation, opening of the caged ether, and vinylogous ester formation, and 3) removal of the carbamate moiety, which was anticipated to be a difficult transformation. A fourth impeding challenge at the time was also the small quantities of spirocycles **165a** and **148** that had been accessed. The material throughput at the time was very limiting for further late-stage investigation until all reactions in the route and the [2+2]-cycloaddition had been considerably altered (with the Honeywell/Philips lamp set up) to allow material throughput (see Section 2.4.2, Scheme 2.9 for details).

Figure 2.5 *Overview of most advanced intermediates and remaining challenges.*

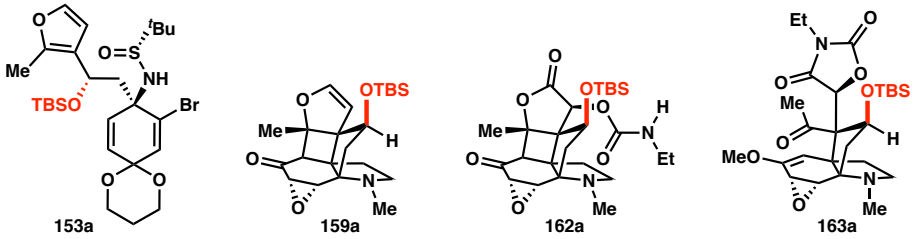


2.5.1 A Difficult TBS-Deprotection

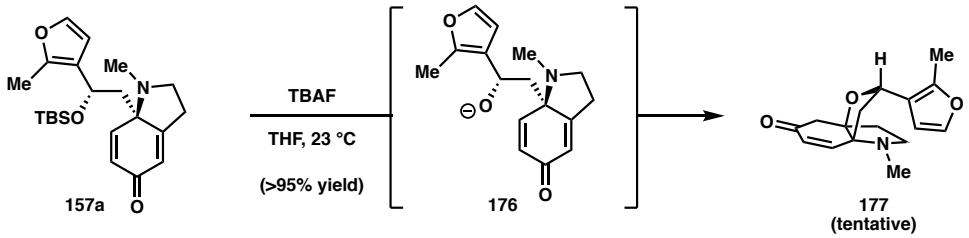
During our 2nd generation synthesis efforts, TBS-deprotection along the route toward spirocycle **165a** were investigated. However, this deprotection was unsuccessful in the majority of intermediates (Figure 2.16a), save for compounds **154a** (Scheme 2.17a) and **159b** in the C10-(*R*)-diastereomeric series (Scheme 2.18). Scheme 2.16a shows a selection

Scheme 2.16 *Failed TBS-deprotections and observed side reactions.*

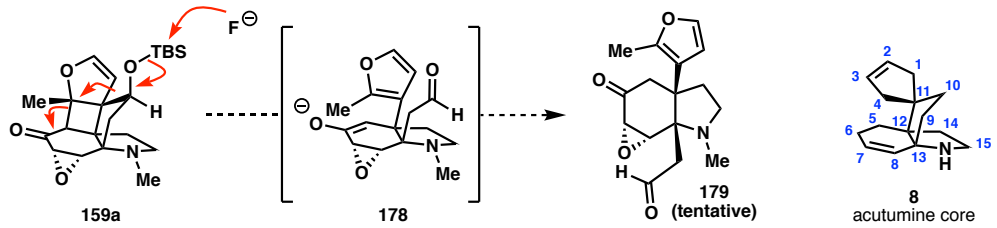
a) Selection of compounds and TBS-deprotection conditions which failed.



b) Cyclic ether formation prior to [2+2]-cycloaddition.



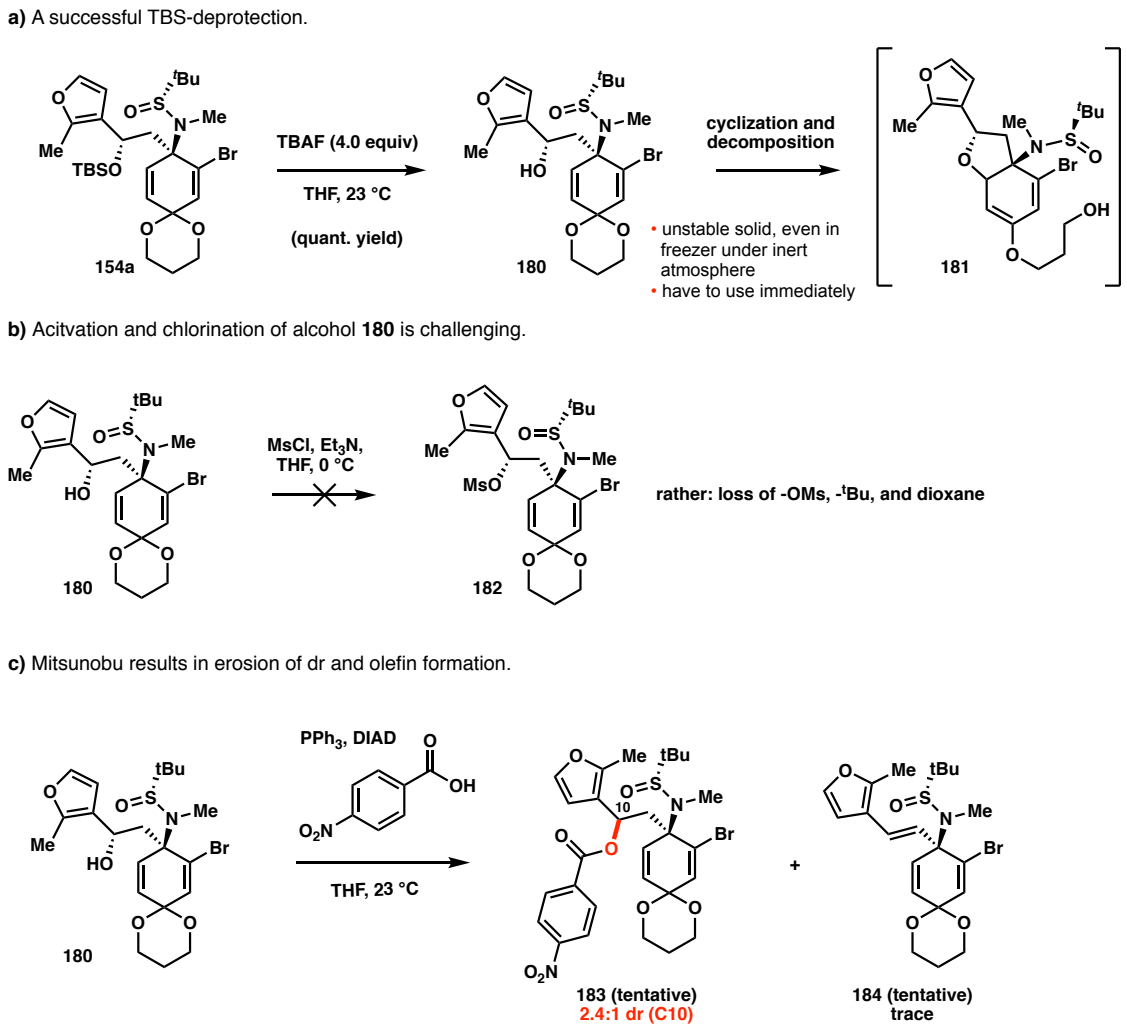
c) Retro-aldol reactivity post [2+2]-cycloaddition.



of compounds that were unsuccessful in this TBS-deprotection, as well as a subsection of conditions what were tried. On compounds prior to [2+2]-cycloaddition, *in situ* oxy-Michael addition of the resulting alcohols were observed, which afforded undesired cyclic ether products, such as compound **177** (Scheme 1.14b). In contrast, for compounds after formation of the C11–C12 bond, retro-aldol side-reactivity was commonly encountered (Scheme 2.16c).

The exception to this challenge was TBS-ether **154a** (Scheme 2.17a), which was the only intermediate prior to the [2+2]-cycloaddition that could be successfully deprotected. The product alcohol **180** could be purified via Florisil flash chromatography; however, it was not stable, even under inert atmosphere and in a freezer, and would cyclize and decompose both as a solid and in solution. It was suitably stable for immediate use, and so was subjected to MsCl at 0 °C (Scheme 2.17b). Unfortunately, these conditions did not afford mesylate **182**, or any chlorination product, but decomposition of the intermediate. In considering chlorination reactions on an alcohol such as **180**, there was a significant concern about the formation of elimination products and erosion of the stereofidelity at C10 due to the benzylic nature of this alcohol with respect to the electron-rich furan. In order to probe the stability of this alcohol under activating conditions, a Mitsunobu reaction was performed with PPh_3, DIAD, and *p*-nitrobenzoic acid (Scheme 2.17c). Indeed, the reaction resulted in formation of undesired olefin **184**, while the substituted product **183** had been formed with an eroded dr as well (single diastereomer to 2.4:1 dr). These results indicated that any substitution at C10 prior to the [2+2]-cycloaddition of the furan would be very challenging.

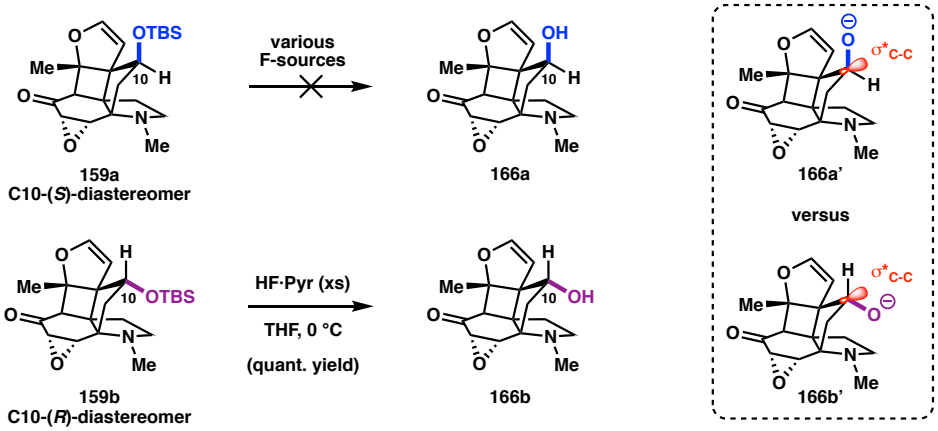
Scheme 2.17 *A successful TBS-deprotection prior to [2+2].*



The second exception to the TBS-deprotection difficulties was cyclobutane **159b** in the C10-(*R*)-diastereomeric series (Scheme 2.18). Prior to accessing this cyclobutane, its (*S*)-isomer **159a** had been subjected to numerous TBS-deprotection trials, always resulting in retro-aldol type products or decomposition. However, when C10-(*R*)-cyclobutane **159b** was subjected to excess HF·Pyr, a remarkably clean reaction afforded quantitative yields of neopentyl alcohol **166b** after a short column. This very drastic difference likely results from the change of orbital overlap of the alcohol lone-pair and the

C–C σ* orbital. Despite the successful TBS-removal, the (*R*)-diastereomeric series proved synthetically intractable, as laid out in Section 2.4.4. Nevertheless, a number of chlorination trials were performed on neopentyl alcohol **166b**. These efforts included standard deoxychlorination reactions, such as the use of Appel conditions, thionyl chloride, and MsCl/TsCl. Unfortunately, the desired deoxychlorination product at C10 was never observed.

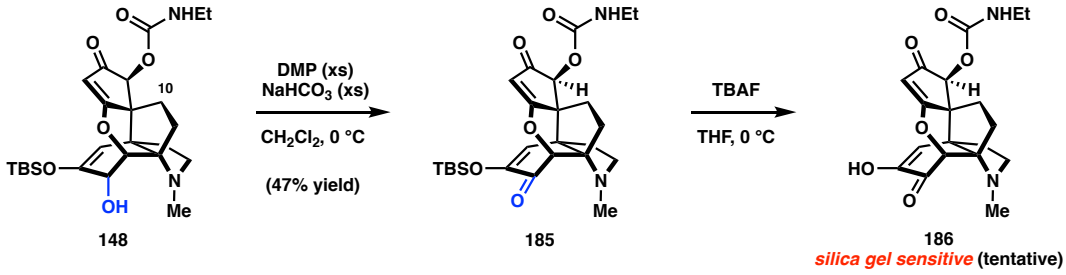
Scheme 2.18 *Different TBS-deprotection results between C10-(S)- and (R)-series.*



2.5.2 Trials to Advance the Caged Ether

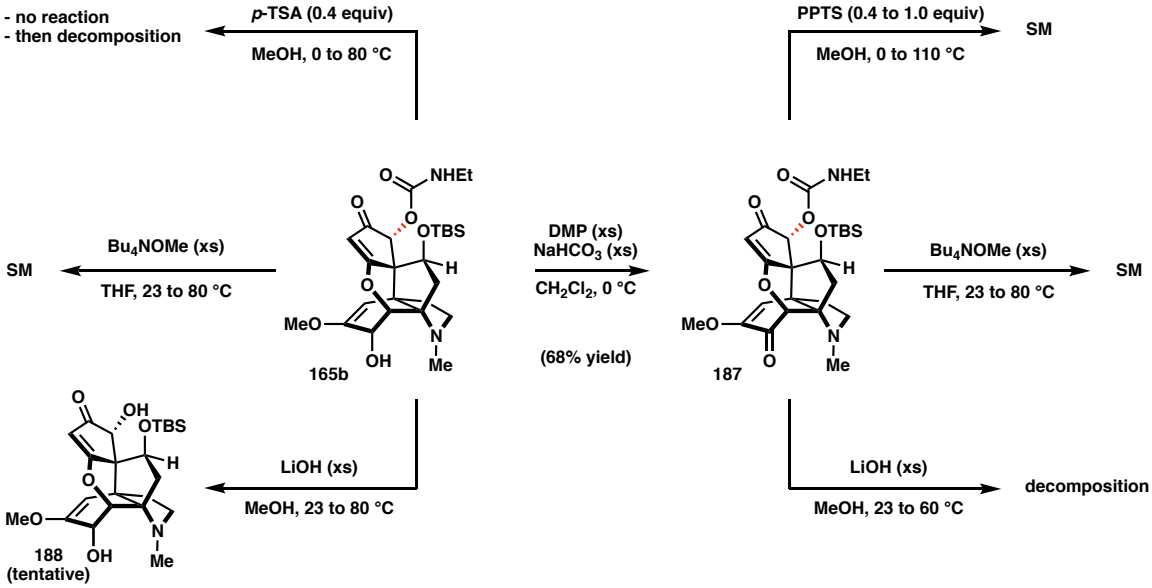
At this point of investigating the C10-deoxy series, there was only minimal amounts of material to begin probing the final functionalizations of the 6-membered ring. Working on small scale, however, Dess-Martin oxidation of **148** to afforded ketone **185**, which now contained the correct oxidation state for the required dimethoxyenone functionality (Scheme 2.19). Subsequent TBS-deprotection of the enol-ether was feasible, although it resulted in a silica gel sensitive enol **186**.

Scheme 2.19 *Advancement of C10-deoxy caged ether* ***148***.



On the analogous C10-oxidized substrate, we could likewise perform the Dess-Martin oxidation – here on the C1-epimer – to afford the ketone **187** (Scheme 2.20), and a number of trials were performed on this limited amount of material to open the caged ether. Unfortunately, both acidic and basic conditions aimed at leveraging MeOH as a nucleophile were unsuccessful and ring-opened products were never observed. Interestingly, when alcohol **165b** was subjected to refluxing MeOH and LiOH, carbamate-deprotected product **188** was observed, tentatively based on LC/MS and ^{1}H NMR. At this

Scheme 2.20 *Trials on C10-oxidized caged ether* ***165b***.



stage, due to the difficulties in material throughput, selectivity, and reactivity, we decided to review the feasibility of this 1st generation rote to (–)-acutumine (**1**).

2.6 CONCLUDING REMARKS

In conclusion, the 1st generation efforts toward the total synthesis of (–)-acutumine (**1**) involved the development of our key strategy utilizing a [2+2]-cycloaddition of furanyl dihydroindolone **127b** in order to install the vicinal quaternary carbon centers found in the natural product. This was then followed by an engineered retro-aldol/aldol sequence that utilized a carbamate as an internal handle to perform this challenging carbonyl chemistry in a controlled fashion. These efforts culminated in the synthesis of the spirocyclic core of dechloroacutumine; however, C–H chlorination efforts at this time remained fruitless.

The 2nd generation efforts resulted in the successful synthesis of the analogous spirocyclic core with oxidation at C10 for subsequent chlorination. This work included the synthesis of both the (*S*)- and (*R*)-diastereomers at C10, spirocycles **165a** and **169**. Many of the steps in the sequence had to be re-optimized, as the chemistry was not identically applicable with a newly oxidized C10-carbon after step five in the sequence. On the small amounts of material that had been obtained in 2014, late-stage trials to access the dimethoxyenone functionality were performed and remained unsuccessful. Furthermore, TBS-deprotection proved incredibly difficult along the sequence, which impeded investigations for subsequent chlorination. The single intermediate that was successfully TBS-deprotected in the C10-(*S*)-series was obtained after the nitrogen methylation, but it was found that the benzylic nature of alcohol **180** resulted in erosion of dr when a

Mitsunobu reaction was attempted. Furthermore, chlorination trials on C10-(*R*)-alcohol **166b** did not afford the desired deoxychlorination.

Overall, while the spirocyclic core of the acutumine alkaloids had been obtained in two series of compounds, it became clear that the installation of the dimethoxyenone functionality on the 6-membered ring was one of the biggest, perhaps underestimated, challenges in the synthesis. While the late-stage chlorination (either C–H or deoxychlorination) was viewed risky as well, this was a particular challenge that was understood from the beginnings of this project. Thus, in the next chapter of these total synthesis efforts, we sought to investigate every mode in which we might modify (open, oxidize, etc.) epoxyketones **158a** and **159a** (see Chapter 3) We fully understood that even with a successful chlorination in hand, we could not complete the total synthesis without the dimethoxyenone functionality.

2.7 EXPERIMENTAL SECTION

2.7.1 Materials and Methods

General Procedures. Unless otherwise stated, reactions were performed under an inert atmosphere (dry N_2 or Ar) using freshly dried solvents utilizing standard Schlenk techniques. Glassware was oven-dried at 120 °C for a minimum of four hours, or flame-dried utilizing a Bunsen burner under high vacuum. Tetrahydrofuran (THF), methylene chloride (CH_2Cl_2), acetonitrile (CH_3CN), benzene (PhH), and toluene (PhMe) were dried by passing through activated alumina columns. HPLC grade methanol (MeOH, A452-4), benzene (PhH, OmniSolv, BX0212-1), acetonitrile (CH_3CN, A998-4), pentane (P399-4),

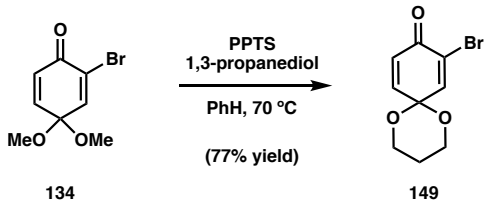
and ACS grade acetone (A18-20) and hexanes (H292-20) were purchased from Fisher and used when specifically indicated, as received. Anhydrous DMF was purchased from VWR (EM-DX1727-6) and used as received. Triethylamine (Et_3N), N,N-diisopropylethylamine (DIPEA) were distilled over calcium hydride prior to use. All reactions were monitored by thin-layer chromatography using EMD/Merck silica gel 60 F254 pre-coated plates (0.25 mm) and were visualized by UV, *p*-anisaldehyde, potassium permanganate ($KMnO_4$), or ceric ammonium molybdate (CAM) staining. Flash column chromatography was performed as described by Still et al.[43] using silica gel (particle size 0.032-0.063) purchased from Silicycle or Florisil (100-200 mesh) purchased from ACROS Organics (CAS 1343-88-0). Preparative HPLC was performed with an Agilent 1100 Series HPLC utilizing an Agilent Eclipse XDB-C18 5µm column (9.4 x 250 mm) or an Agilent Zorbax RX-SIL 5µm column (9.4 x 250 mm). ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance III HD with Prodigy cryoprobe (at 400 MHz and 101 MHz respectively), a Varian 400 MR (at 400 MHz and 101 MHz, respectively), a Varian Inova 500 (at 500 MHz and 126 MHz, respectively), or a Varian Inova 600 (at 600 MHz and 150 MHz, respectively), and are reported relative to internal $CHCl_3$ (^1H, $\delta = 7.26$) and $CDCl_3$ (^{13}C, $\delta = 77.16$), or C_6H_6 (^1H, $\delta = 7.16$) and C_6D_6 (^{13}C, $\delta = 128.06$). Data for ^1H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicity and qualifier abbreviations are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm^{-1}). HRMS were acquired using an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in

electrospray ionization (ESI), or mixed (MM) ionization mode, or obtained from the Caltech Mass Spectral Facility in fast-atom bombardment mode (FAB). Molecular formulas of the compounds "M" are given, with the observed ion fragment in brackets, e.g. $[M+H]^+$. Optical rotations were measured on a Jasco P-2000 polarimeter using a 100 mm path-length cell at 589 nm. Melting points were determined using a Büchi B-545 capillary melting point apparatus and the values reported are uncorrected.

Unless otherwise stated, chemicals and reagents were used as received. Reagents were purchased from commercial vendors as follows: pyridinium *p*-toluenesulfonate (PPTS) and potassium *tert*-butoxide (KO^{t}Bu, 1 M in THF) were purchased from Sigma-Aldrich. (R)-(+)-2-methyl-2-propanesulfinamide was purchased from Combi Blocks. Indium trifluoromethanesulfonate ($InOTf_3$) was purchased from Strem Chemicals Inc. and stored in a nitrogen-filled glovebox. Hexamethylphosphoramide (HMPA) was distilled over calcium hydride and stored in a Schlenk flask over 3Å molecular sieves under Ar. Methyl trifluoromethanesulfonate (MeOTf) was purchased from Sigma-Aldrich, transferred to a Schlenk flask in a nitrogen-filled glovebox, and stored in the Schlenk tube under N_2 at –20 °C. DMP was purchased from Oakwood Chemical and stored in the freezer of a nitrogen-filled glovebox.

2.7.2 Experimental Procedures

Preparation of dioxane ketal 149.



134 149

A 5 L three-neck flask containing a stir bar was flame-dried. Dimethoxyketal[13] **134** (77.8 g, 334 mmol) was taken up in PhH (2 L, in 4 batches; HPLC grade) and transferred to the reaction flask under air by use of a funnel. PPTS (13.0 g, 51.7 mmol, 0.15 equiv) was added, followed rapidly by 1,3-propanediol (63.3 mL, 876 mmol, 2.6 equiv). An oven-dried reflux condenser was attached to the reaction flask, and the mixture was sparged with N_2 for 15 min. To the remaining neck, a thermocouple was added to monitor the internal temperature. Using a heating mantle, the mixture was gradually heated to an internal temperature of 74 °C, which was reached after a total heating time of 1 h and 20 min (the endothermic process required 50 min of heating to reach 62.8 °C, 65 min till 65.7 °C) (*Note*: It was found that close monitoring of this reaction is necessary so that the reaction can be quenched immediately upon completion (as judged by TLC). Prolonged heating will cause formation of undesired side products. On smaller scales (25.0 g or less), the reaction was placed in a 70 °C oil bath, and closely monitored by TLC, typically reaching completion after 30 min). The heating mantle was removed and the reaction rapidly quenched by the addition of pH 7 buffer (1.2 L). The stirring mixture was left to cool to room temperature (40 min). The mixture was transferred to a separatory funnel and the

layers separated. The aqueous layer was set aside, and the organic layer was washed with brine (2 x 1 L), dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The aqueous layer was extracted with Et_2O (5 x 500 mL), and the combined organic layers were washed with brine (2 x 800 mL). The combined brine layers were back-extracted with Et_2O (1 x 500 mL). All combined organic layers were dried with Na_2SO_4, filtered, concentrated under reduced pressure, and combined with the initial PhH crude to give an orange solid (80.4 g). The crude was recrystallized from CH_2Cl_2/hexanes, and stored in the freezer to afford ketal **149** as pale orange crystals (63.15 g total, 77% yield; 58.0 g from first recrystallization, 5.15 g from second recrystallization of filtrate) that were filtered away from the diol. Typically, the filtrate was concentrated and recrystallized a second time to afford more amounts of pure ketal. However, subsequent recrystallizations become increasingly difficult due to the increased ratio of viscous diol present.

TLC: R_f 0.57 (2:1 hexanes/EtOAc, UV & $KMnO_4$).

melting point: 117–121 °C.

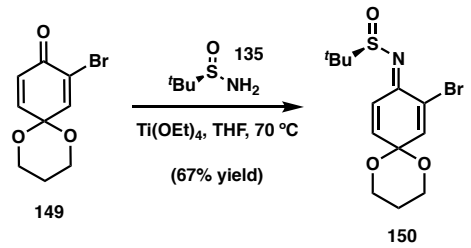
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, J = 3.0 Hz, 1H), 7.05 (dd, J = 10.3, 3.0 Hz, 1H), 6.29 (d, J = 10.3 Hz, 1H), 4.16 – 4.02 (m, 4H), 1.98 (dtt, J = 13.7, 7.7, 4.9 Hz, 1H), 1.83 (dtt, J = 13.9, 5.7, 4.2 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 178.0, 143.2, 141.9, 126.9, 125.5, 91.1, 61.3, 24.9.

FTIR (NaCl, thin film): 2971, 2880, 1680, 1645, 1124, 1048, 994, 953 cm^{-1}.

HRMS (FAB$^+$, *m/z*): $C_9H_9BrO_3$, calc'd for $[M+H]^+$: 244.9813, found: 244.9815.

Preparation of imine 150.



Ketone **149** (13.7 g, 55.78 mmol) was added to a flame-dried 250 mL Schlenk flask with a stir bar. Sulfinyl amine (8.11 g, 66.94 mmol, 1.2 equiv) was added subsequently, and the mixture placed under N_2 atmosphere. THF (35 mL) was added, followed by $Ti(OEt)_4$ (25.7 mL, 122.7 mmol, 2.2 equiv). THF (2 mL) was then used to wash down the viscous titanium reagent from the Schlenk neck and the mixture was sparged with N_2 for 15 min. The Kontes valve was closed, while the N_2 inlet needle was left in place in the side arm. The flask was then thoroughly wrapped in aluminum foil and was immersed in a 70 °C oil bath. The reaction was stirred for 3 days (72 h), giving a deep orange-brown mixture. The reaction was subsequently cooled to room temperature and EtOAc was used to dilute to twice the volume. This mixture was then slowly poured into a well-stirred brine solution (450 mL) in an Erlenmeyer flask (*Note*: Insufficient stirring will cause clumping and solids will not disperse into small particles). The heterogeneous mixture was filtered through a pad of Celite (185 g, pre-compacted with EtOAc) and was washed with EtOAc thoroughy (1.6 L). This filtration can be slow if a fritted filter funnel is used. Commonly a non-fritted filter funnel with a Kim-wipe and sand (below and above Celite) was employed, and the top Celite layer was opened up with a metal spatula during filtration. Once all titanium salts were filtered off, the layers were separated in a separatory funnel and organic layer washed

with brine (2 x 700 mL). The combined aqueous layers (aqueous layer and brine washes) were then extracted with EtOAc (3 x 400 mL). All combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give an orange-brown semi-solid. The residue was purified by silica gel flash chromatography (silica gel oven-dried overnight): 1) equilibrated with 1% Et_3N in 10% EtOAc/hexanes, then 2) flushed two column volumes of 10% EtOAc/hexanes, and 3) loaded the crude and run a gradient of 20–50% EtOAc/hexanes) to afford **150** as a dark orange sticky solid (13.1 g, 67% yield).

TLC: R_f 0.48 (1:1 hexanes/EtOAc, $KMnO_4$).

$[\alpha]_D^{25.0}$: –199.9° (c = 0.70, $CHCl_3$).

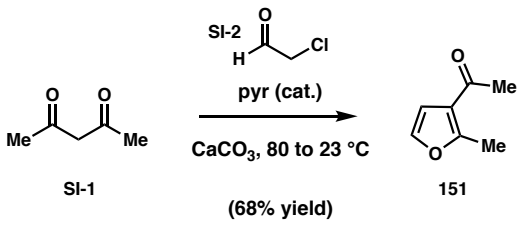
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, *J* = 10.4 Hz, 1H), 7.31 (d, *J* = 2.7 Hz, 1H), 6.73 (dd, *J* = 10.5, 2.7 Hz, 1H), 4.07 (td, *J* = 6.0, 5.5, 2.5 Hz, 4H), 1.97 – 1.77 (m, 2H), 1.32 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 156.6, 136.8, 136.2, 125.3, 120.5, 91.0, 61.1, 61.0, 60.9, 25.0, 23.4.

FTIR (NaCl, thin film): 2962, 2872, 1568, 1362, 1243, 1108, 1047, 991, 933 cm^{-1}.

HRMS (MM, *m/z*): $C_{13}H_{18}BrNO_3S$, calc'd for $[M+H]^+$: 348.0264, found: 348.0263.

Preparation of ketofuran 151.



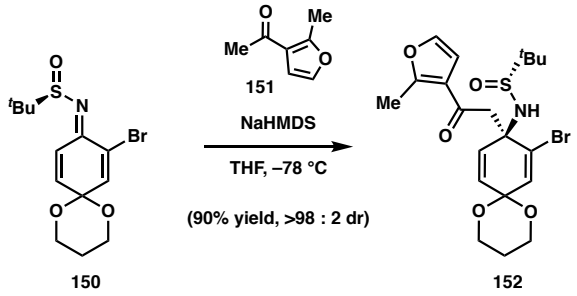
The following procedure was adapted from a literature report[30]:

$CaCO_3$ (114.0 g, 1.14 mol, 0.98 equiv) was added to a 3-neck 500 mL round bottom flask under ambient air. Acetylacetone (**SI-1**, 120 mL, 1.17 mol, 1.0 equiv) was added, followed by pyridine (4.73 mL, 58.4 mmol, 5 mol%). The mixture was mixed to a thick paste utilizing a mechanical stirrer, after which a thermocouple was placed on one neck, and a 250 mL addition funnel on another. Subsequently, acetaldehyde (**SI-2**, 148.4 mL, 1.17 mol, 1.0 equiv, 50% wt in H_2O) was added dropwise via the addition funnel over 2 h, and a slight exotherm to 35 °C was noted. Subsequently, the addition funnel was replaced with a reflux condenser, and the mixture heated to an internal temperature of 80 °C and kept at that temperature for 90 min. The reaction was subsequently cooled to room temperature and stirred for 16 h. Upon reaction completion, the mixture was slowly quenched with 1 M HCl (300 mL), which was added via addition funnel. Once the addition was complete and bubbling had ceased, the mixture was transferred to a 2 L Erlenmeyer flask containing H_2O (200 mL), and the transfer completed with EtOAc (400 mL). Under stirring, concentrated HCl (60 mL) was added slowly dropwise, followed by more H_2O (200 mL), at which point all solids had dissolved. The mixture was then transferred to a separatory funnel and the layers separated. The aqueous layer was extracted with EtOAc (3 x 350 mL) and the combined organic layers were washed with brine (350 mL). All combined organic

layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give an orange-brown oil. Due to product volatility, this crude was not dried under high vacuum, but rather stored under inert atmosphere until purification. The crude was purified via fractional distillation (reported bp = 73–75 °C at 15 mmHg),[44] starting at 10 mmHg and 35 °C to remove remaining EtOAc and acetylacetone. The oil bath was then slowly heated to 60–65 °C (10 mmHg), at which point product began to distill over. Finally, the mixture was gradually heated to a final temperature of 110 °C to ensure all product had distilled over, ultimately affording furan **151** as a clear oil (98.3 g, 68% yield). All spectroscopic data matched the literature reported values.[30,44–46]

Note: The product was stored in an oven-dried bottle over activated 3Å MS under Ar at –20 °C. This maintained the integrity and clear color of the furan for prolonged time (> 1 year). When exposed to air during storage or for prolonged times, the furan gradually turned yellow; however, discolored batches showed no adverse effects on the yield of the following 1,2-addition chemistry.

Preparation of ketone 152.



A 1 L flask with stir bar was flame-dried. Furan **151** (10.7 g, 86.1 mmol, 1.5 equiv) was added, placed under N_2, and THF (38 mL) was added. The mixture was cooled to –78 °C,

and NaHMDS (86 mL, 86.1 mmol, 1 M in THF, 1.5 equiv) was added via cannula over 1 h and 15 min (approximately 2 drops per second). While this yellow mixture was stirred at –78 °C for an additional 40 min, imine **150** (20 g, 57.4 mmol), under N_2, in a flame-dried flask, was taken up in THF (90 mL). The imine solution was then added to the stirred enolate at –78 °C by syringe pump at 15 mL/h (on this scale, 3 syringe pumps with a 50 mL syringe each were required), overall taking 3 h and 30 min. As the addition progressed, the yellow mixture turned brown. It is important to maintain the reaction at –78 °C as warming will cause decomposition. THF (20 mL) was used to rinse all three syringes and complete imine addition. After an additional 15 min, all starting material was consumed by TLC analysis (the contents of the capillary was quenched with saturated aqueous $NaHCO_3$, which enabled clearer visualization of the reaction). The reaction was quenched at –78 °C with saturated aqueous $NaHCO_3$ (200 mL). The mixture was subsequently warmed to room temperature, and EtOAc (100 mL) was added. The mixture was transferred to a separatory funnel, and brine (100 mL) and H_2O (50 mL) were added to aid layer separation and to dissolve salts. The aqueous layer was extracted with EtOAc (5 x 200 mL) and the combined organic layers were washed with brine (2 x 500 mL). The brine layer was back-extracted with EtOAc (1 x 400 mL). All combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure to an off-white foam. The residue was purified by silica gel flash chromatography (equilibrated with 30% EtOAc/hexanes and utilized a gradient of 40–100% EtOAc/hexanes after loading) to afford **152** as an off-white solid (24.4 g, 90% yield).

TLC: R_f 0.29 (2:1 EtOAc/hexanes, UV, $KMnO_4$, and CAM).

$[\alpha]_D^{25.0}$: –42.1° (c = 1.50, $CHCl_3$).

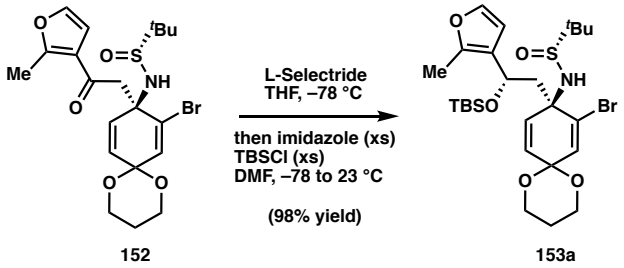
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22 (d, *J* = 2.1 Hz, 1H), 6.77 (d, *J* = 2.2 Hz, 1H), 6.53 (d, *J* = 2.1 Hz, 1H), 6.44 (d, *J* = 10.4 Hz, 1H), 6.35 (dd, *J* = 10.4, 2.2 Hz, 1H), 5.77 (s, 1H), 4.12 – 3.92 (m, 4H), 3.31 (d, *J* = 16.2 Hz, 1H), 2.92 (d, *J* = 16.3 Hz, 1H), 2.57 (s, 3H), 1.94 – 1.80 (m, 1H), 1.79 – 1.66 (m, 1H), 1.26 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 194.9, 160.4, 140.7, 133.6, 132.8, 131.5, 123.2, 121.3, 110.1, 91.9, 60.7, 60.6, 59.4, 56.8, 49.1, 25.2, 23.0, 14.8.

FTIR (NaCl, thin film): 3258, 2960, 2870, 1667, 1574, 1409, 1240, 1113, 1049 cm^{-1}.

HRMS (MM, *m/z*): $C_{20}H_{26}BrNO_5S$, calc'd for $[M+H]^+$: 472.0788, found 472.0792.

Preparation of TBS-ether 153a.



152 153a

Note 1: This reaction was set up in duplicate (2 x 12.2 g) and, after quenching, the batches were combined for extraction and purification. This reaction can be done on larger scale and it is recommended that a reliable large-scale flask is available that can be dried and kept under inert atmosphere. An analogous experiment with 23.6 g (49.96 mmol) was conducted in a 3 L three-neck flask under a bed of argon, using an overhead stirrer. In this case, a slight decrease in yield was observed (83%).

Note 2: It is important to plan ahead and swiftly prepare the quenching mixture (TBSCl, imidazole, DMF) once the reductant has been added to the ketone. It takes approximately 10 min for the solids to dissolve in DMF on large scale. To prepare the quenching mixture, a 1 L flask with stir bar was flame-dried. TBSCl (38.9 g, 258 mmol, 10.0 equiv) and imidazole (26.8 g, 387 mmol, 15.0 equiv) were added, and the solids placed under nitrogen atmosphere. The solids were taken up in DMF (172 mL, added via cannula) and stirred to speed up dissolving.

Ketone **152** (12.2 g, 25.8 mmol) was added to a flame-dried 2 L flask and placed under N_2 atmosphere. THF (520 mL) was added, and the mixture cooled to –78 °C. L-Selectride (51.7 mL, 51.7 mmol, 2.0 equiv) was added via cannula over 35 min (approximately 2 drops per second). At this point, the quenching mixture was prepared (see *Note 2* above). After a total time of 85 min (starting from beginning of reductant cannulation), TLC analysis indicated consumption of starting material. At this stage, the prepared DMF mixture was added to the reaction at –78 °C via cannula over 30 min. Specifically, the addition was started at 2 drops per second. Upon significant quenching of the reaction, the mixture began to solidify, at which point the addition rate of the DMF mixture was increased to a steady stream. After complete addition of the DMF mixture, the reaction was kept at –78 °C for 5 min and then warmed to room temperature and stirred overnight (between 15–18 h). The reaction was subsequently quenched by cooling to 0 °C and adding H_2O (500 mL) under high stirring. EtOAc (300 mL) was added and the mixture warmed to room temperature and vigorously stirred for 1 h. The two batches were combined at this

point and added to a separatory funnel and the layers separated. The organic layer was set aside, and the aqueous layer was extracted with EtOAc (5 x 300 mL). These extractions were washed with brine (3 x 300 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure. While concentrating the first portion of the workup, the first organic layer was washed with brine (5 x 500 mL) to remove most DMF, subsequently dried with Na_2SO_4, filtered, and concentrated under reduced pressure and combined with the second part of the crude. Overall, 135 g crude oil was obtained (*Note*: A heavier crude will likely contain too much DMF to enable a successful column), which was stored in the freezer overnight. The residue was purified by silica gel flash chromatography (10–100% EtOAc/hexanes) to afford **153a** as an off-white foam (29.8 g, 98% yield).

TLC: R_f 0.42 (4:1 EtOAc/hexanes, UV & $KMnO_4$).

$[\alpha]_D^{25.0}$: –101.8° (c = 1.01, $CHCl_3$).

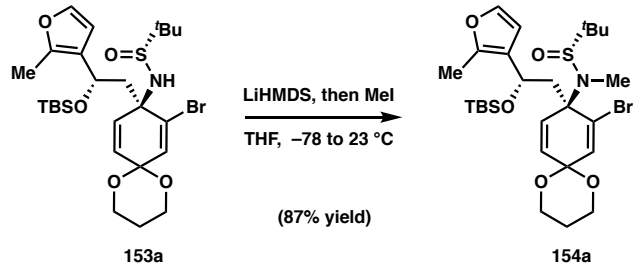
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21 (d, *J* = 2.0 Hz, 1H), 6.70 (d, *J* = 2.3 Hz, 1H), 6.34 – 6.28 (m, 2H), 5.98 (d, *J* = 10.3 Hz, 1H), 4.55 (dd, *J* = 8.0, 4.1 Hz, 1H), 4.09 – 3.93 (m, 4H), 3.53 (s, 1H), 2.34 (dd, *J* = 13.7, 4.1 Hz, 1H), 2.26 (dd, *J* = 13.8, 8.1 Hz, 1H), 2.22 (s, 3H), 1.91 – 1.69 (m, 2H), 1.12 (s, 9H), 0.80 (s, 9H), 0.00 (s, 3H), -0.20 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 147.8, 140.8, 133.5, 133.1, 131.5, 124.3, 122.8, 109.8, 91.9, 63.4, 60.8, 60.3, 59.3, 56.4, 50.0, 25.9, 25.2, 22.7, 18.1, 12.3, -4.6, -4.9.

FTIR (NaCl, thin film): 3336, 2929, 2857, 1669, 1255, 1052, 836 cm^{-1}.

HRMS (ESI, *m/z*): $C_{26}H_{42}BrNO_5SSi$, calc'd for $[M+H]^+$: 588.1809, found 588.1789.

Preparation of methylated sulfinamide 154a.



Sulfinamide **153a** (29.77 g, 50.57 mmol) in THF (505 mL) was transferred to a flame-dried 2 L flask via cannula, all under a nitrogen atmosphere. The mixture was cooled to –78 °C, after which LiHMDS (70.8 mL, 70.8 mmol, 1 M in THF, 1.4 equiv) was added over 50 min via cannula (approximately 2 drops per second) to give a yellow-brown solution. Once the addition was complete, the mixture was further stirred at –78 °C for 30 min, after which MeI (12.6 mL, 202.3 mmol, 4.0 equiv) was added dropwise. After stirring at –78 °C for 10 min, the reaction was warmed to room temperature. TLC analysis indicated only trace starting material after 1 h after cooling bath removal (approximately 20–25 min after the mixture had reached room temperature). At this point the reaction had turned a deeper orange brown. The reaction was quenched at room temperature with saturated aqueous NH_4Cl (450 mL), which generated some solids that were dissolved upon the addition of H_2O (20 mL). The mixture was stirred vigorously for 1.5 h to quench the excess MeI. EtOAc (200 mL) was added and the mixture transferred to a separatory funnel. The layers were separated, and the aqueous layer was extracted with EtOAc (4 x 200 mL). The combined organic layers were washed with brine (1 x 300 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure (in a fumehood for safety) to give an orange foam. The residue was purified by silica gel flash chromatography (equilibrated 10%

EtOAc/hexanes and utilized a gradient of 40–70% EtOAc/hexanes after loading) to afford **154a** as a pale champagne-colored foam (26.4 g, 87% yield).

TLC: R_f 0.45 (1:1 hexanes/EtOAc, UV & *p*-anisaldehyde).

$[\alpha]_D^{25.0}$: +24.8° (c = 0.94, $CHCl_3$).

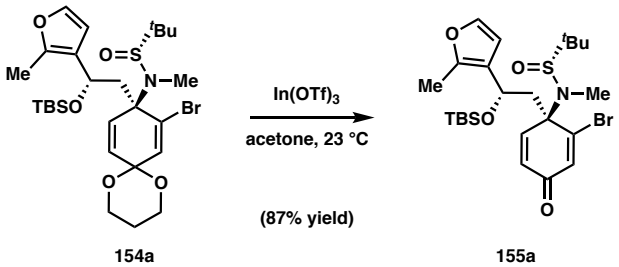
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.17 (d, *J* = 1.9 Hz, 1H), 7.09 (d, *J* = 2.3 Hz, 1H), 6.27 (d, *J* = 1.9 Hz, 1H), 6.01 (dd, *J* = 10.1, 2.3 Hz, 1H), 5.34 (d, *J* = 10.1 Hz, 1H), 4.31 (dd, *J* = 7.0, 3.0 Hz, 1H), 4.16 – 3.88 (m, 4H), 3.05 (dd, *J* = 13.5, 3.1 Hz, 1H), 2.33 (s, 3H), 2.15 (s, 3H), 2.03 (dd, *J* = 13.5, 7.0 Hz, 1H), 1.93 (dtt, *J* = 13.4, 9.0, 4.6 Hz, 1H), 1.71 (dtt, *J* = 12.8, 5.2, 3.7 Hz, 1H), 1.18 (s, 9H), 0.80 (s, 9H), 0.01 (s, 3H), -0.24 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 147.5, 140.3, 133.1, 131.6, 131.4, 127.1, 124.0, 109.9, 91.9, 66.2, 63.9, 61.0, 60.2, 59.0, 48.0, 25.9, 25.8, 25.1, 24.4, 18.1, 12.3, -4.6, -4.9.

FTIR (NaCl, thin film): 2954, 2857, 1472, 1246, 1111, 1071, 988, 936, 836 cm^{-1}.

HRMS (ESI, *m/z*): $C_{27}H_{44}BrNO_5SSi$, calc'd for $[M+H]^+$: 602.1966, found 602.1960.

Preparation of enone 155a.



154a 155a

Ketal **154a** (26.4 g, 43.8 mmol) was taken up in acetone (438 mL, ACS certified) under air in a 1 L flask. $In(OTf)_3$ (1.23 g, 2.19 mmol, 5 mol%) was weighed out, removed from the

glovebox, and added to the stirring ketal at room temperature in one portion. The vial containing the Lewis Acid was rinsed with acetone (2 mL) and the mixture added to the stirring reaction. The orange mixture was stirred at room temperature for 30 min, at which point TLC analysis indicated consumption of starting material. The reaction was worked up after 40 min by the addition of saturated aqueous $NaHCO_3$ (250 mL), giving a light orange milky mixture. EtOAc (200 mL) was added and the mixture stirred vigorously for 5 min. The heterogeneous mixture was transferred to a separatory funnel and H_2O (20 mL) was used to help transfer the solids. The layers were separated, and the aqueous layer subsequently extracted with EtOAc (2 x 150 mL, and then 2 x 100 mL). The combined organic layers were washed with brine (200 mL), and the brine layer was back-extracted with EtOAc (1 x 150 mL). All combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give an orange foam. The residue was purified by silica gel flash chromatography (equilibrated 20% EtOAc/hexanes and utilized a gradient of 30–60% EtOAc/hexanes after loading) to afford **155a** as a pale orange solid (20.8 g, 87% yield).

TLC: R_f 0.47 (1:1 hexanes/EtOAc, UV & *p*-anisaldehyde).

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25.0}}$**:** –12.8° (c = 0.98, $CHCl_3$).

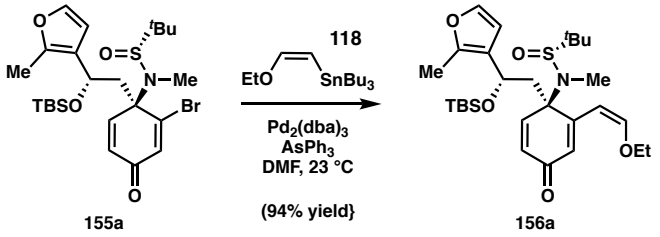
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18 (d, *J* = 1.9 Hz, 1H), 6.88 (d, *J* = 1.8 Hz, 1H), 6.43 (d, *J* = 10.0 Hz, 1H), 6.21 (d, *J* = 1.9 Hz, 1H), 6.07 (dd, *J* = 9.9, 1.8 Hz, 1H), 4.40 (dd, *J* = 7.8, 4.5 Hz, 1H), 3.12 (dd, *J* = 13.3, 4.6 Hz, 1H), 2.38 (s, 3H), 2.13 (dd, *J* = 13.3, 7.8 Hz, 1H), 2.05 (s, 3H), 1.23 (s, 9H), 0.80 (s, 9H), -0.03 (s, 3H), -0.23 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 183.4, 150.6, 149.8, 147.6, 141.0, 136.2, 128.0, 122.8, 109.4, 66.7, 63.7, 59.5, 46.9, 26.0, 25.8, 24.4, 18.1, 12.3, -4.5, -4.7.

FTIR (NaCl, thin film): 2954, 2857, 1670, 1472, 1255, 1073, 952, 836 cm^{-1}.

HRMS (ESI, *m/z*): $C_{24}H_{38}BrNO_4SSi$, calc'd for $[M+H]^+$: 544.1547, found 544.1549.

Preparation of vinyl ether 156a.



A 250 mL round bottom flask with a stir bar was flame-dried, and Ph_3As (2.34 g, 7.64 mmol, 20 mol %) was added in a fumehood. Vinyl bromide **155a** (20.8 g, 38.19 mmol), in a 500 mL round bottom flask, the reaction flask with ligand, and an oven-dried 100 mL graduated cylinder were brought into a nitrogen-filled glovebox. DMF (55 mL) was added to the flask containing vinyl bromide **155a** and was left to dissolve. $Pd(OAc)_2$ (1.75 g, 1.90 mmol, 5 mol %) was then added to the ligand and slurried in DMF (5 mL). Subsequently, vinyl bromide **155a** was added to the reaction flask, and the enone flask rinsed with DMF (15 mL), and the solution transferred. The flask was then rinsed a final time with DMF (2 x 2.5 mL) to complete the transfer to the reaction flask. The reaction flask was capped with a plastic septum, sealed with electrical tape, and removed from the glovebox. Under stirring (600 rpm) and at room temperature, the mixture was sparged with N_2 for 15 min. Subsequently, stannane **118**[19] (19.8 mL, 57.3 mmol, 1.50 equiv) was added and the mixture

continuously sparged with N_2 for 20 min at room temperature. After a total of 2.5 h, all of **155a** was consumed, as monitored by TLC analysis. The reaction was quenched by slowly pouring the mixture into brine (700 mL) in a 2 L Erlenmeyer flask. EtOAc (250 mL) was added and the mixture vigorously stirred. The biphasic mixture was then filtered through a pad of silica gel (4 x 8 cm), the filtrate transferred to a separatory funnel, the layers separated, and the organic layer set aside for later washing. The aqueous layer was extracted with EtOAc (3 x 200 mL), and these extracts were combined with the resulting filtrate after rinsing the silica gel pad with EtOAc (6 x 250 mL). These combined organic layers were washed with brine (1 x 300 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure in a fumehood. During this time, the first organic layer (containing a significant amount of DMF) was washed with brine (2 x 300 mL) and the combined brine layers were back-extracted with EtOAc (1 x 200 mL).These combined organic layers were also dried with Na_2SO_4, filtered, combined with the previously concentrated batch, and concentrated under reduced pressure in a fumehood. The crude residue was purified by silica gel flash chromatography (10–70% EtOAc/hexanes) to afford **156a** as a brown-gold foam (19.21 g, 94% yield).

TLC: R_f 0.36 (1:1 hexanes/EtOAc, UV & *p*-anisaldehyde).

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25.0}}$: –74.4° (c = 1.38, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18 – 7.14 (m, 2H), 6.60 (d, *J* = 7.2 Hz, 1H), 6.19 (d, *J* = 2.0 Hz, 1H), 6.11 (d, *J* = 10.0 Hz, 1H), 5.95 (dd, *J* = 10.0, 2.0 Hz, 1H), 5.18 (d, *J* = 7.2 Hz, 1H), 4.28 (dd, *J* = 8.5, 3.4 Hz, 1H), 4.14 – 3.95 (m, 2H), 2.78 (dd, *J* = 13.2, 3.4 Hz, 1H),

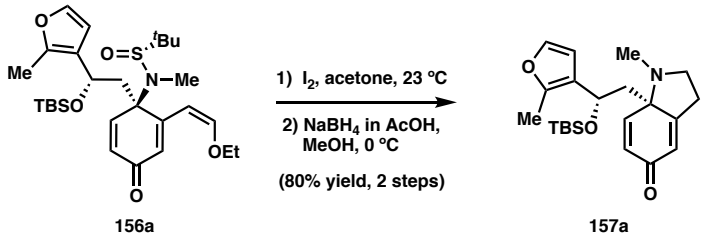
2.33 (s, 3H), 2.20 (dd, J = 13.2, 8.5 Hz, 1H), 2.02 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H), 1.22 (s, 9H), 0.74 (s, 9H), -0.11 (s, 3H), -0.27 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 186.8, 154.6, 153.3, 149.2, 147.7, 140.8, 128.9, 128.7, 123.1, 109.2, 99.4, 70.8, 64.5, 63.8, 59.1, 47.0, 26.3, 25.8, 24.6, 18.1, 15.6, 12.3, -4.7, -4.9.

FTIR (NaCl, thin film): 2955, 2857, 1662, 1626, 1472, 1258, 1067, 836 cm^{-1}.

HRMS (ESI, *m/z*): $C_{28}H_{45}NO_5SSi$, calc'd for $[M+H]^+$: 536.2860, found 536.2853.

Preparation of pyrrolidine 157a.



Step 1: Vinyl ether **156a** (19.18 g, 35.8 mmol) was taken up in acetone (716 mL, ACS certified) in a 2 L round bottom flask containing a stir bar. Iodine (9.54 g, 37.6 mmol, 1.05 equiv) was added in one portion and the deep purple-brown solution was stirred at room temperature for 40 min. The reaction was quenched by the addition of sodium sulfite (14.2 g, 112.8 mmol, 3.15 equiv) and saturated aqueous $NaHCO_3$ (450 mL). EtOAc (250 mL) was added, and the mixture stirred vigorously at room temperature for 10 min. The mixture was transferred to a 4 L separatory funnel, and H_2O (100 mL) was used to help transfer the residual solids (*Note*: This extraction normally contains some solids, and it is recommended that on smaller scale that at least a 250 mL separatory funnel is used to avoid clogging). The aqueous and organic layers were separated, and the aqueous layer extracted with

EtOAc (4 x 200 mL). The combined organic layers were washed with brine (2 x 350 mL), and the combined brine layers were back-extracted with EtOAc (2 x 200 mL). The combined organic layers were dried with Na_2SO_4, filtered through a pad of Celite (100 g, compacted with EtOAc), and concentrated under reduced pressure to give a dark red foam, which was dried under high vacuum for 1 h prior to Step 2.

Step 2: The crude from Step 1 was taken up in MeOH (716 mL, HPLC grade) in a 2 L round bottom flask and cooled to 0 °C. The reductant solution was prepared separately by adding $NaBH_4$ (2.7 g, 71.6 mmol) to a 250 mL round bottom flask. While at 0 °C, AcOH (240 mL, 0.3 M) was slowly added to the $NaBH_4$. *Caution:* significant fumes develop, so it is recommended to perform this at the back of a well-ventilated fumehood. The mixture was swirled, and care was taken not to freeze the AcOH. The remaining $NaBH_4$ was left to dissolve at room temperature after all vigorous fuming had ceased. The reductant was cannulated into the reaction at 0 °C over 50 min, between at 2–4 drops per second. As the cannulation was proceeding, a 50% w/w aqueous KOH quench solution was prepared: H_2O (1 L) was added to a 3 L three-neck flask containing a stir bar, and was cooled to 0 °C. KOH (500 g) was added in seven portions. The mixture was continued to stir at 0 °C to ensure cooling back to 0 °C after the exothermic process. The reduction reaction was quenched after a total time of 1.5 h (since start of reductant cannulation), after a worked up TLC sample (50% w/w aqueous KOH and EtOAc) had shown consumption of all starting material. The quench and reaction solutions were kept in a 0 °C bath for the entirety of the quenching process. The 3-neck flask was equipped with a thermocouple to measure the

internal temperature (2.6 °C at start), as well as an addition funnel containing EtOAc (500 mL). The reaction was cannulated to the KOH solution (well-stirred) over 40 min so that the internal temperature never exceeded 25 °C (this was the endpoint temperature). The EtOAc was added in four portions during this quench time. Once the quench was complete, EtOAc (3 x 20 mL) was added to the reaction flask to rinse the flask and cannula. The worked up mixture was then stirred vigorously at room temperature for 10 min, then transferred to a 4 L separatory funnel. Brine (200 mL) and EtOAc (500 mL) were added to aid layer separation. The resulting aqueous layer was then extracted with EtOAc (4 x 500 mL), and the combined organic layers were washed with brine (2 x 400 mL). The combined brine layers were back-extracted with EtOAc (2 x 400 mL), and all combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give a dark red oil. The residue was purified by Florisil flash chromatography: 1) equilibrated with 0.5% Et_3N in 10% EtOAc/hexanes, then 2) flushed two column volumes of 10% EtOAc/hexanes, and 3) loaded compound onto 30 g of Celite and utilize a gradient of 10–80% EtOAc/hexanes after loading) to afford **157a** as a red oil (11.06 g, 80% yield, 2 steps). *Note:* This compound is fairly sensitive and should be used in the next step within a few days, and stored in a freezer. It is important to use a Celite plug after Step 1, as it has been found that fine solids can be carried through fritted or Kim-Wipe-plugged filters, which affects the next step and overall yield. It is also crucial to quench the reaction slowly in Step 2, as overheating causes a significant amount of decomposition.

TLC: R_f 0.40 (4:1 EtOAc/hexanes, UV & *p*-anisaldehyde).

$[\alpha]_D^{25.0}$**:** +31.4° (c = 0.63, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18 (d, *J* = 2.0 Hz, 1H), 6.94 (d, *J* = 10.0 Hz, 1H), 6.22 (d, *J* = 1.9 Hz, 1H), 6.20 (dd, *J* = 10.0, 1.6 Hz, 1H), 6.16 (dt, *J* = 2.8, 1.5 Hz, 1H), 4.49 (dd, *J* = 7.5, 3.1 Hz, 1H), 3.09 (qdd, *J* = 10.9, 9.0, 5.4 Hz, 2H), 2.85 (dddd, *J* = 17.6, 9.4, 4.4,

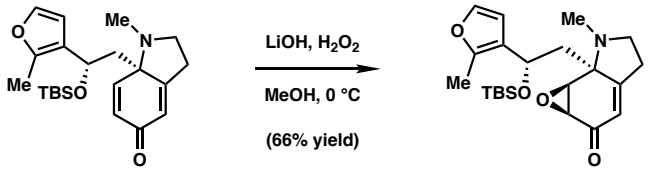
2.4 Hz, 1H), 2.69 (dddd, *J* = 17.4, 8.9, 6.4, 1.4 Hz, 1H), 2.31 (s, 3H), 2.15 (s, 3H), 2.13 (dd, *J* = 14.2, 7.5 Hz, 1H), 1.79 (dd, *J* = 14.2, 3.2 Hz, 1H), 0.79 (s, 9H), -0.04 (s, 3H), -0.31 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 186.7, 168.1, 147.6, 146.4, 140.6, 129.4, 123.5, 123.4, 109.5, 66.0, 63.3, 51.7, 42.5, 37.5, 28.3, 25.9, 18.1, 12.1, -4.5, -4.9.

FTIR (NaCl, thin film): 2953, 2856, 1669, 1645, 1472, 1256, 1076, 894, 836 cm^{-1}.

HRMS (ESI, *m/z*): $C_{22}H_{33}NO_3Si$, calc'd for $[M+H]^+$: 388.2302, found 388.2313.

Preparation of epoxide 158a.



157a 158a

Safety note: Large quantities of 50% H_2O_2 are utilized in this reaction and proper quenching protocols were used for safe practices. H_2O_2 was first transferred to a clean graduated cylinder with a glass pipette and was then further measured and transferred to the reaction using a plastic syringe (so as to avoid metal-catalyzed decomposition of H_2O_2 in the reagent bottle). Residual hydrogen peroxide in the cylinder and syringe was immediately diluted with H_2O and then quenched with excess sodium thiosulfate. Before disposal of the aqueous layers and concentration of the crude product, all extraction layers were checked for peroxides with test strips (MilliporeSigma EM1.10081.0001). With the described reaction quenching protocol, no remaining peroxides were found. However, in

the event of remaining peroxides, excess sodium thiosulfate was used to finalize quench of all aqueous layers before disposal.

Enone **157a** (11.0 g, 28.38 mmol) was taken up in MeOH (284 mL total, HPLC grade) in a 1 L round bottom flask containing a stir bar. It was cooled to 0 °C under ambient air. LiOH (1.36 g, 56.8 mmol, 2.0 equiv) was powdered with a mortar and pestle and added to the enone at 0 °C in one portion. Subsequently, H_2O_2 was added (3.22 mL, 56.8 mmol, 50% w/w in H_2O, 2.0 equiv) dropwise, and the reaction stirred at 0 °C. After one hour, powdered LiOH (680 mg, 28.38 mmol, 1.0 equiv) was added, followed by H_2O_2 (1.6 mL, 28.38 mmol, 50% w/w in H_2O, 1.0 equiv), and the reaction continued to stir at 0 °C. After a total of 2 h and 50 min the reaction was quenched at 0 °C by the addition of sodium thiosulfate (14 g, 56.8 mmol, 2.0 equiv) in 150 mL H_2O. EtOAc (200 mL) was added and the mixture stirred vigorously at 0 °C for 10 min. After warming to room temperature, the mixture was transferred to a 2 L separatory funnel, using H_2O (50 mL) to aid in the transfer of the resulting salts. Brine (150 mL) was added to aid in separation of the layers, and the organic layer was removed and set aside. The resulting aqueous layer was extracted with EtOAc (2 x 250 mL, then 3 x 200 mL). All organic layers were combined and subsequently washed with brine (200 mL) and the brine layer was back-extracted with EtOAc (1 x 100 mL). All combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give a red-brown solid. The residue was purified by silica gel flash chromatography (15–50% EtOAc/hexanes) to afford **158a** as a light brown-gold solid (7.52 g, 66% yield).

TLC: R_f 0.51 (1:1 hexanes/EtOAc, UV & *p*-anisaldehyde).

$[\alpha]_D^{25.0}$**:** –180.9° (c = 1.15, $CHCl_3$).

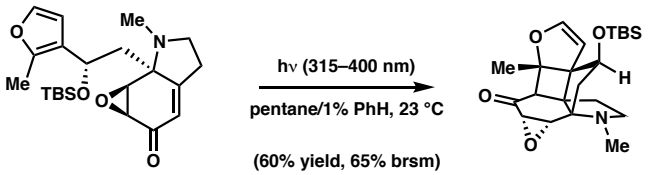
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21 (d, *J* = 2.0 Hz, 1H), 6.27 (d, *J* = 1.9 Hz, 1H), 5.78 (q, *J* = 1.9 Hz, 1H), 4.59 (t, *J* = 6.1 Hz, 1H), 3.69 (dd, *J* = 4.2, 0.6 Hz, 1H), 3.12 (dd, *J* = 4.2, 1.8 Hz, 1H), 3.07 (ddd, *J* = 10.1, 7.6, 4.7 Hz, 1H), 2.91 (ddd, *J* = 10.1, 9.0, 6.7 Hz, 1H), 2.75 – 2.58 (m, 2H), 2.53 (s, 3H), 2.16 (s, 3H), 2.04 (dd, *J* = 14.5, 6.5 Hz, 1H), 1.93 (dd, *J* = 14.5, 5.6 Hz, 1H), 0.80 (s, 9H), -0.01 (s, 3H), -0.24 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 194.7, 163.8, 147.2, 140.8, 122.9, 118.3, 109.5, 65.1, 63.6, 54.4, 53.1, 51.2, 41.1, 36.5, 28.6, 25.9, 18.1, 12.2, -4.4, -4.8.

FTIR (NaCl, thin film): 2954, 2857, 1680, 1472, 1255, 1057, 897, 836 cm^{-1}.

HRMS (ESI, *m/z*): $C_{22}H_{33}NO_4Si$, calc'd for $[M+H]^+$: 404.2252, found 404.2237.

Preparation of cyclobutane 159a.



158a 159a

Background information on setup: For scale-up purposes, this reaction was typically set up in triplicate batches. Any borosilicate round bottom flask can be used for this UVA chemistry, but longer reaction times were observed for heavy-walled glassware. Typically, thin Pyrex glassware gave the most rapid conversion. Glassware was cleaned in a base-bath for 7–12 h prior to use in order to remove any residue that could impact absorption of

light. A medium-pressure, 450W mercury lamp (Hanovia PC451050) with a Uranium glass filter was also successfully used for this transformation, which gave more rapid conversion. However, due to the emitted heat of this lamp, pentane was deemed an unsafe solvent and hexanes was used as an alternative with comparable overall yields, with somewhat decreased conversion due to heavier precipitate formation over the course of the reaction. Photoboxes made in-house were used that contained computer fans (Coolerguys Dual 80mm USB cooling fans, B002NVC1DS) for ventilation, assuring reaction temperatures remained at 23 °C.

Procedure: Three 2 L Pyrex round-bottom flasks (Corning, 70320-2L) containing a stir bar were flame-dried. Enone **158a** (400 mg, 0.991 mmol) was added to each, followed by PhH (10 mL). Once the solid was dissolved, pentane (HPLC grade) was added till the flasks were filled half way (approximately 1.1 L). The flasks were capped with plastic septa, sealed with electrical tape, and a vent needle was put in place. Large ice baths were placed in three photoboxes, where the three reactions were sparged with N_2 for 2 h at 0 °C (so as not to evaporate large portions of pentane). Once sparging was complete, the vent needles were removed and the resulting holes in the septa taped with electrical tape. Under N_2 flow, the flasks were warmed to room temperature (*Note:* It is important to allow sufficient time for the pentane to warm up so as not to cause over pressurization during irradiation). The flasks were subsequently irradiated with a Philipps UVA light (Philips 232934, 36W UVA-PL-L/4P lamp, 315–400nm; Honeywell curing system base was used – Honeywell UV100A1059) for 39.5 h at a distance between 13–16 cm, with periodic checking of

functional stirring and continuous N_2 flow. Once complete, the solvent was removed under reduced pressure, and the combined batches were purified by silica gel flash chromatography (equilibrated with 5% EtOAc/hexanes and utilized a gradient of 10–50% EtOAc/hexanes after loading) to afford **159a** as a beige solid (724 mg, 60% yield), along with recovered starting material (58 mg, 5% yield, 65% brsm).

TLC: R_f 0.50 (1:1 hexanes/EtOAc, UV & $KMnO_4$).

$[\alpha]_D^{25.0}$: –2.7° (c = 1.11, $CHCl_3$).

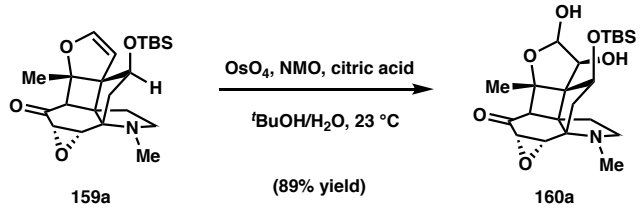
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.45 (d, *J* = 2.9 Hz, 1H), 4.65 (d, *J* = 2.9 Hz, 1H), 4.15 (dd, *J* = 10.7, 7.1 Hz, 1H), 3.60 (d, *J* = 4.1 Hz, 1H), 3.22 (dd, *J* = 4.1, 0.6 Hz, 1H), 3.18 (s, 1H), 2.94 (td, *J* = 8.4, 5.7 Hz, 1H), 2.62 (ddd, *J* = 8.7, 7.4, 5.7 Hz, 1H), 2.47 (s, 3H), 2.31 (dd, *J* = 13.5, 7.0 Hz, 1H), 2.21 (ddd, *J* = 13.0, 7.5, 5.7 Hz, 1H), 1.94 – 1.83 (m, 1H), 1.82 (dd, *J* = 13.5, 10.7 Hz, 1H), 1.42 (s, 3H), 0.84 (s, 9H), 0.02 (s, 3H), 0.00 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 203.8, 148.3, 102.5, 89.4, 75.4, 67.7, 67.2, 60.1, 58.8, 56.3, 55.5, 54.2, 39.8, 34.8, 32.0, 25.8, 19.4, 18.0, -4.6, -4.7.

FTIR (NaCl, thin film): 2955, 2856, 1701, 1608, 1472, 1252, 1139, 1119, 1032 cm^{-1}.

HRMS (ESI, *m/z*): $C_{22}H_{33}NO_4Si$, calc'd for $[M+H]^+$: 404.2252, found 404.2262.

Preparation of diol 160a.



159a 160a

Cyclobutane **159a** (452.5 mg, 1.12 mmol) and citric acid (471 mg, 2.24 mmol, 2.0 equiv) were added to a round bottom flask containing a stir bar. The solids were taken up in ^{t}BuOH/H_2O (1:1, 22.4 mL) and the mixture was sonicated until all solids had dissolved. At room temperature, under stirring, OsO_4 (1.40 mL, 0.11 mmol, 2.5 wt % in ^{t}BuOH, 0.10 equiv) was added dropwise, followed by NMO (144.5 mg, 1.23 mmol, 1.10 equiv) in three portions. The mixture was stirred at room temperature for 4 h, after which it was quenched by the addition of aqueous Na_2SO_4 (5 g in 30 mL H_2O, 20.1 mmol, 9.0 equiv) and saturated aqueous $NaHCO_3$ (25 mL). EtOAc (20 mL) was added and the mixture stirred vigorously for 5 min. The mixture was transferred to a separatory funnel and the layers separated. The aqueous layer was extracted with EtOAc (3 x 20 mL), and the combined organic layers were washed with brine (2 x 40 mL). The combined organic layers were then dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give a golden foam. The residue was purified via silica gel flash chromatography (1–4% MeOH/CH_2Cl_2) to afford **160a** as an off-white foam (438 mg, 89% yield). *Note:* The diol is isolated as an inconsequential mixture of diastereomers at the lactol position (see two TLC R_f below).

TLC: R_f 0.38 and 0.29 (2:1 EtOAc/hexanes, UV & *p*-anisaldehyde).

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25.0}}$**:** +51.4° (c = 0.69, $CHCl_3$).

Major diastereomer = ‡

Minor diastereomer = *

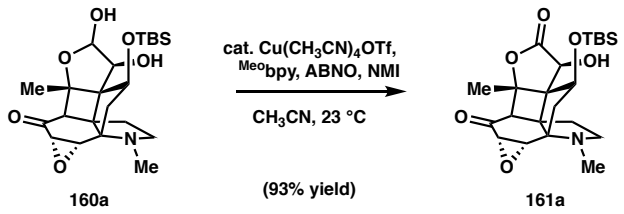
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.49 (s, 1H*), 5.27 (d, *J* = 7.4 Hz, 1H‡), 4.75 – 4.64 (m, 1H‡, 1H*), 4.27 (d, *J* = 7.0 Hz, 1H*), 4.16 (d, *J* = 10.9 Hz, 1H‡), 3.93 (dd, *J* = 6.3, 2.6 Hz, 1H‡), 3.75 (d, *J* = 7.1 Hz, 1H*), 3.62 (d, *J* = 4.3 Hz, 1H‡), 3.61 (d, *J* = 4.2 Hz, 1H*), 3.45 (d, *J* = 6.3 Hz, 1H‡), 3.34 (s, 1H*), 3.24 (dd, *J* = 4.3, 0.5 Hz, 1H‡), 3.21 (dd, *J* = 4.2, 0.6 Hz, 1H*), 3.07 (br, 1H*), 3.03 – 2.88 (m, 1H‡, 1H*), 2.90 (s, 1H‡), 2.87 – 2.74 (m, 1H‡, 1H*), 2.49 (s, 3H‡, 3H*), 2.41 – 2.32 (m, 1H‡, 1H*), 2.08 – 1.97 (m, 1H‡), 1.90 (dddd, *J* = 19.3, 13.9, 8.6, 5.2 Hz, 1H‡, 1H*), 1.79 – 1.62 (m, 1H‡, 1H*), 1.43 (s, 3H‡, 3H*), 0.87 (s, 9H‡), 0.86 (s, 9H*), 0.14 (s, 3H‡), 0.13 (s, 3H*), 0.12 (s, 3H‡), 0.11 (s, 3H*).

^{13}C NMR (101 MHz, $CDCl_3$): δ 204.1*, 203.3, 106.1*, 98.1‡, 88.4‡, 84.4‡, 80.3*, 75.6*, 75.5, 74.6, 68.7‡, 68.4‡, 63.7‡, 61.8‡, 58.7*, 58.3, 56.9*, 55.0, 54.9, 54.2*, 54.0, 51.4‡, 50.3‡, 38.0*, 38.0, 34.7*, 34.5, 32.0*, 30.4, 25.7*, 25.7, 21.6‡, 17.8, -3.5*, -3.6, -5.2‡.

FTIR (NaCl, thin film): 3468, 2933, 2858, 1700, 1447, 1255, 1172, 1082, 838 cm^{-1}.

HRMS (ESI, *m/z*): $C_{22}H_{35}NO_6Si$, calc'd for $[M+H]^+$: 438.2306, found 438.2293.

Preparation of α-hydroxyketone 161a.



Diol **160a** (418 mg, 0.955 mmol) was taken up in CH_3CN (11.9 mL, HPLC grade) in a round bottom flask containing a stir bar. $Cu(CH_3CN)_4OTf$ (36 mg, 0.0955 mmol, 0.10

equiv), ^{MeO}bpy (20.7 mg, 0.0955, 0.10 equiv), ABNO (2.7 mg, 0.0191 mmol, 0.02 equiv), and NMI (15.2 µl, 0.191 mmol, 0.20 equiv) were added in that order, and the orange-brown mixture was stirred vigorously (800–900 rpm) at room temperature under air for 4 h. The reaction was then filtered through a plug of silica gel (1.5 x 3 cm) with EtOAc (40 mL), and complete elution was confirmed by TLC analysis. The pale gold foam was then purified via silica gel flash chromatography (10–80% EtOAc/hexanes) to afford **161a** as a white foam (388 mg, 93% yield).

TLC: R_f 0.36 (2:1 EtOAc/hexanes, UV, $KMnO_4$, and CAM).

$[\alpha]_D^{25.0}$: +15.1° (c = 1.25, $CHCl_3$).

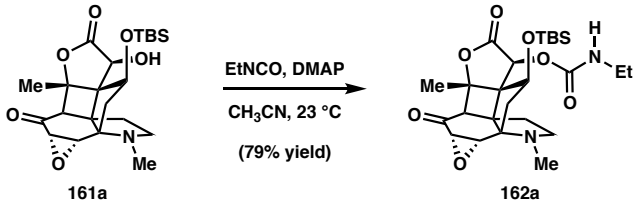
^{1}H NMR (400 MHz, $CDCl_3$): δ 4.67 (dd, *J* = 10.8, 6.9 Hz, 1H), 4.27 (d, *J* = 3.9 Hz, 1H), 3.66 (d, *J* = 4.4 Hz, 1H), 3.36 (d, *J* = 5.9 Hz, 1H), 3.32 (d, *J* = 4.4 Hz, 1H), 2.96 (td, *J* = 8.9, 5.4 Hz, 1H), 2.91 (s, 1H), 2.84 (ddd, *J* = 9.0, 7.7, 5.7 Hz, 1H), 2.47 (s, 3H), 2.42 (dd, *J* = 13.4, 6.9 Hz, 1H), 2.10 – 1.92 (m, 2H), 1.61 (s, 3H), 1.59 – 1.53 (m, 1H), 0.84 (s, 9H), 0.09 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 203.0, 174.9, 90.2, 74.4, 72.2, 69.4, 58.8, 58.5, 55.4, 54.5, 53.9, 53.5, 38.6, 34.3, 30.3, 25.7, 20.9, 17.8, -4.0, -5.1.

FTIR (NaCl, thin film): 3460, 2954, 2857, 1772, 1707, 1472, 1255, 1107, 838 cm^{-1}.

HRMS (ESI, *m/z*): $C_{22}H_{33}NO_6Si$, calc'd for $[M+H]^+$: 436.2150, found 436.2145.

Preparation of carbamate 162a.



α-Hydroxyketone **161a** (275 mg, 0.63 mmol) and DMAP (77.1 mg, 0.63 mmol, 1.0 equiv) were added to a flame-dried scintillation vial containing a stir bar. The solids were placed under an atmosphere of nitrogen and taken up in CH_3CN (3.2 mL). At room temperature, EtNCO (0.11 mL, 1.39 mmol, 2.20 equiv) was then added dropwise, and the mixture was stirred for 24 h. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (25 mL); EtOAc (5 mL) was added and the mixture vigorously stirred. The mixture was transferred to a separatory funnel and the aqueous layer extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with brine (1 x 20 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give an orange oil. The crude residue was purified via Florisil flash chromatography (10–70% EtOAc/hexanes) to afford carbamate **162a** as a white foam (252 mg, 79% yield).

TLC: R_f 0.26 (1:1 hexanes/EtOAc, UV, $KMnO_4$, and CAM).

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25.0}}$**:** +9.6° (c = 0.73, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.54 (s, 1H), 4.76 (t, *J* = 5.8 Hz, 1H), 4.40 (dd, *J* = 9.9, 6.9 Hz, 1H), 3.64 (d, *J* = 4.3 Hz, 1H), 3.33 (d, *J* = 4.3 Hz, 1H), 3.26 (qd, *J* = 7.3, 5.8 Hz, 2H), 2.98 (td, *J* = 8.6, 4.5 Hz, 1H), 2.92 (s, 1H), 2.88 (dt, *J* = 9.0, 7.2 Hz, 1H), 2.45 (s, 3H),

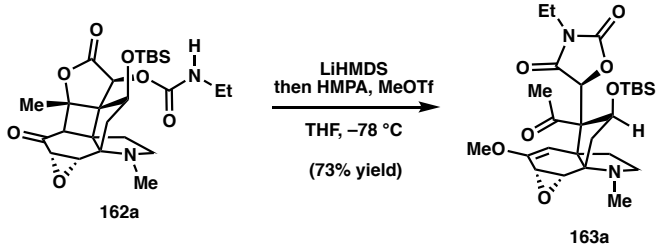
2.40 (dd, J = 13.7, 6.9 Hz, 1H), 2.19 – 2.02 (m, 2H), 1.59 (s, 3H), 1.64 – 1.53 (m, 1H), 1.16 (t, J = 7.3 Hz, 3H), 0.85 (s, 9H), 0.04 (s, 3H), 0.02 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 202.8, 172.4, 155.1, 90.5, 74.0, 71.5, 69.1, 59.5, 59.0, 56.0, 54.8, 54.2, 53.7, 39.8, 36.5, 34.6, 30.9, 25.8, 21.0, 18.0, 15.1, -3.9, -5.2.

FTIR (NaCl, thin film): 3368, 2933, 2857, 1782, 1716, 1516, 1250, 1107, 839 cm^{-1}.

HRMS (ESI, *m/z*): $C_{25}H_{38}N_2O_7Si$, calc'd for $[M+H]^+$: 507.2521, found 507.2516.

Preparation of oxazolidinedione 163a.



162a 163a

Carbamate **162a** (115.8 mg, 0.229 mmol) was added to a flame-dried 15 mL round bottom flask and placed under nitrogen atmosphere. THF (2.9 mL) was added, and the mixture cooled to –78 °C. LiHMDS (0.32 mL, 0.32 mmol, 1 M in THF, 1.4 equiv) was added dropwise to give a bright yellow solution, which was stirred for 45 min at –78 °C. In the meantime, a 2 M stock solution of HMPA in THF was prepared under N_2. After the 45 min, HMPA (0.57 mL, 1.14 mmol, 2M, 5.0 equiv) was added dropwise, giving a darker yellow/orange solution, followed by MeOTf (75 mL, 0.686 mmol, 3.0 equiv), upon which the reaction color disappeared. This mixture was further stirred at –78 °C for 2 h, and LC/MS analysis indicated complete conversion of **162a**. The reaction was then quenched by the dropwise addition of 2,6-lutidine (0.1 mL, 3.76 mmol, 3.8 equiv), followed by pH

7 buffer (5 mL). The mixture was vigorously stirred and warmed to room temperature, during which time EtOAc (5 mL) was added. The mixture was transferred to a separatory funnel and the reaction flask rinsed with pH 7 buffer (5 mL) and EtOAc (2 mL). The layers were separated and the aqueous layer extracted with EtOAc (5 x 10 mL). The combined organic layers were washed with brine (1 x 10 mL) and the brine layer was back-extracted with EtOAc (1 x 5 mL). All combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give a yellow oil. The residue was purified by silica gel flash chromatography (5–50% EtOAc/hexanes) to afford **163a** as a white foam (87 mg, 73% yield).

TLC: R_f 0.57 (2:1 EtOAc/hexanes, UV & DNP).

$[\alpha]_D^{25.0}$: –73.1° (c = 0.49, $CHCl_3$).

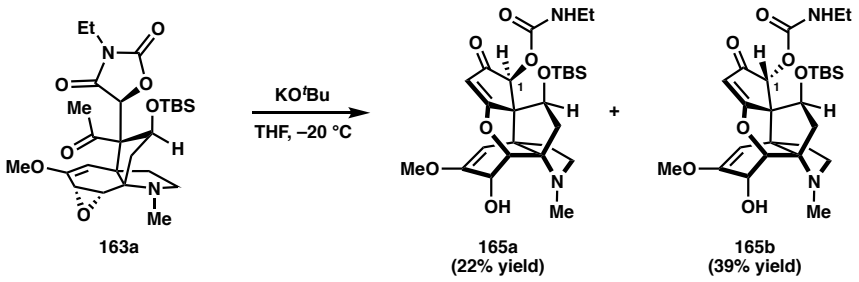
^{1}H NMR (400 MHz, $CDCl_3$): δ 4.89 (s, 1H), 4.84 (s, 1H), 4.69 (s, 1H), 3.63 (qd, *J* = 7.2, 1.7 Hz, 2H), 3.49 (s, 3H), 3.46 (d, *J* = 4.2 Hz, 1H), 3.25 (dd, *J* = 4.2, 2.2 Hz, 1H), 2.90 (td, *J* = 9.3, 6.4 Hz, 1H), 2.70 (t, *J* = 7.9 Hz, 1H), 2.64 (s, 3H), 2.46 – 2.26 (m, 2H), 2.20 (s, 3H), 2.17 – 2.08 (m, 1H), 1.96 – 1.81 (m, 1H), 1.32 (t, *J* = 7.2 Hz, 3H), 0.87 (s, 9H), 0.15 (s, 3H), 0.11 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 205.8, 173.0, 155.5, 151.2, 102.5, 82.6, 77.3 (HSQC), 74.0, 68.3, 57.8, 56.2, 55.1, 52.1, 49.3, 43.2, 37.8, 35.3, 35.1, 32.4, 25.9, 17.9, 12.5, -4.4, -5.0.

FTIR (NaCl, thin film): 2950, 2857, 1808, 1734, 1698, 1448, 1220, 1120, 840 cm^{-1}.

HRMS (ESI, *m/z*): $C_{26}H_{40}N_2O_7Si$, calc'd for $[M+H]^+$: 521.2678, found 521.2664.

Preparation of spirocycles 165a and 165b.



Ketone **163a** (40 mg, 0.077 mmol) was added to a flame-dried round bottom flask and placed under nitrogen atmosphere. The solid was taken up in THF (3.8 mL) and cooled to –20 °C. KO′Bu (0.38 mL, 0.38 mmol, 1 M in THF, 5.0 equiv) was then added dropwise, resulting in a bright yellow solution. The mixture was stirred 40 min at –20 °C, after which it was quenched with pH 7 buffer (6 mL), 10% IPA/CH_2Cl_2 (6 mL) was added, and the mixture warmed to room temperature. The aqueous layer was extracted with 10% IPA/CH_2Cl_2 (8 x 10 mL). The combined organic layers were washed with brine (1 x 20 mL), and the brine layer back-extracted with 10% IPA/CH_2Cl_2 (1 x 5 mL). All combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give a white solid. The residue was purified by preparative reverse phase HPLC (60–75% H_2O/CH_3CN over 10 minutes, t_R(**165b**) = 7.2–7.9 min, t_R(**165a**) = 8.5–9.0 min), affording epimers **165a** (8.6 mg, 22% yield, 56% pure, contains unidentified side product of equal MW; the yield is adjusted accordingly to 12%) and **165b** (15.5 mg, 39% yield) as white solids. Epimer **165a** was repurified for characterization via preparatory reverse phase HPLC (0.1% AcOH aqueous modifier, gradient 30–40% H_2O/CH_3CN over 10 minutes, t_R(**165a**) = 10.5–11.5 min).

Desired epimer **165a**:

TLC: R_f 0.48 (1:1 acetone/hexanes, UV & CAM).

$[\alpha]_D^{25.0}$**:** +223.5° (c = 0.10, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.58 (s, 1H), 5.37 (s, 1H), 4.81 (d, *J* = 2.1 Hz, 1H), 4.78 (dd, *J* = 4.8, 2.1 Hz, 1H), 4.67 (t, *J* = 5.7 Hz, 1H), 4.19 – 4.09 (m, 2H), 3.83 (br, 1H), 3.58 (s, 3H), 3.29 (qd, *J* = 7.2, 5.7 Hz, 2H), 3.18 (ddd, *J* = 10.0, 8.7, 2.1 Hz, 1H), 2.55 (dd, *J* = 14.3, 9.2 Hz, 1H), 2.44 (q, *J* = 9.3 Hz, 1H), 2.30 (s, 3H), 1.89 (ddd, *J* = 13.8, 9.0, 2.2 Hz, 1H), 1.76 (dt, *J* = 13.8, 9.0 Hz, 1H), 1.32 (dd, *J* = 14.4, 9.8 Hz, 1H), 1.19 (t, *J* = 7.3 Hz, 3H), 0.81 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 199.0, 182.1, 156.1, 155.4, 115.8, 102.9, 80.5, 74.3, 73.7, 70.8, 69.2, 68.6, 55.3, 54.4, 53.4, 37.5, 36.4, 36.0, 32.6, 25.7, 17.9, 15.2, -3.9, -4.8.

FTIR (NaCl, thin film): 3392, 2933, 2859, 1716, 1604, 1515, 1248, 1138, 838 cm^{-1}.

HRMS (ESI, *m/z*): $C_{26}H_{40}N_2O_7Si$, calc'd for $[M+H]^+$: 521.2678, found 521.2683.

Major epimer **165b**:

TLC: R_f 0.61 (1:1 acetone/hexanes, UV & CAM).

$[\alpha]_D^{25.0}$**:** +125.1° (c = 0.78, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.40 (s, 1H), 5.22 (s, 1H), 5.10 (s, 1H), 4.79 (t, *J* = 5.8 Hz, 1H), 4.72 (d, *J* = 3.3 Hz, 1H), 4.59 (s, 1H), 4.35 (dd, *J* = 9.8, 5.2 Hz, 1H), 4.00 (d, *J* = 3.3 Hz, 1H), 3.57 (s, 3H), 3.36 – 3.14 (m, 3H), 2.54 (td, *J* = 10.6, 3.9 Hz, 1H), 2.47 (dd, *J* = 14.3, 9.9 Hz, 1H), 2.35 (s, 3H), 1.94 (ddd, *J* = 13.7, 10.9, 7.4 Hz, 1H), 1.84 (ddd, *J* = 13.3,

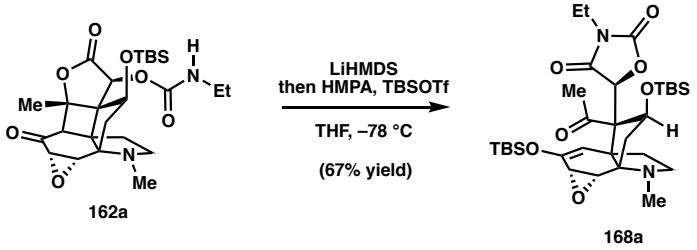
8.6, 3.8 Hz, 1H), 1.34 (dd, J = 14.3, 5.2 Hz, 1H), 1.16 (t, J = 7.3 Hz, 3H), 0.81 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 198.5, 183.1, 155.7, 155.3, 107.6, 96.4, 83.8, 71.7, 69.7, 68.5, 68.4, 64.5, 55.4, 53.0, 50.1, 37.2, 36.4, 33.8, 31.9, 25.6, 17.8, 15.2, -4.0, -5.0.

FTIR (NaCl, thin film): 3363, 2931, 2856, 1713, 1605, 1514, 1249, 1138, 839 cm^{-1}.

HRMS (ESI, *m/z*): $C_{26}H_{40}N_2O_7Si$, calc'd for $[M+H]^+$: 521.2678, found 521.2667.

Preparation of oxazolidinedione 168a.

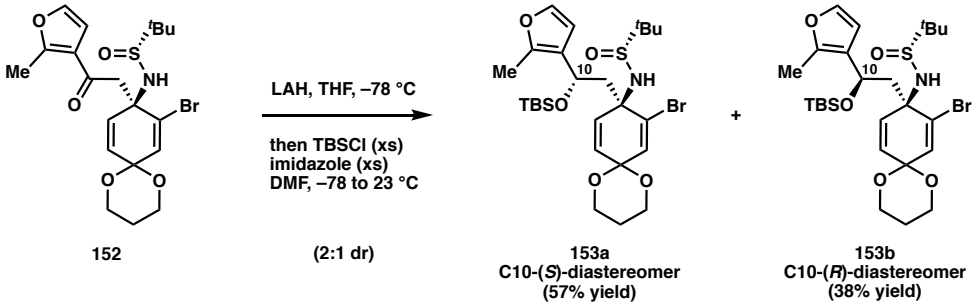


Carbamate **162a** (30 mg, 0.059 mmol) was added to a flame-dried 2 dram vial and placed under nitrogen atmosphere. THF (0.66 mL) was added, and the mixture cooled to –78 °C. LiHMDS (83 μL, 0.083 mmol, 1 M in THF, 1.4 equiv) was added dropwise to give a bright yellow solution, which was stirred for 40 min at –78 °C. HMPA (50 μL, 0.296 mmol, 5.0 equiv) was added, followed by TBSOTf (20 μL, 0.089 mmol, 1.5 equiv). This mixture was further stirred at –78 °C for 2 h, and was then quenched by the addition of two drops of 2,6-lutidine, followed by pH 7 buffer (3 mL). The mixture was vigorously stirred and warmed to room temperature. The layers were separated and the aqueous layer extracted with EtOAc (5 x 2 mL). The combined organic layers were washed with brine (1 x 4 mL) and the brine layer was back-extracted with EtOAc (1 x 2 mL). All combined organic layers

were dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (5–60% EtOAc/hexanes) to afford **168a** (24.3 mg, 67% yield).

^{1}H NMR (600 MHz, $CDCl_3$): δ 5.07 (s, 1H), 4.86 (s, 1H), 4.68 (s, 1H), 3.71 – 3.52 (m, 2H), 3.42 (d, *J* = 4.1 Hz, 1H), 3.14 (dd, *J* = 4.1, 2.0 Hz, 1H), 2.90 (q, *J* = 8.2 Hz, 1H), 2.75 – 2.60 (m, 1H), 2.64 (s, 3H), 2.43 – 2.32 (m, 1H), 2.31 – 2.22 (m, 1H), 2.24 (s, 3H), 2.15 (t, *J* = 11.6 Hz, 1H), 1.96 – 1.76 (m, 1H), 1.31 (t, *J* = 7.2 Hz, 3H), 0.92 (s, 9H), 0.87 (s, 9H), 0.17 (s, 3H), 0.15 (s, 3H), 0.13 (s, 3H), 0.11 (s, 3H).

Preparation of diastereomeric ethers 153a and 153b.



Ketone **152** (6.15 g, 13.02 mmol) was taken up in THF (65 mL) in a flame-dried flask under N_2 atmosphere. To a separate, flame-dried 1 L flask LAH (1.24 g, 32.55 mmol, 2.5 equiv) was added and placed under N_2. The LAH was slowly suspended in THF (65 mL) at –78 °C, while the bubbling was carefully monitored. After a few minutes, the THF solution of ketone **152** was added via cannula down the wall of the 1 L flask at –78 °C. Care was taken during the vigorous bubbling. The flask with ketone **152** was rinsed with THF (5 mL) and the solution transferred to the reaction flask as well. In a separate, flame-

dried flask under N_2 a solution of TBSCl (29.43 g, 195.3 mmol, 15.0 equiv) and imidazole (17.99 g, 260.4 mmol, 20.0 equiv) was prepared in DMF (130 mL). After 3 h, the TBSCl/imidazole solution was slowly added to the 1 L flask at –78 °C via cannula. Again, vigorous bubbling was observed. The reaction mixture was warmed to room temperature and stirred overnight (15–18 h). Subsequently, TBSCl (5.89 g, 39.06 mmol, 3.0 equiv) and imidazole (5.40 g, 78.10 mmol, 6.0 equiv) were added as a solution DMF (26 mL), and the reaction stirred for another 3 h at room temperature, giving full consumption of the alkoxide. Brine (400 mL) was added to a 1 L Erlenmeyer flask and cooled to 0 °C. The reaction mixture was slowly added to the brine, and EtOAc (30 mL) was used to complete the transfer. After diluting the quenched mixture with more EtOAc (100 mL), it was warmed to room temperature, and filtered through a large pad of Celite (80 g). The Celite was washed with EtOAc (300 mL) to ensure elution. The mixture was then transferred to a separatory funnel, the layers separated, and the aqueous layer was then extracted with EtOAc (3 x 250 mL). The combined organic layers were washed with brine (4 x 400 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was first purified by a large silica gel plug (20–40% EtOAc/hexanes) to rid of most silanol, yielding 7.35 g of a fluffy white solid. This solid was repurified by silica gel flash chromatography (20–40% EtOAc/hexanes) to afford **153a** (C10-(*S*)-diastereomer, 4.35 g, 57%) and **153b** (C10-(*R*)-diastereomer, 2.89 g, 38% yield).

153a (C10-(*S*)-diastereomer): See page 80.

153b (C10-(*R*)-diastereomer):

TLC: R_f 0.45 (4:1 EtOAc/hexanes, UV & $KMnO_4$).

$[\alpha]_D^{25}$: –56.7° (c = 1.77, $CHCl_3$).

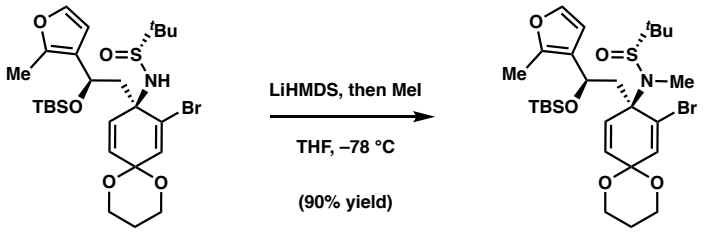
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18 (d, *J* = 2.0 Hz, 1H), 6.66 (d, *J* = 2.3 Hz, 1H), 6.52 (dd, *J* = 10.3, 2.3 Hz, 1H), 6.35 (d, *J* = 10.3 Hz, 1H), 6.30 (d, *J* = 1.9 Hz, 1H), 4.60 (dd, *J* = 8.0, 3.4 Hz, 1H), 4.17 – 3.90 (m, 4H), 2.31 (dd, *J* = 14.2, 7.9 Hz, 1H), 2.21 (s, 3H), 2.01 (dd, *J* = 14.2, 3.5 Hz, 1H), 1.88 (dddd, *J* = 12.4, 8.0, 4.4, 3.4 Hz, 1H), 1.82 – 1.68 (m, 1H), 1.21 (s, 9H), 0.80 (s, 9H), 0.03 (s, 3H), -0.21 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 147.0, 140.4, 133.7, 132.8, 131.9, 124.5, 123.2, 109.9, 92.0, 64.5, 60.8, 60.4, 60.0, 56.5, 50.4, 26.1, 25.2, 23.0, 18.2, 12.1, -4.5, -4.5.

FTIR (NaCl, thin film): 3277, 3191, 2956, 2857, 2231, 1676, 1517, 1405, 1246, 1140, 986 cm^{-1}.

HRMS (MM, *m/z*): $C_{26}H_{42}BrNO_5SSi$, calc'd for $[M+H]^+$ 588.1809, found 588.1776.

Preparation of methylated sulfinamide 154b.



153b 154b

Sulfinamide **153b** (4.0 g, 6.80 mmol) was added to a flame-dried flask containing a stir bar, and was dissolved in THF (68 mL) under N_2. It was cooled to –78 °C, and LiHMDS (9.51 ml, 9.51 mmol, 1 M in THF, 1.40 equiv) was subsequently added dropwise.

The mixture was stirred for 35 min at –78 °C, after which MeI (1.70 ml, 27.18 mmol, 4.0 equiv) was added dropwise. After stirring for 5 min at –78 °C, the mixture was warmed to room temperature and stirred for 1 h. The reaction was quenched with saturated aqueous NH_4Cl (100 mL) and extracted with EtOAc (5 x 40 mL). The combined organic layers were washed brine (2 x 40 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified via silica flash chromatography (20–100% EtOAc/hexanes) to afford **154b** (3.70 g, 90% yield) as a fluffy solid.

TLC: R_f 0.37 (1:1 hexanes/EtOAc, UV & *p*-anisaldehyde).

$[\alpha]_D^{25}$: –1.23° (c = 0.74, $CHCl_3$).

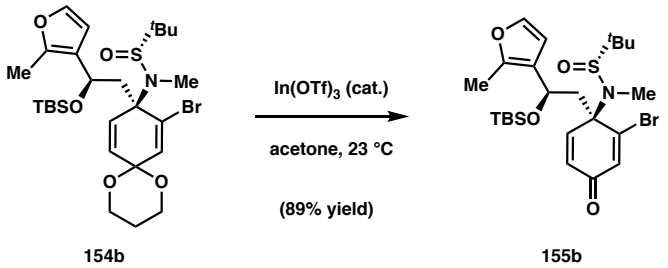
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.17 (d, *J* = 2.0 Hz, 1H), 6.90 (d, *J* = 2.3 Hz, 1H), 6.32 (dd, *J* = 10.2, 2.3 Hz, 1H), 6.28 (d, *J* = 1.9 Hz, 1H), 5.83 (d, *J* = 10.1 Hz, 1H), 4.32 (t, *J* = 4.6 Hz, 1H), 4.07 – 3.91 (m, 4H), 2.85 (dd, *J* = 13.7, 4.2 Hz, 1H), 2.36 (s, 3H), 2.20 (s, 3H), 2.13 – 2.01 (m, 1H), 1.95 – 1.82 (m, 1H), 1.82 – 1.72 (m, 1H), 1.21 (s, 9H), 0.79 (s, 9H), -0.06 (s, 3H), -0.31 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 147.0, 140.2, 133.3, 132.3, 131.6, 126.9, 123.5, 110.1, 91.9, 66.6, 63.9, 60.9, 60.2, 59.0, 48.0, 26.0, 25.9, 25.2, 24.4, 18.1, 12.0, -4.4, -5.0.

FTIR (NaCl, thin film): 2954, 2857, 1674, 1630, 1471, 1393, 1218, 1046, 914, 860 cm^{-1}.

HRMS (MM, *m/z*): $C_{27}H_{44}BrNO_5SSi$, calc'd for $[M+H]^+$ 602.1.1966, found 602.1923.

Preparation of enone 155b.



Ketal **154b** (3.7 g, 6.14 mmol) was taken up in acetone (61 mL, certified ACS grade) under air. $In(OTf)_3$ (173 mg, 0.31 mmol, 5 mol %) was weighed out, removed from the glovebox, and was added to the ketal solution at room temperature in one portion. The solution immediately turned from pale yellow to orange. The mixture was stirred for 30 min at room temperature, after which it was quenched with saturated aqueous $NaHCO_3$ (100 mL). The aqueous layer was extracted with EtOAc (5 x 40 mL), and the combined organic layers were washed brine (2 x 40 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give an off-white, sticky solid. The residue was purified via silica flash chromatography (30–70% EtOAc/hexanes and 80% EtOAc/hexanes to flush) to afford ketone **155b** (2.98 g, 89% yield).

TLC: R_f 0.39 (1:1 hexanes/EtOAc, UV & *p*-anisaldehyde).

$[\alpha]_D^{25}$: +28.4° (c = 0.79, $CHCl_3$).

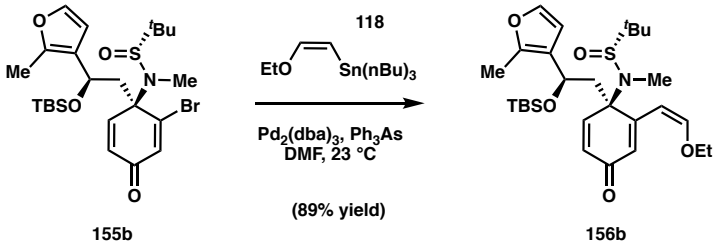
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20 (d, *J* = 2.0 Hz, 1H), 6.90 (d, *J* = 10.0 Hz, 1H), 6.83 (d, *J* = 1.8 Hz, 1H), 6.35 (dd, *J* = 10.0, 1.8 Hz, 1H), 6.25 (d, *J* = 2.0 Hz, 1H), 4.40 (dd, *J* = 7.3, 3.9 Hz, 1H), 2.85 (dd, *J* = 13.7, 3.9 Hz, 1H), 2.40 (s, 3H), 2.25 (dd, *J* = 13.6, 7.3 Hz, 1H), 2.17 (s, 3H), 1.24 (s, 9H), 0.79 (s, 9H), -0.15 (s, 3H), -0.33 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 183.5, 151.0, 150.2, 146.9, 140.7, 136.5, 128.5, 122.8, 109.6, 67.4, 63.9, 59.5, 47.5, 26.2, 25.9, 24.3, 18.1, 12.2, -4.4, -4.9.

FTIR (NaCl, thin film): 2953, 2856, 1634, 1515, 1411, 1361, 1256, 1138, 952 cm^{-1}.

HRMS (MM, *m/z*): $C_{24}H_{38}BrNO_4SSi$, calc'd for $[M+H]^+$ 544.1547, found 544.1477.

Preparation of vinyl ether 156b.



Triphenylarsine (335 mg, 1.09 mmol, 20 mol %) was added to a flame-dried flask with a stir bar, which, along with the vinyl bromide **155b** (2.98 g, 5.47 mmol) in a separate flask, was brought into a nitrogen-filled glovebox. **155b** was taken up in DMF (10 mL) and allowed to dissolve. $Pd_2(dba)_3$ (251 mg, 0.27 mmol, 5 mol %) was then added to the reaction flask containing the ligand, and taken up in DMF (1 mL). The solution of **155b** was subsequently added to the reaction flask containing the ligand and catalyst, and DMF (1 mL) was used to complete the transfer. The reaction was brought out of the glovebox and was sparged with N_2 for 5 min, after which stannane **118** (2.75 ml, 8.21 mmol, 1.5 equiv) was added, and the mixture was sparged with N_2 for another 5 min. The mixture was stirred for 2.75 h at room temperature, after which the reaction was quenched with brine (40 mL) and diluted with EtOAc (20 mL). The aqueous layer was extracted with EtOAc (5 x 20 mL), and the combined organic layers washed with brine (4 x 40 mL). The

combined brine layers were back-extracted EtOAc (2 x 50 mL) and the combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified via silica flash chromatography (10–70% EtOAc/hexanes) to afford vinyl ether **156b** (2.60 g, 89% yield).

$[\alpha]_D^{25}$: –73.7° (c = 1.10, $CHCl_3$).

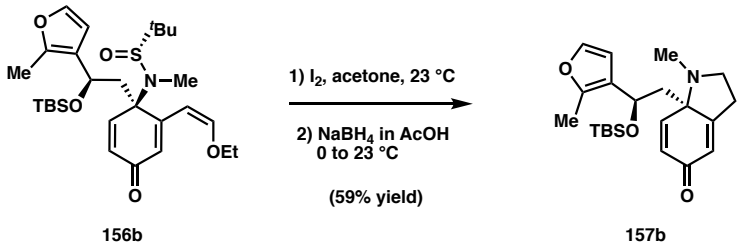
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.13 (d, *J* = 1.9 Hz, 1H), 7.09 (d, *J* = 2.0 Hz, 1H), 6.62 (d, *J* = 10.0 Hz, 1H), 6.39 (d, *J* = 7.1 Hz, 1H), 6.32 (dd, *J* = 10.0, 2.0 Hz, 1H), 6.21 (d, *J* = 2.0 Hz, 1H), 4.87 (d, *J* = 7.2 Hz, 1H), 4.28 (t, *J* = 5.1 Hz, 1H), 4.03 – 3.87 (m, 2H), 2.61 (dd, *J* = 13.4, 4.6 Hz, 1H), 2.37 (s, 3H), 2.23 (dd, *J* = 13.4, 5.6 Hz, 1H), 2.04 (s, 3H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.24 (s, 9H), 0.77 (s, 9H), -0.13 (s, 3H), -0.34 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 186.9, 154.3, 153.3, 150.0, 146.8, 140.3, 129.8, 128.8, 123.4, 109.7, 99.2, 70.7, 65.2, 63.8, 59.2, 47.9, 26.6, 25.9, 24.6, 18.0, 15.5, 12.0, -4.4, -4.9.

FTIR (NaCl, thin film): 2954, 2895, 2238, 1661, 1575, 1463, 1385, 1217, 1064 cm^{-1}.

HRMS (MM, *m/z*): $C_{28}H_{45}NO_5SSi$, calc'd for $[M+H]^+$ 536.2860, found 536.2839.

Preparation of pyrrolidine 157b.



156b 157b

Vinyl ether **156b** (2.60 g, 4.85 mmol) was taken up in acetone (100 mL, ACS certified grade), cooled to 0 °C, and sparged with N_2 for 20 min. It was then warmed to room temperature, under N_2, after which iodine (1.29 g, 5.10 mmol, 1.05 equiv) was added. After 35 min, the reaction was quenched with sodium sulfite (10 g) and saturated aqueous $NaHCO_3$ (80 mL). The mixture was diluted with EtOAc (100 mL), and the aqueous layers extracted with EtOAc (5 x 50 mL). The combined organic layers were then washed with brine (2 x 150 mL) and the brine layers back-extracted EtOAc (3 x 150 mL). The combined organic layers were then dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give a dark-orange oil. It was dried under high vacuum for 1 h, after which the residue was taken up in MeOH (100 mL, HPLC grade) and cooled to 0 °C. $NaBH_4$ (367 mg, 9.70 mmol, 2.0 equiv) was added to an Erlenmeyer flask, cooled to 0 °C, and AcOH (32.4 mL) was added. While carefully watching the bubbling, the mixture was only briefly swirled in the ice bath so as not to freeze the AcOH. As soon as the reductant was dissolved, the solution was added to the reaction mixture at 0 °C at a fast dropping rate over 10 min. The reaction mixture was warmed to room temperature and stirred for 1.5 h. Another 2.0 equiv of $NaBH_4$ (367 mg, 9.70 mmol) in AcOH (32.4 mL) was prepared and added at room temperature. After another 2 h, another 1.0 equiv of $NaBH_4$ (183.5 mg, 4.85 mmol) in

AcOH (16.2 mL) was added. After a total reaction time of 5 h, the mixture was quenched: aqueous 50% w/w KOH (200 mL) was cooled to 0 °C, to which the cold reaction mixture was added via pipette, gradually moving to a slow pour. Upon completion of addition, EtOAc (100 mL) was added immediately and the reaction flask rinsed with EtOAc (20 mL). After a few minutes of stirring, the mixture was warmed to room temperature. The aqueous layer was extracted with EtOAc (3 x 80 mL and 2 x 50 mL) and the combined organic layers washed with brine (3 x 150 mL). The combined brine layers were back-extracted with EtOAc (2 x 100 mL) and the total combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give a red oil. The residue was purified via silica flash chromatography (30–80% EtOAc/hexanes and 100% EtOAc to flush) to afford pyrrolidine **157b** (1.10 g, 59% yield).

TLC: R_f 0.27 (4:1 EtOAc/hexanes, UV & *p*-anisaldehyde).

$[\alpha]_D^{25}$: +39.2° (c = 0.32, $CHCl_3$).

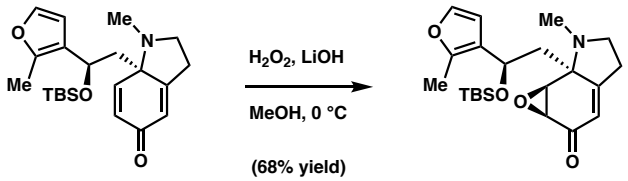
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19 (d, *J* = 2.0 Hz, 1H), 6.89 (d, *J* = 10.0 Hz, 1H), 6.29 – 6.22 (m, 2H), 5.98 (dd, *J* = 2.5, 1.4 Hz, 1H), 4.31 (t, *J* = 5.9 Hz, 1H), 3.07 (ddd, *J* = 10.7, 8.9, 3.9 Hz, 1H), 2.96 (td, *J* = 10.3, 6.4 Hz, 1H), 2.51 (dddd, *J* = 16.7, 9.0, 6.3, 1.4 Hz, 1H), 2.46 – 2.36 (m, 1H), 2.35 (s, 3H), 2.12 (d, *J* = 5.9 Hz, 2H), 2.10 (s, 3H), 0.80 (s, 9H), -0.06 (s, 3H), -0.25 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 186.5, 167.2, 147.6, 146.9, 140.7, 130.0, 123.1, 109.4, 64.9, 63.3, 51.7, 40.8, 36.7, 27.9, 25.9, 18.1, 12.3, -4.5, -4.9.

FTIR (NaCl, thin film): 2927, 2854, 1667, 1644, 1463, 1254, 1138, 1054, 916 cm^{-1}.

HRMS (MM, *m/z*): $C_{22}H_{33}NO_3Si$, calc'd for $[M+H]^+$ 388.2302, found 388.2511.

Preparation of epoxide 158b.



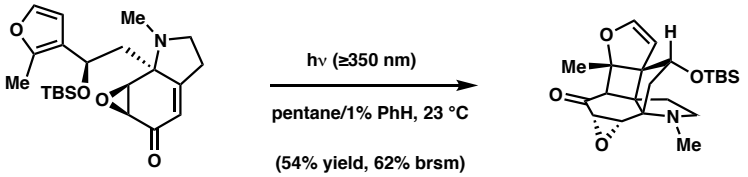
157b 158b

Pyrrolidine **157b** (1.1 g, 2.84 mmol) was taken up in MeOH (28 mL, HPLC grade) and cooled to 0 °C. LiOH (136 mg, 5.68 mmol, 2.0 equiv) was powdered with a mortar and pestle, and was subsequently added to the solution of **157b**, followed by H_2O_2 (0.322 ml, 5.68 mmol, 50 wt % in H_2O, 2.0 equiv). After stirring for 1.5 h at 0 °C, powdered LiOH (136 mg, 5.68 mmol, 2.0 equiv) was added, followed by H_2O_2 (0.322 ml, 5.68 mmol, 50 wt % in H_2O, 2.0 equiv), and the mixture stirred another 1.5 h at 0 °C. The reaction was then diluted with H_2O (50 mL) and EtOAc (50 mL). The aqueous layer was then extracted with EtOAc (5 x 30 mL), and the combined organic layers were washed with brine (1 x 30 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give a red oil. The residue was purified via silica flash chromatography (10–50% EtOAc/hexanes) to afford epoxide **158b** (780 mg, 68% yield).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.20 (d, *J* = 2.0 Hz, 1H), 6.26 (d, *J* = 1.9 Hz, 1H), 5.78 – 5.72 (m, 1H), 4.44 (t, *J* = 5.6 Hz, 1H), 3.64 (d, *J* = 4.1 Hz, 1H), 3.43 (dd, *J* = 4.1, 1.8 Hz, 1H), 3.07 (ddd, *J* = 9.7, 8.4, 3.7 Hz, 1H), 2.78 (td, *J* = 9.5, 6.4 Hz, 1H), 2.61 (dd, *J* = 18.0,

7.3 Hz, 1H), 2.53 (s, 3H), 2.50 – 2.34 (m, 1H), 2.22 (dd, *J* = 14.5, 5.9 Hz, 1H), 2.15 (s, 3H), 1.90 (dd, *J* = 14.5, 5.4 Hz, 1H), 0.81 (s, 9H), -0.04 (s, 3H), -0.30 (s, 3H).

Preparation of cyclobutane 159b.



158b 159b

Epoxide **158b** (385 mg, 0.954 mmol) was taken up PhH (9.5 mL) and transferred to a flame-dried 2 L flask containing a stir bar. It was diluted further with pentane (1 L, HPLC grade), cooled to 0 °C and sparged with N_2 for 1.5 h, after which the mixture was warmed back to room temperature. The reaction was irradiated with ≥350 nm light (Hanovia PC451050 lamp with a Uranium glass filter) in a photobox for 6.5 h. The reaction was subsequently concentrated under reduced pressure and the residue purified via silica flash chromatography (10–50% EtOAc/hexanes) to afford cyclobutane **159b** (207 mg, 54% yield; 62% brsm). This reaction can alternatively be conducted in 0.003 M hexanes (HPLC grade) to avoid issues of the pentane heating up rapidly and escaping the flask. First efforts to scale up with 163 mg epoxide **158b** (0.398 mmol) resulted in 103 mg cyclobutane **159b** (63% yield).

TLC: R_f 0.47 (1:1 hexanes/EtOAc, UV & $KMnO_4$).

$[\alpha]_D^{25}$: –4.0° (c = 0.42, $CHCl_3$).

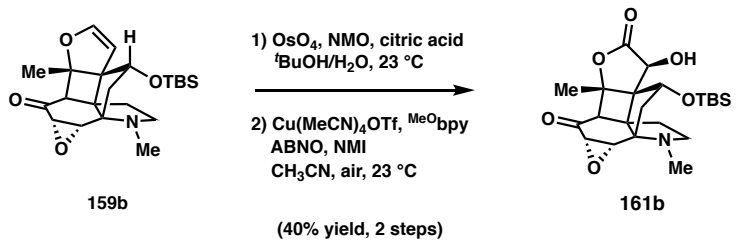
^{1}H NMR (600 MHz, $CDCl_3$): δ 6.40 (d, *J* = 2.7 Hz, 1H), 4.81 (d, *J* = 2.7 Hz, 1H), 4.07 (d, *J* = 5.0 Hz, 1H), 3.58 (d, *J* = 3.8 Hz, 1H), 3.32 (d, *J* = 3.8 Hz, 1H), 3.18 (d, *J* = 2.0 Hz, 1H), 2.91 (t, *J* = 7.4 Hz, 1H), 2.66 (ddd, *J* = 11.7, 8.0, 5.1 Hz, 1H), 2.49 (d, *J* = 1.9 Hz, 3H), 2.43 – 2.36 (m, 1H), 2.05 (dd, *J* = 12.0, 4.9 Hz, 1H), 1.98 (td, *J* = 11.8, 6.7 Hz, 1H), 1.88 – 1.79 (m, 1H), 1.19 (d, *J* = 1.9 Hz, 3H), 0.91 (d, *J* = 1.7 Hz, 9H), 0.07 (d, *J* = 2.2 Hz, 3H), 0.03 (d, *J* = 2.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 204.6, 147.5, 100.7, 88.2, 74.3, 70.9, 69.4, 63.3, 63.2, 58.2, 55.1, 52.0, 39.8, 35.8, 31.5, 26.2, 18.5, 17.2, -4.5, -4.9.

FTIR (NaCl, thin film): 2959, 2929, 2856, 2807, 1695, 1472, 1248, 1076, 940 cm^{-1}.

HRMS (MM, *m/z*): $C_{22}H_{33}NO_4Si$, calc'd for $[M+H]^+$ 404.2252, found 404.2518.

Preparation of lactone 161b.



Cyclobutane **75b** (40 mg, 0.099 mmol) and citric acid monohydrate (41.7 mg, 0.198 mmol, 2.0 equiv) were added to a vial and suspended in ^{t}BuOH/H_2O (2 mL, 1:1). OsO_4 (0.12 ml, 0.0099 mmol, 2.5 wt % in ^{t}BuOH, 10 mol%) was added, followed by NMO (12.8 mg, 0.11 mmol, 1.1 equiv), and the vial was capped and the mixture stirred at room temperature for 17 h. The reaction was quenched with saturated aqueous $Na_2S_2O_3$ (2 mL) and diluted with EtOAc (5 mL). The aqueous layers were extracted with EtOAc (5 x 3 mL),

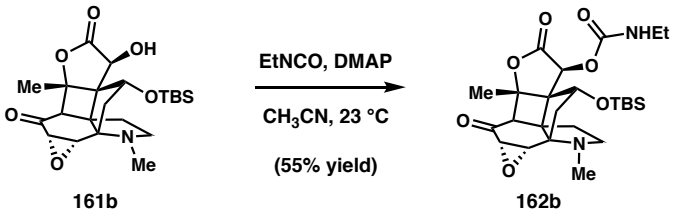
and the combined organic layers were washed with brine (2 x 5 mL), dried with Na_2SO_4, and filtered through a short silica plug, while rinsing with EtOAc (20 mL). The brine layers still contained desired diol **99**, as well as the silica plug. So the brine layer was extracted with 10% MeOH/CH_2Cl_2 (5 x 3 mL), and those combined organic layers were dried with Na_2SO_4, filtered through Celite, while the silica plug was thoroughly rinsed with 10% MeOH/CH_2Cl_2 (30 mL). All combined organic filtrates were then concentrated under reduced pressure to give 34.1 mg of diol **99** (79% crude yield), which is very insoluble and is present as both lactol diastereomers and ring-opened aldehyde in the crude ^{1}H NMR spectra. Diol **99** was subsequently suspended up in ^{t}BuOH (0.5 mL) and CH_3CN (0.34 mL, HPLC grade), after which $Cu(CH_3CN)_4$ (2.9 mg, 0.008 mmol, in 0.1 mL CH_3CN, 8 mol %), solid ^{MeO}bpy (1.7 mg, 0.008 mmol, 8 mol %), ABNO (0.22 mg, 0.002 mmol; in 40 µL CH_3CN, 2 mol %), and NMI (1.2 µl, 0.016 mmol, in 20 µL CH_3CN, 16 mol %) were added in that order. The heterogeneous solution quickly turned from a brown-orange to an olive green. The mixture was heated at 50 °C in a heating block, while using sonication to aid dissolution of diol **99** on the walls of the vial. The reaction stagnated after several hours, so $Cu(CH_3CN)_4$ (2.9 mg, 0.008 mmol, in 0.1 mL CH_3CN, 8 mol %), solid ^{MeO}bpy (1.7 mg, 0.008 mmol, 8 mol %), ABNO (0.22 mg, 0.002 mmol, in 40 µL CH_3CN, 2 mol %), and NMI (1.2 µl, 0.016 mmol, in 20 µL CH_3CN, 16 mol %) were added again in that order. After stirring overnight (18 h) at 50 °C, diol **99** was still observed via LC/MS analysis, so the reagents were added a third time (same as above), upon which the heterogeneous reaction mixture became homogenous. Total reaction time was 24 h. The reaction was worked up by filtering through a silica plug with EtOAc (40 mL). The filtrate was

concentrated under reduced pressure to give a yellow oil. The residue was purified via silica flash chromatography (10–100% EtOAc/hexanes) to afford lactone **100** (17.1 mg, 40% over two steps).

^{1}H NMR (300 MHz, $CDCl_3$): δ 4.40 (dd, *J* = 5.6, 2.9 Hz, 1H), 4.35 (s, 1H), 3.64 (d, *J* = 4.2 Hz, 1H), 3.38 (d, *J* = 4.2 Hz, 1H), 3.09 – 3.02 (m, 1H), 2.93 (s, 1H), 2.80 (ddd, *J* = 10.2, 8.6, 5.6 Hz, 1H), 2.50 (s, 3H), 2.33 (dd, *J* = 15.0, 2.9 Hz, 1H), 2.12 (ddd, *J* = 13.1, 10.1, 7.5 Hz, 1H), 1.89 (ddd, *J* = 13.1, 5.6, 2.0 Hz, 1H), 1.71 (dd, *J* = 15.0, 5.5 Hz, 1H), 1.46 (s, 3H), 0.91 (s, 9H), 0.17 (s, 3H), 0.12 (s, 3H).

HRMS (MM, *m/z*): $C_{22}H_{33}NO_6Si$, calc'd for $[M+H]^+$ 436.2150, found 436.2169.

Preparation of carbamate 106.

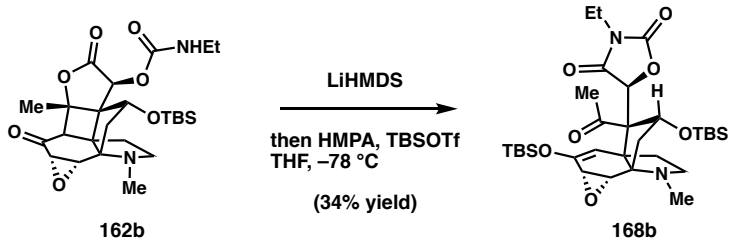


Lactone **161b** (8 mg, 0.018 mmol) and DMAP (2.25 mg, 0.018 mmol, 1.0 equiv) were added to an oven-dried vial and placed under N_2. The solids were dissolved in CH_3CN (0.1 mL), after which ethyl isocyanate (3.2 μL, 0.04 mmol, 2.2 equiv) was added. The reaction was stirred at room temperature for 24 h, after which mostly starting material was observed via LC/MS. Thus, DMAP (2.25 mg, 0.018 mmol, 1.0 equiv) and excess ethyl isocyanate (14.6 μL, 0.180 mmol, 10 equiv) were added, along with CH_3CN (0.1 mL). The reaction was stirred overnight (16 h), resulting in consumption of the starting material. The

reaction was quenched with saturated aqueous $NaHCO_3$ (5 mL) and extracted with EtOAc (4 x 3 mL). The combined organic layers were washed with brine (1 x 3 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified via silica flash chromatography (10–100% EtOAc/hexanes) to afford carbamate **162b** (5.1 mg, 55% yield).

HRMS (MM, *m/z*): $C_{25}H_{38}N_2O_7Si$, calc'd for $[M+H]^+$ 507.2521, found 507.2511.

Preparation of succinimide 168b.



162b 168b

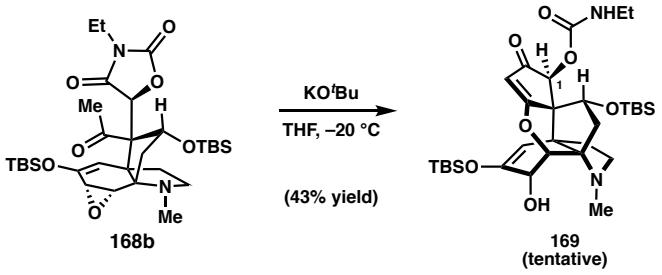
Carbamate **162b** (5.1 mg, 0.01 mmol) was added to an oven-dried vial, placed under N_2 atmosphere, and dissolved in THF (0.13 mL). It was cooled to –78 °C, after which LiHMDS (14.1 μL, 0.014 mmol, 1 M in THF, 1.4 equiv) was added slowly, followed by TBSOTf (3.5 μL, 0.015 mmol, 1.5 equiv). The mixture was stirred at –78 °C for 30 min, after which HMPA (8.8 μL, 0.050 mmol, 5.0 equiv) was added and the reaction stirred further at –78 °C for 2 h. The reaction was quenched with 1 drop of 2,6-lutidine and diluted with pH 7 buffer (5 mL) and EtOAc (5 mL), then warmed to room temperature. The aqueous layer was then extracted with EtOAc (4 x 3 mL), and the combined organic layers washed with brine (1 x 3 mL), dried with Na_2SO_4, filtered, and concentrated under reduced

pressure to give a crude oil. The residue was purified via silica flash chromatography (10–50% EtOAc/hexanes) to afford **168b** (2.1 mg, 34% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.36 (s, 1H), 5.09 (s, 1H), 4.59 (d, *J* = 5.0 Hz, 1H), 3.70 – 3.53 (m, 2H), 3.33 (d, *J* = 2.6 Hz, 1H), 3.07 (d, *J* = 2.1 Hz, 1H), 3.01 – 2.93 (m, 1H), 2.81 – 2.76 (m, 1H), 2.60 (s, 3H), 2.51 (q, *J* = 9.2, 8.1 Hz, 1H), 2.39 – 2.18 (m, 2H), 2.04 (s, 3H), 1.85 (d, *J* = 12.1 Hz, 1H), 1.32 (t, *J* = 7.2 Hz, 3H), 0.91 (s, 9H), 0.90 (s, 9H), 0.18 (s, 3H), 0.15 (s, 3H), 0.12 (d, *J* = 2.3 Hz, 6H).

HRMS (MM, *m/z*): $C_{31}H_{52}N_2O_7Si_2$, calc'd for $[M+H]^+$ 621.3386, found 621.3387.

Preparation of spirocycle 169.



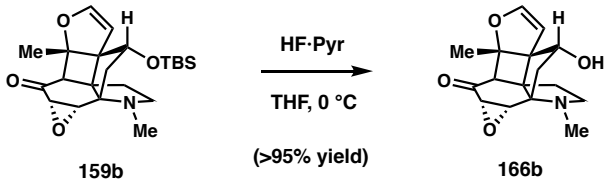
Ketone **168b** (2.1 mg, 0.0034 mmol) was added to an oven-dried vial, placed under nitrogen atmosphere, and taken up in THF (0.11 mL). The mixture was cooled to –20 °C and KO^{t}Bu (03.7 μL, 0.0037 mmol, 1 M in THF, 1.1 equiv) was added, resulting in a bright yellow solution. The reaction was stirred at –20 °C for 1 h, after which it was quenched with saturated aqueous $NaHCO_3$ (4 mL). EtOAc/CH_2Cl_2 (4:1, 2 mL) was added and the mixture warmed to room temperature. The layers were separated and the aqueous layer extracted with EtOAc/CH_2Cl_2 (4:1, 6 x 2 mL). The combined organic layers were dried

with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified via silica gel flash chromatography (10–100% EtOAc/hexanes) to afford **169** (0.9 mg, 43% yield), tentatively assigned as the caged ether.

^{1}H NMR (600 MHz, $CDCl_3$): δ 5.43 (s, 1H), 5.29 (d, *J* = 0.6 Hz, 1H), 4.98 (s, 1H), 4.78 (t, *J* = 5.6 Hz, 1H), 4.62 (d, *J* = 3.2 Hz, 1H), 4.34 (dd, *J* = 7.5, 1.8 Hz, 1H), 3.80 (d, *J* = 3.2 Hz, 1H), 3.34 – 3.21 (m, 2H), 3.17 (dt, *J* = 12.9, 6.4 Hz, 1H), 2.91 (ddd, *J* = 13.9, 11.3, 6.6 Hz, 1H), 2.51 (td, *J* = 10.7, 4.2 Hz, 1H), 2.34 (s, 3H), 2.14 (dd, *J* = 14.6, 7.3 Hz, 1H), 1.93 (dd, *J* = 14.6, 1.4 Hz, 1H), 1.84 (ddd, *J* = 13.5, 9.0, 4.8 Hz, 1H), 1.15 (t, *J* = 7.2 Hz, 3H), 0.92 (s, 9H), 0.89 (s, 9H), 0.15 (s, 3H), 0.12 (s, 3H), 0.06 (s, 6H).

HRMS (MM, *m/z*): $C_{31}H_{52}N_2O_7Si_2$, calc'd for $[M+H]^+$ 621.3386, found 621.3379.

Preparation of alcohol 166b.



Cyclobutane **159b** (15 mg, 0.037 mmol) was added to a plastic Eppendorf tube and dissolved in THF (0.25 mL). It was cooled to 0 °C, after which HF·Pyr (4.8 µL, 0.186 mmol, in 0.1 mL THF, 5.0 equiv) was added. After 1.5 h, the reaction was carefully quenched with saturated aqueous $NaHCO_3$ (4 mL), diluted with EtOAc (4 mL), and warmed to room temperature. The aqueous layers was extracted with EtOAc (5 x 2 mL) and the combined organic layers washed with brine (1 x 4 mL). The brine layer was back-

extracted with EtOAc (1 x 4 mL) and the combined organic layers dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude oil. The residue was purified via silica flash chromatography (10–100% EtOAc/hexanes) to afford alcohol **166b** as a white solid (22 mg, > 95% yield).

TLC: R_f 0.22 (3:1 EtOAc/hexanes, UV & $KMnO_4$).

$[\alpha]_D^{25}$: +39.9° (c = 0.74, $CHCl_3$).

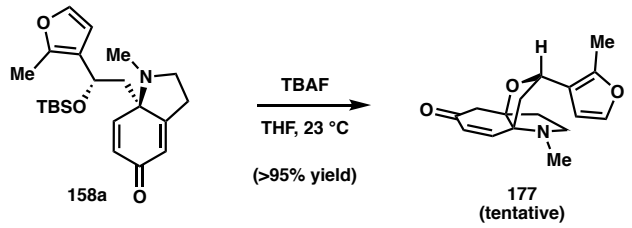
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.47 (d, *J* = 2.8 Hz, 1H), 5.04 (d, *J* = 2.8 Hz, 1H), 3.97 (d, *J* = 4.5 Hz, 1H), 3.68 (d, *J* = 4.4 Hz, 1H), 3.23 (d, *J* = 4.4 Hz, 1H), 3.18 (s, 1H), 3.11 (td, *J* = 9.2, 2.6 Hz, 1H), 2.94 (td, *J* = 9.4, 7.8 Hz, 1H), 2.52 (s, 3H), 2.51 – 2.43 (m, 1H), 2.32 (d, *J* = 14.7 Hz, 1H), 1.97 (ddd, *J* = 13.6, 9.8, 2.6 Hz, 1H), 1.82 (dd, *J* = 14.7, 4.5 Hz, 1H), 1.22 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 204.3, 148.3, 100.7, 89.1, 75.6, 72.5, 71.2, 61.3, 57.1, 55.9, 54.4, 54.3, 39.5, 34.3, 31.2, 17.0.

FTIR (NaCl, thin film): 3306, 2932, 2849, 1703, 1605, 1450, 1350, 1155, 983 cm^{-1}.

HRMS (MM, *m/z*): $C_{16}H_{19}NO_4$, calc'd for $[M+H]^+$ 290.1387, found 290.1513.

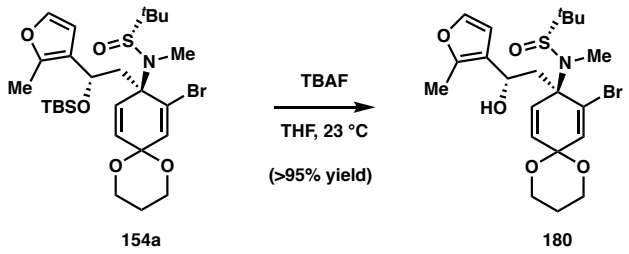
Preparation of bridging ether 177.



Silyl ether **158a** (5 mg, 0.013 mmol) was added to an oven-dried 1 dram vial, placed under N_2 atmosphere, and dissolved in THF (0.1 mL). TBAF (14 μL, 0.014 mmol, 1 M THF, 1.1 equiv) was then added and the mixture stirred at room temperature for 1 h. The reaction was quenched with saturated aqueous Na_2SO_4 (2 mL). The aqueous layers was extracted with EtOAc (5 x 1 mL). The combined organic layers washed with brine (1 x 1 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by PTLC (100% EtOAc) to afford alcohol **177** as a yellow solid (3.5 mg, >95% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26 – 7.25 (m, 1H, partially covered by solvent peak), 6.89 (d, *J* = 10.3 Hz, 1H), 6.39 (d, *J* = 1.9 Hz, 1H), 6.10 (d, *J* = 10.3 Hz, 1H), 4.84 (dd, *J* = 9.7, 6.1 Hz, 1H), 2.92 – 2.84 (m, 2H), 2.86 (d, *J* = 16.5 Hz, 1H), 2.76 (d, *J* = 16.4 Hz, 1H), 2.44 (s, 3H), 2.34 (dd, *J* = 13.0, 9.7 Hz, 1H), 2.26 (s, 3H), 2.17 (ddd, *J* = 13.4, 5.9, 3.6 Hz, 1H), 1.91 (dd, *J* = 13.0, 6.2 Hz, 1H), 1.85 – 1.71 (m, 1H).

Preparation of alcohol 180.

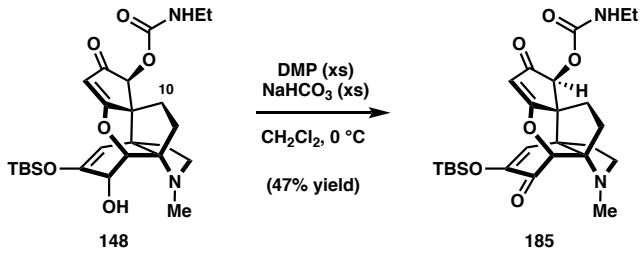


154a 180

Silyl ether **154a** (10 mg, 0.017 mmol) was added to an oven-dried 1 dram vial, placed under N_2 atmosphere, and dissolved in THF (0.17 mL). TBAF (66 µL, 0.066 mmol, 1 M THF, 4.0 equiv) was then added dropwise and the mixture stirred at room temperature for 3 h. The reaction was quenched with pH 7 buffer (4 mL). The aqueous layers was extracted with EtOAc (5 x 2 mL). The combined organic layers washed with brine (2 x 4 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give a pale yellow oil. The residue was purified via Florisil flash chromatography (10–70% EtOAc/hexanes) to afford alcohol **180** as a white solid (9 mg, >95% yield).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.23 (d, *J* = 1.9 Hz, 1H), 7.04 (d, *J* = 2.3 Hz, 1H), 6.33 (d, *J* = 1.9 Hz, 1H), 6.25 (dd, *J* = 10.2, 2.3 Hz, 1H), 5.65 (d, *J* = 10.2 Hz, 1H), 4.57 (dt, *J* = 7.1, 3.1 Hz, 1H), 4.20 – 3.90 (m, 4H), 3.00 (dd, *J* = 13.8, 7.7 Hz, 1H), 2.37 (s, 3H), 2.29 (d, *J* = 4.1 Hz, 1H), 2.21 (s, 3H), 1.91 (dq, *J* = 12.7, 4.0 Hz, 1H), 1.80 (dd, *J* = 13.8, 4.1 Hz, 1H), 1.19 (s, 9H).

Preparation of ketone 185.



Note: It is imperative to utilize pure DMP for successful reaction conversion. The reaction was reproducible when commercial DMP was utilized that was stored in the freezer a nitrogen-filled glovebox for its time of use.

Spirocycle **148** (17.7 mg, 0.036 mmol) and $NaHCO_3$ (30 mg, 0.361 mmol, 10.0 equiv) were added to an oven-dried vial and placed under N_2 atmosphere. CH_2Cl_2 (1.8 mL) was added, and the mixture cooled to 0 °C. DMP (76 mg, 0.18 mmol, 5.0 equiv, stored in freezer of a nitrogen-filled glovebox) was added and the mixture stirred for 4 h at 0 °C. The reaction was quenched by the addition of a 1:1 mixture of saturated aqueous $Na_2S_2O_3$/saturated aqueous $NaHCO_3$ (8 mL). EtOAc (3 mL) was added and the mixture warmed to room temperature. The aqueous layer was extracted with EtOAc (5 x 3 mL). and the combined organic layers washed with brine (1 x 5 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was first purified by silica gel flash chromatography (5–50% EtOAc/hexanes), and then by preparative reverse phase HPLC (75–85% CH_3CN/H_2O over 14 min, t_R(**185**) = 10.5–11.5 min) to afford **185** (8.2 mg, 47% yield).

TLC: R_f 0.36 (1:1 EtOAc/hexanes, UV & CAM).

$[\alpha]_D^{25}$: –39.9° (c = 0.31, $CHCl_3$).

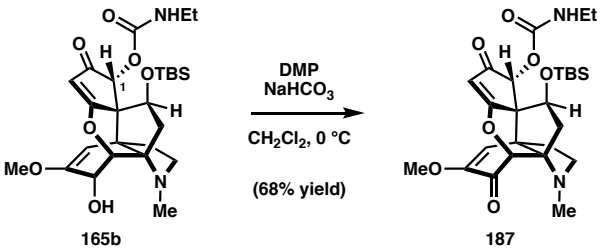
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.86 (s, 1H), 5.38 (s, 1H), 5.31 (s, 1H), 4.97 (t, *J* = 5.4 Hz, 1H), 4.61 (s, 1H), 3.34 – 3.14 (m, 3H), 2.58 (ddd, *J* = 11.1, 9.9, 3.7 Hz, 1H), 2.25 (s, 3H), 2.30 – 2.17 (m, 1H), 2.12 – 1.93 (m, 2H), 1.90 – 1.74 (m, 2H), 1.69 – 1.60 (m, 1H), 1.17 (t, *J* = 7.3 Hz, 3H), 0.92 (s, 9H), 0.12 (s, 3H), 0.08 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 198.4, 188.6, 188.5, 155.5, 146.4, 126.0, 105.8, 88.5, 73.1, 72.5, 59.5, 53.8, 52.9, 36.4, 35.9, 31.1, 28.4, 25.7, 21.7, 18.5, 15.2, -4.6, -4.7.

FTIR (NaCl, thin film): 3313, 2934, 2858, 1704, 1600, 1248, 840 cm^{-1}.

HRMS (ESI, *m/z*): $C_{25}H_{36}N_2O_6Si$, calc'd for $[M+H]^+$: 489.2415, found 489.2434.

Preparation of ketone 187.



165b 187

Note: It is imperative to utilize pure DMP for successful reaction conversion. The reaction was reproducible when commercial DMP was utilized that was stored in the freezer a nitrogen-filled glovebox for its time of use.

Spirocycle **165b** (10 mg, 0.0192 mmol) and $NaHCO_3$ (16.1 mg, 0.19 mmol, 10.0 equiv) were added to an oven-dried vial and placed under N_2 atmosphere. CH_2Cl_2 (1.5 mL) was

added, and the mixture cooled to 0 °C. DMP (40.8 mg, 0.096 mmol, 5.0 equiv, stored in freezer of a nitrogen-filled glovebox) was added quickly and the mixture stirred for 1.5 h at 0 °C. The reaction was quenched by the addition of a 1:1 mixture of saturated aqueous $Na_2S_2O_3$/saturated aqueous $NaHCO_3$ (5 mL). EtOAc (3 mL) was added and the mixture warmed to room temperature. The aqueous layer was extracted with EtOAc (5 x 3 mL). and the combined organic layers washed with brine (1 x 5 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by silica gel flash chromatography (0–80% EtOAc/hexanes) to afford **187** as a white foam (6.8 mg, 68% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.55 (s, 1H), 5.48 (s, 1H), 5.29 (s, 1H), 4.84 (t, *J* = 5.8 Hz, 1H), 4.61 (s, 1H), 4.40 (dd, *J* = 9.8, 5.2 Hz, 1H), 3.62 (s, 3H), 3.33 – 3.11 (m, 3H), 2.56 (td, *J* = 10.4, 4.6 Hz, 1H), 2.47 (dd, *J* = 14.4, 9.8 Hz, 1H), 2.24 (s, 3H), 2.01 – 1.81 (m, 2H), 1.32 (dd, *J* = 14.4, 5.3 Hz, 1H), 1.18 (t, *J* = 7.2 Hz, 3H), 0.82 (s, 9H), 0.05 (s, 6H).
HRMS (ESI, *m/z*): $C_{26}H_{38}N_2O_7Si$, calc'd for $[M+H]^+$: 519.2521, found 519.2523.

2.8 NOTES AND REFERENCES

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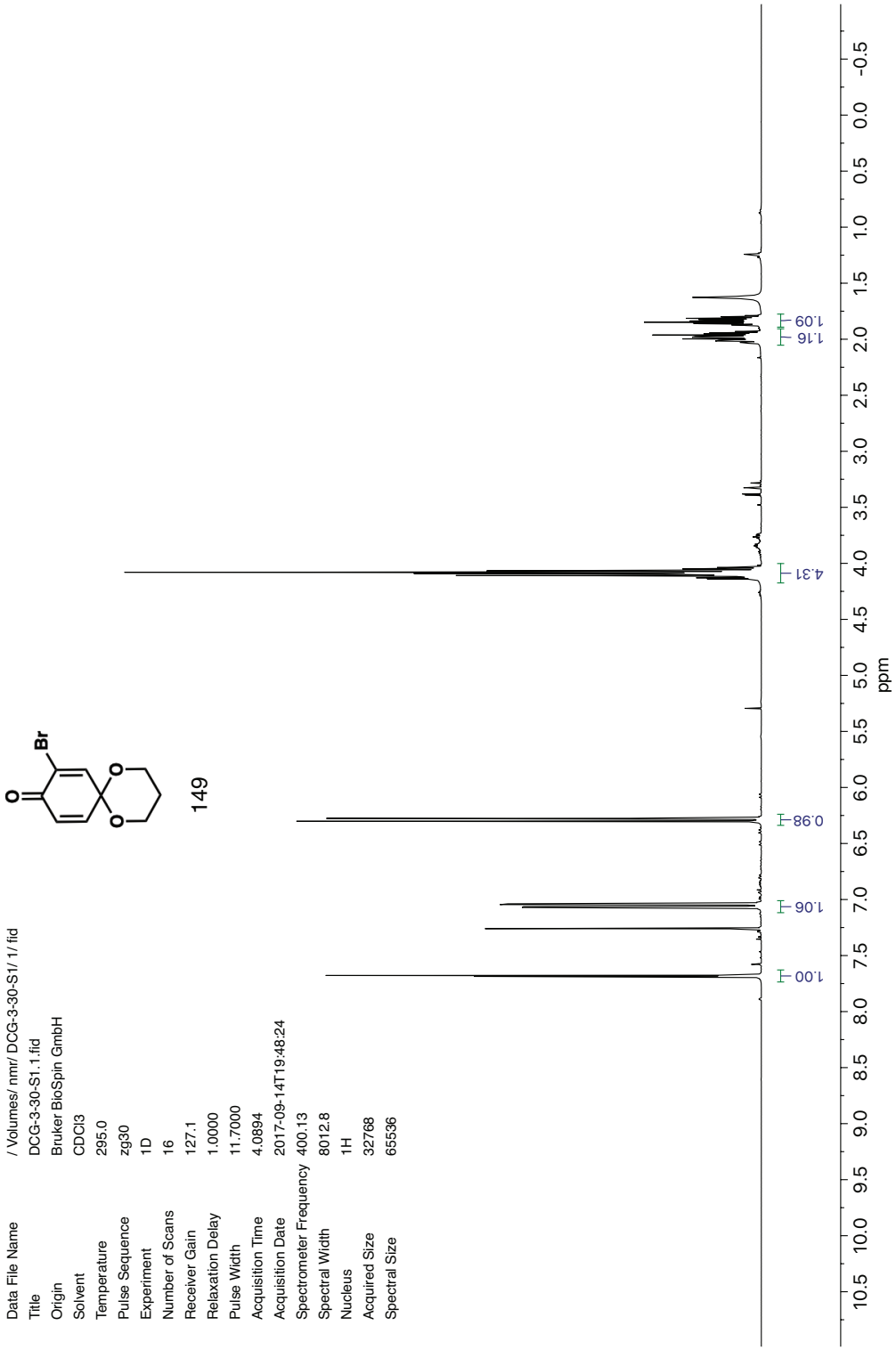
Appendix 1

Spectra Relevant to Chapter 2:

The Reisman Strategy Toward (–)-Acutumine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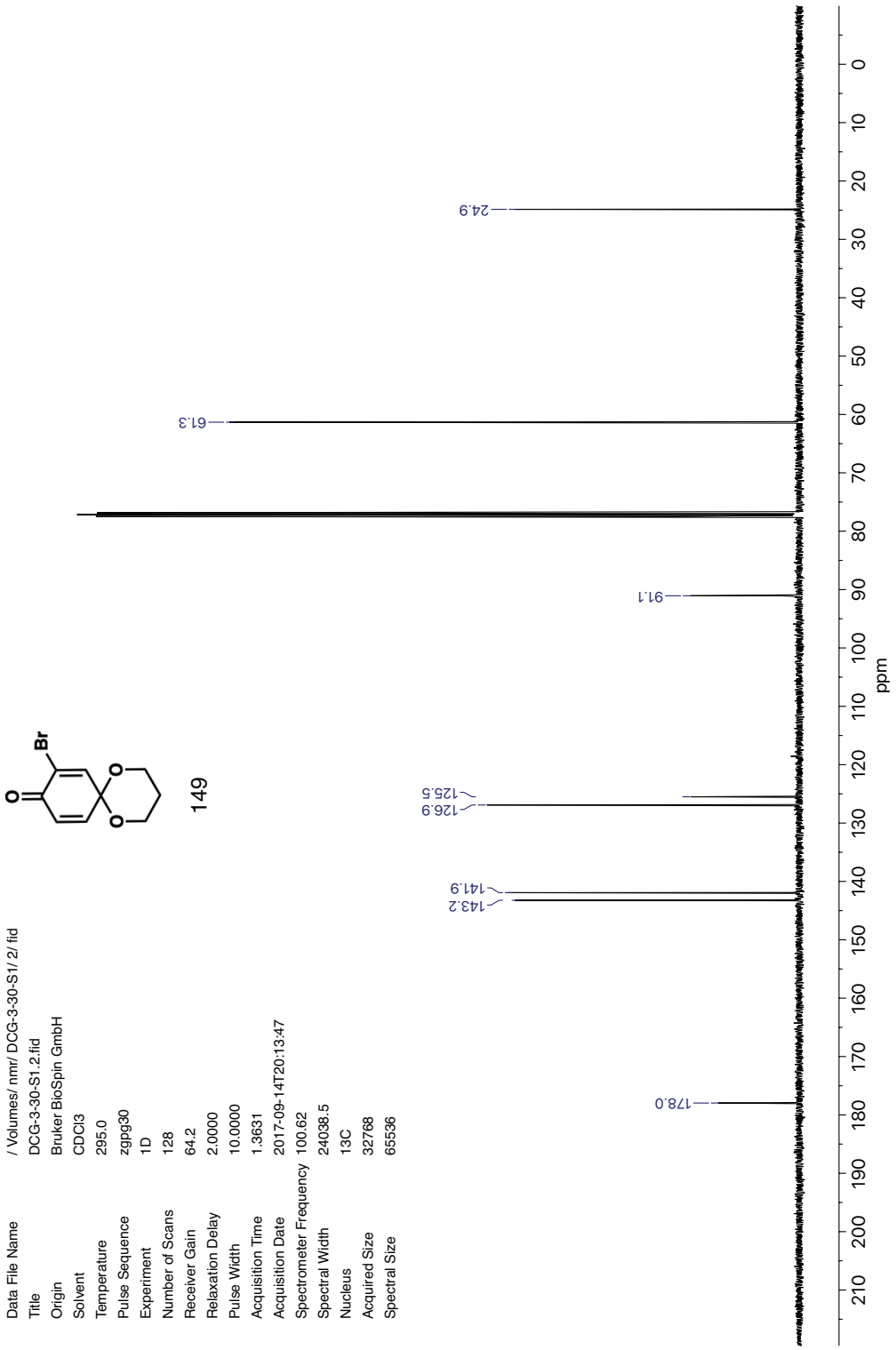
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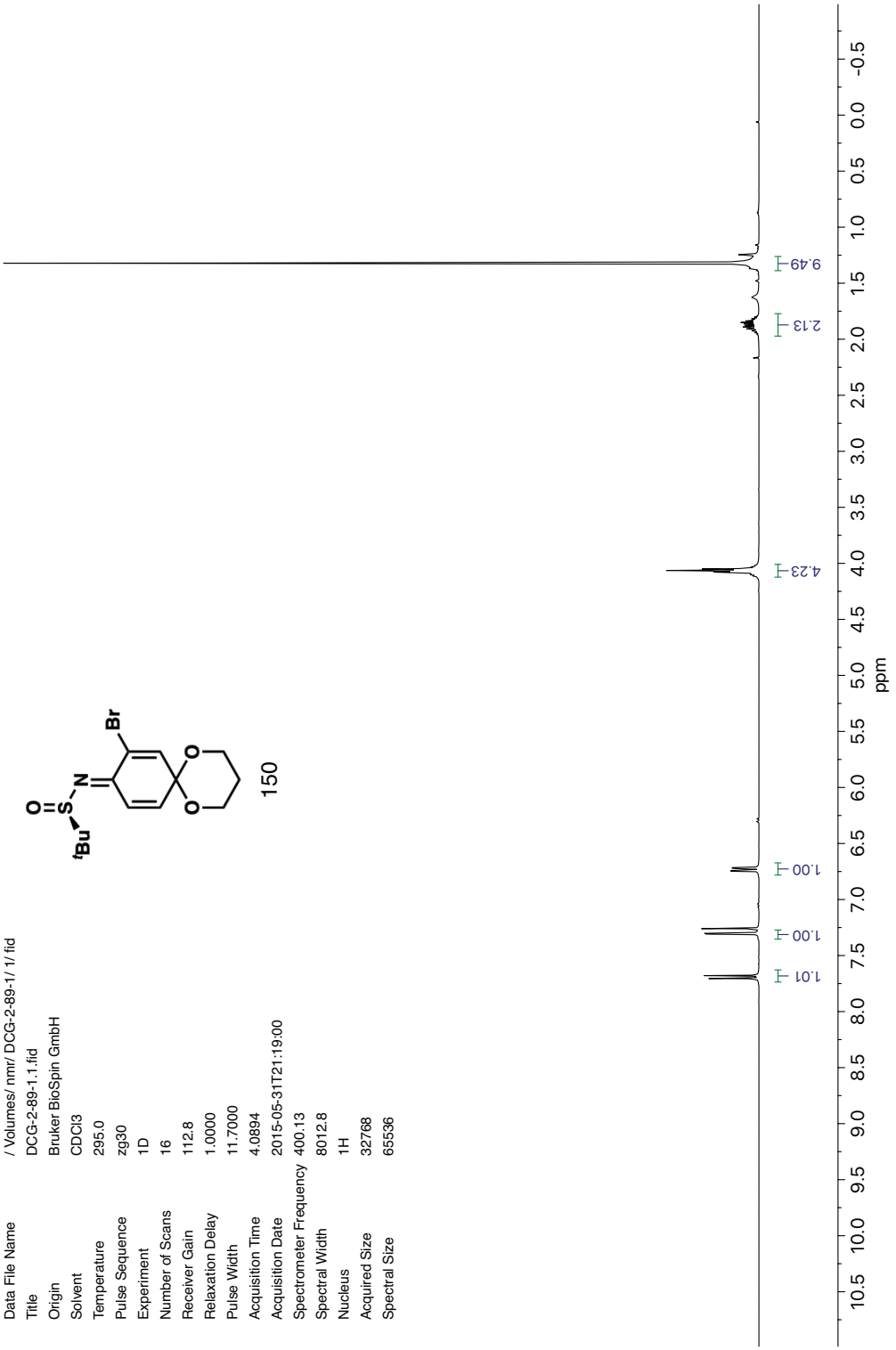
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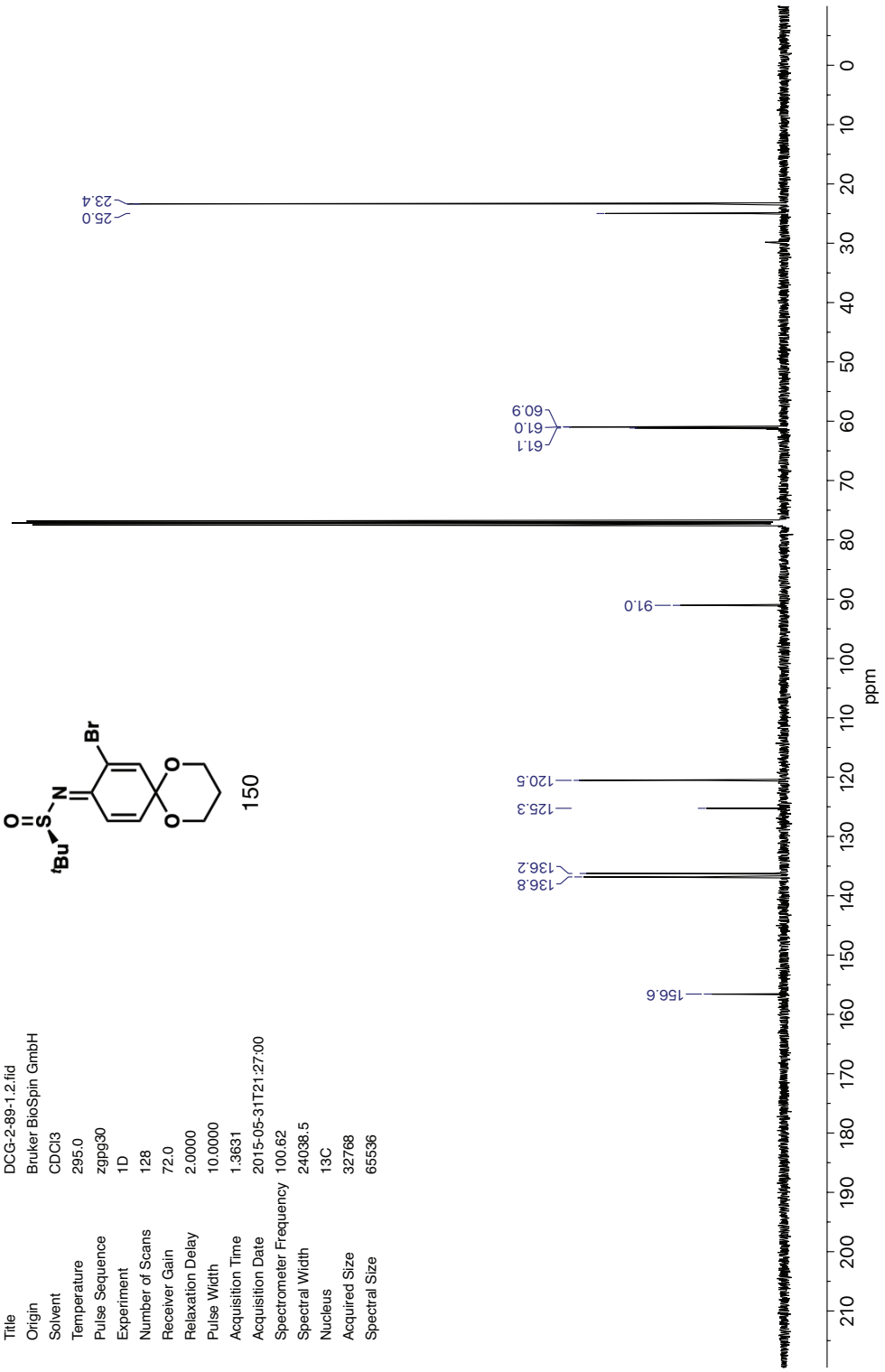
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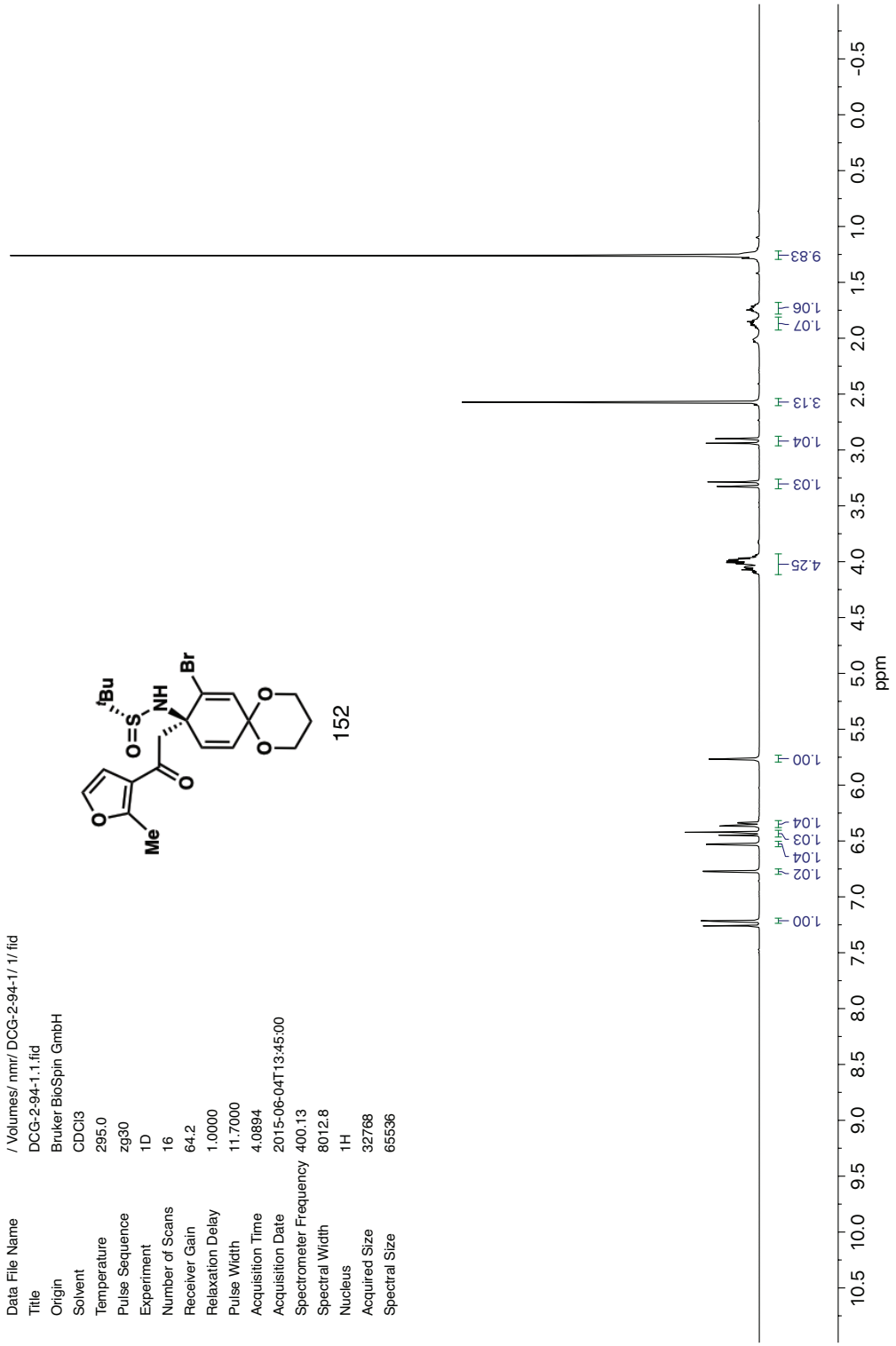
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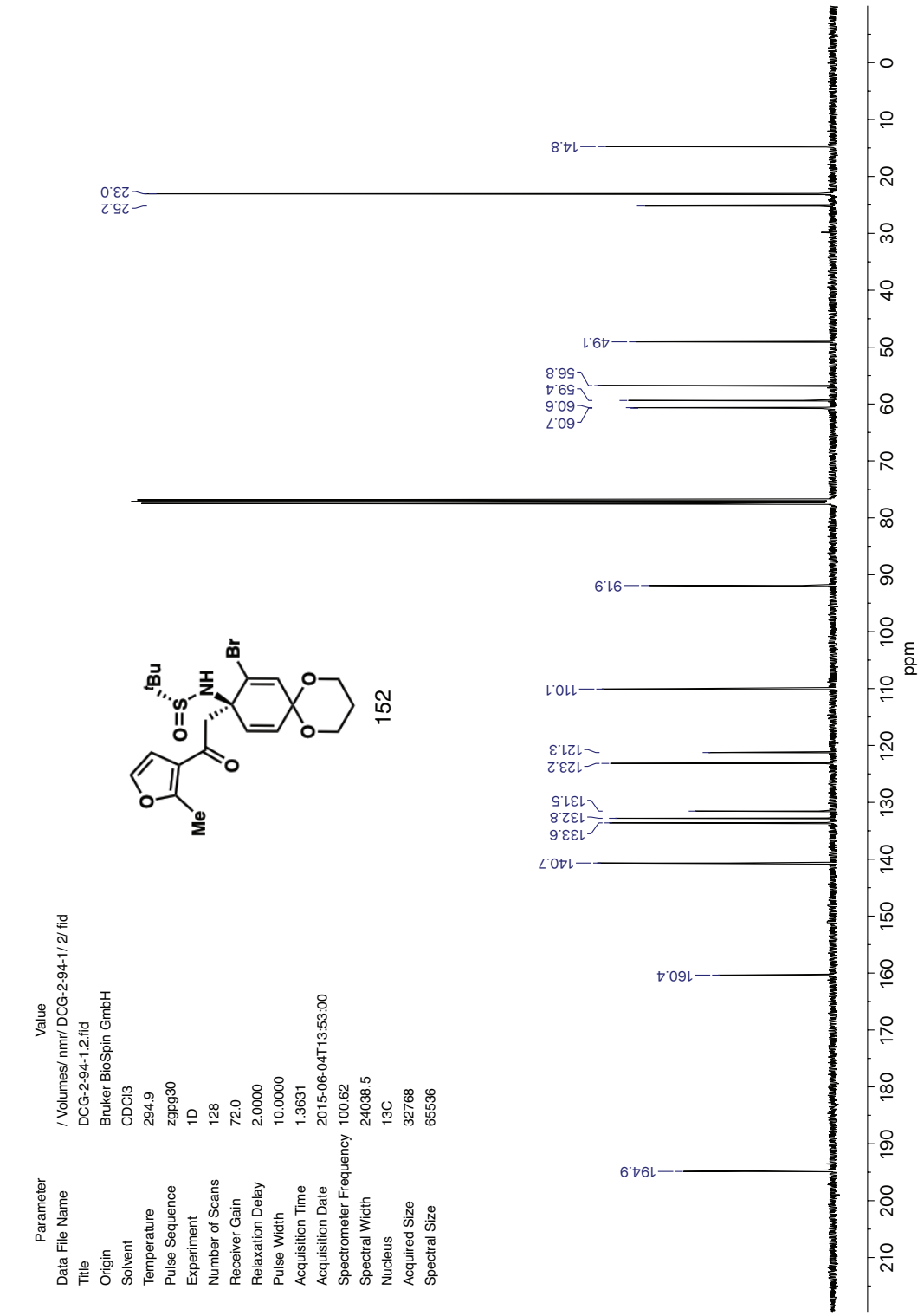
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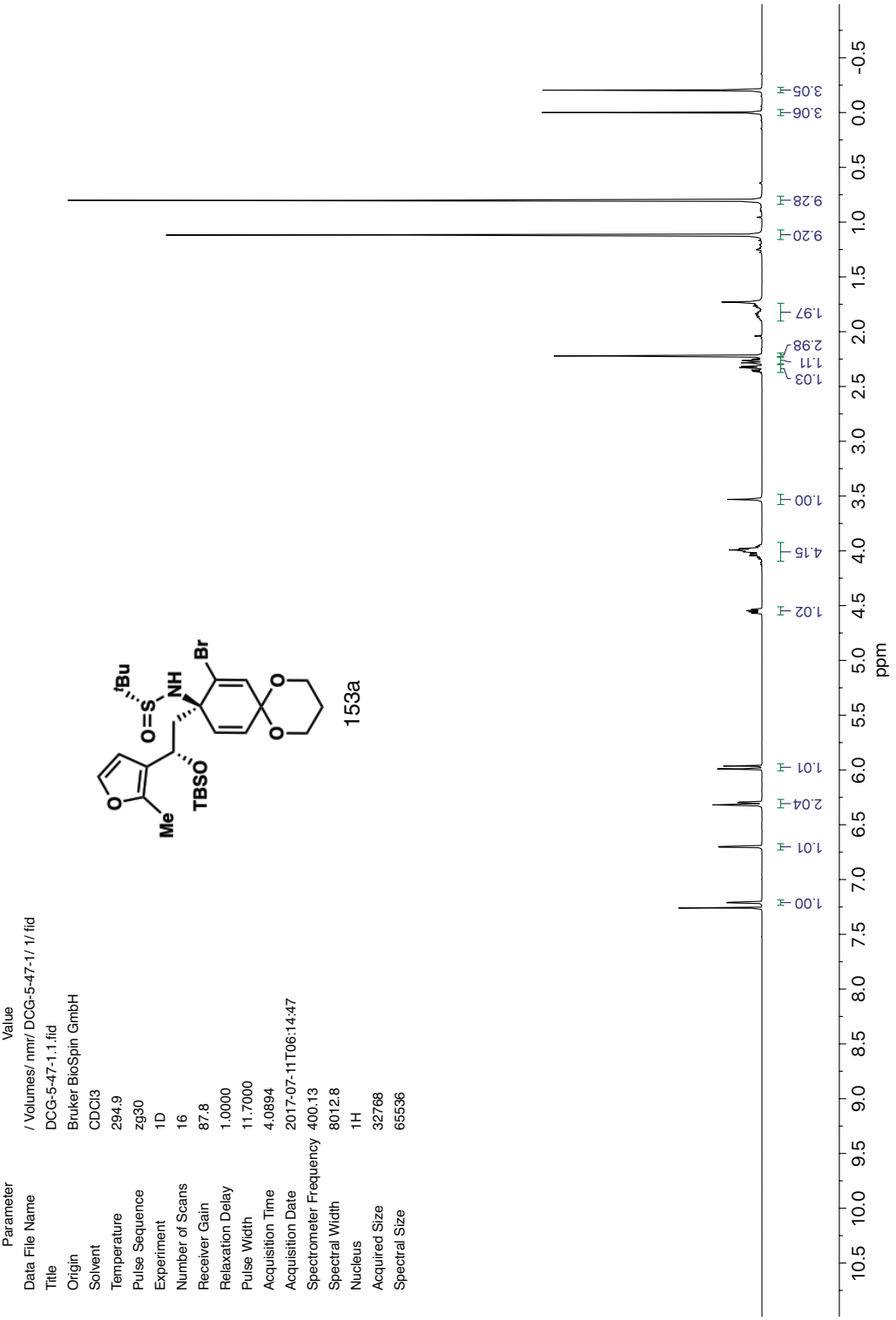
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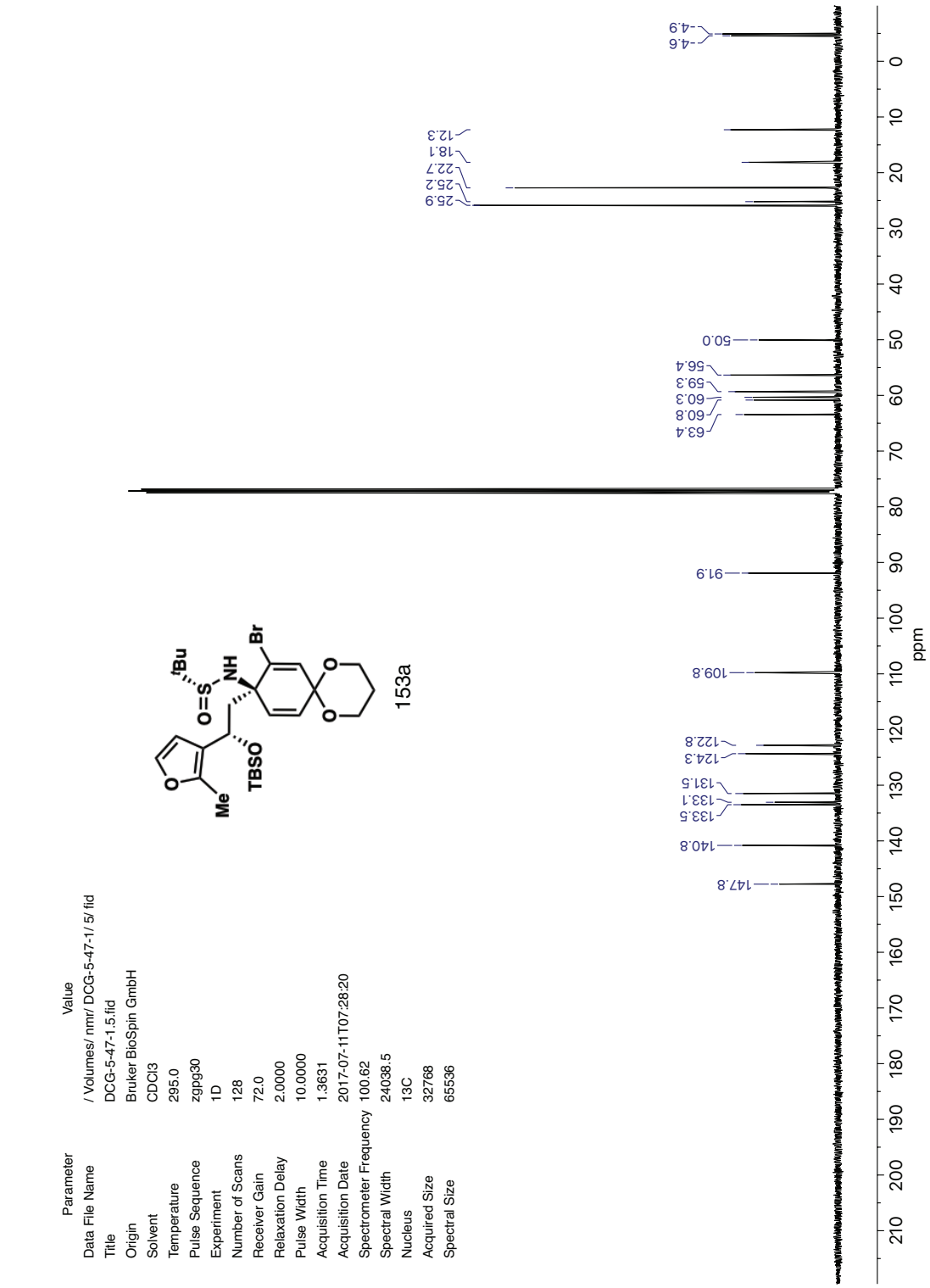
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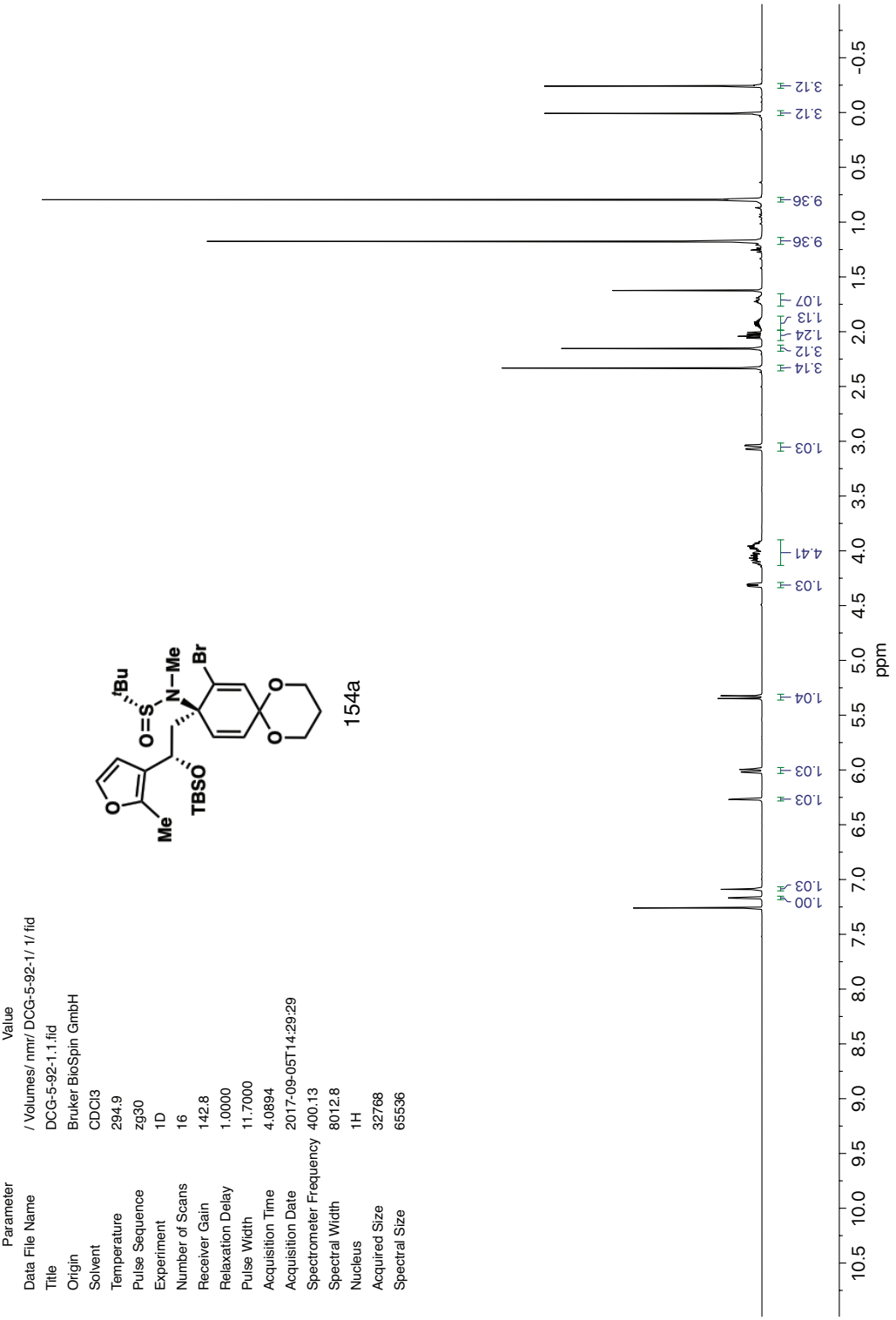
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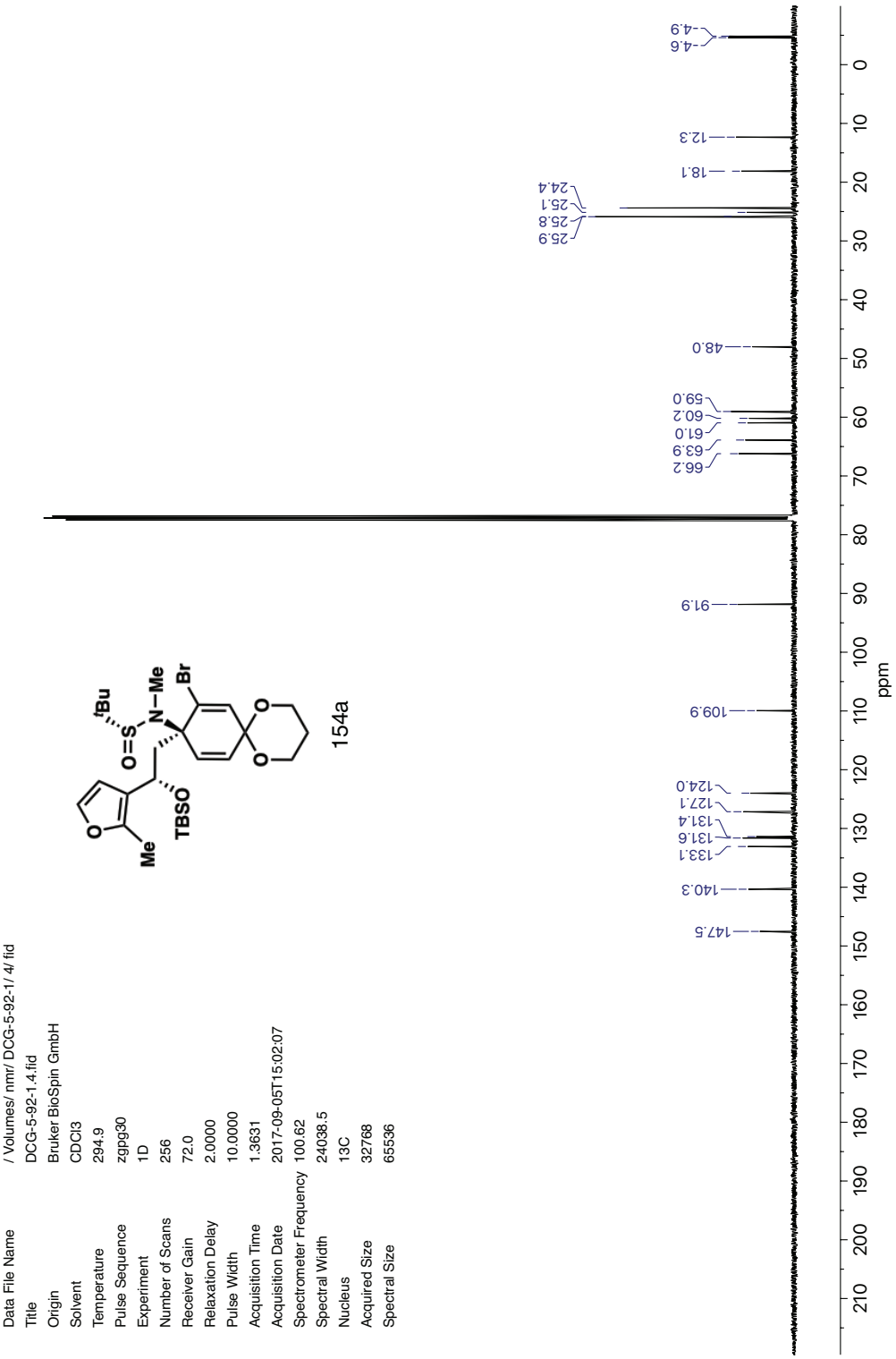
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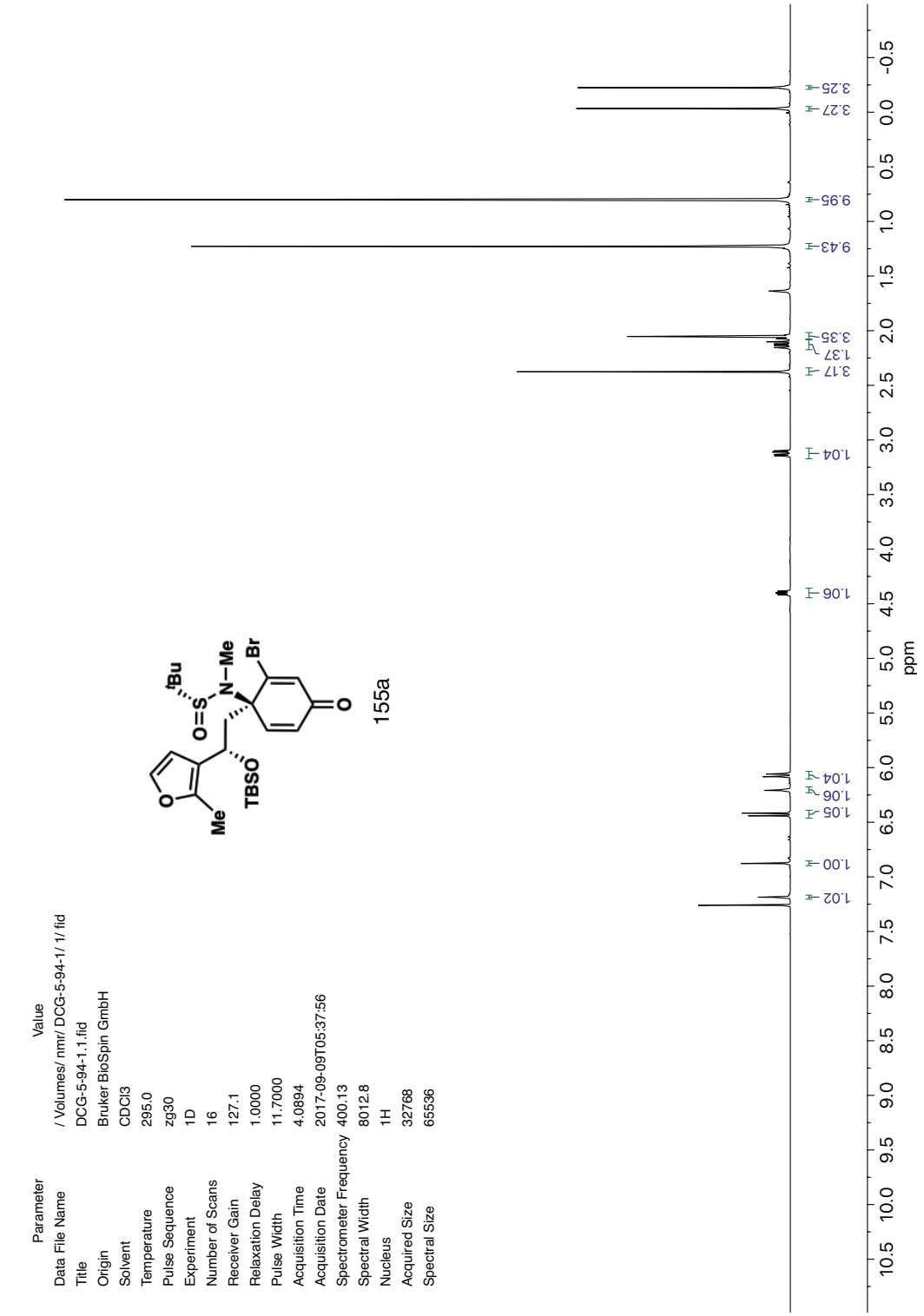
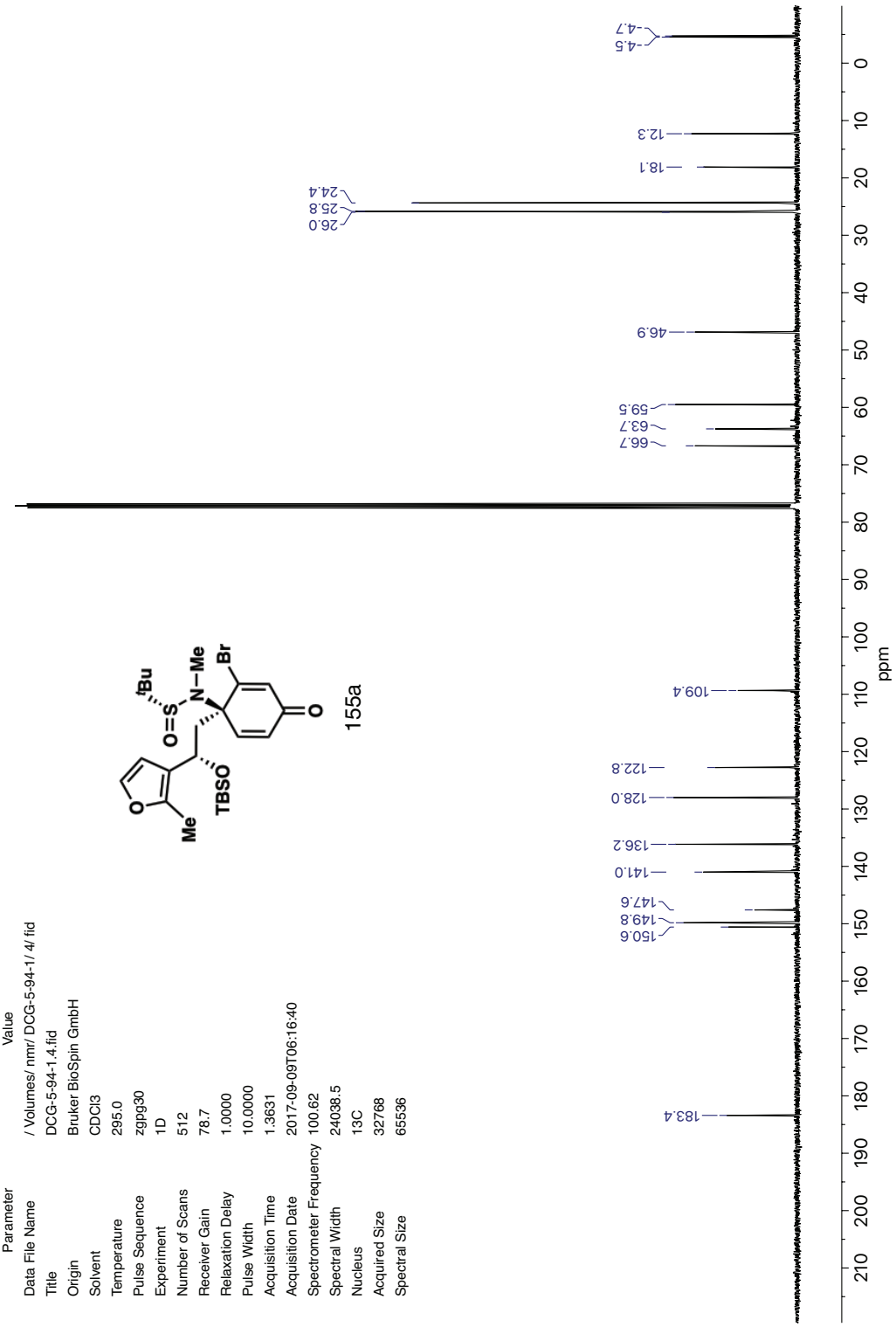
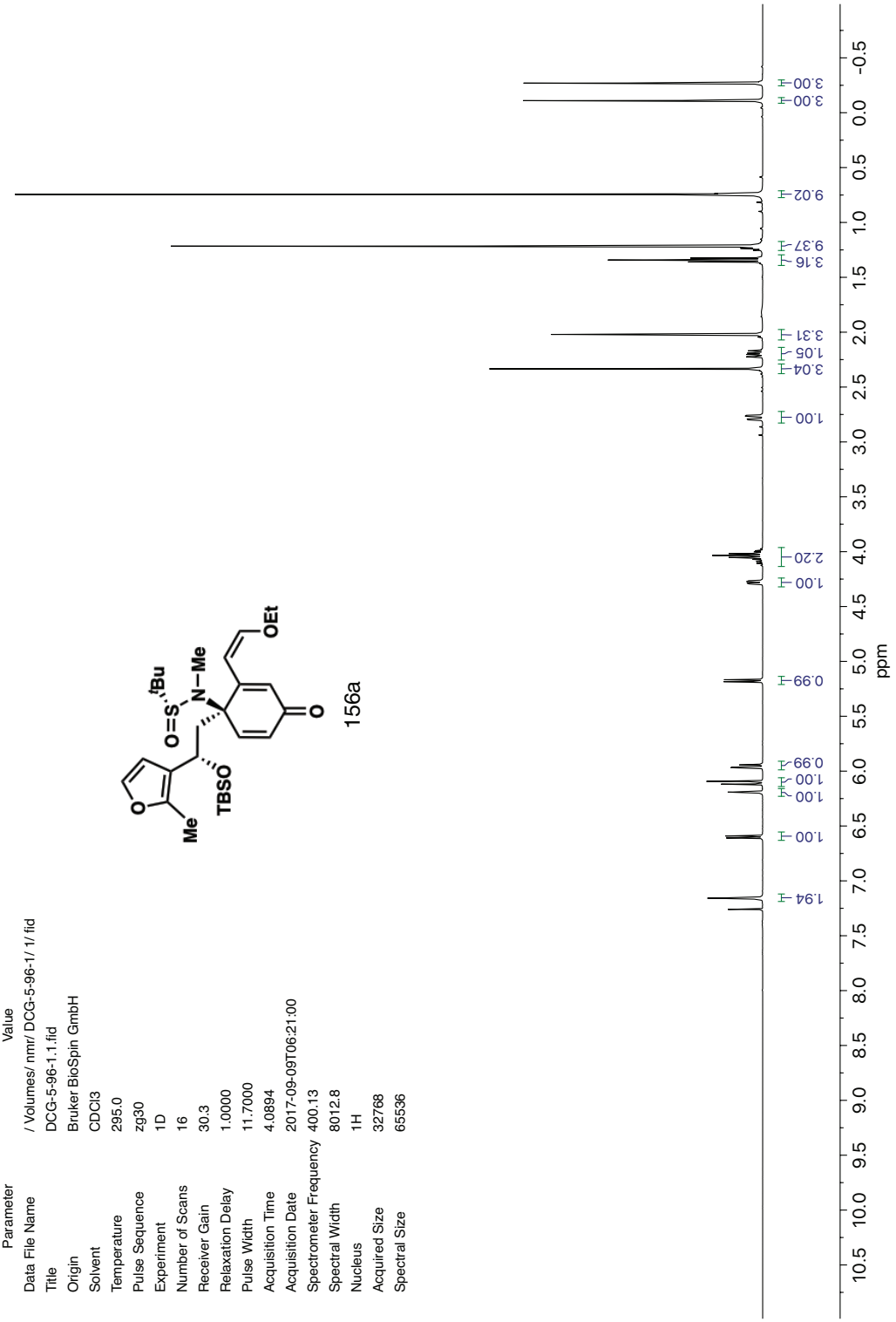
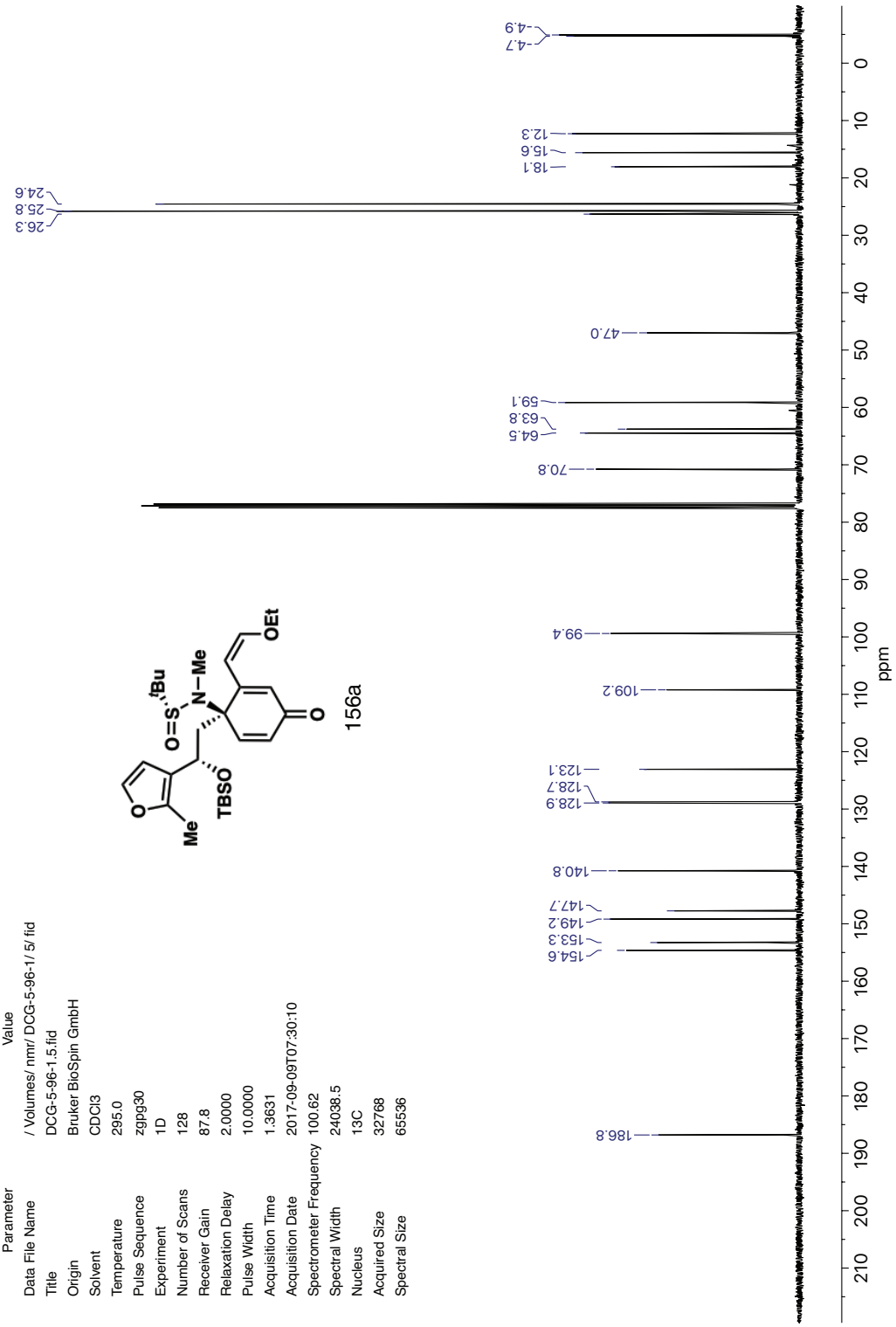
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-09-05T15:02:07
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
tBu
O=S
N–Me
Br
TBSO
Me
O
O
O
154a
-4.9
-4.6
12.3
18.1
24.4
25.1
25.8
25.9
48.0
59.0
60.2
61.0
63.9
66.2
91.9
109.9
124.0
127.1
131.4
131.6
133.1
140.3
147.5
ppm

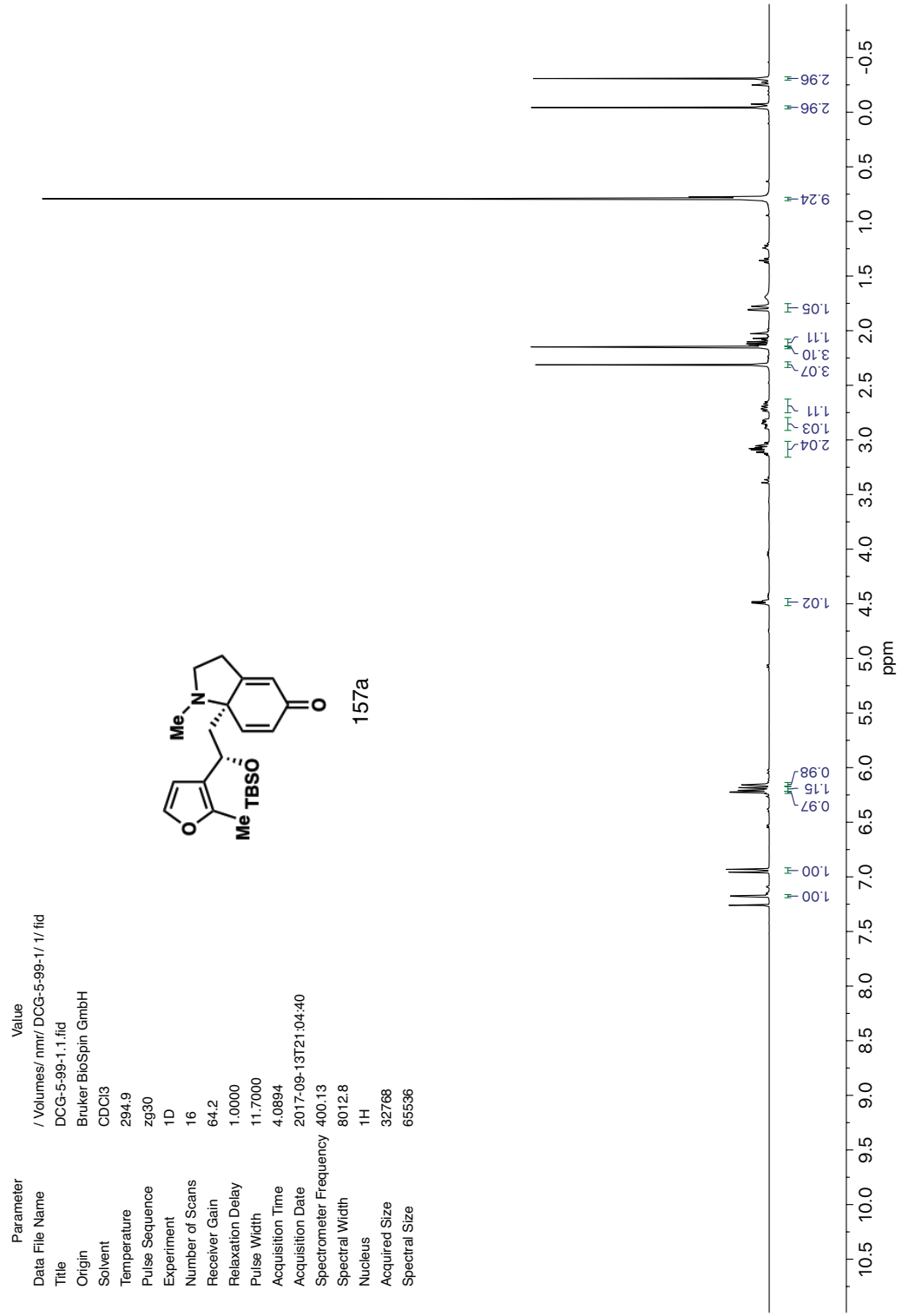

Parameter
Value
Data File Name / Volumes/ nmr/ DCG-5-94-1/ 1/ fid
Title DCG-5-94-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 127.1
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-09-09T05:37:56
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
155a
ppm

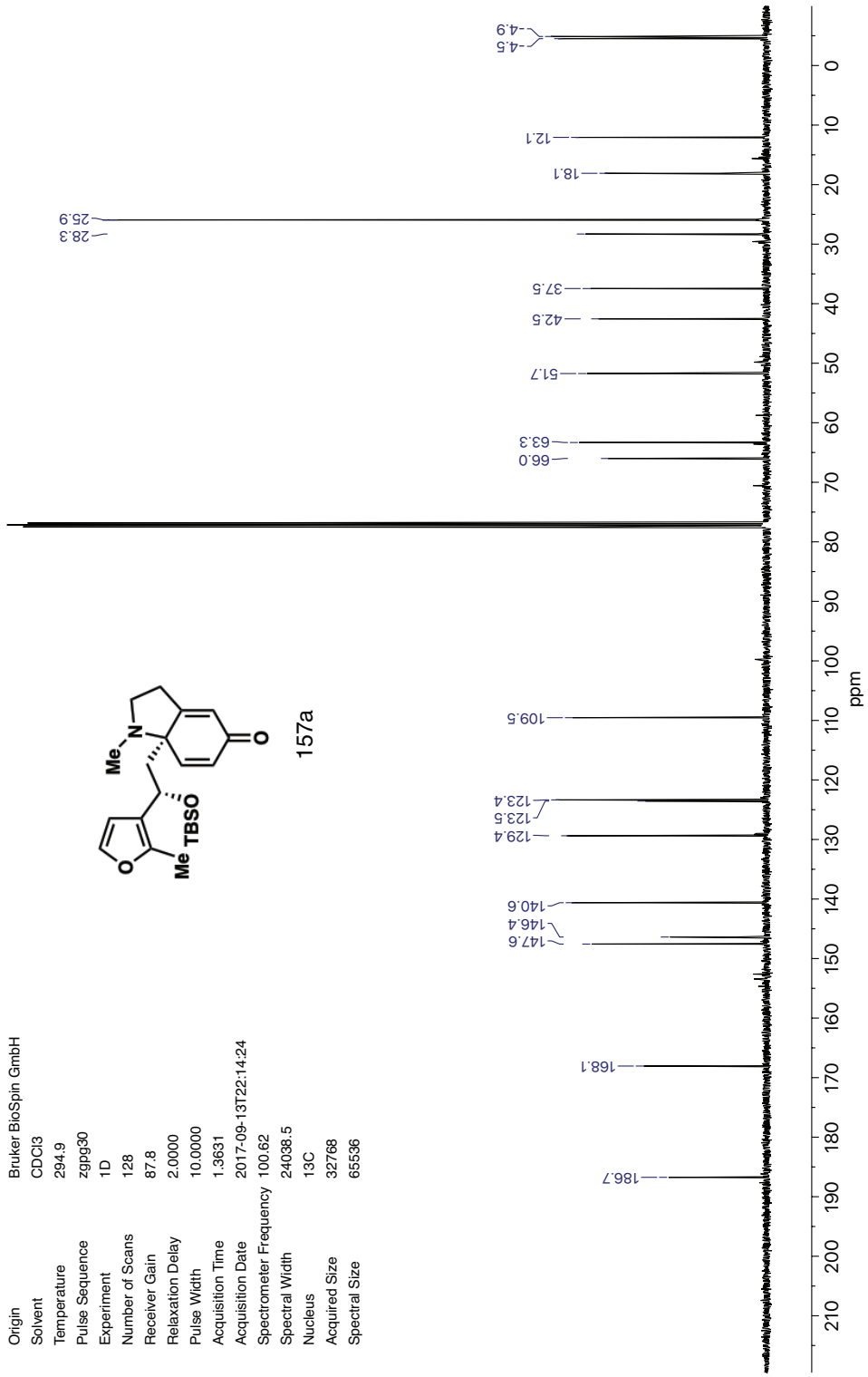

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-94-1/ 4/ fid
Title DCG-5-94-1.4.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 512
Receiver Gain 78.7
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-09-09T06:16:40
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
tBu
O=S
N–Me
Br
TBSO
Me
O
O
155a
-4.7
-4.5
12.3
18.1
24.4
25.8
26.0
46.9
59.5
63.7
66.7
109.4
122.8
128.0
136.2
141.0
147.6
149.8
150.6
183.4
ppm

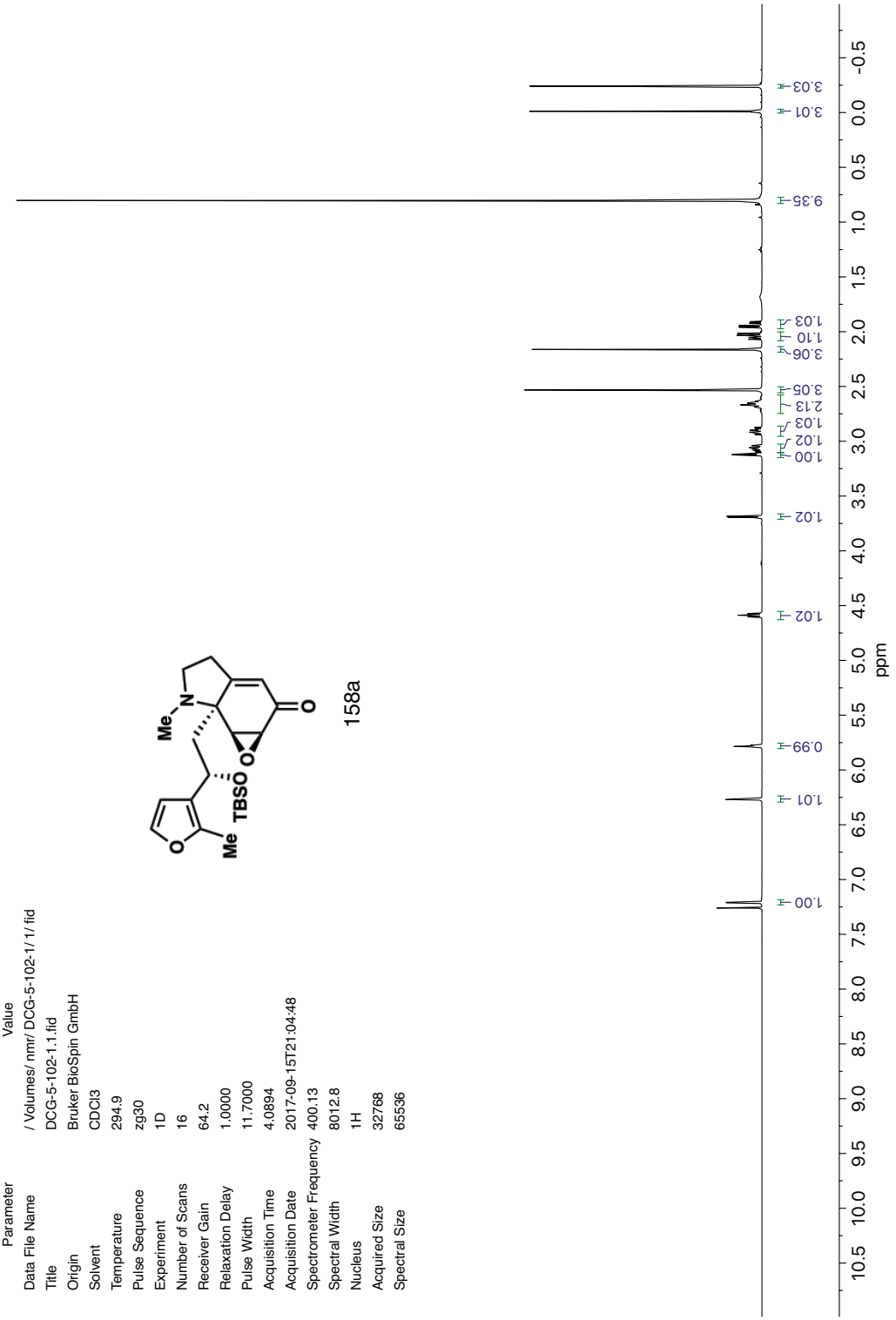

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-96-1/ 1/ fid
Title DCG-5-96-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 30.3
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-09-09T06:21:00
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
O=S
tBu
N–Me
OEt
TBSO
Me
O
156a
1.94
1.00
1.00
1.00
0.99
1.00
0.99
2.20
1.00
0.99
3.04
1.05
3.31
1.00
3.16
9.37
9.02
3.00
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm

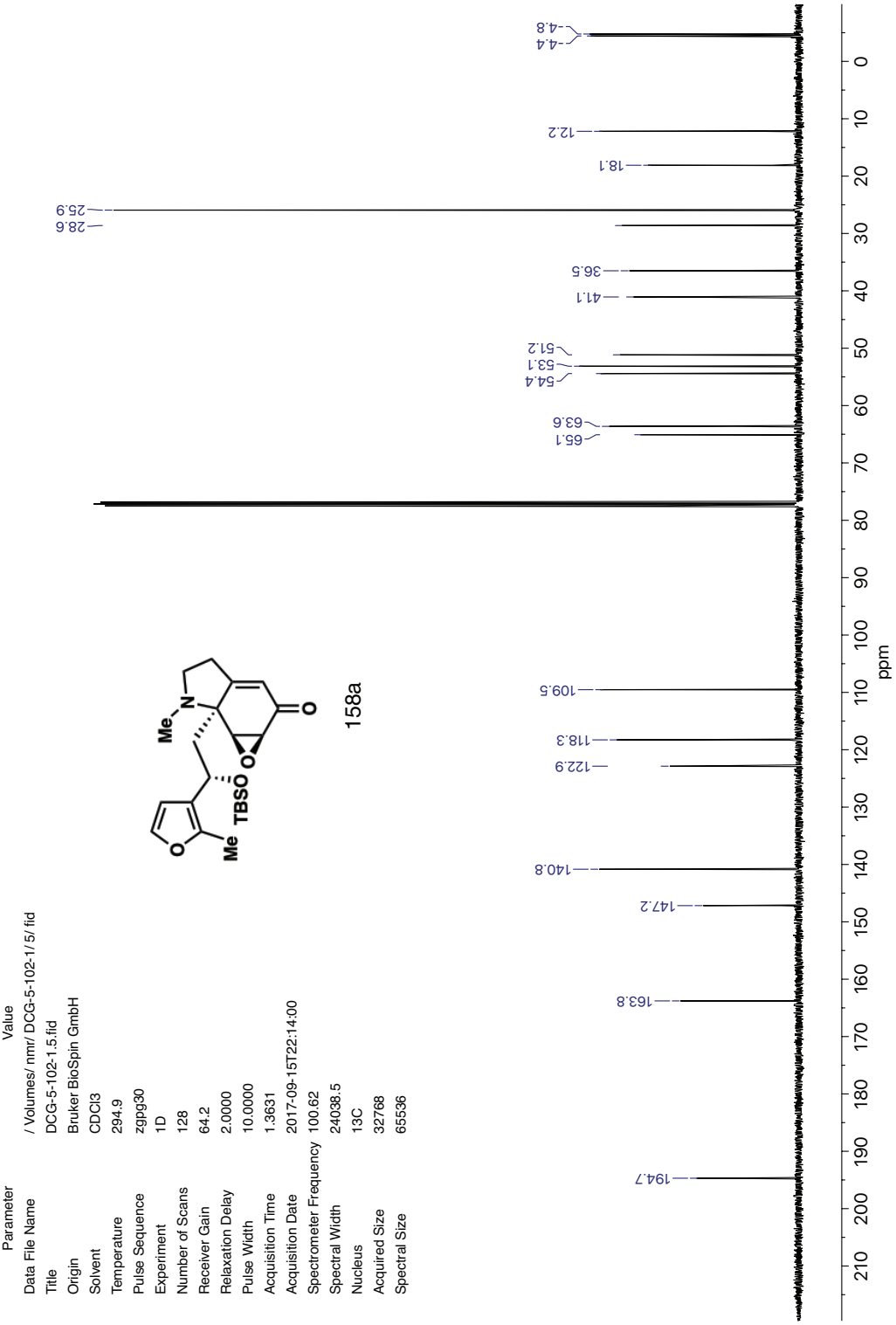


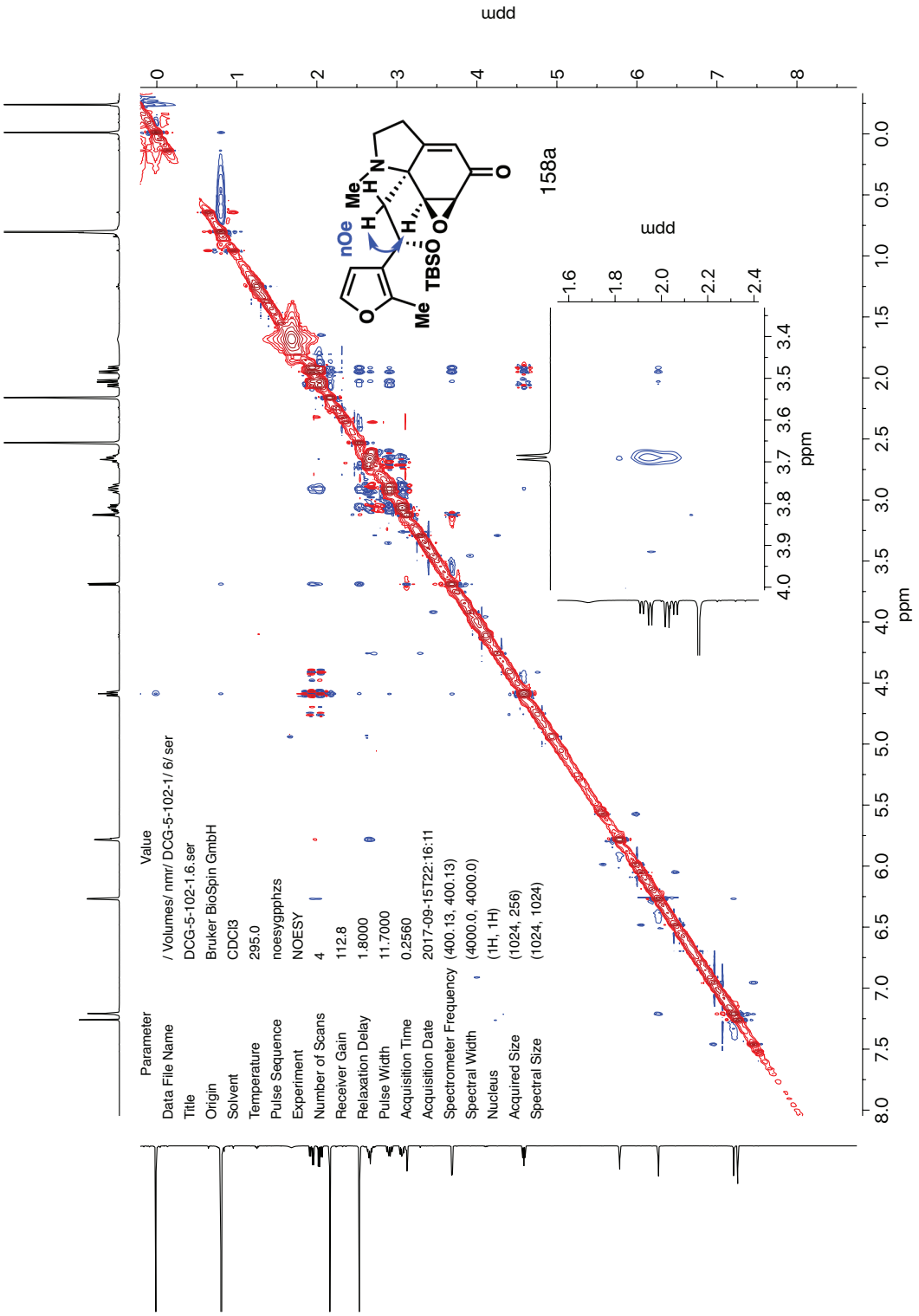
Parameter	Value
Data File Name	/ Volumes/ nmr/ DCG-5-96-1/ 5/ fid
Title	DCG-5-96-1.5.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	128
Receiver Gain	87.8
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2017-09-09T07:30:10
Spectrometer Frequency	100.62
Spectral Width	24038.5
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

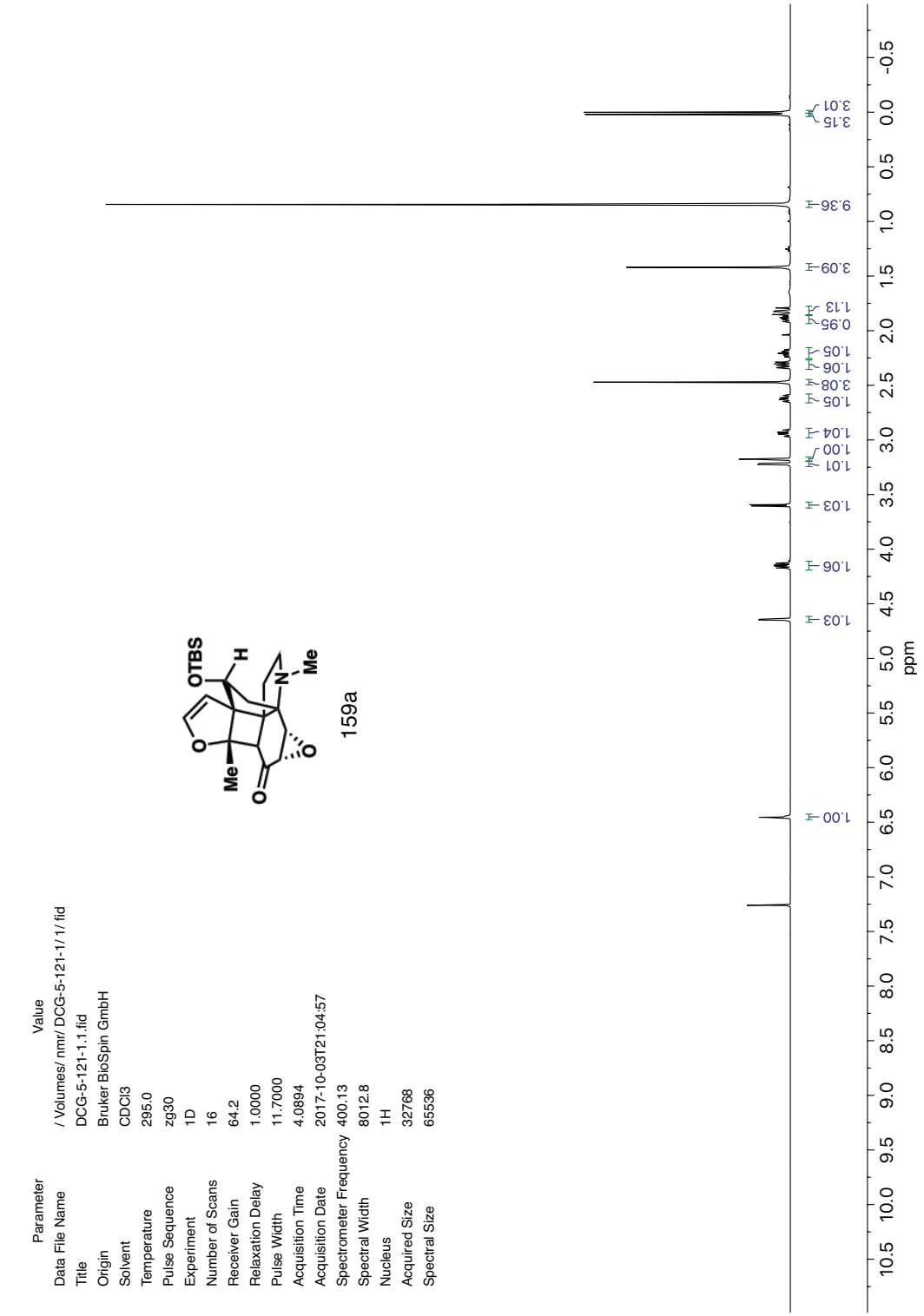

Parameter
Value
Data File Name / Volumes/ nmr/ DCG-5-99-1/ 1/ fid
Title DCG-5-99-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 64.2
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-09-13T21:04:40
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
Me
N
O
Me
TBSO
157a
1.00
1.00
0.97
1.15
0.98
1.02
2.04
1.03
1.11
3.07
3.10
1.11
1.05
9.24
2.96
2.96
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
ppm

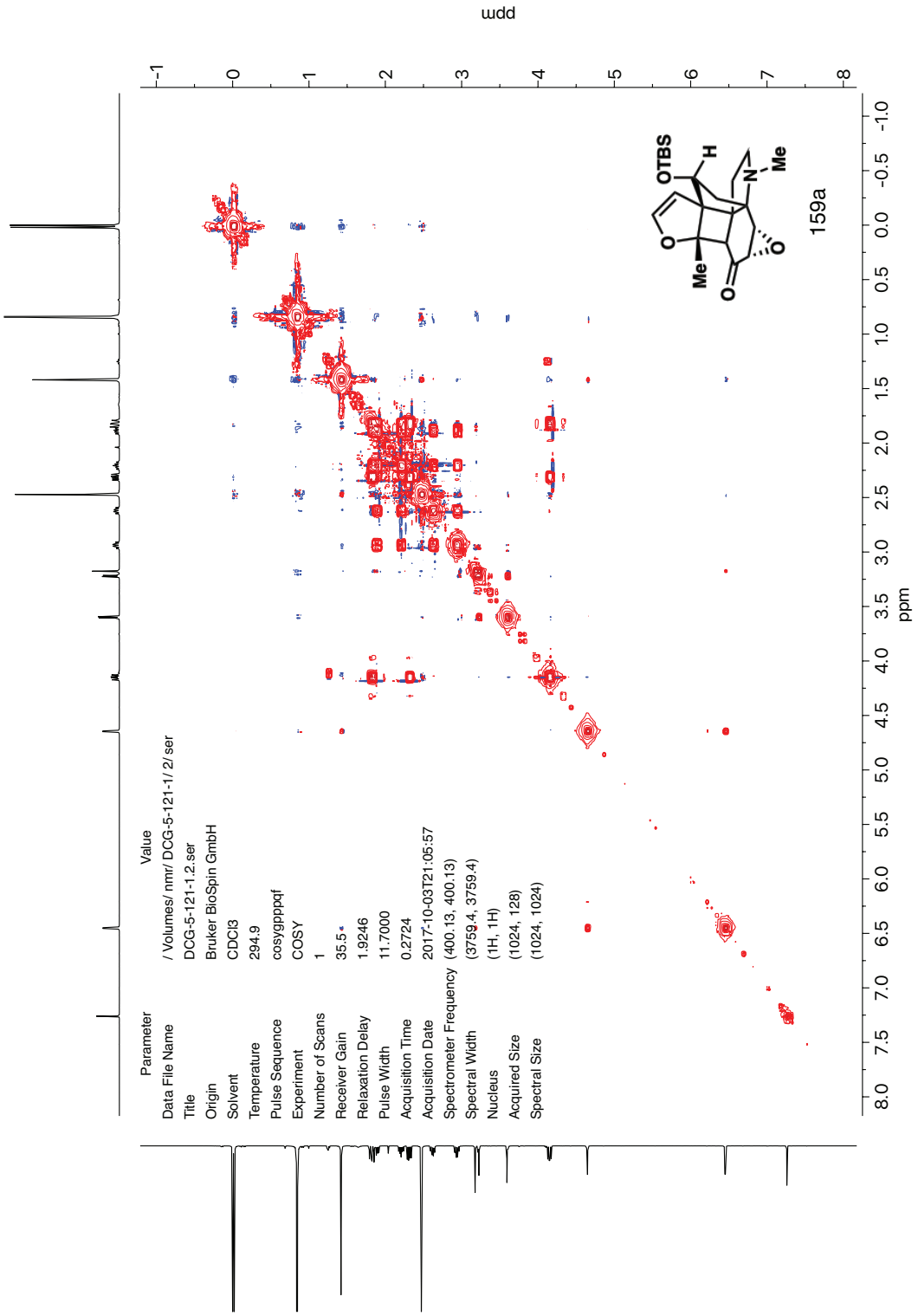

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-99-1/ 5/ fid
Title DCG-5-99-1.5.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 128
Receiver Gain 87.8
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-09-13T22:14:24
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
N
O
Me
TBSO
157a
-4.9
-4.5
12.1
18.1
25.9
28.3
37.5
42.5
51.7
63.3
66.0
109.5
123.4
123.5
129.4
140.6
146.4
147.6
168.1
186.7
ppm

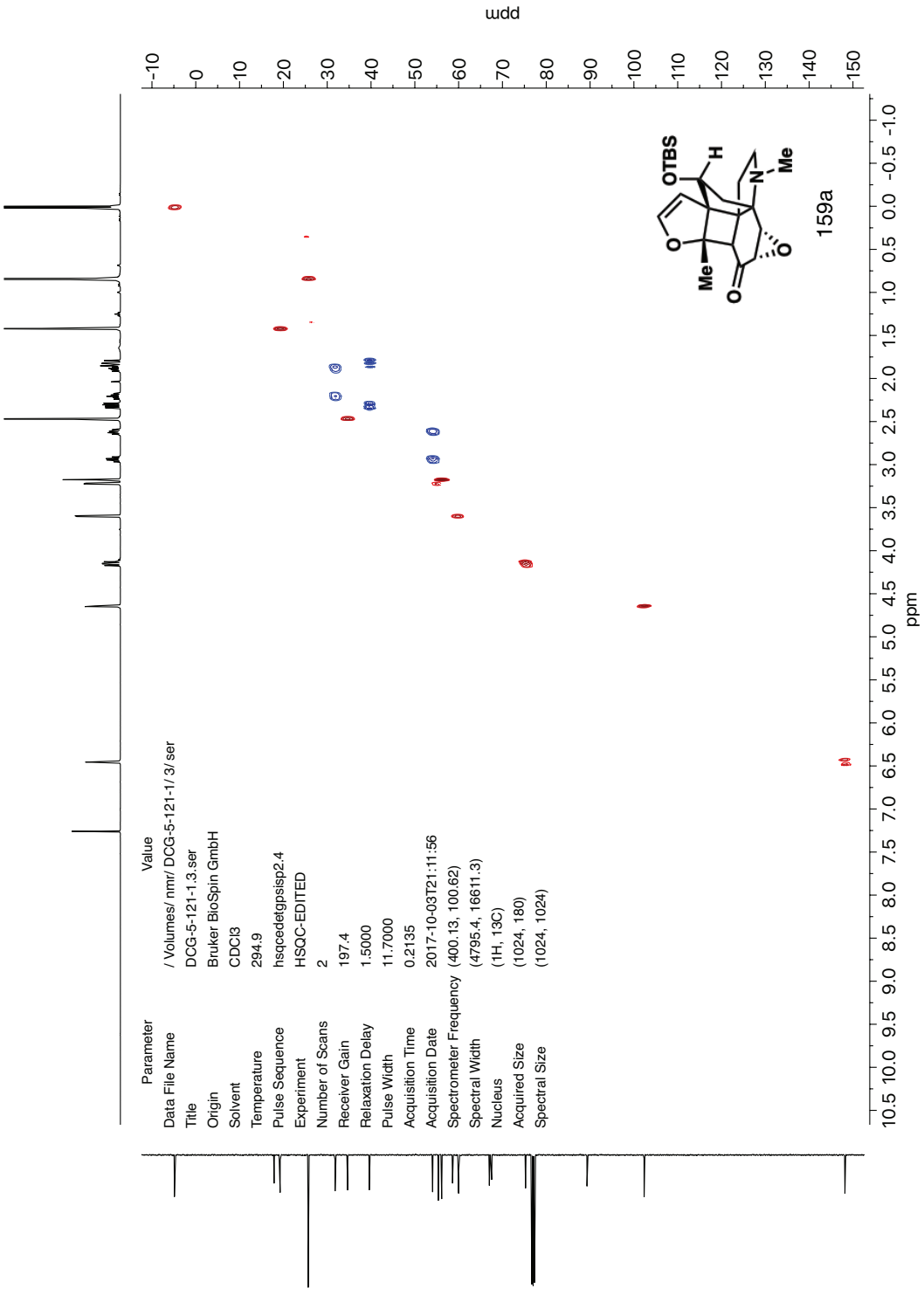

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-102-1/1/ fid
Title DCG-5-102-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 64.2
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-09-15T21:04:48
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
Me
N
TBSO
O
Me
O
158a
1.00
1.01
0.99
1.02
1.02
1.00
1.02
1.03
2.13
3.05
3.06
1.10
1.03
9.35
3.01
3.03
ppm

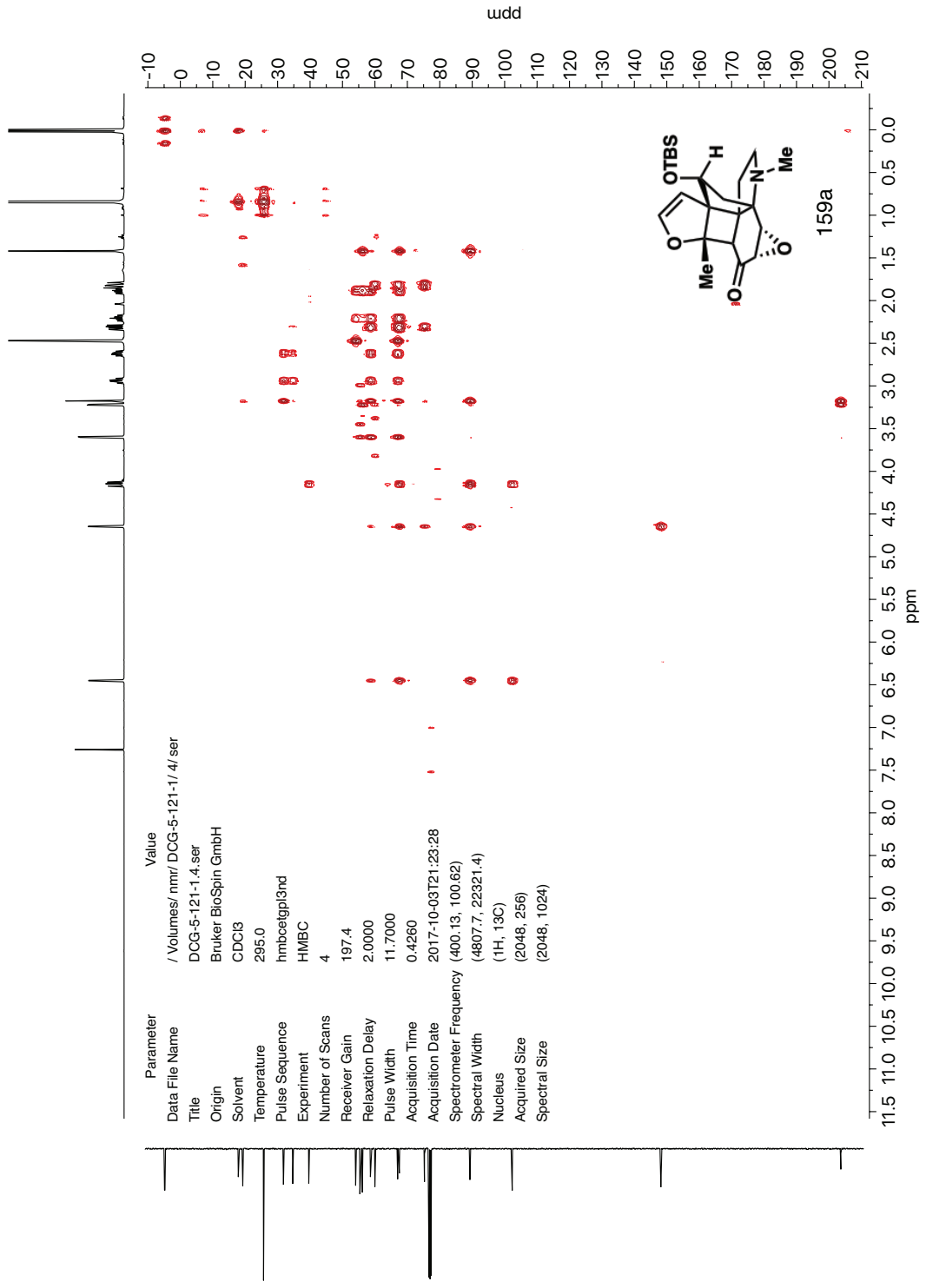

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-102-1/5/ fid
Title DCG-5-102-1.5.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 128
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-09-15T22:14:00
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
N
TBSO
O
Me
O
158a
-4.8
-4.4
12.2
18.1
25.9
28.6
36.5
41.1
51.2
53.1
54.4
63.6
65.1
109.5
118.3
122.9
140.8
147.2
163.8
194.7
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
ppm

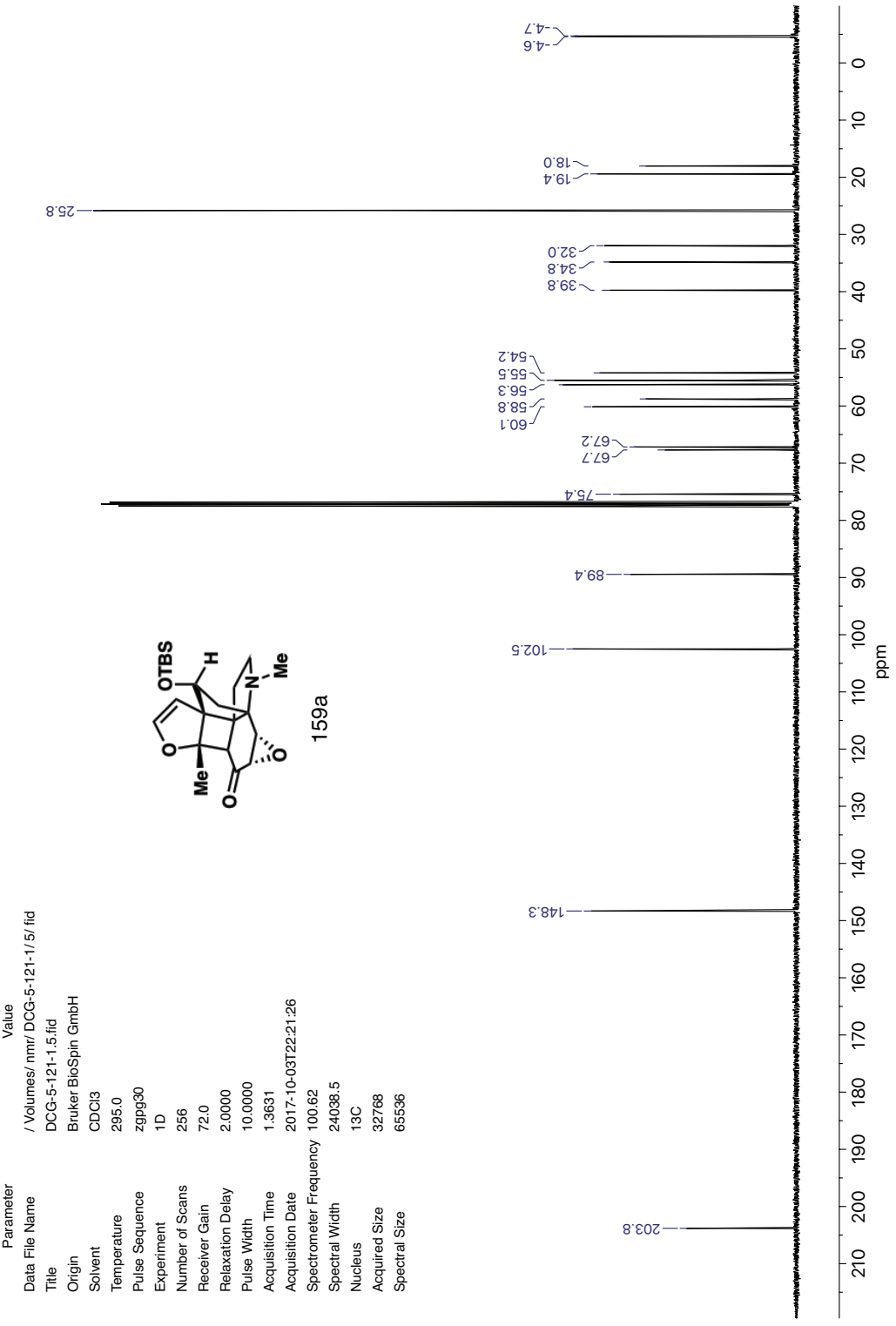

ppm
158a
nOe
Me
TBSO
Me
ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-102-1/ 6/ ser
Title DCG-5-102-1.6.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence noesygpphzs
Experiment NOESY
Number of Scans 4
Receiver Gain 112.8
Relaxation Delay 1.8000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2017-09-15T22:16:11
Spectrometer Frequency (400.13, 400.13)
Spectral Width (4000.0, 4000.0)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)


Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-121-1/1/ fid
Title DCG-5-121-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 64.2
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-10-03T21:04:57
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
OTBS
H
N
Me
Me
O
O
O
159a
1.00
1.03
1.06
1.03
1.01
1.00
1.04
1.05
3.08
1.06
1.05
0.95
1.13
3.09
9.36
3.15
3.01
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm

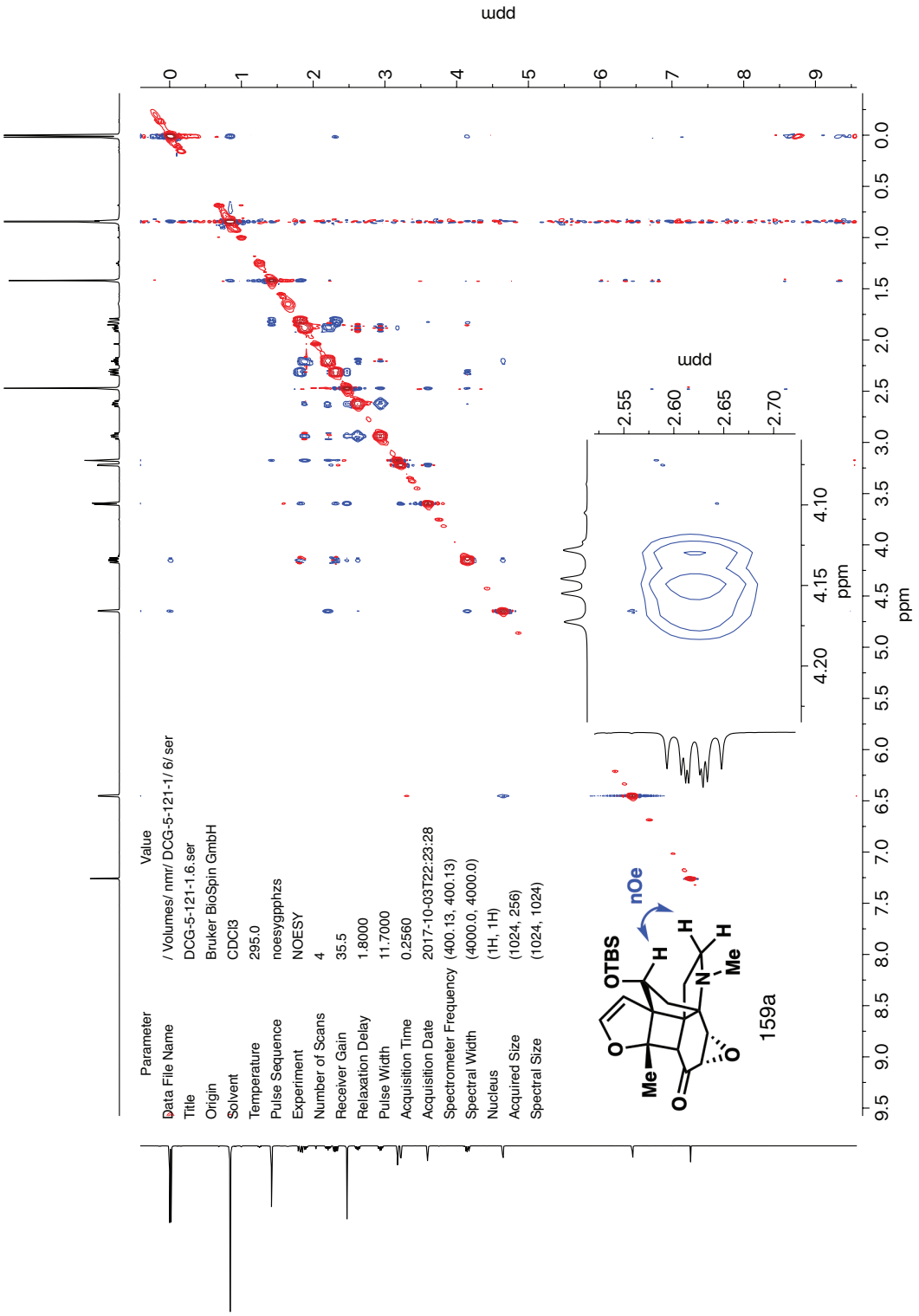

ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-121-1/ 2/ ser
Title DCG-5-121-1.2.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 35.5
Relaxation Delay 1.9246
Pulse Width 11.7000
Acquisition Time 0.2724
Acquisition Date 2017-10-03T21:05:57
Spectrometer Frequency (400.13, 400.13)
Spectral Width (3759.4, 3759.4)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)
OTBS
H
N
Me
Me
O
O
O
159a
ppm

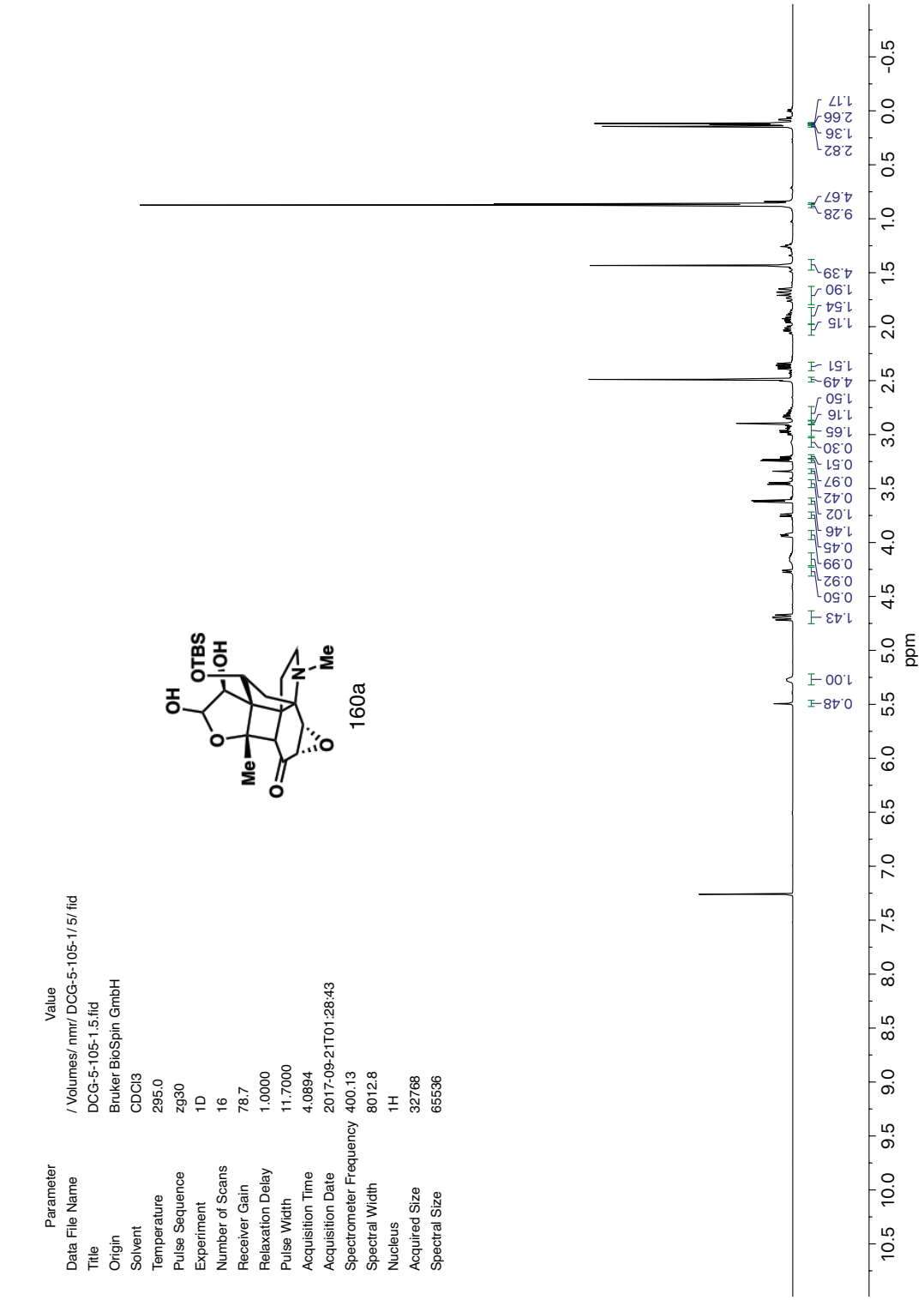

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-121-1/ 3/ ser
Title DCG-5-121-1.3.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2017-10-03T21:11:56
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 180)
Spectral Size (1024, 1024)
OTBS
H
N
Me
Me
O
O
O
159a
ppm
ppm

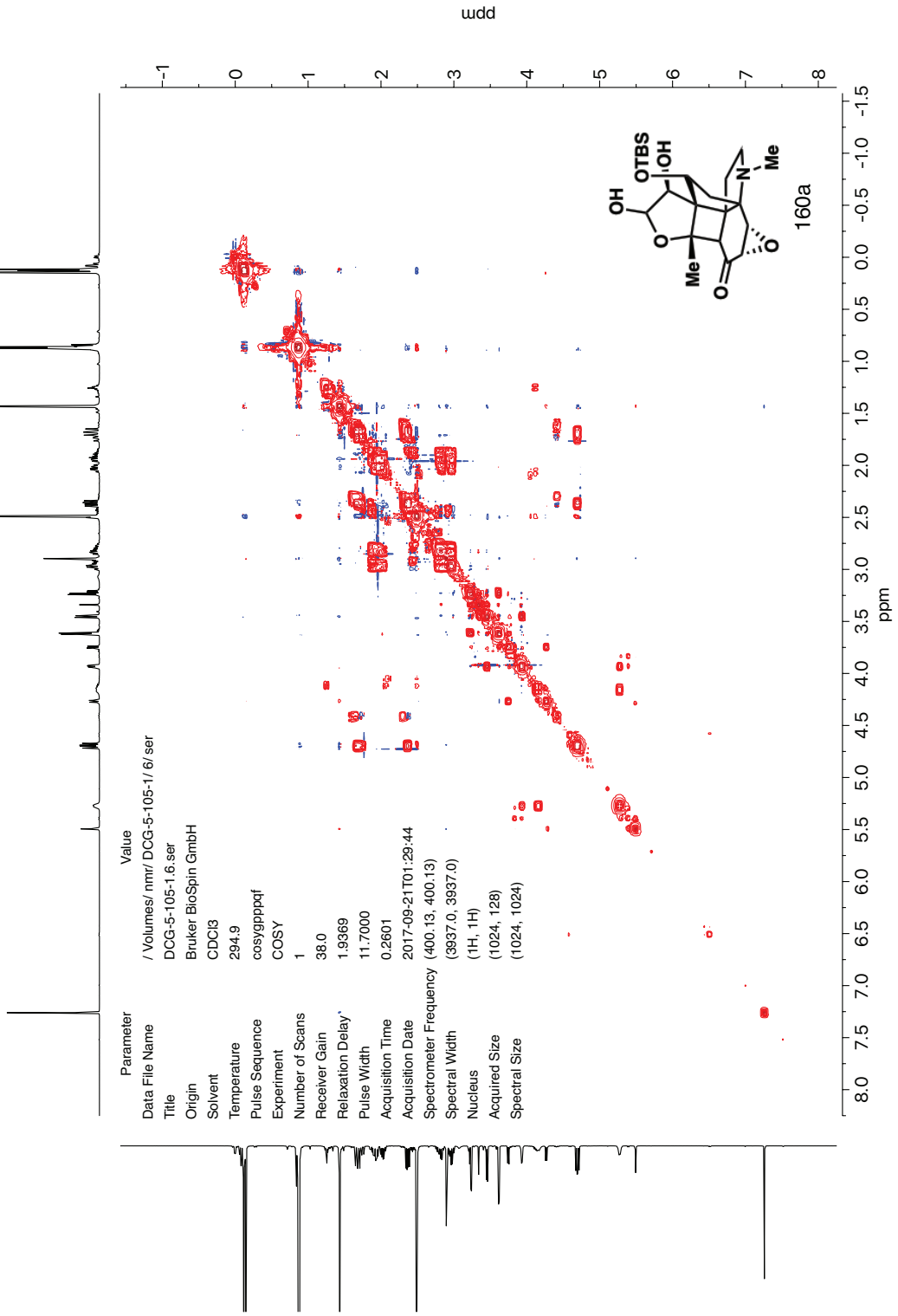

ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-121-1/ 4/ ser
Title DCG-5-121-1.4.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2017-10-03T21:23:28
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
OTBS
H
N
Me
Me
O
O
O
159a
ppm

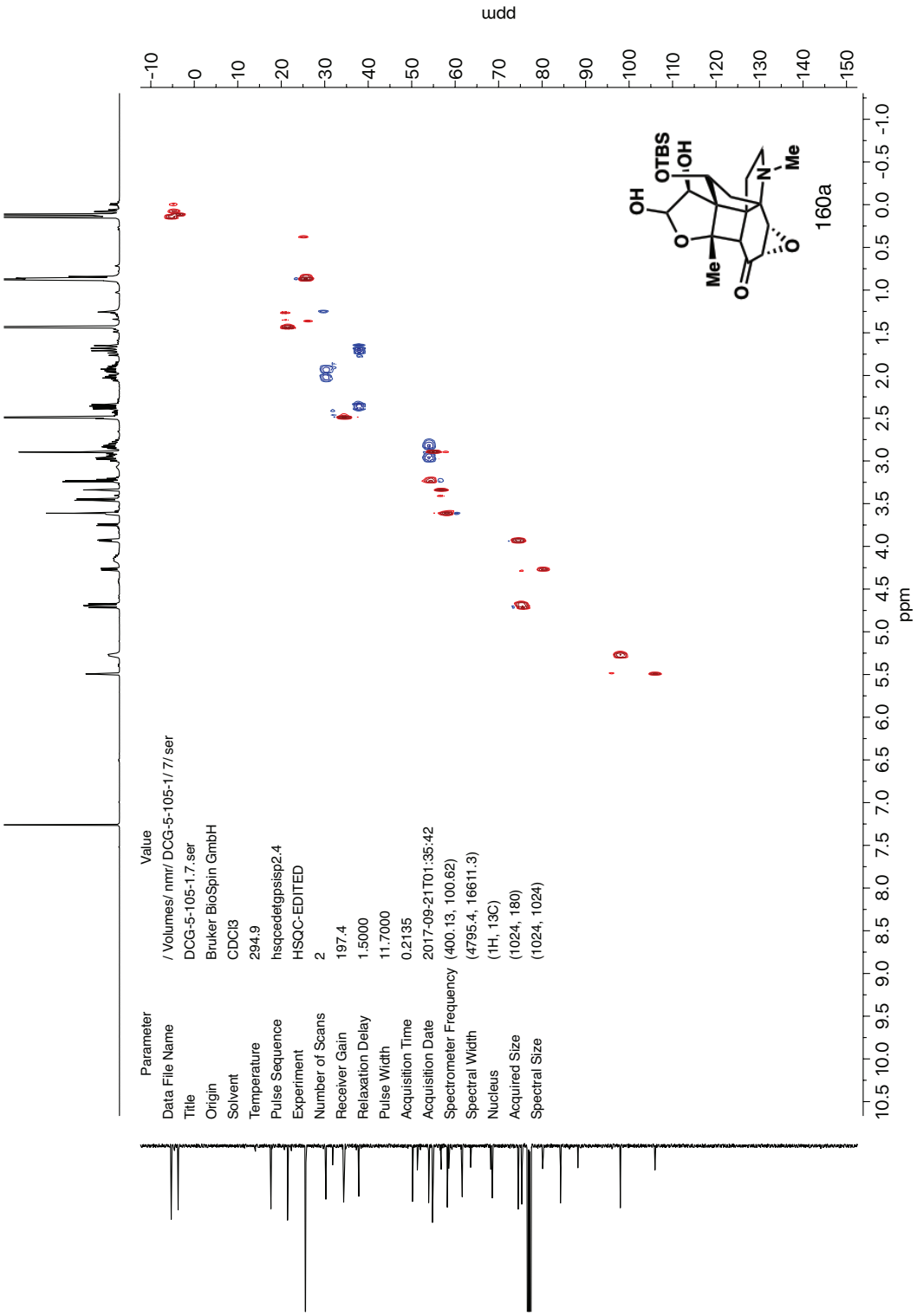


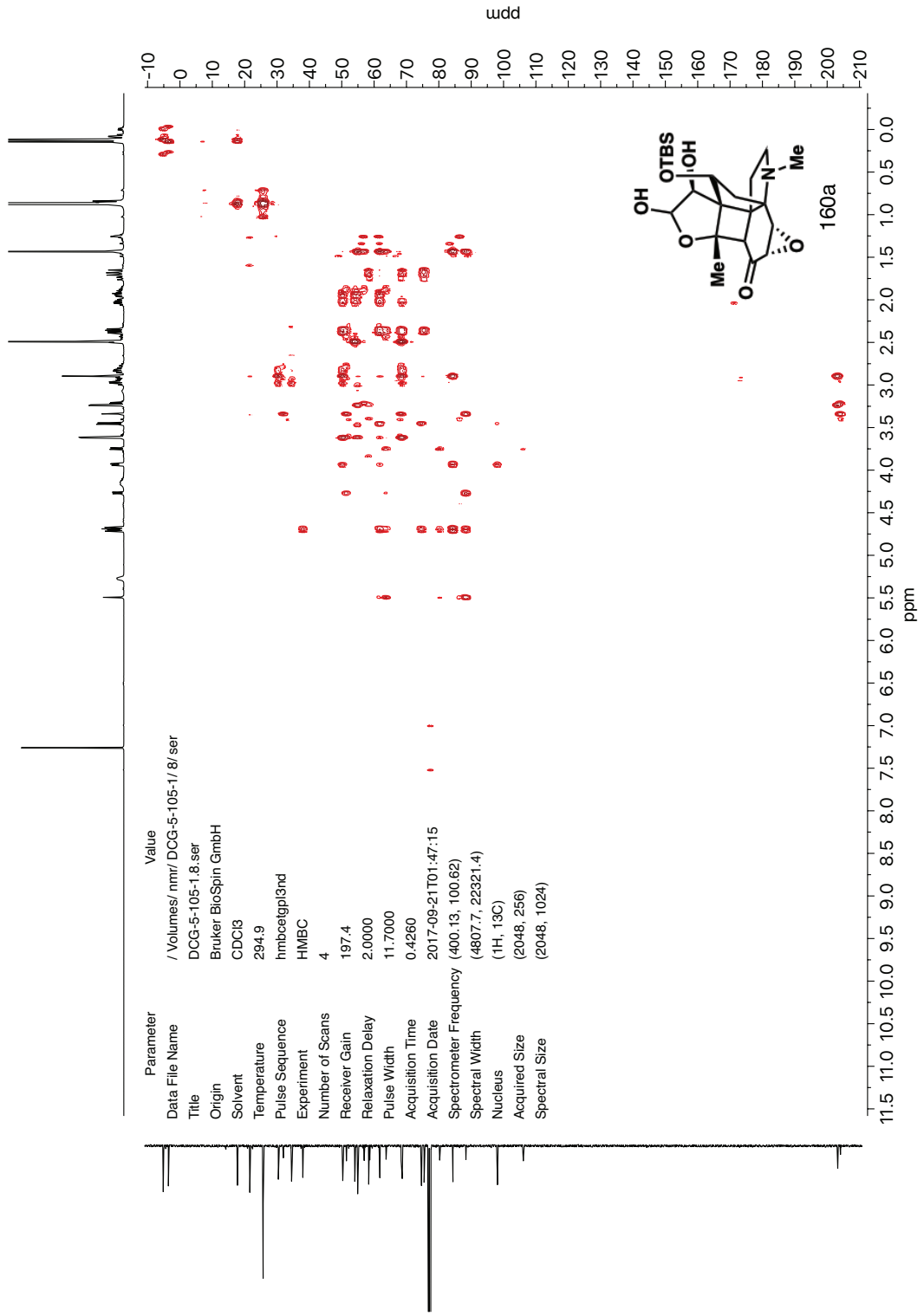
Parameter	Value
Data File Name	/ Volumes/ nmr/ DCG-5-121-1/5/ fid
Title	DCG-5-121-1.5.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	256
Receiver Gain	72.0
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2017-10-03T22:21:26
Spectrometer Frequency	100.62
Spectral Width	24038.5
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

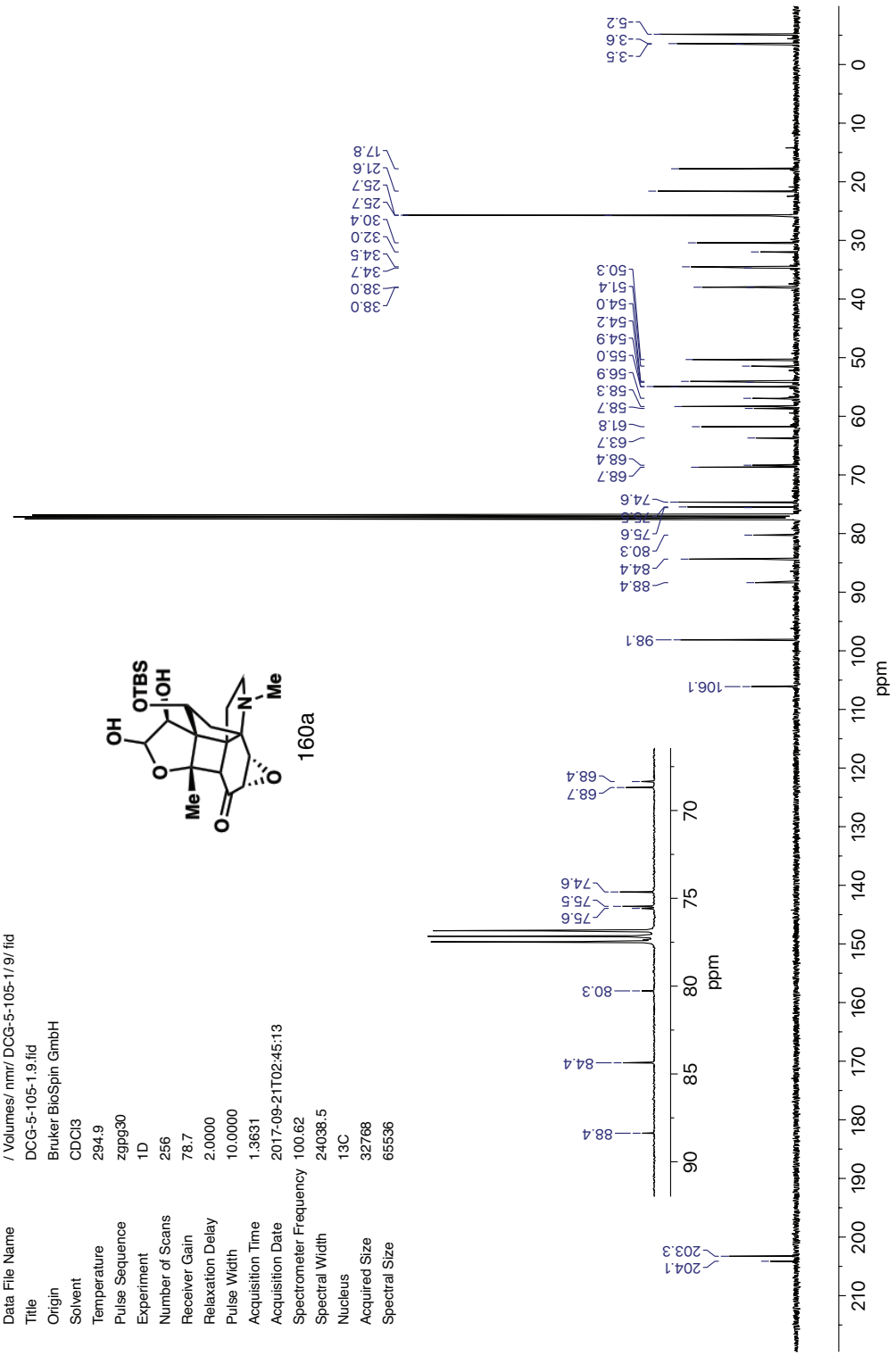

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-121-1/ 6/ ser
Title DCG-5-121-1.6.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence noesygpphzs
Experiment NOESY
Number of Scans 4
Receiver Gain 35.5
Relaxation Delay 1.8000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2017-10-03T22:23:28
Spectrometer Frequency (400.13, 400.13)
Spectral Width (4000.0, 4000.0)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
ppm
OTBS
nOe
Me
H
N
Me
O
159a


Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-105-1/5/ fid
Title DCG-5-105-1.5.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 78.7
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-09-21T01:28:43
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
OH
OTBS
OH
Me
Me
O
O
O
N
160a
ppm


ppm
ppm
OH
OTBS
OH
Me
N
O
Me
O
O
160a
Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-105-1/ 6/ ser
Title DCG-5-105-1.6.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 38.0
Relaxation Delay 1.9369
Pulse Width 11.7000
Acquisition Time 0.2601
Acquisition Date 2017-09-21T01:29:44
Spectrometer Frequency (400.13, 400.13)
Spectral Width (3937.0, 3937.0)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)


Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-105-1/ 7/ ser
Title DCG-5-105-1.7.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2017-09-21T01:35:42
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 180)
Spectral Size (1024, 1024)
ppm
OH
OTBS
OH
Me
N
Me
O
O
O
160a


ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-105-1/ 8/ ser
Title DCG-5-105-1.8.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2017-09-21T01:47:15
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
OH
OTBS
OH
Me
Me
160a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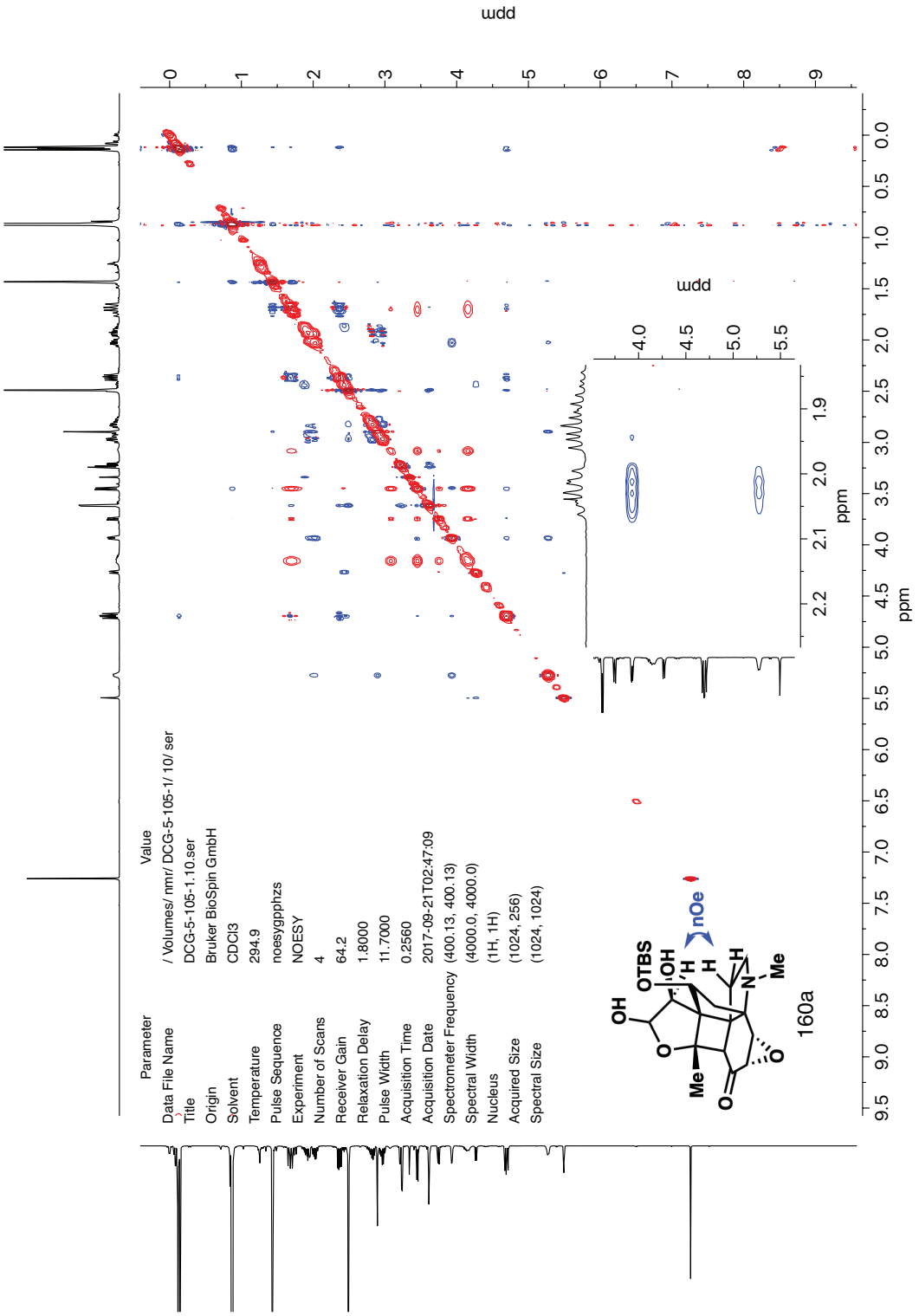
Title DCG-5-105-1.9.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 78.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-09-21T02:45:13
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OH
OTBS
OH
Me
N
Me
O
O
O
160a
ppm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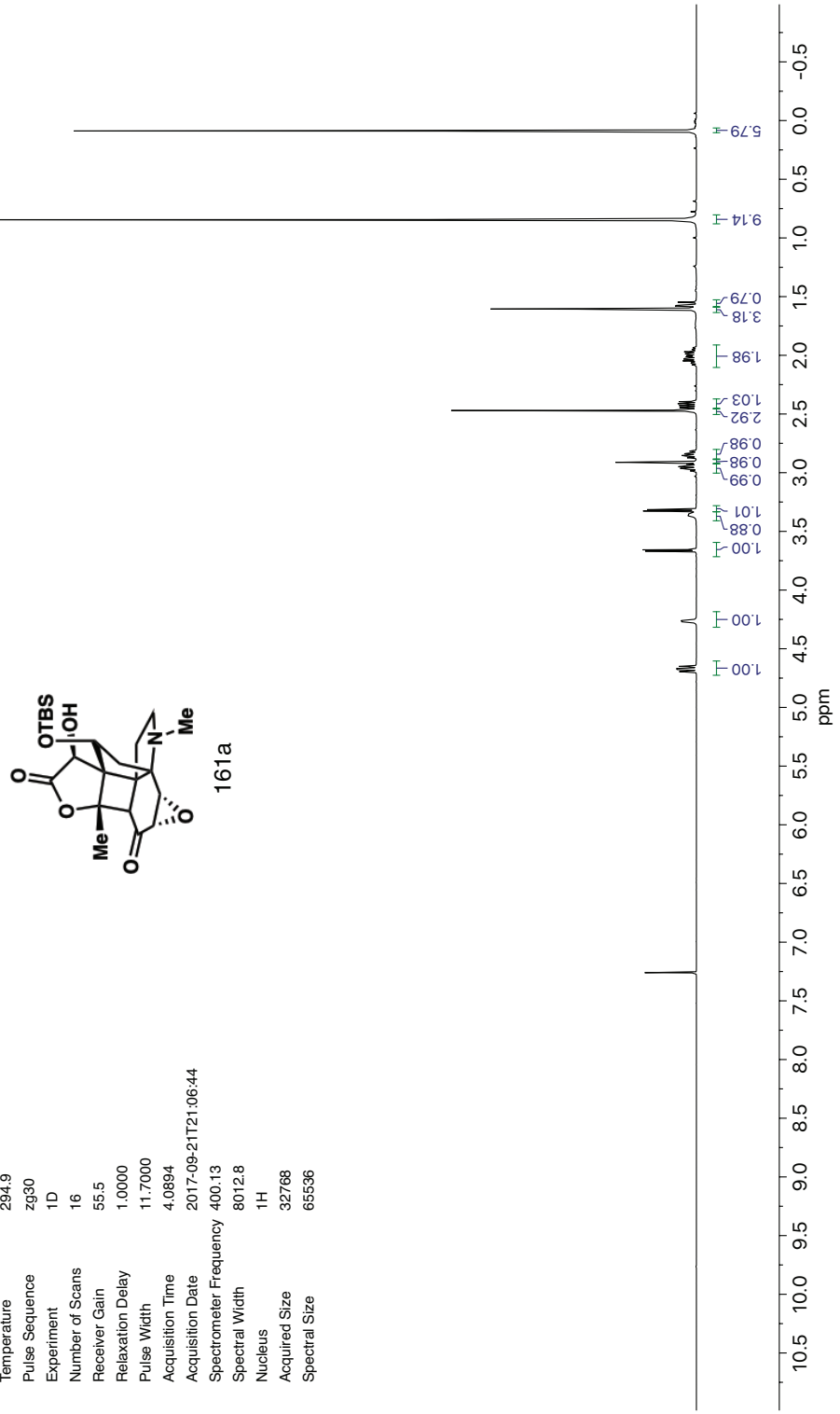
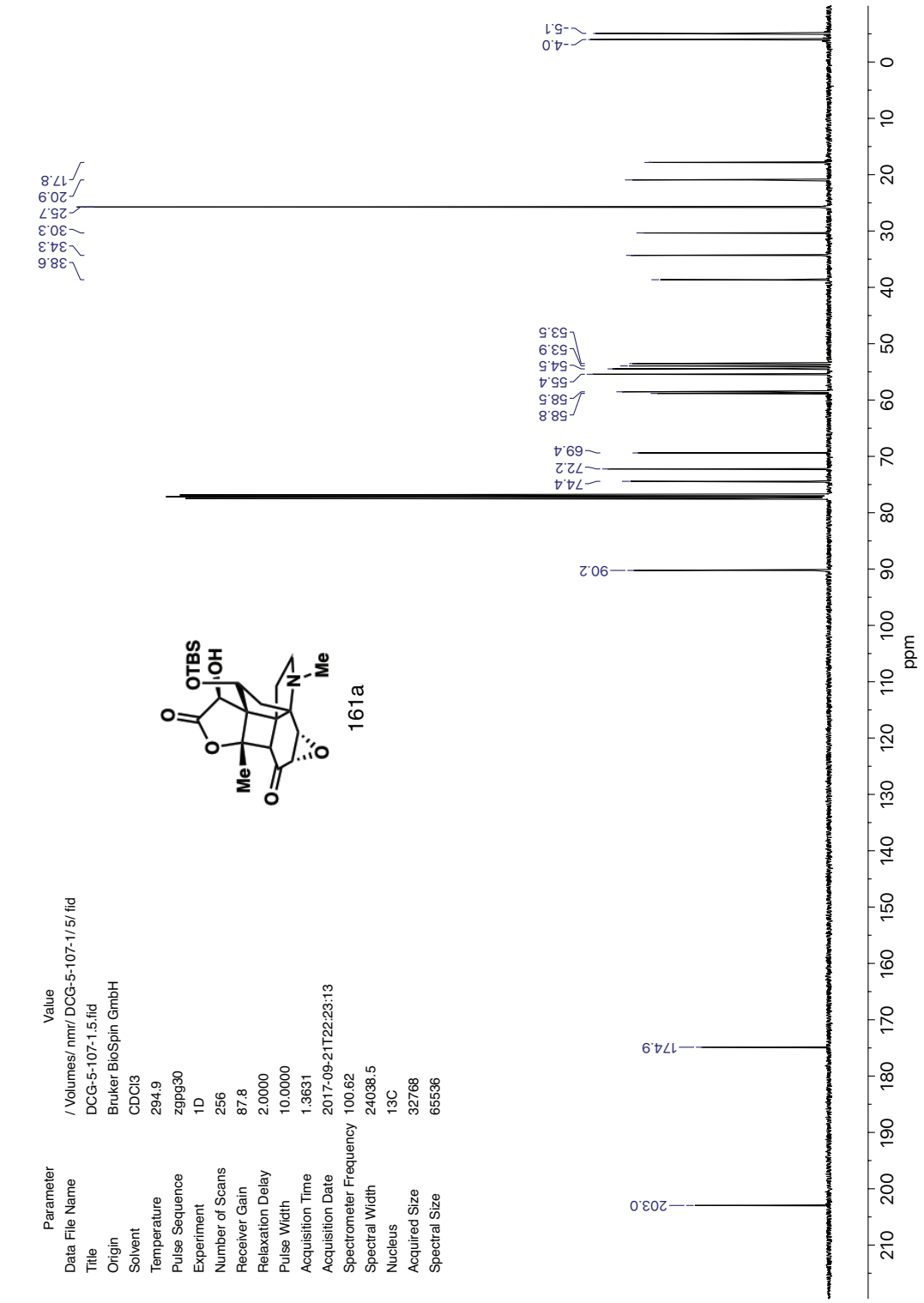
Title DCG-5-105-1.10.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence noesygpphzs
Experiment NOESY
Number of Scans 4
Receiver Gain 64.2
Relaxation Delay 1.8000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2017-09-21T02:47:09
Spectrometer Frequency (400.13, 400.13)
Spectral Width (4000.0, 4000.0)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
ppm
OH
OTBS
OH
H
H
nOe
Me
O
O
N
H
Me
O
160a


Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-107-1/1/ fid
Title DCG-5-107-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 55.5
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-09-21T21:06:44
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
OTBS
OH
Me
Me
N
O
O
O
O
O
161a
1.00
1.00
1.00
0.88
1.01
0.99
0.98
0.98
2.92
1.03
1.98
3.18
0.79
9.14
5.79
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm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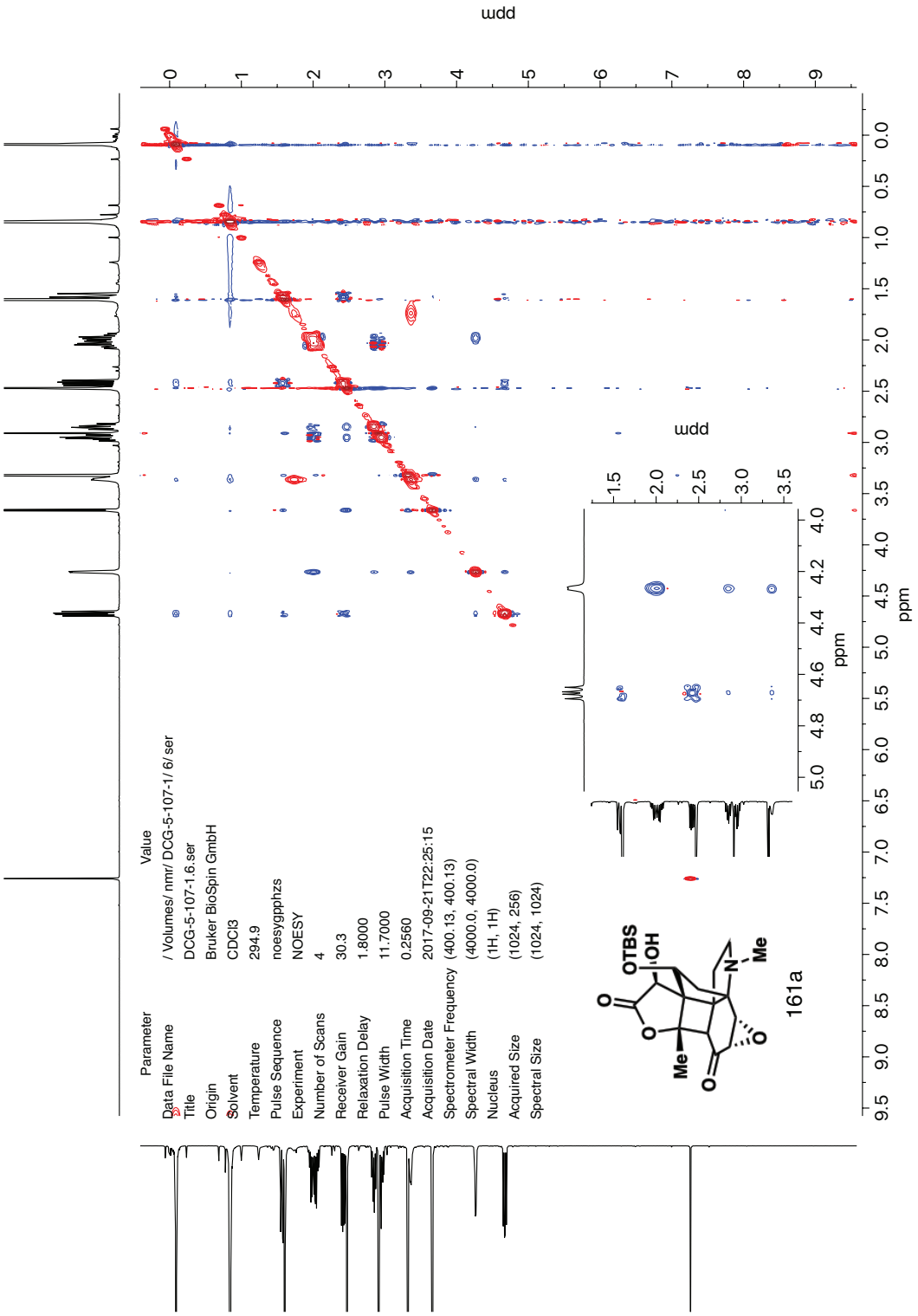
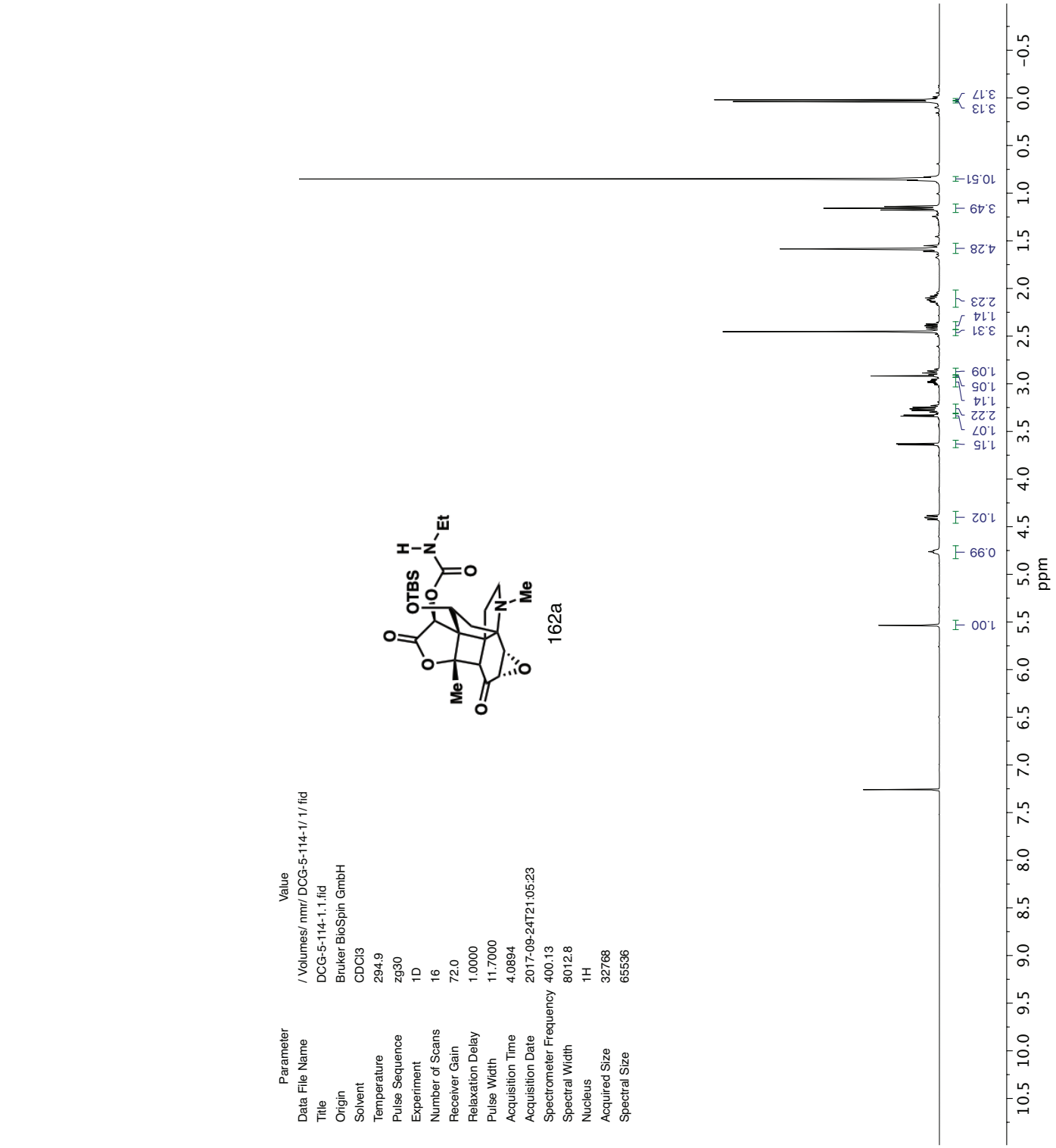
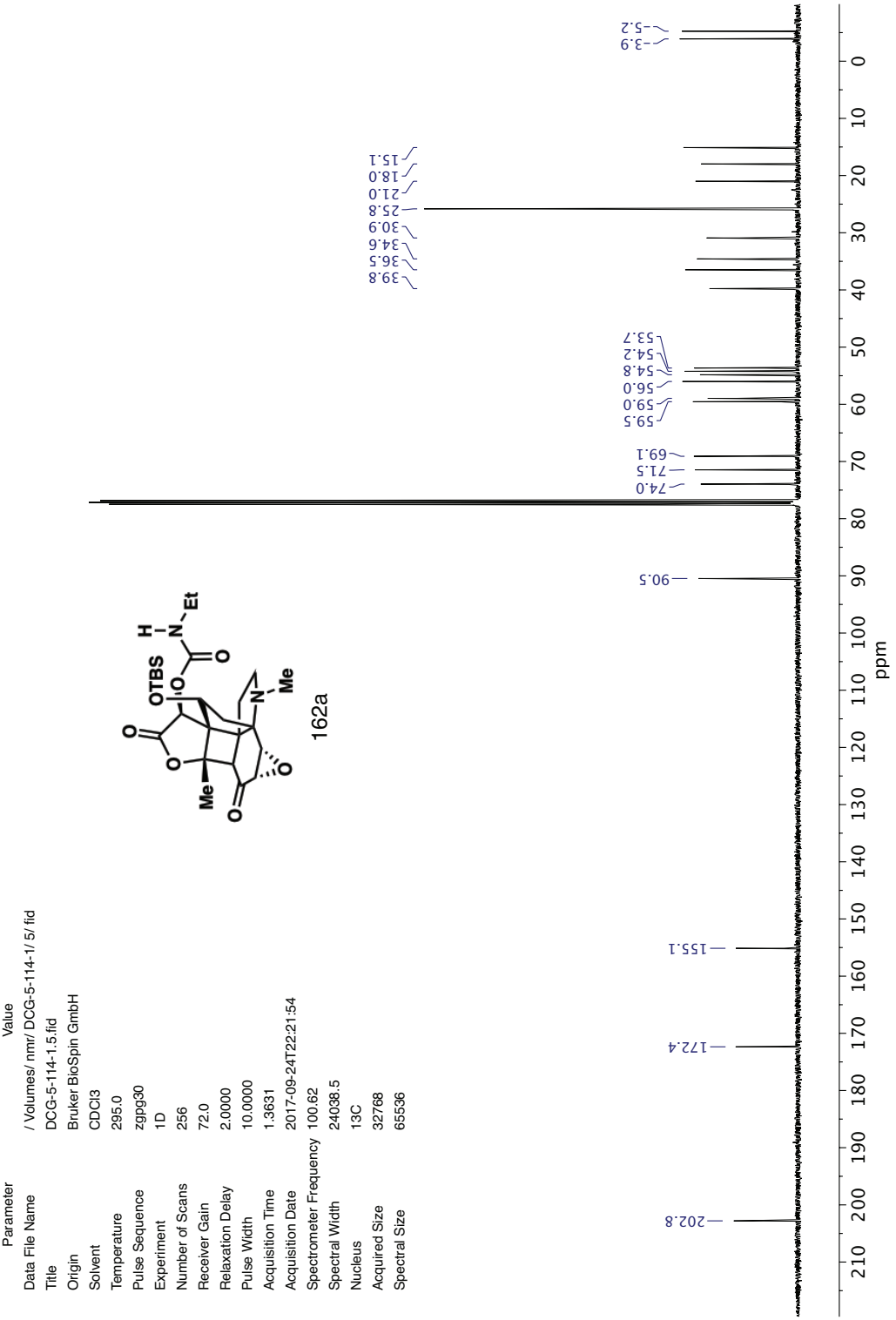
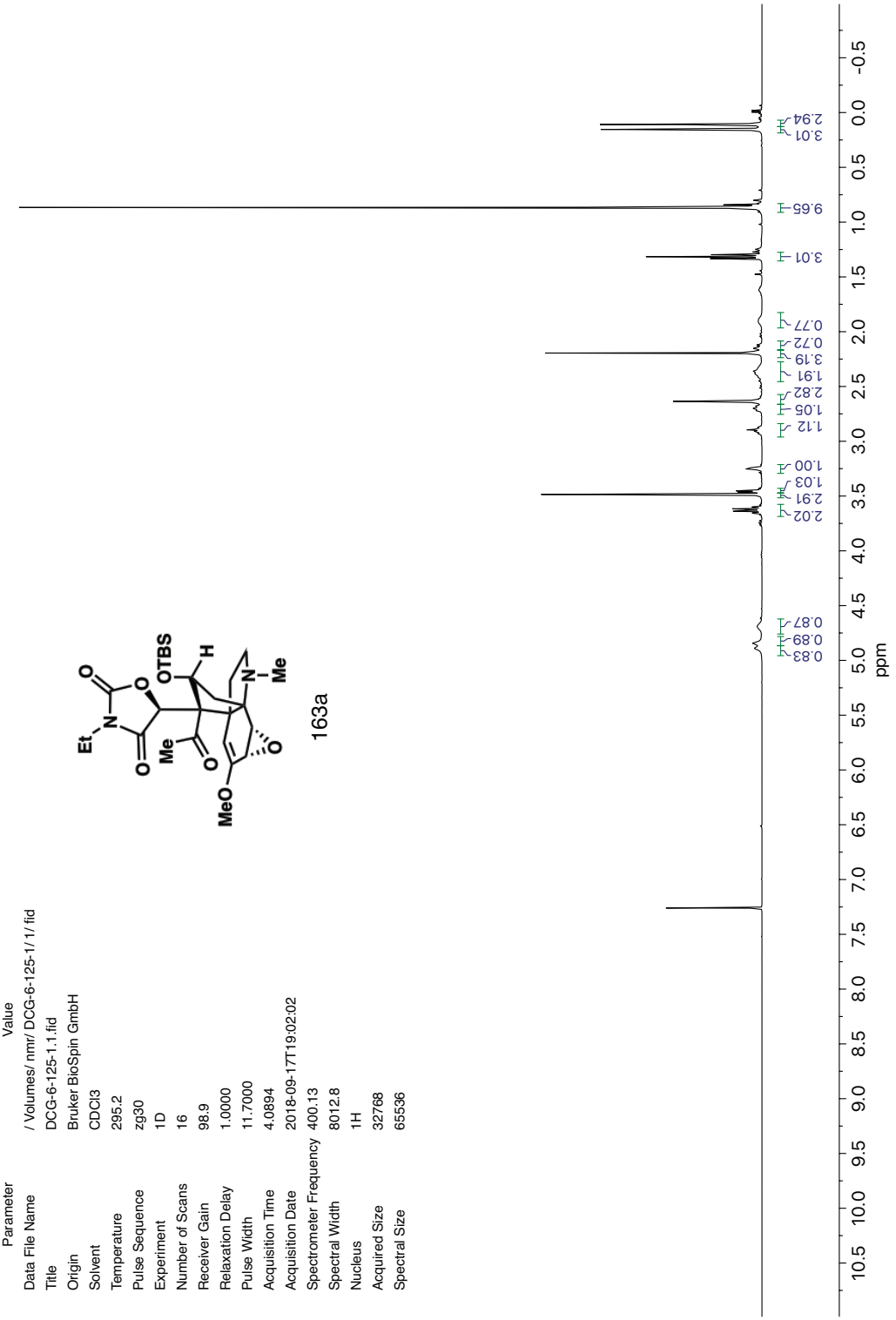
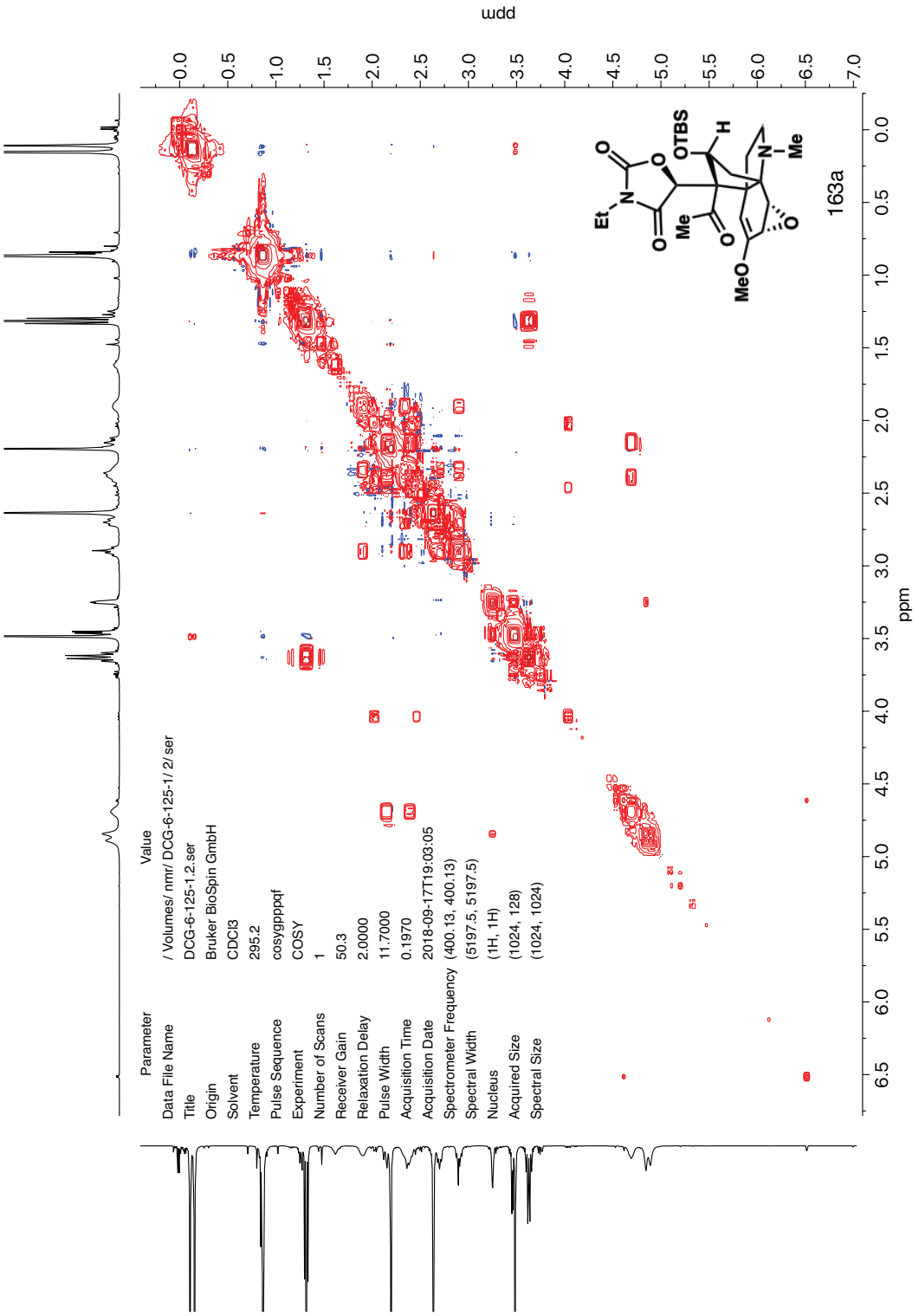
Title DCG-5-107-1.5.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 87.8
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-09-21T22:23:13
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OTBS
OH
Me
Me
O
O
O
O
O
N
161a
203.0
174.9
90.2
74.4
72.2
69.4
58.8
58.5
55.4
54.5
53.9
53.5
38.6
34.3
30.3
25.7
20.9
17.8
-4.0
-5.1
ppm

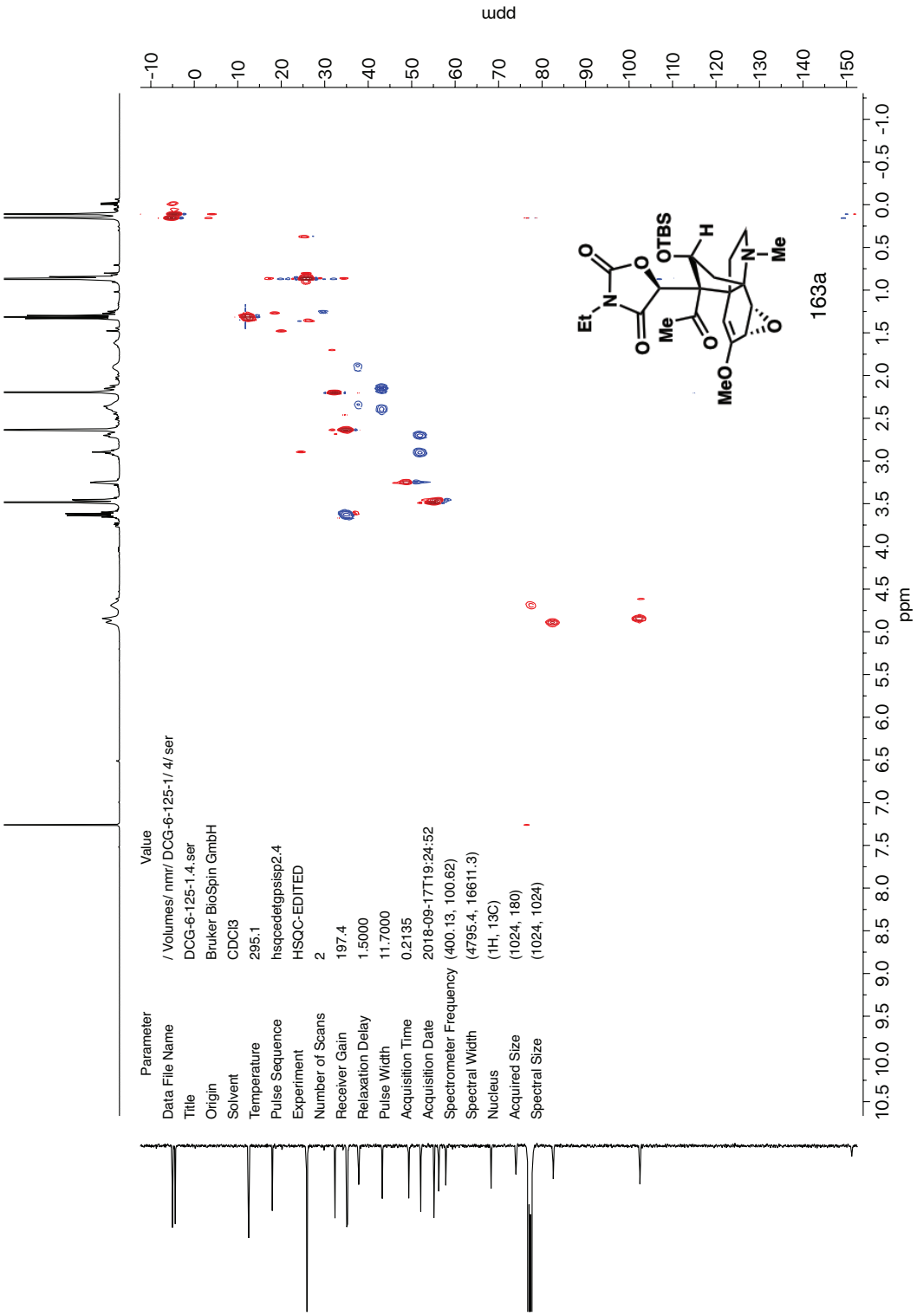

ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-107-1/ 6/ ser
Title DCG-5-107-1.6.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence noesygpphzs
Experiment NOESY
Number of Scans 4
Receiver Gain 30.3
Relaxation Delay 1.8000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2017-09-21T22:25:15
Spectrometer Frequency (400.13, 400.13)
Spectral Width (4000.0, 4000.0)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
OTBS
OH
Me
Me
O
O
O
O
N
161a

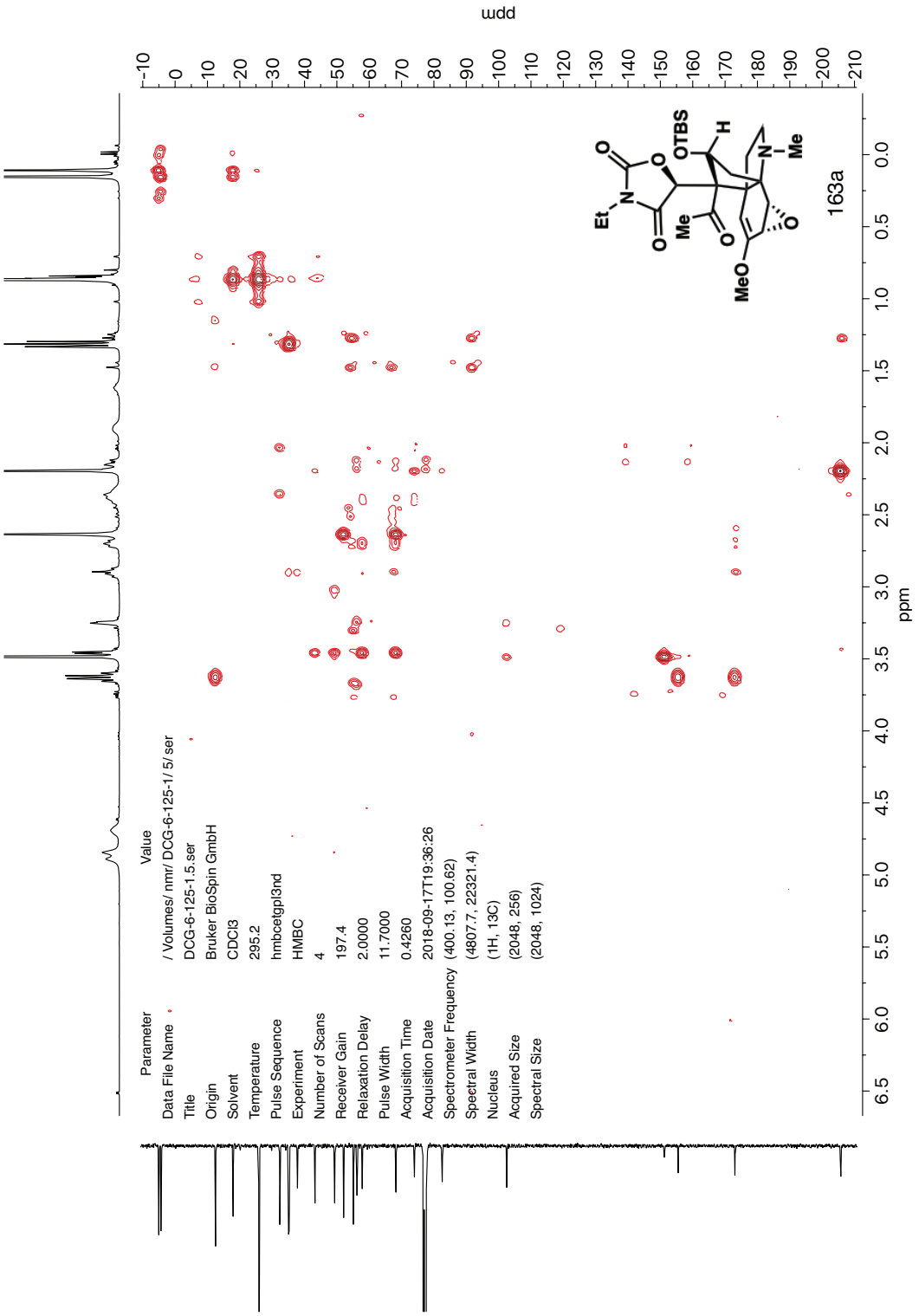

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-114-1/ 1/ fid
Title DCG-5-114-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 72.0
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-09-24T21:05:23
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
OTBS
H
N
Et
O
O
O
O
Me
N
Me
O
O
O
Me
162a
1.00
0.99
1.02
1.15
1.07
2.22
1.14
1.05
1.09
3.31
1.14
2.23
4.28
3.49
10.51
3.13
3.17
ppm

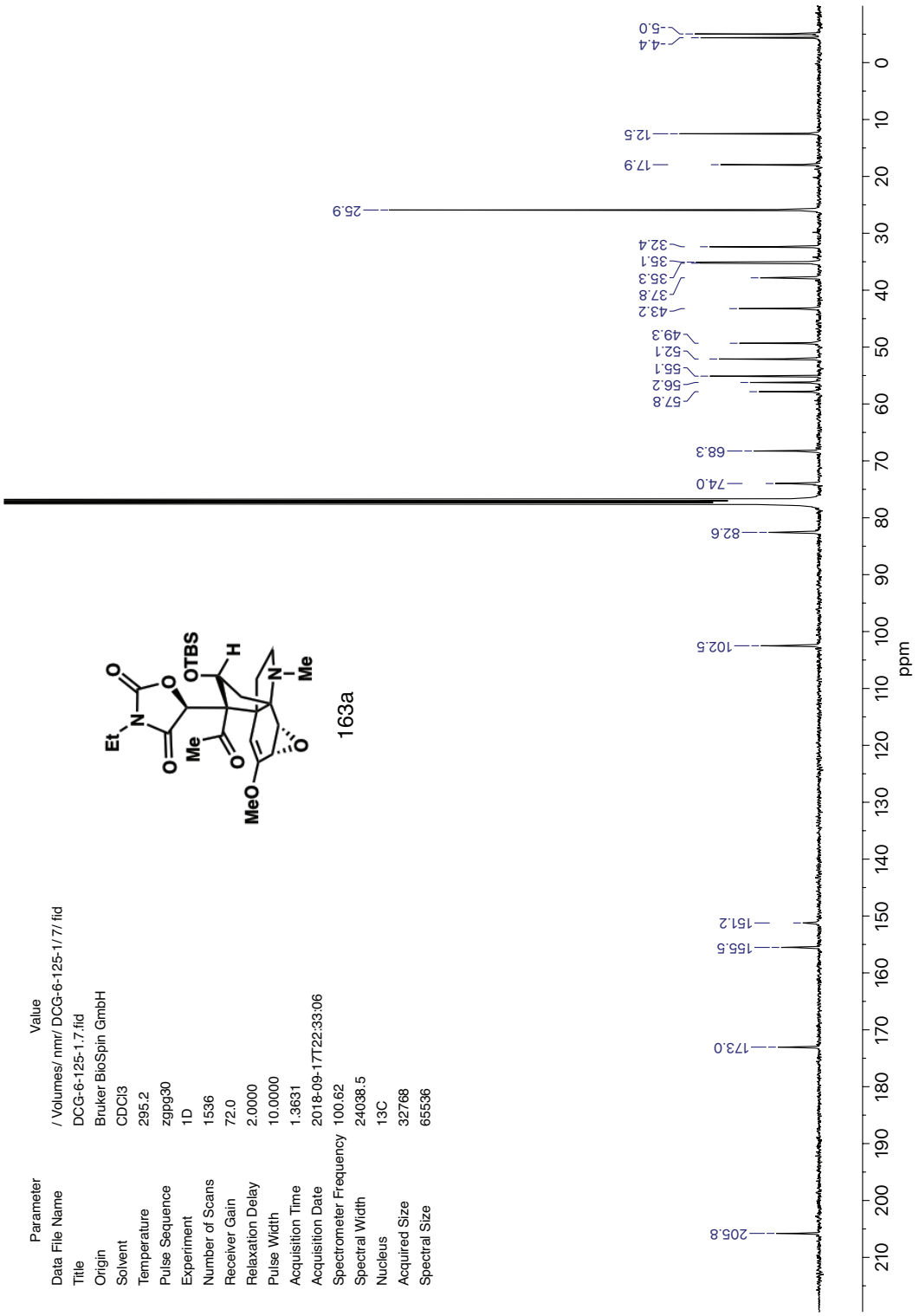

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-114-1/ 5/ fid
Title DCG-5-114-1.5.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-09-24T22:21:54
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OTBS
H
N
Et
O
O
O
O
Me
N
Me
O
O
O
O
162a
202.8
172.4
155.1
90.5
74.0
71.5
69.1
59.5
59.0
56.0
54.8
54.2
53.7
39.8
36.5
34.6
30.9
25.8
21.0
18.0
15.1
3.9
-5.2
ppm


Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-125-1/1/ fid
Title DCG-6-125-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 98.9
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-09-17T19:02:02
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
Et
Me
MeO
OTBS
H
Me
163a
0.83
0.89
0.87
2.02
2.91
1.03
1.00
1.12
1.05
2.82
1.91
3.19
0.72
0.77
3.01
9.65
3.01
2.94
ppm


ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-125-1/ 2/ ser
Title DCG-6-125-1.2.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 50.3
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.1970
Acquisition Date 2018-09-17T19:03:05
Spectrometer Frequency (400.13, 400.13)
Spectral Width (5197.5, 5197.5)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)
OTBS
H
Et
Me
MeO
Me
163a
ppm


Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-125-1/ 4/ ser
Title DCG-6-125-1.4.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2018-09-17T19:24:52
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 180)
Spectral Size (1024, 1024)
ppm
ppm
Et
N
O
O
O
Me
O
OTBS
H
N
Me
O
MeO
163a


Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-125-1/ 5/ ser
Title DCG-6-125-1.5.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2018-09-17T19:36:26
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
ppm
ppm
163a
Et
Me
OTBS
H
MeO
Me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Data File Name / Volumes/ nmr/ DCG-6-125-1/7/ fid
Title DCG-6-125-1.7.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 1536
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-09-17T22:33:06
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OTBS
H
Et
Me
MeO
Me
163a
205.8
173.0
155.5
151.2
102.5
82.6
74.0
68.3
57.8
56.2
55.1
52.1
49.3
43.2
37.8
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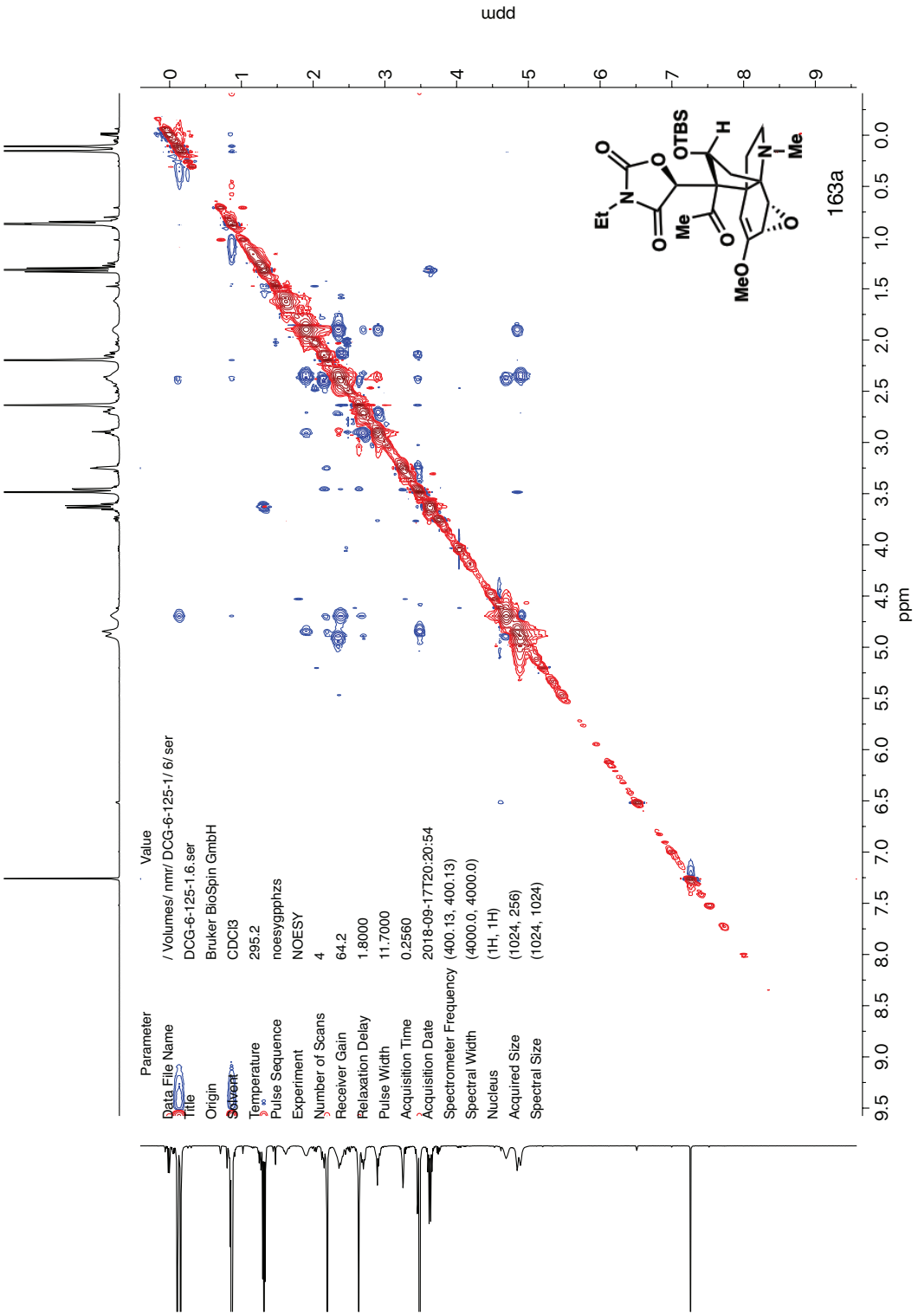
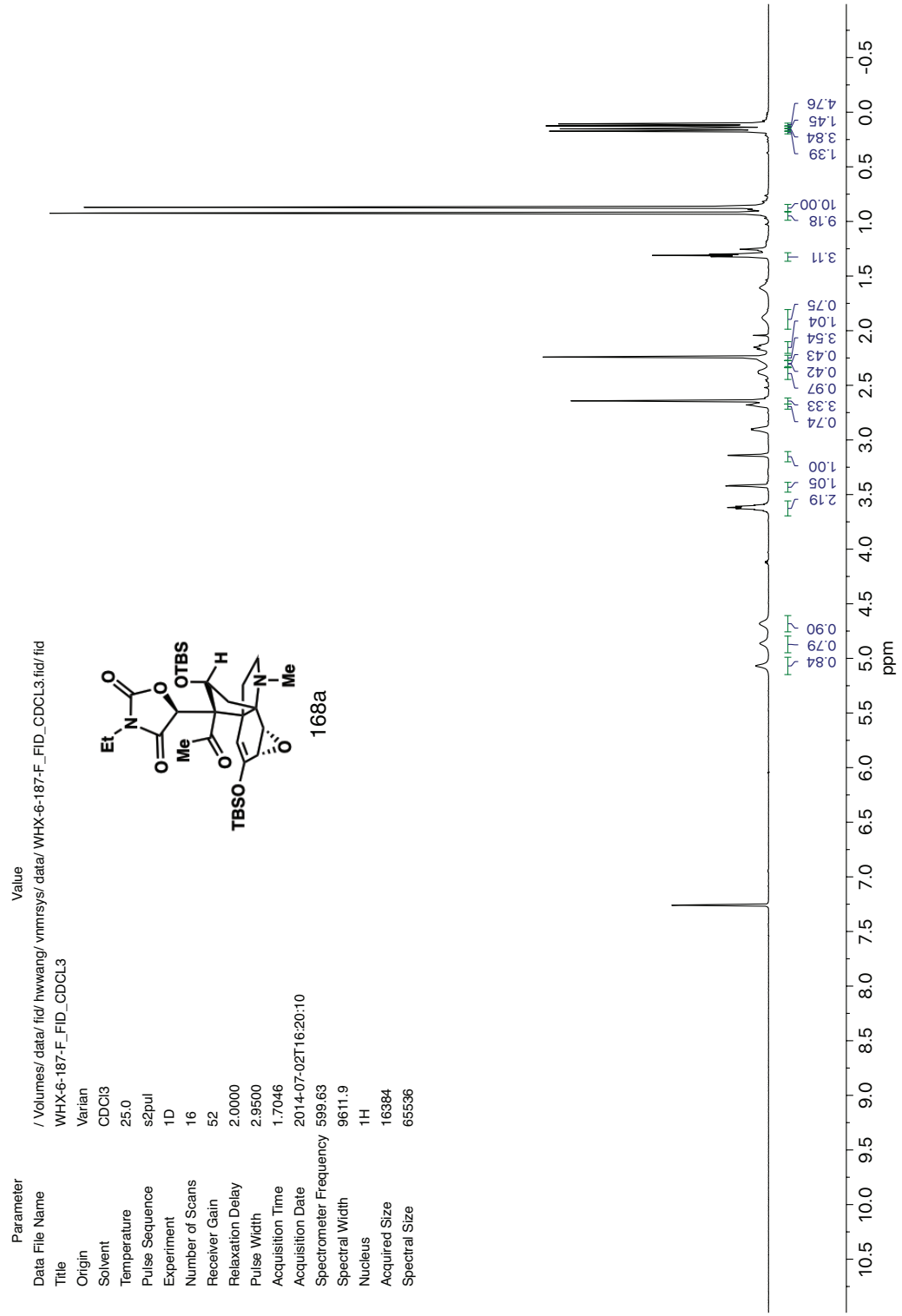
35.1
32.4
25.9
17.9
12.5
-4.4
-5.0
ppm


ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-125-1/ 6/ ser
Title DCG-6-125-1.6.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence noesygpphzs
Experiment NOESY
Number of Scans 4
Receiver Gain 64.2
Relaxation Delay 1.8000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2018-09-17T20:20:54
Spectrometer Frequency (400.13, 400.13)
Spectral Width (4000.0, 4000.0)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
Et
Me
OTBS
H
MeO
Me
163a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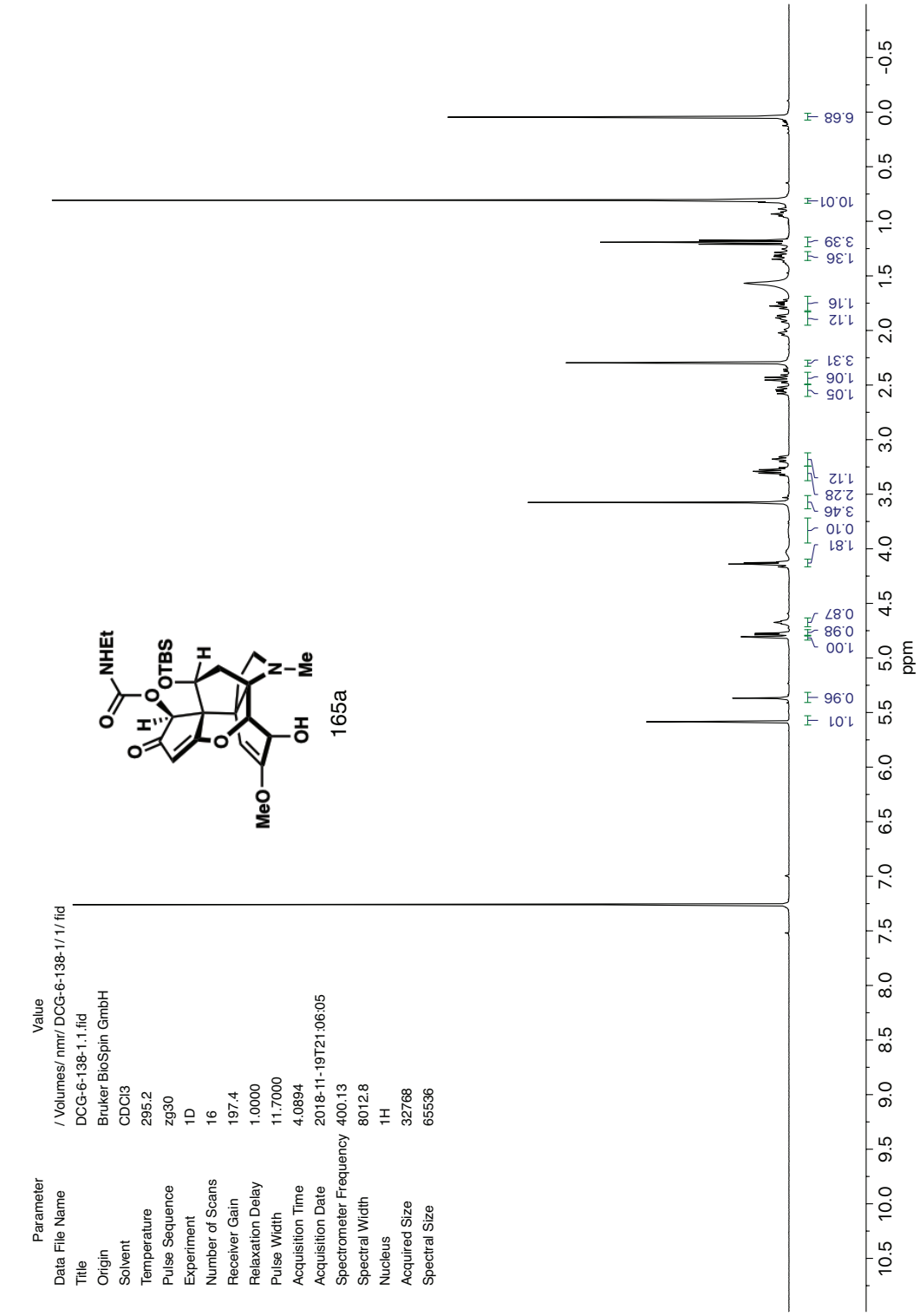
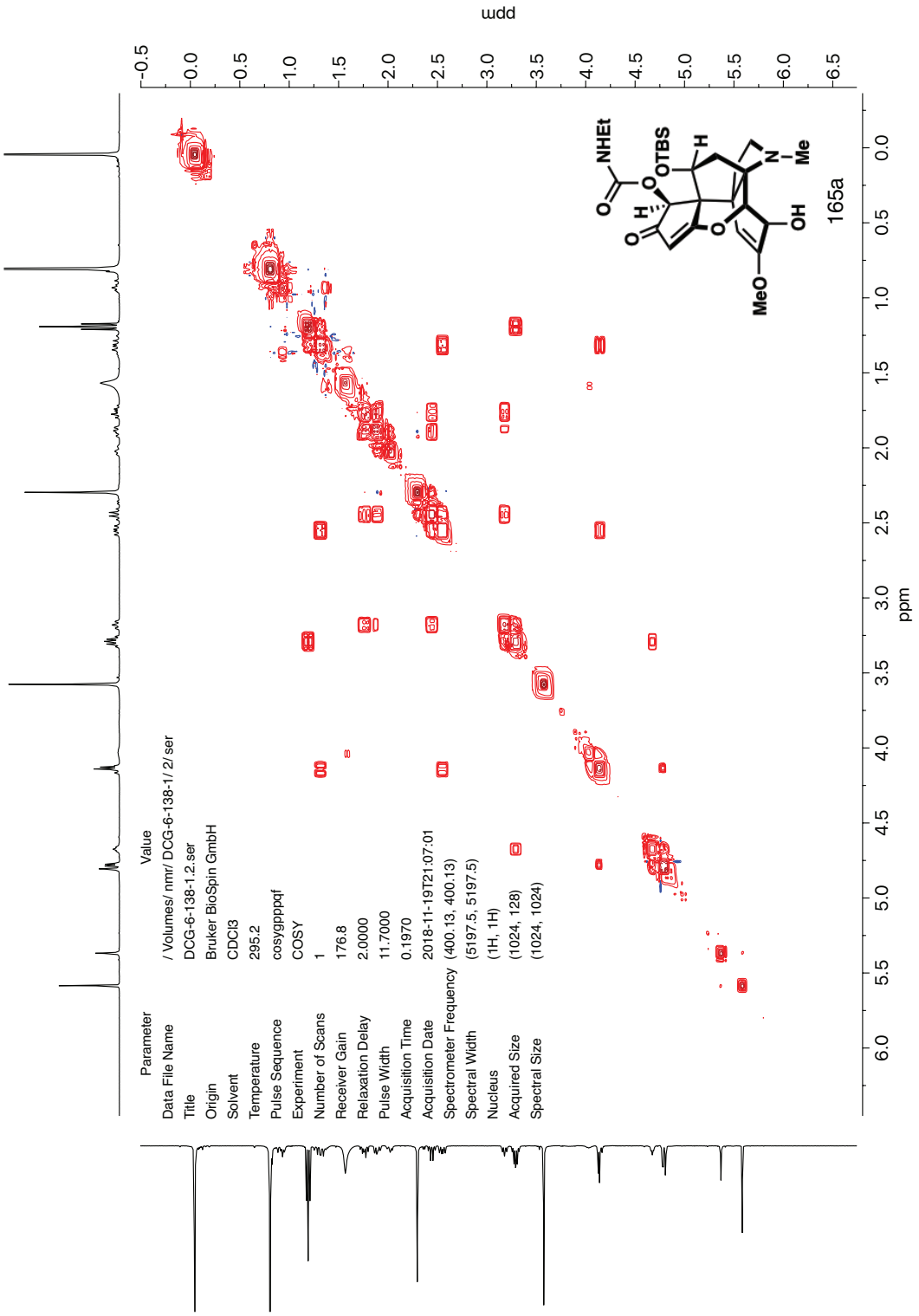
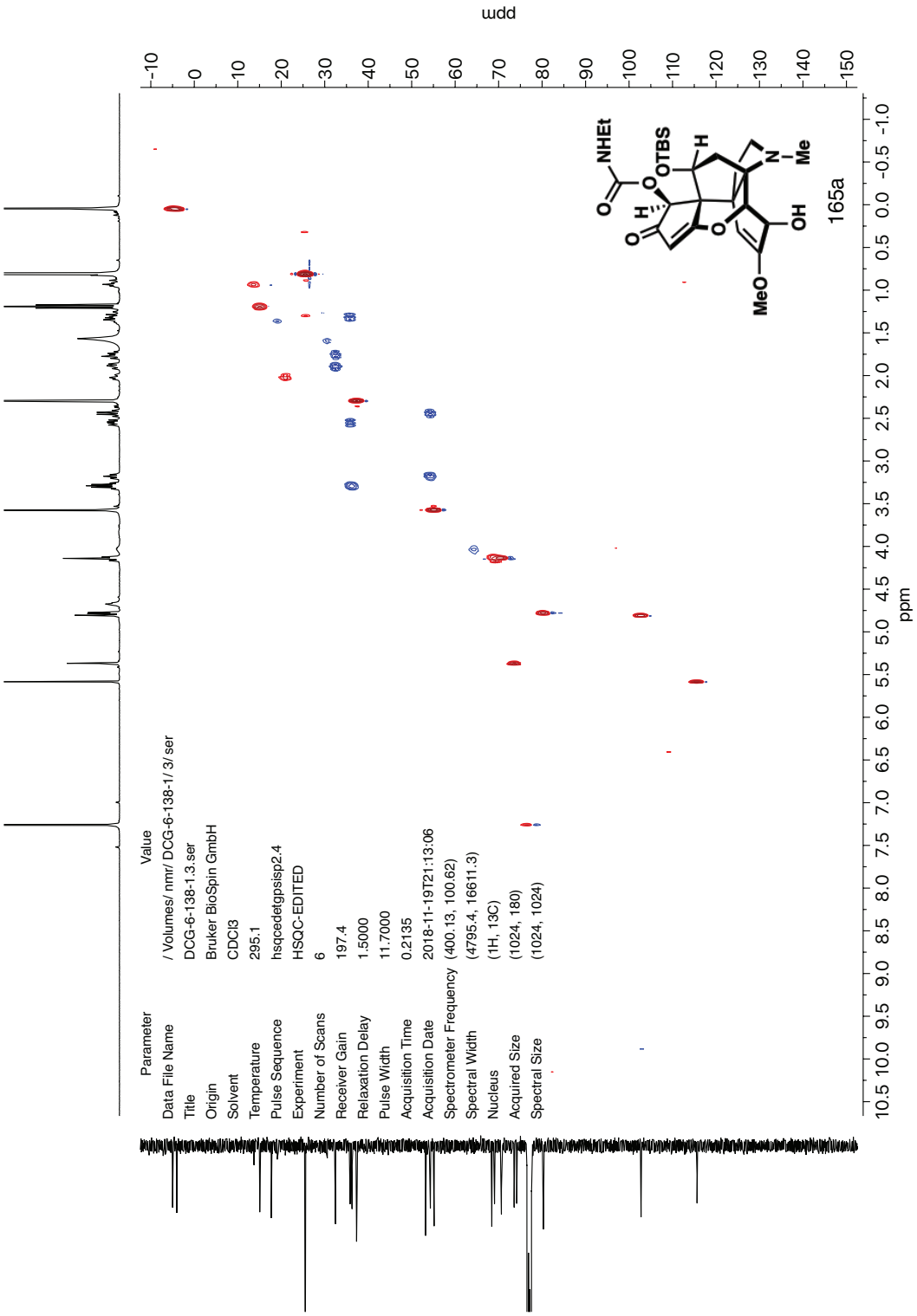
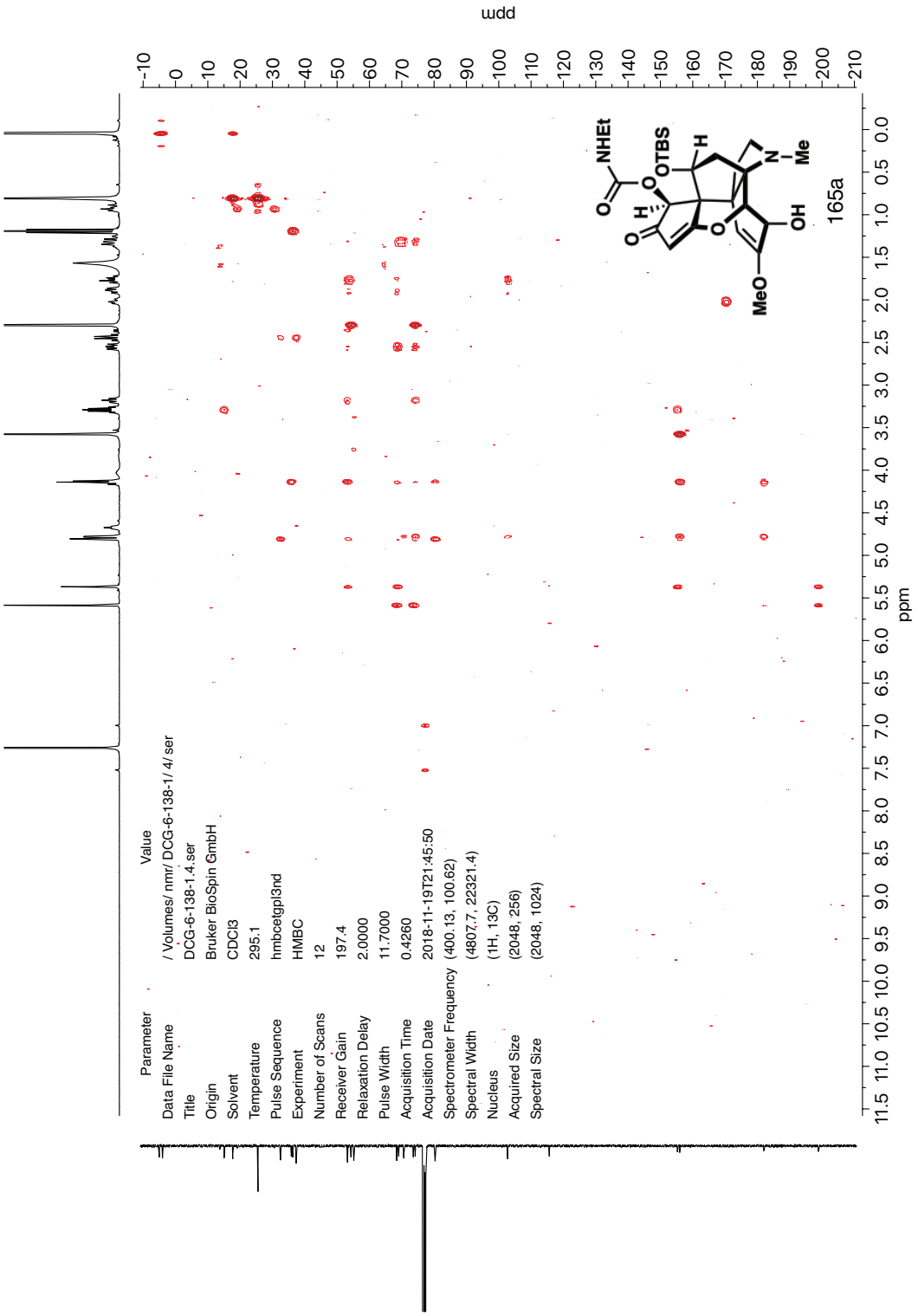
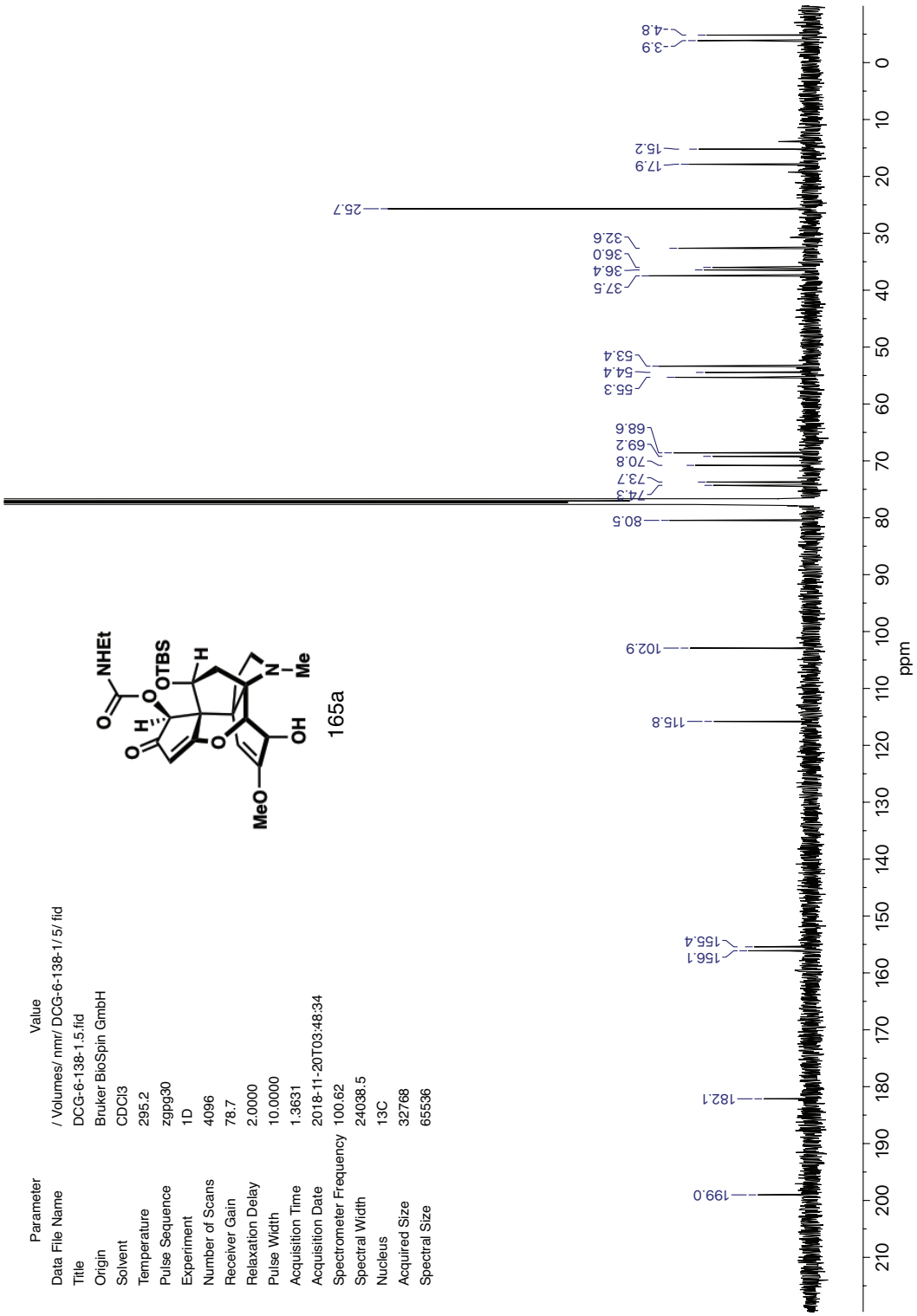
Value
Data File Name / Volumes/ data/ fid/ hwwang/ vnmrsys/ data/ WHX-6-187-F_FID_CDCL3.fid/ fid
Title WHX-6-187-F_FID_CDCL3
Origin Varian
Solvent CDCl3
Temperature 25.0
Pulse Sequence s2pul
Experiment 1D
Number of Scans 16
Receiver Gain 52
Relaxation Delay 2.0000
Pulse Width 2.9500
Acquisition Time 1.7046
Acquisition Date 2014-07-02T16:20:10
Spectrometer Frequency 599.63
Spectral Width 9611.9
Nucleus 1H
Acquired Size 16384
Spectral Size 65536
Et
Me
OTBS
H
TBSO
Me
168a
0.84
0.79
0.90
2.19
1.05
1.00
0.74
3.33
0.97
0.42
0.43
3.54
1.04
0.75
3.11
9.18
10.00
1.39
3.84
1.45
4.76
ppm

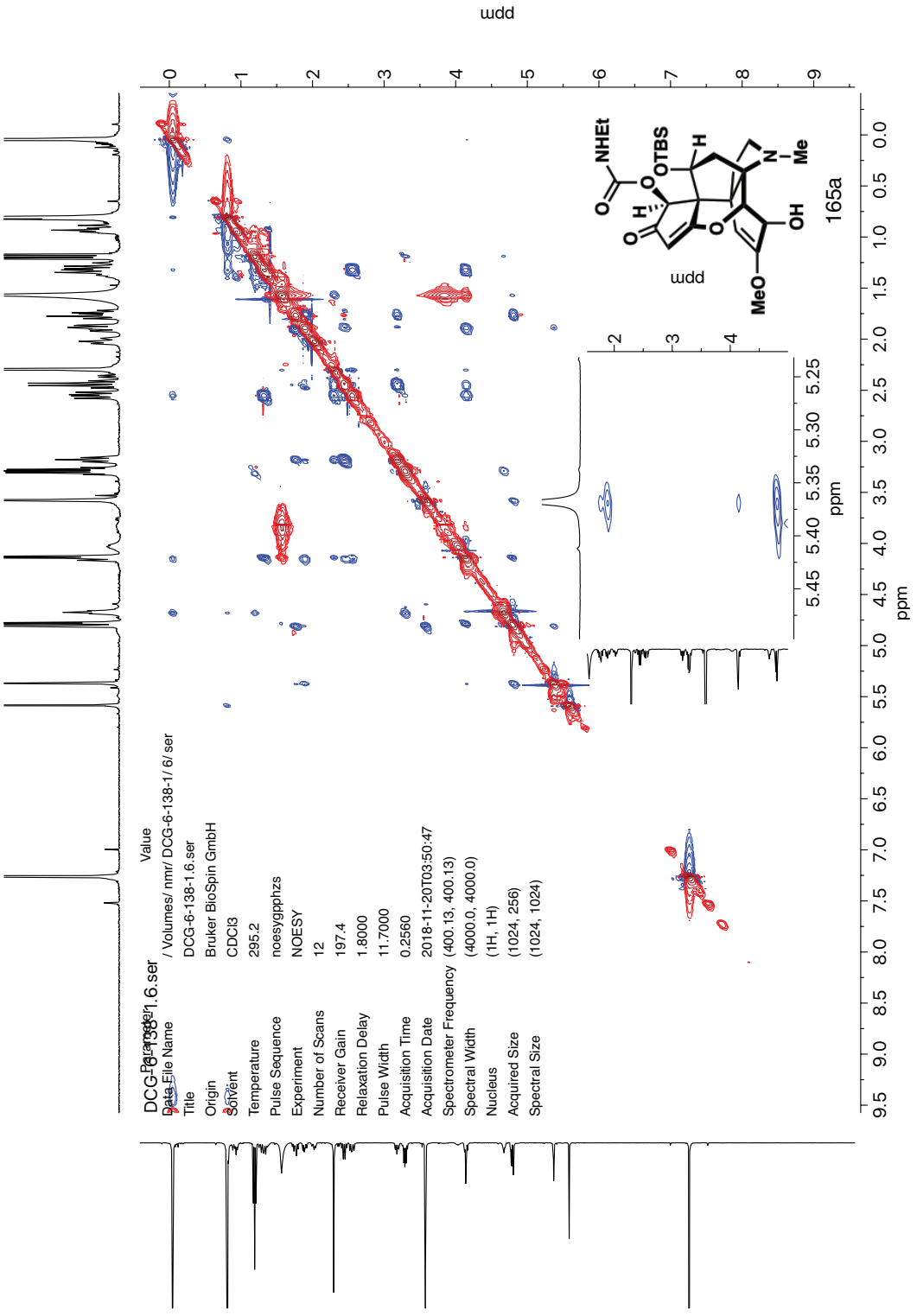

Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-138-1/1/ fid
Title DCG-6-138-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 197.4
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-11-19T21:06:05
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
NHEt
OTBS
H
O
H
O
O
OH
N
Me
MeO
165a
1.01
0.96
1.00
0.98
0.87
1.81
0.10
3.46
2.28
1.12
1.05
1.06
3.31
1.12
1.16
1.36
3.39
10.01
6.68
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm

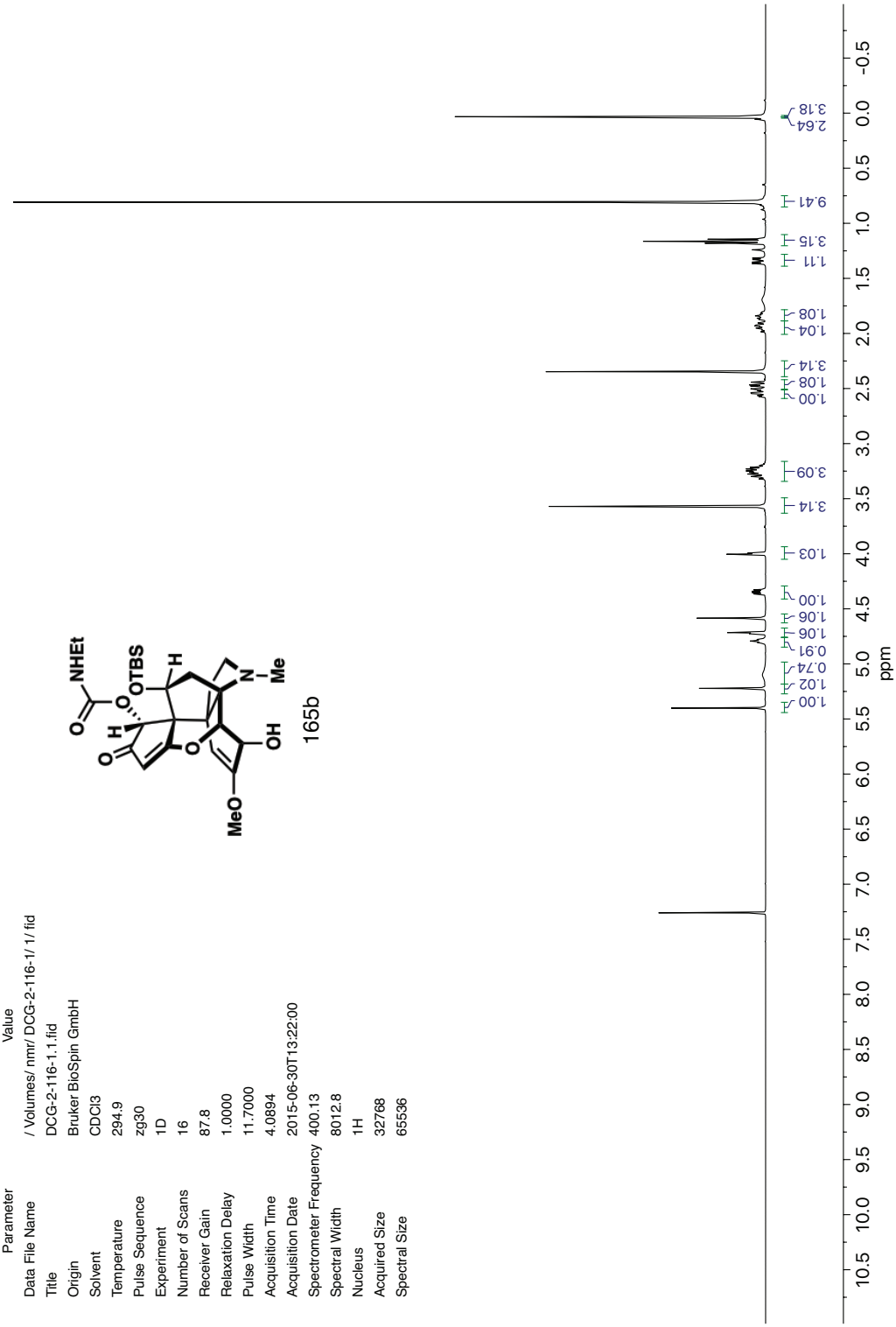

ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-138-1/ 2/ ser
Title DCG-6-138-1.2.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 176.8
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.1970
Acquisition Date 2018-11-19T21:07:01
Spectrometer Frequency (400.13, 400.13)
Spectral Width (5197.5, 5197.5)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)
NHEt
OTBS
H
Me
OH
MeO
165a

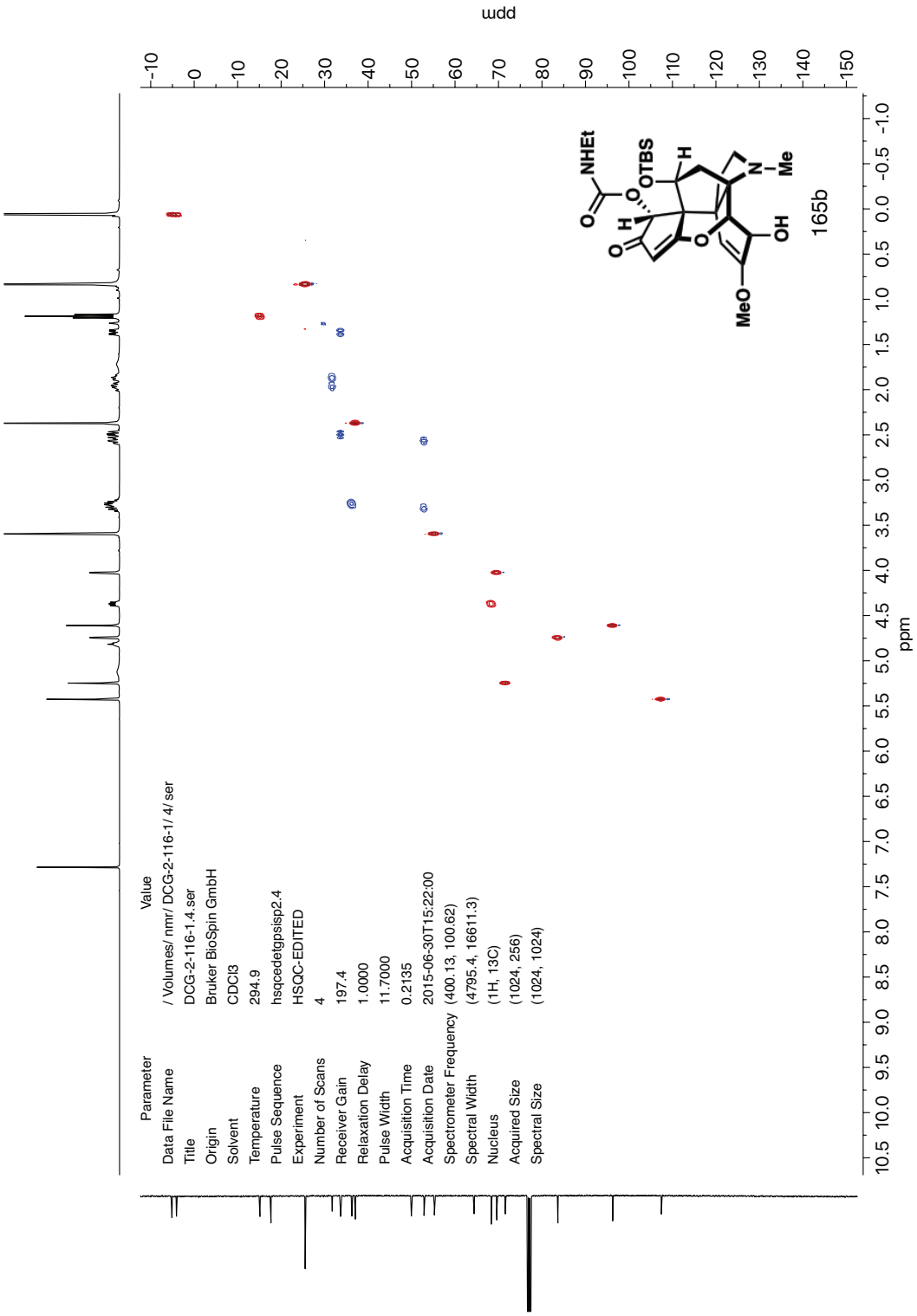

Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-138-1/ 3/ ser
Title DCG-6-138-1.3.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 6
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2018-11-19T21:13:06
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 180)
Spectral Size (1024, 1024)
ppm
NHEt
OTBS
OH
MeO
Me
165a

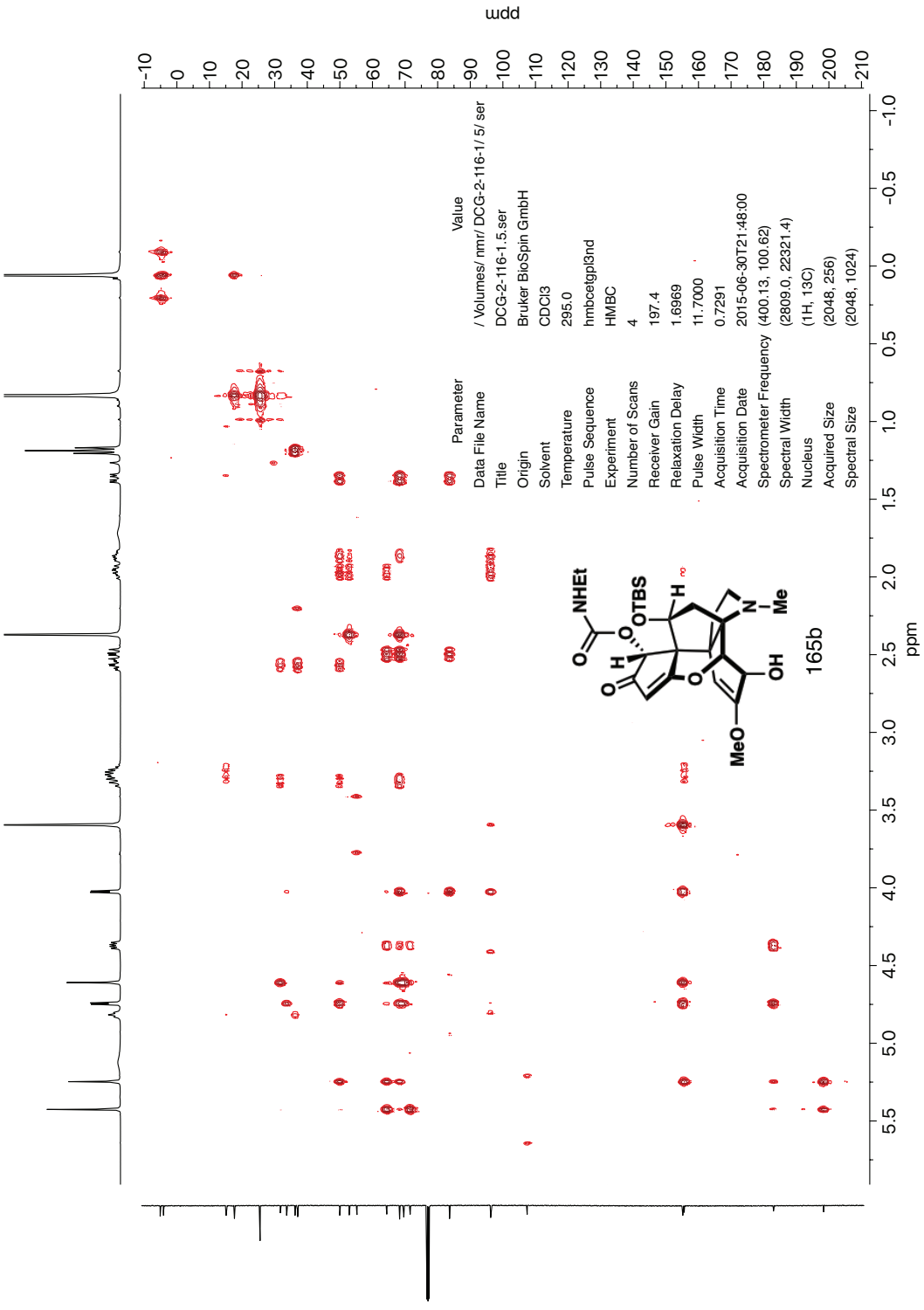

ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-138-1/ 4/ ser
Title DCG-6-138-1.4.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 12
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2018-11-19T21:45:50
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
NHEt
OTBS
H
Me
OH
MeO
165a
ppm

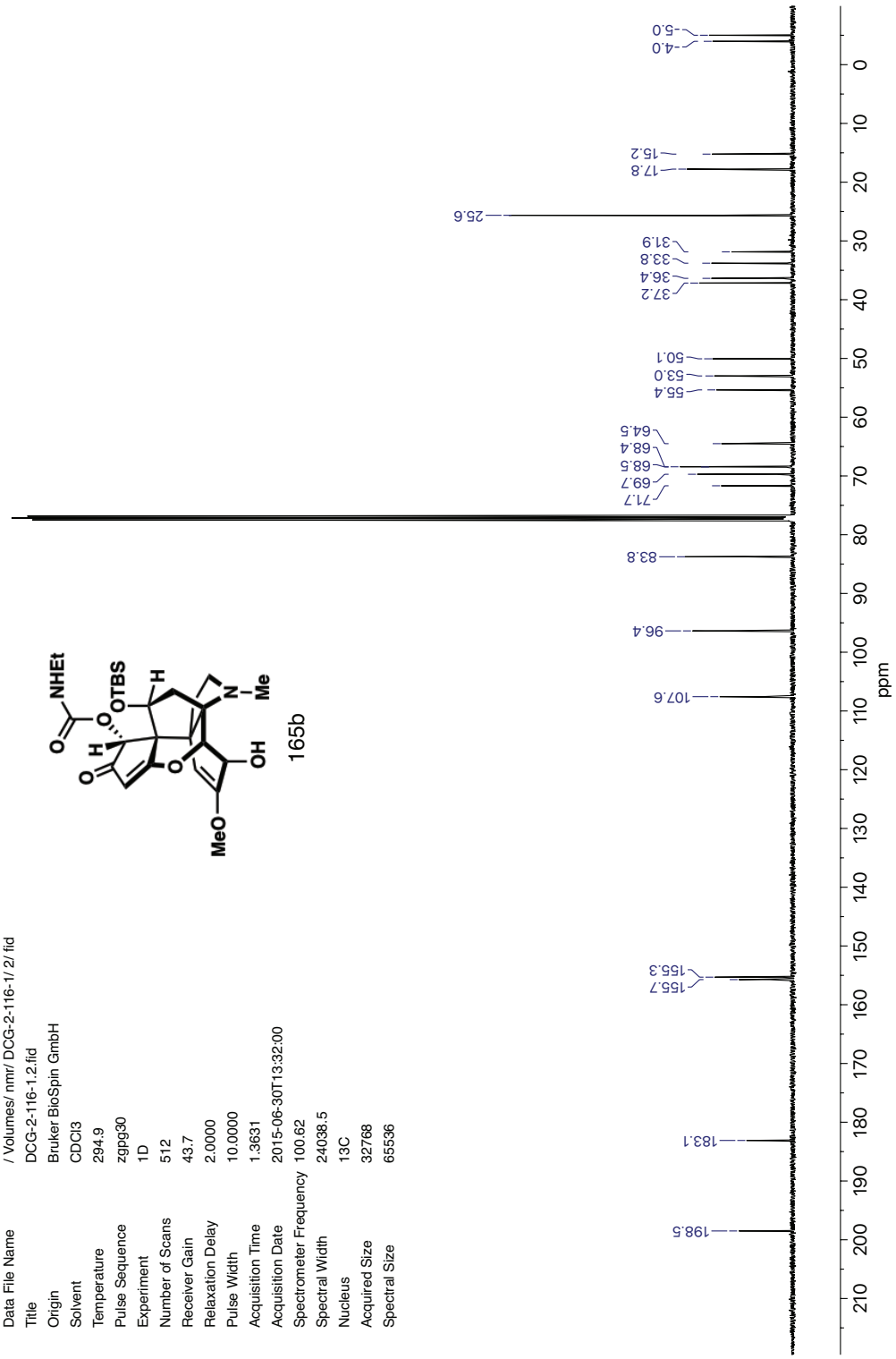

Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-138-1/5/ fid
Title DCG-6-138-1.5.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 4096
Receiver Gain 78.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-11-20T03:48:34
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
NHEt
OTBS
H
Me
OH
MeO
165a
199.0
182.1
156.1
155.4
115.8
102.9
80.5
74.3
73.7
70.8
69.2
68.6
55.3
54.4
53.4
37.5
36.4
36.0
32.6
25.7
17.9
15.2
-3.9
-4.8
ppm

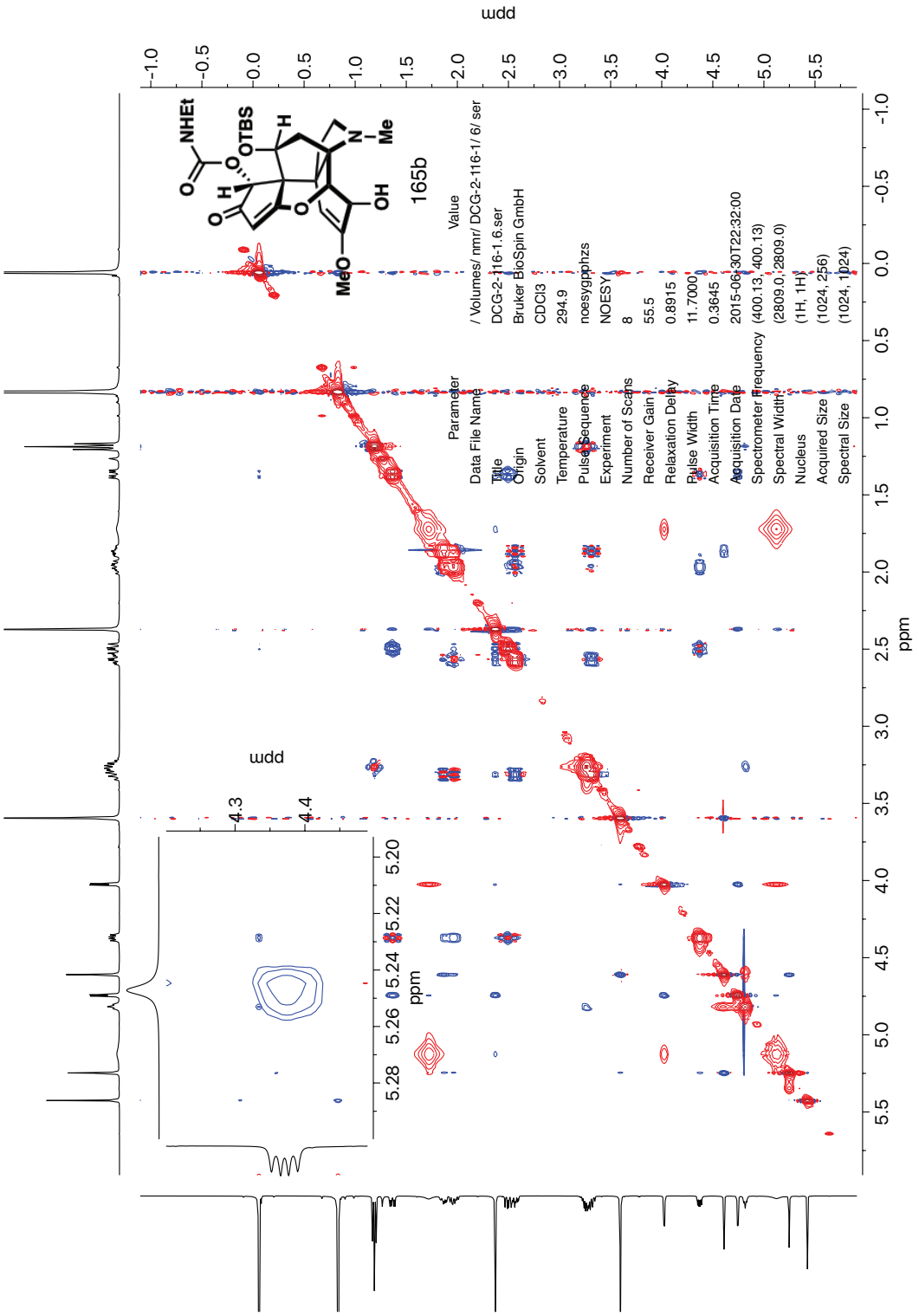

DCG-6-138-1.6.ser
Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-138-1/ 6/ ser
Title DCG-6-138-1.6.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence noesygpphzs
Experiment NOESY
Number of Scans 12
Receiver Gain 197.4
Relaxation Delay 1.8000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2018-11-20T03:50:47
Spectrometer Frequency (400.13, 400.13)
Spectral Width (4000.0, 4000.0)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
NHEt
OTBS
H
N
Me
OH
MeO
165a
ppm

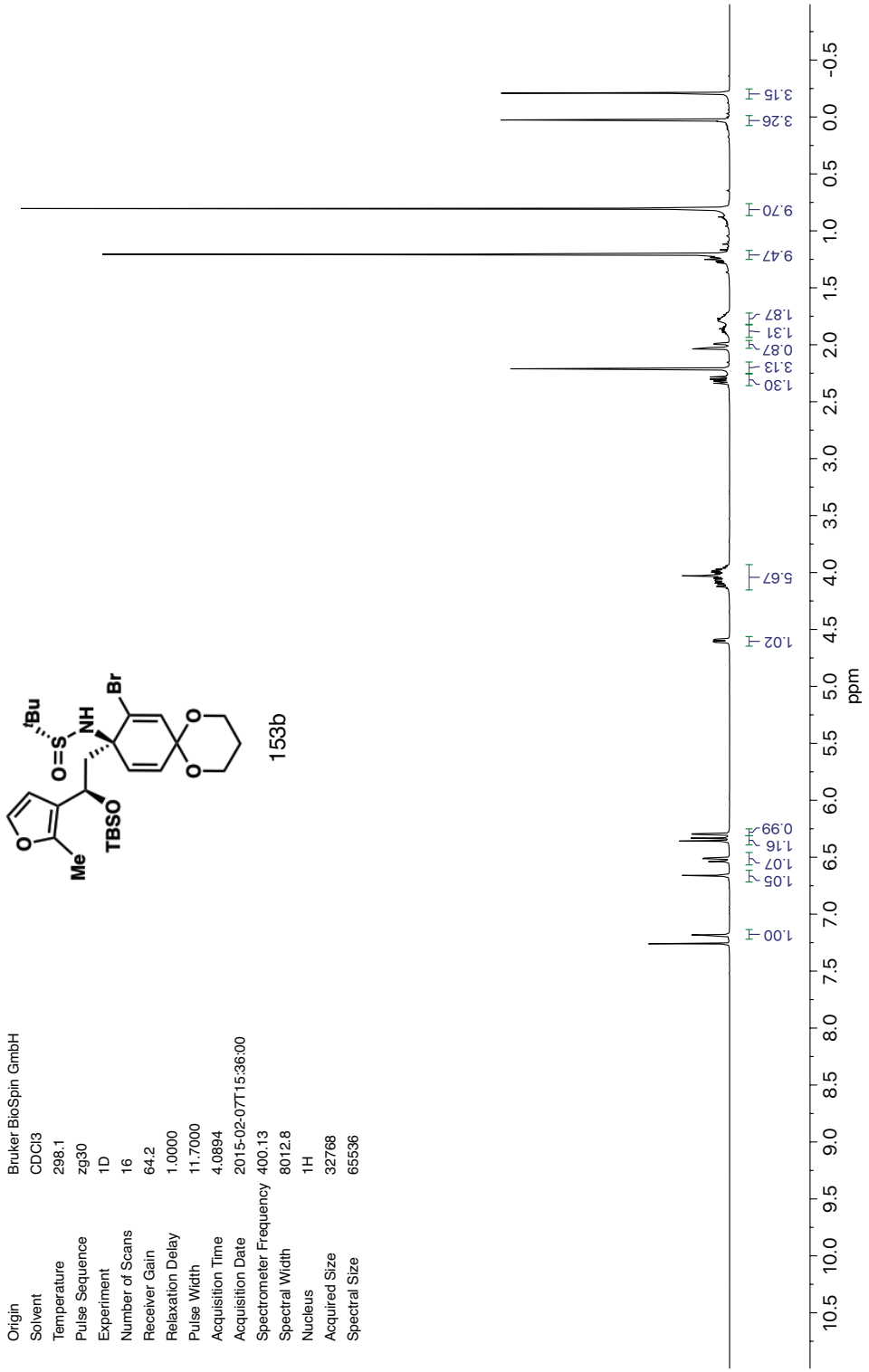

Parameter Value
Data File Name / Volumes/ nmr/ DCG-2-116-1/ 1/ fid
Title DCG-2-116-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 87.8
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2015-06-30T13:22:00
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
NHEt
OTBS
H
O
H
O
N
Me
OH
MeO
165b
1.00
1.02
0.74
1.00
0.91
1.06
1.06
1.00
1.03
3.14
3.09
1.00
1.08
3.14
1.04
1.08
1.11
3.15
9.41
2.64
3.18
ppm

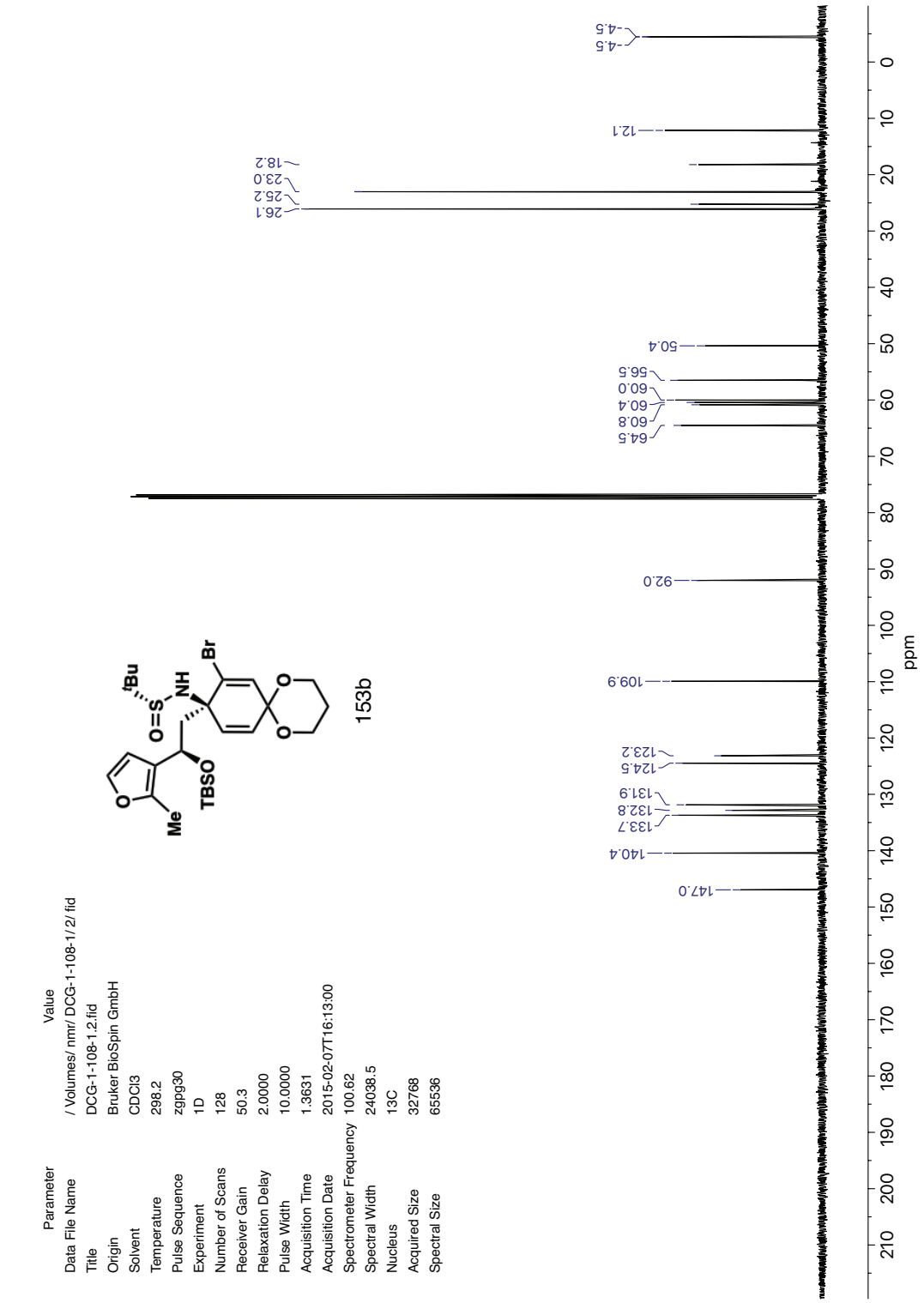

Parameter Value
Data File Name / Volumes/ nmr/ DCG-2-116-1/ 4/ ser
Title DCG-2-116-1.4.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2015-06-30T15:22:00
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
NHEt
OTBS
MeO
OH
Me
165b
ppm
ppm

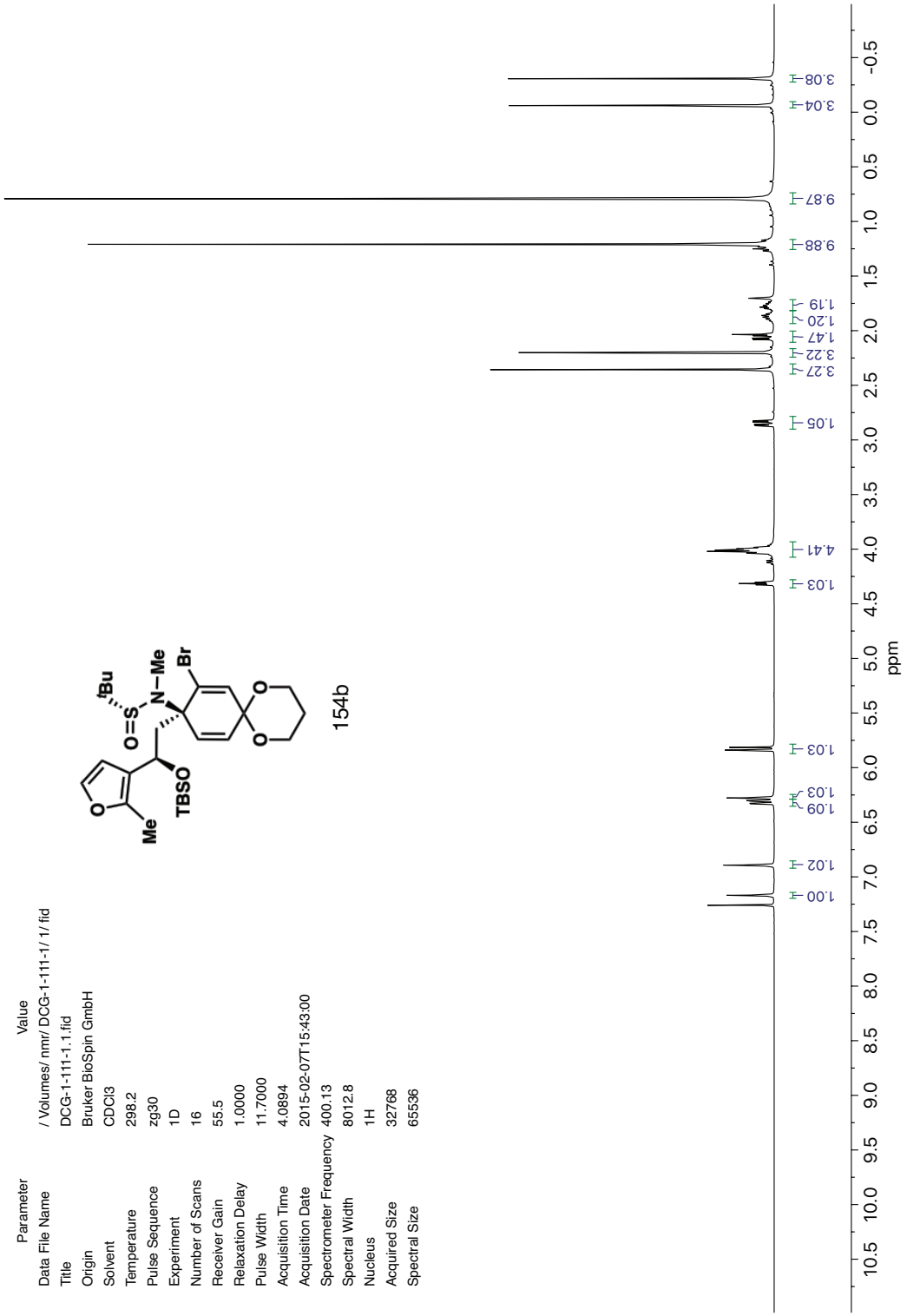

ppm
Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-2-116-1/ 5/ ser
Title
DCG-2-116-1.5.ser
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.0
Pulse Sequence
hmbcetgpl3nd
Experiment
HMBC
Number of Scans
4
Receiver Gain
197.4
Relaxation Delay
1.6969
Pulse Width
11.7000
Acquisition Time
0.7291
Acquisition Date
2015-06-30T21:48:00
Spectrometer Frequency
(400.13, 100.62)
Spectral Width
(2809.0, 22321.4)
Nucleus
(1H, 13C)
Acquired Size
(2048, 256)
Spectral Size
(2048, 1024)
NHEt
OTBS
H
Me
OH
MeO
165b

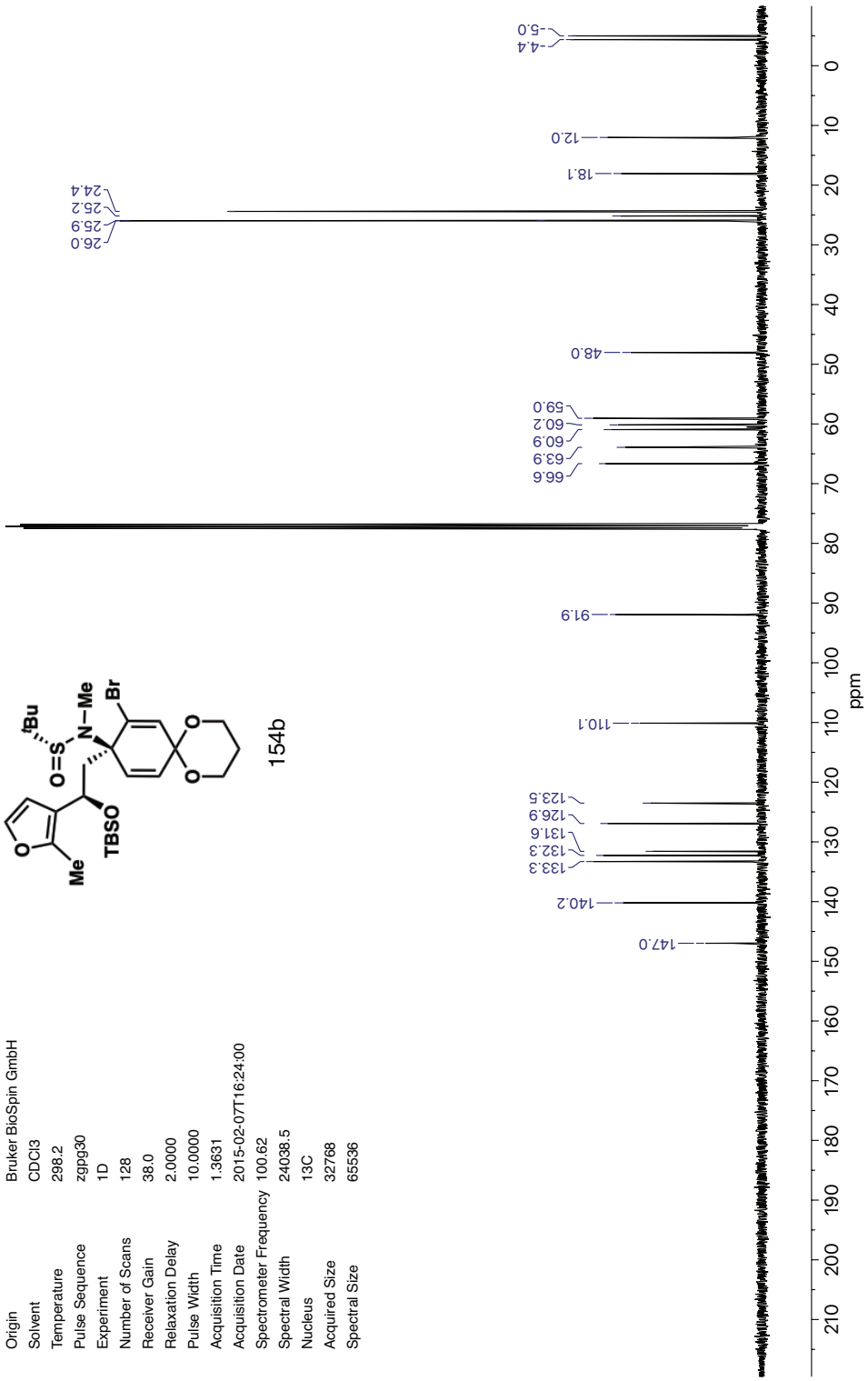

Parameter Value
Data File Name / Volumes/ nmr/ DCG-2-116-1/ 2/ fid
Title DCG-2-116-1.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 512
Receiver Gain 43.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2015-06-30T13:32:00
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
NHEt
OTBS
H
O
H
O
N
Me
OH
MeO
165b
198.5
183.1
155.7
155.3
107.6
96.4
83.8
71.7
69.7
68.5
68.4
64.5
55.4
53.0
50.1
37.2
36.4
33.8
31.9
25.6
17.8
15.2
-4.0
-5.0
ppm


NHEt
OTBS
H
N
Me
OH
MeO
165b
Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-2-116-1/ 6/ ser
Title
DCG-2-116-1.6.ser
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
noesygpphzs
Experiment
NOESY
Number of Scans
8
Receiver Gain
55.5
Relaxation Delay
0.8915
Pulse Width
11.7000
Acquisition Time
0.3645
Acquisition Date
2015-06-30T22:32:00
Spectrometer Frequency
(400.13, 400.13)
Spectral Width
(2809.0, 2809.0)
Nucleus
(1H, 1H)
Acquired Size
(1024, 256)
Spectral Size
(1024, 1024)
ppm
ppm
ppm

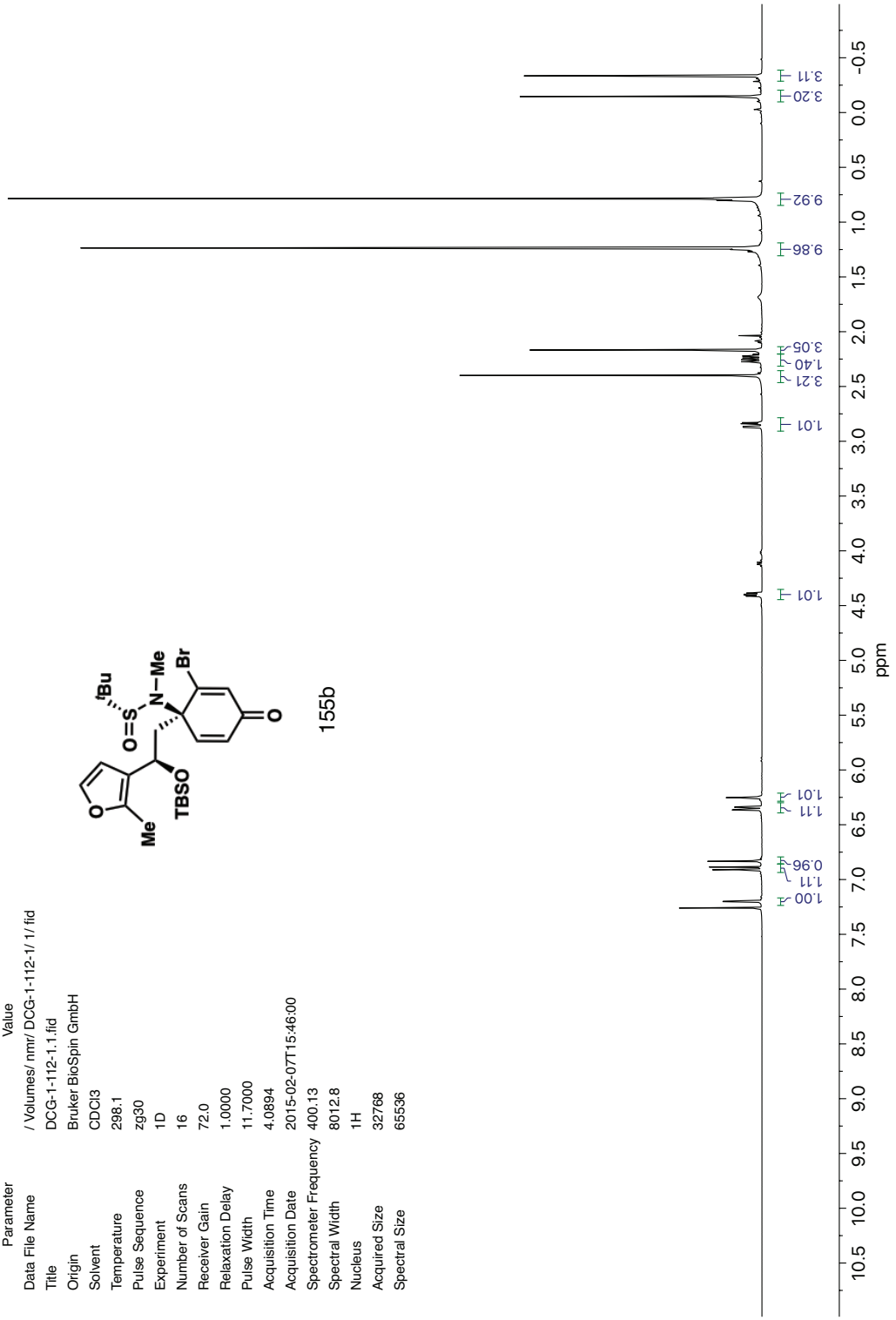

Parameter Value
Data File Name / Volumes/ nmr/ DCG-1-108-1/1/ fid
Title DCG-1-108-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 298.1
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 64.2
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2015-02-07T15:36:00
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
tBu
O=S
NH
Br
TBSO
Me
O
O
O
153b
1.00
1.05
1.07
1.16
0.99
1.02
5.67
1.30
3.13
0.87
1.31
1.87
9.47
9.70
3.26
3.15
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm

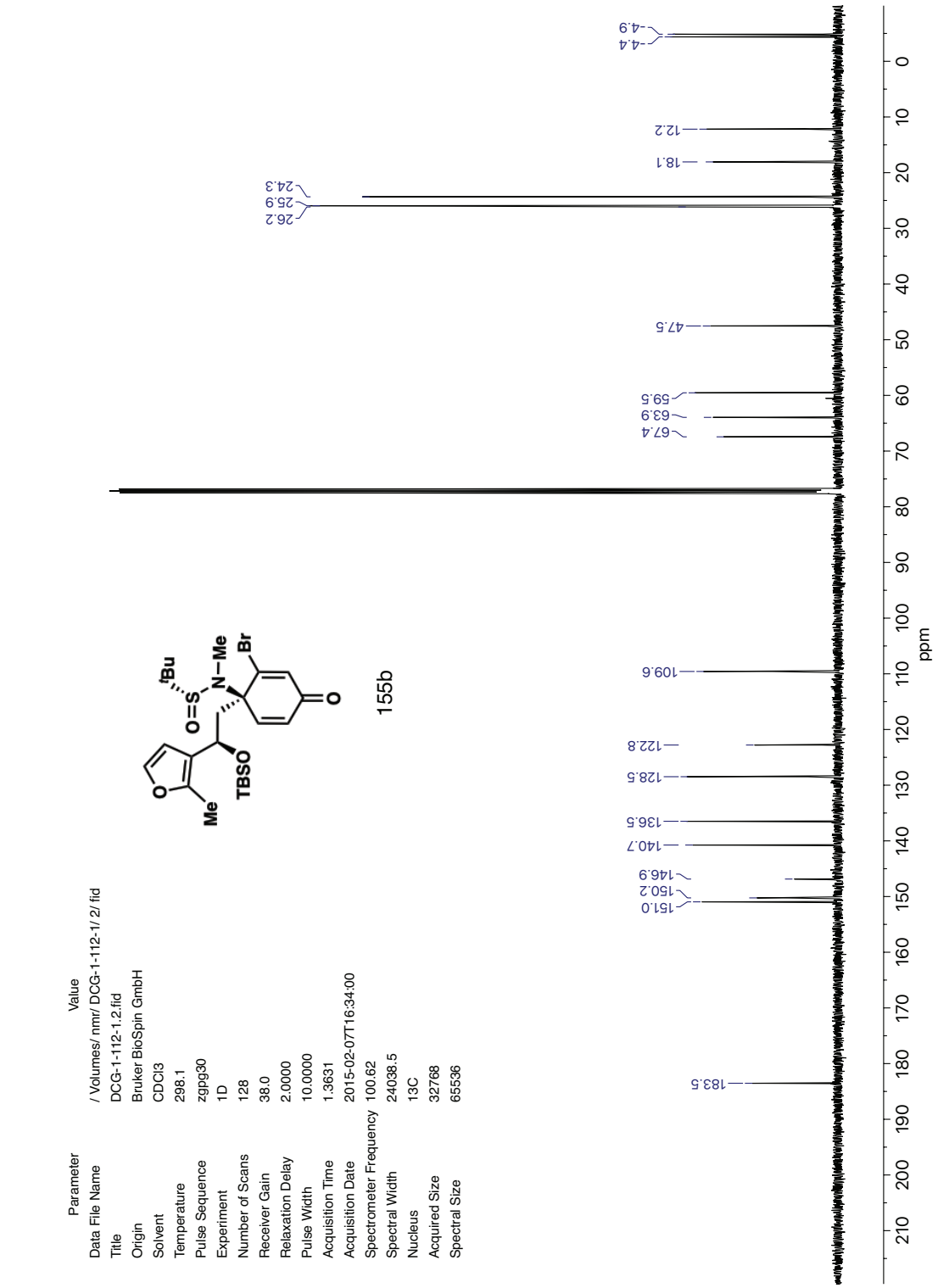

Parameter Value
Data File Name / Volumes/ nmr/ DCG-1-108-1/2/ fid
Title DCG-1-108-1.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 298.2
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 128
Receiver Gain 50.3
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2015-02-07T16:13:00
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
153b
ppm

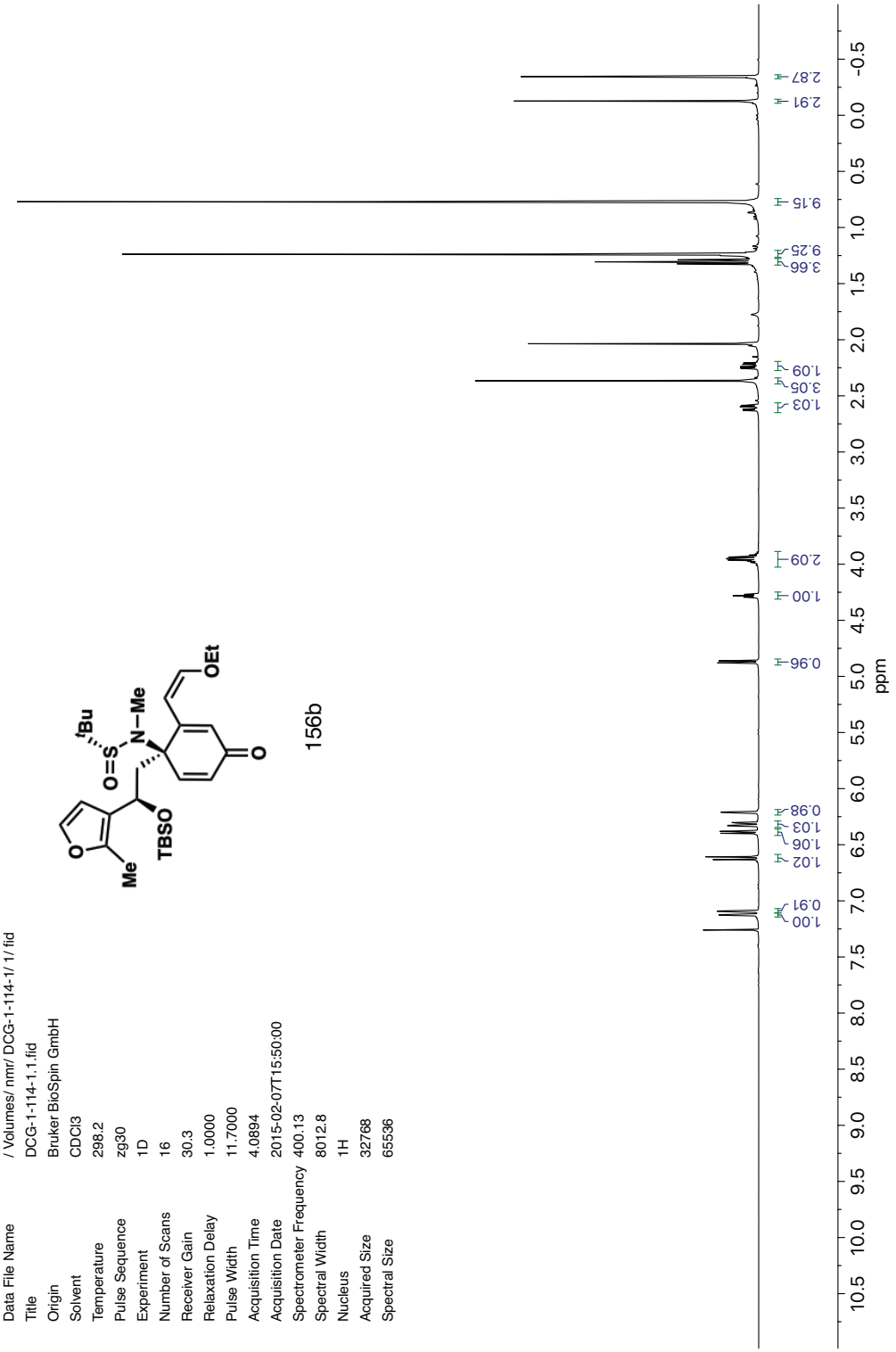

Parameter Value
Data File Name / Volumes/ nmr/ DCG-1-111-1/ 1/ fid
Title DCG-1-111-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 298.2
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 55.5
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2015-02-07T15:43:00
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
tBu
O=S
N–Me
Br
TBSO
Me
O
O
O
154b
1.00
1.02
1.09
1.03
1.03
1.03
4.41
1.05
3.27
3.22
1.47
1.20
1.19
9.88
9.87
3.04
3.08
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm

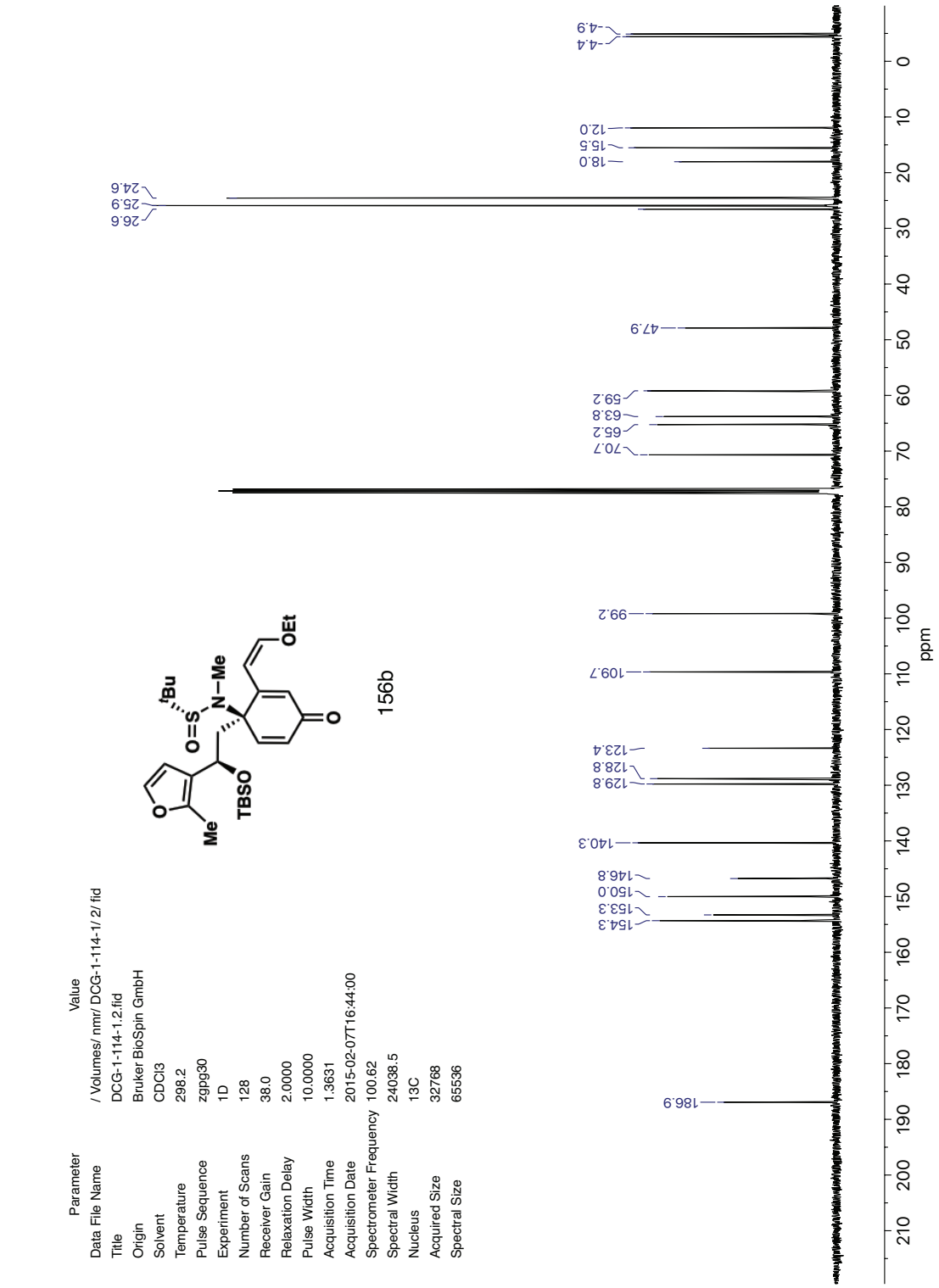


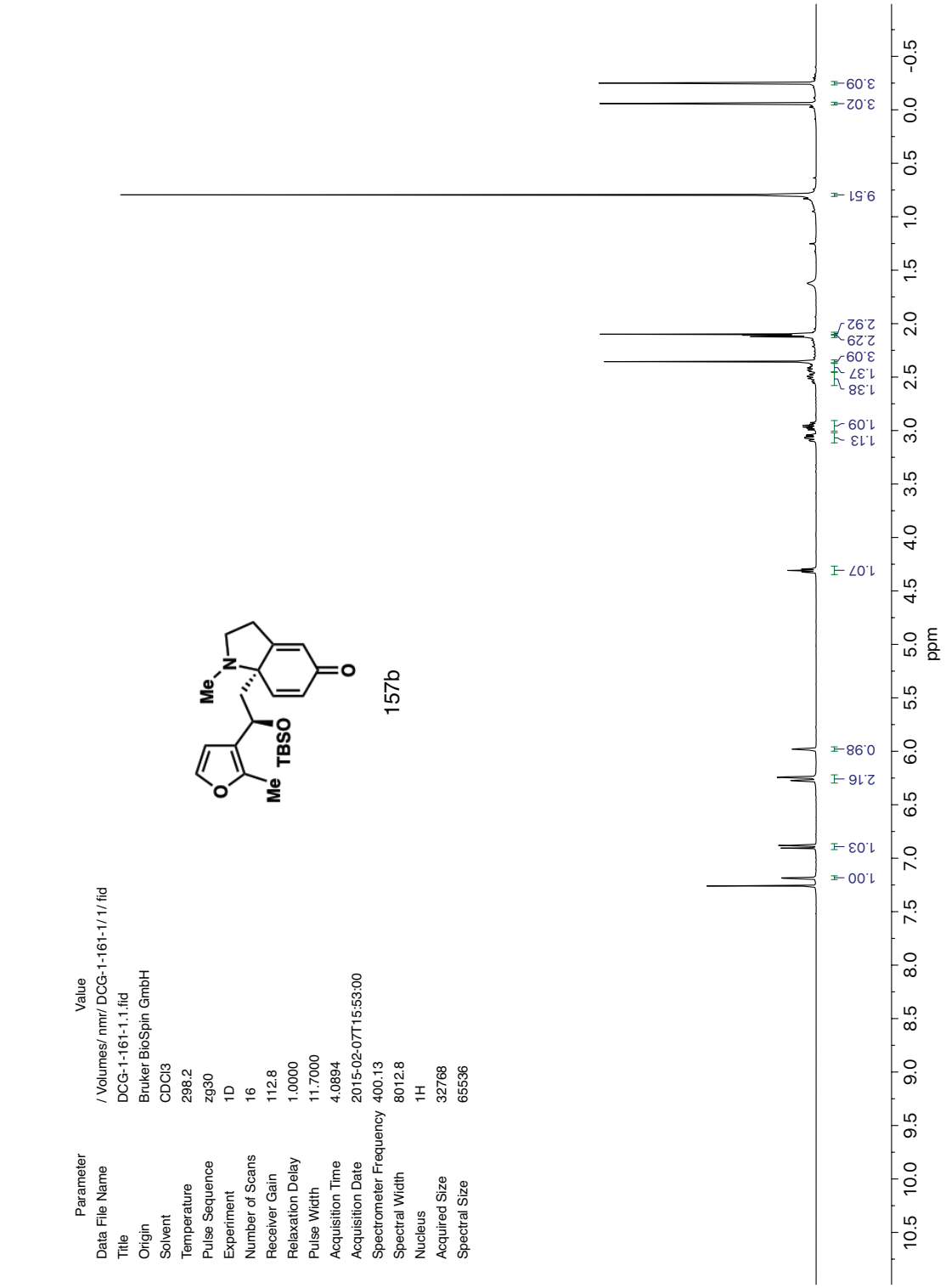
Parameter	Value
Data File Name	/ Volumes/ nmr/ DCG-1-111-1/ 2/ fid
Title	DCG-1-111-1.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	298.2
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	128
Receiver Gain	38.0
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2015-02-07T16:24:00
Spectrometer Frequency	100.62
Spectral Width	24038.5
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

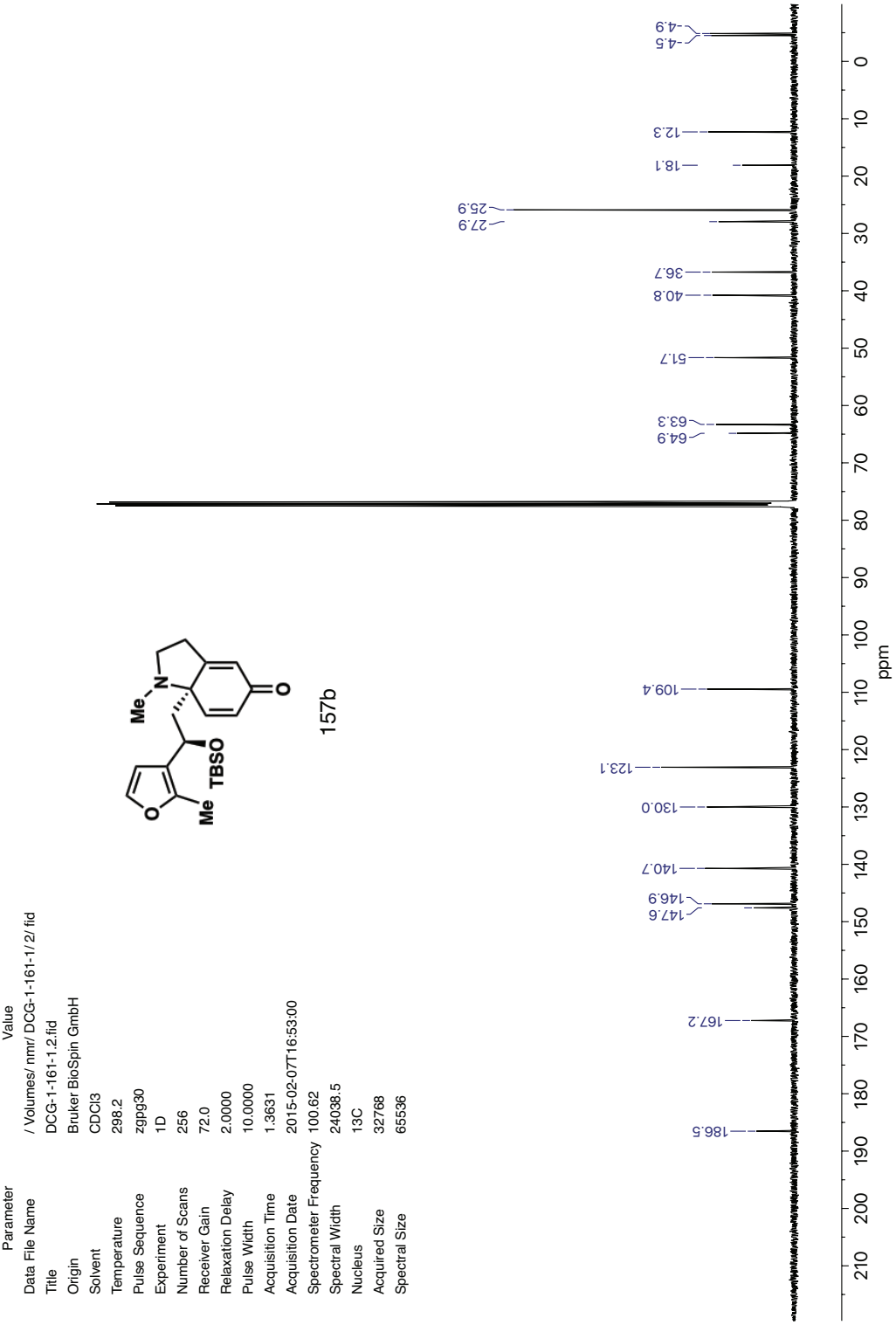

Parameter Value
Data File Name / Volumes/ nmr/ DCG-1-112-1/ 1/ fid
Title DCG-1-112-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 298.1
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 72.0
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2015-02-07T15:46:00
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
tBu
O=S
N–Me
Br
O
TBSO
Me
O
155b
1.00
1.11
0.96
1.11
1.01
1.01
3.21
1.40
3.05
1.01
9.86
9.92
3.20
3.11
ppm

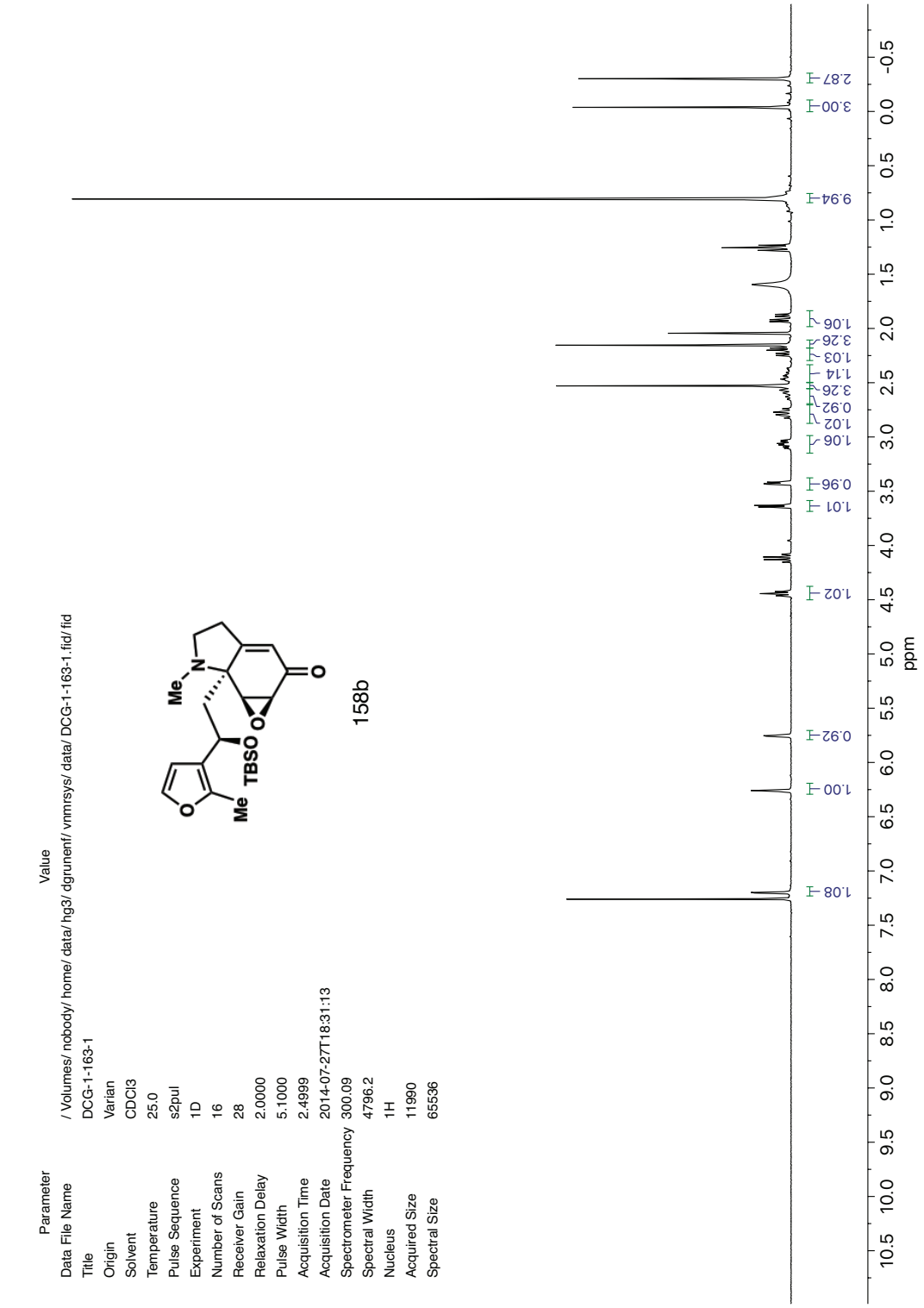

Parameter Value
Data File Name / Volumes/ nmr/ DCG-1-112-1/ 2/ fid
Title DCG-1-112-1.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 298.1
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 128
Receiver Gain 38.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2015-02-07T16:34:00
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
155b
-4.4
-4.9
12.2
18.1
24.3
25.9
26.2
47.5
59.5
63.9
67.4
109.6
122.8
128.5
136.5
140.7
146.9
150.2
151.0
183.5
ppm

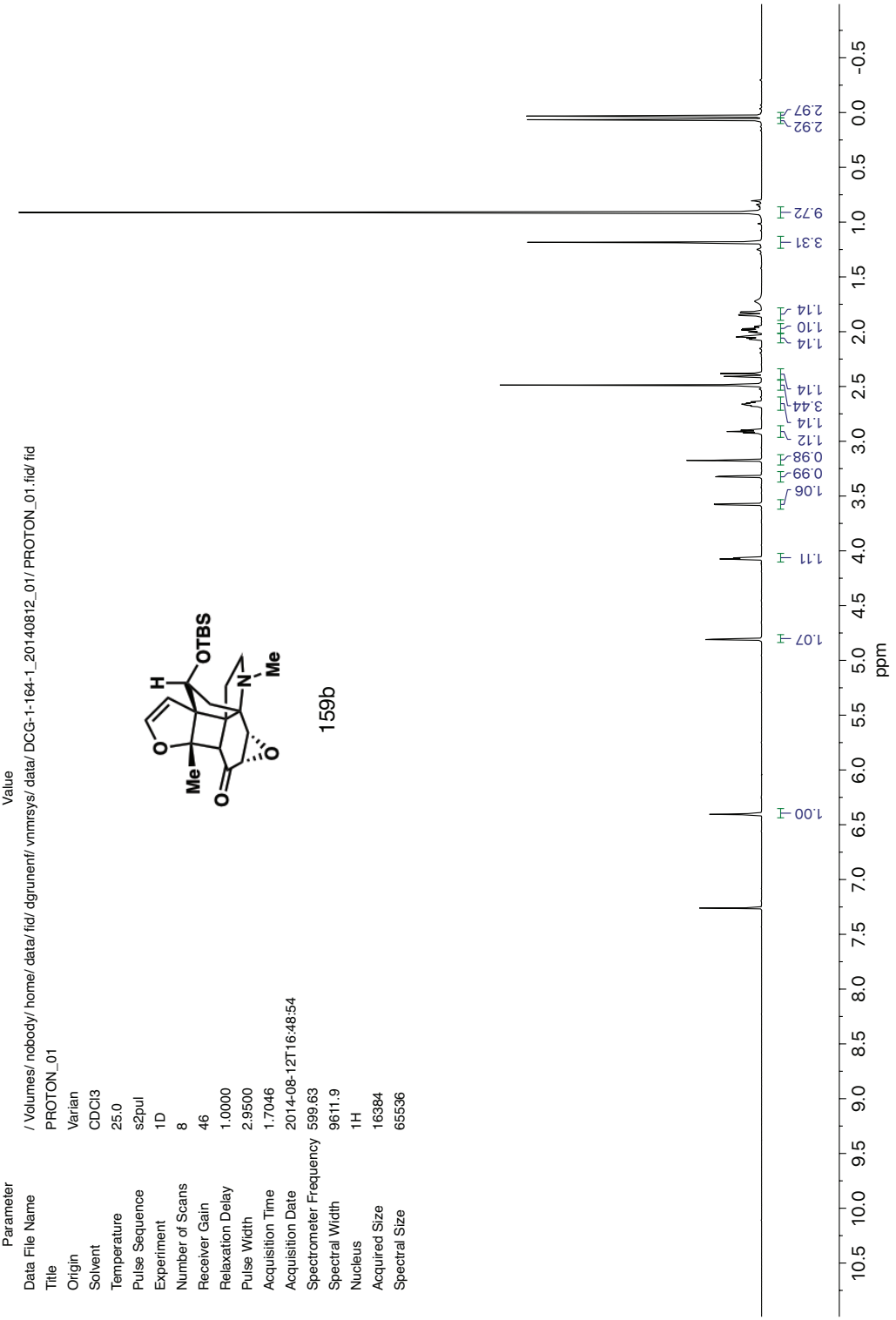

Parameter Value
Data File Name / Volumes/ nmr/ DCG-1-114-1/ 1/ fid
Title DCG-1-114-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 298.2
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 30.3
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2015-02-07T15:50:00
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
tBu
O=S
N–Me
OEt
O
TBSO
Me
O
156b
2.87
2.91
9.15
3.66
9.25
1.03
3.05
1.09
2.09
1.00
0.96
0.98
1.03
1.06
1.02
1.00
0.91
ppm

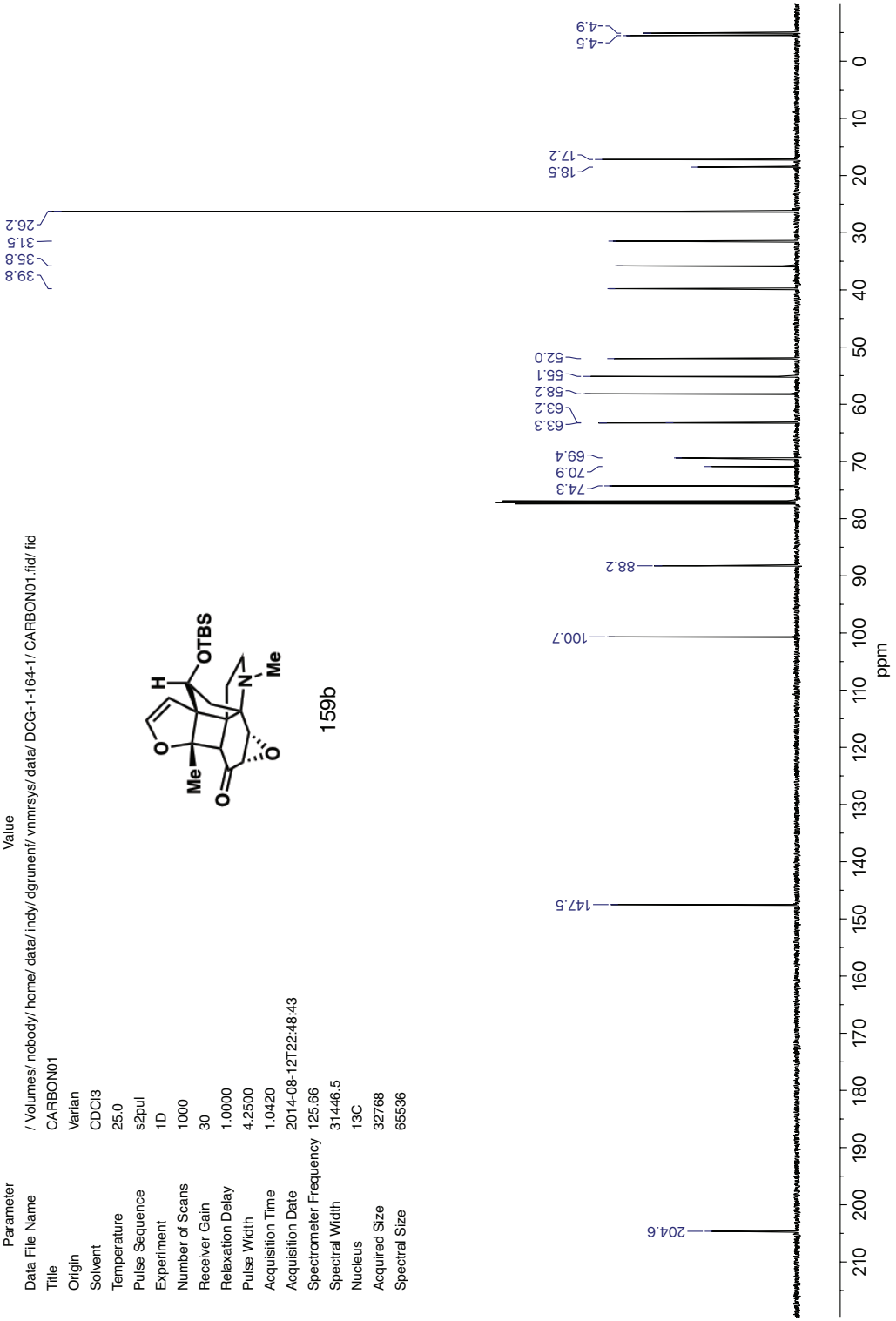

Parameter Value
Data File Name / Volumes/ nmr/ DCG-1-114-1/ 2/ fid
Title DCG-1-114-1.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 298.2
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 128
Receiver Gain 38.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2015-02-07T16:44:00
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
156b
tBu
O=S
N–Me
OEt
O
TBSO
Me
O
-4.9
-4.4
12.0
15.5
18.0
24.6
25.9
26.6
47.9
59.2
63.8
65.2
70.7
99.2
109.7
123.4
128.8
129.8
140.3
146.8
150.0
153.3
154.3
186.9
ppm


Parameter Value
Data File Name / Volumes/ nmr/ DCG-1-161-1/1/1/ fid
Title DCG-1-161-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 298.2
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 112.8
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2015-02-07T15:53:00
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
Me
N
O
TBSO
Me
O
157b
1.00
1.03
2.16
0.98
1.07
1.09
1.13
1.37
1.38
3.09
2.29
2.92
9.51
3.02
3.09
ppm


Parameter Value
Data File Name / Volumes/ nmr/ DCG-1-161-1/2/ fid
Title DCG-1-161-1.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 298.2
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2015-02-07T16:53:00
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
N
O
TBSO
Me
O
157b
-4.9
-4.5
12.3
18.1
25.9
27.9
36.7
40.8
51.7
63.3
64.9
109.4
123.1
130.0
140.7
146.9
147.6
167.2
186.5
ppm


Parameter
Value
Data File Name / Volumes/ nobody/ home/ data/ hg3/ dgrunenf/ vnmrsys/ data/ DCG-1-163-1.fid/ fid
Title DCG-1-163-1
Origin Varian
Solvent CDCl3
Temperature 25.0
Pulse Sequence s2pul
Experiment 1D
Number of Scans 16
Receiver Gain 28
Relaxation Delay 2.0000
Pulse Width 5.1000
Acquisition Time 2.4999
Acquisition Date 2014-07-27T18:31:13
Spectrometer Frequency 300.09
Spectral Width 4796.2
Nucleus 1H
Acquired Size 11990
Spectral Size 65536
Me
N
TBSO
Me
O
O
O
158b
1.08
1.00
0.92
1.02
1.01
0.96
1.06
1.02
0.92
3.26
1.14
1.03
3.26
1.06
9.94
3.00
2.87
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm


Parameter
Value
Data File Name / Volumes/ nobody/ home/ data/ fid/ dgrunenf/ vnmrsys/ data/ DCG-1-164-1_20140812_01/ PROTON_01.fid/ fid
Title PROTON_01
Origin Varian
Solvent CDCl3
Temperature 25.0
Pulse Sequence s2pul
Experiment 1D
Number of Scans 8
Receiver Gain 46
Relaxation Delay 1.0000
Pulse Width 2.9500
Acquisition Time 1.7046
Acquisition Date 2014-08-12T16:48:54
Spectrometer Frequency 599.63
Spectral Width 9611.9
Nucleus 1H
Acquired Size 16384
Spectral Size 65536
OTBS
H
Me
Me
159b
1.00
1.07
1.11
1.06
0.99
0.98
1.12
1.14
3.44
1.14
1.14
1.10
1.14
3.31
9.72
2.92
2.97
ppm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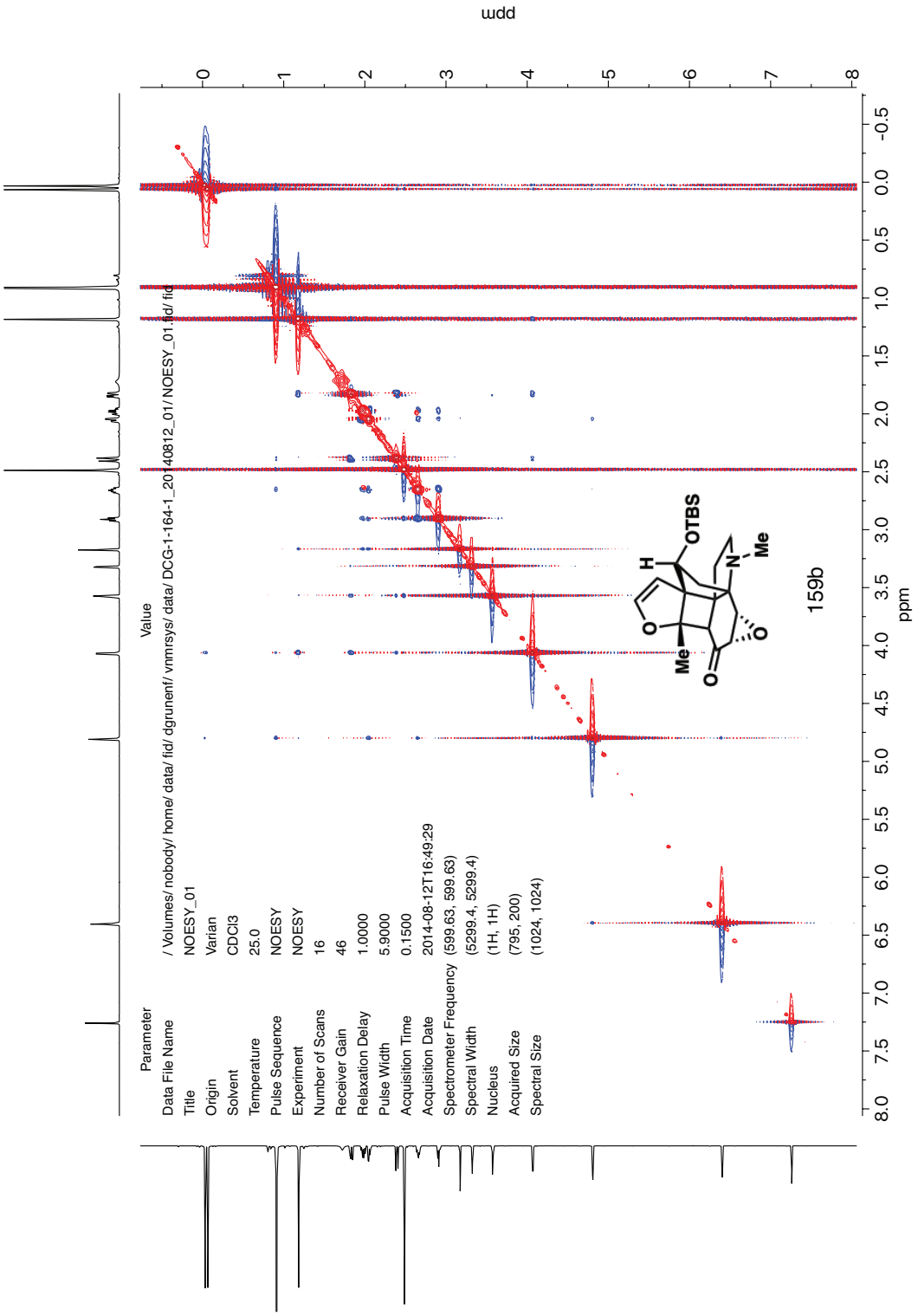
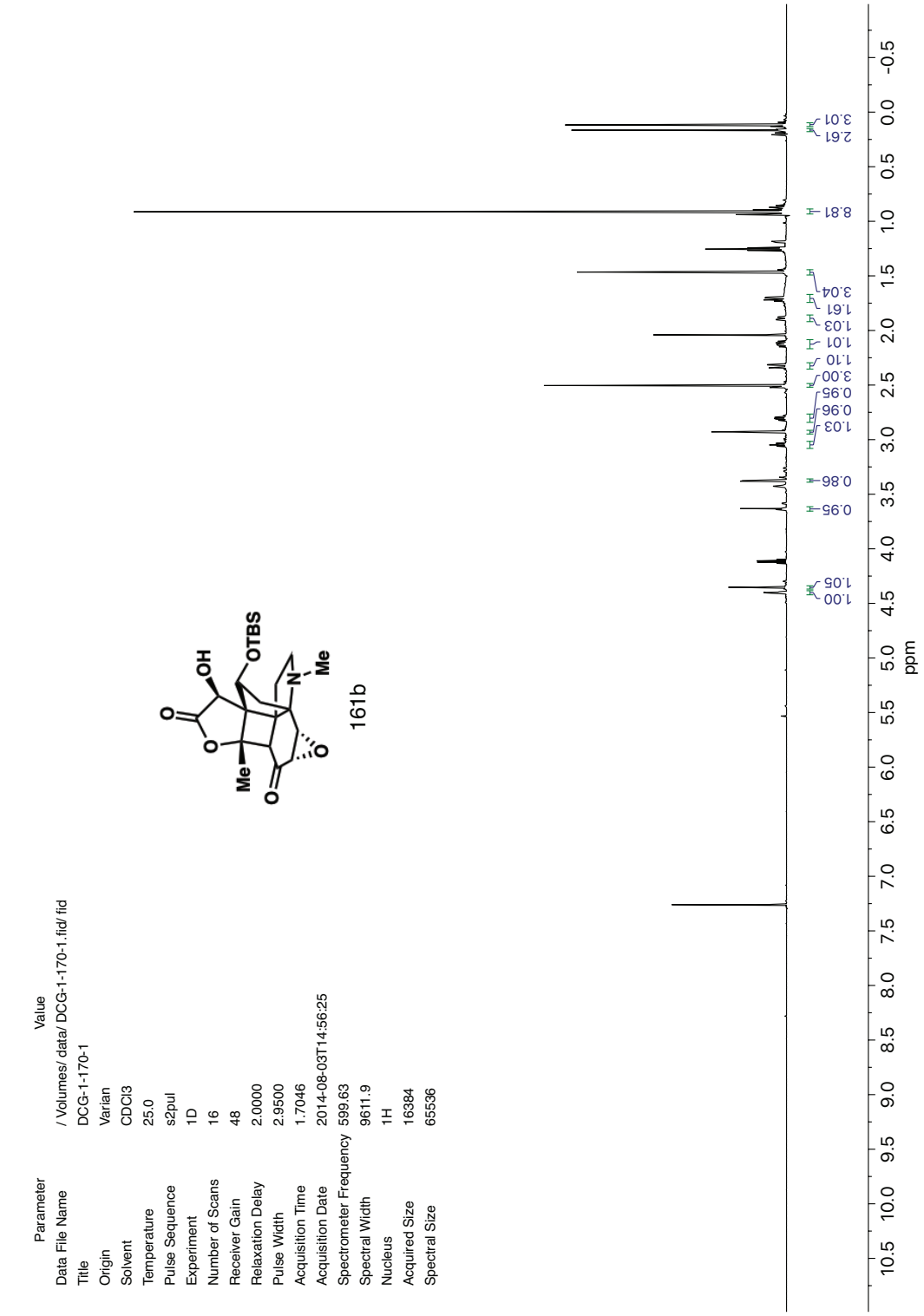
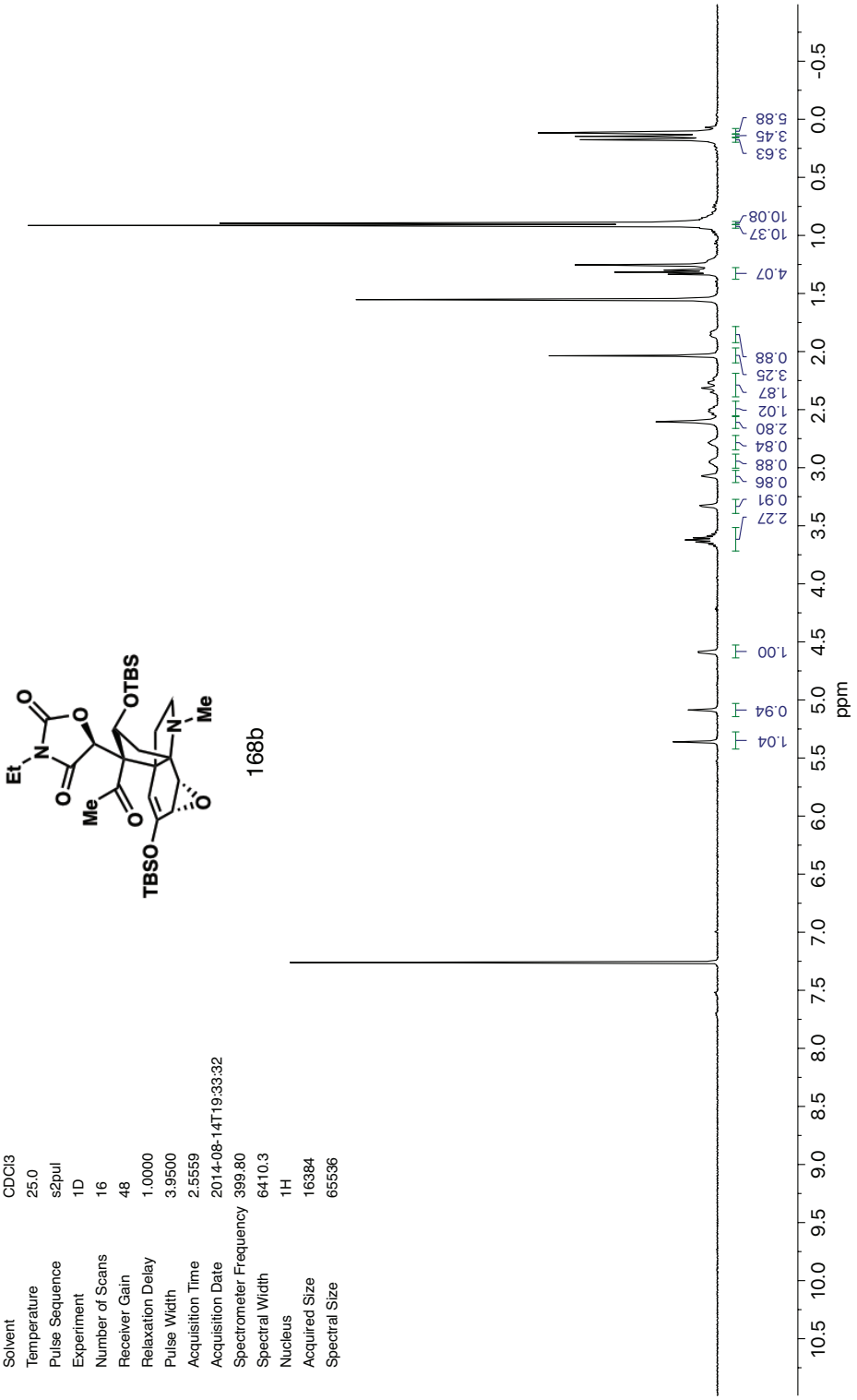
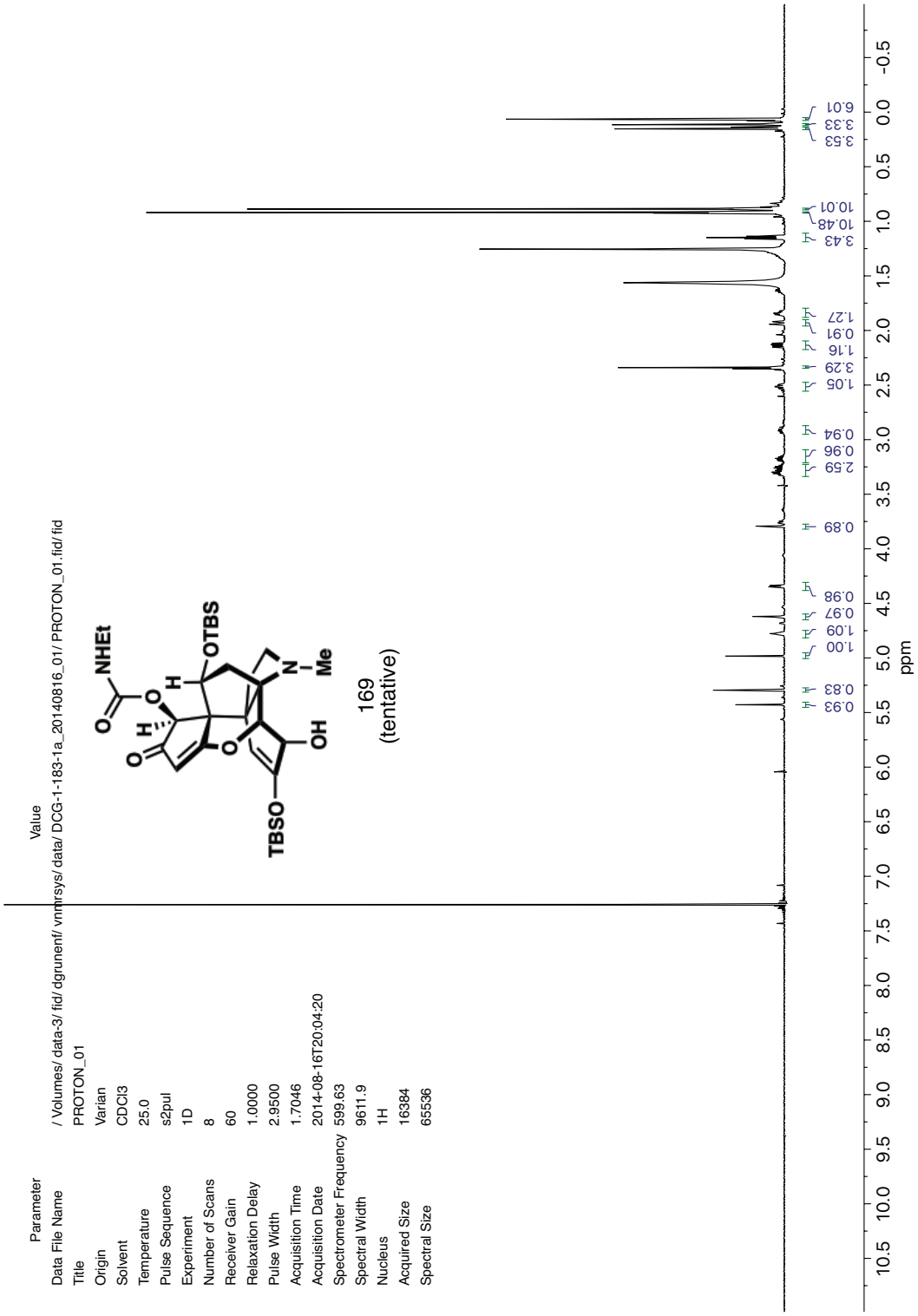
Value
Data File Name / Volumes/ nobody/ home/ data/ indy/ dgrunenf/ vnmrsys/ data/ DCG-1-164-1/ CARBON01.fid/ fid
Title CARBON01
Origin Varian
Solvent CDCl3
Temperature 25.0
Pulse Sequence s2pul
Experiment 1D
Number of Scans 1000
Receiver Gain 30
Relaxation Delay 1.0000
Pulse Width 4.2500
Acquisition Time 1.0420
Acquisition Date 2014-08-12T22:48:43
Spectrometer Frequency 125.66
Spectral Width 31446.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OTBS
H
Me
N
Me
O
O
O
159b
204.6
147.5
100.7
88.2
74.3
70.9
69.4
63.3
63.2
58.2
55.1
52.0
39.8
35.8
31.5
26.2
18.5
17.2
-4.5
-4.9
ppm


ppm
Parameter
Value
Data File Name / Volumes/ nobody/ home/ data/ fid/ dgrunenf/ vnmrsys/ data/ DCG-1-164-1_20140812_01/ NOESY_01.fid/ fid
Title NOESY_01
Origin Varian
Solvent CDCl3
Temperature 25.0
Pulse Sequence NOESY
Experiment NOESY
Number of Scans 16
Receiver Gain 46
Relaxation Delay 1.0000
Pulse Width 5.9000
Acquisition Time 0.1500
Acquisition Date 2014-08-12T16:49:29
Spectrometer Frequency (599.63, 599.63)
Spectral Width (5299.4, 5299.4)
Nucleus (1H, 1H)
Acquired Size (795, 200)
Spectral Size (1024, 1024)
OTBS
H
Me
N
Me
O
O
O
159b
ppm


Parameter Value
Data File Name / Volumes/ data/ DCG-1-170-1.fid/ fid
Title DCG-1-170-1
Origin Varian
Solvent CDCl3
Temperature 25.0
Pulse Sequence s2pul
Experiment 1D
Number of Scans 16
Receiver Gain 48
Relaxation Delay 2.0000
Pulse Width 2.9500
Acquisition Time 1.7046
Acquisition Date 2014-08-03T14:56:25
Spectrometer Frequency 599.63
Spectral Width 9611.9
Nucleus 1H
Acquired Size 16384
Spectral Size 65536
OH
OTBS
Me
Me
O
O
O
O
O
N
161b
1.00
1.05
0.95
0.86
1.03
0.96
0.95
3.00
1.10
1.01
1.03
1.61
3.04
8.81
2.61
3.01
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm


Parameter
Value
Data File Name / Volumes/ data-3/ siena/ dgrunenf/ vnmrsys/ data/ DCG-1-181-1/ PROTON01.fid/ fid
Title PROTON01
Origin Varian
Solvent CDCl3
Temperature 25.0
Pulse Sequence s2pul
Experiment 1D
Number of Scans 16
Receiver Gain 48
Relaxation Delay 1.0000
Pulse Width 3.9500
Acquisition Time 2.5559
Acquisition Date 2014-08-14T19:33:32
Spectrometer Frequency 399.80
Spectral Width 6410.3
Nucleus 1H
Acquired Size 16384
Spectral Size 65536
Et
Me
OTBS
TBSO
Me
168b
1.04
0.94
1.00
2.27
0.91
0.86
0.88
0.84
2.80
1.02
1.87
3.25
0.88
4.07
10.37
10.08
3.63
3.45
5.88
ppm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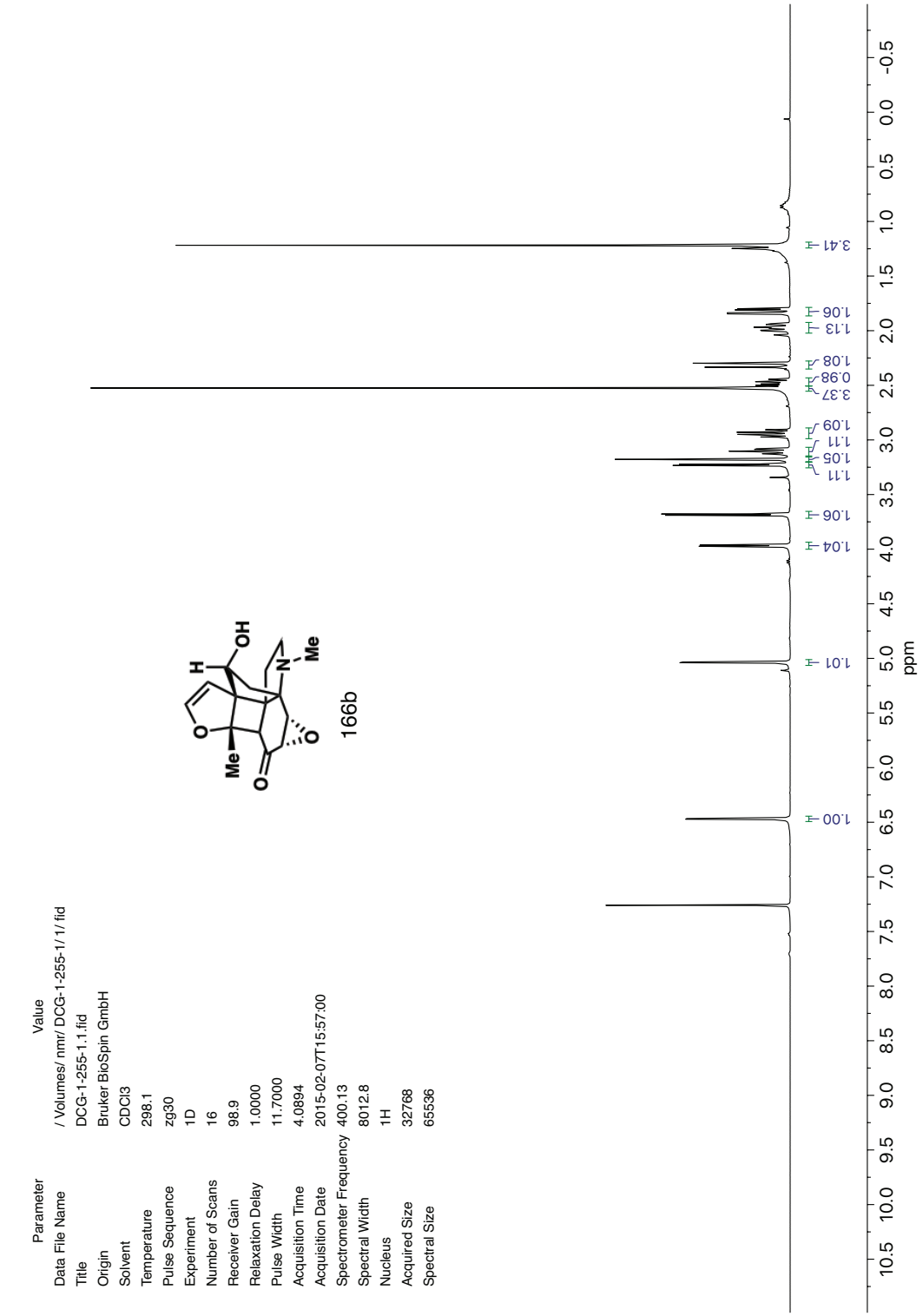
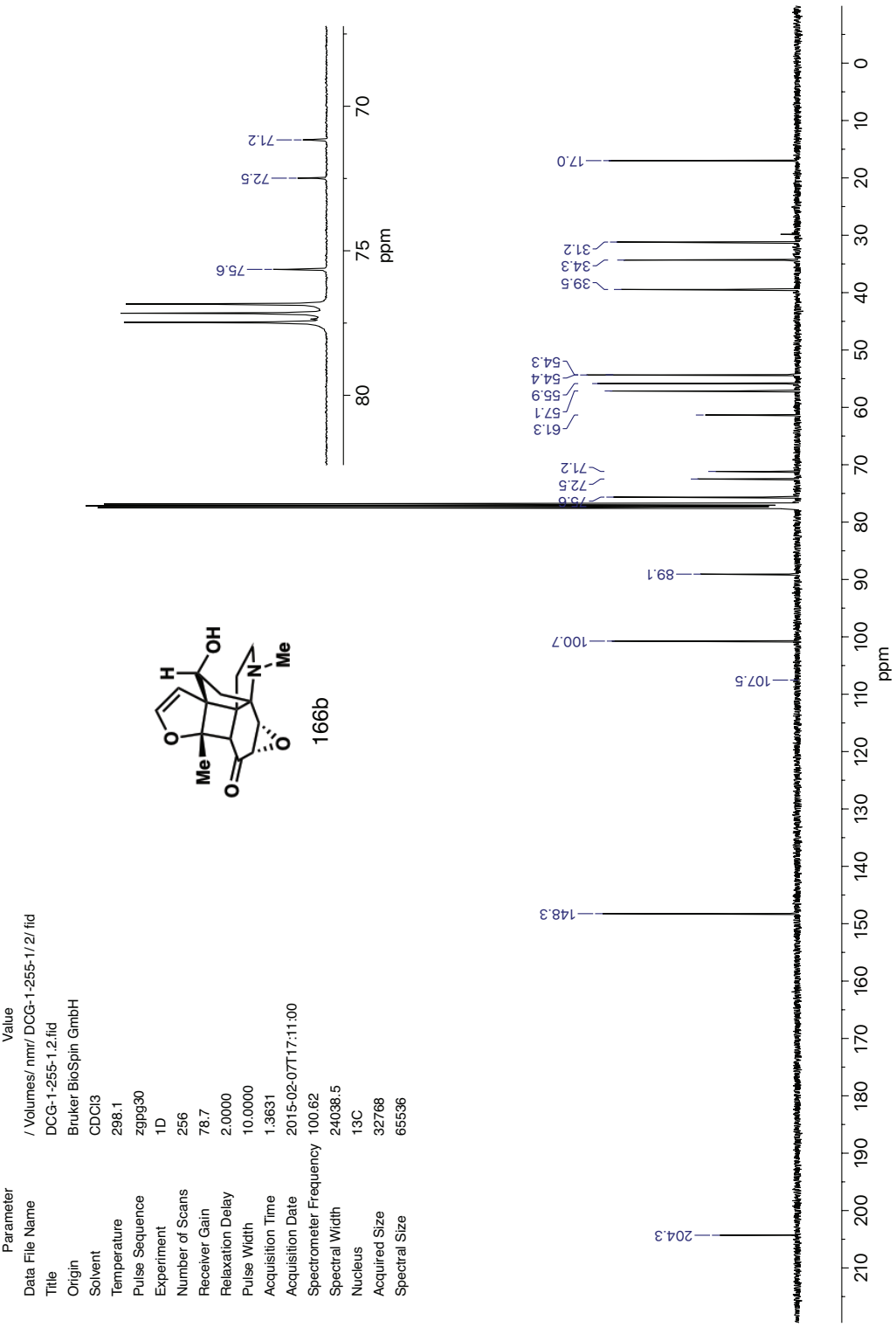
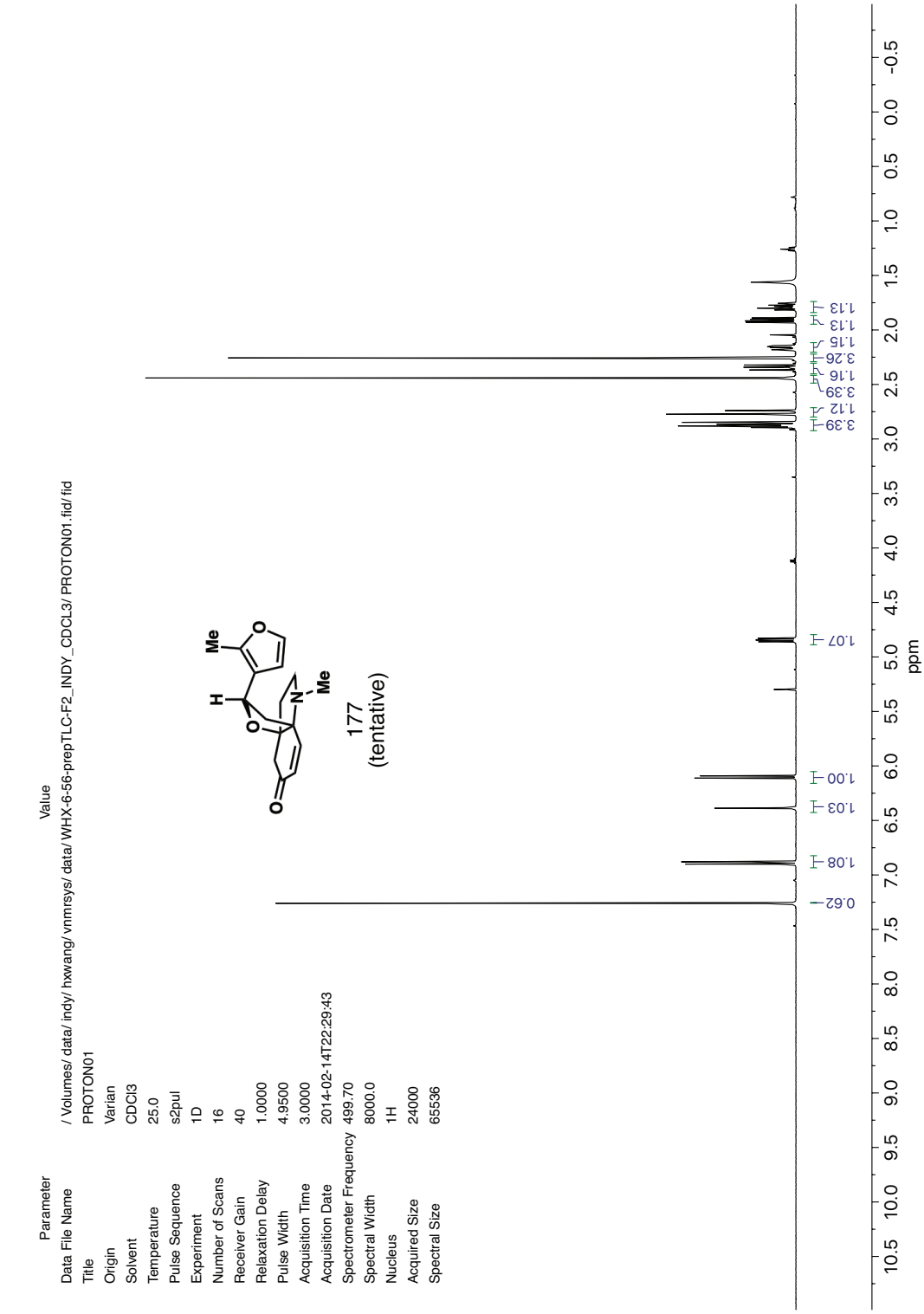
Value
Data File Name / Volumes/ data-3/ fid/ dgrunenf/ vnmrsys/ data/ DCG-1-183-1a_20140816_01/ PROTON_01.fid/ fid
Title PROTON_01
Origin Varian
Solvent CDCl3
Temperature 25.0
Pulse Sequence s2pul
Experiment 1D
Number of Scans 8
Receiver Gain 60
Relaxation Delay 1.0000
Pulse Width 2.9500
Acquisition Time 1.7046
Acquisition Date 2014-08-16T20:04:20
Spectrometer Frequency 599.63
Spectral Width 9611.9
Nucleus 1H
Acquired Size 16384
Spectral Size 65536
NHEt
OTBS
TBSO
OH
N
Me
169
(tentative)
0.93
0.83
1.00
1.09
0.97
0.98
0.89
2.59
0.96
0.94
1.05
3.29
1.16
0.91
1.27
3.43
10.48
10.01
3.53
3.33
6.01
ppm


Parameter Value
Data File Name / Volumes/ nmr/ DCG-1-255-1/1/ fid
Title DCG-1-255-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 298.1
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 98.9
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2015-02-07T15:57:00
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
H
OH
N
Me
O
Me
O
O
166b
1.00
1.01
1.04
1.06
1.11
1.05
1.11
1.09
3.37
0.98
1.08
1.06
1.13
3.41
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm


Parameter Value
Data File Name / Volumes/ nmr/ DCG-1-255-1/2/ fid
Title DCG-1-255-1.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 298.1
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 78.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2015-02-07T17:11:00
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
166b
ppm
204.3
148.3
107.5
100.7
89.1
75.6
72.5
71.2
61.3
57.1
55.9
54.4
54.3
39.5
34.3
31.2
17.0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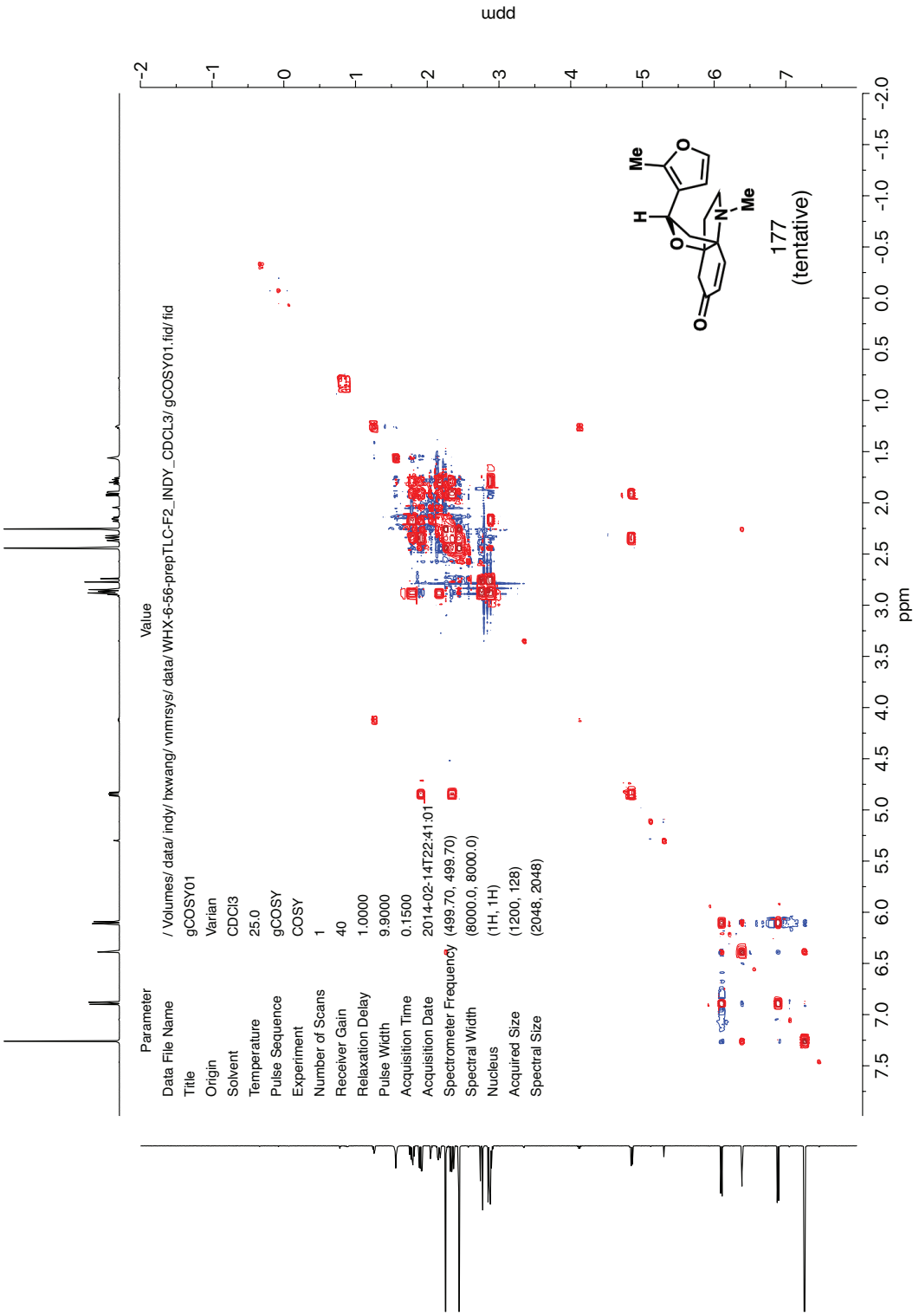
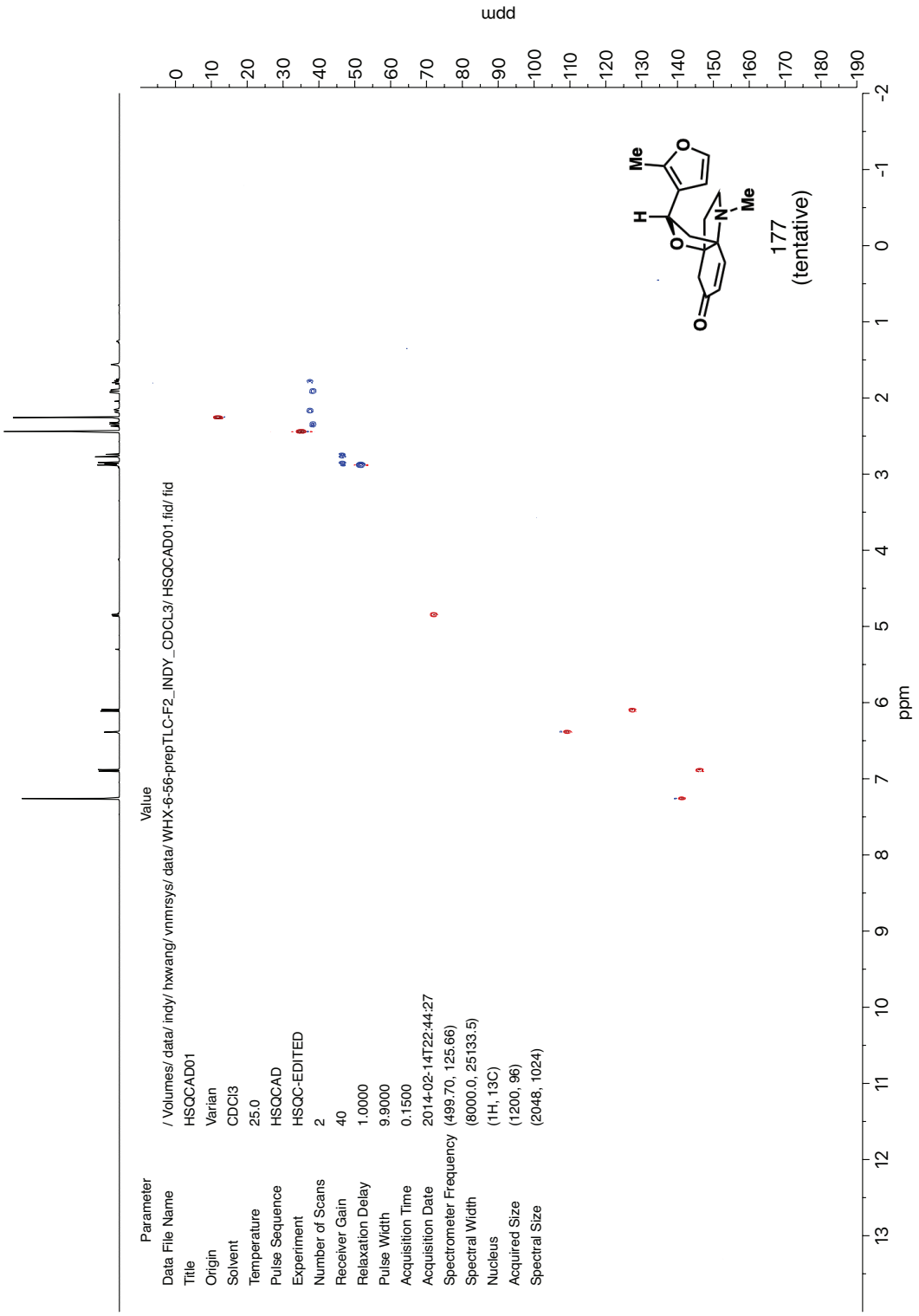
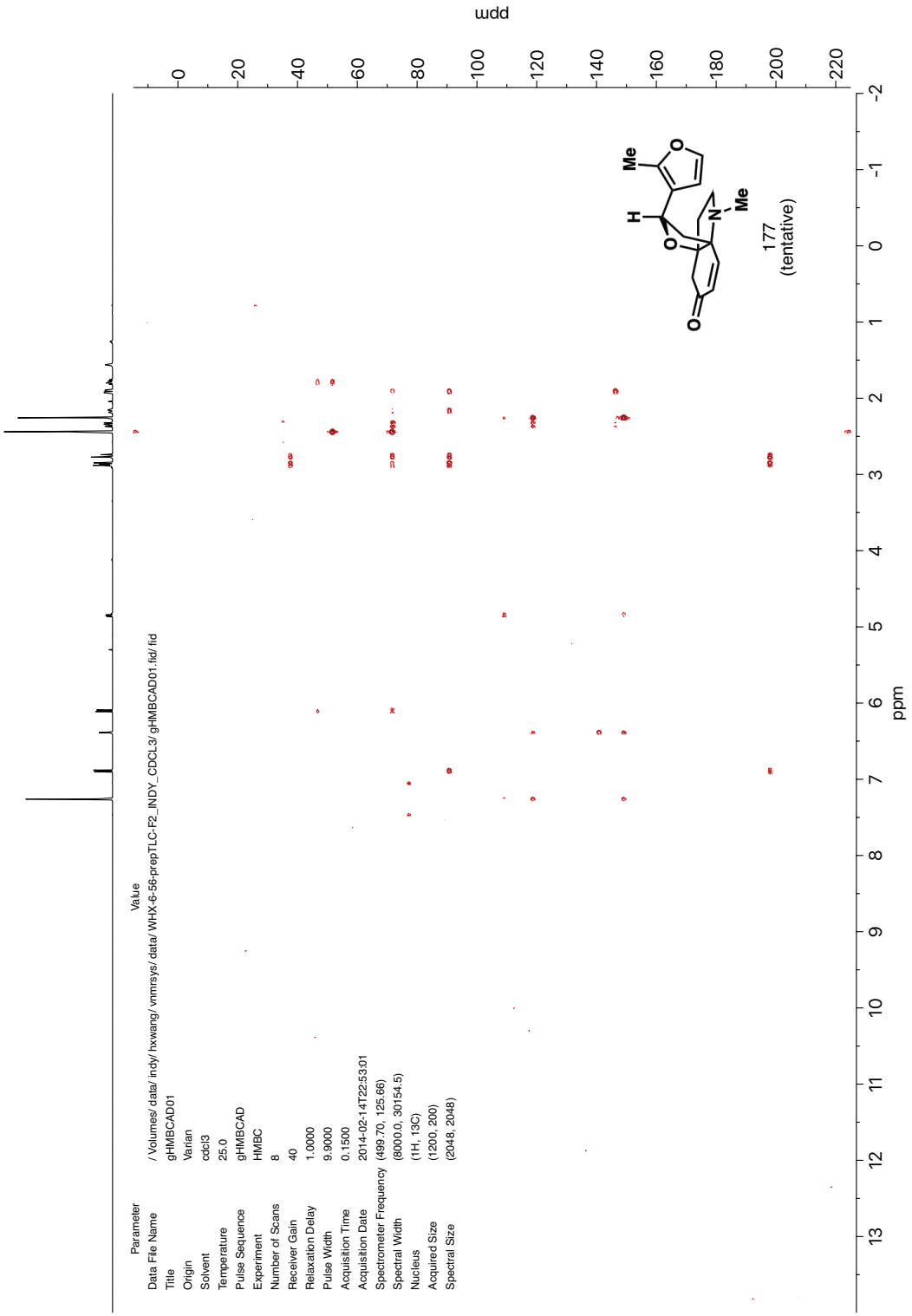
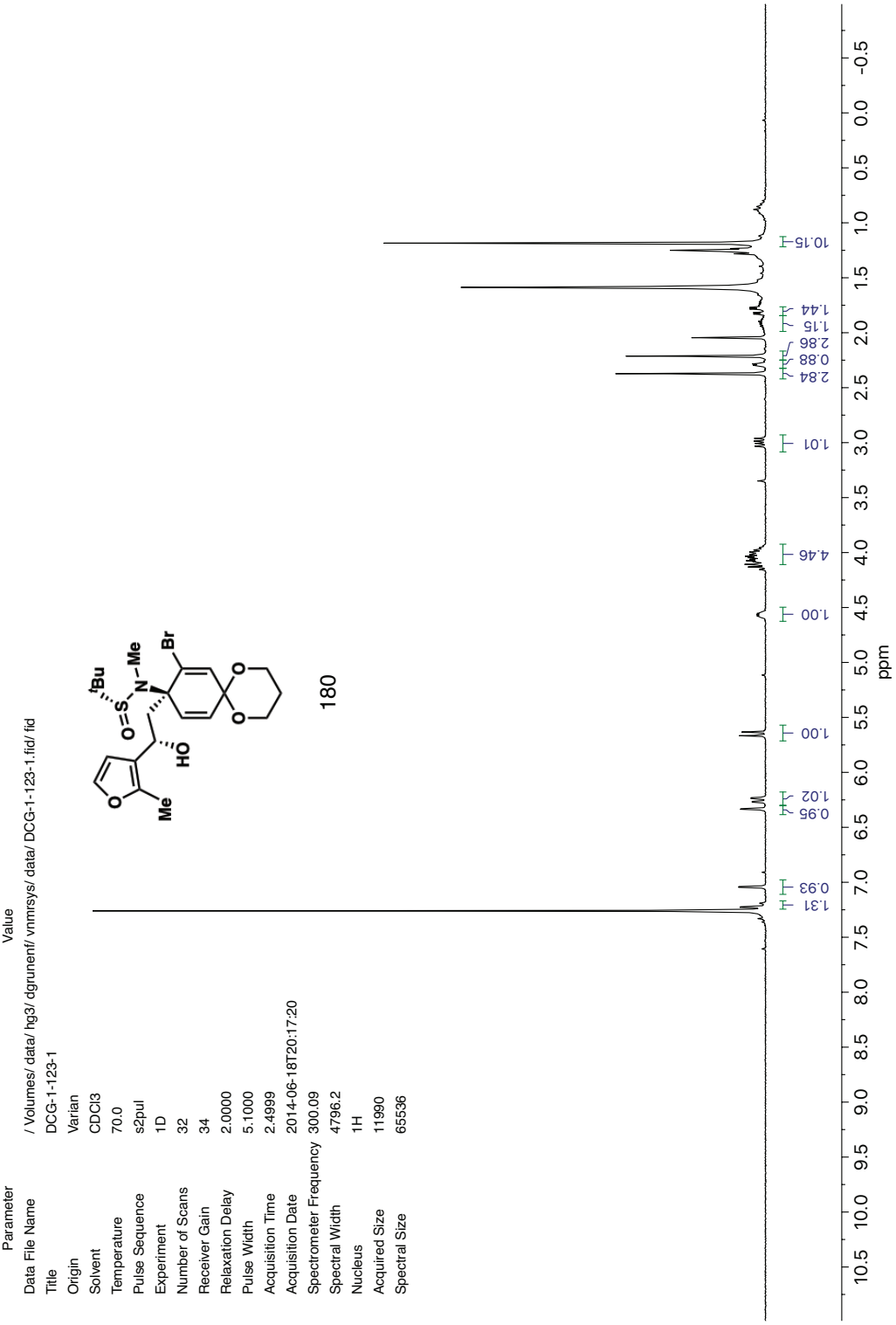
Value
Data File Name / Volumes/ data/ indy/ hxwang/ vnmrsys/ data/ WHX-6-56-prepTLC-F2_INDY_CDCL3/ PROTON01.fid/ fid
Title PROTON01
Origin Varian
Solvent CDCl3
Temperature 25.0
Pulse Sequence s2pul
Experiment 1D
Number of Scans 16
Receiver Gain 40
Relaxation Delay 1.0000
Pulse Width 4.9500
Acquisition Time 3.0000
Acquisition Date 2014-02-14T22:29:43
Spectrometer Frequency 499.70
Spectral Width 8000.0
Nucleus 1H
Acquired Size 24000
Spectral Size 65536
Me
H
O
N
Me
O
O
177
(tentative)
0.62
1.08
1.03
1.00
1.07
3.39
1.12
3.39
1.16
3.26
1.15
1.13
1.13
ppm
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5

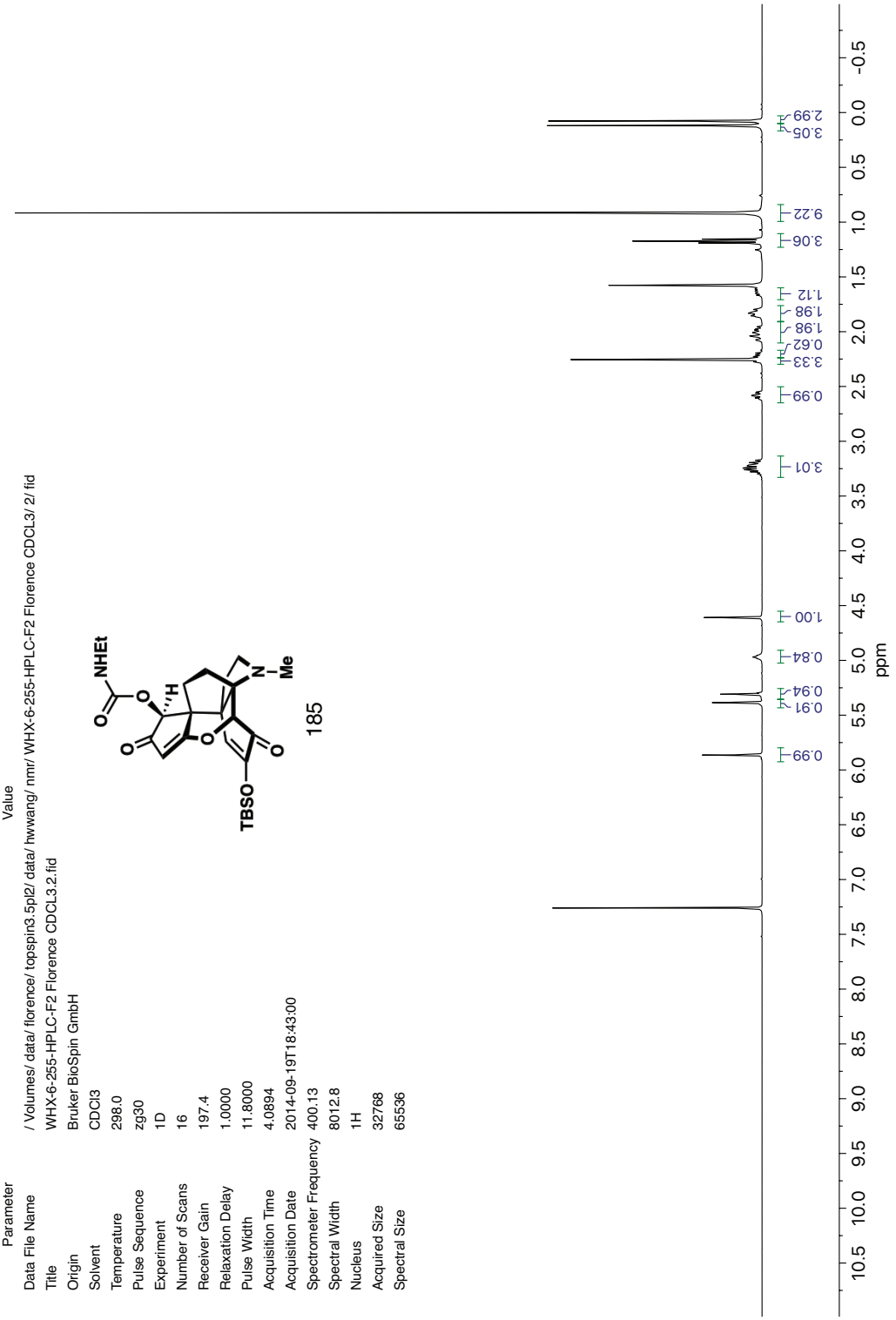

ppm
Parameter
Value
Data File Name / Volumes/ data/ indy/ hxwang/ vnmrsys/ data/ WHX-6-56-prepTLC-F2_INDY_CDCL3/ gCOSY01.fid/ fid
Title gCOSY01
Origin Varian
Solvent CDCl3
Temperature 25.0
Pulse Sequence gCOSY
Experiment COSY
Number of Scans 1
Receiver Gain 40
Relaxation Delay 1.0000
Pulse Width 9.9000
Acquisition Time 0.1500
Acquisition Date 2014-02-14T22:41:01
Spectrometer Frequency (499.70, 499.70)
Spectral Width (8000.0, 8000.0)
Nucleus (1H, 1H)
Acquired Size (1200, 128)
Spectral Size (2048, 2048)
Me
H
O
N
Me
O
177
(tentative)
ppm

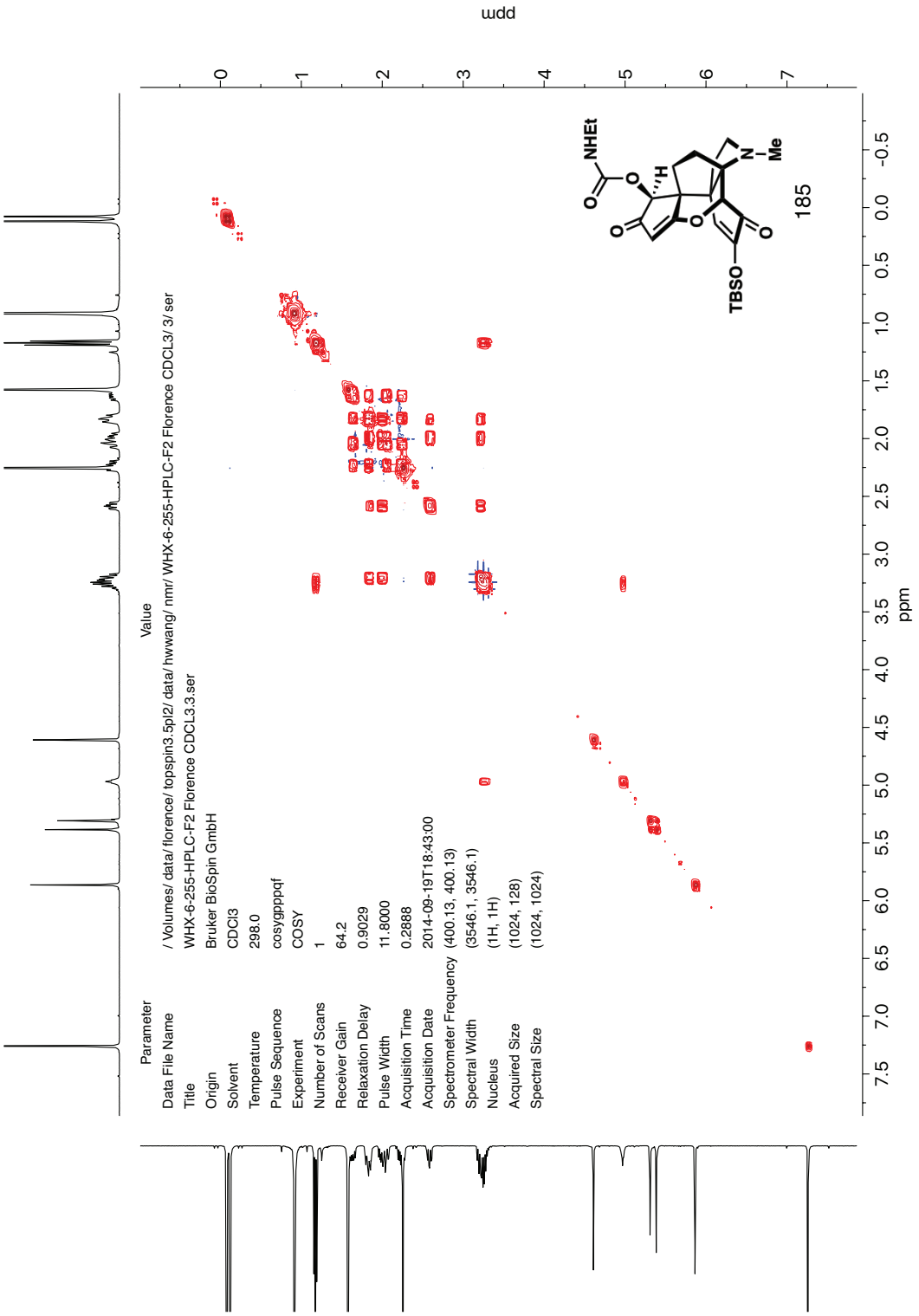


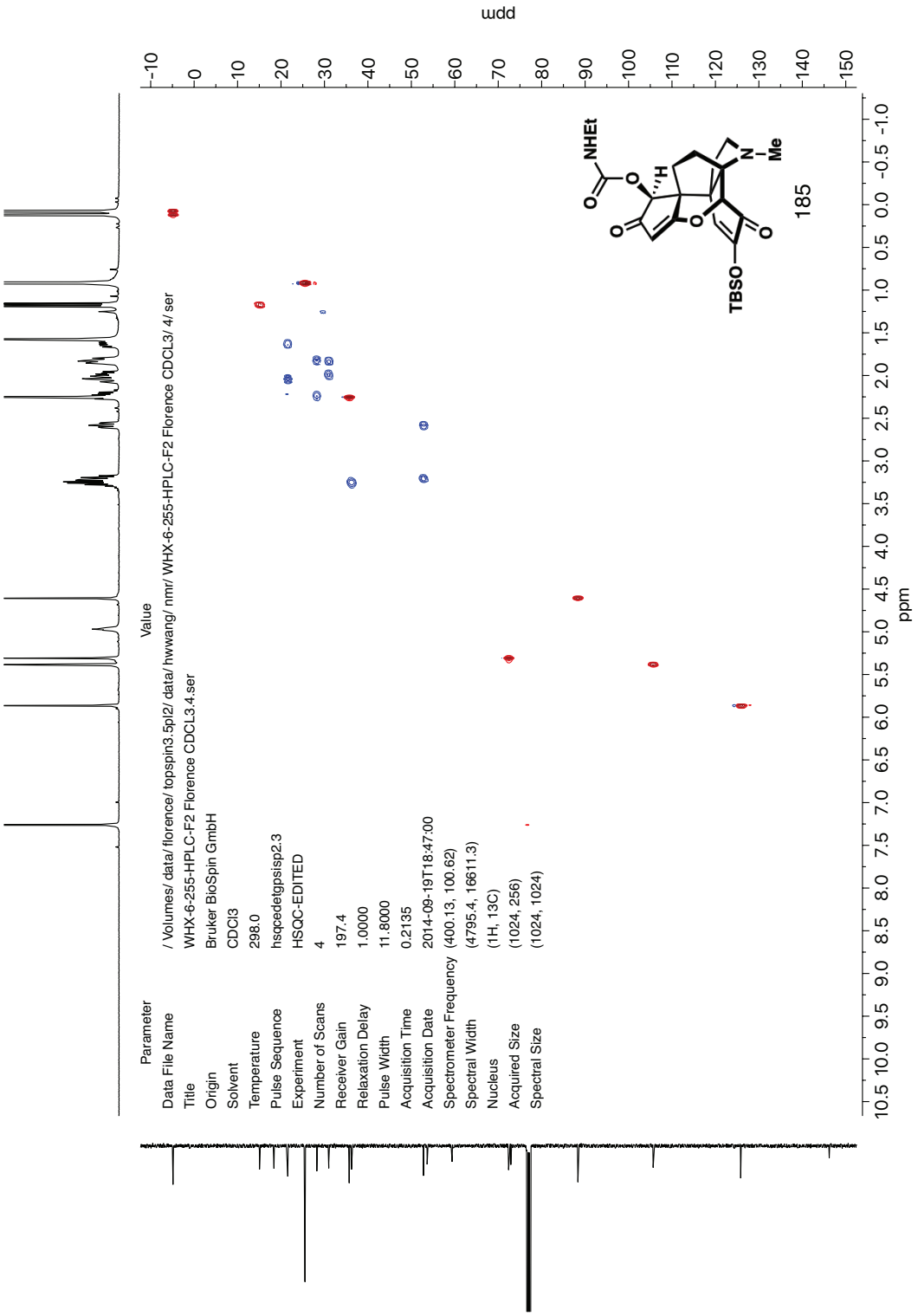
Parameter	Value
Data File Name	/ Volumes/ data/ indy/ hxwang/ vnmrsys/ data/ WHX-6-56-prepTLC-F2_INDY_CDCL3/ HSQCAD01.fid/ fid
Title	HSQCAD01
Origin	Varian
Solvent	CDCl3
Temperature	25.0
Pulse Sequence	HSQCAD
Experiment	HSQC-EDITED
Number of Scans	2
Receiver Gain	40
Relaxation Delay	1.0000
Pulse Width	9.9000
Acquisition Time	0.1500
Acquisition Date	2014-02-14T22:44:27
Spectrometer Frequency	(499.70, 125.66)
Spectral Width	(8000.0, 25133.5)
Nucleus	(1H, 13C)
Acquired Size	(1200, 96)
Spectral Size	(2048, 1024)

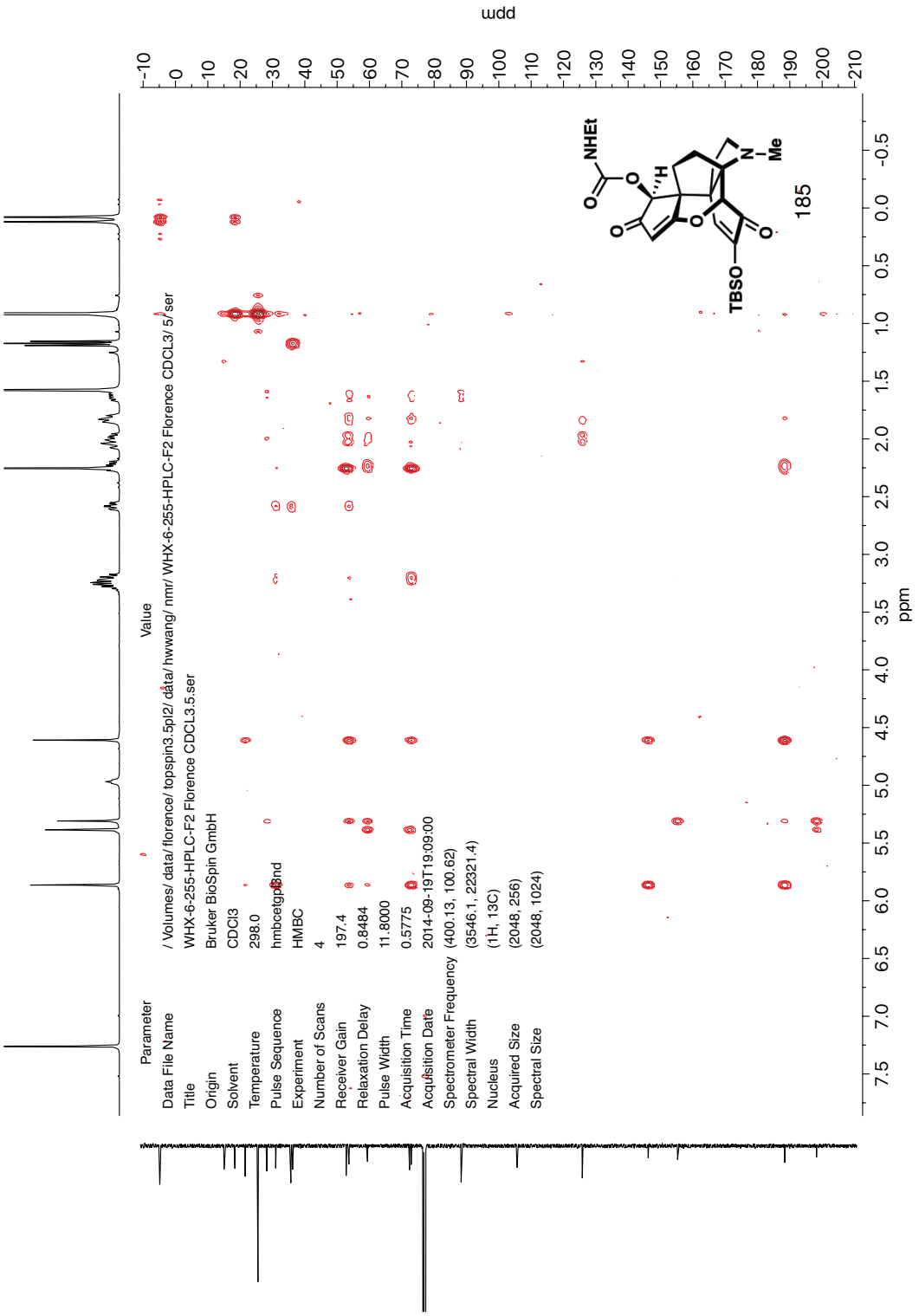

Parameter Value
Data File Name / Volumes/ data/ indy/ hxwang/ vnmrsys/ data/ WHX-6-56-prepTLC-F2_INDY_CDCL3/ gHMBCAD01.fid/ fid
Title gHMBCAD01
Origin Varian
Solvent cdcl3
Temperature 25.0
Pulse Sequence gHMBCAD
Experiment HMBC
Number of Scans 8
Receiver Gain 40
Relaxation Delay 1.0000
Pulse Width 9.9000
Acquisition Time 0.1500
Acquisition Date 2014-02-14T22:53:01
Spectrometer Frequency (499.70, 125.66)
Spectral Width (8000.0, 30154.5)
Nucleus (1H, 13C)
Acquired Size (1200, 200)
Spectral Size (2048, 2048)
ppm
ppm
Me
H
O
N
Me
O
O
177
(tentative)

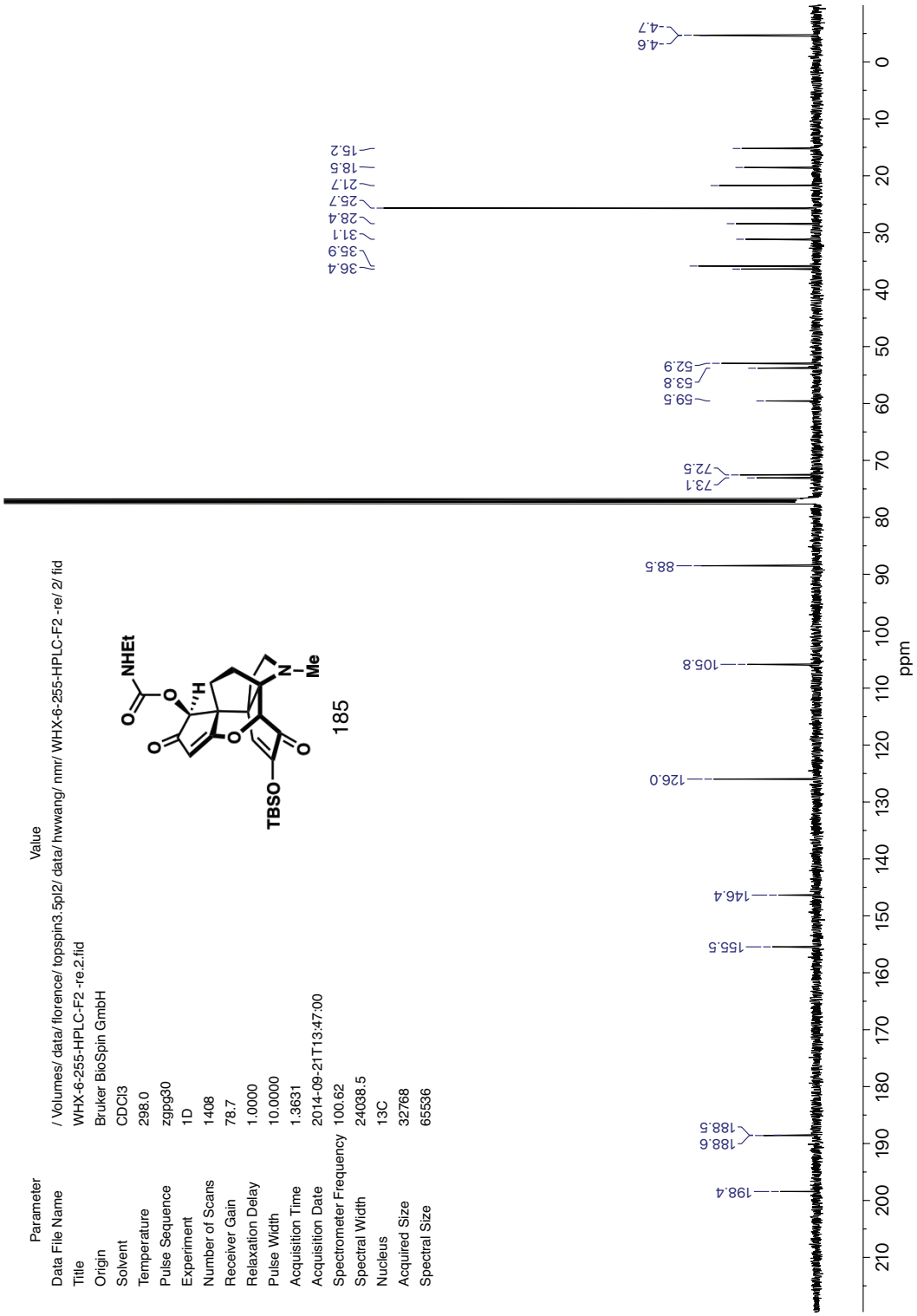

Parameter
Value
Data File Name / Volumes/ data/ hg3/ dgrunenf/ vnmrsys/ data/ DCG-1-123-1.fid/ fid
Title DCG-1-123-1
Origin Varian
Solvent CDCl3
Temperature 70.0
Pulse Sequence s2pul
Experiment 1D
Number of Scans 32
Receiver Gain 34
Relaxation Delay 2.0000
Pulse Width 5.1000
Acquisition Time 2.4999
Acquisition Date 2014-06-18T20:17:20
Spectrometer Frequency 300.09
Spectral Width 4796.2
Nucleus 1H
Acquired Size 11990
Spectral Size 65536
180
ppm

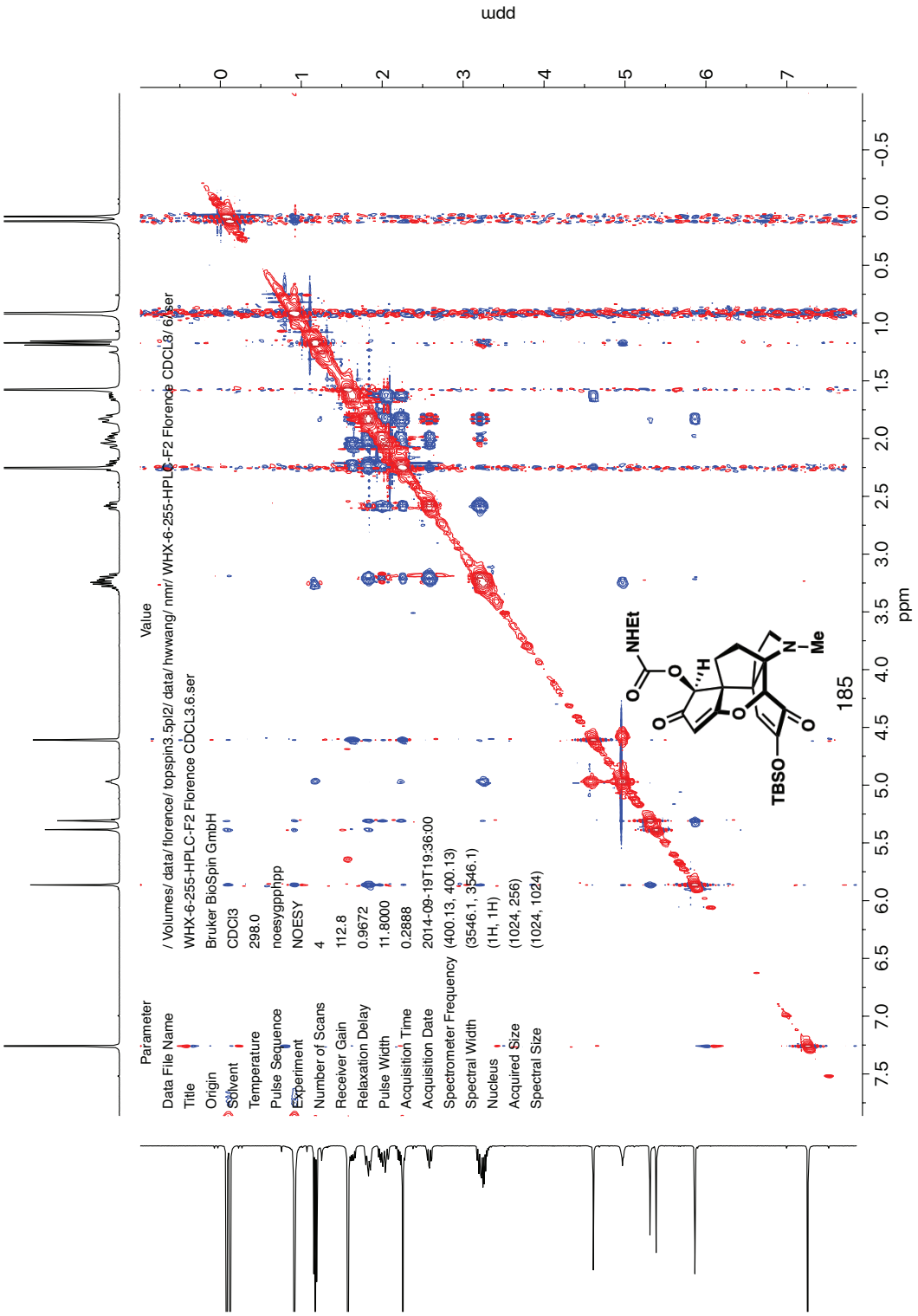

Parameter
Value
Data File Name / Volumes/ data/ florence/ topspin3.5pl2/ data/ hwwang/ nmr/ WHX-6-255-HPLC-F2 Florence CDCL3/ 2/ fid
Title WHX-6-255-HPLC-F2 Florence CDCL3.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 298.0
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 197.4
Relaxation Delay 1.0000
Pulse Width 11.8000
Acquisition Time 4.0894
Acquisition Date 2014-09-19T18:43:00
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
NHEt
TBSO
Me
185
0.99
0.91
0.94
0.84
1.00
3.01
0.99
3.33
0.62
1.98
1.98
1.12
3.06
9.22
3.05
2.99
ppm

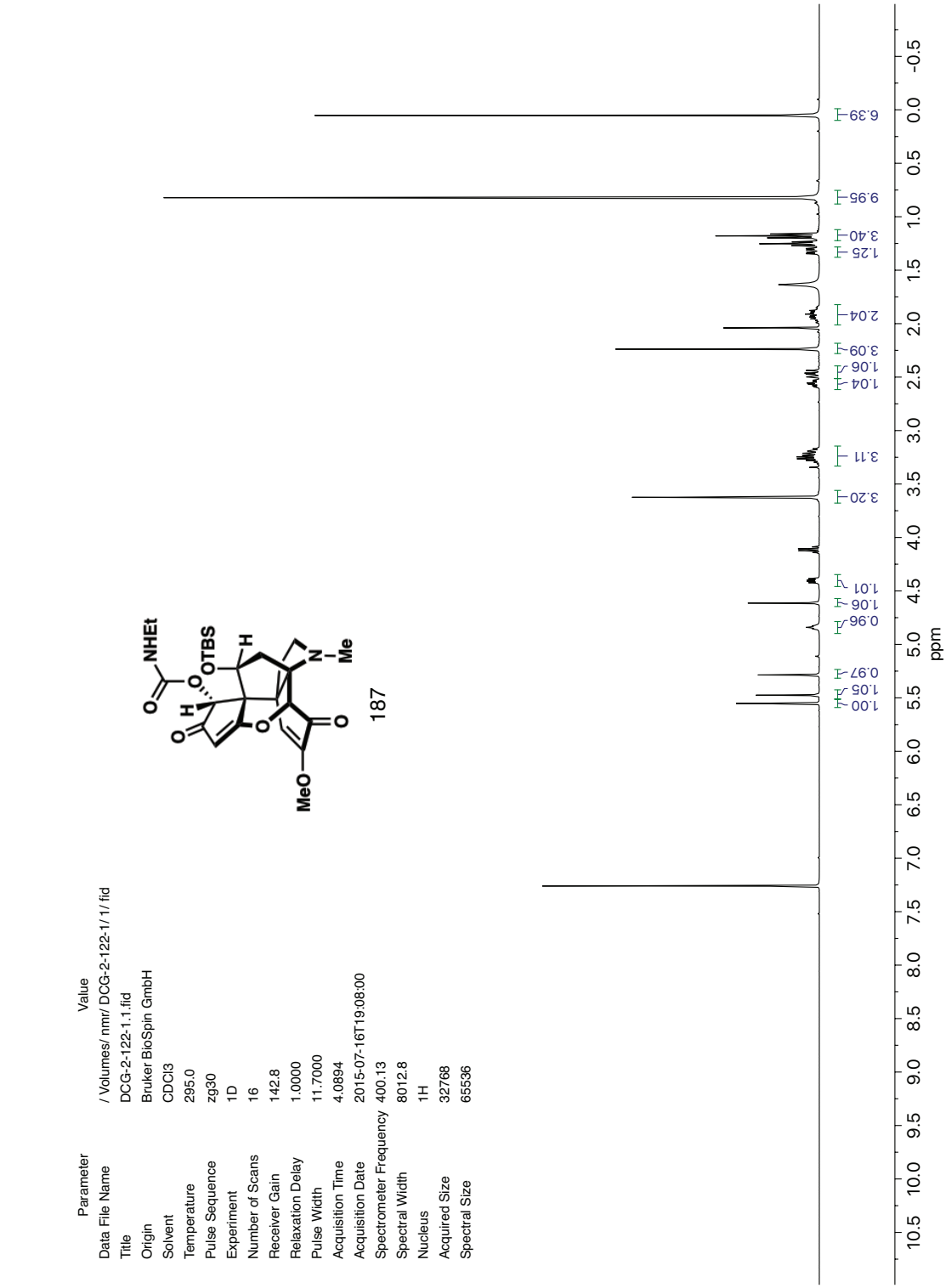

ppm
Parameter Value
Data File Name / Volumes/ data/ florence/ topspin3.5pl2/ data/ hwwang/ nmr/ WHX-6-255-HPLC-F2 Florence CDCL3/ 3/ ser
Title WHX-6-255-HPLC-F2 Florence CDCL3.3.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 298.0
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 64.2
Relaxation Delay 0.9029
Pulse Width 11.8000
Acquisition Time 0.2888
Acquisition Date 2014-09-19T18:43:00
Spectrometer Frequency (400.13, 400.13)
Spectral Width (3546.1, 3546.1)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)
NHEt
TBSO
Me
185
ppm


Parameter
Value
Data File Name / Volumes/ data/ florence/ topspin3.5pl2/ data/ hwwang/ nmr/ WHX-6-255-HPLC-F2 Florence CDCL3/ 4/ ser
Title WHX-6-255-HPLC-F2 Florence CDCL3.4.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 298.0
Pulse Sequence hsqcedetgpsisp2.3
Experiment HSQC-EDITED
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 1.0000
Pulse Width 11.8000
Acquisition Time 0.2135
Acquisition Date 2014-09-19T18:47:00
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
NHEt
TBSO
Me
185
ppm
ppm


Parameter Value
Data File Name / Volumes/ data/ florence/ topspin3.5pl2/ data/ hwwang/ nmr/ WHX-6-255-HPLC-F2 Florence CDCL3/ 5/ ser
Title WHX-6-255-HPLC-F2 Florence CDCL3.5.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 298.0
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 0.8484
Pulse Width 11.8000
Acquisition Time 0.5775
Acquisition Date 2014-09-19T19:09:00
Spectrometer Frequency (400.13, 100.62)
Spectral Width (3546.1, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
NHEt
TBSO
Me
185
ppm
ppm


Parameter
Value
Data File Name / Volumes/ data/ florence/ topspin3.5pl2/ data/ hwwang/ nmr/ WHX-6-255-HPLC-F2 -re/ 2/ fid
Title WHX-6-255-HPLC-F2 -re.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 298.0
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 1408
Receiver Gain 78.7
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2014-09-21T13:47:00
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
NHEt
TBSO
Me
185
198.4
188.6
188.5
155.5
146.4
126.0
105.8
88.5
73.1
72.5
59.5
53.8
52.9
36.4
35.9
31.1
28.4
25.7
21.7
18.5
15.2
-4.6
-4.7
ppm


ppm
Parameter
Value
Data File Name / Volumes/ data/ florence/ topspin3.5pl2/ data/ hwwang/ nmr/ WHX-6-255-HPLC-F2 Florence CDCL3/ 6/ ser
Title WHX-6-255-HPLC-F2 Florence CDCL3.6.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 298.0
Pulse Sequence noesygpphpp
Experiment NOESY
Number of Scans 4
Receiver Gain 112.8
Relaxation Delay 0.9672
Pulse Width 11.8000
Acquisition Time 0.2888
Acquisition Date 2014-09-19T19:36:00
Spectrometer Frequency (400.13, 400.13)
Spectral Width (3546.1, 3546.1)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
NHEt
TBSO
Me
185


Parameter Value
Data File Name / Volumes/ nmr/ DCG-2-122-1/1/ fid
Title DCG-2-122-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 142.8
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2015-07-16T19:08:00
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
NHEt
OTBS
H
MeO
Me
187
1.00
1.05
0.97
0.96
1.06
1.01
3.20
3.11
1.04
1.06
3.09
2.04
1.25
3.40
9.95
6.39
ppm

Chapter 3

Revised Strategies for the Asymmetric Total Synthesis of Acutumine Alkaloids

3.1 INTRODUCTION

After successfully constructing the spirocyclic core of (–)-acutumine (**1**) in two different series, an impasse had been reached in our synthetic efforts since 1) material throughput to the advanced intermediates was limited, 2) opening of the caged-ether **165b** had not been accomplished in preliminary trials (see Chapter 2, Section 2.5.2), 3) TBS-deprotection had proven challenging, and 4) installation of the dimethoxyenone motif had been unsuccessful thus far. As a result, we turned our focus toward strategies which circumvented the use of a carbamate as part of our retro-aldol approach to address these challenges. In particular, elaboration of epoxyketone **159a** to the dimethoxyenone functionality was pursued more vigorously since this motif is conserved across the acutumine alkaloids. This chapter details these efforts, which culminated in the synthesis

of a key late-stage spirocycle bearing the entire carbocyclic core and oxidation pattern of the natural product (–)-acutuminine (**18**).

3.2 EARLY EFFORTS TO INSTALL THE DIMETHOXYENONE MOTIF

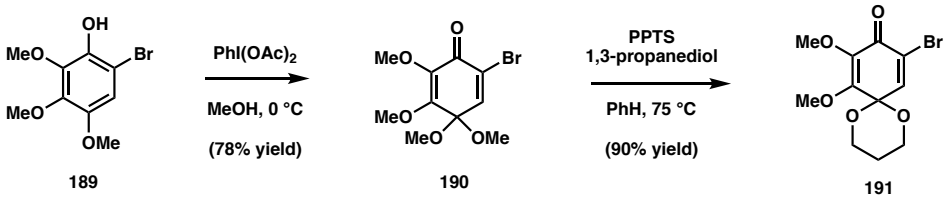
3.2.1 Strategy to Begin Synthesis with Requisite Oxidation State

As efforts were underway to open epoxyketones **158a** and **159a** (*vide infra*), the first steps of the synthesis were investigated with a more highly oxidized phenol (Scheme 3.1). It was thought that, as in the case of the total syntheses published by Castle and Herzon, it would be advantageous to begin the total synthesis with the requisite oxidation state at C7–C8 for the dimethoxyenone. While known phenol **189**[1–3] could indeed be advanced in the oxidative dearomatization/transketalization sequence to afford bis-enone **191** (Scheme 3.1a), subsequent imine formation with sulfinyl amine **135** proved challenging (Scheme 3.1b). The conditions previously developed, utilizing THF and $Ti(OEt)_4$ did not afford the desired product, but left unreacted starting material. Significant amount of experimentation was undertaken to effect this imine formation. It was found that heating **191** in neat $Ti(OEt)_4$ in the presence of amine **135** in the microwave at 80 °C could afford conversion to a new product by TLC analysis (not shown). However, this product was not stable to isolation; aqueous workup, as well as quench with EtOAc, consistently returned enone **191**. It was hypothesized that the new product may be the resulting aminal **194**; however, efforts to confirm this product or utilize it in subsequent steps *in situ* remained fruitless. It is hypothesized that the encountered difficulty in forming the desired imine **192** may arise from the increase in electron density on the enone carbonyl as a

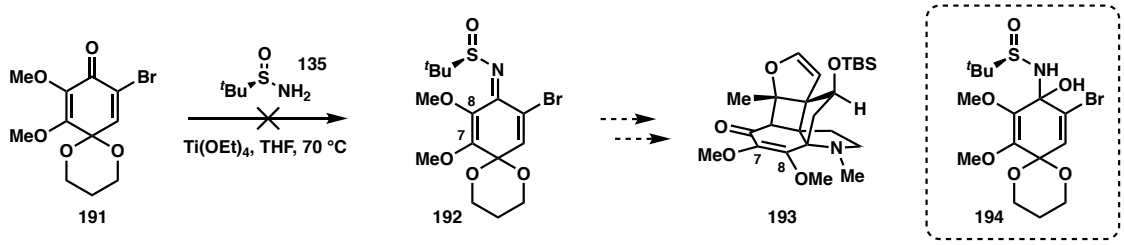
vinylogous ester, as well as the increased steric hindrance at the α-position of the enone via the addition of a methoxy group.

Scheme 3.1 *Strategy to employ C7–C8-oxidized phenol at the beginning.*

a) Oxidative dearomatization/transketalization to enone **191**.



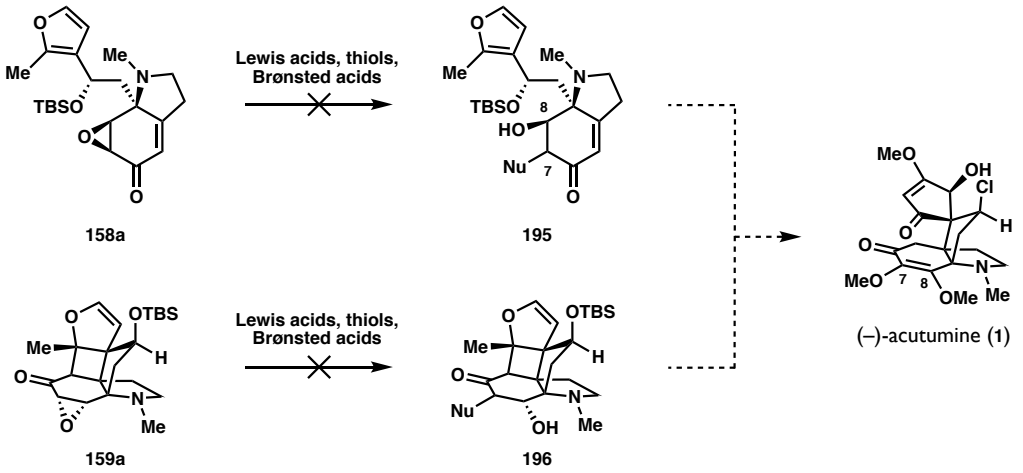
b) A challenging imine formation.



3.2.2 Recalcitrant Epoxyketones

During our optimization efforts of the C10-oxidized series, opening of epoxyketones **158a** and **159a** were pursued as well (Scheme 3.2). However, screens of both Brønsted acids[4] and Lewis acids,[5–7] as well as investigations into epoxide-openings with thiol nucleophiles, were unsuccessful.[7] In most cases, unreacted starting material was observed, which upon more forcing conditions would undergo decomposition. The first successful epoxide-opening/modification occurred when a Wharton rearrangement was attempted (*vide infra*). This series led us down an exciting path for a retro-aldol/Dieckmann sequence which did not require a carbamate nucleophile.

Scheme 3.2 *Epoxide-opening: early trials.*



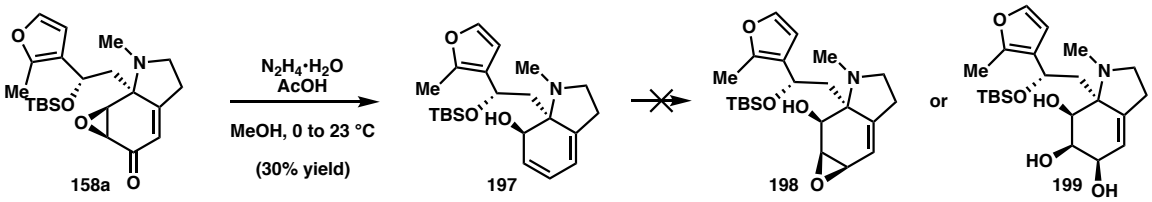
3.3 WHARTON SERIES

3.3.1 Wharton Rearrangement

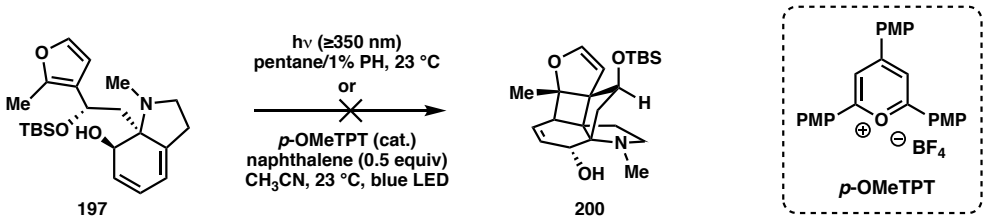
When subjected to hydrazine hydrate and AcOH in MeOH, we were pleased to see clean Wharton rearrangement of epoxyketone **159a** to allylic alcohol **197** (Scheme 3.3a).[8]

Scheme 3.3 *Wharton rearrangement prior to [2+2]-cycloaddition.*

a) Wharton rearrangement to diene **197**.



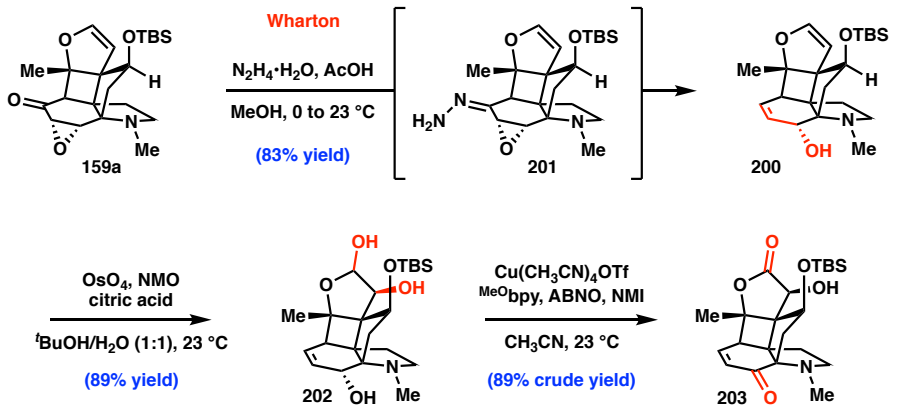
b) [2+2]-cycloaddition of diene.



While the yield was moderate, it allowed us to pursue subsequent oxidation chemistry of this allylic alcohol. Unfortunately, various epoxidation and dihydroxylation conditions were unsuccessful, and allylic epoxide **198** and triol **199** were never observed. A number of [2+2]-cycloaddition trials were performed as well (Scheme 3.3b).[9] However, cyclobutane **200** was never obtained; rather, diene **197** tended to decompose quite readily.

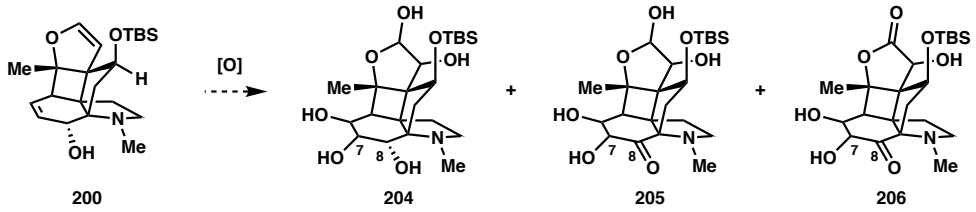
Fortunately, the Wharton rearrangement translated very well to cyclobutane **159a**, to afford allylic alcohol **200** in 83% yield (Scheme 3.4). Subsequent furan dihydroxylation proceeded smoothly utilizing the conditions established for the carbamate series, with OsO_4 and citric acid to provide lactol **202** in 89% yield. Finally, Stahl oxidation furnished the desired lactone **203**,[10,11] which was formed with concomitant allylic alcohol oxidation on the 6-membered ring. Interestingly, this intermediate was fairly sensitive to purification (both silica and Florisil flash chromatography, even when neutralized with Et_3N), and it was found that it was best to perform an aqueous workup after the Stahl oxidation utilizing aqueous $NaHCO_3$ and postpone flash chromatography until subsequent steps.

Scheme 3.4 *Wharton rearrangement post [2+2]-cycloaddition.*



While lactone **203** could be accessed very efficiently, significant interest remained in the possibility for a bis-dihydroxylation of allylic alcohol **200** to afford **204** in a single step (Scheme 3.5). Further oxidized ketones **205** and **206** were also of interest because these products would approach the required oxidation states at C7 and C8 for the dimethoxyenone functionality. Unfortunately, multiple screens of dihydroxylation reactions never cleanly afforded the desired products. These investigations included variations of the Upjohn dihydroxyation, such as solvent screen, stoichiometric OsO_4 trials, and investigations into amine additives.[12–15] Furthermore, the conditions reported by Plietker utilizing $RuCl_3$ proved unfruitful as well.[16–20]

Scheme 3.5 *Bis-dihydroxylation of allylic alcohol* ***200****.*

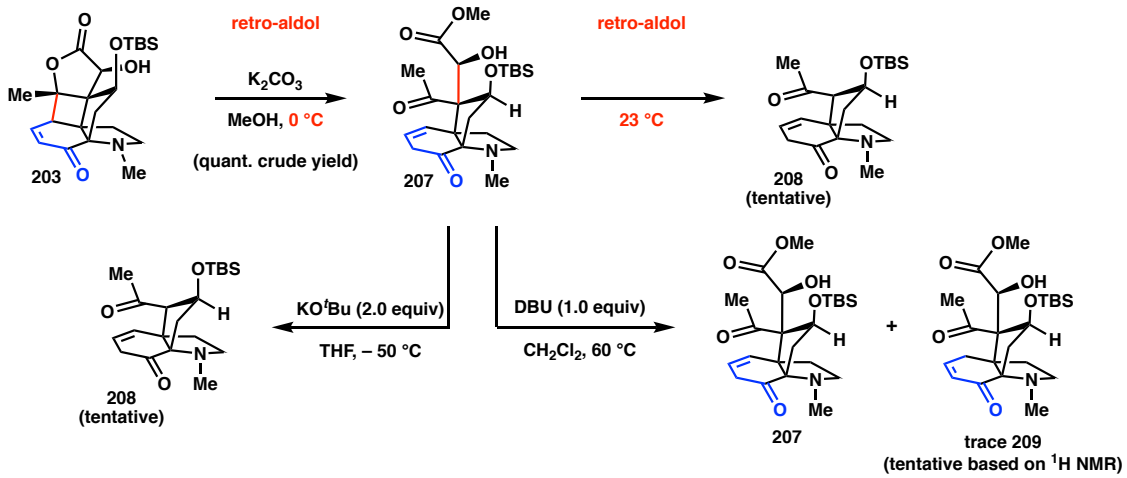


3.3.2 Retro-Aldol/Dieckmann – Wharton Series

Since a more highly oxidized intermediate could not be obtained, subsequent chemistry on lactone **203** was pursued (Scheme 3.6). Gratifyingly, subjecting **203** to K_2CO_3 in MeOH at 0 °C afforded the desired retro-aldol product **207**, which interestingly contains a skipped enone. When the retro-aldol reaction was warmed to room temperature, a second retro-aldol event occurred to afford ketone **208** in which the ester side-chain was eliminated (based on LC/MS analysis). Similarly, when ketone **207** was subjected to Dieckmann cyclization conditions, such as KO^{t}Bu in THF, undesired retro-aldol product **208** was

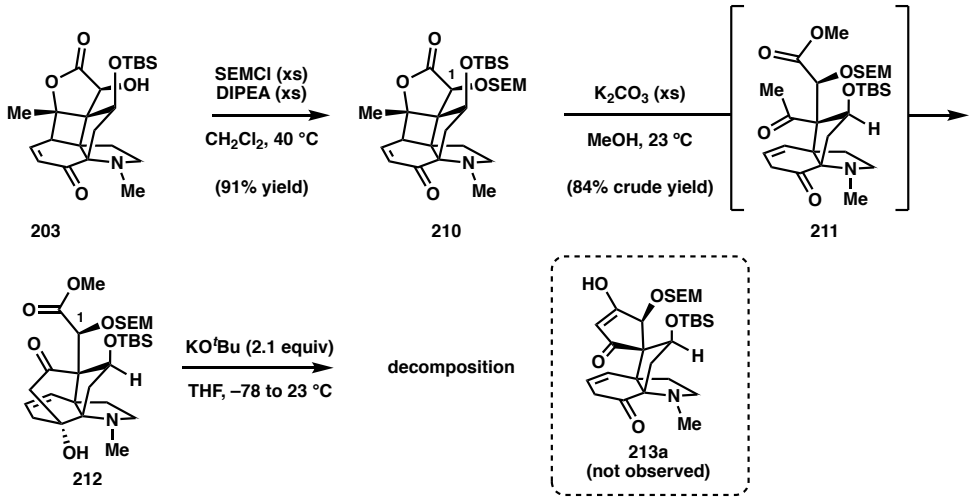
observed as the sole product, even at low temperatures. To advance skipped enone **207** to conjugated enone **209**, **207** was subjected to DBU in refluxing CH_2Cl_2; however, only traces of the conjugated enone **209** could be observed by ^1H NMR, indicating that skipped enone **207** is most likely thermodynamically favored.

Scheme 3.6 *Successful retro-aldol with MeOH.*



In an effort to avoid the second retro-aldol fragmentation of ketone **207**, two avenues were pursued: 1) protection of α-hydroxylactone **203**, and 2) protection of retro-aldol product **207**. In the first case, the C1-alcohol was protected as the SEM ether to furnish **210** (Scheme 3.7). Subsequent retro-aldol proceeded smoothly, affording bridging ketone **212**. Unfortunately, subjecting tertiary alcohol **212** to various basic reaction conditions did not afford the desired spirocycle via Dieckmann cyclization. Instead, many of the conditions surveyed resulted in epimerization at C1 or decomposition. Similar epimerization reactivity was observed in the carbamate series (see Chapter 2, Section 2.4.3).

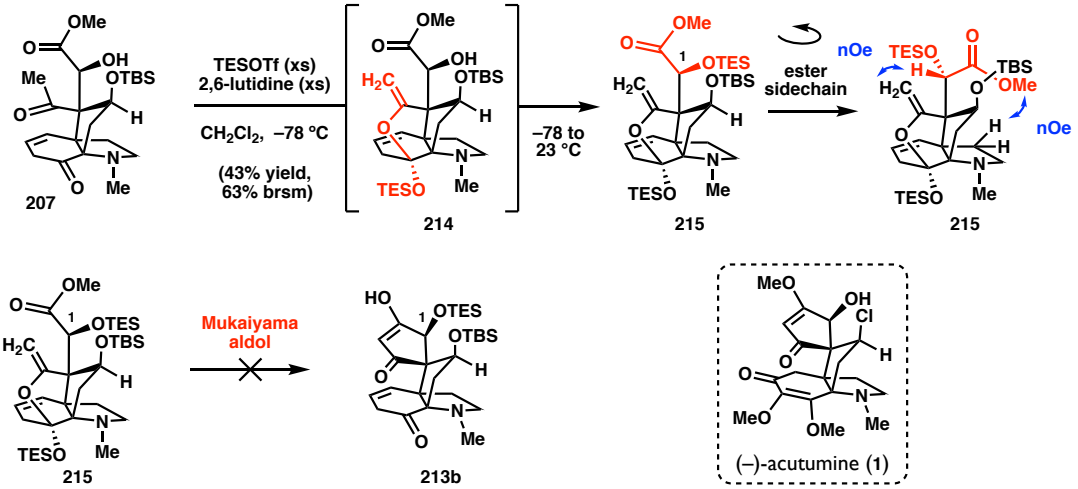
Scheme 3.7 *Retro-aldol/Dieckmann trial of SEM-protected lactone* ***210***.



The alternative protection of retro-aldol product **207** was pursued next. Subjecting **207** to excess TESOTf and 2,6-lutidine furnished TES-ether **215** (Scheme 3.8). During this reaction, the methyl ketone was also converted to the bridging silyl enol ether, so a number of reaction conditions were investigated to perform a Mukaiyama-aldol to close the spirocycle to vinylogous acid **213b**. Unfortunately, only reformation of the ketone functionality occurred when subjecting **215** to various Lewis acids,[21–23] and the desired spirocycle **213b** was never observed.

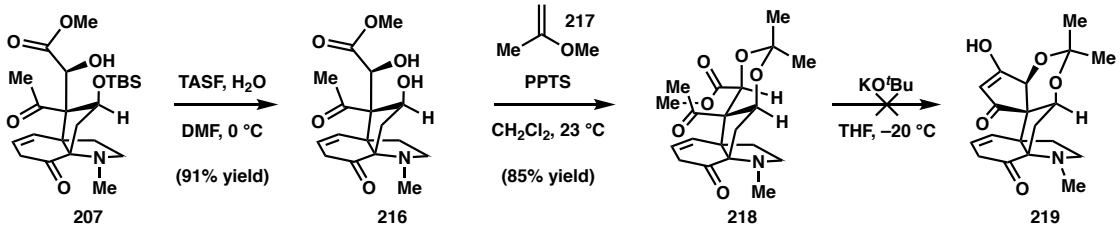
nOe studies were performed on bridging silyl enol ether **215**, which indicated that the silyl protecting groups at C1 and C10 favored an undesired orientation of the ester side chain (Scheme 3.8). Specifically, an nOe was observed between the methoxy group of the ester and the pyrrolidine ring, thus placing the ester and bridging silyl enol ether functionalities, the reaction partners of a Mukaiyama aldol, away from each other. This orientation is likely favored since it places the C1–OTES group away from the C10–OTBS group, effectively relieving non-bonding steric interactions. Thus, it was hypothesized that

Scheme 3.8 *Formation of silyl enol ether* ***215*** *and Mukaiyama aldol trials.*



installing a cyclic ketal protecting group between the C10 and C1 alcohols might place the ester in proximity to the C3 methyl ketone for the purposes of a Dieckmann cyclization (Scheme 3.9). Toward that end, TBS-ether **207** was deprotected using TASF,[24] and the resulting diol **216** was subjected to 2-methoxypropene (**217**) to afford cyclic ketal **218**. Unfortunately, subsequent Dieckmann trials again proved unfruitful and the desired spirocycle **219** could not be obtained. In fact, it was found that the protection reaction to ketal **218** was difficult to scale above a 5 mg scale; in particular, conversion was slow and subsequent prolonged stirring resulted in decomposition of the substrate.

Scheme 3.9 *Cyclic ketal* ***218*** *to bring ester and ketone in proximity for Dieckmann.*

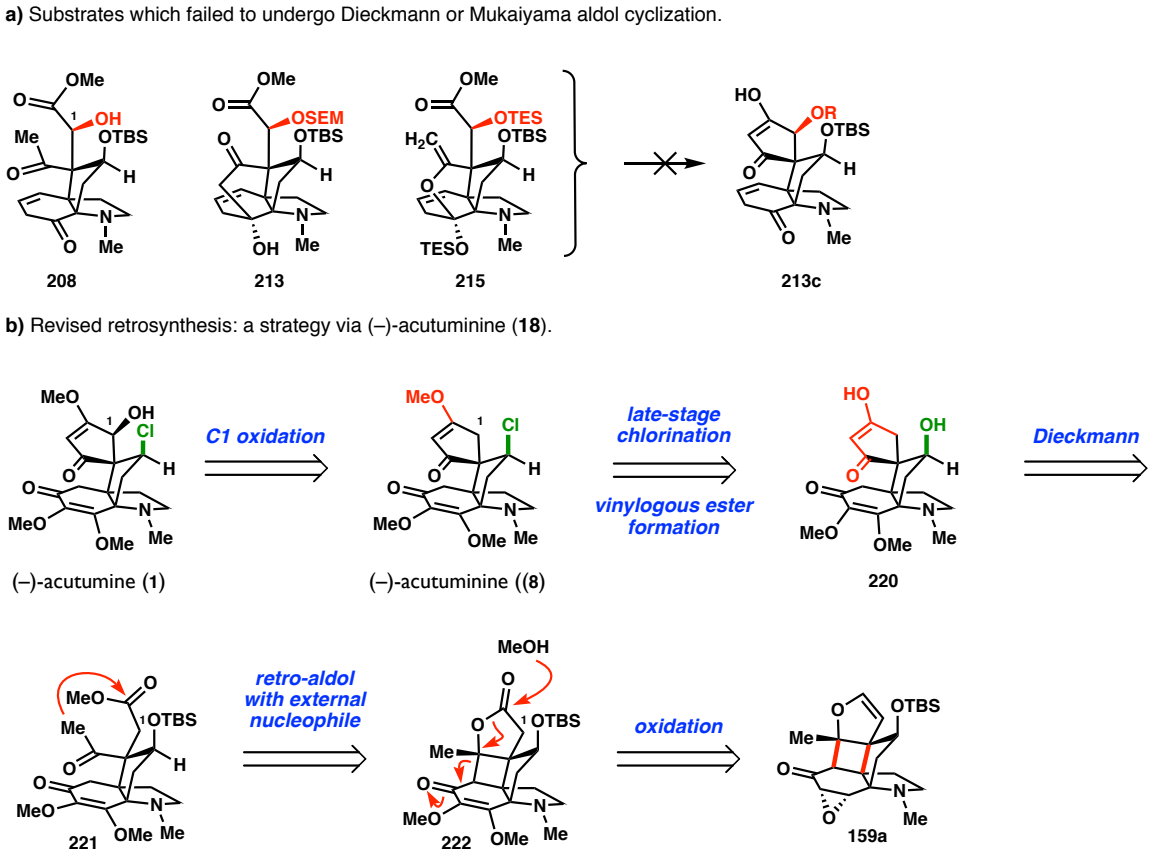


3.4 C1-DEOXY SERIES

3.4.1 Revised Retrosynthesis

Looking at the substrates that had failed to undergo the Dieckmann cyclization (Figure 3.1a), it became evident that the presence of the C1-substituent was causing the bulk of the reactivity challenges. When the C1 alcohol was unprotected, retro-aldol chemistry dominated, while protected analogues failed to undergo Dieckmann cyclization, likely due to the unfavorable orientation of the ester side chain. As a result, we became interested in removing the C1 oxidation in order to probe whether the spirocycle formation might be achieved. The retrosynthesis was thus slightly revised such that C1 oxidation was

Figure 3.1 *A difficult Dieckmann cyclization leading to revised retrosynthesis.*



removed from (–)-acutumine (**1**) via a late-stage allylic oxidation to reveal the related natural product (–)-acutuminine (**18**).[25] (–)-Acutuminine (**18**) was further disconnected via the same late-stage deoxychlorination of spirocycle **220**, a key element of our past retrosynthetic strategy. In order to access the spirocycle lacking oxidation at C1, it was thought that a retro-aldol/Dieckmann cyclization sequence of lactone **222** could be performed. Finally, it was imagined that lactone **222** could be accessed from the common cyclobutane intermediate **159a**.

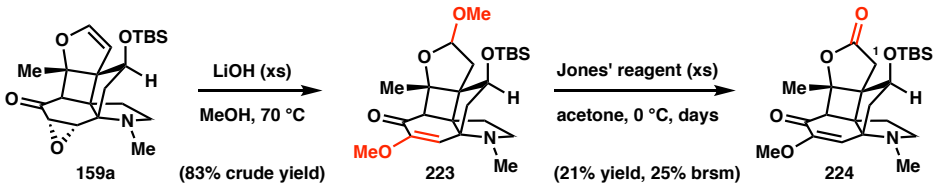
3.4.2 Lactone Series

C1-deoxy lactone **224** could be readily accessed in a two-step sequence from cyclobutane **159a** (Scheme 3.10a). While conceptually simple, the hydration/oxidation[26] of cyclobutyl furan **159a** required non-canonical reaction conditions in order to avoid TBS-deprotection and decomposition (Scheme 3.10a). Surprisingly, we found that addition of methoxide to the enol ether occurs at room temperature, and that upon heating, a second equivalent of methoxide opens the epoxide to afford acetal **223**. Subsequent oxidation to lactone **224** could be achieved under Jones' oxidation conditions; however, due to large amounts of decomposition the yield was low (21%). Fortunately, utilizing $BF_3 \cdot Et_2O$ and *m*-CPBA (**225**) proved to be a suitable alternative to the Jones' conditions.[27] It was crucial in this case to use sufficient Lewis acid in order to mask the basic amine, which was otherwise rapidly oxidized by *m*-CPBA. From a brief screen (Scheme 3.10b), it was apparent that the isolated yield dropped significantly upon scale up (entries 1–2). It was hypothesized that the purity of *m*-CPBA could affect the reaction yield; indeed, when 99%

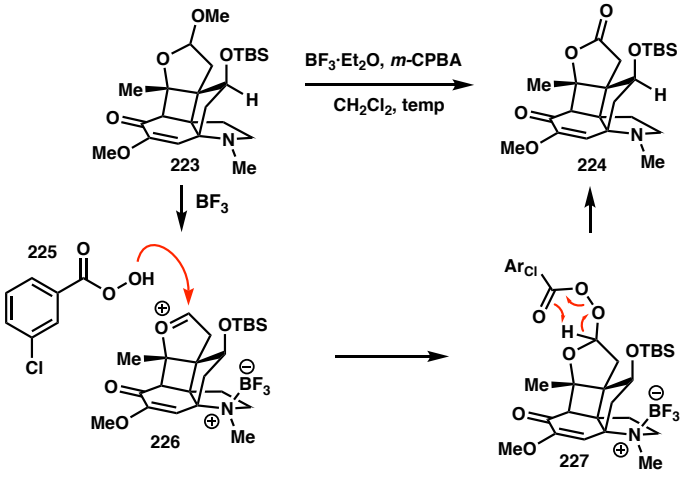
m-CPBA was utilized, the yield dropped even more significantly to 39% (entry 3). Ultimately, it proved crucial to use 75% *m*-CPBA and maintain the reaction at 0 °C for prolonged reaction times in order to obtain reliable yields upon scale up (entries 4–5). It is hypothesized that trace benzoic acid in the reaction may assist in the conversion of intermediate peroxide **227** to the product **224**.

Scheme 3.10 *Synthesis of C1-deoxy lactone* ***224***.

a) Two-step sequence to lactone **224**.



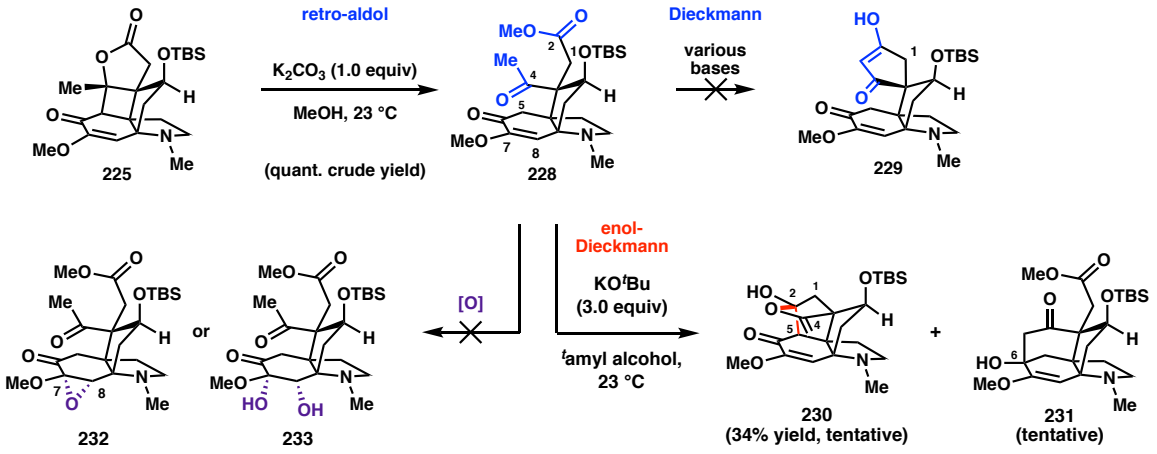
b) Improved conditions for lactone formation.



entry	% *m*-CPBA	temp (°C)	yield (%)	scale (mg)
1	75	0 to 23	71	5
2	75	0 to 23	52	20
3	99	0 to 23	39	20
4	75	0	73	60
5	75	0	72	180

Gratifyingly, lactone **224** underwent smooth retro-aldol to ester **228** when subjected to K_2CO_3 in MeOH. At this stage, we were poised to investigate whether removing the C1 alcohol might enable Dieckmann cyclization. Unfortunately, when ketone was subjected to a variety of bases, spirocycle **229** was never obtained. Several conditions afforded recovered starting material, and conditions such as KO^{t}Bu in ^{t}amyl alcohol[28] afforded moderate yields of the enol-Dieckamnn product **230**, as well as tentatively assigned bridging ketone **231**. Efforts to further advance intermediate **228** were then focused on installation of the dimethoxyenone at C7–C8. Thus, a variety of oxidations were investigated, including dihydroxylation and epoxidation reactions. Unfortunately, efforts to access diol **233** were unfruitful, as was the epoxidation to methoxy epoxide **232**.

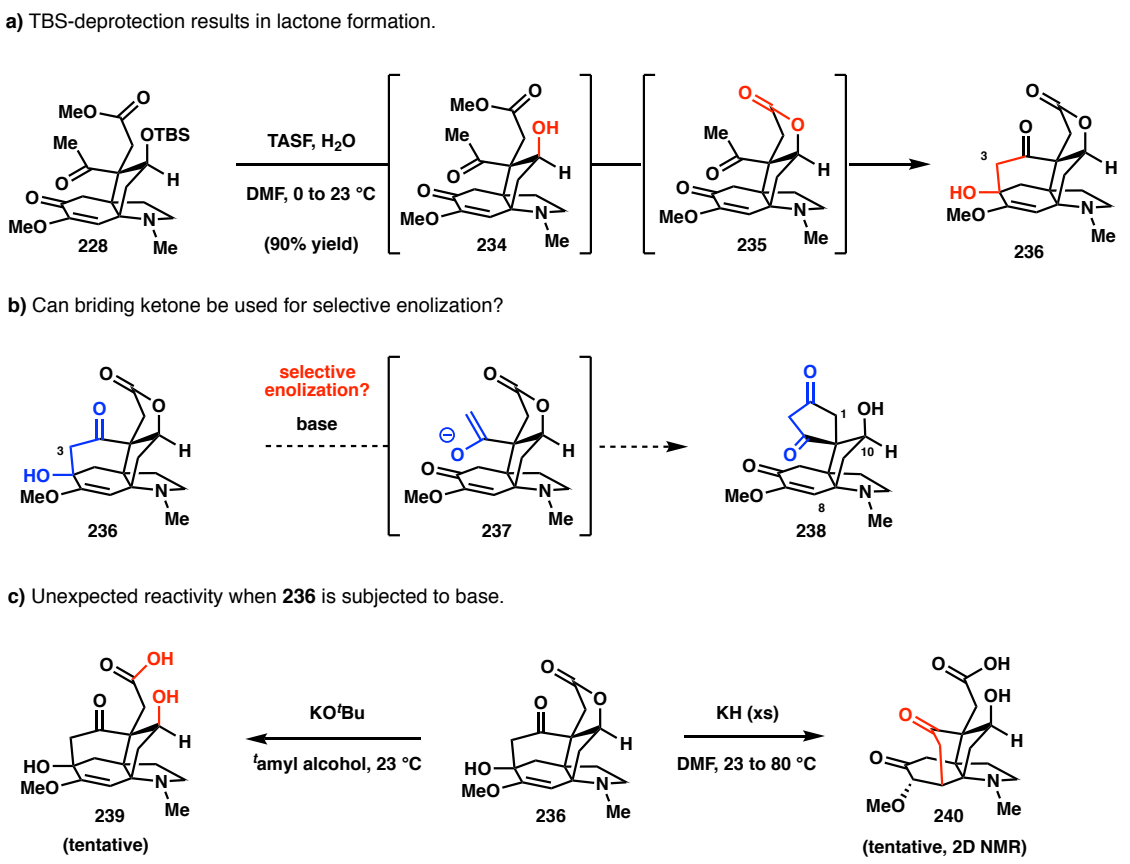
Scheme 3.11 *Retro-aldol/Dieckmann without oxidation at C1.*



Upon exploring further late-stage chemistry, it was discovered that TBS-deprotection of silyl ether **228** proceeded smoothly with TASF (Scheme 3.12a),[24] giving rise to bridged pentacycle **236** via *in situ* lactone formation. We hoped that this bridging ketone could undergo retro-aldol upon deprotonation of the tertiary alcohol to selectively generate the enolate, and thus promote the desired spirocycle formation (Scheme 3.12b).

However, subjecting **236** to various bases has thus far not afforded the desired Dieckmann cyclization (Scheme 3.12c). Instead, unreacted starting material was observed by LC/MS and TLC, and the strained lactone opened upon quenching with HCl or AcOH. When bridging ketone **236** was subjected to more forcing conditions utilizing excess anhydrous potassium hydride in DMF at 80 °C, enolization began to occur; however, 2D-NMR analysis indicated that tentatively assigned diketone **240** was formed. Ketone **236** had thus undergone a surprising Michael addition into the enone of the 6-membered ring, rather than reacting with the lactone to close the spirocycle.

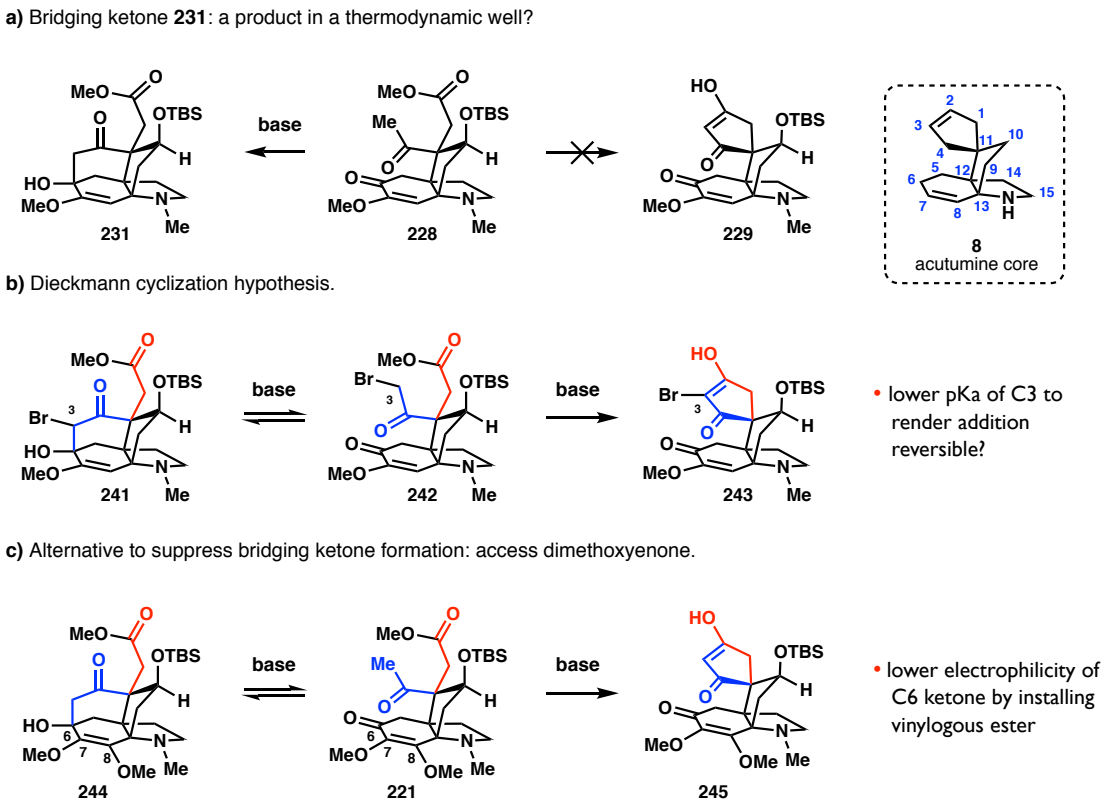
Scheme 3.12 *Lactone* ***236*** *and Dieckmann trials.*



3.5 DIECKMANN CYCLIZATION HYPOTHESIS

The fact that bridging ketone **231** was so resistant to enolization led us to the hypothesize that it is formed kinetically, and that it resides in a local energy minimum, thermodynamically (Scheme 13a). However, the Dieckmann condensation product **229**, once obtained, should be thermodynamically favored overall. Thus, it was anticipated that lowering the pK_a of the C3 methyl ketone could shift the aldol/retro-aldol equilibrium and drive the reaction to the spirocyclic product (Scheme 3.13b). It was thought that installing a bromide functionality at C3 might allow this envisioned shift in pK_a and reactivity. The decision to employ an α-bromoketone as the substrate was attractive because it would allow investigations of other ring closures, including 1) Reformatsky and other reductive

Scheme 3.13 *Dieckmann cyclization hypothesis.*



cyclizations, and 2) a Horner-Wadsworth-Emmons cyclization (HWE) following an Arbuzov displacement of the bromide.

In addition to increasing the acidity of the C3 ketone, it was hypothesized that a substrate possessing the required dimethoxyenone would be less electrophilic at the C6 carbonyl (Scheme 3.13c). It was hypothesized that attenuating the electrophilicity of the C6 carbonyl might enable the Dieckmann cyclization by rendering formation of the bridging ketone **244** less favorable (Scheme 3.13c). In this case, the electron-donating nature of the vinylogous ester –OMe group may aid the retro-aldol process from bridging ketone **244** to methyl ketone **221**. Ultimately, formation of the vinylogous acid **245** via Dieckmann cyclization would then drive the reaction toward the spirocyclic product.

3.6 THE ROAD TO SUCCESSFUL DIECKMANN CYCLIZATION

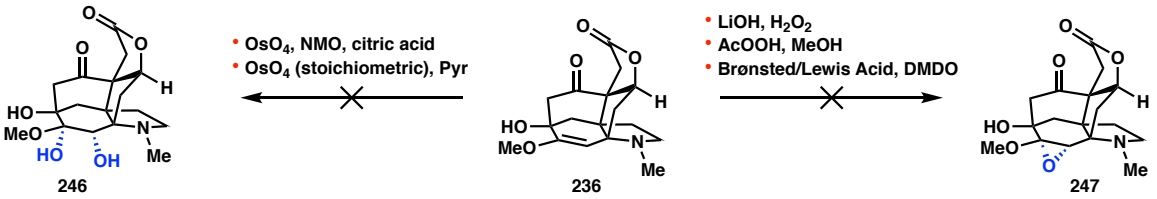
3.6.1 C3-Bromination and Dieckmann Cyclization

Various oxidation approaches to install the dimethoxyenone motif were pursued concomitantly with the installation of the bromide at C3. Unfortunately, many oxidation trials across various substrates failed to afford any desired diols or epoxides (Scheme 3.14). This presented an impasse with respect to investigating the hypothesis that the presence of the dimethoxyenone might enable Dieckmann cyclization by lowering the electrophilicity of the C6 carbonyl.

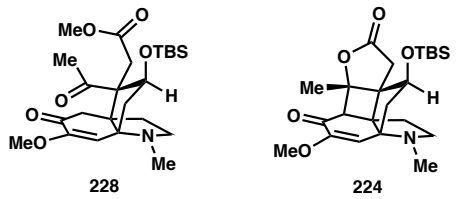
Fortuitously, epoxidation of enone **223** was successful to afford methoxy-epoxide **248** (Scheme 3.15). Furthermore, it was found that the methoxide addition/epoxidation sequence could be performed in one pot, first by subjecting cyclobutane**159a** to LiOH in

Scheme 3.14 *Overview of unsuccessful oxidations on methoxyenone functionality.*

a) Unsuccessful dihydroxylation and epoxidation of alkene **236**.

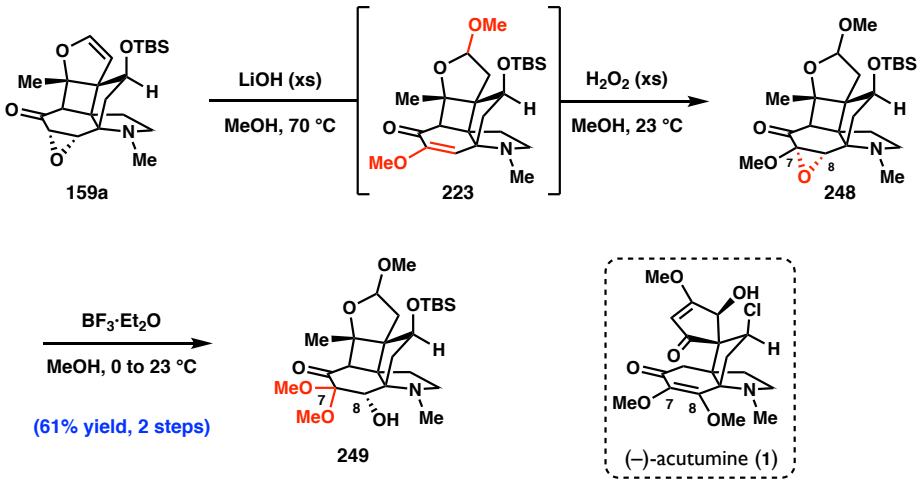


b) Other substrates subjected to dihydroxylation and epoxidation trials.



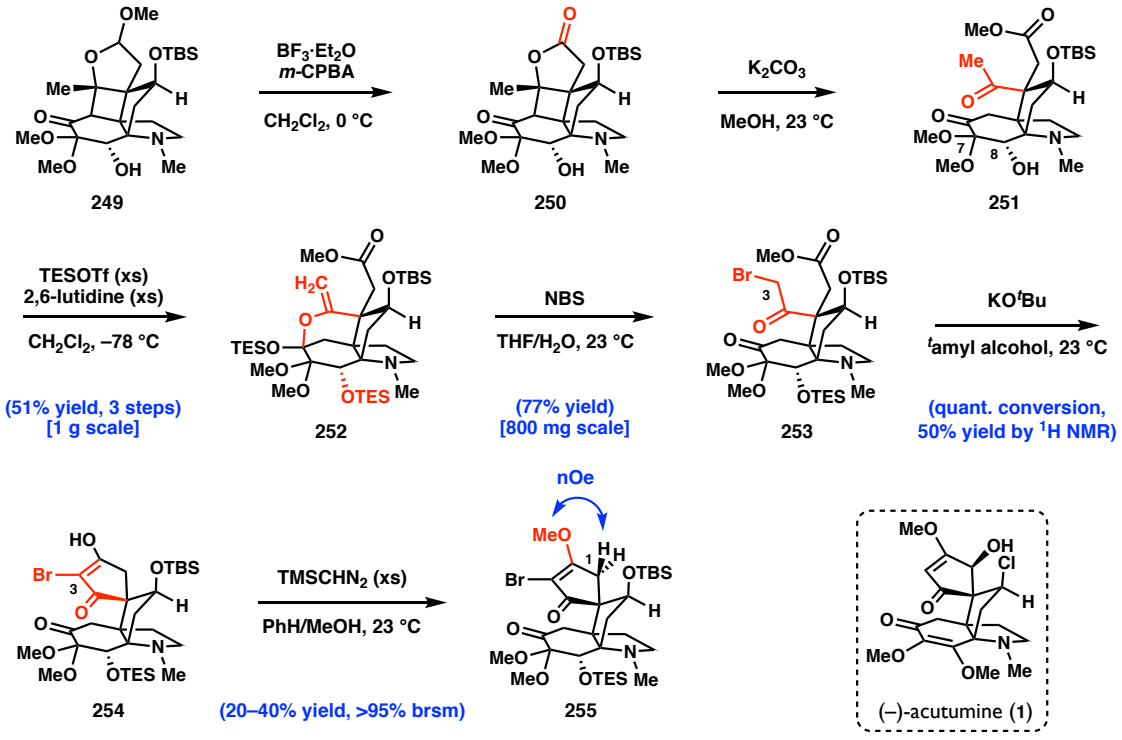
MeOH at 70 °C, and then cooling the reaction to room temperature and adding H_2O_2. With the correct oxidation state at C7 and C8, epoxide opening was investigated, which occurred readily with $BF_3{\cdot}Et_2O$ in MeOH. It is important to note that this methoxy-epoxide functionality is particularly activated towards epoxide-opening. Previous trials to open the epoxide pre- and post [2+2]-cycloaddition had all been unsuccessful (Section 3.2.2).

Scheme 3.15 *Accessing oxidation state of dimethoxyenone at C7–C8.*



The oxidation to lactone **250** proceeded smoothly (Scheme 3.16), leaving the methoxy ketal functionality intact despite the use of Lewis acid in the reaction. Subsequent retro-aldol afforded ketone **251**,[29] which could now be converted to α-bromoketone **253** via a two-step sequence. First, ketone **251** was subjected to excess TESOTf and 2,6-lutidine to afford bridging silyl enol ether **252**. Second, the enol ether could be brominated using NBS to provide bromide **253**. It was crucial here to brominate via the silyl enol ether **252** because the pyrrolidine functionality is otherwise rapidly oxidized by NBS. Additionally, careful portion-wise addition of NBS was also critical, as a fast addition rate was also accompanied by pyrrolidine oxidation. With this key intermediate in hand, bromide **253** was subjected to KO^{t}Bu in ^{t}amyl alcohol and we were delighted to see complete conversion to the desired spirocycle **254**. The successful Dieckmann cyclization with the C3 bromide

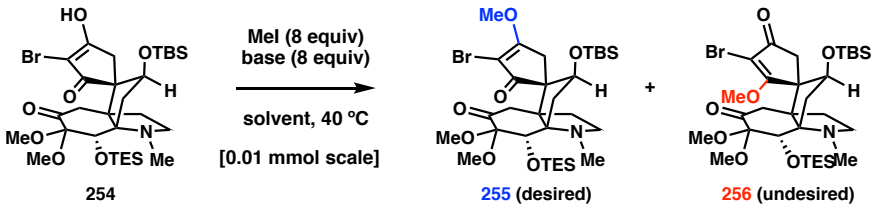
Scheme 3.16 *Access to spirocycle* ***255****: a successful Dieckmann cyclization.*



in place indicated that our hypothesis may be indeed operative (Scheme 3.13b). Although the yield of the Dieckmann cyclization initially appeared to be modest by ^{1}H NMR, we were encouraged that a single isomer of the vinylogous acid was observed in CD_3CN. When subjected to excess $TMSCHN_2$, acid **254** was smoothly converted to vinylogous ester **255** as a single isomer, which was confirmed via a key nOe signal between the vinylogous ester –OMe to the C1 methylene. The methylation yield was, however, variable and conversion decreased dramatically upon scale-up. Although vinylogous acid **254** could be recovered in case of poor conversion (>95% brsm), investigations for a suitable alternative were pursued.

It was found that using MeI and an inorganic base could afford vinylogous ester **255** when heated at 40 °C (Table 3.1). A screen of reaction solvent showed that polar solvents such as CH_3CN and DMF were beneficial for conversion (entries 2 and 4). In these

Table 3.1. *Methylation screen of spirocyclic vinylogous acid* ***254****.*



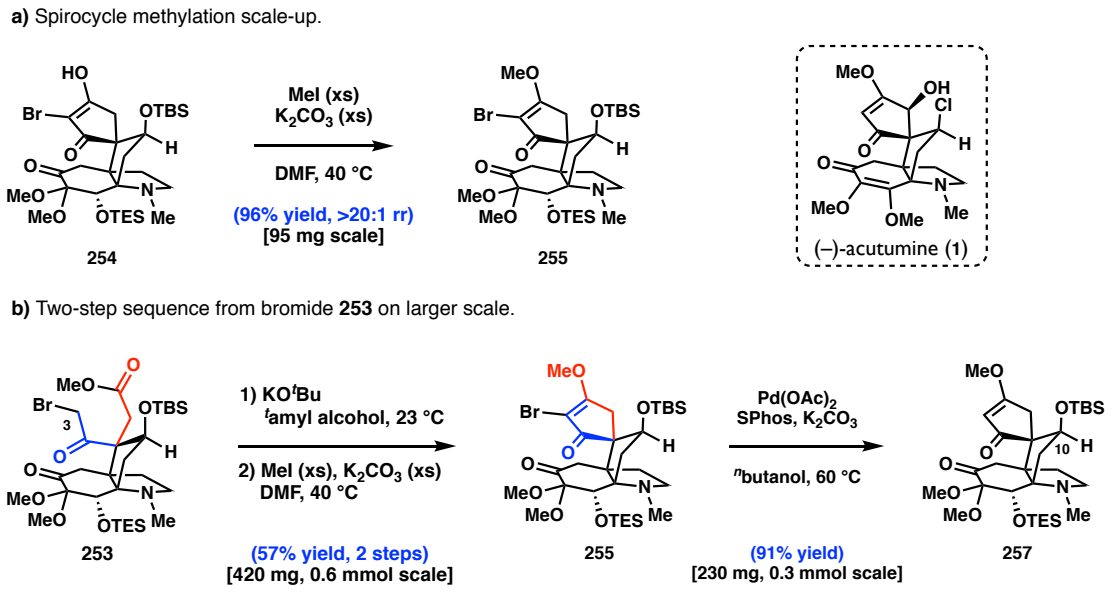
entry	solvent	base	yield 255	yield 256	yield 254
1	THF	K_2CO_3	20%	19%	9%
2	dioxane	K_2CO_3	7%	15%	82%
3	CH_3CN	K_2CO_3	74%	27%	0%
4	DMF	K_2CO_3	69%[a]	0%	0%
5	DMF	Na_2CO_3	65%[a]	0%	0%
6	DMF	Cs_2CO_3	61%[a]	0%	0%

Yields determined by ^{1}H NMR with pyrazine as an internal standard.
[a] Aqueous workup performed.

cases, the zwitterionic vinylogous acid **254** also showed the highest solubility. In fact, DMF gave the cleanest reaction profile (entries 4–6), whereby formation of the undesired isomer **256** was suppressed. Counter-ion effects of the inorganic base employed were not observed (entries 4–6).

Scale up of the optimized methylation conditions were then investigated, and we were pleased to see that we could obtain **255** in 96% yield and >20:1 rr on 95 mg scale (Scheme 3.17a). Subsequent scale-up campaigns (up to 0.6 mmol scale) revealed that conducting the silyl enol ether bromination, Dieckmann cyclizaition, and vinylogous acid methylation steps in a single day (methylation proceeds overnight) improved the yield of the sequence. Thus, Dieckmann cyclization/methylation was accomplished in a 57% yield over two steps (Scheme 3.17b), as opposed to 48%. It is believed that this difference is due to the slight instability of vinylogous acid **254** when stored in the freezer for several days or weeks.

Scheme 3.17 *Scale-up campaigns of cyclopentenone* ***255***.

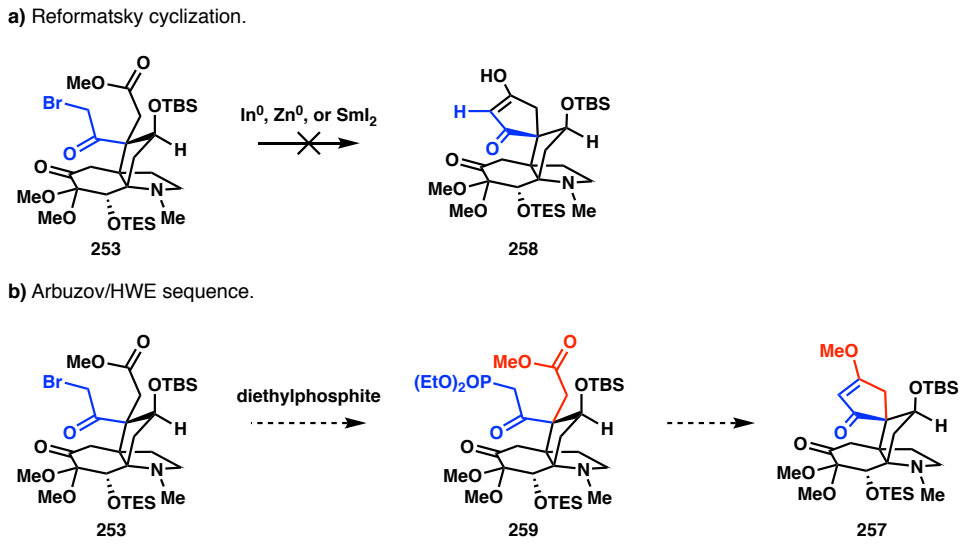


With vinylogous ester **255** in hand, subsequent debromination proceeded smoothly utilizing $Pd(OAc)_2$, SPhos, and K_2CO_3 in ^{n}butanol at 60 °C.[30] This culminated in the synthesis of the spirocyclic cyclopentenone found in (–)-acutumine (**1**), which had not been achieved to date. Having solved the retro-aldol and Dieckmann sequence, there were two key challenges remaining in the synthesis: 1) installation of the dimethoxyenone motif, and 2) TBS-deprotection and chlorination at C10.

3.6.2 Reductive and HWE Cyclizations

While the Dieckmann cyclization/debromination sequence was successful, it remained of interest whether spirocycle **257** could be accessed in a more direct manner. This could either be accomplished via a reductive cyclization of α-bromoketone **253** (Scheme 3.18a), or an HWE cyclization[31] of its corresponding phosphonate **259**, which could provide direct access to the desired vinylogous ester isomer **257** (Scheme 3.18b).

Scheme 3.18 *Other cyclizations attempted with α-bromoketone* ***253***.



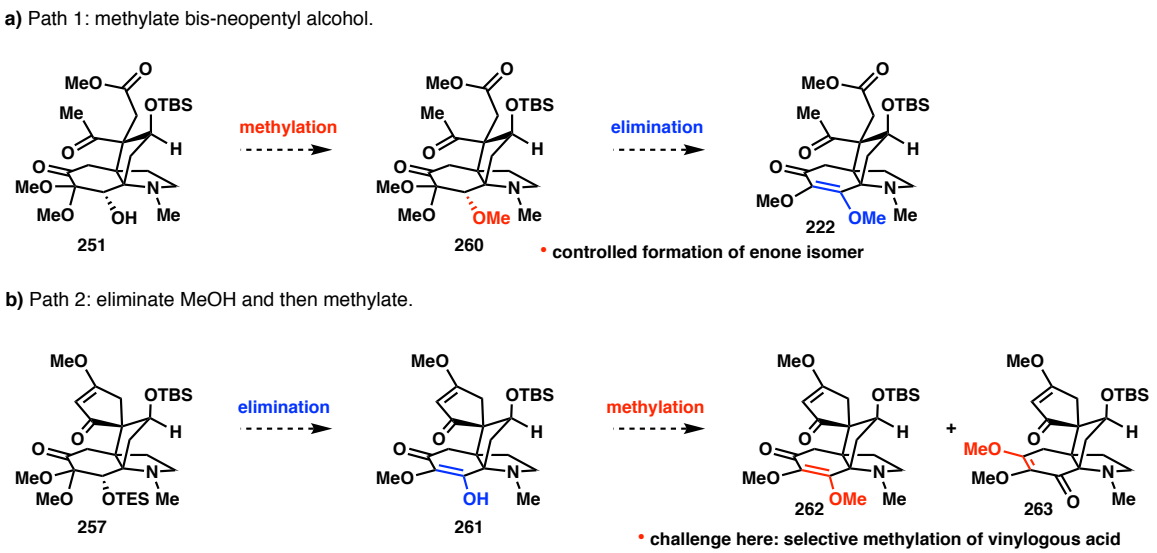
Unfortunately, Reformatsky and other reductive cyclization trials of α-bromoketone **253** never afforded the desired spirocycle, and the Arbuzov displacement necessary to access the organophosphonate **259** was very challenging. The primary bromide proved surprisingly resistant to substitution, only affording conversions with TBAI (not shown). Ultimately, failure to confirm synthesis of phosphonate **259**, and unsuccessful HWE trials on tentatively assigned products led us to remain focused on our current bromination/Dieckmann cyclization route.

3.7 INSTALLATION OF THE DIMETHOXYENONE

3.7.1 Remaining Strategies and Failed Pathways

There were two possible avenues to finalize the dimethoxyenone functionality: first, methylation of the bis-neopentyl alcohol, such as in **251** (Scheme 3.19a), followed by elimination of MeOH to afford the desired enone isomer **222** in a controlled fashion;

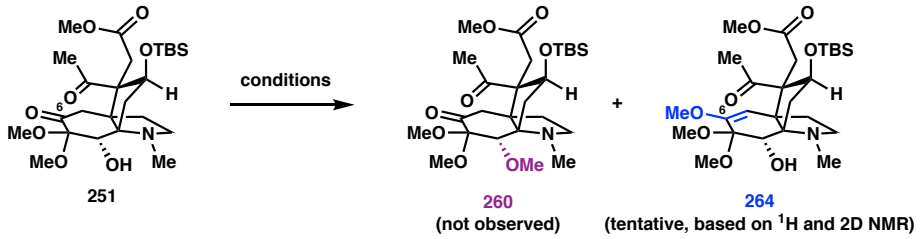
Scheme 3.19 *Possible avenues for dimethoxyenone installation.*



second, elimination of MeOH first on ketal **257** (Scheme 3.19b), followed by methylation of the resulting vinylogous acid **261**. In this case, selectivity in the methylation reaction was expected to be a challenge given that vinylogous acid **261** will be in equilibrium with its isomer.

To investigate the first pathway (Scheme 3.19a), methylation screens were performed on a number of intermediates along the route. Unfortunately, in the case of retro-aldol product **251** (Table 3.2), enolization and methylation of the C6 ketone predominated, and both acidic ($TiCl_4$ in MeOH)[32] and neutral conditions (Ag_2O and MeI)[33] afforded vinyl ether **264** (entries 1 and 2). Johnson-Robert methylation conditions[34,35] and the use of Meerwein's salt in the presence of a Lewis acid to mask the basic amine left unreacted starting material (entries 3 and 4).

Table 3.2. *Methylation trials on bis-neopentyl alcohol* ***251***.

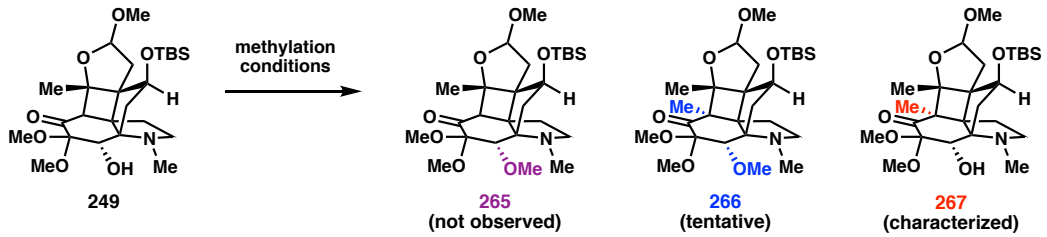


entry	conditions	result
1	Ag_2O (xs), MeI (xs), CH_3CN, 23 to 50 °C	264
2	$TiCl_4$ (xs), MeOH, 23 to 50 °C	264
3	$BF_3{\cdot}Et_2O$ (1.5 equiv), diazomethane (xs), Et_2O, 0 to 23 °C	251
4	Meerwein's salt (1.0 equiv), proton sponge (2.0 equiv), CH_2Cl_2, 23 to 50 °C	251 & trace bis-methylation

To prevent enolization and methylation of the C6-ketone, methylation of cyclobutane **149** was investigated (Table 3.3). Surprisingly, neutral conditions and those employing base and MeI afforded bis-methylated product **266** (entries 1–6), in which the

cyclobutane bridgehead proton was methylated. Most likely this occurs in a concerted process, as previously described by Shair and Maimone in their syntheses of hyperforin.[36,37] In an effort to test weaker bases, **249** was subjected to K_2CO_3 and MeI; however, only trace methylation was observed (entry 7). Finally, conditions reported to afford methylation via displacement of triflate failed to afford the desired product **265** as well,[38,39] only resulting in successful triflate formation (observed via LC/MS).

Table 3.3. *Methylation trials on cyclobutane* ***149***.

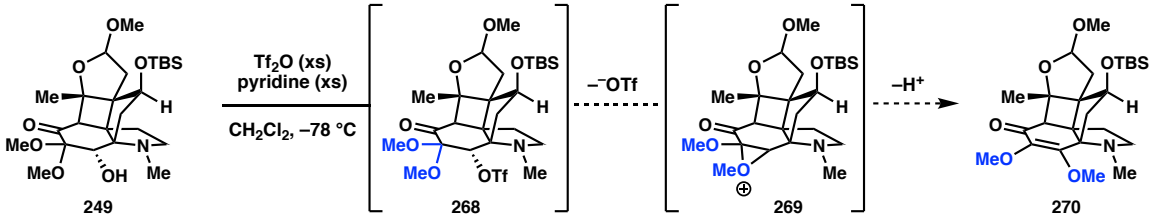


entry	conditions	result
1	NaH (5 equiv), MeI (3 equiv), THF, 0 to 23 °C	266
2	KH (5 equiv), MeI (3 equiv), THF, 0 to 23 °C	266
3	KH (5 equiv), MeI (1 equiv), THF, –78 to –60 °C	266 + 267
4	KH (5 equiv), MeI (1 equiv), THF, –78 to –60 °C	266 + 267
5	Ag_2O (4 equiv), MeI (5 equiv), CH_3CN, 23 to 70 °C	mostly 249, trace bis-methylation
6	KO^{t}Bu (3 equiv), MeI (5 equiv), THF, 23 °C	266
7	K_2CO_3 (xs), MeI (xs), DMF, 23 to 70 °C	mostly 249, trace mono-methylation
8	Tf_2O (xs), Pyr (xs), CH_2Cl_2, –78 °C, then MeOH/Et_3N/DBU warm to 23 °C	triflate formation, no methylation

In 1997, Myers and coworkers reported an unexpected 1,2-shift of a MeO– group from a neighboring dimethoxyketal to displace an adjacent C–OSO_2CF_3.[40] Having successfully formed the triflate from alcohol **249**, we sought to apply the reported conditions to our substrate (Scheme 3.20). When hindered alcohol **249** was subjected to triflic anhydride in pyridine at –78 °C, trace desired mass of enone **270** was observed by

LC/MS. Unfortunately, this hit proved irreproducible and impervious to improvement, leaving the installation of the dimethoxyenone an unsolved challenge.

Scheme 3.20 *Triflate formation/1,2-shift to afford dimethoxyenone.*

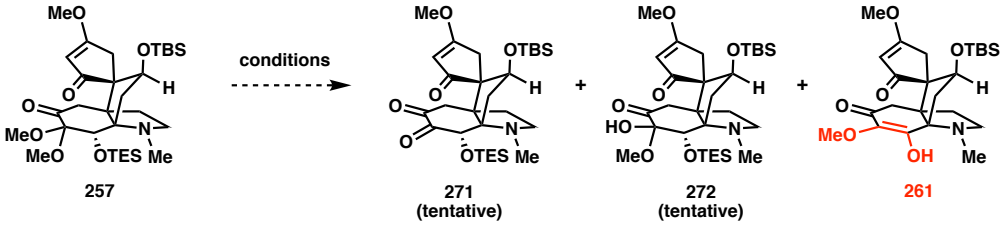


3.7.2 Successful Installation of the Dimethoxyenone

Having little success in the methylation of the hindered bis-neopentyl alcohol, investigation of the second pathway commenced, in which elimination of MeOH would occur first, followed by methylation to the vinylogous acid (Scheme 3.19b). Reported conditions to afford this type of elimination were surveyed first, but it was found that basic conditions returned unreacted starting material (not shown).[41–43] Utilizing Brønsted acid either left unreacted starting material **257** or afforded complete ketal deprotection **271** (Table 3.4, entries 1 and 2).[44–46] Lewis acids — such as AlC_3 (entry 3) [47] — afforded mono-demethylation to give hemiketal **272**, followed by decomposition. Encouraged by this differing reactivity with Lewis acids, we moved to BCl_3,[48,32] which at 1.5 equivalents afforded diketone **271** and starting ketal **257** (entry 4). Conversion in the reaction was low, so the equivalents of BCl_3 were increased (1.5 to 3.0 equivalents), revealing that at 3.0 equivalents hemiketal **272** and vinylogous acid **261** were formed as well (entry 5). Increasing the amounts of the Lewis acid to excess quantities finally resulted in clean

formation of vinylogous acid **261** (entry 6), along with large quantities of unreacted starting material **257** as well. While the conversion was incomplete, it was found that prolonged reaction times resulted in formation of the undesired hemiketal **272** and diketone **271**. Thus, the use of excess Lewis acid and short reaction times could result in clean formation of **261**, and starting ketal **257** could be re-isolated and re-subjected.

Table 3.4. *Brønsted and Lewis acid screen toward ketal elimination.*



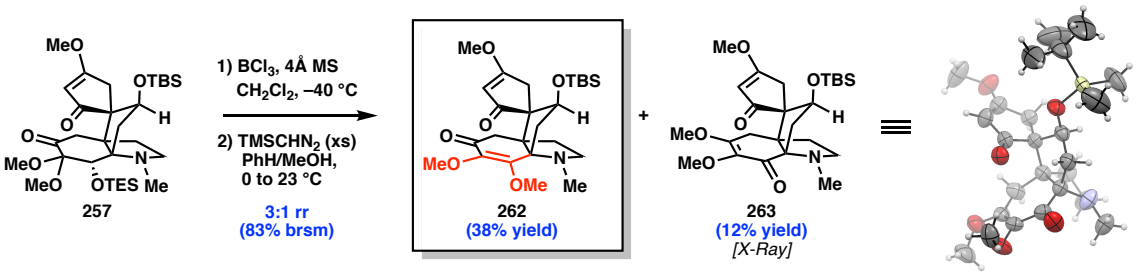
entry	conditions	result
1	*p*-TsOH (1.0 equiv), PhH, 23 to 80 °C	257, then decomposition
2	AcCl (4.4 equiv), MeOH, 23 to 60 °C	271 + 257
3	$AlCl_3$ (2.0 equiv), CH_2Cl_2, 23 to 60 °C	demethylation, then decomposition
4	BCl_3 (1.5 equiv), 4Å MS, CH_2Cl_2, –40 °C	271 + 257
5	BCl_3 (3.0 equiv), 4Å MS, CH_2Cl_2, –40 °C	271 + 272 + 261 + 257
6	BCl_3 (6.0 equiv), 4Å MS, CH_2Cl_2, –40 °C	261 + 257

Note: BCl_3-mediated reactions are at incomplete conversion of 257.

The crude mixture of ketal **257** and vinylogous acid **261** was then subjected to excess $TMSCHN_2$ (Scheme 3.21). Gratifyingly, desired dimethoxyenone **262** was obtained, along with its isomer **263**. Analysis via ^1H NMR indicated that the methylation occurred in a 3:1 rr, favoring the desired isomer **262**, which was a foam. The undesired isomer **263** was a crystalline solid and suitable crystals for X-Ray diffraction were grown. X-Ray structural analysis allowed us to unambiguously confirm the absolute configuration, as well as the stereochemistry of the two vinylogous esters. While the conversion in the

BCl_3-mediated ketal elimination reaction has not been improved to date, this sequence allowed us to synthesize sufficient material for subsequent late-stage investigations.

Scheme 3.21 *Two-step sequence for the formation of dimethoxyenone* ***262****.*

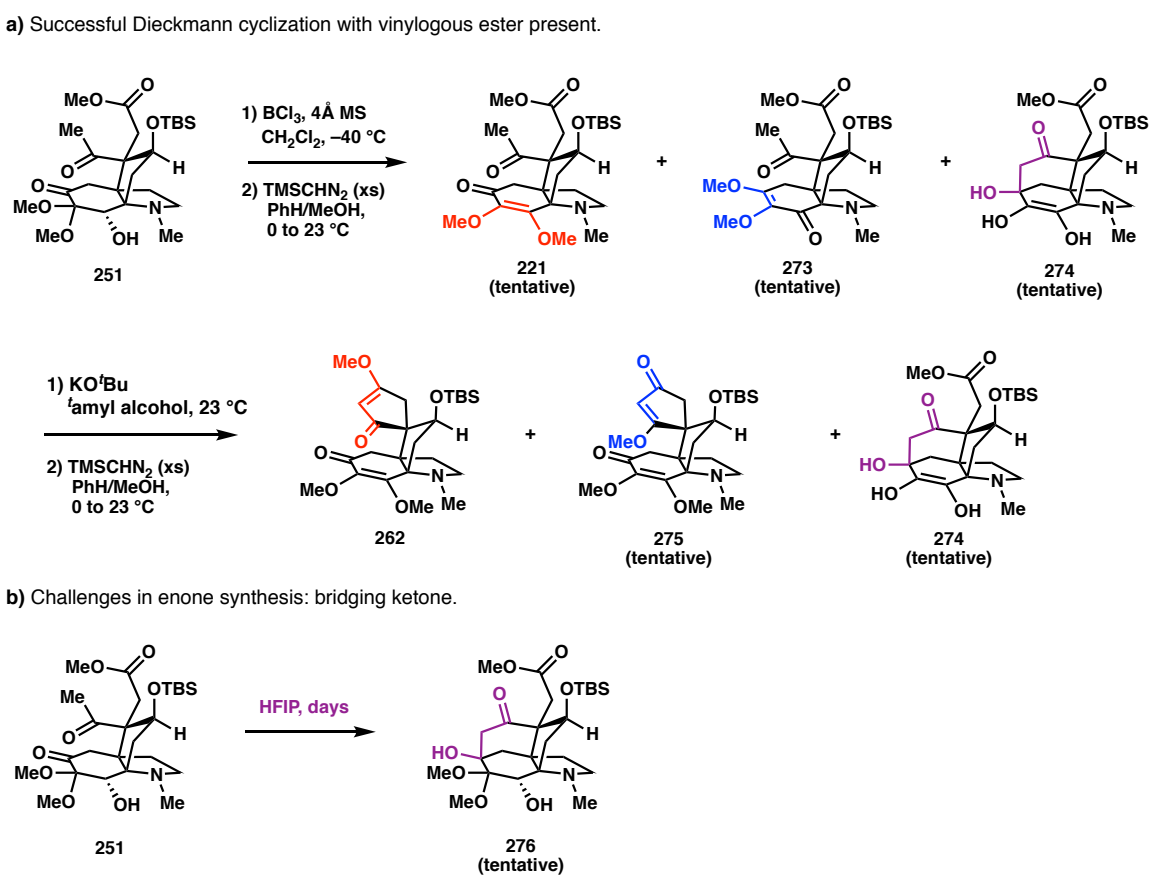


3.7.3 Access to Dimethoxyenone Modifies C6-Carbonyl — Revisiting the Dieckmann Cyclization Hypothesis

Having successfully installed the dimethoxyenone motif, the Dieckmann cyclization hypothesis was revisited to investigate whether reducing the electrophilicity of the C6 carbonyl would indeed enable successful Dieckmann as an alternative to the bromination route. Subjecting ketal **251**, an intermediate from earlier in the synthesis, to BCl_3 in CH_2Cl_2 indeed induced the desired elimination of MeOH, although the reaction was accompanied by large amounts of ketal deprotection (Scheme 3.22). The crude of the elimination reaction was subsequently methylated with $TMSCHN_2$; however, conversion was low, and only small quantities of enone **221** were accessed. The resulting vinylogous ester **221** was subjected to the Dieckmann cyclization conditions, and gratifyingly resulted in successful spirocycle closure. This was confirmed via methylation of the crude reaction mixture to **262**, and comparing the NMR data to the material obtained from the bromination

route. These studies were very exciting because they showed that 1) our Dieckmann cyclization hypothesis with respect to the electrophilicity of the C6 carbonyl was likely operative, and 2) that it was feasible to cut three steps from our synthesis if needed (silyl enol ether formation, bromination, and then debromination). Efforts at optimizing this sequence are currently ongoing, although results thus far have shown that subjecting ketal **251** to Lewis acids, or stirring for prolonged periods of time in hexafluoroisopropanol (HFIP), results in formation of bridging ketone **276**. It is believed that formation of this bridging motif, such as in **276** and **274**, is the underlying reason for low conversion on the methylation step, which with $TMSCHN_2$ relies on the acidity of the vinylogous acid.

Scheme 3.22 *Investigating C6 modification for Dieckmann cyclization.*

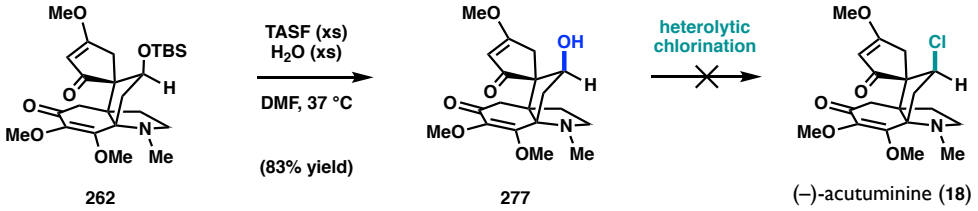


3.8 TOWARD TBS-DEPROTECTION AND CHLORINATION

3.8.1 Deoxychlorination Efforts

At this point in our investigations, we were eager to remove the TBS-group and investigate chlorination chemistry. While TBS-deprotection proceeded uneventfully to neopentyl alcohol **277** (Scheme 3.23), subsequent heterolytic chlorination trials proved very challenging. Specifically, when reagents such as thionyl chloride or Appel conditions were employed, unreacted starting material was observed. Preliminary investigations using MsCl also proved unfruitful, which could either proceed via a S_N2 or double inversion mechanism with assistance of the basic amine.

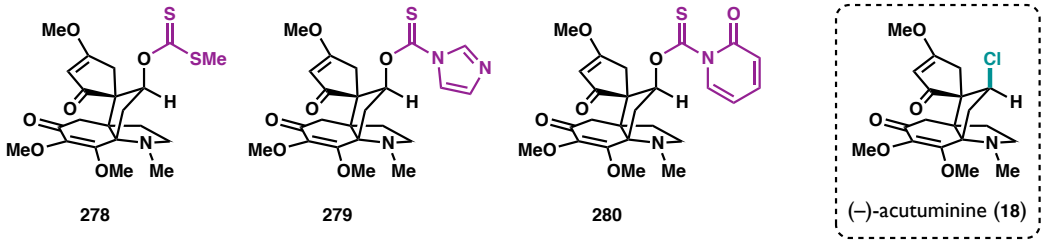
Scheme 3.23 *Neopyentyl alcohol* ***277*** *and (–)-acutuminine (****18****).*



While investigating heterolytic deoxychlorination reactions, a variety of activating groups were appended to neopentyl alcohol **277** in order to begin radical deoxychlorination trials (Figure 3.2). During the entire development of the C10-OH series of our acutumine synthesis, we had been working on the development of a variety of radical deoxychlorination reactions (see Chapter 4). Amongst those efforts, the deoxychlorination of 2° and 3° cesium oxalates utilizing visible light photocatalysis and ethyl 2,2,2-trichloroacetate (ETCA) was successful (Chapter 4, Section 4.3); however, a functional group tolerance screen demonstrated that the reaction does not tolerate basic amines, likely

due to oxidation by the excited state [Ir] catalyst. We were thus aware that many photoredox-catalyzed processes would be challenging in that regard. Indeed, most chlorination trials that had been conducted resulted in decomposition of the substrate.

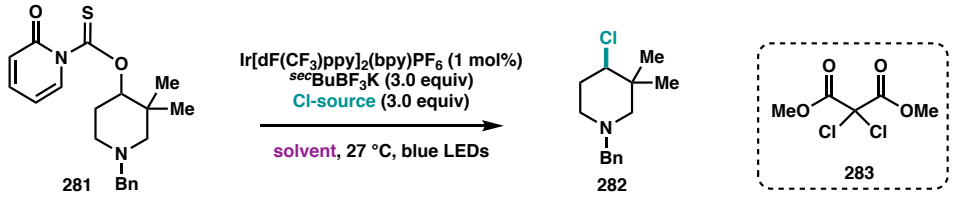
Figure 3.2 *Fragmentation groups synthesized to investigate chlorination reactions.*



One of the few chlorination hits (observed via LC/MS and HRMS) occurred during trials utilizing pyridone **280**. In 2017, Molander reported mild fragmentation of methyl xanthates derived from benzylic alcohols utilizing potassium trifluoroborate salts as radical initiators in the presence of an [Ir] catalyst and visible light.[49] The resulting carbon centered radical was then coupled with aryl bromide electrophiles utilizing a nickel catalyst. For the purposes of deoxychlorination, and based on our ongoing investigations into such methods (*vide infra*, Chapter 4), it was hypothesized that the radical deoxygenation of an *unactivated* or *unstabilized* 2° alcohol to the carbon centered radical could be achieved under these conditions if the pyridone fragmentation group was employed. These efforts had demonstrated that this fragmentation group was more reactive for such 2° alcohols. Gratifyingly, utilizing model substrate **281**, the desired chloride **282** could be obtained in 50% yield when subjected to $Ir[dF(CF_3)ppy]_2(bpy)PF_6$, $^{sec}BuBF_3K$, and ETCA under irradiation with a blue LED light (Table 3.5, entry 1). Interestingly, when the solvent was switched from EtOAc to CH_2Cl_2, the product yield decreased, and larger quantities of

deoxygenation were observed via LC/MS. The reaction performed comparably with malonate **283** as a Cl-source. The observed moderate mass balance seemed to imply that decomposition of the substrate was occurring. It was also hypothesized that the product chloride **282** may be consumed under the reaction conditions, especially given that several equivalents of the radical initiator ($^{sec}BuBF_3K$) were employed. Thus, further parameters were investigated, including equivalents of reagents, various trifluoroborate salts, and reaction time. However, the yield of **282** could not be increased.

Table 3.5. *Radical deoxychlorination of neopentyl alcohol via photoredox catalysis.*

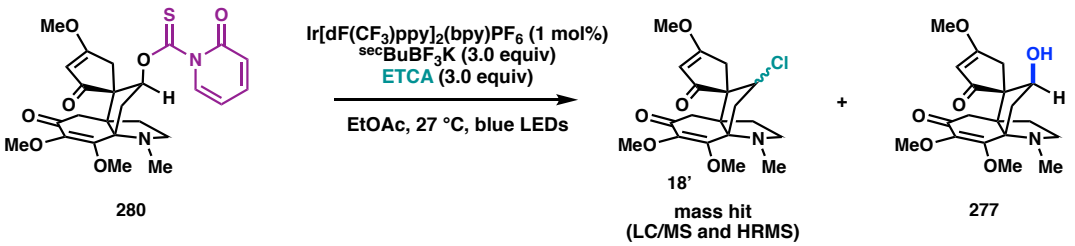


entry	Cl-source	solvent	yield 282
1	ETCA	EtOAc	50%
2	ETCA	CH_2Cl_2	39%
3	malonate 285	EtOAc	46%

Having successfully performed a radical deoxychlorination of a neopentyl alcohol, the discovered conditions were applied to the acutumine substrate **280** (Scheme 3.24). While the desired mass for deoxychlorination was observed in traces, it appeared that large amounts of decomposition were occurring because pyridone **280** was consumed, while the only other product that was observed was the corresponding neopentyl alcohol **277**. Deoxygenation was never observed. Unfortunately, these traces of chlorination product were insufficient in quantity for NMR analysis and structural confirmation. Even performing this reaction on 4 mg scale, the yield of chlorination could not be improved for

further studies. Since significant amounts of valuable late-stage material were being lost to this reaction, other avenues of chlorination were pursued.

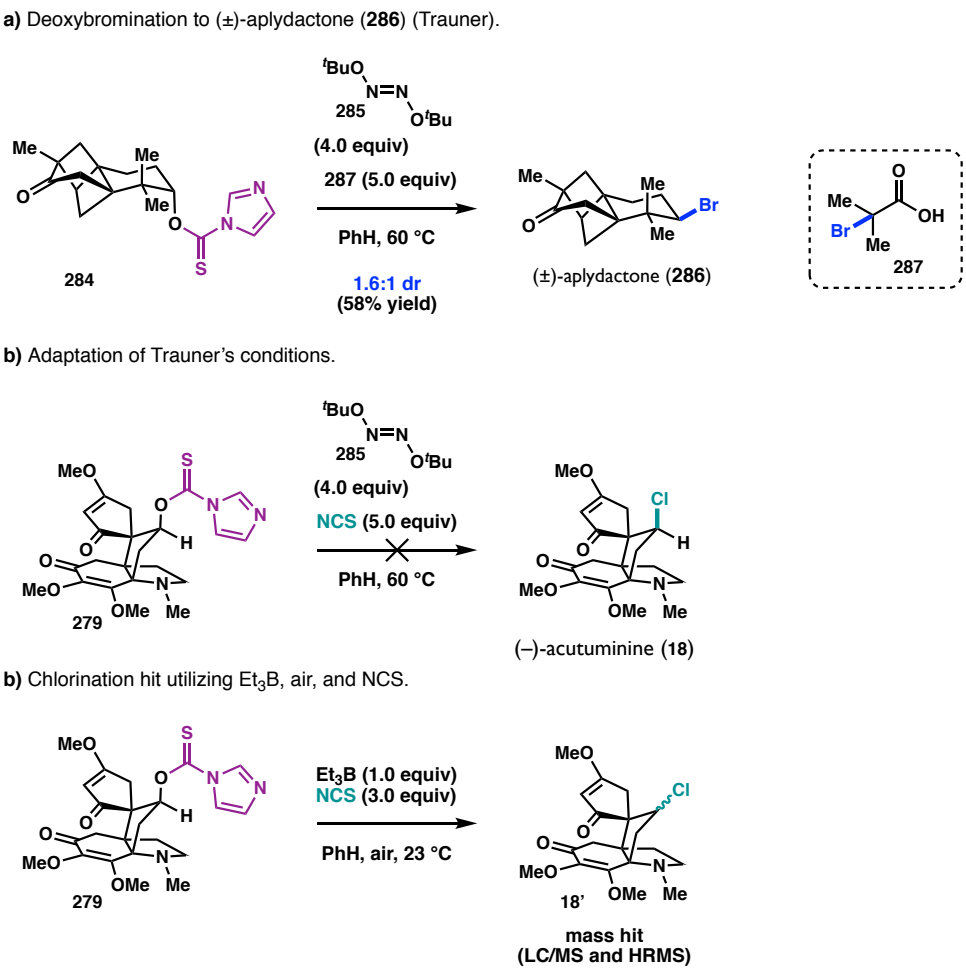
Scheme 3.24 *Application of radical deoxychlorination to the acutumine system.*



Given that the acutumine substrates might not be stable to photoredox-catalyzed deoxychlorination reactions since the basic amine is labile to oxidation chemistry, other radical deoxychlorination conditions were pursued with more classical initiators. Of particular interest was the report by Trauner and coworkers, who successfully installed a neopentyl bromide via a deoxybromination reaction in their total synthesis of (±)-aplydactone (**286**, Scheme 3.25a).[50] The authors subjected imidazolyl thiocarbamate **284** to radical initiator **285** and bromide source **287**, affording good yield of the brominated products in a 1.6:1 dr. In order to adapt these conditions, model substrates were first subjected to similar conditions (not shown), and chlorination was accomplished when NCS was substituted for bromide **287**. Unfortunately, when these conditions were then applied to the acutumine system, rapid decomposition of thiocarbamate **279** occurred (Scheme 3.25b). The reaction conditions appeared to be too harsh for our sensitive substrate, so the reaction was pursued with milder conditions instead. In this case, subjection to Et_3B and oxygen at room temperature afforded trace chlorination product (observed via LC/MS, Scheme 3.25c). We were very encouraged by this chlorination hit because the retention

time of the product peak overlapped with the hit utilizing photoredox catalysis (*vide supra*). Unfortunately, conversion of this reaction was slow, and it furthermore proved irreproducible on large scale. Again, sufficient quantities for thorough NMR analysis could never be obtained. It is also worth noting that trials to induce deoxygenation to the dechloroacutumine spirocycle have thus far been unsuccessful as well. Employing standard conditions such as AIBN and $^{n}Bu_3SnH$ on xanthate or thiocarbamate activating groups led to decomposition.

Scheme 3.25 *Deoxychlorination trials with classical radical initiators.*



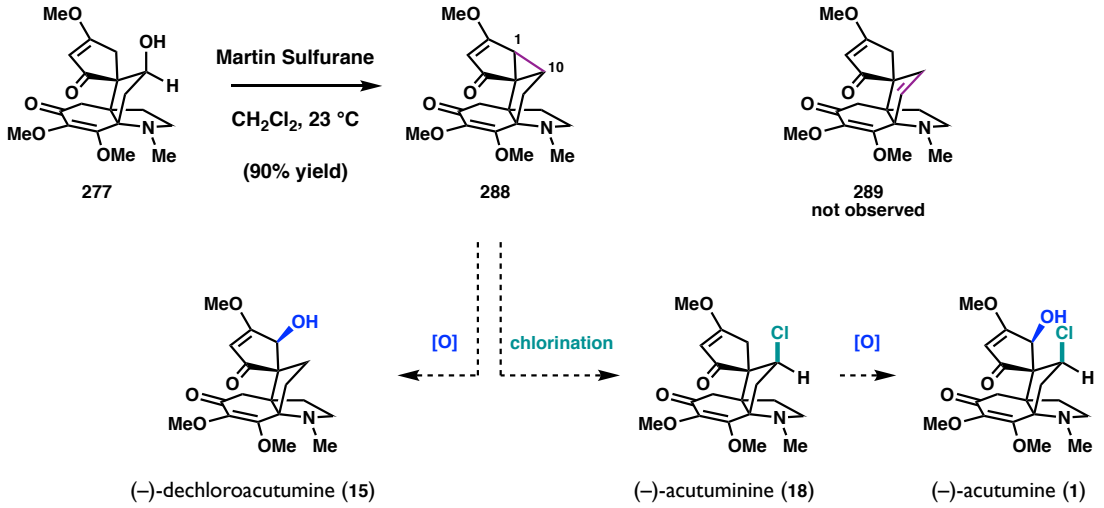
3.8.2 Other Pathways for Chloride Installation

Having had little success in performing a deoxychlorination to access (–)-acutuminine (**18**), other avenues for chlorination were considered. Various functional group interconversions can be conceived of to convert an alcohol to a chloride. For instance, the neopentyl alcohol could be oxidized and the resulting ketone chlorinated directly,[51] or the ketone could be further converted to the vinyl triflate for halogenation. These avenues were not attractive, however, because they would either require preparation of a sensitive hydrazone on milligram scale, or would necessitate the addition of numerous steps to our synthesis (again a challenge with limited material on hand).

Thus, a pathway via dehydration and hydrochlorination was pursued, and it was thought that accessing the olefin **289** would be feasible based on King's work in the Herzon group.[52] Unfortunately, when alcohol **277** was subjected to Burgess' reagent, dehydration did not occur. As a result, Martin Sulfurane was employed instead, which incredibly afforded cyclopropane **288** in excellent yield (Scheme 3.26). Similar reactivity has been observed before in the literature,[53,54] in which Martin Sulfurane aided in generating a strained cyclobutane from a hindered alcohol, rather than dehydrating to the olefin. Having accessed this unexpected product was particularly exciting because a C–C bond was formed between C1 and C10, the two carbons that required modification to access either (–)-dechloroacutumine (**15**), (–)-acutuminine (**18**), or (–)-acutumine (**1**). It was hypothesized that cyclopropane opening and chlorination might be accomplished with assistance from the basic amine in order afford the desired diastereomer. This was a particularly interesting thought because Barton's biosynthetic proposal invokes a

mechanism with a neopentyl cation (see Chapter 1, Section 1.3.4), which conceivably could be stabilized by the proximal tertiary amine.[55] Furthermore, difunctionalization of the cyclopropane could potentially provide a more direct path toward (–)-acutumine (**1**).[56]

Scheme 3.26 *Cyclopropanation with Martin Sulfurane.*



Preliminary results showed that cyclopropane **288** is surprisingly stable (Scheme 3.26). When cyclopropane-opening and chlorination was attempted with HCl,[57] BCl_3, or TMSCl/NaCl,[58] very little to no conversion was observed. Excitingly, HCl in Et_2O afforded traces of a chlorination product (via LC/MS and HRMS). Upon scaling to 3 mg and increasing the reaction time to one day at room temperature, conversion could unfortunately not be increased, and demethylation of the vinylogous ester was observed instead, along with large quantities of unreacted cyclopropane. As of the writing of this dissertation, the identity of this product has not been confirmed. Current efforts are directed at optimizing this chlorination and pursuing oxidation chemistry at C1 as well.

3.9 CONCLUDING REMARKS

(–)-Acutumine (**1**) is a complex spirocyclic alkaloid present in plant extracts used in traditional Chinese medicine.[59,60] This propellane natural product has an interesting history, starting from its isolation in 1929[61] and spanning landmark publications on its structural elucidation,[62–65] proposed biosynthesis,[55] and total synthesis efforts published over the past thirteen years.[48,52,66–75] The spirocyclic core, 5 contiguous stereocenters, and neopentyl chloride present in (–)-acutumine (**1**) have cemented it as one of the most challenging synthetic targets known to synthetic organic chemists.

The Reisman group began their synthetic efforts toward acutumine alkaloids in 2011. The foundation of our work was inspired by previous efforts in the laboratory which enabled enantioselective access to a number of hasubanan alkaloids,[76,77] which are related propellane natural products. Specifically, the stereoselective 1,2-addition of organometal species to benzoquinone-derived imines **112** was developed (see Chapter 2, Section 2.2),[76] which allowed entry into chiral intermediates containing the C–N bond present in both hasubanan (C14–N)[60] and acutumine (C13–N) alkaloids. Building on the expertise developed in our group on these stereoselective 1,2-additions, the synthetic strategy to access acutumine alkaloids relied on a key [2+2]-cycloaddition/retro-aldol/aldol sequence to install the spirocyclic core. Noteworthy is that the photo-mediated [2+2]-cycloaddition installs the vicinal all-carbon quaternary centers in a single step.

Over the course of our work on the acutumine alkaloids, we have successfully accessed the spirocyclic core in three different series. The first two proceeded via a carbamate-enable retro-aldol/aldol sequence, which culminated in the synthesis of the

spirocyclic core of (–)-dechloroacutumine (**15**) and a C10-oxidized analogue **165a**, which contains a neopentyl alcohol functional group handle for chlorination (see Chapter 2). The third series proceeded via a retro-aldol/Dieckmann sequence as had been originally proposed in our retrosynthetic analysis (see Chapter 2, Section 2.3.1, Figure 2.3), whereby MeOH served as an external nucleophile to fragment cyclobutyl lactone **125b** in a retro-aldol event. Subsequent Dieckmann cyclization proved capricious in a number of routes (see Chapter 3), highlighting the difficult carbonyl chemistry we hoped to accomplish.

The challenge presented in the ring-closure to the spirocycle inspired a Dieckmann cyclization hypothesis, which postulates that the stereoelectronics of the carbonyls on the acutumine core (C6 and C3/C4) can be modified to enable to Dieckmann cyclization. This hypothesis culminated in modification of the C3-methyl ketone to α-bromoketone **253**, which underwent successful Dieckmann cyclization and methylation to spirocycle **255**. This result was particularly significant because we had, for the first time, accessed the spirocyclic cyclopentenone found in (–)-acutumine (**1**). At this stage, the remaining challenges were investigated, which included installation of the dimethoxyenone motif and C10-chlorination. After extensive experimentation, elimination/methylation of ketal **257** was at last successful to forge vinylogous ester **262**. Subsequent TBS-deprotection afforded neopentyl alcohol **277**, a key intermediate which contains the complete carboskeleton and oxidation pattern of the natural product (–)-acutuminine (**18**).

With the total synthesis of (–)-acutuminine (**18**) and (–)-acutumine (**1**) within close reach, deoxychlorination reactions of alcohol **277** were pursued. To date, heterolytic deoxychlorination reactions have been unsuccessful, while two radical deoxychlorination

reactions have afforded mass hits of chlorination products (*vide supra*). Thus far, optimization of these conditions has proven challenging, given the propensity for the intermediates to decompose under radical conditions. It is hypothesized that decomposition may occur via a variety of mechanisms. Under photoredox-catalysis, oxidation of the tertiary amine and redox reactions of the electron-rich vinylogous esters may be operative, while general fragmentation and decomposition of the spirocyclic core upon formation of the C10 carbon centered radical may occur as well. Overall, efforts in our laboratory are directed at continued development of radical deoxychlorinations that can be implemented in challenging contexts like natural product total synthesis (see Chapter 4).

Upon investigation of other pathways toward successful C10-chlorination, or a synthesis of (–)-dechloroacutumine (**15**), cyclopropane **288** was surprisingly formed when alcohol **277** was subjected to Martin Sulfurane. This remarkable intermediate, which contains a C1–C10 bond, is primed for modification at the precise carbons required for completion of a total synthesis of (–)-acutumine (**1**), (–)-acutuminine (**18**), and (–)-dechloroacutumine (**15**). Current efforts are directed at investigating C10 and C1 modifications of cyclopropane **288**, as well as investigating its biological activity.

3.10 EXPERIMENTAL SECTION

3.10.1 Materials and Methods

General Procedures. Unless otherwise stated, reactions were performed under an inert atmosphere (dry N_2 or Ar) using freshly dried solvents utilizing standard Schlenk techniques. Glassware was oven-dried at 120 °C for a minimum of four hours, or flame-dried utilizing a Bunsen burner under high vacuum. Tetrahydrofuran (THF), methylene chloride (CH_2Cl_2), acetonitrile (CH_3CN), methanol (MeOH), benzene (PhH), and toluene (PhMe) were dried by passing through activated alumina columns. MeOH was stored over 4Å molecular sieves in a flame-dried Schlenk flask under Ar and was used for reaction procedures, unless the use of wet HPLC grade methanol (0.2 micron filtered HPLC grade, Fisher A452-4) is specifically indicated. HPLC grade benzene (PhH, OmniSolv, BX0212-1), acetonitrile (CH_3CN, A998-4), pentane (P399-4), and ACS grade acetone (A18-20) and ^{n}Butanol (certified ACS grade, A399-4) were purchased from Fisher and used when specifically indicated, as received. Anhydrous DMF was purchased from VWR (EM-DX1727-6) and used as received. Anhydrous *tert*-amyl alcohol was purchased from Sigma-Aldrich and used as received. Triethylamine (Et_3N) and *N*,*N*-diisopropylethylamine (DIPEA) were distilled over calcium hydride prior to use, and 2,6-lutidine was distilled over calcium hydride and stored in a dried Schlenk tube under N_2. All reactions were monitored by thin-layer chromatography using EMD/Merck silica gel 60 F254 pre-coated plates (0.25 mm) and were visualized by UV, *p*-anisaldehyde, potassium permanganate ($KMnO_4$), ceric ammonium molybdate (CAM), or 2,4-dinitrophenylhydrazine staining. Flash column chromatography was performed as described by Still et al.[78] using silica gel

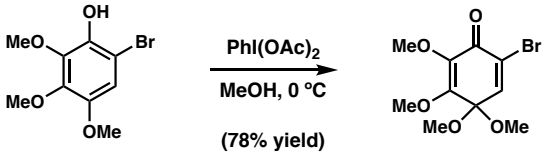
(particle size 0.032-0.063) purchased from Silicycle or Florisil (100-200 mesh) purchased from ACROS Organics (CAS 1343-88-0). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance III HD with Prodigy cryoprobe (at 400 MHz and 101 MHz respectively), a Varian 400 MR (at 400 MHz and 101 MHz, respectively), a Varian Inova 500 (at 500 MHz and 126 MHz, respectively), or a Varian Inova 600 (at 600 MHz and 150 MHz, respectively), and are reported relative to internal $CHCl_3$ (^{1}H, $\delta = 7.26$) and $CDCl_3$ (^{13}C, $\delta = 77.16$), C_6H_6 (^{1}H, $\delta = 7.16$) and C_6D_6 (^{13}C, $\delta = 128$), or CH_3CN (^{1}H, $\delta = 1.94$) and CD_3CN (^{13}C, $\delta = 118.26$). Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicity and qualifier abbreviations are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, bt = broad triplet. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm^{-1}). HRMS were acquired using an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI), or mixed (MM) ionization mode, or obtained from the Caltech Mass Spectral Facility in fast-atom bombardment mode (FAB). Molecular formulas of the compounds M are given, with the observed ion fragment in brackets, e.g. $[M+H]^+$. Optical rotations were measured on a Jasco P-2000 polarimeter using a 100 mm path-length cell at 589 nm. Melting points were determined using a Büchi B-545 capillary melting point apparatus and the values reported are uncorrected.

Unless otherwise stated, chemicals and reagents were used as received. Reagents were purchased from commercial vendors as follows: Triethylsilyl trifluoromethanesulfonate (TESOTf) was purchased from Oakwood Chemicals Inc. and

stored in the freezer of a nitrogen-filled glovebox. TASF was purchased from Sigma-Aldrich, Martin Sulfurane was purchased from TCI Chemicals Inc., and potassium *tert*-butoxide (KO^{t}Bu) was purchased from AK Scientific Inc., and all were stored in a nitrogen-filled glovebox. Lithium hydroxide (LiOH) was purchased from Sigma-Aldrich and stored in a desiccator. Hydrogen peroxide (30% H_2O_2 in H_2O, stabilized) was purchased from MilliporeSigma. Boron trifluoride diethyl etherate ($BF_3{\cdot}Et_2O$, ≥ 46.5% in Et_2O), boron trichloride (BCl_3, 1 M in CH_2Cl_2), and trimethylsilyl diazomethane ($TMSCHN_2$, 2 M in Et_2O) were purchased from Sigma-Aldrich, and 3-chloroperoxybenzoic acid (*m-CPBA*, 75%) was purchased from AK Scientific Inc. *N*-bromosuccinimide (NBS) was recrystallized from H_2O before use (reliable over at least 6 months when stored in an amber flask in a freezer at –20 °C).

3.10.2 Experimental Procedures

Preparation of ketal 190.



189 190

6-Bromo-2,3,4-trimethoxyphenol[79] (**189**, 4.8 g, 18.32 mmol) was taken up in MeOH (20 mL, HPLC grade) and cooled to 0 °C. A solution of $PhI(OAc)_2$ (6.20 g, 19.24 mmol, 1.05 equiv) in MeOH (72 mL, HPLC grade) was prepared and added dropwise to phenol **189** over 10 min. The mixture was stirred for an additional 20 min at 0 °C, after which the

reaction was quenched with saturated aqueous $NaHCO_3$ (150 mL), diluted with EtOAc (100 mL), and warmed to room temperature. The MeOH was removed under reduced pressure, and the remaining aqueous layer was extracted with EtOAc (4 x 80 mL). The combined organic layers were washed with brine (1 x 200 mL), dried with Na_2SO_3, filtered, and concentrated under reduced pressure to give an orange oil. The crude residue was purified by silica gel flash chromatography (5–40% EtOAc/hexanes) to afford **190** (4.16 g, 78% yield) as an orange oil.

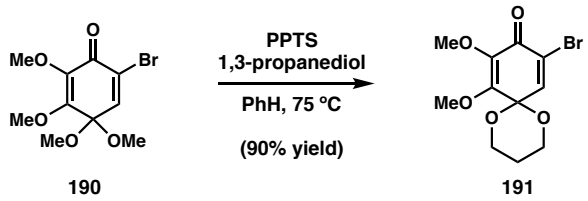
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.78 (s, 1H), 3.94 (s, 3H), 3.50 (s, 3H), 3.11 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 175.5, 155.4, 140.3, 136.9, 124.5, 96.7, 60.7, 60.1, 51.0.

FTIR (NaCl, thin film): 3320, 3055, 2949, 2833, 1668, 1456, 1297, 1080, 974 cm^{-1}.

HRMS (MM, *m/z*): $C_{10}H_{13}BrO_5$, calc'd for $[M+H]^+$: 293.0019, found 293.0000.

Preparation of dioxane 191.



190 **191**

Ketal **190** (4.16 g, 14.23 mmol) and PPTS (537 mg, 2.14 mmol, 15 mol %) were added to a flame-dried round bottom flask. A reflux condenser was added and the system placed under N_2 atmosphere. PhH (84 mL) was added, followed by 1,3-propanediol (2.61 ml, 36.15 mmol, 2.5 equiv). The flask was placed in a preheated oil bath at 75 °C, upon which the temperature dropped. The heating bath returned to 75 °C after 12 min, and the

reaction was further heated for one additional hour (*Note*: During the reaction monitoring, the flask was always removed from the heating bath, as prolonged heating of the reaction mixture causes the decomposition of the product). The reaction was quenched with pH 7 buffer (110 mL), diluted with Et_2O (60 mL), and cooled to room temperature. The aqueous layer was extracted with Et_2O (5 x 60 mL), and the combined organic layers were washed with brine (1 x 100 mL), dried with Na_2SO_3, filtered, and concentrated under reduced pressure to give an orange oil. The crude was purified via Florisil flash chromatography (5–80% EtOAc/hexanes) to afford **191** (3.91 g, 90%) as a thick oil that crystallizes to a yellow solid on large scale.

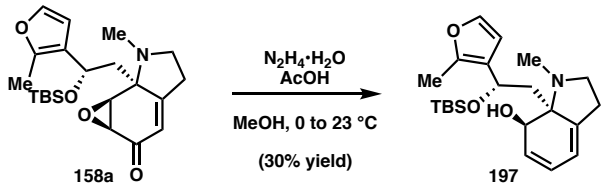
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (s, 1H), 4.16 (s, 3H), 4.22 – 4.09 (m, 4H), 3.71 (s, 3H), 2.20 (dtt, *J* = 13.7, 10.0, 6.4 Hz, 1H), 1.63 (dp, *J* = 13.5, 3.3 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 176.1, 157.5, 136.4, 135.9, 123.8, 93.0, 61.5, 61.3, 61.1, 24.4.

FTIR (NaCl, thin film): 3062, 2880, 1666, 1450, 1353, 1281, 1190, 1085, 1032 cm^{-1}.

HRMS (MM, *m/z*): $C_{11}H_{13}BrO_5$, calc'd for $[M+H]^+$: 305.0019, found 305.0000.

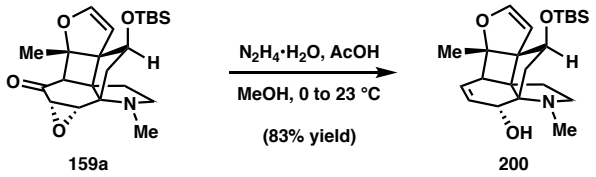
Preparation of allylic alcohol 197.



Epoxyketone **158a** (60 mg, 0.15 mmol) was added to a 2 dram vial containing a stir bar and was taken up in MeOH (1.5 mL, HPLC grade). The mixture was cooled to 0 °C, after which the mixture was sparged with N_2 for 15 min. Subsequently, hydrazine monohydrate (14.5 μL, 0.30 mmol, 2.0 equiv, 64–65%) was added. After 1 min, AcOH (17 μL, 0.30 mmol, 2.0 equiv) was added. The mixture was stirred at 0 °C for 5 min, then warmed to room temperature and stirred for 5 h. Upon consumption of epoxide **158a**, saturated aqueous $NaHCO_3$ (8 mL) was added, as well as EtOAc (3 mL), and the mixture was transferred to a separatory funnel. The aqueous layer was extracted with EtOAc (5 x 3 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (1 x 8 mL), then brine (1 x 8 mL), and dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified via Florisil flash chromatography (10–100% EtOAc/hexanes) to afford allylic alcohol **197** (17.5 mg, 30% yield).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.17 (d, *J* = 1.9 Hz, 1H), 6.23 (d, *J* = 1.9 Hz, 1H), 6.06 (dd, *J* = 9.3, 5.1 Hz, 1H), 5.91 (dd, *J* = 9.4, 5.5 Hz, 1H), 5.73 (dt, *J* = 4.9, 2.4 Hz, 1H), 4.63 (t, *J* = 5.5 Hz, 1H), 3.60 (d, *J* = 5.5 Hz, 1H), 3.23 (td, *J* = 8.9, 3.0 Hz, 1H), 2.91 (q, *J* = 8.7 Hz, 1H), 2.61 – 2.47 (m, 2H), 2.44 (s, 3H), 2.18 (s, 3H), 1.91 (qd, *J* = 14.9, 5.6 Hz, 2H), 0.82 (s, 9H), -0.01 (s, 3H), -0.28 (s, 3H).

Preparation of allylic alcohol 200.



159a 200

Cyclobutane **159a** (324 mg, 0.80 mmol) was added to a 25 mL round bottom flask and was taken up in MeOH (8 mL, HPLC grade). The flask was sealed with a plastic septum and cooled to 0 °C, after which the mixture was sparged with N_2 for 15 min. Subsequently, hydrazine monohydrate (120 μL, 1.60 mmol, 2.0 equiv, 64–65%) was added. After 1 min, AcOH (92 μL, 1.60 mmol, 2.0 equiv) was added. The mixture was stirred at 0 °C for 5 min, then warmed to room temperature and stirred for 4 h. Upon consumption of the cyclobutane, saturated aqueous $NaHCO_3$ (30 mL) was added, as well as EtOAc (10 mL), and the mixture was transferred to a separatory funnel. The aqueous layer was extracted with EtOAc (5 x 10 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (1 x 15 mL), then brine (1 x 15 mL), and the combined washes were back-extracted with EtOAc (1 x 10 mL). All combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give an orange oil. The crude residue was purified via Florisil flash chromatography (10–60% EtOAc/hexanes) to afford allylic alcohol **200** as a pale yellow solid (259 mg, 83% yield). *Note:* A rapid gradient increase and chromatography run is necessary to avoid decomposition upon purification.

TLC: R_f 0.49 (3:1 EtOAc/hexanes, CAM) and 0.40 (60% EtOAc/CH_2Cl_2, CAM).

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25.0}}$**:** –64.5° (c = 0.125, $CHCl_3$).

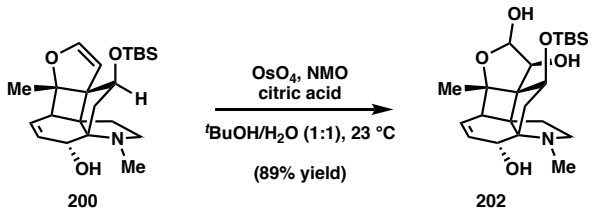
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.51 (d, *J* = 2.8 Hz, 1H), 6.17 (ddd, *J* = 10.1, 5.8, 2.2 Hz, 1H), 5.88 (dd, *J* = 10.1, 4.4 Hz, 1H), 5.03 (br, 1H), 4.56 (d, *J* = 2.9 Hz, 1H), 3.78 (dd, *J* = 11.6, 6.8 Hz, 1H), 3.70 (d, *J* = 5.8 Hz, 1H), 3.06 (dd, *J* = 4.4, 2.2 Hz, 1H), 3.01 (dd, *J* = 8.6, 6.5 Hz, 1H), 2.34 (s, 3H), 2.17 (dd, *J* = 14.1, 6.8 Hz, 1H), 2.10 (ddd, *J* = 12.1, 8.6, 4.9 Hz, 1H), 2.01 (dd, *J* = 12.2, 4.8 Hz, 1H), 1.82 (ddd, *J* = 14.1, 11.6, 0.9 Hz, 1H), 1.66 (td, *J* = 12.1, 6.6 Hz, 1H), 1.37 (s, 3H), 0.85 (s, 9H), 0.02 (s, 3H), 0.01 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 148.36, 128.07, 127.16, 101.60, 90.14, 74.77, 68.06, 66.86, 62.54, 55.87, 53.94, 47.74, 40.79, 34.56, 30.52, 25.83, 18.09, 18.06, -4.67, -4.75.

FTIR (NaCl, thin film): 3278, 2928, 2855, 1605, 1250, 1148, 1119, 1038, 836 cm^{-1}.

HRMS (ESI, *m/z*): $C_{22}H_{35}NO_3Si$, calc'd for $[M+H]^+$: 390.2459, found 390.2470.

Preparation of triol 202.



Allylic alcohol **200** (50 mg, 0.13 mmol) and citric acid monohydrate (108 mg, 0.51 mmol, 4.0 equiv) were added to a scintillation vial and taken up in ^{t}BuOH/H_2O (1.3 mL, 1:1) under ambient air at room temperature. OsO_4 (0.26 mL, 0.013 mmol, 0.10 equiv, 0.05 M in PhMe) was added, followed by portion-wise addition of NMO (18 mg, 0.15 mmol, 1.20 equiv), and the mixture was stirred for 1.75 h. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (5 mL) and saturated aqueous $Na_2S_2O_3$ (5 mL). EtOAc (5 mL) was added and the mixture was stirred vigorously for 2 h. The layers were separated

and the aqueous layer extracted with EtOAc (4 x 10 mL), and the combined organic layers were washed with saturated aqueous $NaHCO_3$ (1 x 10 mL) and brine (1 x 10 mL). All combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give a pale yellow oil. The crude residue was purified via Florisil gel flash chromatography (0–10% MeOH/CH_2Cl_2) to afford triol **202** as a white foam (48.5 mg, 89% yield) as a mixture of diastereomers at the lactol position (1:0.6 dr).

TLC: R_f 0.35 and 0.38 (10% MeOH/CH_2Cl_2, CAM).

$[\alpha]_D^{25.0}$: –10.0° (c = 0.77, $CHCl_3$).

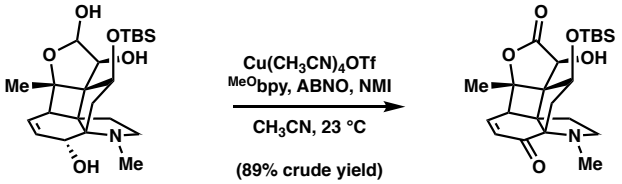
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.15 (ddd, *J* = 10.0, 5.9, 2.1 Hz, 1H), 6.17 – 6.08 (m, 1H), 5.90 – 5.80 (m, 2H), 5.53 (s, 1H), 5.38 (d, *J* = 8.7 Hz, 1H), 4.79 (s, 2H), 4.31 – 4.21 (m, 2H), 4.18 (s, 1H), 4.15 (d, *J* = 7.2 Hz, 1H), 3.86 – 3.78 (m, 2H), 3.73 – 3.65 (m, 2H), 3.54 (d, *J* = 6.4 Hz, 1H), 3.21 (dd, *J* = 4.5, 2.2 Hz, 1H), 3.14 – 3.00 (m, 2H), 2.91 (dd, *J* = 4.4, 2.2 Hz, 1H), 2.40 (s, 3H), 2.36 – 2.25 (m, 1H), 2.23 (ddd, *J* = 13.7, 6.7, 2.8 Hz, 1H), 1.84 – 1.70 (m, 3H), 1.65 (td, *J* = 12.8, 6.6 Hz, 0H), 1.40 (s, 2H), 1.39 (s, 3H), 0.87 (s, 9H), 0.86 (s, 5H), 0.15 (s, 3H), 0.14 (s, 1H), 0.12 (s, 3H), 0.11 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 127.42, 127.25, 126.89, 126.83, 106.12, 98.09, 89.24, 84.28, 79.90, 74.52, 74.43, 73.88, 69.13, 68.81, 63.65, 62.79, 62.64, 61.64, 53.97, 53.90, 48.02, 47.72, 46.70, 46.31, 39.46, 34.46, 34.39, 30.27, 29.45, 25.75, 25.72, 20.05, 19.88, 17.74, -3.40, -3.48, -5.26.

FTIR (NaCl, thin film): 3403, 2929, 2856, 1461, 1252, 1114, 1038, 1003, 837 cm^{-1}.

HRMS (ESI, *m/z*): $C_{22}H_{37}NO_5Si$, calc'd for $[M+H]^+$: 424.2514, found 424.2507.

Preparation of α-hydroxylactone 203.



202 203

Diol **202** (48 mg, 0.11 mmol) was taken up in CH_3CN (1.4 mL, HPLC grade) in a scintillation vial. $Cu(CH_3CN)_4OTf$ (4.3 mg, 0.011 mmol, 10 mol %), ^{MeO}bpy (2.5 mg, 0.011, 10 mol %), ABNO (0.3 mg, 0.0023 mmol, 2 mol %), and NMI (1.8 μl, 0.023 mmol, 20 mol %) were added in that order, and the orange-brown mixture was stirred vigorously (800–900 rpm) at room temperature under air for 7 h. The reaction was then quenched by the addition of saturated aqueous $NaHCO_3$ (10 mL), and the aqueous layer was extracted with EtOAc (5 x 5 mL). The combined organic layers were washed with brine (1 x 7 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure to afford lactone **203** as a beige foam (42.1 mg, 89% crude yield), which was typically carried forward without purification.

TLC: R_f 0.53 (100% EtOAc, UV & CAM).

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25.0}}$**:** –65.9° (c = 1.32, $CHCl_3$).

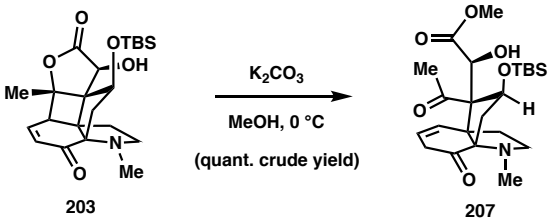
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.66 (dd, *J* = 10.2, 5.1 Hz, 1H), 6.15 (dd, *J* = 10.2, 1.8 Hz, 1H), 4.46 (dd, *J* = 10.9, 6.9 Hz, 1H), 4.34 (s, 1H), 3.38 (br, 1H), 3.06 (dd, *J* = 5.1, 1.8 Hz, 1H), 2.94 (ddd, *J* = 9.2, 7.0, 2.3 Hz, 1H), 2.64 (s, 3H), 2.53 (dd, *J* = 14.0, 6.9 Hz, 1H), 2.36 (td, *J* = 9.4, 5.6 Hz, 1H), 1.92 (dd, *J* = 14.0, 10.9 Hz, 1H), 1.90 – 1.81 (m, 1H), 1.68 (ddd, *J* = 13.5, 9.9, 7.1 Hz, 1H), 1.62 (s, 3H), 0.85 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 200.2, 175.4, 140.6, 129.6, 90.1, 73.8, 73.2, 70.8, 59.6, 53.3, 52.9, 48.0, 39.8, 36.5, 30.2, 25.8, 19.7, 17.8, -4.0, -5.1.

FTIR (NaCl, thin film): 3406, 2930, 2857, 1779, 1677, 1251, 1128, 838 cm^{-1}.

HRMS (ESI, *m/z*): $C_{22}H_{33}NO_5Si$, calc'd for $[M+H]^+$: 420.2201, found 420.2208.

Preparation of ketone 207.



Lactone **203** (20 mg, 0.048 mmol) was added to a flame-dried 2 dram vial and placed under nitrogen atmosphere. It was taken up in MeOH (0.95 mL) and cooled to 0 °C. The septum was briefly removed and solid K_2CO_3 (6.6 mg, 0.048 mmol, 1.0 equiv) was added. The mixture was then stirred vigorously at 0 °C for 20 min, upon which LC/MS analysis indicated consumption of lactone **203**. The reaction was then quenched by the addition of pH 7 buffer (5 mL), and EtOAc (5 mL) and brine (5 mL) were added. After warming to room temperature, the layers were separated, and the aqueous layer extracted with EtOAc (5 x 8 mL). All combined organic layers were then dried with Na_2SO_4, filtered, and concentrated under reduced pressure to afford ester **207** as a pale orange foam (22 mg, quantitative crude yield), which was typically carried forward without further purification.

TLC: R_f 0.50 (60% EtOAc/CH_2Cl_2, UV & CAM).

$[\alpha]_D^{25.0}$: +75.9° (c = 0.850, $CHCl_3$).

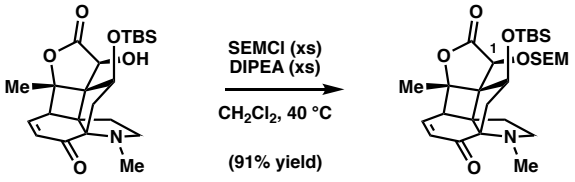
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.70 (ddd, *J* = 10.2, 2.9, 1.4 Hz, 1H), 5.60 (ddd, *J* = 10.1, 4.6, 2.3 Hz, 1H), 5.02 (s, 1H), 4.79 (t, *J* = 9.1 Hz, 1H), 3.91 (s, 3H), 3.27 (br, 1H), 2.96 (dd, *J* = 21.2, 4.7 Hz, 1H), 2.74 – 2.62 (m, 2H), 2.56 (dt, *J* = 21.2, 2.6 Hz, 1H), 2.33 (s, 3H), 2.22 (s, 3H), 1.99 – 1.79 (m, 2H), 1.66 – 1.50 (m, 2H), 0.87 (s, 9H), 0.12 (s, 3H), 0.09 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 208.8, 205.4, 174.8, 131.6, 122.2, 74.8, 73.7, 72.1, 70.6, 62.7, 53.2, 52.4, 38.8, 37.5, 35.4, 35.3, 31.1, 25.9, 18.0, -4.0, -4.9.

FTIR (NaCl, thin film): 3422, 2930, 2856, 1704, 1255, 1192, 1119, 838 cm^{-1}.

HRMS (ESI, *m/z*): $C_{23}H_{37}NO_6Si$, calc'd for $[M+H]^+$: 452.2463, found 452.2455.

Preparation of ether 210.



203 **210**

α-Hydroxyketone **203** (39.6 mg, 0.095 mmol) was added to a flame-dried 2 dram vial and placed under nitrogen atmosphere. It was taken up in CH_2Cl_2 (1.9 mL), and DIPEA (41 μL, 0.24 mmol, 2.5 equiv) was added, followed by SEMCl (33 μL, 0.19 mmol, 2.0 equiv). The septum was quickly replaced with a Teflon-lined screw cap, which was sealed with electrical tape. The vial was subsequently heated at 40 °C for 8 h, at which point significant amount of unreacted starting material **203** was observed via LC/MS. Thus, at room temperature more DIPEA (41 μL, 0.24 mmol, 2.5 equiv) was added, followed by SEMCl

(33 μL, 0.19 mmol, 2.0 equiv), and the reaction heated at 40 °C for 14 h. At this point, more DIPEA (21 μL, 0.12 mmol, 1.25 equiv) and SEMCl (17 μL, 0.095 mmol, 1.0 equiv) were added at room temperature, and the reaction heated at 40 °C for a final 9 h, resulting in complete consumption of **203**. The mixture was cooled to room temperature and quenched with saturated aqueous NH_4Cl (10 mL). The mixture was transferred to a separatory funnel, and extracted with EtOAc (4 x 5 mL). The combined organic layers were washed with brine (1 x 7 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by Florisil flash chromatography: 1) equilibrated with 10% EtOAc/hexanes with 1% Et_3N, 2) flushed with two column volumes of 10% EtOAc/hexanes, and 3) ran gradient of 10–50% EtOAc/hexanes to afford **210** as a faintly yellow oil (47.1 mg, 91% yield).

TLC: R_f 0.47 (1:1 EtOAc/hexanes, UV & faint with CAM).

$[\alpha]_D^{25.0}$: –94.0° (c = 0.46, $CHCl_3$).

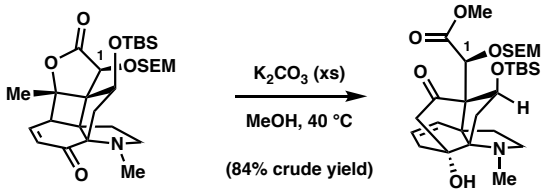
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.66 (dd, *J* = 10.2, 5.1 Hz, 1H), 6.15 (dd, *J* = 10.2, 1.8 Hz, 1H), 5.29 (d, *J* = 7.0 Hz, 1H), 4.72 (d, *J* = 7.0 Hz, 1H), 4.42 (s, 1H), 4.35 (dd, *J* = 9.8, 6.9 Hz, 1H), 3.76 (ddd, *J* = 11.6, 9.5, 5.6 Hz, 1H), 3.59 (ddd, *J* = 11.5, 9.5, 5.7 Hz, 1H), 3.01 (dd, *J* = 5.2, 1.8 Hz, 1H), 2.93 (ddd, *J* = 8.9, 6.9, 2.0 Hz, 1H), 2.60 (s, 3H), 2.44 (dd, *J* = 14.2, 6.9 Hz, 1H), 2.24 (ddt, *J* = 10.6, 8.4, 5.3 Hz, 1H), 1.98 – 1.85 (m, 2H), 1.70 (ddd, *J* = 13.6, 10.3, 6.9 Hz, 1H), 1.59 (s, 3H), 1.02 (ddd, *J* = 13.7, 11.6, 5.7 Hz, 1H), 0.92 (ddd, *J* = 13.7, 11.6, 5.6 Hz, 1H), 0.84 (s, 9H), 0.04 (s, 6H), 0.04 (s, 9H).

^{f13}C NMR (101 MHz, $CDCl_3$): δ 200.0, 174.6, 140.9, 129.7, 93.7, 90.0, 73.2, 73.0, 70.8, 66.5, 60.1, 54.0, 52.9, 48.2, 40.3, 36.8, 30.9, 25.8, 19.9, 18.3, 18.0, -1.3, -4.6, -5.0.

FTIR (NaCl, thin film): 2952, 2894, 1780, 1682, 1250, 1127, 1020, 838 cm^{-1}.

HRMS (ESI, *m/z*): $C_{28}H_{47}NO_6Si_2$, calc'd for $[M+H]^+$: 550.3015, found 550.3001.

Preparation of bridging ketone 212.



210 212

Lactone **210** (9 mg, 0.0164 mmol) and K_2CO_3 (25 mg, 0.18 mmol, 11.0 equiv) were added to a flame-dried 1 dram vial and placed under N_2. At room temperature, MeOH (0.36 mL) was added and the mixture heated at 40 °C for 23 h. The reaction was then cooled to room temperature and quenched with pH 7 buffer (5 mL) and EtOAc (5 mL) was added. The mixture was transferred to a separatory with help of pH 7 buffer (10 mL) and EtOAc (5 mL), and the aqueous layer was extracted with EtOAc (5 x 7 mL). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure to afford **212** (8 mg, 84% crude yield), which was typically carried forward without purification. For the purposes of characterization, the crude residue was purified via silica gel flash chromatography (5–60% EtOAc/hexanes) to afford **212** as a clear oil (2 mg, 21% yield)

TLC: R_f 0.42 (2:1 EtOAc/hexanes, faintly UV active & CAM).

$[\alpha]_D^{25.0}$: +20.7° (c = 0.10, $CHCl_3$).

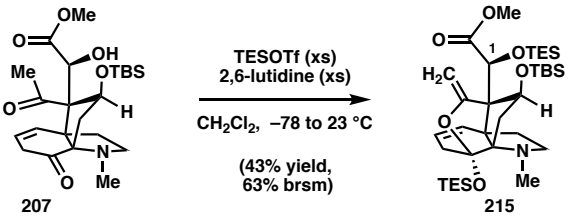
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.67 (dd, *J* = 9.9, 2.7 Hz, 1H), 5.54 – 5.45 (m, 1H), 4.82 (d, *J* = 6.6 Hz, 1H), 4.69 – 4.61 (m, 1H), 4.64 (d, *J* = 6.5 Hz, 1H), 4.61 (s, 1H), 3.80 – 3.68 (m, 1H), 3.73 (s, 3H), 3.50 (ddd, *J* = 11.5, 9.5, 5.7 Hz, 1H), 3.24 – 3.11 (m, 1H), 2.75 – 2.67 (m, 2H), 2.50 (d, *J* = 17.4 Hz, 1H), 2.52 – 2.38 (m, 1H), 2.45 (s, 3H), 2.31 (dd, *J* = 14.8, 10.4 Hz, 1H), 2.04 – 1.90 (m, 2H), 1.76 – 1.64 (m, 2H), 0.99 – 0.76 (m, 2H), 0.84 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H), 0.01 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 203.6, 172.8, 133.5, 122.6, 96.5, 75.7, 75.5, 73.5, 71.5, 68.4, 66.4, 60.0, 53.9, 53.2, 51.9, 39.2, 38.1, 30.0, 29.5, 25.8, 18.2, 17.9, -1.3, -4.2, -4.9.

FTIR (NaCl, thin film): 3482, 2951, 2854, 1720, 1251, 1058, 835 cm^{-1}.

HRMS (ESI, *m/z*): $C_{29}H_{51}NO_7Si_2$, calc'd for $[M+H]^+$: 582.3277, found 582.3254.

Preparation of silyl enol ether 215.



Ketone **207** (10 mg, 0.022 mmol) was added to a flame-dried 1 dram vial containing a stir bar and was placed under N_2 atmosphere. It was taken up in CH_2Cl_2 (0.55 mL) and cooled to –78 °C. 2,6-Lutidine (21 mL, 0.18 mmol, 8.0 equiv) was added, followed by TESOTf (25 mL, 0.11 mmol, 5.0 equiv). The mixture was stirred at –78 °C for 10 min, and was then warmed to room temperature. After stirring at room temperature for 1 h, additional 2,6-lutidine (10 mL, 0.09 mmol, 4.0 equiv) and TESOTf (10 mL, 0.044 mmol, 2.0 equiv) were added and the mixture was stirred further at room temperature for an additional 30 min.

The reaction was quenched by the addition of pH 7 buffer (4 mL), and the auqueous layer was extracted with CH_2Cl_2 (4 x 4 mL). The combined organic layers were washed with brine (1 x 5 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by Florisil flash chromatography (0–25% EtOAc/hexanes) to afford silyl ether **215** as an off-white foam (6.4 mg, 43% yield), along with recovered **207** (2 mg, 20% yield, 63% brsm).

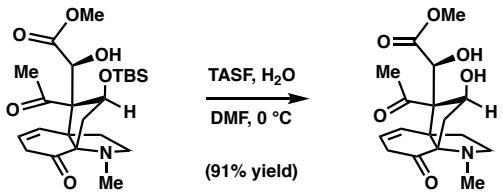
^{1}H NMR (600 MHz, $CDCl_3$): δ 5.58 (dd, *J* = 9.9, 2.6 Hz, 1H), 5.41 (dd, *J* = 10.6, 4.7 Hz, 1H), 4.62 (s, 1H), 4.47 (s, 1H), 4.43 (dd, *J* = 10.1, 5.6 Hz, 1H), 3.88 (s, 1H), 3.72 (s, 3H), 3.07 (q, *J* = 9.0, 8.4 Hz, 1H), 2.54 (d, *J* = 17.6 Hz, 1H), 2.31 (s, 3H), 2.30 (d, *J* = 16.0 Hz, 1H), 2.25 (dd, *J* = 17.4, 5.2 Hz, 1H), 1.90 (dd, *J* = 14.1, 10.0 Hz, 1H), 1.75 (dd, *J* = 14.1, 5.7 Hz, 1H), 1.62 (dd, *J* = 9.4, 5.9 Hz, 2H), 0.97 (t, *J* = 7.9 Hz, 9H), 0.94 (t, *J* = 8.0 Hz, 9H), 0.88 (s, 9H), 0.70 (p, *J* = 7.8 Hz, 6H), 0.57 (q, *J* = 7.9 Hz, 6H), 0.10 (s, 3H), 0.07 (s, 3H).

Note: ^{13}C data was taken from HSQC (*) and HMBC (‡) spectra and is incomplete (cyclohexanone and methyl ketone carbonyls not confidently visible).

^{13}C NMR (151 MHz, $CDCl_3$): δ 173. 4‡, 157.3‡, 133.2*, 120.8*, 90.7*, 72.8*, 71.5‡, 70.4*, 62.1‡, 57.0‡, 52.7*, 51.5*, 36.4*, 37.6*, 27.1*, 30.3*, 7.1*, 6.8*, 25.7*, 6.3*, 4.8*, -5.2*, -3.7*.

HRMS (MM, *m/z*): $C_{35}H_{65}NO_6Si_3$, calc'd for $[M+H]^+$: 680.4192, found 680.4201.

Preparation of neopentyl alcohol 216.

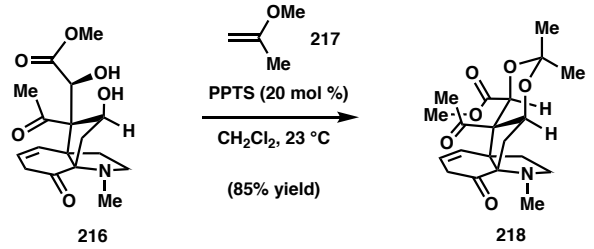


207 216

Silyl ether **207** (19.0 mg, 0.042 mmol) and a stir bar were added to a 2 dram vial, and was taken up in DMF (0.2 mL) and cooled to 0 °C. TASF (34.8 mg, 0.13 mmol, 3.0 equiv) was weighed into a vial, sealed with a screw cap, and removed from the glovebox. The TASF was taken up in DMF (1 mL) under ambient air, after which H_2O (7.5 μL, 0.42 mmol, 10.0 equiv) was added. The TASF solution was subsequently added dropwise to silyl ether **207** at 0 °C, and the mixture was stirred for 1 h. The reaction was quenched by the addition of pH 7 buffer (8 mL), and the aqueous layer was extracted with 10% IPA/$CHCl_3$ (5 x 5 mL). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by Florisil flash chromatography (0–10% MeOH/CH_2Cl_2) to afford **216** (13.5 mg, 95% yield; adjusted yield is 91% based on purity of 96%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.83 (ddd, *J* = 10.3, 3.0, 1.3 Hz, 1H), 5.66 (ddd, *J* = 10.3, 5.1, 2.5 Hz, 1H), 4.73 (dd, *J* = 10.4, 8.7 Hz, 1H), 4.61 (s, 1H), 3.86 (s, 3H), 3.32 (br, 1H), 2.99 – 2.85 (m, 1H), 2.87 – 2.70 (m, 3H), 2.43 (dd, *J* = 14.8, 10.4 Hz, 1H), 2.29 (s, 3H), 2.22 (dd, *J* = 14.9, 8.8 Hz, 1H), 2.18 – 2.11 (m, 1H), 2.10 (s, 3H), 1.95 – 1.85 (m, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 208.3, 206.3, 173.5, 131.9, 122.4, 76.1, 74.7, 71.7, 64.2, 53.1, 52.6, 38.5, 37.4, 35.3, 35.2, 31.4.

Preparation of cyclic ketal 218.



Note: This reaction proved challenging to reproduce and resulted in large amounts of decomposition on >3 mg scale.

Diol **216** (3.1 mg, 0.0056 mmol) and PPTS (0.3 mg, 0.0011 mmol, 20 mol %) were added to a flame-dried 1 dram vial containing a stir bar and placed under N_2 atmosphere. The solids were taken up in CH_2Cl_2 (0.19 mL) and 2-methoxypropene (**217**) was added (2 μL, 0.0167 mmol, 3.0 equiv). The reaction was heated at 40 °C for 5 h, after which PPTS (0.3 mg, 0.0011 mmol, 20 mol %) and 2-methoxypropene (2 μL, 0.0167 mmol, 3.0 equiv) were added. The mixture was stirred at 40 °C overnight, then cooled to room temperature and quenched by the addition of pH 7 buffer (3 mL). The aqueous layer was extracted with CH_2Cl_2 (5 x 1.5 mL), and the combined organic layers dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by Florisil flash chromatography (10–100% EtOAc/pentane) to afford **218** (2.95 mg, 85% yield).

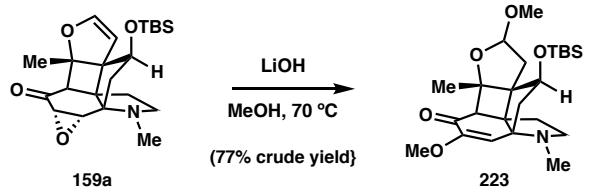
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.73 – 5.50 (m, 2H), 4.99 (d, *J* = 3.3 Hz, 1H), 4.76 (t, *J* = 9.0 Hz, 1H), 3.89 (s, 3H), 2.95 (dd, *J* = 21.3, 3.0 Hz, 1H), 2.78 – 2.62 (m, 2H), 2.62 (d, *J* = 21.5 Hz, 1H), 2.36 (s, 3H), 2.21 (s, 3H), 2.12 – 1.89 (m, 2H), 1.78 – 1.67 (m, 1H), 1.62 (dd, *J* = 11.5, 2.6 Hz, 1H), 1.42 (s, 3H), 1.35 (s, 3H).

Note: ^{13}C data was taken from HSQC (*) and HMBC (‡) spectra.

^{13}C NMR (101 MHz, $CDCl_3$): δ 208.5‡, 205.0‡, 174.2‡, 130.9*, 122.5*, 75.2‡, 72.4*, 73.7*, 69.9‡, 62.1‡, 53.0*, 49.7*, 52.2*, 38.5*, 31.2*, 35.3*, 35.0*, 35.0*, 24.9*, 25.0*.

HRMS (MM, *m/z*): $C_{20}H_{27}NO_6$, calc'd for $[M+H]^+$: 378.1911, found 378.1910.

Preparation of acetal 223.



159a 223

A 100 mL two-neck round bottom flask, stir bar, and waterless condenser were flame-dried. Cyclobutane **159a** (907 mg, 2.24 mmol) was added and placed under N_2. MeOH (22.5 mL) was added, followed by powdered LiOH (269 mg, 11.24 mmol, 5.0 equiv). The mixture was heated at 70 °C (oil bath temperature) for 15 h, after which additional powdered LiOH (269 mg, 11.24 mmol, 5.0 equiv) was added and the reaction stirred at 70 °C for 23 h. The reaction was cooled to room temperature and quenched with saturated aqueous NH_4Cl (15 mL). The mixture was transferred to a separatory funnel and H_2O (10 mL) and EtOAc (30 mL) were used to help in the transfer of the solids. The layers were separated and the aqueous layer was extracted with EtOAc (5 x 20 mL). The combined organic layers were washed with brine (1 x 40 mL), and the brine layer back-extracted with EtOAc (1 x 20 mL). All combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give an orange-beige foam (781 mg, 77% crude yield), which was typically carried on without purification. A small portion was purified

for characterization by Florisil flash chromatography: 1) equilibrated with hexanes, 2) used hexanes and minimal CH_2Cl_2 to load, and 3) ran a gradient of 10–80% EtOAc/hexanes to afford **223** as a white foam.

TLC: R_f 0.28 (3:1 EtOAc/hexanes, $KMnO_4$).

$[\alpha]_D^{25.0}$: +73.8° (c = 0.50, $CHCl_3$).

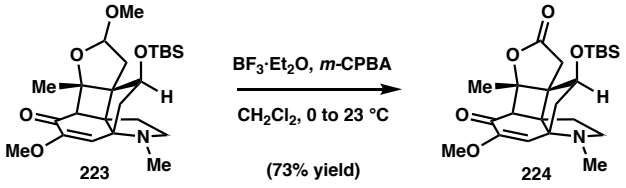
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.91 (s, 1H), 5.13 (d, *J* = 5.4 Hz, 1H), 4.09 (dd, *J* = 10.4, 7.6 Hz, 1H), 3.61 (s, 3H), 3.40 (s, 3H), 3.36 (s, 1H), 2.64 (ddd, *J* = 9.0, 7.5, 3.4 Hz, 1H), 2.53 – 2.35 (m, 2H), 2.41 (s, 3H), 2.24 – 2.12 (m, 2H), 2.08 (d, *J* = 13.8 Hz, 1H), 1.71 (dd, *J* = 13.6, 10.4 Hz, 1H), 1.60 (ddd, *J* = 13.8, 6.9, 3.4 Hz, 1H), 1.34 (s, 3H), 0.85 (s, 9H), 0.03 (s, 3H), 0.03 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 190.14, 151.45, 115.77, 106.48, 89.20, 73.70, 69.60, 63.47, 59.12, 55.00, 54.98, 53.88, 50.40, 44.86, 36.67, 34.65, 32.71, 25.81, 19.41, 17.94, -4.28, -4.89.

FTIR (NaCl, thin film): 2932, 2857, 1676, 1617, 1457, 1254, 1156, 1034, 838 cm^{-1}.

HRMS (ESI, *m/z*): $C_{24}H_{39}NO_5Si$, calc'd for $[M+H]^+$: 450.2670, found 450.2678.

Preparation of lactone 224.



Note: This reaction can be set up without particular care for a dry set up or inert atmosphere. However, it is crucial to utilize wet *m-CPBA* (75% here), as a significant drop in yield was observed for 99% *m-CPBA*.

In a round bottom flask with a stir bar, acetal **223** (300 mg, 0.67 mmol) was taken up in CH_2Cl_2 (10 mL). It was cooled to 0 °C and a septum with N_2 inlet added (in case gases develop). $BF_3{\cdot}Et_2O$ (0.44 mL, 1.67 mmol, 2.5 equiv; 46.5%) was added dropwise, giving a pale red solution, which was stirred for 10 min. In the meantime, *m-CPBA* (161 mg, 0.70 mmol, 1.05 equiv; 75%) was added to a 2 dram vial and taken up in CH_2Cl_2 (3 mL). Once dissolved, the *m-CPBA* solution was added to the reaction dropwise at 0 °C. The syringe and vial of *m-CPBA* were rinsed with CH_2Cl_2 (1 mL), and the solution transferred dropwise to the reaction. The resulting reaction was stirred at 0 °C for 22 h, and conversion was monitored by LC/MS. At 0 °C, the reaction was then quenched with saturated aqueous $NaHCO_3$ (15 mL) and 0.1 M sodium thiosulfate (4 mL, 0.57 equiv to oxidant). EtOAc (15 mL) and brine (15 mL) were added and the reaction warmed to room temperature. The layers were separated, and the aqueous layer was then extracted with EtOAc (4 x 15 mL), and the combined organic layers were washed with brine (1 x 20 mL), and the brine layer was back-extracted with EtOAc (1 x 5 mL). All combined organic layers were dried with

Na_2SO_4, filtered, and concentrated under reduced pressure to give an orange-brown foam. The crude residue was purified by Florisil flash chromatography (30–100% EtOAc/hexanes) to afford **224** (210 mg, 73% yield) as a white foam.

TLC: R_f 0.21 (100% EtOAc, DNP and CAM).

$[\alpha]_D^{25.0}$: +65.6° (c = 0.76, $CHCl_3$).

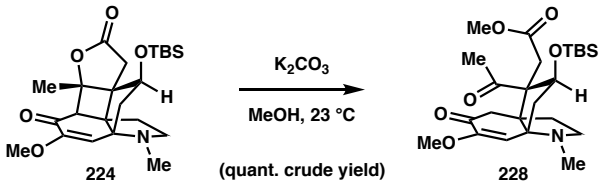
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.94 (s, 1H), 4.15 (dd, *J* = 10.4, 7.5 Hz, 1H), 3.62 (s, 3H), 3.17 (s, 1H), 2.77 (s, 2H), 2.73 (ddd, *J* = 9.1, 7.8, 2.9 Hz, 1H), 2.52 (dd, *J* = 13.7, 7.5 Hz, 1H), 2.45 (td, *J* = 8.9, 7.4 Hz, 1H), 2.40 (s, 3H), 2.02 (dt, *J* = 13.4, 8.1 Hz, 1H), 1.72 – 1.61 (m, 2H), 1.51 (s, 3H), 0.85 (s, 9H), 0.05 (s, 3H), 0.05 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 187.6, 175.1, 151.8, 115.0, 89.4, 74.4, 69.8, 59.2, 58.4, 55.1, 53.5, 51.5, 45.1, 34.3, 33.0, 31.5, 25.7, 18.8, 17.9, -4.3, -4.9.

FTIR (NaCl, thin film): 2953, 2857, 1773, 1683, 1616, 1457, 1381, 1159, 961 cm^{-1}.

HRMS (FAB^+, *m/z*): $C_{23}H_{35}NO_5Si$, calc'd for $[M+H]^+$: 434.2363, found 434.2368.

Preparation of ketone 228.



In a round bottom flask with flame-dried stir bar and under N_2, lactone **224** (365 mg, 0.84 mmol) was taken up in MeOH (42 mL). At room temperature, solid K_2CO_3 (122 mg, 0.88 mmol, 1.05 equiv) was added and the mixture stirred vigorously. After 1.5 h, it was

quenched by the addition of pH 7 buffer (35 mL), and EtOAc (30 mL) and brine (30 mL) were added. The layers were separated and the aqueous layer extracted with EtOAc (5 x 20 mL). The combined organic layers were washed with brine (1 x 60 mL) and the brine layer back-extracted with EtOAc (1 x 20 mL). All combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give a pale orange foam (400 mg, quantitative crude yield), which was typically carried forward without further purification. For characterization, a sample was purified by Florisil flash chromatography (10–100% EtOAc/hexanes) to afford **228** as a white foam.

TLC: R_f 0.14 and 0.40 (100% EtOAc and 10% MeOH in CH_2Cl_2, UV & CAM).

$[\alpha]_D^{25.0}$: –6.4° (c = 0.77, $CHCl_3$).

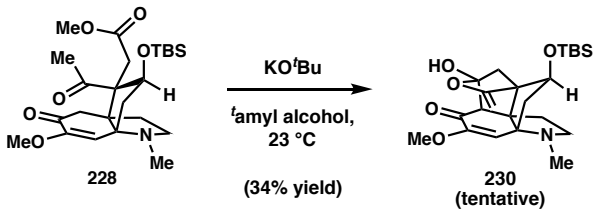
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.38 (s, 1H), 4.19 (dd, *J* = 9.0, 6.1 Hz, 1H), 3.68 (s, 3H), 3.63 (s, 3H), 3.34 (d, *J* = 17.0 Hz, 1H), 3.12 (d, *J* = 17.5 Hz, 1H), 2.82 (d, *J* = 17.0 Hz, 1H), 2.73 (dd, *J* = 9.5, 6.1 Hz, 1H), 2.39 – 2.26 (m, 1H), 2.31 (s, 3H), 2.25 (s, 3H), 2.12 (d, *J* = 17.5 Hz, 1H), 2.05 (dd, *J* = 12.6, 6.2 Hz, 1H), 1.98 (dt, *J* = 11.4, 5.8 Hz, 1H), 1.54 (dd, *J* = 12.5, 9.0 Hz, 1H), 1.37 (dd, *J* = 12.1, 4.5 Hz, 1H), 0.85 (s, 9H), 0.11 (s, 3H), 0.05 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 210.2, 191.7, 172.1, 150.2, 111.3, 77.5, 68.2, 65.6, 54.9, 54.8, 52.1, 51.7, 46.9, 44.5, 38.9, 38.6, 35.4, 31.9, 25.9, 18.0, -4.2, -4.7.

FTIR (NaCl, thin film): 2954, 2857, 1736, 1698, 1438, 1360, 1257, 1208, 1092 cm^{-1}.

HRMS (FAB$^+$, *m/z*): $C_{24}H_{39}NO_6Si$, calc'd for $[M+H]^+$: 466.2625, found 466.2607.

Preparation of lactol 230.



Ketone **228** (5 mg, 0.011 mmol) was added to a flame-dried 2 dram vial, placed under N_2 atmosphere, and taken up in ^{t}amyl alcohol (0.45 mL). KO^{t}Bu (3.6 mg, 0.032 mmol) was then weighed out into a ½ dram vial, sealed with a plastic septum, removed from the glovebox, and placed under N_2. The solid was taken up in ^{t}amyl alcohol (120 μL), and, once dissolved, added to the ketone solution at room temperature. The mixture was stirred at room temperature for 20 min and was then quenched with aqueous 1 M HCl (32 μL, 3.0 equiv). The resulting mixture was then concentrated under reduced pressure and the crude residue purified by silica gel preparatory TLC (10% MeOH/CH_2Cl_2) to afford tentatively assigned enol ether aldol product **230** (1.6 mg, 34% yield). *Note*: After 20 min of reaction time, LC/MS analysis indicated that starting ketone **228** was still present, indicating that the reaction conversion was not complete.

Note: NMR spectra contain traces of CH_2Cl_2 and AcOH.

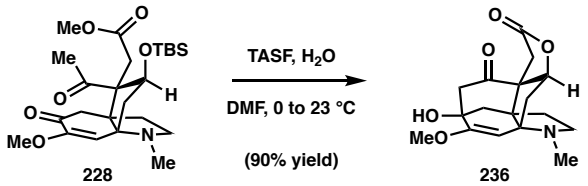
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.91 (s, 1H), 5.28 (d, *J* = 3.7 Hz, 1H), 5.16 (d, *J* = 3.0 Hz, 1H), 4.11 – 3.95 (m, 2H), 3.62 (s, 3H), 2.87 (d, *J* = 16.2 Hz, 1H), 2.84 – 2.75 (m, 1H), 2.64 (d, *J* = 16.1 Hz, 1H), 2.42 (s, 3H), 2.41 – 2.33 (m, 2H), 2.23 – 2.08 (m, 1H), 1.74 (ddd, *J* = 14.1, 7.4, 2.4 Hz, 1H), 1.65 (dd, *J* = 13.1, 10.1 Hz, 1H), 0.88 (s, 9H), 0.08 (s, 2H), 0.05 (s, 3H).

Note: ^{13}C data was taken from HSQC (*) and HMBC (‡) spectra.

^{13}C NMR (101 MHz, $CDCl_3$): δ 189.1‡, 174.8‡, 151.3‡, 143.5‡, 114.6*, 111.5*, 76.1*, 70.0‡, 59.7‡, 55.3‡, 53.9*, 54.9*, 54.3*, 44.2*, 37.8*, 34.0*, 30.2*, 25.7*, -4.9*, -4.3*.

HRMS (MM, *m/z*): $C_{23}H_{35}NO_5Si$, calc'd for $[M+H]^+$: 434.2357, found 434.2362.

Preparation of lactone 236.



Silyl ether **228** (370 mg, 0.79 mmol) was taken up in DMF (15 mL) in a round bottom flask. TASF (657 mg, 2.38 mmol, 3.0 equiv) was weighed into a scintillation vial, sealed with a screw cap, and removed from the glovebox. The solid TASF was taken up in DMF (4.9 mL) under ambient air, after which H_2O (0.14 mL, 7.90 mmol, 10.0 equiv) was added. The reaction flask was cooled to 0 °C and the TASF solution was subsequently added dropwise. After stirring at 0 °C for 5 min, the reaction was warmed to room temperature and stirred overnight. After a total of 41 h, the stir bar was removed and briefly rinsed with CH_2Cl_2. The reaction was transferred to a 200 mL round bottom flask, rinsing with CH_2Cl_2 (5 mL). Celite (20 g) was added so that all DMF had been absorbed, and the vial was carefully placed under high vacuum. The dry-loaded crude residue was first run through a Florisil plug (5 x 7.5 cm, 0–10% MeOH/CH_2Cl_2) to remove any excess DMF. Subsequently, the material was dry-loaded again onto Celite (3 g) and purified via Florisil

flash chromatography (0–10% MeOH/CH_2Cl_2) to afford **236** as a white foam (229 mg, 90% yield).

TLC: R_f 0.45 (10% MeOH in CH_2Cl_2, CAM).

$[\alpha]_D^{25.0}$: +26.5° (c = 1.14, $CHCl_3$).

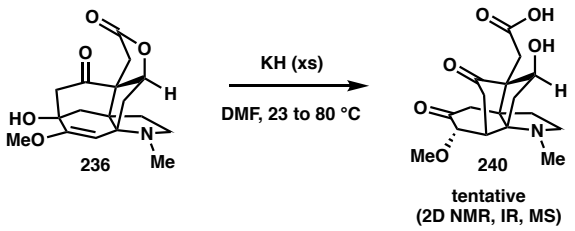
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.18 (dd, *J* = 8.2, 4.0 Hz, 1H), 4.45 (s, 1H), 3.56 (s, 3H), 3.25 (ddd, *J* = 10.1, 9.1, 4.2 Hz, 1H), 3.04 (br, 1H), 2.83 (dd, *J* = 15.8, 3.2 Hz, 1H), 2.66 (d, *J* = 17.9 Hz, 1H), 2.54 (d, *J* = 18.1 Hz, 1H), 2.61 – 2.46 (m, 2H), 2.49 (d, *J* = 15.8 Hz, 1H), 2.25 (s, 3H), 2.13 (dd, *J* = 15.0, 4.0 Hz, 1H), 1.94 (d, *J* = 13.0 Hz, 1H), 1.87 (dd, *J* = 15.0, 8.3 Hz, 1H), 1.76 (ddd, *J* = 13.6, 10.7, 4.3 Hz, 1H), 1.62 (ddd, *J* = 13.6, 9.1, 6.2 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 209.0, 174.5, 157.2, 95.9, 87.1, 74.3, 68.9, 62.1, 55.3, 54.2, 52.7, 51.2, 41.1, 38.9, 35.8, 34.0, 31.3.

FTIR (NaCl, thin film): 3468, 2941, 1775, 1705, 1451, 1184, 1127, 1037, 731 cm^{-1}.

HRMS (ESI, *m/z*): $C_{17}H_{21}NO_5$, calc'd for $[M+H]^+$: 320.1492, found: 320.1478.

Preparation of Michael adduct 240.

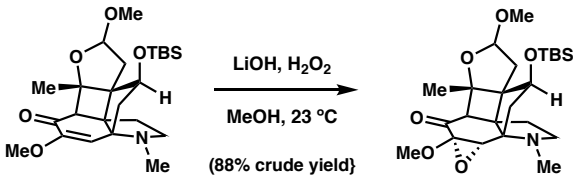


Tertiary alcohol **236** (4 mg, 0.0125 mmol) was added to a flame-dried 1 dram vial containing a stir bar. It was brought into a nitrogen-filled glovebox, where anhydrous KH

(0.8 mg, 0.019 mmol, 1.5 equiv) was added. The solids were dissolved in DMF (0.4 mL), the vial sealed with a Teflon lined cap, sealed with electrical tape, and removed from the glovebox. Conversion of **236** was not observed until additional KH (3 mg, 0.075 mmol, 6.0 equiv) was added in the glovebox and the reaction was heated at 80 °C (aluminum block temperature) for 2 h. The reaction was cooled to room temperature and quenched by the addition of AcOH (5.5 μL, 0.094 mmol, 7.5 equiv), and the residue was concentrated under reduced pressure between 38–40 °C. The crude product was directly analyzed by NMR, which led to the tentative structural assignment of **240**.

^{1}H NMR (400 MHz, CD_3OD): δ 4.67 (dd, *J* = 10.7, 4.1 Hz, 1H), 4.49 (d, *J* = 3.7 Hz, 1H), 3.39 (s, 3H), 3.46 – 3.33 (m, 1H), 2.92 – 2.74 (m, 3H), 2.74 – 2.62 (m, 2H), 2.48 – 2.37 (m, 2H), 2.41 (s, 3H), 2.25 (d, *J* = 16.1 Hz, 1H), 2.14 (d, *J* = 16.3 Hz, 1H), 1.95 – 1.85 (m, 1H), 1.64 (dd, *J* = 14.7, 4.0 Hz, 1H), 1.44 – 1.33 (m, 1H).

Preparation of methoxy-epoxide 248.



223 248

Methoxyenone **223** (763 mg, 1.7 mmol) was taken up in MeOH (34 mL, HPLC grade) in a 200 mL round bottom flask with stir bar. At room temperature, powdered LiOH (325 mg, 13.6 mmol, 8.0 equiv) was added, followed by dropwise addition of H_2O_2 (1.39 mL, 13.6 mmol, 8.0 equiv; 30 wt %). The resulting heterogeneous reaction was stirred vigorously at

room temperature for 30 h, after which it was quenched by the addition of solid sodium thiofulfate (2.95 g, 11.9 mmol, 7.0 equiv), H_2O (10 mL), and saturated aqueous $NaHCO_3$ (30 mL). After stirring at room temperature for 10 min, the layers were separated and the aqueous layer extracted with EtOAc (6 x 20 mL). The combined organic layers were washed with brine (1 x 60 mL), and the brine layer back-extracted with EtOAc (1 x 20 mL). All combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give an orange-beige foam (698 mg, 88% crude yield), which was typically carried on without purification. A small portion was purified for characterization by Florisil flash chromatography (minimal CH_2Cl_2 to load; purified with a gradient of 10–50% EtOAc/hexanes) to afford **248** as a beige foam.

TLC: R_f 0.50 (2:1 hexanes/EtOAc, $KMnO_4$ & CAM).

$[\alpha]_D^{25.0}$: +112.6° (c = 0.46, $CHCl_3$).

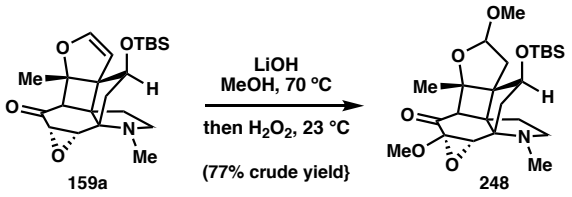
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.08 (d, *J* = 5.2 Hz, 1H), 4.06 (dd, *J* = 10.9, 7.0 Hz, 1H), 3.75 (s, 1H), 3.54 (s, 3H), 3.36 (s, 3H), 3.16 (s, 1H), 2.89 (td, *J* = 8.4, 5.8 Hz, 1H), 2.62 (ddd, *J* = 8.7, 7.5, 5.6 Hz, 1H), 2.47 (s, 3H), 2.35 (ddd, *J* = 13.5, 7.5, 5.8 Hz, 1H), 2.23 (dd, *J* = 13.4, 7.1 Hz, 1H), 2.11 (dd, *J* = 13.9, 5.3 Hz, 1H), 2.01 (d, *J* = 13.8 Hz, 1H), 1.80 (ddd, *J* = 13.8, 8.1, 5.5 Hz, 1H), 1.71 (dd, *J* = 13.4, 10.9 Hz, 1H), 1.35 (s, 3H), 0.85 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 201.0, 106.2, 87.8, 82.2, 75.3, 68.9, 64.9, 62.8, 57.6, 54.9, 54.7, 54.3, 51.5, 38.3, 36.4, 34.9, 32.1, 25.8, 20.4, 17.9, -4.4, -4.9.

FTIR (NaCl, thin film): 2933, 2857, 1714, 1457, 1254, 1100, 1033, 870, 837, 776 cm^{-1}.

HRMS (ESI, *m/z*): $C_{24}H_{39}NO_6Si$, calc'd for $[M+H]^+$: 466.2619, found 466.2641.

One-pot preparation of methoxy-epoxide 248.

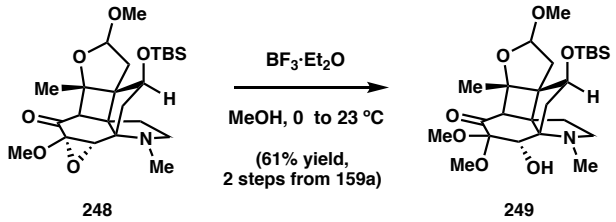


Note: This reaction was set up in duplicate. The batches were quenched and then combined for the extraction step.

A 100 mL two-neck round bottom flask, stir bar, and waterless condenser were flame-dried. Cyclobutane **159a** (700 mg, 1.73 mmol) was added and placed under N_2. MeOH (17.3 mL) was added, followed by powdered LiOH (208 mg, 8.67 mmol, 5.0 equiv). The mixture was heated at 70 °C (oil bath temperature) for 17 h, after which additional powdered LiOH (208 mg, 8.67 mmol, 5.0 equiv) was added, and the reaction stirred at 70 °C for 9 h. The reaction was cooled to room temperature and diluted with MeOH (17.3 mL, HPLC grade). To this mixture, hydrogen peroxide (1.42 mL, 13.87 mmol, 8.0 equiv, 30% in H_2O) was added dropwise at room temperature. The beige-orange mixture became heterogeneous after a few min and was stirred at room temperature for 36 h. The reaction was carefully quenched by the addition of saturated aqueous $NaHCO_3$ (30 mL), solid sodium thiosulfate (2.95 g, 11.9 mmol, 7.0 equiv), and H_2O (10 mL). After stirring vigorously at room temperature for 10 min, the two batches were transferred to a separatory funnel. H_2O (2 x 10 mL) and EtOAc (2 x 10 mL) were used to rinse the reaction flasks and

transfer any residue to the separatory funnel. The layers were separated and the aqueous layer was extracted with EtOAc (6 x 60 mL). The combined organic layers were washed with brine (1 x 150 mL) and the brine layer back-extracted with EtOAc (1 x 50 mL). All combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure to afford **248** as an orange-beige foam (1.24 g, 77 % crude yield), which was typically carried on without purification.

Preparation of ketal 249.



248 249

Crude methoxy-epoxide **248** (1.24 g, 2.66 mmol), under N_2 in a 200 mL round bottom flask with a flame-dried stir bar, was taken up in MeOH (53 mL). It was cooled to 0 °C, and $BF_3{\cdot}Et_2O$ (1.55 mL, 5.86 mmol, ≥46.5% in Et_2O, 2.2 equiv) was added dropwise. The reaction was stirred at 0 °C for 5 min, and was then warmed to room temperature. After 4.5 h, the reaction was quenched by the addition of pH 7 buffer (50 mL). After transferring to a separatory funnel, brine (30 mL) was used to aid in layer separation. The separated aqueous layer was then extracted with EtOAc (5 x 40 mL), and the combined organic layers washed were washed with brine (1 x 80 mL), and the brine layer back-extracted with EtOAc (1 x 30 mL). All combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give a light salmon-colored foam. The crude product was purified by Florisil flash chromatography: 1) equilibrated with 1% Et_3N/

CH_2Cl_2, 2) flushed two column volumes with CH_2Cl_2, and 3) loaded compound in CH_2Cl_2 and utilized a gradient of 2–10% MeOH/CH_2Cl_2 to afford **249** (1.05 g, 61% yield over two steps) as a white foam.

TLC: R_f 0.57 (CH_2Cl_2/10% MeOH, CAM).

$[\alpha]_D^{25.0}$: +86.3° (c = 0.49, $CHCl_3$).

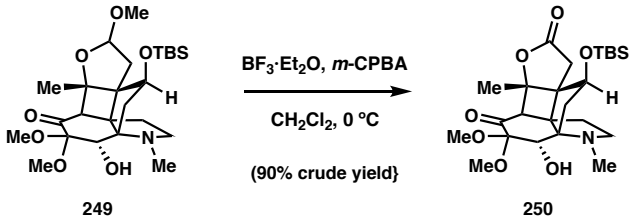
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.09 (d, *J* = 5.6 Hz, 1H), 4.85 (br, 1H), 3.78 (dd, *J* = 11.7, 7.1 Hz, 1H), 3.70 (s, 1H), 3.41 (s, 3H), 3.38 (s, 3H), 3.29 (s, 3H), 3.20 (s, 1H), 3.05 (dd, *J* = 8.8, 6.6 Hz, 1H), 2.71 (dd, *J* = 14.7, 11.7 Hz, 1H), 2.40 – 2.29 (m, 1H), 2.35 (s, 3H), 2.27 – 2.08 (m, 2H), 1.89 (d, *J* = 13.9 Hz, 1H), 1.94 – 1.81 (m, 1H), 1.42 (s, 3H), 0.87 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 201.0, 106.0, 95.7, 88.7, 75.8, 71.4, 70.4, 62.7, 57.8, 55.1, 54.7, 51.4, 49.9, 49.3, 37.5, 35.9, 34.6, 31.4, 25.8, 19.5, 18.0, -4.3, -5.0.

FTIR (NaCl, thin film): 3306, 2932, 2856, 1704, 1449, 1253, 1104, 1033, 838 cm^{-1}.

HRMS (FAB$^+$, *m/z*): $C_{25}H_{43}NO_7Si$, calc'd for $[M+H]^+$: 498.2887, found 498.2886.

Preparation of lactone 250.



Note: This reaction can be set up without particular care for a dry set up or inert atmosphere. However, it is crucial to utilize wet *m-CPBA* (75% here), as a significant drop in yield was observed for 99% *m-CPBA*.

In a round bottom flask with a stir bar, ketal **249** (1.05 g, 2.11 mmol) was taken up in CH_2Cl_2 (32.3 mL). It was cooled to 0 °C and a septum with N_2 inlet added (in case gases develop). $BF_3 \cdot Et_2O$ (1.4 mL, 5.28 mmol, ≥46.5% in Et_2O, 2.5 equiv) was added dropwise, giving a pale red solution, which was stirred for 10 min. In the meantime, *m-CPBA* (511 mg, 2.22 mmol, 1.05 equiv; 75%) was added to a scintillation vial and taken up in CH_2Cl_2 (6 mL). Once dissolved, the *m-CPBA* solution was added to the reaction dropwise at 0 °C. The syringe and vial of *m-CPBA* were rinsed with CH_2Cl_2 (2 x 2 mL), and the solution transferred dropwise to the reaction. The resulting wine-red reaction was stirred at 0 °C for 5 h, and conversion was monitored by LC/MS. The reaction was quenched at 0 °C with 0.1 M sodium thiosulfate (14 mL, 0.6 equiv with respect to oxidant) and saturated aqueous $NaHCO_3$ (80 mL). The mixture was stirred at 0 °C for 10 min until all bubbling had ceased, and was then warmed to room temperature. The mixture was transferred to a separatory funnel and EtOAc (10 mL) and brine (20 mL) were used to assist layer separation. The aqueous layer was then extracted with EtOAc (5 x 40 mL), and the combined organic layers

were washed with saturated aqueous $NaHCO_3$ (4 x 50 mL) and brine (1 x 50 mL). All combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure to afford **250** as a beige foam (919 mg, 90% crude yield), which was carried forward without further purification. For characterization, a sample was purified by Florisil flash chromatography: 1) equilibrated with 1% Et_3N in 20% EtOAc/hexanes, then 2) flushed with two column volumes of 20% EtOAc/hexanes, and 3) loaded the crude and purified with a gradient of 20–100% EtOAc/hexanes) to afford **250** as a white foam.

TLC: R_f 0.45 (3:1 EtOAc/hexanes, CAM).

$[\alpha]_D^{25.0}$: +67.6° (c = 0.58, $CHCl_3$).

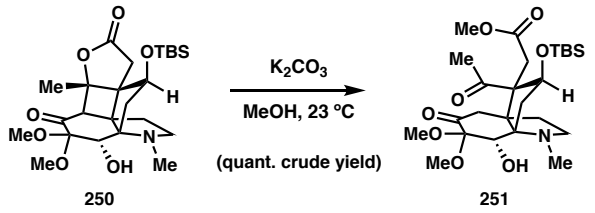
^{1}H NMR (400 MHz, $CDCl_3$): δ 4.98 (br, 1H), 3.75 (dd, *J* = 11.0, 7.8 Hz, 1H), 3.65 (s, 1H), 3.37 (s, 3H), 3.32 (s, 3H), 3.22 – 3.15 (m, 1H), 3.17 (s, 1H), 2.72 (d, *J* = 18.6 Hz, 1H), 2.46 (d, *J* = 18.5 Hz, 1H), 2.36 (s, 3H), 2.36 – 2.20 (m, 2H), 2.27 – 2.12 (m, 2H), 1.83 (d, *J* = 8.3 Hz, 1H), 1.59 (s, 3H), 0.87 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 200.7, 174.2, 96.6, 89.4, 75.7, 72.9, 70.4, 58.0, 55.7, 54.8, 54.1, 50.4, 50.0, 39.3, 34.5, 32.2, 30.4, 25.7, 19.2, 17.9, -4.4, -5.0.

FTIR (NaCl, thin film): 3304, 2952, 2857, 1775, 1710, 1462, 1250, 1123, 958, 837 cm^{-1}.

HRMS (FAB$^+$, *m/z*): $C_{24}H_{39}NO_7Si$, calc'd for $[M+H]^+–H_2$: 480.2418, found 480.2415.

Preparation of ketone 251.



Lactone **250** (919 mg, 1.9 mmol), under N_2, was taken up in MeOH (47.7 mL) in a round bottom flask containing a flame-dried stir bar. At room temperature, solid K_2CO_3 (277 mg, 1.0 mmol, 1.05 equiv) was added and the mixture stirred vigorously, resulting in an orange solution. After 5 h, the reaction was quenched by the addition of pH 7 buffer (70 mL). EtOAc (25 mL) and brine (25 mL) were added, the layers separated, and the aqueous layer extracted with EtOAc (5 x 80 mL). The combined organic layers were washed with brine (1 x 100 mL) and the brine layer back-extracted with EtOAc (1 x 50 mL). All combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give a beige-orange foam (987 mg, quant. crude yield), which was typically carried forward without further purification. For characterization, a sample was purified by Florisil flash chromatography (10–100% EtOAc in hexanes) to afford **251** as a white foam.

TLC: R_f 0.36 (100% EtOAc, CAM).

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25.0}}$**:** –8.7° (c = 0.69, $CHCl_3$).

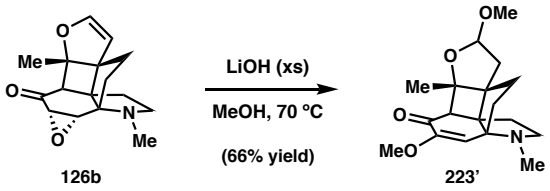
^{1}H NMR (400 MHz, $CDCl_3$): δ 3.89 (s, 1H), 3.71 (s, 3H), 3.66 – 3.63 (m, 1H), 3.61 (s, 3H), 3.45 (s, 3H), 3.28 (d, *J* = 18.6 Hz, 1H), 3.21 – 3.11 (m, 1H), 3.06 (d, *J* = 17.0 Hz, 1H), 2.72 – 2.59 (m, 2H), 2.37 (s, 3H), 2.44 – 2.28 (m, 2H), 2.13 (s, 3H), 2.03 – 1.90 (m, 2H), 1.78 – 1.64 (m, 1H), 0.86 (s, 9H), 0.09 (s, 3H), 0.06 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 208.7, 200.7, 172.3, 94.0, 79.7, 71.8, 70.8, 64.6, 55.5, 55.4, 52.3, 50.7, 50.1, 49.0, 40.7, 38.1, 35.8, 34.8, 31.5, 25.9, 18.1, -4.3, -4.6.

FTIR (NaCl, thin film): 3508, 3286, 2952, 2857, 1734, 1438, 1254, 1061, 915 cm^{-1}.

HRMS (ESI, *m/z*): $C_{25}H_{43}NO_8Si$, calc'd for $[M+H]^+$: 514.2831, found 514.2843.

Preparation of acetal 223'.



A 2 dram vial containing a stir bar was flame-dried. Cyclobutane **126b** (40 mg, 0.15 mmol) was added and placed under N_2. MeOH (1.46 mL) was added, followed by powdered LiOH (17.5 mg, 0.73 mmol, 5.0 equiv). The mixture was heated at 70 °C (aluminum block temperature) for 7 h, after which additional powdered LiOH (17.5 mg, 0.73 mmol, 5.0 equiv) was added and the reaction stirred at 70 °C for 12 h. The reaction was cooled to room temperature and quenched with saturated aqueous NH_4Cl (2 mL). EtOAc (1 mL) and brine (1 mL) were added and the mixture stirred vigorously. The layers were separated and the aqueous layer was extracted with EtOAc (5 x 5 mL). The combined organic layers were washed with brine (1 x 15 mL), and the brine layer back-extracted with EtOAc (1 x 5 mL). All combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by Florisil flash chromatography (0–10% MeOH/CH_2Cl_2) to afford acetal **223'** (30.8 mg, 66% yield) as a pale yellow foam, after azeotroping with pentane. *Note*: The reaction affords **223'** as an inseparable and

inconsequential mixture of diastereomers (3.8:1 dr) at the acetal position. The major isomer was characterized below.

TLC: R_f 0.46 (10% MeOH in CH_2Cl_2, UV & CAM).

$[\alpha]_D^{25.0}$: +37.9° (c = 1.54, $CHCl_3$).

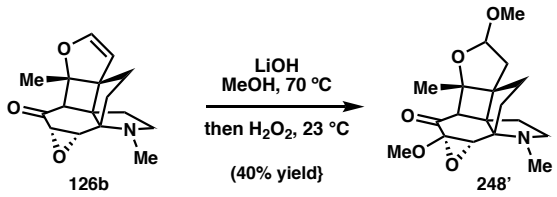
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.99 (s, 1H), 5.08 (d, *J* = 5.5 Hz, 1H), 3.61 (s, 3H), 3.39 (s, 3H), 3.32 (s, 1H), 2.73 (dddd, *J* = 10.4, 6.8, 3.9, 2.8 Hz, 1H), 2.56 – 2.44 (m, 1H), 2.42 (s, 3H), 2.39 – 2.24 (m, 2H), 2.21 (d, *J* = 14.2 Hz, 1H), 1.99 (dd, *J* = 14.3, 5.5 Hz, 1H), 1.89 – 1.65 (m, 2H), 1.64 – 1.48 (m, 2H), 1.17 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 190.28, 151.64, 116.76, 106.67, 88.43, 73.37, 61.42, 59.09, 55.03, 54.99, 54.69, 53.75, 38.67, 37.67, 34.70, 32.56, 30.05, 17.70.

FTIR (NaCl, thin film): 2933, 2782, 1676, 1613, 1449, 1376, 1157, 1097, 1031 cm^{-1}.

HRMS (ESI, *m/z*): $C_{18}H_{25}NO_4$, calc'd for $[M+H]^+$: 320.1856, found 320.1860.

One-pot preparation of ketal 248'.



A 2 dram vial containing a stir bar was flame-dried. Cyclobutane **126b** (40 mg, 0.15 mmol) was added and placed under N_2. MeOH (1.46 mL) was added, followed by powdered LiOH (17.5 mg, 0.73 mmol, 5.0 equiv). The mixture was heated at 70 °C (aluminum block temperature) for 7 h, after which additional powdered LiOH (17.5 mg, 0.73 mmol, 5.0

equiv) was added and the reaction stirred at 70 °C for 12 h. The reaction was cooled to room temperature and diluted with MeOH (1.46 mL, HPLC grade). To this mixture, hydrogen peroxide (0.12 mL, 1.17 mmol, 8.0 equiv, 30% in H_2O) was added dropwise at room temperature. The mixture became heterogeneous after a few min and was stirred at room temperature for 24 h. The reaction was carefully quenched by the addition of saturated aqueous $NaHCO_3$ (2 mL), sodium thiosulfate (254 mg in 1 mL H_2O, 1.02 mmol, 7.0 equiv). After stirring vigorously at room temperature for 10 min, the layers were separated and the aqueous layer was extracted with EtOAc (5 x 10 mL). The combined organic layers were washed with brine (1 x 10 mL) and the brine layer back-extracted with EtOAc (2 x 5 mL). All combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by Florisil flash chromatography (0–10% MeOH/CH_2Cl_2) to afford methoxy-epoxide **248'** (19.8 mg, 40% yield) as a clear semi-solid, after azeotroping with pentane.

TLC: R_f 0.42 (5% MeOH in CH_2Cl_2, UV & $KMnO_4$).

$[\alpha]_D^{25.0}$: +124.9° (c = 0.99, $CHCl_3$).

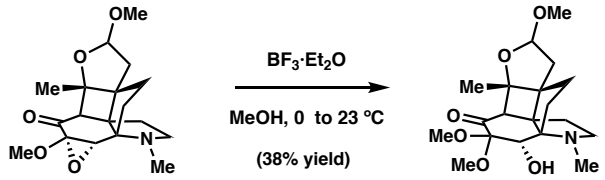
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.03 (dd, *J* = 5.4, 0.5 Hz, 1H), 3.79 (s, 1H), 3.53 (s, 3H), 3.36 (s, 3H), 3.14 (s, 1H), 2.92 (td, *J* = 8.5, 6.0 Hz, 1H), 2.78 (ddd, *J* = 8.6, 7.7, 5.2 Hz, 1H), 2.48 (s, 3H), 2.52 – 2.38 (m, 1H), 2.15 (d, *J* = 14.2 Hz, 1H), 2.01 (ddd, *J* = 13.9, 5.5, 2.7 Hz, 1H), 1.90 (dd, *J* = 14.3, 5.4 Hz, 1H), 1.87 – 1.71 (m, 3H), 1.48 (ddd, *J* = 13.9, 11.6, 8.6 Hz, 1H), 1.16 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 202.0, 106.5, 87.6, 82.6, 72.9, 65.2, 60.8, 57.7, 55.1, 54.9 (two overlapping peaks, HSQC & HMBC), 54.6, 38.3, 34.9, 32.0, 31.2, 31.0, 18.3.

FTIR (NaCl, thin film): 2934, 2835, 1712, 1450, 1183, 1096, 1030, 977 cm^{-1}.

HRMS (ESI, *m/z*): $C_{18}H_{25}NO_5$, calc'd for $[M+H]^+$: 336.1805, found 336.1798.

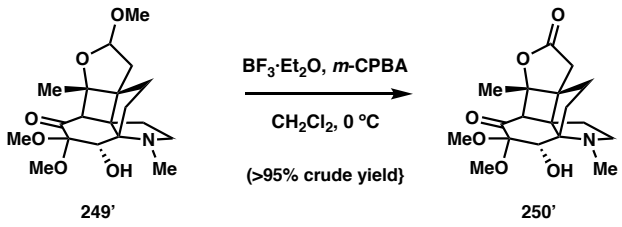
Preparation of ketal 249'.



248' 249'

A 2 dram vial containing a stir bar was flame-dried. Methoxy-epoxide **248'** (19.8 mg, 0.06 mmol) was added, placed under N_2 atmosphere, and taken up in MeOH (1.2 mL). It was cooled to 0 °C, and $BF_3{\cdot}Et_2O$ (34.5 μL, 0.13 mmol, ≥46.5% in Et_2O, 2.2 equiv) was added dropwise. The reaction was stirred at 0 °C for 5 min, and was then warmed to room temperature. After 2.5 h, the reaction was quenched by the addition of pH 7 buffer (5 mL). After transferring to a separatory funnel, brine (5 mL) was used to aid in layer separation. The separated aqueous layer was then extracted with 10% IPA/$CHCl_3$ (6 x 5 mL), and the combined organic layers washed were washed with brine (1 x 5 mL), and the brine layer back-extracted with 10% IPA/$CHCl_3$ (2 x 5 mL). All combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by Florisil flash chromatography (0–10% MeOH/CH_2Cl_2) to afford **249'** (8.3 mg, 38% yield) as an off-white foam.

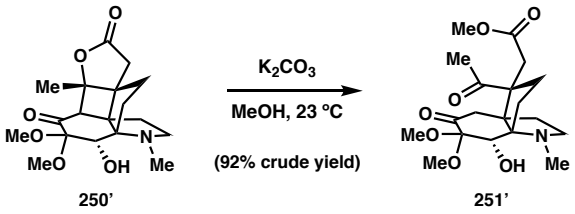
Preparation of lactone 250'.



Ketal **249'** (8.3 mg, 0.023 mmol) was taken up in CH_2Cl_2 (0.2 mL). It was cooled to 0 °C and a septum with N_2 inlet added. $BF_3{\cdot}Et_2O$ (15 μL, 0.056 mmol, ≥46.5% in Et_2O, 2.5 equiv) was added dropwise and the mixture was stirred for 10 min. In the meantime, *m-CPBA* (5.4 mg, 0.024 mmol, 1.05 equiv; 75%) was added to a 1 dram vial and taken up in CH_2Cl_2 (0.15 mL). Once dissolved, the *m-CPBA* solution was added to the reaction dropwise at 0 °C. The syringe and vial of *m-CPBA* were rinsed with CH_2Cl_2 (0.1 mL), and the solution transferred dropwise to the reaction. The resulting mixture was stirred at 0 °C for 11 h, and conversion was monitored by LC/MS. The reaction was quenched at 0 °C with 0.1 M sodium thiosulfate (0.12 mL, 0.5 equiv with respect to oxidant) and saturated aqueous $NaHCO_3$ (5 mL). The mixture was stirred at 0 °C for 10 and was warmed to room temperature. The aqueous layer was then extracted with 10% IPA/$CHCl_3$ (6 x 5 mL), and the combined organic layers were washed with saturated aqueous $NaHCO_3$ (4 x 5 mL) and brine (1 x 5 mL). The combined aqueous extracts were back-extracted with 10% IPA/$CHCl_3$ (1 x 5 mL). All combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure to afford **250'** as a beige foam (8 mg, >95% crude yield), which was carried forward without further purification.

^{1}H NMR (600 MHz, $CDCl_3$): δ 3.65 (s, 1H), 3.40 (s, 3H), 3.29 (s, 3H), 3.18 (dd, *J* = 9.0, 6.8 Hz, 1H), 3.16 (s, 1H), 2.62 (d, *J* = 18.8 Hz, 1H), 2.52 (d, *J* = 18.8 Hz, 1H), 2.38 (s, 3H), 2.35 – 2.28 (m, 1H), 2.22 (td, *J* = 12.7, 6.8 Hz, 1H), 2.16 (ddd, *J* = 15.0, 7.8, 3.0 Hz, 1H), 2.10 (ddd, *J* = 14.1, 7.5, 3.0 Hz, 1H), 1.93 (dd, *J* = 13.0, 4.8 Hz, 1H), 1.74 (ddd, *J* = 15.0, 11.3, 7.5 Hz, 1H), 1.50 – 1.43 (m, 1H), 1.42 (s, 3H).

Preparation of ketone 251'.

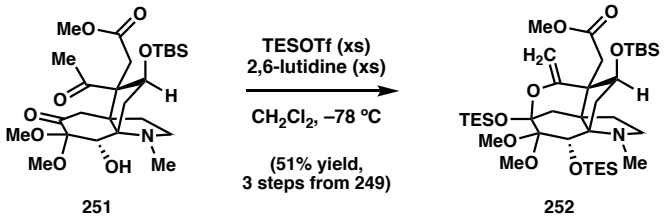


Crude lactone **250'** (8 mg, 0.023 mmol theoretical), under N_2, was taken up in MeOH (0.75 mL) in flame-dried 2 dram vial containing stir bar. At room temperature, solid K_2CO_3 (3.3 mg, 0.024 mmol, 1.05 equiv) was added and the mixture stirred vigorously for 50 min. The reaction was quenched by the addition of pH 7 buffer (5 mL). The mixture was transferred to a separatory funnel, using 10% IPA/$CHCl_3$ (10 mL) and brine (10 mL) to help the transfer. The layers were separated and the aqueous layer extracted with 10% IPA/$CHCl_3$ (6 x 5 mL). The combined organic layers were washed with brine (1 x 5 mL) and the brine layer back-extracted with 10% IPA/$CHCl_3$ (1 x 2 mL). All combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure to afford **251'** as a foam (8 mg, 92% crude yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.17 (s, 1H), 3.63 (s, 3H), 3.51 – 3.42 (m, 1H), 3.35 (s, 3H), 3.24 (s, 3H), 3.12 – 3.07 (m, 1H), 3.04 (dd, *J* = 16.5, 2.0 Hz, 1H), 2.86 (q, *J* = 8.0 Hz, 1H), 2.71 – 2.60 (m, 1H), 2.55 (d, *J* = 13.9 Hz, 1H), 2.42 (s, 3H), 2.22 (s, 3H), 2.19 (d, *J* = 13.9 Hz, 1H), 2.22 – 2.08 (m, 2H), 2.00 – 1.75 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 211.1, 205.2, 173.0, 99.3, 75.4, 74.2, 63.8, 62.1, 55.3, 51.9, 51.2, 48.7, 44.4, 39.1, 33.0, 32.9, 31.7, 30.6, 29.3.

Preparation of silyl enol ether 252.



251 252

Ketone **251** (980 mg, 1.9 mmol), under N_2, was taken up in CH_2Cl_2 (47.7 mL) in a round bottom flask containing a flame-dried stir bar. 2,6-Lutidine (2.7 mL, 22.9 mmol, 12.0 equiv) was added, and the mixture was cooled to –78 °C. TESOTf (3.5 mL, 15.3 mmol, 8.0 equiv) was added dropwise, and the mixture stirred at –78 °C for 5 h. The reaction was quenched at –78 °C by the addition of saturated aqueous $NaHCO_3$ (100 mL), and the mixture was warmed to room temperature. EtOAc (50 mL) was added and the layers separated. The aqueous layer was extracted with EtOAc (3 x 40 mL), the combined organic layers were washed with brine (2 x 100 mL), and the brine layer was back-extracted with EtOAc (1 x 40 mL). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure and dried under high vacuum overnight to remove excess silanol (~90 mTorr). The crude residue was dry-loaded onto Celite (4.6 g) and

purified by Florisil flash chromatography: 1) equilibrated with 1% Et_3N/hexanes, 2) flushed with two column volumes of hexanes, and 3) utilized a gradient of 0–20% EtOAc/hexanes to afford silyl enol ether **252** (800 mg, 57%, 51% over 3 steps from ketal **249**) as a white foam (after azeotroping with pentane). *Note*: It is crucial to dry this intermediate under high vacuum overnight in order to remove any residual silanol and have an accurate yield. Adding any excess NBS in the next step will cause rapid overoxidation on the pyrrolidine ring.

TLC: R_f 0.52 (4:1 hexanes/EtOAc, CAM).

$[\alpha]_D^{25.0}$: +70.4° (c = 0.53, $CHCl_3$).

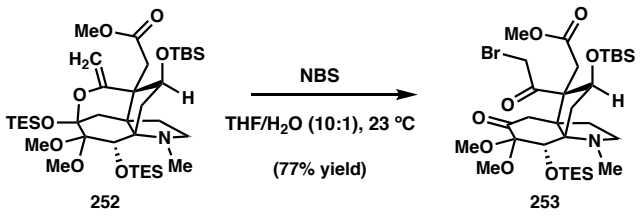
^{1}H NMR (400 MHz, $CDCl_3$): δ 4.65 (d, *J* = 1.2 Hz, 1H), 4.25 (d, *J* = 1.2 Hz, 1H), 3.74 (s, 1H), 3.63 (s, 3H), 3.42 (s, 3H), 3.39 (dd, *J* = 11.9, 6.8 Hz, 1H), 3.28 (s, 3H), 2.96 (ddd, *J* = 8.9, 7.2, 1.6 Hz, 1H), 2.74 (d, *J* = 16.6 Hz, 1H), 2.64 – 2.50 (m, 1H), 2.42 (d, *J* = 13.2 Hz, 1H), 2.37 (d, *J* = 16.7 Hz, 1H), 2.33 (d, *J* = 13.1 Hz, 1H), 2.31 – 2.20 (m, 1H), 2.24 (s, 3H), 2.05 (ddd, *J* = 13.2, 5.8, 1.7 Hz, 1H), 1.77 (dd, *J* = 13.1, 6.7 Hz, 1H), 1.71 – 1.57 (m, 1H), 1.02 – 0.90 (m, 18H), 0.86 (s, 9H), 0.71 – 0.54 (m, 12H), 0.03 (s, 3H), 0.02 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 171.93, 155.82, 101.75, 100.54, 98.68, 77.34 (HSQC), 76.06, 71.87, 58.01, 55.88, 51.60, 51.48, 51.46, 49.81, 39.22, 36.81, 36.04, 34.95, 34.61, 26.00, 18.18, 7.53, 7.20, 6.54, 5.62, -3.76, -4.57.

FTIR (NaCl, thin film): 2952, 2877, 1744, 1461, 1239, 1140, 1078, 1006, 838 cm^{-1}.

HRMS (ESI, *m/z*): $C_{37}H_{71}NO_8Si_3$, calc'd for $[M+H]^+$: 742.4560, found 742.4576.

Preparation of α-bromoketone 253.



Note: Bromide **253** is somewhat light- and acid-sensitive. The reaction is performed and purified in the dark, without the use of a fumehood light. Aluminum foil is used to cover the flask during drying under high vacuum, as well as concentration on the rotary evaporator.

Silyl enol ether **252** (800 mg, 1.08 mmol) was taken up in THF (36 mL) under air. A syringe with H_2O (3.3 mL) was prepared and set aside. Recrystallized NBS (191.8 mg, 1.08 mmol, 1.0 equiv) was weighed out onto a weigh paper. Under good stirring (at least 650 rpm), at room temperature and under air, the H_2O was added in one portion, immediately followed by gradual, portion-wise addition of the solid NBS (~20 portions using a small spatula, VWR 82027-524) (*Note:* If NBS is added too quickly, the reaction will briefly turn yellow and then again colorless. This is an indication of overoxidation on the pyrrolidine ring and should be avoided by careful portion-wise addition of the NBS). Once the addition was complete, the reaction was stirred at room temperature for 2 min, and the starting material **252** was consumed by TLC analysis. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (100 mL), and the mixture was stirred vigorously. The mixture was transferred to a separatory funnel with the help of EtOAc (30 mL), and the layers separated. The aqueous layer was extracted with EtOAc (5 x 40 mL), and the combined

organic layers were washed with brine (50 mL). The brine layer was back-extracted with EtOAc (1 x 25 mL), and all combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give a clear oil. The residue was loaded onto Celite (2.6 g), and purified via Florisil flash chromatography: 1) equilibrated with hexanes and 2) utilized a gradient of 10–40% EtOAc/hexanes to afford **253** as a white foam (590 mg, 77% yield), after azeotroping with pentane.

TLC: R_f 0.26 (4:1 hexanes/EtOAc, CAM).

$[\alpha]_D^{25.0}$: –38.8° (c = 0.75, $CHCl_3$).

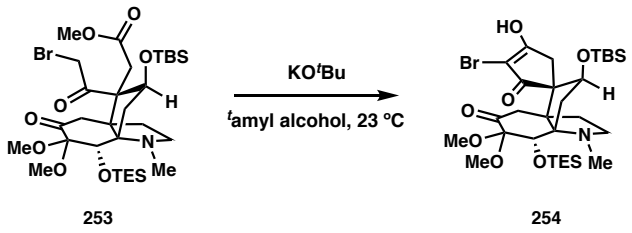
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.22 (br, 1H), 4.51 (d, *J* = 14.9 Hz, 1H), 4.44 (d, *J* = 14.9 Hz, 1H), 3.88 (dd, *J* = 11.3, 6.6 Hz, 1H), 3.69 (s, 3H), 3.57 (s, 3H), 3.36 – 3.22 (m, 2H), 3.19 (s, 3H), 2.84 (d, *J* = 18.0 Hz, 1H), 2.77 (ddd, *J* = 9.7, 7.1, 3.0 Hz, 1H), 2.50 (s, 3H), 2.25 – 2.11 (m, 2H), 1.85 (d, *J* = 13.1 Hz, 1H), 1.80 (ddd, *J* = 14.0, 6.1, 2.7 Hz, 1H), 1.64 – 1.47 (m, 2H), 1.02 (t, *J* = 7.9 Hz, 9H), 0.90 (s, 9H), 0.82 – 0.66 (m, 6H), 0.11 (s, 3H), 0.08 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 204.1, 201.5, 171.6, 96.8, 82.2, 79.9, 70.8, 65.1, 56.3, 53.9, 53.2, 52.5, 50.4, 44.2, 40.2, 38.6, 37.4, 36.0, 34.8, 25.9, 18.1, 7.2, 5.4, -4.4, -4.7.

FTIR (NaCl, thin film): 2953, 2879, 1729, 1438, 1362, 1206, 1124, 1096, 838 cm^{-1}.

HRMS (FAB$^+$, *m/z*): $C_{31}H_{56}BrNO_8Si_2$, calc'd for $[M+H]^+–H_2$: 706.2629, found 706.2609.

Preparation of spirocyclic acid 254.



253 254

A flame-dried stir bar was added to α-bromoketone **253** (421 mg, 0.60 mmol) in a round bottom flask, and was placed under N_2 atmosphere. The solid was taken up in anhydrous ^{t}amyl alcohol (8 mL). KO^{t}Bu (200.5 mg, 1.79 mmol, 3.0 equiv) was weighed out into a scintillation vial in a nitrogen-filled glovebox; the vial was sealed and removed from the glovebox and kept under N_2 in the fumehood. Subsequently, the base was taken up in *tert*-amyl alcohol (5 mL) and briefly sonicated to speed up dissolving. At room temperature and under good stirring (700 rpm), the base mixture was added dropwise to the flask containing **253**. The faintly yellow solution gradually turned deep yellow and then orange-brown. As the reaction progressed, a heterogeneous mixture developed, which was stirred for a total of 90 min. AcOH (0.1 mL, 1.79 mmol, 3.0 equiv) was added to quench, rapidly returning the yellow color. The stir bar was removed, rinsed with MeOH (1 mL), and the residue concentrated under reduced pressure at 38 °C, and a pale yellow solid was obtained after azeotroping with heptane (1 x 30 mL, HPLC grade). The crude was typically taken forward without purification. For characterization purposes, acid **254** was dry-loaded onto Celite and purified by Florisil flash chromatography (equilibrated with CH_2Cl_2 and utilized a gradient of 0–10% MeOH/CH_2Cl_2, whereby a rapid increase of MeOH and flushing with 10% MeOH/ CH_2Cl_2 was necessary to elute all of **254**) to afford vinylogous acid **254** as a

beige solid. *Note*: Due to the slight light sensitivity of product **254**, the same precautions were taken as in the synthesis, purification, and handling of bromide **253**.

TLC: R_f 0.25 (CH_2Cl_2/10% MeOH, UV & CAM).

$[\alpha]_D^{25.0}$: –20.8° (c = 0.45, $CHCl_3$).

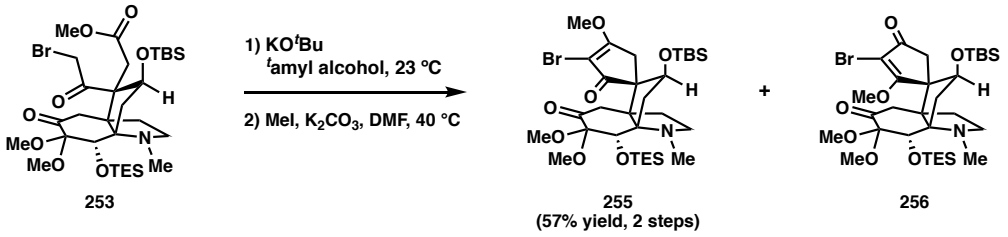
^{1}H NMR (400 MHz, CD_3CN): δ 5.70 (s, 1H), 3.98 (dd, *J* = 10.5, 7.8 Hz, 1H), 3.53 (s, 3H), 3.09 (s, 3H), 2.68 (d, *J* = 12.0 Hz, 1H), 2.68 – 2.58 (m, 1H), 2.45 (s, 3H), 2.36 (d, *J* = 16.1 Hz, 1H), 2.29 – 2.04 (m, 4H), 1.77 (d, *J* = 12.0 Hz, 1H), 1.76 – 1.66 (m, 1H), 1.47 (ddd, *J* = 13.5, 10.1, 8.1 Hz, 1H), 1.02 (t, *J* = 7.9 Hz, 9H), 0.81 (s, 9H), 0.87 – 0.74 (m, 6H), 0.02 (s, 3H), -0.01 (s, 3H).

^{13}C NMR (101 MHz, CD_3CN): δ 203.6, 194.5, 191.8, 99.4, 92.8, 82.6, 79.9, 71.2 (HMBC, quat. carbon), 64.7, 55.9, 54.9, 53.5, 50.9, 43.8, 43.4, 38.6, 35.8, 34.5, 26.1, 18.6, 7.4, 6.0, -4.1, -4.8.

FTIR (NaCl, thin film): 3388, 2952, 2879, 1726, 1552, 1250, 1120, 1006, 830 cm^{-1}.

HRMS (ESI, *m/z*): $C_{30}H_{52}BrNO_7Si_2$, calc'd for $[M+H]^+$: 674.2538, found 674.2547.

Preparation of vinylogous ester 255.



For preparation of vinylogous acid (Step 1), see procedure immediately above. Step 2: A flame-dried 150 mL pressure flask containing a stir bar was charged with K_2CO_3 (330 mg, 2.38 mmol, 4.0 equiv) and placed under nitrogen atmosphere. Crude spirocyclic acid **254** (0.60 mmol theoretical), under N_2, was taken up in DMF (20 mL) and transferred to the pressure reaction flask. The residue was further rinsed with DMF (3 x 9 mL) and transferred to the reaction flask. Subsequently, MeI (0.15 mL, 2.38 mmol, 4.0 equiv) was added. The pressure flask was then tightly sealed with a screw cap, and the reaction heated at 40 °C (oil bath), while shielded from light with aluminum foil. A blast shield was added as a precautionary measure. After 15 h, small quantities of the acid **254** were observed via LC/MS, so at room temperature K_2CO_3 (165 mg, 1.19 mmol, 2.0 equiv) was added, followed by MeI (75 μL, 1.19 mmol, 2.0 equiv). The mixture was sealed and heated at 40 °C for another 3 h, upon which all acid **254** had been consumed. The mixture was cooled to room temperature and quenched with saturated aqueous NH_4Cl (50 mL). EtOAc (20 mL) was added and the mixture stirred vigorously for 1 h (1000 rpm). The mixture was transferred to a separatory funnel, using H_2O (20 mL) and EtOAc (10 mL) to help the transfer. The layers were separated, and the aqueous layer extracted with EtOAc (4 x 35 mL). The combined organic layers were washed with brine (3 x 50 mL), and the combined

brine layers were back-extracted with EtOAc (1 x 35 mL). All combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give an orange-brown oil. The residue was dried under high vacuum overnight to remove residual DMF, resulting in an orange-brown solid. The crude residue was dry-loaded onto Celite (3.0 g) and purified by Florisil flash chromatography (25 g): 1) equilibrated with 1% Et_3N/hexanes, 2) flushed with two column volumes of hexanes, and 3) purified with a slow gradient (0–10% acetone/hexanes), followed by a fast gradient (15–30% acetone/hexanes) to afford **255** as a bright yellow foam (232.7 mg, 57% yield). On large scale, sufficient quantities of minor isomer **256** were formed in the reaction; however, it eluted in the first band, which also contained traces of the desired debromination product **257** and an unidentified side product. For characterization purposes, this first band was repurified by preparatory TLC (equilibrated plate with 1% Et_3N/hexanes and utilized a gradient of 15% acetone in PhMe/hexanes 1:1) to afford minor isomer **256** as a clear oil. *Note*: Minor isomer **256** is particularly sensitive (to purification, light, and in solution away from light). This was noted by formation of a pink baseline upon purification trials, even on neutralized stationary phases. The sensitivity was also noted by discoloration over time when stored as a foam in the freezer. Storage in PhH at –20 °C, away from light, is recommended.

Desired isomer **255**:

TLC: R_f 0.42 and 0.13 (10% MeOH/CH_2Cl_2 and 20% acetone/hexanes, UV & CAM).

$\boldsymbol{[\alpha]_D^{25.0}}$**:** –56.0° (c = 0.58, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.33 (s, 1H), 4.09 (s, 3H), 4.13 – 3.95 (m, 1H), 3.61 (s, 3H), 3.11 (s, 3H), 2.80 – 2.69 (m, 3H), 2.58 (d, *J* = 17.0 Hz, 1H), 2.48 (s, 3H), 2.21 – 2.02 (m, 3H), 1.75 (d, *J* = 11.6 Hz, 1H), 1.71 (ddd, *J* = 13.2, 9.3, 7.7 Hz, 1H), 1.58 (ddd, *J* = 13.4, 7.2, 2.3 Hz, 1H), 1.02 (t, *J* = 7.8 Hz, 9H), 0.87 – 0.75 (m, 6H), 0.81 (s, 9H), 0.03 (s, 3H), 0.01 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 202.0, 198.0, 181.1, 98.6, 97.9, 82.2, 79.7, 71.5, 65.3, 57.9, 54.5, 53.9, 53.3, 50.4, 42.6, 37.6, 37.0, 35.6, 33.3, 25.6, 17.8, 7.2, 5.4, -4.2, -5.2.

FTIR (NaCl, thin film): 2951, 2782, 1732, 1620, 1461, 1349, 1122, 1056, 831 cm^{-1}.

HRMS (ESI, *m/z*): $C_{31}H_{54}BrNO_7Si_2$, calc'd for $[M+H]^+$: 688.2695, found 688.2714.

Minor isomer **256**:

TLC: R_f 0.28 (20% acetone/hexanes, UV & CAM);

R_f 0.60 (15% acetone in hexanes/PhMe 1:1, UV & CAM).

$[\alpha]_D^{25.0}$: +22.8° (c = 0.1, PhH). *Note*: The optical rotation is opposite sign to that of **255**.

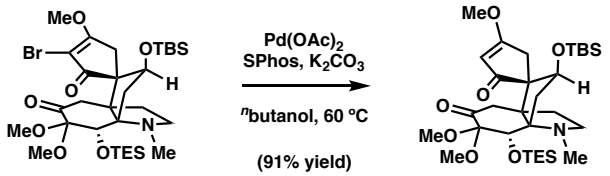
^{1}H NMR (400 MHz, C_6D_6): δ 4.61 (s, 1H), 3.90 (s, 3H), 3.86 (dd, *J* = 10.8, 7.8 Hz, 1H), 3.69 (s, 3H), 3.23 (s, 3H), 2.51 (s, 3H), 2.55 – 2.45 (m, 1H), 2.42 (d, *J* = 12.6 Hz, 1H), 2.34 (dd, *J* = 13.6, 7.8 Hz, 1H), 2.19 (d, *J* = 6.6 Hz, 2H), 1.96 – 1.82 (m, 2H), 1.70 (d, *J* = 12.6 Hz, 1H), 1.35 (ddd, *J* = 13.5, 9.1, 7.5 Hz, 1H), 1.23 – 1.14 (m, 1H), 1.10 (t, *J* = 7.9 Hz, 9H), 0.88 (s, 9H), 0.87 – 0.65 (m, 6H), -0.01 (s, 3H), -0.04 (s, 3H).

^{13}C NMR (101 MHz, C_6D_6): δ 200.7, 194.1, 181.3, 99.7, 98.8, 83.7, 79.4, 71.4, 64.6, 59.8, 55.8, 54.1, 53.9, 50.0, 43.8, 43.2, 38.3, 36.8, 36.6, 25.7, 17.9, 7.3, 5.6, -4.5, -5.2.

FTIR (NaCl, thin film): 2951, 2878, 1721, 1599, 1455, 1260, 1128, 1006 cm^{-1}.

HRMS (ESI, *m/z*): $C_{31}H_{54}BrNO_7Si_2$, calc'd for $[M+H]^+$: 688.2695, found 688.2701.

Preparation of spirocyclic cyclopentenone 257.



255 **257**

A 50 mL round bottom flask and stir bar were flame-dried and brought into a nitrogen-filled glovebox. $Pd(OAc)_2$ (15.2 mg, 0.068 mmol, 20 mol %), SPhos (55.5 mg, 0.135 mmol, 40 mol %), and K_2CO_3 (70.0 mg, 0.51 mmol, 1.5 equiv) were added, and the capped flask was removed from the glovebox. Under air, vinylogous ester **255** (232.7 mg, 0.34 mmol) was added, followed by *n*butanol (11.3 mL, ACS grade). The flask was sealed with a rubber septum and electrical tape, and the mixture was sparged with N_2 for 15 min, after which it was heated at 60 °C (oil bath) for 90 min, at which point LC/MS analysis showed consumption of the vinyl bromide. The reaction was cooled to room temperature and quenched with saturated aqueous $NaHCO_3$ (30 mL) and stirred vigorously for 10 min. The mixture was transferred to a separatory funnel, utilizing brine (20 mL) and CH_2Cl_2 (20 mL) to rinse the flask. The aqueous layer was then extracted with CH_2Cl_2 (4 x 20 mL) and the combined organic layers washed with brine (1 x 20 mL). The brine layer was back-extracted with CH_2Cl_2 (1 x 10 mL) and all combined organic layers dried with Na_2SO_4, filtered, and concentrated under reduced pressure at no more than 37 °C. The residual *n*butanol was removed under high vacuum (~90 mTorr) overnight to give a red-brown crude (*Note:* This reaction may also be worked up by filtering through a pad of Celite with

hexanes/acetone (2:1) and concentration of the filtrate at 38–41 °C. However, in these cases, reduced yields (70–80%) were observed). The crude residue was dry-loaded onto Celite (1.0 g) and purified by Florisil flash chromatography: 1) equilibrated with 1% Et_3N/hexanes, 2) flushed with two column volumes of hexanes, and 3) purified with 0–20% acetone/hexanes to afford **257** as a pale yellow foam (187 mg, 91% yield) after azeotroping with pentane.

TLC: R_f 0.46 (hexanes/20% acetone, UV & $KMnO_4$).

$[\alpha]_D^{25.0}$: –65.7° (c = 0.69, $CHCl_3$).

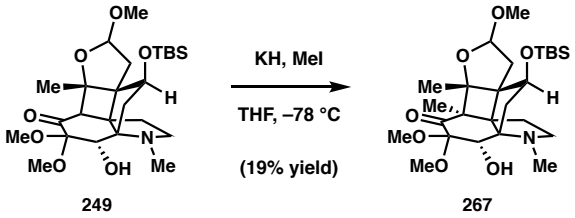
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.39 (s, 1H), 5.21 (s, 1H), 4.02 (t, *J* = 9.2 Hz, 1H), 3.77 (s, 3H), 3.61 (s, 3H), 3.12 (s, 3H), 2.79 – 2.72 (m, 1H), 2.74 (d, *J* = 11.7 Hz, 1H), 2.67 (dd, *J* = 17.3, 1.4 Hz, 1H), 2.46 (s, 3H), 2.50 – 2.39 (m, 1H), 2.17 – 2.10 (m, 1H), 2.08 (d, *J* = 9.2 Hz, 2H), 1.78 (d, *J* = 11.6 Hz, 1H), 1.70 (ddd, *J* = 13.3, 9.9, 7.9 Hz, 1H), 1.54 (ddd, *J* = 13.4, 7.1, 1.8 Hz, 1H), 1.03 (t, *J* = 7.9 Hz, 9H), 0.90 – 0.71 (m, 6H), 0.81 (s, 9H), 0.03 (s, 3H), -0.00 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 205.5, 202.2, 187.7, 106.0, 98.2, 82.1, 79.5, 71.5, 66.4, 58.4, 54.5, 54.1, 53.3, 50.4, 42.7, 38.9, 37.7, 35.8, 32.7, 25.7, 18.0, 7.2, 5.5, -4.2, -5.2.

FTIR (NaCl, thin film): 2950, 2857, 1734, 1693, 1611, 1460, 1361, 1074, 834 cm^{-1}.

HRMS (ESI, *m/z*): $C_{31}H_{55}NO_7Si_2$, calc'd for $[M+H]^+$: 610.3590, found 610.3564.

Preparation of methylated cyclobutane 267.



249 267

In a nitrogen-filled glovebox, anhydrous potassium hydride (13.0 mg, 0.32 mmol, 8.0 equiv) was added to a flame-dried 1 dram vial containing a stir bar. The vial was sealed with a plastic septum, sealed with electrical tape, and removed from the glovebox. The vial was put under an atmosphere of N_2, THF (0.1 mL) was added, and the mixture cooled to 0 °C. Bis-neopentyl alcohol **249** (20 mg, 0.040 mmol), under N_2, was taken up in THF (0.4 mL) and transferred to the reaction vial containing the base at 0 °C. The vial containing the alcohol was rinsed with THF (0.1 mL) and transferred to the reaction vial. The mixture was stirred at 0 °C for 30 min, after which it was cooled to –78 °C. MeI (7.5 mL, 0.12 mmol, 3.0 equiv) was added, and the reaction stirred at –78 °C for 2 h. The reaction was quenched with saturated aqueous NH_4Cl (3 mL), and transferred to a separatory funnel, using H_2O (2 mL) and EtOAc (5 mL) to aid the transfer. The layers were separated and the aqueous layer was extracted with EtOAc (5 x 3 mL). The combined organic layers washed with brine (1 x 5 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give a pale orange oil. The crude residue was purified by Florisil flash chromatography (5–50% EtOAc/hexanes) to afford **267** (4 mg, 19% yield) as a pale yellow oil.

TLC: R_f 0.44 (1:1 EtOAc/hexanes, CAM).

$\boldsymbol{[\alpha]_D^{25.0}}$**:** +104.4° (c = 0.20, $CHCl_3$).

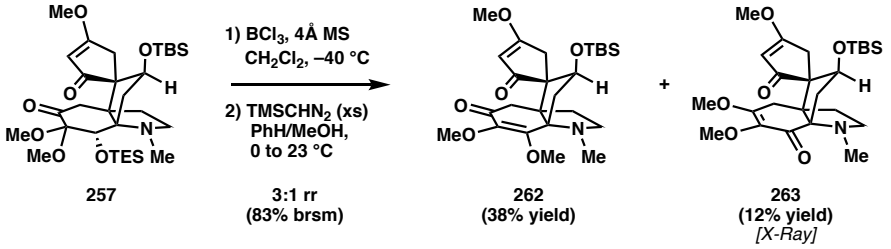
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.10 (dd, *J* = 6.7, 1.2 Hz, 1H), 4.43 (br, 1H), 3.80 – 3.59 (m, 2H), 3.43 (s, 3H), 3.37 (s, 3H), 3.35 (s, 3H), 3.06 (dd, *J* = 8.7, 6.3 Hz, 1H), 2.77 (dd, *J* = 14.8, 11.9 Hz, 1H), 2.33 (s, 3H), 2.26 (dd, *J* = 14.5, 6.8 Hz, 1H), 2.19 – 2.03 (m, 2H), 2.08 – 1.98 (m, 1H), 1.99 – 1.85 (m, 1H), 1.87 (dd, *J* = 14.5, 1.2 Hz, 1H), 1.29 (s, 3H), 1.26 (s, 3H), 0.87 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 205.9, 106.5, 94.1, 92.1, 77.0 (HSQC), 70.5, 70.5, 62.3, 55.4, 55.0, 54.2, 54.1, 49.7, 49.3, 37.3, 35.9, 34.3, 28.6, 25.8, 21.8, 18.8, 18.0, -4.3, -5.0.

FTIR (NaCl, thin film): 3392, 2931, 2854, 1701, 1458, 1226, 1107, 1041 cm^{-1}.

HRMS (FAB$^+$, *m/z*): $C_{26}H_{45}NO_7Si$, calc'd for $[M+H]^+$: 512.3038, found 512.3050.

Preparation of dimethoxyenones 262 and 263.



Note: Due to decreased conversion to the vinylogous acid upon scale-up, the first step of this procedure utilizing BCl_3 was performed in two batches (100 mg and 85 mg respectively), which were then combined for the methylation step. Reaction procedure and reagent quantities for the elimination step are described for the 100 mg scale reaction.

Powdered 4Å MS (1.0 g, 1000 wt %) were added to a 100 mL two-neck round bottom flask containing a stir bar. The flask and MS were flame-dried under high vacuum for 5 min.

Subsequently, ketal **257** (100 mg, 0.16 mmol) was added, and the flask placed under nitrogen atmosphere. The solids were taken up in CH_2Cl_2 (16.4 mL), and the heterogeneous mixture was stirred at room temperature for 10 min, and was then cooled to –40 °C. BCl_3 (1.5 mL, 1.5 mmol, 9.0 equiv; 1 M in CH_2Cl_2) was then added dropwise, and the reaction stirred for 1 h at –40 °C. After this time, the BCl_3 and CH_2Cl_2 were removed under high vacuum at –40 °C in the fumehood (slow decrease to ~90 mTorr). This was performed by distilling into a 200 mL two-neck round bottom flask at –78 °C, utilizing a U-shaped joint. Once approximately 4 mL of solvent distilled over, the reaction flask was removed from the cooling bath and slowly let warm to room temperature to speed up distillation. The crude reaction was then further dried under high vacuum for 10 min. At this stage, the two crudes (100 mg and 85 mg scale) were combined. The crudes were taken up in CH_3CN (10 mL) and filtered through a fine fritted filter to remove the MS, which were washed with CH_3CN (10 x 10 mL). The filtrate was concentrated under reduced pressure and dried under high vacuum. The crude vinylogous acid mixture was taken forward immediately without further purification.

The crude mixture of vinylogous acid isomers and remaining ketal **257** was taken up in PhH (8 mL) and MeOH (2 mL, HPLC grade). The flask was fitted with a plastic septum and nitrogen inlet needle, and cooled to 0 °C. $TMSCHN_2$ (0.76 mL, 0.1.5 mmol, 5.0 equiv, 2 M in Et_2O) was then added dropwise, and the mixture stirred at 0 °C for 5 min, after which it was warmed to room temperature and stirred for 1 h. The reaction was quenched by first cooling to 0 °C and then slowly adding in AcOH (0.35 mL, 6.07 mmol, 20 equiv). The mixture was stirred briefly at 0 °C, and was then warmed to room temperature and

stirred vigorously for another 15 min. All solvent was then removed under reduced pressure, and the acetic acid removed by azeotroping with heptane (1 x 20 mL). The residue was purified by silica gel flash chromatography (25 g, 0–50% acetone/hexanes) to afford dimethoxyenone **262** as an off-white foam (54.5 mg, 38% yield) and dimethoxyenone **263** as a pale yellow solid (17.7 mg, 12% yield), along with recovered ketal **257** (62 mg, 33% yield, 83% brsm). Minor isomer **263** was recrystallized by vapor diffusion ($CDCl_3$/pentane) and the structure confirmed via X-ray crystallography.

Data for desired isomer **262**:

TLC: R_f 0.43 (2:1 hexanes/acetone, UV & CAM).

$[\alpha]_D^{25.0}$: –70.3° (c = 0.90, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.16 (s, 1H), 4.27 (dd, *J* = 10.7, 6.8 Hz, 1H), 4.08 (s, 3H), 3.78 (s, 3H), 3.68 (s, 3H), 2.73 – 2.59 (m, 3H), 2.51 – 2.44 (m, 1H), 2.46 (d, *J* = 18.1 Hz, 1H), 2.36 (td, *J* = 10.5, 4.8 Hz, 1H), 2.31 (s, 3H), 2.15 (d, *J* = 15.9 Hz, 1H), 1.95 (dd, *J* = 12.7, 6.7 Hz, 1H), 1.84 (td, *J* = 11.0, 6.8 Hz, 1H), 1.53 (ddd, *J* = 11.8, 4.9, 1.5 Hz, 1H), 0.79 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 205.8, 194.0, 188.4, 160.9, 138.5, 106.0, 77.7, 72.6, 65.2, 60.6, 60.4, 58.5, 51.7, 50.5, 46.6, 40.7, 38.9, 37.1, 36.3, 25.7, 17.9, -4.0, -5.0.

FTIR (NaCl, thin film): 2948, 2856, 1672, 1605, 1359, 1233, 1121, 838 cm^{-1}.

HRMS (ESI, *m/z*): $C_{25}H_{39}NO_6Si$, calc'd for $[M+H]^+$: 478.2619, found: 478.2610.

Data for isomer **263**:

TLC: R_f 0.27 (2:1 hexanes/acetone, UV & CAM).

$[\alpha]_D^{25.0}$**:** –71.1° (c = 0.24, $CHCl_3$).

melting point: 184–185 °C.

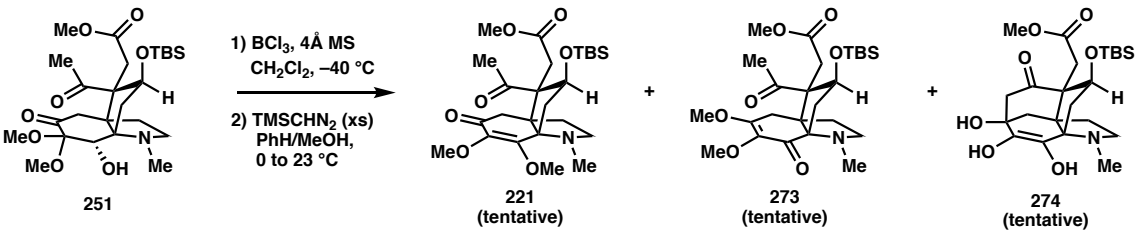
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.21 (s, 1H), 4.08 – 3.99 (m, 1H), 3.91 (s, 3H), 3.79 (s, 3H), 3.74 (s, 3H), 2.88 (ddd, *J* = 9.5, 7.2, 5.1 Hz, 1H), 2.69 (dd, *J* = 17.5, 1.4 Hz, 1H), 2.56 – 2.27 (m, 4H), 2.30 (s, 3H), 2.08 (dd, *J* = 14.0, 8.1 Hz, 1H), 1.92 (ddd, *J* = 12.8, 7.7, 5.1 Hz, 1H), 1.78 (dt, *J* = 12.9, 7.0 Hz, 1H), 0.78 (s, 9H), 0.02 (s, 3H), -0.00 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 204.3, 193.1, 188.2, 158.5, 136.3, 105.9, 77.9, 74.5, 66.6, 60.7, 58.6, 58.4, 52.5, 50.9, 41.6, 37.6, 36.9, 36.0, 33.5, 25.7, 17.9, -4.1, -5.2.

FTIR (NaCl, thin film): 2948, 2855, 1693, 1602, 1461, 1359, 1246, 1120, 836 cm^{-1}.

HRMS (ESI, *m/z*): $C_{25}H_{39}NO_6Si$, calc'd for $[M+H]^+$: 478.2619, found: 478.2630.

Preparation of dimethoxyenone 221.



Step 1: Powdered 4Å MS (500 mg, 1000 wt %) were flame-dried under high vacuum in a 10 mL round bottom flask containing a stir bar. Ketone (50 mg, 0.097 mmol) was added, the flask put under N_2 atmosphere, and CH_2Cl_2 (2 mL) was added. The flask was cooled to –40 °C, after which BCl_3 (0.58 mL, 0.58 mmol, 6.0 equiv; 1 M in CH_2Cl_2) was added

dropwise, and the reaction stirred for 1 h at –40 °C. After this time, the BCl_3 and CH_2Cl_2 were removed under high vacuum at –40 °C in the fumehood (slow decrease to ~90 mTorr). The crude was taken up in CH_3CN (5 mL) and filtered through a fine fritted filter to remove the MS, which were washed with CH_3CN (10 x 5 mL). The filtrate was concentrated under reduced pressure and dried under high vacuum. The crude mixture was taken forward immediately without further purification.

Step 2: The crude was taken up in PhH (2.6 mL) and MeOH (0.65 mL, HPLC grade) and cooled to 0 °C. $TMSCHN_2$ (0.24 mL, 0.49 mmol, 5.0 equiv, 2 M in Et_2O) was added and the mixture stirred for 5 min at 0 °C. The reaction was warmed to room temperature and stirred for 30 min. It was then cooled to 0 °C and quenched with AcOH (0.28 mL) at 0 °C. The solvent was removed under reduced pressure in the fumehood and the crude dried under high vacuum. The crude residue was purified by silica gel preparatory TLC (40% acetone/hexanes) to afford tentatively assigned vinylogous ester **221** (5 mg, contaminated with an unidentified side product that still contains a dimethoxyketal, <10% yield) and isomer **273** (7.1 mg, 1:1 mixture with an unidentified side product that still contains a dimethoxyketal).

Data for isomer **221**:

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.19 (dd, *J* = 9.4, 6.3 Hz, 1H), 4.09 (s, 3H), 3.70 (s, 3H), 3.68 (s, 3H), 3.32 (d, *J* = 17.2 Hz, 1H), 3.04 – 2.98 (m, 1H), 2.80 – 2.70 (m, 1H), 2.70 – 2.59 (m, 1H), 2.27 (s, 3H), 2.25 (s, 3H), 2.31 – 2.20 (m, 1H), 2.16 – 2.07 (m, 1H), 2.02 –

1.84 (m, 2H), 1.86 – 1.77 (m, 1H), 1.54 – 1.39 (m, 1H), 0.89 (s, 9H), 0.12 (s, 3H), 0.09 (s, 3H).

Note: ^{13}C data was taken from HSQC (*) and HMBC (‡) spectra (TBS ^{t}Bu quaternary carbon not assigned).

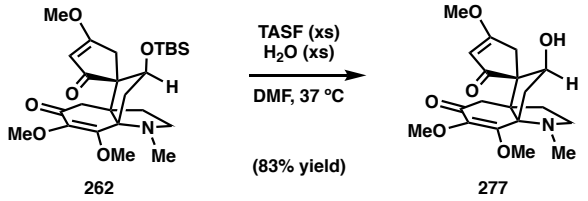
^{13}C NMR (101 MHz, $CDCl_3$): δ 210.7‡, 201.5‡, 171.8‡, 160.2‡, 137.8‡, 77.9*, 72.7‡, 65.2‡, 60.4*, 60.3*, 52.6‡, 52.0*, 51.4*, 48.7*, 39.9*, 39.6*, 37.9*, 35.5*, 31.9*, 25.8*, -4.9*, -4.5*.

Preparation of bridging ketone 276.

251 **276 (tentative)**

Methyl ketone **251** (5 mg, 0.0078 mmol) was added to a flame-dried 1 dram vial containing a stir bar and brought into a nitrogen-filled glovebox. HFIP (0.2 mL) was added, the vial sealed with a screw cap. The vial was removed from the glovebox and stirred at room temperature for 5 days. Gradual conversion to a new peak with the same mass as 251 was observed via LC/MS. The reaction was then concentrated under reduced pressure and dried under high vacuum. The crude residue was analyzed by ^{1}H NMR ($CDCl_3$), indicating disappearance of the methyl ketone signal. *Note*: Crude contains phthalate contamination from screw cap.

Preparation of neopentyl alcohol 277.



262 277

Silyl ether **262** (54.5 mg, 0.11 mmol) and a stir bar were added to a scintillation vial and taken up in DMF (2.7 mL). TASF (157 mg, 0.57 mmol, 5.0 equiv) was weighed into a scintillation vial, sealed with a screw cap, and removed from the glovebox. The TASF was taken up in DMF (2 mL) under ambient air, after which H_2O (20.5 μL, 1.14 mmol, 10.0 equiv) was added. The TASF solution was subsequently added to silyl ether **262** at room temperature. The vial containing TASF was then rinsed with DMF (1 mL), which was transferred to the reaction vial to complete the transfer. The reaction vial was subsequently sealed with a Teflon-lined cap, sealed with electrical tape, and heated at 37 °C (aluminum block temperature) and stirred for 16 h. *Note:* Due to product polarity, no aqueous workup is performed. Upon consumption of silyl enol ether **262**, Celite (3.0 g) was added and the heterogeneous mixture was carefully placed under high vacuum (~90 mTorr), and all solvent was removed by gentle heating in the reaction heating block at 37 °C. The dry-loaded crude residue was purified by Florisil gel flash chromatography (0–100% acetone/hexanes) to afford **277** as a white foam (34.6 mg, 83% yield) after azeotroping with pentane (2 x 7 mL). *Note*: Using 100% acetone on the Florisil column affords acetone self-aldol side products (visible in ^{1}H NMR). However, prolonged drying of alcohol **277** under high vacuum (~90 mTorr) readily removes these volatile products.

TLC: R_f 0.25 (80% acetone in hexanes, UV & CAM).

$[\alpha]_D^{25.0}$: –75.0° (c = 0.82, $CHCl_3$).

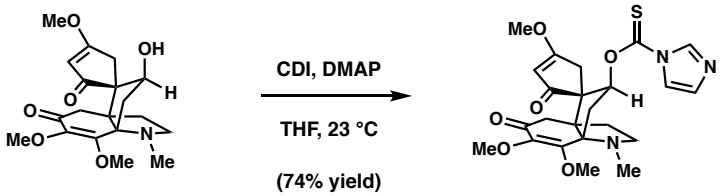
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.24 (s, 1H), 4.30 (bt, 1H), 4.08 (s, 3H), 3.84 (s, 3H), 3.67 (s, 3H), 2.86 – 2.74 (m, 2H), 2.76 – 2.67 (m, 1H), 2.65 (dd, *J* = 18.1, 1.1 Hz, 1H), 2.54 – 2.37 (m, 2H), 2.34 (s, 3H), 2.25 (d, *J* = 15.9 Hz, 1H), 2.23 (dd, *J* = 13.4, 7.0 Hz, 1H), 1.85 (dt, *J* = 12.6, 8.7 Hz, 1H), 1.53 (ddd, *J* = 12.6, 6.2, 2.6 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 206.6, 193.8, 190.2, 160.7, 138.3, 105.8, 78.2, 73.3, 64.3, 60.7, 60.5, 58.9, 53.2, 52.2, 46.6, 39.7, 38.6, 37.8, 36.4.

FTIR (NaCl, thin film): 3401, 2945, 2788, 1668, 1599, 1445, 1361, 1080, 994 cm^{-1}.

HRMS (ESI, *m/z*): $C_{19}H_{25}NO_6$, calc'd for $[M+H]^+$: 364.1755, found: 364.1749.

Preparation of imidazolyl thiocarbamate 279.



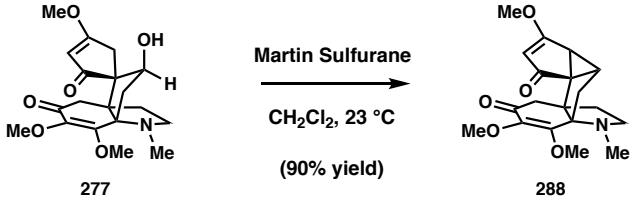
277 279

Neopentyl alcohol **277** (13 mg, 0.036 mmol), DMAP (4.4 mg, 0.036 mmol, 1.0 equiv), and CDI (12.7 mg, 0.072 mmol, 2.0 equiv) were added to a flame-dried 2 dram vial containing a stir bar and the vial wasfz placed under N_2 atmosphere. The solids were taken up in THF (0.7 mL) and the mixture stirred at room temperature for 2 h. The reaction was concentrated under reduced pressure and directly purified by silica gel flash chromatography (10–80% acetone/hexanes) to afford thiocarbamate **279** (12.5 mg, 74% yield).

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.17 (s, 1H), 7.52 – 7.46 (m, 1H), 6.99 (dd, *J* = 1.7, 0.9 Hz, 1H), 5.94 (dd, *J* = 10.1, 7.5 Hz, 1H), 5.30 (d, *J* = 1.2 Hz, 1H), 4.10 (s, 3H), 3.82 (s, 3H), 3.70 (s, 3H), 2.78 (dd, *J* = 2.9, 1.2 Hz, 2H), 2.72 (ddd, *J* = 9.7, 6.9, 2.6 Hz, 1H), 2.70 – 2.59 (m, 2H), 2.52 (td, *J* = 9.8, 5.4 Hz, 1H), 2.38 (s, 3H), 2.29 (d, *J* = 16.1 Hz, 1H), 2.04 – 1.92 (m, 1H), 1.67 (dq, *J* = 12.1, 2.7 Hz, 2H).

HRMS (ESI, *m/z*): $C_{23}H_{27}N_3O_6S$, calc'd for $[M+H]^+$: 474.1693, found: 474.1697.

Preparation of cyclopropane 288.



Neopentyl alcohol **277** (10 mg, 0.028 mmol) was added to a flame-dried 2 dram vial containing a stir bar, and was brought into a nitrogen-filled glovebox. The solid was taken up in CH_2Cl_2 (2.8 mL). At room temperature, Martin Sulfurane (55.5 mg, 0.083 mmol, 3.0 equiv) was then added, and the mixture rapidly turned bright yellow. It was stirred for 90 min, and then brought out of the glovebox. LC/MS analysis at this stage indicated complete consumption of alcohol **277**. The reaction was quenched with saturated aqueous $NaHCO_3$ (4 mL) and transferred to a separatory funnel, utilizing EtOAc (5 mL) and saturated aqueous $NaHCO_3$ (10 mL) to rinse the vial. The layers were separated and the aqueous layer extracted with EtOAc (5 x 4 mL). All combined organic layers were washed with brine (1 x 5 mL) and the brine layer back-extracted with EtOAc (1 x 3 mL). All combined organic layers were dried with Na_2SO_4, filtered, and concentrated under

reduced pressure to give a crude oil. The crude residue was purified by Florisil flash chromatography: 1) equilibrated with 1% Et_3N/hexanes, 2) flushed with two column volumes of hexanes, and 3) purified with a gradient of 0–20% acetone/hexanes to afford cyclopropane **288** as an off-white foam (8.6 mg, 90% yield) after azeotroping with pentane (2 x 4 mL). *Note:* NMR analysis can be performed in $CDCl_3$ if desired; however, the product is mildly acid sensitive, thus rendering C_6D_6 a more preferable choice for longer studies.

TLC: R_f 0.40 (1:1 hexanes/acetone, UV & CAM).

$[\alpha]_D^{25.0}$: –82.5° (c = 0.11, $CHCl_3$).

^{1}H NMR (400 MHz, C_6D_6): δ 4.58 (d, *J* = 1.5 Hz, 1H), 4.22 (d, *J* = 15.4 Hz, 1H), 3.53 (s, 3H), 3.50 (s, 3H), 3.04 (dd, *J* = 2.3, 1.6 Hz, 1H), 2.94 (s, 3H), 2.79 (d, *J* = 15.5 Hz, 1H), 2.43 (td, *J* = 9.3, 2.2 Hz, 1H), 2.23 – 2.16 (m, 1H), 2.15 (dd, *J* = 5.6, 2.2 Hz, 1H), 2.08 (s, 3H), 1.94 – 1.83 (m, 2H), 1.54 (ddd, *J* = 13.2, 9.0, 2.2 Hz, 1H), 1.43 (dd, *J* = 15.0, 5.5 Hz, 1H).

^{13}C NMR (101 MHz, C_6D_6): δ 198.5, 193.1, 186.9, 157.9, 137.7, 98.8, 76.8, 60.3, 60.1, 57.7, 53.5, 52.9, 51.7, 49.0, 45.6, 35.9, 33.1, 33.0, 32.3.

FTIR (NaCl, thin film): 2940, 1681, 1586, 1454, 1354, 1234, 1111, 1067, 1010 cm^{-1}.

HRMS (ESI, *m/z*): $C_{19}H_{23}NO_5$, calc'd for $[M+H]^+$: 346.1649, found: 346.1642.

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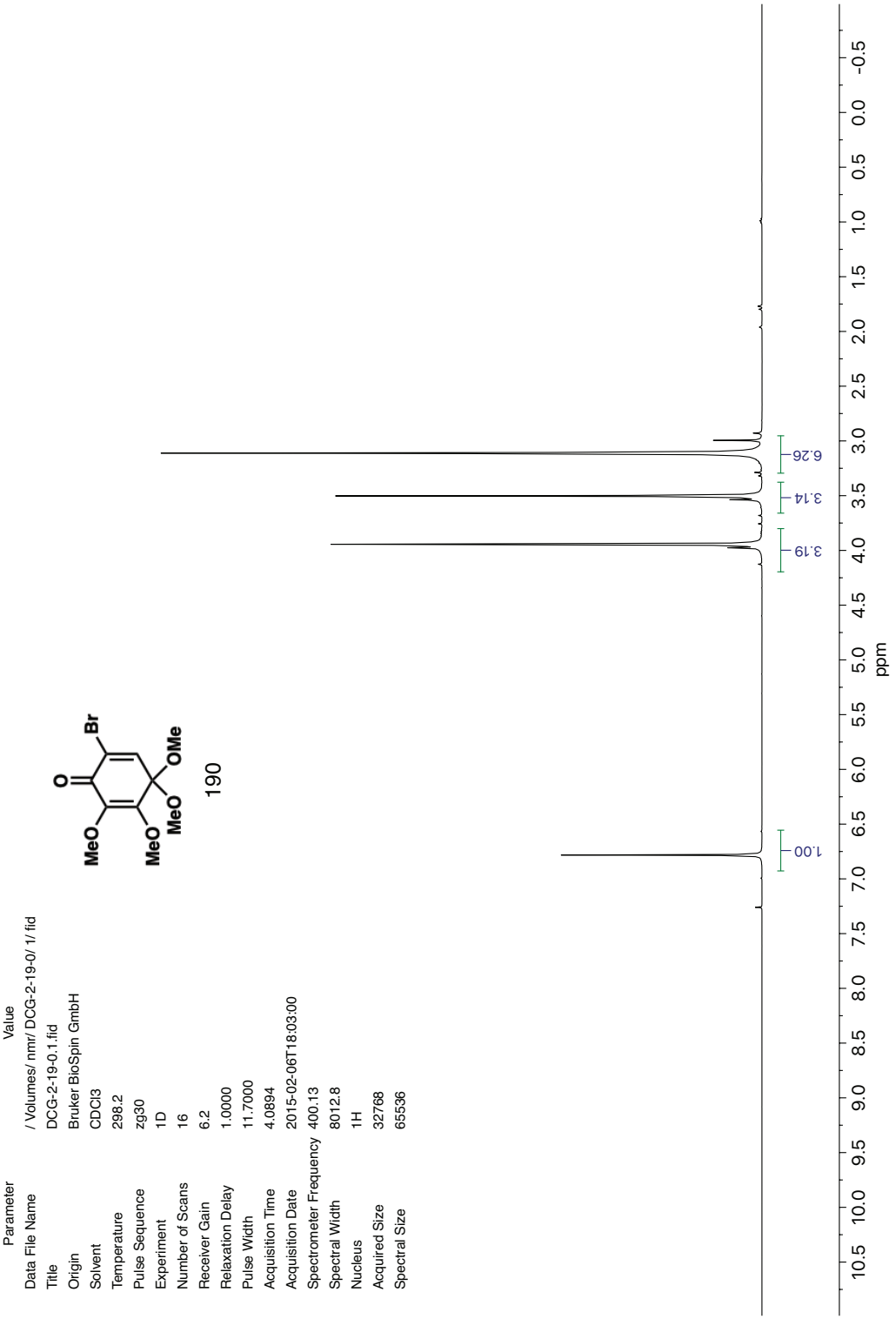
Appendix 2

Spectra Relevant to Chapter 3:

Revised Strategies for the Asymmetric

Total Synthesis of Acutumine Alkaloids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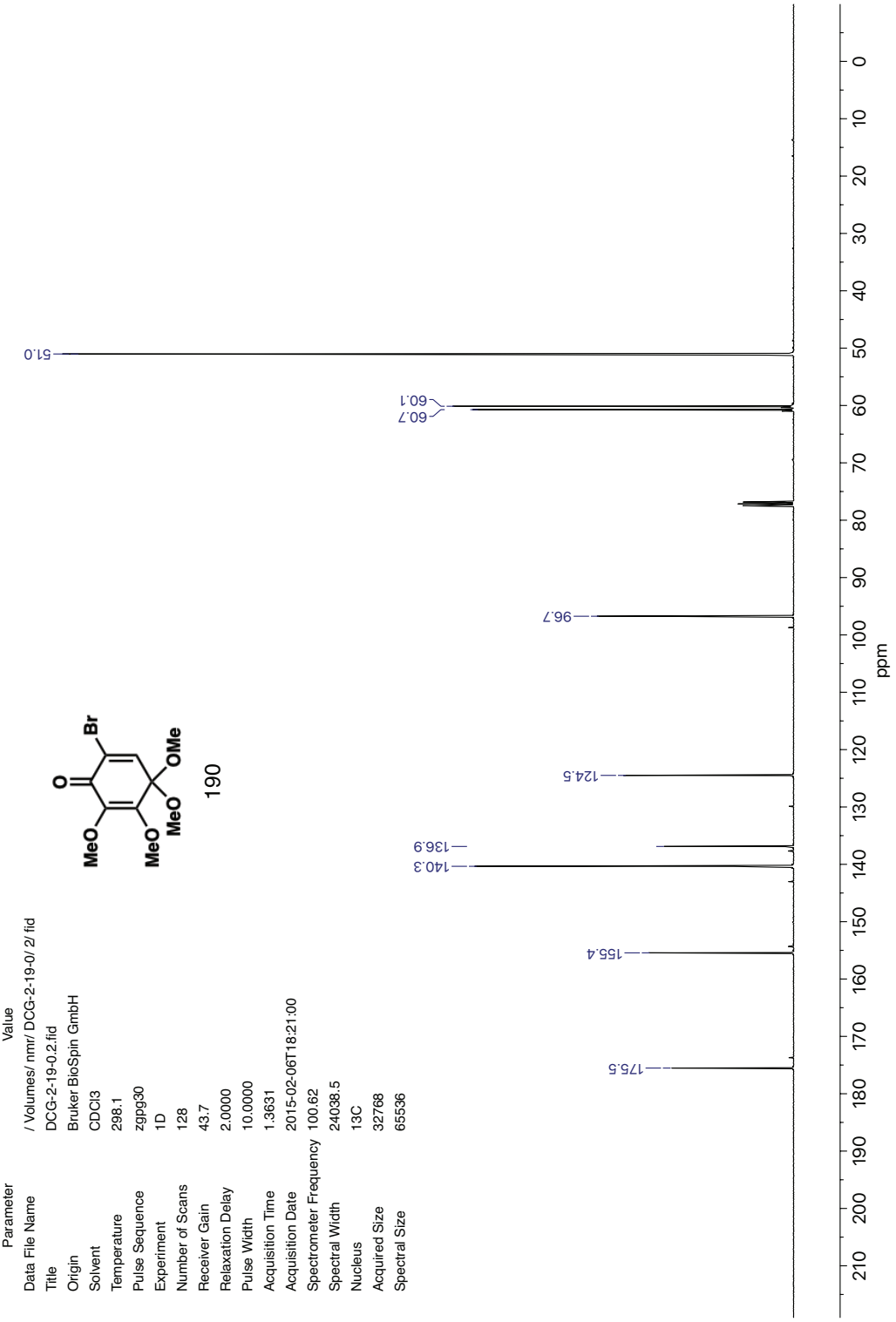
DCG-2-19-0.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
298.2
Pulse Sequence
zg30
Experiment
1D
Number of Scans
16
Receiver Gain
6.2
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2015-02-06T18:03:00
Spectrometer Frequency
400.13
Spectral Width
8012.8
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
190
MeO
MeO
MeO
OMe
Br
O
1.00
3.19
3.14
6.26
ppm
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5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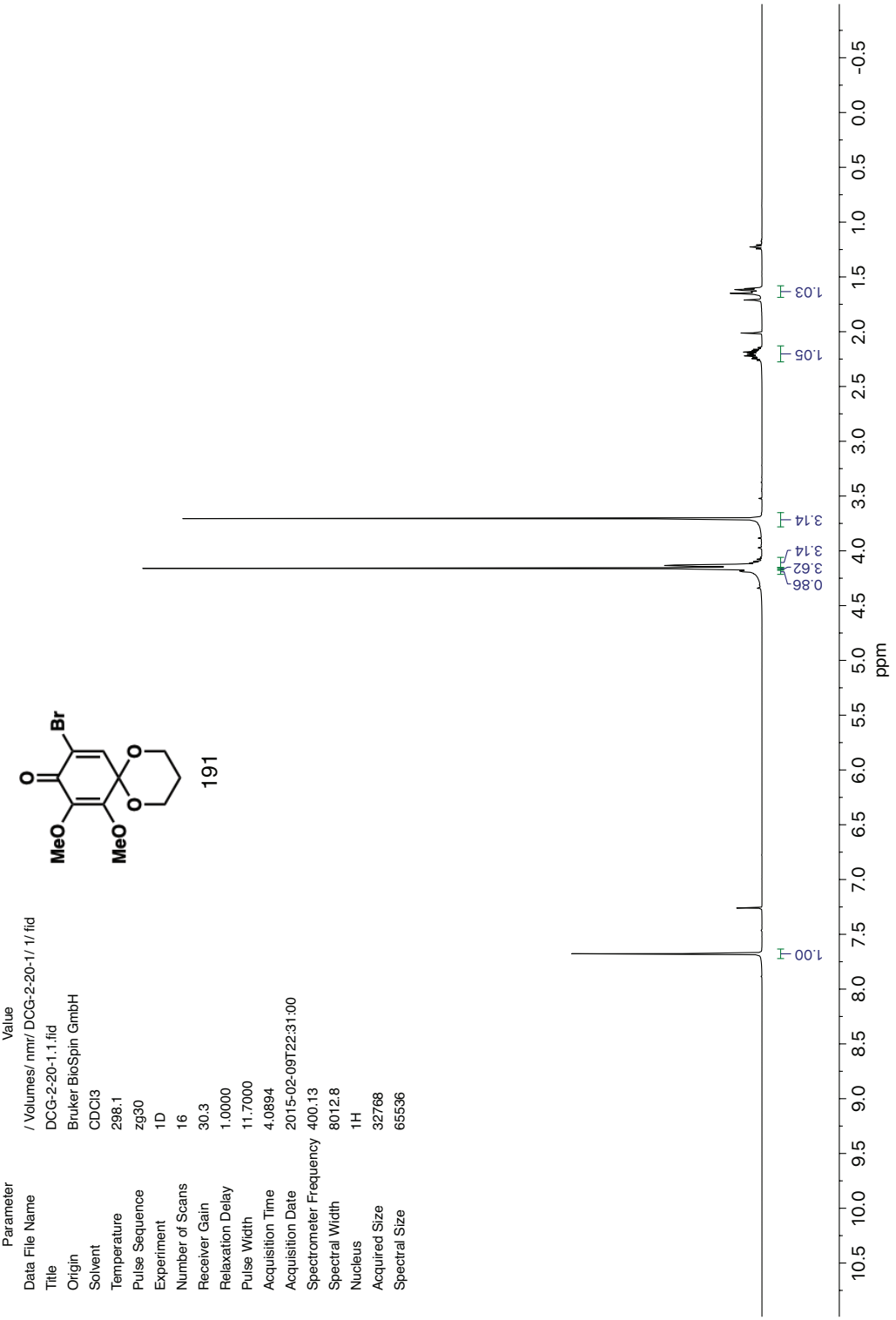
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 298.1
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 128
Receiver Gain 43.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2015-02-06T18:21:00
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
O
Br
MeO
MeO
MeO
OMe
190
51.0
60.7
60.1
96.7
124.5
136.9
140.3
155.4
175.5
ppm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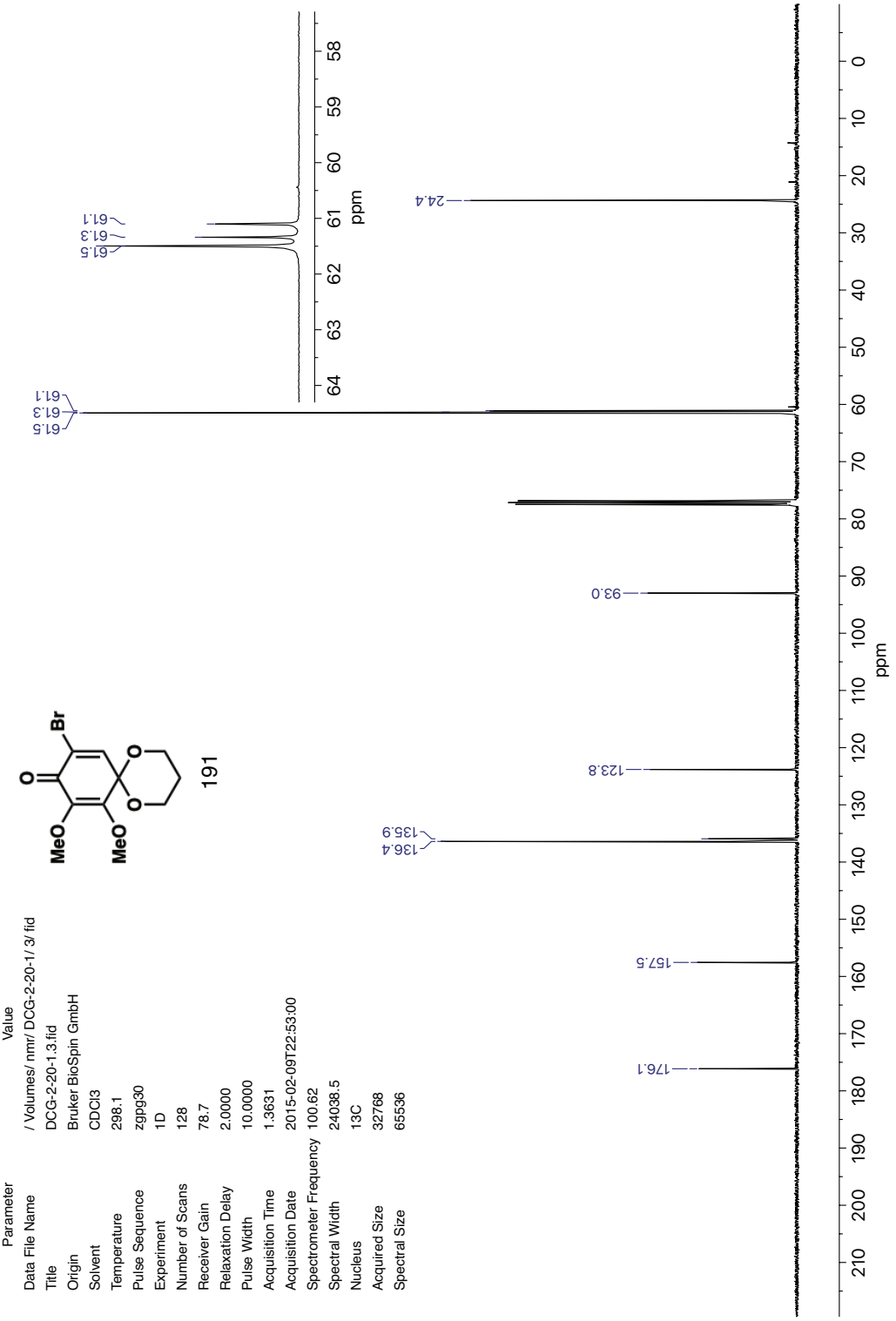
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 298.1
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 30.3
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2015-02-09T22:31:00
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
Br
O
MeO
MeO
O
O
191
1.00
3.14
3.14
3.62
0.86
1.05
1.03
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm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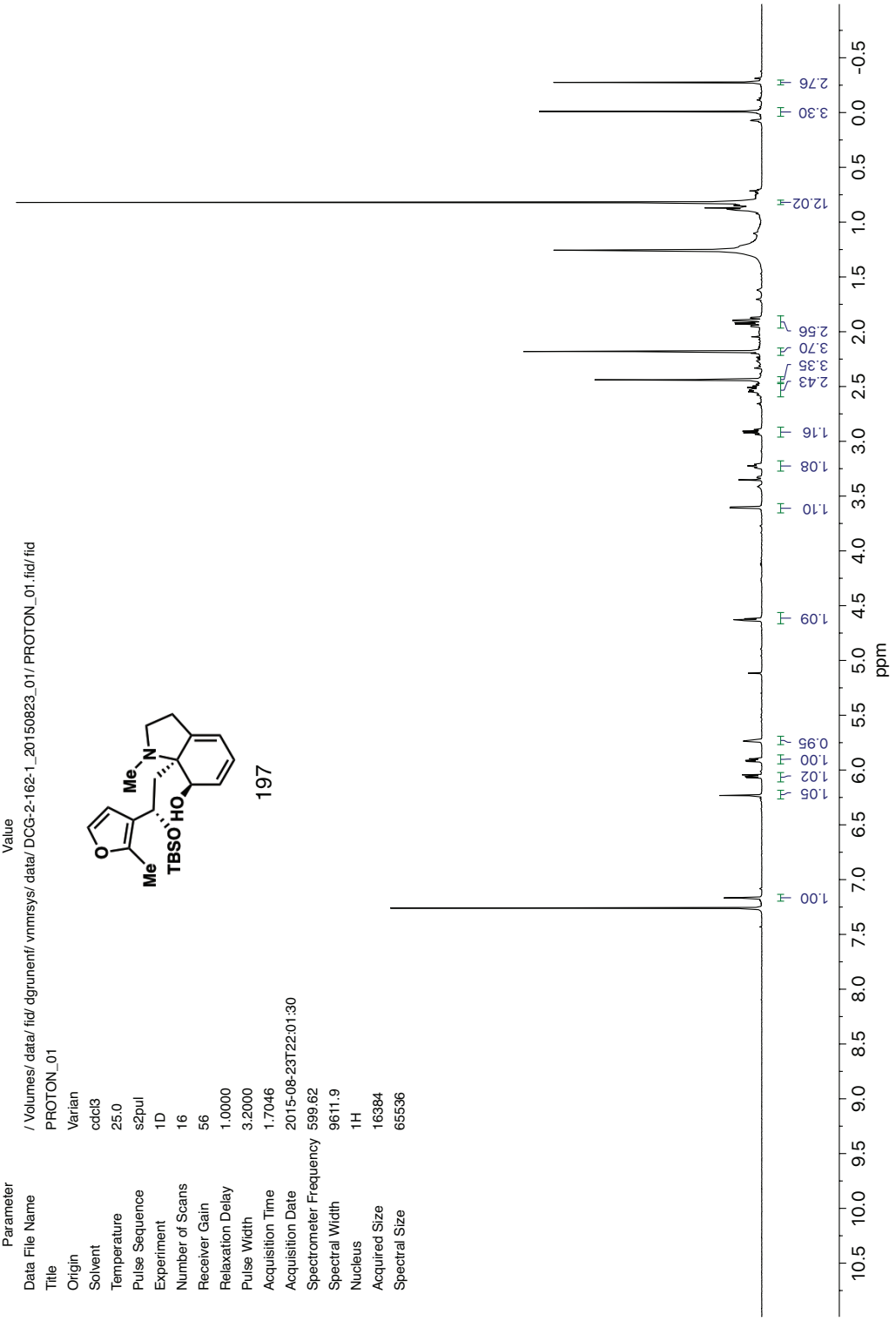
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 298.1
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 128
Receiver Gain 78.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2015-02-09T22:53:00
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Br
MeO
MeO
O
O
O
191
61.5
61.3
61.1
24.4
93.0
123.8
135.9
136.4
157.5
176.1
ppm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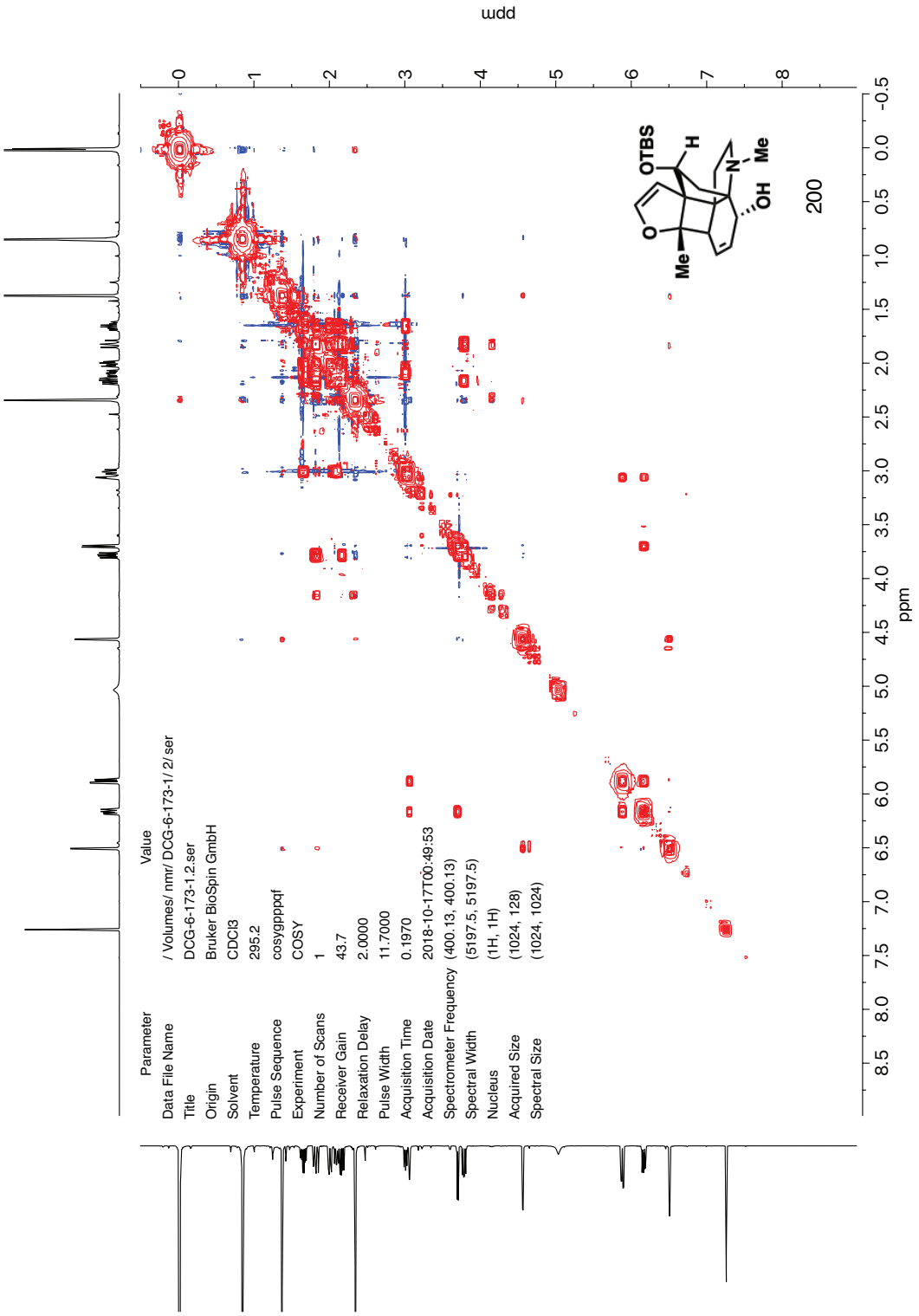
Title PROTON_01
Origin Varian
Solvent cdcl3
Temperature 25.0
Pulse Sequence s2pul
Experiment 1D
Number of Scans 16
Receiver Gain 56
Relaxation Delay 1.0000
Pulse Width 3.2000
Acquisition Time 1.7046
Acquisition Date 2015-08-23T22:01:30
Spectrometer Frequency 599.62
Spectral Width 9611.9
Nucleus 1H
Acquired Size 16384
Spectral Size 65536
Me
N
O
Me
TBSO
HO
197
1.00
1.05
1.02
1.00
0.95
1.09
1.10
1.08
1.16
2.43
3.35
3.70
2.56
12.02
3.30
2.76
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm


Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-173-1/1/1/ fid
Title DCG-6-173-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 87.8
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-10-17T00:48:53
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
OTBS
H
N
Me
OH
Me
O
Me
200
1.00
0.99
0.99
0.86
0.99
1.01
0.99
1.00
1.02
3.11
1.14
0.90
1.00
1.03
1.15
3.12
9.79
3.04
3.04
ppm


ppm
ppm
OTBS
H
N
Me
OH
Me
O
Me
200
Parameter Value
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Title DCG-6-173-1.2.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 43.7
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.1970
Acquisition Date 2018-10-17T00:49:53
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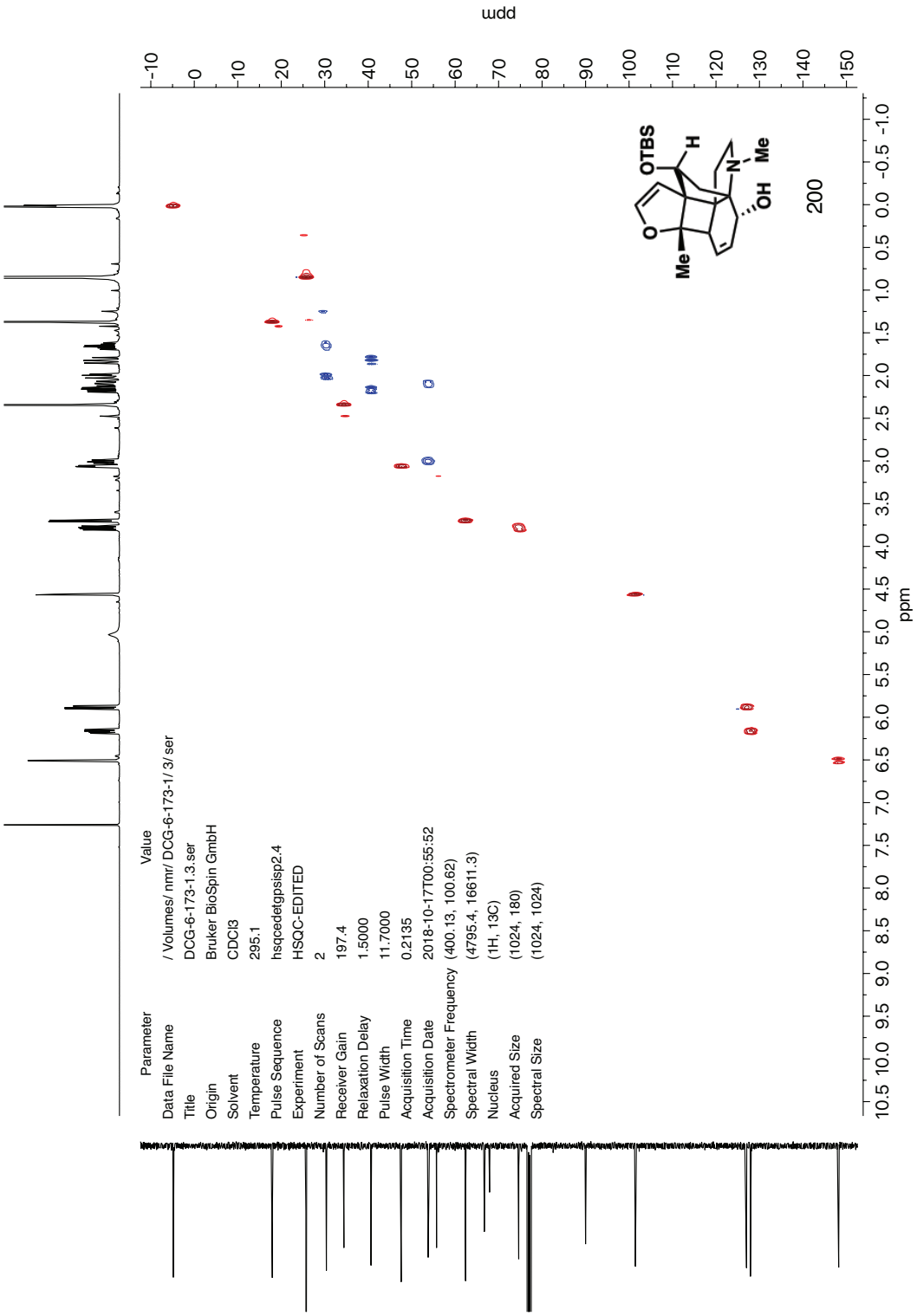
Spectral Width (5197.5, 5197.5)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)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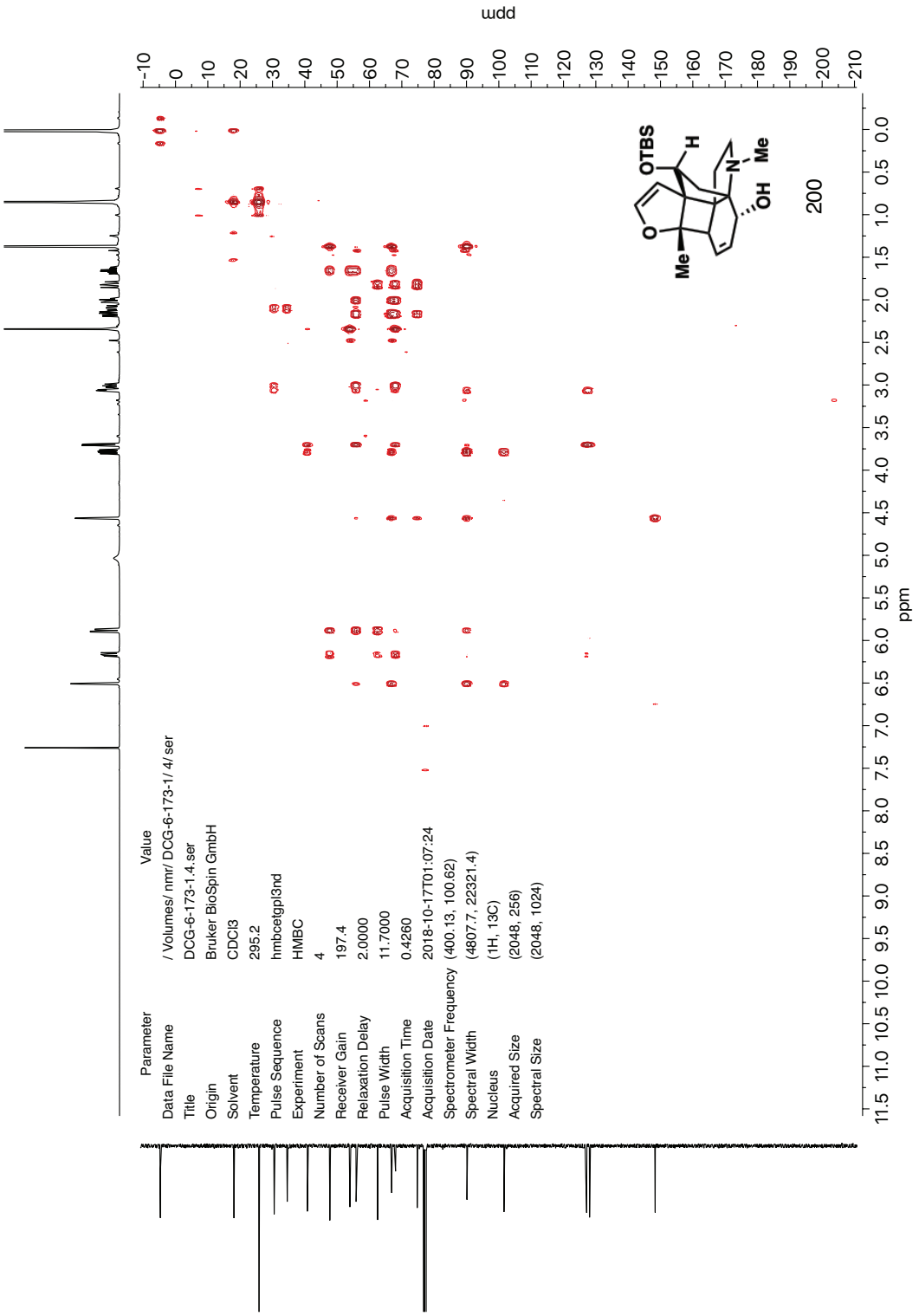
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2018-10-17T00:55:52
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 180)
Spectral Size (1024, 1024)
OTBS
H
O
Me
N
Me
OH
200
ppm
ppm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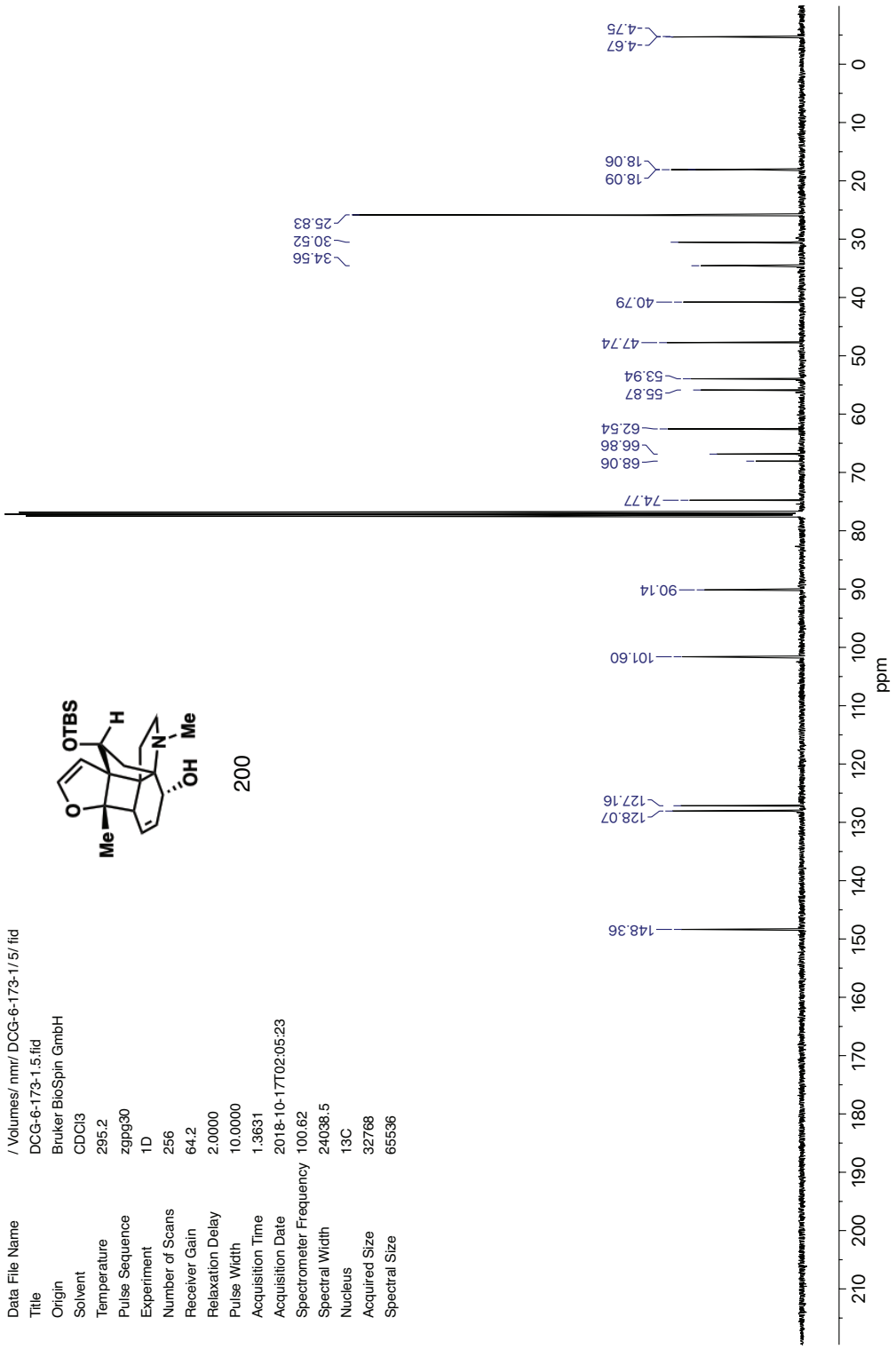
Title DCG-6-173-1.4.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2018-10-17T01:07:24
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
ppm
ppm
OTBS
H
Me
OH
Me
N
O
200



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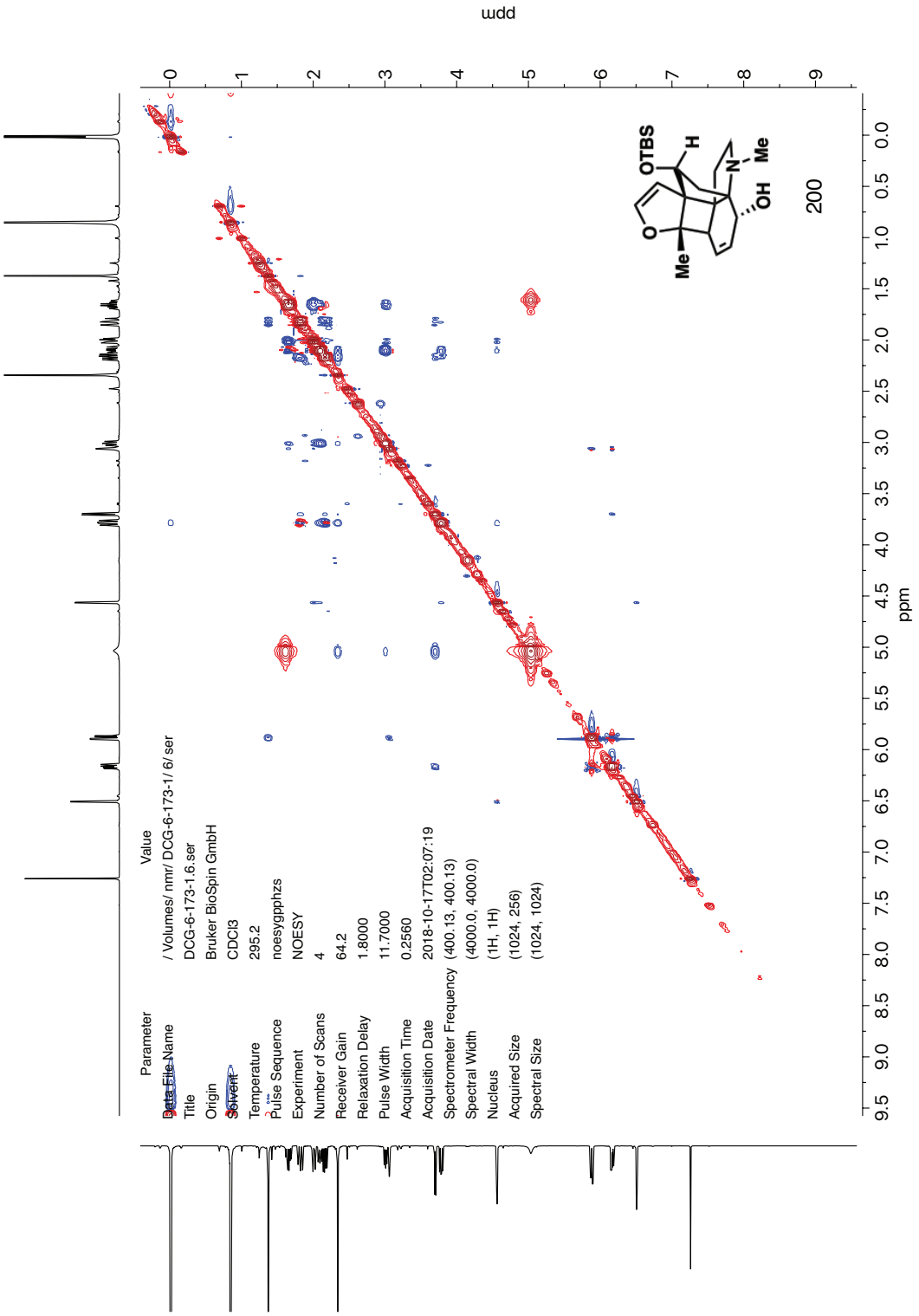
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	256
Receiver Gain	64.2
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-10-17T02:05:23
Spectrometer Frequency	100.62
Spectral Width	24038.5
Nucleus	13C
Acquired Size	32768
Spectral Size	65536


ppm
ppm
OTBS
H
N
Me
OH
Me
O
Me
200
Parameter Value
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Title DCG-6-173-1.6.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence noesygpphzs
Experiment NOESY
Number of Scans 4
Receiver Gain 64.2
Relaxation Delay 1.8000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2018-10-17T02:07:19
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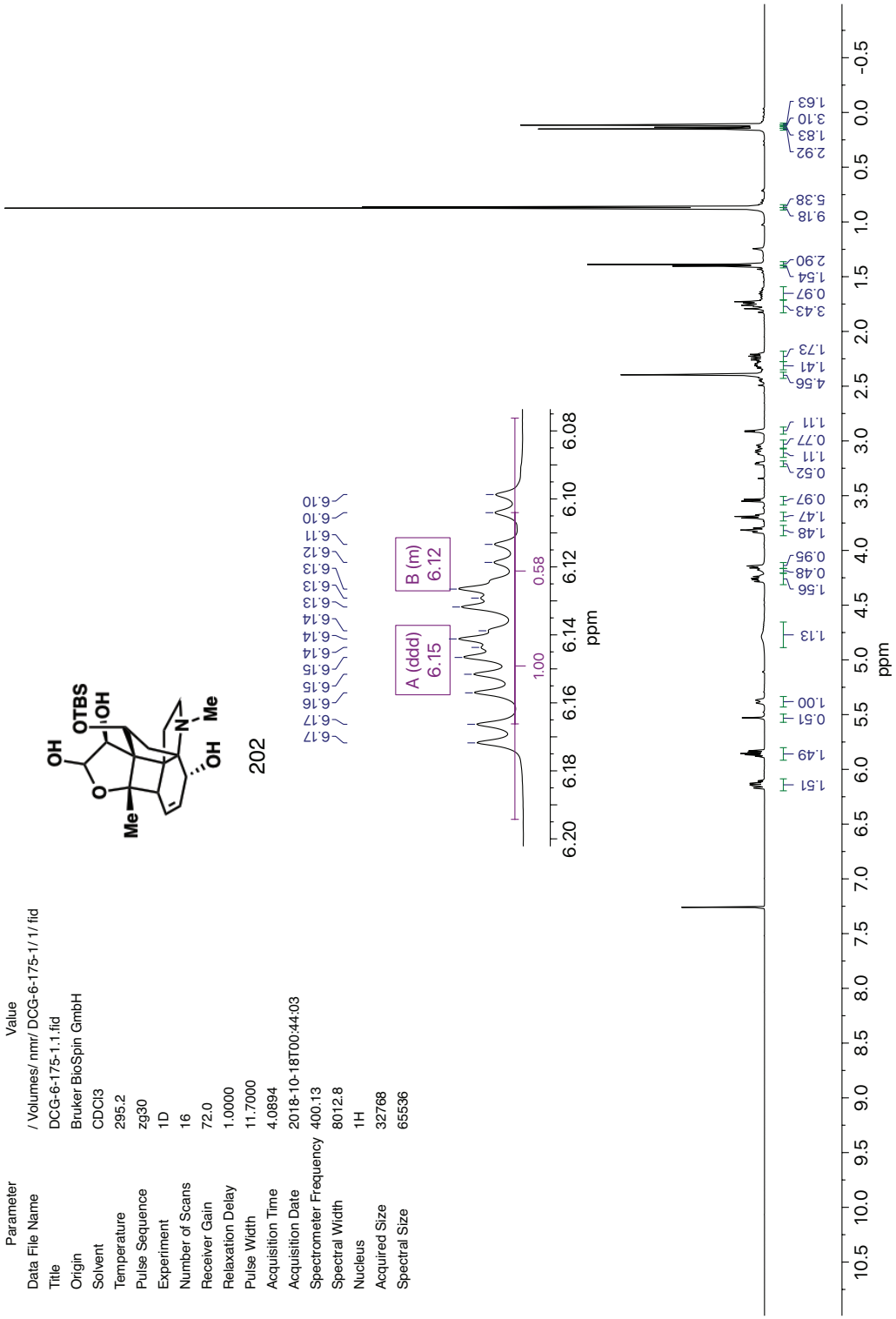
Spectral Width (4000.0, 4000.0)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)


Parameter Value
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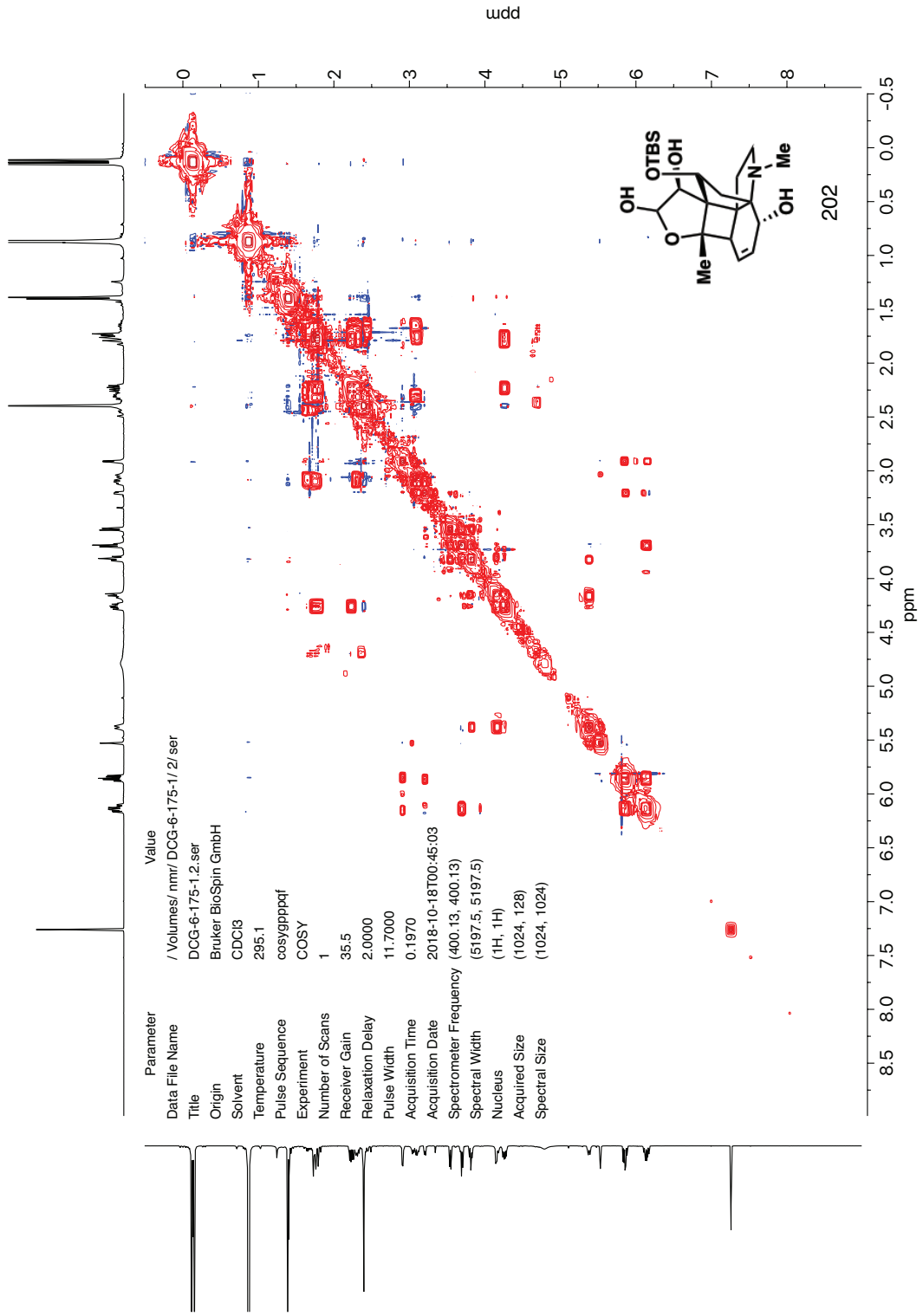
Title DCG-6-175-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 72.0
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-10-18T00:44:03
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
OH
OTBS
OH
O
Me
N
Me
OH
202
A (ddd) 6.15
B (m) 6.12
1.00
0.58
ppm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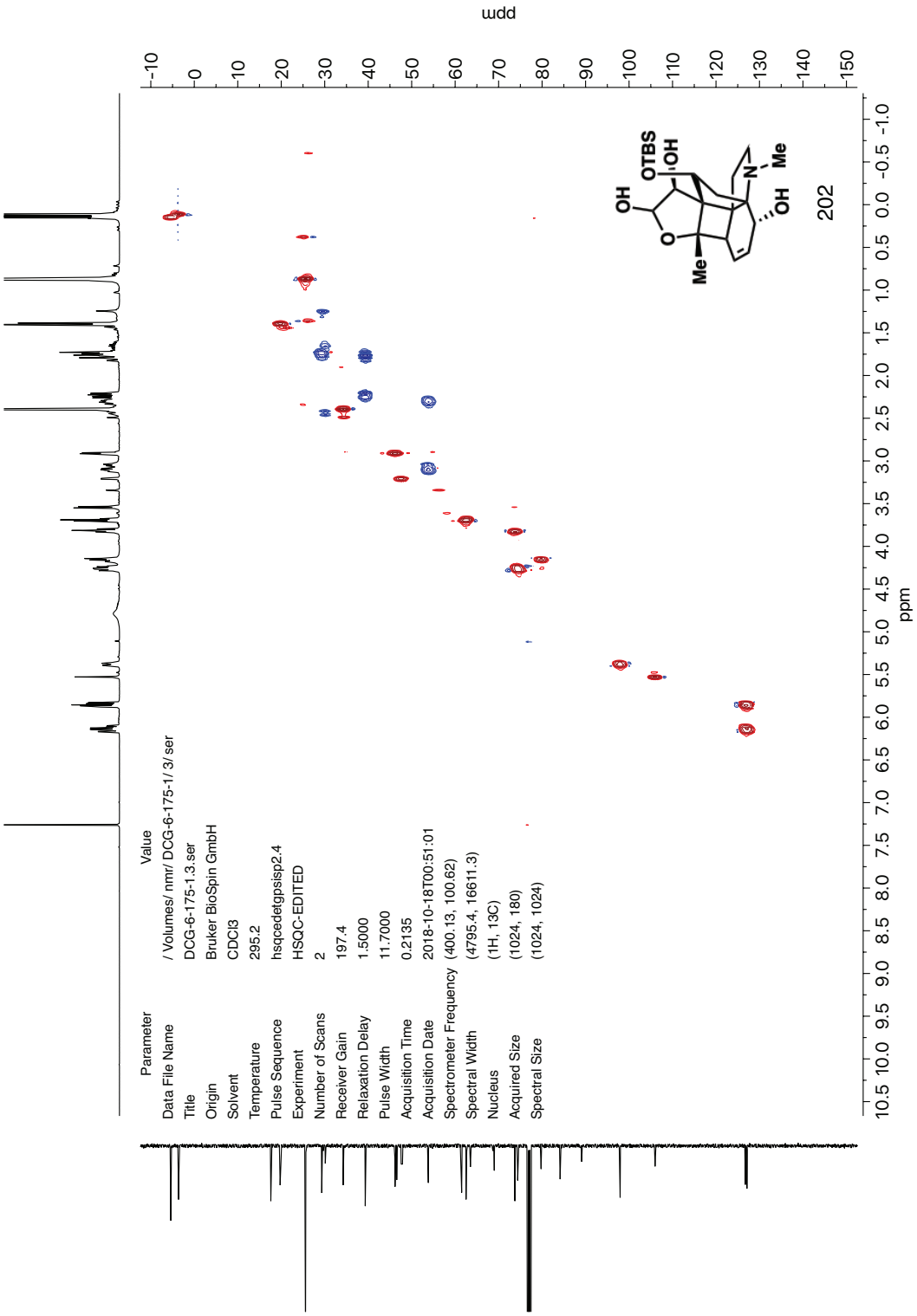
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 35.5
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.1970
Acquisition Date 2018-10-18T00:45:03
Spectrometer Frequency (400.13, 400.13)
Spectral Width (5197.5, 5197.5)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)
OH
OTBS
OH
Me
OH
Me
202
ppm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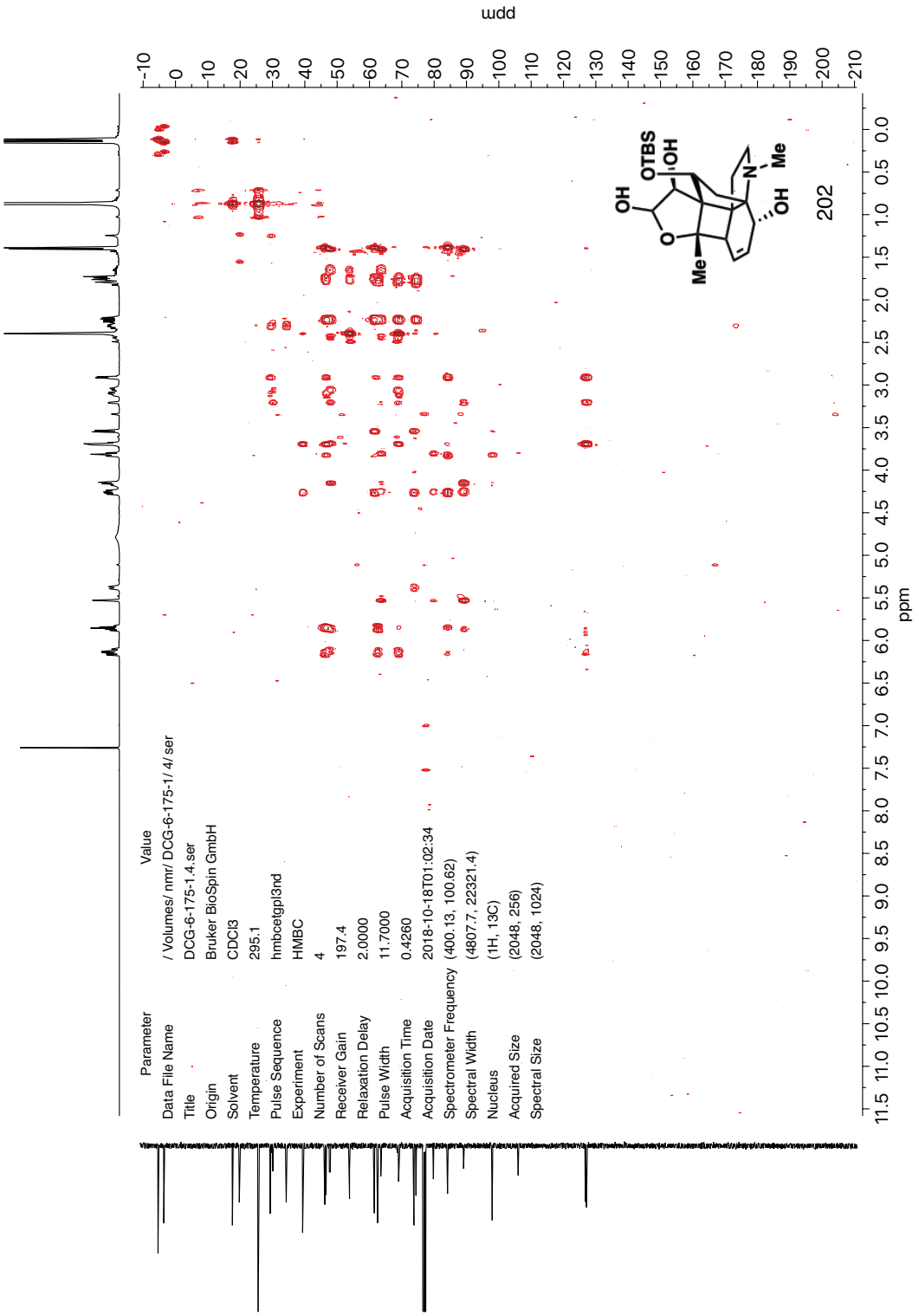
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2018-10-18T00:51:01
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 180)
Spectral Size (1024, 1024)
ppm
ppm
OH
OTBS
OH
O
Me
N
Me
OH
202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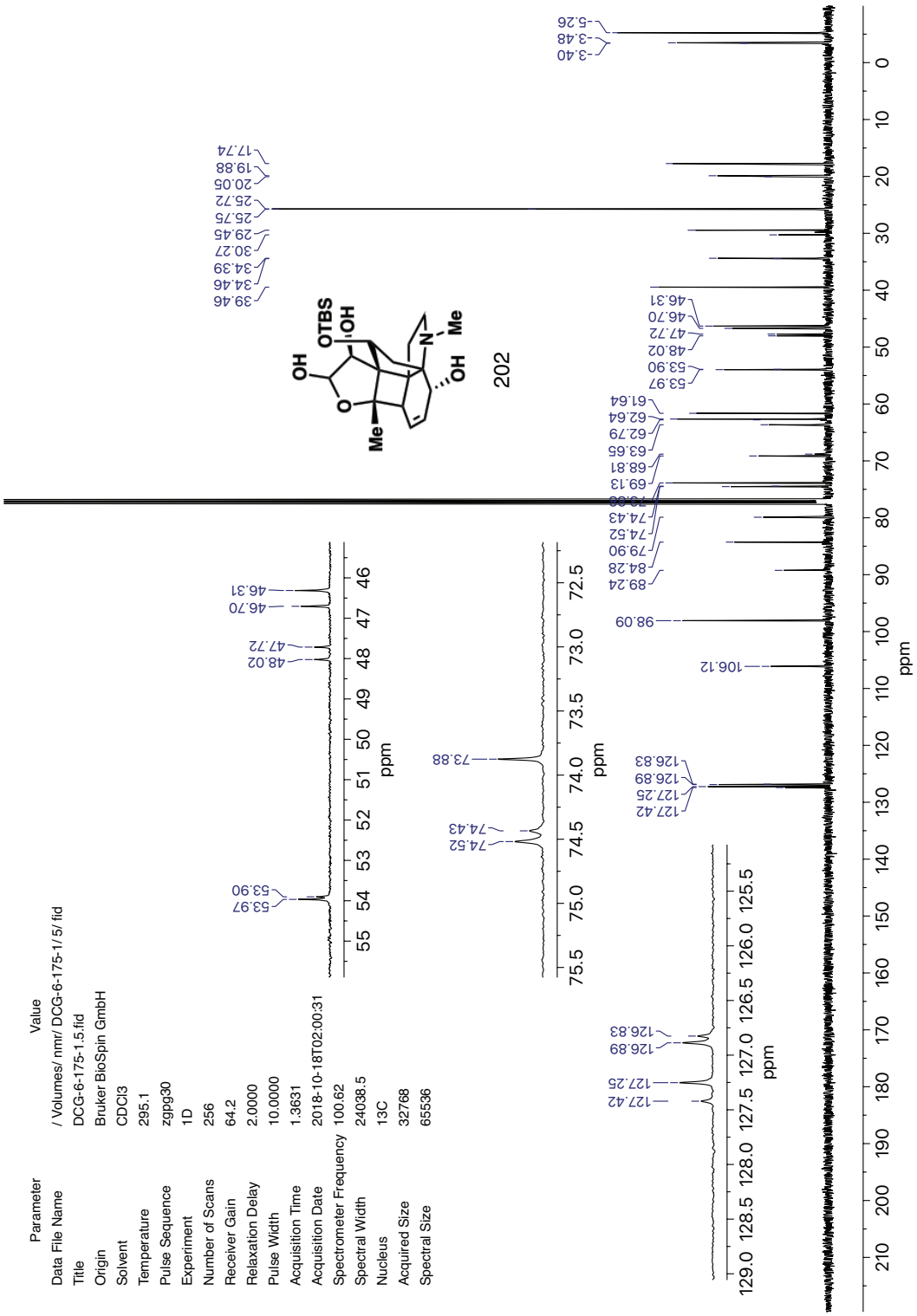
Solvent CDCl3
Temperature 295.1
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2018-10-18T01:02:34
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
OH
OTBS
OH
Me
OH
Me
202
ppm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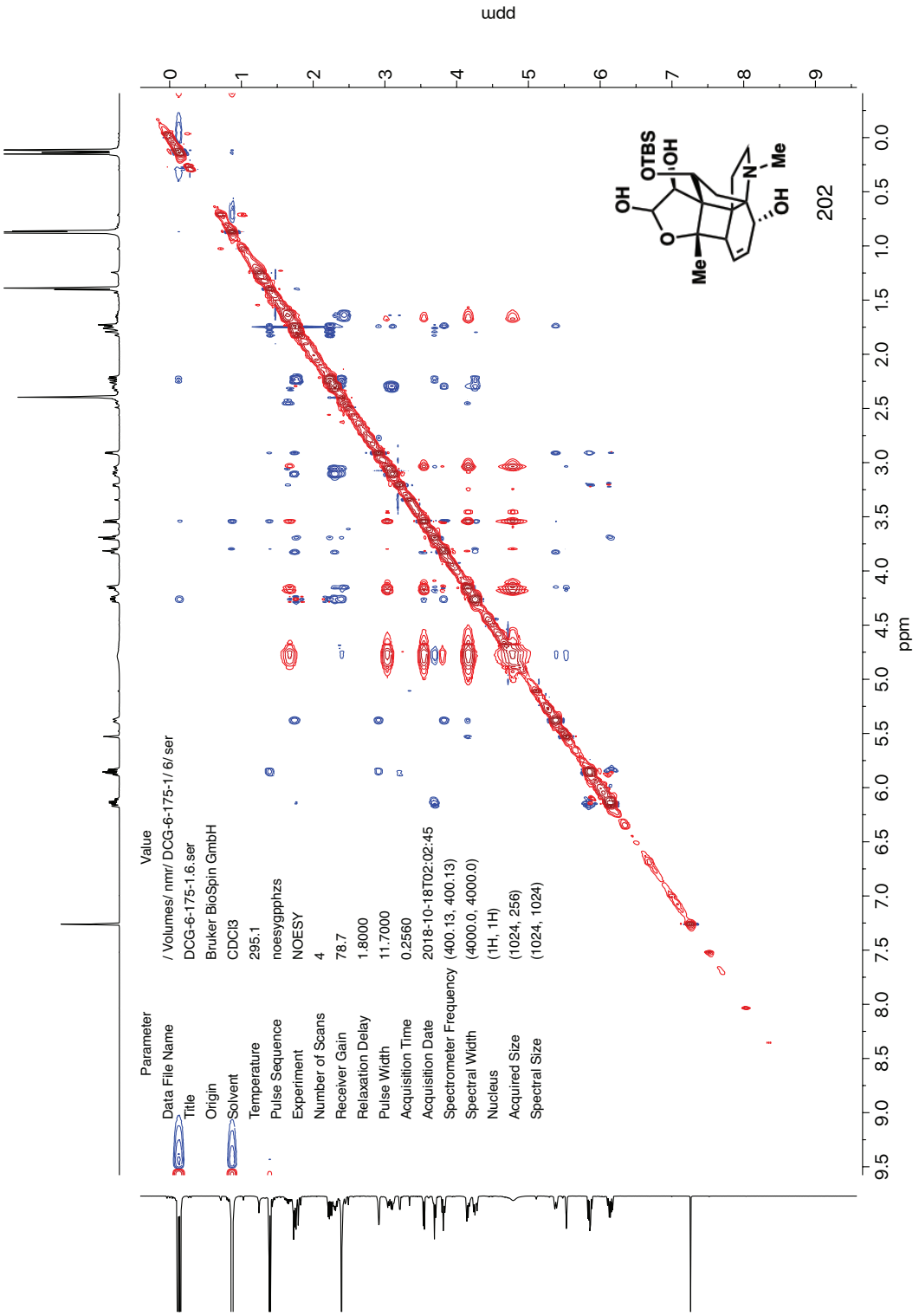
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-10-18T02:00:31
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OTBS
OH
OH
O
Me
N
Me
OH
202
ppm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Value
Data File Name
/ Volumes/ nmr/ DCG-6-175-1/ 6/ ser
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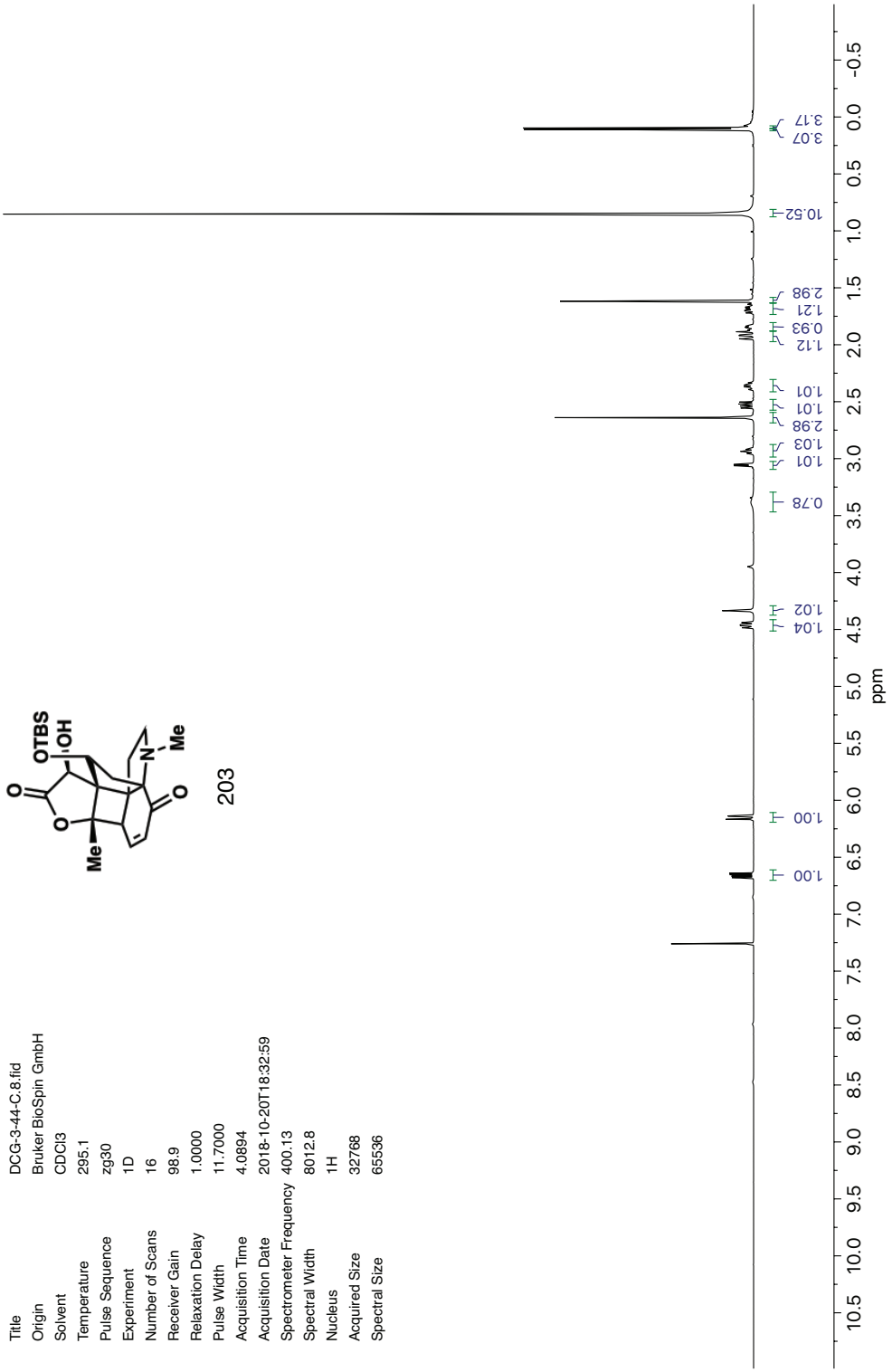
DCG-6-175-1.6.ser
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.1
Pulse Sequence
noesygpphzs
Experiment
NOESY
Number of Scans
4
Receiver Gain
78.7
Relaxation Delay
1.8000
Pulse Width
11.7000
Acquisition Time
0.2560
Acquisition Date
2018-10-18T02:02:45
Spectrometer Frequency
(400.13, 400.13)
Spectral Width
(4000.0, 4000.0)
(1H, 1H)
Nucleus
Acquired Size
(1024, 256)
Spectral Size
(1024, 1024)
OH
OTBS
OH
Me
OH
Me
202
ppm



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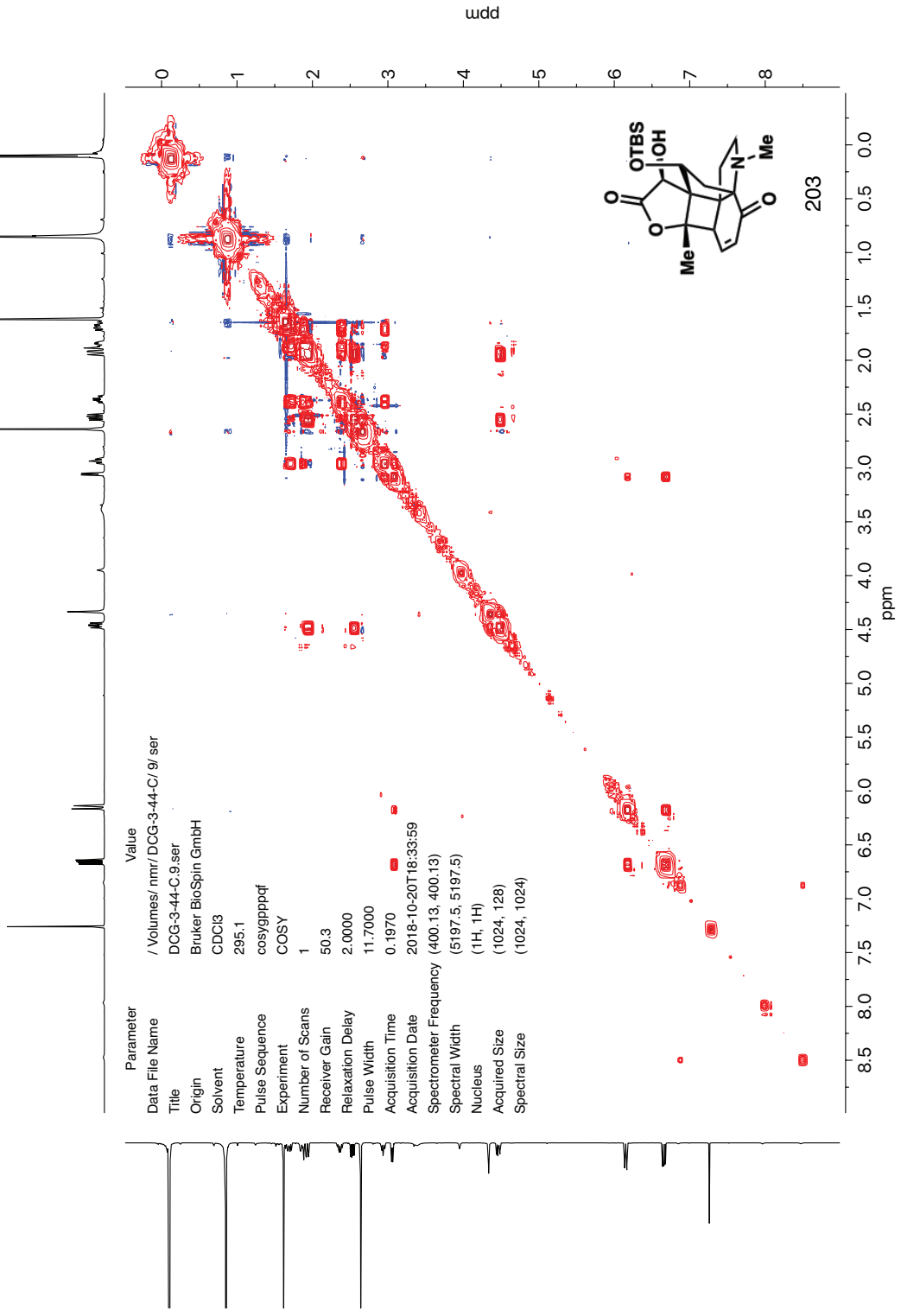
Title	DCG-3-44-C.8.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	16
Receiver Gain	98.9
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-10-20T18:32:59
Spectrometer Frequency	400.13
Spectral Width	8012.8
Nucleus	1H
Acquired Size	32768
Spectral Size	65536


ppm
ppm
OTBS
OH
Me
N
Me
O
O
O
203
Parameter Value
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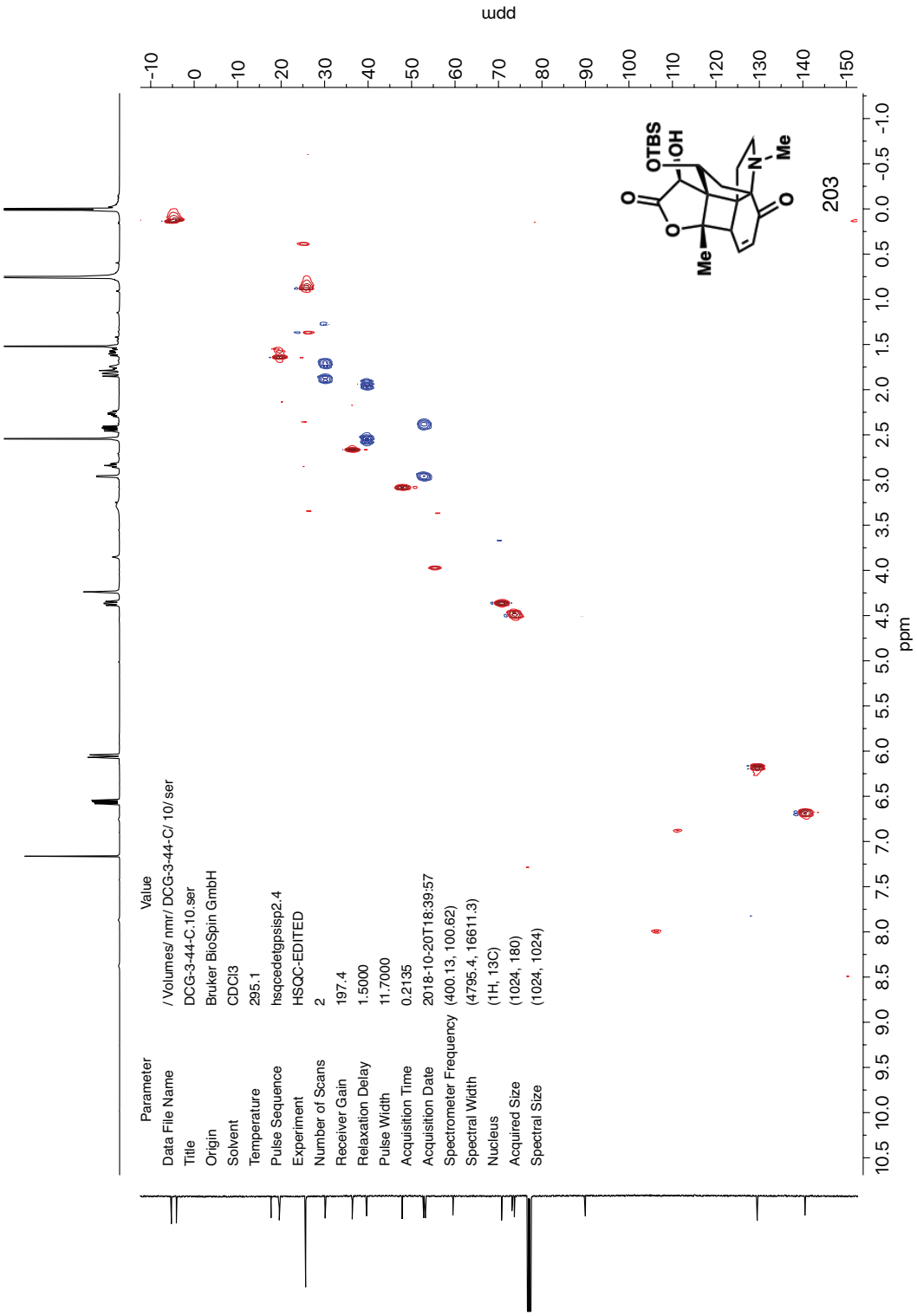
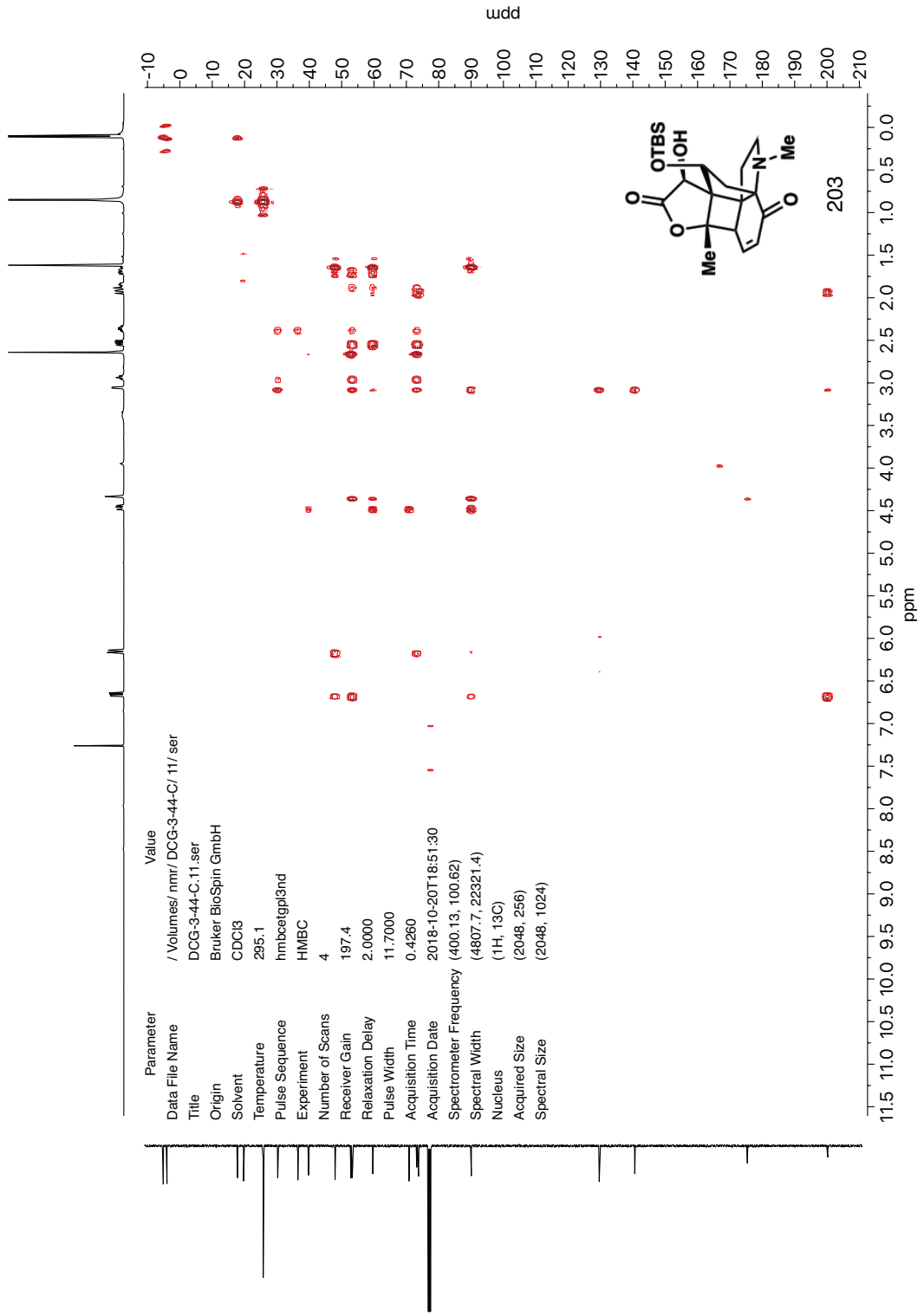
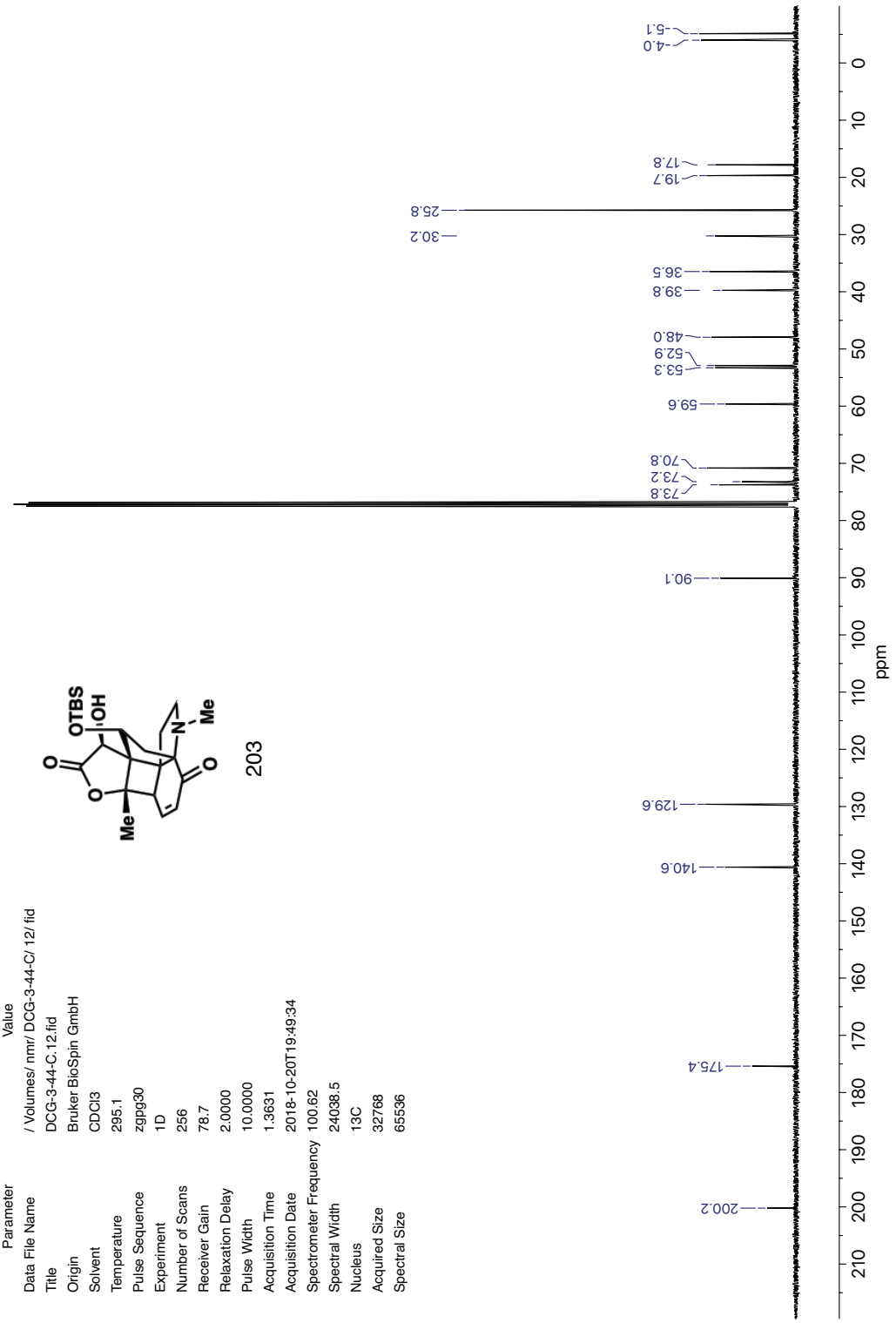
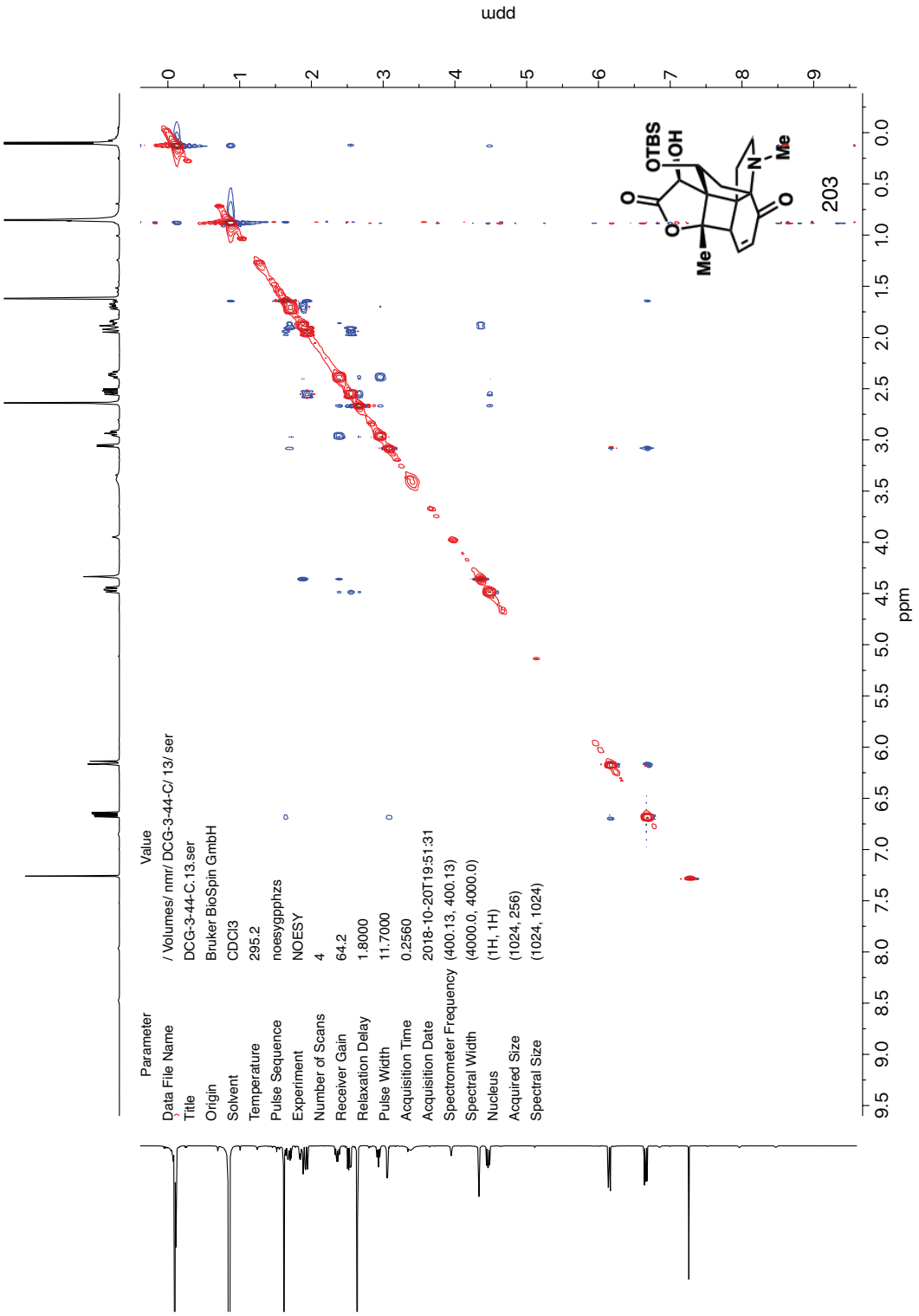
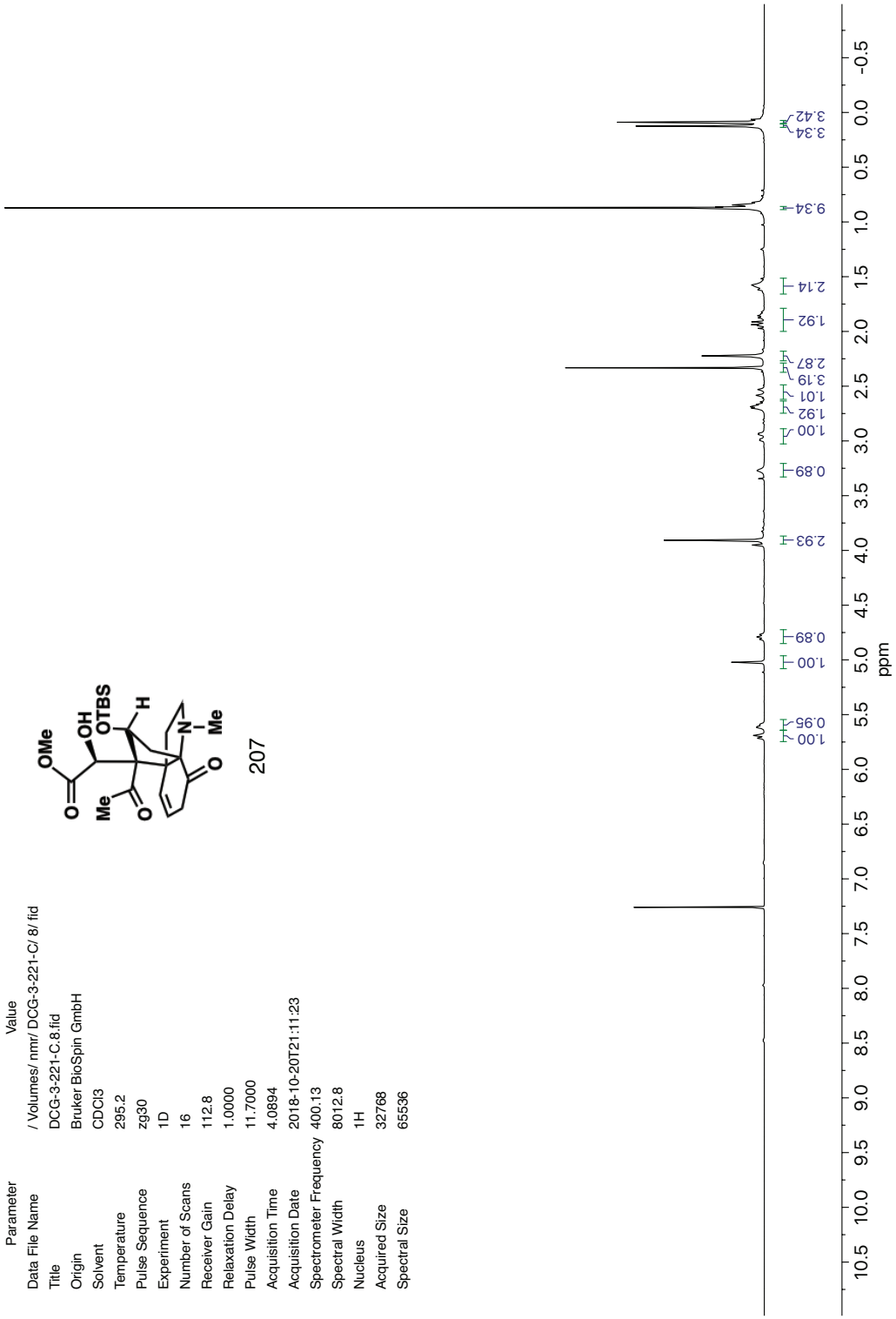
Title DCG-3-44-C.9.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 50.3
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.1970
Acquisition Date 2018-10-20T18:33:59
Spectrometer Frequency (400.13, 400.13)
Spectral Width (5197.5, 5197.5)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)


Parameter Value
Data File Name / Volumes/ nmr/ DCG-3-44-C/ 10/ ser
Title DCG-3-44-C.10.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2018-10-20T18:39:57
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 180)
Spectral Size (1024, 1024)
OTBS
OH
Me
Me
N
O
O
O
203
ppm
ppm

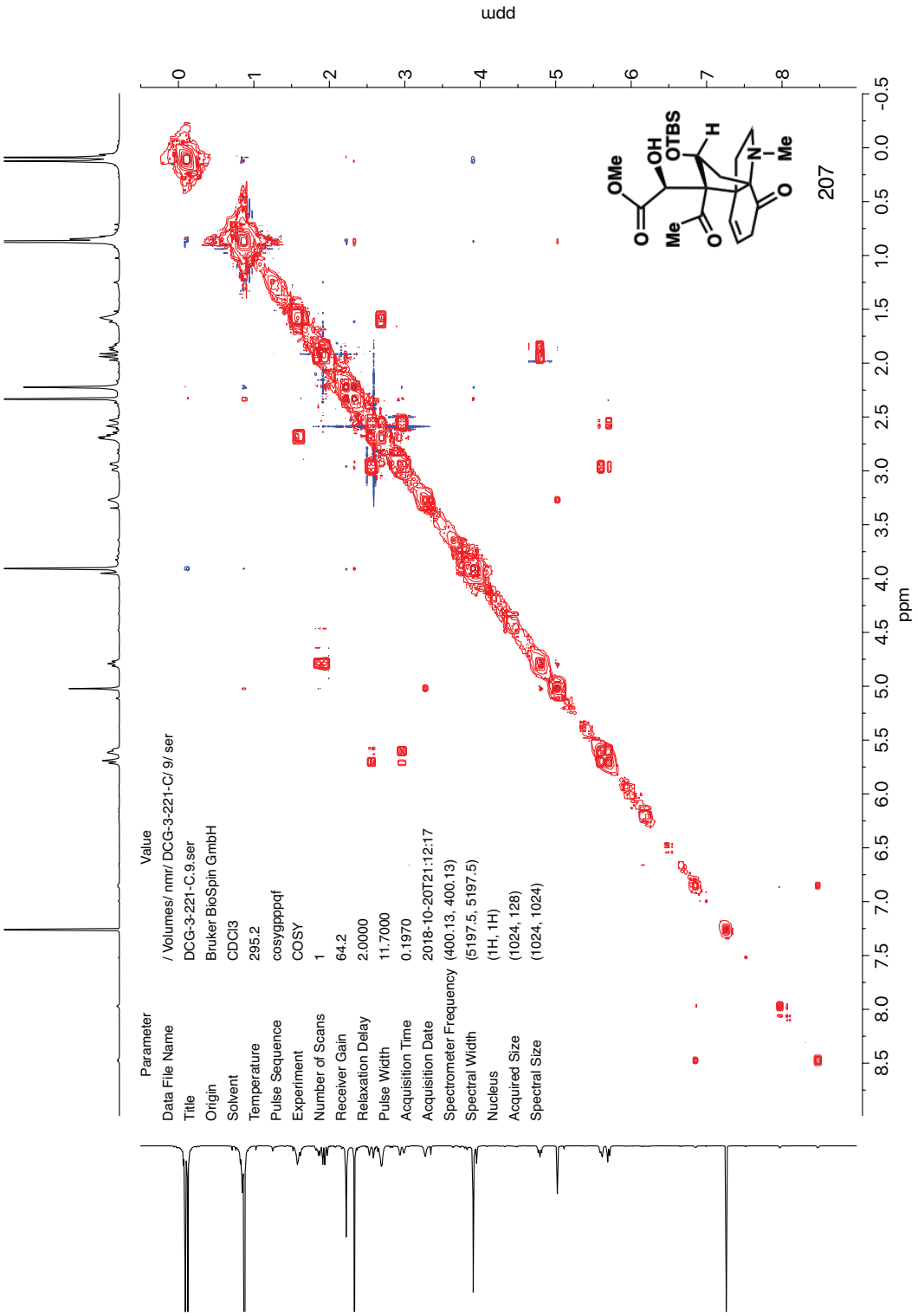

ppm
ppm
OTBS
OH
O
O
Me
N
Me
O
203
Parameter Value
Data File Name / Volumes/ nmr/ DCG-3-44-C/ 11/ ser
Title DCG-3-44-C.11.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2018-10-20T18:51:30
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)

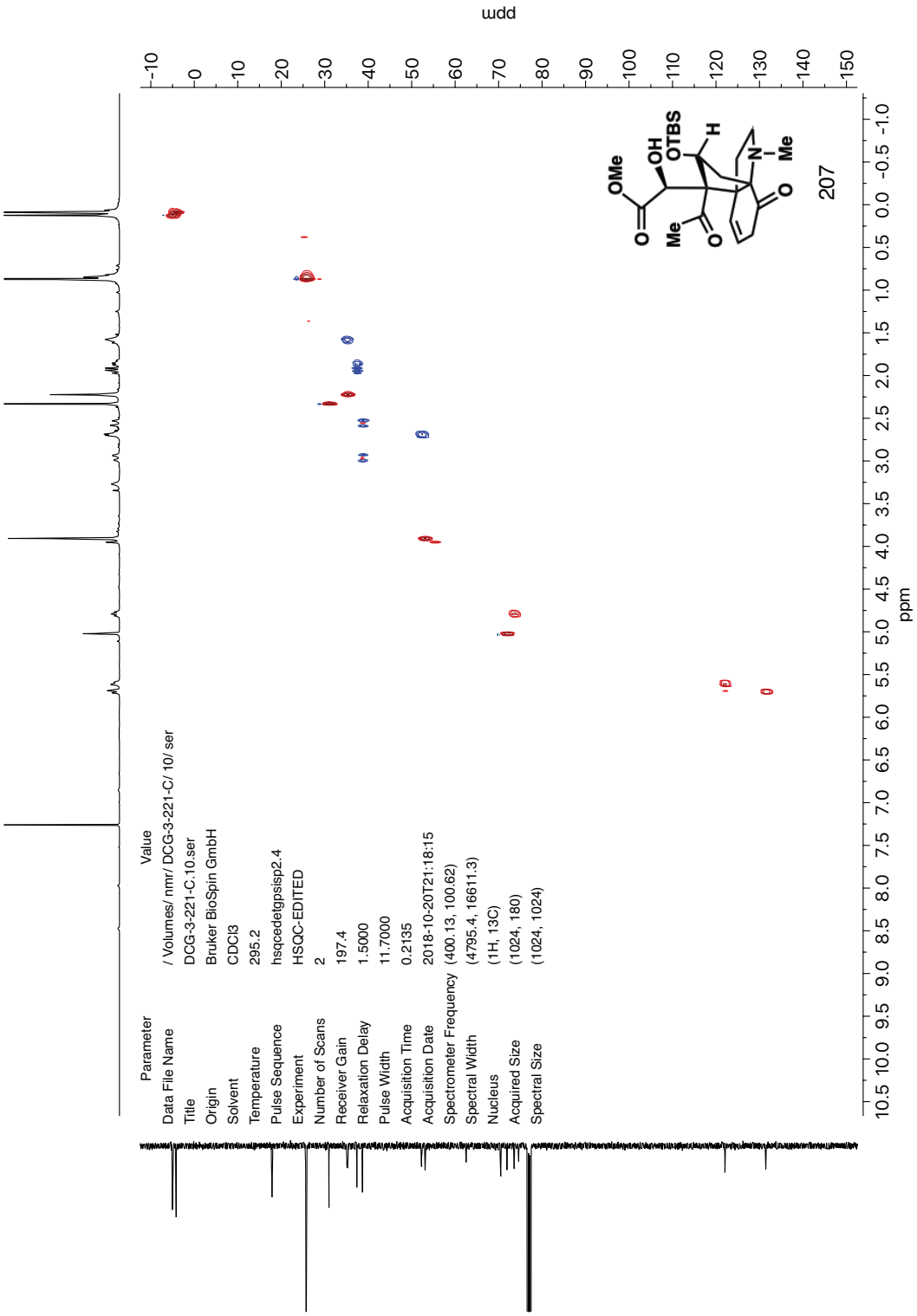

Parameter Value
Data File Name / Volumes/ nmr/ DCG-3-44-C/ 12/ fid
Title DCG-3-44-C.12.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 78.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-10-20T19:49:34
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OTBS
OH
Me
Me
O
O
O
N
203
-5.1
-4.0
17.8
19.7
25.8
30.2
36.5
39.8
48.0
52.9
53.3
59.6
70.8
73.2
73.8
90.1
129.6
140.6
175.4
200.2
ppm

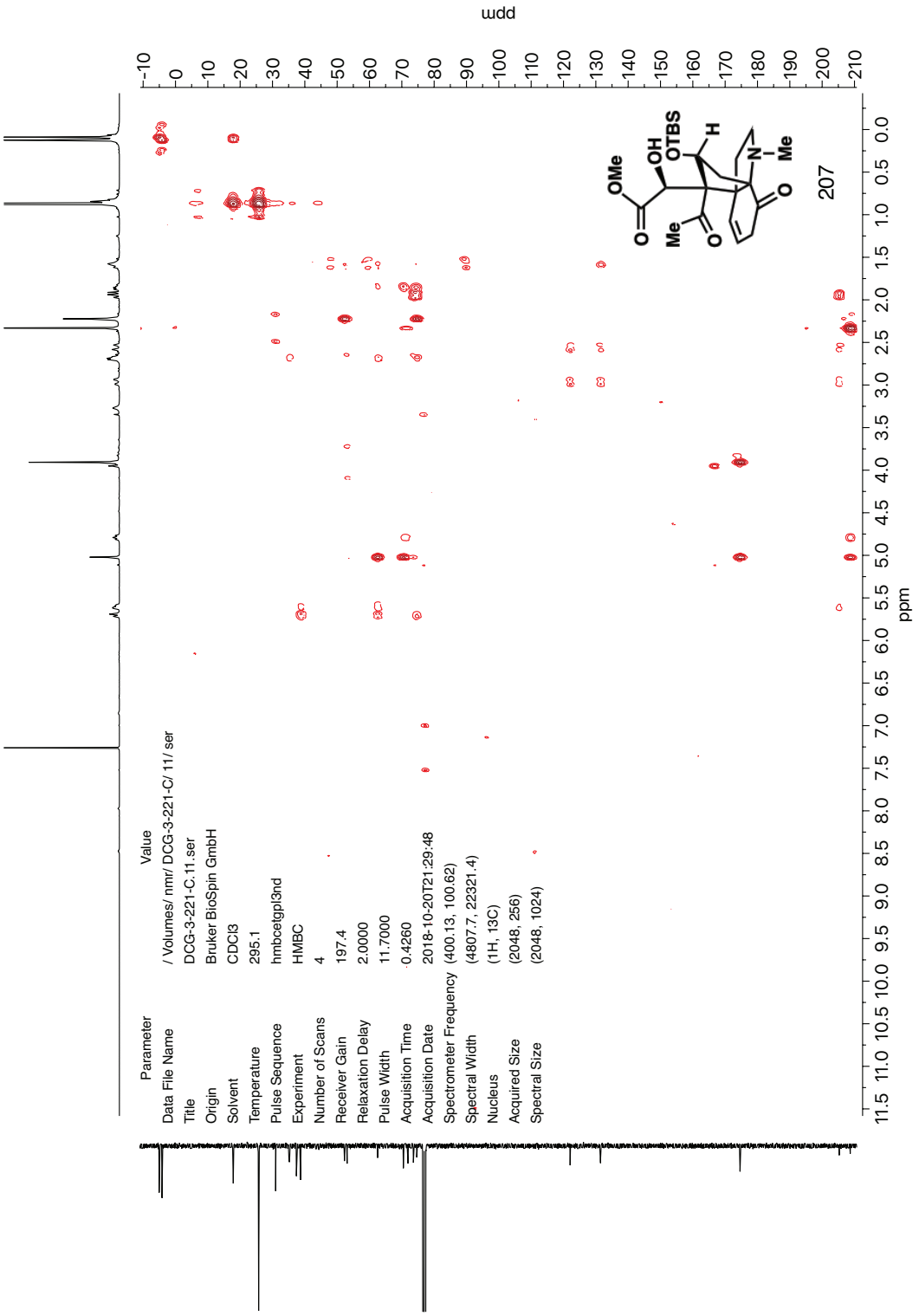

ppm
ppm
OTBS
OH
N
Me
Me
O
O
O
203
Parameter Value
Data File Name / Volumes/ nmr/ DCG-3-44-C/ 13/ ser
Title DCG-3-44-C.13.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence noesygpphzs
Experiment NOESY
Number of Scans 4
Receiver Gain 64.2
Relaxation Delay 1.8000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2018-10-20T19:51:31
Spectrometer Frequency (400.13, 400.13)
Spectral Width (4000.0, 4000.0)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)

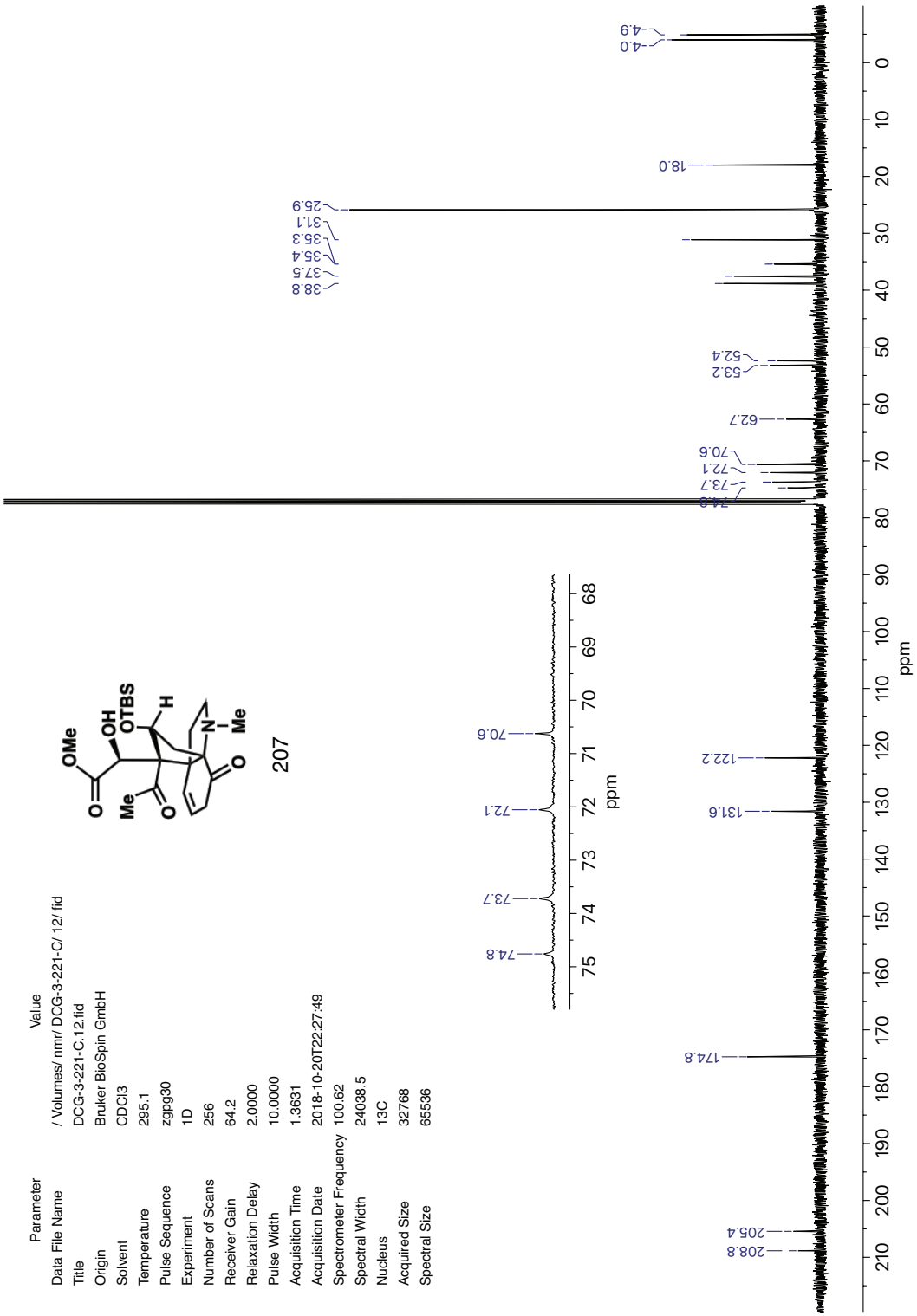


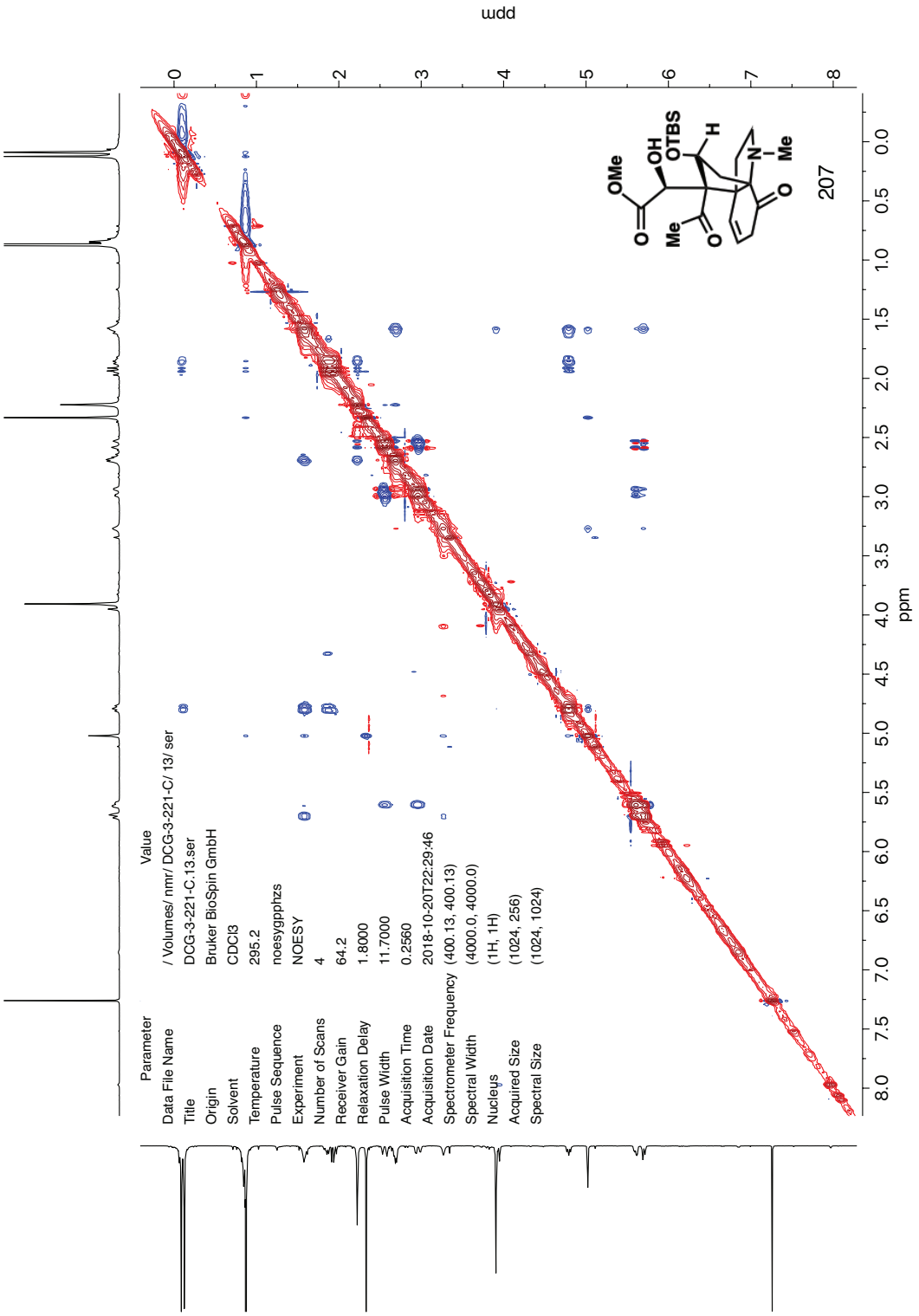
Parameter	Value
Data File Name	/ Volumes/ nmr/ DCG-3-221-C/ 8/ fid
Title	DCG-3-221-C.8.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zg30
Experiment	1D
Number of Scans	16
Receiver Gain	112.8
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-10-20T21:11:23
Spectrometer Frequency	400.13
Spectral Width	8012.8
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

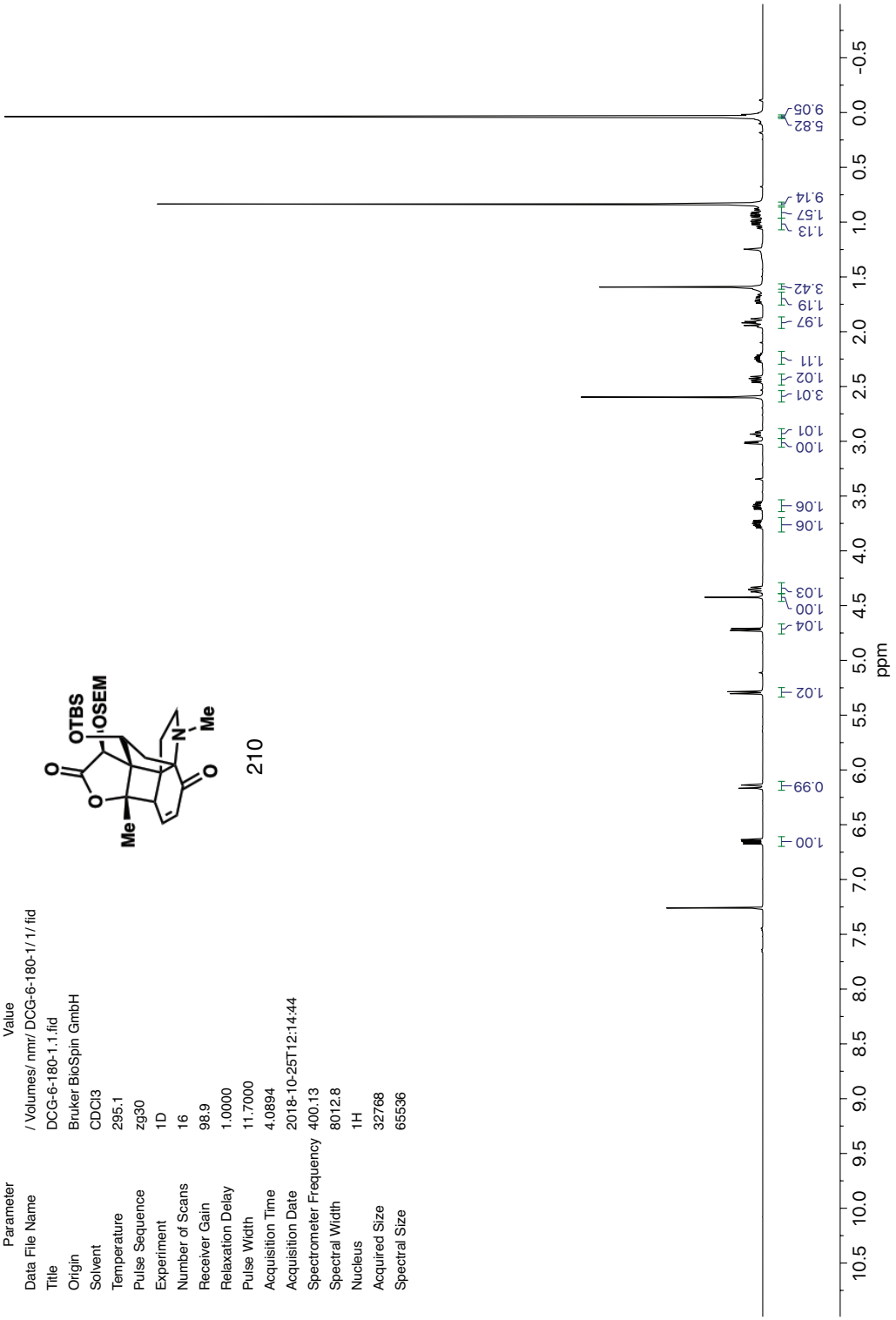

ppm
ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-3-221-C/ 9/ ser
Title DCG-3-221-C.9.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.1970
Acquisition Date 2018-10-20T21:12:17
Spectrometer Frequency (400.13, 400.13)
Spectral Width (5197.5, 5197.5)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)
OMe
OH
OTBS
H
Me
N
Me
O
O
O
207


Parameter Value
Data File Name / Volumes/ nmr/ DCG-3-221-C/ 10/ ser
Title DCG-3-221-C.10.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2018-10-20T21:18:15
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 180)
Spectral Size (1024, 1024)
ppm
ppm
OMe
OH
OTBS
H
Me
N
Me
O
O
O
207

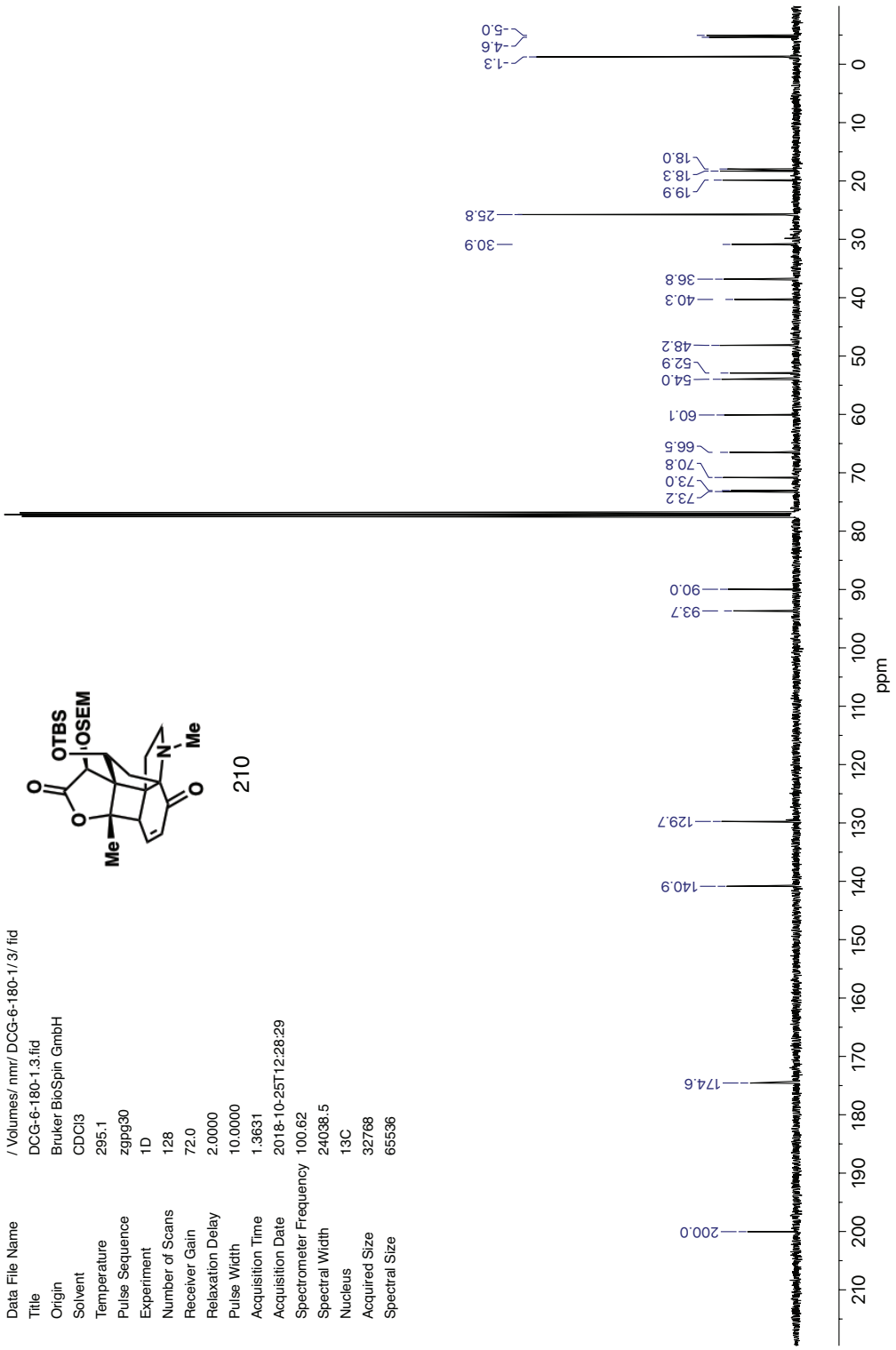

ppm
ppm
OMe
OH
OTBS
H
Me
O
O
N
Me
O
207
Parameter Value
Data File Name / Volumes/ nmr/ DCG-3-221-C/ 11/ ser
Title DCG-3-221-C.11.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2018-10-20T21:29:48
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)

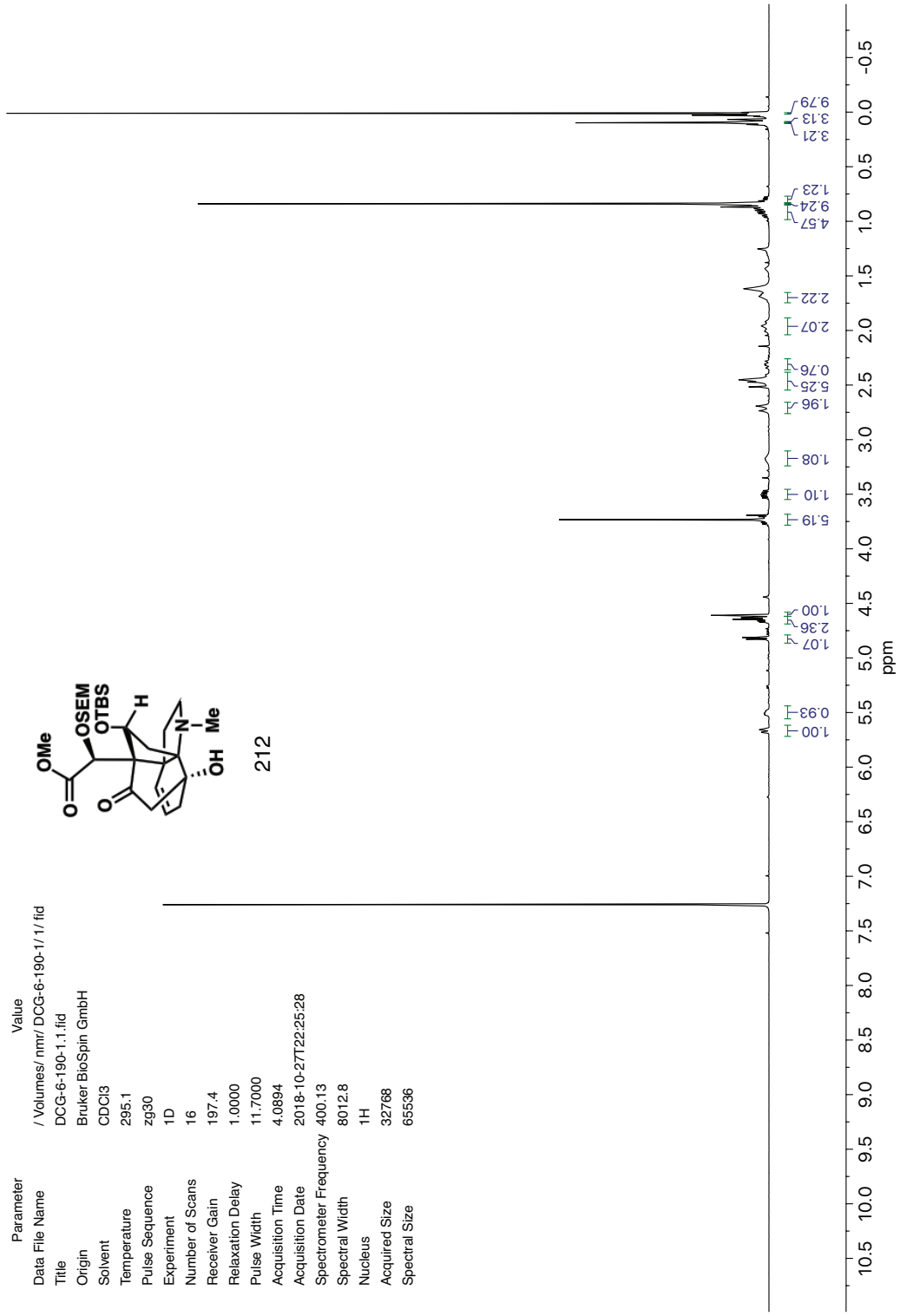

Parameter Value
Data File Name / Volumes/ nmr/ DCG-3-221-C/ 12/ fid
Title DCG-3-221-C.12.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-10-20T22:27:49
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OMe
OH
OTBS
H
N
Me
Me
O
O
O
207
ppm
ppm


ppm
ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-3-221-C/ 13/ ser
Title DCG-3-221-C.13.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence noesygpphzs
Experiment NOESY
Number of Scans 4
Receiver Gain 64.2
Relaxation Delay 1.8000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2018-10-20T22:29:46
Spectrometer Frequency (400.13, 400.13)
Spectral Width (4000.0, 4000.0)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
OMe
OH
OTBS
H
Me
Me
N
O
O
O
207

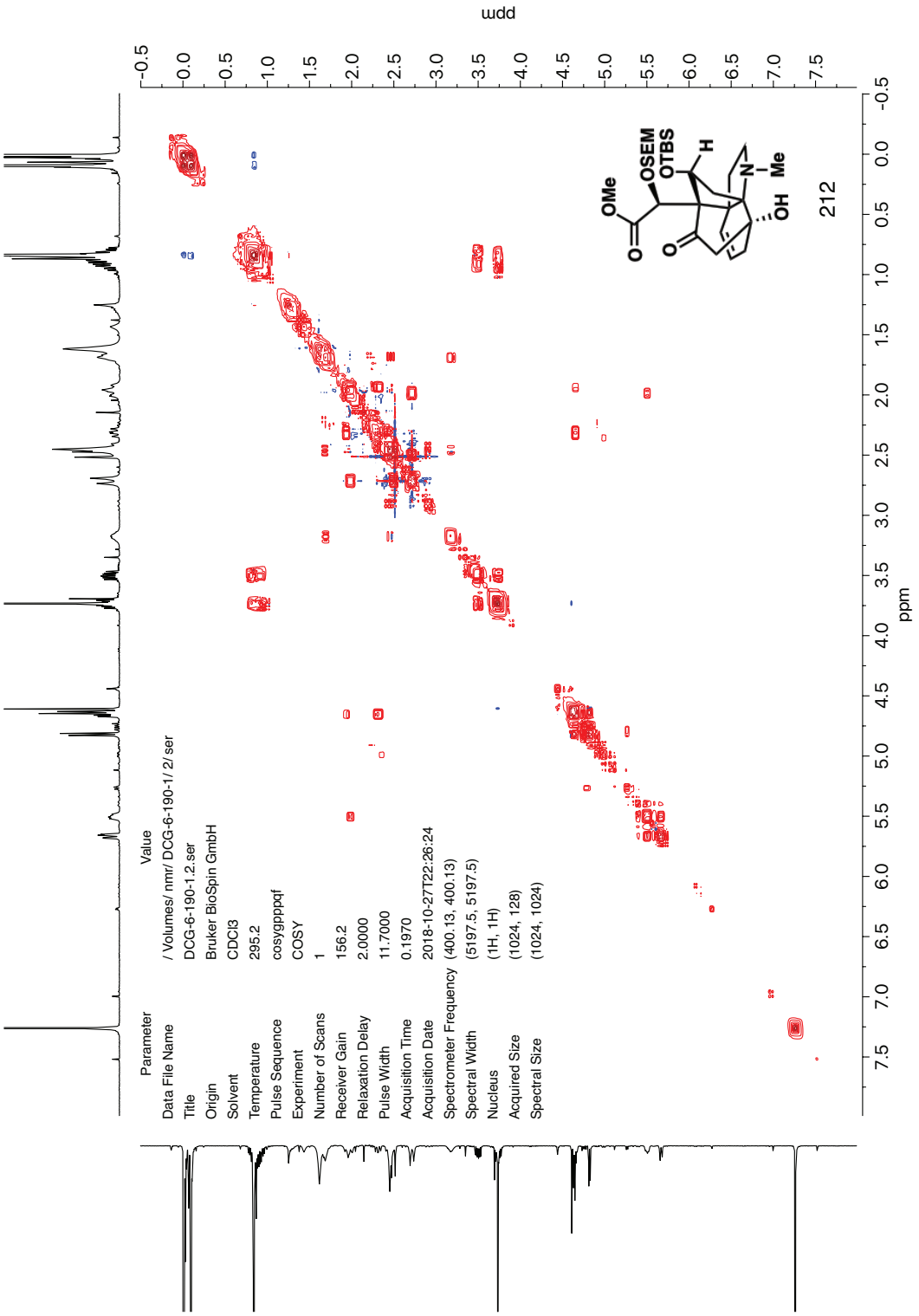


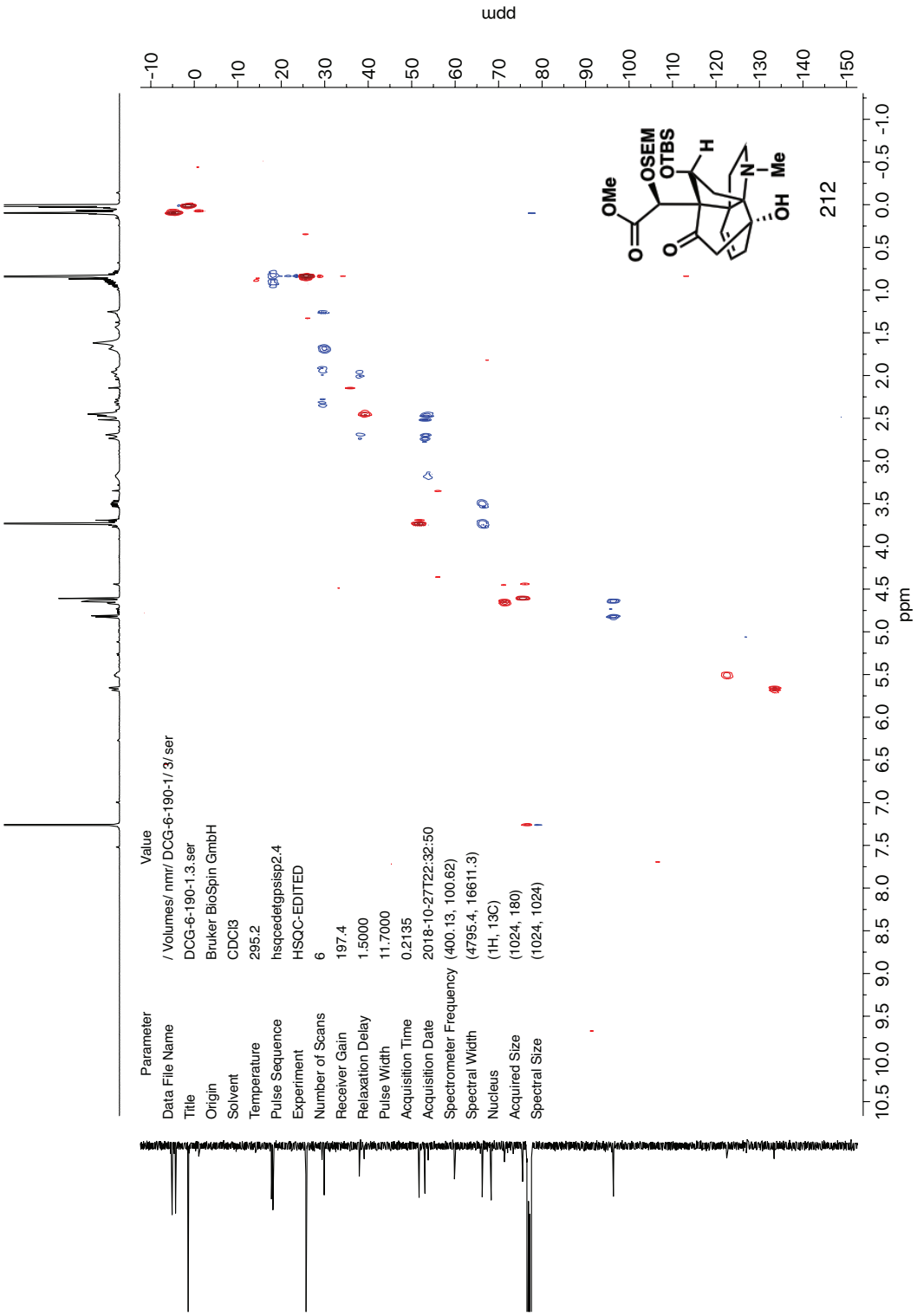
Parameter	Value
Data File Name	/ Volumes/ nmr/ DCG-6-180-1/ 1/ fid
Title	DCG-6-180-1.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	16
Receiver Gain	98.9
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-10-25T12:14:44
Spectrometer Frequency	400.13
Spectral Width	8012.8
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

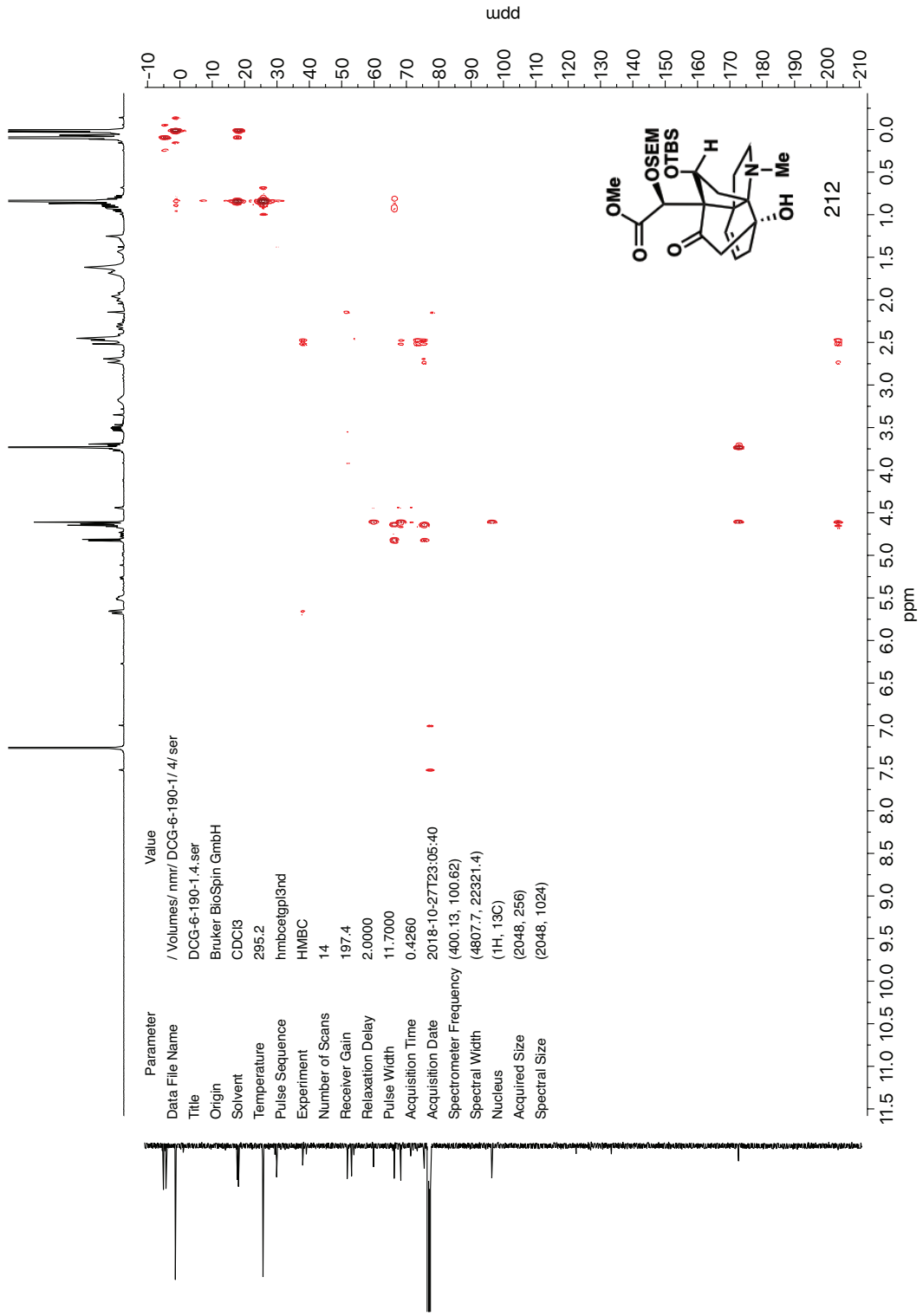

Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-180-1/3/ fid
Title DCG-6-180-1.3.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 128
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-10-25T12:28:29
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OTBS
OSEM
Me
N
Me
O
O
O
210
-1.3
-4.6
-5.0
18.0
18.3
19.9
25.8
30.9
36.8
40.3
48.2
52.9
54.0
60.1
66.5
70.8
73.0
73.2
90.0
93.7
129.7
140.9
174.6
200.0
ppm

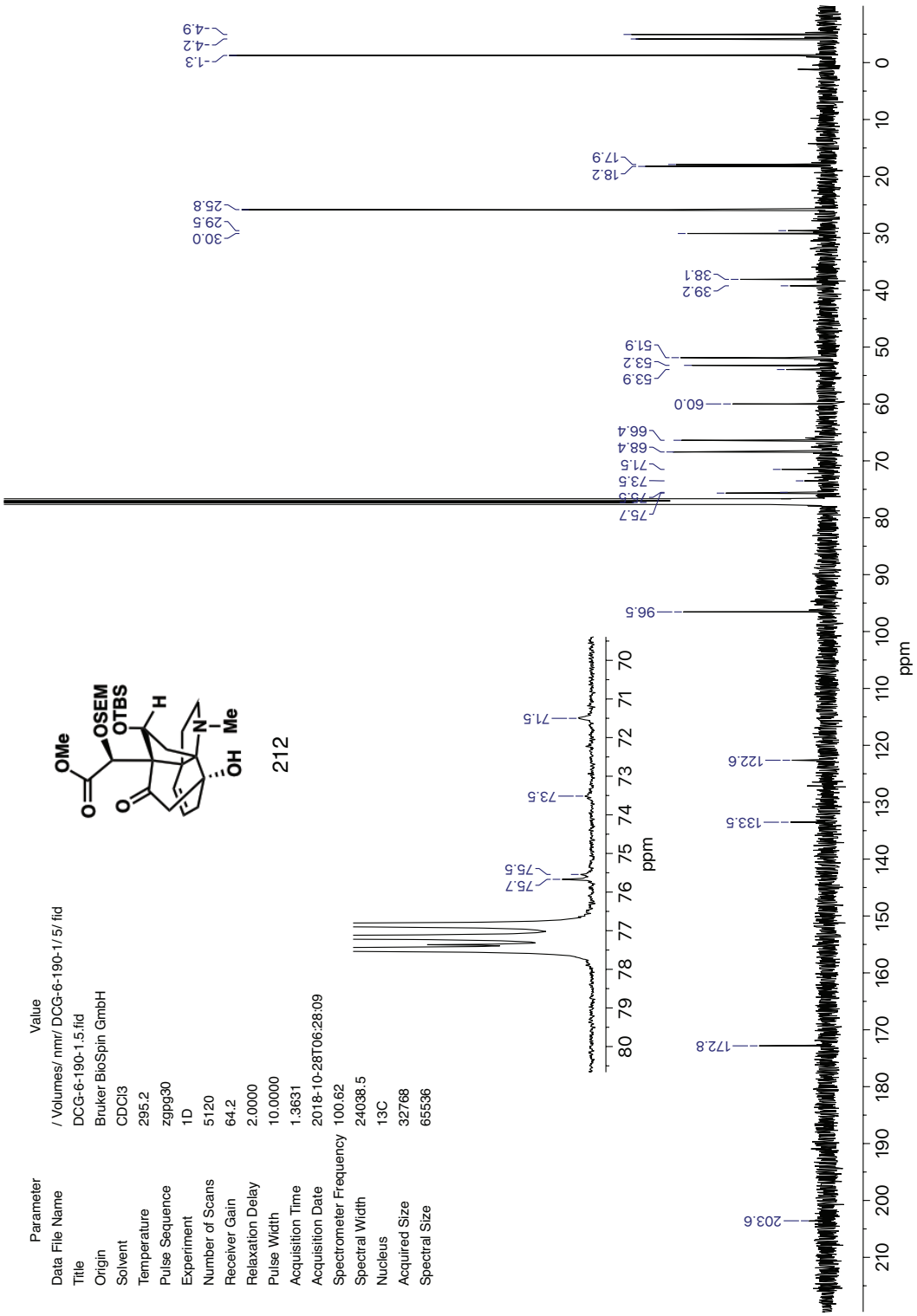


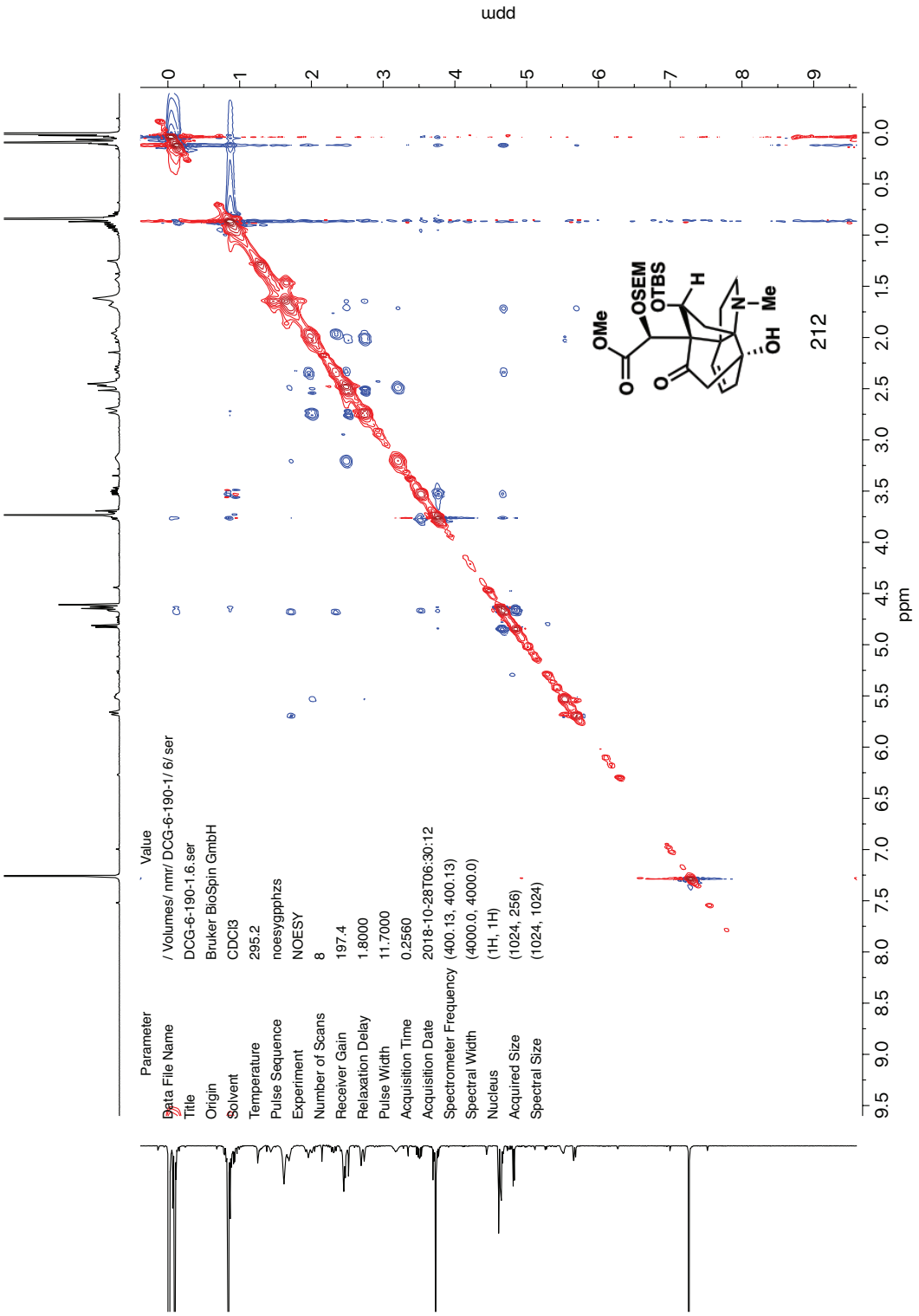
Parameter	Value
Data File Name	/ Volumes/ nmr/ DCG-6-190-1/ 1/ fid
Title	DCG-6-190-1.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	16
Receiver Gain	197.4
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-10-27T22:25:28
Spectrometer Frequency	400.13
Spectral Width	8012.8
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

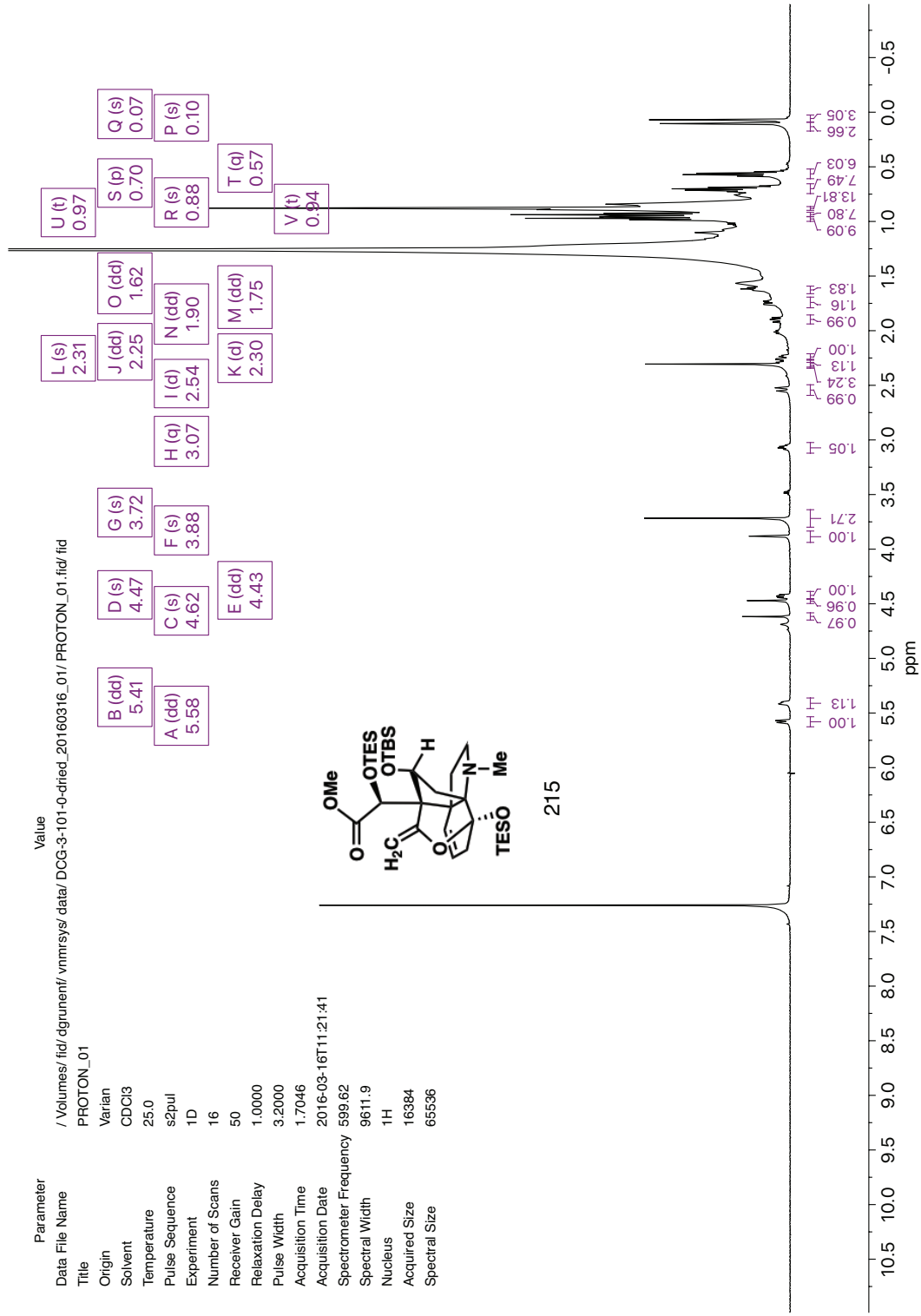

ppm
OMe
OSEM
OTBS
H
N
Me
OH
O
O
212
Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-190-1/ 2/ ser
Title DCG-6-190-1.2.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 156.2
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.1970
Acquisition Date 2018-10-27T22:26:24
Spectrometer Frequency (400.13, 400.13)
Spectral Width (5197.5, 5197.5)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)

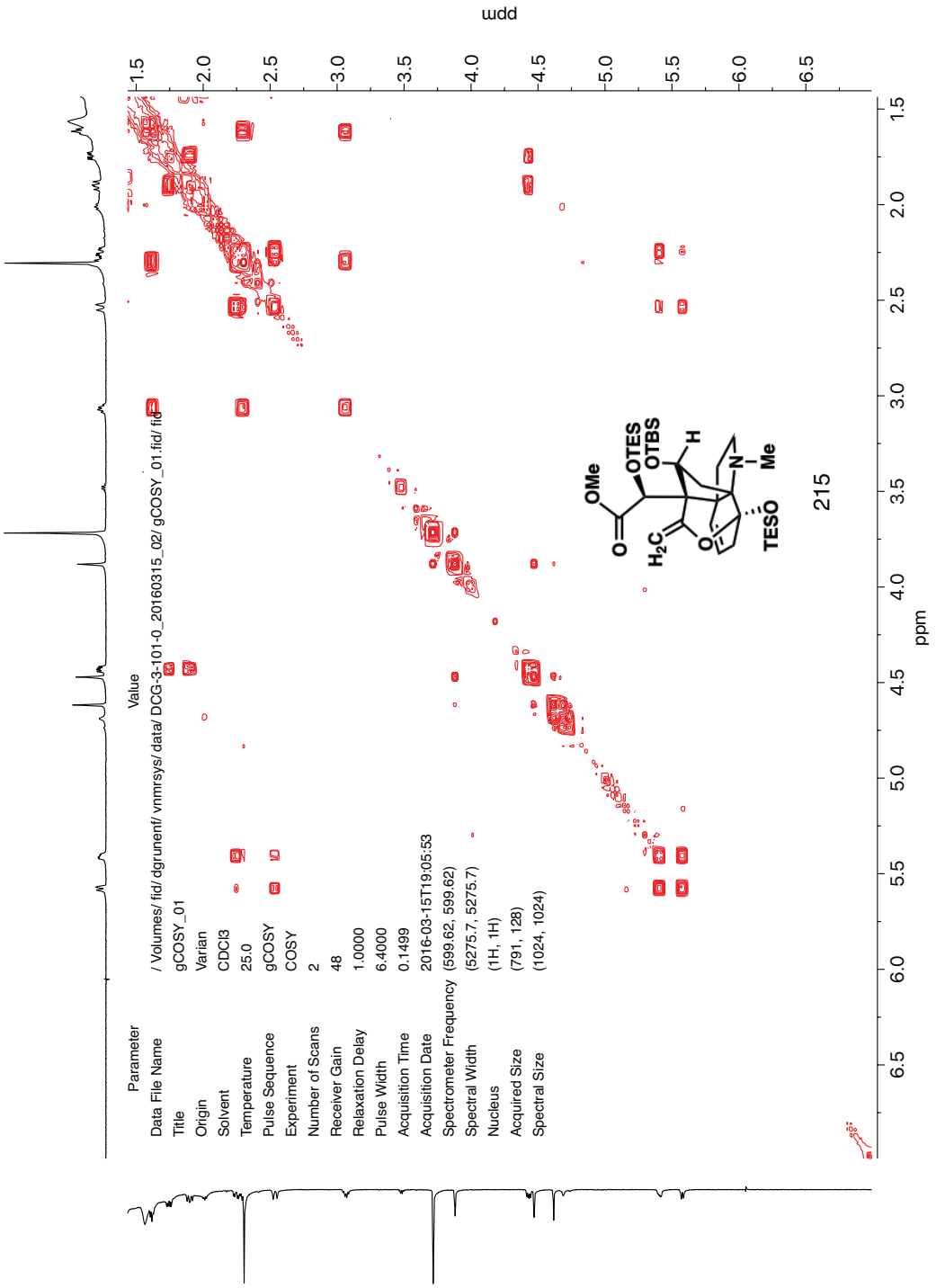

Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-190-1/ 3/ ser
Title DCG-6-190-1.3.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 6
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2018-10-27T22:32:50
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 180)
Spectral Size (1024, 1024)
OMe
OSEM
OTBS
H
N
Me
OH
O
O
212
ppm
ppm

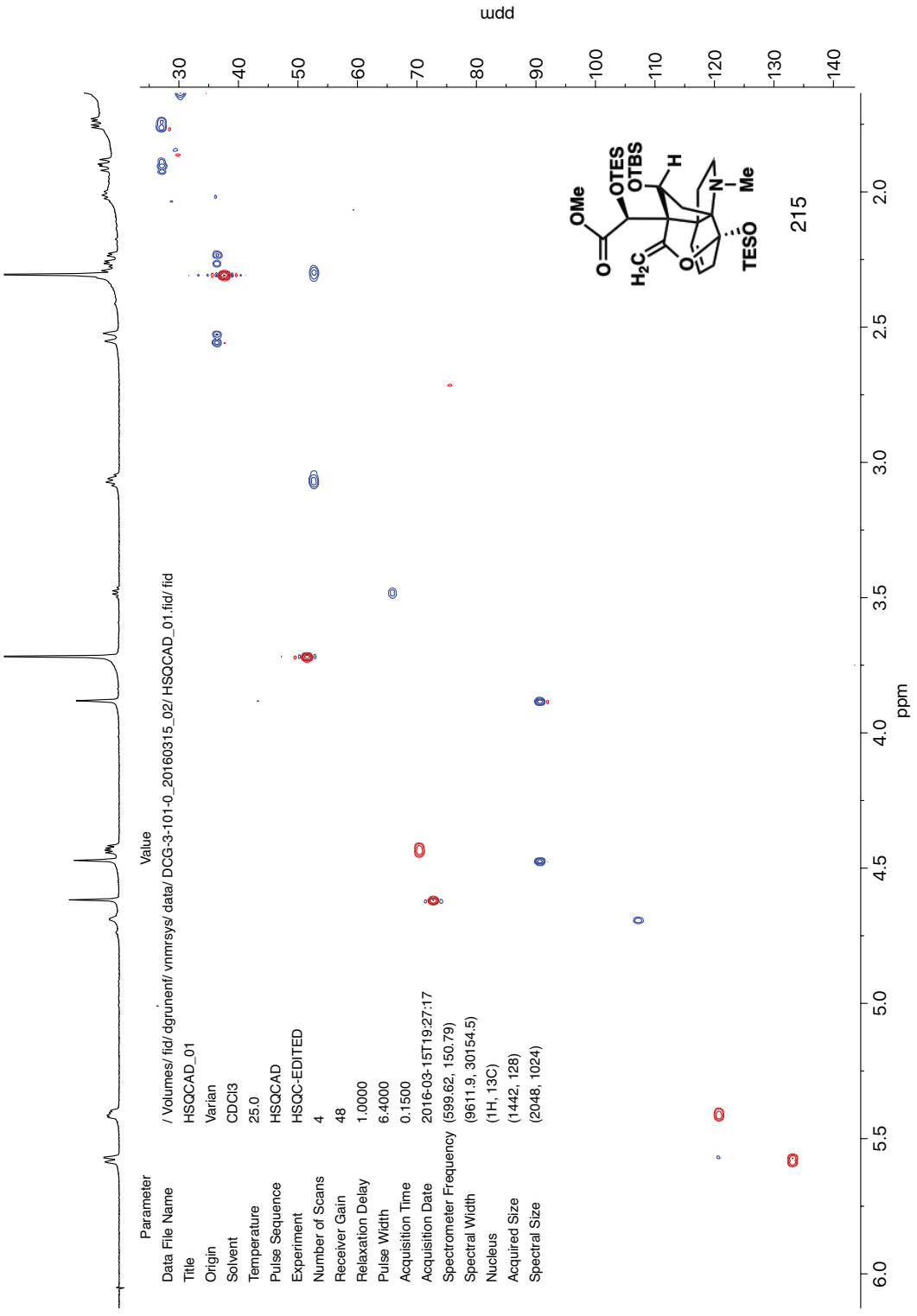

ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-190-1/ 4/ ser
Title DCG-6-190-1.4.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 14
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2018-10-27T23:05:40
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
OMe
OSEM
OTBS
H
N
Me
OH
O
O
212
ppm


Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-190-1/5/ fid
Title DCG-6-190-1.5.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 5120
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-10-28T06:28:09
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OMe
OSEM
OTBS
H
N
Me
OH
O
O
212
ppm


ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-190-1/ 6/ ser
Title DCG-6-190-1.6.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence noesygpphzs
Experiment NOESY
Number of Scans 8
Receiver Gain 197.4
Relaxation Delay 1.8000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2018-10-28T06:30:12
Spectrometer Frequency (400.13, 400.13)
Spectral Width (4000.0, 4000.0)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
OMe
OSEM
OTBS
H
N
Me
OH
O
212
ppm


Parameter
Value
Data File Name / Volumes/ fid/ dgrunenf/ vnmrsys/ data/ DCG-3-101-0-dried_20160316_01/ PROTON_01.fid/ fid
Title PROTON_01
Origin Varian
Solvent CDCl3
Temperature 25.0
Pulse Sequence s2pul
Experiment 1D
Number of Scans 16
Receiver Gain 50
Relaxation Delay 1.0000
Pulse Width 3.2000
Acquisition Time 1.7046
Acquisition Date 2016-03-16T11:21:41
Spectrometer Frequency 599.62
Spectral Width 9611.9
Nucleus 1H
Acquired Size 16384
Spectral Size 65536
A (dd) 5.58
B (dd) 5.41
C (s) 4.62
D (s) 4.47
E (dd) 4.43
F (s) 3.88
G (s) 3.72
H (q) 3.07
I (d) 2.54
J (dd) 2.25
K (d) 2.30
L (s) 2.31
M (dd) 1.75
N (dd) 1.90
O (dd) 1.62
P (s) 0.10
Q (s) 0.07
R (s) 0.88
S (p) 0.70
T (q) 0.57
U (t) 0.97
V (t) 0.94
OMe
OTES
OTBS
H
H2C
O
N
Me
TESO
215
ppm


Parameter
Value
Data File Name
/ Volumes/ fid/ dgrunenf/ vnmrsys/ data/ DCG-3-101-0_20160315_02/ gCOSY_01.fid/ fid
Title
gCOSY_01
Origin
Varian
Solvent
CDCl3
Temperature
25.0
Pulse Sequence
gCOSY
Experiment
COSY
Number of Scans
2
Receiver Gain
48
Relaxation Delay
1.0000
Pulse Width
6.4000
Acquisition Time
0.1499
Acquisition Date
2016-03-15T19:05:53
Spectrometer Frequency
(599.62, 599.62)
Spectral Width
(5275.7, 5275.7)
Nucleus
(1H, 1H)
Acquired Size
(791, 128)
Spectral Size
(1024, 1024)
ppm
OMe
OTES
OTBS
H
H2C
N
Me
TESO
215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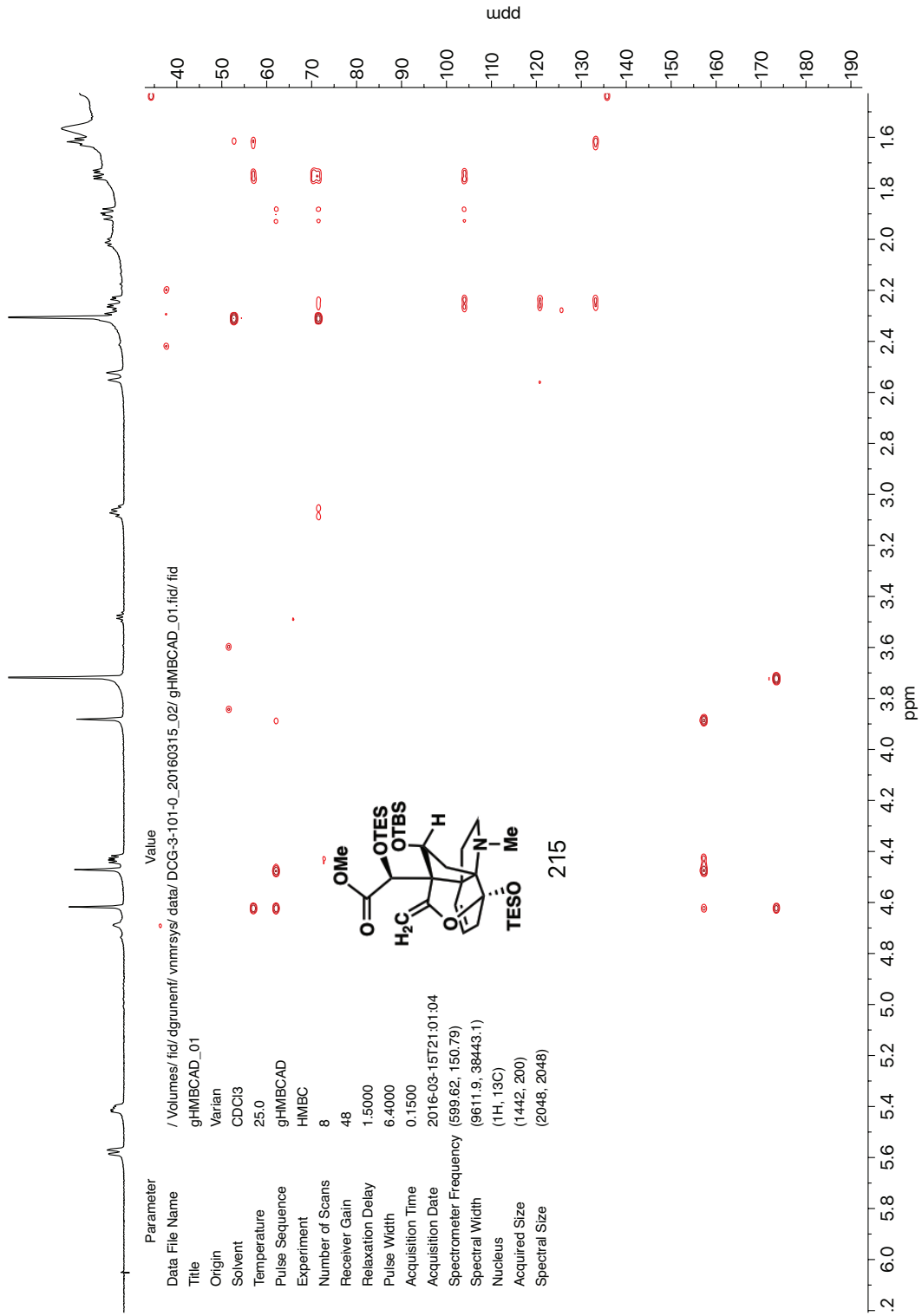
Value
Data File Name / Volumes/ fid/ dgrunenf/ vnmrsys/ data/ DCG-3-101-0_20160315_02/ HSQCAD_01.fid/ fid
Title HSQCAD_01
Origin Varian
Solvent CDCl3
Temperature 25.0
Pulse Sequence HSQCAD
Experiment HSQC-EDITED
Number of Scans 4
Receiver Gain 48
Relaxation Delay 1.0000
Pulse Width 6.4000
Acquisition Time 0.1500
Acquisition Date 2016-03-15T19:27:17
Spectrometer Frequency (599.62, 150.79)
Spectral Width (9611.9, 30154.5)
Nucleus (1H, 13C)
Acquired Size (1442, 128)
Spectral Size (2048, 1024)
ppm
ppm
OMe
OTES
OTBS
H
N
Me
TESO
H2C
O
215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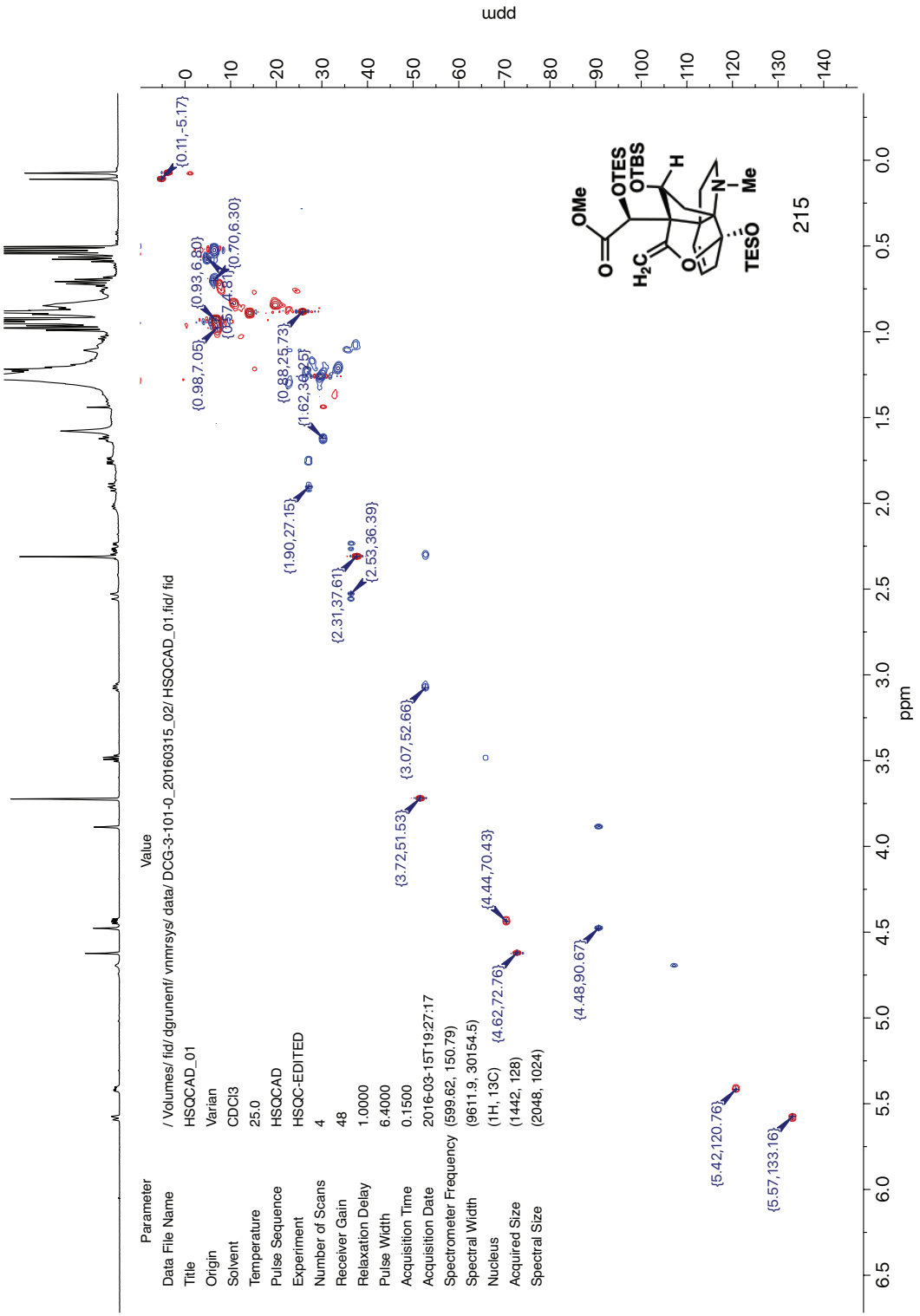
Data File Name
/ Volumes/ fid/ dgrunenf/ vnmrsys/ data/ DCG-3-101-0_20160315_02/ gHMBCAD_01.fid/ fid
Title
gHMBCAD_01
Origin
Varian
Solvent
CDCl3
Temperature
25.0
Pulse Sequence
gHMBCAD
Experiment
HMBC
Number of Scans
8
Receiver Gain
48
Relaxation Delay
1.5000
Pulse Width
6.4000
Acquisition Time
0.1500
Acquisition Date
2016-03-15T21:01:04
Spectrometer Frequency
(599.62, 150.79)
Spectral Width
(9611.9, 38443.1)
Nucleus
(1H, 13C)
Acquired Size
(1442, 200)
Spectral Size
(2048, 2048)
OMe
OTES
OTBS
H
H2C
O
O
N
Me
TESO
215
ppm
ppm


ppm
ppm
{0.11,-5.17}
{0.98,7.05}
{0.93,6.80}
{0.70,6.30}
{1.90,27.15}
{2.31,37.61}
{2.53,36.39}
{3.72,51.53}
{3.07,52.66}
{4.44,70.43}
{4.62,72.76}
{4.48,90.67}
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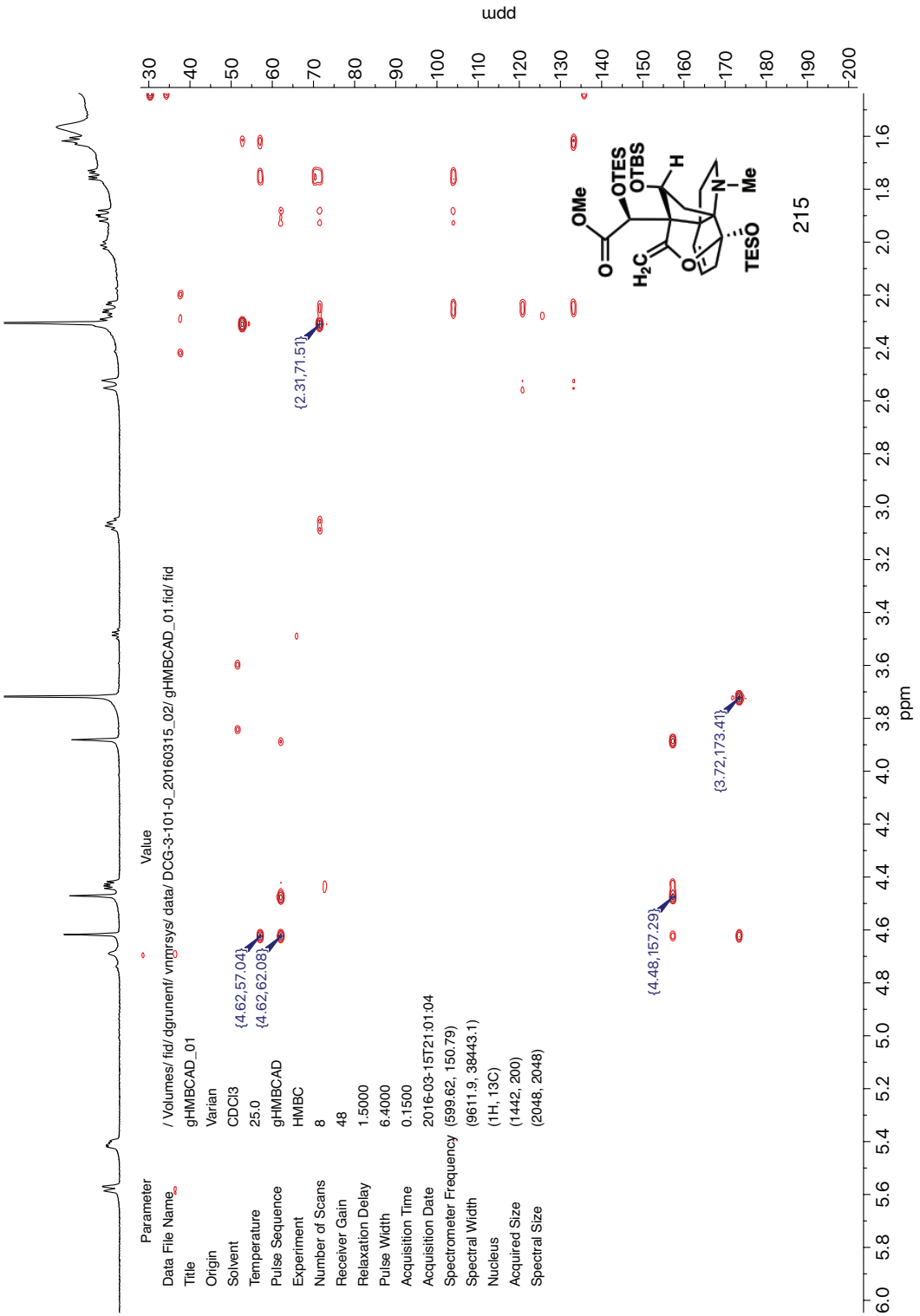
OMe
OTES
OTBS
H
N
Me
TESO
O
H2C
215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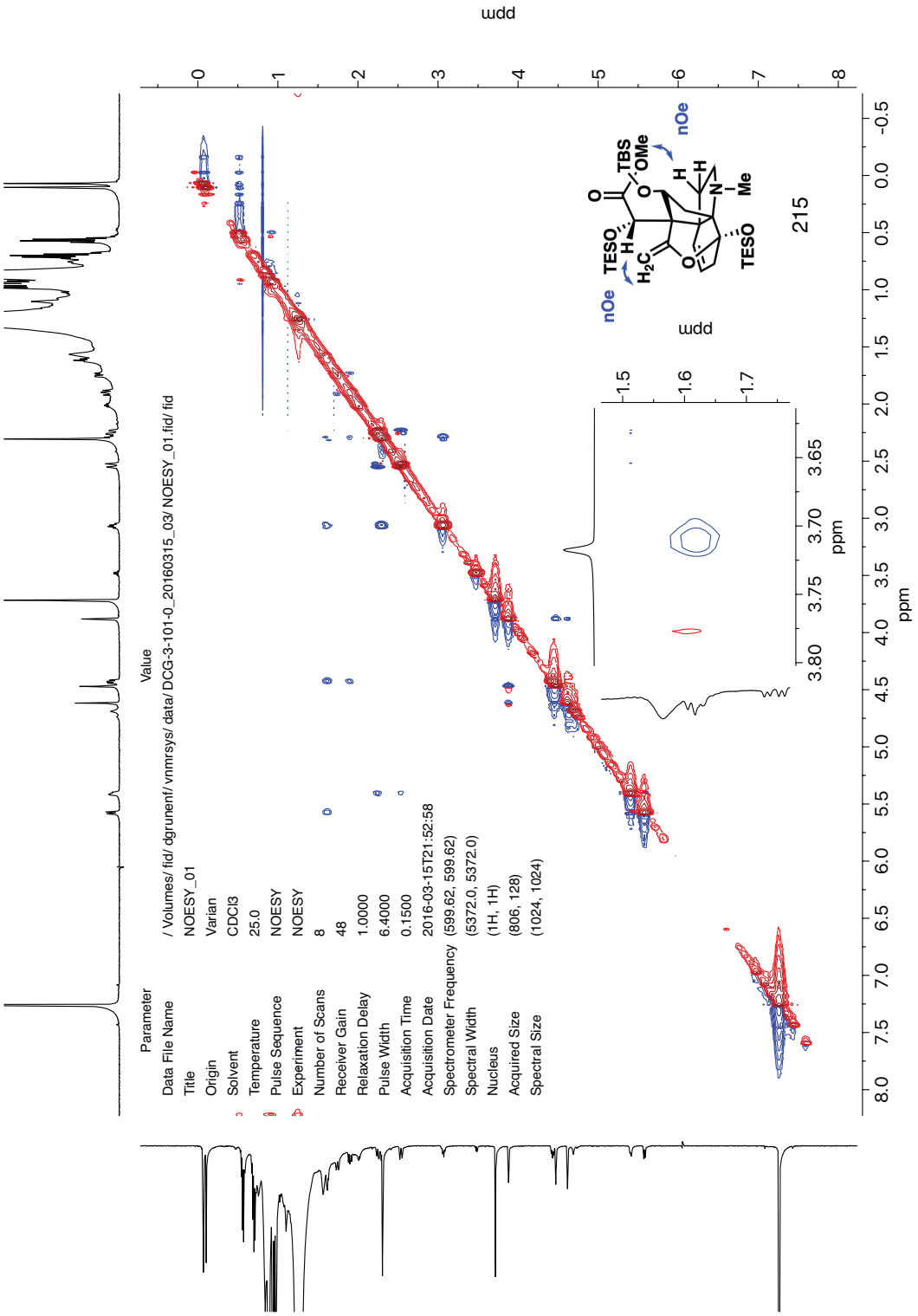
Value
Data File Name
/ Volumes/ fid/ dgrunenf/ vnmrsys/ data/ DCG-3-101-0_20160315_02/ gHMBCAD_01.fid/ fid
Title
gHMBCAD_01
Origin
Varian
Solvent
CDCl3
Temperature
25.0
Pulse Sequence
gHMBCAD
Experiment
HMBC
Number of Scans
8
Receiver Gain
48
Relaxation Delay
1.5000
Pulse Width
6.4000
Acquisition Time
0.1500
Acquisition Date
2016-03-15T21:01:04
Spectrometer Frequency
(599.62, 150.79)
Spectral Width
(9611.9, 38443.1)
Nucleus
(1H, 13C)
Acquired Size
(1442, 200)
Spectral Size
(2048, 2048)
{4.62,57.04}
{4.62,62.08}
{2.31,71.51}
{4.48,157.29}
{3.72,173.41}
OMe
OTES
OTBS
H
H2C
O
N
Me
TESO
215
ppm
ppm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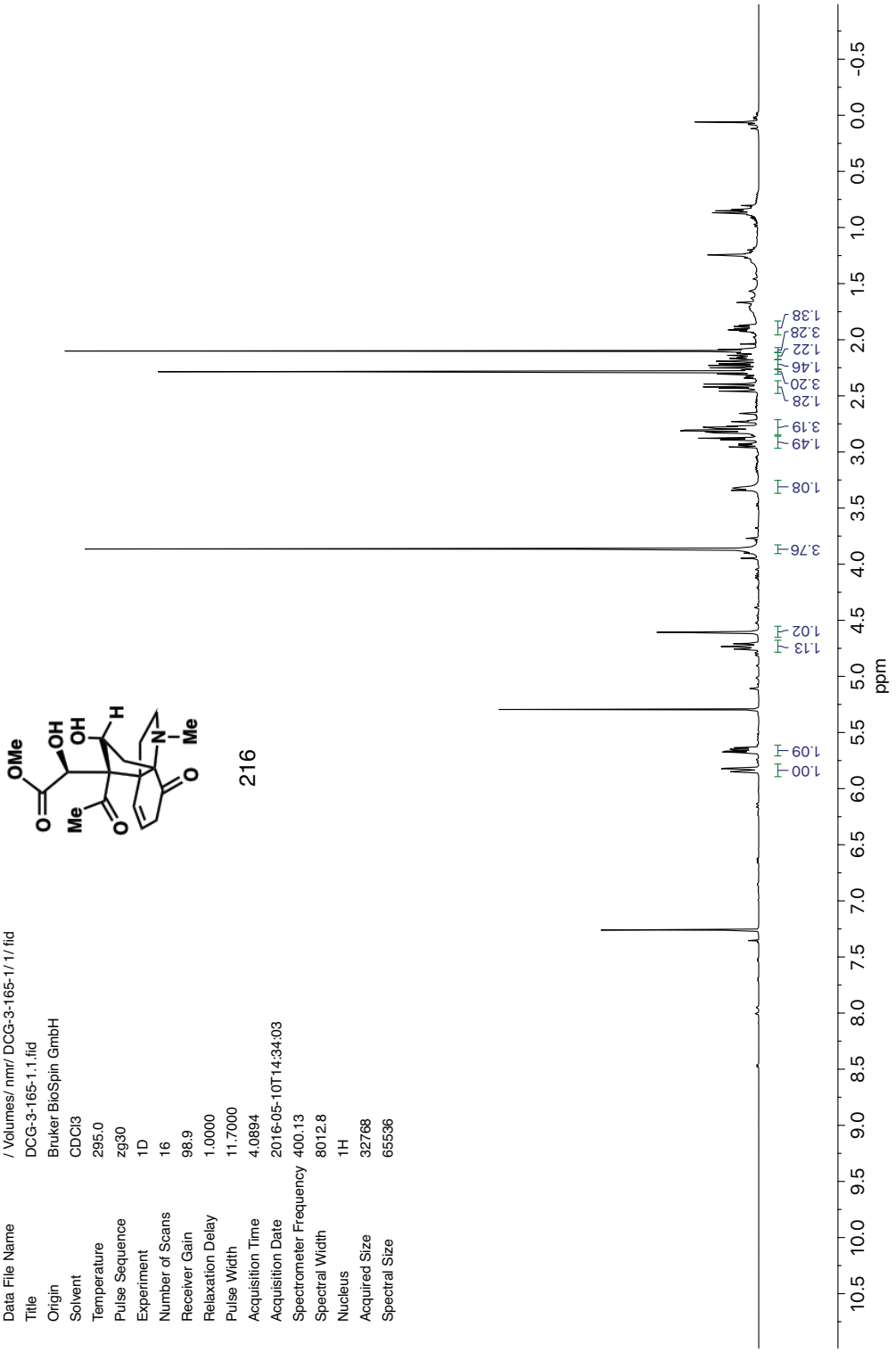
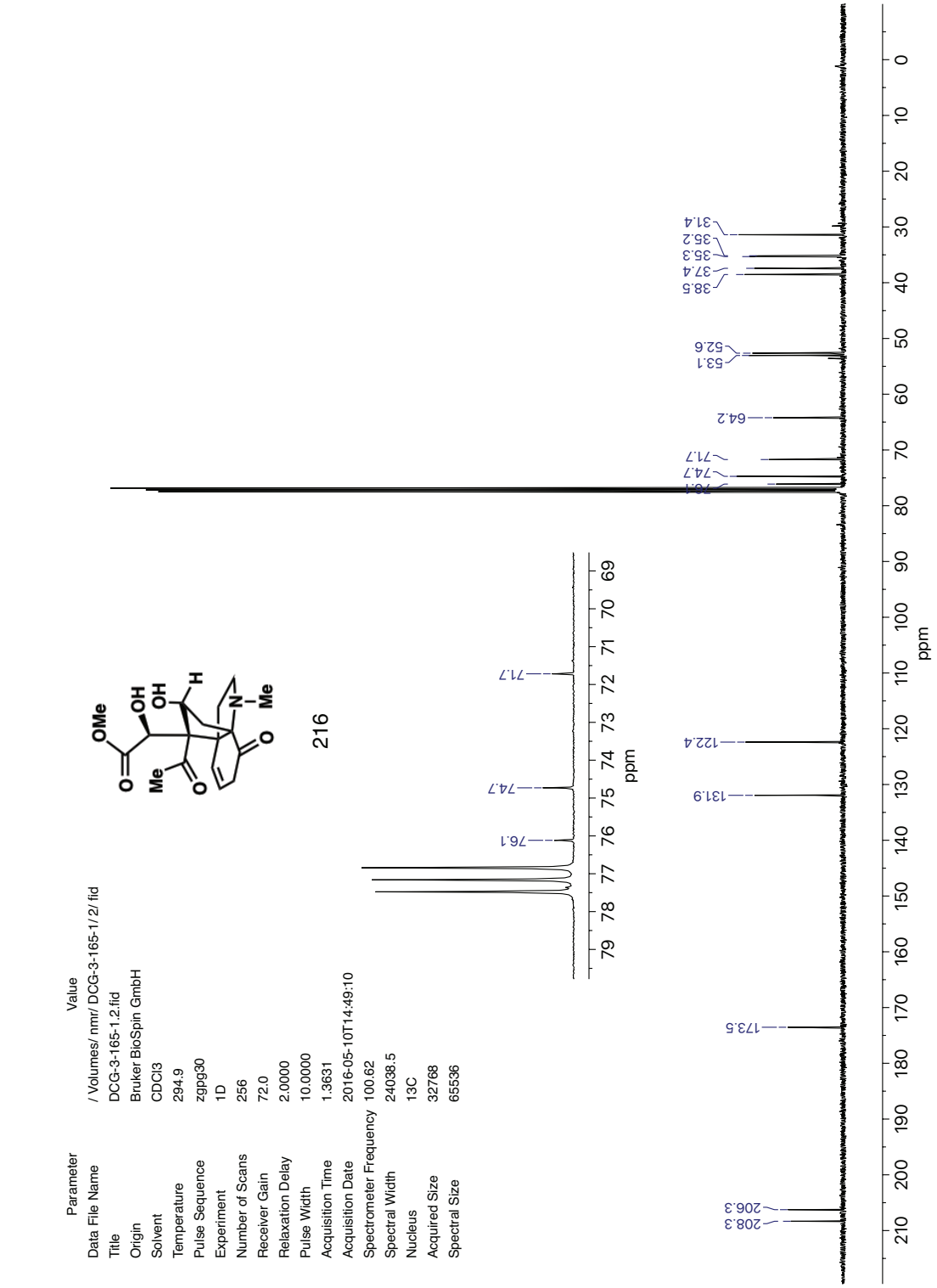
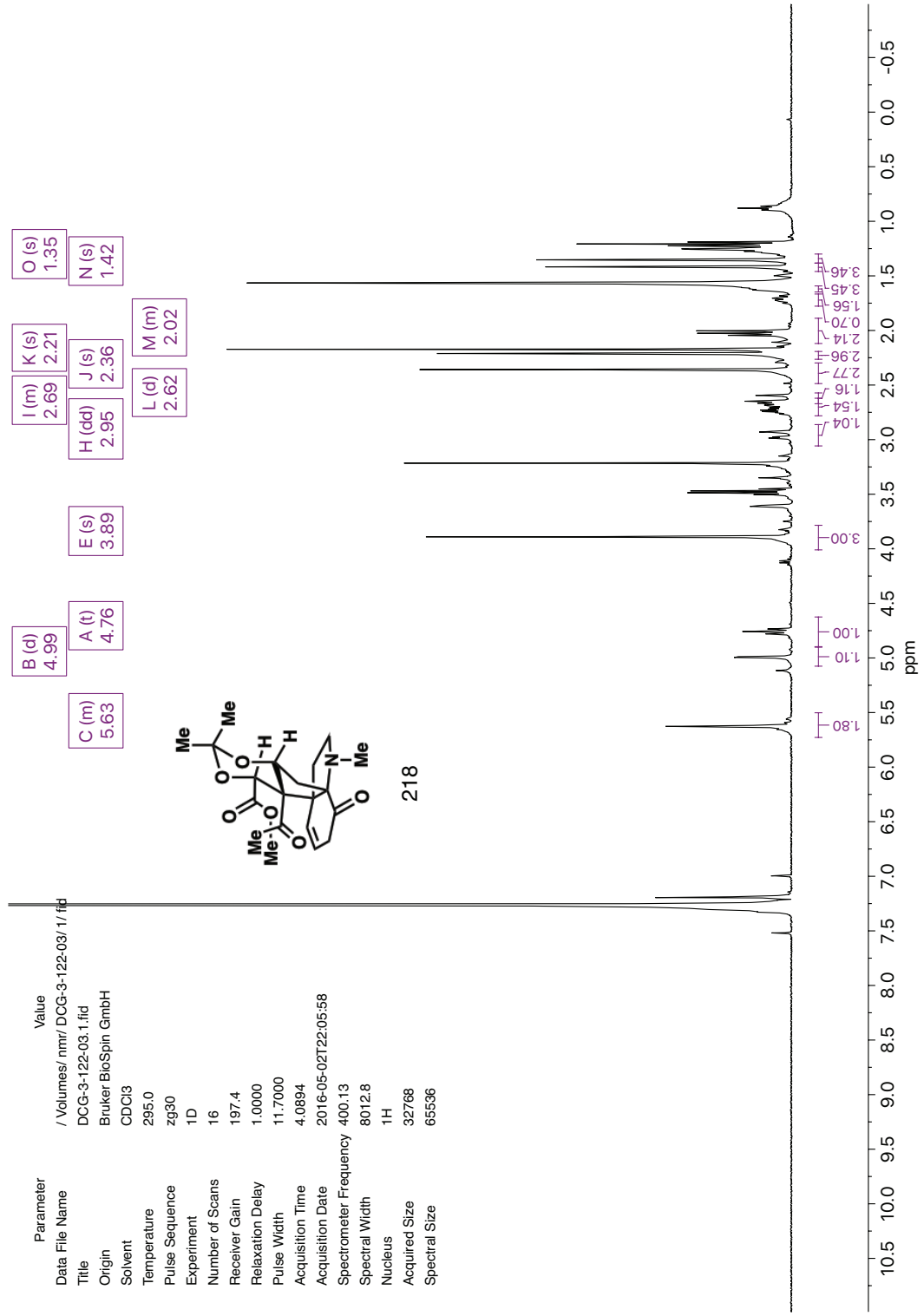
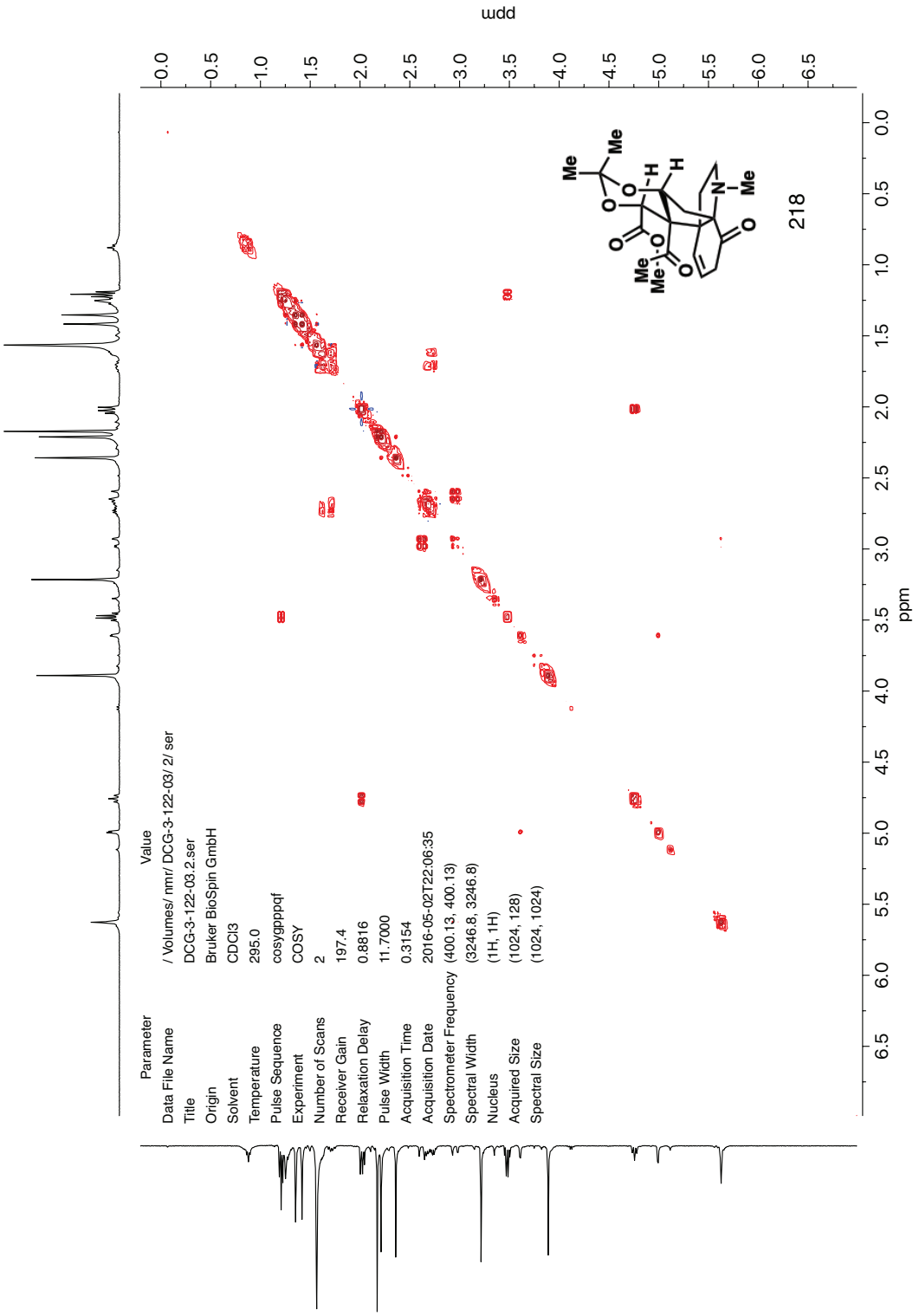
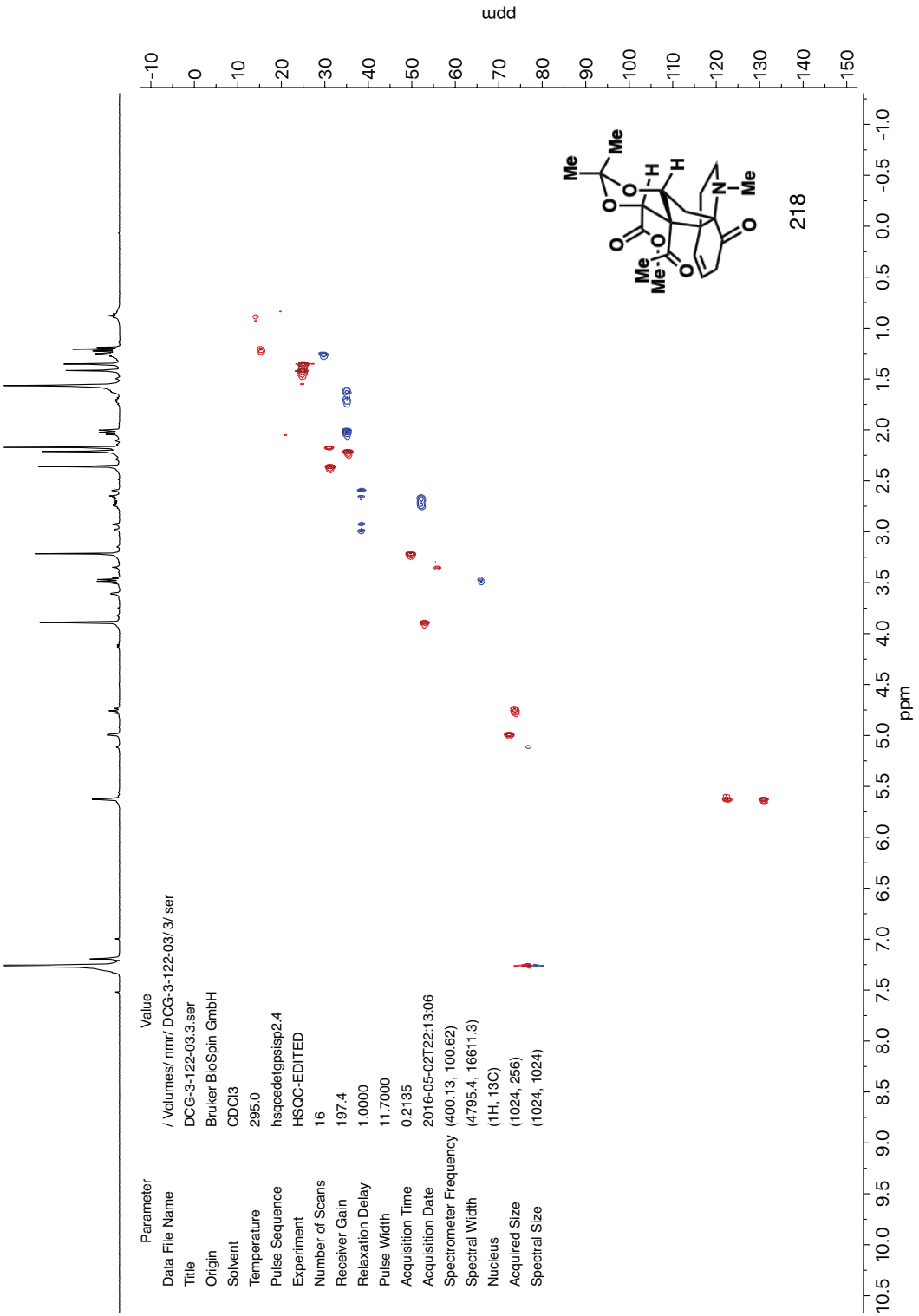
Data File Name / Volumes/ fid/ dgrunenf/ vnmrsys/ data/ DCG-3-101-0_20160315_03/ NOESY_01.fid/ fid
Title NOESY_01
Origin Varian
Solvent CDCl3
Temperature 25.0
Pulse Sequence NOESY
Experiment NOESY
Number of Scans 8
Receiver Gain 48
Relaxation Delay 1.0000
Pulse Width 6.4000
Acquisition Time 0.1500
Acquisition Date 2016-03-15T21:52:58
Spectrometer Frequency (599.62, 599.62)
Spectral Width (5372.0, 5372.0)
Nucleus (1H, 1H)
Acquired Size (806, 128)
Spectral Size (1024, 1024)
ppm
nOe
nOe
TESO
TBS
OMe
Me
TESO
215

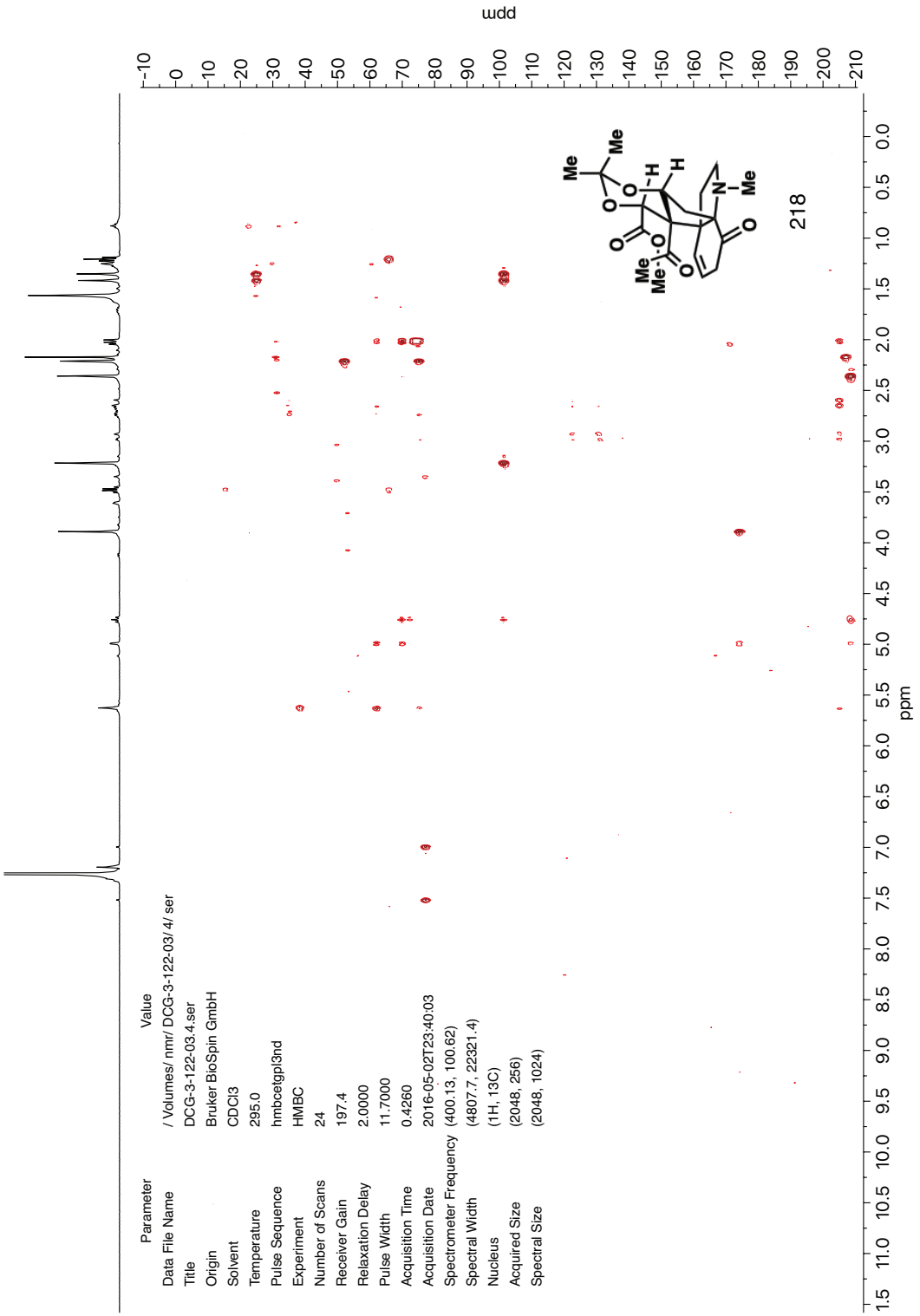

Parameter Value
Data File Name / Volumes/ nmr/ DCG-3-165-1/1/1/ fid
Title DCG-3-165-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 98.9
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2016-05-10T14:34:03
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
OMe
OH
OH
H
N
Me
O
Me
O
O
216
1.00
1.09
1.02
1.13
3.76
1.08
1.49
3.19
1.28
3.20
1.46
1.22
3.28
1.38
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm

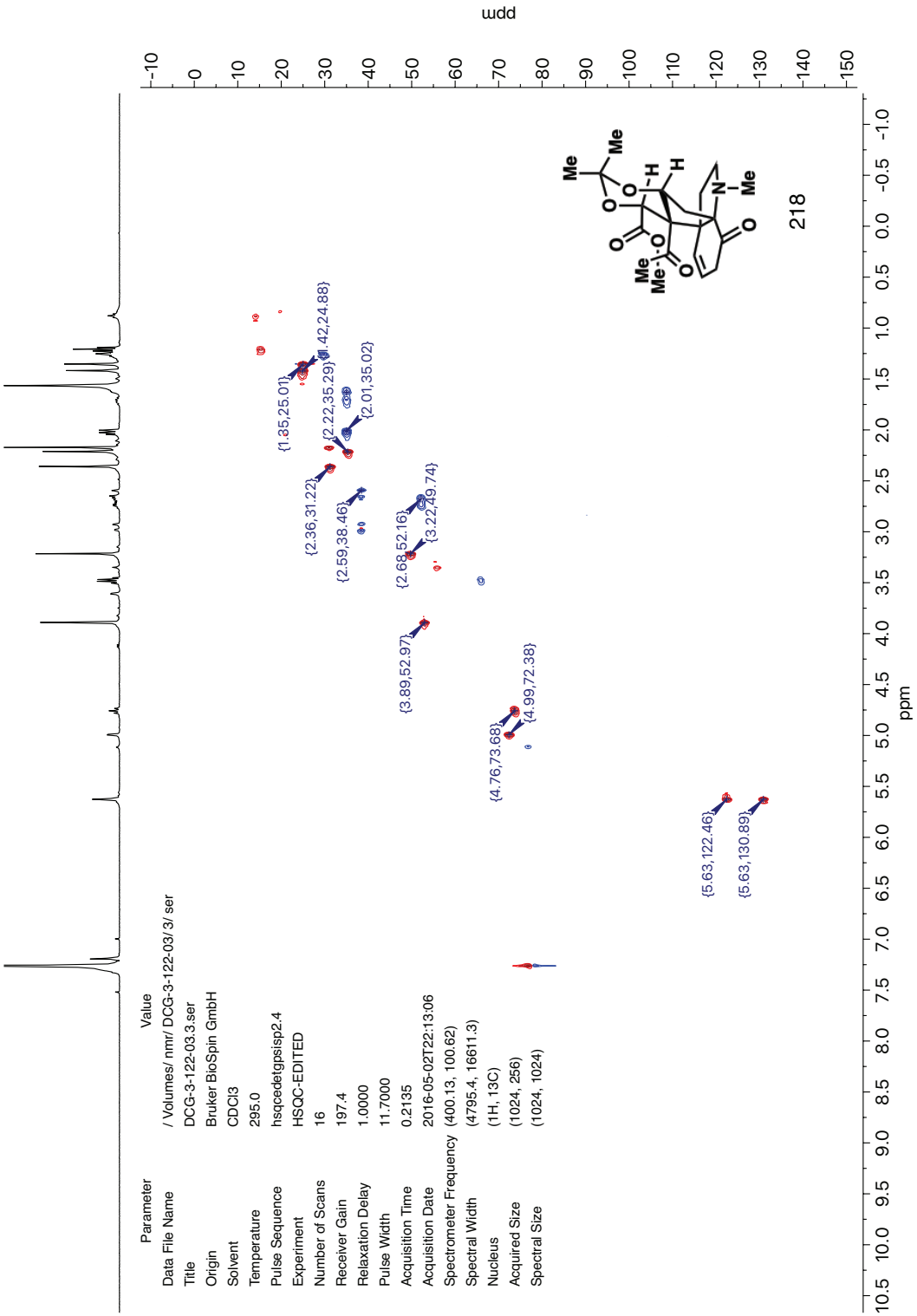

Parameter Value
Data File Name / Volumes/ nmr/ DCG-3-165-1/2/ fid
Title DCG-3-165-1.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-05-10T14:49:10
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OMe
OH
OH
H
N
Me
O
Me
O
O
216
71.7
74.7
76.1
ppm
208.3
206.3
173.5
131.9
122.4
64.2
53.1
52.6
38.5
37.4
35.3
35.2
31.4
ppm

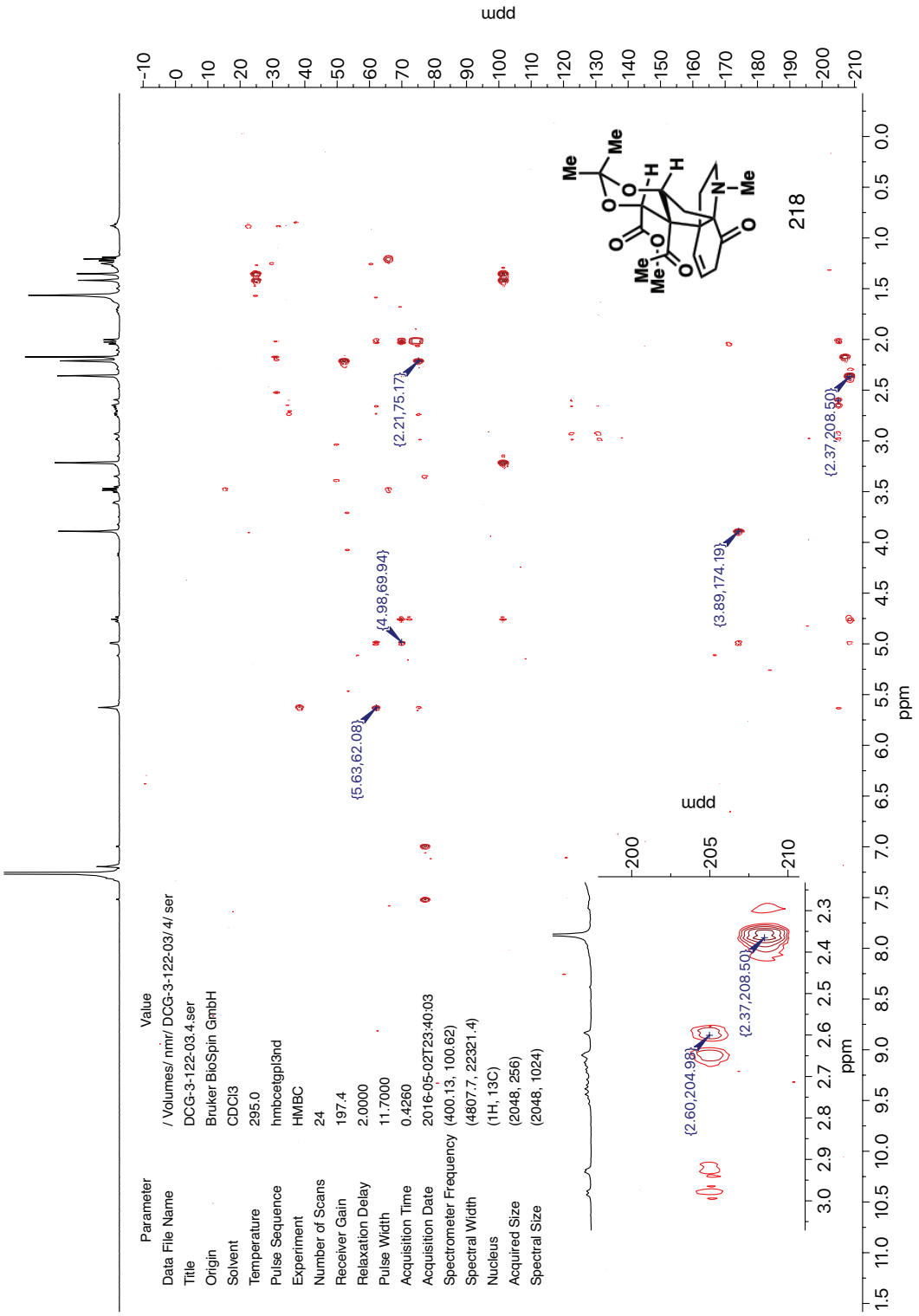

Parameter Value
Data File Name / Volumes/ nmr/ DCG-3-122-03/ 1/ fid
Title DCG-3-122-03.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 197.4
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2016-05-02T22:05:58
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
B (d) 4.99
A (t) 4.76
C (m) 5.63
E (s) 3.89
H (dd) 2.95
I (m) 2.69
J (s) 2.36
K (s) 2.21
L (d) 2.62
M (m) 2.02
N (s) 1.42
O (s) 1.35
218
1.80
1.10
1.00
3.00
1.04
1.54
1.16
2.77
2.96
2.14
0.70
1.56
3.45
3.46
ppm

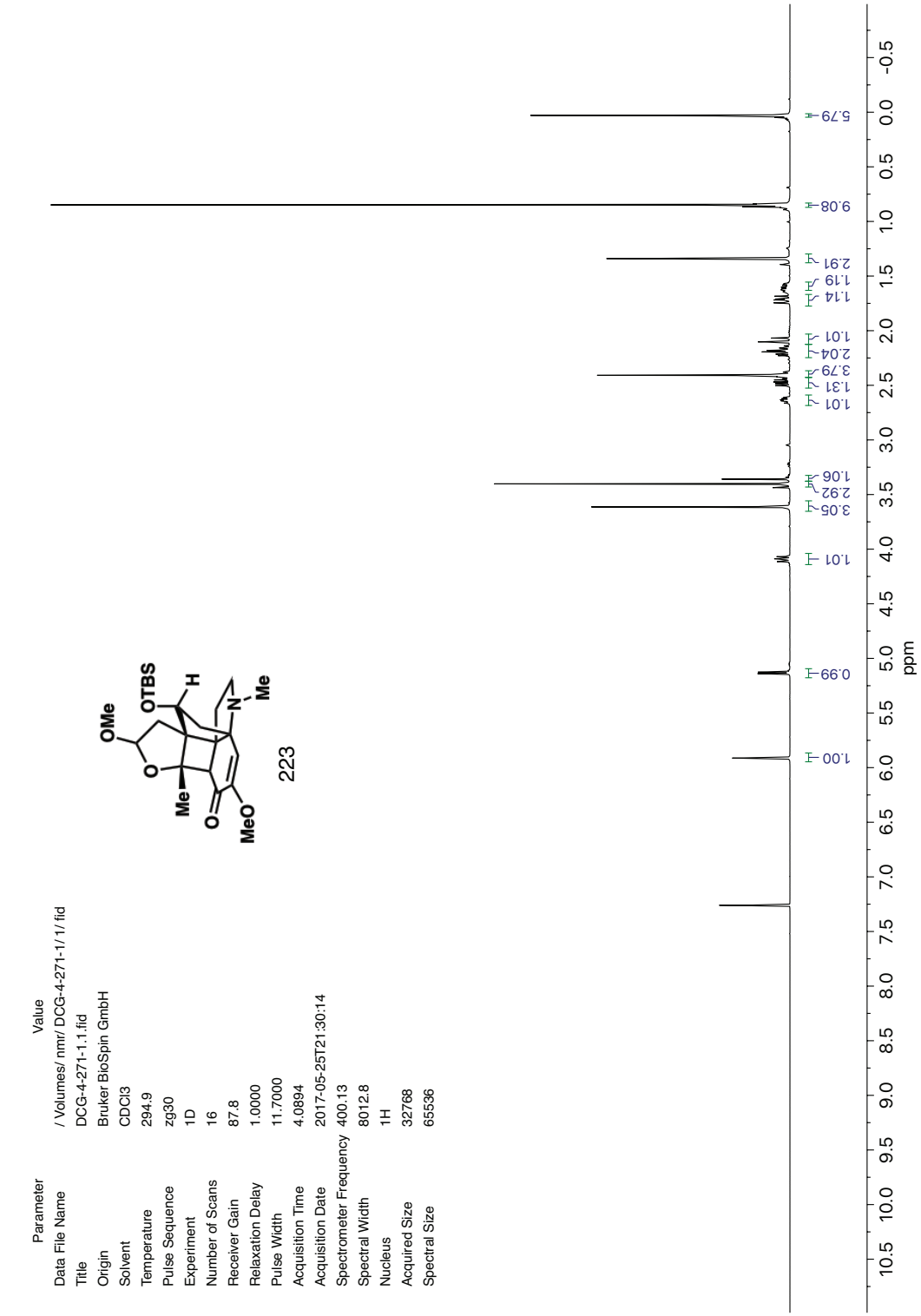

Parameter Value
Data File Name / Volumes/ nmr/ DCG-3-122-03/ 2/ ser
Title DCG-3-122-03.2.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 0.8816
Pulse Width 11.7000
Acquisition Time 0.3154
Acquisition Date 2016-05-02T22:06:35
Spectrometer Frequency (400.13, 400.13)
Spectral Width (3246.8, 3246.8)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)
ppm
218


Parameter Value
Data File Name / Volumes/ nmr/ DCG-3-122-03/ 3/ ser
Title DCG-3-122-03.3.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 16
Receiver Gain 197.4
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2016-05-02T22:13:06
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
ppm
ppm
218


Parameter Value
Data File Name / Volumes/ nmr/ DCG-3-122-03/ 4/ ser
Title DCG-3-122-03.4.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 24
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2016-05-02T23:40:03
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
ppm
ppm
218
Me
Me
H
H
N
Me
O
Me
Me
O


Parameter Value
Data File Name / Volumes/ nmr/ DCG-3-122-03/ 3/ ser
Title DCG-3-122-03.3.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 16
Receiver Gain 197.4
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2016-05-02T22:13:06
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
{1.35,25.01}
{1.42,24.88}
{2.22,35.29}
{2.01,35.02}
{2.36,31.22}
{2.59,38.46}
{2.68,52.16}
{3.22,49.74}
{3.89,52.97}
{4.76,73.68}
{4.99,72.38}
{5.63,122.46}
{5.63,130.89}
Me
Me
H
H
Me
Me
Me
O
O
O
O
O
O
N
218
ppm
ppm


Parameter Value
Data File Name / Volumes/ nmr/ DCG-3-122-03/ 4/ ser
Title DCG-3-122-03.4.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 24
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2016-05-02T23:40:03
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
{5.63,62.08}
{4.98,69.94}
{2.21,75.17}
{3.89,174.19}
{2.37,208.50}
{2.60,204.98}
{2.37,208.50}
218
Me
Me
Me
Me
H
H
O
O
O
O
O
O
N
O
ppm
ppm
ppm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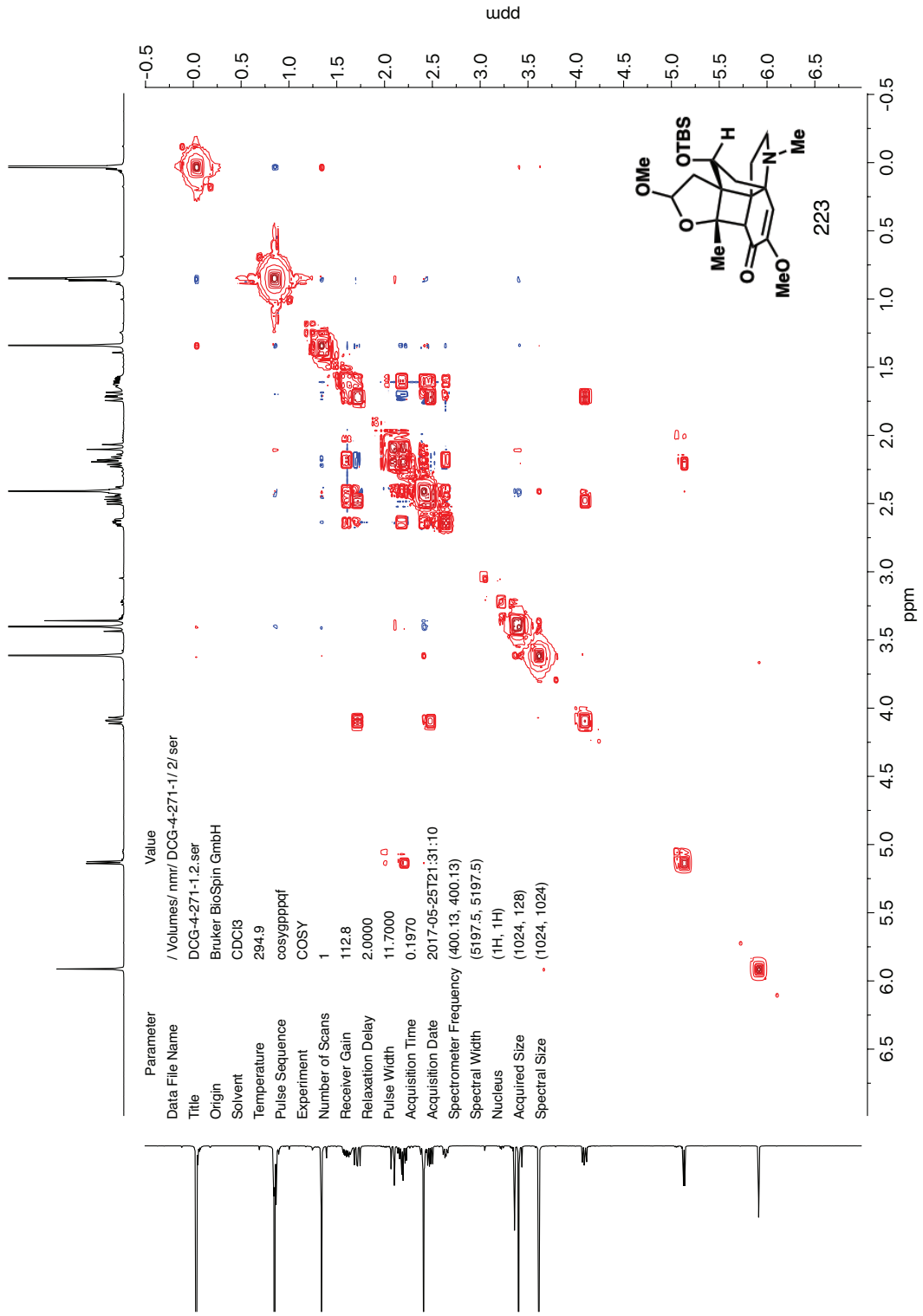
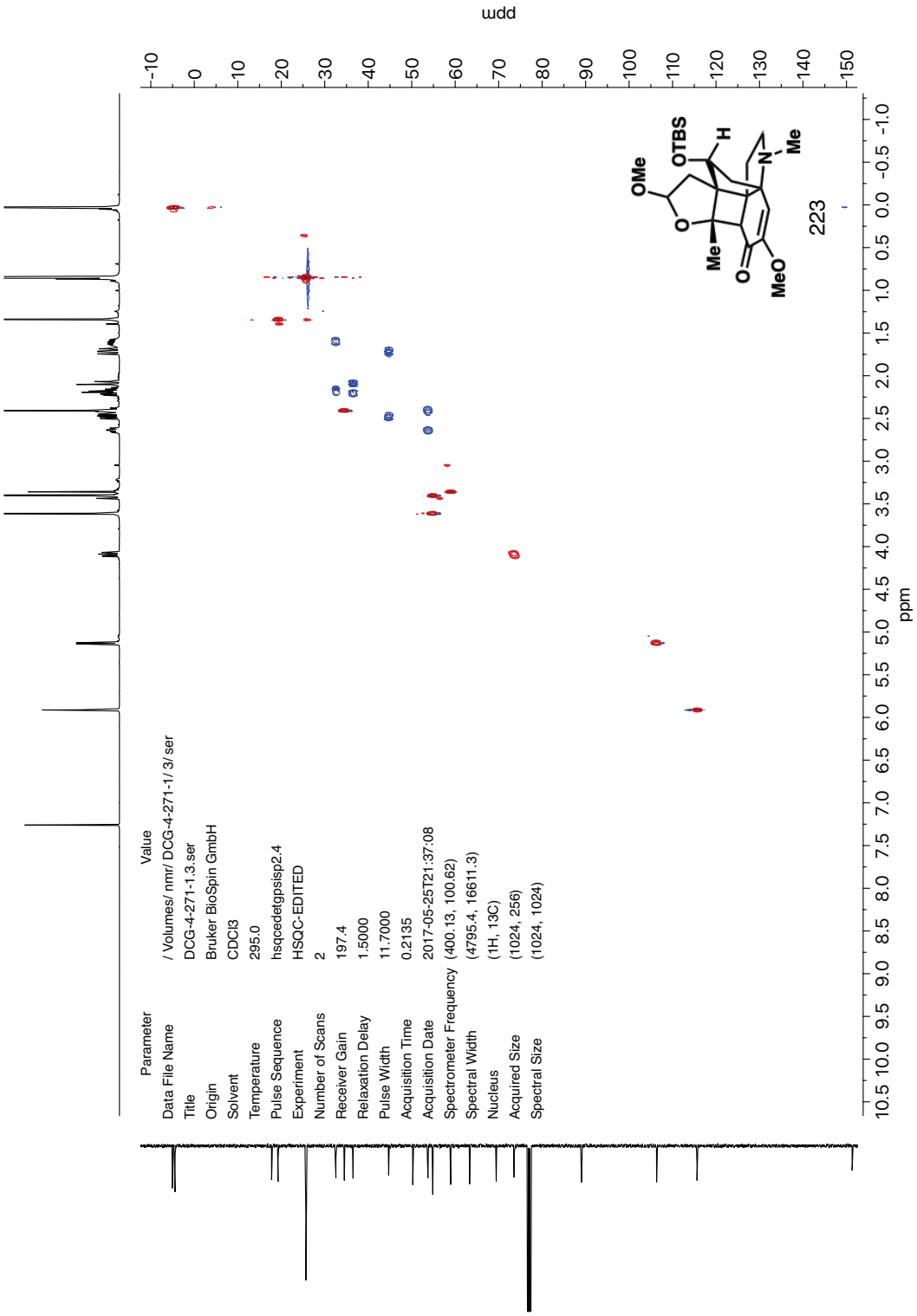
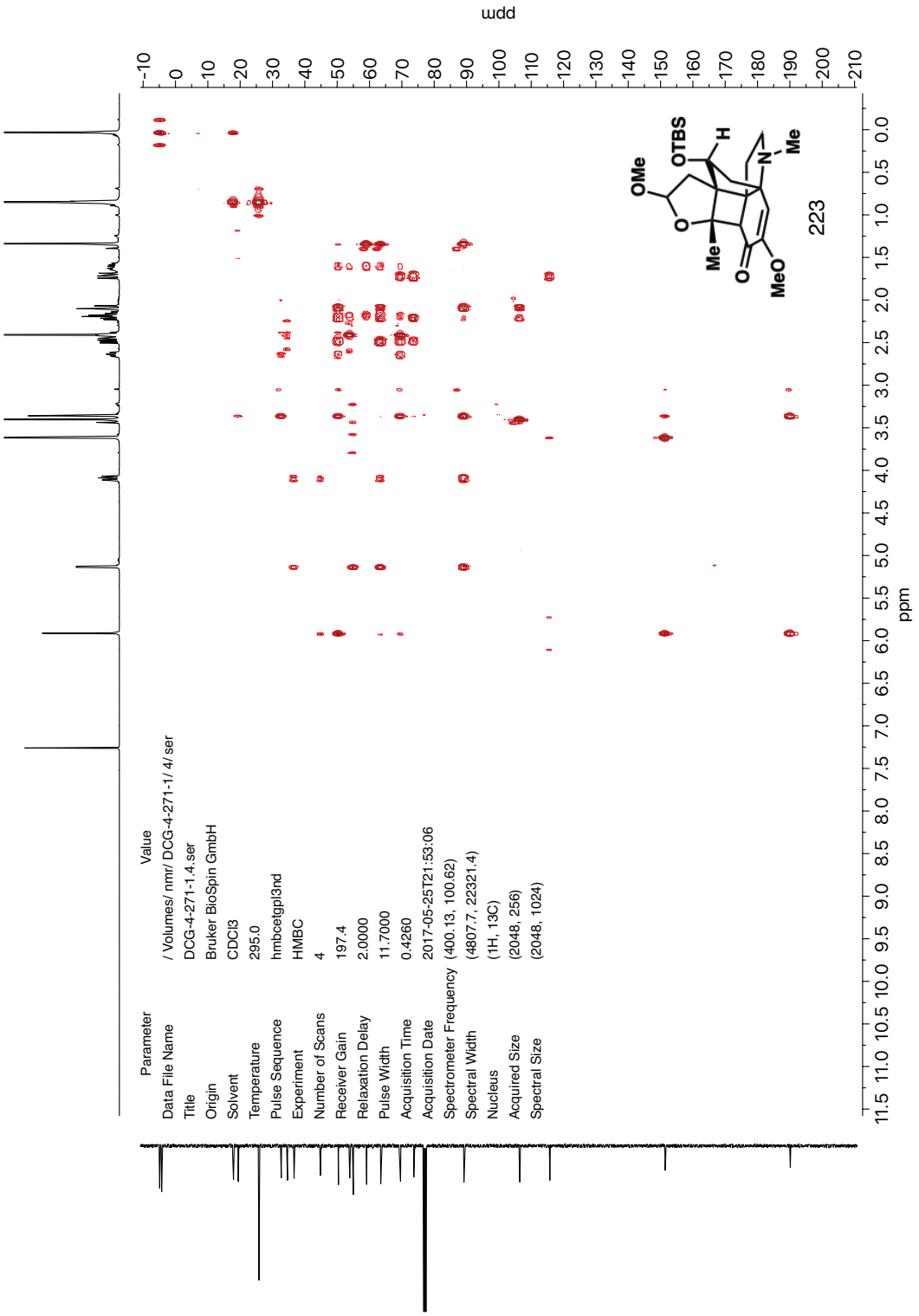
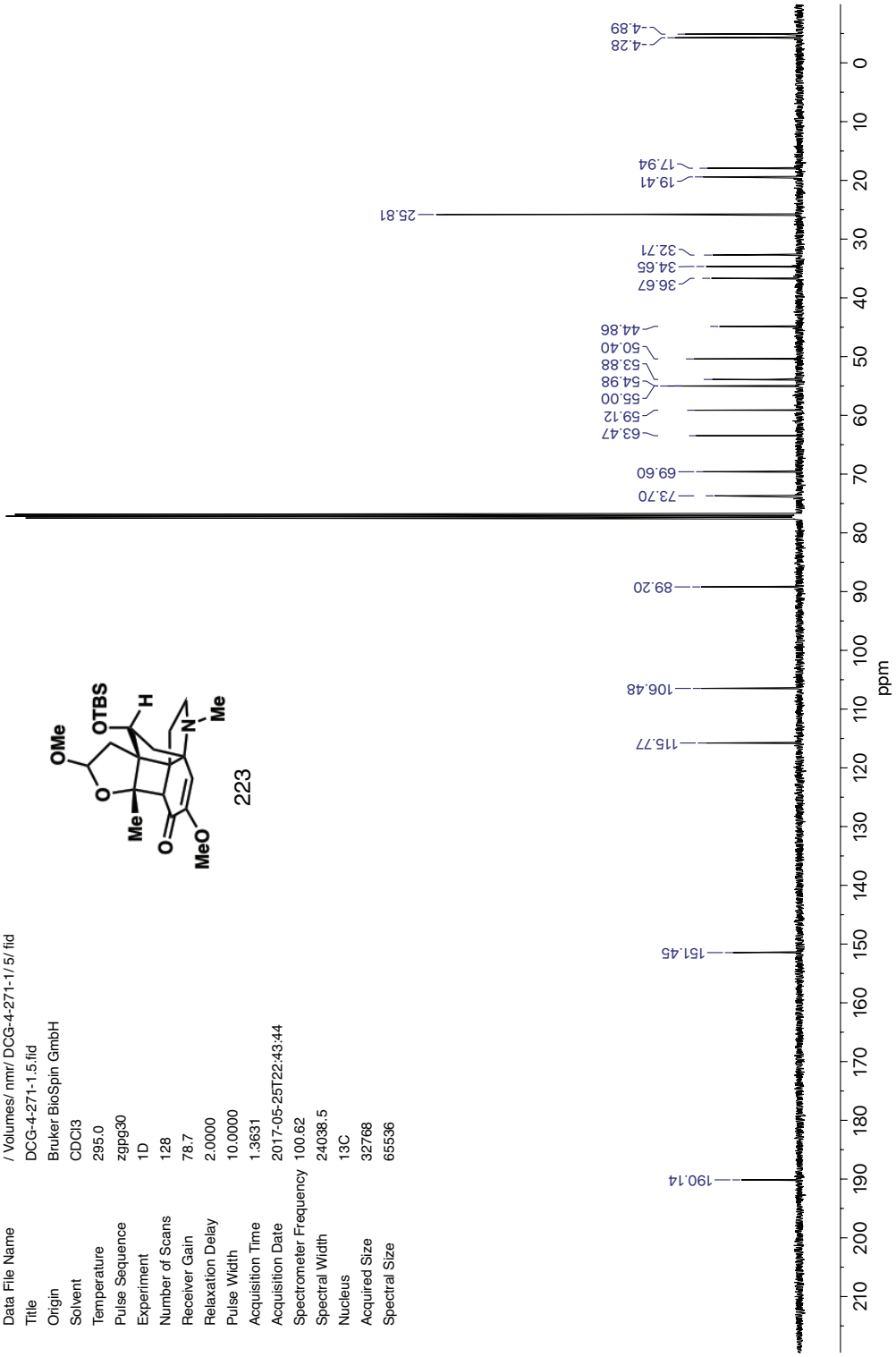
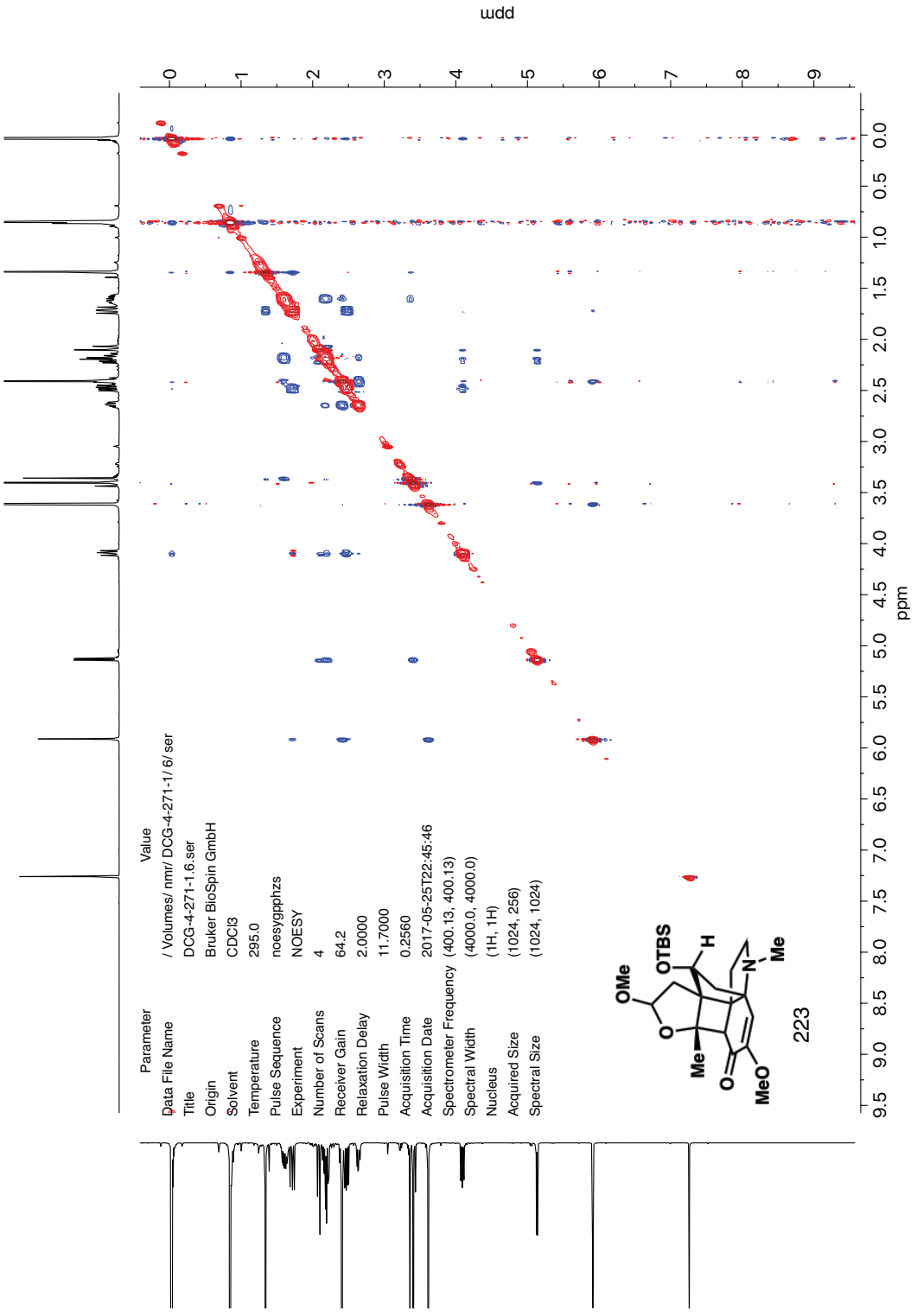
Data File Name / Volumes/ nmr/ DCG-4-271-1/1/1/ fid
Title DCG-4-271-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 87.8
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-05-25T21:30:14
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
OMe
OTBS
H
Me
N
Me
O
O
MeO
223
1.00
0.99
1.01
3.05
2.92
1.06
1.01
1.31
3.79
2.04
1.01
1.14
1.19
2.91
9.08
5.79
ppm

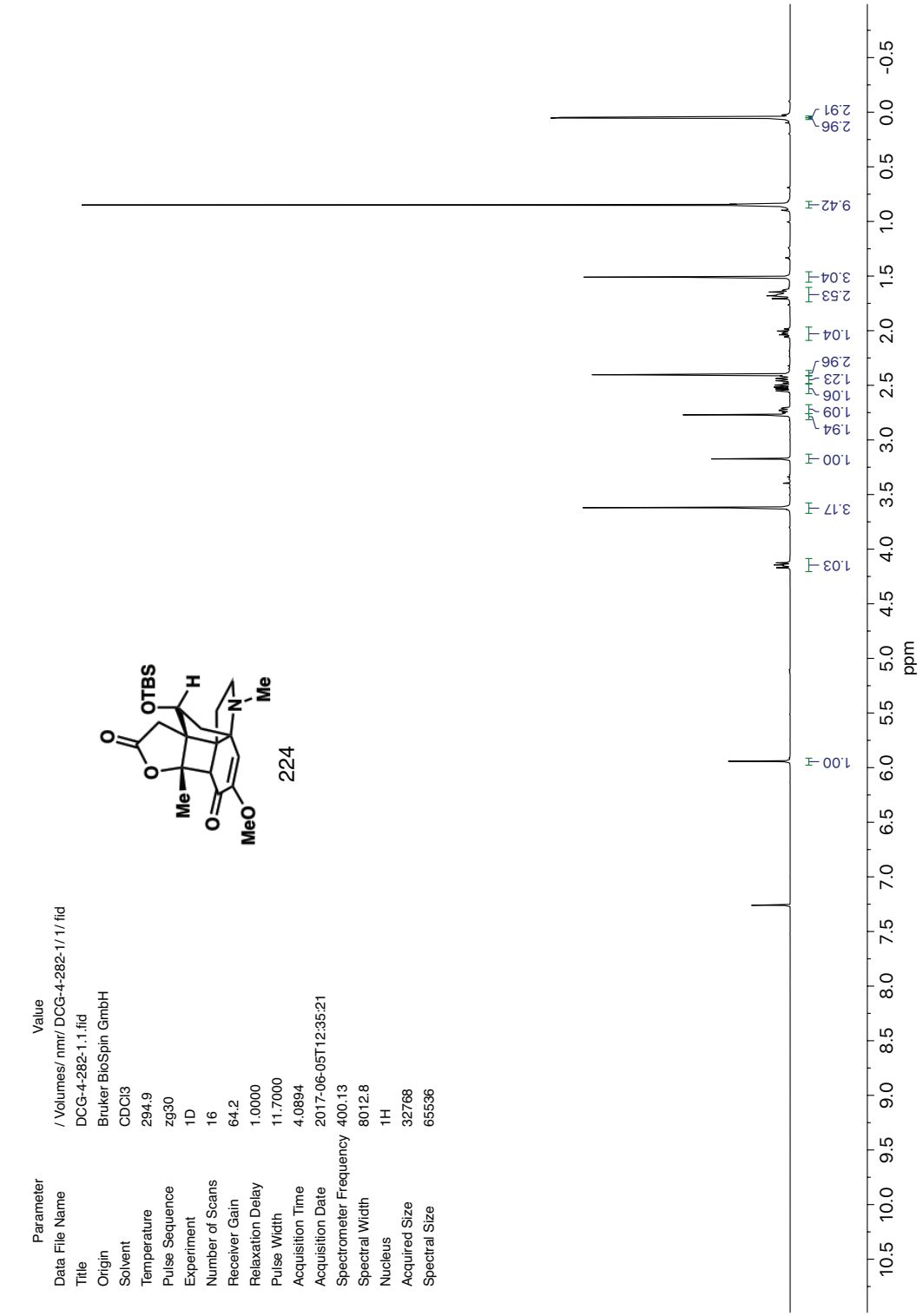

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-271-1/ 2/ ser
Title DCG-4-271-1.2.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 112.8
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.1970
Acquisition Date 2017-05-25T21:31:10
Spectrometer Frequency (400.13, 400.13)
Spectral Width (5197.5, 5197.5)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)
OMe
OTBS
H
Me
N
Me
O
Me
O
MeO
223
ppm
ppm

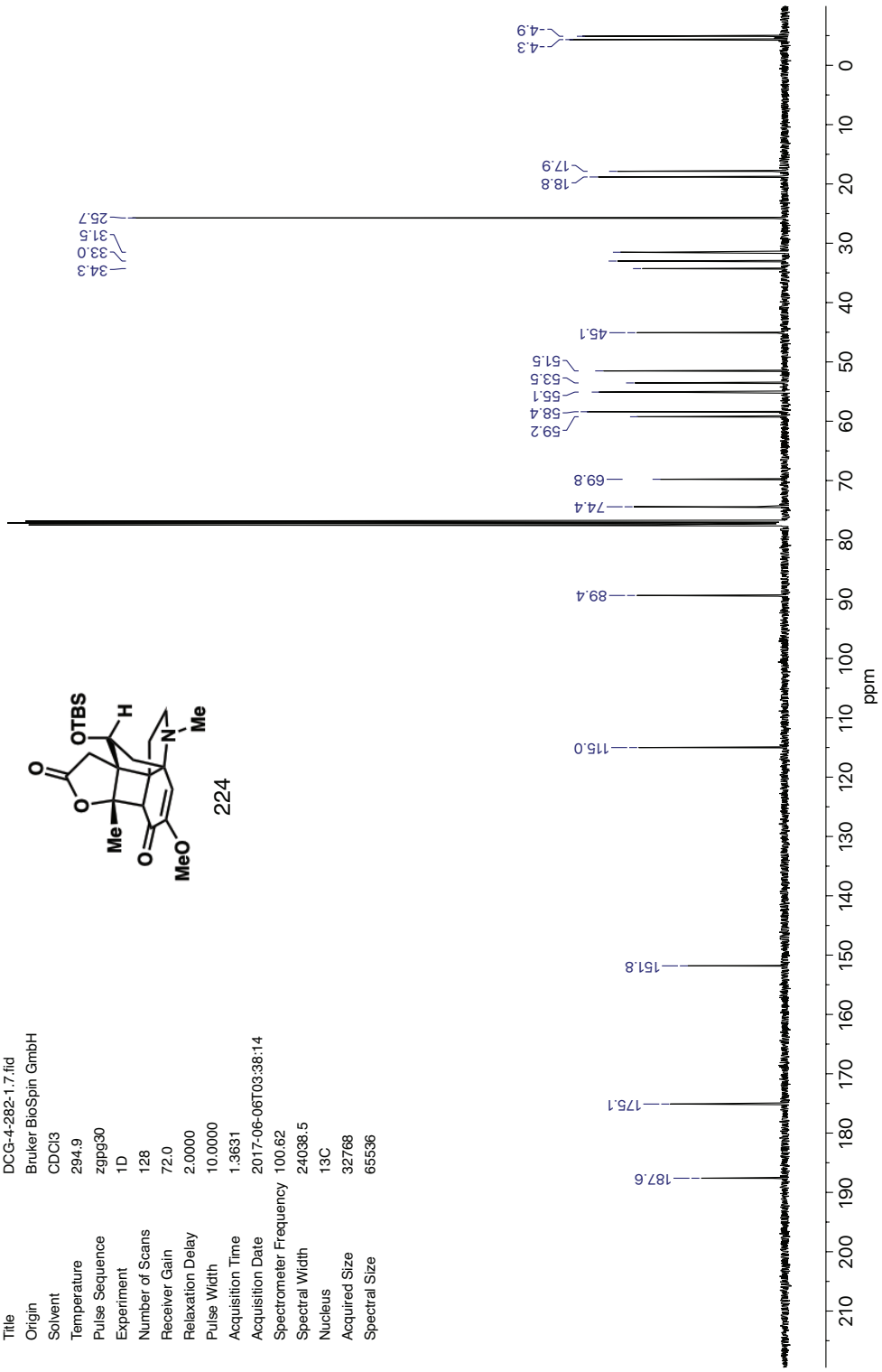

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-271-1/ 3/ ser
Title DCG-4-271-1.3.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2017-05-25T21:37:08
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
ppm
OMe
OTBS
H
Me
O
MeO
N
Me
223

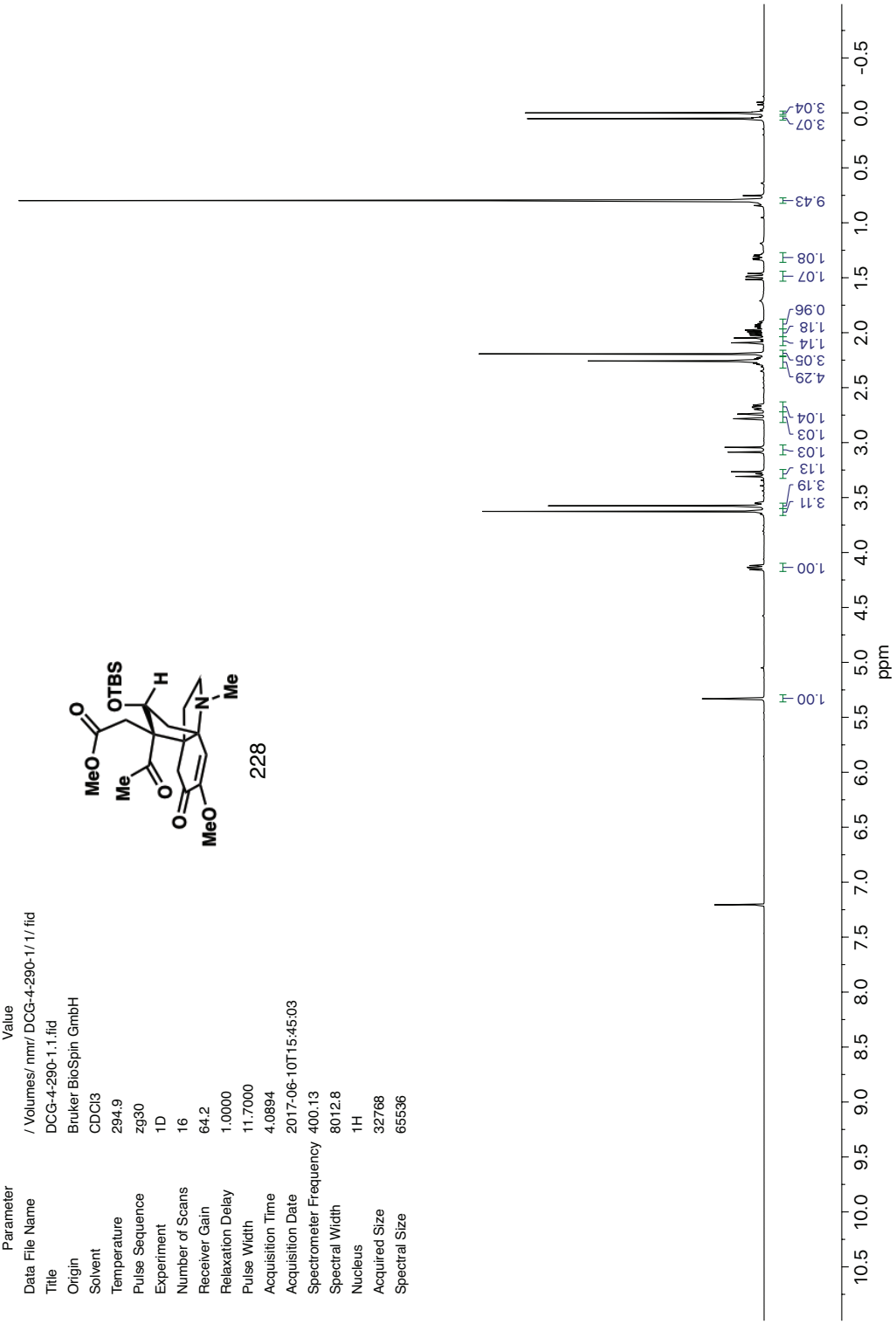

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-271-1/ 4/ ser
Title DCG-4-271-1.4.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2017-05-25T21:53:06
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
ppm
ppm
OMe
OTBS
H
Me
N
Me
O
MeO
223

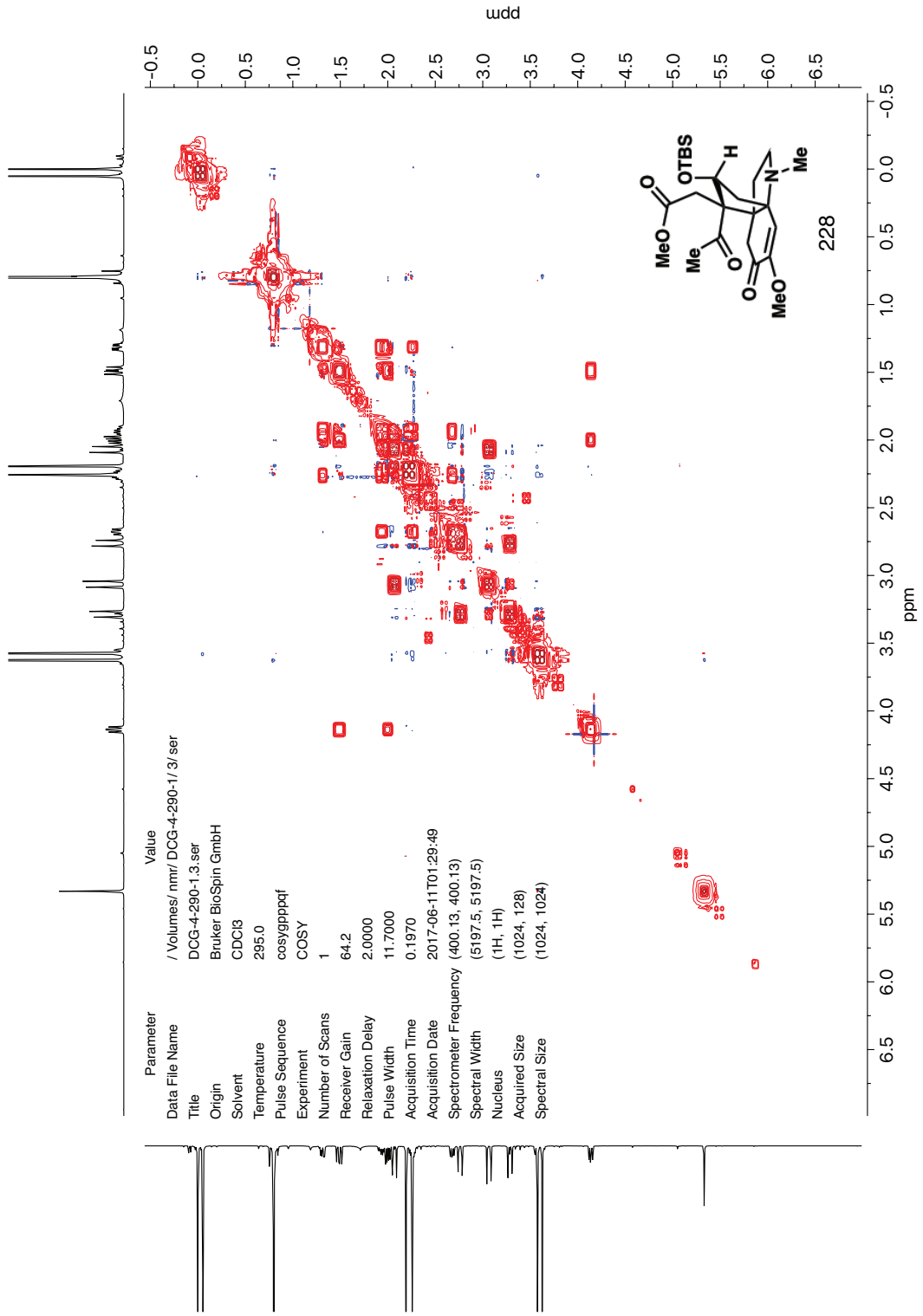

Parameter
Value
Data File Name / Volumes/ nmr/ DCG-4-271-1/5/ fid
Title DCG-4-271-1.5.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 128
Receiver Gain 78.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-05-25T22:43:44
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OMe
OTBS
H
N
Me
O
Me
O
MeO
223
190.14
151.45
115.77
106.48
89.20
73.70
69.60
63.47
59.12
55.00
54.98
53.88
50.40
44.86
36.67
34.65
32.71
25.81
19.41
17.94
-4.28
-4.89
ppm

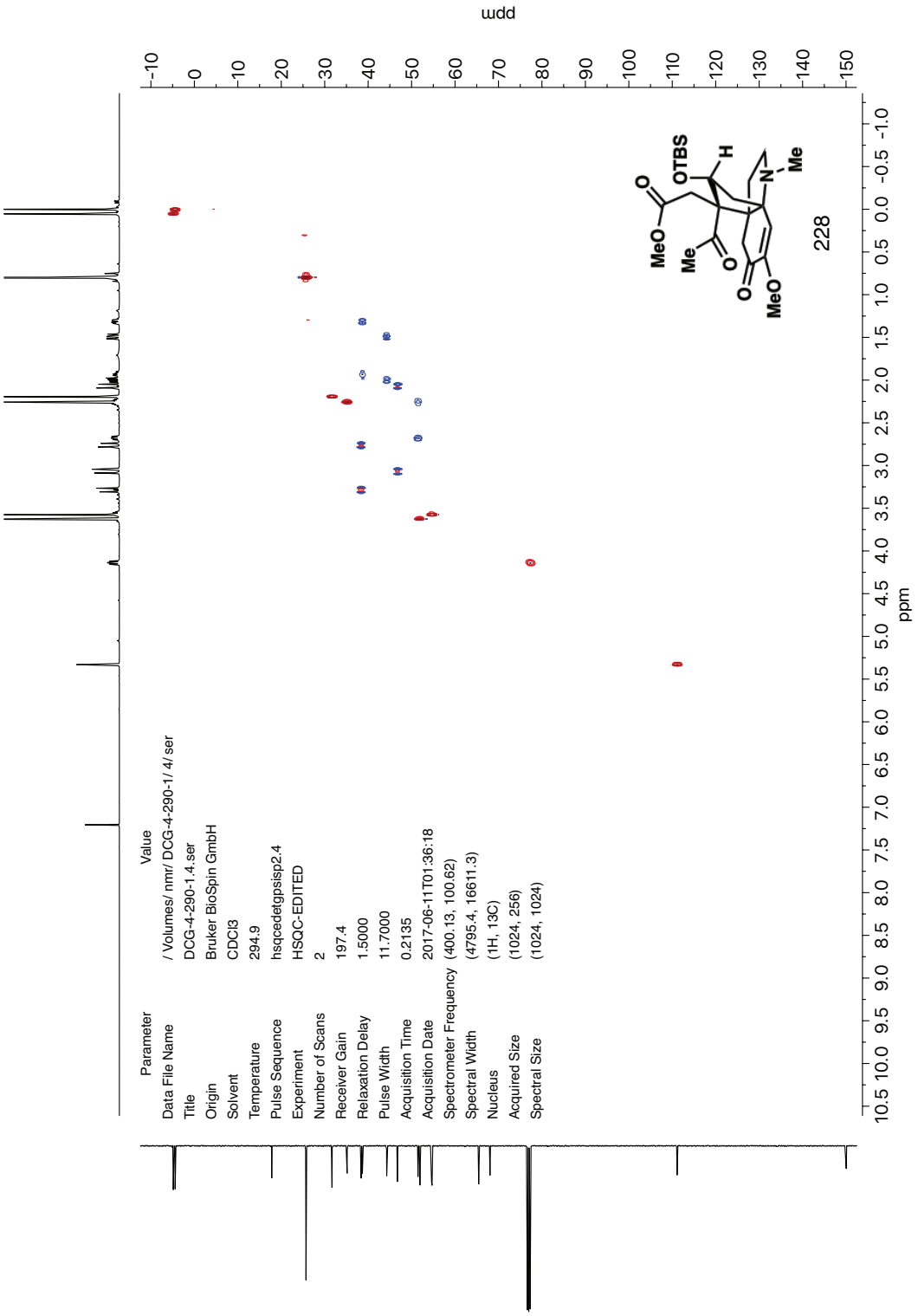

ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-271-1/ 6/ ser
Title DCG-4-271-1.6.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence noesygpphzs
Experiment NOESY
Number of Scans 4
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2017-05-25T22:45:46
Spectrometer Frequency (400.13, 400.13)
Spectral Width (4000.0, 4000.0)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
OMe
OTBS
H
Me
O
MeO
N
Me
223

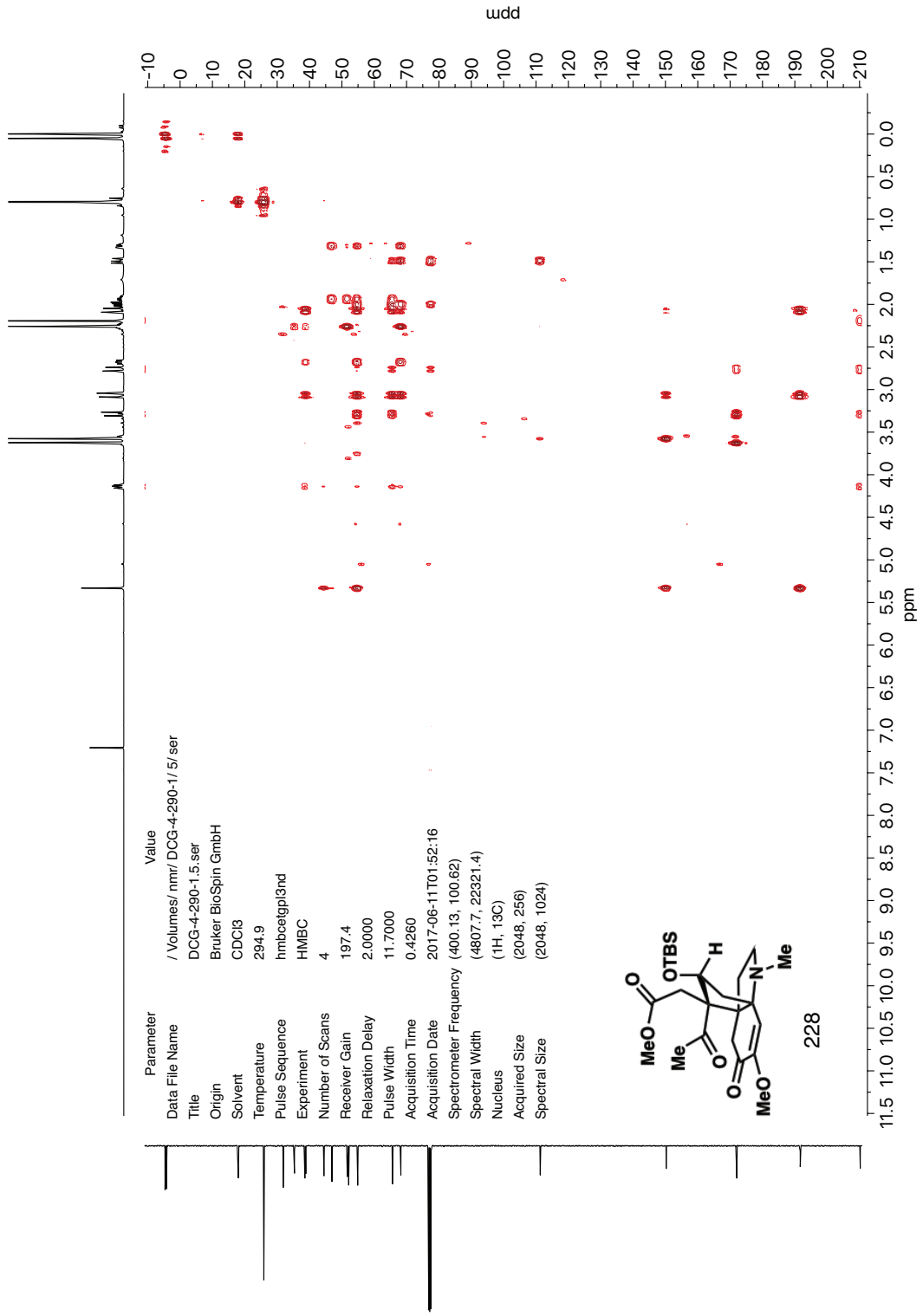

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-282-1/1/ fid
Title DCG-4-282-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 64.2
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-06-05T12:35:21
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
OTBS
H
Me
N
O
O
O
Me
O
MeO
224
1.00
3.17
1.03
1.00
1.94
1.09
1.06
1.23
2.96
1.04
2.53
3.04
9.42
2.96
2.91
ppm

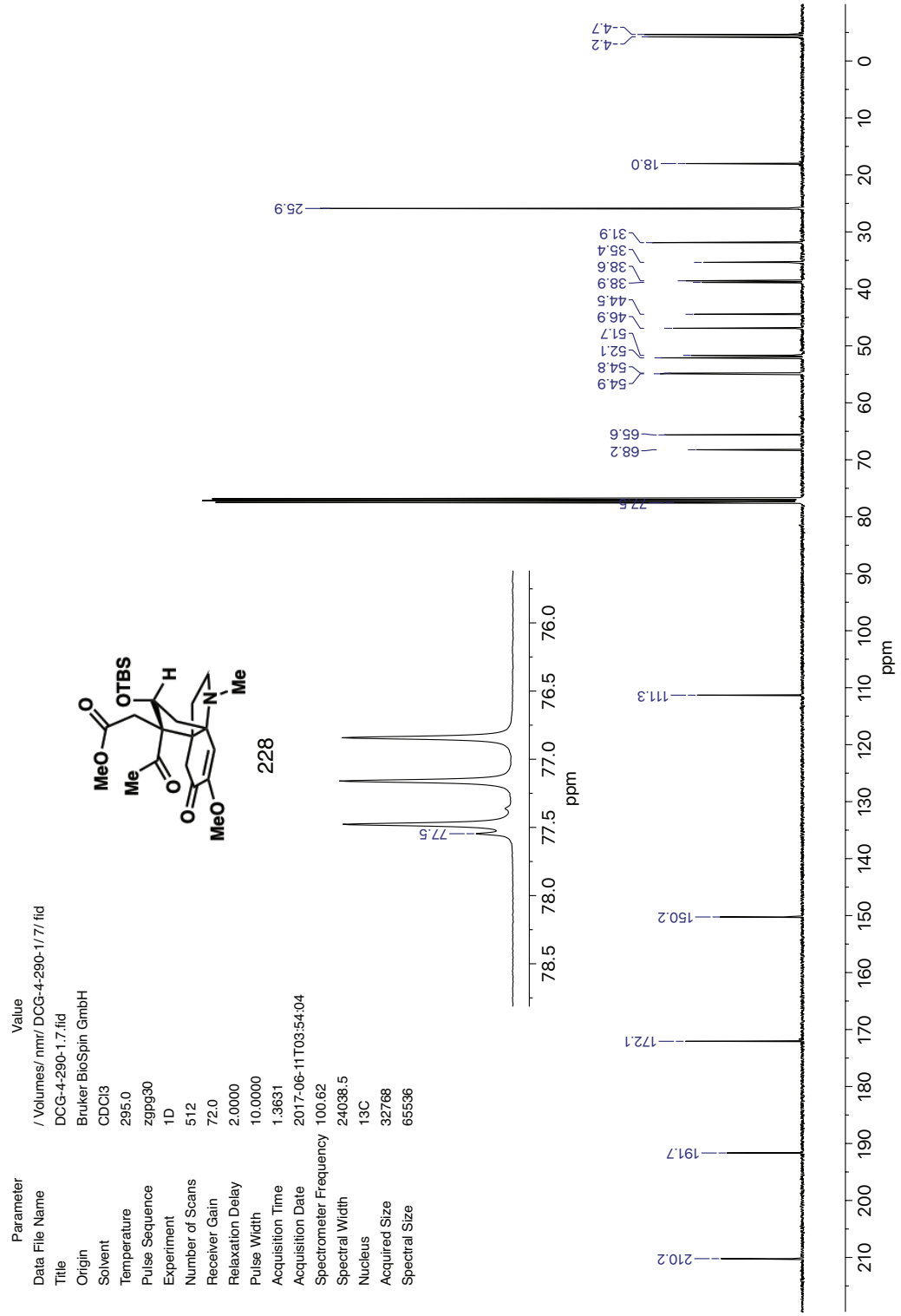

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-282-1/7/ fid
Title DCG-4-282-1.7.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 128
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-06-06T03:38:14
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OTBS
H
Me
N
O
O
O
Me
O
MeO
224
187.6
175.1
151.8
115.0
89.4
74.4
69.8
59.2
58.4
55.1
53.5
51.5
45.1
34.3
33.0
31.5
25.7
18.8
17.9
-4.3
-4.9
ppm

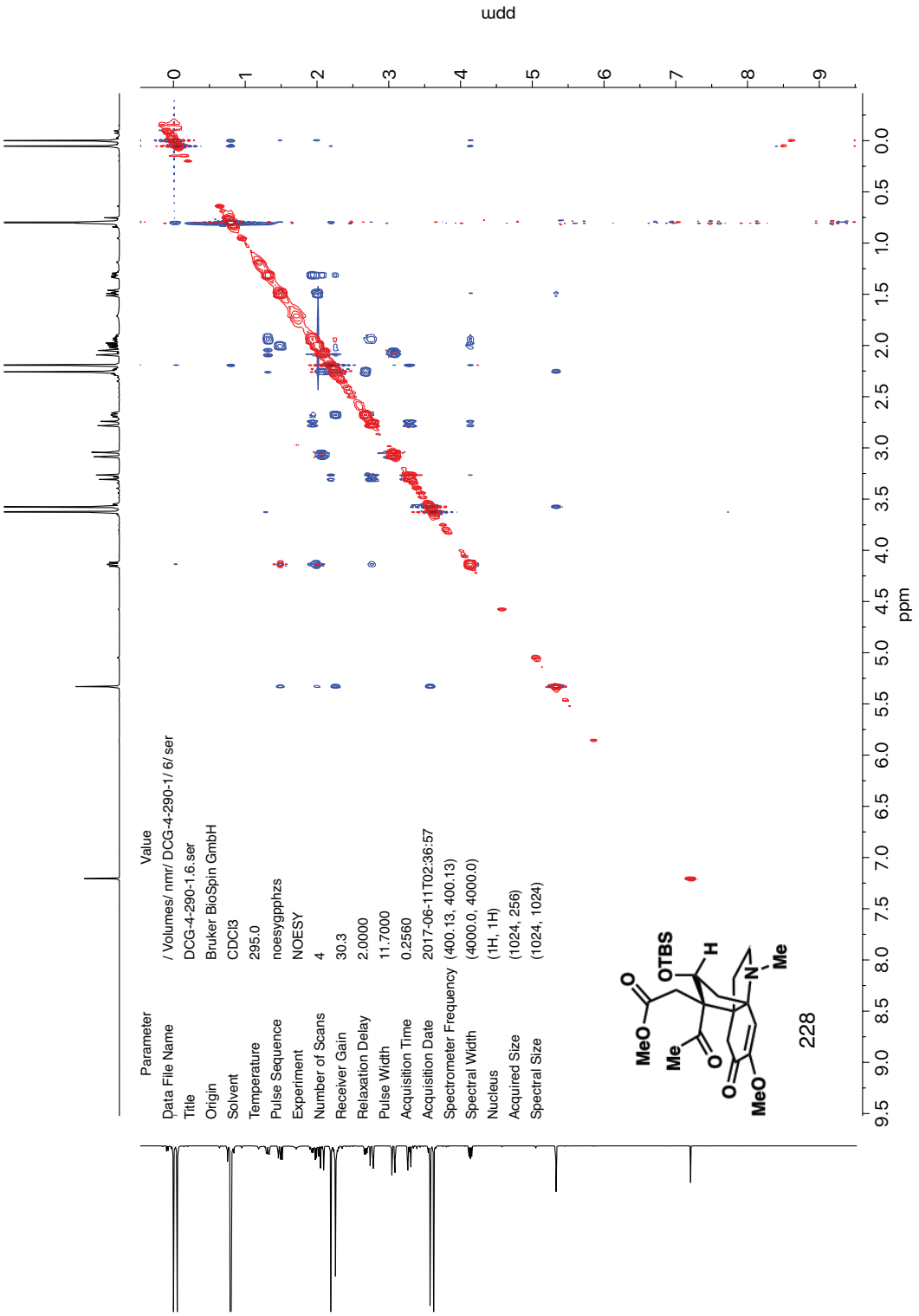

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-290-1/1/1/ fid
Title DCG-4-290-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 64.2
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-06-10T15:45:03
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
MeO
O
OTBS
H
Me
O
N
Me
O
MeO
228
1.00
3.11
3.19
1.13
1.03
1.03
1.04
4.29
3.05
1.14
1.18
0.96
1.07
1.08
9.43
3.07
3.04
ppm

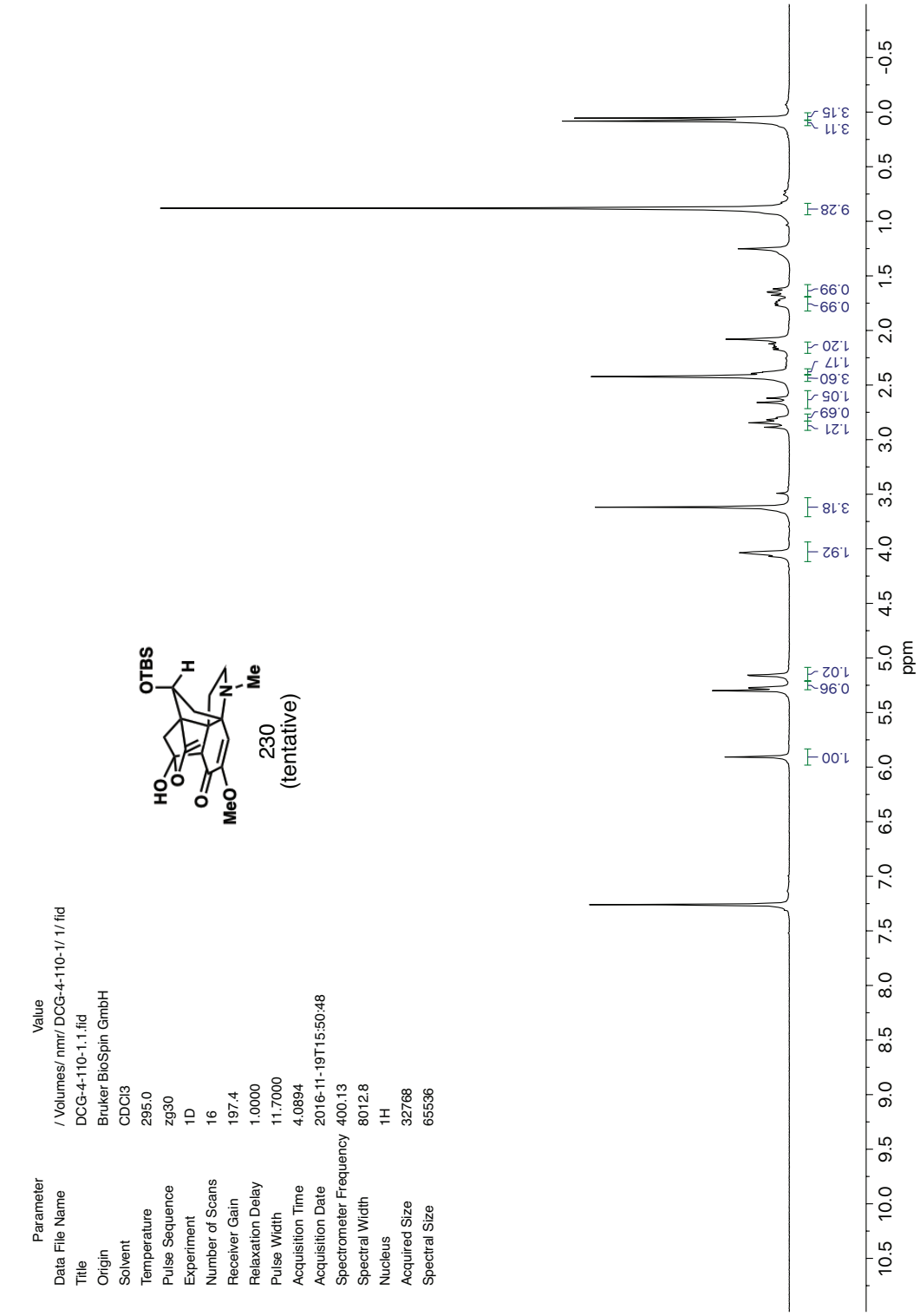

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-290-1/ 3/ ser
Title DCG-4-290-1.3.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.1970
Acquisition Date 2017-06-11T01:29:49
Spectrometer Frequency (400.13, 400.13)
Spectral Width (5197.5, 5197.5)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)
ppm
MeO
Me
O
OTBS
H
N
Me
MeO
228

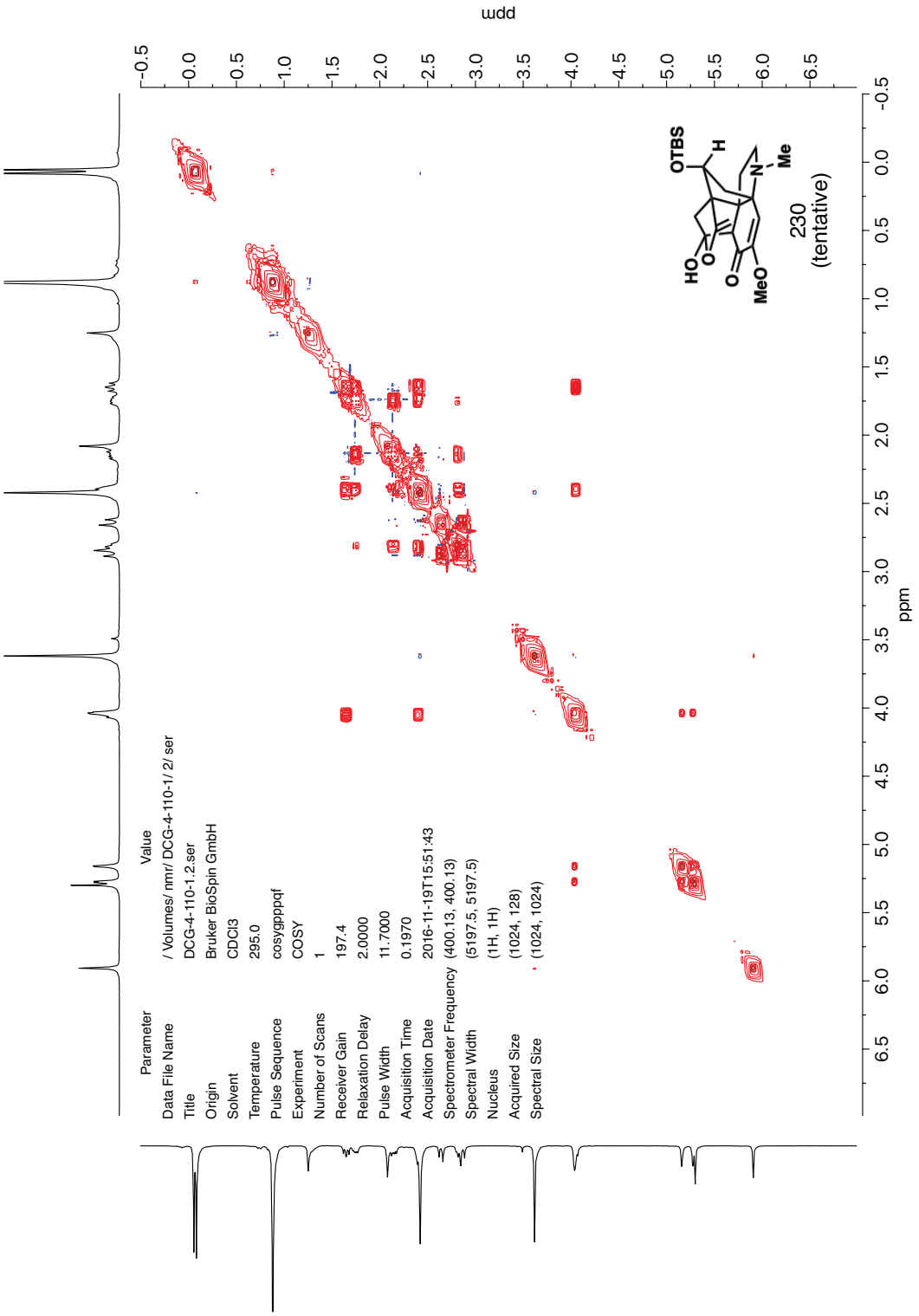

ppm
ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-290-1/ 4/ ser
Title DCG-4-290-1.4.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2017-06-11T01:36:18
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
MeO
Me
O
OTBS
H
N
Me
O
MeO
228

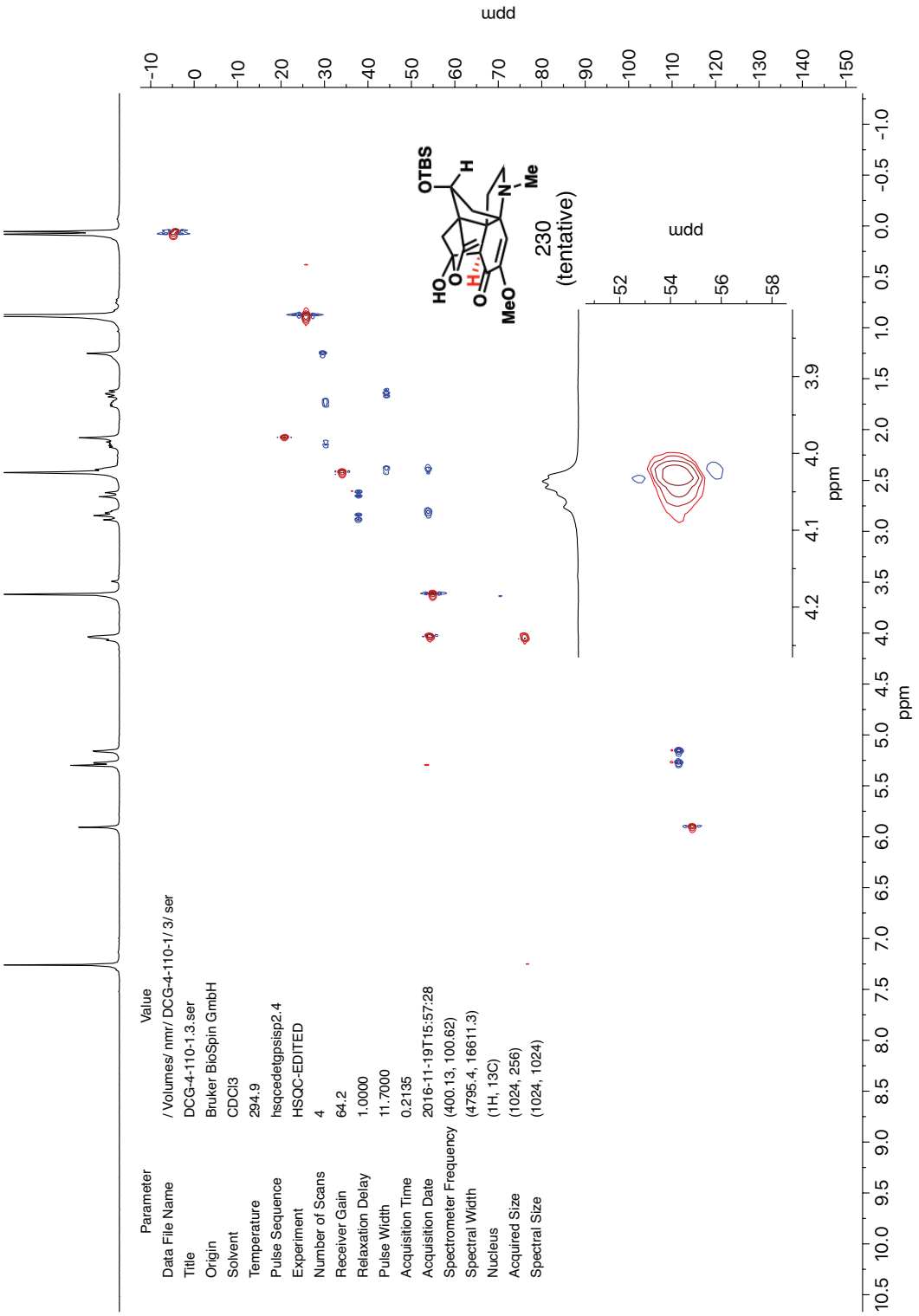

ppm
ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-290-1/ 5/ ser
Title DCG-4-290-1.5.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2017-06-11T01:52:16
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
MeO
Me
OTBS
O
O
O
H
N
Me
MeO
228

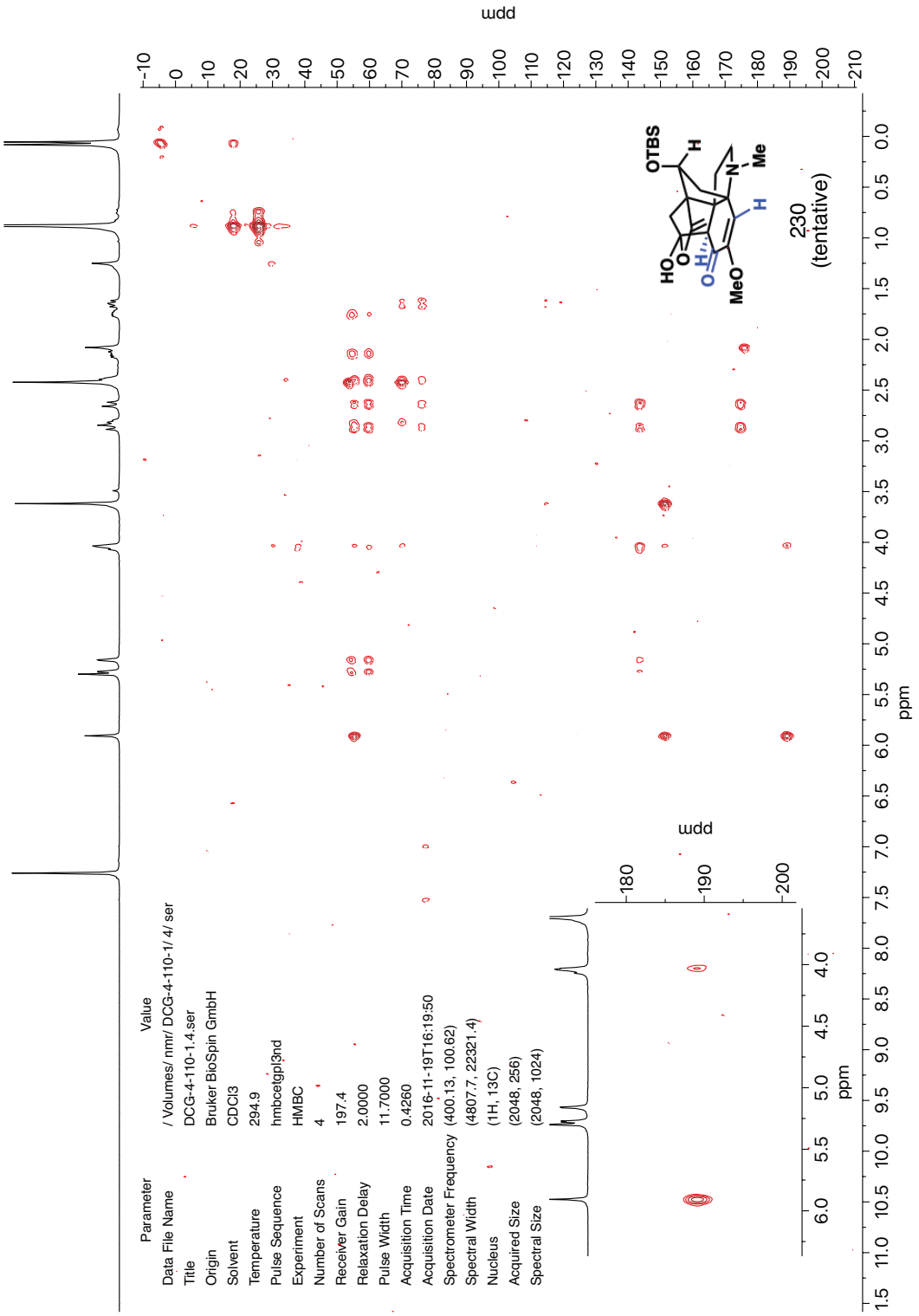

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-290-1/7/ fid
Title DCG-4-290-1.7.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 512
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-06-11T03:54:04
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
MeO
Me
O
OTBS
H
N
Me
O
MeO
228
ppm
ppm

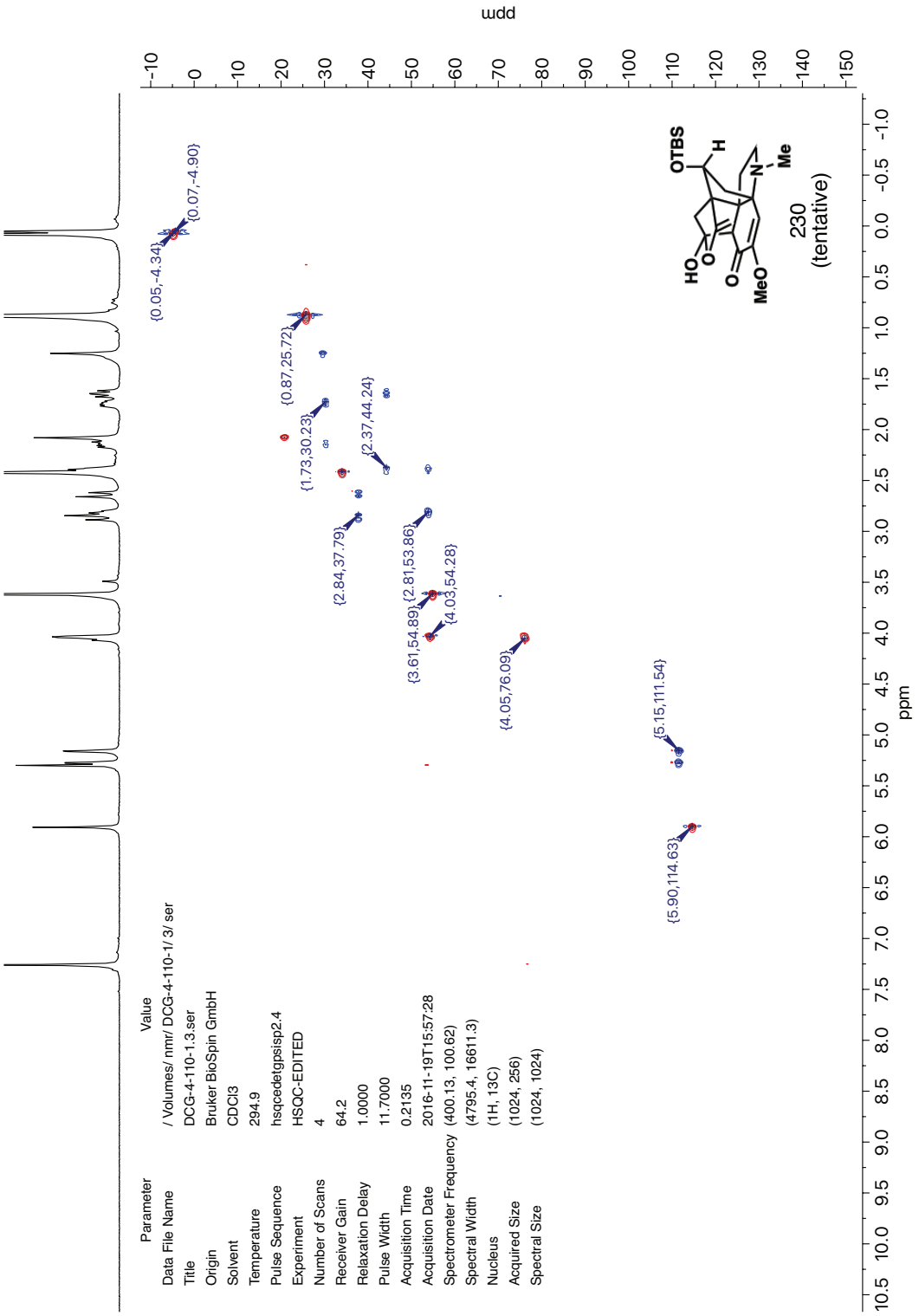

ppm
ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-290-1/ 6/ ser
Title DCG-4-290-1.6.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence noesygpphzs
Experiment NOESY
Number of Scans 4
Receiver Gain 30.3
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2017-06-11T02:36:57
Spectrometer Frequency (400.13, 400.13)
Spectral Width (4000.0, 4000.0)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
MeO
Me
OTBS
H
N
Me
MeO
228

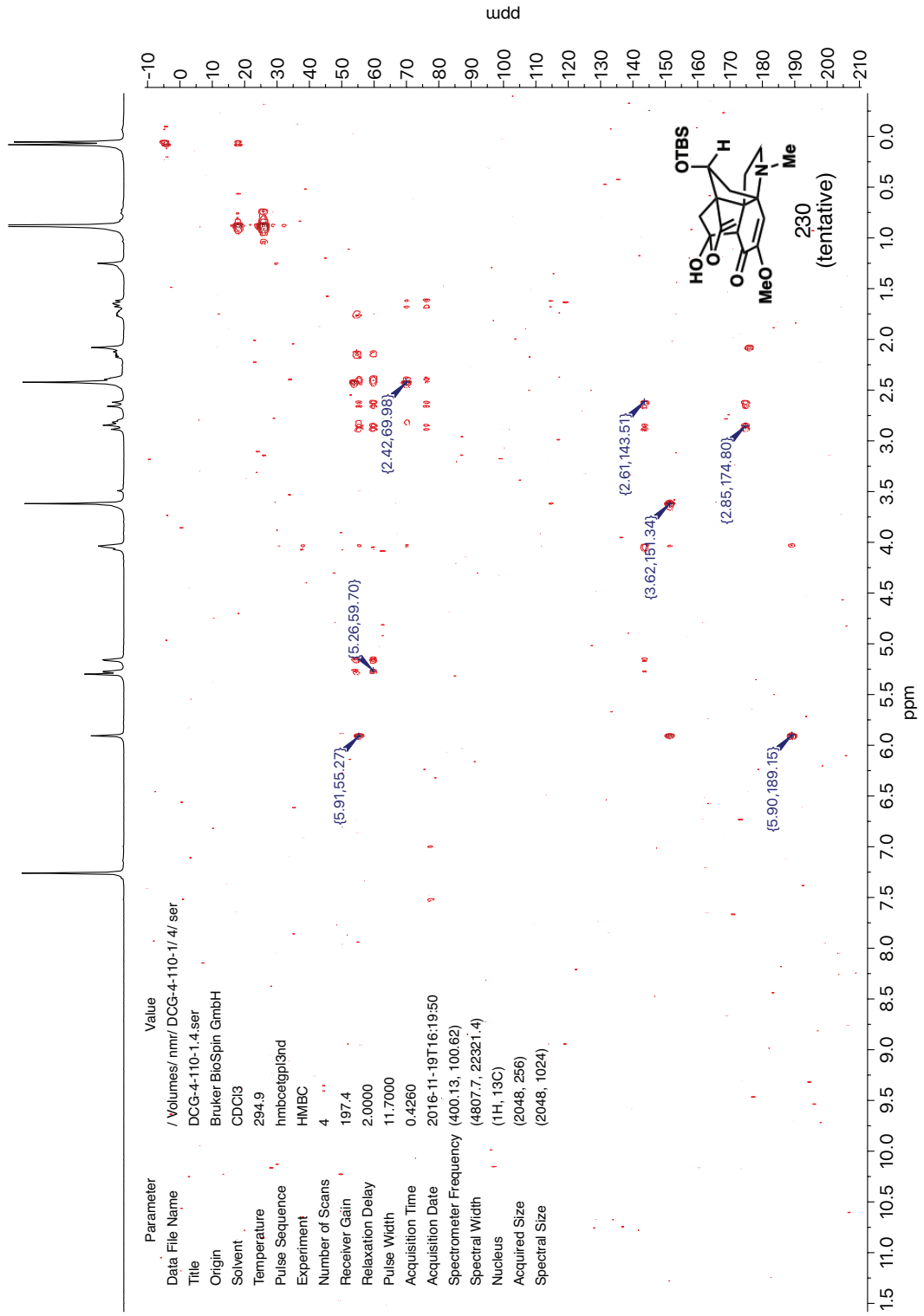

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-110-1/ 1/ fid
Title DCG-4-110-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 197.4
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2016-11-19T15:50:48
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
OTBS
H
HO
O
O
MeO
N
Me
230
(tentative)
1.00
0.96
1.02
3.18
1.92
1.21
0.69
1.05
3.60
1.17
1.20
0.99
0.99
9.28
3.11
3.15
ppm


Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-110-1/ 2/ ser
Title DCG-4-110-1.2.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.1970
Acquisition Date 2016-11-19T15:51:43
Spectrometer Frequency (400.13, 400.13)
Spectral Width (5197.5, 5197.5)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)
OTBS
H
Me
N
HO
O
O
MeO
230
(tentative)
ppm
ppm

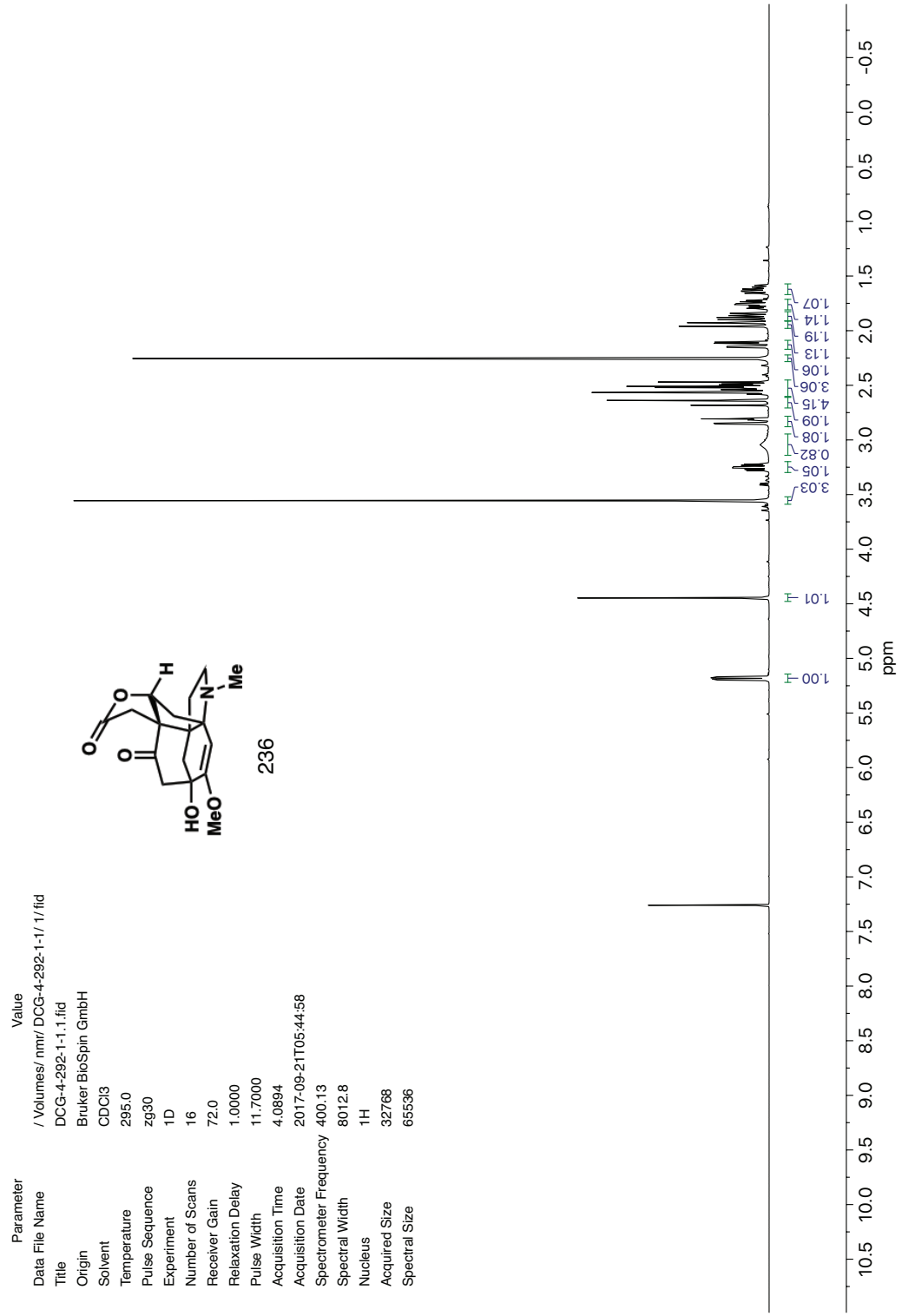

Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-4-110-1/ 3/ ser
Title
DCG-4-110-1.3.ser
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
hsqcedetgpsisp2.4
Experiment
HSQC-EDITED
Number of Scans
4
Receiver Gain
64.2
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
0.2135
Acquisition Date
2016-11-19T15:57:28
Spectrometer Frequency
(400.13, 100.62)
Spectral Width
(4795.4, 16611.3)
Nucleus
(1H, 13C)
Acquired Size
(1024, 256)
Spectral Size
(1024, 1024)
OTBS
H
N
Me
HO
O
O
MeO
230
(tentative)
ppm
ppm
ppm
ppm

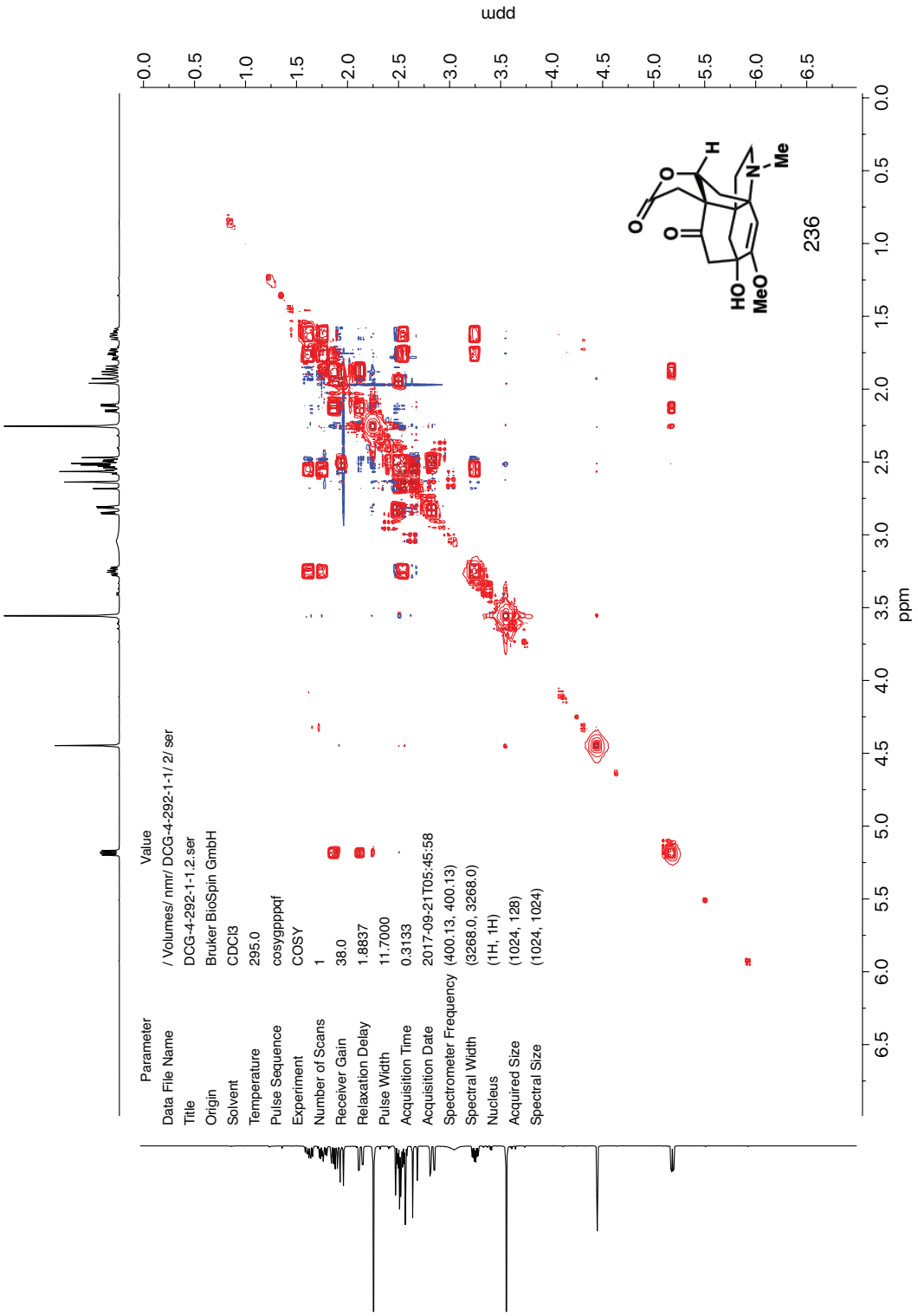

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-110-1/ 4/ ser
Title DCG-4-110-1.4.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2016-11-19T16:19:50
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
ppm
OTBS
HO
O
MeO
N
Me
H
230
(tentative)

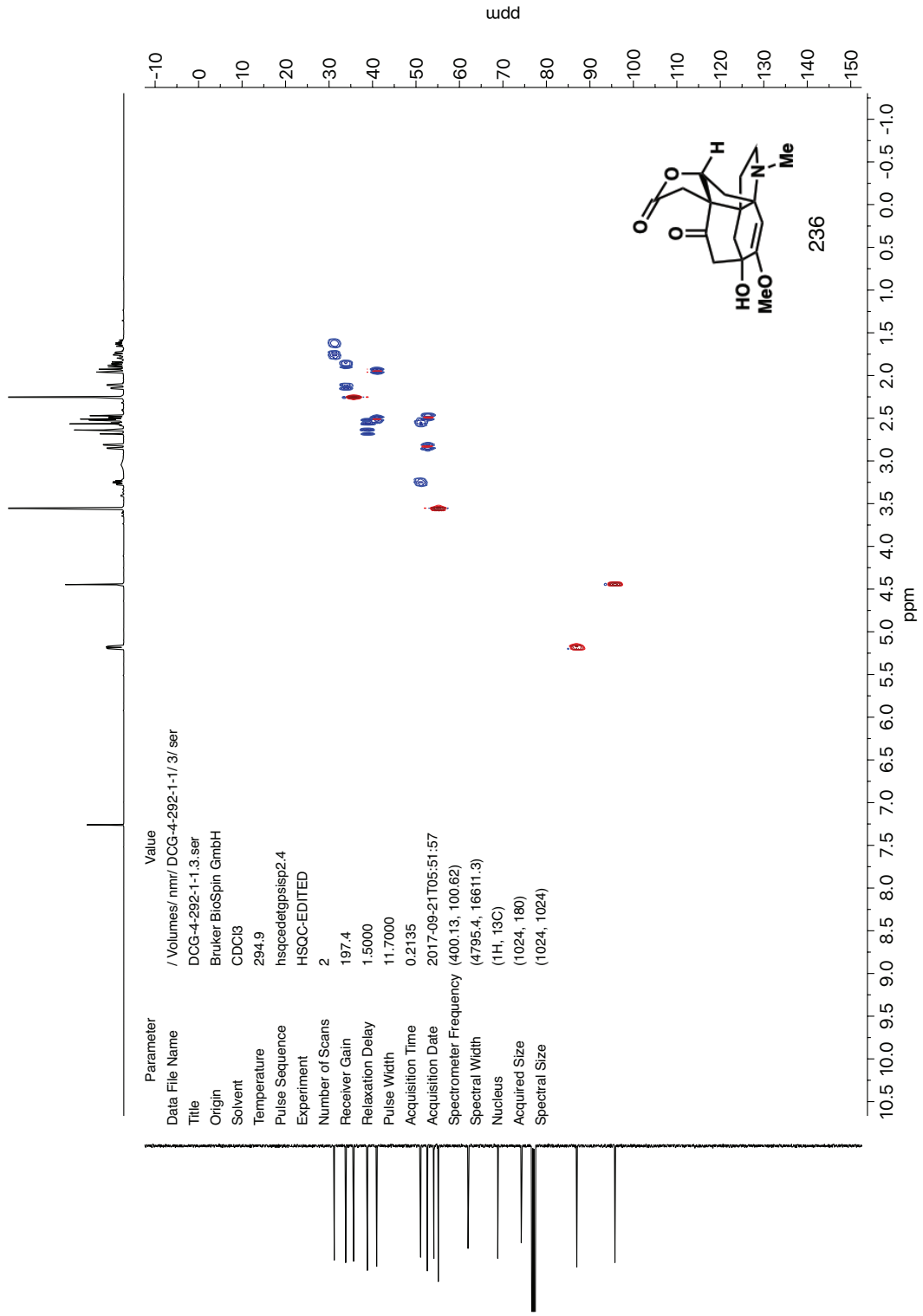

ppm
{0.05,-4.34}
{0.07,-4.90}
{0.87,25.72}
{1.73,30.23}
{2.37,44.24}
{2.84,37.79}
{2.81,53.86}
{3.61,54.89}
{4.03,54.28}
{4.05,76.09}
{5.15,111.54}
{5.90,114.63}
OTBS
H
HO
O
N
Me
O
MeO
230
(tentative)
Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-110-1/ 3/ ser
Title DCG-4-110-1.3.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 4
Receiver Gain 64.2
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2016-11-19T15:57:28
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)



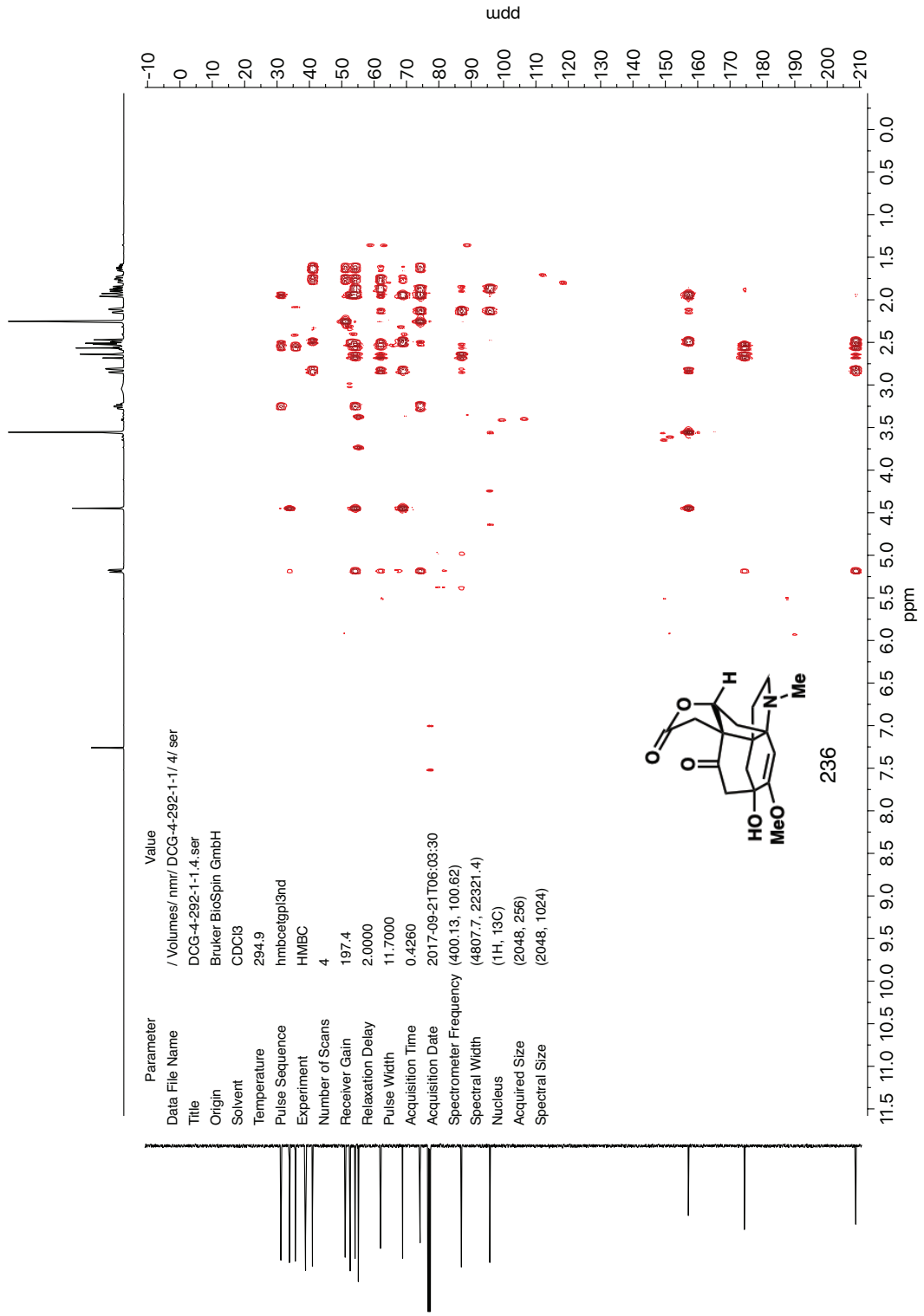
Parameter	Value
Data File Name	/ Volumes/ nmr/ DCG-4-110-1/ 4/ ser
Title	DCG-4-110-1.4.ser
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	294.9
Pulse Sequence	hmbcetgpl3nd
Experiment	HMBC
Number of Scans	4
Receiver Gain	197.4
Relaxation Delay	2.0000
Pulse Width	11.7000
Acquisition Time	0.4260
Acquisition Date	2016-11-19T16:19:50
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(4807.7, 22321.4)
Nucleus	(1H, 13C)
Acquired Size	(2048, 256)
Spectral Size	(2048, 1024)

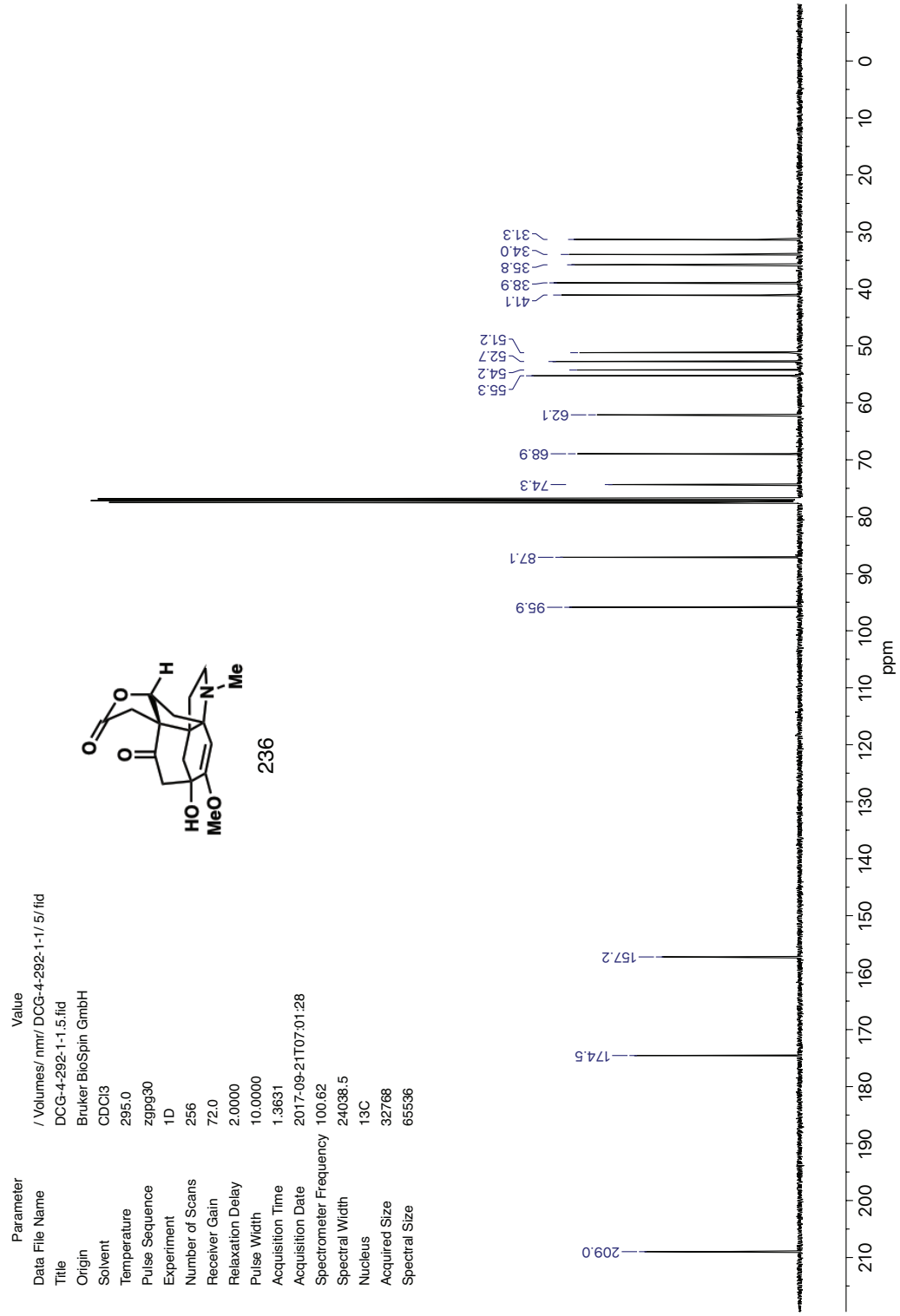

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-292-1-1/ 1/ fid
Title DCG-4-292-1-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 72.0
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-09-21T05:44:58
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
236
HO
MeO
O
O
O
H
N
Me
1.00
1.01
3.03
1.05
0.82
1.08
1.09
4.15
3.06
1.06
1.13
1.19
1.14
1.07
ppm
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5

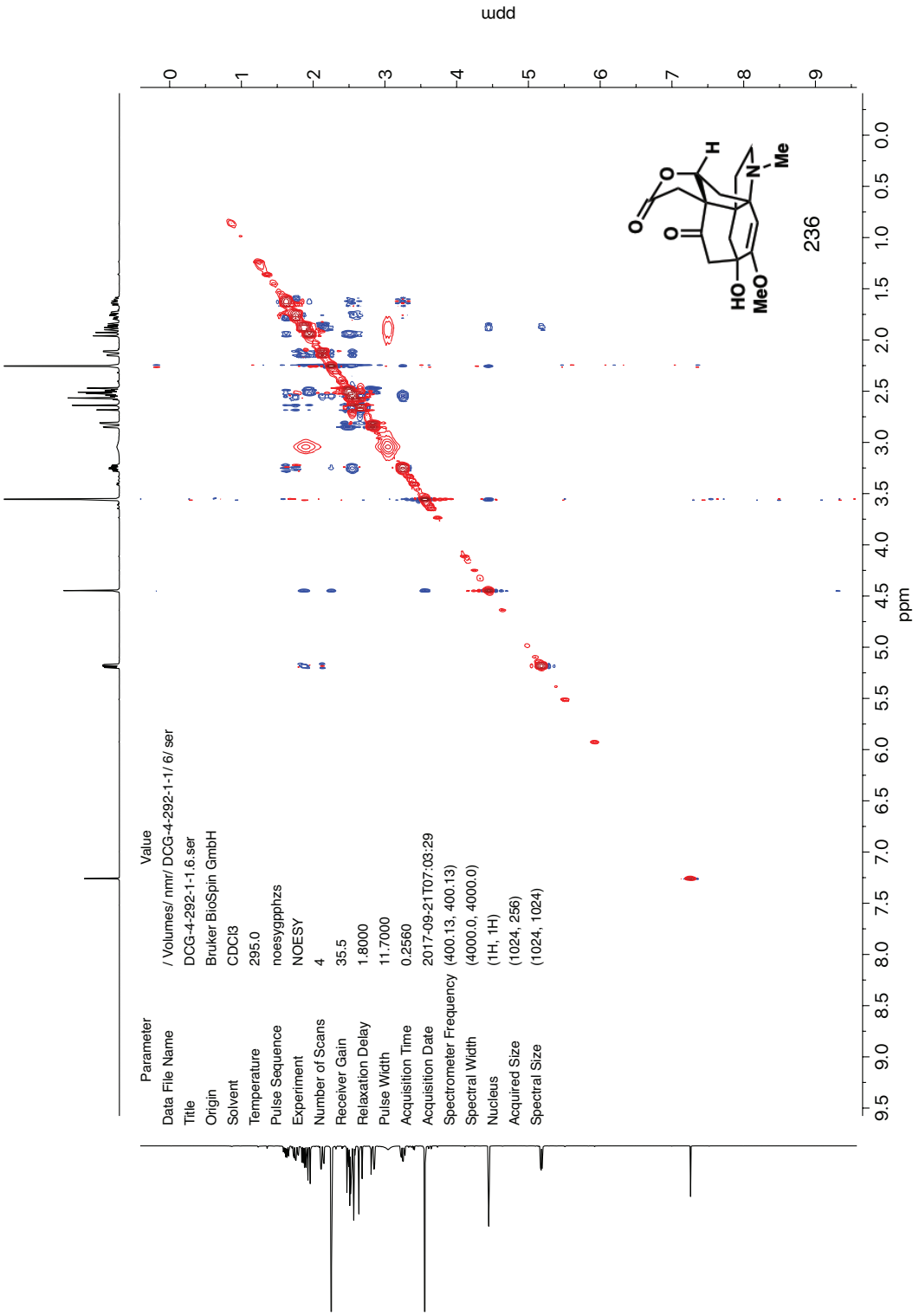

ppm
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-292-1-1/ 2/ ser
Title DCG-4-292-1-1.2.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 38.0
Relaxation Delay 1.8837
Pulse Width 11.7000
Acquisition Time 0.3133
Acquisition Date 2017-09-21T05:45:58
Spectrometer Frequency (400.13, 400.13)
Spectral Width (3268.0, 3268.0)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)
H
Me
HO
MeO
236

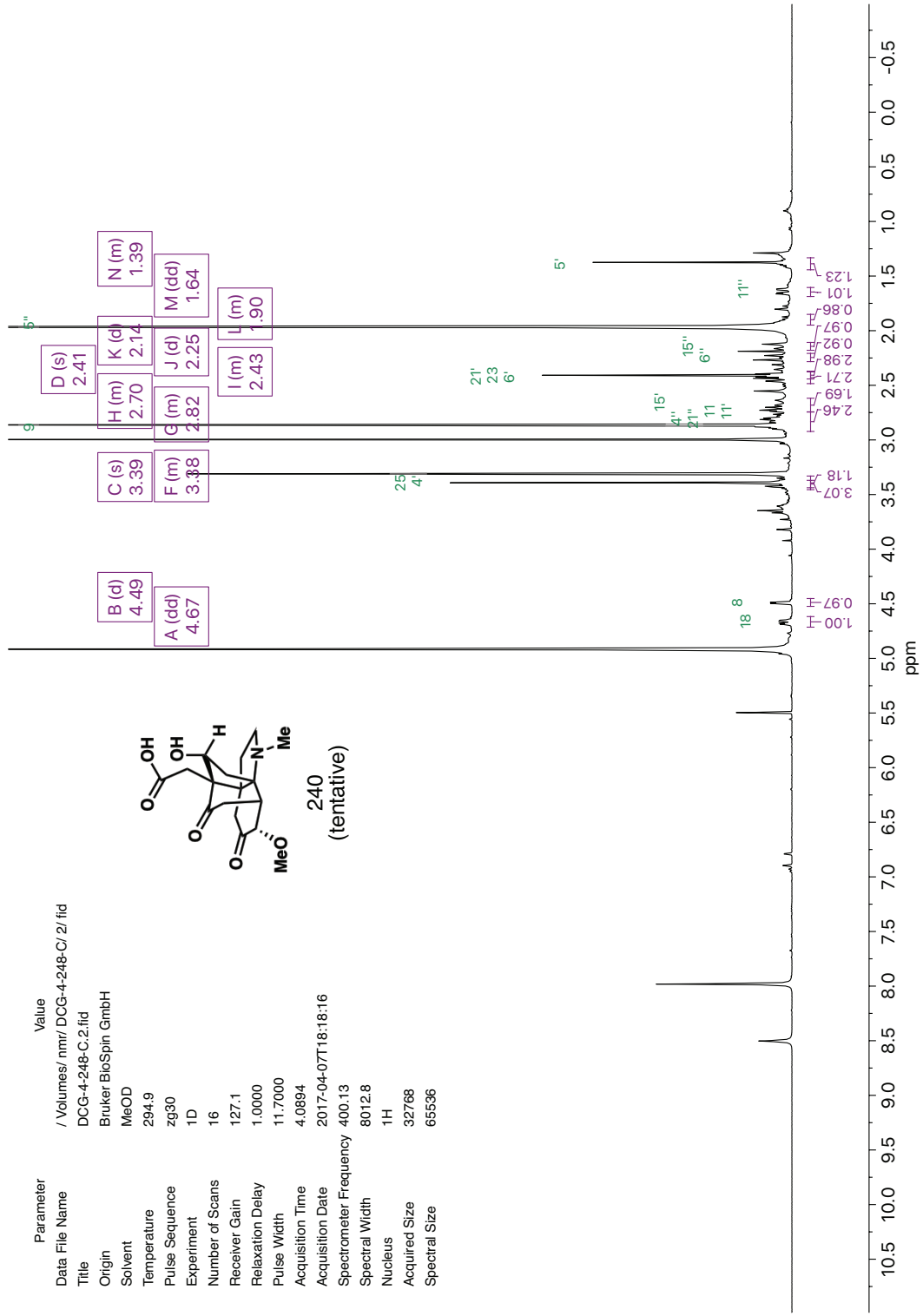


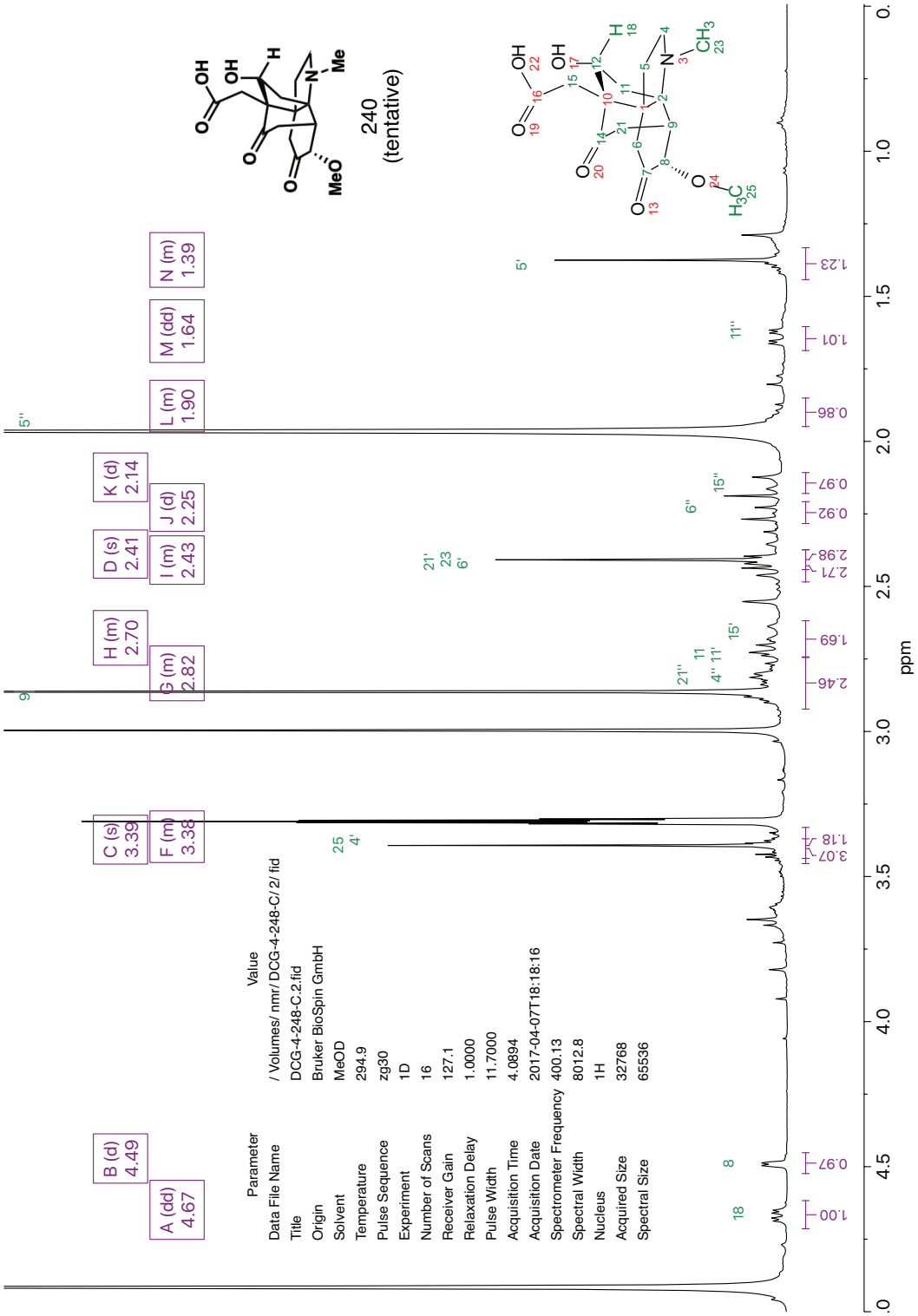
Parameter	Value
Data File Name	/ Volumes/ nmr/ DCG-4-292-1-1/ 3/ ser
Title	DCG-4-292-1-1.3.ser
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	294.9
Pulse Sequence	hsqcedetgpsisp2.4
Experiment	HSQC-EDITED
Number of Scans	2
Receiver Gain	197.4
Relaxation Delay	1.5000
Pulse Width	11.7000
Acquisition Time	0.2135
Acquisition Date	2017-09-21T05:51:57
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(4795.4, 16611.3)
Nucleus	(1H, 13C)
Acquired Size	(1024, 180)
Spectral Size	(1024, 1024)

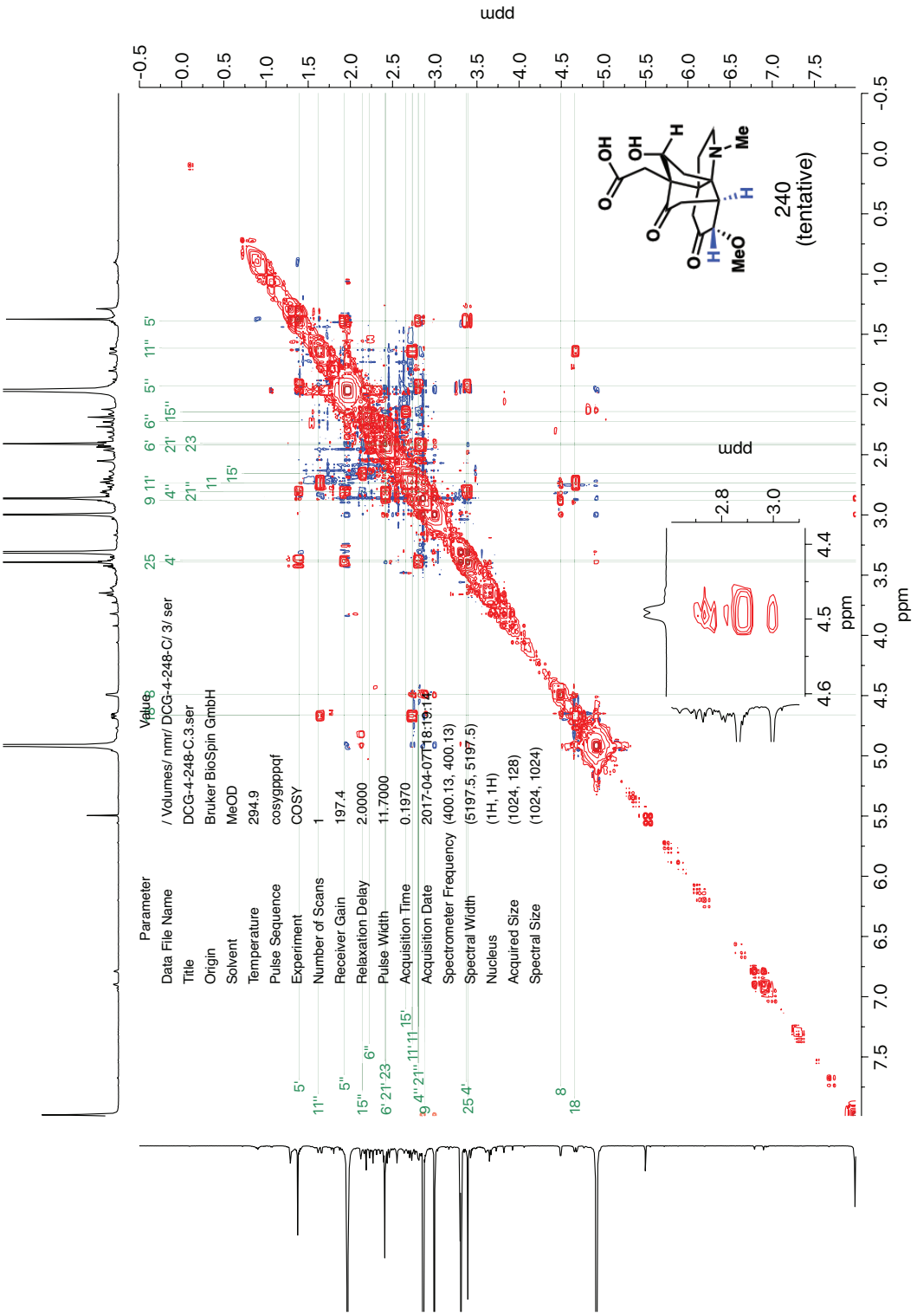

ppm
ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-292-1-1/ 4/ ser
Title DCG-4-292-1-1.4.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2017-09-21T06:03:30
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
H
O
O
N
Me
HO
MeO
236

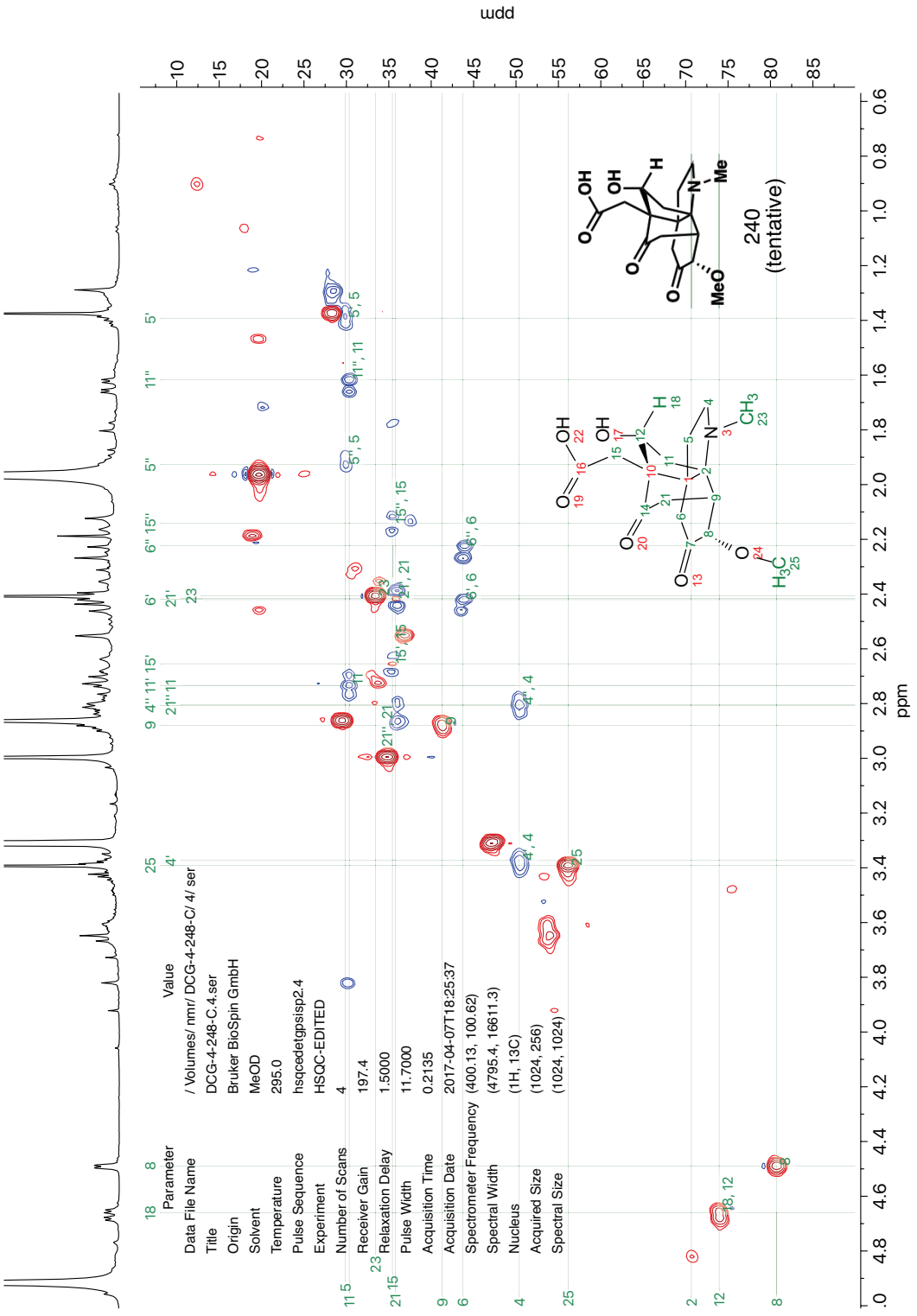

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-292-1-1/ 5/ fid
Title DCG-4-292-1-1.5.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-09-21T07:01:28
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
236
209.0
174.5
157.2
95.9
87.1
74.3
68.9
62.1
55.3
54.2
52.7
51.2
41.1
38.9
35.8
34.0
31.3
ppm

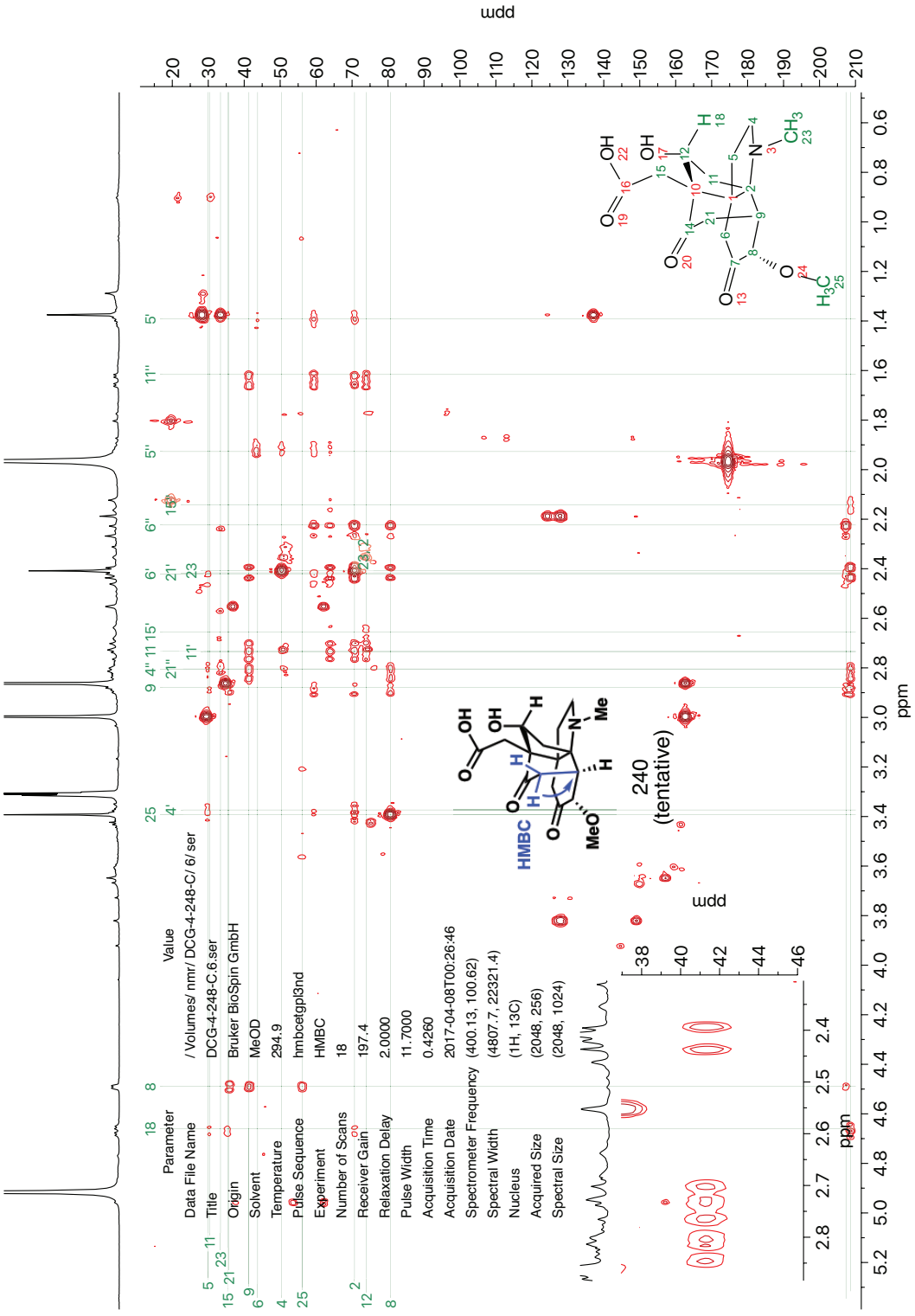

ppm
ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-292-1-1/ 6/ ser
Title DCG-4-292-1-1.6.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence noesygpphzs
Experiment NOESY
Number of Scans 4
Receiver Gain 35.5
Relaxation Delay 1.8000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2017-09-21T07:03:29
Spectrometer Frequency (400.13, 400.13)
Spectral Width (4000.0, 4000.0)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
H
N
Me
O
O
HO
MeO
236

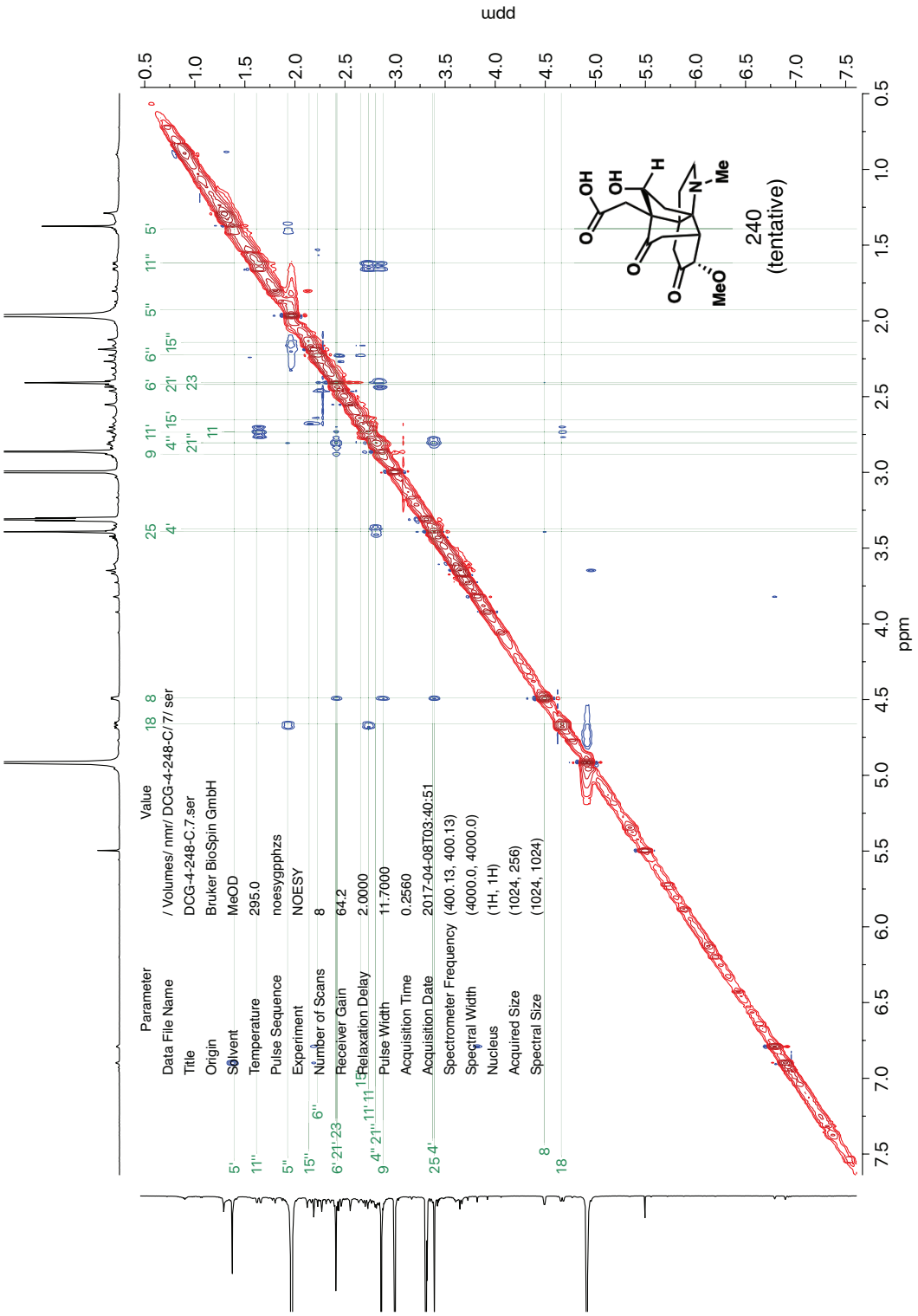

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-248-C/ 2/ fid
Title DCG-4-248-C.2.fid
Origin Bruker BioSpin GmbH
Solvent MeOD
Temperature 294.9
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 127.1
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-04-07T18:18:16
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
240
(tentative)
A (dd) 4.67
B (d) 4.49
C (s) 3.39
D (s) 2.41
F (m) 3.88
G (m) 4.82
H (m) 2.70
I (m) 2.43
J (d) 2.25
K (d) 2.14
L (m) 1.90
M (dd) 1.64
N (m) 1.39
ppm

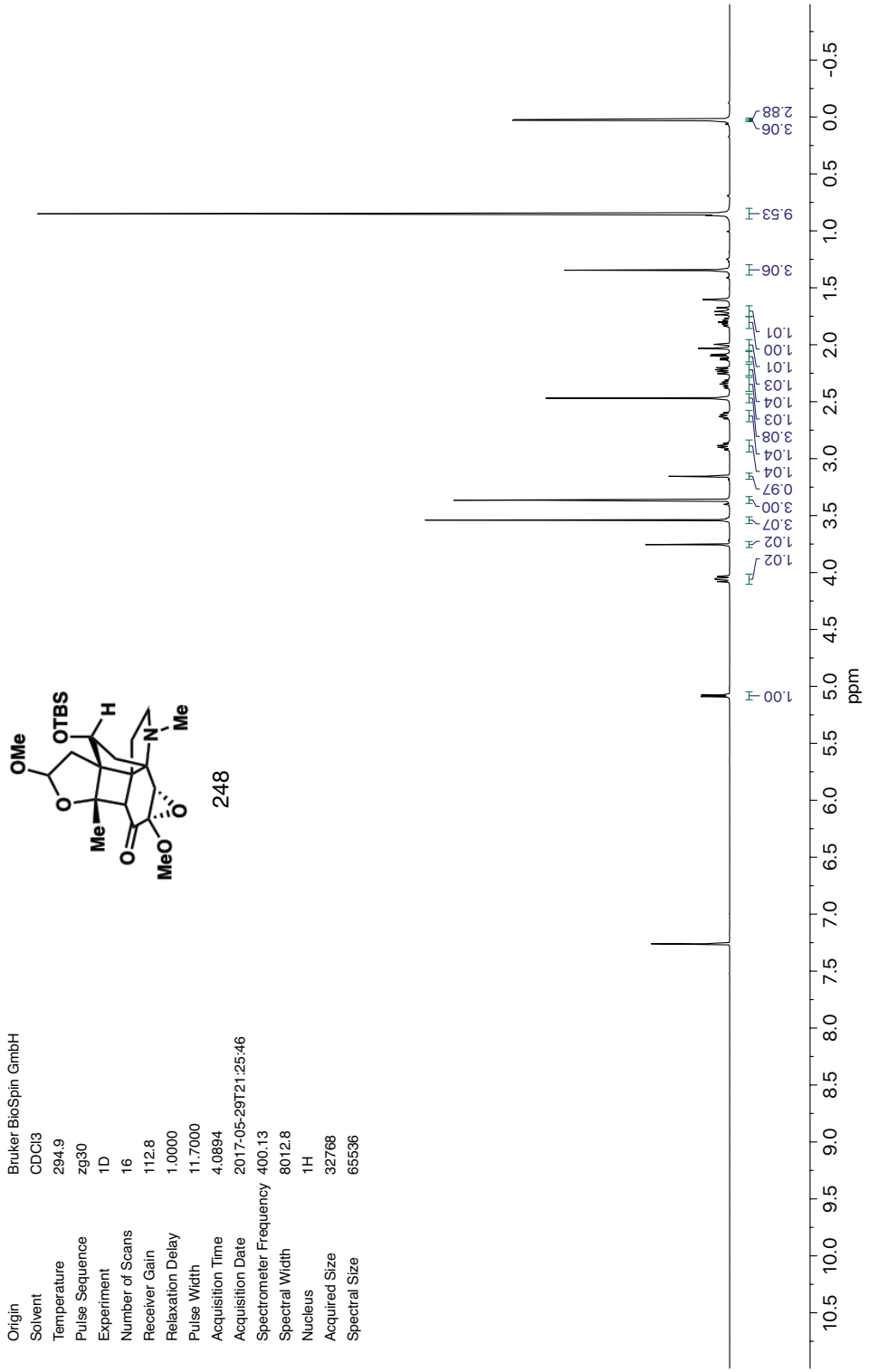

240
(tentative)
A (dd) 4.67
B (d) 4.49
C (s) 3.39
F (m) 3.38
G (m) 2.82
H (m) 2.70
D (s) 2.41
I (m) 2.43
J (d) 2.25
K (d) 2.14
L (m) 1.90
M (dd) 1.64
N (m) 1.39
Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-248-C/ 2/ fid
Title DCG-4-248-C.2.fid
Origin Bruker BioSpin GmbH
Solvent MeOD
Temperature 294.9
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 127.1
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-04-07T18:18:16
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
ppm

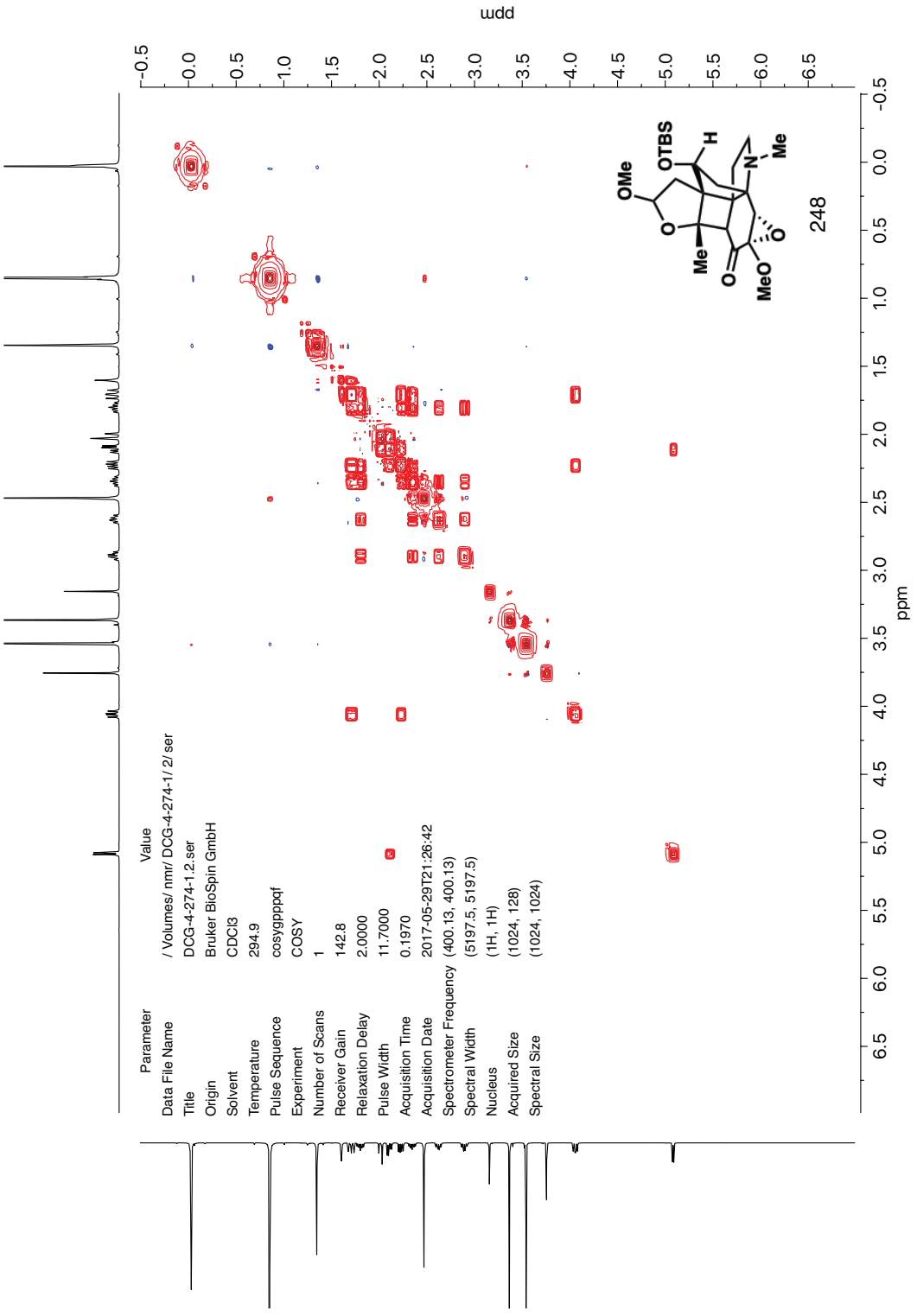

Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-4-248-C/ 3/ ser
Title
DCG-4-248-C.3.ser
Origin
Bruker BioSpin GmbH
Solvent
MeOD
Temperature
294.9
Pulse Sequence
cosygpppqf
Experiment
COSY
Number of Scans
1
Receiver Gain
197.4
Relaxation Delay
2.0000
Pulse Width
11.7000
Acquisition Time
0.1970
Acquisition Date
2017-04-07T18:19:17
Spectrometer Frequency
(400.13, 400.13)
Spectral Width
(5197.5, 5197.5)
Nucleus
(1H, 1H)
Acquired Size
(1024, 128)
Spectral Size
(1024, 1024)
ppm
240
(tentative)
OH
OH
O
O
H
N
Me
H
H
MeO

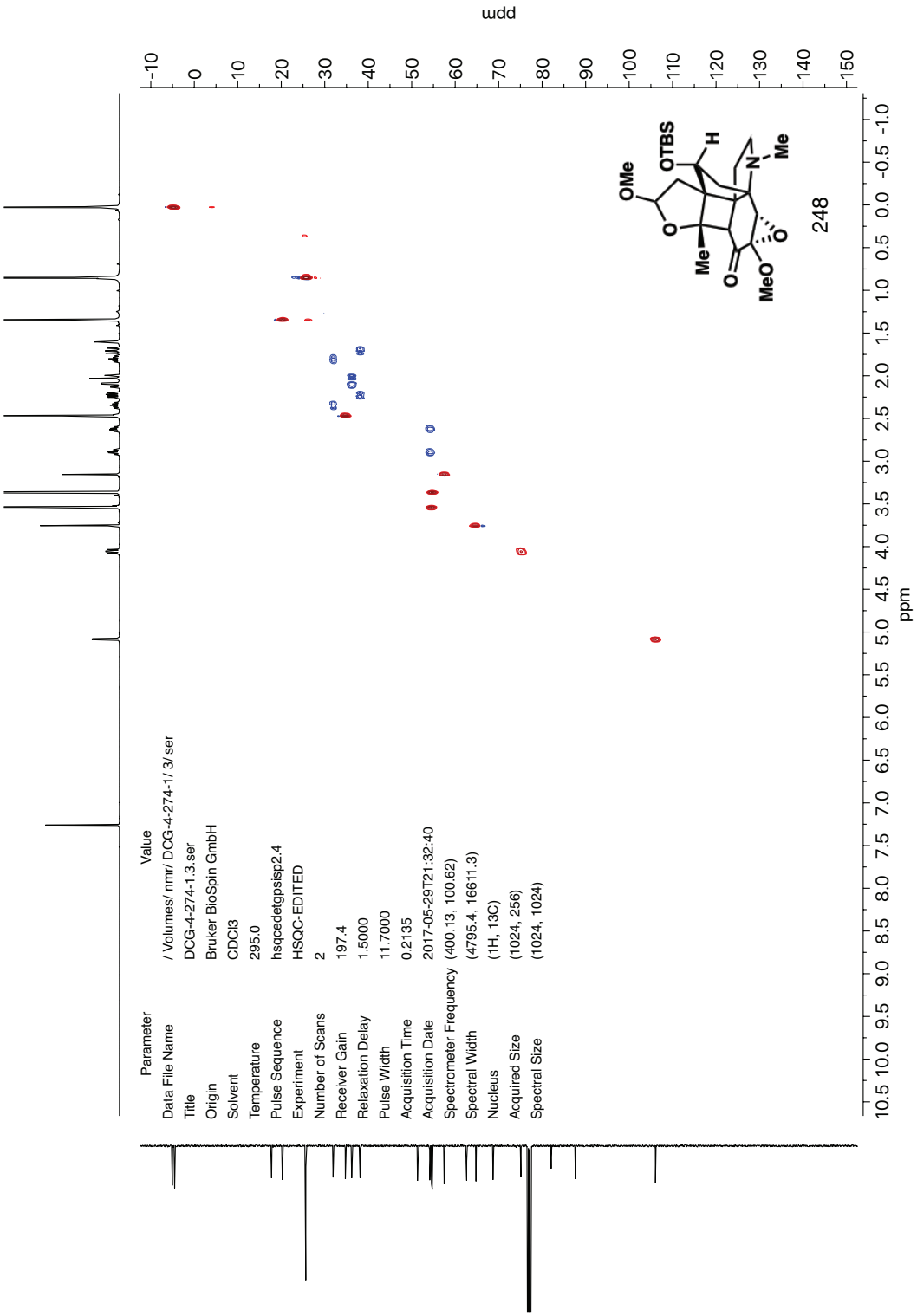

ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-248-C/ 4/ ser
Title DCG-4-248-C.4.ser
Origin Bruker BioSpin GmbH
Solvent MeOD
Temperature 295.0
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2017-04-07T18:25:37
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
MeO
Me
240
(tentative)

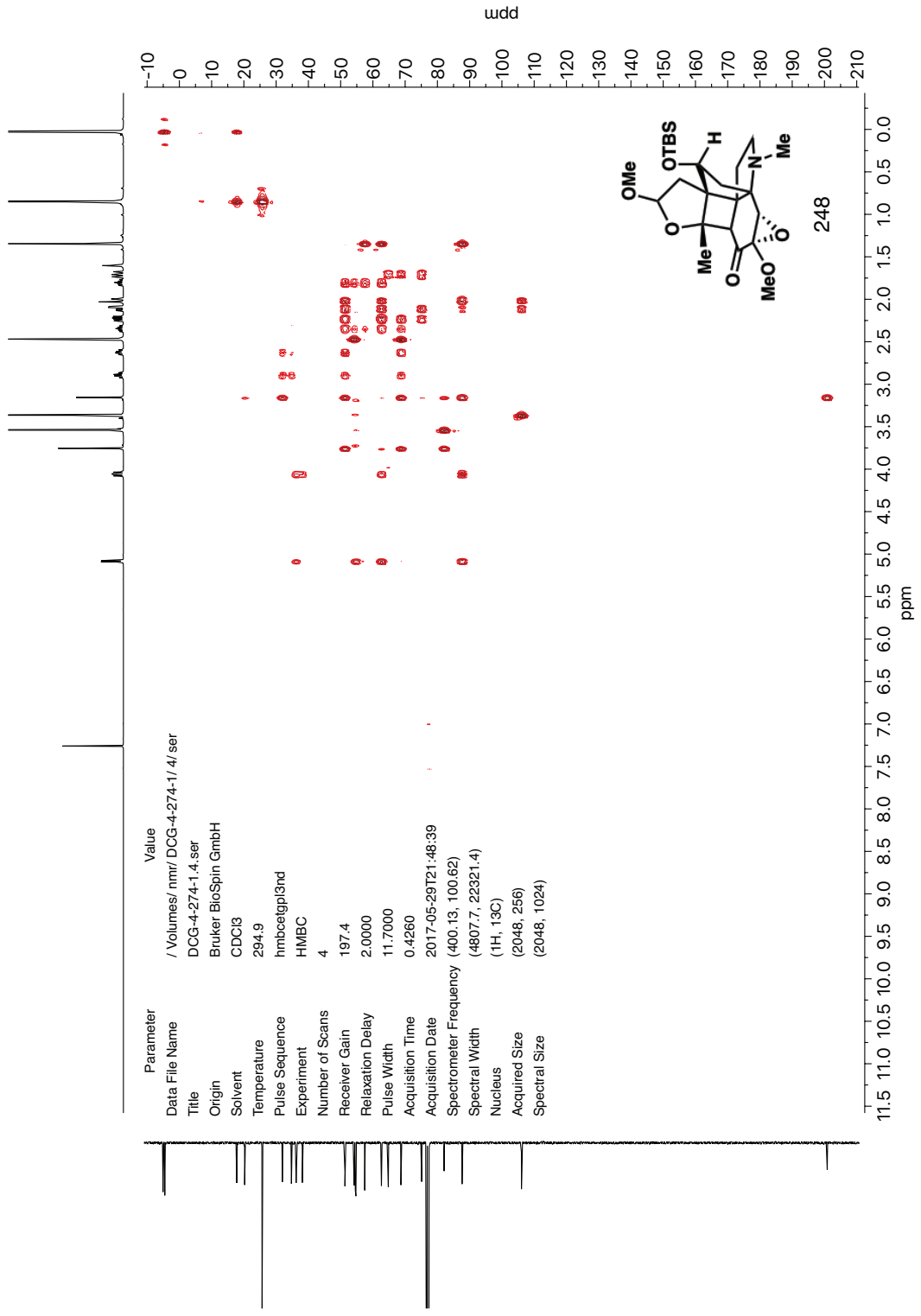

Parameter
Value
Data File Name / Volumes/ nmr/ DCG-4-248-C/ 6/ ser
Title DCG-4-248-C.6.ser
Origin Bruker BioSpin GmbH
Solvent MeOD
Temperature 294.9
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 18
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2017-04-08T00:26:46
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
HMBC
MeO
Me
240
(tentative)
ppm
ppm

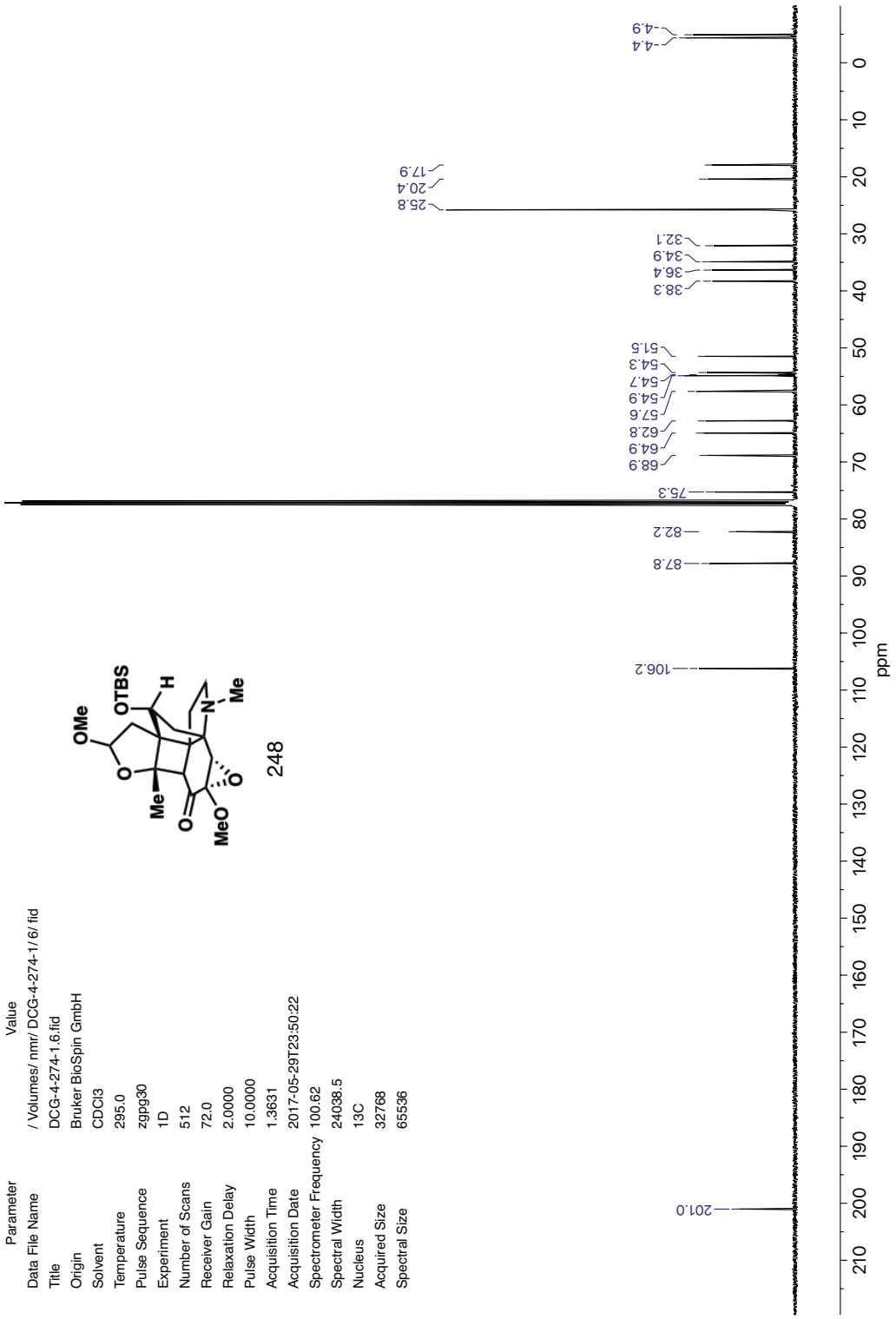

Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-4-248-C/ 7/ ser
Title
DCG-4-248-C.7.ser
Origin
Bruker BioSpin GmbH
Solvent
MeOD
Temperature
295.0
Pulse Sequence
noesygpphzs
Experiment
NOESY
Number of Scans
8
Receiver Gain
64.2
Relaxation Delay
2.0000
Pulse Width
11.7000
Acquisition Time
0.2560
Acquisition Date
2017-04-08T03:40:51
Spectrometer Frequency
(400.13, 400.13)
Spectral Width
(4000.0, 4000.0)
Nucleus
(1H, 1H)
Acquired Size
(1024, 256)
Spectral Size
(1024, 1024)
240
(tentative)
ppm

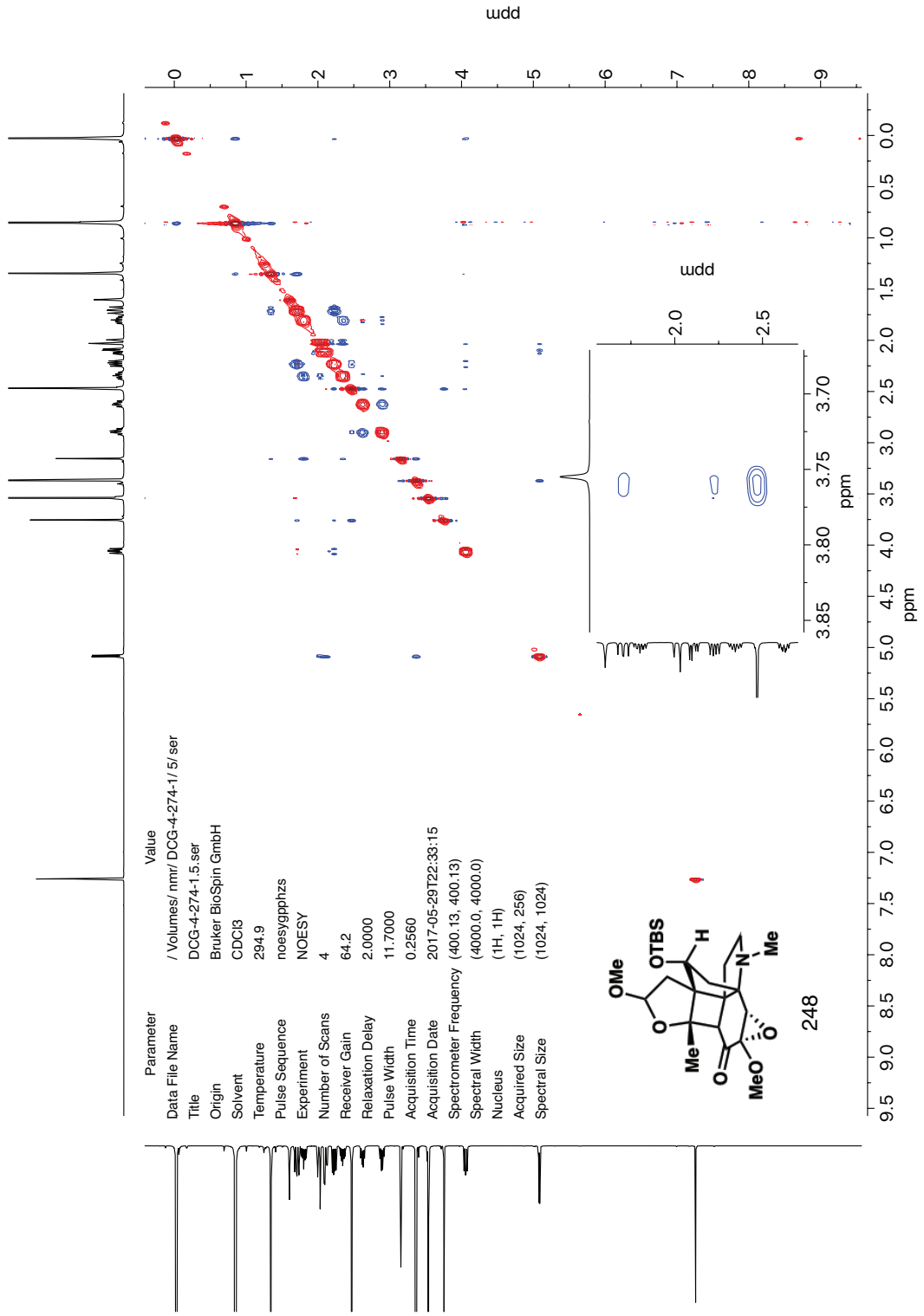

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-274-1/1/1/ fid
Title DCG-4-274-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 112.8
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-05-29T21:25:46
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
OMe
OTBS
H
N
Me
O
Me
O
MeO
O
248
1.00
1.02
3.07
3.00
0.97
1.04
1.04
3.08
1.03
1.04
1.03
1.01
1.00
1.01
3.06
9.53
3.06
2.88
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm

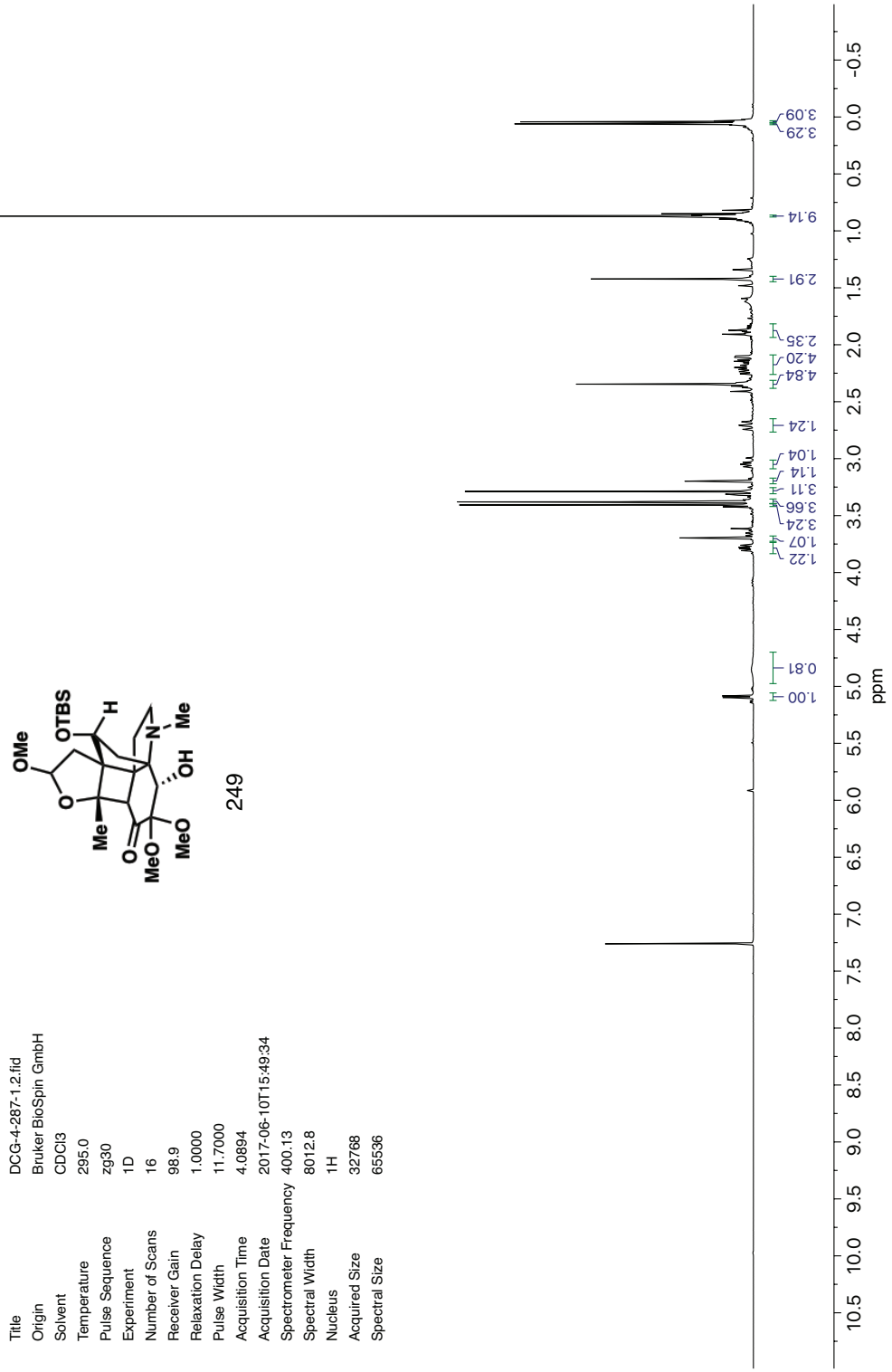

ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-274-1/ 2/ ser
Title DCG-4-274-1.2.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 142.8
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.1970
Acquisition Date 2017-05-29T21:26:42
Spectrometer Frequency (400.13, 400.13)
Spectral Width (5197.5, 5197.5)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)
OMe
OTBS
H
Me
N
Me
O
O
Me
O
MeO
248

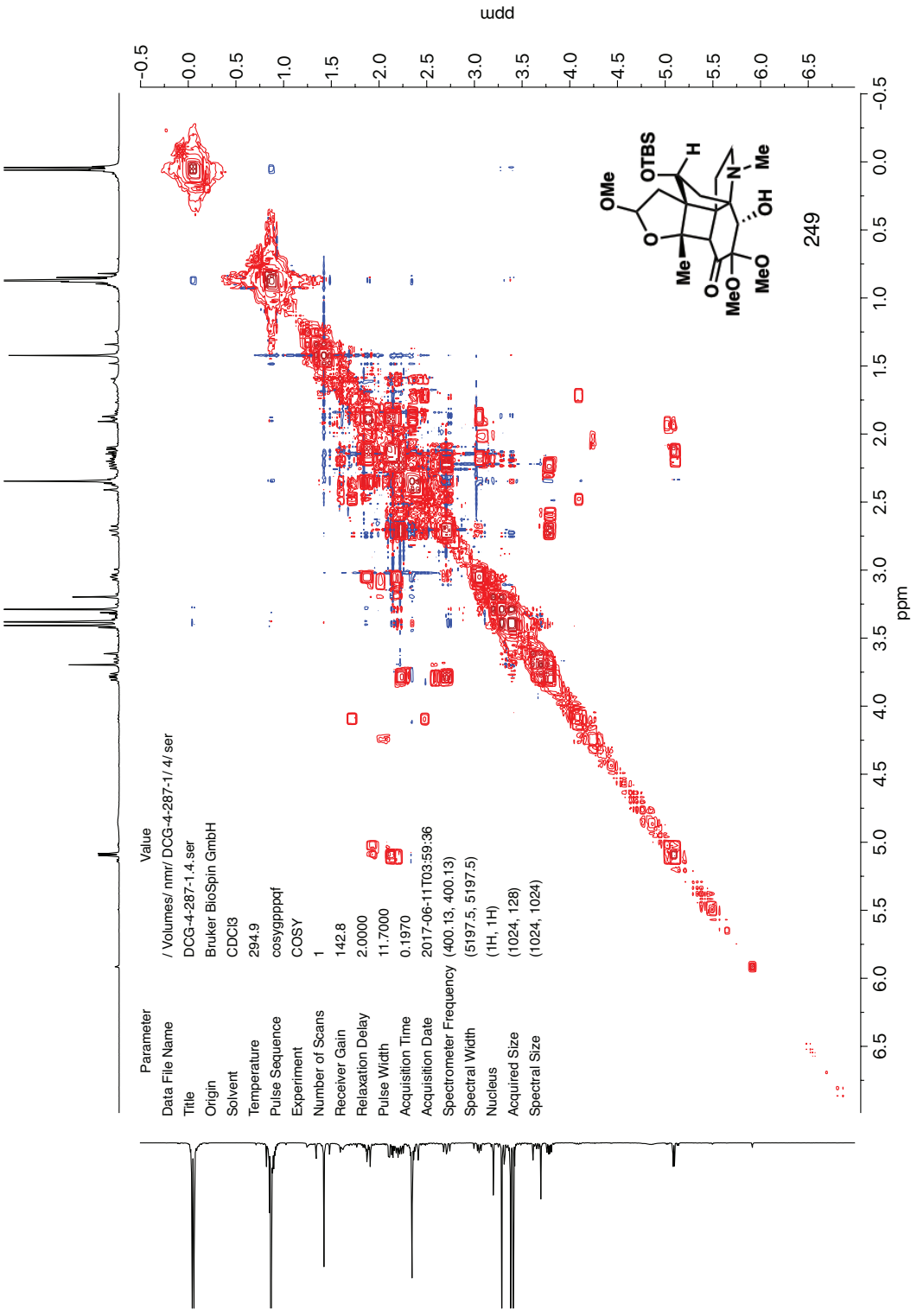

ppm
ppm
OMe
OTBS
H
Me
N
Me
O
O
O
MeO
248
Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-274-1/ 3/ ser
Title DCG-4-274-1.3.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2017-05-29T21:32:40
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)

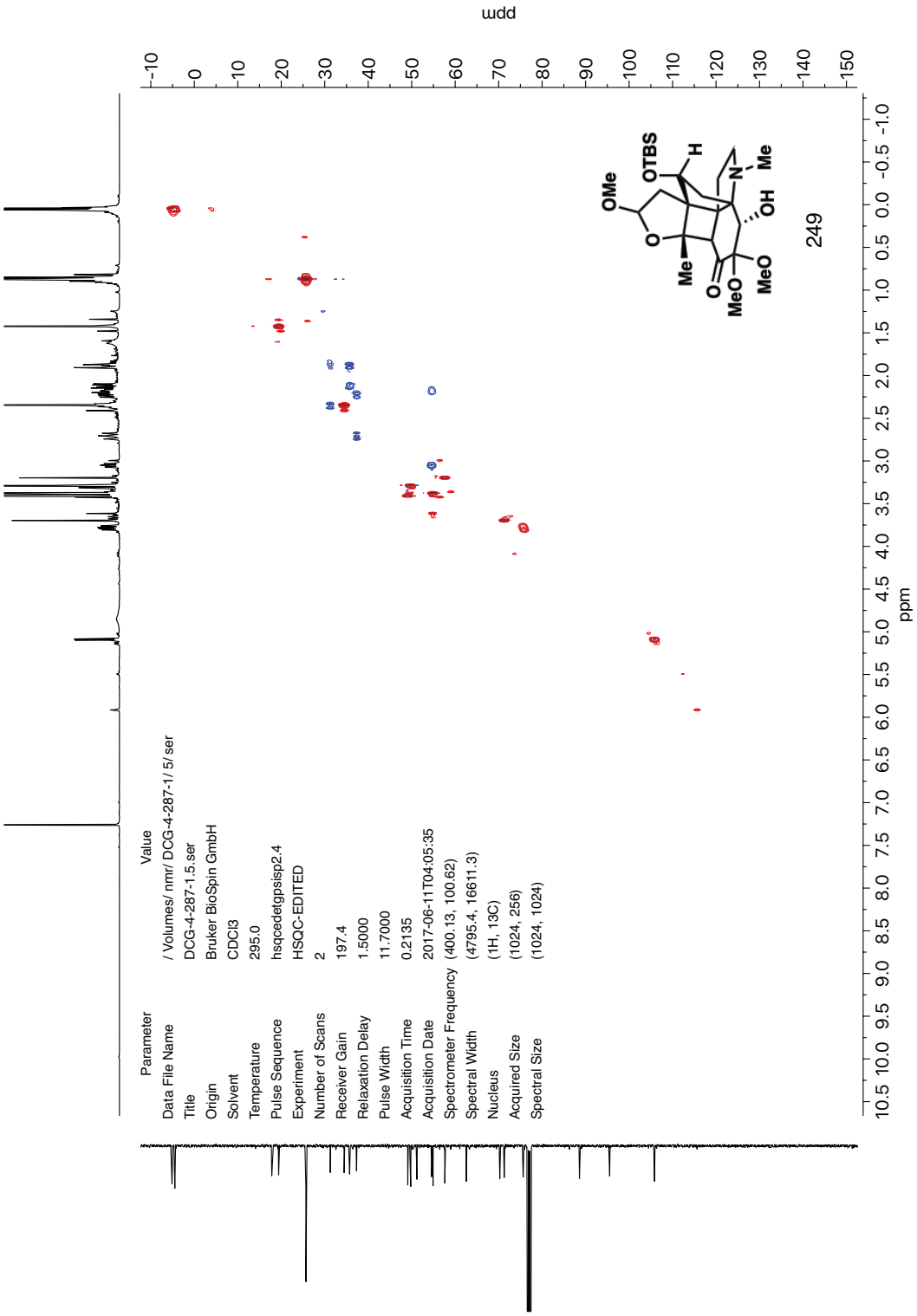

ppm
ppm
OMe
OTBS
H
Me
N
Me
O
O
MeO
248
Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-274-1/ 4/ ser
Title DCG-4-274-1.4.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2017-05-29T21:48:39
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)

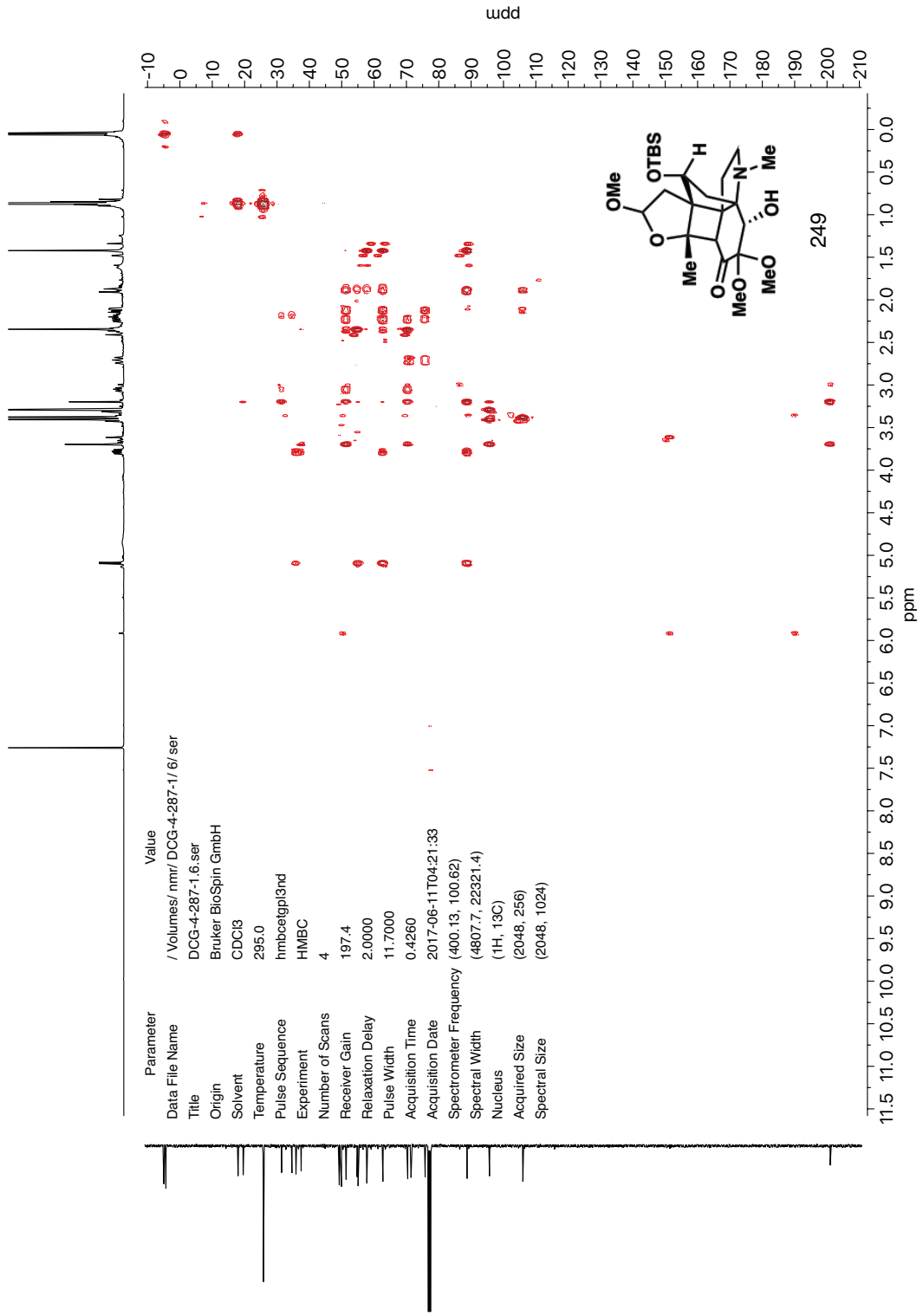

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-274-1/ 6/ fid
Title DCG-4-274-1.6.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 512
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-05-29T23:50:22
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OMe
OTBS
H
N
Me
O
Me
O
O
MeO
248
201.0
106.2
87.8
82.2
75.3
68.9
64.9
62.8
57.6
54.9
54.7
54.3
51.5
38.3
36.4
34.9
32.1
25.8
20.4
17.9
-4.4
-4.9
ppm

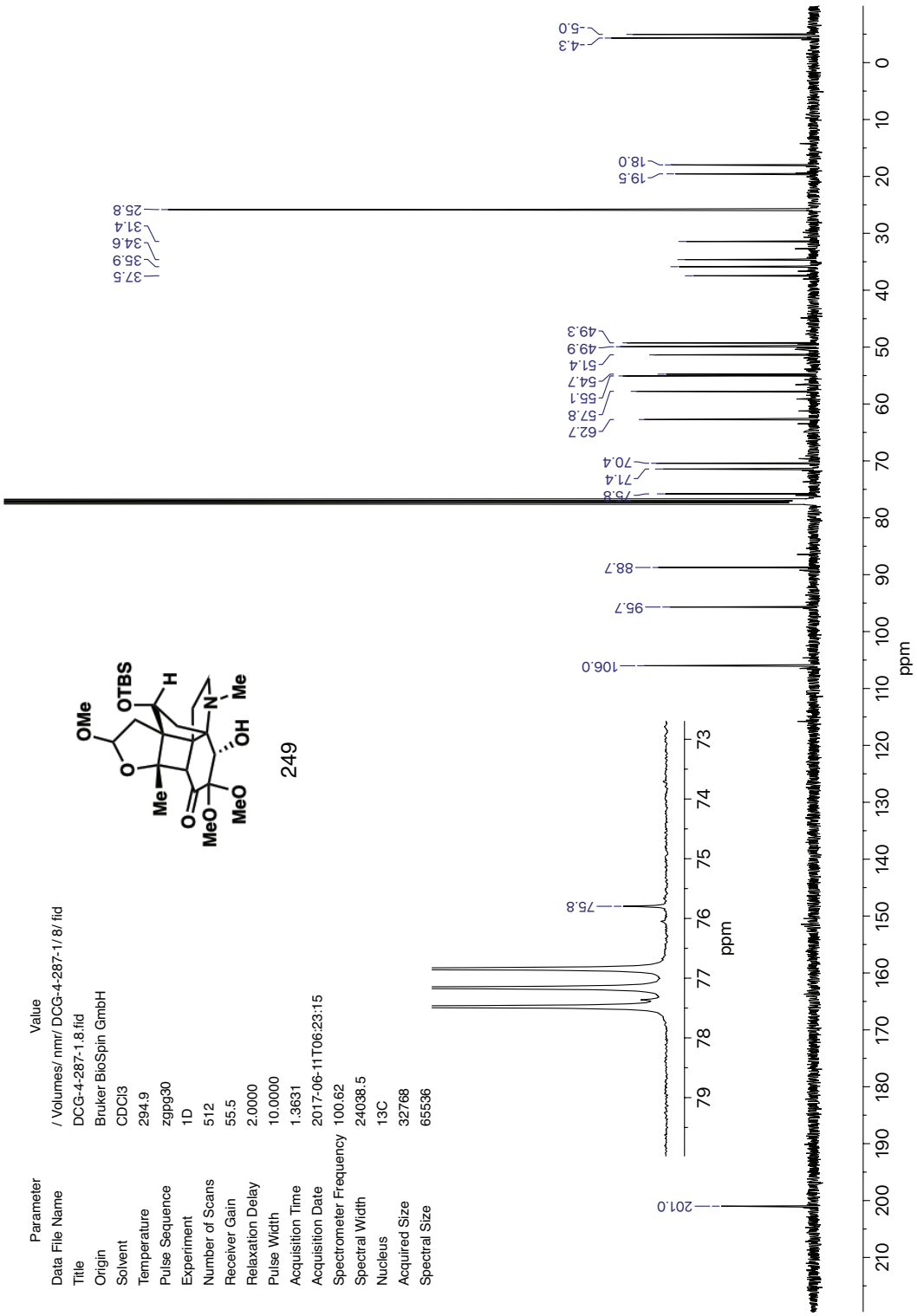

Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-4-274-1/ 5/ ser
Title
DCG-4-274-1.5.ser
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
noesygpphzs
Experiment
NOESY
Number of Scans
4
Receiver Gain
64.2
Relaxation Delay
2.0000
Pulse Width
11.7000
Acquisition Time
0.2560
Acquisition Date
2017-05-29T22:33:15
Spectrometer Frequency
(400.13, 400.13)
Spectral Width
(4000.0, 4000.0)
Nucleus
(1H, 1H)
Acquired Size
(1024, 256)
Spectral Size
(1024, 1024)
OMe
OTBS
H
Me
N
Me
O
O
MeO
248
ppm
ppm
ppm

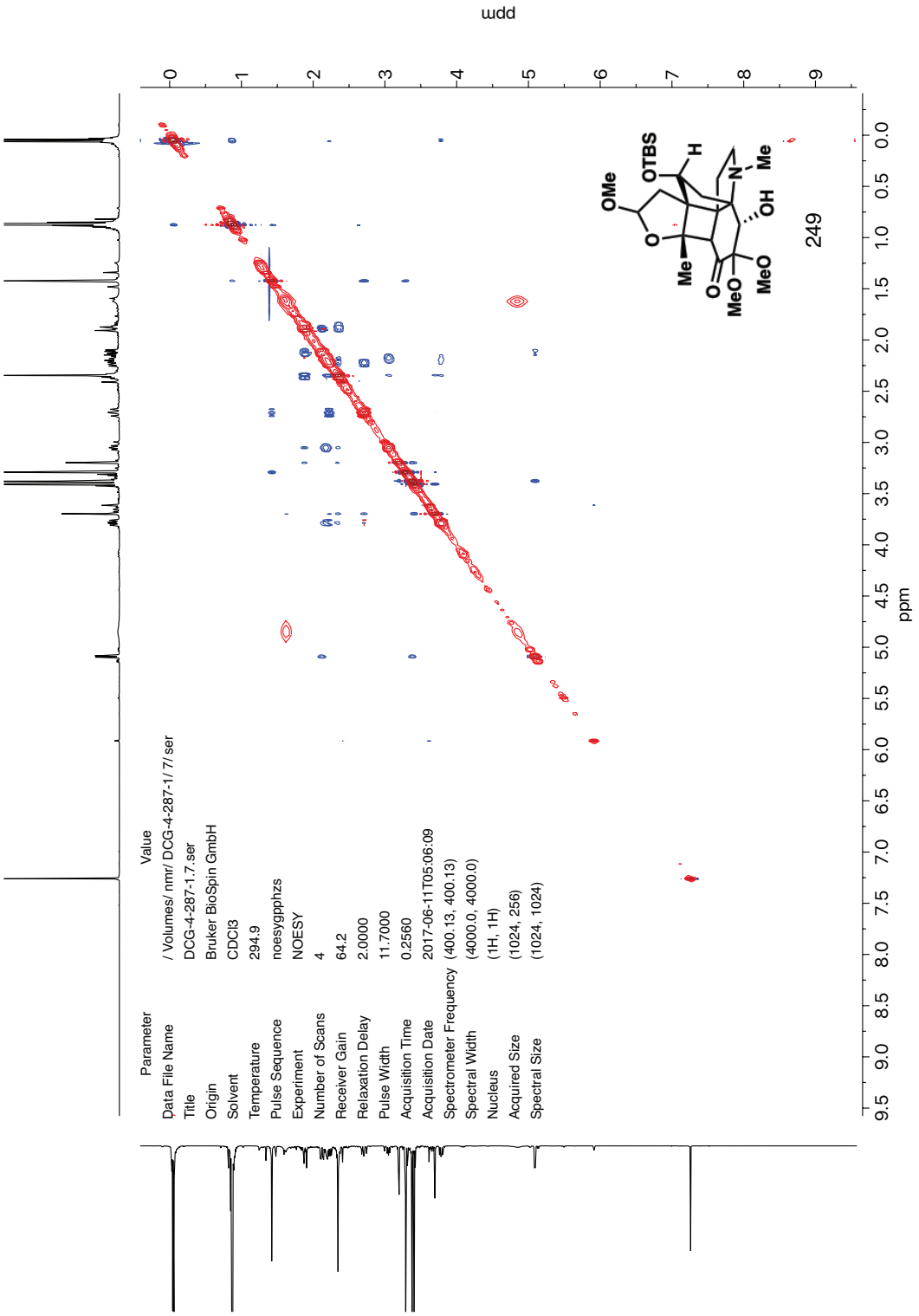

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-287-1/2/ fid
Title DCG-4-287-1.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 98.9
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-06-10T15:49:34
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
OMe
OTBS
H
N
Me
OH
Me
O
MeO
MeO
249
1.00
0.81
1.22
1.07
3.24
3.66
3.11
1.14
1.04
1.24
4.84
4.20
2.35
2.91
9.14
3.29
3.09
ppm

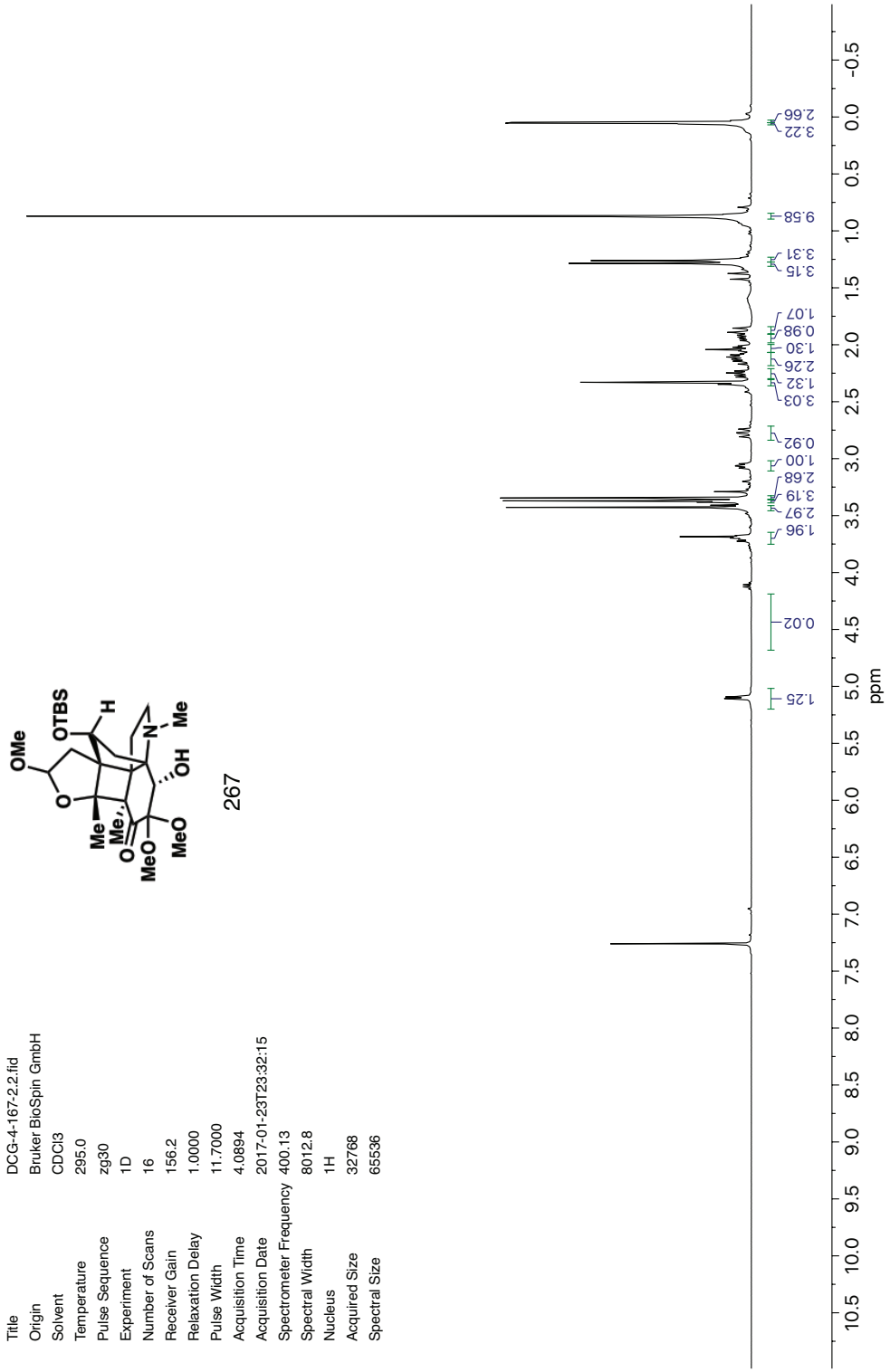

ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-287-1/ 4/ ser
Title DCG-4-287-1.4.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 142.8
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.1970
Acquisition Date 2017-06-11T03:59:36
Spectrometer Frequency (400.13, 400.13)
Spectral Width (5197.5, 5197.5)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)
OMe
OTBS
H
N
Me
OH
Me
O
Me
MeO
MeO
249

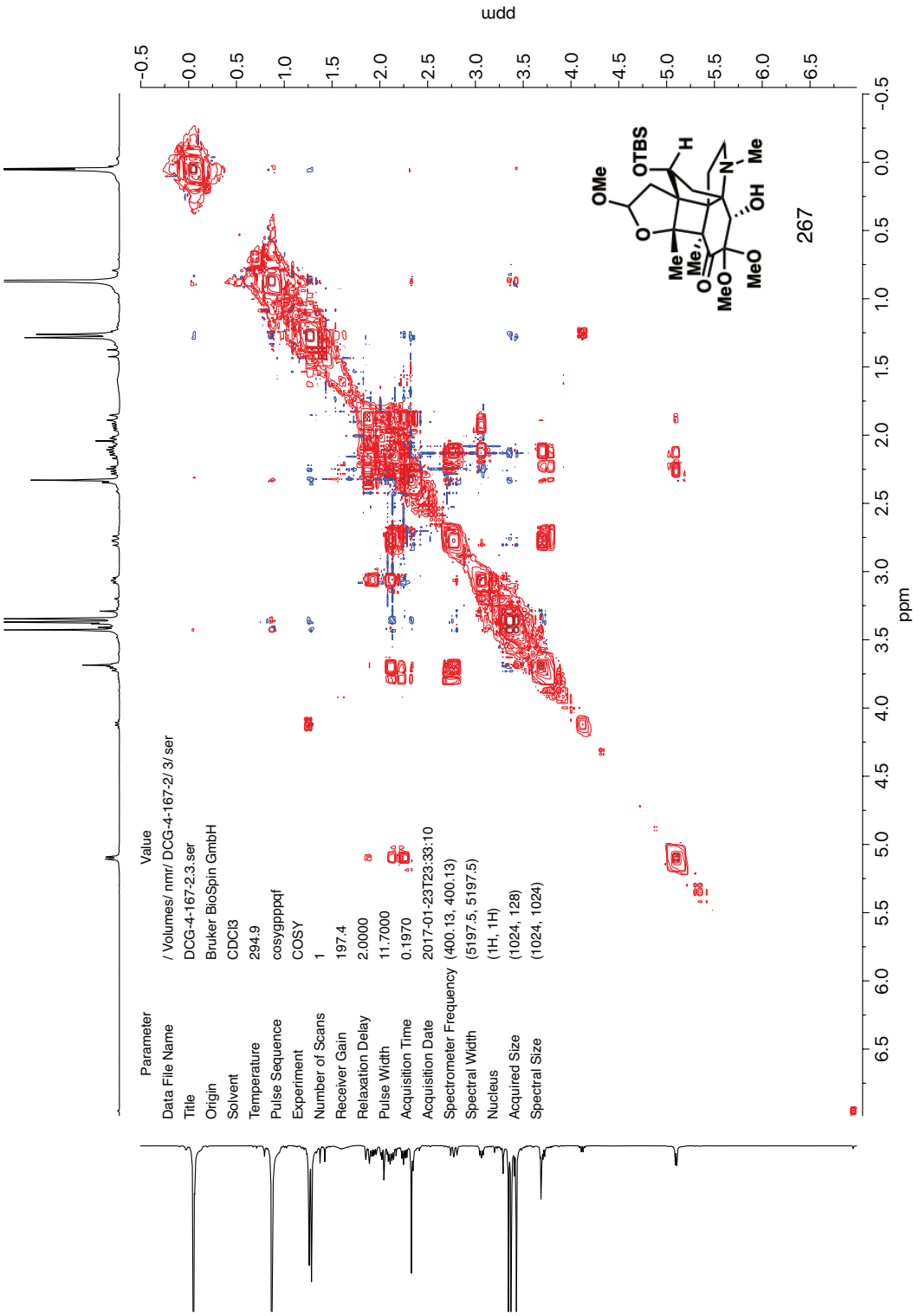

ppm
ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-287-1/ 5/ ser
Title DCG-4-287-1.5.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2017-06-11T04:05:35
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
OMe
OTBS
H
N
Me
OH
Me
O
MeO
MeO
Me
O
249

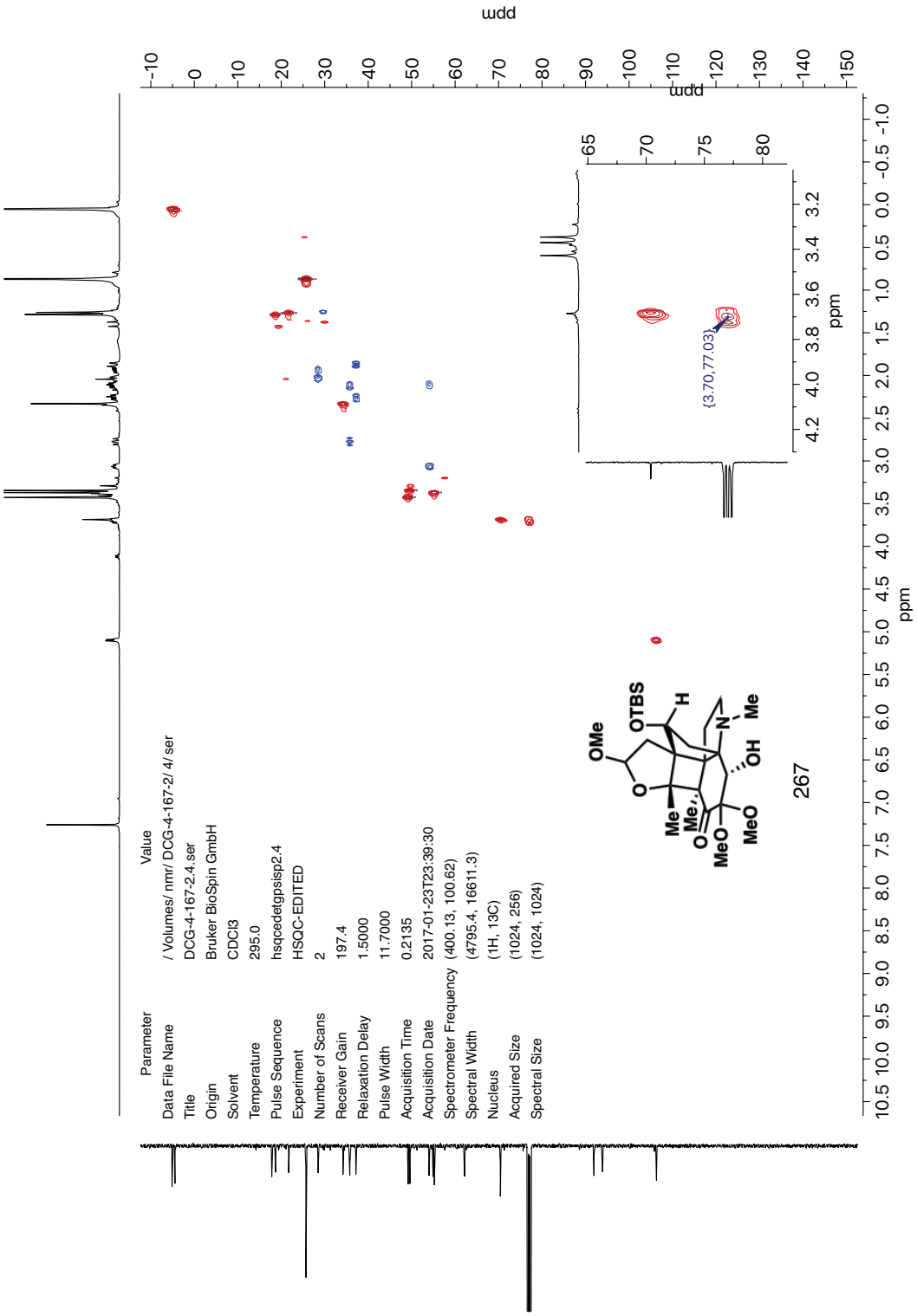

ppm
ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-287-1/ 6/ ser
Title DCG-4-287-1.6.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2017-06-11T04:21:33
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
OMe
OTBS
H
Me
N
Me
O
OH
MeO
MeO
249

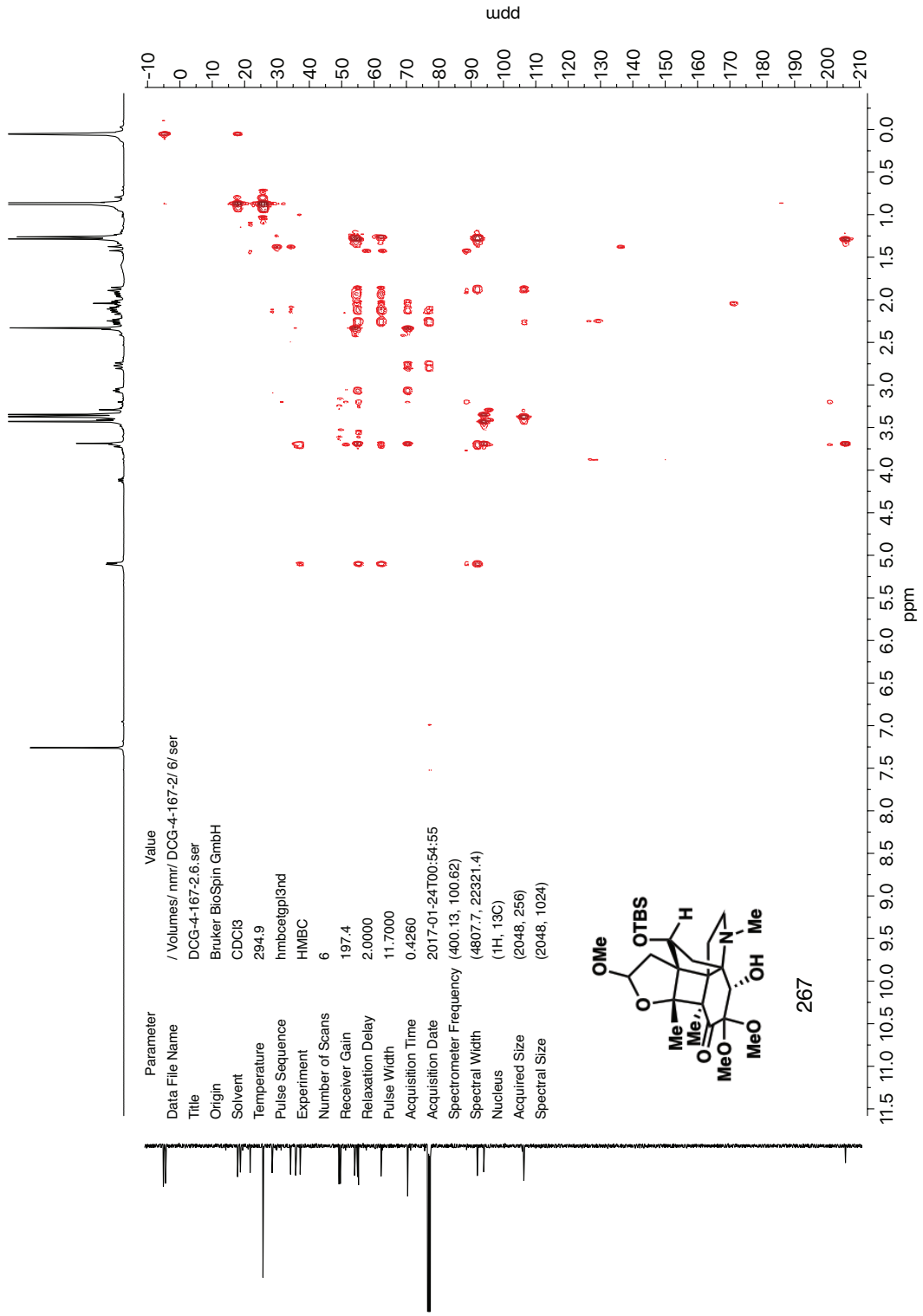

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-287-1/ 8/ fid
Title DCG-4-287-1.8.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 512
Receiver Gain 55.5
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-06-11T06:23:15
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OMe
OTBS
H
N
Me
OH
O
Me
MeO
MeO
O
249
ppm
ppm

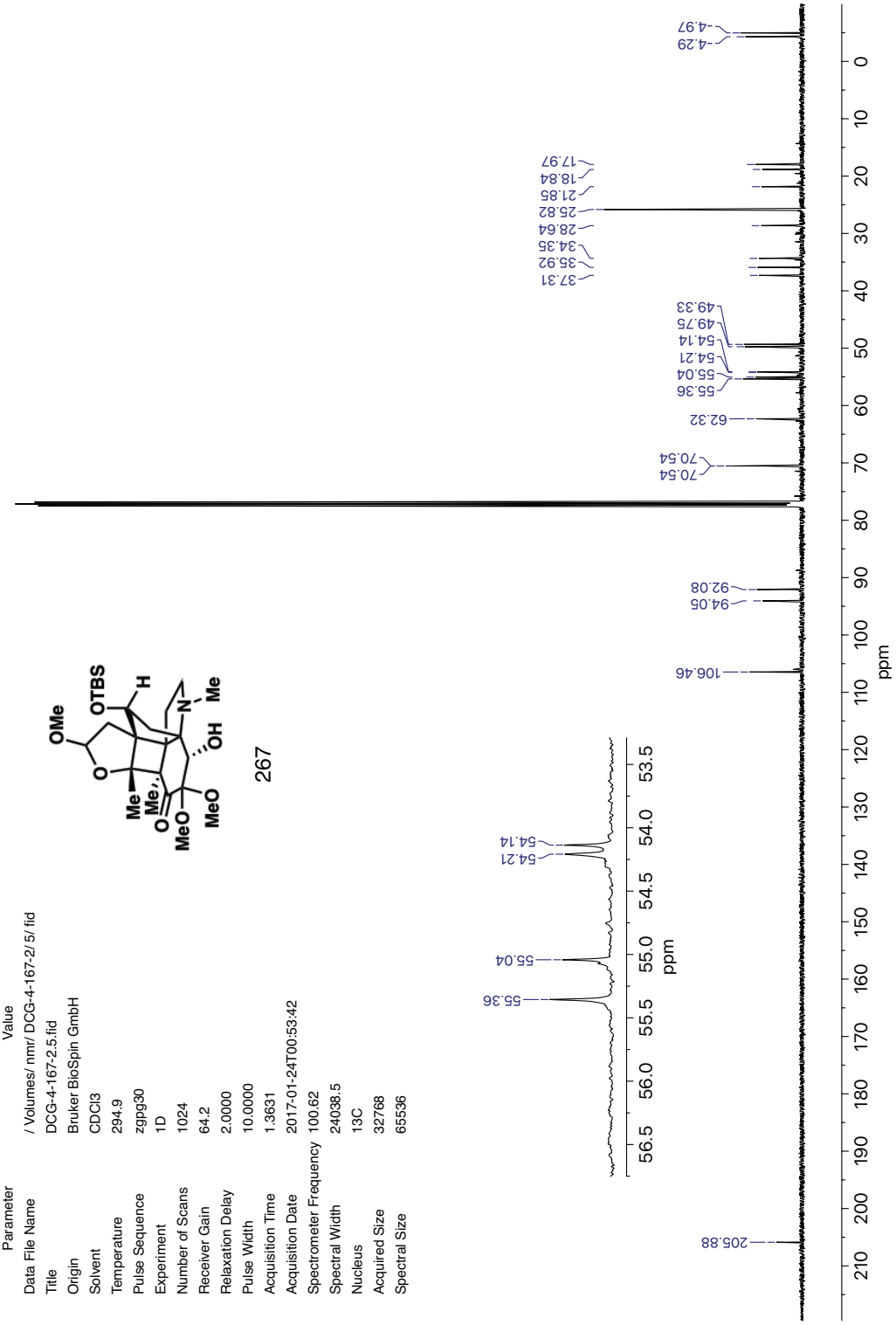

ppm
ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-287-1/ 7/ ser
Title DCG-4-287-1.7.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence noesygpphzs
Experiment NOESY
Number of Scans 4
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2017-06-11T05:06:09
Spectrometer Frequency (400.13, 400.13)
Spectral Width (4000.0, 4000.0)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
OMe
OTBS
H
Me
N
Me
OH
O
MeO
MeO
O
249

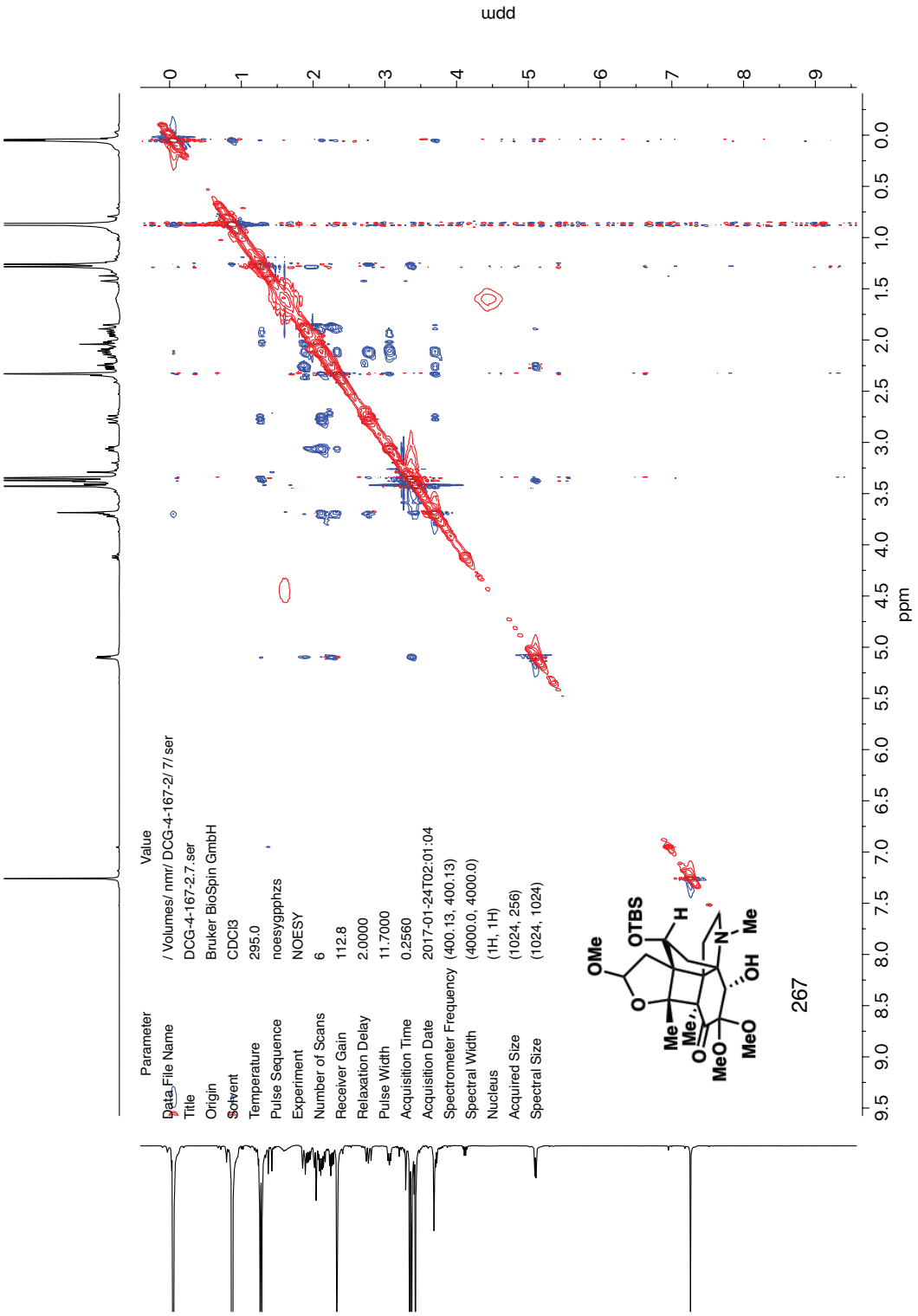

OMe
OTBS
H
N
Me
OH
O
Me
Me
O
MeO
MeO
267
Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-167-2/2/ fid
Title DCG-4-167-2.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 156.2
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-01-23T23:32:15
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
1.25
0.02
1.96
2.97
3.19
2.68
1.00
0.92
3.03
1.32
2.26
1.30
0.98
1.07
3.15
3.31
9.58
3.22
2.66
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm

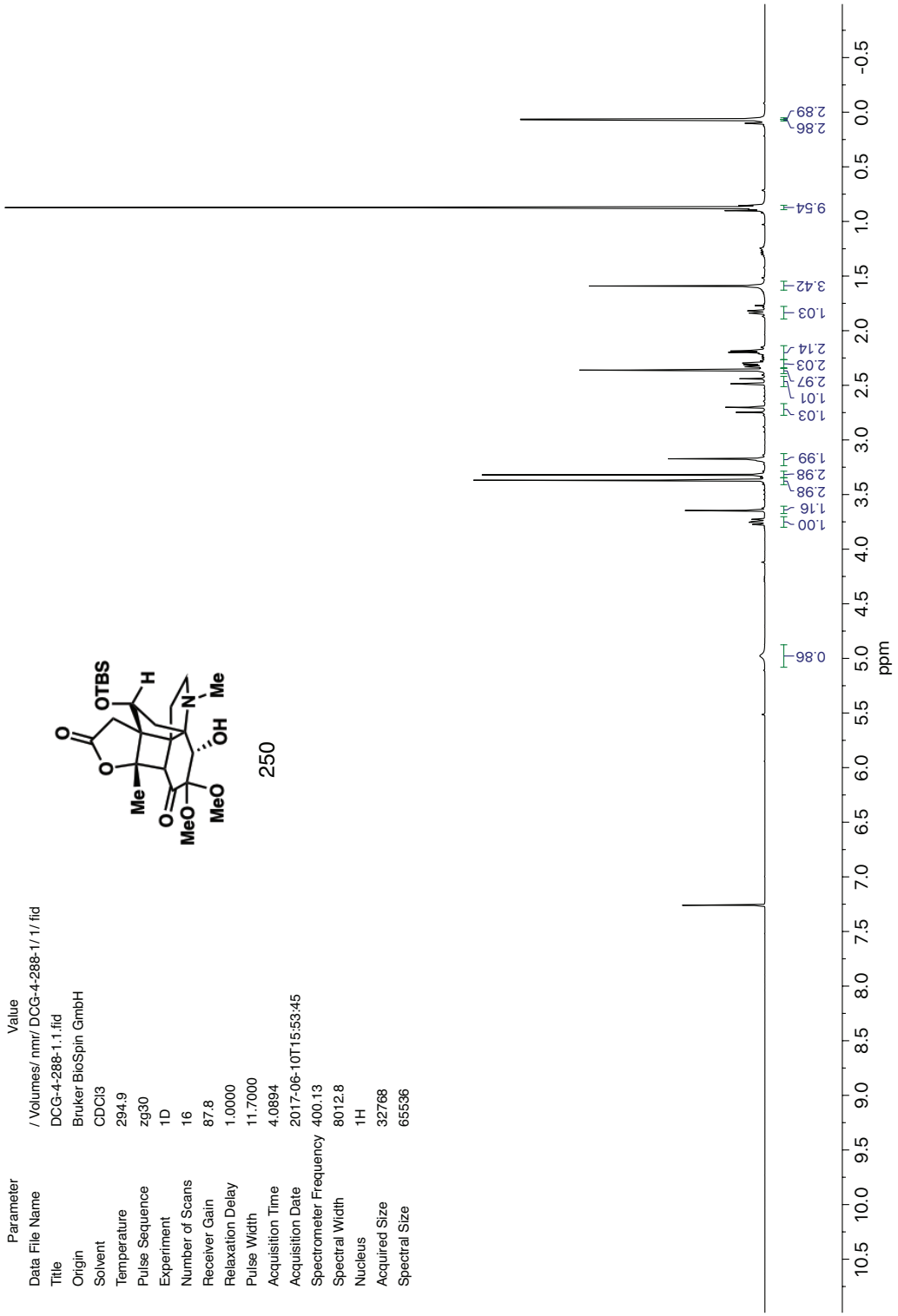

ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-167-2/ 3/ ser
Title DCG-4-167-2.3.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.1970
Acquisition Date 2017-01-23T23:33:10
Spectrometer Frequency (400.13, 400.13)
Spectral Width (5197.5, 5197.5)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)
OMe
OTBS
H
N
Me
OH
Me
Me
O
MeO
MeO
267

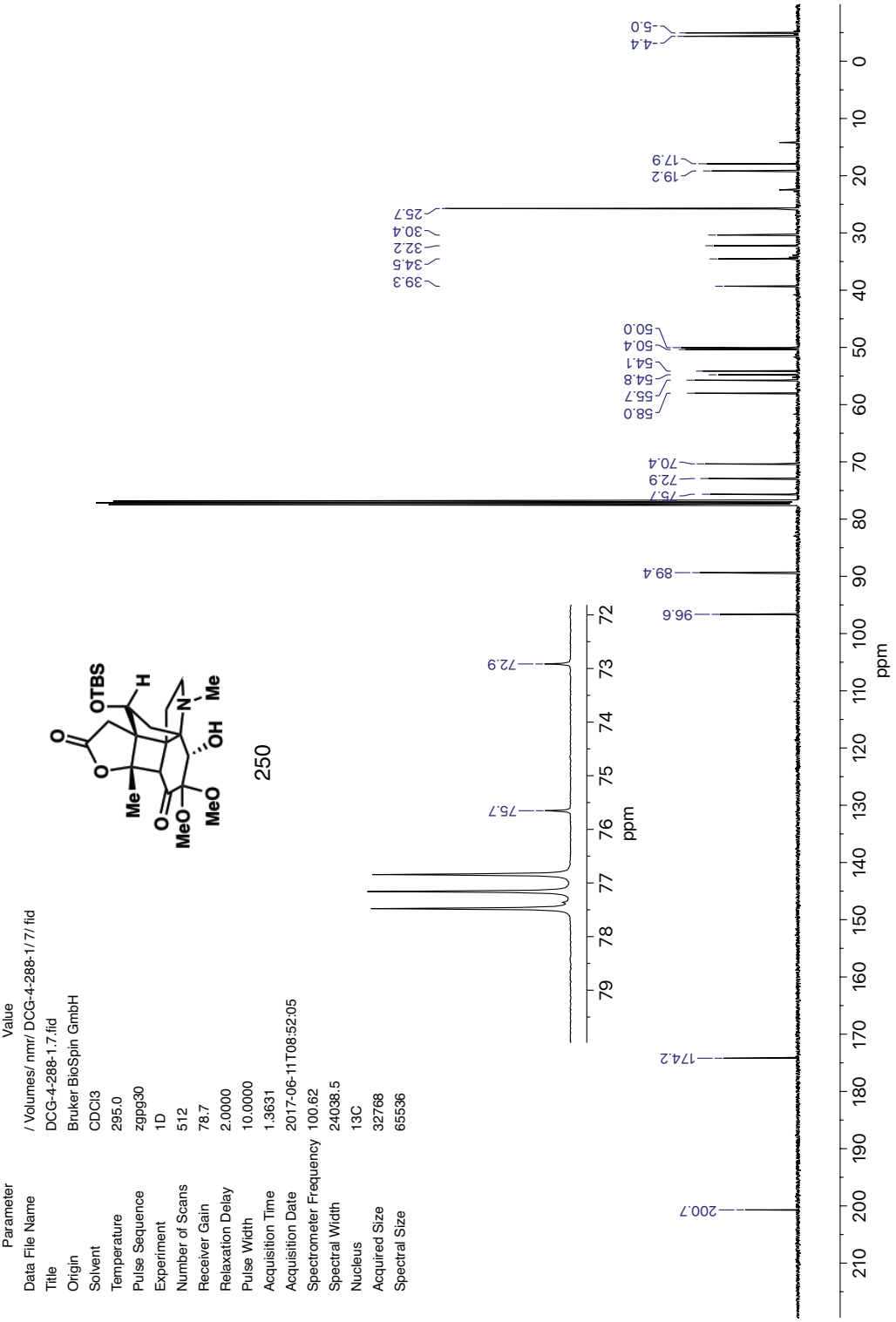

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-167-2/ 4/ ser
Title DCG-4-167-2.4.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2017-01-23T23:39:30
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
{3.70,77.03}
OMe
OTBS
H
Me
Me
O
MeO
MeO
OH
Me
N
267
ppm
ppm
ppm
ppm

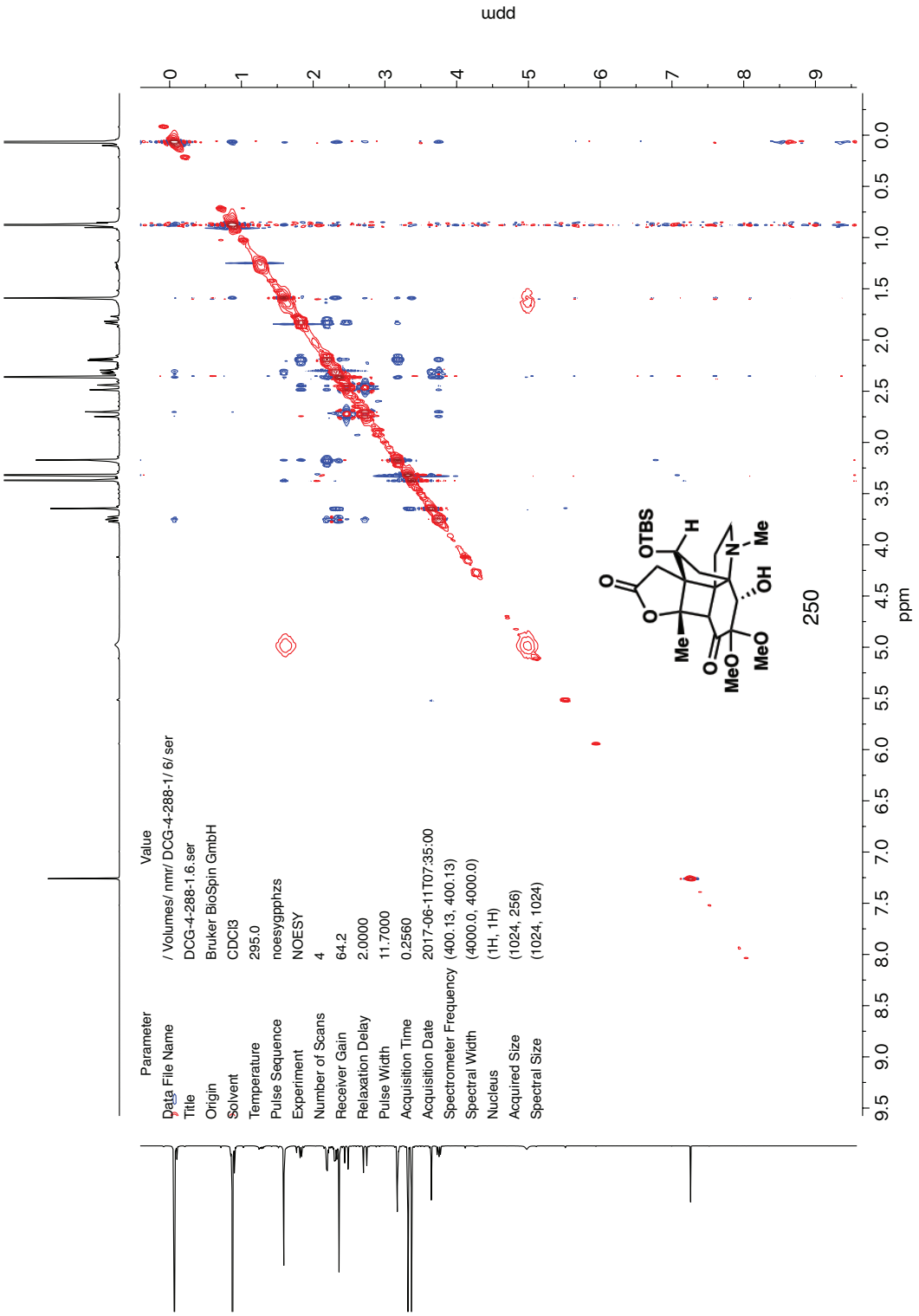

ppm
ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-167-2/ 6/ ser
Title DCG-4-167-2.6.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 6
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2017-01-24T00:54:55
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
OMe
OTBS
H
Me
Me
O
MeO
N
OH
Me
MeO
267

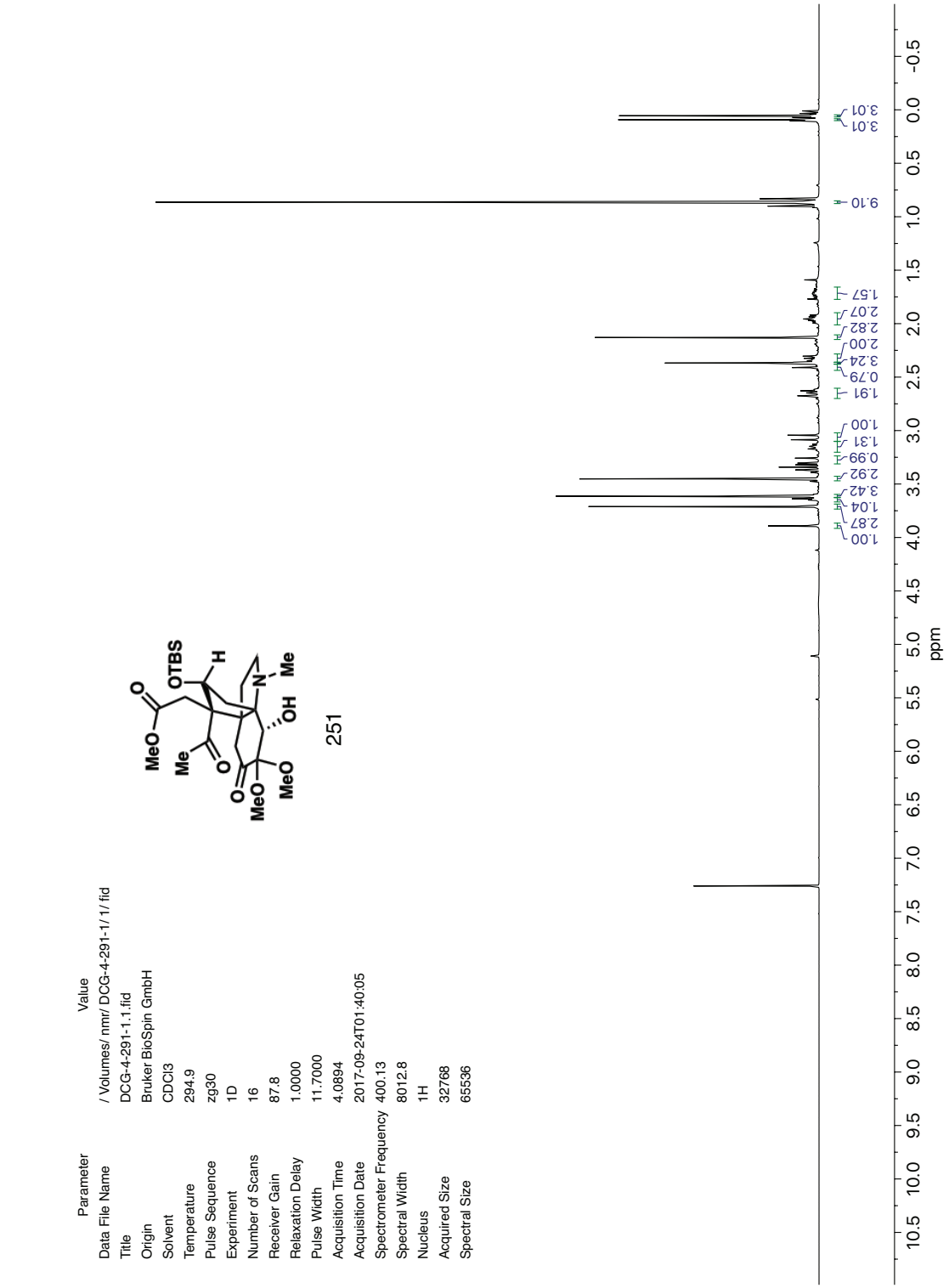

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-167-2/5/ fid
Title DCG-4-167-2.5.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 1024
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-01-24T00:53:42
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OMe
OTBS
H
N
Me
OH
Me
Me
Me
O
MeO
MeO
267
205.88
106.46
94.05
92.08
70.54
70.54
62.32
55.36
55.04
54.21
54.14
49.75
49.33
37.31
35.92
34.35
28.64
25.82
21.85
18.84
17.97
-4.29
-4.97
55.36
55.04
54.21
54.14
ppm
ppm

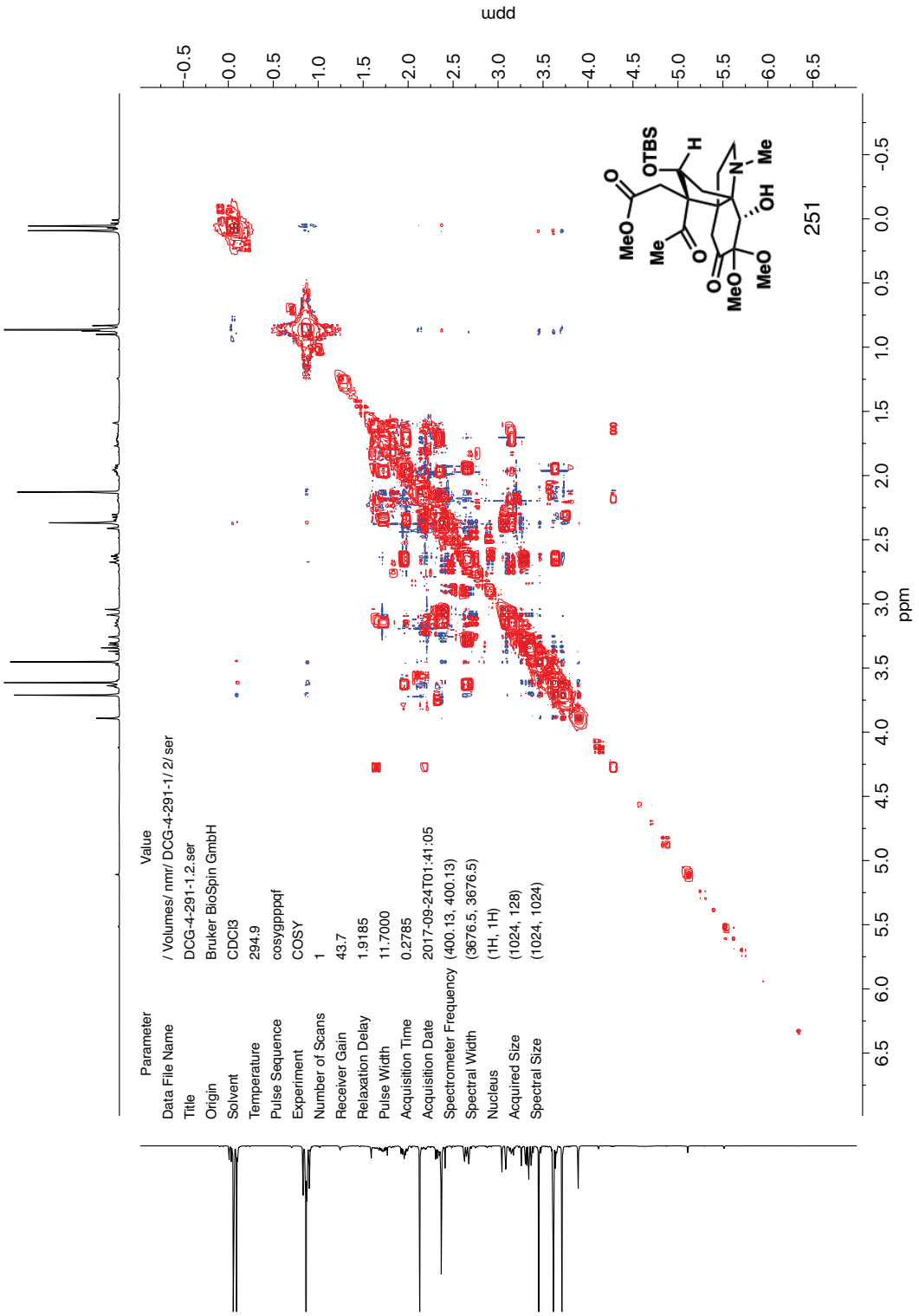

ppm
ppm
Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-4-167-2/ 7/ ser
Title
DCG-4-167-2.7.ser
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.0
Pulse Sequence
noesygpphzs
Experiment
NOESY
Number of Scans
6
Receiver Gain
112.8
Relaxation Delay
2.0000
Pulse Width
11.7000
Acquisition Time
0.2560
Acquisition Date
2017-01-24T02:01:04
Spectrometer Frequency
(400.13, 400.13)
Spectral Width
(4000.0, 4000.0)
Nucleus
(1H, 1H)
Acquired Size
(1024, 256)
Spectral Size
(1024, 1024)
OMe
OTBS
H
Me
Me
O
MeO
MeO
N
OH
Me
267

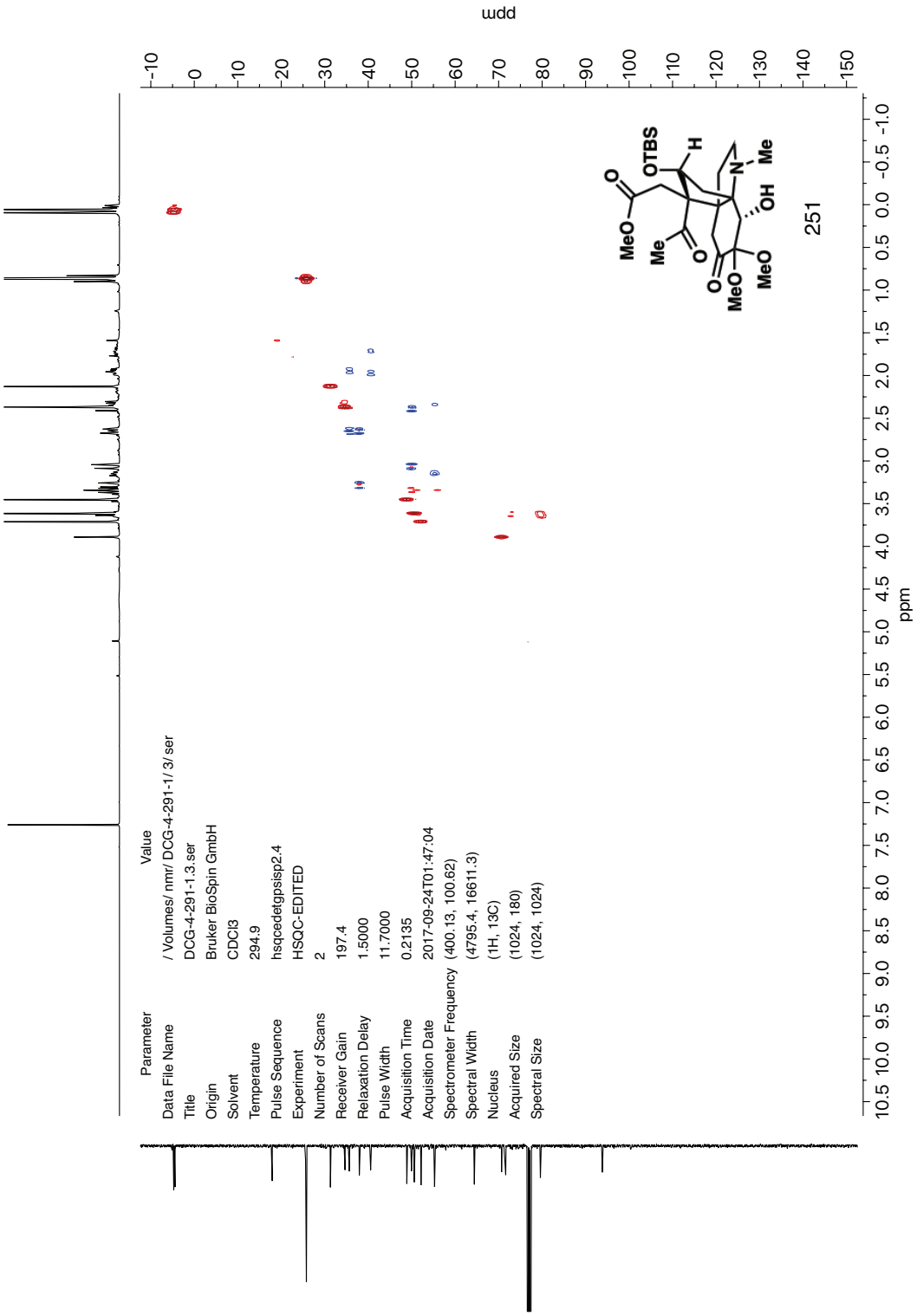

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-288-1/1/ fid
Title DCG-4-288-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 87.8
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-06-10T15:53:45
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
OTBS
H
N
Me
OH
MeO
MeO
Me
O
O
O
250
0.86
1.00
1.16
2.98
2.98
1.99
1.03
1.01
2.97
2.03
2.14
1.03
3.42
9.54
2.86
2.89
ppm

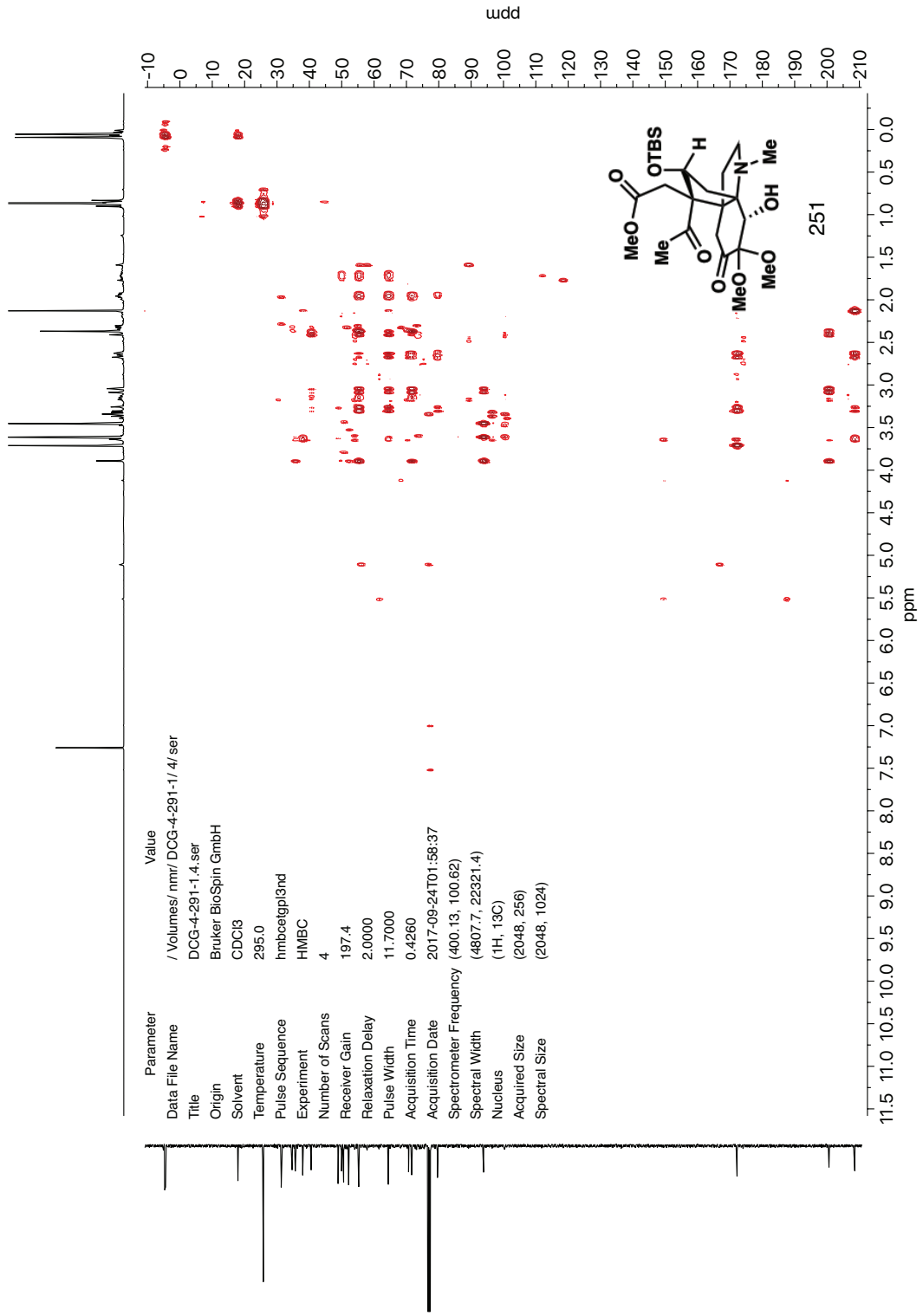

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-288-1/7/ fid
Title DCG-4-288-1.7.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 512
Receiver Gain 78.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-06-11T08:52:05
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OTBS
H
N
Me
OH
Me
O
O
Me
O
MeO
MeO
250
ppm
ppm

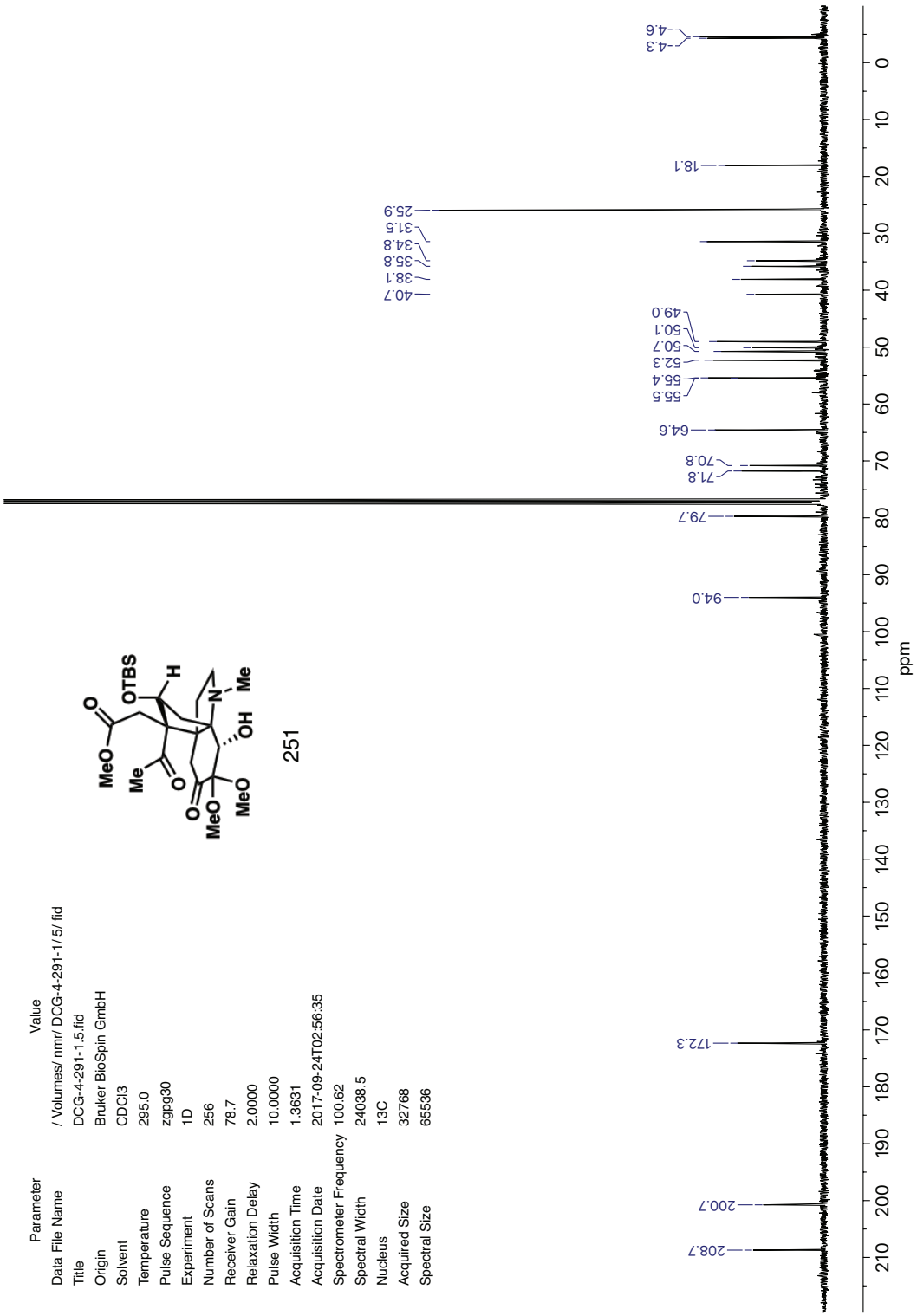

ppm
Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-4-288-1/ 6/ ser
Title
DCG-4-288-1.6.ser
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.0
Pulse Sequence
noesygpphzs
Experiment
NOESY
Number of Scans
4
Receiver Gain
64.2
Relaxation Delay
2.0000
Pulse Width
11.7000
Acquisition Time
0.2560
Acquisition Date
2017-06-11T07:35:00
Spectrometer Frequency
(400.13, 400.13)
Spectral Width
(4000.0, 4000.0)
Nucleus
(1H, 1H)
Acquired Size
(1024, 256)
Spectral Size
(1024, 1024)
OTBS
H
N
Me
OH
Me
O
O
Me
O
MeO
MeO
250
ppm

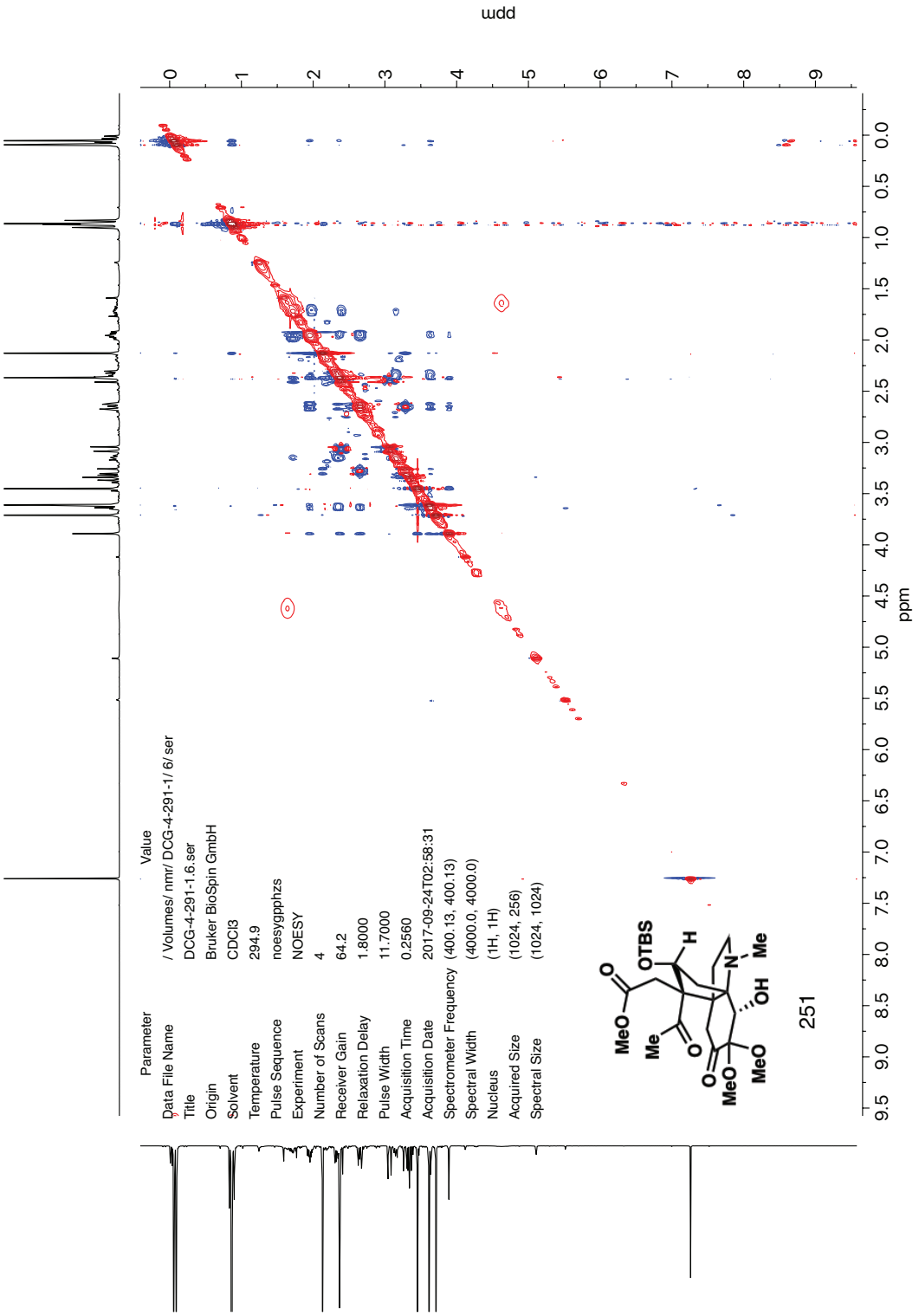

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-291-1/1/ fid
Title DCG-4-291-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 87.8
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-09-24T01:40:05
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
MeO
Me
O
OTBS
H
N
Me
OH
MeO
MeO
O
O
251
3.01
9.10
1.57
2.07
2.82
2.00
3.24
0.79
1.91
1.00
1.31
0.99
2.92
3.42
1.04
2.87
1.00
ppm

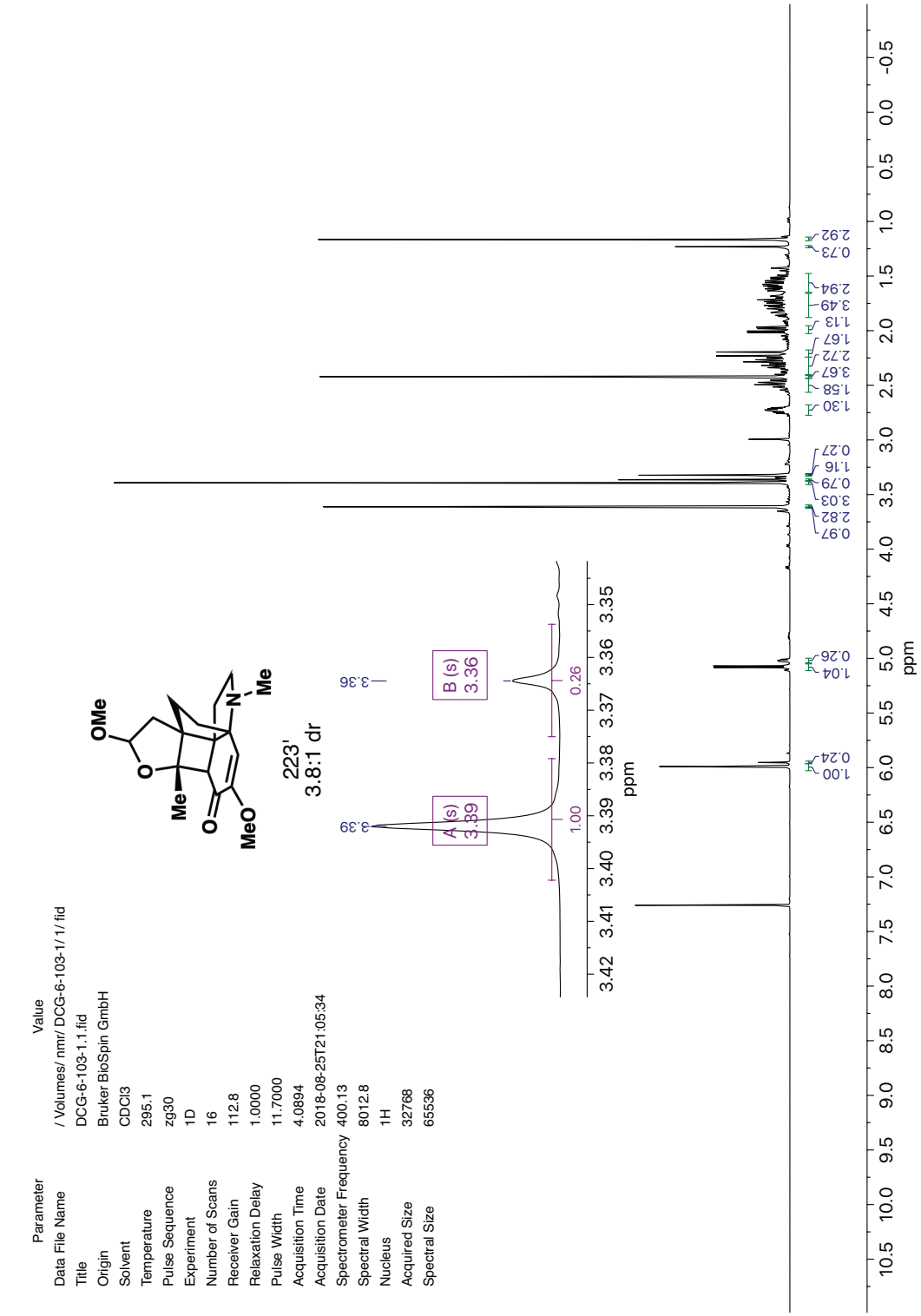

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-291-1/ 2/ ser
Title DCG-4-291-1.2.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 43.7
Relaxation Delay 1.9185
Pulse Width 11.7000
Acquisition Time 0.2785
Acquisition Date 2017-09-24T01:41:05
Spectrometer Frequency (400.13, 400.13)
Spectral Width (3676.5, 3676.5)
(1H, 1H)
Nucleus (1024, 128)
Acquired Size (1024, 1024)
Spectral Size
ppm
MeO
Me
OTBS
H
N
Me
OH
MeO
MeO
251

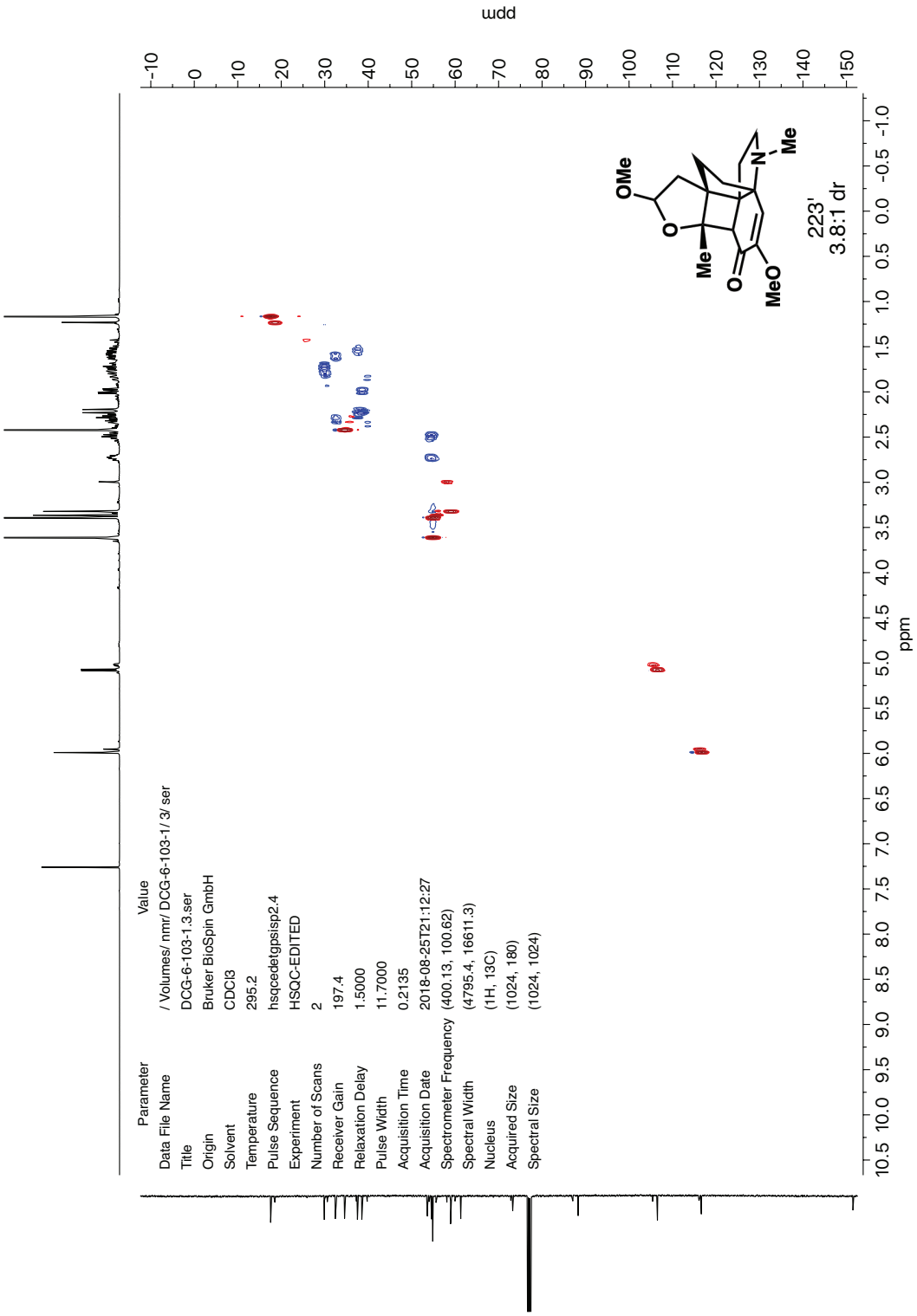

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-291-1/ 3/ ser
Title DCG-4-291-1.3.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2017-09-24T01:47:04
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 180)
Spectral Size (1024, 1024)
ppm
ppm
MeO
Me
OTBS
H
N
Me
OH
MeO
MeO
O
O
O
251

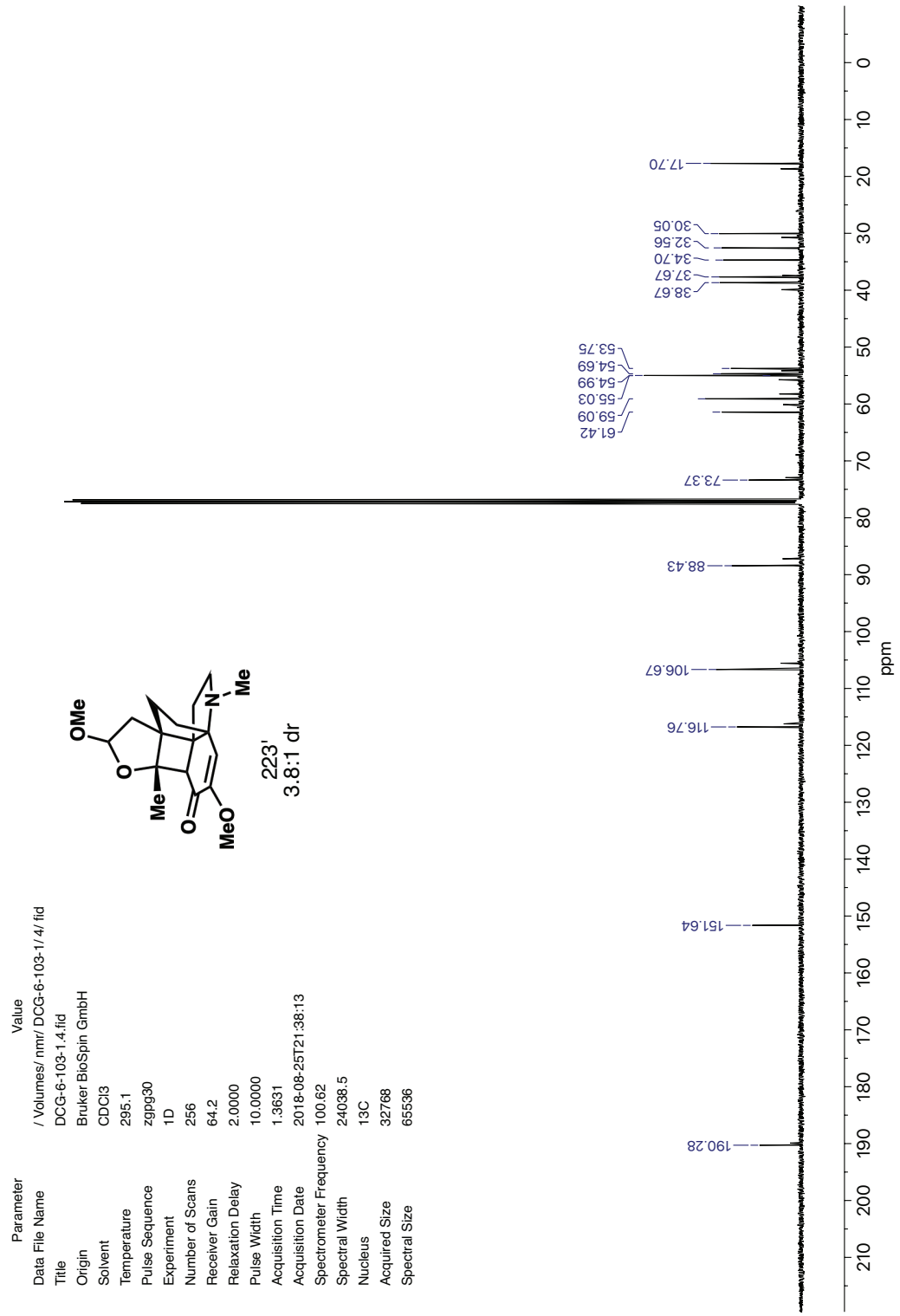

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-291-1/ 4/ ser
Title DCG-4-291-1.4.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2017-09-24T01:58:37
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
ppm
ppm
MeO
Me
OTBS
H
N
Me
OH
MeO
MeO
251

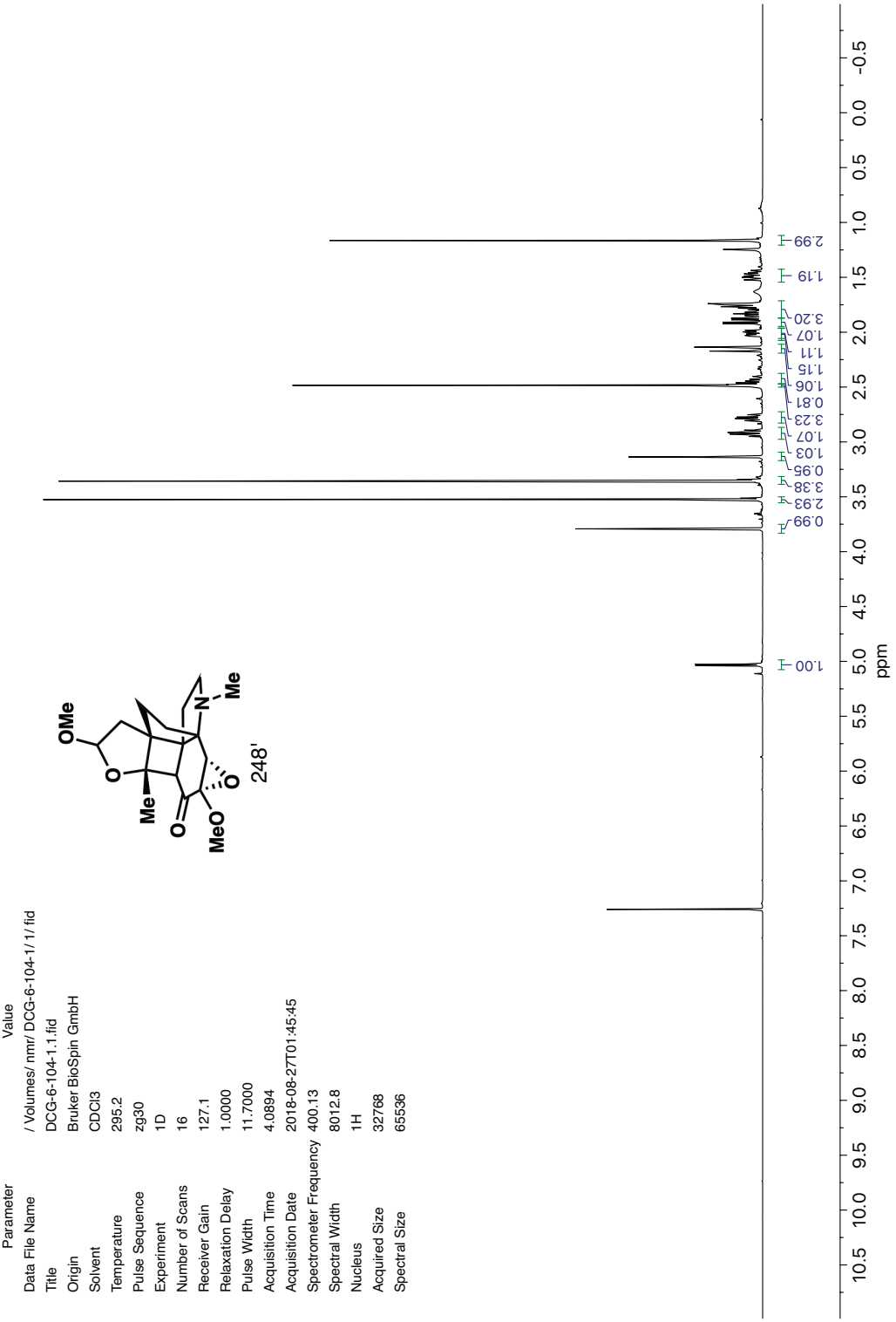

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-291-1/5/ fid
Title DCG-4-291-1.5.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 78.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-09-24T02:56:35
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
MeO
Me
O
O
OTBS
H
N
Me
OH
MeO
MeO
O
251
208.7
200.7
172.3
94.0
79.7
71.8
70.8
64.6
55.5
55.4
52.3
50.7
50.1
49.0
40.7
38.1
35.8
34.8
31.5
25.9
18.1
-4.3
-4.6
ppm

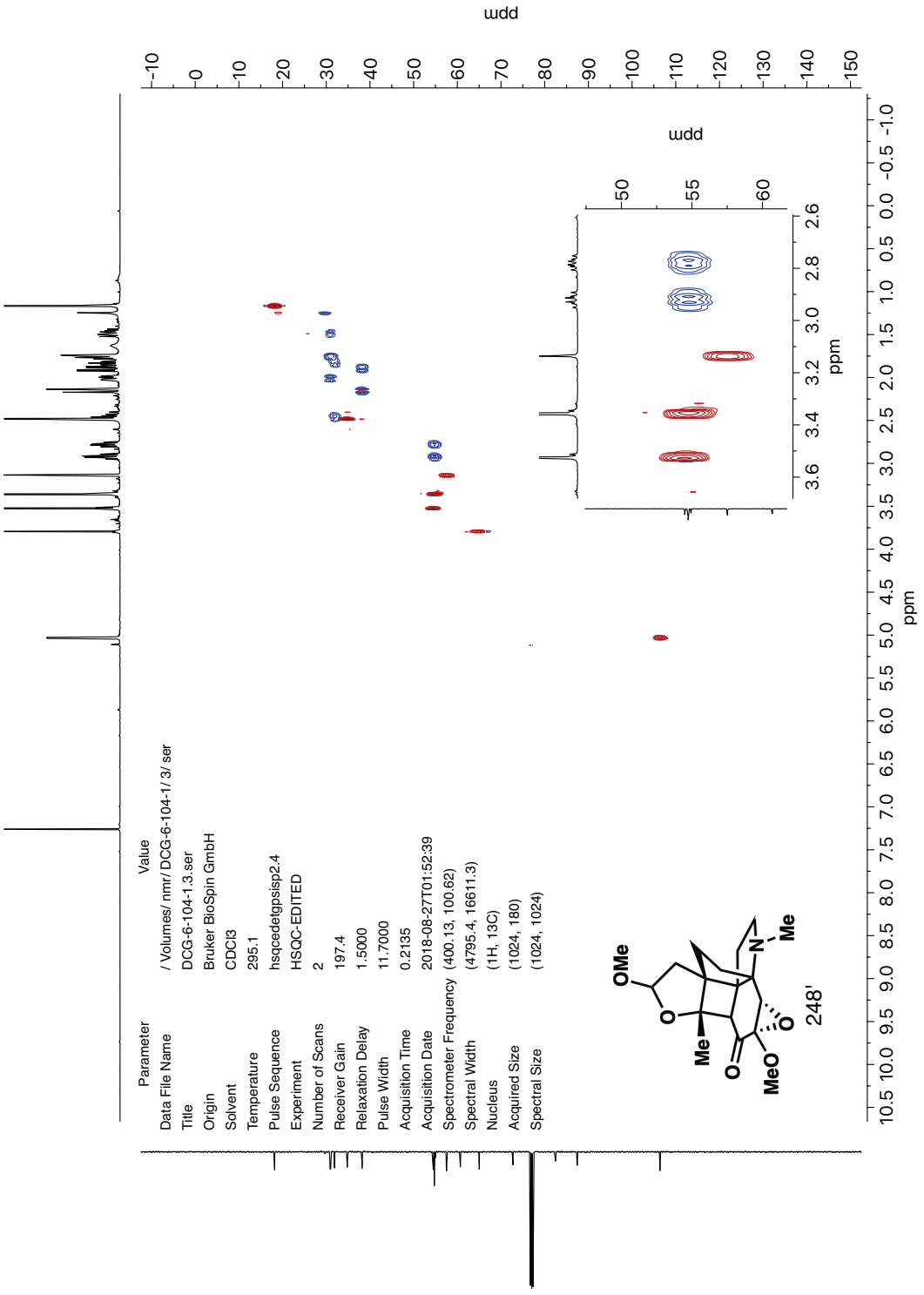

ppm
ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-291-1/ 6/ ser
Title DCG-4-291-1.6.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence noesygpphzs
Experiment NOESY
Number of Scans 4
Receiver Gain 64.2
Relaxation Delay 1.8000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2017-09-24T02:58:31
Spectrometer Frequency (400.13, 400.13)
Spectral Width (4000.0, 4000.0)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
MeO
Me
OTBS
H
O
O
N
Me
OH
MeO
MeO
O
251

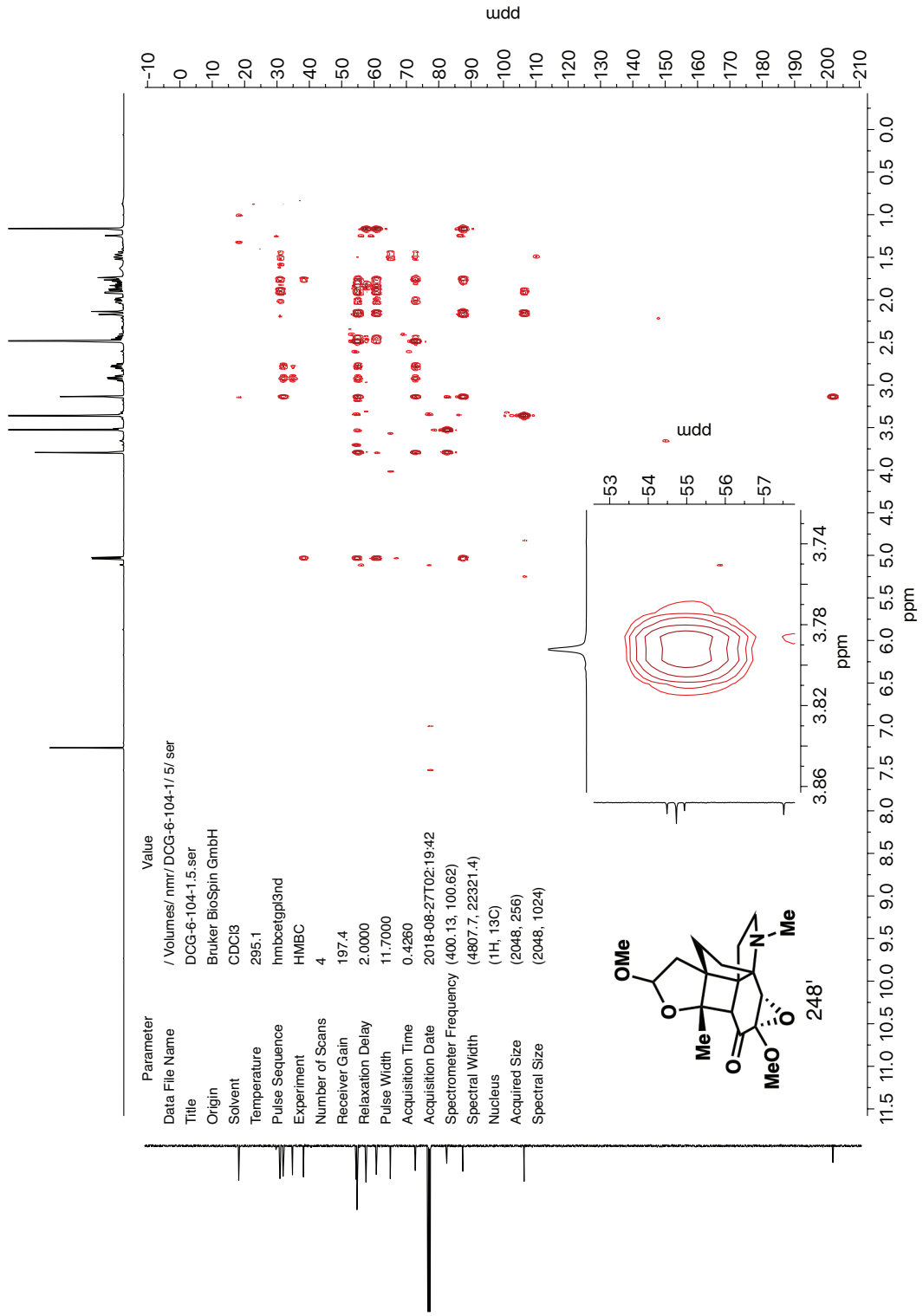

Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-103-1/1/1/ fid
Title DCG-6-103-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 112.8
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-08-25T21:05:34
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
OMe
Me
MeO
Me
223'
3.8:1 dr
3.39
3.36
A (s) 3.39
B (s) 3.36
1.00
0.26
ppm
1.00
0.24
1.04
0.26
0.97
2.82
3.03
0.79
1.16
0.27
1.30
1.58
3.67
2.72
1.67
1.13
3.49
2.94
0.73
2.92

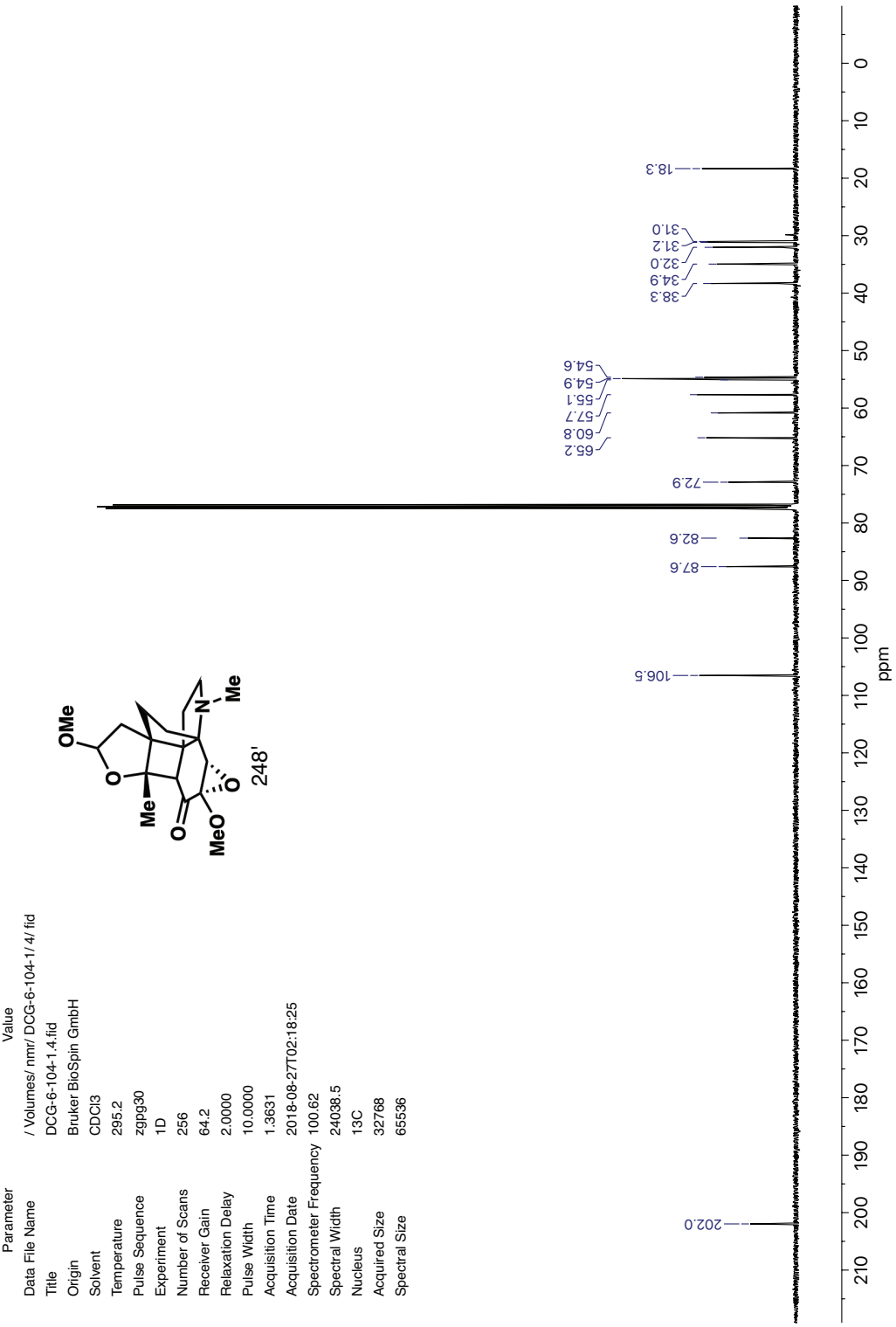

Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-103-1/ 3/ ser
Title DCG-6-103-1.3.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2018-08-25T21:12:27
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 180)
Spectral Size (1024, 1024)
OMe
O
Me
O
MeO
N
Me
223'
3.8:1 dr
ppm
ppm

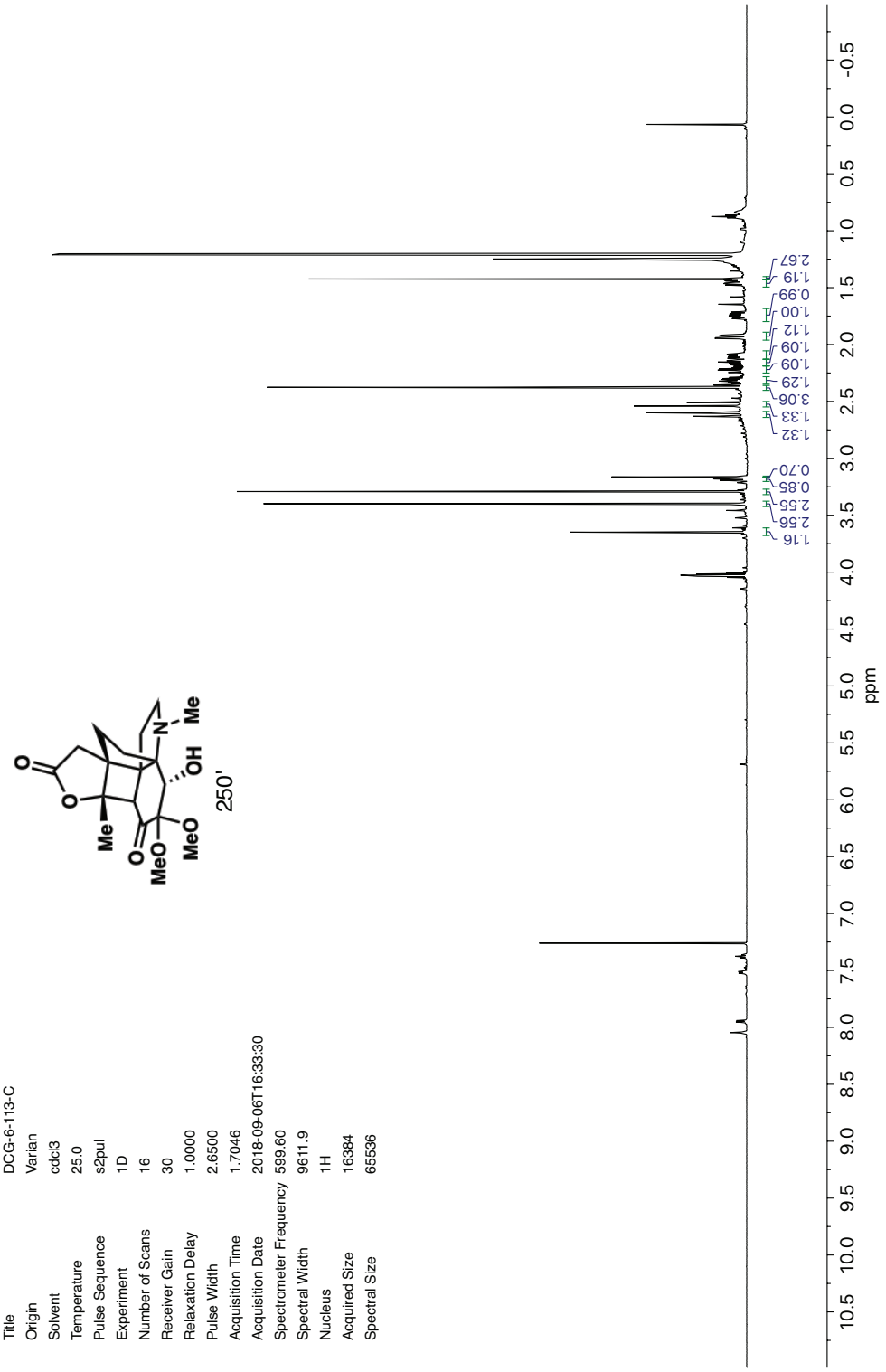

Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-103-1/ 4/ fid
Title DCG-6-103-1.4.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-08-25T21:38:13
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OMe
O
Me
O
MeO
N
Me
223'
3.8:1 dr
190.28
151.64
116.76
106.67
88.43
73.37
61.42
59.09
55.03
54.99
54.69
53.75
38.67
37.67
34.70
32.56
30.05
17.70
ppm

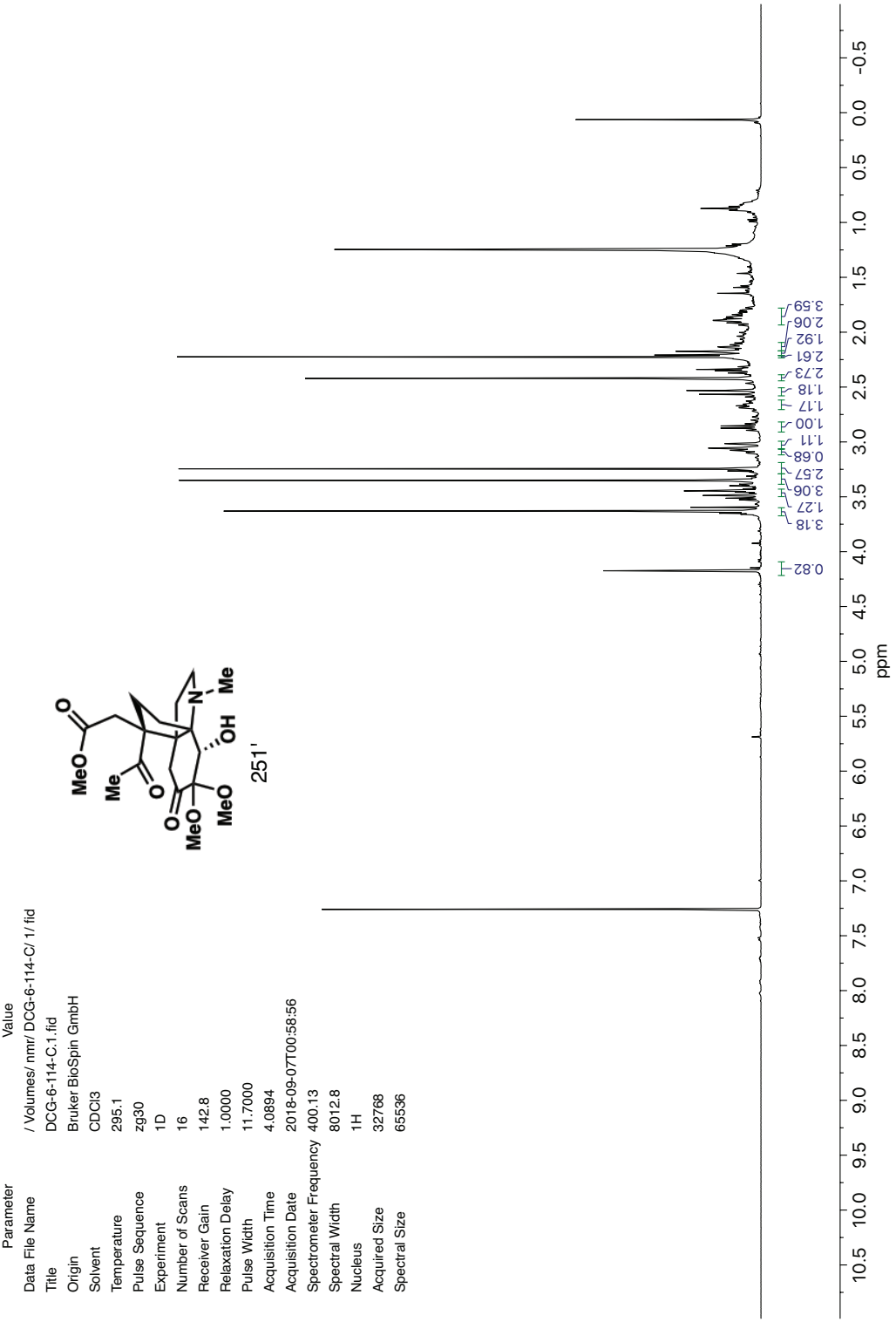

Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-104-1/1/ fid
Title DCG-6-104-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 127.1
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-08-27T01:45:45
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
OMe
Me
MeO
248'
1.00
0.99
2.93
3.38
0.95
1.03
1.07
3.23
0.81
1.06
1.15
1.11
1.07
3.20
1.19
2.99
ppm

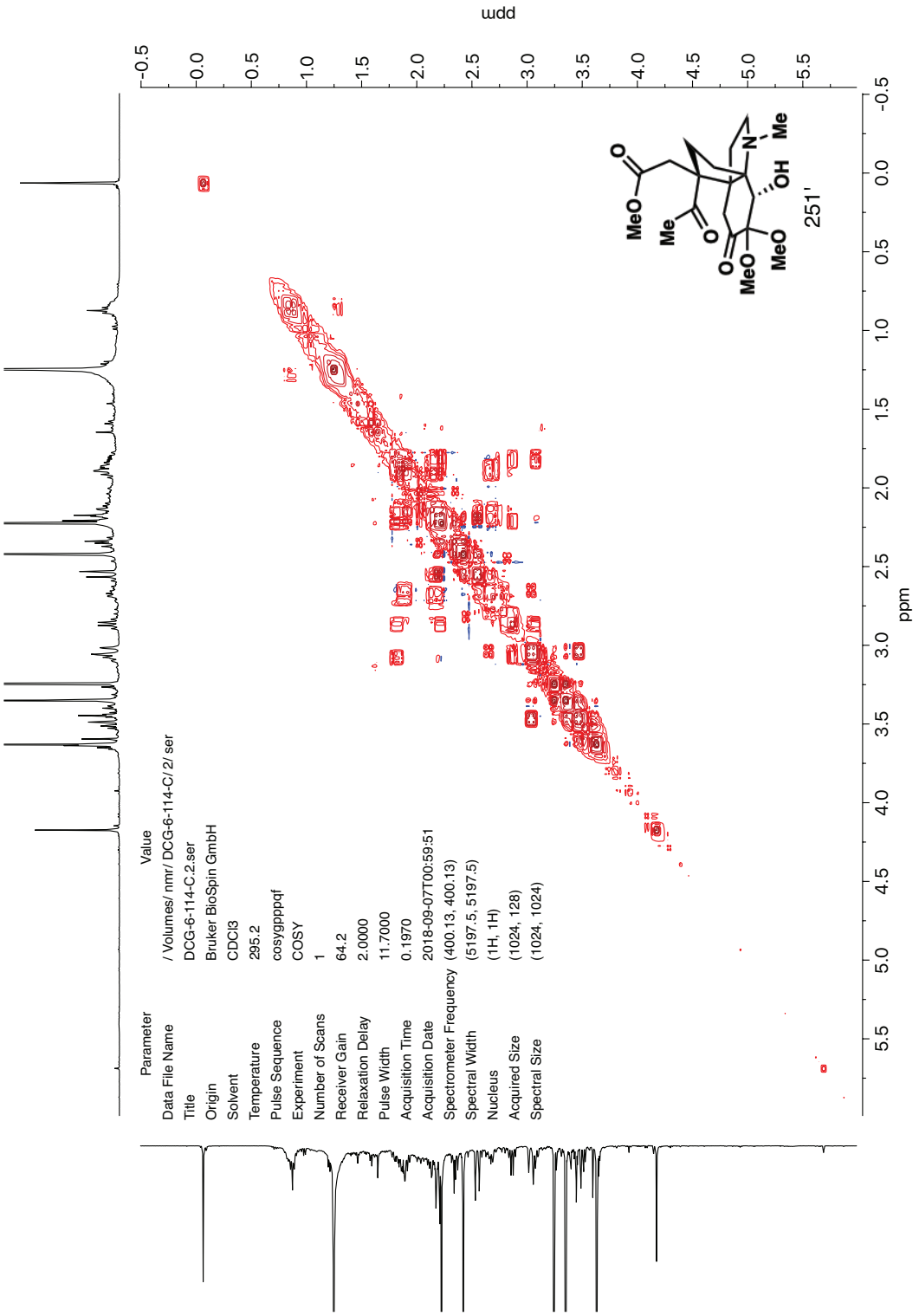

Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-104-1/ 3/ ser
Title DCG-6-104-1.3.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2018-08-27T01:52:39
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 180)
Spectral Size (1024, 1024)
OMe
Me
MeO
Me
248'
ppm
ppm
ppm
ppm

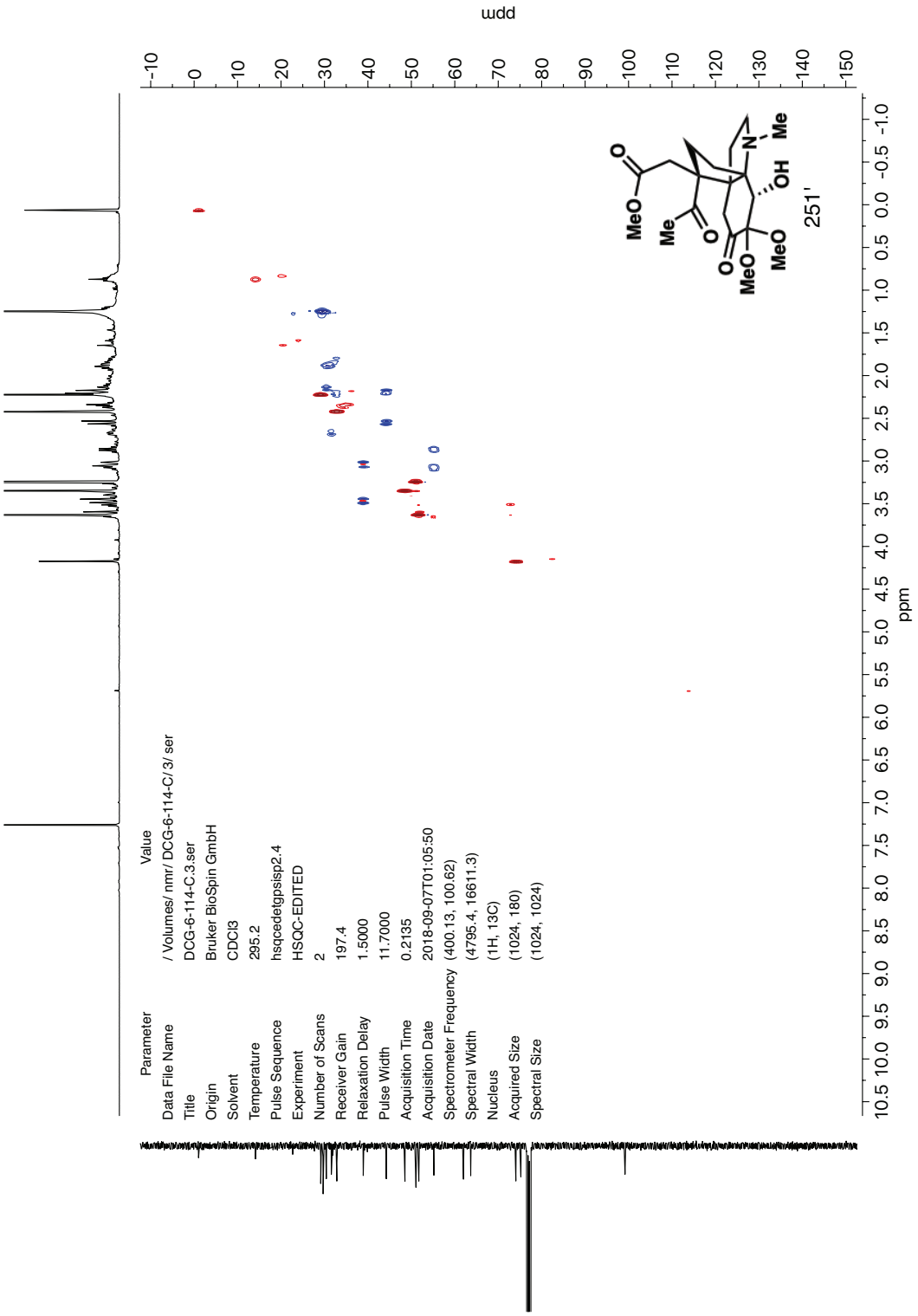

Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-104-1/ 5/ ser
Title DCG-6-104-1.5.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2018-08-27T02:19:42
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
ppm
OMe
Me
MeO
Me
248'

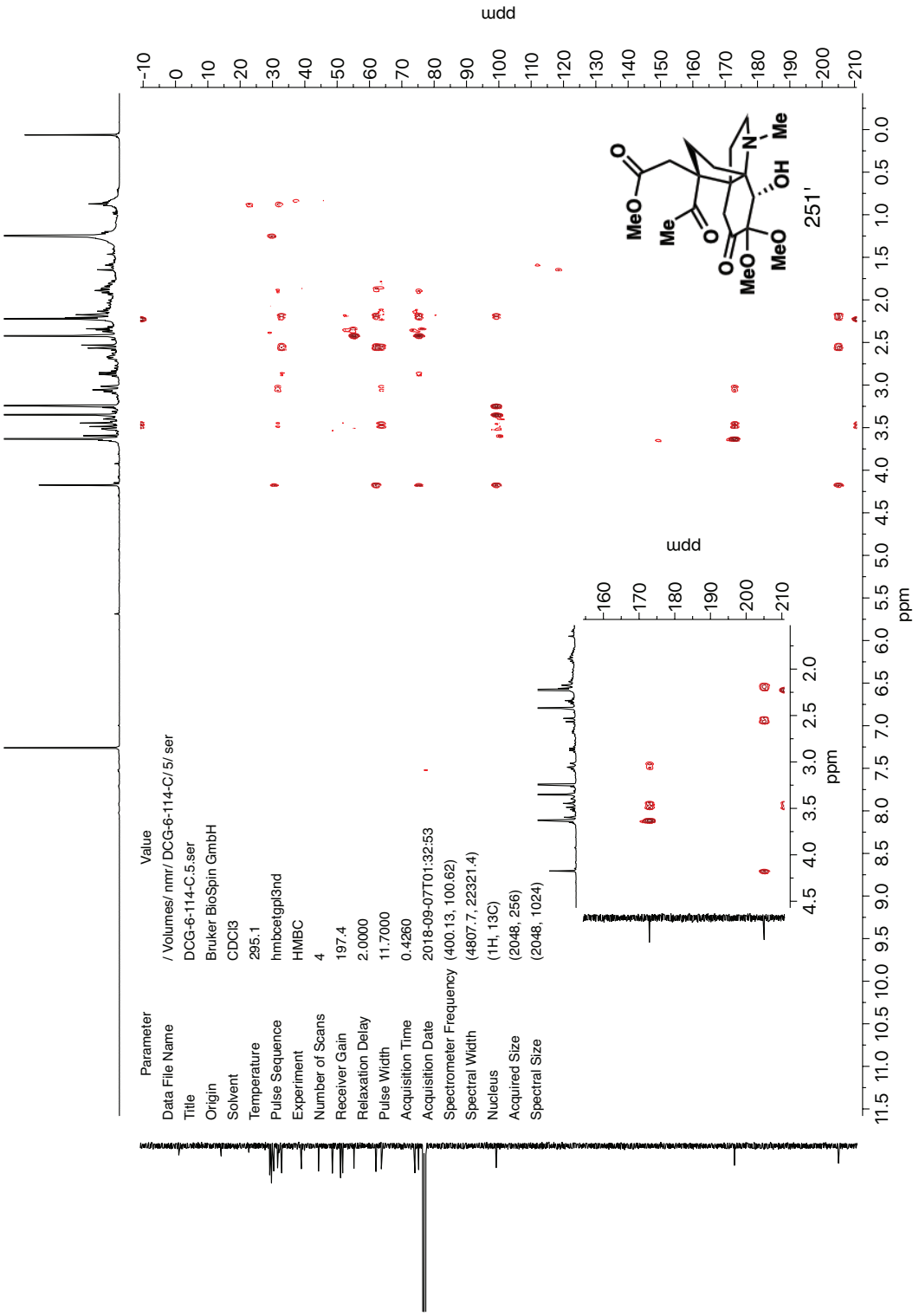

Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-104-1/ 4/ fid
Title DCG-6-104-1.4.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-08-27T02:18:25
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OMe
Me
MeO
Me
248'
202.0
106.5
87.6
82.6
72.9
65.2
60.8
57.7
55.1
54.9
54.6
38.3
34.9
32.0
31.2
31.0
18.3
ppm

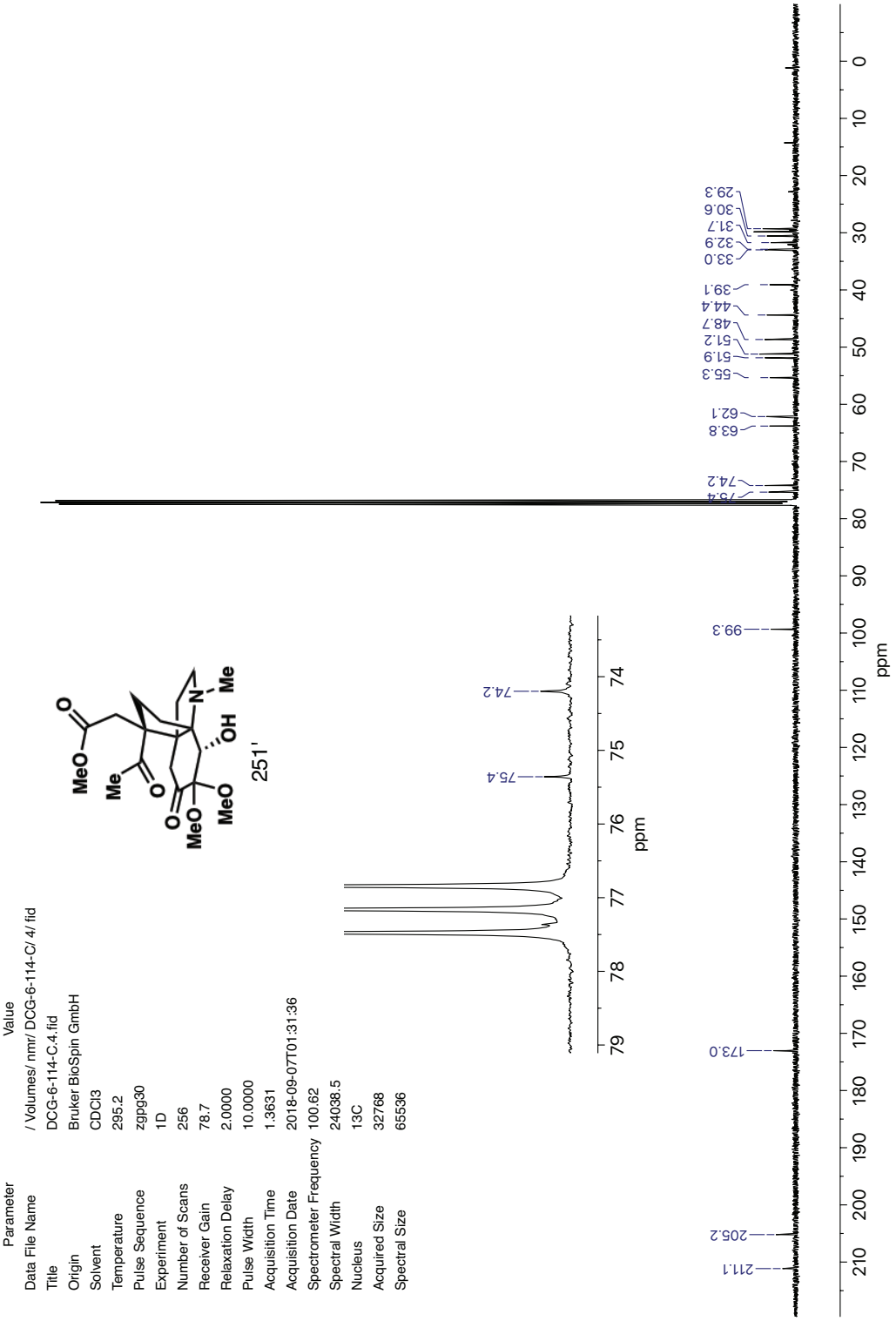

Parameter Value
Data File Name / Volumes/ data/ DCG-6-113-C.fid/ fid
Title DCG-6-113-C
Origin Varian
Solvent cdcl3
Temperature 25.0
Pulse Sequence s2pul
Experiment 1D
Number of Scans 16
Receiver Gain 30
Relaxation Delay 1.0000
Pulse Width 2.6500
Acquisition Time 1.7046
Acquisition Date 2018-09-06T16:33:30
Spectrometer Frequency 599.60
Spectral Width 9611.9
Nucleus 1H
Acquired Size 16384
Spectral Size 65536
250'
1.16
2.56
2.55
0.85
0.70
1.32
1.33
3.06
1.29
1.09
1.09
1.12
1.00
0.99
1.19
2.67
ppm

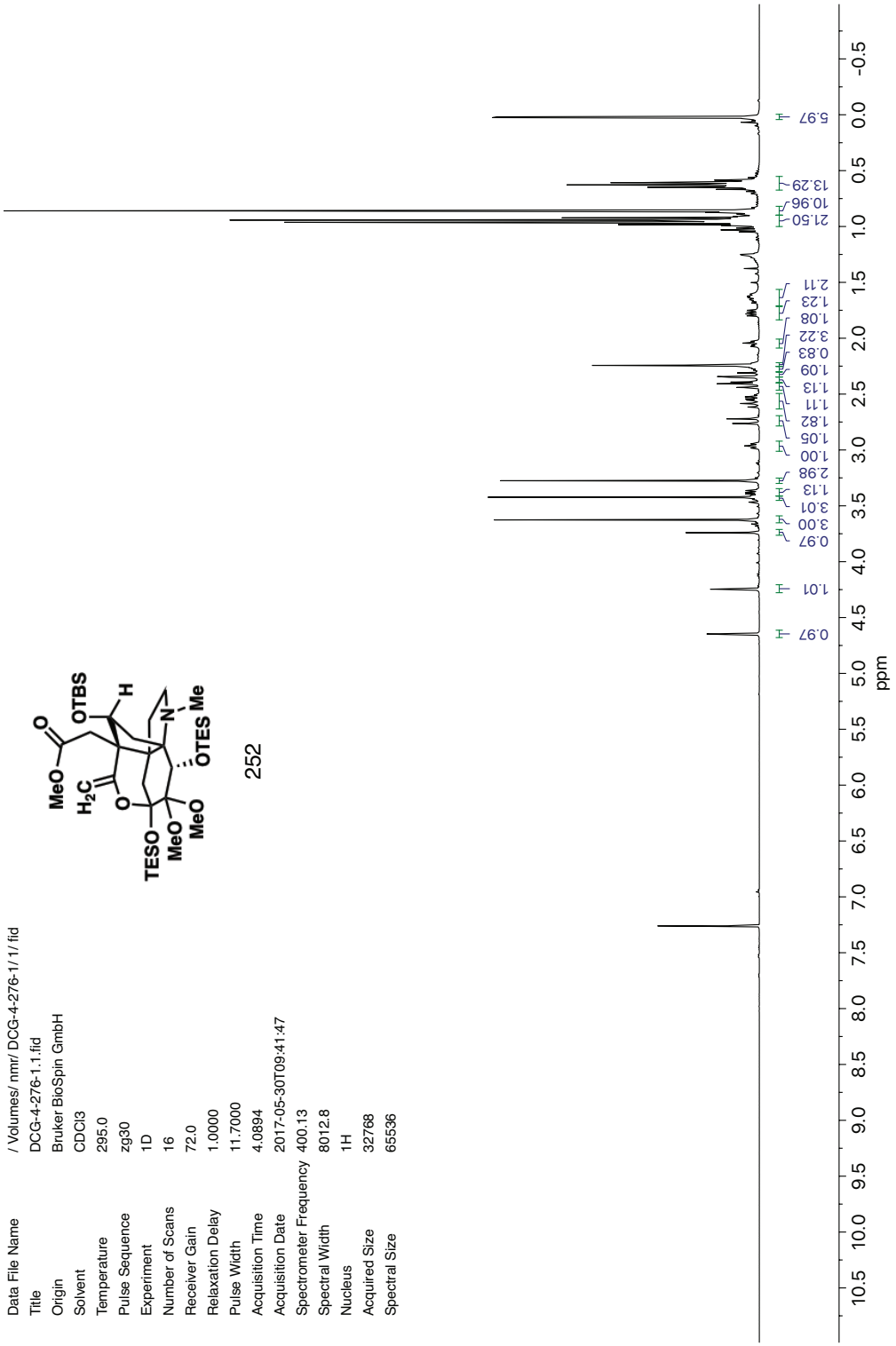

Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-114-C/ 1/ fid
Title DCG-6-114-C.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 142.8
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-09-07T00:58:56
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
MeO
Me
O
O
MeO
MeO
OH
N
Me
251'
0.82
3.18
1.27
3.06
2.57
0.68
1.11
1.00
1.17
1.18
2.73
2.61
1.92
2.06
3.59
ppm

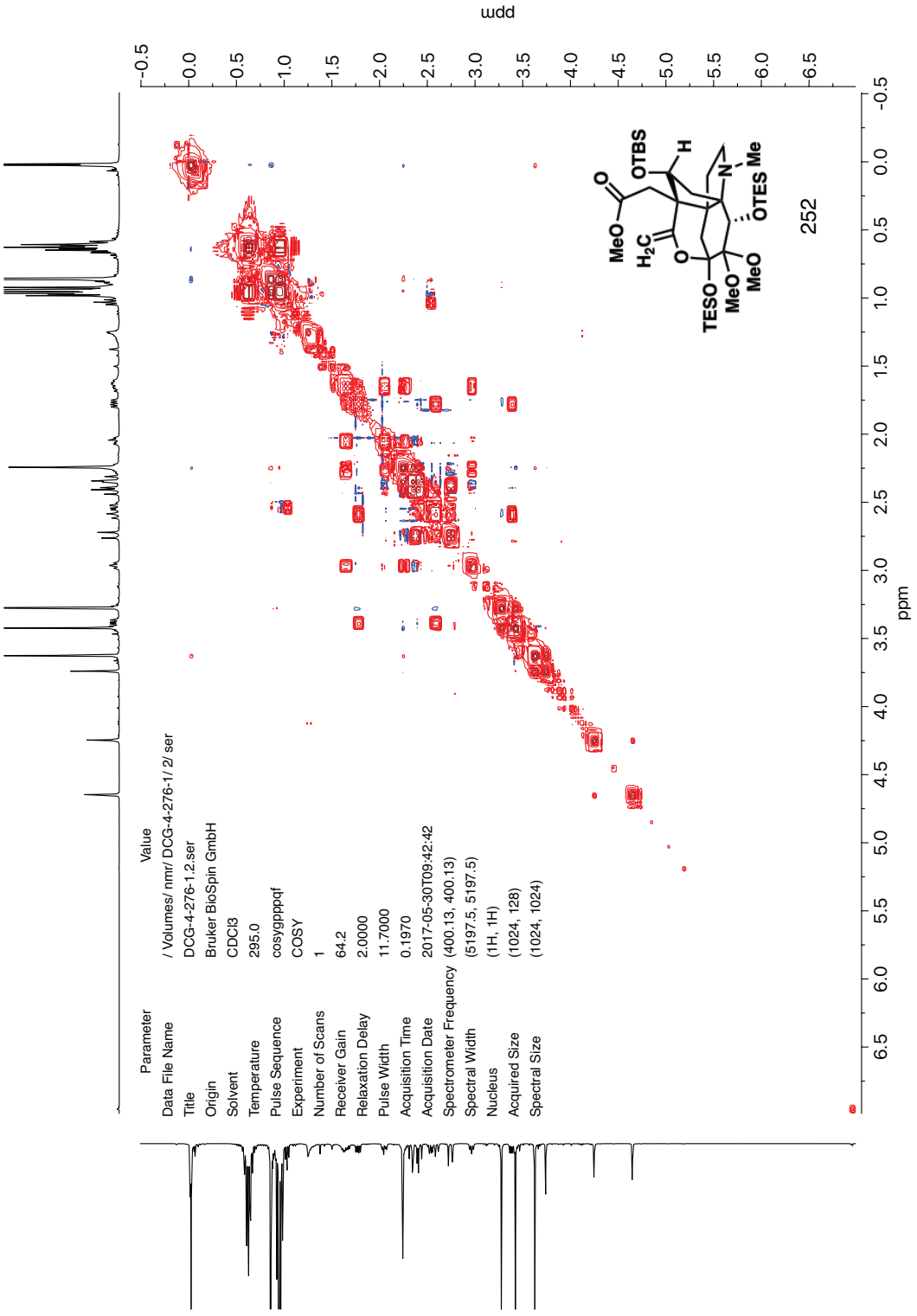

ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-114-C/ 2/ ser
Title DCG-6-114-C.2.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.1970
Acquisition Date 2018-09-07T00:59:51
Spectrometer Frequency (400.13, 400.13)
Spectral Width (5197.5, 5197.5)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)
MeO
Me
O
MeO
MeO
OH
N
Me
251'

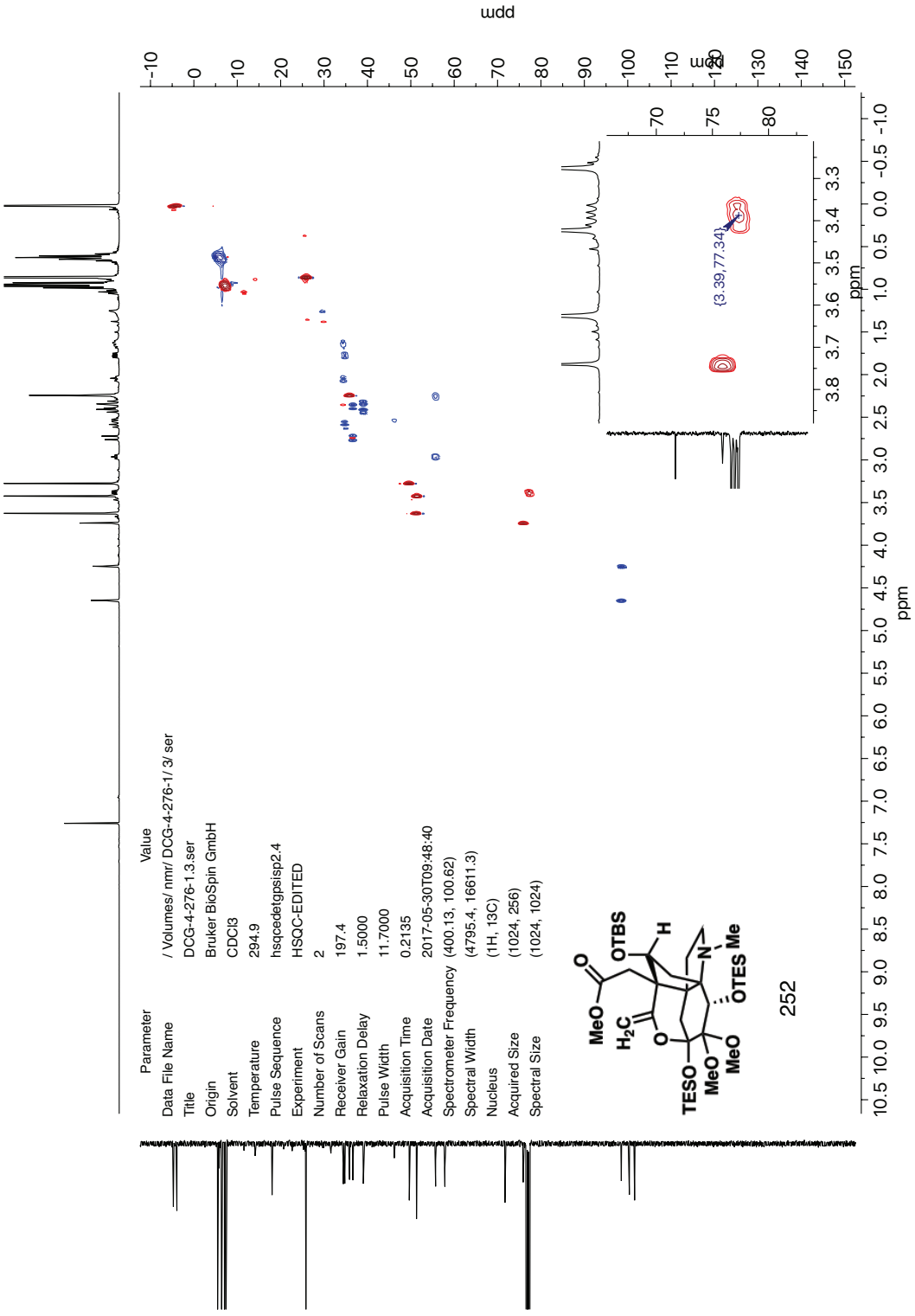

ppm
ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-114-C/ 3/ ser
Title DCG-6-114-C.3.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2018-09-07T01:05:50
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 180)
Spectral Size (1024, 1024)
MeO
Me
O
O
MeO
MeO
OH
N
Me
251'

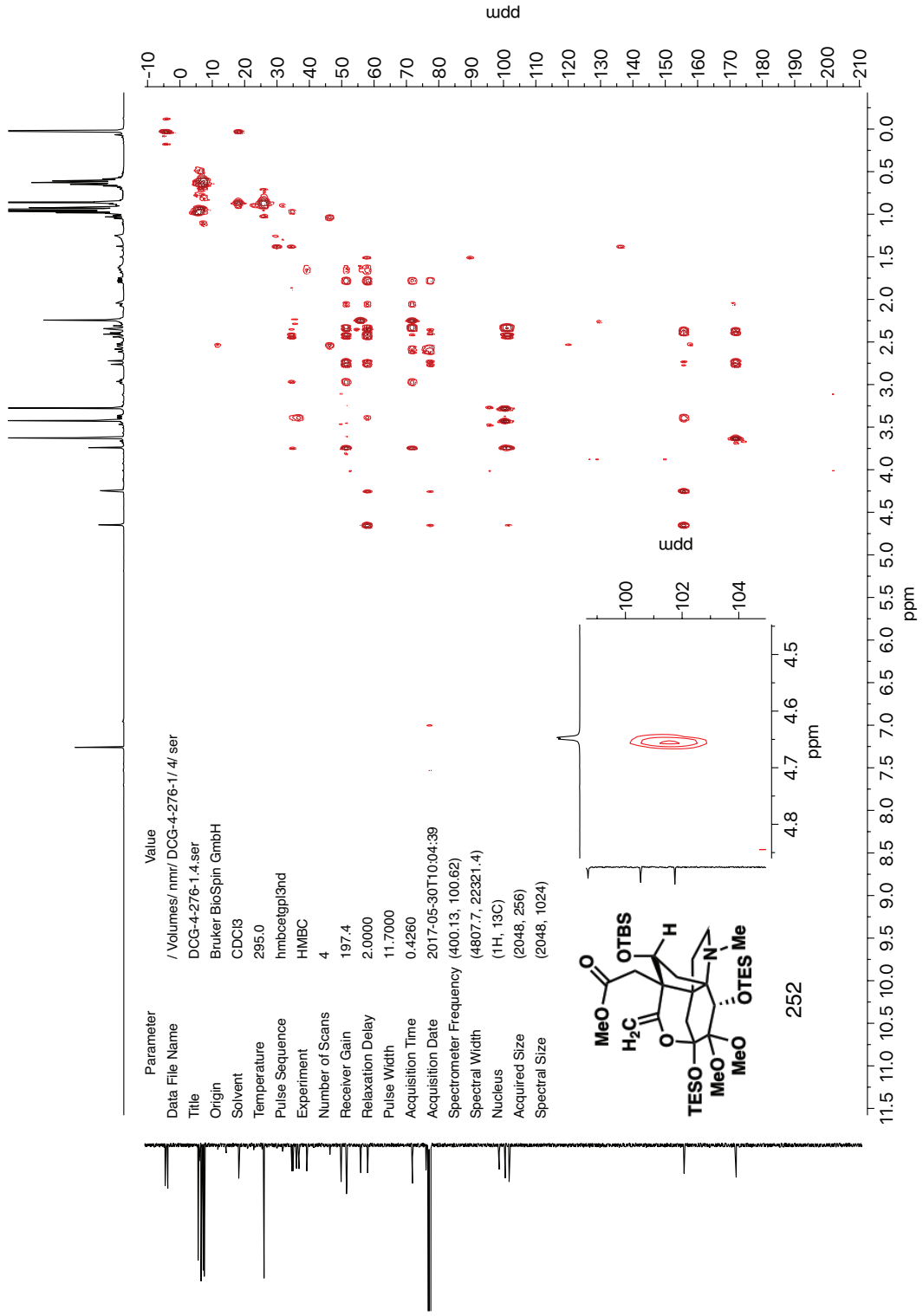

Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-114-C/ 5/ ser
Title DCG-6-114-C.5.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2018-09-07T01:32:53
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
ppm
MeO
Me
MeO
MeO
OH
N
Me
251'

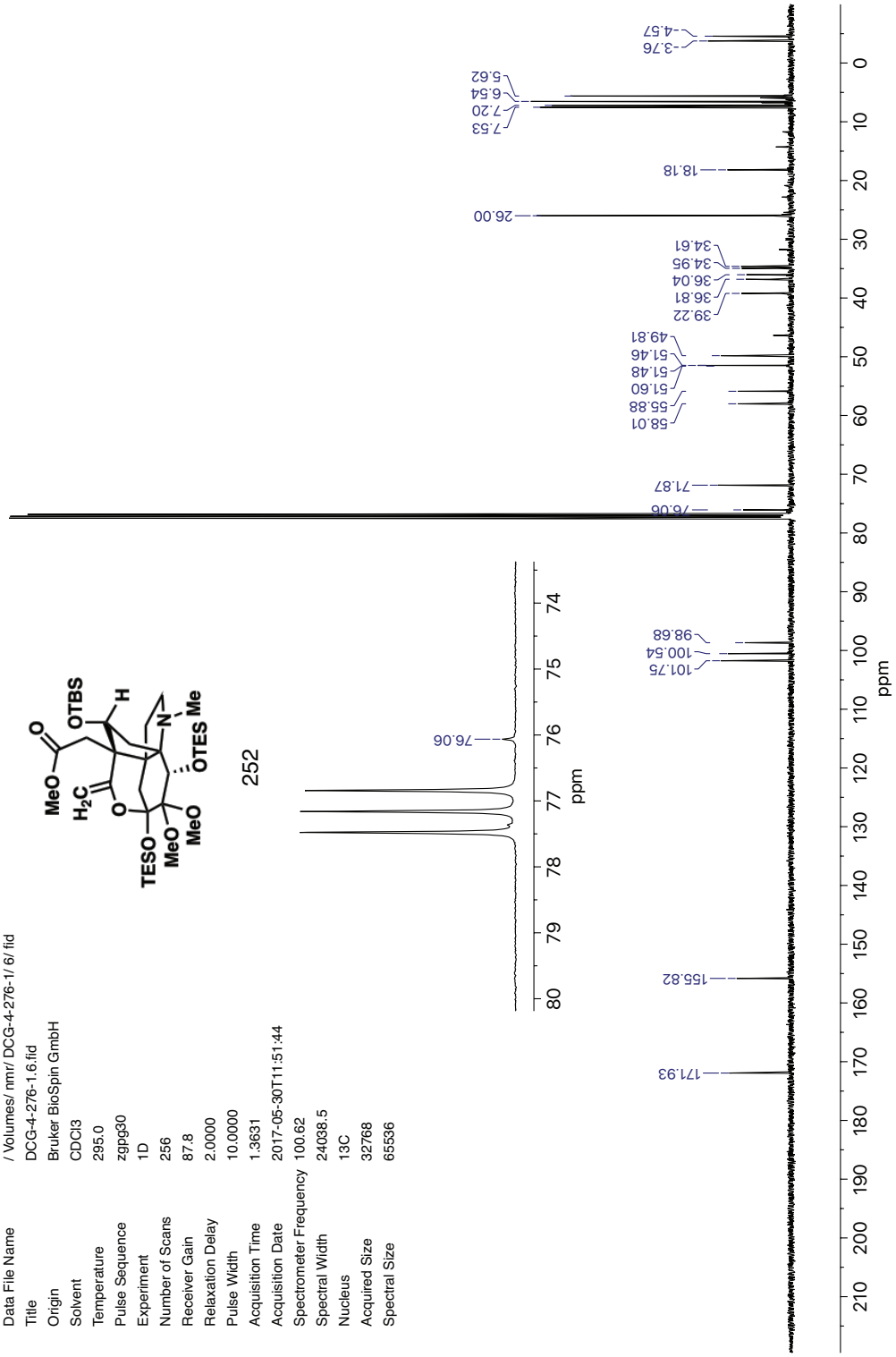

Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-114-C/ 4/ fid
Title DCG-6-114-C.4.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 78.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-09-07T01:31:36
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
MeO
Me
O
O
MeO
MeO
OH
N
Me
251'
74.2
75.4
ppm
211.1
205.2
173.0
99.3
75.4
74.2
63.8
62.1
55.3
51.9
51.2
48.7
44.4
39.1
33.0
32.9
31.7
30.6
29.3
ppm

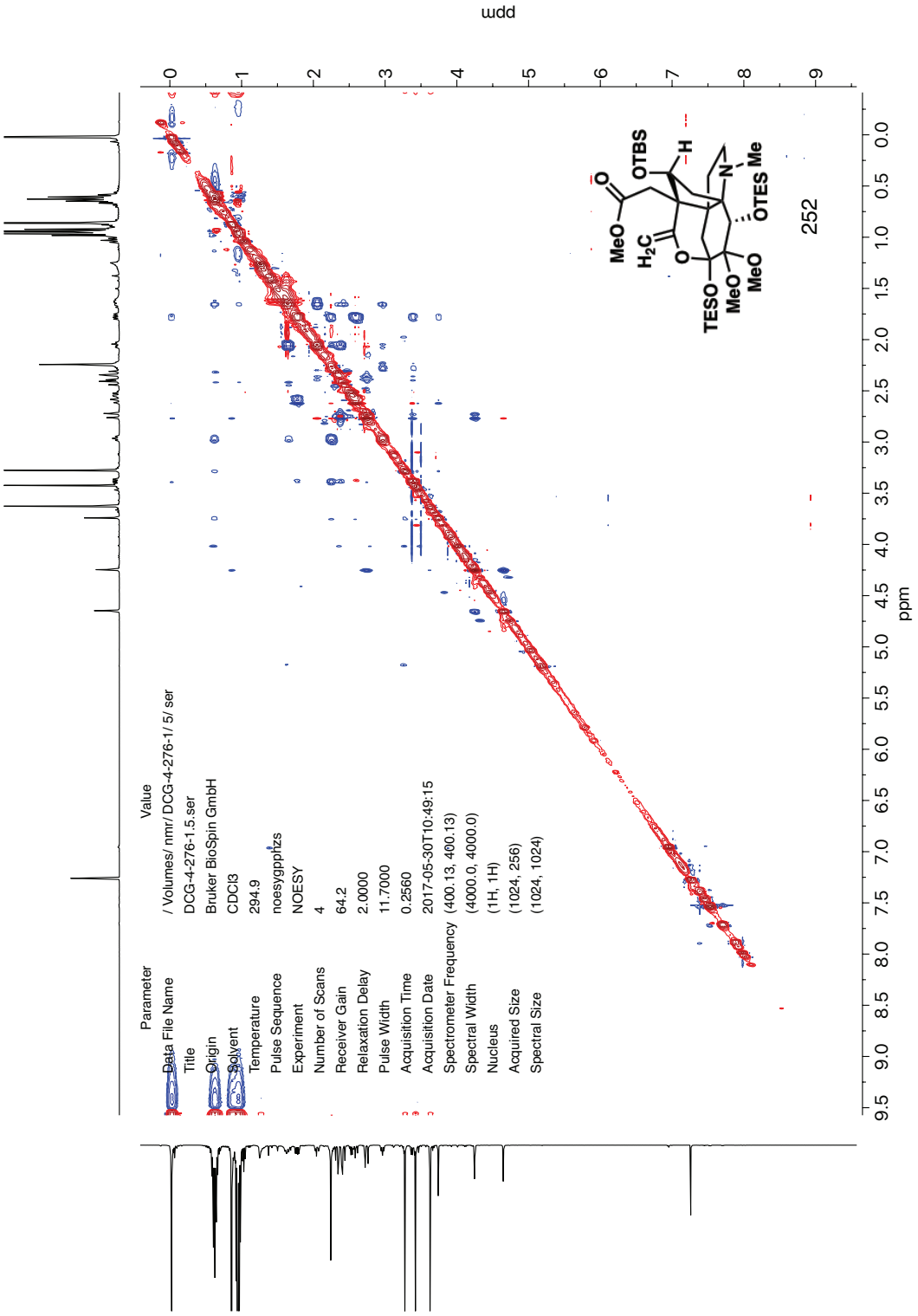

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-276-1/1/1/ fid
Title DCG-4-276-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 72.0
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-05-30T09:41:47
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
MeO
H2C
O
OTBS
H
N
Me
OTES
TESO
MeO
MeO
252
0.97
1.01
0.97
3.00
3.01
1.13
2.98
1.00
1.05
1.82
1.11
1.13
1.09
0.83
3.22
1.08
1.23
2.11
21.50
10.96
13.29
5.97
ppm

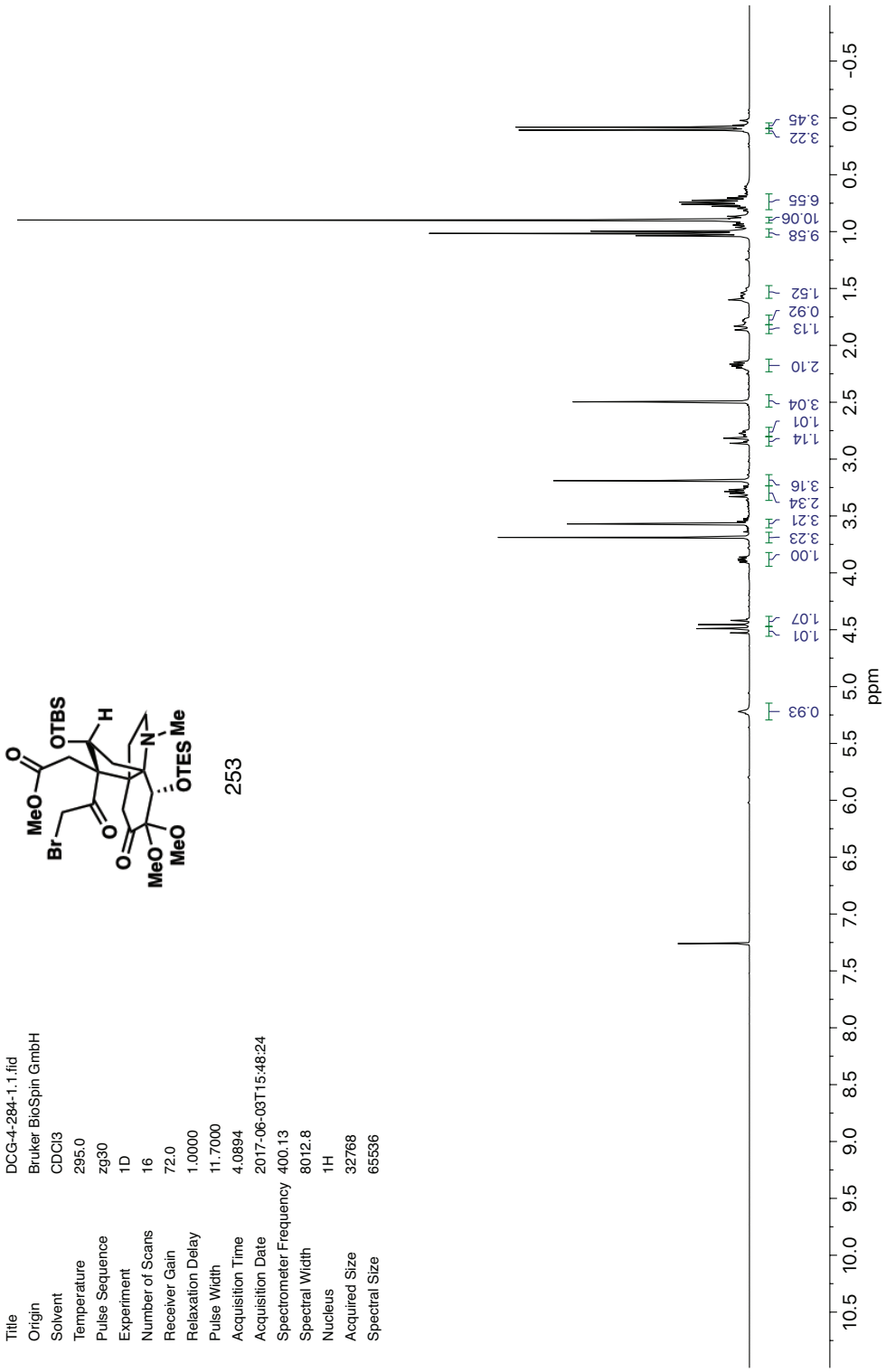

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-276-1/ 2/ ser
Title DCG-4-276-1.2.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.1970
Acquisition Date 2017-05-30T09:42:42
Spectrometer Frequency (400.13, 400.13)
Spectral Width (5197.5, 5197.5)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)
ppm
252

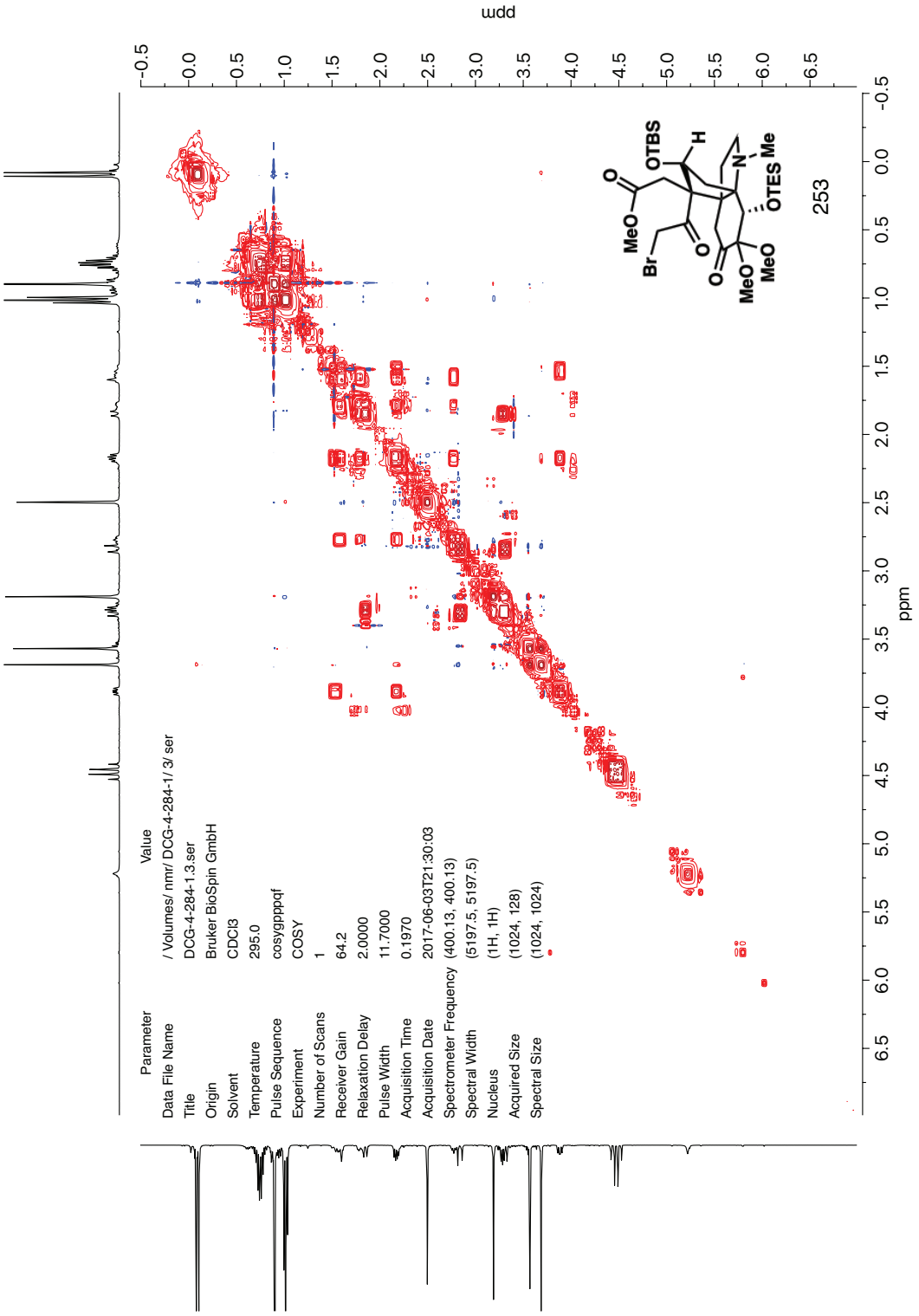

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-276-1/ 3/ ser
Title DCG-4-276-1.3.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2017-05-30T09:48:40
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
MeO
H2C
OTBS
H
N
TESO
MeO
MeO
OTES
Me
252
{3.39,77.34}
ppm
ppm

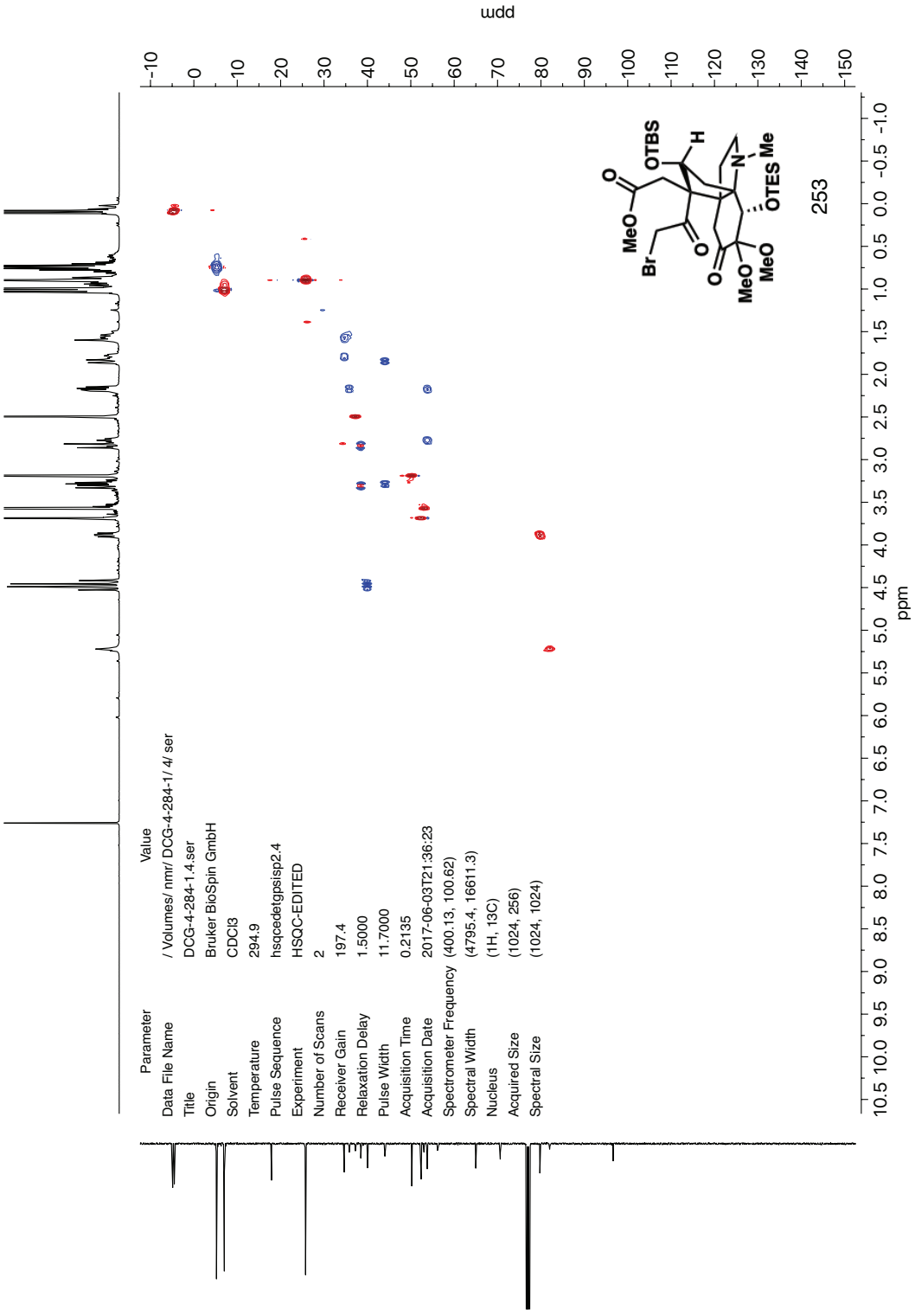

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-276-1/ 4/ ser
Title DCG-4-276-1.4.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2017-05-30T10:04:39
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
MeO
H2C
OTBS
H
TESO
MeO
MeO
N
OTES
Me
252
ppm
ppm
ppm

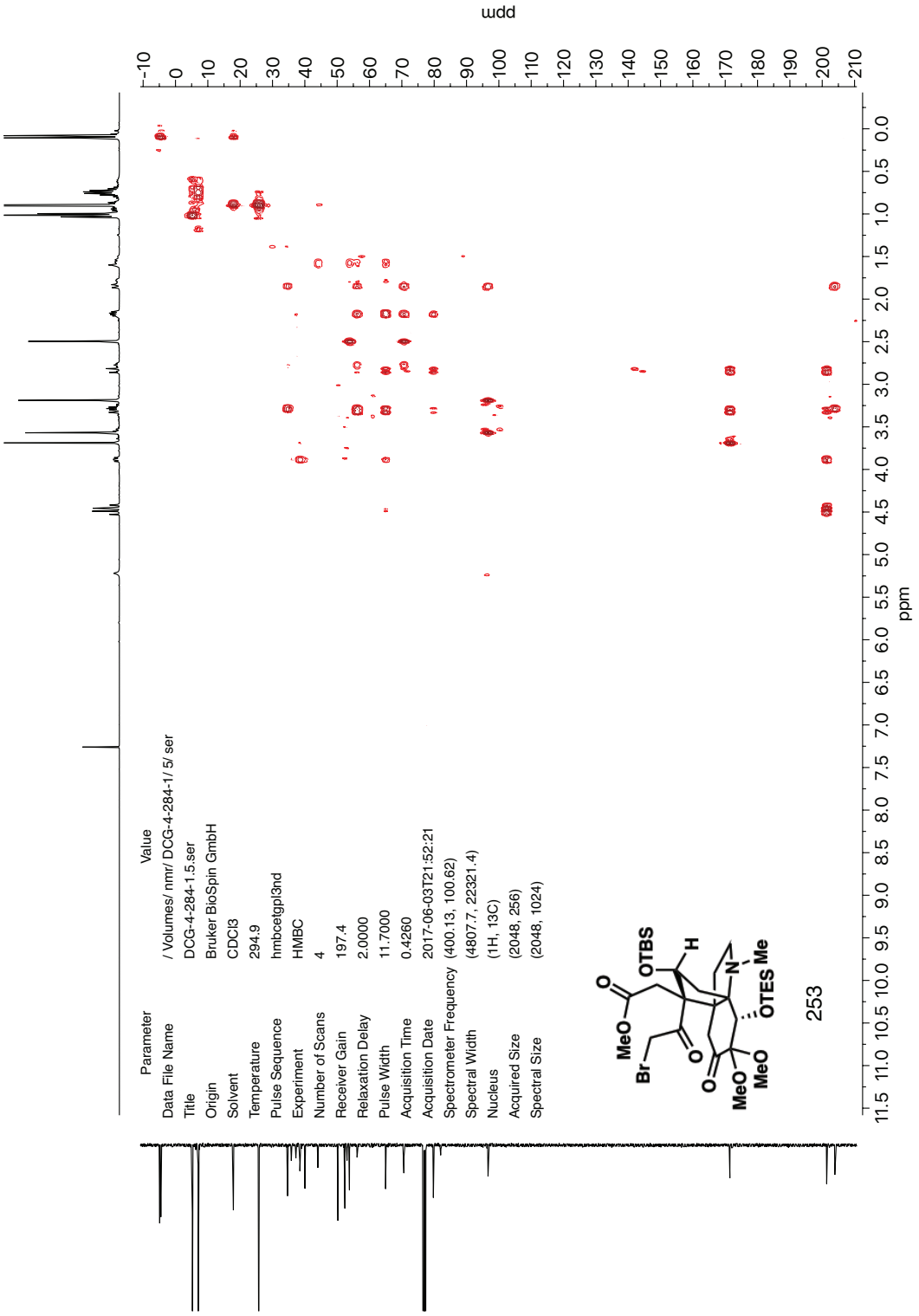

Parameter
Value
Data File Name / Volumes/ nmr/ DCG-4-276-1/ 6/ fid
Title DCG-4-276-1.6.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 87.8
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-05-30T11:51:44
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
MeO
H2C
O
OTBS
H
N
Me
OTES
TESO
MeO
MeO
252
76.06
ppm
-3.76
-4.57
5.62
6.54
7.20
7.53
18.18
26.00
34.61
34.95
36.04
36.81
39.22
49.81
51.46
51.48
51.60
55.88
58.01
71.87
76.06
98.68
100.54
101.75
155.82
171.93
ppm

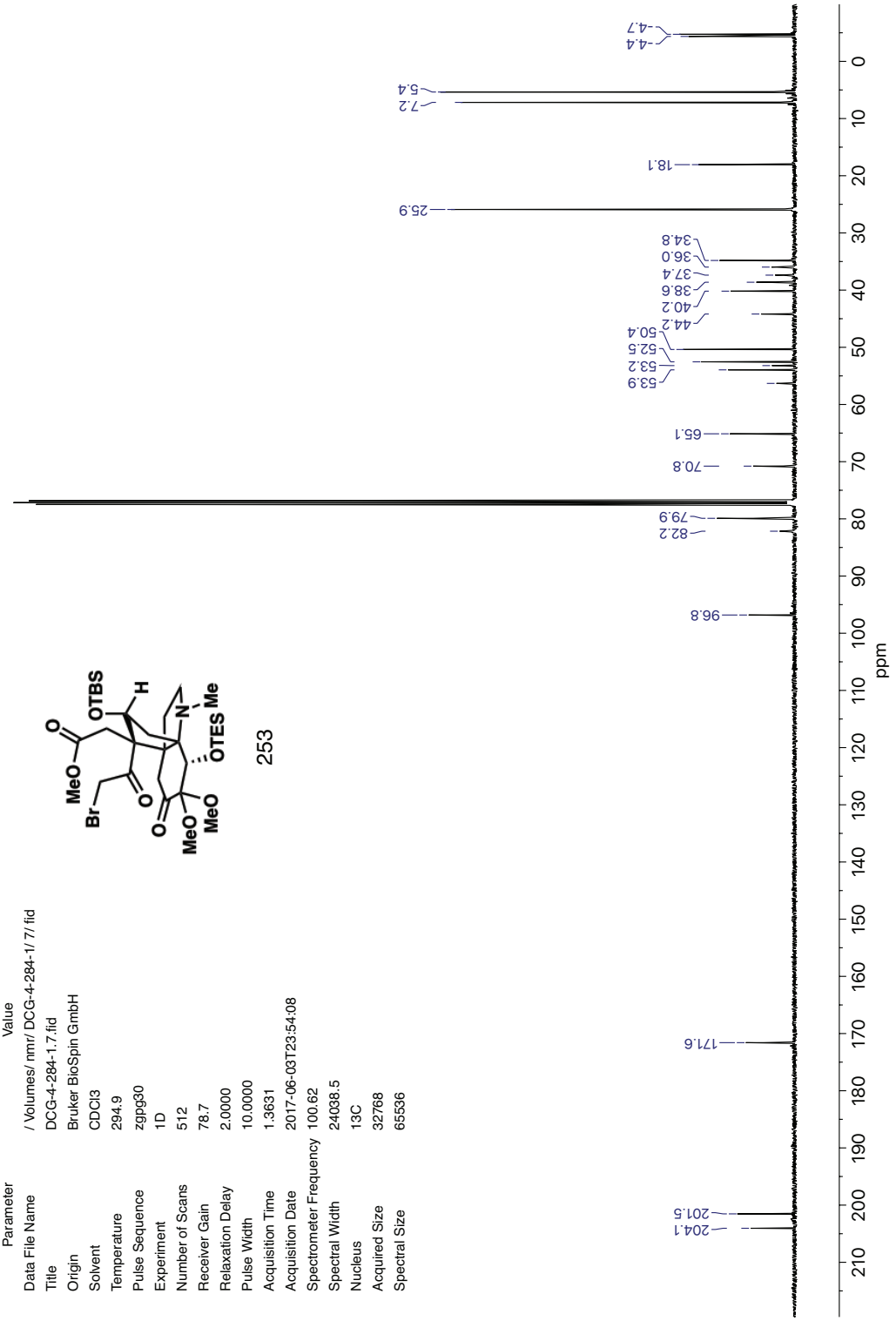

Parameter
Value
Data File Name / Volumes/ nmr/ DCG-4-276-1/ 5/ ser
Title DCG-4-276-1.5.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence noesygpphzs
Experiment NOESY
Number of Scans 4
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2017-05-30T10:49:15
Spectrometer Frequency (400.13, 400.13)
Spectral Width (4000.0, 4000.0)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
ppm
252

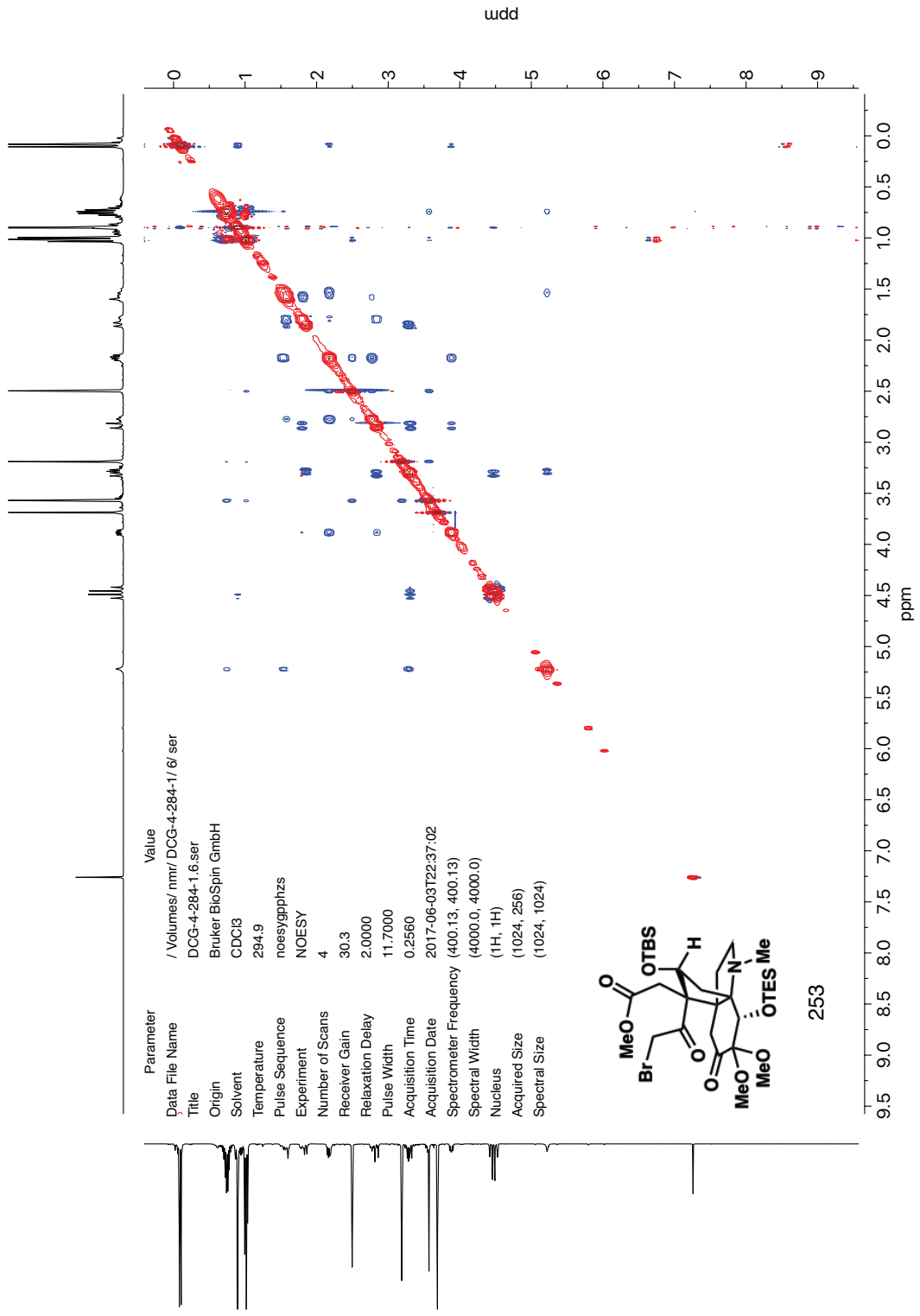

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-284-1/ 1/ fid
Title DCG-4-284-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 72.0
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-06-03T15:48:24
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
MeO
Br
O
OTBS
H
N
Me
OTES
MeO
MeO
253
0.93
1.01
1.07
1.00
3.23
3.21
2.34
3.16
1.14
1.01
3.04
2.10
1.13
0.92
1.52
9.58
10.06
6.55
3.22
3.45
ppm

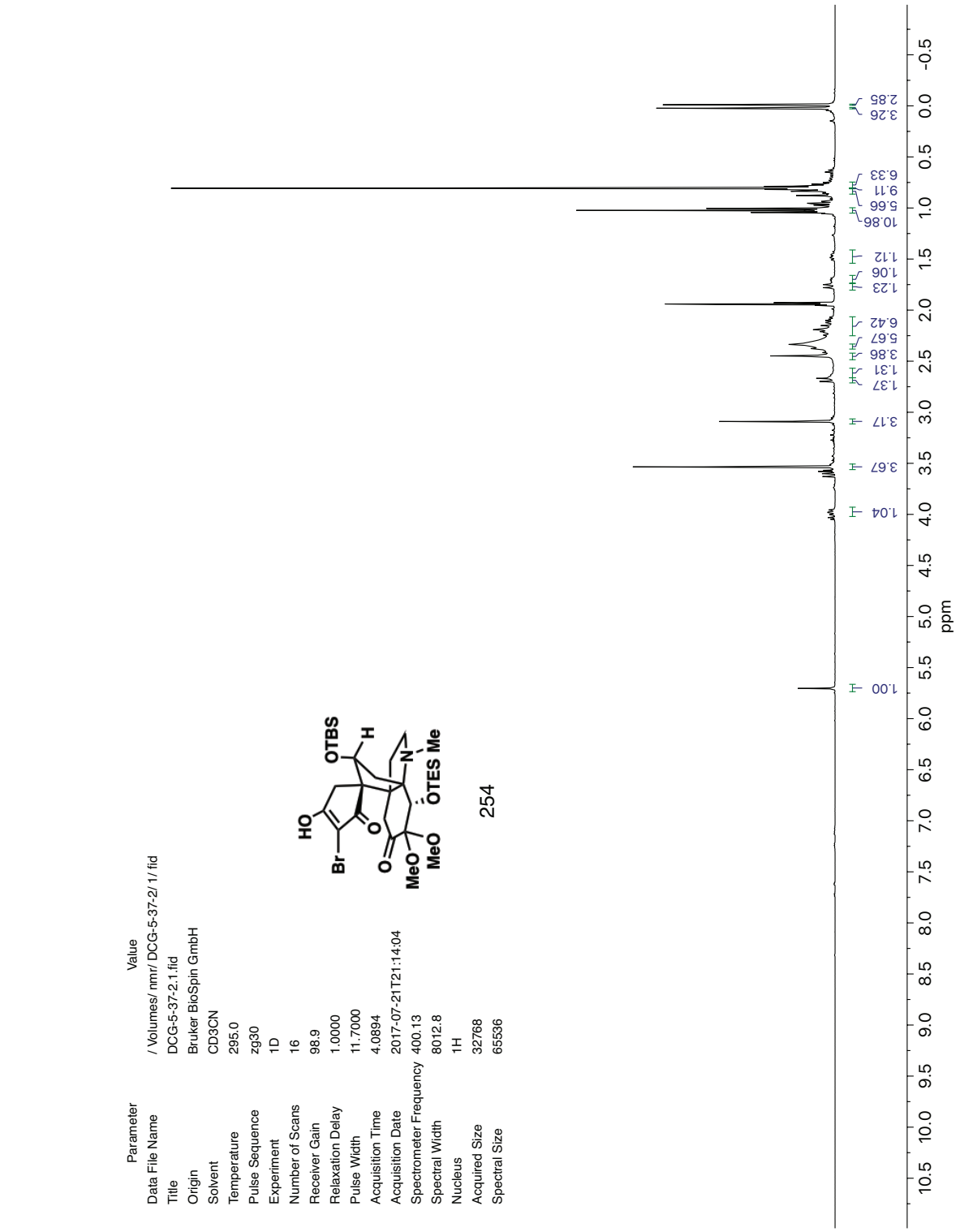

ppm
-0.5
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-4-284-1/ 3/ ser
Title
DCG-4-284-1.3.ser
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.0
Pulse Sequence
cosygpppqf
Experiment
COSY
Number of Scans
1
Receiver Gain
64.2
Relaxation Delay
2.0000
Pulse Width
11.7000
Acquisition Time
0.1970
Acquisition Date
2017-06-03T21:30:03
Spectrometer Frequency
(400.13, 400.13)
Spectral Width
(5197.5, 5197.5)
Nucleus
(1H, 1H)
Acquired Size
(1024, 128)
Spectral Size
(1024, 1024)
MeO
Br
O
OTBS
H
N
OTES
Me
MeO
MeO
253

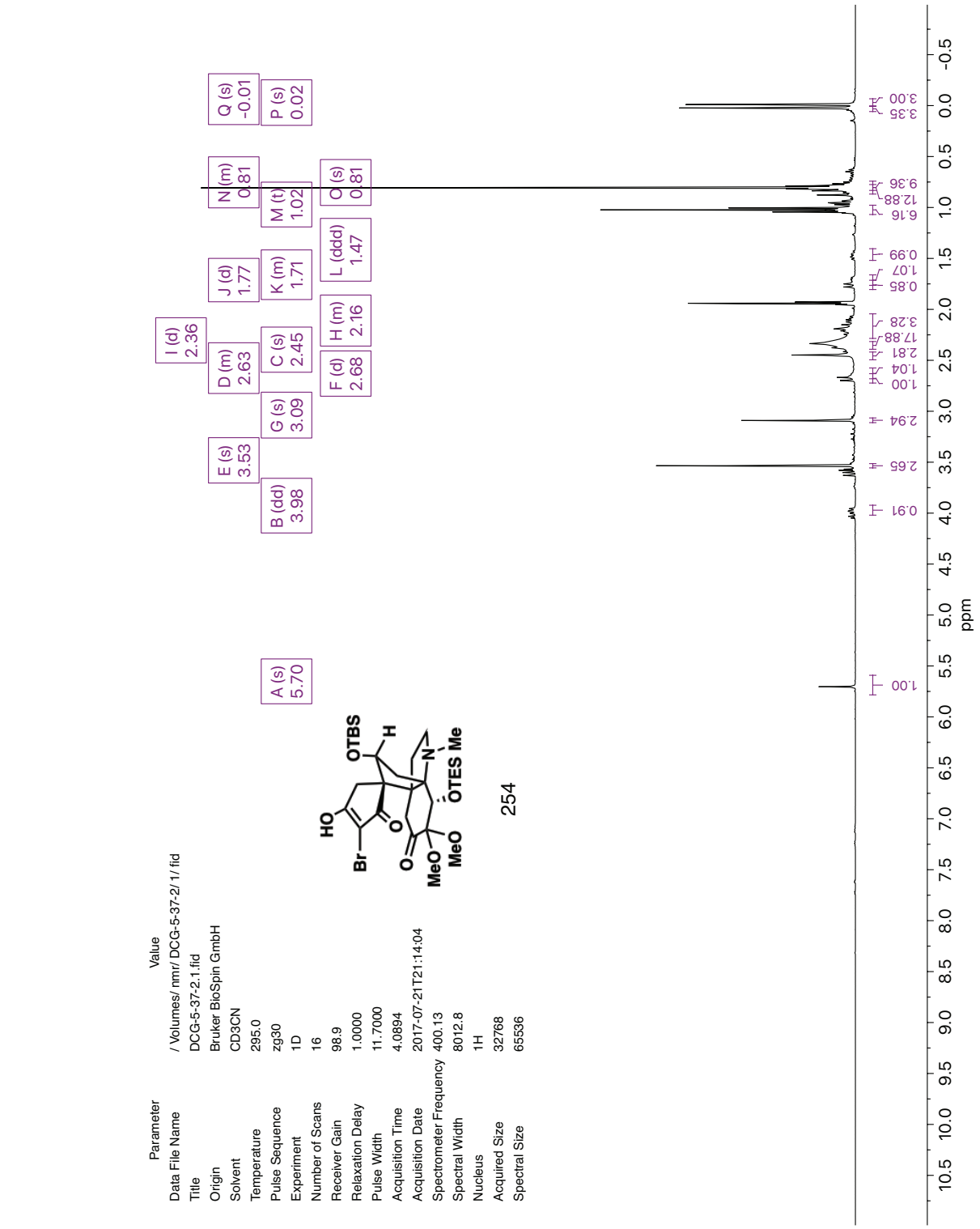

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-284-1/ 4/ ser
Title DCG-4-284-1.4.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2017-06-03T21:36:23
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
ppm
ppm
253

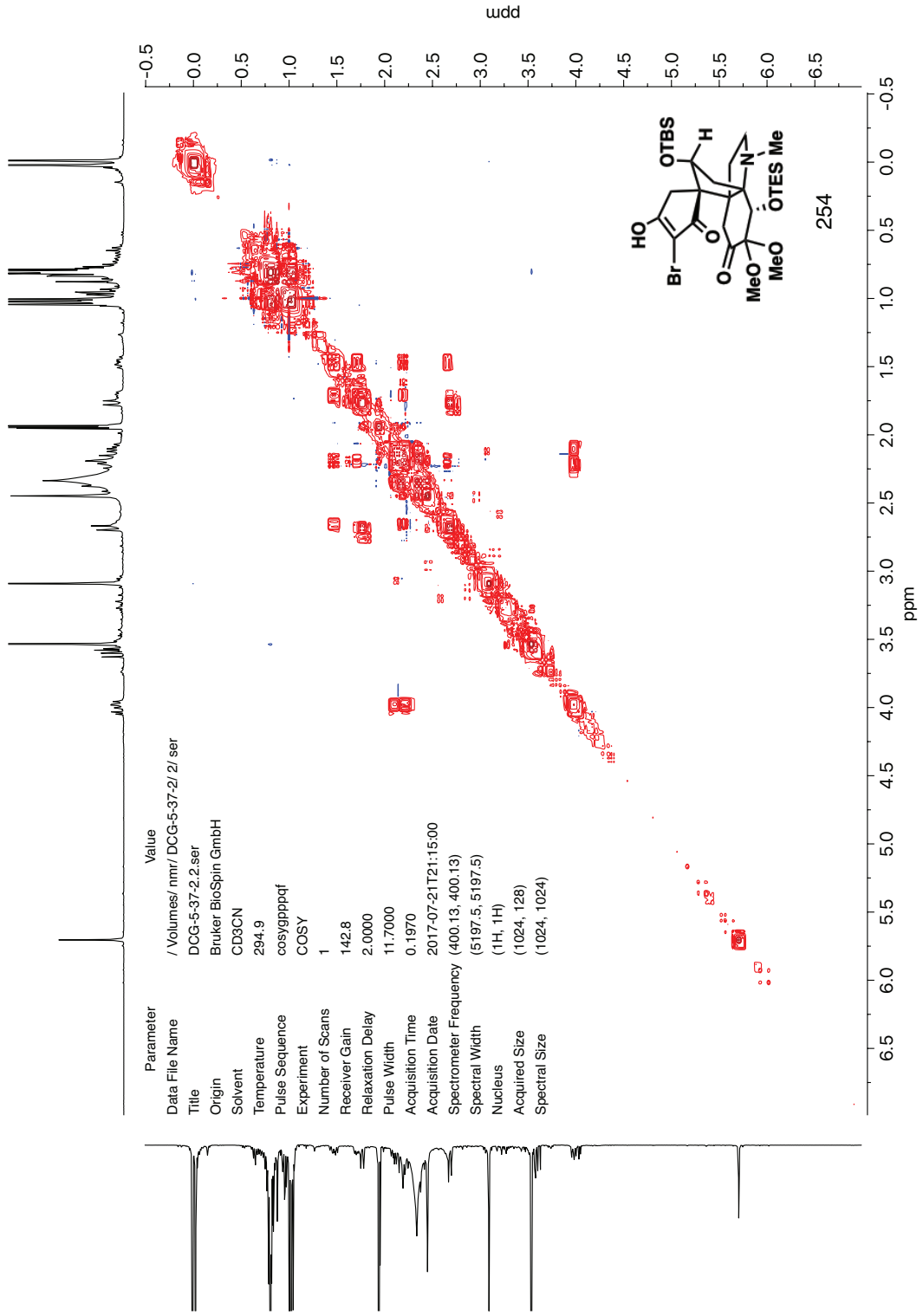

Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-4-284-1/ 5/ ser
Title
DCG-4-284-1.5.ser
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
hmbcetgpl3nd
Experiment
HMBC
Number of Scans
4
Receiver Gain
197.4
Relaxation Delay
2.0000
Pulse Width
11.7000
Acquisition Time
0.4260
Acquisition Date
2017-06-03T21:52:21
Spectrometer Frequency
(400.13, 100.62)
Spectral Width
(4807.7, 22321.4)
Nucleus
(1H, 13C)
Acquired Size
(2048, 256)
Spectral Size
(2048, 1024)
MeO
Br
OTBS
H
N
OTES
Me
MeO
MeO
253
ppm
ppm

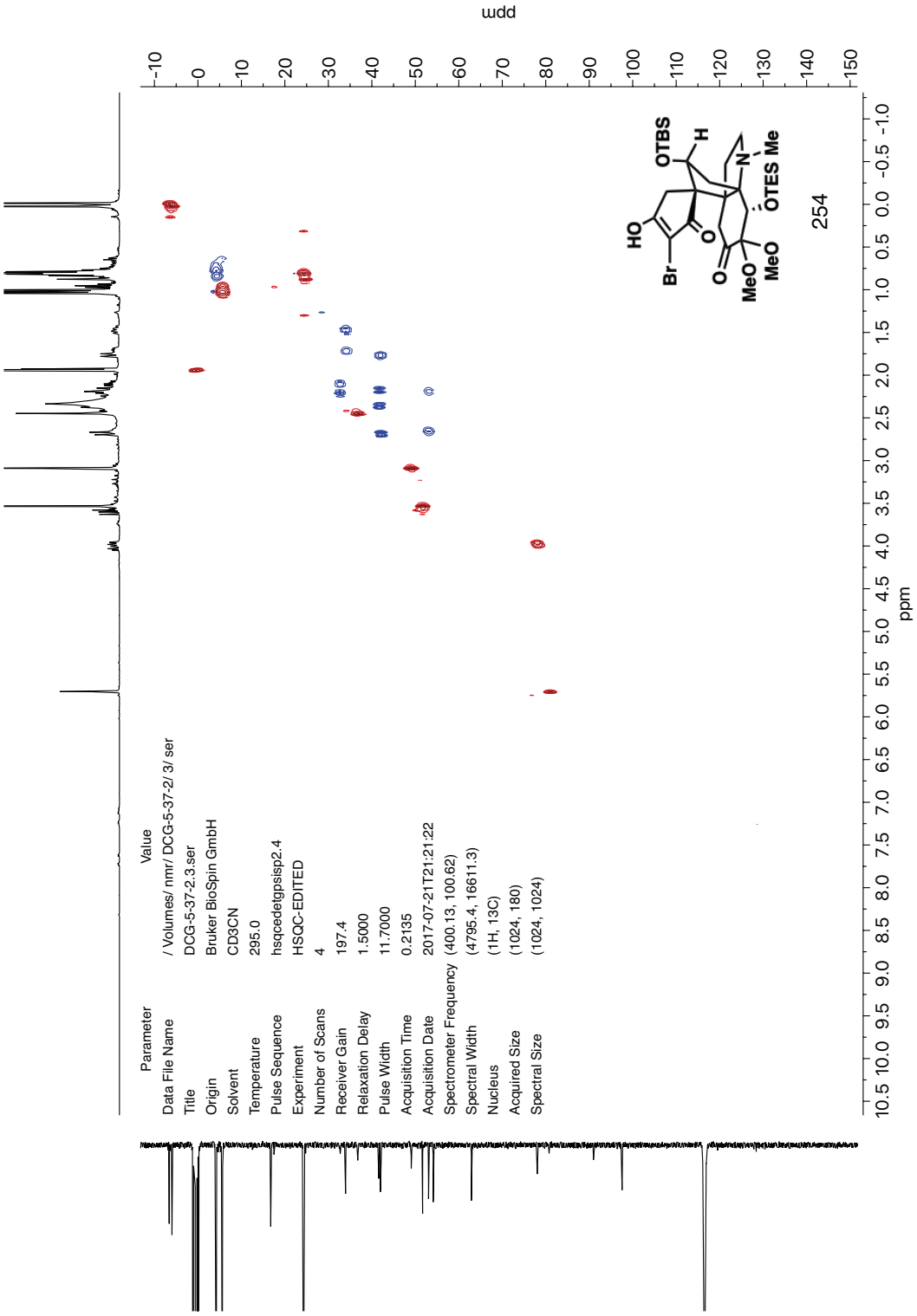

Parameter
Value
Data File Name / Volumes/ nmr/ DCG-4-284-1/ 7/ fid
Title DCG-4-284-1.7.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 512
Receiver Gain 78.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-06-03T23:54:08
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
253
MeO
Br
O
OTBS
H
N
Me
OTES
MeO
MeO
O
O
-4.7
-4.4
5.4
7.2
18.1
25.9
34.8
36.0
37.4
38.6
40.2
44.2
50.4
52.5
53.2
53.9
65.1
70.8
79.9
82.2
96.8
171.6
201.5
204.1
ppm

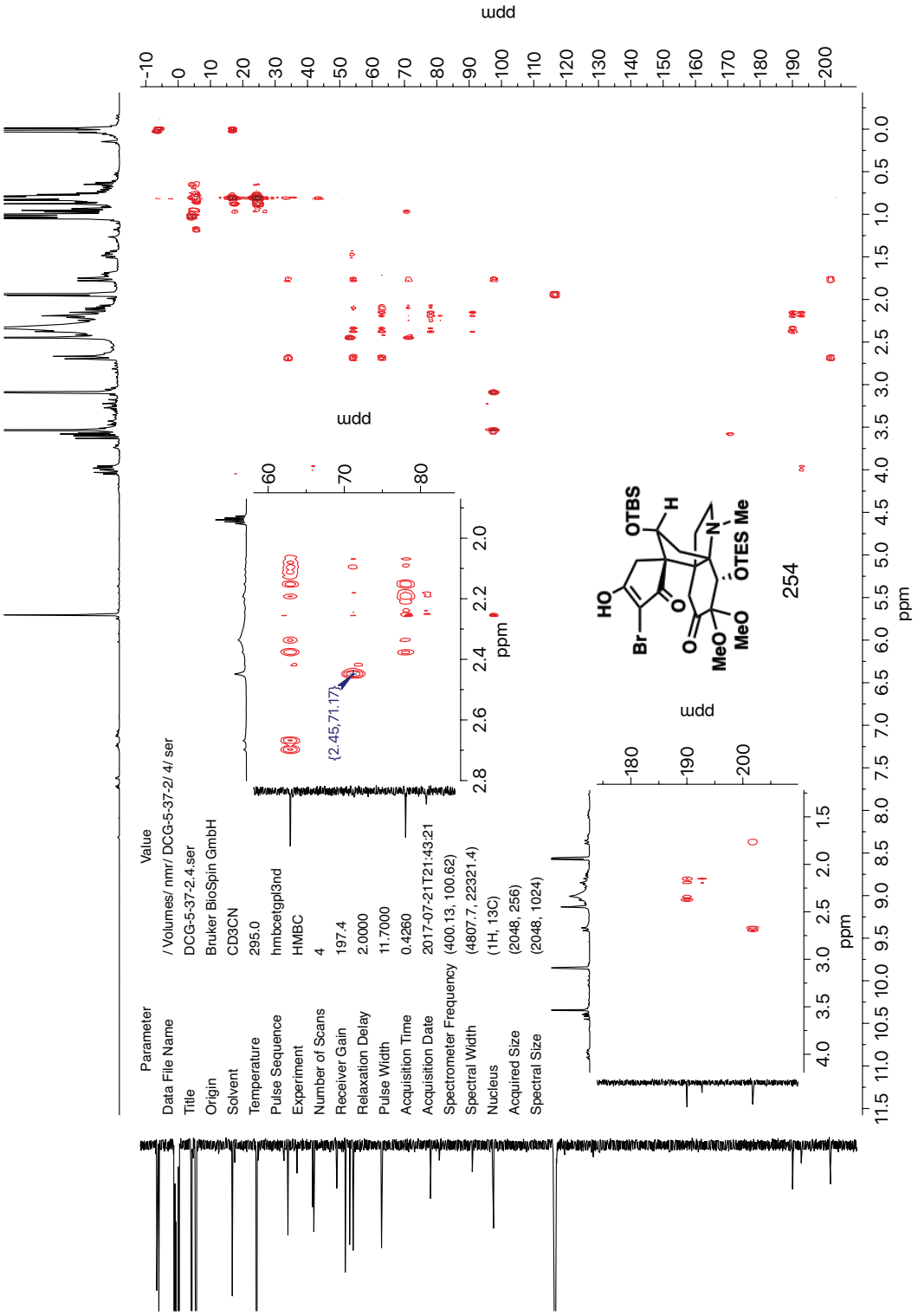

ppm
ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-284-1/ 6/ ser
Title DCG-4-284-1.6.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence noesygpphzs
Experiment NOESY
Number of Scans 4
Receiver Gain 30.3
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2017-06-03T22:37:02
Spectrometer Frequency (400.13, 400.13)
Spectral Width (4000.0, 4000.0)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
MeO
Br
OTBS
H
N
OTES
Me
MeO
MeO
253

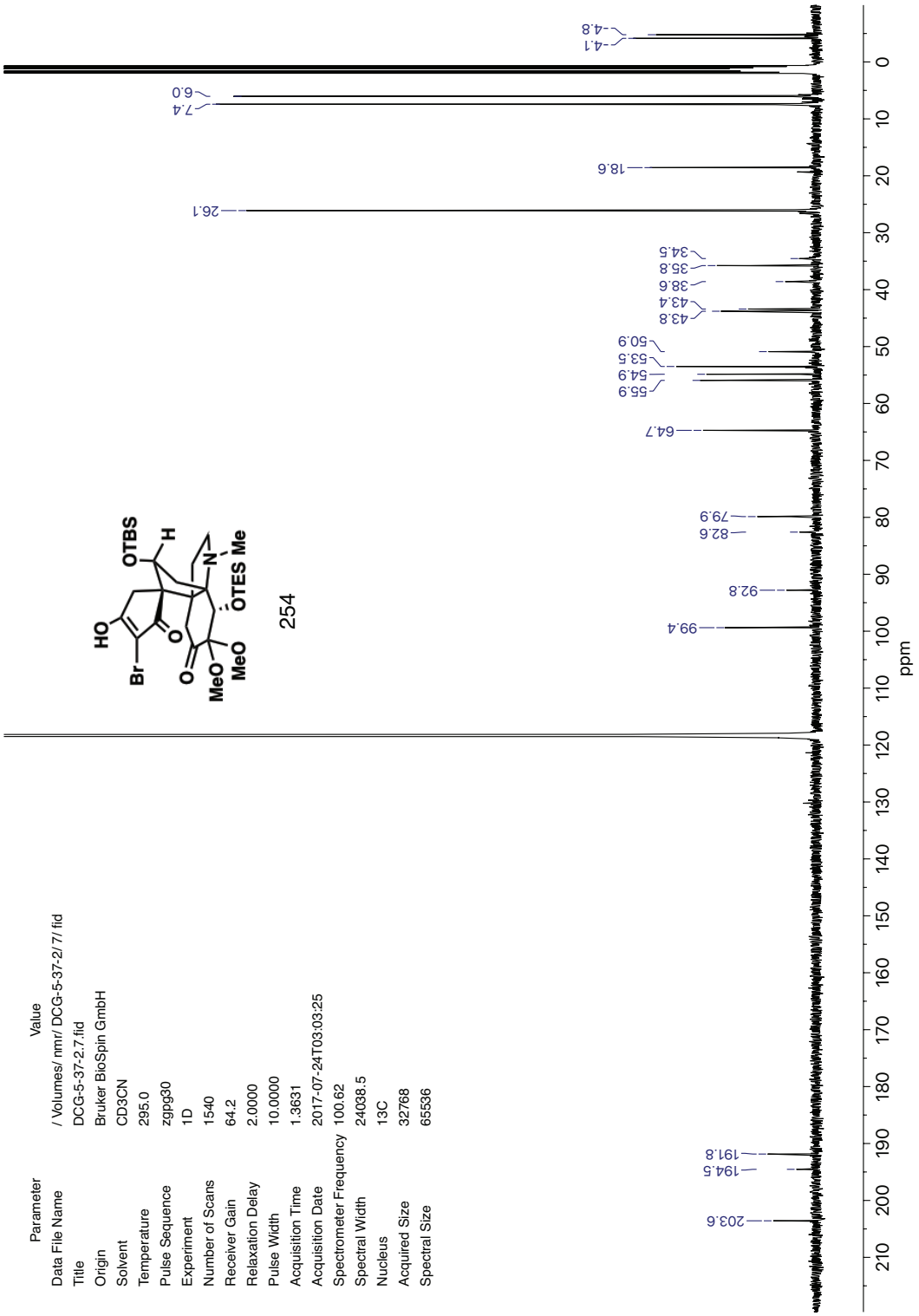

Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-5-37-2/ 1/ fid
Title
DCG-5-37-2.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CD3CN
Temperature
295.0
Pulse Sequence
zg30
Experiment
1D
Number of Scans
16
Receiver Gain
98.9
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2017-07-21T21:14:04
Spectrometer Frequency
400.13
Spectral Width
8012.8
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
HO
OTBS
H
Br
O
O
MeO
MeO
N
OTES
Me
254
1.00
1.04
3.67
3.17
1.37
1.31
3.86
5.67
6.42
1.23
1.06
1.12
10.86
5.66
9.11
6.33
3.26
2.85
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
ppm

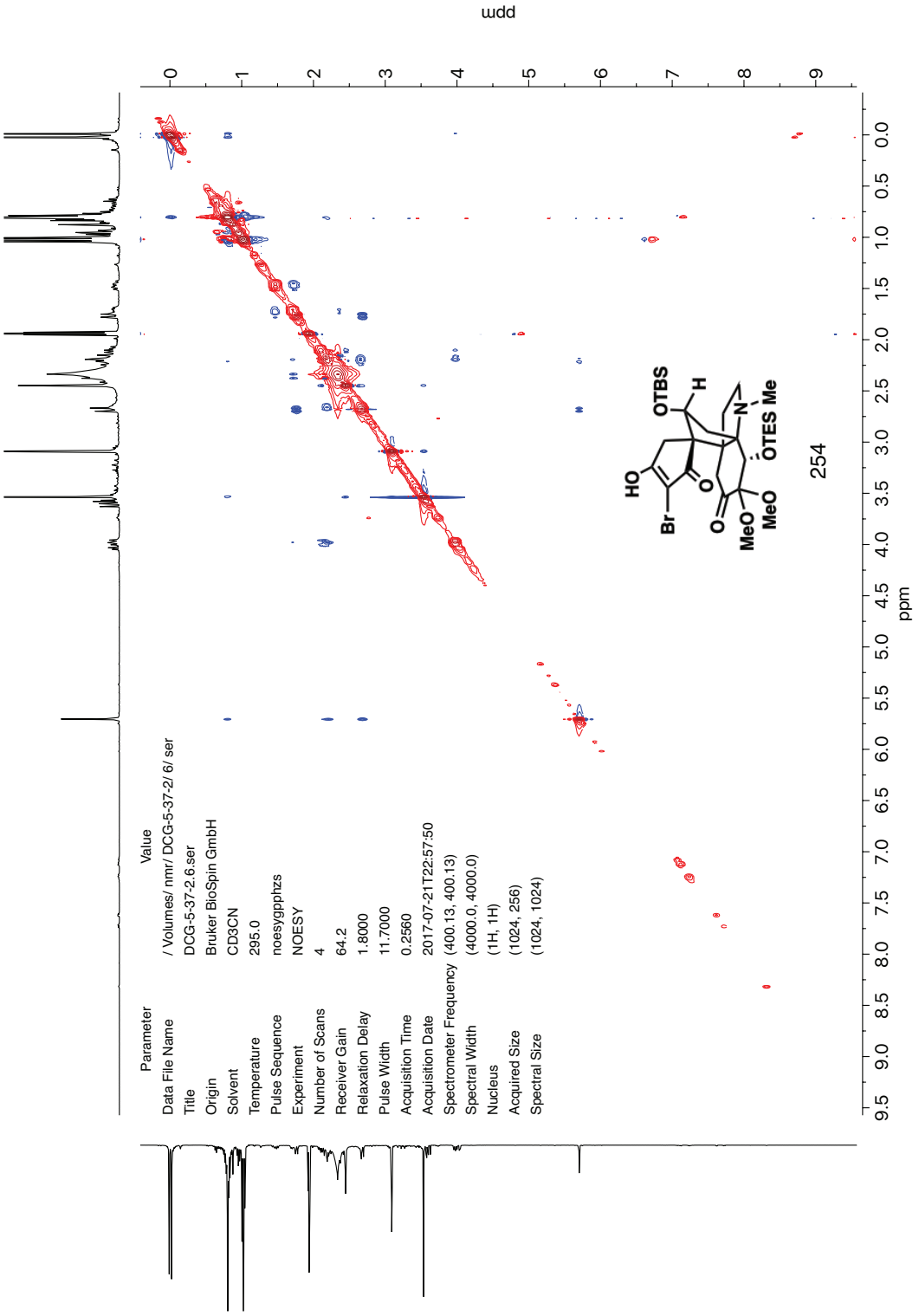

Parameter
Value
Data File Name / Volumes/ nmr/ DCG-5-37-2/ 1/ fid
Title DCG-5-37-2.1.fid
Origin Bruker BioSpin GmbH
Solvent CD3CN
Temperature 295.0
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 98.9
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-07-21T21:14:04
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
A (s) 5.70
B (dd) 3.98
C (s) 2.45
D (m) 2.63
E (s) 3.53
F (d) 2.68
G (s) 3.09
H (m) 2.16
I (d) 2.36
J (d) 1.77
K (m) 1.71
L (ddd) 1.47
M (t) 1.02
N (m) 0.81
O (s) 0.81
P (s) 0.02
Q (s) -0.01
HO
OTBS
H
Br
O
O
N
MeO
MeO
OTES
Me
254
1.00
0.91
2.65
2.94
1.00
1.04
2.81
17.88
3.28
0.85
1.07
0.99
6.16
12.88
9.36
3.35
3.00
ppm

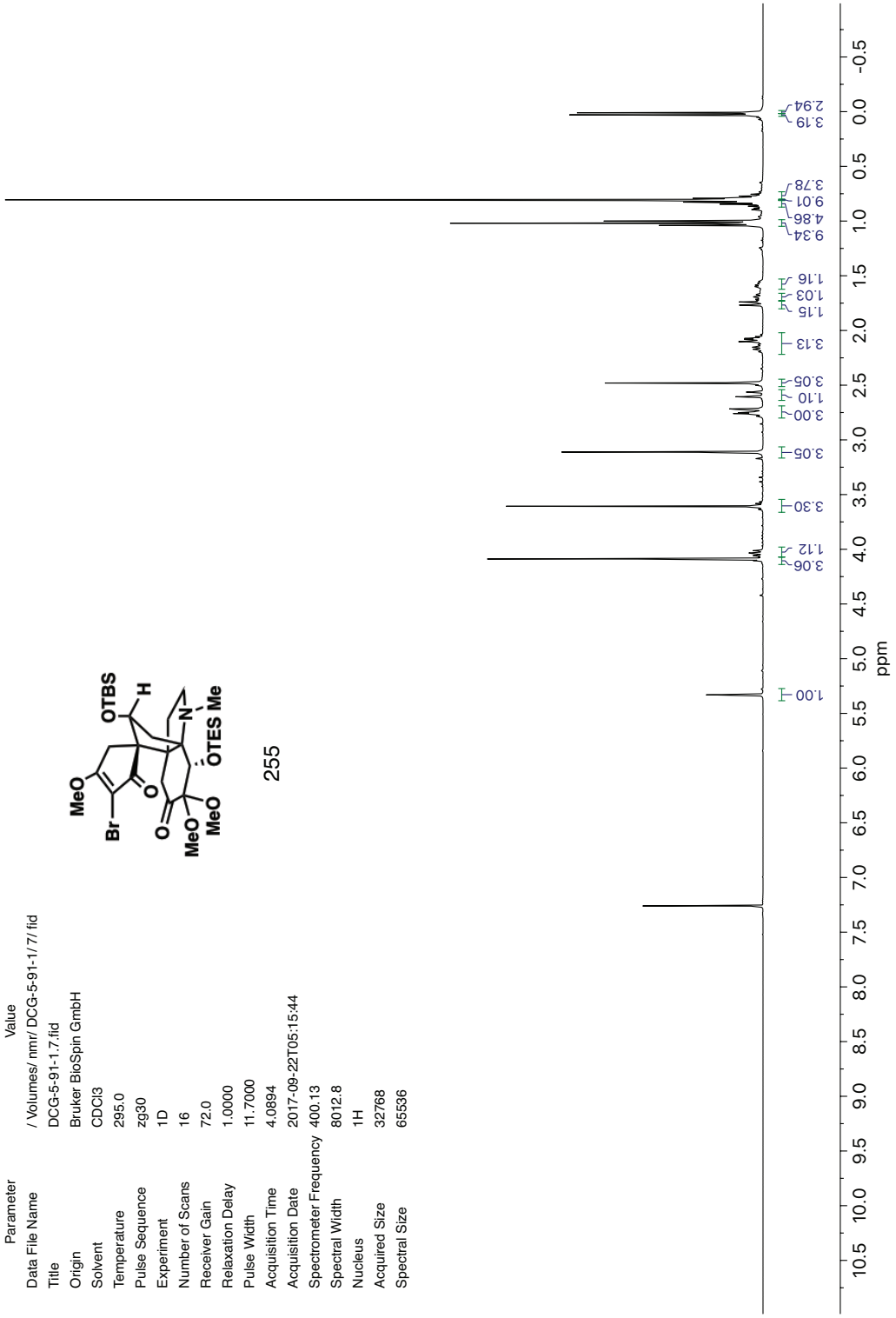

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-37-2/ 2/ ser
Title DCG-5-37-2.2.ser
Origin Bruker BioSpin GmbH
Solvent CD3CN
Temperature 294.9
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 142.8
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.1970
Acquisition Date 2017-07-21T21:15:00
Spectrometer Frequency (400.13, 400.13)
Spectral Width (5197.5, 5197.5)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)
ppm
HO
OTBS
H
Br
O
O
MeO
MeO
N
OTES Me
254

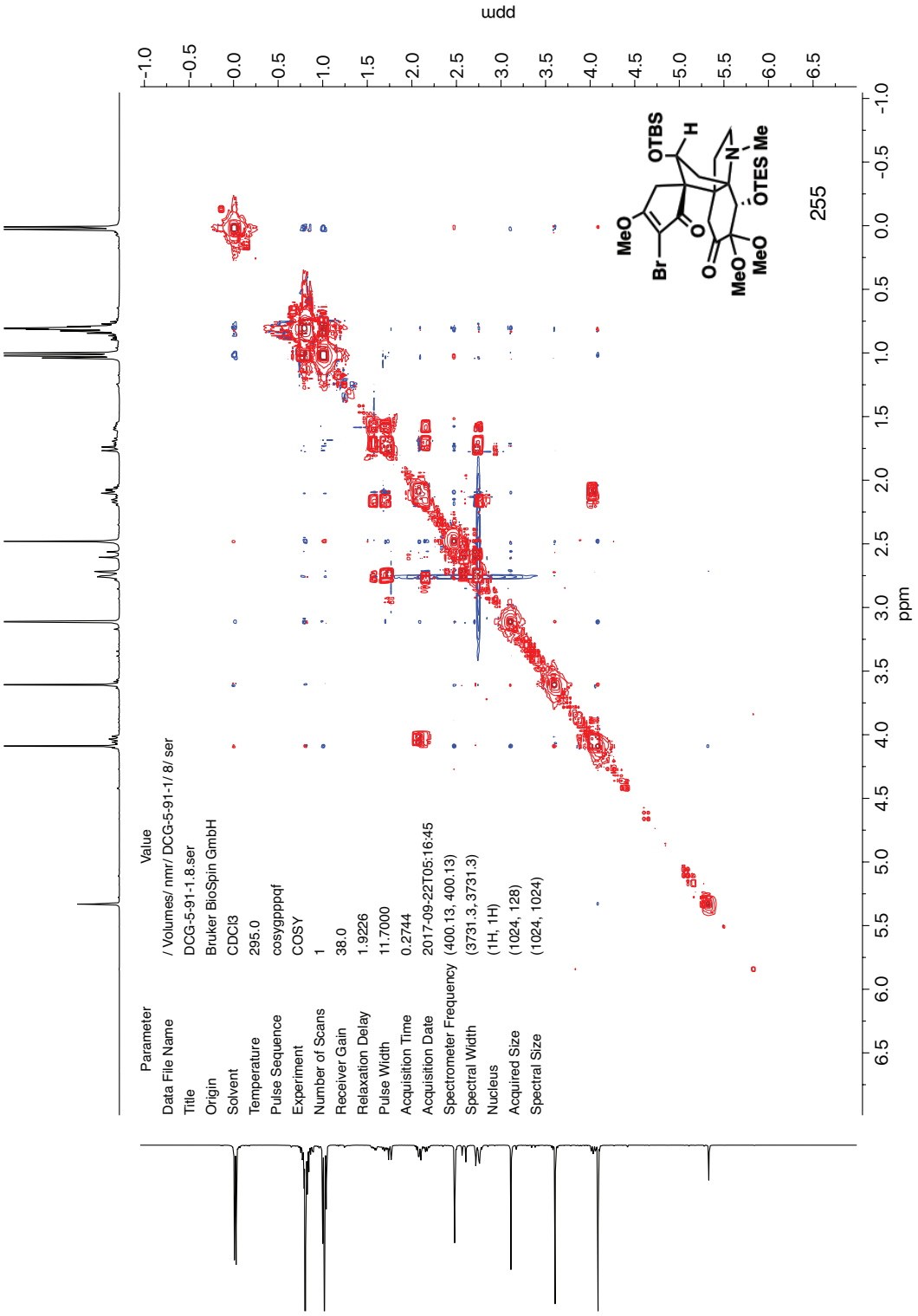

Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-5-37-2/ 3/ ser
Title
DCG-5-37-2.3.ser
Origin
Bruker BioSpin GmbH
Solvent
CD3CN
Temperature
295.0
Pulse Sequence
hsqcedetgpsisp2.4
Experiment
HSQC-EDITED
Number of Scans
4
Receiver Gain
197.4
Relaxation Delay
1.5000
Pulse Width
11.7000
Acquisition Time
0.2135
Acquisition Date
2017-07-21T21:21:22
Spectrometer Frequency
(400.13, 100.62)
Spectral Width
(4795.4, 16611.3)
Nucleus
(1H, 13C)
Acquired Size
(1024, 180)
Spectral Size
(1024, 1024)
ppm
ppm
HO
Br
O
O
MeO
MeO
O
N
OTBS
H
OTES
Me
254

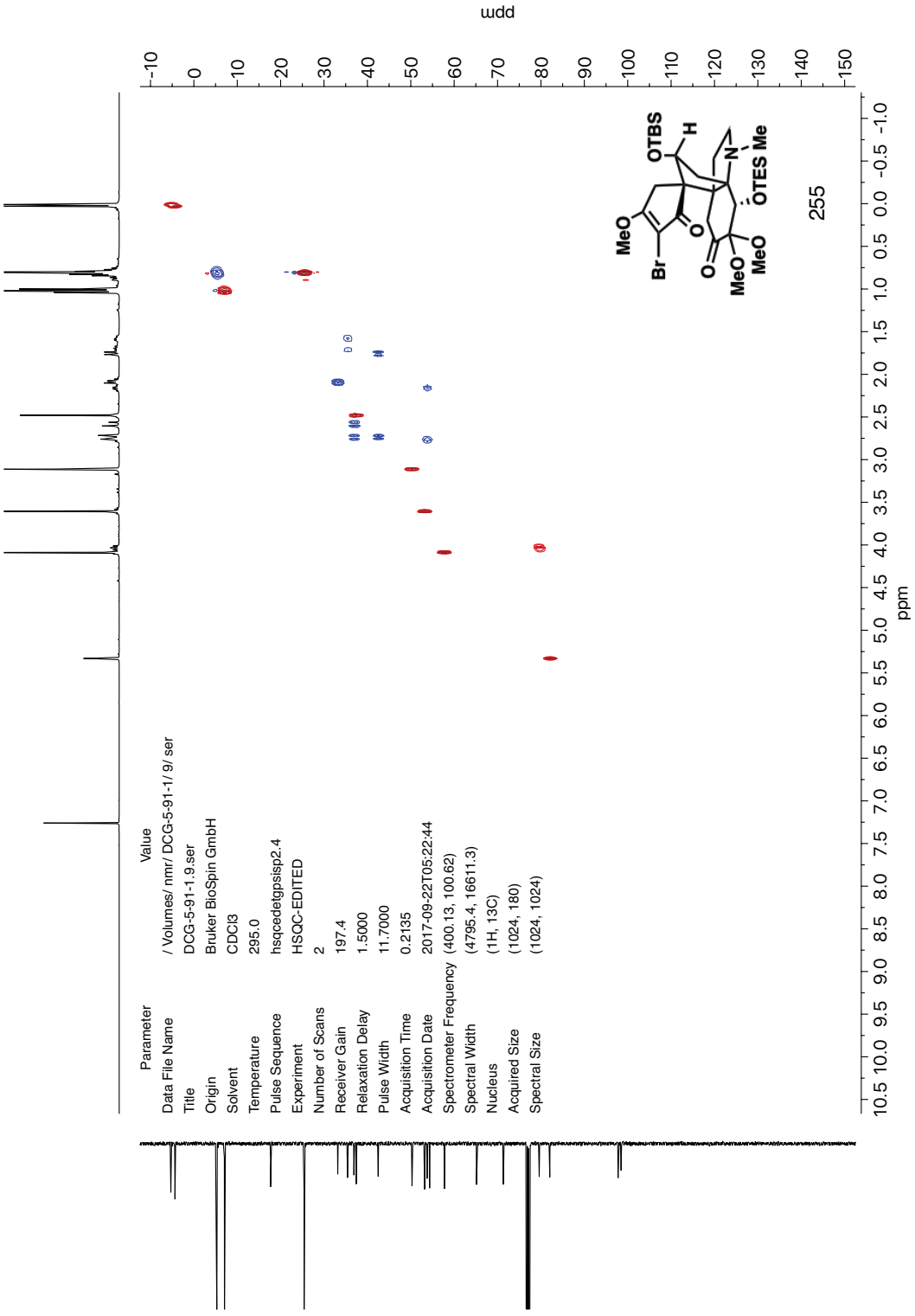

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-37-2/ 4/ ser
Title DCG-5-37-2.4.ser
Origin Bruker BioSpin GmbH
Solvent CD3CN
Temperature 295.0
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2017-07-21T21:43:21
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
(2.45,71.17)
HO
Br
O
O
MeO
MeO
OTBS
H
N
OTES Me
254
ppm

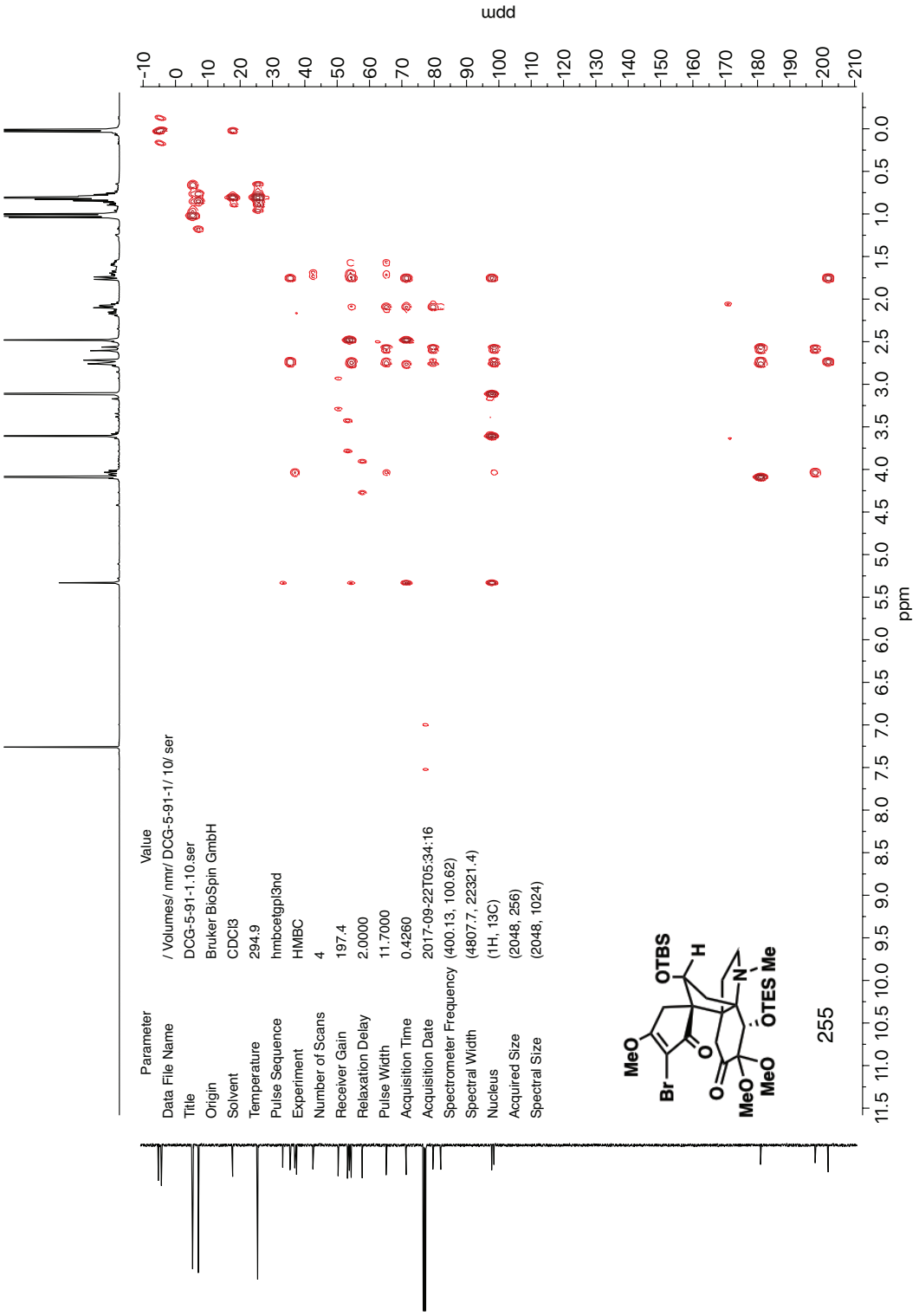

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-37-2/ 7/ fid
Title DCG-5-37-2.7.fid
Origin Bruker BioSpin GmbH
Solvent CD3CN
Temperature 295.0
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 1540
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-07-24T03:03:25
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
-4.8
-4.1
6.0
7.4
18.6
26.1
34.5
35.8
38.6
43.4
43.8
50.9
53.5
54.9
55.9
64.7
79.9
82.6
92.8
99.4
191.8
194.5
203.6
HO
Br
O
O
MeO
MeO
OTBS
H
N
OTES Me
254
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
ppm

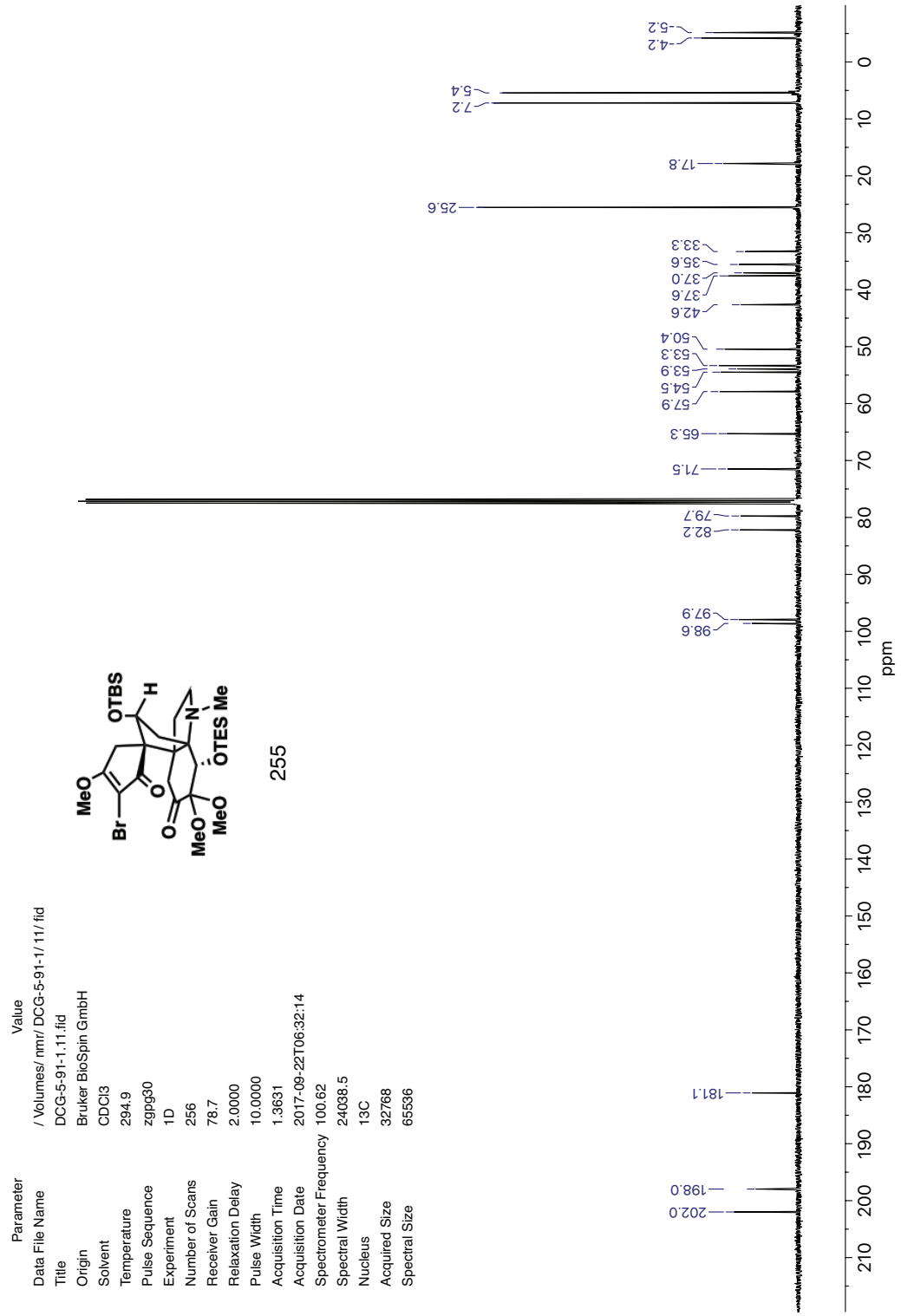

Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-5-37-2/ 6/ ser
Title
DCG-5-37-2.6.ser
Origin
Bruker BioSpin GmbH
Solvent
CD3CN
Temperature
295.0
Pulse Sequence
noesygpphzs
Experiment
NOESY
Number of Scans
4
Receiver Gain
64.2
Relaxation Delay
1.8000
Pulse Width
11.7000
Acquisition Time
0.2560
Acquisition Date
2017-07-21T22:57:50
Spectrometer Frequency
(400.13, 400.13)
Spectral Width
(4000.0, 4000.0)
Nucleus
(1H, 1H)
Acquired Size
(1024, 256)
Spectral Size
(1024, 1024)
ppm
ppm
HO
Br
OTBS
H
N
OTES Me
MeO
MeO
O
O
254

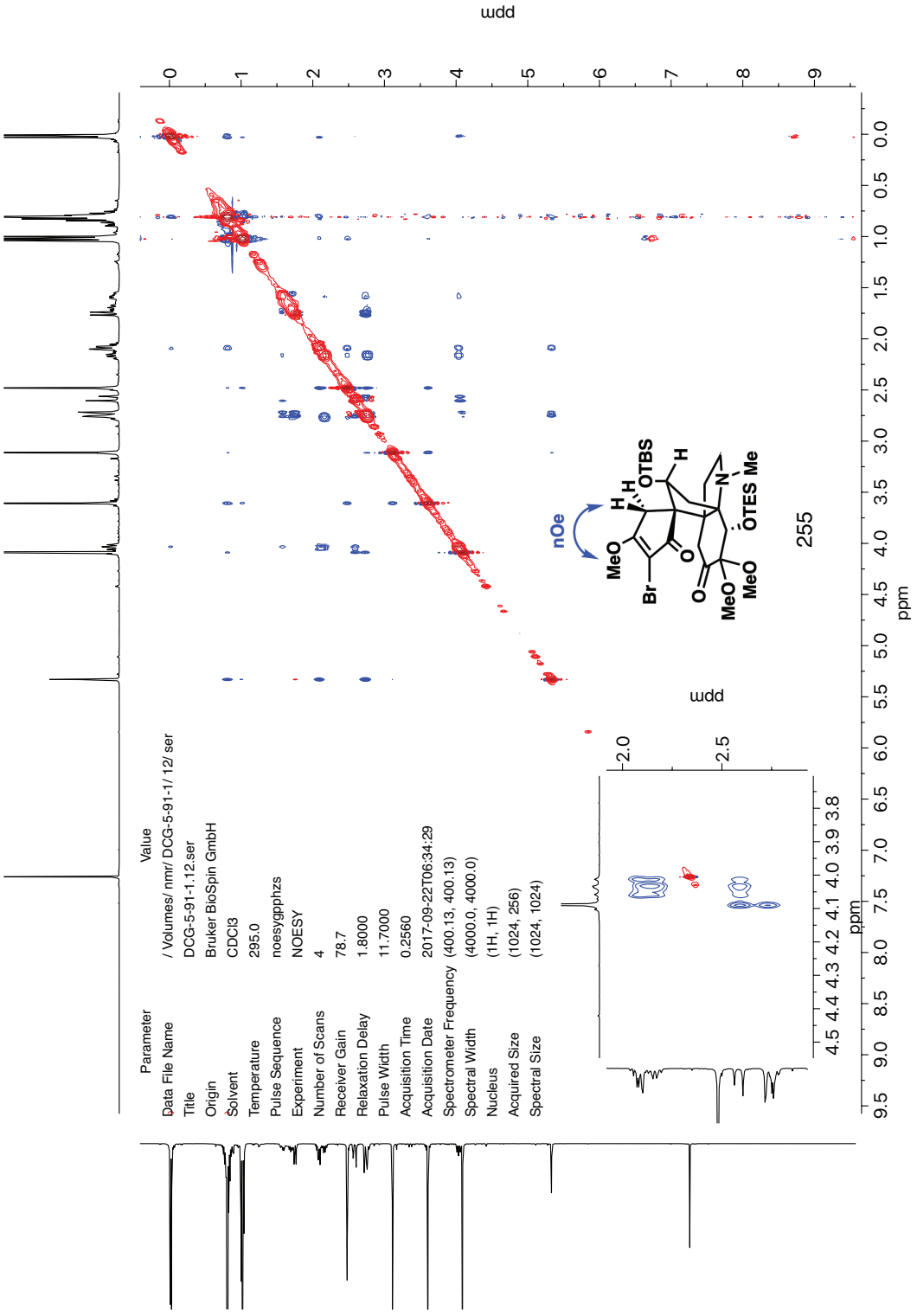

Parameter
Value
Data File Name / Volumes/ nmr/ DCG-5-91-1/7/ fid
Title DCG-5-91-1.7.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 72.0
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-09-22T05:15:44
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
MeO
Br
OTBS
H
N
OTES Me
MeO
MeO
255
1.00
3.06
1.12
3.30
3.05
3.00
1.10
3.05
3.13
1.15
1.03
1.16
9.34
4.86
9.01
3.78
3.19
2.94
ppm

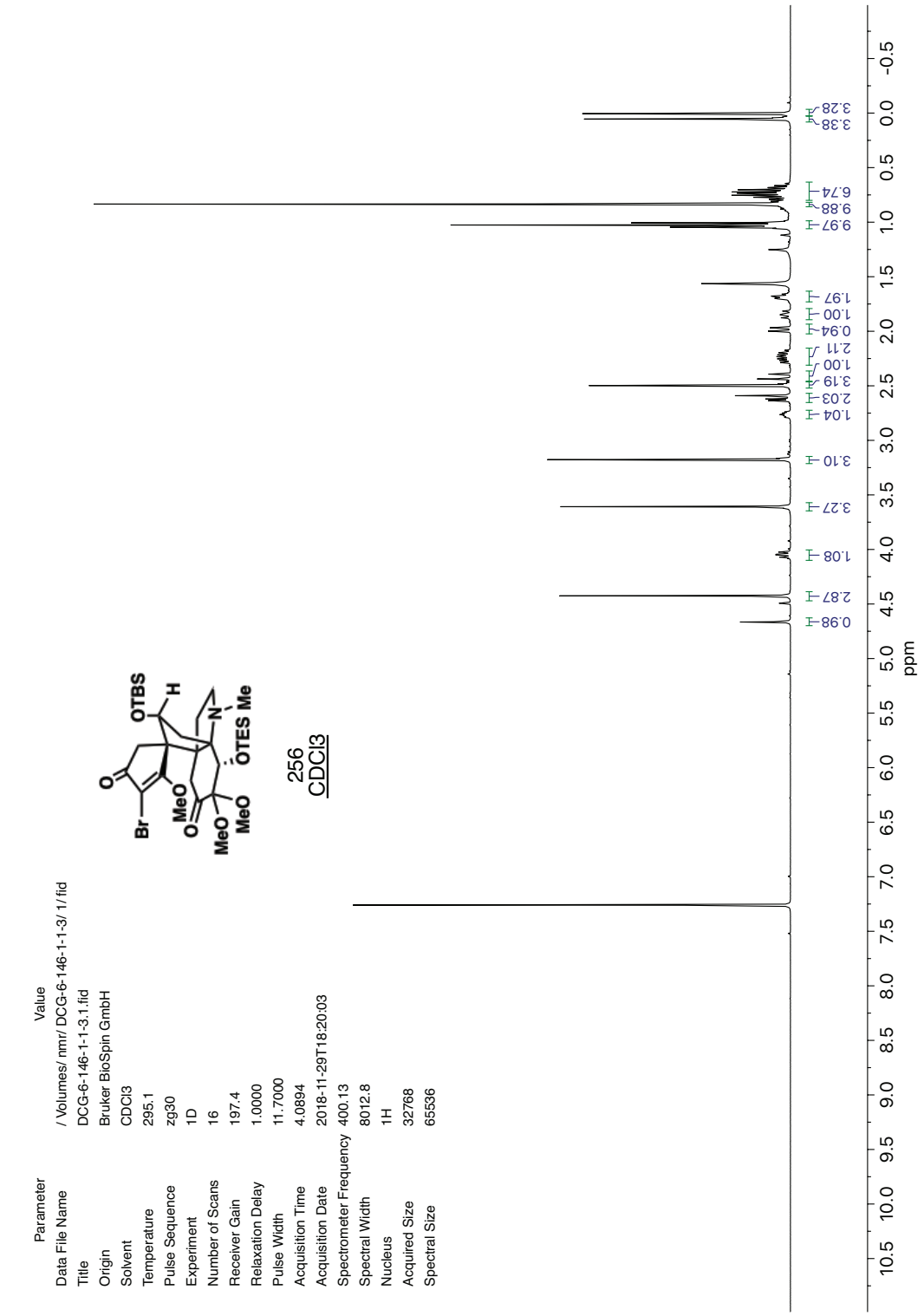

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-91-1/ 8/ ser
Title DCG-5-91-1.8.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 38.0
Relaxation Delay 1.9226
Pulse Width 11.7000
Acquisition Time 0.2744
Acquisition Date 2017-09-22T05:16:45
Spectrometer Frequency (400.13, 400.13)
Spectral Width (3731.3, 3731.3)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)
OTBS
H
N
OTES Me
MeO
Br
O
MeO
MeO
255
ppm
ppm

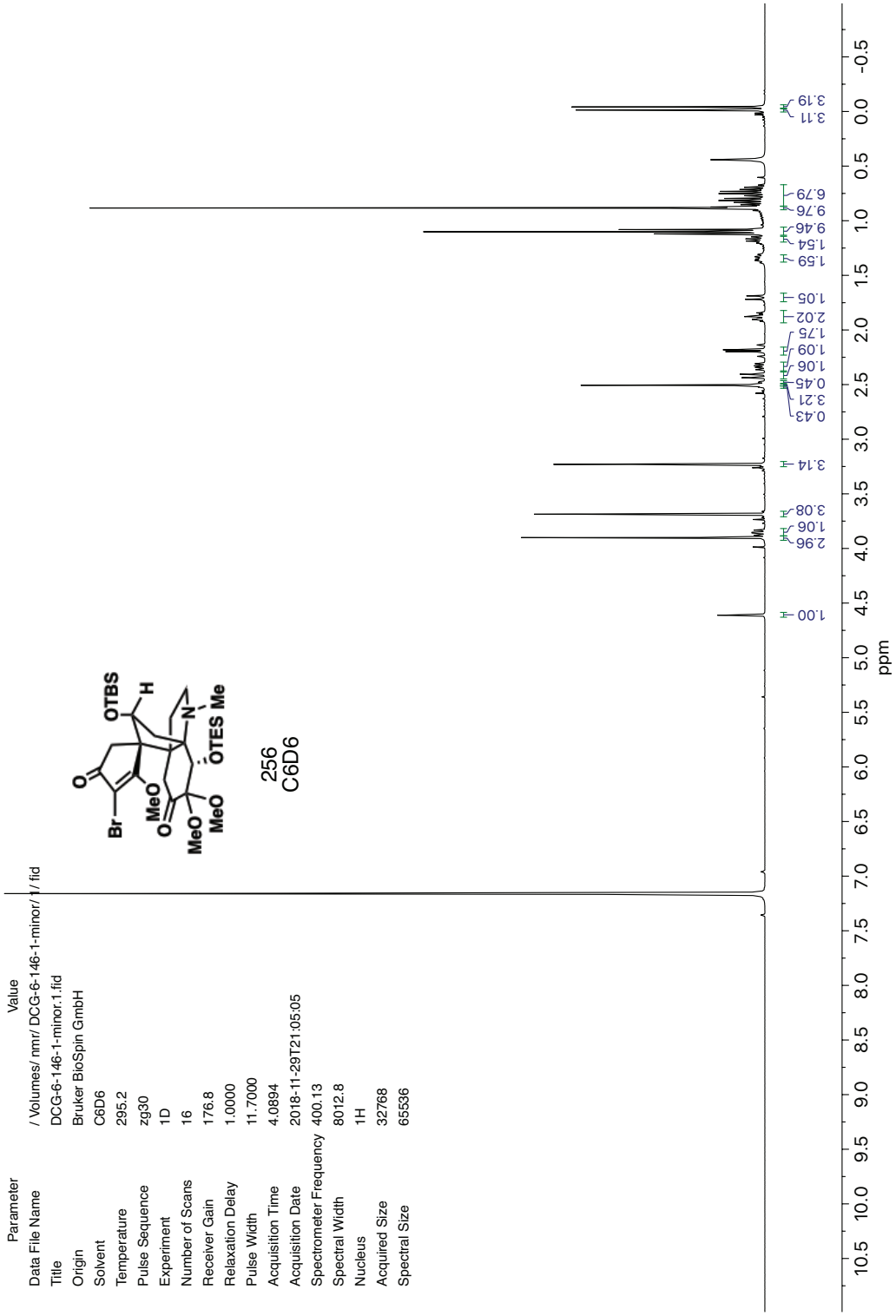

Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-5-91-1/ 9/ ser
Title
DCG-5-91-1.9.ser
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.0
Pulse Sequence
hsqcedetgpsisp2.4
Experiment
HSQC-EDITED
Number of Scans
2
Receiver Gain
197.4
Relaxation Delay
1.5000
Pulse Width
11.7000
Acquisition Time
0.2135
Acquisition Date
2017-09-22T05:22:44
Spectrometer Frequency
(400.13, 100.62)
Spectral Width
(4795.4, 16611.3)
Nucleus
(1H, 13C)
Acquired Size
(1024, 180)
Spectral Size
(1024, 1024)
ppm
ppm
OTBS
H
N
OTES Me
MeO
Br
O
MeO
MeO
255

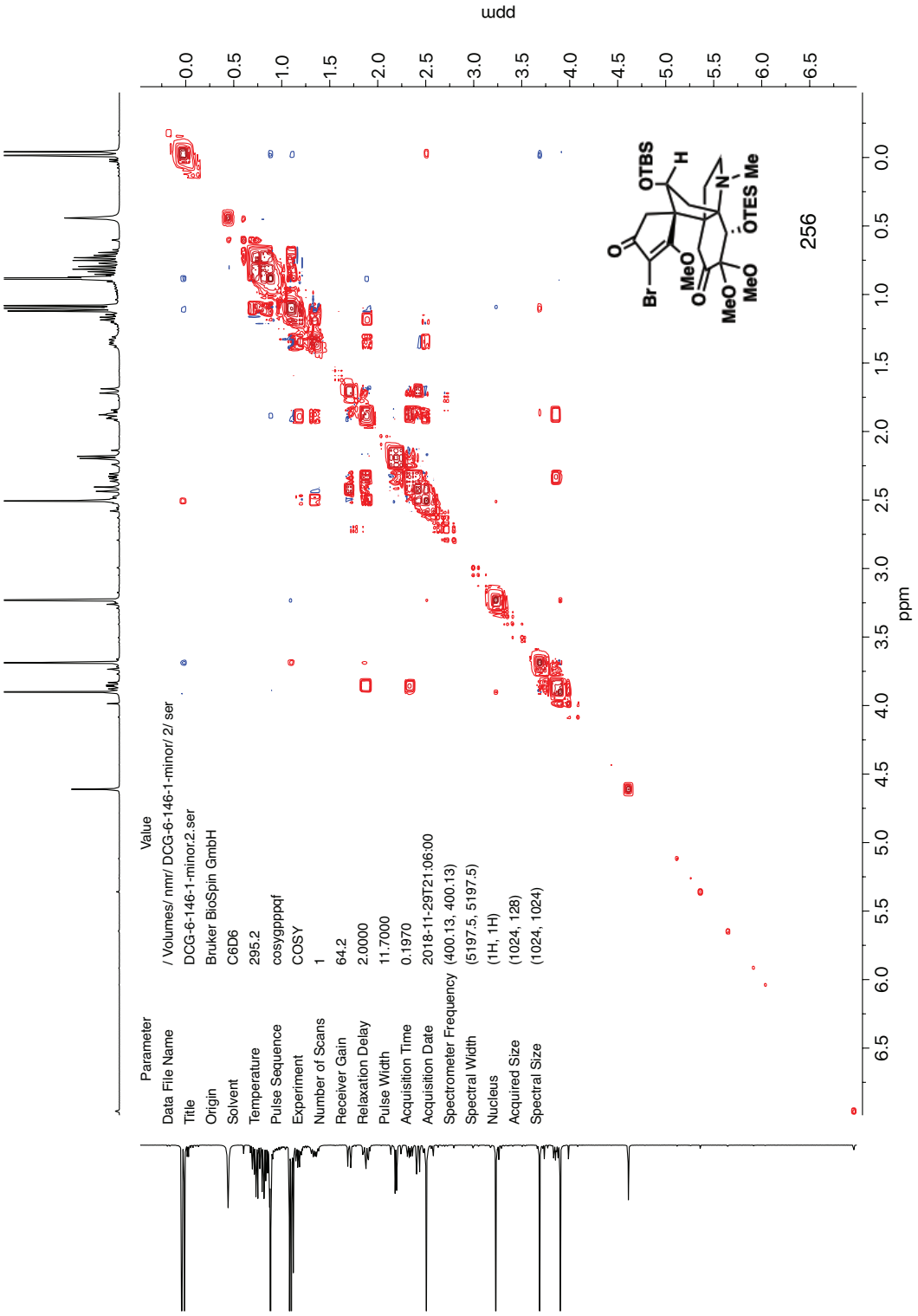

Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-5-91-1/ 10/ ser
Title
DCG-5-91-1.10.ser
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
hmbcetgpl3nd
Experiment
HMBC
Number of Scans
4
Receiver Gain
197.4
Relaxation Delay
2.0000
Pulse Width
11.7000
Acquisition Time
0.4260
Acquisition Date
2017-09-22T05:34:16
Spectrometer Frequency
(400.13, 100.62)
Spectral Width
(4807.7, 22321.4)
Nucleus
(1H, 13C)
Acquired Size
(2048, 256)
Spectral Size
(2048, 1024)
MeO
Br
OTBS
H
O
O
N
MeO
MeO
OTES
Me
255
ppm
ppm


Parameter
Value
Data File Name / Volumes/ nmr/ DCG-5-91-1/ 11/ fid
Title DCG-5-91-1.11.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 78.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-09-22T06:32:14
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
MeO
Br
O
OTBS
H
N
OTES Me
MeO
MeO
O
255
-5.2
-4.2
5.4
7.2
17.8
25.6
33.3
35.6
37.0
37.6
42.6
50.4
53.3
53.9
54.5
57.9
65.3
71.5
79.7
82.2
97.9
98.6
181.1
198.0
202.0
ppm


Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-91-1/ 12/ ser
Title DCG-5-91-1.12.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence noesygpphzs
Experiment NOESY
Number of Scans 4
Receiver Gain 78.7
Relaxation Delay 1.8000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2017-09-22T06:34:29
Spectrometer Frequency (400.13, 400.13)
Spectral Width (4000.0, 4000.0)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
nOe
MeO
Br
OTBS
H
H
O
O
MeO
MeO
N
OTES Me
255
ppm
ppm
ppm


Parameter
Value
Data File Name / Volumes/ nmr/ DCG-6-146-1-1-3/ 1/ fid
Title DCG-6-146-1-3.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 197.4
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-11-29T18:20:03
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
OTBS
H
N
OTES
Me
O
MeO
O
Br
MeO
MeO
256
CDCl3
0.98
2.87
1.08
3.27
3.10
1.04
2.03
3.19
1.00
2.11
0.94
1.00
1.97
9.97
9.88
6.74
3.38
3.28
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm


Parameter
Value
Data File Name / Volumes/ nmr/ DCG-6-146-1-minor/ 1/ fid
Title DCG-6-146-1-minor.1.fid
Origin Bruker BioSpin GmbH
Solvent C6D6
Temperature 295.2
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 176.8
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-11-29T21:05:05
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
OTBS
H
N
OTES
Me
O
Br
MeO
O
MeO
MeO
256
C6D6
1.00
2.96
1.06
3.08
3.14
0.43
3.21
0.45
1.06
1.09
1.75
2.02
1.05
1.59
1.54
9.46
9.76
6.79
3.11
3.19
ppm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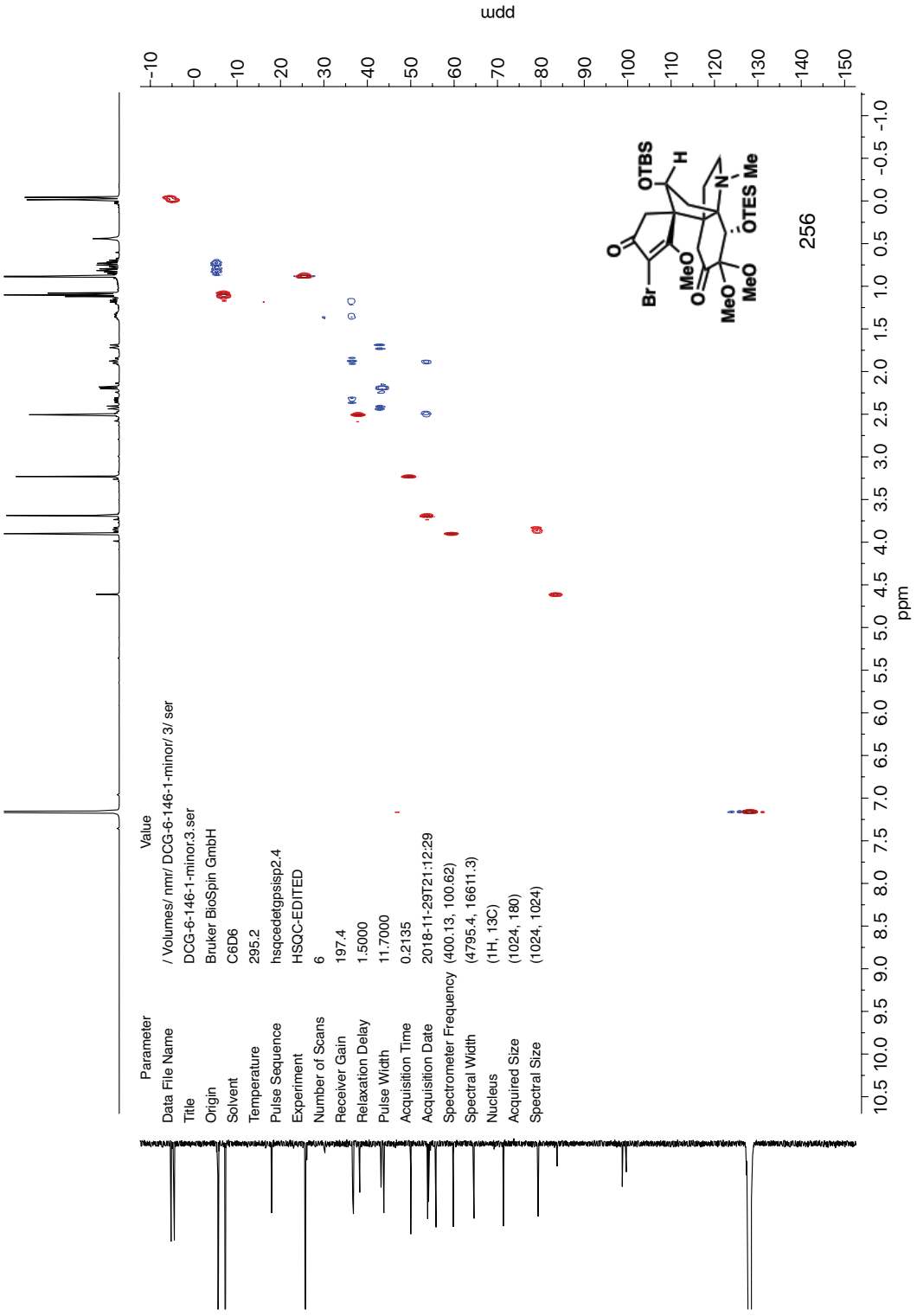
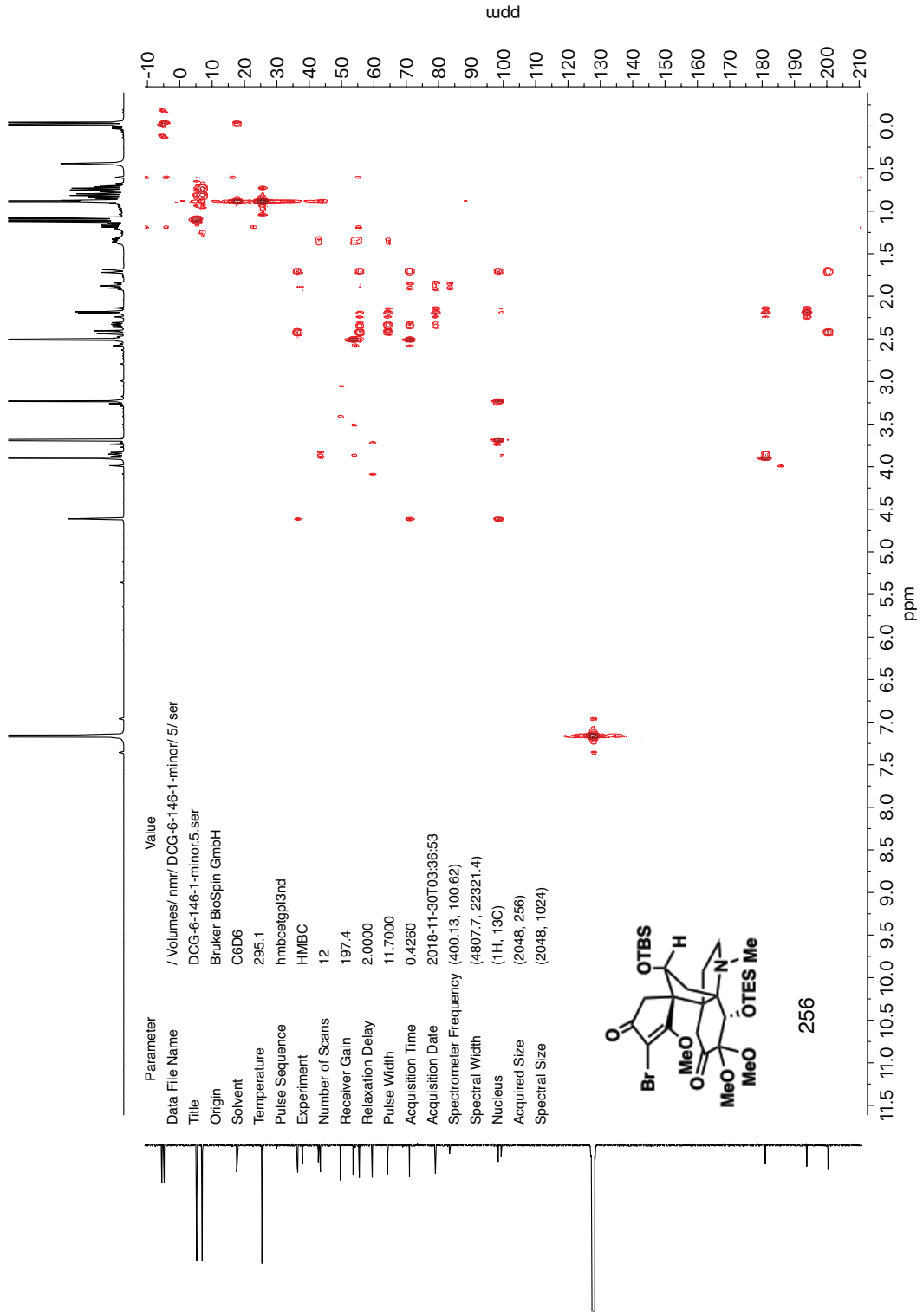
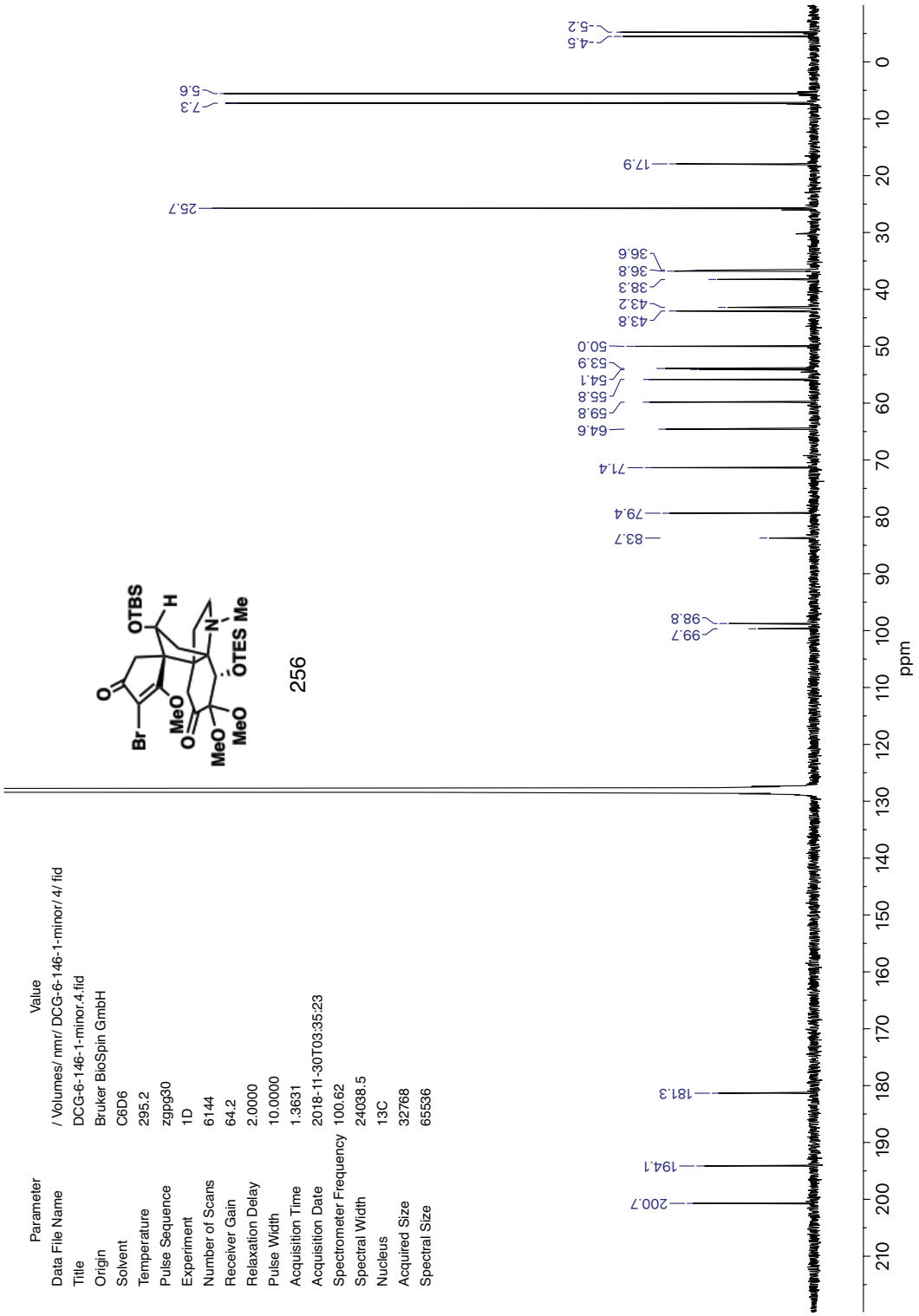
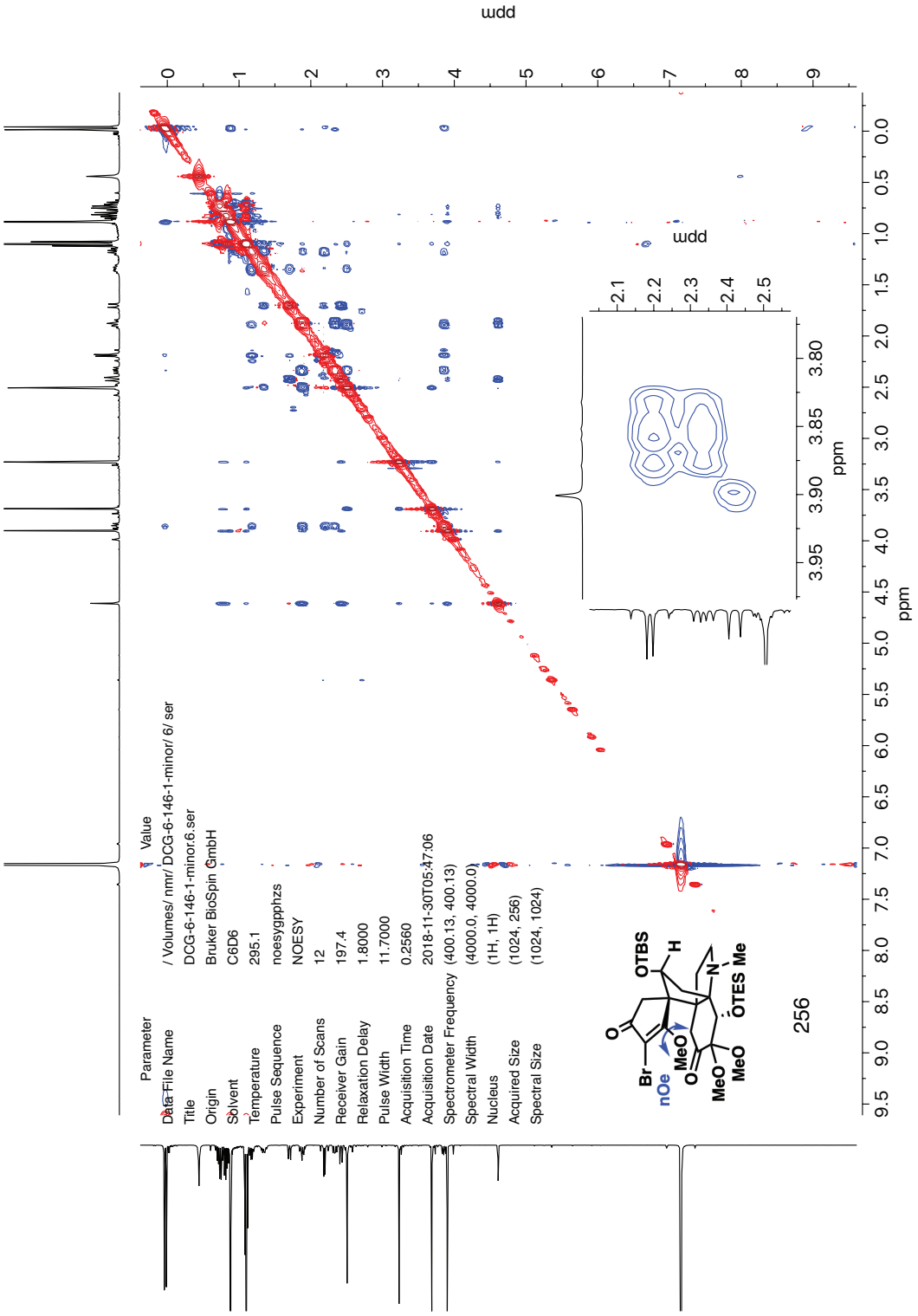
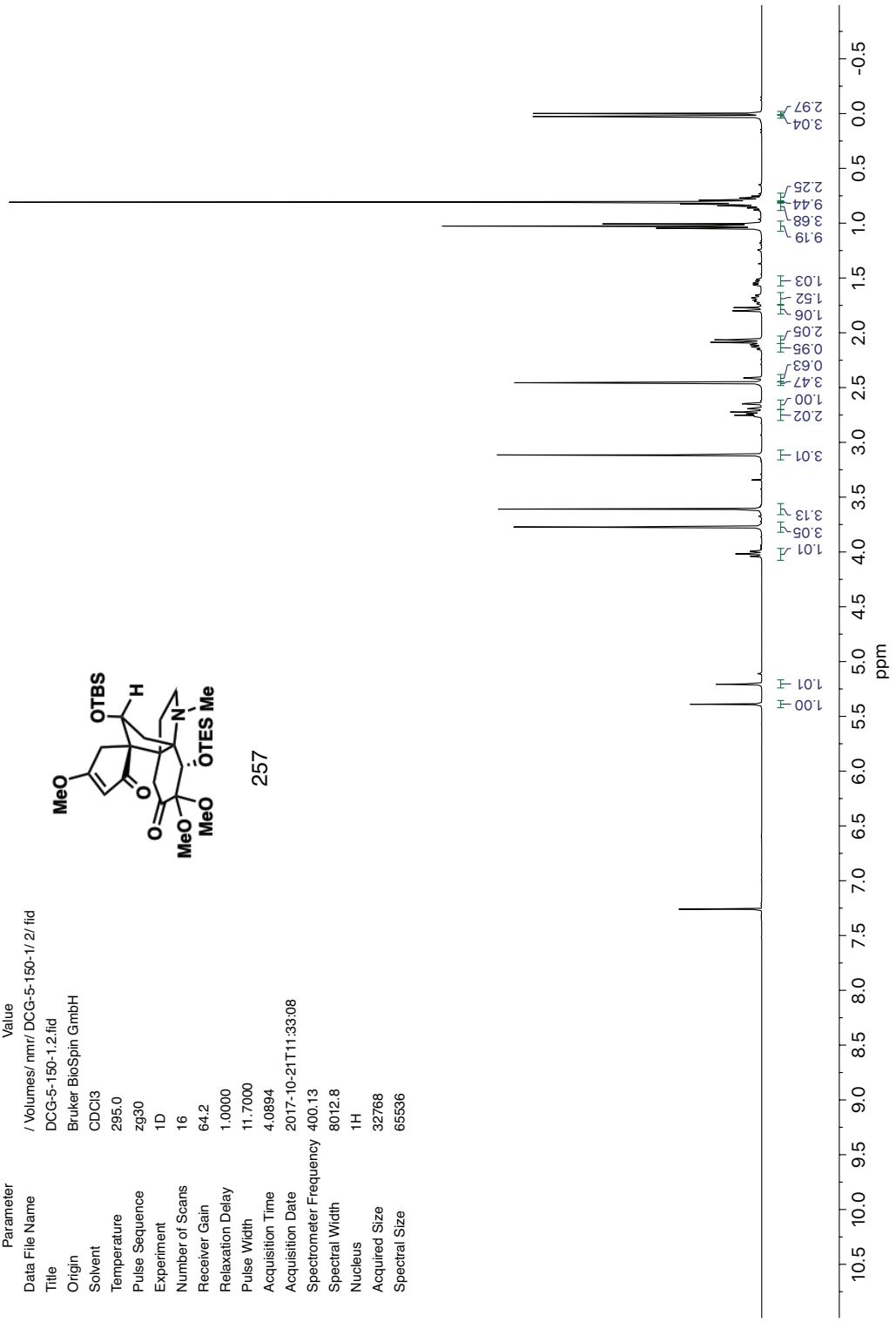
Data File Name / Volumes/ nmr/ DCG-6-146-1-minor/ 2/ ser
Title DCG-6-146-1-minor.2.ser
Origin Bruker BioSpin GmbH
Solvent C6D6
Temperature 295.2
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.1970
Acquisition Date 2018-11-29T21:06:00
Spectrometer Frequency (400.13, 400.13)
Spectral Width (5197.5, 5197.5)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)
ppm
OTBS
H
OTES
Me
O
Br
MeO
O
MeO
MeO
N
256

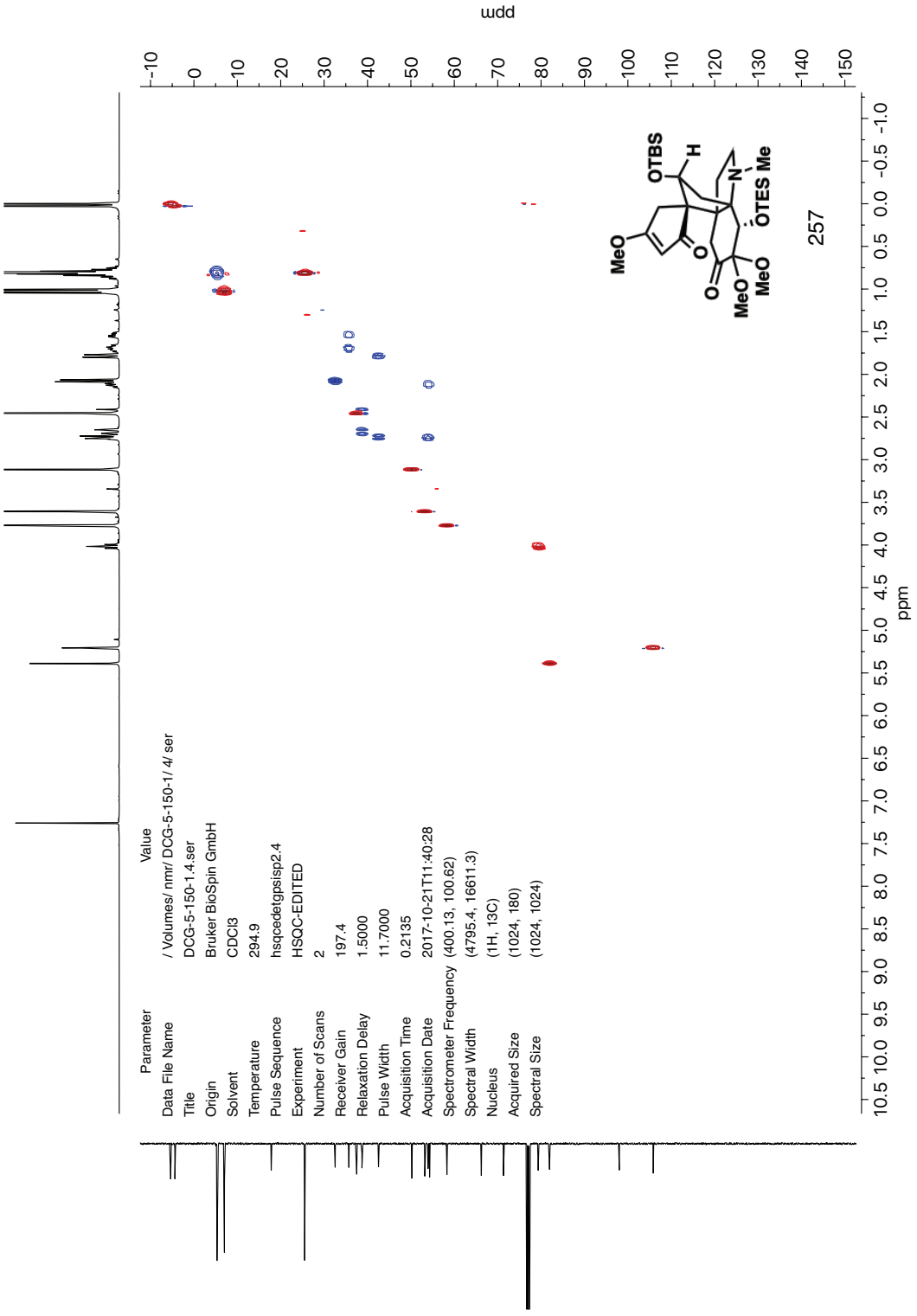

Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-146-1-minor/ 3/ ser
Title DCG-6-146-1-minor:3.ser
Origin Bruker BioSpin GmbH
Solvent C6D6
Temperature 295.2
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 6
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2018-11-29T21:12:29
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 180)
Spectral Size (1024, 1024)
ppm
ppm
OTBS
H
N
OTES
Me
O
Br
MeO
O
MeO
MeO
256

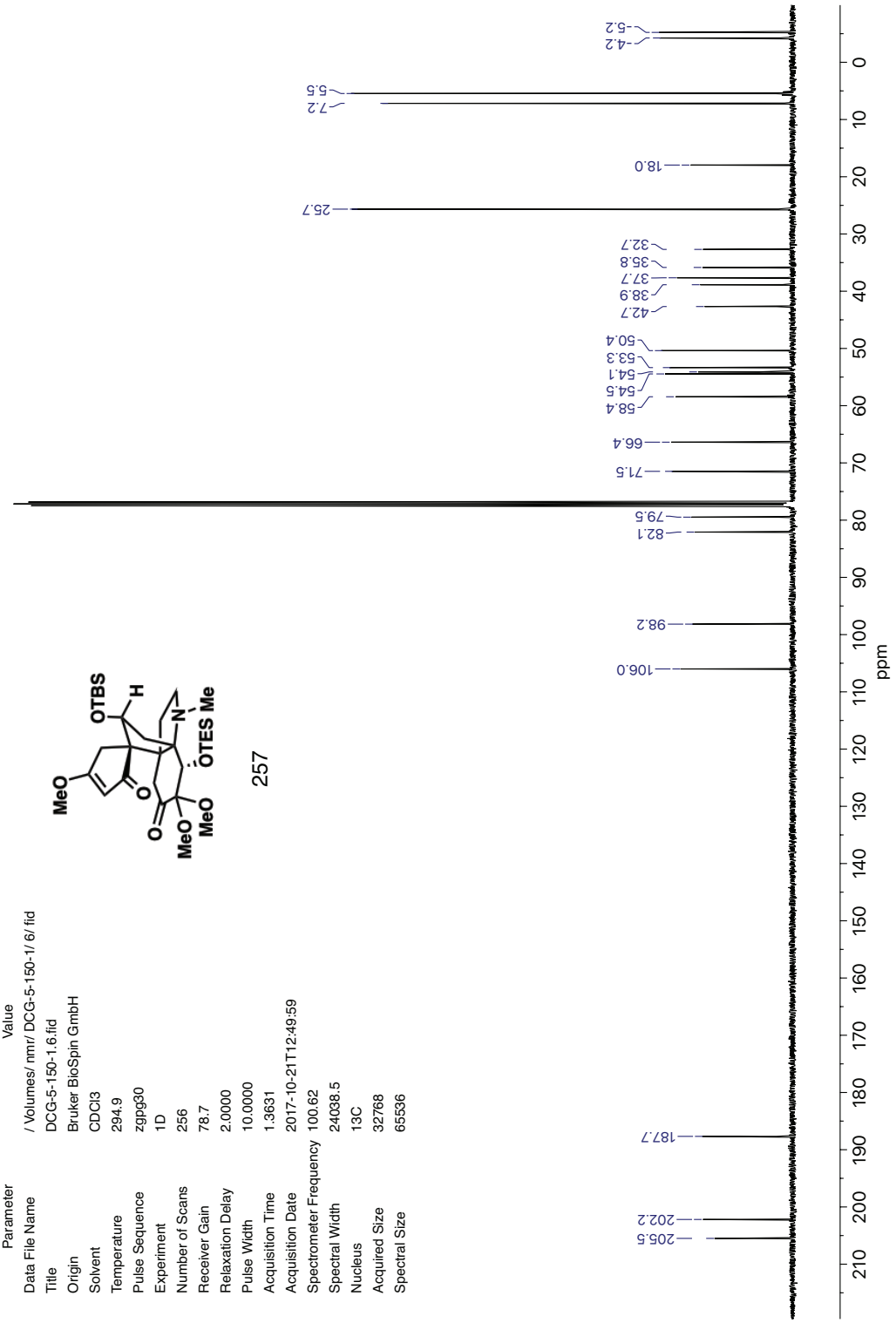

Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-146-1-minor/ 5/ ser
Title DCG-6-146-1-minor:5.ser
Origin Bruker BioSpin GmbH
Solvent C6D6
Temperature 295.1
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 12
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2018-11-30T03:36:53
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
OTBS
H
N
OTES
Me
MeO
MeO
MeO
O
O
Br
256
ppm
ppm

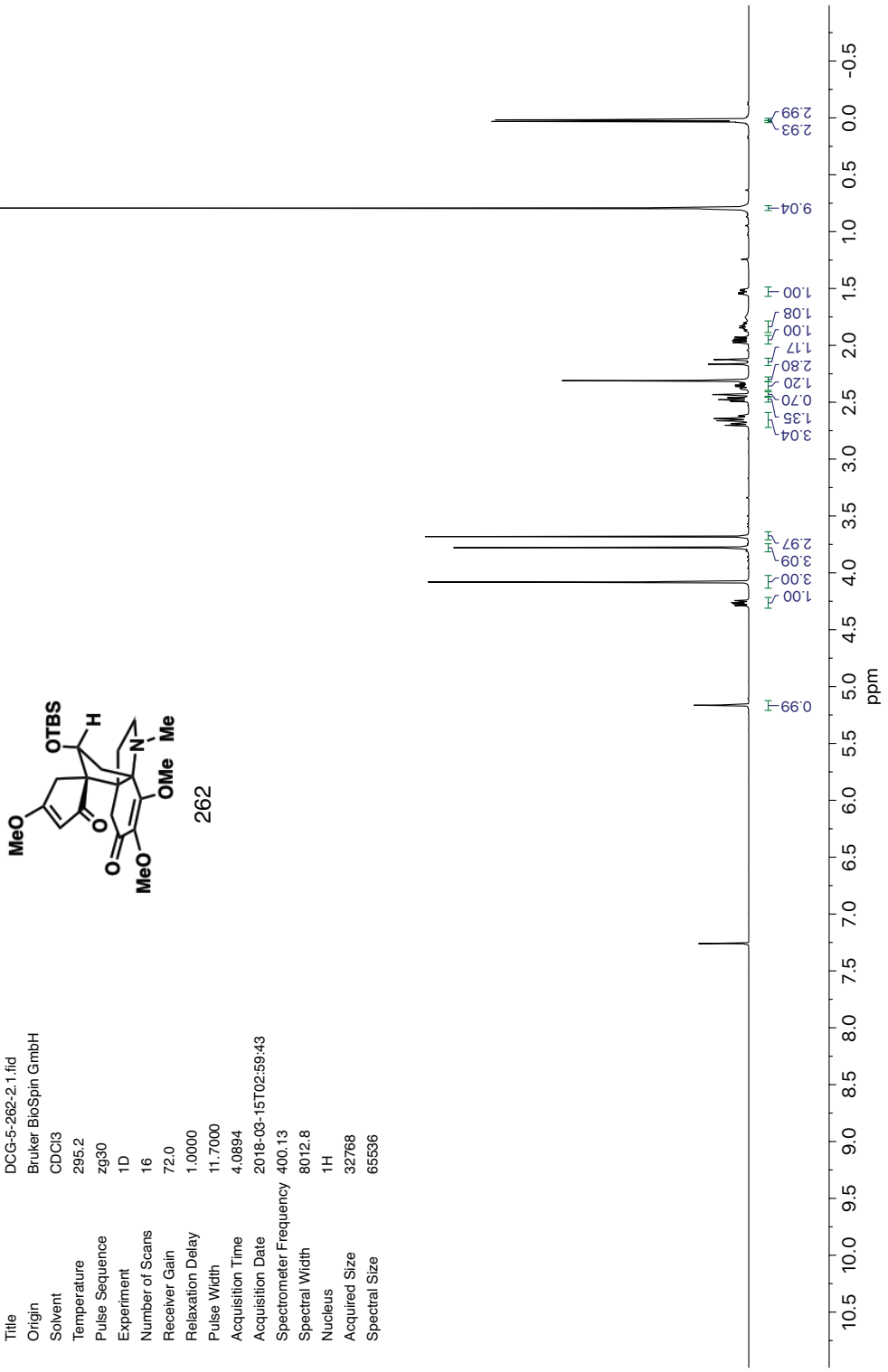

Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-146-1-minor/ 4/ fid
Title DCG-6-146-1-minor.4.fid
Origin Bruker BioSpin GmbH
Solvent C6D6
Temperature 295.2
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 6144
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-11-30T03:35:23
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OTBS
H
N
OTES
Me
O
MeO
O
Br
MeO
MeO
256
200.7
194.1
181.3
99.7
98.8
83.7
79.4
71.4
64.6
59.8
55.8
54.1
53.9
50.0
43.8
43.2
38.3
36.8
36.6
25.7
17.9
7.3
5.6
-4.5
-5.2
ppm

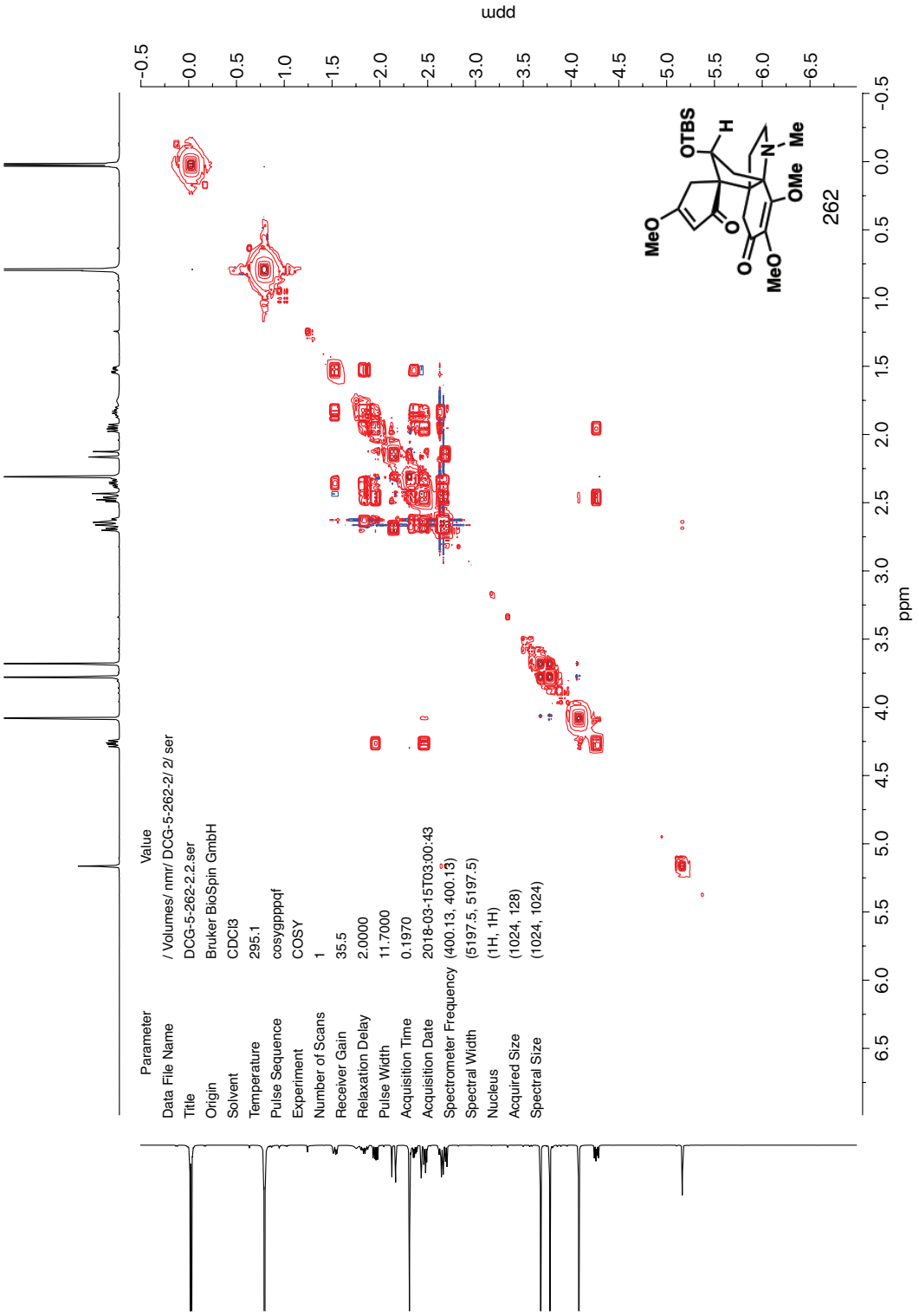

Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-146-1-minor/ 6/ ser
Title DCG-6-146-1-minor.6.ser
Origin Bruker BioSpin GmbH
Solvent C6D6
Temperature 295.1
Pulse Sequence noesygpphzs
Experiment NOESY
Number of Scans 12
Receiver Gain 197.4
Relaxation Delay 1.8000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2018-11-30T05:47:06
Spectrometer Frequency (400.13, 400.13)
Spectral Width (4000.0, 4000.0)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
OTBS
H
Br
nOe
O
MeO
O
N
MeO
MeO
OTES Me
256
ppm
ppm

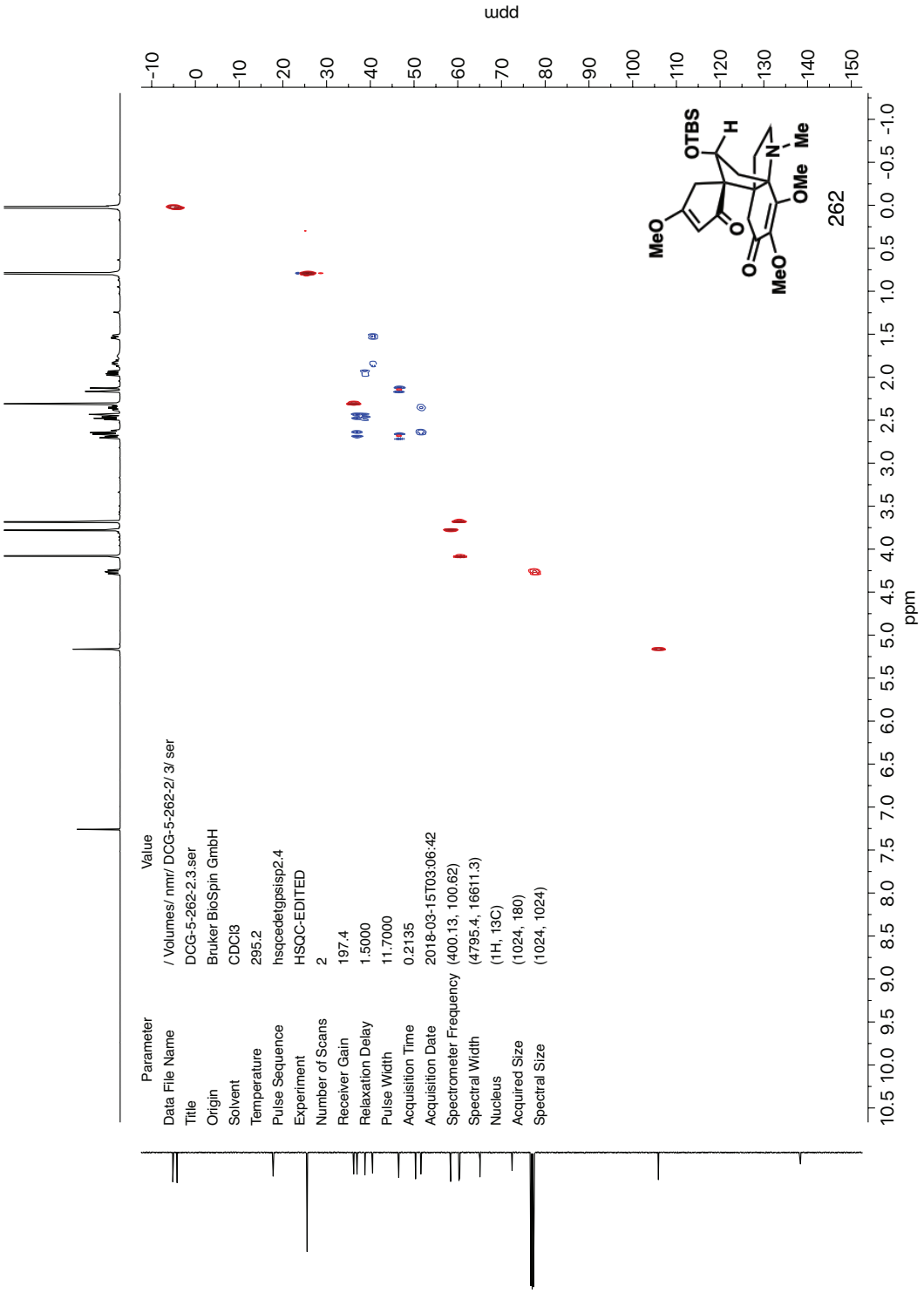

Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-5-150-1/ 2/ fid
Title
DCG-5-150-1.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.0
Pulse Sequence
zg30
Experiment
1D
Number of Scans
16
Receiver Gain
64.2
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2017-10-21T11:33:08
Spectrometer Frequency
400.13
Spectral Width
8012.8
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
MeO
OTBS
H
N
OTES Me
O
O
MeO
MeO
257
1.00
1.01
3.01
1.01
3.05
3.13
3.01
2.02
1.00
3.47
0.63
0.95
2.05
1.06
1.52
1.03
9.19
3.68
9.44
2.25
3.04
2.97
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
ppm

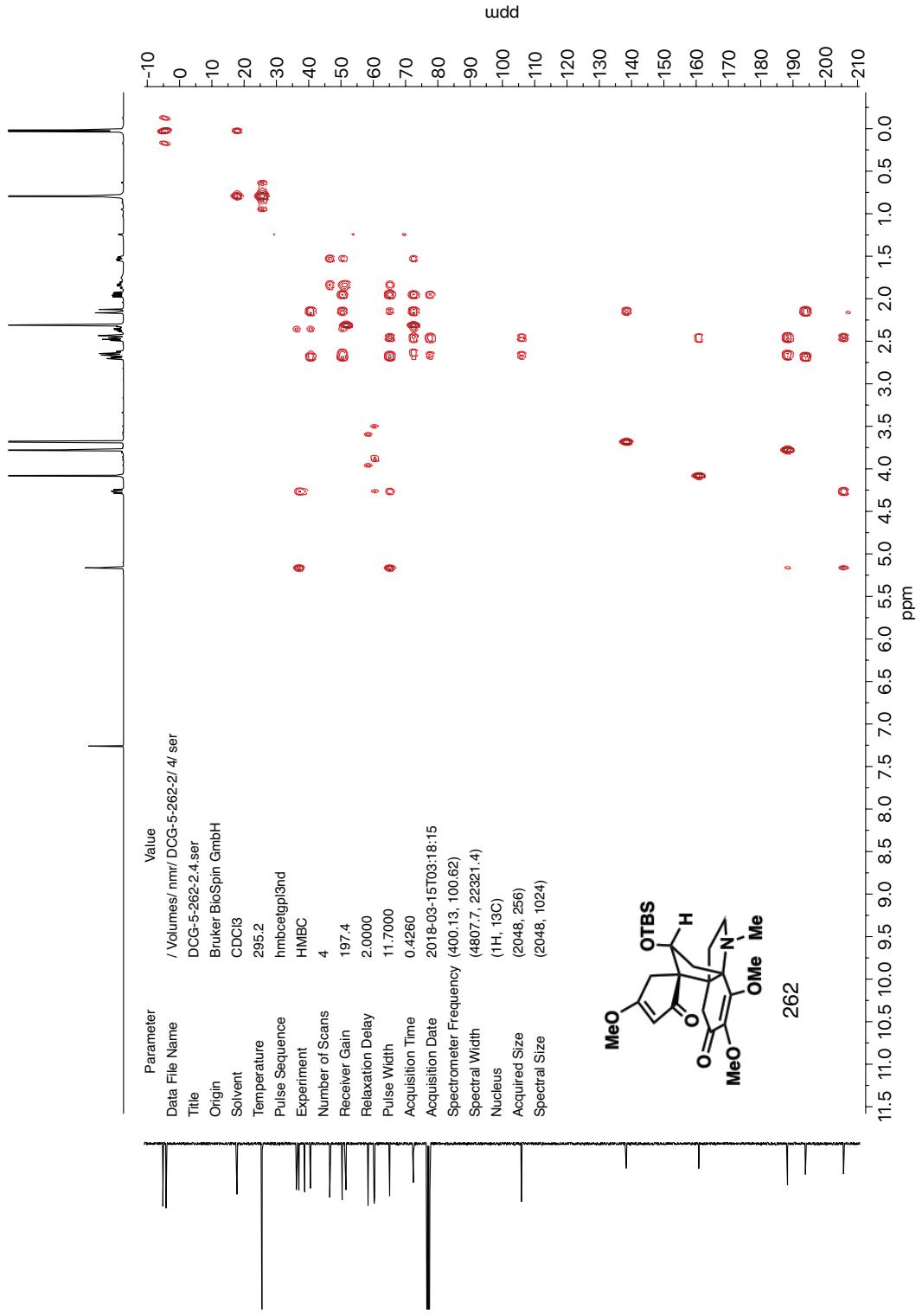

Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-5-150-1/ 4/ ser
Title
DCG-5-150-1.4.ser
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
hsqcedetgpsisp2.4
Experiment
HSQC-EDITED
Number of Scans
2
Receiver Gain
197.4
Relaxation Delay
1.5000
Pulse Width
11.7000
Acquisition Time
0.2135
Acquisition Date
2017-10-21T11:40:28
Spectrometer Frequency
(400.13, 100.62)
Spectral Width
(4795.4, 16611.3)
Nucleus
(1H, 13C)
Acquired Size
(1024, 180)
Spectral Size
(1024, 1024)
ppm
ppm
MeO
OTBS
H
N
OTES Me
MeO
MeO
O
O
257

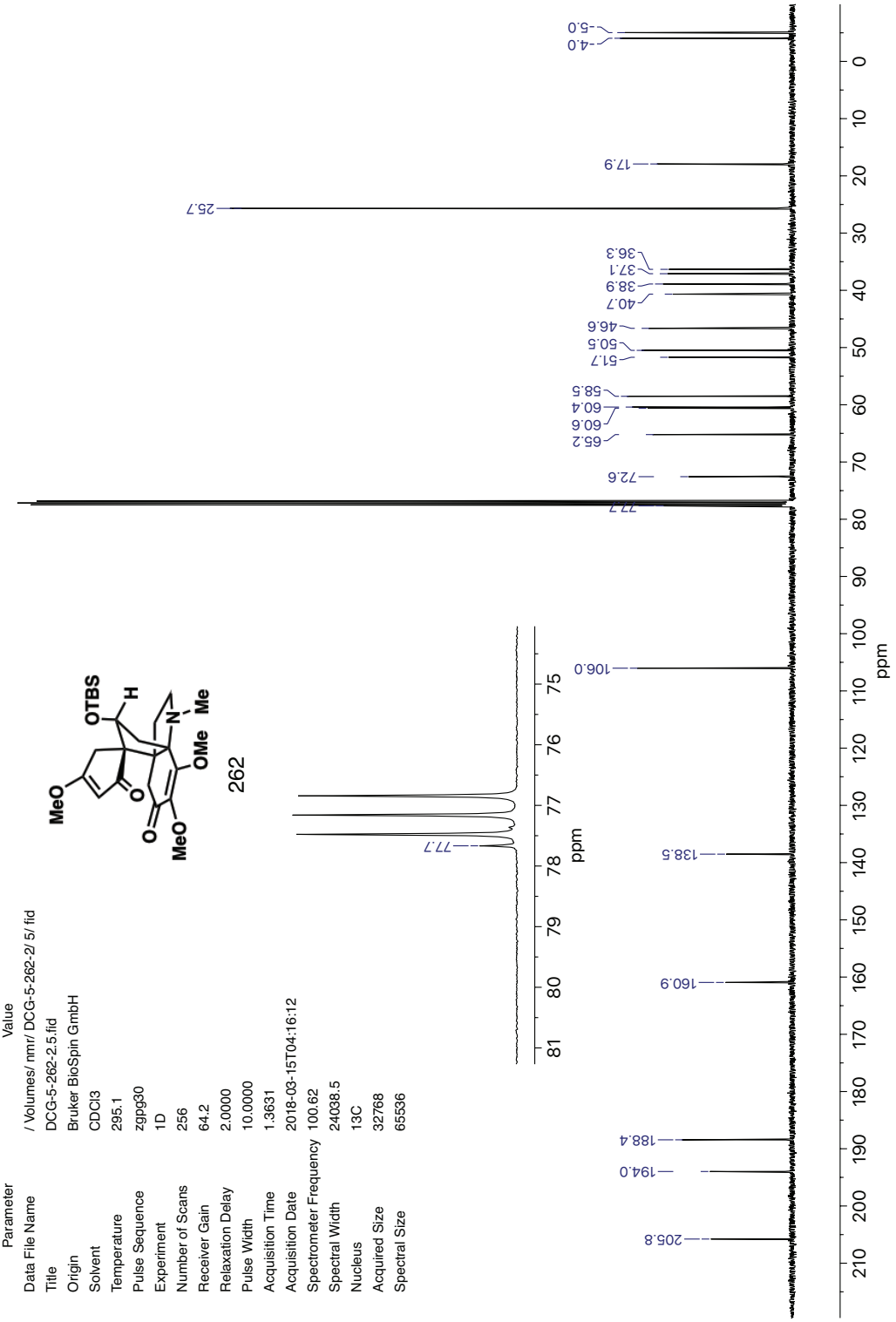

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-150-1/ 6/ fid
Title DCG-5-150-1.6.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 78.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-10-21T12:49:59
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
MeO
OTBS
H
N
OTES Me
O
O
MeO
MeO
257
-5.2
-4.2
5.5
7.2
18.0
25.7
32.7
35.8
37.7
38.9
42.7
50.4
53.3
54.1
54.5
58.4
66.4
71.5
79.5
82.1
98.2
106.0
187.7
202.2
205.5
ppm

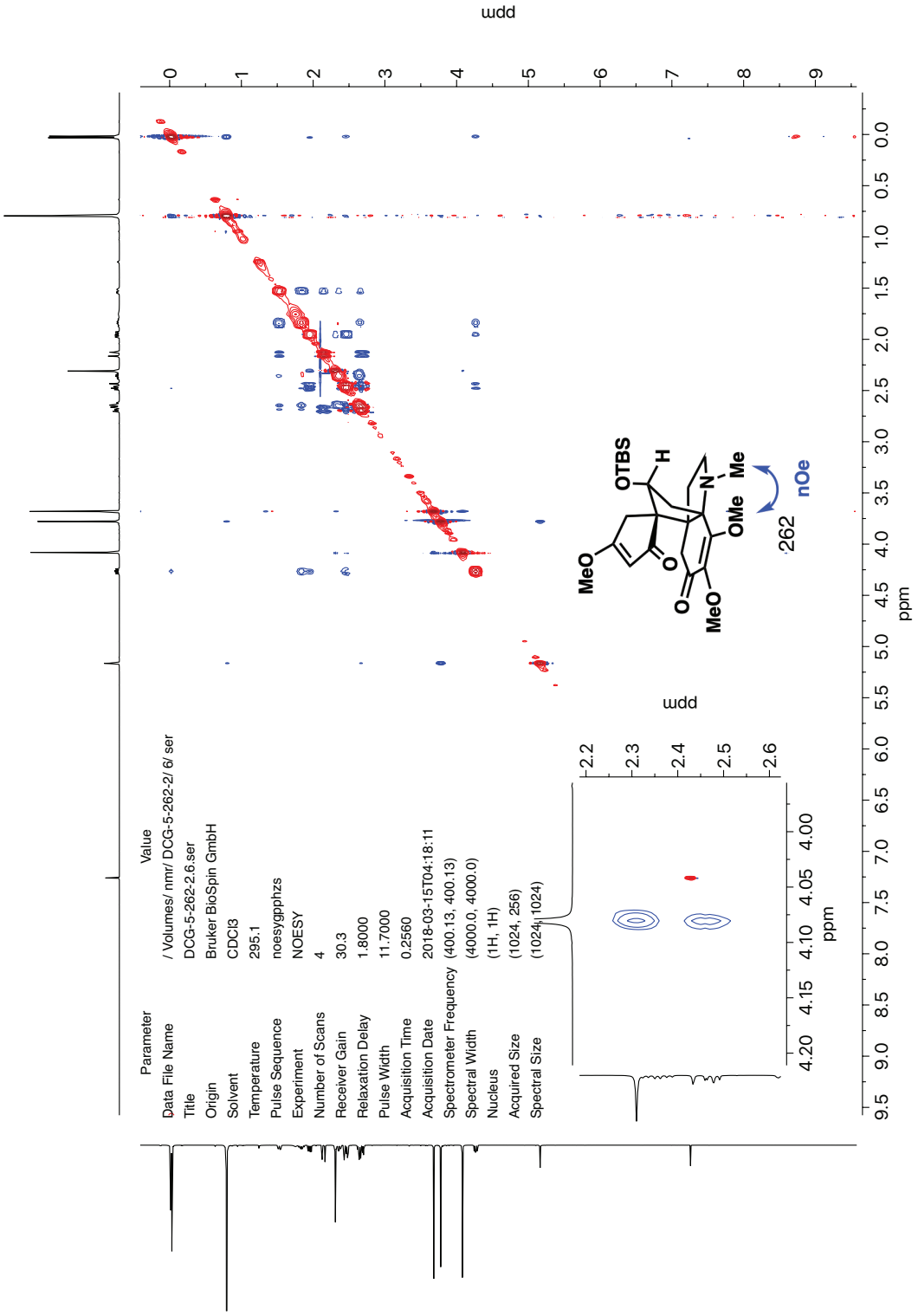

Parameter
Value
Data File Name / Volumes/ nmr/ DCG-5-262-2/ 1/ fid
Title DCG-5-262-2.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 72.0
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-03-15T02:59:43
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
OTBS
H
N
Me
OMe
MeO
MeO
O
O
262
0.99
1.00
3.00
3.09
2.97
9.04
1.00
3.04
1.35
0.70
1.20
2.80
1.17
1.00
1.08
2.93
2.99
ppm

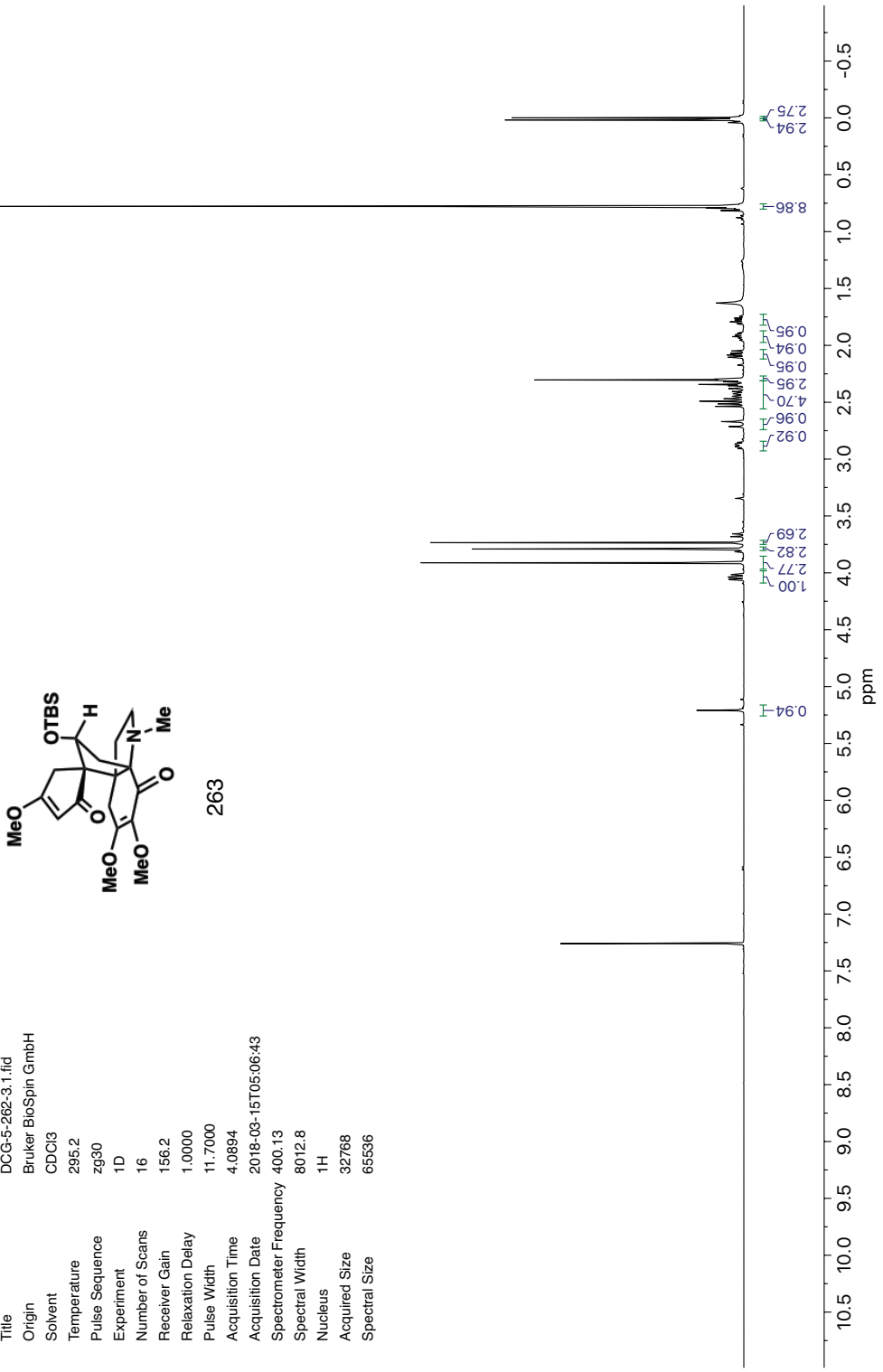

ppm
-0.5
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
OTBS
H
N
Me
OMe
MeO
O
MeO
262
Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-262-2/ 2/ ser
Title DCG-5-262-2.2.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 35.5
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.1970
Acquisition Date 2018-03-15T03:00:43
Spectrometer Frequency (400.13, 400.13)
Spectral Width (5197.5, 5197.5)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)

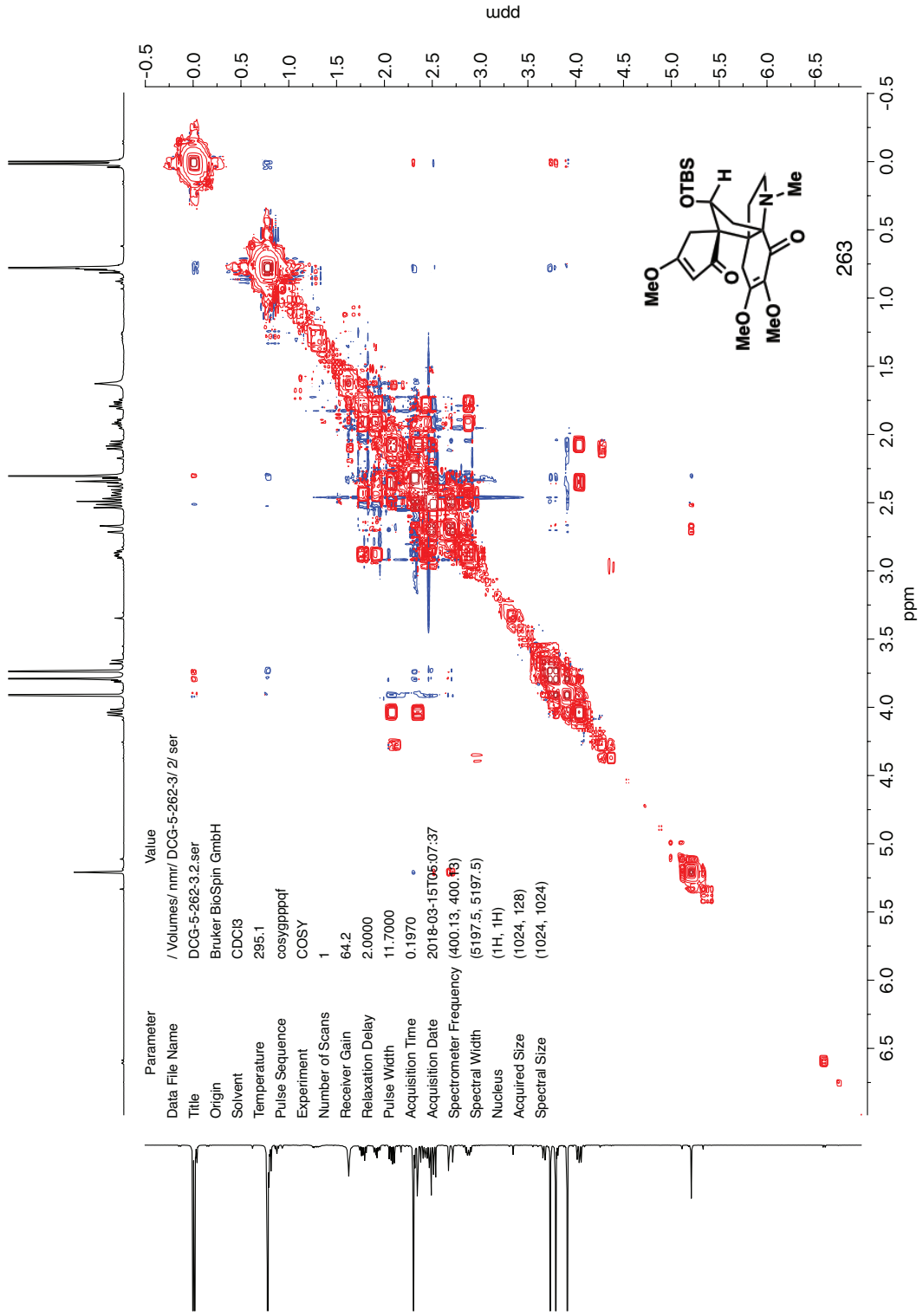

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-262-2/ 3/ ser
Title DCG-5-262-2.3.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2018-03-15T03:06:42
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 180)
Spectral Size (1024, 1024)
ppm
ppm
OTBS
H
N
Me
OMe
MeO
O
O
MeO
262

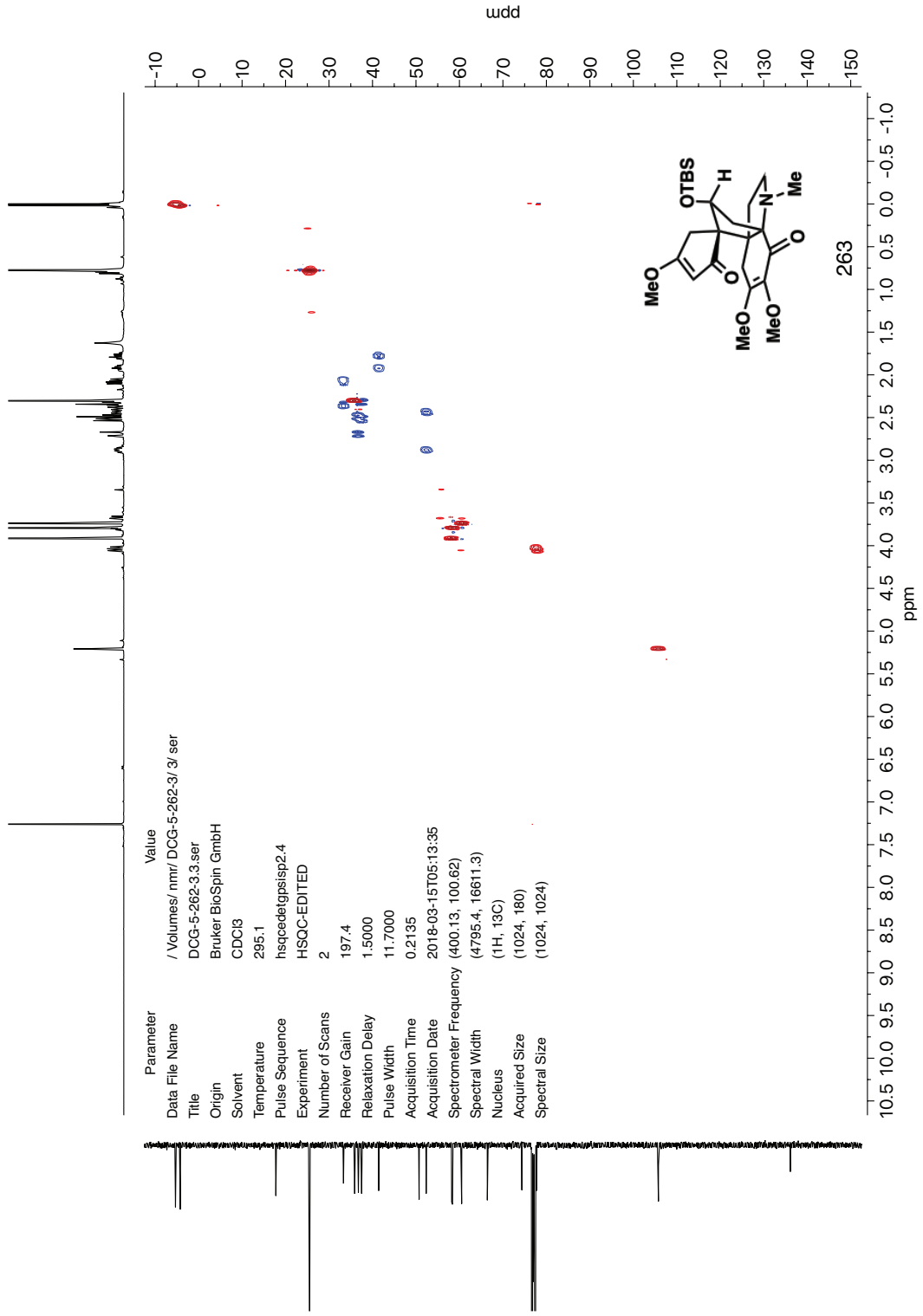

Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-5-262-2/ 4/ ser
Title
DCG-5-262-2.4.ser
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
hmbcetgpl3nd
Experiment
HMBC
Number of Scans
4
Receiver Gain
197.4
Relaxation Delay
2.0000
Pulse Width
11.7000
Acquisition Time
0.4260
Acquisition Date
2018-03-15T03:18:15
Spectrometer Frequency
(400.13, 100.62)
Spectral Width
(4807.7, 22321.4)
Nucleus
(1H, 13C)
Acquired Size
(2048, 256)
Spectral Size
(2048, 1024)
MeO
OTBS
H
O
O
MeO
N
OMe
Me
262
ppm
ppm

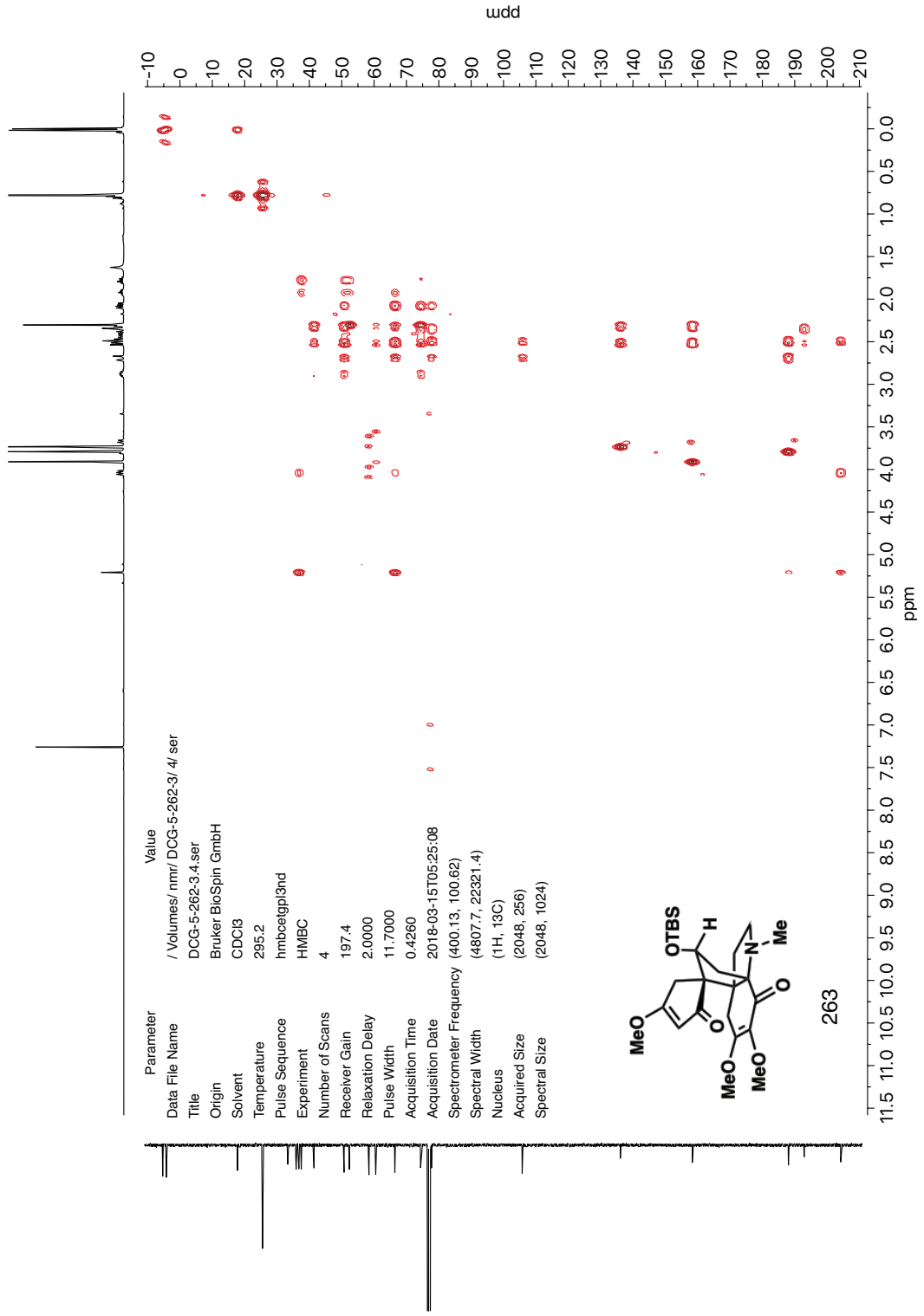

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-262-2/ 5/ fid
Title DCG-5-262-2.5.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-03-15T04:16:12
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OTBS
H
N
Me
OMe
MeO
O
O
MeO
262
ppm
ppm

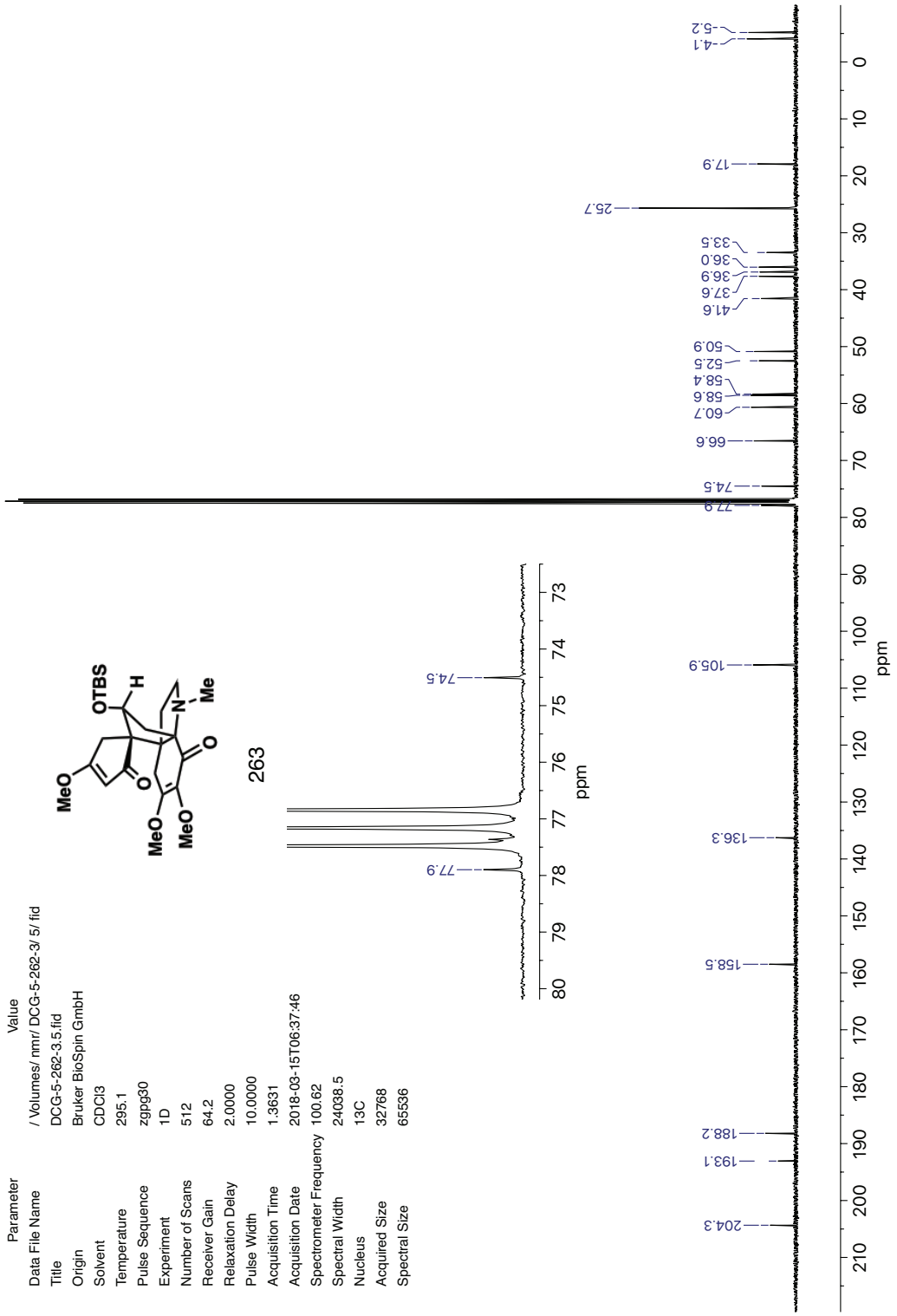

Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-5-262-2/ 6/ ser
Title
DCG-5-262-2.6.ser
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.1
Pulse Sequence
noesygpphzs
Experiment
NOESY
Number of Scans
4
Receiver Gain
30.3
Relaxation Delay
1.8000
Pulse Width
11.7000
Acquisition Time
0.2560
Acquisition Date
2018-03-15T04:18:11
Spectrometer Frequency
(400.13, 400.13)
Spectral Width
(4000.0, 4000.0)
Nucleus
(1H, 1H)
Acquired Size
(1024, 256)
Spectral Size
(1024, 1024)
OTBS
H
N
Me
OMe
MeO
O
O
MeO
nOe
262
ppm
ppm
ppm

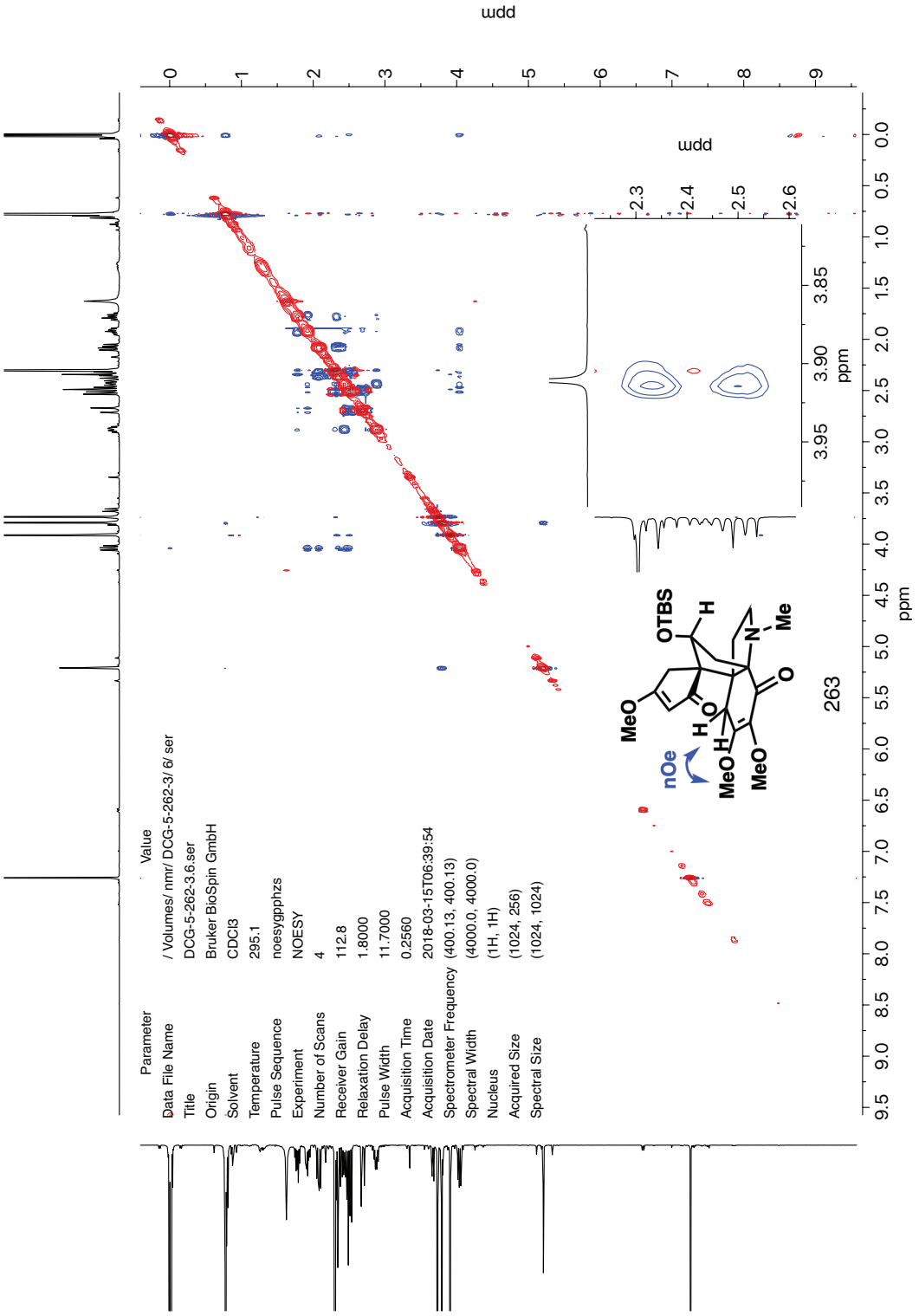

Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-5-262-3/ 1/ fid
Title
DCG-5-262-3.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
zg30
Experiment
1D
Number of Scans
16
Receiver Gain
156.2
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-03-15T05:06:43
Spectrometer Frequency
400.13
Spectral Width
8012.8
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
OTBS
H
N
Me
O
MeO
MeO
MeO
O
263
0.94
1.00
2.77
2.82
2.69
0.92
0.96
4.70
2.95
0.95
0.94
0.95
8.86
2.94
2.75
ppm

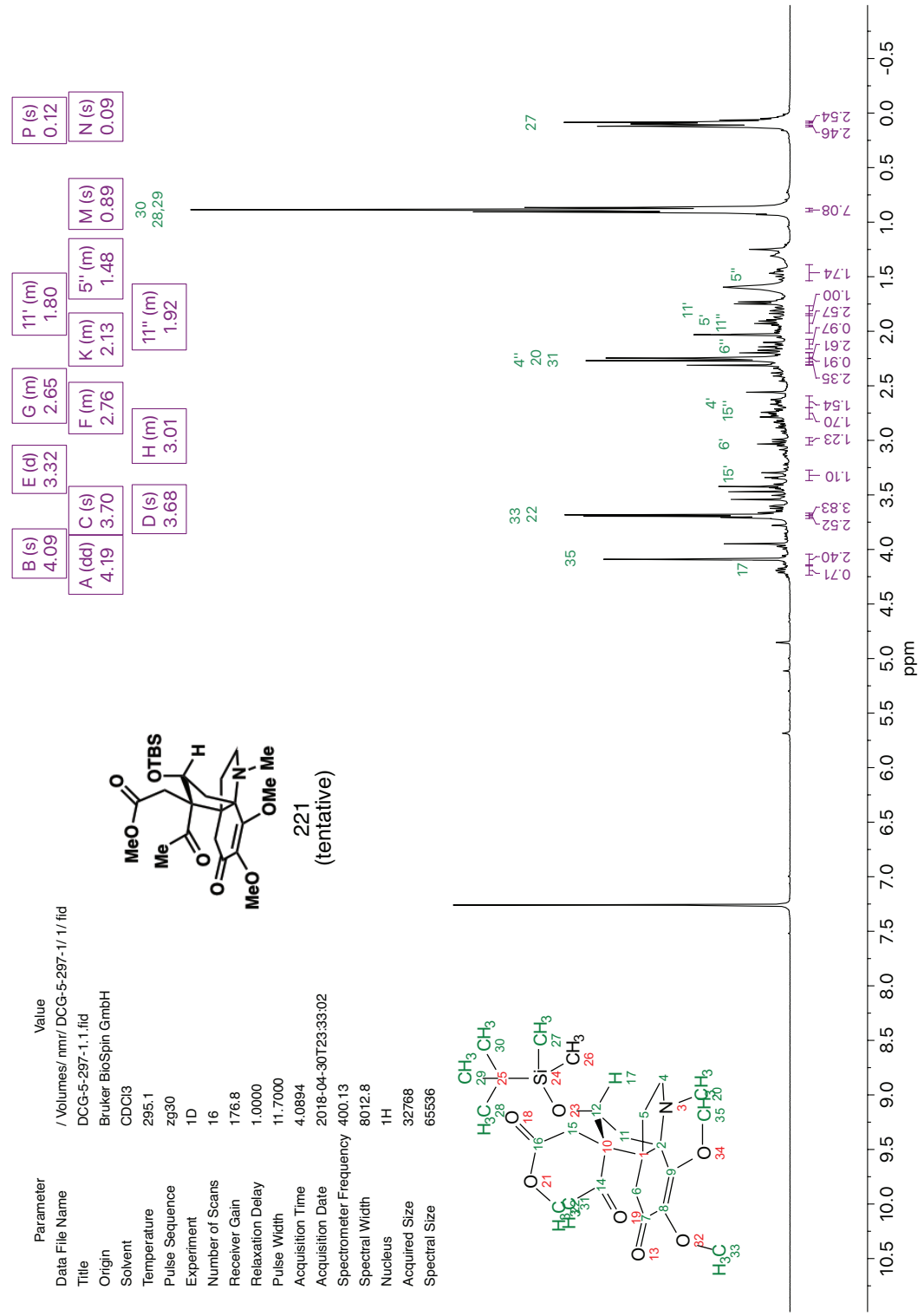

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-262-3/ 2/ ser
Title DCG-5-262-3.2.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.1970
Acquisition Date 2018-03-15T05:07:37
Spectrometer Frequency (400.13, 400.13)
Spectral Width (5197.5, 5197.5)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)
OTBS
H
N
Me
O
MeO
MeO
MeO
263
ppm
ppm

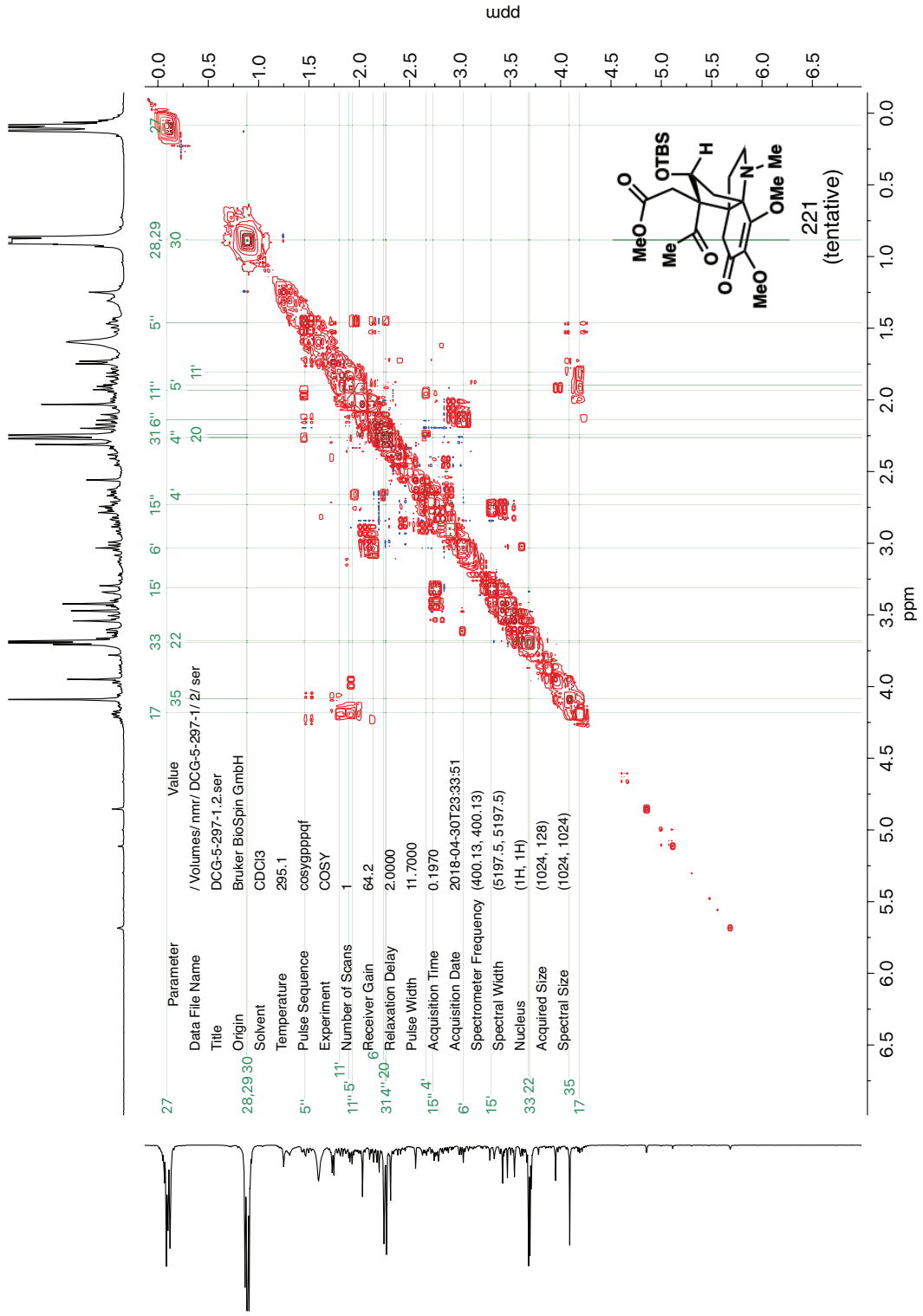

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-262-3/ 3/ ser
Title DCG-5-262-3.3.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2018-03-15T05:13:35
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 180)
Spectral Size (1024, 1024)
ppm
ppm
OTBS
H
N
Me
O
MeO
MeO
MeO
263

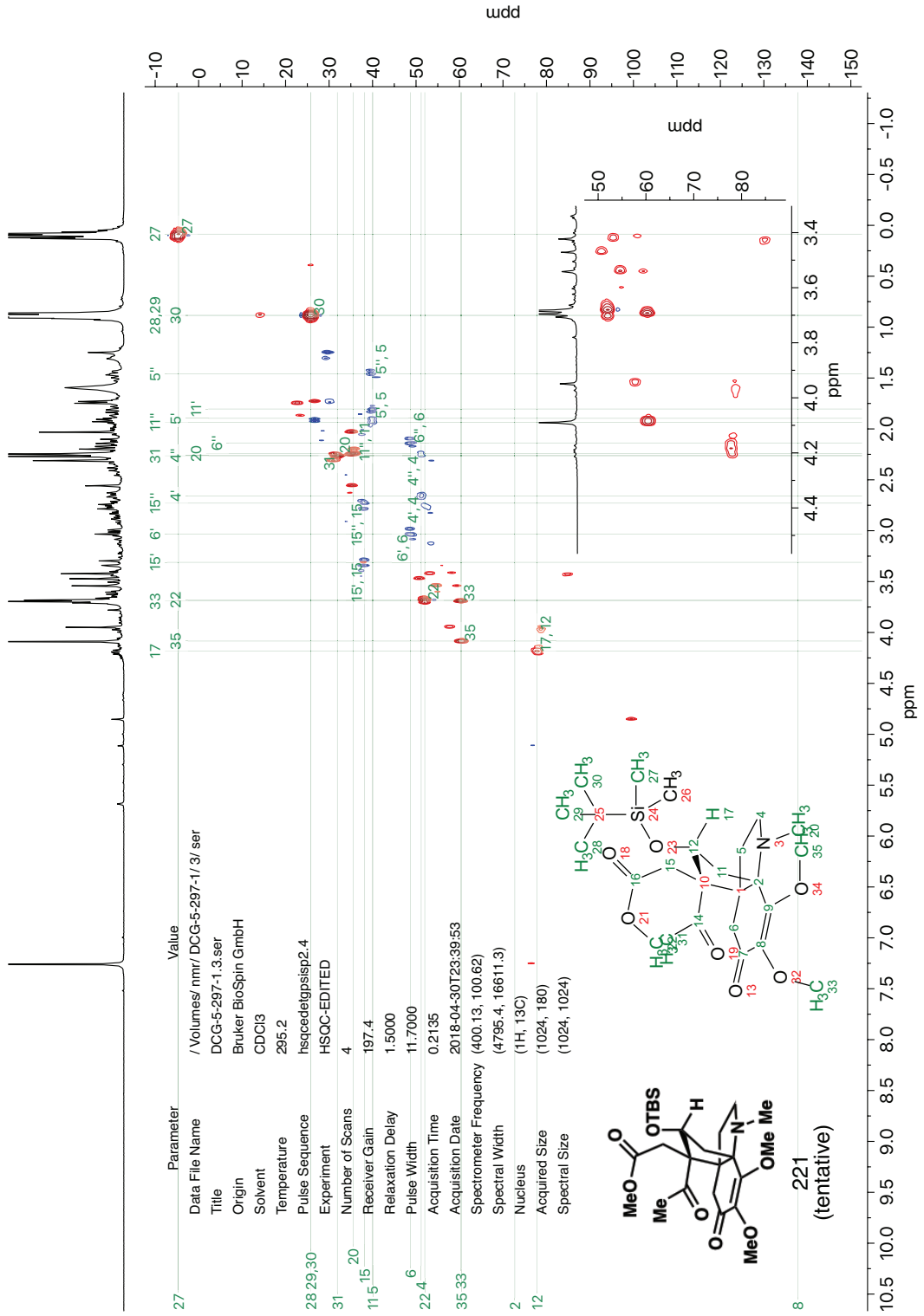

Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-5-262-3/ 4/ ser
Title
DCG-5-262-3.4.ser
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
hmbcetgpl3nd
Experiment
HMBC
Number of Scans
4
Receiver Gain
197.4
Relaxation Delay
2.0000
Pulse Width
11.7000
Acquisition Time
0.4260
Acquisition Date
2018-03-15T05:25:08
Spectrometer Frequency
(400.13, 100.62)
Spectral Width
(4807.7, 22321.4)
Nucleus
(1H, 13C)
Acquired Size
(2048, 256)
Spectral Size
(2048, 1024)
OTBS
H
MeO
O
N
Me
MeO
MeO
O
263
ppm
ppm

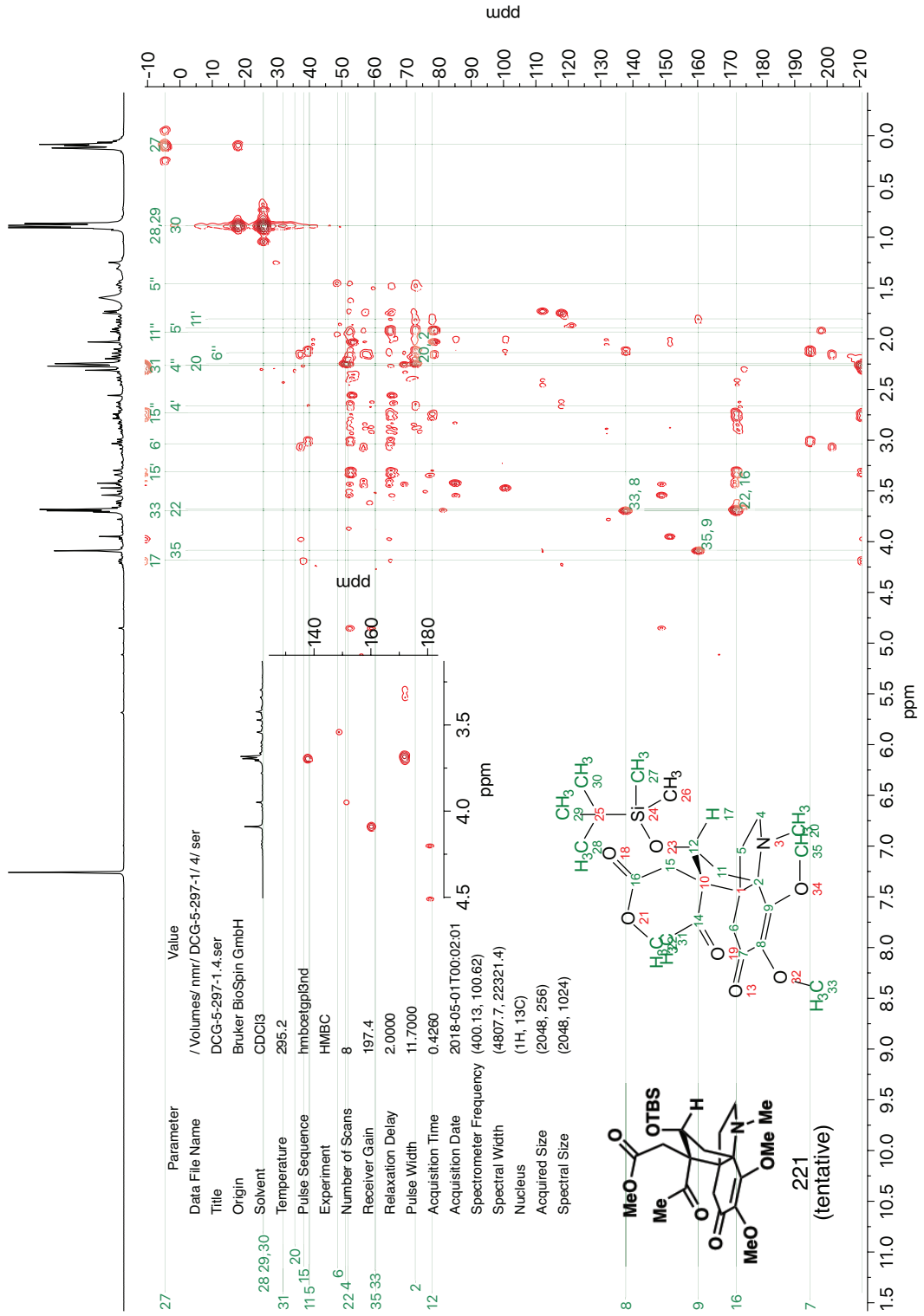

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-262-3/ 5/ fid
Title DCG-5-262-3.5.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 512
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-03-15T06:37:46
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OTBS
H
N
Me
O
O
MeO
MeO
MeO
263
74.5
77.9
ppm
204.3
193.1
188.2
158.5
136.3
105.9
77.9
74.5
66.6
60.7
58.6
58.4
52.5
50.9
41.6
37.6
36.9
36.0
33.5
25.7
17.9
-4.1
-5.2
ppm

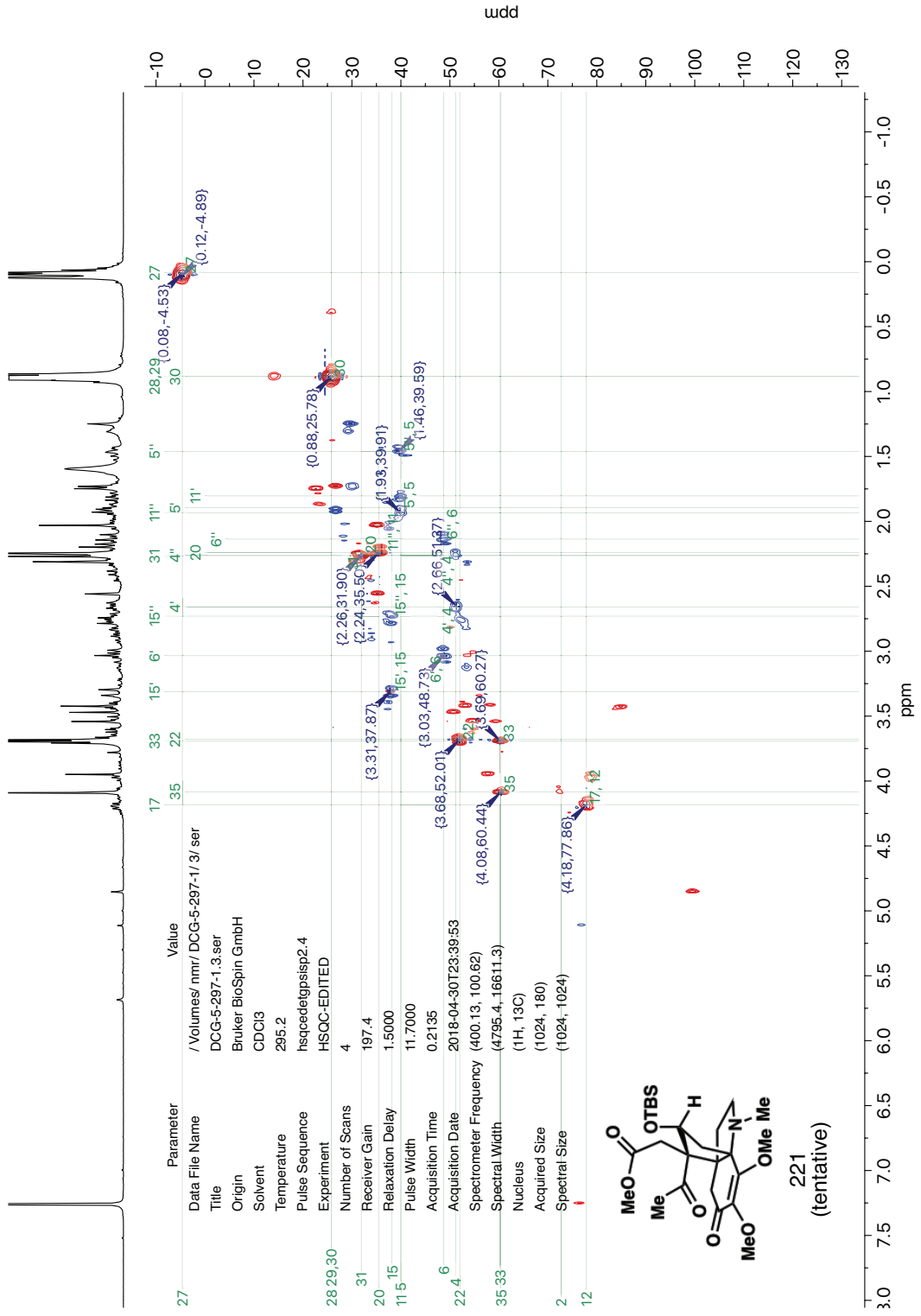

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-262-3/ 6/ ser
Title DCG-5-262-3.6.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence noesygpphzs
Experiment NOESY
Number of Scans 4
Receiver Gain 112.8
Relaxation Delay 1.8000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2018-03-15T06:39:54
Spectrometer Frequency (400.13, 400.13)
Spectral Width (4000.0, 4000.0)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
ppm
nOe
OTBS
MeO
MeO
MeO
Me
263

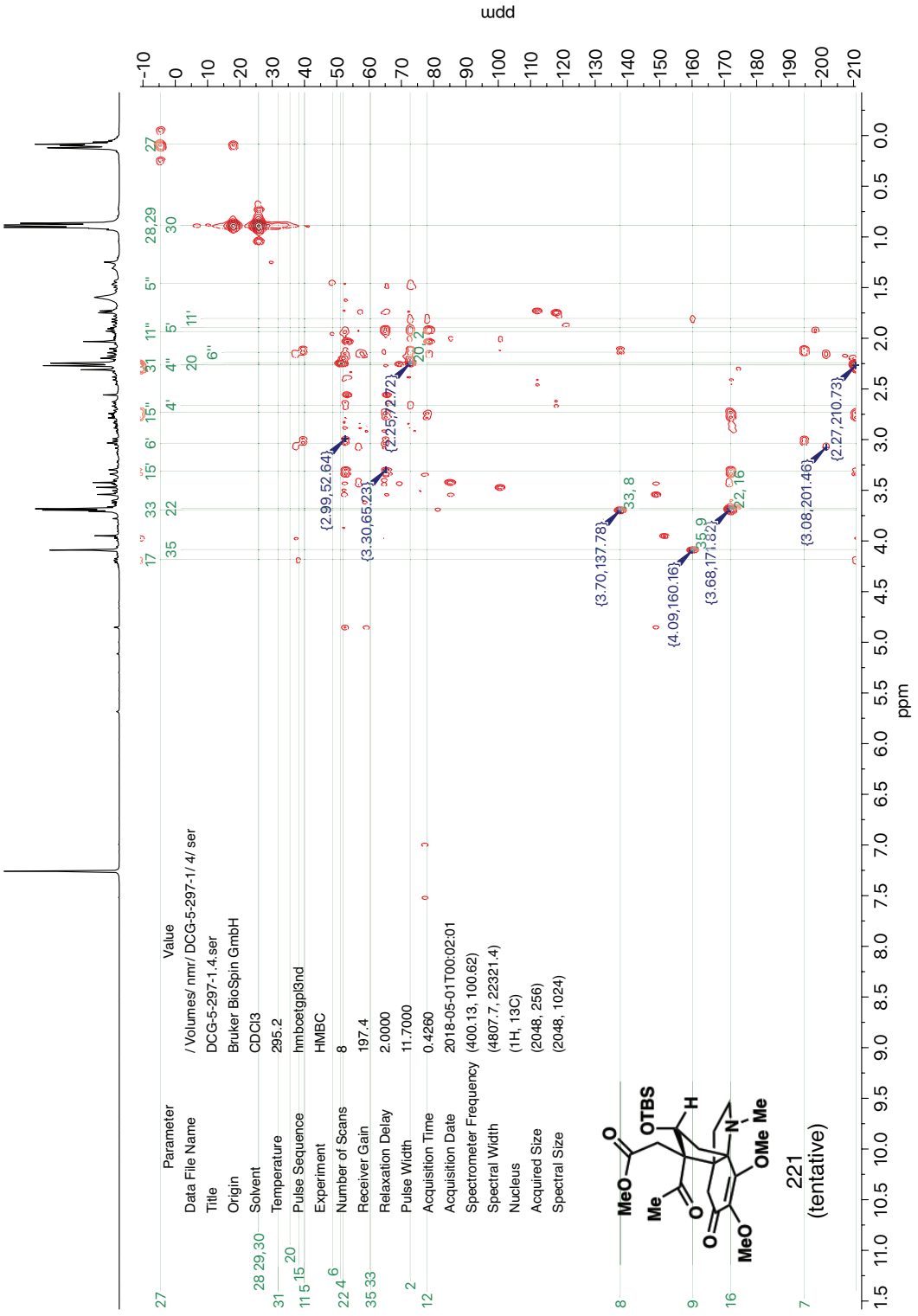

Parameter
Value
Data File Name / Volumes/ nmr/ DCG-5-297-1/ 1/ fid
Title DCG-5-297-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 176.8
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-04-30T23:33:02
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
A (dd) 4.19
B (s) 4.09
C (s) 3.70
D (s) 3.68
E (d) 3.32
F (m) 2.76
G (m) 2.65
H (m) 3.01
K (m) 2.13
11' (m) 1.80
11'' (m) 1.92
5'' (m) 1.48
M (s) 0.89
N (s) 0.09
P (s) 0.12
MeO
OTBS
Me
OMe Me
MeO
221
(tentative)
ppm

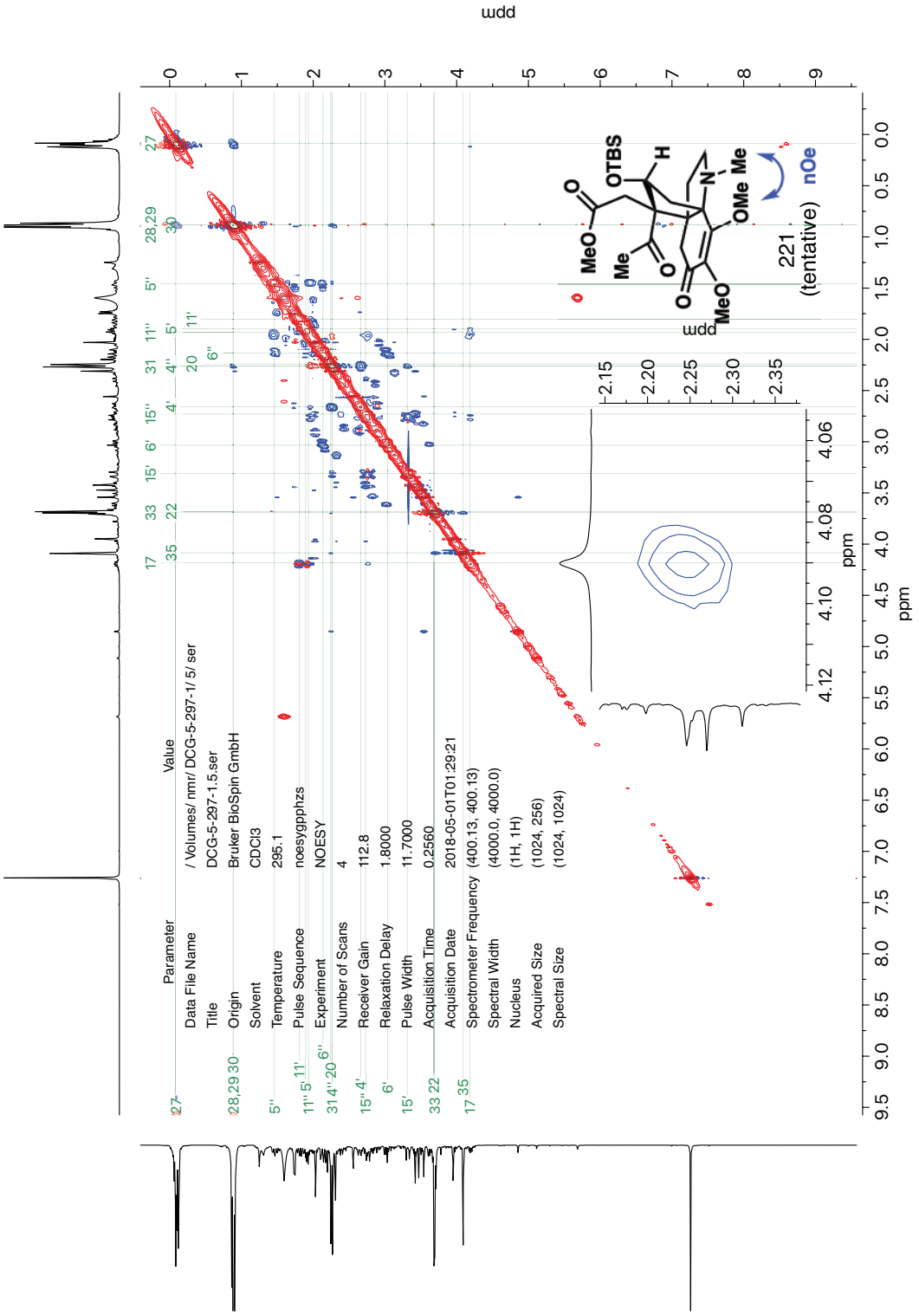

ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-297-1/ 2/ ser
Title DCG-5-297-1.2.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.1970
Acquisition Date 2018-04-30T23:33:51
Spectrometer Frequency (400.13, 400.13)
Spectral Width (5197.5, 5197.5)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)
MeO
Me
OTBS
H
N
OMe
Me
MeO
221
(tentative)

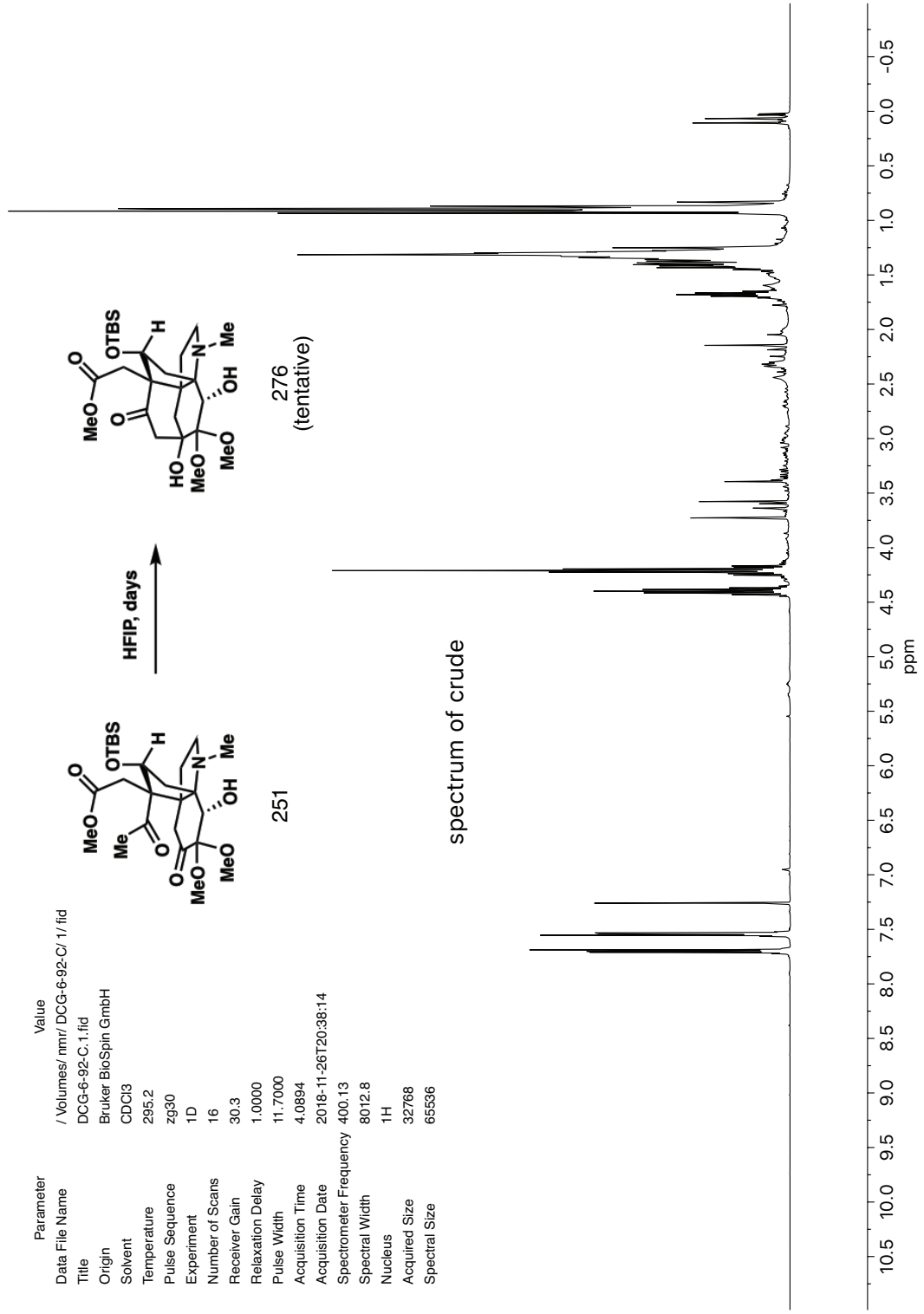

Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-5-297-1/ 3/ ser
Title
DCG-5-297-1.3.ser
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
hsqcedetgpsisp2.4
Experiment
HSQC-EDITED
Number of Scans
4
Receiver Gain
197.4
Relaxation Delay
1.5000
Pulse Width
11.7000
Acquisition Time
0.2135
Acquisition Date
2018-04-30T23:39:53
Spectrometer Frequency
(400.13, 100.62)
Spectral Width
(4795.4, 16611.3)
Nucleus
(1H, 13C)
Acquired Size
(1024, 180)
Spectral Size
(1024, 1024)
MeO
Me
OTBS
H
OMe
Me
MeO
221
(tentative)
ppm
ppm
ppm

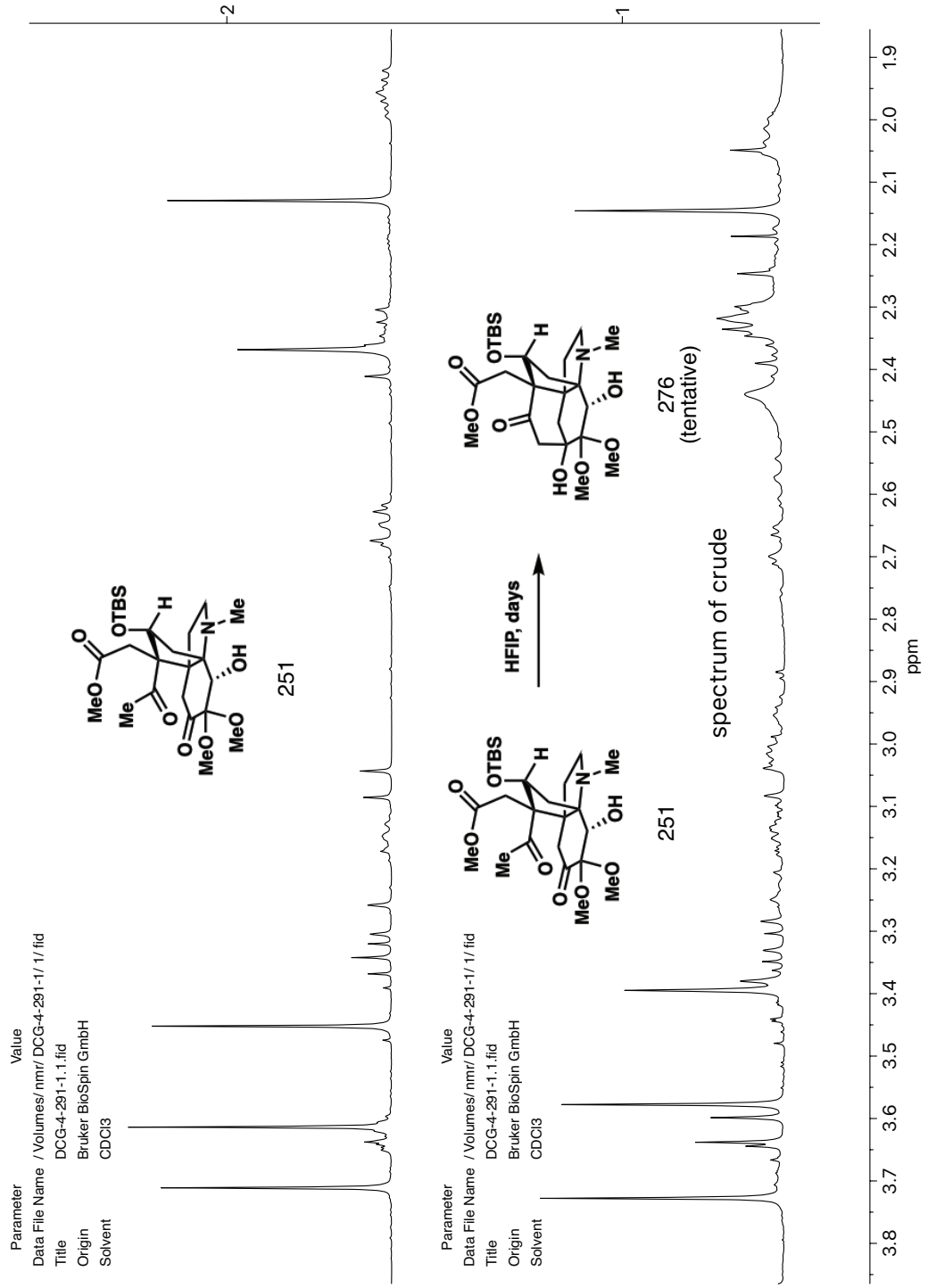

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-297-1/ 4/ ser
Title DCG-5-297-1.4.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 8
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2018-05-01T00:02:01
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
221
(tentative)
ppm
ppm

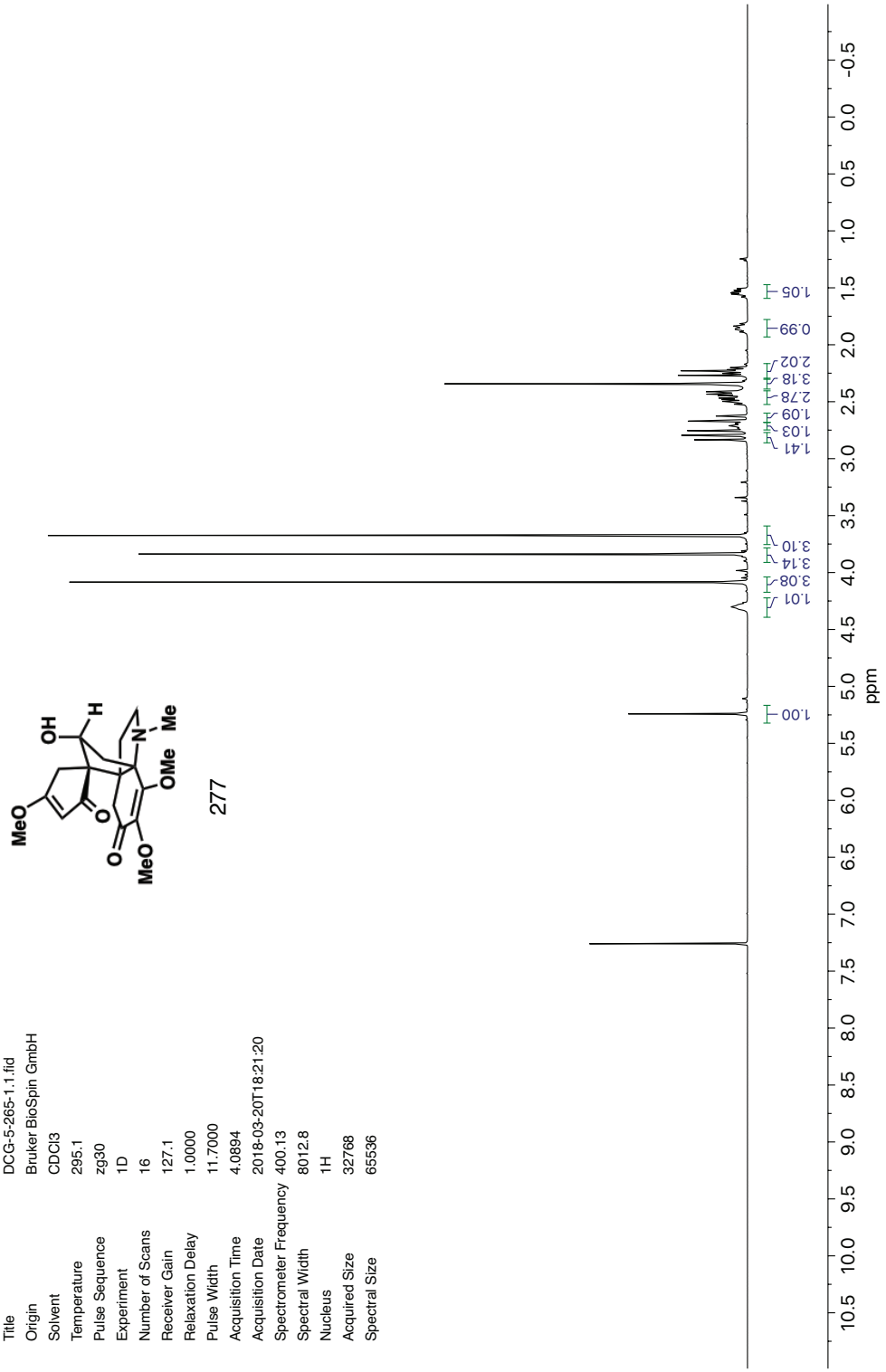

Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-5-297-1/ 3/ ser
Title
DCG-5-297-1.3.ser
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
hsqcedetgpsisp2.4
Experiment
HSQC-EDITED
Number of Scans
4
Receiver Gain
197.4
Relaxation Delay
1.5000
Pulse Width
11.7000
Acquisition Time
0.2135
Acquisition Date
2018-04-30T23:39:53
Spectrometer Frequency
(400.13, 100.62)
Spectral Width
(4795.4, 16611.3)
Nucleus
(1H, 13C)
Acquired Size
(1024, 180)
Spectral Size
(1024, 1024)
ppm
MeO
Me
OTBS
H
O
O
N
MeO
OMe Me
221
(tentative)

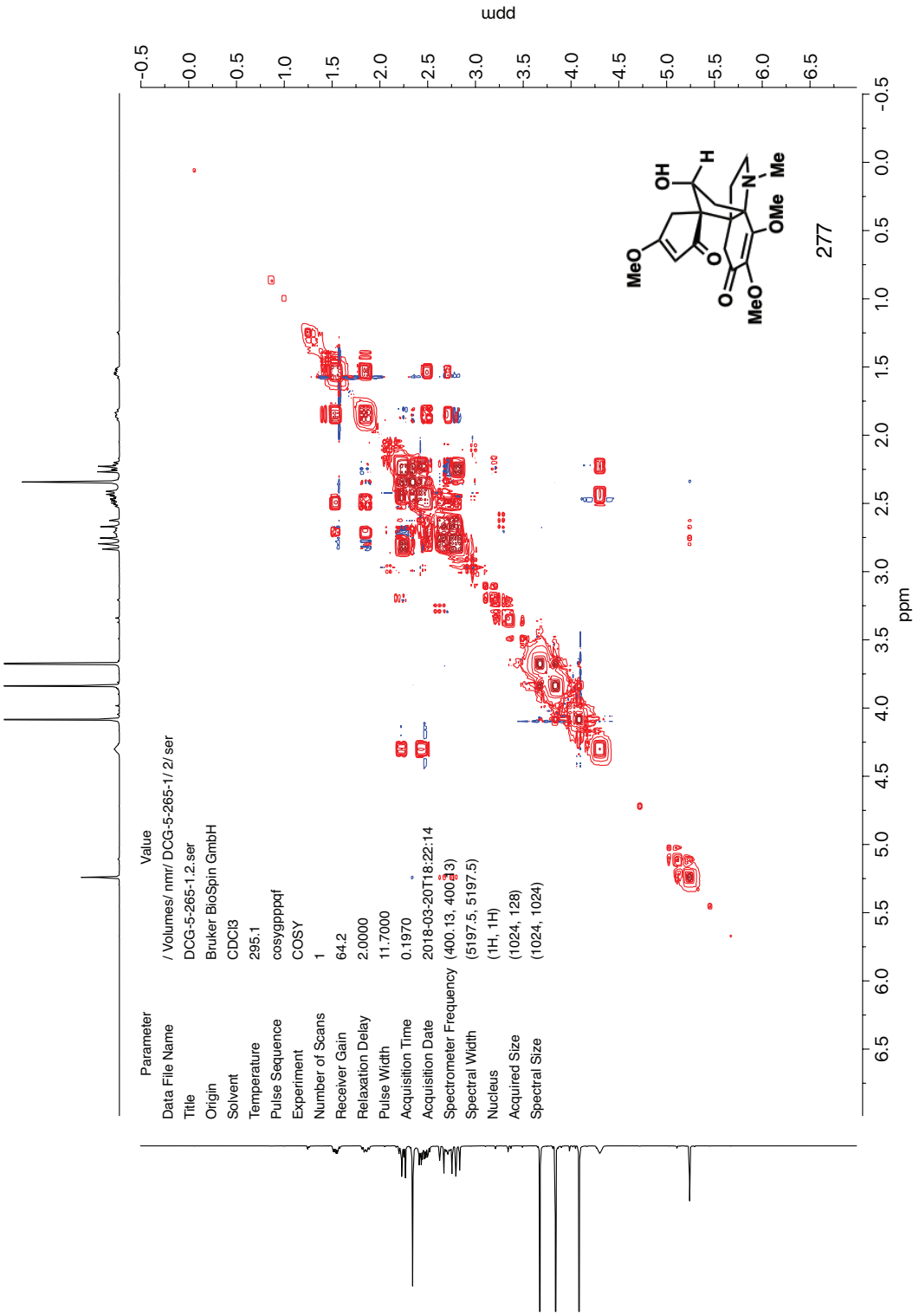

Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-5-297-1/ 4/ ser
Title
DCG-5-297-1.4.ser
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
hmbcetgpl3nd
Experiment
HMBC
Number of Scans
8
Receiver Gain
197.4
Relaxation Delay
2.0000
Pulse Width
11.7000
Acquisition Time
0.4260
Acquisition Date
2018-05-01T00:02:01
Spectrometer Frequency
(400.13, 100.62)
Spectral Width
(4807.7, 22321.4)
Nucleus
(1H, 13C)
Acquired Size
(2048, 256)
Spectral Size
(2048, 1024)
{2.99,52.64}
{3.30,65.23}
{3.70,137.78}
{4.09,160.16}
{3.68,171.82}
{3.08,201.46}
{2.27,210.73}
MeO
OTBS
Me
H
O
N
OMe Me
221
(tentative)
ppm

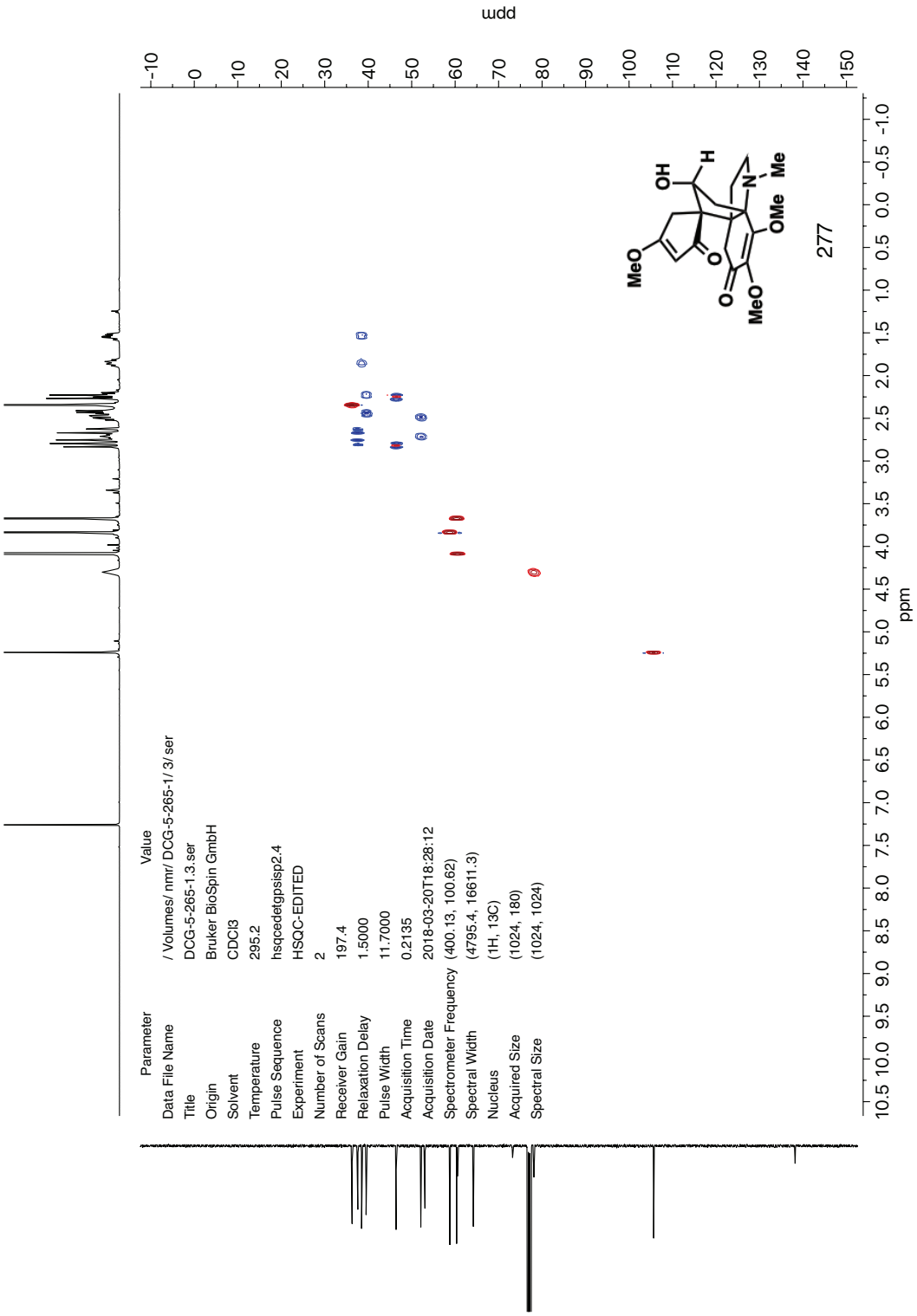

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-297-1/ 5/ ser
Title DCG-5-297-1.5.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence noesygpphzs
Experiment NOESY
Number of Scans 4
Receiver Gain 112.8
Relaxation Delay 1.8000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2018-05-01T01:29:21
Spectrometer Frequency (400.13, 400.13)
Spectral Width (4000.0, 4000.0)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
MeO
Me
OTBS
H
N
OMe Me
MeO
221
(tentative)
nOe
ppm

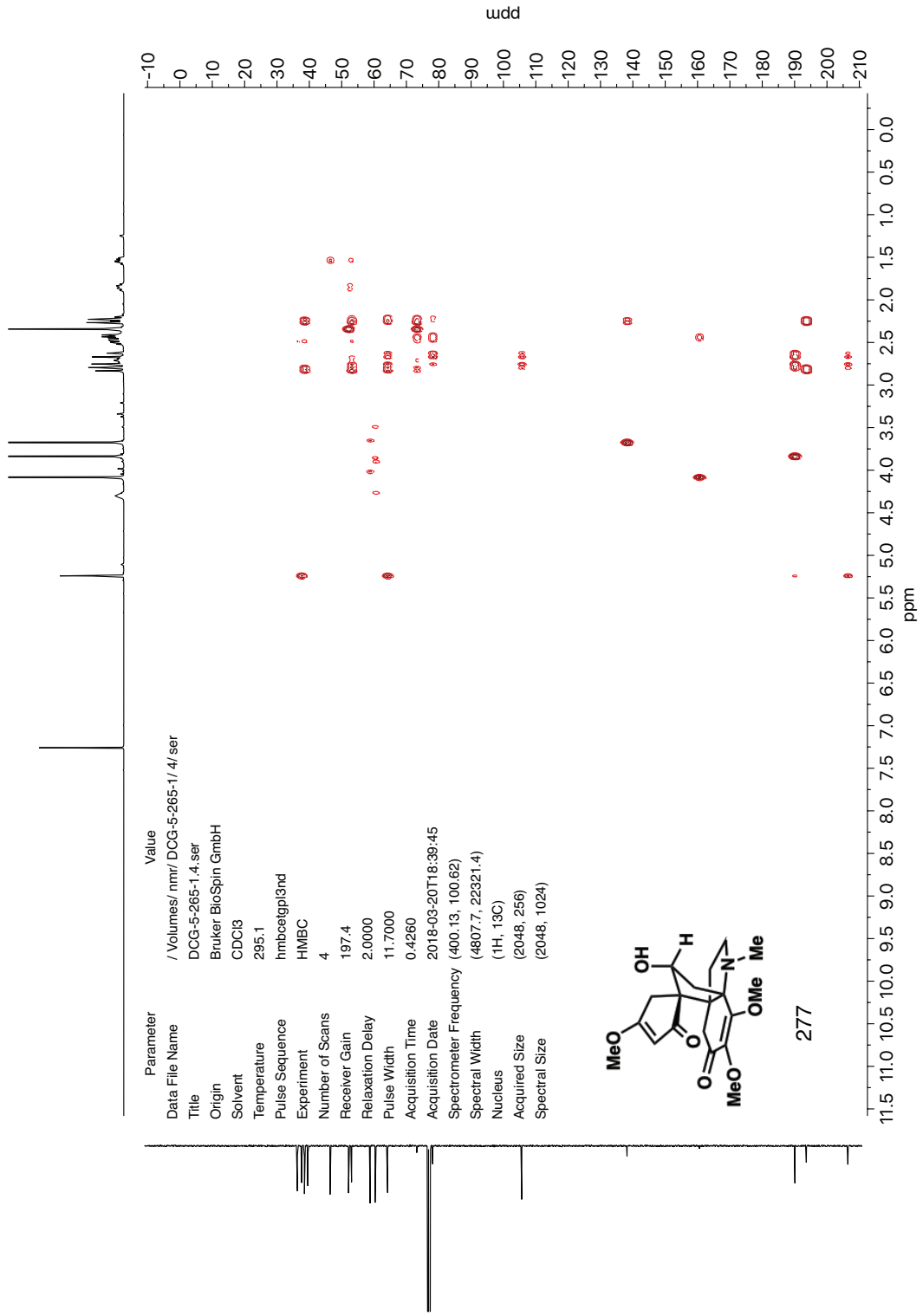

Parameter
Value
Data File Name / Volumes/ nmr/ DCG-6-92-C/ 1/ fid
Title DCG-6-92-C.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 30.3
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-11-26T20:38:14
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
HFIP, days
251
276
(tentative)
spectrum of crude
ppm

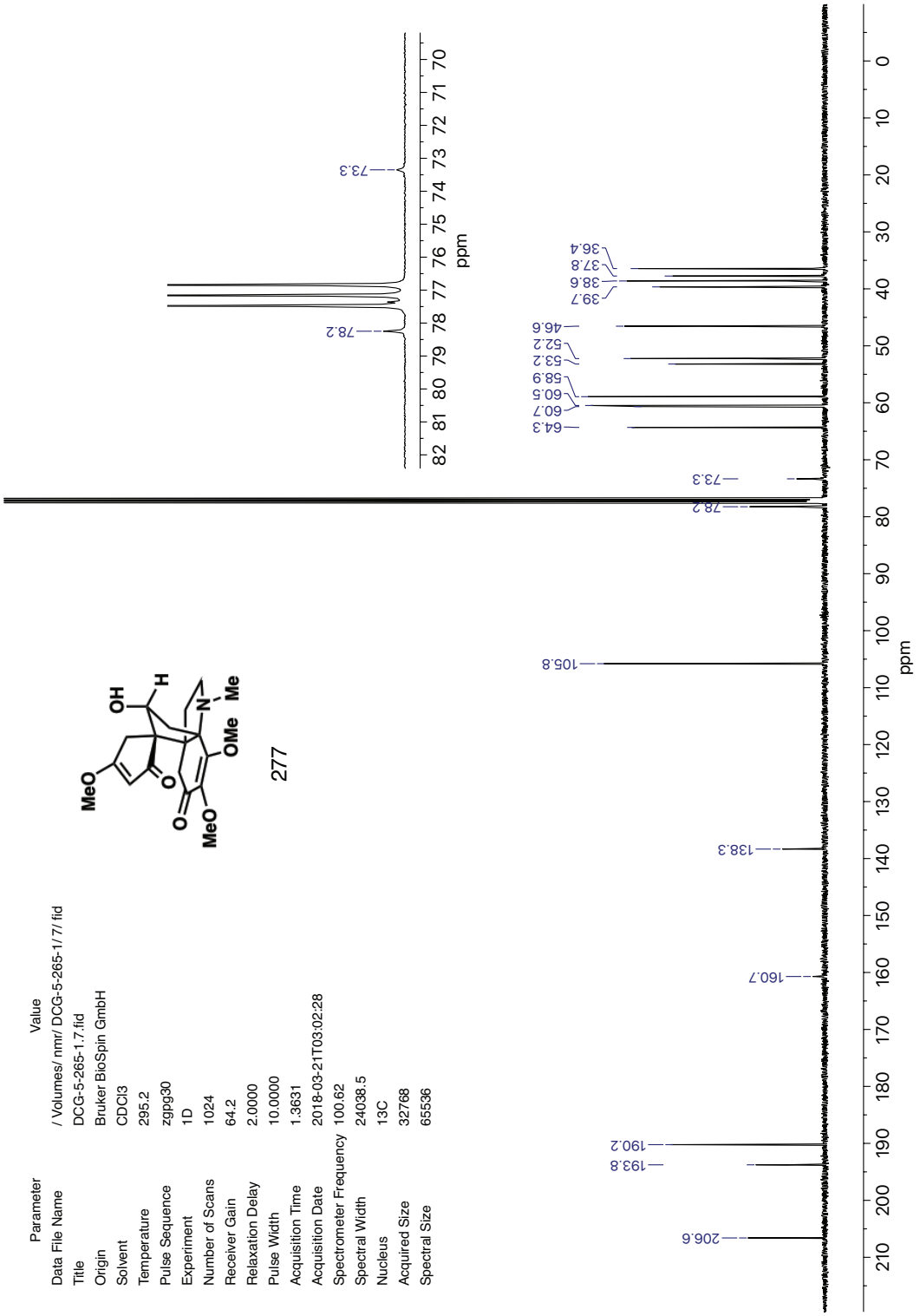

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-291-1/ 1/ fid
Title DCG-4-291-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
251
HFIP, days
276
(tentative)
spectrum of crude
ppm


Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-265-1/1/ fid
Title DCG-5-265-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 127.1
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-03-20T18:21:20
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
277
MeO
OH
H
N
Me
OMe
MeO
O
O
1.00
1.01
3.08
3.14
3.10
1.41
1.03
1.09
2.78
3.18
2.02
0.99
1.05
ppm


Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-265-1/ 2/ ser
Title DCG-5-265-1.2.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.1970
Acquisition Date 2018-03-20T18:22:14
Spectrometer Frequency (400.13, 400.13)
Spectral Width (5197.5, 5197.5)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)
ppm
277
OH
H
N
Me
OMe
MeO
O
MeO


Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-265-1/ 3/ ser
Title DCG-5-265-1.3.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2018-03-20T18:28:12
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 180)
Spectral Size (1024, 1024)
ppm
277
MeO
OH
H
N
Me
OMe
O
MeO


Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-265-1/ 4/ ser
Title DCG-5-265-1.4.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2018-03-20T18:39:45
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
277
ppm
ppm


Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-265-1/7/ fid
Title DCG-5-265-1.7.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 1024
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-03-21T03:02:28
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
277
MeO
OH
H
N
Me
OMe
O
O
MeO
206.6
193.8
190.2
160.7
138.3
105.8
78.2
73.3
64.3
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60.5
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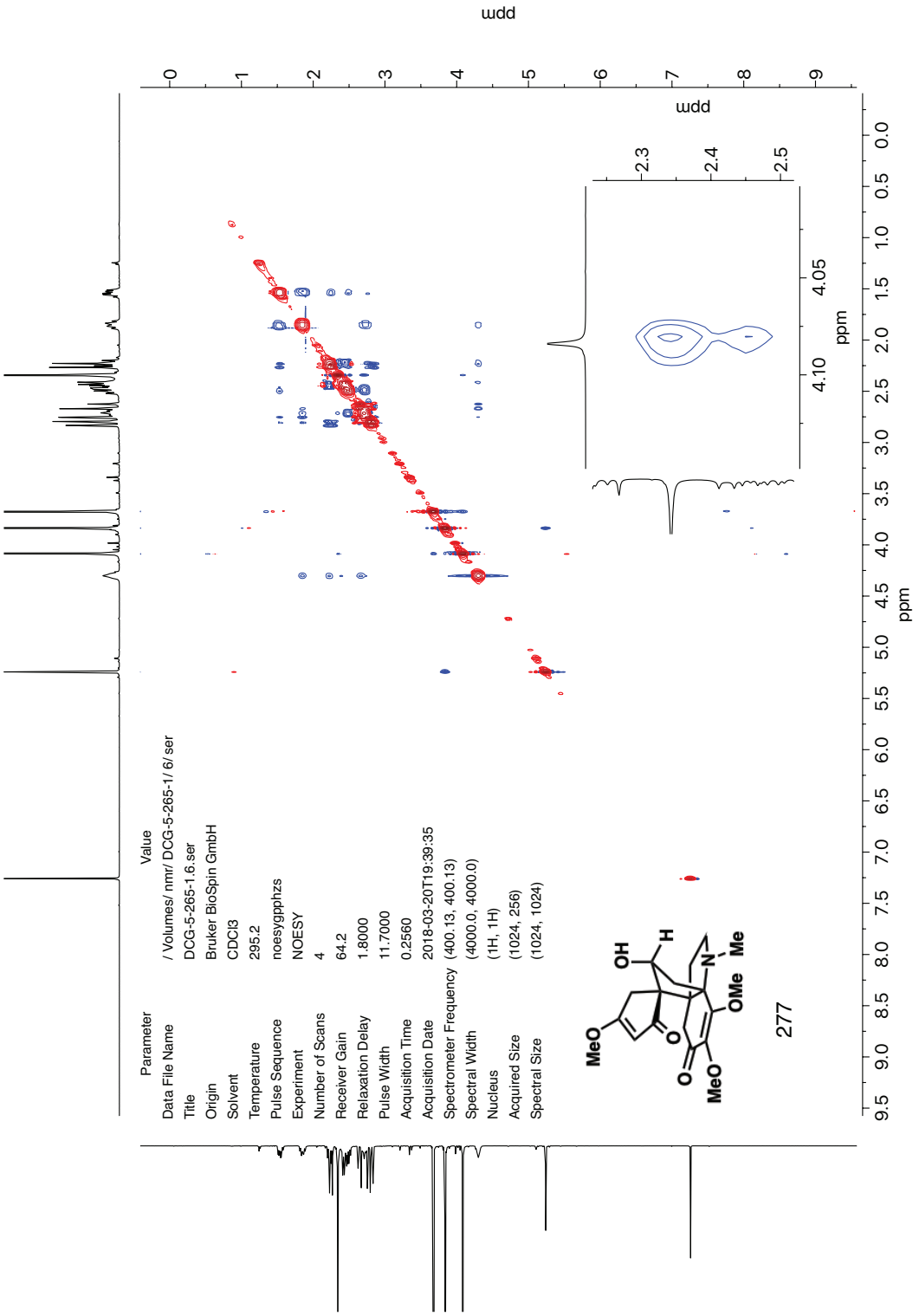
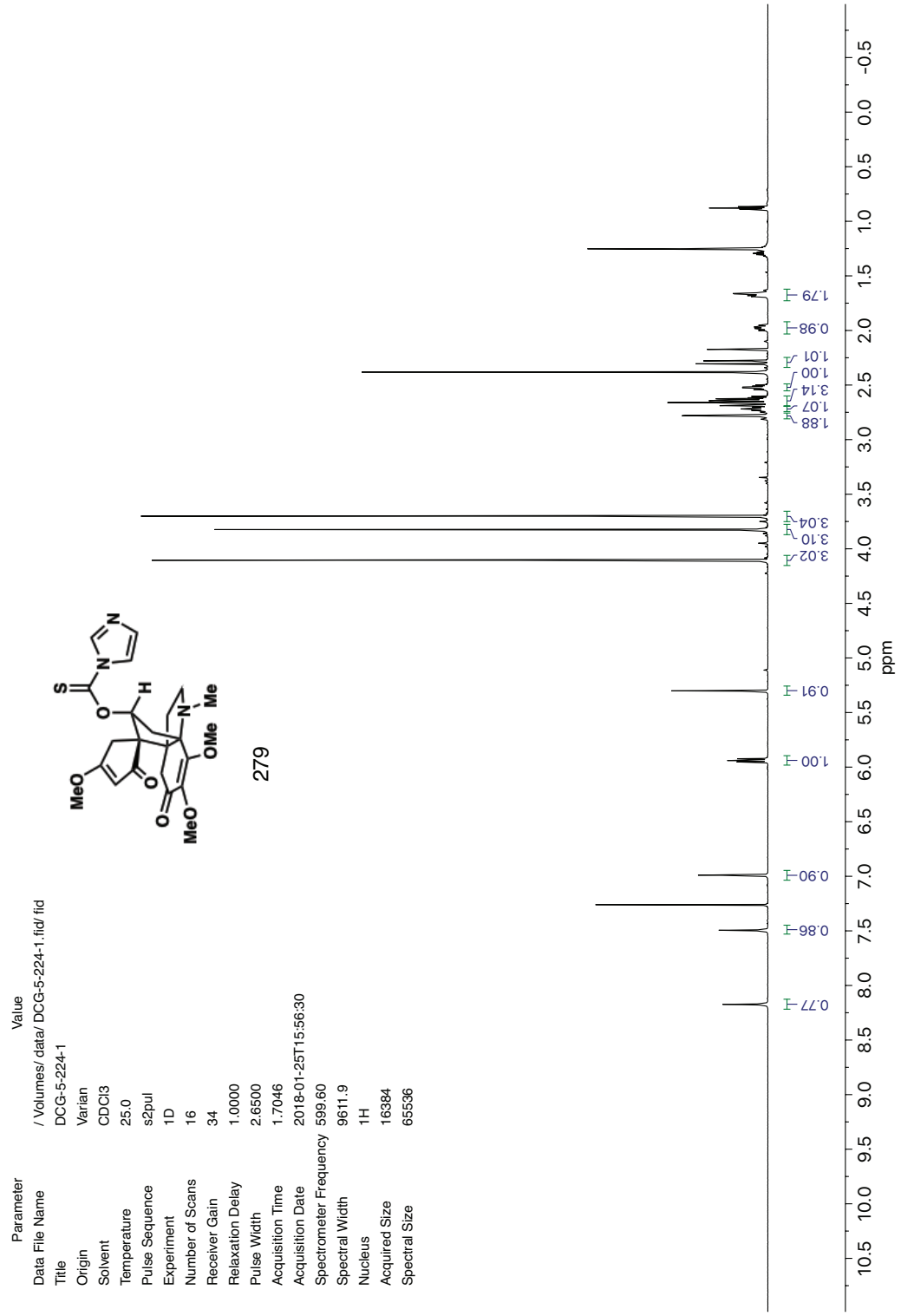
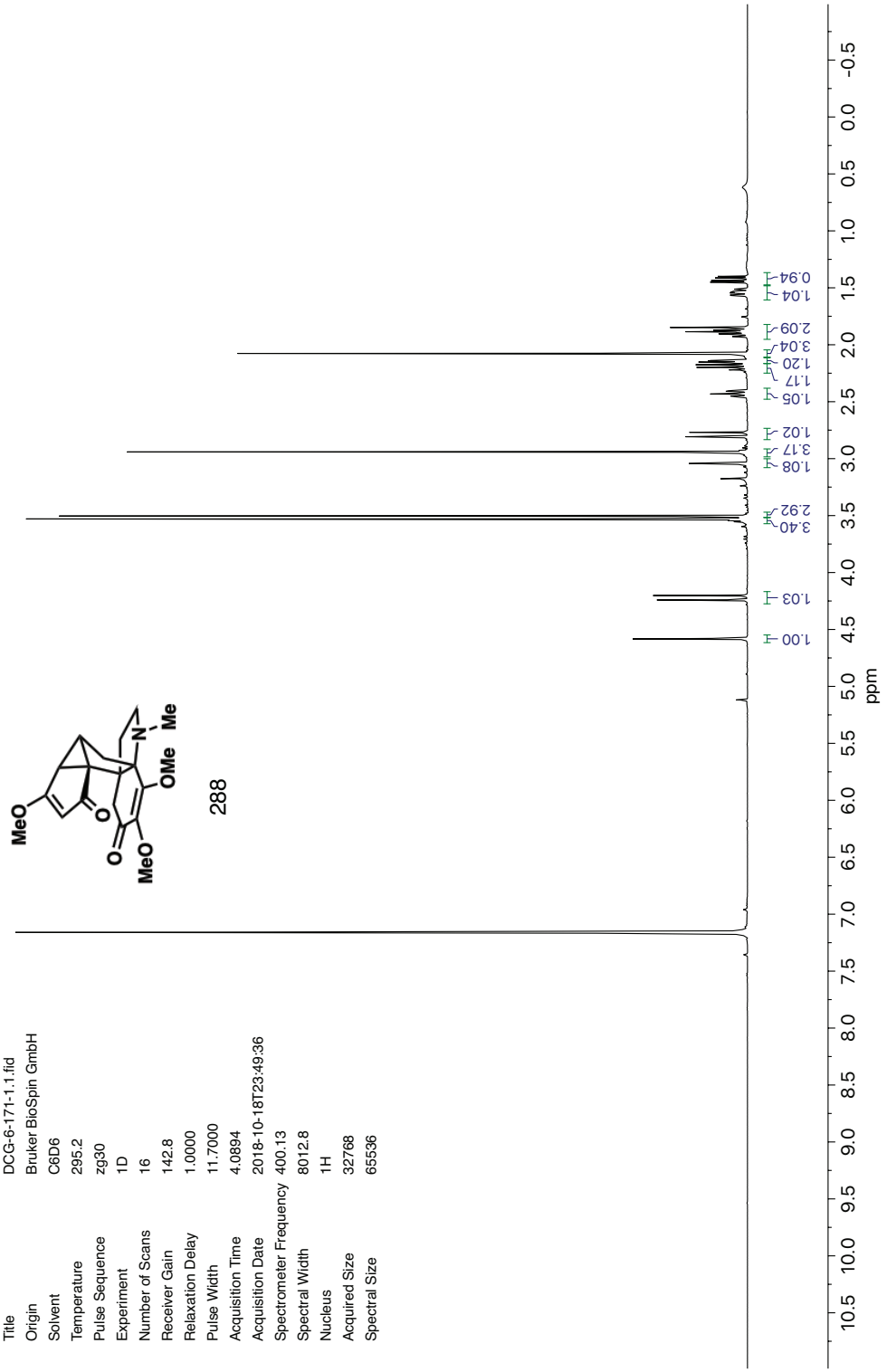
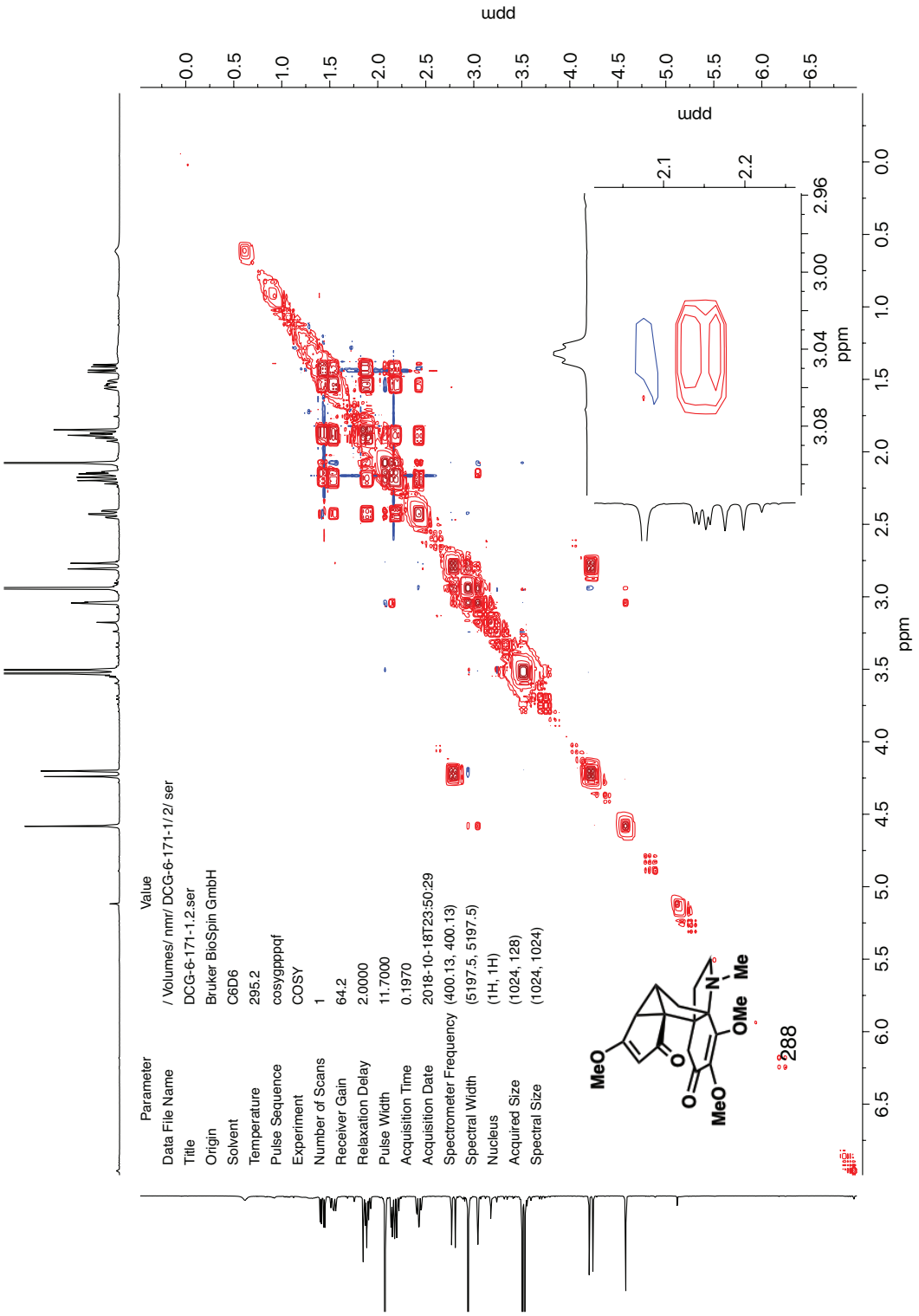
46.6
39.7
38.6
37.8
36.4
ppm


Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-265-1/ 6/ ser
Title DCG-5-265-1.6.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence noesygpphzs
Experiment NOESY
Number of Scans 4
Receiver Gain 64.2
Relaxation Delay 1.8000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2018-03-20T19:39:35
Spectrometer Frequency (400.13, 400.13)
Spectral Width (4000.0, 4000.0)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
MeO
OH
H
O
N
Me
OMe
MeO
O
277
ppm
ppm
ppm
ppm


Parameter Value
Data File Name / Volumes/ data/ DCG-5-224-1.fid/ fid
Title DCG-5-224-1
Origin Varian
Solvent CDCl3
Temperature 25.0
Pulse Sequence s2pul
Experiment 1D
Number of Scans 16
Receiver Gain 34
Relaxation Delay 1.0000
Pulse Width 2.6500
Acquisition Time 1.7046
Acquisition Date 2018-01-25T15:56:30
Spectrometer Frequency 599.60
Spectral Width 9611.9
Nucleus 1H
Acquired Size 16384
Spectral Size 65536
279
MeO
MeO
OMe
Me
Me
0.77
0.86
0.90
1.00
0.91
3.02
3.10
3.04
1.88
1.07
3.14
1.00
1.01
0.98
1.79
ppm


Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-171-1/1/ fid
Title DCG-6-171-1.1.fid
Origin Bruker BioSpin GmbH
Solvent C6D6
Temperature 295.2
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 142.8
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-10-18T23:49:36
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
MeO
O
O
MeO
OMe
N
Me
288
1.00
1.03
3.40
2.92
1.08
3.17
1.02
1.05
1.17
1.20
3.04
2.09
1.04
0.94
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm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Title DCG-6-171-1.2.ser
Origin Bruker BioSpin GmbH
Solvent C6D6
Temperature 295.2
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.1970
Acquisition Date 2018-10-18T23:50:29
Spectrometer Frequency (400.13, 400.13)
Spectral Width (5197.5, 5197.5)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)
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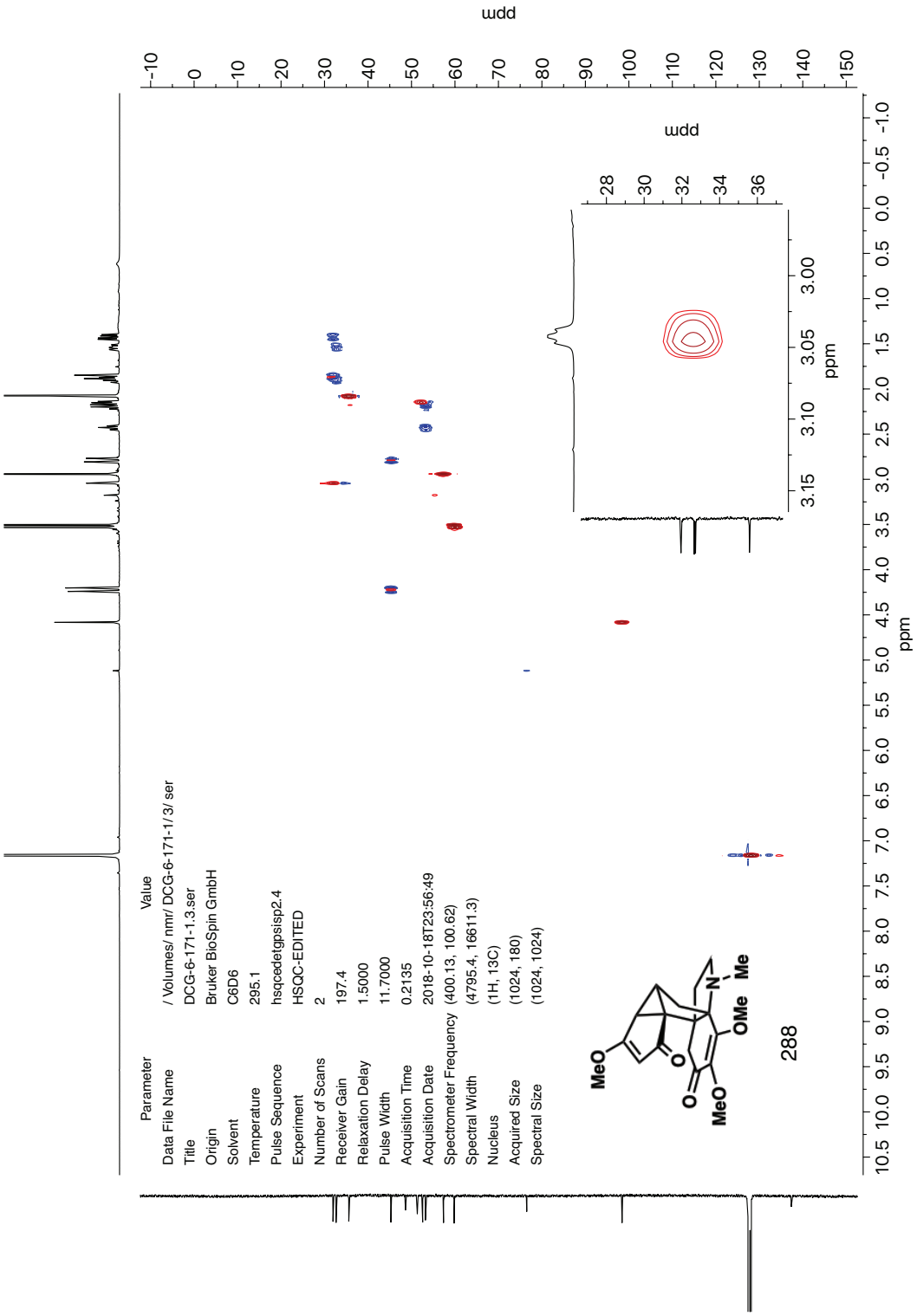
MeO
OMe
Me
N
O
O
288
ppm
ppm
ppm
ppm


Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-171-1/3/ ser
Title DCG-6-171-1.3.ser
Origin Bruker BioSpin GmbH
Solvent C6D6
Temperature 295.1
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2018-10-18T23:56:49
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 180)
Spectral Size (1024, 1024)
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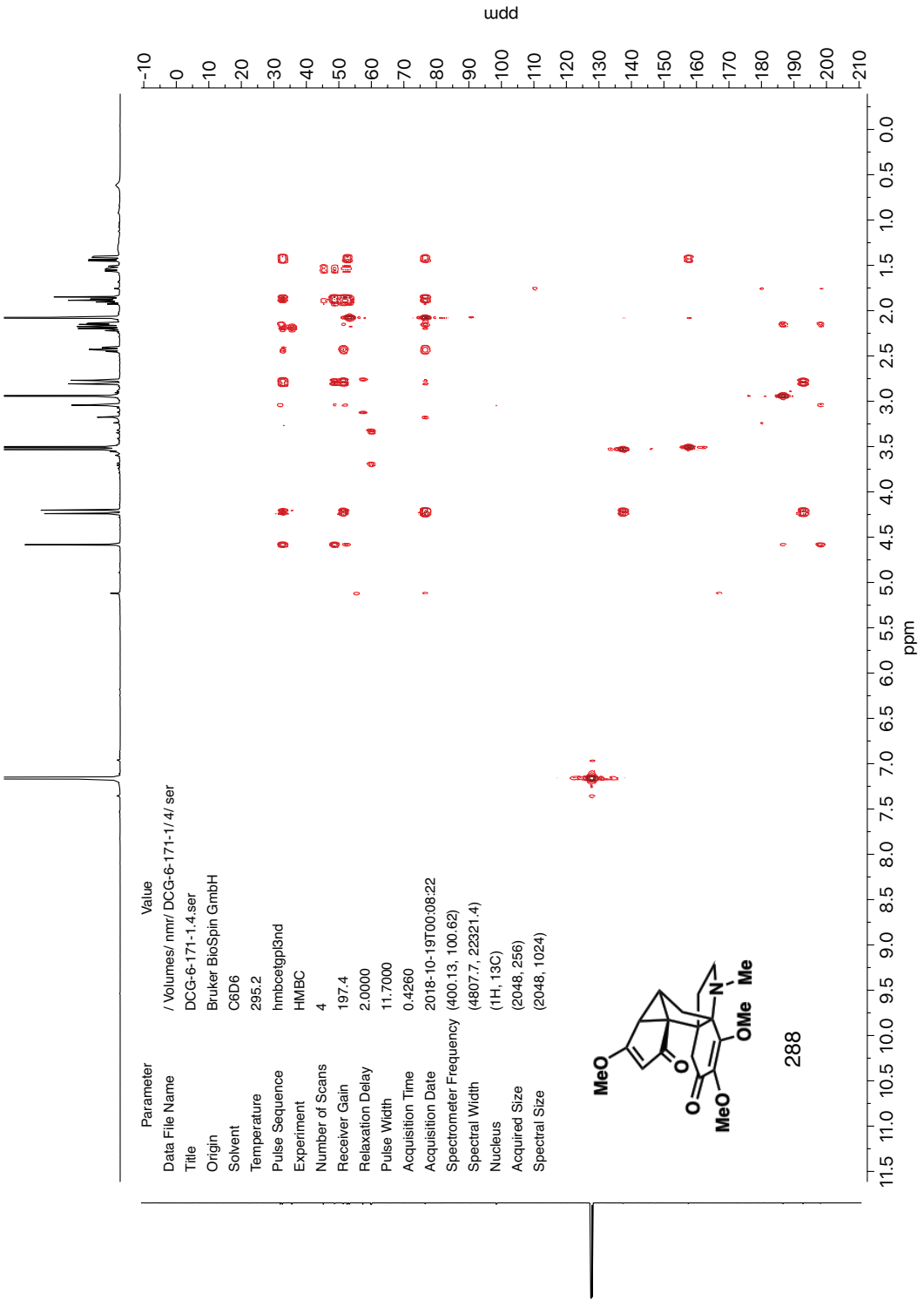
O
MeO
OMe
Me
N
288
ppm
ppm
ppm
ppm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Parameter Value
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Title DCG-6-171-1.4.ser
Origin Bruker BioSpin GmbH
Solvent C6D6
Temperature 295.2
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2018-10-19T00:08:22
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
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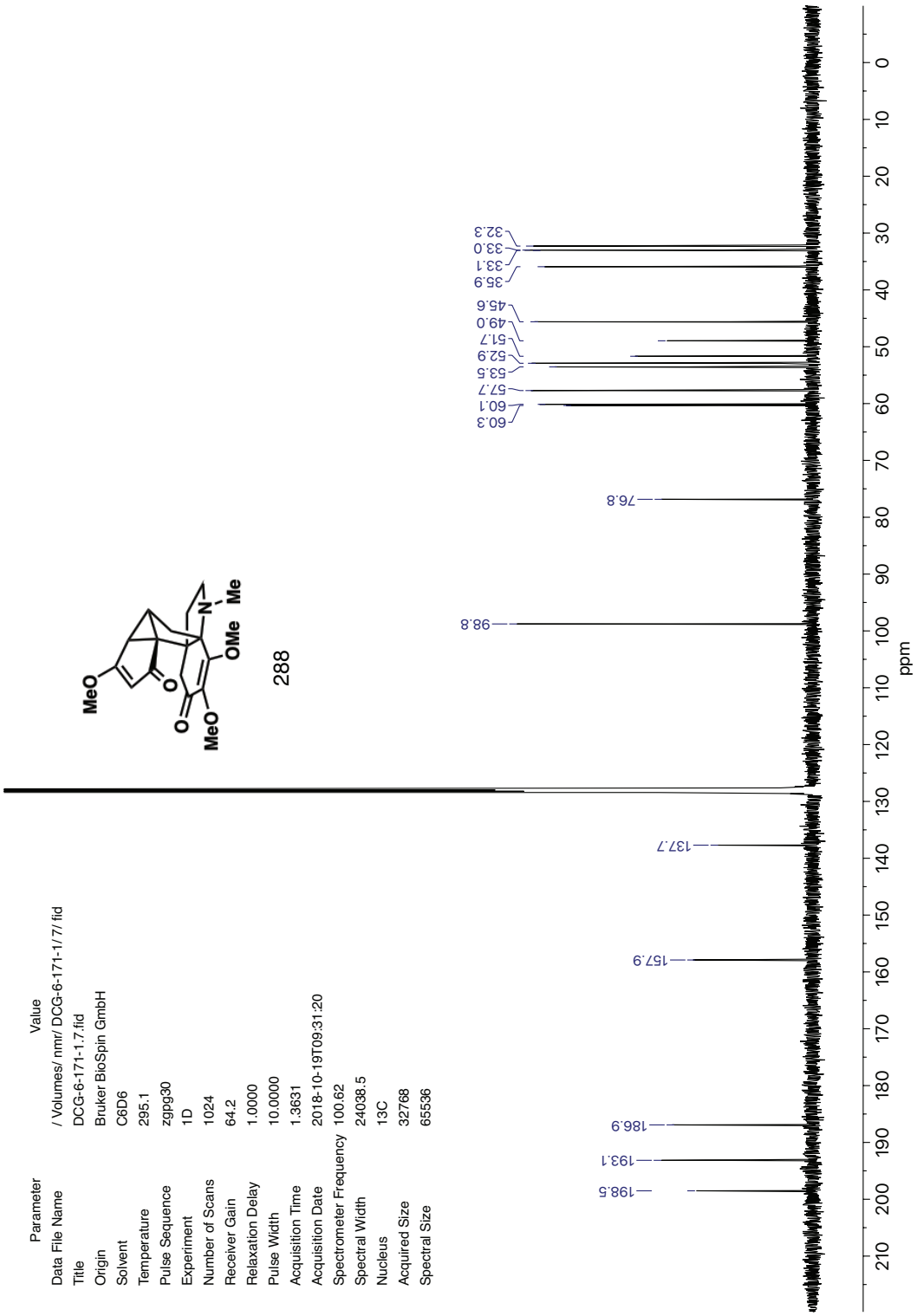
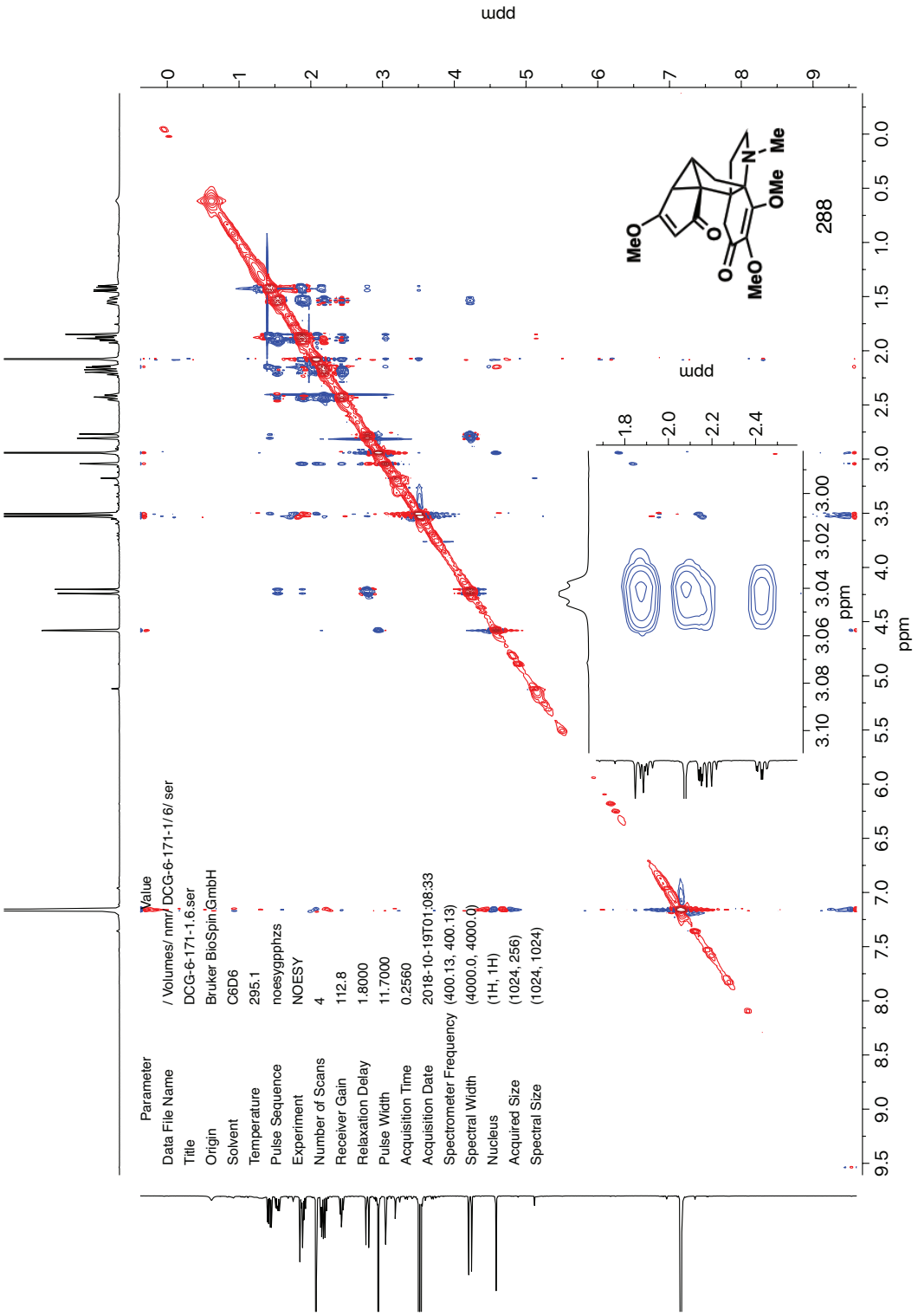
O
O
MeO
OMe
N
Me
288



Parameter	Value
Data File Name	/ Volumes/ nmr/ DCG-6-171-1/7/ fid
Title	DCG-6-171-1.7.fid
Origin	Bruker BioSpin GmbH
Solvent	C6D6
Temperature	295.1
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1024
Receiver Gain	64.2
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-10-19T09:31:20
Spectrometer Frequency	100.62
Spectral Width	24038.5
Nucleus	13C
Acquired Size	32768
Spectral Size	65536


Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-171-1/ 6/ ser
Title DCG-6-171-1.6.ser
Origin Bruker BioSpin GmbH
Solvent C6D6
Temperature 295.1
Pulse Sequence noesygpphzs
Experiment NOESY
Number of Scans 4
Receiver Gain 112.8
Relaxation Delay 1.8000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2018-10-19T01:08:33
Spectrometer Frequency (400.13, 400.13)
Spectral Width (4000.0, 4000.0)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
MeO
O
O
MeO
OMe
N
Me
288
ppm
ppm

Appendix 3

X-Ray Crystallography Report Relevant to Chapter 3:

Revised Strategies for the Asymmetric

Total Synthesis of Acutumine Alkaloids

A3.1 X-RAY CRYSTAL STRUCTURE ANALYSIS

Figure A3.1 *Rendering of dimethoxyenone* ***263****.*

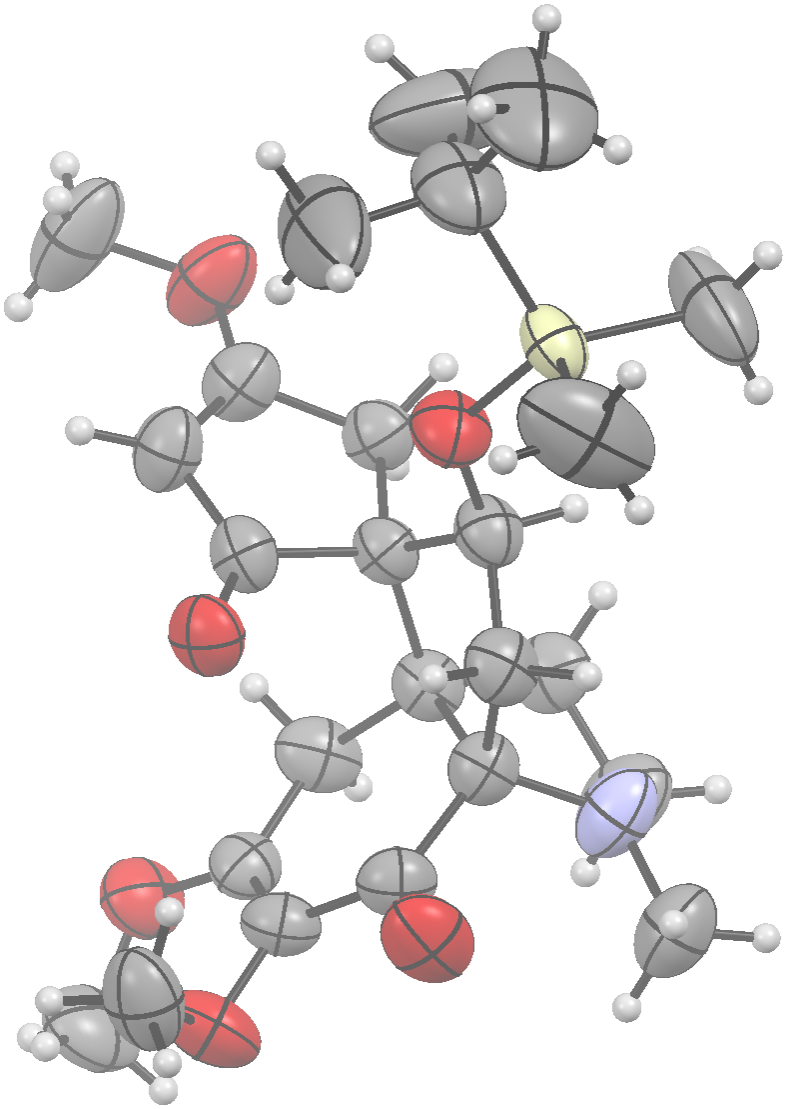


Table A3.1. *Crystal and refinement data for compound* ***263***.

Identification code	**263**	
Empirical formula	$C_{25}H_{39}NO_6Si$	
Formula weight	477.66	
Temperature	275(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 7.5603(4) Å	α= 90°.
	b = 13.2950(7) Å	β= 90°.
	c = 26.4513(13) Å	γ = 90°.
Volume	2658.7(2) $Å^3$	
Z	4	
Density (calculated)	1.193 Mg/m^3	
Absorption coefficient	1.089 mm^{-1}	
F(000)	1032	
Crystal size	0.200 x 0.150 x 0.050 mm^3	
Theta range for data collection	3.721 to 74.470°.	
Index ranges	-9<=h<=9, -15<=k<=16, -33<=l<=32	
Reflections collected	52017	
Independent reflections	5441 [R(int) = 0.0411]	
Completeness to theta = 67.679°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.0000 and 0.8731	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5441 / 757 / 446	
Goodness-of-fit on F^2	1.045	
Final R indices [I>2sigma(I)]	R1 = 0.0485, wR2 = 0.1352	
R indices (all data)	R1 = 0.0510, wR2 = 0.1375	
Absolute structure parameter	0.034(9)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.312 and -0.174 $e.Å^{-3}$	

A3.1.1 Crystallographic Analysis and Refinement Details

Low-temperature diffraction data (ϕ-and ω-scans) were collected on a Bruker AXS D8 VENTURE KAPPA diffractometer coupled to a PHOTON II CPAD detector with Cu K_α radiation (λ = 1.54178 Å) from an IμS micro-source for the structure of compound V18021. The structure was solved by direct methods using SHELXS[1] and refined against F^2 on all data by full-matrix least squares with SHELXL-2016[2] using established refinement techniques.[3] All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were included into the model at geometrically calculated positions and refined using a riding model. The isotropic displacement parameters of all hydrogen atoms were fixed to 1.2 times the U value of the atoms they are linked to (1.5 times for methyl groups). All disordered atoms were refined with the help of similarity restraints on the 1,2- and 1,3-distances and displacement parameters as well as enhanced rigid bond restraints for anisotropic displacement parameters.

Compound **263** crystallizes in the orthorhombic space group $P2_12_12_1$ with one molecule in the asymmetric unit. Absolute configuration was determined by anomalous dispersion (Flack = 0.034(9)).[4] The $SiMe_2{}^tBu$ group was modeled as a three-component disorder.

Table A3.2. *Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for* ***263****. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.*

	x	y	z	U(eq)
C(1)	1829(4)	6143(2)	3663(1)	55(1)
C(2)	1400(4)	5112(2)	3477(1)	62(1)
O(1)	-230(3)	4795(2)	3563(1)	85(1)
C(17)	-698(6)	3836(3)	3354(3)	113(2)
C(3)	2759(4)	4672(2)	3239(1)	64(1)
C(4)	4266(4)	5328(2)	3234(1)	52(1)
O(2)	5703(3)	5171(2)	3042(1)	64(1)
C(11)	3769(3)	6315(2)	3515(1)	47(1)
C(12)	4117(3)	7266(2)	3192(1)	48(1)
C(5)	3557(4)	7157(3)	2636(1)	62(1)
C(6)	4925(4)	6973(2)	2249(1)	52(1)
O(3)	4134(4)	6754(2)	1806(1)	75(1)
C(18)	4954(7)	6977(4)	1340(1)	99(1)
C(7)	6673(4)	7040(2)	2339(1)	54(1)
O(4)	7907(3)	6876(2)	1965(1)	81(1)
C(19)	8951(6)	5995(4)	2038(2)	89(1)
C(8)	7360(4)	7308(2)	2832(1)	56(1)
O(5)	8959(3)	7374(2)	2899(1)	81(1)
C(13)	6131(3)	7520(2)	3276(1)	51(1)
N(1)	6117(4)	8597(2)	3427(1)	74(1)
C(16)	7677(6)	9210(3)	3346(2)	85(1)
C(15)	4456(5)	9033(3)	3303(2)	83(1)
C(14)	3167(4)	8208(2)	3404(1)	64(1)
C(9)	6720(4)	6868(2)	3734(1)	57(1)
C(10)	5020(4)	6481(2)	3965(1)	55(1)
O(6)	5219(3)	5593(2)	4251(1)	66(1)
Si(1)	5852(4)	5550(2)	4857(1)	57(1)
C(20)	8320(11)	5569(14)	4918(5)	138(5)

C(21)	4910(20)	6583(9)	5234(4)	122(4)
C(22)	4933(15)	4310(7)	5061(4)	94(3)
C(23)	5740(30)	3521(8)	4697(5)	173(8)
C(24)	2892(17)	4390(15)	5054(7)	173(7)
C(25)	5710(40)	4090(20)	5597(6)	164(10)
Si(1A)	4817(9)	5456(5)	4867(2)	94(2)
C(20A)	6210(40)	6457(19)	5182(8)	147(9)
C(21A)	2580(30)	5770(30)	5085(9)	159(10)
C(22A)	5780(30)	4241(13)	5050(8)	106(6)
C(23A)	7670(40)	4110(30)	4829(13)	177(14)
C(24A)	4420(50)	3500(20)	4803(10)	153(10)
C(25A)	5710(70)	4160(40)	5641(9)	166(16)
Si(1B)	6118(12)	5129(7)	4758(3)	67(2)
C(20B)	7640(50)	4040(30)	4611(14)	127(13)
C(21B)	7510(50)	6070(30)	5078(12)	116(11)
C(22B)	4250(30)	4647(19)	5130(8)	99(6)
C(23B)	3120(60)	5590(30)	5280(15)	154(14)
C(24B)	5020(50)	4020(30)	5579(11)	91(9)
C(25B)	3260(50)	3930(30)	4748(11)	113(11)

Table A3.3. *Bond lengths [Å] and angles [°] for* ***263****.*

C(1)-C(2)	1.492(4)
C(1)-C(11)	1.536(4)
C(1)-H(1A)	0.9700
C(1)-H(1B)	0.9700
C(2)-O(1)	1.322(4)
C(2)-C(3)	1.340(5)
O(1)-C(17)	1.435(5)
C(17)-H(17A)	0.9600
C(17)-H(17B)	0.9600
C(17)-H(17C)	0.9600

C(3)-C(4)	1.435(4)
C(3)-H(3)	0.9300
C(4)-O(2)	1.218(3)
C(4)-C(11)	1.553(4)
C(11)-C(10)	1.536(4)
C(11)-C(12)	1.548(4)
C(12)-C(5)	1.539(4)
C(12)-C(14)	1.548(4)
C(12)-C(13)	1.576(4)
C(5)-C(6)	1.475(4)
C(5)-H(5A)	0.9700
C(5)-H(5B)	0.9700
C(6)-C(7)	1.346(4)
C(6)-O(3)	1.348(3)
O(3)-C(18)	1.411(5)
C(18)-H(18A)	0.9600
C(18)-H(18B)	0.9600
C(18)-H(18C)	0.9600
C(7)-O(4)	1.376(4)
C(7)-C(8)	1.449(4)
O(4)-C(19)	1.426(5)
C(19)-H(19A)	0.9600
C(19)-H(19B)	0.9600
C(19)-H(19C)	0.9600
C(8)-O(5)	1.225(4)
C(8)-C(13)	1.524(4)
C(13)-N(1)	1.486(4)
C(13)-C(9)	1.555(4)
N(1)-C(15)	1.421(5)
N(1)-C(16)	1.449(5)
C(16)-H(16A)	0.9600
C(16)-H(16B)	0.9600
C(16)-H(16C)	0.9600
C(15)-C(14)	1.492(5)

C(15)-H(15A)	0.9700
C(15)-H(15B)	0.9700
C(14)-H(14A)	0.9700
C(14)-H(14B)	0.9700
C(9)-C(10)	1.513(4)
C(9)-H(9A)	0.9700
C(9)-H(9B)	0.9700
C(10)-O(6)	1.411(4)
C(10)-H(10)	0.9800
O(6)-Si(1B)	1.624(7)
O(6)-Si(1A)	1.667(5)
O(6)-Si(1)	1.673(3)
Si(1)-C(21)	1.842(8)
Si(1)-C(22)	1.869(10)
Si(1)-C(20)	1.873(8)
C(20)-H(20A)	0.9600
C(20)-H(20B)	0.9600
C(20)-H(20C)	0.9600
C(21)-H(21A)	0.9600
C(21)-H(21B)	0.9600
C(21)-H(21C)	0.9600
C(22)-C(24)	1.547(14)
C(22)-C(23)	1.549(13)
C(22)-C(25)	1.564(14)
C(23)-H(23A)	0.9600
C(23)-H(23B)	0.9600
C(23)-H(23C)	0.9600
C(24)-H(24A)	0.9600
C(24)-H(24B)	0.9600
C(24)-H(24C)	0.9600
C(25)-H(25A)	0.9600
C(25)-H(25B)	0.9600
C(25)-H(25C)	0.9600
Si(1A)-C(21A)	1.834(16)

Si(1A)-C(22A)	1.838(15)
Si(1A)-C(20A)	1.888(16)
C(20A)-H(20D)	0.9600
C(20A)-H(20E)	0.9600
C(20A)-H(20F)	0.9600
C(21A)-H(21D)	0.9600
C(21A)-H(21E)	0.9600
C(21A)-H(21F)	0.9600
C(22A)-C(23A)	1.550(18)
C(22A)-C(24A)	1.566(19)
C(22A)-C(25A)	1.568(18)
C(23A)-H(23D)	0.9600
C(23A)-H(23E)	0.9600
C(23A)-H(23F)	0.9600
C(24A)-H(24D)	0.9600
C(24A)-H(24E)	0.9600
C(24A)-H(24F)	0.9600
C(25A)-H(25D)	0.9600
C(25A)-H(25E)	0.9600
C(25A)-H(25F)	0.9600
Si(1B)-C(22B)	1.836(19)
Si(1B)-C(21B)	1.841(17)
Si(1B)-C(20B)	1.890(19)
C(20B)-H(20G)	0.9600
C(20B)-H(20H)	0.9600
C(20B)-H(20I)	0.9600
C(21B)-H(21G)	0.9600
C(21B)-H(21H)	0.9600
C(21B)-H(21I)	0.9600
C(22B)-C(24B)	1.563(19)
C(22B)-C(23B)	1.564(19)
C(22B)-C(25B)	1.573(19)
C(23B)-H(23G)	0.9600
C(23B)-H(23H)	0.9600

C(23B)-H(23I)	0.9600
C(24B)-H(24G)	0.9600
C(24B)-H(24H)	0.9600
C(24B)-H(24I)	0.9600
C(25B)-H(25G)	0.9600
C(25B)-H(25H)	0.9600
C(25B)-H(25I)	0.9600

C(2)-C(1)-C(11)	105.1(2)
C(2)-C(1)-H(1A)	110.7
C(11)-C(1)-H(1A)	110.7
C(2)-C(1)-H(1B)	110.7
C(11)-C(1)-H(1B)	110.7
H(1A)-C(1)-H(1B)	108.8
O(1)-C(2)-C(3)	131.1(3)
O(1)-C(2)-C(1)	116.0(3)
C(3)-C(2)-C(1)	112.9(3)
C(2)-O(1)-C(17)	116.5(3)
O(1)-C(17)-H(17A)	109.5
O(1)-C(17)-H(17B)	109.5
H(17A)-C(17)-H(17B)	109.5
O(1)-C(17)-H(17C)	109.5
H(17A)-C(17)-H(17C)	109.5
H(17B)-C(17)-H(17C)	109.5
C(2)-C(3)-C(4)	110.3(3)
C(2)-C(3)-H(3)	124.8
C(4)-C(3)-H(3)	124.8
O(2)-C(4)-C(3)	127.4(3)
O(2)-C(4)-C(11)	124.1(3)
C(3)-C(4)-C(11)	108.5(2)
C(1)-C(11)-C(10)	114.3(2)
C(1)-C(11)-C(12)	115.1(2)
C(10)-C(11)-C(12)	101.8(2)
C(1)-C(11)-C(4)	103.1(2)

C(10)-C(11)-C(4)	110.0(2)
C(12)-C(11)-C(4)	112.7(2)
C(5)-C(12)-C(11)	113.8(2)
C(5)-C(12)-C(14)	107.2(2)
C(11)-C(12)-C(14)	112.5(2)
C(5)-C(12)-C(13)	114.9(2)
C(11)-C(12)-C(13)	105.2(2)
C(14)-C(12)-C(13)	102.9(2)
C(6)-C(5)-C(12)	119.1(2)
C(6)-C(5)-H(5A)	107.6
C(12)-C(5)-H(5A)	107.6
C(6)-C(5)-H(5B)	107.6
C(12)-C(5)-H(5B)	107.6
H(5A)-C(5)-H(5B)	107.0
C(7)-C(6)-O(3)	127.1(3)
C(7)-C(6)-C(5)	123.7(3)
O(3)-C(6)-C(5)	109.1(3)
C(6)-O(3)-C(18)	121.2(3)
O(3)-C(18)-H(18A)	109.5
O(3)-C(18)-H(18B)	109.5
H(18A)-C(18)-H(18B)	109.5
O(3)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5
C(6)-C(7)-O(4)	121.9(3)
C(6)-C(7)-C(8)	121.8(3)
O(4)-C(7)-C(8)	116.3(3)
C(7)-O(4)-C(19)	114.1(3)
O(4)-C(19)-H(19A)	109.5
O(4)-C(19)-H(19B)	109.5
H(19A)-C(19)-H(19B)	109.5
O(4)-C(19)-H(19C)	109.5
H(19A)-C(19)-H(19C)	109.5
H(19B)-C(19)-H(19C)	109.5

O(5)-C(8)-C(7)	120.2(3)
O(5)-C(8)-C(13)	118.4(3)
C(7)-C(8)-C(13)	121.4(2)
N(1)-C(13)-C(8)	113.0(3)
N(1)-C(13)-C(9)	109.3(3)
C(8)-C(13)-C(9)	108.8(2)
N(1)-C(13)-C(12)	103.7(2)
C(8)-C(13)-C(12)	116.2(2)
C(9)-C(13)-C(12)	105.4(2)
C(15)-N(1)-C(16)	117.1(3)
C(15)-N(1)-C(13)	109.7(3)
C(16)-N(1)-C(13)	119.7(3)
N(1)-C(16)-H(16A)	109.5
N(1)-C(16)-H(16B)	109.5
H(16A)-C(16)-H(16B)	109.5
N(1)-C(16)-H(16C)	109.5
H(16A)-C(16)-H(16C)	109.5
H(16B)-C(16)-H(16C)	109.5
N(1)-C(15)-C(14)	103.6(3)
N(1)-C(15)-H(15A)	111.0
C(14)-C(15)-H(15A)	111.0
N(1)-C(15)-H(15B)	111.0
C(14)-C(15)-H(15B)	111.0
H(15A)-C(15)-H(15B)	109.0
C(15)-C(14)-C(12)	103.1(3)
C(15)-C(14)-H(14A)	111.1
C(12)-C(14)-H(14A)	111.1
C(15)-C(14)-H(14B)	111.1
C(12)-C(14)-H(14B)	111.1
H(14A)-C(14)-H(14B)	109.1
C(10)-C(9)-C(13)	105.2(2)
C(10)-C(9)-H(9A)	110.7
C(13)-C(9)-H(9A)	110.7
C(10)-C(9)-H(9B)	110.7

C(13)-C(9)-H(9B)	110.7
H(9A)-C(9)-H(9B)	108.8
O(6)-C(10)-C(9)	114.3(3)
O(6)-C(10)-C(11)	111.2(2)
C(9)-C(10)-C(11)	105.0(2)
O(6)-C(10)-H(10)	108.7
C(9)-C(10)-H(10)	108.7
C(11)-C(10)-H(10)	108.7
C(10)-O(6)-Si(1B)	143.7(4)
C(10)-O(6)-Si(1A)	126.7(3)
C(10)-O(6)-Si(1)	125.0(2)
O(6)-Si(1)-C(21)	112.5(4)
O(6)-Si(1)-C(22)	101.6(4)
C(21)-Si(1)-C(22)	111.0(6)
O(6)-Si(1)-C(20)	111.5(4)
C(21)-Si(1)-C(20)	109.3(8)
C(22)-Si(1)-C(20)	110.9(7)
Si(1)-C(20)-H(20A)	109.5
Si(1)-C(20)-H(20B)	109.5
H(20A)-C(20)-H(20B)	109.5
Si(1)-C(20)-H(20C)	109.5
H(20A)-C(20)-H(20C)	109.5
H(20B)-C(20)-H(20C)	109.5
Si(1)-C(21)-H(21A)	109.5
Si(1)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21B)	109.5
Si(1)-C(21)-H(21C)	109.5
H(21A)-C(21)-H(21C)	109.5
H(21B)-C(21)-H(21C)	109.5
C(24)-C(22)-C(23)	115.6(14)
C(24)-C(22)-C(25)	113.5(14)
C(23)-C(22)-C(25)	106.7(14)
C(24)-C(22)-Si(1)	107.8(8)
C(23)-C(22)-Si(1)	105.8(8)

C(25)-C(22)-Si(1)	106.9(13)
C(22)-C(23)-H(23A)	109.5
C(22)-C(23)-H(23B)	109.5
H(23A)-C(23)-H(23B)	109.5
C(22)-C(23)-H(23C)	109.5
H(23A)-C(23)-H(23C)	109.5
H(23B)-C(23)-H(23C)	109.5
C(22)-C(24)-H(24A)	109.5
C(22)-C(24)-H(24B)	109.5
H(24A)-C(24)-H(24B)	109.5
C(22)-C(24)-H(24C)	109.5
H(24A)-C(24)-H(24C)	109.5
H(24B)-C(24)-H(24C)	109.5
C(22)-C(25)-H(25A)	109.5
C(22)-C(25)-H(25B)	109.5
H(25A)-C(25)-H(25B)	109.5
C(22)-C(25)-H(25C)	109.5
H(25A)-C(25)-H(25C)	109.5
H(25B)-C(25)-H(25C)	109.5
O(6)-Si(1A)-C(21A)	116.8(8)
O(6)-Si(1A)-C(22A)	106.3(7)
C(21A)-Si(1A)-C(22A)	118.8(11)
O(6)-Si(1A)-C(20A)	104.6(9)
C(21A)-Si(1A)-C(20A)	102.5(14)
C(22A)-Si(1A)-C(20A)	106.4(11)
Si(1A)-C(20A)-H(20D)	109.5
Si(1A)-C(20A)-H(20E)	109.5
H(20D)-C(20A)-H(20E)	109.5
Si(1A)-C(20A)-H(20F)	109.5
H(20D)-C(20A)-H(20F)	109.5
H(20E)-C(20A)-H(20F)	109.5
Si(1A)-C(21A)-H(21D)	109.5
Si(1A)-C(21A)-H(21E)	109.5
H(21D)-C(21A)-H(21E)	109.5

Si(1A)-C(21A)-H(21F)	109.5
H(21D)-C(21A)-H(21F)	109.5
H(21E)-C(21A)-H(21F)	109.5
C(23A)-C(22A)-C(24A)	112(2)
C(23A)-C(22A)-C(25A)	113(2)
C(24A)-C(22A)-C(25A)	111(2)
C(23A)-C(22A)-Si(1A)	111.6(15)
C(24A)-C(22A)-Si(1A)	100.6(15)
C(25A)-C(22A)-Si(1A)	107.9(19)
C(22A)-C(23A)-H(23D)	109.5
C(22A)-C(23A)-H(23E)	109.5
H(23D)-C(23A)-H(23E)	109.5
C(22A)-C(23A)-H(23F)	109.5
H(23D)-C(23A)-H(23F)	109.5
H(23E)-C(23A)-H(23F)	109.5
C(22A)-C(24A)-H(24D)	109.5
C(22A)-C(24A)-H(24E)	109.5
H(24D)-C(24A)-H(24E)	109.5
C(22A)-C(24A)-H(24F)	109.5
H(24D)-C(24A)-H(24F)	109.5
H(24E)-C(24A)-H(24F)	109.5
C(22A)-C(25A)-H(25D)	109.5
C(22A)-C(25A)-H(25E)	109.5
H(25D)-C(25A)-H(25E)	109.5
C(22A)-C(25A)-H(25F)	109.5
H(25D)-C(25A)-H(25F)	109.5
H(25E)-C(25A)-H(25F)	109.5
O(6)-Si(1B)-C(22B)	104.6(8)
O(6)-Si(1B)-C(21B)	111.2(14)
C(22B)-Si(1B)-C(21B)	115.5(14)
O(6)-Si(1B)-C(20B)	112.1(13)
C(22B)-Si(1B)-C(20B)	108.1(16)
C(21B)-Si(1B)-C(20B)	105.5(18)
Si(1B)-C(20B)-H(20G)	109.5

Si(1B)-C(20B)-H(20H)	109.5
H(20G)-C(20B)-H(20H)	109.5
Si(1B)-C(20B)-H(20I)	109.5
H(20G)-C(20B)-H(20I)	109.5
H(20H)-C(20B)-H(20I)	109.5
Si(1B)-C(21B)-H(21G)	109.5
Si(1B)-C(21B)-H(21H)	109.5
H(21G)-C(21B)-H(21H)	109.5
Si(1B)-C(21B)-H(21I)	109.5
H(21G)-C(21B)-H(21I)	109.5
H(21H)-C(21B)-H(21I)	109.5
C(24B)-C(22B)-C(23B)	116(2)
C(24B)-C(22B)-C(25B)	110(2)
C(23B)-C(22B)-C(25B)	113(2)
C(24B)-C(22B)-Si(1B)	108.0(18)
C(23B)-C(22B)-Si(1B)	106(2)
C(25B)-C(22B)-Si(1B)	103.4(15)
C(22B)-C(23B)-H(23G)	109.5
C(22B)-C(23B)-H(23H)	109.5
H(23G)-C(23B)-H(23H)	109.5
C(22B)-C(23B)-H(23I)	109.5
H(23G)-C(23B)-H(23I)	109.5
H(23H)-C(23B)-H(23I)	109.5
C(22B)-C(24B)-H(24G)	109.5
C(22B)-C(24B)-H(24H)	109.5
H(24G)-C(24B)-H(24H)	109.5
C(22B)-C(24B)-H(24I)	109.5
H(24G)-C(24B)-H(24I)	109.5
H(24H)-C(24B)-H(24I)	109.5
C(22B)-C(25B)-H(25G)	109.5
C(22B)-C(25B)-H(25H)	109.5
H(25G)-C(25B)-H(25H)	109.5
C(22B)-C(25B)-H(25I)	109.5
H(25G)-C(25B)-H(25I)	109.5

H(25H)-C(25B)-H(25I) 109.5

Table A3.4. *Anisotropic displacement parameters ($Å^2 x\ 10^3$) for* ***263****. The anisotropic displacement factor exponent takes the form:* $-2\pi^2[\ h^2\ a^{*2}U^{11} + \ldots + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	49(1)	55(2)	61(2)	-1(1)	5(1)	5(1)
C(2)	53(2)	57(2)	76(2)	0(1)	-3(1)	2(1)
O(1)	56(1)	66(1)	133(2)	-5(1)	7(1)	-7(1)
C(17)	71(3)	76(3)	191(6)	-23(3)	-7(3)	-20(2)
C(3)	59(2)	53(2)	79(2)	-10(1)	-6(2)	4(1)
C(4)	50(1)	55(1)	49(1)	-4(1)	-4(1)	12(1)
O(2)	56(1)	66(1)	70(1)	-8(1)	7(1)	13(1)
C(11)	44(1)	51(1)	46(1)	-1(1)	0(1)	5(1)
C(12)	41(1)	54(1)	49(1)	3(1)	-4(1)	9(1)
C(5)	45(1)	87(2)	54(2)	12(2)	-11(1)	2(1)
C(6)	58(2)	54(2)	45(1)	8(1)	-8(1)	-1(1)
O(3)	78(2)	96(2)	51(1)	5(1)	-14(1)	-11(1)
C(18)	111(3)	137(4)	49(2)	12(2)	-13(2)	-15(3)
C(7)	51(1)	62(2)	50(1)	11(1)	3(1)	2(1)
O(4)	67(1)	115(2)	60(1)	11(1)	14(1)	12(1)
C(19)	67(2)	109(3)	92(3)	-31(2)	4(2)	13(2)
C(8)	43(1)	64(2)	60(2)	8(1)	-2(1)	1(1)
O(5)	43(1)	121(2)	78(2)	-9(1)	-2(1)	-2(1)
C(13)	43(1)	54(1)	55(1)	1(1)	-8(1)	3(1)
N(1)	61(2)	55(1)	106(2)	-3(1)	-8(2)	1(1)
C(16)	78(2)	66(2)	110(3)	-6(2)	-8(2)	-12(2)
C(15)	72(2)	59(2)	118(3)	7(2)	8(2)	9(2)
C(14)	54(2)	58(2)	79(2)	4(1)	2(1)	14(1)
C(9)	50(1)	68(2)	53(1)	2(1)	-14(1)	2(1)
C(10)	61(2)	57(2)	46(1)	1(1)	-5(1)	4(1)

O(6)	76(1)	70(1)	51(1)	10(1)	-10(1)	4(1)
Si(1)	68(1)	65(1)	38(1)	-4(1)	-4(1)	14(1)
C(20)	58(4)	254(17)	102(7)	17(9)	-17(4)	5(7)
C(21)	196(13)	109(7)	62(5)	-15(4)	15(7)	59(8)
C(22)	132(8)	89(5)	62(5)	18(4)	-9(6)	19(6)
C(23)	340(20)	61(5)	118(9)	0(5)	41(14)	16(10)
C(24)	122(8)	228(17)	169(14)	92(13)	-25(9)	-73(10)
C(25)	250(20)	160(19)	86(10)	48(11)	-43(13)	27(19)
Si(1A)	71(3)	140(4)	71(2)	40(3)	7(2)	27(3)
C(20A)	220(30)	154(18)	72(12)	-25(13)	-29(19)	0(20)
C(21A)	147(16)	250(30)	82(12)	18(16)	39(12)	103(17)
C(22A)	128(12)	118(10)	73(9)	27(8)	1(10)	38(9)
C(23A)	148(16)	220(30)	160(30)	80(20)	25(17)	94(17)
C(24A)	220(30)	145(16)	89(14)	17(14)	-1(19)	-39(19)
C(25A)	230(40)	200(30)	64(11)	72(16)	-16(16)	10(30)
Si(1B)	76(4)	66(4)	59(4)	1(3)	-19(3)	6(4)
C(20B)	140(30)	150(20)	90(20)	-2(19)	-1(18)	90(20)
C(21B)	120(30)	150(30)	78(19)	-39(18)	-17(18)	-20(20)
C(22B)	111(14)	143(16)	42(9)	22(10)	7(10)	19(11)
C(23B)	150(30)	210(30)	110(30)	10(20)	-12(19)	90(20)
C(24B)	120(20)	100(20)	54(14)	21(12)	18(12)	10(16)
C(25B)	120(20)	140(20)	76(15)	30(15)	19(15)	-37(19)

Table A3.5. *Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for* ***263***.

	x	y	z	U(eq)
H(1A)	1682	6184	4027	66
H(1B)	1069	6639	3505	66
H(17A)	-481	3840	2996	169
H(17B)	-1929	3706	3415	169
H(17C)	2	3320	3510	169
H(3)	2730	4033	3096	76
H(5A)	2712	6610	2617	74
H(5B)	2932	7766	2541	74
H(18A)	5380	7657	1345	148
H(18B)	4113	6900	1071	148
H(18C)	5928	6526	1287	148
H(19A)	10182	6167	2017	134
H(19B)	8672	5512	1780	134
H(19C)	8703	5713	2364	134
H(16A)	7842	9315	2990	127
H(16B)	8693	8873	3482	127
H(16C)	7528	9847	3511	127
H(15A)	4421	9235	2951	100
H(15B)	4214	9614	3514	100
H(14A)	2057	8326	3230	77
H(14B)	2941	8139	3764	77
H(9A)	7460	6314	3623	69
H(9B)	7375	7269	3976	69
H(10)	4523	7006	4182	66
H(20A)	8824	5075	4695	207
H(20B)	8645	5417	5260	207
H(20C)	8757	6223	4829	207
H(21A)	5337	7215	5108	184

H(21B)	5252	6506	5581	184
H(21C)	3640	6567	5210	184
H(23A)	5308	2864	4783	260
H(23B)	7006	3531	4726	260
H(23C)	5408	3679	4356	260
H(24A)	2387	3727	5055	260
H(24B)	2523	4740	4754	260
H(24C)	2499	4751	5347	260
H(25A)	4767	3909	5823	246
H(25B)	6307	4673	5722	246
H(25C)	6533	3537	5575	246
H(20D)	7421	6375	5083	221
H(20E)	6109	6394	5542	221
H(20F)	5799	7109	5079	221
H(21D)	2214	6394	4938	239
H(21E)	2578	5827	5447	239
H(21F)	1776	5245	4985	239
H(23D)	8307	3627	5030	265
H(23E)	8273	4739	4833	265
H(23F)	7583	3866	4487	265
H(24D)	5032	3049	4580	229
H(24E)	3558	3875	4616	229
H(24F)	3841	3119	5064	229
H(25D)	6896	4160	5773	249
H(25E)	5126	3550	5736	249
H(25F)	5078	4726	5775	249
H(20G)	7348	3480	4825	191
H(20H)	8842	4237	4670	191
H(20I)	7498	3847	4263	191
H(21G)	6917	6708	5078	174
H(21H)	8618	6130	4904	174
H(21I)	7720	5862	5421	174
H(23G)	3536	5849	5596	230
H(23H)	1902	5391	5313	230

H(23I)	3225	6091	5023	230
H(24G)	4975	4413	5883	137
H(24H)	6220	3839	5507	137
H(24I)	4324	3420	5623	137
H(25G)	3693	4056	4412	170
H(25H)	2017	4067	4761	170
H(25I)	3481	3246	4839	170

Table A3.6. *Torsion angles [°] for* ***263****.*

C(11)-C(1)-C(2)-O(1)	-179.9(3)
C(11)-C(1)-C(2)-C(3)	-1.2(4)
C(3)-C(2)-O(1)-C(17)	-2.9(6)
C(1)-C(2)-O(1)-C(17)	175.5(4)
O(1)-C(2)-C(3)-C(4)	179.0(3)
C(1)-C(2)-C(3)-C(4)	0.4(4)
C(2)-C(3)-C(4)-O(2)	-178.6(3)
C(2)-C(3)-C(4)-C(11)	0.5(4)
C(2)-C(1)-C(11)-C(10)	-118.0(3)
C(2)-C(1)-C(11)-C(12)	124.5(3)
C(2)-C(1)-C(11)-C(4)	1.3(3)
O(2)-C(4)-C(11)-C(1)	177.9(3)
C(3)-C(4)-C(11)-C(1)	-1.2(3)
O(2)-C(4)-C(11)-C(10)	-59.8(3)
C(3)-C(4)-C(11)-C(10)	121.2(3)
O(2)-C(4)-C(11)-C(12)	53.1(3)
C(3)-C(4)-C(11)-C(12)	-125.9(3)
C(1)-C(11)-C(12)-C(5)	-75.7(3)
C(10)-C(11)-C(12)-C(5)	160.0(2)
C(4)-C(11)-C(12)-C(5)	42.2(3)
C(1)-C(11)-C(12)-C(14)	46.4(3)
C(10)-C(11)-C(12)-C(14)	-77.9(3)

C(4)-C(11)-C(12)-C(14)	164.3(2)
C(1)-C(11)-C(12)-C(13)	157.7(2)
C(10)-C(11)-C(12)-C(13)	33.4(3)
C(4)-C(11)-C(12)-C(13)	-84.4(3)
C(11)-C(12)-C(5)-C(6)	-102.2(3)
C(14)-C(12)-C(5)-C(6)	132.8(3)
C(13)-C(12)-C(5)-C(6)	19.1(4)
C(12)-C(5)-C(6)-C(7)	-10.2(5)
C(12)-C(5)-C(6)-O(3)	170.9(3)
C(7)-C(6)-O(3)-C(18)	-27.5(5)
C(5)-C(6)-O(3)-C(18)	151.4(4)
O(3)-C(6)-C(7)-O(4)	-0.3(5)
C(5)-C(6)-C(7)-O(4)	-179.0(3)
O(3)-C(6)-C(7)-C(8)	178.4(3)
C(5)-C(6)-C(7)-C(8)	-0.3(5)
C(6)-C(7)-O(4)-C(19)	-112.5(4)
C(8)-C(7)-O(4)-C(19)	68.6(4)
C(6)-C(7)-C(8)-O(5)	-179.1(3)
O(4)-C(7)-C(8)-O(5)	-0.2(5)
C(6)-C(7)-C(8)-C(13)	0.4(5)
O(4)-C(7)-C(8)-C(13)	179.2(3)
O(5)-C(8)-C(13)-N(1)	69.2(4)
C(7)-C(8)-C(13)-N(1)	-110.3(3)
O(5)-C(8)-C(13)-C(9)	-52.4(4)
C(7)-C(8)-C(13)-C(9)	128.1(3)
O(5)-C(8)-C(13)-C(12)	-171.1(3)
C(7)-C(8)-C(13)-C(12)	9.4(4)
C(5)-C(12)-C(13)-N(1)	106.2(3)
C(11)-C(12)-C(13)-N(1)	-127.9(2)
C(14)-C(12)-C(13)-N(1)	-9.9(3)
C(5)-C(12)-C(13)-C(8)	-18.4(3)
C(11)-C(12)-C(13)-C(8)	107.5(3)
C(14)-C(12)-C(13)-C(8)	-134.5(3)
C(5)-C(12)-C(13)-C(9)	-138.9(3)

C(11)-C(12)-C(13)-C(9)	-13.0(3)
C(14)-C(12)-C(13)-C(9)	105.0(3)
C(8)-C(13)-N(1)-C(15)	110.6(3)
C(9)-C(13)-N(1)-C(15)	-128.1(3)
C(12)-C(13)-N(1)-C(15)	-16.0(4)
C(8)-C(13)-N(1)-C(16)	-29.0(4)
C(9)-C(13)-N(1)-C(16)	92.3(4)
C(12)-C(13)-N(1)-C(16)	-155.7(3)
C(16)-N(1)-C(15)-C(14)	177.3(4)
C(13)-N(1)-C(15)-C(14)	36.6(4)
N(1)-C(15)-C(14)-C(12)	-41.5(4)
C(5)-C(12)-C(14)-C(15)	-90.6(3)
C(11)-C(12)-C(14)-C(15)	143.6(3)
C(13)-C(12)-C(14)-C(15)	30.9(3)
N(1)-C(13)-C(9)-C(10)	98.0(3)
C(8)-C(13)-C(9)-C(10)	-138.2(2)
C(12)-C(13)-C(9)-C(10)	-13.0(3)
C(13)-C(9)-C(10)-O(6)	156.8(2)
C(13)-C(9)-C(10)-C(11)	34.6(3)
C(1)-C(11)-C(10)-O(6)	68.6(3)
C(12)-C(11)-C(10)-O(6)	-166.5(2)
C(4)-C(11)-C(10)-O(6)	-46.8(3)
C(1)-C(11)-C(10)-C(9)	-167.3(2)
C(12)-C(11)-C(10)-C(9)	-42.4(3)
C(4)-C(11)-C(10)-C(9)	77.3(3)
C(9)-C(10)-O(6)-Si(1B)	65.4(8)
C(11)-C(10)-O(6)-Si(1B)	-175.9(7)
C(9)-C(10)-O(6)-Si(1A)	117.8(4)
C(11)-C(10)-O(6)-Si(1A)	-123.5(4)
C(9)-C(10)-O(6)-Si(1)	83.8(3)
C(11)-C(10)-O(6)-Si(1)	-157.5(2)
C(10)-O(6)-Si(1)-C(21)	38.4(7)
C(10)-O(6)-Si(1)-C(22)	157.0(4)
C(10)-O(6)-Si(1)-C(20)	-84.8(7)

O(6)-Si(1)-C(22)-C(24)	-67.2(10)
C(21)-Si(1)-C(22)-C(24)	52.5(11)
C(20)-Si(1)-C(22)-C(24)	174.2(10)
O(6)-Si(1)-C(22)-C(23)	57.0(10)
C(21)-Si(1)-C(22)-C(23)	176.7(11)
C(20)-Si(1)-C(22)-C(23)	-61.6(11)
O(6)-Si(1)-C(22)-C(25)	170.4(13)
C(21)-Si(1)-C(22)-C(25)	-69.9(14)
C(20)-Si(1)-C(22)-C(25)	51.8(14)
C(10)-O(6)-Si(1A)-C(21A)	57.3(14)
C(10)-O(6)-Si(1A)-C(22A)	-167.5(8)
C(10)-O(6)-Si(1A)-C(20A)	-55.2(12)
O(6)-Si(1A)-C(22A)-C(23A)	45.4(19)
C(21A)-Si(1A)-C(22A)-C(23A)	180(2)
C(20A)-Si(1A)-C(22A)-C(23A)	-66(2)
O(6)-Si(1A)-C(22A)-C(24A)	-73.4(15)
C(21A)-Si(1A)-C(22A)-C(24A)	60.7(19)
C(20A)-Si(1A)-C(22A)-C(24A)	175.5(16)
O(6)-Si(1A)-C(22A)-C(25A)	171(2)
C(21A)-Si(1A)-C(22A)-C(25A)	-55(2)
C(20A)-Si(1A)-C(22A)-C(25A)	60(2)
C(10)-O(6)-Si(1B)-C(22B)	121.0(10)
C(10)-O(6)-Si(1B)-C(21B)	-4.3(17)
C(10)-O(6)-Si(1B)-C(20B)	-122.2(18)
O(6)-Si(1B)-C(22B)-C(24B)	170.2(19)
C(21B)-Si(1B)-C(22B)-C(24B)	-67(3)
C(20B)-Si(1B)-C(22B)-C(24B)	51(2)
O(6)-Si(1B)-C(22B)-C(23B)	-65.0(19)
C(21B)-Si(1B)-C(22B)-C(23B)	58(2)
C(20B)-Si(1B)-C(22B)-C(23B)	175(2)
O(6)-Si(1B)-C(22B)-C(25B)	53.7(19)
C(21B)-Si(1B)-C(22B)-C(25B)	176(2)
C(20B)-Si(1B)-C(22B)-C(25B)	-66(2)

A3.2 REFERENCES

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(2) Sheldrick, G. M. *Acta Cryst.* **2015**, *C71*, 3.

(3) Müller, P. *Crystallogr. Rev.* **2009**, *15*, 57.

(4) Parsons, S.; Flack, H. D.; Wagner, T. *Acta Cryst.* **2013**, *B69*, 249.

Chapter 4

Development of Radical Deoxychlorination Reactions: Preparation of Hindered Alkyl Chlorides†

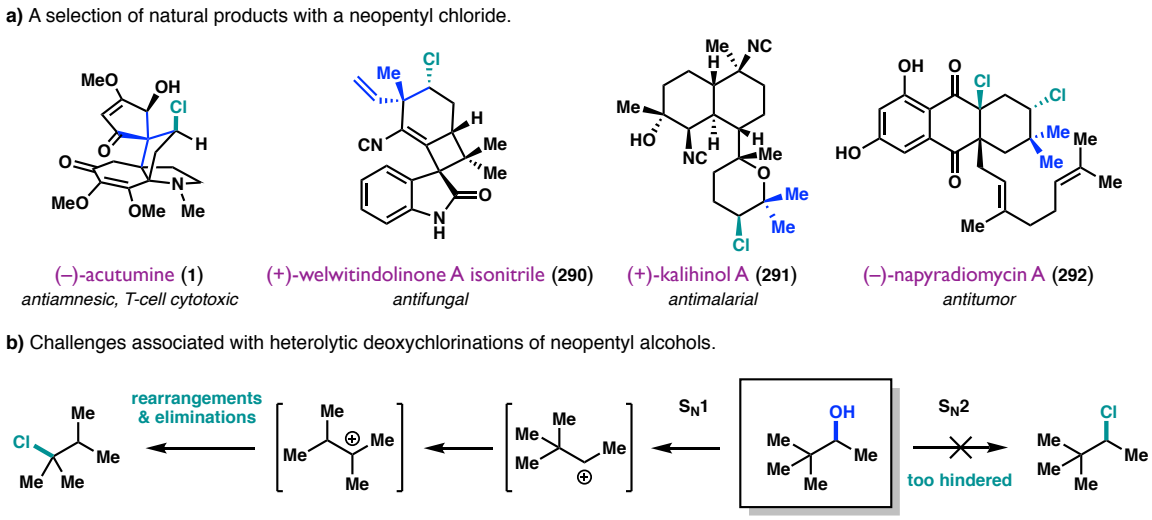
4.1 INTRODUCTION

Alkyl chlorides are useful building blocks for organic synthesis,[1–3] and the chloride substituent is present in many natural products and bioactive compounds (**1** and **290**–**292**,[4–7] Figure 4.1a).[8–10] In the context of fine chemical synthesis, this functionality is often introduced by deoxychlorination of alcohols with reagents such as thionyl chloride[11–13] or CCl_4/PPh_3 (Appel conditions),[14] which proceed by polar mechanisms involving heterolytic cleavage of the C–O bond.[15–20] Depending on the substrate, these reactions can proceed by

† Portions of this chapter were adapted from the following communication: Su, J. Y.; Grünenfelder, D. C.; Takeuchi, K.; Reisman, S. E. *Org. Lett.* **2018**, *20*, 4912, DOI: 10.1021/acs.orglett.8b02045, copyright 2018 American Chemical Society. Deoxychlorination studies of cesium oxalates were conducted in collaboration with Dr. Justin Y. Su (post-doc, Reisman group) and Dr. Kohei Takeuchi (visiting graduate student, Tanino group).

either S_N1 (3° alcohols) or S_N2 (1° alcohols) pathways. Hindered 2° alcohols (such as neopentyl alcohols) are typically the most difficult substrates for deoxychlorination: S_N1 pathways can result in carbocation rearrangement and competing elimination reactions, while S_N2 pathways are impeded by steric hindrance of the nucleophile trajectory (Figure 4.1b).

Figure 4.1 *Natural products containing neopentyl chlorides and challenges in heterolytic deoxychlorination of hindered alcohols.*

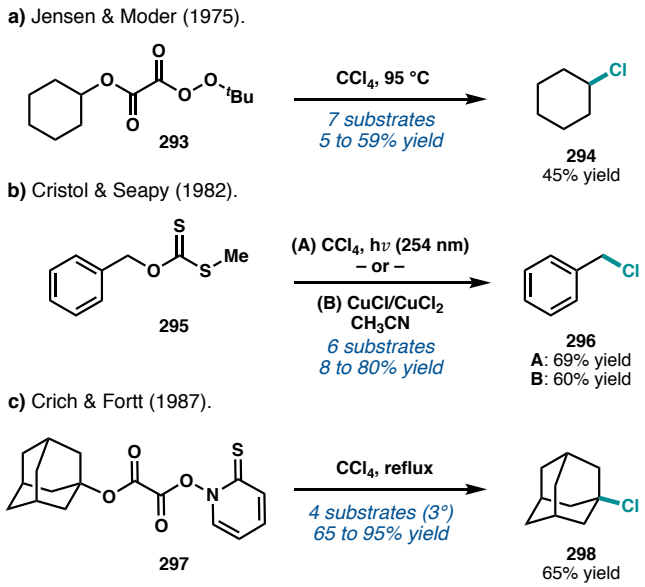


In recent years, chemists have begun to address these limitations by developing new reactions that afford alkyl chlorides via reductive chlorination of ketones,[21] C(sp^3)–H chlorination,[22–30] and hydrogen atom transfer-mediated olefin hydrochlorination[31–33] and alkenyl chloride hydrogenation.[34,35] Nonetheless, a mild method for the radical deoxychlorination of hindered 2° and 3° alcohols would provide a new tool for the preparation of complex alkyl chlorides.

As part of our synthetic efforts toward a total synthesis of (–)-acutumine (**1**), we required a method to prepare a secondary neopentyl chloride. We envisioned that a radical

deoxychlorination could circumvent some of the challenges presented by heterolytic deoxychlorination, since chlorine atom transfer to a highly reactive carbon-centered radical would likely be less sensitive to steric encumbrance, while also avoiding counterion and aggregation effects.[36–43] The feasibility of radical deoxychlorination was first established in 1975 by Jensen and Moder, who reported that thermolysis of peroxyglyoxalates in the presence of CCl_4 produced the corresponding alkyl chlorides (Scheme 4.1a).[44] Subsequently, Crich and Fortt disclosed a related deoxychlorination of tertiary alcohols using *N*-hydroxypyridine-2-thionyl oxalates as a more practical activating group (Scheme 4.c).[45,46] In 1982, Cristol and Seapy disclosed that photolysis of methyl xanthates with 254 nm light in CCl_4 also gives rise to C–Cl bond formation (Scheme 4.1b).[47,48]

Scheme 4.1 *Literature examples of radical deoxychlorination reactions.*



While promising, these early methods suffer from modest yields and limited substrate scope, which might result from the formation of promiscuous $^{\bullet}CCl_3$ radicals that can lead to side product formation. It was anticipated that catalytic generation of carbon-

centered radicals under mild conditions using visible light could minimize non-productive pathways and improve the chlorination yield. Moreover, such methods would avoid the formation of shock-sensitive peroxyglyoxalates and the use of carbon tetrachloride, a carcinogen and ozone depleter.[49]

At the outset of this project, we hypothesized that the use of visible, rather than UV light, would be important since the calculated C–Cl bond dissociation energy (BDE) of the desired chlorination products, such as (–)-acutumine (**1**), are in the UVA region (357 nm, Table 4.1).[50] Thus, the use of UVC light might result in undesired product C–Cl bond homolysis under the reaction conditions. Many of the known chlorinating reagents, such as NCS, hexachloroethane, and HCA have BDEs that lie between the product C–Cl bond and the region for visible light.[51,52] Thus, Cl-abstraction of the chloride source by the substrate carbon centered radical was deemed favorable.

Table 4.1. *BDEs of a selection of chloride sources and product-like C–Cl bonds.*

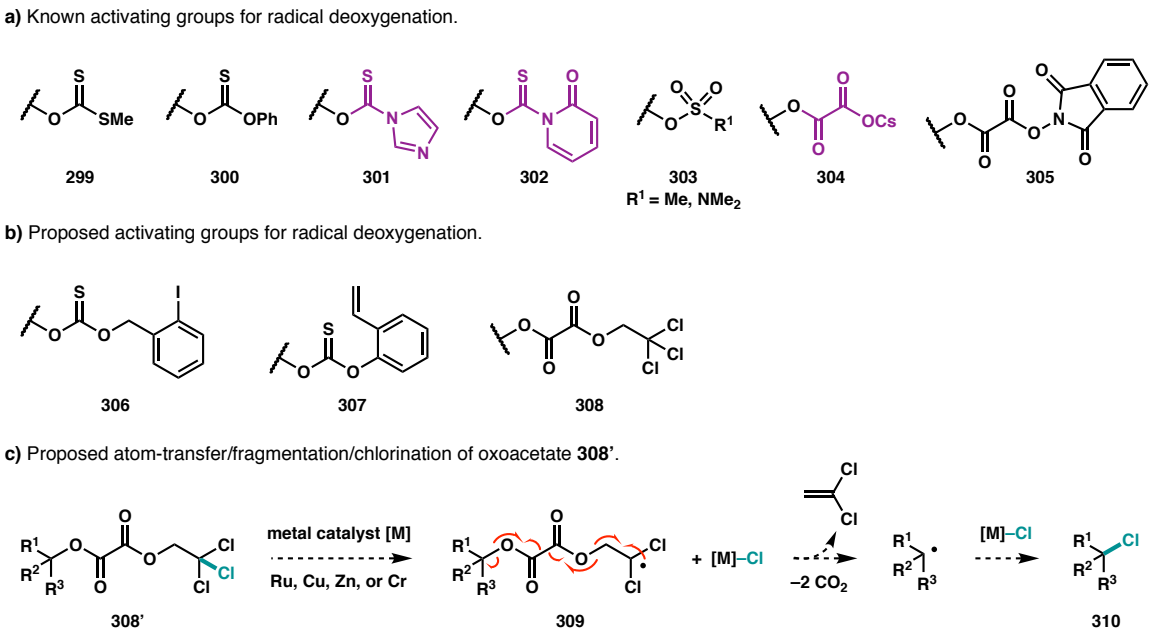
Cl-source	BDE (kcal/mol)	BDE (nm)*
$Cl–CCl_2COCCl_3$	54.3	498
$Cl–CCl_3$	70.9	381
$Cl–CCl_2CCl_3$	72.6	372
NCS	73.4	368
$Cl–C(CH_3)_3$	84.1	321
alkyl chloride	**BDE (kcal/mol)**	**BDE (nm)***
C–Cl	84.0	322
Acutumine C–Cl**	75.7	357

*as calculated from kcal/mol (Planck-Einstein equation)
** Spartan: unrestricted HF-DFT with literature control.

A large variety of activating groups have been developed in order to promote radical deoxygenations (Figure 4.2a),[53–56] including xanthates (**299**),[57–59] thiocarbamates (**301**),[60,61] and oxalates[62,63] (**304** and **305**). At the outset of our investigations into a radical

deoxychlorination, we were interested in investigating a broad set of activating groups in the presence of a number of chloride sources, such as those shown in Table 4.1. Inspired by the known Barton decarboxylation[39,64] and deoxygenation,[57] we also proposed a number of novel fragmentation groups (Figure 4.2b, **306**–**308**) that might afford the desired radical deoxygenation as well. For one fragmentation group, trichloroethyl oxoacetate **308'**, we envisioned that Cl–atom abstraction and oxalate fragmentation might be followed by Cl-atom transfer[65] to effect the desired deoxychlorination, without the need for an additional chloride source (Figure 4.2c). Over the course of our investigations into the activating groups listed in Figure 4.2, radical deoxychlorinations were successfully performed solely with thiocarbamate **301**, pyridone **302**, and cesium oxalate **304** activating groups (Figure 4.2a) utilizing photoredox catalysis. The specific details of these investigations are outlined in this chapter.

Figure 4.2 *Known and proposed activating groups for radical deoxychlorination.*



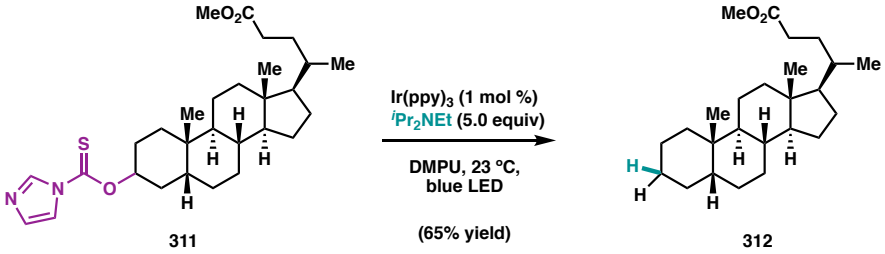
4.2 EARLY INVESTIGATIONS INTO PHOTOREDOX-MEDIATED DEOXYCHLORINATIONS

4.2.1 Preliminary Studies with Imidazolyl Thiocarbamates

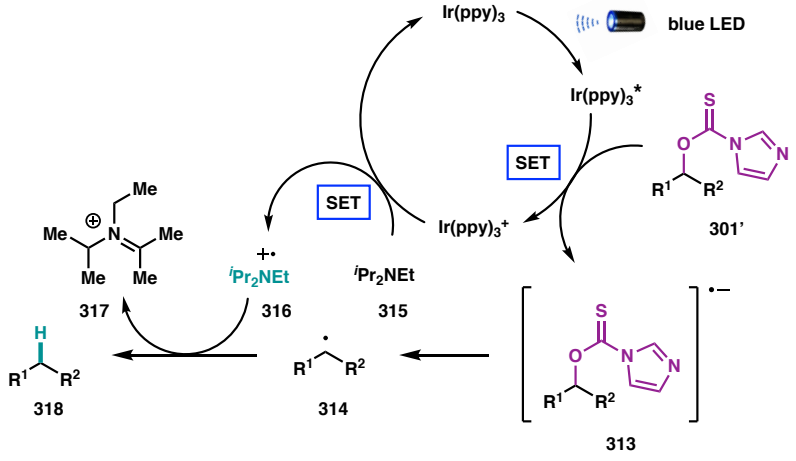
Our efforts within the arena of photoredox catalysis began with fragmentation groups that have been utilized in deoxygenation reactions, and the first screens were set up utilizing these fragmentation conditions in the presence of a chloride source. Specifically, Fensterbank and coworkers demonstrated in 2014 that imidazolyl thiocarbamate **311** undergoes mild deoxygenation in the presence of $Ir(ppy)_3$ and Hünig's base as a reductant (Scheme 4.2a).[61,66] The authors proposed the deoxygenation is initiated by single electron

Scheme 4.2 *Photoredox-mediated deoxygenation of imidazolyl thiocarbamates.*

a) Fensterbank, Goddard, and Ollivier (2014).



b) Proposed mechanism of deoxygenation.

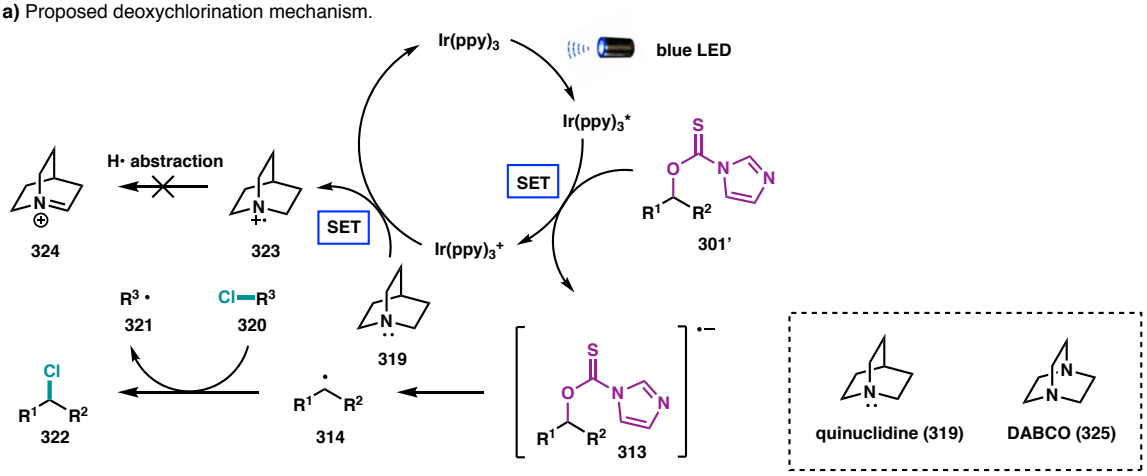


transfer (SET) of excited state $Ir(ppy)_3^*$ to thiocarbamate **301'** (Scheme 4.2b), which fragments to afford carbon centered radical **314**. Hünig's base (**315**) may then undergo SET with the iridium catalyst to regenerate $Ir(ppy)_3$. Finally, hydrogen atom transfer (HAT) of the resulting aminyl radical **316** may afford the desired deoxygenated product **318**.

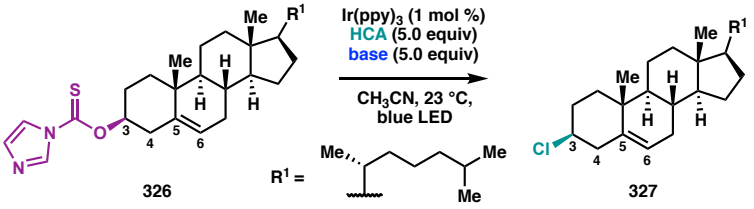
For the purposes of a deoxychlorination reaction, it was hypothesized that 1) employing a reductant which could not undergo HAT with the carbon centered radical, such as quinuclidine (**319**, Scheme 4.3a), and 2) conducting the reaction in the presence of

Scheme 4.3 *Preliminary screen of deoxychlorination with HCA.*

a) Proposed deoxychlorination mechanism.



b) Initial hit on activated cholesterol **326**.



entry	base	isolated yield
1	quinuclidine (319)	57%
2	$^iPr_2NEt$	0%[a]
3	DABCO (325)	0%

[a] 78% of 326 recovered.

c) Application to menthol substrate **328**.

a chloride source **320** might afford the desired chlorination products. However, at this stage the fate of the resulting chloride source radical **321** and quinuclidine aminyl radical **323** were uncertain, and it was envisioned that these species could negatively affect the chlorination reaction.

Initial screening on activated cholesterol **326** was conducted with HCA as the chloride source (Scheme 4.3b).‡ Indeed, in the presence of quinuclidine (**319**), desired chloride **327** was obtained in good yield (entry 1), while no product was observed when Hünig's base or DABCO (**325**) were employed (entries 2 and 3). Unfortunately, this reaction did not translate well to other activated alcohols, which was not surprising given that cholesterol is a privileged substrate for deoxyfunctionalization: it has been proposed that these reactions proceed via intermediacy of an *i*-steroid (C3,C5-cyclo analogue).[67,68] It is hypothesized that the assistance from the C5–C6 olefin may stabilize the resulting carbocation or radical at C3, in heterolytic or homolytic mechanisms respectively.

With respect to other substrates, when activated menthol **328** was subjected to the reaction conditions (Scheme 4.3c), only traces of neomenthyl chloride **329** and menthyl chloride **300** were observed by ^{1}H NMR, along with 80% unreacted thiocarbamate **328** and larger quantities of transacylated ester **331**. These results indicated that 1) fragmentation of an unactivated or unstabilized secondary alcohol, as opposed to cholesterol **326**, was much more challenging, and that 2) some hydrolysis to the starting alcohol may be occurring, which when acylated with HCA *in situ* could form ester **331**. It thus became

‡ Initial screening was performed in collaboration with Sanae Izumi, a visiting graduate student from the Takemoto group.

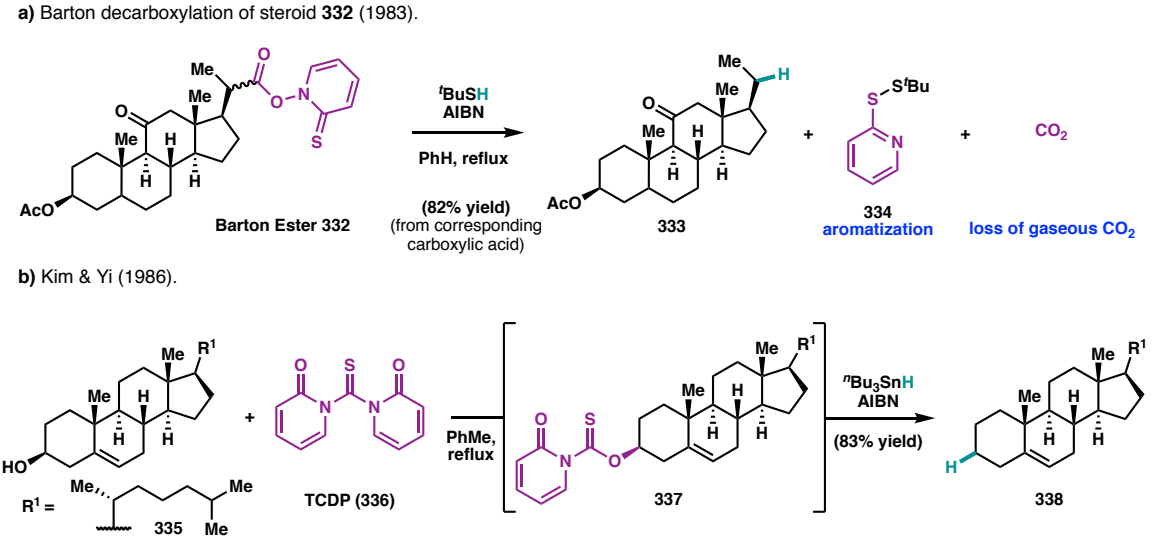
apparent that there was a need to replace the imidazolyl thiocarbamate activating group with a motif that would be more prone to deoxygenation on an unactivated, secondary alcohol in order generate the desired carbon centered radical.

4.2.2 Renaissance of the Pyridone Activating Group

Along these lines, the activating group of the Barton *decarboxylation* reaction (Scheme 4.4a),[39,64] a thiopyridone, was of particular interest. In this case, aromatization of the pyridone group and release of gaseous CO_2 are the main driving forces which enable smooth decarboxylation, even of unactivated 2° acids. We thus reasoned that an analogous fragmentation group could resolve our challenges with conversion in a radical *deoxygenation* reaction.

Interestingly, Kim and Yi reported on such an activating group in 1986 (Scheme 4.4b),[69] although it has not been widely employed in the literature. The authors reported

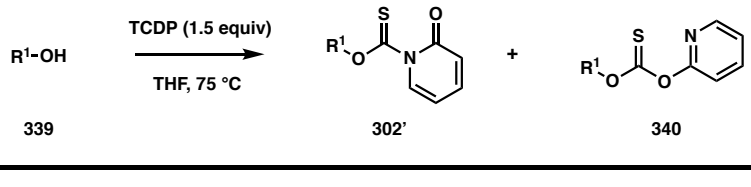
Scheme 4.4 *Barton decarboxylation thiopyridone* ***332*** *and deoxygenation of* ***335****.*



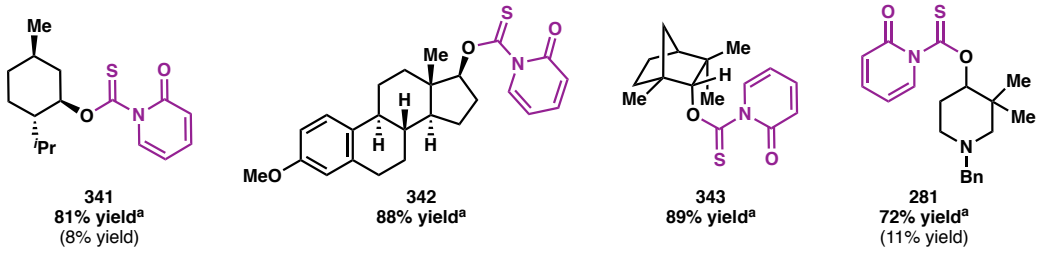
that pyridone **337** could be formed from alcohol **335** and thiocarbonyl dipyridone (TCDP, **336**), a reagent which the authors developed primarily for the formation of nitriles, carbodiimides, isocthiocyanates and cyclic thionocarbonates in this particular publication. Subsequent *in situ* deoxygenation of pyridone **337** was then accomplished by the addition of $^{n}Bu_3SnH$ and AIBN, affording deoxygenated product **338** in excellent yield. We were particularly excited about employing this thiopyridone activating group for secondary alcohols since 1) its formation occurs in a single step from commercially available TCDP, and 2) its fragmentation should be more facile on challenging 2° substrates given the driving forces mentioned above.

A number of activated alcohols were then synthesized utilizing TCDP; however, it was found that the literature reported conditions in refluxing PhMe afforded large quantities of the rearranged pyridyl thiocarbonate product (**340**, Table 4.2). Fortunately, running the pyridone formation at 75 °C in THF instead afforded much higher yields of the desired pyridones **302'** and diminished quantities (0–11%) of the undesired thiocarbonate

Table 4.2. *Synthesis of pyridone substrates.*



339 302' 340



341
81% yield[a]
(8% yield)

342
88% yield[a]

343
89% yield[a]

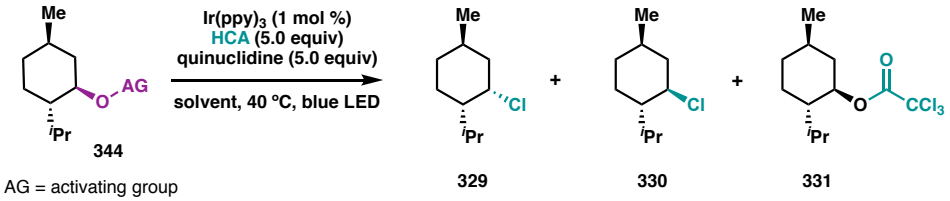
281
72% yield[a]
(11% yield)

[a] Isolated yields are reported. [b] Yields of pyridyl thiocarbonate 340 given in brackets.

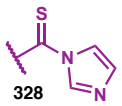
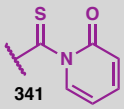
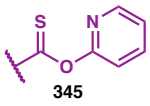
products **340**. The identity of these acylated species was confirmed via ^{15}N–^{1}H-HMBC, as a pyridine nitrogen (~290 ppm, with respect to NH_3) is much more downfield than that of a pyridone nitrogen (~200 ppm, with respect to NH_3). A number of activated alcohols were synthesized according to this procedure (**281** and **341–343**, Table 4.2), and the deoxychlorination conditions with $Ir(ppy)_3$, quinuclidine, and HCA were then screened on menthol derivative **341**.

In a preliminary screen, imidazolyl thiocarbamate, pyridone, and pyridyl thiocarbonate activating groups were evaluated (Table 4.3, entries 1–3). Compared to the imidazolyl thiocarbamate **328** (entry 1), we were gratified that the use of pyridone **341** did

Table 4.3. *First screen utilizing the pyridone activating group.*



AG = activating group

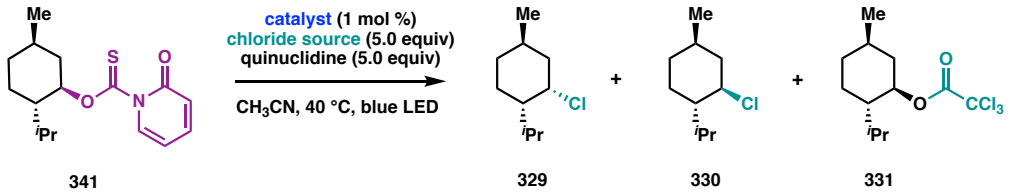
entry	activating group	solvent	yield[a] 329	330	331	344 (SM)
1	 328	CH_3CN	trace	trace	trace	80%
2	 341	CH_3CN	17%	15%	7%	0%
3	 345	CH_3CN	3%	10%	5%	trace
4	341	CH_2Cl_2	1%	0%	9%	90%
5	341	dioxane	0%	0%	0%	98%
6	341	dioxane/DMSO (4:1)	0%	0%	0%	100%

[a] Determined by ^{1}H NMR with pyrazine as an internal standard.

indeed give complete conversion of the starting material and a 32% yield of menthyl chloride diastereomers **329** and **330** (entry 2). Formation of acylated species **331** was mitigated as well (7%). In contrast, pyridyl thiocarbonate **345** performed poorly, while also showing a slight preference for the formation of menthyl chloride **330** over neomenthyl chloride **329** (entry 3). A brief screen of solvents indicated that the use of polar solvents, such as CH_3CN were preferable (entry 2), where CH_2Cl_2 afforded more modest yields of products (entry 4). Interestingly, the use of ethereal solvents, such as dioxane or a dioxane/DMSO mixture, inhibited the reaction (entries 5–6).

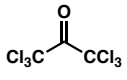
Following the initial chlorination hit (Table 4.4, entry 1), a number of chloride sources were screened, including malonates **283** and **346**, ETCA, and CCl_4 (entries 2–5). Unfortunately, in all cases the chlorination products were formed in considerably diminished yield, which was accompanied by much decreased conversion as well. A brief

Table 4.4. *Chloride source and catalyst screen.*

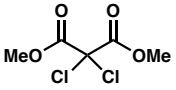


341 329 330 331

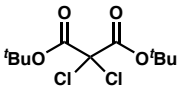
entry	catalyst	Cl-source	yield[a] 329	330	331	341 (SM)
1	$Ir(ppy)_3$	HCA	17%	15%	7%	0%
2	$Ir(ppy)_3$	283	trace	trace	0%	76%
3	$Ir(ppy)_3$	346	4%	0%	0%	8%
4	$Ir(ppy)_3$	ETCA	0%	0%	trace	>95%
5	$Ir(ppy)_3$	CCl_4	1%	trace	2%	82%
6	$Ir(Fppy)_3$	HCA	2%	trace	9%	89%
7	$Cu(dap)_2Cl_2$	HCA	1%	0%	9%	90%



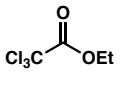
HCA



283



346



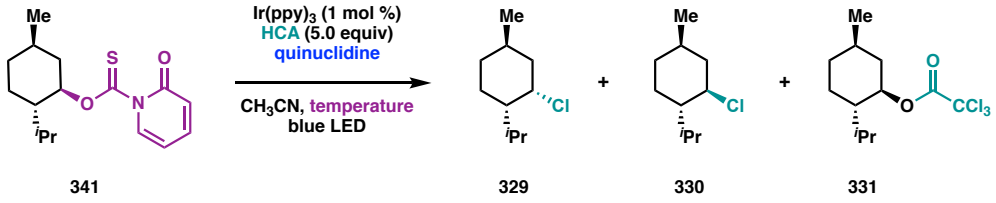
ETCA

[a] Determined by ^1H NMR with pyrazine as an internal standard.

survey of other catalysts, such as $Ir(Fppy)_3$ (entry 6) and $Cu(dap)_2Cl_2$ (entry 7), again showed diminished product formation. Interestingly, the quantity of ester **331** formed in these cases remained similar.

It was hypothesized that temperature could have a large impact on the reaction. Reducing the reaction temperature slightly from 40 °C (entry 1, Table 4.5) to 30 °C (entry 2) resulted in a similar reaction profile. However, increasing the reaction temperature markedly depreciated product formation (entries 3–4). The effects of the base loading were investigated next, which showed that using the standard reaction temperature at 40 °C and 1.0 equivalent of quinuclidine resulted in a dramatic drop in conversion (entry 5), with only trace chloride formation. Gratifyingly, lowering the reaction temperature and maintaining

Table 4.5. *Temperature and base equivalent screen.*



341 329 330 331

entry	base (equiv)	temperature[b]	yield[a] 329	330	331	341 (SM)
1	5.0	40 °C	17%	15%	7%	0%
2	5.0	30 °C	8%	10%	3%	0%
3	5.0	70 °C	7%	9%	5%	0%
4	5.0	80 °C	3%	trace	4%	4%
5	1.0	40 °C	3%	trace	7%	~90%
6	1.0	30 °C	14%	14%	4%	0%
7	1.0	0 °C	13%	19%	4%	0%
8	1.0	–20 °C	7%	15%	4%	0%

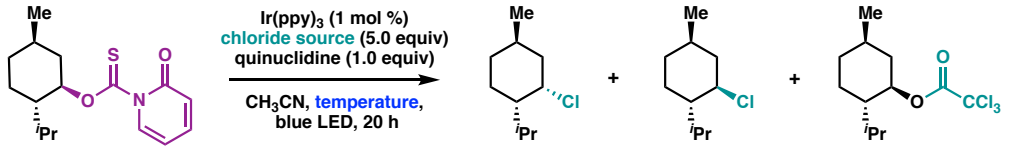
[a] Determined by ^1H NMR with pyrazine as an internal standard.
[b] Based on literature reports and measurements with external thermometer. Number of lamps and distances: 40 °C = 1 lamp, 5 cm; 30 °C = 1 lamp, 5 cm with fan; 70 °C = 1 lamp, 1 cm; 80 °C = 2 lamps, 1 cm; 0 °C and –20 °C = 2 lamps, cryocool controlled bath.

the 1.0 equivalent of base was sufficient to rescue conversion (6–8), with comparable yields of product formation at 0 °C (32% yield combined of **329** and **330**, entry 7). One important note on the difference between entries 1 and 7 is the reaction appearance. At higher temperatures, such as entry 1 at 40 °C, the reaction rapidly turned dark brown/black, whereas it remained orange at 0 °C. It was hypothesized that the remaining starting pyridone **341** most likely is undergoing decomposition, given the low mass balance of the reaction.

Upon successful chlorination at 0 °C, a few chloride sources were surveyed again at that temperature. Compared to HCA (Table 4.6, entry 1), ETCA and malonate **283** still gave depreciated product formation (entries 2–3). However, malonate **283** was of interest because the overall mass balance, with 54% remaining pyridone **341**, was much improved (entry 3). Unfortunately, running the reaction longer to increase conversion did not result in increased product formation (entry 4). Instead, the mass balance was decreased greatly, with only 2% remaining pyridone **341**. Other modifications of the conditions, including changes in concentration (entry 5) and temperature (entry 6) diminished product formation as well. Overall, it became clear that various reaction parameters, including equivalents of base, chloride source, photocatalyst, reaction temperature, concentration, and reaction time did not improve the reaction. Indeed, most runs that provided full conversion had very poor mass balance, indicating that large amounts of decomposition may be occurring. This decomposition may be due the resulting aminyl radical **323** and chloride source radical **321** that are generated *in situ* (Figure 4.4a), whose fate at this stage remain uncertain (*vide supra*). Given these observations, it is not surprising that application to other substrates

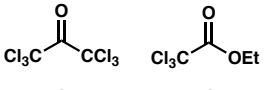
was challenging. In fact, at this stage of reaction development we had discovered other radical deoxychlorinations (*vide infra*), so this particular reaction was deprioritized for the time being. However, these investigations have demonstrated that the pyridone activating group is a valuable tool over the much more commonly utilized imidazolyl thiocarbamate, which in our case gave only trace conversion.

Table 4.6. *Second Cl-source and concentration screen.*

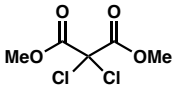


341 329 330 331

entry	Cl-source	temperature	conc.	yield[a] 329	330	331	341 (SM)
1	HCA	0 °C	0.06 M	13%	19%	4%	0%
2	ETCA	0 °C	0.06 M	0%	3%	0%	20%
3	283	0 °C	0.06 M	0%	11%	0%	54%
4[b]	283	0 °C	0.06 M	0%	3%	0%	2%
5	283	0 °C	0.20 M	1%	6%	0%	13%
6	283	40 °C	0.06 M	trace	3%	0%	17%



HCA ETCA



283

[a] Determined by ^{1}H NMR with pyrazine as an internal standard.
[b] Run for 72 h instead of 20 h.

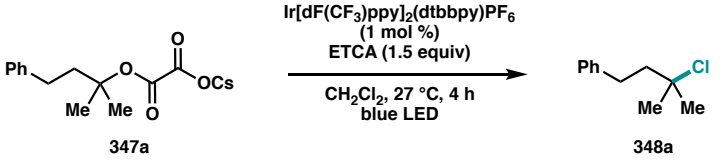
4.3 DEOXYCHLORINATION OF CESIUM OXALATES

4.3.1 Reaction Optimization and Substrate Scope

Whilst investigating the pyridone activating group, cesium oxalates were also surveyed as a possible fragmentation group in a radical deoxychlorination. In our preliminary studies, the deoxychlorination of cesium oxalate **347a** was investigated with Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$ as a catalyst under irradiation with a blue light-emitting diode

(LED).[62,63,70] A variety of chlorine atom sources and solvents were examined, the results of which are summarized in Table 4.7.[71,72] When ETCA was employed in CH_2Cl_2, 3° chloride **348a** was produced in 82% yield (entry 1).[73] Use of NCS or HCA instead of ETCA delivered **348a** in lower yields (entries 2 and 3), and when ethyl chloroacetate (**349**) was employed, none of the chloride product was formed (entry 4). When malonate (**283**)[74] was

Table 4.7. *Optimization studies of cesium oxalate deoxychlorination.*



347a 348a

entry[a]	deviation from standard conditions	yield 345a (%)[b]
1	None	82
2	NCS instead of ETCA	32
3	HCA instead of ETCA	17
4	349 instead of ETCA	0
5	283 instead of ETCA	75
6	CH_3CN instead of CH_2Cl_2	20
7	dioxane instead of CH_2Cl_2	36
8	THF instead of CH_2Cl_2	34
9	With 10 equiv H_2O	72
10	No ETCA	0
11	No [Ir] catalyst	0
12	In dark	0

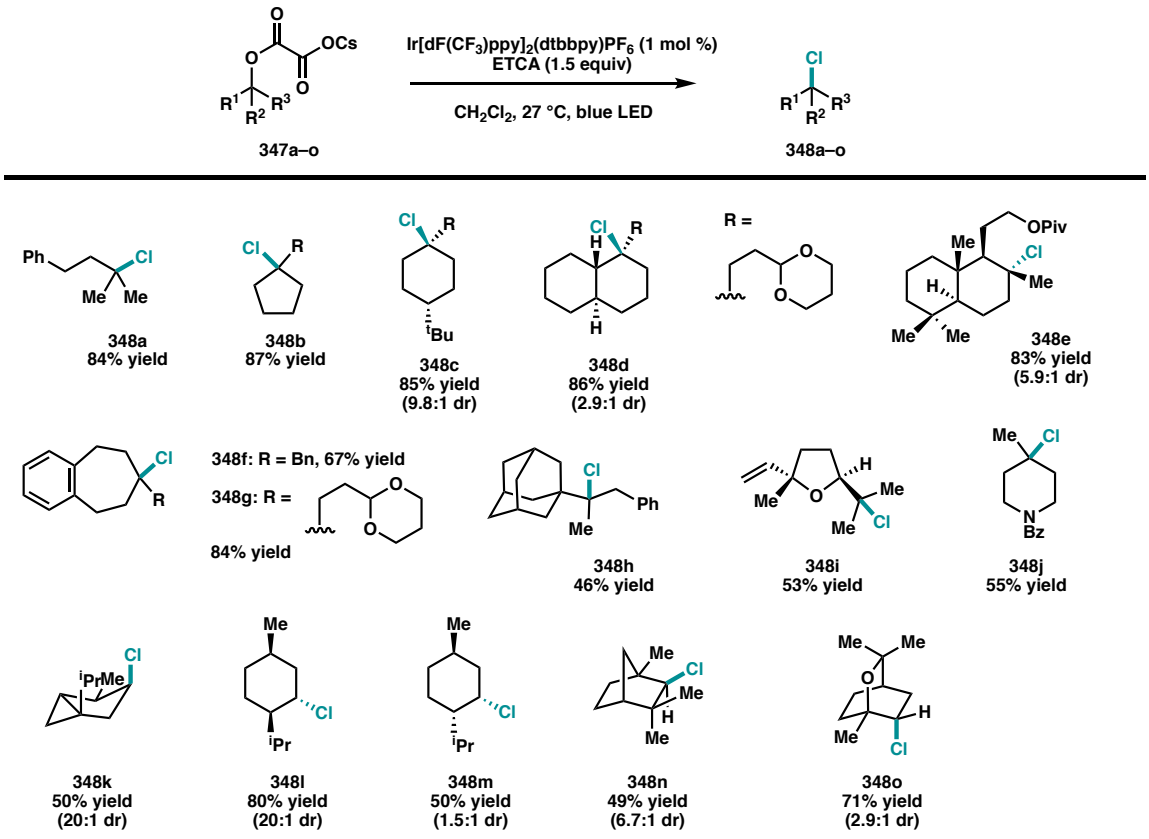
[a] Reactions were conducted under inert atmosphere on 0.1 mmol scale. [b] Determined by ^1H NMR versus pyrazine as an internal standard.

used, chloride **348a** was obtained in 75% yield (entry 5); ultimately, ETCA was selected as the chlorine atom source since it is more readily available. Use of MeCN, dioxane, or THF as the solvent led to a significantly diminished yield relative to CH_2Cl_2 (entries 6–8). The addition of 10 equivalents of water improved the solubility of the oxalate **347a**, but led to a slight decrease in yield (entry 9). Control experiments in which ETCA, [Ir] catalyst,

or light was omitted confirmed that each of these components is necessary for the reaction to proceed (entries 10–12).

Using the established protocol, we first examined the scope of the reaction with several tertiary alcohol-derived cesium oxalates (Table 4.8). Cyclopentyl, cyclohexyl, and cycloheptyl oxalates all performed well under the reaction conditions, providing the corresponding chlorides in 67–87% yield (entries **348b–g**). For cyclohexyl substrate **347c**, a 2.5:1 mixture of diastereomeric oxalates was converged to **348c** with greater than 9:1 dr,[75] demonstrating that in certain contexts radical deoxychlorination can be advantageous

Table 4.8. *Substrate scope of deoxychlorination of Cs-oxalates.*



Reactions were conducted on 0.3 mmol scale. Isolated yields are reported. Reactions for products 348a–j were run for 4 h; reactions for products 348k–o were run for 24 h. Chloride 348b was isolated in 92% yield as a 94:6 mixture of 348b to alkene side product as determined by ^{1}H NMR. Chloride 348e was isolated in 90% yield as a 92:8 mixture of 348e to alkene side products as determined by ^{1}H NMR. Chloride 348h was isolated in 54% yield as a 85:15 mixture of 348h to alkene side products as determined by ^{1}H NMR.

over reactions that proceed through stereospecific mechanisms.[76] The cesium oxalate **347e**, derived from the natural product (+)-sclareolide, provided the corresponding alkyl chloride **348e** in 83% yield. The preparation of neopentyl 3° chloride **348h** demonstrates the ability of sterically encumbered oxalates to undergo the chlorination. Oxalates derived from linalool oxide and a benzoyl-protected piperidine delivered the tertiary chloride products **348i** and **348j**, respectively, in moderate yield.

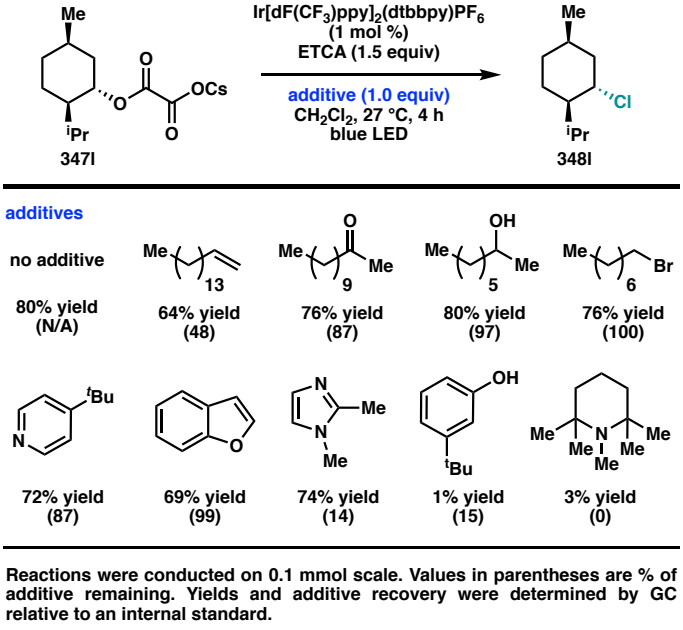
Secondary alcohol-derived substrates were found to react under identical reaction conditions, but with longer reaction times (24 h) required to achieve high conversions. The cesium oxalates derived from (−)-thujone and (+)-isomenthol provided the secondary alkyl chlorides **348k** and **348l** with high diastereoselectivity (20:1 dr, Table 4.8).[77] Unsurprisingly, the (−)-menthol-derived oxalate provided chloride **348m** with only modest diastereoselectivity (1.5:1 dr). Notably, chlorination of sterically demanding, bridged bicyclic ring systems (**347n** and **347o**) were also enabled by the reaction conditions.[78] A 1.3 mmol scale procedure in which **347l** was prepared and subjected directly to the chlorination conditions delivered **348l** in 65% overall yield for the cesium oxalate formation and deoxychlorination sequence.

4.3.2 Functional Group Tolerance — A Robustness Screen

To further probe the functional group tolerance of the reaction, we investigated how the addition of exogenous molecules bearing functional groups impacted the conversion of cesium oxalate **347l** to secondary chloride **348l** (Table 4.9).[79,80] The reaction proceeded without significant reduction in yield in the presence of a ketone, alcohol, alkyl bromide,

benzofuran, or pyridine, and the respective additives were recovered in good yields. The reaction also proceeded in the presence of a terminal alkene and imidazole; however, these additives were consumed to a greater extent. The reaction was inhibited by 3-*tert*-butylphenol and 1,2,2,6,6-pentamethylpiperidine, and these additives were consumed. It is likely that under the reaction conditions, the tertiary amine was oxidized by the excited state [Ir] catalyst.

Table 4.9. *Functional group tolerance of the radical deoxychlorination.*



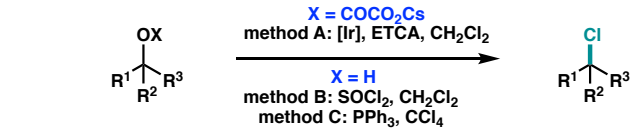
Reactions were conducted on 0.1 mmol scale. Values in parentheses are % of additive remaining. Yields and additive recovery were determined by GC relative to an internal standard.

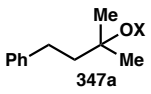
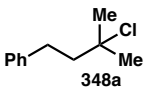
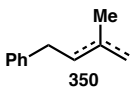
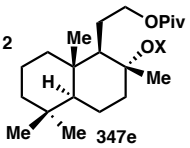
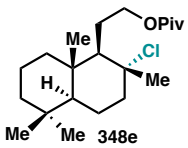
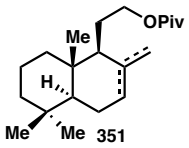
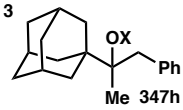
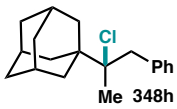
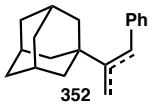
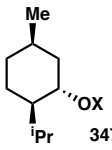
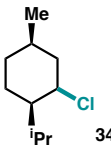
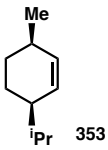
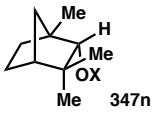
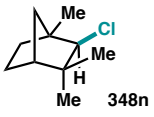
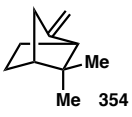
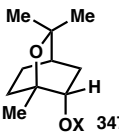
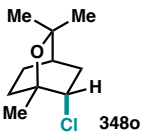
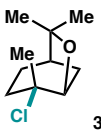
4.3.3 Comparison with Standard Heterolytic Deoxychlorinations

To provide a comparison with more conventional heterolytic deoxychlorination processes, we evaluated a subset of the alcohol substrates from Figure 1 under standard thionyl chloride and Appel reaction conditions (Table 4.10). For the 3° alcohols **347a-OH**, **347e-OH**, and **347h-OH**, the radical deoxychlorination conditions gave improved results

overall relative to the use of thionyl chloride; in particular, a decrease in the formation of alkenes resulting from competitive E1 pathways was observed (entries 1–3, **method B**). For example, the $SOCl_2$-mediated chlorination of sclareolide-derived alcohol **347e-OH** produced chloride **348e** in only 45% yield; the mass balance is a mixture of alkene isomers (**351**, 55% yield, entry 2). A similar reaction outcome was observed for adamantyl-derived

Table 4.10. *Comparison with nonradical deoxychlorination processes.*



entry	substrate	chloride	A B C	yield (%)	side product	A B C	yield (%)
1	 347a	 348a		82 66 0	 350		0 0 76
2	 347e	 348e		83 45 0	 351		6 55 80
3	 347h	 348h		46 51 0	 352		8 41 0
4	 347l	 348l		80 9 16	 353		0 0 63
5	 347n	 348n		49 0 63	 354		0 0 21
6	 347o	 348o		71 49 47	 355		0 51 53

[a] Reactions were conducted on 0.1 mmol scale. Yields determined by ^1H NMR analysis of the crude reaction mixture using pyrazine as an internal standard.

alcohol **347h-OH**, where $SOCl_2$ delivering chloride **348h** in 51% yield and 41% yield of alkene isomers **352** (entry 3). In contrast, the radical deoxychlorination conditions (**method A**) only gave 8% yield of alkenes **352**, allowing for easier chromatographic purification of chloride **348h**. Unsurprisingly, no chlorination of the 3° alcohols was observed under traditional Appel conditions (**method C**).

For secondary alcohols **347l-OH** and **347n-OH**, thionyl chloride afforded poor yields of the corresponding chlorides (entries 4–5, **method B**). Under the Appel conditions (**method C**), (+)-isomenthol (**347l-OH**) predominantly underwent elimination to cyclohexene **353** (entry 4).[81] The relatively hindered framework of (+)-fenchol (**347n-OH**) gave chloride **348n** in 63% yield using **method C**; however rearrangement also occurred to give α-fenchene (**354**) in 21% yield (entry 5). Subjection of oxabicycle **347o-OH** to either $SOCl_2$ or Appel conditions delivered a ~1:1 mixture of chloride **348o** and rearranged chloride **355** in near quantitative yield (entry 6).[82] This reactivity study demonstrates an advantage of the radical deoxychlorination developed here, which minimized the formation of elimination and rearrangement products and consistently delivered the alkyl chlorides across a range of secondary and tertiary alcohol-derived oxalates.

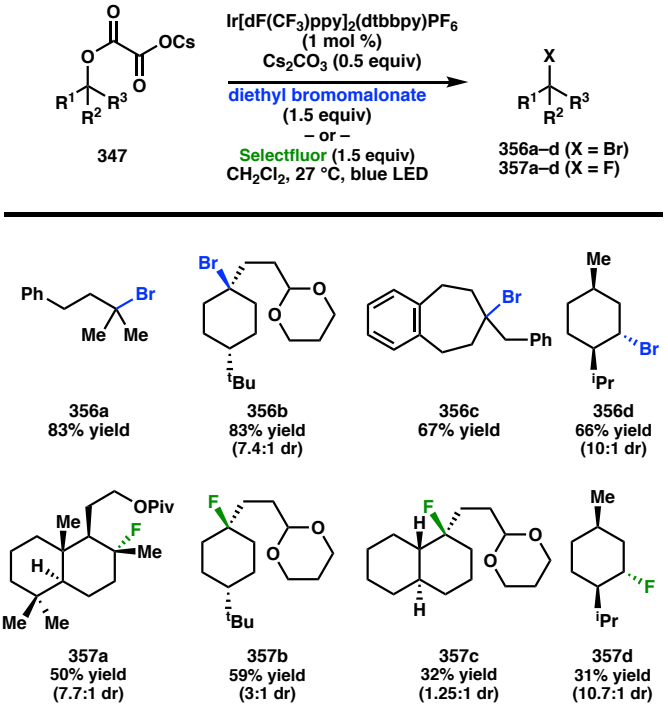
4.3.4 Application to Deoxybromination and Deoxyfluorination

Although the primary focus of this study was the development of radical deoxychlorination reactions, preliminary investigations revealed that these conditions can be adapted for deoxybromination and deoxyfluorination.[83,84] Novel methods for the installation of C–F bonds are of particular interest since this functionality has gained

marked interest in drug discovery.[85,86] More specifically, it has been shown that installation of a C–F bond can effect drug pharmacokinetics, intrinsic potency, as well as other parameters such as pK_a.[87] ^{18}F has also gained an important place in *in vivo* imaging technology as well.

When pursuing a deoxybromination, diethyl bromomalonate was used in place of ETCA, and the alkyl bromides were obtained (Table 4.11). For these reactions, addition of 0.5 equiv of Cs_2CO_3 was found to improve the yield of the bromide product. Alternatively, use of Selectfluor as the halide source provided the corresponding alkyl fluorides, although

Table 4.11. *Radical deoxybromination and deoxyfluorination.*



Reactions were conducted on 0.3 mmol scale with 1.5 equiv of halide source in CH_2Cl_2. Reactions for products 356a–c and 357a–c were run for 4 h; reactions for products 356d and 357d were run for 24 h. Isolated yields are reported. Reaction for 357d was performed in CD_2Cl_2, and the yield was determined by ^1H NMR analysis of the crude reaction mixture using pyrazine as an internal standard.

the yields were generally lower.[88] These findings show the flexibility of this deoxyhalogenation approach to prepare either the alkyl chlorides, bromides, or fluorides.

4.4 CONCLUDING REMARKS

In conclusion, several visible light-mediated methods for radical deoxychlorination of activated alcohols were investigated. When imidazolyl thiocarbamate **328** — derived from the unactivated 2° alcohol (–)-menthol — was subjected to $Ir(ppy)_3$ as a photocatalyst, quinuclidine, and hexachloroacetone, in the presence of blue LED light, only trace chlorination products were observed. However, it was found that the underutilized pyridone activating group, as in substrate **341**, was much more amenable to this deoxychlorination, affording moderate yields of chlorination products **329** and **330**. Unfortunately, the mass balance of this particular chlorination was fairly poor, as it was accompanied by significant amounts of decomposition. Although the development of these conditions has been halted for the time being, we are confident that the pyridone activating group will be of promising use in future radical deoxygenation chemistry.

Additionally, a method for the radical deoxychlorination of cesium oxalates under photoredox catalysis was developed for the preparation of hindered 2° and 3° chlorides.[71] The reactions proceed at room temperature with visible light, and ethyl trichloroacetate was identified as an effective and readily available chlorine atom source. A comparison study of the radical deoxychlorination reaction with thionyl chloride and Appel reaction conditions demonstrated a diminished propensity for rearrangements and elimination processes compared to the nucleophilic substitution-based chemistry. The conditions were

successfully translated to the synthesis of alkyl bromides and fluorides by using diethyl bromomalonate or Selectfluor, respectively.

As of the writing of this dissertation, application of the reactions outlined in this chapter to the acutumine system have been unsuccessful. Undesired deoxygenation and protonation was never observed either, and the substrates appeared to readily decompose under the reaction conditions. This observed decomposition can be rationalized given the ability of the excited state [Ir] catalyst to oxidize basic amines. Nonetheless, efforts in our laboratory are directed toward continued development of radical deoxychlorination reactions and their application in the context of complex natural product total synthesis.

4.5 EXPERIMENTAL SECTION

4.5.1 Materials and Methods

General Procedures. Unless otherwise stated, reactions were performed under a nitrogen atmosphere using freshly dried solvents. Methylene chloride (CH_2Cl_2), diethyl ether (Et_2O), tetrahydrofuran (THF), and 1,4-dioxane were dried by passing through activated alumina columns. Triethylamine (Et_3N) was distilled over calcium hydride prior to use. Halogenation reactions were performed in a Hepatochem EvoluChem™ PhotoRedOx Box device and irradiated with a Kessil A160WE blue LED lamp. Cooling with the internal fan afforded reaction temperatures of 27 °C, as measured with a thermocouple. Unless otherwise stated, reactions were stirred at a rate of 430 rpm. Reaction screens in 1 dram vials were performed with a Biotage 355543 stir bar, while those in a ½ dram vial utilized a V&P Scientific VP 774-7 stir bar. Chlorination reactions in 20 mL scintillation vials were

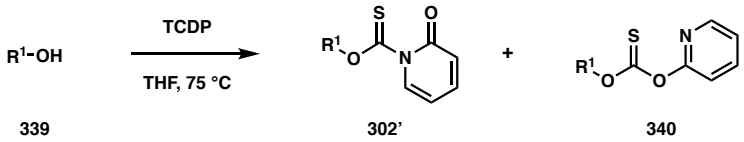
performed with an egg-shaped stir bar (VWR 58949-010). Bromination and fluorination reactions in 20 mL scintillation vials were performed with a "+"-shaped stir bar (VWR 58947-822) for better stirring with added Cs_2CO_3. All reactions were monitored by thin-layer chromatography using EMD/Merck silica gel 60 F254 pre-coated plates (0.25 mm). Silica gel column chromatography was performed as described by Still et al.[89] using silica gel (particle size 0.032–0.063) purchased from Silicycle. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Inova 500 (at 500 MHz and 125 MHz respectively) or a Bruker Avance III HD with Prodigy cyroprobe (at 400 MHz and 101 MHz respectively). NMR data is reported relative to internal chloroform, DMSO, or methanol solvent peaks (with respect to TMS (tetramethylsilane)): $CDCl_3$, ^{1}H, δ = 7.26, ^{13}C, δ = 77.16; DMSO-d_6, ^{1}H, δ = 2.50, ^{13}C, δ = 39.52; CD_3OD, ^{1}H, δ = 3.31, ^{13}C, δ = 49.00). NMR data in D_2O is reported relative to DSS (4,4-dimethyl-4-silapentane-1-sulfonic acid): D_2O, ^{1}H, δ = 4.79. ^{19}F spectra were recorded on a Varian 400 MR spectrometer (at 376 MHz); chemical shifts are reported in parts per million and are referenced to $CFCl_3$ (δ 0 ppm). ^{1}H–^{15}N HMBC data is reported with respect to NH_3 (10.13 ppm) for nitrogen chemical shift referencing. NMR data are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicity and qualifier abbreviations are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm^{-1}). HRMS were acquired using either an Agilent 6200 Series TOF with an Agilent G1978A Multimode source using electrospray ionization (ESI) or from the Caltech Mass Spectral Facility using electrospray ionization (ESI), electron ionization (EI), or fast atom

bombardment (FAB). Molecular formulas of the compounds "M" are given, with the observed ion fragment in brackets, e.g. $[M+H]^+$. GC-Flame ionization detection analysis was performed on a Agilent Technologies 6850 Network GC system using a Agilent HP-1 capillary column (19091Z-413E: length 30 m, diameter 0.320 mm, film 0.25 μm).

Unless otherwise stated, chemicals and reagents were used as received. Reagents were purchased from commercial vendors as follows: Ethyl trichloroacetate (ETCA) was purchased from Sigma-Aldrich, distilled prior to use, and stored in a Schlenk tube under an atmosphere of nitrogen. HCA was purchased from Sigma-Aldrich and stored in a nitrogen-filled glovebox. Selectfluor was purchased from Sigma-Aldrich and was stored in the freezer of a nitrogen-filled glovebox. 1,1'-thiocarbonyldi-2(1H)-pyridone (TCDP) was purchased from Sigma-Aldrich. Dimethyl 2,2-dichloromalonate was prepared according to literature procedure.[74]

4.5.2 Experimental Procedures — Pyridones

General Procedure #1 (Pyridone Formation):

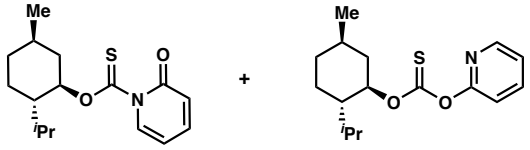


339 302' 340

The alcohol (1.0 equiv) and 1,1'-thiocarbonyldi-2(1H)-pyridone (TCDP, 1.5 equiv) were added to a flame dried vial containing a stir bar. The solids were put under an atmosphere of nitrogen and taken up in THF (0.4 M). The vial was then sealed with a Teflon-lined cap, sealed with electrical tape, and heated at 75 °C (aluminum heating block) for the indicated

time below. Upon reaction completion, the mixture was cooled and transferred to a separatory funnel with CH_2Cl_2. The organic layer was washed with H_2O and then brine, and the combined aqueous layers were back-extracted with CH_2Cl_2 (3x). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The residues were purified via silica gel flash chromatography with the indicated conditions below.

Preparation of menthol-derived pyridone 341 and carbonate 345.



341 (81% yield) **345 (8% yield)**

Performed according to the general procedure with (–)-menthol (500 mg, 3.2 mmol) and heated for 13 h. Purified by silica gel chromatography (0–25% EtOAc/hexanes), affording pyridone **341** (763 mg, 81% yield) as a bright yellow oil and thiocarbonate **345** (75.5 mg, 8% yield) as a faintly yellow solid.

Pyridone **341**:

TLC: R_f 0.40 (3:1 hexanes/EtOAc, UV & $KMnO_4$).

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25.0}}$**:** –46.6° (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (ddd, *J* = 7.1, 2.1, 0.8 Hz, 1H), 7.31 – 7.22 (m, 1H), 6.48 (ddd, *J* = 9.4, 1.3, 0.8 Hz, 1H), 6.13 (ddd, *J* = 7.1, 6.5, 1.2 Hz, 1H), 5.35 (td, *J* = 10.9, 4.5 Hz, 1H), 2.35 (dddd, *J* = 12.0, 4.4, 3.4, 1.9 Hz, 1H), 2.11 (pd, *J* = 7.0, 2.8 Hz, 1H), 1.80

– 1.63 (m, 3H), 1.53 (dddd, *J* = 18.6, 12.1, 6.6, 3.4 Hz, 1H), 1.27 – 1.04 (m, 2H), 0.95 (d, *J* = 6.6 Hz, 3H), 1.00 – 0.85 (m, 1H), 0.91 (d, *J* = 7.0 Hz, 3H), 0.82 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 192.8, 160.0, 140.1, 135.5, 122.7, 105.5, 87.3, 47.0, 38.6, 34.1, 31.6, 26.0, 23.2, 22.1, 20.8, 16.5.

^{15}N NMR (41 MHz, $CDCl_3$): δ 205.4.

FTIR (NaCl, thin film): 2954, 2870, 1688, 1609, 1534, 1305, 1221, 1017 cm^{-1}.

HRMS (ESI, *m/z*): $C_{16}H_{23}NO_2S$, calc'd for $[M+H]^+$: 294.1522, found: 294.1511.

Thiocarbonate **345**:

TLC: R_f 0.57 (3:1 hexanes/EtOAc, UV & $KMnO_4$).

$[\alpha]_D^{25.0}$: –73.3° (c = 0.52, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.44 (ddd, *J* = 5.0, 2.0, 0.8 Hz, 1H), 7.82 (ddd, *J* = 8.1, 7.3, 2.0 Hz, 1H), 7.27 (ddd, *J* = 7.3, 4.9, 1.0 Hz, 1H), 7.12 – 7.04 (m, 1H), 5.16 (td, *J* = 10.8, 4.6 Hz, 1H), 2.37 – 2.27 (m, 1H), 2.10 – 1.97 (m, 1H), 1.78 – 1.58 (m, 3H), 1.51 (dddq, *J* = 15.0, 9.6, 6.4, 3.1 Hz, 1H), 1.19 – 0.99 (m, 2H), 0.94 (d, *J* = 6.6 Hz, 3H), 0.93 (d, *J* = 7.0 Hz, 3H), 1.00 – 0.85 (m, 1H), 0.84 (d, *J* = 7.0 Hz, 3H).

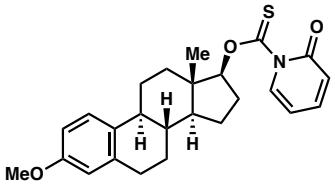
^{13}C NMR (101 MHz, $CDCl_3$): δ 193.6, 159.8, 148.9, 139.9, 122.9, 117.4, 86.0, 47.3, 39.6, 34.4, 31.7, 26.6, 23.8, 22.3, 21.0, 17.1.

^{15}N NMR (41 MHz, $CDCl_3$): δ 291.2.

FTIR (NaCl, thin film): 2957, 2871, 1592, 1433, 1292, 1173, 1014 cm^{-1}.

HRMS (ESI, *m/z*): $C_{16}H_{23}NO_2S$, calc'd for $[M+H]^+$: 294.1522, found: 294.1509.

Preparation of estradiol-derived pyridone 342.



342

Performed according to the general procedure with estrone-derived alcohol[90] (250 mg, 0.87 mmol) and heated for 13 h. Purified by silica gel chromatography (0–20% EtOAc/hexanes), affording pyridone **342** (325 mg, 88% yield) as an off-white solid.

TLC: R_f 0.42 (3:1 hexanes/EtOAc, UV & $KMnO_4$).

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25.0}}$**:** +13.1° (c = 0.52, $CHCl_3$).

^{f1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (ddd, *J* = 7.2, 2.1, 0.8 Hz, 1H), 7.32 – 7.23 (m, 1H), 7.21 (dd, *J* = 8.7, 1.1 Hz, 1H), 6.71 (dd, *J* = 8.6, 2.8 Hz, 1H), 6.63 (d, *J* = 2.7 Hz, 1H), 6.49 (dt, *J* = 9.3, 1.2 Hz, 1H), 6.14 (ddd, *J* = 7.2, 6.5, 1.3 Hz, 1H), 5.31 (dd, *J* = 9.1, 7.4 Hz, 1H), 3.78 (s, 3H), 2.91 – 2.83 (m, 2H), 2.50 (dtd, *J* = 14.2, 9.8, 9.4, 6.3 Hz, 1H), 2.37 – 2.18 (m, 2H), 2.15 (dd, *J* = 8.8, 2.6 Hz, 1H), 1.91 (ddt, *J* = 12.7, 5.6, 2.7 Hz, 1H), 1.87 – 1.72 (m, 2H), 1.59 – 1.46 (m, 4H), 1.46 – 1.32 (m, 2H), 0.96 (s, 3H).

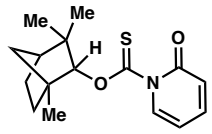
^{13}C NMR (101 MHz, $CDCl_3$): δ 193.3, 160.0, 157.6, 140.1, 138.0, 135.7, 132.4, 126.5, 122.8, 113.9, 111.6, 105.5, 94.3, 55.3, 49.6, 44.2, 43.9, 38.6, 37.0, 29.9, 27.4, 26.6, 26.3, 23.6, 12.7.

^{15}N NMR (41 MHz, $CDCl_3$): δ 204.8.

FTIR (NaCl, thin film): 2926, 2872, 1682, 1610, 1500, 1318, 1223, 1186, 1034 cm^{-1}.

HRMS (ESI, *m/z*): $C_{25}H_{29}NO_3S$, calc'd for $[M+H]^+$: 424.1941, found: 424.1938.

Preparation of fenchol-derived pyridone 343.



343

Performed according to the general procedure with (+)-fenchol (400 mg, 2.48 mmol) and heated for 12 h. Purified by silica gel chromatography (0–15% EtOAc/hexanes), affording pyridone **343** (646 mg, 89% yield) as a pastel yellow solid.

TLC: R_f 0.60 (3:1 hexanes/EtOAc, UV & $KMnO_4$).

$[\alpha]_D^{25.0}$: not observed (acquired three times).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (ddd, *J* = 7.2, 2.1, 0.8 Hz, 1H), 7.32 – 7.22 (m, 1H), 6.49 (ddd, *J* = 9.4, 1.3, 0.8 Hz, 1H), 6.13 (ddd, *J* = 7.6, 6.5, 1.3 Hz, 1H), 5.15 (d, *J* = 2.0 Hz, 1H), 1.87 – 1.64 (m, 4H), 1.49 (tdd, *J* = 12.5, 5.3, 4.0 Hz, 1H), 1.31 – 1.23 (m, 1H), 1.26 (s, 3H), 1.21 (s, 3H), 1.20 – 1.12 (m, 1H), 0.93 (s, 3H).

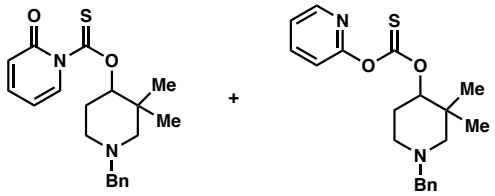
^{13}C NMR (101 MHz, $CDCl_3$): δ 194.0, 159.8, 139.9, 135.7, 122.9, 105.5, 98.0, 49.7, 48.9, 41.6, 41.2, 30.1, 27.3, 25.7, 20.5, 19.5.

^{15}N NMR (41 MHz, $CDCl_3$): δ 205.0.

FTIR (NaCl, thin film): 2955, 2876, 1679, 1610, 1536, 1320, 1220, 1034 cm^{-1}.

HRMS (ESI, *m/z*): $C_{16}H_{21}NO_2S$, calc'd for $[M+H]^+$: 292.1366, found: 292.1353.

Preparation of neopentyl pyridone 281 and carbonate SI-3.



281 (72% yield) **SI-3 (11% yield)**

Performed according to the general procedure with known neopentyl alcohol[91] (2.0 g, 9.11 mmol) and heated for 15 h. The crude reaction mixture was dry-loaded onto Celite (5g) and purified by silica gel flash chromatography (5–30% EtOAc/hexanes) to afford pyridone **281** (2.34 g, 72% yield) as a bright yellow oil and thiocarbonate **SI-3** (351 mg, 11% yield) as a clear oil.

Pyridone **281**:

TLC: R_f 0.39 (2:1 hexanes/EtOAc, UV & $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 (ddd, *J* = 7.2, 2.0, 0.8 Hz, 1H), 7.35 – 7.27 (m, 5H), 7.26 – 7.22 (m, 1H), 6.50 (dt, *J* = 9.4, 1.1 Hz, 1H), 6.13 (ddd, *J* = 7.4, 6.5, 1.2 Hz, 1H), 5.24 (dd, *J* = 8.7, 4.3 Hz, 1H), 3.52 (d, *J* = 13.4 Hz, 1H), 3.45 (d, *J* = 13.5 Hz, 1H), 2.83 – 2.68 (m, 1H), 2.41 (d, *J* = 11.5 Hz, 1H), 2.36 – 2.25 (m, 1H), 2.11 (ddt, *J* = 13.7, 5.8, 3.9 Hz, 1H), 1.99 (dtd, *J* = 13.2, 9.2, 4.2 Hz, 2H), 1.11 (s, 3H), 1.08 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 193.0, 159.9, 140.0, 139.1, 135.6, 128.8, 128.3, 127.0, 122.9, 105.6, 90.3, 63.5, 62.6, 51.4, 36.0, 26.2, 25.5, 21.3.

^{15}N NMR (41 MHz, $CDCl_3$): δ 205.4, 44.8.

FTIR (NaCl, thin film): 2953, 2805, 1682, 1609, 1537, 1305, 1227, 1183, 1026 cm^{-1}.

HRMS (ESI, *m/z*): $C_{20}H_{24}N_2O_2S$, calc'd for $[M+H]^+$: 357.1631, found: 357.1642.

Thiocarbonate **SI-3**:

TLC: R_f 0.56 (2:1 hexanes/EtOAc, UV & $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.44 (ddd, *J* = 4.9, 2.0, 0.8 Hz, 1H), 7.83 (ddd, *J* = 8.2, 7.3, 2.0 Hz, 1H), 7.36 – 7.24 (m, 5H), 7.29 – 7.20 (m, 1H), 7.10 (dt, *J* = 8.1, 0.9 Hz, 1H), 5.05 (dd, *J* = 8.7, 4.2 Hz, 1H), 3.50 (d, *J* = 13.4 Hz, 1H), 3.44 (d, *J* = 13.4 Hz, 1H), 2.80 – 2.58 (m, 1H), 2.43 – 2.23 (m, 2H), 2.15 – 2.05 (m, 1H), 2.05 – 1.85 (m, 2H), 1.08 (s, 3H), 1.03 (s, 3H).

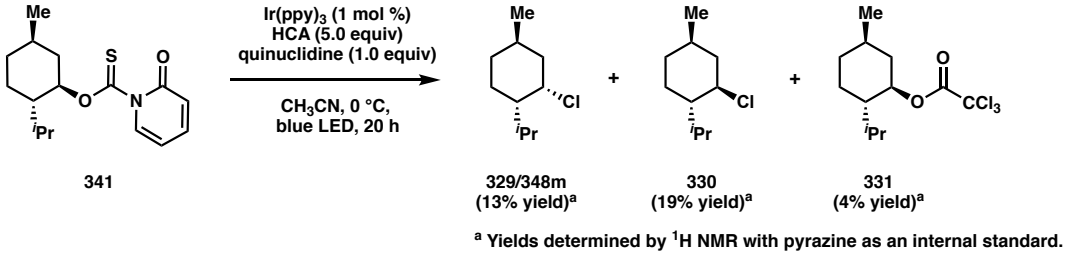
^{13}C NMR (101 MHz, $CDCl_3$): δ 193.4, 159.6, 148.8, 139.8, 139.1, 128.8, 128.3, 127.1, 122.8, 117.1, 88.8, 63.4, 62.6, 51.3, 35.7, 26.5, 25.5, 21.3.

^{15}N NMR (41 MHz, $CDCl_3$): δ 291.7, 44.8.

FTIR (NaCl, thin film): 2958, 2806, 1592, 1432, 1292, 1181, 1026 cm^{-1}.

HRMS (ESI, *m/z*): $C_{20}H_{24}N_2O_2S$, calc'd for $[M+H]^+$: 357.1631, found: 357.1634.

Procedure for the Deoxychlorination of Pyridone 341:



Note: For the purposes of running the deoxychlorination at 0 °C, small Schlenk tubes were used to enable absorption of blue LED light in a dewar. When the reaction was run at ambient temperature, 1 dram vials were utilized.

Pyridone **341** (15 mg, 0.051 mmol), $Ir(ppy)_3$ (0.3 mg, 0.0005 mmol, 1 mol %), and quinuclidine (5.7 mg, 0.051 mmol, 1.0 equiv) were added to a flame-dried Schlenk tube containing a stir bar. The Schlenk tube was brought into a nitrogen-filled glovebox, after which CH_3CN (0.8 mL) was added, followed by HCA (38.8 mL, 0.256 mmol, 5.0 equiv). The tube was sealed and brought out of the glovebox, cooled to 0 °C (utilizing a cryocool), and irradiated with blue LED light for 20 h (two Kessil lamps at a distance of ~10 cm). The reaction was quenched by the addition of saturated aqueous LiCl (3 mL) and the aqueous layer was extracted with Et_2O (5 x 1.5 mL). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure at 23 °C (at a pressure of ~60–100 mmHg). Due to product volatility, the crude was not dried under high vacuum. Pyrazine was utilized as an internal standard and ^1H NMR indicated formation of neomenthyl chloride **329/348m** (13% yield), menthyl chloride **330** (19% yield), and ester **331** (4% yield). The ^1H NMR spectrum of the mixture of products was consistent with

those reported for the individual chloride diastereomers (**329**/**348m** and **330**)[92] and ester **331**.[93]

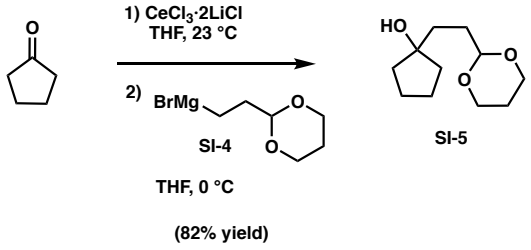
4.5.3 Experimental Procedures — Cesium Oxalates

1. Substrate Preparation

Known cesium oxalates: Substrates **347a**, **347e**, **347i**, **347j**, and **347l** were prepared according to literature procedures and the NMR data were consistent with those reported in the literature.[94]

a. Preparation of cesium oxalate 347b:

Preparation of cyclopentanol SI-5.



A flame-dried 25 mL round bottom flask was charged with cyclopentanone (100 mg, 1.19 mmol) and put under an atmosphere of argon. A solution of $CeCl_3$•2LiCl[95] (4 mL, 1.19 mmol, 0.3 M in THF, 1.0 equiv) was added at 23 °C, and the pale yellow mixture stirred for 1 h. The mixture was then cooled to 0 °C and Grignard **SI-4**[96] (3.2 mL, 1.19 mmol, 0.37 M in THF, 1.0 equiv) was added dropwise. After 15 min, TLC analysis indicated full conversion, and the mixture was quenched with a saturated aqueous solution of NH_4Cl (3

mL) and stirred at 0 °C for 5 min. H_2O (7 mL) and EtOAc (5 mL) were added and the mixture warmed to room temperature and transferred to a separatory funnel. A saturated aqueous solution of Rochelle's salt (10 mL) was added, after which the aqueous layer was extracted with EtOAc (4 x 15 mL). The combined organic layers were washed with a saturated aqueous solution of NaCl (1 x 15 mL), and the aqueous layer back-extracted with EtOAc (1 x 10 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (5–50% EtOAc/hexanes) to afford tertiary alcohol **SI-5** (195 mg, 82% yield) as a clear oil.

TLC: R_f 0.32 (50% EtOAc/hexanes, *p*-anisaldehyde).

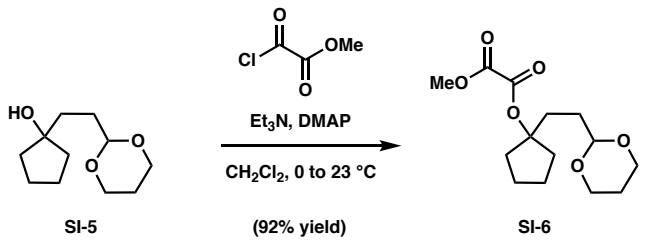
^{1}H NMR (400 MHz, $CDCl_3$): δ 4.58 (t, *J* = 4.6 Hz, 1H), 4.11 (ddt, *J* = 10.5, 5.0, 1.2 Hz, 2H), 3.83 – 3.72 (m, 2H), 2.15 – 2.01 (m, 1H), 2.08 (s, 1H), 1.78 (dddd, *J* = 7.6, 5.6, 4.5, 1.7 Hz, 4H), 1.71 (ddd, *J* = 8.3, 6.1, 1.8 Hz, 2H), 1.68 – 1.57 (m, 4H), 1.57 – 1.48 (m, 2H), 1.34 (dtt, *J* = 13.5, 2.5, 1.3 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 102.5, 81.8, 66.9, 39.7, 35.4, 30.8, 25.7, 23.8.

FTIR (NaCl, thin film): 3450, 2959, 2852, 1378, 1240, 1145, 994 cm^{-1}.

HRMS (EI, *m/z*): $C_{11}H_{20}O_3$, calc'd for $(M+\cdot)^+$: 200.1413, found: 200.1411.

Preparation of methyl oxalate SI-6.



To a 50 mL round bottom flask containing a solution of alcohol **SI-5** (146 mg, 0.73 mmol) in CH_2Cl_2 (6.6 mL) at 0 °C was added Et_3N (150 µL, 1.09 mmol, 1.5 equiv), DMAP (9 mg, 0.073 mmol, 0.1 equiv), and methyl oxalyl chloride (80 µL, 1.17 mmol, 1.2 equiv) dropwise by syringe. The reaction was stirred at room temperature for 2.5 h followed by the addition of H_2O (4 mL). The organic layer was collected and the aqueous layer was extracted with CH_2Cl_2 (4 x 6 mL). The combined organic extracts were washed with a saturated aqueous solution of NaCl (2 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (10–33% EtOAc/hexanes) to afford methyl oxalate **SI-6** (193 mg, 92% yield) as a clear colorless oil.

TLC: R_f 0.27 (20% EtOAc/hexanes, *p*-anisaldehyde).

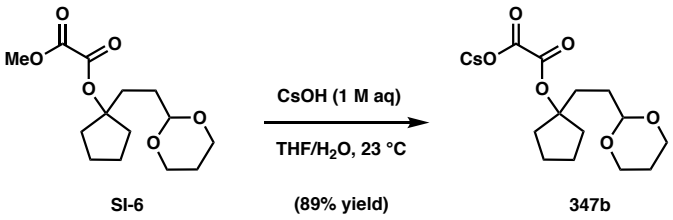
^{1}H NMR (500 MHz, $CDCl_3$): δ 4.48 (t, *J* = 5.2 Hz, 1H), 4.07 (ddt, *J* = 10.5, 5.0, 1.4 Hz, 2H), 3.84 (s, 3H), 3.72 (dddd, *J* = 11.9, 10.5, 2.6, 1.6 Hz, 2H), 2.25 – 2.15 (m, 2H), 2.14 – 2.08 (m, 2H), 2.08 – 1.99 (m, 1H), 1.80 – 1.69 (m, 4H), 1.67 – 1.57 (m, 4H), 1.32 (dtt, *J* = 13.5, 2.7, 1.4 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 159.0, 157.0, 102.0, 97.1, 67.0, 53.4, 37.4, 31.1, 30.3, 25.9, 24.0.

FTIR (NaCl, thin film): 2960, 2853, 2733, 2658, 1766, 1739, 1454, 1332, 1202, 1146, 1079, 997 cm^{-1}.

HRMS (FAB+, *m/z*): $C_{14}H_{21}O_6$, calc'd for $(M+H-H_2)^+$: 285.1338, found: 285.1317.

Preparation of cesium oxalate 347b.



A 20 mL scintillation vial was charged with methyl oxalate **SI-6** (119 mg, 0.42 mmol), THF (2.6 mL), and H_2O (0.27 mL). A 1 M aqueous solution of CsOH (0.420 mL, 0.42 mmol, 1.0 equiv) was then added dropwise to the solution with vigorous stirring. After the addition was complete, the solution was stirred for an additional 5 min. The reaction was concentrated under reduced pressure to remove the THF and the aqueous layer was washed 1:1 pentane/Et_2O (4 x 2 mL). The aqueous layer was then concentrated using rotary evaporation followed by high vacuum (~50 mTorr) to deliver cesium oxalate **347b** as a white amorphous solid (149 mg, 89% yield).

^{1}H NMR (400 MHz, CD_3OD): δ 4.54 (t, *J* = 5.1 Hz, 1H), 4.03 (ddt, *J* = 10.4, 4.9, 1.4 Hz, 2H), 3.83 – 3.69 (m, 2H), 2.28 – 2.13 (m, 2H), 2.12 – 2.05 (m, 2H), 1.98 (dtt, *J* = 13.4,

12.5, 5.0 Hz, 1H), 1.84 – 1.67 (m, 4H), 1.67 – 1.53 (m, 4H), 1.34 (dtt, *J* = 13.4, 2.7, 1.4 Hz, 1H).

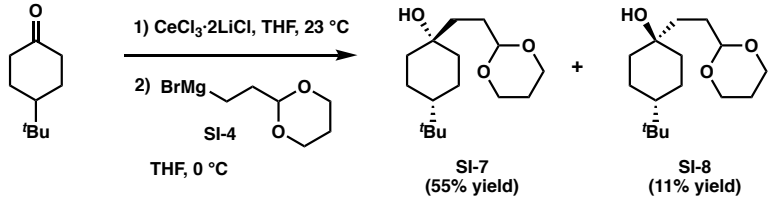
^{13}C NMR (101 MHz, CD_3OD): δ 166.3, 166.1, 103.4, 94.9, 67.8, 38.5, 32.3, 31.3, 27.0, 24.9.

FTIR (NaCl, thin film): 2960, 2856, 1715, 1645, 1455, 1404, 1200, 1078, 995 cm^{-1}.

HRMS (TOF-ESI, *m/z*): $C_{13}H_{19}O_6^-$, calc'd for $(M–Cs)^-$: 271.1187, found: 271.1187.

b. Preparation of cesium oaxalate 347c:

Preparation of alcohols SI-7 and SI-8.



A flame-dried 100 mL round bottom flask was charged with 4-*tert*-butylcyclohexanone (306 mg, 1.98 mmol) and placed under an atmosphere of argon. A solution of $CeCl_3$•2LiCl[3] (6.6 mL, 1.98 mmol, 0.3 M in THF, 1.0 equiv) was added at room temperature and the pale yellow solution was stirred for 1 h. The mixture was then cooled to 0 ºC and a solution of Grignard reagent SI-1[4] (5.0 mL, 2.18 mmol, 0.44 M in THF, 1.1 equiv) was added dropwise. The reaction was stirred at 0 °C for 1 h. A saturated aqueous solution of NH_4Cl (10 mL) was added and the reaction was stirred for 25 min while warming to room temperature. A saturated aqueous solution of Rochelle's salt (5 mL) was added and the aqueous layer was extracted with Et_2O (3 x 12 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue

was purified by silica gel chromatography (10–50% EtOAc/hexanes) to afford alcohol **SI-7** (295 mg, 55% yield) as a white solid and alcohol **SI-8** (60 mg, 11% yield) as a white solid.

Alcohol **SI-7**:

TLC: R_f 0.31 (40% EtOAc/hexanes, $KMnO_4$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 4.53 (t, *J* = 4.9 Hz, 1H), 4.08 (ddt, *J* = 10.4, 5.0, 1.4 Hz, 2H), 3.74 (dddd, *J* = 11.9, 10.5, 2.6, 1.6 Hz, 2H), 2.06 (dtt, *J* = 13.5, 12.5, 5.0 Hz, 1H), 1.88 (br s, 1H), 1.78 – 1.61 (m, 4H), 1.60 – 1.42 (m, 4H), 1.40 – 1.16 (m, 5H), 0.99 – 0.86 (m, 1H), 0.83 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 102.8, 69.9, 67.0, 48.1, 38.0, 37.7, 32.5, 29.1, 27.7, 25.8, 22.6.

FTIR (NaCl, thin film): 3481, 2949, 2847, 2732, 2654, 1456, 1432, 1402, 1365, 1242, 1145, 1073, 1006, 979 cm^{-1}.

HRMS (FAB+, *m/z*): $C_{16}H_{29}O_3$, calc'd for $(M+H-H_2)^+$: 269.2117, found: 269.2095.

Alcohol **SI-8**:

TLC: R_f 0.18 (40% EtOAc/hexanes, $KMnO_4$).

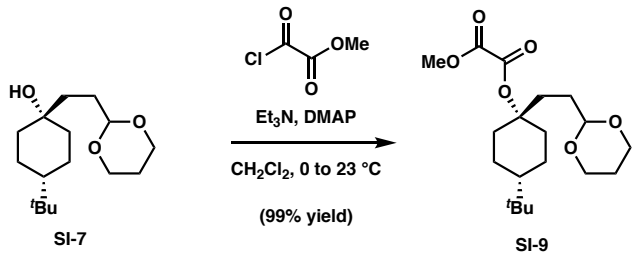
^{1}H NMR (400 MHz, $CDCl_3$): δ 4.56 (t, *J* = 4.7 Hz, 1H), 4.10 (ddt, *J* = 10.4, 5.0, 1.4 Hz, 2H), 3.76 (dddd, *J* = 11.9, 10.5, 2.6, 1.6 Hz, 2H), 2.17 (br s, *J* = 3.4 Hz, 1H), 2.08 (dtt, *J* = 13.5, 12.5, 5.0 Hz, 1H), 1.77 (ddd, *J* = 13.8, 3.9, 2.2 Hz, 2H), 1.74 – 1.58 (m, 6H), 1.42 – 1.30 (m, 3H), 1.12 – 0.98 (m, 3H), 0.84 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 102.8, 71.5, 67.0, 47.7, 38.8, 32.4, 30.3, 28.8, 27.8, 25.8, 24.5.

FTIR (NaCl, thin film): 3296, 2941, 2863, 2729, 2656, 1455, 1365, 1283, 1239, 1211, 1148, 1102, 1007, 984 cm^{-1}.

HRMS (FAB+, *m/z*): $C_{16}H_{29}O_3$, calc'd for $(M+H-H_2)^+$: 269.2117, found: 269.2123.

Preparation of methyl oxalate SI-9.



To a 50 mL round bottom flask containing a solution of alcohol **SI-7** (231 mg, 0.85 mmol) in CH_2Cl_2 (7.8 mL) at 0 °C was added Et_3N (0.18 mL, 1.28 mmol, 1.5 equiv), DMAP (10 mg, 0.09 mmol, 0.1 equiv), and methyl oxalyl chloride (0.09 mL, 1.03 mmol, 1.2 equiv) dropwise via syringe. The reaction was stirred at room temperature for 3 h followed by the addition of a 1:1 mixture of a saturated aqueous solution of NaCl and H_2O (3 mL). The organic layer was collected and the aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (10–20% EtOAc/hexanes) to give methyl oxalate **SI-9** (301 mg, 99% yield) as a pale yellow oil.

TLC: R_f 0.56 (40% EtOAc/hexanes, UV, $KMnO_4$).

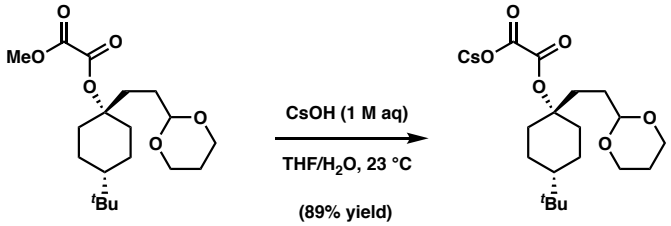
^{1}H NMR (400 MHz, $CDCl_3$): δ 4.47 (t, *J* = 5.2 Hz, 1H), 4.07 (ddt, *J* = 10.4, 5.0, 1.4 Hz, 2H), 3.85 (s, 3H), 3.72 (dddd, *J* = 11.9, 10.5, 2.6, 1.6 Hz, 2H), 2.49 – 2.37 (m, 2H), 2.13 – 1.95 (m, 3H), 1.68 – 1.51 (m, 4H), 1.40 – 1.16 (m, 6H), 1.09 – 0.94 (m, 1H), 0.83 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 159.1, 156.7, 102.2, 88.1, 67.0, 53.3, 47.2, 34.6, 32.5, 32.4, 29.1, 27.6, 25.9, 22.3.

FTIR (NaCl, thin film): 2954, 2866, 2732, 2658, 1767, 1740, 1453, 1366, 1331, 1205, 1165, 1004, 977 cm^{-1}.

HRMS (FAB+, *m/z*): $C_{19}H_{31}O_6$, calc'd for $(M+H-H_2)^+$: 355.2121, found: 355.2133.

Preparation of cesium oxalate 347c.



SI-9 347c

A 20 mL scintillation vial was charged with methyl oxalate **SI-9** (118 mg, 0.33 mmol), THF (2.1 mL), and H_2O (0.22 mL). A 1 M aqueous solution of CsOH (0.33 mL, 0.33 mmol, 1.0 equiv) was then added dropwise to the solution with vigorous stirring. After the addition was complete, the mixture was stirred for an additional 5 min. The reaction was then concentrated under reduced pressure to remove the THF and the aqueous layer was washed with 1:1 pentane/Et_2O (4 x 2 mL). The aqueous layer was then concentrated under reduced pressure using rotary evaporation followed by high vacuum (~50 mTorr) to afford cesium oxalate **347c** as a white solid (141 mg, 90% yield).

^{1}H NMR (400 MHz, CD_3OD): δ 4.51 (t, *J* = 5.1 Hz, 1H), 4.02 (ddt, *J* = 10.4, 5.0, 1.4 Hz, 2H), 3.83 – 3.69 (m, 2H), 2.52 – 2.39 (m, 2H), 2.04 – 1.91 (m, 3H), 1.67 – 1.52 (m, 4H), 1.46 – 1.30 (m, 3H), 1.24 (td, *J* = 13.5, 3.6 Hz, 2H), 1.04 (tt, *J* = 12.0, 3.3 Hz, 1H), 0.86 (s, 9H).

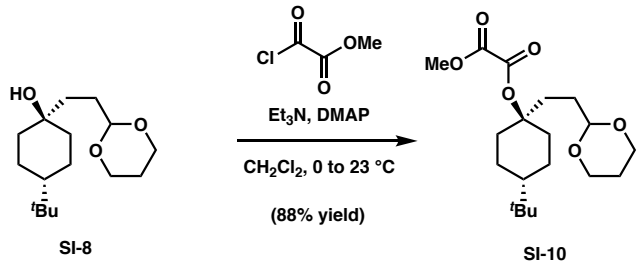
^{13}C NMR (101 MHz, CD_3OD): δ 166.4, 166.1, 103.6, 85.4, 67.8, 35.8, 33.6, 33.2, 30.1, 28.0, 27.0, 23.4.

FTIR (NaCl, thin film): 2952, 2851, 2734, 1704, 1622, 1452, 1399, 1212, 979 cm^{-1}.

HRMS (TOF-ESI, *m/z*): $C_{18}H_{29}O_6^-$, calc'd for $(M–Cs)^-$: 341.1970, found: 341.1974.

c. Preparation of cesium oaxalate 347c':

Preparation of methyl oxalate SI-7.



To a 50 mL round bottom flask containing a solution of alcohol **SI-8** (136 mg, 0.50 mmol) in CH_2Cl_2 (4.6 mL) at 0 °C was added Et_3N (0.11 mL, 0.75 mmol, 1.5 equiv), DMAP (6 mg, 0.05 mmol, 0.1 equiv), and methyl oxalyl chloride (0.06 mL, 0.60 mmol, 1.2 equiv) dropwise via syringe. The reaction was stirred at room temperature for 3 h followed by the addition of a 1:1 mixture of saturated aqueous NaCl and H_2O (2 mL). The organic layer was collected and the aqueous layer was extracted with CH_2Cl_2 (4 x 4 mL). The combined

organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (10–20% EtOAc/hexanes) to furnish methyl oxalate **SI-10** (159 mg, 88% yield) as a clear colorless oil.

TLC: R_f 0.54 (40% EtOAc/hexanes, UV, $KMnO_4$).

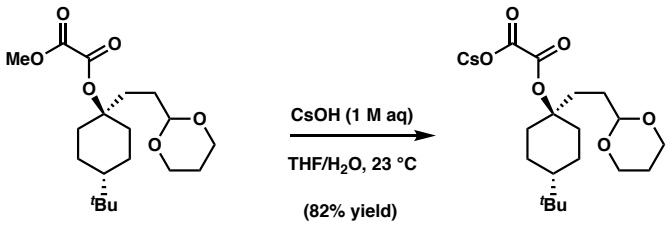
^{1}H NMR (400 MHz, $CDCl_3$): δ 4.49 (t, *J* = 5.2 Hz, 1H), 4.07 (ddt, *J* = 10.4, 5.0, 1.4 Hz, 2H), 3.83 (s, 3H), 3.73 (dddd, *J* = 11.9, 10.4, 2.6, 1.6 Hz, 2H), 2.33 – 2.19 (m, 2H), 2.14 – 1.96 (m, 3H), 1.82 – 1.66 (m, 4H), 1.66 – 1.52 (m, 2H), 1.32 (dtt, *J* = 13.5, 2.7, 1.4 Hz, 1H), 1.26 – 1.02 (m, 3H), 0.83 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 159.0, 156.6, 102.2, 90.0, 67.0, 53.4, 47.3, 34.6, 32.3, 28.8, 27.7, 26.4, 25.9, 24.1.

FTIR (NaCl, thin film): 2954, 2868, 2731, 2658, 1767, 1740, 1461, 1367, 1326, 1206, 1166, 1093, 1010, 973 cm^{-1}.

HRMS (FAB+, *m/z*): $C_{19}H_{31}O_6$, calc'd for $(M+H-H_2)^+$: 355.2121, found: 355.2133.

Preparation of cesium oxalate 347c'.



SI-10 347c'

A 20 mL scintillation vial was charged with methyl oxalate **SI-10** (118 mg, 0.33 mmol), THF (2.1 mL), and H_2O (0.22 mL). A 1 M aqueous solution of CsOH (1 M in H_2O, 0.33

mL, 0.33 mmol, 1.0 equiv) was added dropwise to the solution with vigorous stirring. After the addition was complete, the mixture was stirred for an additional 5 min. The reaction was concentrated under reduced pressure to remove the THF and the aqueous layer was washed with 1:1 pentane/Et_2O (4 x 2 mL). The aqueous layer was concentrated under reduced pressure using rotary evaporation followed by high vacuum (~50 mTorr) to afford cesium oxalate **347c'** as a white solid (129 mg, 82% yield).

^{1}H NMR (400 MHz, CD_3OD): δ 4.56 (t, *J* = 5.2 Hz, 1H), 4.04 (ddt, *J* = 10.5, 5.1, 1.4 Hz, 2H), 3.78 (dddd, *J* = 12.0, 10.5, 2.6, 1.6 Hz, 2H), 2.36 – 2.26 (m, 2H), 2.15 – 2.07 (m, 2H), 2.00 (dtt, *J* = 13.4, 12.5, 5.0 Hz, 1H), 1.71 (td, *J* = 11.5, 5.9 Hz, 4H), 1.64 – 1.52 (m, 2H), 1.35 (dtt, *J* = 13.4, 2.6, 1.4 Hz, 1H), 1.24 – 1.06 (m, 3H), 0.88 (s, 9H).

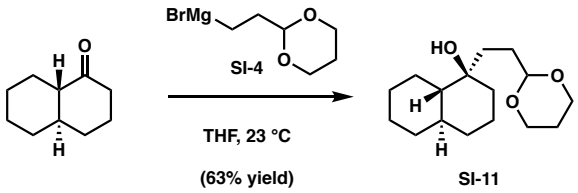
^{13}C NMR (101 MHz, CD_3OD): δ 166.5, 165.9, 103.6, 87.2, 67.9, 35.9, 33.0, 29.8, 28.0, 27.2, 27.0, 25.0.

FTIR (NaCl, thin film): 2952, 2867, 2732, 2662, 1713, 1645, 1462, 1373, 1210, 1146, 1091, 1006, 972 cm^{-1}.

HRMS (TOF-ESI, *m/z*): $C_{18}H_{29}O_6^-$, calc'd for $(M–Cs)^-$: 341.1970, found: 341.1972.

d. Preparation of cesium oxalate 347d:

Preparation of alcohol SI-11.



A flame-dried 50 mL round bottom flask was charged with *trans*-decalone (500 mg, 3.28 mmol) and put under an atmosphere of nitrogen. THF (3.3 mL) was added, followed by dropwise addition of a solution of Grignard reagent **SI-4**[4] (8.2 mL, 1.25 mmol, 0.5 M in THF, 1.25 equiv) at 23 °C. TLC analysis indicated full conversion after 2 h, and the mixture was quenched with a saturated aqueous solution of NH_4Cl (5 mL) and stirred vigorously for 10 min. The biphasic mixture was concentrated under rotary evaporation to remove the THF. A saturated aqueous solution of NaCl (3 mL) was added and the resulting solution was extracted with EtOAc (4 x 15 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (0–40% EtOAc/hexanes) to provide tertiary alcohol **SI-11** (553 mg, 63% yield) as a white solid.

TLC: R_f 0.31 (33% EtOAc/hexanes, *p*-anisaldehyde).

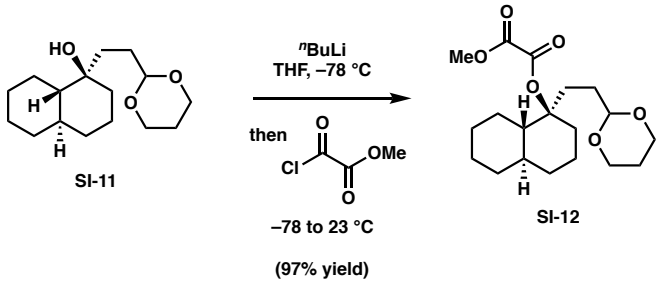
^{1}H NMR (400 MHz, $CDCl_3$): δ 4.50 (t, *J* = 4.7 Hz, 1H), 4.09 (ddt, *J* = 10.4, 5.0, 1.4 Hz, 2H), 3.75 (td, *J* = 12.3, 2.5 Hz, 2H), 2.07 (dtt, *J* = 13.5, 12.4, 5.0 Hz, 1H), 1.81 – 1.71 (m, 2H), 1.60 (dddd, *J* = 19.4, 10.4, 4.6, 2.5 Hz, 7H), 1.55 – 1.46 (m, 3H), 1.39 – 1.25 (m, 3H), 1.19 (tdd, *J* = 8.8, 4.2, 2.5 Hz, 2H), 1.13 – 1.01 (m, 1H), 0.98 – 0.82 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 102.8, 72.4, 67.1, 49.0, 37.2, 36.7, 34.8, 34.6, 34.3, 29.7, 26.9, 26.3, 25.9, 24.9, 21.3.

FTIR (NaCl, thin film): 3495, 2925, 2849, 1448, 1377, 1145, 999 cm^{-1}.

HRMS (EI, *m/z*): $C_{16}H_{28}O_3$, calc'd for $(M+\cdot)^+$: 268.2039, found: 268.2054.

Preparation of methyl oxalate SI-12.



A flame-dried 25 mL round bottom flask was charged with alcohol **SI-11** (240 mg, 0.89 mmol) and THF (3.6 mL). The flask was cooled to –78 ºC followed by dropwise addition of ^{n}BuLi (2.5 M in hexanes, 0.46 mL, 1.16 mmol, 1.3 equiv). The reaction was then stirred for an additional 30 min. Methyl oxalyl chloride (30 µL, 0.31 mmol, 1.7 equiv) was added dropwise by syringe. The solution was stirred at –78 ºC for 30 min and then warmed to room temperature over 2 h. The reaction was quenched with a 1:1 mixture of a saturated aqueous solution of $NaHCO_3$ and a saturated aqueous solution of NaCl (3 mL). The biphasic mixture was concentrated under rotary evaporation to remove the THF and the resulting solution was extracted with EtOAc (4 x 5 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (0–25% EtOAc/hexanes) to afford methyl oxalate **SI-12** (306 mg, 97% yield) as a viscous yellow oil.

TLC: R_f 0.35 (15% EtOAc/hexanes, *p*-anisaldehyde).

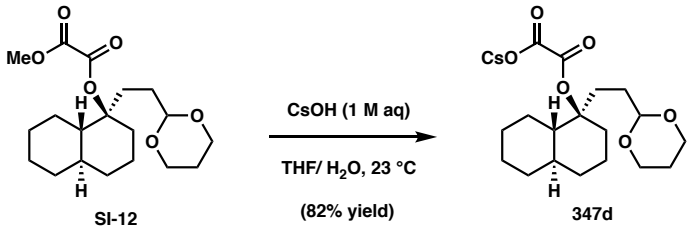
^{1}H NMR (500 MHz, $CDCl_3$): δ 4.47 (t, *J* = 5.1 Hz, 1H), 4.12 – 4.04 (m, 2H), 3.86 (s, 3H), 3.73 (tdd, *J* = 12.0, 5.0, 2.6 Hz, 2H), 2.72 – 2.63 (m, 1H), 2.39 (ddd, *J* = 13.4, 11.3, 5.8 Hz, 1H), 2.06 (dtt, *J* = 13.5, 12.5, 5.0 Hz, 1H), 1.94 – 1.84 (m, 1H), 1.83 – 1.71 (m, 2H), 1.70 – 1.61 (m, 2H), 1.61 – 1.10 (m, 11H), 1.02 (ddd, *J* = 11.6, 10.4, 3.0 Hz, 1H), 0.99 – 0.86 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 159.2, 156.8, 102.2, 91.2, 67.02, 66.99, 53.3, 47.8, 36.6, 34.6, 33.7, 31.9, 30.3, 29.4, 26.7, 26.1, 25.8, 24.7, 21.1.

FTIR (NaCl, thin film): 2931, 2851, 2732, 2662, 1766, 1739, 1450, 1330, 1205, 1170, 1144, 1002 cm^{-1}.

HRMS (FAB+, *m/z*): $C_{19}H_{29}O_6$, calc'd for $(M+H-H_2)^+$: 353.1964, found: 353.1969.

Preparation of cesium oxalate 347d.



A 20 mL scintillation vial was charged with methyl oxalate **SI-12** (141 mg, 0.40 mmol), THF (2.5 mL), and H_2O (0.26 mL). A 1 M aqueous solution of CsOH (1 M in H_2O, 0.40 mL, 0.40 mmol, 1.0 equiv) was added dropwise to the solution with vigorous stirring. After the addition was complete, the mixture was stirred for an additional 5 min. The reaction was then concentrated under reduced pressure to remove the THF and the aqueous layer

was washed with 1:1 pentane/Et_2O (4 x 2 mL). The aqueous layer was concentrated under reduced pressure using rotary evaporation and then high vacuum (~50 mTorr) to deliver cesium oxalate **347d** as a hygroscopic white solid (177 mg, 94% yield).

^{1}H NMR (400 MHz, CD_3OD): δ 4.51 (t, *J* = 5.1 Hz, 1H), 4.04 (ddt, *J* = 10.5, 5.0, 1.4 Hz, 2H), 3.78 (dddd, *J* = 14.6, 10.6, 3.5, 2.0 Hz, 2H), 2.76 – 2.63 (m, 1H), 2.51 – 2.32 (m, 1H), 1.99 (dtt, *J* = 13.4, 12.5, 5.0 Hz, 1H), 1.87 (ddd, *J* = 13.4, 10.2, 7.7 Hz, 1H), 1.82 – 1.70 (m, 2H), 1.69 – 1.14 (m, 13H), 1.09 – 0.87 (m, 3H).

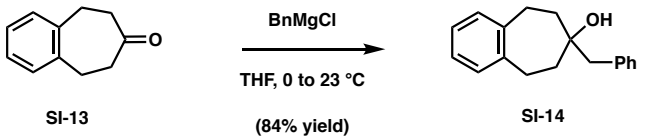
^{13}C NMR (101 MHz, CD_3OD): δ 167.3, 166.8, 103.5, 88.6, 67.9, 37.5, 35.9, 35.1, 33.2, 31.2, 30.4, 27.7, 27.2, 27.0, 25.6, 22.1.

FTIR (NaCl, thin film): 2930, 2850, 2732, 2665, 1706, 1632, 1448, 1404, 1217, 1145, 1076, 1026, 1001 cm^{-1}.

HRMS (TOF-ESI, *m/z*): $C_{18}H_{27}O_6^-$, calc'd for $(M–Cs)^-$: 339.1813, found: 339.1812.

e. Preparation of cesium oxalate 347f:

Preparation of alcohol SI-14.



To a 50 mL round bottom flask containing a solution of cycloheptanone **SI-13** (100 mg, 0.62 mmol)[97] in THF (2.5 mL) at 0 °C was added a solution of benzylmagnesium chloride (2.0 M in THF, 0.47 mL, 0.94 mmol, 1.5 equiv) dropwise. The reaction was stirred at room temperature for 16 h and a saturated aqueous solution of NH_4Cl (2 mL) was slowly added.

The biphasic mixture was concentrated under rotary evaporation to remove the THF. A saturated aqueous solution of NaCl (2 mL) was added and the resulting mixture was extracted with Et_2O (4 x 5 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (5–15% EtOAc/hexanes) to furnish tertiary alcohol **SI-14** (132 mg, 84% yield) as a white solid.

TLC: R_f 0.23 (10% EtOAc/hexanes, UV, $KMnO_4$).

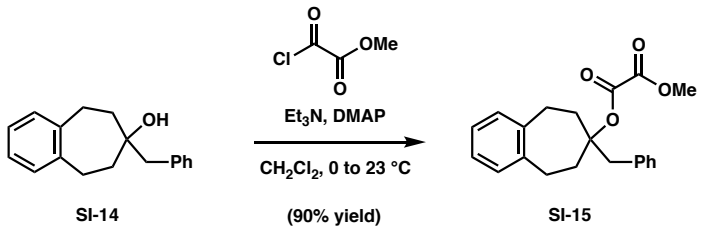
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 – 7.21 (m, 3H), 7.21 – 7.15 (m, 2H), 7.09 (s, 4H), 3.16 (t, *J* = 13.3 Hz, 2H), 2.74 (s, 2H), 2.50 (dd, *J* = 14.6, 7.3 Hz, 2H), 1.80 (dd, *J* = 14.0, 7.4 Hz, 2H), 1.58 (t, *J* = 13.1 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 142.9, 136.9, 130.9, 128.8, 128.4, 126.7, 126.3, 73.6, 50.8, 39.1, 29.6.

FTIR (NaCl, thin film): 3557, 3455, 3060, 3026, 2931, 2853, 1493, 1454, 1223, 1086, 1042, 909 cm^{-1}.

HRMS (EI, *m/z*): $C_{18}H_{19}O$, calc'd for $(M+H-H_2)^+$: 251.1436, found: 251.1433.

Preparation of methyl oxalate SI-15.



SI-14 (90% yield) SI-15

To a 50 mL round bottom flask containing a solution of alcohol **SI-14** (245 mg, 0.97 mmol) in CH_2Cl_2 (8.8 mL) at 0 °C was added Et_3N (0.2 mL, 1.46 mmol, 1.5 equiv), DMAP (12 mg, 0.10 mmol, 0.1 equiv), and methyl oxalyl chloride (0.11 mL, 1.17 mmol, 1.2 equiv) dropwise by syringe. The reaction was stirred at room temperature for 4.5 h followed by the addition of a 4:1 mixture of a saturated aqueous solution of NH_4Cl and a saturated aqueous solution of NaCl (5 mL). The organic layer was collected and the aqueous layer was extracted with Et_2O (4 x 8 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (5–10% EtOAc/hexanes) to afford methyl oxalate **SI-15** (297 mg, 90% yield) as a clear crystalline solid.

TLC: R_f 0.52 (15% EtOAc/hexanes, UV, $KMnO_4$).

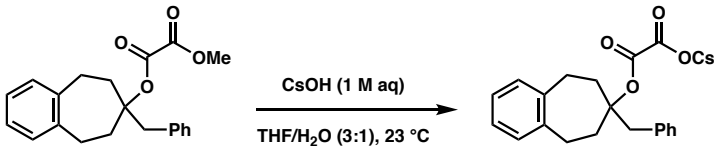
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 – 7.19 (m, 4H), 7.15 – 7.10 (m, 2H), 7.08 (q, *J* = 1.2 Hz, 4H), 3.88 (s, 3H), 3.30 (s, 2H), 3.14 – 2.99 (m, 2H), 2.67 (dd, *J* = 14.2, 7.3 Hz, 2H), 2.56 (ddd, *J* = 14.9, 7.3, 1.3 Hz, 2H), 1.69 – 1.48 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 159.0, 157.3, 142.1, 135.7, 130.7, 129.0, 128.4, 127.0, 126.5, 91.2, 53.5, 45.0, 35.9, 29.3.

FTIR (NaCl, thin film): 3028, 2952, 1766, 1738, 1494, 1454, 1326, 1202, 981 cm^{-1}.

HRMS (EI, *m/z*): $C_{21}H_{21}O_4$, calc'd for $(M+H-H_2)^+$: 337.1440, found: 337.1435.

Preparation of cesium oxalate 347f.



SI-15 (99% yield) 347f

A 20 mL scintillation vial was charged with methyl oxalate **SI-15** (253 mg, 0.75 mmol), THF (4.7 mL), and H_2O (0.8 mL). A 1 M aqueous solution of CsOH (1 M in H_2O, 0.75 mL, 0.75 mmol, 1.0 equiv) was added dropwise to the solution with vigorous stirring. After the addition was complete, the mixture was stirred for an additional 5 min. The reaction was concentrated under reduced pressure using rotary evaporation and then high vacuum (~50 mTorr) to provide cesium oxalate **347f** as a white solid (339 mg, 99% yield).

^{1}H NMR (400 MHz, DMSO-d_6): δ 7.28 – 7.14 (m, 5H), 7.11 – 6.99 (m, 4H), 3.20 (s, 2H), 3.01 (t, J = 12.9 Hz, 2H), 2.48 – 2.36 (m, 4H), 1.32 (t, J = 13.1 Hz, 2H).

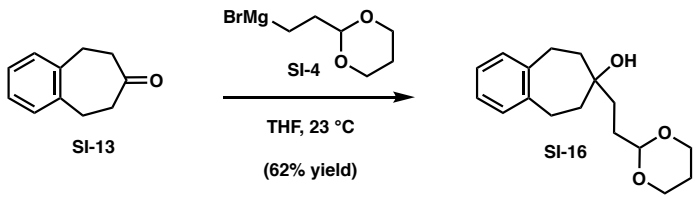
^{13}C NMR (101 MHz, DMSO-d_6): δ 167.9, 163.3, 142.4, 136.9, 130.7, 128.5, 127.8, 126.2, 126.0, 83.7, 44.1, 35.8, 28.4.

IR (ATR): 3374, 2965, 1712, 1627, 1396, 1208, 1185 cm^{-1}.

HRMS (TOF-ESI, *m/z*): $C_{20}H_{19}O_4$, calc'd for $(M-Cs)^-$: 323.1289, found: 323.1292.

f. Preparation of cesium oxalate 347g.

Preparation of alcohol SI-16.



For the preparation of **SI-4**, a flame-dried 25 mL round bottom flask was charged with magnesium turnings (99 mg, 4.06 mmol, 2.6 equiv). The vessel was exchanged three times with argon and THF (1.0 mL) was added. With vigorous stirring, 1,2-dibromoethane (35 μL, 0.41 mmol, 0.26 equiv) was added dropwise to the suspension. After 10 min, a solution of 2-(2-bromoethyl)-1,3-dioxane (517 mg, 2.65 mmol, 1.7 equiv) in THF (2.0 mL) was added dropwise over 10 min. Upon completion of addition, the reaction was stirred for an additional 1.5 h, yielding Grignard **SI-4** as a grey solution. A separate flame-dried 50 mL round bottom flask was charged with cyclopentanone **SI-13** (250 mg, 1.56 mmol)[5] and THF (2.0 mL) to which the Grignard reagent was added dropwise via syringe. The Grignard reagent flask was rinsed with THF (1.0 mL) and added to the reaction for quantitative transfer. The resulting solution was stirred for 22 h and then quenched with the addition of a saturated aqueous solution of NH_4Cl (3 mL) and stirred vigorously for 10 min. The biphasic mixture was concentrated under rotary evaporation to remove the THF. A saturated aqueous solution of NaCl (2 mL) was added and the resulting solution was extracted with Et_2O (4 x 10 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by silica

gel chromatography (10–50% EtOAc/hexanes) to give tertiary alcohol **SI-16** (267 mg, 62% yield) as a clear crystalline solid.

TLC: R_f 0.34 (50% EtOAc/hexanes, UV, $KMnO_4$).

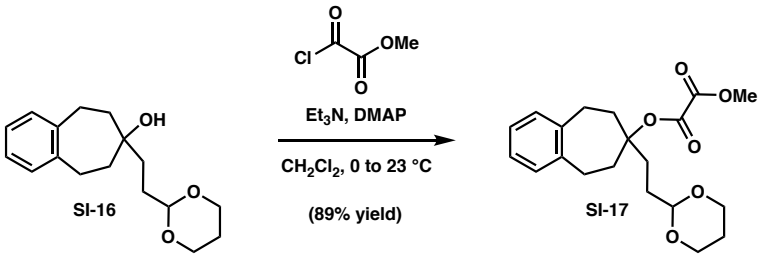
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.10 (s, 4H), 4.57 (t, *J* = 4.8 Hz, 1H), 4.12 (ddt, *J* = 10.5, 5.0, 1.4 Hz, 2H), 3.83 – 3.66 (m, 2H), 3.18 (t, *J* = 13.2 Hz, 2H), 2.52 (ddd, *J* = 14.6, 7.7, 1.4 Hz, 2H), 2.32 (t, *J* = 11.3 Hz, 1H), 2.18 – 2.00 (m, 1H), 1.84 (dd, *J* = 13.9, 7.8 Hz, 2H), 1.75 (dtd, *J* = 10.6, 5.1, 2.8 Hz, 2H), 1.61 (dd, *J* = 8.9, 6.4 Hz, 2H), 1.51 (t, *J* = 12.9 Hz, 2H), 1.35 (dtt, *J* = 13.5, 2.6, 1.4 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 143.1, 128.8, 126.1, 102.6, 72.9, 67.0, 39.2, 38.0, 29.7, 29.0, 25.8.

FTIR (NaCl, thin film): 3457, 2932, 2853, 1492, 1454, 1404, 1144, 1097, 998, 903 cm^{-1}.

HRMS (EI, *m/z*): $C_{17}H_{23}O_3$, calc'd for $(M+H-H_2)^+$: 275.1647, found: 275.1638.

Preparation of methyl oxalate SI-17.



To a 50 mL round bottom flask containing a solution of alcohol **SI-16** (202 mg, 0.73 mmol) in CH_2Cl_2 (6.6 mL) at 0 °C was added Et_3N (0.15 mL, 1.09 mmol, 1.5 equiv), DMAP (9 mg, 0.07 mmol, 0.1 equiv), and methyl oxalyl chloride (0.11 mL, 1.17 mmol, 1.2 equiv)

dropwise by syringe. The reaction was stirred at room temperature for 3 h followed by the addition of a 3:1 mixture of a saturated aqueous solution of NH_4Cl and a saturated aqueous solution of NaCl (4 mL). The organic layer was collected and the aqueous layer was extracted with CH_2Cl_2 (3 x 6 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (10–33% EtOAc/hexanes) to afford methyl oxalate **SI-17** (237 mg, 89% yield) as a white crystalline solid.

TLC: R_f 0.34 (33% EtOAc/hexanes, UV, $KMnO_4$).

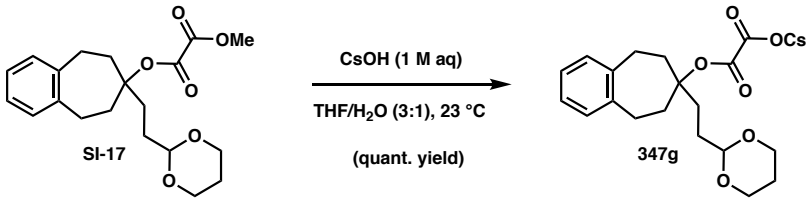
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.10 (s, 4H), 4.48 (t, *J* = 5.1 Hz, 1H), 4.07 (ddt, *J* = 10.4, 5.0, 1.4 Hz, 2H), 3.88 (s, 3H), 3.72 (dddd, *J* = 11.9, 10.5, 2.6, 1.6 Hz, 2H), 3.15 – 2.95 (m, 2H), 2.59 (ddt, *J* = 14.0, 10.5, 6.6 Hz, 4H), 2.15 – 1.94 (m, 3H), 1.72 – 1.43 (m, 4H), 1.32 (dtt, *J* = 13.4, 2.6, 1.4 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 158.9, 156.6, 142.1, 129.0, 126.5, 102.0, 91.2, 67.0, 53.5, 36.0, 32.9, 29.4, 29.2, 25.8.

FTIR (NaCl, thin film): 2954, 2852, 2732, 1765, 1740, 1494, 1454, 1327, 1206, 1168, 1085, 1009, 894 cm^{-1}.

HRMS (EI, *m/z*): $C_{20}H_{25}O_6$, calc'd for $(M+H-H_2)^+$: 361.1651, found: 361.1652.

Preparation of cesium oxalate 347g.



A 20 mL scintillation vial was charged with methyl oxalate **SI-17** (180 mg, 0.50 mmol), THF (3.1 mL), and H_2O (0.53 mL). A 1 M aqueous solution of CsOH (1 M in H_2O, 0.5 mL, 0.50 mmol, 1.0 equiv) was added dropwise to the solution with vigorous stirring. After the addition was complete, the mixture was stirred for an additional 5 min. The reaction was concentrated under reduced pressure using rotary evaporation and then high vacuum (~50 mTorr) to give cesium oxalate **347g** as a hygroscopic white solid (242 mg, quant. yield).

^{1}H NMR (400 MHz, D_2O): δ 7.24 – 7.01 (m, 4H), 4.66 (t, *J* = 5.3 Hz, 1H), 4.05 (ddd, *J* = 12.2, 5.0, 1.3 Hz, 2H), 3.83 (td, *J* = 12.4, 2.4 Hz, 2H), 2.98 (dd, *J* = 14.6, 11.6 Hz, 2H), 2.56 (dd, *J* = 14.7, 7.7 Hz, 2H), 2.47 (dd, *J* = 14.5, 7.7 Hz, 2H), 2.10 – 1.82 (m, 3H), 1.72 – 1.34 (m, 5H).

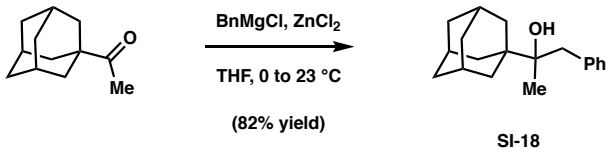
^{13}C NMR (101 MHz, D_2O): δ 167.5, 166.5, 145.2, 131.4, 129.1, 104.6, 91.9, 69.5, 38.0, 34.6, 31.1, 30.9, 27.6.

IR (ATR): 3399, 2933, 2856, 1711, 1638, 1375, 1206, 1145 cm^{-1}.

HRMS (TOF-ESI, *m/z*): $C_{19}H_{23}O_6$, calc'd for $(M–Cs)^-$: 347.1500, found: 347.1503.

g. Preparation of cesium oxalate 347h.

Preparation of tertiary alcohol SI-18.



A flame-dried 25 mL round bottom flask was charged with $ZnCl_2$ (38 mg, 0.28 mmol, 0.25 equiv) and THF (1.7 mL). A solution of BnMgCl (2.0 M in THF, 1.1 mL, 02.24 mmol, 2.0 equiv) was added dropwise and the reaction was stirred for 1 h. The contents were then cooled to 0 ºC and a solution of 1-adamantyl methyl ketone (200 mg, 1.12 mmol) in THF (2.0 mL) was added dropwise. The reaction was stirred for 2 h at 0 ºC then warmed to room temperature over 12 h. A 4:1 mixture of a saturated aqueous solution of NH_4Cl and H_2O (2.5 mL) was slowly added and the biphasic mixture was concentrated under rotary evaporation to remove the THF. The resulting solution was extracted with Et_2O (4 x 4 mL). The combined organic extracts were washed with saturated aqueous NaCl (3 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude ratio of benzyl adduct **SI-18** to 1-adamantyl methyl ketone starting material was ~8:1. The crude residue was purified by silica gel chromatography (5–10% Et_2O/hexanes) to afford tertiary alcohol **SI-18** (247 mg, 82% yield) as a white solid.

TLC: R_f 0.36 (15% Et_2O/hexanes, UV, $KMnO_4$).

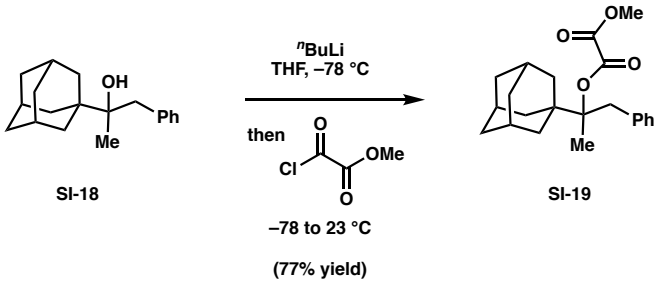
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 – 7.15 (m, 5H), 2.92 (d, *J* = 13.1 Hz, 1H), 2.56 (d, *J* = 13.1 Hz, 1H), 2.13 – 1.94 (m, 3H), 1.76 (d, *J* = 3.1 Hz, 7H), 1.69 (ddt, *J* = 13.3, 9.4, 2.2 Hz, 5H), 1.13 – 1.03 (br s, 1H), 0.92 (d, *J* = 0.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 138.7, 131.2, 128.1, 126.2, 75.8, 41.1, 39.3, 37.3, 36.4, 28.9, 20.8.

FTIR (NaCl, thin film): 3496, 2905, 2850, 1679, 1492, 1379, 1191, 1090, 927 cm^{-1}.

HRMS (EI, *m/z*): $C_{19}H_{25}O$, calc'd for $(M+H-H_2)^+$: 269.1905, found: 269.1900.

Preparation of methyl oxalate SI-19.



A flame-dried 25 mL round bottom flask was charged with alcohol **SI-18** (50 mg, 0.19 mmol) and THF (0.74 mL). The flask was cooled to –78 ºC followed by dropwise addition of ^{n}BuLi (2.05 M in hexanes, 0.11 mL, 0.22 mmol, 1.2 equiv). The reaction was stirred for an additional 30 min at the same temperature. Methyl oxalyl chloride (30 µL, 0.31 mmol, 1.7 equiv) was added dropwise via syringe. The reaction was stirred at –78 ºC for 1 h and then warmed to room temperature over 3 h. The reaction was diluted with Et_2O (1.5 mL) and quenched with a 1:1 mixture of a saturated aqueous solution of $NaHCO_3$ and a saturated aqueous solution of NaCl (2 mL). The biphasic mixture was concentrated under rotary evaporation to remove the THF and the resulting solution was extracted with Et_2O (4 x 3 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by silica gel

chromatography (5–15% Et_2O/hexanes) to provide methyl oxalate **SI-19** (51 mg, 77% yield) as a white crystalline solid.

TLC: R_f 0.40 (10% EtOAc/hexanes, UV, $KMnO_4$).

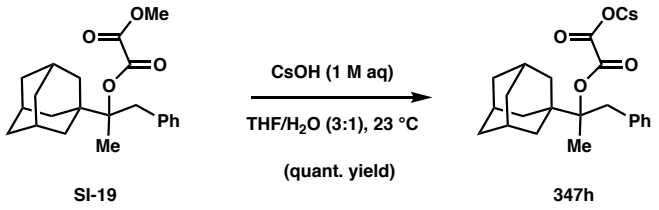
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 – 7.05 (m, 5H), 3.89 (s, 3H), 3.33 (d, *J* = 13.6 Hz, 1H), 2.73 (dd, *J* = 13.9, 2.6 Hz, 1H), 2.15 – 1.97 (m, 3H), 1.92 – 1.80 (m, 3H), 1.71 (p, *J* = 12.7, 12.2 Hz, 9H), 1.48 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 159.3, 156.9, 137.4, 131.1, 128.1, 126.6, 96.0, 53.4, 41.4, 40.9, 37.0, 36.9, 28.6, 18.6.

FTIR (NaCl, thin film): 3028, 2906, 2850, 1766, 1604, 1496, 1323, 1158, 984 cm^{-1}.

HRMS (EI, *m/z*): $C_{22}H_{27}O_4$, calc'd for $(M+H-H_2)^+$: 355.1909, found: 355.1921.

Preparation of cesium oxalate 347h.



SI-19 347h

A 20 mL scintillation vial was charged with methyl oxalate **SI-19** (292 mg, 0.82 mmol), THF (5.1 mL), and H_2O (0.88 mL). A 1 M aqueous solution of CsOH (0.82 mL, 0.82 mmol, 1.0 equiv) was then added dropwise with vigorous stirring. After the addition was complete, the mixture was stirred for an additional 5 min. The vial was then concentrated under reduced pressure using rotary evaporation followed by high vacuum (~50 mTorr) to afford cesium oxalate **347h** as a white solid (391 mg, quant. yield).

^{1}H NMR (400 MHz, DMSO-d_6): δ 7.39 – 7.26 (m, 2H), 7.26 – 7.08 (m, 3H), 3.16 (d, J = 13.8 Hz, 1H), 2.79 (d, J = 13.9 Hz, 1H), 2.03 – 1.88 (m, 3H), 1.82 – 1.70 (m, 3H), 1.71 – 1.49 (m, 9H), 1.22 (s, 3H).

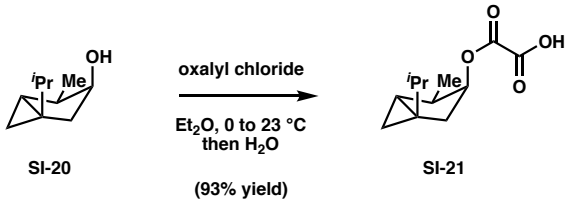
^{13}C NMR (101 MHz, DMSO- d_6): δ 167.8, 163.7, 138.8, 130.8, 127.7, 125.8, 88.3, 40.7, 36.6, 36.1, 28.1, 19.4.

IR (ATR): 3398, 2902, 2846, 1711, 1616, 1453, 1239, 1086, 893 cm^{-1}.

HRMS (TOF-ESI, *m/z*): $C_{21}H_{25}O_4$, calc'd for $(M–Cs)^–$: 341.1758, found: 341.1763.

h. Preparation of cesium oxalate 347k.

Preparation of acid SI-21.



A flame-dried 25 mL round bottom flask was charged with Et_2O (5 mL) and cooled to 0 °C. Oxalyl chloride (165 µL, 2.05 mmol, 2.05 equiv) was added. In a separate, flame-dried 2 dram vial, (–)-Thujol **SI-20** (158 mg, 1.02 mmol)[98] was dissolved in Et_2O (2 mL). The alcohol was added dropwise to the oxalyl chloride solution at 0 °C, and the vial containing the alcohol was rinsed with Et_2O (1 mL), which was then also added dropwise to the reaction flask. The mixture was stirred for 2 h at 0 °C and 1 h at 23 °C. Oxalyl chloride (40 µL, 0.51 mmol, 0.5 equiv) was then added at 23 °C, and the reaction was stirred for an additional 2 h, until all alcohol had been consumed by TLC analysis. The mixture was

concentrated under reduced pressure and dried under high vacuum (~90 mTorr) for 10 min. The residue was subsequently taken up in Et_2O (20 mL), and H_2O (20 mL) was added carefully, dropwise. The mixture was stirred vigorously until bubbling ceased (10 min), and the layers were separated. The aqueous layer was extracted with Et_2O (3 x 10 mL), and the combined organic layers were extracted with saturated aqueous $NaHCO_3$ (2 x 25 mL). The combined bicarbonate layers were washed with Et_2O (1 x 20 mL), and were subsequently acidified with 1 M HCl (35 mL), which was slowly added in portions of 5 mL to give a pH of 3. The resulting acidified aqueous layer was extracted with Et_2O (4 x 20 mL), and the combined organic layers washed with a saturated aqueous solution of NaCl (1 x 40 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure to afford **SI-21** as a clear oil (216 mg, 93% yield). *Note:* this oil will slowly decompose, even under high vacuum, if left for extended periods of time (>6 h). This decomposition was noted with slight color change to purple. The oil should be dried and carried forward as quickly as possible.

$[\alpha]_D^{25}$: –38.2° (c = 0.18, $CHCl_3$).

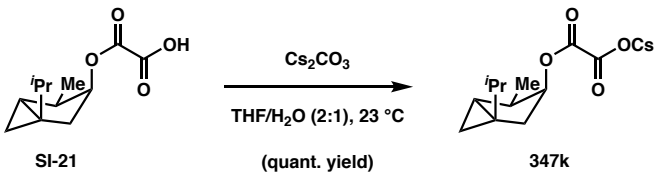
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.78 (s, 1H), 4.87 (dt, *J* = 9.0, 7.3 Hz, 1H), 2.49 (p, *J* = 7.0 Hz, 1H), 2.10 (dd, *J* = 12.4, 7.6 Hz, 1H), 1.96 – 1.85 (m, 1H), 1.30 (dt, *J* = 13.7, 6.8 Hz, 1H), 0.98 (d, *J* = 6.7 Hz, 3H), 1.00 – 0.88 (m, 1H), 0.94 (d, *J* = 5.1 Hz, 3H), 0.92 (d, *J* = 5.0 Hz, 3H), 0.42 – 0.30 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 157.8, 157.7, 79.8, 35.9, 33.1, 31.1, 30.0, 27.9, 20.2, 19.7, 15.3, 14.6.

FTIR (NaCl, thin film): 3178, 2960, 2874, 1744, 1203, 979 cm^{-1}.

HRMS (TOF-ESI, *m/z*): $C_{12}H_{17}O_4$, calc'd for $(M–H)^–$: 225.1127, found: 225.1122.

Preparation of cesium oxalate 347k.



SI-21 347k

A 20 mL scintillation vial was charged with oxalic acid **SI-21** (211 mg, 0.93 mmol) and THF (3.1 mL). Cs_2CO_3 (152 mg, 0.47 mmol, 0.5 equiv) was taken up in H_2O (1.05 mL) in a separate vial, and transferred to the vigorously stirred acid at room temperature. The vial containing the base was rinsed with H_2O (0.5 mL) and transferred dropwise to the reaction. After stirring vigorously at room temperature for 5 min, the mixture was concentrated under reduced pressure and azeotroped with PhMe (6 x 5 mL) to afford **347k** as a white solid (333 mg, quant. yield).

^{1}H NMR (400 MHz, DMSO-d_6): δ 4.54 (dt, *J* = 9.3, 7.3 Hz, 1H), 2.26 (p, *J* = 6.9 Hz, 1H), 1.86 (dd, *J* = 12.2, 7.7 Hz, 1H), 1.65 (ddd, *J* = 12.2, 9.4, 1.4 Hz, 1H), 1.27 (hept, *J* = 6.7 Hz, 1H), 0.93 (d, *J* = 6.8 Hz, 3H), 0.88 (d, *J* = 6.9 Hz, 3H), 0.91 – 0.82 (m, 1H), 0.78 (d, *J* = 7.0 Hz, 3H), 0.39 (dd, *J* = 5.1, 3.9 Hz, 1H), 0.25 (ddd, *J* = 8.3, 5.1, 1.4 Hz, 1H).

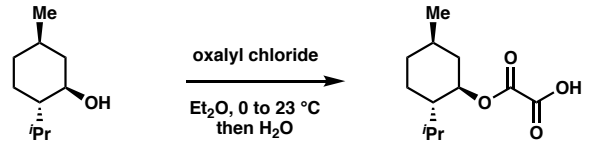
^{13}C NMR (101 MHz, DMSO-d_6): δ 167.2, 162.8, 72.6, 35.1, 32.4, 30.3, 29.6, 27.5, 20.1, 19.5, 15.1, 13.8.

IR (ATR): 3408, 2957, 1718, 1633, 1375, 1202, 1037 cm^{-1}.

HRMS (TOF-ESI, *m/z*): $C_{12}H_{17}O_4$, calc'd for $(M–Cs)^–$: 225.1127, found: 225.1135.

i. Preparation of cesium oxalate 347m:

Preparation of acid SI-22.



(–)-menthol (quant. yield) SI-22

A flame-dried 100 mL round bottom flask was charged with (–)-menthol (400 mg, 2.56 mmol) and Et_2O (20 mL). The flask was cooled to 0 °C, and oxalyl chloride (0.41 mL, 5.12 mmol, 2.0 equiv) was added dropwise. The mixture was warmed to room temperature after 10 min, and after an additional 1.5 h, TLC analysis indicated consumption of (–)-menthol. The reaction was carefully quenched at 0 °C by the dropwise addition of H_2O (30 mL) after addition of a vent needle. The mixture was stirred vigorously and warmed to room temperature. The layers were separated, and the aqueous layer extracted with Et_2O (3 x 15 mL), and the combined organic layers dried with $MgSO_4$, filtered, and concentrated under reduced pressure and azeotroped with pentane (4 x 20 mL) to afford **SI-22** as a clear oil (584 mg, quant. yield).

$[\alpha]_D^{25}$: –80.8° (c = 0.89, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.08 (bs, 1H), 4.87 (td, *J* = 11.0, 4.5 Hz, 1H), 2.05 (dddd, *J* = 11.9, 4.4, 3.4, 1.9 Hz, 1H), 1.88 (heptd, *J* = 6.9, 2.7 Hz, 1H), 1.78 – 1.67 (m, 2H), 1.63

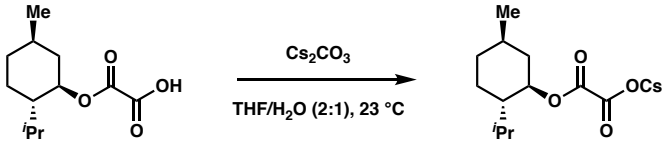
– 1.45 (m, 2H), 1.18 (td, *J* = 12.0, 11.0 Hz, 1H), 1.13 – 1.01 (m, 1H), 0.94 (d, *J* = 6.5 Hz, 3H), 0.99 – 0.84 (m, 1H), 0.91 (d, *J* = 7.0 Hz, 3H), 0.77 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 158.0, 157.5, 79.7, 46.7, 40.3, 34.0, 31.6, 26.3, 23.4, 22.0, 20.7, 16.3.

FTIR (NaCl, thin film): 3180, 2957, 2872, 1739, 1456, 1202, 950 cm^{-1}.

HRMS (TOF-ESI, *m/z*): $C_{12}H_{19}O_4$, calc'd for $(M-H)^-$: 227.1289, found: 227.1283.

Preparation of cesium oxalate 347m.



Oxalic acid **SI-22** (566 mg, 2.48 mmol) was taken up in THF (8.3 mL). Cs_2CO_3 (404 mg, 1.24 mmol, 0.5 equiv) was taken up in H_2O (3.1 mL) in a vial, and transferred dropwise to the vigorously stirred acid at room temperature. The vial containing the base was rinsed with H_2O (1 mL) and transferred dropwise to the reaction. After stirring vigorously at room temperature for 10 min, the mixture was concentrated under reduced pressure and azeotroped with PhMe (6 x 20 mL) to afford **347m** as a white solid (889 mg, quant. yield). This resulting cesium oxalate is moderately hygroscopic, and was typically stored and weighed out in a nitrogen-filled glovebox.

^{1}H NMR (400 MHz, D_2O): δ 4.75 (td, *J* = 11.0, 4.5 Hz, 1H), 1.94 (dtd, *J* = 13.0, 3.9, 1.9 Hz, 1H), 1.80 (heptd, *J* = 7.0, 2.6 Hz, 1H), 1.68 (ddt, *J* = 12.6, 9.1, 3.0 Hz, 2H), 1.55 – 1.40

(m, 2H), 1.17 – 1.01 (m, 2H), 0.89 (d, J = 6.5 Hz, 3H), 0.96 – 0.81 (m, 1H), 0.87 (d, J = 7.1 Hz, 3zH), 0.73 (d, J = 7.1 Hz, 3H).

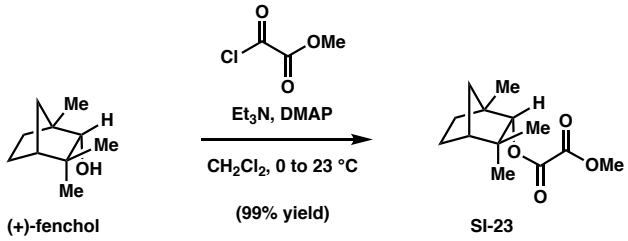
^{13}C NMR (101 MHz, D_2O): δ 167.3, 167.2, 80.0, 49.1, 42.6, 36.3, 33.7, 28.6, 25.8, 24.0, 22.5, 18.4.

IR (ATR): 2954, 1708, 1645, 1370, 1196, 963 cm^{-1}.

HRMS (TOF-ESI, *m/z*): $C_{12}H_{19}O_4$, calc'd for $(M–Cs)^-$: 227.1289, found: 227.1280.

j. Preparation of cesium oxalate 347n.

Preparation of methyl oxalate SI-23.



To a 100 mL round bottom flask containing a solution of (+)-fenchol (400 mg, 2.59 mmol) in CH_2Cl_2 (24 mL) at 0 °C was added Et_3N (0.54 mL, 3.89 mmol, 1.5 equiv), DMAP (32 mg, 0.26 mmol, 0.1 equiv), and methyl oxalyl chloride (0.29 mL, 3.11 mmol, 1.2 equiv) dropwise via syringe. The reaction was stirred at room temperature for 3 h followed by the addition of a 3:1 mixture of a saturated aqueous solution of NH_4Cl and a saturated aqueous solution of NaCl (8 mL). The organic layer was collected and the aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified

by silica gel chromatography (5–10% Et_2O/hexanes) to furnish methyl oxalate **SI-23** (617 mg, 99% yield) as a transparent crystalline solid.

TLC: R_f 0.63 (20% EtOAc/hexanes, UV, $KMnO_4$).

$[\alpha]_D^{25}$: +48.8° (c = 1.00, $CHCl_3$).

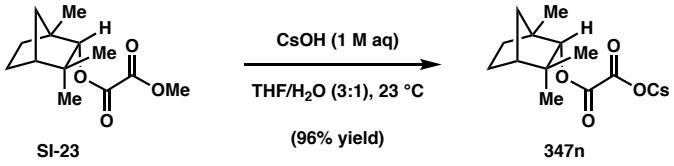
^{1}H NMR (400 MHz, $CDCl_3$): δ 4.50 (d, *J* = 2.0 Hz, 1H), 3.89 (s, 3H), 1.89 – 1.66 (m, 4H), 1.66 – 1.56 (m, 1H), 1.47 (tdd, *J* = 12.6, 5.7, 4.0 Hz, 1H), 1.23 (dd, *J* = 10.4, 1.6 Hz, 1H), 1.19 – 1.08 (m, 1H), 1.12 (s, 3H), 1.07 (s, 3H), 0.81 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 158.7, 158.4, 89.6, 53.5, 48.6, 48.4, 41.5, 39.9, 29.8, 26.6, 25.9, 20.2, 19.4.

FTIR (NaCl, thin film): 2960, 2877, 1770, 1747, 1462, 1322, 1202, 1170, 968 cm^{-1}.

HRMS (TOF-ESI, *m/z*): $C_{13}H_{20}O_4Na$, calc'd for $(M+Na)^+$: 263.1254, found: 263.1259.

Preparation of cesium oxalate 347n.



SI-23 347n

A 20 mL scintillation vial was charged with methyl oxalate **SI-23** (755 mg, 3.14 mmol), THF (9.8 mL), and H_2O (0.17 mL). A 1 M aqueous solution of CsOH (3.14 mL, 3.14 mmol, 1.0 equiv) was added dropwise to the solution with vigorous stirring. After the addition was complete, the mixture was stirred for an additional 5 min. The reaction was concentrated under rotary evaporation to remove the THF. The aqueous layer was washed with Et_2O (3 x 2.5 mL) and then concentrated under reduced pressure using rotary

evaporation followed by high vacuum (~50 mTorr) to afford cesium oxalate **347n** as a white solid (1.078 g, 96% yield).

$[\alpha]_D^{25}$: +25.1° (c = 0.98, MeOH).

^{1}H NMR (400 MHz, DMSO-d_6): δ 4.17 (d, *J* = 1.9 Hz, 1H), 1.76 – 1.51 (m, 4H), 1.40 (tdd, *J* = 12.3, 5.6, 4.0 Hz, 1H), 1.14 (dd, *J* = 10.0, 1.6 Hz, 1H), 1.06 – 1.01 (m, 1H), 1.03 (s, 3H), 0.99 (s, 3H), 0.71 (s, 3H).

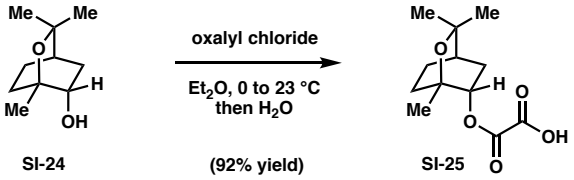
^{13}C NMR (101 MHz, DMSO-d_6): δ 168.2, 163.1, 83.6, 47.80, 47.78, 40.9, 29.5, 26.2, 25.5, 20.1, 19.4.

IR (ATR): 3413, 2940, 2874, 1710, 1640, 1364, 1203, 1032, 1003 cm^{-1}.

HRMS (TOF-ESI, *m/z*): $C_{12}H_{17}O_4$, calc'd for $(M–Cs)^-$: 225.1132, found: 225.1128.

k. Preparation of cesium oxalate 347o.

Preparation of acid SI-25.



SI-24 (92% yield) SI-25

A flame-dried 100 mL round bottom flask was charged with eucalyptol derivative **SI-24** (400 mg, 2.35 mmol)[99] and Et_2O (18 mL). The flask was cooled to 0 ºC, and oxalyl chloride (0.38 mL, 4.70 mmol, 2.0 equiv) was added dropwise. The clear mixture was stirred for 1.5 h, and then warmed to room temperature. After stirring for 24 h, the solution was cooled to 0 °C, and oxalyl chloride (0.1 mL, 1.18 mmol, 0.5 equiv) was added. The mixture was

warmed to room temperature and stirred for an additional 4 h, until all alcohol had been consumed by TLC analysis. The mixture was concentrated under reduced pressure and dried under high vacuum (~90 mTorr) for 5 min. The residue was subsequently taken up in Et_2O (30 mL) and H_2O (30 mL) was added carefully, dropwise. The mixture was stirred vigorously until bubbling ceased (10 min), and the layers were separated. The aqueous layer was extracted with Et_2O (3 x 15 mL), and the combined organic layers were extracted with saturated aqueous $NaHCO_3$ (3 x 30 mL). The combined bicarbonate layers were acidified with 1 M HCl (110 mL), which was slowly added in portions of 10 mL to give a pH of 1. The resulting acidified aqueous layer was extracted with Et_2O (3 x 80 mL), and the combined organic layers washed with a saturated aqueous solution of NaCl (1 x 60 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure to afford **SI-25** as a white solid (522 mg, 92% yield) after azeotroping with pentane.

$[\alpha]_D^{25}$: –9.5° (c = 0.53, $CHCl_3$).

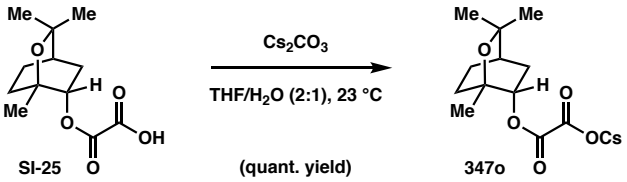
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.01 (s, 1H), 4.88 (ddd, *J* = 9.8, 3.7, 2.0 Hz, 1H), 2.69 (ddt, *J* = 14.7, 9.7, 3.3 Hz, 1H), 2.09 – 2.01 (m, 1H), 1.97 (ddd, *J* = 14.7, 11.6, 2.9 Hz, 1H), 1.74 – 1.64 (m, 1H), 1.64 – 1.53 (m, 2H), 1.43 (ddd, *J* = 14.6, 3.6, 2.4 Hz, 1H), 1.33 (s, 3H), 1.26 (s, 3H), 1.12 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 158.3, 158.0, 76.3, 75.1, 71.6, 33.9, 32.1, 28.7, 28.4, 25.7, 23.9, 21.8.

FTIR (NaCl, thin film): 3078, 2975, 1745, 1184, 1004 cm^{-1}.

HRMS (TOF-ESI, *m/z*): $C_{12}H_{17}O_5$, calc'd for $(M–H)^-$: 241.1081, found: 241.1083.

Preparation of cesium oxalate 347o.



A 20 mL scintillation vial was charged with oxalic acid **SI-25** (507 mg, 2.09 mmol) and THF (7 mL). Cs_2CO_3 (340.7 g, 1.05 mmol, 0.5 equiv) was taken up in H_2O (2.5 mL) in a separate vial, and transferred to the vigorously stirred acid at room temperature. The vial containing the base was rinsed with H_2O (1 mL) and transferred dropwise to the reaction. After stirring vigorously at room temperature for 5 min, the mixture was concentrated under reduced pressure and azeotroped with PhMe (8 x 6 mL) to afford **347o** as a white solid (780 mg, quant. yield). This resulting cesium oxalate is moderately hygroscopic, and was typically stored and weighed out in a nitrogen-filled glovebox.

^{1}H NMR (400 MHz, D_2O): δ 4.75 (ddd, *J* = 9.7, 3.6, 1.4 Hz, 1H), 2.63 (ddt, *J* = 13.1, 9.8, 3.2 Hz, 1H), 2.08 – 1.87 (m, 2H), 1.70 – 1.52 (m, 3H), 1.44 (dt, *J* = 14.7, 3.2 Hz, 1H), 1.30 (s, 3H), 1.23 (s, 3H), 1.05 (s, 3H).

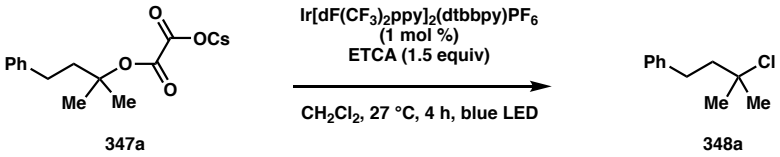
^{13}C NMR (101 MHz, D_2O): δ 167.1, 167.0, 78.5, 77.1, 74.7, 35.9, 33.9, 30.6, 30.2, 27.9, 25.8, 23.5.

IR (ATR): 2969, 1714, 1634, 1377, 1196, 1005, 874 cm^{-1}.

HRMS (TOF-ESI, *m/z*): $C_{12}H_{17}O_5$, calc'd for $(M–Cs)^–$: 241.1081, found: 241.1090.

2. Deoxychlorination Reactions

Optimization of Reaction Parameters



Entry[a]	Deviation from standard conditions	NMR yield **348a** (%)[b]
1	None	82
2	ETCA (not distilled)	32
3	HCA instead of ETCA	17
4	A instead of ETCA	0
5	B instead of ETCA	5
6	C instead of ETCA	75
7	NCS instead of ETCA	32
8	CCl_4 (10 equiv) instead of ETCA	42
9	MeCN instead of CH_2Cl_2	20
10	1,4-dioxane instead of CH_2Cl_2	36
11	THF instead of CH_2Cl_2	34
12	1,2-dichloroethane instead of CH_2Cl_2	0
13	With H_2O (10 equiv)	72
14	In dark	0
15	No [Ir] catalyst	0
16	No ETCA	0
17[c]	36 °C	82

[a]Performed on 37 mg (0.1 mmol) scale. A = ethyl chloroacetate, B = diethyl 2-chloromalonate, C = dimethyl 2,2-dichloromalonate. Internal temperature measured using a thermocouple as 27 °C.

[b]Yields determined by quantitative ^{1}H NMR spectrometry using pyrazine as a standard.

[c]Reaction directly irradiated with a Kessil A160WE blue LED lamp ~ 4 cm away. Internal temperature measured using a thermocouple.

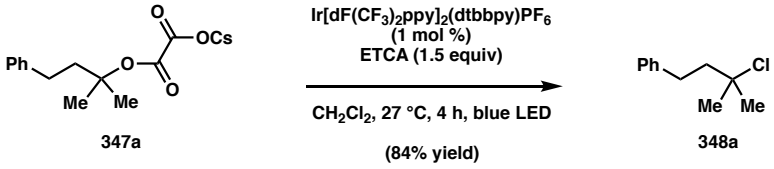
General Procedure #1 (reaction optimization): On a benchtop, 1 dram vials each containing a stir bar were successively charged with cesium oxalate **347a** (37 mg, 0.10 mmol), $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (1.1 mg, 0.001 mmol, 0.01 equiv), degassed solvent (0.5 mL) that was sparged with a balloon of argon for 15 min, and chlorinating agent (0.15 mmol, 1.5 equiv). The vials were sparged with argon for an additional 10–15 seconds and then sealed under a stream of argon with a screw cap. The vials were subsequently irradiated with blue LED light for 4 h in a Hepatochem device. Following this time, each of the vials was removed from the Hepatochem device. A 1:1 mixture of a saturated aqueous solution of NaCl and H_2O (1.5 mL) was added to each vial and then each reaction was extracted with Et_2O (3 x 3 mL). Each of the combined organic extracts was dried over $MgSO_4$, filtered, and concentrated under rotary evaporation in a rotavap water bath at 27 °C (at a pressure of ~60–100 mmHg for volatile products). NMR yields were determined using quantitative ^1H NMR spectroscopy with pyrazine as an added standard. The ^1H NMR data for tertiary chloride 2a was consistent with those reported in the literature.[100]

General Procedure #2 (substrate scope): On a benchtop, a 20 mL scintillation vial containing a stir bar was successively charged with cesium oxalate (1 equiv), $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (0.01 equiv), degassed CH_2Cl_2 (1.5 mL, sparged with a balloon of argon for 15 min), and ETCA (1.5 equiv). The vial was sparged with argon for an additional 10–15 seconds and then sealed under a stream of argon with a screw cap. The vial was placed in a Hepatochem device and irradiated with blue LED light. Tertiary

alcohol-derived cesium oxalates were irradiated for 4 h and secondary alcohol-derived cesium oxalates were irradiated for 24 h. The vial was subsequently removed from the Hepatochem device and transferred to a separatory funnel with a 1:1 mixture of a saturated aqueous solution of NaCl and H_2O (1.5 mL). The mixture was extracted with Et_2O (3 x 3 mL) and the combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under rotary evaporation in a rotavap water bath at 27 °C (at a pressure of ~60–100 mmHg for volatile products). The crude residue was purified by silica gel chromatography to afford the chlorinated products. To mitigate elimination of tertiary chlorides to the corresponding alkenes during purification, silica gel columns were treated with Et_3N as needed for selected products (see below).

Chlorides **348a**, **348b**, **348c**, **348d**, **348f**, **348i**, and **348o** were contaminated with ETCA following purification by column chromatography. For these products, the remaining ETCA was removed by dissolving in THF (0.9 mL) and MeOH (0.45 mL), cooling to 0 ºC, and then adding a 3 M aqueous solution of NaOH (0.3 mL) dropwise. After stirring at 0 ºC for 5 min and room temperature for 25 min, the solution was diluted with H_2O (1 mL) and extracted with Et_2O (4 x 2 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford the chloride products.

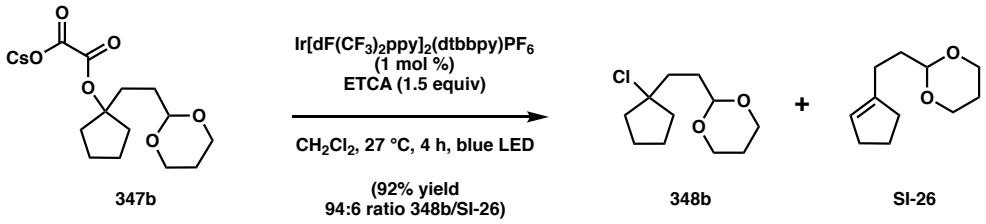
Preparation of chloride 348a.



Prepared according to general procedure #2 using cesium oxalate **347a** (115 mg, 0.31 mmol).[2] Purification of the orange-colored crude residue by silica gel column chromatography (0–2% Et_2O/pentane). Residual ETCA was removed by treatment with aqueous NaOH according to general procedure #2 to provide chloride **348a** as a pale yellow oil (48 mg, 84% yield). The ^1H NMR data for tertiary chloride 2a was consistent with those reported in the literature.[8]

TLC: R_f 0.34 (hexanes, *p*-anisaldehyde)

Preparation of chloride 348b.



Prepared according to general procedure #2 using cesium oxalate **347b** (119 mg, 0.29 mmol). A silica gel column was eluted with two column volumes of 3% Et_3N/5% Et_2O/pentane. Purification of the crude residue was then performed on this column (5–15% Et_2O/pentane). Residual ETCA was removed by treatment with aqueous NaOH according to general procedure #2 to furnish a 94:6 mixture of chloride **348b** and alkene **SI-26** as pale

yellow oil (61 mg, 92% yield: 87% 2b, 5% SI-23). ^{1}H NMR analysis indicated that alkene SI-23 did not form until after the NaOH hydrolysis procedure.

TLC (348b): R_f 0.37 (15% Et_2O/pentane, *p*-anisaldehyde).

TLC (SI-26): R_f 0.43 (15% Et_2O/pentane, *p*-anisaldehyde).

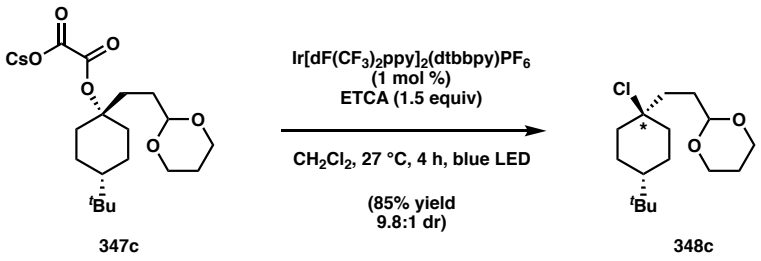
^{1}H NMR (348b, 400 MHz, $CDCl_3$): δ 4.55 (t, *J* = 4.6 Hz, 1H), 4.09 (ddt, *J* = 10.5, 5.0, 1.4 Hz, 2H), 3.83 – 3.67 (m, 2H), 2.15 – 1.99 (m, 3H), 1.99 – 1.82 (m, 6H), 1.78 – 1.62 (m, 4H), 1.33 (dtt, *J* = 13.5, 2.6, 1.4 Hz, 1H).

^{13}C NMR (348b, 101 MHz, $CDCl_3$): δ 102.1, 82.7, 67.0, 42.4, 37.5, 31.9, 25.9, 23.2.

FTIR (NaCl, thin film): 2964, 2850, 2730, 2657, 1449, 1378, 1241, 1080, 998 cm^{-1}.

HRMS (FAB+, *m/z*): $C_{11}H_{18}ClO_2$, calc'd for $(M+H-H_2)^+$: 217.0995, found: 217.0983.

Preparation of chloride 348c.



Prepared according to general procedure #2 using cesium oxalate **347c** (140 mg, 0.30 mmol). A silica gel column was eluted with two column volumes of 3% Et_3N/2% Et_2O/pentane. Purification of the crude residue was then performed on this column (5–10% pentane/Et_2O). Residual ETCA was removed by treatment with aqueous NaOH according

to general procedure #2 to give chloride **348c** as a 9.8:1 mixture of inseparable diastereomers as a clear colorless oil (72 mg, 85% yield).

TLC: R_f 0.23 (10% Et_2O/hexanes, $KMnO_4$).

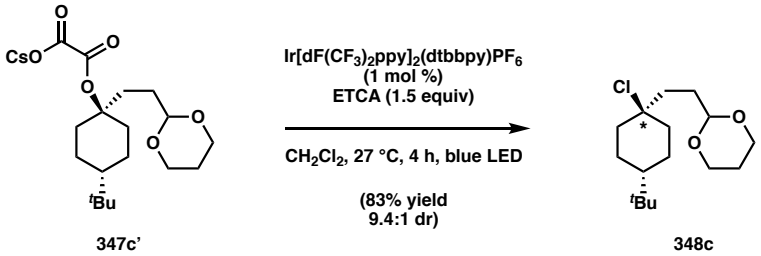
^{1}H NMR (major diastereomer, 400 MHz, $CDCl_3$): δ 4.55 (t, *J* = 4.5 Hz, 1H), 4.10 (ddt, *J* = 10.4, 5.0, 1.4 Hz,2H), 3.76 (dddd, *J* = 12.7, 10.5, 2.6, 1.5 Hz, 2H), 2.20 – 2.03 (m, 1H), 2.05 – 1.96 (m, 2H), 1.93 – 1.75 (m, 4H), 1.70 – 1.57 (m, 2H), 1.57 – 1.30 (m, 5H), 0.93 (tt, *J* = 11.8, 3.5 Hz, 1H), 0.86 (s, 9H).

^{13}C NMR (major diastereomer, 101 MHz, $CDCl_3$): δ 102.4, 75.5, 67.1, 47.7, 40.2, 40.1, 32.6, 30.0, 27.7, 25.9, 23.0.

FTIR (NaCl, thin film): 2947, 2849, 2730, 1448, 1366, 1287, 1147, 1042, 975 cm^{-1}.

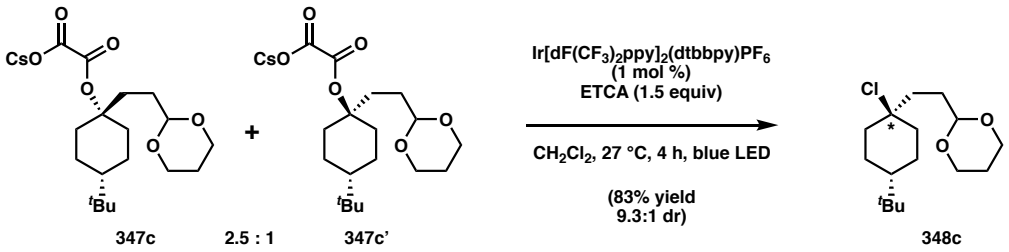
HRMS (FAB+, *m/z*): $C_{16}H_{28}ClO_2$, calc'd for $(M+H-H_2)^+$: 287.1778, found: 287.1755.

Preparation of chloride 348c.



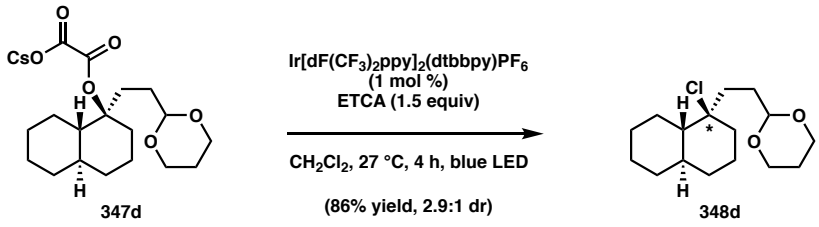
Prepared according to general procedure #2 using the epimer of cesium oxalate **347c**, cesium oxalate 1c' (114 mg, 0.24 mmol). Purification of the crude residue was then performed as above to provide chloride **348c** as a 9.4:1 mixture of inseparable diastereomers as a clear colorless oil (58 mg, 83% yield).

Preparation of chloride 348c.



Prepared according to the general procedure #2 using a 2.5:1 mixture of cesium oxalates **347c** and **347c'** respectively (139 mg, 0.29 mmol). Purification of the crude residue was then performed as above to give chloride **348c** as a 9.3:1 mixture of inseparable diastereomers as a clear colorless oil (70 mg, 83% yield).

Preparation of chloride 348d.



Prepared according to general procedure #2 using cesium oxalate **347d** (147 mg, 0.31 mmol). A silica gel column was eluted with two column volumes of 3% Et_3N/5% Et_2O/pentane. Purification of the crude residue was then performed on this column (5–15% pentane/Et_2O). Residual ETCA was removed by treatment with aqueous NaOH according to general procedure #2 to deliver chloride **348d** as a 2.9:1 mixture of inseparable diastereomers as a clear colorless oil (77 mg, 86% yield).

TLC: R_f 0.29 (15% Et_2O/pentane, *p*-anisaldehyde).

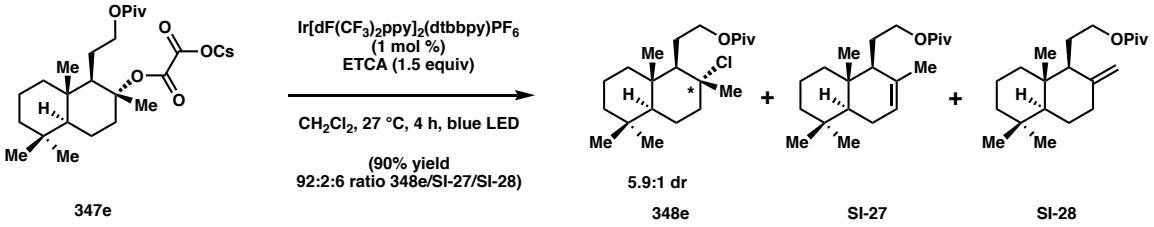
^{1}H NMR (2.4:1 dr, asterisk denotes minor diastereomer, 400 MHz, $CDCl_3$): δ *4.55 – 4.53 (m, 0.3H), 4.51 (dd, *J* = 5.5, 4.1 Hz, 1H), 4.10 (ddq, *J* = 10.2, 5.0, 1.8, 1.4 Hz, 2.7H), 3.85 – 3.67 (m, 2.7H), *2.30 – 2.20 (m, 0.5H), 2.16 – 1.96 (m, 2.8H), 1.98 – 1.87 (m, 1.6H), 1.87 – 1.70 (m, 6.4H), 1.70 – 1.40 (m, 9.6H), 1.40 – 1.08 (m, 7.7H), 1.08 – 0.77 (m, 4.3H).

^{13}C NMR (asterisk denotes minor diastereomer, 101 MHz, $CDCl_3$): δ *102.5, 102.4, *79.8, 79.0, 67.1, *55.8, 51.1, *40.5, *39.8, 38.9, 37.0, *35.0, 34.6, 34.0, *33.9, 30.2, *29.9, *28.1, *26.9, *26.7, 26.6, 26.3, 26.1, *25.93, 25.91, *23.3, 21.9.

FTIR (NaCl, thin film): 2928, 2850, 2730, 2662, 1449, 1377, 1286, 1144, 1001 cm^{-1}.

HRMS (FAB+, *m/z*): $C_{16}H_{26}ClO_2$, calc'd for $(M+H-H_2)^+$: 285.1621, found: 285.1650.

Preparation of chloride 348e.



Prepared according to general procedure #2 using cesium oxalate **347e** (165 mg, 0.30 mmol). A silica gel column was eluted with two column volumes of 3% Et_3N/2% Et_2O/pentane. Purification of the crude residue was then performed on this column (isocratic: 2% Et_2O/hexanes) to afford a 92:2:6 mixture of chloride **348e**, alkene **SI-27**, and alkene **SI-28** as a viscous yellow oil (96 mg, 90% yield: 83% **348e** 5.9:1 dr, 2% **SI-27**, 5% **SI-28**).

TLC (348e): R_f 0.28 (3% Et_2O/pentane, *p*-anisaldehyde).

$[\alpha]_D^{25}$: +3.6° (c = 1.01, $CHCl_3$).

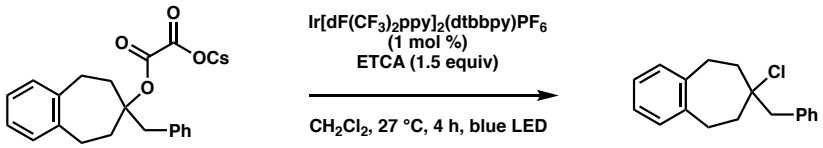
^{1}H NMR (348e, asterisk denotes minor diastereomer, 400 MHz, $CDCl_3$): δ 4.17 (td, *J* = 10.3, 6.0 Hz, 1H), 4.07 (td, *J* = 10.2, 6.1 Hz, 1H), *4.05 – 3.98 (m, 0.34 H), (dt, *J* = 12.9, 3.3 Hz, 1H), 2.12 – 1.98 (m, 1H), 1.92 – 1.75 (m, 1H), 1.74 – 1.61 (m, 3H), 1.59 – 1.51 (m, 4H), 1.52 – 1.24 (m, 3H), 1.19 (d, *J* = 1.6 Hz, 11H), 1.16 – 1.07 (m, 1H), 1.05 – 0.90 (m, 3H), 0.86 (d, *J* = 1.7 Hz, 4H), 0.85 – 0.79 (m, 3H), 0.77 (s, 3H).

^{13}C NMR (348e, asterisk denotes minor diastereomer, 101 MHz, $CDCl_3$): δ *178.83, 178.80, 78.0, *75.7, 66.4, *66.0, 58.9, *57.2, *56.1, 56.0, 46.5, *45.2, *42.0, 41.8, 40.7, 39.9, *39.6, *39.4, 38.83*, 38.82, *34.3, *33.5, 33.4, 33.3, 27.4, *26.9, *26.4, 26.2, *21.8, 21.6, 21.1, *18.8, 18.4, *18.2, 15.7, *15.5.

FTIR (NaCl, thin film): 2953, 1728, 1480, 1460, 1390, 1230, 1157, 1035, 979 cm^{-1}.

HRMS (EI, *m/z*): $C_{21}H_{37}O_2Cl$, calc'd for $(M+\cdot)^+$: 356.2480, found: 356.2482.

Preparation of chloride 348f.



Prepared according to general procedure #2 using cesium oxalate **347f** (139 mg, 0.31 mmol). A silica gel column was eluted with two column volumes of 2% Et_3N/hexanes. Purification of the crude material was then performed on this column (isocratic: 2% Et_2O/hexanes). Residual ETCA was removed by treatment with aqueous NaOH according

to general procedure #2 to give chloride **348f** as a white crystalline solid (55 mg, 67% yield).

TLC: R_f 0.35 (3% Et_2O/pentane, *p*-anisaldehyde).

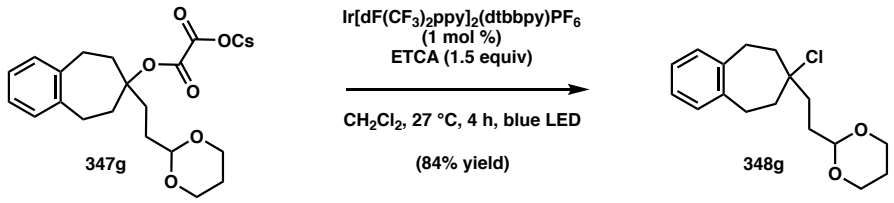
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 – 7.17 (m, 5H), 7.09 (d, *J* = 1.1 Hz, 4H), 3.32 (t, *J* = 13.4 Hz, 2H), 3.09 (s, 2H), 2.58 (dd, *J* = 14.9, 7.0 Hz, 2H), 2.27 – 2.06 (m, 2H), 1.72 (t, *J* = 13.3 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 142.4, 136.1, 131.4, 129.0, 128.0, 127.0, 126.4, 78.9, 53.0, 41.0, 31.0.

FTIR (NaCl, thin film): 3062, 3028, 2935, 1948, 1881, 1604, 1494, 1208, 1080 cm^{-1}.

HRMS (EI, *m/z*): $C_{18}H_{19}Cl$, calc'd for $(M+\cdot)^+$: 270.1175, found: 270.1169.

Preparation of chloride 348g.



Prepared according to general procedure #2 using cesium oxalate **347g** (149 mg, 0.31 mmol). A silica gel column was eluted with two column volumes of 2% Et_3N/5% Et_2O/hexanes. Purification of the crude material was then performed on this column (3–5% EtOAc/hexanes) to afford chloride **348g** as a viscous yellow oil (76 mg, 84% yield).

TLC: R_f 0.21 (5% EtOAc/hexanes, *p*-anisaldehyde).

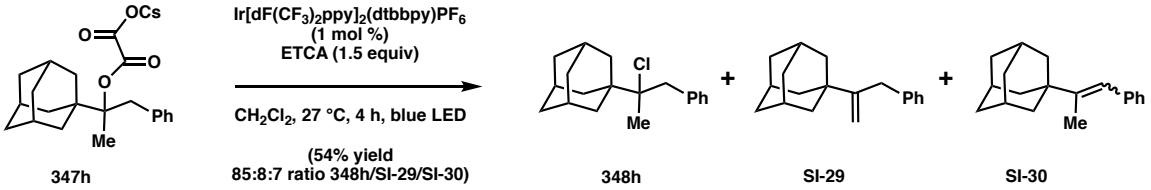
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.12 (s, 4H), 4.65 – 4.48 (m, 1H), 4.10 (ddt, *J* = 10.4, 5.0, 1.4 Hz, 2H), 3.86 – 3.61 (m, 2H), 3.15 – 3.45 (br d, *J* = 14.4 Hz, 2H), 2.75 – 2.47 (m, 2H), 2.27 – 2.15 (m, 2H), 2.07 (dtt, *J* = 13.5, 12.5, 5.0 Hz, 1H), 1.97 – 1.80 (m, 4H), 1.66 (d, *J* = 14.0 Hz, 2H), 1.40 – 1.29 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 142.4, 128.9, 126.4, 102.2, 79.1, 67.0, 41.1, 31.0, 30.1, 25.9.

FTIR (NaCl, thin film): 2938, 2852, 1764, 1493, 1453, 1377, 1239, 1145, 1086 cm^{-1}.

HRMS (EI, *m/z*): $C_{17}H_{22}O_2Cl$, calc'd for $(M+H-H_2)^+$: 293.1308, found: 293.1322.

Preparation of chloride 348h.



Prepared according to general procedure #2 using cesium oxalate **347h** (146 mg, 0.31 mmol). A silica gel column was eluted with two column volumes of 2% Et_3N/pentane. Purification of the crude residue was then performed on this column (isocratic: 2% Et_2O/pentane) to afford an inseparable 85:8:7 mixture of chloride **348h**, alkene **SI-29**, and alkene **SI-30** as a white crystalline solid (49 mg, 54% yield: 46% **348h**, 4% **SI-29**, 4% **SI-30**).

TLC: R_f 0.43 (2% EtOAc/hexanes, $KMnO_4$).

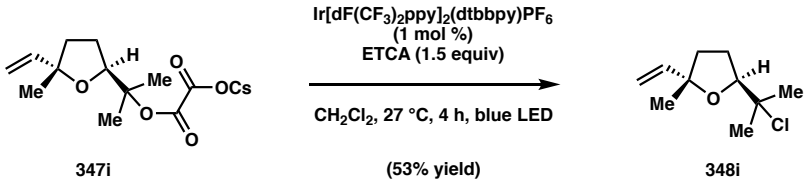
^{1}H NMR (348h, 400 MHz, $CDCl_3$): δ 7.33 – 7.19 (m, 5H), 3.19 (d, *J* = 13.7 Hz, 1H), 2.91 (d, *J* = 13.7 Hz, 1H), 2.13 – 1.96 (m, 3H), 1.88 (d, *J* = 3.0 Hz, 6H), 1.82 – 1.58 (m, 9H), 1.29 (d, *J* = 0.8 Hz, 3H).

^{13}C NMR (348h, 101 MHz, $CDCl_3$): δ 137.8, 131.8, 127.7, 126.6, 82.6, 43.0, 41.2, 37.1, 37.0, 28.9, 23.1.

FTIR (NaCl, thin film): 2905, 2849, 1763, 1604, 1496, 1451, 1082, 972 cm^{-1}.

HRMS (TOF-ES+, *m/z*): $C_{19}H_{25}ClH$, calc'd for $(M+H)^+$: 289.1718, found: 289.1723.

Preparation of chloride 348i.



347i (53% yield) 348i

Prepared according to general procedure #2 using cesium oxalate **347i** (126 mg, 0.34 mmol). The crude residue was purified by silica gel chromatography (3–5% Et_2O/pentane). Residual ETCA was removed by treatment with aqueous NaOH according to general procedure #2 to provide chloride **348i** as a white crystalline solid (33.4 mg, 53% yield).

TLC: R_f 0.37 (3% Et_2O/pentane, *p*-anisaldehyde).

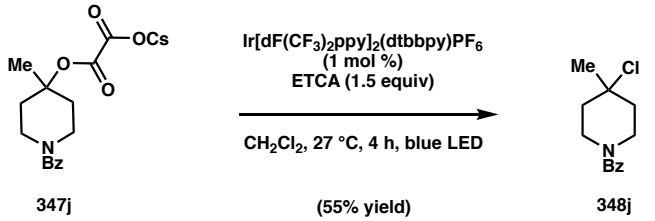
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.85 (dd, *J* = 17.3, 10.6 Hz, 1H), 5.18 (dd, *J* = 17.3, 1.6 Hz, 1H), 5.00 (dd, *J* = 10.6, 1.6 Hz, 1H), 3.98 (dd, *J* = 7.4, 6.1 Hz, 1H), 2.03 – 1.93 (m, 2H), 1.88 (ddd, *J* = 12.0, 8.0, 4.9 Hz, 1H), 1.81 – 1.68 (m, 1H), 1.55 (d, *J* = 1.5 Hz, 6H), 1.34 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 143.5, 111.6, 85.8, 84.1, 71.5, 37.1, 29.9, 27.8, 27.7, 26.7.

FTIR (NaCl, thin film): 3088, 2979, 2871, 1750, 1643, 1461, 1386, 1302, 1242, 1119, 1063, 1028, 921 cm^{-1}.

HRMS (GC-EI, *m/z*): $C_{10}H_{17}OCl$, calc'd for $(M+H-H_2)^+$: 188.0943, found: 188.0968.

Preparation of chloride 348j.



347j (55% yield) 348j

Prepared according to general procedure #2 using cesium oxalate **347j** (146 mg, 0.31 mmol). The crude residue was purified by silica gel chromatography (10–40% EtOAc/hexanes), furnishing **348j** as a light yellow solid (41 mg, 55% yield).

TLC: R_f 0.28 (33% EtOAc/hexanes, UV, $KMnO_4$).

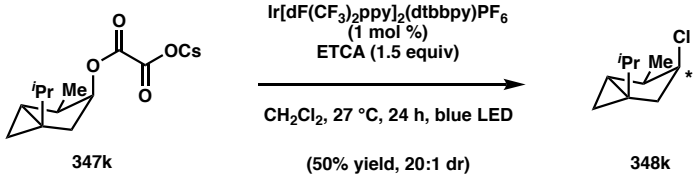
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 – 7.34 (m, 5H), 4.49 – 4.68 (br d, J = 13.4 Hz, 1H), 3.55 – 3.73 (br s, 1H), 3.55 – 3.37 (m, 1H), 3.34 – 3.11 (br s, 1H), 2.11 – 1.90 (m, 1H), 1.92 – 1.73 (m, 2H), 1.73 – 1.55 (m, 1H), 1.66 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 170.5, 136.0, 129.8, 128.6, 127.0, 69.3, 44.5, 41.2, 40.3, 38.8, 33.4.

FTIR (NaCl, thin film): 3059, 2946, 2873, 1634, 1578, 1433, 1372, 1288, 1254, 1168, 1130, 1107, 967 cm^{-1}.

HRMS (TOF-ESI, *m/z*): $C_{13}H_{16}ClNOH$, calc'd for $(M+H)^+$: 238.0993, found: 238.0986.

Preparation of chloride 348k.



Prepared according to general procedure #2 using cesium oxalate **347k** (114 mg, 0.32 mmol). The crude residue was purified by silica gel chromatography (isocratic: hexanes) to afford chloride **348k** as a fragrant clear colorless oil (27.4 mg, 50% yield, 20:1 dr). The spectral data was consistent with those reported in the literature.[21]

TLC: R_f 0.70 (pentane, *p*-anisaldehyde).

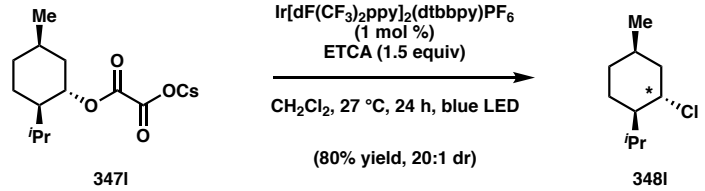
$[\alpha]_D^{25}$: –18.5° (c = 0.96, $CHCl_3$).

^{1}H NMR (19:1 dr, major diastereomer, 400 MHz, $CDCl_3$): δ 3.95 – 3.80 (m, 1H), 2.38 (ddd, *J* = 14.5, 7.9, 1.9 Hz, 1H), 2.17 (qd, *J* = 7.1, 3.0 Hz, 1H), 1.79 (dd, *J* = 14.4, 3.5 Hz, 1H), 1.28 (dt, *J* = 13.4, 6.7 Hz, 1H), 1.06 (d, *J* = 7.2 Hz, 3H), 0.98 – 0.94 (m, 1H), 0.93 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.9 Hz, 3H), 0.86 (ddt, *J* = 8.4, 3.9, 1.0 Hz, 1H), 0.57 (ddd, *J* = 8.4, 4.8, 1.7 Hz, 1H).

^{13}C NMR (19:1 dr, major diastereomer, 101 MHz, $CDCl_3$): δ 65.7, 47.2, 38.0, 35.2, 33.1, 29.9, 20.7, 20.3, 19.9, 19.0.

FTIR (NaCl, thin film): 2959, 2872, 1458, 1382, 1298, 1252, 1064, 1032, 940 cm^{-1}.

Preparation of chloride 348l.



Prepared according to general procedure #2 using cesium oxalate **347l** (110 mg, 0.31 mmol). The crude residue was purified by silica gel chromatography (isocratic: pentane) to furnish chloride **348l** as a clear colorless oil (42.5 mg, 80% yield, 20:1 dr).

TLC: R_f 0.90 (pentane, *p*-anisaldehyde).

$[\alpha]_D^{25}$: +31.8° (c = 0.95, $CHCl_3$).

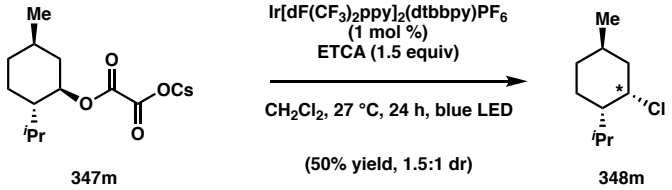
^{1}H NMR (400 MHz, $CDCl_3$): δ 4.26 (td, *J* = 7.5, 4.0 Hz, 1H), 2.02 (ddt, *J* = 14.2, 7.3, 5.0 Hz, 2H), 1.91 – 1.76 (m, 2H), 1.76 – 1.65 (m, 1H), 1.60 – 1.37 (m, 2H), 1.36 – 1.19 (m, 2H), 0.93 (dd, *J* = 6.9, 1.6 Hz, 6H), 0.86 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 62.0, 49.9, 41.1, 30.3, 28.0, 27.4, 21.1, 20.5, 19.9, 18.2.

FTIR (NaCl, thin film): 2959, 2928, 2872, 1461, 1386, 1210, 1022, 975 cm^{-1}.

HRMS (GC-EI, *m/z*): $C_{10}H_{19}Cl$, calc'd for $(M+\cdot)^+$: 174.1175, found: 174.1162.

Preparation of chloride 348m.

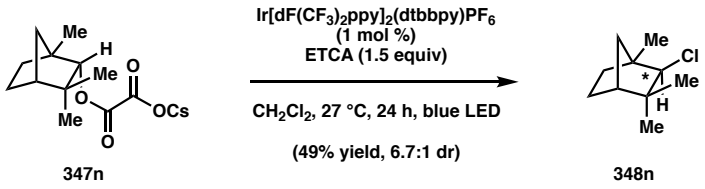


Prepared according to general procedure #2 using cesium oxalate **347m** (108.5 mg, 0.30 mmol). The crude residue was purified by silica gel chromatography (isocratic: pentane) to afford chloride **348m/329** as a clear colorless oil (25.3 mg, 50% yield, 1.5:1 dr). The ^{1}H NMR spectrum of the mixture of diastereomers was consistent with those reported for the individual diastereomers, neomenthyl chloride[92] and commercially available (−)-menthyl chloride.

TLC: R_f 0.72 (pentane, *p*-anisaldehyde).

FTIR (NaCl, thin film): 2956, 2928, 2870, 1454, 1370, 1278 cm^{-1}.

Preparation of chloride 348n.



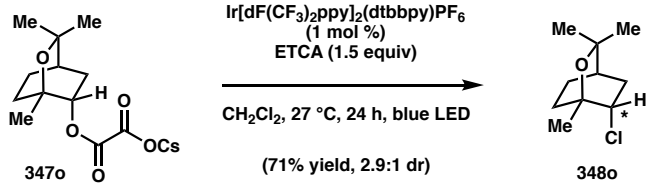
Prepared according to general procedure#2 using cesium oxalate **347n** (109 mg, 0.30 mmol). The crude residue was purified by silica gel chromatography (isocratic: pentane) to provide chloride **348n** as a clear colorless oil (25.5 mg, 49% yield, 6.7:1 dr). The ^{1}H

NMR spectrum of the mixture of diastereomers was consistent with those reported in the literature for each of the individual diastereomers.[101]

TLC: R_f 0.93 (pentane, *p*-anisaldehyde).

FTIR (NaCl, thin film): 2953, 2870, 1468, 1366, 1274, 906 cm^{-1}.

Preparation of chloride 348o.



Prepared according to the general procedure using cesium oxalate **347o** (117 mg, 0.31 mmol). The crude residue was purified by silica gel chromatography (3–10% Et_2O/pentane). Residual ETCA was removed by treatment with aqueous NaOH according to general procedure #2 to afford chloride **348o** as a clear colorless fragrant oil (41.7 mg, 71% yield, 2.9:1 dr). The spectral data were consistent with those reported in the literature.[102]

TLC (major diastereomer): R_f 0.29 (3% Et_2O/pentane, *p*-anisaldehyde).

TLC (minor diastereomer): R_f 0.24 (3% Et_2O/pentane, *p*-anisaldeyde).

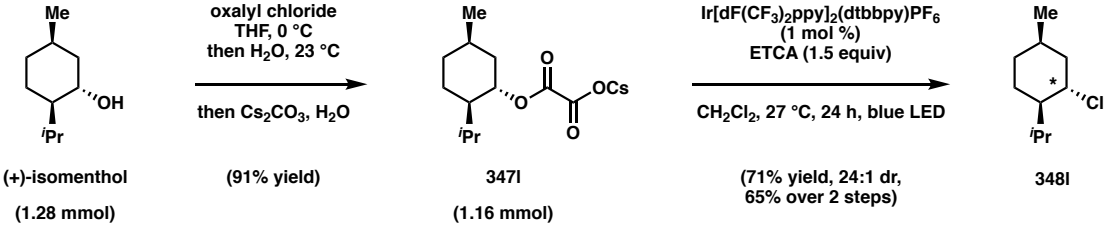
^{1}H NMR (major diastereomer, 400 MHz, $CDCl_3$): δ 3.94 (ddd, *J* = 10.2, 4.4, 2.0 Hz, 1H), 2.74 (ddt, *J* = 14.8, 10.2, 3.4 Hz, 1H), 2.15 – 2.02 (m, 1H), 2.02 – 1.86 (m, 1H), 1.81

(ddd, J = 14.8, 4.4, 2.7 Hz, 1H), 1.69 – 1.56 (m, 2H), 1.54 (tt, J = 3.5, 2.4 Hz, 1H), 1.28 (s, 3H), 1.20 (d, J = 0.7 Hz, 3H), 1.17 (s, 3H).

^{13}C NMR (major diastereomer, 101 MHz, $CDCl_3$): δ 74.2, 73.5, 59.7, 36.3, 34.6, 28.9, 28.4, 25.4, 25.2, 21.9.

FTIR (NaCl, thin film): 3362, 2970, 2935, 1723, 1460, 1379, 1200, 1129, 1090, 1069, 1051, 987 cm^{-1}.

3. 1.3 mmol Scale Deoxychlorination Sequence.



Step 1: Preparation of cesium oxalate 347l.

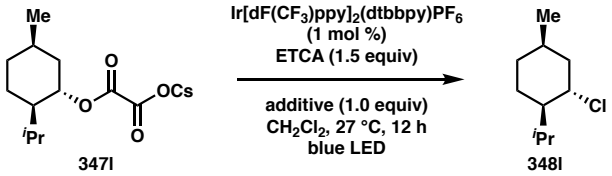
A flame-dried 100 mL round bottom flask attached to a 10 mL dropping funnel was charged with a solution of oxalyl chloride (0.11 mL, 1.29 mmol, 1.01 equiv) in THF (6.0 mL). The solution was cooled to 0 ºC followed by dropwise addition of a solution of (+)-isomenthol (200 mg, 1.28 mmol) in THF (6 mL) over 15 min. The transfer was made quantitative using an additional amount of THF (2 x 0.5 mL). After the reaction was stirred at this temperature for 1 h, H_2O (4.3 mL) was added and the resulting solution was warmed to room temperature while stirring for an additional 1 h. A saturated aqueous solution of NaCl (8 mL) was added, the contents were transferred to a separatory funnel, and the flask was rinsed with THF (2 mL) to make the transfer quantitative. The aqueous layer was

separated and the organic layer was washed with a 2:1 mixture of a saturated aqueous solution of NaCl and H_2O (12 mL) followed by a 1:2 mixture of saturated aqueous solution of NaCl and H_2O (2 x 12 mL). A solution of Cs_2CO_3 (213 mg, 0.51 equiv) in H_2O (1.0 mL) was then added. The contents were shaken thoroughly and then concentrated under rotary evaporation to remove the THF. The aqueous solution was washed with 1:1 pentane/Et_2O (3 x 3 mL) and then concentrated using rotary evaporation followed by high vacuum (~50 mTorr) to afford cesium oxalate **347l** (419 mg, 91% yield) as a white solid.

Step 2: Preparation of chloride 348l.

A 15 mL Schlenk tube was charged with cesium oxalate **347l** (419 mg, 1.16 mmol), $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (13 mg, 0.012 mmol, 0.01 equiv), and a magnetic stir bar. The flask was evacuated and backfilled with argon (x 3) and CH_2Cl_2 (5.8 mL) that was degassed by sparging with argon for 15 min and ETCA (0.24 mL, 1.74 mmol, 1.5 equiv) were added. The flask was sealed and irradiated with a Kessil A160WE blue LED lamp placed approximately 4 cm away and cooled using a fan. The reaction was stirred vigorously for 24 h under these conditions (550 rpm). The blue LED was turned off and H_2O (5 mL) was added to the orange suspension. The contents were transferred to a separatory funnel and extracted with Et_2O (4 x 10 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under rotary evaporation in a rotavap water bath at 27 °C (at a pressure of ~60–100 mmHg). The crude orange material was purified by silica gel chromatography (isocratic: pentane) to afford chloride **348l** as a clear colorless oil (144 mg, 71% yield, 24:1 dr).

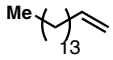
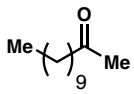
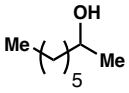
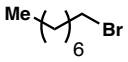
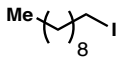
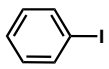
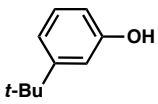
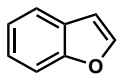
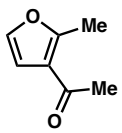
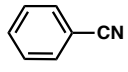
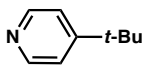
4. Functional Group Tolerance of the Radical Deoxychlorination.

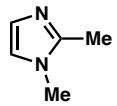
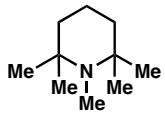
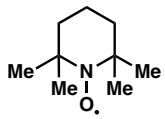
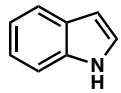
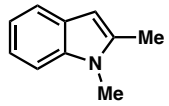
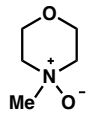


General Procedure #3: On a benchtop, 1/2 dram vials each containing a stir bar were successively charged with **347l** (37 mg, 0.10 mmol), Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (1.2 mg, 0.001 mmol, 0.01 equiv), additive (0.10 mmol, 1.0 equiv), CH_2Cl_2 (0.5 mL) that was degassed by sparging with a balloon of argon for 15 min, and ETCA (29 mg, 0.15 mmol, 1.5 equiv). The vials were sparged with argon for an additional 5 seconds, sealed under a stream of argon, and irradiated with blue LED light in a Hepatochem device for 12 h. After removing the vials from the Hepatochem device, a 1:1 mixture of saturated aqueous solution of NaCl and H_2O (0.5 mL) was added to each vial. Each reaction was extracted with Et_2O (4 x 1 mL). Each of the combined organic extracts was then dried over $MgSO_4$ and filtered. A solution of a measured amount of *n*-dodecane standard in hexanes was added to each of the combined organic extracts. After thoroughly mixing the resulting solutions, a ~1 mL aliquot was taken for each sample and analyzed by GC-flame ionization detection. The yields of **348l** and additive were calculated based on a calibrated response factor (RF).

Response Factor (RF) = (Area standard/Area additive) x (mmol additive/mmol standard)

RF 2l (major diastereomer) = 1.209 RF 2l (minor diastereomer) = 1.553

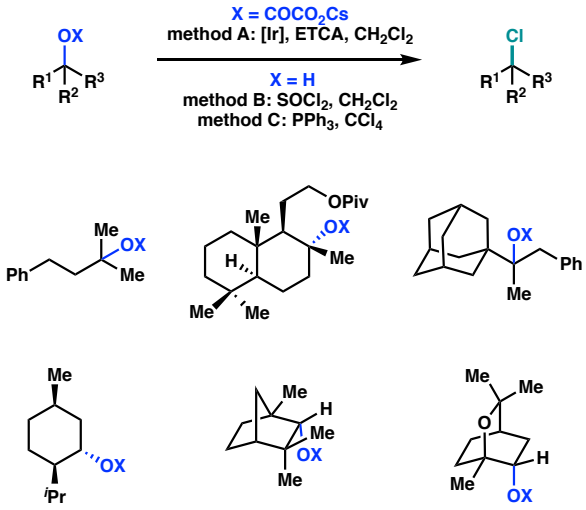
Additive	Area % **348l**[a]	Area % std	Area % additive	RF additive:std	Mass std (mg)	GC yield of **348l**	Additive recovery
None	55.7	24.3	N/A	N/A	5.0	80%	N/A
	36.8	18.3	31.6	1.065	4.6	64%	48%
	30.6	16.2	34.9	1.237	5.7	76%	87%
	36.8	16.8	22.5	2.426	5.3	80%	97%
	31.8	15.3	33.1	1.564	5.3	76%	101%
	30.7	16.5	33.4	1.563	4.9	65%	90%
	33.4	19.2	28.2	1.914	5.7	70%	92%
	0.7	44.0	13.4	1.586	5.3	1%	15%
	39.0	18.1	35.3	1.954	4.6	69%	99%
	42.1	19.5	24.7	2.291	4.6	69%	75%
	38.9	17.1	30.1	1.761	4.9	79%	87%
	17.3	31.1	32.3	1.432	5.7	72%	87%

	0.6	37.2	ND	ND	5.8	1%	ND[b]
	58.0	31.9	3.9	3.598	5.8	74%	14%
	3.9	50.7	0.6	1.379	4.9	3%	0%
	2.9	52.1	3.7	1.279	5.8	2%	3%
	0.0	48.0	10.0	2.165	5.7	0%	15%
	0.0	21.1	32.7	1.377	4.6	0%	55%
$BF_3 \bullet OEt_2$	1.4	35.3	ND	ND	4.9	2%	ND
	49.0	31.8	ND	ND	4.9	53%	ND

[a]Area % 348l = combined area of major and minor diastereomers of 348l

[b]Not determined due to overlapping peaks in GC trace.

5. Comparison with Non-Radical Deoxychlorination Processes.



Method A (Radical deoxychlorination conditions; X=$COCO_2Cs$): Experimental procedures listed in the above deoxychlorination reactions section.

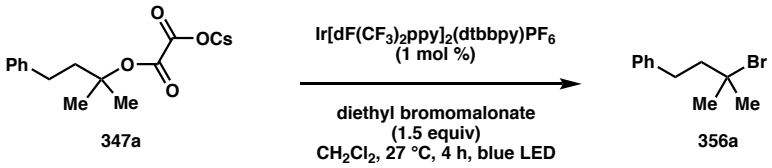
Method B (Appel reaction conditions; X=H): A 2 dram vial containing a stir bar was successively charged with alcohol substrate (0.1 mmol), triphenyl phosphine (52.5 mg, 0.2 mmol, 2.0 equiv), and CCl_4 (0.33 mL). The vial was sealed and the reaction contents were stirred at 70 ºC for 14 h. The reaction was then cooled to room temperature and diluted with Et_2O (2 mL). The resulting slurry was filtered through Celite, rinsed with Et_2O (10 mL), and concentrated under rotary evaporation in a rotavap water bath at 27 °C (at a pressure of ~60–100 mmHg for volatile products). NMR yields were determined using quantitative ^1H NMR spectroscopy with pyrazine as an added standard.

Method C ($SOCl_2$ conditions; X=H): A 2 dram vial containing a stir bar was successively charged with alcohol substrate (0.1 mmol) and CH_2Cl_2 (1.0 mL) and the contents were then

placed under an argon atmosphere and cooled to 0 ºC. To the stirred solution was added $SOCl_2$ (35 µL, 0.50 mmol, 5.0 equiv) dropwise. The reaction was then allowed to warm to room temperature and stirred for 20 h. The reaction was slowly quenched with a 1:1 mixture of a saturated aqueous solution of NaCl and a saturated aqueous solution of $NaHCO_3$ (1.0 mL) and then extracted with Et_2O (4 x 3 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under rotary evaporation in a rotavap water bath at 27 °C (at a pressure of ~60–100 mmHg for volatile products). NMR yields were determined using quantitative ^1H NMR spectroscopy with pyrazine as an added standard.

6. Deoxybromination Reactions

Optimization of Reaction Parameters



Entry[a]	Deviation from above conditions	NMR yield **356a** (%)[b]
1	None	66
2	NBS	0
3	CBr_4	4
4	1,1,2,2-tetrabromoethane	15
5	Ethyl tribromoacetate	9
6	2-bromo-2-methyl propionic acid	0
7	0.2 equiv Cs_2CO_3	80
8	0.5 equiv Cs_2CO_3	89
9	1.0 equiv C s_2CO_3	64

[a]Performed on 37 mg (0.1 mmol) scale.

[b]Yields determined by quantitative ^{1}H NMR spectrometry using pyrazine as a standard.

General Procedure #4 (reaction optimization): On a benchtop, 1 dram vials each containing a stir bar were successively charged with cesium oxalate **347a** (37 mg, 0.10 mmol, 1 equiv), Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (1.1 mg, 0.001 mmol, 0.01 equiv), CH_2Cl_2 (0.5 mL) that was degassed by sparging with a balloon of argon for 15 min, and brominating agent (0.15 mmol, 1.5 equiv). The vials were sparged with argon for an additional 10–15 seconds and then sealed with a screw cap under a stream of argon. The vials were subsequently irradiated with blue LED light for 4 h in a Hepatochem device.

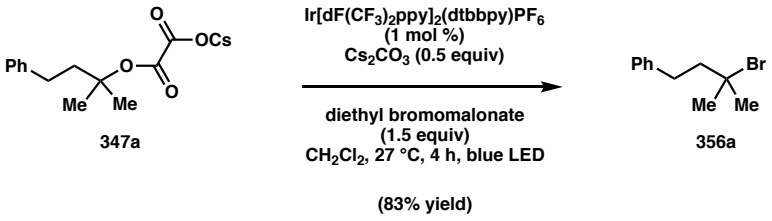
Following this time, each of the vials was removed from the Hepatochem device. A 1:1 mixture of a saturated aqueous solution of NaCl and H_2O (1.5 mL) was added to each vial and then each reaction was extracted with Et_2O (3 x 3 mL). Each of the combined organic extracts was dried over $MgSO_4$, filtered, and concentrated under rotary evaporation in a rotavap water bath at 27 °C (at a pressure of ~60–100 mmHg for volatile products). NMR yields were determined using quantitative ^1H NMR spectroscopy with pyrazine as an added standard. The ^1H NMR data for the tertiary bromide **356a** was consistent with those reported in the literature.[100]

General Procedure #5 (substrate scope): A 20 mL scintillation vial containing a stir bar was successively charged with cesium oxalate (1 equiv), $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (0.01 equiv), cesium carbonate (0.5 equiv), CH_2Cl_2 (1.5 mL) that was degassed by sparging with a balloon of argon for 15 min, and diethyl bromomalonate (1.5 equiv) were added. The vial was sparged with argon for an additional 10–15 seconds and then sealed with a screw cap under a stream of argon. The vial was placed in a Hepatochem device and irradiated with blue LED light. Tertiary alcohol-derived cesium oxalates were irradiated for 4 h and secondary alcohol-derived cesium oxalates were irradiated for 24 h. The vial was subsequently removed from the Hepatochem device and transferred to a separatory funnel with a 1:1 mixture of a saturated aqueous solution of NaCl and H_2O (1.5 mL) and then extracted with Et_2O (3 x 3 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under rotary evaporation in a rotavap water bath at 27 °C (at a pressure of ~60–100 mmHg for volatile products). The crude residue was purified by silica

gel chromatography to afford the brominated products. To mitigate elimination of tertiary bromides to the corresponding alkenes during purification, silica gel columns were treated with Et_3N as needed (see below).

Bromides **356a** and **356b** were contaminated with diethyl bromomalonate and diethyl malonate following purification by column chromatography. For these products, the diethyl bromomalonate and diethyl malonate were removed by dissolving in THF (0.9 mL) and MeOH (0.45 mL), cooling to 0 ºC, and then adding a 3 M aqueous solution of NaOH (0.3 mL) dropwise. After stirring at 0 ºC for 5 min and room temperature for 25 min, the solution was diluted with H_2O (1 mL) and extracted with Et_2O (4 x 2 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford the bromide products.

Preparation of bromide 356a.

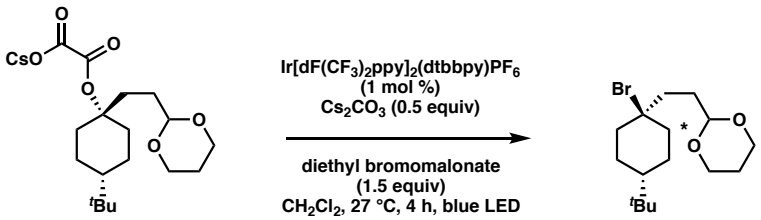


Prepared according to general procedure #5 using cesium oxalate **347a** (111 mg, 0.30 mmol). A silica gel column was eluted with two column volumes of 3% Et_3N/2% Et_2O/pentane. The crude material was then purified using this column (isocratic: 2% Et_2O/pentane). Residual diethyl bromomalonate and diethylmalonate were removed by treatment with aqueous NaOH according to general procedure #5 to deliver bromide **356a**

as a pale yellow oil (57 mg, 83% yield). The ^{1}H NMR data for tertiary bromide **356a** was consistent with those reported in the literature.[100]

TLC: R_f 0.37 (hexanes, *p*-anisaldehyde).

Preparation of bromide 356b.



347c (83% yield, 7.4:1 dr) **356b**

Prepared according to general procedure #5 using cesium oxalate **347c** (128 mg, 0.27 mmol). A silica gel column was eluted with two column volumes of 3% Et_3N/5% Et_2O/pentane. The crude material was then purified using this column (isocratic: 2% Et_2O/pentane). Residual diethyl bromomalonate and diethylmalonate were removed by treatment with aqueous NaOH according to general procedure #5 to afford bromide **356b** as a mixture of inseparable diastereomers as a clear colorless oil (75 mg, 83% yield, 7.4:1 dr).

TLC: R_f 0.28 (10% Et_2O/hexanes, *p*-anisaldehyde).

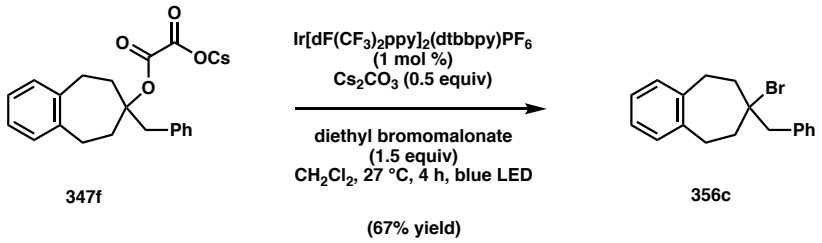
^{1}H NMR (400 MHz, $CDCl_3$): δ 4.56 (t, *J* = 4.2 Hz, 1H), 4.10 (ddt, *J* = 10.4, 5.0, 1.4 Hz, 2H), 3.76 (dddd, *J* = 11.9, 10.4, 2.6, 1.6 Hz, 2H), 2.18 – 2.08 (m, 2H), 2.08 – 2.00 (m, 1H), 1.98 – 1.85 (m, 4H), 1.73 – 1.47 (m, 4H), 1.40 – 1.27 (m, 3H), 0.95 (tt, *J* = 11.9, 3.6 Hz, 1H), 0.86 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 102.3, 76.6, 67.1, 47.6, 41.5, 41.4, 32.6, 31.2, 27.6, 25.9, 23.9.

FTIR (NaCl, thin film): 2948, 2849, 2729, 2657, 1446, 1366, 1286, 1248, 1147, 1079, 1040, 1009, 974 cm^{-1}.

HRMS (FAB+, *m/z*): $C_{16}H_{28}BrO_2$, calc'd for $(M+H-H_2)^+$: 331.1273, found: 331.1251.

Preparation of bromide 356c.



Prepared according to general procedure #5 using cesium oxalate **347f** (136 mg, 0.30 mmol). A silica gel column was eluted with two column volumes of 2% Et_3N/pentane. The crude material was then purified using this column (isocratic: 2% Et_2O/pentane) to provide bromide **356c** as a viscous clear colorless oil (63 mg, 67% yield).

TLC: R_f 0.33 (3% Et_2O/pentane, *p*-anisaldehyde).

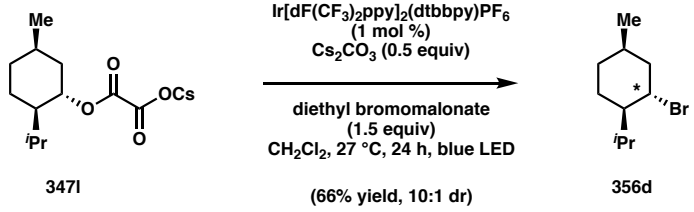
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 – 7.22 (m, 5H), 7.09 (s, 4H), 3.46 – 3.31 (m, 2H), 3.29 (s, 2H), 2.66 (dd, *J* = 14.9, 7.1 Hz, 2H), 2.33 (dddd, *J* = 14.9, 7.4, 2.3, 1.4 Hz, 2H), 1.83 – 1.56 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 142.3, 136.4, 131.5, 129.1, 128.0, 127.1, 126.5, 80.3, 54.2, 41.9, 32.6.

FTIR (NaCl, thin film): 3017, 2946, 1604, 1494, 1453, 1270, 1077, 1034, 936 cm^{-1}.

HRMS (EI, *m/z*): $C_{18}H_{18}Br$, calc'd for $(M+H-H_2)^+$: 313.0592, found: 313.0606.

Preparation of bromide 356d.



Prepared according to general procedure #5 using cesium oxalate **347l** (110 mg, 0.31 mmol). The crude residue was purified by silica gel chromatography (isocratic: 1% Et_2O/pentane) to give bromide **356d** as a clear colorless oil (44.1 mg, 66% yield, 10:1 dr).

TLC: R_f 0.66 (pentane, *p*-anisaldehyde).

$[\alpha]_D^{25}$: +36.2° (c = 1.00, $CHCl_3$).

^{1}H NMR (major diastereomer, 400 MHz, $CDCl_3$): δ 4.51 (tt, *J* = 7.2, 3.2 Hz, 1H), 2.11 – 1.94 (m, 3H), 1.88 (ddt, *J* = 11.3, 7.6, 5.1 Hz, 1H), 1.81 – 1.72 (m, 1rH), 1.60 – 1.40 (m, 3H), 1.38 – 1.23 (m, 1H), 0.93 (dd, *J* = 6.8, 2.3 Hz, 6H), 0.85 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (major diastereomer, 101 MHz, $CDCl_3$): δ 57.4, 50.2, 41.9, 30.4, 28.9, 28.5, 21.2, 21.1, 19.8, 18.3.

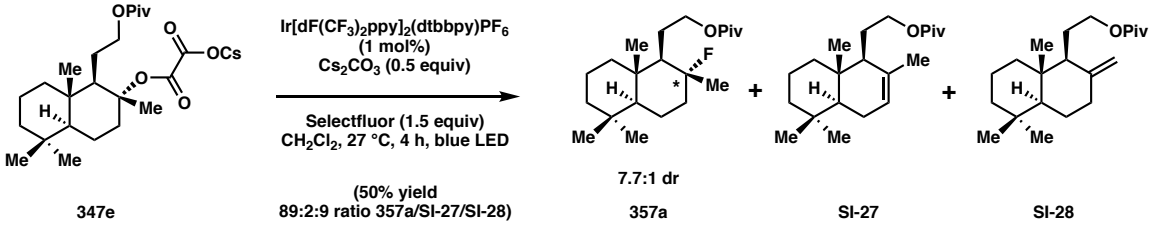
FTIR (NaCl, thin film): 2959, 1458, 1386, 1190, 1020, 974 cm^{-1}.

HRMS (GC-EI, *m/z*): $C_{10}H_{18}Br$, calc'd for $(M-H)^+$: 217.0592, found: 217.0562.

7. Deoxyfluorination Reactions

General Procedure #6: In a nitrogen-filled glovebox, a 20 mL scintillation vial was charged with Selectfluor (1.5 equiv) and Cs_2CO_3 (0.5 equiv). The vial was sealed with a screw cap and removed from the glovebox. A stir bar was then added, followed by cesium oxalate (1.0 equiv) and $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (0.01 equiv). The vial was layered with argon for 45 seconds and CH_2Cl_2 (1.5 mL) was added (degassed by sparging with a balloon of argon for 20 min). The vial was sparged with argon for an additional 10–15 seconds and then sealed with a screw cap. The vial was placed in a Hepatochem device and irradiated with blue LED light. Tertiary alcohol-derived cesium oxalates were irradiated for 4 h and secondary alcohol-derived cesium oxalates were irradiated for 24 h. Following this time, the reaction was removed from the Hepatochem device. The solid was removed by filtering through a pipette plug and rinsing with CH_2Cl_2 (15 mL), and the solvent was removed under rotary evaporation. For volatile fluoride **357d**, the reaction was performed in CD_2Cl_2 and a crude yield obtained directly using ^1H NMR and pyrazine as an internal standard (no evaporation of solvent was performed). The crude residues were then purified by silica gel chromatography to afford the fluorinated products. To mitigate elimination of tertiary fluorides to the corresponding alkenes during purification, silica gel columns were pre-eluted with Et_3N-containing solvent as needed for selected products (see below).

Preparation of fluoride 357a.



Prepared according to general procedure #6 using cesium oxalate **347e** (163 mg, 0.30 mmol). A silica gel column was pre-eluted with two column volumes of 3% Et_3N/pentane, followed by two column volumes of pentane. Purification of the crude residue was then performed on this column (isocratic: 2% Et_2O/pentane) to afford a 89:2:9 mixture of **357**a (7.7:1 dr), **SI-27**, and **SI-28** in (51 mg, 50% yield: 45% **357a**, 1% **SI-27**, 4% **SI-28**).

TLC: R_f 0.37 (5% Et_2O/pentane, *p*-anisaldehyde).

$[\alpha]_D^{25}$: +9.9° (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.13 – 4.03 (m, 2H), 1.98 (ddd, *J* = 12.3, 4.1, 3.0 Hz, 1H), 1.76 – 1.50 (m, 6H), 1.51 – 1.36 (m, 3H), 1.34 (dd, *J* = 24.1, 1.1 Hz, 3H), 1.27 – 1.20 (m, 1H), 1.19 (s, 9H), 1.16 – 1.06 (m, 1H), 1.04 – 0.89 (m, 2H), 0.88 (s, 3H), 0.78 (s, 3H), 0.78 (s, 3H).

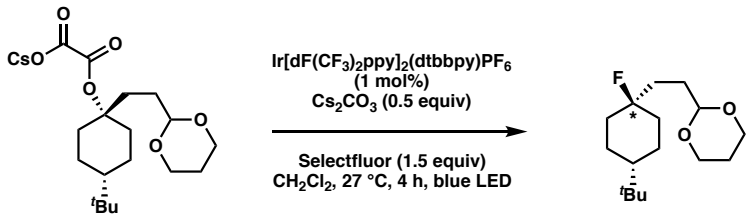
^{13}C NMR (101 MHz, $CDCl_3$): δ 178.8, 98.5 (d, *J* = 166.5 Hz), 65.6 (d, *J* = 5.2 Hz), 55.8 (d, *J* = 1.9 Hz), 55.4 (d, *J* = 17.4 Hz), 41.9, 41.1 (d, *J* = 20.7 Hz), 39.6, 38.8, 38.7 (d, *J* = 10.8 Hz), 33.5, 33.4, 27.4, 24.4, 22.5 (d, *J* = 26.6 Hz), 21.6, 20.4 (d, *J* = 11.7 Hz), 18.5, 15.3.

^{19}F NMR (376 MHz, $CDCl_3$): δ *major diastereomer:*-118.24 (qt, *J* = 24.2, 14.8 Hz), *minor diastereomer:* -156.64 – -157.46 (m).

FTIR (NaCl, thin film): 2955, 2870, 1728, 1459, 1284, 1157 cm^{-1}.

HRMS (ESI+, *m/z*): $C_{21}H_{37}FO_2$, calc'd for $(M+Na)^+$: 363.2675, found: 363.2678.

Preparation of fluoride 357b.



347c 357b

Prepared according to general procedure #6 using cesium oxalate **347c** (142 mg, 0.30 mmol). A silica gel column was pre-eluted with two column volumes of 3% Et_3N/pentane, followed by two column volumes of pentane. Purification of the crude residue was then performed on this column (0–10% Et_2O/pentane) to afford fluoride **357b** as a clear oil (48.5 mg, 59% yield, 3:1 dr).

TLC (major diastereomer): R_f 0.48 (10% Et_2O/pentane, *p*-anisaldehyde).

TLC (minor diastereomer): R_f 0.55 (90:20 pentane/Et_2O, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$): *major diastereomer:* δ 4.52 (t, J = 4.8 Hz, 1H), 4.15 – 4.05 (m, 2H), 3.81 – 3.70 (m, 2H), 2.15 – 2.00 (m, 1H), 1.98 – 1.86 (m, 2H), 1.83 – 1.64 (m, 4H), 1.65 – 1.52 (m, 2H), 1.40 – 1.28 (m, 3H), 1.27 – 1.17 (m, 1H), 1.07 – 0.90 (m, 2fH), 0.85 (s, 9H).

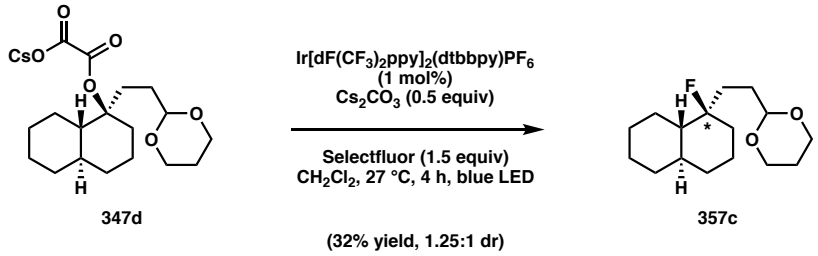
^{13}C NMR (101 MHz, $CDCl_3$): *major diastereomer:* δ 102.5, 94.9 (d, *J* = 169.9 Hz), 67.1, 47.5, 36.1 (d, *J* = 20.3 Hz), 35.5 (d, *J* = 22.8 Hz), 35.1 (d, *J* = 23.2 Hz), 32.6, 29.0 (d, *J* = 4.7 Hz), 27.7, 26.0, 24.7 (d, *J* = 11.9 Hz), 22.6.

^{19}F NMR (376 MHz, $CDCl_3$): δ *minor diastereomer:* –138.26 (tt, *J* = 24.9, 12.8 Hz), *major diastereomer:* -161.48 – -162.22 (m).

FTIR (NaCl, thin film): 2949, 2848, 1469, 1366, 1240, 1148, 1007, 926 cm^{-1}.

HRMS (FAB+, *m/z*): $C_{16}H_{29}FO_2$, calc'd for $(M+H-H_2)^-$: 271.2073, found: 271.2084.

Preparation of fluoride 357c.



Prepared according to general procedure #6 using cesium oxalate **347d** (142 mg, 0.30 mmol). A silica gel column (20 g) was pre-eluted with two column volumes of 3% Et_3N/pentane, followed by two column volumes of 2% Et_2O/pentane. The crude material was dry-loaded onto 400 mg Celite, then purified using this column (2–10% Et_2O/pentane) to afford a diastereomeric mixture of fluoride **357c** as a clear oil (26 mg, 32% yield, 1.25:1 dr).

TLC: R_f 0.43 (20% Et_2O/pentane, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$): *Note: mixture of diastereomers*: δ 4.57 – 4.50 (m, 1H), 4.50 (t, *J* = 5.0 Hz, 1H), 4.15 – 4.05 (m, 4H), 3.81 – 3.68 (m, 4H), 2.15 – 1.99 (m, 3H), 1.90 – 1.49 (m, 23H), 1.46 – 1.26 (m, 6H), 1.26 – 1.05 (m, 7H), 1.02 – 0.85 (m, 5H).

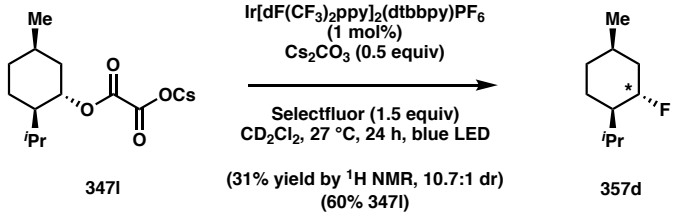
^{13}C NMR (101 MHz, $CDCl_3$): *Note: mixture of diastereomers*: δ 102.7, 102.5, 98.6 (d, *J* = 172.4 Hz), 97.1 (d, *J* = 172.4 Hz), 67.1, 52.0 (d, *J* = 19.0 Hz), 47.8 (d, *J* = 21.1 Hz), [aliphatic region: 39.6, 39.5, 37.4, 35.0, 35.0, 34.8, 34.8, 34.68, 34.67, 33.80, 33.78, 33.76, 31.7, 31.4, 30.5, 29.9, 29.8, 28.78, 28.75, 26.8, 26.5, 26.4, 26.2, 26.0, 25.9, 25.2, 25.2, 24.9, 24.83, 24.81, 24.7, 22.8, 22.6, 21.28, 21.26].

^{19}F NMR (376 MHz, $CDCl_3$): δ -146.05 – -146.60 (m), -166.95 (tdd, *J* = 39.5, 19.5, 8.3 Hz).

FTIR (NaCl, thin film): 2928, 2851, 1449, 1376, 1146, 1002, 934 cm^{-1}.

HRMS (FAB+, *m/z*): $C_{16}H_{27}FO_2$, calc'd for $(M+\cdot - H)^-$: 269.1917, found: 269.1918.

Preparation of fluoride 357d.



Prepared according to general procedure #6 using cesium oxalate **347l** (108 mg, 0.30 mmol) and CD_2Cl_2 as a solvent. Fluoride **357d** was formed in 31% yield (with 60% oxalate **347l** remaining), which was determined by ^{1}H NMR with pyrazine as an internal standard. For characterization, the crude material in CD_2Cl_2 was loaded onto a silica gel column and

purified using pentane (isocratic) to afford fluoride **357d** as a clear oil (4 mg, 8% yield, 10.7:1 dr).

TLC: R_f 0.65 (2% Et_2O/pentane, *p*-anisaldehyde).

$[\alpha]_D^{25}$: +17.4° (c = 0.20, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.70 (dtd, *J* = 47.8, 6.9, 3.3 Hz, 1H), 1.97 (dtd, *J* = 8.4, 4.8, 3.9, 2.6 Hz, 1H), 1.83 (dq, *J* = 13.5, 6.7 Hz, 1H), 1.78 – 1.67 (m, 1H), 1.66 – 1.48 (m, 2H), 1.49 – 1.36 (m, 3H), 1.29 – 1.16 (m, 1H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.92 (d, *J* = 7.0 Hz, 3H), 0.91 – 0.88 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 91.5 (d, *J* = 167.8 Hz), 47.0 (d, *J* = 16.8 Hz), 37.0 (d, *J* = 19.3 Hz), 30.0 (d, *J* = 1.4 Hz), 27.7 (d, *J* = 6.8 Hz), 26.5 (d, *J* = 6.6 Hz), 20.9, 20.7 (d, *J* = 5.1 Hz), 20.5, 19.3.

^{19}F NMR (376 MHz, $CDCl_3$): δ -179.53 – -179.86 (m).

FTIR (NaCl, thin film): 2928, 2872, 1460, 1369, 1261, 1028 cm^{-1}.

HRMS (EI+, *m/z*): $C_{10}H_{19}F$, calc'd for $(M+\cdot)^+$: 158.1471, found: 158.1445.

4.6 NOTES AND REFERENCES

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(73) Ethyl trichloroacetate was distilled prior to use; residual HCl neutralizes the oxalate salt and decreases the yield.

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(77) The reductive ketone deoxychlorination developed by Rawal and co-workers provides the opposite diastereomer of **348k**, which demonstrates the complementarity of the two methods (see ref 21).

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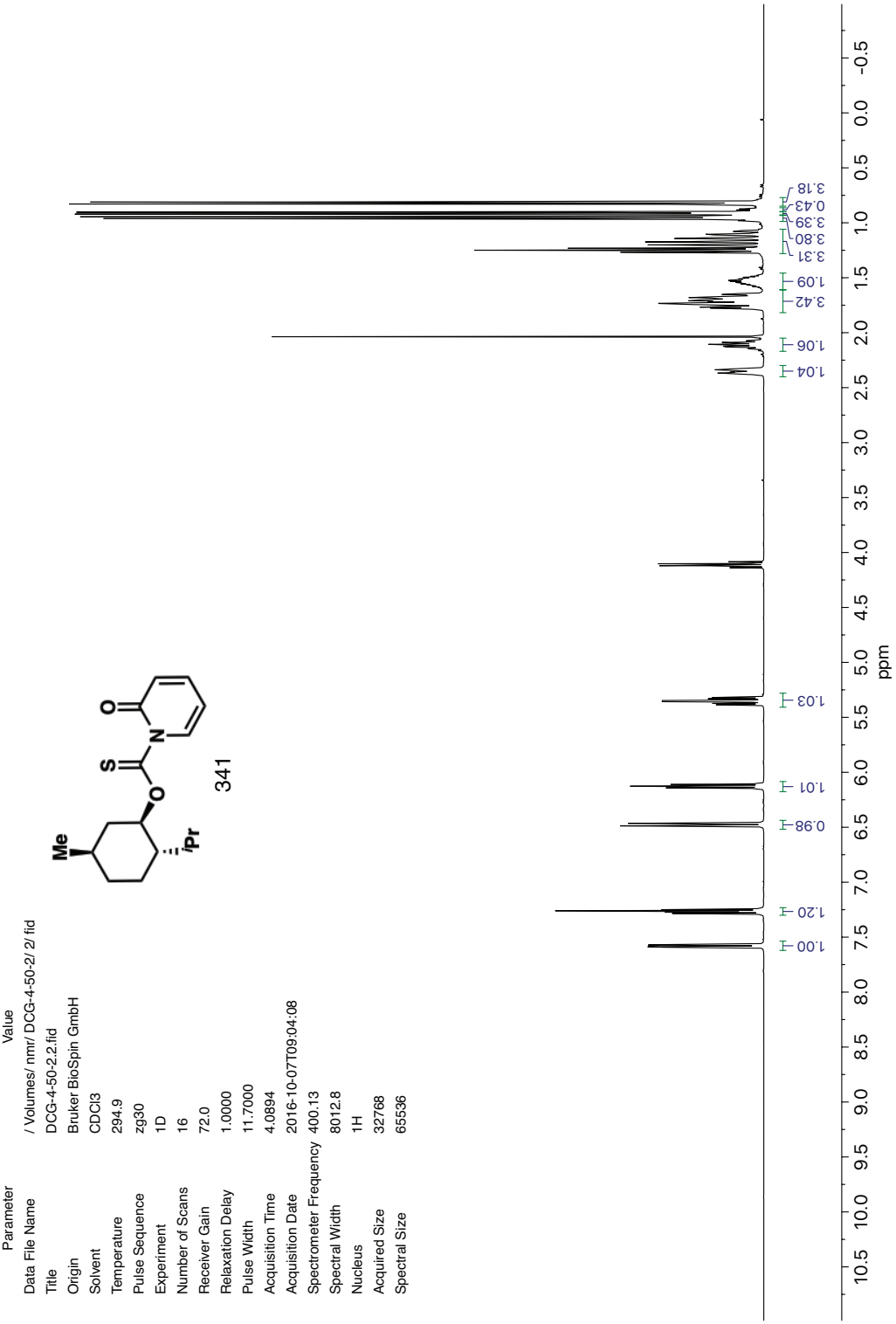
Appendix 4

Spectra Relevant to Chapter 4:

Development of Radical Deoxychlorination Reactions:

Preparation of Hindered Alkyl Chlorides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Receiver Gain 72.0
Relaxation Delay 1.0000
Pulse Width 11.7000
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Acquired Size 32768
Spectral Size 65536
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iPr
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S
N
O
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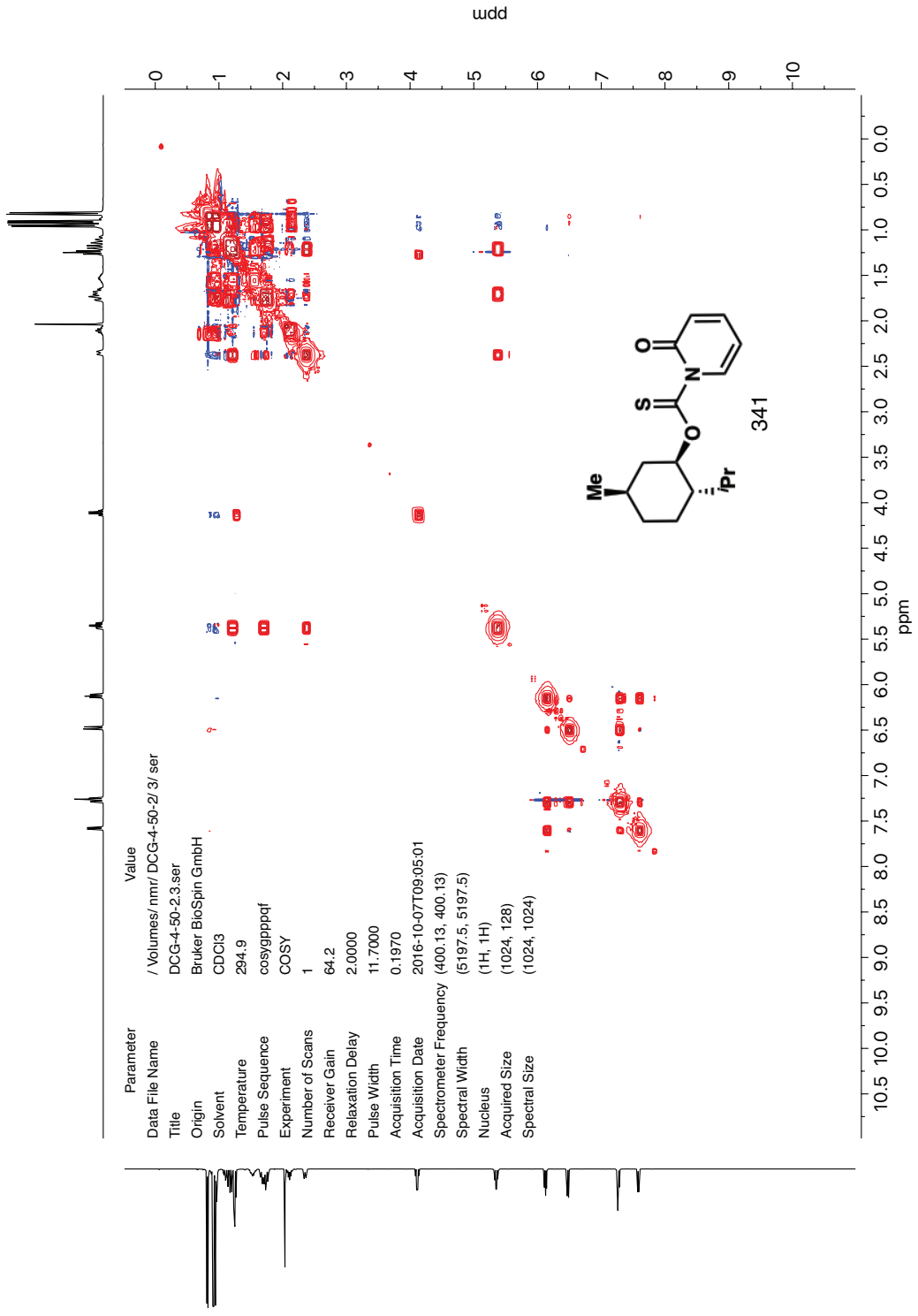
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Spectral Width (5197.5, 5197.5)
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O
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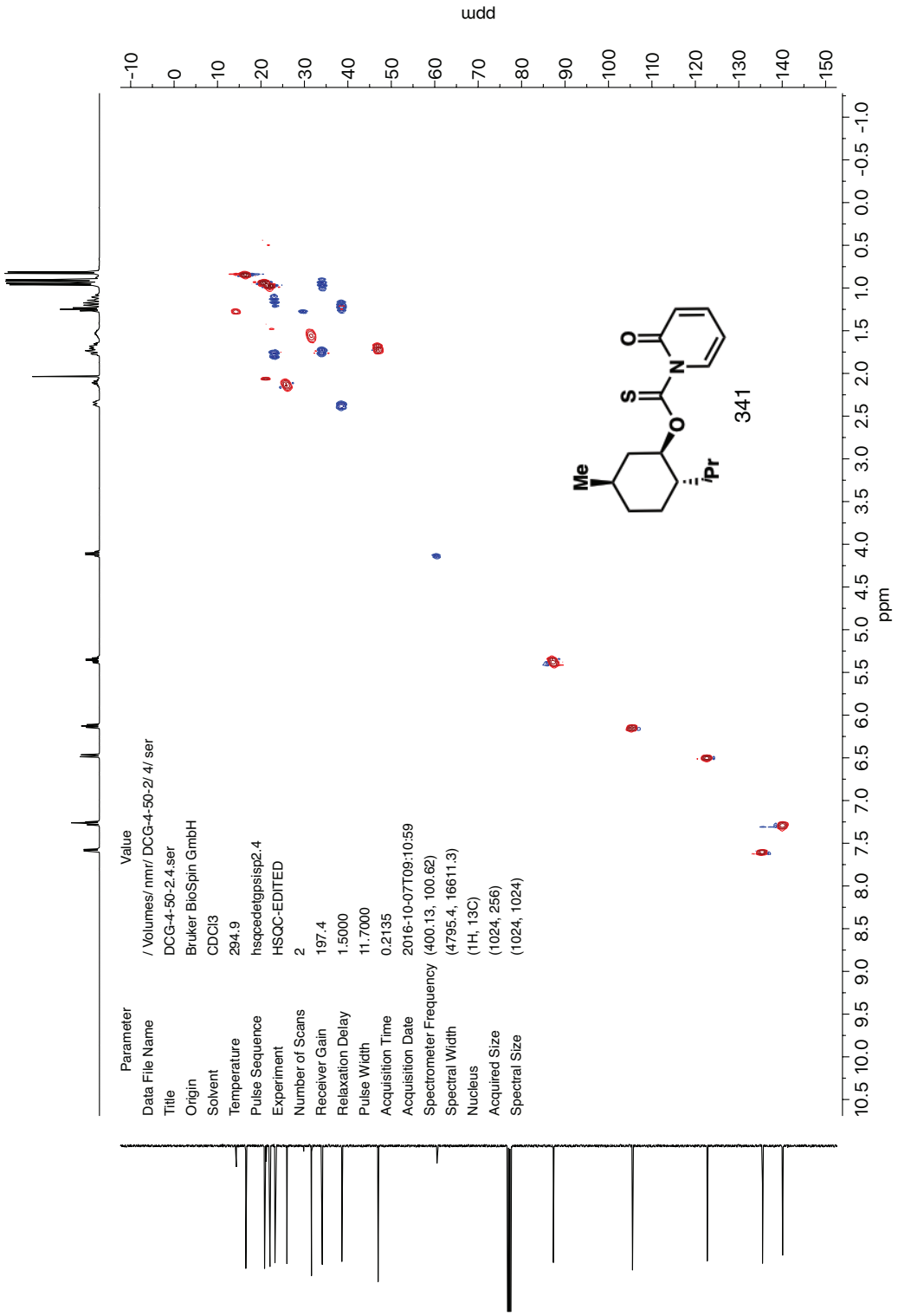
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Pulse Sequence hsqcedetgpsisp2.4
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Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
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ppm
Me
iPr
O
S
N
O
O
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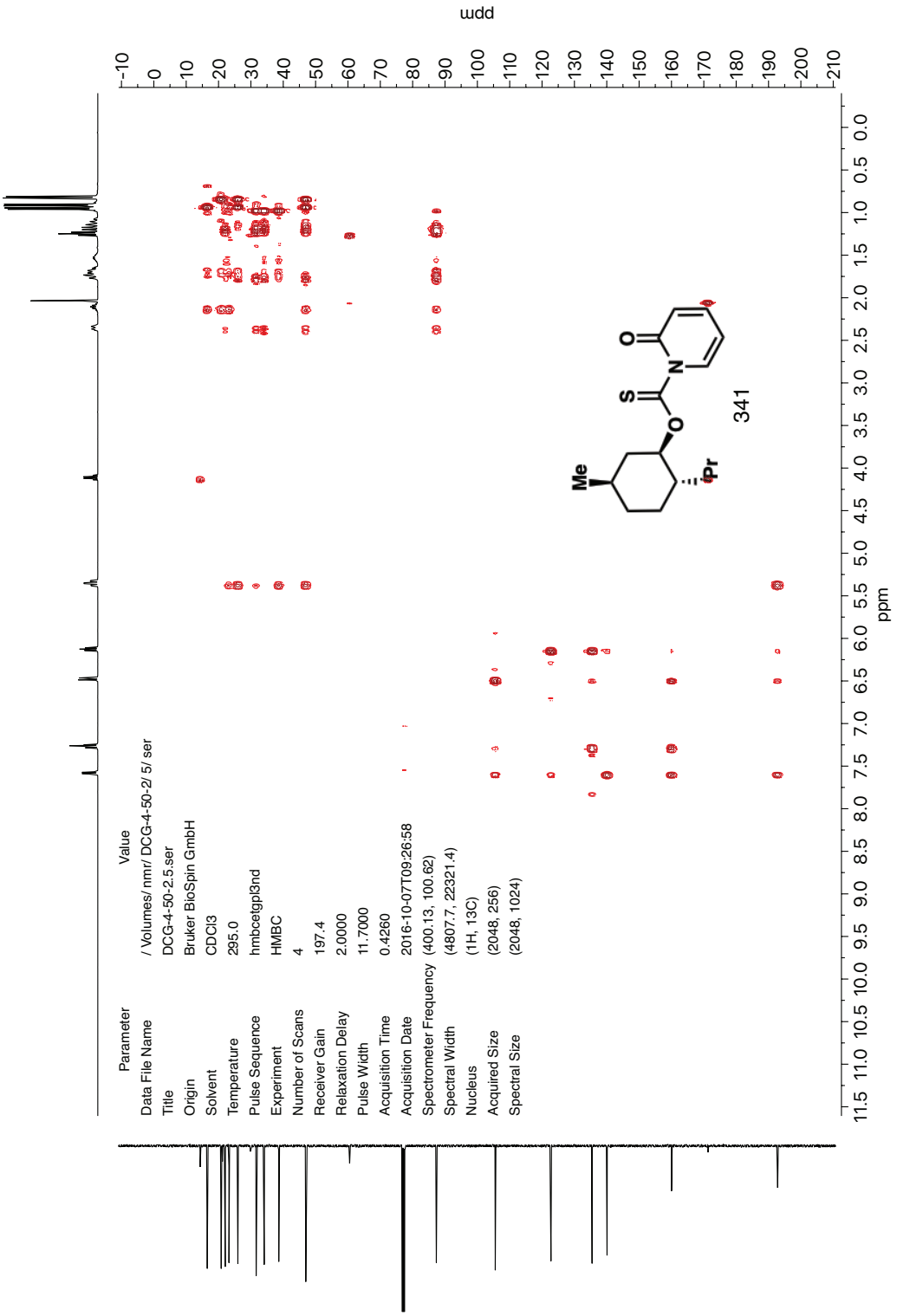
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ppm
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S
N
O
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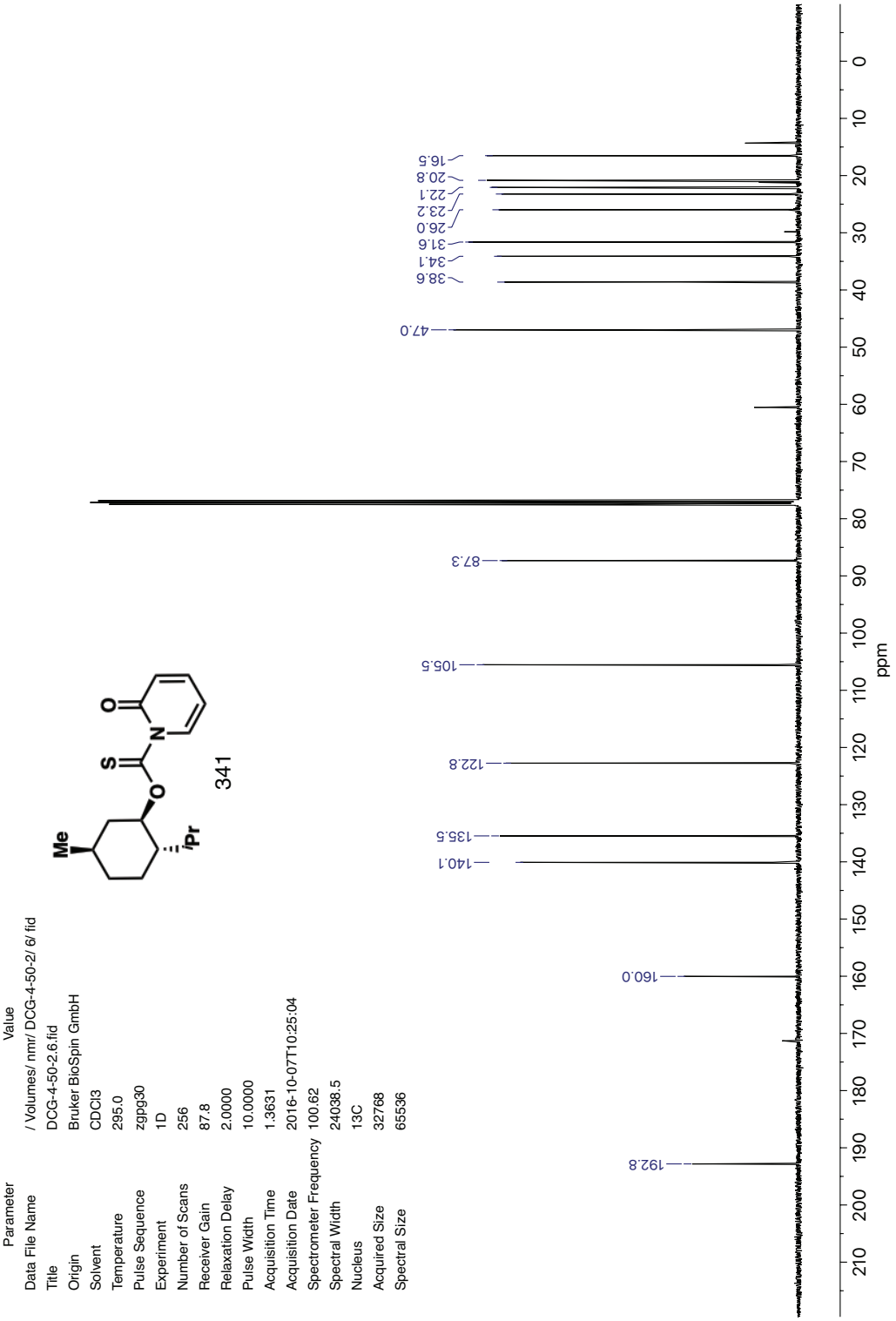
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Pulse Width 10.0000
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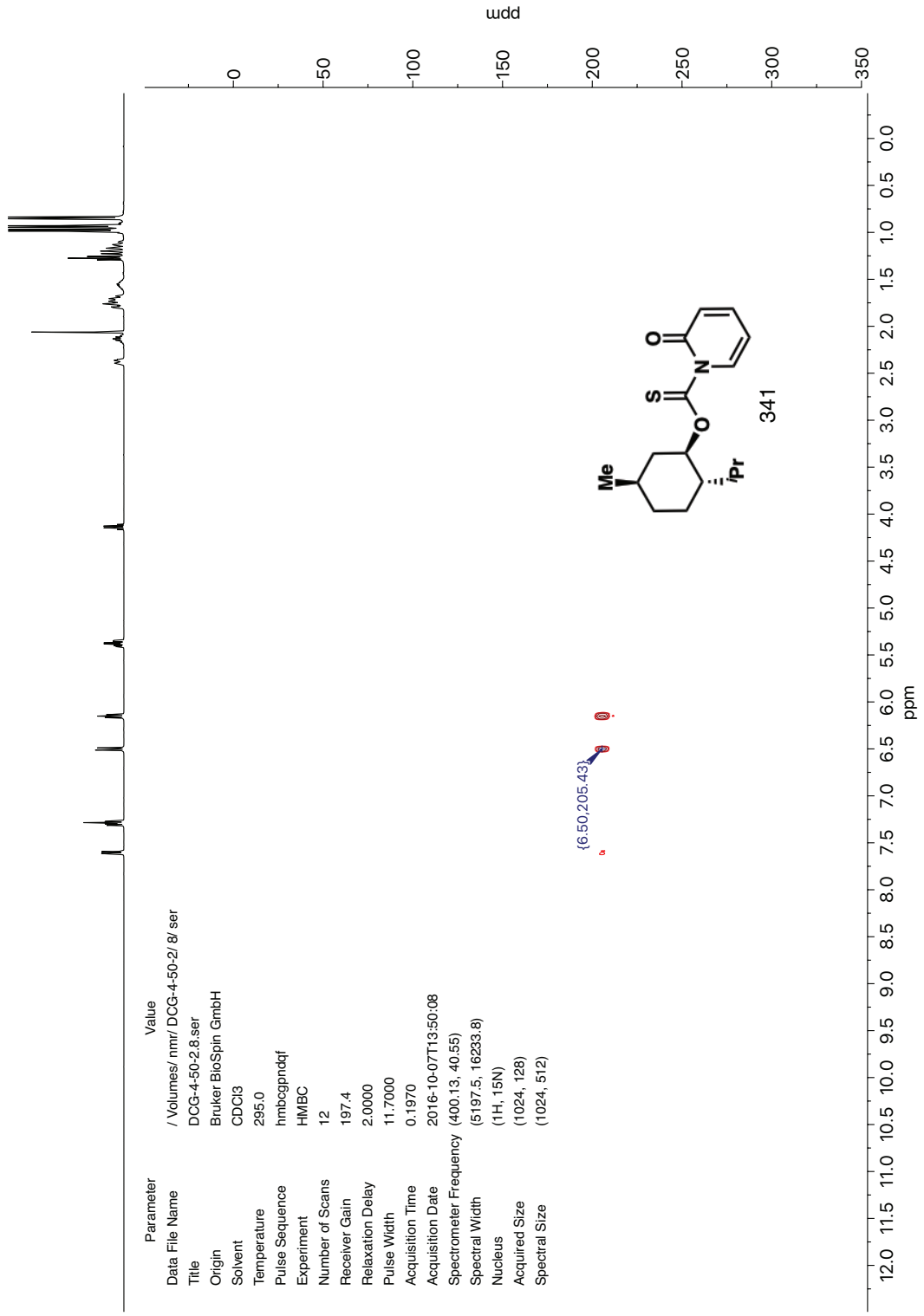
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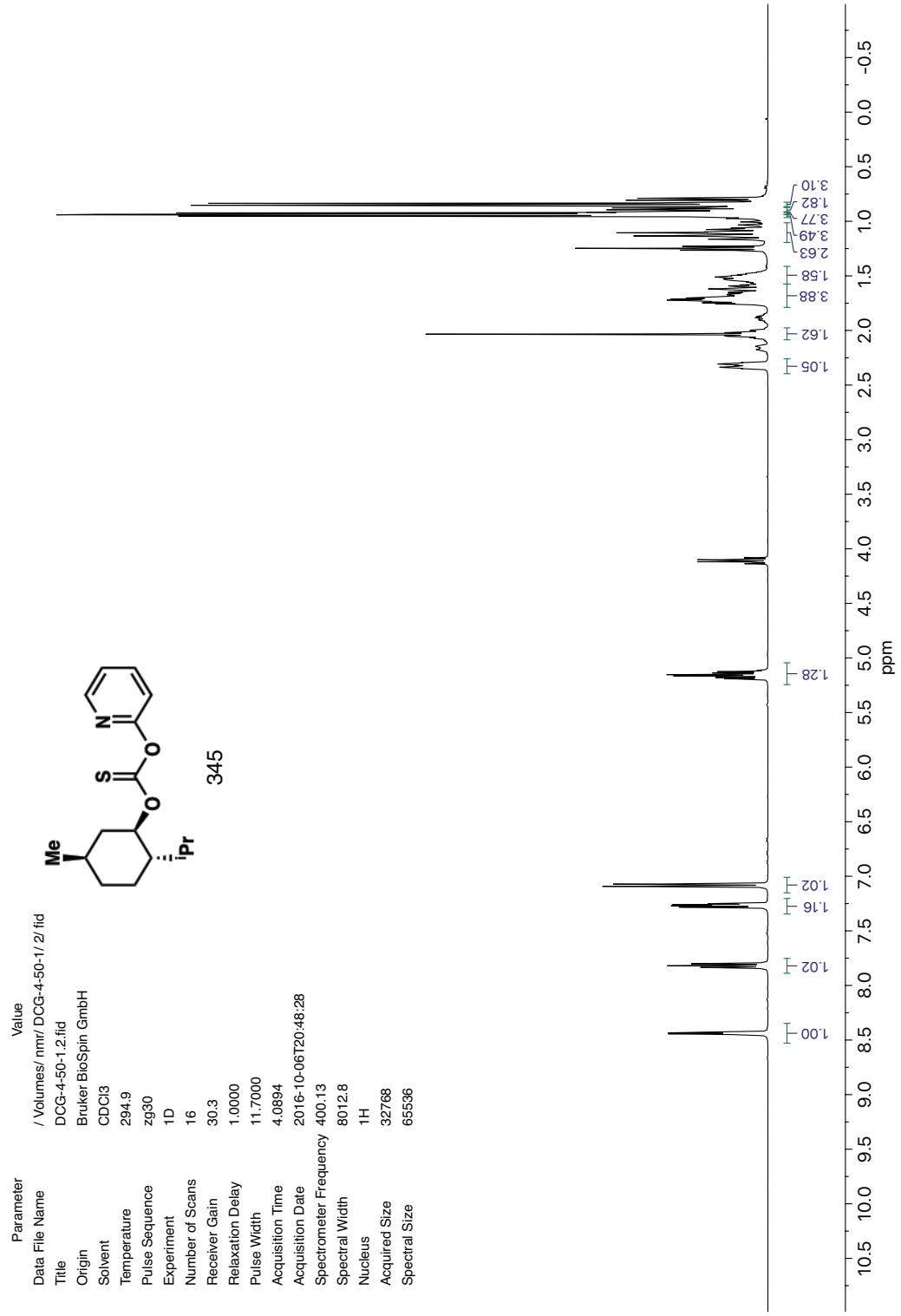
ppm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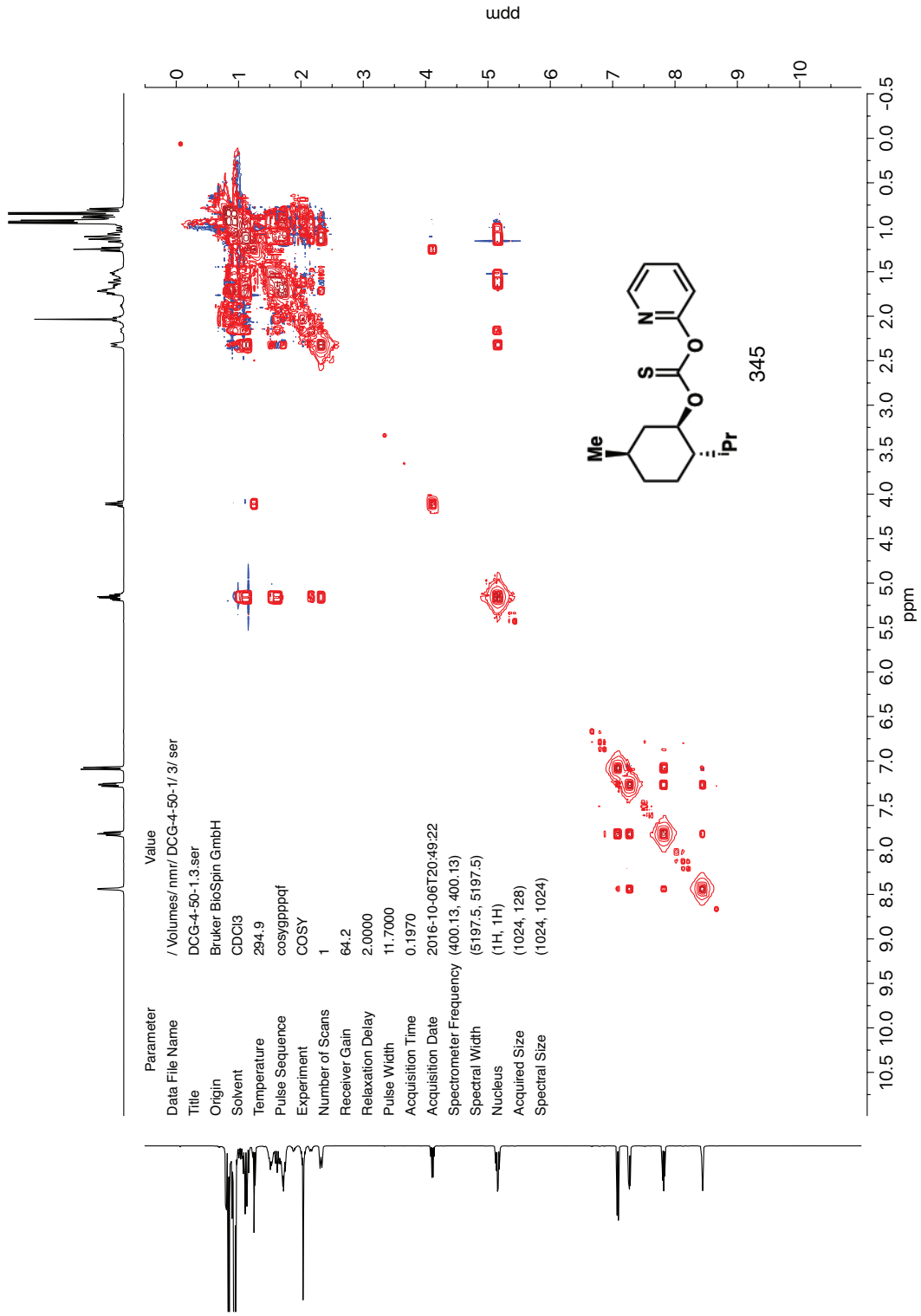
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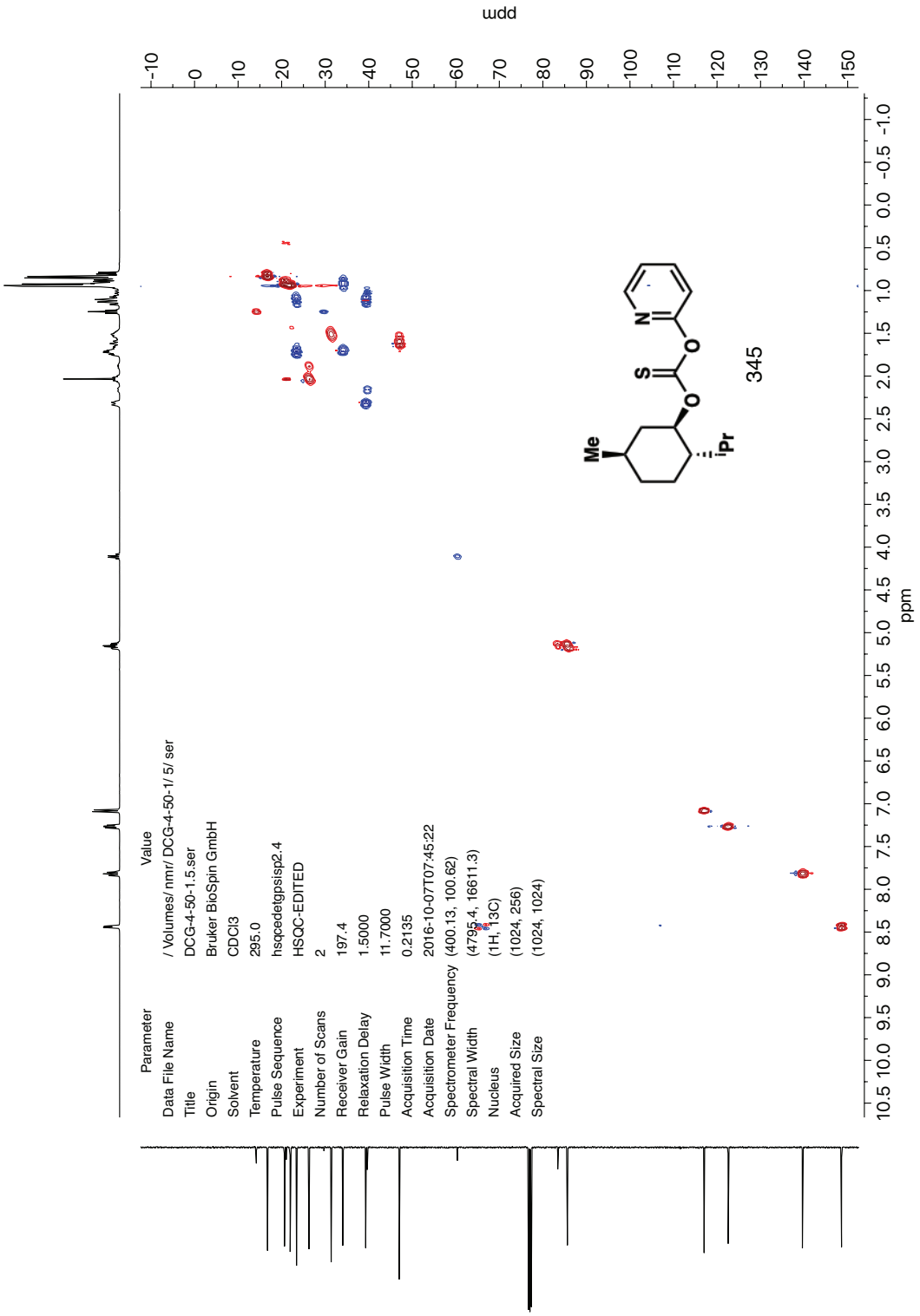
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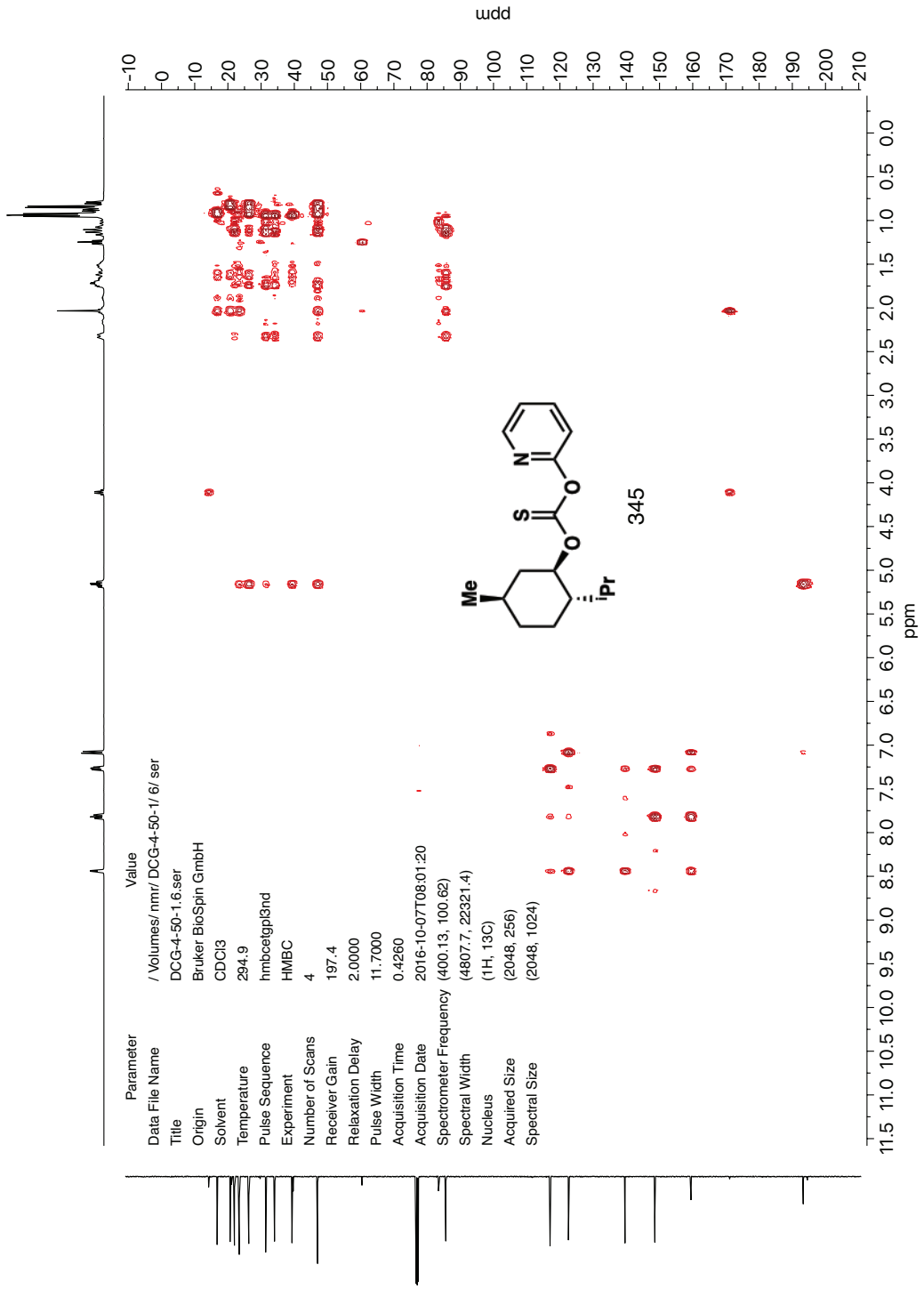
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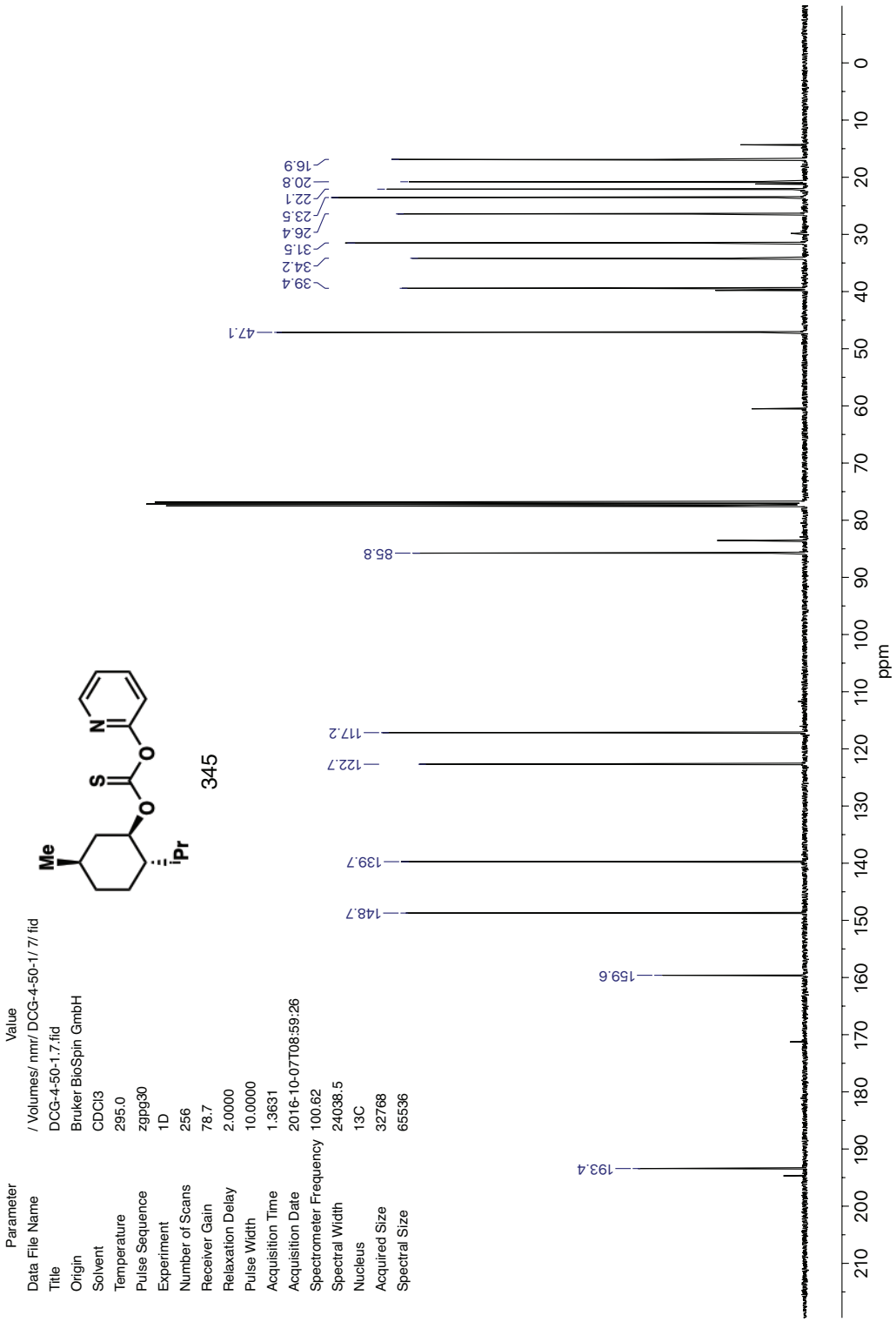
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Experiment 1D
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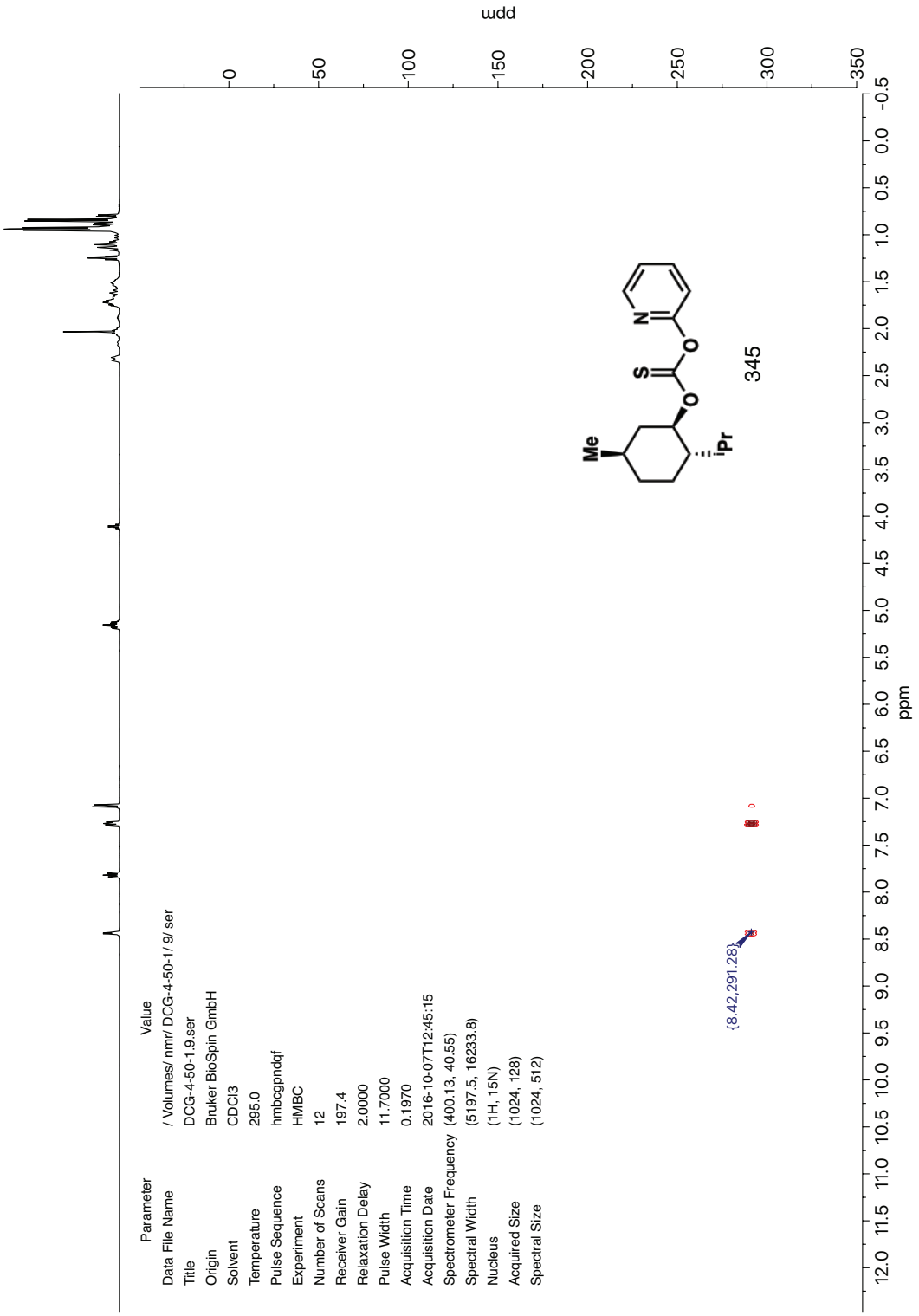
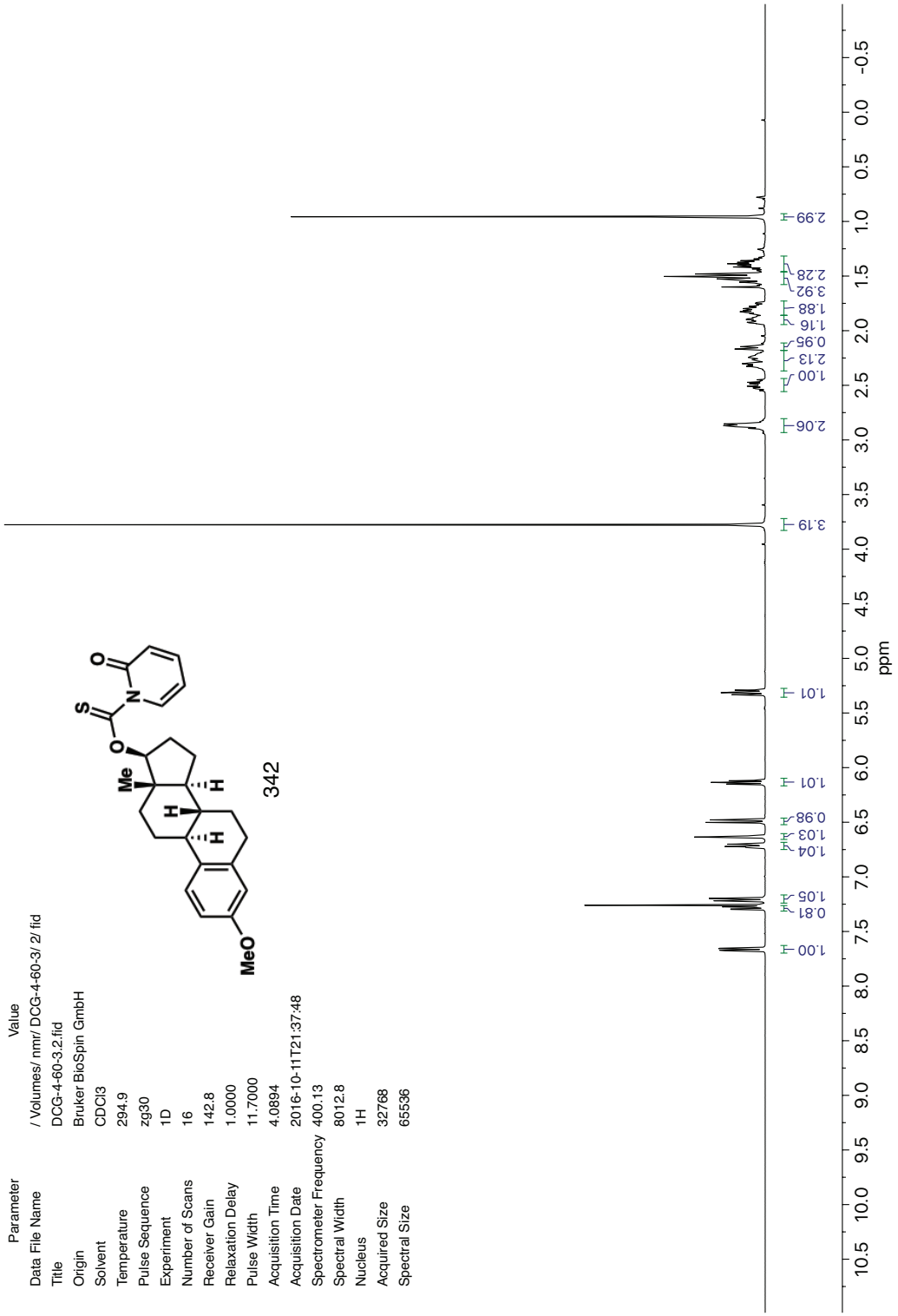
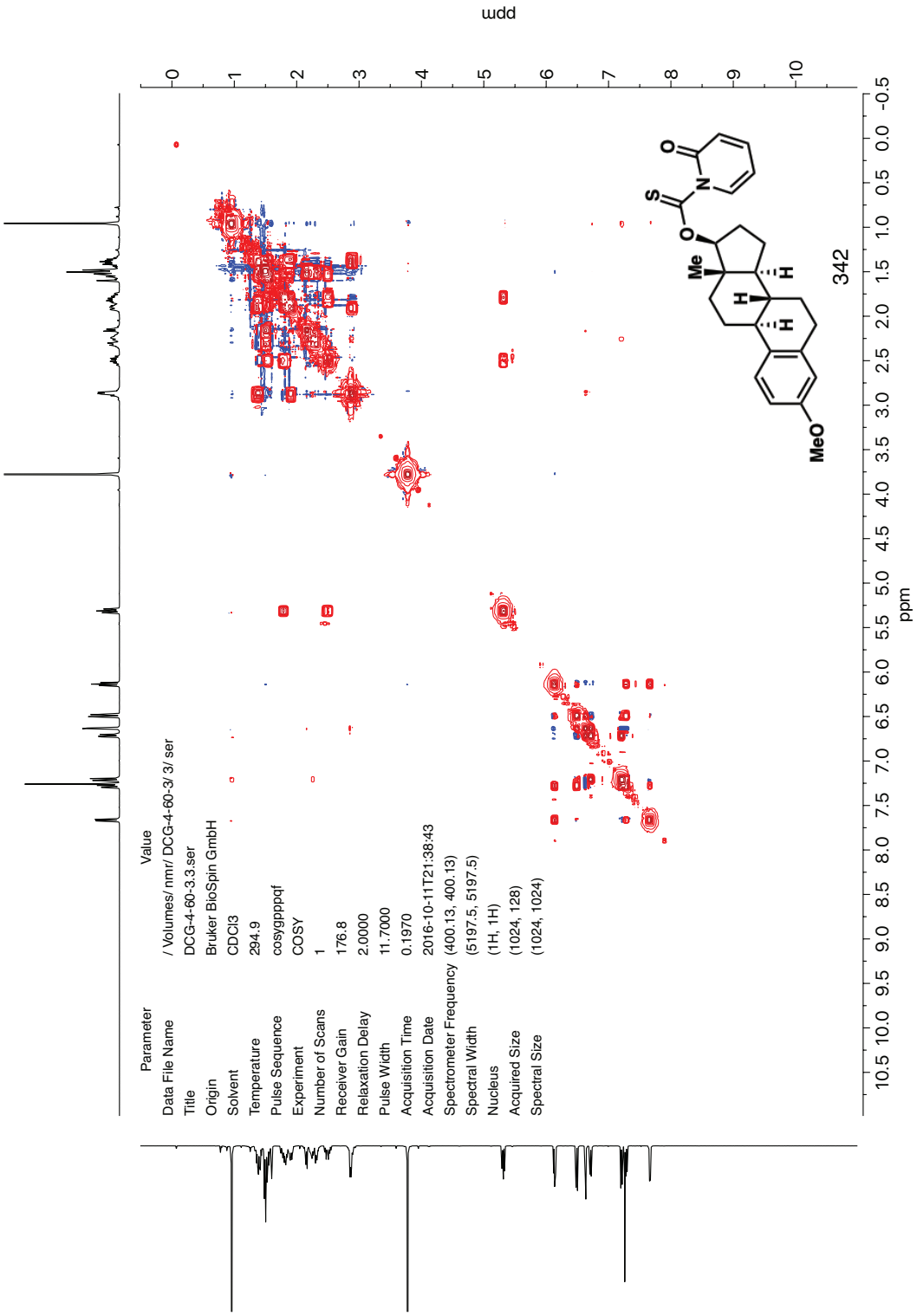
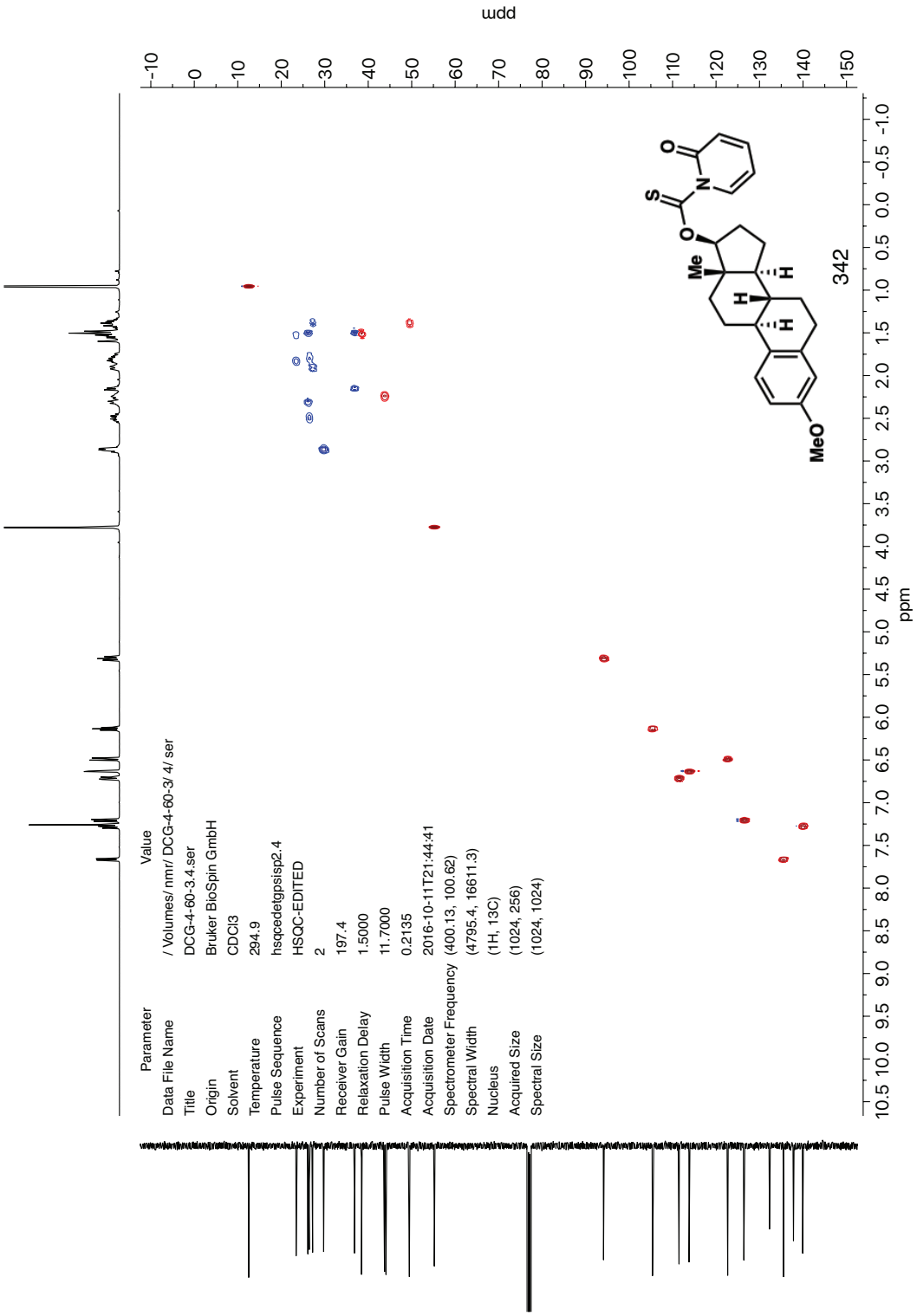
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-10-07T08:59:26
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
iPr
S
O
O
N
345
193.4
159.6
148.7
139.7
122.7
117.2
85.8
47.1
39.4
34.2
31.5
26.4
23.5
22.1
20.8
16.9
ppm

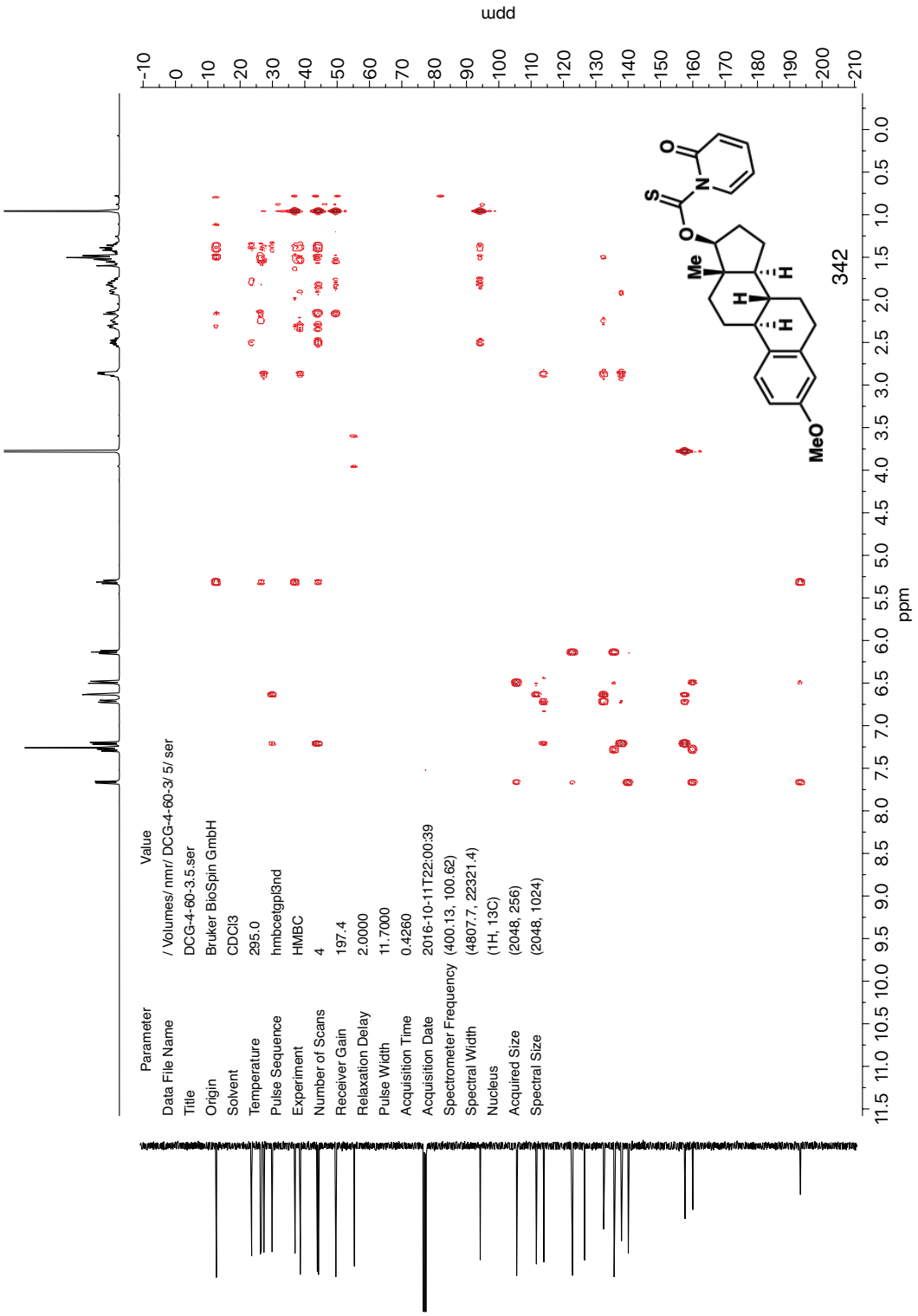


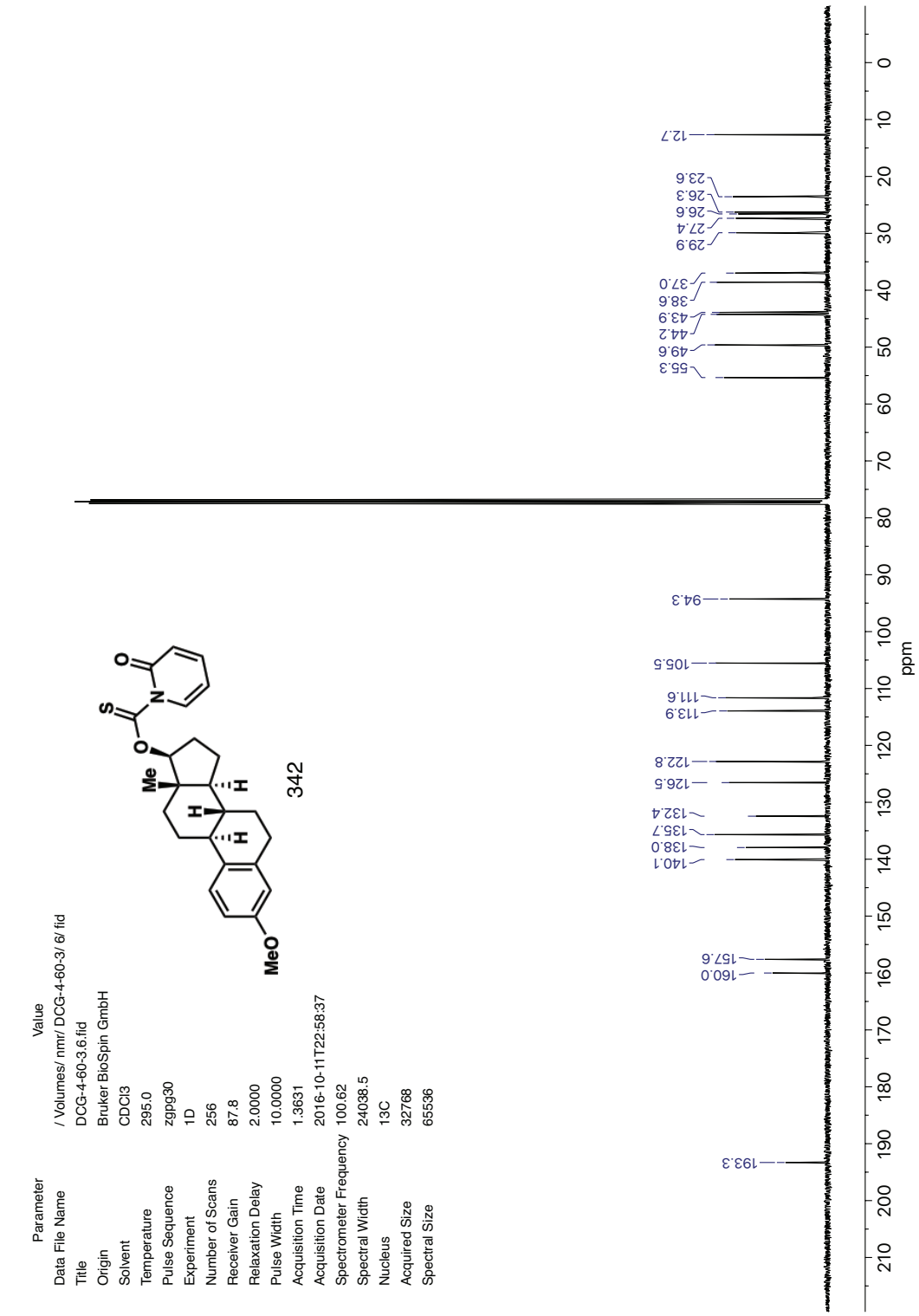
Parameter	Value
Data File Name	/ Volumes/ nmr/ DCG-4-50-1/ 9/ ser
Title	DCG-4-50-1.9.ser
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	hmbcgpndqf
Experiment	HMBC
Number of Scans	12
Receiver Gain	197.4
Relaxation Delay	2.0000
Pulse Width	11.7000
Acquisition Time	0.1970
Acquisition Date	2016-10-07T12:45:15
Spectrometer Frequency	(400.13, 40.55)
Spectral Width	(5197.5, 16233.8)
Nucleus	(1H, 15N)
Acquired Size	(1024, 128)
Spectral Size	(1024, 512)

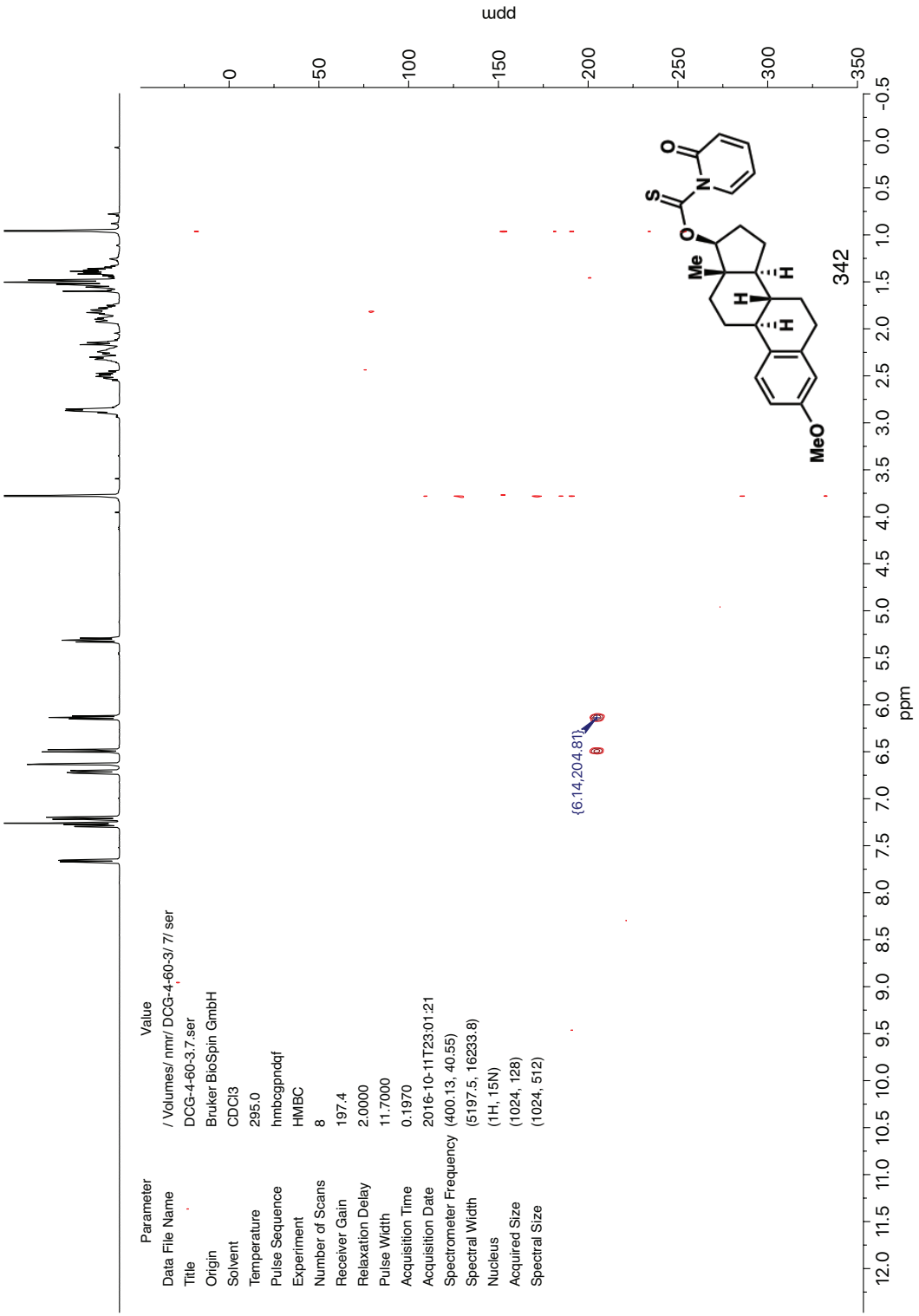

Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-4-60-3/ 2/ fid
Title
DCG-4-60-3.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zg30
Experiment
1D
Number of Scans
16
Receiver Gain
142.8
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2016-10-11T21:37:48
Spectrometer Frequency
400.13
Spectral Width
8012.8
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
Me
H
H
H
O
S
O
N
O
MeO
342
1.00
0.81
1.05
1.04
1.03
0.98
1.01
1.01
3.19
2.06
1.00
2.13
0.95
1.16
1.88
3.92
2.28
2.99
ppm

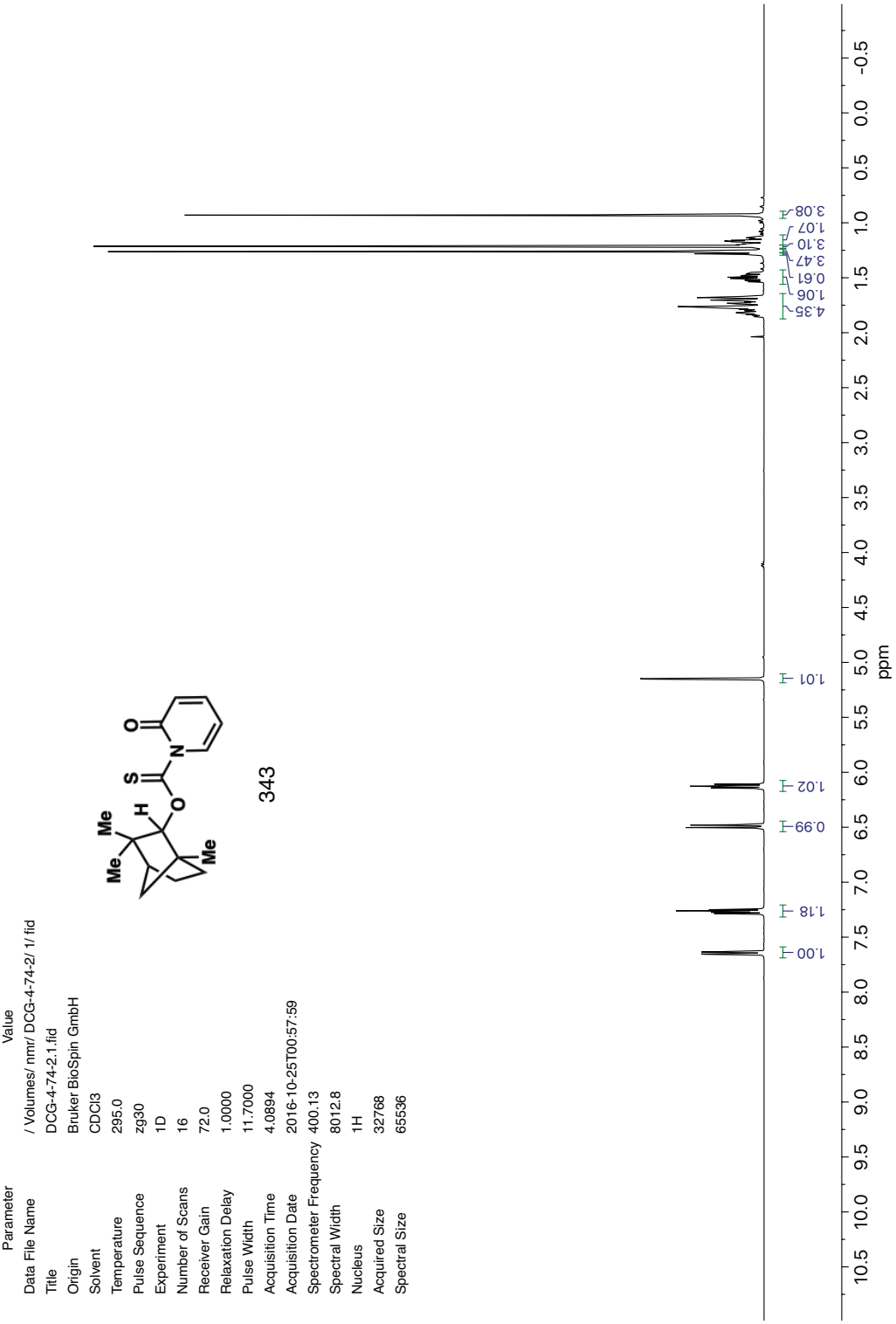

ppm
ppm
Me
H
H
H
O
N
S
O
MeO
342
Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-60-3/ 3/ ser
Title DCG-4-60-3.3.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 176.8
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.1970
Acquisition Date 2016-10-11T21:38:43
Spectrometer Frequency (400.13, 400.13)
Spectral Width (5197.5, 5197.5)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)

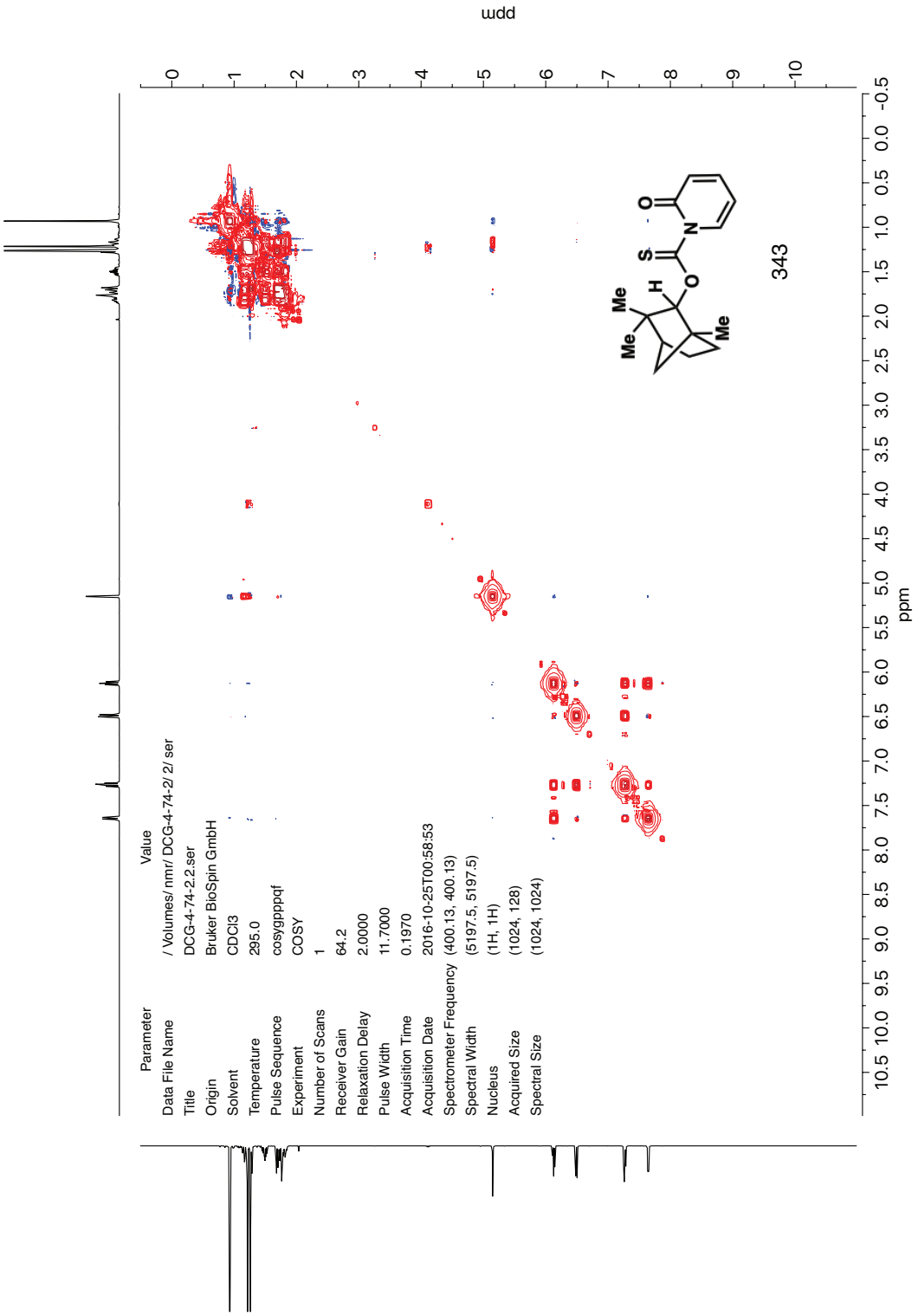

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-60-3/ 4/ ser
Title DCG-4-60-3.4.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2016-10-11T21:44:41
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
ppm
ppm
Me
H
H
H
MeO
342

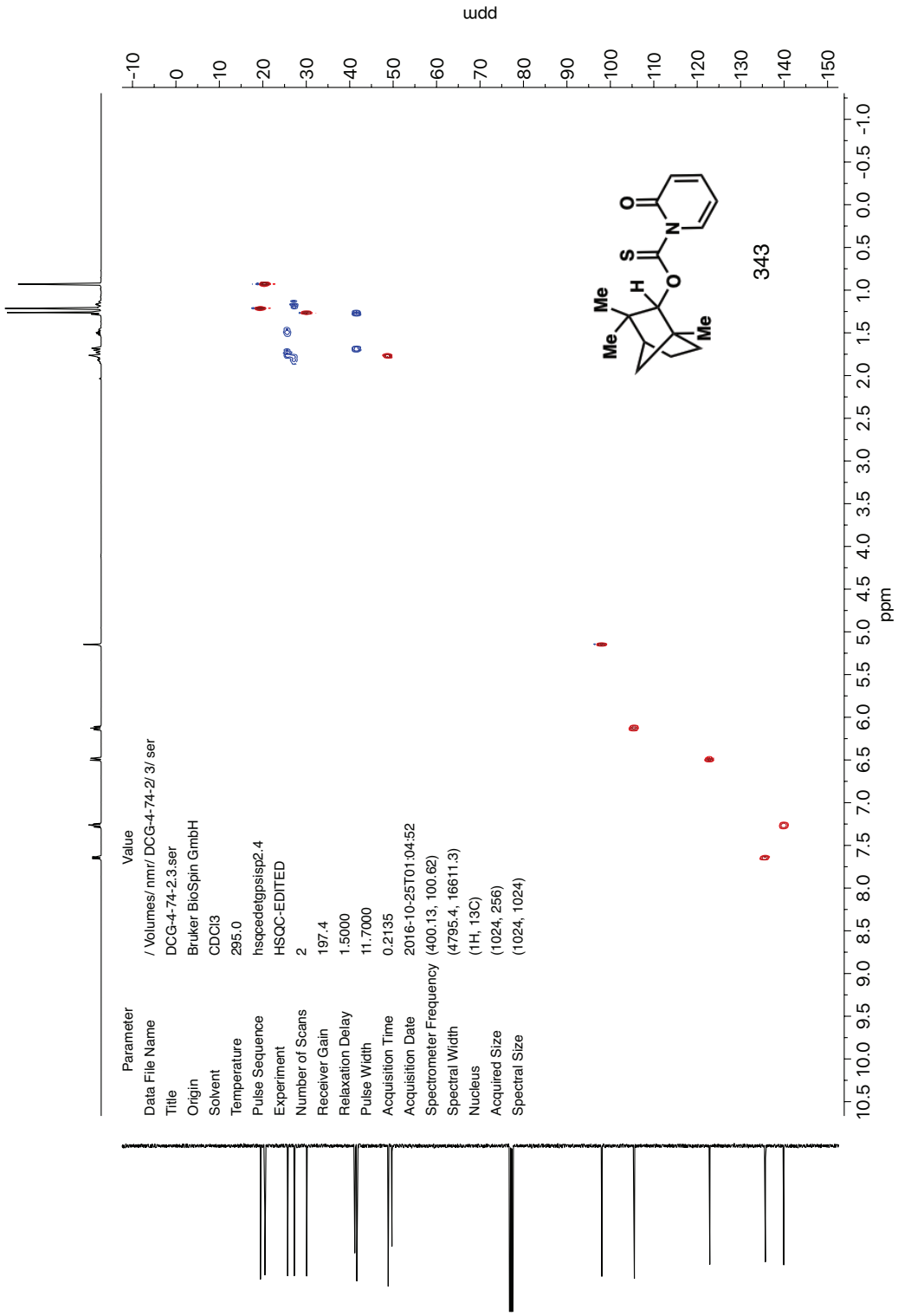

ppm
ppm
Me
H
H
H
O
N
S
O
MeO
342
Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-60-3/ 5/ ser
Title DCG-4-60-3.5.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2016-10-11T22:00:39
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)

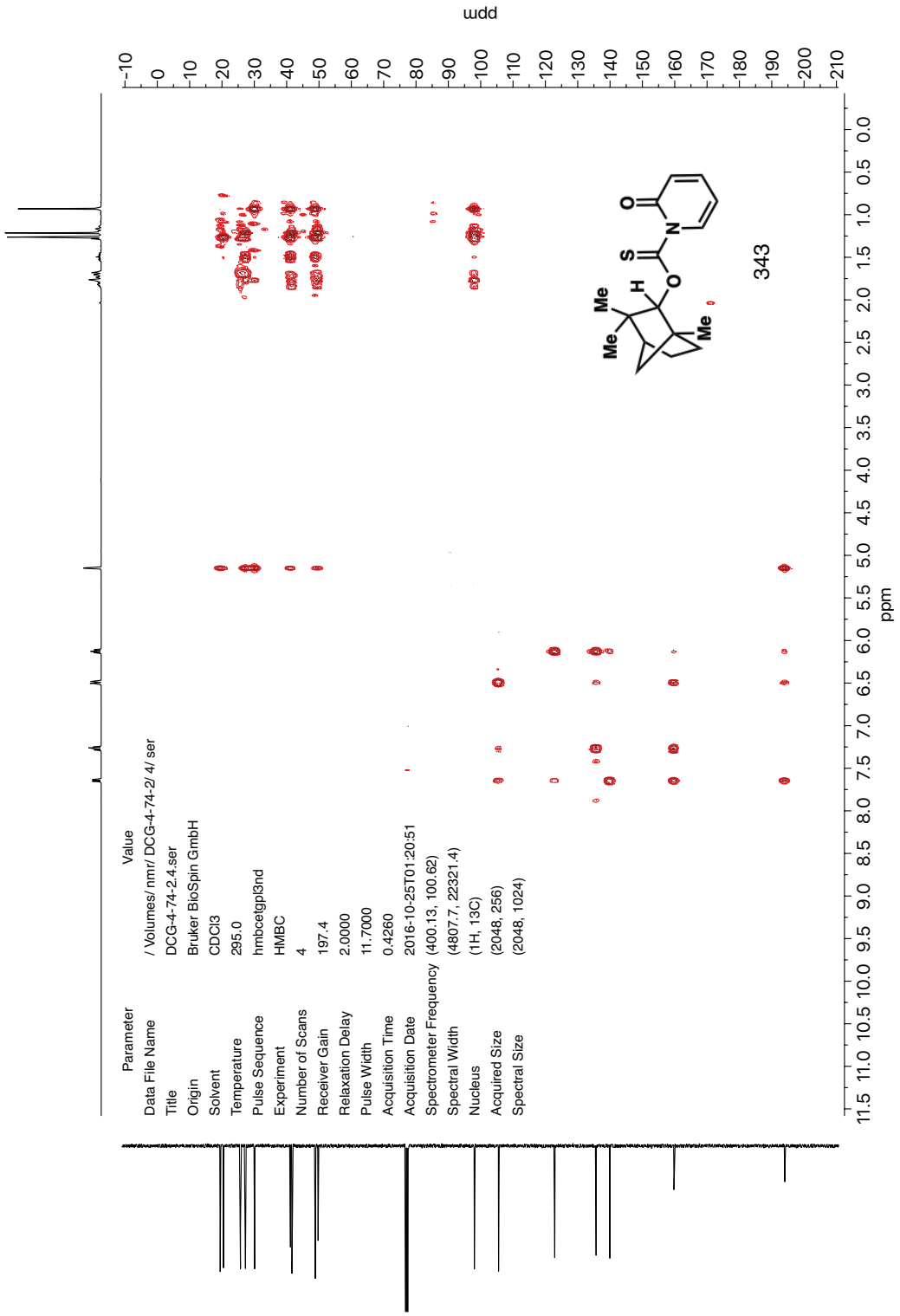

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-60-3/ 6/ fid
Title DCG-4-60-3.6.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 87.8
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-10-11T22:58:37
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
H
H
H
MeO
342
193.3
160.0
157.6
140.1
138.0
135.7
132.4
126.5
122.8
113.9
111.6
105.5
94.3
55.3
49.6
44.2
43.9
38.6
37.0
29.9
27.4
26.6
26.3
23.6
12.7
ppm

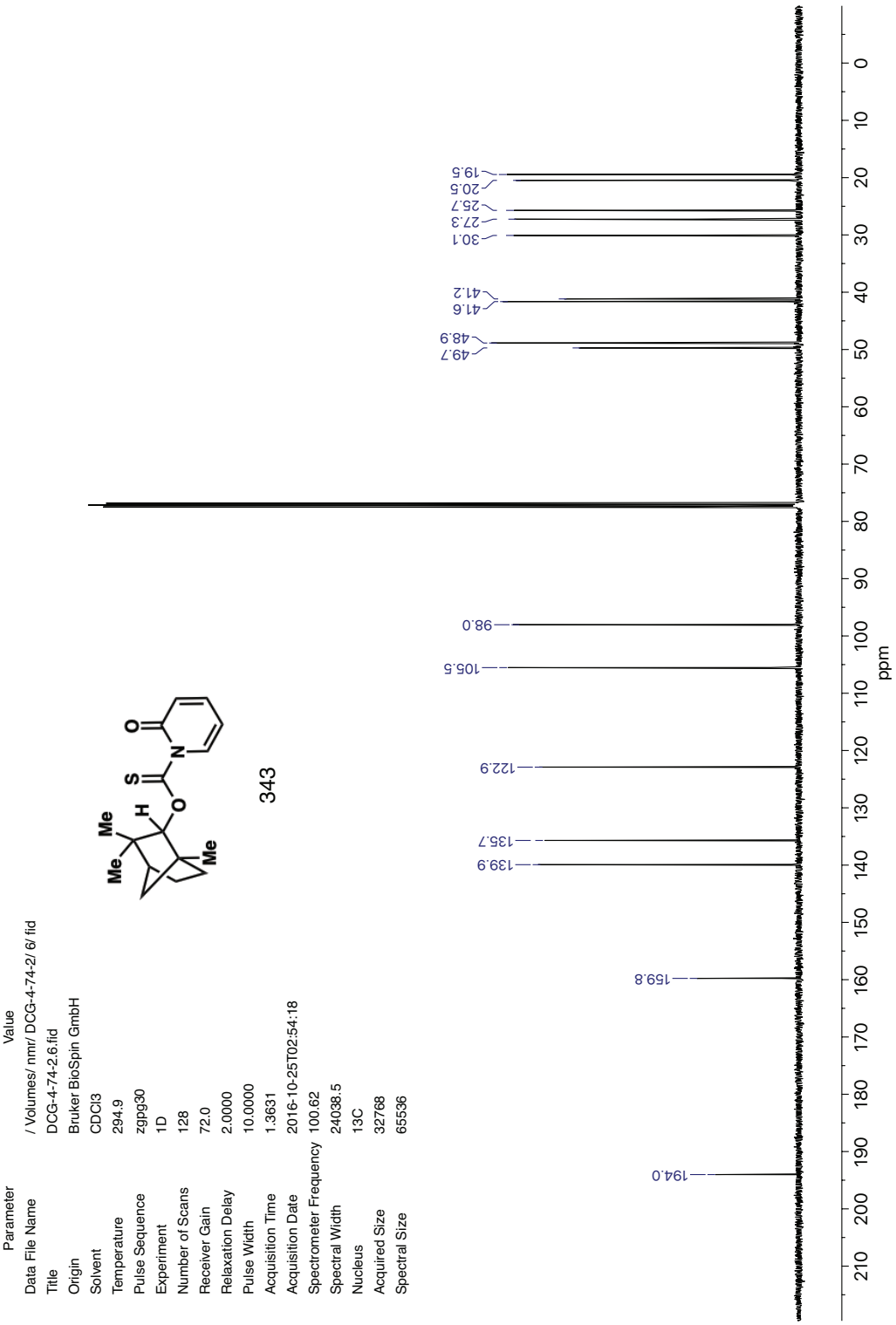

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-60-3/ 7/ ser
Title DCG-4-60-3.7.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence hmbcgpndqf
Experiment HMBC
Number of Scans 8
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.1970
Acquisition Date 2016-10-11T23:01:21
Spectrometer Frequency (400.13, 40.55)
Spectral Width (5197.5, 16233.8)
Nucleus (1H, 15N)
Acquired Size (1024, 128)
Spectral Size (1024, 512)
{6.14,204.81}
ppm
ppm
342
MeO
Me
H
H
H
O
N
S
O

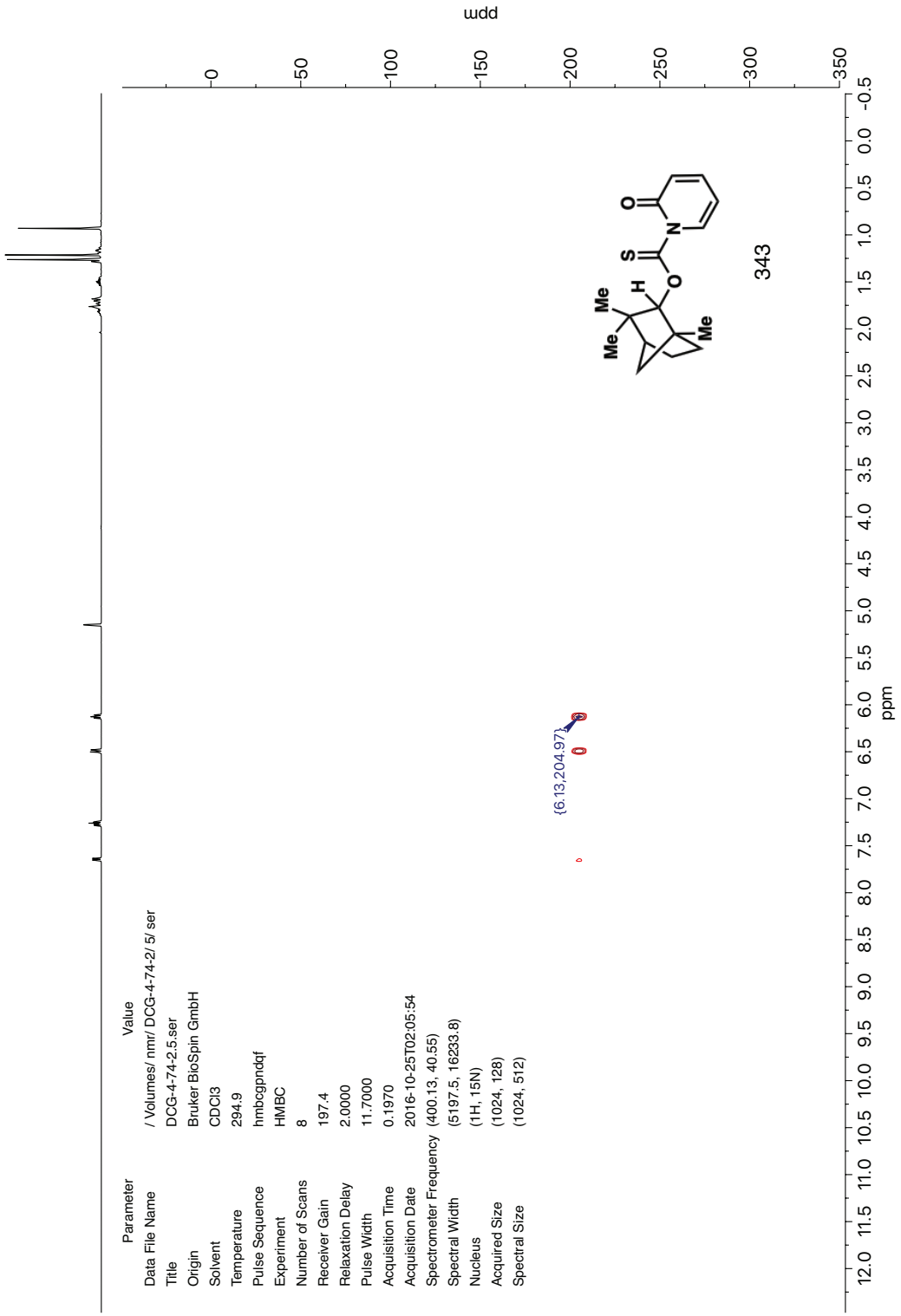

Parameter
Value
Data File Name / Volumes/ nmr/ DCG-4-74-2/ 1/ fid
Title DCG-4-74-2.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 72.0
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2016-10-25T00:57:59
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
343
Me
Me
H
O
S
O
N
Me
1.00
1.18
0.99
1.02
1.01
4.35
1.06
0.61
3.47
3.10
1.07
3.08
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm


ppm
ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-74-2/ 2/ ser
Title DCG-4-74-2.2.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.1970
Acquisition Date 2016-10-25T00:58:53
Spectrometer Frequency (400.13, 400.13)
Spectral Width (5197.5, 5197.5)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)
Me
Me
H
O
S
N
O
O
Me
343

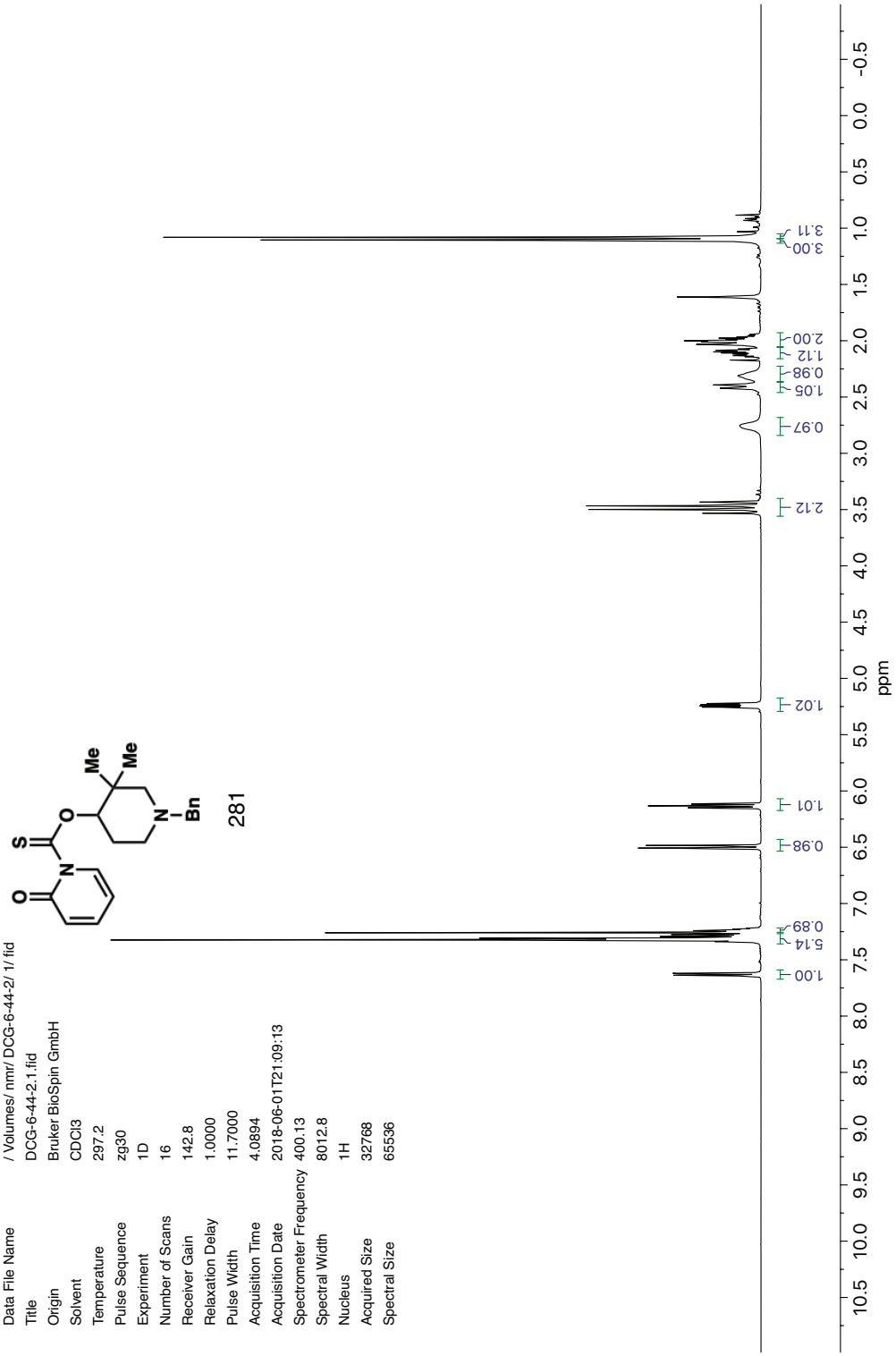

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-74-2/ 3/ ser
Title DCG-4-74-2.3.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2016-10-25T01:04:52
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
Me
Me
H
O
S
N
O
Me
343
ppm
ppm

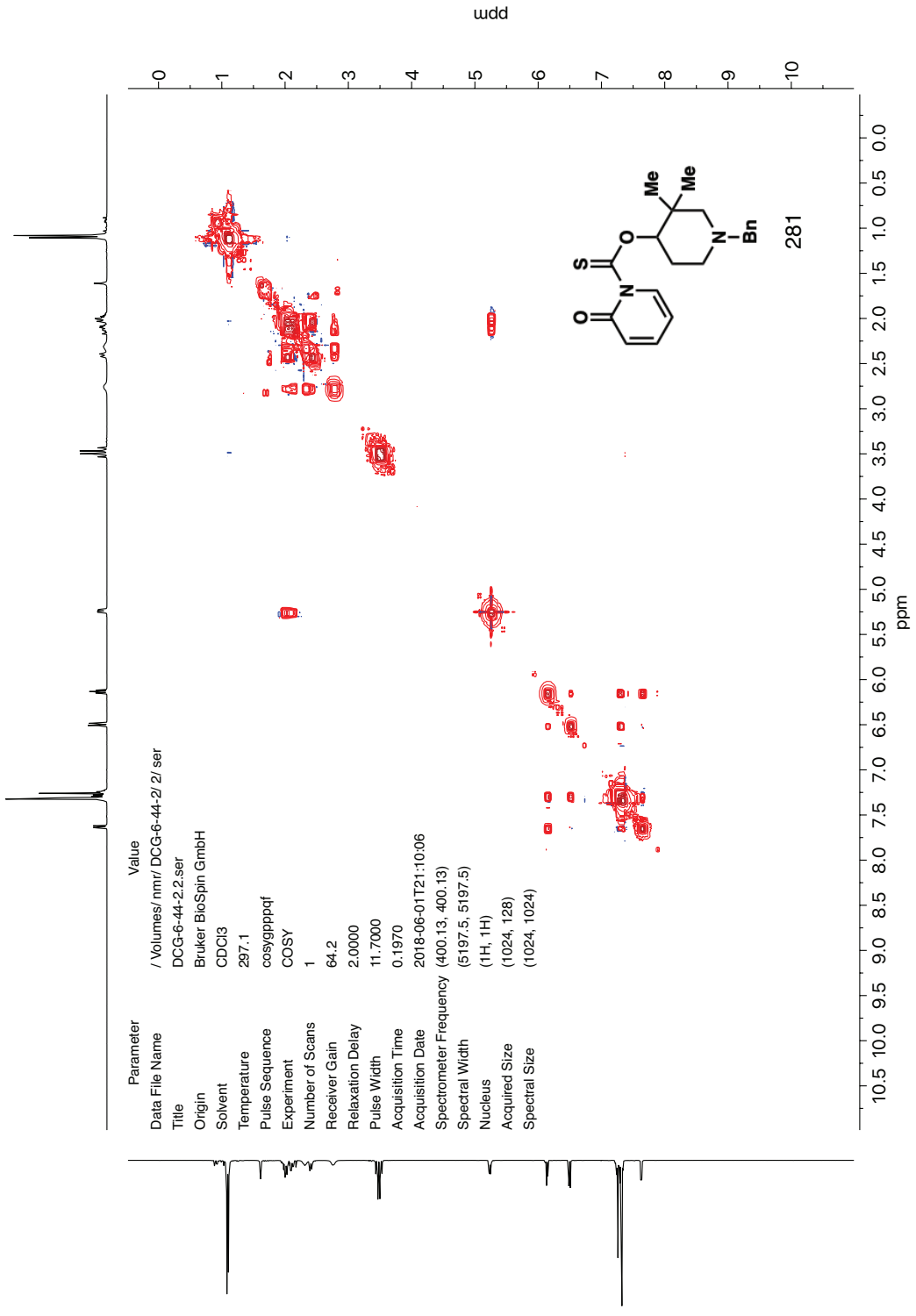

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-74-2/ 4/ ser
Title DCG-4-74-2.4.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2016-10-25T01:20:51
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
ppm
ppm
343
Me
Me
Me
H
S
O
N
O

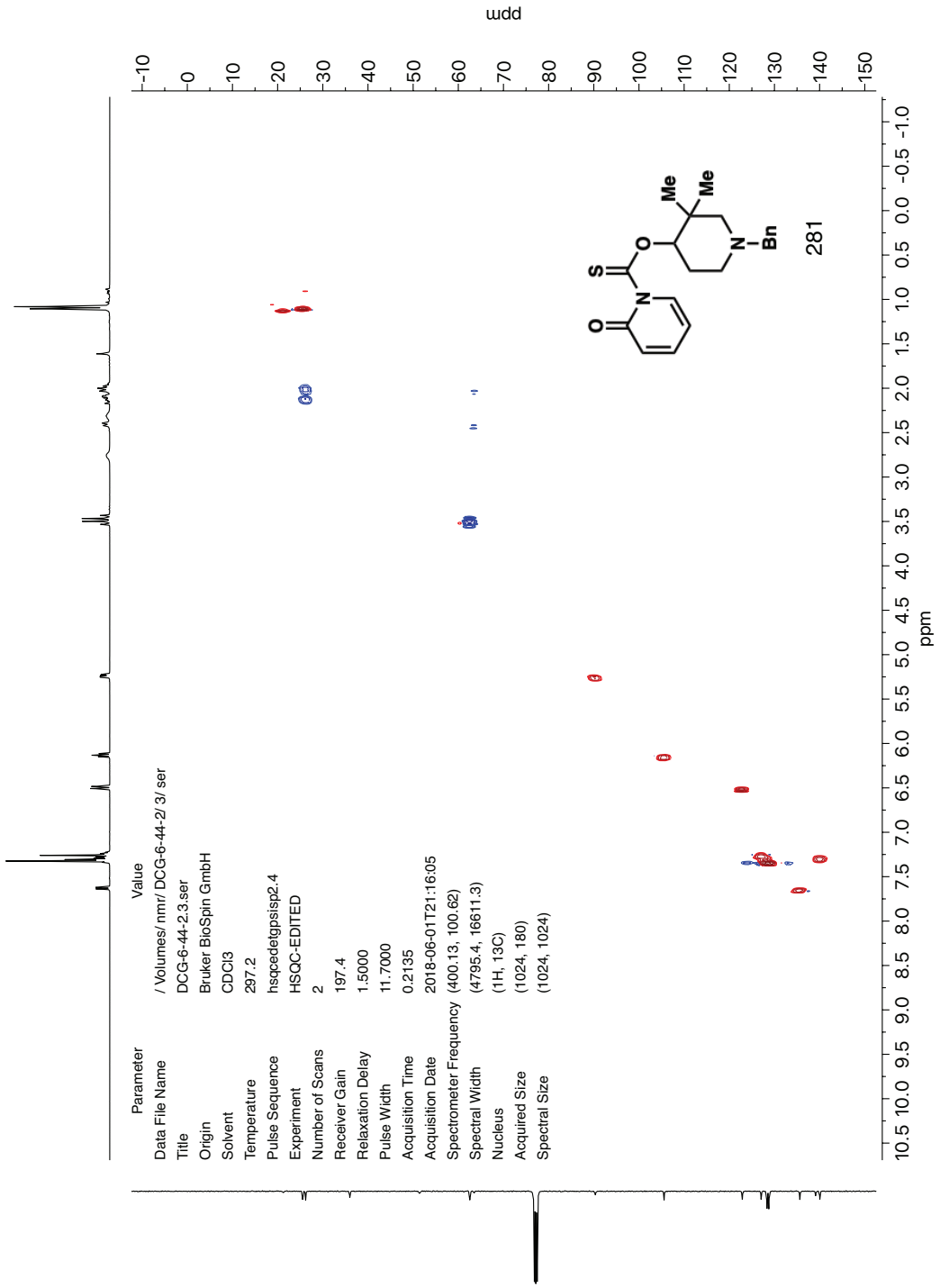

Parameter Value
Data File Name / Volumes/ nmr/ DCG-4-74-2/ 6/ fid
Title DCG-4-74-2.6.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 128
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-10-25T02:54:18
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
343
Me
Me
H
O
S
O
N
O
Me
194.0
159.8
139.9
135.7
122.9
105.5
98.0
49.7
48.9
41.6
41.2
30.1
27.3
25.7
20.5
19.5
ppm

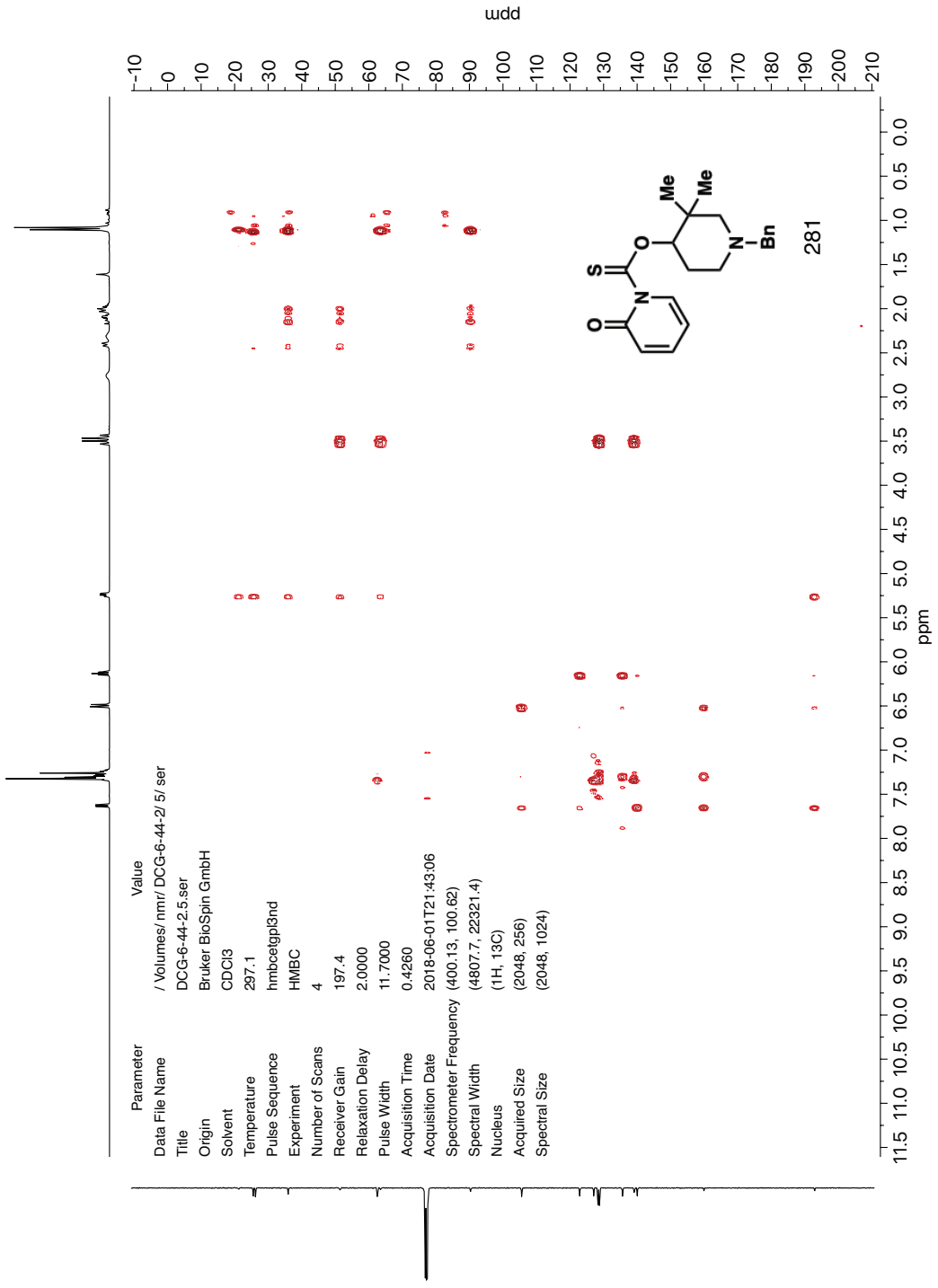


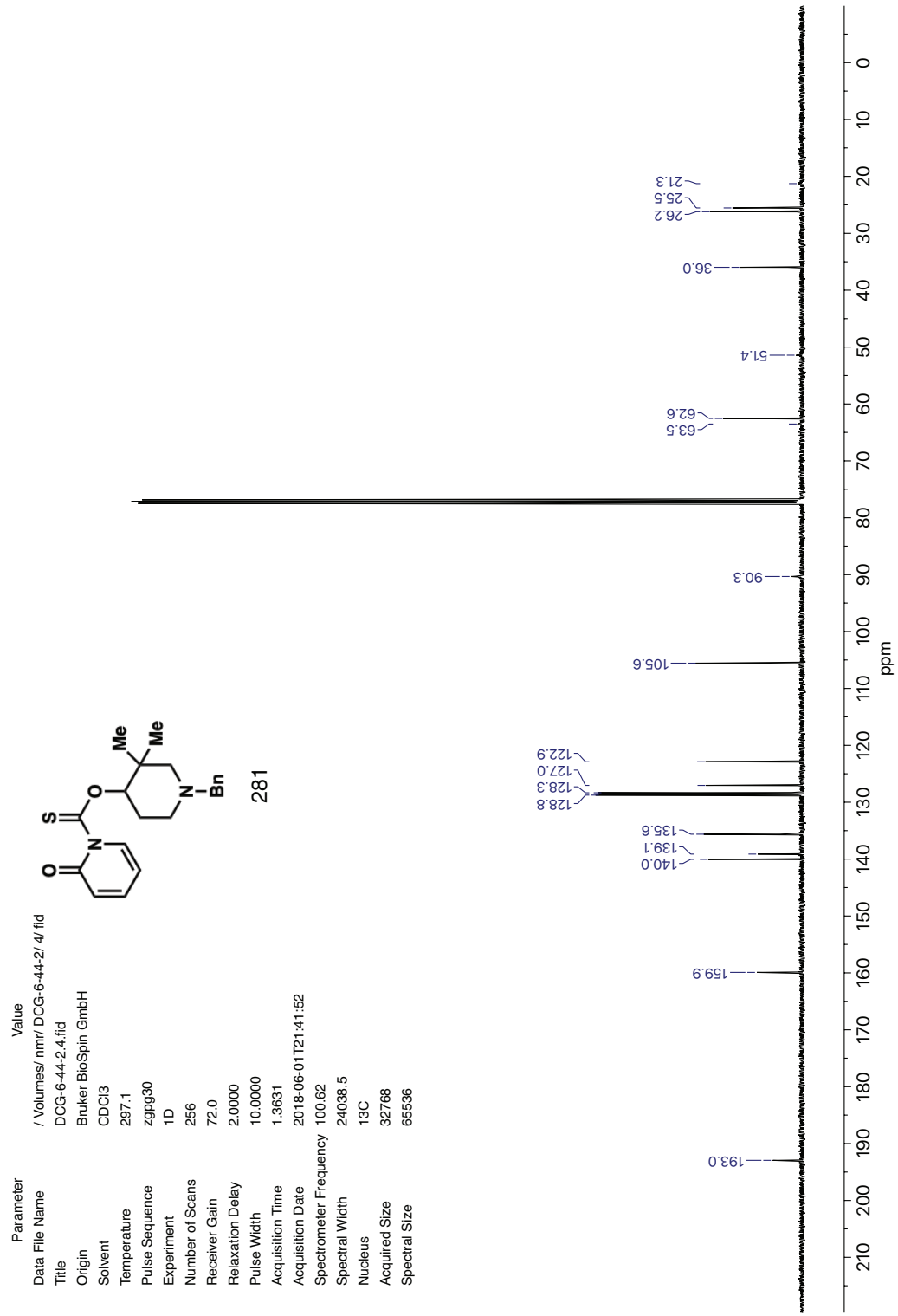
Parameter	Value
Data File Name	/ Volumes/ nmr/ DCG-4-74-2/ 5/ ser
Title	DCG-4-74-2.5.ser
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	294.9
Pulse Sequence	hmbcgpndqf
Experiment	HMBC
Number of Scans	8
Receiver Gain	197.4
Relaxation Delay	2.0000
Pulse Width	11.7000
Acquisition Time	0.1970
Acquisition Date	2016-10-25T02:05:54
Spectrometer Frequency	(400.13, 40.55)
Spectral Width	(5197.5, 16233.8)
Nucleus	(1H, 15N)
Acquired Size	(1024, 128)
Spectral Size	(1024, 512)

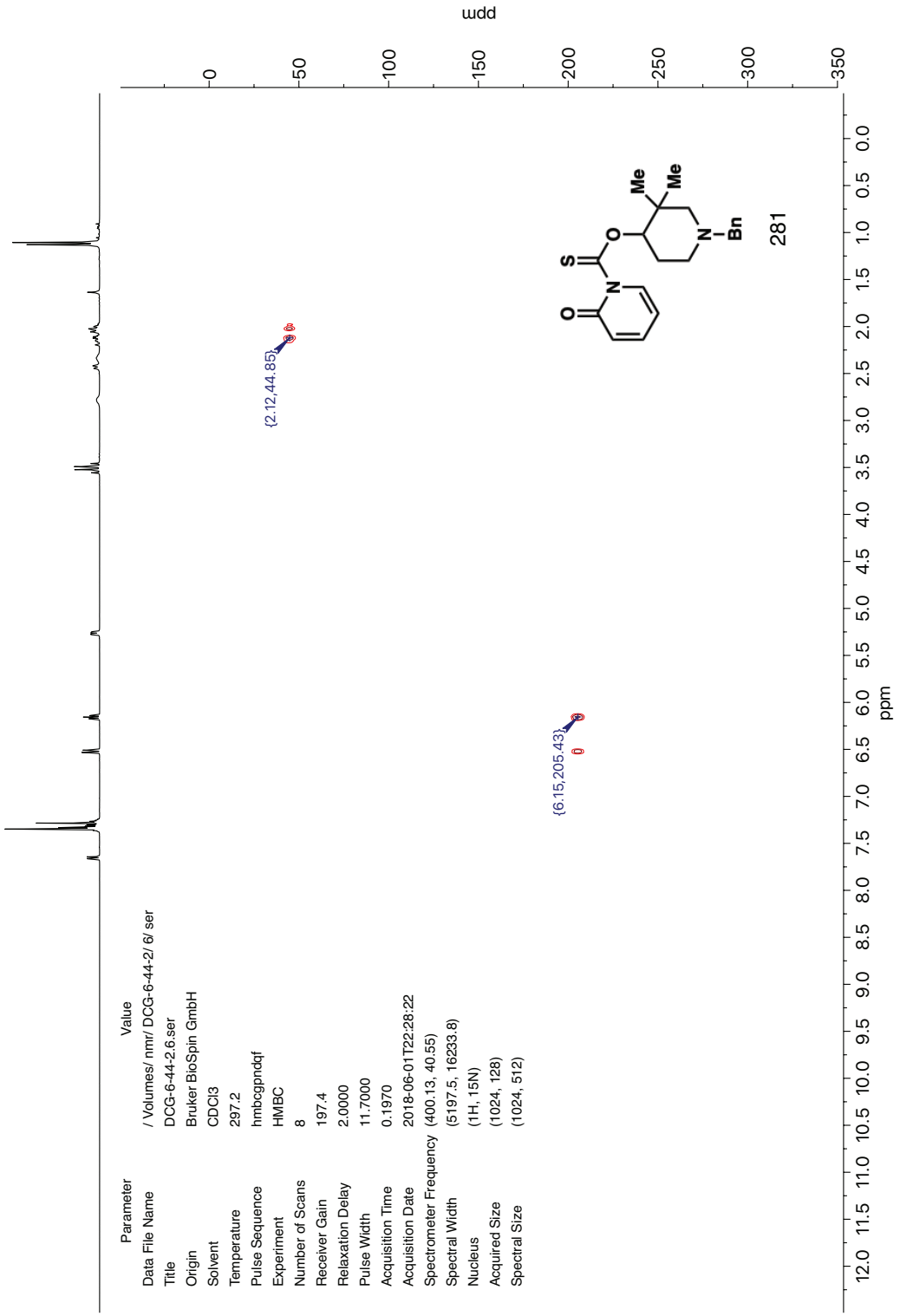

Parameter
Value
Data File Name / Volumes/ nmr/ DCG-6-44-2/ 1/ fid
Title DCG-6-44-2.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 297.2
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 142.8
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-06-01T21:09:13
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
281
Me
Me
Bn
1.00
5.14
0.89
0.98
1.01
1.02
2.12
0.97
1.05
0.98
1.12
2.00
3.00
3.11
ppm


ppm
ppm
Me
Me
O
N
Bn
S
O
N
281
Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-44-2/ 2/ ser
Title DCG-6-44-2.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 297.1
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.1970
Acquisition Date 2018-06-01T21:10:06
Spectrometer Frequency (400.13, 400.13)
Spectral Width (5197.5, 5197.5)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)

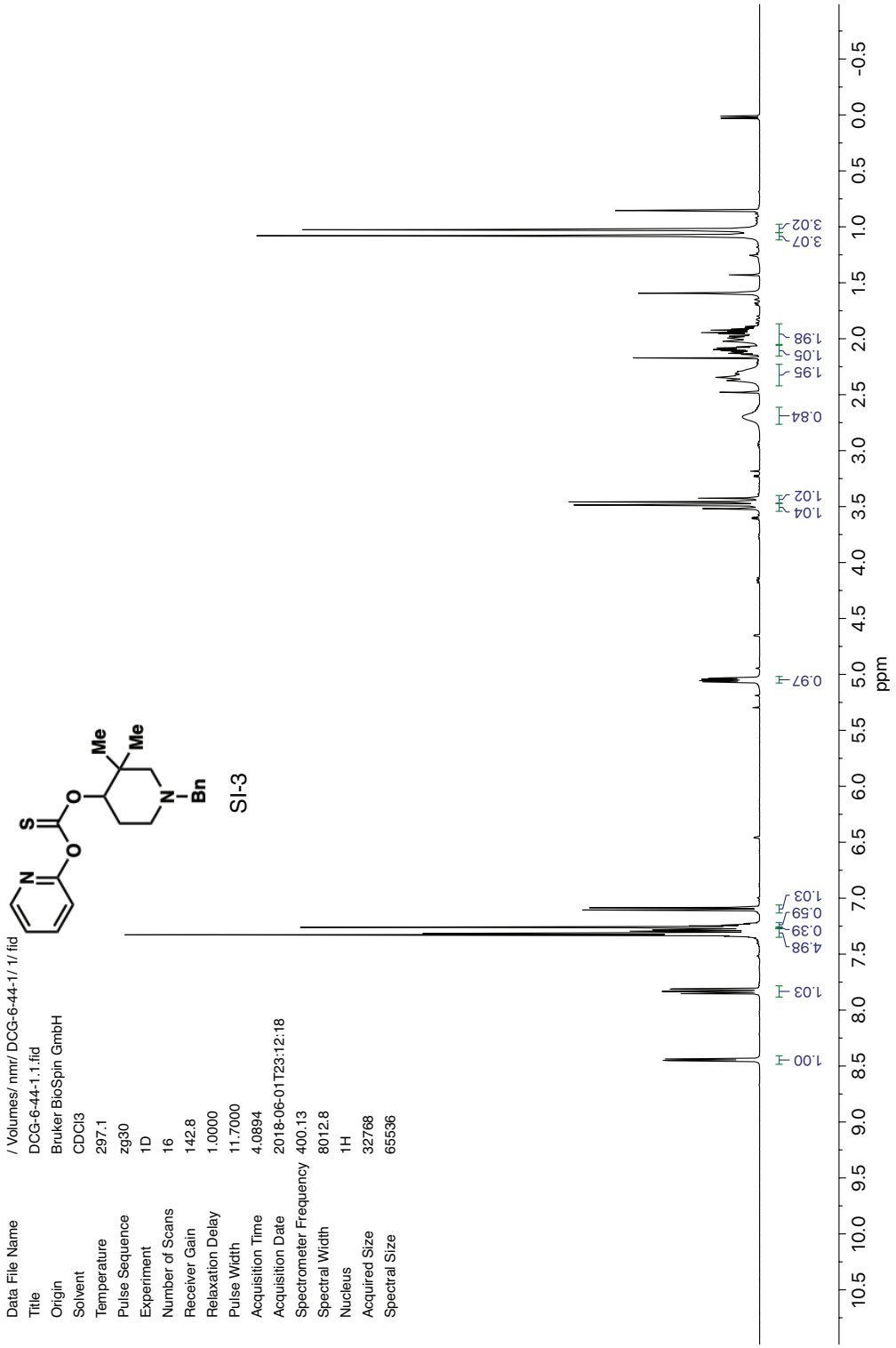

Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-44-2/ 3/ ser
Title DCG-6-44-2.3.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 297.2
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2018-06-01T21:16:05
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 180)
Spectral Size (1024, 1024)
ppm
ppm
Me
Me
Bn
281

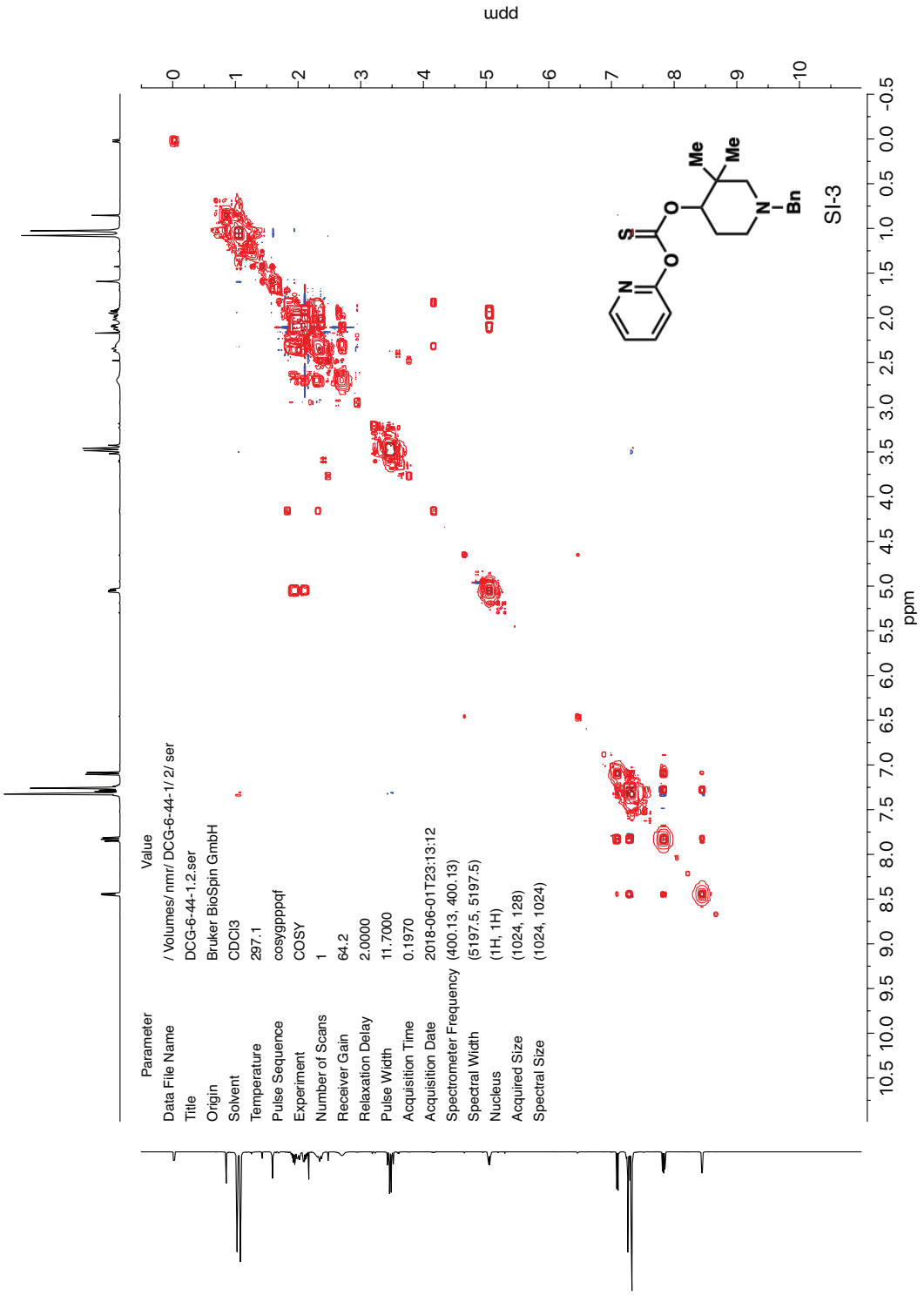

Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-44-2/ 5/ ser
Title DCG-6-44-2.5.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 297.1
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2018-06-01T21:43:06
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
ppm
ppm
Me
Me
Bn
281

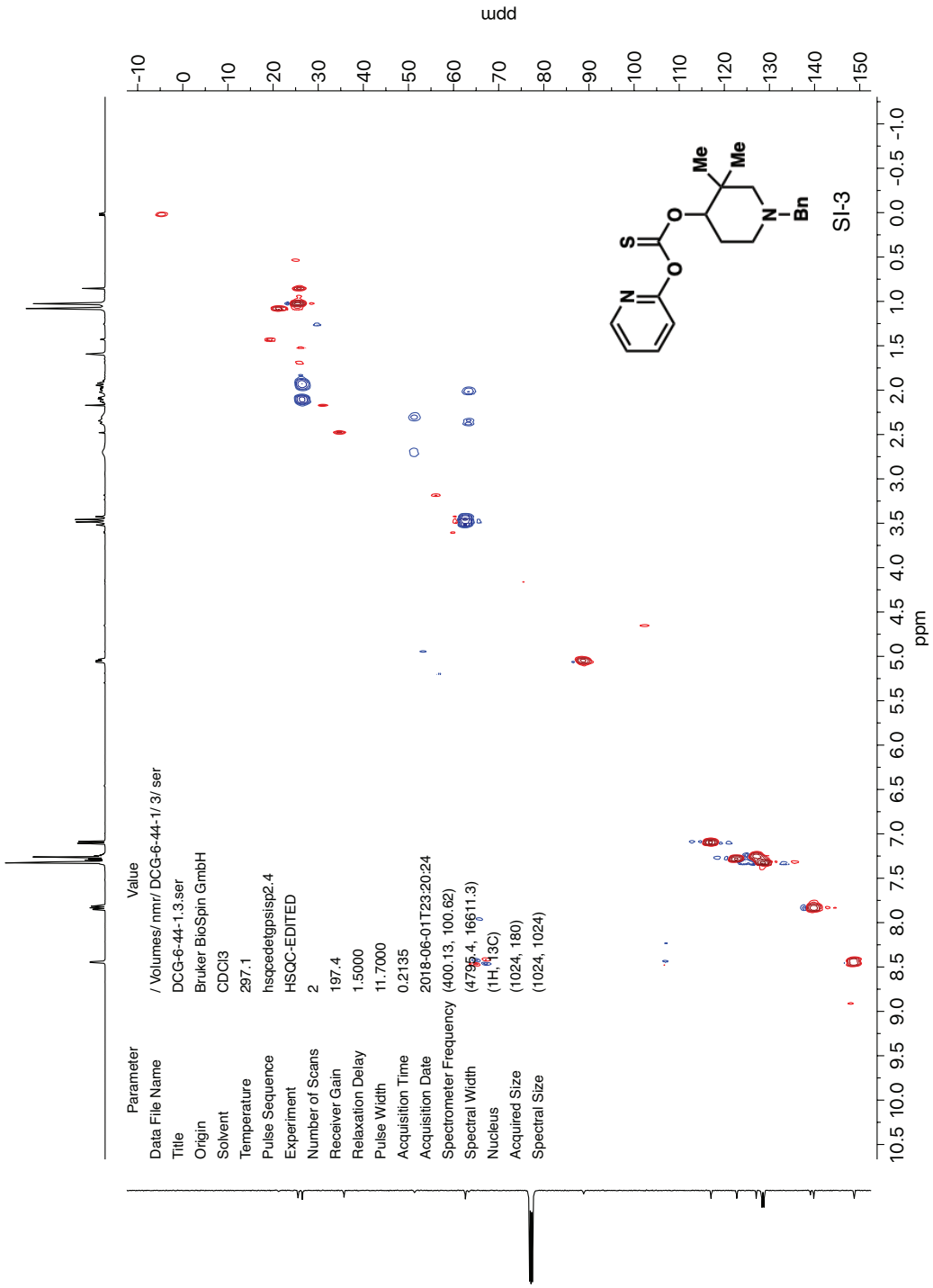

Parameter
Value
Data File Name / Volumes/ nmr/ DCG-6-44-2/ 4/ fid
Title DCG-6-44-2.4.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 297.1
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-06-01T21:41:52
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
281
193.0
159.9
140.0
139.1
135.6
128.8
128.3
127.0
122.9
105.6
90.3
63.5
62.6
51.4
36.0
26.2
25.5
21.3
ppm

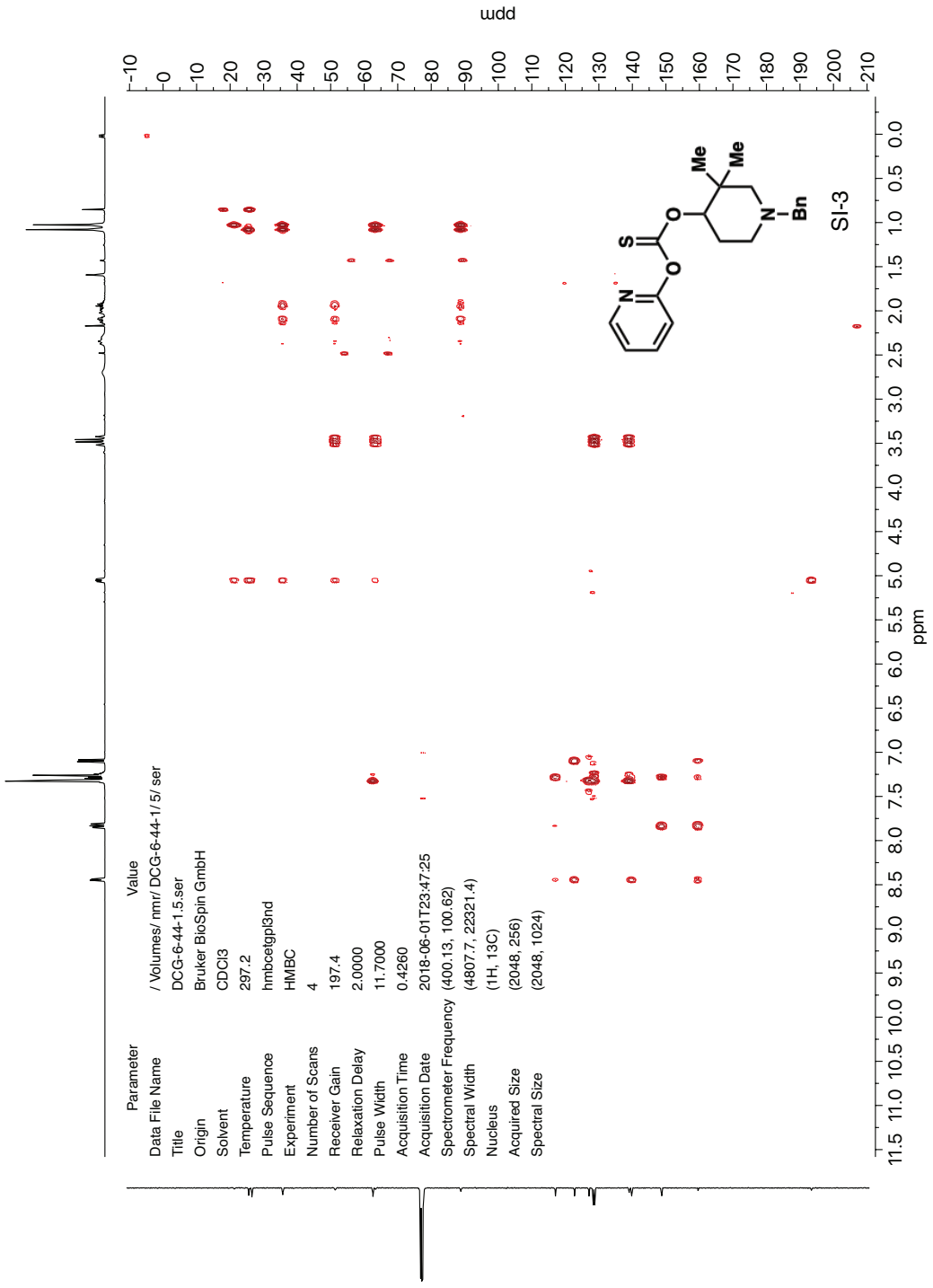


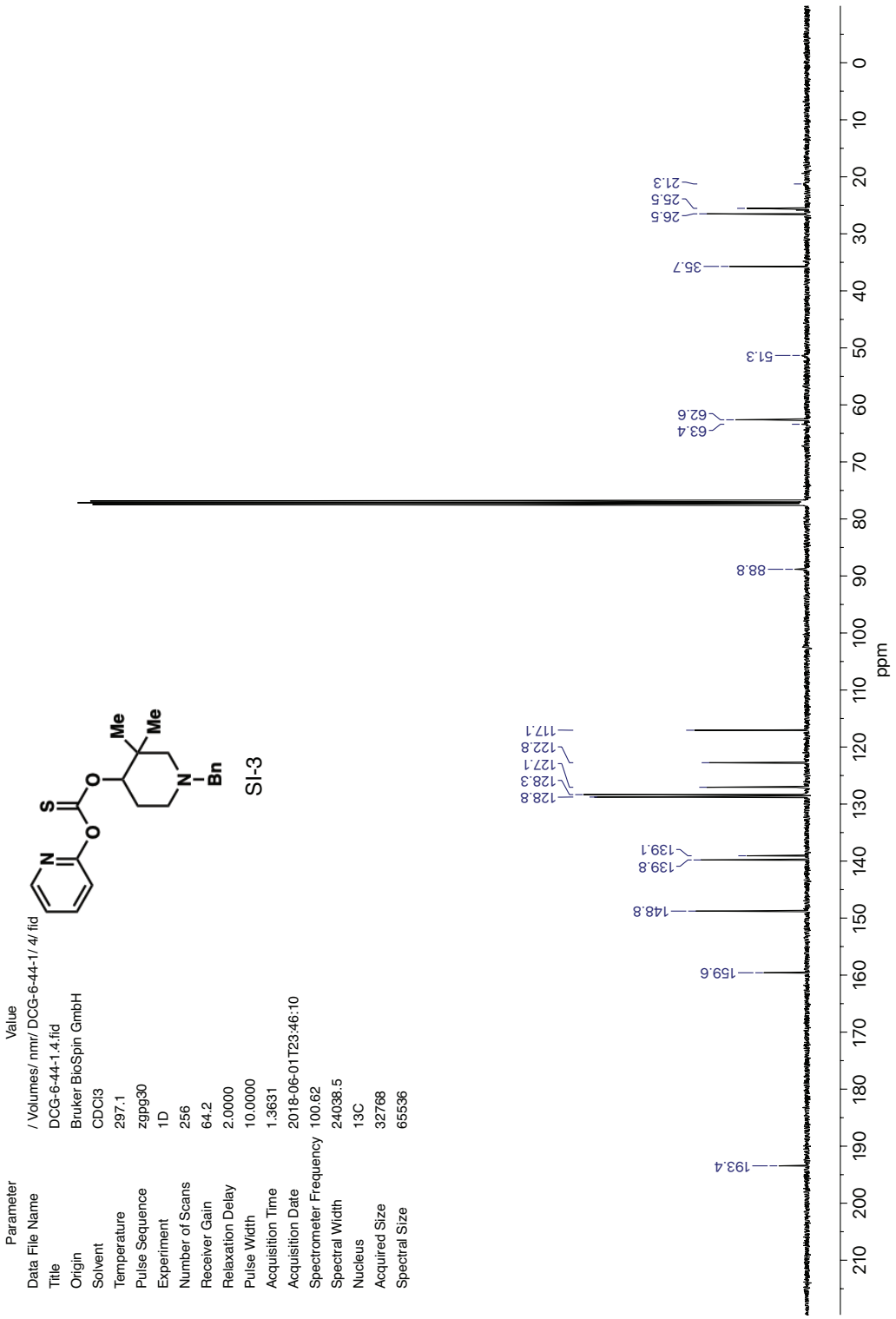
Parameter	Value
Data File Name	/ Volumes/ nmr/ DCG-6-44-2/ 6/ ser
Title	DCG-6-44-2.6.ser
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	297.2
Pulse Sequence	hmbcgpndqf
Experiment	HMBC
Number of Scans	8
Receiver Gain	197.4
Relaxation Delay	2.0000
Pulse Width	11.7000
Acquisition Time	0.1970
Acquisition Date	2018-06-01T22:28:22
Spectrometer Frequency	(400.13, 40.55)
Spectral Width	(5197.5, 16233.8)
Nucleus	(1H, 15N)
Acquired Size	(1024, 128)
Spectral Size	(1024, 512)

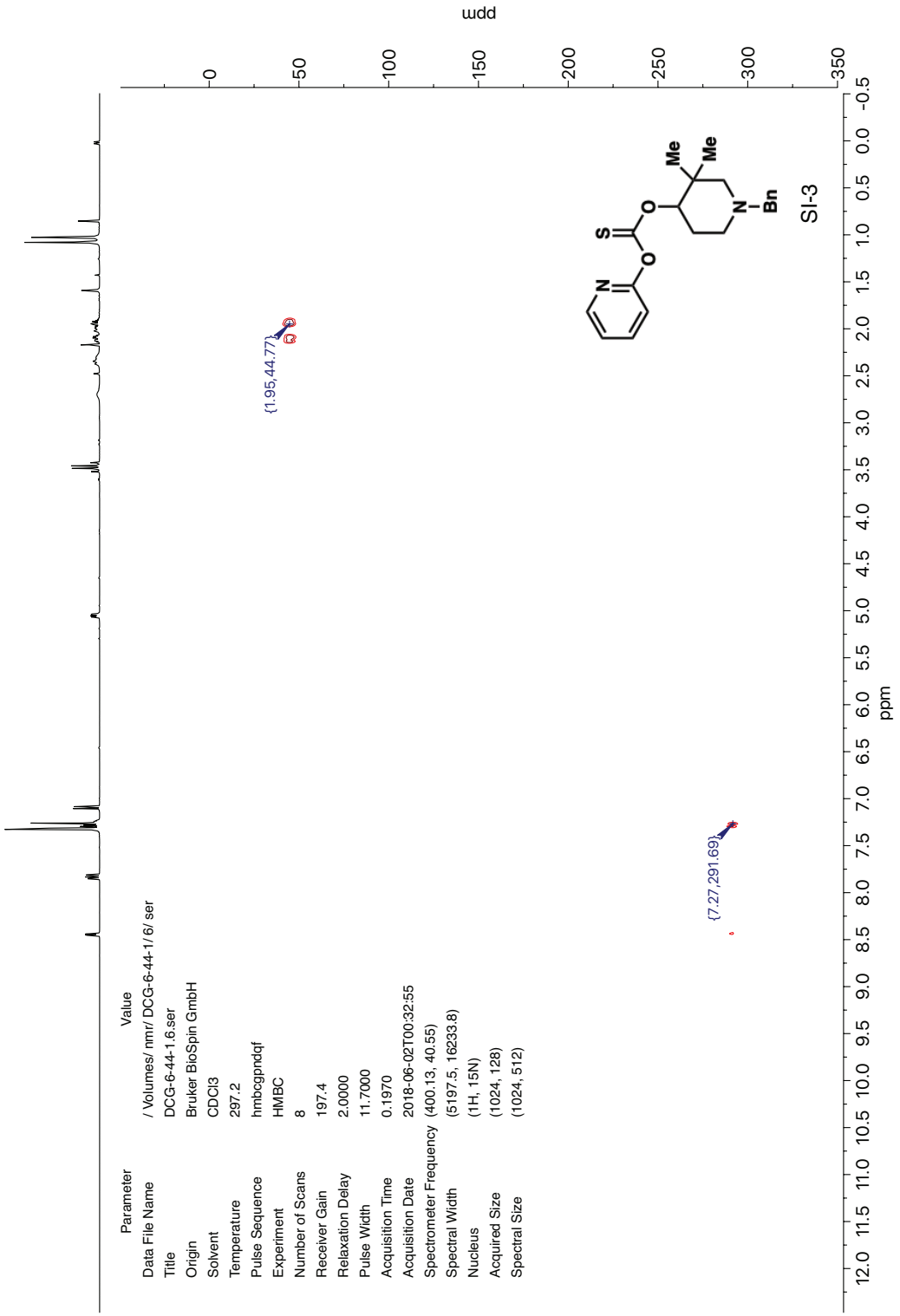

Parameter
Value
Data File Name / Volumes/ nmr/ DCG-6-44-1/ 1/ fid
Title DCG-6-44-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 297.1
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 142.8
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-06-01T23:12:18
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
Me
Me
Bn
SI-3
1.00
1.03
4.98
0.39
0.59
1.03
0.97
1.04
1.02
0.84
1.95
1.05
1.98
3.07
3.02
ppm


ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-44-1/ 2/ ser
Title DCG-6-44-1.2.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 297.1
Pulse Sequence cosygpppqf
Experiment COSY
Number of Scans 1
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.1970
Acquisition Date 2018-06-01T23:13:12
Spectrometer Frequency (400.13, 400.13)
Spectral Width (5197.5, 5197.5)
Nucleus (1H, 1H)
Acquired Size (1024, 128)
Spectral Size (1024, 1024)
Me
Me
Bn
SI-3

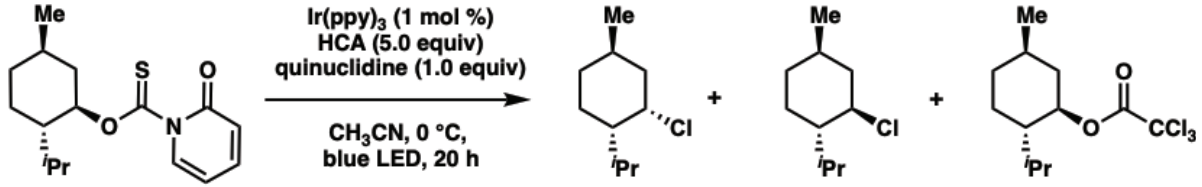

Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-44-1/ 3/ ser
Title DCG-6-44-1.3.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 297.1
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2018-06-01T23:20:24
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4796.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 180)
Spectral Size (1024, 1024)
ppm
ppm
SI-3
Me
Me
Bn
N
O
O
S
N


Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-44-1/5/ ser
Title DCG-6-44-1.5.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 297.2
Pulse Sequence hmbcetgpl3nd
Experiment HMBC
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 2.0000
Pulse Width 11.7000
Acquisition Time 0.4260
Acquisition Date 2018-06-01T23:47:25
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4807.7, 22321.4)
Nucleus (1H, 13C)
Acquired Size (2048, 256)
Spectral Size (2048, 1024)
ppm
ppm
SI-3
Me
Me
Bn
N
O
O
S
N


Parameter
Value
Data File Name / Volumes/ nmr/ DCG-6-44-1/ 4/ fid
Title DCG-6-44-1.4.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 297.1
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-06-01T23:46:10
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
SI-3
193.4
159.6
148.8
139.8
139.1
128.8
128.3
127.1
122.8
117.1
88.8
63.4
62.6
51.3
35.7
26.5
25.5
21.3
ppm


ppm
{1.95,44.77}
{7.27,291.69}
Me
Me
Bn
SI-3
Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-6-44-1/ 6/ ser
Title
DCG-6-44-1.6.ser
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
297.2
Pulse Sequence
hmbcgpndqf
Experiment
HMBC
Number of Scans
8
Receiver Gain
197.4
Relaxation Delay
2.0000
Pulse Width
11.7000
Acquisition Time
0.1970
Acquisition Date
2018-06-02T00:32:55
Spectrometer Frequency
(400.13, 40.55)
Spectral Width
(5197.5, 16233.8)
Nucleus
(1H, 15N)
Acquired Size
(1024, 128)
Spectral Size
(1024, 512)

Parameter	Value
Data File Name	/ Volumes/ nmr/ DCG-4-131-A-C/ 2/ fid
Title	DCG-4-131-A-C.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	zg30
Experiment	1D
Number of Scans	1
Receiver Gain	13.7
Relaxation Delay	10.0000
Pulse Width	11.7000
Acquisition Time	9.9998
Acquisition Date	2016-12-10T19:42:46
Spectrometer Frequency	400.13
Spectral Width	8012.8
Nucleus	1H
Acquired Size	80127
Spectral Size	262144



341

329/348m
peak B

(13% yield)

330
peak C

(19% yield)

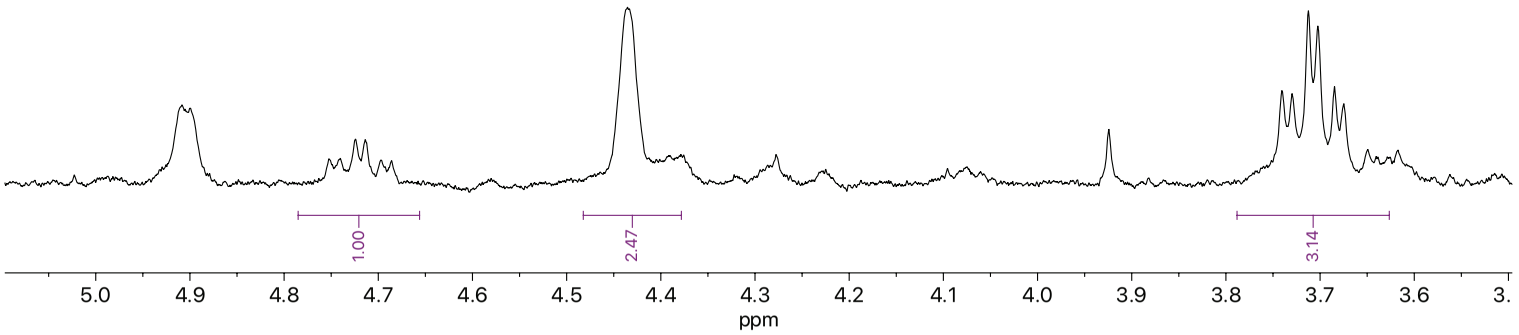
331
peak A

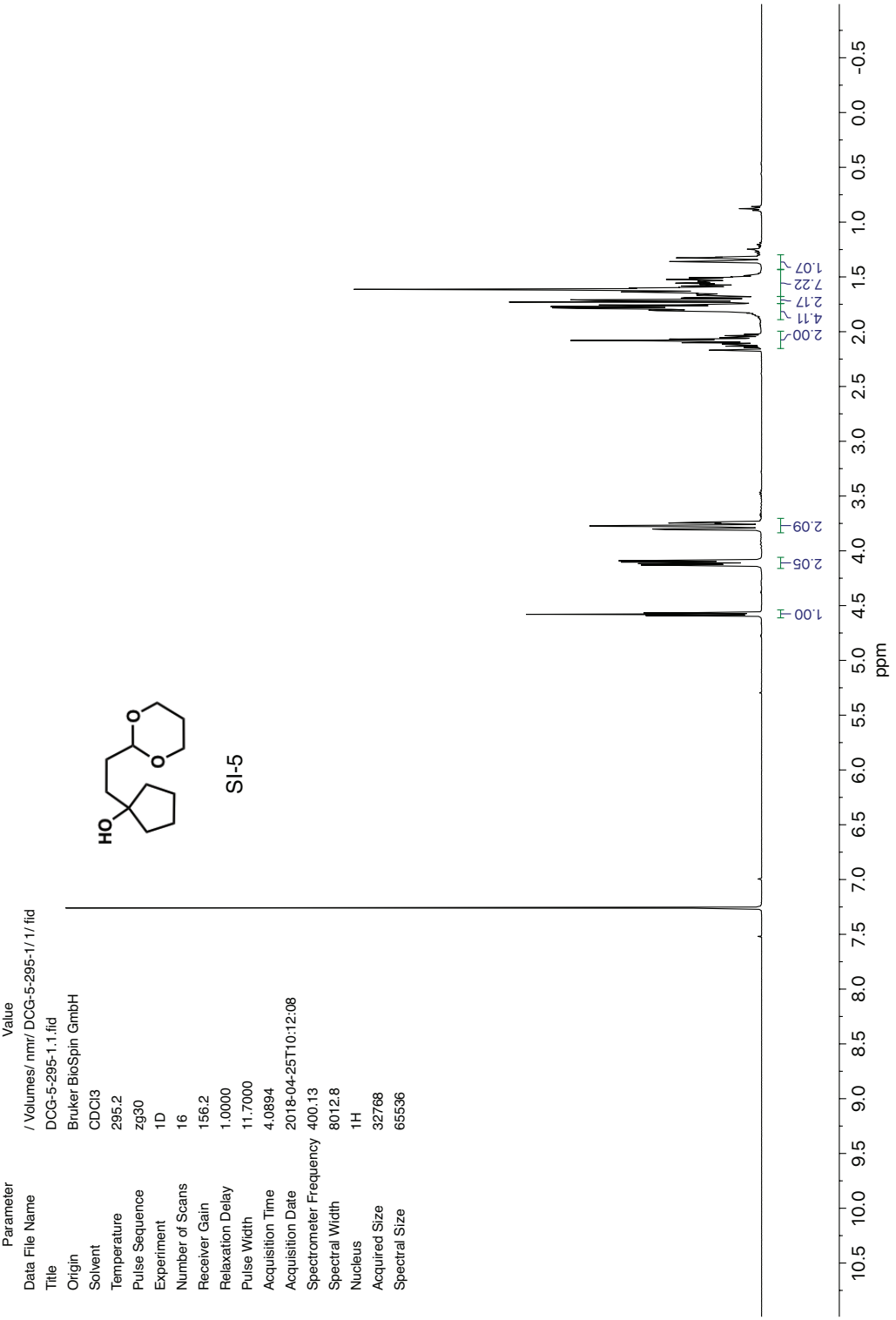
(4% yield)

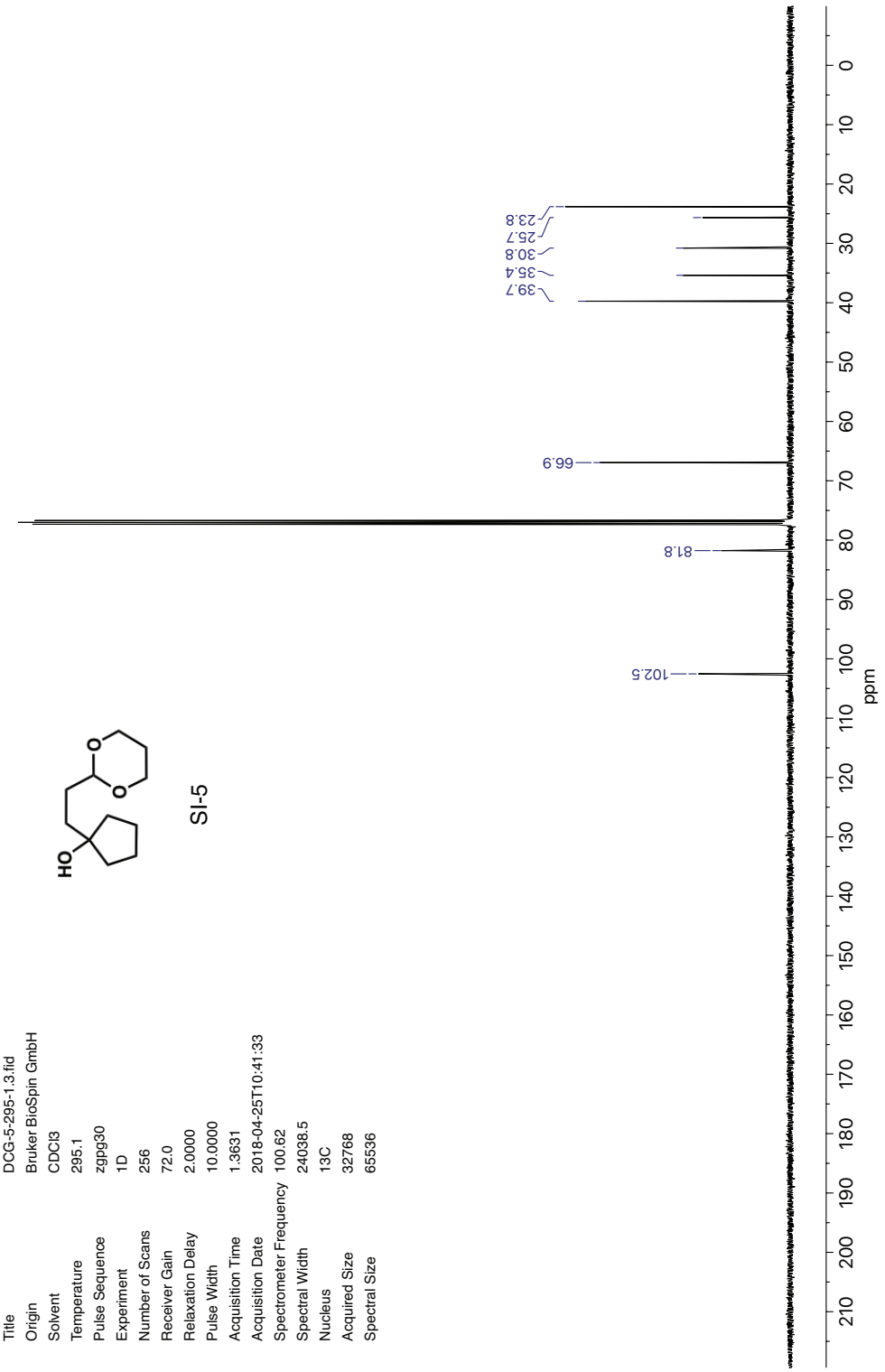
A (td)
4.72

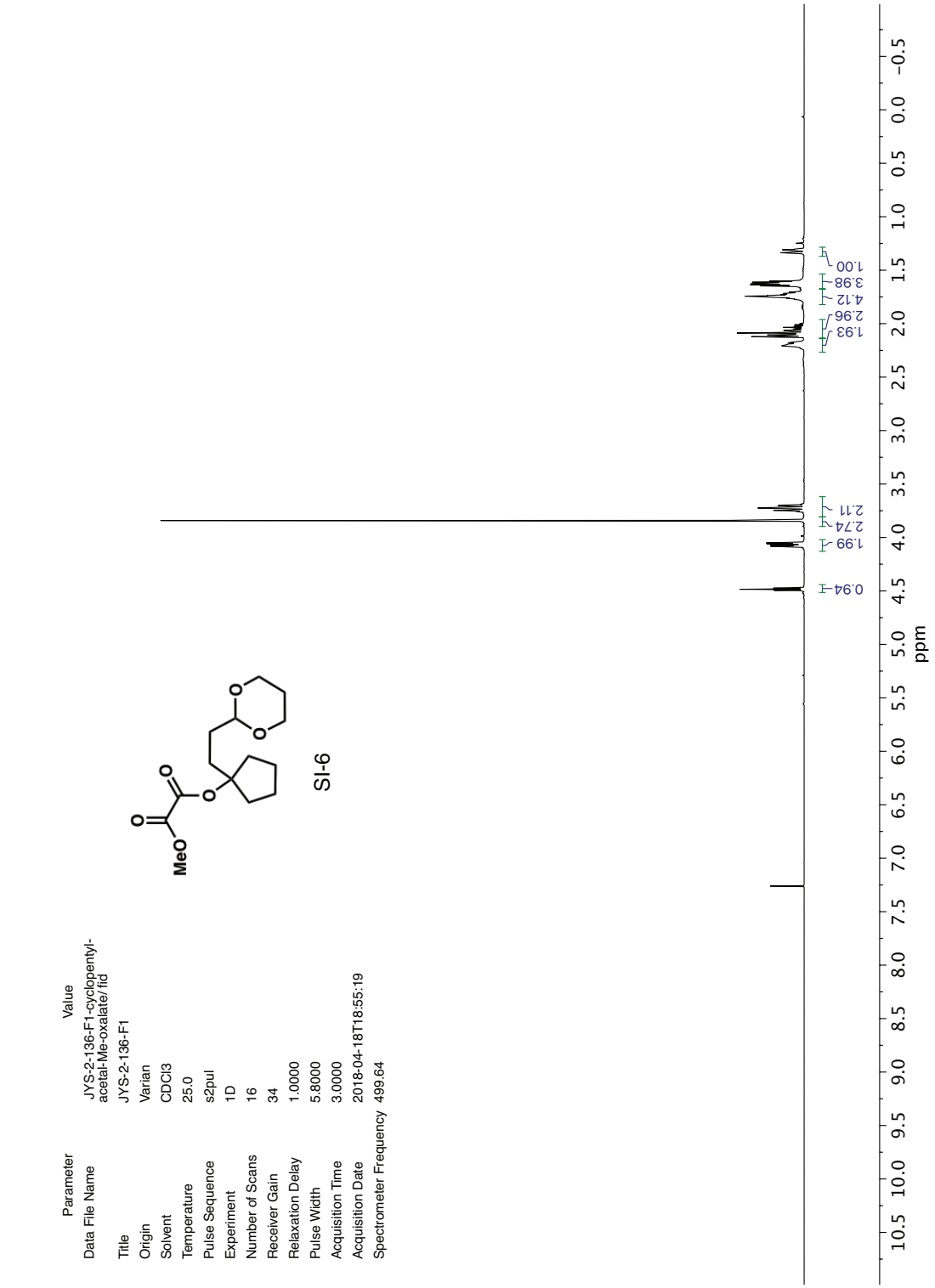
B (s)
4.43

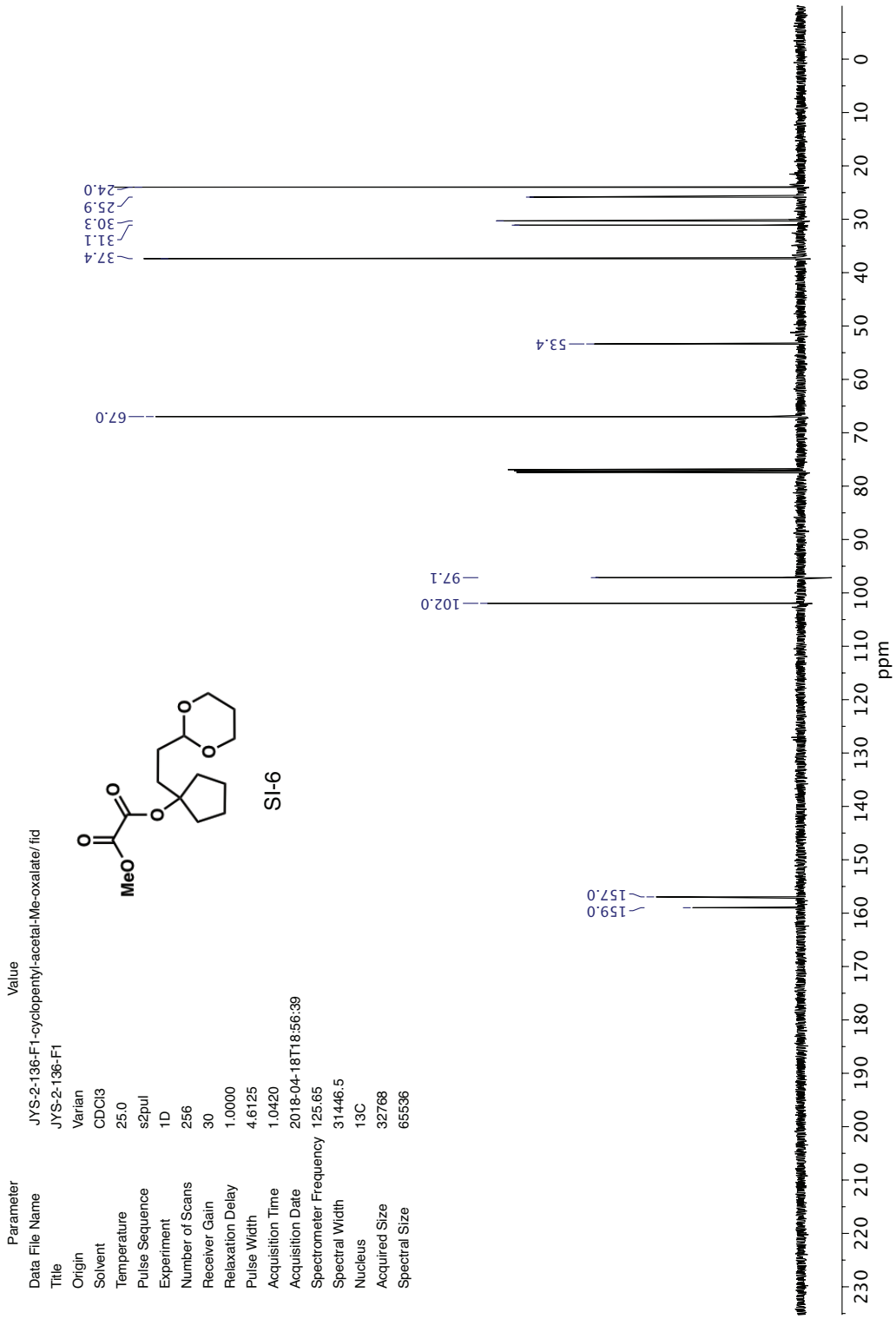
C (td)
3.71

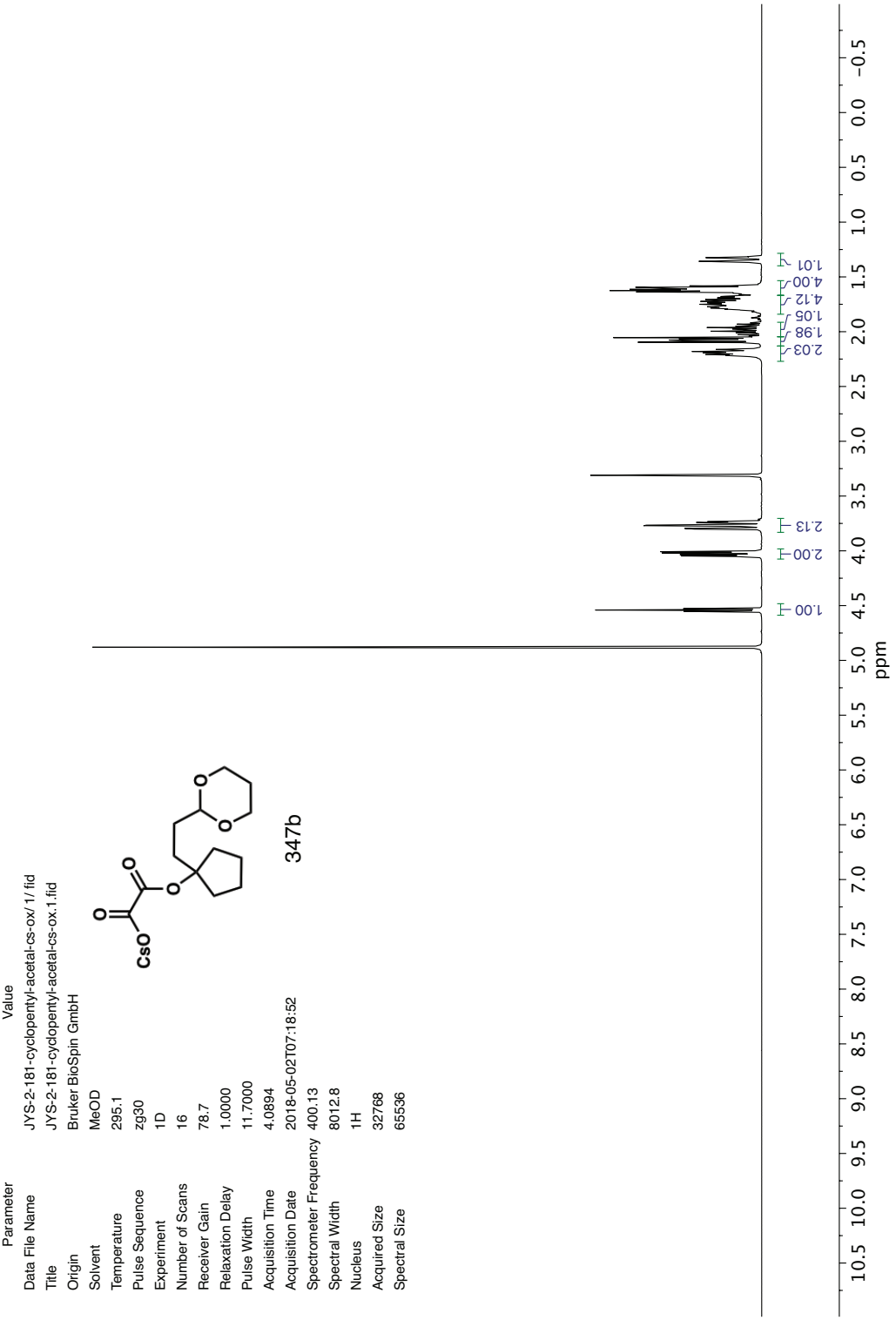


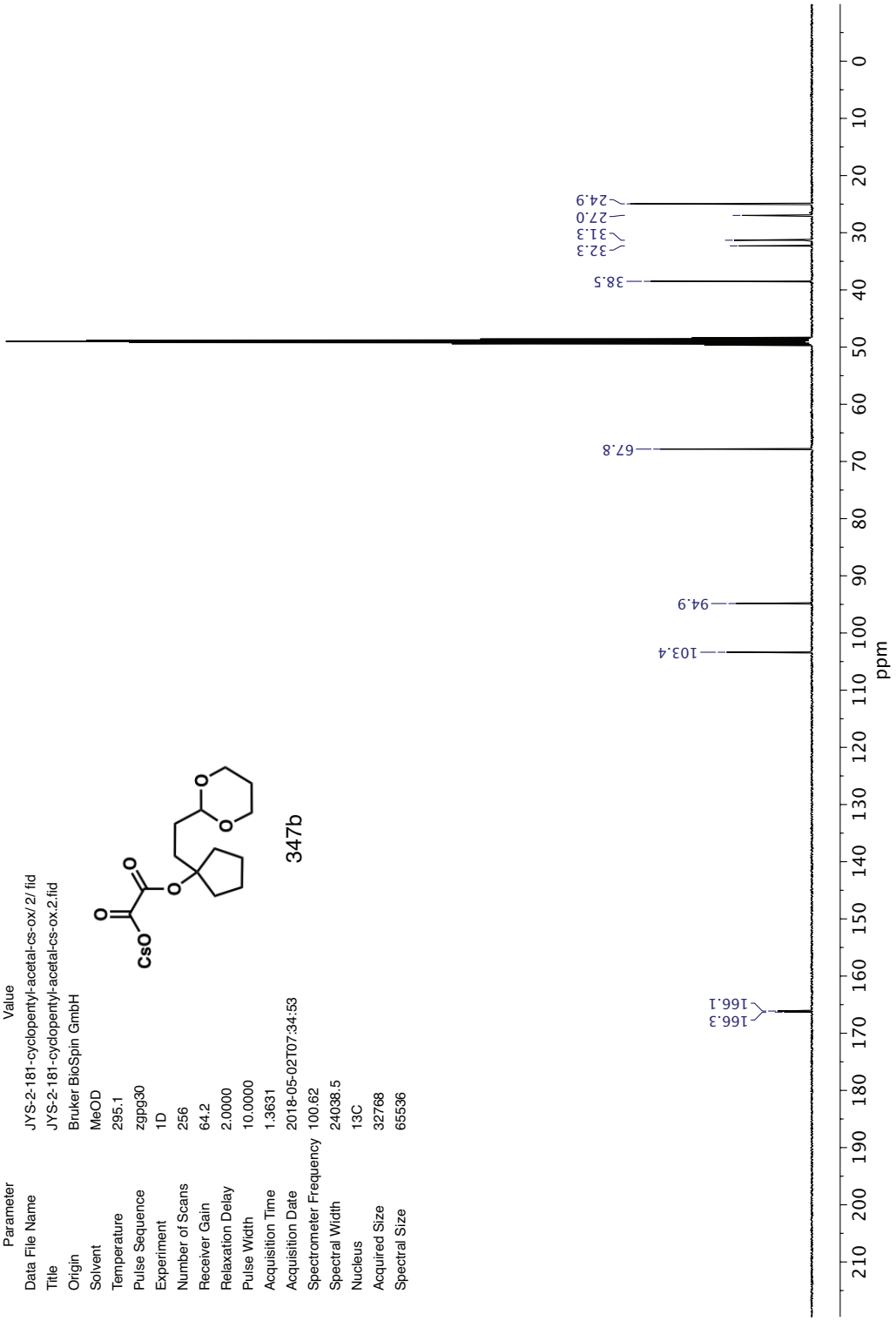

Parameter
Value
Data File Name / Volumes/ nmr/ DCG-5-295-1/1/ fid
Title DCG-5-295-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 156.2
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-04-25T10:12:08
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
HO
SI-5
1.00
2.05
2.09
2.00
4.11
2.17
7.22
1.07
ppm

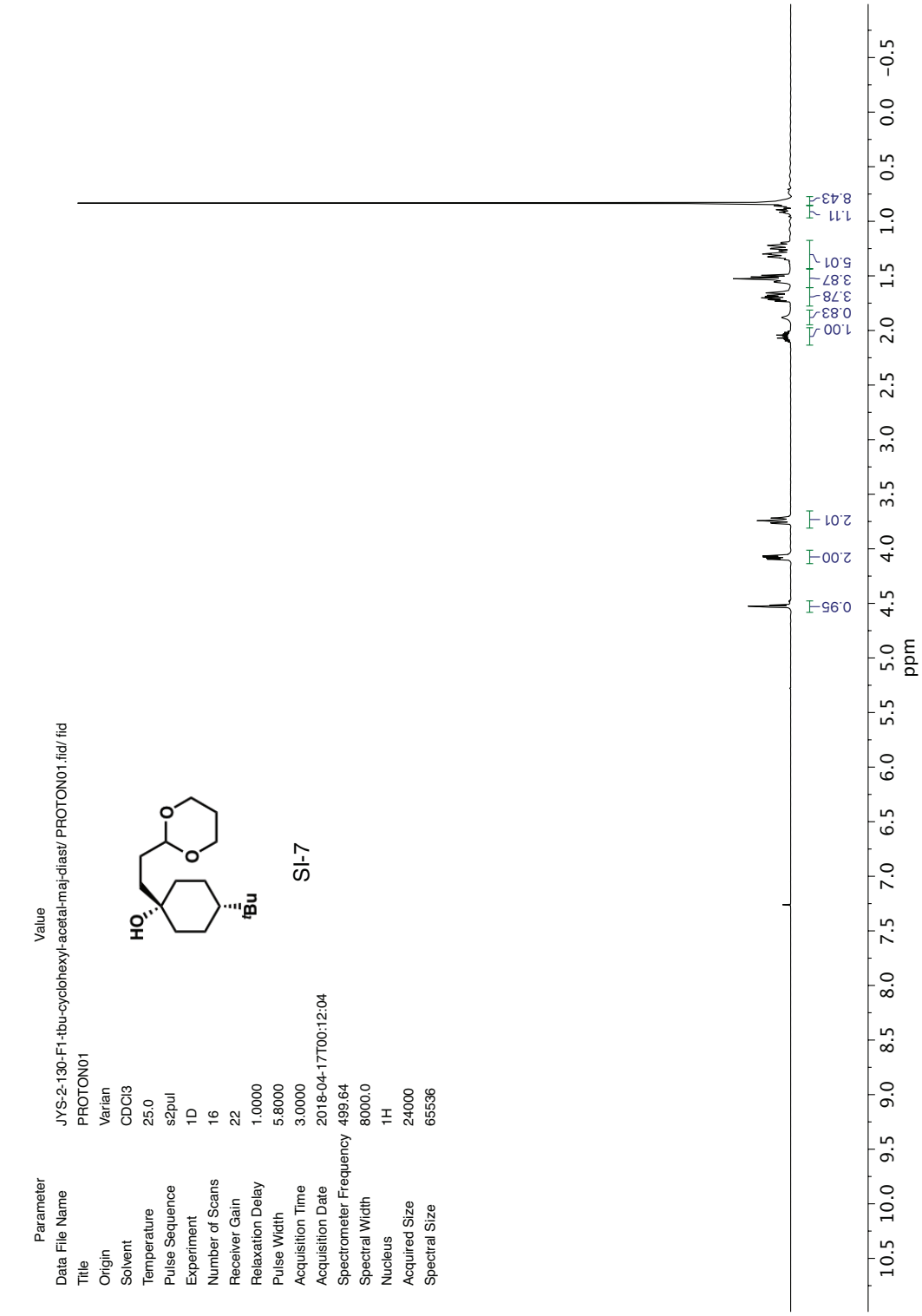

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-295-1/ 3/ fid
Title DCG-5-295-1.3.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-04-25T10:41:33
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
HO
SI-5
102.5
81.8
66.9
39.7
35.4
30.8
25.7
23.8
ppm

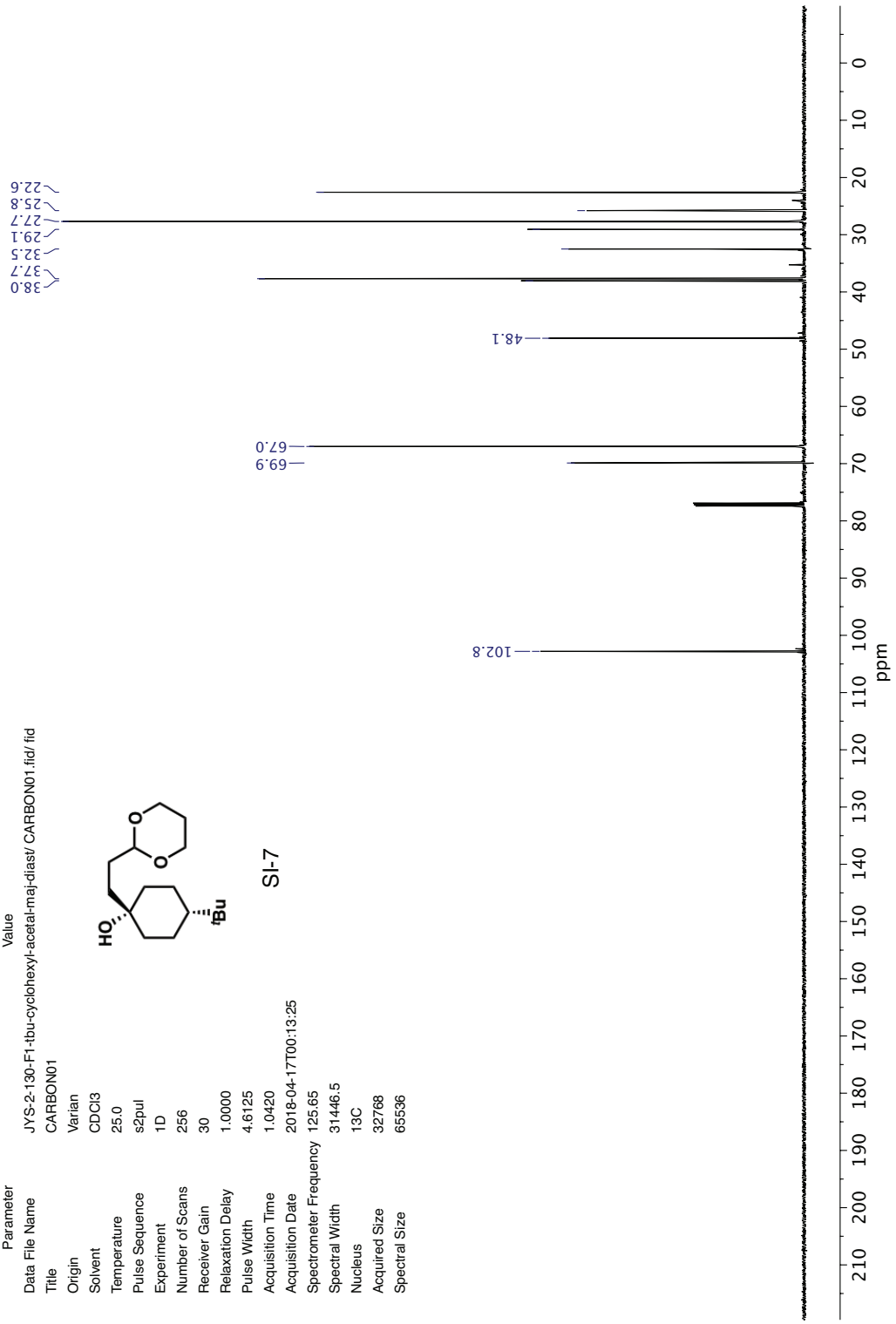

Parameter Value
Data File Name JYS-2-136-F1-cyclopentyl-acetal-Me-oxalate/ fid
Title JYS-2-136-F1
Origin Varian
Solvent CDCl3
Temperature 25.0
Pulse Sequence s2pul
Experiment 1D
Number of Scans 16
Receiver Gain 34
Relaxation Delay 1.0000
Pulse Width 5.8000
Acquisition Time 3.0000
Acquisition Date 2018-04-18T18:55:19
Spectrometer Frequency 499.64
MeO
SI-6
0.94
1.99
2.74
2.11
1.93
2.96
4.12
3.98
1.00
ppm


Parameter
Value
Data File Name JYS-2-136-F1-cyclopentyl-acetal-Me-oxalate/ fid
Title JYS-2-136-F1
Origin Varian
Solvent CDCl3
Temperature 25.0
Pulse Sequence s2pul
Experiment 1D
Number of Scans 256
Receiver Gain 30
Relaxation Delay 1.0000
Pulse Width 4.6125
Acquisition Time 1.0420
Acquisition Date 2018-04-18T18:56:39
Spectrometer Frequency 125.65
Spectral Width 31446.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
MeO
SI-6
157.0
159.0
97.1
102.0
53.4
67.0
24.0
25.9
30.3
31.1
37.4
ppm


Parameter
Value
Data File Name
JYS-2-181-cyclopentyl-acetal-cs-ox/1/fid
Title
JYS-2-181-cyclopentyl-acetal-cs-ox.1.fid
Origin
Bruker BioSpin GmbH
Solvent
MeOD
Temperature
295.1
Pulse Sequence
zg30
Experiment
1D
Number of Scans
16
Receiver Gain
78.7
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-05-02T07:18:52
Spectrometer Frequency
400.13
Spectral Width
8012.8
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
CsO
O
O
O
O
O
347b
1.00
2.00
2.13
2.03
1.98
1.05
4.12
4.00
1.01
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
ppm


Parameter
Value
Data File Name
JYS-2-181-cyclopentyl-acetal-cs-ox/2/fid
Title
JYS-2-181-cyclopentyl-acetal-cs-ox.2.fid
Origin
Bruker BioSpin GmbH
Solvent
MeOD
Temperature
295.1
Pulse Sequence
zgpg30
Experiment
1D
Number of Scans
256
Receiver Gain
64.2
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-05-02T07:34:53
Spectrometer Frequency
100.62
Spectral Width
24038.5
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
CsO
O
O
O
O
O
347b
166.3
166.1
103.4
94.9
67.8
38.5
32.3
31.3
27.0
24.9
ppm


Parameter
Value
Data File Name JYS-2-130-F1-tbu-cyclohexyl-acetal-maj-diast/ PROTON01.fid/ fid
Title PROTON01
Origin Varian
Solvent CDCl3
Temperature 25.0
Pulse Sequence s2pul
Experiment 1D
Number of Scans 16
Receiver Gain 22
Relaxation Delay 1.0000
Pulse Width 5.8000
Acquisition Time 3.0000
Acquisition Date 2018-04-17T00:12:04
Spectrometer Frequency 499.64
Spectral Width 8000.0
Nucleus 1H
Acquired Size 24000
Spectral Size 65536
HO
tBu
SI-7
0.95
2.00
2.01
1.00
0.83
3.78
3.87
5.01
1.11
8.43
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
ppm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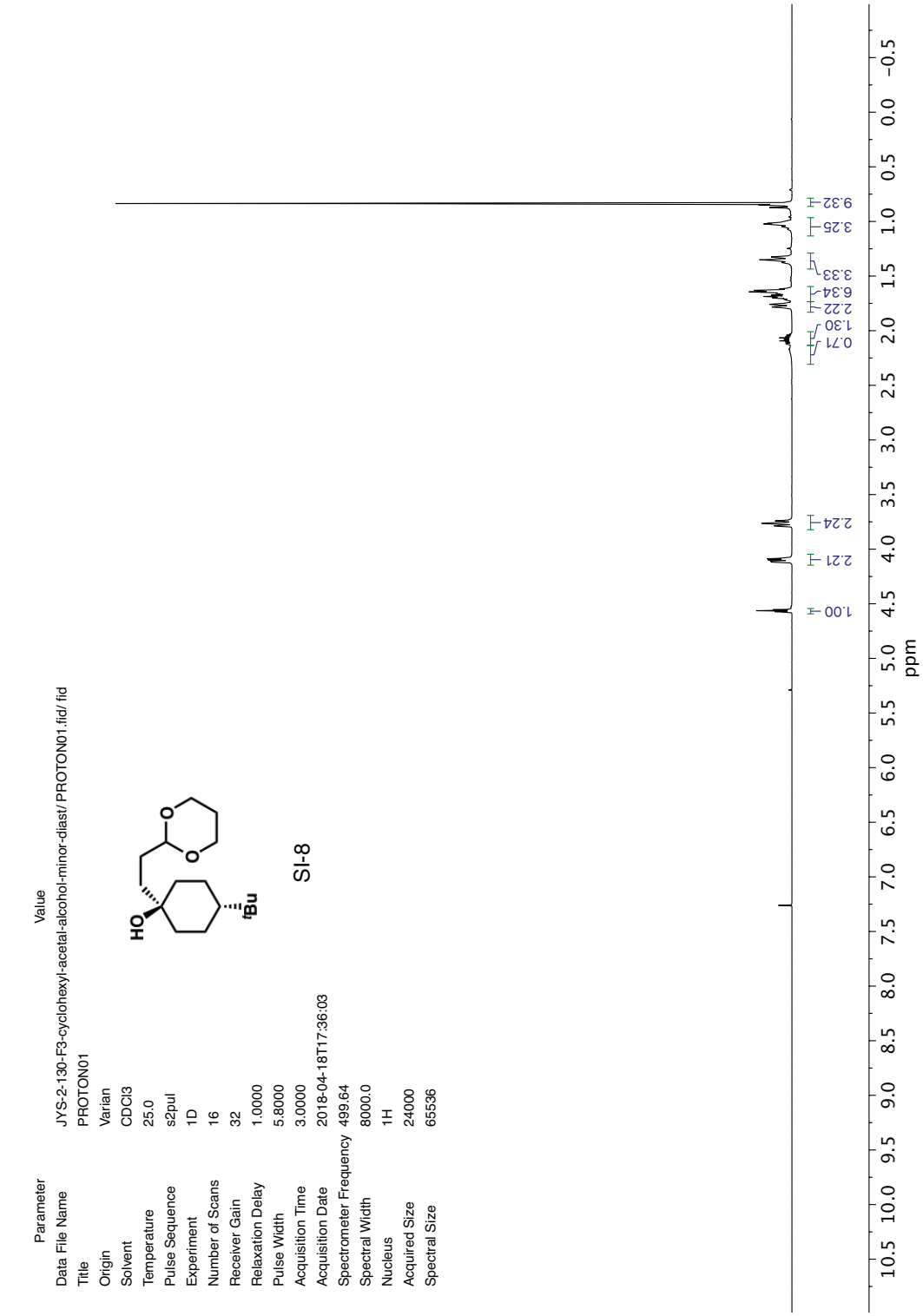
Data File Name JYS-2-130-F1-tbu-cyclohexyl-acetal-maj-diast/ CARBON01.fid/ fid
Title CARBON01
Origin Varian
Solvent CDCl3
Temperature 25.0
Pulse Sequence s2pul
Experiment 1D
Number of Scans 256
Receiver Gain 30
Relaxation Delay 1.0000
Pulse Width 4.6125
Acquisition Time 1.0420
Acquisition Date 2018-04-17T00:13:25
Spectrometer Frequency 125.65
Spectral Width 31446.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
HO
tBu
SI-7
102.8
69.9
67.0
48.1
38.0
37.7
32.5
29.1
27.7
25.8
22.6
ppm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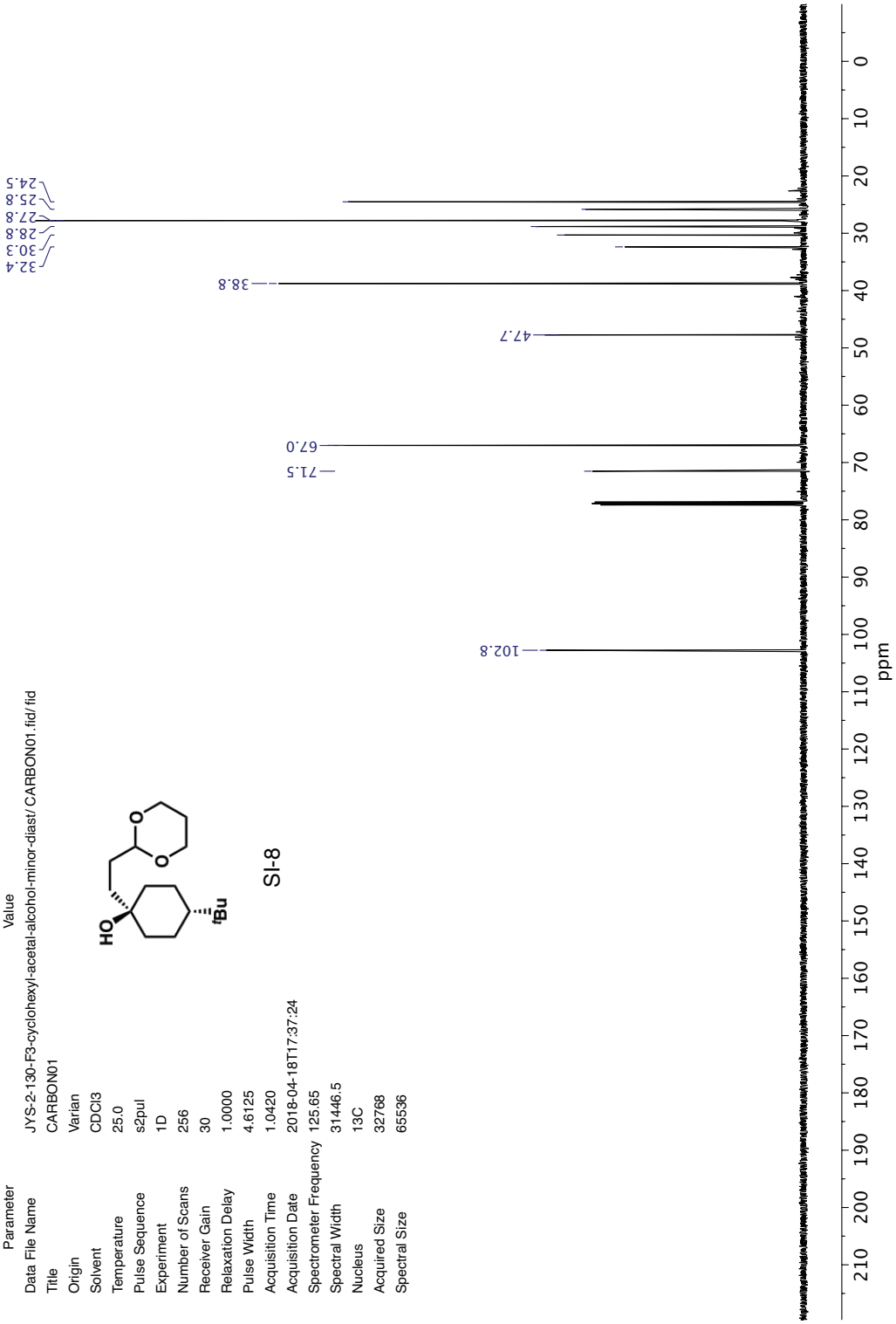
Data File Name JYS-2-130-F3-cyclohexyl-acetal-alcohol-minor-diast/ PROTON01.fid/ fid
Title PROTON01
Origin Varian
Solvent CDCl3
Temperature 25.0
Pulse Sequence s2pul
Experiment 1D
Number of Scans 16
Receiver Gain 32
Relaxation Delay 1.0000
Pulse Width 5.8000
Acquisition Time 3.0000
Acquisition Date 2018-04-18T17:36:03
Spectrometer Frequency 499.64
Spectral Width 8000.0
Nucleus 1H
Acquired Size 24000
Spectral Size 65536
SI-8
HO
tBu
1.00
2.21
2.24
0.71
1.30
2.22
6.34
3.33
3.25
9.32
ppm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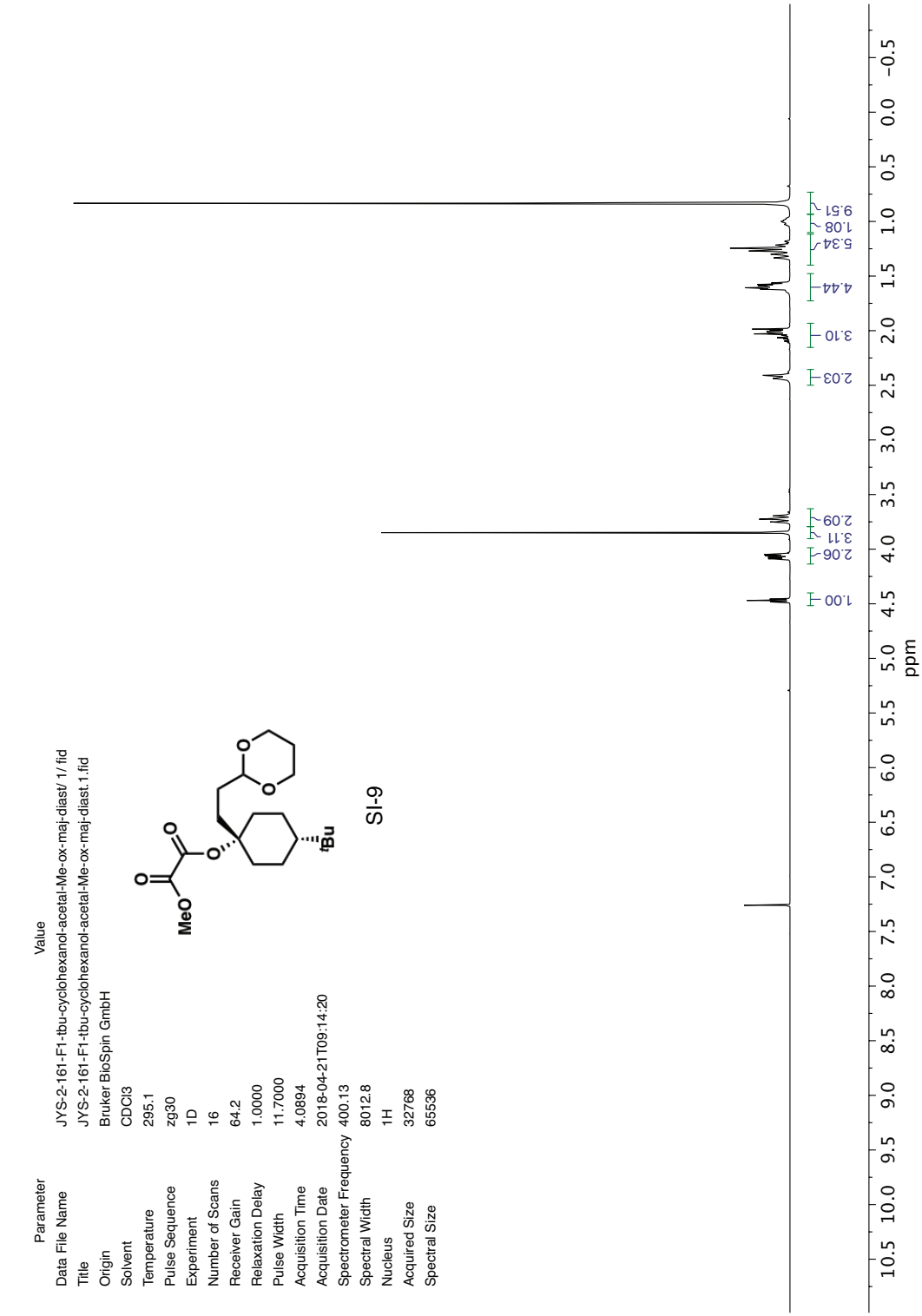
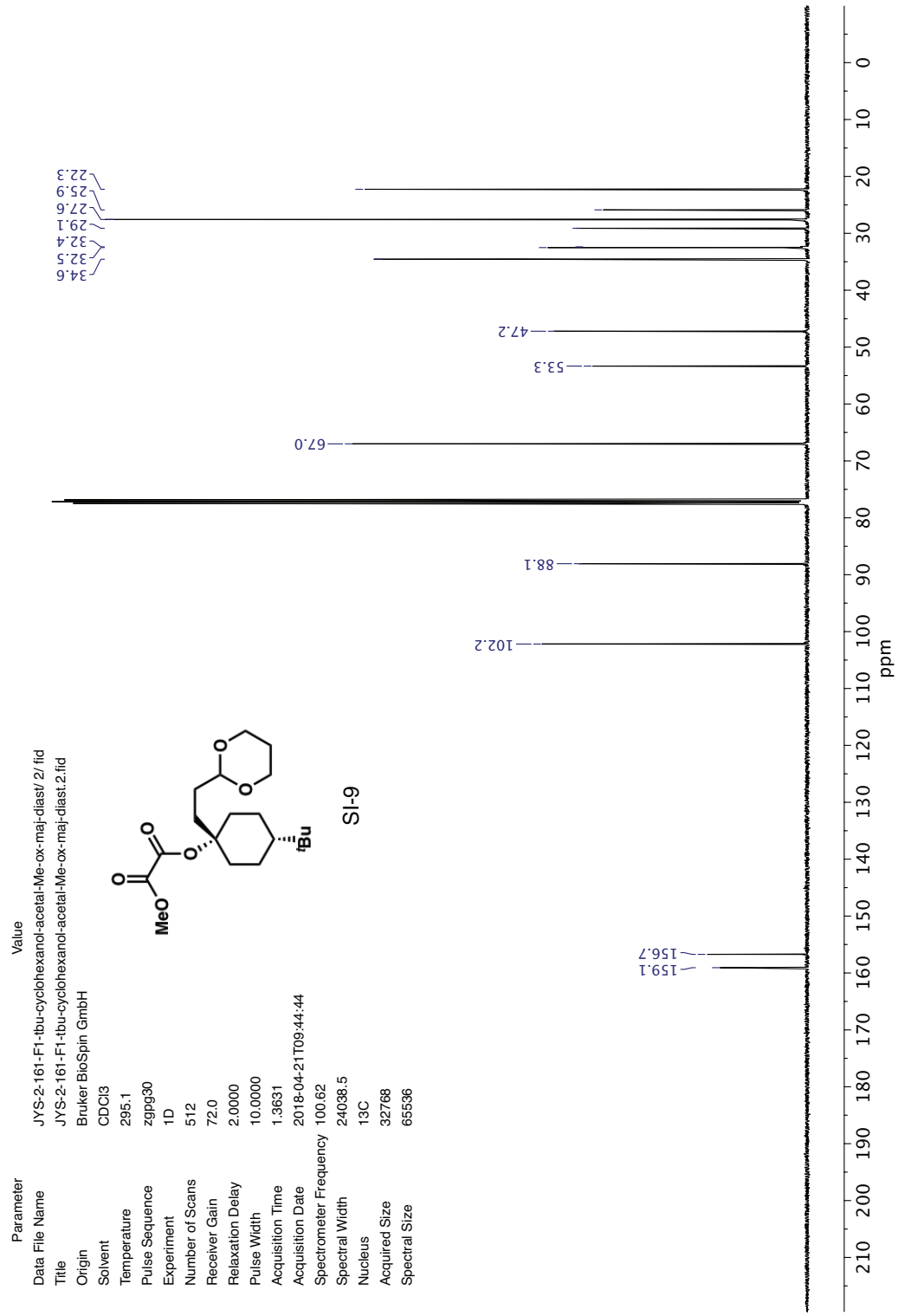
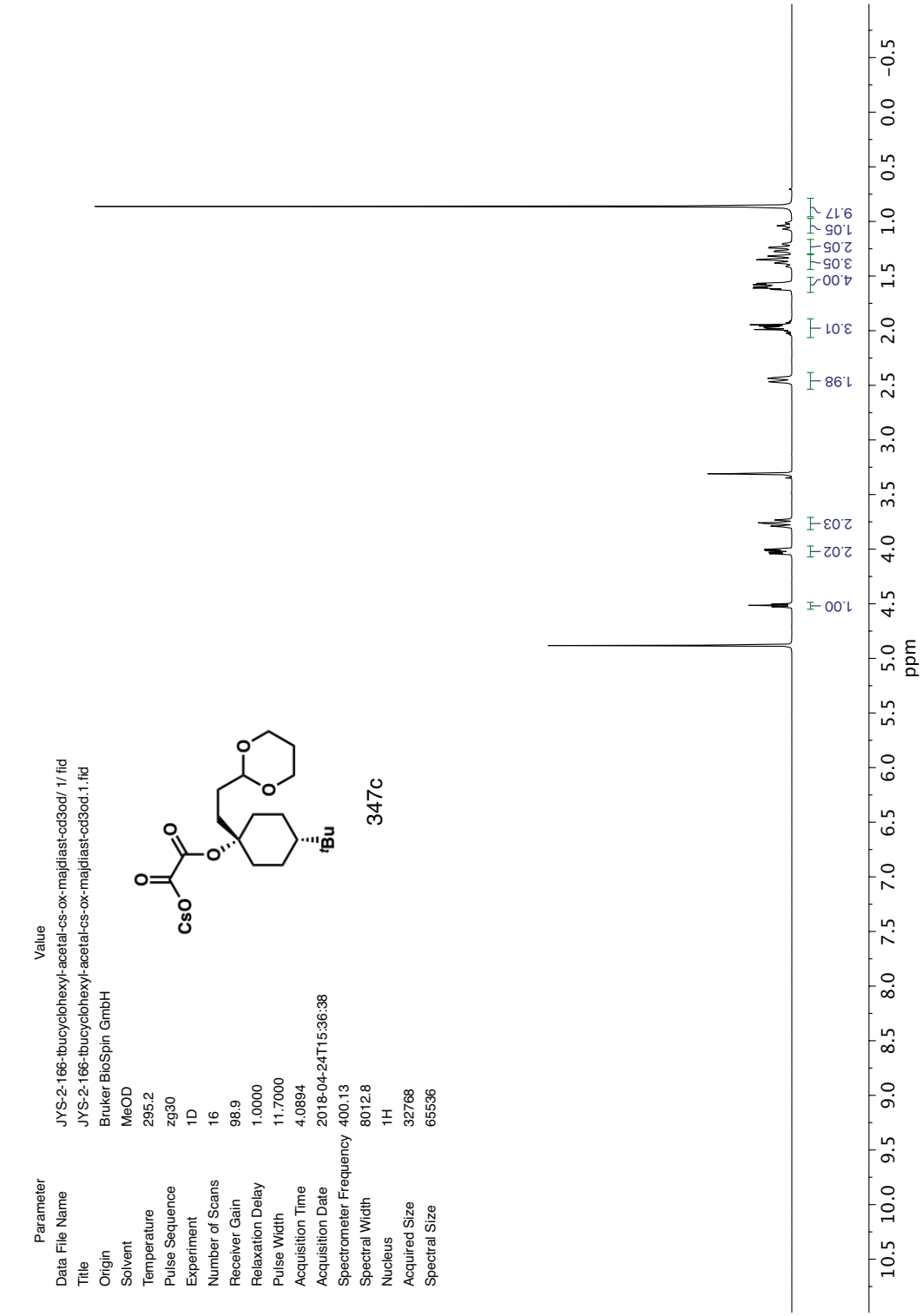
Data File Name JYS-2-130-F3-cyclohexyl-acetal-alcohol-minor-diast/ CARBON01.fid/ fid
Title CARBON01
Origin Varian
Solvent CDCl3
Temperature 25.0
Pulse Sequence s2pul
Experiment 1D
Number of Scans 256
Receiver Gain 30
Relaxation Delay 1.0000
Pulse Width 4.6125
Acquisition Time 1.0420
Acquisition Date 2018-04-18T17:37:24
Spectrometer Frequency 125.65
Spectral Width 31446.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
SI-8
HO
tBu
O
O
102.8
71.5
67.0
47.7
38.8
32.4
30.3
28.8
27.8
25.8
24.5
ppm


Parameter
Value
Data File Name JYS-2-161-F1-tbu-cyclohexanol-acetal-Me-ox-maj-diast/ 1/ fid
Title JYS-2-161-F1-tbu-cyclohexanol-acetal-Me-ox-maj-diast.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 64.2
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-04-21T09:14:20
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
MeO
tBu
SI-9
1.00
2.06
3.11
2.09
2.03
3.10
4.44
5.34
1.08
9.51
ppm


Parameter
Value
Data File Name JYS-2-161-F1-tbu-cyclohexanol-acetal-Me-ox-maj-diast/ 2/ fid
Title JYS-2-161-F1-tbu-cyclohexanol-acetal-Me-ox-maj-diast.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 512
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-04-21T09:44:44
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
MeO
tBu
SI-9
156.7
159.1
102.2
88.1
67.0
53.3
47.2
34.6
32.5
32.4
29.1
27.6
25.9
22.3
ppm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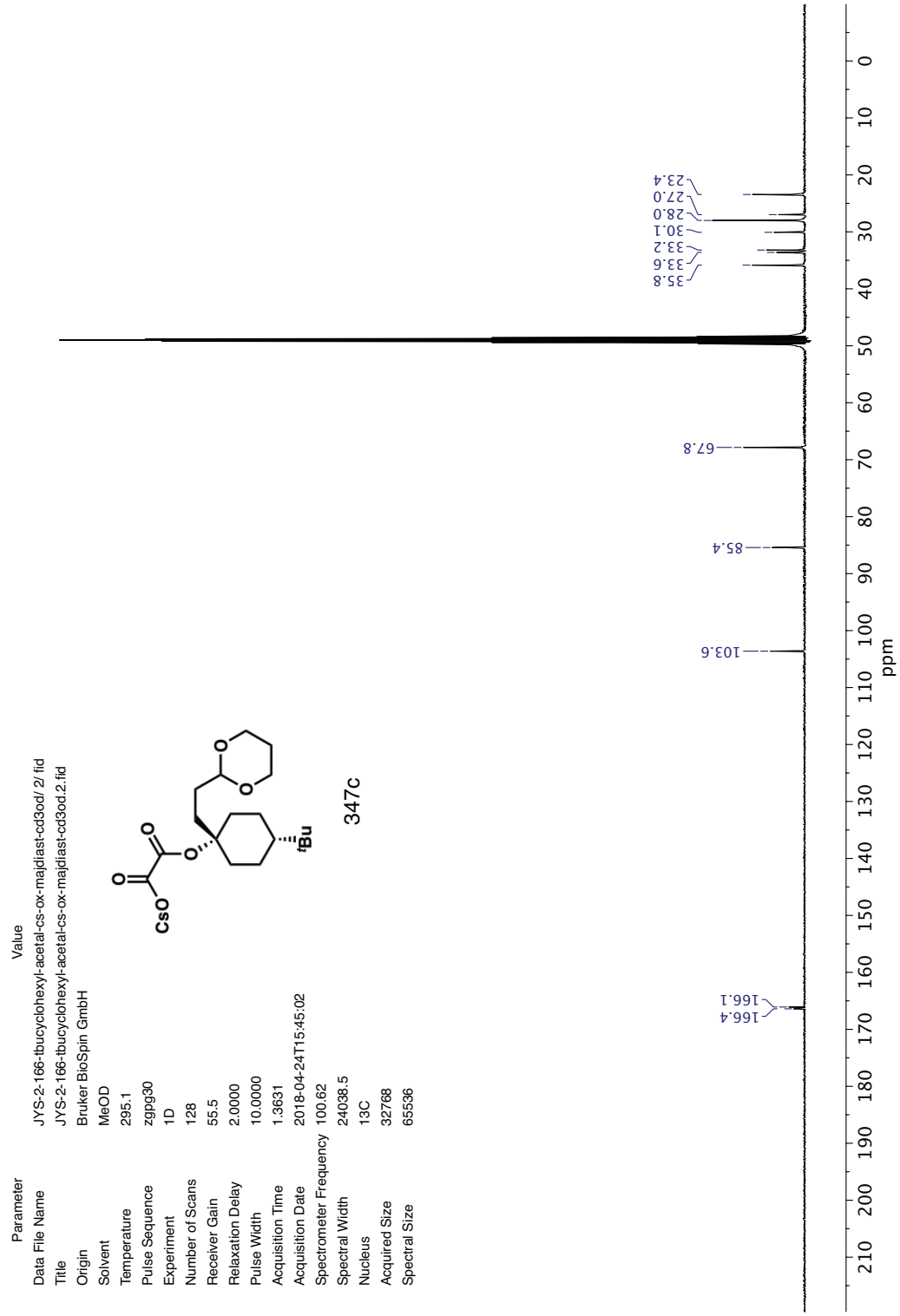
Data File Name
JYS-2-166-tbucyclohexyl-acetal-cs-ox-majdiast-cd3od/ 1/ fid
Title
JYS-2-166-tbucyclohexyl-acetal-cs-ox-majdiast-cd3od.1.fid
Origin
Bruker BioSpin GmbH
Solvent
MeOD
Temperature
295.2
Pulse Sequence
zg30
Experiment
1D
Number of Scans
16
Receiver Gain
98.9
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-04-24T15:36:38
Spectrometer Frequency
400.13
Spectral Width
8012.8
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
CsO
O
O
O
O
O
tBu
347c
1.00
2.02
2.03
1.98
3.01
4.00
3.05
2.05
1.05
9.17
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
ppm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Data File Name
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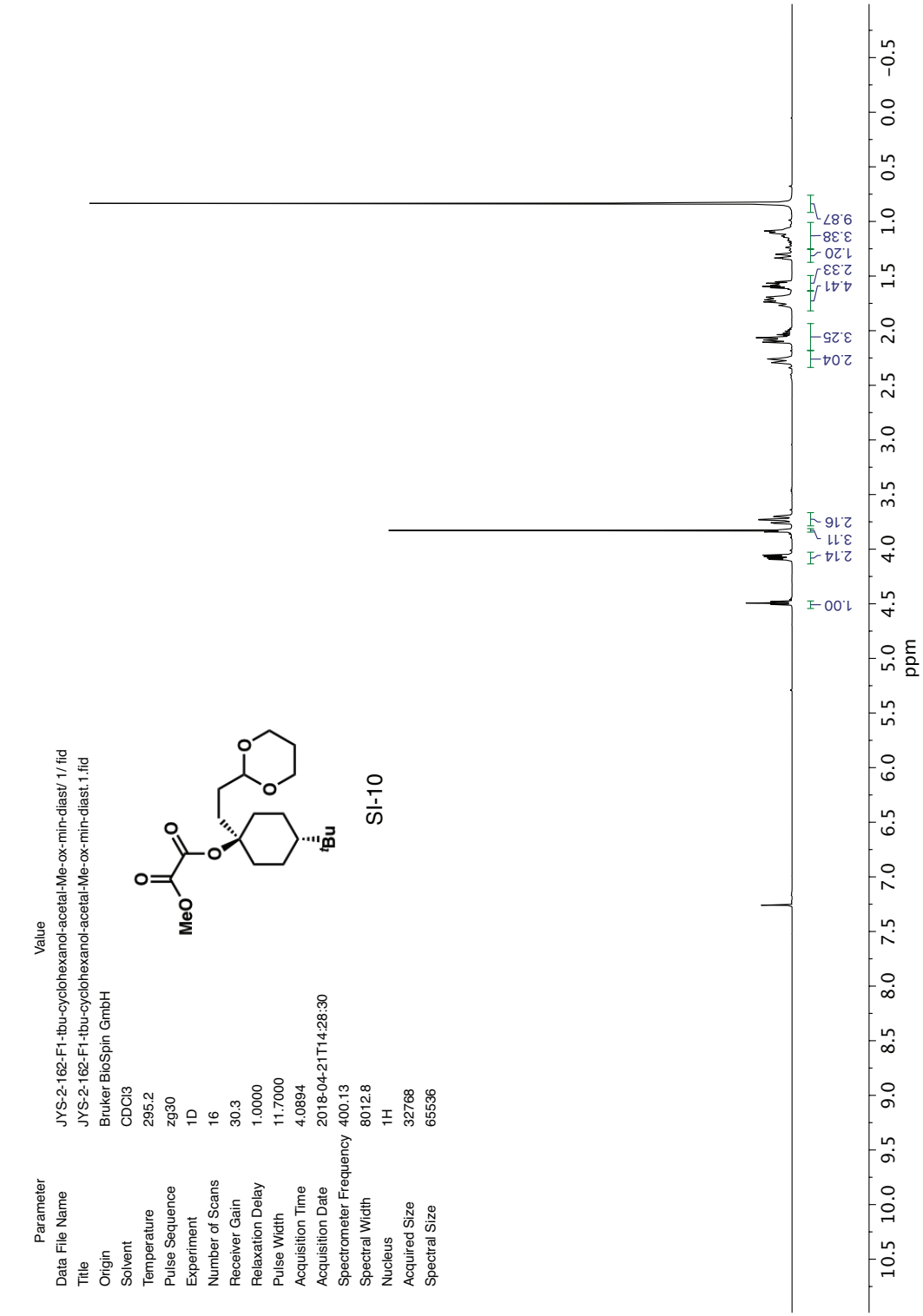
Title
JYS-2-166-tbucyclohexyl-acetal-cs-ox-majdiast-cd3od.2.fid
Origin
Bruker BioSpin GmbH
Solvent
MeOD
Temperature
295.1
Pulse Sequence
zgpg30
Experiment
1D
Number of Scans
128
Receiver Gain
55.5
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-04-24T15:45:02
Spectrometer Frequency
100.62
Spectral Width
24038.5
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
CsO
O
O
O
O
O
tBu
347c
166.4
166.1
103.6
85.4
67.8
35.8
33.6
33.2
30.1
28.0
27.0
23.4
ppm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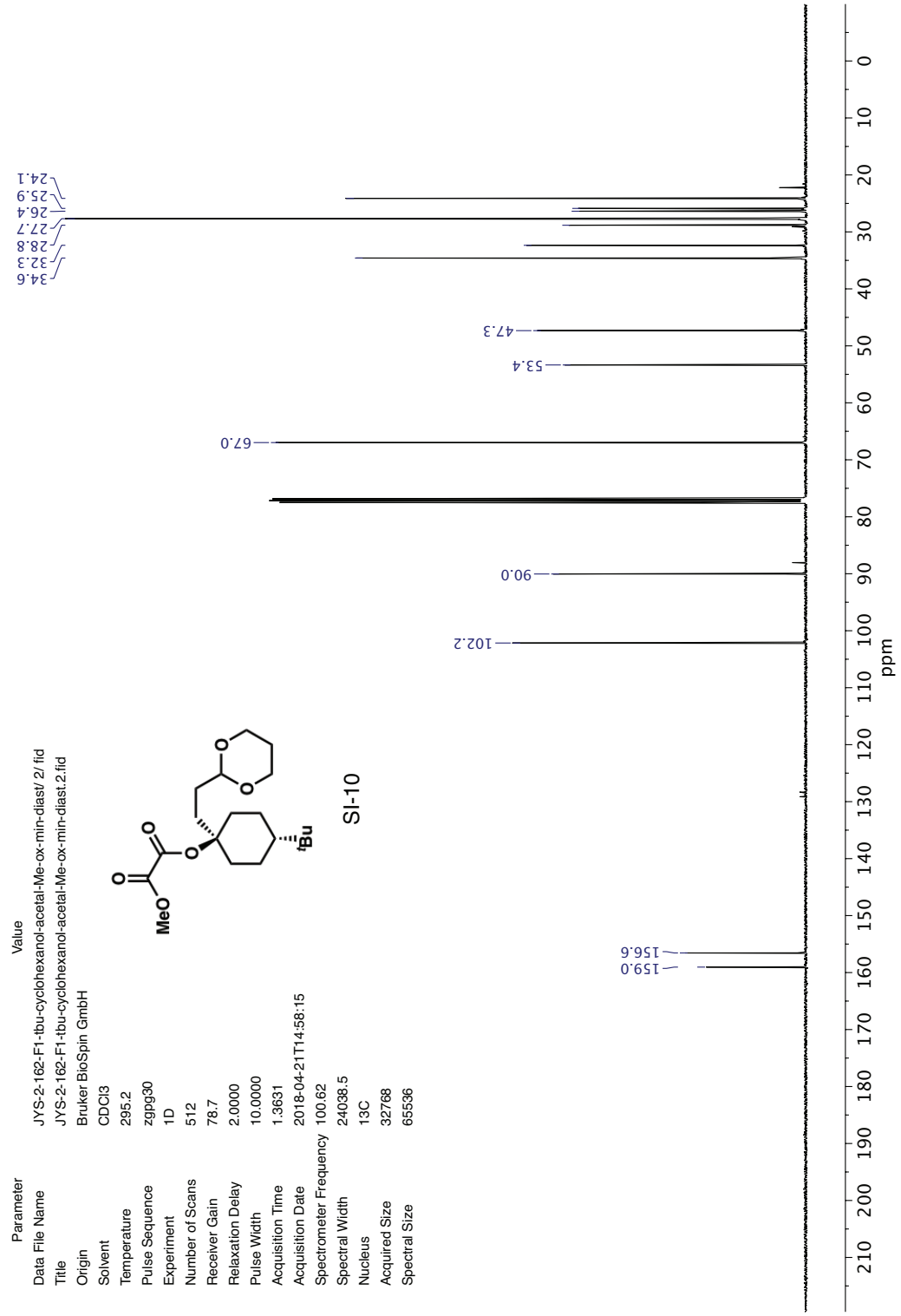
Data File Name JYS-2-162-F1-tbu-cyclohexanol-acetal-Me-ox-min-diast/ 1/ fid
Title JYS-2-162-F1-tbu-cyclohexanol-acetal-Me-ox-min-diast.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 30.3
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-04-21T14:28:30
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
MeO
tBu
SI-10
1.00
2.14
3.11
2.16
2.04
3.25
4.41
2.33
1.20
3.38
9.87
ppm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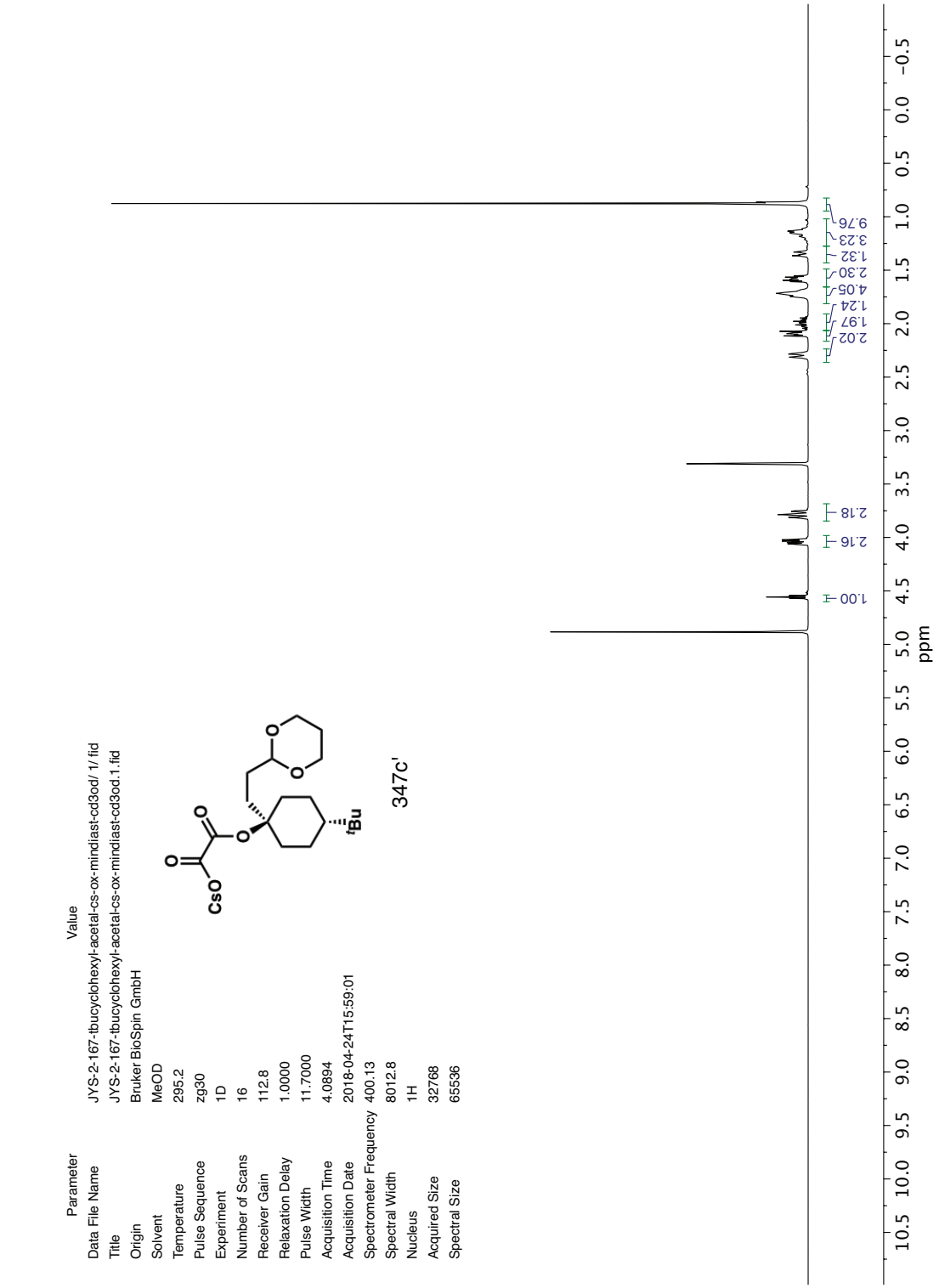
Data File Name JYS-2-162-F1-tbu-cyclohexanol-acetal-Me-ox-min-diast/ 2/ fid
Title JYS-2-162-F1-tbu-cyclohexanol-acetal-Me-ox-min-diast.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 512
Receiver Gain 78.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-04-21T14:58:15
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
MeO
tBu
SI-10
159.0
156.6
102.2
90.0
67.0
53.4
47.3
34.6
32.3
28.8
27.7
26.4
25.9
24.1
ppm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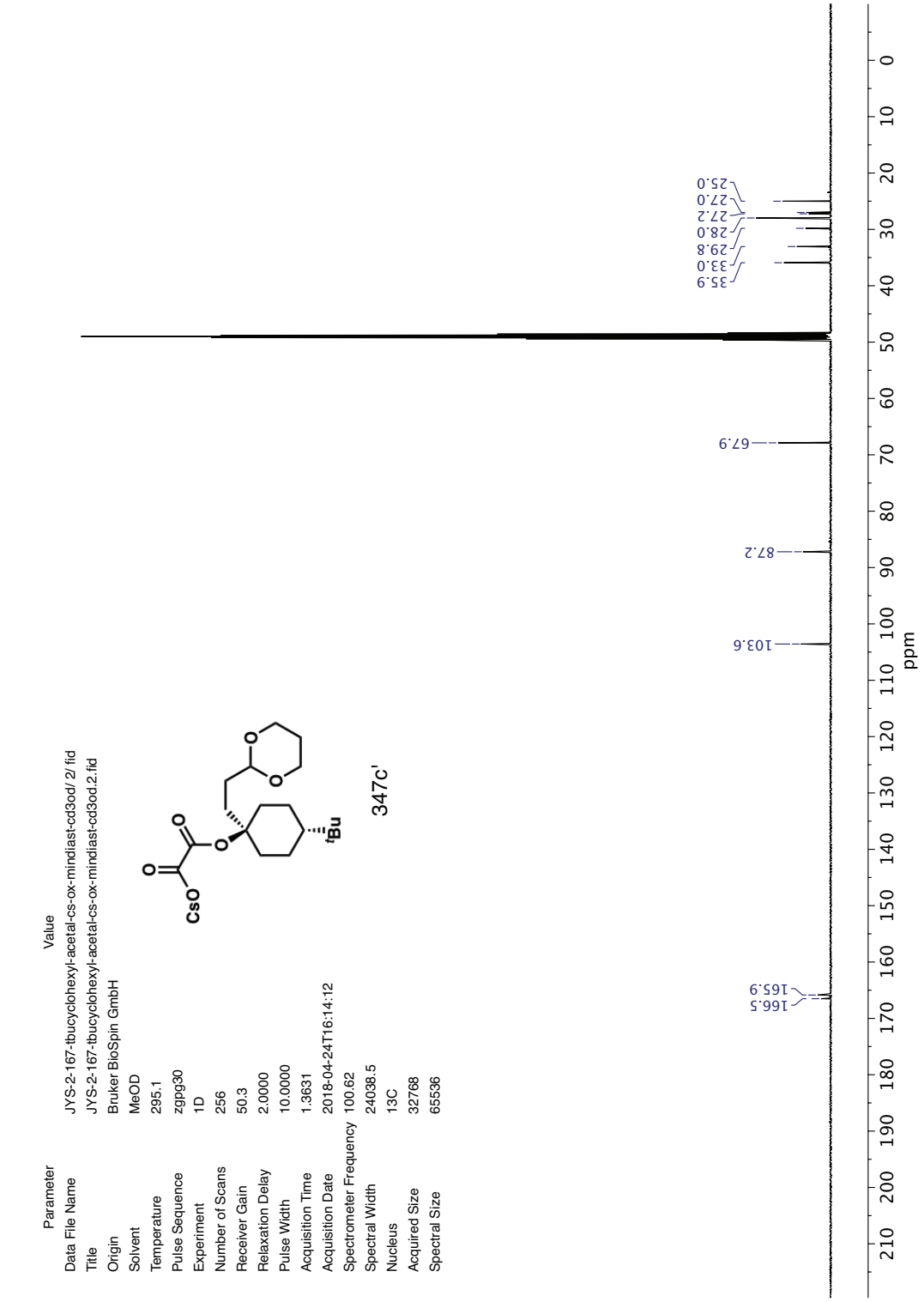
Data File Name JYS-2-167-tbucyclohexyl-acetal-cs-ox-mindiast-cd3od/ 1/ fid
Title JYS-2-167-tbucyclohexyl-acetal-cs-ox-mindiast-cd3od.1.fid
Origin Bruker BioSpin GmbH
Solvent MeOD
Temperature 295.2
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 112.8
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-04-24T15:59:01
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
CsO
tBu
347c'
1.00
2.16
2.18
2.02
1.97
1.24
4.05
2.30
1.32
3.23
9.76
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
ppm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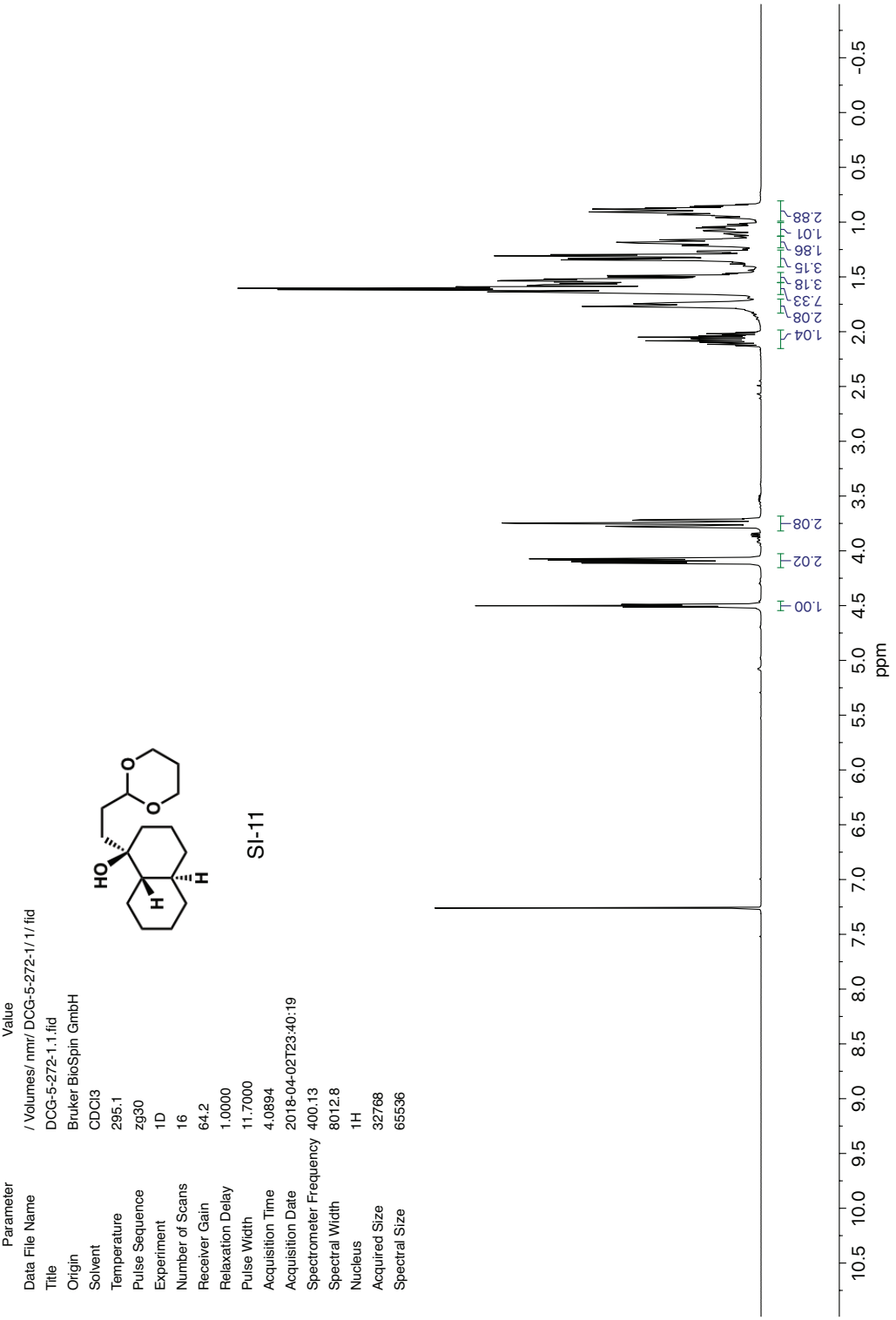
Value
Data File Name JYS-2-167-tbucyclohexyl-acetal-cs-ox-mindiast-cd3od/ 2/ fid
Title JYS-2-167-tbucyclohexyl-acetal-cs-ox-mindiast-cd3od.2.fid
Origin Bruker BioSpin GmbH
Solvent MeOD
Temperature 295.1
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 50.3
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-04-24T16:14:12
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
CsO
tBu
347c'
166.5
165.9
103.6
87.2
67.9
35.9
33.0
29.8
28.0
27.2
27.0
25.0
ppm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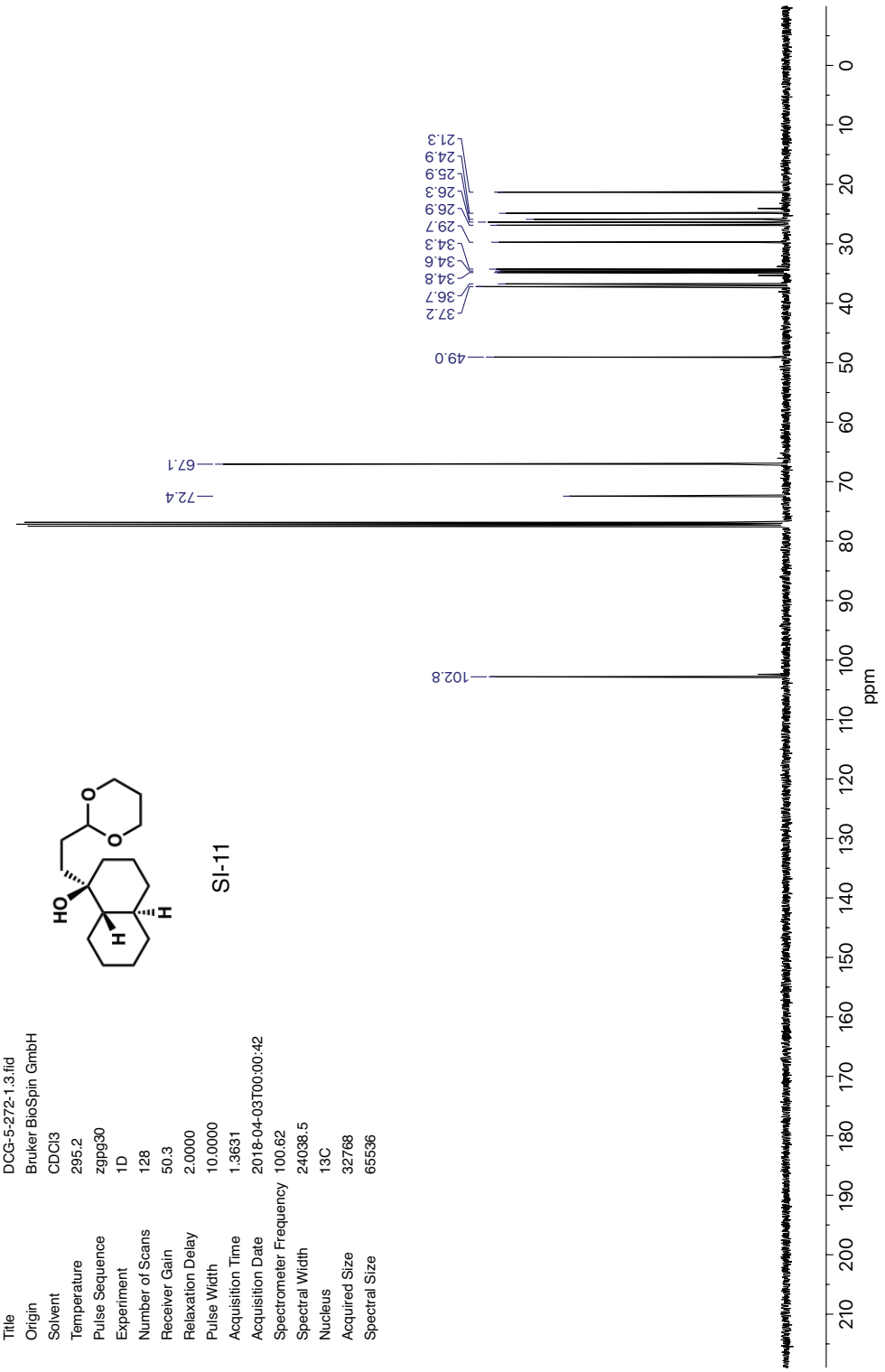
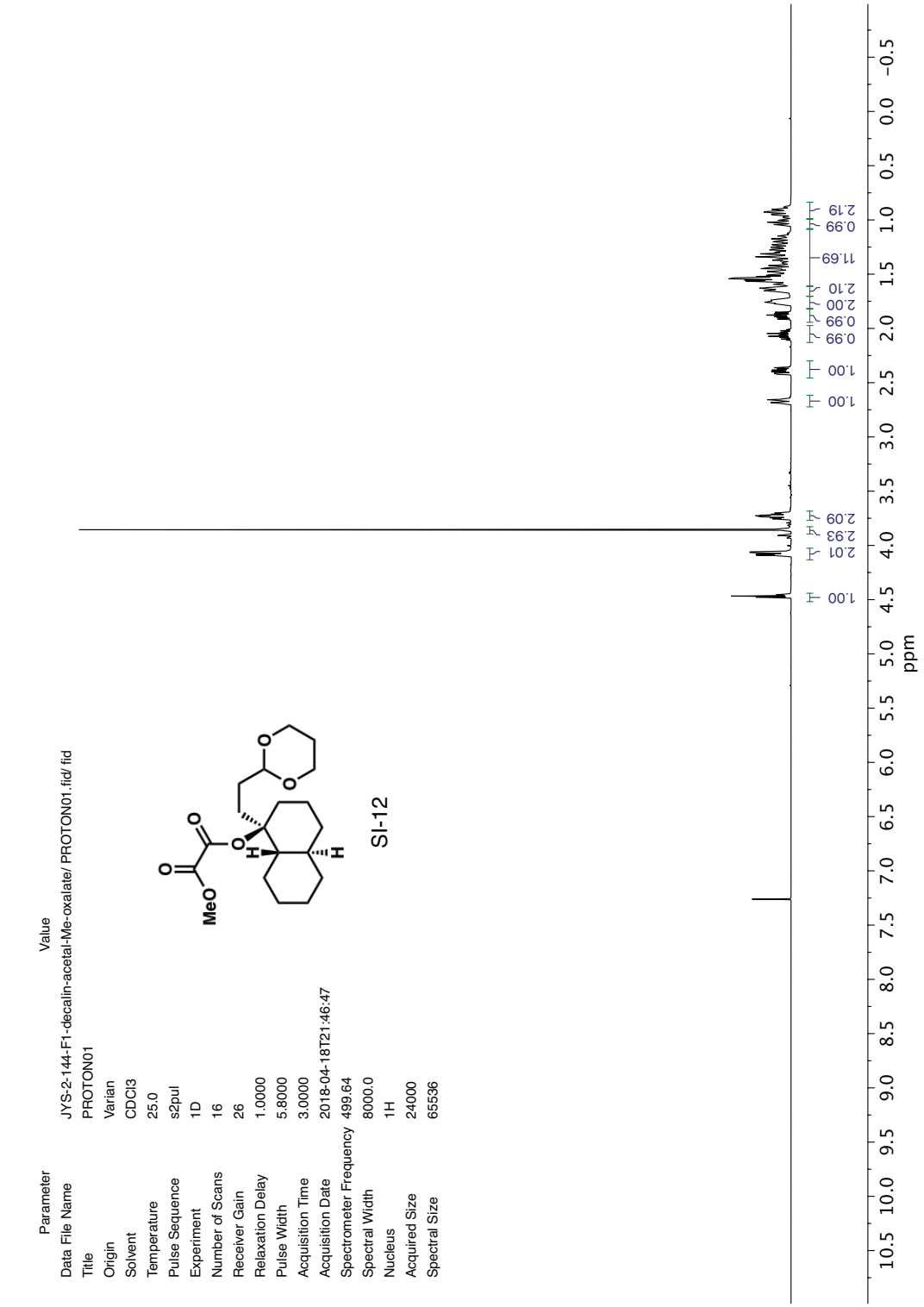
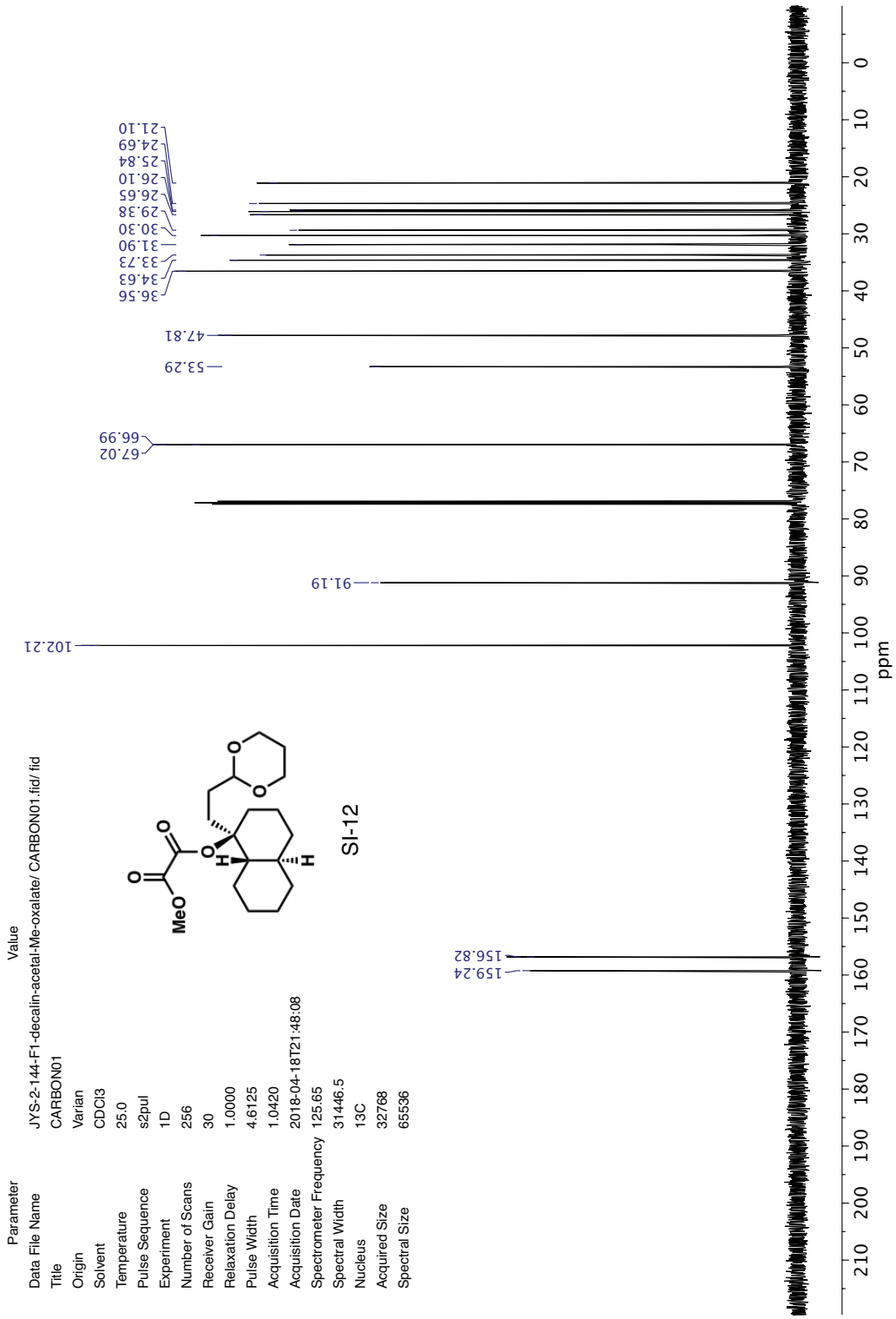
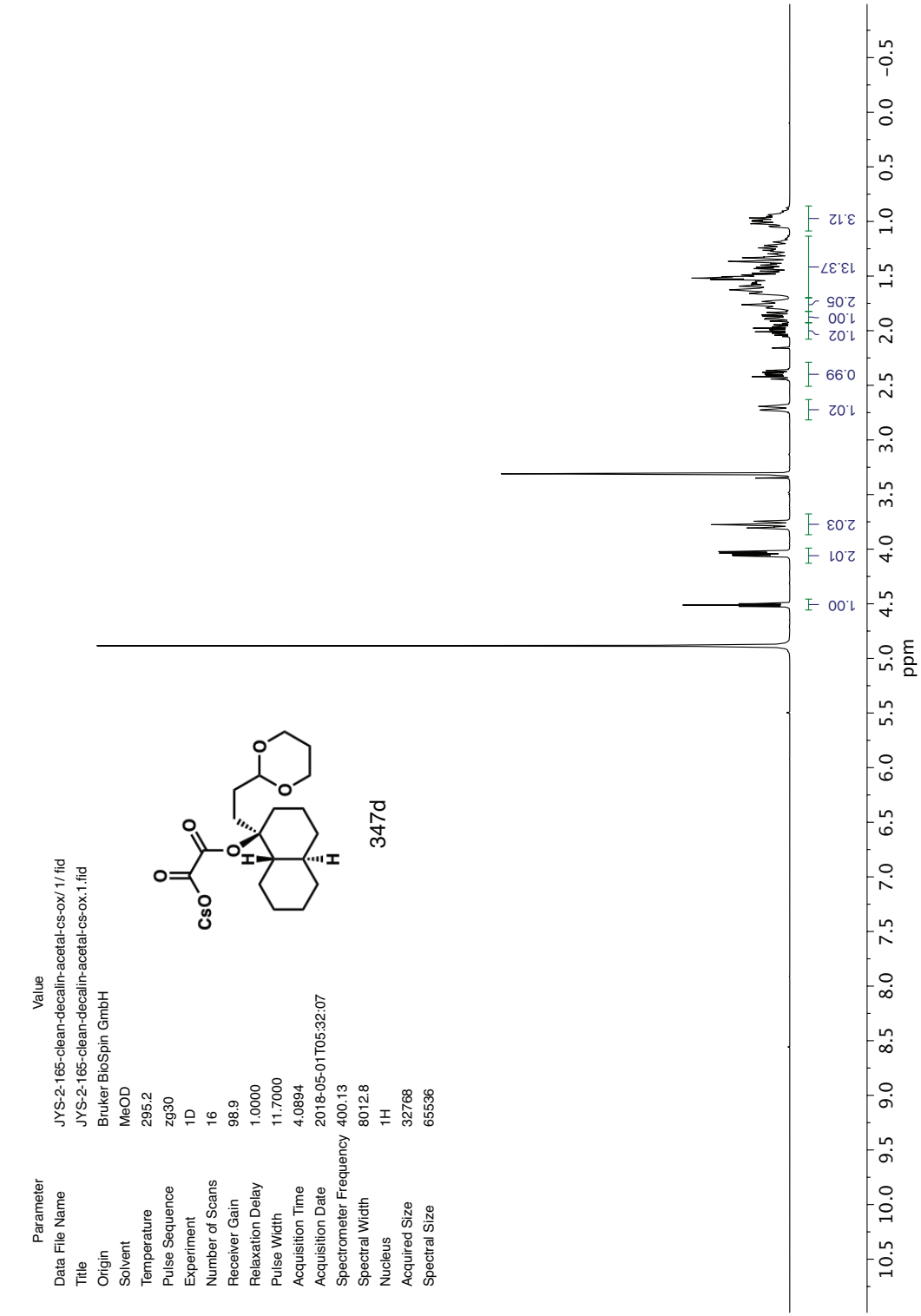
Data File Name / Volumes/ nmr/ DCG-5-272-1/1/ fid
Title DCG-5-272-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 64.2
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-04-02T23:40:19
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
SI-11
HO
H
H
O
O
1.00
2.02
2.08
1.04
2.08
7.33
3.18
3.15
1.86
1.01
2.88
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm


Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-272-1/3/ fid
Title DCG-5-272-1.3.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 128
Receiver Gain 50.3
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-04-03T00:00:42
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
SI-11
102.8
72.4
67.1
49.0
37.2
36.7
34.8
34.6
34.3
29.7
26.9
26.3
25.9
24.9
21.3
ppm


Parameter
Value
Data File Name
JYS-2-144-F1-decalin-acetal-Me-oxalate/ PROTON01.fid/ fid
Title
PROTON01
Origin
Varian
Solvent
CDCl3
Temperature
25.0
Pulse Sequence
s2pul
Experiment
1D
Number of Scans
16
Receiver Gain
26
Relaxation Delay
1.0000
Pulse Width
5.8000
Acquisition Time
3.0000
Acquisition Date
2018-04-18T21:46:47
Spectrometer Frequency
499.64
Spectral Width
8000.0
Nucleus
1H
Acquired Size
24000
Spectral Size
65536
MeO
SI-12
1.00
2.01
2.93
2.09
1.00
1.00
0.99
0.99
2.00
2.10
11.69
0.99
2.19
ppm


Parameter Value
Data File Name JYS-2-144-F1-decalin-acetal-Me-oxalate/ CARBON01.fid/ fid
Title CARBON01
Origin Varian
Solvent CDCl3
Temperature 25.0
Pulse Sequence s2pul
Experiment 1D
Number of Scans 256
Receiver Gain 30
Relaxation Delay 1.0000
Pulse Width 4.6125
Acquisition Time 1.0420
Acquisition Date 2018-04-18T21:48:08
Spectrometer Frequency 125.65
Spectral Width 31446.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
MeO
SI-12
102.21
91.19
67.02
66.99
53.29
47.81
36.56
34.63
33.73
31.90
30.30
29.38
26.65
26.10
25.84
24.69
21.10
159.24
156.82
ppm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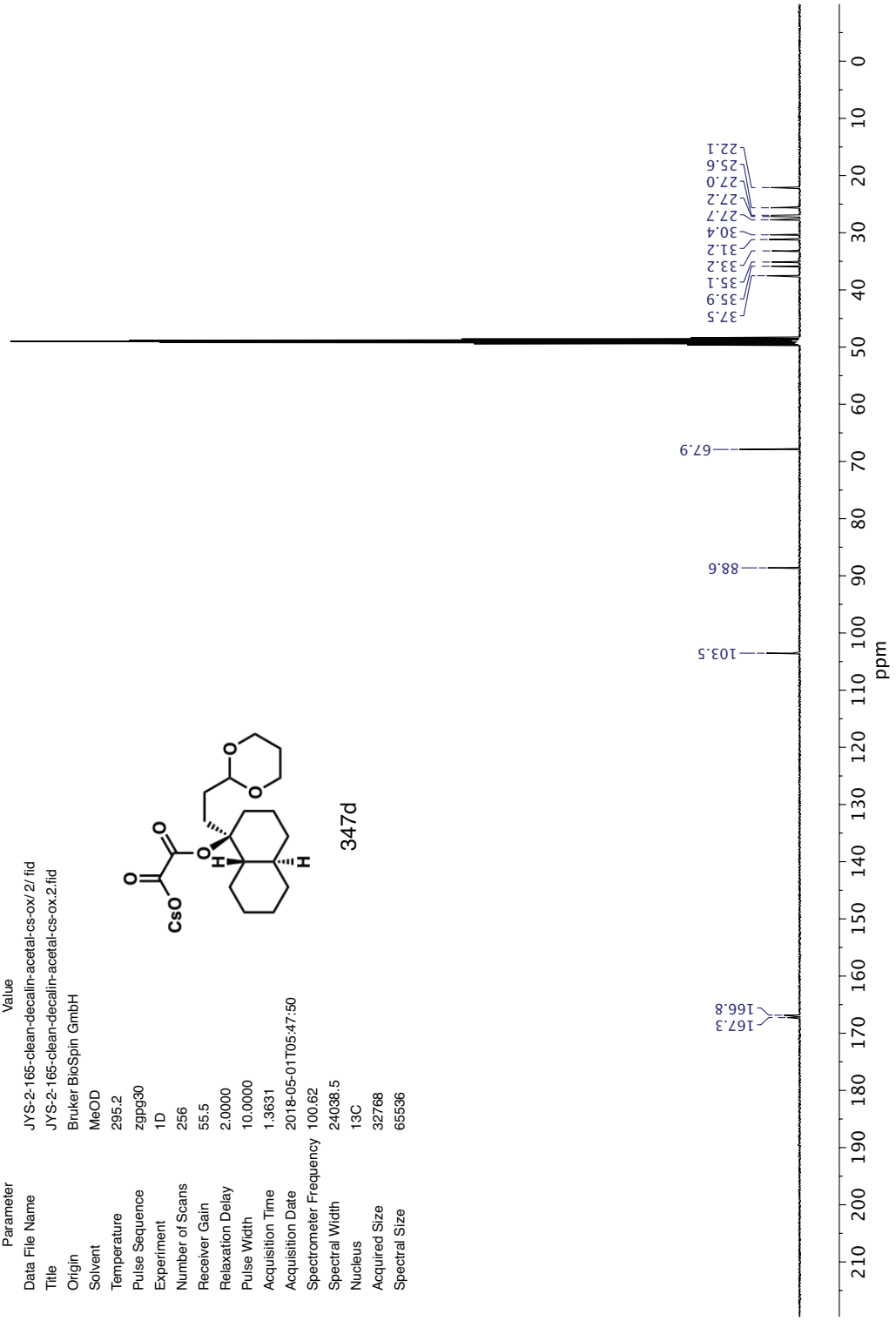
Value
Data File Name
JYS-2-165-clean-decalin-acetal-cs-ox/1/fid
Title
JYS-2-165-clean-decalin-acetal-cs-ox.1.fid
Origin
Bruker BioSpin GmbH
Solvent
MeOD
Temperature
295.2
Pulse Sequence
zg30
Experiment
1D
Number of Scans
16
Receiver Gain
98.9
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-05-01T05:32:07
Spectrometer Frequency
400.13
Spectral Width
8012.8
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
CsO
347d
1.00
2.01
2.03
1.02
0.99
1.02
1.00
2.05
13.37
3.12
ppm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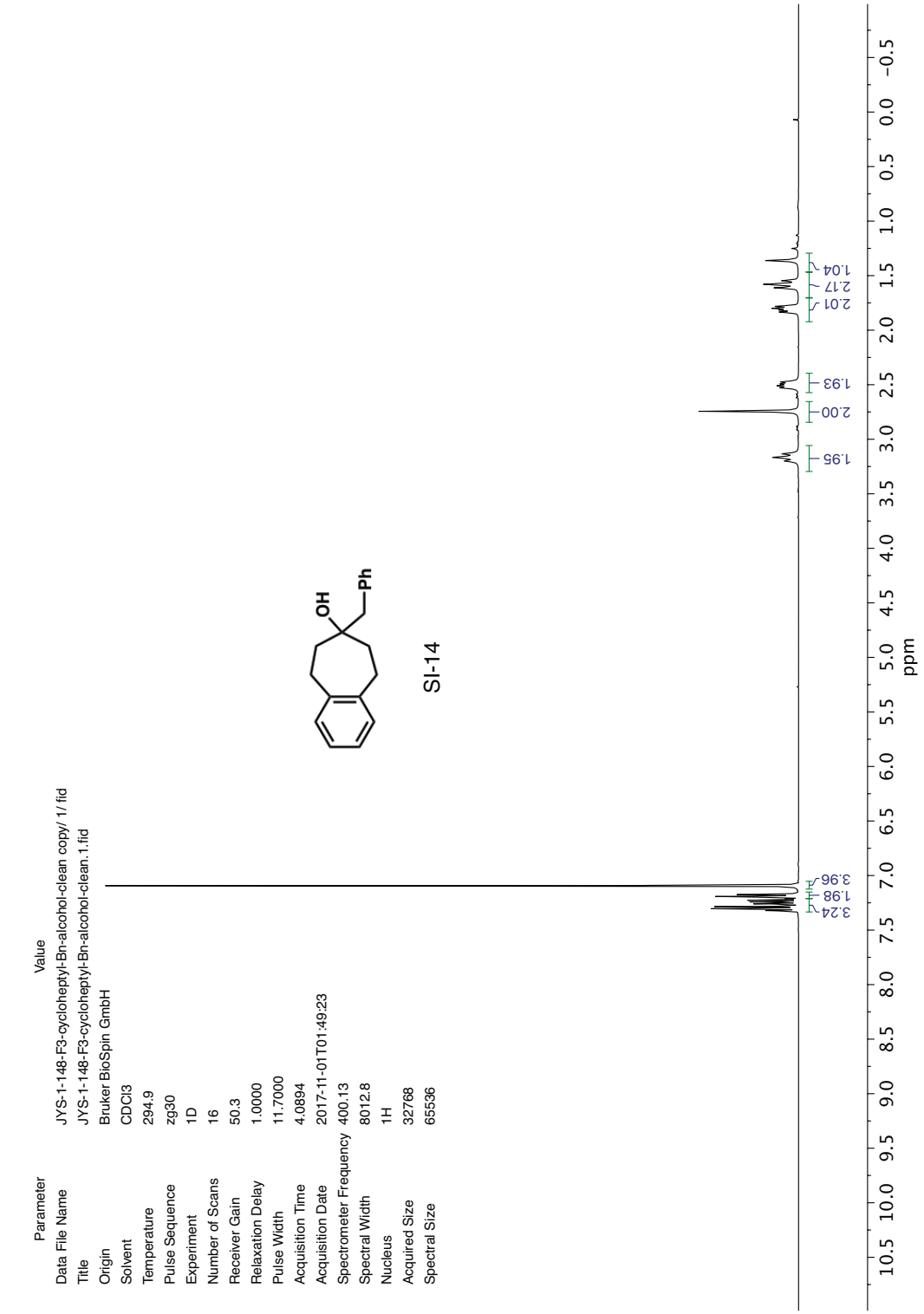
Value
Data File Name
JYS-2-165-clean-decalin-acetal-cs-ox/2/fid
Title
JYS-2-165-clean-decalin-acetal-cs-ox.2.fid
Origin
Bruker BioSpin GmbH
Solvent
MeOD
Temperature
295.2
Pulse Sequence
zgpg30
Experiment
1D
Number of Scans
256
Receiver Gain
55.5
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-05-01T05:47:50
Spectrometer Frequency
100.62
Spectral Width
24038.5
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
CsO
347d
167.3
166.8
103.5
88.6
67.9
37.5
35.9
35.1
33.2
31.2
30.4
27.7
27.2
27.0
25.6
22.1
ppm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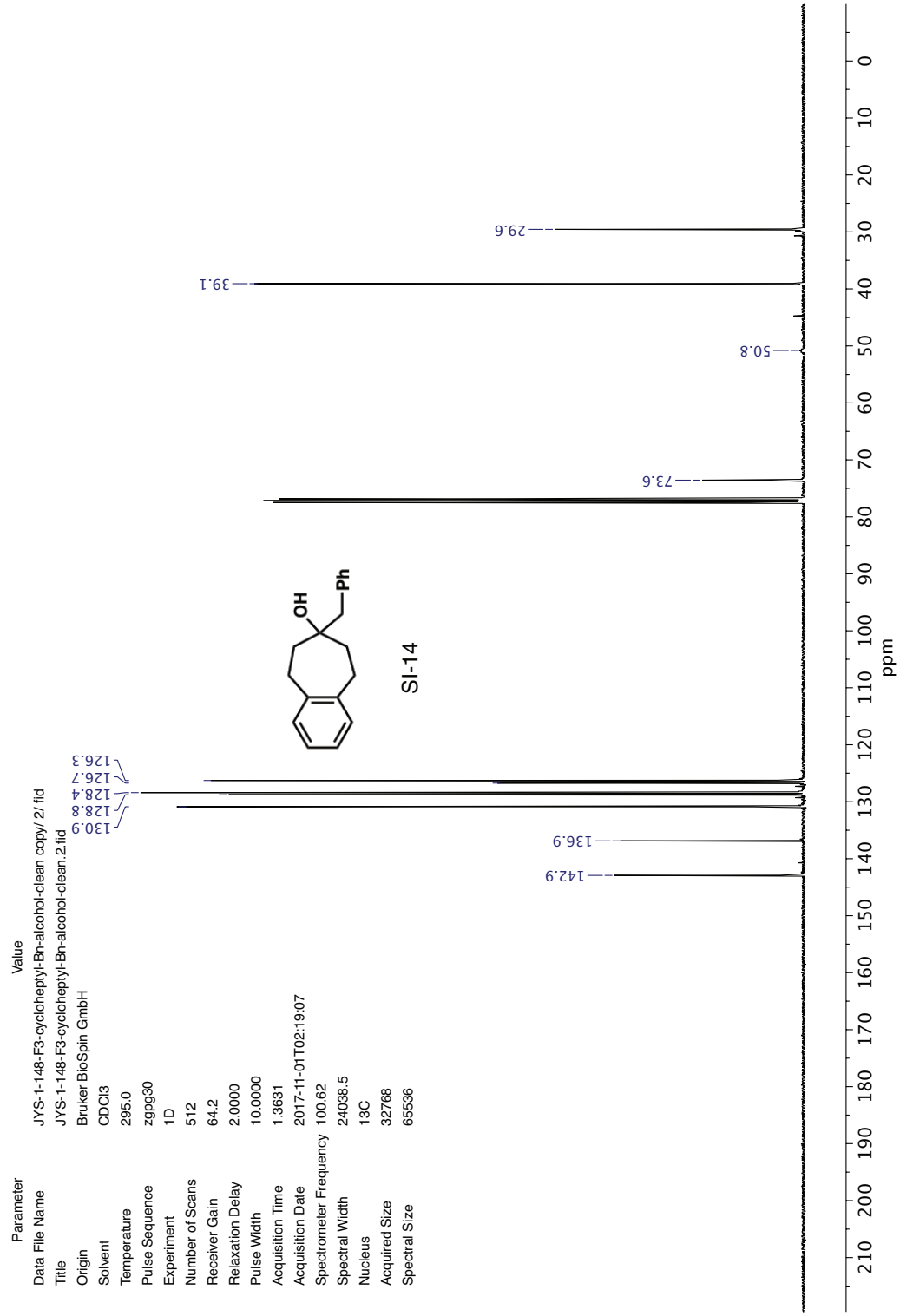
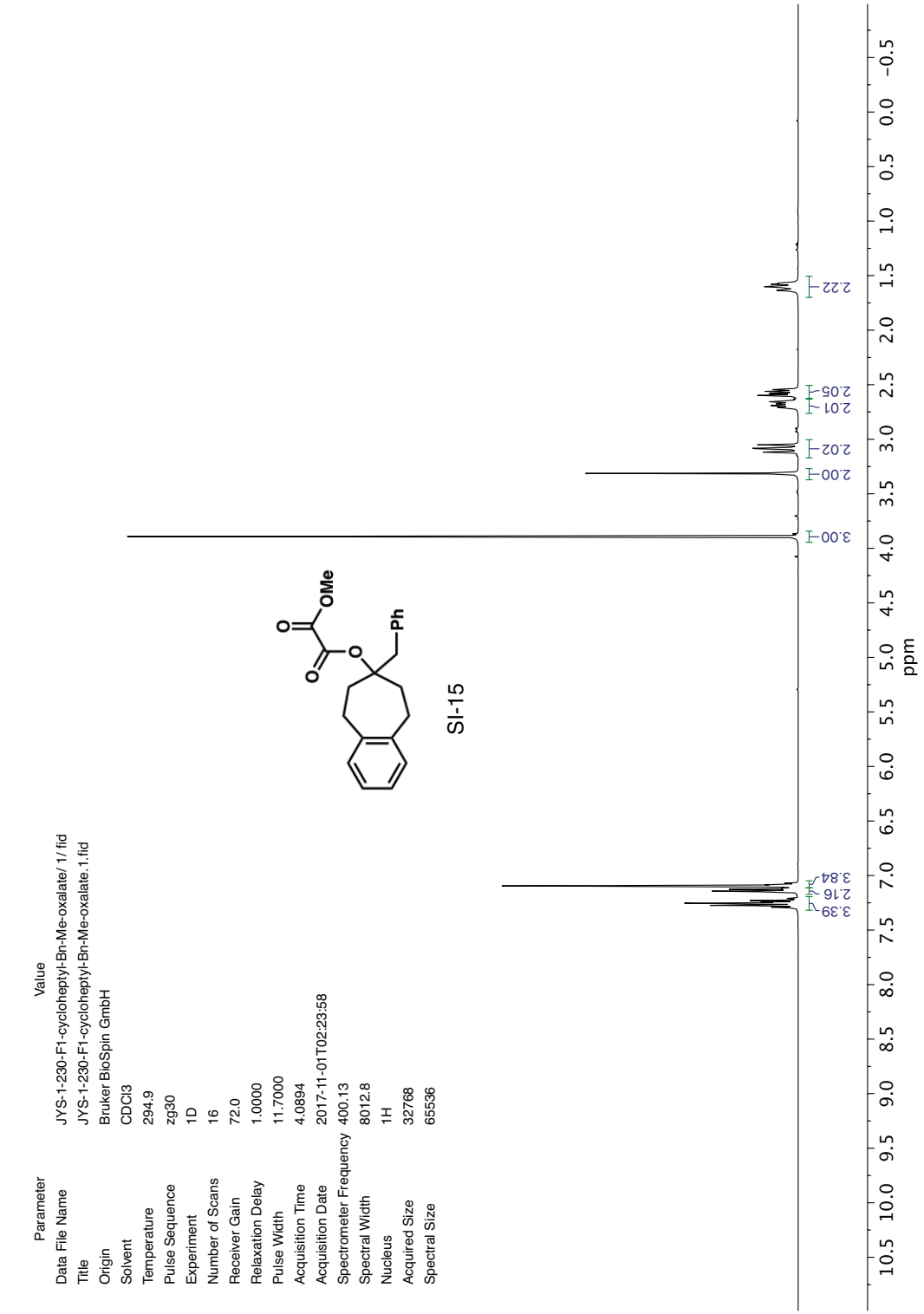
Data File Name JYS-1-148-F3-cycloheptyl-Bn-alcohol-clean copy/ 1/ fid
Title JYS-1-148-F3-cycloheptyl-Bn-alcohol-clean.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 50.3
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-11-01T01:49:23
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
OH
Ph
SI-14
3.24
1.98
3.96
1.95
2.00
1.93
2.01
2.17
1.04
ppm


Parameter
Value
Data File Name JYS-1-148-F3-cycloheptyl-Bn-alcohol-clean copy/ 2/ fid
Title JYS-1-148-F3-cycloheptyl-Bn-alcohol-clean.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 512
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-11-01T02:19:07
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OH
Ph
SI-14
142.9
136.9
130.9
128.8
128.4
126.7
126.3
73.6
50.8
39.1
29.6
ppm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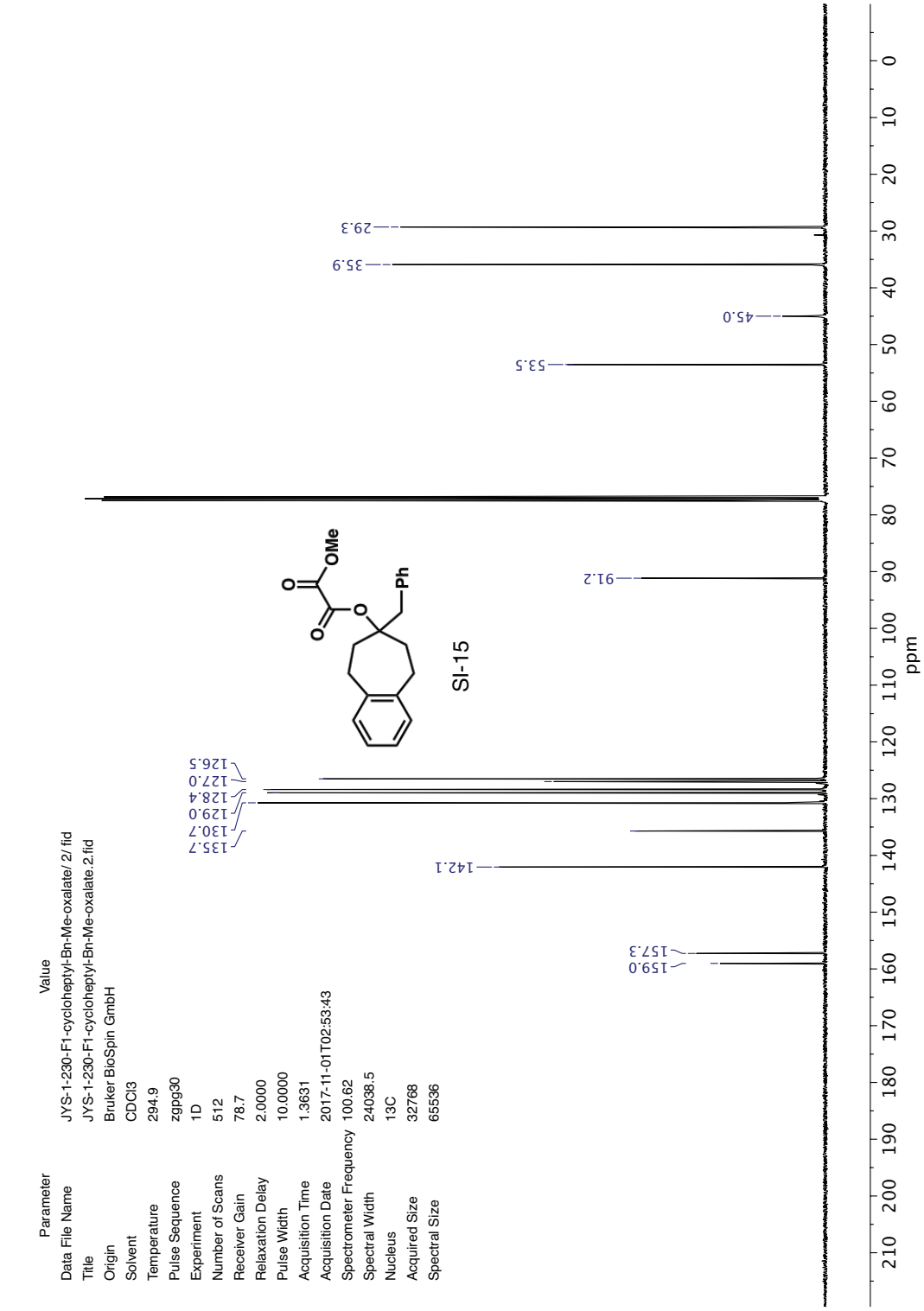
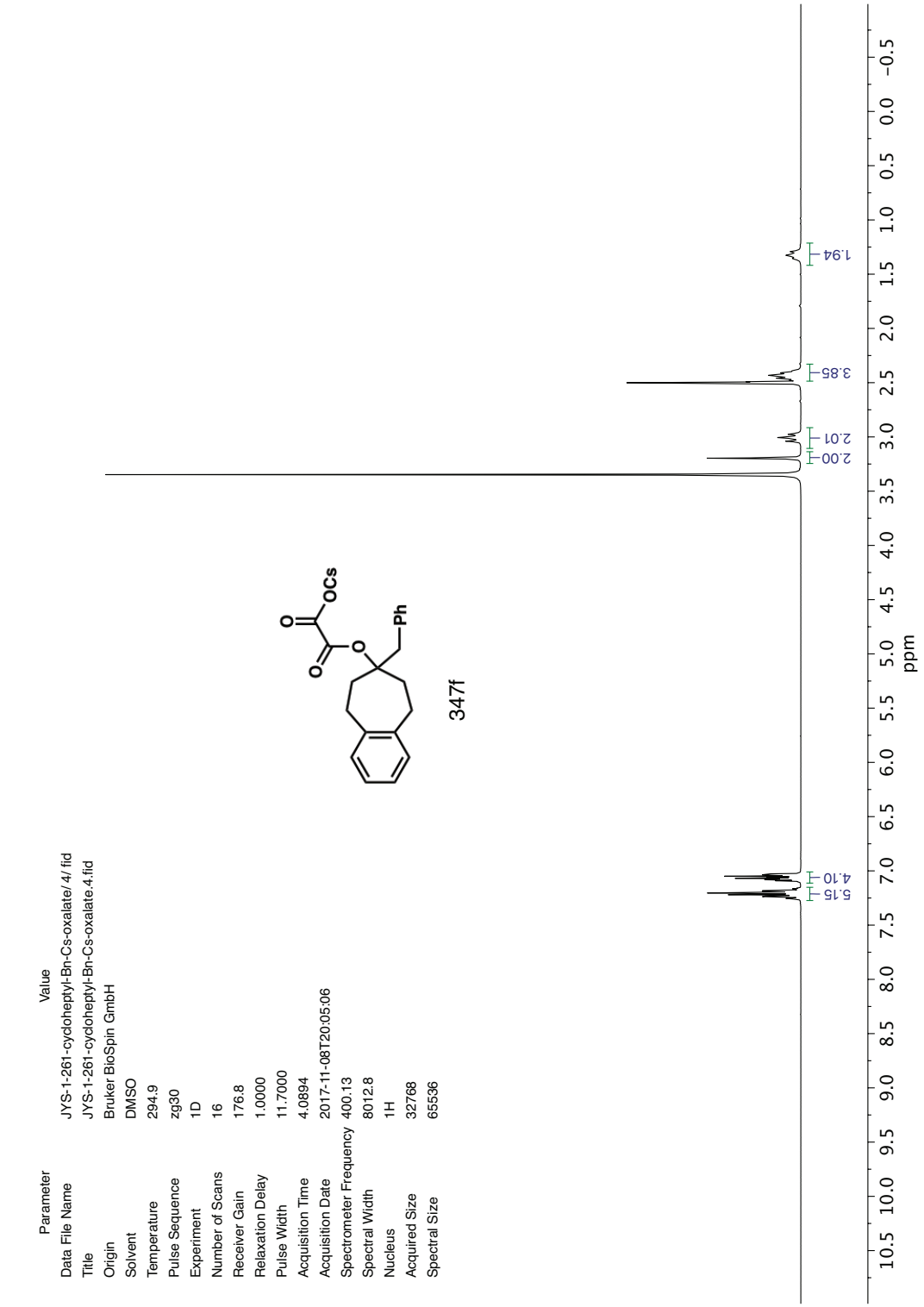
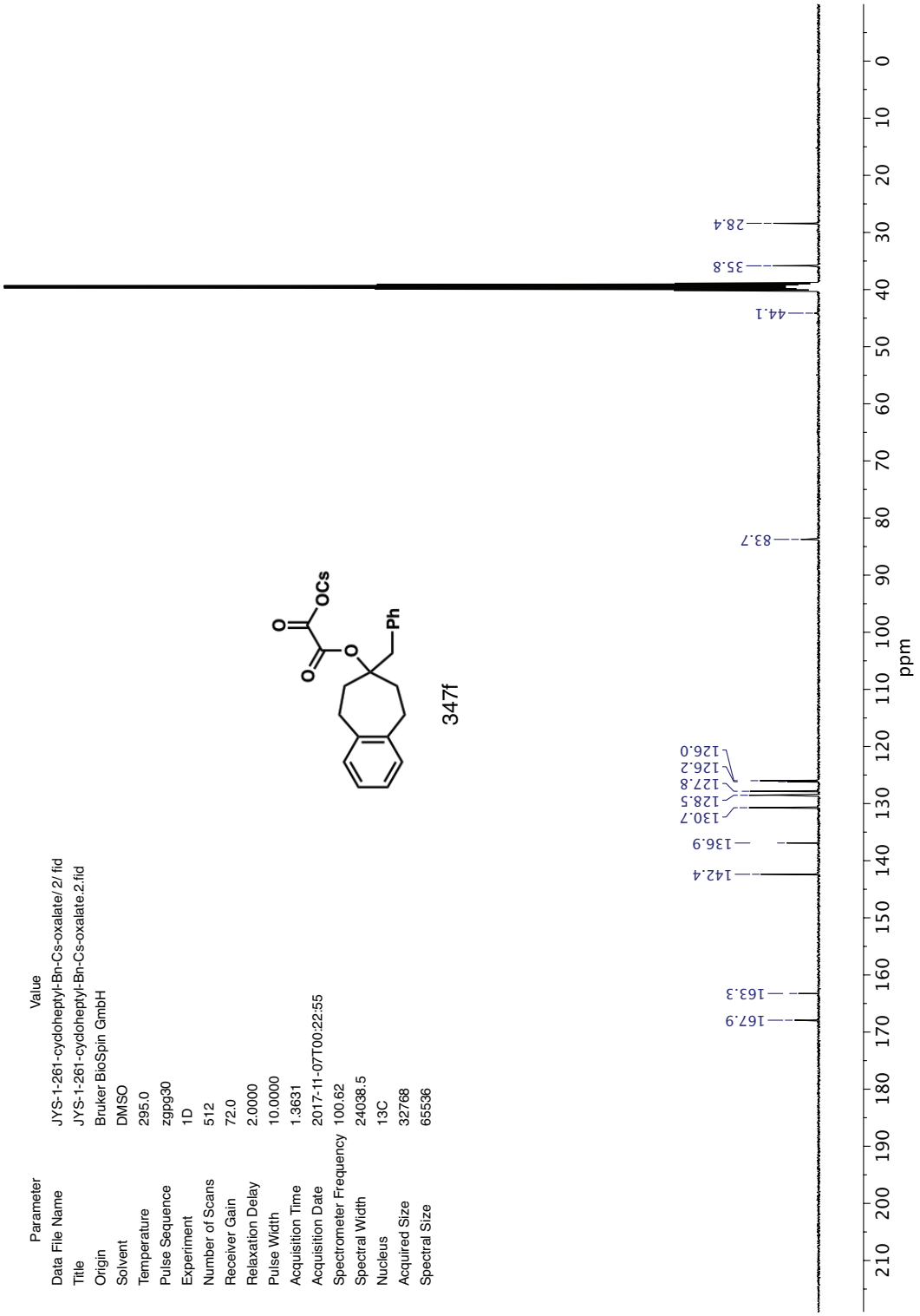
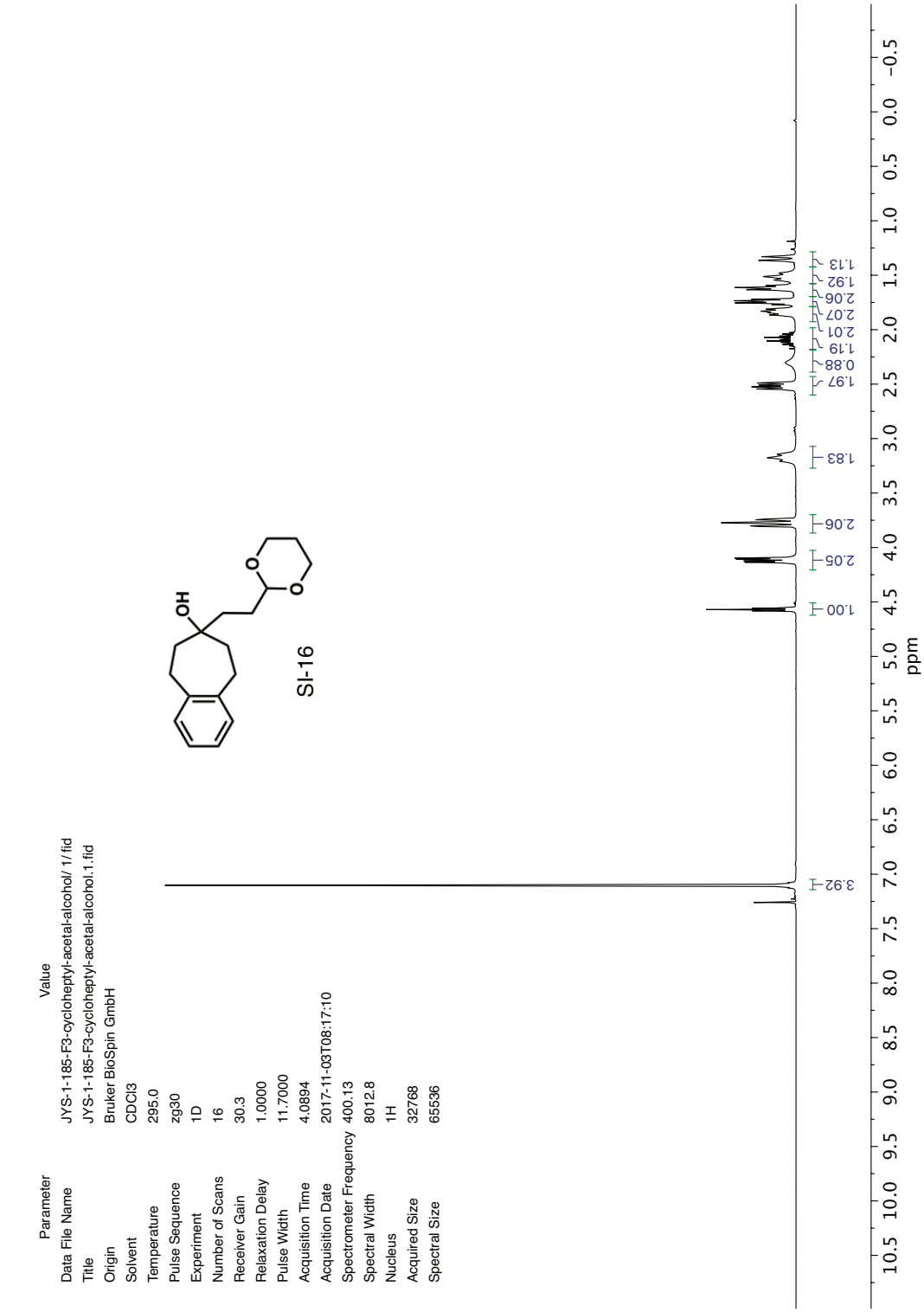
Data File Name
JYS-1-230-F1-cycloheptyl-Bn-Me-oxalate/ 1/ fid
Title
JYS-1-230-F1-cycloheptyl-Bn-Me-oxalate.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zg30
Experiment
1D
Number of Scans
16
Receiver Gain
72.0
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2017-11-01T02:23:58
Spectrometer Frequency
400.13
Spectral Width
8012.8
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
OMe
Ph
SI-15
3.39
2.16
3.84
3.00
2.00
2.02
2.01
2.05
2.22
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
ppm


Parameter
Value
Data File Name
JYS-1-230-F1-cycloheptyl-Bn-Me-oxalate/ 2/ fid
Title
JYS-1-230-F1-cycloheptyl-Bn-Me-oxalate.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zgpg30
Experiment
1D
Number of Scans
512
Receiver Gain
78.7
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2017-11-01T02:53:43
Spectrometer Frequency
100.62
Spectral Width
24038.5
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
157.3
159.0
142.1
135.7
130.7
129.0
128.4
127.0
126.5
91.2
53.5
45.0
35.9
29.3
OMe
Ph
SI-15
ppm


Parameter Value
Data File Name JYS-1-261-cycloheptyl-Bn-Cs-oxalate/ 4/ fid
Title JYS-1-261-cycloheptyl-Bn-Cs-oxalate.4.fid
Origin Bruker BioSpin GmbH
Solvent DMSO
Temperature 294.9
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 176.8
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-11-08T20:05:06
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
OCs
Ph
347f
5.15
4.10
2.00
2.01
3.85
1.94
ppm


Parameter Value
Data File Name JYS-1-261-cycloheptyl-Bn-Cs-oxalate/2/ fid
Title JYS-1-261-cycloheptyl-Bn-Cs-oxalate.2.fid
Origin Bruker BioSpin GmbH
Solvent DMSO
Temperature 295.0
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 512
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-11-07T00:22:55
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OCs
Ph
347f
28.4
35.8
44.1
83.7
126.0
126.2
127.8
128.5
130.7
136.9
142.4
163.3
167.9
ppm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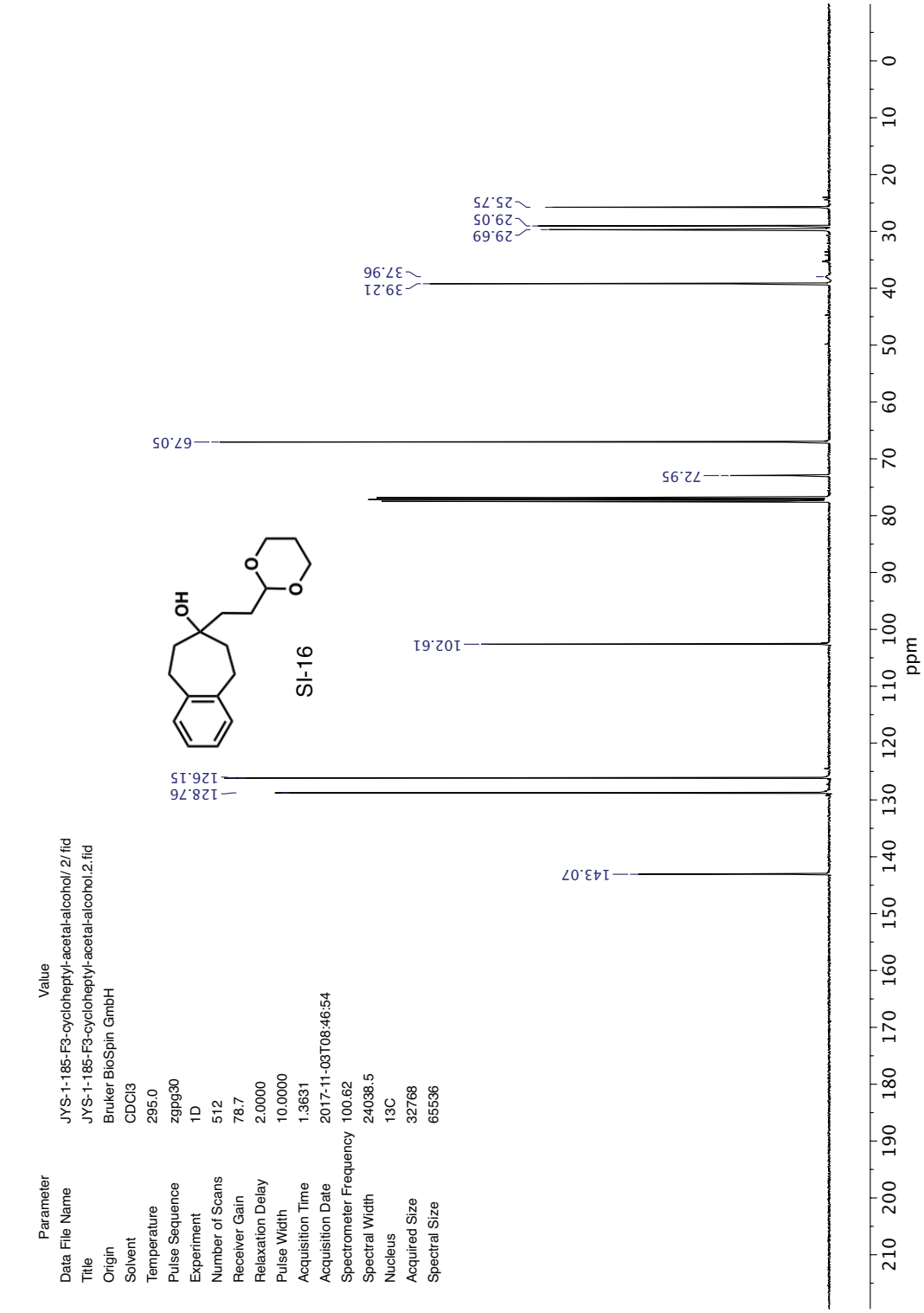
Value
Data File Name
JYS-1-185-F3-cycloheptyl-acetal-alcohol/ 1/ fid
Title
JYS-1-185-F3-cycloheptyl-acetal-alcohol.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.0
Pulse Sequence
zg30
Experiment
1D
Number of Scans
16
Receiver Gain
30.3
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2017-11-03T08:17:10
Spectrometer Frequency
400.13
Spectral Width
8012.8
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
OH
O
O
SI-16
3.92
1.00
2.05
2.06
1.83
1.97
0.88
1.19
2.01
2.07
2.06
1.92
1.13
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
ppm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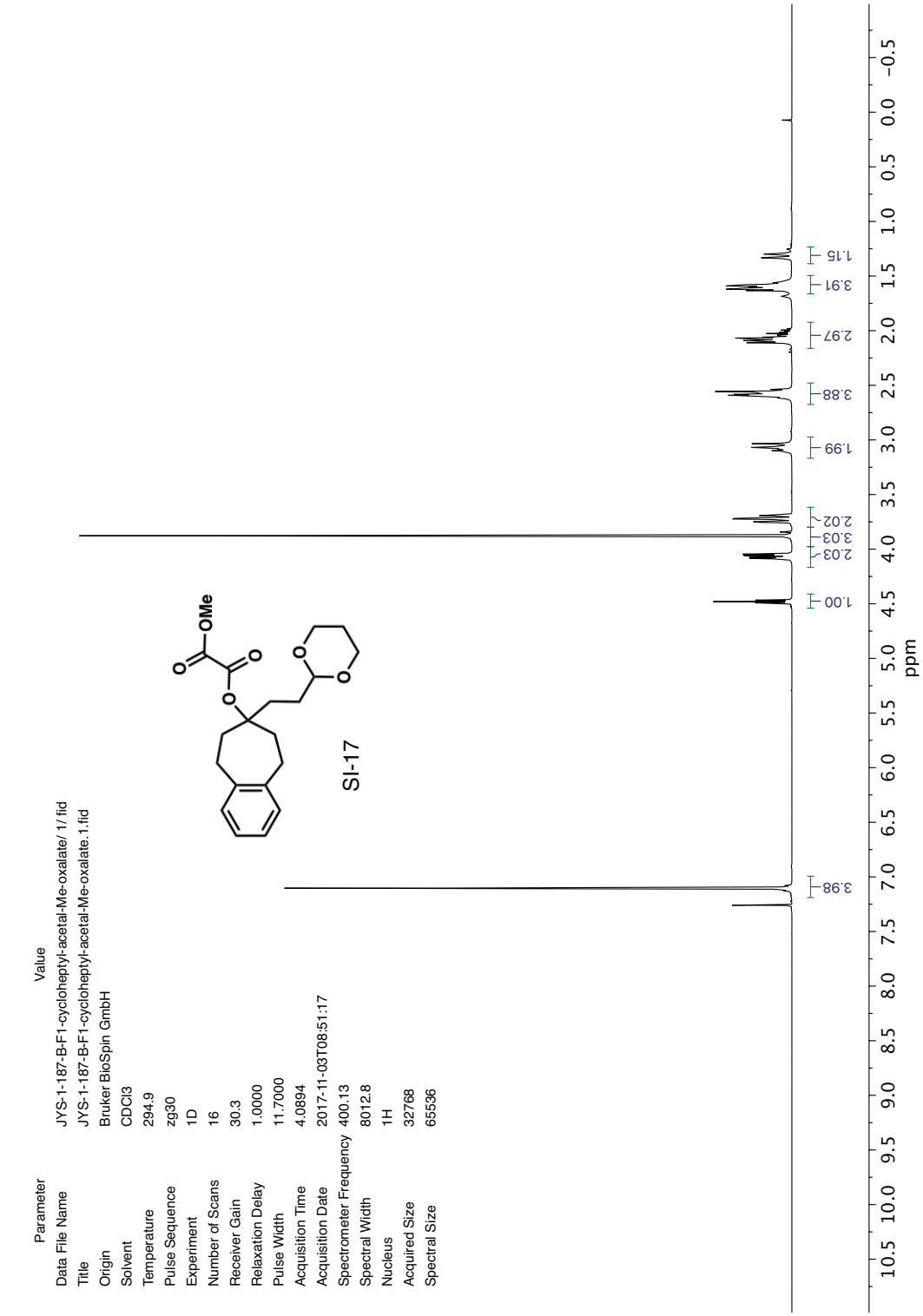
Value
Data File Name
JYS-1-185-F3-cycloheptyl-acetal-alcohol/ 2/ fid
Title
JYS-1-185-F3-cycloheptyl-acetal-alcohol.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.0
Pulse Sequence
zgpg30
Experiment
1D
Number of Scans
512
Receiver Gain
78.7
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2017-11-03T08:46:54
Spectrometer Frequency
100.62
Spectral Width
24038.5
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
SI-16
OH
O
O
143.07
128.76
126.15
102.61
72.95
67.05
39.21
37.96
29.69
29.05
25.75
ppm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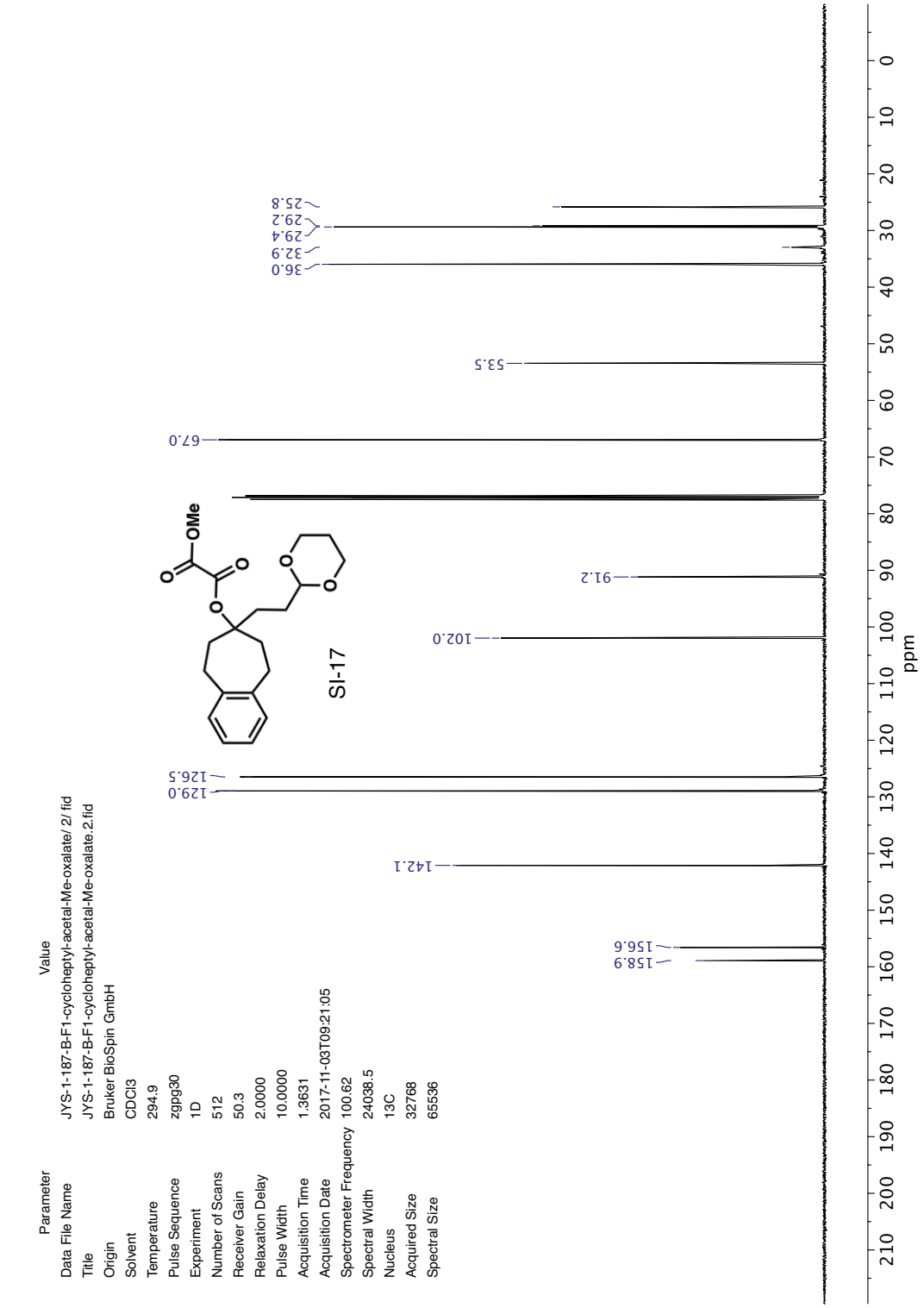
Value
Data File Name JYS-1-187-B-F1-cycloheptyl-acetal-Me-oxalate/ 1/ fid
Title JYS-1-187-B-F1-cycloheptyl-acetal-Me-oxalate. 1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 30.3
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-11-03T08:51:17
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
OMe
SI-17
3.98
1.00
2.03
3.03
2.02
1.99
3.88
2.97
3.91
1.15
ppm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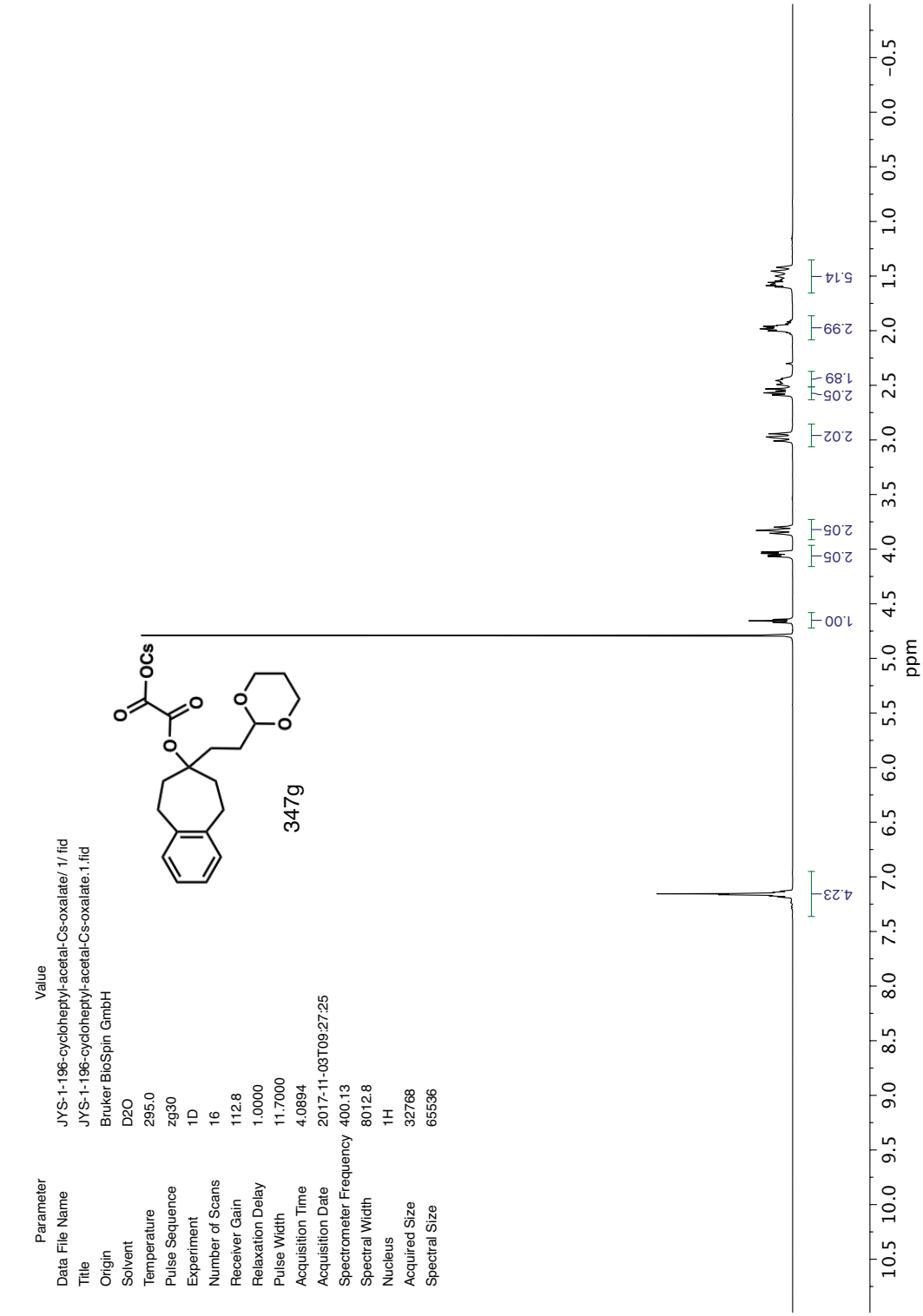
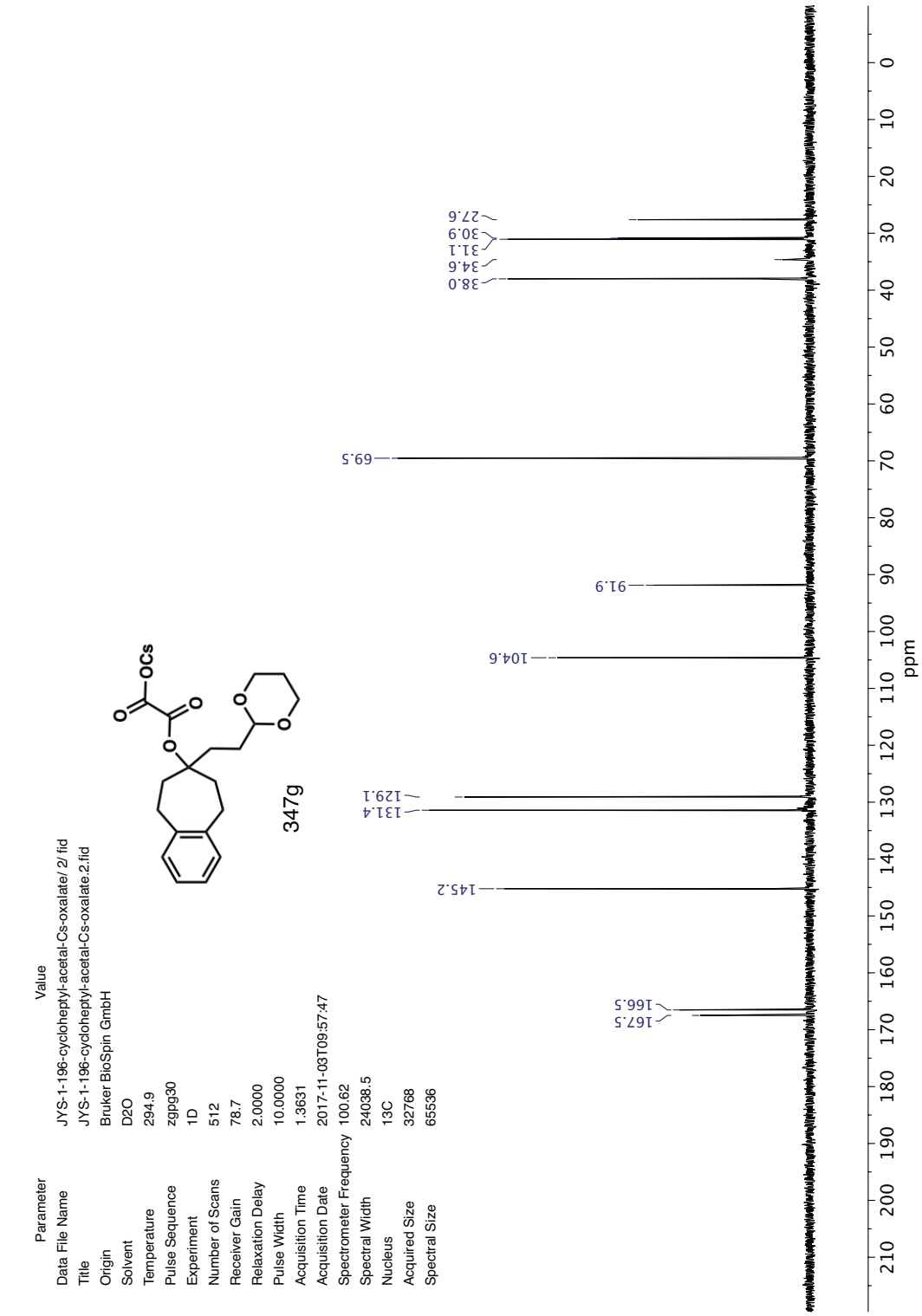
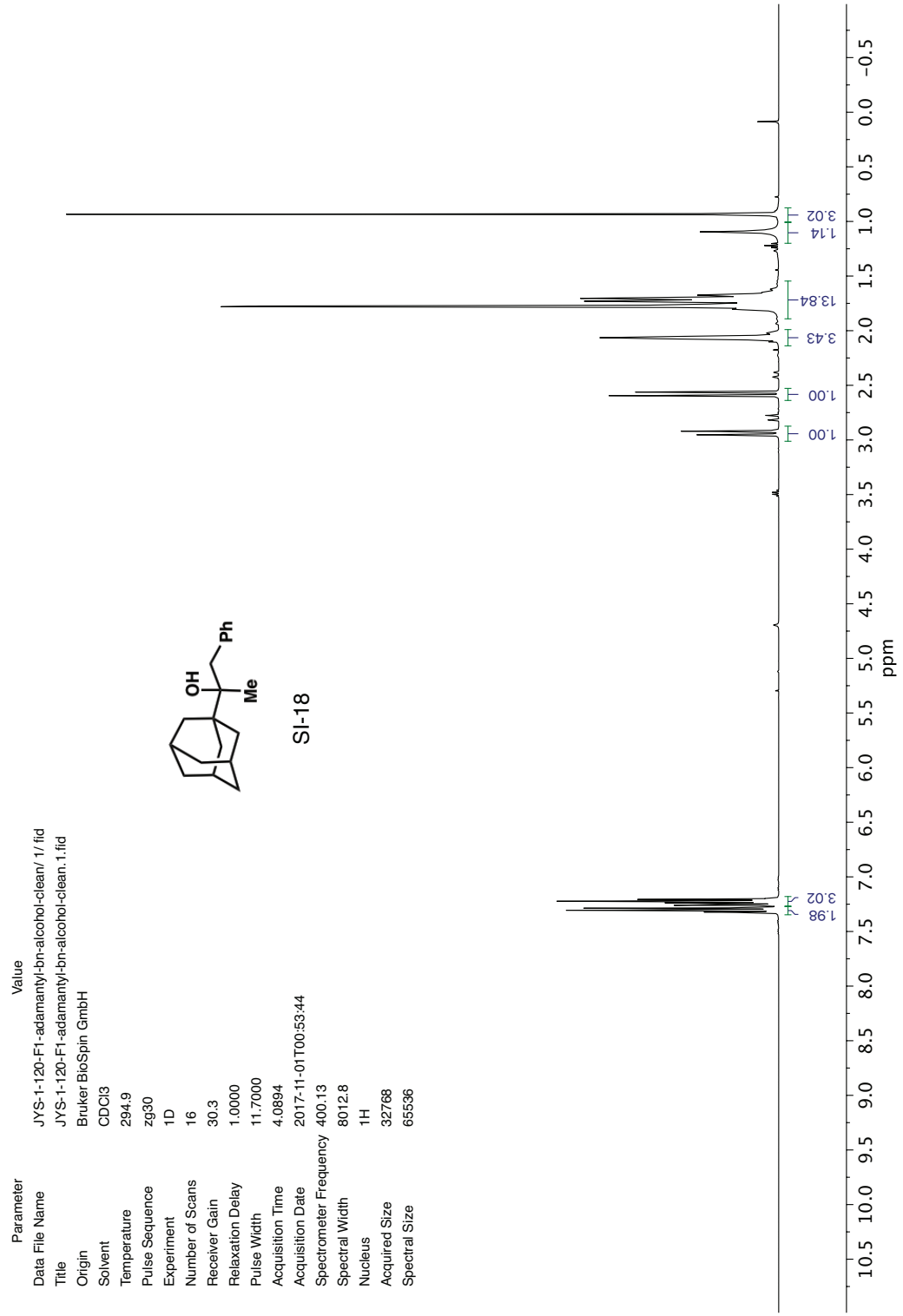
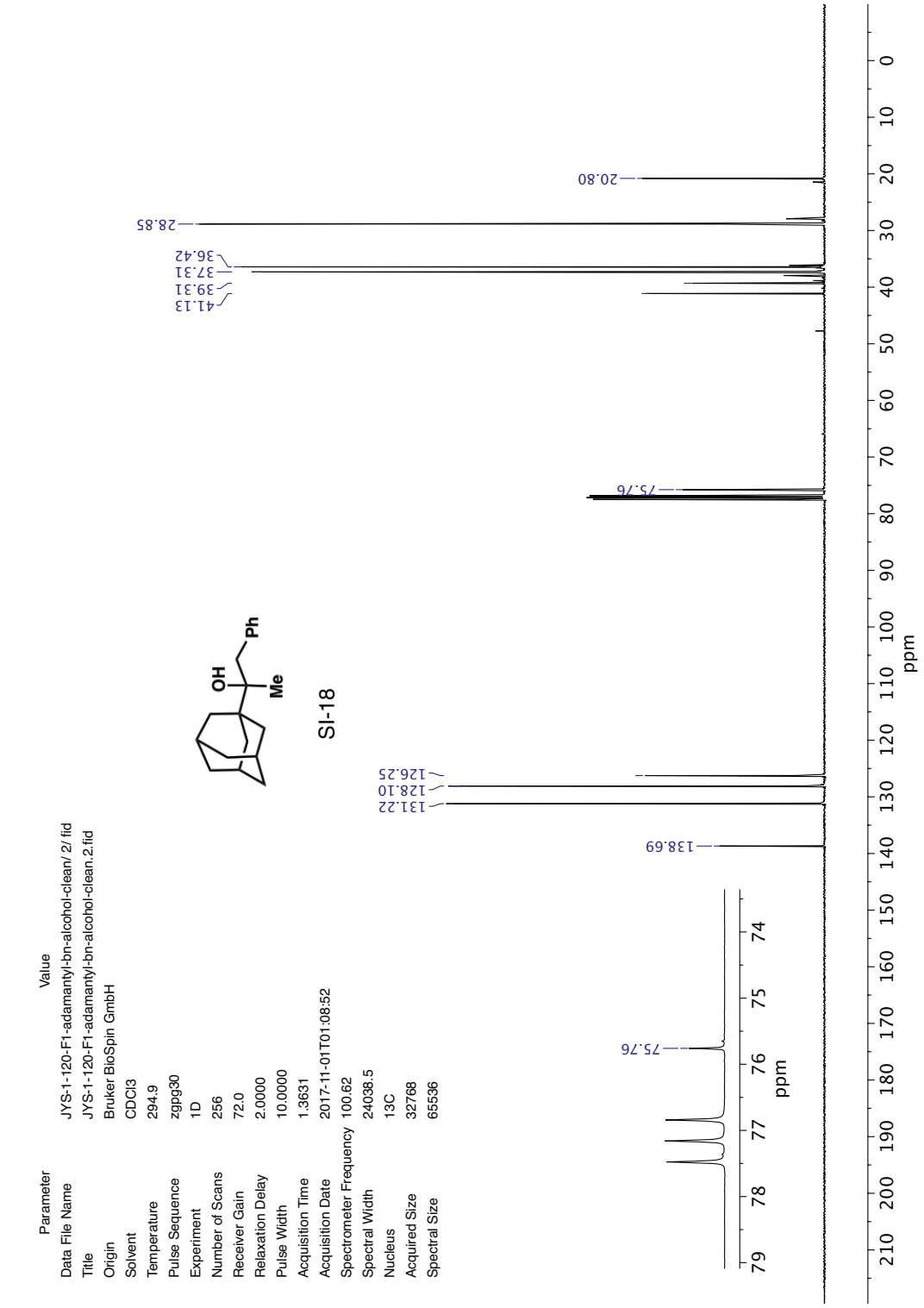
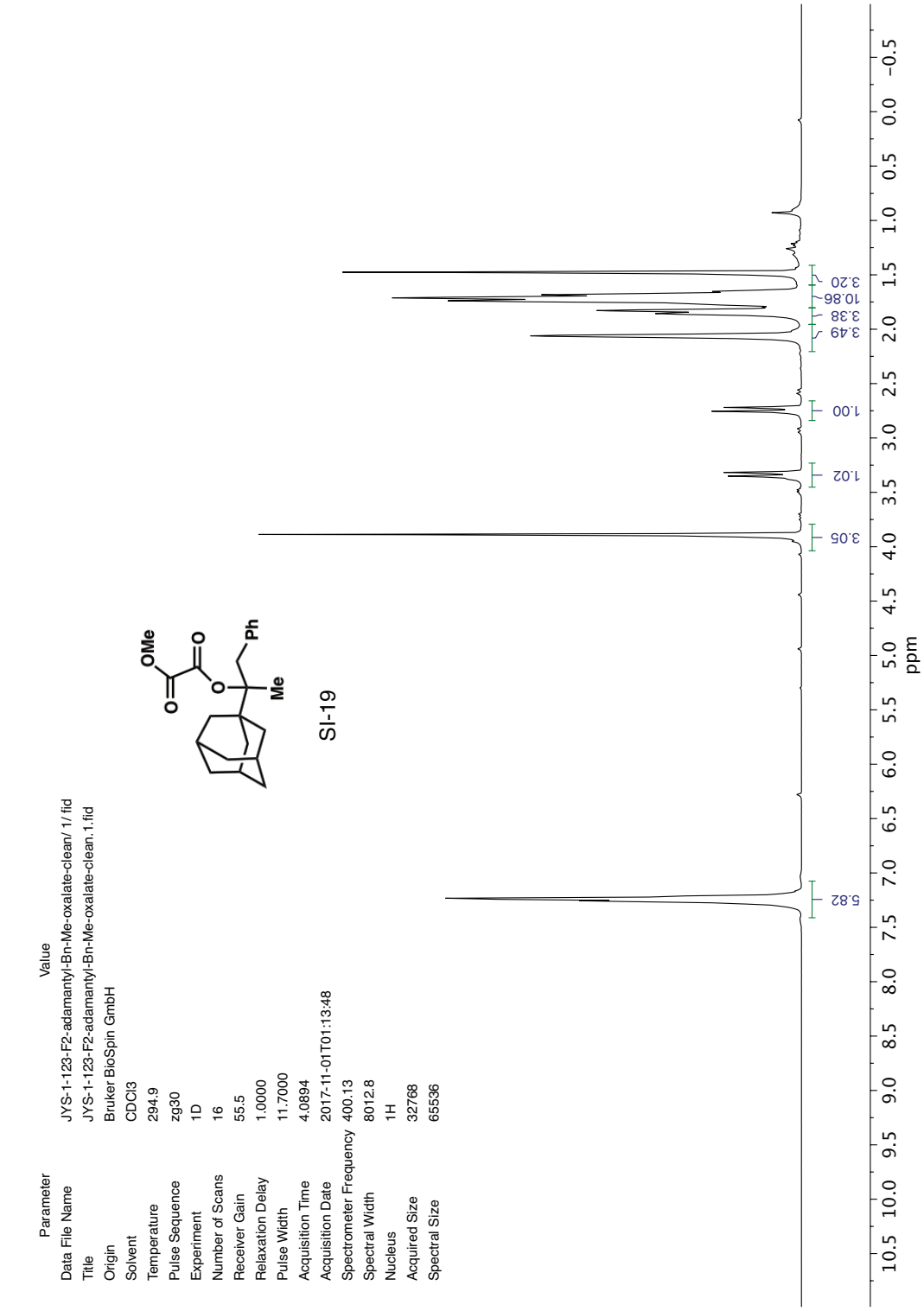
Data File Name JYS-1-187-B-F1-cycloheptyl-acetal-Me-oxalate/ 2/ fid
Title JYS-1-187-B-F1-cycloheptyl-acetal-Me-oxalate.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 512
Receiver Gain 50.3
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-11-03T09:21:05
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OMe
SI-17
158.9
156.6
142.1
129.0
126.5
102.0
91.2
67.0
53.5
36.0
32.9
29.4
29.2
25.8
ppm

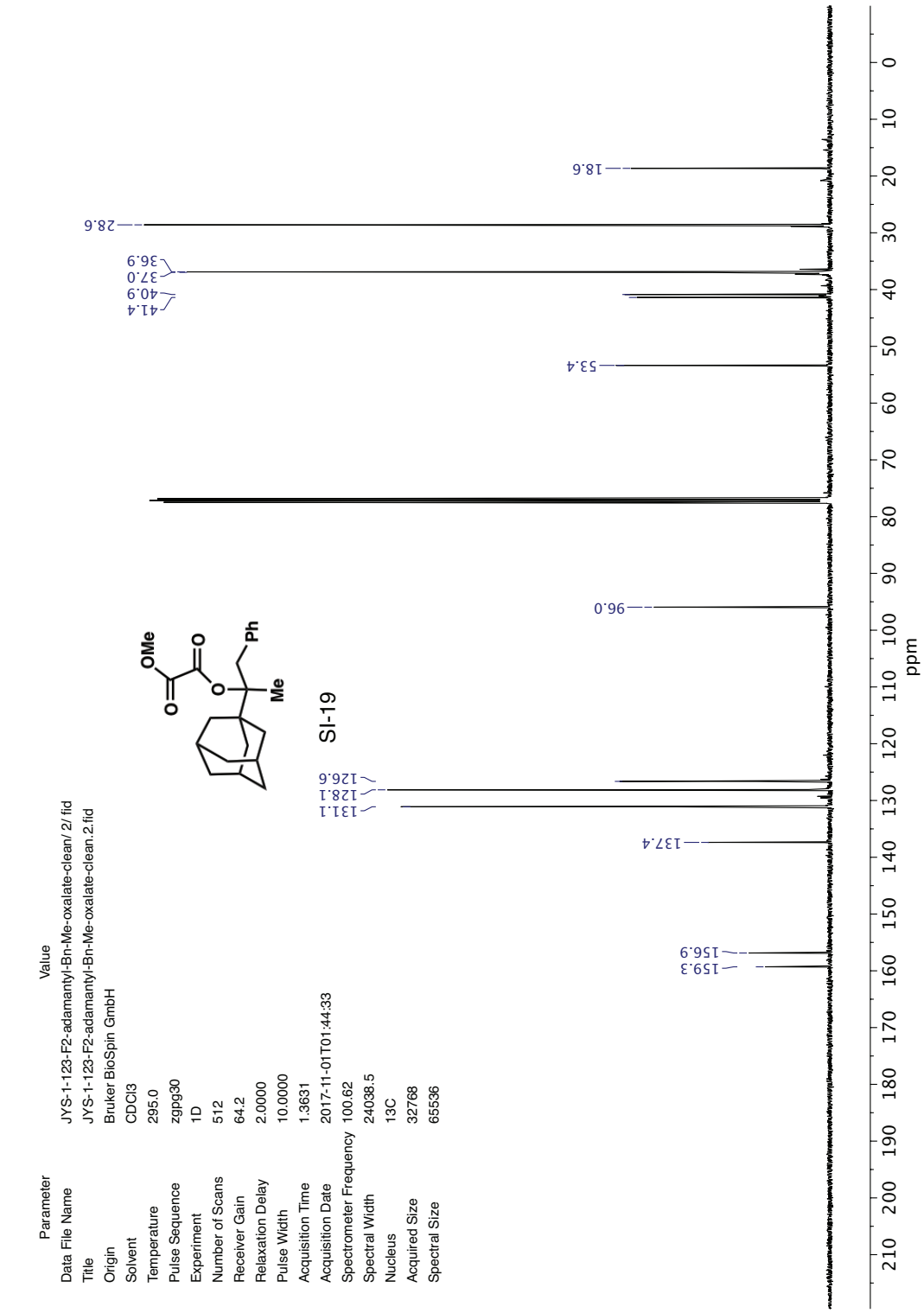

Parameter
Value
Data File Name
JYS-1-196-cycloheptyl-acetal-Cs-oxalate/ 1/ fid
Title
JYS-1-196-cycloheptyl-acetal-Cs-oxalate.1.fid
Origin
Bruker BioSpin GmbH
Solvent
D2O
Temperature
295.0
Pulse Sequence
zg30
Experiment
1D
Number of Scans
16
Receiver Gain
112.8
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2017-11-03T09:27:25
Spectrometer Frequency
400.13
Spectral Width
8012.8
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
OCs
347g
4.23
1.00
2.05
2.05
2.02
2.05
1.89
2.99
5.14
ppm

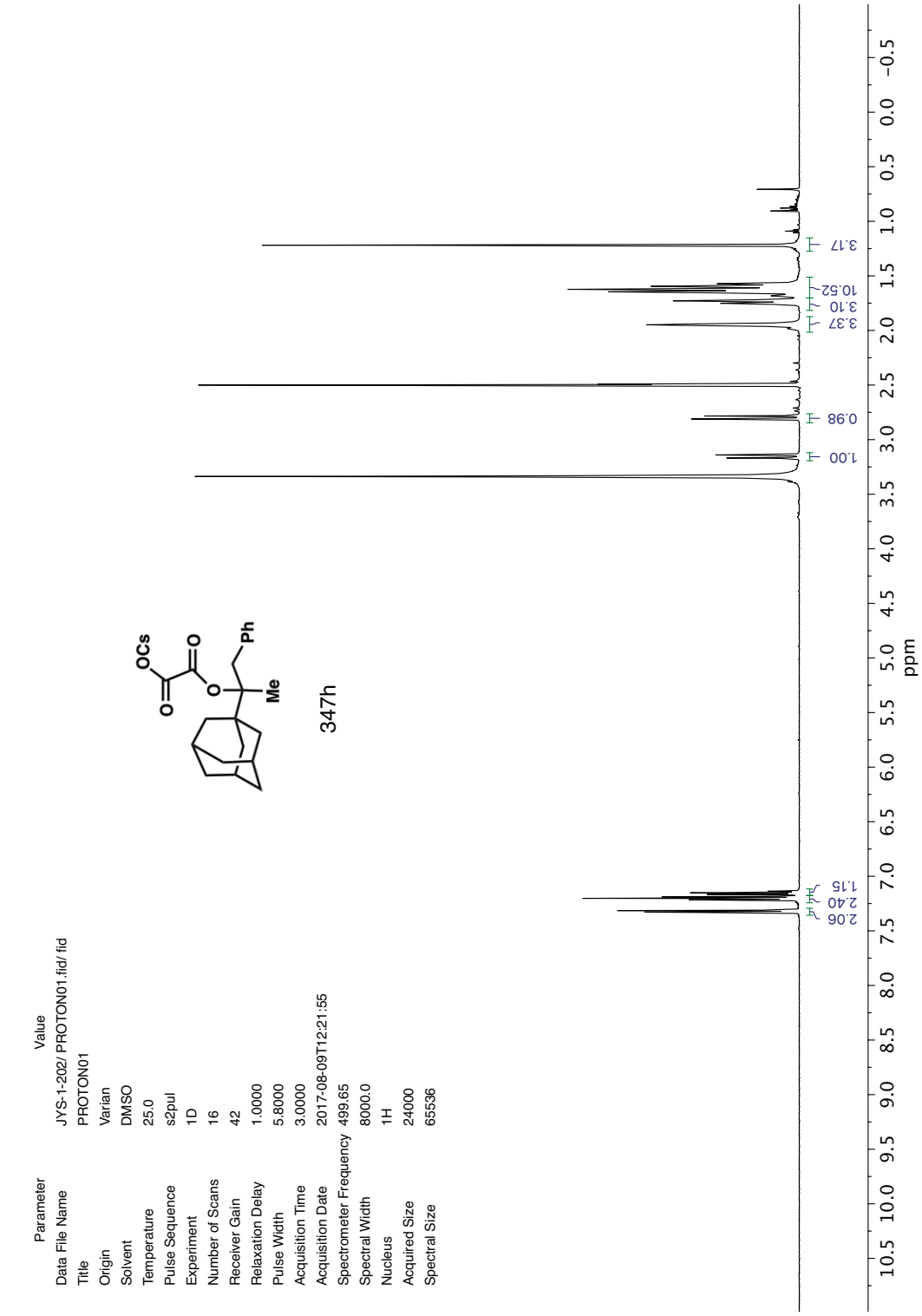

Parameter
Value
Data File Name JYS-1-196-cycloheptyl-acetal-Cs-oxalate/ 2/ fid
Title JYS-1-196-cycloheptyl-acetal-Cs-oxalate.2.fid
Origin Bruker BioSpin GmbH
Solvent D2O
Temperature 294.9
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 512
Receiver Gain 78.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-11-03T09:57:47
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OCs
347g
166.5
167.5
145.2
131.4
129.1
104.6
91.9
69.5
38.0
34.6
31.1
30.9
27.6
ppm

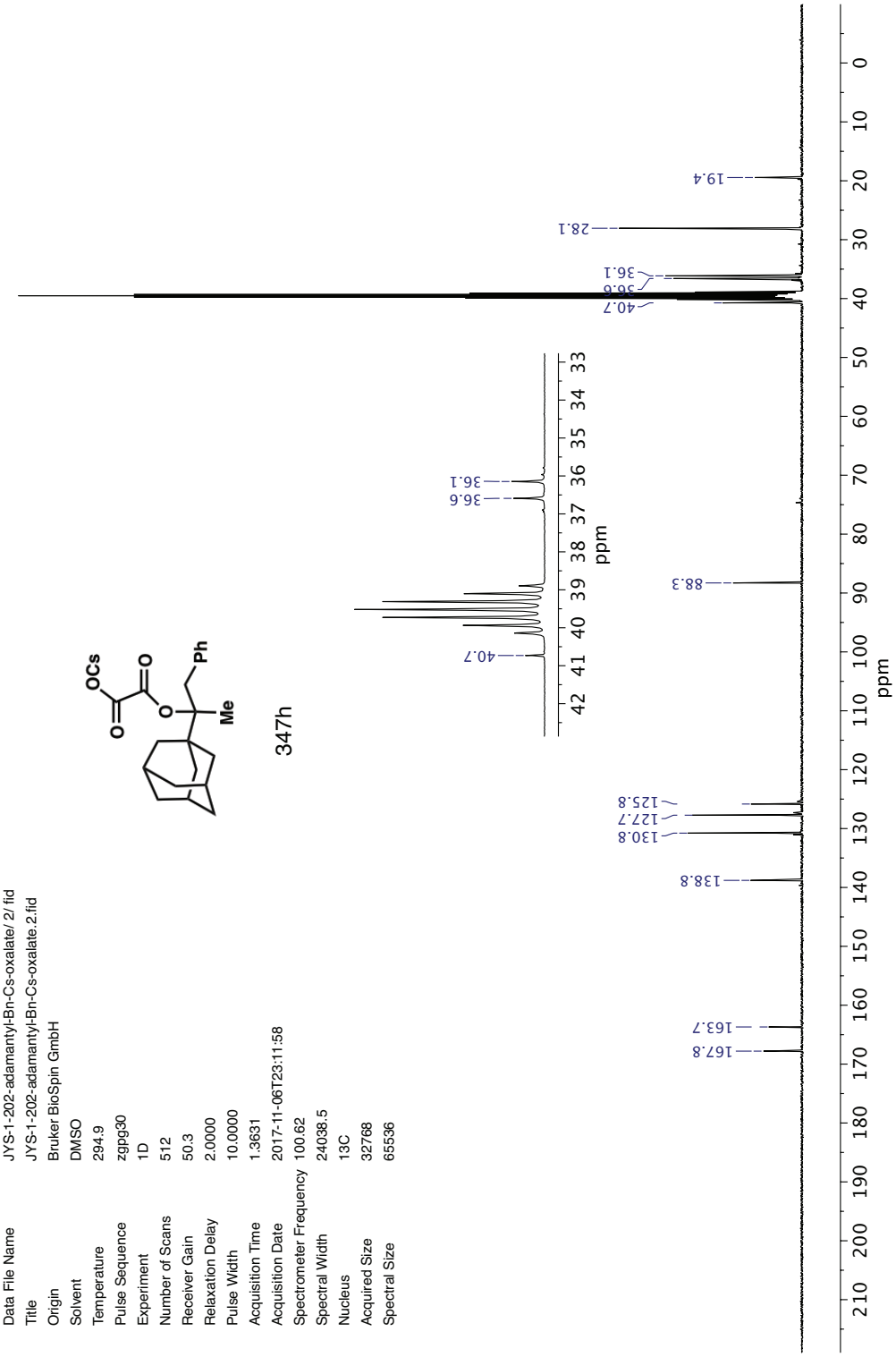

Parameter
Value
Data File Name
JYS-1-120-F1-adamantyl-bn-alcohol-clean/ 1/ fid
Title
JYS-1-120-F1-adamantyl-bn-alcohol-clean.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zg30
Experiment
1D
Number of Scans
16
Receiver Gain
30.3
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2017-11-01T00:53:44
Spectrometer Frequency
400.13
Spectral Width
8012.8
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
OH
Ph
Me
SI-18
1.98
3.02
1.00
1.00
3.43
13.84
1.14
3.02
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
ppm


Parameter
Value
Data File Name JYS-1-120-F1-adamantyl-bn-alcohol-clean/ 2/ fid
Title JYS-1-120-F1-adamantyl-bn-alcohol-clean.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-11-01T01:08:52
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OH
Ph
Me
SI-18
138.69
131.22
128.10
126.25
75.76
41.13
39.31
37.31
36.42
28.85
20.80
ppm


Parameter
Value
Data File Name
JYS-1-123-F2-adamantyl-Bn-Me-oxalate-clean/ 1/ fid
Title
JYS-1-123-F2-adamantyl-Bn-Me-oxalate-clean.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zg30
Experiment
1D
Number of Scans
16
Receiver Gain
55.5
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2017-11-01T01:13:48
Spectrometer Frequency
400.13
Spectral Width
8012.8
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
OMe
O
O
O
Ph
Me
SI-19
5.82
3.05
1.02
1.00
3.49
3.38
10.86
3.20
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
ppm


Parameter
Value
Data File Name JYS-1-123-F2-adamantyl-Bn-Me-oxalate-clean/ 2/ fid
Title JYS-1-123-F2-adamantyl-Bn-Me-oxalate-clean.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 512
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-11-01T01:44:33
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
SI-19
OMe
O
O
O
Ph
Me
159.3
156.9
137.4
131.1
128.1
126.6
96.0
53.4
41.4
40.9
37.0
36.9
28.6
18.6
ppm


Parameter Value
Data File Name JYS-1-202/ PROTON01.fid/ fid
Title PROTON01
Origin Varian
Solvent DMSO
Temperature 25.0
Pulse Sequence s2pul
Experiment 1D
Number of Scans 16
Receiver Gain 42
Relaxation Delay 1.0000
Pulse Width 5.8000
Acquisition Time 3.0000
Acquisition Date 2017-08-09T12:21:55
Spectrometer Frequency 499.65
Spectral Width 8000.0
Nucleus 1H
Acquired Size 24000
Spectral Size 65536
OCs
O
O
O
Ph
Me
347h
2.06
2.40
1.15
1.00
0.98
3.37
3.10
10.52
3.17
ppm


Parameter Value
Data File Name JYS-1-202-adamantyl-Bn-Cs-oxalate/ 2/ fid
Title JYS-1-202-adamantyl-Bn-Cs-oxalate.2.fid
Origin Bruker BioSpin GmbH
Solvent DMSO
Temperature 294.9
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 512
Receiver Gain 50.3
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-11-06T23:11:58
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OCs
O
O
O
Ph
Me
347h
ppm
ppm
40.7
36.6
36.1
19.4
28.1
36.1
36.6
40.7
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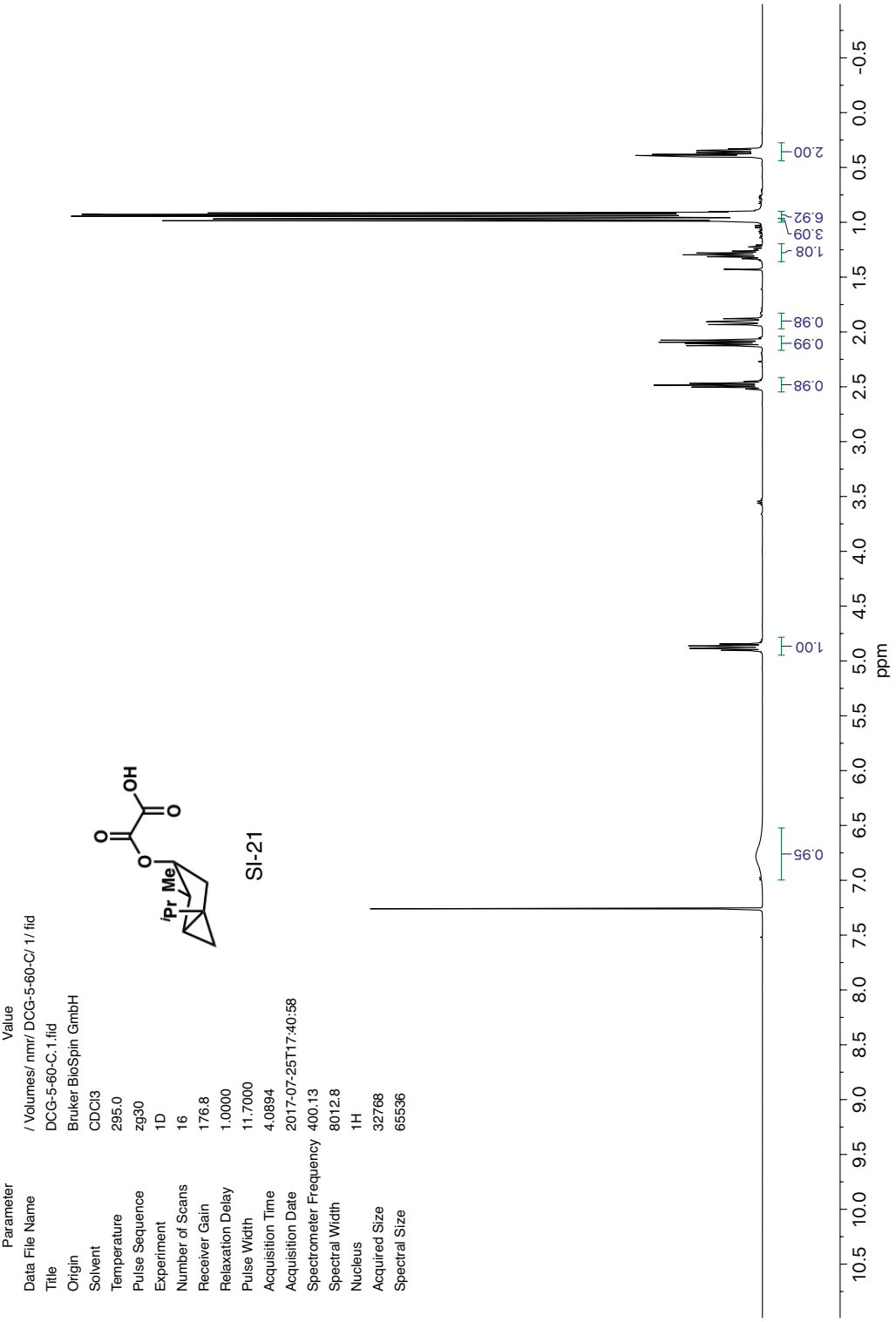
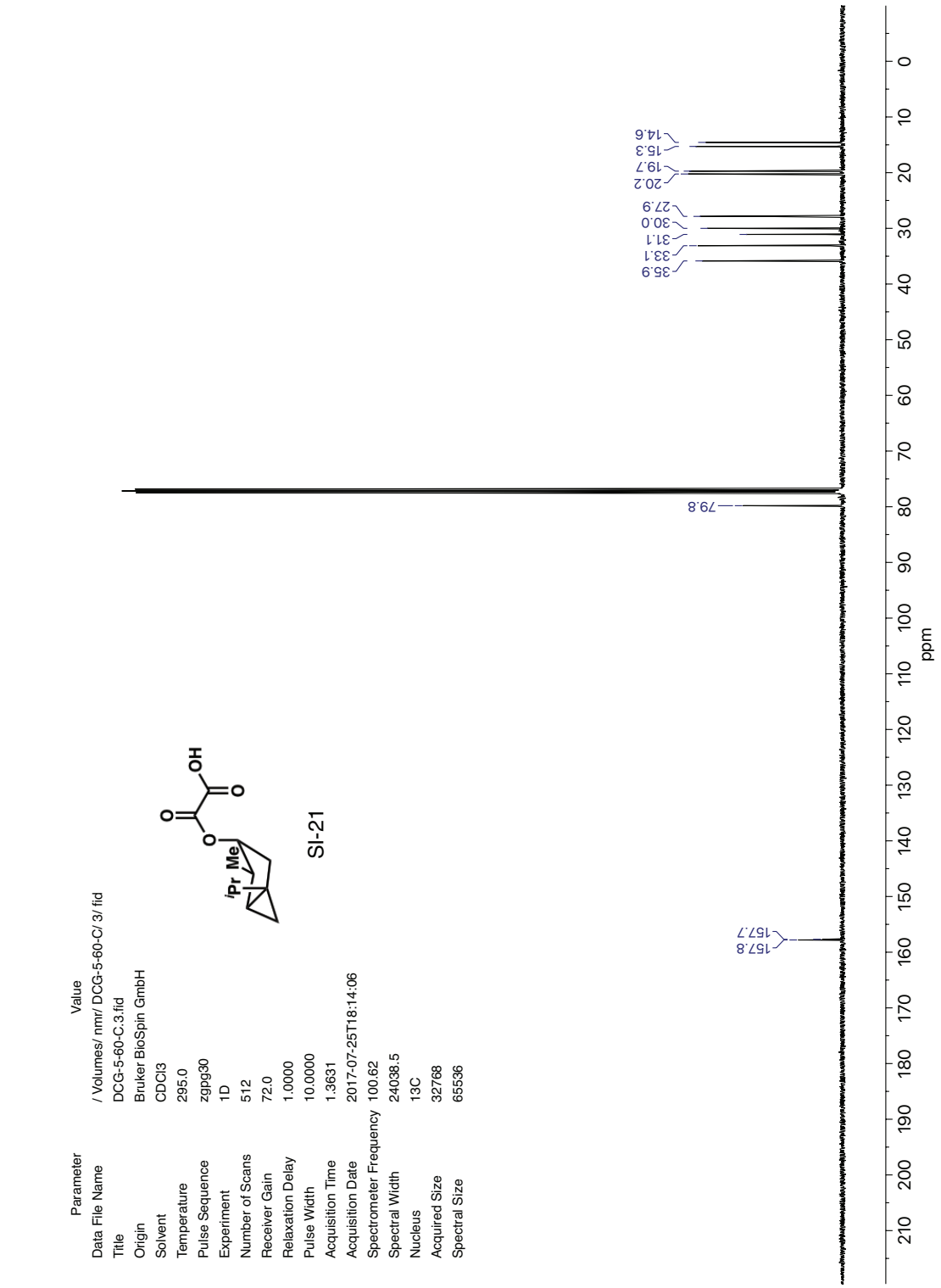
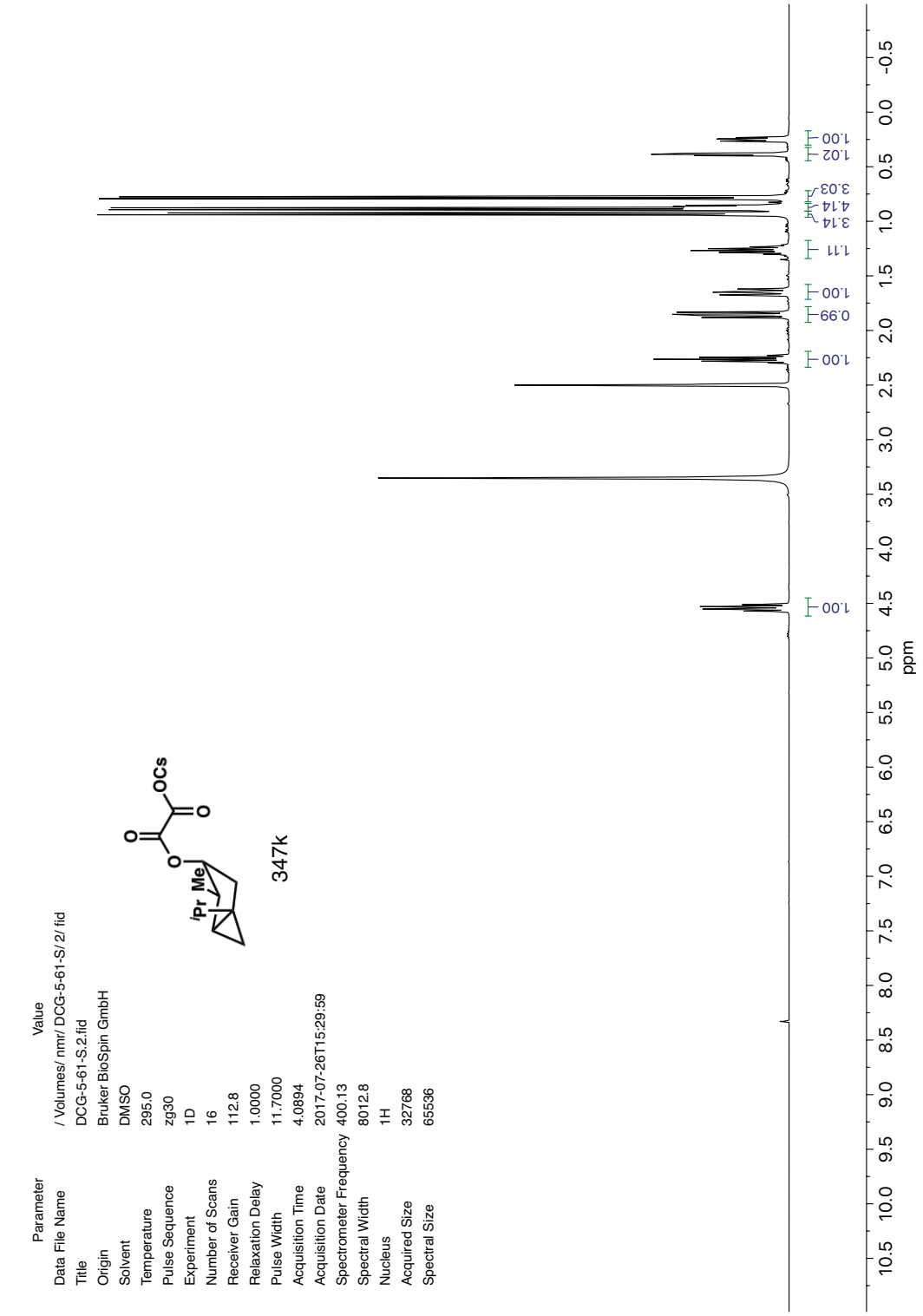
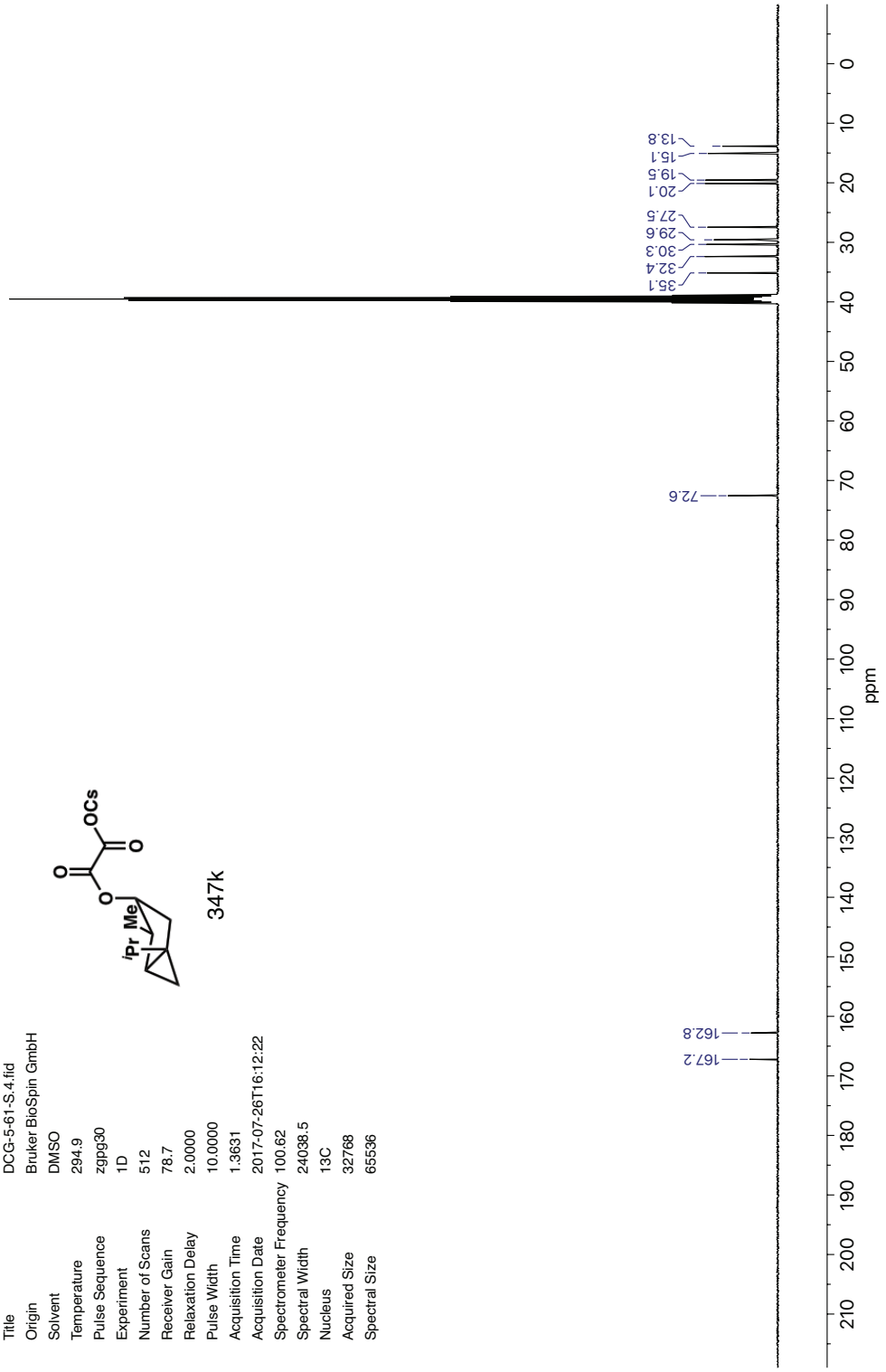
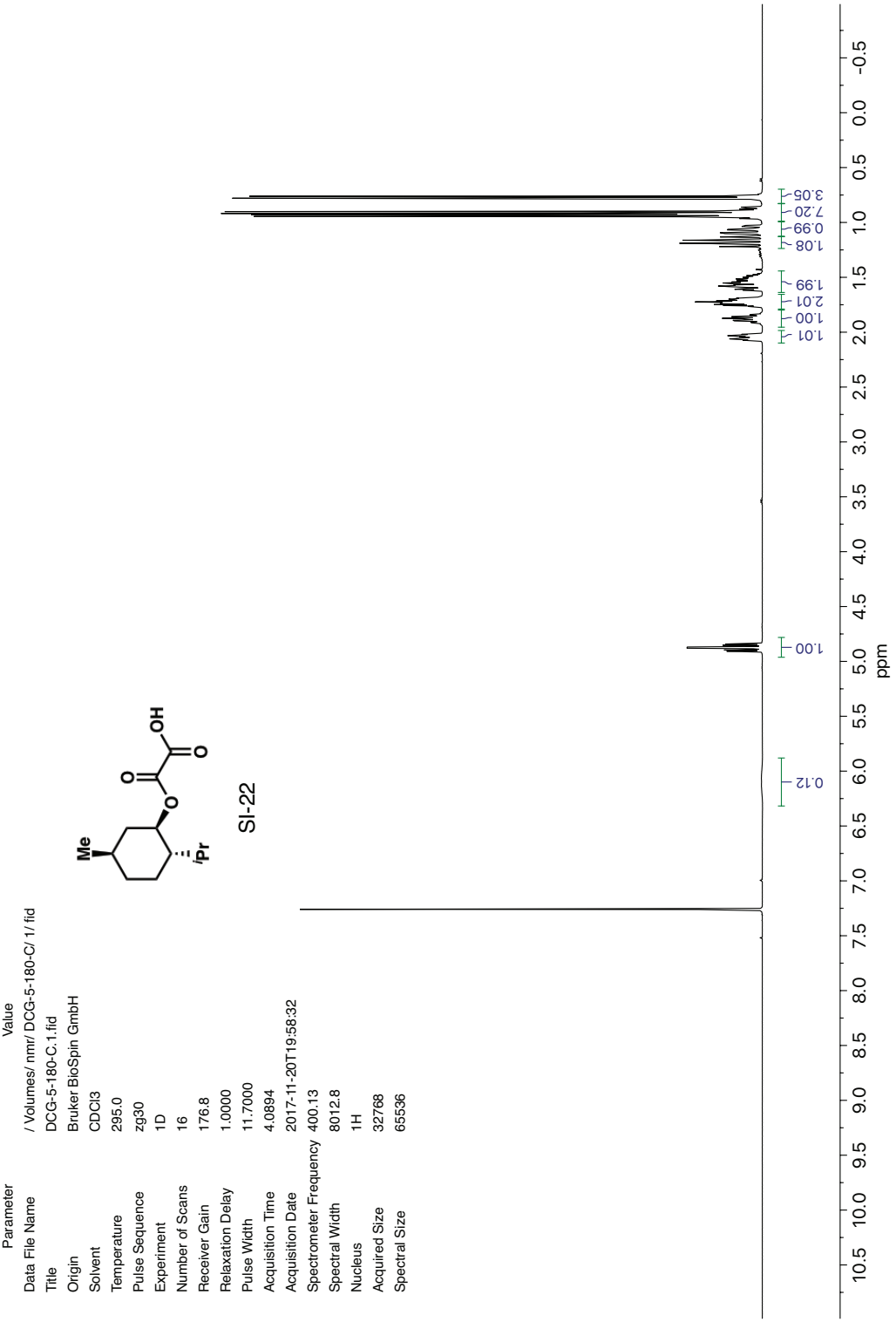
138.8
130.8
127.7
125.8
167.8
163.7

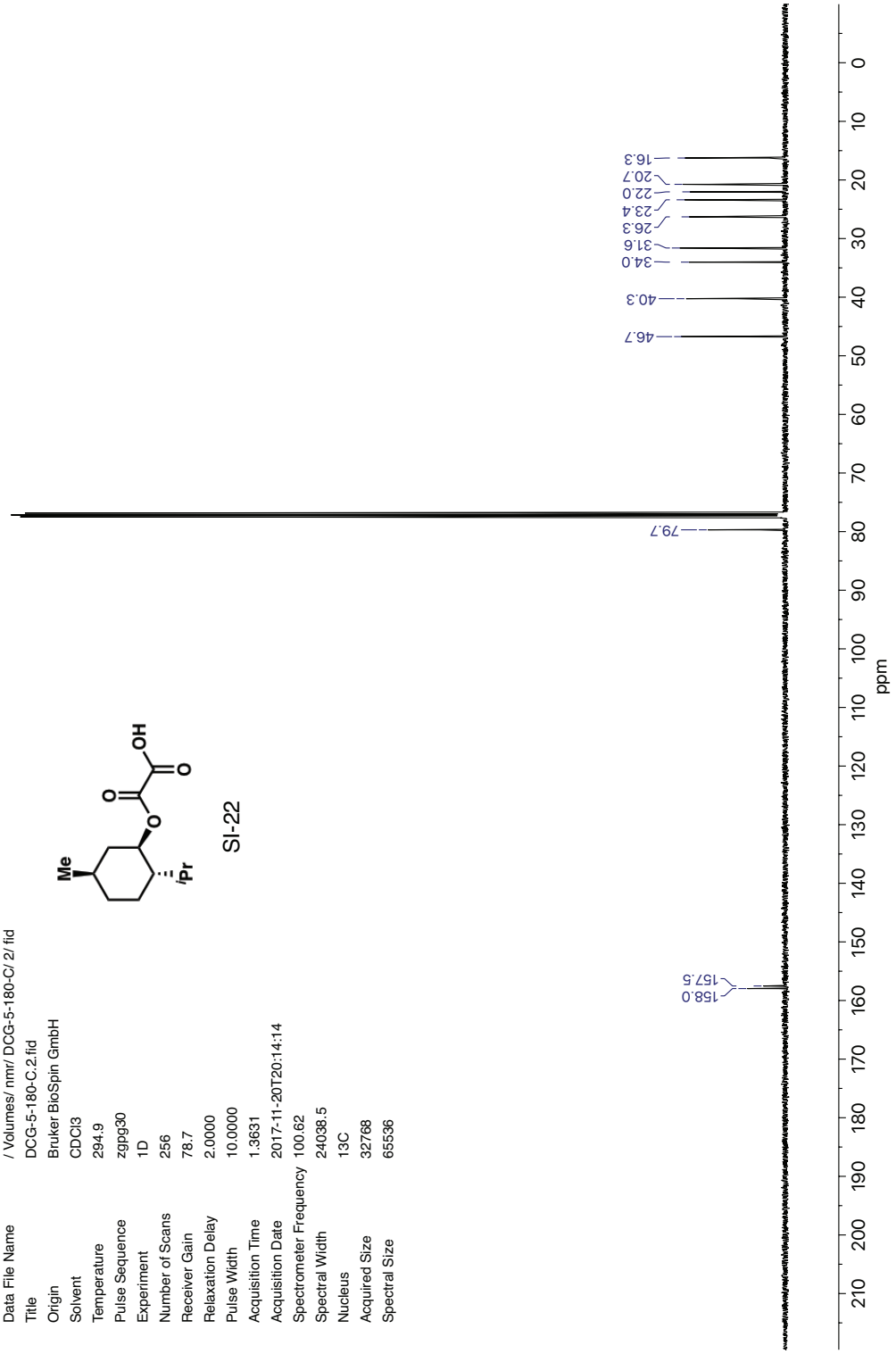

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-60-C/ 1/ fid
Title DCG-5-60-C.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 176.8
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-07-25T17:40:58
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
SI-21
iPr
Me
OH
O
O
O
0.95
1.00
0.98
0.99
0.98
1.08
3.09
6.92
2.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm

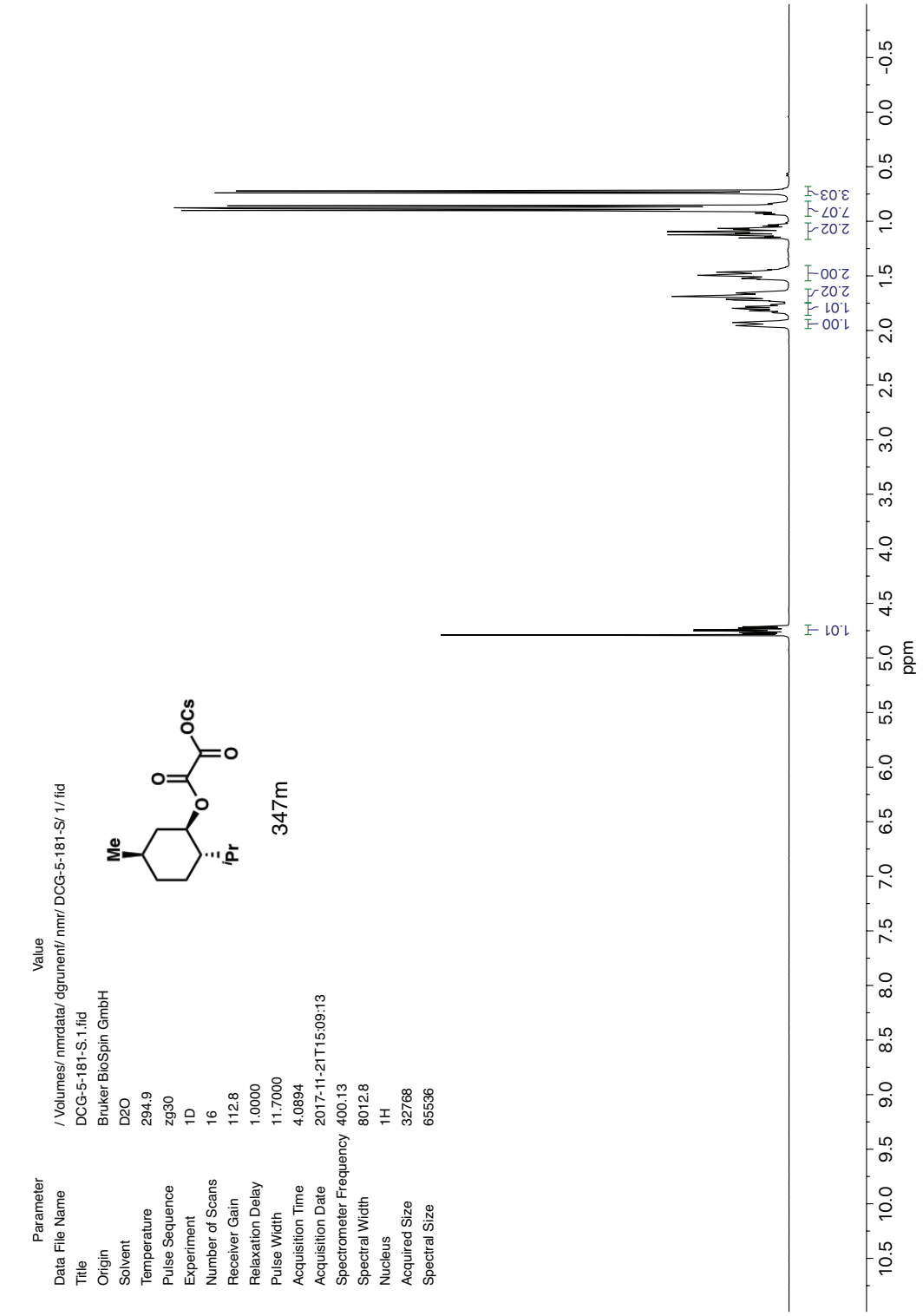

Parameter
Value
Data File Name / Volumes/ nmr/ DCG-5-60-C/ 3/ fid
Title DCG-5-60-C.3.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 512
Receiver Gain 72.0
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-07-25T18:14:06
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
SI-21
157.8
157.7
79.8
35.9
33.1
31.1
30.0
27.9
20.2
19.7
15.3
14.6
ppm

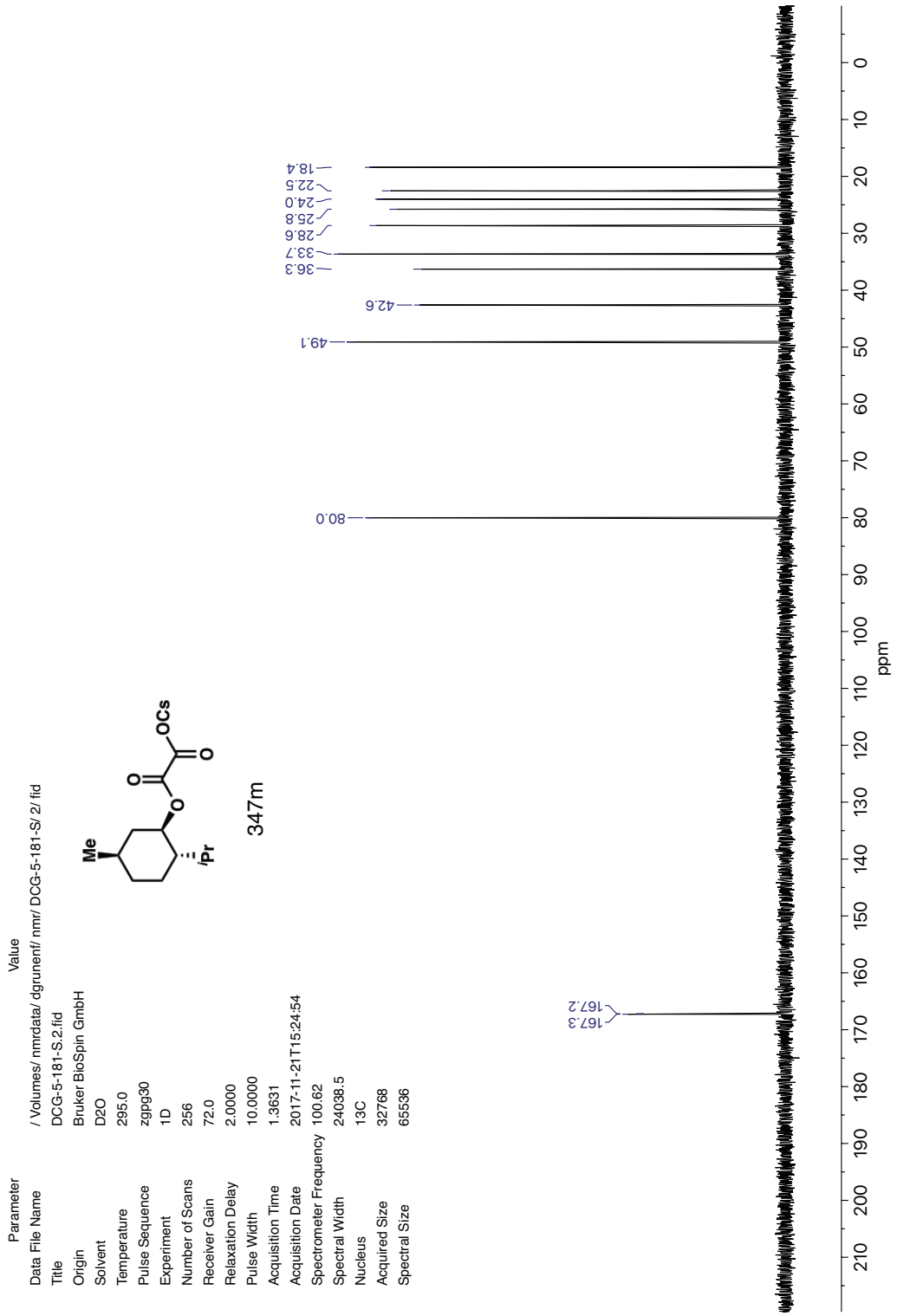

Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-5-61-S/ 2/ fid
Title
DCG-5-61-S.2.fid
Origin
Bruker BioSpin GmbH
Solvent
DMSO
Temperature
295.0
Pulse Sequence
zg30
Experiment
1D
Number of Scans
16
Receiver Gain
112.8
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2017-07-26T15:29:59
Spectrometer Frequency
400.13
Spectral Width
8012.8
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
OCs
O
O
O
iPr
Me
347k
1.00
1.02
3.14
4.14
3.03
1.11
1.00
0.99
1.00
1.00
ppm

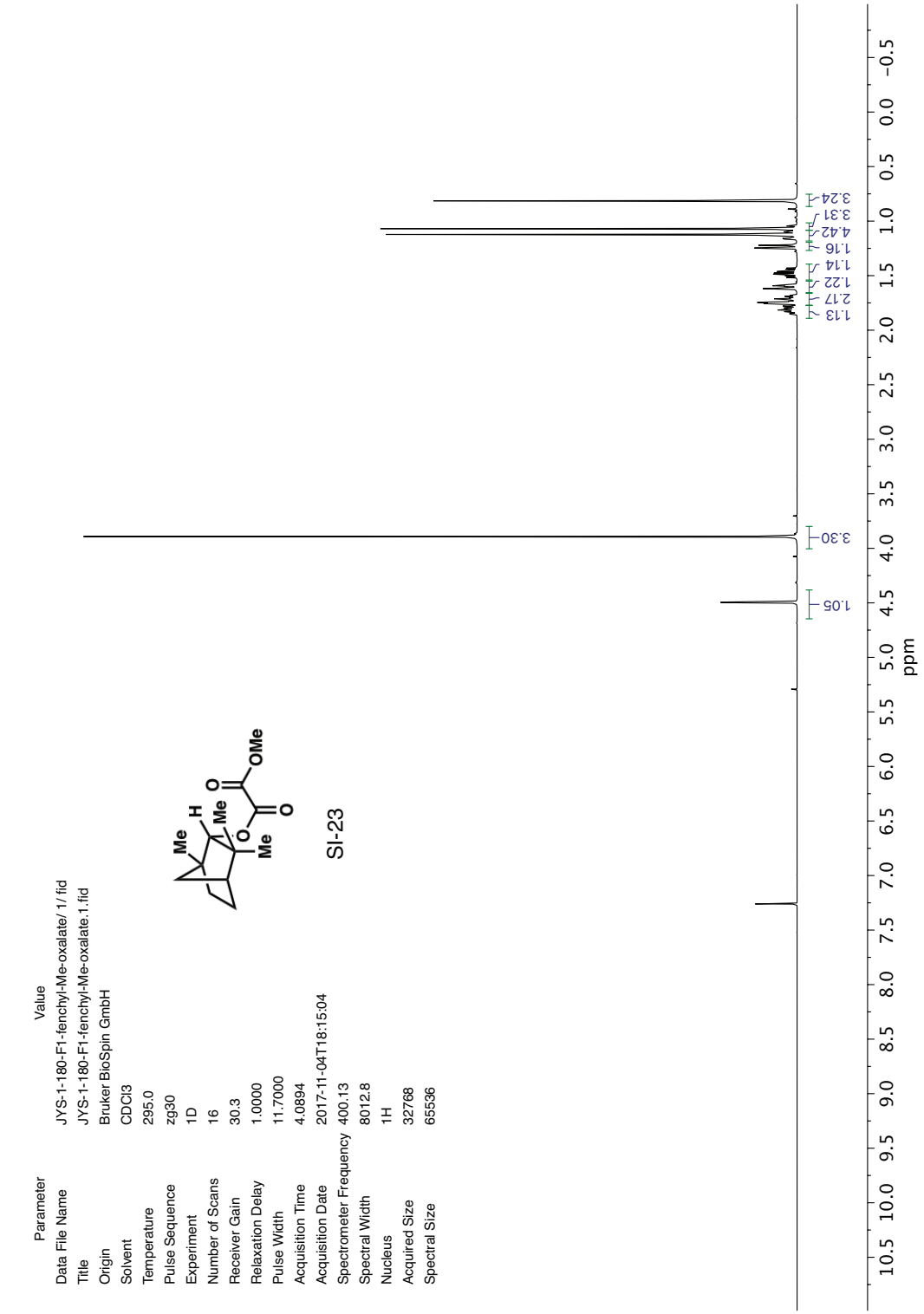

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-61-S/ 4/ fid
Title DCG-5-61-S.4.fid
Origin Bruker BioSpin GmbH
Solvent DMSO
Temperature 294.9
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 512
Receiver Gain 78.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-07-26T16:12:22
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OCs
O
O
O
iPr
Me
347k
167.2
162.8
72.6
35.1
32.4
30.3
29.6
27.5
20.1
19.5
15.1
13.8
ppm

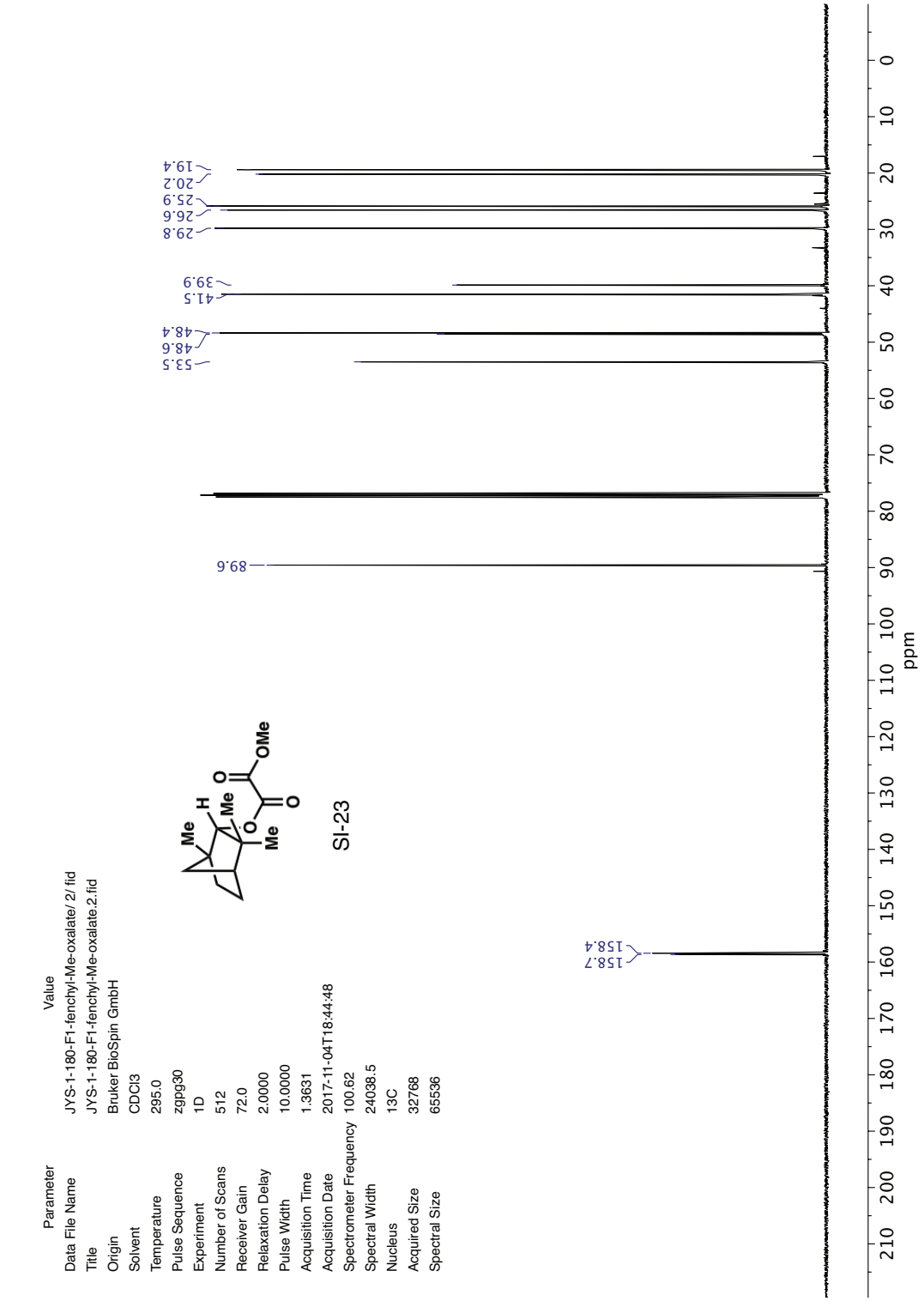

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-180-C/ 1/ fid
Title DCG-5-180-C.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 176.8
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-11-20T19:58:32
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
Me
iPr
O
O
O
OH
SI-22
0.12
1.00
1.01
1.00
2.01
1.99
1.08
0.99
7.20
3.05
ppm

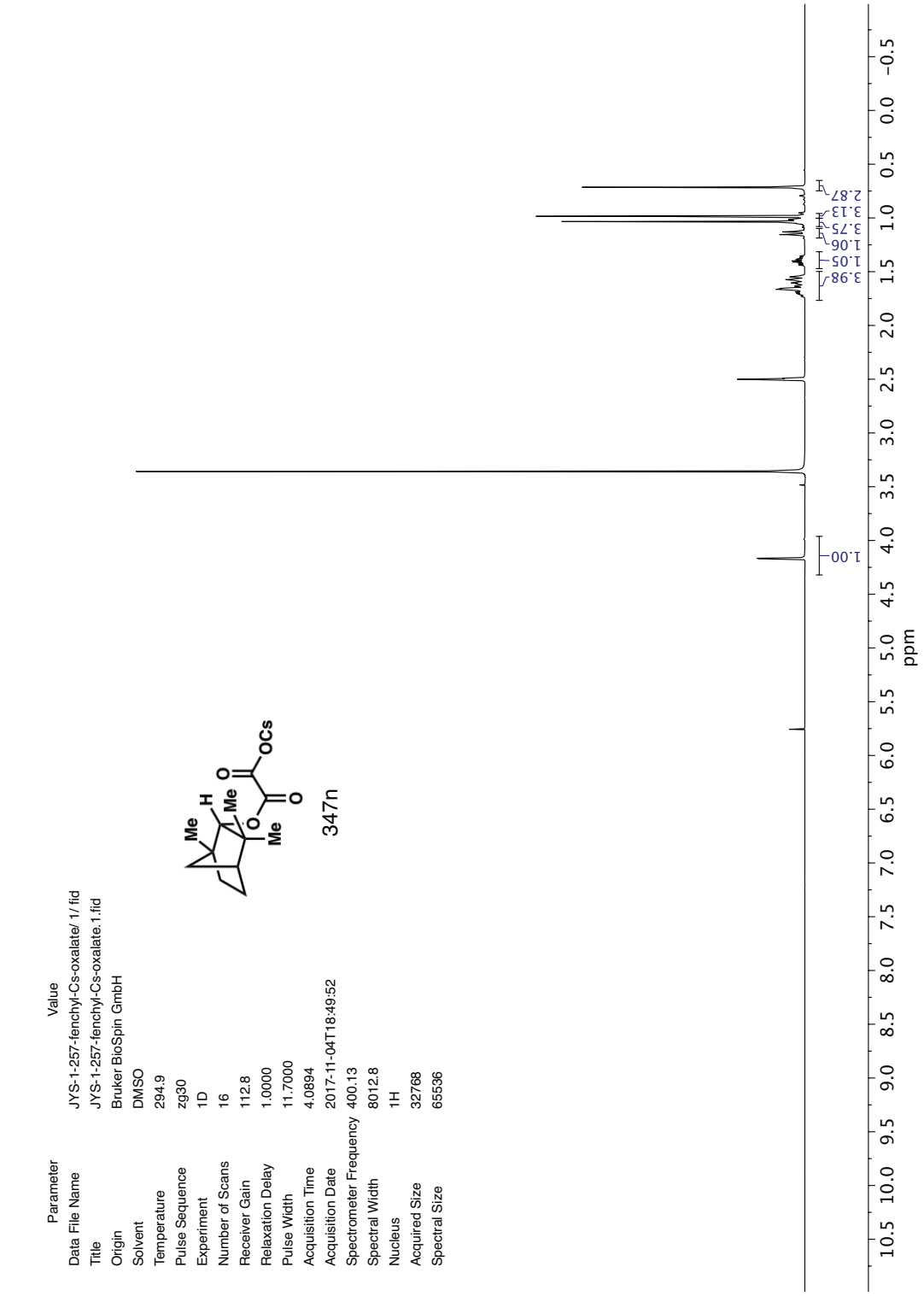

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-180-C/ 2/ fid
Title DCG-5-180-C.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 78.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-11-20T20:14:14
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
iPr
O
O
O
OH
SI-22
158.0
157.5
79.7
46.7
40.3
34.0
31.6
26.3
23.4
22.0
20.7
16.3
ppm

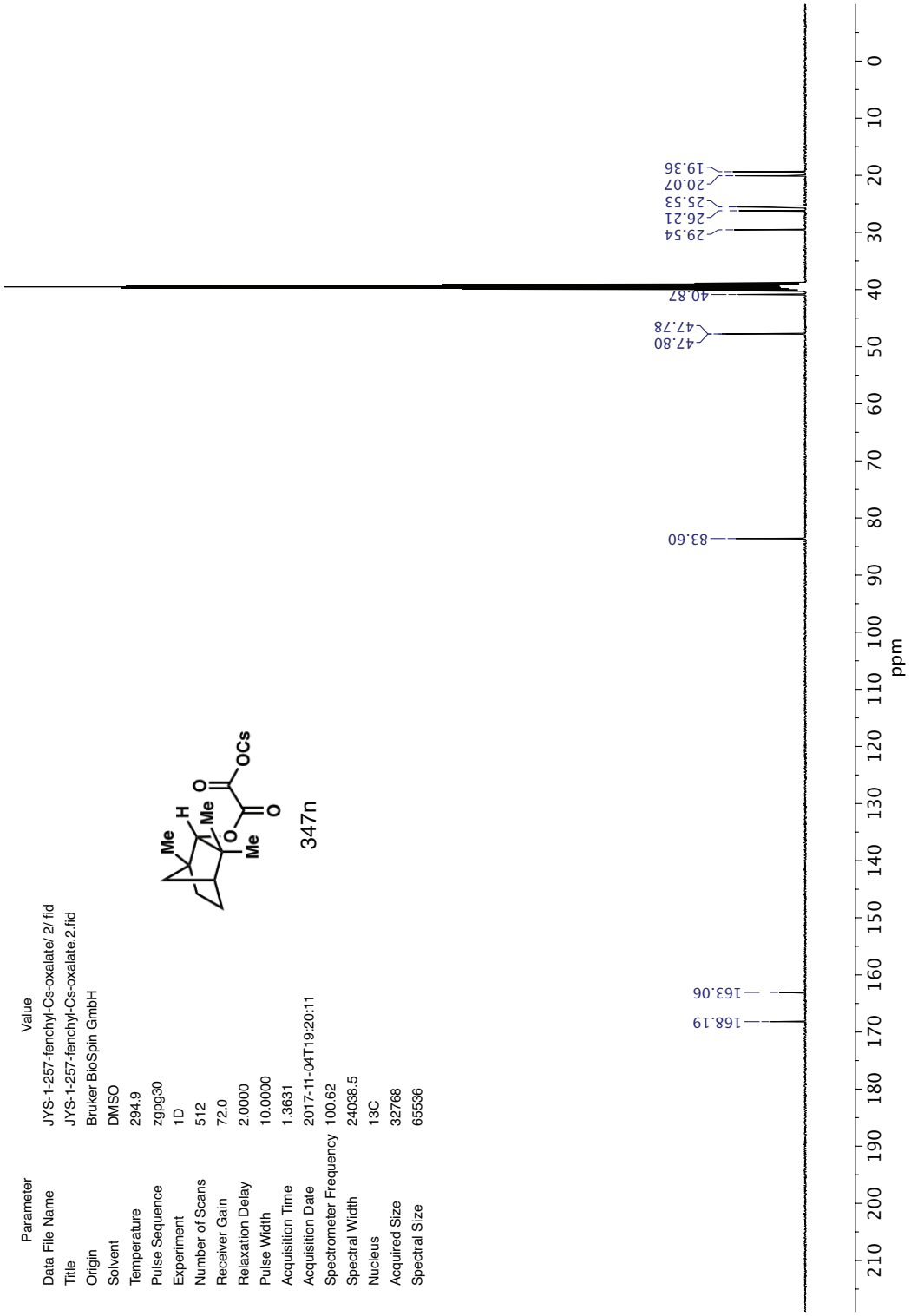

Parameter
Value
Data File Name / Volumes/ nmrdata/ dgrunenf/ nmr/ DCG-5-181-S/ 1/ fid
Title DCG-5-181-S.1.fid
Origin Bruker BioSpin GmbH
Solvent D2O
Temperature 294.9
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 112.8
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-11-21T15:09:13
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
Me
iPr
OCs
347m
1.01
1.00
2.01
2.02
2.00
2.02
7.07
3.03
ppm

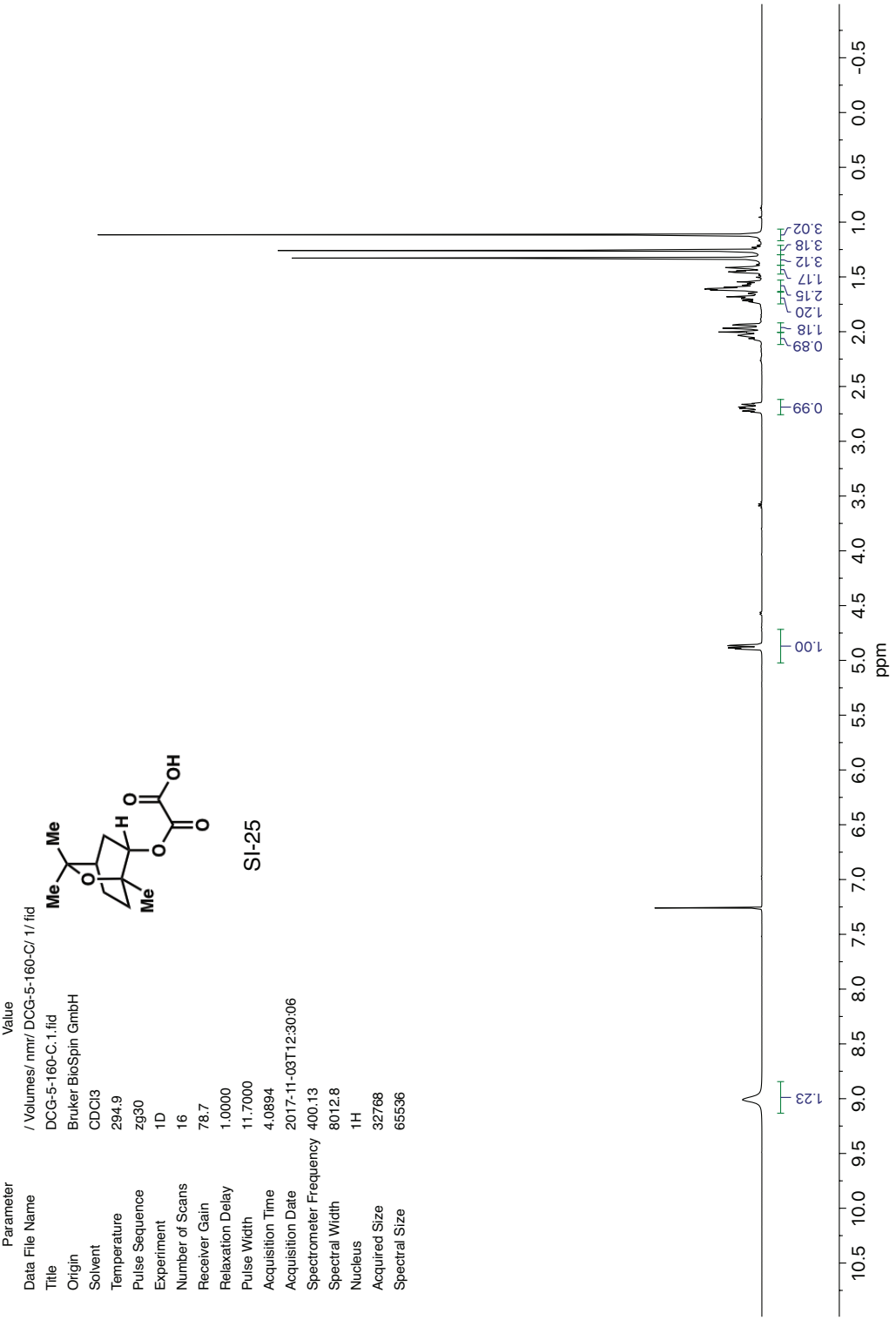

Parameter
Value
Data File Name / Volumes/ nmrdata/ dgrunenf/ nmr/ DCG-5-181-S/ 2/ fid
Title DCG-5-181-S.2.fid
Origin Bruker BioSpin GmbH
Solvent D2O
Temperature 295.0
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-11-21T15:24:54
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
iPr
OCs
347m
167.3
167.2
80.0
49.1
42.6
36.3
33.7
28.6
25.8
24.0
22.5
18.4
ppm

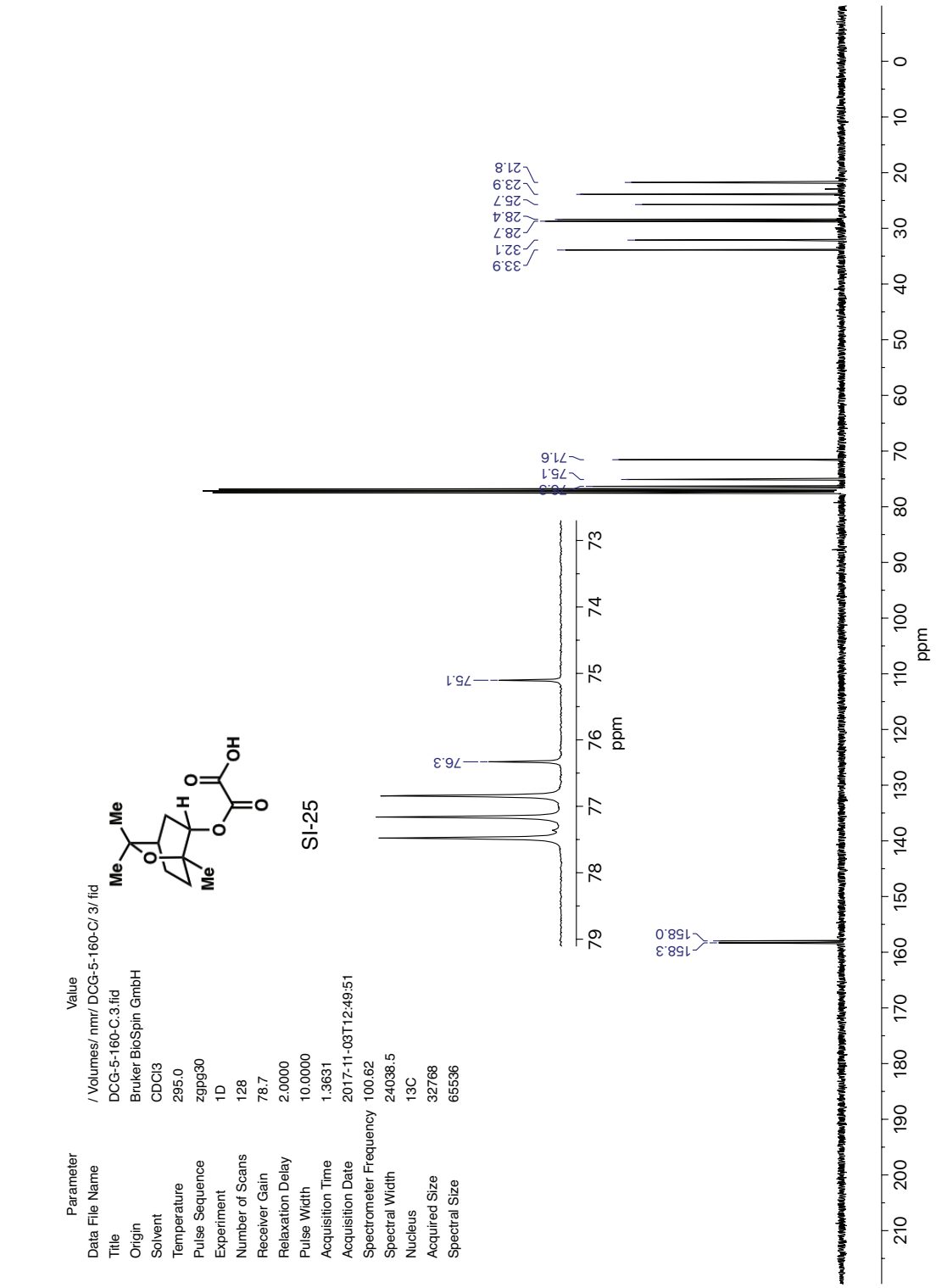

Parameter
Value
Data File Name
JYS-1-180-F1-fenchyl-Me-oxalate/ 1/ fid
Title
JYS-1-180-F1-fenchyl-Me-oxalate.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.0
Pulse Sequence
zg30
Experiment
1D
Number of Scans
16
Receiver Gain
30.3
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2017-11-04T18:15:04
Spectrometer Frequency
400.13
Spectral Width
8012.8
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
Me
H
Me
O
OMe
O
Me
O
SI-23
1.05
3.30
1.13
2.17
1.22
1.14
1.16
4.42
3.31
3.24
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
ppm

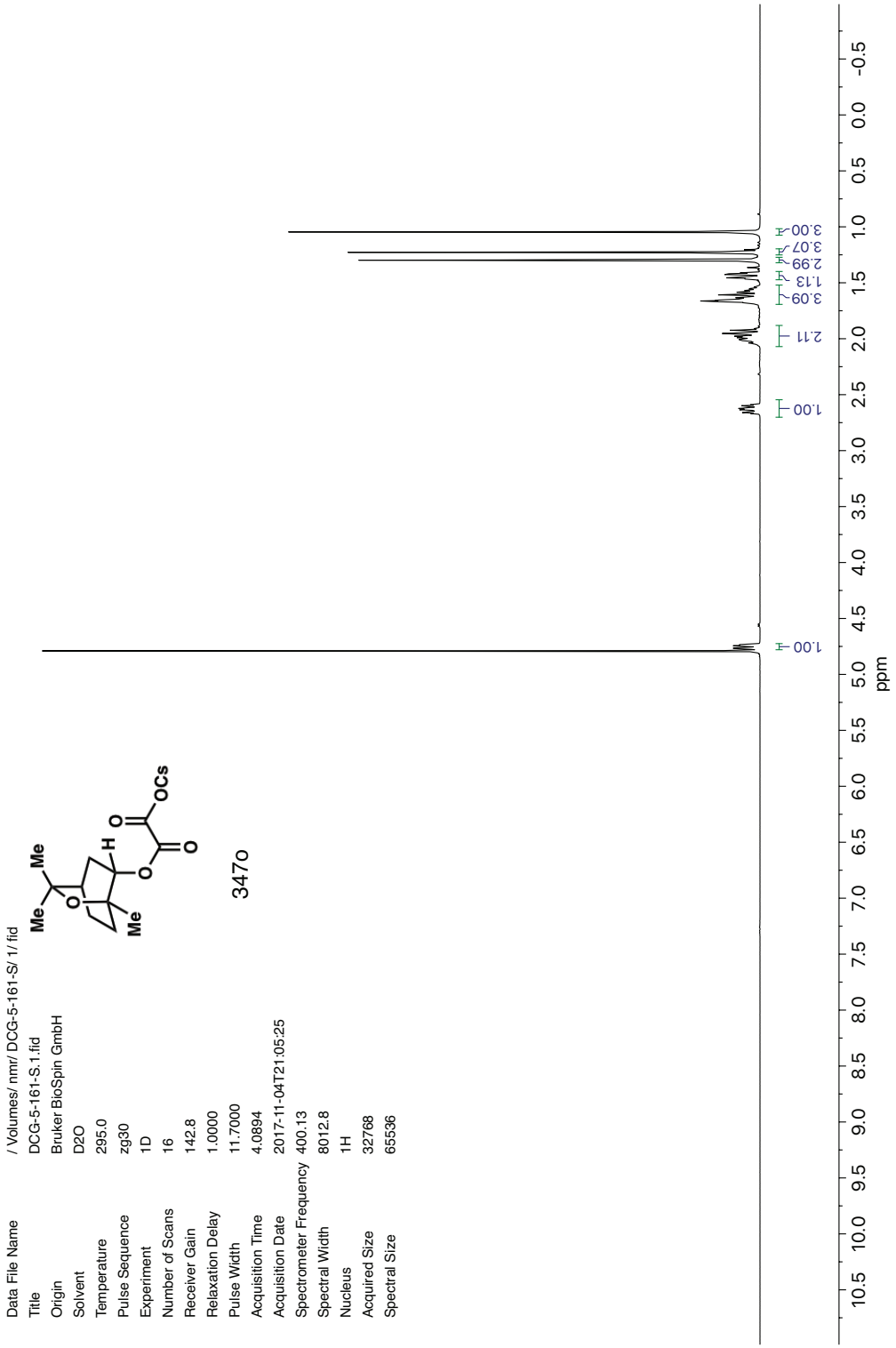

Parameter Value
Data File Name JYS-1-180-F1-fenchyl-Me-oxalate/ 2/ fid
Title JYS-1-180-F1-fenchyl-Me-oxalate.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 512
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-11-04T18:44:48
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
H
Me
O
OMe
O
Me
O
SI-23
158.7
158.4
89.6
53.5
48.6
48.4
41.5
39.9
29.8
26.6
25.9
20.2
19.4
ppm

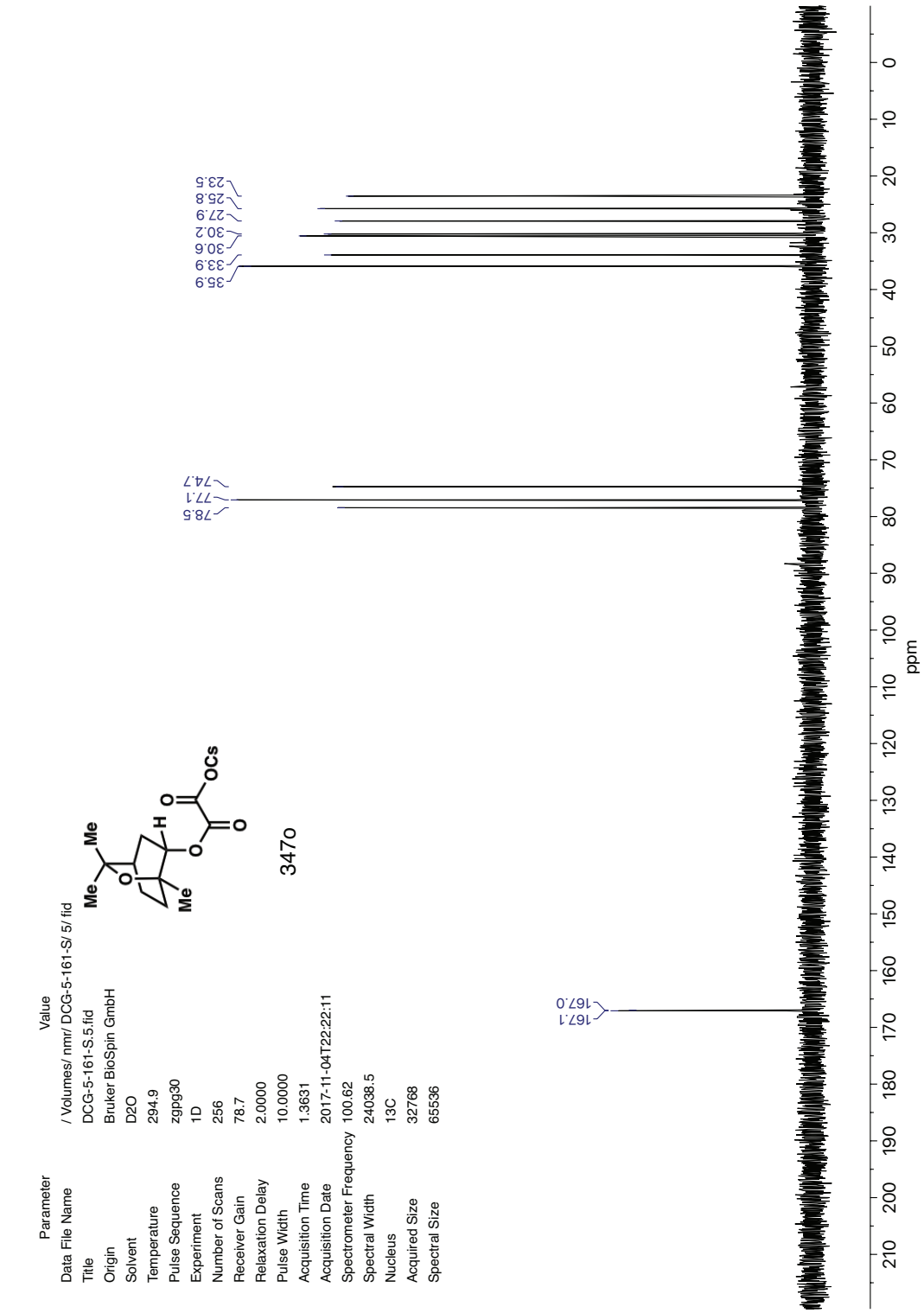

Parameter Value
Data File Name JYS-1-257-fenchyl-Cs-oxalate/ 1/ fid
Title JYS-1-257-fenchyl-Cs-oxalate.1.fid
Origin Bruker BioSpin GmbH
Solvent DMSO
Temperature 294.9
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 112.8
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-11-04T18:49:52
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
Me
H
Me
O
OCs
O
Me
O
347n
1.00
3.98
1.05
1.06
3.75
3.13
2.87
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm

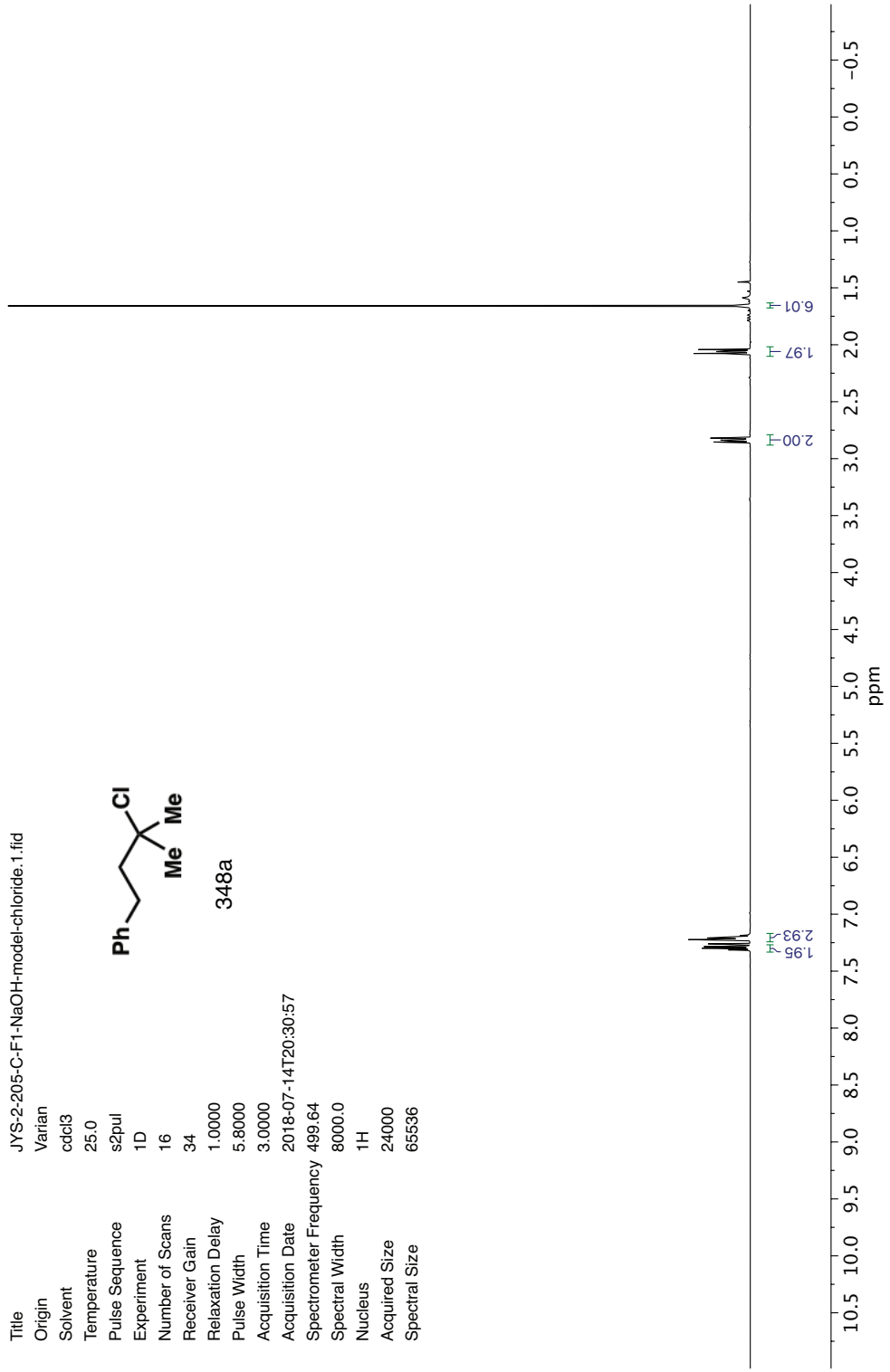

Parameter Value
Data File Name JYS-1-257-fenchyl-Cs-oxalate/ 2/ fid
Title JYS-1-257-fenchyl-Cs-oxalate.2.fid
Origin Bruker BioSpin GmbH
Solvent DMSO
Temperature 294.9
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 512
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-11-04T19:20:11
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
H
Me
O
OCs
O
O
Me
347n
168.19
163.06
83.60
47.80
47.78
40.87
29.54
26.21
25.53
20.07
19.36
ppm

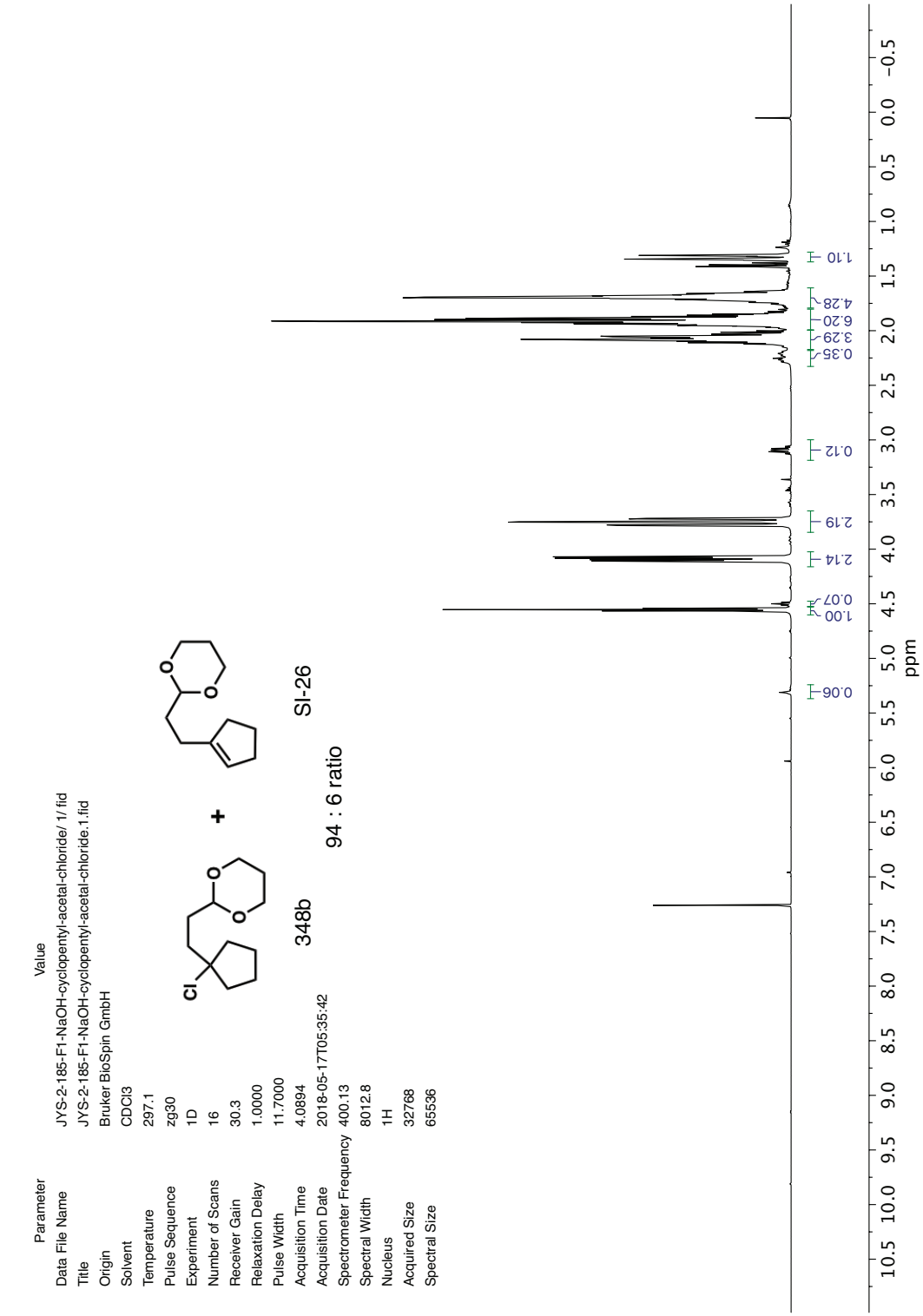

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-160-C/ 1/ fid
Title DCG-5-160-C.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 78.7
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-11-03T12:30:06
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
SI-25
1.23
1.00
0.99
0.89
1.18
1.20
2.15
1.17
3.12
3.18
3.02
ppm

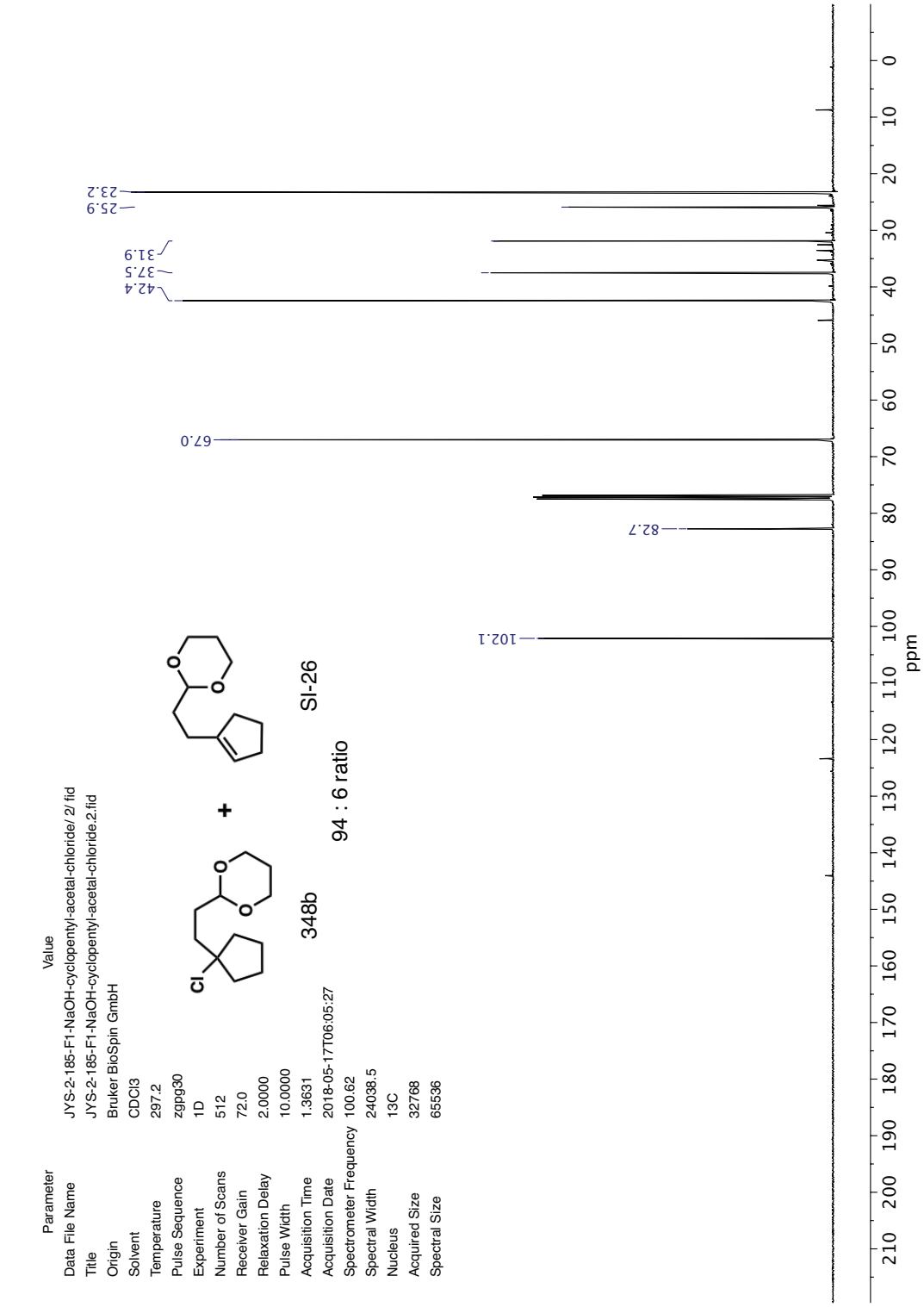

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-160-C/ 3/ fid
Title DCG-5-160-C.3.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 128
Receiver Gain 78.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-11-03T12:49:51
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
SI-25
158.3
158.0
76.3
75.1
77.3
75.1
71.6
33.9
32.1
28.7
28.4
25.7
23.9
21.8
ppm

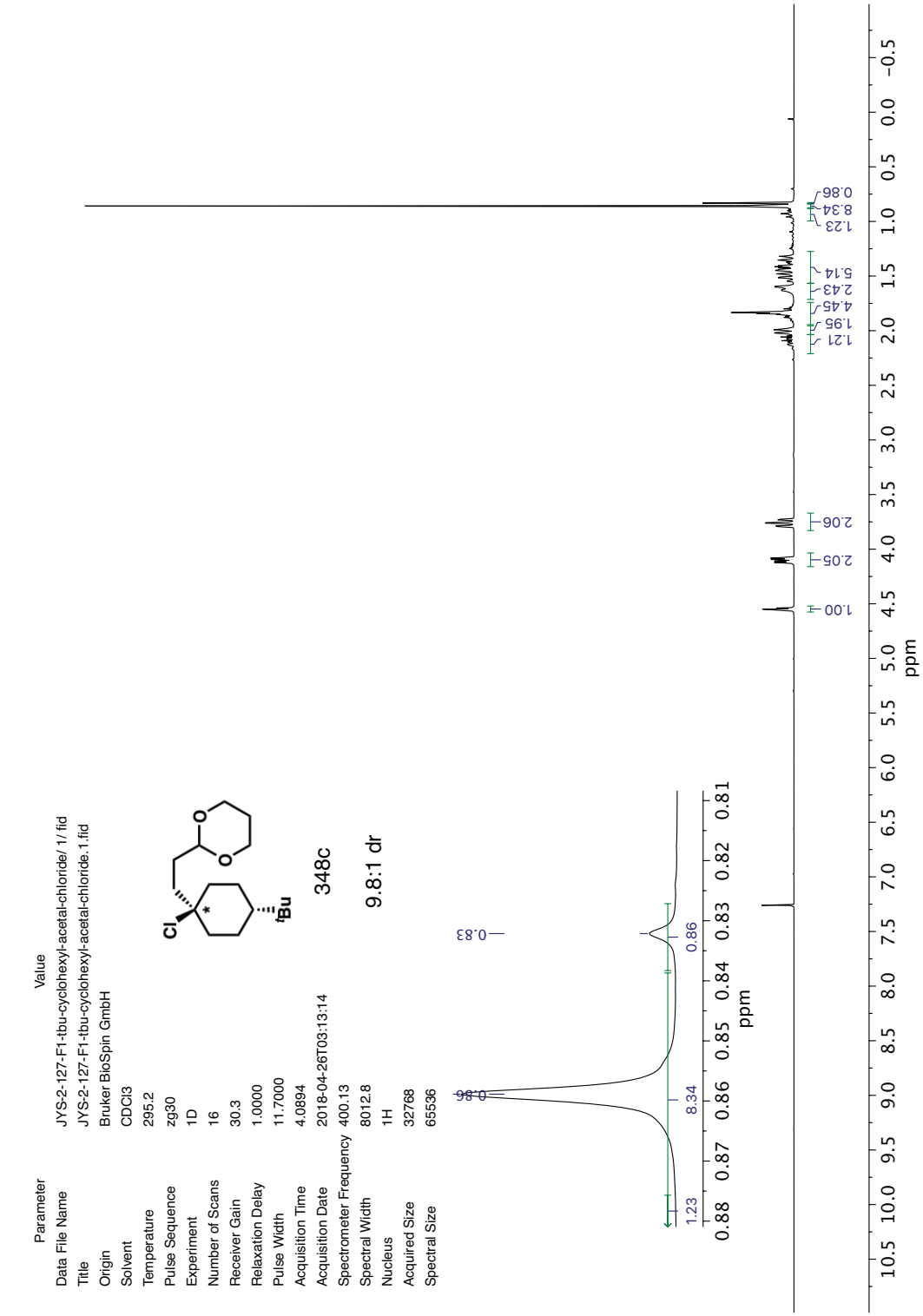

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-161-S/ 1/ fid
Title DCG-5-161-S.1.fid
Origin Bruker BioSpin GmbH
Solvent D2O
Temperature 295.0
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 142.8
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-11-04T21:05:25
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
Me
Me
O
H
O
OCs
O
O
Me
347o
1.00
2.11
3.09
1.13
2.99
3.07
3.00
1.00
ppm
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5

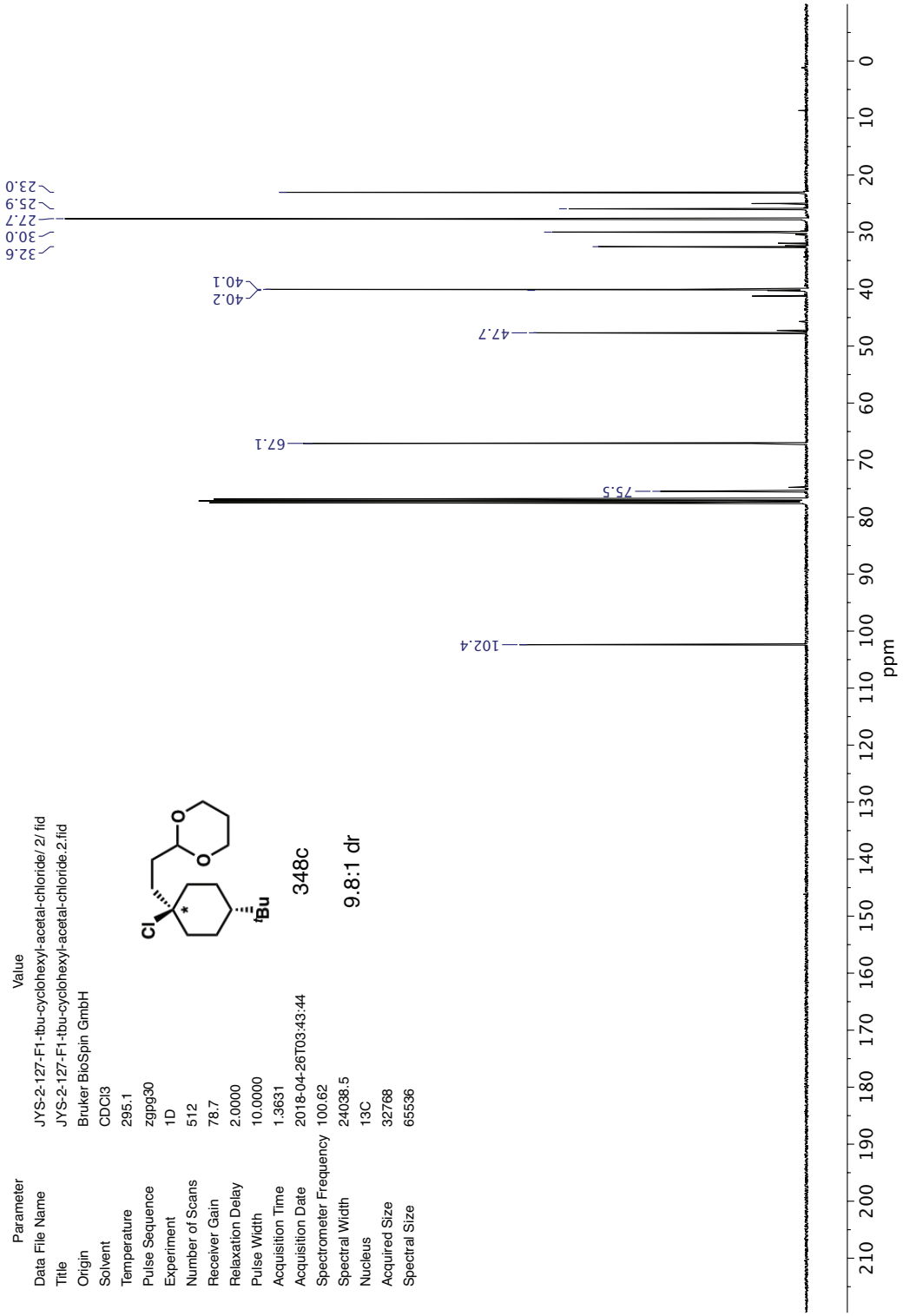

Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-161-S/ 5/ fid
Title DCG-5-161-S.5.fid
Origin Bruker BioSpin GmbH
Solvent D2O
Temperature 294.9
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 78.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-11-04T22:22:11
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
Me
O
H
O
O
O
OCs
Me
347o
167.1
167.0
78.5
77.1
74.7
35.9
33.9
30.6
30.2
27.9
25.8
23.5
ppm

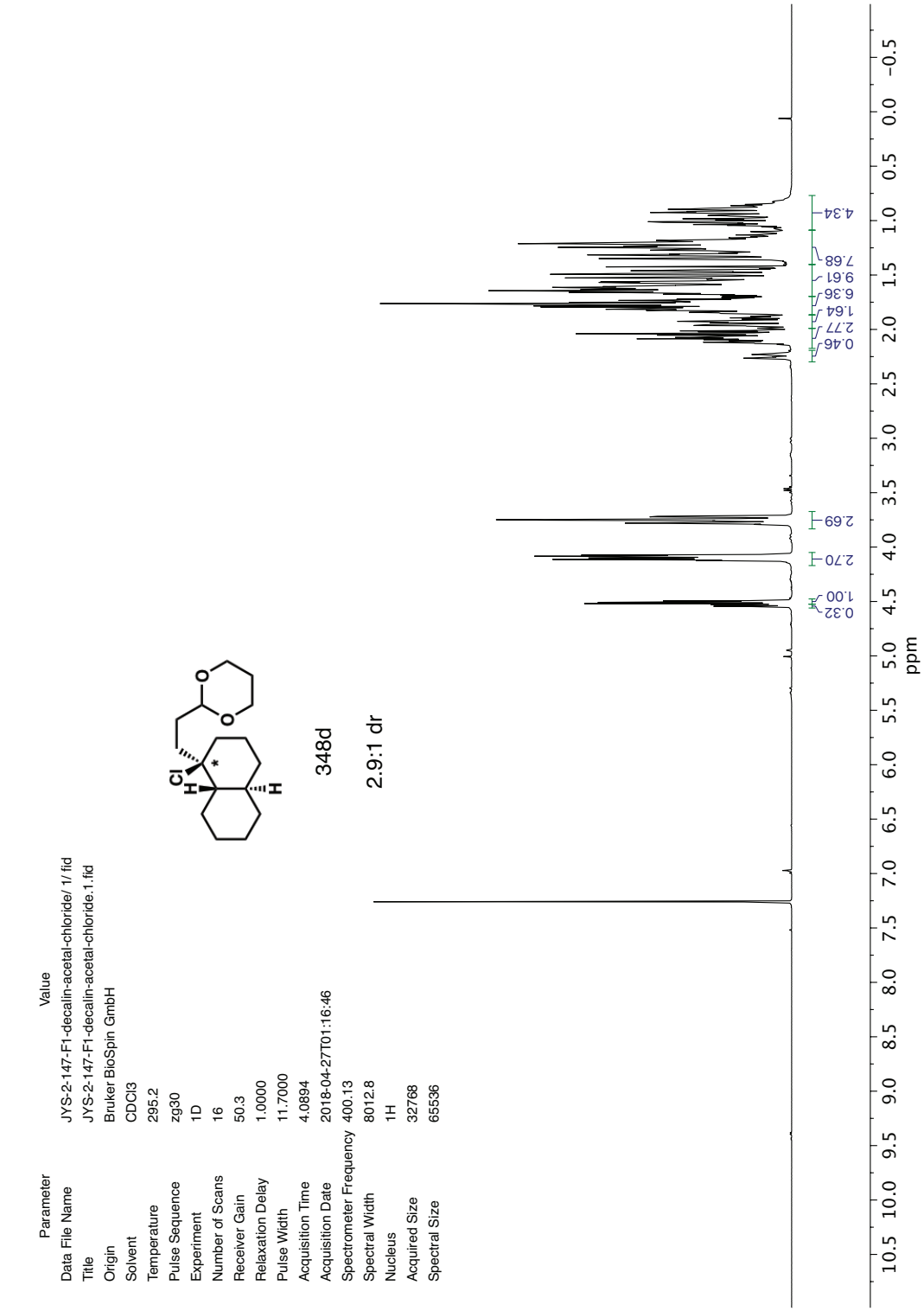

Parameter
Value
Data File Name
JYS-2-205-C-F1-NaOH-model-chloride/1/fid
Title
JYS-2-205-C-F1-NaOH-model-chloride.1.fid
Origin
Varian
Solvent
cdcl3
Temperature
25.0
Pulse Sequence
s2pul
Experiment
1D
Number of Scans
16
Receiver Gain
34
Relaxation Delay
1.0000
Pulse Width
5.8000
Acquisition Time
3.0000
Acquisition Date
2018-07-14T20:30:57
Spectrometer Frequency
499.64
Spectral Width
8000.0
Nucleus
1H
Acquired Size
24000
Spectral Size
65536
Ph
Cl
Me
Me
348a
1.95
2.93
2.00
1.97
6.01
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
ppm

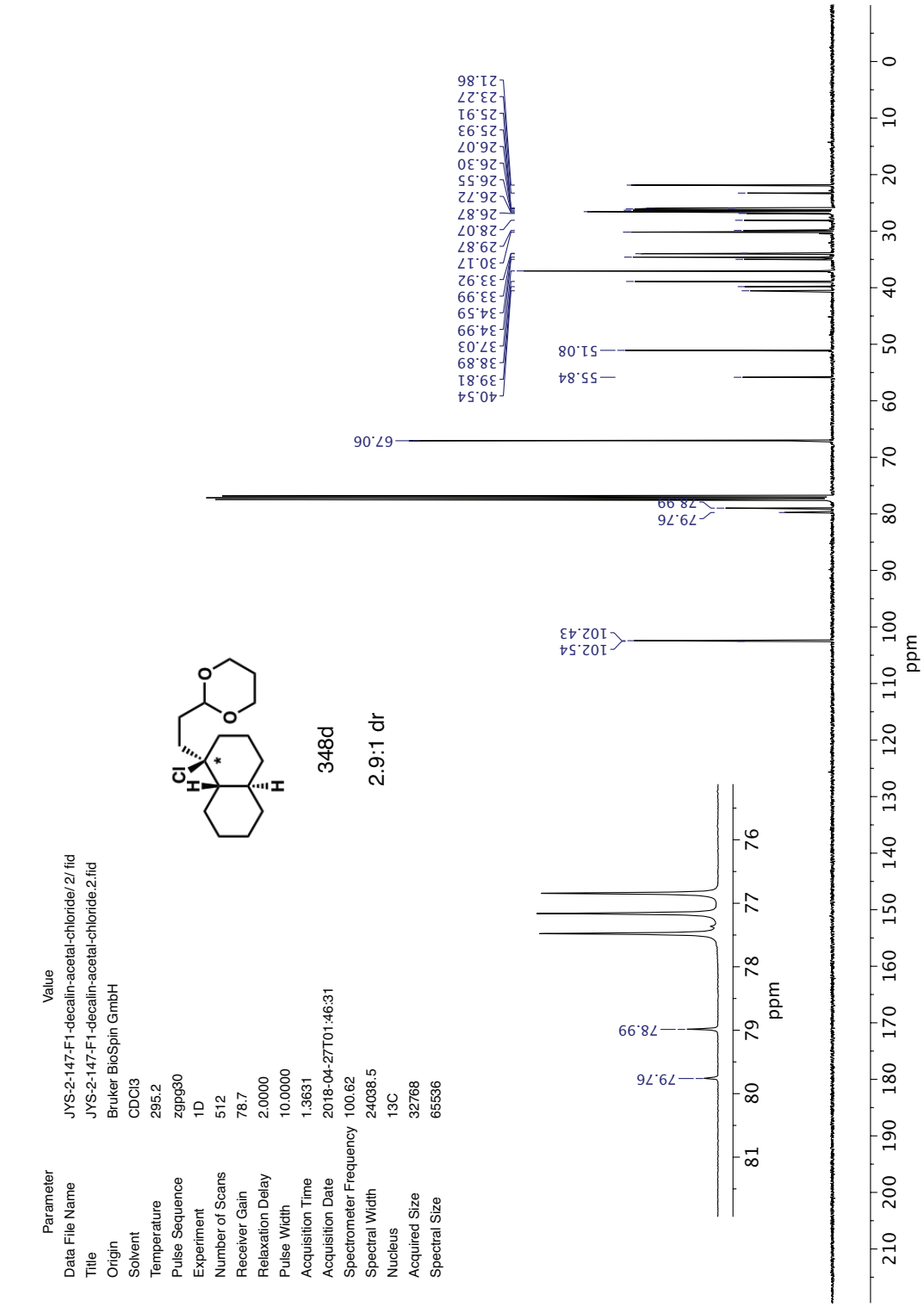

Parameter
Value
Data File Name JYS-2-185-F1-NaOH-cyclopentyl-acetal-chloride/ 1/ fid
Title JYS-2-185-F1-NaOH-cyclopentyl-acetal-chloride.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 297.1
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 30.3
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-05-17T05:35:42
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
Cl
348b
+
SI-26
94 : 6 ratio
0.06
1.00
0.07
2.14
2.19
0.12
0.35
3.29
6.20
4.28
1.10
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
ppm

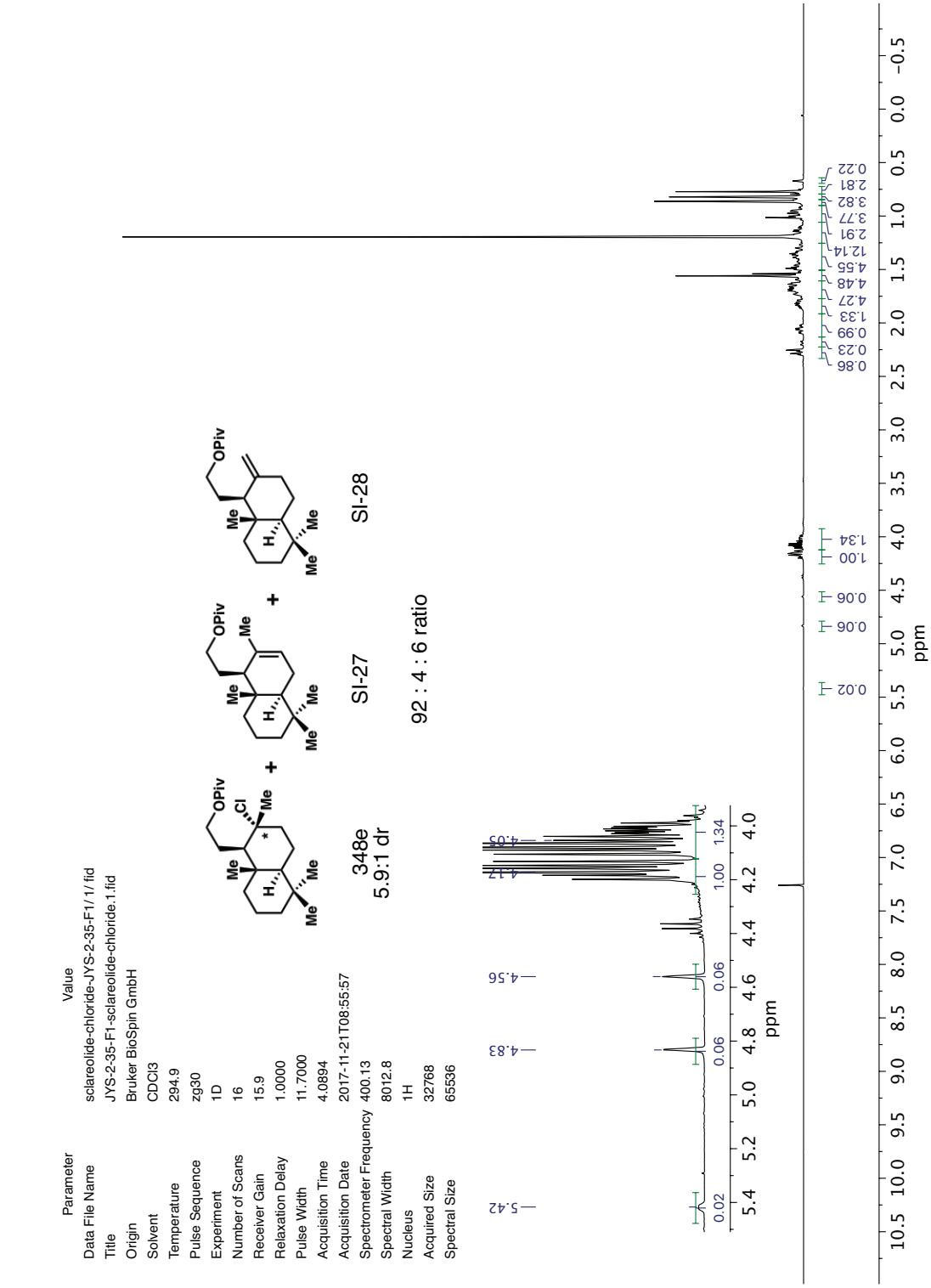

Parameter
Value
Data File Name JYS-2-185-F1-NaOH-cyclopentyl-acetal-chloride/ 2/ fid
Title JYS-2-185-F1-NaOH-cyclopentyl-acetal-chloride.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 297.2
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 512
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-05-17T06:05:27
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
348b
+
94 : 6 ratio
SI-26
Cl
23.2
25.9
31.9
37.5
42.4
67.0
82.7
102.1
ppm

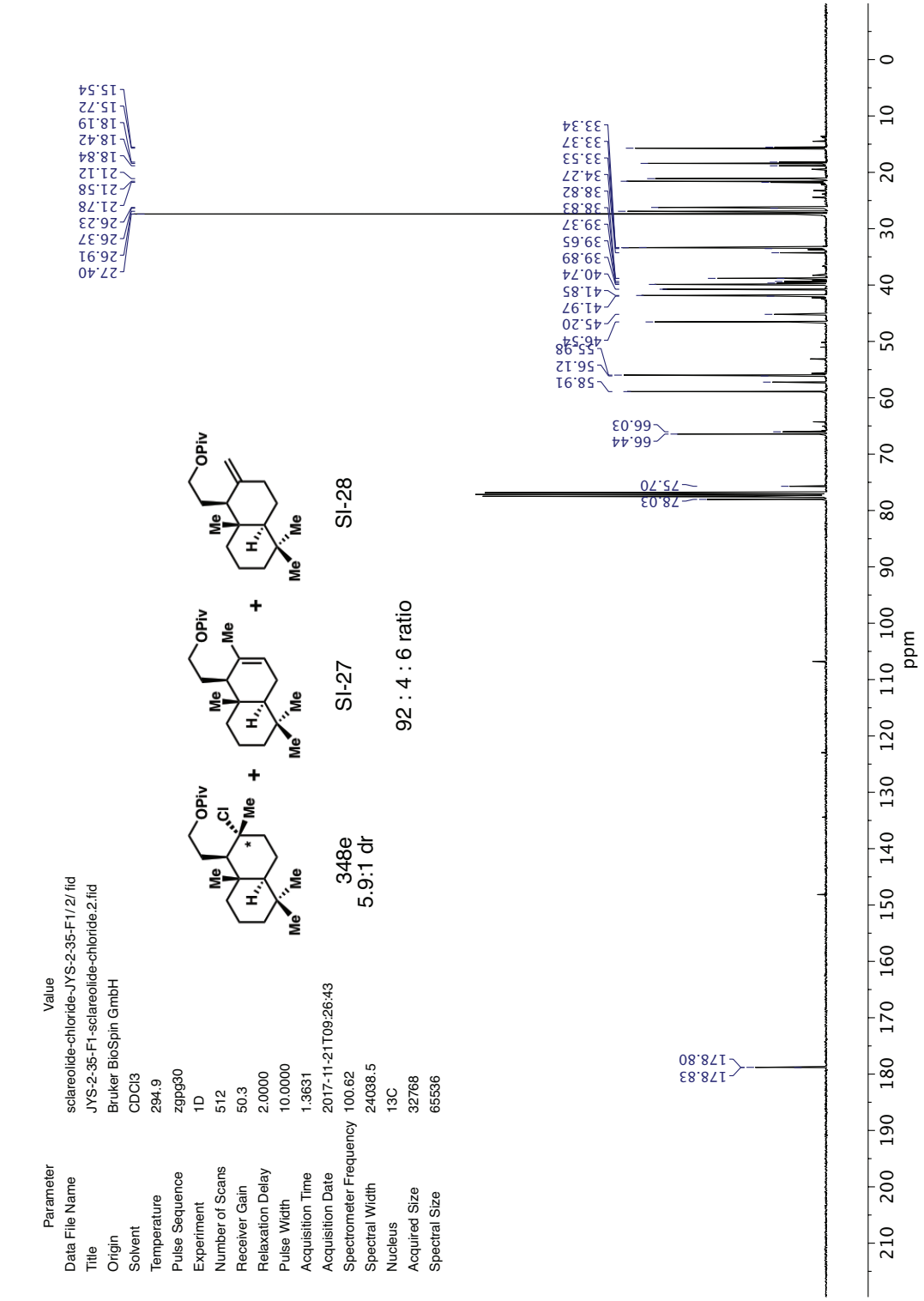

Parameter
Value
Data File Name JYS-2-127-F1-tbu-cyclohexyl-acetal-chloride/ 1/ fid
Title JYS-2-127-F1-tbu-cyclohexyl-acetal-chloride. 1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 30.3
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-04-26T03:13:14
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
348c
9.8:1 dr
Cl
tBu
0.83
0.86
1.23
8.34
0.88 0.87 0.86 0.85 0.84 0.83 0.82 0.81
ppm
1.00
2.05
2.06
1.21
1.95
4.45
2.43
5.14
1.23
8.34
0.86
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
ppm

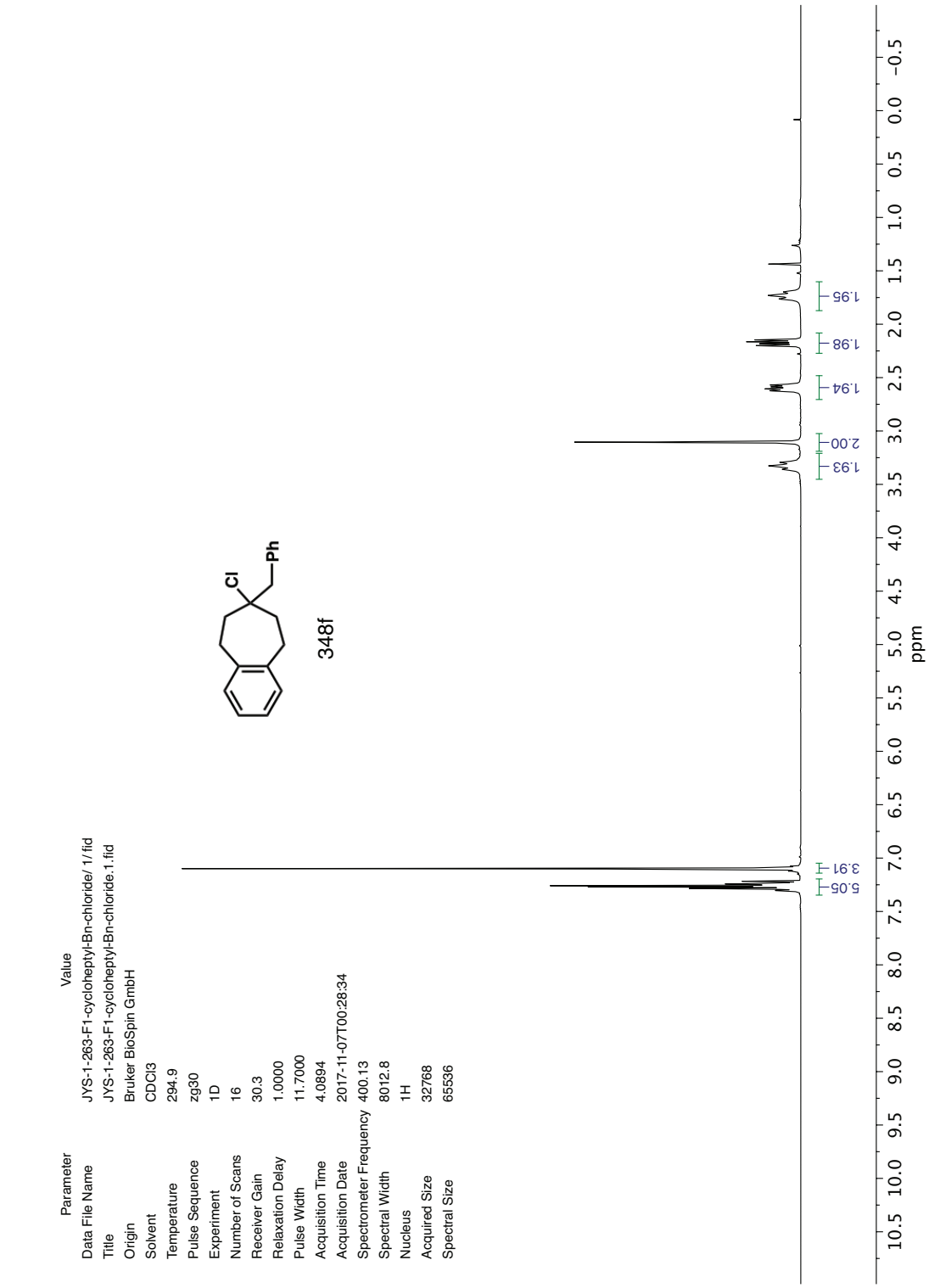

Parameter
Value
Data File Name
JYS-2-127-F1-tbu-cyclohexyl-acetal-chloride/ 2/ fid
Title
JYS-2-127-F1-tbu-cyclohexyl-acetal-chloride.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.1
Pulse Sequence
zgpg30
Experiment
1D
Number of Scans
512
Receiver Gain
78.7
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-04-26T03:43:44
Spectrometer Frequency
100.62
Spectral Width
24038.5
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
348c
9.8:1 dr
Cl
tBu
O
O
102.4
75.5
67.1
47.7
40.2
40.1
32.6
30.0
27.7
25.9
23.0
ppm

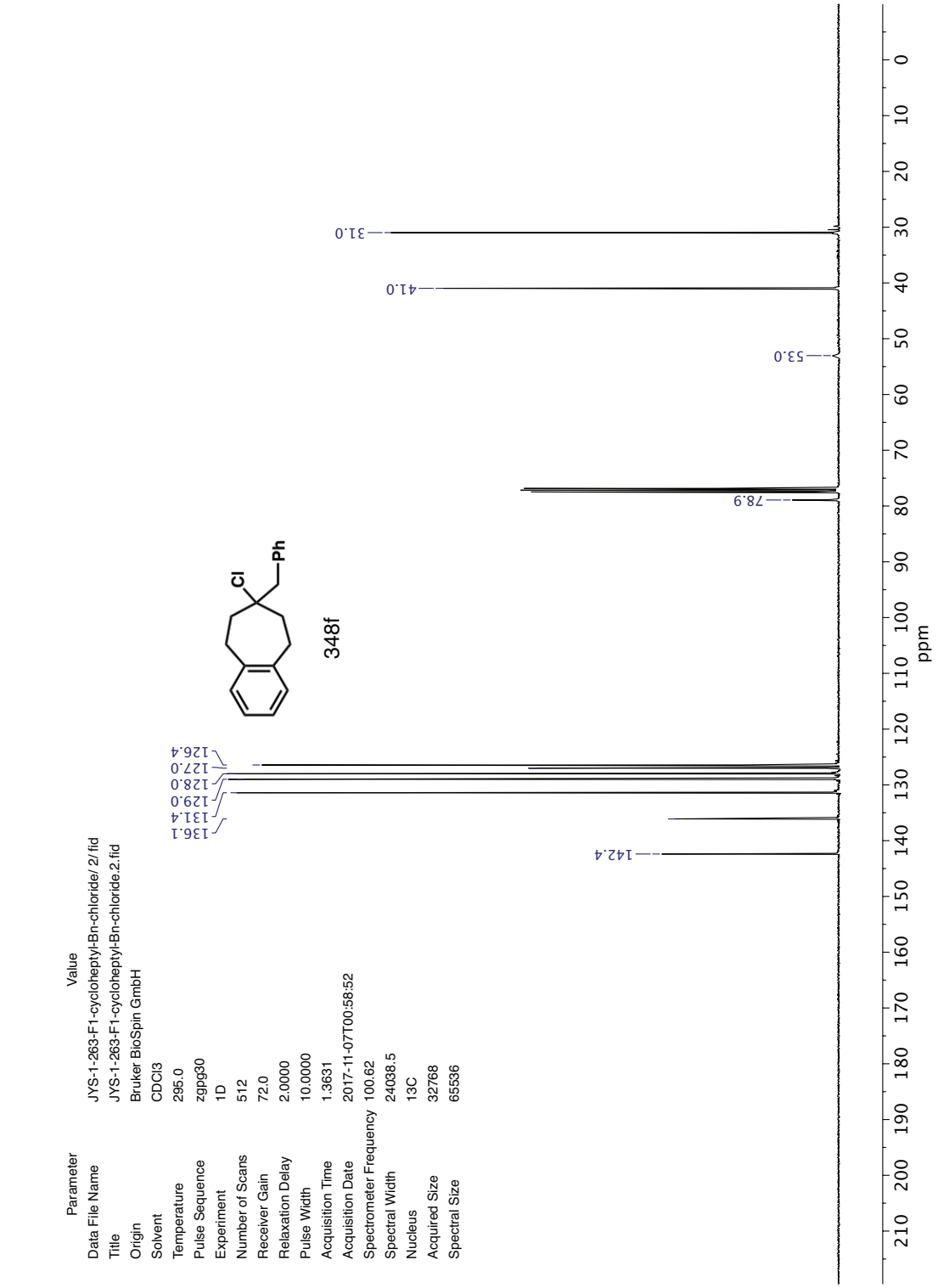

Parameter Value
Data File Name JYS-2-147-F1-decalin-acetal-chloride/ 1/ fid
Title JYS-2-147-F1-decalin-acetal-chloride.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 50.3
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-04-27T01:16:46
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
348d
2.9:1 dr
Cl
H
H
0.32
1.00
2.70
2.69
0.46
2.77
1.64
6.36
9.61
7.68
4.34
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
ppm

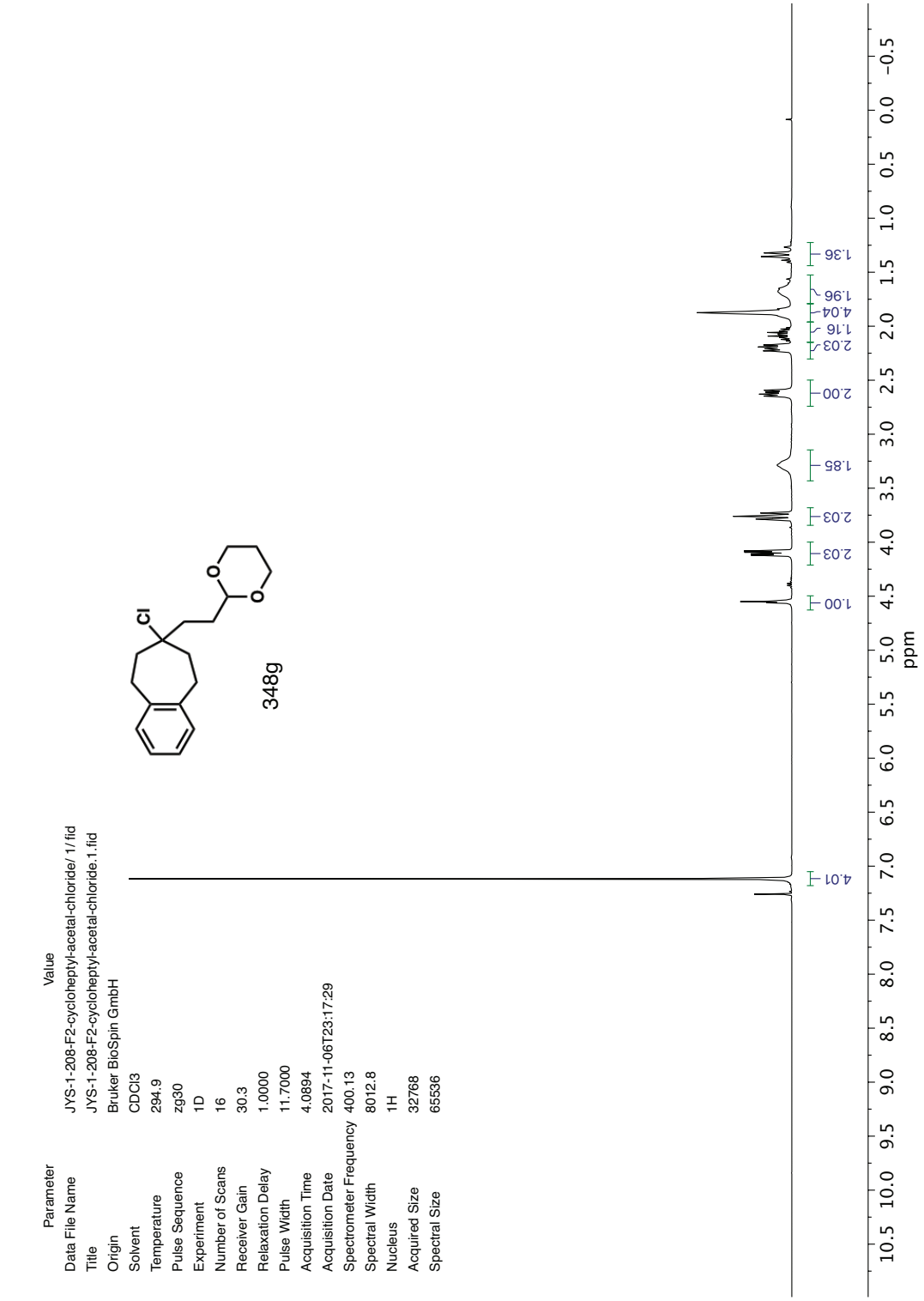

Parameter Value
Data File Name JYS-2-147-F1-decalin-acetal-chloride/ 2/ fid
Title JYS-2-147-F1-decalin-acetal-chloride.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 512
Receiver Gain 78.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-04-27T01:46:31
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
348d
2.9:1 dr
Cl
H
H
O
O
*
102.54
102.43
79.76
78.99
67.06
55.84
51.08
40.54
39.81
38.89
37.03
34.99
34.59
33.99
33.92
30.17
29.87
28.07
26.87
26.72
26.55
26.30
26.07
25.93
25.91
23.27
21.86
ppm
ppm

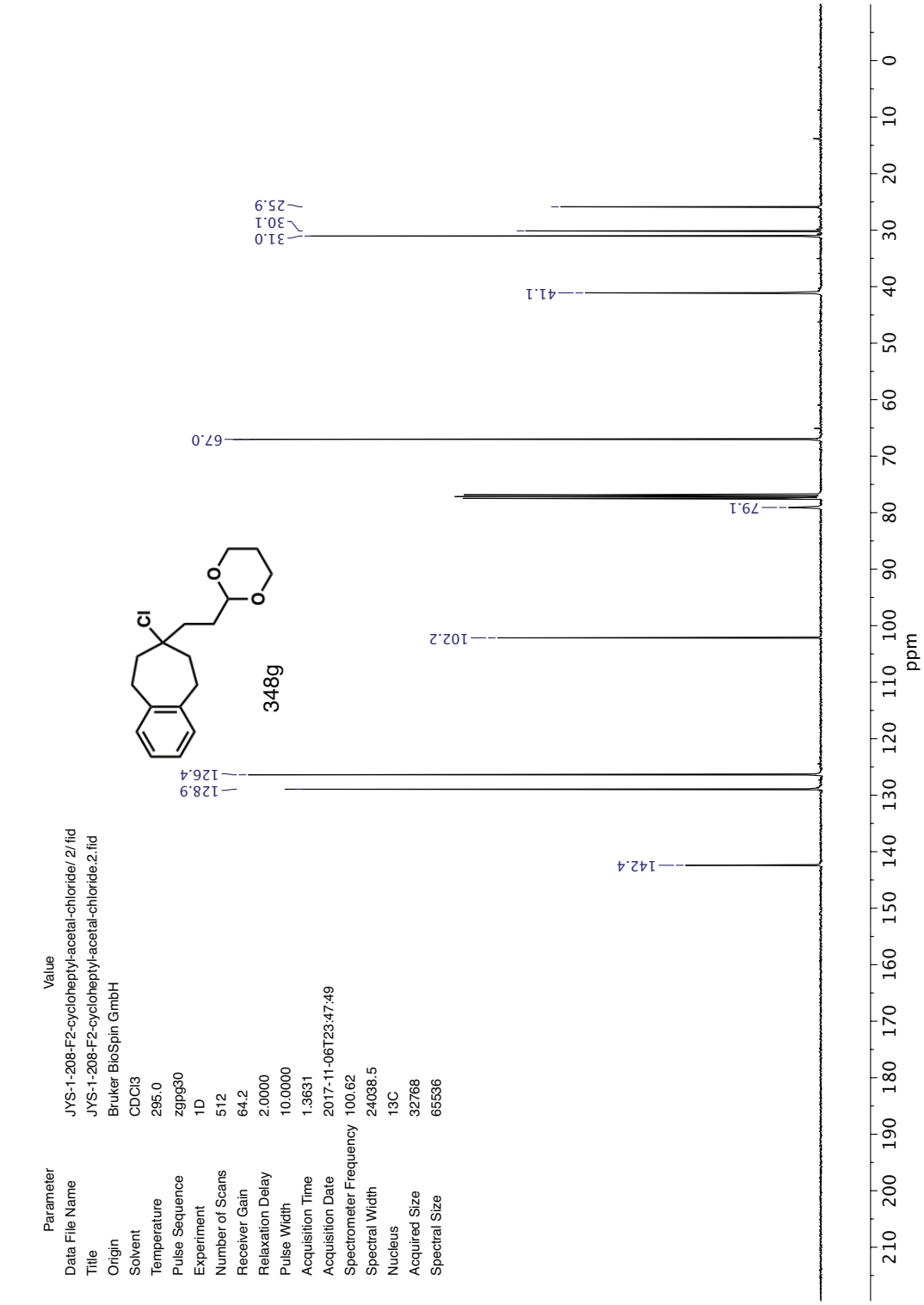

Parameter Value
Data File Name sclareolide-chloride-JYS-2-35-F1/1/fid
Title JYS-2-35-F1-sclareolide-chloride.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 15.9
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-11-21T08:55:57
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
OPiv
Cl
Me
H
Me
Me
348e
5.9:1 dr
Sl-27
Sl-28
92 : 4 : 6 ratio
5.42
4.83
4.56
4.17
4.05
0.02
0.06
0.06
1.00
1.34
0.02
0.06
0.06
1.00
1.34
0.86
0.23
0.99
1.33
4.27
4.48
4.55
12.14
2.91
3.77
3.82
2.81
0.22
ppm

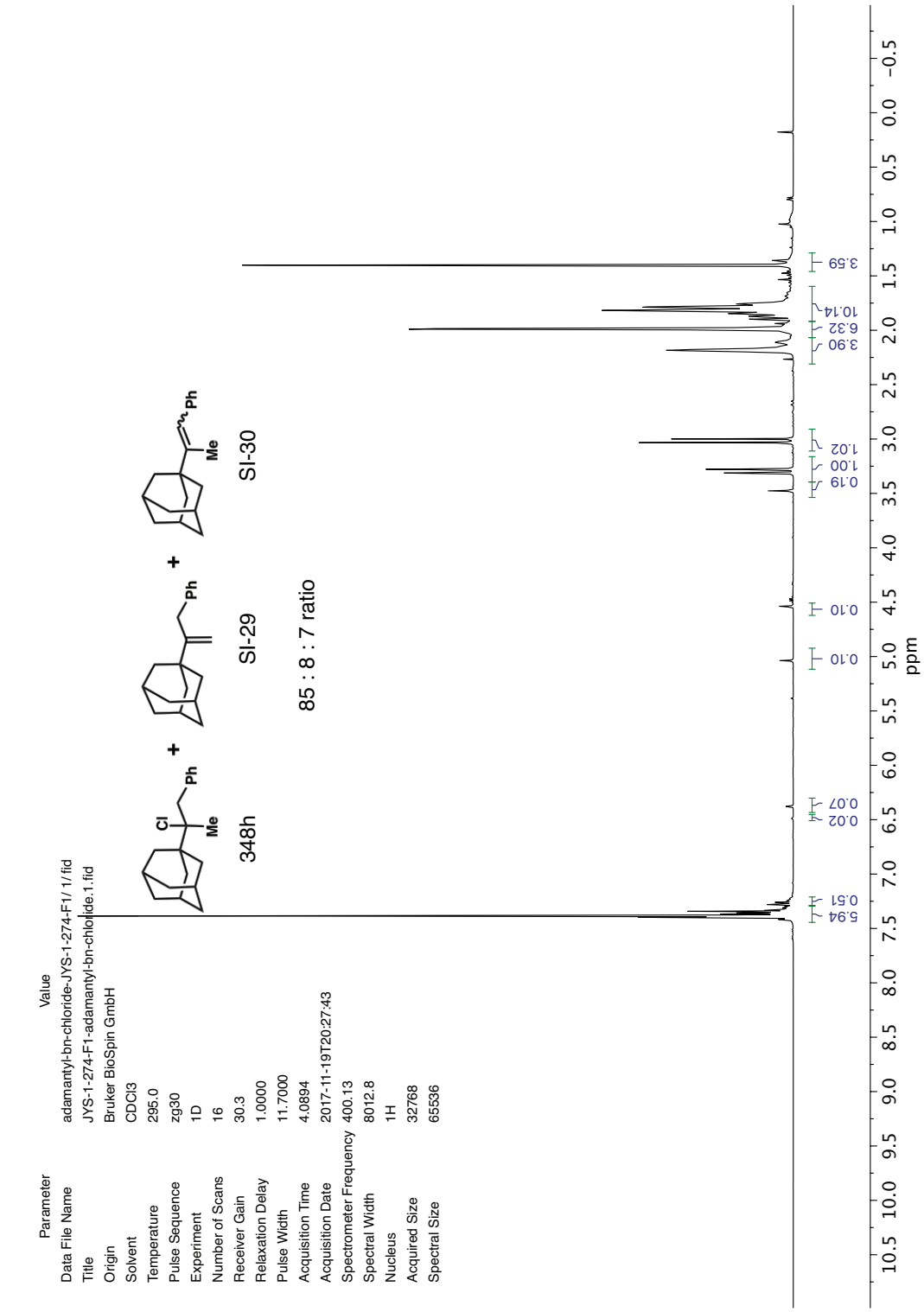

Parameter Value
Data File Name sclareolide-chloride-JYS-2-35-F1/2/ fid
Title JYS-2-35-F1-sclareolide-chloride.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 512
Receiver Gain 50.3
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-11-21T09:26:43
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
348e
5.9:1 dr
Sl-27
Sl-28
92 : 4 : 6 ratio
OPiv
Cl
Me
H
ppm

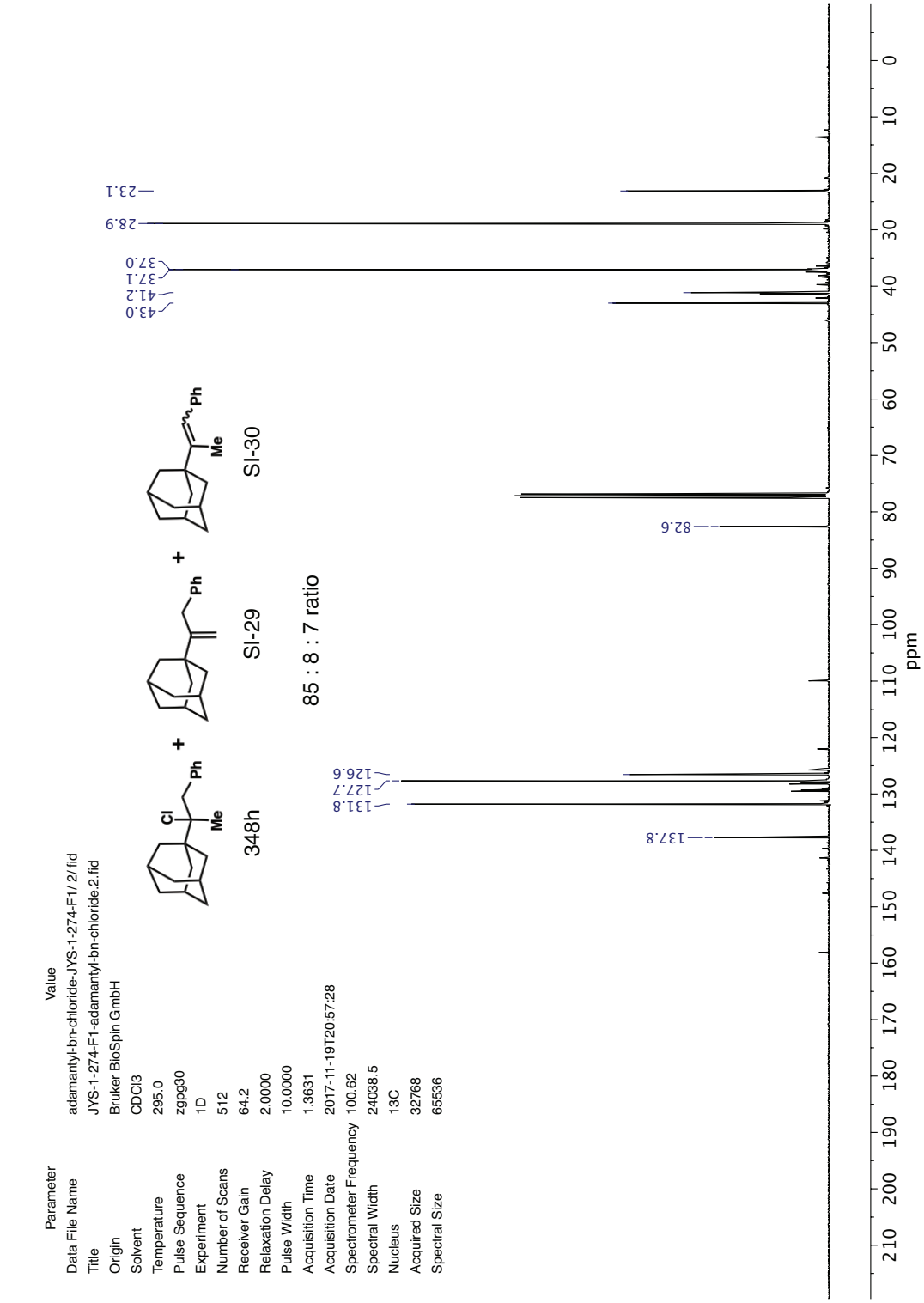

Parameter
Value
Data File Name
JYS-1-263-F1-cycloheptyl-Bn-chloride/ 1/ fid
Title
JYS-1-263-F1-cycloheptyl-Bn-chloride.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zg30
Experiment
1D
Number of Scans
16
Receiver Gain
30.3
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2017-11-07T00:28:34
Spectrometer Frequency
400.13
Spectral Width
8012.8
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
Cl
Ph
348f
5.05
3.91
1.93
2.00
1.94
1.98
1.95
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
ppm

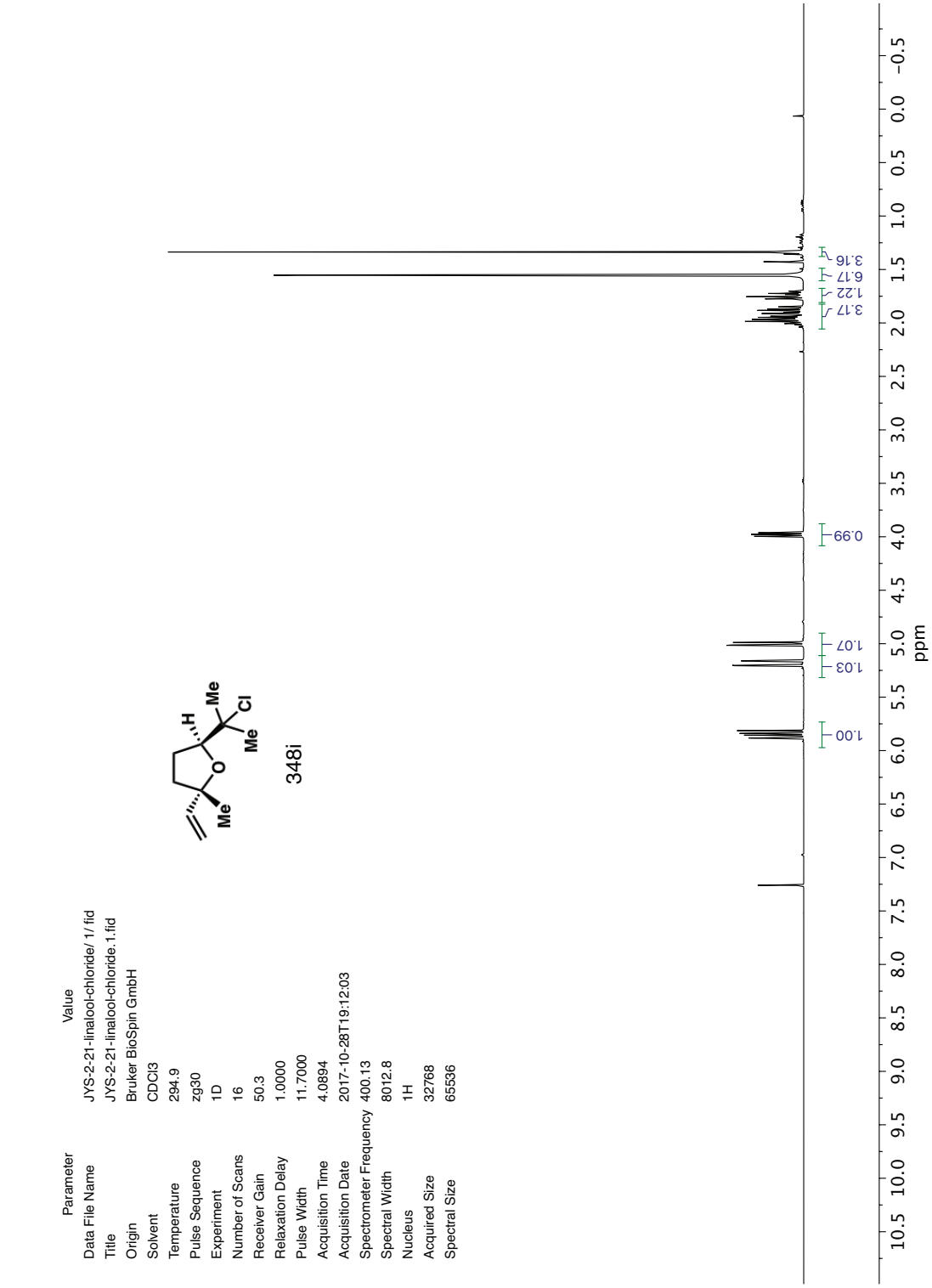

Parameter Value
Data File Name JYS-1-263-F1-cycloheptyl-Bn-chloride/ 2/ fid
Title JYS-1-263-F1-cycloheptyl-Bn-chloride.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 512
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-11-07T00:58:52
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
136.1
131.4
129.0
128.0
127.0
126.4
142.4
78.9
53.0
41.0
31.0
Cl
Ph
348f
ppm

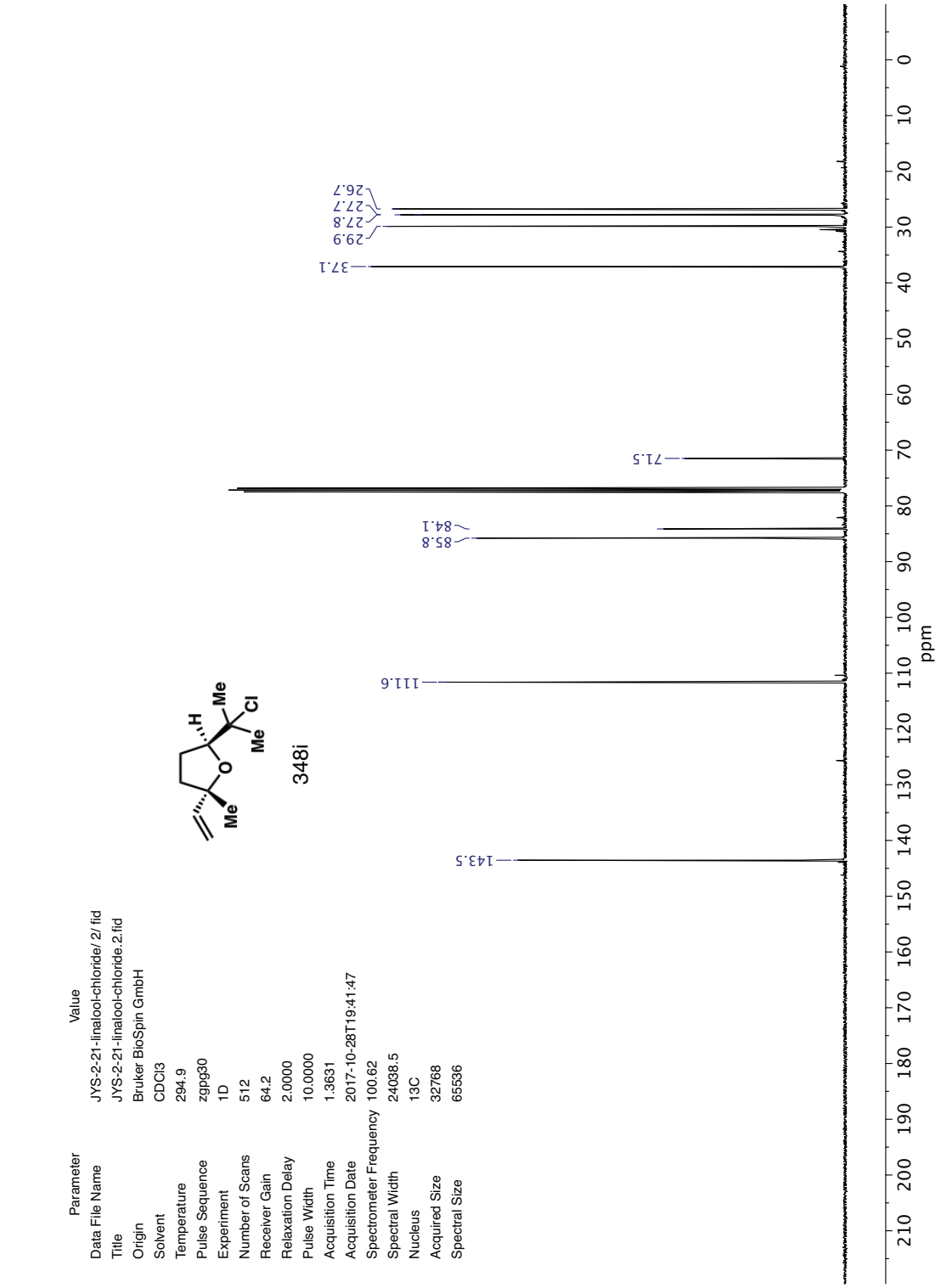

Parameter
Value
Data File Name
JYS-1-208-F2-cycloheptyl-acetal-chloride/ 1/ fid
Title
JYS-1-208-F2-cycloheptyl-acetal-chloride.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zg30
Experiment
1D
Number of Scans
16
Receiver Gain
30.3
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2017-11-06T23:17:29
Spectrometer Frequency
400.13
Spectral Width
8012.8
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
Cl
O
O
348g
4.01
1.00
2.03
2.03
1.85
2.00
2.03
1.16
4.04
1.96
1.36
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
ppm

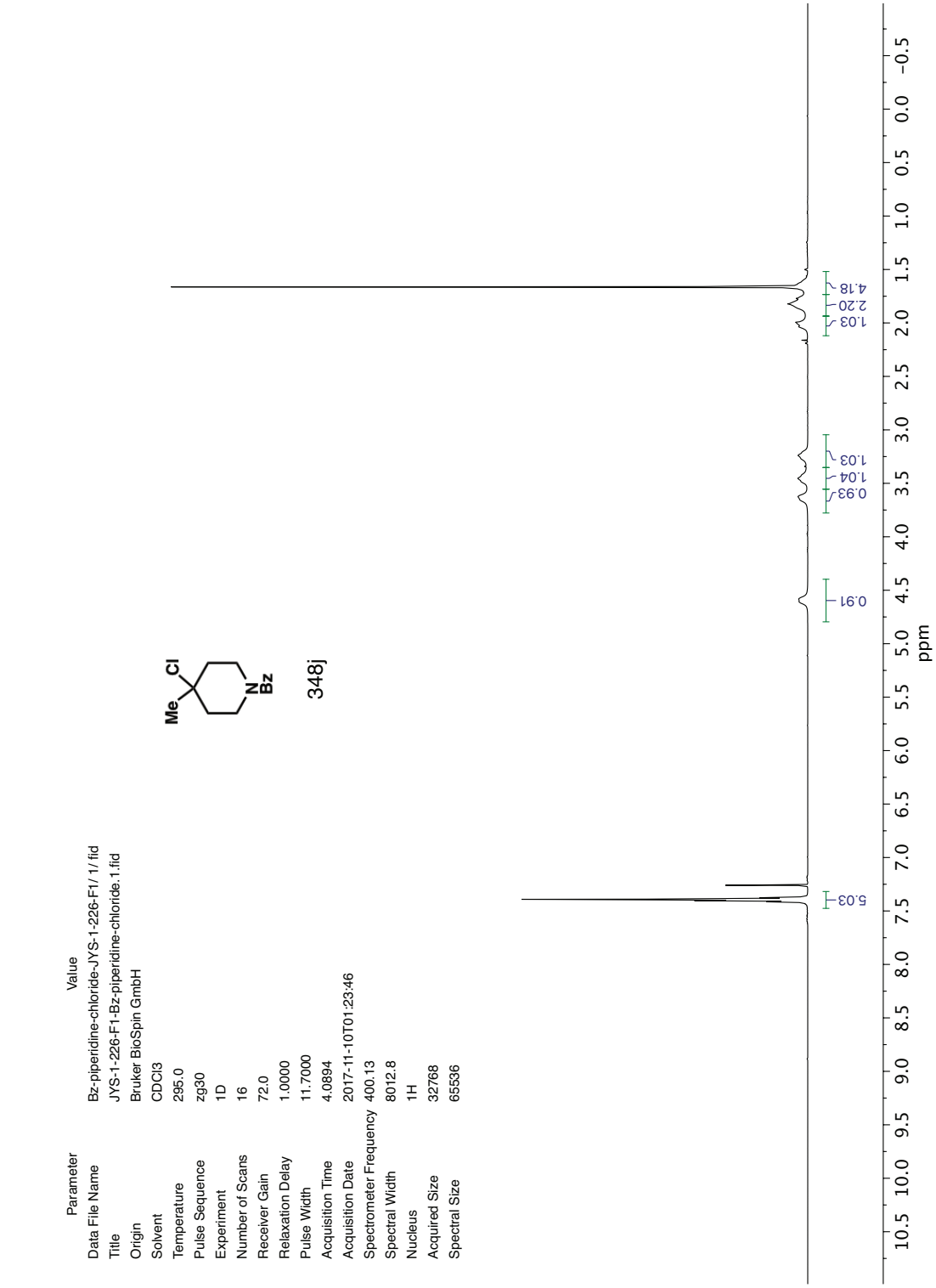

Parameter
Value
Data File Name
JYS-1-208-F2-cycloheptyl-acetal-chloride/ 2/ fid
Title
JYS-1-208-F2-cycloheptyl-acetal-chloride.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.0
Pulse Sequence
zgpg30
Experiment
1D
Number of Scans
512
Receiver Gain
64.2
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2017-11-06T23:47:49
Spectrometer Frequency
100.62
Spectral Width
24038.5
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
348g
Cl
O
O
142.4
128.9
126.4
102.2
79.1
67.0
41.1
31.0
30.1
25.9
ppm


Parameter Value
Data File Name adamantyl-bn-chloride-JYS-1-274-F1/ 1/ fid
Title JYS-1-274-F1-adamantyl-bn-chloride.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 30.3
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-11-19T20:27:43
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
Cl
Ph
Me
+
Ph
+
Ph
Me
348h
SI-29
SI-30
85 : 8 : 7 ratio
5.94
0.51
0.02
0.07
0.10
0.10
0.19
1.00
1.02
3.90
6.32
10.14
3.59
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
ppm


Parameter
Value
Data File Name
adamantyl-bn-chloride-JYS-1-274-F1/ 2/ fid
Title
JYS-1-274-F1-adamantyl-bn-chloride.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.0
Pulse Sequence
zgpg30
Experiment
1D
Number of Scans
512
Receiver Gain
64.2
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2017-11-19T20:57:28
Spectrometer Frequency
100.62
Spectral Width
24038.5
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Cl
Ph
Me
348h
+
Ph
SI-29
+
Ph
Me
SI-30
85 : 8 : 7 ratio
137.8
131.8
127.7
126.6
82.6
43.0
41.2
37.1
37.0
28.9
23.1
ppm


Parameter Value
Data File Name JYS-2-21-linalool-chloride/ 1/ fid
Title JYS-2-21-linalool-chloride.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 50.3
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-10-28T19:12:03
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
348i
Me
H
Me
Cl
Me
O
1.00
1.03
1.07
0.99
3.17
1.22
6.17
3.16
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm


Parameter Value
Data File Name JYS-2-21-linalool-chloride/ 2/ fid
Title JYS-2-21-linalool-chloride.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 512
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-10-28T19:41:47
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
348i
Me
H
Me
Cl
Me
O
143.5
111.6
85.8
84.1
71.5
37.1
29.9
27.8
27.7
26.7
ppm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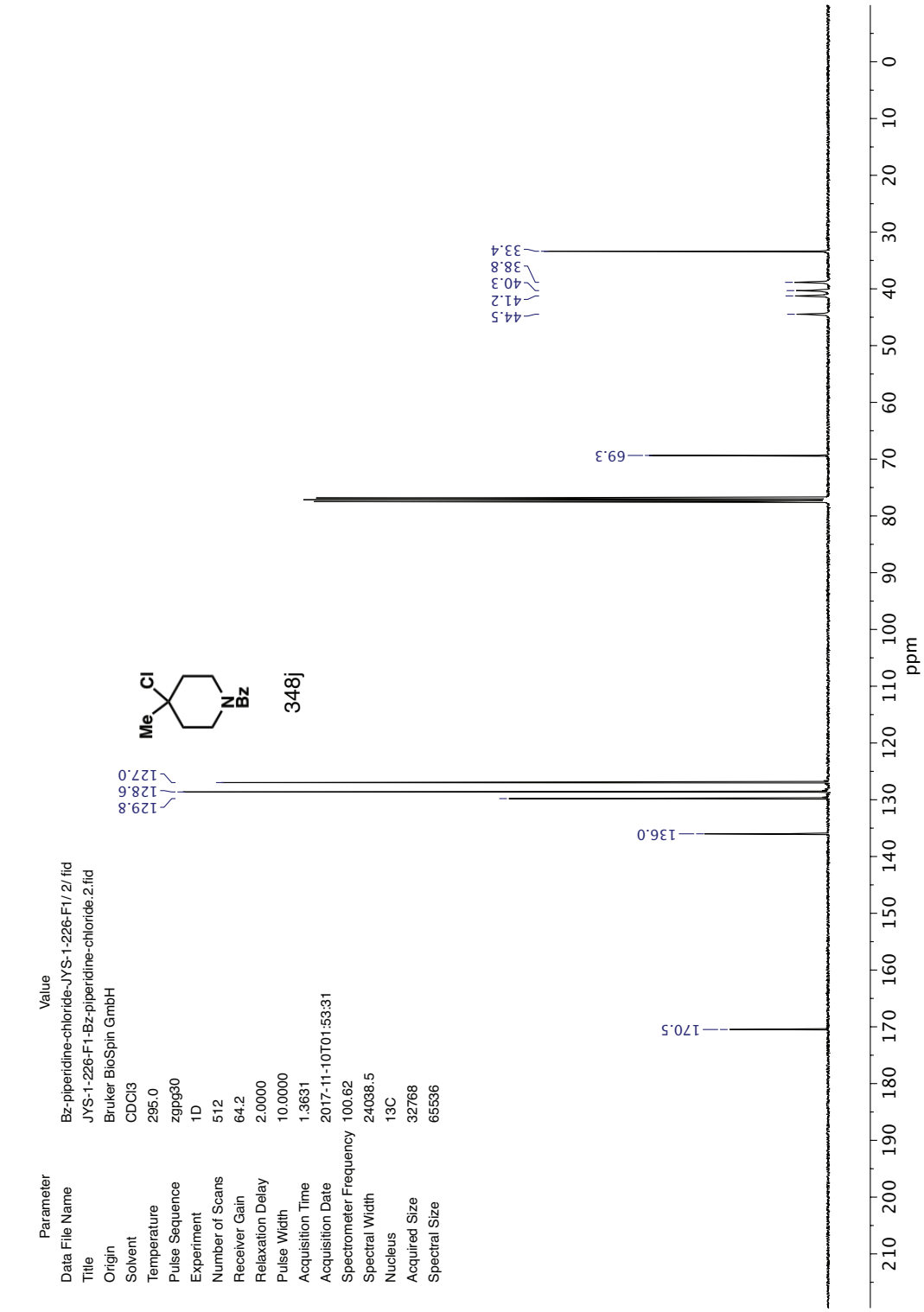
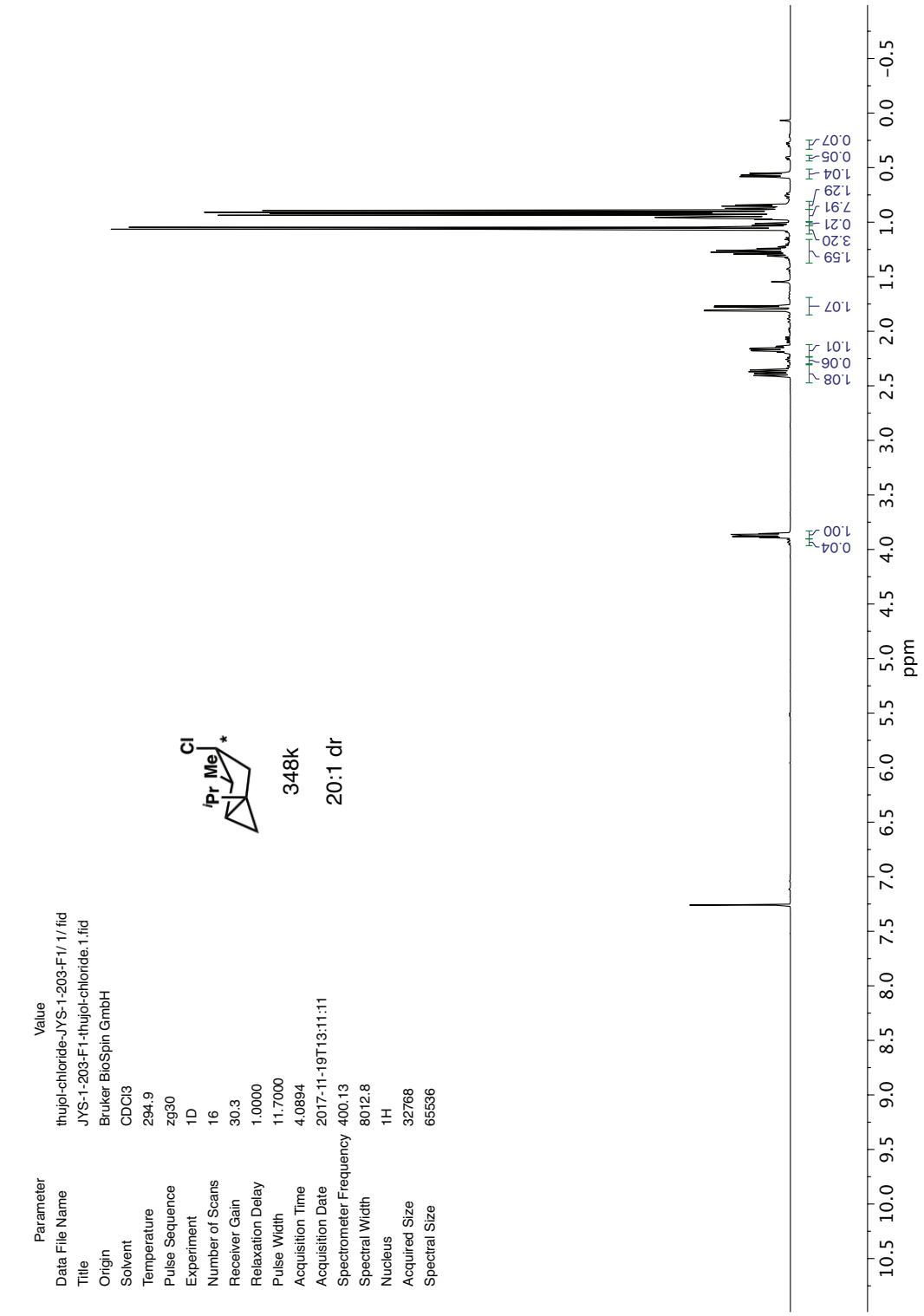
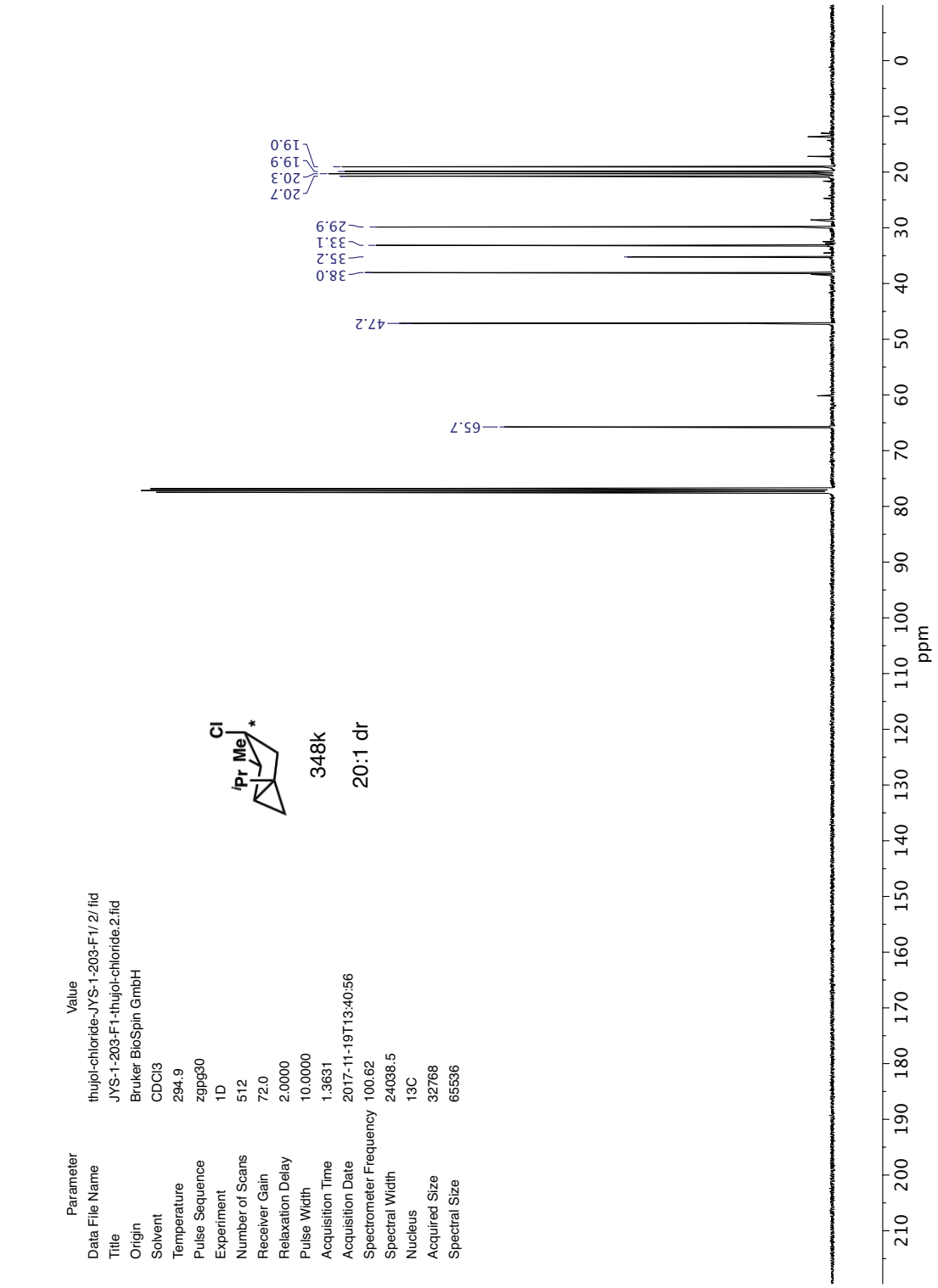
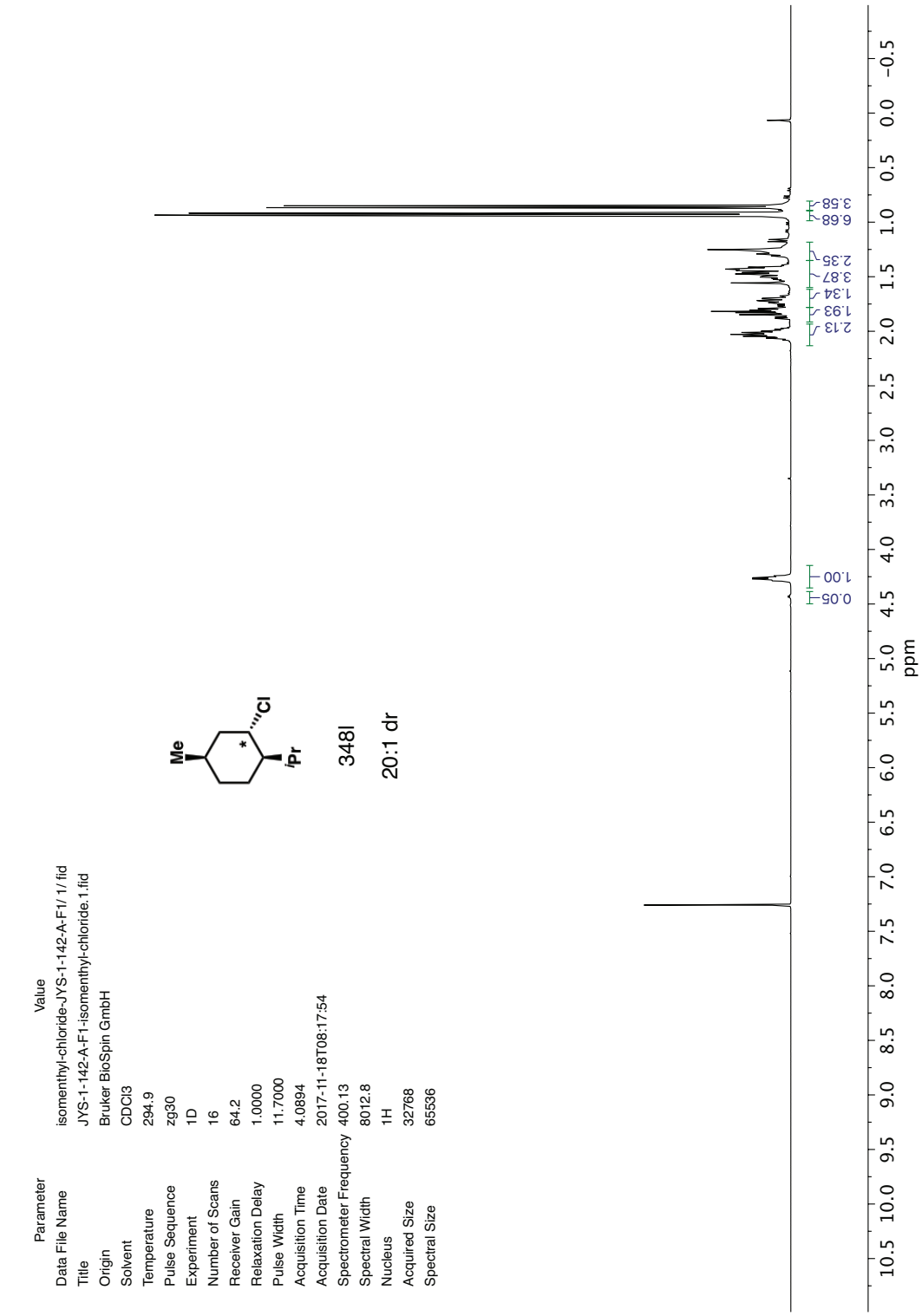
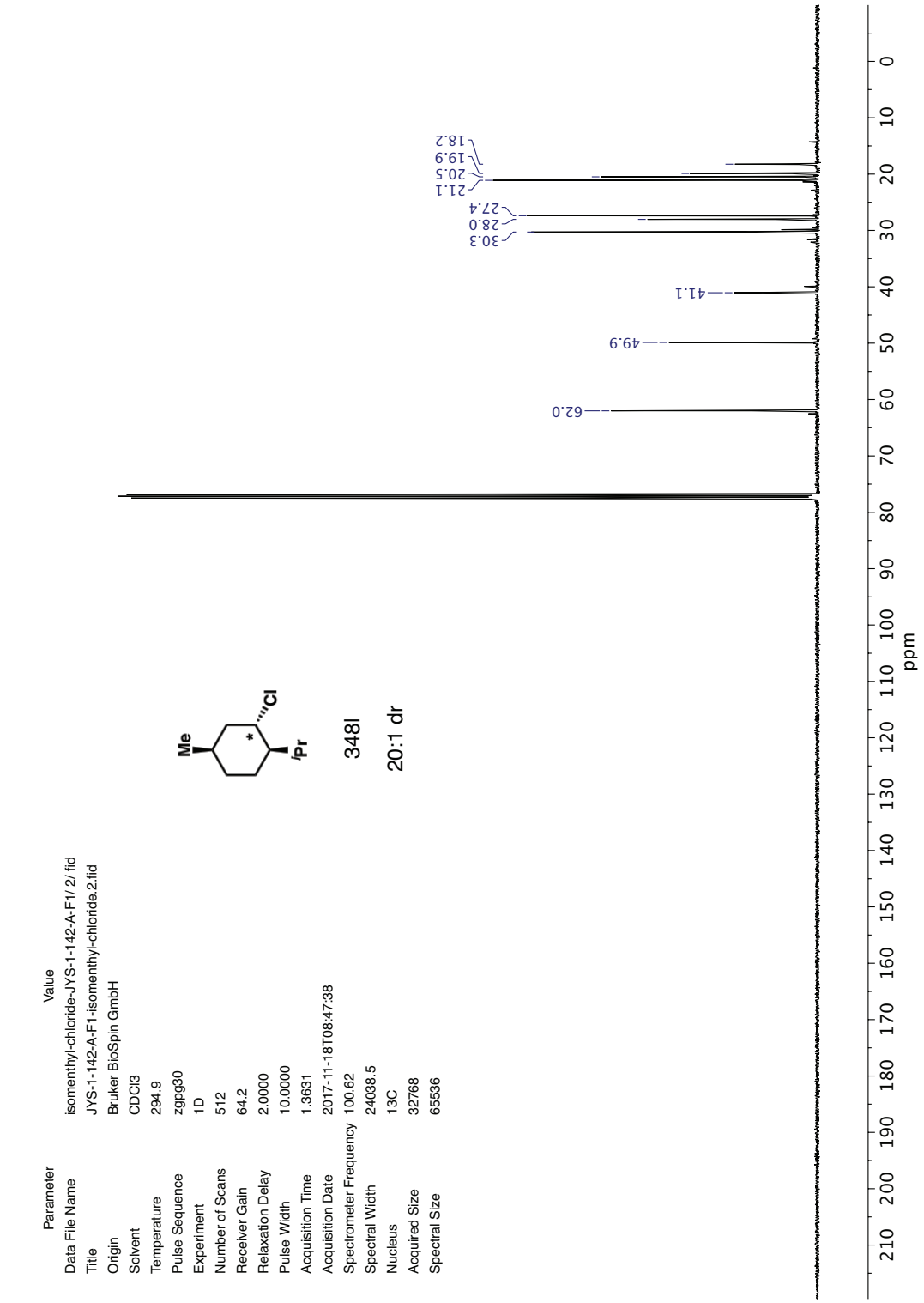
Value
Data File Name
Bz-piperidine-chloride-JYS-1-226-F1/ 1/ fid
Title
JYS-1-226-F1-Bz-piperidine-chloride.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.0
Pulse Sequence
zg30
Experiment
1D
Number of Scans
16
Receiver Gain
72.0
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2017-11-10T01:23:46
Spectrometer Frequency
400.13
Spectral Width
8012.8
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
Me
Cl
N
Bz
348j
5.03
0.91
0.93
1.04
1.03
1.03
2.20
4.18
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
ppm

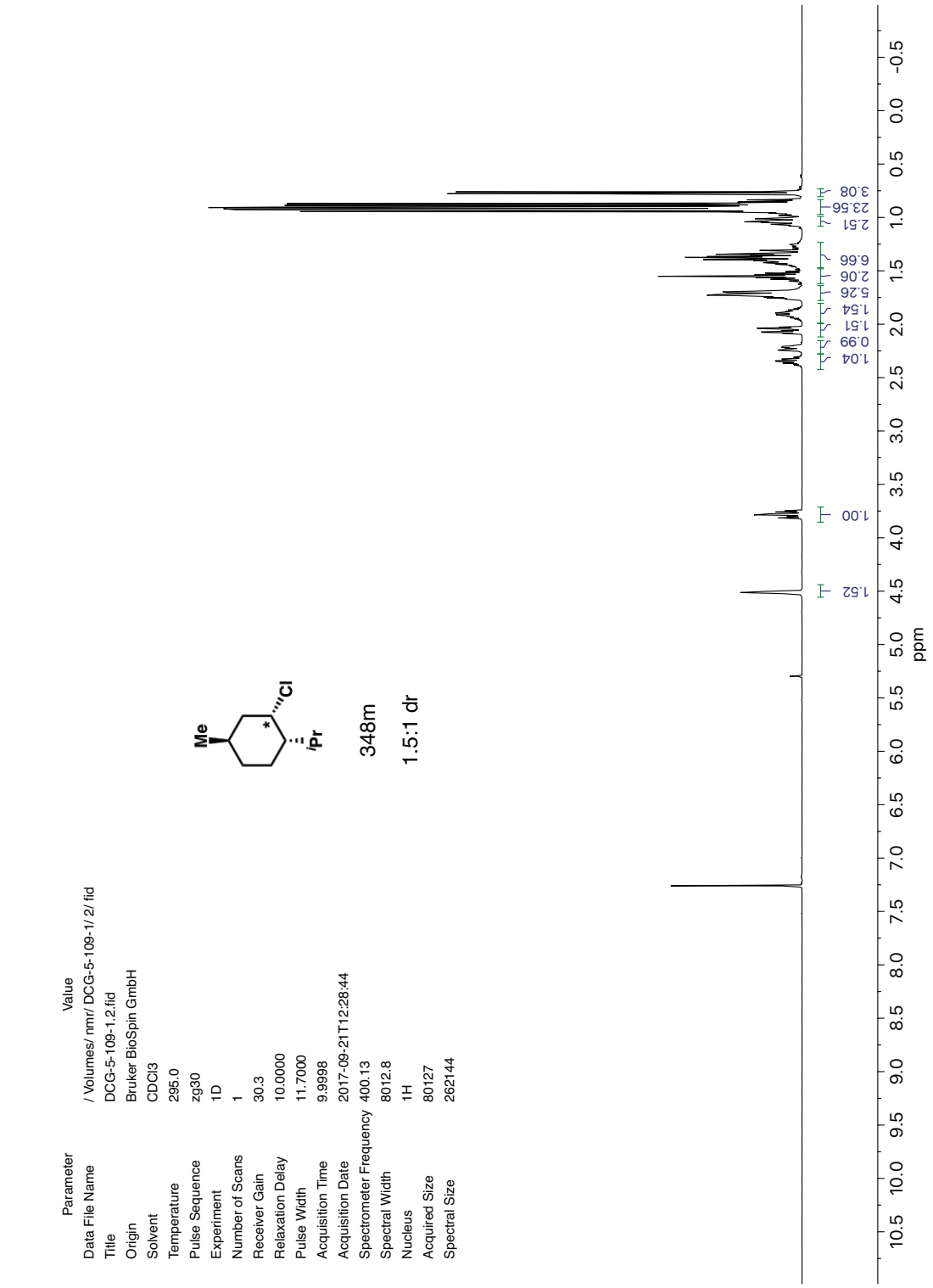

Parameter Value
Data File Name Bz-piperidine-chloride-JYS-1-226-F1/ 2/ fid
Title JYS-1-226-F1-Bz-piperidine-chloride.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 512
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-11-10T01:53:31
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
Cl
N
Bz
348j
170.5
136.0
129.8
128.6
127.0
69.3
44.5
41.2
40.3
38.8
33.4
ppm

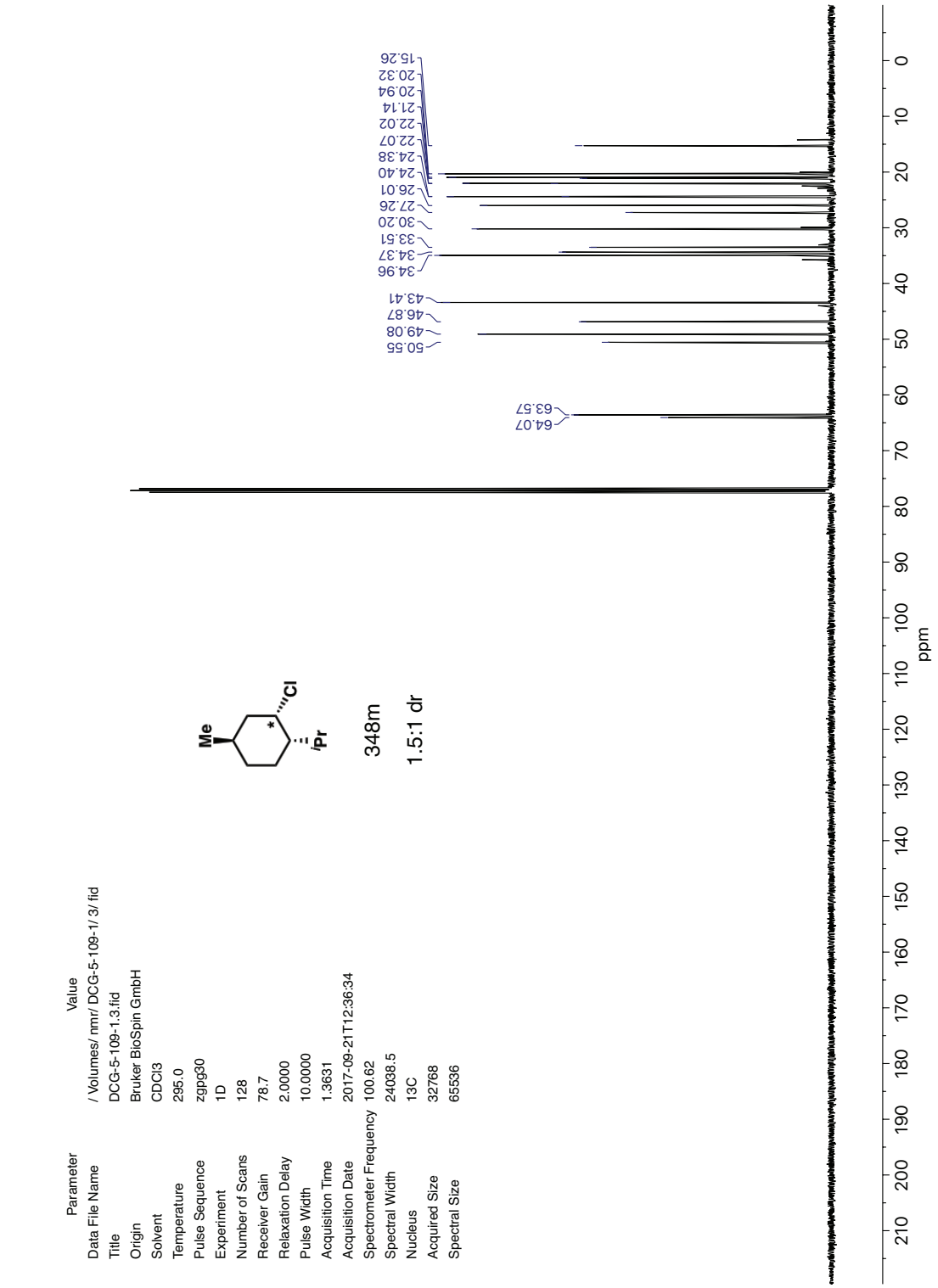

Parameter Value
Data File Name thujol-chloride-JYS-1-203-F1/ 1/ fid
Title JYS-1-203-F1-thujol-chloride.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 30.3
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-11-19T13:11:11
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
Cl
iPr
Me
*
348k
20:1 dr
0.04
1.00
1.08
0.06
1.01
1.07
1.59
3.20
0.21
7.91
1.29
1.04
0.05
0.07
ppm

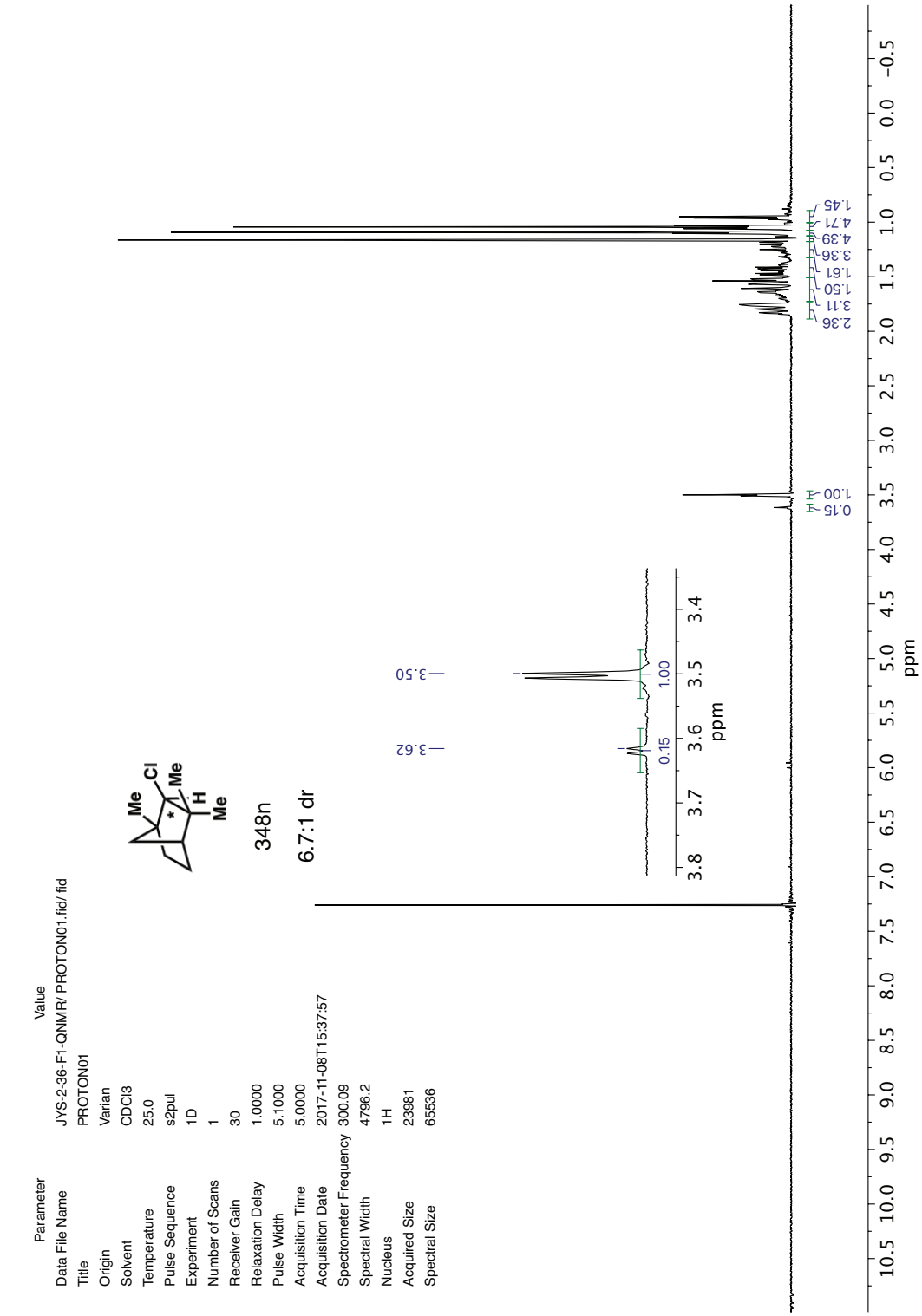

Parameter
Value
Data File Name
thujol-chloride-JYS-1-203-F1/ 2/ fid
Title
JYS-1-203-F1-thujol-chloride.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zgpg30
Experiment
1D
Number of Scans
512
Receiver Gain
72.0
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2017-11-19T13:40:56
Spectrometer Frequency
100.62
Spectral Width
24038.5
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Cl
iPr
Me
348k
20:1 dr
65.7
47.2
38.0
35.2
33.1
29.9
20.7
20.3
19.9
19.0
ppm

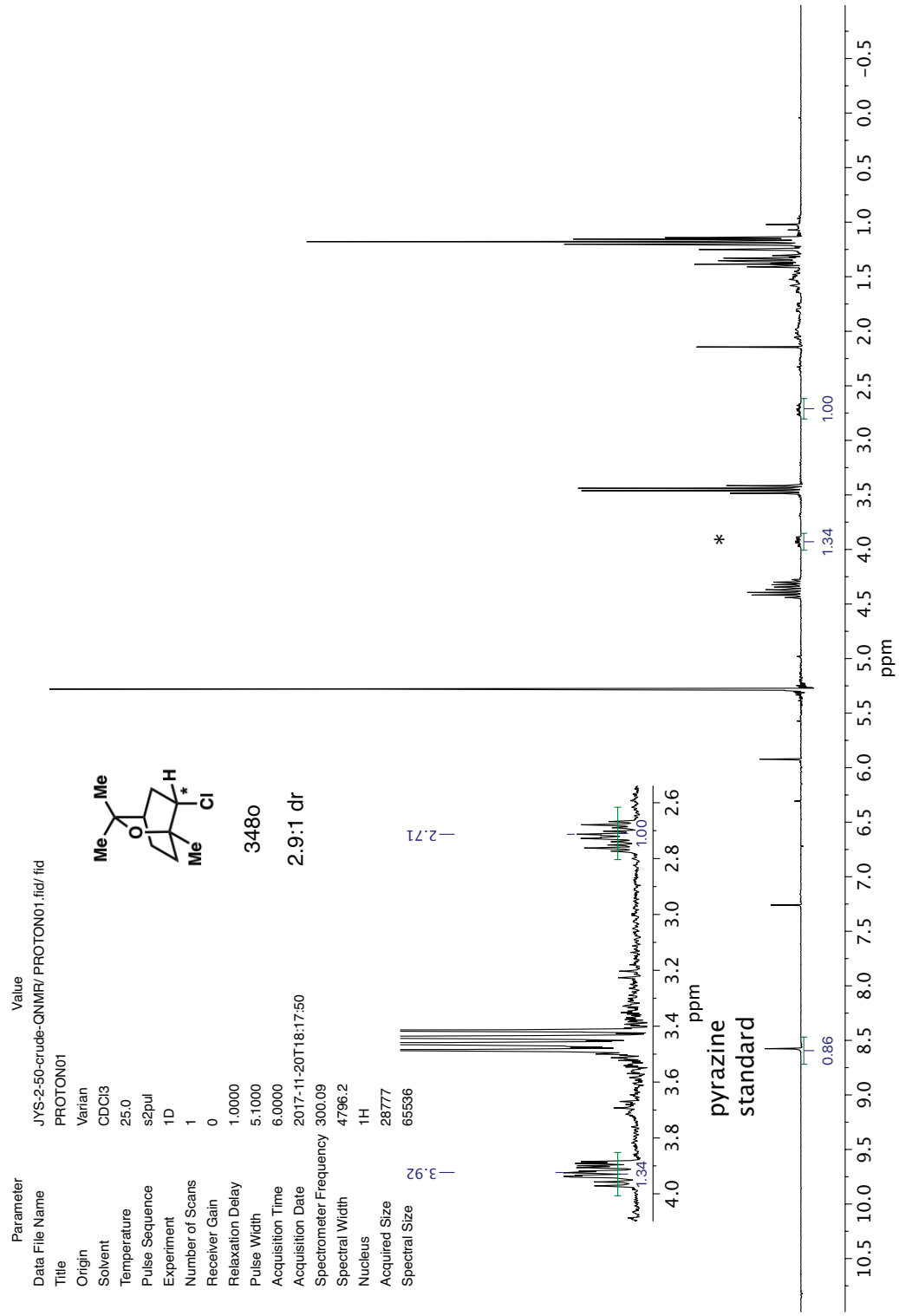

Parameter
Value
Data File Name
isomenthyl-chloride-JYS-1-142-A-F1/ 1/ fid
Title
JYS-1-142-A-F1-isomenthyl-chloride.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zg30
Experiment
1D
Number of Scans
16
Receiver Gain
64.2
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2017-11-18T08:17:54
Spectrometer Frequency
400.13
Spectral Width
8012.8
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
Me
Cl
iPr
348l
20:1 dr
0.05
1.00
2.13
1.93
1.34
3.87
2.35
6.68
3.58
ppm

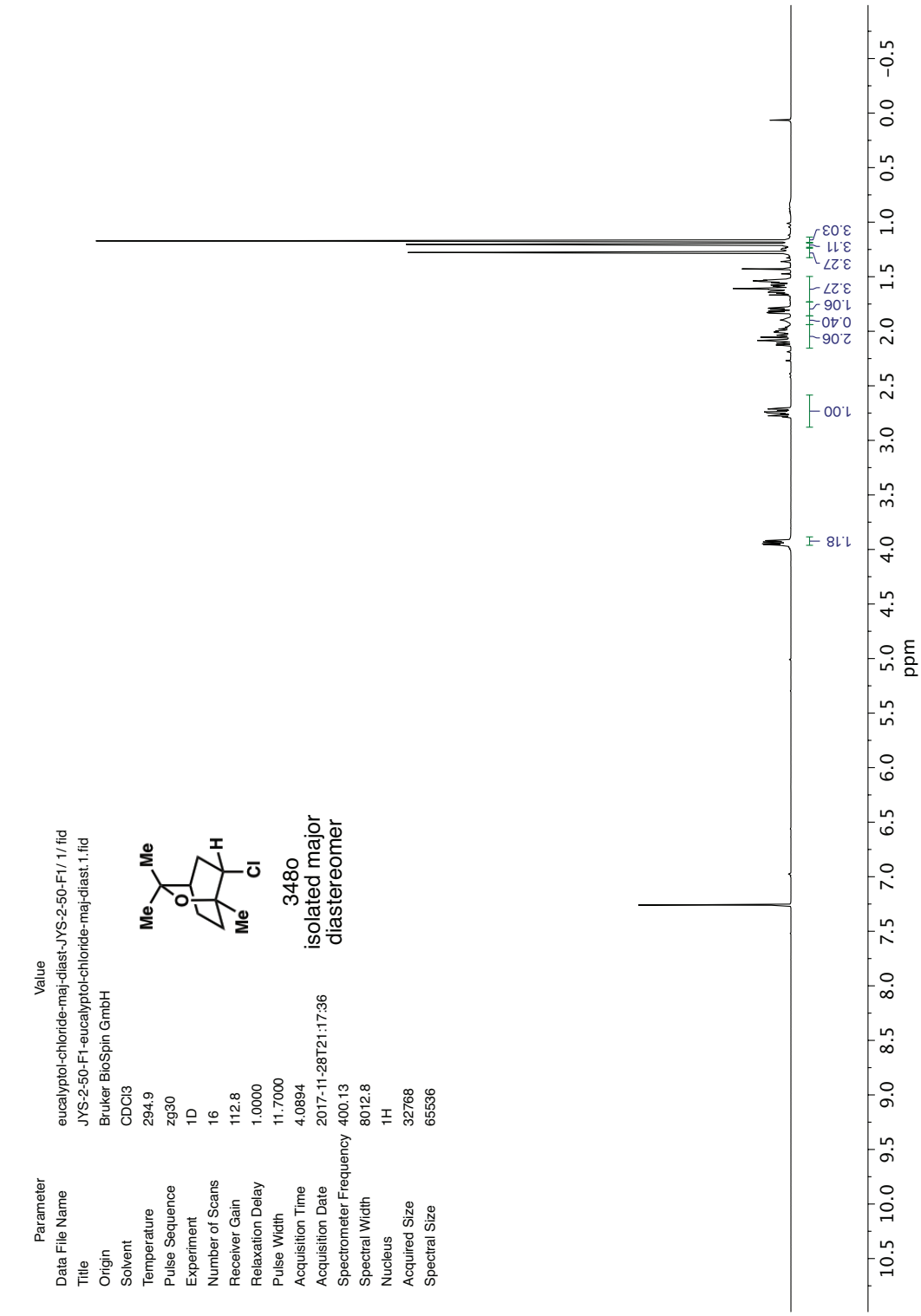

Parameter
Value
Data File Name
isomenthyl-chloride-JYS-1-142-A-F1/ 2/ fid
Title
JYS-1-142-A-F1-isomenthyl-chloride.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zgpg30
Experiment
1D
Number of Scans
512
Receiver Gain
64.2
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2017-11-18T08:47:38
Spectrometer Frequency
100.62
Spectral Width
24038.5
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Me
Cl
iPr
348l
20:1 dr
62.0
49.9
41.1
30.3
28.0
27.4
21.1
20.5
19.9
18.2
ppm


Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-109-1/ 2/ fid
Title DCG-5-109-1.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Experiment 1D
Number of Scans 1
Receiver Gain 30.3
Relaxation Delay 10.0000
Pulse Width 11.7000
Acquisition Time 9.9998
Acquisition Date 2017-09-21T12:28:44
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 80127
Spectral Size 262144
Me
Cl
iPr
348m
1.5:1 dr
1.52
1.00
1.04
0.99
1.51
1.54
5.26
2.06
6.66
2.51
23.56
3.08
ppm


Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-109-1/ 3/ fid
Title DCG-5-109-1.3.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 128
Receiver Gain 78.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2017-09-21T12:36:34
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
Cl
iPr
348m
1.5:1 dr
64.07
63.57
50.55
49.08
46.87
43.41
34.96
34.37
33.51
30.20
27.26
26.01
24.40
24.38
22.07
22.02
21.14
20.94
20.32
15.26
ppm


Parameter Value
Data File Name JYS-2-36-F1-QNMR/ PROTON01.fid/ fid
Title PROTON01
Origin Varian
Solvent CDCl3
Temperature 25.0
Pulse Sequence s2pul
Experiment 1D
Number of Scans 1
Receiver Gain 30
Relaxation Delay 1.0000
Pulse Width 5.1000
Acquisition Time 5.0000
Acquisition Date 2017-11-08T15:37:57
Spectrometer Frequency 300.09
Spectral Width 4796.2
Nucleus 1H
Acquired Size 23981
Spectral Size 65536
Me
Cl
Me
H
Me
348n
6.7:1 dr
3.62
3.50
0.15
1.00
2.36
3.11
1.50
1.61
3.36
4.39
4.71
1.45
0.15
1.00
ppm
ppm


Parameter Value
Data File Name JYS-2-50-crude-QNMR/ PROTON01.fid/ fid
Title PROTON01
Origin Varian
Solvent CDCl3
Temperature 25.0
Pulse Sequence s2pul
Experiment 1D
Number of Scans 1
Receiver Gain 0
Relaxation Delay 1.0000
Pulse Width 5.1000
Acquisition Time 6.0000
Acquisition Date 2017-11-20T18:17:50
Spectrometer Frequency 300.09
Spectral Width 4796.2
Nucleus 1H
Acquired Size 28777
Spectral Size 65536
Me
Me
O
H
*
Me
Cl
348o
2.9:1 dr
3.92
2.71
1.34
1.00
0.86
pyrazine
standard
*
ppm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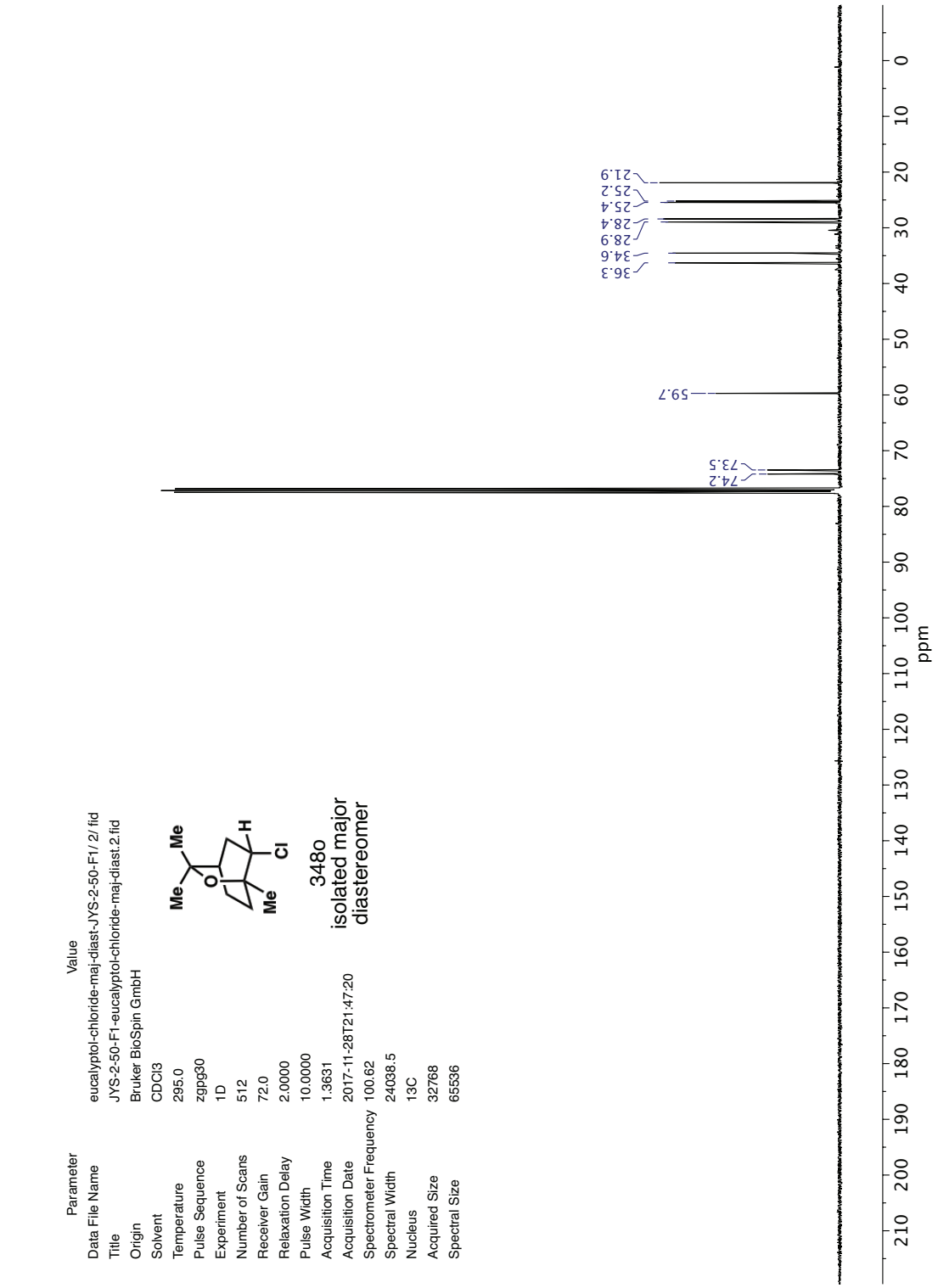
Data File Name
eucalyptol-chloride-maj-diast-JYS-2-50-F1/ 1/ fid
Title
JYS-2-50-F1-eucalyptol-chloride-maj-diast.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zg30
Experiment
1D
Number of Scans
16
Receiver Gain
112.8
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2017-11-28T21:17:36
Spectrometer Frequency
400.13
Spectral Width
8012.8
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
Me
Me
O
H
Me
Cl
348o
isolated major
diastereomer
1.18
1.00
2.06
0.40
1.06
3.27
3.27
3.11
3.03
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm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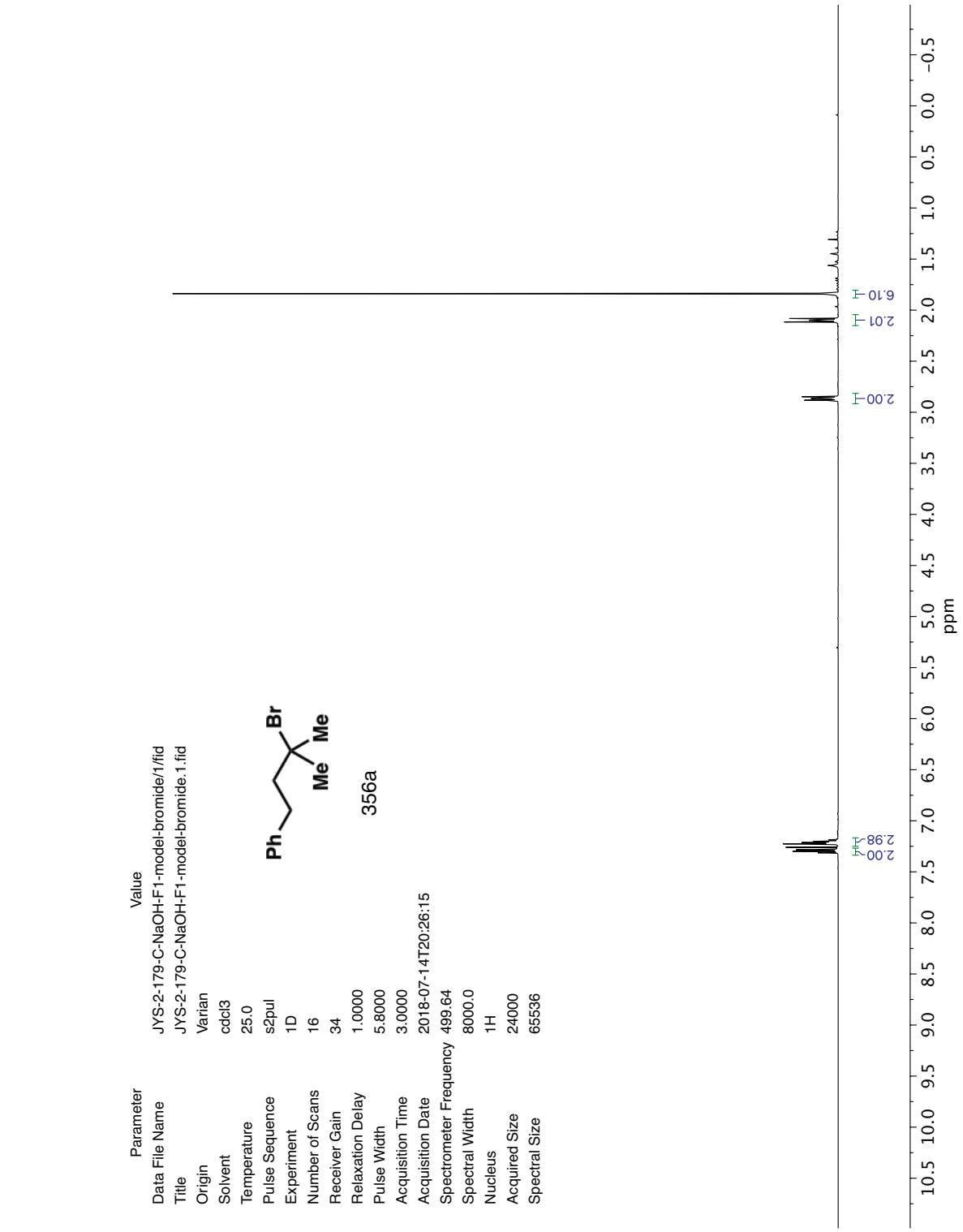
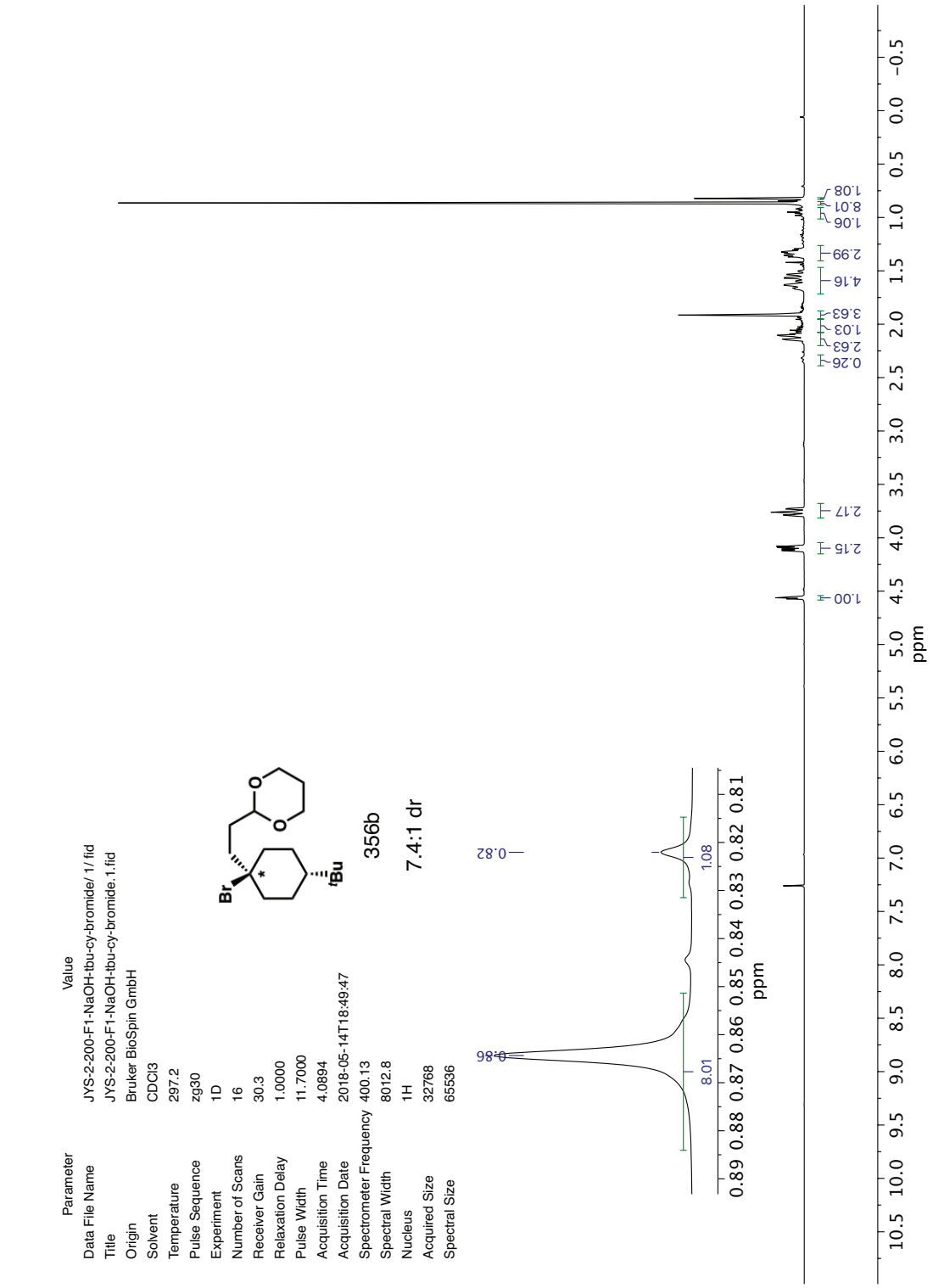
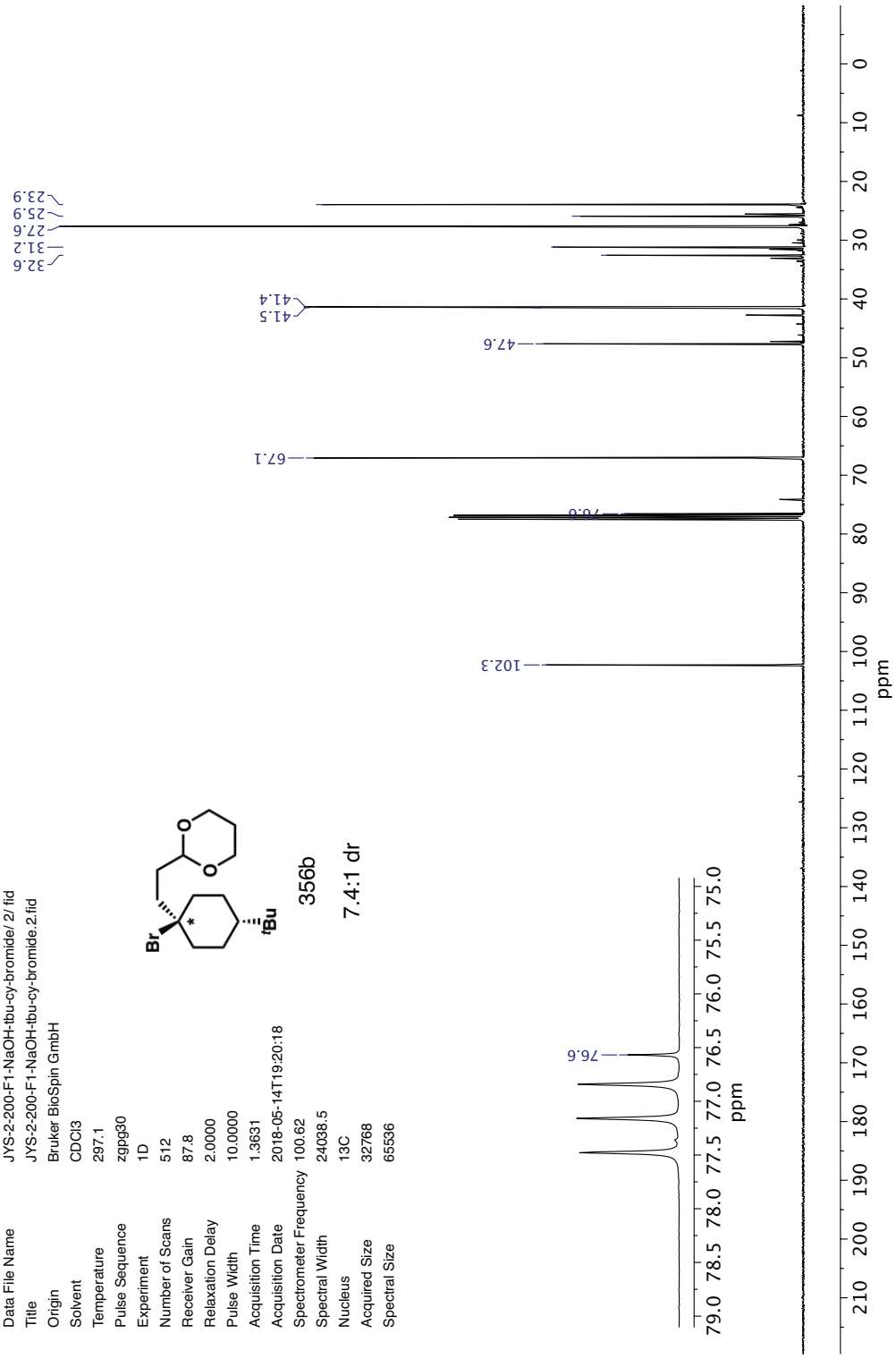
Data File Name
eucalyptol-chloride-maj-diast-JYS-2-50-F1/ 2/ fid
Title
JYS-2-50-F1-eucalyptol-chloride-maj-diast.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.0
Pulse Sequence
zgpg30
Experiment
1D
Number of Scans
512
Receiver Gain
72.0
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2017-11-28T21:47:20
Spectrometer Frequency
100.62
Spectral Width
24038.5
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Me
Me
O
H
Me
Cl
348o
isolated major
diastereomer
74.2
73.5
59.7
36.3
34.6
28.9
28.4
25.4
25.2
21.9
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm


Parameter
Value
Data File Name
JYS-2-179-C-NaOH-F1-model-bromide/1/fid
Title
JYS-2-179-C-NaOH-F1-model-bromide.1.fid
Origin
Varian
Solvent
cdcl3
Temperature
25.0
Pulse Sequence
s2pul
Experiment
1D
Number of Scans
16
Receiver Gain
34
Relaxation Delay
1.0000
Pulse Width
5.8000
Acquisition Time
3.0000
Acquisition Date
2018-07-14T20:26:15
Spectrometer Frequency
499.64
Spectral Width
8000.0
Nucleus
1H
Acquired Size
24000
Spectral Size
65536
Ph
Br
Me
Me
356a
2.00
2.98
2.00
2.01
6.10
ppm


Parameter Value
Data File Name JYS-2-200-F1-NaOH-tbu-cy-bromide/ 1/ fid
Title JYS-2-200-F1-NaOH-tbu-cy-bromide.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 297.2
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 30.3
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-05-14T18:49:47
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
Br
tBu
356b
7.4:1 dr
0.82
0.86
8.01
1.08
1.00
2.15
2.17
0.26
2.63
1.03
3.63
4.16
2.99
1.06
8.01
1.08
ppm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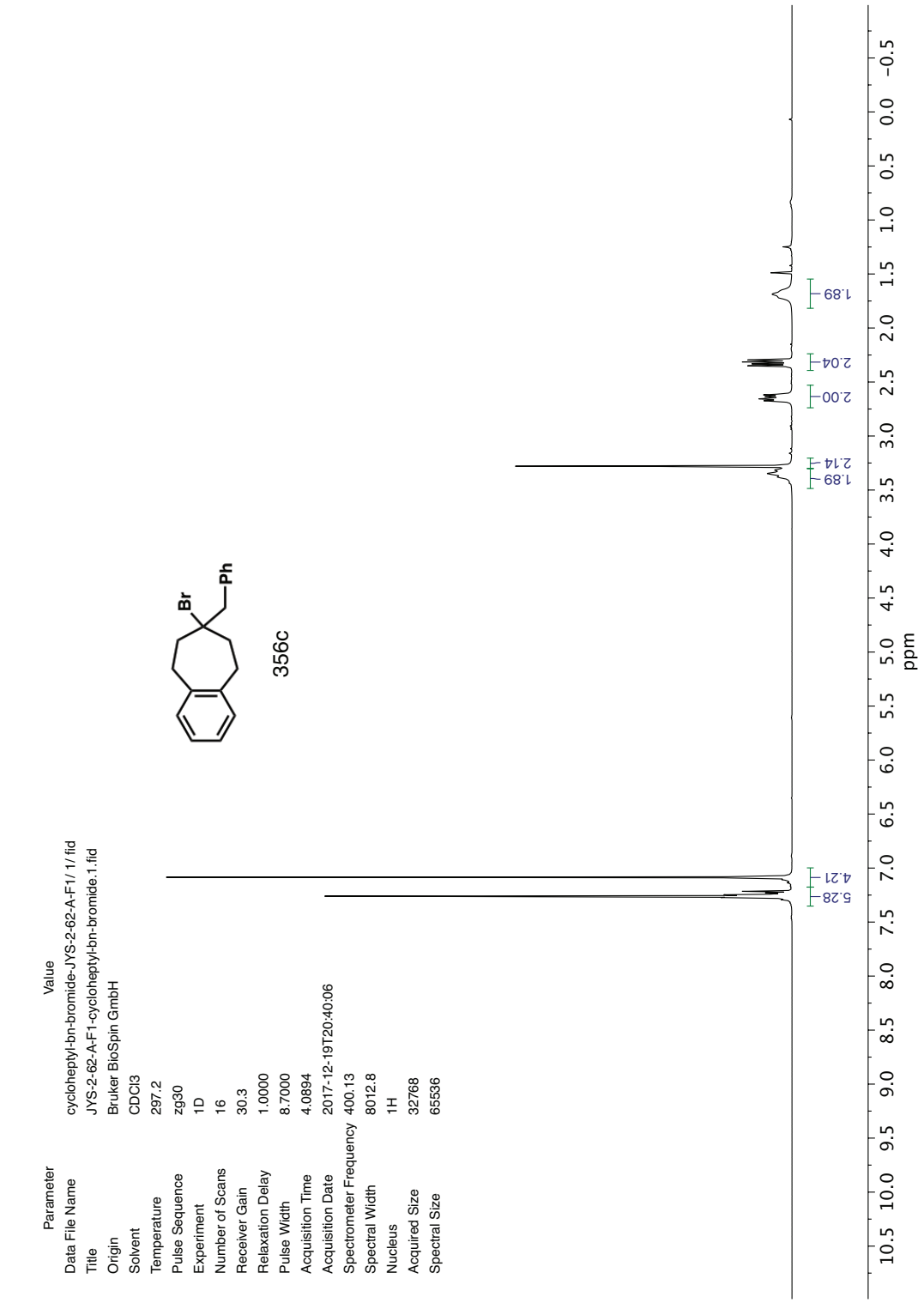
Value
Data File Name
JYS-2-200-F1-NaOH-tbu-cy-bromide/ 2/ fid
Title
JYS-2-200-F1-NaOH-tbu-cy-bromide.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
297.1
Pulse Sequence
zgpg30
Experiment
1D
Number of Scans
512
Receiver Gain
87.8
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-05-14T19:20:18
Spectrometer Frequency
100.62
Spectral Width
24038.5
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Br
tBu
356b
7.4:1 dr
102.3
76.8
76.6
67.1
47.6
41.5
41.4
32.6
31.2
27.6
25.9
23.9
ppm
ppm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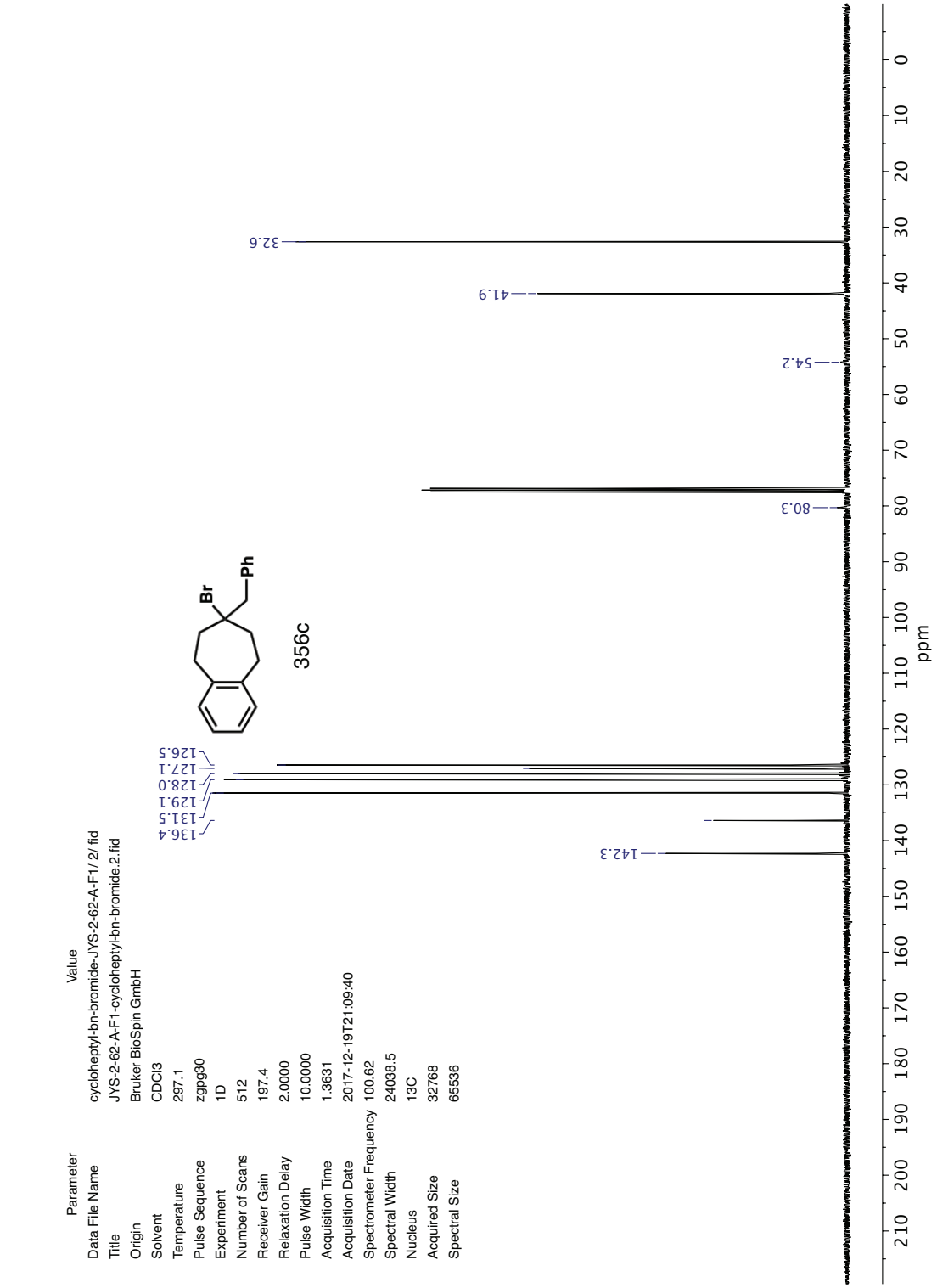
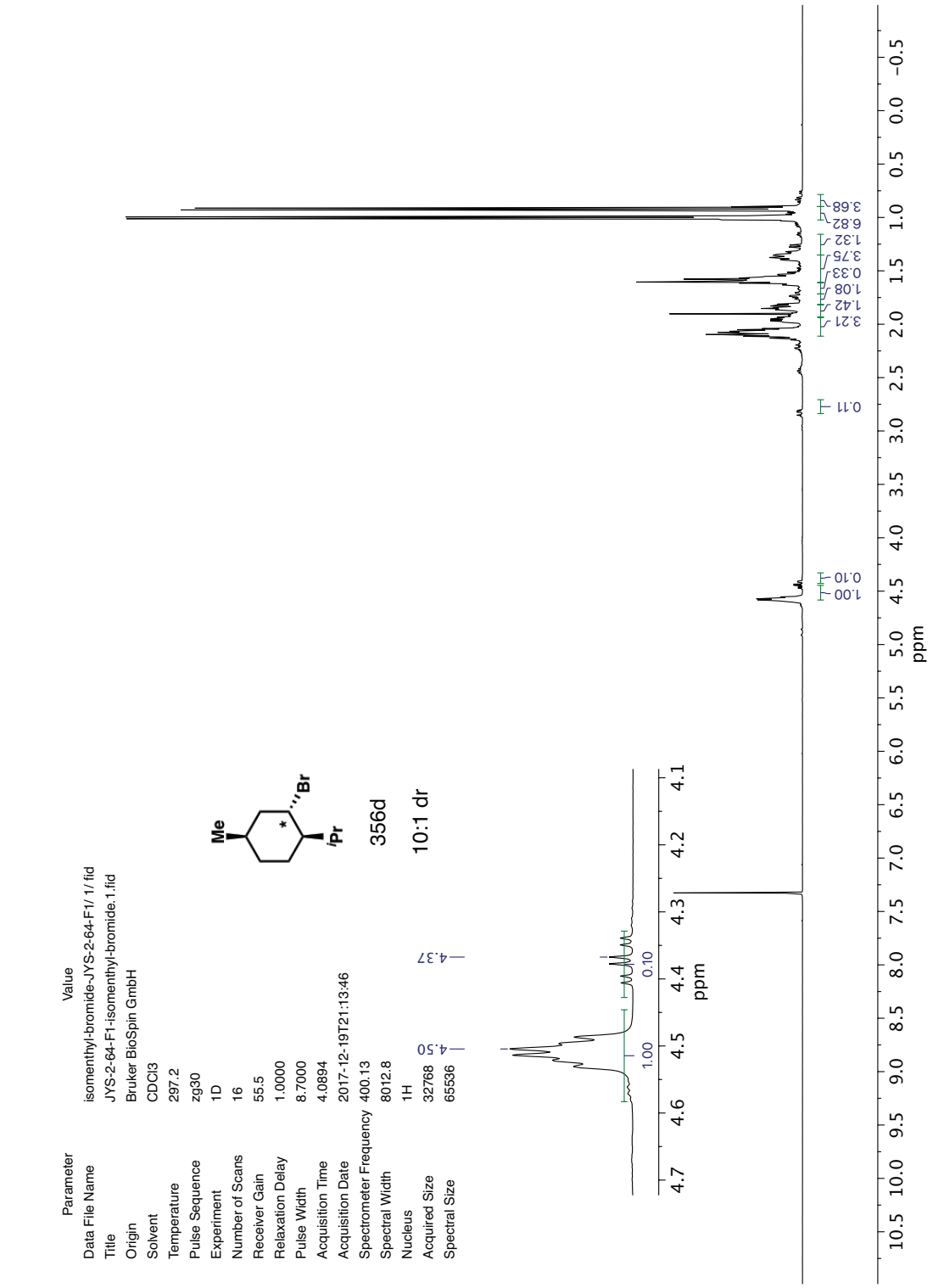
Value
Data File Name
cycloheptyl-bn-bromide-JYS-2-62-A-F1/ 1/ fid
Title
JYS-2-62-A-F1-cycloheptyl-bn-bromide.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
297.2
Pulse Sequence
zg30
Experiment
1D
Number of Scans
16
Receiver Gain
30.3
Relaxation Delay
1.0000
Pulse Width
8.7000
Acquisition Time
4.0894
Acquisition Date
2017-12-19T20:40:06
Spectrometer Frequency
400.13
Spectral Width
8012.8
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
Br
Ph
356c
5.28
4.21
1.89
2.14
2.00
2.04
1.89
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm


Parameter
Value
Data File Name
cycloheptyl-bn-bromide-JYS-2-62-A-F1/ 2/ fid
Title
JYS-2-62-A-F1-cycloheptyl-bn-bromide.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
297.1
Pulse Sequence
zgpg30
Experiment
1D
Number of Scans
512
Receiver Gain
197.4
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2017-12-19T21:09:40
Spectrometer Frequency
100.62
Spectral Width
24038.5
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Br
Ph
356c
32.6
41.9
54.2
80.3
126.5
127.1
128.0
129.1
131.5
136.4
142.3
ppm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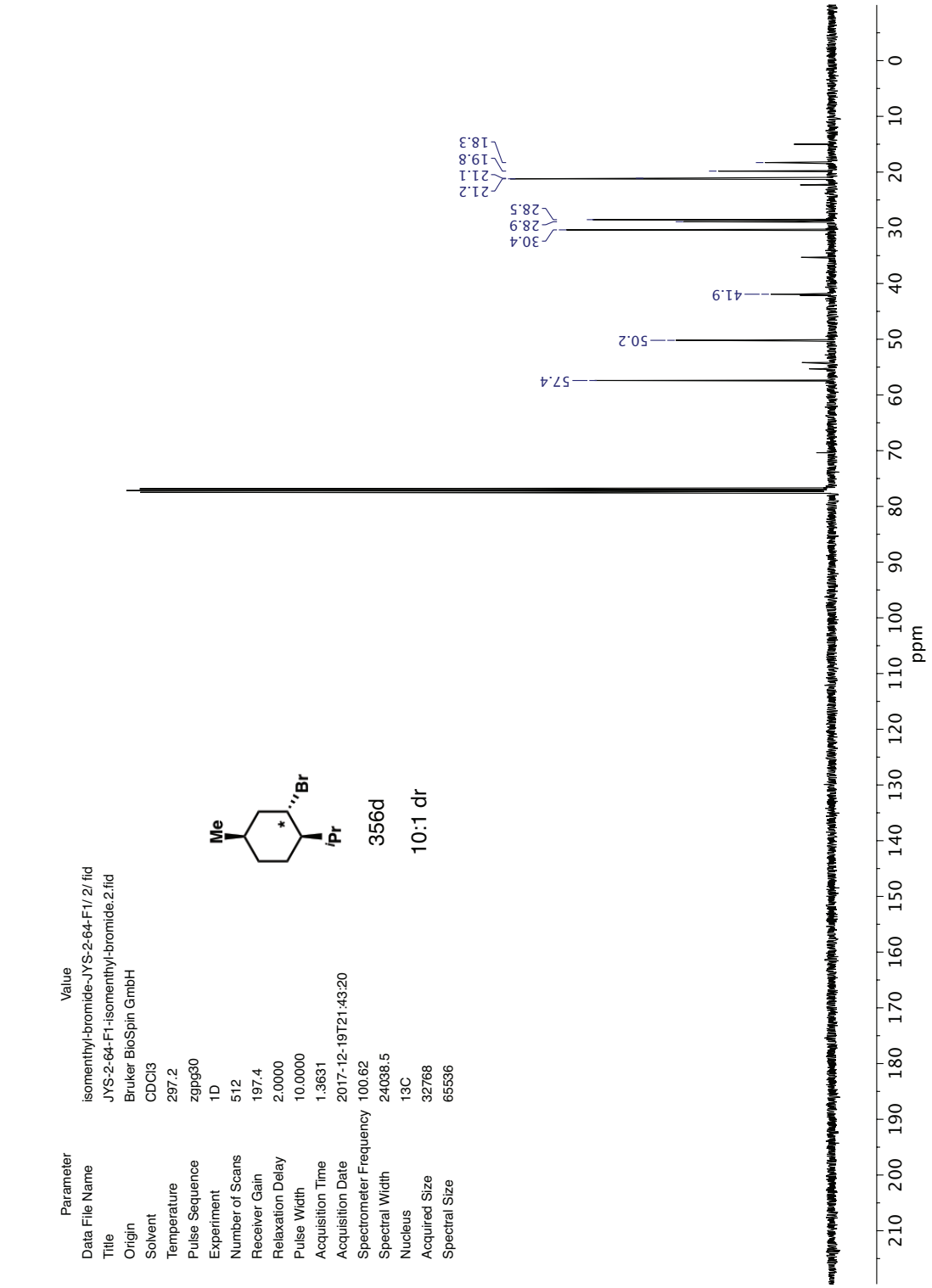
Data File Name
isomenthyl-bromide-JYS-2-64-F1/ 1/ fid
Title
JYS-2-64-F1-isomenthyl-bromide.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
297.2
Pulse Sequence
zg30
Experiment
1D
Number of Scans
16
Receiver Gain
55.5
Relaxation Delay
1.0000
Pulse Width
8.7000
Acquisition Time
4.0894
Acquisition Date
2017-12-19T21:13:46
Spectrometer Frequency
400.13
Spectral Width
8012.8
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
Me
Br
iPr
356d
10:1 dr
4.37
4.50
1.00
0.10
0.11
1.00
0.10
3.21
1.42
1.08
0.33
3.75
1.32
6.82
3.68
ppm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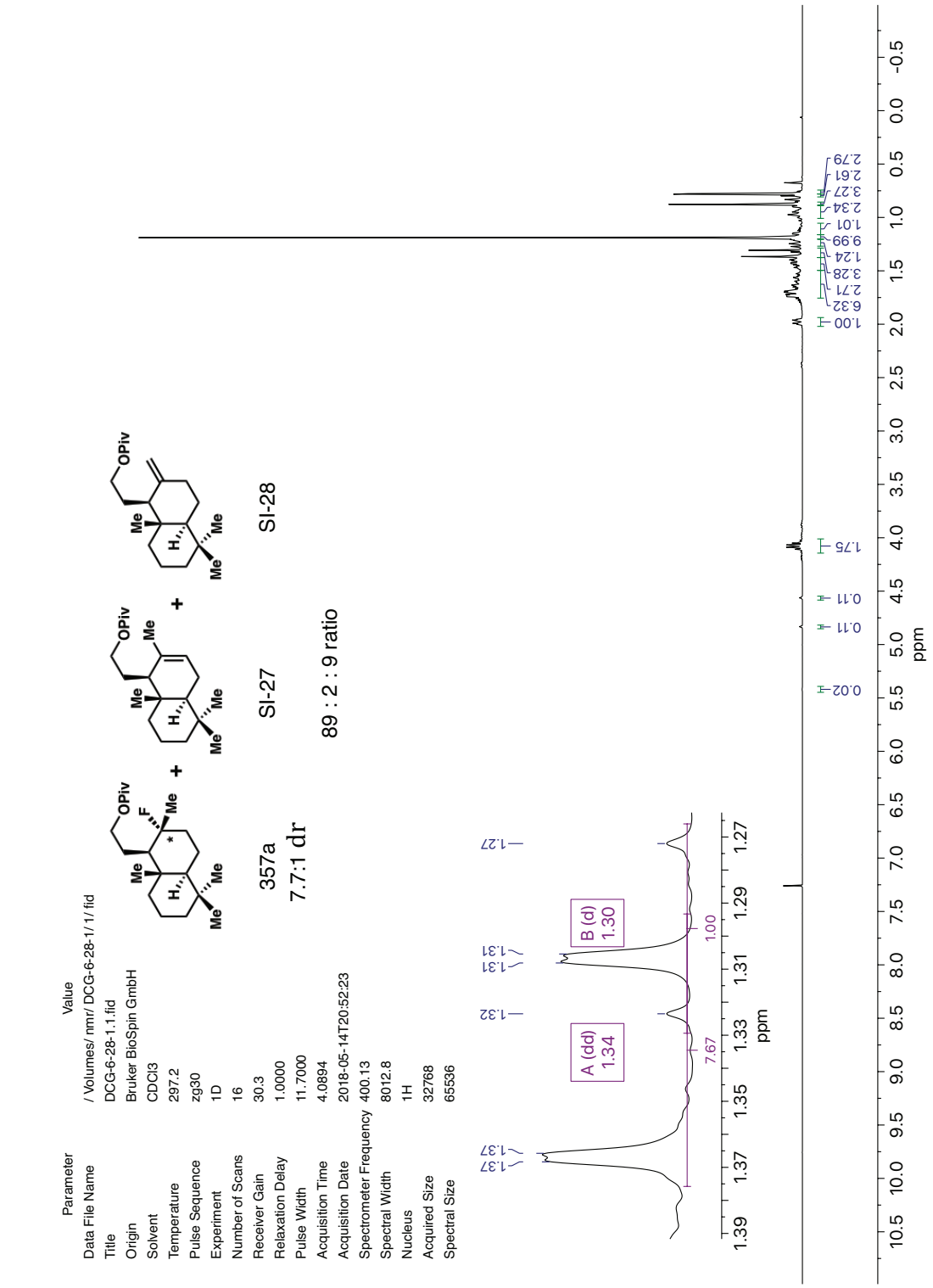
Data File Name
isomenthyl-bromide-JYS-2-64-F1/ 2/ fid
Title
JYS-2-64-F1-isomenthyl-bromide.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
297.2
Pulse Sequence
zgpg30
Experiment
1D
Number of Scans
512
Receiver Gain
197.4
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2017-12-19T21:43:20
Spectrometer Frequency
100.62
Spectral Width
24038.5
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Me
Br
iPr
356d
10:1 dr
57.4
50.2
41.9
30.4
28.9
28.5
21.2
21.1
19.8
18.3
ppm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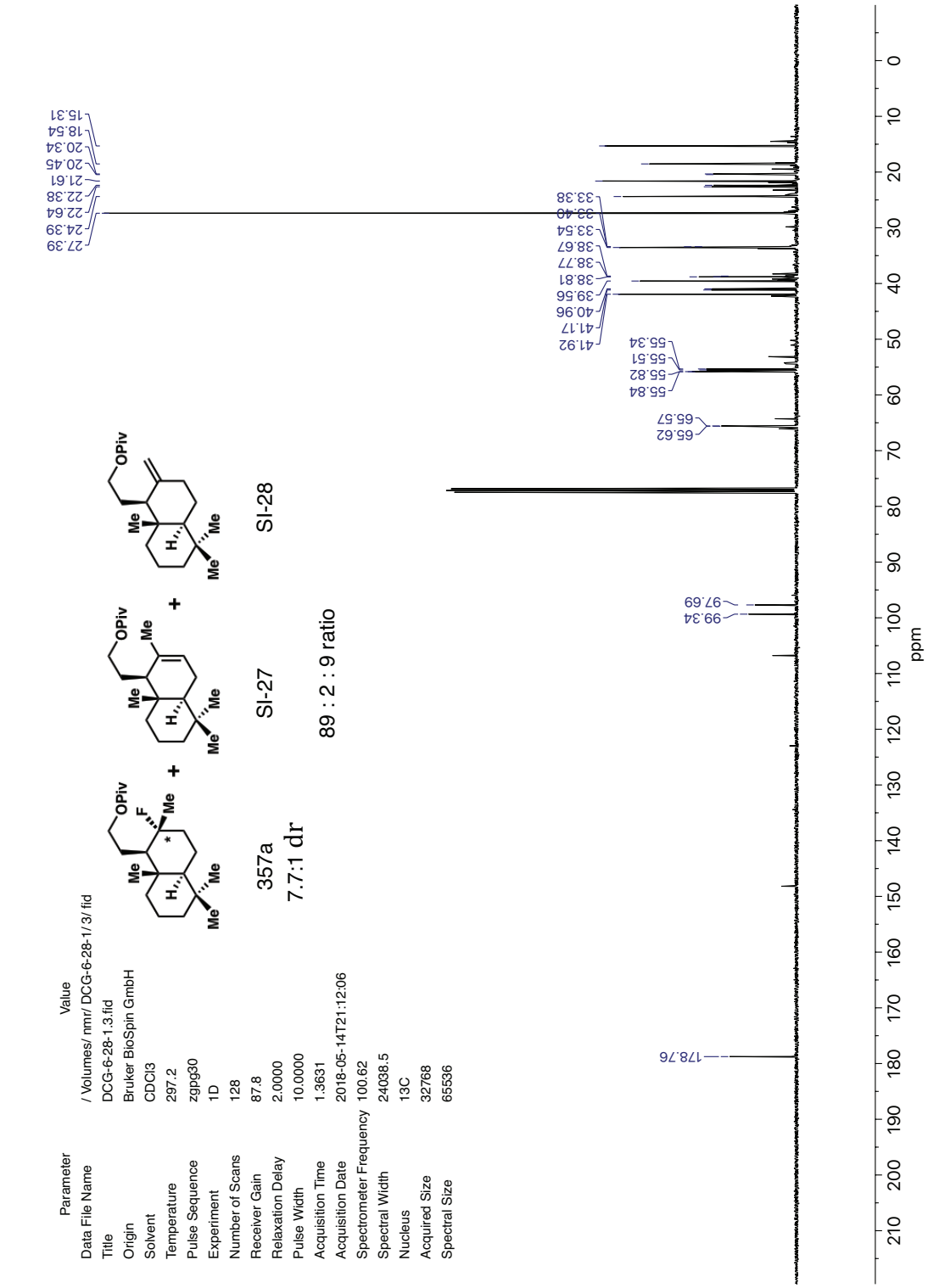
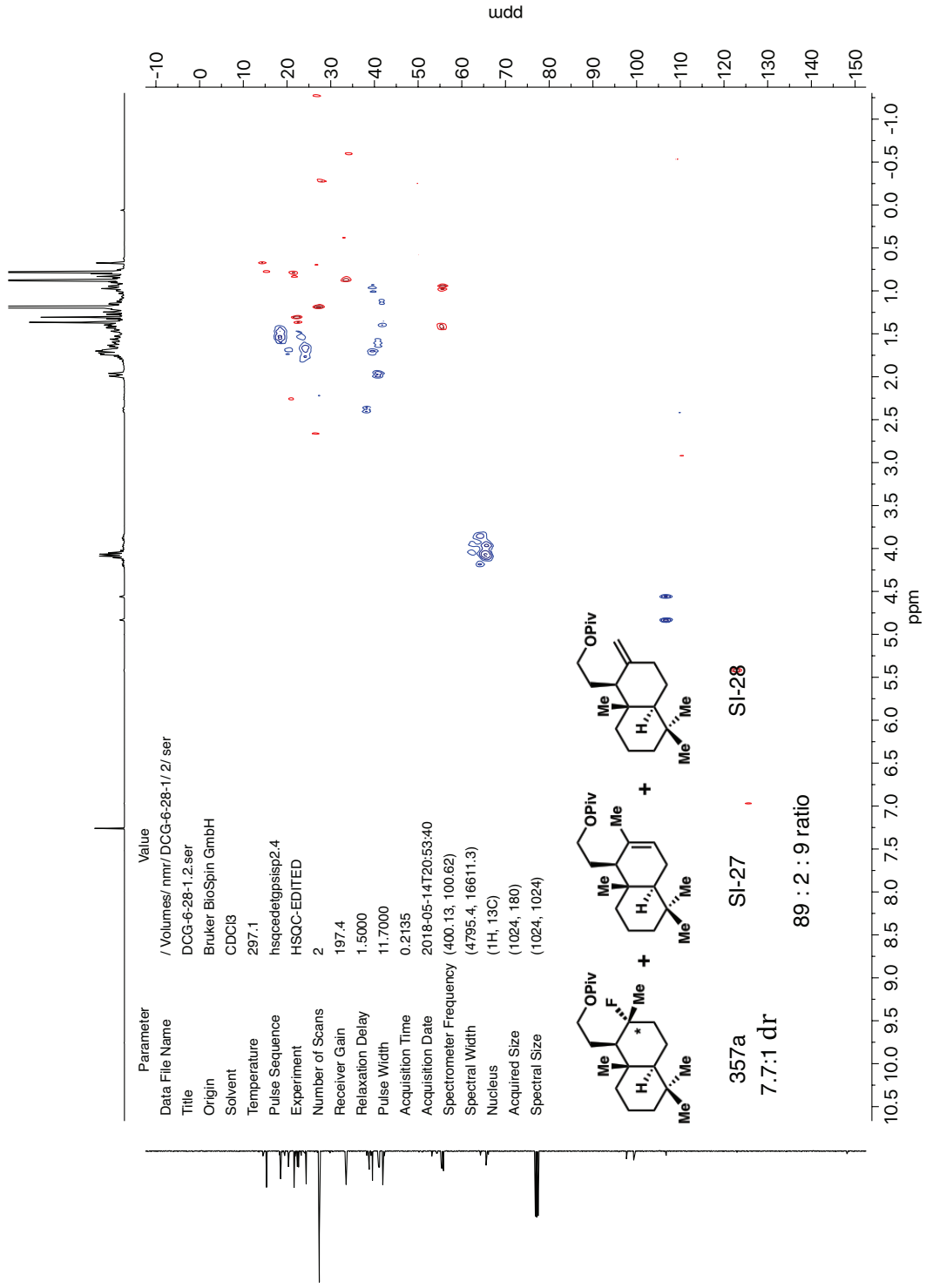
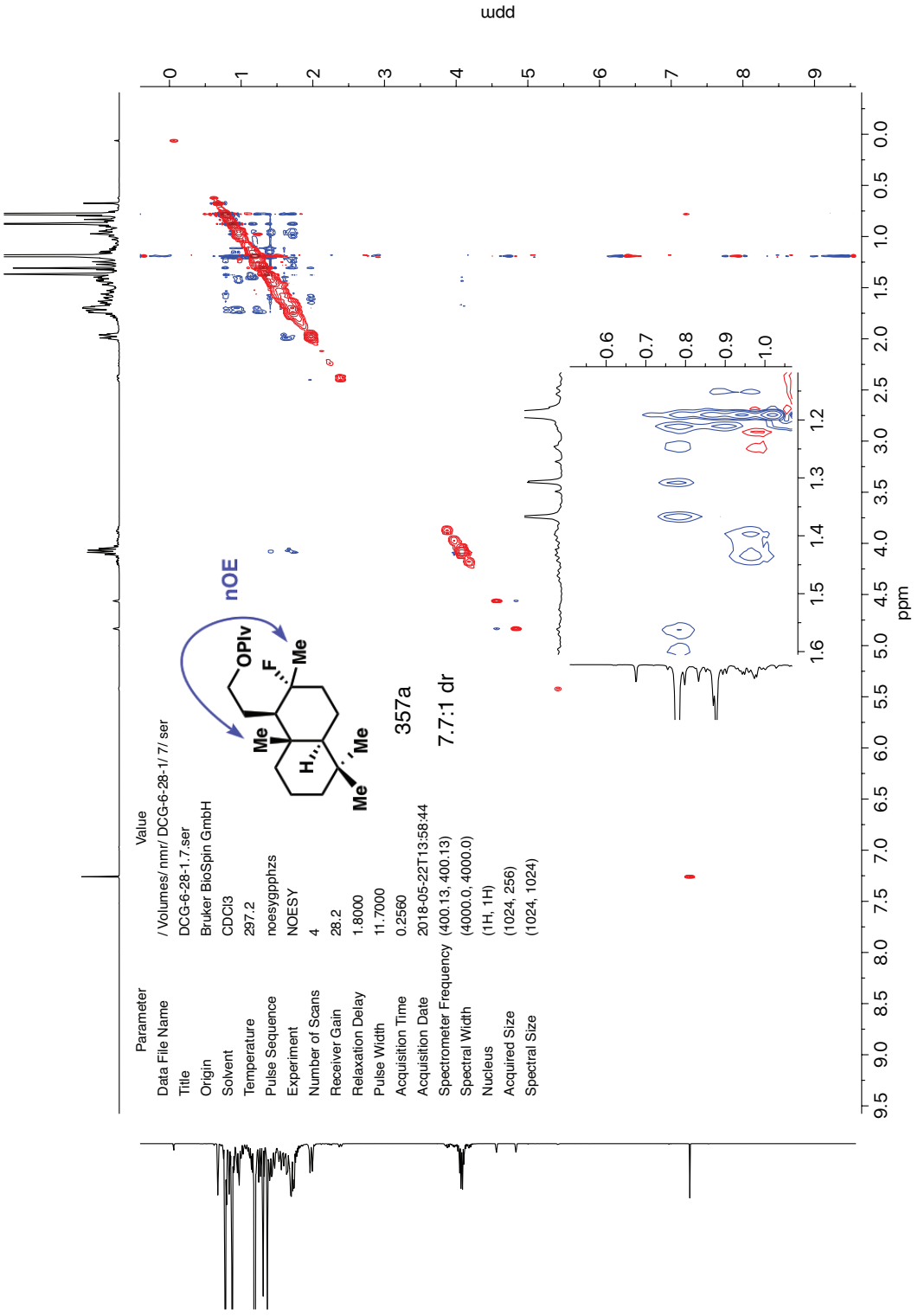
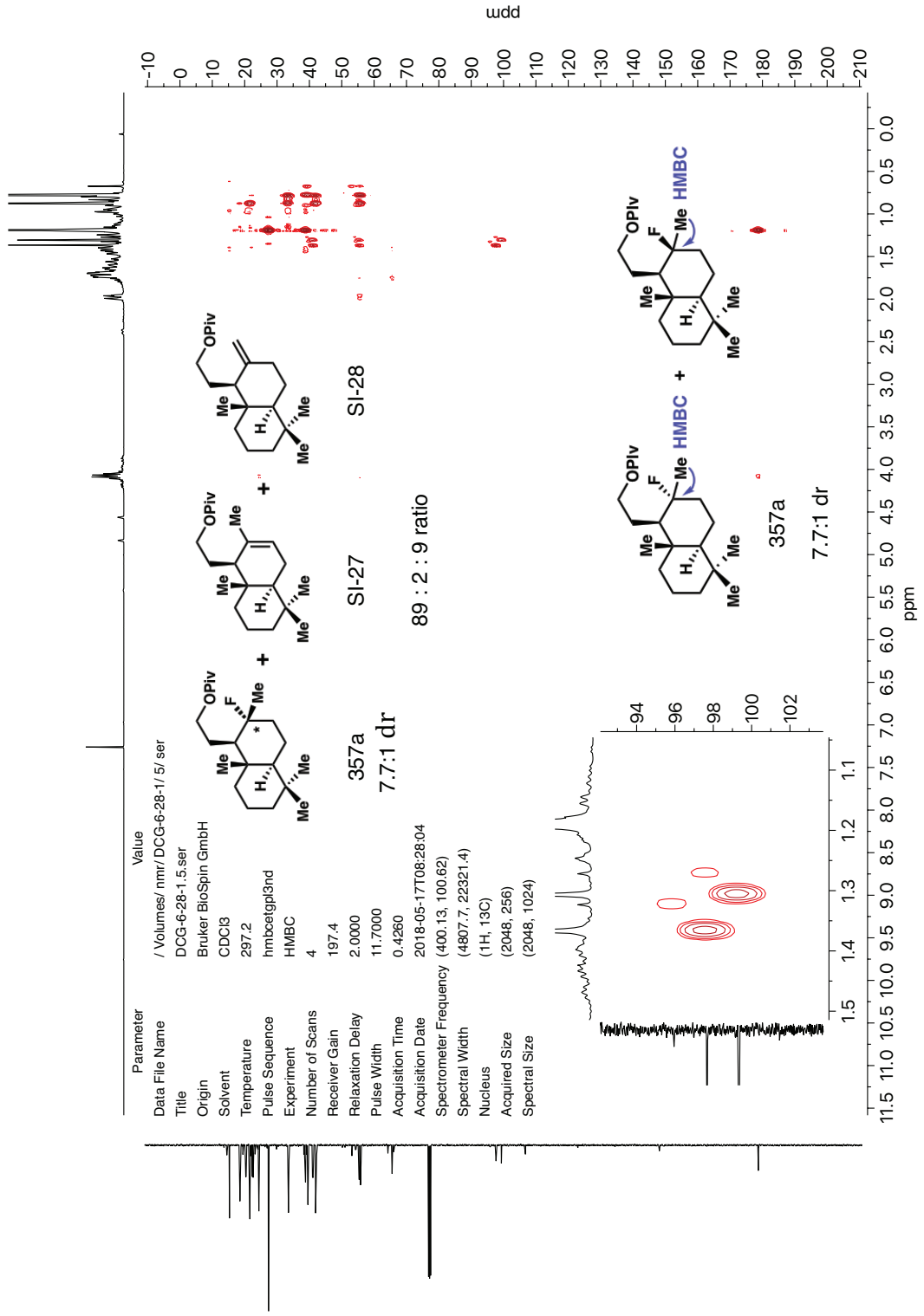
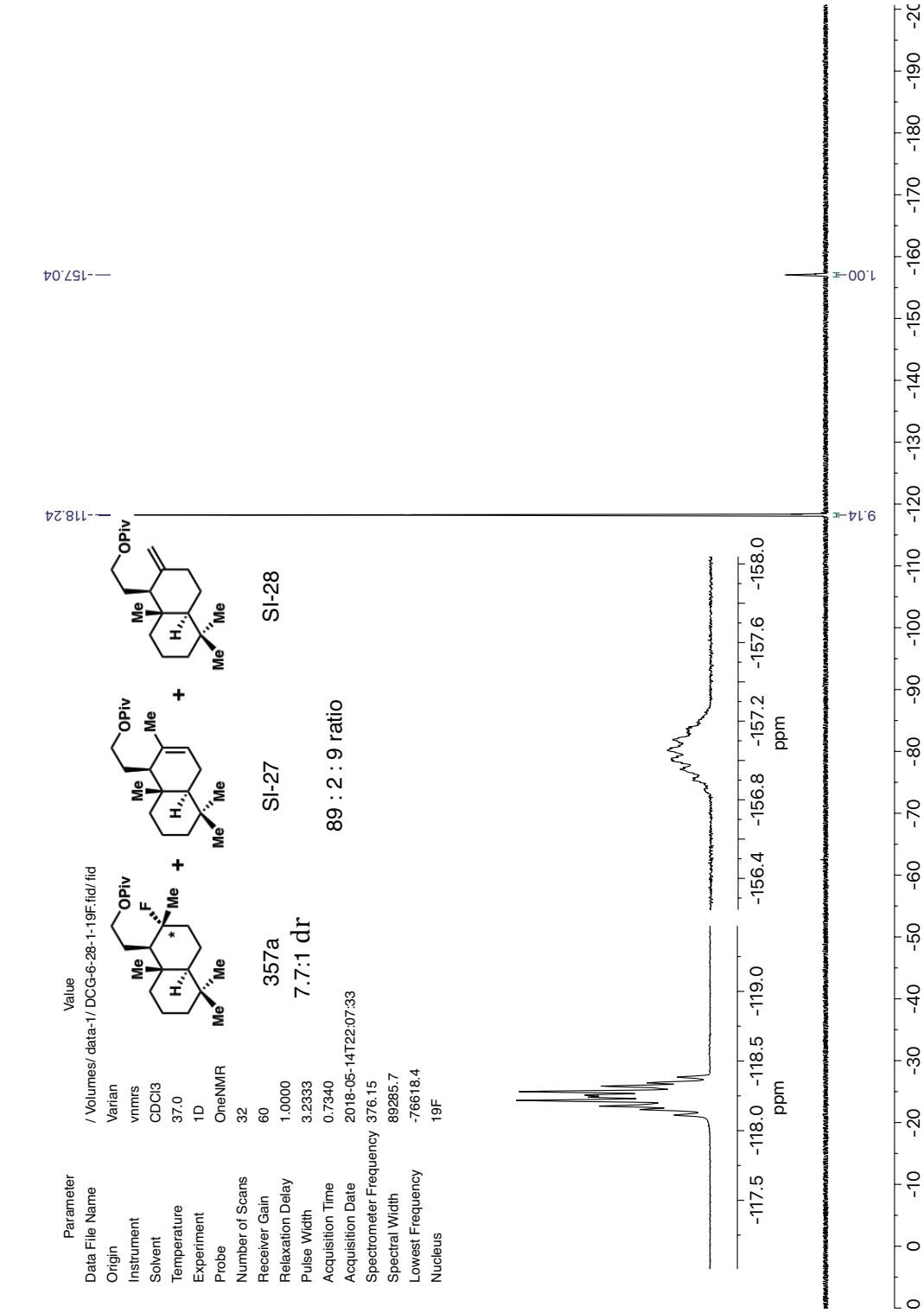
Data File Name / Volumes/ nmr/ DCG-6-28-1/ 1/ fid
Title DCG-6-28-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 297.2
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 30.3
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-05-14T20:52:23
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
357a
7.7:1 dr
SI-27
SI-28
89 : 2 : 9 ratio
A (dd) 1.34
B (d) 1.30
7.67
1.00
ppm


Parameter
Value
Data File Name / Volumes/ nmr/ DCG-6-28-1/3/ fid
Title DCG-6-28-1.3.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 297.2
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 128
Receiver Gain 87.8
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-05-14T21:12:06
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
357a
7.7:1 dr
SI-27
89 : 2 : 9 ratio
SI-28
178.76
99.34
97.69
65.62
65.57
55.84
55.82
55.51
55.34
41.92
41.17
40.96
39.56
38.81
38.77
38.67
33.54
33.40
33.38
27.39
24.39
22.64
22.38
21.61
20.45
20.34
18.54
15.31
ppm


ppm
ppm
Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-28-1/ 2/ ser
Title DCG-6-28-1.2.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 297.1
Pulse Sequence hsqcedetgpsisp2.4
Experiment HSQC-EDITED
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2018-05-14T20:53:40
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Nucleus (1H, 13C)
Acquired Size (1024, 180)
Spectral Size (1024, 1024)
OPiv
Me
F
Me
H
Me
Me
+
OPiv
Me
Me
H
Me
Me
+
OPiv
Me
H
Me
Me
357a
7.7:1 dr
SI-27
SI-28
89 : 2 : 9 ratio


Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-28-1/ 7/ ser
Title DCG-6-28-1.7.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 297.2
Pulse Sequence noesygpphzs
Experiment NOESY
Number of Scans 4
Receiver Gain 28.2
Relaxation Delay 1.8000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2018-05-22T13:58:44
Spectrometer Frequency (400.13, 400.13)
Spectral Width (4000.0, 4000.0)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
nOE
OPiv
F
Me
Me
H
Me
Me
357a
7.7:1 dr
ppm
ppm


Parameter
Value
Data File Name
/ Volumes/ nmr/ DCG-6-28-1/ 5/ ser
Title
DCG-6-28-1.5.ser
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
297.2
Pulse Sequence
hmbcetgpl3nd
Experiment
HMBC
Number of Scans
4
Receiver Gain
197.4
Relaxation Delay
2.0000
Pulse Width
11.7000
Acquisition Time
0.4260
Acquisition Date
2018-05-17T08:28:04
Spectrometer Frequency
(400.13, 100.62)
Spectral Width
(4807.7, 22321.4)
Nucleus
(1H, 13C)
Acquired Size
(2048, 256)
Spectral Size
(2048, 1024)
OPiv
F
Me
Me
Me
Me
H
357a
7.7:1 dr
SI-27
SI-28
89 : 2 : 9 ratio
HMBC
357a
7.7:1 dr
ppm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Instrument vnmrs
Solvent CDCl3
Temperature 37.0
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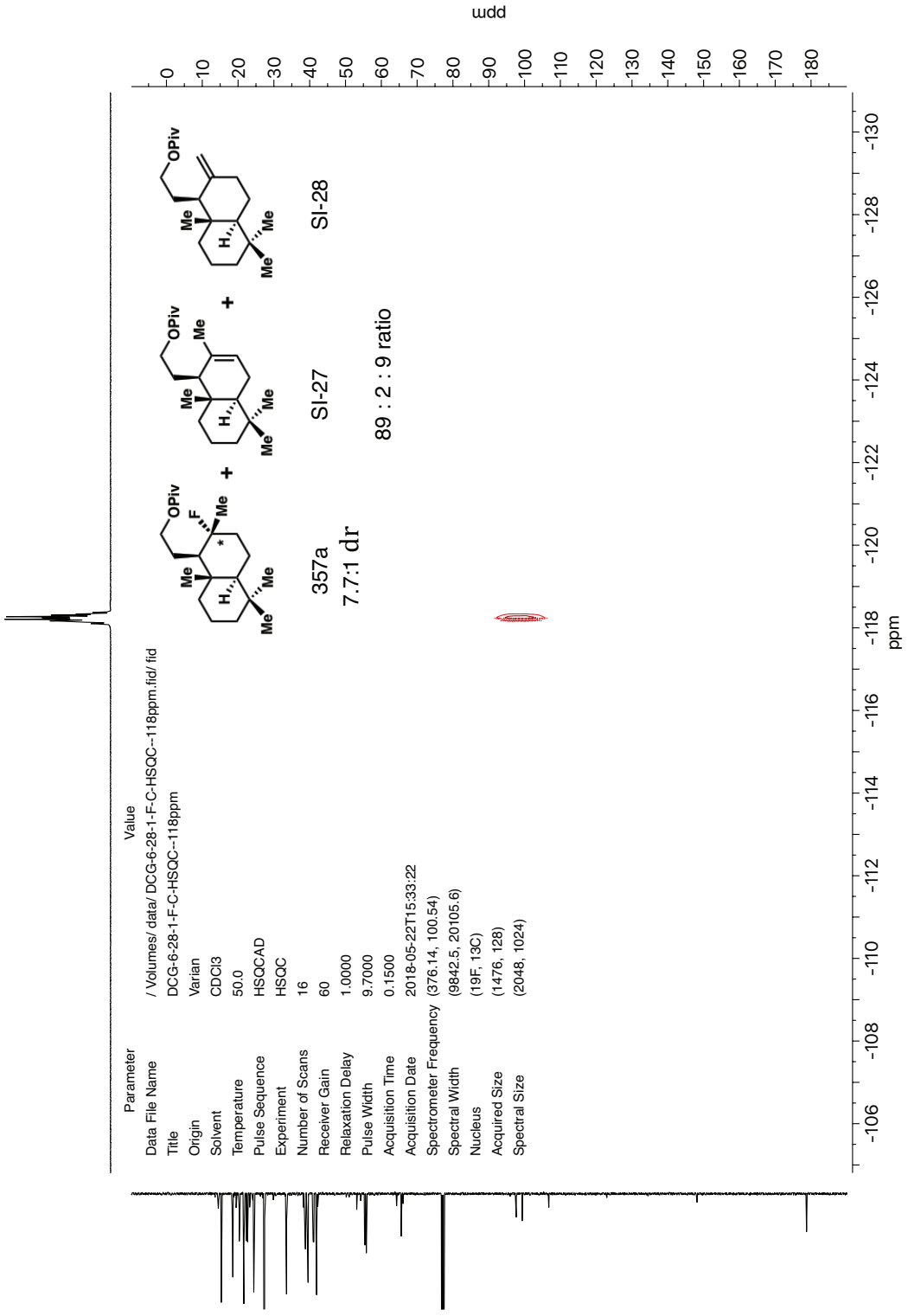
Probe OneNMR
Number of Scans 32
Receiver Gain 60
Relaxation Delay 1.0000
Pulse Width 3.2333
Acquisition Time 0.7340
Acquisition Date 2018-05-14T22:07:33
Spectrometer Frequency 376.15
Spectral Width 89285.7
Lowest Frequency -76618.4
Nucleus 19F
357a
7.7:1 dr
SI-27
SI-28
89 : 2 : 9 ratio
-118.24
-157.04
9.14
1.00
-117.5 -118.0 -118.5 -119.0
-156.4 -156.8 -157.2 -157.6 -158.0
ppm
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
ppm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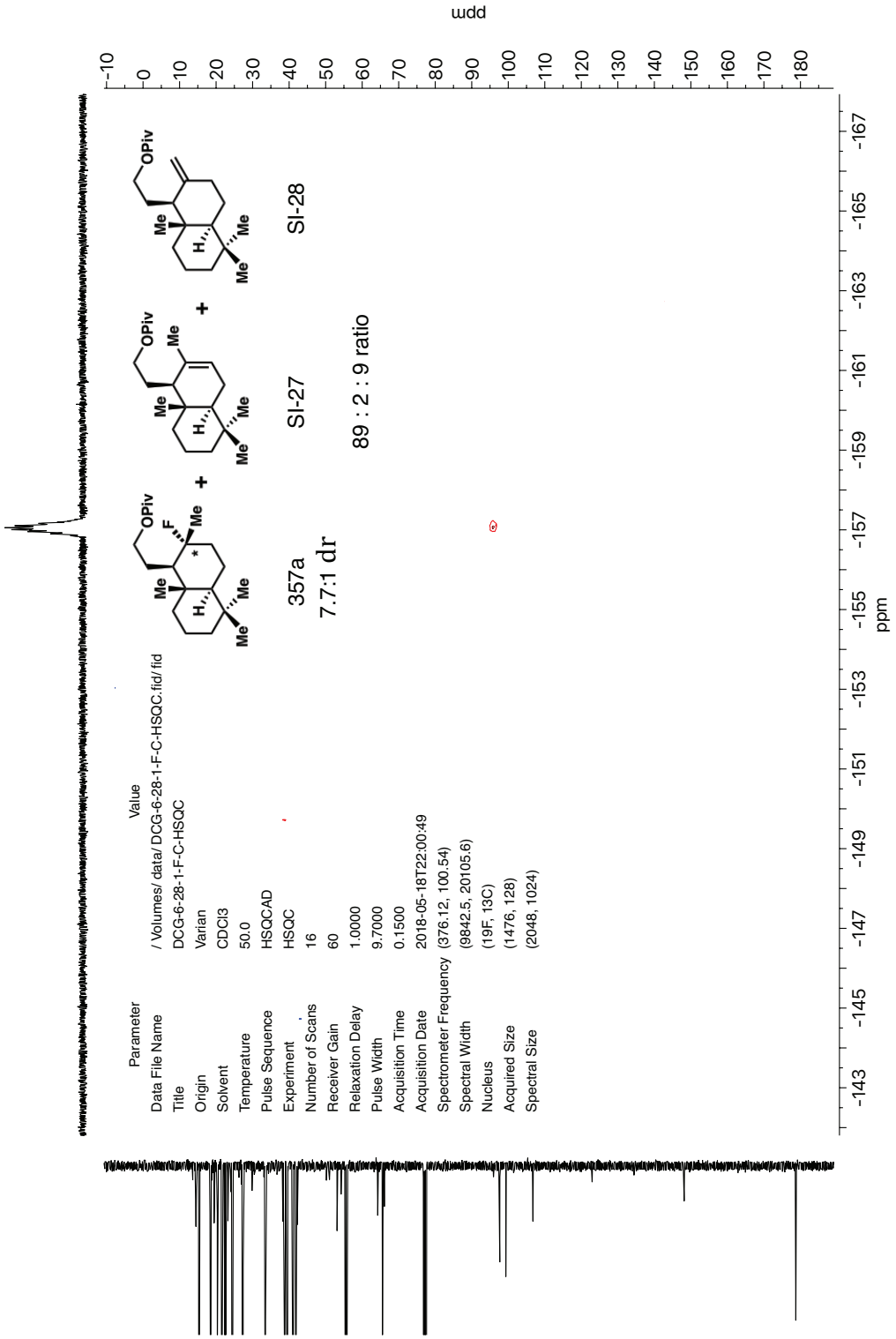
Origin
Varian
Solvent
CDCl3
Temperature
50.0
Pulse Sequence
HSQCAD
Experiment
HSQC
Number of Scans
16
Receiver Gain
60
Relaxation Delay
1.0000
Pulse Width
9.7000
Acquisition Time
0.1500
Acquisition Date
2018-05-22T15:33:22
Spectrometer Frequency
(376.14, 100.54)
Spectral Width
(9842.5, 20105.6)
Nucleus
(19F, 13C)
Acquired Size
(1476, 128)
Spectral Size
(2048, 1024)
357a
7.7:1 dr
SI-27
89 : 2 : 9 ratio
SI-28
ppm
ppm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10
20
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40
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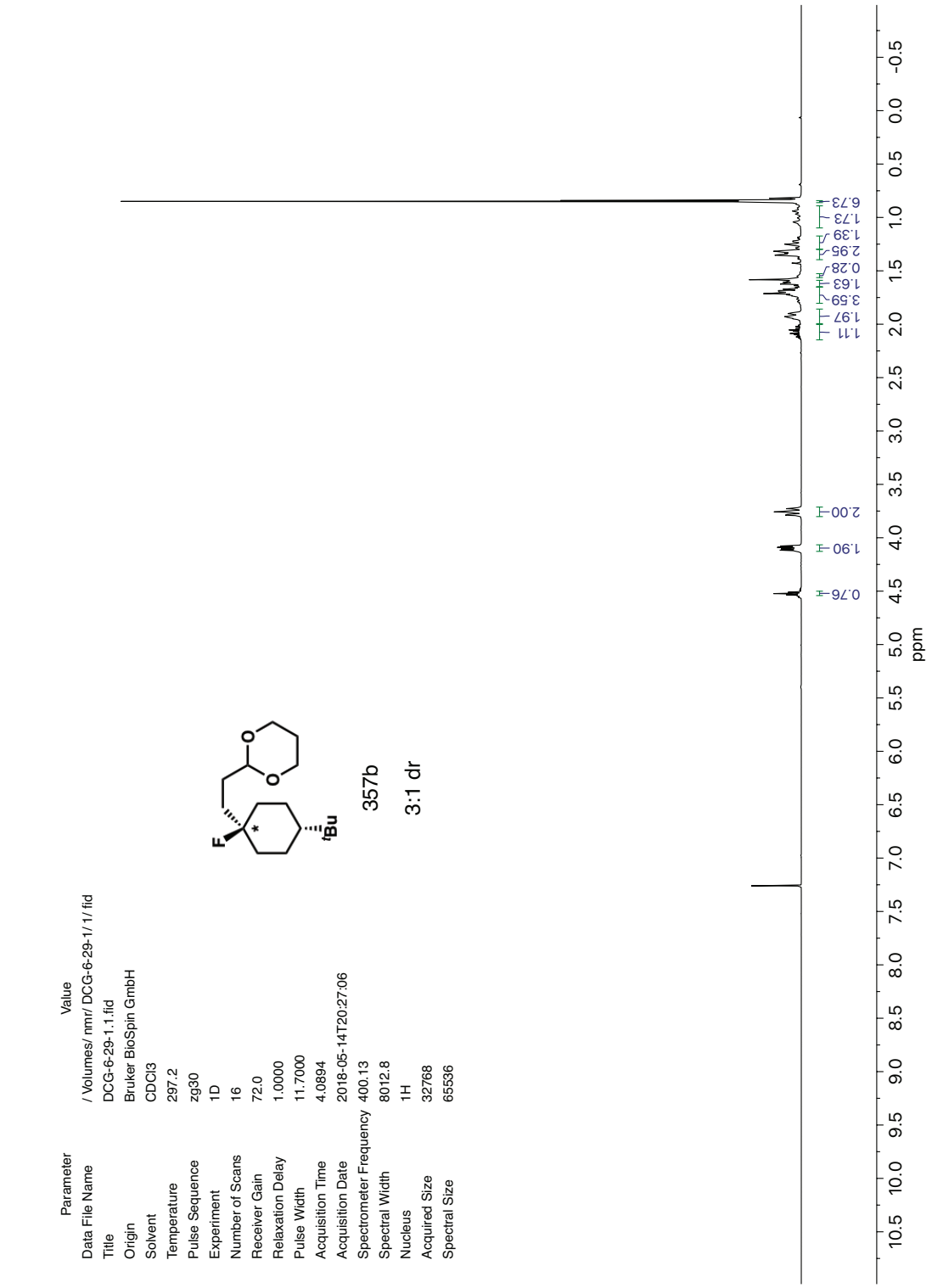
60
70
80
90
100
110
120
130
140
150
160
170
180
-143
-145
-147
-149
-151
-153
-155
-157
-159
-161
-163
-165
-167
ppm
Parameter
Value
Data File Name
/ Volumes/ data/ DCG-6-28-1-F-C-HSQC.fid/ fid
Title
DCG-6-28-1-F-C-HSQC
Origin
Varian
Solvent
CDCl3
Temperature
50.0
Pulse Sequence
HSQCAD
Experiment
HSQC
Number of Scans
16
Receiver Gain
60
Relaxation Delay
1.0000
Pulse Width
9.7000
Acquisition Time
0.1500
Acquisition Date
2018-05-18T22:00:49
Spectrometer Frequency
(376.12, 100.54)
Spectral Width
(9842.5, 20105.6)
Nucleus
(19F, 13C)
Acquired Size
(1476, 128)
Spectral Size
(2048, 1024)
OPiv
F
Me
Me
Me
Me
H
*
+
OPiv
Me
Me
Me
Me
H
+
OPiv
Me
Me
Me
Me
H
357a
7.7:1 dr
SI-27
89 : 2 : 9 ratio
SI-28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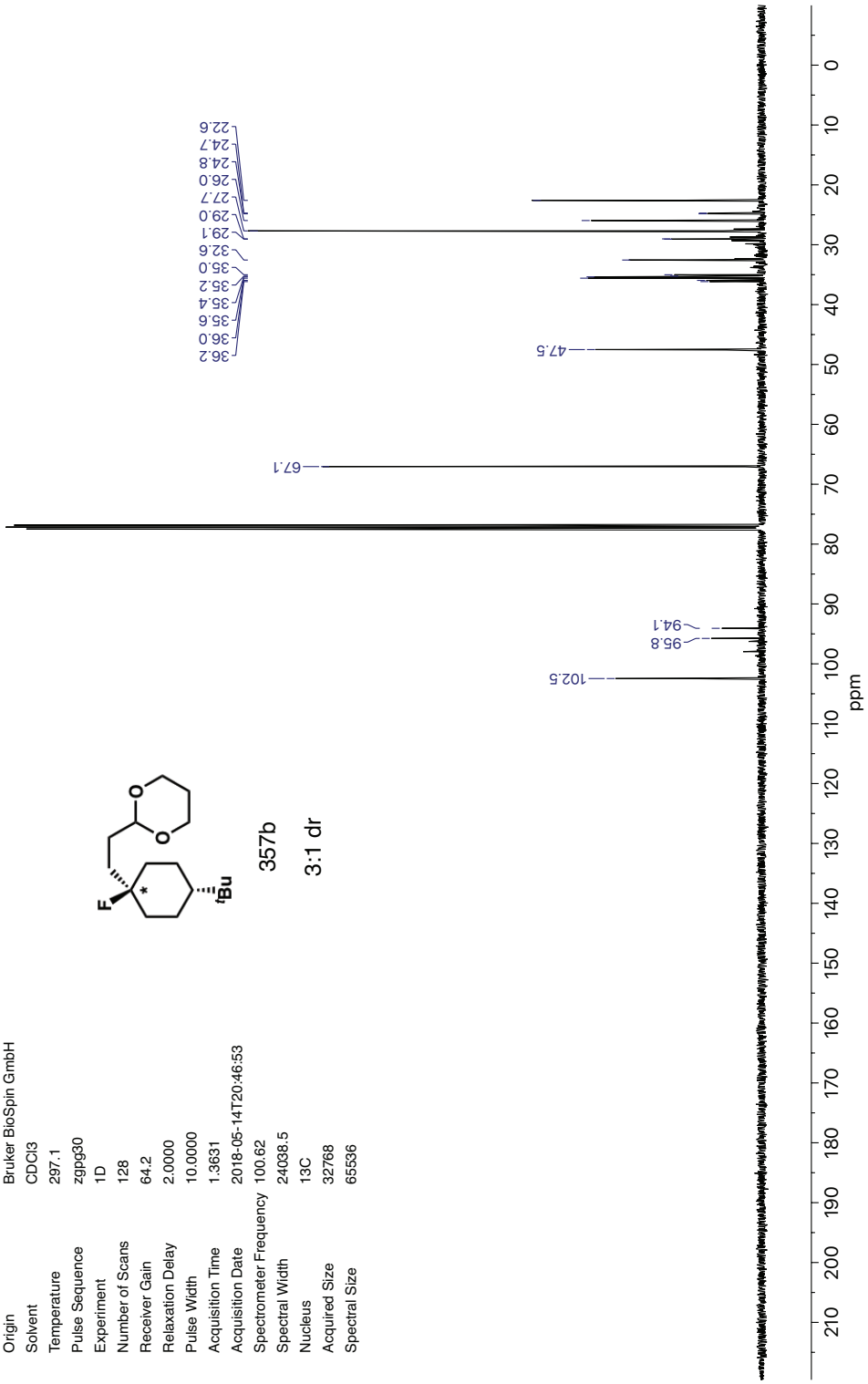
Title
DCG-6-29-1.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
297.2
Pulse Sequence
zg30
Experiment
1D
Number of Scans
16
Receiver Gain
72.0
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-05-14T20:27:06
Spectrometer Frequency
400.13
Spectral Width
8012.8
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
F
tBu
357b
3:1 dr
0.76
1.90
2.00
1.11
1.97
3.59
1.63
0.28
2.95
1.39
1.73
6.73
ppm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Data File Name / Volumes/ nmr/ DCG-6-29-1/3/ fid
Title DCG-6-29-1.3.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 297.1
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 128
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-05-14T20:46:53
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
F
tBu
357b
3:1 dr
102.5
95.8
94.1
67.1
47.5
36.2
36.0
35.6
35.4
35.2
35.0
32.6
29.1
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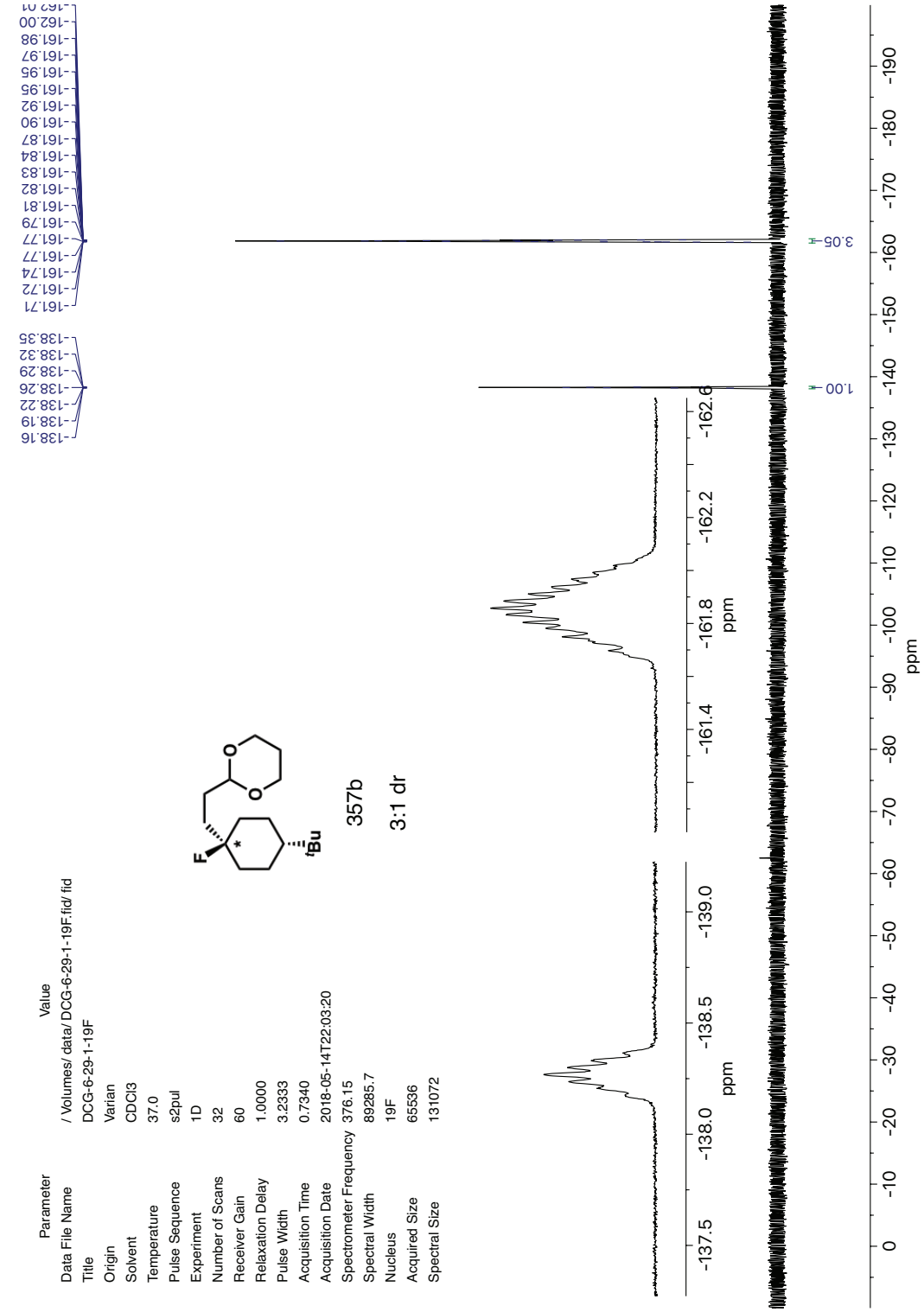
26.0
24.8
24.7
22.6
ppm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Data File Name / Volumes/ data/ DCG-6-29-1-19F.fid/ fid
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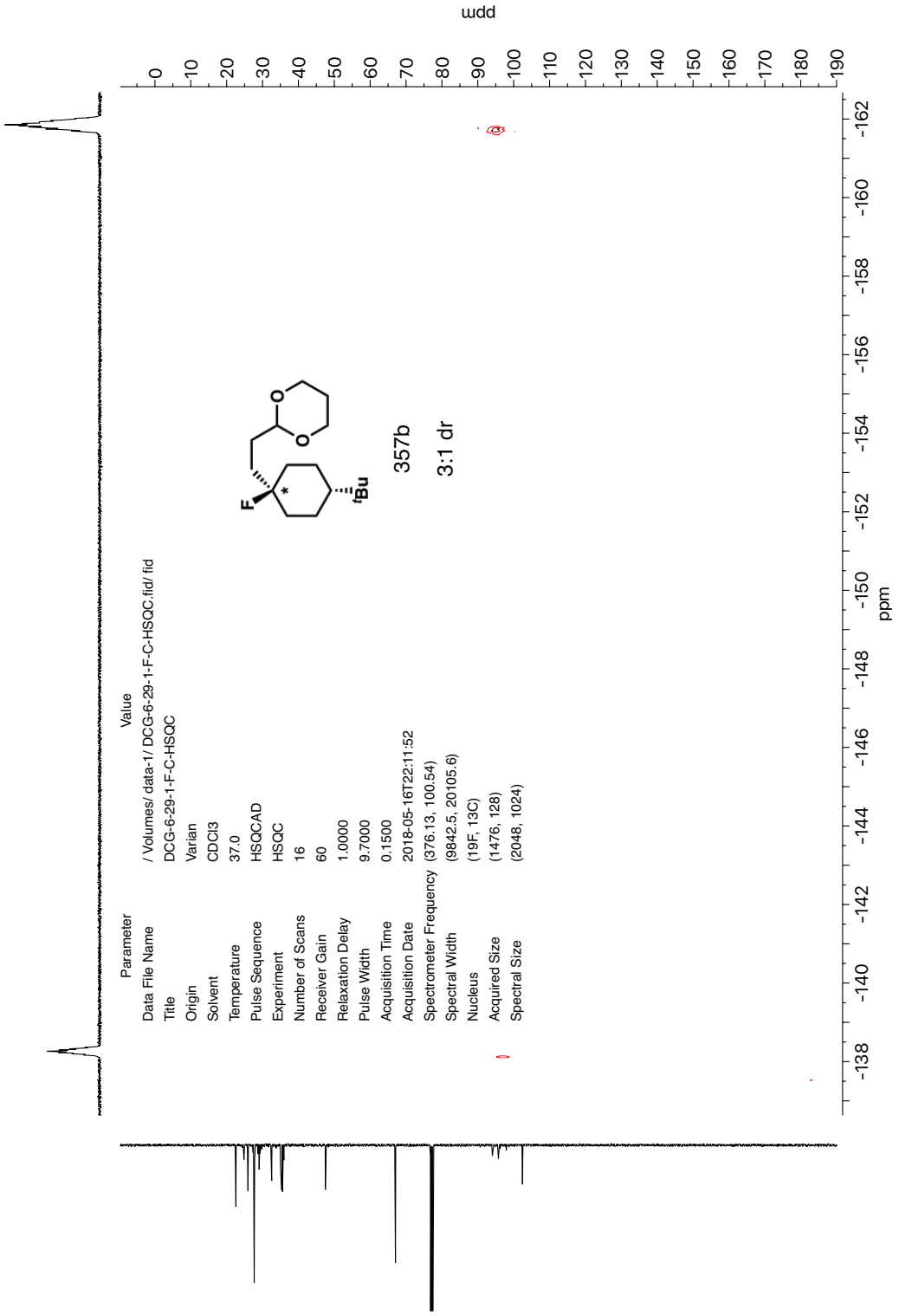
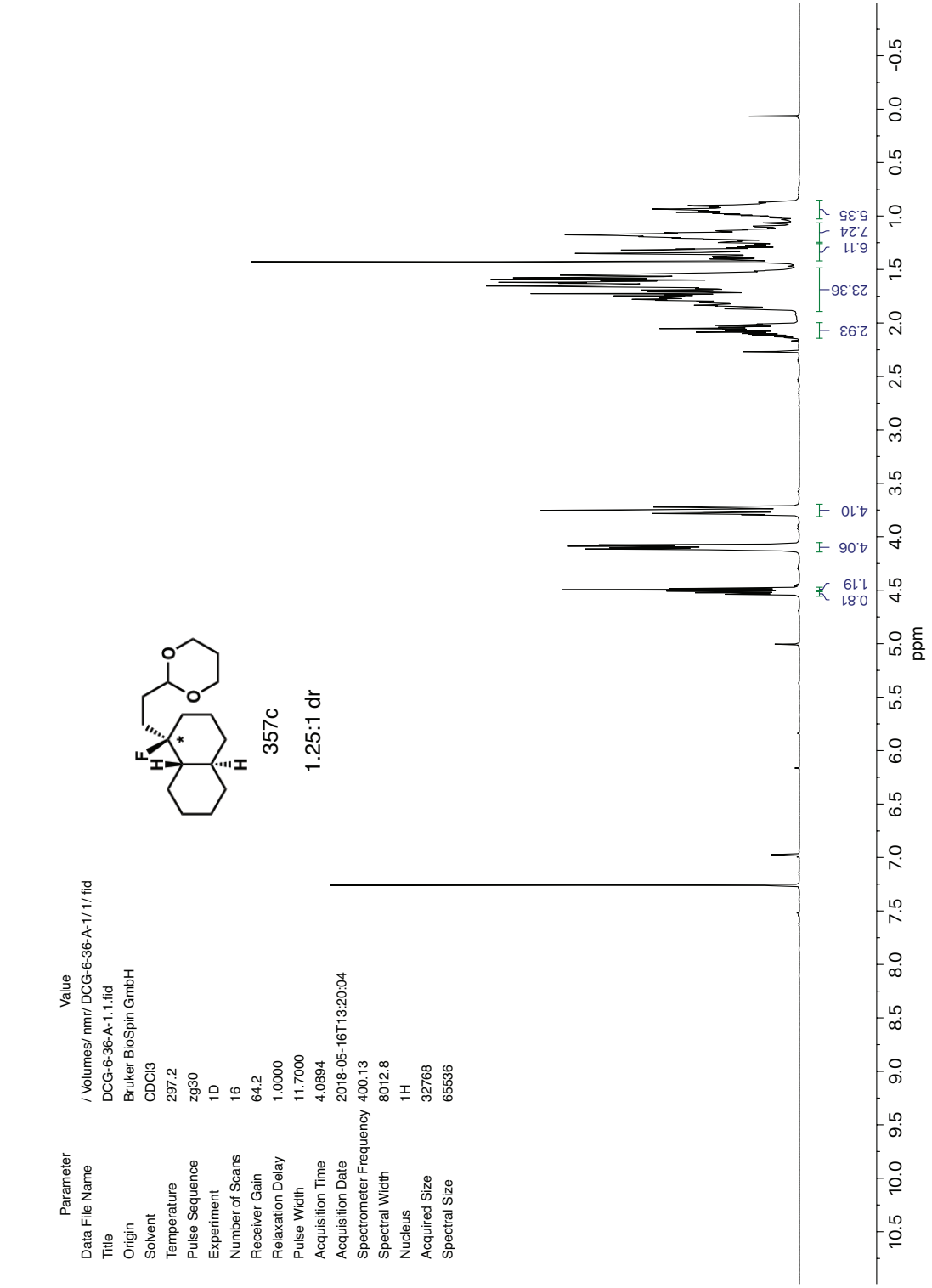
Origin Varian
Solvent CDCl3
Temperature 37.0
Pulse Sequence s2pul
Experiment 1D
Number of Scans 32
Receiver Gain 60
Relaxation Delay 1.0000
Pulse Width 3.2333
Acquisition Time 0.7340
Acquisition Date 2018-05-14T22:03:20
Spectrometer Frequency 376.15
Spectral Width 89285.7
Nucleus 19F
Acquired Size 65536
Spectral Size 131072
357b
3:1 dr
F
O
O
tBu
-138.16
-138.19
-138.22
-138.26
-138.29
-138.32
-138.35
-161.71
-161.72
-161.74
-161.77
-161.77
-161.79
-161.81
-161.82
-161.83
-161.84
-161.87
-161.90
-161.92
-161.95
-161.96
-161.97
-161.98
-162.00
-162.01
-137.5
-138.0
-138.5
-139.0
ppm
-161.4
-161.8
-162.2
-162.6
ppm
1.00
3.05
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
ppm


ppm
ppm
357b
3:1 dr
F
tBu
Parameter Value
Data File Name / Volumes/ data-1/ DCG-6-29-1-F-C-HSQC.fid/ fid
Title DCG-6-29-1-F-C-HSQC
Origin Varian
Solvent CDCl3
Temperature 37.0
Pulse Sequence HSQCAD
Experiment HSQC
Number of Scans 16
Receiver Gain 60
Relaxation Delay 1.0000
Pulse Width 9.7000
Acquisition Time 0.1500
Acquisition Date 2018-05-16T22:11:52
Spectrometer Frequency (376.13, 100.54)
Spectral Width (9842.5, 20105.6)
Nucleus (19F, 13C)
Acquired Size (1476, 128)
Spectral Size (2048, 1024)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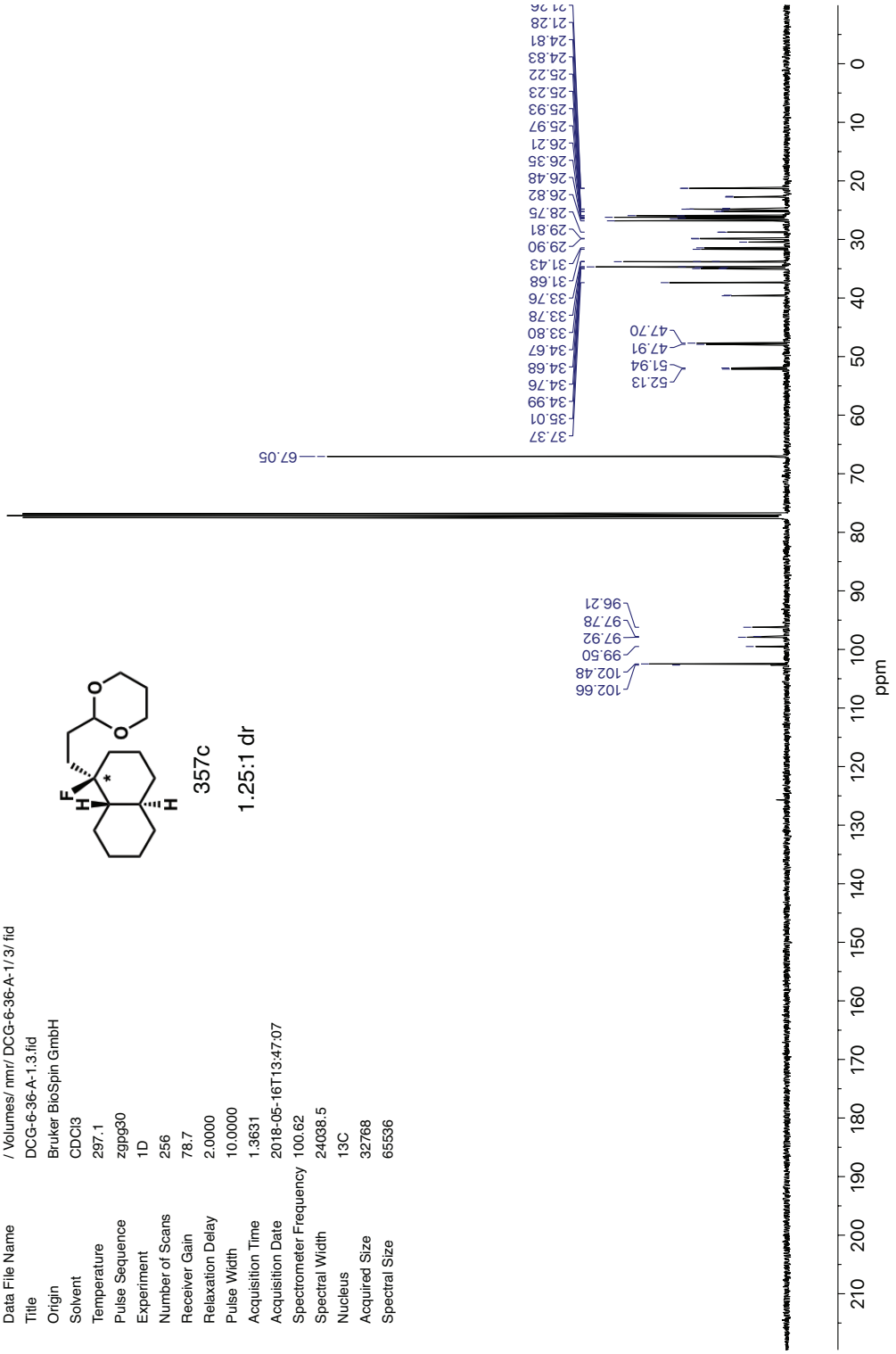
Data File Name / Volumes/ nmr/ DCG-6-36-A-1/ 1/ fid
Title DCG-6-36-A-1.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 297.2
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 64.2
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-05-16T13:20:04
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
357c
1.25:1 dr
0.81
1.19
4.06
4.10
2.93
23.36
6.11
7.24
5.35
ppm


Parameter Value
Data File Name / Volumes/ nmr/ DCG-6-36-A-1/3/ fid
Title DCG-6-36-A-1.3.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 297.1
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 256
Receiver Gain 78.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-05-16T13:47:07
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
357c
1.25:1 dr
67.05
102.66
102.48
99.50
97.92
97.78
96.21
52.13
51.94
47.91
47.70
37.37
35.01
34.99
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34.68
34.67
33.80
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33.76
31.68
31.43
29.90
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25.23
25.22
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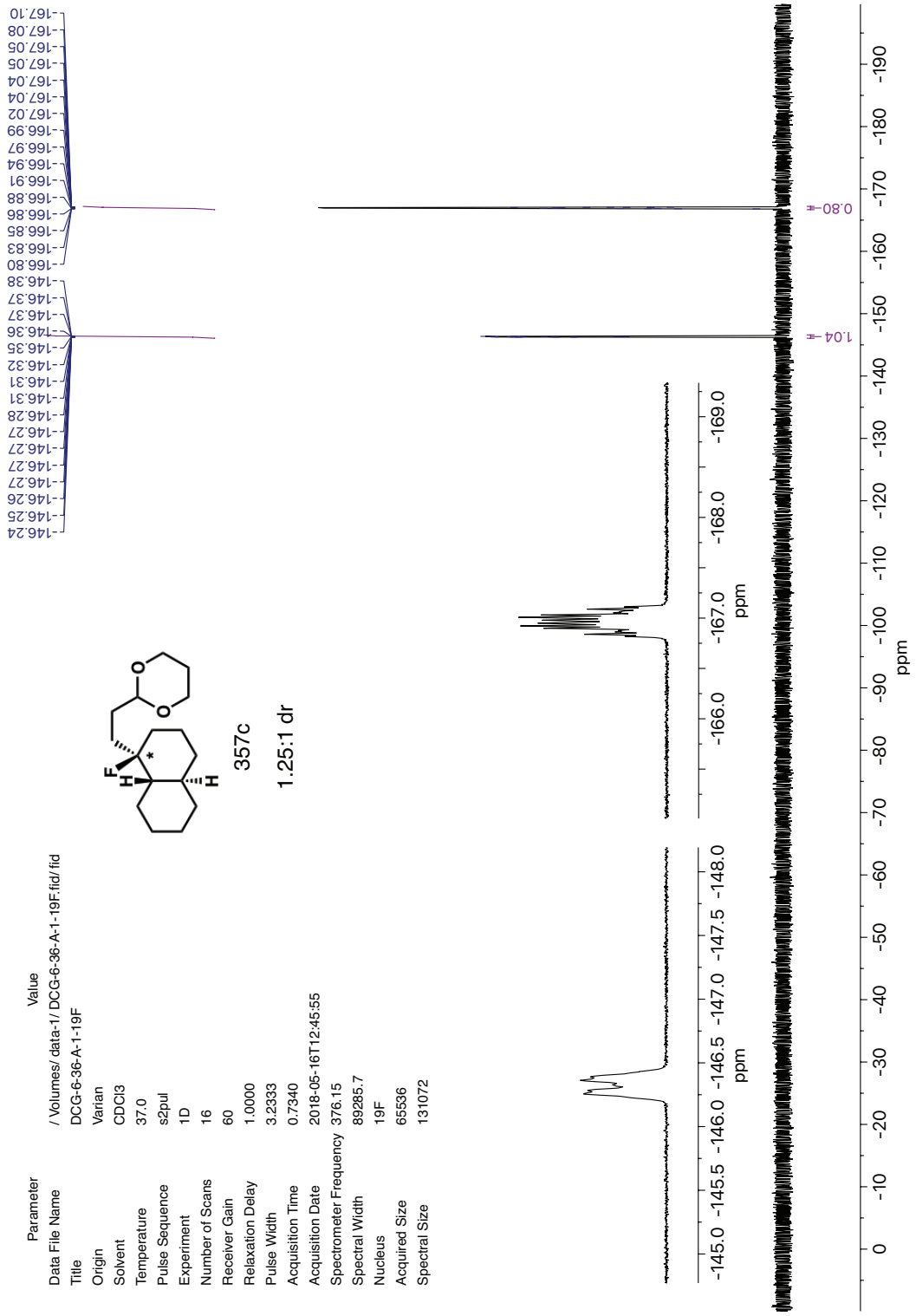
ppm


Parameter
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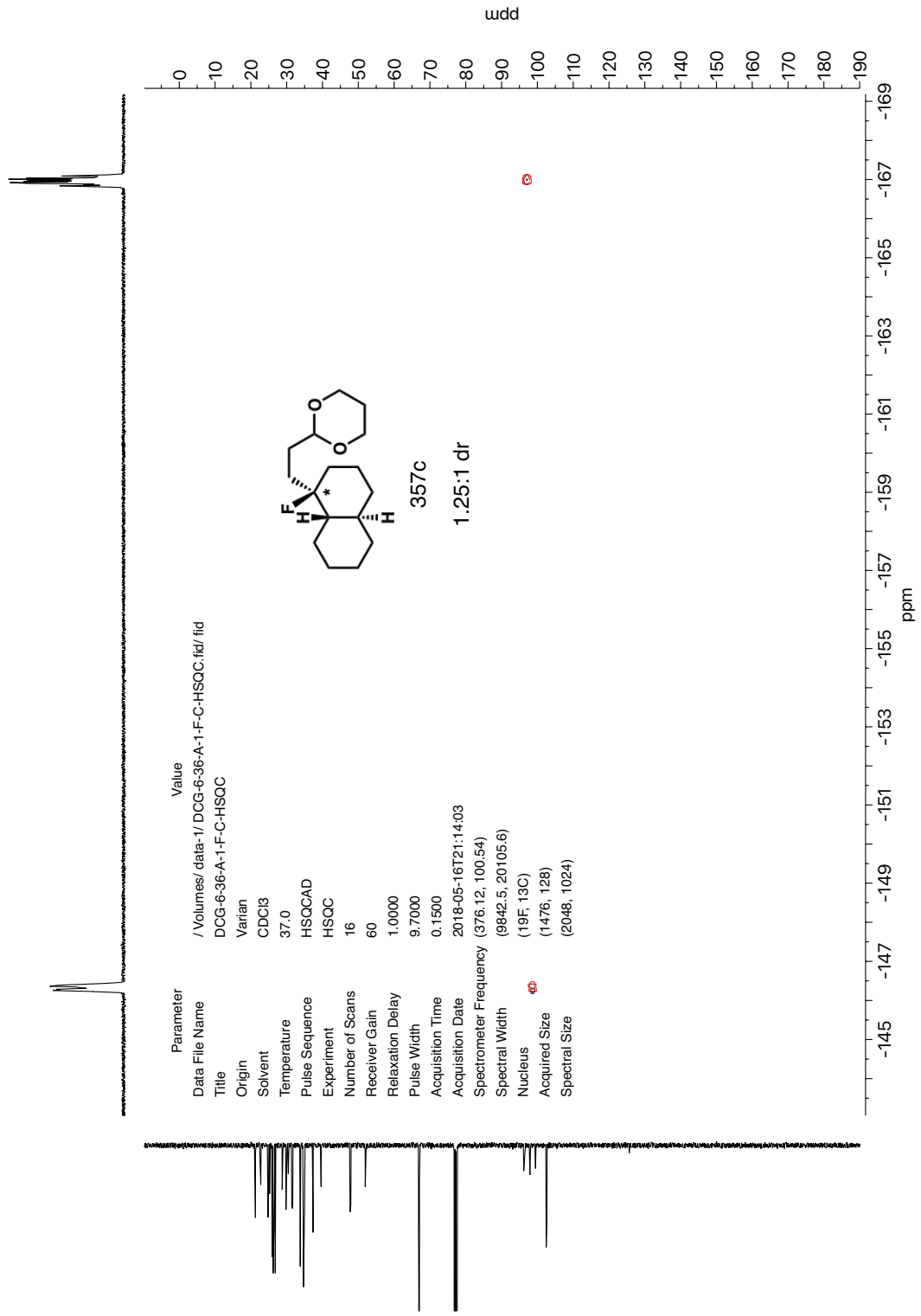
Data File Name / Volumes/ data-1/ DCG-6-36-A-1-19F.fid/ fid
Title DCG-6-36-A-1-19F
Origin Varian
Solvent CDCl3
Temperature 37.0
Pulse Sequence s2pul
Experiment 1D
Number of Scans 16
Receiver Gain 60
Relaxation Delay 1.0000
Pulse Width 3.2333
Acquisition Time 0.7340
Acquisition Date 2018-05-16T12:45:55
Spectrometer Frequency 376.15
Spectral Width 89285.7
Nucleus 19F
Acquired Size 65536
Spectral Size 131072
357c
1.25:1 dr
F
H
H
0.80
1.04
ppm
ppm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10
20
30
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90
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110
120
130
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150
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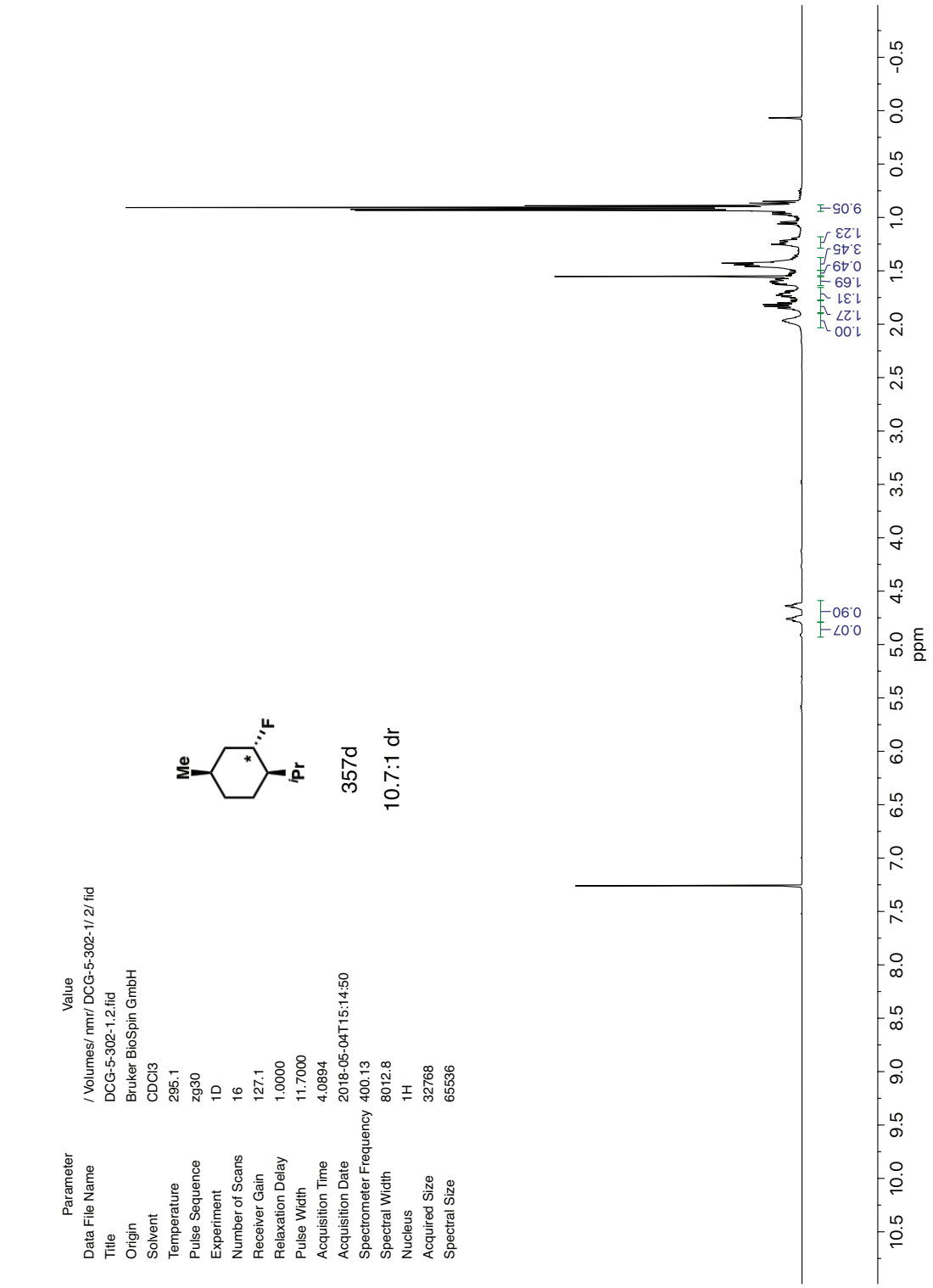
170
180
190
-145
-147
-149
-151
-153
-155
-157
-159
-161
-163
-165
-167
-169
ppm
Parameter
Value
Data File Name
/ Volumes/ data-1/ DCG-6-36-A-1-F-C-HSQC.fid/ fid
Title
DCG-6-36-A-1-F-C-HSQC
Origin
Varian
Solvent
CDCl3
Temperature
37.0
Pulse Sequence
HSQCAD
Experiment
HSQC
Number of Scans
16
Receiver Gain
60
Relaxation Delay
1.0000
Pulse Width
9.7000
Acquisition Time
0.1500
Acquisition Date
2018-05-16T21:14:03
Spectrometer Frequency
(376.12, 100.54)
Spectral Width
(9842.5, 20105.6)
Nucleus
(19F, 13C)
Acquired Size
(1476, 128)
Spectral Size
(2048, 1024)
F
H
H
O
O
357c
1.25:1 dr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Title DCG-5-302-1.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zg30
Experiment 1D
Number of Scans 16
Receiver Gain 127.1
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-05-04T15:14:50
Spectrometer Frequency 400.13
Spectral Width 8012.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
Me
F
iPr
357d
10.7:1 dr
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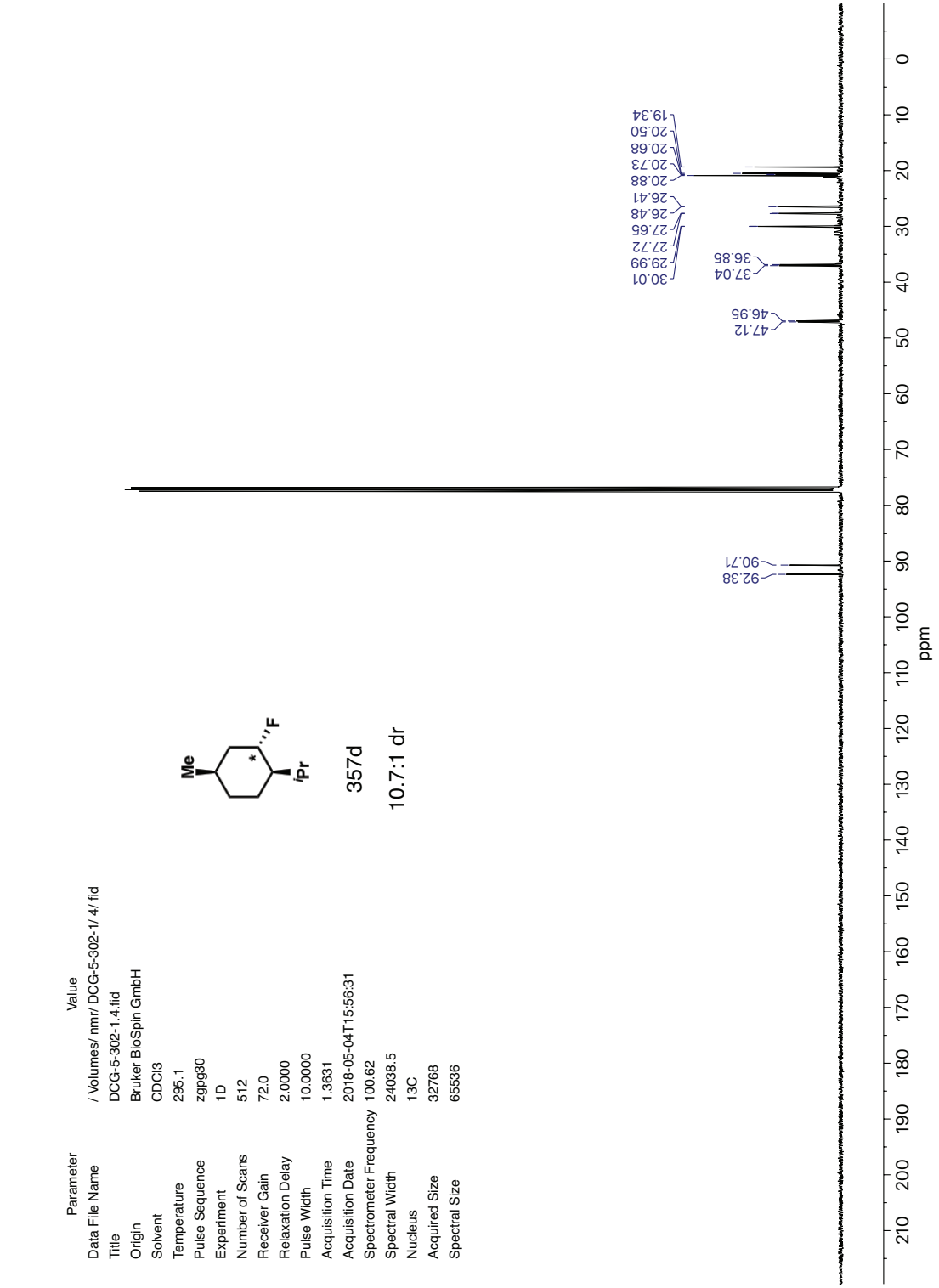
0.90
1.00
1.27
1.31
1.69
0.49
3.45
1.23
9.05
ppm


Parameter Value
Data File Name / Volumes/ nmr/ DCG-5-302-1/ 4/ fid
Title DCG-5-302-1.4.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zgpg30
Experiment 1D
Number of Scans 512
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-05-04T15:56:31
Spectrometer Frequency 100.62
Spectral Width 24038.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
F
iPr
357d
10.7:1 dr
92.38
90.71
47.12
46.95
37.04
36.85
30.01
29.99
27.72
27.65
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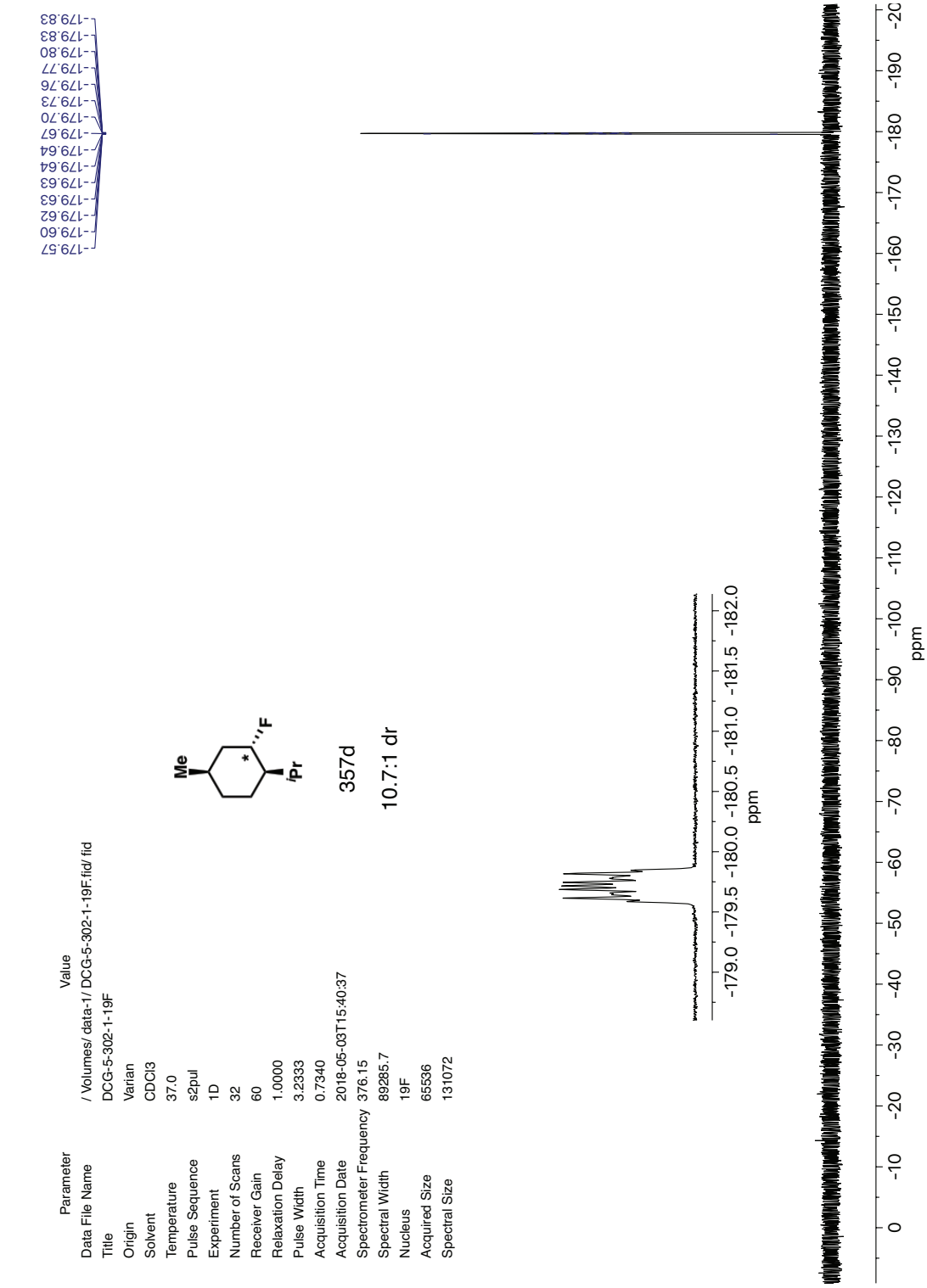
26.41
20.88
20.73
20.68
20.50
19.34
ppm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Title DCG-5-302-1-19F
Origin Varian
Solvent CDCl3
Temperature 37.0
Pulse Sequence s2pul
Experiment 1D
Number of Scans 32
Receiver Gain 60
Relaxation Delay 1.0000
Pulse Width 3.2333
Acquisition Time 0.7340
Acquisition Date 2018-05-03T15:40:37
Spectrometer Frequency 376.15
Spectral Width 89285.7
Nucleus 19F
Acquired Size 65536
Spectral Size 131072
Me
iPr
F
357d
10.7:1 dr
-179.57
-179.60
-179.62
-179.63
-179.63
-179.64
-179.64
-179.67
-179.70
-179.73
-179.76
-179.77
-179.80
-179.83
-179.83
-179.0 -179.5 -180.0 -180.5 -181.0 -181.5 -182.0
ppm
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -20
ppm

ABOUT THE AUTHOR

Denise Christine Grünenfelder was born on March 24th, 1987 to Janet M. Grünenfelder (Fetrow) and Karl R. Grünenfelder in Sursee, LU, Switzerland. She grew up in the neighboring canton of Zug, where she spent her childhood playing outside with her sister Diana. During her high school years in the Kantonsschule Zug, Denise chose to emphasize on chemistry and biology, largely due to the inspiring and contagious passion of her high school chemistry teacher. Without any hesitation, she went on to pursue a chemistry degree in college.

In 2006, Denise moved across the Atlantic to attend Boston University, where she earned her B.A. in chemistry in 2010. During this time, she had the privilege of joining the laboratory of Professor John A. Porco, where she conducted undergraduate research under the mentorship of Dr. Suwei Dong. Part of this time was spent pursuing total syntheses of bisorbicillinoid natural products, including bisorbicillinol and (–)-sorbicillactone A. Denise also completed two summer internships in the pharmaceutical industry, the first in the medicinal chemistry team at Novartis Institutes for BioMedical Research (NIBR), and the second in the process group at Millennium Pharmaceuticals.

Following her graduation from BU, Denise joined the oncology department at NIBR as an associate chemist where she worked for three years before returning to academia. In 2013, she moved to Pasadena to pursue her graduate studies under the direction of Professor Sarah E. Reisman at the California Institute of Technology. Her graduate research has focused on the total synthesis of spirocyclic acutumine alkaloids and the development of radical deoxychlorination reactions. Following the completion of her Ph.D., Denise will return to Boston, where she will join the medicinal chemistry team at Bristol-Myers Squibb.