TOTAL SYNTHESES OF THE C_{19} DITERPENOID ALKALOID NATURAL PRODUCTS (–)-LILJESTRANDISINE AND (–)-LILJESTRANDININE

Thesis by

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ABSTRACT

A unified synthetic strategy to access diterpenoid alkaloid natural products is presented. The highly bridged hexacyclic natural products are characterized as having a hydrindane bridged piperidyl motif that is common to the C_{19} *aconitine* type diterpenoid alkaloids and the C_{20} *napelline* and *denudatine* type diterpenoid alkaloids. A unified strategy to the C_{19} and C_{20} diterpenoid alkaloids is developed. An asymmetric synthesis of an epoxy-hydrindane fragment enables the development of the key unified strategy, involving a 1,2-addition followed by a semipinacol rearrangement in a key fragment coupling process. The fragment coupling is demonstrated generally with a variety of substrates, including an aromatic substrate that is advanced to a key bicyclo[2.2.1]heptane intermediate towards the C_{20} diterpenoid alkaloids.

The developed 1,2-addition/semipinacol-rearrangement strategy is ultimately leveraged in the total synthesis of two different C_{19} *aconitine* type diterpenoid alkaloids. An asymmetric synthesis of a bridged bicyclo[3.2.1]octane fragment is presented. The bridged bicyclo[3.2.1]octane fragment is advanced through the developed 1,2-addition/semipinacol rearrangement fragment coupling strategy affording a key tetracyclic intermediate. This work ultimately culminates in the total syntheses of two natural products (–)-liljestrandisine and (–)-liljestrandinine. Key steps for the completion of the total syntheses include advancement of the key tetracyclic intermediate from the fragment coupling through a series of C–N and C–C bond forming reactions, including an intramolecular aziridination reaction and a radical cyclization.

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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
p-ABSA	para-acetamidobenzenesulfonyl azide
Ac	acetyl
acac	acetylacetonate
AIBN	azobisisobutyronitrile
aq	aqueous
Ar	aryl group
atm	atmosphere(s)
BINOL	1,1'-bi-2,2'-naphthol
bipy	2,2'-bipyridine
Bn	benzyl
Boc	tert-butoxycarbonyl
bp	boiling point
br	broad
Bu	butyl
i-Bu	*iso*-butyl
n-Bu	butyl or *norm*-butyl
t-Bu	*tert*-butyl
BQ	1,4-benzoquinone

Bz	benzoyl
c	concentration of sample for measurement of optical rotation
^{13}C	carbon-13 isotope
/C	supported on activated carbon charcoal
°C	degrees Celsius
calc’d	calculated
CAN	ceric ammonium nitrate
cat.	catalyst
Cbz	benzyloxycarbonyl
cf.	consult or compare to (Latin: confer)
cis	(zusammen) on the same side
cm^{-1}	wavenumber(s)
CoA	Coenzyme A
conc.	concentrated
conv.	conversion
Cp	cyclopentadienyl
CSA	camphor sulfonic acid
Cy	cyclohexyl
Δ	heat or difference
δ	chemical shift in ppm
d	doublet
d	deutero or dextrorotatory
D	deuterium

dba	dibenzylideneacetone
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCE	1,2-dichloroethane
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
de novo	starting from the beginning; anew
DIPEA	*N,N*-diisopropylethylamine
DHQ	dihydroquinine
DHQD	dihydroquinidine
DIBAL	diisobutylaluminum hydride
DMAP	4-(dimethylamino)pyridine
DME	1,2-dimethoxyethane
DMEDA	N,N'-dimethylethylenediamine
DMF	*N,N*-dimethylformamide
DMP	Dess-Martin Periodinane
DMPU	1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone
DMSO	dimethylsulfoxide
dppe	1,2-bis(diphenylphosphino)ethane
dppf	1,1'-bis(diphenylphosphino)ferrocene
dr	diastereomeric ratio
ee	enantiomeric excess
E	methyl carboxylate (CO_2CH_3)
E^+	electrophile
E	trans (entgegen) olefin geometry

EDCI	N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride
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*)
FAB	fast atom bombardment
FTIR	fourier transform infrared spectroscopy
g	gram(s)
h	hour(s)
1H	proton
[H]	reduction
HDA	hetero-Diels–Alder
HFIP	hexafluoroisopropanol
HMBC	heteronuclear multiple-bond correlation spectroscopy
HMDS	hexamethyldisilazide
HMPA	hexamethylphosphoramide
hν	irradiation with light
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectrometry

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 or neutral ligand
l	levorotatory
LA	Lewis acid
LC/MS	liquid chromatography–mass spectrometry
LDA	lithium diisopropylamide
m	multiplet or meter(s)
M	molar or molecular ion
m	meta
µ	micro
m-CPBA	meta-chloroperbenzoic acid
Me	methyl
mg	milligram(s)
MHz	megahertz
MIC	minimum inhibitory concentration

min	minute(s)
mL	milliliter(s)
MM	mixed method
mol	mole(s)
MOM	methoxymethyl
Ms	methanesulfonyl (mesyl)
MS	molecular sieves
MTT	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide
m/z	mass-to-charge ratio
NBS	*N*-bromosuccinimide
nd	not determined
NHC	N-heterocyclic carbene
nm	nanometer(s)
nM	nanomolar
NMO	*N*-methylmorpholine N-oxide
NMR	nuclear magnetic resonance
NOE	nuclear Overhauser effect
NOESY	nuclear Overhauser enhancement spectroscopy
NPh	naphthyl
Nu	nucleophile
o	ortho
[O]	oxidation
P	peak

p	para
PCC	pyridinium chlorochromate
PDC	pyridinium dichromate
Ph	phenyl
pH	hydrogen ion concentration in aqueous solution
PHAL	1,4-phthalazinediyl diether
PIFA	[bis(trifluoroacetoxy)iodo]benzene
Pin	pinacol
PivOH	pivalic acid
pK_a	acid dissociation constant
pm	picometer(s)
PMB	*para*-methoxybenzyl
ppm	parts per million
PPTS	pyridinium para-toluenesulfonate
Pr	propyl
i-Pr	*iso*propyl
n-Pr	propyl or *norm*-propyl
psi	pounds per square inch
py	pyridine
PYR	2,5-diphenyl-4,6-pyrimidinediyl diether
q	quartet
QD	Quinidine
QN	Quinine

quant.	quantitative
R	generic (alkyl) group
RL	large group
R	rectus
RCM	ring-closing metathesis
recry.	recrystallization
ref	reference
Rf	retention factor
rgt.	reagent
rt	room temperature
s	singlet or seconds
sat.	saturated
t	triplet
TBAF	tetra-*n*-butylammonium fluoride
TBME	*tert*-butyl methyl ether
TBS	*tert*-butyldimethylsilyl
TC	thiophene-2-carboxylate
temp	temperature
Tf	trifluoromethanesulfonyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TIPS	tri*iso*propylsilyl
TLC	thin layer chromatography

TMS	trimethylsilyl
TOF	time-of-flight
tol	tolyl
TPAP	tetrapropylammonium perruthenate
trans	on the opposite side
Ts	para-toluenesulfonyl (tosyl)
UV	ultraviolet
vide infra	see below
w/v	weight per volume
X	anionic ligand or halide
xs	excess
Z	*cis* (zusammen) olefin geometry

Chapter 1

Development of a Unified Strategy Towards Diterpenoid Alkaloids

1.1 INTRODUCTION

The diterpenoid alkaloids are a diverse class of over 1200 natural products, which are primarily isolated from the *Aconitum* and *Delphinium* genera of plants.[1,2] Famously, these plants are known for their beautiful purple flowers commonly known as "monk's hood", "devil's helmet", or "queen of poisons." While the name "queen of poisons" highlights their toxicity, the herbs and roots of these plants have also been used in traditional Chinese and Japanese folk medicines for centuries. Indeed, the diterpenoid alkaloids display a variety of biological activities including antiarrhythmic, anti-inflammatory, anticancer, and antihypertensive, among others. These compounds are also known to modulate voltage-gated ion channels.[3] It is their complex structure and pharmacological activity that have long interested scientists and drawn them to study their phytochemistry, medicinal properties, structure and synthesis.

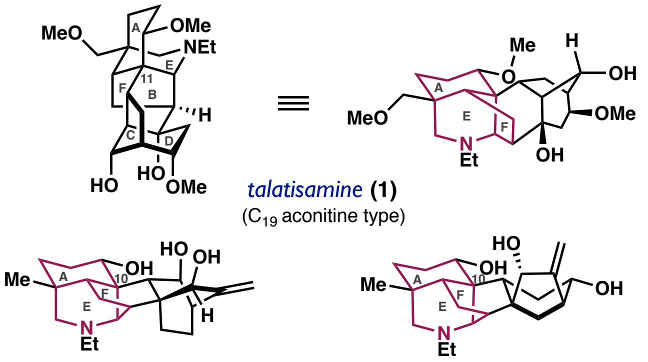
The diterpenoid alkaloids originate from terpene biosynthesis pathways through a series of enzymatic cyclizations, further skeletal rearrangements, oxidations and incorporation of nitrogen resulting in highly caged hexacyclic natural products.[4] These compounds are often called "pseudoalkaloids" because these molecules arise from prenyl units, and the nitrogen is incorporated at a late stage.[4] The structures have been known for decades and as a result, many strategies towards these natural products have been reported to date, as well as numerous total syntheses of both the C_{19}[5] and C_{20}[6] diterpenoid alkaloids. However, strategic, efficient, and fully synthetic access to these complex alkaloids remains an unfulfilled challenge.

1.2 SYNTHETIC STRATEGY

The targets of our research efforts (compounds **1–3**) are shown in Figure 1.1. Notably, these molecules each possess the same hydrindane-bridged piperidyl motif (AEF tricycle) highlighted in each structure. We sought to devise a unified synthetic towards these alkaloids that takes advantage of this common structural motif.

Our primary research efforts focused around the total synthesis of the C_{19} *aconitine* alkaloid talatisamine (**1**), due to its interesting activity as a non-cytotoxic blocker of voltage-gated K^+ channels with selectivity over voltage-gated Na^+ and Ca^{2+} ion channels as well as its ability to attenuate the cytotoxicity of β-amyloid oligomers by restoring cell viability.[7] We were also interested in the development of a unified synthetic strategy that would enable total syntheses of different members of the diterpenoid alkaloid family of natural products, such as the C_{20} diterpenoid alkaloid napelline (**2**) and lepenine (**3**).

Figure 1.1. Examples of C_{19}- and C_{20}-Diterpenoid Alkaloids.



talatisamine **(1)**
(C_{19} aconitine type)

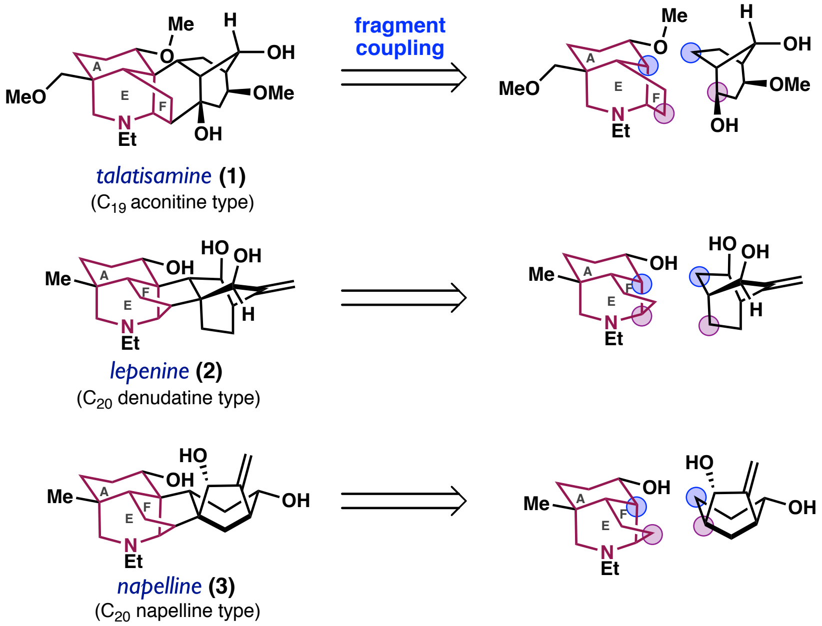
lepenine **(2)**
(C_{20} denudatine type)

napelline **(3)**
(C_{20} napelline type)

1.2.1 SYNTHETIC STRATEGY FOR C_{19} DITERPENOID ALKALOIDS

Our goals for this project included developing a unified synthetic strategy that would enable the synthesis of other types of diterpenoid alkaloids (e.g. **2** or **3**), in addition to our primary target (**1**). Specifically, identification of the AEF tricycle common to the C_{19} and C_{20} diterpenoid alkaloids guided the retrosynthetic strategy. While our first goal was to develop a total synthesis of a C_{19} diterpenoid alkaloid such as **1**, it was believed that developing a synthetic strategy that could be extended to other members of the family would ultimately provide the greatest contribution to the area of diterpenoid alkaloids total synthesis. Furthermore, while others have reported total syntheses of these molecules, convergent strategies remain an unfulfilled challenge. Having identified the AEF tricycle common to **1**–**3**, we sought to develop a convergent fragment coupling approach in which the AEF tricycle could be coupled with the appropriate bicycle to potentially access **1**–**3**. The idealized retrosynthetic concept that we hoped to achieve in this work is shown in Figure 1.2. That is, our ultimate goal was to identify general bond formation strategies that would enable C–C bond formations, retrosynthetically disconnecting to the AEF tricyclic unit, and a bridged bicyclic motif necessary for each class of natural products.

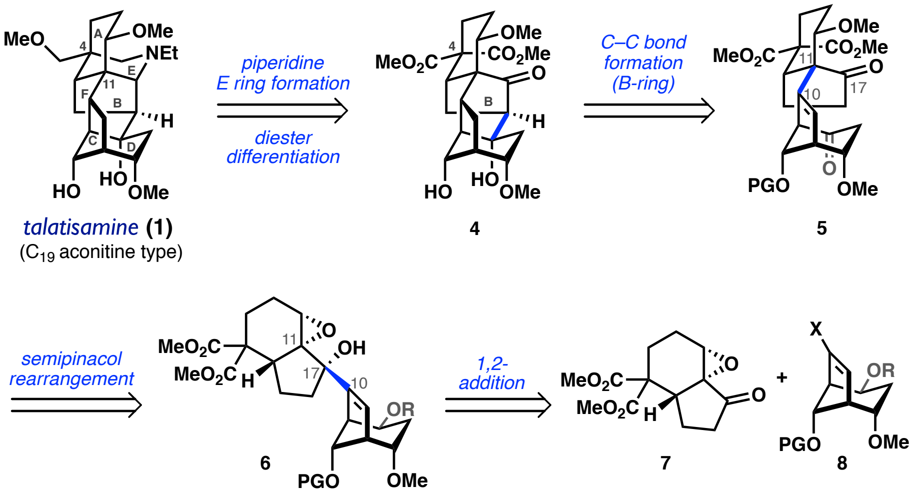
Figure 1.2. Key Retrosynthetic Concept for C_{19}- and C_{20}-Diterpenoid Alkaloids.



This chapter focuses on the development of a 1,2-addition and subsequent semipinacol rearrangement, ultimately enabling the fragment coupling synthetic strategy. This strategy was ultimately utilized in the context of the total synthesis of the C_{19} diterpenoid alkaloids (–)-liljestrandisine and (–)-liljestrandinine (Chapters 2 and 3). A retrosynthetic analysis that was envisioned for the C_{19} diterpenoid alkaloids is provided here (and is discussed in more detail in Chapters 2 and 3), as this guided our work in strategy development.

For the C_{19} diterpenoid alkaloid **1**, we envisioned a key disconnection through the piperidine E-ring through C–N bond formation and differentiation of diester **4** (Figure 1.3). Introducing the C4 quaternary center as the diester is simplifying because this center could be generated through the simple α-functionalization of a diester. Furthermore, by introducing the C_4 quaternary center as the diester, this obviates the need to diastereoselectively form this center, and was believed that it could be more easily differentiated at a late stage through substrate control. The B ring in **4** could be assembled through a C–C bond formation from **5** via α-functionalization of the C17 ketone. The C10–C11 bond and hindered C11 quaternary center in **5** would arise from a semipinacol rearrangement of epoxy-alcohol **6**. **6** would arise from the convergent union of two bicyclic fragments of similar size and complexity, namely a 1,2-addition of a vinyl-nucleophile **8** into epoxyketone **7**. Notably, both fragments for this coupling event are chiral, necessitating asymmetric syntheses of each fragment.

Figure 1.3. Retrosynthetic strategy towards C_{19} diterpenoid alkaloids.

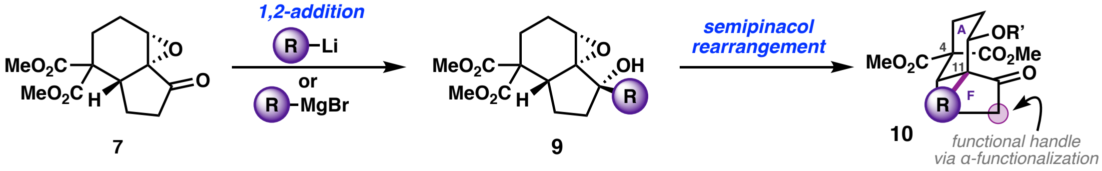


1.2.2 1,2-ADDITION/SEMIPINACOL FRAGMENT COUPLING STRATEGY

Our 1,2-addition and subsequent semipinacol rearrangement approach is central to the synthetic strategy, and we envisioned that developing this strategy would ultimately be enabling for the total synthesis. By investigating the substrate scope for the 1,2-

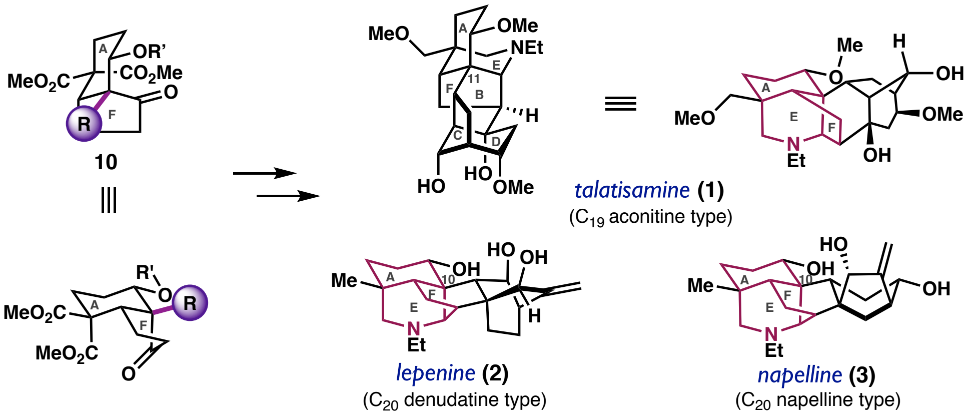
addition and subsequent semipinacol rearrangement, we hoped to develop an understanding of this key disconnection in the context of diterpenoid alkaloid total synthesis. Diastereoselective addition of an organometallic reagent or Grignard reagent to epoxyketone **7** should provide epoxy-alcohol **9** (Figure 1.4). It is proposed that the organometallic reagent would preferentially add to the opposite face of the epoxide. Subsequent treatment with a Lewis acid should then facilitate an epoxide-opening semipinacol rearrangement, providing **10**. This strategy proposes to leverage a number of key features: 1) use of robust 1,2-addition chemistry to diastereoselectively form a crucial C–C bond and unify two complex fragments, 2) the enthalpic driving force of epoxide opening to generate a hindered all carbon quaternary center.

Figure 1.4. 1,2-Addition and Semipinacol Rearrangement Strategy.



It is envisioned that the 1,2-addition/semipinacol rearrangement strategy would enable a unified strategy to both the C_{19} and C_{20} diterpenoid alkaloids (Figure 1.5). The semipinacol rearrangement product **10** maps onto the A and F rings of both the C_{19} and C_{20} diterpenoid alkaloids, as highlighted in Figure 1.4. It is proposed that introduction of a variety of different R groups, such as aryl fragments with a variety of different oxidation and functional handles could lead to the core framework of the C_{20} diterpenoid alkaloids.

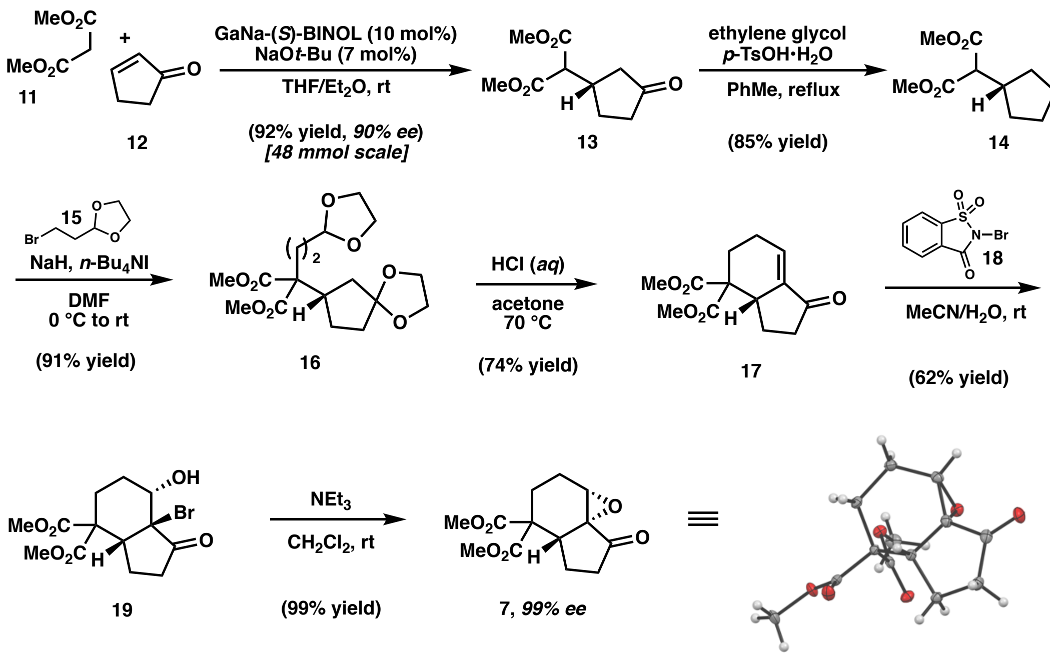
Figure 1.5. Unified Synthetic Strategy via 1,2-Addition and Semipinacol Rearrangement.



1.3 ASYMMETRIC SYNTHESIS OF EPOXYKETONE FRAGMENT

Our first goal was to develop a route to synthesize epoxyketone **7** enantioselectively, and evaluate the key convergent 1,2-addition/semipinacol-rearrangement strategy.[8] Our asymmetric synthesis of **7** begins with an asymmetric conjugate addition using Shibasaki's GaNa-BINOL catalyst[9] of dimethyl malonate (**11**) onto 2-cyclo-penten-1-one (**12**) to afford cyclopentanone **13** in 90% ee (Figure 1.6). Subsequent ketal protection afforded **14**, which was subsequently alkylated with bromide **15** affording bis-ketal **16**. Treatment of **16** with aqueous hydrochloric acid at elevated temperatures affected a bis-deprotection followed by intramolecular aldol condensation to afford enone **17**. To furnish the crucial *trans* ring-fusion of the hydrindane subunit, a two-step protocol was used wherein **17** was treated with *N*-bromosaccharin[10] in the presence of water to facilitate bromohydrin formation, followed by elimination of the bromide with triethylamine to afford epoxyketone **7**, which could be recrystallized to enrich the **7** to >99% ee. Furthermore, the structure of **7** was confirmed via single crystal X-ray diffraction analysis.

Figure 1.6. Asymmetric Synthesis of Epoxyketone **7**.



1.4 SUBSTRATE SCOPE FOR FRAGMENT COUPLING

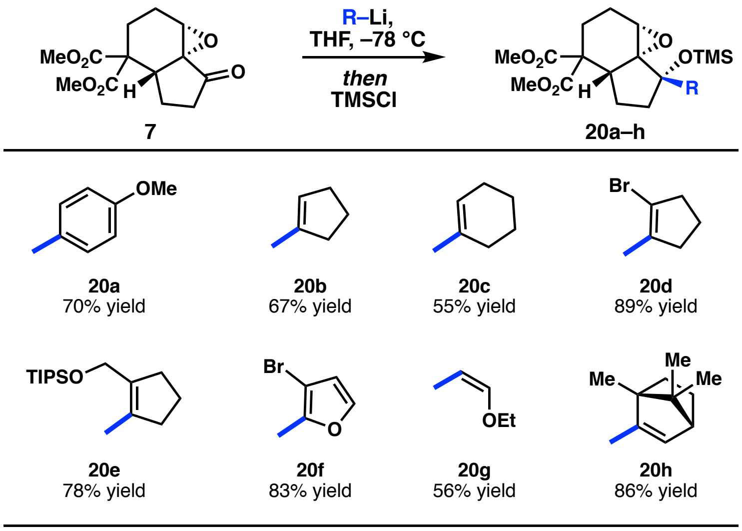
With a scalable route to epoxyketone **7** established, we focused our attention on the development of the scope of the 1,2-addition/semipinacol rearrangement fragment coupling.

1.4.1 SUBSTRATE SCOPE FOR 1,2-ADDITION

After some optimization, it was discovered that the epoxyketone could undergo 1,2-additions with a variety of different vinyl lithium reagents[11] (Table 1.1). A noteworthy realization in the optimization for the 1,2-addition was the realization that this reaction was extremely sensitive to trace water[12] (see experimental information).

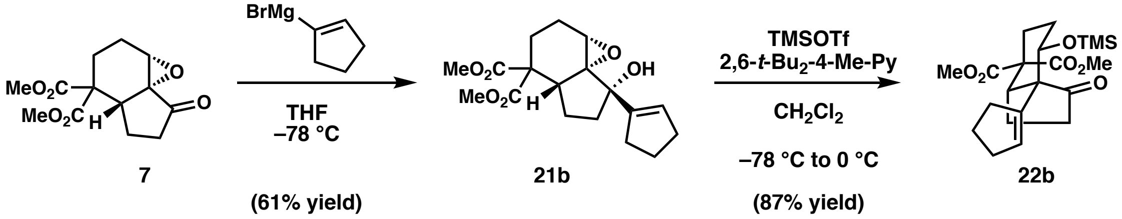
After the 1,2-addition was complete, it was found that the reaction could be quenched *in situ* with TMSCl, resulting in the tertiary TMS protected alcohol as the final product. We ultimately opted to run the reactions with *in situ* TMS protection because this enabled a Lewis-acid catalyzed semipinacol rearrangement (TMS protection was a requirement to effect catalyst turnover). These semipinacol rearrangement studies are ongoing using the Lewis acid $TMSNTf_2$[13].

Table 1.1. Substrate scope for 1,2-addition with organolithiums and *in situ* TMS protection.



An alternative reaction sequence and conditions could be utilized to effect the semipinacol rearrangement (Figure 1.7), 1,2-addition of cyclopentenyl magnesium bromide to **7** furnished epoxy-alcohol **21b.** Subjection of **21b** to a stoichiometric amount of TMSOTf facilitated a high-yielding semipinacol rearrangement on gram-scale. While a stoichiometric, rather than a catalytic quantity of the Lewis acid was required to effect the rearrangement, it is possible to directly effect the rearrangement from the epoxy-alcohol rather than the tertiary TMS protected epoxy-alcohol.

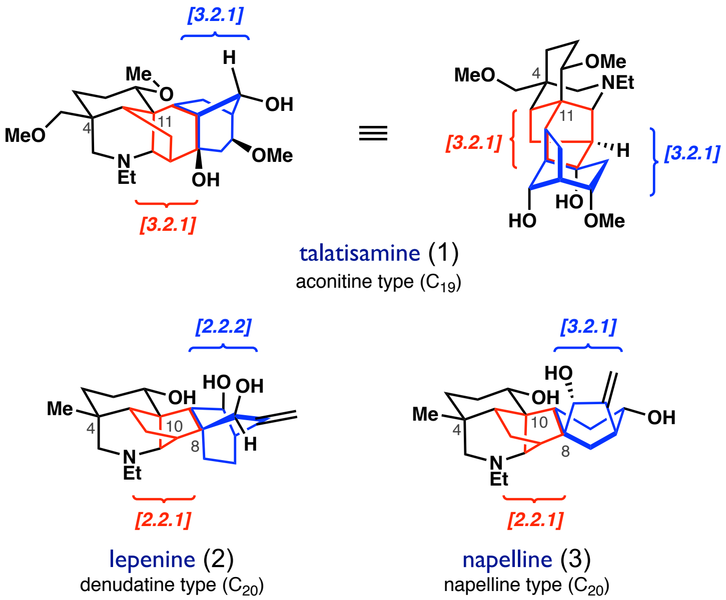
Figure 1.7. An example of a semipinacol rearrangement from an epoxy-alcohol.



1.5 UNIFIED STRATEGY TO C_{20} DITERPENOID ALKALOIDS

With the feasibility of the convergent fragment coupling via the developed 1,2-addition and subsequent semipinacol rearrangement established, we turned our attention to evaluate our proposed unified strategy towards the C_{20} diterpenoid alkaloid natural products, specifically the *napelline* and *denudatine* types. As highlighted above, a common feature to both C_{19} and C_{20} diterpenoid alkaloids is the AEF tricycle (Figure 1.1). However, there are important differences to consider in the structural variation between the C_{19} and C_{20} diterpenoid alkaloids (Figure 1.8). The aconitine type C_{19} diterpenoid alkaloids possess a central bicyclo[3.2.1]octane, whereas the napelline type and denudatine type diterpenoid alkaloids possess a central bicyclo[2.2.1]heptane motif (highlighted in red). The central bicyclo[3.2.1]octane or bicyclo[2.2.1]heptane is then fused to a final bridged bicyclic motif for each structure. In developing a unified synthetic strategy to the C_{19} and C_{20} diterpenoid alkaloids, our goal was to devise a strategy that would enable the synthesis of both the bicyclo[3.2.1]octane and bicyclo[2.2.1]heptane ring systems necessary for the core carbocyclic framework of these natural products. Our next goal was to develop a strategy that would enable the synthesis a second C–C bond for the central bicyclo[2.2.1]heptane for the *napelline* and *denudatine* natural products, allowing us to establish a convergent fragment coupling strategy, and generate the central ring system of the natural products.

Figure 1.8. Structural differences in C_{19} and C_{20} diterpenoid alkaloids.



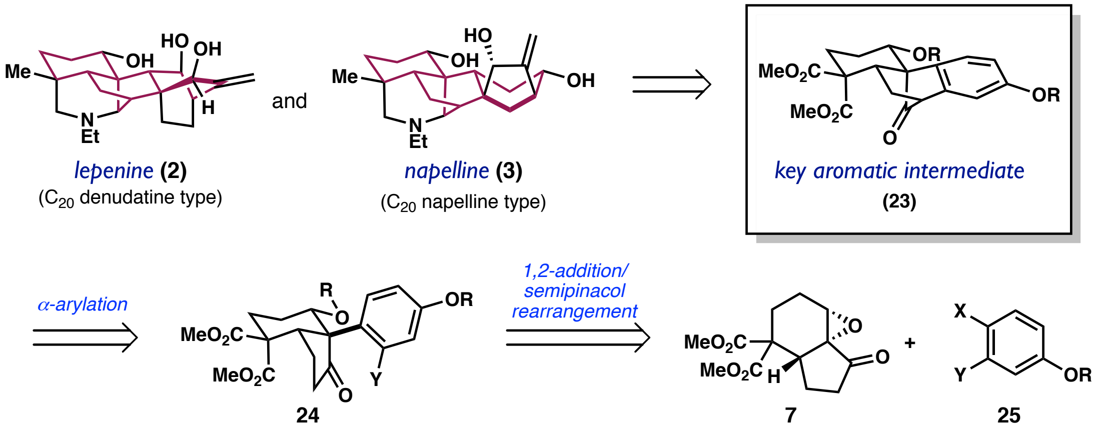
talatisamine (1)
aconitine type (C_{19})

lepenine (2)
denudatine type (C_{20})

napelline (3)
napelline type (C_{20})

In a retrosynthetic sense, it was envisioned that key aromatic intermediate **23** could be advanced to both **2** and **3** (Figure 1.9). Key aromatic intermediate **23** contains the majority of the carbon skeleton necessary for the C_{20} diterpenoid alkaloids **2** and **3** (highlighted in **2** and **3** in Figure 1.9). It was thought that the central bicyclo[2.2.1]heptane could be formed via an intramolecular α-arylation reaction of aryl halide **24**. The crucial all carbon quaternary center could arise from the developed 1,2-addition/semipinacol rearrangement approach. Specifically, an aryl halide nucleophile (**25**) with an additional ortho substituent (denoted as Y) would enable a second C–C bond formation, which would enable the cyclization to form the central bicyclo[2.2.1]heptane necessary for **23**.

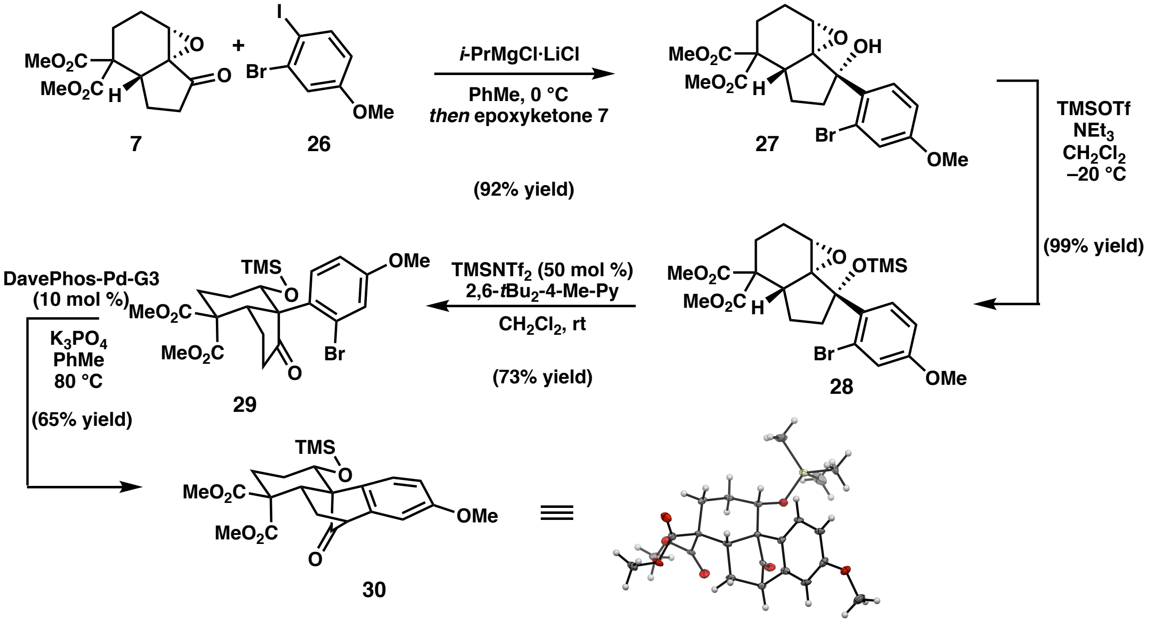
Figure 1.9. Unified Strategy to Diterpenoid Alkaloids via Aromatic Intermediate **23**.



1.5.1 SYNTHESIS OF A KEY AROMATIC INTERMEDIATE

To that end, a route to the proposed key aromatic intermediate was developed. Under heavily optimized conditions, it was found that selective magnesiation of aryl iodide **26** with *i*PrMgCl•2LiCl in toluene and subsequent addition into **7** afforded epoxy-alcohol **27** in high yield (Figure 1.10). Next, the isolated tertiary alcohol was protected as the TMS ether to afford **28**. Subjection of **28** to TMSNTf$_2$ (50 mol %) in the presence of 2,6-(*t*-Bu)$_2$-4-Me-Py facilitated a semipinacol rearrangement, providing **29**. Aryl bromide **29** was then treated with Buchwald's Pd-catalyzed conditions[14] to facilitate an intramolecular α-arylation reaction, giving bridged bicyclo[2.2.1]heptane **30**. The structure of **30** was confirmed via single crystal X-ray diffraction analysis. With the realization of the convergent coupling strategy towards the C$_{20}$ diterpenoid alkaloids through the synthesis of aromatic intermediate **30**, our focus shifted to C$_{19}$ diterpenoid alkaloid **1**.

Figure 1.10. Route to Key Aromatic Intermediate **30**.



1.6 CONCLUDING REMARKS

This chapter details a unified, fragment coupling based strategy to the C_{19} and C_{20} diterpenoid alkaloids via a 1,2-addition and subsequent semipinacol rearrangement. A broad substrate scope, including bulky bridged bicyclic fragments is presented. The developed synthetic strategy was ultimately used in the total syntheses of C_{19} diterpenoid alkaloid natural products (see Chapters 2 and 3). Lastly, the developed fragment coupling was utilized in the synthesis of a key aromatic intermediate towards the C_{20} diterpenoid alkaloids.

1.7 EXPERIMENTAL SECTION

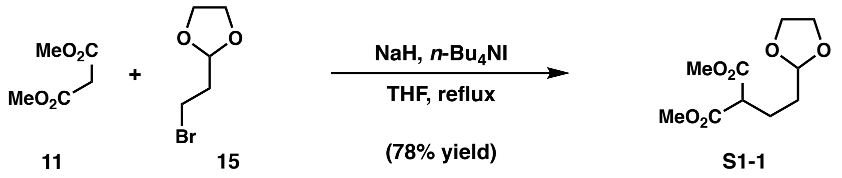
1.7.1 MATERIALS AND METHODS

Unless otherwise stated, reactions were performed under an inert atmosphere (dry N_2 or Ar) with 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), diethyl ether (Et_2O), methylene chloride (CH_2Cl_2), acetonitrile (MeCN), *tert*-butyl methyl ether (TBME), benzene (PhH), and toluene (PhMe) were dried by passing through activated alumina columns. Absolute ethanol (200 proof) was purchased from Koptec, and stored over activated 3Å MS in a Schlenk Tube under N_2. Triethylamine (Et_3N), *N*,*N*-diisopropylethylamine (DIPEA), and 2,6-lutidine were distilled over calcium hydride prior to use. Unless otherwise stated, chemicals and reagents were used as received. 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, $KMnO_4$, CAM, or ninhydrin staining. Flash column chromatography was performed using silica gel (SiliaFlash® P60, particle size 40-63 microns [230 to 400 mesh]) purchased from Silicycle. Optical rotations were measured on a Jasco P-2000 polarimeter using a 100 mm path-length cell at 589 nm. ^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, $\delta = 77.0$). 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, app = apparent. 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).

1.7.2 PREPARATIVE PROCEDURES AND SPECTROSCOPIC DATA

Preparation of racemic and enantiopure 7:

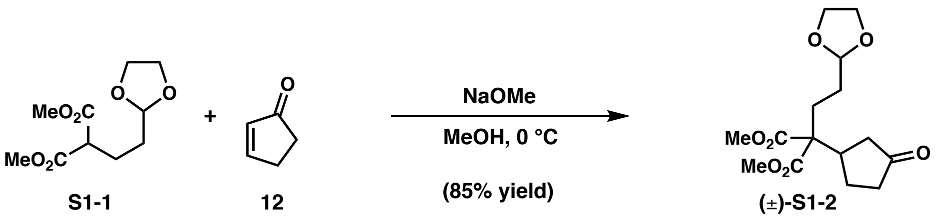
Preparation of diester S1-1:



In a 250-mL, round-bottomed flask equipped with a reflux condenser, NaH (60% dispersion in mineral oil, 1.05 g, 43.7 mmol, 1.17 equiv) was suspended in THF (44 mL) and cooled to 0 °C. To this suspension was added dimethyl malonate (**11**, 5.0 mL, 43.7 mmol, 1.17 equiv) dropwise with a vent needle to allow pressure release caused by H_2 evolution. The reaction was then warmed to room temperature with stirring for 30 minutes, after which *n*-Bu_4NI (1.38 g, 3.74 mmol, 0.10 equiv) and 2-(2-bromoethyl)-1,3-dioxolane (**15**, 4.4 mL, 37.4 mmol, 1.0 equiv) was added. The solution was heated to reflux and stirred for 4 h, and then quenched by addition of sat. NH_4Cl (100 mL). The aqueous phase was extracted with Et_2O (3 x 200 mL), and the combined organic extracts were washed with 1 N HCl (100 mL) and brine (100 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by silica gel chromatography (20 to 23% EtOAc in hexanes) provided diester **S1--1** (6.76 g, 29.1 mmol, 78% yield) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.88 (t, *J* = 4.5 Hz, 1H), 4.00 – 3.91 (m, 2H), 3.90 – 3.80 (m, 2H), 3.74 (s, 6H), 3.47 (t, *J* = 7.5 Hz, 1H), 2.08 – 2.01 (m, 2H), 1.74 – 1.68 (m, 2H).

Preparation of racemic ketal S1-2:



In a 500-mL, round-bottomed flask, Na (2.18 g, 94.9 mmol, 1.1 equiv) was added to MeOH (110 mL). After consumption of the solid Na, the solution was cooled to 0 °C, and a solution of diester **S1-1** (20.0 g, 86.3 mmol, 1.0 equiv) in MeOH (30 mL) was added via cannula, followed by dropwise addition of a solution of 2-cyclopenten-1-one (**12**, 7.95 mL, 94.9 mmol, 1.1 equiv) in MeOH (30 mL) over 20 minutes. The reaction was stirred for an additional 2 h, and then quenched with sat. NH_4Cl (300 mL). The mixture was concentrated *in vacuo* to remove MeOH, and the resulting solution was extracted with EtOAc (3 x 150 mL). The combined organic extracts were washed with brine (150 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification by silica gel chromatography (20% acetone in hexanes) afforded ketal (±)-**S1-2** (23.1 g, 73.5 mmol, 85% yield) as a white solid.

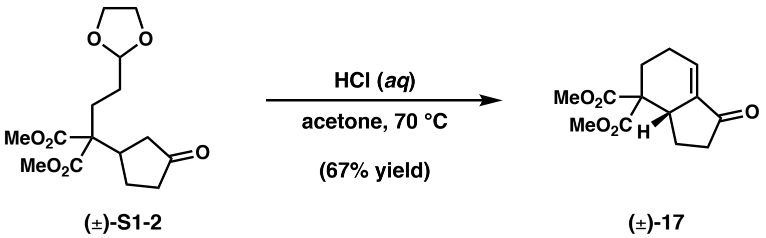
^{1}H NMR (400 MHz, CDCl$_3$): δ 4.85 (td, *J* = 4.4, 0.9 Hz, 1H), 4.01 – 3.91 (m, 2H), 3.89 – 3.80 (m, 2H), 3.74 – 3.73 (m, 6H), 2.85 – 2.74 (m, 1H), 2.48 (dd, *J* = 18.5, 7.6 Hz, 1H), 2.31 (dd, *J* = 17.2, 8.4 Hz, 1H), 2.25 – 2.11 (m, 3H), 2.08 – 2.03 (m, 2H), 1.73 – 1.58 (m, 3H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 217.4, 170.9, 170.8, 103.7, 59.4, 52.4, 52.4, 41.1, 40.2, 38.5, 28.9, 27.7, 24.9.

FTIR (NaCl, thin film): 2956, 2890, 1743, 1730, 1451, 1435, 1407, 1222, 1147, 1036 cm^{-1}.

HRMS: (FAB) calc'd for $C_{15}H_{23}O_7$ [M + H]$^+$ 315.1444, found 315.1438.

Preparation of enone (±)-17:

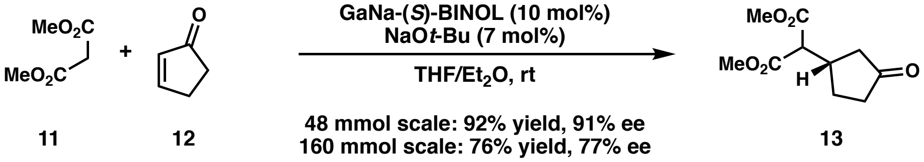


In a 1L, round-bottomed flask equipped with a reflux condenser, racemic ketal **(±)-S1-2** (10 g, 31.8 mmol, 1.0 equiv) was dissolved in acetone (280 mL). Aqueous HCl (31.8 mL, 2 N, 63.6 mmol, 2.0 equiv) was added, and the reaction was heated to 70 °C with stirring for 16 h. The reaction was cooled to room temperature and quenched with sat. $NaHCO_3$ (200 mL) and partially concentrated *in vacuo* to remove acetone. The resulting mixture was extracted with CH_2Cl_2 (3 x 300 mL), and the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by silica gel chromatography (10 to 40% EtOAc in hexanes) to afford enone (±)-**17** (5.37 g, 21.3 mmol, 67% yield) as a white solid.

See below for full characterization data on enantioenriched material.

^{1}H NMR (500 MHz, CDCl$_3$): δ 6.69 (q, *J* = 3.8 Hz, 1H), 3.78 (s, 3H), 3.67 (s, 3H), 3.10 (qdd, *J* = 7.4, 3.5, 2.1 Hz, 1H), 2.53 – 2.37 (m, 4H), 2.32 – 2.22 (m, 2H), 2.11 –1.90 (m, 2H).

Preparation of diester 13:



Preparation of GaNa-(*S*)-BINOL solution (0.05 M in 9:1 THF:Et$_2$O):[9] In a 500-mL, round-bottomed flask, a solution of NaO*t*-Bu (3.29 g, 34.2 mmol, 4.0 equiv) in THF (60 mL) was added to a solution of (*S*)-BINOL (4.90 g, 17.1 mmol, 2.0 equiv) in THF (52 mL), and the resulting mixture was stirred for 30 minutes. This was then cannulated into a solution of GaCl$_3$ (1.51 g, 8.55 mmol, 1.0 equiv) in THF (43 mL) and Et$_2$O (17 mL). This mixture was stirred for 2 h, and then allowed to stand un-agitated for at least 22 h.

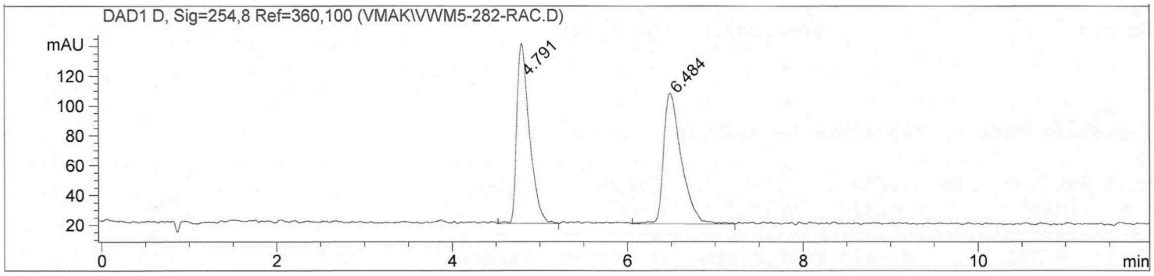
Enantioselective Michael addition: A solution of GaNa-(*S*)-BINOL (96 mL, 0.05 M in 9:1 THF:Et$_2$O, 4.80 mmol, 0.10 equiv) was transferred via syringe to a 500-mL, round-bottomed flask. To this was added a solution of NaO*t*-Bu (323 mg, 3.36 mmol. 0.07 equiv) in THF (7.5 mL), followed by dimethyl malonate (**11**, 5.5 mL, 48 mmol, 1.0 equiv) and 2-cyclopenten-1-one (**12**, 4.0 mL, 48 mmol, 1.0 equiv). The reaction was stirred for 37 h, then quenched with 1 N HCl (300 mL). The mixture was extracted with EtOAc (3 x 200 mL), and the combined organic extracts were washed with brine (300 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Vacuum distillation of the crude residue afforded diester **13** (9.44 g, 44.1 mmol, 92% yield) as a colorless oil. Spectroscopic data matched that reported in the literature.[15]

^{1}H NMR (500 MHz, Chloroform-*d*): δ 3.76 (s, 3H), 3.74 (s, 3H), 3.37 (d, *J* = 9.4 Hz, 1H), 2.91 – 2.80 (m, 1H), 2.49 (dd, *J* = 18.4, 7.5 Hz, 1H), 2.37 – 2.30 (m, 1H), 2.27 – 2.15 (m, 2H), 2.00 (ddd, *J* = 18.4, 11.0, 1.5 Hz, 1H), 1.69 – 1.60 (m, 1H).

TLC (2:1 Hexanes:EtOAc), R_f: 0.2 (purple in *p*-anisaldehyde)

Diester **13** was carried forward to enone **17**, where enantiomeric excess was determined to be 91%:

SFC data for racemic enone 17:



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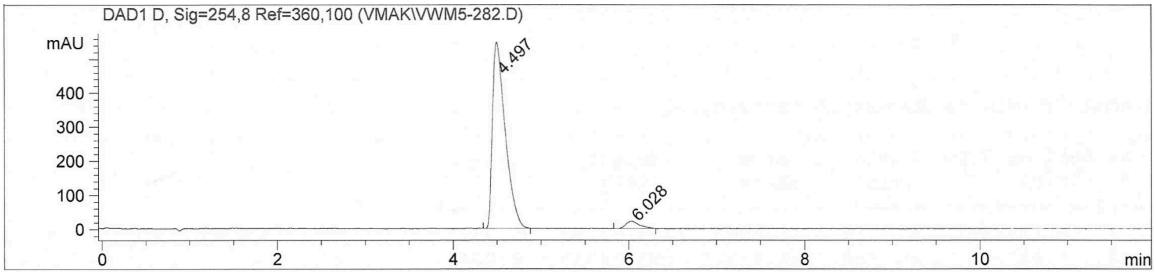
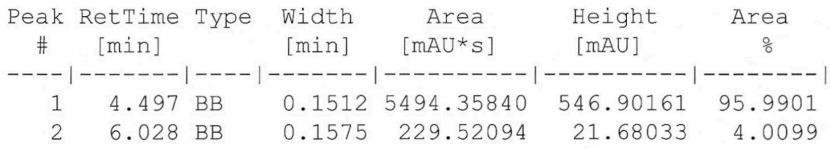
Peak RetTime Type  Width      Area       Height      Area
  #   [min]        [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   4.791 VV    0.1489 1209.87744  120.72012  49.2621
   2   6.484 VV    0.2134 1246.12061   87.90836  50.7379
```

SFC data for enantioenriched enone 17 (three steps from diester 13):





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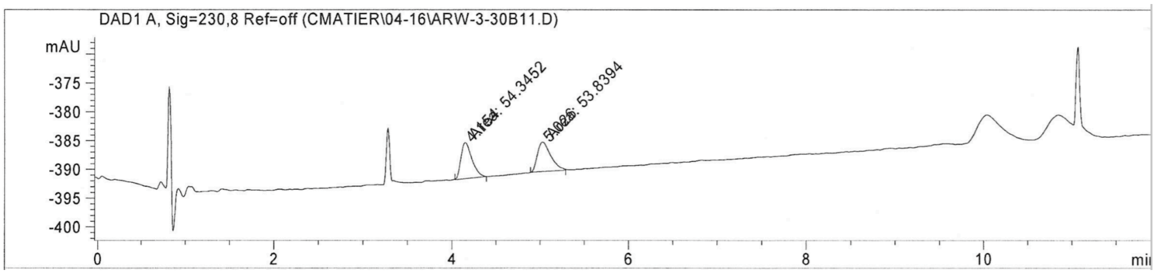
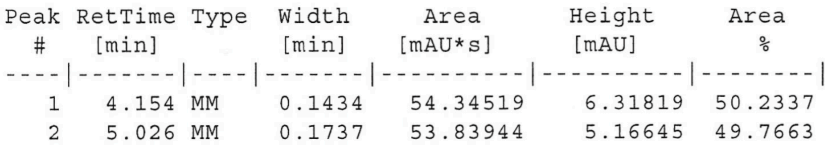
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   4.497 BB    0.1512 5494.35840  546.90161 95.9901
   2   6.028 BB    0.1575  229.52094   21.68033  4.0099
```

Large-scale preparation of diester 13: The above protocol was reproduced using 160 mmols of dimethyl malonate (**11**) and 160 mmols of 2-cyclopenten-1-one (**12**), affording a 76% yield of diester **13** in 77% ee.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = –46° (c = 0.84, CHCl$_3$).

SFC data for racemic diester 13:





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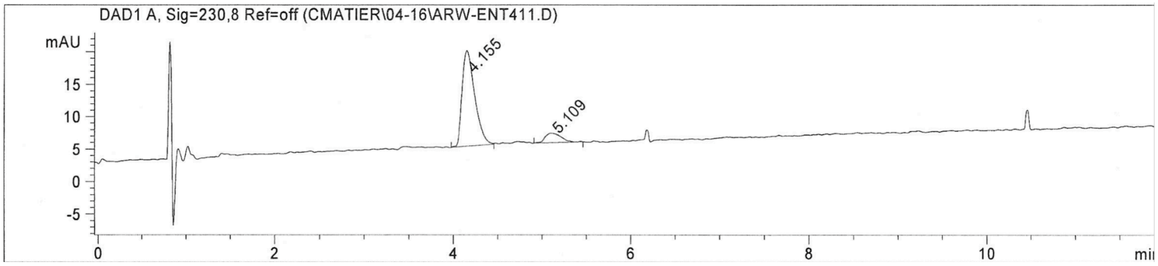
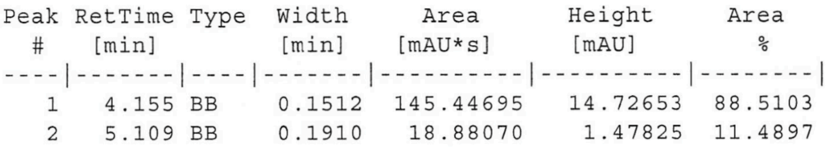
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   4.154 MM    0.1434   54.34519    6.31819 50.2337
   2   5.026 MM    0.1737   53.83944    5.16645 49.7663
```

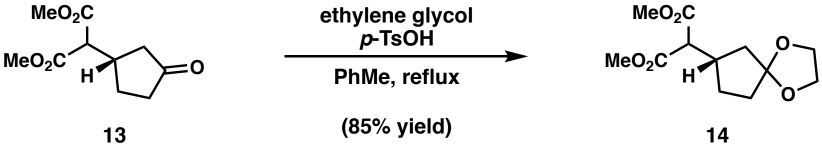
SFC data for enantioenriched diester 13 prepared on 160 mmol scale:





```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   4.155 BB    0.1512  145.44695   14.72653 88.5103
   2   5.109 BB    0.1910   18.88070    1.47825 11.4897
```

Preparation of ketal 14:



In a flame dried 1-L, round-bottomed flask equipped with a reflux condenser and Dean–Stark trap, ketone **13** (38.6 g, 180 mmol, 1.0 equiv) was dissolved in toluene (600 mL). To this solution was added ethylene glycol (20.2 mL, 360 mmol, 2.0 equiv) and *p*-TsOH•H_2O (3.42 g, 18.0 mmol, 0.10 equiv), and the reaction was heated to reflux for 11 h. The reaction was then cooled to room temperature and diluted with Et_2O (1200 mL). The solution was washed with saturated aqueous $NaHCO_3$ (2 x 400 mL), and the combined aqueous phase was extracted with Et_2O (750 mL). The combined organic phase was washed with brine (500 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification by silica gel chromatography (25% EtOAc in hexanes with 2% NEt_3) provided ketal **14** (39.6 g, 153 mmol, 85% yield) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.93 – 3.84 (m, 4H), 3.72 (m, 6H), 3.31 (d, *J* = 10.2 Hz, 1H), 2.75 – 2.62 (m, 1H), 2.08 (ddd, *J* = 13.7, 8.0, 1.2 Hz, 1H), 1.99 – 1.86 (m, 2H), 1.85 – 1.75 (m, 1H), 1.56 (dd, *J* = 13.6, 9.5 Hz, 1H), 1.48 – 1.36 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 169.0, 168.9, 117.0, 64.3, 64.2, 56.7, 52.4, 52.4, 40.6, 36.8, 35.5, 28.2.

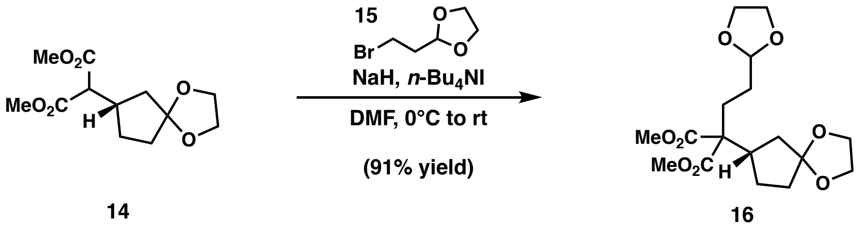
FTIR (NaCl, thin film): 2956, 2885, 1754, 1734, 1435, 1316, 1216, 1151, 1079, 1017, 947 cm^{-1}.

HRMS: (PMM) calc'd for $C_{12}H_{19}O_6$ $[M + H]^+$ 259.1176, found 259.1169.

$[\alpha]_D^{25}$ = +2.2° (*c* = 1.4, $CHCl_3$).

TLC (2:1 Hexanes:EtOAc), R$_f$: 0.3 (purple in *p*-anisaldehyde)

Preparation of bis-ketal 16:



A flame dried 1-L round-bottomed flask was charged with diester **14** (39.9 g, 155 mmol, 1.0 equiv) and DMF (386 mL). The solution was cooled to 0 °C before NaH (60% dispersion in mineral oil, 7.42 g, 185 mmol, 1.2 equiv) was added in portions. *n*-Bu_4NI (11.39 g, 30.8 mmol, 0.20 equiv) and 2-(2-bromoethyl)-1,3-dioxolane (**16**, 27.2 mL, 232 mmol, 1.5 equiv) were added sequentially, and the reaction was allowed to warm to room temperature and stirred for 72 hours. The reaction was then quenched by addition of sat. NH_4Cl (600 mL). The mixture was extracted with EtOAc (3 x 1 L), and the combined organic extracts were washed with sat. NH_4Cl (2 x 400 mL) followed by brine (400 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification by silica gel chromatography (10 to 50% EtOAc in hexanes) afforded bis-ketal **16** (50.4 g, 141 mmol, 91% yield) as a colorless oil.

^{1}H NMR (500 MHz, CDCl$_3$): δ 4.83 (td, *J* = 4.5, 1.9 Hz, 1H), 3.97 – 3.81 (m, 8H), 3.71 (s, 3H), 3.71 (s, 3H), 2.70 – 2.60 (m, 1H), 2.05 – 1.95 (m, 3H), 1.91 – 1.80 (m, 2H), 1.80 – 1.66 (m, 2H), 1.64 – 1.50 (m, 3H).

^{13}C NMR (126 MHz, CDCl$_3$): δ 171.2, 171.1, 116.6, 103.9, 64.9, 64.9, 64.2, 64.1, 59.8, 52.2, 52.1, 40.4, 38.0, 35.3, 29.0, 27.9, 25.4.

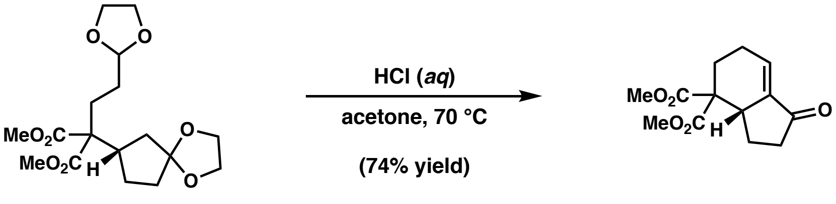
FTIR (NaCl, thin film): 2954, 2915, 2877, 1728, 1434, 1227, 1141, 1024 cm^{-1}.

HRMS: (FAB) calc'd for $C_{17}H_{27}O_8$ $[M + H]^+$ 359.1706, found 359.1716.

$[\alpha]_D^{25}$ = –0.69° (*c* = 0.60, $CHCl_3$).

TLC (1:1 Hexanes:EtOAc), R*f*: 0.3 (turquoise in *p*-anisaldehyde)

Preparation of enone 17:



16 17

In a 1L, round-bottomed flask equipped with a reflux condenser, bis-ketal **16** (25.2 g, 70.3 mmol, 1.0 equiv) was dissolved in acetone (280 mL). Aqueous HCl (70 mL, 2 N, 140 mmol, 2.0 equiv) was added, and the reaction was heated to 70 °C with stirring for 16 h. The reaction was cooled to room temperature and quenched with sat. $NaHCO_3$ (300 mL) and partially concentrated *in vacuo* to remove acetone. The resulting mixture was extracted with CH_2Cl_2 (3 x 450 mL), and the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by silica gel chromatography (10 to 40% EtOAc in hexanes) to afford enone **17** (13.03 g, 51.6 mmol, 74% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.69 (q, *J* = 3.8 Hz, 1H), 3.78 (s, 3H), 3.67 (s, 3H), 3.10 (qdd, *J* = 7.4, 3.5, 2.1 Hz, 1H), 2.53 – 2.37 (m, 4H), 2.32 – 2.22 (m, 2H), 2.11 –1.90 (m, 2H).

^{13}C NMR (126 MHz, CDCl$_3$): δ 204.6, 171.8, 169.5, 137.1, 131.3, 55.0, 52.7, 52.2, 42.8, 37.7, 29.4, 23.9, 23.2.

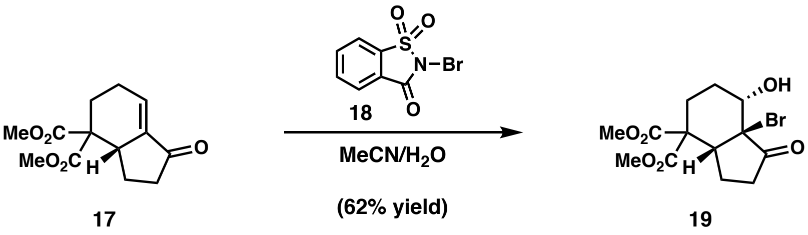
FTIR (NaCl, thin film): 3022, 2956, 2898, 2848, 1732, 1659, 1451, 1434, 1283, 1256, 1214, 1174, 1143, 1064 cm^{-1}.

HRMS: (FAB) calc'd for $C_{13}H_{17}O_5$ $[M + H]^+$ 253.1076, found 253.1076.

$[\alpha]_D^{25}$ = –34° (c = 1.7, CHCl$_3$).

TLC (1:1 Hexanes:EtOAc), R$_f$: 0.6 (UV, blue in *p*-anisaldehyde)

Preparation bromohydrin 19:



A 250-mL, round-bottomed flask was charged with enone **190** (3.91 g, 15.5 mmol, 1.0 equiv), MeCN (64 mL), and H_2O (12 mL), followed lastly by *N*-bromosaccharin (**191**, 5.28 g, 20.1 mmol, 1.3 equiv). The reaction was stirred for 6.5 h, then quenched by addition of sat. $Na_2S_2O_3$ (150 mL). The mixture was extracted with Et_2O (3 x 250 mL), and the combined organic extracts were washed with sat. $NaHCO_3$ (2 x 150 mL), brine (150 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo* to afford a crude white solid. This was dissolved in Et_2O (600 mL) at 35 °C. Ca. 300 mL was concentrated off, and then hexanes (300 mL) was added. The solution was concentrated until ca. 300 mL of solvent remained, with white solids suspended within. The solvent was decanted into a Büchner funnel, washing the flask carefully with hexanes. The residual solids in the flask were collected, affording bromohydrin **192** (3.37 g, 9.65 mmol, 62% yield) as a white solid.

^{1}H NMR (500 MHz, Chloroform-*d*): δ 4.37 (t, *J* = 2.8 Hz, 1H), 3.77 (s, 3H), 3.74 (s, 3H), 3.10 (ddd, *J* = 12.3, 5.9, 1.6 Hz, 1H), 2.81 (d, *J* = 1.7 Hz, 1H), 2.79 – 2.71 (m, 1H), 2.51 (dd, *J* = 18.0, 7.3 Hz, 1H), 2.41 – 2.32 (m, 2H), 2.30 – 2.17 (m, 2H), 2.07 – 1.98 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 211.6, 171.3, 171.1, 76.5, 55.5, 53.0, 52.5, 47.9, 42.2, 36.2, 28.2, 27.6, 21.3.

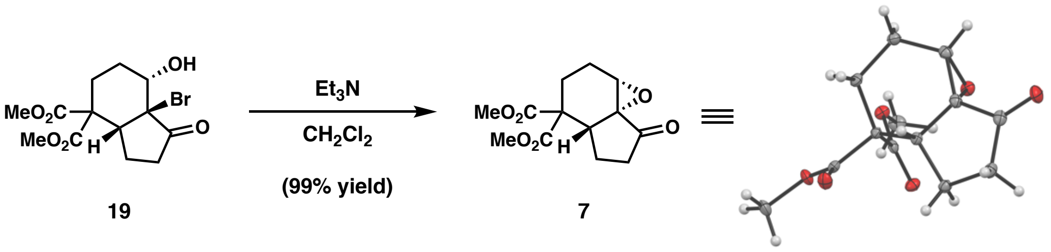
FTIR (NaCl, thin film): 3436, 2998, 2955, 2847, 1748, 1732, 1435, 1403, 1252, 1213, 1152, 1091, 1073, 1056, 980 cm^{-1}.

HRMS: (FAB) calc'd for $C_{13}H_{18}BrO_6$ $[M + H]^+$ 349.0287, found 349.0275.

$[\alpha]_D^{25}$ = –49° (*c* = 0.17, $CHCl_3$).

TLC (1:1 Hexanes:EtOAc), R*f*: 0.6 (orange in *p*-anisaldehyde)

Preparation of epoxyketone 7:



In a 250-mL, round-bottomed flask, bromohydrin **19** (3.35 g, 9.59 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (96 mL). Et_3N (1.60 mL, 11.5 mmol, 1.2 equiv) was added, and the reaction was stirred for 9 h. The mixture was loaded directly onto a column of silica gel (slurried in hexanes), and purification by chromatography (100% hexanes, then 40% EtOAc in hexanes) afforded epoxyketone **7** (2.54 g, 9.47 mmol, 99% yield) as a white solid. The resulting solid was recrystallized from acetone layered with hexanes to afford epoxyketone **7** in >99% ee.

^{1}H NMR (500 MHz, CDCl$_3$): δ 3.76 (s, 1H), 3.76 – 3.73 (m, 4H), 2.93 (dd, *J* = 12.5, 5.8 Hz, 1H), 2.68 (qd, *J* = 11.7, 7.4 Hz, 1H), 2.58 (ddd, *J* = 18.7, 7.6, 1.6 Hz, 1H), 2.48 – 2.28 (m, 4H), 2.12 – 2.01 (m, 1H), 1.72 – 1.61 (m, 1H).

^{13}C NMR (126 MHz, CDCl$_3$): δ 212.0, 171.4, 169.8, 63.0, 56.1, 55.2, 53.1, 52.4, 43.8, 38.4, 29.3, 23.0, 21.7.

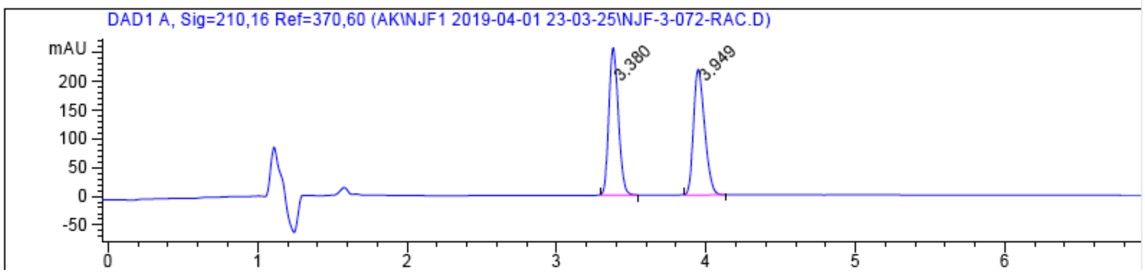
FTIR (NaCl/thin film): 3006, 2956, 2903, 2848, 1755, 1732, 1453, 1434, 1408, 1372, 1306, 1251, 1214, 1176, 1139, 1058, 890 cm^{-1}.

HRMS: (FAB) calc'd for $C_{13}H_{17}O_6$ $[M + H]^+$ 269.1025, found 269.1050.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = –171° (*c* = 0.60, CHCl$_3$).

TLC (1:1 Hexanes:EtOAc), R*$_f$*: 0.6 (yellow/orange in *p*-anisaldehyde)

SFC data for racemic epoxyketone 7:



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Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   3.380 BB    0.0683 1135.58337  253.08704  50.0585
   2   3.949 BB    0.0845 1132.93115  218.41344  49.9415

Totals :                  2268.51453  471.50047
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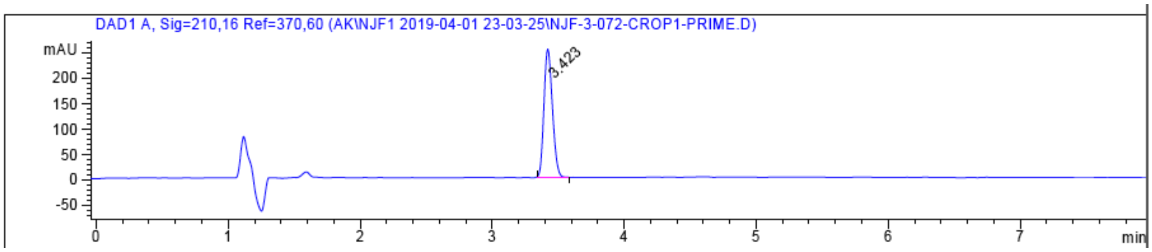
SFC data for enantiopure epoxyketone 7:



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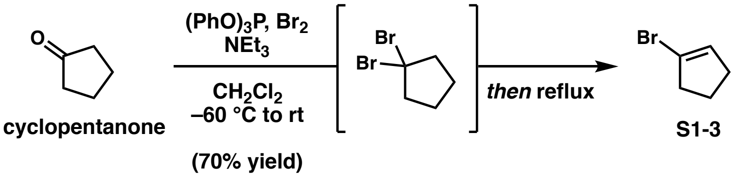
Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   3.423 BB    0.0728 1129.82751  249.84152 100.0000

Totals :                  1129.82751  249.84152
```

Preparation of vinyl halides for 1,2-additions:

Preparation of vinyl bromide S1-3:



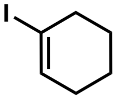
A flame-dried 500-mL round-bottomed flask was charged with triphenyl phosphite (27.6 mL, 105 mmol, 1.1 equiv) and CH_2Cl_2 (300 mL), and cooled to –60 °C. Br_2 (5.9 mL, 115.5 mmol, 1.2 equiv) was added, followed by NEt_3 (17.6 mL, 126 mmol, 1.3 equiv). Cyclopentanone (8.53 mL, 96 mmol, 1 equiv) was added, and the reaction was allowed to warm to room temperature and stirred for an additional 6 hours at room temperature. The reaction was monitored by TLC (100% hexanes), indicating full conversion to the dibromide (note: only stains with $KMnO_4$). The flask was then equipped with a reflux condenser, and was allowed to reflux for 1 hour. The reaction was monitored by TLC, which indicated full consumption of the dibromide and conversion to the vinyl bromide. The reaction was then cooled to room temperature, and the mixture was transferred to a separatory funnel. The organics were washed with aqueous 2 N HCl (2 x 300 mL), and the combined aqueous was extracted with pentanes (2 x 150 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo* (with ice in the bath because the product is volatile). Purification of the crude residue by a silica gel chromatography (100% pentanes), provided vinyl bromide **S1-3** (10 g, 67.2 mmol, ~70% yield but was volatile so was not put on high vacuum) as a clear oil.

^{1}H NMR data agrees with characterization data reported by Hayashi.[16] The procedure was adapted from a procedure reported in the literature by Liang.[17] More general information about $TPPBr_2$ can be found in a report by Spaggiarri.[18]

TLC (100% Hexanes), R*f*: 0.6 (UV, $KMnO_4$)

^{1}H NMR (600 MHz, Chloroform-*d*): δ 5.83 (p, *J* = 2.3 Hz, 1H), 2.58 (tq, *J* = 7.5, 2.4 Hz, 2H), 2.33 (tq, *J* = 7.8, 2.6 Hz, 2H), 1.98 (tt, *J* = 8.3, 6.8 Hz, 2H).

Preparation of vinyl iodide S1-4:

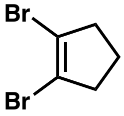


S1-4

Vinyl iodide S1-4 was prepared according to a procedure by Wiemer,[19] ^{1}H NMR data agrees with characterization data reported by Prabhu.[20] The attached ^{1}H NMR spectrum contains pyrazine (used for QNMR).

^{1}H NMR (500 MHz, Chloroform-*d*): δ 6.32 (tt, *J* = 4.0, 1.8 Hz, 1H), 2.51 – 2.47 (m, 2H), 2.10 – 2.05 (m, 2H), 1.72 – 1.61 (m, 4H).

Preparation of S1-5:

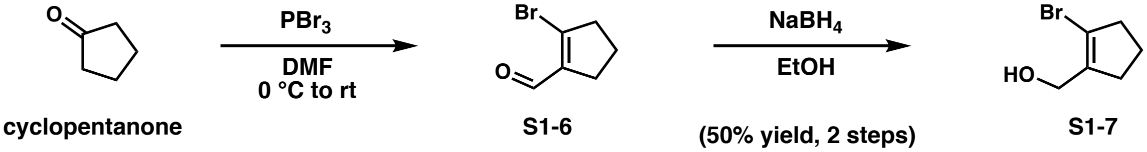


S1-5

S1-5 was prepared according a procedure reported by Feringa,[21] and 1H NMR data matched their report.

^{1}H NMR (500 MHz, Chloroform-*d*): δ 2.66 – 2.60 (m, 2H), 2.10 – 2.03 (m, 2H).

Preparation of allylic alcohol S1-7:



In a 1-L, round-bottomed flask, PBr_3 (14.3 mL, 153 mmol, 2.7 equiv) was added via syringe to a solution of DMF (14.0 mL, 181 mmol, 3.2 equiv) in CH_2Cl_2 (80 mL) at 0 °C. After stirring for 1 h, a solution of cyclopentanone (5.0 mL, 56.5 mmol, 1.0 equiv) in CH_2Cl_2 (30 mL, 10 mL rinse) was added via cannula. The reaction was allowed to warm to ambient temperature, and stirred for an additional 21 h. The reaction was cooled again to 0 °C, and quenched *carefully* with sat. $NaHCO_3$ (500 mL). Solid $NaHCO_3$ was added periodically as needed until bubbling ceased. The resulting mixture was extracted with Et_2O (3 x 250 mL), and the combined organic extracts were washed with H_2O (2 x 500 mL) and brine (500 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was purified by silica gel chromatography (15% EtOAc in hexanes) to afford bromoenal **S1-6** (ca. 5.8 g), which was used in the next step without rigorous removal of solvent.

In a 500-mL, round-bottomed flask, bromoenal **S1-6** (ca. 5.8 g) was dissolved in EtOH (33 mL) and cooled to 0 °C. $NaBH_4$ (1.5 g, 39.8 mmol, 1.2 equiv) was added, and the reaction was stirred for 1 h. The reaction was quenched with H_2O (200 mL), and the mixture was concentrated *in vacuo* to remove ethanol. The resulting aqueous solution was extracted with Et_2O (3 x 200 mL), and the combined organic extracts were washed with brine (200 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by silica gel chromatography (15% EtOAc in hexanes) afforded allylic alcohol **S1-7** (5.05 g, 28.5 mmol, 50% yield over two steps) as a colorless oil. Spectroscopic data for bromoenal **S1-6** and allylic alcohol **S1-7** matched that reported in the literature.[22]

Caution: Bromoenal **S1-6** was found to decompose exothermically upon standing for several hours. It could be safely stored as a solution in Et_2O in a –20 °C freezer, but in most cases was immediately used in subsequent reactions.

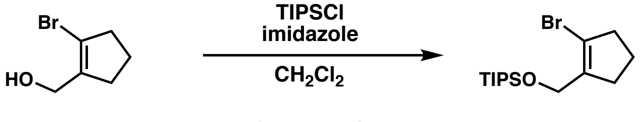
Bromoenal S1-6:

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.90 (s, 1H), 2.94 – 2.86 (m, 4H), 2.57 – 2.49 (m, 4H), 2.02 (pd, J = 7.9, 1.1 Hz, 4H).

Allylic alcohol S1-7:

^{1}H NMR (300 MHz, CDCl$_3$): δ 4.29 – 4.21 (m, 2H), 2.73 – 2.59 (m, 2H), 2.54 – 2.40 (m, 2H), 1.97 (tt, *J* = 8.3, 6.6 Hz, 2H).

Preparation of silyl ether S1-8:



S1-7 S1-8

In a 200-mL, round-bottomed flask, allylic alcohol **S1-7** (5.05 g, 28.5 mmol, 1.0 equiv) and imidazole (4.66 g, 68.5 mmol, 2.4 equiv) were dissolved in DMF (57 mL). To this solution was added TIPSCl (6.59 g, 34.2 mmol, 1.2 equiv), and the reaction was stirred for 12 h. The reaction was quenched with sat. NaHCO$_3$ (100 mL) and H$_2$O (100 mL), and extracted with Et$_2$O (3 x 200 mL). The combined organic extracts were washed with H$_2$O (200 mL) and brine (200 mL), dried over MgSO$_4$, filtered, and concentrated *in vacuo*. The crude oil was purified by silica gel chromatography (0.5% Et$_3$N/5% EtOAc in hexanes) to afford TIPS ether **S1-8** (7.24 g, 21.8 mmol, 76% yield) as a colorless oil.

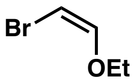
^{1}H NMR (500 MHz, CDCl$_3$): δ 4.35 (tq, *J* = 1.7, 0.9 Hz, 2H), 2.68 – 2.62 (m, 2H), 2.52 – 2.45 (m, 2H), 1.99 – 1.91 (m, 2H), 1.18 – 1.10 (m, 3H), 1.10 – 1.04 (m, 18H).

^{13}C NMR (126 MHz, CDCl$_3$): δ 140.7, 115.2, 61.4, 40.2, 32.3, 21.5, 18.0, 12.0.

FTIR (NaCl, thin film): 2960, 2941, 2892, 2866, 1657, 1463, 1383, 1369, 1104, 1066 cm^{-1}.

HRMS: (FAB) calc'd for C$_{15}$H$_{28}$BrOSi [M + H – H$_2$]$^+$ 331.1093, found 331.1089.

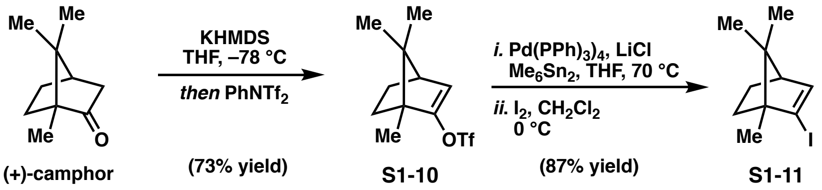
Preparation of S1-9:



S1-9 was prepared according a procedure reported by Valenti[23], and 1H NMR and characterization data matched a reported data by Stalick.[24]

^{1}H NMR (500 MHz, Chloroform-*d*): δ 6.60 (d, *J* = 4.2 Hz, 1H), 5.09 (d, *J* = 4.2 Hz, 1H), 3.97 (q, *J* = 7.1 Hz, 2H), 1.33 (t, *J* = 7.1 Hz, 3H).

Synthetic sequence for preparation of camphor-derived vinyl iodide S1-11:



Preparation of enol triflate S1-10:

A 500-mL, round-bottomed flask was charged with (+)-camphor (4.58 g, 30mmol, 1.0 equiv), which was subsequently dissolved in THF (250 mL) and cooled to –78 °C. KHMDS (63 mL, 0.5 M in toluene, 31.5 mmol, 1.05 equiv) was added, causing the solution to turn yellow, and the reaction was stirred for 45 minutes. In a separate flask, a solution of $PhNTf_2$ (11.25 g, 31.5 mmol, 1.05 equiv) in THF (50 mL) was prepared and cannulated into the first reaction flask, causing the solution to turn clear. The resulting mixture was allowed to warm to room temperature over 12 hours, and then quenched with sat. NH_4Cl (100 mL). This mixture was extracted with Et_2O (3 x 200 mL), and the combined organic extracts were washed with aqueous 1 M NaOH (4 x 100 mL) and brine (1 x 100 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*.

Purification of the crude organic residue by filtering through a plug of silica gel, eluting with hexanes afforded vinyl triflate **S1-8** (6.20 g, 21.9 mmol, 73% yield) as a clear oil.

Proton NMR data for **S1-10**:

^{1}H NMR (600 MHz, Chloroform-*d*): δ 5.67 (d, *J* = 3.8 Hz, 1H), 2.45 (t, *J* = 3.7 Hz, 1H), 1.93 (ddt, *J* = 12.2, 8.5, 3.7 Hz, 1H), 1.65 (dddd, *J* = 12.3, 8.6, 3.6, 0.7 Hz, 1H), 1.34 (ddd, *J* = 12.5, 9.1, 3.6 Hz, 1H), 1.15 (ddd, *J* = 12.5, 9.1, 3.7 Hz, 1H), 1.03 (s, 3H), 0.92 (s, 3H), 0.79 (s, 3H).

Preparation of vinyl iodide S1-11:

In an N_2-filled glovebox, LiCl (447 mg, 10.55 mmol, 3.0 equiv) and $Pd(PPh_3)_4$ (163 mg, 0.141 mmol, 0.04 equiv) were a 100-mL round-bottomed flask containing vinyl triflate **S1-10** (1.00 g, 3.52 mmol, 1.0 equiv). The contents were dissolved in THF (35 mL), and then Me_6Sn_2 (1.15 g, 3.52 mmol, 1.0 equiv) was added. The flask was brought out of the glovebox, carefully equipped with a reflux condenser, and heated to reflux (bath temperature set to 70 °C) with vigorous stirring for 3 h, then cooled to room temperature, diluted with hexanes (ca. 75 mL), and quenched with H_2O (25 mL). The solution was extracted with hexanes (3 x 75 mL), and then the combined organic extracts were washed with H_2O (25 mL), 10% NH_4OH (25 mL), and H_2O (25 mL) again. After drying over Na_2SO_4 and filtration, the filtrate was concentrated *in vacuo* to afford the crude vinyl stannane.

The crude vinyl stannane was dissolved in CH_2Cl_2 (25 mL) and cooled to 0 °C. To this solution was cannulated a solution of I_2 (0.938 g, 3.70 mmol, 1.05 equiv) in CH_2Cl_2 (10 mL). After stirring for 30 min at 0 °C, the reaction was quenched with sat.

$Na_2S_2O_3$ (50 mL), and diluted with H_2O (25 mL) and CH_2Cl_2 (25 mL). The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 x 75 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the crude residue by a silica gel plug, eluting with hexanes provided vinyl iodide **S1-11** (800 mg, 3.06 mmol, 87% yield) as a clear oil.

Note: vinyl iodide **S1-11** is slightly volatile, so it should not be left on the high vacuum for extended time.

Proton NMR data for **S1-11**:

^{1}H NMR (600 MHz, Chloroform-*d*): δ 6.40 – 6.39 (m, 1H), 2.36 (t, *J* = 3.6 Hz, 1H), 1.79 (ddt, *J* = 11.9, 8.4, 3.6 Hz, 2H), 1.43 (dddd, *J* = 11.9, 8.6, 3.3, 0.7 Hz, 1H), 1.32 – 1.24 (m, 1H), 0.99 – 0.94 (m, 1H), 0.89 (s, 3H), 0.85 (s, 3H), 0.84 (s, 3H).

Preparative procedures for 1,2-additions followed by TMS trapping:

General Procedure A (Regular Addition)

To a 50 mL oven dried N_2 flushed flask was added the epoxyketone **7** (80.5 mg, 0.30 mmol, 1.00 equiv). The epoxyketone was concentrated from PhMe (2 x 5 mL, 45 °C bath temperature), followed by high vacuum to dry the solids. To a separate 10 mL flask under N_2 was weighed the alkenyl halide (0.36 mmol, 1.20 equiv), followed by THF (3 mL). The alkenyl halide solution was cooled to –78 °C, followed by addition of the *t*-BuLi (1.7M in pentane, 0.44 mL, 0.74 mmol, 2.45 equiv), and was stirred for 20 minutes at this temperature. The epoxyketone was dissolved in THF (6 mL) and was cooled to –94 °C in an acetone/liq. N_2 bath. The vinyl lithium solution was cannulated into the epoxyketone solution over the course of 5 minutes, then the solution was stirred at this temperature for 20 minutes. The reaction was warmed to –78 °C by putting it into an acetone/CO_2 bath. After stirring at –78 °C for 2 minutes TMSCl (76 μL, 0.60 mmol, 2.00 equiv) was added. The reaction was allowed to warm to room temperature and was stirred for 15 minutes at this temperature. The reaction was concentrated under reduced pressure and purified by SiO_2 column chromatography.

General Procedure B (Inverse Addition)

To a 25 mL oven dried N_2 flushed flask was added the epoxyketone **7** (80.5 mg, 0.30 mmol, 1.00 equiv). The epoxyketone was concentrated from PhMe (2 x 5 mL, 45 °C bath temperature), followed by high vacuum to dry the solids. To a separate 50 mL flask under N_2 was weighed the alkenyl halide (0.36 mmol, 1.20 equiv), followed by THF (3 mL). The alkenyl halide solution was cooled to –78 °C, followed by addition of the *t*-BuLi (1.7 M in pentane, 0.44 mL, 0.74 mmol, 2.45 equiv), and was stirred for 20 minutes at this temperature. The alkenyl lithium solution was cooled to –94 °C in an acetone/liq. N_2 bath. The epoxyketone **7** was dissolved in THF (6 mL) and cannulated into the vinyl lithium solution over the course of 5 minutes, then the solution was stirred at this temperature for 20 minutes. The reaction was warmed to –78 °C by putting it into an acetone/CO_2 bath. After stirring at –78 °C for 2 minutes TMSCl (76 μL, 0.60 mmol, 2.00 equiv) was added. The reaction was allowed to warm to room temperature and was stirred for 15 minutes at this temperature. The reaction was concentrated under reduced pressure and purified by SiO_2 column chromatography.

Procedure C (LDA Lithiation of furan)

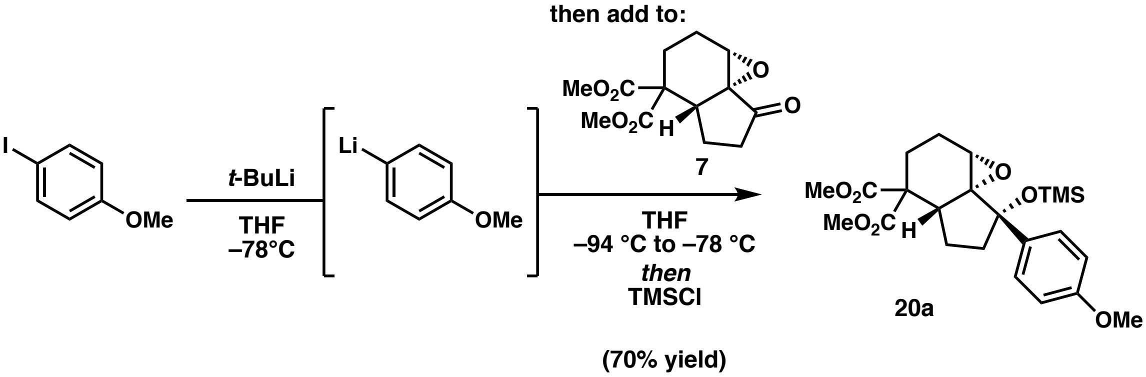
To a 25 mL oven dried N_2 flushed flask was added the epoxyketone **7** (80.5 mg, 0.30 mmol, 1.00 equiv). The epoxyketone was concentrated from PhMe (2 x 5 mL, 45 °C bath temperature), followed by high vacuum to dry the solids. To a separate 50 mL flask under N_2 was added *i*Pr_2NH (54 µL, 0.38 mmol, 1.25 equiv), and THF (3 mL). The solution was cooled to –78 °C, followed by adding *n*-BuLi (137 µL, 0.38 mmol, 1.25 equiv). The solution was stirred at –78 °C for 30 minutes. To a 10 mL oven dried N_2 flushed flask was added 3-bromofuran (52.9 mg, 0.36 mmol, 1.20 equiv), and THF (2 mL). The 3-bromofuran solution was cannulated into the LDA solution over the course of 5 minutes, and the flask was rinsed with THF (2 x 1 mL). The resulting solution was stirred at –78 °C for 30 minutes, followed by cooling the solution to –94 °C. The epoxyketone **7** was dissolved in THF (4 mL), and was cannulated into the furan solution over the course of 5 minutes, followed by rinsing the flask with THF (2 x 1 mL). Once the addition was complete, the reaction was stirred at –94 °C for 20 minutes, followed by warming the reaction to –78 °C with an acetone/CO_2 bath. The reaction was stirred at –78 °C for 5 minutes, followed by adding TMSCl (101.5 µL, 0.90 mmol, 3.00 equiv). The reaction was allowed to warm to r.t. and was stirred for 15 minutes. The reaction was concentrated under reduced pressure, and was purified by SiO_2 chromatography.

Notes

1. It is extremely important for this reaction to be rigorously dry. Trace water diminishes yield. To achieve this the epoxyketone was concentrated from PhMe twice, followed by drying under high vacuum to remove traces of water.
2. The alkenyl halides were dried by passing them through a SiO_2 plug with pentane, followed by concentrated under reduced pressure. The purity of the alkenyl halides were then quantified using QNMR (pyrazine internal standard).

3. It is important to run an SiO_2 column immediately following the concentration of the reaction under reduced pressure, because the product is not stable in the crude reaction mixture.
4. For larger scale reactions it is recommended to quench the reaction with sat. $NaHCO_3$, and perform an aqueous workup (extract with Et_2O, wash combined organic extracts with brine, and dry organic extracts over $MgSO_4$).

Preparation of 1,2-addition product 20a:



Prepared via General Procedure A, 70% isolated yield.

^{1}H NMR (500 MHz, Chloroform-*d*): δ 7.35 – 7.31 (m, 2H), 6.88 – 6.85 (m, 2H), 3.82 (s, 3H), 3.77 (s, 3H), 3.65 (s, 3H), 3.47 (d, *J* = 4.1 Hz, 1H), 2.73 (dddd, *J* = 13.1, 11.0, 8.7, 3.6 Hz, 1H), 2.55 (dd, *J* = 9.9, 8.8 Hz, 1H), 2.46 (ddd, *J* = 13.0, 8.4, 3.7 Hz, 1H), 2.33 (dddd, *J* = 15.4, 10.2, 8.1, 0.7 Hz, 1H), 2.27 – 2.17 (m, 2H), 1.98 – 1.87 (m, 2H), 1.35 (ddd, *J* = 13.3, 10.3, 8.5 Hz, 1H), -0.08 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 172.1, 170.4, 158.9, 136.7, 127.2, 113.6, 79.4, 72.2, 55.2, 55.0, 54.8, 52.7, 52.1, 41.7, 36.4, 29.6, 22.2, 21.3, 1.9.

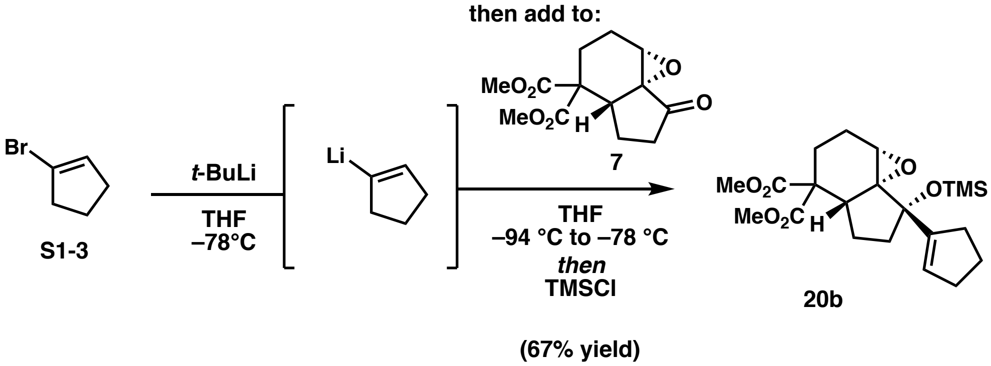
FTIR (NaCl, thin film): 2998, 2952, 2838, 1732, 1609, 1511, 1250, 887, 841 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{23}H_{32}O_7Si$ $[M+H]^+$ 449.1990, found 449.1998.

$[\alpha]_D^{25}$ = +37.5° (c = 1.00, $CHCl_3$).

TLC (20%EtOAc/80% Hexanes), R$_f$: 0.24, (dark blue in *p*-anisaldehyde stain).

Preparation of 1,2-addition product 20b:



Prepared via General Procedure A, 67% isolated yield.

^{1}H NMR (500 MHz, Chloroform-*d*): δ 5.67 (p, J = 2.0 Hz, 1H), 3.74 (s, 3H), 3.68 (s, 3H), 3.28 (dd, J = 3.6, 0.8 Hz, 1H), 2.65 – 2.55 (m, 2H), 2.43 – 2.18 (m, 7H), 2.04 – 1.79 (m, 5H), 1.54 – 1.44 (m, 1H), 0.05 (s, 9H).

^{13}C NMR (126 MHz, CDCl$_3$): δ 172.3, 170.4, 146.1, 126.4, 77.5, 70.3, 55.0, 54.3, 52.7, 52.0, 41.7, 35.3, 32.4, 31.3, 29.8, 23.2, 22.0, 21.2, 1.9.

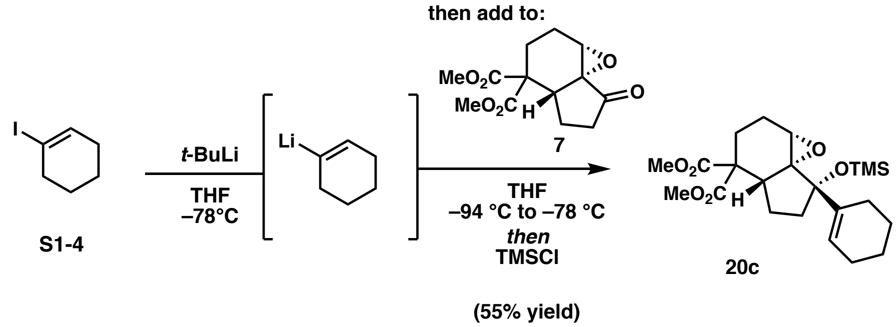
FTIR (NaCl, thin film): 2952, 2847, 1733, 1449, 1433, 1248, 840 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{26}H_{33}O_6Si$ $[M+H]^+$ 409.2041, found 409.2059.

$[\alpha]_D^{25}$ = +32.7° (c = 1.00, $CHCl_3$).

TLC (10%EtOAc/90% Hexanes), R$_f$: 0.12, (navy blue in *p*-anisaldehyde stain).

Preparation of 1,2-addition product 20c:



Prepared via General Procedure A, 55% isolated yield.

^{1}H NMR (500 MHz, Chloroform-*d*): δ 5.76 – 5.73 (m, 1H), 3.74 (s, 3H), 3.68 (s, 3H), 3.31 (d, *J* = 3.8 Hz, 1H), 2.63 (dd, *J* = 9.7, 8.2 Hz, 1H), 2.55 (dddd, *J* = 12.7, 10.5, 8.2, 3.2 Hz, 1H), 2.37 – 2.27 (m, 2H), 2.21 (ddd, *J* = 12.7, 8.2, 3.2 Hz, 1H), 2.16 – 2.00 (m, 3H), 1.98 – 1.85 (m, 3H), 1.82 – 1.75 (m, 1H), 1.75 – 1.68 (m, 1H), 1.67 – 1.60 (m, 1H), 1.59 – 1.45 (m, 3H), 0.05 (s, 9H).

^{13}C NMR (126 MHz, CDCl$_3$): δ 172.3, 170.5, 138.1, 122.5, 80.5, 70.3, 55.1, 55.0, 52.7, 52.0, 41.7, 34.1, 29.8, 25.3, 24.0, 22.8, 22.2, 21.9, 21.2, 2.0.

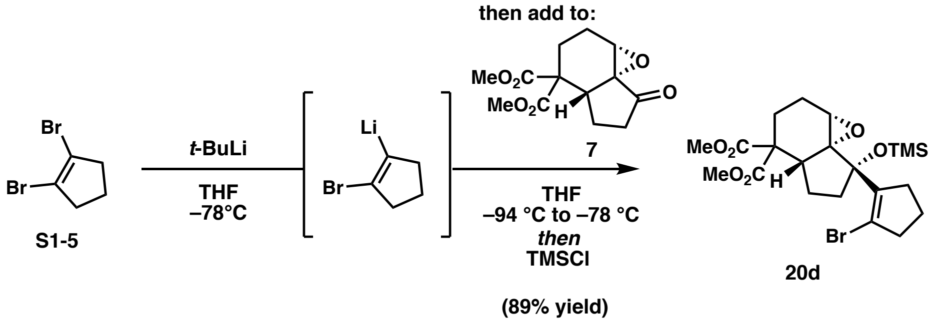
FTIR (NaCl, thin film): 2950, 2859, 1733, 1449, 1434, 1248, 841 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{22}H_{34}O_6Si$ $[M+H]^+$ 423.2197, found 423.2189.

$[\alpha]_D^{25}$ = +11.1° (*c* = 1.00, CHCl$_3$).

TLC (10%EtOAc/90% Hexanes), R*f*: 0.40, (navy blue in *p*-anisaldehyde stain).

Preparation of 1,2-addition product 20d:



Prepared via General Procedure A, 89% isolated yield.

^{1}H NMR (500 MHz, Chloroform-*d*): δ 3.75 (s, 3H), 3.69 (s, 3H), 3.42 (d, *J* = 3.6 Hz, 1H), 2.82 (t, *J* = 9.1 Hz, 1H), 2.78 – 2.62 (m, 2H), 2.55 – 2.39 (m, 4H), 2.36 – 2.26 (m, 2H), 2.04 – 1.96 (m, 2H), 1.94 – 1.83 (m, 3H), 1.62 – 1.54 (m, 1H), 0.08 (s, 9H).

^{13}C NMR (126 MHz, CDCl$_3$): δ 172.2, 170.5, 141.1, 115.3, 78.9, 70.1, 56.5, 55.2, 52.8, 52.0, 43.3, 42.9, 36.8, 34.3, 29.4, 22.4, 21.5, 21.3, 2.0.

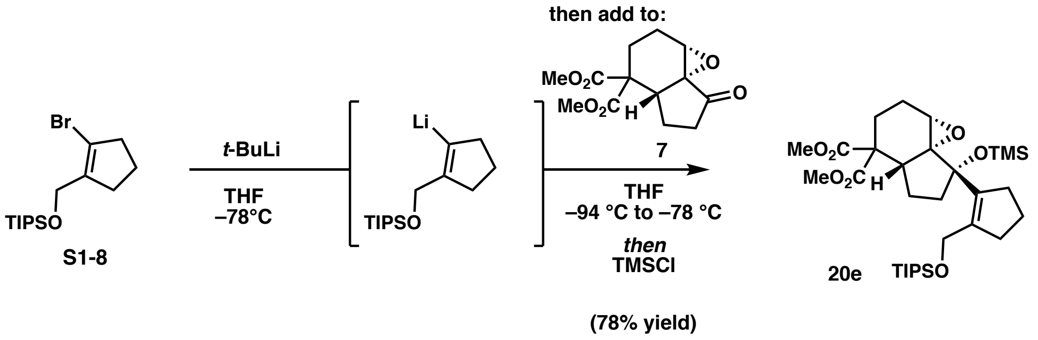
FTIR (NaCl, thin film): 2952, 2851, 1733, 1448, 1433, 1248, 840 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{21}H_{31}O_6SiBr$ $[M+H]^+$ 487.1146, found 487.1145.

$[\alpha]_D^{25}$ = +52.6° (*c* = 1.00, CHCl$_3$).

TLC (10%EtOAc/90% Hexanes), R*f*: 0.17, (dark blue in *p*-anisaldehyde stain).

Preparation of 1,2-addition product 20e:



Prepared via General Procedure A, 78% isolated yield.

^{1}H NMR (500 MHz, Chloroform-*d*): δ 4.58 (dt, *J* = 13.4, 1.6 Hz, 1H), 4.47 (dt, *J* = 13.9, 2.0 Hz, 1H), 3.74 (s, 3H), 3.69 (s, 3H), 3.27 (d, *J* = 3.7 Hz, 1H), 2.67 (dd, *J* = 10.4, 8.5 Hz, 1H), 2.58 – 2.46 (m, 4H), 2.46 – 2.40 (m, 1H), 2.39 – 2.33 (m, 1H), 2.32 – 2.26 (m, 1H), 2.18 (ddd, *J* = 13.2, 8.2, 6.6 Hz, 1H), 2.03 (ddd, *J* = 13.3, 10.0, 5.4 Hz, 1H), 1.97 – 1.85 (m, 2H), 1.77 (p, *J* = 7.5 Hz, 2H), 1.50 (ddd, *J* = 13.3, 10.3, 8.4 Hz, 1H), 1.10 – 1.05 (m, 21H), 0.07 (s, 9H).

^{13}C NMR (126 MHz, CDCl$_3$): δ 172.2, 170.4, 140.3, 137.6, 79.3, 71.2, 61.3, 55.2, 55.1, 52.8, 52.1, 43.7, 38.0, 35.5, 35.1, 29.6, 23.1, 21.8, 21.4, 18.1, 12.0, 2.2.

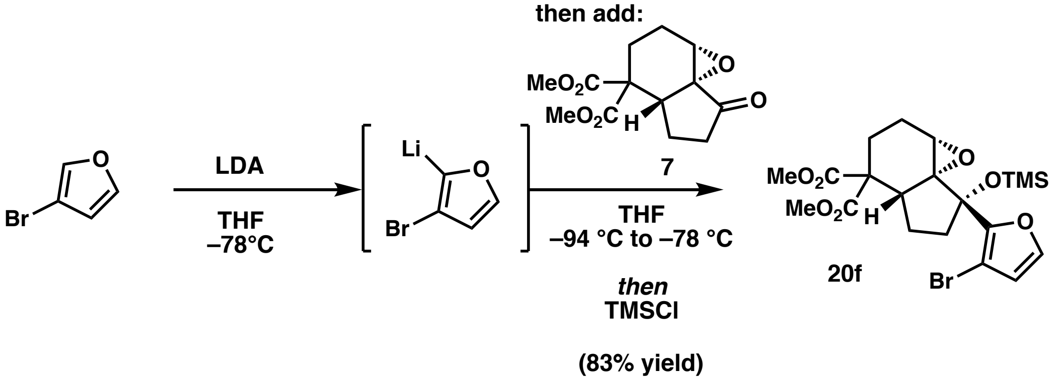
FTIR (NaCl, thin film): 2949, 2866, 1738, 1463, 1434, 1248, 1219, 881, 841 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{31}H_{54}O_7Si$ $[M+NH_4]^+$ 612.3746, found 612.3751.

$[\alpha]_{\mathrm{D}}^{25}$ = +17.8° (*c* = 1.00, CHCl$_3$).

TLC (10%EtOAc/90% Hexanes), R*f*: 0.30, (navy blue in *p*-anisaldehyde stain).

Preparation of 1,2-addition product 20f:



Prepared via General Procedure C, 83% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.34 (d, *J* = 1.9 Hz, 1H), 6.42 (d, *J* = 1.9 Hz, 1H), 3.76 (s, 3H), 3.68 (d, *J* = 3.7 Hz, 1H), 3.66 (s, 3H), 2.79 (ddd, *J* = 12.3, 8.2, 2.4 Hz, 1H), 2.65 (dddd, *J* = 12.4, 10.1, 7.8, 2.4 Hz, 1H), 2.57 (dd, *J* = 10.0, 7.8 Hz, 1H), 2.38 – 2.25 (m, 2H), 2.13 – 2.05 (m, 1H), 2.03 – 1.97 (m, 1H), 1.90 – 1.79 (m, 1H), 1.58 – 1.45 (m, 1H), -0.05 (s, 9H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 172.1, 170.4, 150.9, 141.6, 116.0, 97.3, 76.6, 70.0, 56.2, 55.1, 52.7, 52.1, 41.4, 35.1, 29.7, 21.3, 21.1, 1.1.

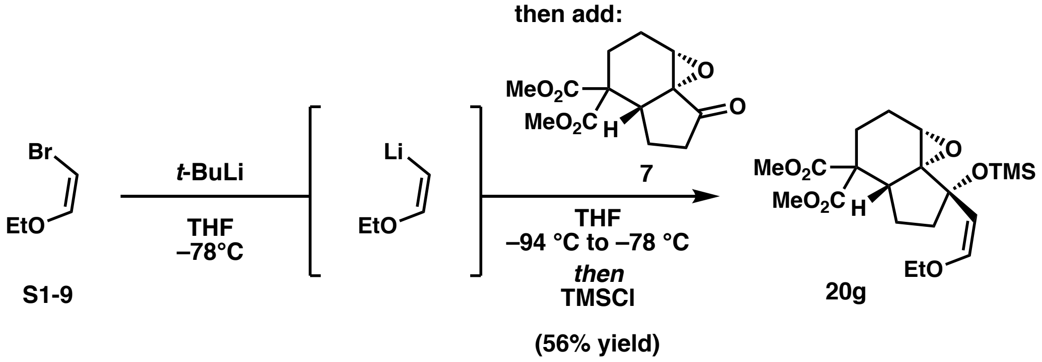
FTIR (NaCl, thin film): 3151, 2993, 2952, 2847, 1733, 1567, 1432, 1250, 873, 843 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{20}H_{27}O_7SiBr$ [M+H]$^+$ 487.0782, found 487.0780.

$[\alpha]_D^{25}$ = +57.4° (*c* = 1.00, CHCl$_3$).

TLC (15%EtOAc/85% Hexanes), R*f*: 0.29, (light brown in *p*-anisaldehyde stain).

Preparation of 1,2-addition product 20g:



Prepared via General Procedure B, 56% isolated yield.

^{1}H NMR (500 MHz, Chloroform-*d*): δ 5.90 (d, *J* = 7.1 Hz, 1H), 4.34 (dd, *J* = 7.1, 0.6 Hz, 1H), 3.83 (d, *J* = 7.1 Hz, 1H), 3.81 (d, *J* = 7.1 Hz, 1H), 3.73 (s, 3H), 3.68 (s, 3H), 3.33 (d, *J* = 3.6 Hz, 1H), 2.88 (dd, *J* = 9.9, 8.6 Hz, 1H), 2.49 (dddd, *J* = 12.6, 10.4, 8.5, 3.8 Hz, 1H), 2.34 – 2.25 (m, 2H), 2.12 (ddd, *J* = 12.1, 8.3, 3.8 Hz, 1H), 2.01 – 1.96 (m, 1H), 1.95 – 1.87 (m, 1H), 1.86 – 1.80 (m, 1H), 1.57 – 1.49 (m, 1H), 1.28 (t, *J* = 7.1 Hz, 3H), 0.08 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 172.5, 170.7, 146.0, 109.6, 76.7, 70.9, 68.6, 55.3, 55.2, 52.6, 51.9, 42.1, 38.5, 29.8, 21.6, 21.5, 15.4, 2.3.

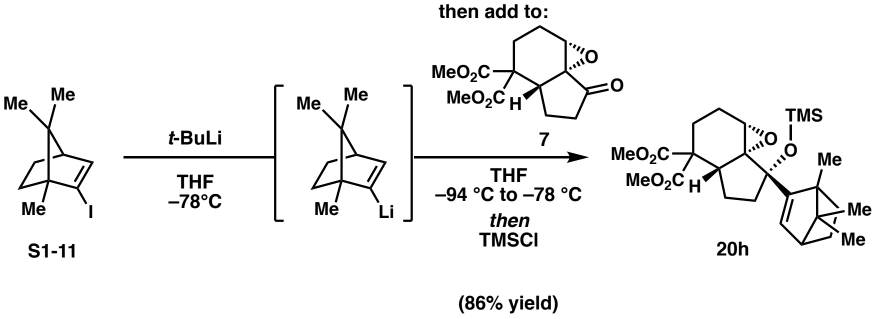
FTIR (NaCl, thin film): 2952, 1733, 1659, 1433, 1248, 1101, 841 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{20}H_{32}O_7Si$ $[M+H]^+$ 413.1990, found 413.2000.

$[\alpha]_D^{25}$ = +57.5° (*c* = 1.00, $CHCl_3$).

TLC (20%EtOAc:80% Hexanes), R*f*: 0.30, (pink in *p*-anisaldehyde stain).

Preparation of 1,2-addition product 20h:



Prepared via General Procedure B, 86% isolated yield.

^{1}H NMR (500 MHz, Chloroform-*d*): δ 5.71 (d, *J* = 3.4 Hz, 1H), 3.75 (s, 3H), 3.68 (s, 3H), 3.34 (d, *J* = 3.6 Hz, 1H), 2.78 (t, *J* = 9.3 Hz, 1H), 2.52 (dddd, *J* = 12.8, 10.8, 9.0, 4.6 Hz, 1H), 2.41 – 2.28 (m, 2H), 2.25 (t, *J* = 3.5 Hz, 1H), 2.19 (ddd, *J* = 13.0, 8.6, 4.6 Hz, 1H), 2.05 – 1.94 (m, 2H), 1.87 – 1.79 (m, 2H), 1.56 – 1.44 (m, 2H), 1.23 (ddd, *J* = 12.2, 9.2, 3.6 Hz, 1H), 1.10 (s, 3H), 1.01 (ddd, *J* = 11.6, 9.2, 3.7 Hz, 1H), 0.77 (s, 3H), 0.74 (s, 3H), 0.06 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 172.2, 170.6, 150.0, 128.7, 79.3, 70.1, 57.1, 55.3, 55.2, 55.0, 52.7, 51.9, 51.2, 42.4, 36.1, 32.9, 29.8, 25.4, 22.7, 21.2, 19.7, 19.5, 13.5, 2.4.

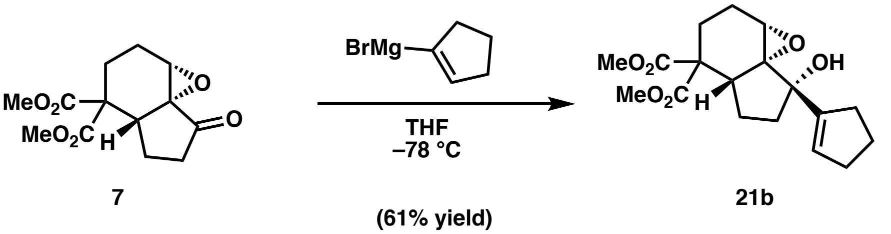
FTIR (NaCl, thin film): 2952, 2873, 1734, 1450, 1434, 1247, 839, 887 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{26}H_{41}O_6Si$ $[M + H]^+$ 477.2667, found 477.2673.

$[\alpha]_D^{25}$ = -11.8° (*c* = 1.00, $CHCl_3$).

TLC (20%EtOAc:80% Hexanes), R*f*: 0.29, (blue in *p*-anisaldehyde stain).

Example of gram-scale procedure, using stoichiometric TMSOTf to facilitate the semipinacol rearrangement:



In a 200-mL, round-bottomed flask, epoxyketone **7** (1.59 g, 5.93 mmol, 1.0 equiv) was dissolved in THF (59 mL) and cooled to –78 °C. To this solution was added cyclopentyl magnesium bromide (prepared from cyclopentenyl bromide, Mg(0) and I_2 activation, 0.3M in THF, 25 mL, 7.50 mmol, 1.27 equiv) via cannula. The reaction was allowed to stir for an additional 10 minutes at –78 °C, then quenched with sat. NH_4Cl solution (30 mL) and H_2O (30 mL), and was allowed to warm to room temperature. The biphasic mixture was then transferred to a separatory funnel with Et_2O (50 mL), and the layers were separated. The aqueous layer was extracted with more Et_2O (3 x 75 mL). The combined organics were washed with brine (1 x 100 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by silica gel chromatography (12% to 13% to 14% acetone in hexanes to elute the product and then 20% acetone in hexanes to recover the unreacted epoxyketone starting material) to afford epoxy alcohol **21b** (1.20 g, 3.61 mmol, 61% yield) as a white solid.

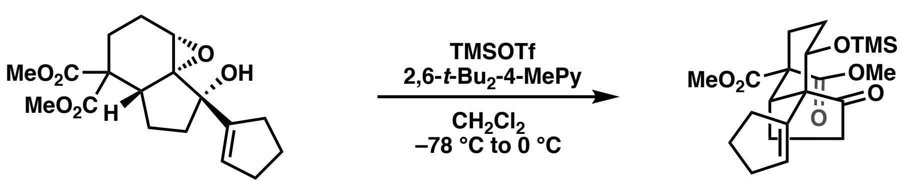
^{1}H NMR (400 MHz, Chloroform-*d*): δ 5.67 (t, *J* = 1.8 Hz, 1H), 3.75 (s, 3H), 3.70 (s, 3H), 3.34 (d, *J* = 3.8 Hz, 1H), 2.74 (dd, *J* = 10.5, 7.8 Hz, 1H), 2.52 – 2.40 (m, 2H), 2.39 – 2.28 (m, 6H), 2.19 – 2.08 (m, 1H), 2.05 – 1.96 (m, 1H), 1.95 – 1.85 (m, 4H), 1.62 – 1.52 (m, 1H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 171.9, 170.3, 145.4, 126.0, 75.4, 71.4, 56.5, 55.1, 52.9, 52.1, 44.0, 37.8, 32.3, 31.7, 29.3, 23.4, 23.2, 21.4.

FTIR (NaCl, thin film): 3503, 2952, 1732, 1433, 1244, 1218, 1174 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{18}H_{25}O_6$ $[M + H]^+$ 337.1646, found 337.1635.

TLC (33%EtOAc/ 67% Hexanes), R$_f$: 0.40 (blue/purple in *p*-anisaldehyde)



21b (87% yield) **22b**

A 100-mL, round-bottomed flask was charged with epoxy alcohol **21b** (1.37 g, 4.07 mmol, 1.0 equiv), 2,6-*t*-Bu$_2$-4-MePy (2.51 g, 12.2 mmol, 3 equiv) and CH_2Cl_2 (41 mL), and the solution was cooled to –78 °C in a dry/ice acetone bath. TMSOTf added dropwise via syringe (1.47 mL, 8.15 mmol, 2 equiv), causing the solution to turn a faint pink color. The reaction was allowed to stir at – 78 °C for 5 minutes, and then the dry//ice acetone bath was replaced with an ice bath, allowing the reaction to warm to 0 °C. The reaction was allowed to stir for an additional 10 minutes at 0 °C, then the reaction was quenched with sat. $NaHCO_3$ (50 mL), and the mixture was allowed to warm to room temperature. The biphasic mixture was transferred to a separatory funnel and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (3 x 75 mL), and the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (10% to 12% to

15% ethyl acetate in hexanes) to afford ketone **22b** (1.45 g, 4.07 mmol, 87% yield) as a white solid.

^{1}H NMR (500 MHz, Chloroform-*d*): δ 5.38 (t, *J* = 2.2 Hz, 1H), 4.33 (t, *J* = 2.5 Hz, 1H), 3.74 (s, 3H), 3.64 (s, 3H), 3.37 (dd, *J* = 12.5, 6.9 Hz, 1H), 2.57 – 2.49 (m, 1H), 2.45 (td, *J* = 13.9, 3.9 Hz, 1H), 2.41 – 2.23 (m, 3H), 2.22 – 2.08 (m, 3H), 1.97 – 1.89 (m, 1H), 1.87 – 1.81 (m, 2H), 1.81 – 1.71 (m, 2H), 1.68 (dq, *J* = 14.3, 3.6 Hz, 1H), 0.06 (s, 9H).

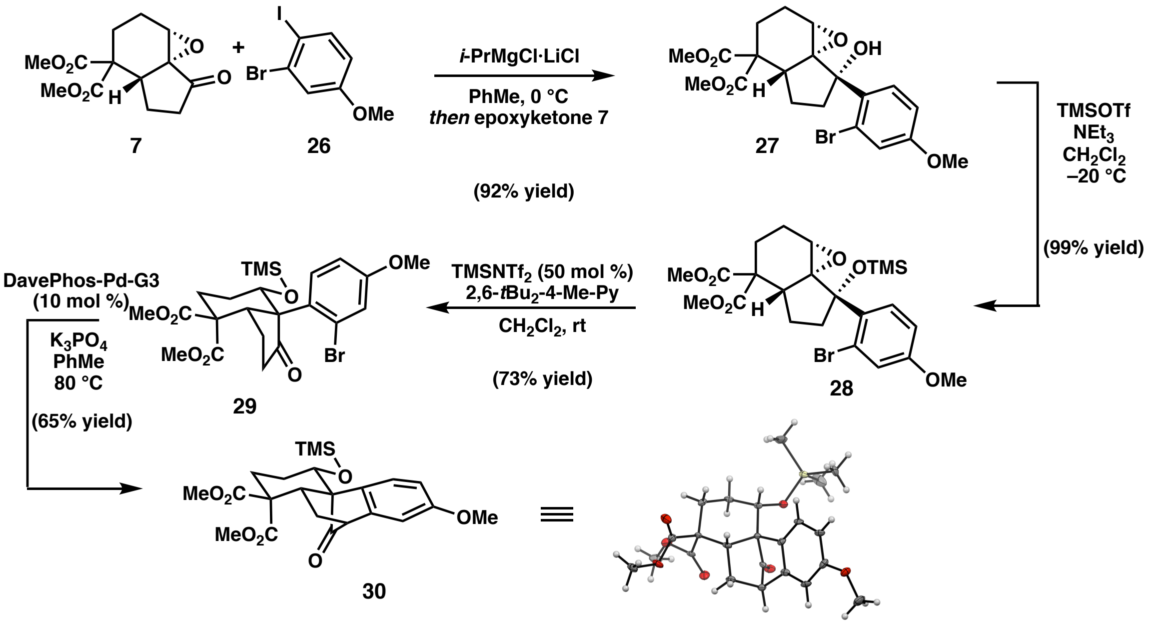
^{13}C NMR (126 MHz, $CDCl_3$): δ 219.2, 170.8, 170.5, 142.9, 127.3, 70.3, 57.8, 56.1, 52.7, 52.5, 41.9, 39.1, 32.9, 32.7, 27.8, 23.5, 22.8, 19.6, -0.0.

FTIR (NaCl, thin film): 2952, 2846, 1740, 1434, 1252, 1171, 1058, 841 cm^{-1}.

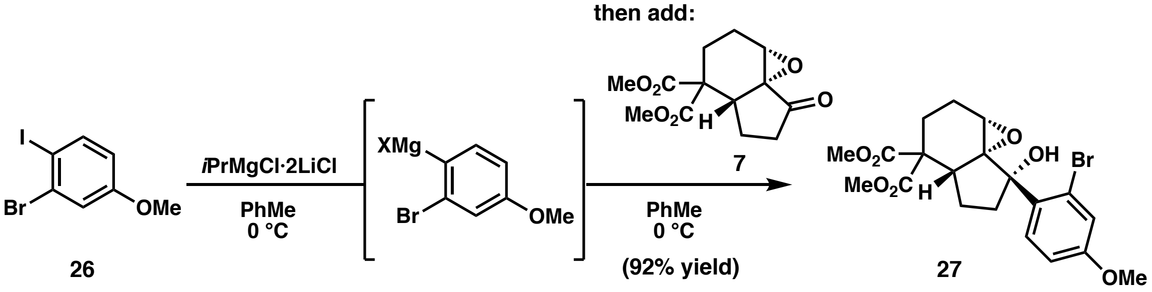
HRMS: (ESI-TOF) calc'd for $C_{21}H_{33}O_6Si$ $[M + H]^+$ 409.2041, found 409.2056.

TLC (15%EtOAc/ 85% Hexanes), R*f*: 0.40 (grey/blue/black in *p*-anisaldehyde)

Preparative procedures and characterization data is shown in this section are for the following route:



Preparation of epoxy-alcohol 27:



In a 250-mL, round-bottomed flask, aryl iodide **26** (4.85 g, 15.49 mmol, 1.7 equiv) was dissolved in PhMe (27 mL) and cooled to 0 °C. To this solution was added *i*-PrMgCl•2LiCl (1.3M in THF, 11.9 mL, 15.49 mmol, 1.7 equiv) dropwise via syringe, and was allowed to continue to stir at 0 °C for 1 hour. Meanwhile, in a separate 100-mL round-bottomed flask, epoxyketone **7** (2.54 g, 9.45 mmol, 1 equiv) was dissolved in PhMe (48 mL) under N_2 (to get the **7** to dissolve, the PhMe solution was heated slightly in a warm water bath). After the metal-halogen exchange flask had been stirring for 1 hour at 0 °C, the epoxyketone solution was added dropwise via cannula, and the flask was rinsed with PhMe (1 x 20mL), and was stirred for an additional 30 minutes at 0 °C. Caution: the epoxyketone begins to crash out of solution, be careful that the cannula does not get clogged. The reaction was then quenched with H_2O (30 mL), and was allowed to warm to room temperature. The biphasic mixture was then transferred to a 1000-mL Erlenmeyer flask, and aqueous sat. Rochelle's salt solution (150 mL) and Et_2O were added (150 mL), and this biphasic mixture was allowed to vigorously stir for 30 minutes. The mixture was then transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with Et_2O (4 x 150 mL). The combined organic extracts were washed with brine (2 x 100 mL), and dried over Na_2SO_4, filtered and then concentrated *in vacuo*. The crude residue was purified by silica gel chromatography (25% to 30% ethyl acetate in hexanes) to afford epoxy alcohol **27** (3.95 g, 8.70 mmol, 92% yield) as a white solid.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.74 (d, *J* = 8.9 Hz, 1H), 7.10 (d, *J* = 2.7 Hz, 1H), 6.83 (dd, *J* = 8.8, 2.7 Hz, 1H), 3.78 (s, 6H), 3.73 (s, 3H), 3.43 (dd, *J* = 12.8, 6.1 Hz, 1H), 3.25 – 3.19 (m, 1H), 3.07 (d, *J* = 1.3 Hz, 1H), 2.67 – 2.52 (m, 1H), 2.42 – 2.30 (m, 2H), 2.25 (dtd, *J* = 15.7, 8.7, 1.2 Hz, 1H), 2.13 – 2.00 (m, 3H), 1.78 (dt, *J* = 13.4, 8.8 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 172.0, 170.8, 159.1, 134.1, 129.9, 120.5, 119.7, 112.7, 78.1, 72.8, 61.1, 55.5, 55.2, 52.9, 52.0, 45.7, 40.1, 28.2, 25.7, 21.7.

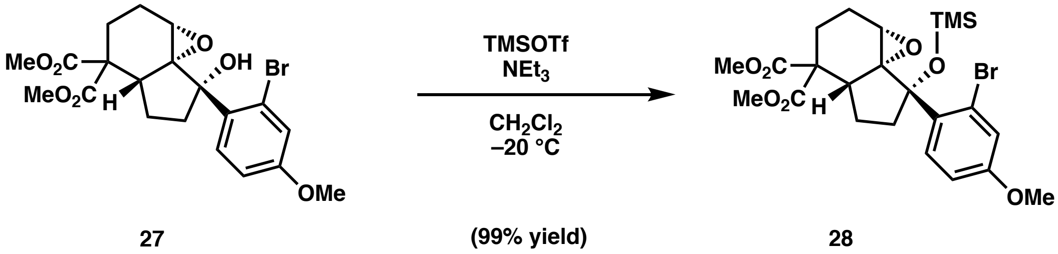
FTIR (NaCl, thin film): 3491, 2995, 2952, 2838, 2255, 1731, 1602, 1487, 1291, 1234, 1031, 917, 731 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{20}H_{25}O_8Br$ $[M + H_2O]^+$ 472.0727, found 472.0750.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = +58.1° (*c* = 1.35, $CHCl_3$).

TLC (30%EtOAc/ 70% Hexanes), R*f*: 0.4 (blue in *p*-anisaldehyde)

Preparation of silyl ether 28:



In a 500-mL, round-bottomed flask, epoxy alcohol **27** (3.95 g, 8.67 mmol, 1.0 equiv) was azeotroped with PhMe (from the solvent system, 3 x 10 mL), and dried under high vacuum. The flask was equipped with a rubber septum and purged with N_2, dissolved in CH_2Cl_2 (87 mL) and cooled to –20 °C. Et_3N (3.63 mL, 26.0 mmol, 3.0 equiv) was added, followed by TMSOTf (1.49 mL, 10.41 mmol, 1.2 equiv). The reaction was stirred for 30 minutes, during which time the reaction was allowed to reach 0 °C. At this time, an additional portion of TMSOTf was added (0.63 mL, 3.47 mmol, 0.4 equiv). The reaction was monitored by TLC, indicating its completion, and then quenched by the addition of sat. $NaHCO_3$ (150 mL), and the reaction was allowed to warm to room temperature. The biphasic mixture was transferred to a separatory funnel, the layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 x 200 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by silica gel chromatography (10% to 15% to 20% ethyl acetate in hexanes) to afford silyl ether **28** (4.52 g, 8.59 mmol, 99% yield) as a white solid.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.30 (d, *J* = 8.8 Hz, 1H), 7.18 (d, *J* = 2.7 Hz, 1H), 6.79 (dd, *J* = 8.8, 2.7 Hz, 1H), 3.79 (s, 3H), 3.77 (s, 3H), 3.68 (s, 3H), 3.47 (d, *J* =

3.5 Hz, 1H), 2.93 (dd, *J* = 10.9, 7.7 Hz, 1H), 2.61 – 2.50 (m, 1H), 2.50 – 2.27 (m, 4H), 2.14 – 2.07 (m, 1H), 1.97 – 1.88 (m, 1H), 1.65 – 1.53 (m, 1H), 0.06 (s, 9H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 172.1, 170.4, 158.8, 135.7, 128.1, 122.7, 121.0, 112.3, 82.1, 70.6, 56.7, 55.5, 55.2, 52.8, 52.1, 43.8, 40.3, 29.2, 24.1, 21.4, 2.4.

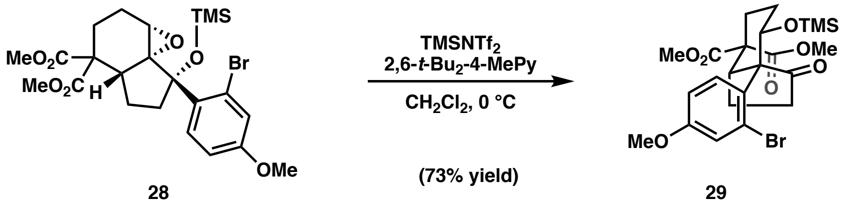
FTIR (NaCl, thin film): 2952, 2389, 1731, 1601, 1488, 1434, 1239, 1032, 883, 842, 734 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{23}H_{35}O_7BrN$ $[M + NH_4]^+$ 544.1361, found 544.1359.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = +34.4° (*c* = 1.30, CHCl$_3$).

TLC (20%EtOAc/ 80% Hexanes), R*f*: 0.4 (blue in *p*-anisaldehyde)

Preparation of rearrangement product 29:



A 500-mL, round-bottomed flask was charged with silyl ether **28** (4.52 g, 8.59 mmol, 1.0 equiv), 2,6-*t*-Bu$_2$-4-MePy (1.94 g, 9.45 mmol, 1.1 equiv) and CH$_2$Cl$_2$ (171.8 mL), and the solution was cooled to 0 °C. In an N$_2$-filled glovebox, a 1-mL syringe was filled with TMSNTf$_2$ (1.52, 4.30 mmol, 0.50 equiv), plugged with a rubber stopper, and removed from the glovebox. The TMSNTf$_2$ was immediately added dropwise to the reaction mixture, causing the solution to turn yellow. After stirring for an additional 30 minutes at 0 °C, the reaction was quenched with sat. NaHCO$_3$ (200 mL), and the solution was allowed to warm to room temperature. The biphasic mixture was transferred to a separatory funnel and the layers were separated. The aqueous phase was extracted with CH$_2$Cl$_2$ (3 x 200 mL), and the combined organic extracts were dried over Na$_2$SO$_4$, filtered, and concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (10% to 12.5% to 15% acetone in hexanes) to afford ketone **29** (3.32 g, 6.27 mmol, 73% yield) as a white solid.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.17 (d, *J* = 2.8 Hz, 1H), 6.98 (d, *J* = 9.0 Hz, 1H), 6.77 (dd, *J* = 8.9, 2.8 Hz, 1H), 4.55 – 4.53 (m, 1H), 4.32 (dd, *J* = 12.0, 8.1 Hz, 1H), 3.75 (s, 3H), 3.71 (s, 3H), 3.07 (s, 3H), 2.75 (dt, *J* = 18.1, 9.6 Hz, 1H), 2.47 (td, *J* = 13.8, 3.8 Hz, 1H), 2.41 – 2.32 (m, 1H), 2.32 – 2.18 (m, 2H), 2.05 – 1.95 (m, 2H), 1.84 (dq, *J* = 14.6, 3.5 Hz, 1H), 0.08 (s, 9H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 219.3, 170.7, 170.3, 158.3, 132.5, 130.1, 123.7, 120.6, 112.4, 70.6, 58.5, 56.1, 55.5, 52.7, 52.2, 41.7, 39.3, 28.4, 23.6, 19.1, -0.1.

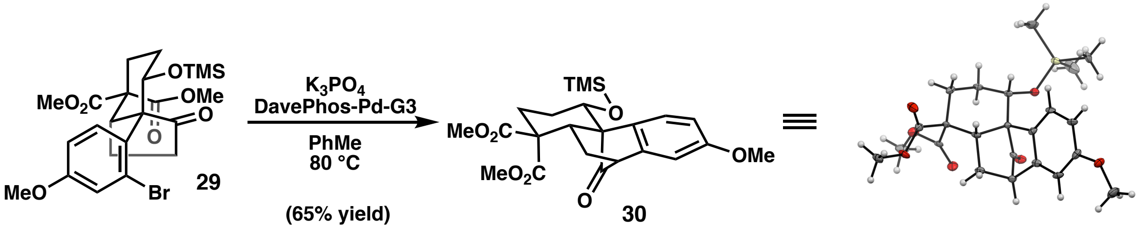
FTIR (NaCl, thin film): 3470, 3083, 2254, 1745, 1732, 1602, 1493, 1456, 1253, 1213, 1173, 1047, 1026, 869, 840, 731 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{23}H_{32}O_7BrSi$ $[M + H]^+$ 527.1095, found 527.1093.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = +52.6° (*c* = 1.40, CHCl$_3$).

TLC (20%EtOAc/ 80% Hexanes), R*f*: 0.35 (yellow in *p*-anisaldehyde)

Preparation of aromatic intermediate 30:



A 40-mL vial containing aryl bromide **29** (480 mg, 0.910 mmol, 1 equiv) was brought into the glovebox, and was charged with K_3PO_4 (882 mg, 3.64 mmol, 4 equiv), and DavePhos-Pd-G3 (69.5 mg, 0.091 mmol, 10 mol %), followed by PhMe (22.75 mL), and the vial was sealed, and brought out of the glovebox, and placed inside a 80 °C oil bath, and allowed to stir for 15 hours. **Note**: it is extremely important to maintain vigorous stirring. A cross-shaped stir bar was used in this reaction. If the stirring is not vigorous, incomplete conversion is observed. The reaction was then cooled to room temperature, and filtered through a plug of silica gel that had been pre-packed with Et_2O, filtered through the silica plug, and flushed with more Et_2O, and concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (15% to 18% to 20% EtOAc in Hexanes) to afford **30** (264 mg, 0.592 mmol, 65% yield) as a white solid. The material was recrystallized from Et_2O to afford crystals suitable for X-ray diffraction analysis.

Note: this reaction was initially developed and performed on racemic material, and the X-ray structure initially obtained was on a racemic material. The route was then repeated and fully characterized using enantiopure epoxyketone **7**.

^{1}H NMR (500 MHz, Chloroform-*d*): δ 7.12 (d, *J* = 8.4 Hz, 1H), 6.84 (d, *J* = 2.4 Hz, 1H), 6.79 (dd, *J* = 8.3, 2.5 Hz, 1H), 4.53 (dd, *J* = 10.0, 5.8 Hz, 1H), 3.79 (s, 3H), 3.73 (s, 3H), 3.67 (s, 3H), 3.36 (d, *J* = 4.4 Hz, 1H), 2.58 (dt, *J* = 12.6, 4.6 Hz, 1H), 2.42 – 2.34 (m, 1H), 2.05 – 1.89 (m, 4H), 1.53 (dd, *J* = 12.4, 11.1 Hz, 1H), 0.11 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 199.5, 171.8, 170.4, 158.8, 142.4, 133.5, 121.5, 112.3, 107.1, 67.9, 56.8, 55.4 (two ^{13}C signals), 52.7, 52.3, 49.0, 43.1, 30.3, 28.7, 28.5, 0.7.

FTIR (NaCl, thin film): 2954, 1790, 1779, 1738, 1732, 1609, 1484, 1455, 1251, 1121, 1043, 908, 875, 842, 732 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{30}H_{31}O_7Si$ $[M + H]^+$ 447.1834, found 447.1824.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = +51.7° (*c* = 0.78, $CHCl_3$).

TLC (20%EtOAc/ 80% Hexanes), R*f*: 0.35 (UV, brown in I_2 stain) note: does not appear in *p*-anisaldehyde or CAM.

1.8 NOTES AND REFERENCES

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(11) The vinyl lithium species were typically generated from the corresponding vinyl bromide or vinyl iodide via lithium-halogen exchange with tert-butyl lithium at low temperature in THF.

(12) If the reaction was not run under strictly anhydrous conditions, the organometallic reagent was quenched, furnishing the protodemetalated species and the recovered epoxyketone. This was especially important in cases where the generated organometallic reagent was valuable, because the functional handle is lost and the nucleophile could not be recovered.
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Chapter 2

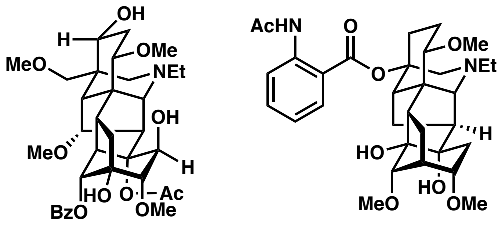
Initial Route Development Towards the C_{19} Diterpenoid Alkaloids

2.1 INTRODUCTION

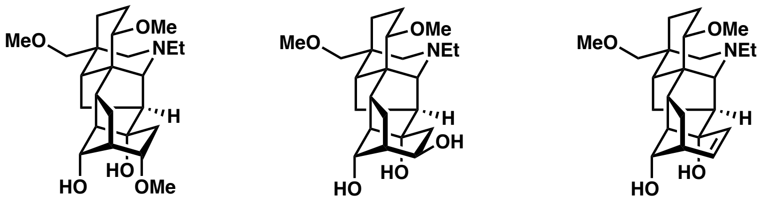
The structural complexity and unique biological activities of the diterpenoid alkaloids have attracted scientists to study their phytochemistry, medicinal properties, structure and synthesis.[1] Our primary research efforts focus around the total synthesis of the C_{19} *aconitine* alkaloids. Representative examples of C_{19} *aconitine* alkaloids are shown in Figure 2.1. Aconitine (**50**) is arguably the most famous of the C_{19} diterpenoid alkaloids, primarily due to its potent toxicity. Diverse biological activity is known across many members of the natural product family,[2] due to their abilities to bind to voltage gated ion channels. Specifically, **50** itself is known to modify voltage-gated Na^+ ion channels, which result in membrane depolarization, thus giving rise to paralysis and respiratory failure. Furthermore, the hydrobromide salt of lappaconitine (**51**) is both approved and marketed in Russia and China as a drug to treat pain and arrhythmia.[3] To contrast this, talatisamine (**1**, Figure 2.1) was found to be a non-cytotoxic blocker of voltage-gated K^+ channels with selectivity over voltage-gated Na^+ and Ca^{2+} ion channels and was shown to attenuate the cytotoxicity of β-amyloid oligomers by restoring cell viability.[4,5] These differences in observed selectivity for voltage-gated ion channels is remarkable considering the structures of the natural products.

As shown in Figure 2.1, the core frameworks of the displayed natural products all possess the same hexacyclic framework, but differ in peripheral oxidation pattern. With this interesting observation in mind, we believed that a tractable initial goal would be to target less oxidized members of the family (e. g. **1**, **52**, or **53**), providing a reasonable synthetic plan. Once a total synthesis has been established, further oxidation on these frameworks could be selectively introduced, which would enable studies leading to a greater understanding of how these oxidation frameworks provide different selectivity of voltage-gated ion channels.

Figure 2.1. Representative examples of C_{19}-Diterpenoid Alkaloids



aconitine (50) lappaconitine (51)



talatisamine (1) liljestrandisine (52) liljestrandinine (53)

This chapter details our retrosynthetic strategy towards the C_{19} diterpenoid alkaloids, and the development of initial synthetic routes. This chapter includes routes that were ultimately unsuccessful in completing the natural product. However, the routes provided here ultimately informed an understanding of the reactivity, guiding the approach to what became the successful routes to **52** and **53** (see Chapter 3).

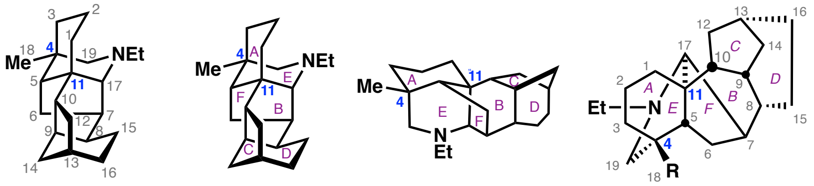
2.2 STRUCTURAL CONSIDERATIONS

The structural complexity of the C_{19} diterpenoid alkaloids has long attracted chemists to study their synthesis. The most difficult features of the diterpenoid alkaloids include the highly caged polycyclic structure, oxidation pattern, and basic amine functionality. These complex 3-dimensional structures can be represented in a number of different drawings (Figure 2.2), and are found throughout the literature in these renditions. Atom numbering and ring labeling that will be used throughout this chapter are shown in Figure 2.2.

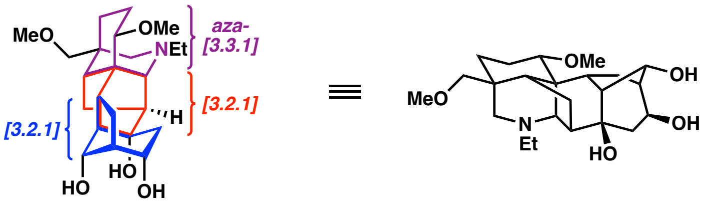
The caged hexacyclic framework contains within it a series of bridged bicyclic motifs (**1**, Figure 2.2), including an AE-azabicyclo[3.3.1]nonane that is then fused to a central FB-bicyclo[3.2.1]octane, and that is then finally fused to a CD-bicyclo[3.2.1]octane, resulting in 12 contiguous stereogenic centers, of which two are all carbon quaternary stereocenters (C4 and C11). In addition to the difficult polycyclic core framework, these frameworks feature a basic *N*-ethylated tertiary amine moiety as a part of a hydrindane bridged piperidyl motif making up the challenging AEF tricycle, and at least 5 free alcohols or ethers.

Figure 2.2. Structural analysis of C_{19}-Diterpenoid Alkaloids

Ring labelling and atom numbering



3-D representations of talatisamine



talatisamine (1)

2.3 SYNTHETIC STRATEGY TO C_{19} DITERPENOID ALKALOIDS

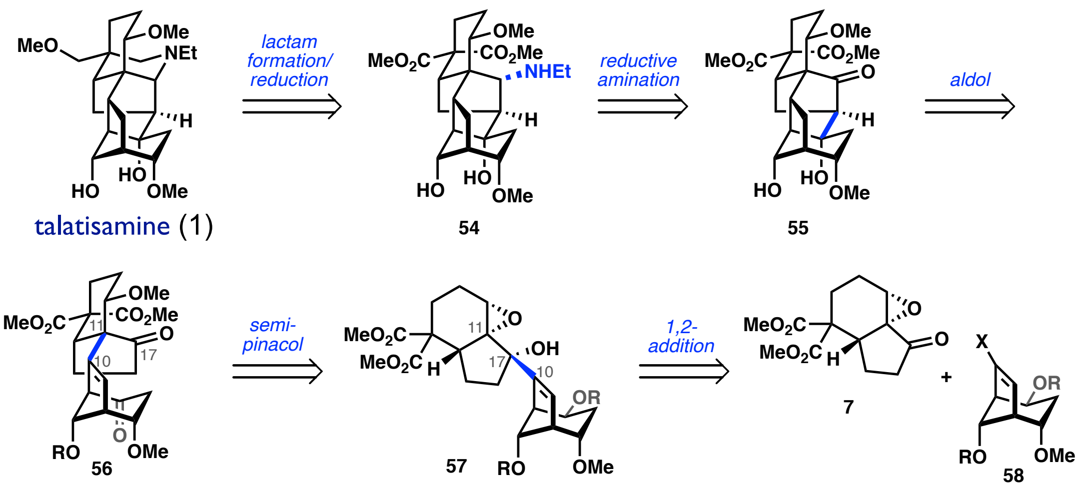
A uniquely convergent approach to these highly caged molecules are non-obvious, and if successful would represent a significant contribution to diterpenoid alkaloids total synthesis. Our work disclosed in Chapter 1 in the development of a synthetic strategy via a 1,2-addition and subsequent semipinacol rearrangement enables the formation of the AE-hydrindane in a convergent fashion.

The most convergent application of this strategy would bring as much complexity as possible through the 1,2-addition and subsequent semipinacol rearrangement. Ideally, addition of a bridged bicyclic motif with appropriate oxidation and functional handles for the natural product would enable the most convergent approach through this strategic disconnection. This strategy would inherently require asymmetric synthesis of each fragment to avoid making mixtures of diastereomers since two chiral fragments will be brought together.

In a retrosynthetic sense, we envisioned a disconnection of **1** through the piperidine E-ring to secondary amine and diester **54** (Figure 2.3). The diester moiety was thought to be a simplifying disconnection to generate the C4 all carbon quaternary stereocenter given that simple α-functionalization chemistry of 1,3-dicarbonyls to generate all carbon quaternary centers is well established. Furthermore, by disconnecting to a diester group, diastereocontrol at this C4 quaternary stereocenter is not required at an early stage, and can be differentiated at a later stage through substrate control. The secondary amine would arise from a reductive amination of ketone **55**, and the central B ring could be assembled through two distinct α-functionalization events of the C17 ketone. Specifically, an intramolecular aldol ring-closing event would close the central B ring of **56**, and the C10–C11 bond would arise from a semipinacol rearrangement of epoxy-alcohol **57**. Epoxy-alcohol **57** would be accessible by the 1,2-addition of an alkenyl nucleophile **58** to epoxyketone **7**. Notably, both fragments for this convergent coupling event are chiral, necessitating asymmetric syntheses of each.

This strategy leverages the developed semipinacol rearrangement[6] strategy disclosed in Chapter 1. Two key features are highlighted through the use of the developed robust strategy: the enthalpic driving force of epoxide-opening to generate the hindered C11 quaternary center, and robust, well-established chemistry of adding vinyl-nucleophiles into ketone electrophiles to generate a crucial C–C bond.

Figure 2.3. Retrosynthetic analysis of C_{19} diterpenoid alkaloids.



2.4 FORWARD SYNTHETIC EFFORTS

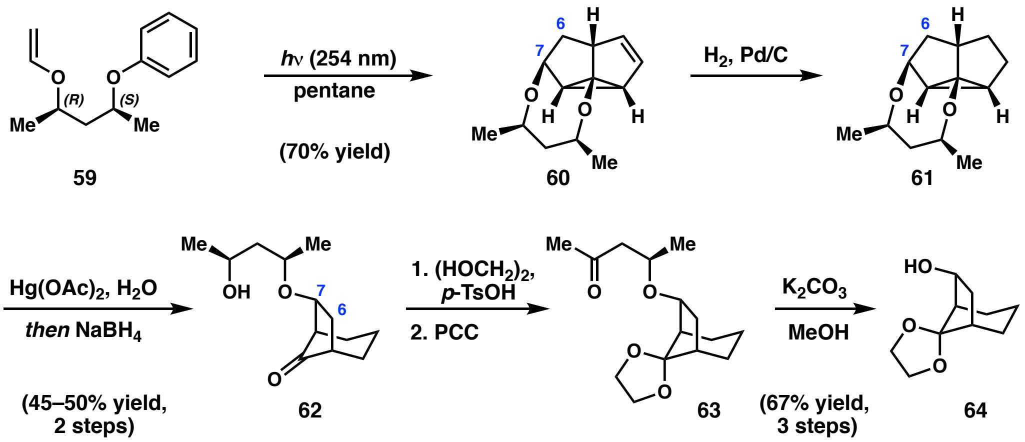
In the following sections, the development of the total synthetic route to the C_{19}-diterpenoid alkaloids (–)-liljestrandisine and (–)-liljestrandinine are disclosed. With our developed enantioselective route to epoxyketone **7** and a broad substrate scope for the 1,2-addition/semipinacol in hand (see Chapter 1), this chapter focuses first on the development of an enantioselective route to a suitably functionalized CD-bicyclo[3.2.1]octane such as **58** for the convergent synthesis. Following this, the development and optimization of the convergent fragment coupling for the C_{19} diterpenoid alkaloids is disclosed. Finally, late-stage studies towards the natural products included. These late-stage studies include failed routes attempting to close the B-ring first and an unsuccessful radical cascade cyclization route to form two rings in one step. The reactivity demonstrated by these failed routes ultimately led to a successful aziridination strategy described in Chapter 3.

2.4.1 ASYMMETRIC SYNTHESIS OF A BICYCLO[3.2.1] OCTANE FRAGMENT

With the establishment of proof of concept for the 1,2-addition and semipinacol rearrangement, especially with sterically demanding bridged bicyclic frameworks (Chapter 2), our next task was to establish an asymmetric synthesis of a suitably functionalized CD-bicyclo[3.2.1]octane fragment for the C19 diterpenoid alkaloids.

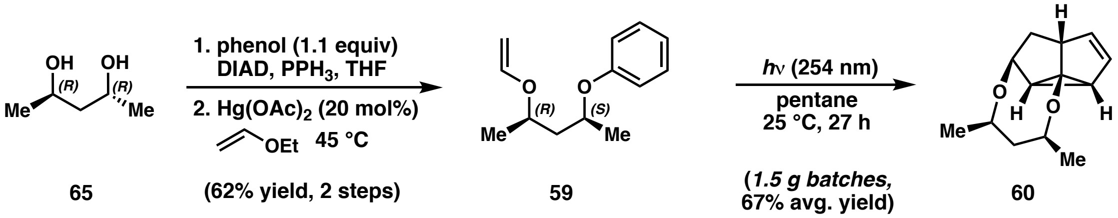
In the development of the enantioselective bicyclo[3.2.1]octane fragment synthesis, it was believed that a *meta*-photocycloaddition strategy[7] would be enabling for the asymmetric synthesis of the desired framework with appropriate oxidation handles. We were inspired by work developed by Sugimura *et al.* wherein a chiral tether was utilized to effect a diastereoselective *meta*-photocycloaddition reaction, thus affording enantiopure *meta*-photocycloaddition products (Figure 2.4).[8,9] Sugimura showed that treatment of **59** under 254 nm light effected a diastereoselective *meta*-photocycloaddition furnishing **60** in 70% yield on small scale. Reduction of the olefin of **60** with H_2 and Pd/C furnished **61**. At this stage, the cyclopropane was cleaved with mercuric acetate, thus revealing bicyclo[3.2.1]octane **62**. The ketone on the one carbon bridge of the bicyclo[3.2.1]octane was protected providing **63**, thus allowing the chiral tether to be liberated by oxidation and subsequent retro-oxy-Michael cleavage under basic conditions, furnishing **64**. We were inspired by Sugimura's route to **64**, and were specifically interested in using the olefin of **60** as a functional handle to install appropriate oxidation on the 3-carbon bridge of the bicyclo[3.2.1]octane fragment. We believed an appropriate functional handle on the 3-carbon bridge would enable B-ring formation at a later stage in the synthesis. It was realized that in using this approach, a variety of different functional handles could be introduced, providing a variety of opportunities to investigate B-ring closure.

Figure 2.4. Sugimura's enantioselective synthesis of **64**.



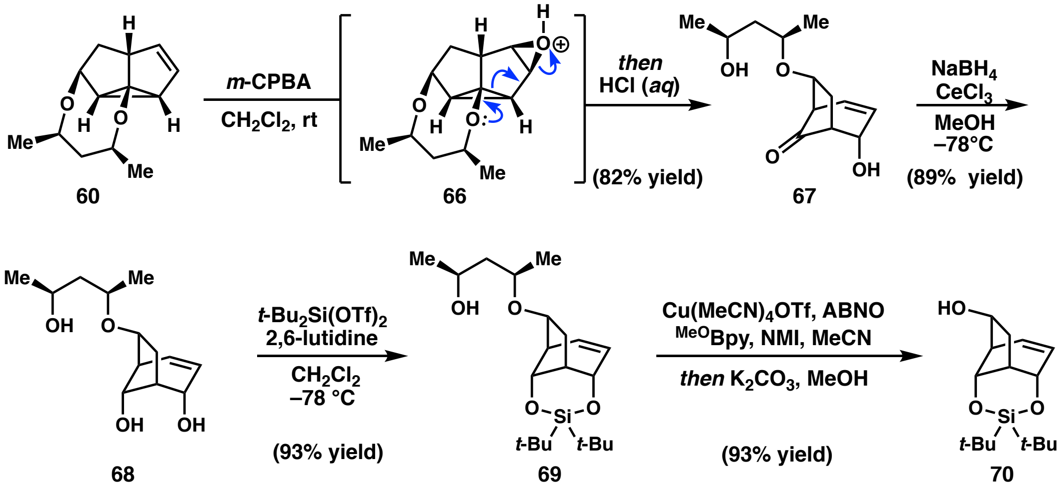
The enantioselective synthesis of the bicyclo[3.2.1]octane fragment began with a diastereoselective *meta*-photocycloaddition of arene **59** following a protocol disclosed in Sugimura *et al.*'s initial report (Figure 2.5).[8] Tetracycle **60** was prepared in three steps, where commercially available (2*R*,4*R*)-(–)-pentane-diol was treated with phenol and DIAD to effect a Mitsunobu reaction, and the remaining alcohol was then vinylated with mercuric acetate and ethyl vinyl ether giving **59** (Figure 2.5). It was found that Sugimura's procedure (reported on small scale) was amenable to scale with an optimization of the reaction setup and operation. It was discovered that we could obtain comparable yields of the **60** on 1.5 g scale after optimizing the photochemistry setup. Furthermore, the reaction profile was clean, allowing us to run the reactions in batches, concentrating the mixtures, and combining the crude residues enabling us to run a single purification providing multigram quantities of **60**, enabling good material throughput.

Figure 2.5. Scalability of the *meta*-photocycloaddition.



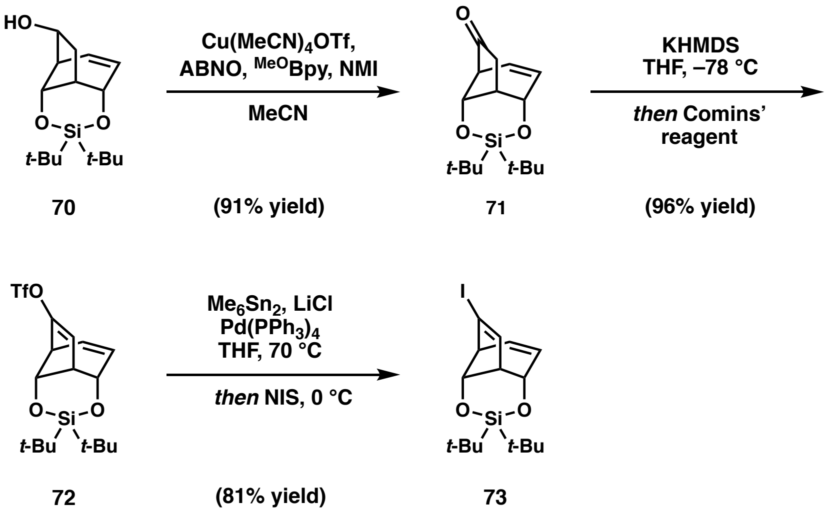
At this stage, subjection of **60** to *meta*-chloroperbenzoic acid effected epoxidation, which upon treatment with aqueous acid facilitated a Grob fragmentation furnishing ketone **67** (Figure 2.6).[10] Diastereoselective 1,2-reduction under Luche conditions afforded triol **68**.[11] The 1,3-diol moiety of **68** was protected as the *tert*-butyl silylene **69**;[12] this protecting group strategy enabled the differentiation of the 1,3-diol moiety, therefore leaving the free alcohol that was then used as a functional handle to cleave the chiral tether. To that end, **69** was subjected to a Stahl oxidation[13] followed by *in situ* treatment with K_2CO_3 and MeOH to facilitate a retro-oxy Michael fragmentation revealing alcohol **70**.

Figure 2.6. Synthesis of **70** from *meta*-photocycloadduct **60**.



Subjection of **70** to a Stahl oxidation furnished ketone **71** (Figure 2.7). To functionalize **70** as the vinyl anion equivalent for the key fragment-coupling event, ketone **70** was converted to vinyl triflate **72**, which was subsequently converted to the corresponding vinyl iodide via a Stille cross-coupling/iodination sequence to afford vinyl iodide **73**.

Figure 2.7. Synthesis of vinyl iodide **73**.



2.4.2 FRAGMENT COUPLING

With both chiral fragments **7** and **73** in hand, conditions to effect the key 1,2-addition/semipinacol rearrangement toward the C_{19} diterpenoid alkaloid framework were evaluated. Lithiation of vinyl iodide **73** with *tert*-butyl lithium followed by addition into **7** afforded epoxy-alcohol **75** (Figure 2.8). Extensive optimization for the fragment coupling was performed, select examples of which are described in Table 2.1. It was crucial at this stage to optimize this reaction, given that the yield of this reaction and material provided would be enabling to the rest of the synthesis. Furthermore, by metalating vinyl iodide

73, if the generated organometallic reagent does not add to the ketone to give the desired product, the reactive species is quenched and cannot be recovered.

Initially, a variety of different additives such as $CeCl_3$, $2LiCl \bullet LaCl_3$, and $MgBr_2$ were evaluated, but these additives did not improve the yield, creating unwanted byproducts instead. The reaction setup was then evaluated, and it was discovered that an inverse addition wherein **7** was added to the generated organometallic reagent was deleterious to reaction yield, creating significant quantities of the addition of the vinyl lithium species to one of the methyl esters (Table 2.1, entry 1). A regular addition protocol was then evaluated, and it was discovered that the vinyl lithium could be successfully added via cannula to a pre-cooled solution of the epoxyketone without decomposing the reactive organometallic species (entry 2). Over the course of these studies, it was also discovered that this 1,2 addition reaction is extremely sensitive to trace water. Specifically, very dry THF was required for the success of this reaction (determined via Karl Fischer titration). For example, the difference between 40 ppm and 7 ppm H_2O in THF (entries 2 and 4) showed a 25% difference in product yield (when calculated, the difference between 40 ppm and 7 ppm is 3 mol % H_2O, but causes a 25% difference in yield). With all of these parameters in mind, the reaction was performed while incrementally increasing scale, showing the scalability of this fragment-coupling event (entries 3–5). Furthermore, the structure of **75** was confirmed via single crystal X-ray diffraction.

Figure 2.8. Fragment coupling to provide epoxy alcohol **75**.

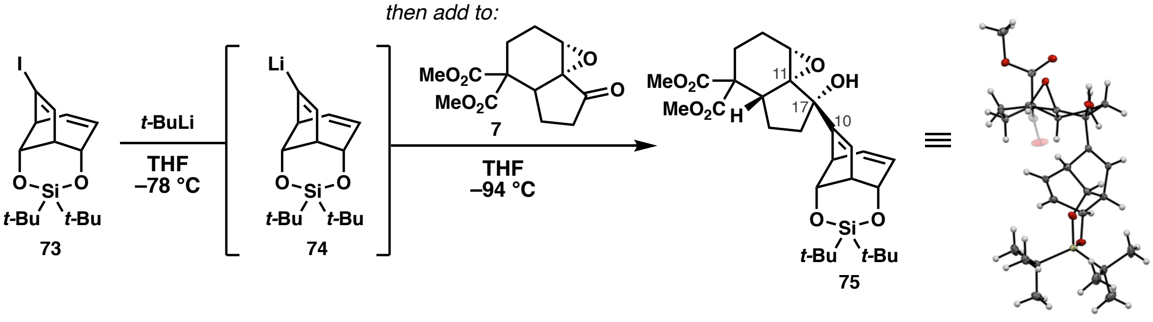


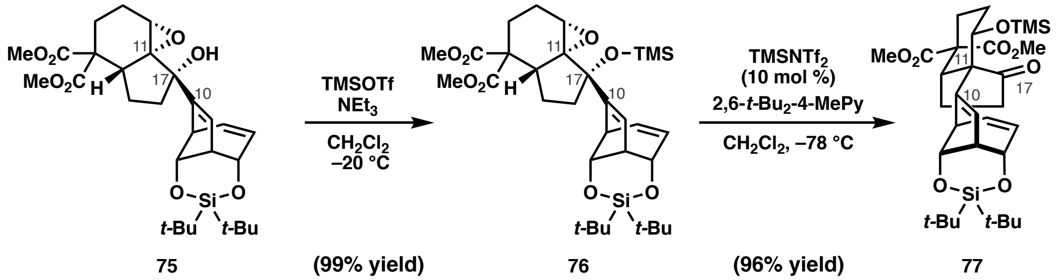
Table 2.1. Screen of reaction parameters for 1,2-addition fragment coupling.

Entry	ppm H_2O in THF*	Scale	Type of Addition**	Result
1	7 pppm	300 mg	inverse	20% yield
2	40 ppm	1 gram	regular	50 % yield
3	7 ppm	300 mg	regular	70% yield
4	7 ppm	1 gram	regular	75% yield
5	7 ppm	3 grams	regular	71% yield

*Determined by Karl Fischer titration.
Inverse: **7 added to **74** via cannula, Regular: **74** added to **7** via cannula

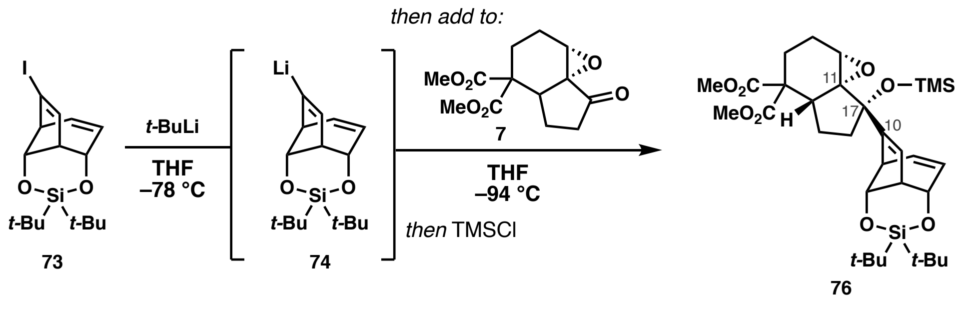
Direct conversion of epoxy-alcohol **75** to rearrangement product **77** could be effected in a single step in 33% yield using a superstoichiometric quantity of TMSOTf at room temperature (Figure 2.9). The low yields observed resulted from decomposition of the bicyclo[3.2.1]octane moiety. After extensive optimization, it was discovered that the rearrangement could proceed in high yield over two steps. First, the tertiary alcohol of **75** was protected as the TMS ether and isolated, furnishing **76**. Subsequent treatment with $TMSNTf_2$ (10 mol %) at low temperatures effected a 98% yield of the desired semipinacol rearrangement product **77**, which notably features the hindered C11 quaternary center and all carbon atoms necessary to complete the carbocyclic core of the aconitine alkaloids.

Figure 2.9. Optimized semipinacol rearrangement to provide **77**.



With the optimized semipinacol rearrangement strategy realized, wherein the tertiary alcohol is protected first and then subjected to a catalytic amount of $TMSNTf_2$, the 1,2-addition procedure was revisited (Figure 2.10). It was discovered that rather than quenching the 1,2-addition reaction with water, *in situ* treatment with TMSCl after the addition was complete provided **76** directly.

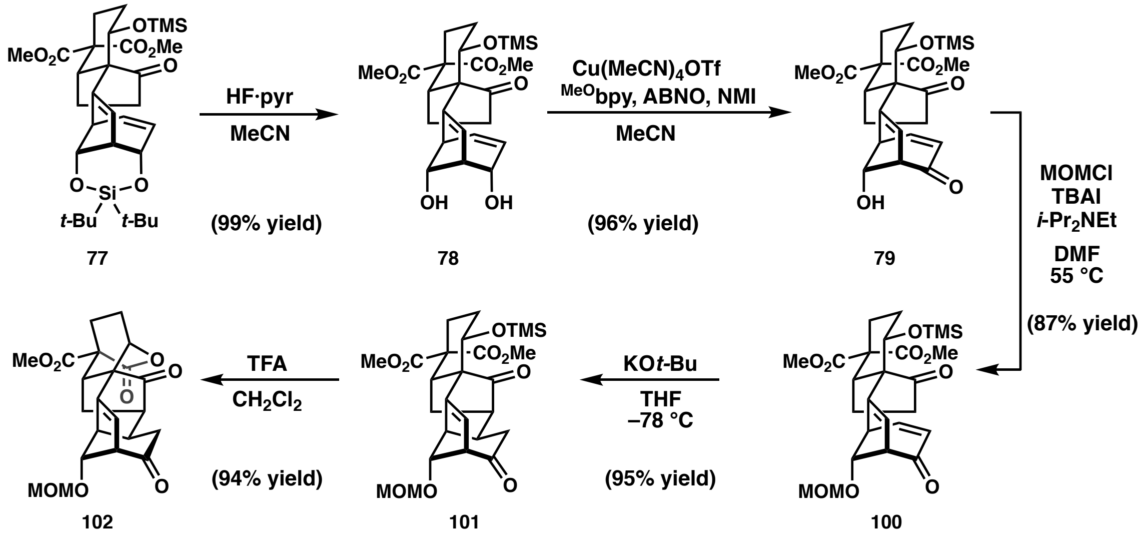
Figure 2.10. Optimized fragment coupling followed by TMS trapping to provide **76**.



2.4.3 ADVANCEMENT TO THE CARBOCYCLIC CORE

To elaborate to the carbocyclic framework of talatisamine, the silylene of tetracycle **77** was selectively deprotected with HF•pyridine, which remarkably preserves the secondary TMS ether (Figure 2.11). Subsequent allylic alcohol oxidation in the presence of the other secondary alcohol under Stahl's conditions[13] gave enone **79**, whose remaining free alcohol was re-protected as the methoxy methyl ether providing **100**. Treatment of **100** with potassium *tert*-butoxide at –78 °C induced an intramolecular Michael addition to provide pentacycle **101** – a compound containing the complete carbon framework of **1** – in 95% yield. **101** was then subjected to TFA which facilitated TMS deprotection and intramolecular lactone formation to afford **102** – this intramolecular cyclization differentiates the two methyl esters.

Figure 2.11. Intramolecular Michael addition route to form the carbocyclic core.

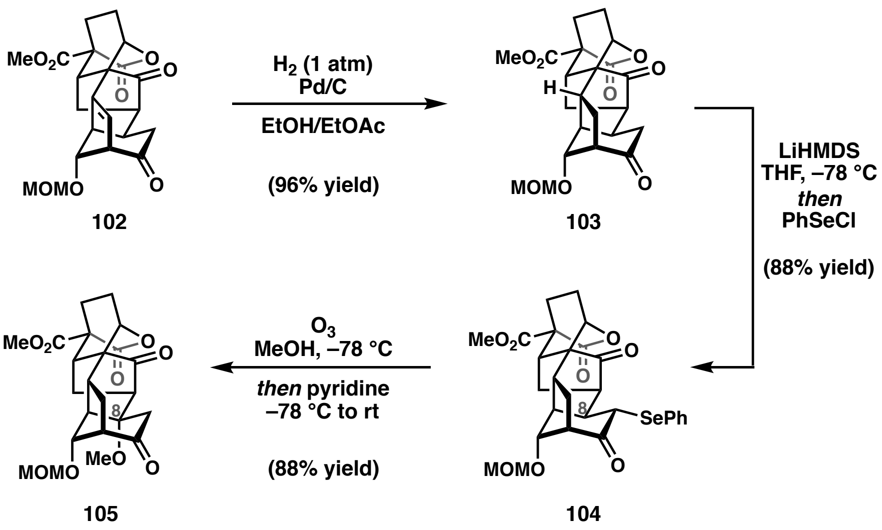


2.4.4 INTRODUCTION OF THE TERTIARY HYDROXYL AT C8

With hexacycle **102** in hand, the next task was to install the tertiary alcohol at C8, necessary for the oxidation pattern of the C_{19} diterpenoid alkaloids (Figure 2.12). A facile hydrogenolysis of the now strained trisubstituted olefin of **102** with Pd/C under an atmosphere of H_2 provided furnished **103**. Notably, once the B-ring has been cyclized, such as on **102**, the trisubstituted olefin is sufficiently strained such that reduction of the olefin is facile.

At this stage, the ketone of **103** could be employed as a functional handle for the installation of the final tertiary hydroxyl group at C8.[14] Treatment of **103** with LiHMDS and PhSeCl furnished α-selenide **104**. Ozonolysis effected oxidation and elimination to the corresponding strained enone, which underwent a spontaneous oxy-Michael addition upon quenching with methanol to furnish β-methoxyketone **105**. While pleased to establish the reactivity necessary to complete the oxidation at C8 necessary for the natural product, we returned to the challenge of forming the final piperidine E-ring. The majority of these studies were performed on material lacking the C8 oxidation.

Figure 2.12. Advancement of lactone to tertiary methyl ether **105**.

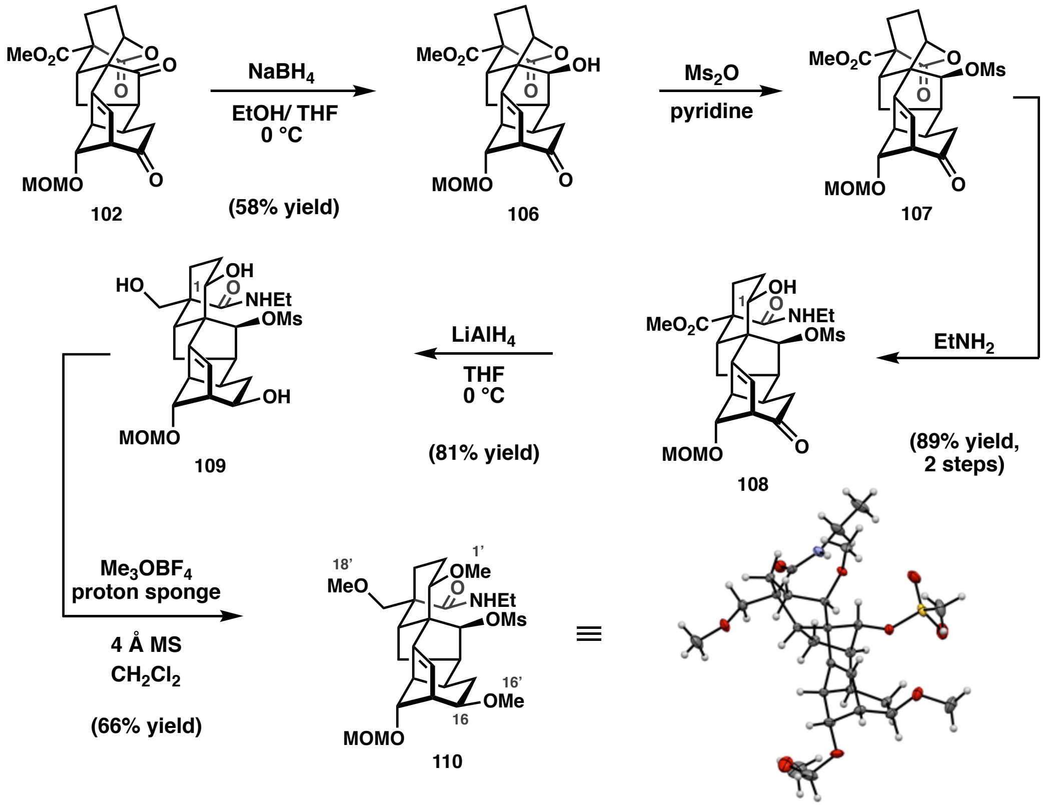


2.4.5 E-RING PIPERIDINE FORMATION: MESYLATE DISPLACEMENT STRATEGY

At this stage, completion of the synthesis requires formation of the piperidine ring and adjustment of the oxidation states. Toward that end, initial investigations sought to utilize an amide to displace a mesylate and close the final piperidine ring. Ketone **102** was selectively reduced with $NaBH_4$ to give alcohol **106** (Figure 2.13). Alcohol **106** was converted to secondary mesylate **107**. Subsequent lactone-opening aminolysis affords secondary amide **108**, a substrate that bears the correct *N*-ethyl group for the natural product. Subjection of **108** to basic conditions at elevated temperatures in an effort to achieve lactam formation via mesylate displacement was unsuccessful – substrates with a free hydroxyl at C1 favored reformation of the lactone, and substrates bearing the methyl ester also afforded decarboxylation as an additional undesired side product. Thus, the material was pushed forward in an effort to mitigate these deleterious side reactions in an effort to synthesize a substrate capable of achieving the desired reactivity.

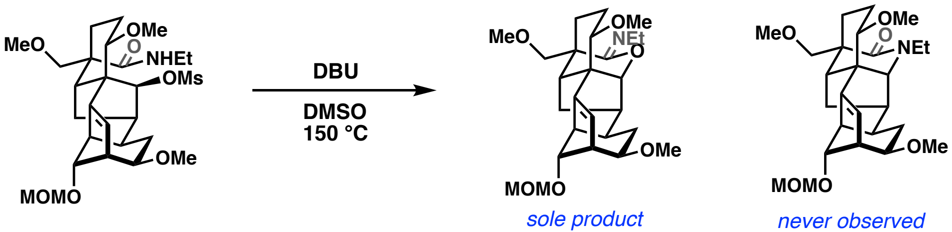
Toward that end, reduction of the methyl ester and ketone of **108** afforded triol **109**. All three alcohols of triol **109** were methylated in one step using trimethyloxonium tetrafluoroborate salt in the presence of Proton Sponge to furnishing **110**, a substrate with the correct C1', C18' and C16' methyl ethers necessary for the natural product. The structure of **110** was confirmed through single crystal X-ray diffraction analysis. While the C16 stereochemistry at this stage was incorrect for the initial target **1**, our initial goal was to establish reactivity and thus synthetic studies were continued on this diastereomer.

Figure 2.13. Advancement of lactone to permethyl ether **110**.



Mesylate **110** was quite unreactive; harsh conditions were required to observe any reactivity. Under forcing conditions, namely subjection of **110** to DBU in DMSO at 150 °C, an intramolecular displacement of the mesylate occurred, providing hexacyclic imidate **111** (Figure 2.14). Formation of desired lactam **112** was never observed. While initially pleased that we could indeed cyclize at the desired position, the desired selectivity for C–N bond formation rather than C–O bond formation could never be realized despite evaluating a variety of different conditions, including unique solvents such as HFIP.

Figure 2.14. Formation of cyclic imidate **111**.

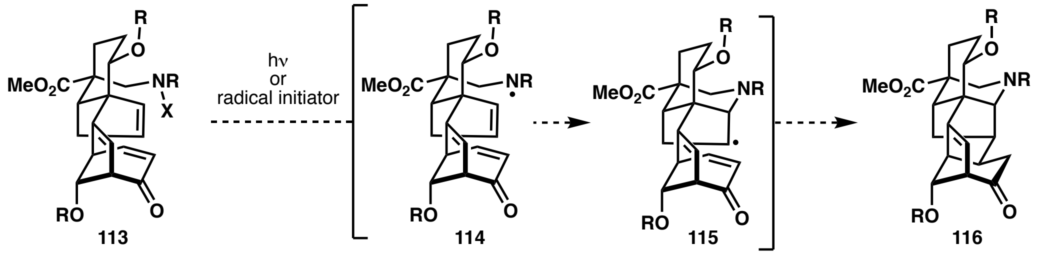


110 **111** **112**

2.4.6 RADICAL CASCADE CYCLIZATION STRATEGY

At this stage, we reevaluated our synthetic plan. A radical cascade cyclization of amine **113** was envisioned (Figure 2.15). It was proposed that treatment of *N*-halo amine **113** with UV light or a radical initiator could generate *N*-centered radical **114**.[15] This aminyl radical could then undergo a 6-*exo*-trig cyclization to generate radical **115**. A second 6-*exo*-trig cyclization could give the stabilized α-keto radical, which upon hydrogen atom abstraction could deliver **116**. Preliminary work suggested that both ring-closing events are geometrically feasible. In particular, the intramolecular base-mediated Michael addition of **100** to give **101** proceeds in 95% yield, indicating that C–C bond formation onto an enone is favorable (Figure 2.11). Additionally, conversion of amide **110** to imidate **111** demonstrates that the formation of a 6 membered ring is possible. It was believed that thorough investigation of this strategy would be worthwhile, because a C–N and C–C bond would be generated in the same step, potentially allowing for a minimization of late-stage redox manipulations in order to access the natural product.

Figure 2.15. Proposed radical cascade cyclization strategy.

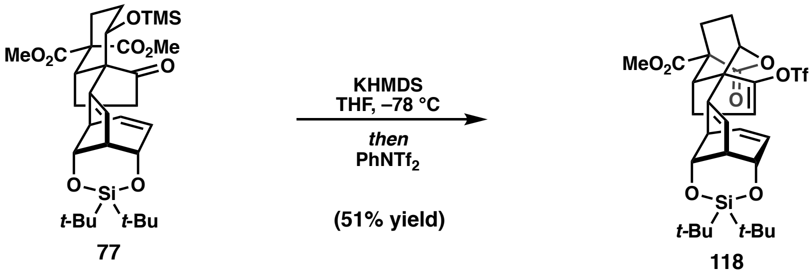


At this time, an initial route towards the radical cyclization precursor was developed (Figure 2.16). Initially, it was proposed that the ketone of **77** could be directly converted to the corresponding cyclopentene via enol triflate formation. Surprisingly, treatment of **77** with KHMDS and trapping of the potassium enolate with Comins' reagent afforded lactone **118**. Presumably, KHMDS facilitates TMS deprotection, intramolecular lactone formation, and generation of the potassium enolate. While this 1-step reaction was serendipitous, consistent yields above 70% could never be achieved, and thus a multistep sequence was developed.

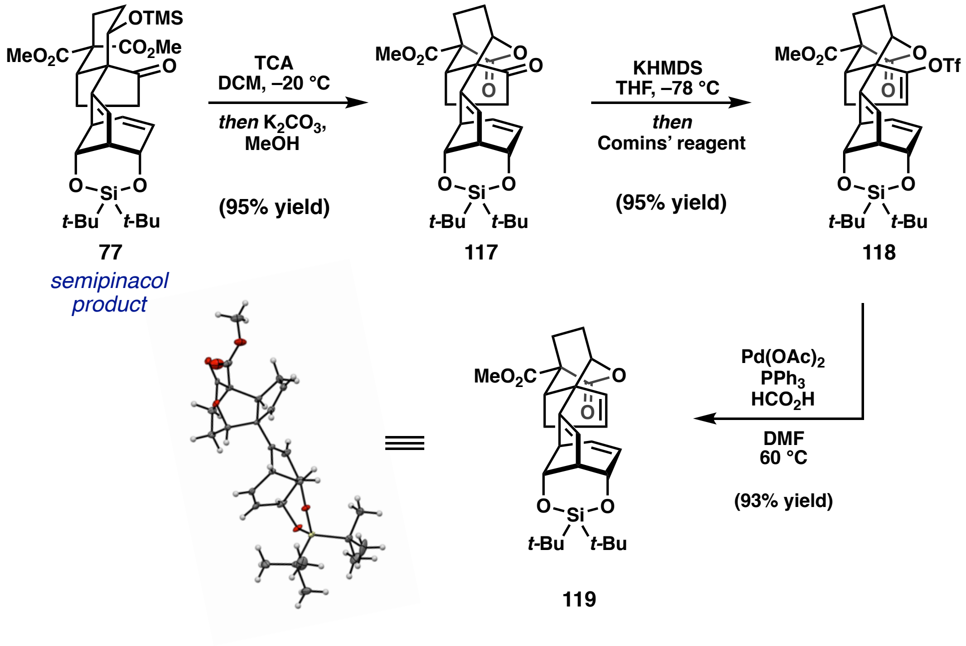
Toward that end, subjection of **77** to trichloroacetic acid facilitated selective cleavage of the TMS ether, followed by treatment with K_2CO_3 to effect an intramolecular lactone formation furnishing **117** (Figure 2.16). This intramolecular lactone formation differentiates the two methyl esters. At this stage, the ketone was then converted to the corresponding vinyl triflate with KHMDS and Comins' reagent providing **118**. Enol triflate **118** was reduced via palladium catalysis to form cyclopentene **119**. The structure of **119** was confirmed via single crystal X-ray diffraction analysis.

Figure 2.16. Synthesis of cyclopentene **119**.

a) Enol triflate formation on **77** directly leads to lactone **118**.

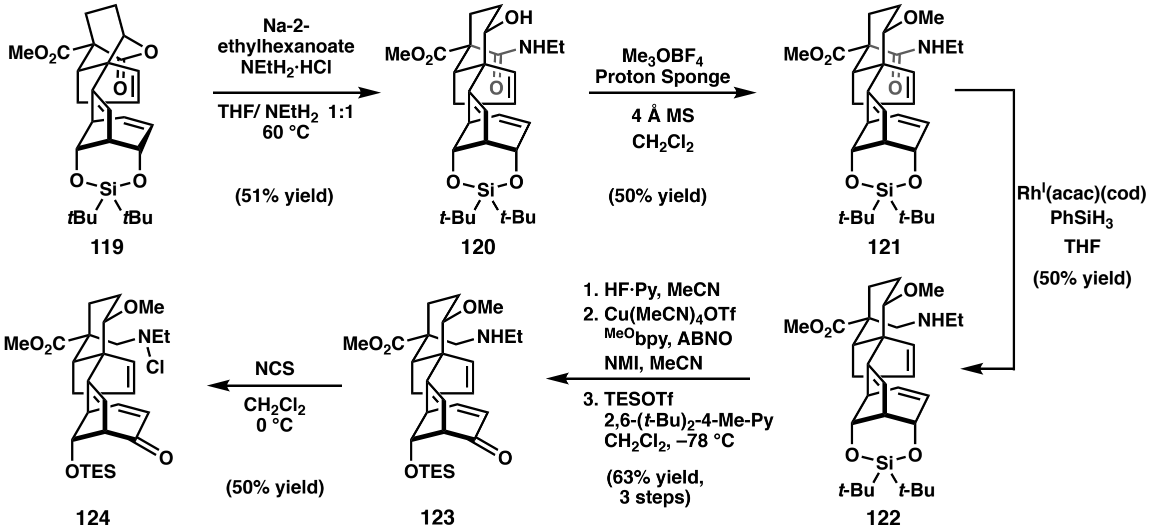


b) Development of a scalable high-yielding multistep protocol:



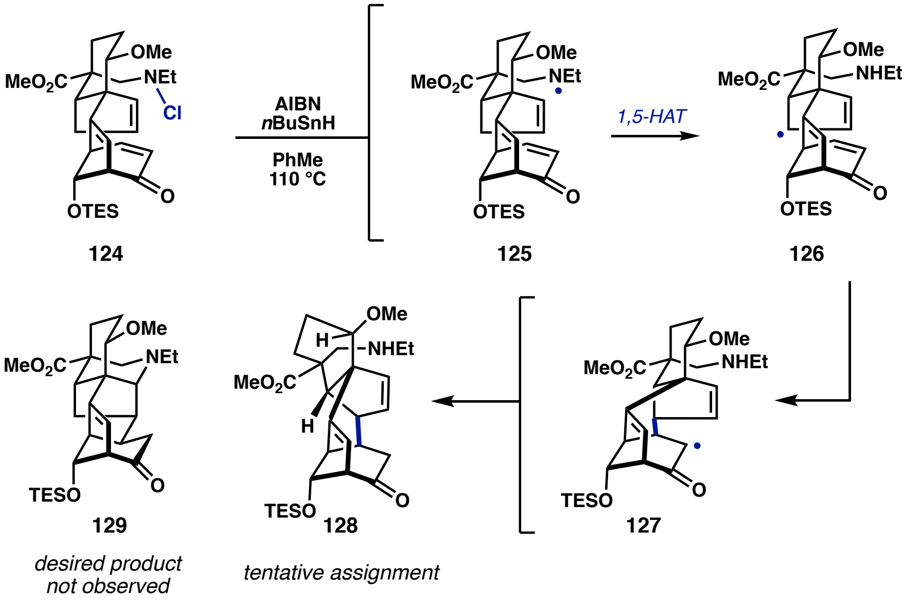
Subsequent lactone-opening aminolysis[16] of **119** furnished ethyl amide **120** (Figure 2.17). The secondary alcohol revealed through the lactone-opening aminolysis was then methylated, providing methyl ether **121**. The secondary amide was reduced via rhodium catalysis,[17] providing ethyl amine **122**. At this stage, our goal was to access a substrate for our proposed radical cascade cyclization event. Thus, we elected to transform the bicyclo[3.2.1]octane moiety into an enone, which could serve as a radical trap. The bicyclo[3.2.1]octane of **122** was transformed to the corresponding enone in three steps via HF•pyridine cleavage of the silylene group, selective Stahl oxidation[13] of the resultant allylic alcohol, and then TES protection of the remaining secondary alcohol, providing enone **123**. To advance to a neutral aminyl radical precursor, the secondary amine was chlorinated with NCS furnishing **124**.

Figure 2.17. Synthesis of *N*-Chloroamine **124**.



Subjection of **124** to AIBN and *n*Bu$_3$Sn–H at elevated temperatures afforded cyclized product **128** (Figure 3.18). Presumably this reaction proceeds via generation of the *N*-centered radical **125** followed by a 1,5-hydrogen atom abstraction to afford allylic radical **126**, which then undergoes cyclization onto the enone to furnish **128**. While undesired, this result establishes the feasibility of a radical cyclization onto an enone to forge the central B ring, and highlights the need for a strategy that is selective for the formation of C–N bonds with the alkene.

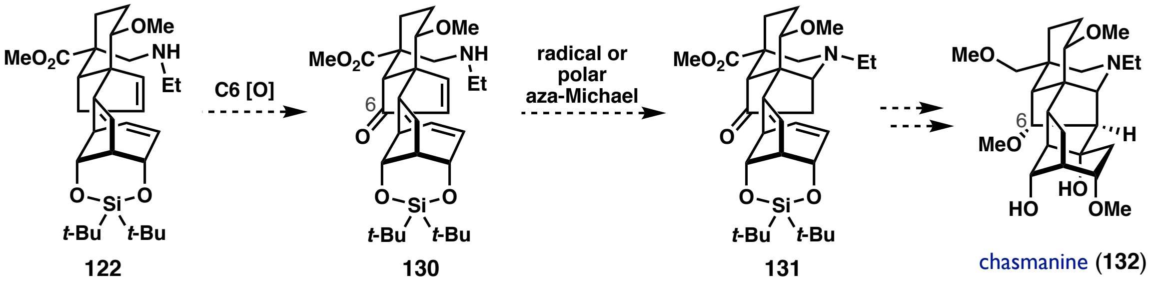
Figure 3.18. Unsuccessful cyclization via a neutral aminyl radical.



2.4.7 INTRODUCTION OF OXIDATION AT C6

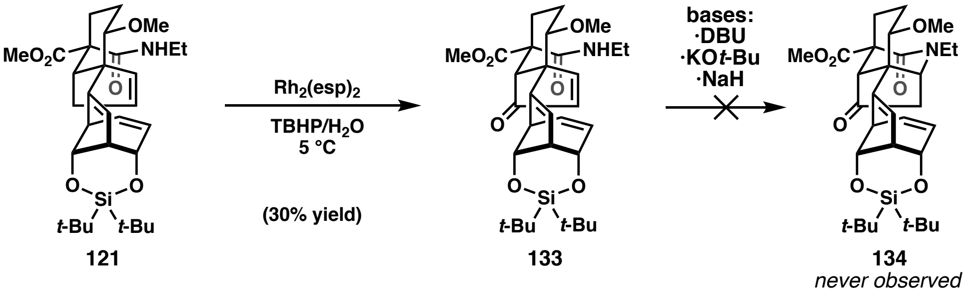
At this stage, our primary focus revolved around forging the C17–N bond and forming the final E ring piperidine. Toward that end, an oxidation strategy was proposed to achieve this goal (Figure 2.19). The methylene at C6 was hypothesized to be problematic, and it was proposed that blocking this position would enable formation of the desired C17–N bond. Introduction of a carbonyl at C6 through allylic oxidation to provide a substrate such as **130** would fulfill a number of goals: 1) C6 would be blocked such that undesirable reactivity at this position could be avoided, 2) an enone would provide bias and favor more desirable electronics for C17–N bond formation and 3) introduction of oxidation at C6 would enable the synthesis of more highly oxidized natural products such as chasmanine (**132**). This oxidation strategy would allow for an aza-Michael reaction either through a radical or polar mechanism.

Figure 2.19. Proposed allylic oxidation strategy towards chasmanine (**132**).



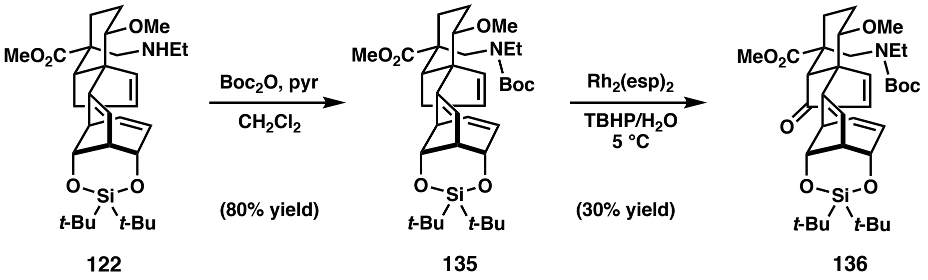
Toward that end, it was discovered that subjection of cyclopentene **121** to $Rh_2(esp)_2$ in *tert*-butyl hydroperoxide provided enone **133** (Figure 2.20).[18] With enone **133** in hand, a variety of different bases were evaluated, but the desired aza-Michael product **134** was never observed.

Figure 2.20. Allylic oxidation of amide **121** providing **134**.



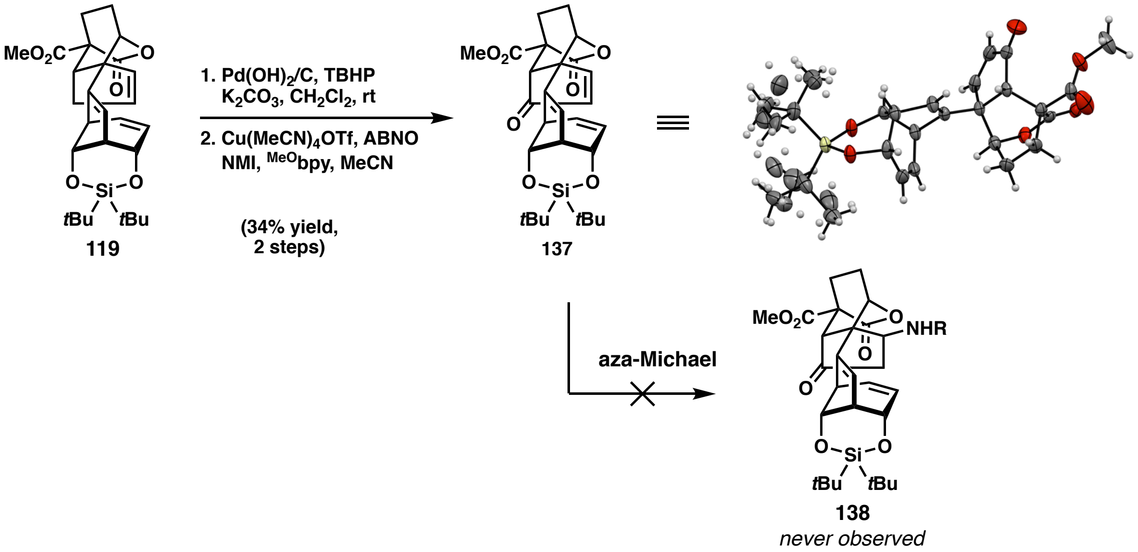
At this stage, we turned our attention to amine substrate **122**, hoping that the amine, rather than an amide would provide the desired product (Figure 2.21). Protection of *N*-ethyl amine **122** with Boc_2O provided carbamate **135**. Subjection of **135** to the developed $Rh_2(esp)_2$ in *tert*-butyl hydroperoxide conditions provided enone **136**. Unfortunately, conditions to cleanly deprotect the *tert*-butyl carbamate group of **136** and affect an intramolecular aza-Michael cyclization could never be realized.

Figure 2.21. Allylic oxidation sequence providing **136**.



Subjection of lactone **119** to $Pd(OH)_2$ and *tert*-butyl hydroperoxide afforded the corresponding allylic alcohol,[19] which could then be advanced to enone **137** under Stahl oxidation conditions (Figure 2.22). With enone **137** in hand, a variety of different conditions were examined to effect an intermolecular aza-Michael reaction, however C–N bond formation through this approach was never realized.

Figure 2.22. Allylic oxidation of lactone provided **137**.



2.5 CONCLUDING REMARKS

To conclude, numerous routes were evaluated in order to advance to the C19 diterpenoid alkaloid core. A few key lessons were learned, which ultimately guided future efforts and resulted in the completion of two natural products (presented in Chapter 3). An intramolecular Michael addition strategy to close the B-ring was established, as well as oxidation chemistry in order to establish the correct C8 tertiary hydroxyl group necessary for the natural product. Taken together, these studies established the feasibility of our approach to the carbocyclic framework of the C19 diterpenoid alkaloids and installation of the appropriate oxidation at C8.

The mesylate displacement route unfortunately gave selectivity for C–O bond rather than C–N bond formation, and thus the alternative radical cascade cyclization route was interrogated. While the radical cascade cyclization route was ultimately unsuccessful, valuable insight was gained from these studies. The feasibility of a radical to cyclize and form a new C–C bond using the enone as a functional handle was established. Furthermore, the studies discussed above highlighted the need for a mode of reactivity that is selective for C–N bond formation between an alkene and an amine. These studies led us to the next route presented (Chapter 3), culminating in the total syntheses of the C_{19} diterpenoid alkaloids (–)-liljestrandisine and (–)-liljestrandinine.

2.6 EXPERIMENTAL SECTION

2.6.1 *Materials and Methods*

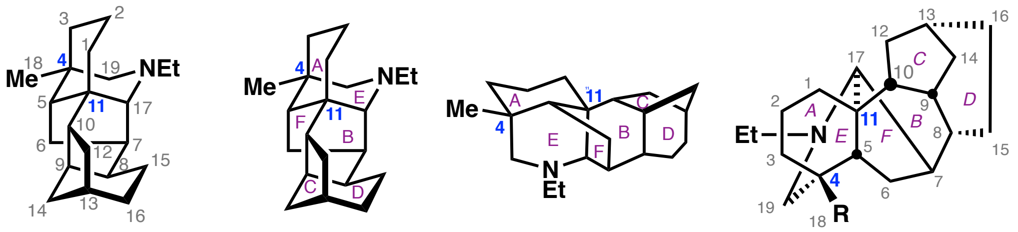
Unless otherwise stated, reactions were performed under an inert atmosphere (dry N_2 or Ar) with freshly dried solvents utilizing standard Schlenk techniques. Glassware was oven-dried at 120 °C for a minimum of four hours, or flame-dried utilizing a Bunsen burner under high vacuum. Tetrahydrofuran (THF), methylene chloride (CH_2Cl_2), acetonitrile (MeCN), *tert*-butyl methyl ether (TBME), benzene (PhH), and toluene (PhMe) were dried by passing through activated alumina columns. Triethylamine (Et_3N) and *N*,*N*-diisopropylethylamine (DIPEA) were distilled over calcium hydride prior to use. Unless otherwise stated, chemicals and reagents were used as received. 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, $KMnO_4$, or CAM staining. Flash column chromatography was performed using silica gel (SiliaFlash® P60, particle size 40-63 microns [230 to 400 mesh]) purchased from Silicycle. Optical rotations were measured on a Jasco P-2000 polarimeter using a 100 mm path-length cell at 589 nm. ^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, $\delta = 77.0$). 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, app = apparent. 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).

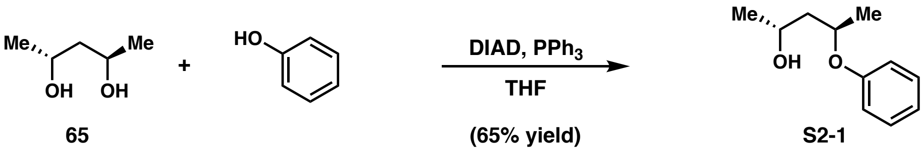
2.6.2 *Preparative Procedures and Spectroscopic Data*

The following ring labeling and atom numbering are used throughout this section:

Ring labelling and atom numbering



Preparation of aryl ether S2-1:



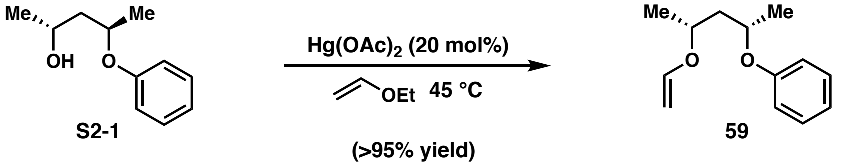
In a flame dried 1-L, round-bottomed flask equipped with an addition funnel, (2*R*, 4*R*)-pentanediol (**65**, 10.42 g, 100 mmol, 1.0 equiv), phenol (10.35 g, 110 mmol, 1.1 equiv), and PPh_3 (31.47 g, 120 mmol, 1.2 equiv) were dissolved in THF (450 mL) and the mixture was cooled to 0 °C. A solution of DIAD (23.6 mL, 120 mmol, 1.2 equiv) in THF (100 mL) was prepared in another flask, and transferred to the addition funnel. The

DIAD solution was added dropwise to the vigorously stirring reaction over 40 min at 0 °C. After complete addition of the DIAD solution, the reaction was allowed to warm to room temperature and stirred for 11 h before being partially concentrated *in vacuo* to a volume of ~200 mL. The mixture was filtered over celite to remove (O)PPh3, and then further concentrated *in vacuo.* Purification of the crude residue by silica gel chromatography (10 to 45% EtOAc in hexanes) afforded arene **S2-1** (11.7 g, 64.9 mmol, 65% yield). Spectroscopic data matched that reported by Sugimura *et al.*[8]

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 – 7.26 (m, 2H), 6.99 – 6.91 (m, 3H), 4.61 (dqd, *J* = 8.6, 6.0, 4.4 Hz, 1H), 4.06 (dqt, *J* = 8.9, 6.1, 2.7 Hz, 1H), 2.56 (s, 1H), 1.95 (dt, *J* = 14.4, 8.8 Hz, 1H), 1.70 (ddd, *J* = 14.4, 4.5, 3.1 Hz, 1H), 1.31 (d, J = 6.0 Hz, 3H), 1.23 (d, J = 6.2 Hz, 3H).

TLC (2:1 Hexanes:EtOAc), R_f: 0.4 (UV, purple in *p*-anisaldehyde)

Preparation of arene olefin 59:

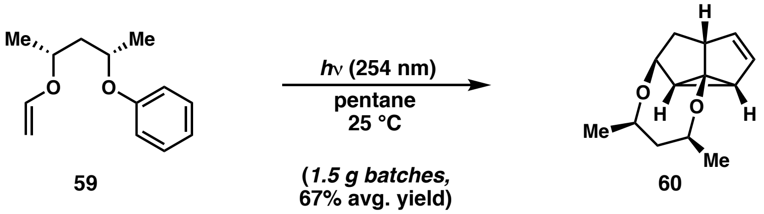


In a 250-mL, round-bottomed flask equipped with a reflux condenser, arene **S2-1** (3.90 g, 21.6 mmol, 1.0 equiv) was dissolved in ethyl vinyl ether (108 mL), and $Hg(OAc)_2$ (689 mg, 2.16 mmol, 0.10 equiv) was added. The mixture was heated to reflux and stirred for 18 h, at which point, the reaction was cooled to room temperature, and another portion of $Hg(OAc)_2$ (689 mg, 2.16 mmol, 0.10 equiv) was added, and the reaction was brought back to reflux. After stirring for another 15 h at reflux, the reaction was quenched by addition of sat. $NaHCO_3$ (100 mL). The layers were separated, and the aqueous phase was extracted with Et_2O (3 x 200 mL). The combined organic extracts were washed with brine (200 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was purified by filtering over a short plug of silica (eluting with 10% EtOAc/1% Et_3N in hexanes) to provide arene olefin **59** (4.5 g, 21.8 mmol, 100% yield) as a colorless oil. Spectroscopic data matched that reported by Sugimura *et al.*[8]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 – 7.24 (m, 2H), 6.97 – 6.86 (m, 3H), 6.34 (dd, J = 14.2, 6.6 Hz, 1H), 4.52 (h, J = 6.2 Hz, 1H), 4.33 (dd, J = 14.2, 1.6 Hz, 1H), 4.12 (h, J = 6.3 Hz, 1H), 4.03 (dd, J = 6.7, 1.6 Hz, 1H), 2.20 (dt, J = 13.9, 6.9 Hz, 1H), 1.65 (dt, J = 14.0, 6.0 Hz, 1H), 1.33 (d, J = 6.1 Hz, 3H), 1.25 (d, J = 6.2 Hz, 3H).

TLC (2:1 Hexanes:EtOAc), R_f: 0.7 (UV, purple in *p*-anisaldehyde)

Preparation of 7-substituted *meta*-photoadduct 60:

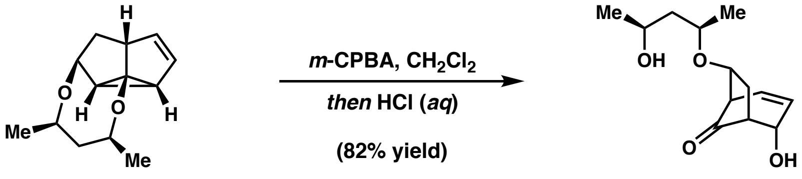


In a 1-L, round-bottomed quartz flask, arene olefin **59** (1.5 g, 7.3 mmol, 1.0 equiv) was dissolved in pentane (700 mL). This solution was sparged with Ar for 75 min, then irradiated with stirring using a Honeywell 254 nm lamp for 27 h. The temperature was deliberately maintained at 25 °C using ventilation fans. Upon completion, the reaction was concentrated *in vacuo* to afford a crude residue. *This procedure was repeated for a total of 5 batches*. All 5 crude batches were combined and purified by silica gel chromatography (9% EtOAc in hexanes) to afford 7-substituted photoadduct **60** (5.0 g, 24.2 mmol, 67% average yield over 5 batches) as a white solid. Spectroscopic data matched that reported by Sugimura *et al.*[8]

^{1}H NMR (400 MHz, Chloroform-*d*): δ 5.66 – 5.58 (m, 1H), 5.43 (dd, *J* = 5.6, 1.8 Hz, 1H), 4.48 (dd, *J* = 6.9, 2.5 Hz, 1H), 4.31 (p, *J* = 6.5 Hz, 1H), 4.05 (p, *J* = 6.6 Hz, 1H), 3.25 (dd, *J* = 8.3, 2.6 Hz, 1H), 2.50 – 2.42 (m, 3H), 2.34 (dt, *J* = 17.4, 7.4 Hz, 1H), 2.09 (ddd, *J* = 14.6, 6.9, 1.1 Hz, 1H), 1.59 (d, *J* = 17.4 Hz, 1H), 1.23 (s, 3H), 1.21 (s, 3H).

TLC (3:1 Hexanes:EtOAc), R*f*: 0.5 (UV, purple in *p*-anisaldehyde)

Preparation of allylic alcohol 67:



60

67

A 2-L, round-bottomed flask was charged with photoadduct **60** (11.84 g, 57.4 mmol, 1.0 equiv) and CH_2Cl_2 (575 mL), and cooled to 0 °C. *m*-CPBA (77% by wt., 14.79 g, 66.0 mmol, 1.15 equiv) was added, and the reaction was stirred for 30 min at 0 °C, then warmed to room temperature. After stirring for an additional 5 h at room temperature, 2 N HCl (115 mL, 230 mmol, 4.0 equiv) was added, and the biphasic mixture was stirred vigorously. After 40 min, the reaction was quenched by careful addition of sat. $NaHCO_3$ (330 mL), and stirred until bubbling ceased (ca. 30 min). The layers were separated, and the aqueous phase was extracted with 3:1 $CHCl_3$:*i*-PrOH (3 x 600 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo.* Purification by silica gel chromatography (40 to 45% acetone in hexanes) afforded allylic alcohol **67** (11.34 g, 47.2 mmol, 82% yield) as a colorless oil.

^{1}H NMR (400 MHz, CDCl$_3$): δ 5.97 (dd, *J* = 9.0, 7.2 Hz, 1H), 5.77 (ddd, *J* = 9.0, 3.8, 1.2 Hz, 1H), 4.58 (s, 1H), 4.02 (dd, *J* = 6.1, 2.2 Hz, 1H), 3.90 (dqd, *J* = 9.2, 6.2, 3.0 Hz, 1H), 3.70 (dqd, *J* = 8.8, 6.0, 4.3 Hz, 1H), 2.79 (dd, *J* = 7.2, 1.5 Hz, 1H), 2.67 – 2.53 (m, 2H), 2.29 (br s, 1H), 2.18 – 2.05 (m, 2H), 1.61 (dt, *J* = 14.4, 8.9 Hz, 1H), 1.48 (ddd, *J* = 14.5, 4.4, 3.1 Hz, 1H), 1.16 (d, *J* = 3.8 Hz, 3H), 1.14 (d, *J* = 4.1 Hz, 3H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 213.9, 131.4, 129.6, 81.1, 75.2, 73.9, 67.0, 51.6, 49.5, 45.9, 32.2, 23.6, 20.0.

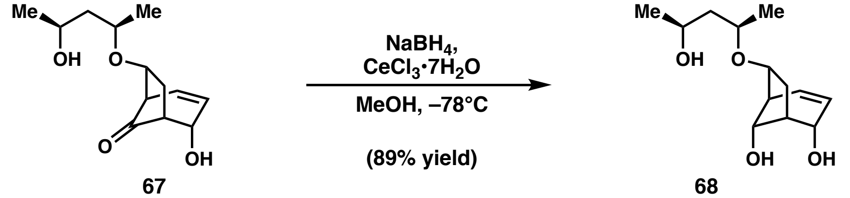
FTIR (NaCl, thin film): 3400, 2969, 2933, 1753, 1458, 1447, 1376, 1329, 1120, 1080, 1048, 926 cm^{-1}.

HRMS: (FAB) calc'd for $C_{13}H_{21}O_4$ $[M + H]^+$ 241.1440, found 241.1421.

$[\alpha]_D^{25}$ = –6.2° (*c* = 1.0, CHCl$_3$).

TLC (1:1 Hexanes:acetone), R*f*: 0.3 (KMnO$_4$)

Preparation of triol 68:



In a 1-L, round-bottomed flask, ketone **67** (6.7 g, 28 mmol, 1.0 equiv) and CeCl$_3$•7H$_2$O (15.6 g, 41.8 mmol, 1.5 equiv) were dissolved in MeOH (280 mL). The solution was then cooled to –78 °C, and NaBH$_4$ (1.27 g, 33.5 mmol, 1.2 equiv) was added. After stirring for 2 h at –78 °C, the reaction was quenched with 1 M NaOH (200 mL), and concentrated *in vacuo* to remove MeOH. The aqueous phase was extracted with EtOAc (8 x 250 mL), and the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Filtration of the crude residue over a short plug of silica (eluting with 50% acetone in hexanes) afforded triol **68** (6.1 g, 25 mmol, 89% yield) as a white solid.

Note: The product is highly water soluble, and thus requires rigorous extraction with a polar solvent such as EtOAc.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.88 (ddt, *J* = 9.9, 3.7, 1.7 Hz, 1H), 5.74 (dd, *J* = 9.4, 7.0 Hz, 1H), 4.46 (s, 1H), 3.97 (dqd, *J* = 8.9, 6.3, 2.7 Hz, 1H), 3.83 (br s, 1H), 3.77 – 3.67 (m, 3H), 3.56 (br s, 2H), 2.63 – 2.58 (m, 1H), 2.46 (appar s, 1H), 1.77 (td, *J* = 4.7, 4.1, 1.7 Hz, 2H), 1.63 – 1.47 (m, 2H), 1.15 (d, *J* = 6.1 Hz, 3H), 1.12 (d, *J* = 6.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 129.7, 126.5, 78.3, 75.4, 72.0, 71.7, 68.1, 45.5, 45.4, 40.8, 33.8, 23.4, 20.1.

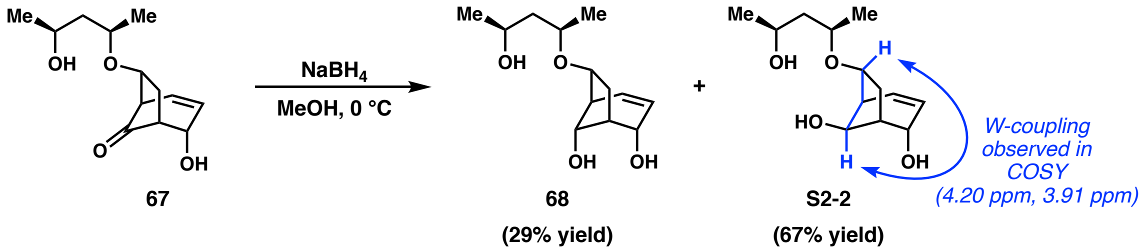
FTIR (NaCl, thin film): 3369, 3032, 2967, 2934, 1757, 1642, 1447, 1420, 1376, 1318, 1180, 1084, 1033, 970, 934 cm^{-1}.

HRMS: (FAB) calc'd for $C_{13}H_{23}O_4$ $[M + H]^+$ 243.1596, found 243.1616.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = –6.2° (*c* = 1.0, $CHCl_3$).

TLC (1:1 Hexanes:acetone), R*f*: 0.4 (UV, blue/green in *p*-anisaldehyde)

Preparation of S2-2:



In a 1-dram vial, ketone **67** (9.2 mg, 38 µmol, 1.0 equiv) was dissolved in MeOH (0.38 mL) and cooled to 0 °C. $NaBH_4$ (2.9 mg, 77 µmol, 2.0 equiv) was added, and the reaction was stirred for 15 minutes, then diluted with acetone (1 mL) and concentrated *in vacuo*. The resulting residue was dissolved in EtOAc (2 mL) and washed with 1 N NaOH (2 mL). The aqueous phase was extracted with EtOAc (3 x 2 mL), and the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by silica gel chromatography (50 to 55% acetone in hexanes) to provide 1,3-*syn*-diol **68** (2.7 mg, 11 µmol, 29% yield) and *anti*-1,3-diol **S2-2** (6.2 mg, 26 µmol, 67% yield).

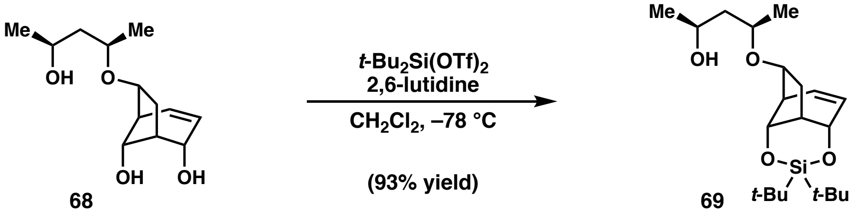
Spectroscopic data for 1,3-*anti*-diol **S2-2**:

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.89 (dd, *J* = 9.3, 7.4 Hz, 1H), 5.53 (ddd, *J* = 9.3, 3.8, 1.5 Hz, 1H), 4.20 (s, 1H), 4.00 (t, *J* = 3.3 Hz, 1H), 3.94 (ddd, *J* = 9.5, 6.4, 2.9 Hz, 1H), 3.91 (d, *J* = 7.1 Hz, 1H), 3.75 – 3.66 (m, 1H), 2.70 (d, J = 7.3 Hz, 1H), 2.58 (br s, 3H), 2.50 (d, *J* = 7.7 Hz, 1H), 2.04 (ddd, *J* = 14.6, 8.2, 1.7 Hz, 1H), 1.79 (dd, *J* = 14.7, 7.2 Hz, 1H), 1.63 (dt, *J* = 14.5, 9.0 Hz, 1H), 1.47 (ddd, *J* = 14.5, 4.3, 2.6 Hz, 1H), 1.16 (d, *J* = 6.3 Hz, 3H), 1.16 (d, *J* = 6.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 132.1, 127.7, 81.0, 74.5, 74.3, 74.1, 67.2, 49.1, 47.3, 45.8, 33.5, 24.0, 19.9.

Additionally, HSQC and COSY spectra are provided below.

Preparation of siliconide 69:



A flame dried 1-L, round-bottomed flask was charged with triol **68** (9.0 g, 37.1 mmol, 1.0 equiv), which was then azeotroped with anhydrous PhMe to remove any trace moisture. CH_2Cl_2 (370 mL) and 2,6-lutidine (10.3 mL, 89.1 mmol, 2.40 equiv.) were added, and the mixture was cooled to –78 °C. To this solution was added *t*-$Bu_2Si(OTf)_2$ (15.0 mL, 44.6 mmol, 1.20 equiv), and the reaction was stirred for 1 h. The reaction was quenched with sat. $NaHCO_3$ (150 mL) and H_2O (150 mL), and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (3 x 180 mL), and the combined organic extracts were washed with 0.1 M HCl (300 mL), washed with sat. $NaHCO_3$ (100 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by silica gel chromatography (10 to 25% acetone in hexanes) to afford siliconide **69** (13.27 g, 34.7 mmol, 93% yield) as a colorless oil.

^{1}H NMR (400 MHz, CDCl$_3$): δ 5.83 (ddd, *J* = 9.5, 4.4, 1.6 Hz, 1H), 5.74 (ddd, *J* = 9.6, 6.3, 1.2 Hz, 1H), 4.59 (t, *J* = 4.8 Hz, 1H), 4.04 – 3.91 (m, 2H), 3.80 – 3.70 (m, 2H), 3.39 (s, 1H), 2.78 (dd, *J* = 6.3, 4.1 Hz, 1H), 2.77 – 2.67 (m, 1H), 1.82 (ddd, *J* = 15.2, 7.5, 1.3 Hz, 1H), 1.71 (dd, *J* = 15.0, 7.9 Hz, 1H), 1.59 (dt, *J* = 14.5, 9.2 Hz, 1H), 1.51 (ddd, *J* = 14.5, 4.0, 2.6 Hz, 1H), 1.16 (d, *J* = 6.2 Hz, 3H), 1.12 (d, *J* = 6.0 Hz, 3H), 1.05 (s, 9H), 0.96 (s, 9H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 129.8, 129.1, 76.4, 74.7, 73.7, 71.0, 67.6, 46.4, 45.9, 38.6, 33.0, 28.7, 28.2, 23.6, 21.2, 20.7, 20.0.

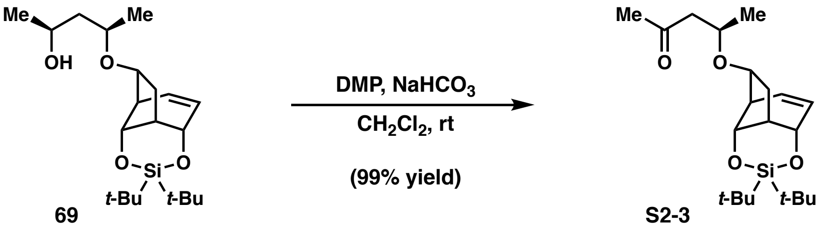
FTIR (NaCl, thin film): 3436, 3032, 2968, 2934, 2900, 2859, 1476, 1388, 1364, 1326, 1196, 1174, 1058, 1036, 1019, 998, 826 cm^{-1}.

HRMS: (FAB) calc'd for $C_{21}H_{39}O_4Si$ $[M + H]^+$ 383.2618, found 383.2630.

$[\alpha]_D^{25}$ = +59° (*c* = 0.90, CHCl$_3$).

TLC (1:1 Hexanes:EtOAc), R*f*: 0.7 (green in *p*-anisaldehyde)

Preparation and isolation of ketone S2-3:



The following protocol could be utilized to access ketone **S2-3**. Initially, S2-3 was isolated, and subjected to KHMDS to facilitate the retro-oxy Michael cleavage to afford **70**. The route was later optimized to access alcohol **70** directly in one step (see below), and thus ketone **S2-3** was not isolated in that procedure. The original procedure to discretely access **S2-3** and concomitant characterization data is provided:

A 500-mL, round-bottomed flask was charged with alcohol **69** (8.5 g, 22 mmol, 1.0 equiv), $NaHCO_3$ (5.60 g, 66.6 mmol, 3.0 equiv), and CH_2Cl_2 (225 mL). Dess–Martin periodinane (12.2 g, 28.9 mmol, 1.3 equiv) was added, and the reaction was stirred for 17 h, after which the reaction was filtered through a plug of silica (eluting with 50% EtOAc in hexanes). The filtrate was concentrated *in vacuo*, and then diluted in CH_2Cl_2 (100 mL), washed with sat. $NaHCO_3$ (2 x 100 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo* to provide ketone **S2-3** (8.5 g, 22 mmol, 99% yield) as a light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.81 (ddd, J = 9.5, 4.4, 1.6 Hz, 1H), 5.73 (ddd, J = 9.5, 6.2, 1.2 Hz, 1H), 4.55 (t, J = 4.8 Hz, 1H), 3.99 (td, J = 4.0, 0.8 Hz, 1H), 3.92 (h, J = 6.1 Hz, 1H), 3.65 (d, J = 7.1 Hz, 1H), 2.74 – 2.64 (m, 3H), 2.42 (dd, J = 16.0, 5.9 Hz, 1H), 2.16 (s, 3H), 1.76 (ddd, J = 14.9, 7.0, 1.4 Hz, 1H), 1.67 (ddt, J = 14.8, 7.7, 1.3 Hz, 1H), 1.11 (d, J = 6.1 Hz, 3H), 1.05 (s, 9H), 0.96 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 207.2, 129.5, 129.4, 76.9, 73.8, 71.1, 70.2, 51.0, 46.7, 38.5, 32.7, 31.2, 28.7, 28.2, 21.2, 20.7, 20.0.

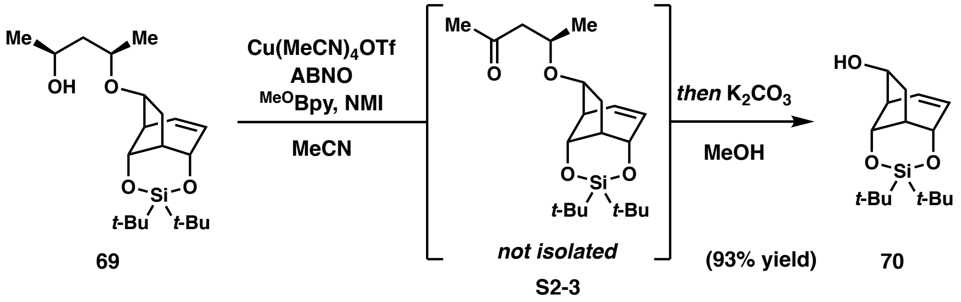
FTIR (NaCl, thin film): 3012, 2970, 2934, 2888, 2859, 1719, 1476, 1388, 1364, 1327, 1176, 1087, 1046, 1018, 999, 826 cm^{-1}.

HRMS: (FAB) calc'd for $C_{21}H_{37}O_4Si$ $[M + H]^+$ 381.2461, found 381.2465.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = +67° (c = 1.6, $CHCl_3$).

TLC (15%EtOAc in Hexanes), R$_f$: 0.4 (purple in *p*-anisaldehyde)

Preparation of alcohol 70:



To a 500 mL, round-bottomed flask was added alcohol **69** (3.92 g, 10.25 mmol, 1 equiv) and MeCN (102 mL). To this solution was added 4,4-dimethoxy-2,2'-bipyridine (111 mg, 0.513 mmol, 5 mol %), *N*-methylimidazole (82.5 µL, 1.03 mmol, 10 mol %), and ABNO (72 mg, 0.513 mmol, 5 mol %). Finally, $Cu(MeCN)_4OTf$ (193 mg, 0.513 mmol, 5 mol %) was added last, causing the solution to turn red/brown. The reaction was vigorously stirred for 60 minutes at room temperature open to air, during which time the reaction mixture turns blue, indicating its completion. At this time, MeOH (205 mL) was added, followed by powdered K_2CO_3 (powdered with mortar and pestle 7.84 g), causing the solution to turn brown, and the mixture was allowed to stir for 20 hours at room temperature. The mixture was filtered through a plug of silica gel and celite (to remove copper and solid K_2CO_3), flushed with excess ethyl acetate and concentrated *in vacuo*. The crude residue was purified by silica gel chromatography (20% ethyl acetate in hexanes, note: streaky on the column) to afford alcohol **70** (2.82 g, 9.53 mmol, 93% yield) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.82 (ddd, $J = 9.4, 4.3, 1.6$ Hz, 1H), 5.77 (ddd, $J = 9.5, 6.1, 1.2$ Hz, 1H), 4.78 (dd, $J = 5.5, 4.1$ Hz, 1H), 4.06 (dd, $J = 6.6, 1.6$ Hz, 1H), 4.01 (t, $J =$

3.9 Hz, 1H), 2.81 – 2.72 (m, 1H), 2.63 (ddd, *J* = 6.0, 4.3, 1.2 Hz, 1H), 1.82 (dd, *J* = 14.8, 6.8 Hz, 1H), 1.70 (ddt, *J* = 15.0, 7.9, 1.2 Hz, 1H), 1.07 (s, 9H), 0.98 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 129.6, 129.0, 73.6, 71.8, 71.0, 50.4, 38.7, 34.1, 28.7, 28.2, 21.2, 20.7.

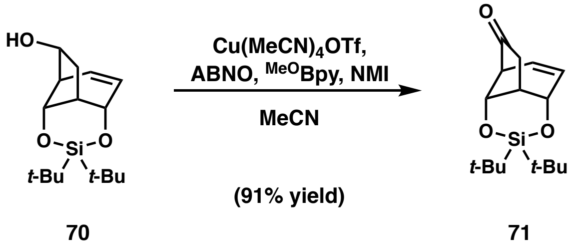
FTIR (NaCl, thin film): 3401, 3033, 2968, 2935, 2896, 2860, 1476, 1442, 1388, 1364, 1321, 1280, 1224, 1175, 1032, 998, 920, 825 cm^{-1}.

HRMS: (FAB) calc'd for $C_{16}H_{27}O_3Si$ $[M + H – H_2]^+$ 295.1747, found 295.1730.

$[\alpha]_D^{25}$ = +89° (*c* = 1.3, $CHCl_3$).

TLC (20%EtOAc in Hexanes), R*f*: 0.4 (blue in *p*-anisaldehyde)

Preparation of ketone 71:



To a 500 mL, round-bottomed flask was added alcohol **70** (2.82 g, 9.53 mmol, 1 equiv) and MeCN (95 mL). To this solution was added 4,4-dimethoxy-2,2'-bipyridine (103 mg, 0.476 mmol, 5 mol %), *N*-methylimidazole (73.6 μL, 0.953 mmol, 10 mol %), and ABNO (66.7 mg, 0.476 mmol, 5 mol %). Finally, Cu(MeCN)$_4$OTf (179 mg, 0.476 mmol, 5 mol %) was added last, causing the solution to turn red/brown. The reaction was vigorously stirred for 60 minutes at room temperature open to air, during which time the reaction mixture turns blue, indicating its completion. The mixture was then filtered through a plug of silica gel, flushed with excess ethyl acetate, and concentrated *in vacuo*. The crude residue was purified by silica gel chromatography (15% ethyl acetate in hexanes) to afford ketone **71** (2.55 g, 8.67 mmol, 91% yield) as a white crystalline solid.

^{1}H NMR (400 MHz, CDCl$_3$): δ 6.08 (ddd, *J* = 9.3, 4.6, 1.6 Hz, 1H), 5.76 (ddd, *J* = 9.2, 6.9, 1.4 Hz, 1H), 4.59 (ddt, *J* = 5.6, 4.1, 1.1 Hz, 1H), 4.27 (ddd, *J* = 4.5, 3.4, 0.9 Hz, 1H), 3.15 (dddd, *J* = 6.8, 4.2, 1.4, 0.7 Hz, 1H), 3.02 (dddq, *J* = 6.8, 5.0, 3.3, 1.6 Hz, 1H), 2.37 – 2.31 (m, 1H), 2.27 (dd, *J* = 19.4, 6.4 Hz, 1H), 1.09 (s, 9H), 0.99 (s, 9H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 206.7, 131.3, 124.8, 71.7, 69.8, 55.1, 38.5, 37.6, 28.6, 28.2, 21.1, 20.8.

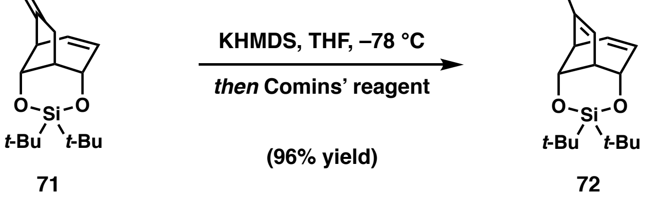
FTIR (NaCl, thin film): 3036, 2968, 2935, 2859, 1743, 1629, 1476, 1404, 1387, 1365, 1298, 1221, 1187, 1145, 1115, 997, 790 cm^{-1}.

HRMS: (FAB) calc'd for $C_{16}H_{27}O_3Si$ $[M + H]^+$ 295.1730, found 295.1731.

$[\alpha]_D^{25}$ = +510° (*c* = 1.1, CHCl$_3$).

TLC (20%EtOAc in Hexanes), R*f*: 0.4 (KMnO$_4$) Note: Does not stain in *p*-anisaldehyde.

Preparation of vinyl triflate 72:



A flame-dried 250-mL, round-bottomed flask was charged with ketone **71** (2.00 g, 6.80 mmol, 1.0 equiv), which was azeotroped with anhydrous PhMe to remove trace moisture.

THF (58 mL) was added, and the mixture was cooled to –78 °C in a dry ice/acetone bath. KHMDS (16.3 mL, 0.5 M in toluene, 8.15 mmol, 1.2 equiv) was added, causing the solution to turn yellow, and the reaction was stirred for 45 minutes while kept at –78 °C. In a separate flask, a solution of Comins' reagent (2.93 g, 7.47 mmol, 1.1 equiv) in THF (10 mL) was prepared and cannulated into the first reaction flask. The resulting mixture was stirred for an additional hour at –78 °C, and then quenched with sat. $NaHCO_3$ (40 mL), and allowed to warm to room temperature. The biphasic mixture was then transferred to a separatory funnel with Et_2O (75 mL), and the layers were separated. The aqueous layer was extracted with more Et_2O (3 x 75 mL). The combined organic layers were then washed with aq. 0.5 M NaOH solution (4 x 75 mL), followed by brine (1 x 100 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the crude residue by silica gel chromatography (0 to 10% EtOAc in hexanes) afforded vinyl triflate **72** (2.77 g, 6.50 mmol, 96% yield) as a yellow oil which solidified on standing.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.21 (ddd, *J* = 9.6, 6.0, 1.1 Hz, 1H), 5.84 (dddd, *J* = 9.6, 4.5, 2.0, 0.8 Hz, 1H), 5.49 (dd, *J* = 4.1, 0.8 Hz, 1H), 4.69 (tt, *J* = 4.8, 1.0 Hz, 1H), 4.28 (ddd, *J* = 4.0, 2.9, 0.8 Hz, 1H), 3.13 (ddddd, *J* = 4.8, 3.9, 2.8, 1.9, 0.9 Hz, 1H), 2.91 (ddq, J = 5.6, 4.7, 0.9 Hz, 1H), 1.08 (s, 9H), 1.01 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 163.3, 131.7, 130.8, 118.5 (q, $J_{C–F}$ =321.3 Hz, SO_2CF_3), 113.2, 75.7, 65.0, 45.2, 44.2, 28.8, 28.2, 21.1, 20.7.

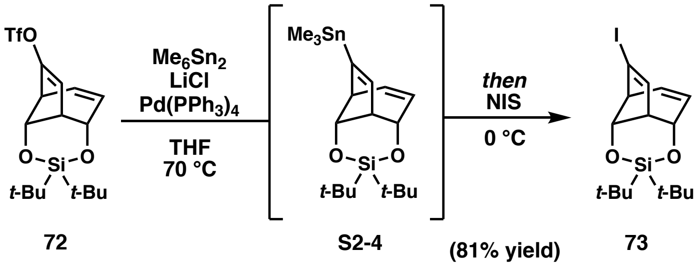
FTIR (NaCl, thin film): 3042, 2976, 2938, 2906, 2852, 1640, 1478, 1429, 1380, 1365, 1258, 1249, 1214, 1141, 1123, 1074, 1001, 926, 901 cm^{-1}.

HRMS: (FAB) calc'd for $C_{17}H_{26}F_3SSiO_5$ $[M + H]^+$ 427.1222, found 427.1205.

$[\alpha]_D^{25}$ = +20° (c = 1.2, $CHCl_3$).

TLC (4:1 Hexanes:EtOAc), R$_f$: 0.8 ($KMnO_4$)

Preparation of vinyl iodide 72 from vinyl triflate 73:



In an N_2-filled glovebox, LiCl (1.29 g, 30.5 mmol, 3.0 equiv), $Pd(PPh_3)_4$ (470 mg, 0.407 mmol, 0.04 equiv), and Me_6Sn_2 (3.33 g, 10.17 mmol, 1 equiv) were added to a 500-mL round bottomed flask containing vinyl triflate **72** (4.34 g, 10.17 mmol, 1.0 equiv), equipped with a rubber septum and brought out of the glovebox, and an N_2 inlet needle was added. The contents were dissolved in THF (102 mL), and then the flask was carefully equipped with a reflux condenser, trying to work quickly to minimize exposure to the atmosphere. The reaction was heated to 70 °C (reflux) in a pre-heated oil bath, and was allowed to stir for 15 h at this temperature, during which time the reaction mixture turns from yellow to black, indicating its completion. The reaction was then cooled to room temperature, the reflux condenser was removed and replaced with a new rubber septum, and then placed into an ice bath and cooled to 0 °C. *N*-iodosuccinimide (2.97 g, 13.11 mmol, 1.3 equiv) was then added in one portion, and the reaction was allowed to stir at 0 °C for an additional 2 hours. An additional portion of *N*-iodosuccinimide (700 mg, 3.11 mmol, 0.3 equiv) was added, and the reaction was allowed to warm to room temperature and stirred for an additional 3 hours. The reaction was then quenched with aqueous sat. $Na_2S_2O_3$ (150 mL), diluted with H_2O (50 mL), and transferred to a separatory funnel with Et_2O (150 mL), the layers were separated, and the aqueous layer was extracted with Et_2O (3 x 150 mL). The combined organic extracts were washed with aqueous sat. $NaHCO_3$ (2 x 150 mL), and brine (1 x 150 mL), and dried over Na2SO4, filtered and concentrated *in vacuo*. The crude organic extracts were purified by silica gel chromatography (22% to 25% to 30% CH_2Cl_2 in hexanes, very streaky but provides good separation), to provide **76** (3.34 g, 8.23 mmol, 81% yield) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.23 (ddd, *J* = 9.6, 6.0, 1.1 Hz, 1H), 6.21 (d, *J* = 3.9 Hz, 1H), 4.63 (tt, *J* = 4.7, 1.0 Hz, 1H), 4.20 (ddd, *J* = 4.4, 3.0, 0.8 Hz, 1H), 2.98 (ddddd, *J* = 4.8, 3.7, 2.8, 1.9, 0.7 Hz, 1H), 2.87 (ddq, *J* = 5.9, 4.5, 0.7 Hz, 1H), 1.07 (s, 9H), 1.00 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 137.3, 133.0, 130.2, 106.7, 76.8, 65.2, 54.5, 48.5, 28.8, 28.2, 21.2, 20.7.

FTIR (NaCl, thin film): 3043, 2971, 2931, 2888, 2856, 1578, 1476, 1382, 1364, 1314, 1286, 1248, 1200, 1119, 1082, 1001, 809 cm^{-1}.

HRMS: (FAB) calc'd for $C_{16}H_{26}IO_2Si$ $[M + H]^+$ 405.0747, found 405.0747.

$[\alpha]_D^{25}$ = +21° (c = 0.96, $CHCl_3$).

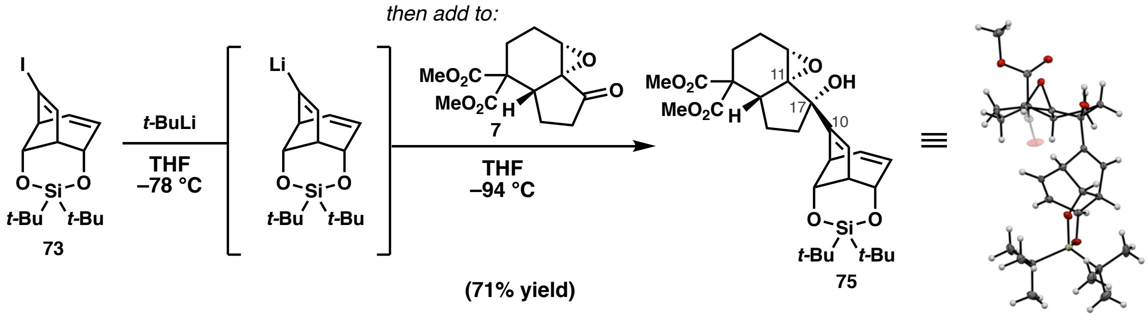
TLC (2:1 Hexanes:CH_2Cl_2), R_f: 0.4 (blue in *p*-anisaldehyde)

Note: In earlier experiments, it was shown that vinyl stannane **S2-4** could be isolated and lithiated with methyl lithium for the 1,2-addition. However, this creates gaseous Me_4Sn as a toxic byproduct, so an improved procedure was created. Furthermore, it was discovered that directly iodinating (and not isolating the vinyl stannane) was preferable for yield, stability, and purity. The procedure for the preparation and isolation of vinyl trimethylstannane **S2-4** and ^{1}H NMR is provided here:

In a N_2-filled glovebox, LiCl (89 mg, 2.11 mmol, 3.0 equiv), $Pd(PPh_3)_4$ (33 mg, 0.028 mmol, 0.04 equiv), and Me_6Sn_2 (0.146 mL, 0.703 mmol, 1.0 equiv) were added to a 40 mL vial with a septum screw-cap containing vinyl triflate **72** (300 mg, 0.703 mmol, 1.0 equiv). The contents were then dissolved in THF (7 mL), the vial was then sealed and brought out of the glovebox. The reaction was heated to 70 °C in an oil bath with vigorous stirring for 15 h, then cooled to room temperature, diluted with hexanes (ca. 20 mL), and quenched with H_2O (20 mL). The solution was extracted with hexanes (3 x 20 mL), and then the combined organic extracts were washed with H_2O (20 mL), 10% NH_4OH (20 mL), and H_2O (20 mL) again. After drying over Na_2SO_4 and filtration, the filtrate was concentrated *in vacuo* to afford crude vinyl stannane **S2-4**. The crude stannane was purified by silica gel (neutralized with a few drops of aq. 28–30% NH_3 in H_2O solution) chromatography (10% to 20% to 30% to 40% to 50% CH_2Cl_2 in hexanes) to afford vinyl trimethyl stannane **S2-4** (209 mg, 0.4713 mmol, 67% yield).

^{1}H NMR (400 MHz, Chloroform-*d*): δ 6.06 (ddd, J = 9.5, 6.1, 1.1 Hz, 1H), 5.96 (d, J = 3.5 Hz, $J_{Sn–H}$= 40.0 Hz, 1H), 5.59 (dddd, J = 9.5, 4.5, 2.0, 0.7 Hz, 1H), 4.47 (ddt, J = 5.2, 4.2, 0.9 Hz, 1H), 4.23 (ddd, J = 4.4, 2.9, 0.6 Hz, 1H), 3.01 – 2.96 (m, 1H), 2.89 (dd, J = 6.2, 4.3 Hz, 1H), 1.08 (s, 9H), 1.01 (s, 9H), 0.14 (s, $J_{Sn–H}$ = 54.9 Hz, 9H).

Preparation of epoxy-alcohol 75:



In a 200-mL, round-bottomed flask, vinyl iodide **73** (3.04 g, 7.51 mmol, 1.0 equiv) was dissolved in THF (75 mL) and cooled to –78 °C. To this solution was added *t*-BuLi (8.8 mL, 1.7 M in pentane, 15.02 mmol, 2.0 equiv) drop wise via syringe. During the last few drops of the addition of *t*-BuLi, the yellow color of *t*-BuLi in THF persisted, indicating that all equivalents of the vinyl iodide had been consumed. The resulting mixture was stirred for an additional 15 minutes at –78 °C. Meanwhile, in a separate 500-mL, round-bottomed flask, epoxyketone **7** (2.62 g, 9.76, 1.3 equiv) was dissolved in THF (75 mL). **7** requires vigorous stirring at room temperature in order to dissolve in THF. After the epoxyketone had dissolved, it was cooled –94 °C (acetone/liquid N_2 bath) and stirred for 10 minutes at this temperature to ensure thorough cooling (some precipitate of **7** forms during this time, but this is not a problem). After the vinyl lithium had been stirred for 15 minutes at –78 °C, the solution of vinyl lithium was then cannulated over 10 minutes into the –94 °C solution of epoxyketone. The reaction was stirred for an additional 30 minutes, allowing the reaction to warm to –78 °C (dry ice was added to the acetone/liquid N_2 bath). The reaction was then quenched with H_2O (150 mL), and was allowed to warm to room temperature. The biphasic mixture was transferred to a separatory funnel, and the aqueous layer was extracted with Et_2O (3 x 150 mL) and CH_2Cl_2 (2 x 150 mL), and the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by silica gel chromatography (10% to 11% to 12% acetone in hexanes and then 30% acetone in hexanes to recover the unreacted **7**) to afford epoxy alcohol **75** (2.91 g, 5.33 mmol, 71% yield) as a white solid. A small sample was recrystallized in hexanes/diethyl ether to obtain crystals suitable for X-ray crystallography.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.10 (ddd, *J* = 9.6, 6.1, 1.1 Hz, 1H), 5.70 (ddd, *J* = 9.4, 4.3, 1.6 Hz, 1H), 5.65 (d, *J* = 3.8 Hz, 1H), 4.48 (t, *J* = 4.7 Hz, 1H), 4.25 (dd, *J* = 4.2, 2.8 Hz, 1H), 3.75 (s, 3H), 3.70 (s, 3H), 3.32 (d, *J* = 3.6 Hz, 1H), 3.05 – 3.01 (m, 1H), 2.83 (ddd, *J* = 5.4, 4.9 Hz, 1H), 2.71 (dd, *J* = 10.7, 7.5 Hz, 1H), 2.53 – 2.42 (m, 2H), 2.42 – 2.29 (m, 2H), 2.10 – 1.98 (m, 2H), 1.97 – 1.86 (m, 2H), 1.61 – 1.47 (m, 1H), 1.08 (s, 9H), 1.02 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 171.7, 170.2, 161.6, 134.5, 129.2, 123.4, 77.7, 75.3, 71.2, 66.1, 56.5, 55.0, 52.9, 52.2, 45.6, 45.2, 44.4, 37.3, 29.3, 28.9, 28.3, 23.3, 21.6, 21.2, 20.7.

FTIR (NaCl, thin film): 3496, 3032, 2950, 2860, 1732, 1476, 1458, 1434, 1383, 1364, 1306, 1244, 1176, 1108, 991 cm^{-1}.

HRMS: (PPM) calc'd for $C_{29}H_{43}O_8Si$ $[M + H]^+$ 547.2722, found 547.2713.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = –5.1° (*c* = 0.30, $CHCl_3$).

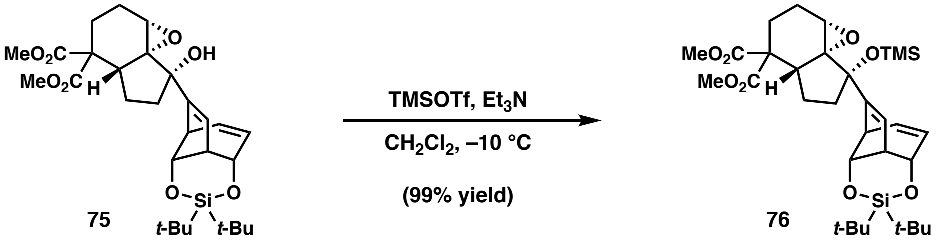
TLC (33%EtOAc/ 67% Hexanes), R*f*: 0.5 (blue in *p*-anisaldehyde)

Notes:

(1) It is extremely important for this reaction to be rigorously dry. Trace water diminishes yield. To achieve this, both substrates were separately azeotroped with PhMe (from the solvent system, 3x) prior to use and dried under high vacuum. Additionally, the THF from the solvent system was titrated. As long as the THF titrated at 7 ppm (or lower), good yields were achieved.

(2) Typically a smaller scale (300 mg) test reaction was done with the same reagent batches, solvent, and substrate prior to scaling up, to ensure that the scale-up run would proceed successfully.

Preparation of tertiary silyl ether 76:



In a 250-mL, round-bottomed flask, epoxy alcohol **75** (3.21 g, 5.88 mmol, 1.0 equiv) was azeotroped with PhMe (from the solvent system, 3 x 15 mL), and dried under high vacuum. The flask was equipped with a rubber septum and purged with N_2, dissolved in CH_2Cl_2 (59 mL) and cooled to –20 °C. Et_3N (2.46 mL, 17.64 mmol, 3.0 equiv) was added, followed by TMSOTf (1.30 mL, 7.06 mmol, 1.2 equiv). The reaction was stirred for 15 minutes, during which time the reaction was allowed to reach –12 °C. The reaction was monitored by TLC, indicating its completion, and then quenched by the addition of sat. $NaHCO_3$ (50 mL). The biphasic mixture was transferred to a separatory funnel, the layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 x

75 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by silica gel chromatography (7 to 8% acetone in hexanes) to afford silyl ether **76** (3.62 g, 5.82 mmol, 99% yield) as a white crystalline solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.03 (ddd, *J* = 9.6, 6.1, 1.1 Hz, 1H), 5.68 (ddd, *J* = 9.5, 4.3, 1.5, 1H), 5.57 (d, *J* = 3.7 Hz, 1H), 4.48 (t, *J* = 4.7 Hz, 1H), 4.26 (ddd, *J* = 4.1, 3.0, 0.7 Hz, 1H), 3.74 (s, 3H), 3.67 (s, 3H), 3.30 (d, *J* = 3.5 Hz, 1H), 3.08 – 3.03 (m, 1H), 2.90 (dd, *J* = 5.5, 4.8 Hz, 1H), 2.74 (t, *J* = 9.3 Hz, 1H), 2.61 (dddd, *J* = 12.8, 11.0, 8.9, 3.9 Hz, 1H), 2.43 – 2.25 (m, 2H), 2.12 (ddd, *J* = 12.7, 8.7, 3.9 Hz, 1H), 2.04 (ddd, *J* = 12.7, 11.0, 7.5 Hz, 1H), 1.96 (ddd, *J* = 15.1, 8.2, 3.7 Hz, 1H), 1.83 (ddt, *J* = 12.7, 9.4, 8.2, 1H), 1.45 (ddd, *J* = 13.3, 10.1, 8.4 Hz, 1H), 1.09 (s, 9H), 1.02 (s, 9H), 0.05 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 172.0, 170.4, 163.2, 135.1, 129.0, 122.5, 77.7, 77.6, 70.1, 66.1, 55.0, 54.0, 52.8, 52.1, 45.8, 44.9, 41.4, 34.5, 29.7, 28.9, 28.3, 22.2, 21.6, 21.2, 20.7, 2.2.

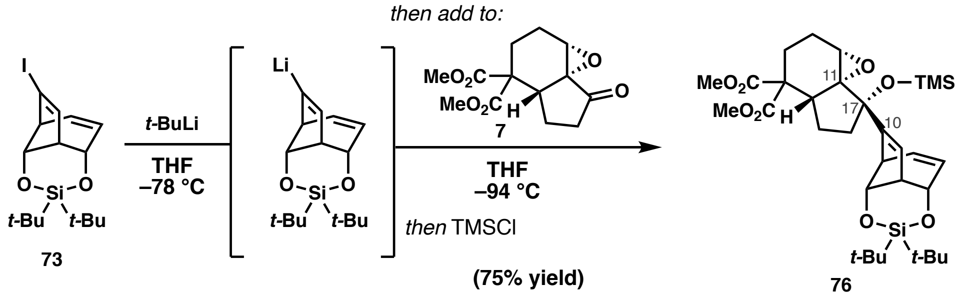
FTIR (NaCl, thin film): 3028, 2952, 2904, 2860, 1732, 1477, 1462, 1434, 1364, 1250, 1175, 1110, 1058, 992, 881, 842 cm^{-1}.

HRMS: (PPM) calc'd for $C_{32}H_{51}O_8Si_2$ $[M + H]^+$ 619.3117, found 619.3106.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = +36° (*c* = 0.35, $CHCl_3$).

TLC (10%EtOAc/ 90% Hexanes), R$_f$: 0.4 (green/black in *p*-anisaldehyde)

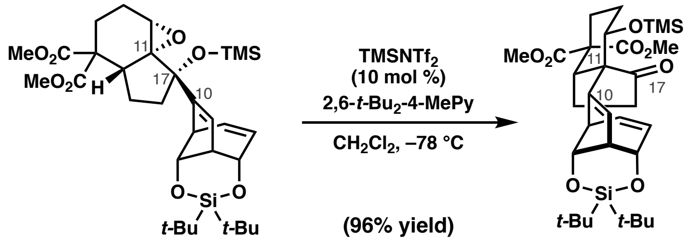
Preparation of silyl ether 76 directly from 1,2-addition of 73 to 7 followed by TMSCl quench:



A flame dried 100 mL pear shaped flask with a magnetic stir bar was charged with vinyl iodide **73** (1.00 g, 2.47 mmol, 1.0 equiv.) and THF (25 mL). The solution was cooled to -78 °C before *t*-BuLi (1.5 M in pentane, 3.3 mL, 4.9 mmol, 2.0 equiv.) was added dropwise. The mixture was stirred at -78 °C for 15 minutes. In a separate 250 mL round-bottomed flask, epoxyketone **7** (0.864 g, 3.22 mmol, 1.3 equiv.) was dissolved in THF (25 mL) and cooled to -94 °C. The solution of vinyl lithium was transferred via cannula to the solution of epoxy ketone, and the reaction was warmed to -78 °C. After 15 minutes, TMSCl (0.63 mL, 4.9 mmol, 2.0 equiv.) was added dropwise. The reaction was warmed to room temperature and stirred for an additional 15 minutes. The reaction was quenched by addition of saturated $NaHCO_3$ (40 mL). The mixture was transferred to a separatory funnel, and the aqueous phase was extracted with EtOAc (5 x 50 mL). The combined organic phases were dried over Na_2SO_4, filtered, and concentrated *in vacuo.* Purification of the crude residue by flash chromatography (silica gel, 5 to 30% EtOAc in hexanes) afforded silyl ether **76** (1.145 g, 1.85 mmol, 75% yield) as a white solid.

Note: this reaction is extremely sensitive to trace water, see notes listed above (for preparation of **75**, which should also be applied to this protocol.

Preparation of ketone 77:



76 **77**

A 500-mL, round-bottomed flask was charged with epoxide **76** (3.62 g, 5.87 mmol, 1.0 equiv), 2,6-(*t*-Bu)$_2$-4-MePy (1.33 g, 6.46 mmol, 1.1 equiv) and CH_2Cl_2 (152 mL), and the solution was cooled to –78 °C in a dry ice/acetone bath. In an N_2-filled glovebox, a 1-mL syringe was filled with $TMSNTf_2$ (208 mg, 0.587 mmol, 0.10 equiv), plugged with a rubber stopper, and removed from the glovebox. The $TMSNTf_2$ was immediately added dropwise to the reaction mixture, causing the solution to turn yellow. After stirring for an additional 50 minutes at –78 °C, the reaction was quenched with sat. $NaHCO_3$ (150 mL), and the solution was allowed to warm to room temperature. The biphasic mixture was transferred to a separatory funnel and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (3 x 150 mL), and the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (3% to 4% acetone in hexanes to elute the 2,6-*t*-Bu$_2$-4-MePy followed by 8% to 10% acetone in hexanes to elute the product) to afford ketone **77** (3.47 g, 5.64 mmol, 96% yield) as a white solid.

Notes:

(1) 2,6-(*t*-Bu)$_2$-4-MePy was purchased from Combi Blocks and repurified before use. The crude brown oil was dissolved in pentanes, and filtered over a plug of silica gel that had been pre-equilibrated with pentanes, eluted with more pentanes and

concentrated *in vacuo,* and dried under high-vacuum. Upon standing, the material turned into a white crystalline solid. This repurification step is crucial for high yields.

(2) If the starting material is not rigorously dry, the reaction may not reach full conversion. It is possible that trace amounts of water can quench $TMSNTf_2$ and result in early termination. In this case, the crude product can simply be resubjected to the reaction conditions. In order to ensure the starting material is sufficiently free of water, it should be azeotroped with toluene or benzene (1–3x) prior to the reaction.

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.88 (ddd, *J* = 9.5, 6.1, 1.1 Hz, 1H), 5.65 (ddd, *J* = 9.5, 4.3, 1.9 Hz, 1H), 5.40 (d, *J* = 3.8 Hz, 1H), 4.66 (t, *J* = 4.7 Hz, 1H), 4.31 (br s, 1H), 4.23 (dd, *J* = 4.0, 3.1 Hz, 1H), 3.74 (s, 3H), 3.67 (s, 3H), 3.40 (dd, *J* = 11.7, 7.3 Hz, 1H), 3.03 – 2.94 (m, 2H), 2.48 (td, *J* = 14.1, 3.4 Hz, 1H), 2.38 – 2.26 (m, 1H), 2.17 – 2.05 (m, 3H), 1.80 – 1.71 (m, 1H), 1.65 – 1.60 (m, 1H), 1.52 (tdd, *J* = 14.3, 2.9, 1.9 Hz, 1H), 1.08 (s, 9H), 1.00 (s, 9H), 0.05 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 215.9, 170.7, 170.6, 158.9, 134.8, 128.2, 124.4, 76.7, 69.9, 66.2, 58.0, 56.2, 52.8, 52.6, 46.2, 46.1, 41.8, 38.8, 28.9, 28.3, 27.4, 23.7, 21.2, 20.7, 19.3, 0.0.

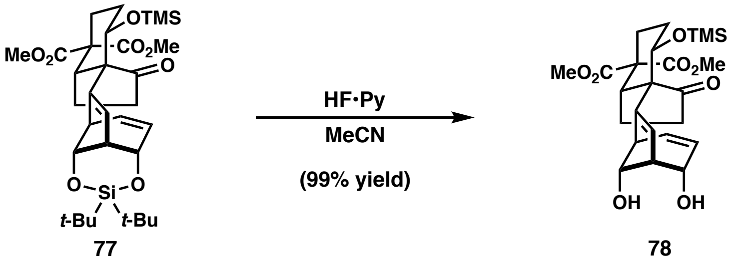
FTIR (NaCl, thin film): 3032, 2952, 2896, 2859, 1741, 1477, 1462, 1443, 1384, 1363, 1252, 1170, 1097, 991, 840 cm^{-1}.

HRMS: (PMM) calc'd for $C_{32}H_{51}O_8Si_2$ $[M + H]^+$ 619.3117, found 619.3105.

$[\alpha]_D^{25}$ = +92° (*c* = 0.73, $CHCl_3$).

TLC (10%EtOAc/ 90% Hexanes), R*f*: 0.4 (blue in *p*-anisaldehyde)

Preparation of diol 78:



A 250-mL plastic-coated round-bottomed flask was charged with silylene **77** (1.07 g, 1.73 mmol, 1.0 equiv) and MeCN (110 mL) and cooled to 0 °C with an ice bath. A solution of HF•Py (pyridine ~30%, HF ~70%, 857 mg, 17.4 equiv) in MeCN (3 mL) was added, and the ice bath was removed to allow the reaction to reach ambient temperature. After stirring for 45 min, the solution was filtered through a plug of silica (that had been pre-equilibrated with EtOAc and eluted with more EtOAc) and concentrated *in vacuo* to provide pure diol **78** (815 mg, 1.71 mmol, 99% yield) as a white solid.

^{1}H NMR (400 MHz, CDCl$_3$): δ 5.83 – 5.75 (m, 2H), 5.47 (d, *J* = 3.6 Hz, 1H), 4.61 (q, *J* = 5.2 Hz, 1H), 4.28 (br s, 1H), 3.94 (appar d, *J* = 8.0 Hz, 1H), 3.74 (s, 3H), 3.67 (s, 3H), 3.38 (dd, *J* = 12.1, 7.3 Hz, 1H), 2.91 (t, *J* = 4.5 Hz, 1H), 2.88 – 2.70 (m, 2H), 2.69 – 2.65 (m, 1H), 2.48 (td, *J* = 14.3, 3.6 Hz, 1H), 2.36 – 2.24 (m, 1H), 2.19 – 2.02 (m, 3H), 1.80 – 1.56 (m, 2H), 1.48 (tdd, *J* = 14.1, 2.8, 2.0 Hz, 1H), 0.03 (s, 9H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 215.9, 170.7, 170.6, 157.0, 130.9, 129.5, 124.8, 74.3, 69.7, 65.7, 57.8, 56.3, 52.9, 52.7, 47.5, 44.3, 41.8, 38.9, 27.4, 23.6, 19.3, -0.0.

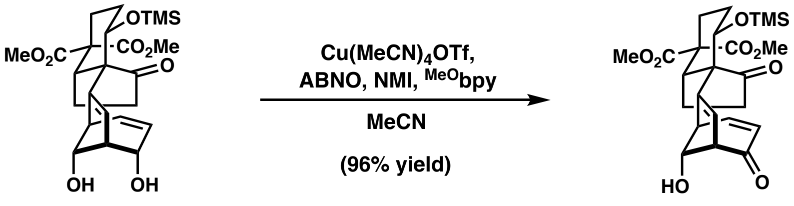
FTIR (NaCl, thin film): 3401, 3025, 2954, 1738, 1434, 1404, 1336, 1313, 1252, 1194, 1171, 1074, 1058, 1020, 980, 892, 862, 842 cm^{-1}.

HRMS: (PMM) calc'd for $C_{24}H_{33}O_7Si$ $[M - OH]^+$ 461.1990, found 461.1980.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = +92° (c = 1.3, $CHCl_3$).

TLC (100%EtOAc), $\mathbf{R_f}$: 0.5 (green/blue in *p*-anisaldehyde)

Preparation of enone 79:



78 **79**

To a 100 mL, round-bottomed flask was added diol **78** (790 mg, 1.65 mmol, 1.0 equiv), MeCN (33 mL), 4,4'-dimethoxy-2,2'-bipyridine (^{MeO}bpy, 10.7 mg, 49.5 μmol, 0.03 equiv), *N*-methylimidazole (13.2 μL, 0.165 mmol, 0.10 equiv) and ABNO (7.9 mg, 56.4 μmol, 0.05 equiv). Lastly, $Cu(MeCN)_4OTf$ (18.9 mg, 45.9 μmol, 0.03 equiv), causing the solution to turn a clear faint red/brown color. The reaction mixture was stirred vigorously while open to air until slightly yellow-green (3 hours). The solution was filtered through a short plug of silica (pre-equilibrated with EtOAc and flushed with more EtOAc) and concentrated *in vacuo*. Purification of the crude residue by silica gel chromatography (50% to 60% to 70% EtOAc in hexanes) afforded enone **79** (757 mg, 1.58 mmol, 96% yield) as a white foam.

Note: This reaction is prone to over-oxidation (to the 1,3-diketone). It is important to only use a minimum amount of catalyst. If the reaction stops, more catalyst can be added. In this case, the reaction should be monitored carefully by TLC.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.87 (ddd, J = 9.7, 6.4, 1.6 Hz, 1H), 5.90 (ddd, J = 9.7, 2.0, 1.2 Hz, 1H), 5.62 (d, J = 3.9 Hz, 1H), 5.06 – 4.96 (m, 1H), 4.24 (br s, 1H), 3.75 (s, 3H), 3.66 (s, 3H), 3.41 (dd, *J* = 12.2, 7.3 Hz, 1H), 3.27 (t, *J* = 5.5 Hz, 1H), 3.26 – 3.18 (br m, 1H), 2.62 – 2.41 (m, 2H), 2.38 – 2.25 (m, 1H), 2.23 – 2.07 (m, 3H), 1.82 – 1.59 (m, 2H), 1.48 (tdd, *J* = 14.3, 3.5, 1.9 Hz, 1H), 0.02 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 215.7, 195.3, 170.8, 170.4, 156.0, 148.7, 127.5, 124.5, 84.3, 69.6, 61.4, 57.9, 56.2, 53.0, 52.8, 47.1, 41.7, 38.8, 27.5, 23.5, 19.3, -0.1.

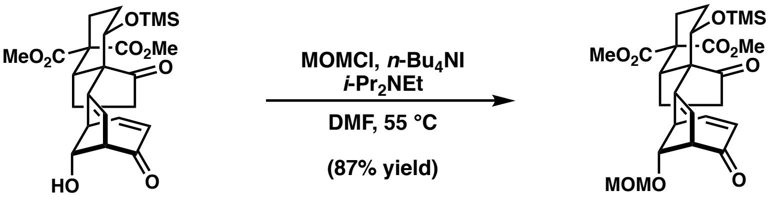
FTIR (NaCl, thin film): 3467, 3009, 3955, 1738, 1674, 1435, 1376, 1314, 1253, 1230, 1172, 1076, 1060, 1021, 981, 843 cm^{-1}.

HRMS: (PMM) calc'd for $C_{24}H_{33}O_8Si$ $[M + H]^+$ 477.1939, found 477.1952.

$[\alpha]_D^{25}$ = +281° (*c* = 1.1, $CHCl_3$).

TLC (100%EtOAc), R*f*: 0.8 (UV, brown in *p*-anisaldehyde)

Preparation of MOM-ether 100:



79 **100**

A 100-mL, round-bottomed flask was charged with alcohol **79** (735 mg, 1.54 mmol, 1.0 equiv), *n*-Bu_4NI (114 mg, 0.308 mmol, 0.20 equiv), *i*-Pr_2NEt (1.50 mL, 9.25 mmol, 6.0 equiv), and DMF (15.4 mL), followed lastly by MOMCl (0.50 mL, 6.55 mmol, 4.25 equiv). The reaction mixture was heated to 55 °C with stirring for 15 h, then cooled to room temperature and diluted with H_2O (15 mL) and Et_2O (20 mL). The layers thoroughly mixed, separated, and then the aqueous phase was extracted with Et_2O (3 x 20 mL). The combined organic extracts were washed with water (3 x 15 mL) and brine (15 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification of the crude residue by silica gel chromatography (30 to 33% to 40% EtOAc in hexanes) afforded methoxymethyl ether **100** (700 mg, 1.34 mmol, 87% yield) as a white solid.

^{1}H NMR (400 MHz, CDCl$_3$): δ 6.82 (ddd, *J* = 9.8, 6.3, 1.6 Hz, 1H), 5.82 (d, *J* = 10.1 Hz, 1H), 5.64 (d, *J* = 3.8 Hz, 1H), 4.75 (td, *J* = 4.6, 1.6 Hz, 1H), 4.71 (s, 2H), 4.25 (br s, 1H), 3.75 (s, 3H), 3.67 (s, 3H), 3.43 (dd, *J* = 12.3, 7.3 Hz, 1H), 3.38 – 3.27 (m, 5H), 2.52 (td, *J* = 14.2, 3.3 Hz, 1H), 2.39 – 2.26 (m, 1H), 2.23 – 2.08 (m, 3H), 1.81 – 1.59 (m, 2H), 1.48 (tdd, *J* = 14.3, 3.3, 1.9 Hz, 1H), 0.03 (s, 9H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 215.5, 195.7, 170.7, 170.4, 155.9, 148.5, 126.7, 124.4, 96.6, 90.5, 69.7, 60.2, 57.8, 56.2, 56.1, 52.9, 52.8, 45.7, 41.7, 38.8, 27.5, 23.5, 19.3, -0.1.

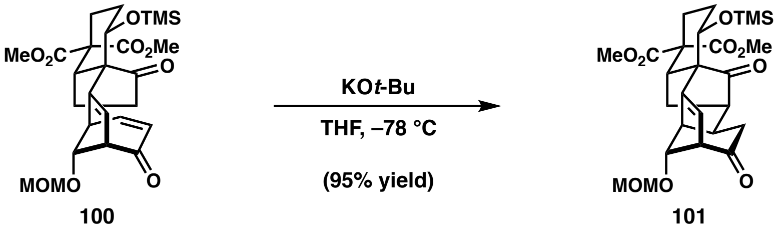
FTIR (NaCl, thin film): 3009, 2954, 1738, 1681, 1462, 1435, 1253, 1230, 1172, 1059, 1040, 981 cm^{-1}.

HRMS: (PMM) calc'd for $C_{26}H_{37}O_9Si$ $[M + H]^+$ 521.2201, found 521.2207.

$[\alpha]_D^{25}$ = +258° (*c* = 1.3, CHCl$_3$).

TLC (33%EtOAc/67%Hexanes), R*f*: 0.3 (UV, brown in *p*-anisaldehyde)

Preparation of pentacycle 101:



A 100-mL, round-bottomed flask was charged with enone **274** (680 mg, 1.305 mmol, 1.0 equiv), followed by THF (26 mL), and this solution was cooled to –78 °C. KO*t*-Bu (1.83 mL, 1.0 M in THF, 1.83 mmol, 1.4 equiv) was added to the reaction, causing the solution to turn yellow. The reaction was allowed to stir for an additional 60 minutes while maintained at –78 °C. The reaction was quenched by addition of sat. NH_4Cl (15 mL) and H_2O (15 mL), and allowed to warm to room temperature. The biphasic mixture was then transferred to a separatory funnel with Et_2O (30 mL), and the layers were separated. The aqueous was extracted with Et_2O (3 x 30 mL). The combined organic extracts were washed with water (1 x 20 mL), and dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification of the crude residue by silica gel chromatography (30% to 33% to 35% to 37% to 40% EtOAc in hexanes) afforded pentacycle **101** (645 mg, 1.24 mmol, 95% yield) as a white solid.

^{1}H NMR (400 MHz, CDCl$_3$): δ 5.54 (d, *J* = 2.6 Hz, 1H), 4.68 (s, 2H), 4.59 (t, *J* = 5.5 Hz, 1H), 4.31 (dd, *J* = 6.5, 3.8 Hz, 1H), 3.76 (s, 3H), 3.65 (s, 3H), 3.36 (s, 3H), 3.32 (dd, *J* = 5.0, 2.6 Hz, 1H), 3.06 (t, *J* = 5.5 Hz, 1H), 2.91 (dd, *J* = 10.2, 5.5 Hz, 1H), 2.61 (dd, *J* = 19.4, 8.7 Hz, 1H), 2.51 – 2.44 (m, 1H), 2.36 – 2.23 (m, 4H), 2.19 (ddd, *J* = 13.3, 7.5, 5.6 Hz, 1H), 1.88 – 1.79 (m, 1H), 1.72 – 1.54 (m, 2H), 0.10 (s, 9H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 203.7, 202.7, 173.0, 170.5, 146.8, 122.6, 96.3, 78.6, 66.4, 60.5, 59.0, 56.6, 56.1, 53.1, 51.9, 51.2, 42.4, 41.4, 37.9, 36.0, 27.1, 26.1, 25.1, 0.3.

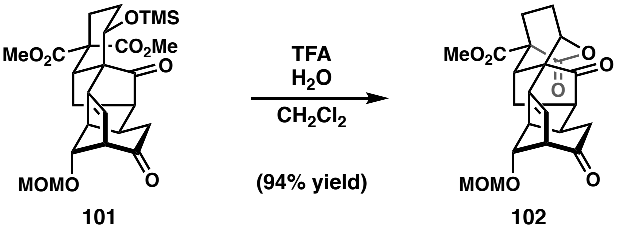
FTIR (NaCl, thin film): 3017, 2954, 2904, 2828, 1747, 1732, 1714, 1589, 1461, 1434, 1406, 1361, 1251, 1215, 1152, 1111, 1043, 866 cm^{-1}.

HRMS: (PMM) calc'd for $C_{26}H_{37}O_9Si$ $[M + H]^+$ 521.2201, found 521.2186.

$[\alpha]_D^{25}$ = +168° (*c* = 1.2, $CHCl_3$).

TLC (33%EtOAc/67%Hexanes), R*f*: 0.35 (UV, purple in *p*-anisaldehyde)

Preparation of lactone 102:



In a 50-mL, round-bottomed flask, diester **101** (200 mg, 0.384 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (7.6 mL). To this solution was added TFA (147 μL, 1.92 mmol, 5.0 equiv) and H_2O (35 μL, 1.92 mmol, 5 equiv). The reaction was stirred for 30 h, and then quenched with sat. $NaHCO_3$ (20 mL). The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo.* Purification of the crude residue by silica gel chromatography (30% to 33% to 35% to 37% to 40% EtOAc in hexanes) afforded lactone **102** (150 mg, 0.361 mmol, 94% yield) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.35 (d, *J* = 2.6 Hz, 1H), 5.20 (dd, J = 4.7, 0.8 Hz, 1H), 4.71 (d, *J* = 6.9 Hz, 1H), 4.68 (d, *J* = 6.9 Hz, 1H), 4.63 (t, *J* = 5.5 Hz, 1H), 3.82 (s, 3H), 3.38 (dd, *J* = 4.9, 2.6 Hz, 1H), 3.36 (s, 3H), 3.11 (t, *J* = 5.7 Hz, 1H), 2.99 (dd, *J* = 9.6, 7.2 Hz, 1H), 2.73 (dd, *J* = 19.3, 9.1 Hz, 1H), 2.63 (dtd, *J* = 9.0, 4.5, 1.8 Hz, 1H), 2.47 – 2.22 (m, 5H), 2.10 – 1.99 (m, 2H), 1.82 (dddd, *J* = 13.8, 11.3, 5.0, 1.0 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 203.7, 200.6, 169.2, 169.1, 143.3, 121.9, 96.6, 78.3, 72.0, 62.2, 60.8, 56.2, 52.8, 52.8 (two overlapping ^{13}C signals), 51.3, 43.7, 43.0, 38.8, 36.0, 28.6, 28.0, 21.2.

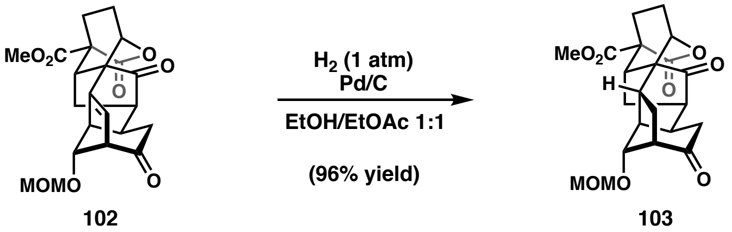
FTIR (NaCl, thin film): 3009, 2954, 1749, 1711, 1444, 1367, 1298, 1264, 1220, 1153, 1108, 1068, 1047, 997 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{22}H_{24}KO_8$ $[M + K]^+$ 455.1103, found 455.1096.

$[\alpha]_D^{25}$ = +183° (c = 0.67, $CHCl_3$).

TLC (33%EtOAc/67%Hexanes), R*f*: 0.3 (UV, blue in *p*-anisaldehyde)

Preparation of carbocycle 103:



To a 50-mL, round-bottomed flask containing lactone **102** (333 mg, 0.80 mmol, 1 equiv) under N_2 was added Pd/C (10 wt%, 333 mg), followed by absolute EtOH (6 mL) and EtOAc (6 mL). The reaction vessel was purged with H_2 for 5 minutes via a double-walled balloon, and stirred for another 22 h under H_2 (1 atm). The H_2 balloon was then removed, and the flask was purged with N_2 for 15 minutes. The suspension was filtered through a plug of silica (eluting with EtOAc), and the resulting solution was concentrated *in vacuo* to provide carbocycle **103** (323 mg, 0.771 mmol, 96% yield) as a white foam.

^{1}H NMR (400 MHz, CDCl$_3$): δ 4.77 (dd, J = 4.5, 1.2 Hz, 1H), 4.63 (d, J = 6.9 Hz, 1H), 4.61 (d, J = 6.9 Hz, 1H), 4.19 (t, J = 4.6 Hz, 1H), 3.82 (s, 3H), 3.34 (s, 3H), 2.88 – 2.73 (m, 5H), 2.65 – 2.53 (m, 1H), 2.47 (dd, J = 14.9, 9.7 Hz, 1H), 2.43–2.30 (m, 2H), 2.23 – 2.09 (m, 2H), 2.05 – 1.86 (m, 3H), 1.80 (dddd, J = 14.1, 11.1, 4.2, 1.2 Hz, 1H), 1.46 (ddd, J = 14.8, 6.6, 0.9 Hz, 1H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 213.9, 210.2, 169.3, 169.1, 96.3, 79.2, 74.1, 56.1, 55.9, 53.1, 52.8 (two overlapping ^{13}C signals) 51.5, 49.6, 45.3, 39.9, 39.0, 37.6, 28.2, 27.9, 24.2, 19.8.

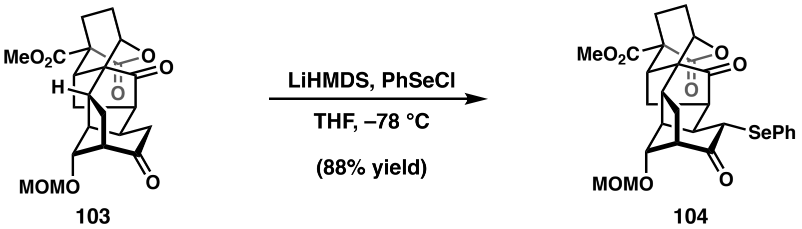
Two ^{13}C signals appear at the same chemical shift, but are resolved in the HSQC spectrum, which is provided below.

FTIR (NaCl, thin film): 2953, 2915, 2854, 1740, 1711, 1458, 1449, 1377, 1298, 1262, 1151, 1103, 1048, 992, 753 cm^{-1}.

HRMS: (ESI) calc'd for $C_{22}H_{28}NO_8$ $[M + NH_4]^+$ 436.1966, found 436.1963.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = +32° (c = 1.0, $CHCl_3$).

Preparation of α-selenide 104:



A 50-mL, round-bottomed flask was charged with diketone **103** (168 mg, 0.401 mmol, 1.0 equiv), which was dissolved in THF (4 mL) and cooled to –78 °C. In a separate flask, a solution of PhSeCl (123 mg, 0.642 mmol, 1.6 equiv) in THF (4 mL) was prepared. LiHMDS (0.60 mL, 1.0 M in THF, 0.60 mmol, 1.5 equiv) was added to the solution of diketone **103**, and the resulting mixture was stirred for 30 minutes at –78 °C. The THF solution of PhSeCl was then added, and the mixture was stirred for another 2 hours. The reaction was quenched with sat $NaHCO_3$ (10 mL), and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by silica gel chromatography (90% ethyl acetate in hexanes) to afford α-selenide **104** as a yellow foam (201.5 mg, 0.351 mmol, 88% yield).

^{1}H NMR (500 MHz, Chloroform-*d*): δ 7.72 – 7.68 (m, 2H), 7.31 – 7.27 (m, 3H), 4.76 – 4.73 (m, 1H), 4.58 (d, *J* = 6.9 Hz, 1H), 4.56 (d, *J* = 6.9 Hz, 1H), 4.22 (t, *J* = 5.0 Hz, 1H), 3.81 (s, 3H), 3.76 (d, *J* = 4.5 Hz, 1H), 3.38 (s, 3H), 3.11 (dtd, *J* = 6.8, 4.5, 2.5 Hz, 1H), 3.05 (dd, *J* = 8.4, 5.4 Hz, 1H), 2.85 (q, *J* = 5.5 Hz, 1H), 2.72 (dd, *J* = 9.8, 7.3 Hz, 1H), 2.59 – 2.53 (m, 1H), 2.44 – 2.34 (m, 2H), 2.21 (dd, *J* = 6.7, 4.2 Hz, 1H), 2.19 – 2.12 (m, 1H), 2.02 – 1.91 (m, 3H), 1.84 – 1.73 (m, 1H), 1.50 (dd, *J* = 15.2, 7.0 Hz, 1H).

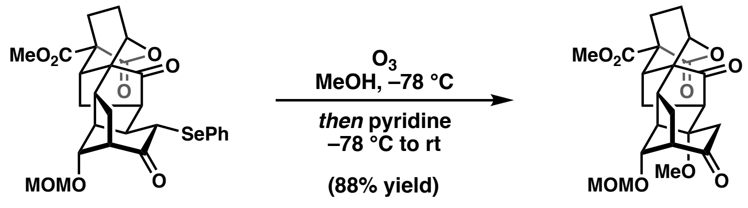
^{13}C NMR (126 MHz, $CDCl_3$): δ 214.0, 207.8, 169.2, 168.9, 134.9, 130.1, 129.1, 128.2, 96.0, 78.7, 73.9, 56.3, 56.2, 53.2, 53.0, 52.8, 51.6, 50.3, 49.2, 47.8, 45.4, 39.5, 28.3, 27.5, 24.4, 19.7.

FTIR (NaCl, thin film): 3017, 2952, 2896, 2854, 1755, 1739, 1713, 1477, 1464, 1438, 1377, 1298, 1262, 1103, 1052, 989 cm^{-1}.

HRMS: (ESI) calc'd for $C_{28}H_{34}NO_8Se$ $[M + NH_4]^+$ 592.1444, found 592.1424.

$[\alpha]_D^{25}$ = +13° (*c* = 0.60, $CHCl_3$).

Preparation of β-methoxyketone 105:



104 105

A 25-mL, round-bottomed flask was charged with α-selenide **104** (90.6 mg, 0.158 mmol, 1.0 equiv), CH_2Cl_2 (4 mL), and methanol (4 mL). The flask was cooled to –78 °C, at which time ozone (as a mixture with O_2) was gently bubbled through the solution (O_2 flow rate = 1/4 L/min, 2 setting on ozone generator) for 20 min. The solution was then sparged with Ar for 15 minutes, and pyridine (64 μL, 0.790 mmol, 5 equiv) was added. The reaction was allowed to warm to ambient temperature, and stirred for a further 48 h. The methanol solvent and pyridine were then removed by concentration *in vacuo*, and the crude residue was purified by silica gel chromatography (44% acetone in hexane) to afford β-methoxyketone **105** as a white solid (62.3 mg, 0.139 mmol, 88% yield) with a small amount of inseperable arene impurity (<10%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.78 (d, *J* = 6.9 Hz, 1H), 4.75 (d, *J* = 4.0 Hz, 1H), 4.56 (d, *J* = 6.9 Hz, 1H), 4.23 (t, *J* = 4.6 Hz, 1H), 3.81 (s, 3H), 3.32 (s, 3H), 3.11 (s, 3H), 2.98 (d, *J* = 17.9 Hz, 1H), 2.79 (dd, *J* = 7.4, 4.5 Hz, 1H), 2.73 (q, *J* = 6.0 Hz, 1H), 2.69 – 2.58 (m, 3H), 2.55 (d, *J* = 6.7 Hz, 1H), 2.46 (dt, *J* = 11.2, 6.5 Hz, 1H), 2.42 – 2.34 (m, 1H), 2.23 – 2.09 (m, 1H), 2.03 – 1.70 (m, 4H), 1.39 (ddd, *J* = 14.9, 6.1, 2.8 Hz, 1H).

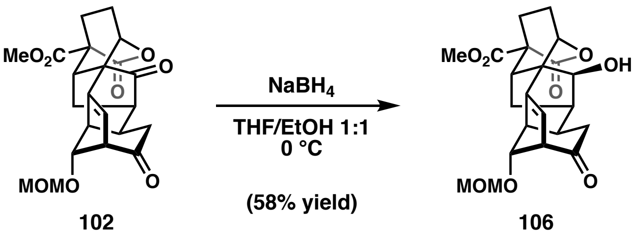
^{13}C NMR (101 MHz, $CDCl_3$): δ 211.5, 208.3, 169.1, 169.1, 95.7, 81.0, 76.9, 74.1, 56.6, 55.8, 53.8, 53.0, 52.8, 52.6, 48.9, 45.8, 45.0, 44.6, 44.5, 28.0, 24.2, 24.2, 20.1.

FTIR (NaCl, thin film): 2954, 2915, 2832, 1746, 1711, 1462, 1443, 1375, 1298, 1262, 1221, 1152, 1103, 1049, 916, 753 cm^{-1}.

HRMS: (FAB) calc'd for $C_{23}H_{29}O_9$ $[M + H]^+$ 449.1811, found 449.1801.

$[\alpha]_D^{25}$ = –14° (*c* = 0.24, $CHCl_3$).

Preparation of alcohol 106:



In a 50-mL round-bottomed flask, diketone **102** was dissolved in THF (3.2 mL) and EtOH (3.2 mL). The solution was cooled to 0 °C in an ice bath, and $NaBH_4$ (61 mg, 1.61 mmol, 5 equiv) was added and stirred for 30 minutes while maintained at 0 °C. At this time the reaction was not done (monitored by LCMS, difficult to monitor by TLC because the starting material and product are nearly indistinguishable), and another portion of $NaBH_4$ was added (61 mg, 1.61 mmol, 5 equiv). The reaction was allowed to stir for another 55 minutes at 0 °C, and then was quenched via the addition of sat. NH_4Cl (6 mL) and H_2O (6 mL). The reaction was allowed to warm to room temperature, and then was diluted with EtOAc (20 mL). The biphasic mixture was transferred to a separatory funnel and the layers were separated. The aqueous layer was extracted with additional EtOAc (4 x 20 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the crude residue by silica gel chromatography (67% to 75% EtOAc in hexanes) afforded secondary alcohol **106** (78 mg, 0.187 mmol, 58% yield) as a white solid.

Notes:

(1) This reaction is difficult to monitor by TLC because the product and starting material appear nearly identical.

(2) Poor yield results from over-reduction of the methyl ester. Some over reduction is inevitable under these conditions while trying to achieve full conversion. However, for good yields, it is still important to monitor this reaction carefully to avoid this as much as possible.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 5.31 (d, *J* = 2.7 Hz, 1H), 4.74 (d, *J* = 4.4 Hz, 1H), 4.72 (d, *J* = 6.8 Hz, 1H), 4.69 (d, *J* = 6.8 Hz, 1H), 4.57 (dd, *J* = 6.0, 4.4 Hz, 1H), 4.09 (t, *J* = 4.7 Hz, 1H), 3.80 (s, 3H), 3.36 (s, 3H), 3.34 (dd, *J* = 4.5, 2.7 Hz, 1H), 2.87 – 2.78 (m, 2H), 2.73 – 2.63 (m, 2H), 2.48 – 2.31 (m, 2H), 2.30 – 2.18 (m, 2H), 2.08 (q, *J* = 4.2 Hz, 1H), 2.03 (d, *J* = 12.5 Hz, 1H), 1.99 – 1.92 (m, 2H), 1.83 – 1.75 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 204.3, 171.5, 169.5, 143.9, 122.1, 96.6, 79.7, 75.3, 73.2, 59.9, 56.0, 55.9, 53.0, 52.6, 44.3, 44.3, 42.4, 42.1, 35.3, 30.5, 29.1, 22.0.

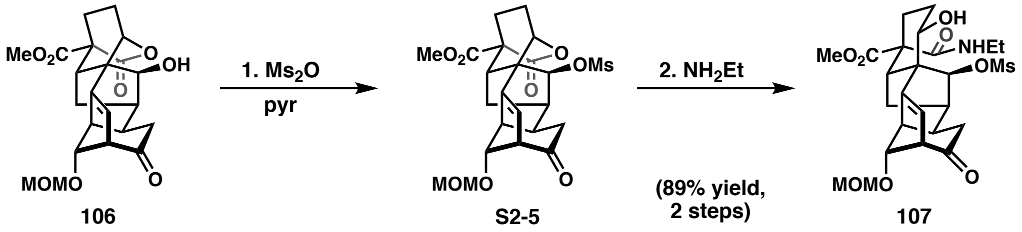
FTIR (NaCl, thin film): 3442, 2949, 1736, 1702, 1436, 1300, 1150, 1112, 1069, 1046, 918, 730 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{22}H_{27}O_8$ $[M + H]^+$ 419.1700, found 419.1703.

$[\alpha]_D^{25}$ = +219° (*c* = 0.34, $CHCl_3$).

TLC (67%EtOAc/33%Hexanes), R*f*: 0.4 (UV, brown in *p*-anisaldehyde)

Preparation of mesylate *N*-ethyl amide 107:



In a 100-mL round-bottom flask, alcohol **106** and Ms_2O (stored in glovebox, brought out a portion in a vial, 801 mg, 4.60 mmol, 10 equiv) added, followed by pyridine (freshly distilled over CaH_2, 7 mL), and was allowed to stir at room temperature for 50 minutes. The reaction was then carefully quenched with sat. $NaHCO_3$ (30 mL), and diluted with EtOAc (30 mL). The biphasic mixture was transferred to a separatory funnel and the layers were separated. The aqueous layer was extracted with EtOAc (3 x

20 mL), and the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the crude residue by silica gel chromatography (1% to 1.5% to 2% MeOH in CH_2Cl_2) afforded mesylate **S2-5**. The material was carried forward into the next step, and a yield was obtained over two steps. ^{1}H NMR data is provided.

^{1}H NMR (500 MHz, Chloroform-*d*): δ 5.44 (d, *J* = 2.7 Hz, 1H), 4.86 – 4.84 (m, 1H), 4.79 (dd, *J* = 4.3, 1.0 Hz, 1H), 4.74 (d, *J* = 6.8 Hz, 1H), 4.72 (d, *J* = 6.8 Hz, 1H), 4.59 (dd, *J* = 6.0, 4.3 Hz, 1H), 3.82 (s, 3H), 3.40 – 3.37 (m, 4H), 3.06 (s, 3H), 2.93 (t, *J* = 6.1 Hz, 1H), 2.86 (dd, *J* = 18.3, 10.6 Hz, 1H), 2.73 – 2.65 (m, 2H), 2.50 (dt, *J* = 10.2, 4.7 Hz, 1H), 2.45 – 2.41 (m, 1H), 2.34 (ddd, *J* = 13.0, 11.5, 5.3 Hz, 1H), 2.26 (tdd, *J* = 11.5, 4.9, 2.8 Hz, 1H), 2.13 – 2.09 (m, 2H), 2.01 (ddd, *J* = 13.2, 11.1, 2.9 Hz, 1H), 1.79 (ddd, *J* = 13.4, 10.8, 5.2 Hz, 1H).

A 2-dram vial was charged with mesylate **S2-5** and neat NH_2Et (3 mL), and sealed with a vial cap. The reaction was stirred for 12 hours at room temperature, and then carefully (caution: NH_2Et boils below room temperature) unscrewed to let the NH_2Et evaporate. Purification of the crude residue by silica gel chromatography (2% to 2.5% MeOH in CH_2Cl_2) afforded secondary amide **107** (221 mg, 0.410 mmol, 89% yield over two steps).

Note: Neat NH_2Et was obtained from distillation of 70%NH_2Et/ 30% H_2O solution, using a cold finger (with dry ice/acetone) to condense the very volatile NH_2Et, and stored over KOH pellets in the freezer.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.62 (t, *J* = 5.4 Hz, 1H), 5.67 (d, *J* = 2.8 Hz, 1H), 5.16 (d, *J* = 4.5 Hz, 1H), 4.74 (d, *J* = 6.8 Hz, 1H), 4.70 (d, *J* = 6.8 Hz, 1H), 4.55 (dd, *J* =

6.0, 4.4 Hz, 1H), 4.09 (td, *J* = 7.0, 3.9 Hz, 1H), 3.77 (s, 3H), 3.72 (d, *J* = 7.7 Hz, 1H), 3.36 (s, 3H), 3.33 (dd, *J* = 4.4, 2.7 Hz, 1H), 3.29 (dd, *J* = 7.4, 5.8 Hz, 1H), 3.27 – 3.22 (m, 1H), 3.08 (s, 3H), 3.05 (d, *J* = 6.1 Hz, 1H), 2.99 (dd, *J* = 9.9, 7.4 Hz, 1H), 2.81 (dd, *J* = 18.2, 10.6 Hz, 1H), 2.58 (d, *J* = 18.2 Hz, 1H), 2.43 (ddd, *J* = 10.2, 6.1, 3.7 Hz, 1H), 2.35 (q, *J* = 4.7 Hz, 1H), 2.29 – 2.23 (m, 2H), 1.96 – 1.84 (m, 3H), 1.78 – 1.72 (m, 1H), 1.14 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 203.6, 175.3, 170.8, 148.3, 124.1, 96.5, 80.5, 79.0, 66.2, 59.4, 56.6, 55.9, 53.1, 52.3, 42.7, 42.5, 41.2, 41.0, 38.4, 36.3, 34.8, 28.9, 26.7, 23.2, 14.3.

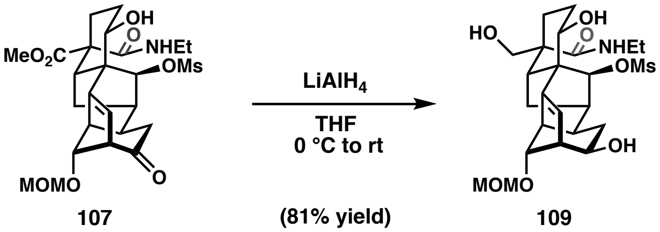
FTIR (NaCl, thin film): 3383, 3285, 2953, 2918, 1732, 1698, 1661, 1652, 1539, 1330, 1174, 1113, 1045, 950, 916, 843, 731 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{25}H_{36}O_{10}NS$ [M + H]$^+$ 542.2054, found 542.2046.

$[\alpha]_D^{25}$ = +175° (*c* = 0.33, $CHCl_3$).

TLC (100% EtOAc), R*f*: 0.5 (UV, brown in *p*-anisaldehyde)

Preparation of triol 109:



A 100-mL round-bottom flask was charged with ester **107** (182 mg, 0.336 mmol, 1 equiv), azeotroped with PhMe (2 x 10 mL) and dried under high vacuum. The substrate was then dissolved in THF (6.7 mL), and cooled to 0 °C in an ice bath. $LiAlH_4$ (1 M in THF, 0.67 mL, 0.67 mmol) was added, and the reaction was allowed to stir for 20 minutes at 0 °C. At this time, additional portions of $LiAlH_4$ were added in 10 minute intervals for a total of (3 x 0.33 mL, 3 x 0.336, 3 x 1 equiv) and the reaction was allowed to stir for an additional 10 minutes after the last portion was added. The reaction was then carefully quenched with H_2O (15 mL) and aqueous sat. Rochelle's salt (20 mL), and diluted with Et_2O (40 mL). The biphasic mixture was then vigorously stirred for 45 minutes, and then transferred to a separatory funnel. The layers were separated, and the aqueous layer was extracted with 20% IPA/ 80% $CHCl_3$ (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the crude residue by silica gel chromatography (2% to 2.5% to 3% to 3.5% to 4% MeOH in CH_2Cl_2) afforded triol **109** (140 mg, 0.271 mmol, 81% yield).

^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.11 (br t, *J* = 5.4 Hz, 1H), 6.02 (d, *J* = 9.1 Hz, 1H), 5.75 (d, *J* = 2.4 Hz, 1H), 4.99 (dd, *J* = 4.5, 0.8 Hz, 1H), 4.72 – 4.70 (m, 1H), 4.70 – 4.68 (m, 1H), 4.28 (t, *J* = 5.5 Hz, 1H), 4.20 (dd, *J* = 8.9, 3.6 Hz, 1H), 4.03 (tdd, *J* = 9.8, 5.5, 2.4 Hz, 1H), 3.72 (dd, *J* = 10.7, 4.1 Hz, 1H), 3.57 (dd, *J* = 10.8, 5.2 Hz, 1H), 3.40 (s, 3H), 3.33 – 3.27 (m, 3H), 3.23 (s, 3H), 2.96 (td, *J* = 5.4, 2.4 Hz, 1H), 2.73 (t, *J* = 5.8 Hz, 1H), 2.54 (ddd, *J* = 16.0, 11.6, 10.2 Hz, 1H), 2.37 (q, *J* = 4.7 Hz, 1H), 2.22 (d, *J* = 9.3 Hz, 1H), 2.15 – 2.09 (m, 2H), 1.95 – 1.65 (m, 5H), 1.47 – 1.29 (m, 2H), 1.18 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 178.7, 147.5, 124.7, 96.1, 84.4, 78.9, 72.1, 65.1, 64.9, 55.8, 52.4, 48.2, 47.2, 42.2, 42.2, 41.5, 38.4, 34.6, 31.4, 31.2, 30.8, 27.1, 23.6, 14.4.

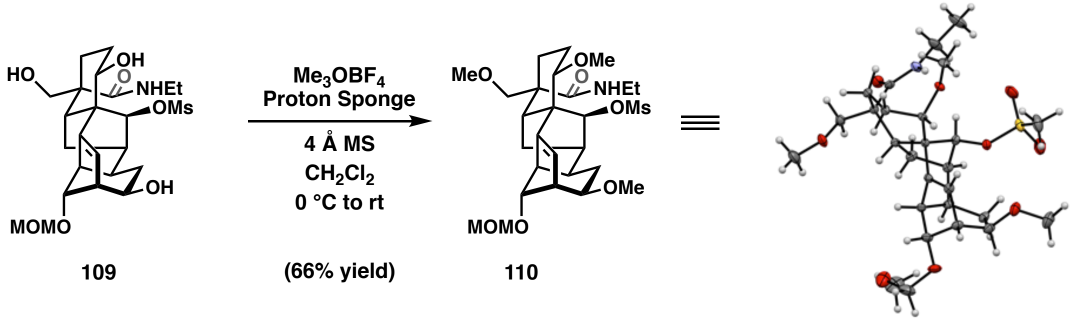
FTIR (NaCl, thin film): 3564, 3304, 2941, 2889, 1620, 1557, 1455, 1397, 1349, 1172, 1042, 998, 971, 941, 916, 846, 734 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{24}H_{38}O_9NS$ $[M + H]^+$ 516.2262, found 516.2260.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = +0.582° (*c* = 0.38, $CHCl_3$).

TLC (100% EtOAc), R*f*: 0.1 (UV, brown in *p*-anisaldehyde)

Preparation of trimethylether 110:



A 100-mL, round-bottomed flask was charged with triol **109** (135 mg, 0.263 mmol, 1.0 equiv), equipped with a rubber septum, purged with N_2, and cooled to 0 °C in an ice bath. Meanwhile, Me_3OBF_4 (0.583 g, 3.94 mmol, 15 equiv), Proton Sponge (0.844 g, 3.94 mmol, 15 equiv), and activated 4 Å MS (850 mg) were added to a 40 mL vial in the glovebox, brought out of the glovebox, and added to the flask containing the substrate. The mixture was then suspended in CH_2Cl_2 (5.2 mL), and allowed to stir for 24 hours, allowing the reaction to warm up to room temperature over this period. The reaction mixture was filtered through a plug of silica gel and celite that had been pre-packed with EtOAc and rinsed further with EtOAc and concentrated *in vacuo*. The resulting crude residue was dissolved in CH_2Cl_2 (20 mL) and ashed with aqueous sat. $NaHSO_3$ (6 x 20 mL), H_2O (1 x 20 mL) and sat. $NaHCO_3$ (1 x 20 mL). The organic layer was then dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (60% to 65% to 67% EtOAc in hexanes) to afford trimethyl ether **110** (96 mg, 0.173 mmol, 66% yield) as a white solid.

A sample was recrystallized by vapor diffusion with EtOAc/Hexanes to afford crystals suitable for X-ray diffraction analysis.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.41 (t, *J* = 4.9 Hz, 1H), 5.65 (d, *J* = 2.4 Hz, 1H), 5.14 (dd, *J* = 4.5, 0.9 Hz, 1H), 4.72 (d, *J* = 6.6 Hz, 1H), 4.70 (d, *J* = 6.6 Hz, 1H), 4.28 (t, *J* = 5.6 Hz, 1H), 3.72 – 3.70 (m, 1H), 3.59 (ddd, *J* = 9.7, 4.9, 3.7 Hz, 1H), 3.42 (s, 3H), 3.39 (s, 3H), 3.4–3.36 (m, 2H), 3.37 (s, 3H), 3.34 – 3.30 (m, 1H), 3.29 (s, 3H), 3.27 – 3.23 (m, 1H), 3.21 – 3.16 (m, 1H), 3.07 (s, 3H), 3.03 (ddd, *J* = 5.5, 4.8, 2.3 Hz, 1H), 2.71 (t, *J* = 5.6 Hz, 1H), 2.43 (dd, *J* = 10.2, 7.0 Hz, 1H), 2.32 – 2.27 (m, 1H), 2.26 – 2.17 (m, 1H), 2.09 – 2.01 (m, 1H), 1.97 (dt, *J* = 15.4, 3.7 Hz, 1H), 1.88 – 1.82 (m, 2H), 1.72 (dt, *J* = 13.6, 6.6 Hz, 1H), 1.57 (dd, *J* = 14.3, 10.2 Hz, 1H), 1.39 – 1.28 (m, 1H), 1.16 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 176.0, 146.4, 124.4, 96.0, 81.5, 78.7, 77.8, 75.2, 74.3, 59.3, 56.0, 55.8, 55.7, 51.6, 47.9, 44.1, 42.5, 41.0, 38.7, 37.3, 34.2, 31.6, 28.3, 27.1, 23.8, 23.0, 13.9.

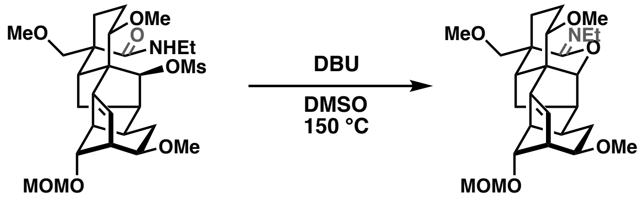
FTIR (NaCl, thin film): 3288, 3076, 2936, 2982, 2822, 1650, 1574, 1557, 1334, 1175, 1099, 1041, 95, 851, 733 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{27}H_{44}O_9NS$ $[M + H]^+$ 558.2731, found 558.2726.

$[\alpha]_D^{25}$ = –3.34° (*c* = 0.62, $CHCl_3$).

TLC (100% EtOAc), R*f*: 0.5 (UV, grey/purple in *p*-anisaldehyde)

Preparation of imidate 111:



110 (76% yield) 111

A 1-dram vial was charged with secondary amide **110** (8 mg, 0.0143 mmol, 1 equiv) and DMSO (0.3 mL). DBU (5 µL, 0.0334 mmol, 2.33 equiv) added, and the headspace of the vial was filled with argon and sealed. The reaction was heated to 150 °C in a pre-heated heating block, and was allowed to stir at this temperature for 20 hours, during which time the reaction mixture turns brown. The reaction was then cooled to room temperature, the vial cap was removed and replaced with a high vacuum adaptor. The vial was placed under vacuum while heating to 70 °C to remove the DMSO. The resulting crude residue was purified by preparative thin layer chromatography (mobile phase: 100% EtOAc). A second preparative thin layer chromatography (mobile phase: 30% acetone/ 70% hexanes) furnished analytically pure hexacyclic imidate **110** (5 mg, 0.0109 mmol, 76% yield).

^{1}H NMR (400 MHz, Chloroform-*d*): δ 6.01 (d, J = 2.3 Hz, 1H), 4.81 (s, 1H), 4.69 (d, J = 6.6 Hz, 1H), 4.66 (d, J = 6.6 Hz, 1H), 4.09 (t, J = 5.5 Hz, 1H), 3.61 (dd, J = 11.0, 6.7 Hz, 1H), 3.58 – 3.51 (m, 3H), 3.40 (s, 3H), 3.39 (s, 3H), 3.34 (s, 3H), 3.28 (s, 3H), 3.24 (dd, J = 7.3, 2.3 Hz, 1H), 3.20 (dd, J = 7.2, 2.2 Hz, 1H), 2.80 (dt, J = 5.6, 2.7 Hz, 1H), 2.66 – 2.58 (m, 1H), 2.39 (dt, J = 7.0, 2.0 Hz, 1H), 2.31 (t, J = 6.0 Hz, 1H), 2.20 (ddt, J =

13.3, 6.8, 3.5 Hz, 1H), 2.10 – 2.02 (m, 1H), 1.87 – 1.77 (m, 2H), 1.76 – 1.70 (m, 2H), 1.46 (tdd, *J* = 12.6, 11.0, 6.7 Hz, 1H), 1.31 – 1.22 (m, 2H), 1.05 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 158.9, 147.5, 125.3, 96.0, 81.2, 78.1, 77.2, 76.3, 73.5, 59.3, 55.9 (two overlapping ^{13}C signals), 55.7, 51.4, 49.1, 46.3, 44.5, 42.1, 40.2, 40.1, 32.4, 31.5, 30.4, 27.2, 26.3, 15.6.

HSQC, HMBC, and ^{1}H-^{15}N HMBC are provided below. The ^{1}H-^{15}N HMBC shows a ^{15}N signal at 235 ppm.

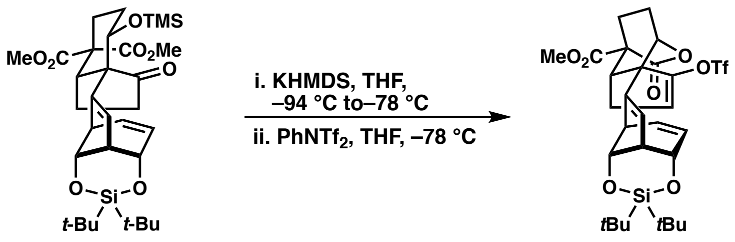
FTIR (NaCl, thin film): 2930, 2822, 1668, 1455, 1368, 1194, 1152, 1104, 1043, 1002, 920, 840, 732 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{27}H_{40}O_6N$ $[M + H]^+$ 462.2850, found 462.2863.

$[\alpha]_D^{25}$ = –92.7° (*c* = 0.25, $CHCl_3$).

TLC (100% EtOAc), R*f*: 0.5 (UV, yellow/purple in *p*-anisaldehyde)

Preparation of enol triflate 77 from 118:



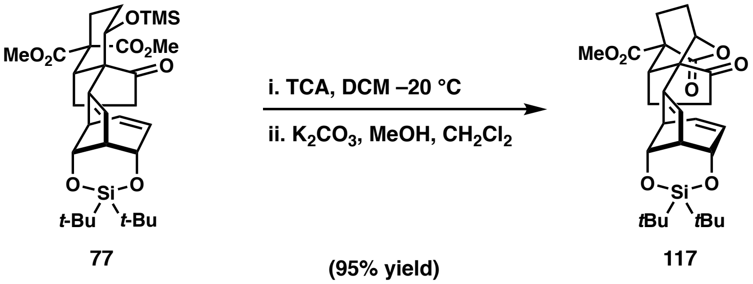
77 118

A 100-mL, round-bottomed flask was charged with ketone **77** (0.526 g, 0.85 mmol, 1.0 equiv), and azeotroped PhMe from the solvent system (3 x 10 mL), and put under high vacuum over night. The following day, the flask was equipped with a stir-bar and rubber septum, purged with N_2, dissolved in THF (43 mL), and cooled to –94 °C in a acetone/ liquid N_2 bath. KHMDS solution (0.5 M in PhMe, 2.04 mL, 1.02 mmol, 1.2

equiv) was added dropwise via syringe, dry ice was added to the bath and the reaction was allowed to warm to –78 °C, and was allowed to stir for an additional 30 minutes at –78 °C. A THF solution of $PhNTf_2$ (0.365 g, 1.02 mmol, 1.2 equiv) in THF (5 mL) was added dropwise via syringe, and the reaction mixture was allowed to stir for an additional 10 minutes at –78 °C. The reaction was then quenched with sat. aqueous NH_4Cl solution (30 mL), and allowed to warm to room temperature. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (4 x 75 mL). The organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (12% ethyl acetate in hexanes to elute recovered starting material, and then 20% ethyl acetate in hexanes to elute the product) afford lactonized enol triflate **118** (0.281 g, 0.434 mmol, 51% yield) as a white foam and recovered **77** (0.298 mmol, 0.184 mmol, 35% yield).

Characterization data shown below.

Preparation of lactone 117:



A 250-mL, round-bottomed flask was charged with silyl ether **77** (1.5 g, 2.43 mmol, 1.0 equiv), and CH_2Cl_2 (50 mL), and cooled to –20 °C in a cryocool. Trichloroacetic acid (15.86 g, 97.04 mmol, 40 equiv) was added, and the reaction vessel was sealed and allowed to continue stirring at –20 °C for 36 hours. The reaction was then carefully quenched with sat. $NaHCO_3$ (100 mL) at –20 °C, and let warm to room temperature. The biphasic mixture was then transferred to a 500-mL Erlenmeyer flask, and vigorously stirred for an additional 10 minutes. The aqueous phase was ensured to be basic with pH paper. The mixture was then transferred to a separatory funnel and the layers were separated. Aqueous phase was extracted with CH_2Cl_2 (3 x 50 mL), and added to a round bottomed flask, and MeOH (20 mL) was added followed by K_2CO_3 (1.5 g). The mixture was allowed to stir at room temperature for 2 hours. The reaction was monitored by TLC and indicated full conversion. If the reaction is going slowly, more K_2CO_3 and MeOH can be added without deleterious effects. At this time, H_2O (20 mL) was added, and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (3 x 30 mL), and the organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (11% acetone in hexanes to 12.5% acetone in hexanes) to afford lactone **117** (1.185 g, 2.303 mmol, 95% yield) as a white foam.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 6.10 (ddd, *J* = 9.5, 6.2, 1.1 Hz, 1H), 5.79 (d, *J* = 3.8 Hz, 1H), 5.75 (ddd, *J* = 9.5, 4.3, 1.9 Hz, 1H), 4.93 (dd, *J* = 3.4, 1.8 Hz, 1H), 4.35 (t, *J* = 4.7 Hz, 1H), 4.21 (ddd, *J* = 4.1, 3.1, 0.8 Hz, 1H), 3.83 (s, 3H), 3.13 – 3.07 (m, 2H), 3.03 (ttd, *J* = 4.2, 2.5, 1.1 Hz, 1H), 2.52 (dddd, *J* = 14.4, 10.6, 9.2, 4.1 Hz, 1H), 2.41 – 2.29 (m, 2H), 2.18 (ddd, *J* = 17.7, 8.8, 4.1 Hz, 1H), 2.04 (ddt, *J* = 13.2, 10.3, 1.9 Hz, 1H), 1.95 (ddd, *J* = 14.3, 6.7, 3.4 Hz, 1H), 1.91 – 1.82 (m, 1H), 1.75 (dddd, *J* = 14.3, 10.4, 8.9, 6.7 Hz, 1H), 1.05 (s, 9H), 0.99 (s, 9H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 212.0, 169.8, 169.6, 156.4, 134.1, 130.1, 127.0, 78.6, 77.5, 65.7, 58.0, 53.5, 52.9, 45.9, 44.8, 43.0, 35.3, 28.8, 28.2, 26.1, 23.5, 22.3, 21.2, 20.7.

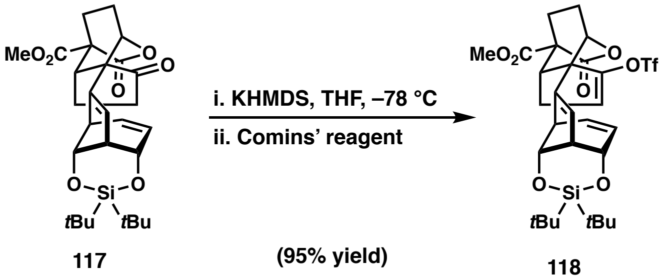
FTIR (NaCl, thin film): 3030, 2974, 2937, 2895, 2860, 1766, 1743, 1476, 1464, 1364, 1271, 1106, 1063, 995, 826 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{28}H_{42}O_7SiN$ $[M + NH_4]^+$ 532.2725, found 532.2720.

$[\alpha]_D^{25}$ = +9.9° (c = 0.66, CHCl$_3$).

TLC (30%EtOAc/70%Hexanes), R$_f$: 0.4 (UV, teal in *p*-anisaldehyde)

Preparation of enol triflate 118 from 117:



A 250-mL, round-bottomed flask was charged with ketone **117** (1.82 g, 3.53 mmol, 1.0 equiv), and azeotroped PhMe from the solvent system (3 x 10 mL), and put under high vacuum over night. The following day, the flask was equipped with a stir-bar and rubber septum, purged with N$_2$, dissolved in THF (35 mL), and cooled to –78 °C in a dry ice/ acetone bath. KHMDS solution (0.5 M in PhMe, 8.48 mL, 4.24 mmol, 1.2 equiv) was added dropwise via syringe causing the reaction mixture to turn yellow. Meanwhile, in a separate flame-dried 50-mL conical flask, Comins' reagent (1.67 g, 4.24 mmol, 1.2 equiv) was dissolved in THF (10 mL) under N$_2$. After the substrate and KHMDS solution had been stirring for 30 minutes at –78 °C, the Comins' reagent solution was added dropwise via cannula, and the solution was allowed to stir for an additional 20 minutes at

–78 °C. The reaction was quenched with sat. $NaHCO_3$ (30 mL), the bath was removed and allowed to warm to room temperature. Diluted with Et_2O (40 mL), transferred to a separatory funnel, and the layers were separated. Aqueous extracted with Et_2O (3 x 40 mL). The organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (11% acetone in hexanes to 12.5% acetone in hexanes) to afford enol triflate **118** (2.171 g, 3.36 mmol, 95% yield) as a white foam.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 6.06 (ddd, *J* = 9.5, 6.1, 1.2 Hz, 1H), 5.73 (ddd, *J* = 9.5, 4.4, 1.6 Hz, 1H), 5.70 (t, *J* = 2.6 Hz, 1H), 5.59 (dd, *J* = 3.8, 0.7 Hz, 1H), 4.78 (dd, *J* = 3.7, 1.7 Hz, 1H), 4.49 (t, *J* = 4.7 Hz, 1H), 4.23 (ddd, *J* = 4.2, 3.0, 0.8 Hz, 1H), 3.82 (s, 3H), 3.10 (m, 1H), 2.95 (ddd, *J* = 17.8, 9.3, 2.3 Hz, 1H), 2.89 – 2.83 (m, 2H), 2.50 (dt, *J* = 17.8, 2.7 Hz, 1H), 2.34 (ddd, *J* = 13.4, 11.4, 3.5 Hz, 1H), 2.20 – 2.04 (m, 2H), 1.79 (ddd, *J* = 13.4, 10.9, 6.6 Hz, 1H), 1.08 (s, 9H), 1.00 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 169.5, 169.0, 156.9, 145.2, 133.4, 129.9, 126.1, 118.3 (q, *J*=321 Hz, SO_2**C**F_3), 114.3, 77.2, 75.3, 65.2, 56.8, 53.0, 52.7, 46.2, 46.2, 43.9, 32.5, 28.8, 28.2, 26.6, 21.9, 21.2, 20.7.

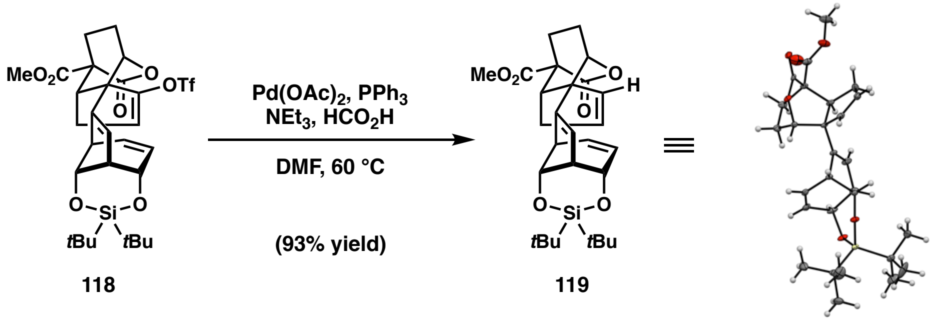
FTIR (NaCl, thin film): 3036, 2938, 2896, 2860, 1769, 1739, 1668, 1476, 1426, 1251, 1217, 1142, 1112, 998, 827 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{29}H_{41}O_9SF_3SiN$ $[M + NH_4]^+$ 664.2218, found 664.2216.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = +123° (*c* = 0.67, $CHCl_3$).

TLC (20%EtOAc/80%Hexanes), R*f*: 0.4 (UV, blue in *p*-anisaldehyde)

Preparation of cyclopentene 119:



A 200-mL, round-bottomed flask was charged with enol triflate **118** (2.28 g, 3.53 mmol, 1.0 equiv), PPh_3 (139 mg, 0.53 mmol, 15 mol %), and $Pd(OAc)_2$ (60 mg, 0.265 mmol, 7.5 mol %). The flask was equipped with a rubber septum, purged with N_2, and dissolved in DMF (35 mL). Then, the reaction mixture was sparged with an Ar balloon for 5 minutes. NEt_3 (3.94 mL, 28.27 mmol, 8 equiv) was added followed by HCO_2H (0.66 mL, 17.67 mmol, 5 equiv) – a cloudy gas was observed upon addition. The reaction was lowered into a 60 °C oil bath, and allowed to continue to stir at that temperature for 20 minutes. The reaction turns black during this time, indicating its completion. The reaction was cooled to room temperature, diluted with sat. NH_4Cl (30 mL), transferred to a separatory funnel and diluted with Et_2O (30 mL). The layers were separated and the aqueous extracted with Et_2O (3 x 30 mL). The organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (10% acetone in hexanes to 12.5% acetone in hexanes, the product is very crystalline, it was loaded in PhMe where some of the product elutes but is collected) to afford olefin **119** (1.64 g, 3.28 mmol, 93% yield) as a crystalline solid.

Crystals suitable for x-ray diffraction could be obtained upon slow evaporation from acetone/hexanes.

Melting Point: 225–230 °C

^{1}H NMR (400 MHz, Chloroform-*d*): δ 6.06 (ddd, *J* = 9.5, 6.1, 1.2 Hz, 1H), 5.76 – 5.68 (m, 2H), 5.51 (d, *J* = 3.8 Hz, 1H), 5.48 – 5.44 (m, 1H), 4.61 (dd, *J* = 3.9, 1.6 Hz, 1H), 4.46 (td, *J* = 4.2, 0.9 Hz, 1H), 4.22 (ddd, *J* = 4.2, 3.1, 0.7 Hz, 1H), 3.80 (s, 3H), 3.04 (ttd, *J* = 4.2, 2.4, 1.0 Hz, 1H), 2.95 – 2.85 (m, 2H), 2.79 (dd, *J* = 4.9, 5.7, 1H), 2.54 – 2.42 (m, 1H), 2.27 (ddd, *J* = 13.1, 11.7, 3.2 Hz, 1H), 2.17 (dddd, *J* = 14.2, 11.1, 3.3, 1.6 Hz, 1H), 1.99 (dddd, *J* = 13.9, 11.6, 6.2, 3.8 Hz, 1H), 1.85 (ddd, *J* = 13.1, 11.0, 6.2 Hz, 1H), 1.07 (s, 9H), 1.00 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 170.4, 170.3, 161.3, 134.7, 132.0, 131.3, 129.1, 121.8, 78.7, 77.3, 65.9, 59.8, 53.4, 52.7, 46.4, 45.7, 44.4, 38.2, 28.8, 28.2, 26.8, 22.4, 21.2, 20.7. A ^{13}C signal is observed to be overlapping with residual $CDCl_3$ at 77.3, resolved peaks are seen in the HSQC spectrum, provided below.

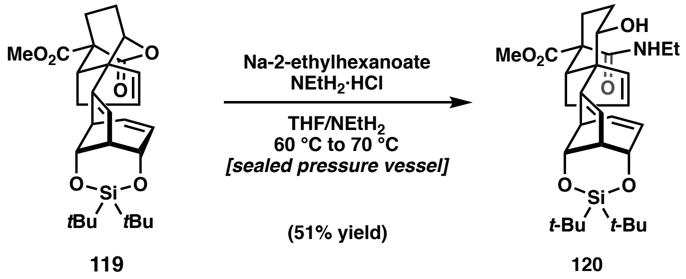
FTIR (NaCl, thin film): 3053, 2937, 2898, 2256, 1760, 1748, 1732, 1476, 1463, 1444, 1364, 1283, 1109, 1063, 993, 911 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{28}H_{39}O_6Si$ $[M + H]^+$ 499.2510, found 499.2512.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = +166° (*c* = 0.40, $CHCl_3$).

TLC (20%EtOAc/80%Hexanes), R*f*: 0.4 (UV, teal in *p*-anisaldehyde)

Preparation of *N*-ethyl amide 120:



To a 75-mL pressure vessel containing lactone **119** (437 mg, 0.877 mmol, 1 equiv), sodium 2-ethylhexanoate (657 mg, 3.95 mmol, 4.5 equiv), ethylamine hydrochloride (161 mg, 1.97 mmol, 2.25 equiv) were added, followed by THF (9 mL) and neat $NEtH_2$ (4 mL). The vessel was sealed (with a Teflon cap that had a perfluoro O-ring), and heated to 60 °C in an oil bath. The reaction was allowed to stir at 60 °C for 2 days, and the reaction progress was monitored. At this time, the reaction had not gone to completion, so the flask was re-sealed and the bath temperature was raised to 70 °C and stirred for another 2 days at this temperature. The reaction was then cooled to room temperature, and transferred to a separatory funnel with EtOAc (30 mL) and aqueous 0.5 M NaOH (20 mL). The layers were separated, and the aqueous phase was extracted with EtOAc (3 x 20 mL) and CH_2Cl_2 (2 x 20 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by silica gel chromatography (20% to 30% to 40% ethyl acetate in hexanes) to afford secondary amide **120** as a white foam (243 mg, 0.447 mmol, 51% yield).

Note: Neat NH_2Et was obtained from distillation of 70%NH_2Et/ 30% H_2O solution, using a cold finger (with dry ice/acetone) to condense the very volatile NH_2Et, and stored over KOH pellets in the freezer.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 6.22 (t, *J* = 5.6 Hz, 1H), 6.16 – 6.05 (m, 2H), 5.65 (ddd, *J* = 9.4, 4.4, 1.9 Hz, 1H), 5.50 (dt, *J* = 5.9, 1.9 Hz, 1H), 5.33 (s, 1H), 4.54 (t, *J* = 4.8 Hz, 1H), 4.17 (ddd, *J* = 4.0, 2.9, 0.7 Hz, 1H), 3.91 (t, *J* = 4.4 Hz, 1H), 3.68 (s, 3H), 3.28 (dqd, *J* = 14.5, 7.2, 5.7 Hz, 1H), 3.22 – 3.10 (m, 2H), 3.01 – 2.96 (m, 1H), 2.90 (t, *J* = 5.3 Hz, 1H), 2.37 – 2.26 (m, 3H), 2.09 – 2.02 (m, 1H), 1.80 – 1.69 (m, 3H), 1.11 – 1.06 (m, 12H), 1.00 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 174.9, 168.6, 163.6, 135.6, 135.1, 132.8, 128.5, 122.0, 76.6, 66.9, 66.2, 56.9, 55.5, 52.9, 46.4, 46.3, 46.2, 35.2, 34.7, 28.9, 28.3, 25.6, 21.2, 20.7, 18.0, 14.6.

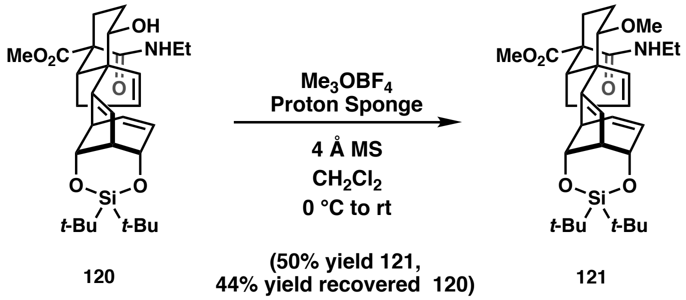
FTIR (NaCl, thin film): 3409, 3033, 3969, 6935, 2896, 2859, 2242, 1713, 1668, 1520, 1229, 1101, 826, 732 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{30}H_{46}O_6NSi$ $[M + H]^+$ 544.3089, found 544.3102.

$[\alpha]_D^{25}$ = +137° (*c* = 1.00, $CHCl_3$).

TLC (50%EtOAc/ 50% Hexanes), R*f*: 0.25 (UV, yellow in *p*-anisaldehyde)

Preparation of methyl ether 121:



A 250-mL, round-bottomed flask was charged with alcohol **120** (787 mg, 1.447 mmol, 1.0 equiv), equipped with a rubber septum, purged with N_2, and cooled to 0 °C in an ice bath. Meanwhile, Me_3OBF_4 (0.856 g, 5.79 mmol, 4 equiv), Proton Sponge (1.24 g, 5.79 mmol, 4 equiv), and activated 4 Å MS (2.36 mg) were added to a 40 mL vial in the glovebox, brought out of the glovebox, and added to the flask containing the substrate. The mixture was then suspended in CH_2Cl_2 (14.5 mL), and allowed to stir for 48 hours, allowing the reaction to warm up to room temperature over this period. The reaction mixture was filtered through a plug of silica gel and celite that had been pre-packed with EtOAc and rinsed further with EtOAc and concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (15% in hexanes to elute the product to 20% acetone in hexanes to elute the starting material) to afford methyl ether **121** (399 mg, 71.6 mmol, 50% yield) as a white solid and recovered alcohol **120** (350 mg, 0.637 mmol, 44% yield).

^{13}C NMR (101 MHz, CDCl$_3$): δ 174.9, 168.7, 164.6, 135.9, 132.8, 131.7, 128.2, 121.1, 77.2, 76.8, 66.4, 57.5, 57.0, 55.7, 52.8, 46.6, 46.1, 46.0, 35.4, 34.8, 28.9, 28.3, 22.0, 21.2, 20.7, 19.2, 14.6.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 6.18 (ddd, *J* = 9.5, 6.1, 1.1 Hz, 1H), 6.11 (t, *J* = 5.6 Hz, 1H), 5.87 (dt, *J* = 5.9, 2.3 Hz, 1H), 5.66 (ddd, *J* = 9.3, 4.4, 1.9 Hz, 1H), 5.45 (dt, *J* = 5.9, 2.0 Hz, 1H), 5.25 (d, *J* = 3.5 Hz, 1H), 4.51 (td, *J* = 4.2, 0.9 Hz, 1H), 4.19 (ddd, *J* = 4.2, 3.1, 0.8 Hz, 1H), 3.70 (s, 3H), 3.38 (dd, *J* = 7.8, 4.0 Hz, 1H), 3.34 – 3.24 (m, 1H), 3.21 (s, 3H), 3.19 – 3.14 (m, 1H), 3.14 – 3.05 (m, 1H), 3.00 – 2.96 (m, 1H), 2.89 – 2.81 (m, 1H), 2.37 (ddt, *J* = 16.4, 8.7, 2.2 Hz, 1H), 2.28 – 2.10 (m, 3H), 1.79 (dddd, *J* = 13.2, 9.0, 7.0, 4.0 Hz, 1H), 1.62 – 1.54 (m, 1H), 1.11 – 1.06 (m, 12H), 1.01 (s, 9H).

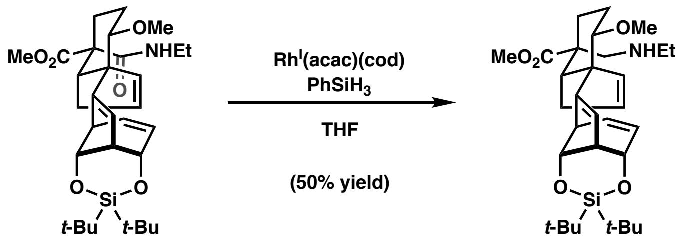
FTIR (NaCl, thin film): 3375, 2970, 2936, 2896, 2860, 1731 1715, 1668, 1652, 1519, 1476, 1463, 1255, 1780, 1104, 991, 826, 732 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{31}H_{48}O_6NSi$ $[M + H]^+$ 558.3245, found 558.3240.

$[\alpha]_D^{25}$ = +122° (*c* = 0.4, $CHCl_3$).

TLC (50%EtOAc/ 50% Hexanes), R*f*: 0.6 (UV, blue in *p*-anisaldehyde)

Preparation of *N*-ethylamine 122:



121 122

A 50-mL, round-bottomed flask was charged with secondary amide **121** (100 mg, 0.179 mmol, 1 equiv), and pumped into the glovebox. Rh^I(acac)(cod) (8.3 mg, 0.0269 mmol, 0.15 equiv) was added followed by THF (1.8 mL) and $PhSiH_3$ (0.44 mL, 3.59

mmol, 20 equiv), was equipped with a rubber septum, brought out of the glovebox and the reaction was put under N_2 via an N_2 inlet needle. The reaction was allowed to stir at room temperature for 13 hours, and was subsequently quenched with aqueous sat. NH_4F solution (6 mL), and the biphasic solution was allowed to stir until the bubbles stopped evolving (30 minutes) The mixture was transferred to a separatory funnel and diluted with EtOAc (15 mL), and the layers were separated. The aqueous layer was extracted with more EtOAc (6 x 15 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (1.25 to 1.4 % 7N NH_3 solution in MeOH/ in CH_2Cl_2) to afford amine **122** (48.7 mg, 0.0895 mmol, 50% yield).

^{1}H NMR (400 MHz, Chloroform-*d*): δ 6.05 (ddd, *J* = 9.5, 6.1, 1.1 Hz, 1H), 5.89 (dt, *J* = 5.9, 2.3 Hz, 1H), 5.64 (ddd, *J* = 9.3, 4.4, 1.9 Hz, 1H), 5.46 (ddd, *J* = 5.8, 2.4, 1.4 Hz, 1H), 5.27 (d, *J* = 3.7 Hz, 1H), 4.45 – 4.37 (m, 1H), 4.23 – 4.19 (m, 1H), 3.58 (s, 3H), 3.54 (dd, *J* = 9.2, 3.3 Hz, 1H), 3.23 (s, 3H), 2.99 – 2.95 (m, 1H), 2.82 – 2.73 (m, 3H), 2.63 – 2.49 (m, 3H), 2.43 (dddd, *J* = 16.0, 9.1, 2.7, 1.5 Hz, 1H), 2.36 – 2.25 (m, 2H), 1.88 – 1.79 (m, 1H), 1.59 – 1.40 (m, 3H), 1.07 (s, 9H), 1.04 – 0.98 (m, 12H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 176.9, 164.6, 135.6, 133.4, 131.1, 128.2, 119.8, 77.7, 76.7, 66.6, 58.7, 57.7, 57.1, 51.5, 47.9, 46.2, 46.1, 46.0, 44.5, 35.4, 28.9, 28.3, 23.7, 21.8, 21.2, 20.6, 15.1.

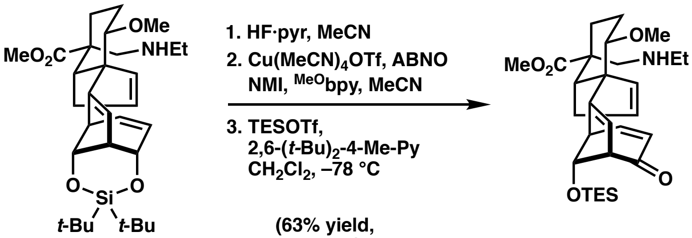
FTIR (NaCl, thin film): 3449, 2965, 2935, 2898, 2859, 1732, 1476, 1103, 992, 827, 731 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{31}H_{50}O_5NSi$ $[M + H]^+$ 544.3453, found 544.3463.

$[\alpha]_D^{25}$ = +84.5° (*c* = 1.26, $CHCl_3$).

TLC (5% 7 N NH_3 in MeOH/ 95% CH_2Cl_2), R_f: 0.5 (UV, blue in *p*-anisaldehyde)

Preparation of enone 123:



122 **123**

A 2-dram vial was charged with silylene **122** (20.2 mg, 0.037 mmol, 1 equiv) and MeCN (1 mL). A solution of HF•Py (pyridine ~30%, HF ~70%, 20.2 mg) in MeCN (0.2 mL) was added, and the reaction was allowed to stir for 40 minutes at room temperature. The reaction was quenched by filtering through a silica gel plug and flushing with lots of 10% 7N NH_3 in MeOH/ 90% CH_2Cl_2 solution, and concentrated *in vacuo*. The crude material was used without further purification.

A 2-dram vial was charged with the crude diol, and dissolved in MeCN (1 mL). A homemade stock-solution [see note below] 0.05M 4,4'-dimethoxy-2,2'-bipyridine (^{MeO}bpy), 0.05 M in ABNO, and 0.2 M *N*-methylimidazole was added to the solution of diol (74 μL, 0.0037 mmol, 0.1 equiv) followed by $Cu(MeCN)_4OTf$ (1.4 mg, 0.0037 mmol, 0.1 equiv) was added, and the clear red/brown reaction mixture was stirred until slightly yellow green, and the TLC indicated the reaction had gone to completion (ca. 90 min), at which point the solution was filtered through a short plug of silica that had been pre-packed with 10% 7N NH_3 in MeOH/ 90% CH_2Cl_2 and flushed with more 10% 7N NH_3 in MeOH/ 90% CH_2Cl_2 to elute the product, and concentrated *in vacuo*. The crude enone was subjected to the next step without further purification.

A 2-dram vial was charged with crude enone, and azeotroped with PhMe (from the solvent system, 2 x 1 mL), and dried under high vacuum. 2,6-(*t*-Bu)$_2$-4-MePy (76 mg, 0.371 mmol, 10 equiv) was added, followed by CH_2Cl_2 (2 mL). The solution was cooled to –78 °C, and TESOTf (40 μL, 0.186 mmol, 5 equiv) was added dropwise via microsyringe. After 10 minutes of stirring at –78 °C, the reaction was quenched via the addition of aqueous sat. $NaHCO_3$ solution 2 mL), and was allowed to warm to room temperature. The layers were separated, and the aqueous layer was extracted with CH2Cl2 (5 x 3 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting crude residue was filtered through a plug of silica gel and filtered with hexanes (to remove the 2,6-(*t*-Bu)$_2$-4-MePy) and then 3% 7N NH_3 solution in MeOH/ 97% CH_2Cl_2 to elute the product, and then concentrated *in vacuo*. The crude residue was purified by preparative thin layer chromatography (3% 7N NH_3 solution in MeOH/ 97% CH_2Cl_2) to afford enone **123** (12 mg, 0.023 mmol, 63% yield) as a clear oil.

Notes for the Stahl oxidation step:

(1) A 0.05 M solution of 4,4’-dimethoxy-2,2’-bipyridine, 0.05M ABNO and 0.2M NMI solution in MeCN could be pre-made and kept in an 8 °C freezer and was stable and good to use for an extended time (>4 months). This homemade stock solution was used in this reaction, and makes it easy to add more catalyst.

(2) This selective oxidation to the enone is very clean and performs well, but oxidation to the diketone has been observed if too much catalyst is added. It is important to monitor this reaction by TLC. It is best to run this reaction carefully,

and start with less catalyst, because more can be added if needed to reach full conversion to the desired product.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 6.94 (ddd, *J* = 9.8, 6.4, 1.6 Hz, 1H), 5.98 – 5.94 (m, 1H), 5.76 (ddd, *J* = 9.8, 2.0, 0.7 Hz, 1H), 5.50 (d, *J* = 3.7 Hz, 1H), 5.38 – 5.35 (m, 1H), 4.65 (td, *J* = 4.5, 1.6 Hz, 1H), 3.61 (s, 3H), 3.46 (dd, *J* = 7.0, 3.0 Hz, 1H), 3.19 (s, 3H), 3.13 – 3.05 (m, 2H), 2.92 (t, *J* = 9.2 Hz, 1H), 2.77 (d, *J* = 11.3 Hz, 1H), 2.64 – 2.52 (m, 3H), 2.43 (dddd, *J* = 15.7, 8.7, 2.6, 1.5 Hz, 1H), 2.33 (ddt, *J* = 15.6, 9.7, 2.2 Hz, 1H), 2.24 – 2.16 (m, 1H), 1.83 – 1.73 (m, 1H), 1.65 – 1.54 (m, 3H), 1.03 (t, *J* = 7.1 Hz, 3H), 0.93 (t, *J* = 7.9 Hz, 9H), 0.64 – 0.53 (m, 6H).

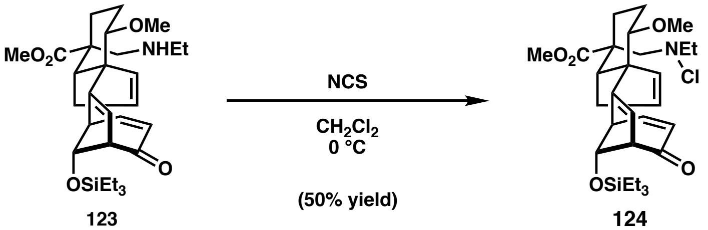
^{13}C NMR (101 MHz, $CDCl_3$): δ 197.0, 176.8, 161.4, 149.2, 132.8, 132.2, 126.6, 120.6, 84.6, 78.2, 62.1, 58.5, 57.4, 57.2, 51.7, 48.2, 47.9, 45.6, 44.5, 34.9, 22.9, 22.5, 15.1, 6.7, 4.7.

HRMS: (ESI-TOF) calc'd for $C_{29}H_{46}O_5NSi$ $[M + H]^+$ 516.3140, found 516.3122.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = +163° (*c* = 0.085, $CHCl_3$).

TLC (5% 7 N NH_3 in MeOH/ 95% CH_2Cl_2), R*f*: 0.5 (UV, blue in *p*-anisaldehyde)

Preparation of *N*-chloroamine 124:



123 **124**

A 10-mL round-bottomed flask was charged with amine **123** (12 mg, 0.0233 mmol, 1 equiv), and CH_2Cl_2 (2.3 mL). The solution was cooled to 0 °C, and *N*-chlorosuccinimide (3.7 mg, 0.028 mmol, 1 equiv) was added. The reaction was allowed to stir for 1 hour at 0 °C, and then the reaction was filtered through a plug of silica gel and flushed with EtOAc. The crude residue was purified by preparative thin layer chromatography (20% EtOAc/ 80% Hexanes) to afford *N*-chloroamine **124** (6 mg, 0.011 mmol, 47% yield) as a clear oil.

Note: This reaction is fairly clean and the poor yield in this case resulted from incomplete conversion (procedure is not optimized). Some starting material was recovered.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 6.93 (ddd, *J* = 9.8, 6.4, 1.6 Hz, 1H), 5.98 – 5.90 (m, 1H), 5.76 (dd, *J* = 9.5, 1.8 Hz, 1H), 5.51 (d, *J* = 3.8 Hz, 1H), 5.37 (ddd, *J* = 5.9, 2.6, 1.5 Hz, 1H), 4.68 (td, *J* = 4.6, 1.6 Hz, 1H), 3.60 (s, 3H), 3.49 (dd, *J* = 7.9, 3.0 Hz, 1H), 3.28 (d, *J* = 14.0 Hz, 1H), 3.19 (s, 3H), 3.13 – 3.01 (m, 3H), 2.97 – 2.88 (m, 3H), 2.46 – 2.26 (m, 3H), 1.84 – 1.75 (m, 1H), 1.70 (dt, *J* = 13.9, 6.6 Hz, 1H), 1.62 – 1.56 (m, 1H), 1.16 (t, *J* = 6.9 Hz, 3H), 0.93 (t, *J* = 7.9 Hz, 9H), 0.58 (q, *J* = 7.7 Hz, 6H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 196.9, 175.9, 161.2, 149.1, 133.0, 131.8, 126.6, 120.6, 84.6, 77.9, 72.3, 62.0, 60.4, 57.3, 57.3, 51.7, 48.4, 47.9, 45.9, 35.3, 23.1, 22.3, 12.8, 6.7, 4.7.

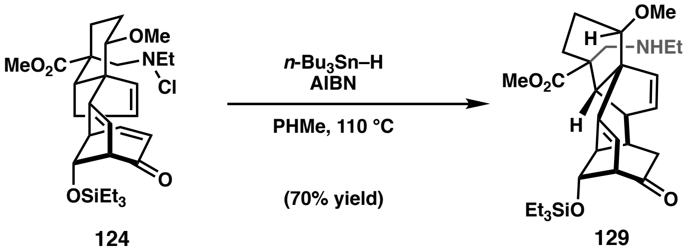
FTIR (NaCl, thin film): 2953, 2933, 2877, 1738, 1731, 1722, 1682, 1455, 1176, 1121, 1100, 1013, 739 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{29}H_{45}O_5NSiCl$ $[M + H]^+$ 550.2750, found 550.2774.

$[\alpha]_D^{25}$ = +122° (c = 0.2, CHCl$_3$).

TLC (20%EtOAc/ 80%Hexanes), R$_f$: 0.5 (UV, blue in *p*-anisaldehyde)

Preparation of cyclization product 129:

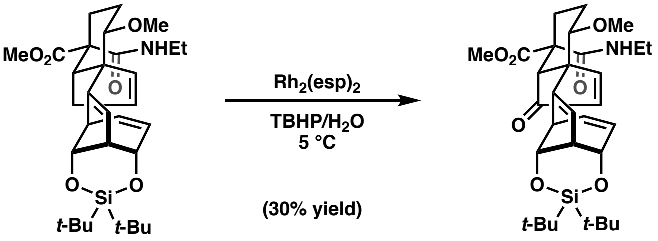


A 1-dram vial was charged with *N*-chloroamine **124** (3 mg, 0.0055 mmol, 1 equiv) and PhMe (1 mL). The reaction was heated to 110 °C in an oil bath, and *n*-Bu$_3$SnH (7.3 µL, 0.027 mmol, 5 equiv) and AIBN (0.45 mg, 0.0028 mmol, 0.5 equiv) was added dropwise as a PhMe solution (0.4 mL). The reaction was allowed to stir for an additional 30 minutes at 110 °C after all of the reagents had been added. The reaction was then cooled to room temperature and concentrated *in vacuo*. The crude residue was purified by preparative thin layer chromatography (2% 7N NH$_3$ solution in MeOH/ 98% CH$_2$Cl$_2$) to afford cyclized **129** (1.8 mg, 0.0035 mmol, 63% yield) as a clear oil.

HRMS: (ESI-TOF) calc'd for $C_{29}H_{46}O_5NSi$ $[M + H]^+$ 516.3140, found 516.3144.

TLC (5% 7 N NH_3 in MeOH/ 95% CH_2Cl_2), R_f: 0.5 (UV, yellow in *p*-anisaldehyde)

Preparation of enone 133:



121 133

A 2-dram vial was charged with cyclopentene **121** (33 mg, 0.0592 mmol, 1 equiv), and *tert*-butyl hydroperoxide solution (70% *tert*-butyl hydroperoxide/ 30% H_2O, 0.8 mL). The solution was cooled to 5 °C in the cryocool, and bis[rhodium(α,α,α’α’-tetramethyl-1,3-benzenedipropionicacid)] ($Rh_2(esp)_2$, 1.5 mg, 0.00198 mmol, 0.03 equiv) was added. The reaction was allowed to stir for 72 hours at 5 °C, and then was quenched by the addition of sat. $Na_2S_2O_3$ (3 mL), and diluted with EtOAc (3 mL). The layers were separated, and the aqueous layer was extracted with more EtOAc (6 x 3 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by preparative thin layer chromatography (50% EtOac/50% hexanes) to afford enone **133** (10 mg, 0.0177 mmol, 30% yield) as a clear oil, that contained ~20% inseparable impurities.

Note: This reaction is not optimized. The poor yield results from unreacted starting material and oxidation to the allylic *tert*-butyl peroxide. Both recovered starting material and allyl *tert*-butyl peroxide could be isolated under these reaction conditions.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.48 (d, *J* = 5.8 Hz, 1H), 6.30 (d, *J* = 5.8 Hz, 1H), 6.17 (ddd, *J* = 9.5, 6.1, 1.1 Hz, 1H), 6.11 (t, *J* = 5.4 Hz, 1H), 5.73 (ddd, *J* = 9.6, 4.5, 1.9 Hz, 1H), 5.38 (dd, *J* = 3.8, 0.7 Hz, 1H), 4.53 (td, *J* = 4.2, 0.9 Hz, 1H), 4.24 – 4.21 (m, 1H), 3.72 (s, 3H), 3.53 (dd, *J* = 10.3, 4.5 Hz, 1H), 3.34 – 3.30 (m, 3H), 3.24 (s, 3H), 3.06 – 3.01 (m, 1H), 2.79 (dd, *J* = 6.2, 4.3 Hz, 1H), 2.38 – 2.30 (m, 1H), 1.99 (td, *J* = 10.9, 10.0, 4.5 Hz, 2H), 1.36 – 1.29 (m, 1H), 1.16 (t, *J* = 7.3 Hz, 3H), 1.08 (s, 9H), 1.02 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 205.7, 173.2, 167.4, 164.7, 161.6, 134.9, 133.8, 129.2, 123.3, 76.4, 66.0, 56.6, 55.7, 55.0, 54.0, 53.2, 46.1, 45.4, 35.2, 28.9, 28.3, 21.3, 21.2, 21.1, 20.7, 14.4.

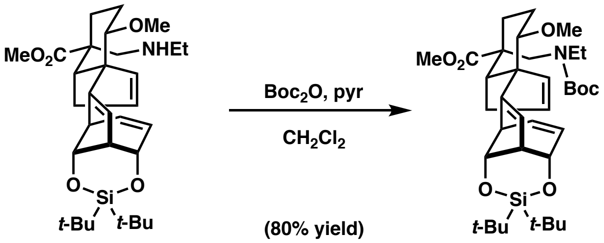
FTIR (NaCl, thin film): 3364, 2973, 2937, 2896, 2860, 1722, 1716, 1682, 1538, 1532, 1476, 1456, 1257, 1234, 1202, 1105, 826, 733 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{31}H_{46}O_7NSi$ $[M + H]^+$ 572.3038, found 572.3460.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = +58.5° (*c* = 0.5, $CHCl_3$).

TLC (50%EtOAc/ 50%Hexanes), R*f*: 0.4 (UV, blue in *p*-anisaldehyde)

Preparation of *tert*-butyl carbamate 135:



122 **135**

To a 100-mL round-bottom flask was added amine **122** (110 mg, 0.202 mmol, 1 equiv), and CH_2Cl_2 (10 mL). Pyridine (0.33 mL, 4.05 mmmol, 20 equiv) added followed by Boc_2O (0.44 g, 2.03 mol, 10 equiv) as a CH_2Cl_2 solution (1 mL). The reaction was allowed to stir for 6 hours at room temperature, and was quenched via the addition of sat.

$NaHCO_3$ (10 mL). The biphasic mixture was transferred to a separatory funnel with CH_2Cl_2 (15 mL) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3x 15 mL) and the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (5% to 10% ethyl acetate in hexanes) to afford *tert*-butyl carbamate **135** (103 mg, 0.162 mmol, 80% yield) as a clear oil.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 6.04 (ddd, *J* = 9.5, 6.2, 1.1 Hz, 1H), 5.89 (dt, *J* = 5.9, 2.3 Hz, 1H), 5.63 (ddd, *J* = 9.3, 4.3, 1.8 Hz, 1H), 5.44 (d, *J* = 5.9 Hz, 1H), 5.25 (d, *J* = 3.7 Hz, 1H), 4.41 (t, *J* = 4.7 Hz, 1H), 4.21 – 4.18 (m, 1H), 3.64 – 3.54 (m, 4H), 3.48 (dd, *J* = 9.2, 2.8 Hz, 1H), 3.29 – 3.18 (m, 5H), 2.98 – 2.94 (m, 1H), 2.89 – 2.73 (m, 3H), 2.43 (m, 2H), 2.21 (m, 1H), 1.79 (m, 2H), 1.49 – 1.42 (m, 10H), 1.07 (s, 9H), 1.00 (s, 12H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 176.7, 164.6, 156.3, 135.7, 133.3, 130.9, 128.2, 119.7, 77.4, 76.7, 66.5, 57.8, 56.9, 54.5, 51.6, 48.3, 46.2 (two overlapping ^{13}C signals), 42.9, 35.6, 29.7, 28.9, 28.4, 28.3, 28.0, 21.9, 21.7, 21.2, 20.6, 13.1.

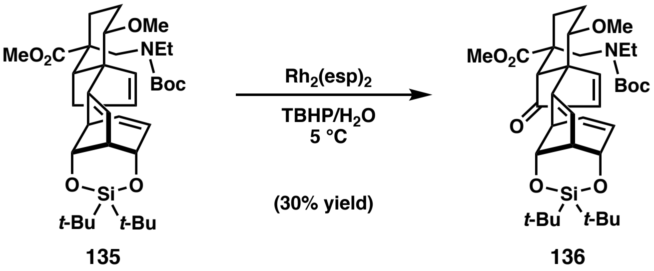
FTIR (NaCl, thin film): 3033, 2934, 2859, 2244, 1431, 1714, 1704, 1694, 1682, 1470, 1455, 1416, 1379, 1256, 1150, 1104, 991, 733 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{36}H_{58}O_7NSi$ $[M + H]^+$ 644.3977, found 644.3960.

$[\alpha]_D^{25}$ = +109° (*c* = 2.1, $CHCl_3$).

TLC (10%EtOAc/ 90%Hexanes), R*f*: 0.4 (UV, blue in *p*-anisaldehyde)

Preparation of enone 136:



A 2-dram vial was charged with cyclopentene **135** (50 mg, 0.078 mmol, 1 equiv), and *tert*-butyl hydroperoxide solution (70% *tert*-butyl hydroperoxide/ 30% H_2O. 1.5 mL). The solution was cooled to 7 °C in the cryocool, and bis[rhodium(α,α,α'α'-tetramethyl-1,3-benzenedipropionicacid)] ($Rh_2(esp)_2$, 3.0 mg, 0.003955 mmol, 0.05 equiv) was added. The reaction was allowed to stir for 72 hours at 5 °C, and then was quenched by the addition of sat. $Na_2S_2O_3$ (3 mL), and diluted with EtOAc (3 mL). The layers were separated, and the aqueous layer was extracted with more EtOAc (6 x 3 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by preparative thin layer chromatography (20% EtOAc/80% hexanes) to afford enone **136** (15 mg, 0.0228 mmol, 29% yield) as a clear oil that contained ~20% inseparable impurities.

Note: This reaction is not optimized. The poor yield results from unreacted starting material and oxidation to the allylic *tert*-butyl peroxide. Both recovered starting material and allyl *tert*-butyl peroxide could be isolated under these reaction conditions.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.49 (d, J = 5.8 Hz, 1H), 6.28 (d, J = 5.8 Hz, 1H), 6.08 (ddd, J = 9.5, 6.1, 1.1 Hz, 1H), 5.69 (ddd, J = 9.5, 4.4, 1.9 Hz, 1H), 5.36 (d, J = 3.8 Hz, 1H), 4.50 (t, J = 4.5 Hz, 1H), 4.25 – 4.20 (m, 1H), 3.88 – 3.70 (m, 2H), 3.64 – 3.57 (m, 4H), 3.52 (dd, J = 11.6, 4.9 Hz, 1H), 3.25 – 3.22 (m, 4H), 3.17 – 3.09 (m, 1H), 3.05 –

3.00 (m, 1H), 2.97 (s, 1H), 2.67 (dd, J = 6.0, 4.5 Hz, 1H), 2.43 – 2.33 (m, 1H), 2.10 – 2.00 (m, 1H), 1.44 – 1.41 (m, 10H), 1.09 – 1.06 (m, 12H), 1.01 (s, 9H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 208.5, 174.0, 165.8, 161.5, 156.2, 134.9, 134.3, 129.1, 122.3, 79.3, 77.2, 76.8, 66.1, 56.6, 56.5, 52.3, 51.3, 48.6, 46.0, 45.3, 43.4, 28.9, 28.4, 28.3, 27.7, 26.4, 24.1, 21.2, 20.7, 13.3.

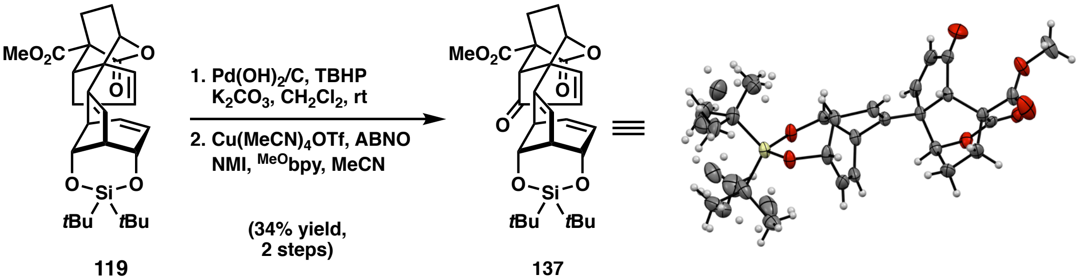
FTIR (NaCl, thin film): 2975, 2936, 2860, 1730, 1702, 1477, 1365, 1255, 1154, 1105, 993, 826, 733 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{36}H_{56}O_8NSi$ $[M + H]^+$ 658.3770, found 658.3737.

$[\alpha]_D^{25}$ = +91° (c = 0.5, CHCl$_3$).

TLC (20%EtOAc/ 80%Hexanes), R$_f$: 0.4 (UV, blue in p-anisaldehyde)

Preparation of enone 137:



119 **137**

A 20-mL round-bottomed flask was charged with cyclopentene **119** (100 mg, 0.2008 mmol, 1 equiv), and CH_2Cl_2 (4 mL). K_2CO_3 (50 mg) and $Pd(OH)_2/C$ (10 wt% Pd, 50 wt% H_2O, 100 mg) were added, followed by *tert*-butyl hydroperoxide (5–6M in decane, 2 mL), and was allowed to stir for 24 hours at room temperature. The reaction was monitored by TLC, and at this time it was not done. Additional portions of *tert*-butyl hydroperoxide (5–6M in decane, 3 x 2 mL) were added over the next 10 hours. The reaction was sluggish by TLC, and was left to stir for an additional 24 hours, at which the reaction mixture was filtered through a plug of silica gel and flushed with EtOAc, and concentrated *in vacuo*. The resulting crude residue was redissolved in CH_2Cl_2 (10 mL), and washed with aqueous sat. $Na_2S_2O_3$ (10 mL), and the layers were separated. The aqueous layer was extracted with additional CH_2Cl_2 (3 x 10 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by silica gel chromatography (20% to 30% to 35% to 40% EtOAc in hexanes) to afford a mixture of enone **137** and the allylic alcohol, which was subjected to the next step.

A 20-mL round-bottom flask was charged with the enone **137** and allylic alcohol mixture, and dissolved in MeCN (5 mL). 4,4'-dimethoxy-2,2'-bipyridine (^{MeO}bpy, 2.2 mg, 10.1 μmol, 0.05 equiv), *N*-methylimidazole (3.2 μL, 40 μmol, 0.20 equiv) and ABNO (1.4 mg, 10.1 μmol, 0.05 equiv) were added followed by $Cu(MeCN)_4OTf$ (3.8 mg, 10.1 μmol, 0.05 equiv), causing the solution to turn a clear faint red/brown color. The solution as then sparged with an O2 balloon for 5 minutes, anad then stirred under an atmosphere of oxygen for 48 hours. The reaction was then quenched by filtering the solution through a short plug of silica (pre-equilibrated with EtOAc and flushed with more EtOAc) and concentrated *in vacuo*. Purification of the crude residue by silica gel chromatography (30% to 40% EtOAc in hexanes) afforded enone **137** (35 mg, 0.068 mmol, 34% yield over 2 steps) as a white solid.

137 was recrystallized from ethyl acetate (slow evaporation) affording crystals suitable for X-ray crystallography.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.53 (d, *J* = 5.5 Hz, 1H), 6.31 (d, *J* = 5.2 Hz, 1H), 6.05 (dd, *J* = 9.5, 5.5 Hz, 1H), 5.78 (ddd, *J* = 9.2, 4.0, 1.5 Hz, 1H), 5.71 (d, *J* = 3.7

Hz, 1H), 4.76 – 4.72 (m, 1H), 4.49 (t, *J* = 4.4 Hz, 1H), 4.27 (dd, *J* = 4.2, 2.7 Hz, 1H), 3.90 (s, 3H), 3.14 – 3.09 (m, 2H), 2.82 (t, *J* = 5.0 Hz, 1H), 2.31 – 2.07 (m, 4H), 1.09 (s, 9H), 1.02 (s, 9H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 203.1, 167.8, 166.2, 162.9, 156.7, 134.2, 133.3, 129.5, 124.9, 76.7, 76.5, 64.9, 54.7, 52.4, 52.0, 50.8, 45.4, 45.3, 28.3, 27.7, 26.5, 22.0, 20.7, 20.1.

FTIR (NaCl, thin film): 2936, 2859, 1784, 1714, 1476, 1364, 1281, 1240, 1109, 1057, 994, 913, 8266, 734 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{28}H_{40}O_7SiN$ [M + NH$_4$]$^+$ 530.2569, found 530.2558.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = +81° (*c* = 6.5, CHCl$_3$).

TLC (40%EtOAc/ 60%Hexanes), R*$_f$*: 0.3 (UV, blue in *p*-anisaldehyde)

2.7 NOTES AND REFERENCES

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Chapter 3

Total Syntheses of the C_{19} Diterpenoid Alkaloids (–)-Liljestrandisine and (–)-Liljestrandinine

3.1. INTRODUCTION

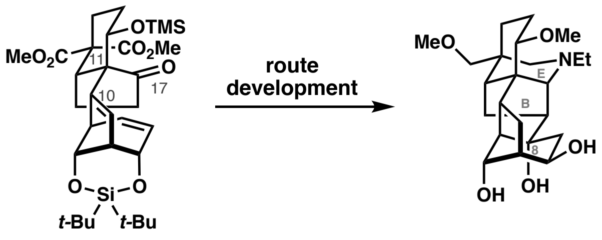
This chapter describes the total synthesis of the C_{19} diterpenoid alkaloids (–)-liljestrandisine and (–)-liljestrandinine. Initial investigations described in Chapter 2 informed the development of the synthetic route.

3.1.1. REMAINING SYNTHETIC CHALLENGES

At this stage, the goal was to complete the total synthesis of a C_{19} diterpenoid alkaloid natural product. The studies described in Chapter 2 focused primarily on C–N and C–C bond forming strategies, with less of an emphasis on achieving the correct functional group and oxidation strategies for the natural product scaffold.

At this stage, we had developed a convergent fragment coupling strategy, providing a scalable route to semipinacol product **77** (Figure 3.1). We focused our attention toward developing a synthetic sequence that would enable the synthesis of the natural product. When comparing the structure of **77** to liljestrandisine (**52**) – what became our initial focus – a few key challenges needed to be addressed in route development. This includes: 1) reduction and differentiation of the two methyl esters 2) installation of the C18’ and C1’ methyl ethers 3) installation of the difficult *N*-ethylated piperidine E-ring 4) formation of the central 6-membered B-ring and 5) installation of the final C8 tertiary alcohol. Based on the studies described in chapter 2, we elected to develop a route using an olefin functionalization strategy. Our failed radical cyclization route (chapter 2) guided our emphasis on investigating strategies for selectively forging a bond between an alkene and an amine, and thus we turned to an aziridination strategy for C–N bond formation.

Figure 3.1. Analysis of remaining challenges in the total synthesis of C_{19} diterpenoid alkaloids.



77

liljestrandisine (**52**)

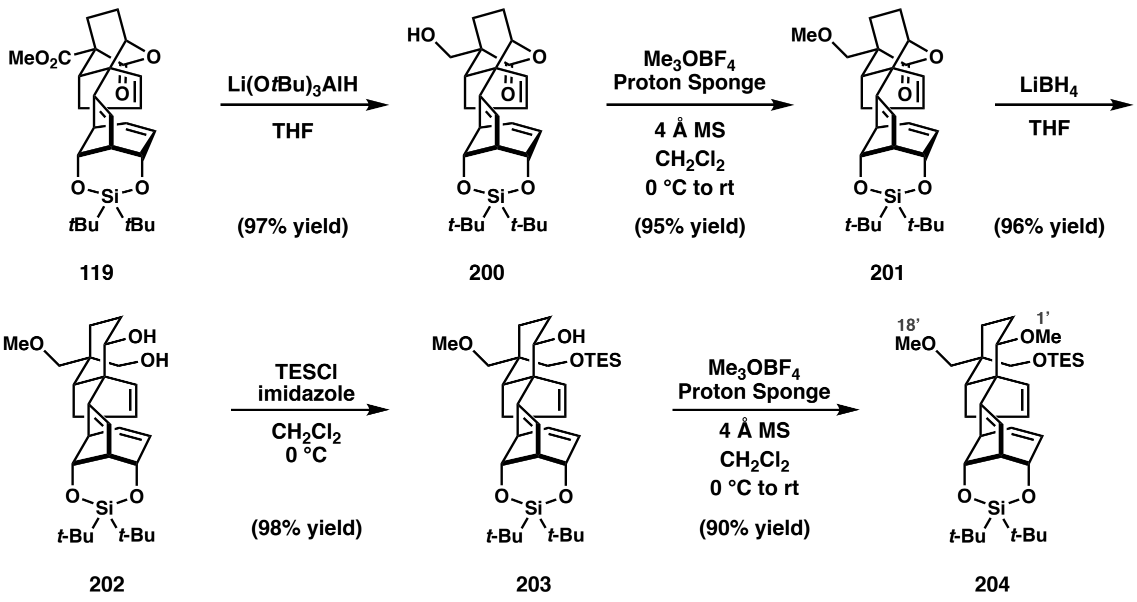
challenges to address in route development:

–differentiation of Me-esters
–selective introduction of methyl ethers
–C–N bond/piperidine E ring formation
–introduction of *N*-ethyl group
–C–C bond/ B ring formation
–C8 oxidation
–oxidation state adjustments

3.2. FORWARD SYNTHETIC ROUTE

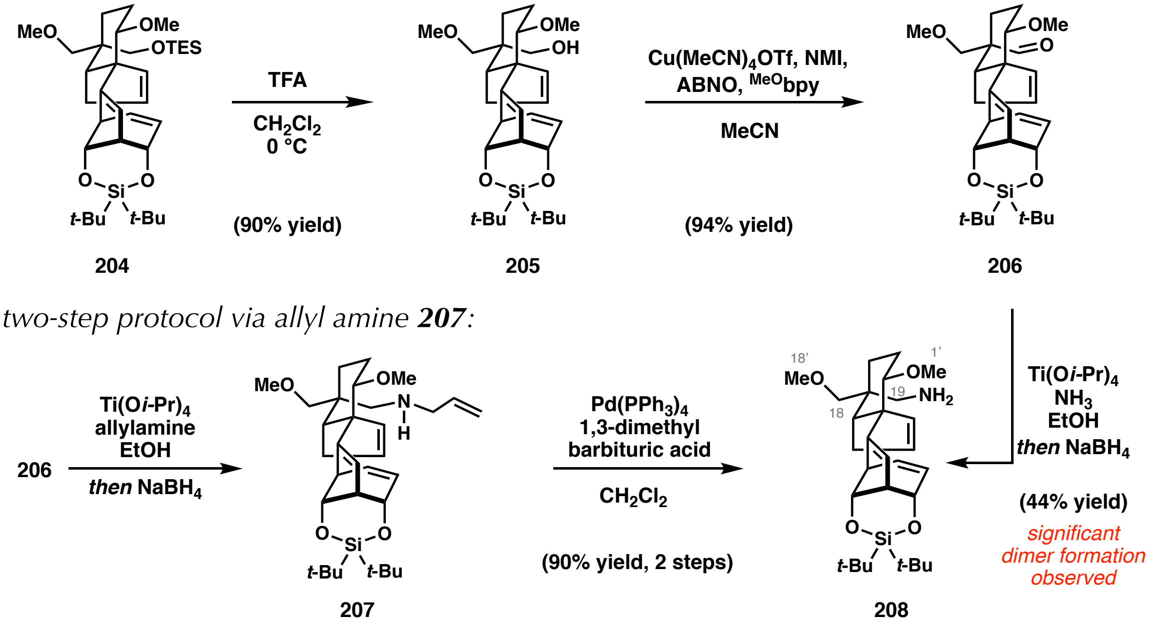
The forward synthetic route began with the route to cyclopentene **119** that was described in Chapter 2 (Figure 2.16). Beginning with intermediate **119**, selective reduction of the methyl ester with lithium tri-*tert*-butoxyaluminum hydride gave primary alcohol **200** (Figure 3.2). Differentiation of the diester moiety via reduction at this stage was enabling for the installation of the correct oxidation and methyl ether pattern for the natural product. Treatment of **200** with trimethyloxonium tetrafluoroborate salt furnished the appropriate C18' methyl ether **201**. At this stage, full reduction of the lactone with lithium borohydride furnished diol **202**. Selective TES ether formation of the primary alcohol furnished **203**, which was followed by a methylation of the remaining secondary alcohol providing bis-methyl ether **204**, a substrate that contains the correct C1' and C18' methyl ethers necessary for **52** and **53**.

Figure 3.2. Route to bis-methyl ether **204** from lactone **119**.



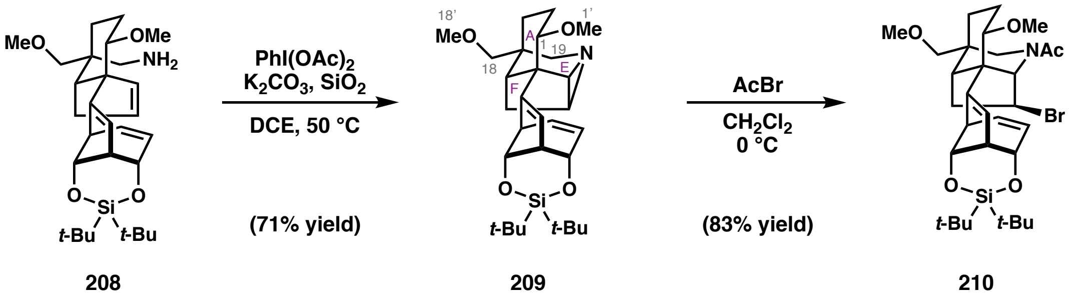
The TES ether was cleaved with trifluoroacetic acid, giving **205** (Figure 3.3). Subsequent oxidation under Stahl's oxidation conditions provided aldehyde **206**. A two-step sequence was employed to convert the aldehyde to the corresponding primary amine. Reductive amination with allylamine provided *N*-allyl amine **207**. The *N*-allyl group was subsequently cleaved via palladium catalysis, providing primary amine **208**. A direct reductive amination with ammonia to provide the primary amine in one-step was possible (44% yield, see experimental section for details), resulting in significant amounts of dimer product, requiring the development of the described two-step protocol.

Figure 3.3. Route to primary amine **208**.



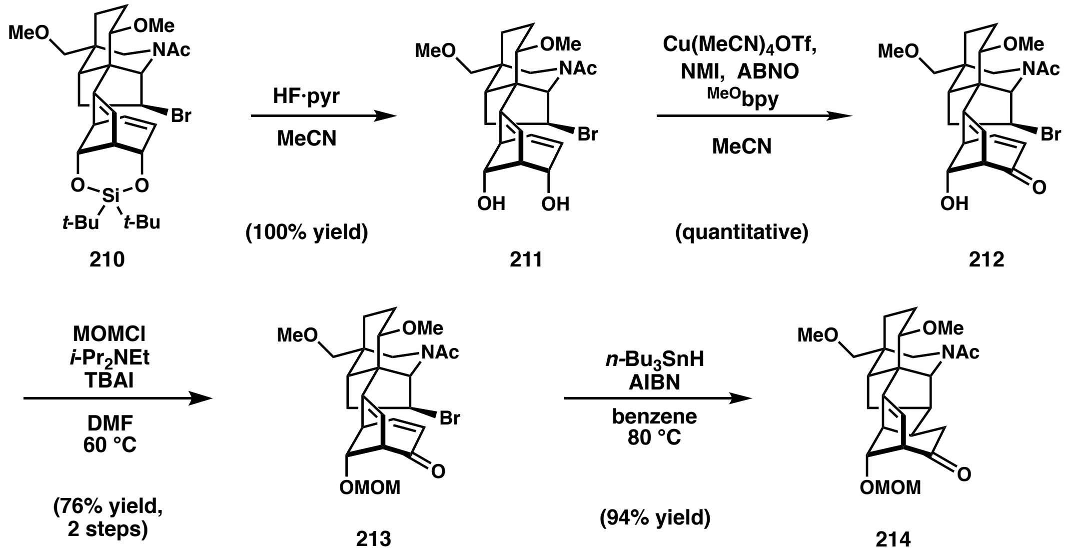
Primary amine **208** was subjected to iodosobenzene diacetate at elevated temperatures furnishing aziridine **209**, providing the difficult piperidine E ring necessary for the C_{19} diterpenoid alkaloid framework (Figure 3.4).[1] To finish the total synthesis, the next crucial tasks to address included installation of the *N*-ethyl group, formation of the central carbocyclic B-ring, and introduction the final tertiary alcohol at C8. Toward that end, treatment of aziridine **209** with acetyl bromide acetylated the nitrogen and regioselectively opened the aziridine, providing alkyl bromide **210**.[2] This aziridination/aziridine opening sequence is strategic because the acetyl group serves as a masked *N*-ethyl group, and the alkyl bromide resulting from the aziridine-opening provides a functional handle for B-ring formation.

Figure 3.4. Intramolecular aziridination and aziridine-opening provides **210**.



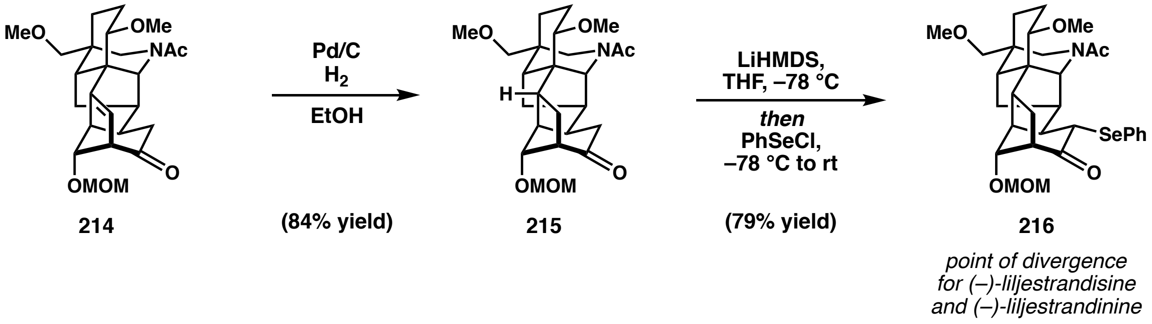
The silylene group of **210** was cleanly deprotected with HF•pyr furnishing diol **211** (Figure 3.5). The two secondary alcohols could be differentiated under Stahl's oxidation conditions,[3] selectively oxidizing the allylic alcohol furnishing enone **212**. The remaining alcohol could be re-protected as the methoxymethyl ether to furnish **213**. Treatment of alkyl bromide **213** with *n*-Bu_3SnH and AIBN at elevated temperatures formed the central B ring – completing the full C_{19} hexacyclic aconitine framework.

Figure 3.5. Synthesis of the C_{19} aconitine core.



The now strained trisubstituted olefin of **214** underwent a facile hydrogenation catalyzed by palladium on carbon furnishing **215** (Figure 3.6). At this stage, the ketone of **215** could be employed as a functional handle for the installation of the final tertiary hydroxyl group at C8.[4] Treatment of **215** with LiHMDS and PhSeCl furnished α-selenide **216**. α-Selenide **216** served as a point of divergence for the two natural products liljestrandisine (**52**) and liljestrandinine (**53**).

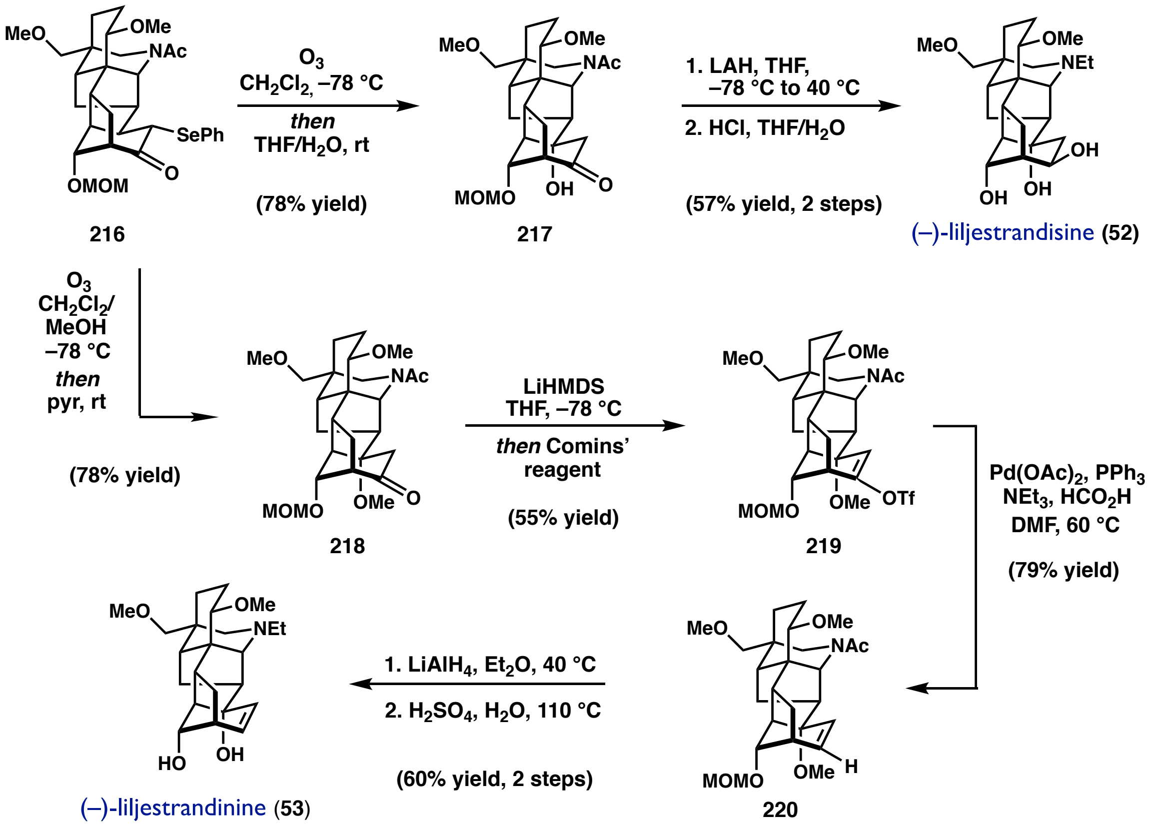
Figure 3.6. Advancement to α-selenide **216.**



Subjection of α-selenide **216** to ozone effected oxidation and elimination to the corresponding strained enone, which underwent a spontaneous oxy-Michael addition with water to furnish β-hydroxyketone **217** (Figure 3.7). Treatment of **217** with lithium aluminum hydride effected both reduction of the ketone to the equatorially disposed alcohol and reduction of the acetyl group to the *N*-ethyl group. Lastly, deprotection of the MOM ether with hydrochloric acid furnished liljestrandisine (**52**).

Alternatively, ozonolysis of α-selenide **216** followed by quenching of the resultant strained enone with methanol furnished β-methoxyketone **218**. At this stage the ketone of **218** was reduced to the alkene via enol triflate **219** and subsequent palladium-catalyzed reduction, giving **220**. Treatment of **220** with $LiAlH_4$ effected reduction of the acetyl group to the *N*-ethyl amine. Subsequent subjection to sulfuric acid at elevated temperatures in water facilitated MOM deprotection and concomitant acid-catalyzed exchange of the methoxy group to the hydroxyl group, providing liljestrandinine (**53**).

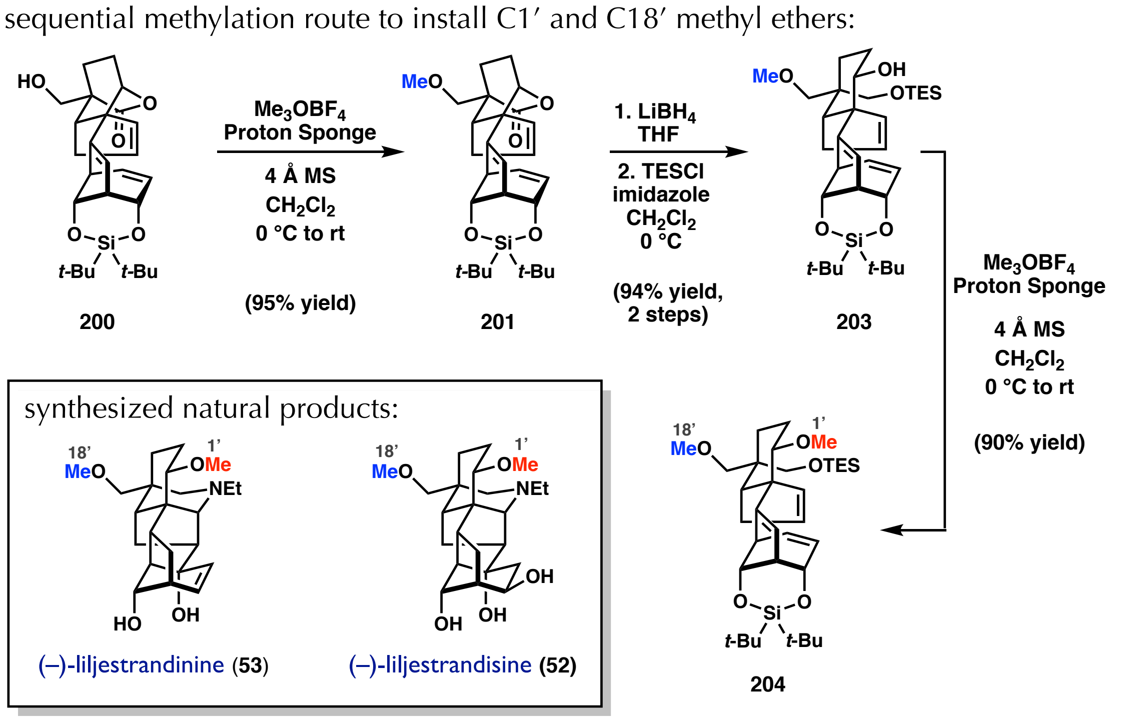
Figure 3.7. Synthesis of (–)-liljestrandisine (**52**) and (–)-liljestrandinine (**53**).



3.3. ANALYSIS OF SYNTHETIC ROUTE

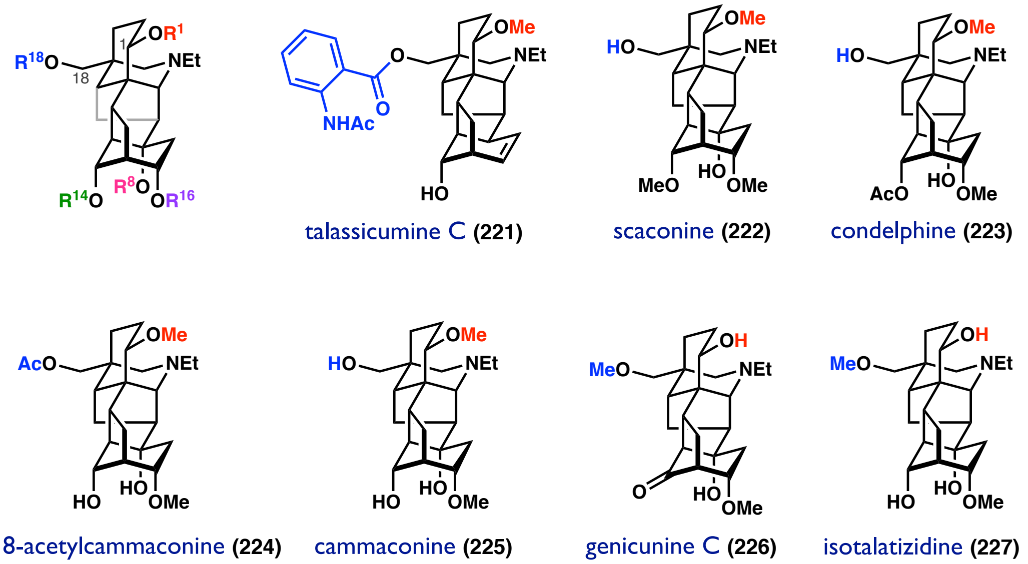
With a route to the C_{19} diterpenoid alkaloid natural products **52** and **53** in hand, an analysis of the advantages and disadvantages of the synthetic route are described. The diterpenoid alkaloids are a large family of natural products, with more than 1200 isolated to date.[5] The total synthetic route provided above could enable access to other natural products in this family. Specifically, our route employs a sequential methylation strategy to install the C1' and C18' methyl ether groups, which are necessary functional groups for **52** and **53** (Figure 3.8). Our route could enable the installation of other functional groups at these positions, and because these are installed in a selective and stepwise fashion, the C1' and C18' groups do not have to be the same.

Figure 3.8. Methylation strategy for total syntheses of **52** and **53**.



Representative examples of C$_{19}$ diterpenoid alkaloid natural products that feature different functional groups at the R1 and R18 positions are depicted (Figure 3.9). As described, our route installs the two methyl groups necessary for **52** and **53** sequentially, and thus if different groups or a protecting group strategy was used instead, natural products with variability at these positions could be selectively accessed using the described synthetic route.

Figure 3.9. Functional group variabiliity across C_{19} diterpenoid alkaloid natural products.



talassicumine C (**221**) scaconine (**222**) condelphine (**223**)

18-acetylcammaconine (**224**) cammaconine (**225**) genicunine C (**226**) isotalatizidine (**227**)

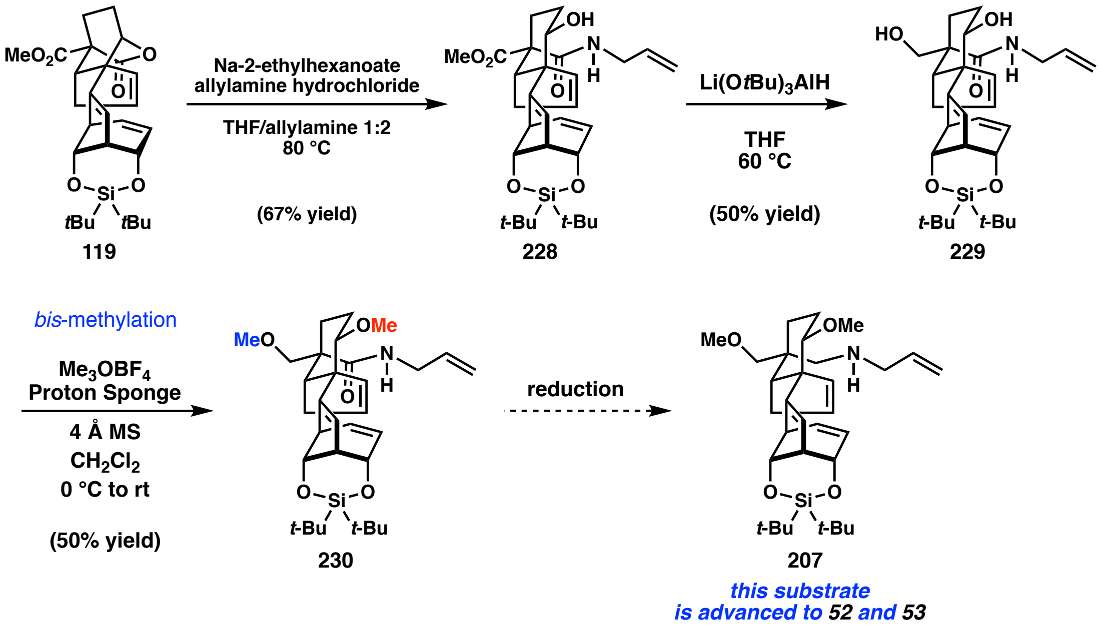
3.3.1. LACTONE OPENING AMINOLYSIS STRATEGIES

It is an advantage that the developed route could provide access to natural products with different functional groups at the R1 and R18 positions (Figure 3.9). However, for the synthesis of natural products featuring the same functional groups at the R1 and R18 positions, such as **52** and **53**, it is believed that a bis-functionalization of these positions would be more efficient.

A *N*-ethyl amine lactone-opening aminolysis strategy (see Figure 2.17) had been developed in our work in accessing a substrate for a proposed radical cascade cyclization reaction. At this time, we proposed using our developed understanding of this reactivity to shorten the synthetic sequence, specifically seeking a route where we could bis-methylate the R1 and R18 positions to more efficiently install the necessary functional groups for **52** and **53**.

To that end, given that the developed synthetic route to **52** and **53** uses *N*-allyl amine **207** as an intermediate, we thought a good starting point in the development of a more efficient route would be through the lactone-opening aminolysis of **119** with *N*-allyl amine (Figure 3.10). It was discovered that the lactone-opening aminolysis conditions developed for the synthesis of *N*-ethyl amide **120** were also amenable for the synthesis of *N*-allyl amide **228**. Subsequent reduction of the methyl ester of **228** furnished diol **229**. At this stage, both C1' and C18' methyl ethers could be installed in one step, furnishing bis-methyl ether **230**. Efforts to advance *N*-allyl amide to **207**, a substrate that is advanced to **52** and **53** is ongoing. If this is successful, this shortens the synthetic sequence to **207**, requiring less redox and functional group manipulations.

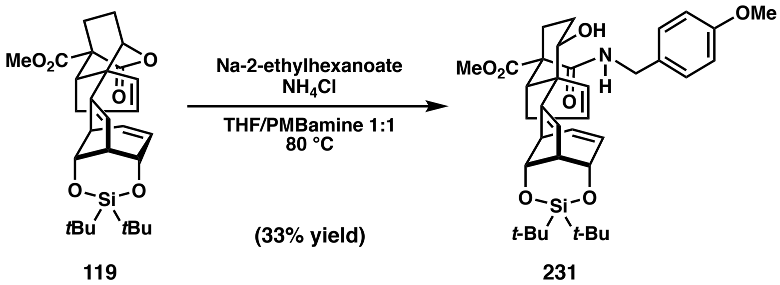
Figure 3.10. *N*-allyl amine lactone-opening aminolysis strategy.



Efforts to investigate alternative amines for the lactone-opening aminolysis of **119** were investigated. Specifically, it was envisioned that a paramethoxybenzyl amine lactone-opening aminolysis could be useful for streamlining the synthetic sequence

(Figure 3.11). It was envisioned that cleavage of the paramethoxy benzyl group could provide the corresponding carboxamide, which could then be reduced to the primary amine. The lactone-opening was possible with 4-methoxybenzylamine, providing amide **231**. Efforts to advance **231** to an intermediate in the synthetic route to **52** and **53** are ongoing.

Figure 3.11. 4-Methoxybenzyl amine lactone-opening aminolysis strategy.



3.4. CONCLUDING REMARKS

This chapter details the total syntheses of the C19 diterpenoid alkaloids (–)-liljestrandisine and (–)-liljestrandinine. The total syntheses were ultimately enabled by an intramolecular aziridination reaction and subsequent acetyl bromide mediated aziridine-opening giving an alkyl bromide. This bromide was then used in a radical Michael reaction forging the final hexacyclic scaffold of the natural products. Lastly, initial investigations to shorten the synthetic sequence involving lactone-opening aminolysis strategies are presented.

3.5. EXPERIMENTAL SECTION

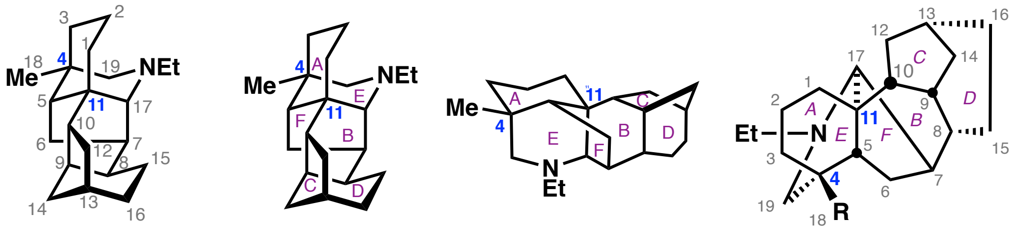
3.5.1 Materials and Methods

Unless otherwise stated, reactions were performed under an inert atmosphere (dry N_2 or Ar) with 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), diethyl ether (Et_2O), methylene chloride (CH_2Cl_2), acetonitrile (MeCN), *tert*-butyl methyl ether (TBME), benzene (PhH), and toluene (PhMe) were dried by passing through activated alumina columns. Absolute ethanol (200 proof) was purchased from Koptec, and stored over activated 3Å MS in a Schlenk Tube under N_2. Triethylamine (Et_3N), *N*,*N*-diisopropylethylamine (DIPEA), and 2,6-lutidine were distilled over calcium hydride prior to use. Unless otherwise stated, chemicals and reagents were used as received. 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, $KMnO_4$, CAM, or ninhydrin staining. Flash column chromatography was performed using silica gel (SiliaFlash® P60, particle size 40-63 microns [230 to 400 mesh]) purchased from Silicycle. Optical rotations were measured on a Jasco P-2000 polarimeter using a 100 mm path-length cell at 589 nm. ^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, $\delta = 77.0$). 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, app = apparent. 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).

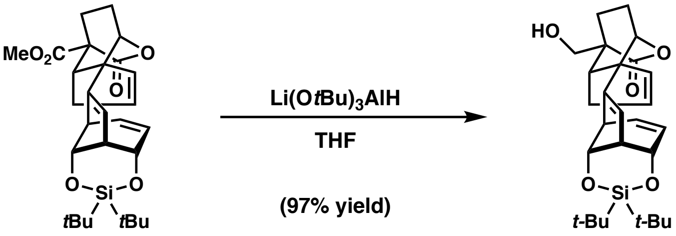
3.5.2 Preparative Procedures and Spectroscopic Data

The following ring labeling and atom numbering are used throughout this section:

Ring labelling and atom numbering



Preparation of alcohol 200:



119 **200**

A 250-mL, round-bottomed flask was charged with methyl ester **119** (1.56 g, 3.13 mmol, 1.0 equiv), equipped with a rubber septum, purged with N_2, and dissolved in THF (31 mL). Then, the reaction was cooled to 0 °C in an ice bath Li(O*t*-Bu)$_3$AlH (2.39 g, 9.39 mmol, 3 equiv) was added, and the ice bath was removed. The reaction was monitored by TLC, and after 100 minutes, trace starting material remained, so an additional portion of Li(O*t*-Bu)$_3$AlH (0.95 g, 3.66 mmol, 1.17 equiv) was added, and allowed to stir for an additional 70 minutes. The reaction was carefully quenched with water (10 mL) followed by sat. Rochelle's salt (30 mL). The biphasic mixture was allowed to stir for 30 minutes, then transferred to a separatory funnel with Et$_2$O (30 mL), and the layers were separated. The aqueous layer was extracted Et$_2$O (3 x 30 mL). The combined organics were washed with brine (1 x 30 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (20% acetone in hexanes to 25 % acetone in hexanes) to afford alcohol **200** (1.42 g, 3.02 mmol, 97% yield) as a white solid.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 6.06 (ddd, *J* = 9.5, 6.1, 1.2 Hz, 1H), 5.74 – 5.68 (m, 2H), 5.51 – 5.48 (m, 2H), 4.62 (dd, *J* = 3.8, 1.6 Hz, 1H), 4.45 (tt, *J* = 4.4, 1.0 Hz, 1H), 4.23 (ddd, *J* = 4.2, 2.9, 0.6 Hz, 1H), 4.03 (dd, *J* = 11.8, 3.7 Hz, 1H), 3.43 (dd, *J* = 11.8, 9.1 Hz, 1H), 3.04 (ddtt, *J* = 4.9, 2.8, 2.0, 1.0 Hz, 1H), 2.77 (dd, *J* = 5.5, 4.7 Hz, 1H), 2.58 (ddt, *J* = 17.9, 9.3, 2.3 Hz, 1H), 2.48 – 2.34 (m, 3H), 2.20 – 2.03 (m, 2H), 1.90 (dddd, *J* = 13.7, 11.4, 6.2, 3.7 Hz, 1H), 1.57 (ddd, *J* = 13.2, 11.1, 6.3 Hz, 1H), 1.07 (s, 9H), 1.00 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 176.6, 161.4, 134.7, 131.9, 131.2, 129.0, 121.6, 78.6, 65.9, 64.2, 60.4, 53.7, 46.4, 46.2, 45.7, 44.5, 35.0, 28.8, 28.2, 24.6, 22.3, 21.2, 20.7.

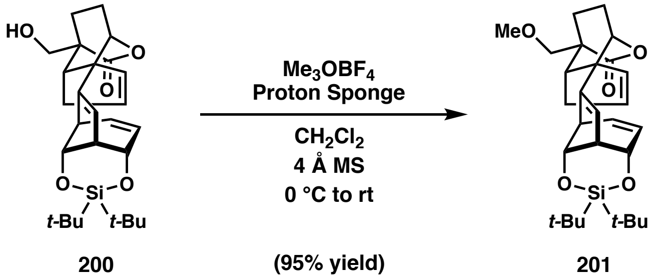
FTIR (NaCl, thin film): 3458, 2935, 2859, 2245, 1738, 1748, 1732, 1476, 1382, 1364, 1364, 1107, 1038, 995, 911 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{27}H_{39}O_5Si$ $[M + H]^+$ 471.2561, found 471.2555.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = +168° (*c* = 0.51, $CHCl_3$).

TLC (50%EtOAc/50%Hexanes), R*f*: 0.5 (UV, blue in *p*-anisaldehyde)

Preparation of methyl ether 201:



A 250-mL, round-bottomed flask was charged with alcohol **200** (1.41 g, 3.00 mmol, 1.0 equiv), equipped with a rubber septum, purged with N_2, and cooled to 0 °C in an ice bath. Meanwhile, Me_3OBF_4 (1.33 g, 9.00 mmol, 3 equiv), Proton Sponge (1.93 g, 9.00 mmol, 3 equiv), and activated 4 Å MS (2.8 g) were added to a 40 mL vial in the glovebox, brought out of the glovebox, and added to the flask containing the substrate. The mixture was then suspended in CH_2Cl_2 (30 mL), and allowed to stir for 24 hours, allowing the reaction to warm up to room temperature over this period. The reaction mixture was filtered through a plug of silica gel and celite that had been pre-packed with a 1:1 Hex/EtOAc mixture and rinsed further with 1:1 Hex/EtOAc and concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (15% ethyl acetate in hexanes to 18% ethyl acetate in hexanes) to afford methyl ether **201** (1.39 g, 2.85 mmol, 95% yield) as a white crystalline solid.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 5.99 (ddd, *J* = 9.5, 6.1, 1.1 Hz, 1H), 5.67 – 5.59 (m, 2H), 5.43 (d, *J* = 3.7 Hz, 1H), 5.40 (dt, *J* = 5.7, 2.1 Hz, 1H), 4.54 – 4.52 (m, 1H), 4.39 (t, *J* = 4.7 Hz, 1H), 4.16 (ddd, *J* = 4.2, 2.9, 0.6 Hz, 1H), 3.58 (d, *J* = 10.0 Hz, 1H), 3.38 (d, *J* = 10.0 Hz, 1H), 3.30 (s, 3H), 2.96 (dtq, *J* = 5.0, 2.9, 0.8 Hz, 1H), 2.71 (dd, *J* = 5.6, 4.8 Hz, 1H), 2.62 – 2.49 (m, 2H), 2.28 (dq, *J* = 17.3, 2.2 Hz, 1H), 2.10 – 2.00 (m, 1H), 1.94 – 1.77 (m, 2H), 1.61 – 1.54 (m, 1H), 1.01 (s, 9H), 0.94 (s, 9H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 175.1, 161.6, 134.9, 132.2, 131.3, 128.8, 121.4, 77.9, 77.3, 72.8, 66.0, 59.8, 59.5, 46.4, 45.8, 44.8, 43.2, 35.0, 28.8, 28.2, 25.5, 21.9, 21.2, 20.7. A ^{13}C signal is observed to be overlapping with residual CDCl$_3$ at 77.3, resolved peaks are seen in the HSQC spectrum, provided below.

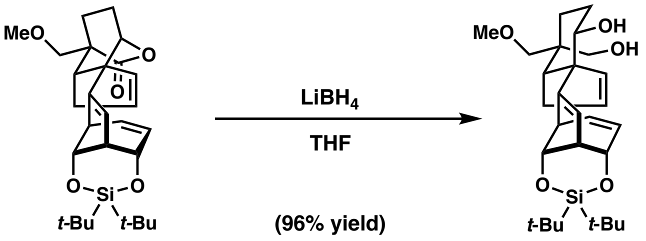
FTIR (NaCl, thin film): 2894, 2933, 2858, 1748, 1475, 1393, 1364, 1109, 994, 825 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{28}H_{41}O_5Si$ $[M + H]^+$ 485.2718, found 485.2716.

$[\alpha]_D^{25}$ = +156° (*c* = 0.75, CHCl$_3$).

TLC (20%EtOAc/80%Hexanes), R*f*: 0.5 (UV, blue in *p*-anisaldehyde)

Preparation of diol 200:



201 **202**

A 250-mL, round-bottomed flask was charged with lactone **201** (1.39 g, 2.88 mmol, 1.0 equiv), was equipped with a rubber septum, purged with N$_2$, and dissolved in THF (29 mL). LiBH$_4$ solution (2 M in THF, 7.2 mL, 14.4 mmol, 5 equiv) was added via syringe, and the reaction was allowed to continue stirring for 20 hours. The reaction was monitored by TLC, which indicated that it had not gone to completion. An additional portion of $LiBH_4$ solution (2 M in THF, 7.2 mL, 14.4 mmol, 5 equiv) was added via syringe. After an additional 3 hours another portion of $LiBH_4$ solution (2 M in THF, 7.2 mL, 14.4 mmol, 5 equiv) was added via syringe (15 equiv total). The reaction was allowed to continue to stir for another 24 hours at room temperature. The reaction was carefully quenched (bubbles evolve) with sat. $NaHCO_3$ (30 mL), and diluted with Et_2O (30 mL), and transferred to a separatory funnel. The layers were separated, and the aqueous layer was extracted with 20%IPA/80%$CHCl_3$ (3 x 30 mL). The combined organics were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (15% acetone in hexanes to 20% acetone in hexanes) to afford diol **202** (1.34 g, 2.76 mmol, 96% yield) as a white solid.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 6.19 (ddd, *J* = 5.8, 2.9, 1.7 Hz, 1H), 6.08 (ddd, *J* = 9.5, 6.1, 1.1 Hz, 1H), 5.67 (ddd, *J* = 9.3, 4.4, 1.9 Hz, 1H), 5.49 (d, *J* = 3.7 Hz, 1H), 5.44 (ddd, *J* = 5.8, 2.7, 1.1 Hz, 1H), 4.44 (td, *J* = 4.3, 0.9 Hz, 1H), 4.22 (ddd, *J* = 4.2, 3.0, 0.7 Hz, 1H), 4.03 (d, *J* = 4.1 Hz, 1H), 3.58 – 3.52 (m, 2H), 3.49 – 3.42 (m, 1H), 3.31 (s, 3H), 3.24 (d, *J* = 8.8 Hz, 1H), 3.08 – 3.01 (m, 2H), 2.91 (t, *J* = 5.3 Hz, 1H), 2.71 – 2.64 (m, 1H), 2.51 (dddd, *J* = 16.0, 8.4, 2.9, 1.1 Hz, 1H), 2.44 – 2.35 (m, 1H), 1.79 – 1.55 (m, 4H), 1.13 – 1.10 (m, 1H), 1.08 (s, 9H), 1.01 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 165.4, 135.9, 135.6, 133.6, 128.3, 120.9, 79.7, 77.1, 72.6, 68.2, 66.3, 59.1, 56.1, 46.5, 46.2, 41.5, 39.6, 35.0, 28.9, 28.3, 24.6, 21.2, 20.7, 20.7.

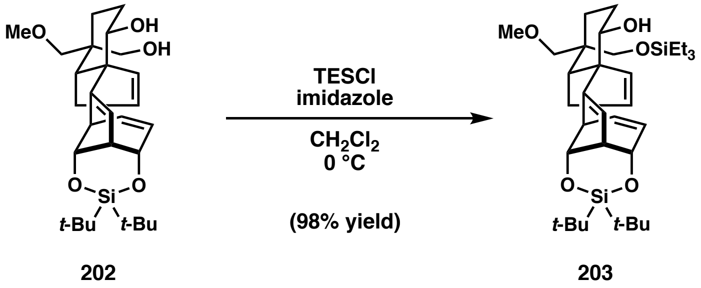
FTIR (NaCl, thin film): 2950, 2910, 2876, 1748, 1476, 1362, 1105, 996, 826 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{28}H_{45}O_5Si$ $[M + H]^+$ 489.3031, found 489.3020.

$[\alpha]_D^{25}$ = +152° (*c* = 0.42, $CHCl_3$).

TLC (50%EtOAc/50%Hexanes), R*f*: 0.5 (UV, brown/pink in *p*-anisaldehyde)

Preparation of silyl ether 203:



A 200-mL, round-bottomed flask was charged with diol **202** (1.35 g, 2.76 mmol, 1.0 equiv), imidazole (0.42 g, 6.20 mmol, 2.25 equiv), dissolved in CH_2Cl_2 (55 mL), and cooled to 0 °C in an ice bath. TESCl (0.69 mL, 4.14 mmol, 1.5 equiv) added via syringe, and was allowed to continue to stir for 25 minutes at 0 °C. The reaction was monitored by TLC, which showed completion of the reaction. The reaction was quenched with sat. $NaHCO_3$ (30 mL), and transferred to a separatory funnel. The layers were separated, and the aqueous was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (10% ethyl acetate in hexanes to 15% ethyl acetate in hexanes) to afford silyl ether **203** (1.63 g, 2.70 mmol, 98% yield) as a white solid.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 6.18 (dt, *J* = 5.9, 2.3 Hz, 1H), 6.07 (ddd, *J* = 9.5, 6.2, 1.1 Hz, 1H), 5.66 (ddd, *J* = 9.4, 4.3, 1.9 Hz, 1H), 5.44 (d, *J* = 3.8 Hz, 1H), 5.40 (dt, *J* = 5.9, 1.8 Hz, 1H), 4.49 (t, *J* = 4.7 Hz, 1H), 4.25 – 4.18 (m, 1H), 4.03 (t, *J* = 3.4 Hz, 1H), 3.49 (d, *J* = 9.3 Hz, 1H), 3.29–3.26 (m, 2H), 3.25 (s, 3H), 3.19 (d, *J* = 8.7 Hz, 1H), 3.08 – 3.04 (m, 1H), 2.87 (t, *J* = 5.3 Hz, 1H), 2.42 – 2.33 (m, 2H), 2.22 (t, *J* = 9.5 Hz, 1H), 1.80 (s, 1H), 1.71 (dt, *J* = 7.6, 3.9 Hz, 2H), 1.46 (dt, *J* = 13.6, 8.2 Hz, 1H), 1.31 (dt, *J* = 13.7, 4.0 Hz, 1H), 1.09 (s, 9H), 1.01 (s, 9H), 0.95 (t, *J* = 7.9 Hz, 9H), 0.62 – 0.54 (m, 6H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 165.5, 136.1, 135.7, 133.9, 128.2, 120.9, 77.1, 72.3, 68.1, 66.3, 66.1, 58.8, 55.9, 46.3, 46.2, 43.1, 40.5, 34.4, 28.9, 28.3, 24.1, 21.3, 20.7, 18.6, 6.9, 4.3.

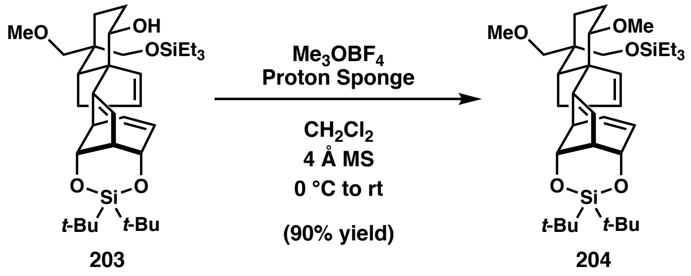
FTIR (NaCl, thin film): 2950, 2910, 2876, 1748, 1476, 1362, 1105, 996, 826 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{34}H_{59}O_5Si_2$ $[M + H]^+$ 603.3896, found 603.3881.

$[\alpha]_D^{25}$ = +103° (*c* = 0.38, CHCl$_3$).

TLC (15%EtOAc/85%Hexanes), R*f*: 0.4 (UV, orange/pink in *p*-anisaldehyde)

Preparation of methyl ether 204:



A 250-mL, round-bottomed flask was charged with alcohol **203** (1.63 g, 2.71 mmol, 1.0 equiv), equipped with a rubber septum, purged with N$_2$, and cooled to 0 °C in an ice bath. Meanwhile, Me$_3$OBF$_4$ (2.00 g, 13.55 mmol, 5 equiv), Proton Sponge (2.91 g, 13.55 mmol, 5 equiv), and activated 4 Å MS (3.3 g) were added to a 40 mL vial in the glovebox, brought out of the glovebox, and added to the flask containing the substrate. The mixture was then suspended in CH$_2$Cl$_2$ (27.1 mL), and allowed to stir for 24 hours, allowing the reaction to warm up to room temperature over this period. The reaction mixture was filtered through a plug of silica gel and celite that had been pre-packed with a 15% ethyl acetate/ 85% hexanes mixture and rinsed further with 15% ethyl acetate/ 85% hexanes and concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (2% to 3% to 4% to 5% to 6% ethyl acetate in hexanes to) to afford methyl ether **204** (1.5 g, 2.43 mmol, 90% yield) as a white solid.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 6.08 (ddd, *J* = 9.5, 6.2, 1.1 Hz, 1H), 5.88 (dt, *J* = 5.8, 2.2 Hz, 1H), 5.65 (ddd, *J* = 9.3, 4.4, 1.9 Hz, 1H), 5.42 – 5.35 (m, 2H), 4.47 (td, *J* = 4.2, 0.9 Hz, 1H), 4.22 (ddd, *J* = 4.4, 3.0, 0.7 Hz, 1H), 3.55 (dd, *J* = 6.9, 2.7 Hz, 1H), 3.45 (d, *J* = 9.2 Hz, 1H), 3.30 (d, *J* = 9.3 Hz, 1H), 3.24 (s, 3H), 3.24 (s, 3H), 3.21 (d, *J* = 8.7 Hz, 1H), 3.16 (d, *J* = 8.7 Hz, 1H), 3.04 (ddddt, *J* = 5.8, 3.8, 2.9, 2.0, 1.0 Hz, 1H), 2.87 (dd, *J* = 6.4, 4.1 Hz, 1H), 2.35 – 2.27 (m, 2H), 2.23 (dd, *J* = 10.2, 7.8 Hz, 1H), 1.67 (dddd, *J* = 13.9, 8.4, 5.6, 2.7 Hz, 1H), 1.57 (dtd, *J* = 13.6, 6.8, 5.1 Hz, 1H), 1.40 – 1.24 (m, 2H), 1.09 (s, 9H), 1.01 (s, 9H), 0.95 (t, *J* = 7.9 Hz, 9H), 0.63 – 0.52 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 166.6, 136.0, 134.0, 131.6, 128.0, 119.8, 79.7, 77.1, 73.4, 66.5, 66.0, 58.7, 57.2, 56.5, 46.2 (2 overlapping ^{13}C signals), 46.2, 43.7, 40.6, 34.8, 28.9, 28.3, 21.4, 21.3, 20.9, 20.7, 6.8, 4.3.

Two ^{13}C signals are observed to be overlapping at 46.2, resolved peaks are seen in the HSQC spectrum, provided below.

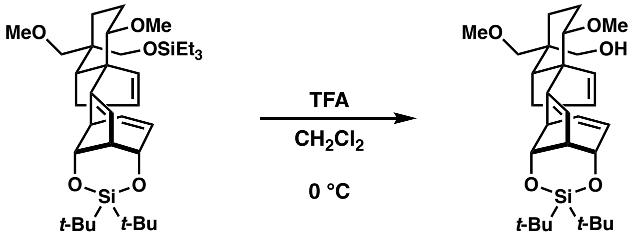
FTIR (NaCl, thin film): 3049, 2936, 2911, 2976, 2808 1476, 1103, 994 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{35}H_{61}O_5Si_2$ $[M + H]^+$ 617.4052, found 617.4045.

$[\alpha]_D^{25}$ = +87° (*c* = 0.57, $CHCl_3$).

TLC (5%EtOAc/95%Hexanes), R*f*: 0.4 (UV, green in *p*-anisaldehyde)

Preparation of alcohol 205:



204 **205**

A 500-mL, round-bottomed flask was charged with silyl ether **204** (1.60 g, 2.59 mmol, 1.0 equiv), and CH_2Cl_2 (52 mL) and cooled to 0 °C in an ice bath. TFA (0.40 mL, 5.18 mmol, 2 equiv) was added via syringe. The reaction was monitored by TLC, and after 45 minutes at 0 °C, additional TFA (0.10 mL, 1.30 mmol, 0.5 equiv) was added. After a further 30 minutes, additional TFA (0.10 mL, 1.30 mmol, 0.5 equiv) was added (3 equiv total). After 15 more minutes, the reaction was done by TLC. The reaction was quenched with sat. $NaHCO_3$ (50 mL), and the pH of the aqueous layer was checked to make sure it was basic. The biphasic mixture was transferred to a separatory funnel, the layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (25% ethyl acetate in hexanes to 30% ethyl acetate in hexanes) to afford alcohol **205** (1.17 g, 2.33 mmol, 90% yield) as a white solid.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 6.08 (ddd, *J* = 9.5, 6.2, 1.1 Hz, 1H), 5.90 (ddd, *J* = 5.8, 2.7, 1.9 Hz, 1H), 5.66 (ddd, *J* = 9.3, 4.4, 1.9 Hz, 1H), 5.45 – 5.42 (m, 2H), 4.44 (td, *J* = 4.2, 0.9 Hz, 1H), 4.26 – 4.19 (m, 1H), 3.57 – 3.52 (m, 2H), 3.46 (dd, *J* = 8.9, 1.3 Hz, 2H), 3.27 (s, 3H), 3.26 (s, 3H), 3.21 (d, *J* = 8.7 Hz, 1H), 3.05 – 2.99 (m, 2H), 2.91 (dd, *J* = 5.9, 4.6 Hz, 1H), 2.64 (t, *J* = 9.2 Hz, 1H), 2.46 (dddd, *J* = 15.7, 8.7, 2.8, 1.4 Hz, 1H), 2.30 (ddt, J = 15.7, 9.9, 2.1 Hz, 1H), 1.67 – 1.61 (m, 1H), 1.61 – 1.42 (m, 2H), 1.17 – 1.10 (m, 1H), 1.08 (s, 9H), 1.01 (s, 9H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 166.5, 135.8, 133.7, 131.5, 128.1, 119.6, 80.5, 79.7, 77.0, 72.4, 66.5, 58.9, 57.2, 56.8, 46.4, 46.2, 42.3, 39.7, 35.5, 28.9, 28.3, 23.2, 21.6, 21.2, 20.7.

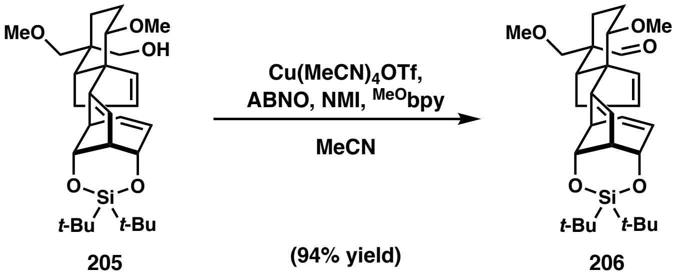
FTIR (NaCl, thin film): 3472, 3048, 2934, 2894, 2859, 1475, 1380, 1101, 991 cm^{-1}.

HRMS: (ESI-TOF) calc’d for $C_{29}H_{47}O_5Si$ $[M + H]^+$ 503.3187, found 503.3184.

$[\alpha]_D^{25}$ = +136° (c = 0.58, CHCl$_3$).

TLC (30%EtOAc/70%Hexanes), R$_f$: 0.4 (UV, pink/orange in *p*-anisaldehyde)

Preparation of aldehyde 206:



A 100-mL, round-bottomed flask was charged with alcohol **205** (218 mg, 0.434 mmol, 1.0 equiv) and MeCN (8.6 mL). 4,4’-dimethoxy-2,2’-bipyridine (^{MeO}bpy, 4.7 mg, 21.7 μmol, 5 mol %), *N*-methylimidazole (6.9 μL, 86.8 μmol, 20 mol %), and ABNO (3.0 mg, 21.7 μmol, 5 mol %). Lastly, Cu(MeCN)$_4$OTf (8.2 mg, 21.7 μmol, 5 mol %) was added, and the clear red/brown reaction mixture was stirred until slightly yellow green, and the TLC indicated the reaction had gone to completion (ca. 90 min), at which point the solution was filtered through a short plug of silica, flushed with ethyl acetate, and concentrated *in vacuo*. Purification of the crude residue by silica gel chromatography (10 to 12% EtOAc in hexanes) afforded aldehyde **206** (204 mg, 0.408 mmol, 94% yield) as a white foam.

Note: The product aldehyde **206** is prone to decomposition, prolonged storage should be avoided if possible. If necessary, it can be stored as a solid in the freezer and should be fine for at least a few weeks. Residual solvent accelerates the decomposition process. It is also possible to run the subsequent step without purification, and using the crude from the silica plug directly. Once the decomposition pathway was discovered, the aldehyde was reproducibly carried through as the crude in the subsequent reductive amination step, to keep the aldehyde for a minimum amount of time.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 9.53 (s, 1H), 6.09 (ddd, *J* = 9.5, 6.1, 1.1 Hz, 1H), 5.85 (dt, *J* = 5.8, 2.3 Hz, 1H), 5.68 (dddd, *J* = 9.5, 4.3, 1.9, 0.6 Hz, 1H), 5.62 (dt, *J* = 5.8, 1.9 Hz, 1H), 5.40 (dd, *J* = 3.9, 0.7 Hz, 1H), 4.45 (tt, *J* = 4.3, 0.9 Hz, 1H), 4.21 (ddd, *J* = 4.3, 3.0, 0.7 Hz, 1H), 3.49 (dd, *J* = 8.9, 3.3 Hz, 1H), 3.39 (d, *J* = 9.2 Hz, 1H), 3.31 (d, *J* = 9.2 Hz, 1H), 3.27 (s, 3H), 3.26 (s, 3H), 3.02 (ddddd, *J* = 4.9, 3.8, 2.9, 2.0, 0.8 Hz, 1H), 2.89 – 2.86 (m, 1H), 2.44 (t, *J* = 7.0 Hz, 1H), 2.29 (ddt, *J* = 16.0, 7.5, 2.2 Hz, 1H), 2.22 (ddt, *J* = 16.0, 6.6, 2.2 Hz, 1H), 2.12 (ddd, *J* = 14.2, 6.7, 4.5 Hz, 1H), 1.83 (dddd, *J* = 13.4, 6.7, 4.6, 3.3 Hz, 1H), 1.55 (dtd, *J* = 13.6, 9.3, 4.6 Hz, 1H), 1.40 (ddd, *J* = 14.3, 9.7, 4.6 Hz, 1H), 1.08 (s, 9H), 1.02 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 204.0, 164.5, 135.2, 134.0, 132.0, 128.5, 121.8, 79.5, 77.3, 76.1, 66.3, 59.3, 58.1, 56.9, 50.8, 46.2, 46.0, 44.1, 34.5, 28.9, 28.3, 21.5, 21.2, 21.1, 20.7.

A ^{13}C signal is observed to be overlapping with residual $CDCl_3$ at 77.3, resolved peaks are seen in the HSQC spectrum, provided below.

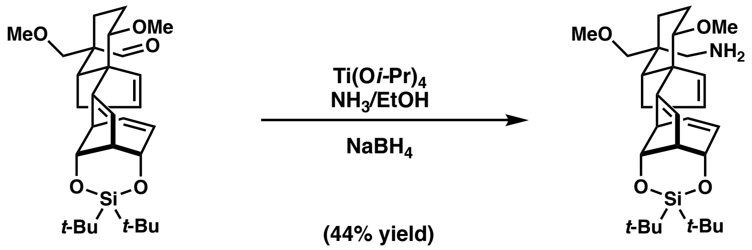
FTIR (NaCl, thin film): 2933, 2894, 2859, 2859, 1724, 1476, 1103, 993 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{29}H_{45}O_5Si$ $[M + H]^+$ 501.3031, found 501.3038.

$[\alpha]_D^{25}$ = +87° (c = 0.60, $CHCl_3$).

TLC (20%EtOAc/80%Hexanes), R*f*: 0.5 (UV, blue in *p*-anisaldehyde)

Preparation of primary amine 208 via reductive amination with NH_3:



206 **208**

A 40-mL vial with a septum cap was charged with the aldehyde **206** (50 mg, 0.10 mmol, 1 equiv), and dissolved in a freshly prepared solution of saturated NH_3/EtOH solution (10 mL). Ti(Oi-Pr)$_4$ (44 μL, 0.15 mmol, 1.5 equiv) was added via microsyringe, and the solution was allowed to stir for 3 hours at room temperature. Over this time, the reaction mixture turned cloudy. $NaBH_4$ (18.9 mg, 0.50 mmol, 5 equiv) was then added, and the reaction was allowed to stir for an additional 30 minutes at room temperature. The reaction was quenched with aqueous 28–30% NH_3 solution (5 mL), and the reaction was allowed to stir overnight. The following day, the reaction mixture was transferred to a round-bottomed flask, and concentrated *in vacuo* to remove the ethanol. The mixture was then transferred to a separatory funnel, and extracted with 10%IPA/90% $CHCl_3$ (5 x 20 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (2% to 3% 7 N NH_3/MeOH solution/ CH_2Cl_2) to primary amine **208** (22 mg, 0.044 mmol, 44% yield) as a clear oil.

Notes:

(1) NH_3/EtOH solution prepared by bubbling a dry 0 °C ethanol with NH_3 for 10 minutes.

(2) The yields of this reaction were somewhat variable, and the majority of the mass-balance was attributed to dimer formation. Despite running the reaction at high dilution, it was never possible to consistently achieve the desired product without the formation of the dimer product. While this reaction can be run in one step, an alternative two-step protocol was developed for scale-up and reproducibility.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 6.06 (ddd, *J* = 9.5, 6.1, 1.1 Hz, 1H), 5.87 (dt, *J* = 5.9, 2.3 Hz, 1H), 5.65 (ddd, *J* = 9.4, 4.4, 1.9 Hz, 1H), 5.44 – 5.39 (m, 2H), 4.46 (t, *J* = 4.7 Hz, 1H), 4.23 (ddd, *J* = 4.3, 3.0, 0.7 Hz, 1H), 3.56 (dd, *J* = 7.7, 2.8 Hz, 1H), 3.26 – 3.24 (m, 6H), 3.22 – 3.19 (m, 1H), 3.18 (d, *J* = 9.2 Hz, 1H), 3.05 – 3.00 (m, 1H), 2.88 (dd, *J* = 5.9, 4.6 Hz, 1H), 2.63 (d, *J* = 13.1 Hz, 1H), 2.58 (d, *J* = 13.1 Hz, 1H), 2.39 (dd, *J* = 10.0, 8.4 Hz, 1H), 2.31 – 2.26 (m, 2H), 1.68 (dddd, *J* = 13.3, 8.0, 5.4, 2.7 Hz, 1H), 1.61 – 1.37 (m, 4H), 1.34 – 1.21 (m, 1H), 1.08 (s, 9H), 1.00 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 166.4, 135.8, 134.1, 131.1, 128.1, 119.7, 79.7, 77.0, 76.1, 66.5, 58.8, 57.2, 56.9, 49.5, 46.3, 46.2, 44.0, 39.7, 35.2, 28.9, 28.3, 23.9, 21.8, 21.2, 20.7.

A ^{13}C signal is observed to be overlapping with residual $CDCl_3$ at 77.00, the peak can be seen in the HSQC spectrum, provided below.

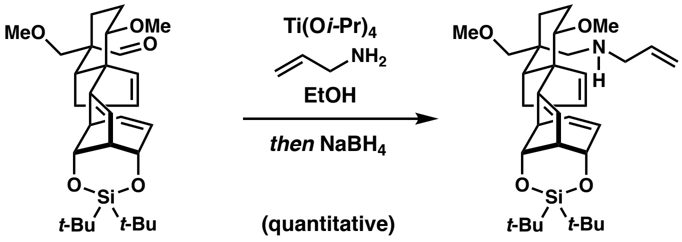
FTIR (NaCl, thin film): 3386, 3050, 2933, 2859, 2362, 1476, 1463, 1106, 992 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{29}H_{48}NO_4Si$ $[M + H]^+$ 502.3347, found 502.3344.

$[\alpha]_D^{25}$ = +105° (c = 0.67, $CHCl_3$).

TLC (10%MeOH/90%CH_2Cl_2), R*f*: 0.15 (UV, blue in *p*-anisaldehyde)

Preparation of *N*-allylamine 207:



206 **207**

A 100-mL, round-bottomed flask was charged with aldehyde **206** (311 mg, 0.621 mmol, 1 equiv), and azeotroped 3x with toluene (from the solvent system) to remove water, and put under high vacuum for 2 hours. The flask was equipped with a rubber septum, purged with N_2, and dissolved in EtOH (stored over 3 Å MS, 21 mL). Allylamine (freshly distilled over $CaCl_2$, 0.19 mL, 248 mmol, 4 equiv) was added followed by Ti(O*i*-Pr)$_4$ (0.39 mL, 1.24 mmol, 2 equv) and let stir for 90 minutes at room temperature. At this time, $NaBH_4$ (117 mg, 3.10 mmol, 5 equiv) was added in one portion, and let stir for 15 minutes further. The reaction was carefully quenched with aqueous 28–30% NH_3 solution (10 mL), and let stir for 10 minutes at room temperature. The reaction was then filtered through a basic alumina plug that had been pre-washed with EtOH, then flushed with ethyl acetate, and concentrated *in vacuo*. Then, the crude mixture was filtered through a silica plug, flushed with 100% CH_2Cl_2 to remove nonpolar impurities, and then with 5% 7 NH_3/95% CH_2Cl_2 to elute the product *N*-allyl amine **207**.

A sample of this material was purified by silica gel chromatography (to 2% to 3% to 4% 7 N NH_3/MeOH solution/ CH_2Cl_2) to afford analytically pure material for characterization:

^{1}H NMR (400 MHz, Chloroform-*d*): δ 6.06 (ddd, *J* = 9.5, 6.2, 1.1 Hz, 1H), 5.93 – 5.81 (m, 2H), 5.64 (ddd, *J* = 9.5, 4.4, 1.9 Hz, 1H), 5.43 – 5.38 (m, 2H), 5.16 (dq, *J* = 17.2, 1.7 Hz, 1H), 5.08 (dq, *J* = 10.3, 1.3 Hz, 1H), 4.47 – 4.42 (m, 1H), 4.22 (ddd, *J* = 4.2, 3.0, 0.7 Hz, 1H), 3.55 (dd, *J* = 7.5, 2.8 Hz, 1H), 3.29 – 3.15 (m, 10H), 3.02 (tdd, *J* = 5.8, 2.8, 1.4 Hz, 1H), 2.90 – 2.86 (m, 1H), 2.49 (s, 2H), 2.41 (dd, *J* = 10.3, 8.0 Hz, 1H), 2.33 – 2.26 (m, 2H), 1.71 – 1.61 (m, 1H), 1.61 – 1.49 (m, 2H), 1.41 – 1.31 (m, 1H), 1.07 (s, 9H), 1.00 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 166.5, 136.8, 135.8, 134.0, 131.3, 128.0, 119.6, 116.1, 79.6, 77.0 (overlapping with $CDCl_3$), 76.5, 66.5, 58.8, 57.2, 56.8, 56.3, 53.0, 46.3, 46.2, 44.5, 39.3, 35.4, 28.9, 28.3, 24.3, 21.7, 21.2, 20.7.

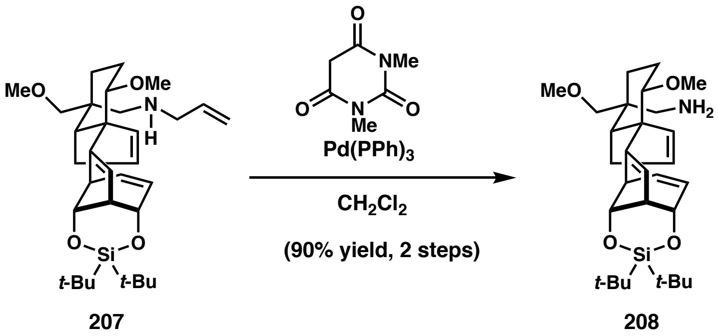
FTIR (NaCl, thin film): 3049, 2934, 2898, 2859, 2859, 1475, 1102, 1106, 992, 825, 732. cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{32}H_{52}NO_4Si$ $[M + H]^+$ 542.3660, found 542.3653.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = +104° (*c* = 2.20, $CHCl_3$).

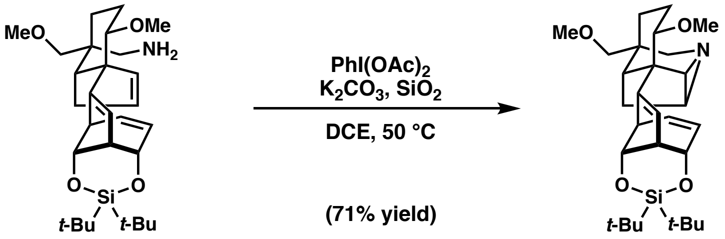
TLC (5% 7N NH_3 in MeOH/95%CH_2Cl_2), R_f: 0.5 (UV, blue in *p*-anisaldehyde)

Preparation of primary amine 208 via deprotection of *N*-allyl 207:



A 100-mL, round-bottomed flask was charged with the crude allylamine **207** and 3,5-dimethylbarbituric acid (0.582 g, 3.72 mmol, 6 equiv), and dissolved in CH_2Cl_2 (12.4 mL) under N_2. Meanwhile, a solution of $Pd(PPh_3)_4$ (72 mg, 0.0621 mmol, 10 mol % in 3 mL CH_2Cl_2) was made inside the glovebox, brought out, and added via syringe to the solution of substrate. The reaction was allowed to stir for 1 hour at room temperature, and was then quenched with sat. $NaHCO_3$ (20 mL). The mixture was then transferred to a separatory funnel, and extracted with 20%IPA/80% $CHCl_3$ (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (1% to 2% to 3% to 4% 7 N NH_3/MeOH solution/ CH_2Cl_2) to afford primary amine **208** (280 mg, 0.559 mmol, 90% yield) as a clear oil.

Preparation of aziridine 209:



208 **209**

A 100-mL, round-bottomed flask was charged with primary amine **208** (281 mg, 0.559 mmol, 1 equiv), PhI(OAc)$_2$ (288 mg, 0.895 mmol, 1.6 equiv), K$_2$CO$_3$ (206 mg, 1.49 mmol, 2.7 equiv), SiO$_2$ gel (13.93 g), and suspended in DCE (55.9 mL) under N$_2$. The mixture was stirred for 30 minutes at room temperature, and then heated to 50 °C in an oil bath and was allowed to stir at 50 °C for 1 hour. At this time, the reaction was allowed to cool to room temperature, and was filtered through a plug of SiO$_2$ and flushed with 8% 7 N NH$_3$/ 92% CH$_2$Cl$_2$ solution to elute the product aziridine, and concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (4% to 6% MeOH in CH$_2$Cl$_2$) to afford aziridine **209** (198 mg, 0.397 mmol, 71% yield) as a clear oil.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 6.11 (ddd, *J* = 9.5, 6.1, 1.1 Hz, 1H), 5.67 (ddd, *J* = 9.3, 4.4, 1.9 Hz, 1H), 5.45 (dd, *J* = 3.9, 0.7 Hz, 1H), 4.51 (t, *J* = 4.7 Hz, 1H), 4.24 – 4.17 (m, 1H), 3.38 – 3.32 (m, 4H), 3.27 (s, 3H), 3.09 (d, *J* = 8.9 Hz, 1H), 3.05 – 3.01 (m, 1H), 2.99 – 2.91 (m, 2H), 2.88 (dd, *J* = 6.0, 4.6 Hz, 1H), 2.78 (d, *J* = 14.3 Hz, 1H), 2.60 – 2.58 (m, 1H), 2.48 – 2.46 (m, 1H), 2.17 – 2.08 (m, 1H), 1.82 (d, *J* = 13.4 Hz, 1H), 1.69 – 1.56 (m, 2H), 1.50 – 1.43 (m, 2H), 1.30 (td, *J* = 14.2, 3.7 Hz, 1H), 1.07 (s, 9H), 1.01 (s, 9H).

^{13}C NMR (101 MHz, CDCl$_3$): δ ^{13}C NMR (101 MHz, CDCl$_3$) δ 162.7, 135.0, 128.8, 123.9, 78.9 (2 overlapping ^{13}C signals), 77.3, 66.3, 59.3, 56.8, 50.2, 50.0, 46.0, 45.1, 38.1, 35.9, 35.6, 33.7, 32.9, 28.9, 28.3, 24.0, 22.6, 21.2, 20.7. Two ^{13}C signals are observed to be overlapping at 78.9. Additionally, a ^{13}C signal is observed to be overlapping with residual CDCl$_3$ at 77.3. Resolved peaks are seen in the HSQC spectrum, provided below.

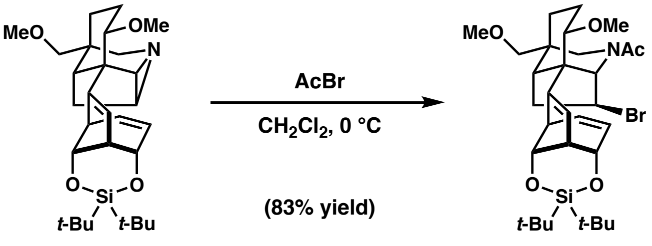
FTIR (NaCl, thin film): 2938, 2859, 2824, 2362, 1476, 1463, 1110, 993 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{29}H_{46}NO_4Si$ $[M + H]^+$ 500.3191, found 500.3178

$[\alpha]_D^{25}$ = +24.6° (c = 1.30, CHCl$_3$).

TLC (10%MeOH/90%CH$_2$Cl$_2$), R$_f$: 0.5 (UV, teal in *p*-anisaldehyde)

Preparation of bromide 210:



209 **210**

A 100-mL, round-bottomed flask was charged with aziridine **209** (198 mg, 0.397 mmol, and CH$_2$Cl$_2$ (7.8 mL) under N$_2$, and cooled to 0 °C in an ice bath. Acetyl bromide (86.1 µL, 1.1645 mmol, 3 equiv) added dropwise via microsyringe, and was allowed to stir for an additional 15 minutes while maintained at 0 °C. Reaction quenched with sat. NaHCO$_3$ (10 mL), transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with CH$_2$Cl$_2$ (3 x 20 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (30% to 40% to 50% ethyl acetate in hexanes) to afford bromide **210** (206 mg, 0.330 mmol, 83% yield) as a white solid.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 6.17 (ddd, *J* = 9.6, 6.1, 1.1 Hz, 1H), 5.73 – 5.68 (m, 2H), 4.76 – 4.71 (m, 1H), 4.65 (s, 1H), 4.24 – 4.19 (m, 1H), 4.09 – 4.03 (m, 2H), 3.29 (s, 3H), 3.23 (s, 3H), 3.14 (d, *J* = 9.2 Hz, 1H), 3.09 – 3.05 (m, 1H), 3.04 – 2.98 (m, 2H), 2.51 (dd, *J* = 14.6, 8.8 Hz, 1H), 2.38 (d, *J* = 14.4 Hz, 1H), 2.34 – 2.23 (m, 2H), 2.18 (s, 3H), 2.07 – 1.98 (m, 1H), 1.74 – 1.67 (m, 1H), 1.50 – 1.32 (m, 2H), 1.16 – 1.08 (m, 1H), 1.08 (s, 9H), 1.03 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 169.0, 135.9, 128.2, 124.9, 80.6, 78.1, 77.6, 66.6, 66.2, 59.4, 55.7, 53.1, 47.3, 46.3, 46.0, 45.7, 42.8, 35.5, 35.4, 32.2, 29.7, 29.0, 28.3, 24.6, 21.8, 21.3, 20.8.

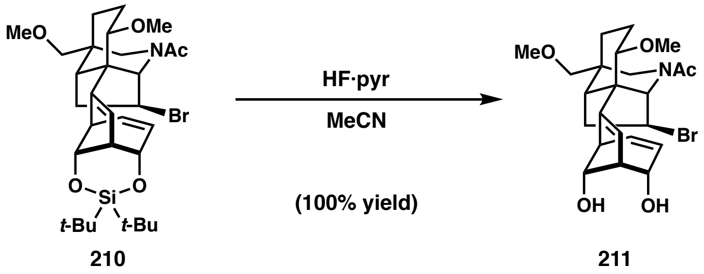
FTIR (NaCl, thin film): 2935, 2867, 2826, 1658, 1631, 1471, 1462, 1427, 1232, 1109 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{31}H_{49}BrNO_5Si$ $[M + H]^+$ 622.2558, found 622.2540

$[\alpha]_D^{25}$ = +50.9° (*c* = 1.32, $CHCl_3$).

TLC (50%EtOAc/50%hexanes), R*f*: 0.4 (UV, green in *p*-anisaldehyde)

Preparation of diol 211:



A 100-mL, round-bottomed flask was charged with silylene **210** (206 mg, 0.331 mmol, 1 equiv) and MeCN (6 mL). A solution of HF•Py (pyridine ~30%, HF ~70%, 206 mg) in MeCN (1 mL) was added, and the reaction was allowed to stir for 30 minutes at room temperature. The reaction was quenched with sat. $NaHCO_3$ (20 mL), transferred to a separatory funnel and extracted with 20%IPA/80%$CHCl_3$ (5 x 20 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting crude residue was dissolved in CH_2Cl_2, filtered through a plug of SiO_2, flushed with CH_2Cl_2 to remove the nonpolar impurities and then 5% MeOH/95% CH_2Cl_2 to elute the product to afford diol **211** (160 mg, 0.331 mmol, 100% yield) as a clear oil.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 6.10 (ddt, *J* = 9.6, 6.3, 1.1 Hz, 1H), 5.84 – 5.78 (m, 2H), 4.70 – 4.61 (m, 2H), 4.09 – 4.02 (m, 2H), 3.96 (s, 1H), 3.29 (s, 3H), 3.21 (s, 3H), 3.18 (dd, *J* = 7.8, 2.4 Hz, 1H), 3.13 (d, *J* = 9.2 Hz, 1H), 3.03 (d, *J* = 9.1 Hz, 1H), 2.96 – 2.88 (m, 1H), 2.84 – 2.78 (m, 1H), 2.77 – 2.73 (m, 1H), 2.55 – 2.47 (m, 1H), 2.38 (dd, *J* = 14.4, 2.1 Hz, 1H), 2.31 – 2.24 (m, 2H), 2.19 (s, 3H), 2.06 – 1.98 (m, 1H), 1.74 – 1.66 (m, 2H), 1.46 (dddd, *J* = 17.2, 12.6, 4.4, 2.2 Hz, 1H), 1.41 – 1.27 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 169.1, 132.4, 129.0, 125.1, 80.8, 78.0, 75.1, 66.6, 65.6, 59.4, 55.8, 52.9, 47.4, 47.4, 45.5, 44.5, 42.8, 35.5, 35.4, 32.2, 24.5, 21.8.

A 13C signal is observed to be missing in the ^{13}C NMR, but can be seen in the HMBC spectrum at 159.5, which is provided below.

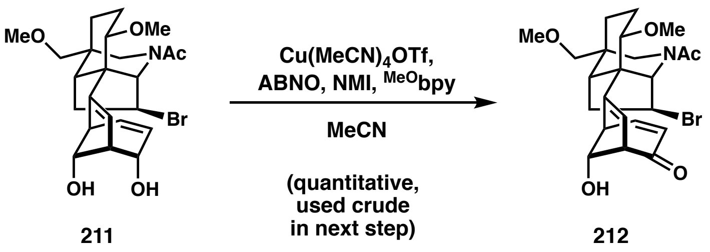
FTIR (NaCl, thin film): 3367, 2930, 2877, 2826, 2239, 1624, 1426, 1234, 1094, 917 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{23}H_{33}BrNO_5$ $[M + H]^+$ 482.1537, found 482.1539

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = +39.1° (*c* = 0.55, $CHCl_3$).

TLC (100%EtOAc), R*f*: 0.25 (UV, green/blue in *p*-anisaldehyde)

Preparation of enone 212:



A 100-mL, round-bottomed flask was charged with diol **211** (159 mg, 0.3308 mmol, 1.0 equiv) and MeCN (3.3 mL). A homemade stock-solution [see note below] 0.05M 4,4'-dimethoxy-2,2'-bipyridine (^{MeO}bpy), 0.05 M in ABNO, and 0.2 M *N*-methylimidazole was added to the solution of diol (0.61 mL, 0.031 mmol, 0.1 equiv) followed by $Cu(MeCN)_4OTf$ (11.6 mg, 0.031 mmol, 0.1 equiv) was added, and the clear red/brown reaction mixture was stirred until slightly yellow green, and the TLC indicated the reaction had gone to completion (ca. 90 min), at which point the solution was filtered through a short plug of silica that had been pre-packed with 5%MeOH/95% CH_2Cl_2, and flushed with more 5%MeOH/95% CH_2Cl_2 to elute the product, and concentrated *in vacuo*. The crude enone was subjected to the next step without further purification. For characterization purposes, **212** could be purified via silica gel chromatography (1% to 2% to 3% to 4% to 5% MeOH in CH_2Cl_2).

Notes:

(1) A 0.05 M solution of 4,4'-dimethoxy-2,2'-bipyridine, 0.05M ABNO and 0.2M NMI solution in MeCN could be pre-made and kept in an 8 °C freezer and was stable and good to use for an extended time (>4 months). This homemade stock solution was used in this reaction, and makes it easy to add more catalyst.

(2) This selective oxidation to the enone is very clean and performs well, but oxidation to the diketone has been observed if too much catalyst is added. It is important to monitor this reaction by TLC. It is best to run this reaction carefully, and start with less catalyst, because more can be added if needed to reach full conversion to the desired product.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.19 (ddd, *J* = 9.8, 6.4, 1.6 Hz, 1H), 5.95 – 5.90 (m, 2H), 5.18 – 5.11 (m, 1H), 4.71 (s, 1H), 4.13 – 4.04 (m, 2H), 3.46 (dd, *J* = 6.4, 4.4 Hz, 1H), 3.33 (dddd, *J* = 4.8, 3.9, 2.0, 1.0 Hz, 1H), 3.29 (s, 3H), 3.29 – 3.20 (m, 1H), 3.21 (s, 3H), 3.14 (d, *J* = 9.2 Hz, 1H), 3.04 (d, *J* = 9.2 Hz, 1H), 2.64 – 2.56 (m, 2H), 2.41 (dd, *J* = 14.6, 2.3 Hz, 1H), 2.36 (d, *J* = 6.3 Hz, 1H), 2.28 (dt, *J* = 15.3, 6.0 Hz, 1H), 2.21 (s, 3H), 2.05 – 1.98 (m, 1H), 1.75 – 1.69 (m, 1H), 1.51 – 1.32 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 195.1, 169.0, 160.1 (br), 150.9, 126.3, 124.1, 85.0, 82.0, 77.9, 66.8, 60.9, 59.4, 55.1, 52.9, 47.8, 47.5, 45.4, 42.7, 35.5, 35.3, 32.0, 24.5, 21.9.

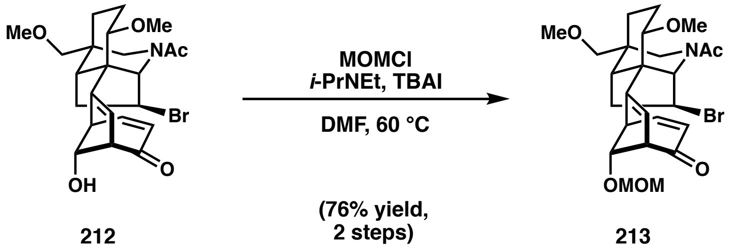
FTIR (NaCl, thin film): 3367, 2930, 2877, 2826, 2239, 1624, 1426, 1234, 1094, 917 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{23}H_{31}BrNO_5$ $[M + H]^+$ 480.1380, found 480.1367

$[\boldsymbol{\alpha}]^{\mathbf{25}}_{\mathbf{D}}$ = +169° (c = 0.50, CHCl$_3$).

TLC (100%EtOAc), R$_f$: 0.25 (UV, pink in *p*-anisaldehyde)

Preparation of methoxymethyl ether 213:



A 100-mL, round-bottomed flask was charged with crude enone **212** (159 mg, 0.3308 mmol, 1.0 equiv), TBAI (61 mg, 0.165 mmol, 0.50 mol %), and DMF (6.6 mL). *i*-Pr$_2$NEt (0.87 mL, 4.96 mmol, 15.0 equiv) added followed by dropwise addition of MOMCl (0.25 mL, 3.31 mmol, 10 equiv), causing a smokiness to evolve from the reaction. The flask was then lowered into a 60 °C oil bath, and let stir for 16 hours at this temperature. The reaction was then cooled to room temperature, diluted with sat. NH$_4$Cl (20 mL), transferred to a separatory funnel and extracted with EtOAc (4 x 20 mL). The combined organic extracts were dried over Na$_2$SO$_4$, filtered, and concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (10% to 20% to 30% to 40% acetone in hexanes) to afford methoxy methyl ether **213** (131 mg, 0.251 mmol, 76% yield over two steps) as a white foam.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.11 (ddd, J = 9.8, 6.4, 1.6 Hz, 1H), 5.95 (d, J = 4.0 Hz, 1H), 5.81 (ddd, J = 9.8, 1.9, 0.6 Hz, 1H), 4.92 (q, J = 4.5 Hz, 1H), 4.70 (s, 1H), 4.65 (s, 2H), 4.12 – 4.04 (m, 2H), 3.50 – 3.46 (m, 1H), 3.41 – 3.37 (m, 1H), 3.32 (s, 3H), 3.27 (s, 3H), 3.27 – 3.19 (m, 1H), 3.19 (s, 3H), 3.13 (d, *J* = 9.2 Hz, 1H), 3.03 (d, *J* = 9.2 Hz, 1H), 2.62 – 2.54 (m, 1H), 2.42 – 2.33 (m, 2H), 2.31 – 2.23 (m, 1H), 2.21 (s, 3H), 2.04 – 1.96 (m, 1H), 1.74 – 1.66 (m, 1H), 1.47 – 1.33 (m, 2H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 195.6, 168.9, 160.0 (br), 150.6, 125.4, 123.9, 96.1, 90.6, 82.0, 77.9, 66.7, 59.4, 59.3, 55.9, 55.1, 52.9, 47.6, 46.2, 45.5, 42.7, 35.4, 35.3, 31.9, 24.5, 21.9.

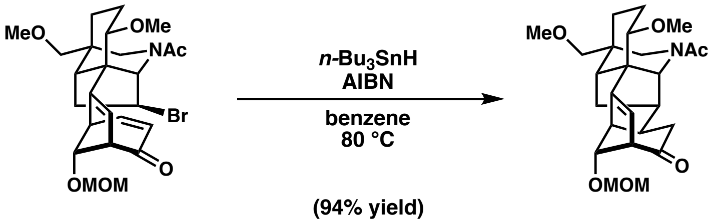
FTIR (NaCl, thin film): 3454, 3056, 2920, 2825, 2244, 1703, 1682, 1654, 1621, 1454, 1109, 1035, 918 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{25}H_{35}BrNO_6$ $[M + H]^+$ 524.1642, found 524.1689

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = +179° (*c* = 0.50, CHCl$_3$).

TLC (100%EtOAc), R*f*: 0.5 (UV, pink in *p*-anisaldehyde)

Preparation of hexacycle 214:



213 **214**

A 100-mL, round-bottomed flask was charged with enone **213** (100 mg, 0.1907 mmol, 1.0 equiv) and dissolved in benzene (19 mL). The solution was sparged with Ar for 20 minutes. Meanwhile, a solution of AIBN (15.7 mg, 0.094 mmol, 0.5 equiv) and *n*-Bu$_3$SnH (1M in cyclohexane solution, 1.14 mL, 1.144 mmol) in benzene (3 mL) was also sparged with Ar for 20 minutes. The round-bottom flask containing the substrate was then heated to 80 °C in an oil bath, and the AIBN/*n*-Bu_3SnH solution was added over 7 hours to the substrate solution via syringe pump. By TLC, the reaction looked done after ~half of the AIBN/*n*-Bu_3SnH solution had been added, but the remainder was still added. After the addition of the AIBN/*n*-Bu_3SnH solution was complete, the reaction was cooled to room temperature and concentrated *in vacuo*. The resulting crude residue was purified by chromatography with a 90% SiO_2/ 10% ground K_2CO_3 solid support[6] eluting (20% to 30% to 40% to 50% acetone in hexanes) to afford hexacycle **214** (80 mg, 0.179 mmol, 94% yield) as a clear oil.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 5.83 (d, *J* = 2.6 Hz, 1H), 4.68 – 4.64 (m, 2H), 4.48 (t, *J* = 5.6 Hz, 1H), 4.07 (s, 1H), 3.74 (d, *J* = 14.6 Hz, 1H), 3.58 (dd, *J* = 10.4, 7.2 Hz, 1H), 3.34 (s, 3H), 3.30 (s, 3H), 3.29 (s, 3H), 3.24 – 3.19 (m, 2H), 3.03 (d, *J* = 9.0 Hz, 1H), 2.91 (t, *J* = 5.7 Hz, 1H), 2.73 – 2.62 (m, 2H), 2.33 – 2.22 (m, 3H), 2.16 – 2.06 (m, 5H), 2.01 – 1.94 (m, 1H), 1.78 – 1.67 (m, 2H), 1.44 (dddd, *J* = 14.9, 13.2, 4.0, 1.7 Hz, 1H), 1.35 – 1.30 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 204.6, 169.8, 153.4, 121.4, 96.3, 80.0, 79.0, 78.2, 65.0, 59.7, 59.4, 55.9, 55.1, 51.5, 46.2, 45.4, 42.5, 42.2, 39.2, 37.7, 33.8, 31.9, 30.5, 24.7, 22.5.

2-dimensional NMR data is included below (HSQC, HMBC, COSY, NOESY).

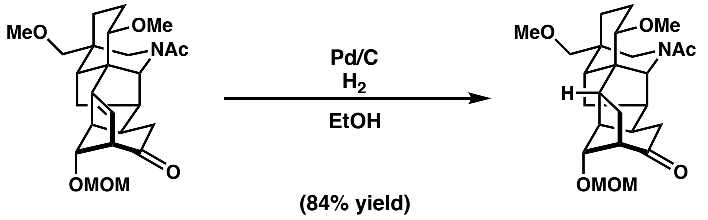
FTIR (NaCl, thin film): 2924, 2825, 1708, 1644, 1418, 1405, 1150, 1112, 1091, 1045, 1001, 919 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{25}H_{39}N_2O_6$ $[M + NH_4]^+$ 463.2803, found 463.2797

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = +84.5° (*c* = 1.0, $CHCl_3$).

TLC (100%EtOAc), R*f*: 0.3 (UV, brown in *p*-anisaldehyde)

Preparation of carbocycle 215:



214 **215**

A 50-mL, round-bottomed flask was charged with alkene **214** (100 mg, 0.224 mmol), Pd/C (10% wt % palladium, contains 67% H_2O, 300 mg, 0.282 mmol, 1.25 equiv), and EtOH (5 mL). The flask was then equipped with a rubber septum, and the suspension was sparged with an H_2 balloon for 10 minutes, then let stir under H_2 for an additional 20 minutes. The reaction was monitored by TLC and LCMS, indicating that the reaction had gone to completion. The reaction mixture was then sparged with an argon balloon for 20 minutes, then filtered through a plug of SiO_2 and celite that had been pre-packed with 5%MeOH/95% CH_2Cl_2, flushed with more 5%MeOH/95% CH_2Cl_2, and then concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (20% to 30% to 40% to 50% acetone in hexanes) to afford **215** (84 mg, 0.187 mmol, 84% yield) as a white foam.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 4.60 (s, 2H), 4.11 (t, *J* = 5.0 Hz, 1H), 3.99 (s, 1H), 3.86 (d, *J* = 14.4 Hz, 1H), 3.31 (s, 3H), 3.28 (s, 3H), 3.20 (m, 5H), 3.09 (dd, *J* = 10.4, 7.1 Hz, 1H), 2.98 (d, *J* = 9.1 Hz, 1H), 2.76 (dd, *J* = 7.8, 5.6 Hz, 1H), 2.70 (dd, *J* = 19.6, 11.4 Hz, 1H), 2.58 (d, *J* = 15.0 Hz, 1H), 2.56 – 2.47 (m, 1H), 2.44 – 2.37 (m, 1H), 2.37 – 2.29 (m, 1H), 2.06 (d, *J* = 8.2 Hz, 7H), 1.92 – 1.85 (m, 2H), 1.71 – 1.64 (m, 2H), 1.43 (tdd, *J* = 13.4, 4.4, 1.9 Hz, 1H), 1.33 – 1.25 (m, 1H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 212.9, 169.7, 96.0, 84.0, 79.7, 78.2, 59.4, 56.8, 55.8, 55.6, 52.3, 48.3, 46.8, 46.1, 44.5, 43.9, 39.1, 37.4, 36.6, 33.8, 32.0, 28.6, 27.3, 25.2, 22.5.

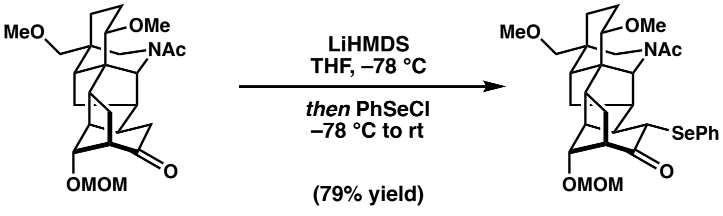
TLC (100%EtOAc), R*f*: 0.3 (UV, yellow in *p*-anisaldehyde)

FTIR (NaCl, thin film): 2913, 2241, 1714, 1698, 1650, 1644, 1634, 1614, 1470, 1454, 1108, 1041, 919 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{25}H_{38}NO_6$ $[M + H]^+$ 448.2694, found 448.2687

$[\alpha]_D^{25}$ = –57.4° (*c* = 2.47, CHCl$_3$).

Preparation of α-selenide 200:



215

216

A 100-mL, round-bottomed flask was charged with ketone **215** (84 mg, 0.189 mmol, 1 equiv), and azeotroped with PhMe (from the solvent system, 2 x 10 mL) to remove H_2O and put under high vacuum for two hours. The flask was then equipped with a rubber septum, purged with N_2, dissolved in THF (5.4 mL), and cooled to –78 °C in a dry ice/acetone bath. LiHMDS (1M in THF, 0.34 mL, 0.340 mmol, 1.8 equiv) was added dropwise via syringe, causing the solution to turn yellow, and was allowed to stir for minutes at –78 °C. At this time, the PhSeCl (72.3 mg, 0.38 mmol, 2 equiv) solution in THF (1 mL) was added dropwise via syringe. This was allowed to stir for an additional 10 minutes at –78 °C, the bath was then removed, and this was allowed to stir for 10 minutes at room temperature. The reaction was quenched with sat. $NaHCO_3$ (10 mL), and the biphasic mixture was transferred to a separatory funnel with Et_2O (15 mL). The layers were separated, and the aqueous layer was extracted CH_2Cl_2 (4 x 15 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (20% to 30% to 35% acetone in hexanes) to afford α-selenide **216** (90 mg, 0.149 mmol, 79%) as a yellow oil.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.74 – 7.67 (m, 2H), 7.28 – 7.26 (m, 1H), 7.26 – 7.19 (m, 2H), 4.60 (d, *J* = 6.8 Hz, 1H), 4.57 (d, *J* = 6.8 Hz, 1H), 4.12 (t, *J* = 5.1 Hz, 1H), 4.00 (s, 1H), 3.78 (d, *J* = 14.4 Hz, 1H), 3.49 (d, *J* = 5.4 Hz, 1H), 3.36 (s, 3H), 3.29 (s, 3H), 3.20 – 3.17 (m, 4H), 3.09 (dd, *J* = 10.3, 7.0 Hz, 1H), 3.02 – 2.96 (m, 2H), 2.63 – 2.50 (m, 3H), 2.38 – 2.31 (m, 1H), 2.14 – 2.01 (m, 4H), 1.91 (d, *J* = 7.3 Hz, 1H), 1.85 (dd, *J* = 14.6, 8.1 Hz, 1H), 1.79 (s, 3H), 1.70 – 1.57 (m, 2H), 1.41 (tdd, *J* = 13.3, 4.3, 1.7 Hz, 1H), 1.30 – 1.25 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 209.8, 169.7, 134.8, 131.1, 129.1, 128.1, 95.8, 84.1, 79.6, 78.1, 59.4, 57.0, 56.1, 55.7, 52.5, 50.8, 48.3, 47.0, 46.0, 44.8, 43.7, 38.5, 37.5, 32.1, 29.2, 28.7, 27.9, 25.0, 22.2.

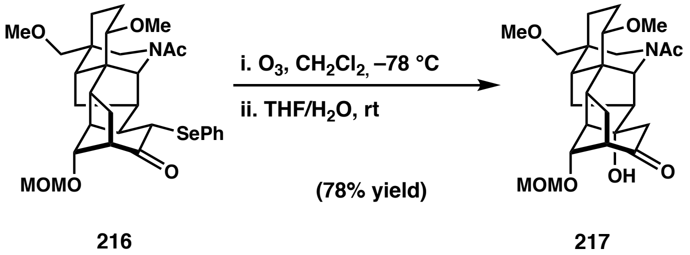
FTIR (NaCl, thin film): 3054, 2922, 2824, 2241, 1714, 1644, 1634, 1579, 1493, 1470, 1434, 1349, 1150, 1043 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{31}H_{42}NO_6Se$ $[M + H]^+$ 604.2172, found 604.2164

$[\alpha]_D^{25}$ = –66.8° (*c* = 3.76, $CHCl_3$).

TLC (100%EtOAc), R*f*: 0.5 (UV, yellow in *p*-anisaldehyde)

Preparation of β-hydroxy ketone 217:



A 50-mL, round-bottomed flask was charged with α-selenide **216** (35 mg, 0.0589 mmol, 1 equiv), and dissolved in CH_2Cl_2 (4 mL). The flask was cooled to –78 °C, at which time ozone (as a mixture with O_2) was gently bubbled through the solution (O_2 flow rate = 1/8 L/min, 1 setting on ozone generator) for 10 min. During this time, the solution turns a faint blue. The reaction was monitored by TLC, and after 10 minutes, all of the starting material had been consumed and converted to the strained enone, visible by TLC/LCMS. The solution was then sparged with Ar for 15 minutes, and pyridine (2 drops) was added. The reaction was allowed to warm to room temperature, and then was concentrated *in vacuo* The crude mixture was then redissolved in THF (1.5 mL) and H_2O (1.5 mL), and was allowed to stir at room temperature for 16 hours. The reaction was then concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (1% to 2% to 3% to 4 % MeOH in CH_2Cl_2) to afford β-hydroxy ketone **217** (21 mg, 0.0453 mmol, 78% yield) as a clear oil.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 4.67 (d, *J* = 6.7 Hz, 1H), 4.65 (d, *J* = 6.7 Hz, 1H), 4.27 (t, *J* = 5.0 Hz, 1H), 3.97 (s, 1H), 3.89 (d, *J* = 14.4 Hz, 1H), 3.35 (s, 3H), 3.30 (s, 3H), 3.22 – 3.13 (m, 7H), 3.01 (d, *J* = 9.1 Hz, 1H), 2.87 (dd, *J* = 7.4, 5.2 Hz, 1H), 2.78 – 2.77 (m, 1H), 2.62 (d, *J* = 13.7 Hz, 1H), 2.50 – 2.44 (m, 2H), 2.14 – 2.01 (m, 8H), 1.94 –

1.89 (m, 1H), 1.79 (dd, J = 15.2, 7.8 Hz, 1H), 1.73 – 1.67 (m, 1H), 1.45 (dddd, J = 15.1, 13.2, 4.4, 1.7 Hz, 1H), 1.35 – 1.26 (m, 1H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 210.4, 169.7, 96.3, 82.7, 80.5, 78.0, 73.4, 59.5, 58.5, 56.1, 55.5, 52.2, 51.7, 50.6, 48.3, 45.6, 45.3, 44.4, 44.3, 37.4, 31.9, 27.0, 25.3, 25.2, 22.5.

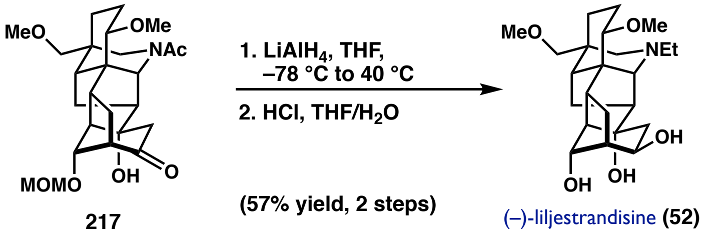
FTIR (NaCl, thin film): 3422, 2926, 2891, 2826, 2242, 1713, 1633, 1462, 1434, 1153, 1106, 1043, 920 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{25}H_{38}NO_7$ [M + H]$^+$ 464.2643, found 464.2646

$[\alpha]_D^{25}$ = –52.6° (c = 0.70, CHCl$_3$).

TLC (10%MeOH/90%CH$_2$Cl$_2$), R$_f$: 0.5 (UV, yellow in p-anisaldehyde)

Preparation of (–)-liljestrandisine (52):



A 2-dram vial was charged with ketone **217** (12 mg, 25 µmol, 1 equiv), azeotroped with toluene (from the solvent system, 2 x 2 mL) and put under high vacuum for 1 hour. The vial was then equipped with a rubber septum, purged with N$_2$, and charged with Et$_2$O (2.5 mL) to dissolve the substrate (takes time to dissolve, **217** is minimally soluble in Et$_2$O). The substrate solution was then cooled to –78 °C in a dry ice/acetone bath, and LiAlH$_4$ solution (1 M in THF, 78 µL, 78 µmol, 3 equiv) was added dropwise via microsyringe. After 10 minutes at –78 °C, the bath was removed and the reaction was allowed to warm up to room temperature. The septum was replaced with a cap, and the reaction was heated to 40 °C in a pre-heated heating block. After 30 minutes at 40 °C, the reaction was cooled to room temperature, and carefully quenched with aqueous 10% NaOH solution (2 mL). The layers were separated, and the aqueous layer was extracted with 20%IPA/80%$CHCl_3$ (5 x 4 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was then transferred to a new 2 dram vial, and used in the next step without further purification.

The 2-dram vial containing the crude residue from the $LiAlH_4$ reduction was dissolved in THF (0.3 mL), H_2O (0.15 mL). 75 μL of concentrated HCl was subsequently added, and the reaction was allowed to stir for 20 hours at room temperature. Monitoring by LCMS indicated full conversion to the product. The reaction as then carefully quenched with aqueous 10% NaOH solution (2 mL), and diluted with 20%IPA/80%$CHCl_3$ (4 mL). The layers were separated, and the aqueous layer was extracted with 20%IPA/80%$CHCl_3$ (5 x 4 mL). As an additional precaution, the aqueous layer was made sure to be basic with pH paper, and an LCMS sample of the aqueous layer was taken to ensure that no product was left behind. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by preparative thin layer chromatography (mobile phase: 10% 7 N NH_3 in MeOH/ 90% CH_2Cl_2) to furnish (–)-liljestrandisine (**52**) (6 mg, 14 μmol, 57% yield over 2 steps).

^{1}H NMR (400 MHz, Chloroform-*d*): δ 4.25 (t, *J* = 5.2 Hz, 1H), 3.89 – 3.84 (m, 1H), 3.30 (s, 3H), 3.26 (s, 3H), 3.18 (s, 1H), 3.09 (d, *J* = 9.0 Hz, 1H), 3.07 (dd, *J* = 10.8, 6.5 Hz, 1H), 2.99 (d, *J* = 9.0 Hz, 1H), 2.63 (dd, *J* = 17.5, 8.8 Hz, 1H), 2.55 – 2.49 (m, 2H), 2.40 – 2.35 (m, 1H), 2.30 – 2.21 (m, 3H), 2.11 – 2.05 (m, 2H), 2.03 – 1.94 (m, 3H), 1.93

– 1.87 (m, 2H), 1.84 – 1.80 (m, 2H), 1.80 – 1.75 (m, 1H), 1.75 – 1.69 (m, 2H), 1.65 (d, *J* = 7.4 Hz, 1H), 1.48 (dd, *J* = 14.9, 7.9 Hz, 1H), 1.44 – 1.34 (m, 1H), 1.05 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 86.2, 79.4, 76.0, 73.6, 72.6, 63.1, 59.5, 56.4, 53.1, 49.6, 48.6, 46.5, 46.4, 46.0, 45.7, 42.4, 40.8, 38.7, 32.8, 27.9, 25.8, 24.6, 13.7.

FTIR (NaCl, thin film): 3330, 2923, 2883, 2814, 1455, 1094 cm^{-1}.

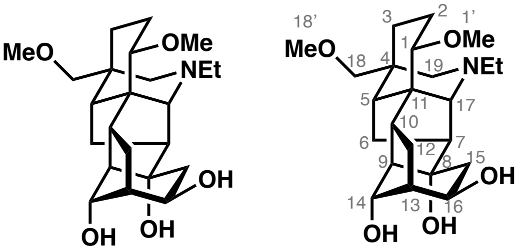
HRMS: (ESI-TOF) calc'd for $C_{23}H_{38}NO_5$ $[M + H]^+$ 408.2744, found 408.2736

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = –9.5° (*c* = 0.15, CHCl$_3$).

TLC (10%7N NH$_3$ in MeOH/90%CH$_2$Cl$_2$), R$_f$: 0.5 (ninhydrin)

^{1}H and ^{13}C line list comparison tables are shown below with natural liljestrandisine.[7]

The following carbon numbering system is used in the line list comparisons:



(–)-liljestrandisine

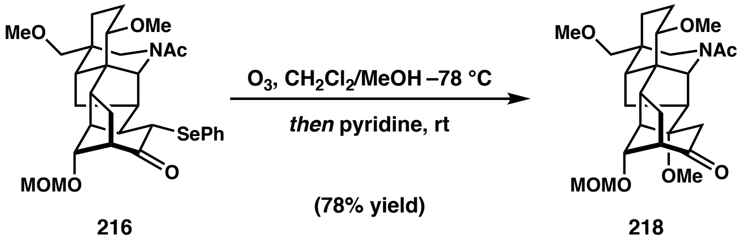
Table S3.1. Comparison of ^{1}H NMR data for Authentic (*ref.* 6) vs. Synthetic (–)-liljestrandisine.

	authentic liljestrandisine Wang, 2004 (*ref.* 6) (400 MHz, $CHCl_3$) $[\alpha]_D$=–12 ° (c =0.5, $CHCl_3$)	synthetic liljestrandisine this report (400 MHz, $CHCl_3$) $[\alpha]_D$=–9.5 ° (c =0.15, $CHCl_3$)
Carbon #, multiplicity	^{1}H (δ) ppm	^{1}H (δ) ppm
1 d	3.07, dd(10.4, 6.4)	3.07, dd(10.8, 6.5), 1H
2 t	1.98, m; 2.19, m	1.98, m, 1H; 2.25, m, 1H
3 t	1.38, dd(11.6); 1.74, m	1.39, m, 1H; 1.77, m, 1H
4 s	–	–
5 d	1.64, d(7.2)	1.65, d(7.4), 1H
6 t	1.47, dd(14.4, 7.6; 1.89, d(7.6)	1.48, dd(14.9, 7.9), 1H; 1.90, m, 1H
7 d	2.07, d(8.0)	2.08, m, 1H
8 s	–	–
9 d	2.25, m	2.25, m, 1H
10 d	1.70, m	1.71, m, 1H
11 s	–	–
12 t	1.78, m; 1.78, m	1.82, m, 1H; 1.82, m, 1H
13 d	2.23, m	2.25, m, 1H
14 d	4.22, t(5.0)	4.25, t(5.2), 1H
15 t	1.95, m; 2.58, m	1.98, m, 1H; 2.63, dd(17.5, 8.8), 1H
16 d	3.82, d(8.0)	3.87, m, 1H
17 d	3.18, s	3.18, s, 1H
18 t	2.99, ABq(9.2); 3.11, ABq(8.4)	2.99, ABq(9.0),1H; 3.09, ABq(9.0), 1H
19 t	2.02, d(11.6); 2.51, m	1.98, m, 1H; 2.52, m, 1H
N CH2	2.39, m; 2.56, m	2.37, m, 1H; 2.52, m, 1H
NCH2CH3	1.05, t(7.2)	1.05, t(7.1), 3H
1’	3.26 s	3.26 s, 3H
18’	3.29 s	3.30 s, 3H

Table S3.2. Comparison of ^{13}C NMR data for Authentic (*ref.* 6) vs. Synthetic (–)-liljestrandisine.

	authentic liljestrandisine Wang, 2004 (*ref.* 6) (100 MHz, $CHCl_3$) $[\alpha]_D$=–12 ° (c =0.5, $CHCl_3$)	synthetic liljestrandisine this report (101 MHz, $CHCl_3$**)** $[\alpha]_D$=–9.5 ° (c =0.15, $CHCl_3$)	chemical shift difference
Carbon #, multiplicity	**^{13}C** (δ) ppm	**^{13}C** (δ) ppm	^{13}C (Δδ) ppm
1 d	86.2	86.2	0
2 t	25.7	25.8	+0.1
3 t	32.7	32.8	+0.1
4 s	38.7	38.7	0
5 d	46.0	46.0	0
6 t	24.6	24.6	0
7 d	46.4	46.4	0
8 s	73.6	73.6	0
9 d	46.5	46.5	0
10 d	45.8	45.7	-0.1
11 s	48.7	48.6	-0.1
12 t	27.9	27.9	0
13 d	40.8	40.8	0
14 d	75.8	76.0	+0.2
15 t	42.3	42.4	+0.1
16 d	72.5	72.6	+0.1
17 d	63.0	63.1	+0.1
18 t	79.4	79.4	0
19 t	53.2	53.1	-0.1
N CH2	49.5	49.6	+0.1
NCH2CH3	13.6	13.7	+0.1
1’	56.2	56.4	+0.2
18’	59.5	59.5	+0.0

Preparation of β-methoxy ketone 218:



A 50-mL, round-bottomed flask was charged with α-selenide **216** (44 mg, 0.0729 mmol, 1 equiv), and dissolved in CH_2Cl_2 (2 mL) and MeOH (2 mL). The flask was cooled to –78 °C, at which time ozone (as a mixture with O_2) was gently bubbled through the solution (O_2 flow rate = 1/8 L/min, 1 setting on ozone generator) for 10 min. During this time, the solution turns a faint blue. The reaction was monitored by TLC, and after 10 minutes, all of the starting material had been consumed and converted to the strained enone, visible by TLC/LCMS. The solution was then sparged with Ar for 15 minutes, and pyridine (3 drops) was added. The reaction was allowed to warm to room temperature, and stirred for 36 hours at room temperature. The reaction was then concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (1% to 1.5% to 2% to 2.5% to 3% MeOH in CH_2Cl_2) to afford β-methoxy ketone **218** (27 mg, 0.0569 mmol, 78% yield) as a clear oil.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 4.77 (d, *J* = 6.8 Hz, 1H), 4.57 (d, *J* = 6.8 Hz, 1H), 4.13 (t, *J* = 4.8 Hz, 1H), 3.91 (d, *J* = 14.4 Hz, 1H), 3.74 (s, 1H), 3.33 (s, 3H), 3.30 (s, 3H), 3.22 – 3.18 (m, 4H), 3.14 (dd, *J* = 9.8, 7.2 Hz, 1H), 3.10 (s, 3H), 3.05 – 2.96 (m, 2H), 2.78 (dd, *J* = 7.6, 4.3 Hz, 1H), 2.61 – 2.50 (m, 2H), 2.44 (t, *J* = 5.7 Hz, 1H), 2.39 (d,

J = 18.3 Hz, 1H), 2.25 (d, J = 7.8 Hz, 1H), 2.10 – 2.02 (m, 7H), 1.88 (d, J = 7.4 Hz, 1H), 1.72 – 1.64 (m, 2H), 1.45 (tdd, J = 13.2, 4.5, 1.7 Hz, 1H), 1.37 – 1.26 (m, 1H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 211.3, 169.7, 95.8, 82.5, 78.2, 77.7, 76.8, 59.5, 58.3, 55.7, 55.5, 52.3, 48.7 (2 overlapping peaks), 47.6, 45.4, 45.3, 44.2, 44.1, 42.7, 37.4, 31.6, 26.8, 25.4, 24.0, 22.4.

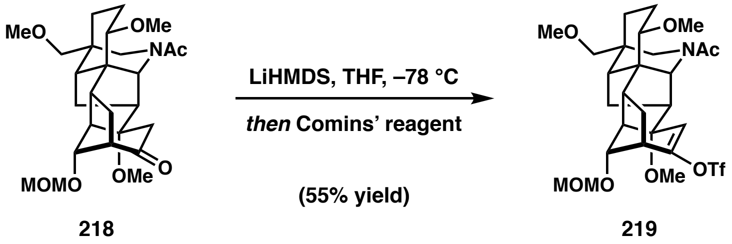
FTIR (NaCl, thin film): 2930, 2890, 2825, 1710, 1639, 1430, 1151, 1114, 1092, 1048 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{26}H_{40}NO_7$ $[M + H]^+$ 478.2799, found 478.2790

$[\alpha]_D^{25}$ = –120° (c = 1.5, CHCl$_3$).

TLC (5%MeOH/95%CH$_2$Cl$_2$), R$_f$: 0.5 (UV, yellow in *p*-anisaldehyde)

Preparation of enol triflate 219:



A 50-mL, round-bottomed flask was charged with ketone **218** (20 mg, 42 µmol, 1 equiv), and azeotroped with PhMe (from the solvent system, 2 x 3 mL) to remove H$_2$O and put under high vacuum for two hours. The flask was then equipped with a rubber septum, purged with N$_2$, dissolved in THF (2 mL), and cooled to –78 °C in a dry ice/acetone bath. LiHMDS (1M in THF, 84 µL, 84 µmol, 2 equiv) was added dropwise via syringe, causing the solution to turn yellow. The LiHMDS/**218** solution was allowed to stir for 30 minutes at –78 °C, and then Comins' reagent (36.9 mg, 94 μmol, 2.25 equiv) solution in THF (1 mL) was added dropwise via syringe. This was allowed to stir for an additional 5 minutes at –78 °C, the bath was then removed, and this was allowed to stir for 20 minutes at room temperature. The reaction was quenched with 0.5 M NaOH (5 mL), and the biphasic mixture was transferred to a separatory funnel with EtOAc (10 mL). The layers were separated, and the aqueous layer was extracted EtOAc (4 x 10 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting crude residue was purified by preparative thin layer silica gel chromatography (mobile phase: 100% ethyl acetate) to afford enol triflate **219** (14 mg, 23 μmol, 55% yield) as a clear oil.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 5.85 (t, *J* = 1.6 Hz, 1H), 4.71 (d, *J* = 6.9 Hz, 1H), 4.60 (d, *J* = 6.9 Hz, 1H), 3.93 – 3.85 (m, 3H), 3.36 (s, 3H), 3.30 (s, 3H), 3.21 (s, 3H), 3.19 – 3.17 (m, 4H), 3.14 – 3.10 (m, 1H), 3.02 (d, *J* = 9.1 Hz, 1H), 2.86 (dd, *J* = 14.2, 5.3 Hz, 1H), 2.72 – 2.64 (m, 1H), 2.61 (d, *J* = 14.4 Hz, 1H), 2.34 (t, *J* = 5.5 Hz, 1H), 2.27 (d, *J* = 7.8 Hz, 1H), 2.09 – 2.03 (m, 6H), 1.96 – 1.90 (m, 1H), 1.83 (d, *J* = 7.4 Hz, 1H), 1.76 – 1.68 (m, 2H), 1.43 (tdd, *J* = 13.2, 4.5, 1.8 Hz, 1H), 1.33 – 1.27 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 170.5, 153.9,114.2, 96.0, 82.6, 78.4, 78.2, 77.2, 59.5, 59.1, 55.6, 55.5, 49.4, 48.0, 45.2, 45.1, 44.3, 43.9, 42.8, 42.6, 37.4, 32.0, 30.7, 25.4, 23.7, 22.5. (Note: triflate carbon was not observed).

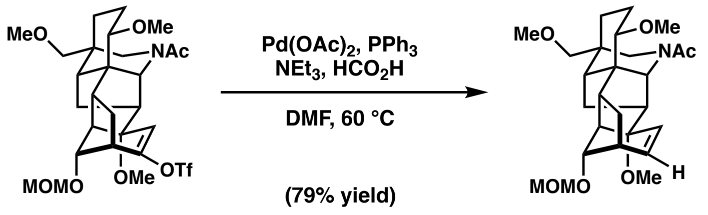
FTIR (NaCl, thin film): 2938, 2829, 1636, 1418, 1210, 1142, 1094 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{27}H_{39}NF_3O_9S$ $[M + H]^+$ 610.2292, found 610.2281

$[\alpha]_D^{25}$ = –37.7° (*c* = 0.50, $CHCl_3$).

TLC (100%EtOAc), R*f*: 0.4 (yellow in *p*-anisaldehyde)

Preparation of alkene 220:



219 **220**

A 50-mL, round-bottomed flask was charged with enol triflate **219** (10 mg, 16.4 μmol, 1.0 equiv), PPh$_3$ (3.4 mg, 12.96 μmol, 0.80 equiv), and Pd(OAc)$_2$ (1.5 mg, 6.68 μmol, 0.40 equiv). The flask was equipped with a rubber septum, purged with N$_2$, and dissolved in DMF (0.8 mL). Then, the reaction mixture was sparged with an Ar balloon for 5 minutes. NEt$_3$ (46 μL, 328 μmol, 20 equiv) was added followed by HCO$_2$H (3 μL, 82.1 μmol, 5 equiv) – a cloudy gas was observed upon addition. The reaction was lowered into a 60 °C oil bath, and allowed to continue to stir at that temperature for 20 minutes. The reaction turns black during this time indicating its completion. The reaction was cooled to room temperature, diluted with sat. NH$_4$Cl (5 mL), transferred to a separatory funnel and diluted with EtOAc (10 mL). The layers were separated and the aqueous extracted with EtOAc (4 x 10 mL). The organic extracts were dried over Na$_2$SO$_4$, filtered, and concentrated *in vacuo*. The resulting crude residue was purified by preparative thin layer silica gel chromatography (mobile phase: 100% ethyl acetate) to afford olefin **220** (6.0 mg, 13.0 μmol, 79% yield) as a clear oil.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 6.17 (ddd, *J* = 9.8, 6.7, 1.1 Hz, 1H), 5.85 (dd, *J* = 9.8, 1.9 Hz, 1H), 4.75 (d, *J* = 6.8 Hz, 1H), 4.59 (d, *J* = 6.8 Hz, 1H), 3.88 (d, *J* = 14.2 Hz, 1H), 3.84 (t, *J* = 4.5 Hz, 1H), 3.79 (s, 1H), 3.36 (s, 3H), 3.30 (s, 3H), 3.23 – 3.18 (m, 4H), 3.17 (s, 3H), 3.11 (dd, *J* = 10.3, 7.6 Hz, 1H), 3.04 (d, *J* = 9.1 Hz, 1H), 2.64 – 2.54 (m, 2H), 2.41 (dd, *J* = 13.9, 5.3 Hz, 1H), 2.33 (t, *J* = 5.5 Hz, 1H), 2.14 (d, *J* = 7.8 Hz, 1H), 2.08 – 1.98 (m, 6H), 1.88 – 1.79 (m, 2H), 1.74 – 1.65 (m, 2H), 1.50 – 1.36 (m, 1H), 1.34 – 1.26 (m, 1H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 169.9, 134.3, 125.3, 95.5, 82.9, 78.6, 77.2, 76.6, 59.5, 59.5, 55.6, 55.5, 49.2, 48.0, 45.6, 45.2, 44.3, 44.2, 42.7, 37.5, 37.4, 32.0, 31.5, 25.5, 23.5, 22.5.

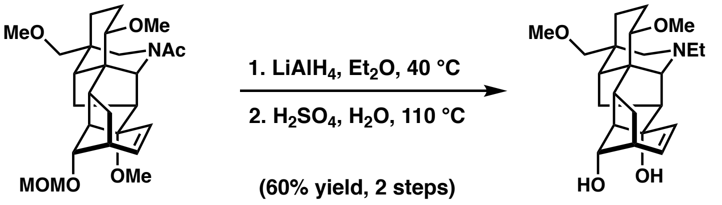
FTIR (NaCl, thin film): 2928, 2886, 2822, 1634, 1428, 1149, 1114, 1091, 1044 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{26}H_{40}NO_6$ $[M + H]^+$ 462.2850, found 462.2835

$[\alpha]_D^{25}$ = –78.2° (*c* = 0.21, CHCl$_3$).

TLC (100%EtOAc), R$_f$: 0.3 (grey/purple in *p*-anisaldehyde)

Preparation of (–)-liljestrandinine (52):



220

(–)-liljestrandinine (**52**)

A 2-dram vial was charged with acetamide **220** (6 mg, 13 µmol, 1 equiv), azeotroped with toluene (from the solvent system, 2 x 1 mL) and put under high vacuum for 1 hour. The vial was then equipped with a rubber septum, purged with N$_2$, and charged with Et$_2$O (1 mL) to dissolve the substrate, and LiAlH$_4$ solution (1 M in THF, 52 µL, 52 µmol, 4 equiv) was added dropwise via microsyringe. The rubber septum was replaced with a vial cap, and heated to 40 °C in a pre-heated heating block. The reaction was allowed to stir at 40 °C for 40 minutes, and then was removed from the heating block and allowed to cool to room temperature. The reaction was carefully quenched with aqueous 10% NaOH solution (4 mL), and diluted with Et_2O (4 mL). The layers were separated, and the aqueous layer was extracted with 20%IPA/80%$CHCl_3$ (5 x 5 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was then transferred to a new 2-dram vial, and used in the next step without further purification.

The 2-dram vial containing the crude residue from the $LiAlH_4$ reduction was dissolved in aqueous 0.5 M H_2SO_4 (1.5 mL), sealed with a cap, and heated to 110 °C in a pre-heated heating block. The reaction was allowed to stir at 110 °C for 3 hours, and then was cooled to room temperature. Monitoring by LCMS indicated full conversion to the product. The reaction as then carefully quenched with aqueous 10% NaOH solution (2 mL), and diluted with 20%IPA/80%$CHCl_3$ (4 mL). The layers were separated, and the aqueous layer was extracted with 20%IPA/80%$CHCl_3$ (8 x 4 mL). As an additional precaution, the aqueous layer was made sure to be basic with pH paper, and an LCMS sample of the aqueous layer was taken to ensure that no product was left behind. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by preparative thin layer chromatography (mobile phase: 10% 7 N NH_3 in MeOH/ 90% CH_2Cl_2) to furnish (–)-liljestrandinine (**52**) (3 mg, 7.8 μmol, 60% yield over 2 steps).

Notes:

(1) Due to rapid protonation and other dynamic effects, the ^{1}H NMR and ^{13}C NMR spectra in $CDCl_3$ are inconsistent and often display broadened and poorly resolved resonances and extra peaks arising from the protonated material. Characterization data

was therefore obtained in benzene-d6, and was compared with synthetic liljestrandinine that had been characterized in benzene-d6.[8] Data collected in chloroform was only of satisfactory resolution and used only to compare to the reported tabulated data for isolated liljestrandinine.[9]

^{1}H NMR (400 MHz, Benzene-*d*$_6$): δ 5.70 (ddd, *J* = 9.5, 6.7, 1.1 Hz, 1H), 5.61 (dd, *J* = 9.4, 1.8 Hz, 1H), 3.78 (q, *J* = 4.8 Hz, 1H), 3.12 (s, 3H), 3.10 – 3.08 (m, 1H), 3.05 (s, 3H), 2.96 (d, *J* = 8.8 Hz, 1H), 2.90 – 2.82 (m, 2H), 2.60 – 2.50 (m, 3H), 2.49 – 2.43 (m, 1H), 2.43 – 2.35 (m, 1H), 2.29 (dq, *J* = 12.0, 7.1 Hz, 1H), 2.19 – 2.11 (m, 2H), 2.10 – 2.07 (m, 1H), 2.05 – 1.97 (m, 2H), 1.97 – 1.88 (m, 2H), 1.76 – 1.72 (m, 1H), 1.64 – 1.47 (m, 5H), 1.04 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 131.9, 129.8, 85.8, 79.6, 74.6, 74.3, 63.2, 59.5, 56.3, 53.2, 49.5, 48.4, 46.4, 45.8, 45.6, 42.4, 39.0, 38.5, 33.1, 32.7, 23.5, 22.7, 13.5.

^{13}C NMR (101 MHz, C_6D_6): δ 132.5, 129.7, 85.6, 80.0, 75.0, 74.5, 63.0, 59.2, 55.7, 53.9, 49.6, 48.6, 46.8, 46.3, 46.0, 42.7, 39.6, 38.9, 33.4, 33.3, 26.7, 24.2, 13.7.

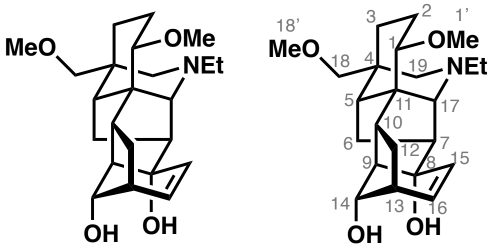
TLC (10%7N NH_3 in MeOH/90%CH_2Cl_2), R$_f$: 0.5 (ninhydrin)

FTIR (NaCl, thin film): 3332, 2921, 2823, 1642, 1462, 1095 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{23}H_{36}NO_4$ $[M + H]^+$ 390.2639, found 390.2622

$[\alpha]_D^{25}$ = –17.6° (*c* = 0.21, $CHCl_3$).

The following carbon numbering system is used in the line list comparisons:



(–)-liljestrandinine

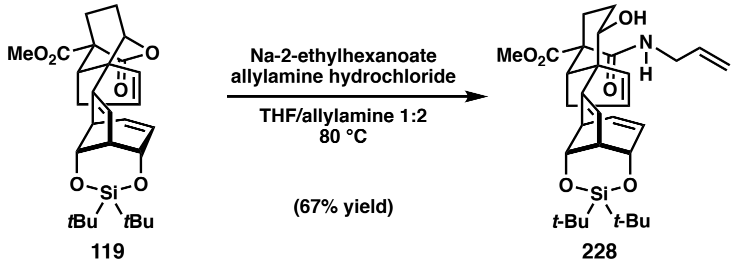
Table S3.3. Comparison of ^{13}C NMR data for Authentic (*ref.* 8) vs. Synthetic (–)-liljestrandinine.

	authentic liljestrandinine Wang, 2003 (*ref.* 8) (100 MHz, $CHCl_3$) $[\alpha]_D$=–10 ° (c =0.5, $CHCl_3$)	synthetic liljestrandinine this report (101 MHz, $CHCl_3$) $[\alpha]_D$=–17.6 ° (c =0.21, $CHCl_3$)	chemical shift difference
Carbon #, multiplicity	^{13}C (δ) ppm	^{13}C (δ) ppm	^{13}C (Δδ) ppm
1 d	85.7	85.8	+0.1
2 t	22.6	22.7	+0.1
3 t	32.6	32.7	+0.1
4 s	38.5	38.5	0
5 d	45.6	45.6	0
6 t	23.4	23.5	+0.1
7 d	42.3	42.4	+0.1
8 s	74.3	74.3	0
9 d	46.3	46.4	+0.1
10 d	45.8	45.8	0
11 s	48.2	48.4	+0.2
12 t	33.0	33.1	+0.1
13 d	38.9	39.0	+0.1
14 d	74.5	74.6	+0.2
15 t	131.7	131.9	+0.2
16 d	129.8	129.8	0
17 d	63.2	63.2	+0.1
18 t	79.6	79.6	0
19 t	53.1	53.2	+0.1
N CH2	49.4	49.5	+0.1
NCH2CH3	13.4	13.5	+0.1
1’	56.2	56.3	+0.1
18’	59.4	59.5	+0.1

Table S3.4. Comparison of ^{13}C NMR data in C_6D_6 of Synthetic (*ref.* 7) vs. Synthetic (–)-liljestrandinine (this report).

synthetic liljestrandinine Sarpong, 2015 (*ref.* 7) (151 MHz, C_6D_6)	synthetic liljestrandinine this report (101 MHz, C_6D_6) $[\alpha]_D$=–17.6 ° (c =0.21, $CHCl_3$)	chemical shift difference
^{13}C (δ) ppm	**^{13}C** (δ) ppm	^{13}C (Δδ) ppm
132.4	132.5	+0.1
129.7	129.7	0
85.6	85.6	0
80.0	80.0	0
74.9	75.0	+0.1
74.5	74.5	0
63.0	63.0	0
59.1	59.2	+0.1
55.6	55.7	+0.1
53.9	53.9	0
49.5	49.6	+0.1
48.6	48.6	0
46.8	46.8	0
46.3	46.3	0
46.0	46.0	0
42.7	42.7	0
39.6	39.6	0
38.9	38.9	0
33.4	33.4	0
33.2	33.3	+0.1
26.7	26.7	0
24.2	24.2	0
13.7	13.7	0

Preparation of *N*-allyl amide 228:



To a 15-mL pressure vessel containing lactone **119** (70 mg, 0.140 mmol, 1 equiv), sodium 2-ethylhexanoate (105 mg, 0.632 mmol, 4.5 equiv), allylamine hydrochloride (30 mg, 0.316 mmol, 2.25 equiv) were added, followed by THF (0.45 mL) and neat *N*-allylamine (0.9 mL). The vessel was sealed (with a Teflon cap that had a perfluoro O-ring), and heated to 80 °C in an oil bath. The reaction was allowed to stir at 80 °C for 2 days. The reaction was then cooled to room temperature, and transferred to a separatory funnel with EtOAc (15 mL) and aqueous 0.5 M NaOH (15 mL). The layers were separated, and the aqueous phase was extracted with EtOAc (4 x 15 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by silica gel chromatography (20% to 30% to 40% ethyl acetate in hexanes) to afford *N*-allyl amide **228** as a white foam (53 mg, 0.094 mmol, 67% yield).

Note: Neat *N*-allylamine was purified just before use by distillation over $CaCl_2$ (using a Hickman distillation apparatus).

^{1}H NMR (500 MHz, Chloroform-*d*): δ 6.33 (t, *J* = 5.7 Hz, 1H), 6.13 (dt, *J* = 5.9, 2.3 Hz, 1H), 6.10 (ddd, *J* = 9.5, 6.2, 1.1 Hz, 1H), 5.82 – 5.73 (m, 1H), 5.68 – 5.63 (m, 1H), 5.51 (dt, *J* = 5.9, 1.9 Hz, 1H), 5.34 (d, *J* = 3.9 Hz, 1H), 5.14 (t, *J* = 1.5 Hz, 1H), 5.11 (dq, *J* = 6.7, 1.4 Hz, 1H), 4.56 – 4.51 (m, 1H), 4.18 (ddd, *J* = 4.1, 3.0, 0.7 Hz, 1H), 3.92 (dd, *J* =

5.3, 3.4 Hz, 1H), 3.88 – 3.77 (m, 2H), 3.70 (s, 3H), 3.17 (td, *J* = 9.1, 1.5 Hz, 1H), 3.00 (dddp, *J* = 5.0, 3.1, 2.1, 1.0 Hz, 1H), 2.92 – 2.89 (m, 1H), 2.39 – 2.30 (m, 3H), 2.09 (dddd, *J* = 14.4, 5.6, 4.0, 1.5 Hz, 1H), 1.86 – 1.70 (m, 3H), 1.08 (s, 9H), 1.01 (s, 9H).

^{13}C NMR (126 MHz, CDCl$_3$): δ 174.9, 168.6, 163.5, 135.6, 135.2, 133.7, 132.8, 128.5, 122.0, 116.7, 76.6, 66.9, 66.2, 57.0, 55.6, 52.9, 46.4, 46.3, 46.2, 42.1, 35.3, 28.9, 28.3, 25.5, 21.2, 20.7, 18.1.

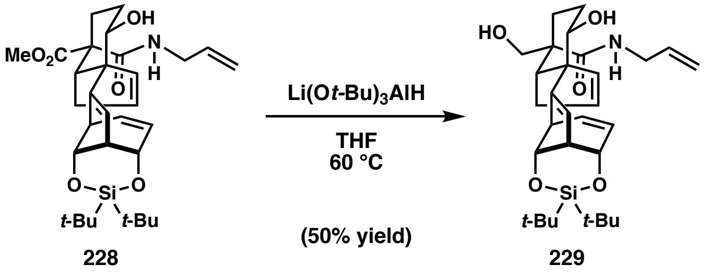
FTIR (NaCl, thin film): 3413, 2934, 3858, 1714, 1674, 1519, 1476, 1252, 1230, 1101, 992, 827, 731 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{31}H_{46}NO_6Si$ $[M + H]^+$ 556.3089, found 556.3085

$[\alpha]_D^{25}$ = +129° (*c* = 1.34, CHCl$_3$).

TLC (70%EtOAc/30%Hexanes), R*f*: 0.5 (brown in *p*-anisaldehyde)

Preparation of diol 229:



A 40-mL vial was charged with ester **228** (52.5 mg, 0.0945 mmol, 1 equiv), Li(O*t*-Bu)$_3$AlH (144 mg, 0.567 mmol, 6 equiv) and THF (1.8 mL), sealed, and heated to 60 °C in a pre-heated oil bath. After 15 hours at this temperature, an additional portion of Li(O*t*-Bu)$_3$AlH (200 mg, 0.788 mmol, 8.3 equiv) was added. After another 24 hours of stirring at 60 °C, an additional portion of Li(O*t*-Bu)$_3$AlH (300 mg, 1.13 mmol, 12 equiv) was added, and the reaction was allowed to stir for another 24 hours at 60 °C. After 5 additional hours, an additional portion of Li(O*t*-Bu)$_3$AlH (200 mg, 0.788 mmol, 8.3 equiv) was added. After a final 24 hours of additional stirring, the reaction was cooled to room temperature, and carefully diluted with H_2O (20 mL). The reaction was transferred to an Erlenmeyer flask and 20 mL aqueous saturated Rochelle's salt was added, and the reaction mixture was allowed to stir vigorously for 1 hour. The biphasic mixture was then transferred to a separatory funnel, and extracted with CH_2Cl_2 (5 x 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by silica gel chromatography (80% ethyl acetate in hexanes to 100% ethyl acetate) to afford diol **228** as a white foam (24.8 mg, 0.025 mmol, 50% yield).

^{1}H NMR (400 MHz, Chloroform-*d*): δ 6.19 (dt, *J* = 5.9, 2.3 Hz, 1H), 6.13 (t, *J* = 5.7 Hz, 1H), 6.06 (ddd, *J* = 9.5, 6.1, 1.1 Hz, 1H), 5.82 (ddt, *J* = 17.2, 10.2, 5.7 Hz, 1H), 5.66 (ddd, *J* = 9.3, 4.4, 1.9 Hz, 1H), 5.54 (d, *J* = 3.7 Hz, 1H), 5.44 (dt, *J* = 5.8, 1.9 Hz, 1H), 5.22 – 5.13 (m, 2H), 4.53 (td, *J* = 4.3, 0.9 Hz, 1H), 4.21 (ddd, *J* = 4.2, 3.0, 0.7 Hz, 1H), 4.02 (t, *J* = 3.1 Hz, 1H), 3.94 (dtt, *J* = 15.6, 5.7, 1.6 Hz, 1H), 3.84 (dtt, *J* = 15.7, 5.7, 1.5 Hz, 1H), 3.76 (d, *J* = 10.8 Hz, 1H), 3.55 (d, *J* = 10.9 Hz, 1H), 3.14 – 3.01 (m, 2H), 2.95 (dd, *J* = 5.9, 4.6 Hz, 1H), 2.86 (t, *J* = 9.7 Hz, 1H), 2.32 – 2.18 (m, 3H), 1.88 – 1.81 (m, 2H), 1.48 – 1.38 (m, 2H), 1.08 (s, 9H), 1.00 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 176.2, 164.4, 136.3, 135.6, 133.9, 133.8, 128.5, 121.8, 116.8, 76.9, 67.2, 66.2, 65.5, 56.0, 47.6, 46.5, 46.2, 41.8, 41.6, 36.1, 28.9, 28.3, 24.1, 21.2, 20.7, 18.0.

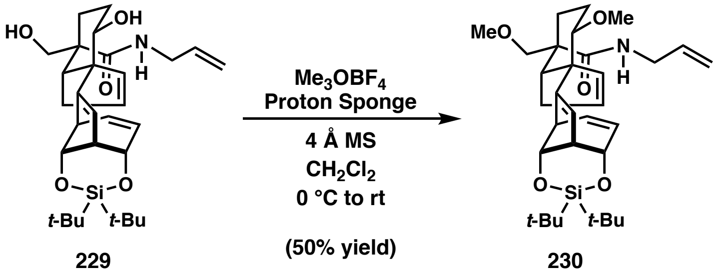
FTIR (NaCl, thin film): 3352, 2931, 2858, 1634, 1539, 1475, 1103, 994, 827, 733 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{30}H_{46}NO_5Si$ $[M + H]^+$ 528.3140, found 528.3130

$[\alpha]_{\mathrm{D}}^{25}$ = +104° (c = 1.08, $CHCl_3$).

TLC (100%EtOAc), R*f*: 0.5 (pink/brown in *p*-anisaldehyde)

Preparation of methyl ether 230:



A 50-mL, round-bottomed flask was charged with alcohol **229** (24.8 g, 0.047 mmol, 1.0 equiv), equipped with a rubber septum, and purged with N_2. Meanwhile, Me_3OBF_4 (83.9 mg, 0.567 mmol, 12 equiv), Proton Sponge (121.5 g, 0.567 mmol, 12 equiv), and activated 4 Å MS (100 mg) were added to a 2-dram vial in the glovebox, brought out of the glovebox, and added to the flask containing the substrate. The mixture was then suspended in CH_2Cl_2 (0.9 mL), and allowed to stir for 16 hours. The reaction mixture was filtered through a plug of silica gel and celite that had been pre-packed with a 50% ethyl acetate/ 50% hexanes mixture and rinsed further with 50% ethyl acetate/ 50% hexanes and concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (30% ethyl acetate in hexanes) to afford methyl ether **230** (12 g, 0.022 mmol, 46% yield) as a white foam.

^{1}H NMR (400 MHz, Chloroform-*d*): δ 6.80 (t, J = 5.7 Hz, 1H), 6.06 (ddd, J = 9.5, 6.2, 1.1 Hz, 1H), 5.88 – 5.77 (m, 2H), 5.67 (ddd, J = 9.4, 4.4, 1.9 Hz, 1H), 5.44 (d, J = 3.8 Hz, 1H), 5.39 (ddd, J = 5.9, 2.6, 1.4 Hz, 1H), 5.19 – 5.08 (m, 2H), 4.49 (t, J = 4.7, 1H), 4.24

(ddd, *J* = 4.1, 3.0, 0.7 Hz, 1H), 3.94 – 3.78 (m, 2H), 3.60 (dd, *J* = 8.2, 2.8 Hz, 1H), 3.42 (d, *J* = 9.4 Hz, 1H), 3.28 (s, 3H), 3.26 (s, 3H), 3.21 (d, *J* = 9.4 Hz, 1H), 3.06 – 3.01 (m, 1H), 2.87 (dd, *J* = 5.9, 4.6 Hz, 1H), 2.69 (t, *J* = 9.4 Hz, 1H), 2.59 (ddd, *J* = 13.9, 7.5, 5.9 Hz, 1H), 2.30 (ddt, *J* = 16.1, 9.8, 2.2 Hz, 1H), 2.20 (dddd, *J* = 16.1, 9.0, 2.7, 1.4 Hz, 1H), 1.79 – 1.69 (m, 1H), 1.66 – 1.62 (m, 1H), 1.22 – 1.13 (m, 1H), 1.08 (s, 9H), 1.01 (s, 9H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 174.9, 166.0, 135.6, 134.6, 133.4, 131.6, 128.2, 119.4, 115.8, 78.9, 76.8, 76.0, 66.5, 58.4, 57.2, 56.9, 47.0, 46.4, 46.2, 43.3, 41.8, 36.5, 28.9, 28.3, 21.5, 21.3, 21.1, 20.7.

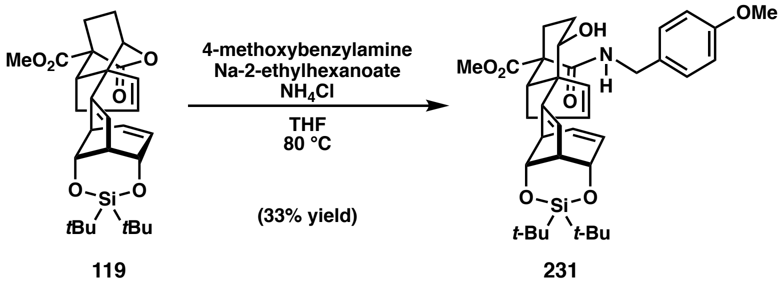
FTIR (NaCl, thin film): 3362, 2932, 2859, 1652, 1531, 1476, 1380, 1258, 1102, 991, 911, 825, 732 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{32}H_{50}NO_5Si$ [M + H]$^+$ 556.3453, found 556.3454

$[\alpha]_D^{25}$ = +103° (*c* = 0.50, CHCl$_3$).

TLC (30%EtOAc/70%Hexanes), R$_f$: 0.4 (blue in *p*-anisaldehyde)

Preparation of 4-methoxybenzylamide 231:



To a 15-mL pressure vessel containing lactone **119** (100 mg, 0.2005 mmol, 1 equiv), sodium 2-ethylhexanoate (150 mg, 0.902 mmol, 4.5 equiv), ammonium chloride (24 mg, 0.45 mmol, 2.25 equiv) were added, followed by THF (0.5 mL) and 4-

methoxybenzylamine (0.5 mL). The vessel was sealed (with a Teflon cap that had a perfluoro O-ring), and heated to 80 °C in an oil bath. The reaction was allowed to stir at 80 °C for 4 days. The reaction was then cooled to room temperature, and transferred to a separatory funnel with EtOAc (15 mL) and aqueous 0.5 M NaOH (15 mL). The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (4 x 15 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by silica gel chromatography (30% to 40% ethyl acetate in hexanes) to afford 4-methoxybenzylamide **231** as a white foam (41.6 mg, 0.066 mmol, 33% yield).

^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.13 (d, *J* = 8.7 Hz, 2H), 6.85 (d, *J* = 8.7 Hz, 2H), 6.44 (t, *J* = 5.6 Hz, 1H), 6.12 – 6.01 (m, 2H), 5.64 (ddd, *J* = 9.2, 4.2, 1.8 Hz, 1H), 5.48 (ddd, *J* = 5.9, 2.5, 1.5 Hz, 1H), 5.32 (d, *J* = 3.7 Hz, 1H), 4.50 (t, *J* = 4.2, 1H), 4.33 (dd, *J* = 14.5, 5.6 Hz, 1H), 4.26 (dd, *J* = 14.4, 5.5 Hz, 1H), 4.16 (ddd, *J* = 4.2, 3.1, 0.8 Hz, 1H), 3.91 (dd, *J* = 5.5, 3.4 Hz, 1H), 3.80 (s, 3H), 3.66 (s, 3H), 3.15 – 3.09 (m, 1H), 2.97 (dtdd, *J* = 5.1, 3.2, 2.4, 1.0 Hz, 1H), 2.88 – 2.84 (m, 1H), 2.38 – 2.25 (m, 3H), 2.10 (dtd, *J* = 14.2, 4.5, 4.1, 1.5 Hz, 1H), 1.80 – 1.69 (m, 3H), 1.06 (s, 9H), 0.99 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 174.7, 168.6, 163.6, 159.0, 135.6, 135.1, 132.8, 129.9, 129.1, 128.4, 121.9, 114.1, 76.6, 66.9, 66.2, 57.0, 55.7, 55.3, 52.9, 46.3, 46.2, 46.1, 43.4, 35.3, 28.9, 28.2, 27.4, 27.2, 25.6, 21.2, 20.6, 18.2.

FTIR (NaCl, thin film): 3404, 3031, 2934, 2858, 1731, 1668, 1614, 1514, 1476, 1361, 1514, 1476, 1380, 1248, 1177, 1102, 1012, 993, 911, 825, 732 cm^{-1}.

HRMS: (ESI-TOF) calc'd for $C_{36}H_{50}NO_7Si$ $[M + H]^+$ 636.3331, found 636.3345

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = +111° (*c* = 0.90, $CHCl_3$).

TLC (50%EtOAc/50%Hexanes), R_f: 0.5 (UV, brown in *p*-anisaldehyde)

3.6 NOTES AND REFERENCES

(1) Examples of intramolecular PhI(OAc)2 promoted intramolecular aziridination reactions can be found in these references: (a) Z.-G.; Cheng, H.; Ge, M.-J.; Xu, L.; Wang, F.-P. Tetrahedron 2013, 69, 5431. (b) Mei, R.-H.; Liu, Z.-G.; Cheng, H.; Xu, L.: Wang, F.-P. Org. Lett. 2013, 15, 2206.

(2) Examples of acetyl bromide opening of aziridines are rare, one example was found in the literature: Larsen, R. D.; Davis, P.; Corley, E.G.; Reider, P. J.; Lamanec, T. R.; Grabowski, E.J.J., J. Org. Chem. 1990, 55, 299.

(3) Steves, J. E.; Stahl, S. S. *Journal of the American Chemical Society* **2013**, *135*, 15742.

(4) This oxidation sequence leveraged known reactivity of C19 diterpenoid alkaloid scaffolds and was further optimized: Shi, Y.; Wilmot, J.T.; Nordstrom, L.U.; Tan, D.S.; Gin, D.Y., JACS 2013, 135, 14313.

(5) Wang, F.-P.; Chen, Q.-H. The C19-Diterpenoid Alkaloids. In *The Alkaloids: Chemistry and Biology*; Elsevier, 2010; Vol. 69, pp 1–577.

(6) Harrowven, D. C.; Curran, D. P.; Kostiuk, S. L.; Wallis-Guy, I. L.; Whiting, S.; Stenning, K. J.; Tang, B.; Packard, E.; Nanson, L. *Chem. Commun.* **2010**, *46*, 6335.

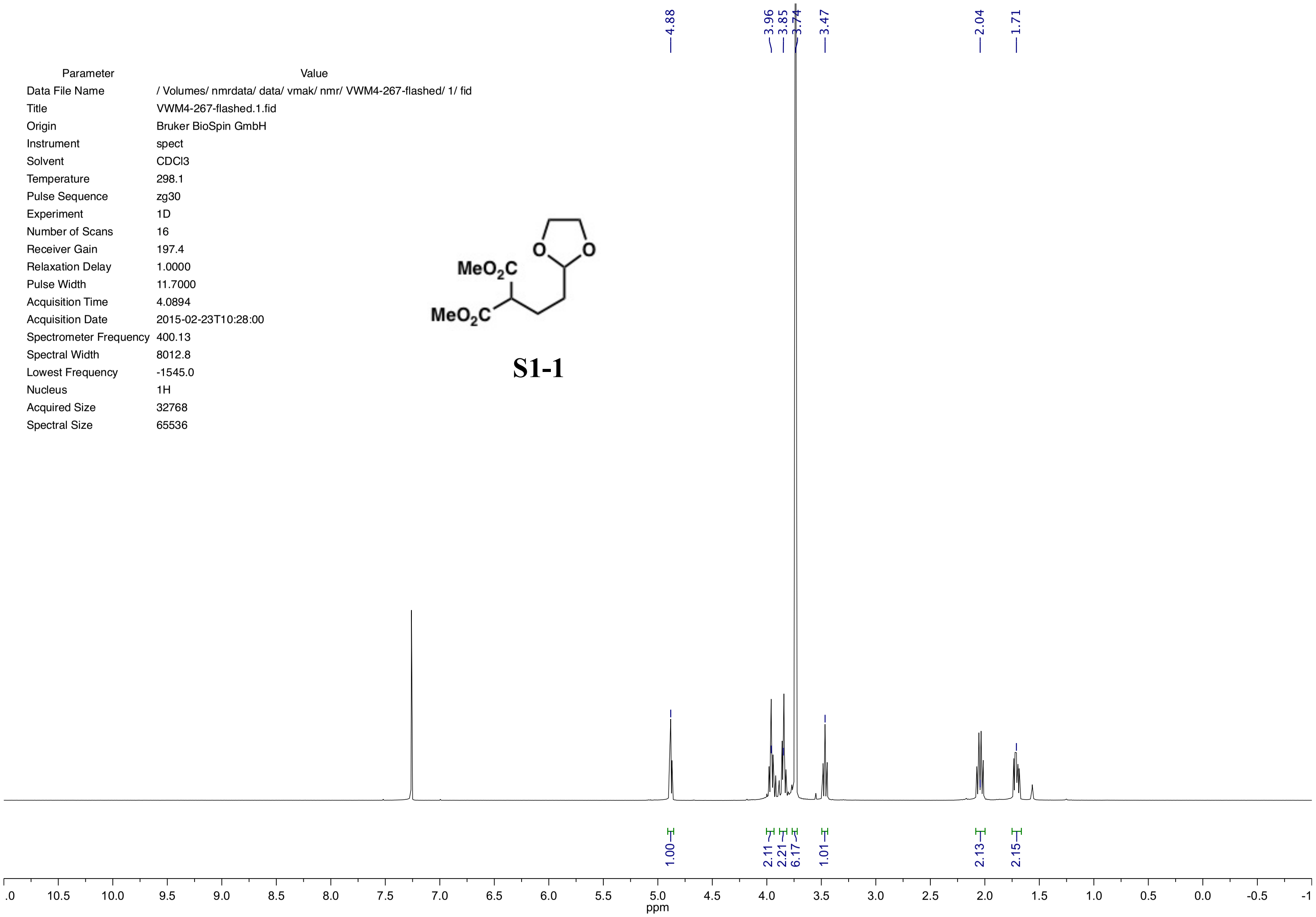
(7) Xie, G.-B.; Wang, F.-P. *Chemical Journal of Chinese Universities* **2004**, *25*, 482.

(8) Marth, C. J.; Gallego, G. M.; Lee, J. C.; Lebold, T. P.; Kulyk, S.; Kou, K. G. M.; Qin, J.; Lilien, R.; Sarpong, R. *Nature* **2015**, *528*, 493.

(9) Wang, F.-P.; Xie, G.-B.; Chen, Q.-H.; Chen, D.-L.; Jian, X.-X. *HETEROCYCLES* **2003**, *60*, 631.

Appendix 1

Spectra Relevant to Chapter 1:
Development of a Unified Strategy Towards Diterpenoid Alkaloids



S1-1

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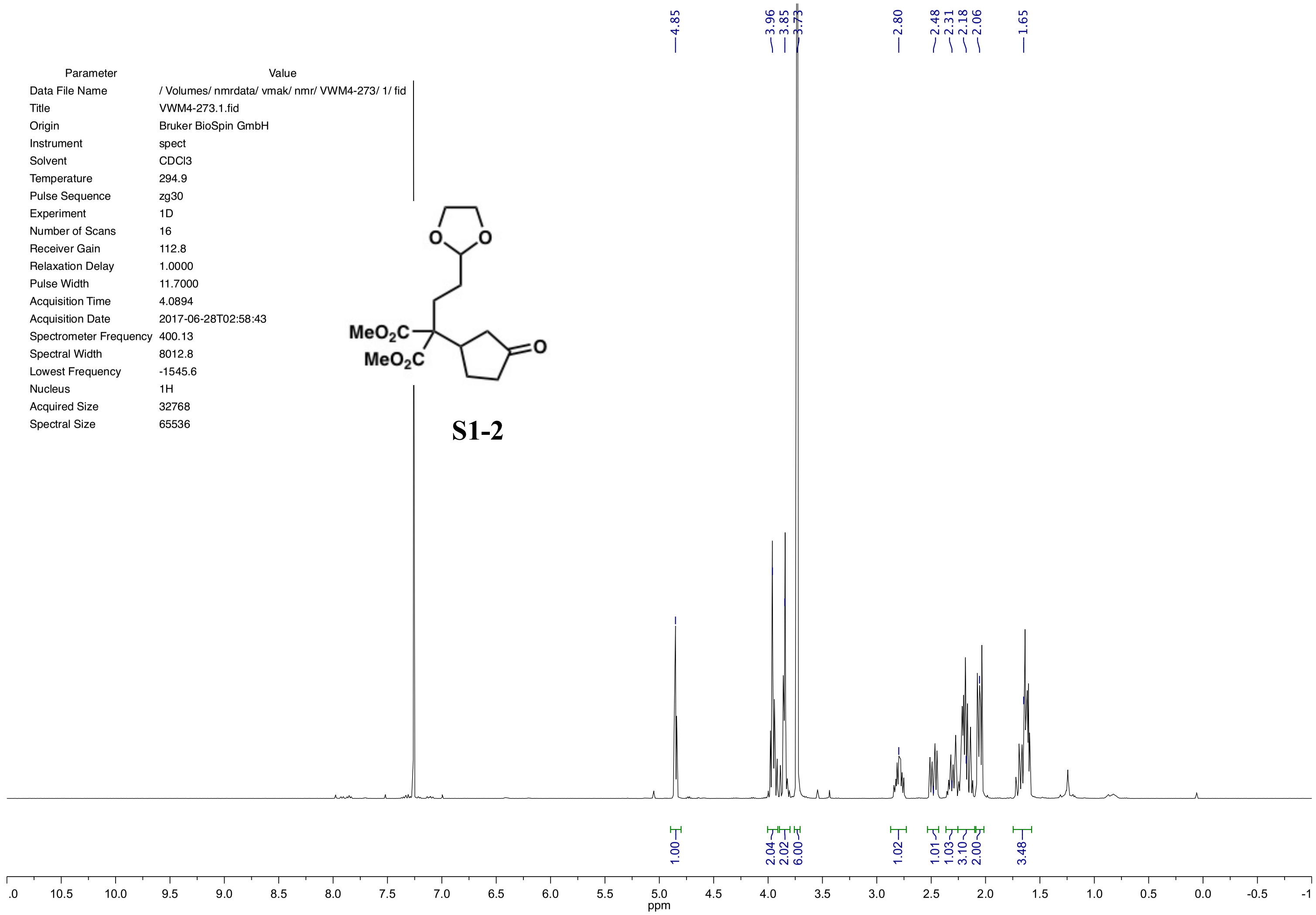
Instrument	spect
Solvent	CDCl3
Temperature	298.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	16
Receiver Gain	197.4
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2015-02-23T10:28:00
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.0
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



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Instrument	spect
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	2017-06-28T02:58:43
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Lowest Frequency	-1545.6
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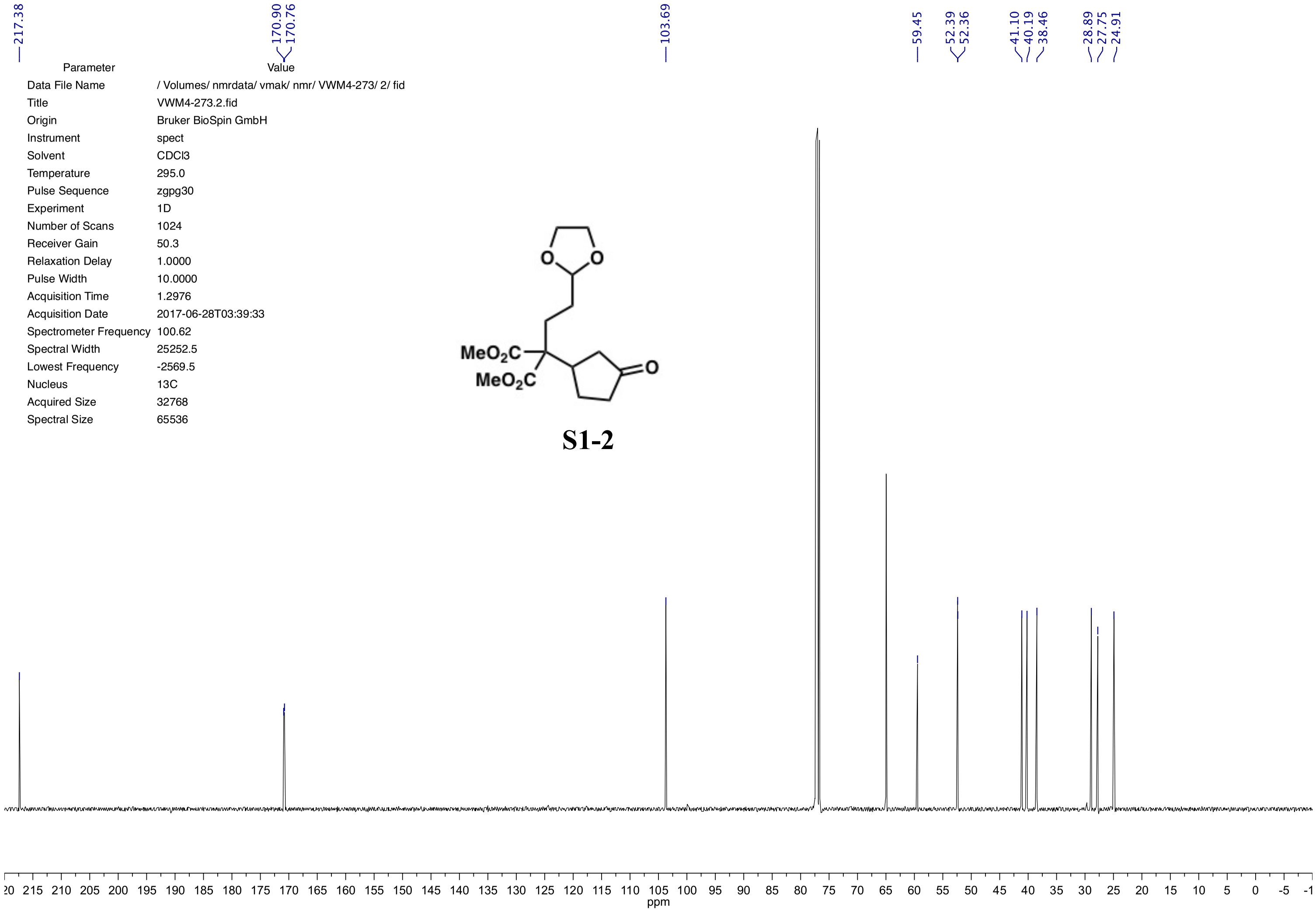
Acquired Size	32768
Spectral Size	65536

S1-2



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Title	VWM4-273.2.fid
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Instrument	spect
Solvent	CDCl3
Temperature	295.0
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Experiment	1D
Number of Scans	1024
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Pulse Width	10.0000
Acquisition Time	1.2976
Acquisition Date	2017-06-28T03:39:33
Spectrometer Frequency	100.62
Spectral Width	25252.5
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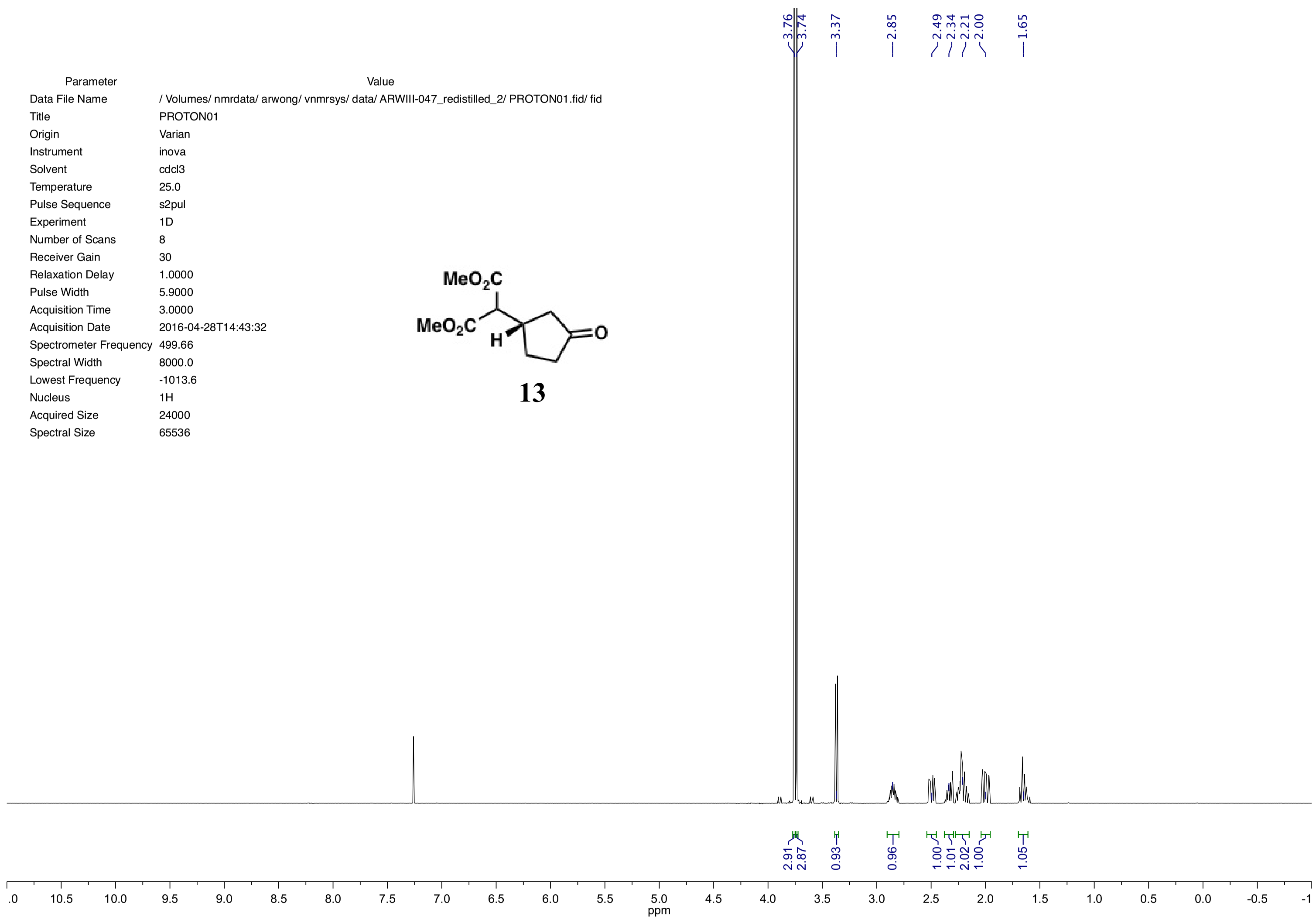
Spectral Size	65536

S1-2



13

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Title	PROTON01
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	8
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	5.9000
Acquisition Time	3.0000
Acquisition Date	2016-04-28T14:43:32
Spectrometer Frequency	499.66
Spectral Width	8000.0
Lowest Frequency	-1013.6
Nucleus	1H
Acquired Size	24000
Spectral Size	65536

Parameter	Value
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Title	VWM7-095.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	294.9
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	2017-05-05T05:03:32
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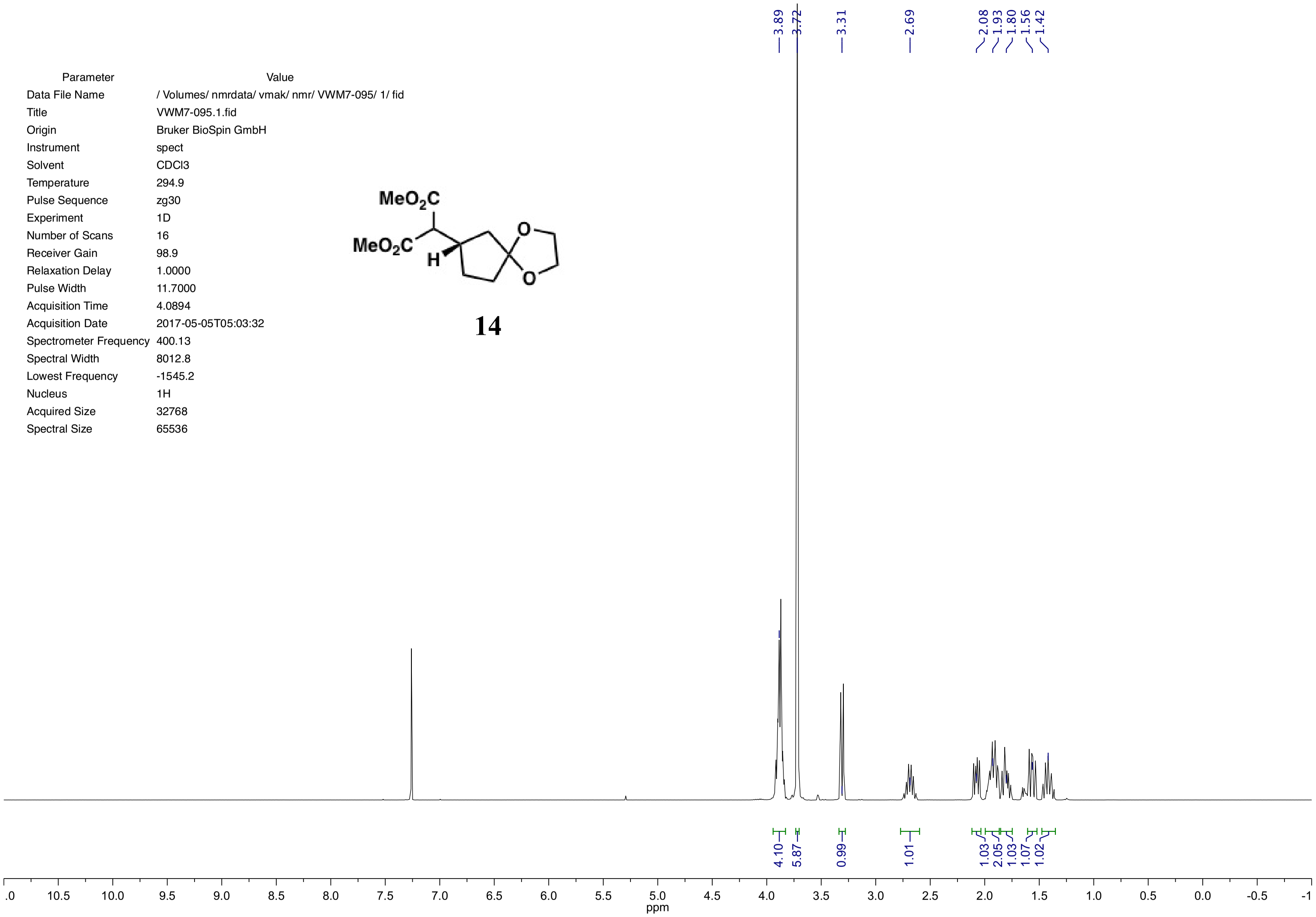
Spectral Width	8012.8
Lowest Frequency	-1545.2
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



14

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Instrument	spect
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1024
Receiver Gain	78.7
Relaxation Delay	2.0000
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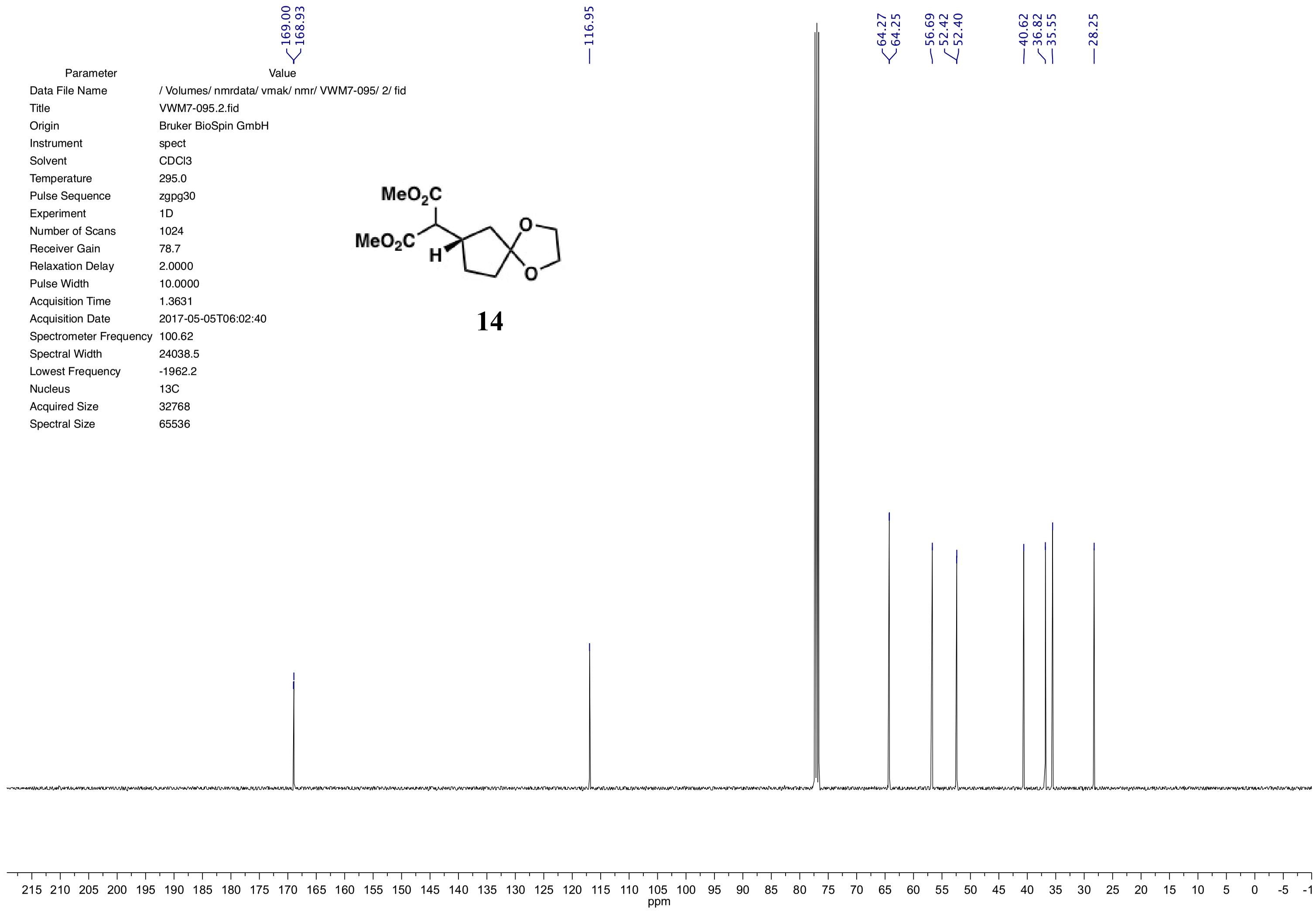
Acquired Size	32768
Spectral Size	65536



14

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Instrument	inova
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	8
Receiver Gain	28
Relaxation Delay	1.0000
Pulse Width	5.8000
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Nucleus	1H
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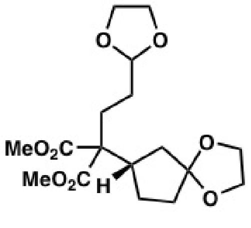

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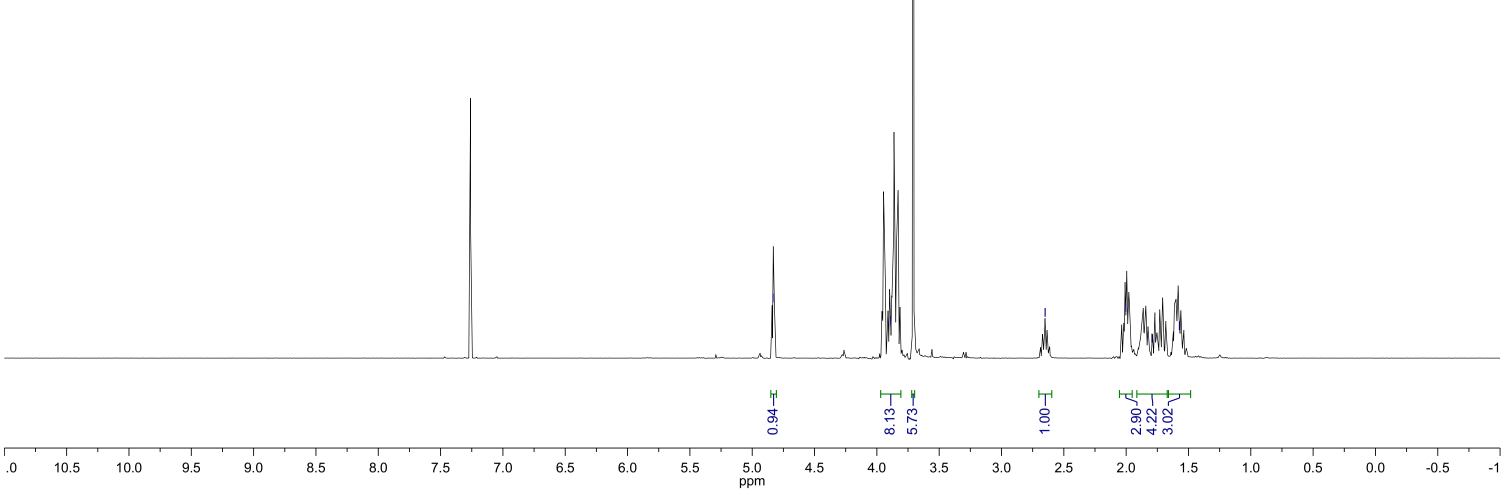

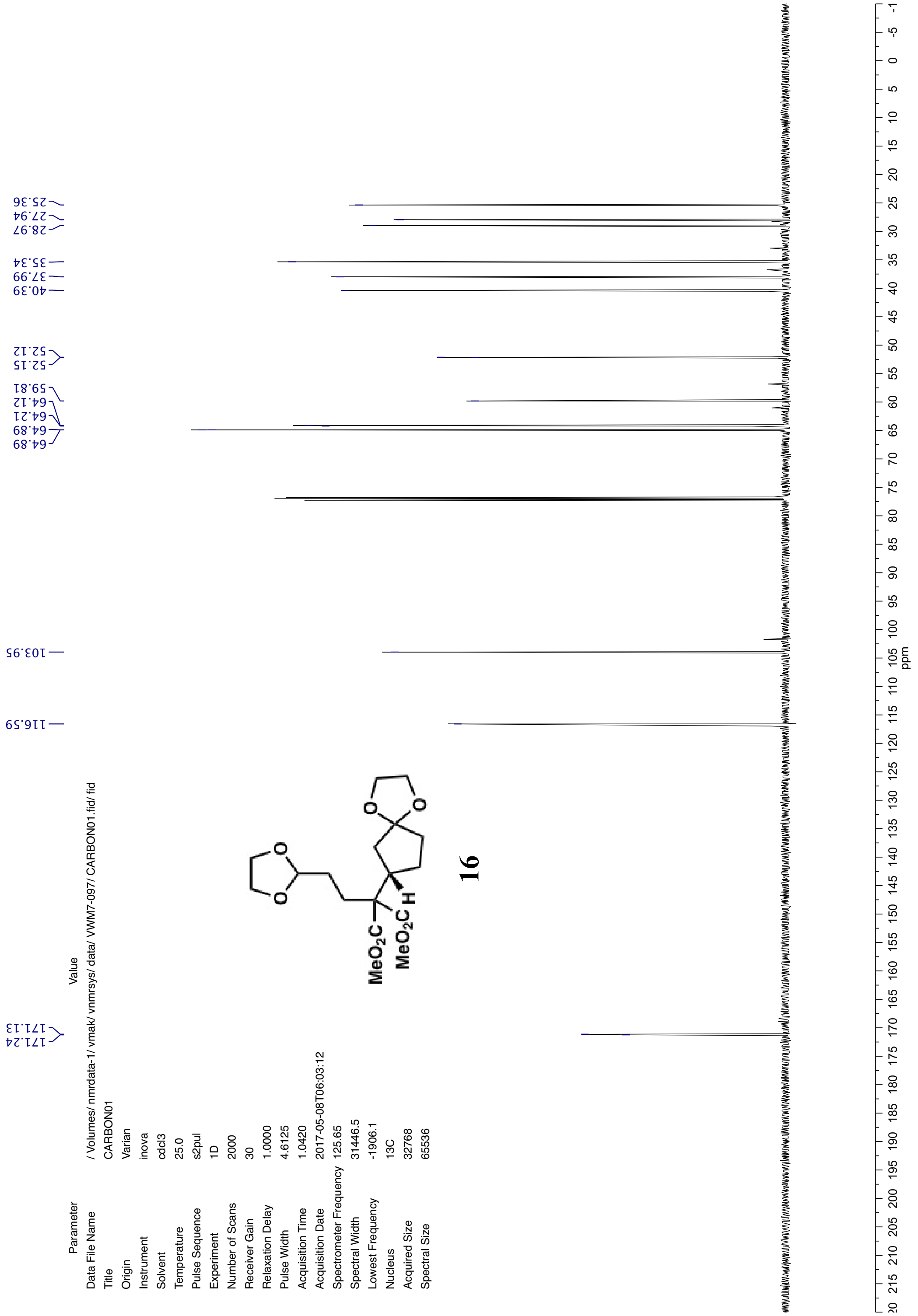

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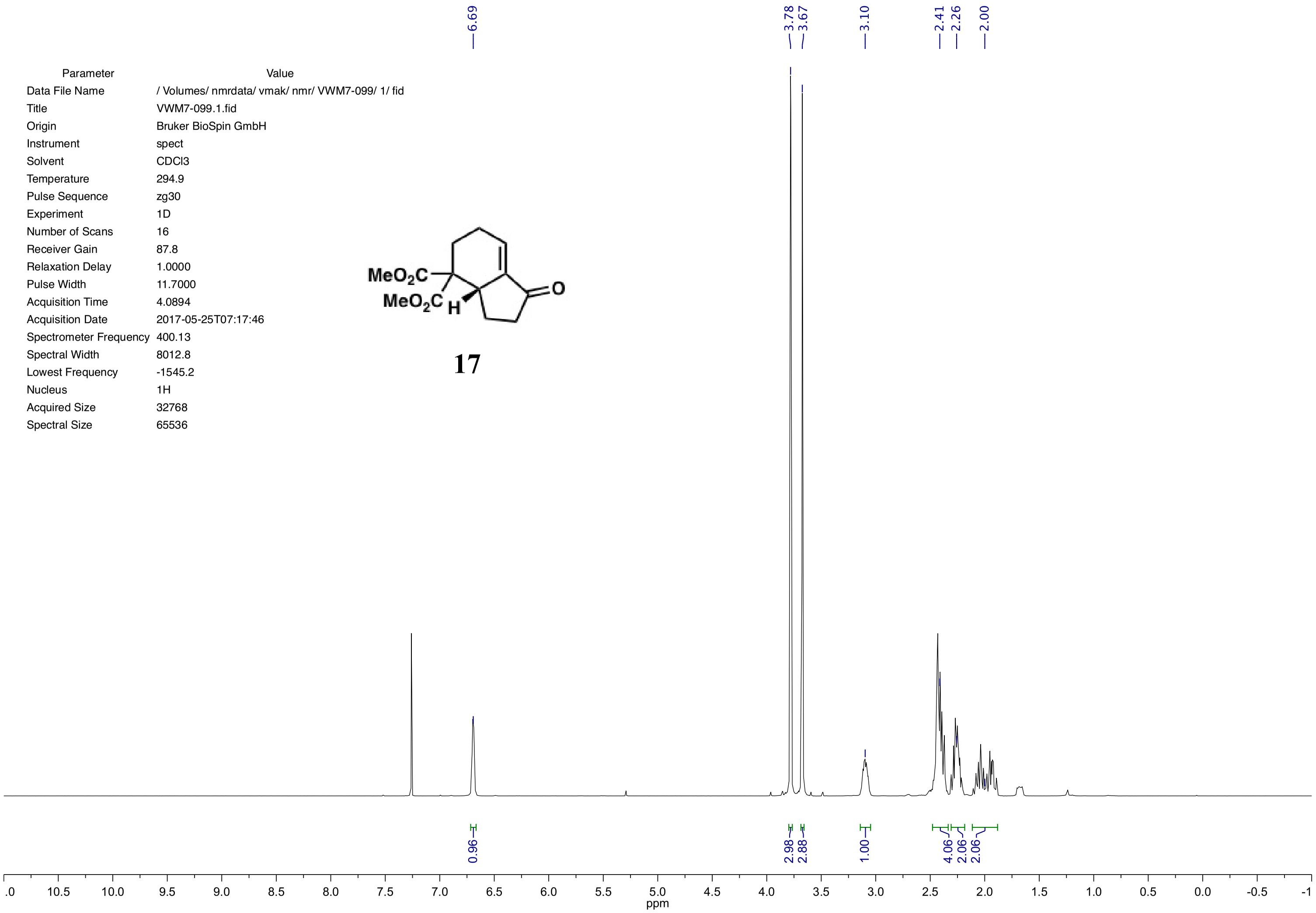
Instrument	inova
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	2000
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	4.6125
Acquisition Time	1.0420
Acquisition Date	2017-05-08T06:03:12
Spectrometer Frequency	125.65
Spectral Width	31446.5
Lowest Frequency	-1906.1
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



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Instrument	spect
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Temperature	294.9
Pulse Sequence	zg30
Experiment	1D
Number of Scans	16
Receiver Gain	87.8
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Pulse Width	11.7000
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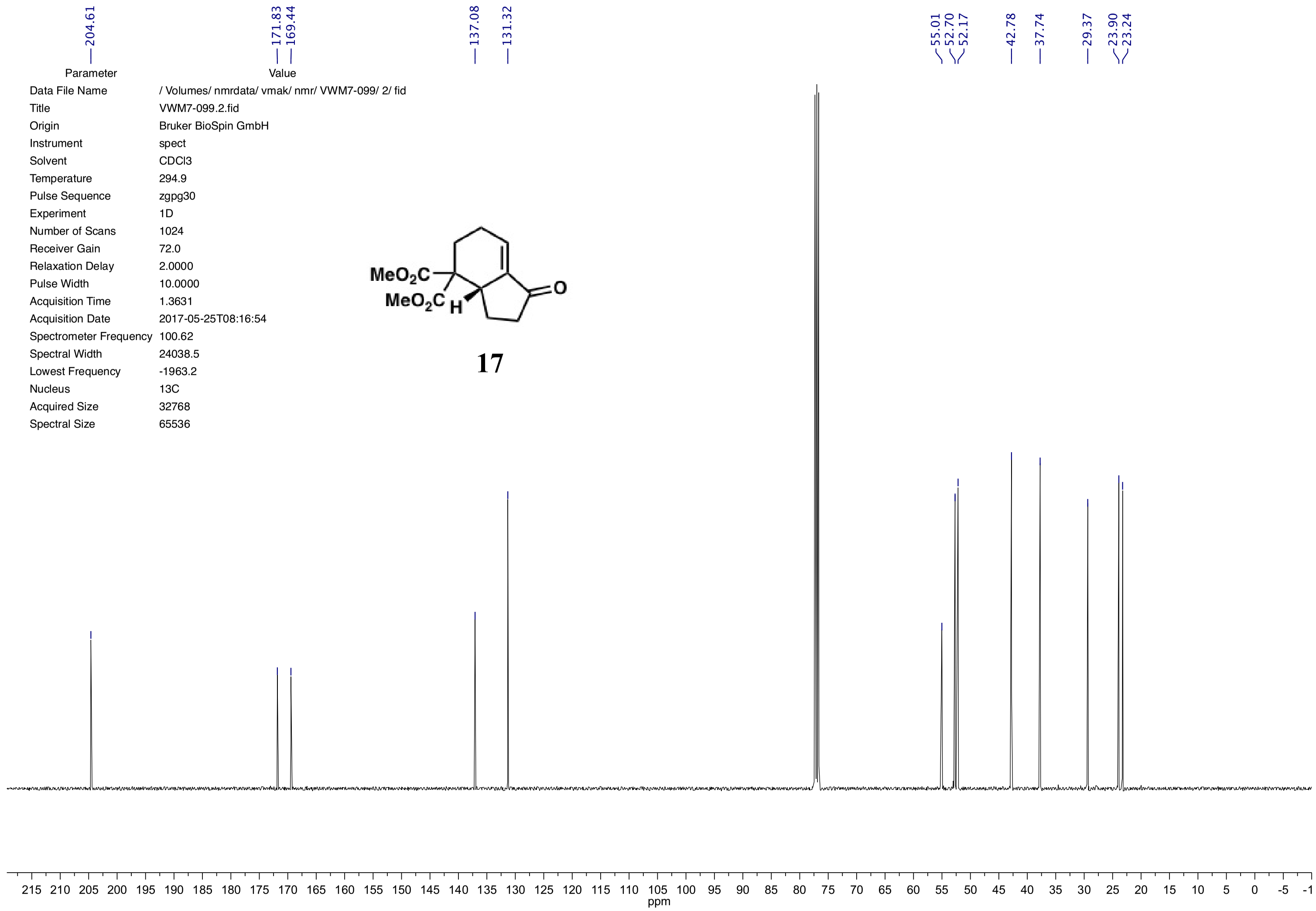
Spectral Size	65536



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Pulse Sequence	zgpg30
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Number of Scans	1024
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Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2017-05-25T08:16:54
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Spectral Width	24038.5
Lowest Frequency	-1963.2
Nucleus	13C
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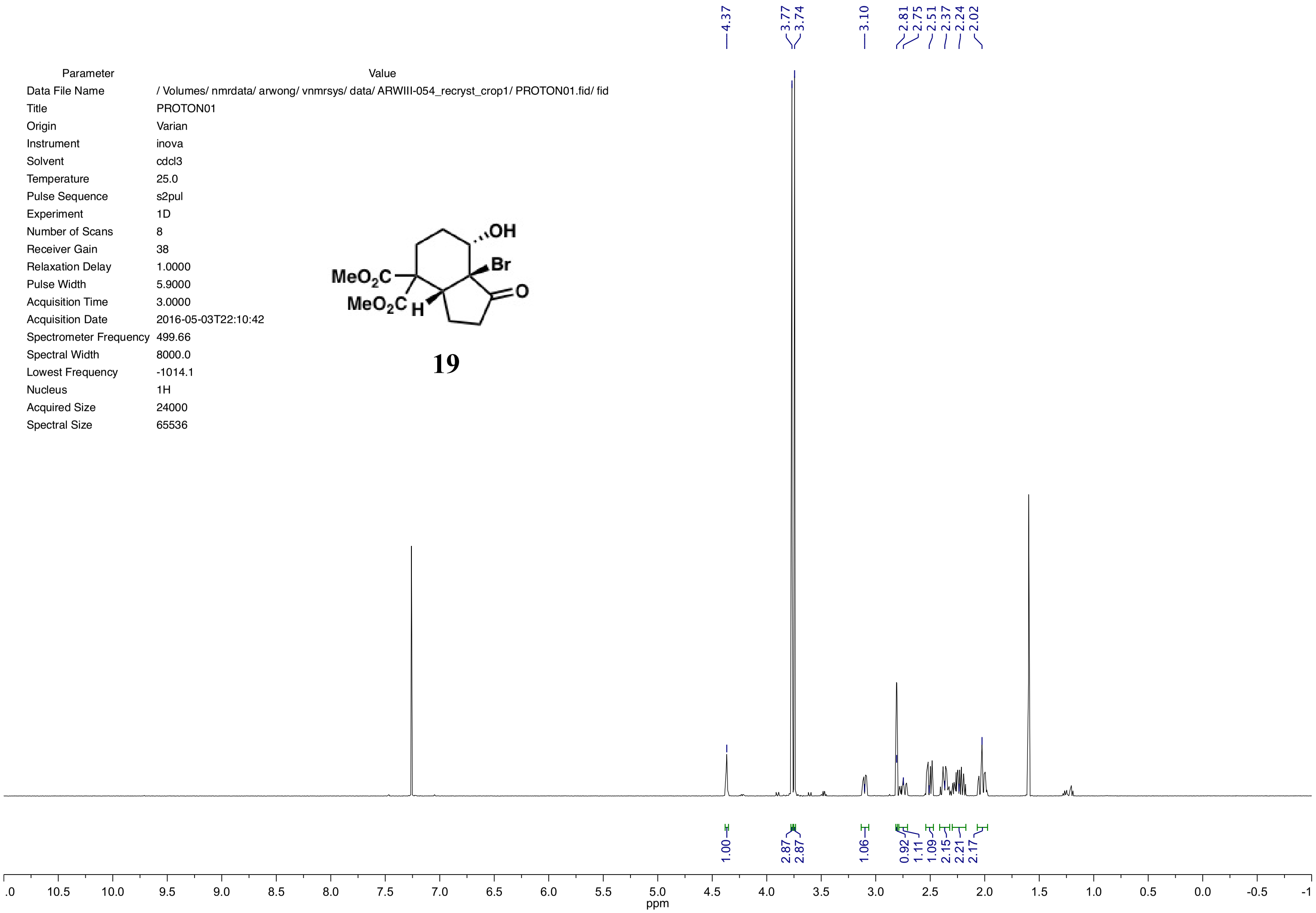
Spectral Size	65536

17



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Instrument	inova
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Experiment	1D
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Nucleus	1H
Acquired Size	24000
Spectral Size	65536

19

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Instrument	spect
Solvent	CDCl3
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Experiment	1D
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Receiver Gain	72.0
Relaxation Delay	2.0000
Pulse Width	10.0000
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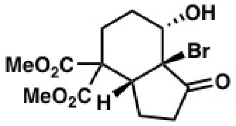
Spectral Size	65536



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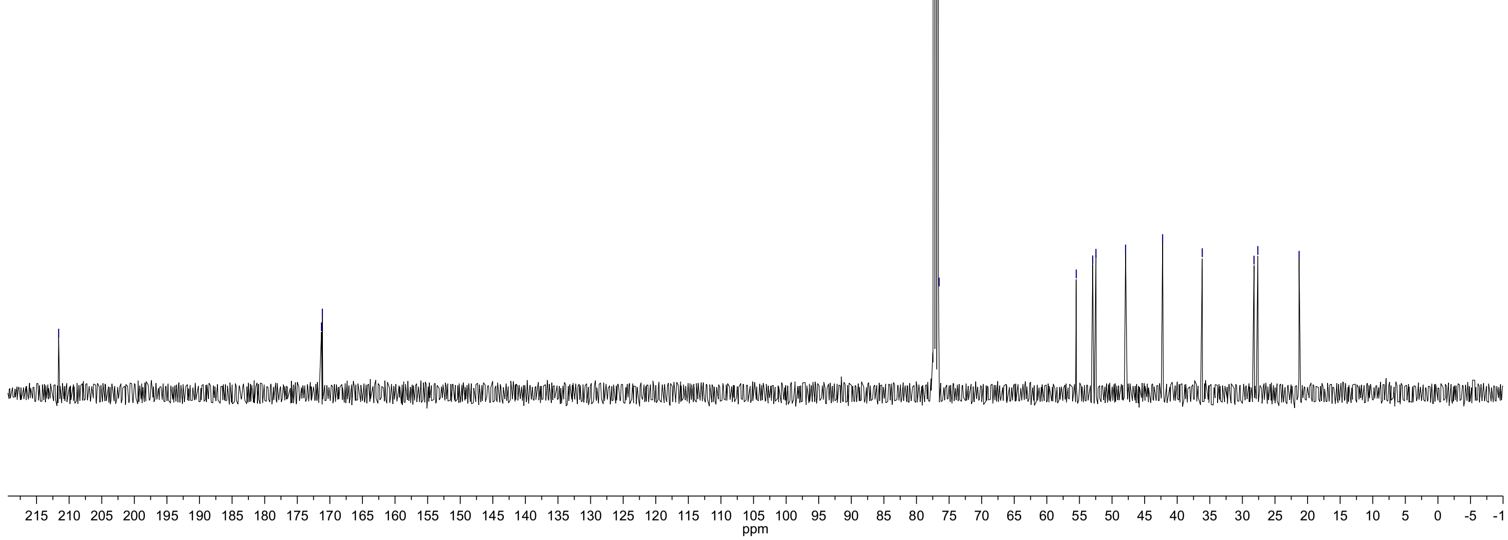

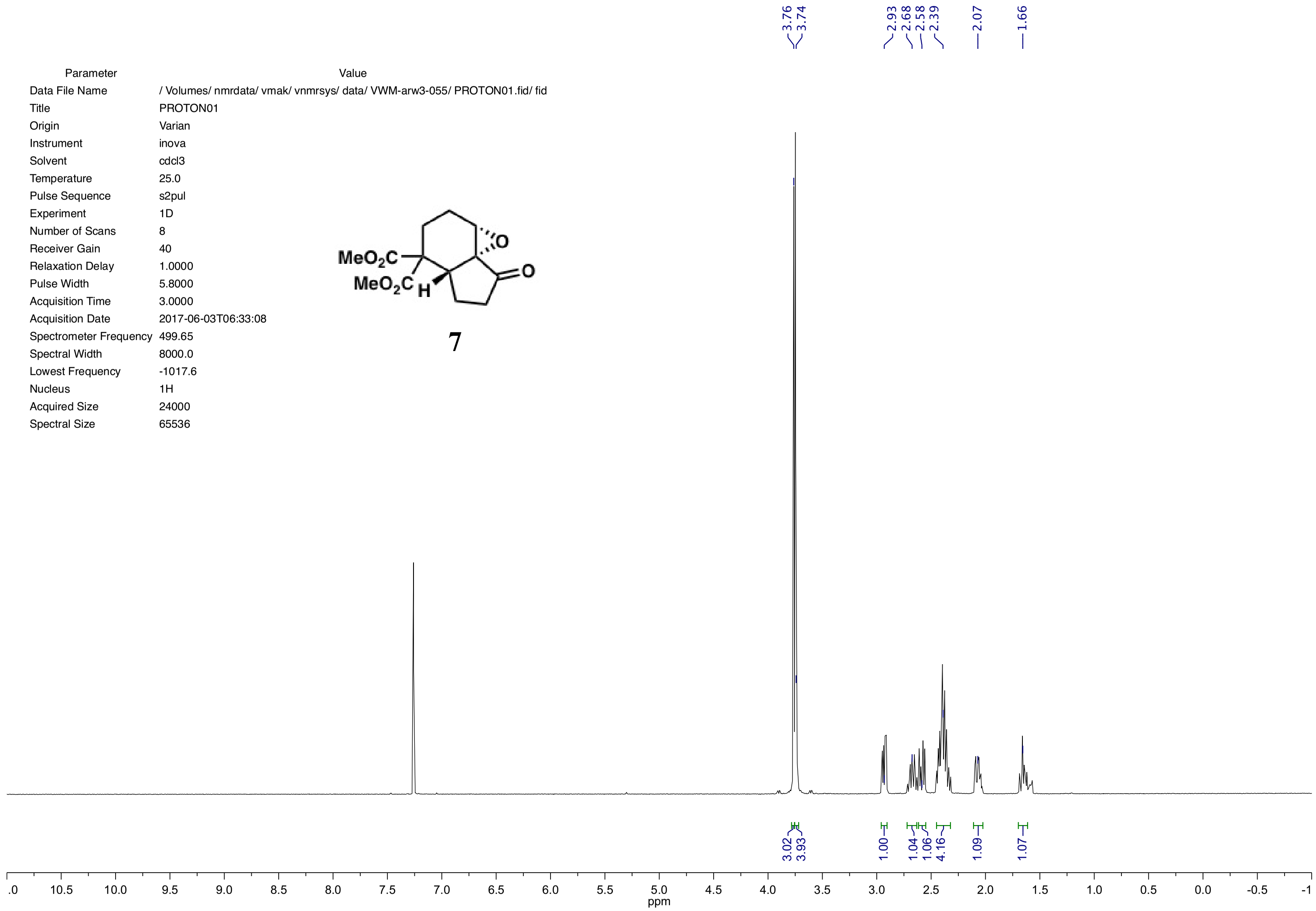

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Instrument	inova
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Temperature	25.0
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Experiment	1D
Number of Scans	8
Receiver Gain	40
Relaxation Delay	1.0000
Pulse Width	5.8000
Acquisition Time	3.0000
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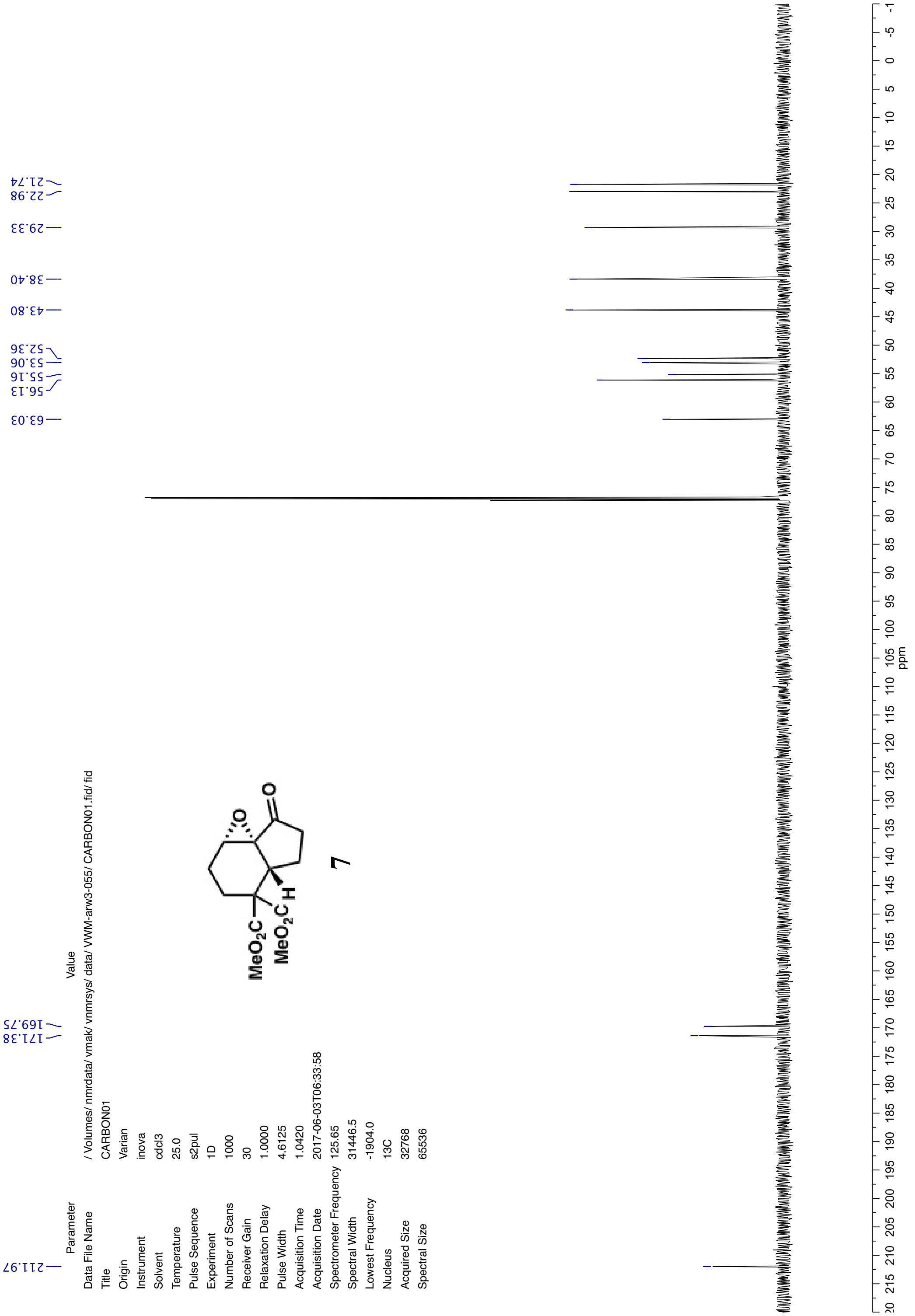
Spectral Size	65536

7



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Experiment	1D
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Lowest Frequency	-1904.0
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

Parameter	Value
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Instrument	inova
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	36
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	2.6500
Acquisition Time	1.7046
Acquisition Date	2018-01-28T13:14:56
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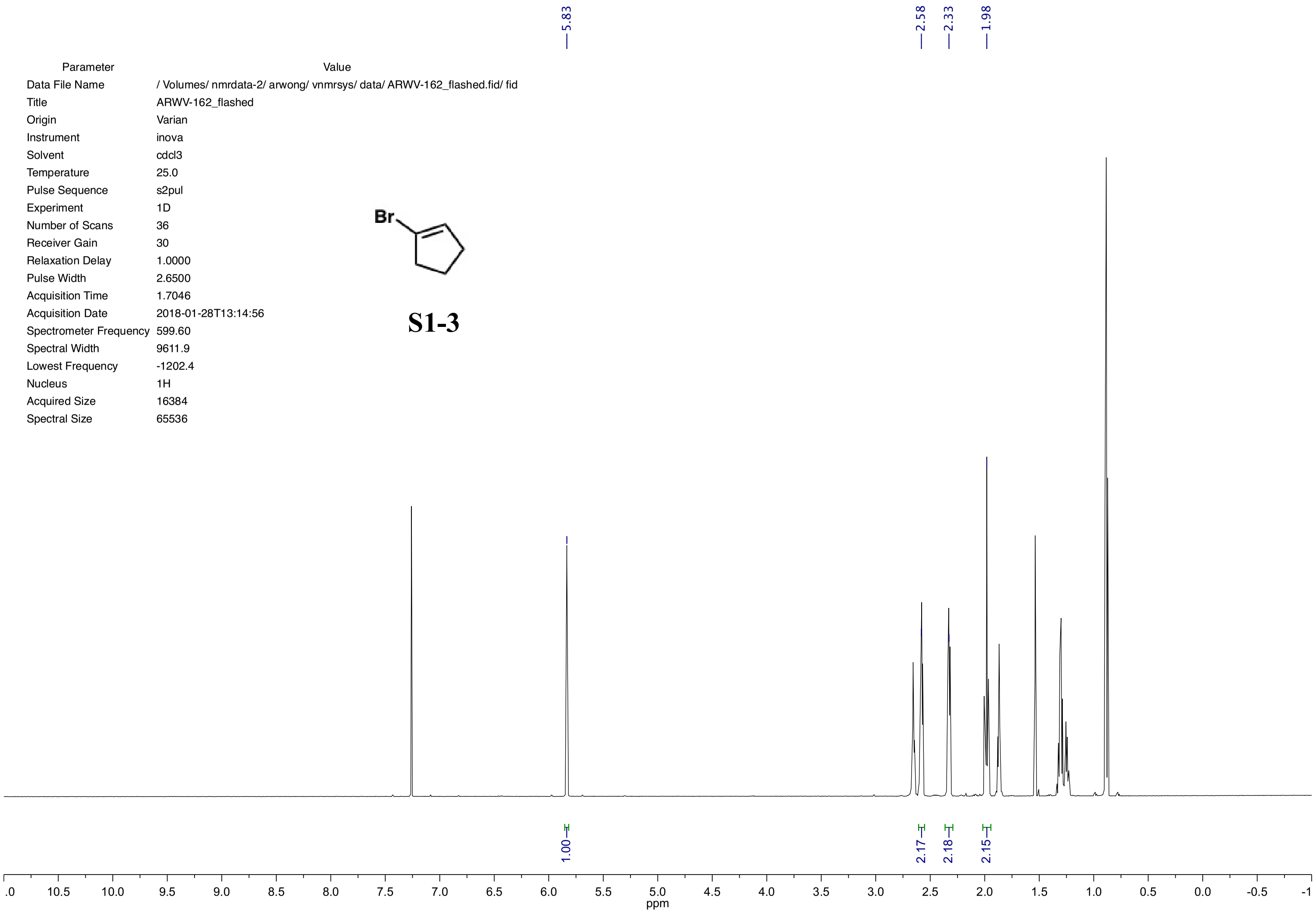
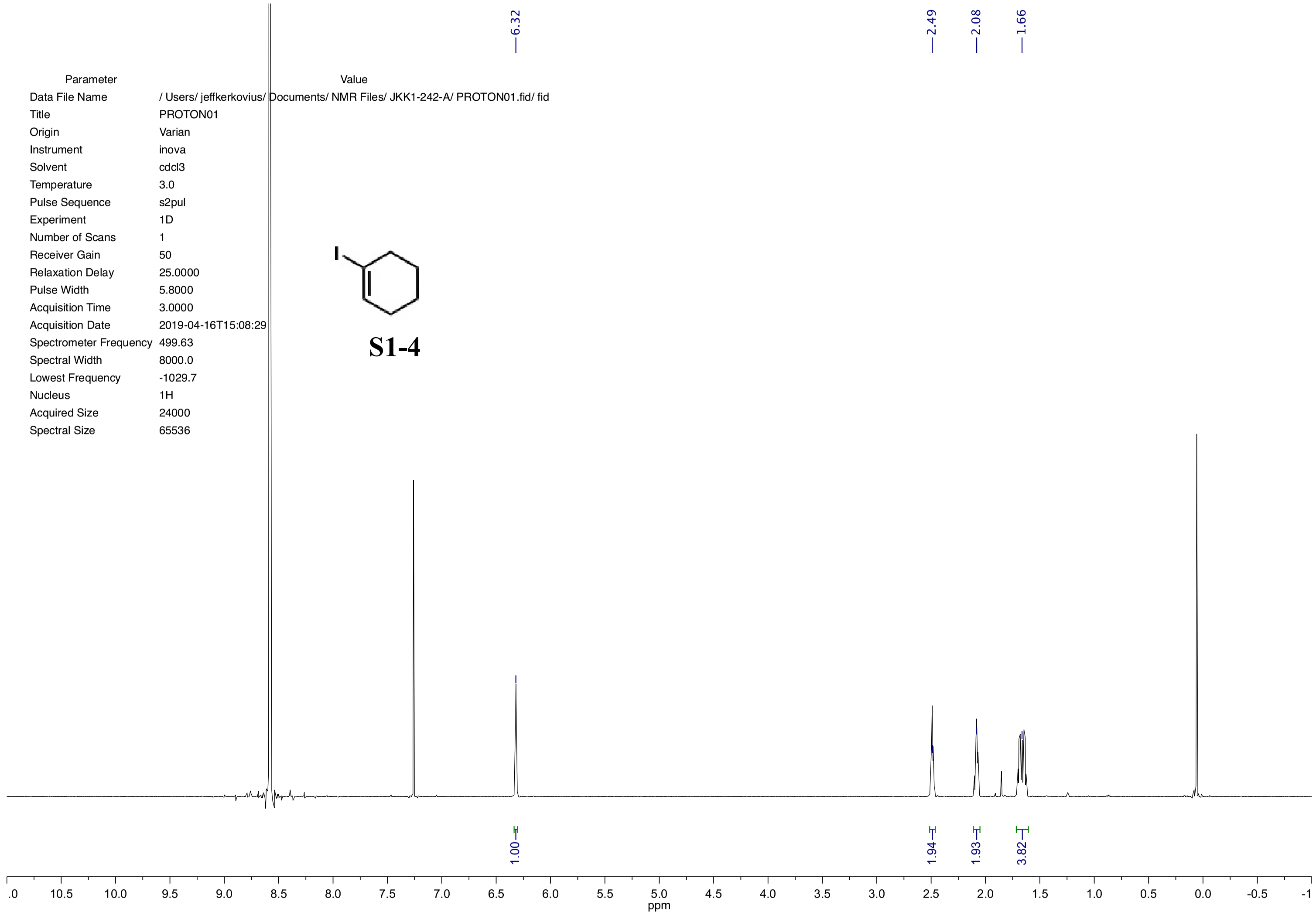
Nucleus	1H
Acquired Size	16384
Spectral Size	65536



S1-3

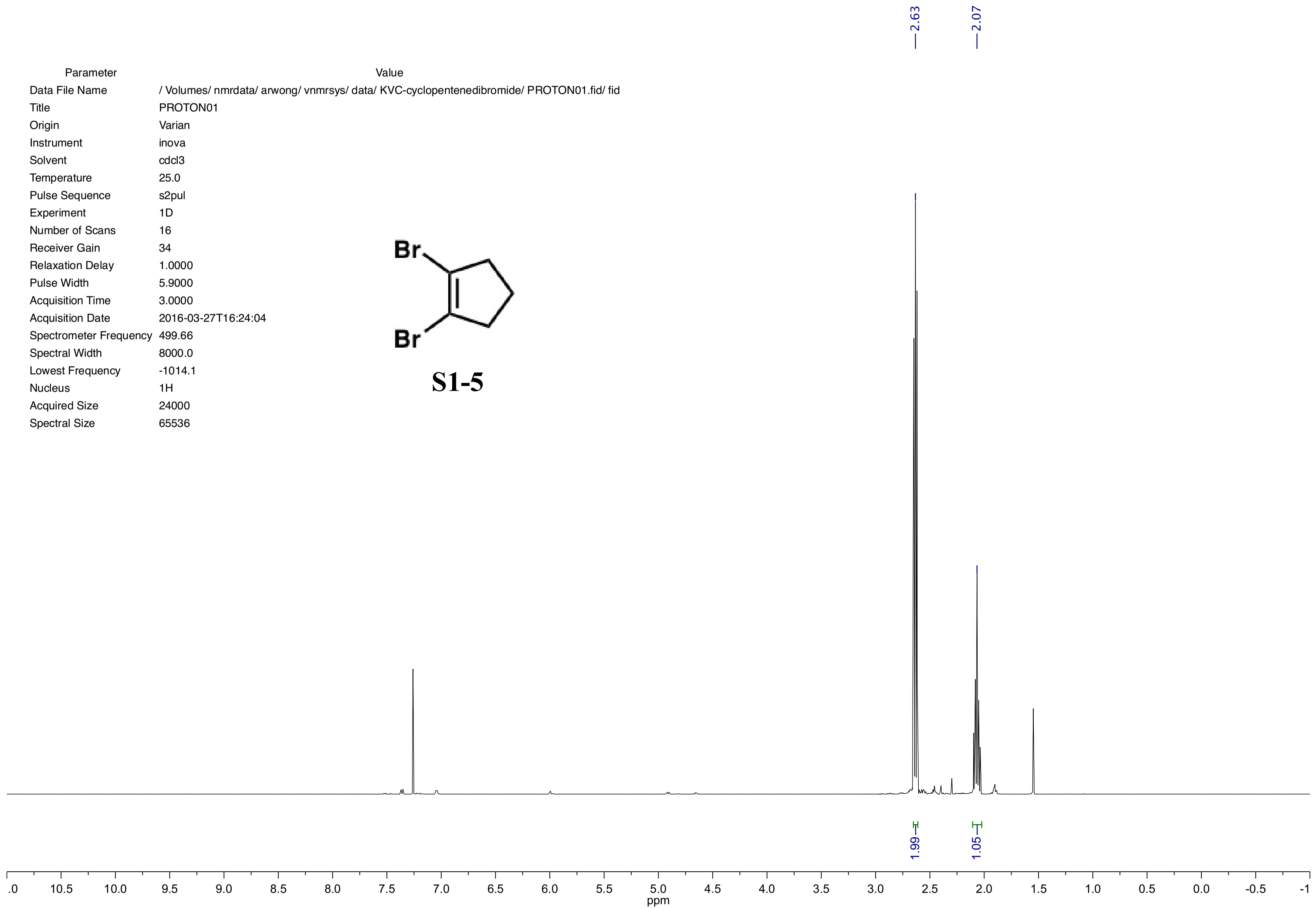


S1-4

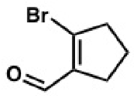
Parameter	Value
Data File Name	/ Users/ jeffkerkovius/ Documents/ NMR Files/ JKK1-242-A/ PROTON01.fid/ fid
Title	PROTON01
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	3.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	1
Receiver Gain	50
Relaxation Delay	25.0000
Pulse Width	5.8000
Acquisition Time	3.0000
Acquisition Date	2019-04-16T15:08:29
Spectrometer Frequency	499.63
Spectral Width	8000.0
Lowest Frequency	-1029.7
Nucleus	1H
Acquired Size	24000
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ vnmrsys/ data/ KVC-cyclopentenedibromide/ PROTON01.fid/ fid
Title	PROTON01
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	16
Receiver Gain	34
Relaxation Delay	1.0000
Pulse Width	5.9000
Acquisition Time	3.0000
Acquisition Date	2016-03-27T16:24:04
Spectrometer Frequency	499.66
Spectral Width	8000.0
Lowest Frequency	-1014.1
Nucleus	1H
Acquired Size	24000
Spectral Size	65536

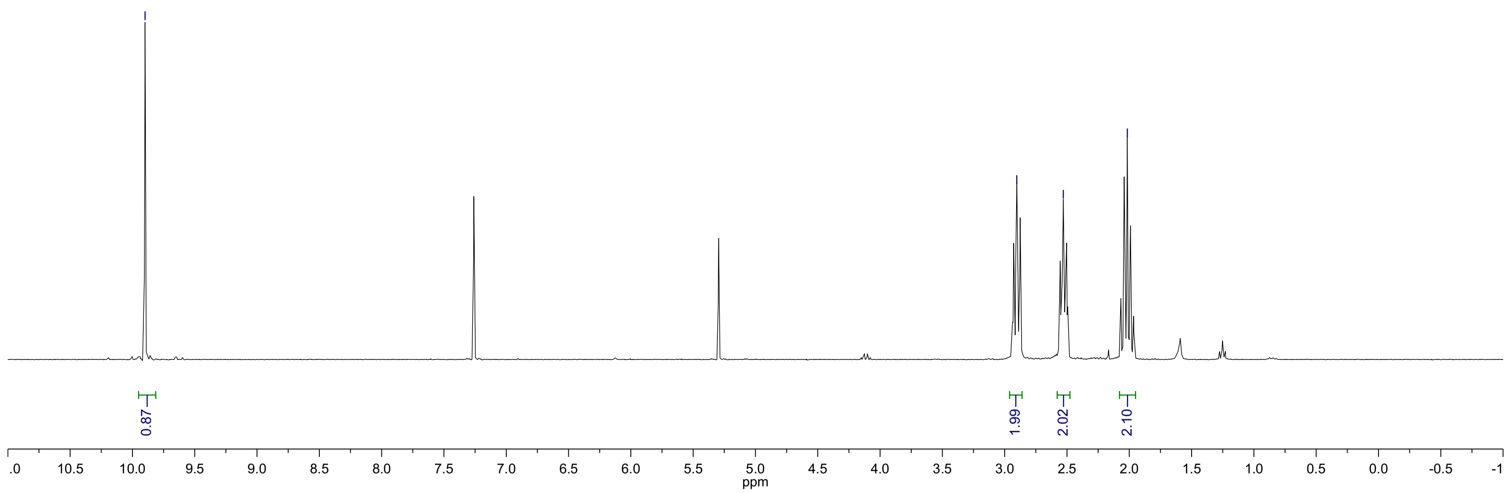
S1-5



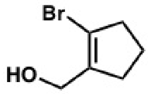
Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ vmak/ vnmrsys/ data/ VWM4-021/ PROTON01.fid/ fid
Title	PROTON01
Origin	Varian
Instrument	mercury
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	8
Receiver Gain	26
Relaxation Delay	1.0000
Pulse Width	5.1000
Acquisition Time	2.4999
Acquisition Date	2014-07-29T08:18:45
Spectrometer Frequency	300.09
Spectral Width	4796.2
Lowest Frequency	-597.2
Nucleus	1H
Acquired Size	11990
Spectral Size	65536



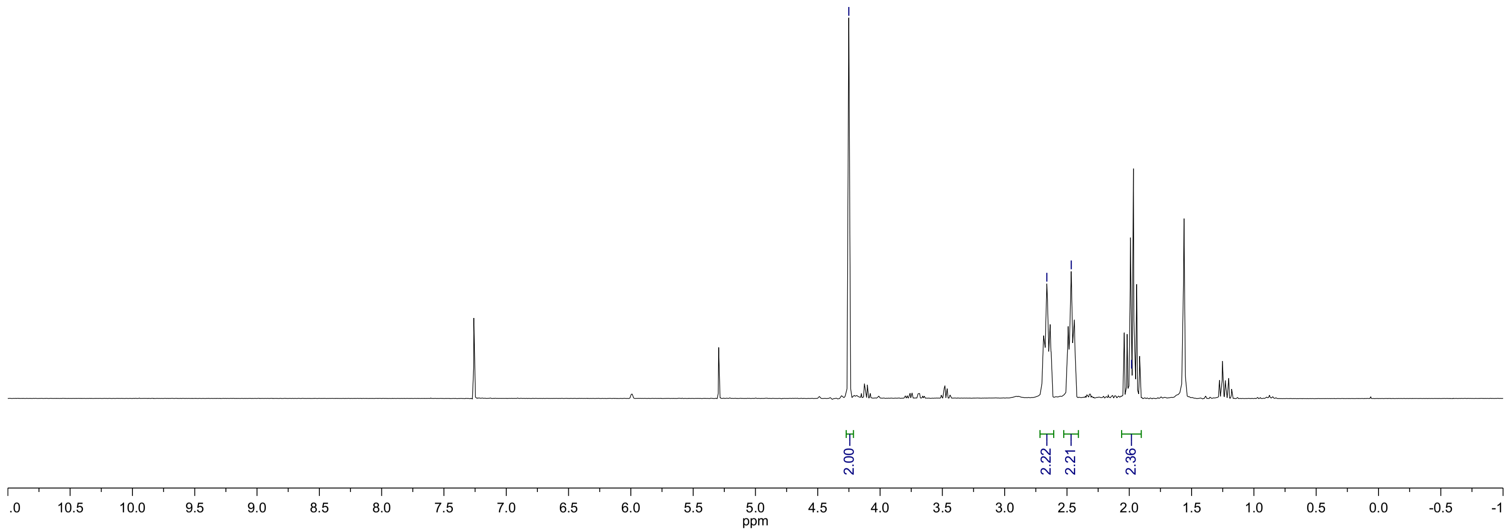
S1-6

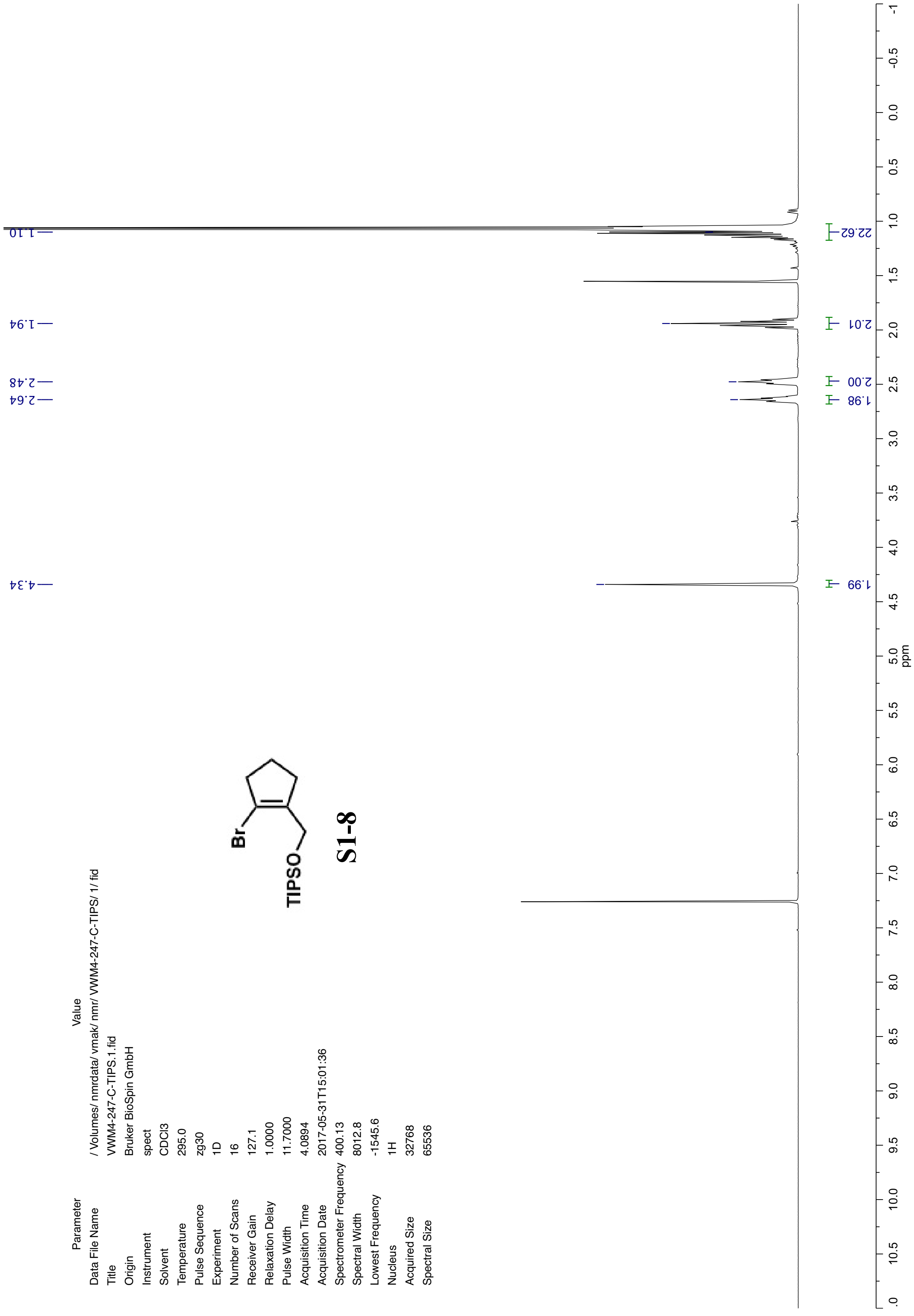


Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ vmak/ vnmrsys/ data/ VWM4-039-f8-12/ PROTON01.fid/ fid
Title	PROTON01
Origin	Varian
Instrument	mercury
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	16
Receiver Gain	20
Relaxation Delay	1.0000
Pulse Width	5.1000
Acquisition Time	2.4999
Acquisition Date	2014-08-12T12:01:01
Spectrometer Frequency	300.09
Spectral Width	4796.2
Lowest Frequency	-597.2
Nucleus	1H
Acquired Size	11990
Spectral Size	65536



S1-7

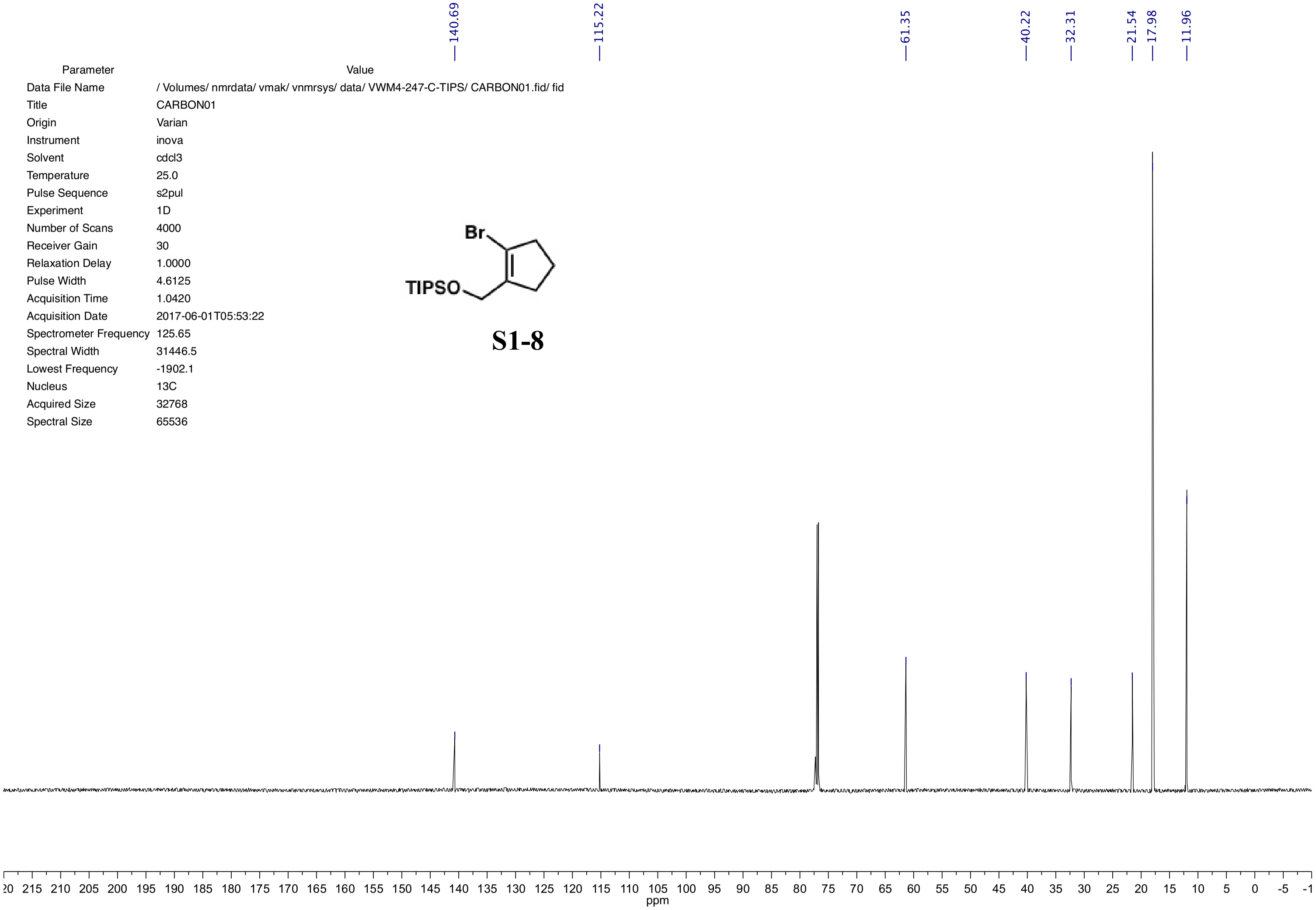




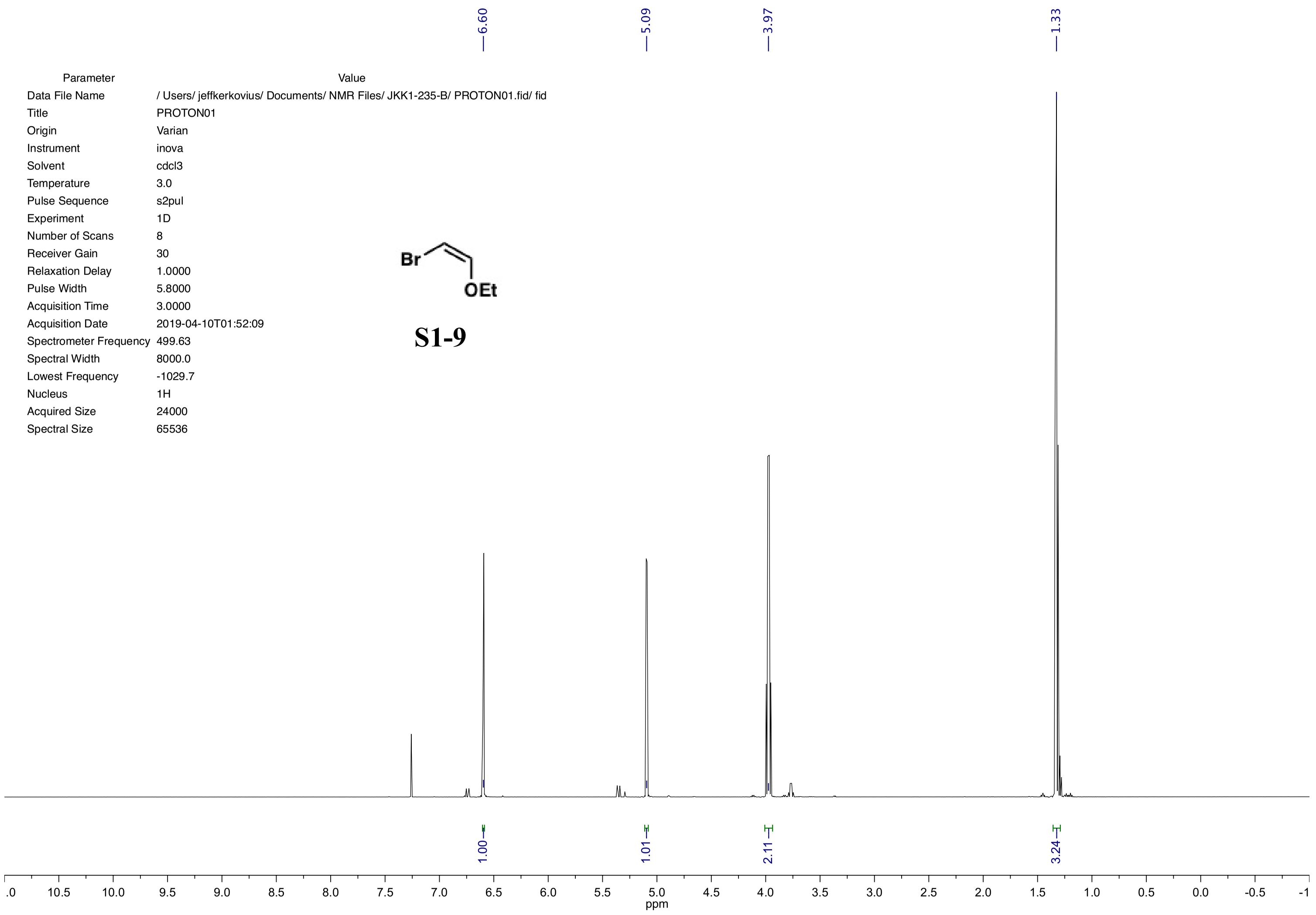
S1-8

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM4-247-C-TIPS/ 1/ fid
Title	VWM4-247-C-TIPS.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
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	2017-05-31T15:01:36
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ vnmrsys/ data/ VWM4-247-C-TIPS/ CARBON01.fid/ fid
Title	CARBON01
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	4000
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	4.6125
Acquisition Time	1.0420
Acquisition Date	2017-06-01T05:53:22
Spectrometer Frequency	125.65
Spectral Width	31446.5
Lowest Frequency	-1902.1
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

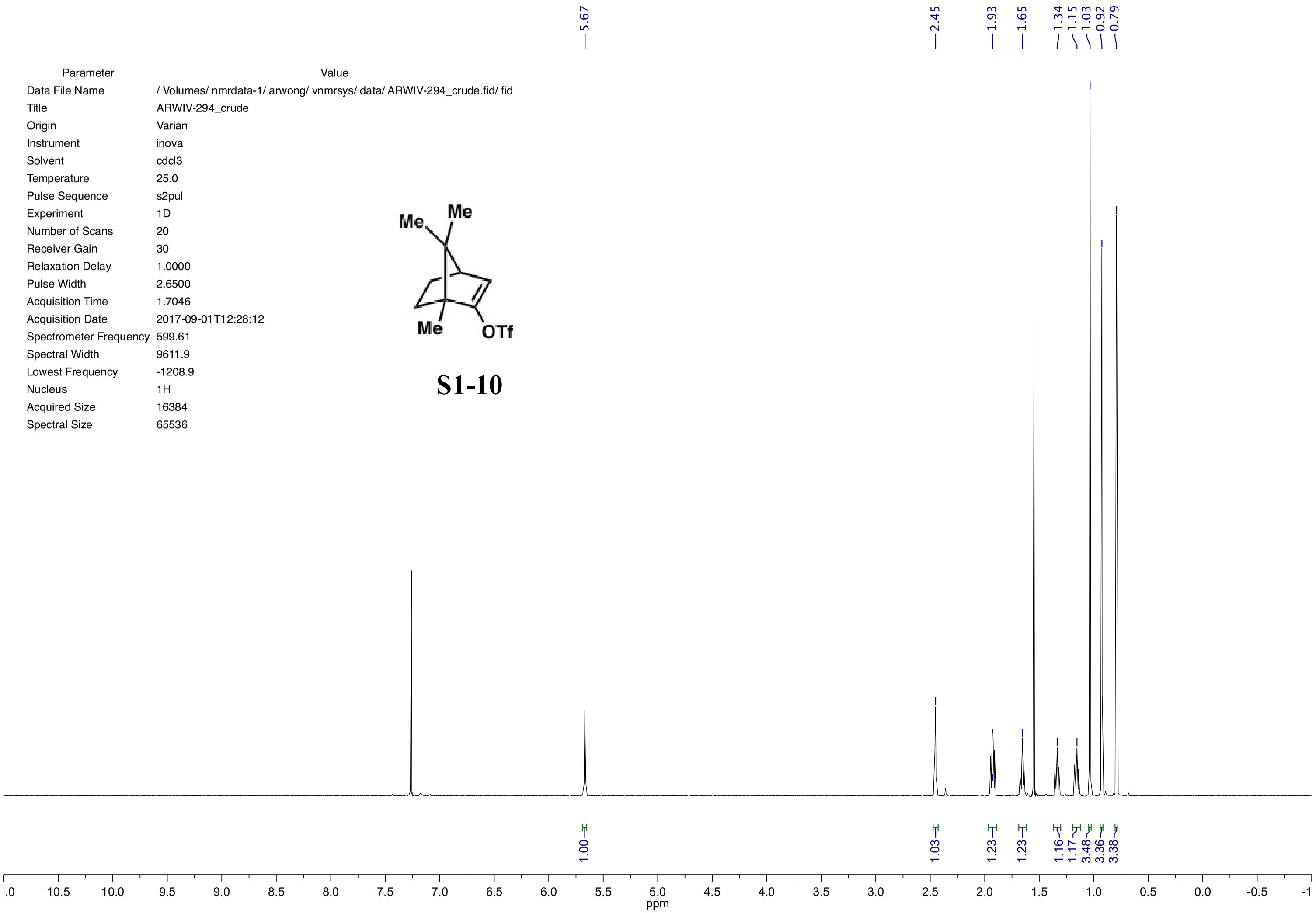


S1-8



S1-9

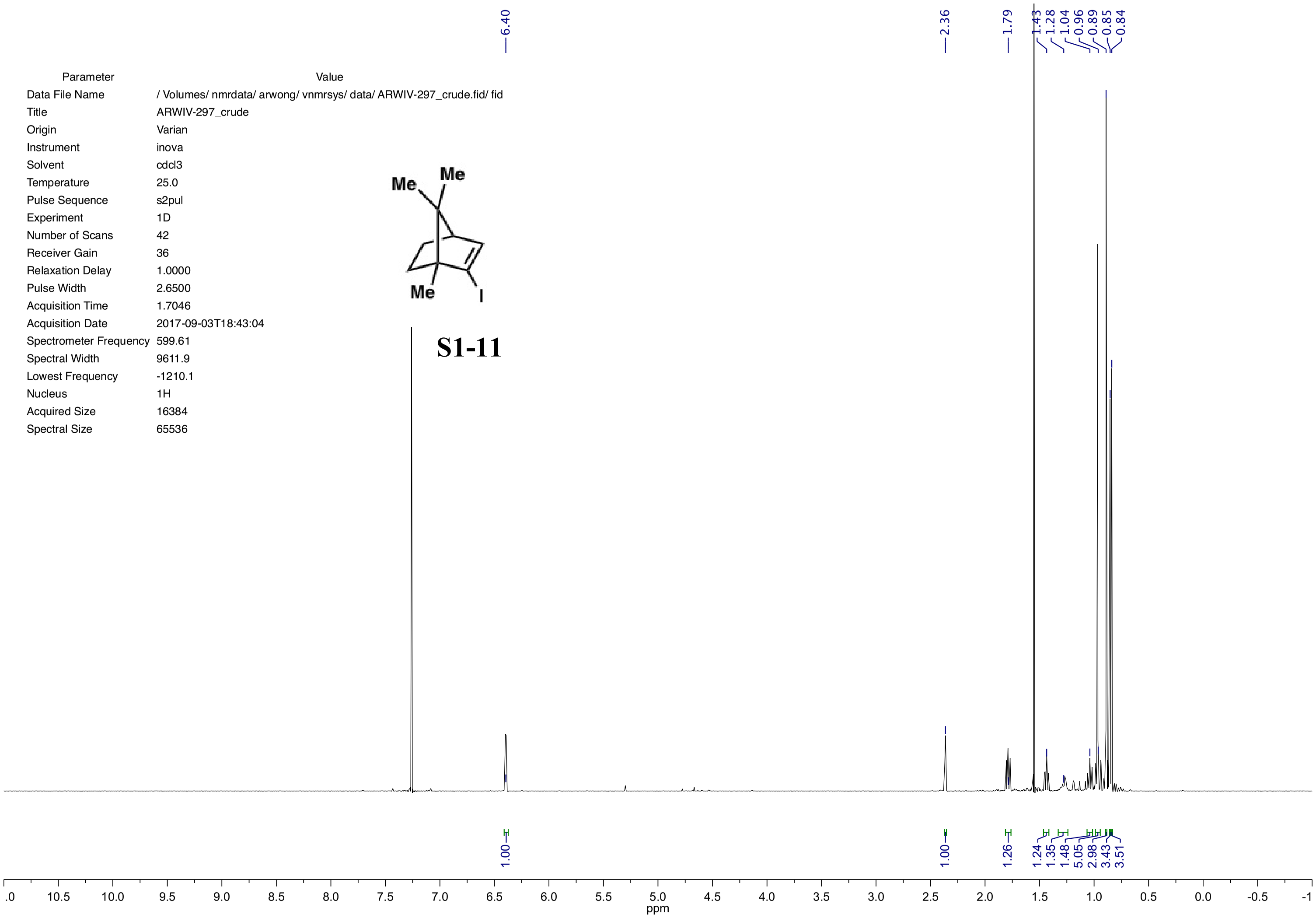
Parameter	Value
Data File Name	/ Users/ jeffkerkovius/ Documents/ NMR Files/ JKK1-235-B/ PROTON01.fid/ fid
Title	PROTON01
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	3.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	8
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	5.8000
Acquisition Time	3.0000
Acquisition Date	2019-04-10T01:52:09
Spectrometer Frequency	499.63
Spectral Width	8000.0
Lowest Frequency	-1029.7
Nucleus	1H
Acquired Size	24000
Spectral Size	65536



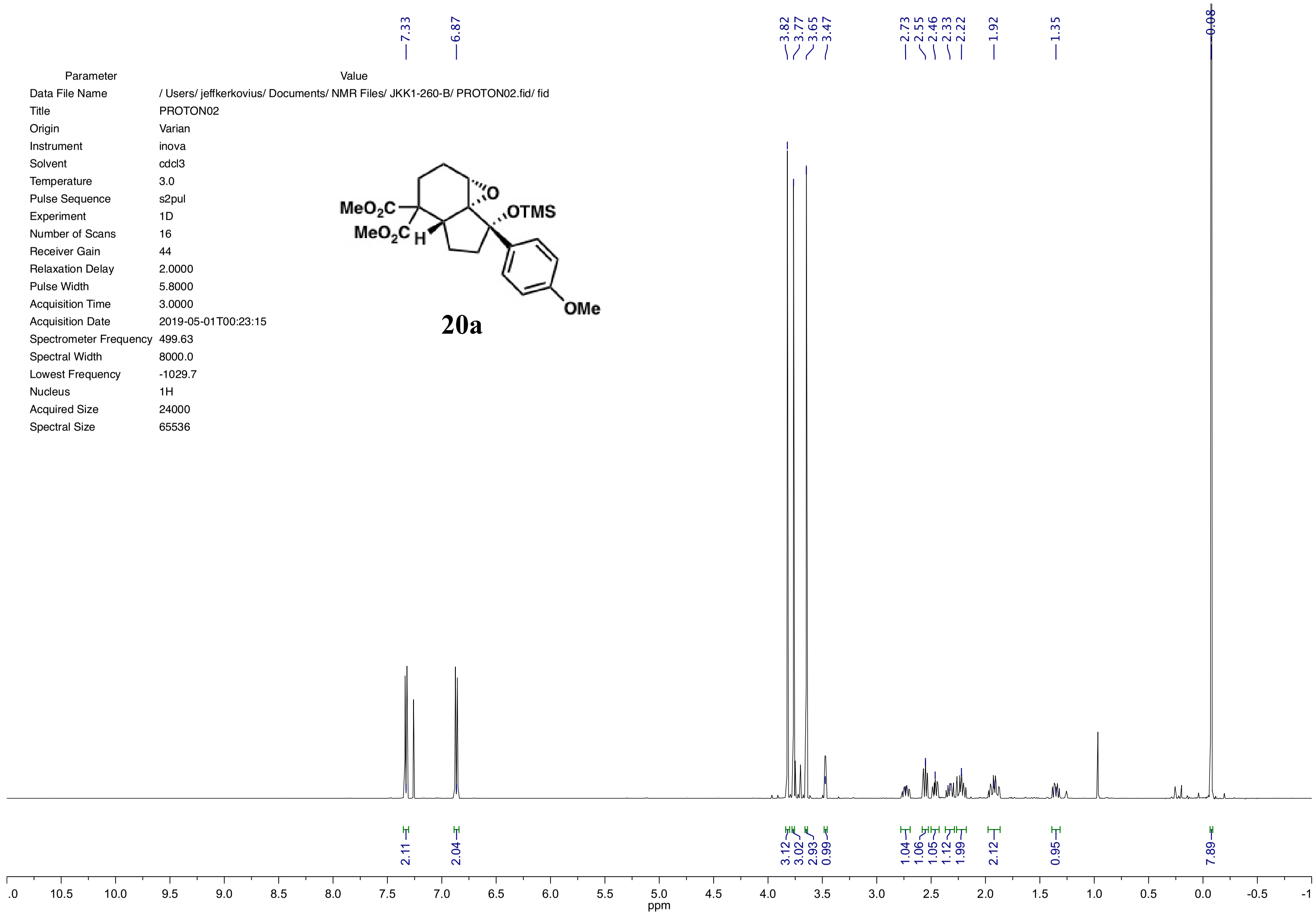
Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ arwong/ vnmrsys/ data/ ARWIV-294_crude.fid/ fid
Title	ARWIV-294_crude
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	20
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	2.6500
Acquisition Time	1.7046
Acquisition Date	2017-09-01T12:28:12
Spectrometer Frequency	599.61
Spectral Width	9611.9
Lowest Frequency	-1208.9
Nucleus	1H
Acquired Size	16384
Spectral Size	65536

S1-10

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ vnmrsys/ data/ ARWIV-297_crude.fid/ fid
Title	ARWIV-297_crude
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	42
Receiver Gain	36
Relaxation Delay	1.0000
Pulse Width	2.6500
Acquisition Time	1.7046
Acquisition Date	2017-09-03T18:43:04
Spectrometer Frequency	599.61
Spectral Width	9611.9
Lowest Frequency	-1210.1
Nucleus	1H
Acquired Size	16384
Spectral Size	65536



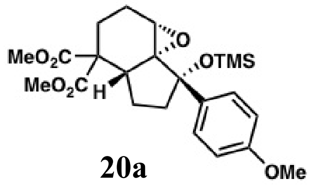
S1-11



20a

Parameter	Value
Data File Name	/ Users/ jeffkerkovius/ Documents/ NMR Files/ JKK1-260-B/ PROTON02.fid/ fid
Title	PROTON02
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	3.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	16
Receiver Gain	44
Relaxation Delay	2.0000
Pulse Width	5.8000
Acquisition Time	3.0000
Acquisition Date	2019-05-01T00:23:15
Spectrometer Frequency	499.63
Spectral Width	8000.0
Lowest Frequency	-1029.7
Nucleus	1H
Acquired Size	24000
Spectral Size	65536

Parameter	Value
Data File Name	/ Users/ jeffkerkovius/ Documents/ NMR Files/ JKK1-260-B/ CARBON01.fid/ fid
Title	CARBON01
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	3.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	512
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	4.8375
Acquisition Time	1.0420
Acquisition Date	2019-05-01T00:24:53
Spectrometer Frequency	125.64
Spectral Width	31446.5
Lowest Frequency	-1907.6
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



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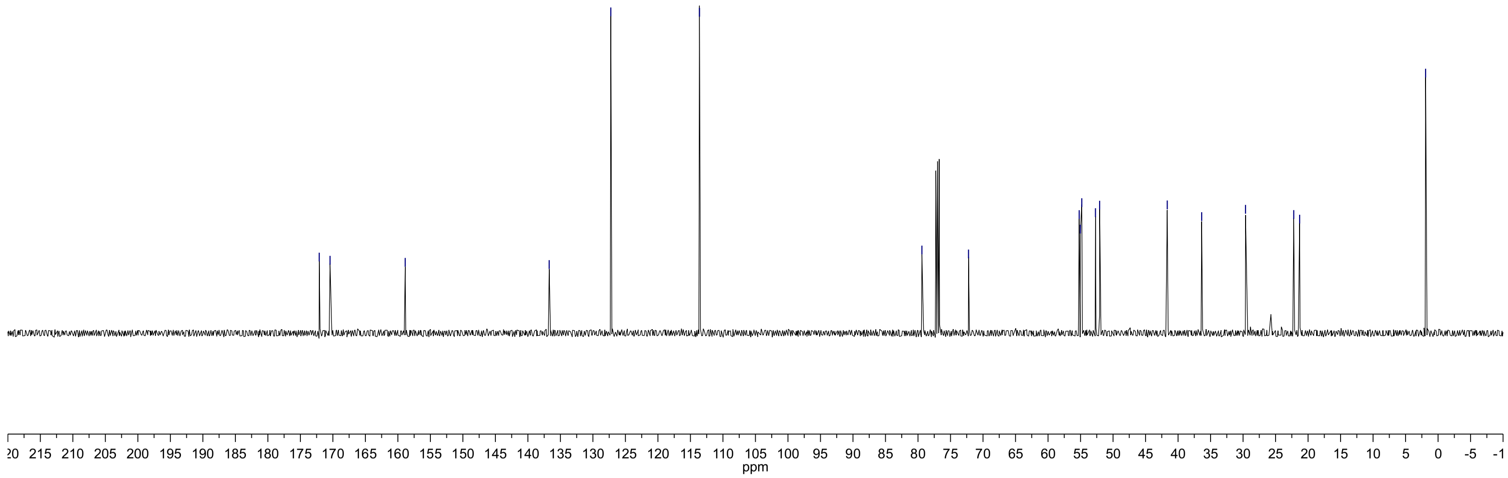
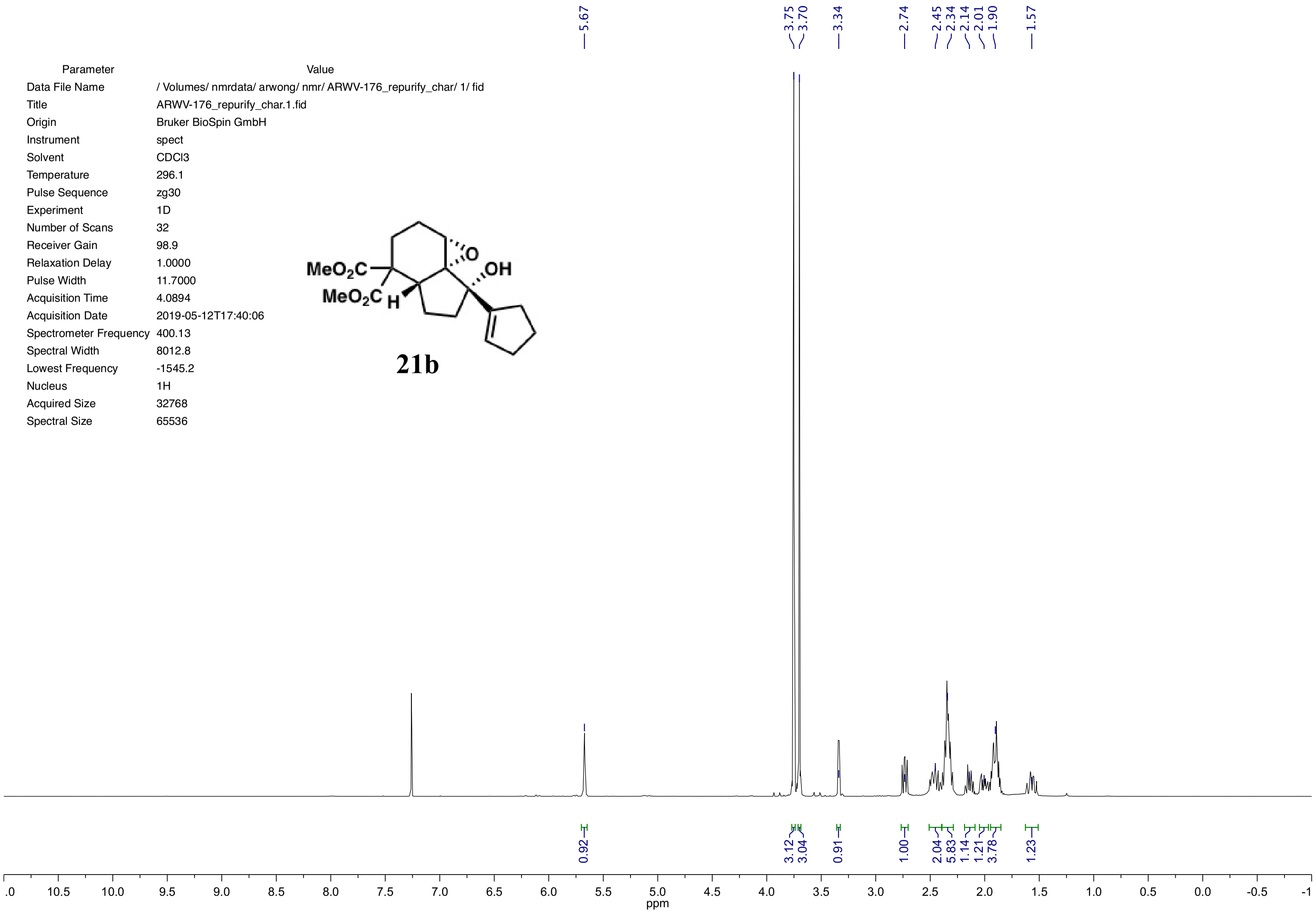
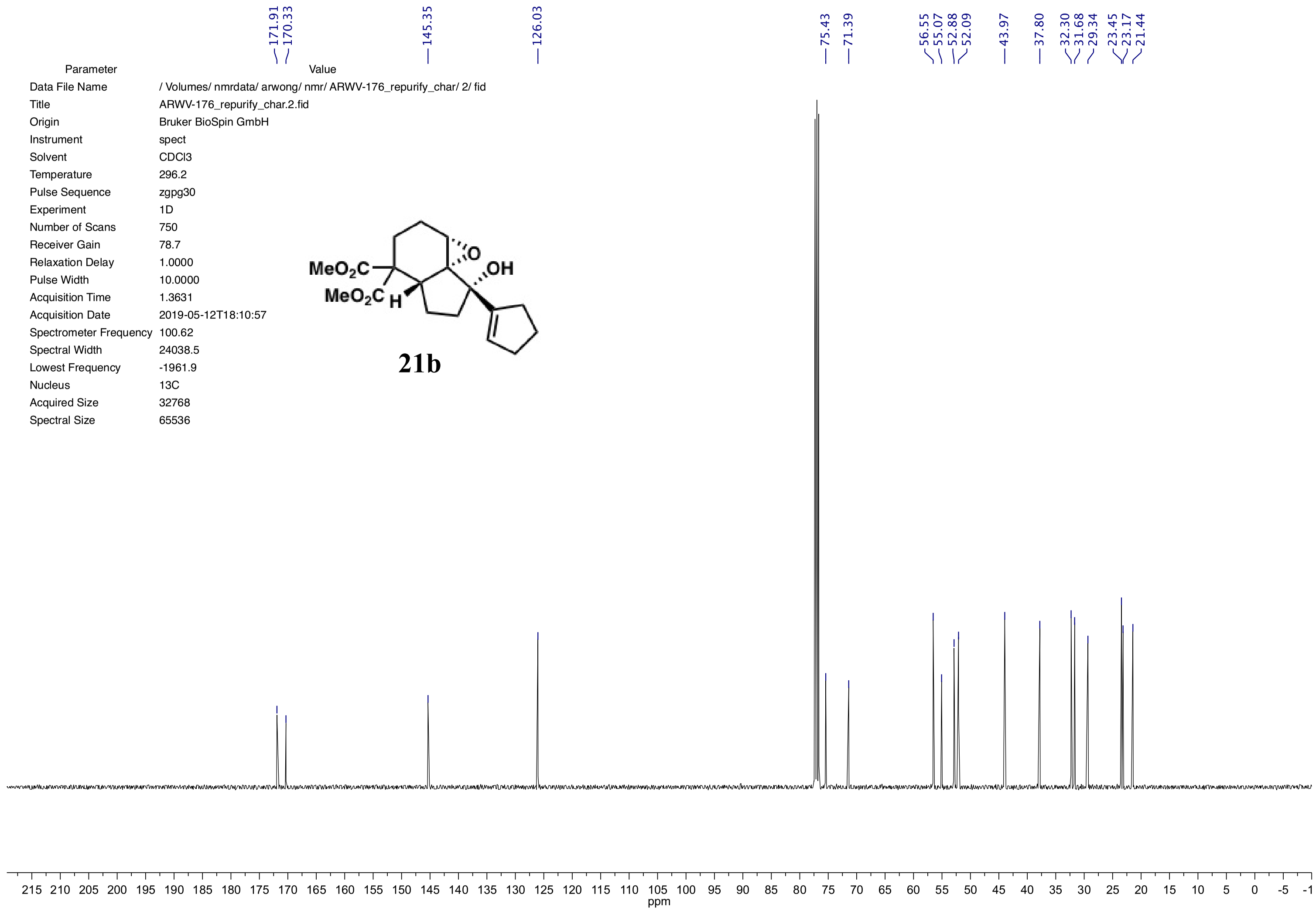


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWV-176_repurify_char/ 1/ fid
Title	ARWV-176_repurify_char.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	296.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	98.9
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2019-05-12T17:40:06
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.2
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



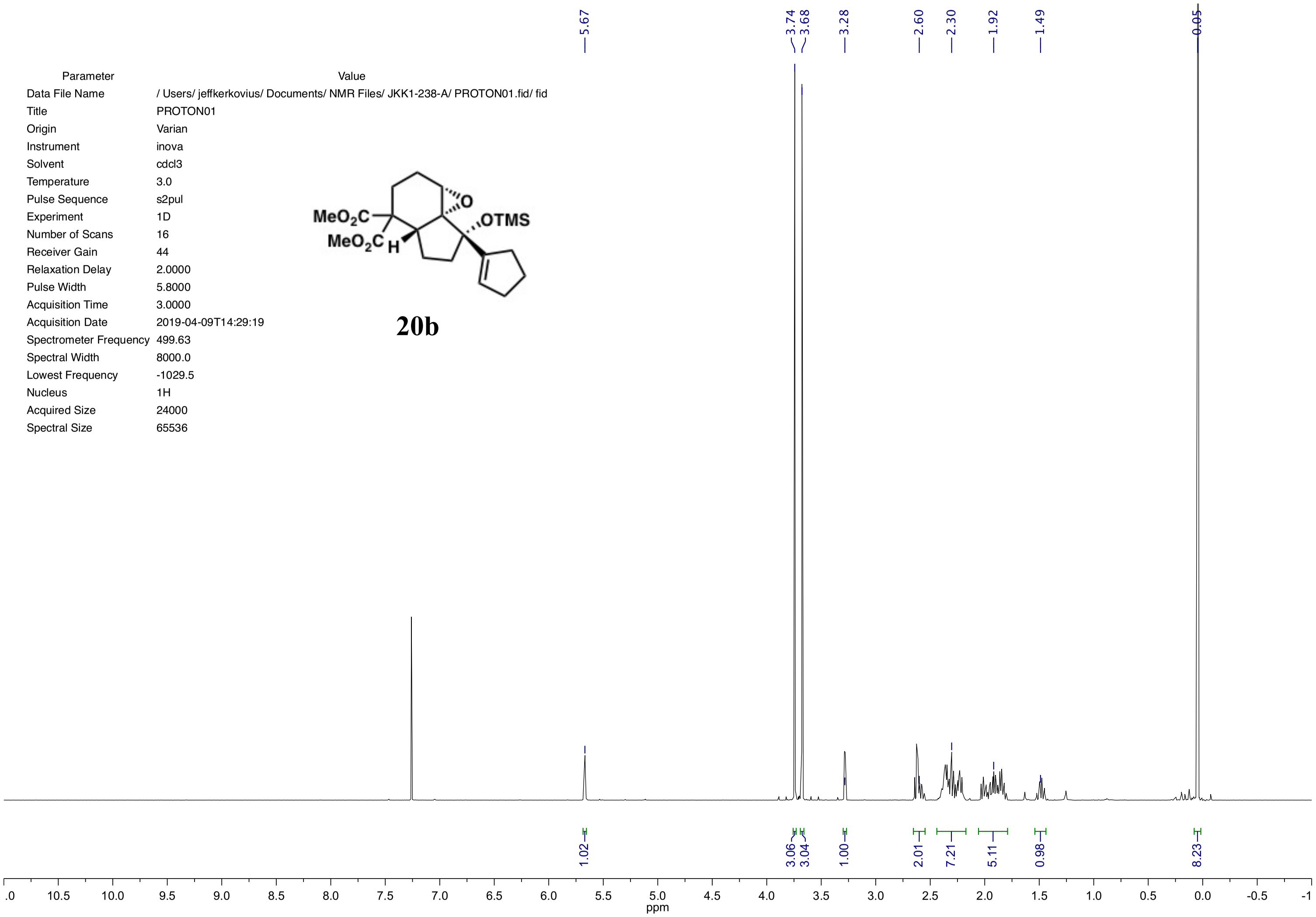
21b



21b

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWV-176_repurify_char/ 2/ fid
Title	ARWV-176_repurify_char.2.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	296.2
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	750
Receiver Gain	78.7
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2019-05-12T18:10:57
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.9
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Data File Name	/ Users/ jeffkerkovius/ Documents/ NMR Files/ JKK1-238-A/ PROTON01.fid/ fid
Title	PROTON01
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	3.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	16
Receiver Gain	44
Relaxation Delay	2.0000
Pulse Width	5.8000
Acquisition Time	3.0000
Acquisition Date	2019-04-09T14:29:19
Spectrometer Frequency	499.63
Spectral Width	8000.0
Lowest Frequency	-1029.5
Nucleus	1H
Acquired Size	24000
Spectral Size	65536



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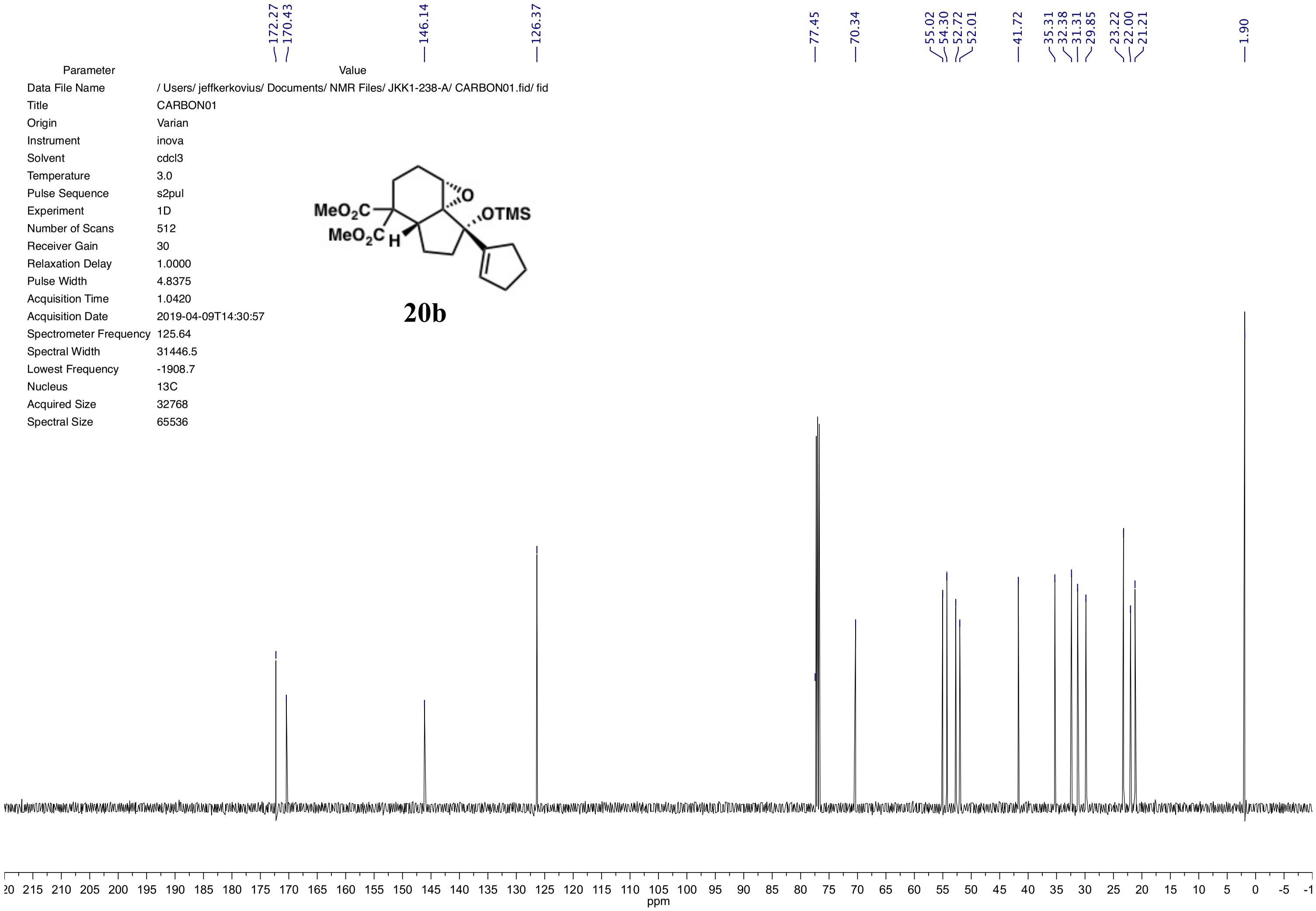
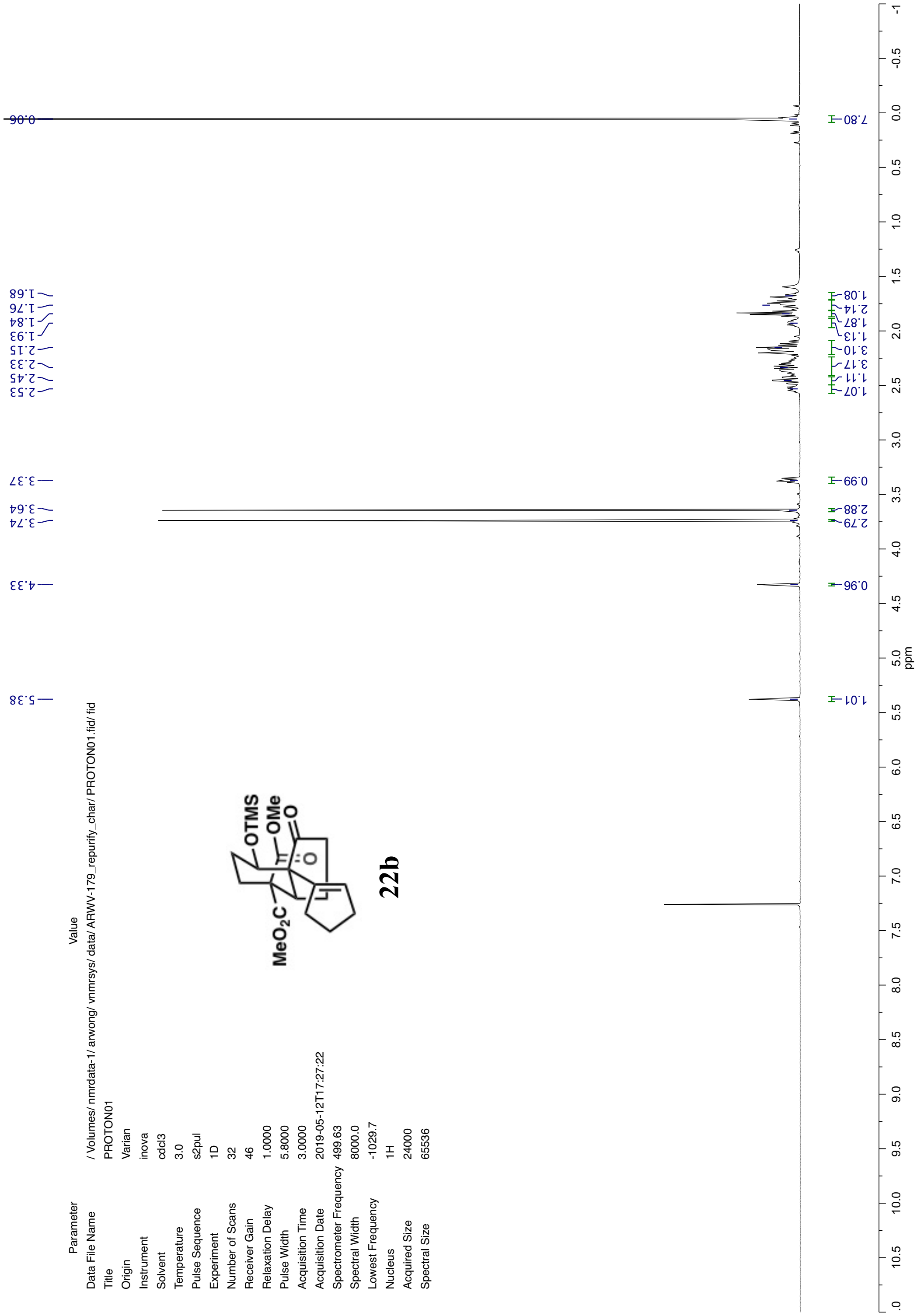


20b

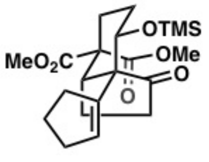
Parameter	Value
Data File Name	/ Users/ jeffkerkovius/ Documents/ NMR Files/ JKK1-238-A/ CARBON01.fid/ fid
Title	CARBON01
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	3.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	512
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	4.8375
Acquisition Time	1.0420
Acquisition Date	2019-04-09T14:30:57
Spectrometer Frequency	125.64
Spectral Width	31446.5
Lowest Frequency	-1908.7
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



22b

Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ arwong/ vnmrsys/ data/ ARWV-179_repurify_char/ PROTON01.fid/ fid
Title	PROTON01
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	3.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	32
Receiver Gain	46
Relaxation Delay	1.0000
Pulse Width	5.8000
Acquisition Time	3.0000
Acquisition Date	2019-05-12T17:27:22
Spectrometer Frequency	499.63
Spectral Width	8000.0
Lowest Frequency	-1029.7
Nucleus	1H
Acquired Size	24000
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ arwong/ vnmrsys/ data/ ARWV-179_repurify_char/ CARBON01.fid/ fid
Title	CARBON01
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	3.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	512
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	4.8375
Acquisition Time	1.0420
Acquisition Date	2019-05-12T17:29:48
Spectrometer Frequency	125.64
Spectral Width	31446.5
Lowest Frequency	-1911.2
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



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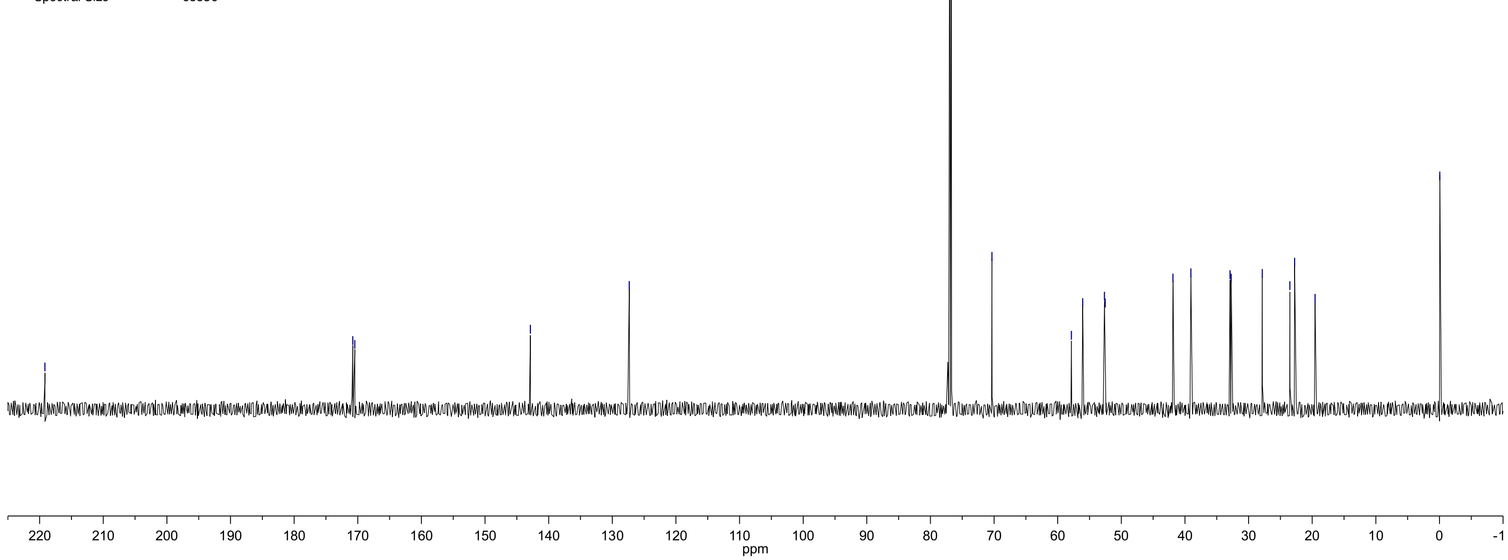
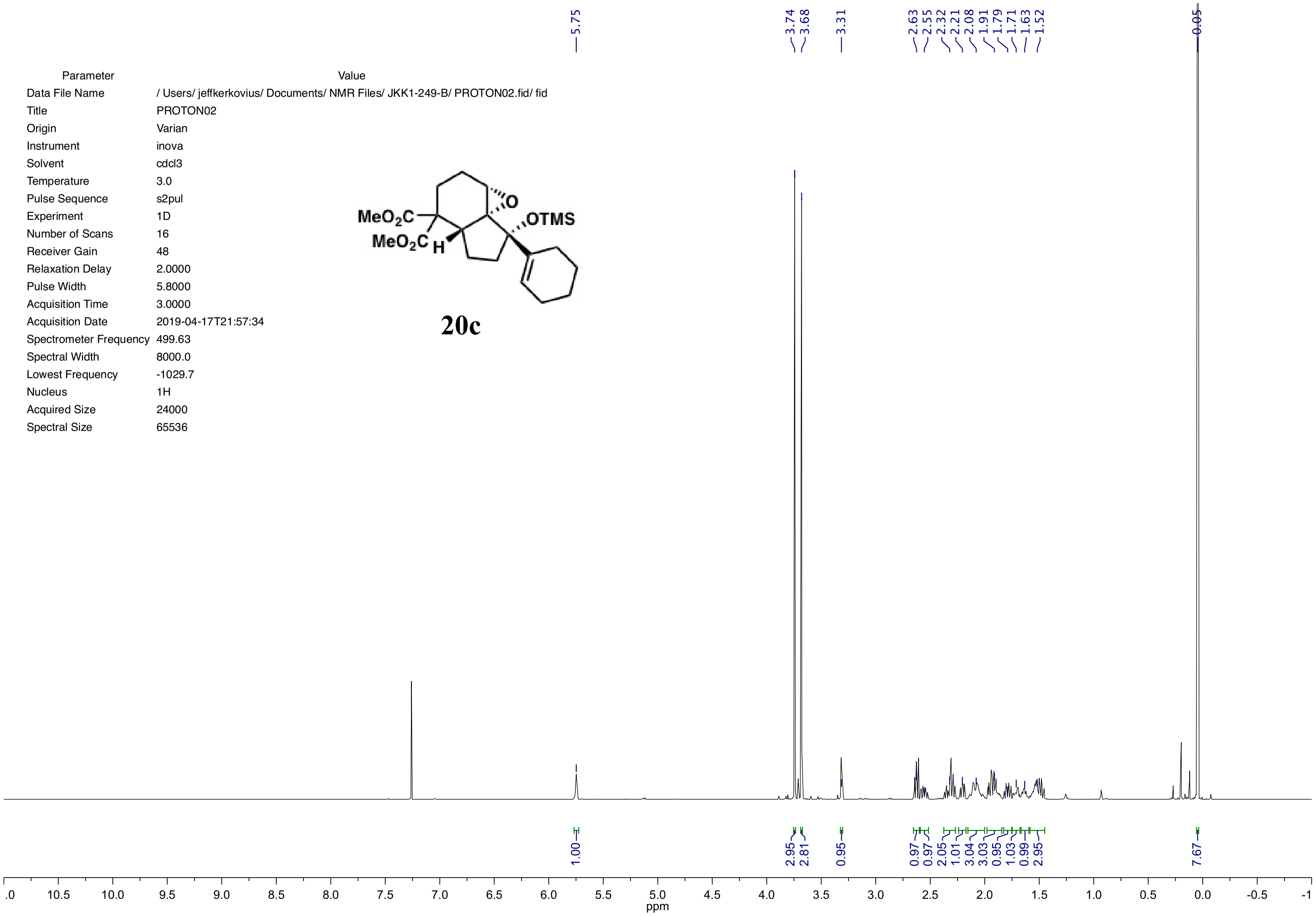
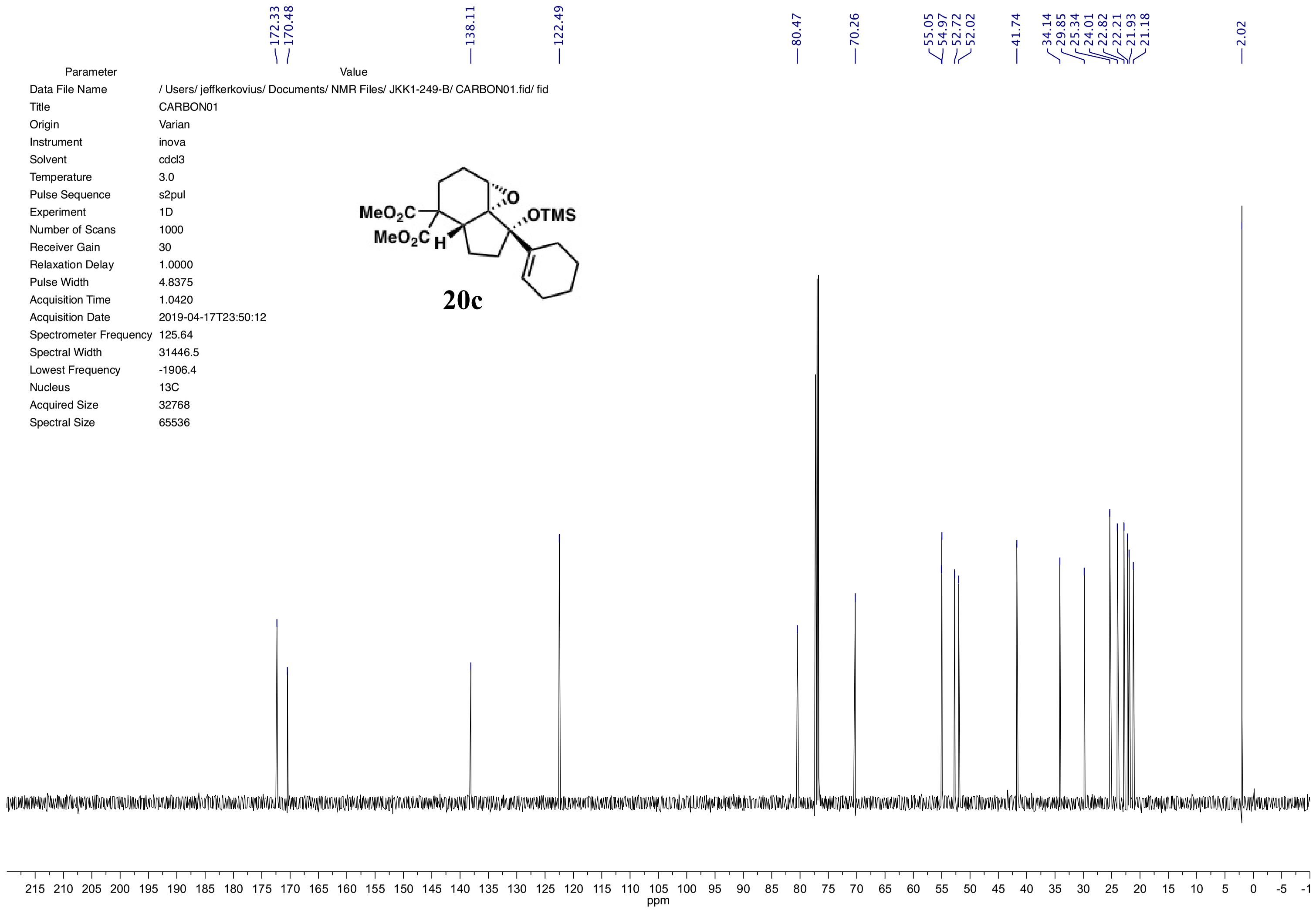


Parameter	Value
Data File Name	/ Users/ jeffkerkovius/ Documents/ NMR Files/ JKK1-249-B/ PROTON02.fid/ fid
Title	PROTON02
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	3.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	16
Receiver Gain	48
Relaxation Delay	2.0000
Pulse Width	5.8000
Acquisition Time	3.0000
Acquisition Date	2019-04-17T21:57:34
Spectrometer Frequency	499.63
Spectral Width	8000.0
Lowest Frequency	-1029.7
Nucleus	1H
Acquired Size	24000
Spectral Size	65536

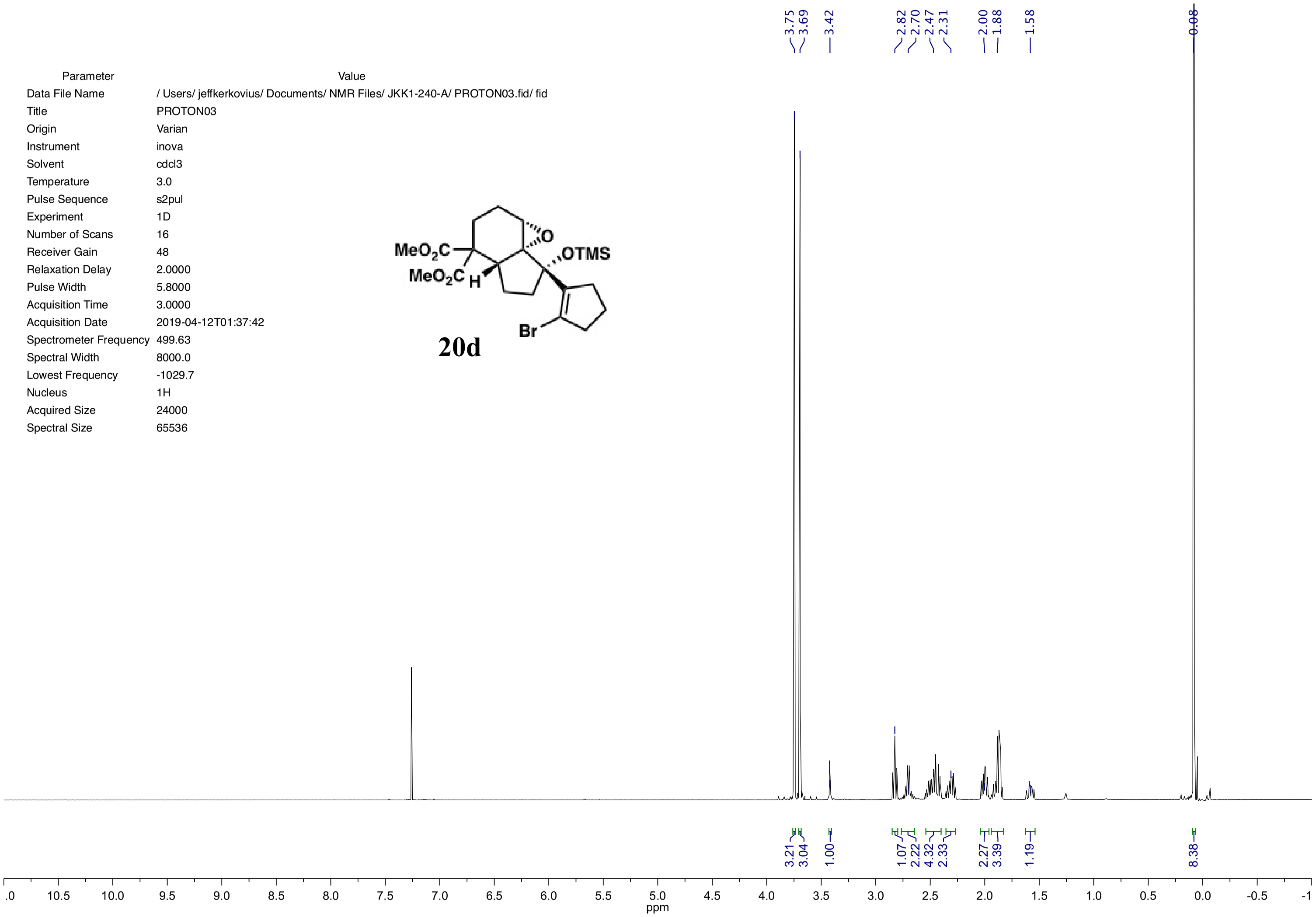


20c



20c

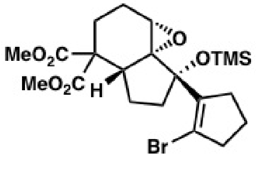
Parameter	Value
Data File Name	/ Users/ jeffkerkovius/ Documents/ NMR Files/ JKK1-249-B/ CARBON01.fid/ fid
Title	CARBON01
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	3.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	1000
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	4.8375
Acquisition Time	1.0420
Acquisition Date	2019-04-17T23:50:12
Spectrometer Frequency	125.64
Spectral Width	31446.5
Lowest Frequency	-1906.4
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



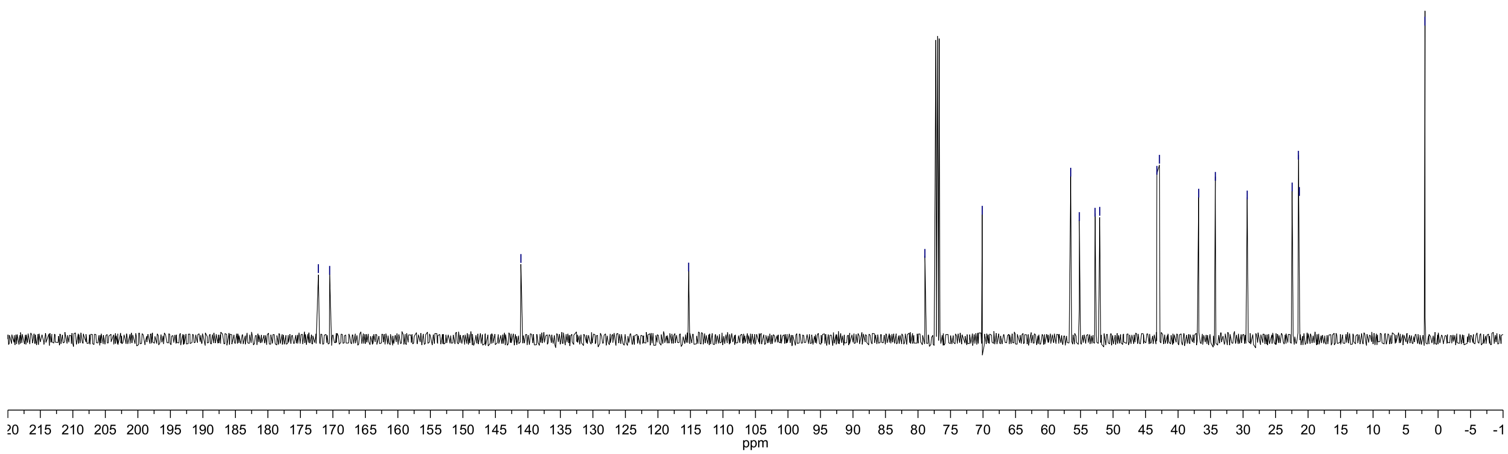
20d

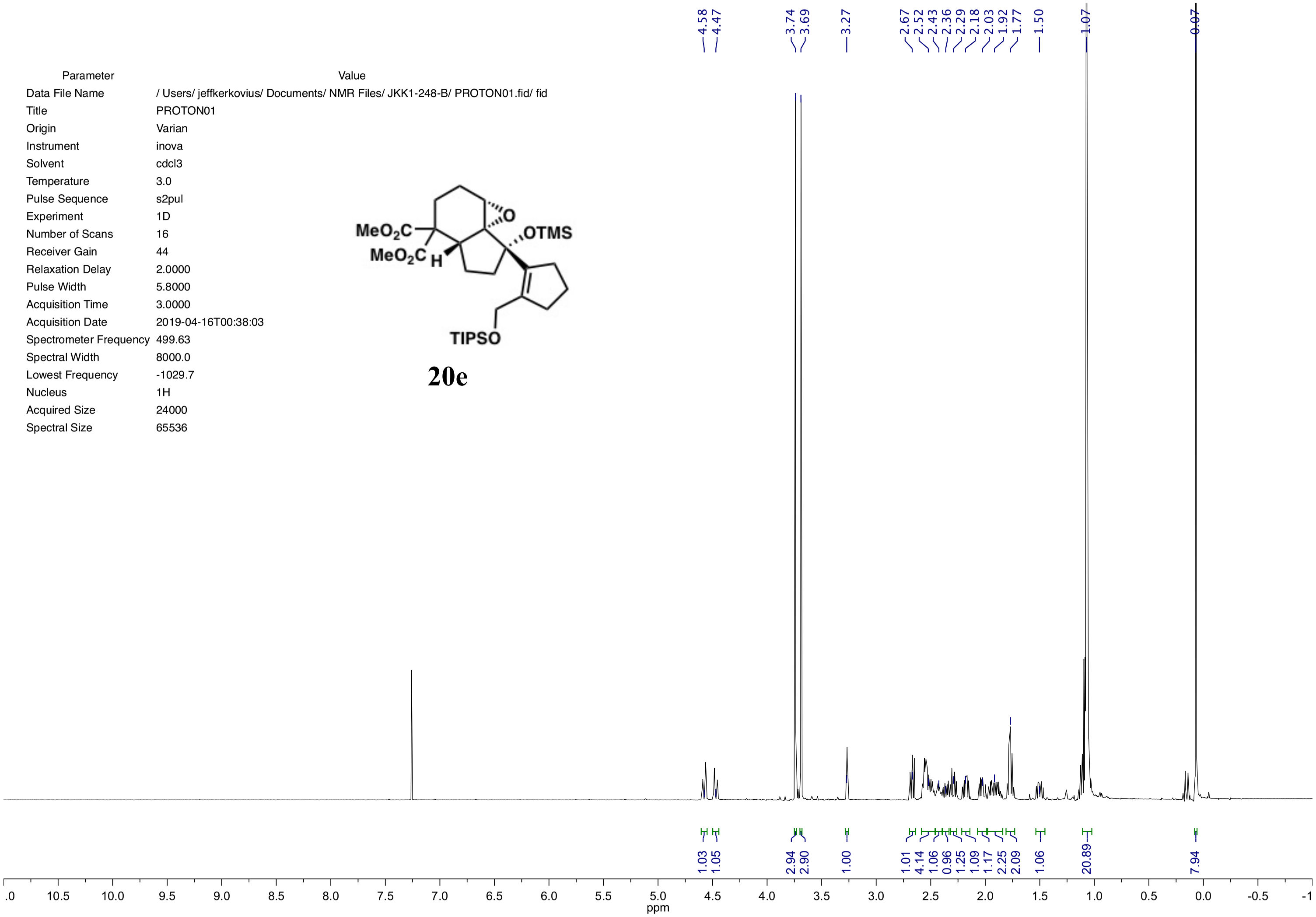
Parameter	Value
Data File Name	/ Users/ jeffkerkovius/ Documents/ NMR Files/ JKK1-240-A/ PROTON03.fid/ fid
Title	PROTON03
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	3.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	16
Receiver Gain	48
Relaxation Delay	2.0000
Pulse Width	5.8000
Acquisition Time	3.0000
Acquisition Date	2019-04-12T01:37:42
Spectrometer Frequency	499.63
Spectral Width	8000.0
Lowest Frequency	-1029.7
Nucleus	1H
Acquired Size	24000
Spectral Size	65536

Parameter	Value
Data File Name	/ Users/ jeffkerkovius/ Documents/ NMR Files/ JKK1-240-A/ CARBON02.fid/ fid
Title	CARBON02
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	3.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	512
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	4.8375
Acquisition Time	1.0420
Acquisition Date	2019-04-12T01:39:20
Spectrometer Frequency	125.64
Spectral Width	31446.5
Lowest Frequency	-1906.8
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



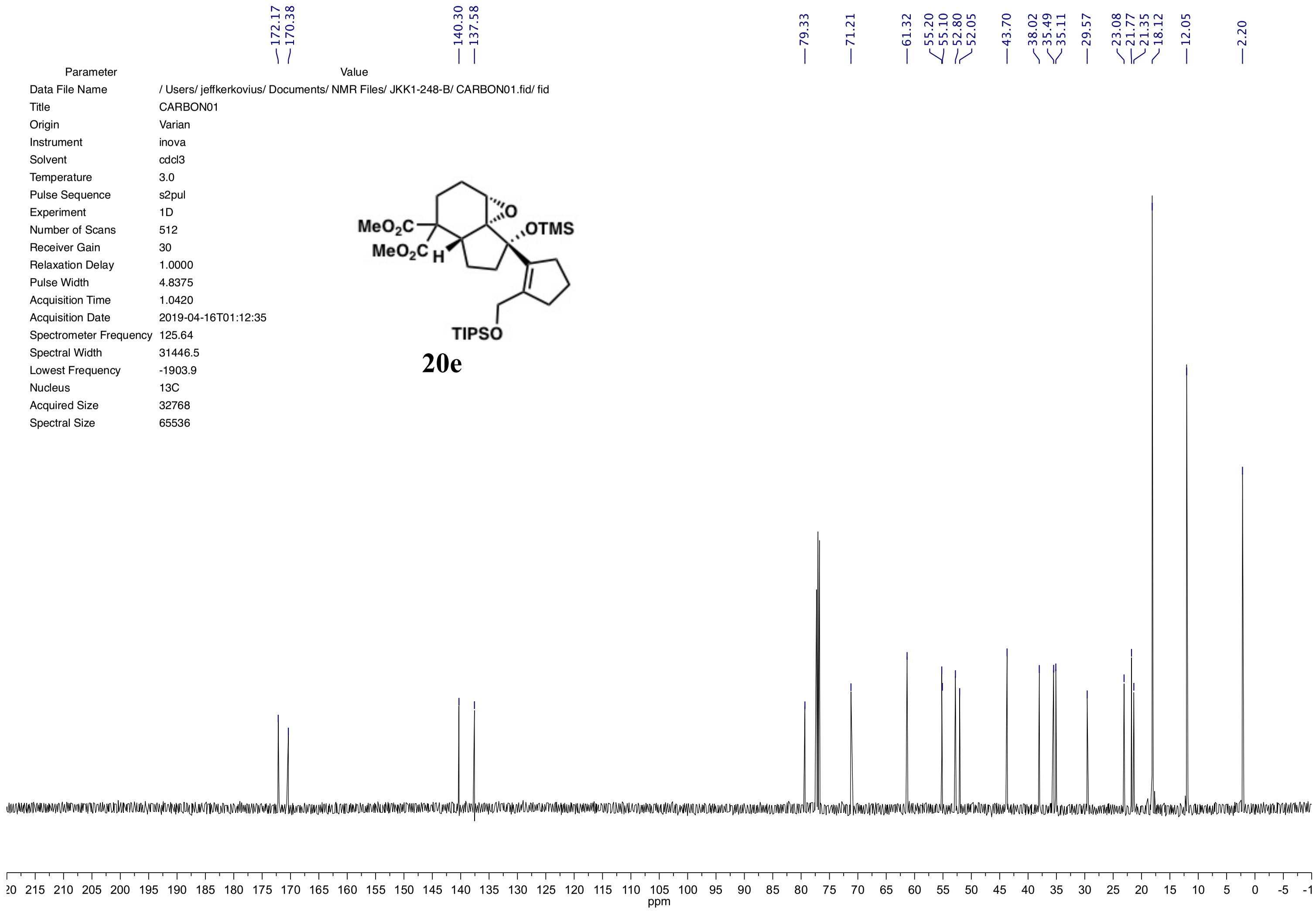
20d





Parameter	Value
Data File Name	/ Users/ jeffkerkovius/ Documents/ NMR Files/ JKK1-248-B/ PROTON01.fid/ fid
Title	PROTON01
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	3.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	16
Receiver Gain	44
Relaxation Delay	2.0000
Pulse Width	5.8000
Acquisition Time	3.0000
Acquisition Date	2019-04-16T00:38:03
Spectrometer Frequency	499.63
Spectral Width	8000.0
Lowest Frequency	-1029.7
Nucleus	1H
Acquired Size	24000
Spectral Size	65536

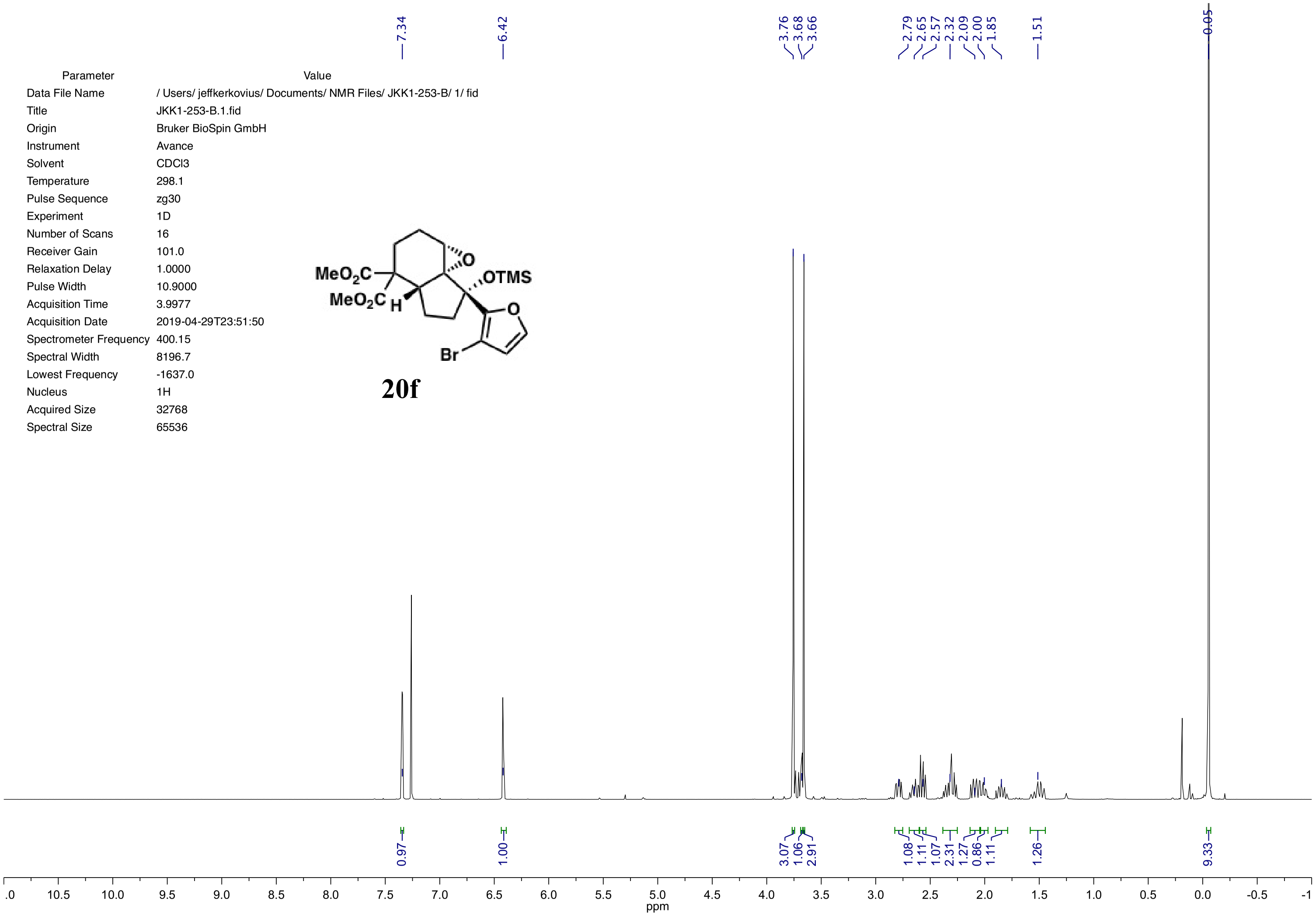
20e



20e

Parameter	Value
Data File Name	/ Users/ jeffkerkovius/ Documents/ NMR Files/ JKK1-248-B/ CARBON01.fid/ fid
Title	CARBON01
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	3.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	512
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	4.8375
Acquisition Time	1.0420
Acquisition Date	2019-04-16T01:12:35
Spectrometer Frequency	125.64
Spectral Width	31446.5
Lowest Frequency	-1903.9
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Data File Name	/ Users/ jeffkerkovius/ Documents/ NMR Files/ JKK1-253-B/ 1/ fid
Title	JKK1-253-B.1.fid
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	16
Receiver Gain	101.0
Relaxation Delay	1.0000
Pulse Width	10.9000
Acquisition Time	3.9977
Acquisition Date	2019-04-29T23:51:50
Spectrometer Frequency	400.15
Spectral Width	8196.7
Lowest Frequency	-1637.0
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



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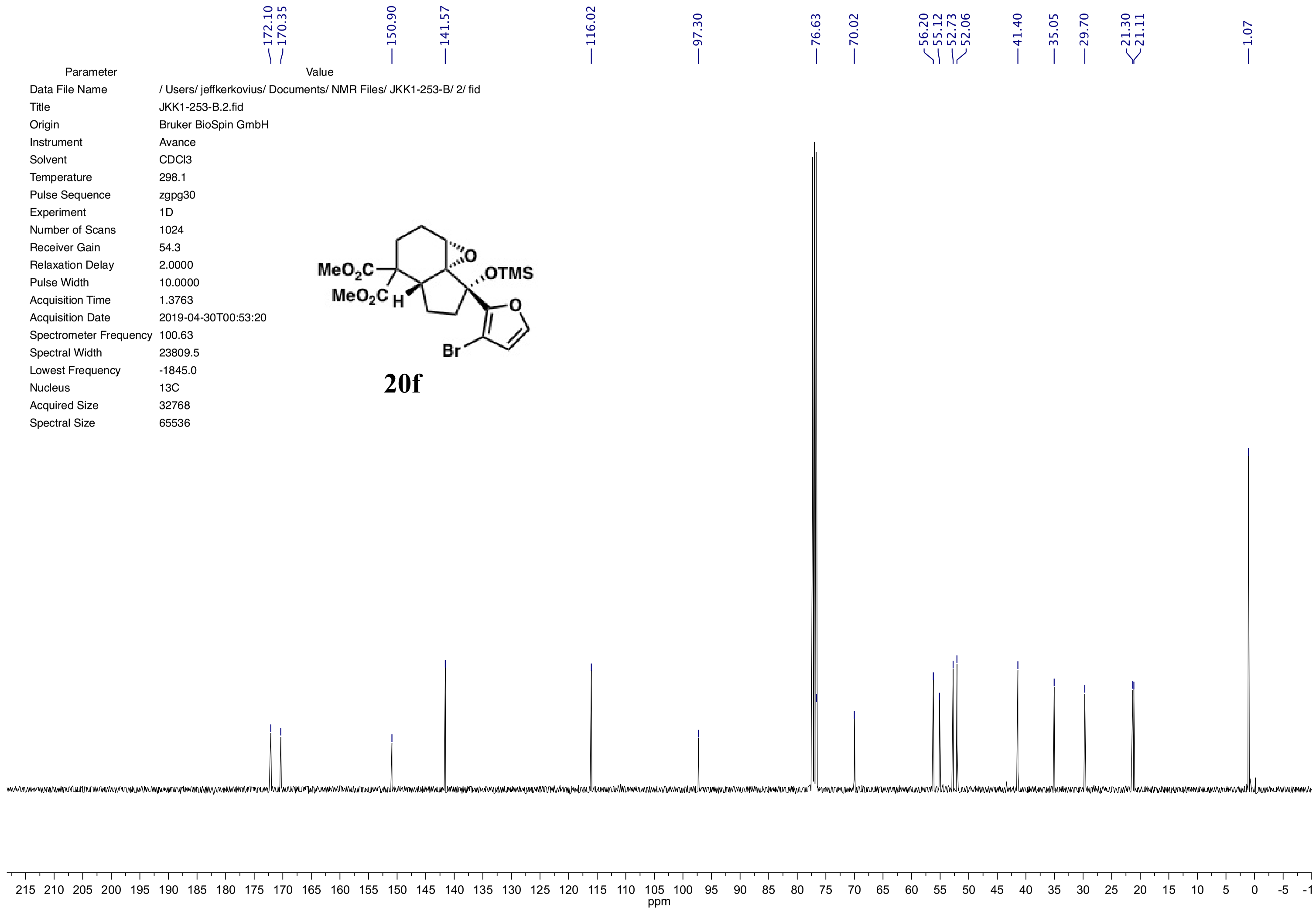
Parameter	Value
Data File Name	/ Users/ jeffkerkovius/ Documents/ NMR Files/ JKK1-253-B/ 2/ fid
Title	JKK1-253-B.2.fid
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298.1
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1024
Receiver Gain	54.3
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.3763
Acquisition Date	2019-04-30T00:53:20
Spectrometer Frequency	100.63
Spectral Width	23809.5
Lowest Frequency	-1845.0
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



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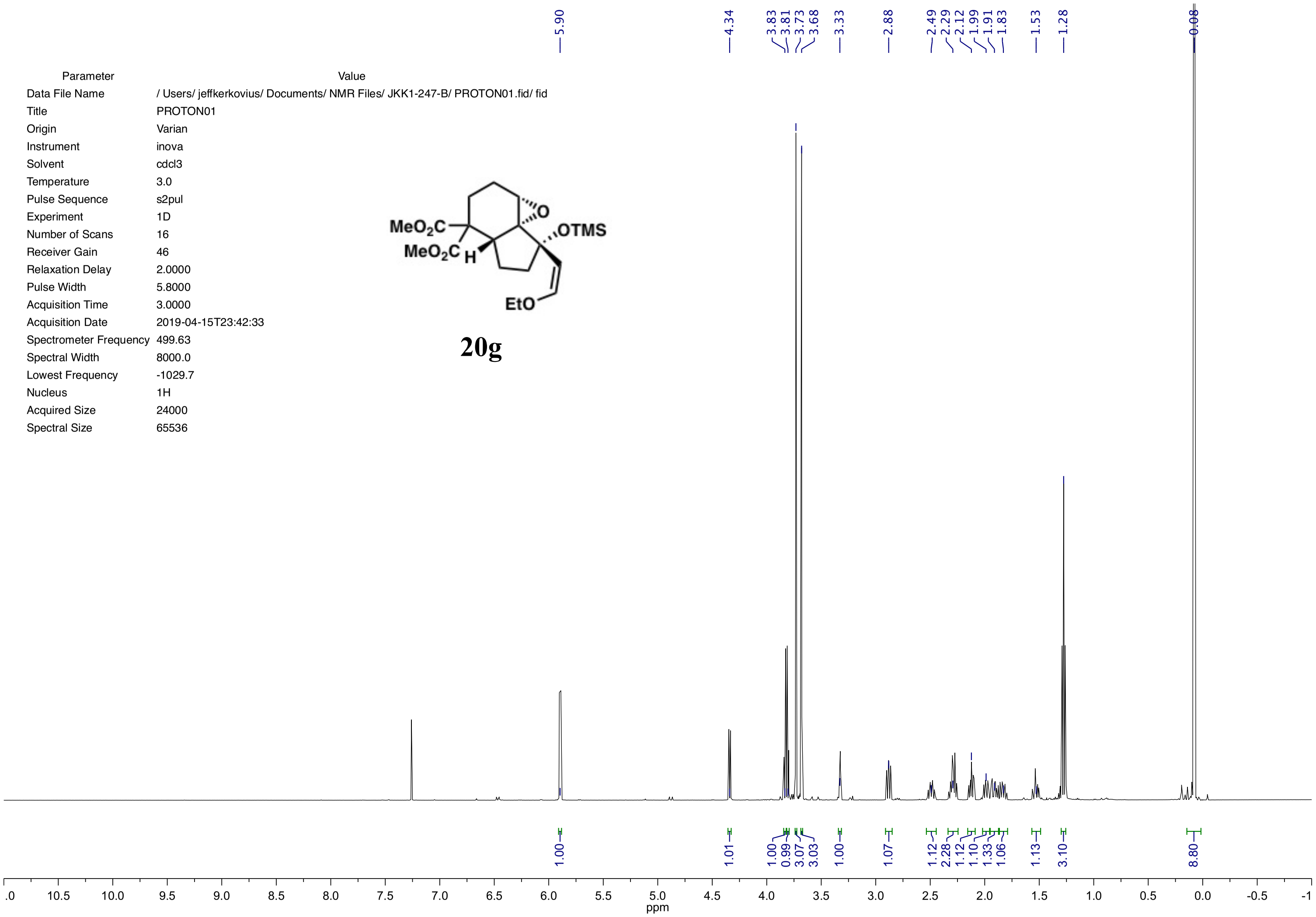
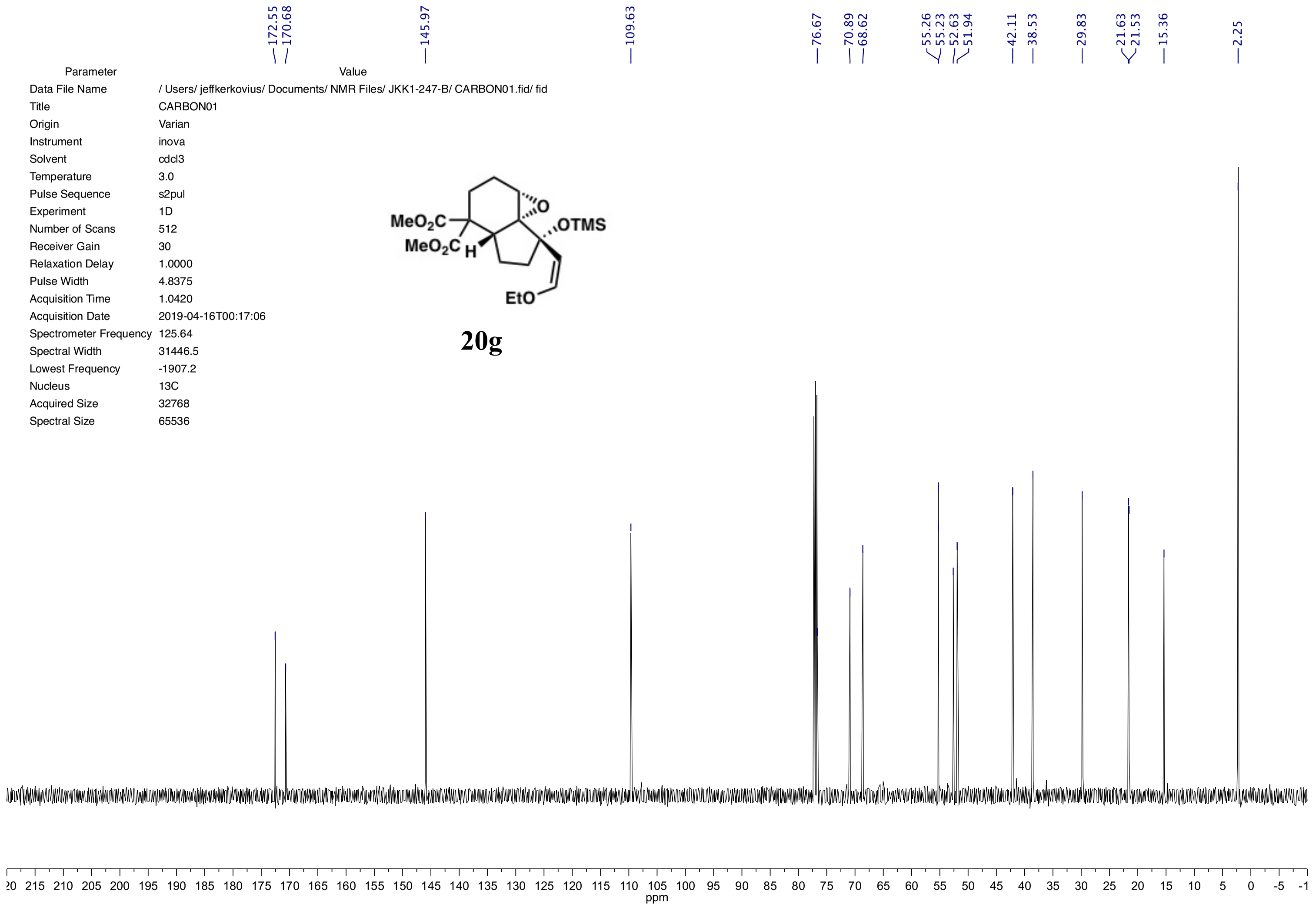


20g

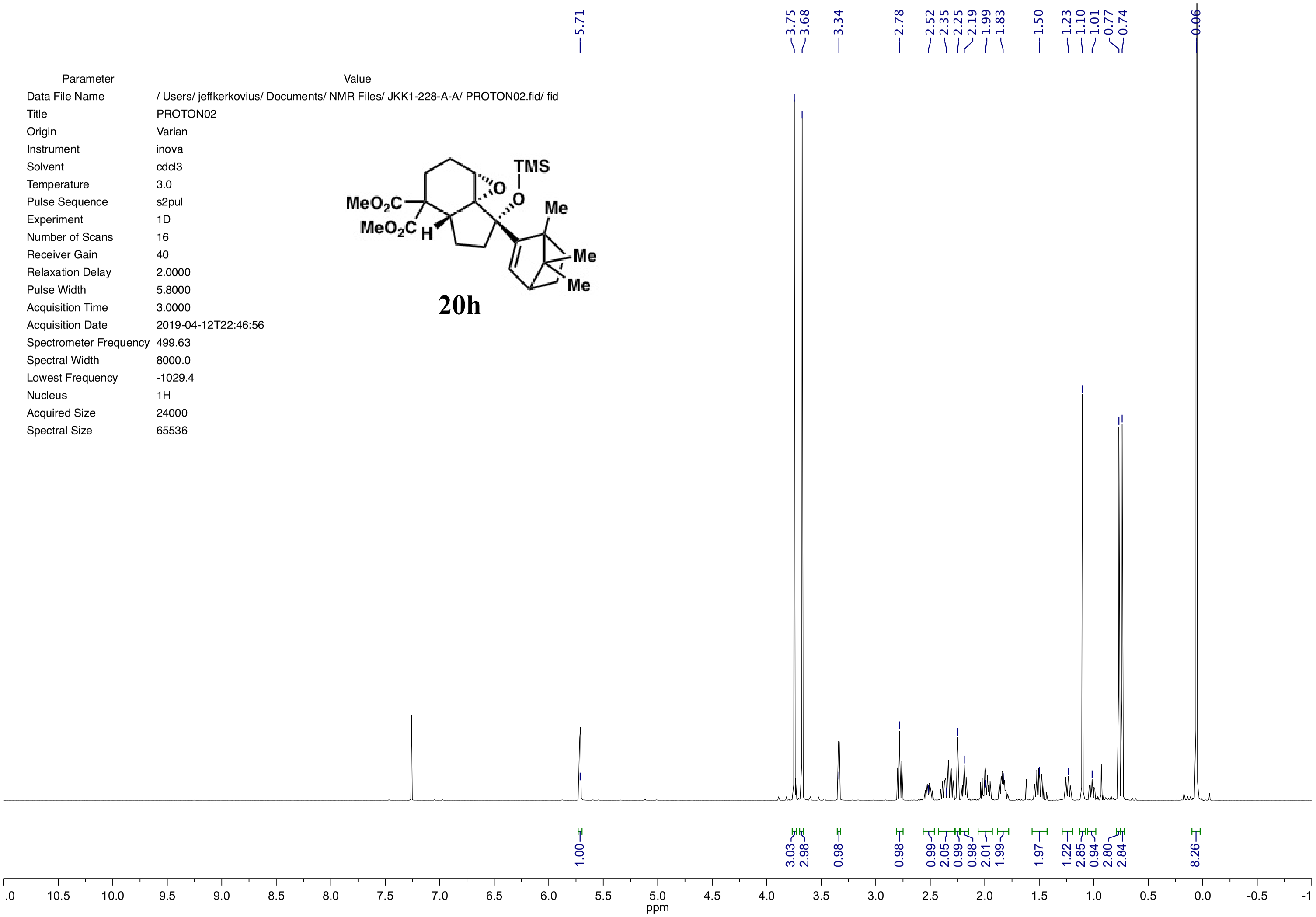
Parameter	Value
Data File Name	/ Users/ jeffkerkovius/ Documents/ NMR Files/ JKK1-247-B/ PROTON01.fid/ fid
Title	PROTON01
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	3.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	16
Receiver Gain	46
Relaxation Delay	2.0000
Pulse Width	5.8000
Acquisition Time	3.0000
Acquisition Date	2019-04-15T23:42:33
Spectrometer Frequency	499.63
Spectral Width	8000.0
Lowest Frequency	-1029.7
Nucleus	1H
Acquired Size	24000
Spectral Size	65536



Parameter	Value
Data File Name	/ Users/ jeffkerkovius/ Documents/ NMR Files/ JKK1-247-B/ CARBON01.fid/ fid
Title	CARBON01
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	3.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	512
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	4.8375
Acquisition Time	1.0420
Acquisition Date	2019-04-16T00:17:06
Spectrometer Frequency	125.64
Spectral Width	31446.5
Lowest Frequency	-1907.2
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

20g

Parameter	Value
Data File Name	/ Users/ jeffkerkovius/ Documents/ NMR Files/ JKK1-228-A-A/ PROTON02.fid/ fid
Title	PROTON02
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	3.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	16
Receiver Gain	40
Relaxation Delay	2.0000
Pulse Width	5.8000
Acquisition Time	3.0000
Acquisition Date	2019-04-12T22:46:56
Spectrometer Frequency	499.63
Spectral Width	8000.0
Lowest Frequency	-1029.4
Nucleus	1H
Acquired Size	24000
Spectral Size	65536



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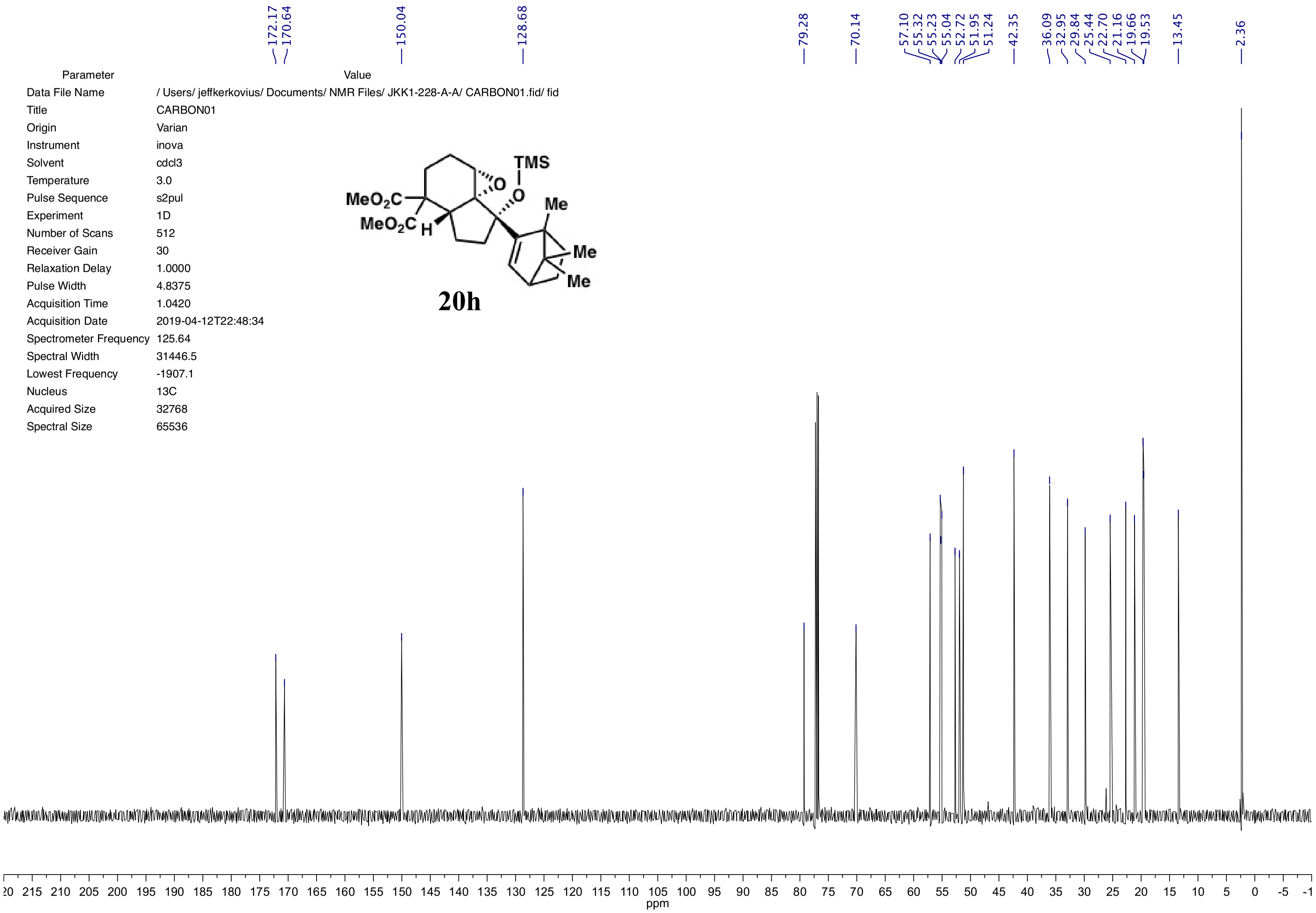

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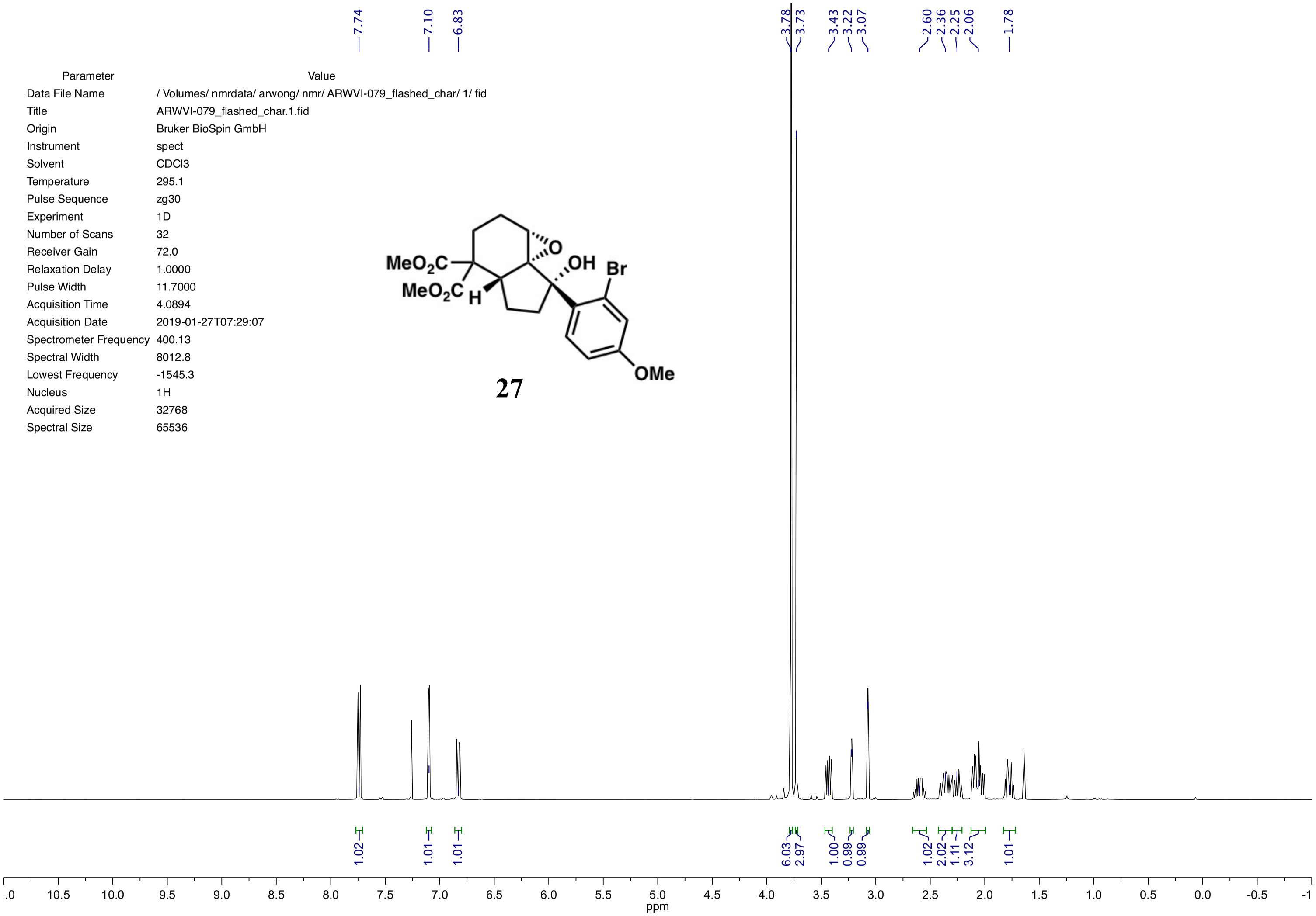
Parameter	Value
Data File Name	/ Users/ jeffkerkovius/ Documents/ NMR Files/ JKK1-228-A-A/ CARBON01.fid/ fid
Title	CARBON01
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	3.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	512
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	4.8375
Acquisition Time	1.0420
Acquisition Date	2019-04-12T22:48:34
Spectrometer Frequency	125.64
Spectral Width	31446.5
Lowest Frequency	-1907.1
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-079_flashed_char/ 1/ fid
Title	ARWVI-079_flashed_char.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2019-01-27T07:29:07
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.3
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



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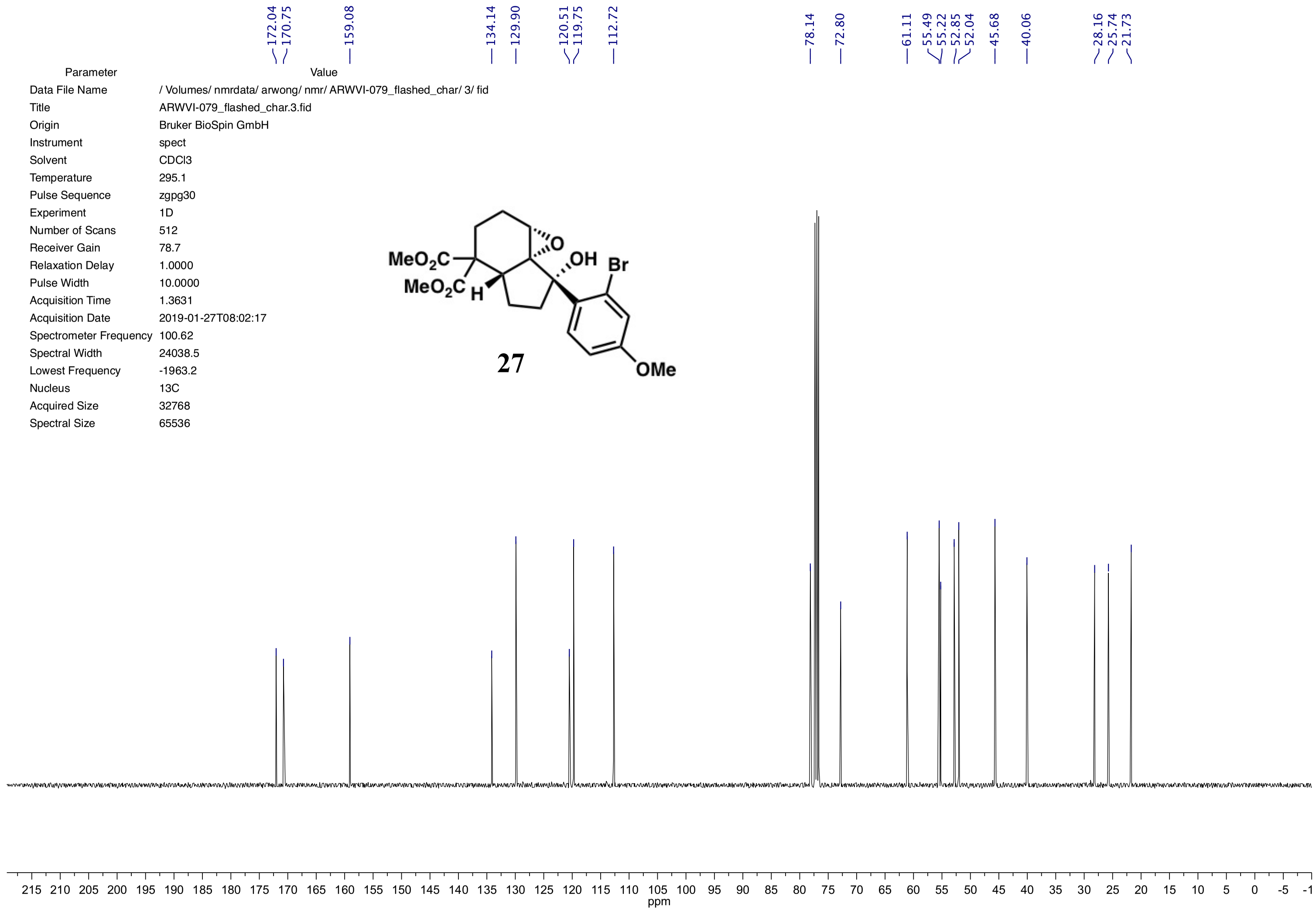
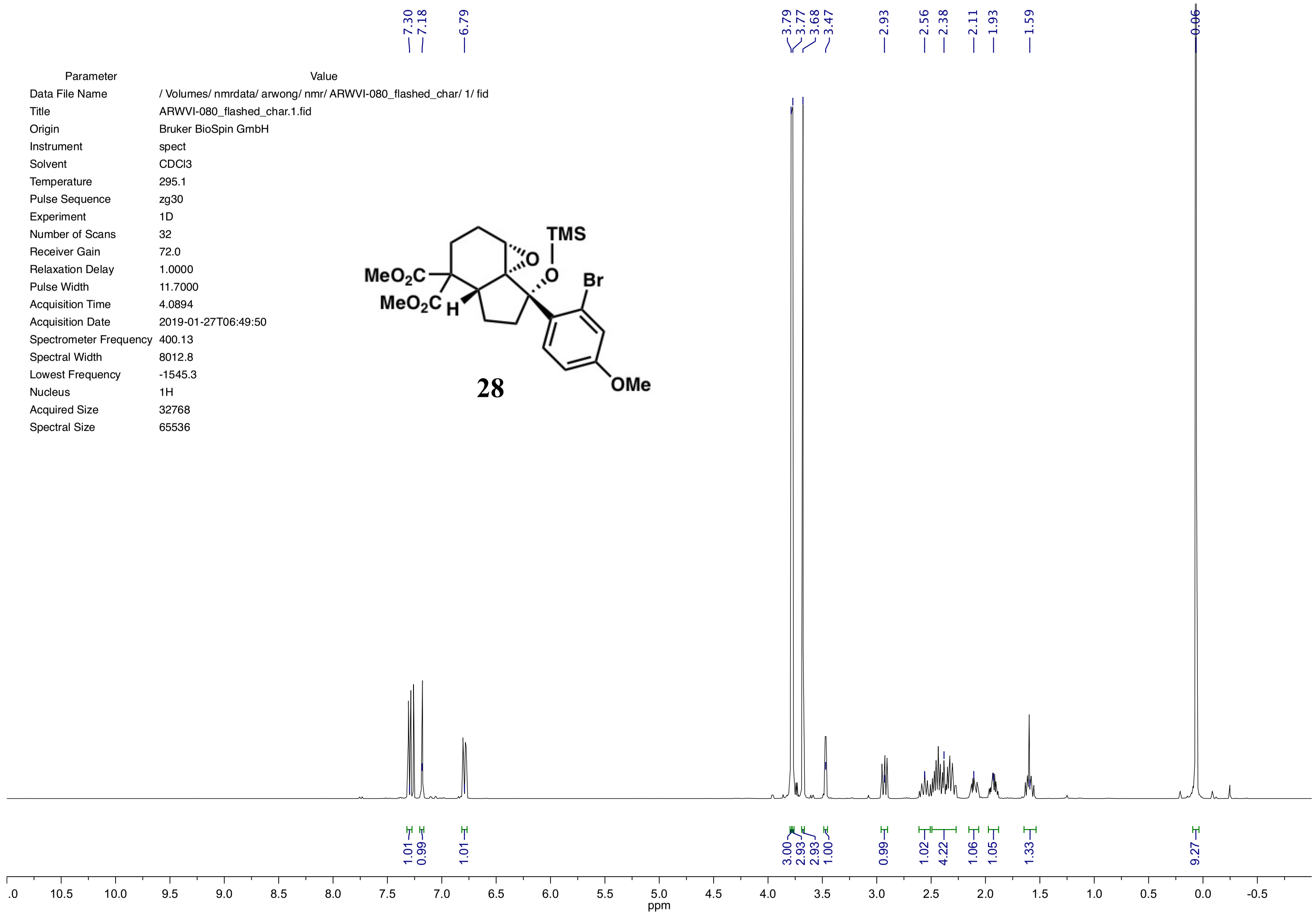


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-079_flashed_char/ 3/ fid
Title	ARWVI-079_flashed_char.3.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	512
Receiver Gain	78.7
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2019-01-27T08:02:17
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1963.2
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-080_flashed_char/ 1/ fid
Title	ARWVI-080_flashed_char.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2019-01-27T06:49:50
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.3
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



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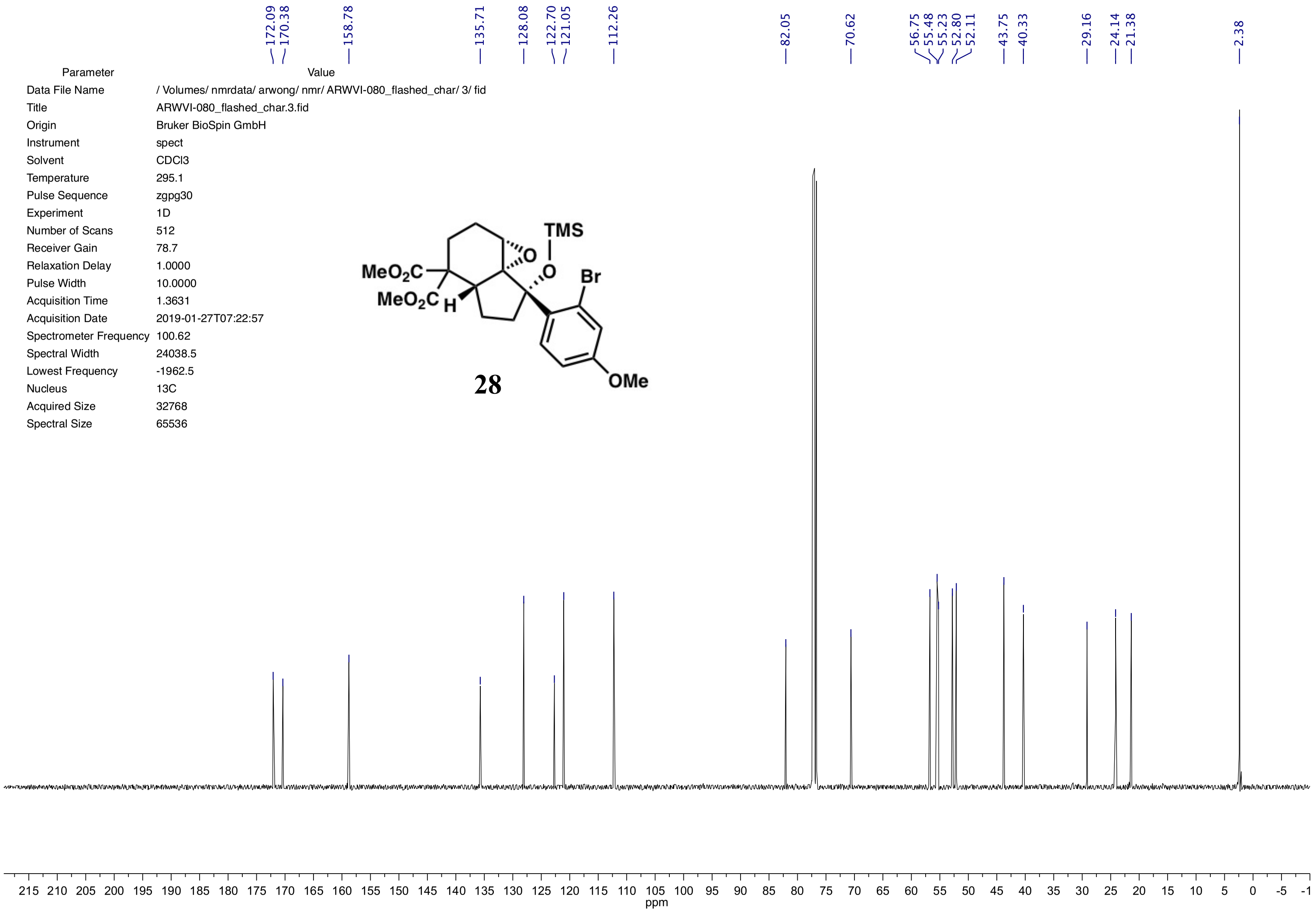
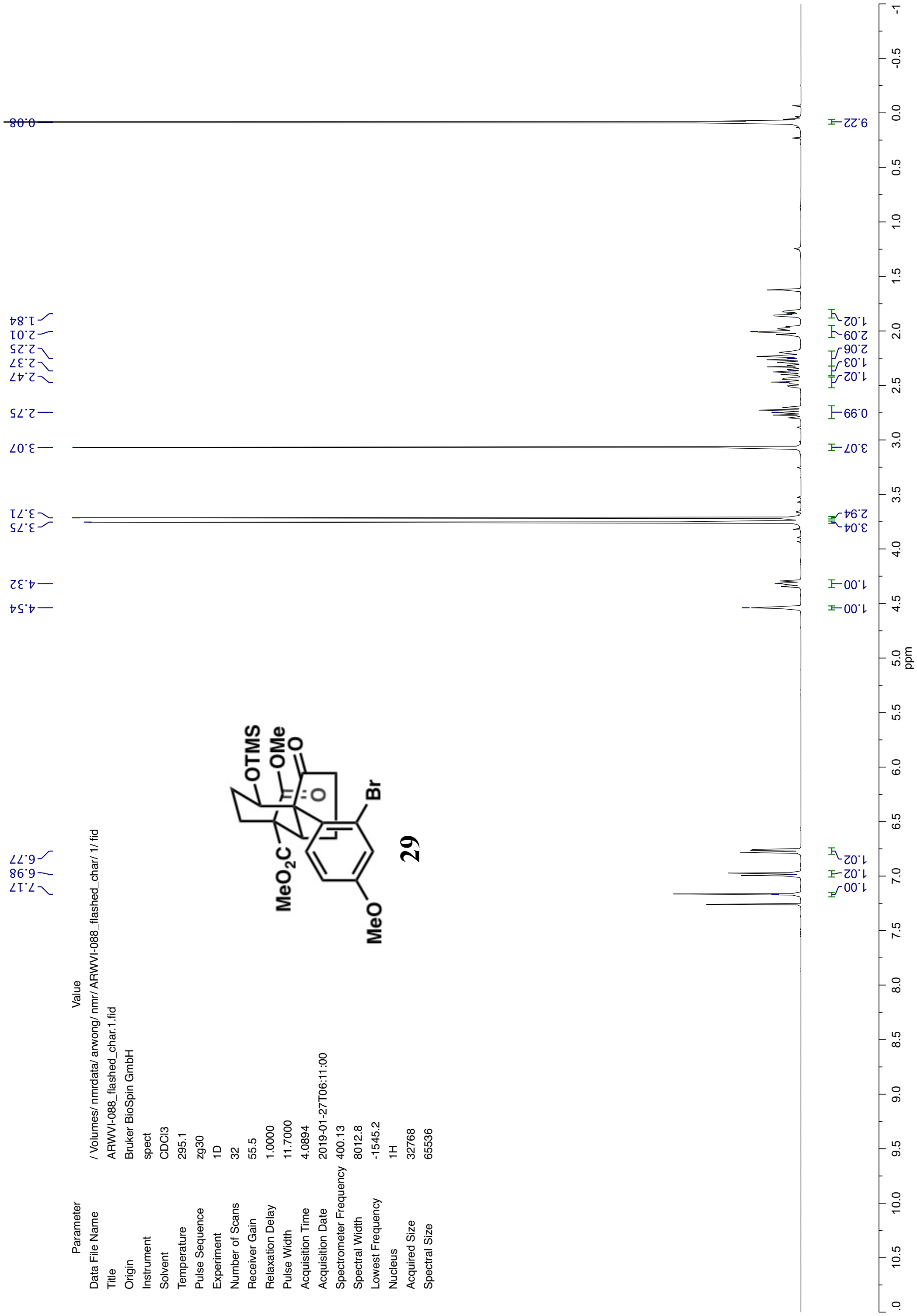


28

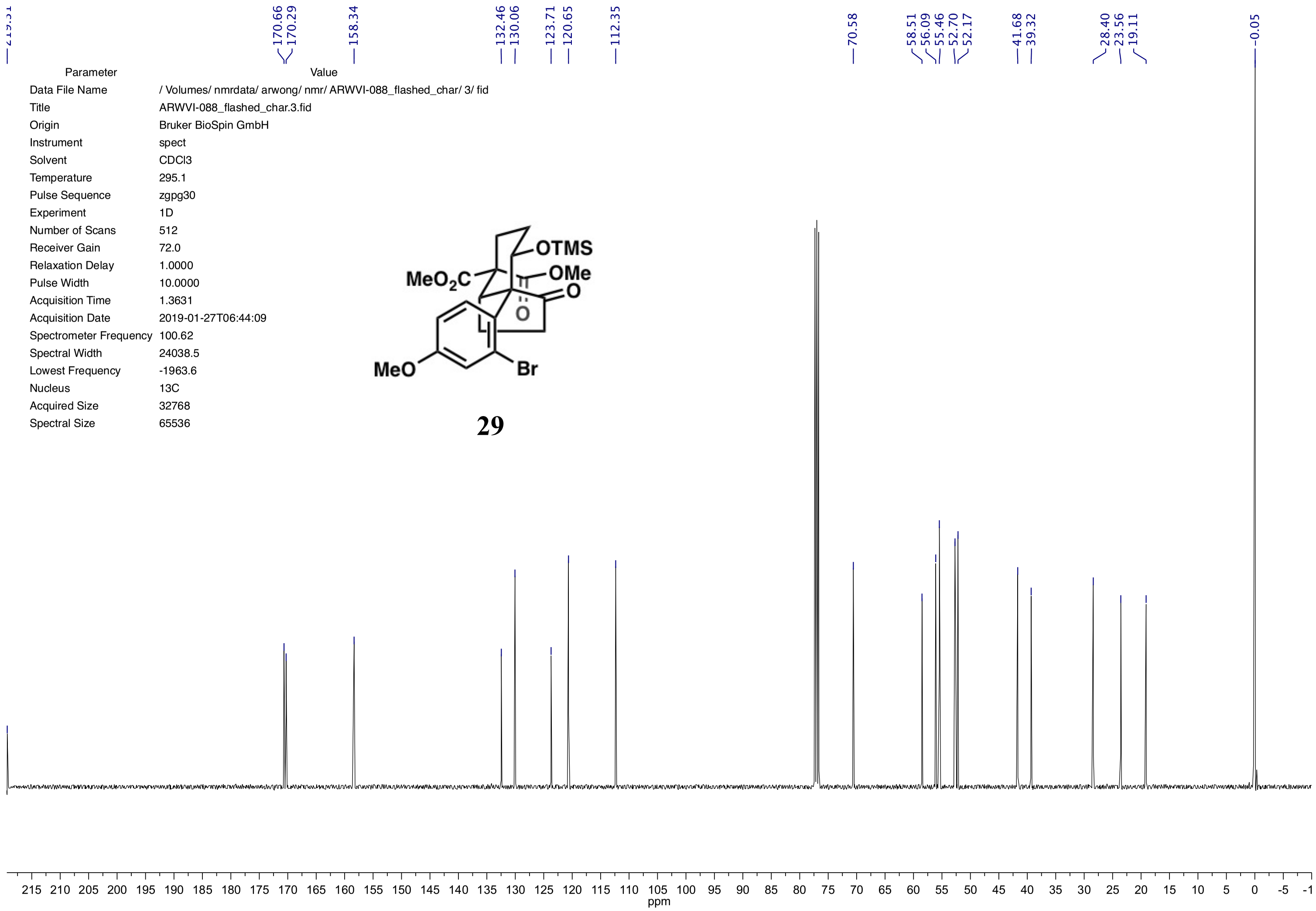
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-080_flashed_char/ 3/ fid
Title	ARWVI-080_flashed_char.3.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	512
Receiver Gain	78.7
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2019-01-27T07:22:57
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1962.5
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



MeO_2C

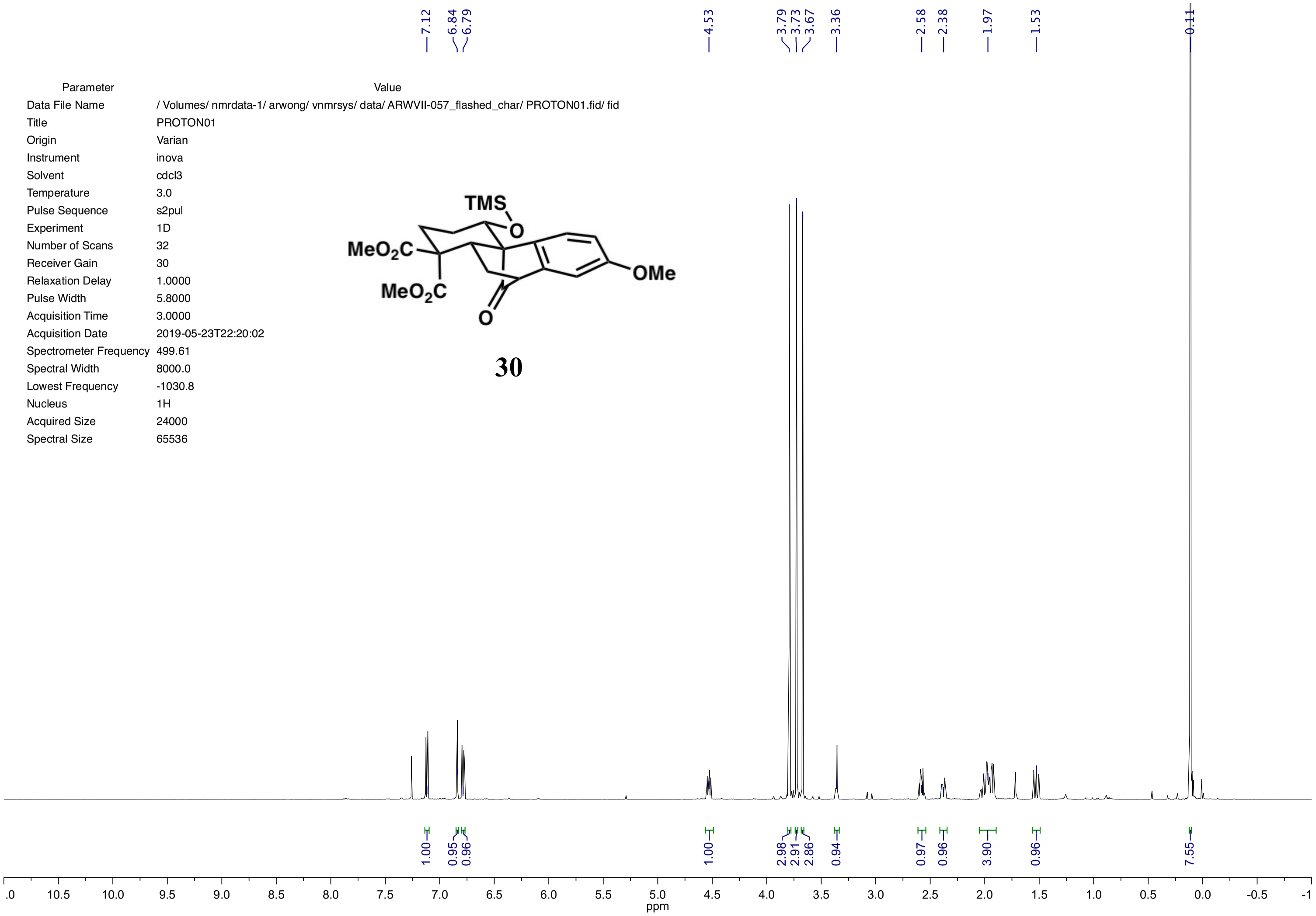
29

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-088_flashed_char/ 1/ fid
Title	ARWVI-088_flashed_char.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	55.5
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2019-01-27T06:11:00
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.2
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-088_flashed_char/ 3/ fid
Title	ARWVI-088_flashed_char.3.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
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	2019-01-27T06:44:09
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1963.6
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

29



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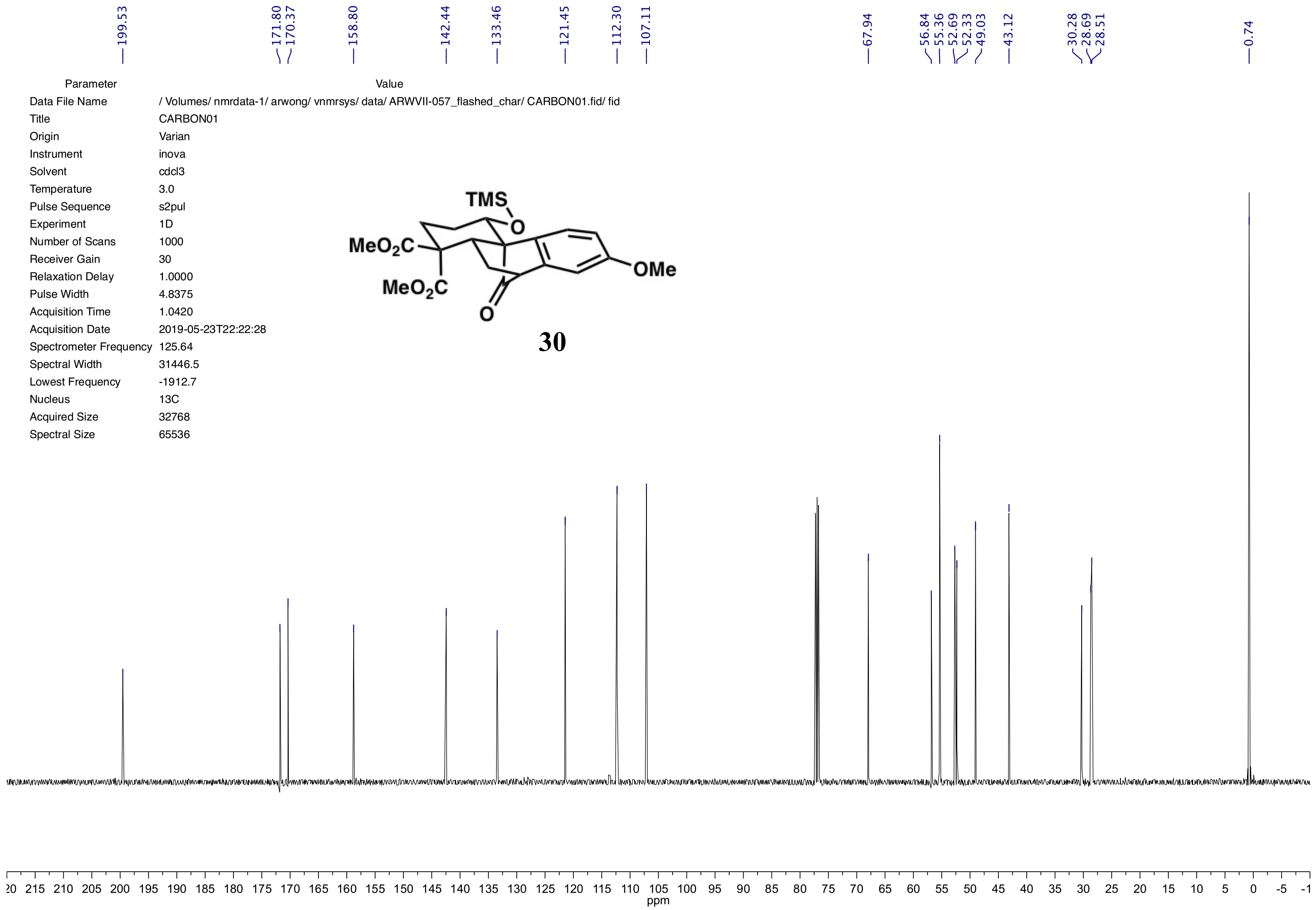
Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ arwong/ vnmrsys/ data/ ARWVII-057_flashed_char/ PROTON01.fid/ fid
Title	PROTON01
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	3.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	32
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	5.8000
Acquisition Time	3.0000
Acquisition Date	2019-05-23T22:20:02
Spectrometer Frequency	499.61
Spectral Width	8000.0
Lowest Frequency	-1030.8
Nucleus	1H
Acquired Size	24000
Spectral Size	65536



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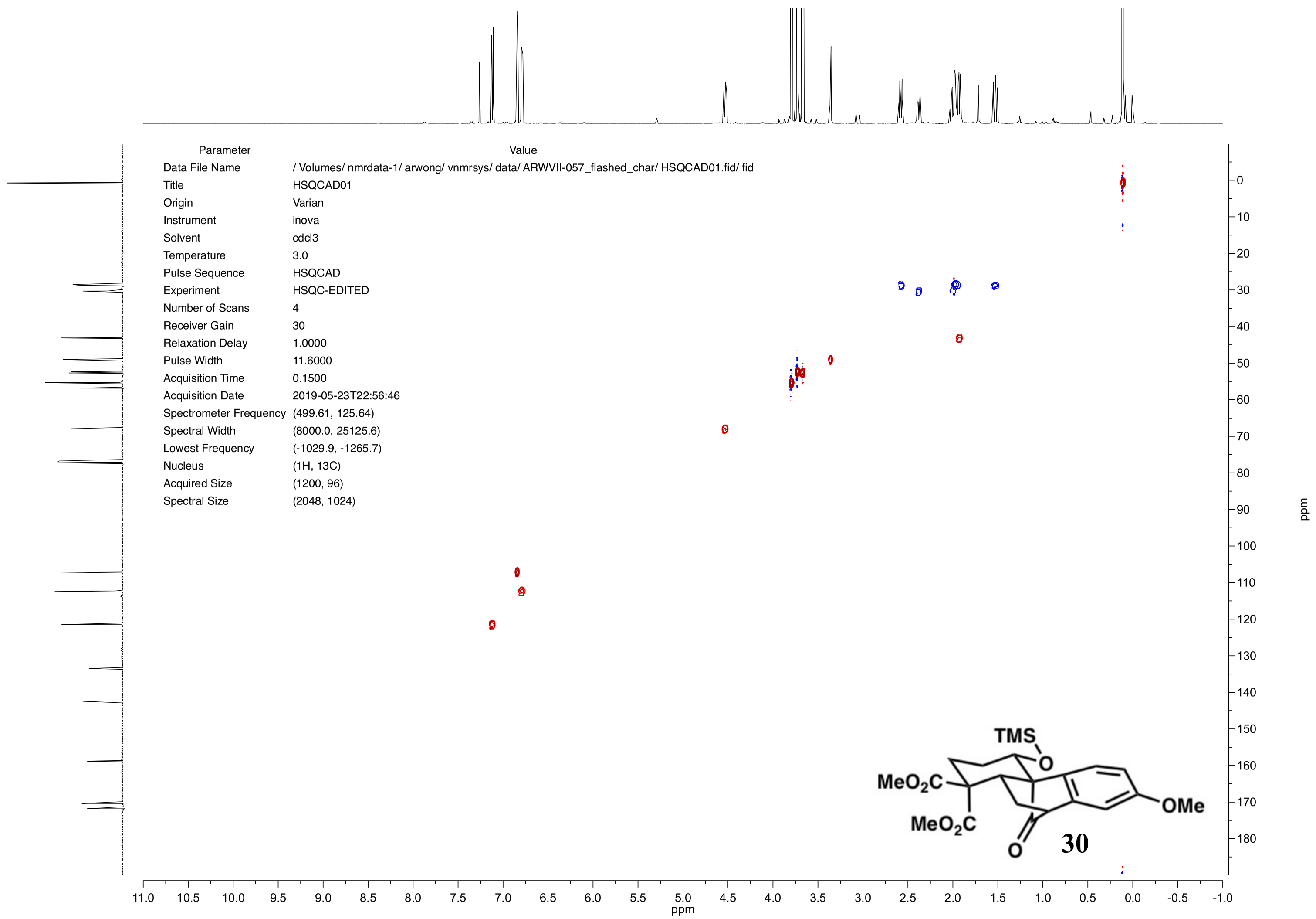
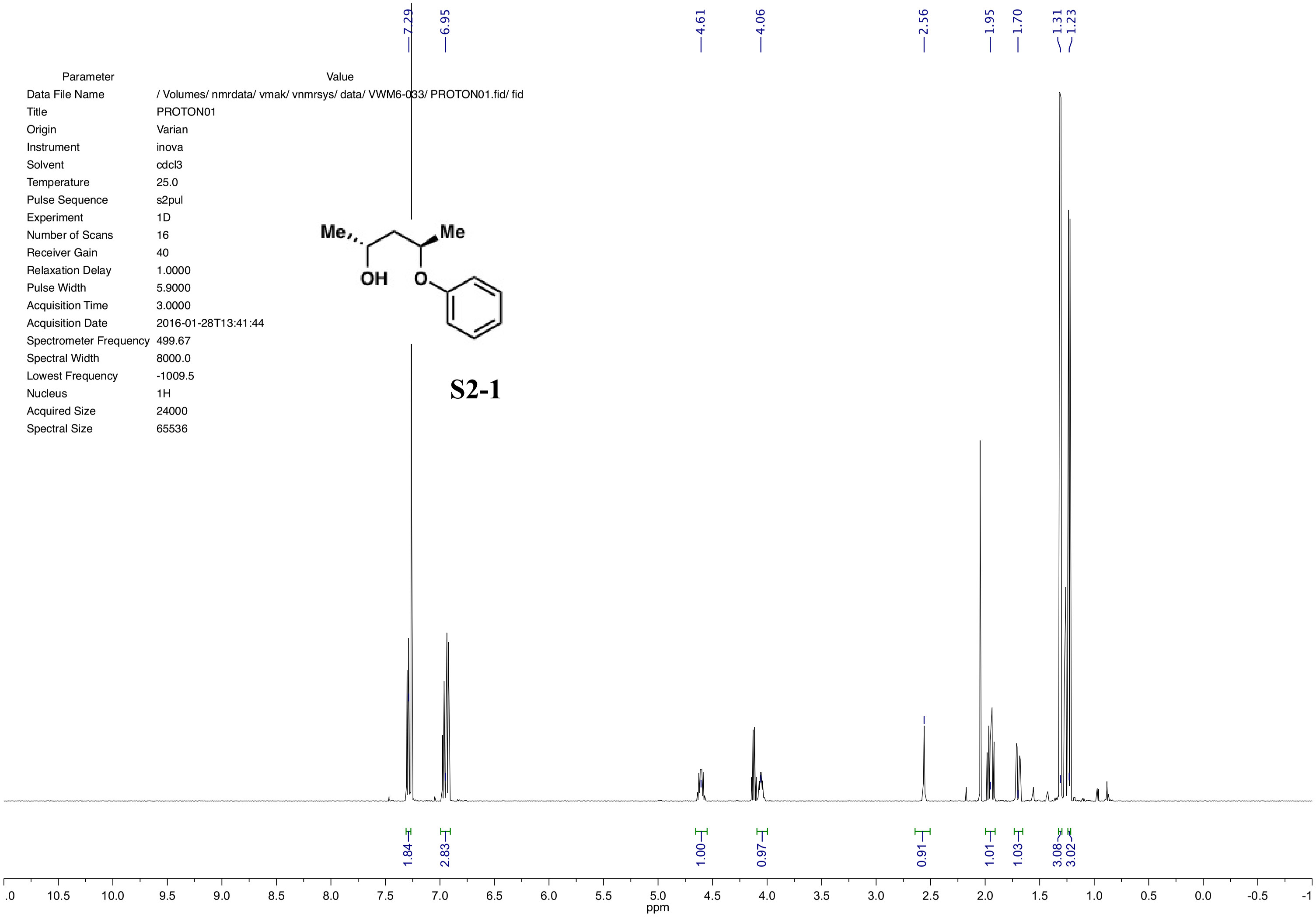
Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ arwong/ vnmrsys/ data/ ARWVII-057_flashed_char/ CARBON01.fid/ fid
Title	CARBON01
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	3.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	1000
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	4.8375
Acquisition Time	1.0420
Acquisition Date	2019-05-23T22:22:28
Spectrometer Frequency	125.64
Spectral Width	31446.5
Lowest Frequency	-1912.7
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ arwong/ vnmrsys/ data/ ARWVII-057_flashed_char/ HSQCAD01.fid/ fid
Title	HSQCAD01
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	3.0
Pulse Sequence	HSQCAD
Experiment	HSQC-EDITED
Number of Scans	4
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	11.6000
Acquisition Time	0.1500
Acquisition Date	2019-05-23T22:56:46
Spectrometer Frequency	(499.61, 125.64)
Spectral Width	(8000.0, 25125.6)
Lowest Frequency	(-1029.9, -1265.7)
Nucleus	(1H, 13C)
Acquired Size	(1200, 96)
Spectral Size	(2048, 1024)

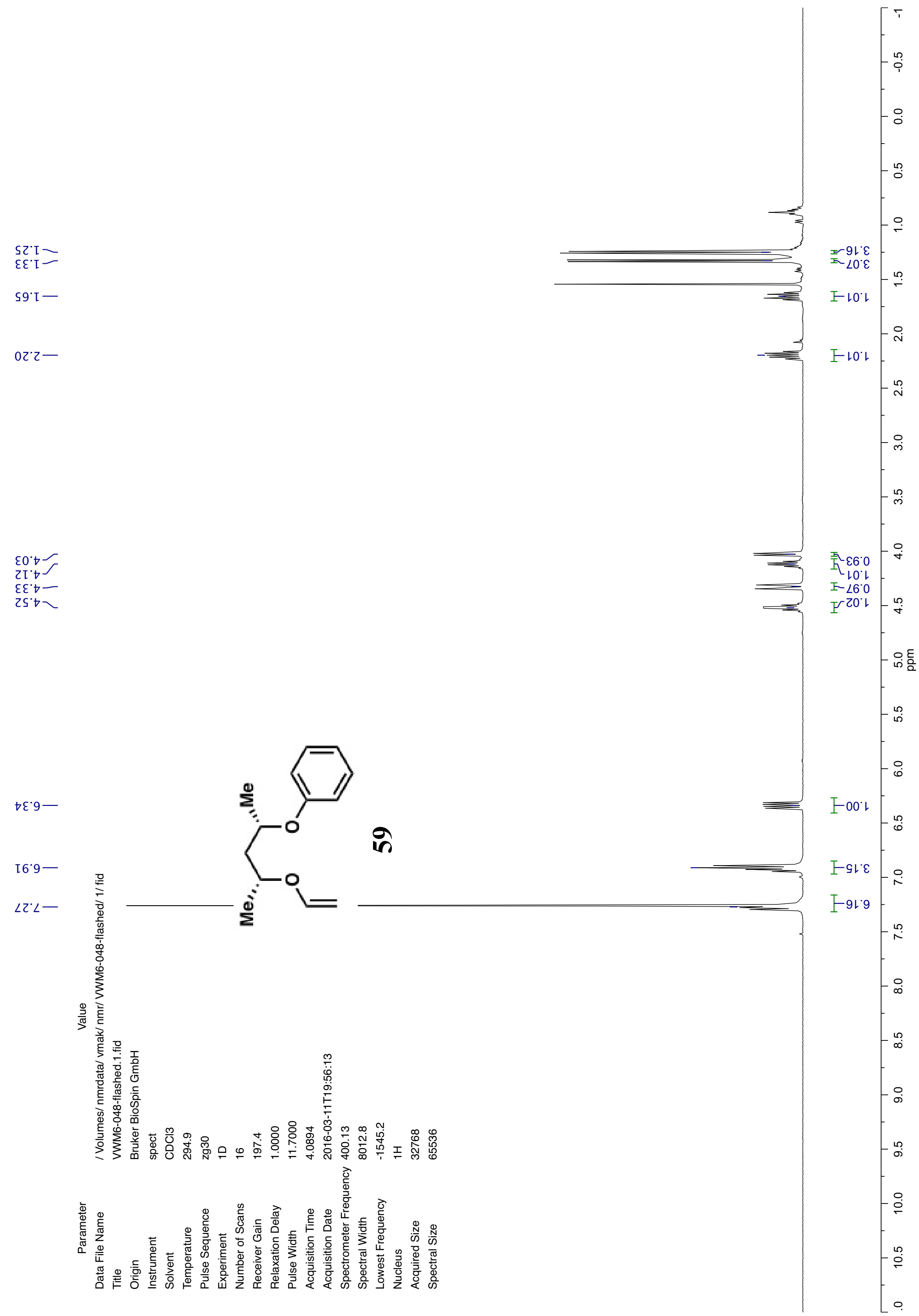
Appendix 2

Spectra Relevant to Chapter 2:
Initial Route Development Towards the C_{19} Diterpenoid Alkaloids



S2-1

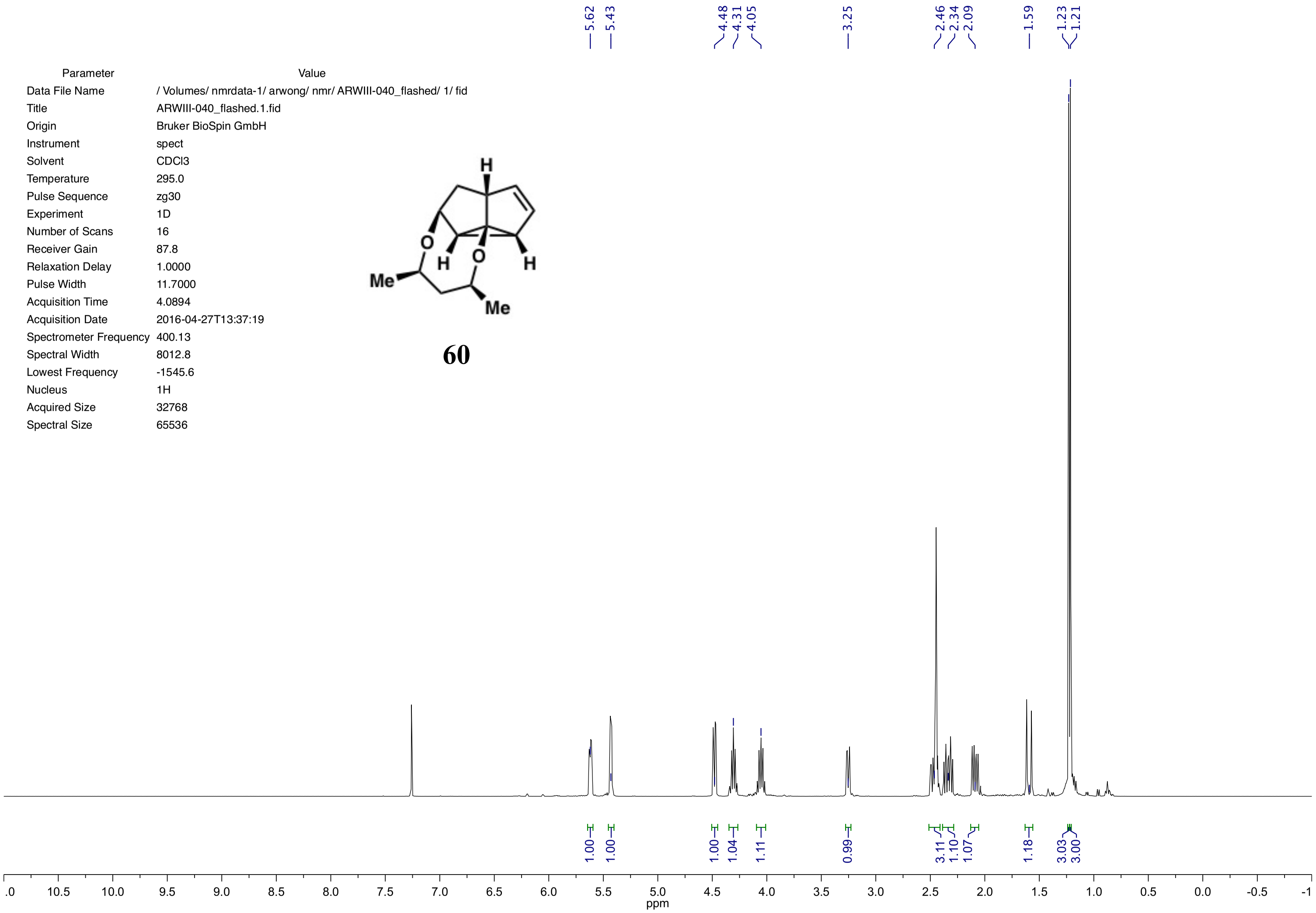
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ vnmrsys/ data/ VWM6-033/ PROTON01.fid/ fid
Title	PROTON01
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	16
Receiver Gain	40
Relaxation Delay	1.0000
Pulse Width	5.9000
Acquisition Time	3.0000
Acquisition Date	2016-01-28T13:41:44
Spectrometer Frequency	499.67
Spectral Width	8000.0
Lowest Frequency	-1009.5
Nucleus	1H
Acquired Size	24000
Spectral Size	65536



59

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM6-048-flashed/ 1/ fid
Title	VWM6-048-flashed.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	294.9
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	2016-03-11T19:56:13
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.2
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ arwong/ nmr/ ARWIII-040_flashed/ 1/ fid
Title	ARWIII-040_flashed.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.0
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	2016-04-27T13:37:19
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



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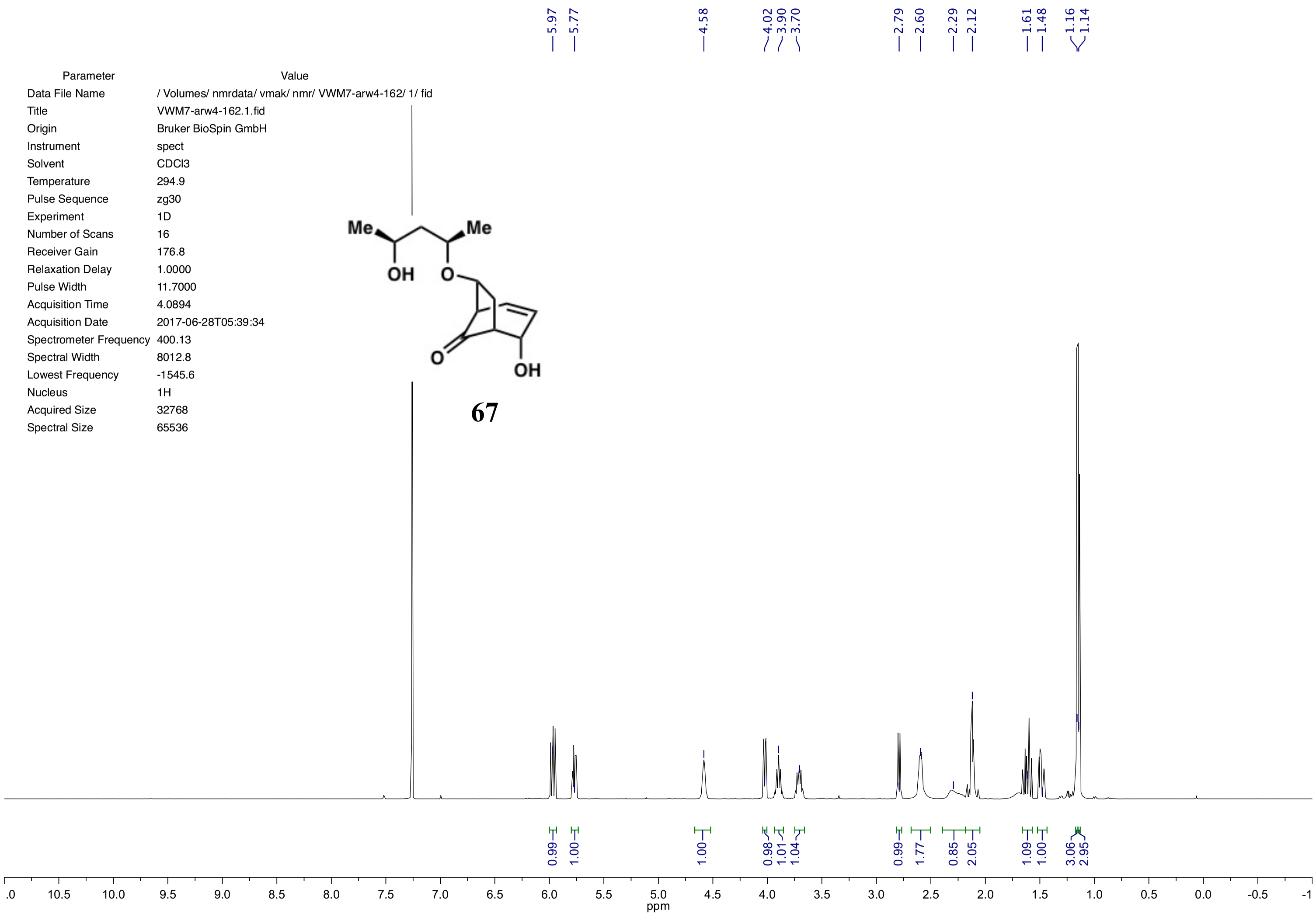
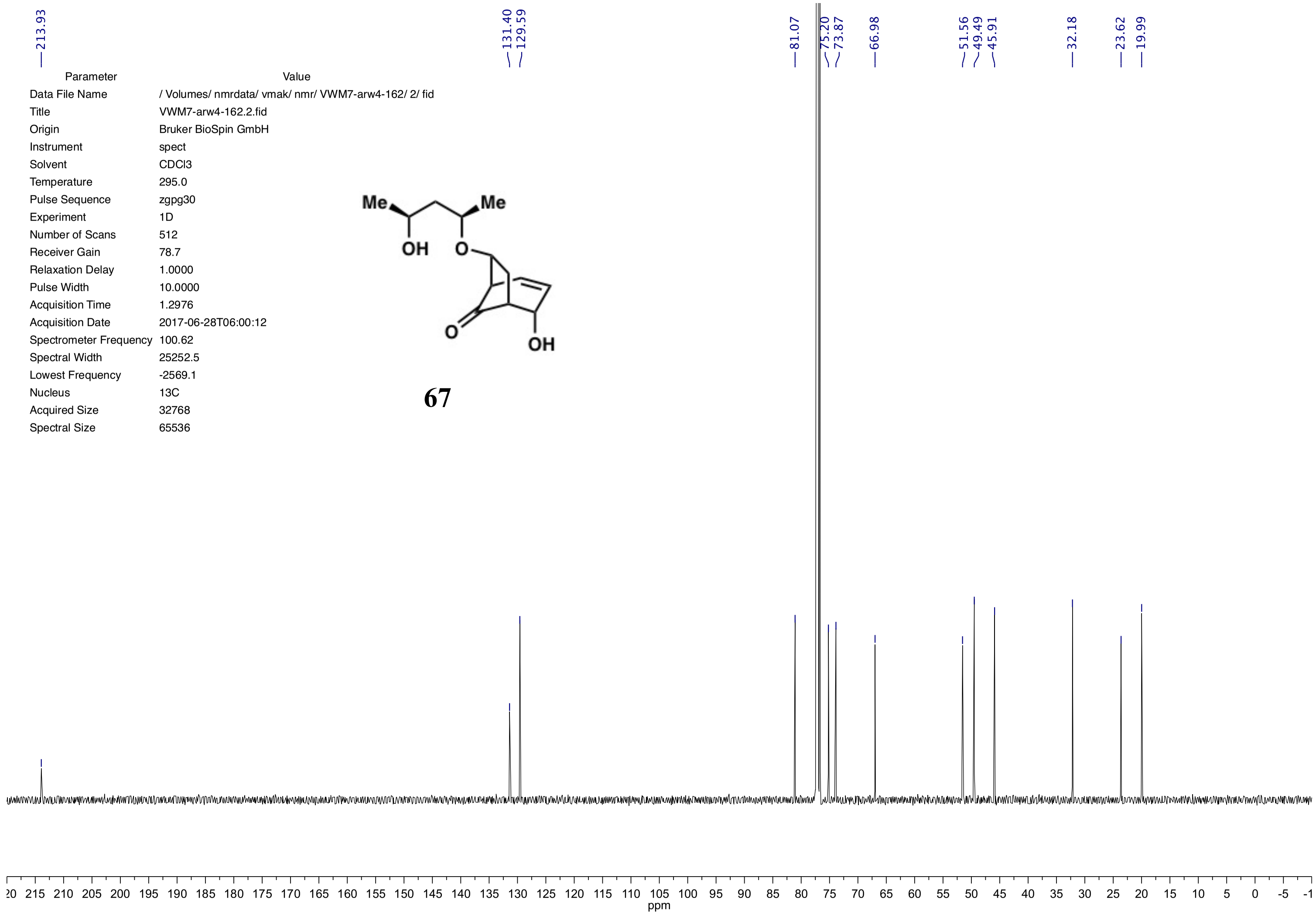


67

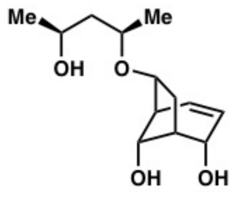
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM7-arw4-162/ 1/ fid
Title	VWM7-arw4-162.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	294.9
Pulse Sequence	zg30
Experiment	1D
Number of Scans	16
Receiver Gain	176.8
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2017-06-28T05:39:34
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



67

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM7-arw4-162/ 2/ fid
Title	VWM7-arw4-162.2.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
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	1.2976
Acquisition Date	2017-06-28T06:00:12
Spectrometer Frequency	100.62
Spectral Width	25252.5
Lowest Frequency	-2569.1
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM7-arw4-163/ 1/ fid
Title	VWM7-arw4-163.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
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	2017-06-28T03:44:24
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



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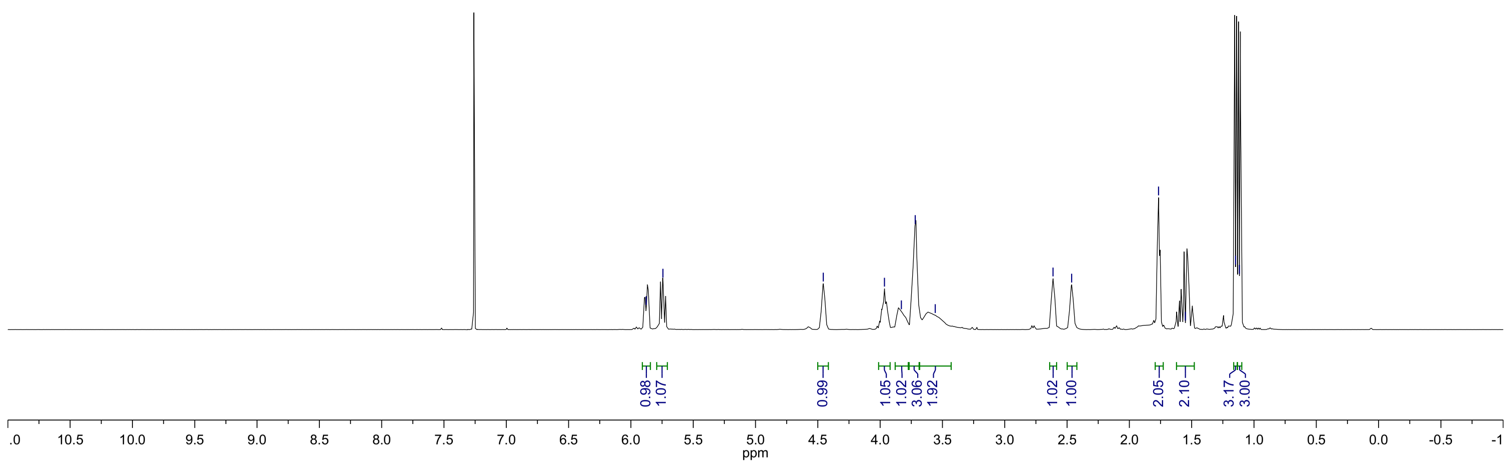
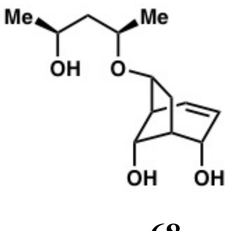


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM7-arw4-163/ 2/ fid
Title	VWM7-arw4-163.2.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1024
Receiver Gain	78.7
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.2976
Acquisition Date	2017-06-28T04:25:11
Spectrometer Frequency	100.62
Spectral Width	25252.5
Lowest Frequency	-2569.4
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



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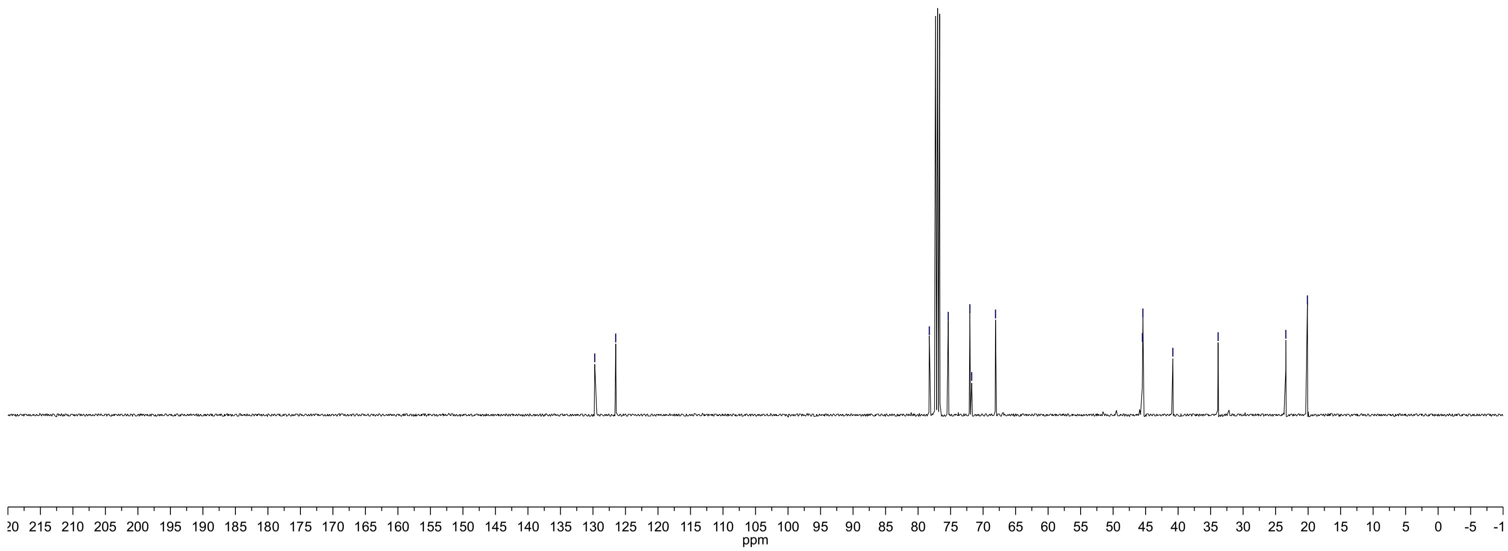
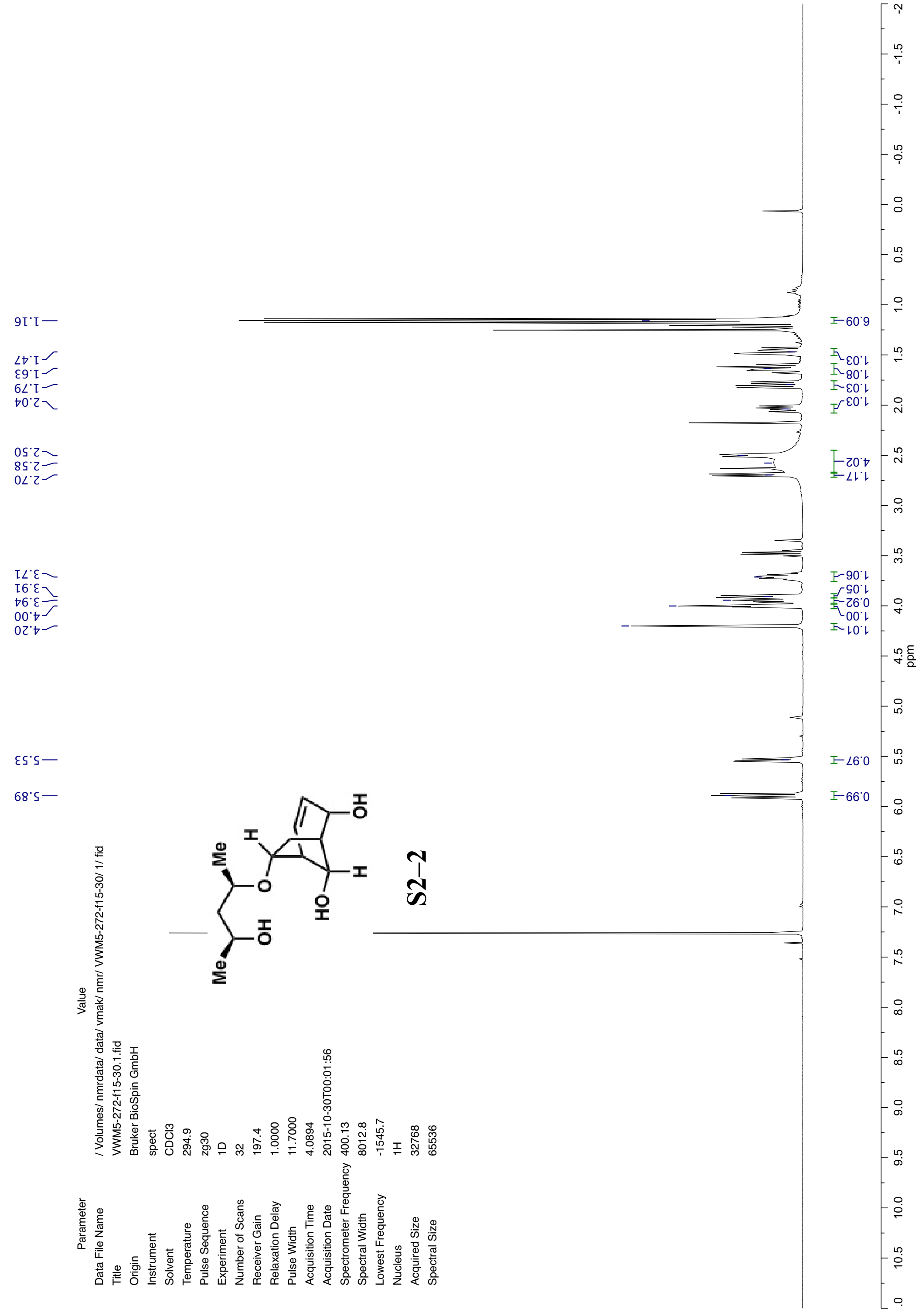
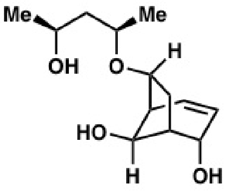




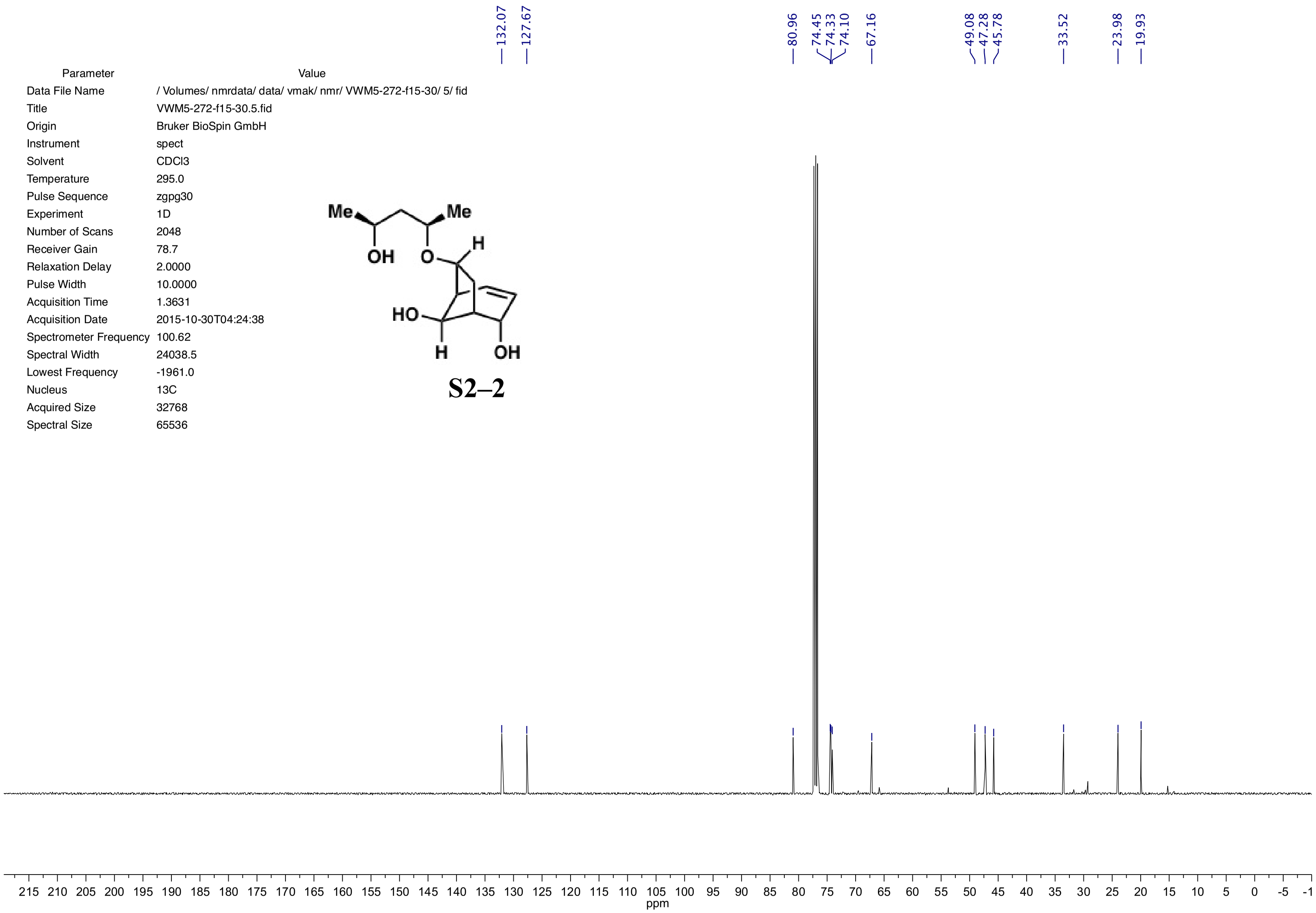
S2–2

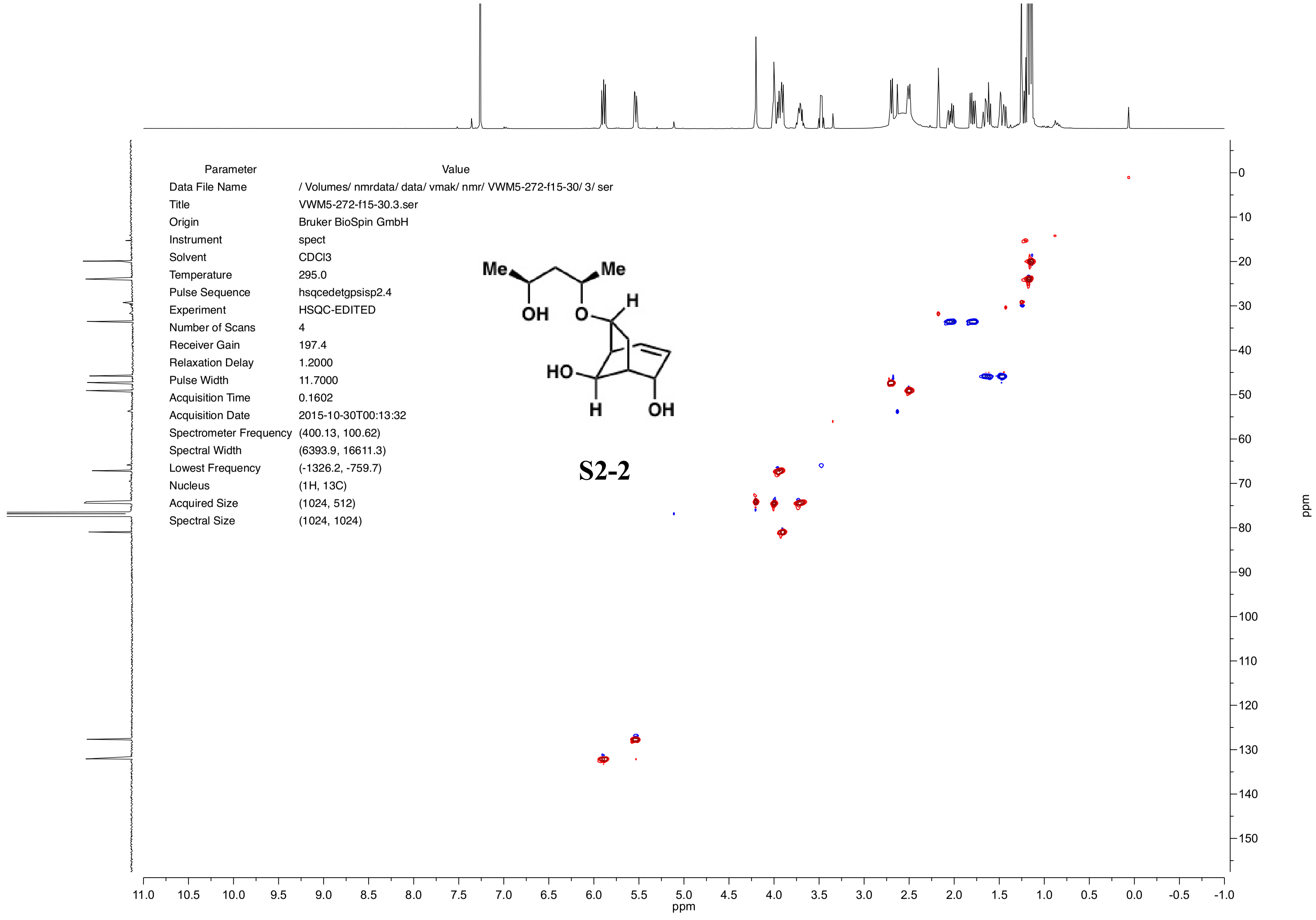
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ data/ vmak/ nmr/ VWM5-272-f15-30/ 1/ fid
Title	VWM5-272-f15-30.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	294.9
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	197.4
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2015-10-30T00:01:56
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.7
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ data/ vmak/ nmr/ VWM5-272-f15-30/ 5/ fid
Title	VWM5-272-f15-30.5.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	2048
Receiver Gain	78.7
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2015-10-30T04:24:38
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.0
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



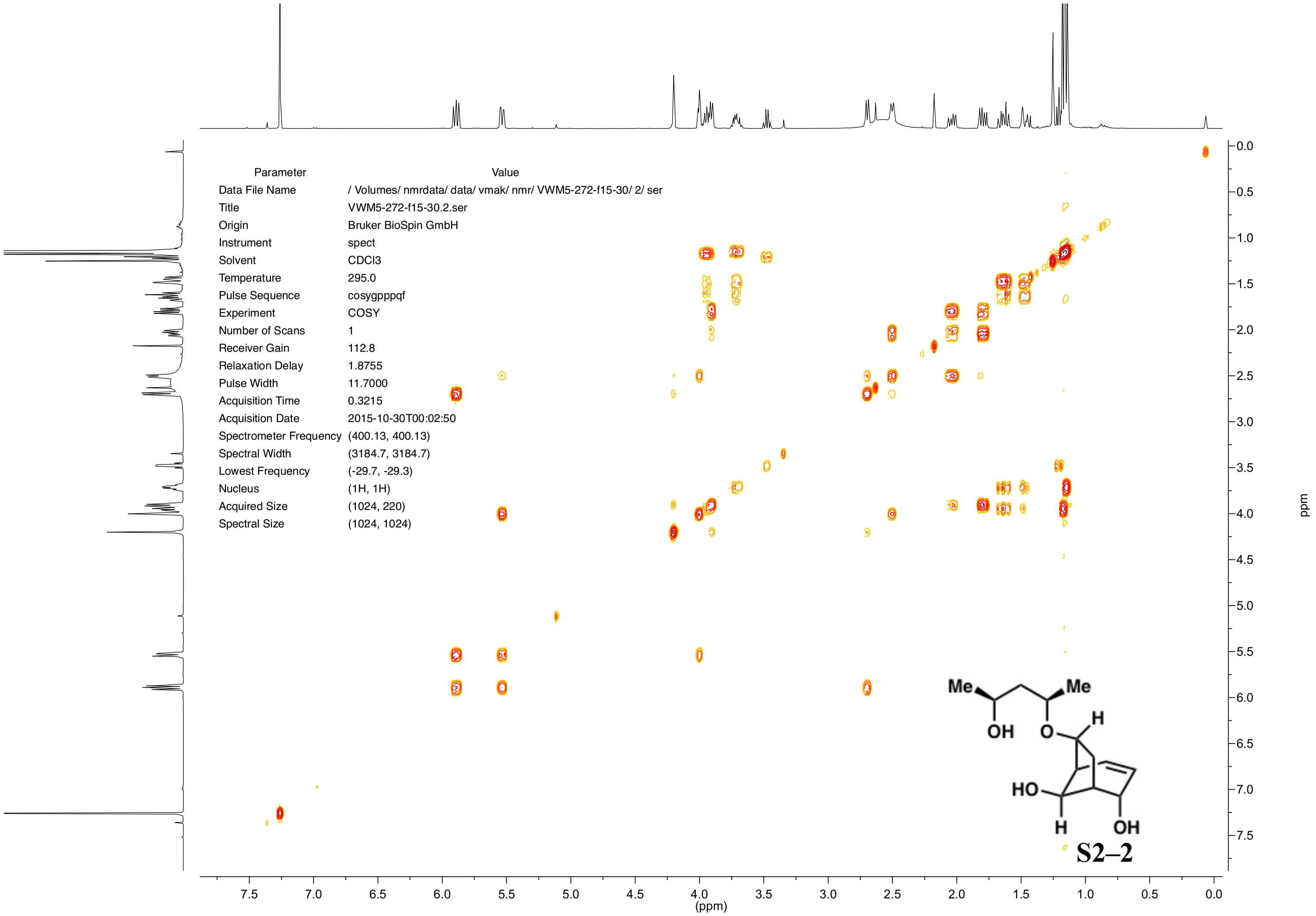
S2–2





S2-2

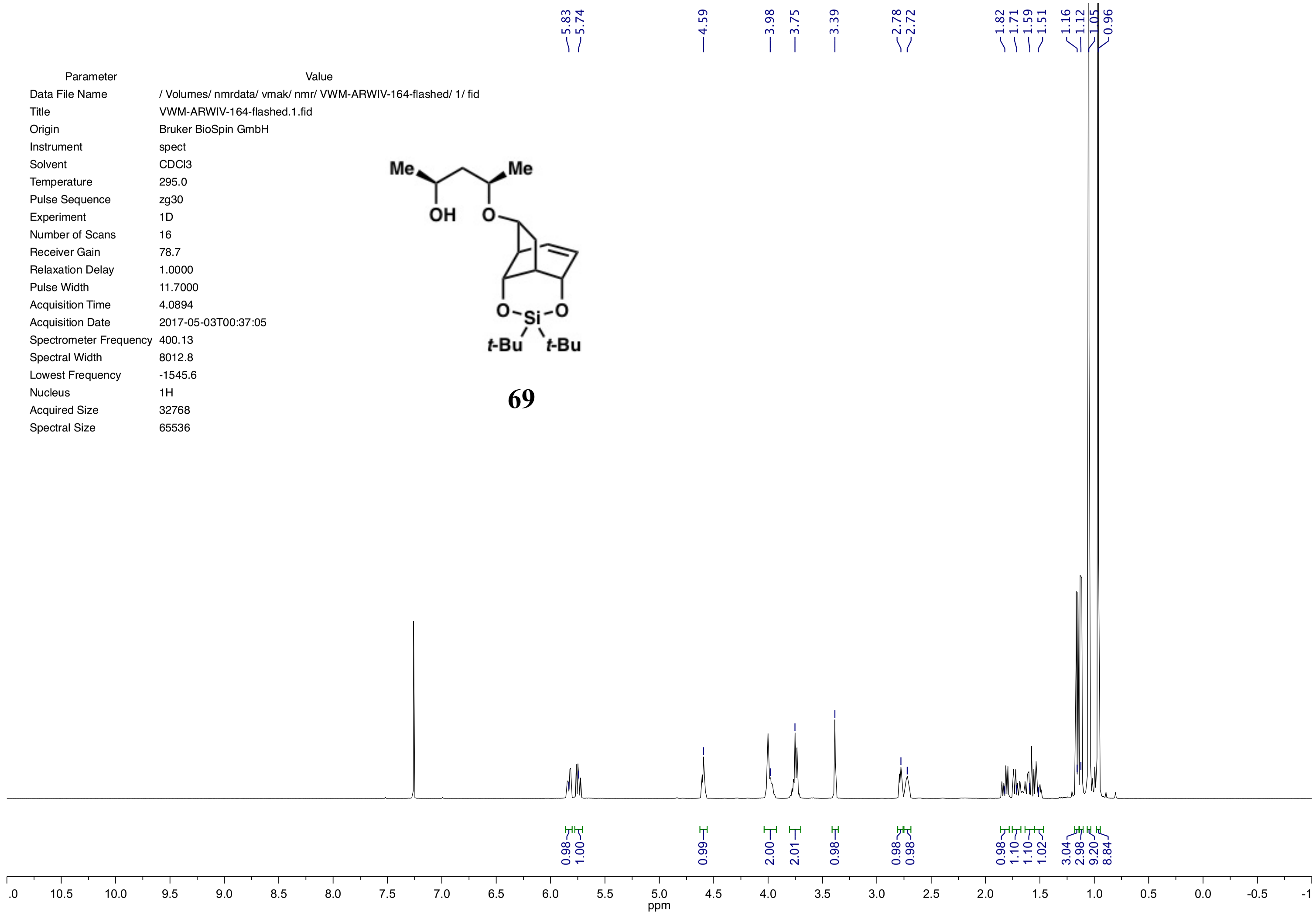
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ data/ vmak/ nmr/ VWM5-272-f15-30/ 3/ ser
Title	VWM5-272-f15-30.3.ser
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	hsqcedetgpsisp2.4
Experiment	HSQC-EDITED
Number of Scans	4
Receiver Gain	197.4
Relaxation Delay	1.2000
Pulse Width	11.7000
Acquisition Time	0.1602
Acquisition Date	2015-10-30T00:13:32
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(6393.9, 16611.3)
Lowest Frequency	(-1326.2, -759.7)
Nucleus	(1H, 13C)
Acquired Size	(1024, 512)
Spectral Size	(1024, 1024)



Parameter	Value
Data File Name	/ Volumes/ nmrdata/ data/ vmak/ nmr/ VWM5-272-f15-30/ 2/ ser
Title	VWM5-272-f15-30.2.ser
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	cosygpppqf
Experiment	COSY
Number of Scans	1
Receiver Gain	112.8
Relaxation Delay	1.8755
Pulse Width	11.7000
Acquisition Time	0.3215
Acquisition Date	2015-10-30T00:02:50
Spectrometer Frequency	(400.13, 400.13)
Spectral Width	(3184.7, 3184.7)
Lowest Frequency	(-29.7, -29.3)
Nucleus	(1H, 1H)
Acquired Size	(1024, 220)
Spectral Size	(1024, 1024)

S2–2

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM-ARWIV-164-flashed/ 1/ fid
Title	VWM-ARWIV-164-flashed.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
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	2017-05-03T00:37:05
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



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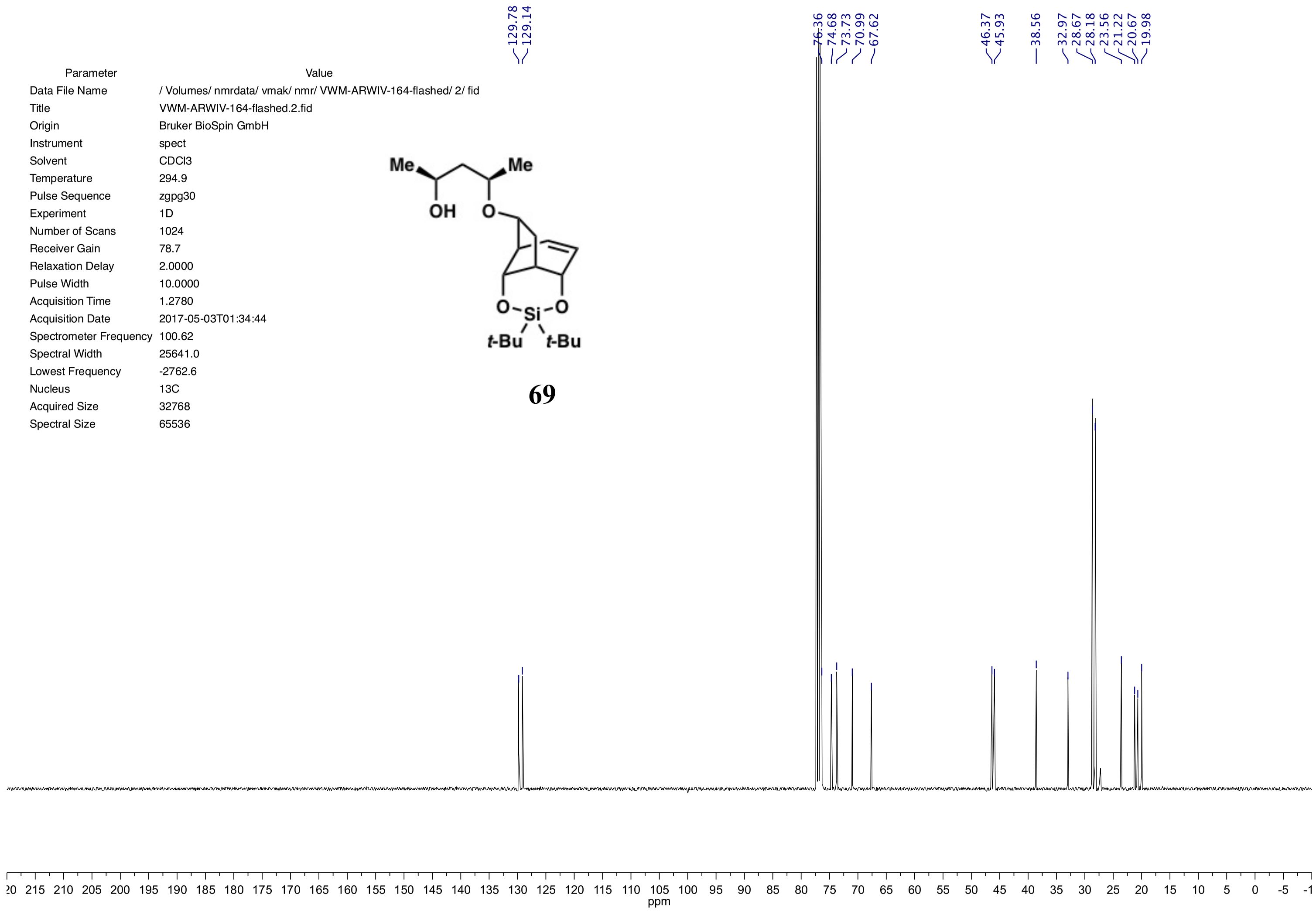
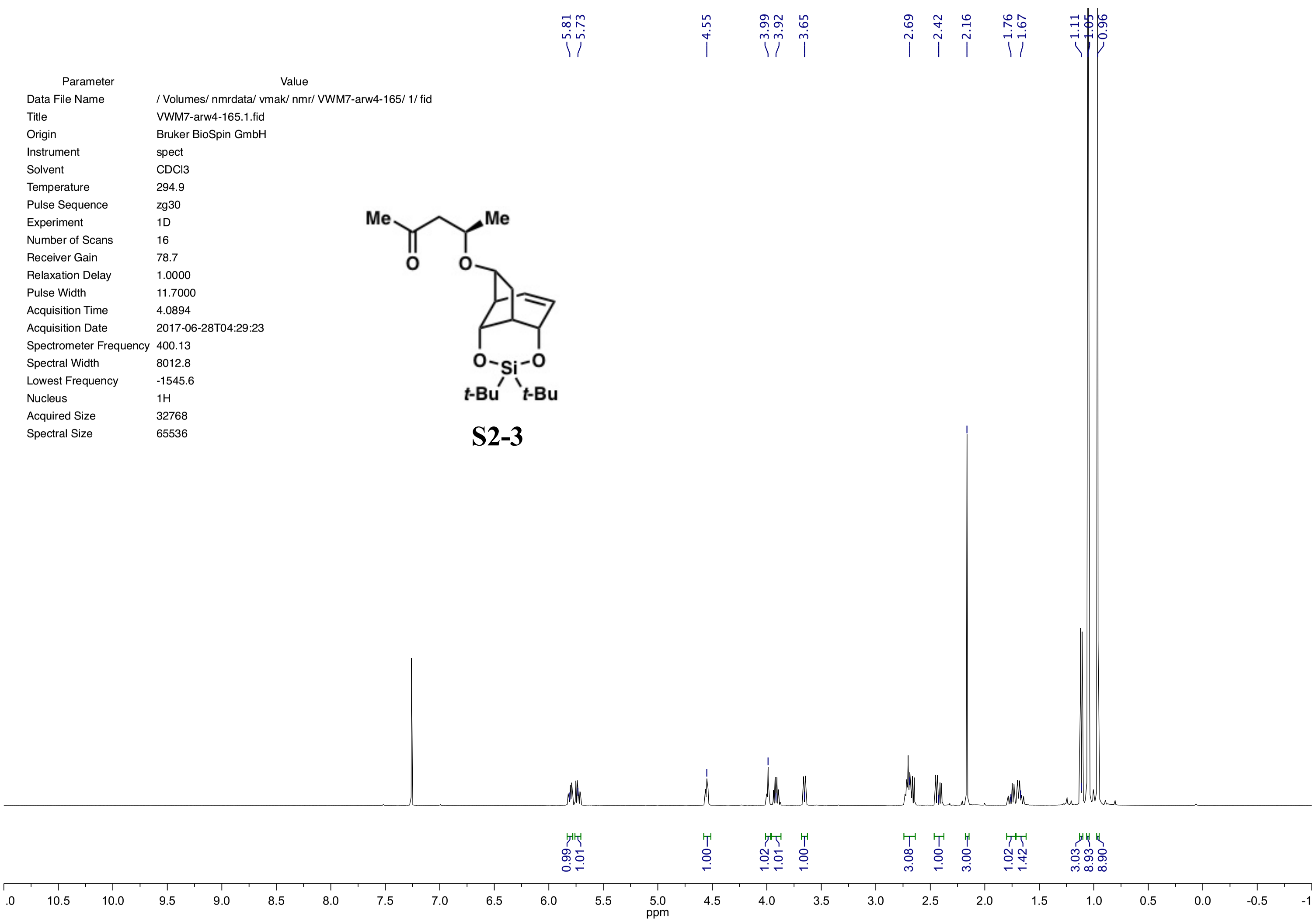


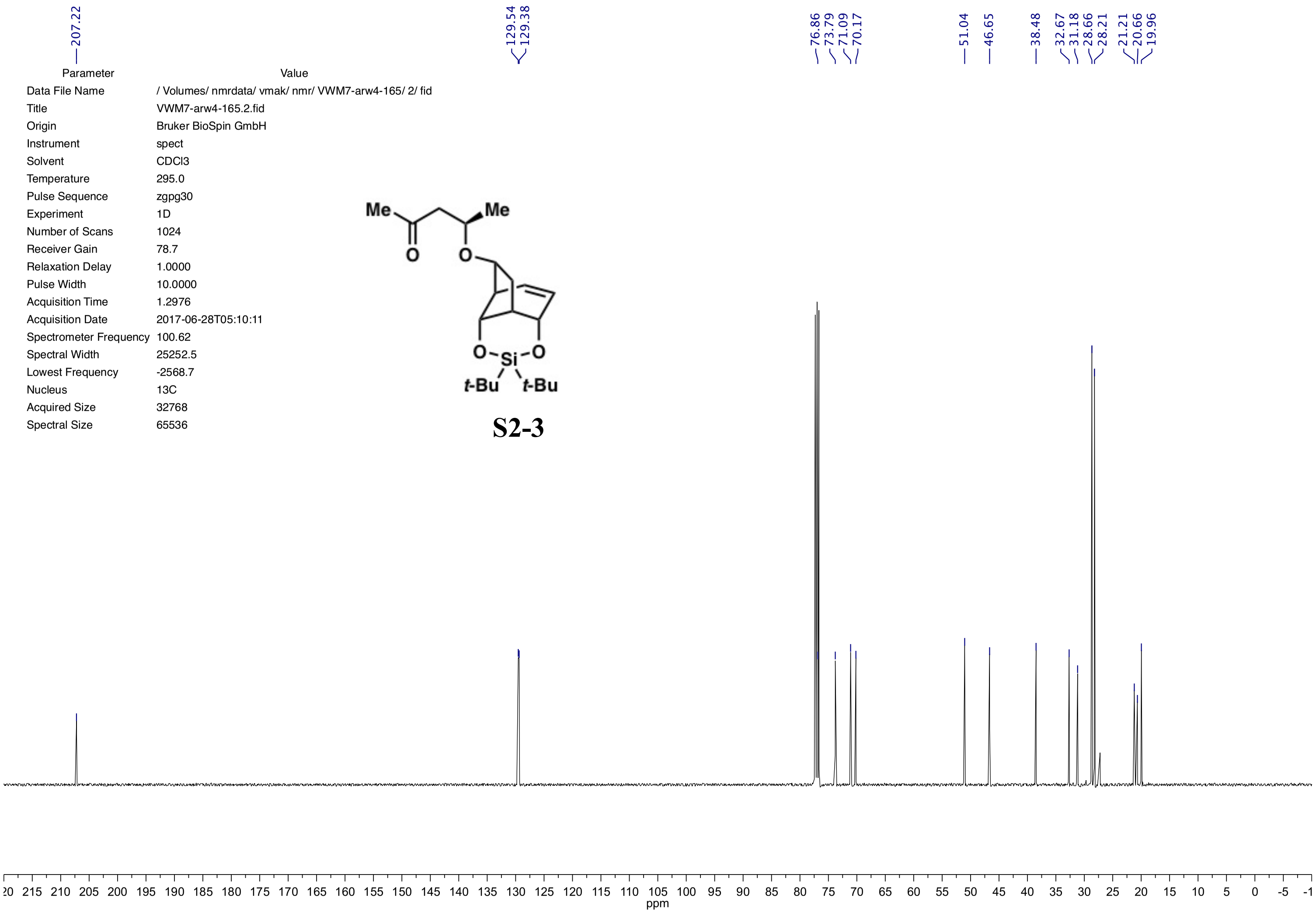
69

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM-ARWIV-164-flashed/ 2/ fid
Title	VWM-ARWIV-164-flashed.2.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	294.9
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1024
Receiver Gain	78.7
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.2780
Acquisition Date	2017-05-03T01:34:44
Spectrometer Frequency	100.62
Spectral Width	25641.0
Lowest Frequency	-2762.6
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



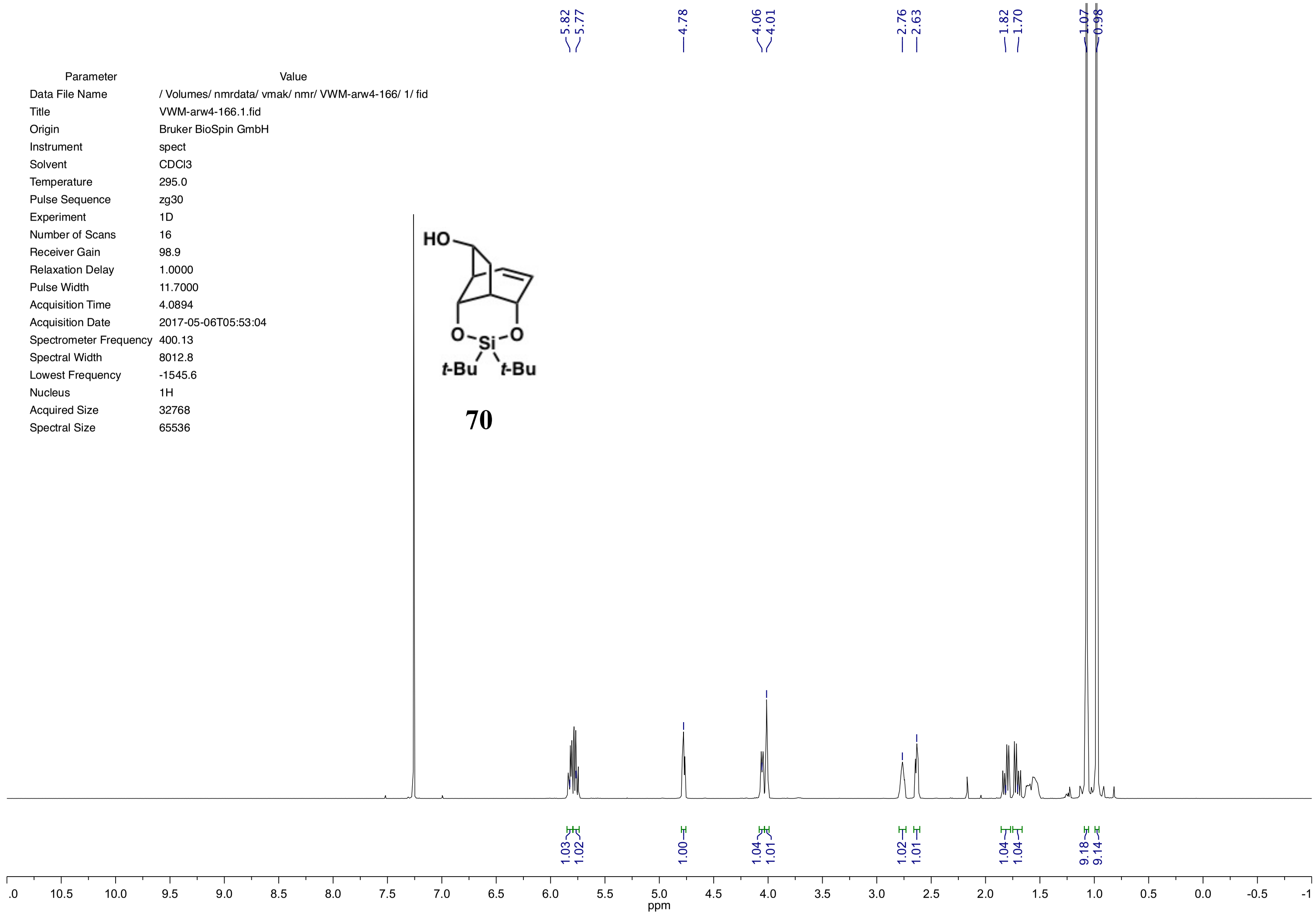
S2-3

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM7-arw4-165/ 1/ fid
Title	VWM7-arw4-165.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
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	2017-06-28T04:29:23
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



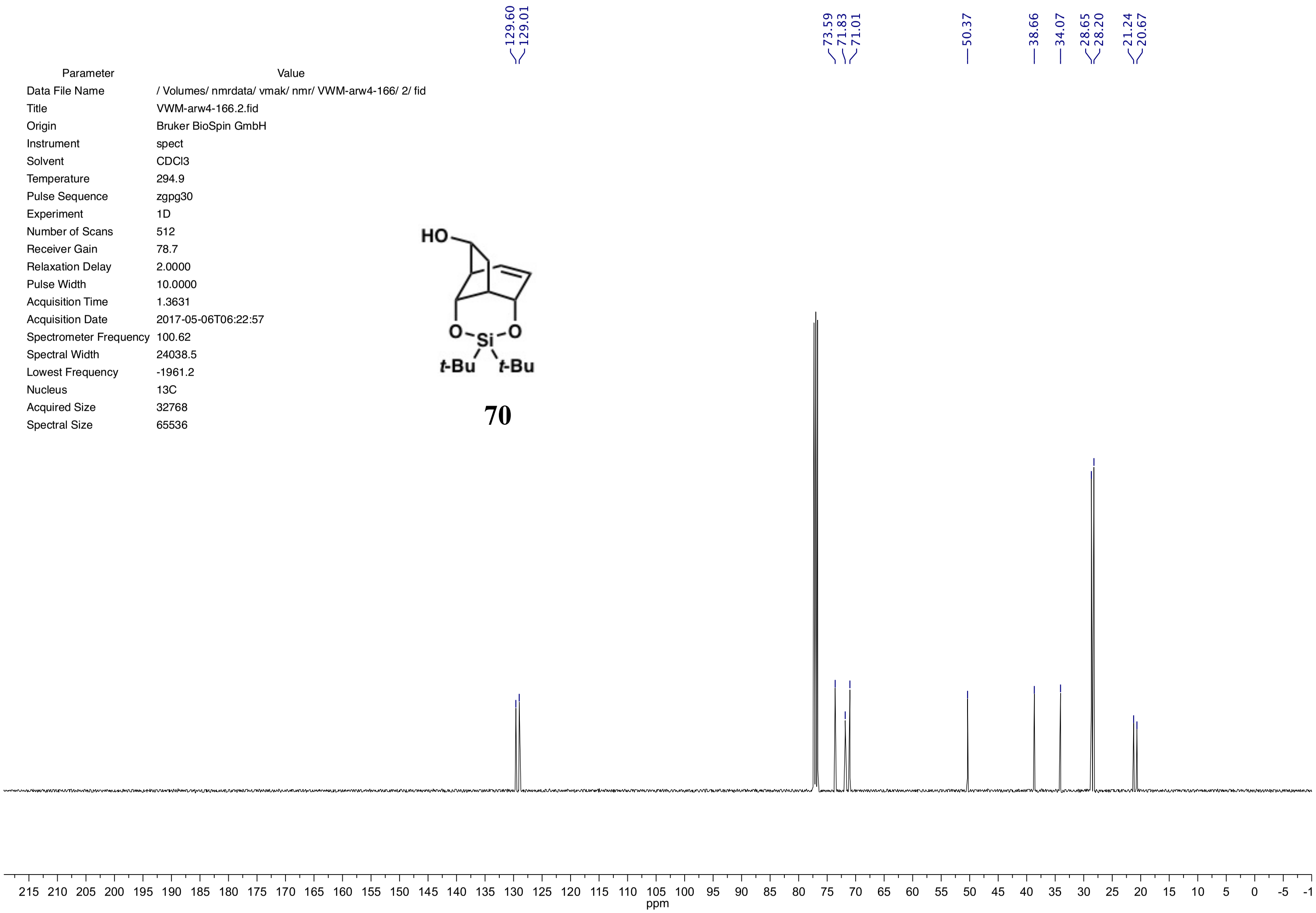
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM7-arw4-165/ 2/ fid
Title	VWM7-arw4-165.2.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1024
Receiver Gain	78.7
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.2976
Acquisition Date	2017-06-28T05:10:11
Spectrometer Frequency	100.62
Spectral Width	25252.5
Lowest Frequency	-2568.7
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

S2-3



70

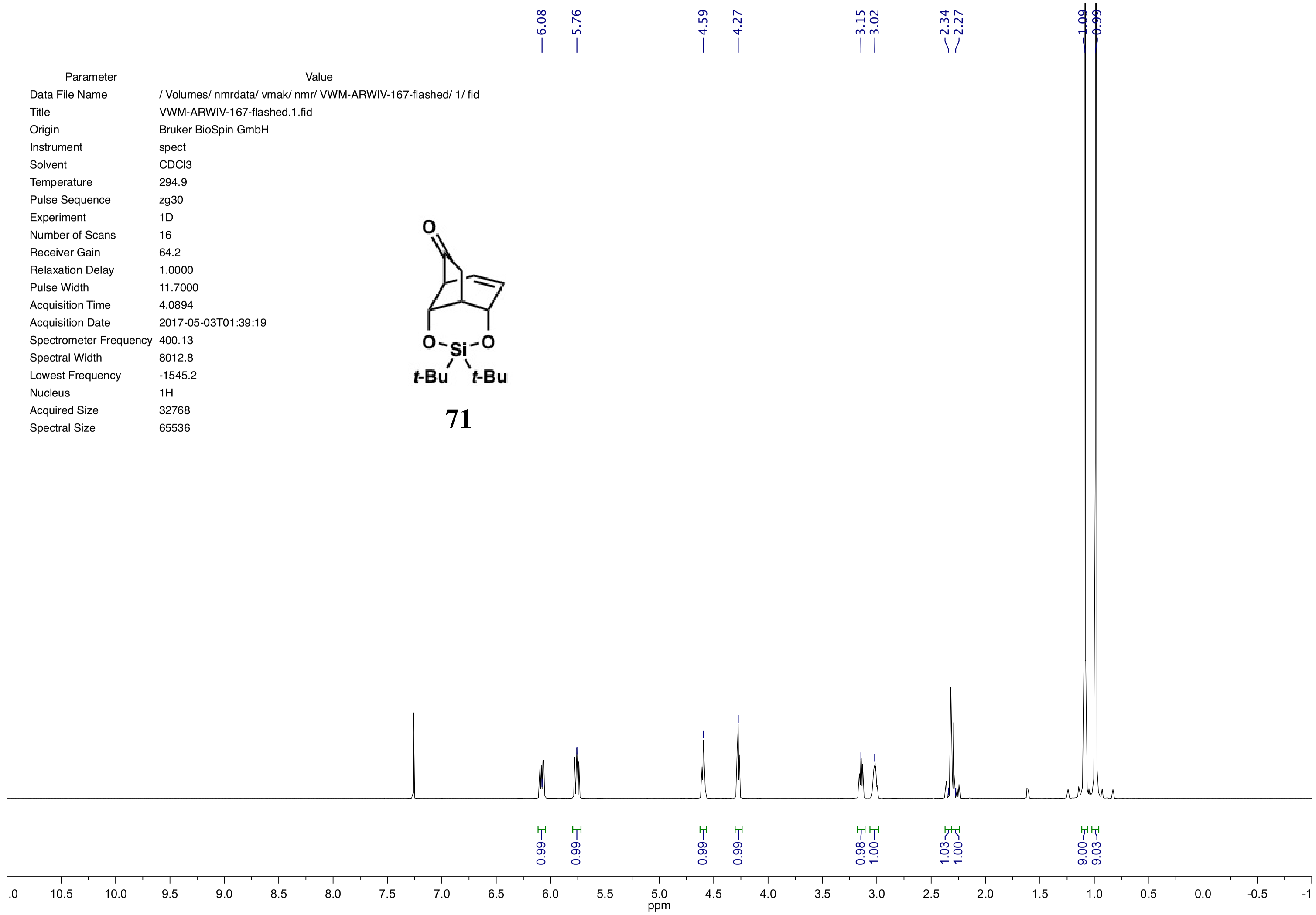
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM-arw4-166/ 1/ fid
Title	VWM-arw4-166.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	zg30
Experiment	1D
Number of Scans	16
Receiver Gain	98.9
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2017-05-06T05:53:04
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



70

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM-arw4-166/ 2/ fid
Title	VWM-arw4-166.2.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
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	2017-05-06T06:22:57
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.2
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM-ARWIV-167-flashed/ 1/ fid
Title	VWM-ARWIV-167-flashed.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
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	2017-05-03T01:39:19
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.2
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



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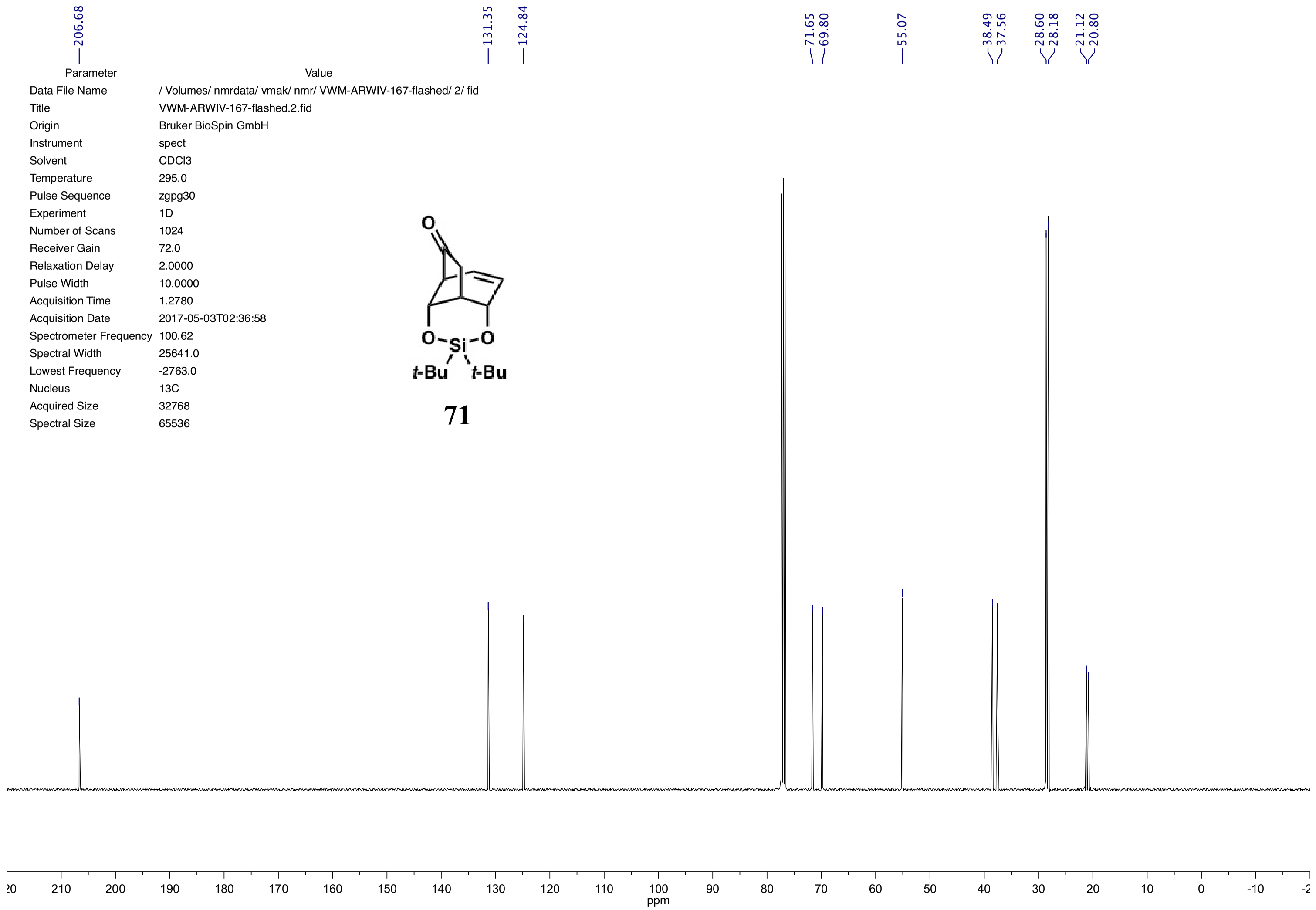

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM-ARWIV-167-flashed/ 2/ fid
Title	VWM-ARWIV-167-flashed.2.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1024
Receiver Gain	72.0
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.2780
Acquisition Date	2017-05-03T02:36:58
Spectrometer Frequency	100.62
Spectral Width	25641.0
Lowest Frequency	-2763.0
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

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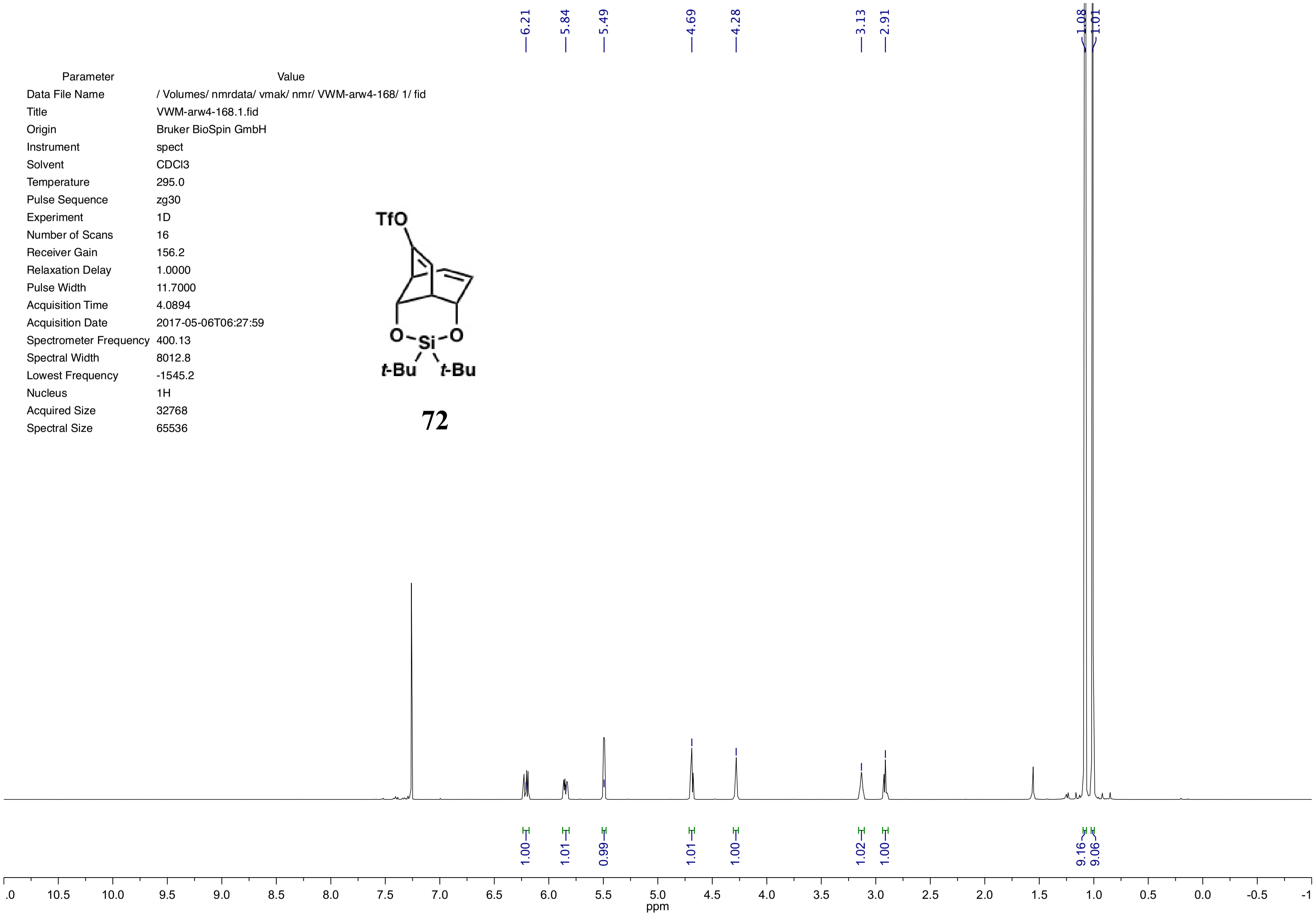
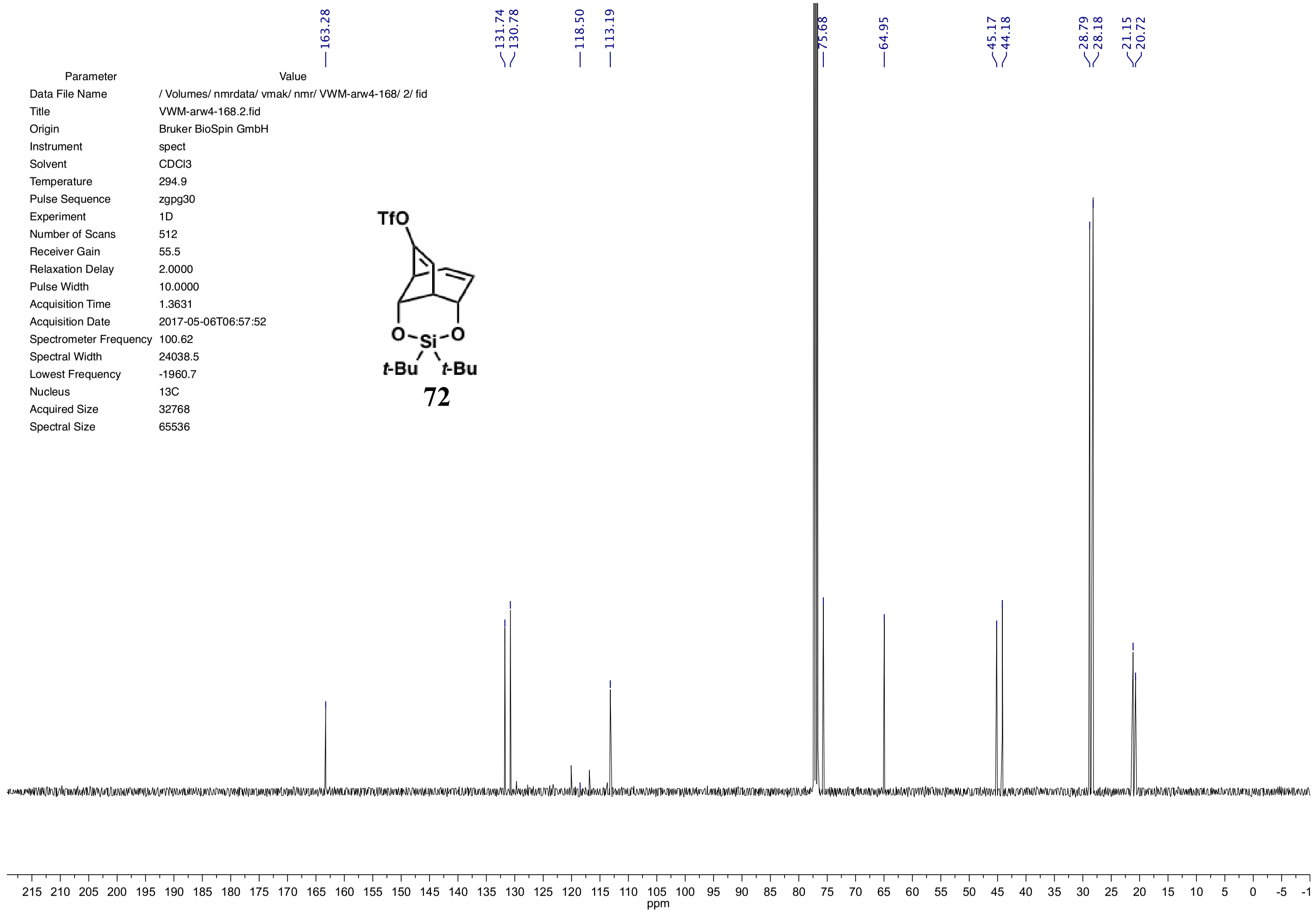


72

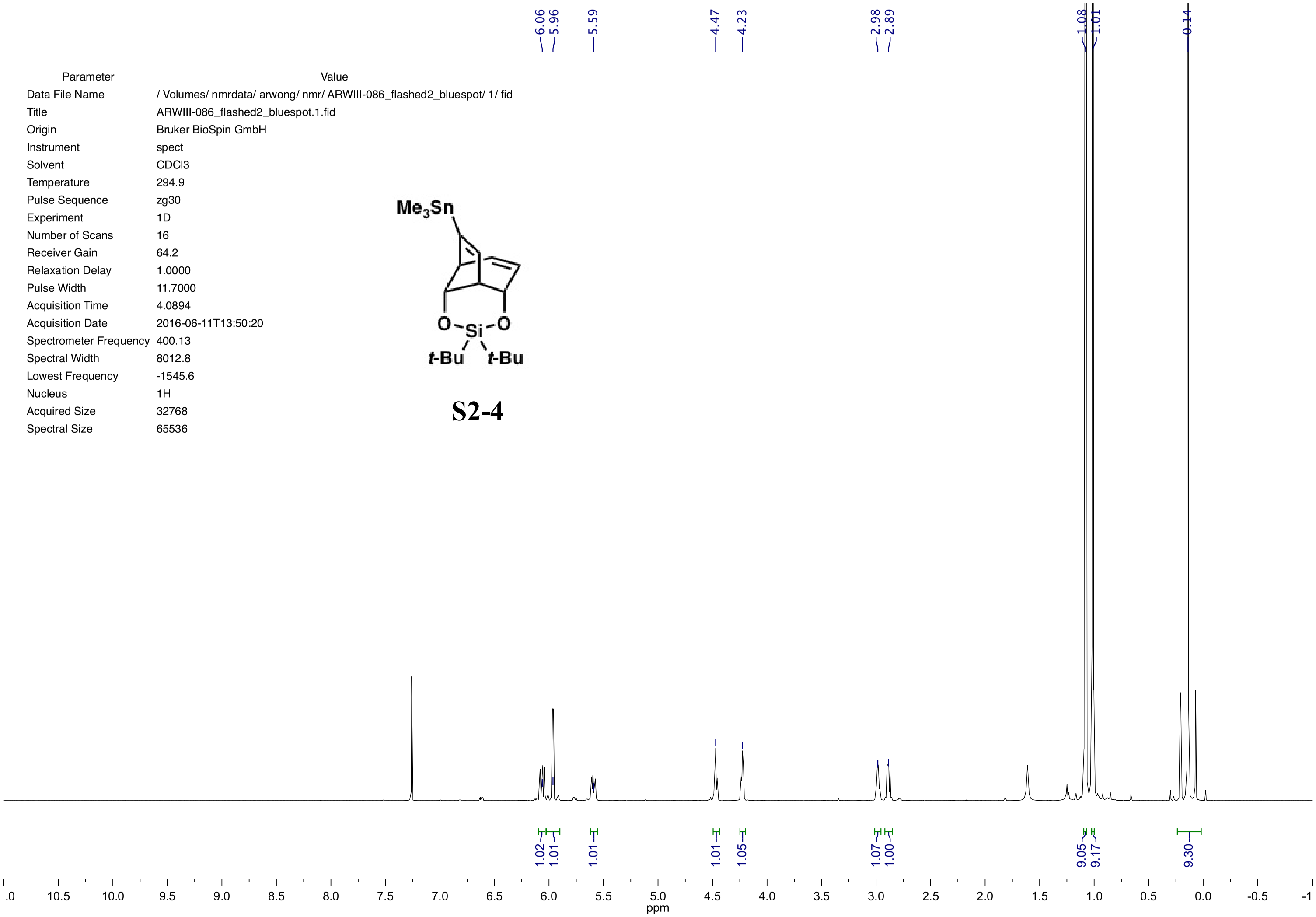
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM-arw4-168/ 1/ fid
Title	VWM-arw4-168.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	zg30
Experiment	1D
Number of Scans	16
Receiver Gain	156.2
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2017-05-06T06:27:59
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.2
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



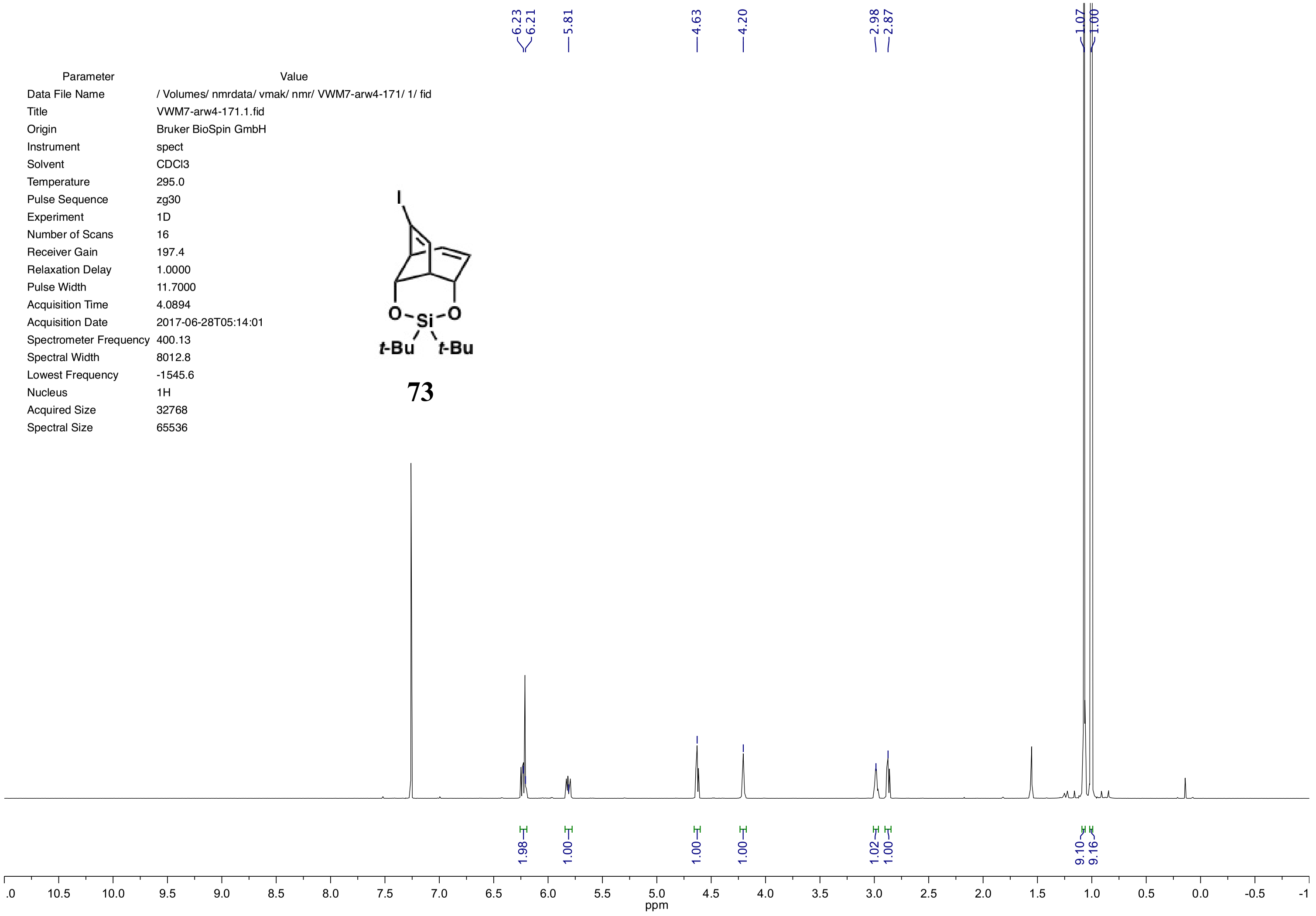
72

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM-arw4-168/ 2/ fid
Title	VWM-arw4-168.2.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
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	2017-05-06T06:57:52
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1960.7
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWIII-086_flashed2_bluespot/ 1/ fid
Title	ARWIII-086_flashed2_bluespot.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
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	2016-06-11T13:50:20
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



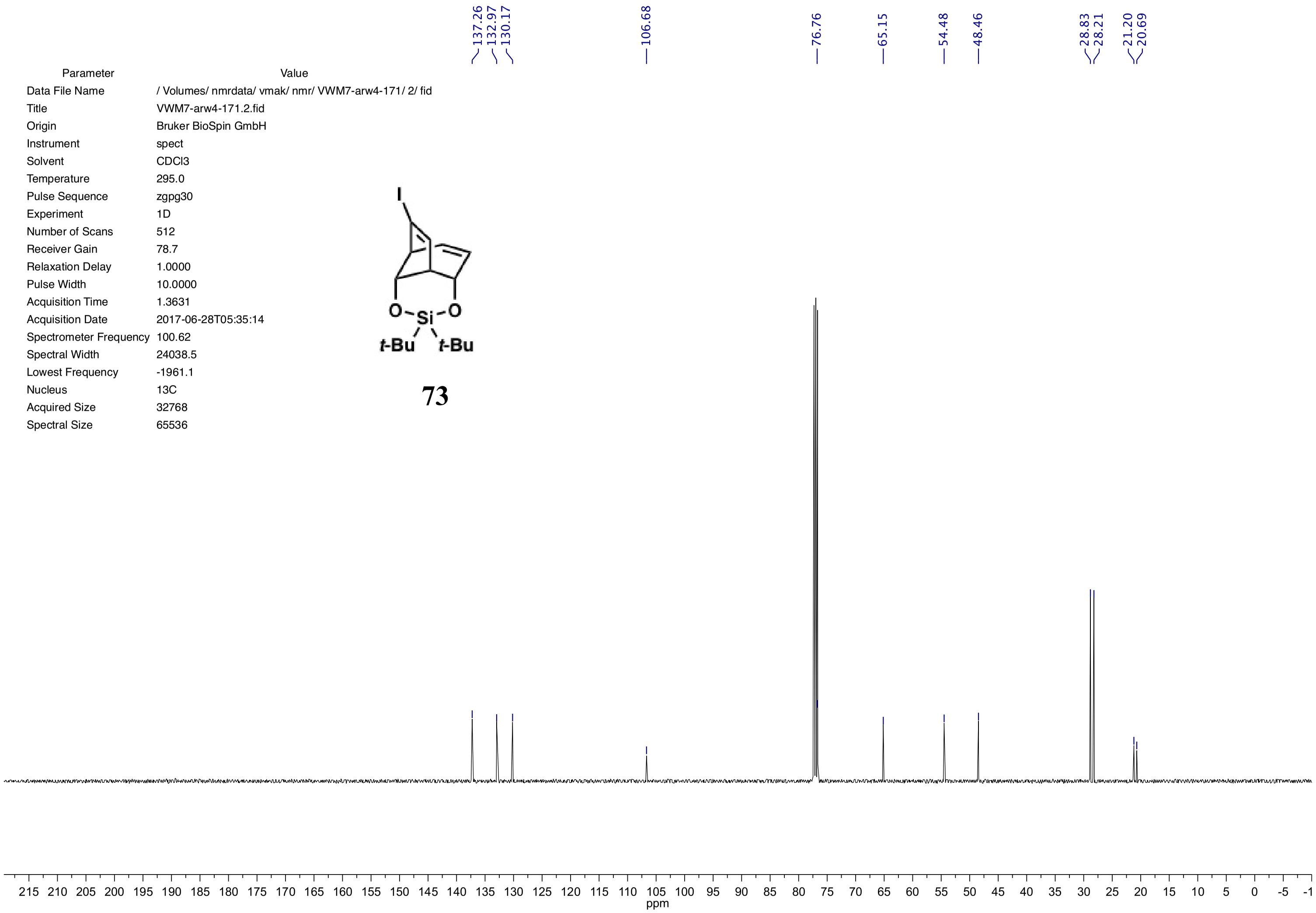
S2-4



73

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM7-arw4-171/ 1/ fid
Title	VWM7-arw4-171.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
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	2017-06-28T05:14:01
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM7-arw4-171/ 2/ fid
Title	VWM7-arw4-171.2.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
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	2017-06-28T05:35:14
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.1
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



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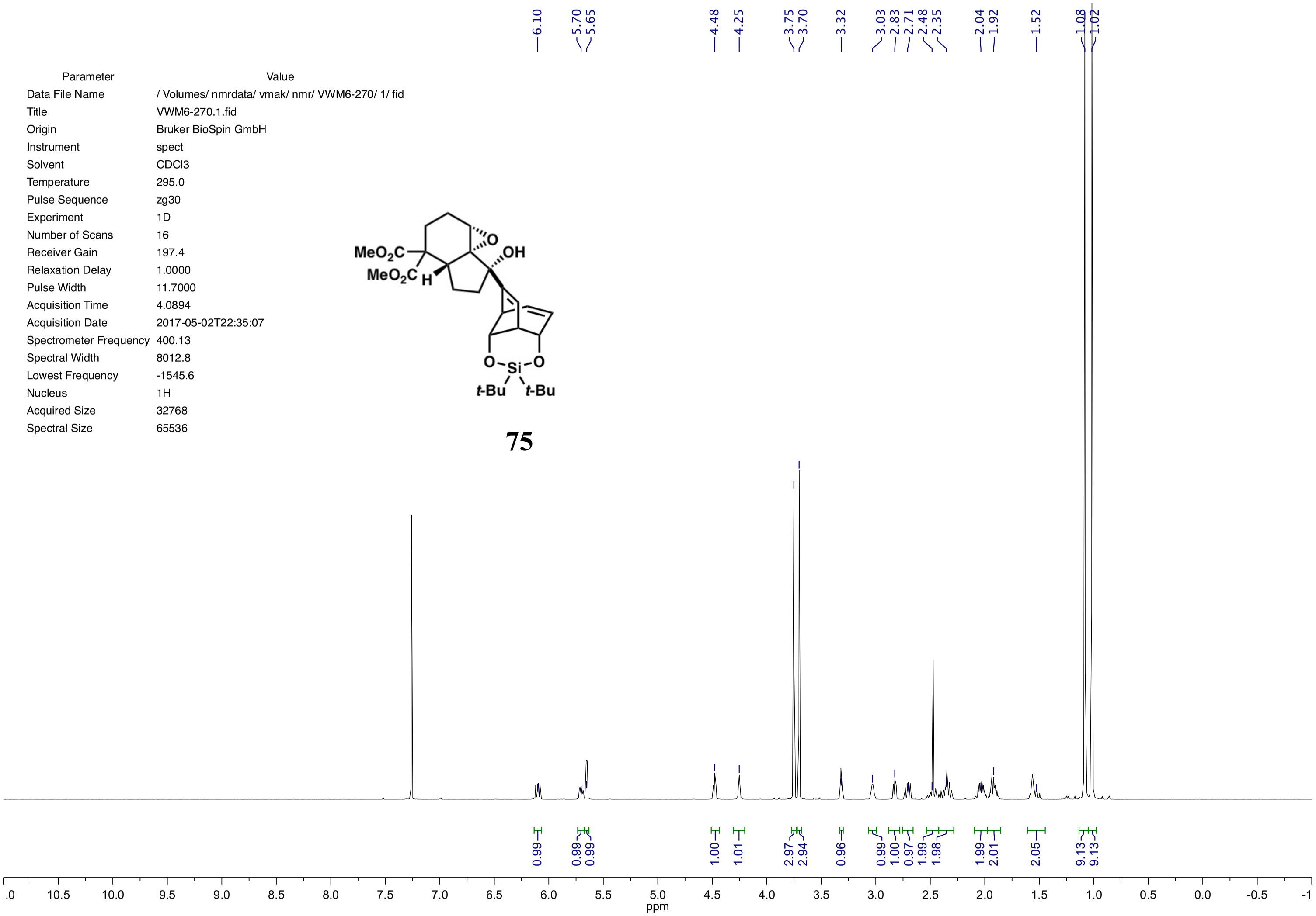
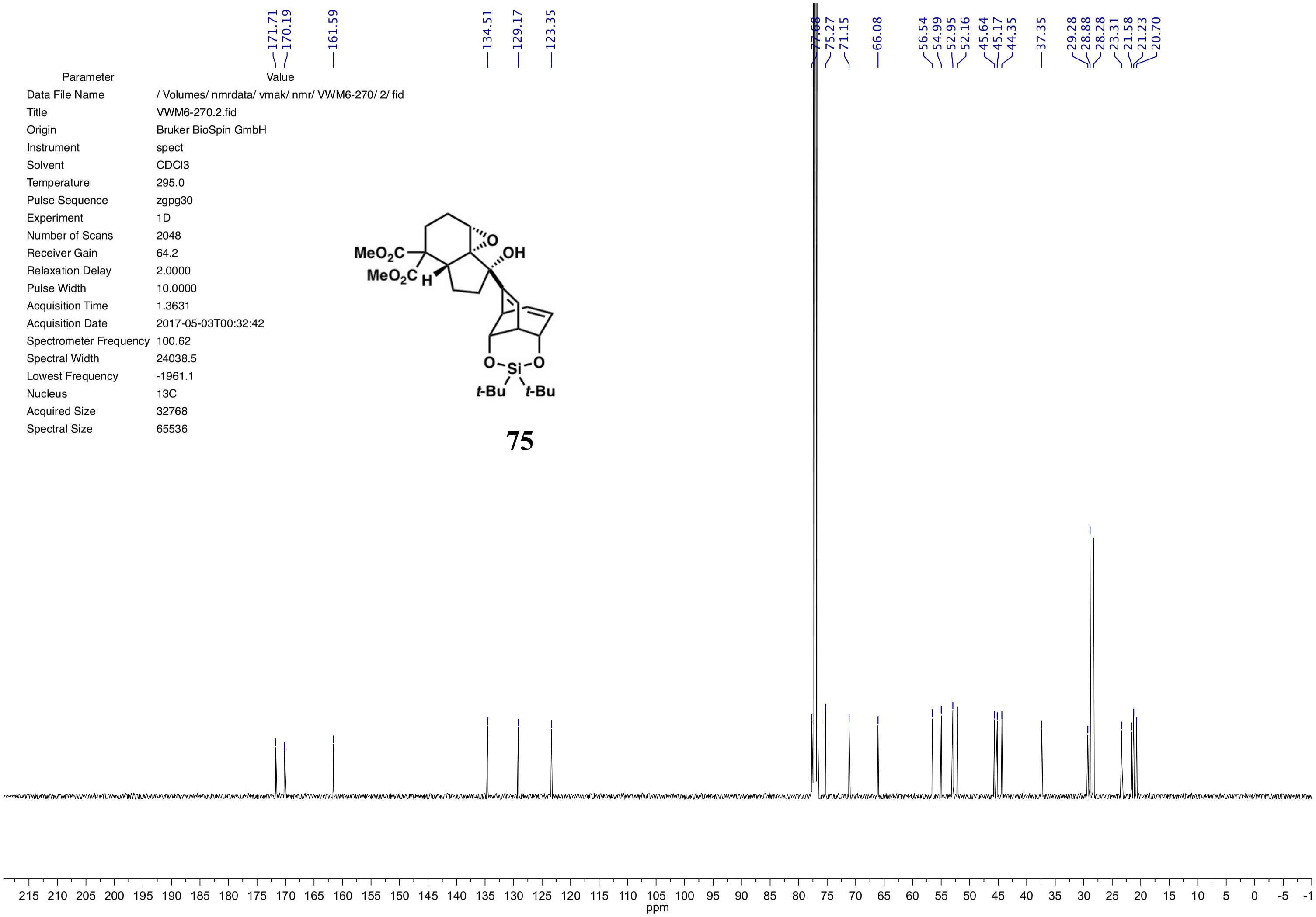


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM6-270/ 1/ fid
Title	VWM6-270.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	zg30
Experiment	1D
Number of Scans	16
Receiver Gain	197.4
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2017-05-02T22:35:07
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

75



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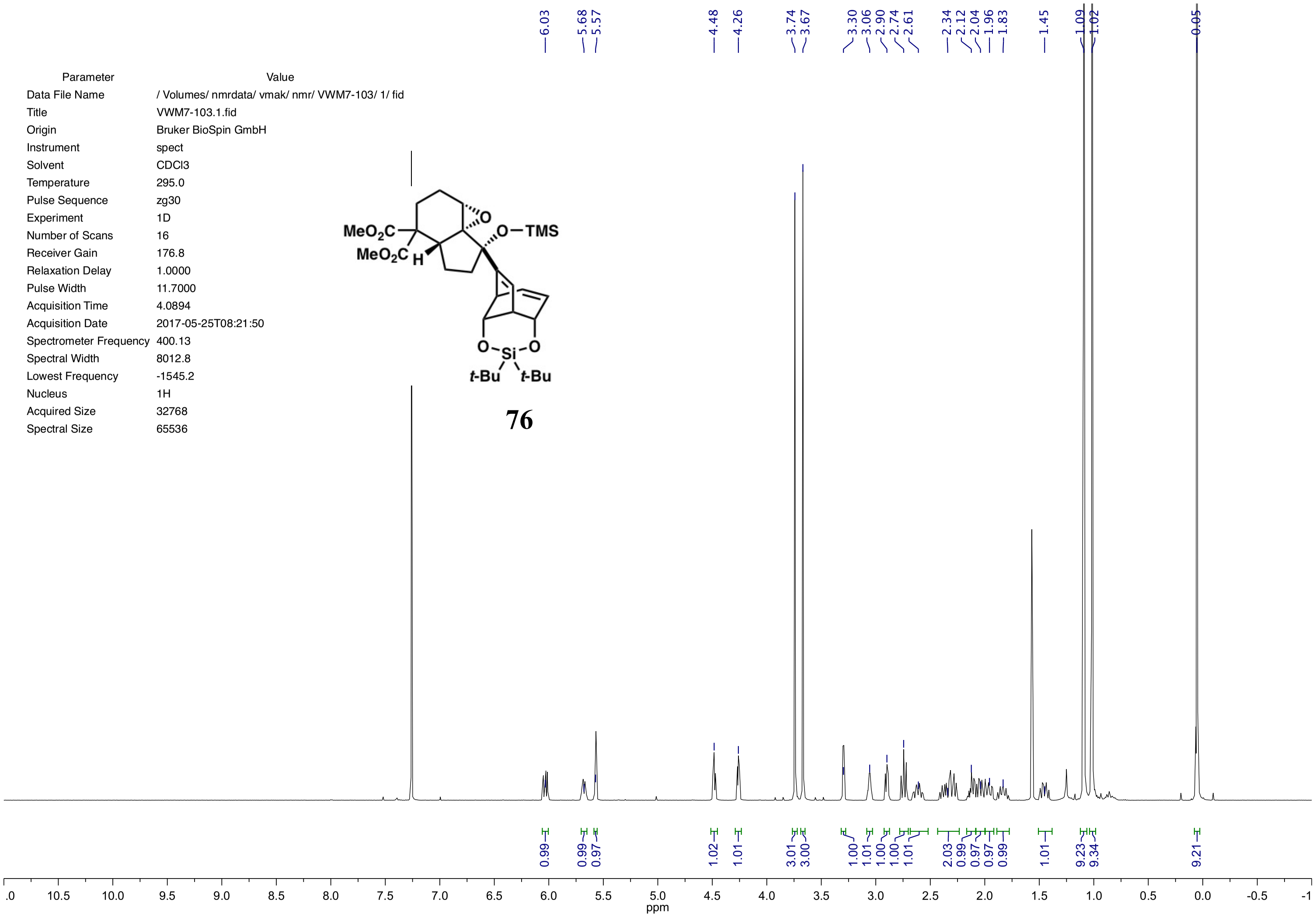
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM6-270/ 2/ fid
Title	VWM6-270.2.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	2048
Receiver Gain	64.2
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2017-05-03T00:32:42
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.1
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM7-103/ 1/ fid
Title	VWM7-103.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
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	2017-05-25T08:21:50
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.2
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



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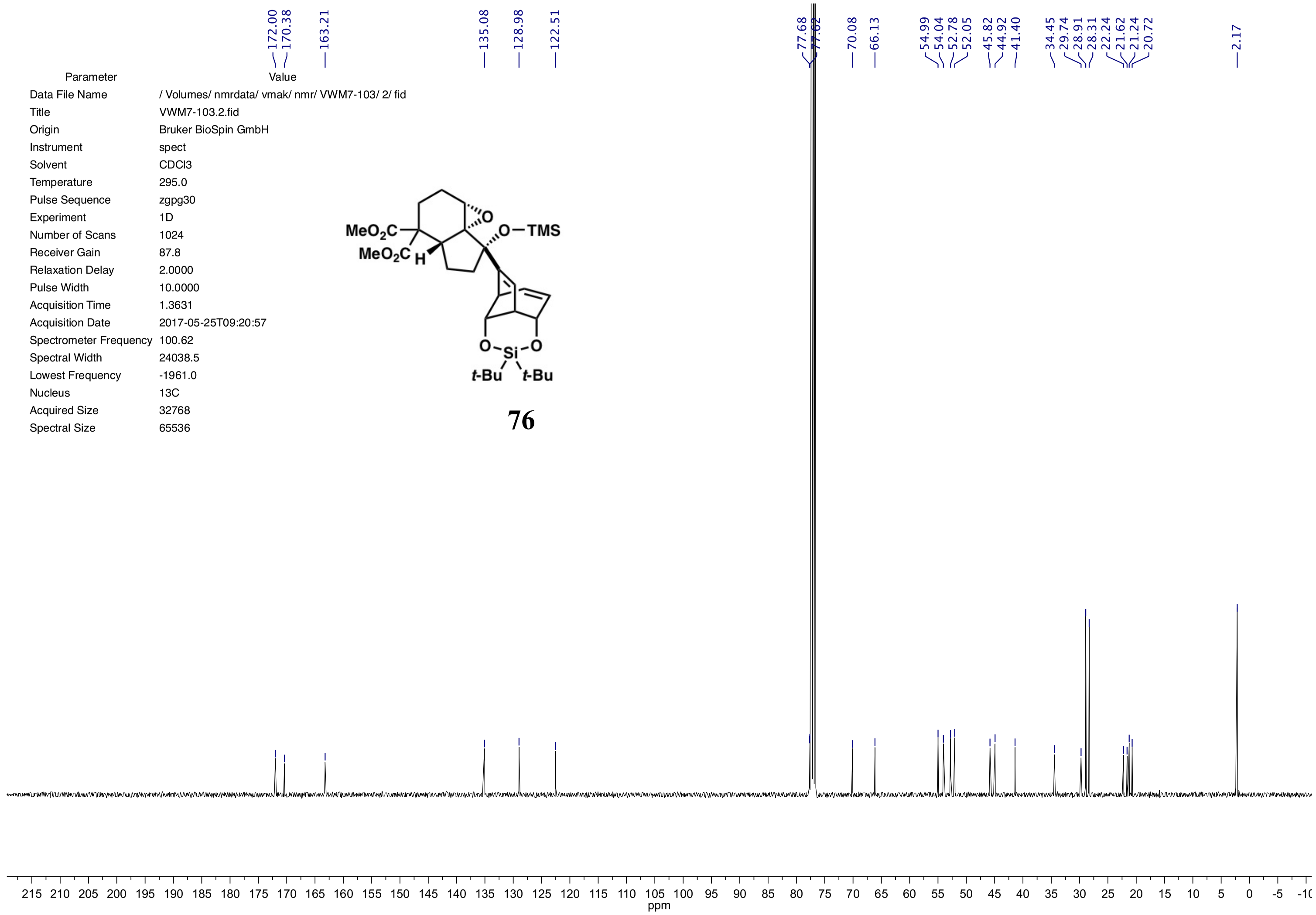

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM7-103/ 2/ fid
Title	VWM7-103.2.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1024
Receiver Gain	87.8
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2017-05-25T09:20:57
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.0
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

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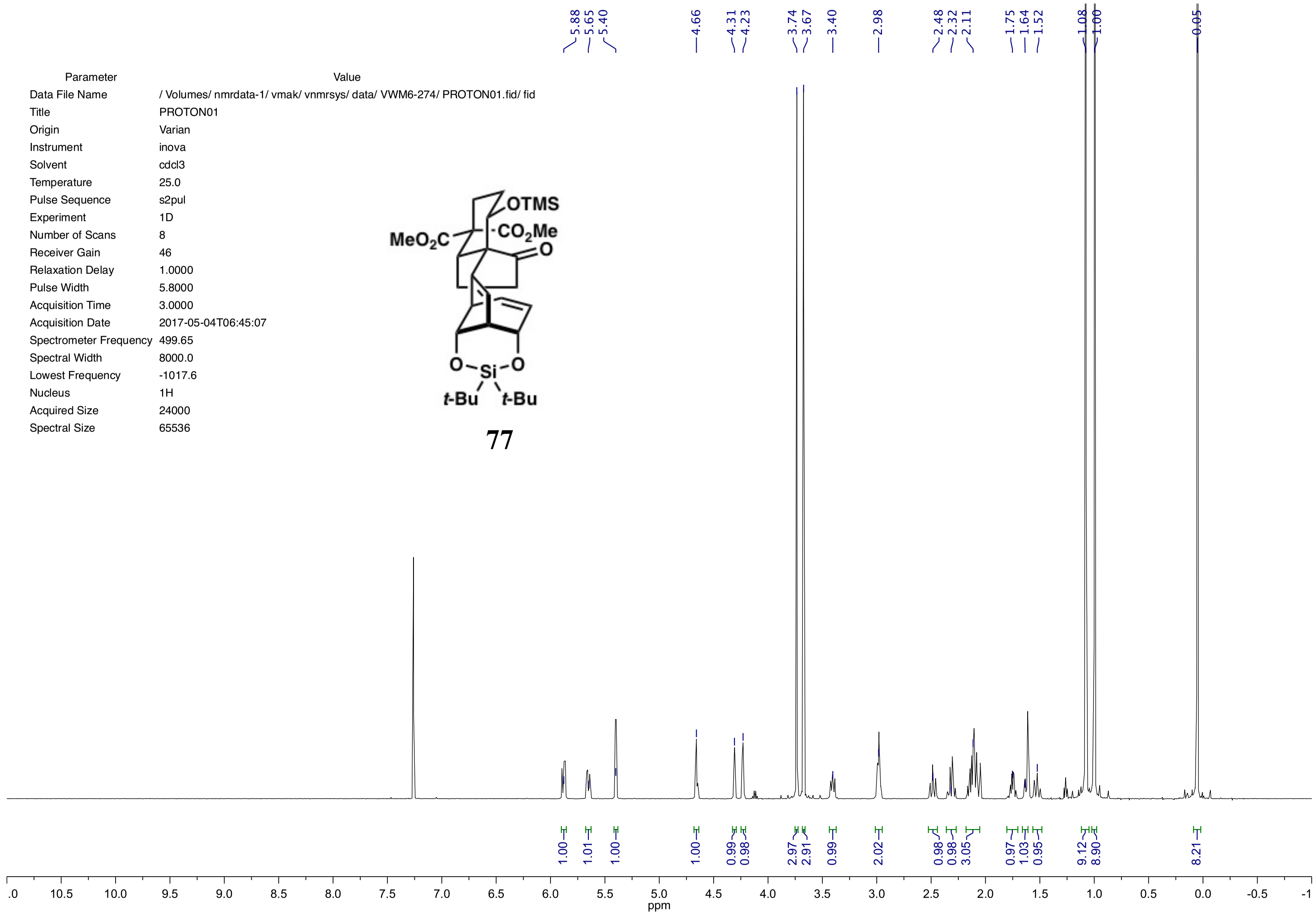

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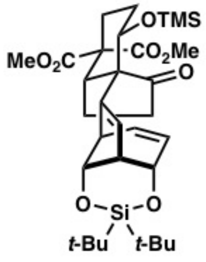
Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ vmak/ vnmrsys/ data/ VWM6-274/ PROTON01.fid/ fid
Title	PROTON01
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	8
Receiver Gain	46
Relaxation Delay	1.0000
Pulse Width	5.8000
Acquisition Time	3.0000
Acquisition Date	2017-05-04T06:45:07
Spectrometer Frequency	499.65
Spectral Width	8000.0
Lowest Frequency	-1017.6
Nucleus	1H
Acquired Size	24000
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ vmak/ vnmrsys/ data/ VWM6-274/ CARBON01.fid/ fid
Title	CARBON01
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	2000
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	4.6125
Acquisition Time	1.0420
Acquisition Date	2017-05-04T06:45:56
Spectrometer Frequency	125.65
Spectral Width	31446.5
Lowest Frequency	-1902.9
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



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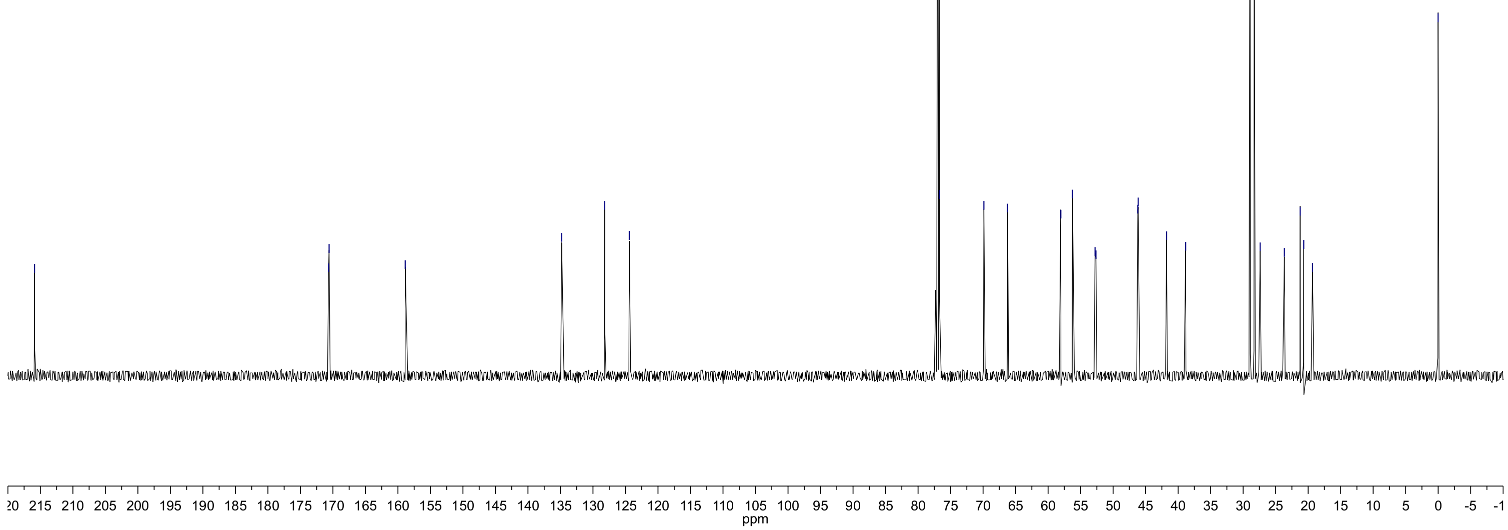
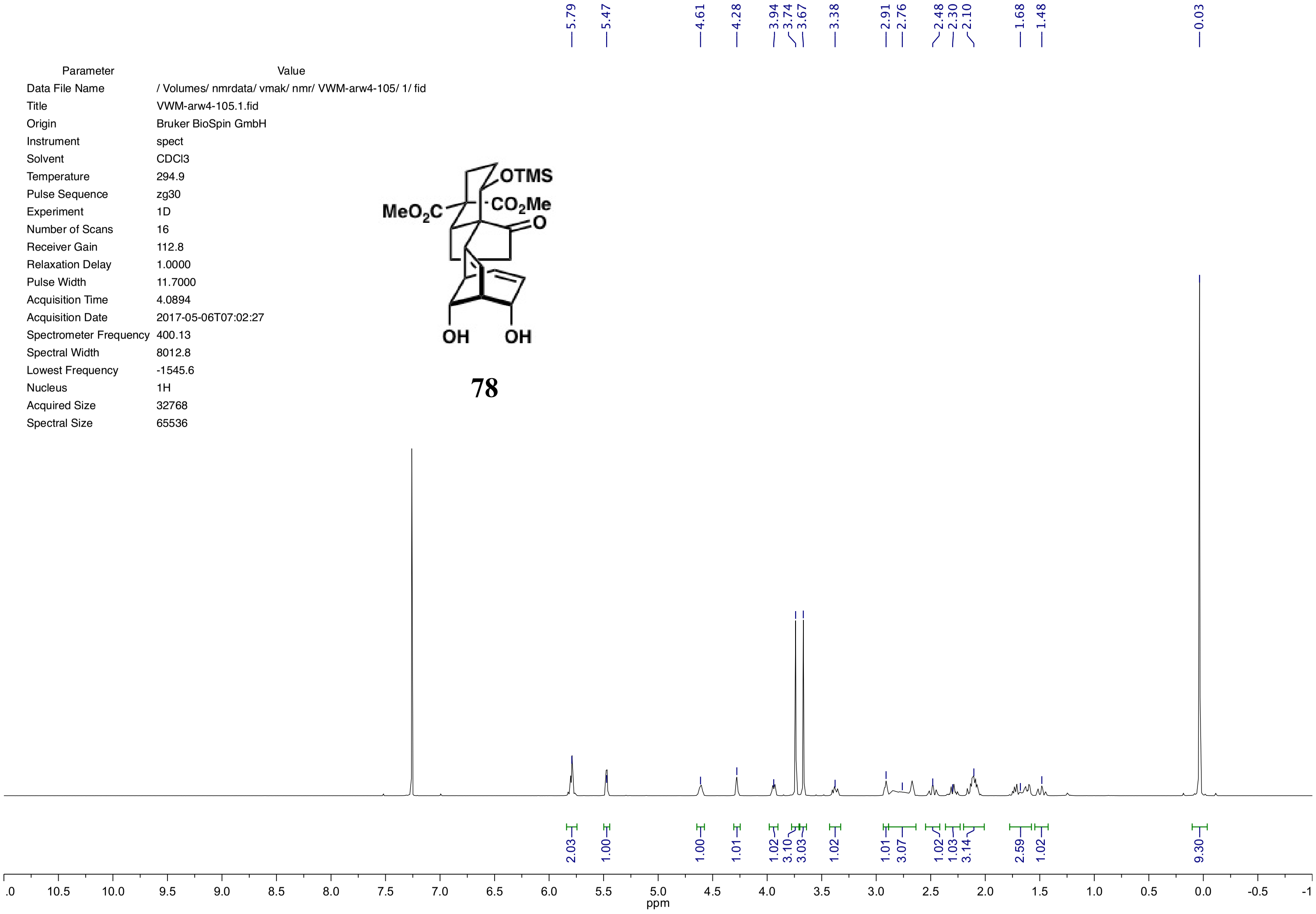


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM-arw4-105/ 1/ fid
Title	VWM-arw4-105.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	294.9
Pulse Sequence	zg30
Experiment	1D
Number of Scans	16
Receiver Gain	112.8
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2017-05-06T07:02:27
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



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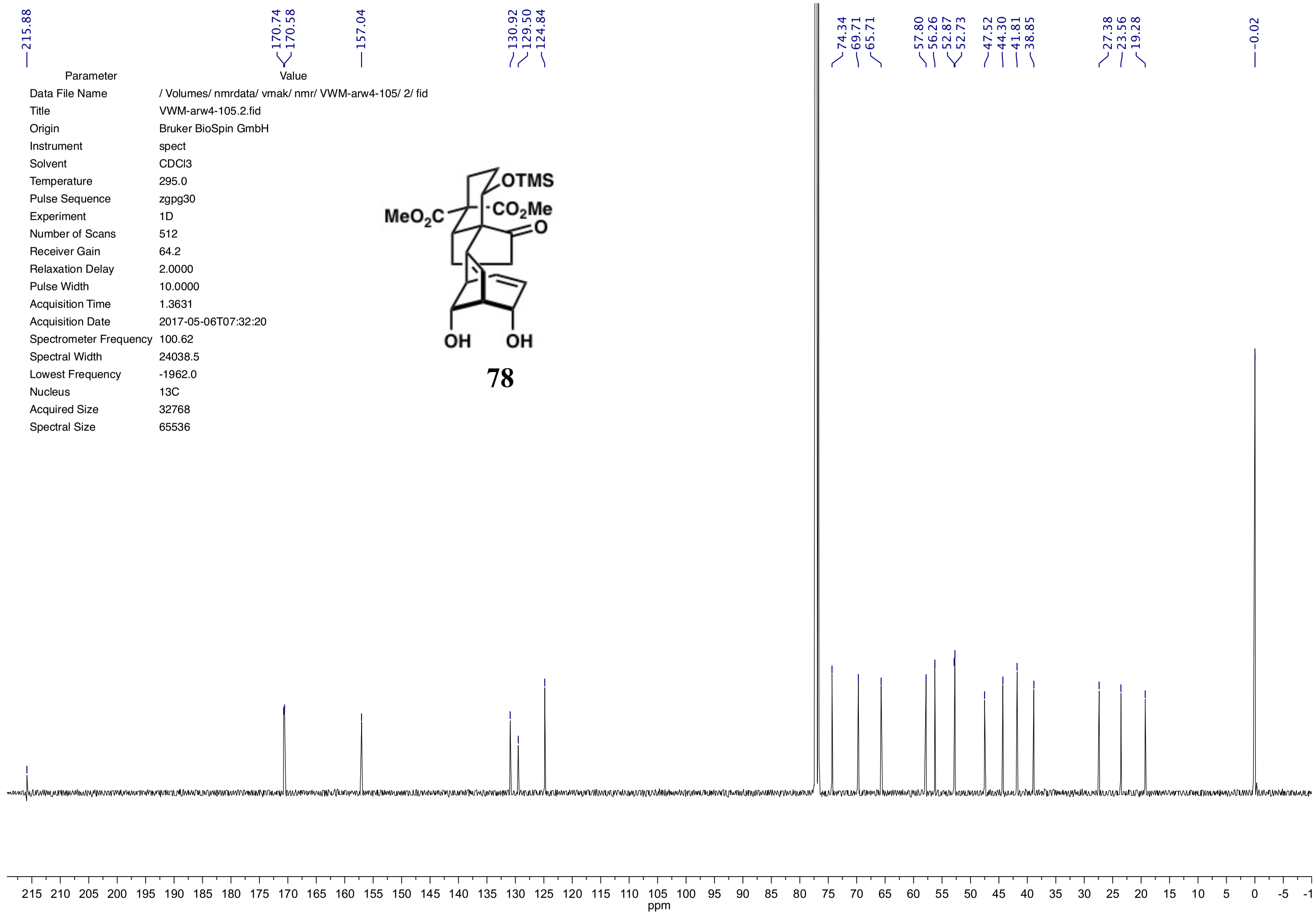

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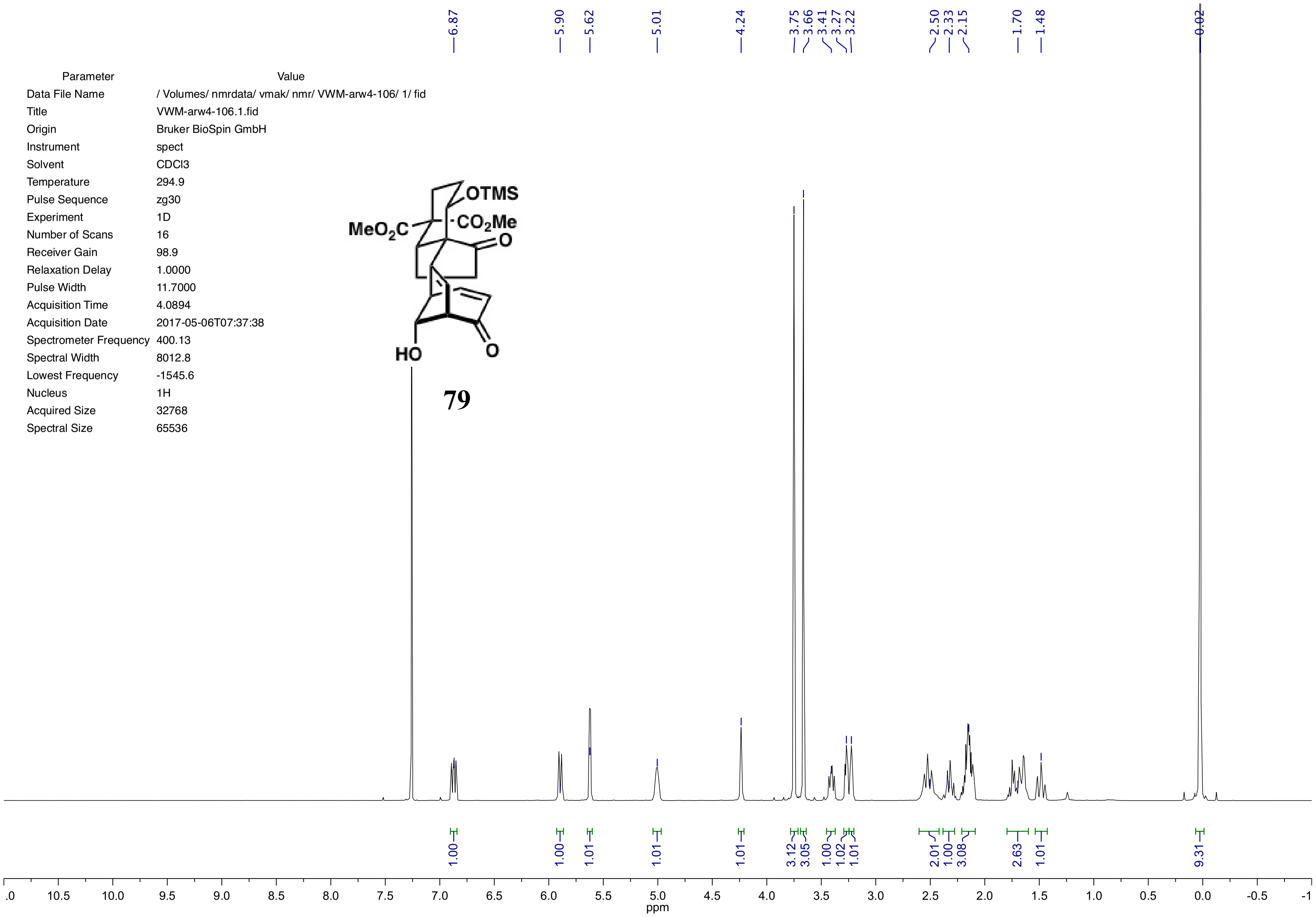
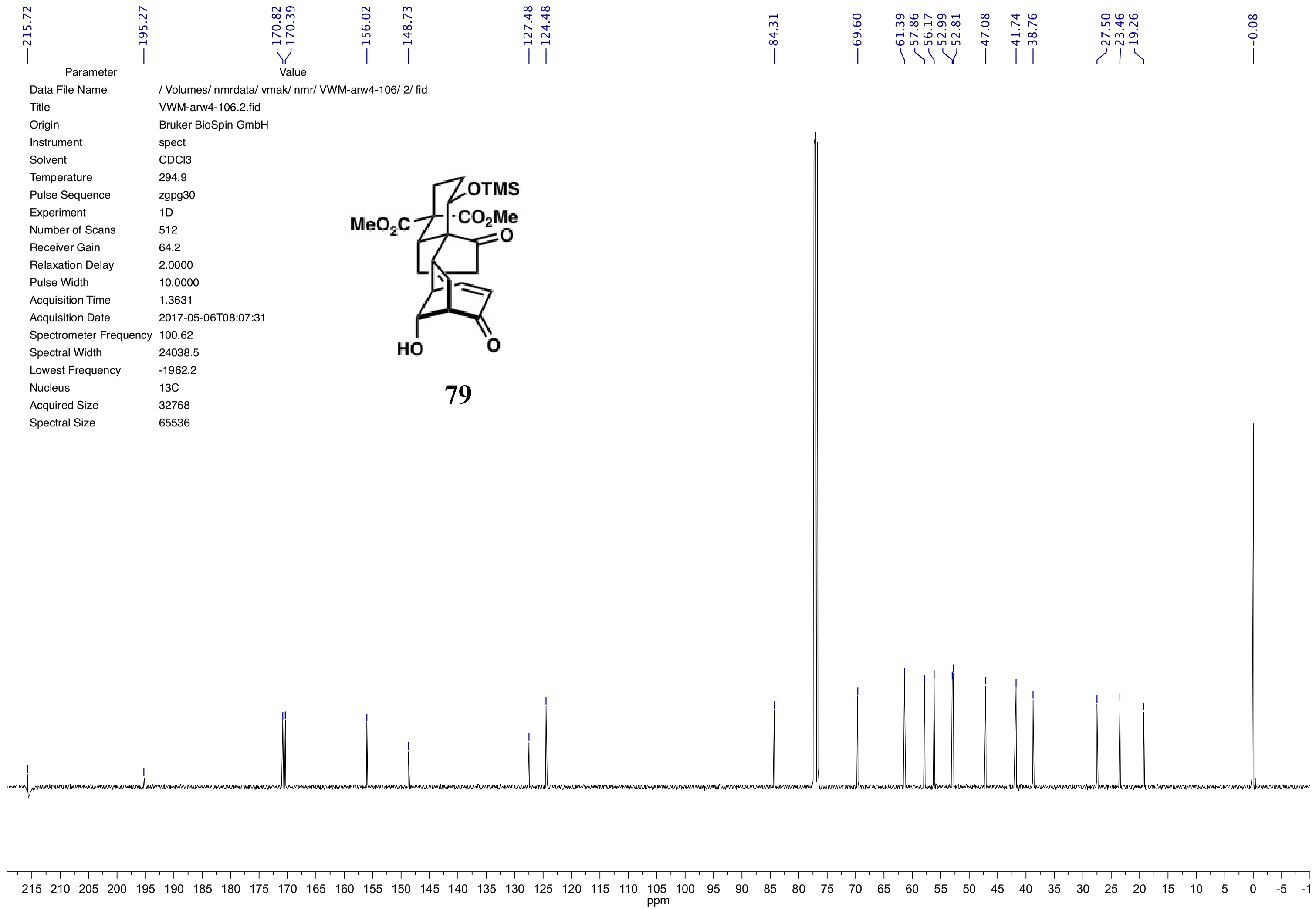
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM-arw4-105/ 2/ fid
Title	VWM-arw4-105.2.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	512
Receiver Gain	64.2
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2017-05-06T07:32:20
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1962.0
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM-arw4-106/ 1/ fid
Title	VWM-arw4-106.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	294.9
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	2017-05-06T07:37:38
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

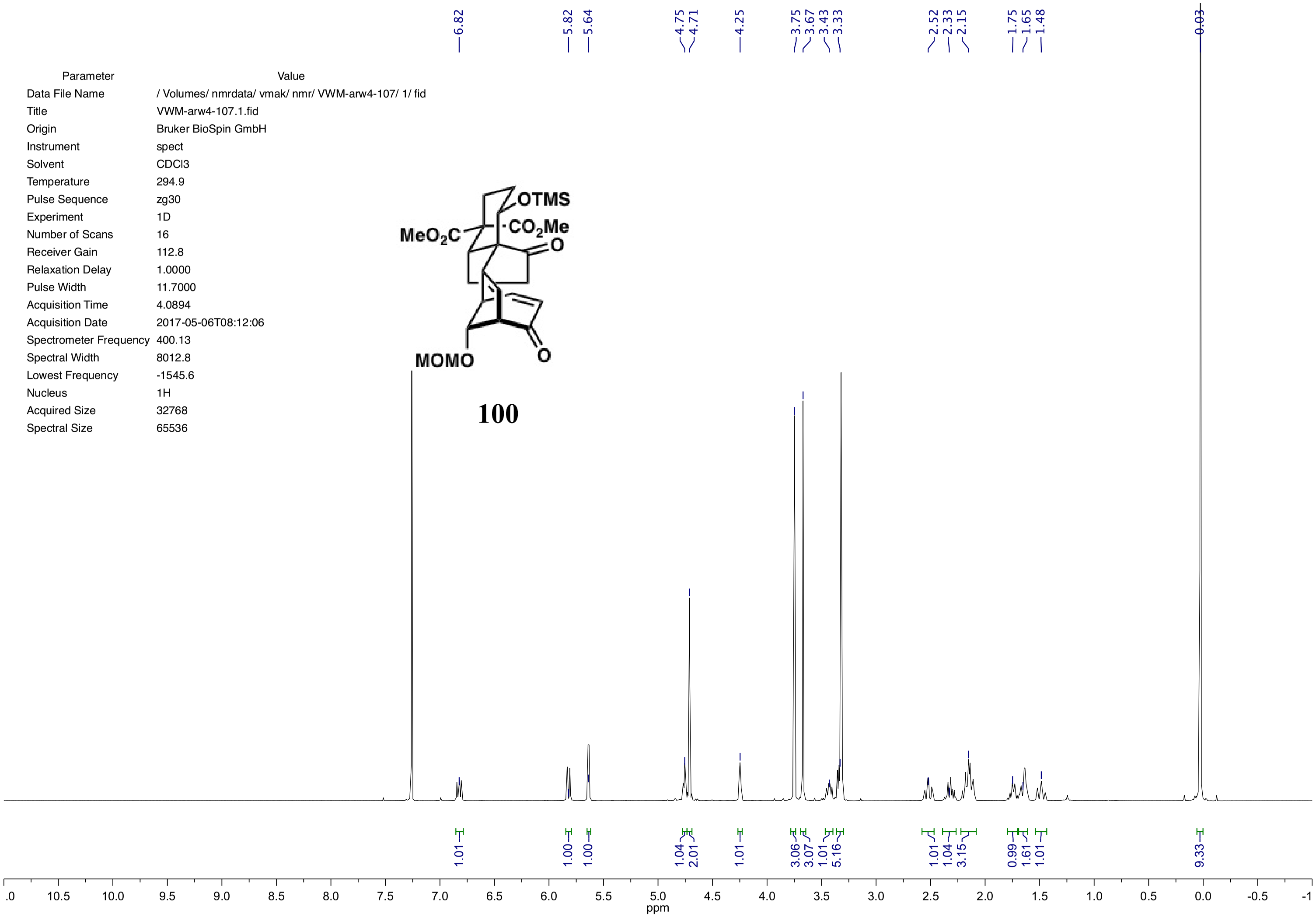


79



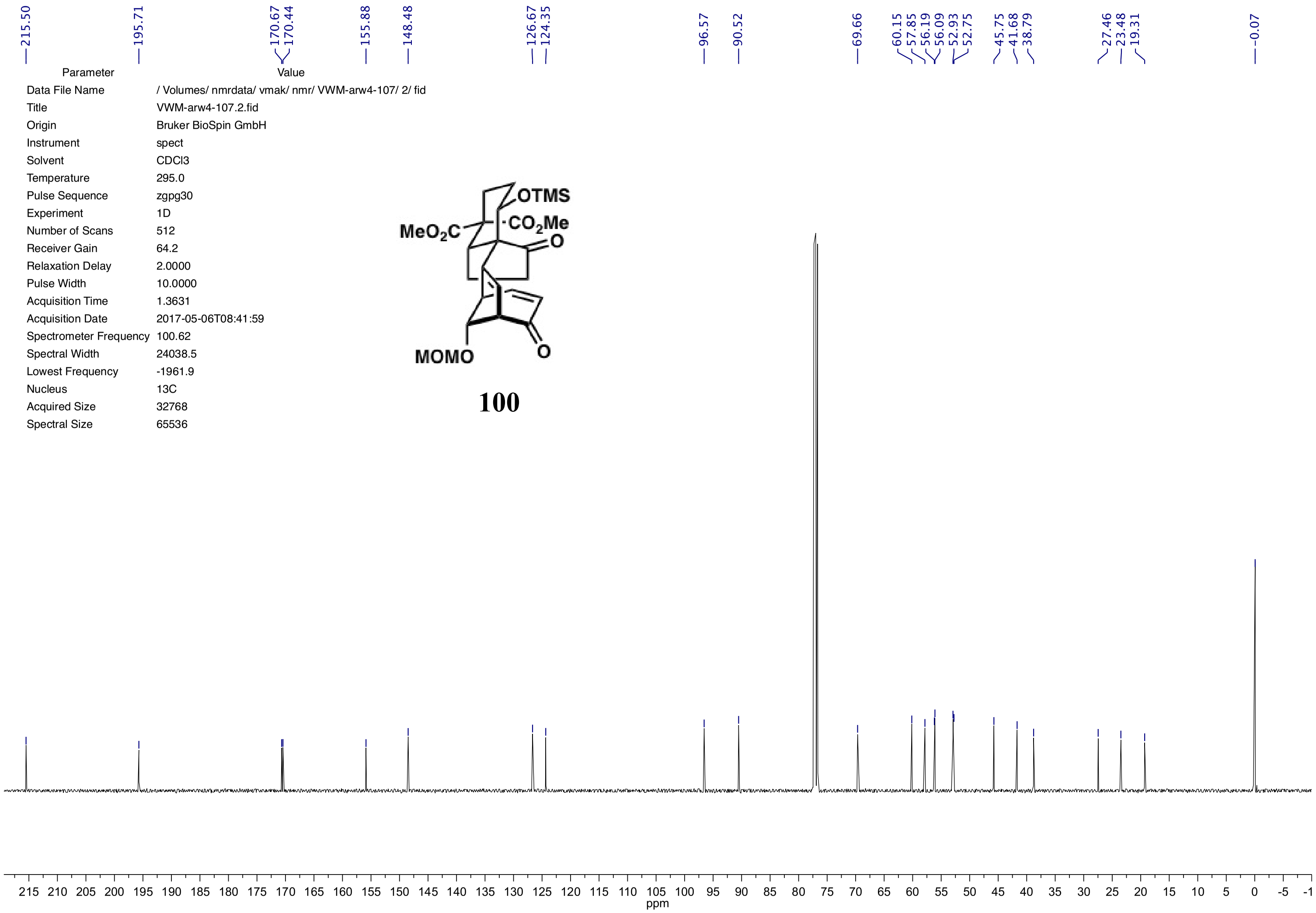
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM-arw4-106/ 2/ fid
Title	VWM-arw4-106.2.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	294.9
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	512
Receiver Gain	64.2
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2017-05-06T08:07:31
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1962.2
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

79



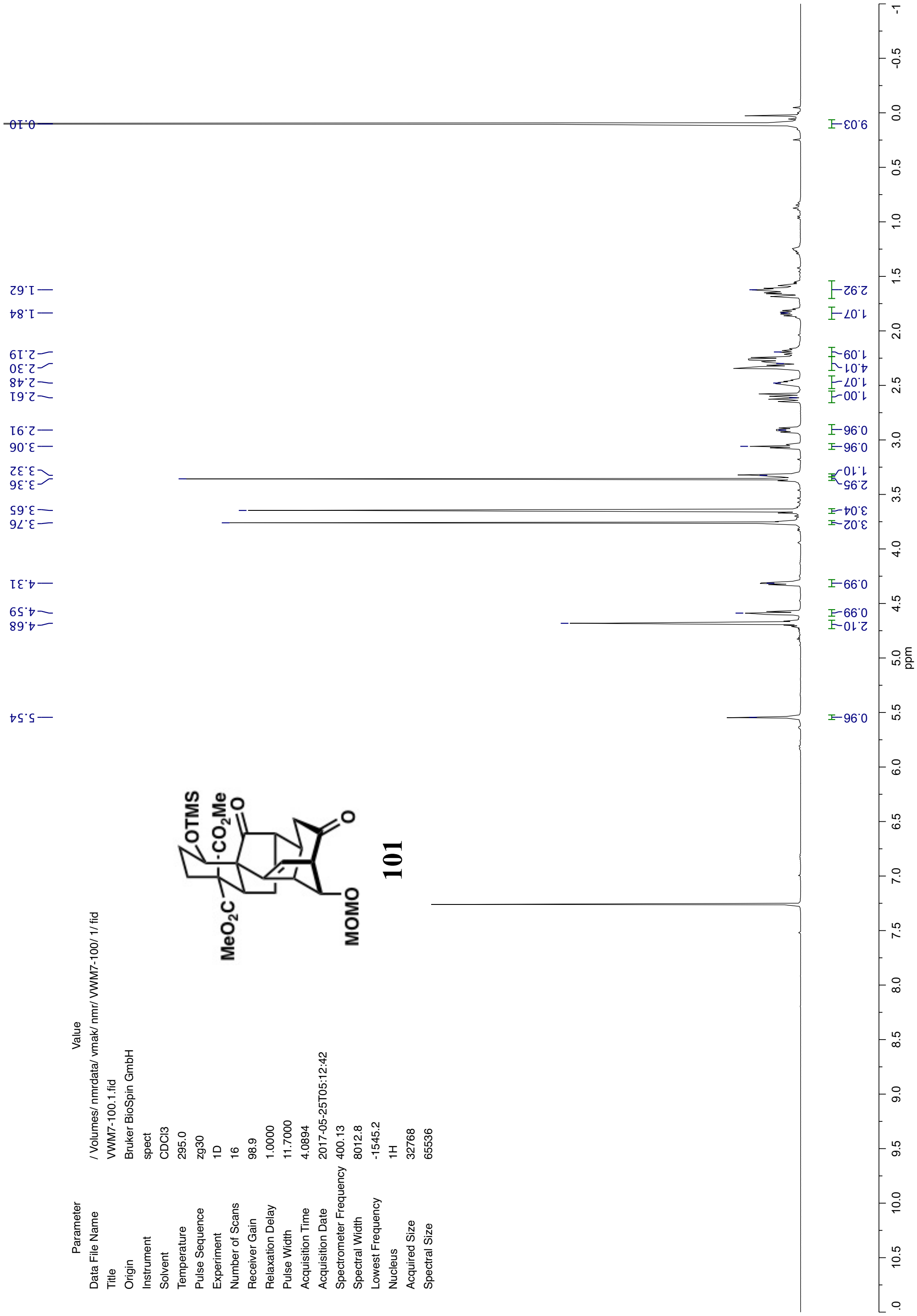
100

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM-arw4-107/ 1/ fid
Title	VWM-arw4-107.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
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	2017-05-06T08:12:06
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



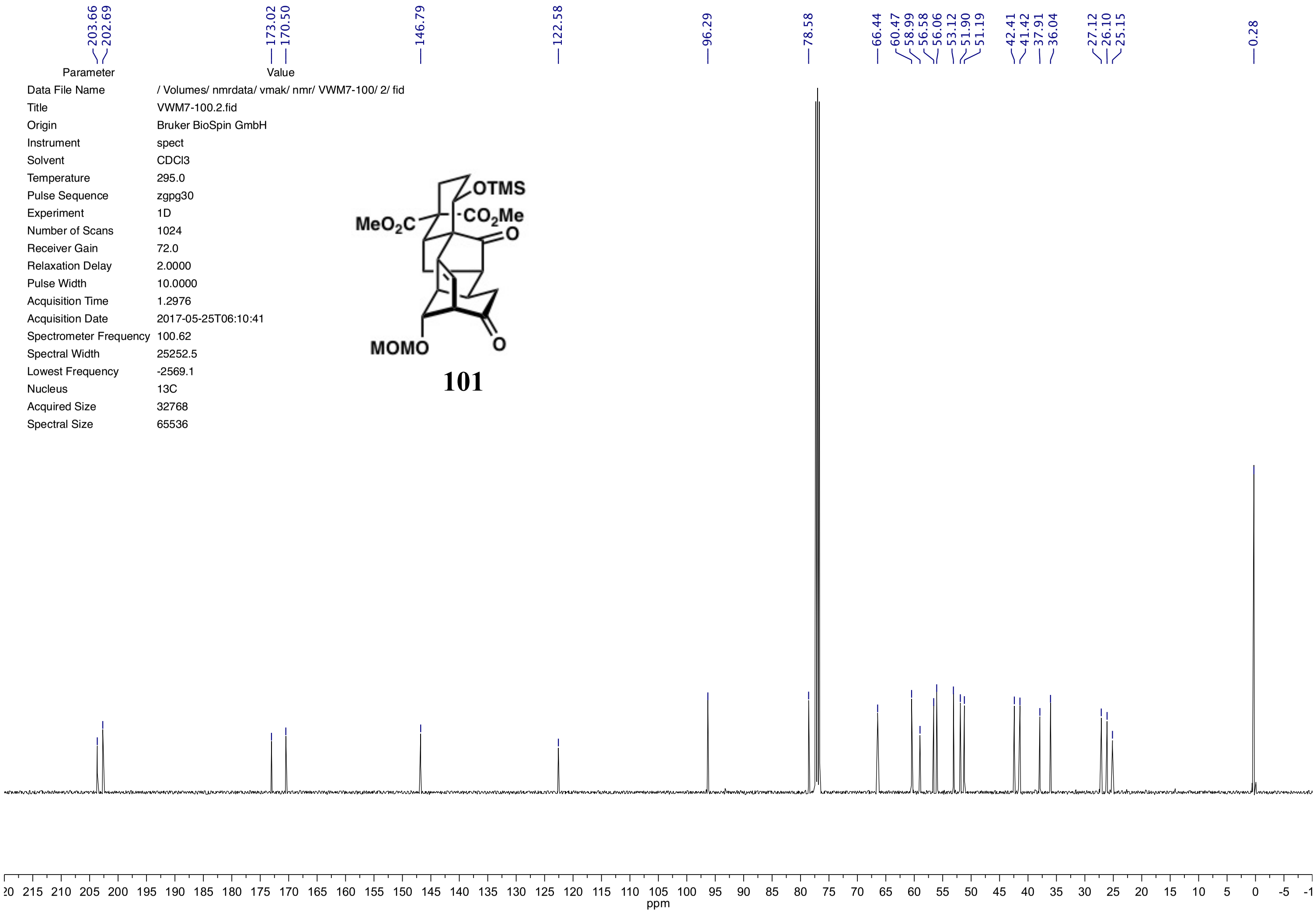
100

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM-arw4-107/ 2/ fid
Title	VWM-arw4-107.2.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
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	2017-05-06T08:41:59
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.9
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



101

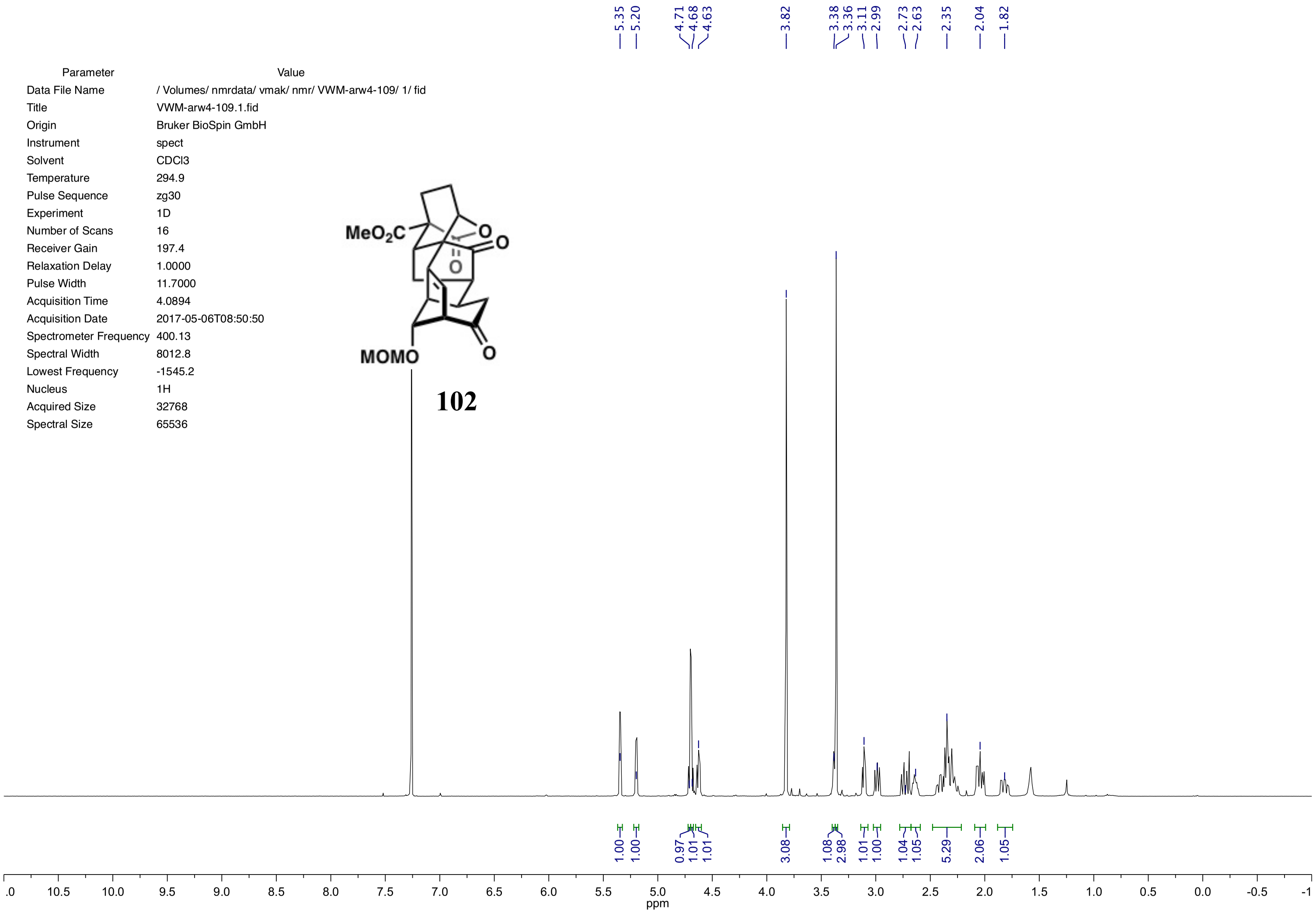
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM7-100/ 1/ fid
Title	VWM7-100.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	zg30
Experiment	1D
Number of Scans	16
Receiver Gain	98.9
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2017-05-25T05:12:42
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.2
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



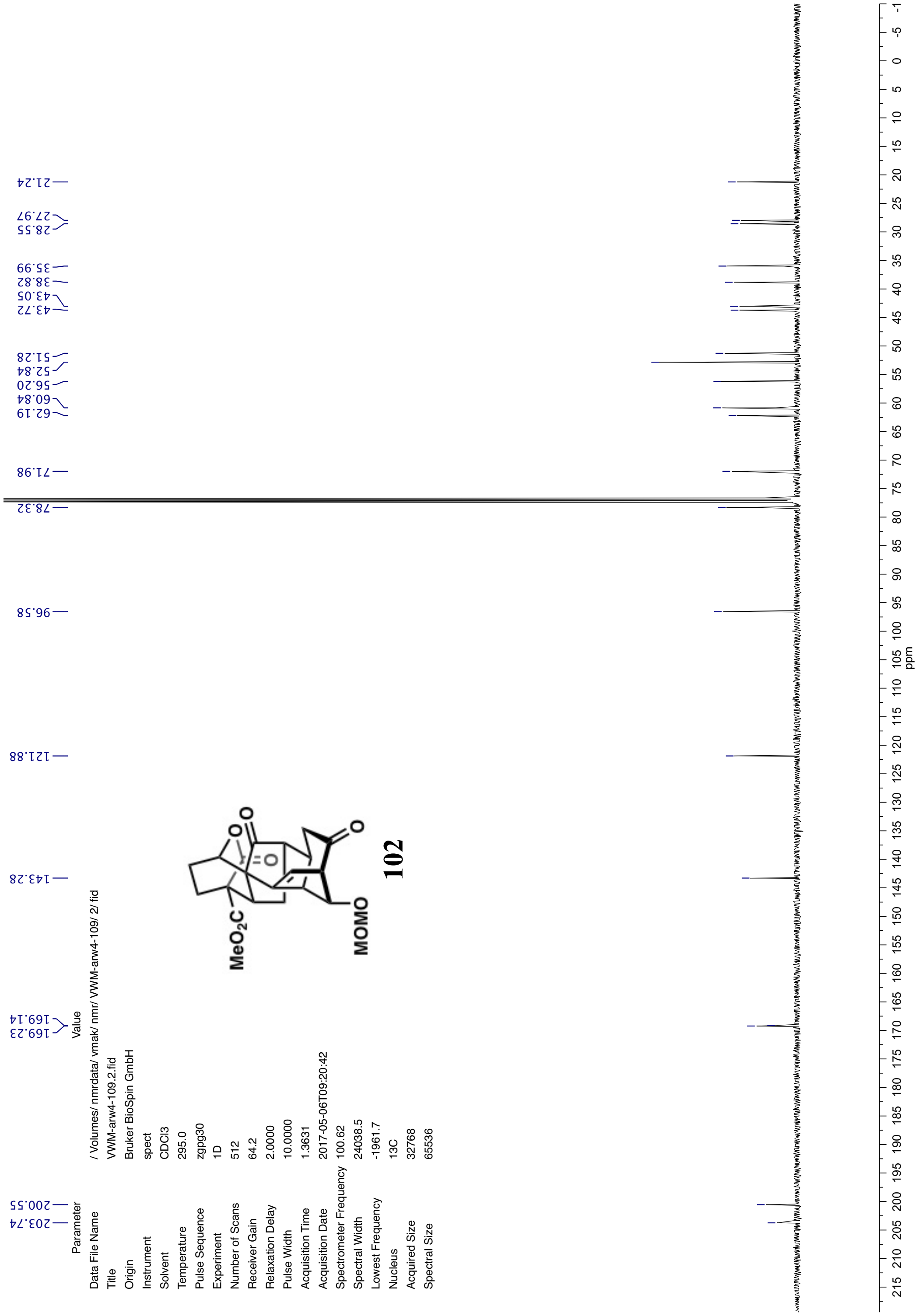
101

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM7-100/ 2/ fid
Title	VWM7-100.2.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1024
Receiver Gain	72.0
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.2976
Acquisition Date	2017-05-25T06:10:41
Spectrometer Frequency	100.62
Spectral Width	25252.5
Lowest Frequency	-2569.1
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM-arw4-109/ 1/ fid
Title	VWM-arw4-109.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	294.9
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	2017-05-06T08:50:50
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.2
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

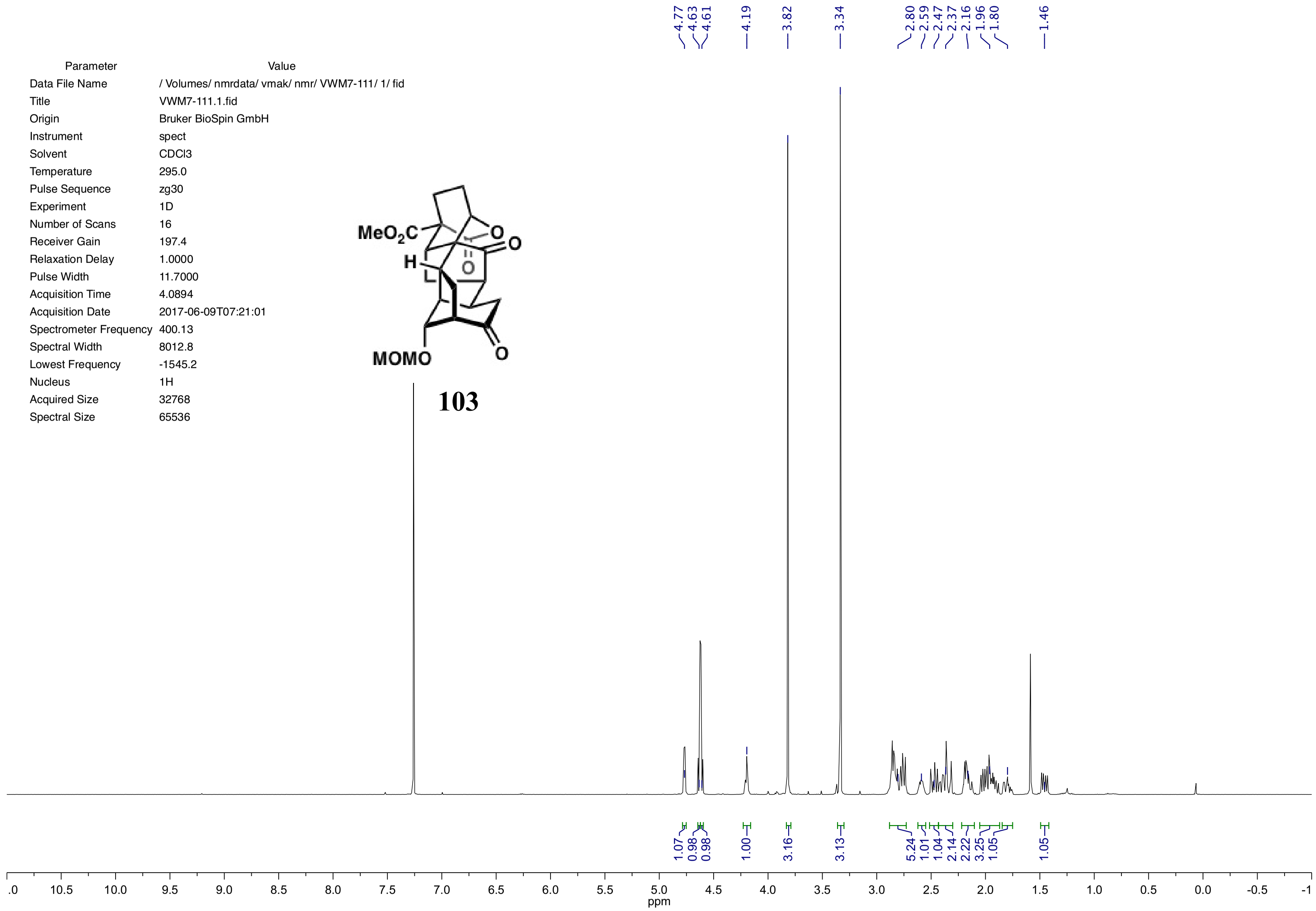


102



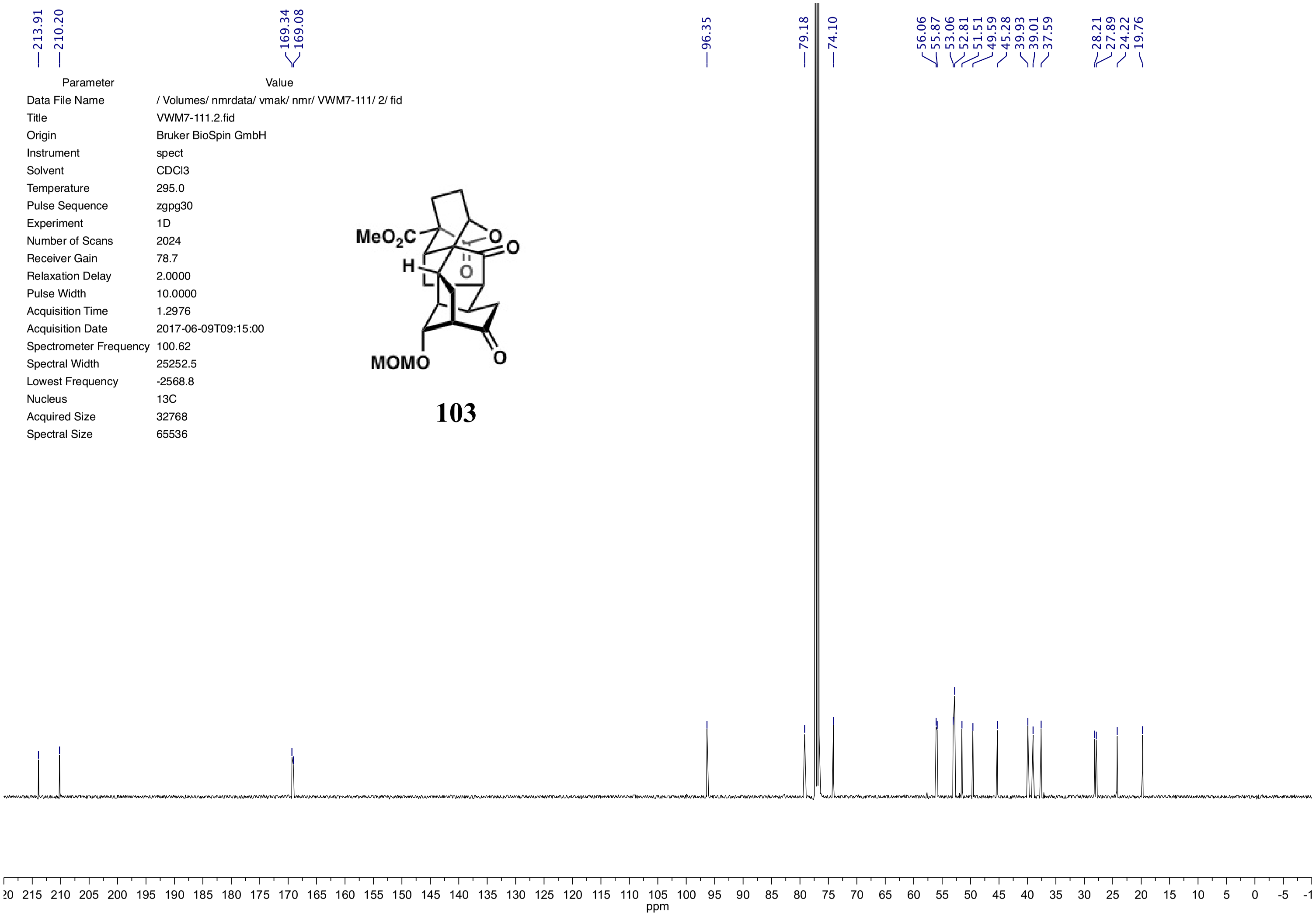
102

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM-arw4-109/ 2/ fid
Title	VWM-arw4-109.2.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
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	2017-05-06T09:20:42
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.7
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



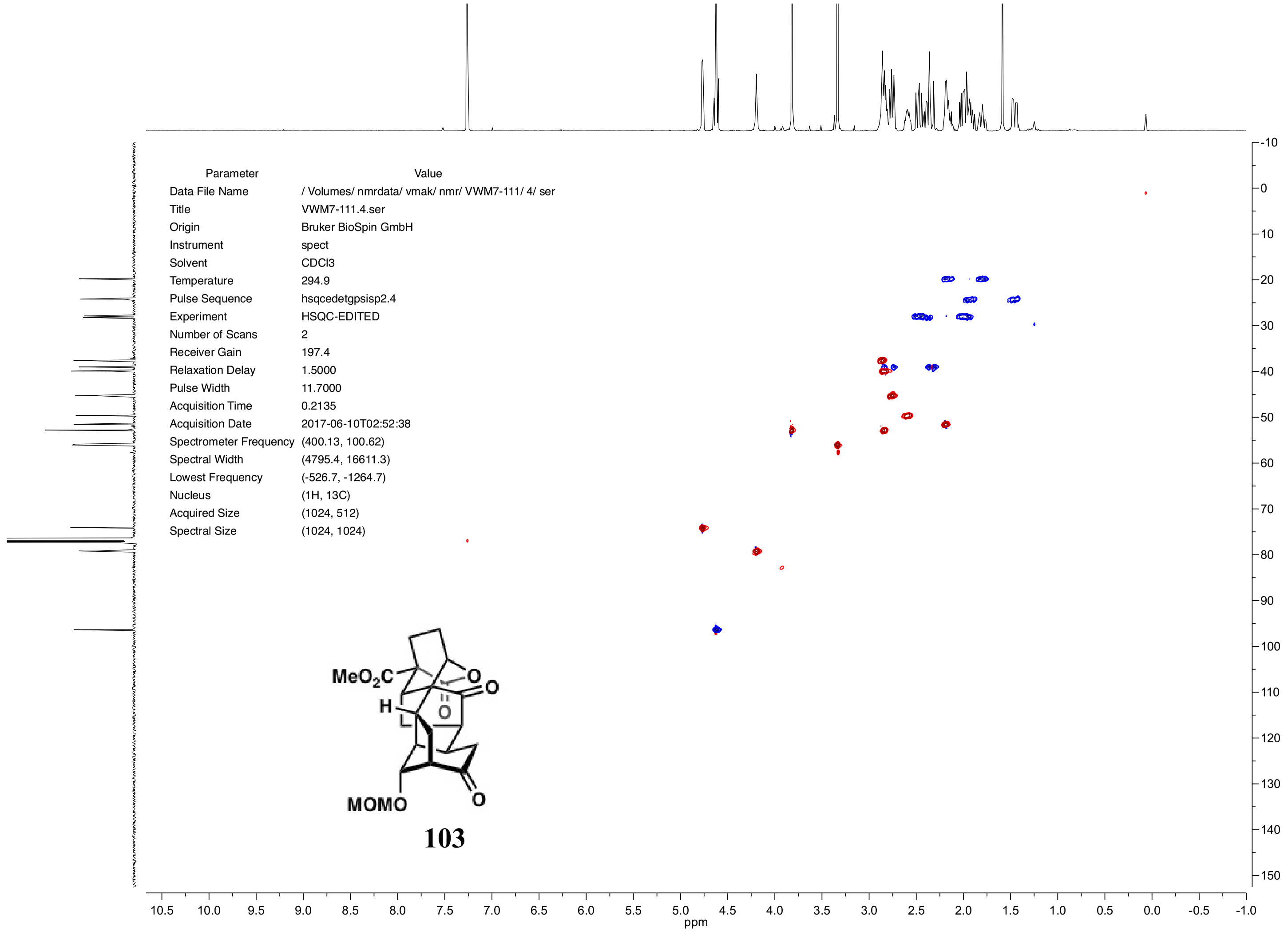
103

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM7-111/ 1/ fid
Title	VWM7-111.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
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	2017-06-09T07:21:01
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.2
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



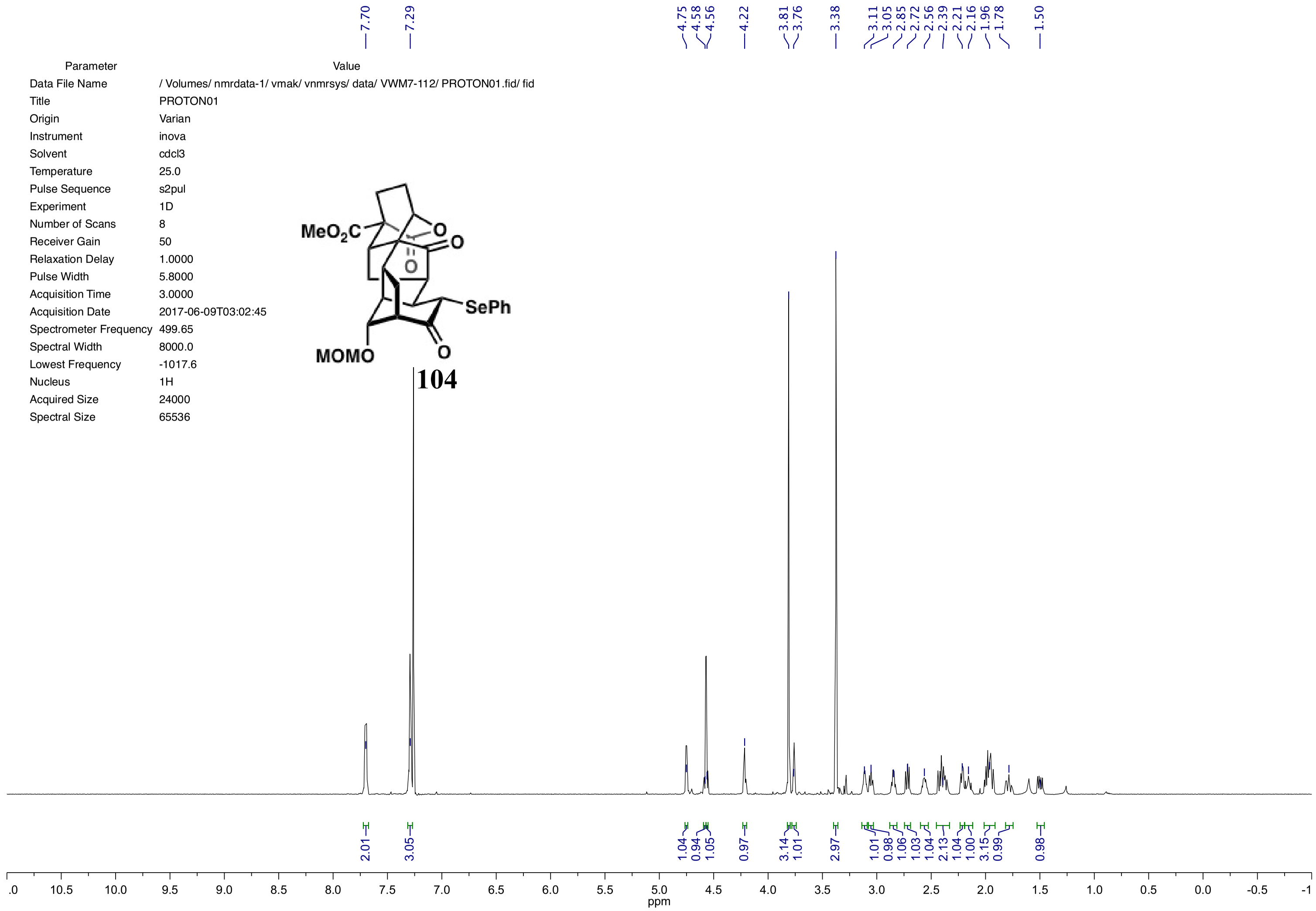
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM7-111/ 2/ fid
Title	VWM7-111.2.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	2024
Receiver Gain	78.7
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.2976
Acquisition Date	2017-06-09T09:15:00
Spectrometer Frequency	100.62
Spectral Width	25252.5
Lowest Frequency	-2568.8
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

103



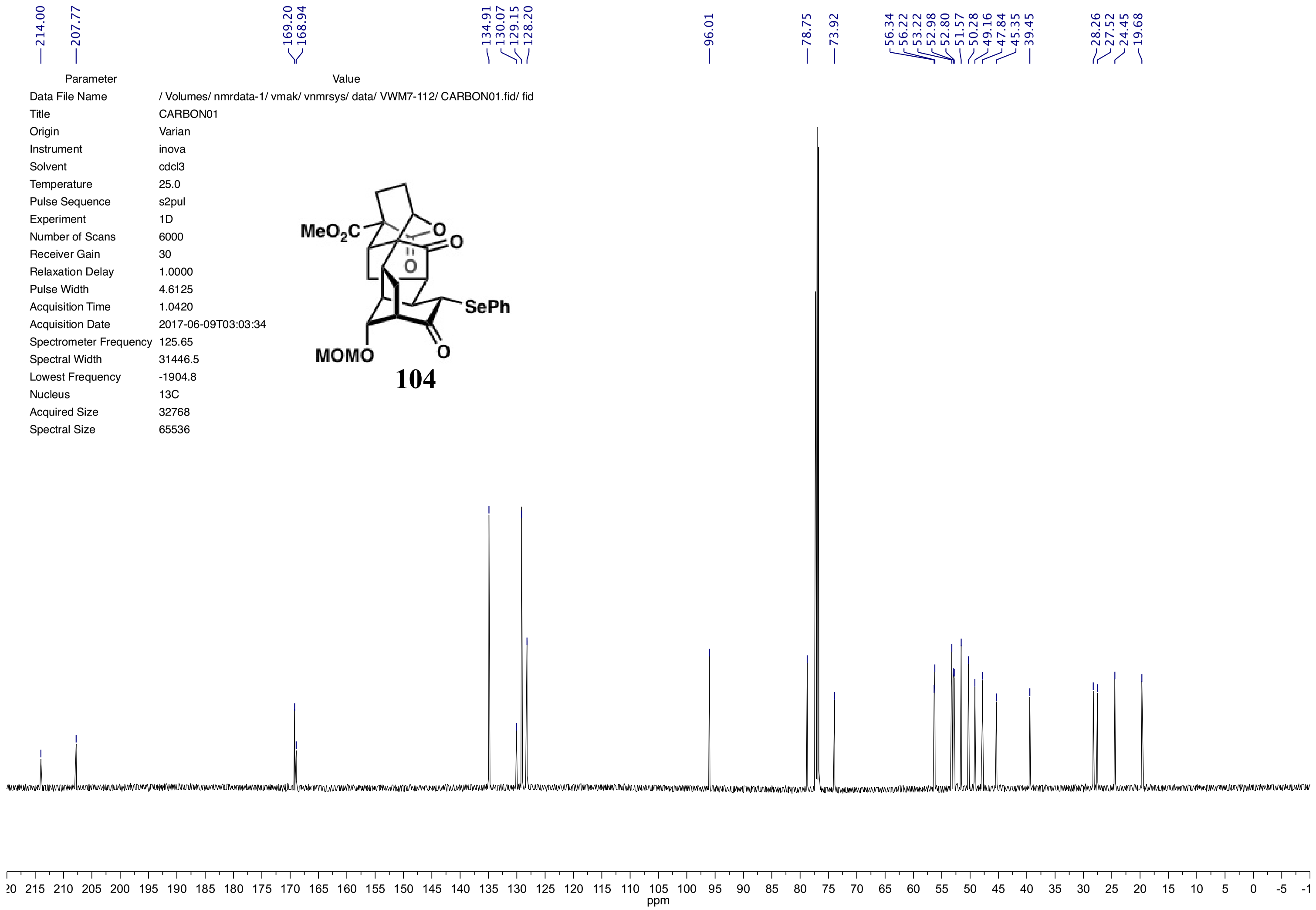
103

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM7-111/ 4/ ser
Title	VWM7-111.4.ser
Origin	Bruker BioSpin GmbH
Instrument	spect
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	2017-06-10T02:52:38
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(4795.4, 16611.3)
Lowest Frequency	(-526.7, -1264.7)
Nucleus	(1H, 13C)
Acquired Size	(1024, 512)
Spectral Size	(1024, 1024)



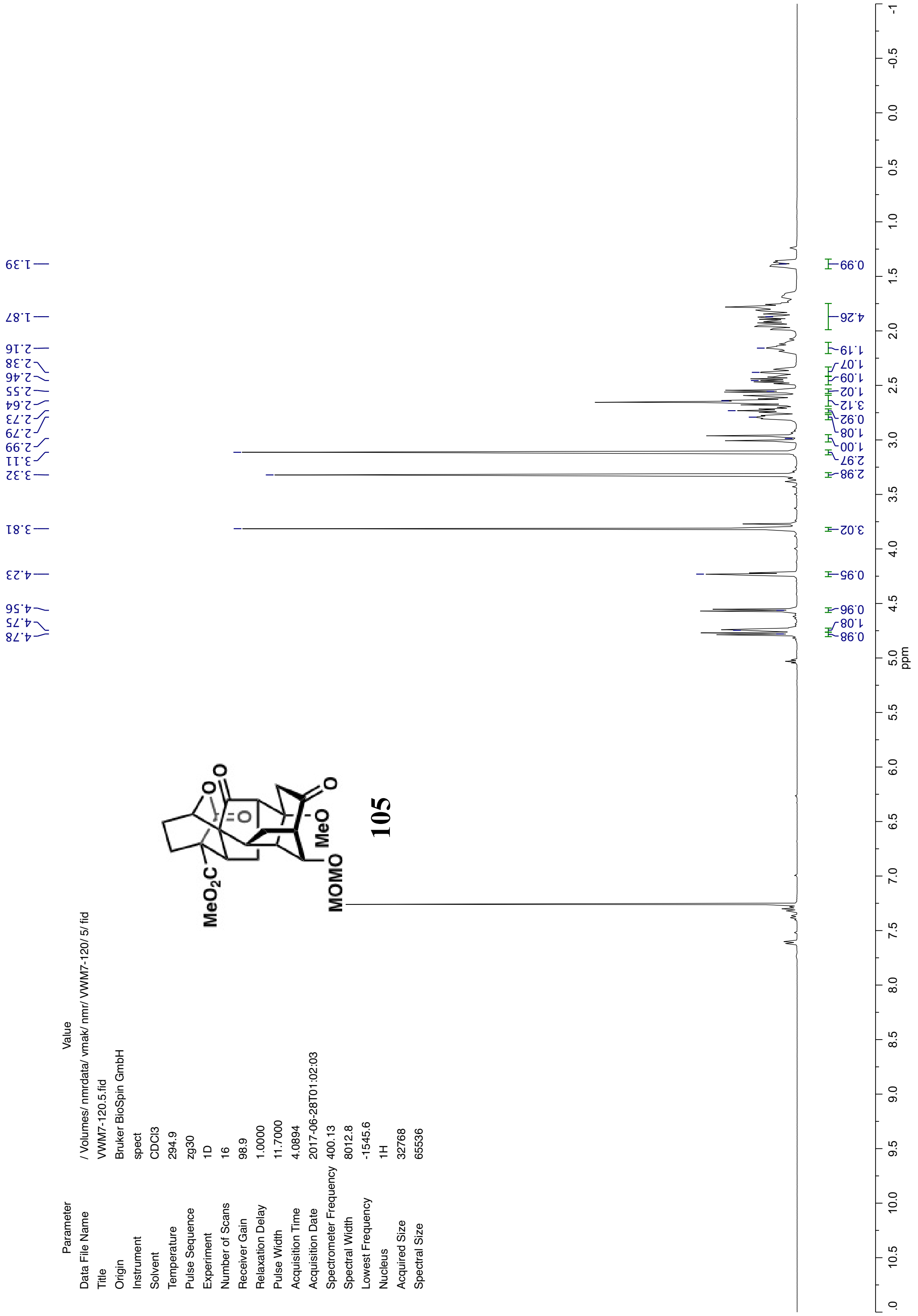
Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ vmak/ vnmrsys/ data/ VWM7-112/ PROTON01.fid/ fid
Title	PROTON01
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	8
Receiver Gain	50
Relaxation Delay	1.0000
Pulse Width	5.8000
Acquisition Time	3.0000
Acquisition Date	2017-06-09T03:02:45
Spectrometer Frequency	499.65
Spectral Width	8000.0
Lowest Frequency	-1017.6
Nucleus	1H
Acquired Size	24000
Spectral Size	65536

104



104

Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ vmak/ vnmrsys/ data/ VWM7-112/ CARBON01.fid/ fid
Title	CARBON01
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	6000
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	4.6125
Acquisition Time	1.0420
Acquisition Date	2017-06-09T03:03:34
Spectrometer Frequency	125.65
Spectral Width	31446.5
Lowest Frequency	-1904.8
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

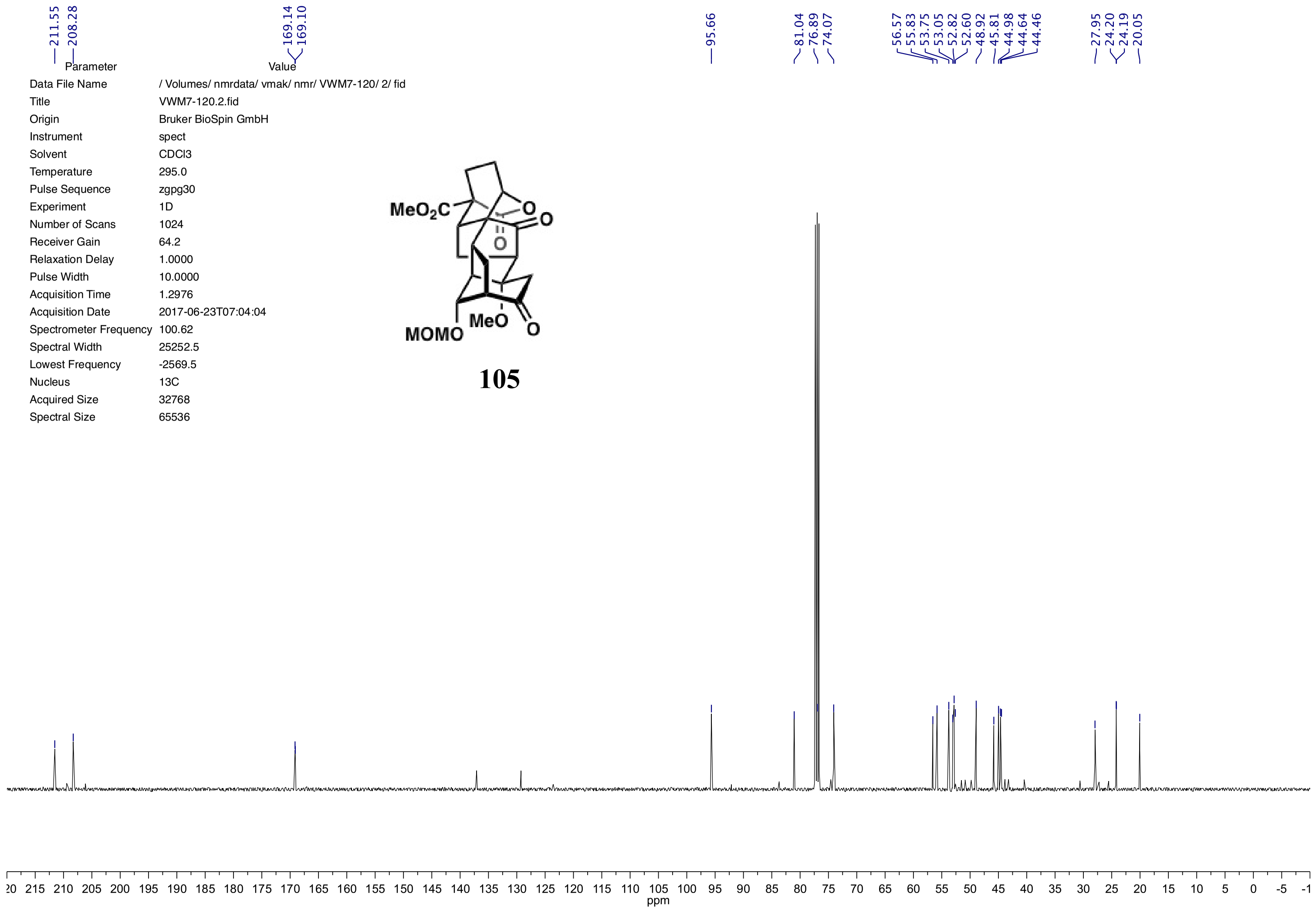


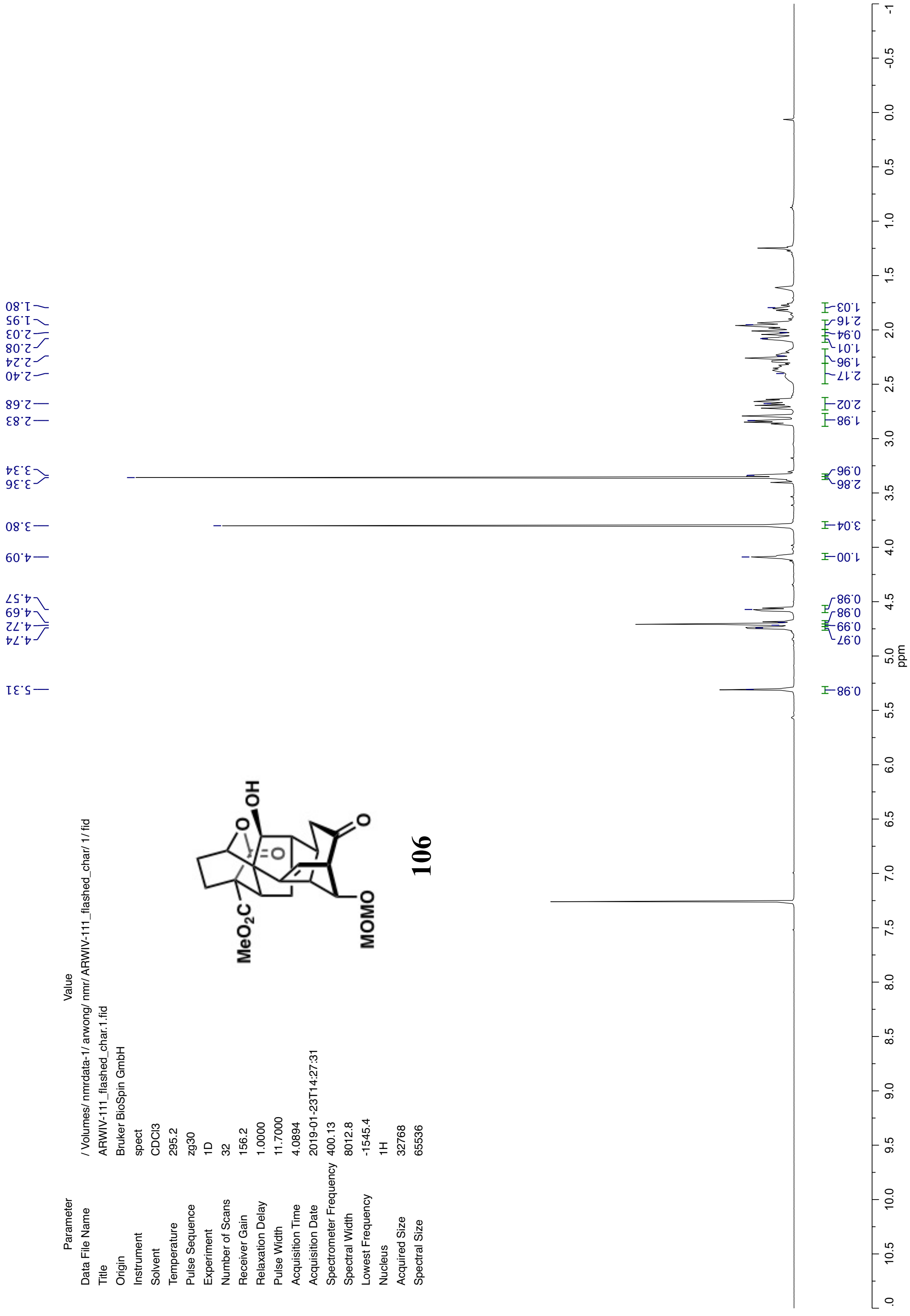
105

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM7-120/ 5/ fid
Title	VWM7-120.5.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	294.9
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	2017-06-28T01:02:03
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ vmak/ nmr/ VWM7-120/ 2/ fid
Title	VWM7-120.2.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1024
Receiver Gain	64.2
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.2976
Acquisition Date	2017-06-23T07:04:04
Spectrometer Frequency	100.62
Spectral Width	25252.5
Lowest Frequency	-2569.5
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

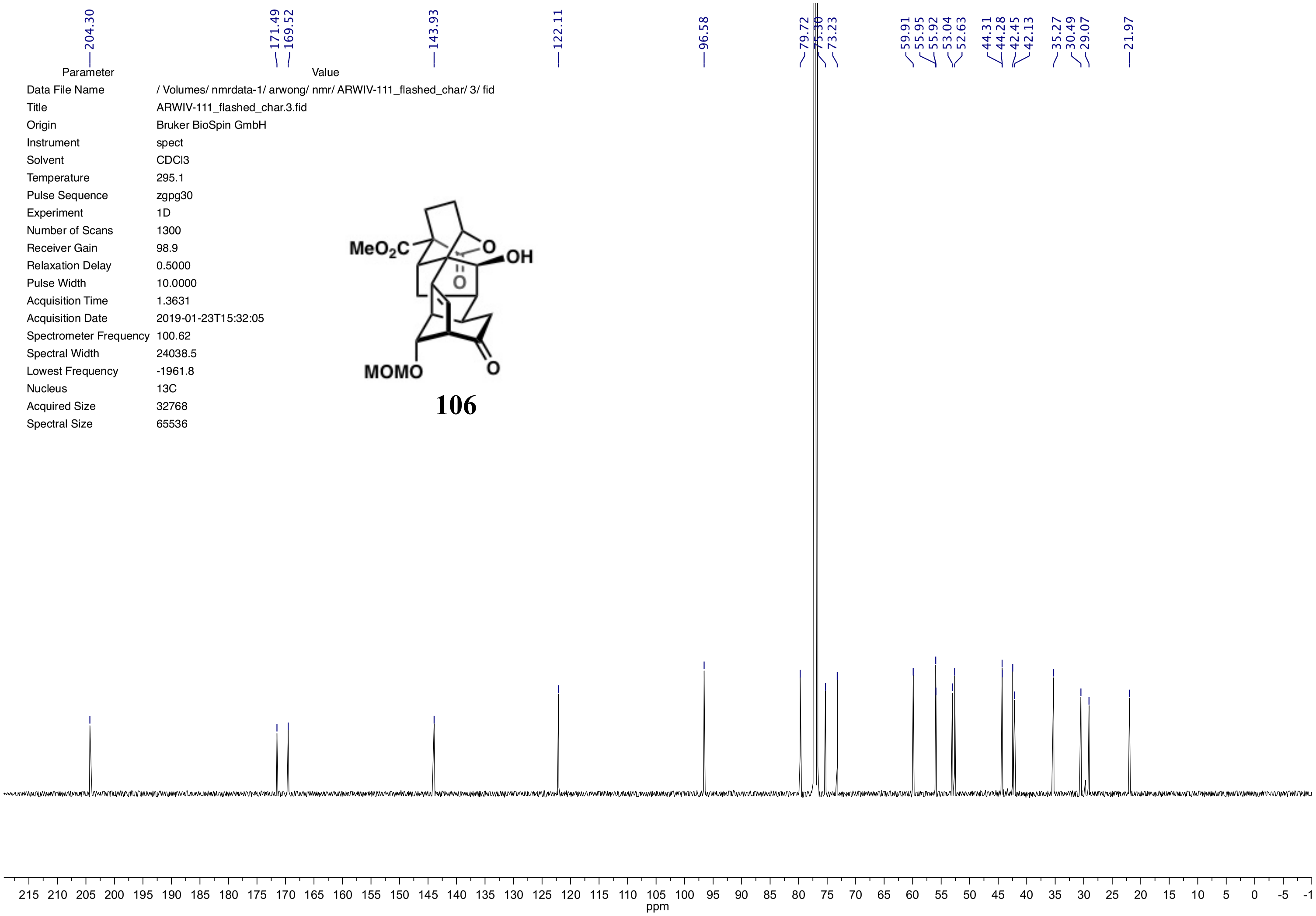
105





106

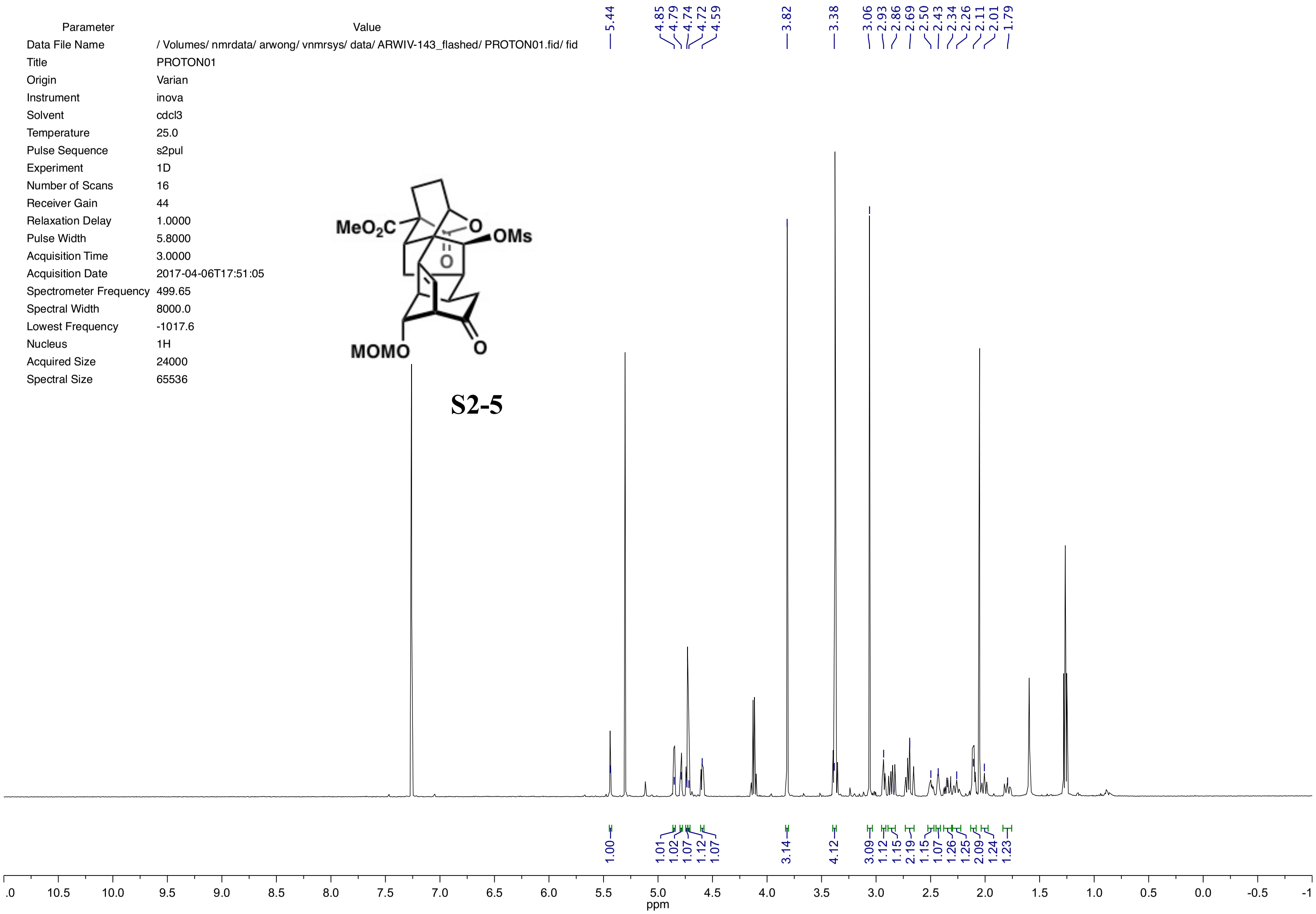
Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ arwong/ nmr/ ARWIV-111_flashed_char/ 1/ fid
Title	ARWIV-111_flashed_char.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	156.2
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2019-01-23T14:27:31
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



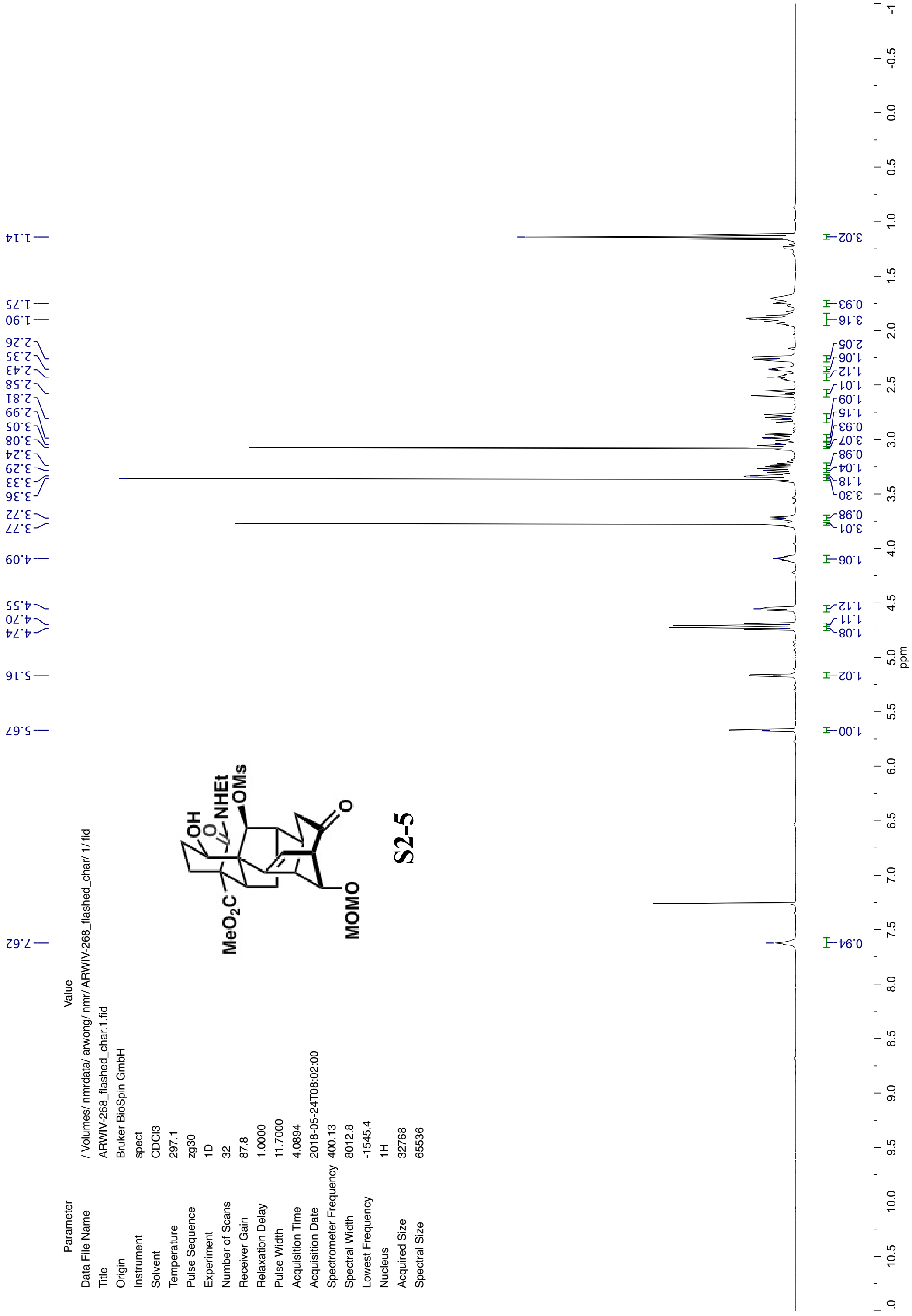
106

Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ arwong/ nmr/ ARWIV-111_flashed_char/ 3/ fid
Title	ARWIV-111_flashed_char.3.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1300
Receiver Gain	98.9
Relaxation Delay	0.5000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2019-01-23T15:32:05
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.8
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ vnmrsys/ data/ ARWIV-143_flashed/ PROTON01.fid/ fid
Title	PROTON01
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	16
Receiver Gain	44
Relaxation Delay	1.0000
Pulse Width	5.8000
Acquisition Time	3.0000
Acquisition Date	2017-04-06T17:51:05
Spectrometer Frequency	499.65
Spectral Width	8000.0
Lowest Frequency	-1017.6
Nucleus	1H
Acquired Size	24000
Spectral Size	65536

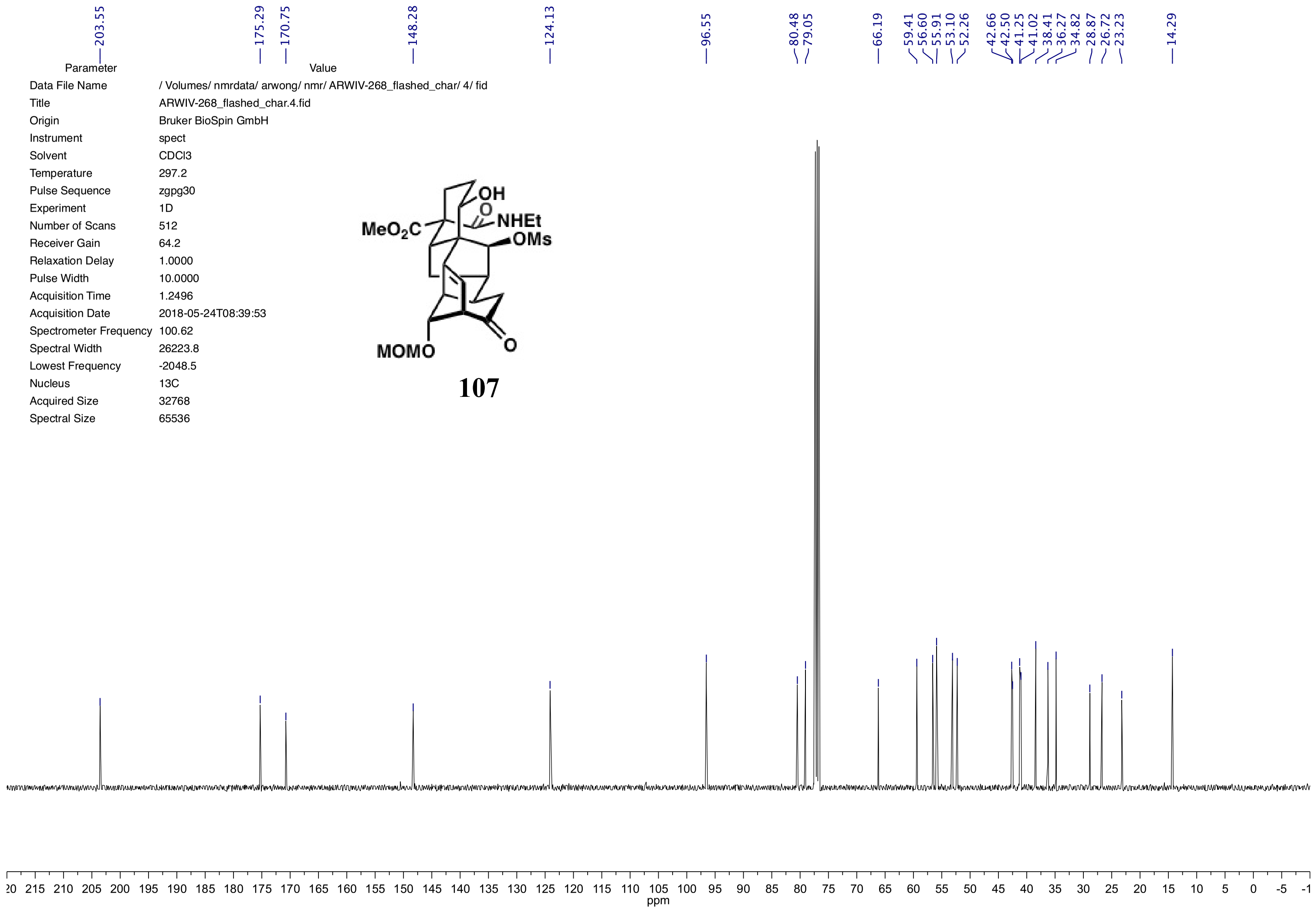


S2-5



S2-5

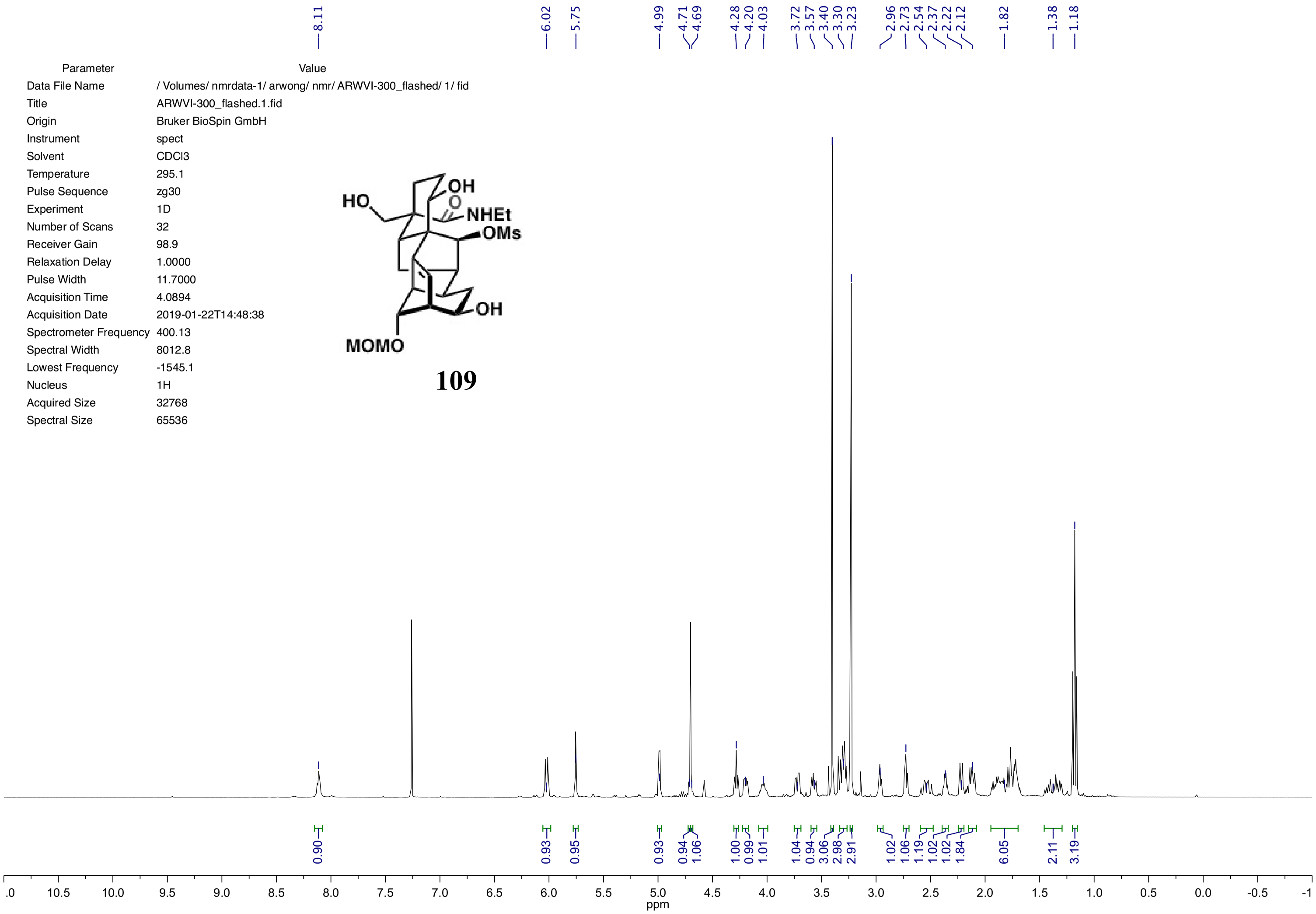
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWIV-268_flashed_char/ 1/ fid
Title	ARWIV-268_flashed_char.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	297.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	87.8
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-05-24T08:02:00
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



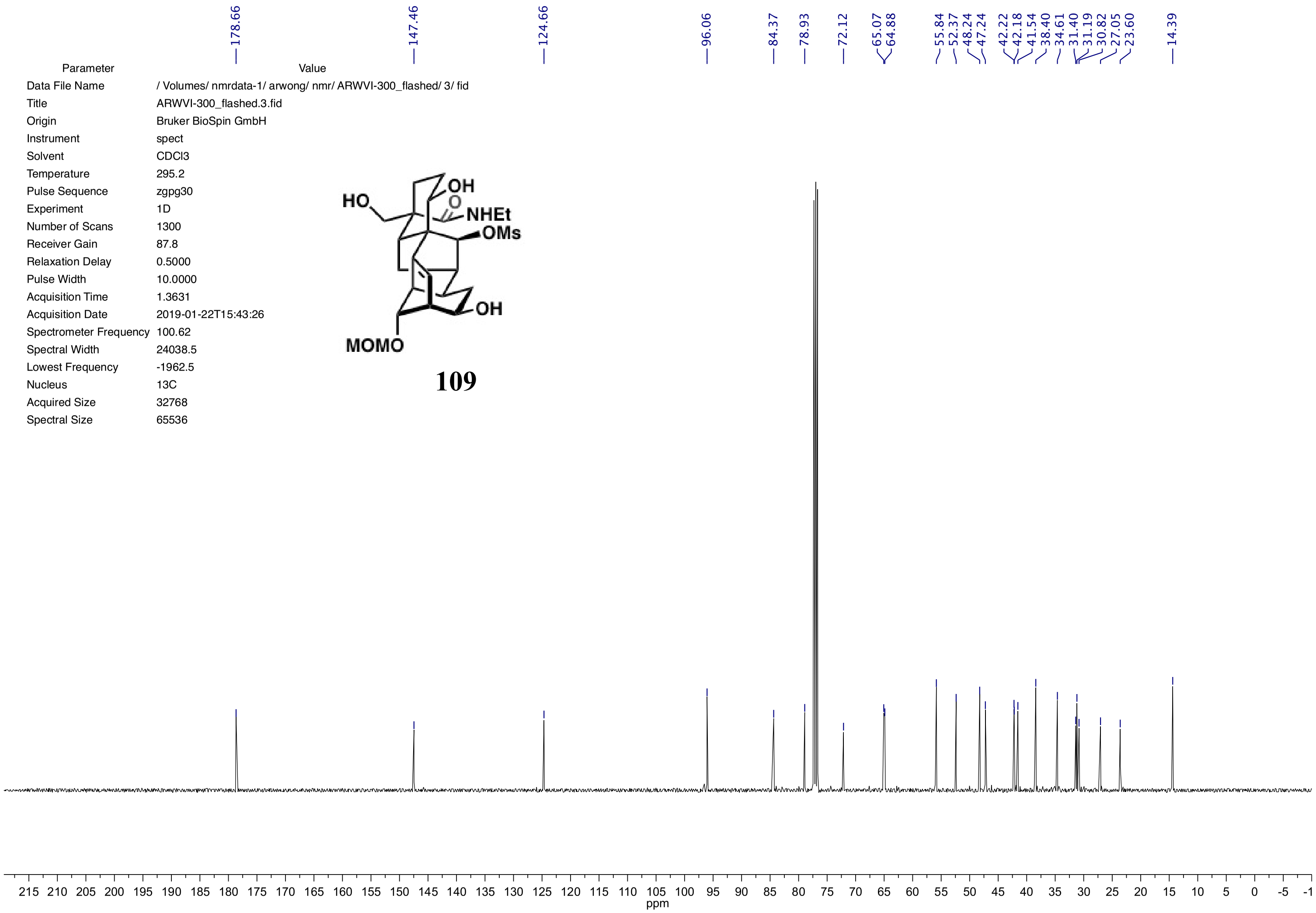
107

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWIV-268_flashed_char/ 4/ fid
Title	ARWIV-268_flashed_char.4.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	297.2
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	512
Receiver Gain	64.2
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.2496
Acquisition Date	2018-05-24T08:39:53
Spectrometer Frequency	100.62
Spectral Width	26223.8
Lowest Frequency	-2048.5
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ arwong/ nmr/ ARWVI-300_flashed/ 1/ fid
Title	ARWVI-300_flashed.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	98.9
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2019-01-22T14:48:38
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.1
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

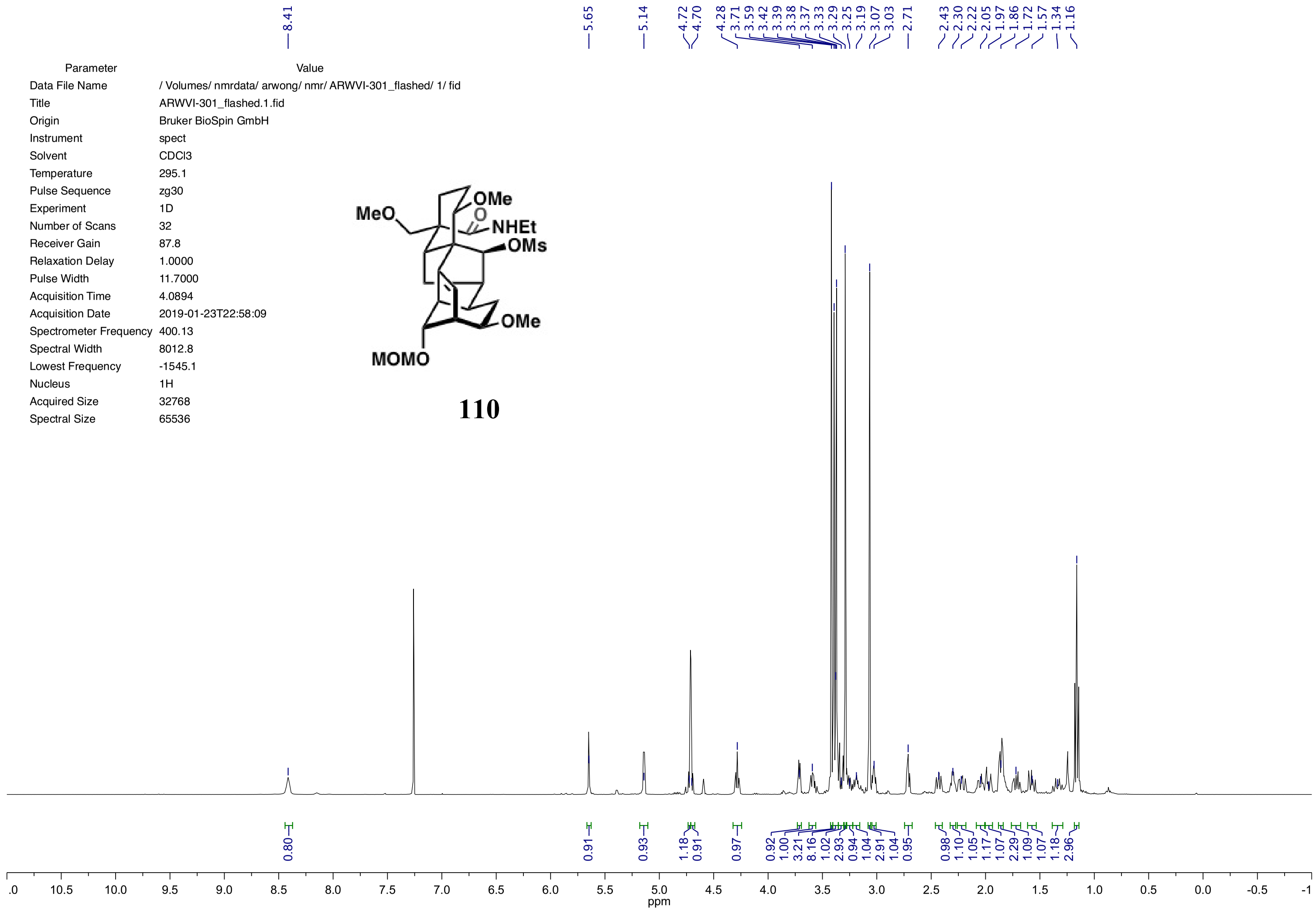


109



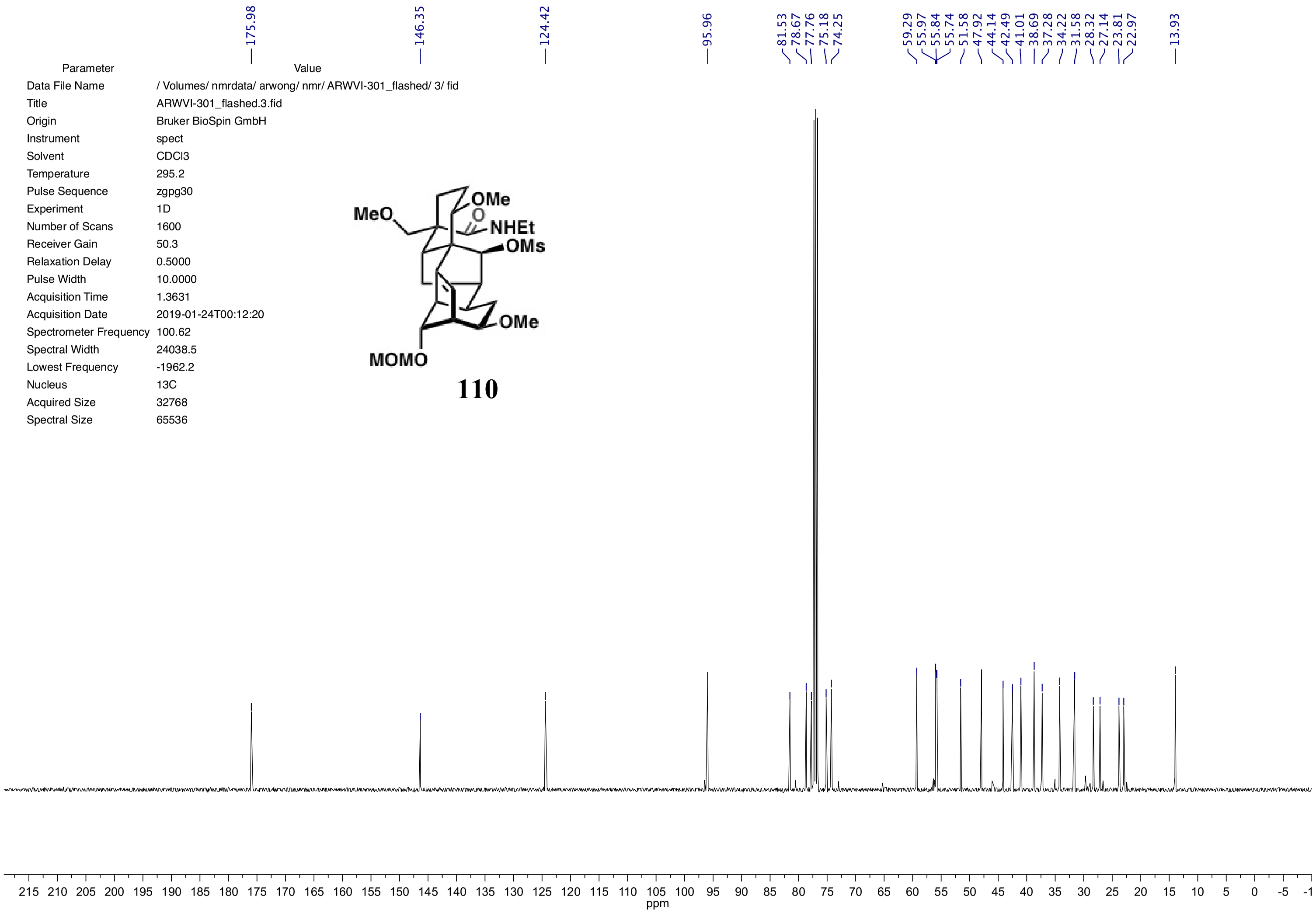
109

Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ arwong/ nmr/ ARWVI-300_flashed/ 3/ fid
Title	ARWVI-300_flashed.3.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1300
Receiver Gain	87.8
Relaxation Delay	0.5000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2019-01-22T15:43:26
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1962.5
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



110

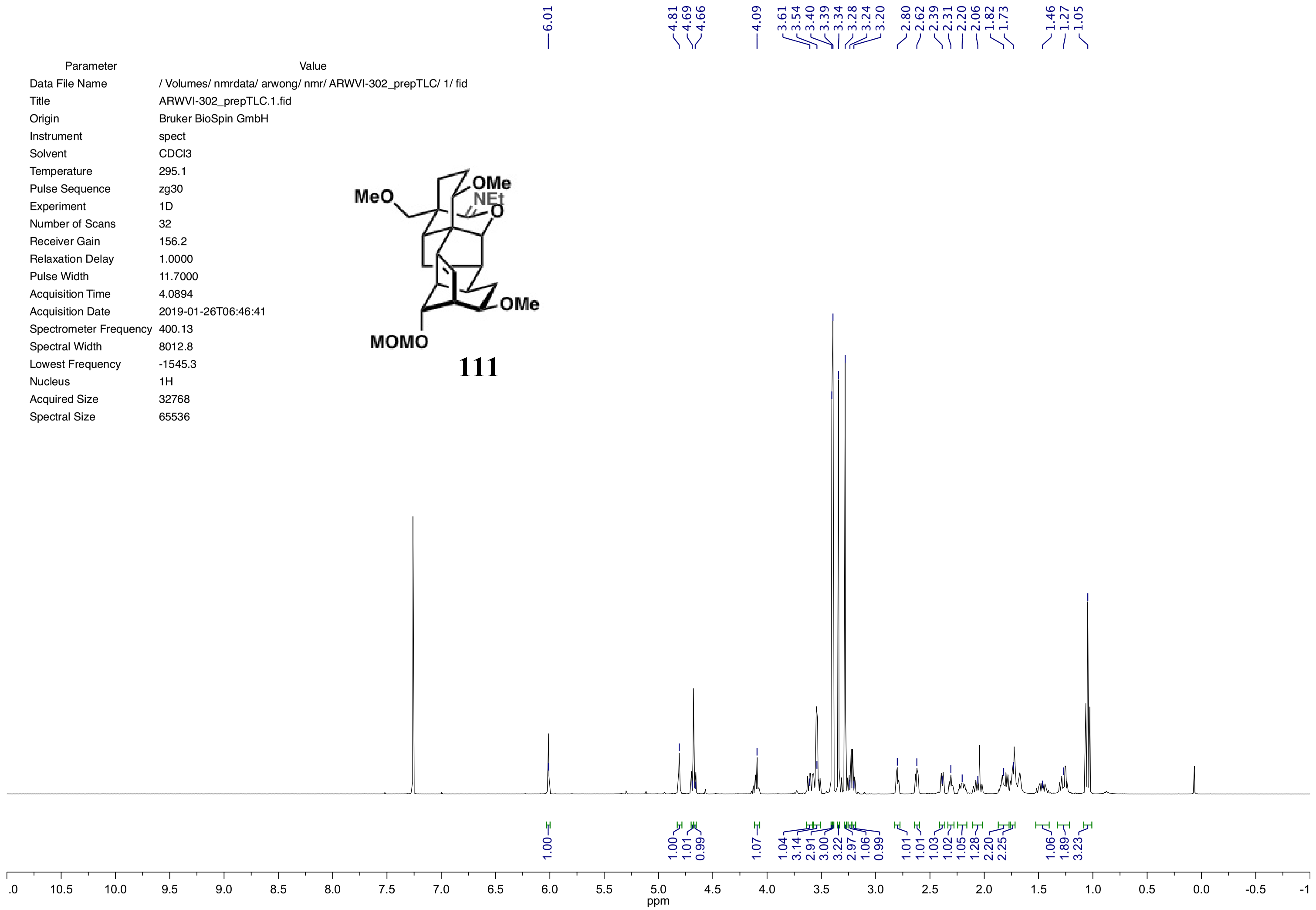
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-301_flashed/ 1/ fid
Title	ARWVI-301_flashed.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	87.8
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2019-01-23T22:58:09
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.1
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

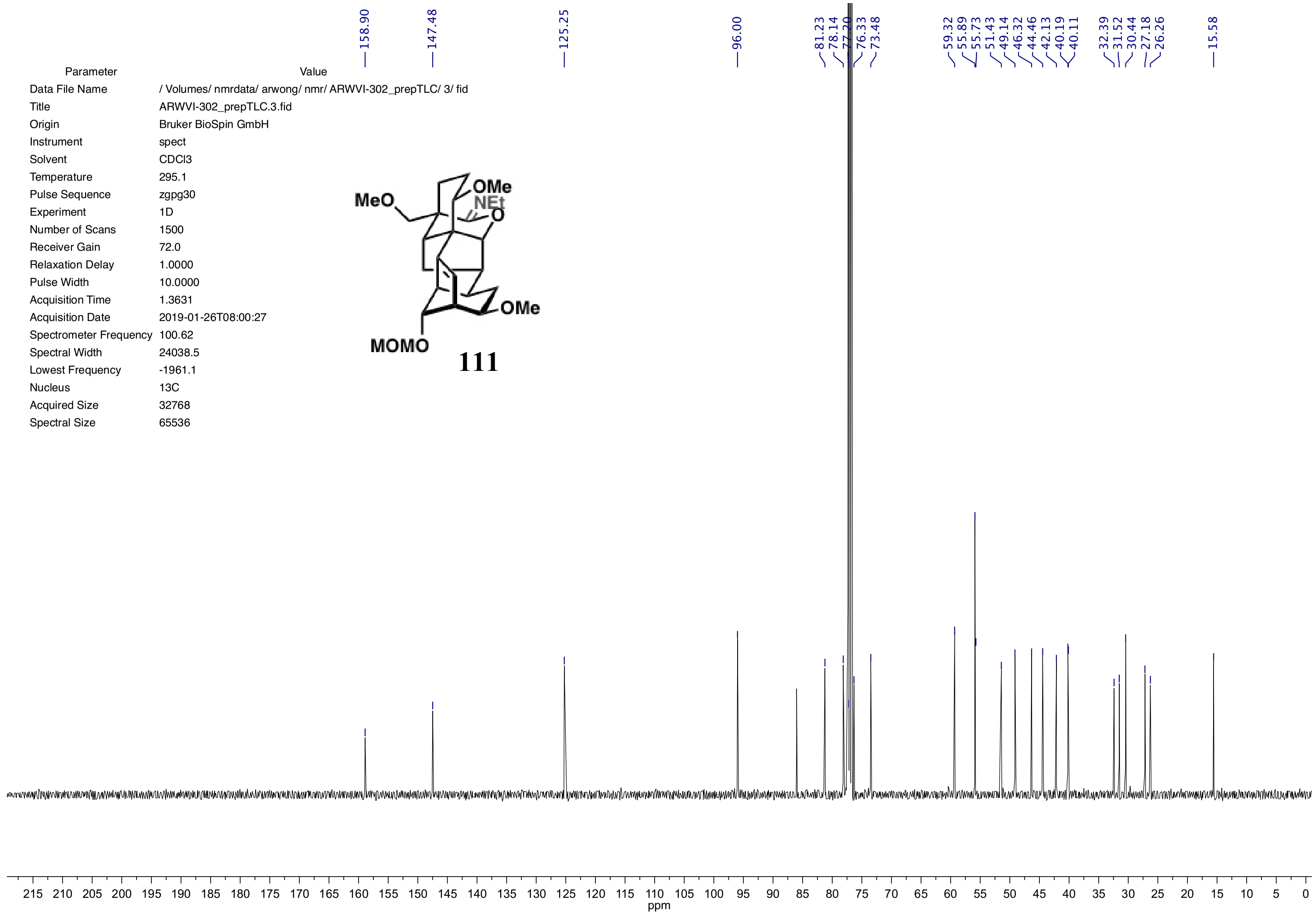


110

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-301_flashed/ 3/ fid
Title	ARWVI-301_flashed.3.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1600
Receiver Gain	50.3
Relaxation Delay	0.5000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2019-01-24T00:12:20
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1962.2
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

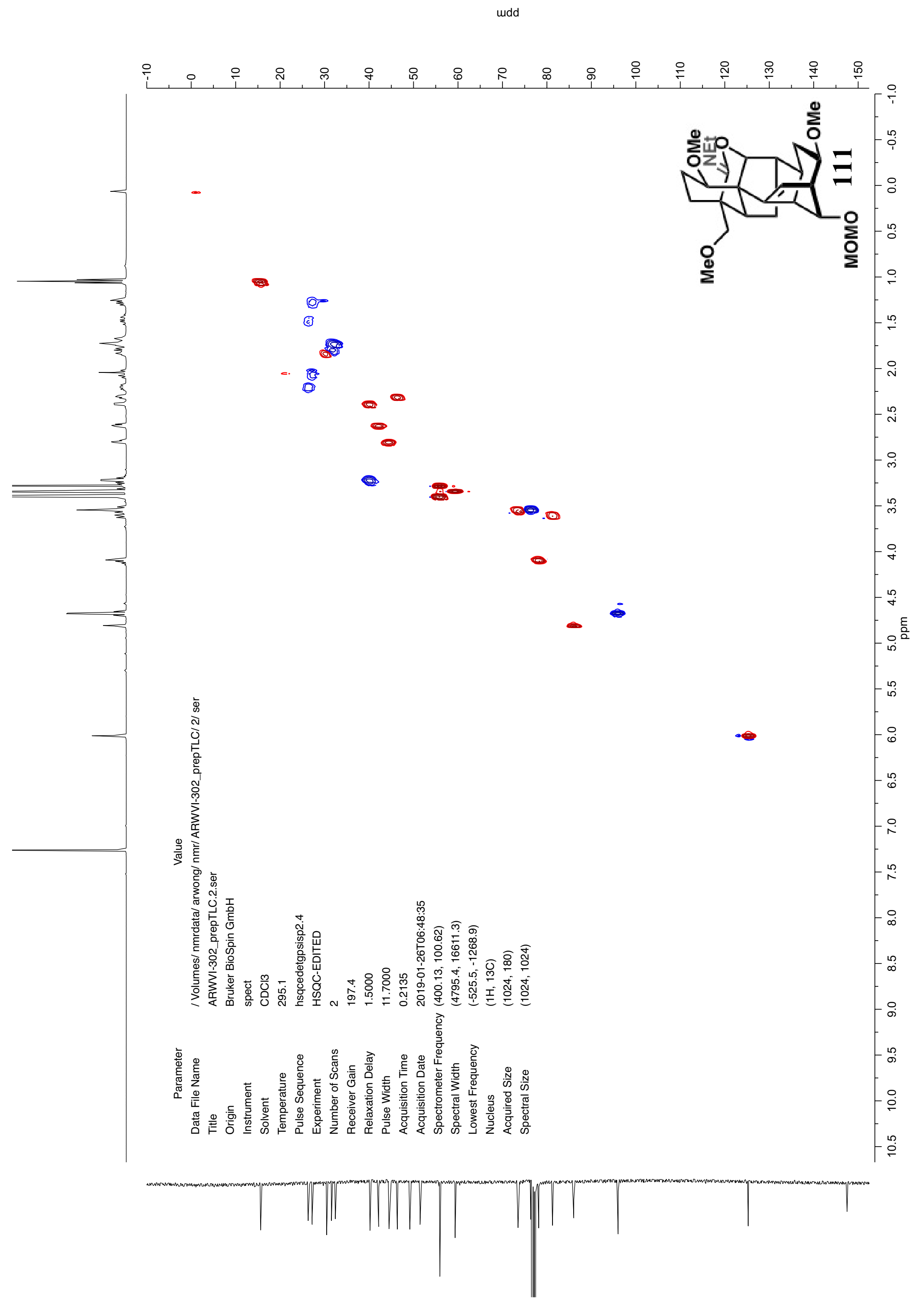
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-302_prepTLC/ 1/ fid
Title	ARWVI-302_prepTLC.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	156.2
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2019-01-26T06:46:41
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.3
Nucleus	1H
Acquired Size	32768
Spectral Size	65536


111



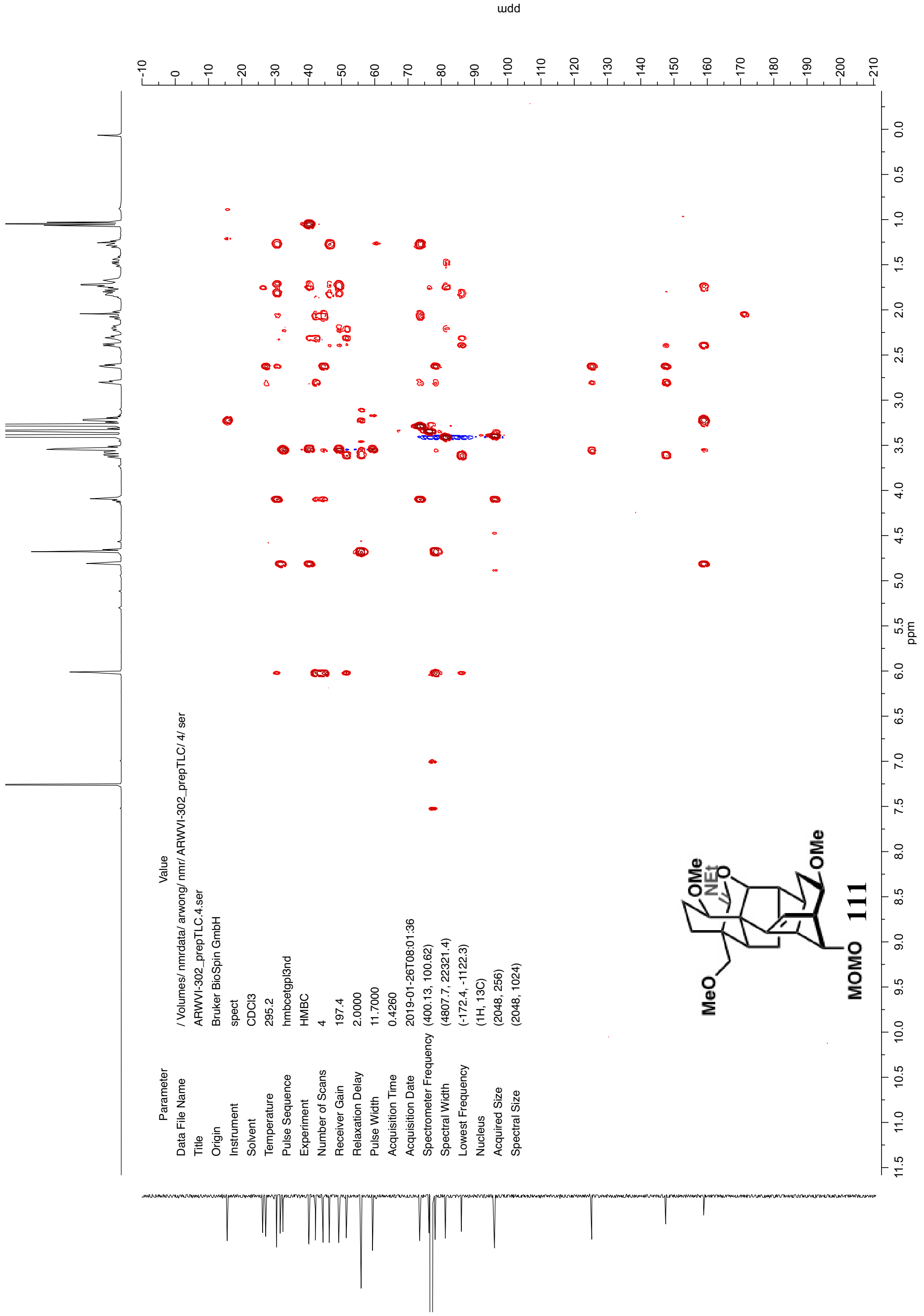
111

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-302_prepTLC/ 3/ fid
Title	ARWVI-302_prepTLC.3.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1500
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2019-01-26T08:00:27
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.1
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



111

Parameter	Value
Data File Name	/Volumes/ nmrdata/ arwong/ nmr/ ARWVI-302_prepTLC/ 2/ ser
Title	ARWVI-302_prepTLC.2.ser
Origin	Bruker BioSpin GmbH
Instrument	spect
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	2019-01-26T06:48:35
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(4795.4, 16611.3)
Lowest Frequency	(-525.5, -1268.9)
Nucleus	(1H, 13C)
Acquired Size	(1024, 180)
Spectral Size	(1024, 1024)

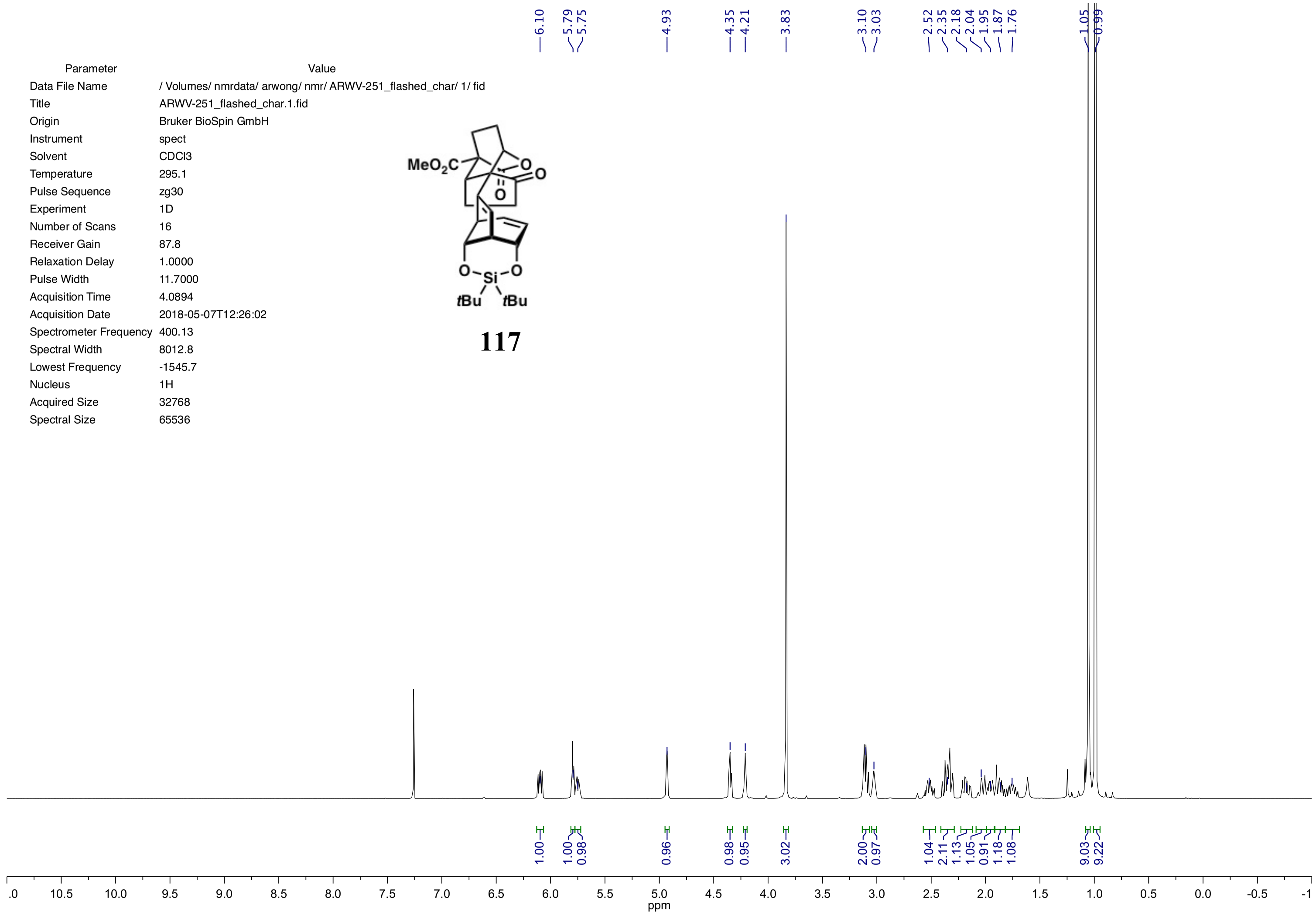


111

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-302_prepTLC/ 4/ ser
Title	ARWVI-302_prepTLC.4.ser
Origin	Bruker BioSpin GmbH
Instrument	spect
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	2019-01-26T08:01:36
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(4807.7, 22321.4)
Lowest Frequency	(-172.4, -1122.3)
Nucleus	(1H, 13C)
Acquired Size	(2048, 256)
Spectral Size	(2048, 1024)

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-302_prepTLC/ 7/ ser
Title	ARWVI-302_prepTLC.7.ser
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
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	2019-01-26T10:12:14
Spectrometer Frequency	(400.13, 40.55)
Spectral Width	(5197.5, 16233.8)
Lowest Frequency	(-207.0, -2035.4)
Nucleus	(1H, 15N)
Acquired Size	(1024, 128)
Spectral Size	(1024, 512)

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWV-251_flashed_char/ 1/ fid
Title	ARWV-251_flashed_char.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
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	2018-05-07T12:26:02
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.7
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



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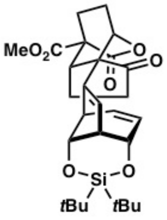
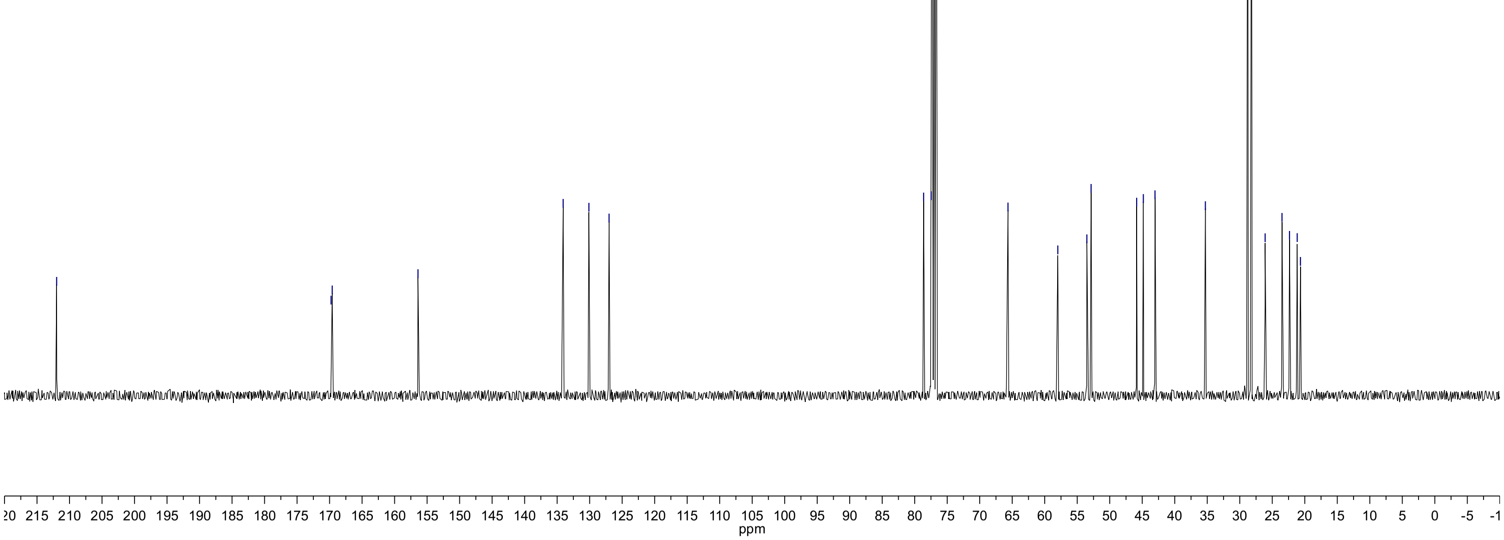
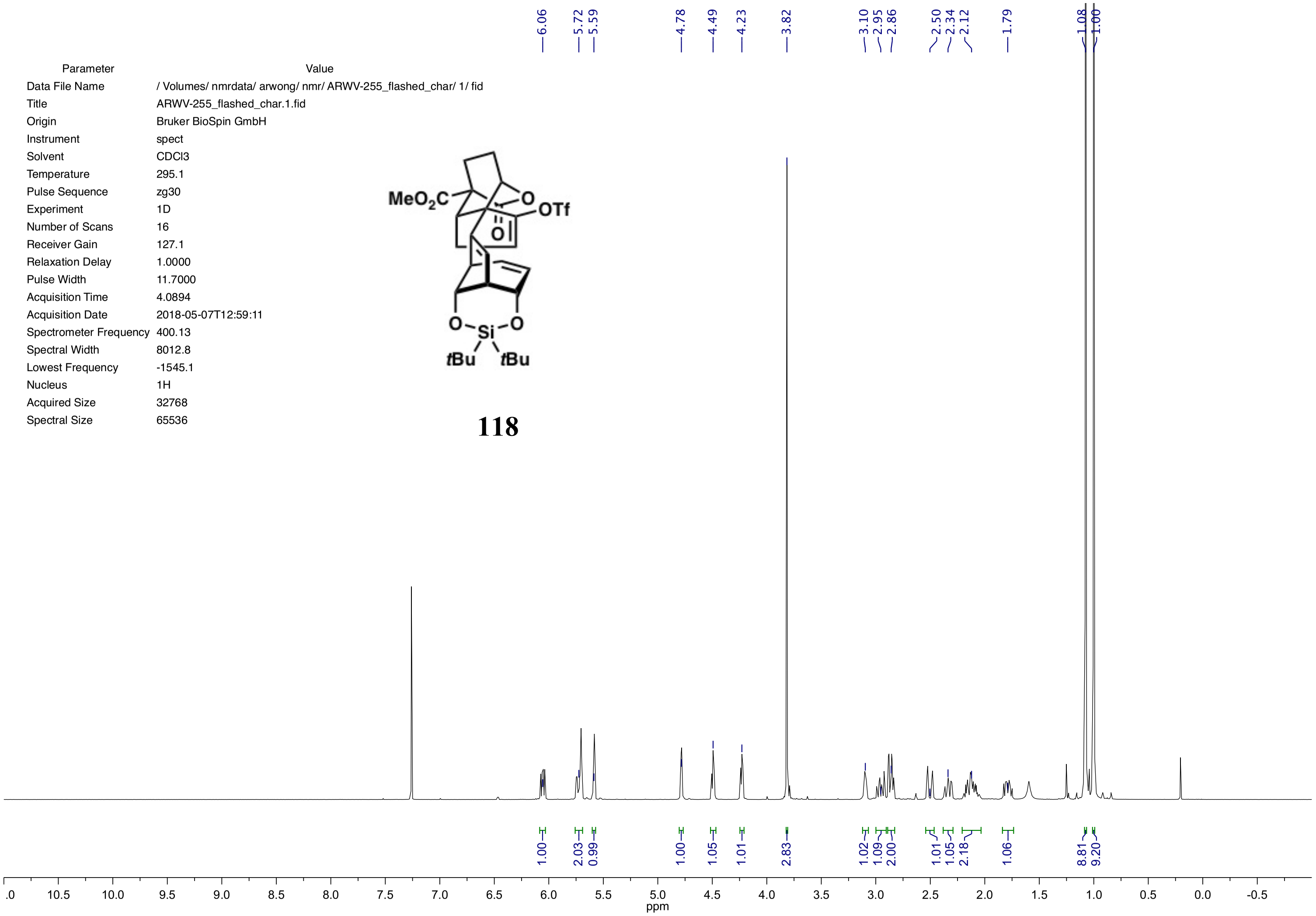
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWV-251_flashed_char/ 4/ fid
Title	ARWV-251_flashed_char.4.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	256
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.2496
Acquisition Date	2018-05-07T12:54:02
Spectrometer Frequency	100.62
Spectral Width	26223.8
Lowest Frequency	-2048.3
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



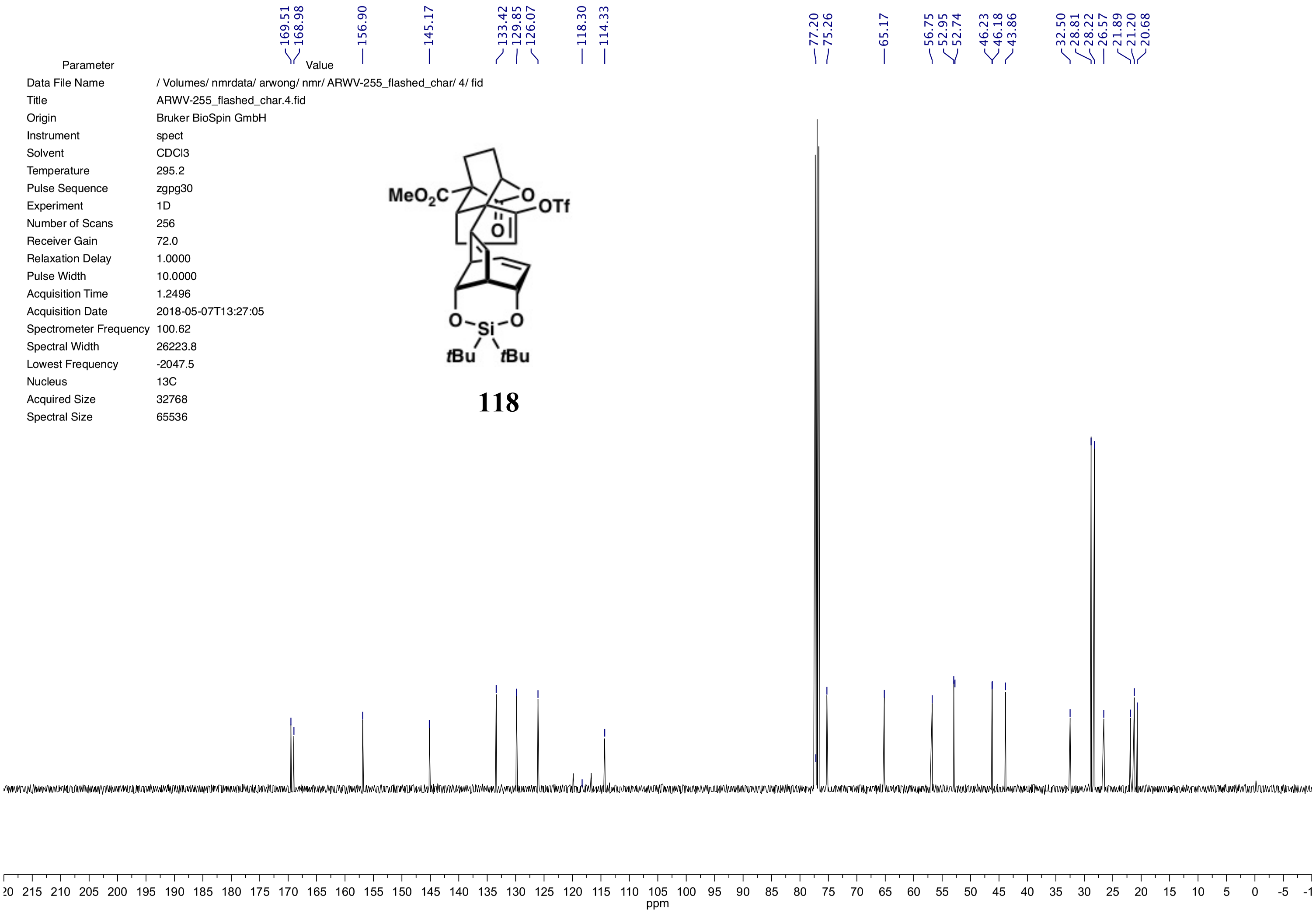
117



Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWV-255_flashed_char/ 1/ fid
Title	ARWV-255_flashed_char.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
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	2018-05-07T12:59:11
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.1
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

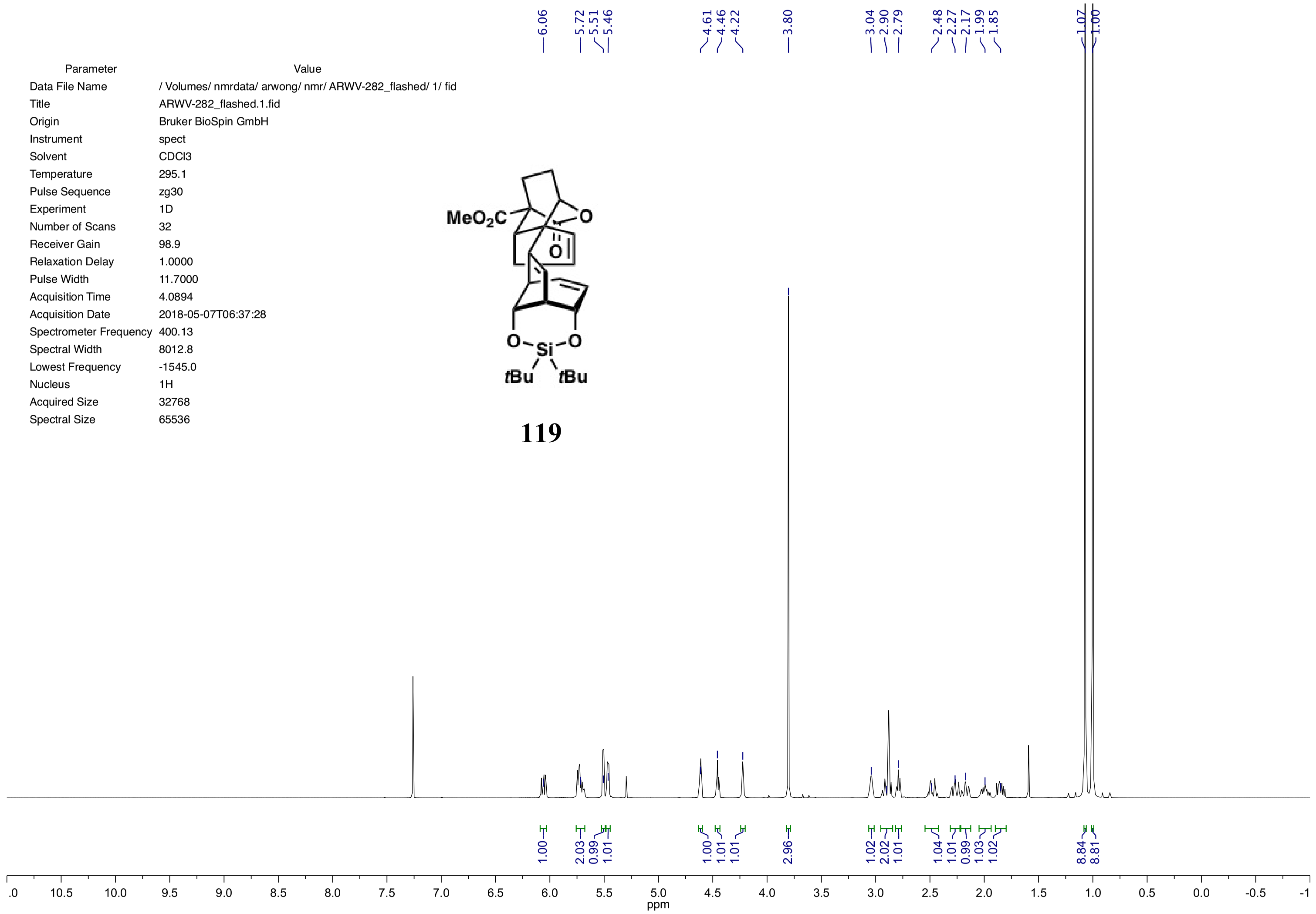


118



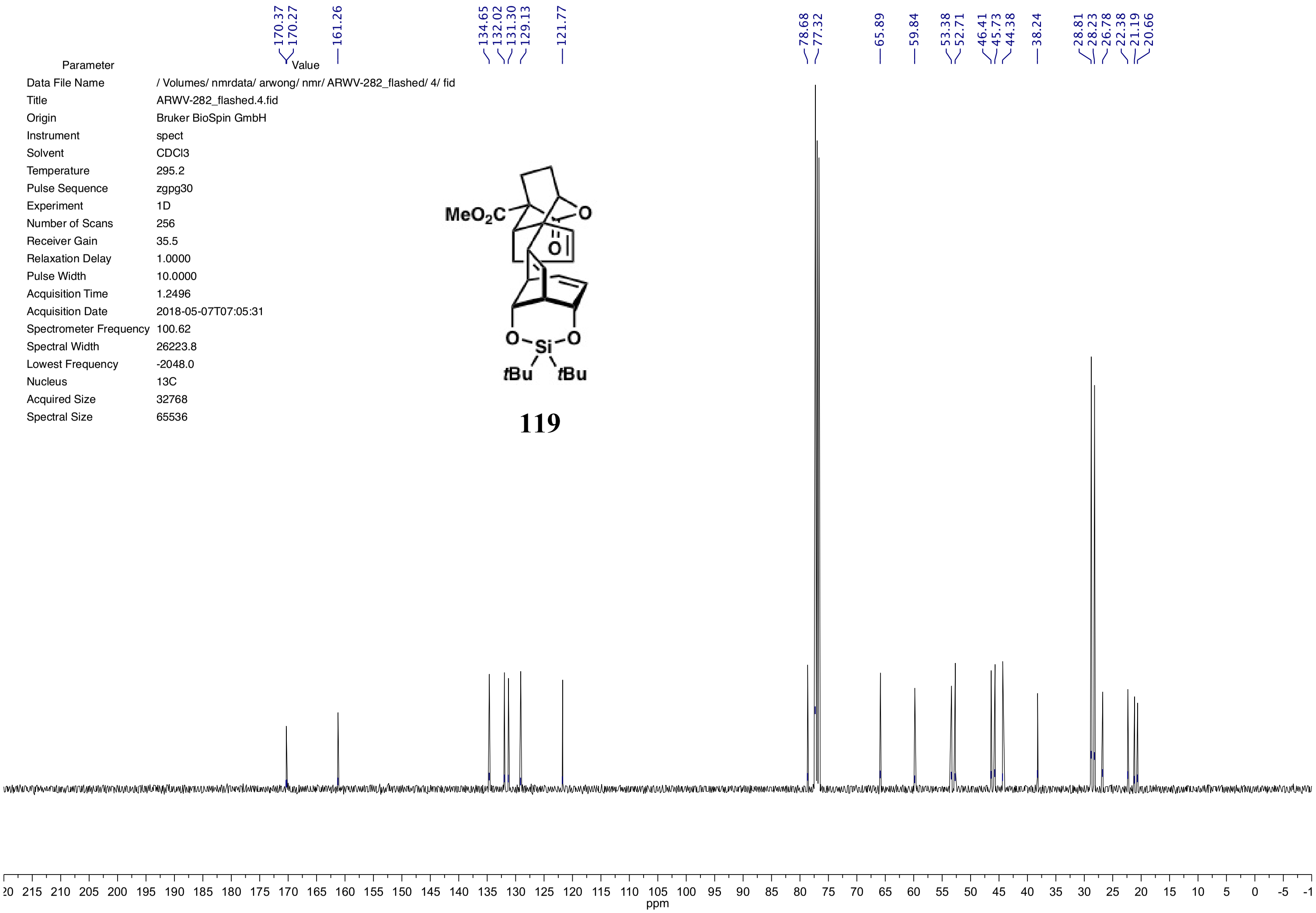
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWV-255_flashed_char/ 4/ fid
Title	ARWV-255_flashed_char.4.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	256
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.2496
Acquisition Date	2018-05-07T13:27:05
Spectrometer Frequency	100.62
Spectral Width	26223.8
Lowest Frequency	-2047.5
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

118



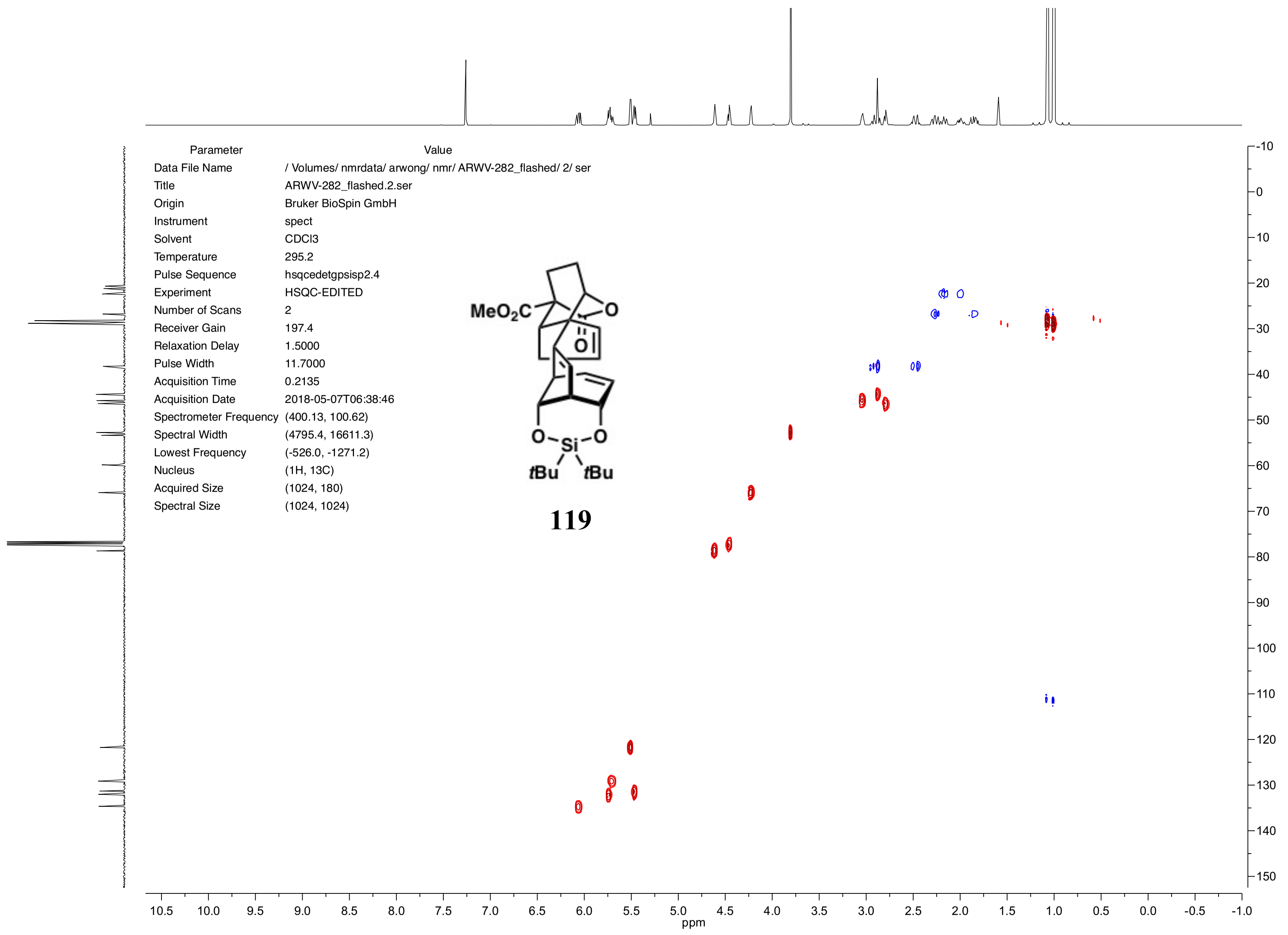
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWV-282_flashed/ 1/ fid
Title	ARWV-282_flashed.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	98.9
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-05-07T06:37:28
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.0
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

119



119

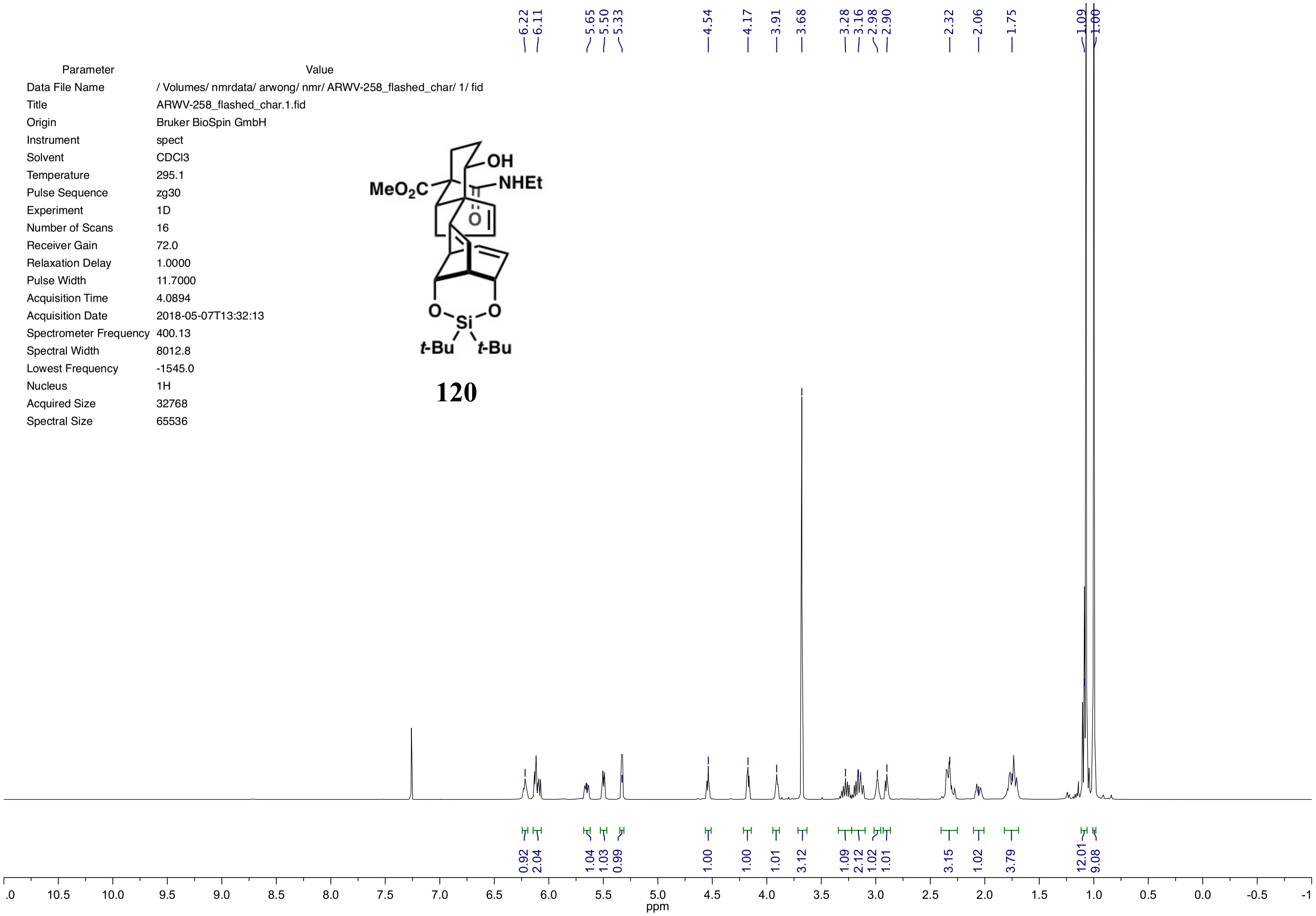
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWV-282_flashed/ 4/ fid
Title	ARWV-282_flashed.4.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	256
Receiver Gain	35.5
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.2496
Acquisition Date	2018-05-07T07:05:31
Spectrometer Frequency	100.62
Spectral Width	26223.8
Lowest Frequency	-2048.0
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



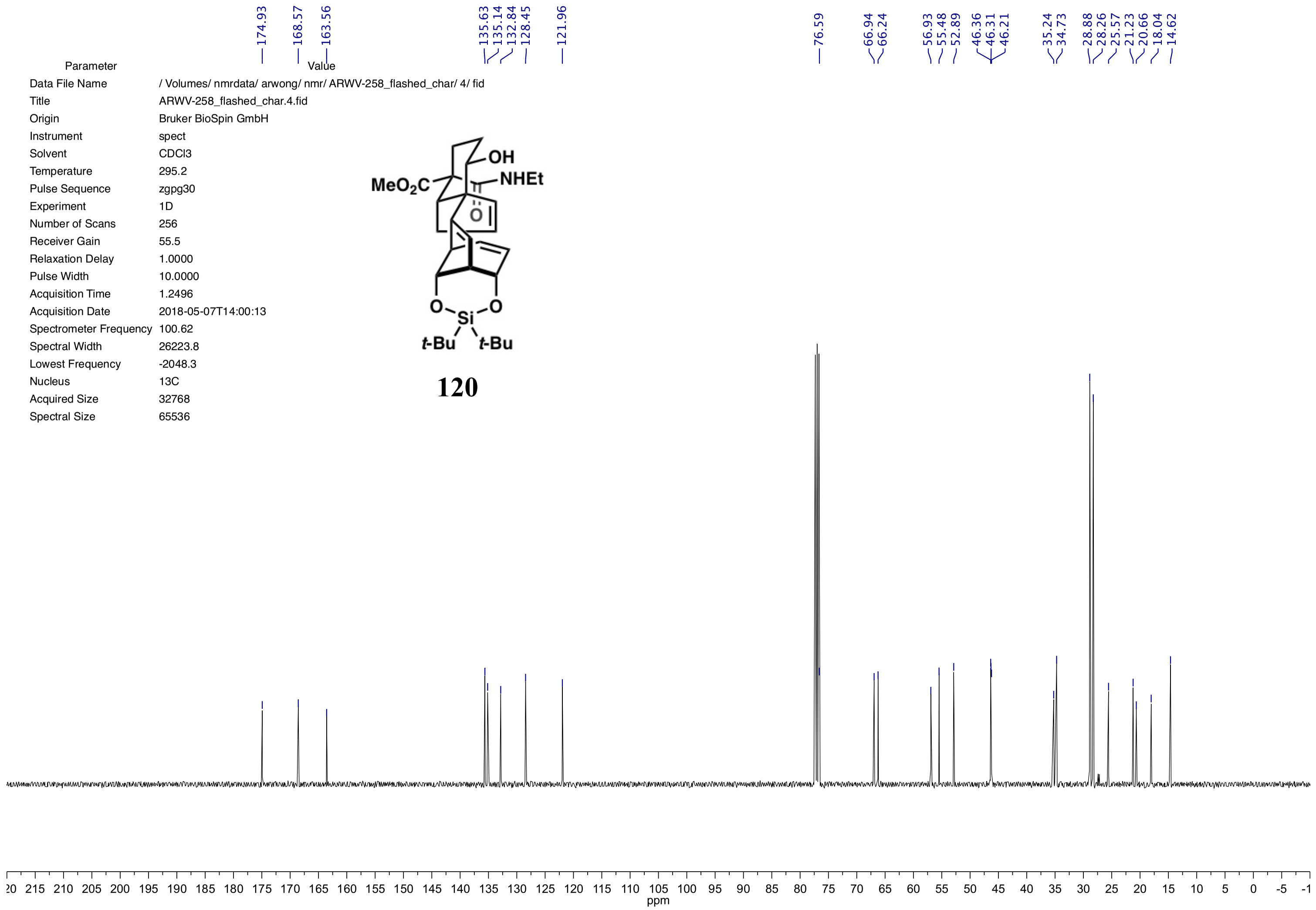
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWV-282_flashed/ 2/ ser
Title	ARWV-282_flashed.2.ser
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	hsqcedetgpsisp2.4
Experiment	HSQC-EDITED
Number of Scans	2
Receiver Gain	197.4
Relaxation Delay	1.5000
Pulse Width	11.7000
Acquisition Time	0.2135
Acquisition Date	2018-05-07T06:38:46
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(4795.4, 16611.3)
Lowest Frequency	(-526.0, -1271.2)
Nucleus	(1H, 13C)
Acquired Size	(1024, 180)
Spectral Size	(1024, 1024)

119

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWV-258_flashed_char/ 1/ fid
Title	ARWV-258_flashed_char.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
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	2018-05-07T13:32:13
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.0
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

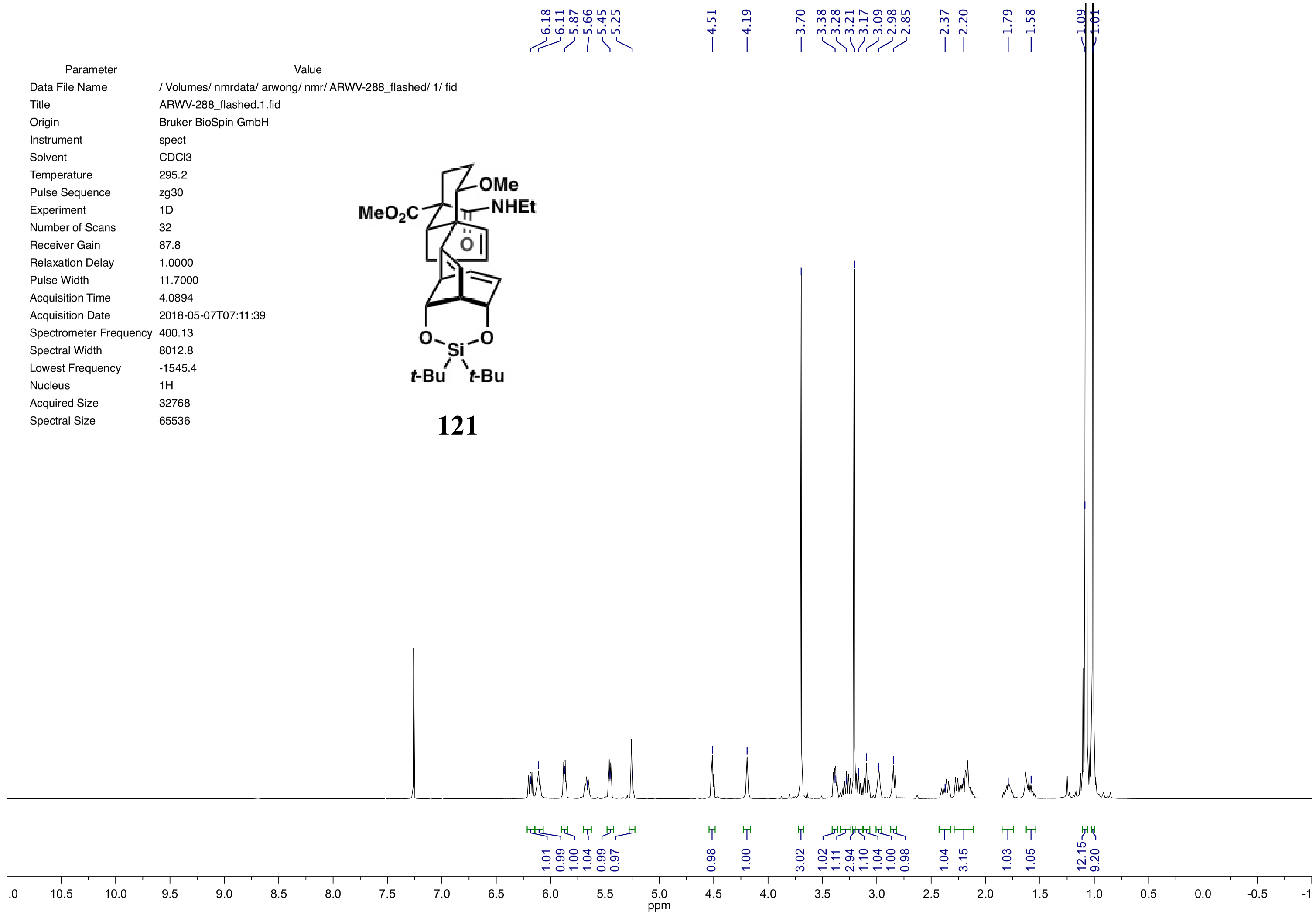


120



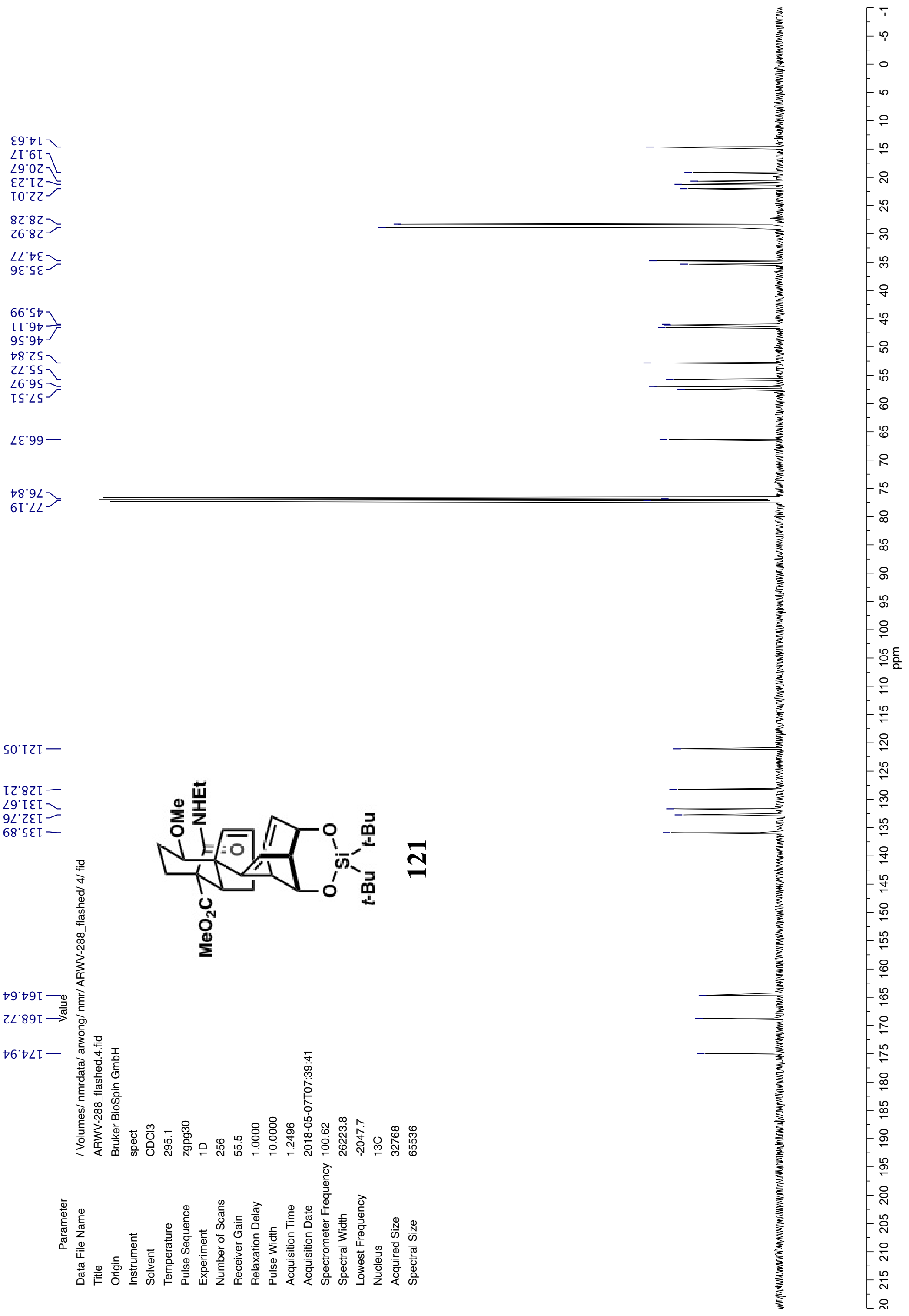
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWV-258_flashed_char/ 4/ fid
Title	ARWV-258_flashed_char.4.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	256
Receiver Gain	55.5
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.2496
Acquisition Date	2018-05-07T14:00:13
Spectrometer Frequency	100.62
Spectral Width	26223.8
Lowest Frequency	-2048.3
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

120



Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWV-288_flashed/ 1/ fid
Title	ARWV-288_flashed.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	87.8
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-05-07T07:11:39
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

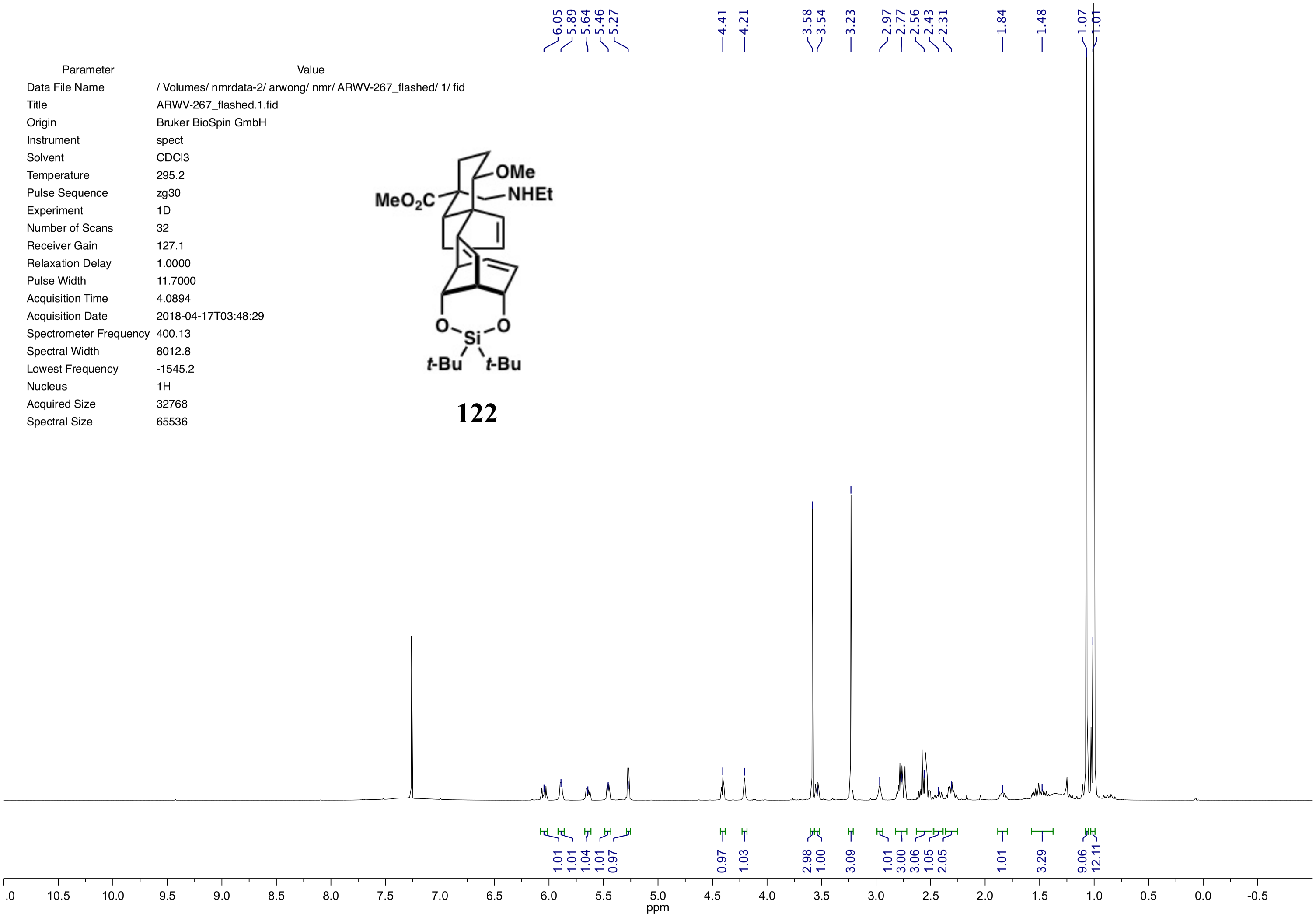
121



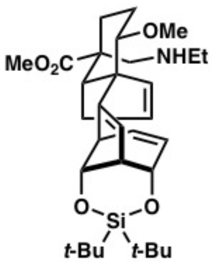
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWV-288_flashed/ 4/ fid
Title	ARWV-288_flashed.4.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	256
Receiver Gain	55.5
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.2496
Acquisition Date	2018-05-07T07:39:41
Spectrometer Frequency	100.62
Spectral Width	26223.8
Lowest Frequency	-2047.7
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata-2/ arwong/ nmr/ ARWV-267_flashed/ 1/ fid
Title	ARWV-267_flashed.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	127.1
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-04-17T03:48:29
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.2
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

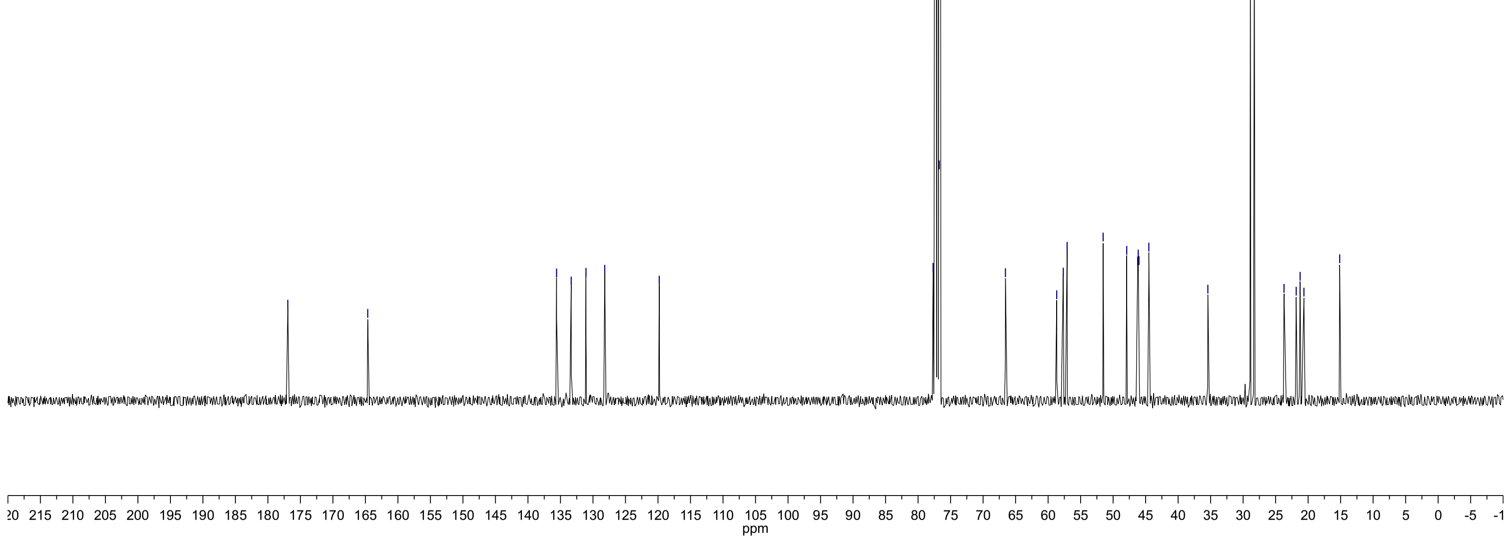
122



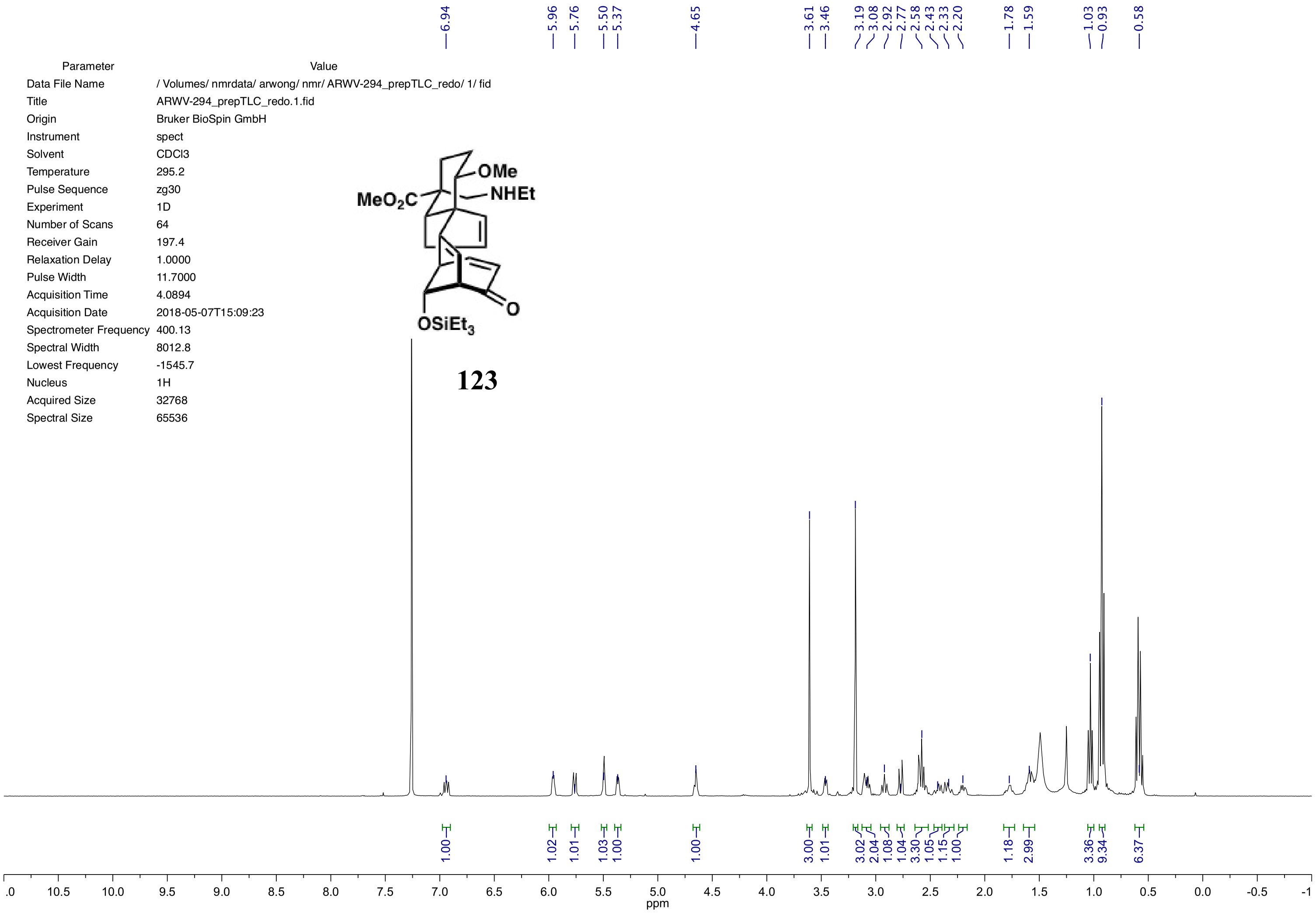
Parameter	Value
Data File Name	/ Volumes/ nmrdata-2/ arwong/ nmr/ ARWV-267_flashed/ 6/ fid
Title	ARWV-267_flashed.6.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1024
Receiver Gain	78.7
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.2496
Acquisition Date	2018-04-17T06:16:34
Spectrometer Frequency	100.62
Spectral Width	26223.8
Lowest Frequency	-2047.2
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



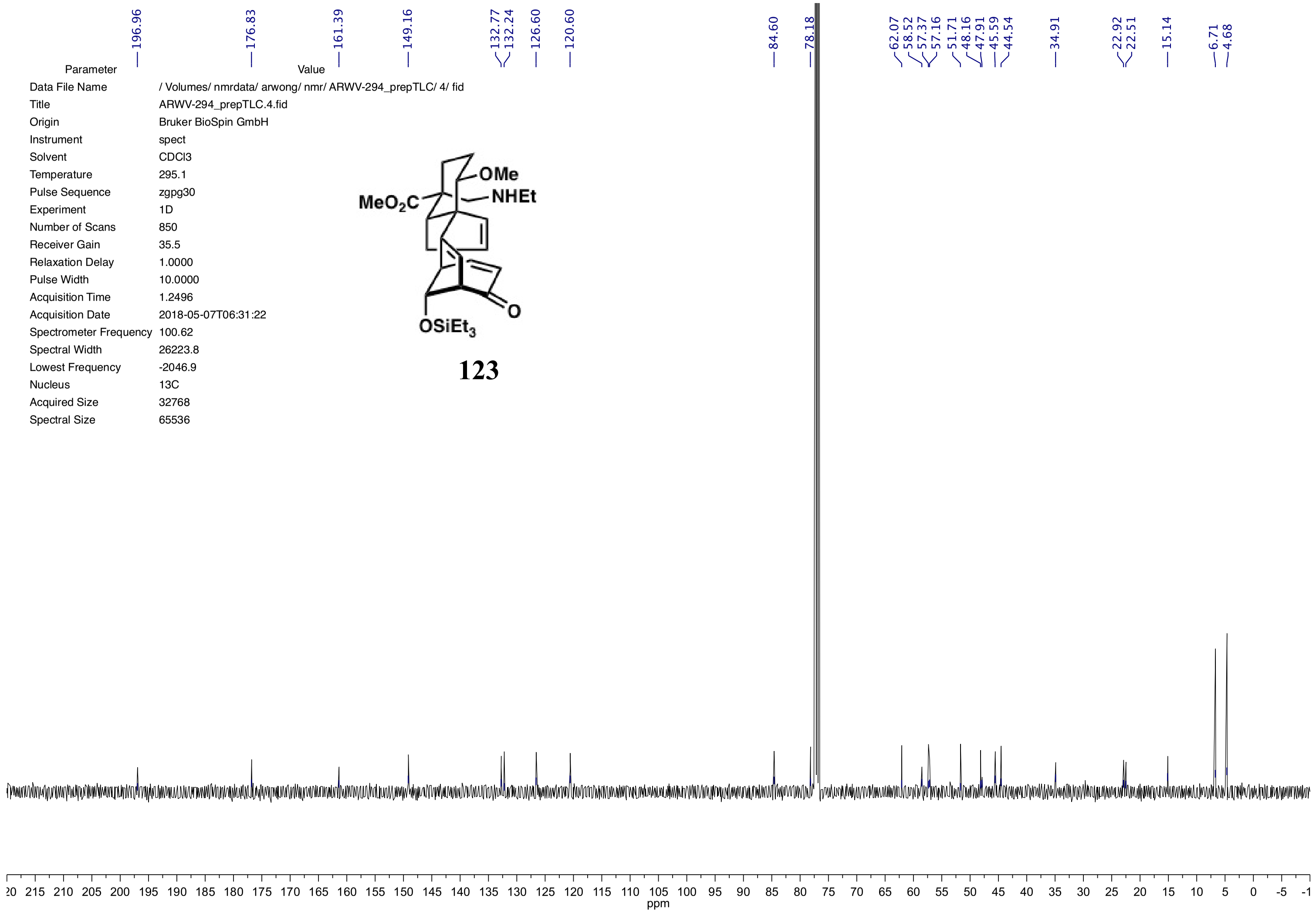
122



Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWV-294_prepTLC_redo/ 1/ fid
Title	ARWV-294_prepTLC_redo.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zg30
Experiment	1D
Number of Scans	64
Receiver Gain	197.4
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-05-07T15:09:23
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.7
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



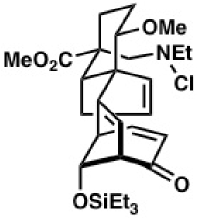
123



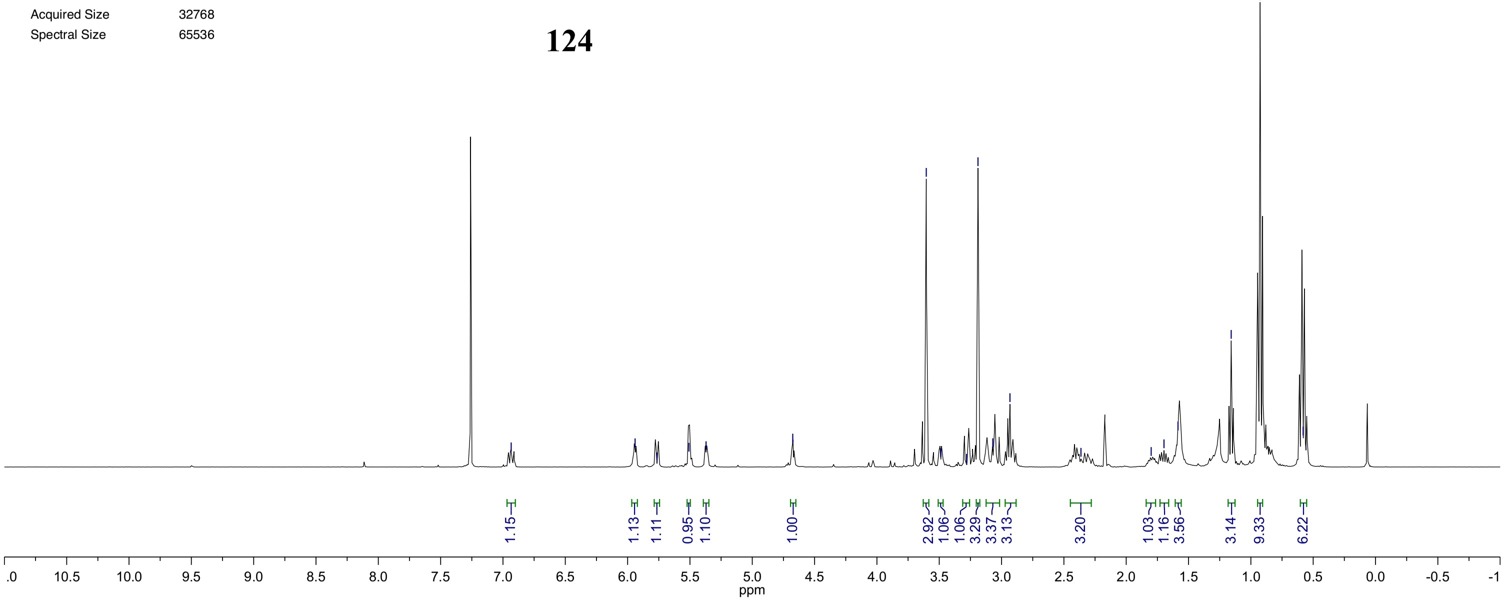
123

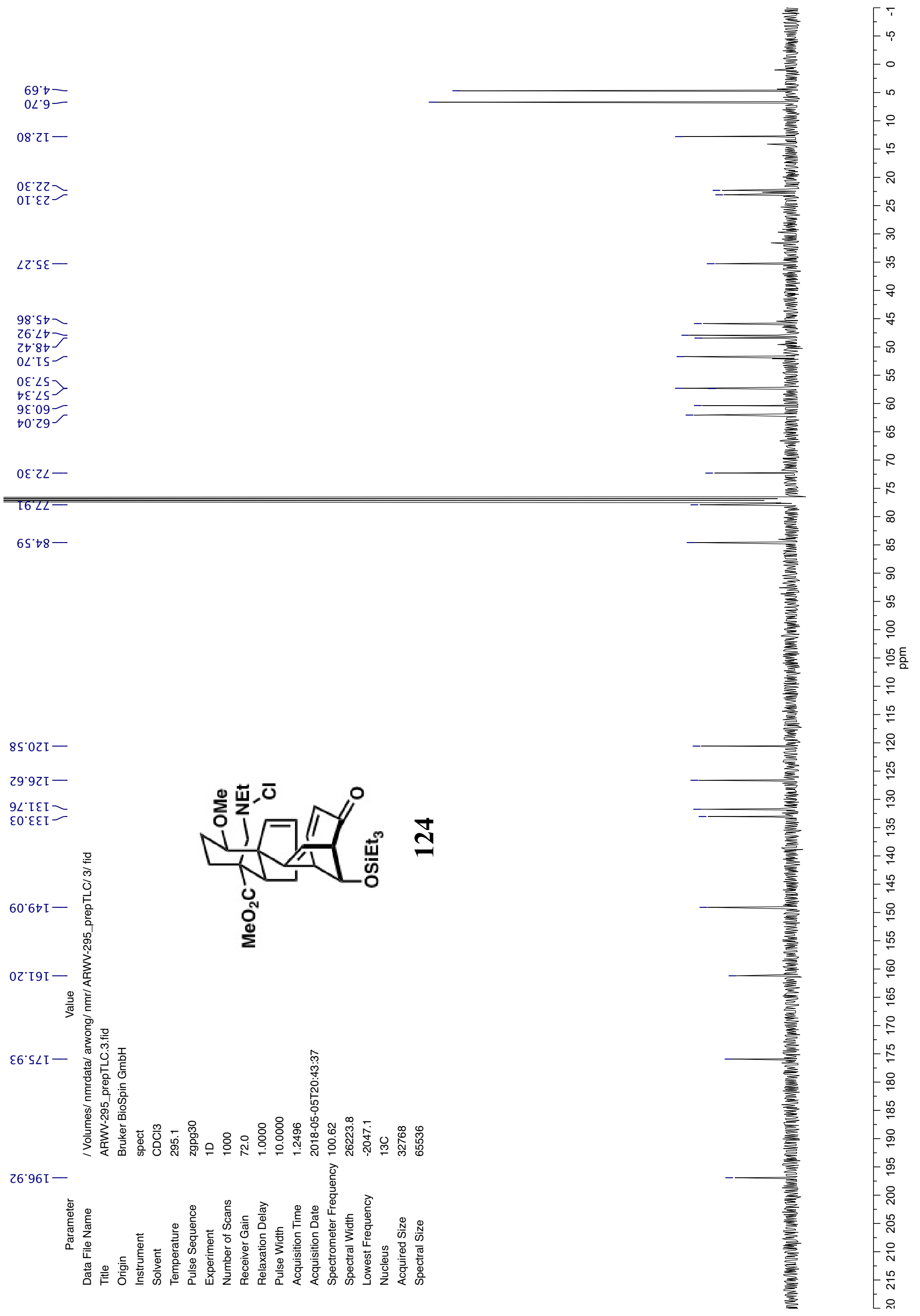
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWV-294_prepTLC/ 4/ fid
Title	ARWV-294_prepTLC.4.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	850
Receiver Gain	35.5
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.2496
Acquisition Date	2018-05-07T06:31:22
Spectrometer Frequency	100.62
Spectral Width	26223.8
Lowest Frequency	-2046.9
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWV-295_prepTLC/ 1/ fid
Title	ARWV-295_prepTLC.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	197.4
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-05-05T19:42:25
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.3
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



124

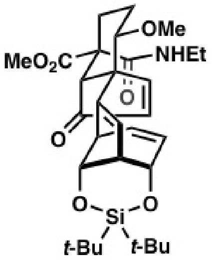




124

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWV-295_prepTLC/ 3/ fid
Title	ARWV-295_prepTLC.3.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1000
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.2496
Acquisition Date	2018-05-05T20:43:37
Spectrometer Frequency	100.62
Spectral Width	26223.8
Lowest Frequency	-2047.1
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ arwong/ nmr/ ARWVI-056_prepTLC_C_char/ 1/ fid
Title	ARWVI-056_prepTLC_C_char.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	297.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	142.8
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-06-20T13:17:58
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



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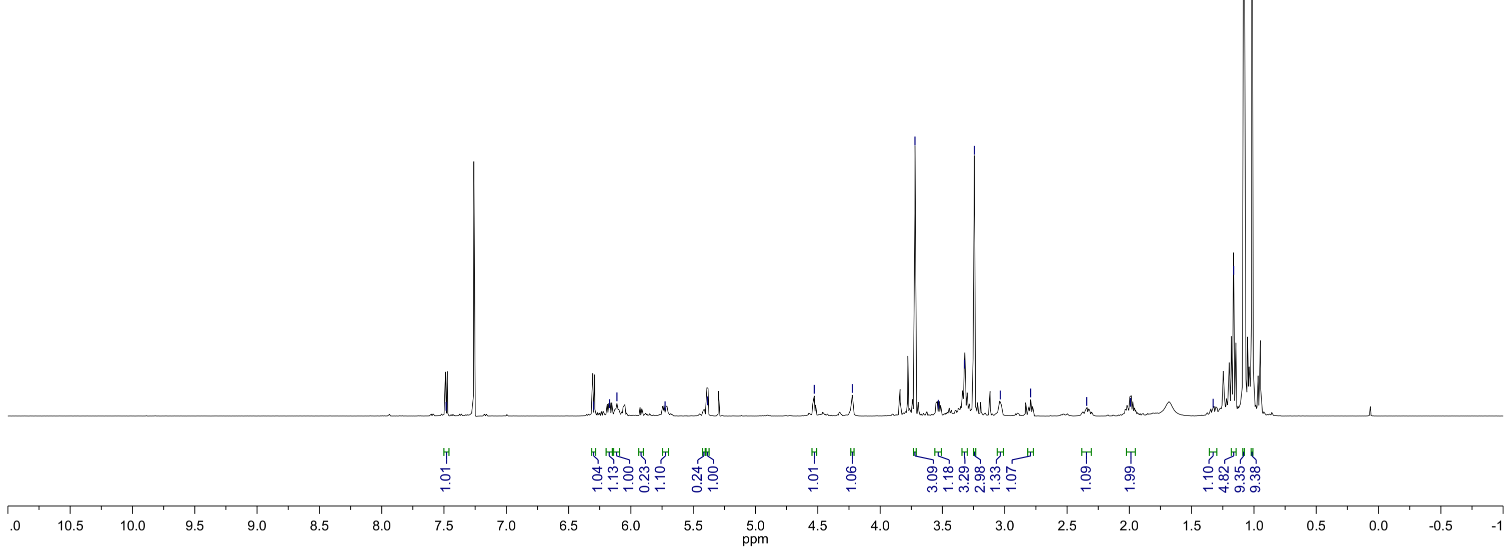

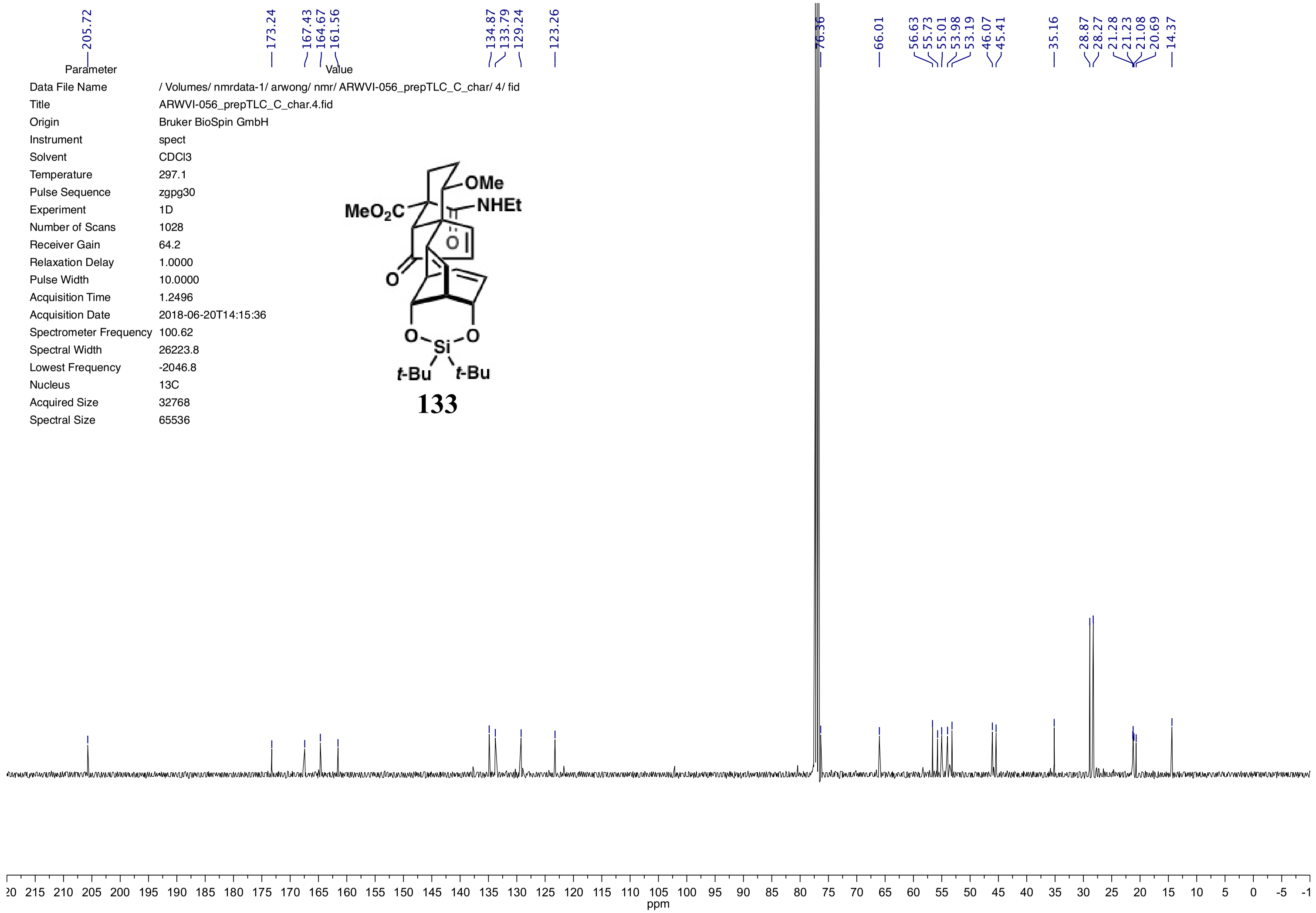

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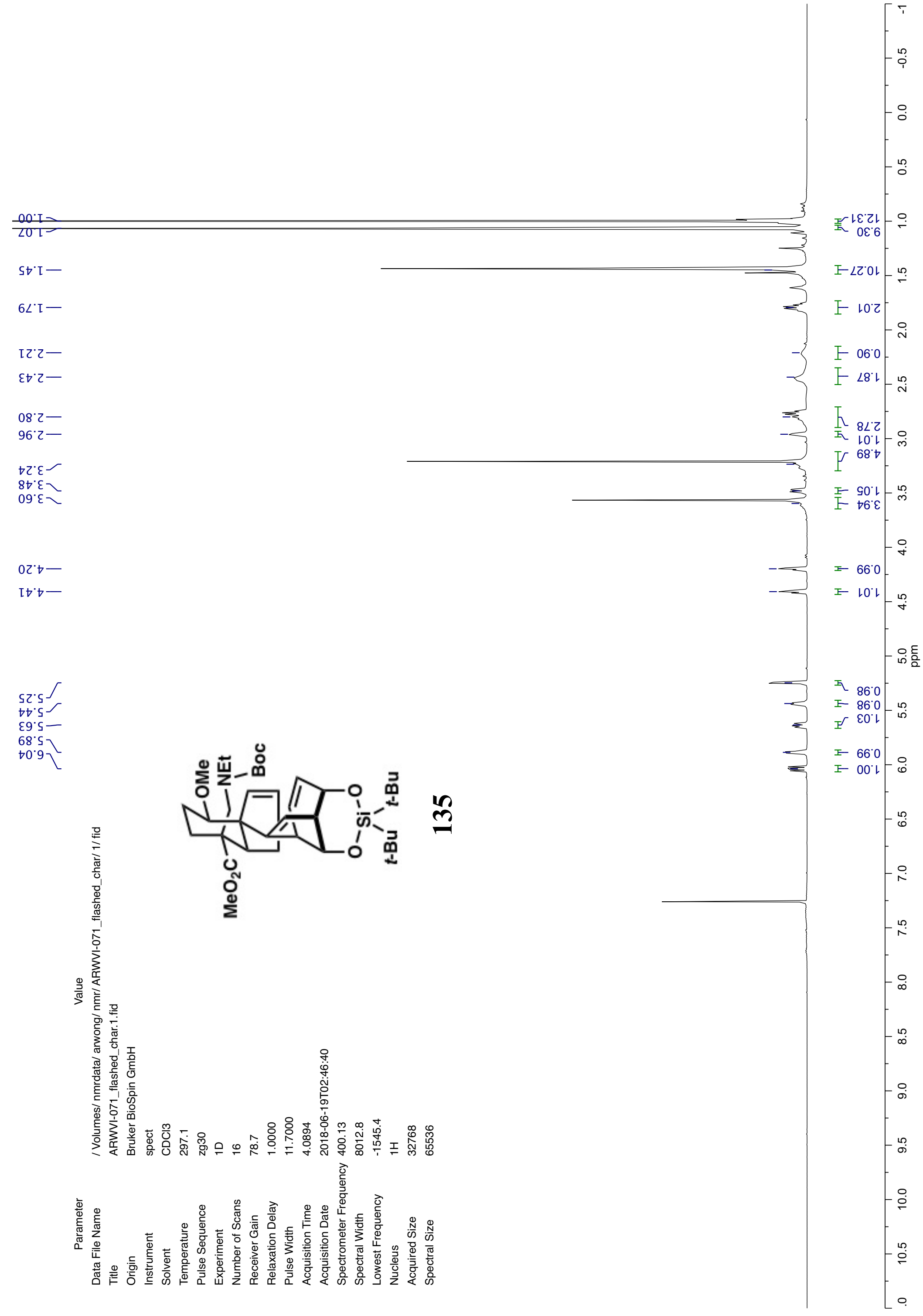
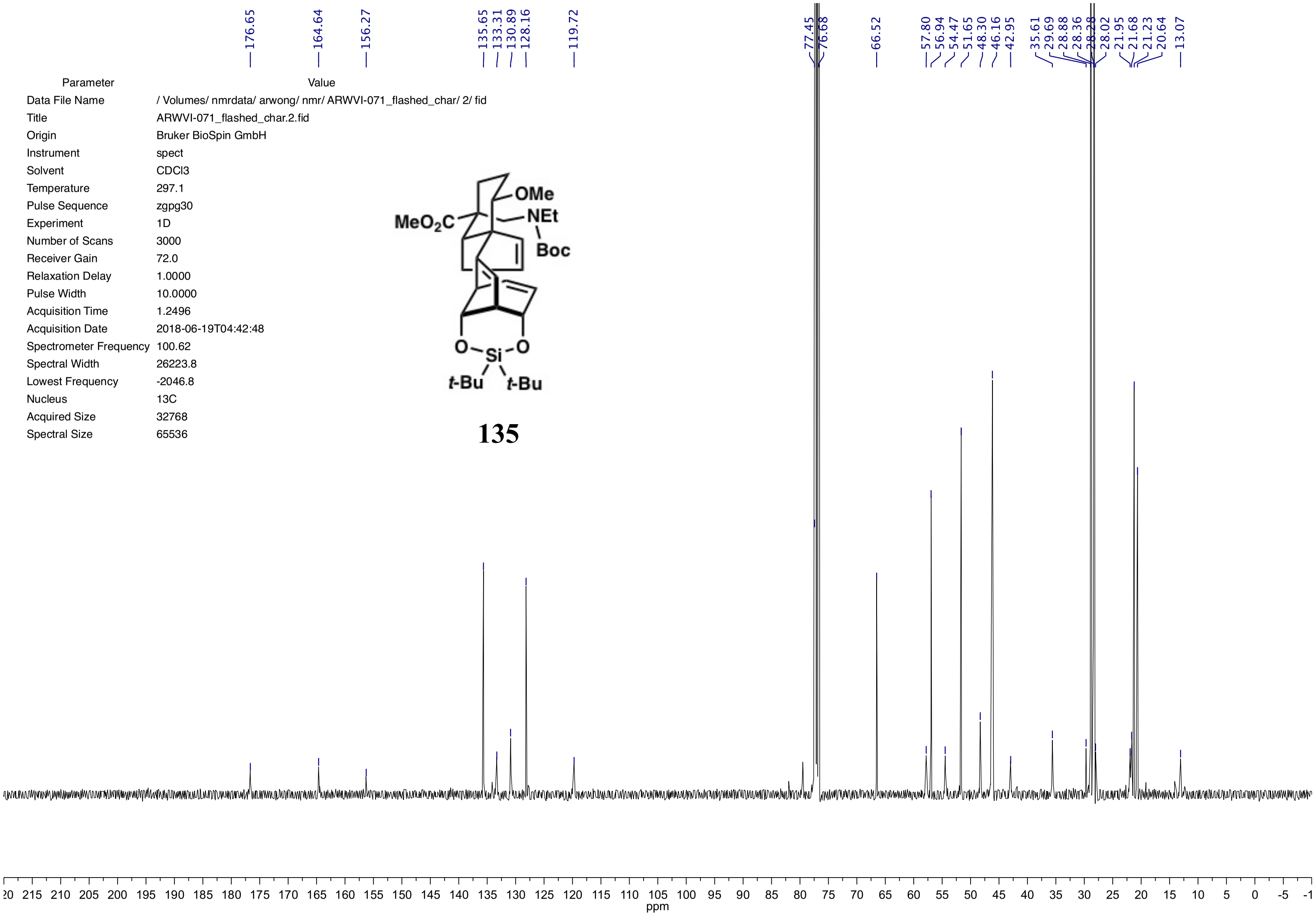
Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ arwong/ nmr/ ARWVI-056_prepTLC_C_char/ 4/ fid
Title	ARWVI-056_prepTLC_C_char.4.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	297.1
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1028
Receiver Gain	64.2
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.2496
Acquisition Date	2018-06-20T14:15:36
Spectrometer Frequency	100.62
Spectral Width	26223.8
Lowest Frequency	-2046.8
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



135

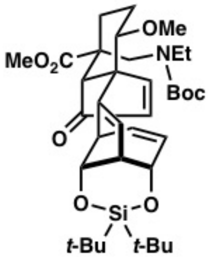
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-071_flashed_char/ 1/ fid
Title	ARWVI-071_flashed_char.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	297.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	16
Receiver Gain	78.7
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-06-19T02:46:40
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



135

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-071_flashed_char/ 2/ fid
Title	ARWVI-071_flashed_char.2.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	297.1
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	3000
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.2496
Acquisition Date	2018-06-19T04:42:48
Spectrometer Frequency	100.62
Spectral Width	26223.8
Lowest Frequency	-2046.8
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-074_prepTLC_B_char/ 1/ fid
Title	ARWVI-074_prepTLC_B_char.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	297.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	112.8
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-06-20T16:31:02
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



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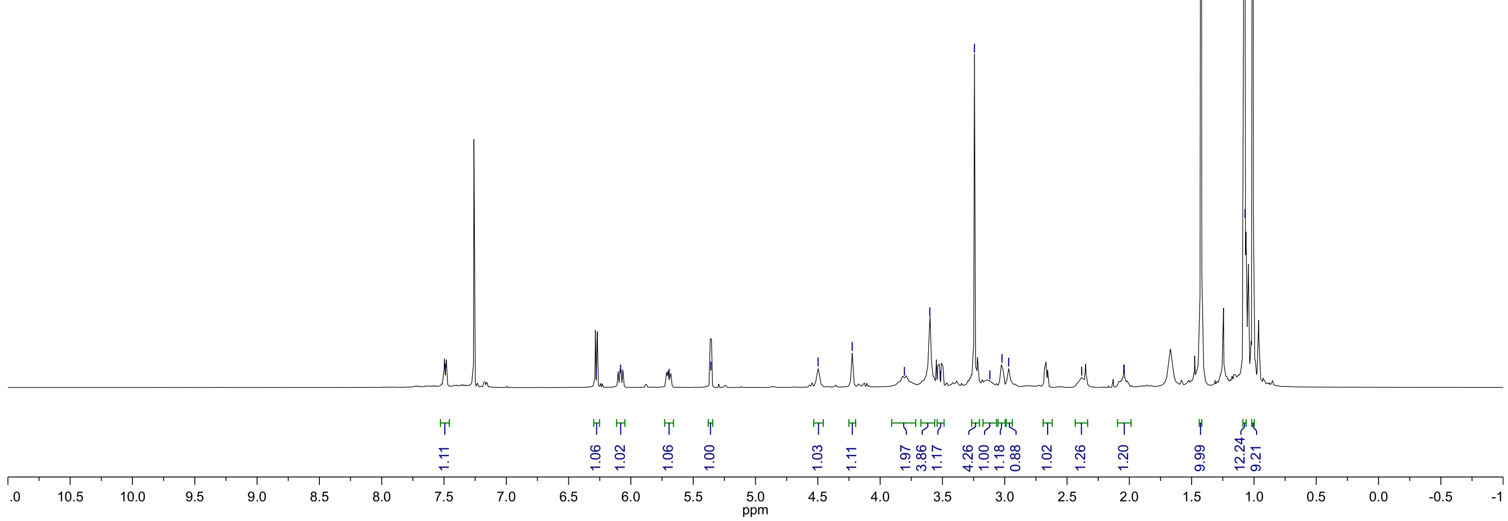
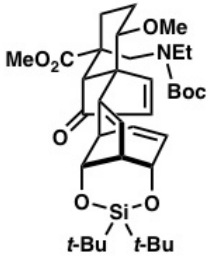
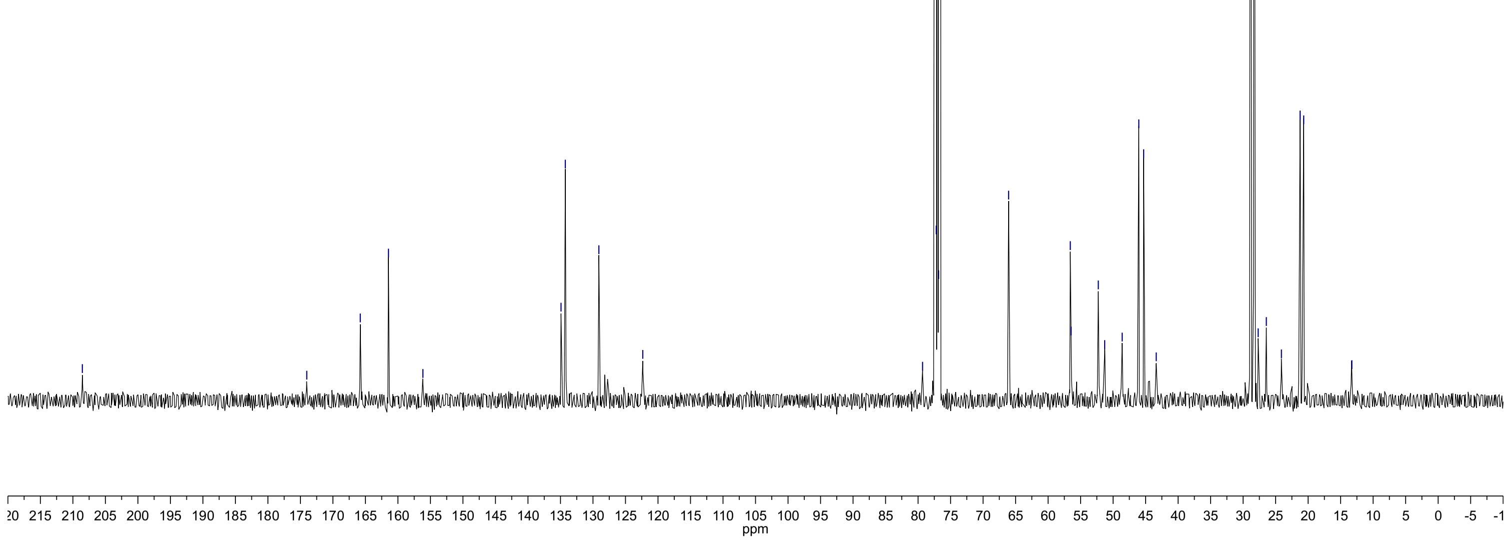
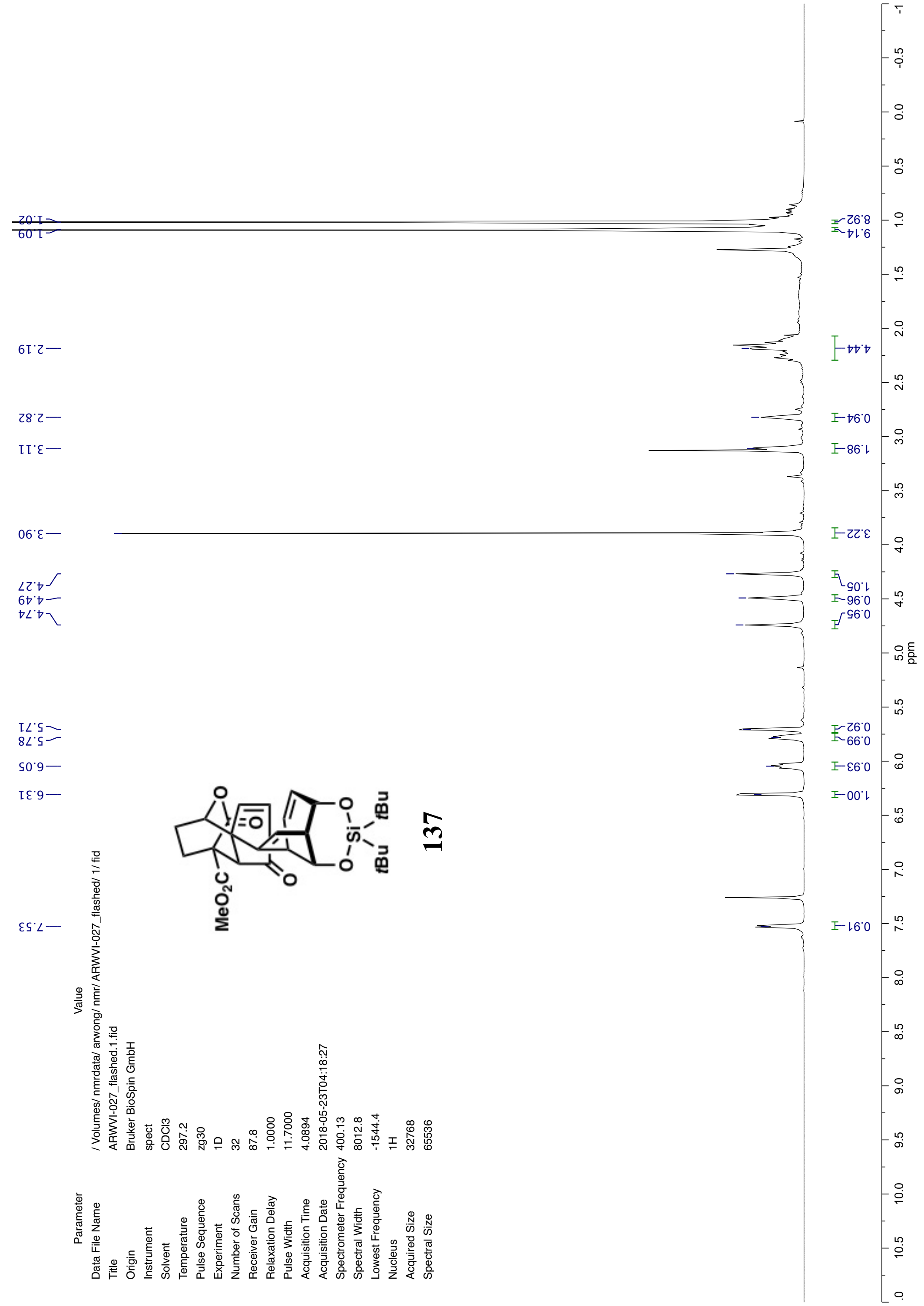


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-074_prepTLC_B_char_2/ 2/ fid
Title	ARWVI-074_prepTLC_B_char_2.2.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	297.2
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	3000
Receiver Gain	55.5
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.2496
Acquisition Date	2018-06-21T03:00:12
Spectrometer Frequency	100.62
Spectral Width	26223.8
Lowest Frequency	-2046.6
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



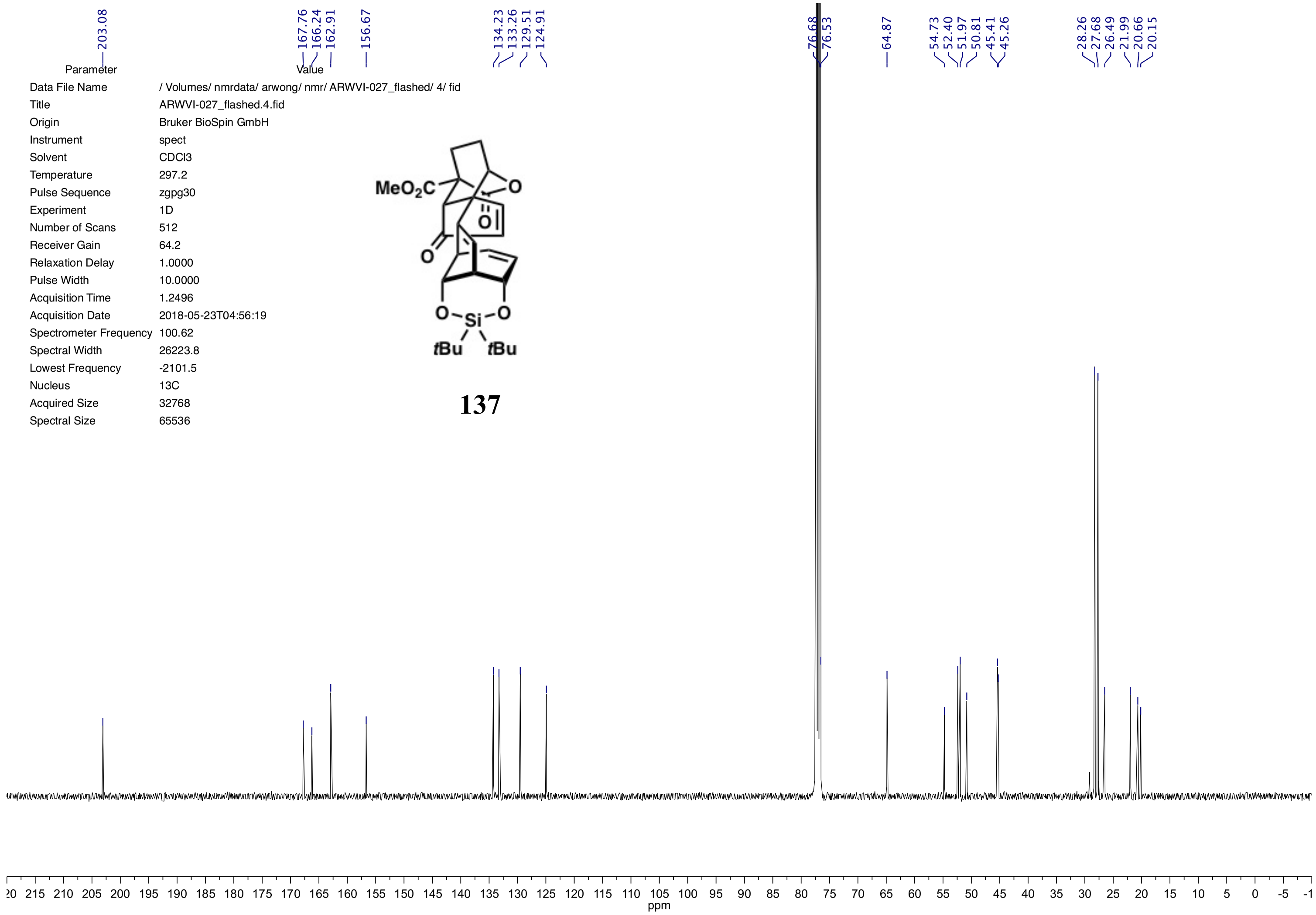
136





137

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-027_flashed/ 1/ fid
Title	ARWVI-027_flashed.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	297.2
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	87.8
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-05-23T04:18:27
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1544.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-027_flashed/ 4/ fid
Title	ARWVI-027_flashed.4.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	297.2
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	512
Receiver Gain	64.2
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.2496
Acquisition Date	2018-05-23T04:56:19
Spectrometer Frequency	100.62
Spectral Width	26223.8
Lowest Frequency	-2101.5
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

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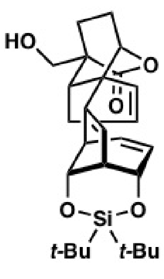
Appendix 3

Spectra Relevant to Chapter 3:

Total Syntheses of the C_{19} Diterpenoid Alkaloids (–)-Liljestrandisine and (–)-Liljestrandinine

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-201_flashed_char/ 1/ fid
Title	ARWVI-201_flashed_char.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	87.8
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2019-01-27T04:11:16
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.1
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



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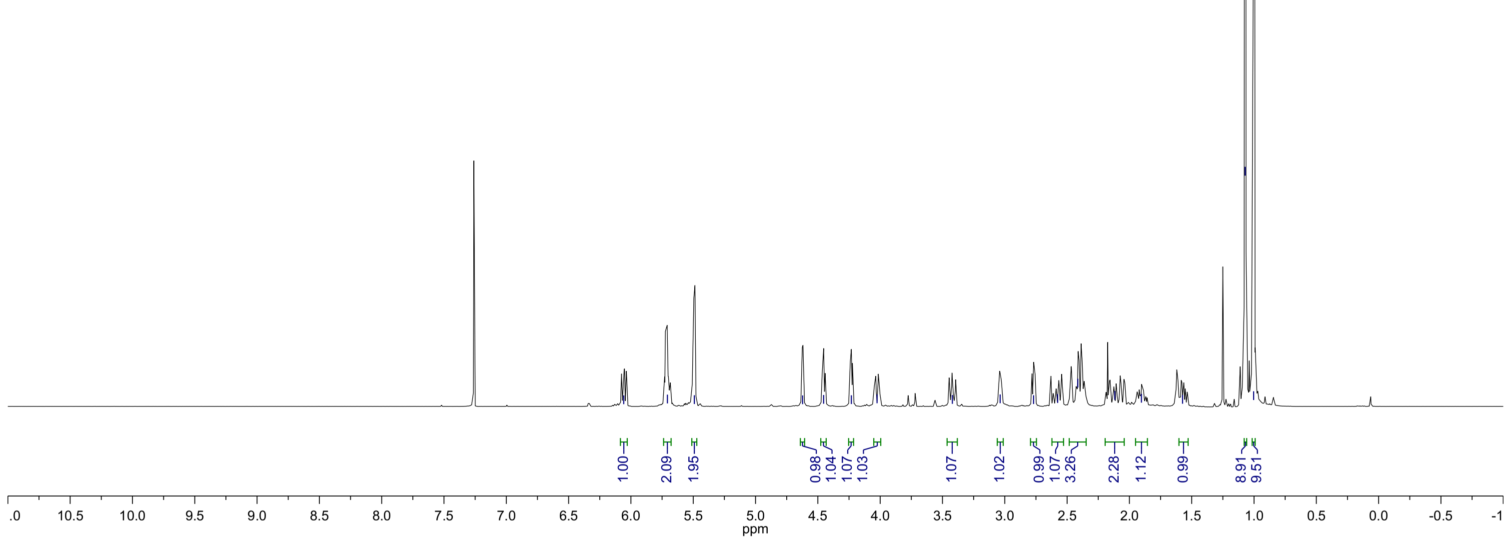
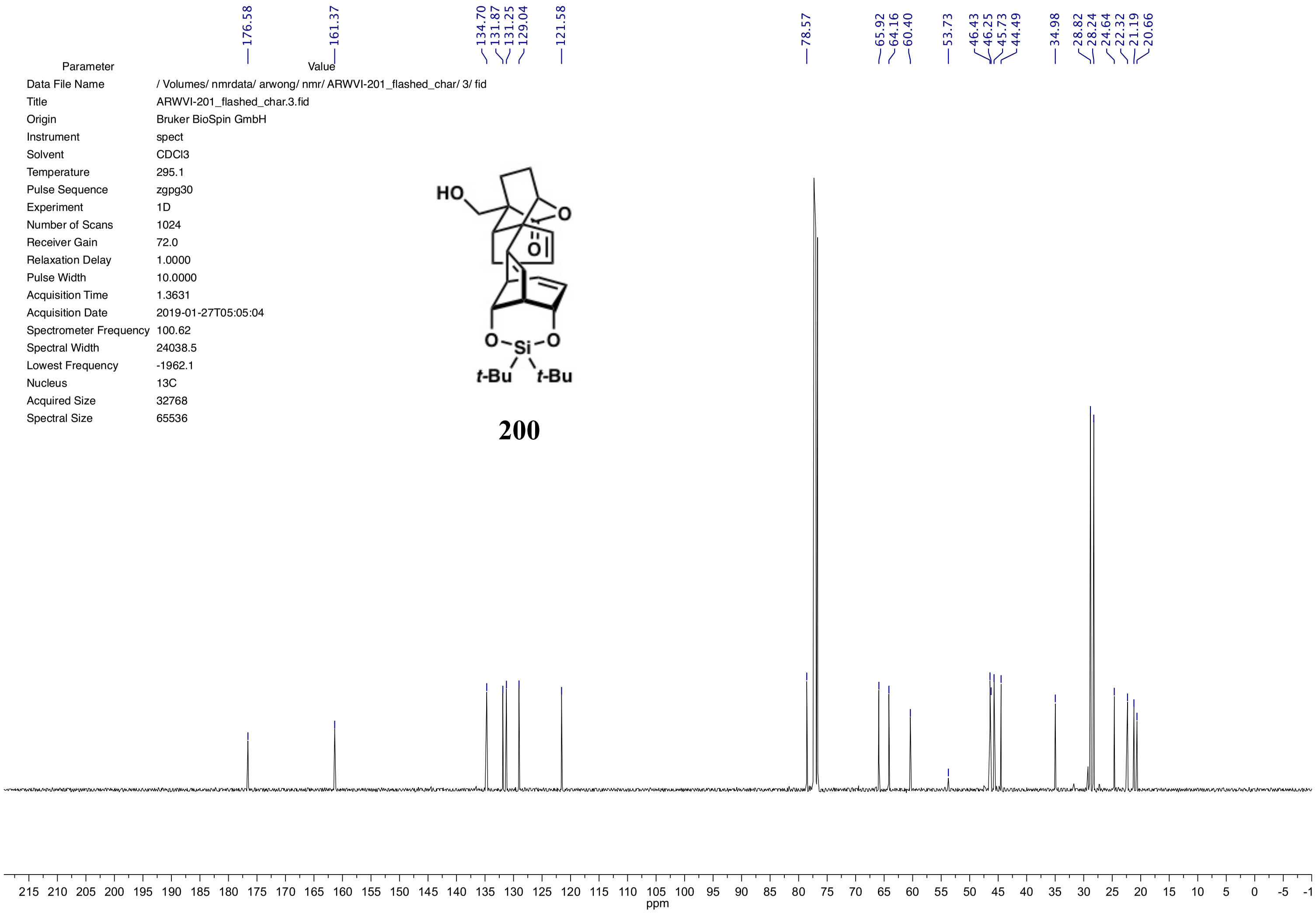
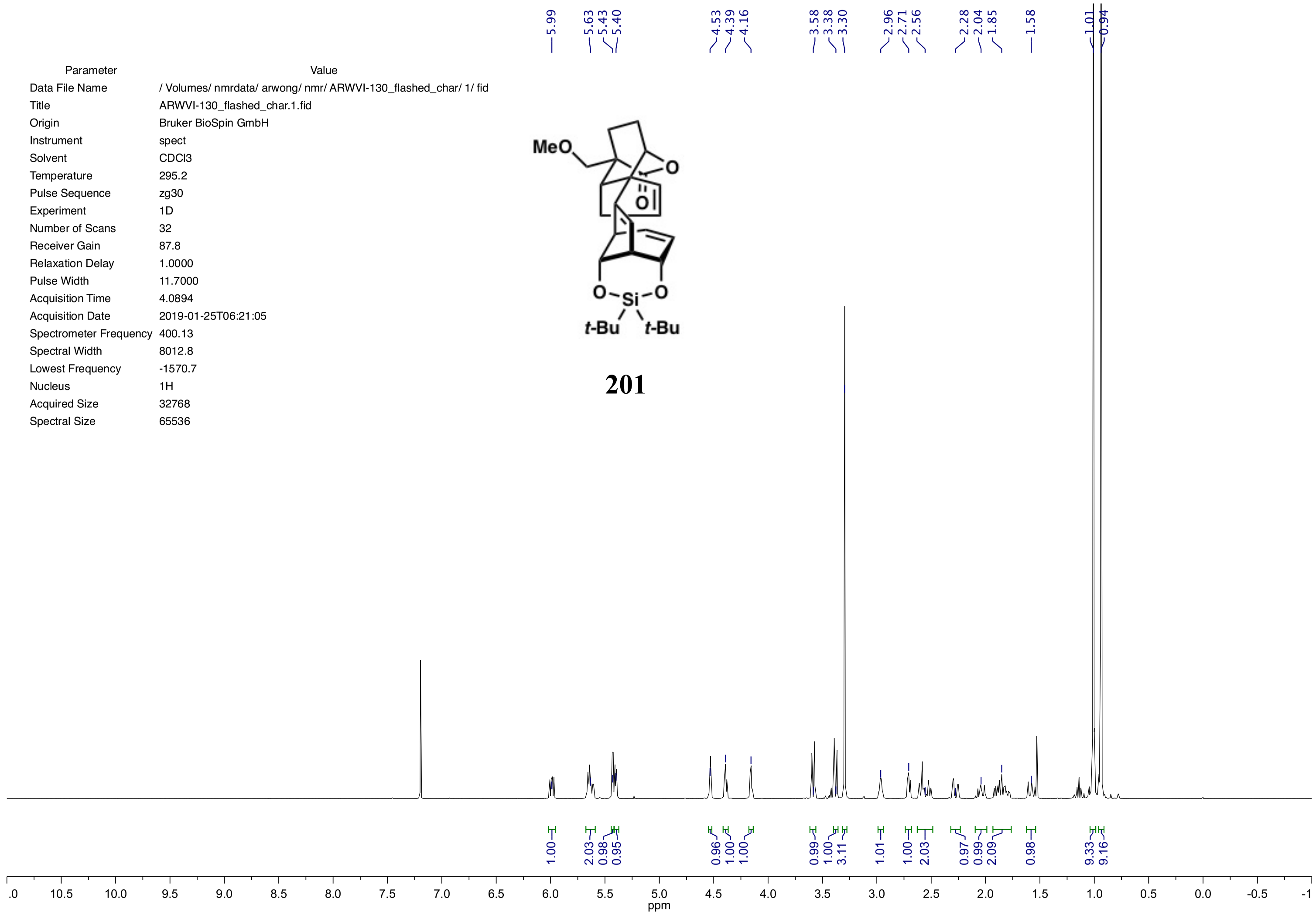




200

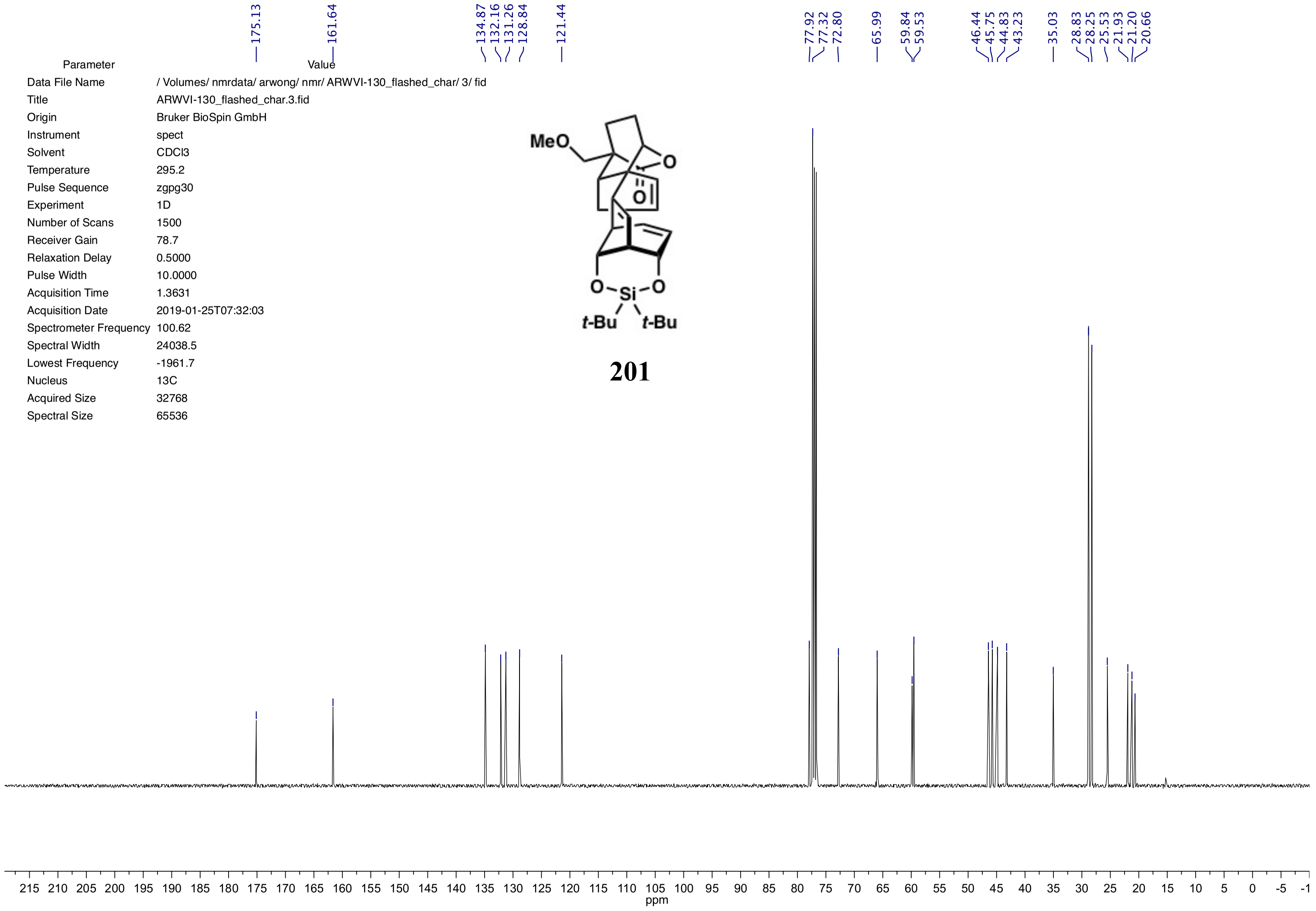
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-201_flashed_char/ 3/ fid
Title	ARWVI-201_flashed_char.3.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1024
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2019-01-27T05:05:04
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1962.1
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



201

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-130_flashed_char/ 1/ fid
Title	ARWVI-130_flashed_char.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	87.8
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2019-01-25T06:21:05
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1570.7
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-130_flashed_char/ 3/ fid
Title	ARWVI-130_flashed_char.3.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1500
Receiver Gain	78.7
Relaxation Delay	0.5000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2019-01-25T07:32:03
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.7
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



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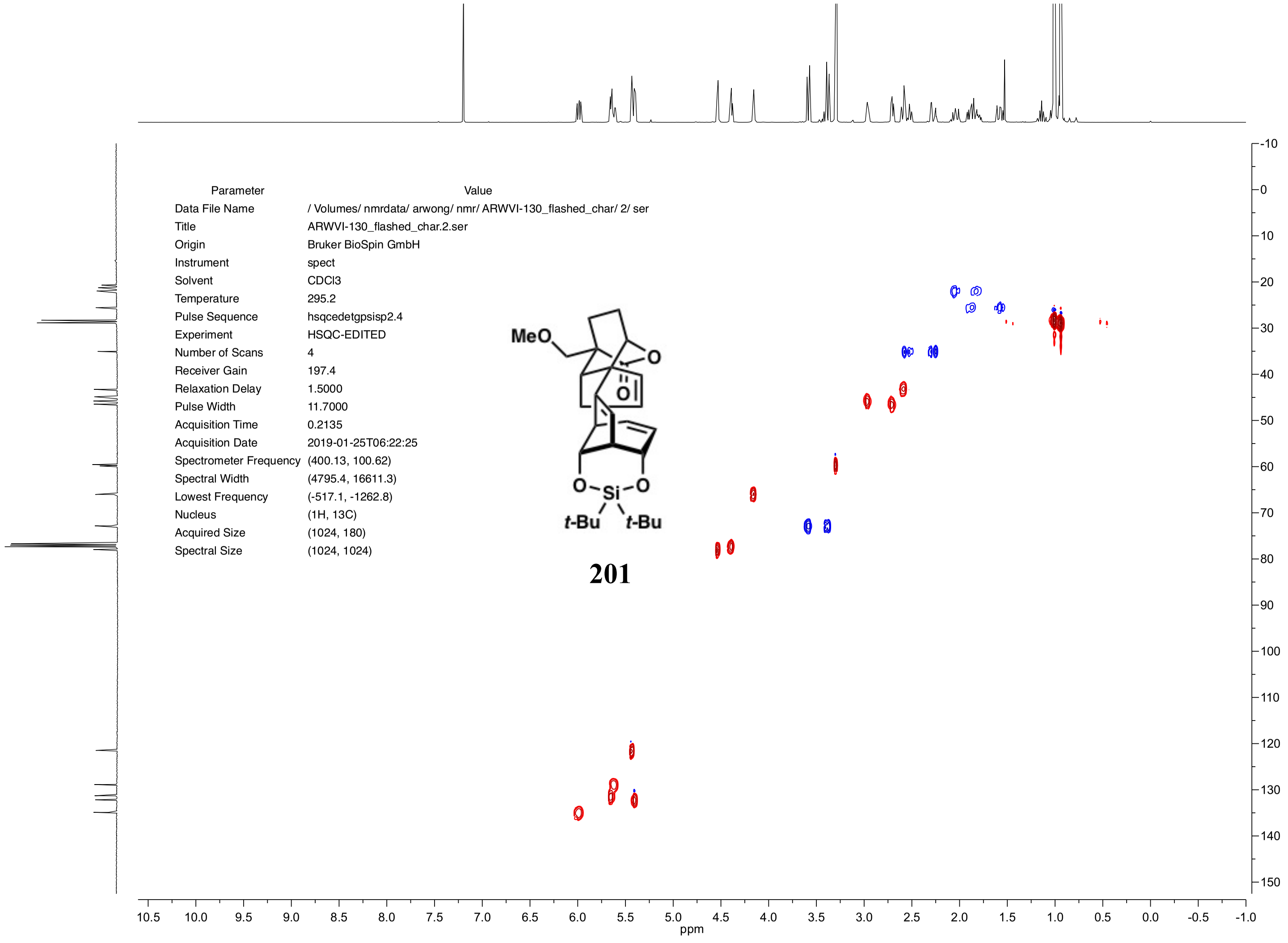
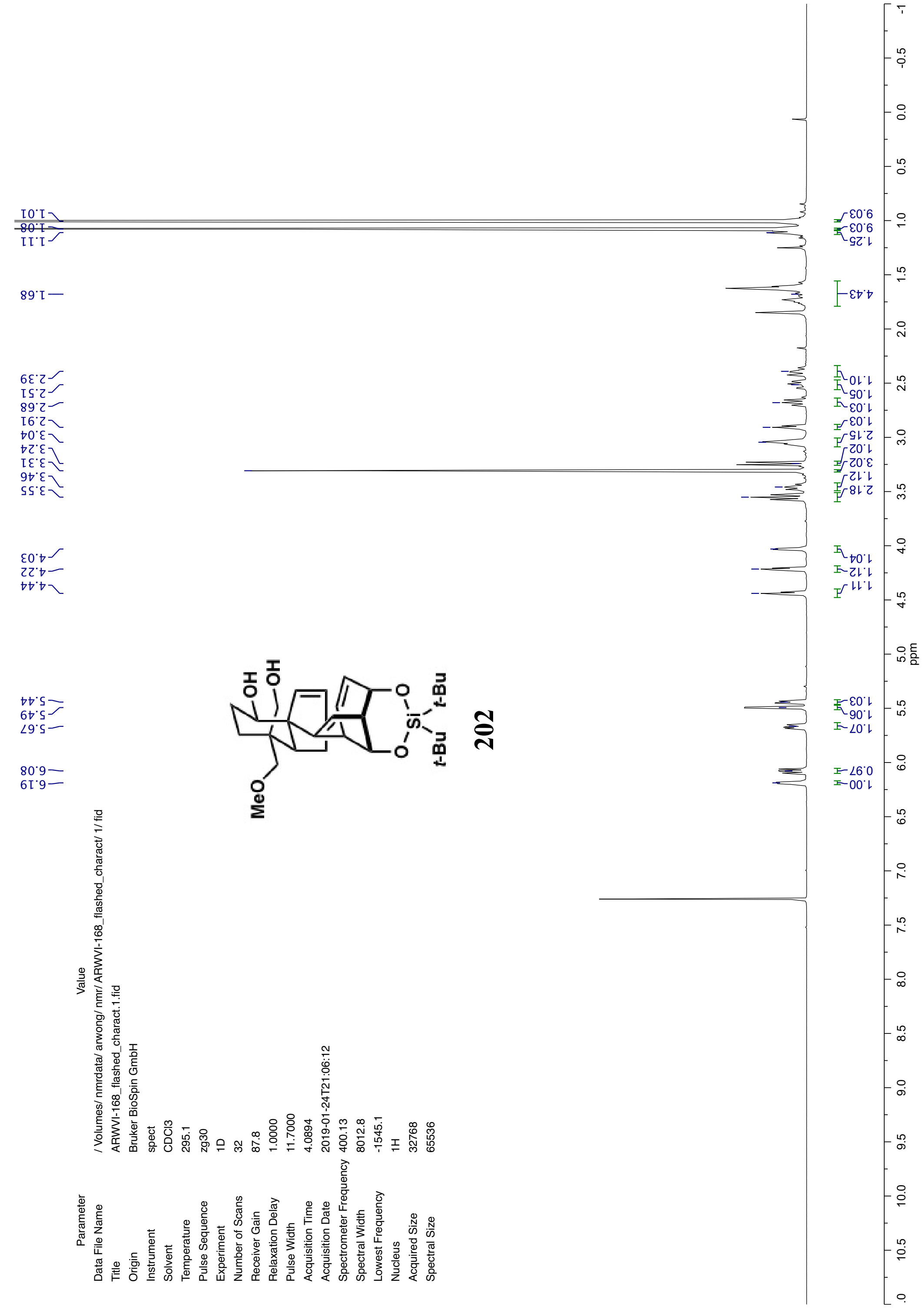


201

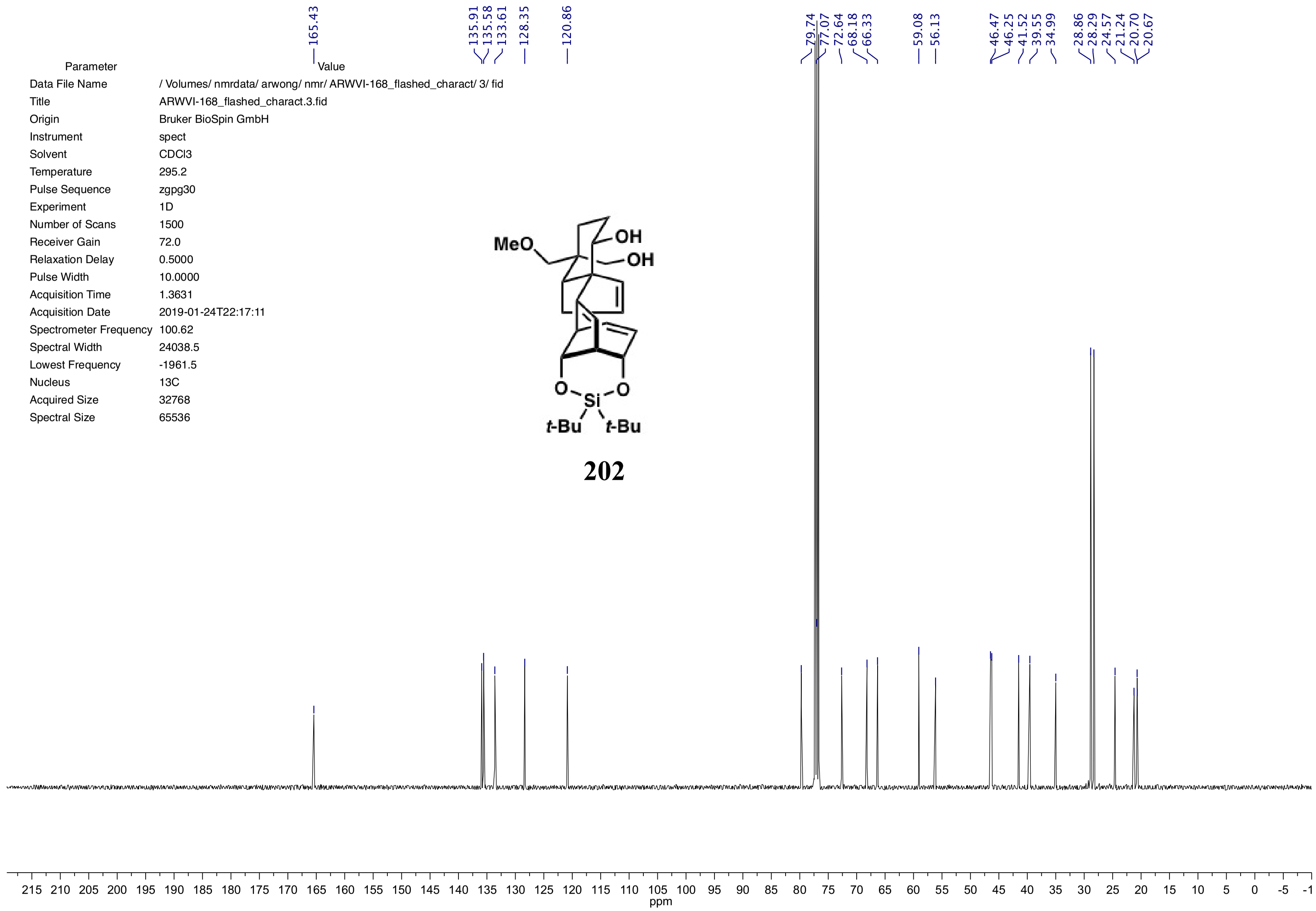
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-130_flashed_char/ 2/ ser
Title	ARWVI-130_flashed_char.2.ser
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	hsqcedetgpsisp2.4
Experiment	HSQC-EDITED
Number of Scans	4
Receiver Gain	197.4
Relaxation Delay	1.5000
Pulse Width	11.7000
Acquisition Time	0.2135
Acquisition Date	2019-01-25T06:22:25
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(4795.4, 16611.3)
Lowest Frequency	(-517.1, -1262.8)
Nucleus	(1H, 13C)
Acquired Size	(1024, 180)
Spectral Size	(1024, 1024)



202

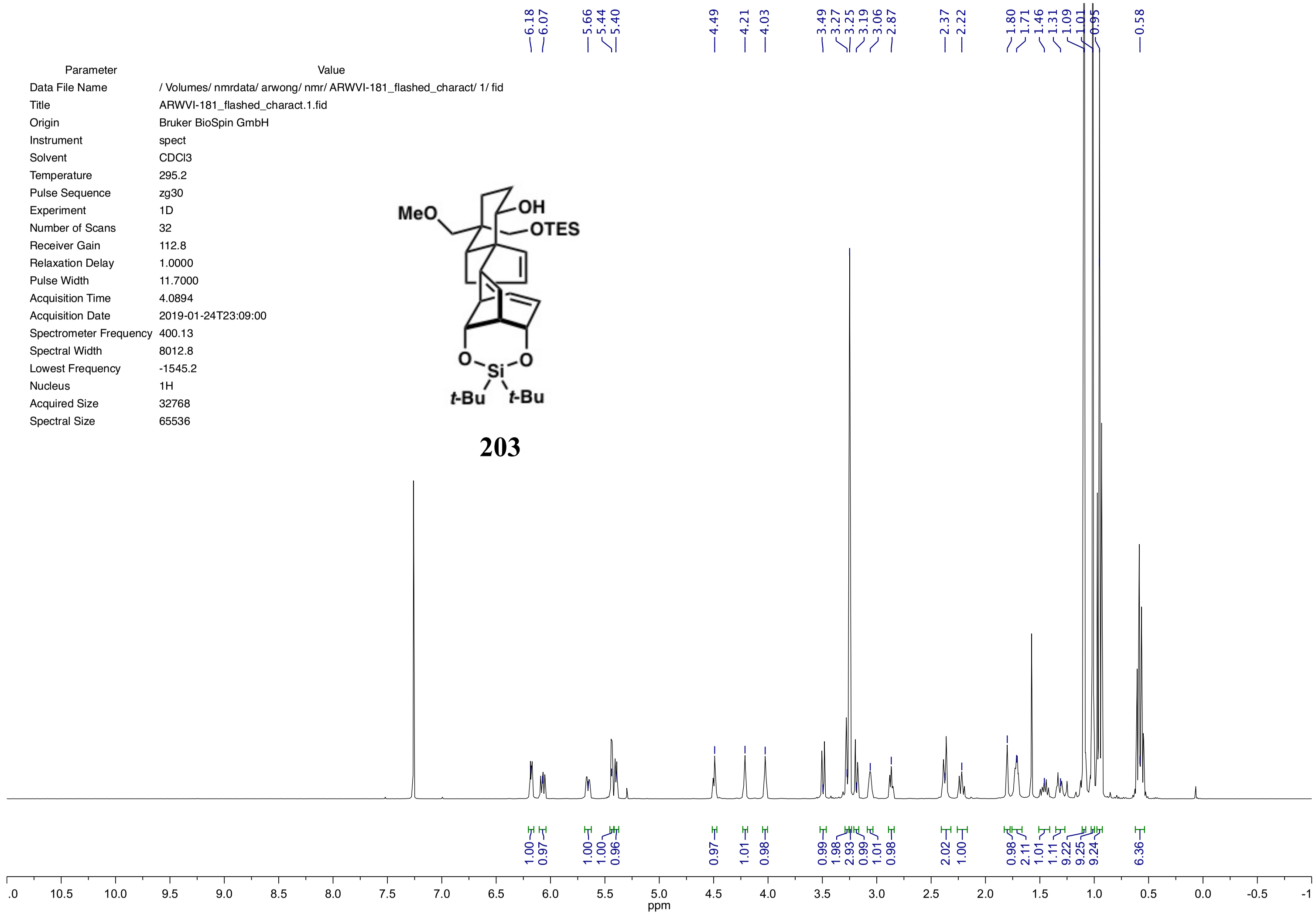
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ awong/ nmr/ ARWVI-168_flashed_charact/ 1/ fid
Title	ARWVI-168_flashed_charact.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	87.8
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2019-01-24T21:06:12
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.1
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-168_flashed_charact/ 3/ fid
Title	ARWVI-168_flashed_charact.3.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1500
Receiver Gain	72.0
Relaxation Delay	0.5000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2019-01-24T22:17:11
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.5
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



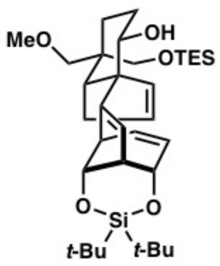
202

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-181_flashed_charact/ 1/ fid
Title	ARWVI-181_flashed_charact.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	112.8
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2019-01-24T23:09:00
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.2
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



203

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-181_flashed_charact/ 3/ fid
Title	ARWVI-181_flashed_charact.3.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1500
Receiver Gain	78.7
Relaxation Delay	0.5000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2019-01-25T00:19:58
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.0
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



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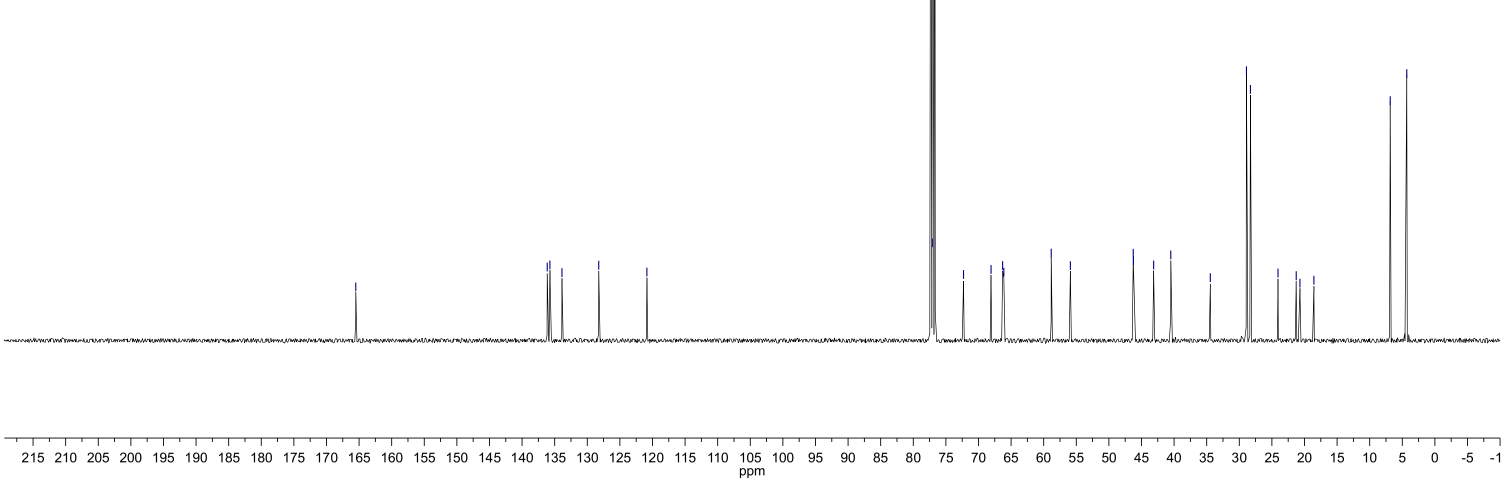
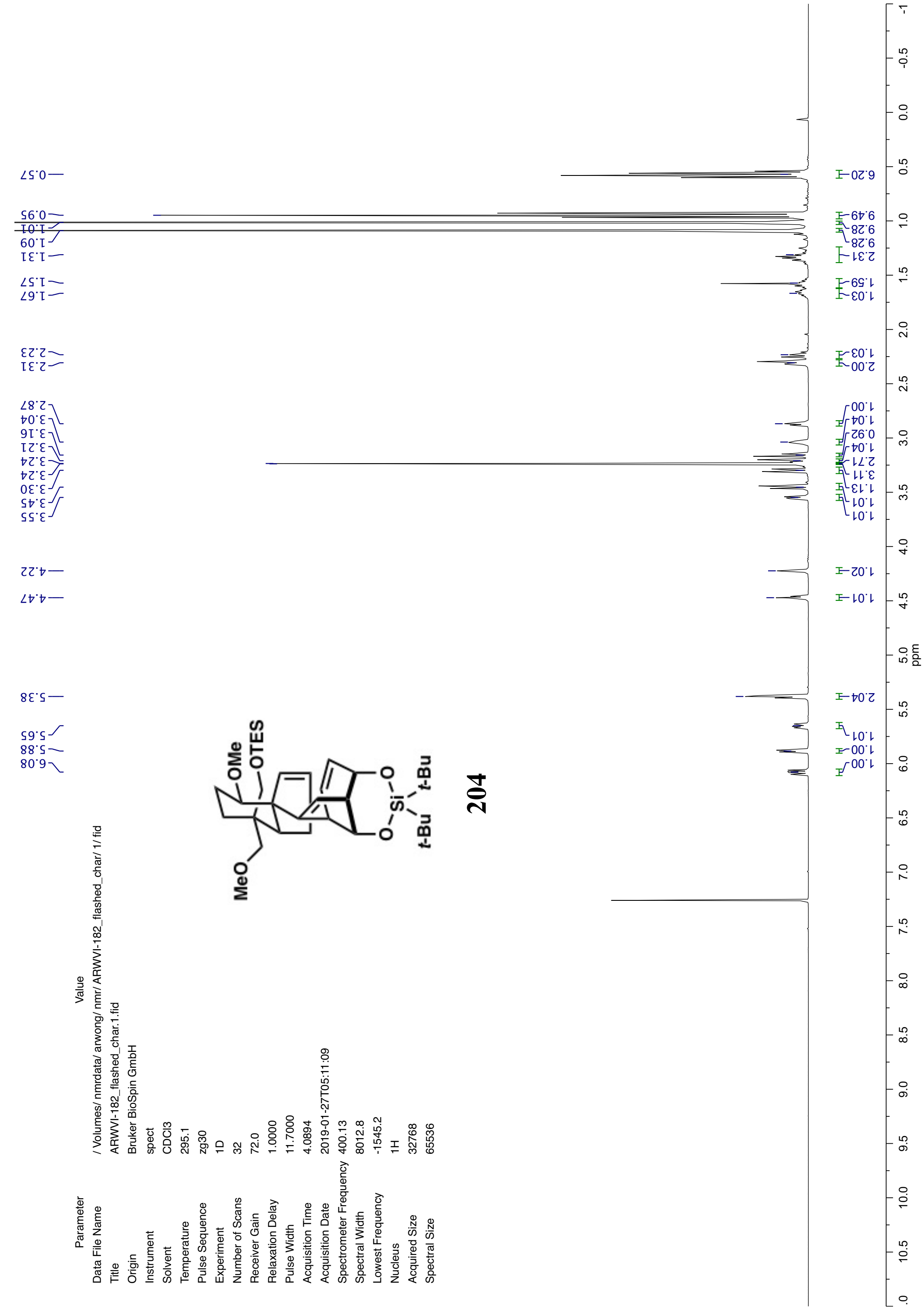
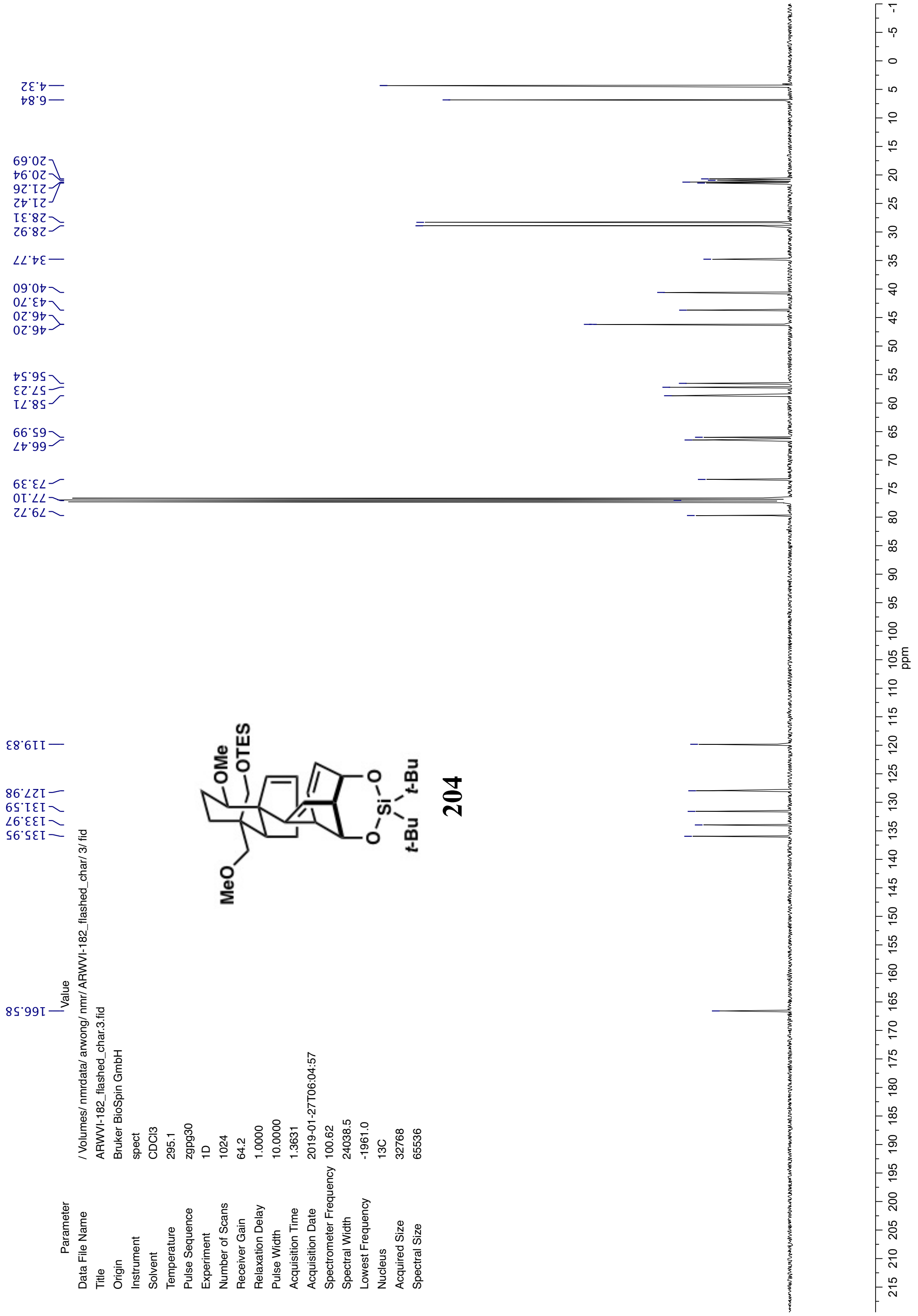




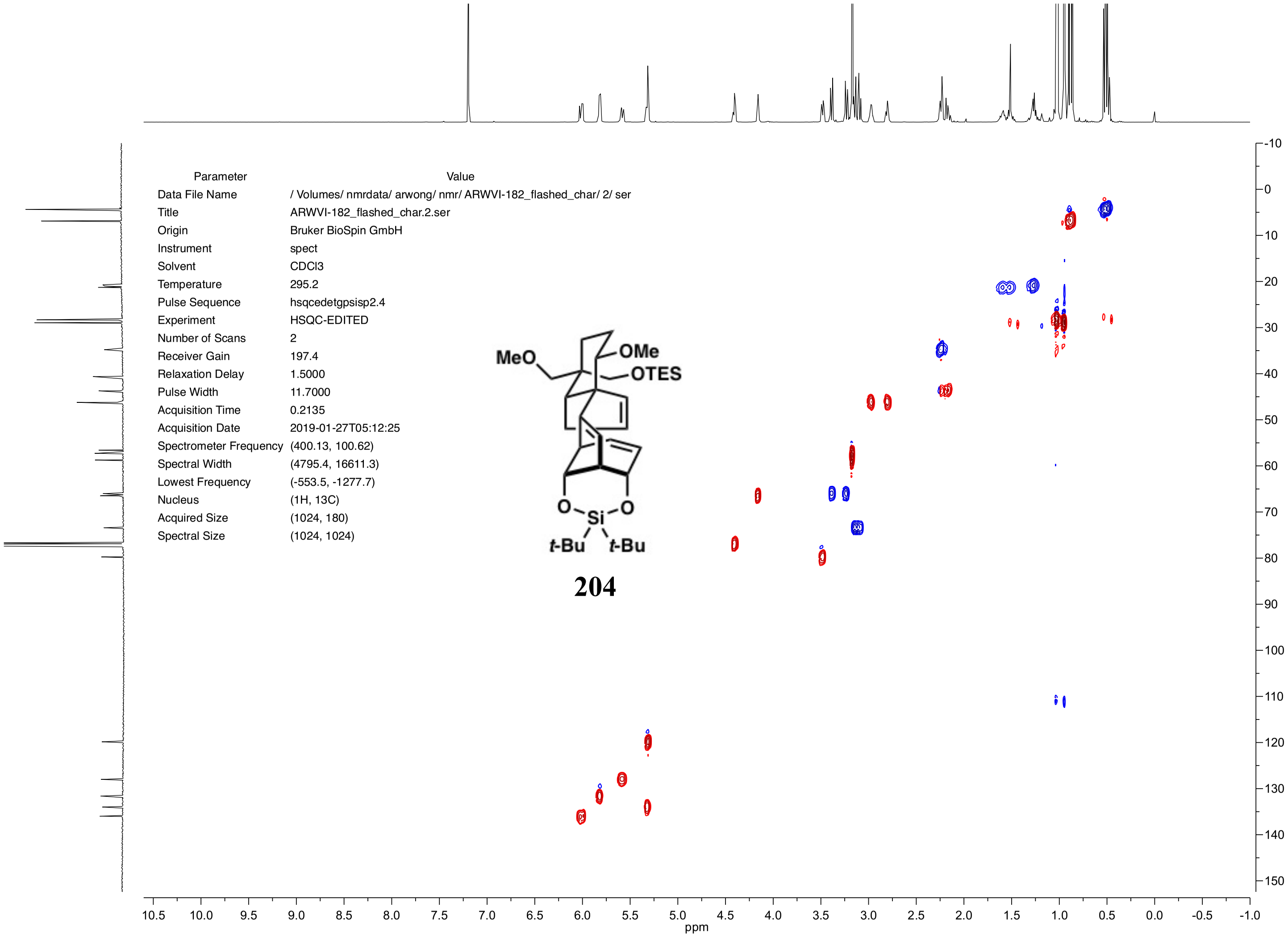
204

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-182_flashed_char/ 1/ fid
Title	ARWVI-182_flashed_char.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2019-01-27T05:11:09
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.2
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



204

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-182_flashed_char/ 3/ fid
Title	ARWVI-182_flashed_char.3.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
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	2019-01-27T06:04:57
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.0
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



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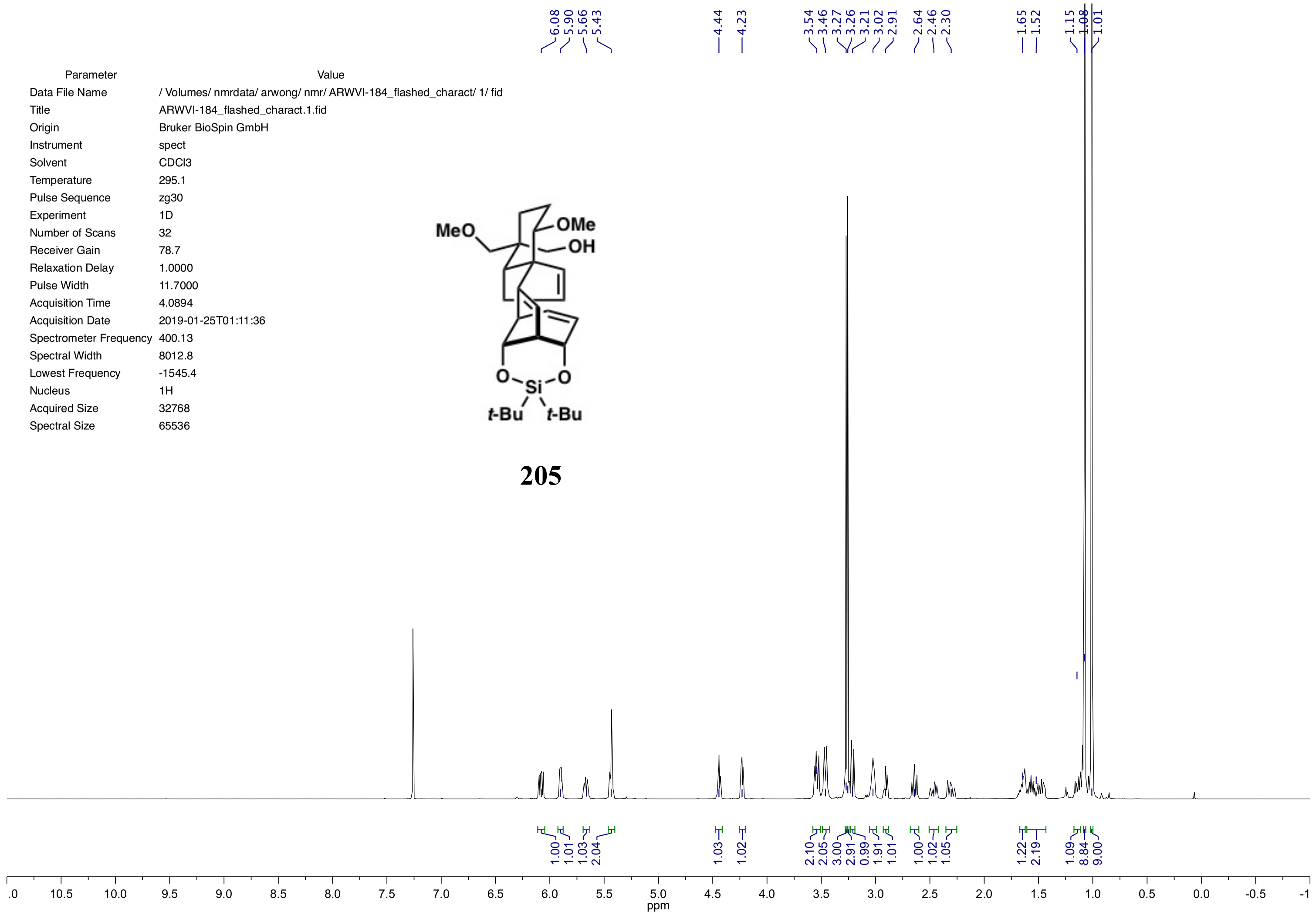
Parameter                    Value
Data File Name               / Volumes/ nmrdata/ arwong/ nmr/ ARWVI-182_flashed_char/ 2/ ser
Title                        ARWVI-182_flashed_char.2.ser
Origin                       Bruker BioSpin GmbH
Instrument                   spect
Solvent                      CDCl3
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             2019-01-27T05:12:25
Spectrometer Frequency       (400.13, 100.62)
Spectral Width               (4795.4, 16611.3)
Lowest Frequency             (-553.5, -1277.7)
Nucleus                      (1H, 13C)
Acquired Size                (1024, 180)
Spectral Size                (1024, 1024)
```

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-184_flashed_charact/ 1/ fid
Title	ARWVI-184_flashed_charact.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	78.7
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2019-01-25T01:11:36
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



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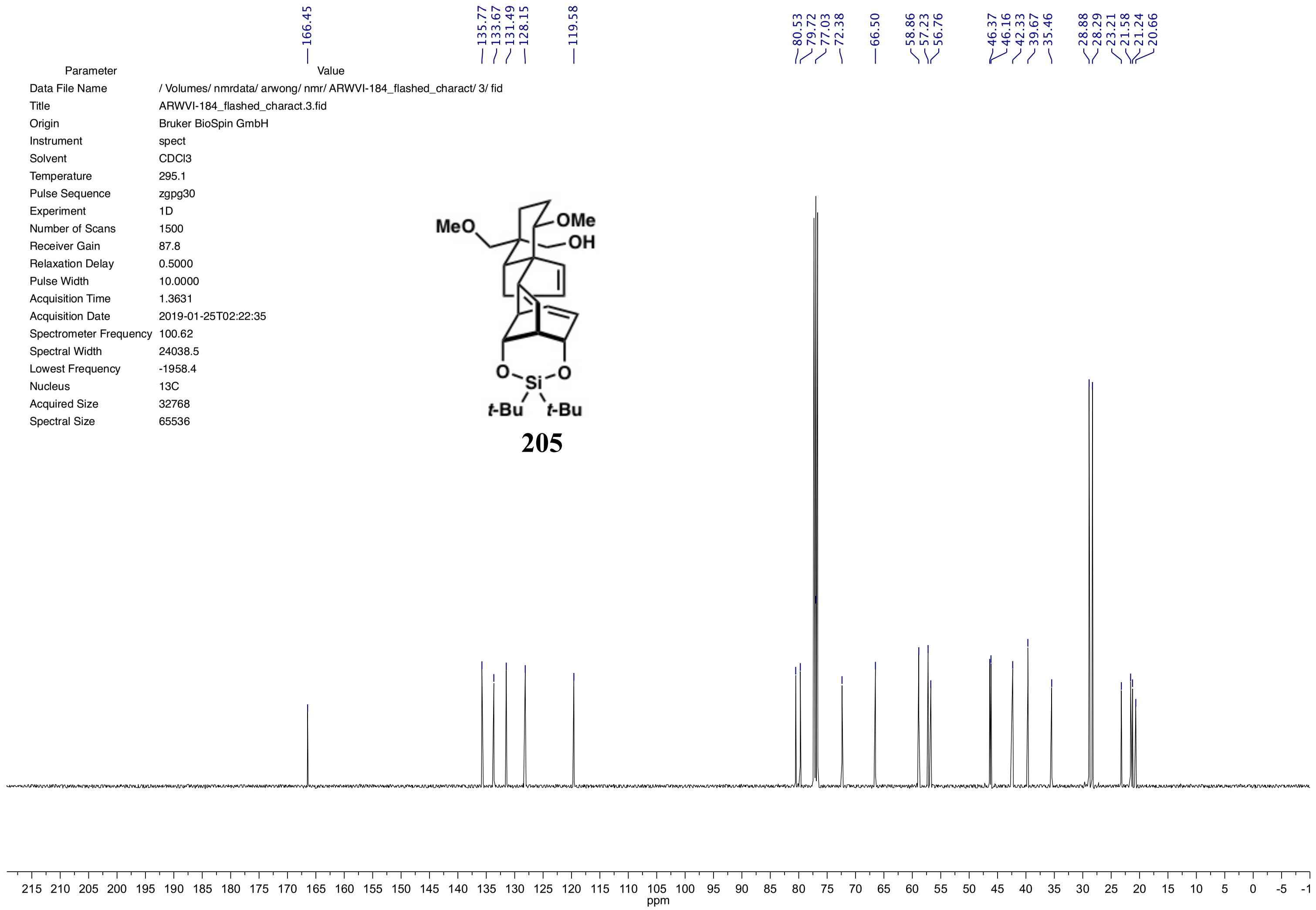
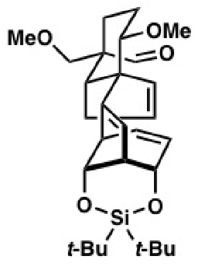


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-184_flashed_charact/ 3/ fid
Title	ARWVI-184_flashed_charact.3.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1500
Receiver Gain	87.8
Relaxation Delay	0.5000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2019-01-25T02:22:35
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1958.4
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

205

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-185_flashed_char/ 1/ fid
Title	ARWVI-185_flashed_char.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	98.9
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2019-01-27T03:10:20
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1570.9
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



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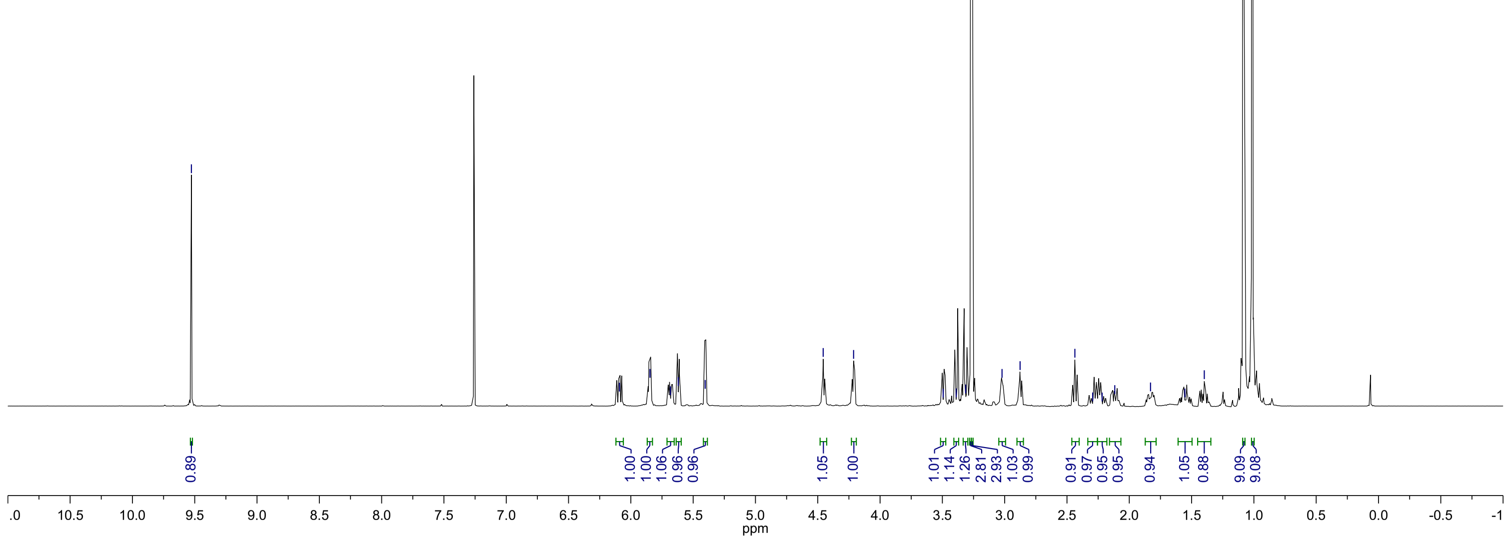
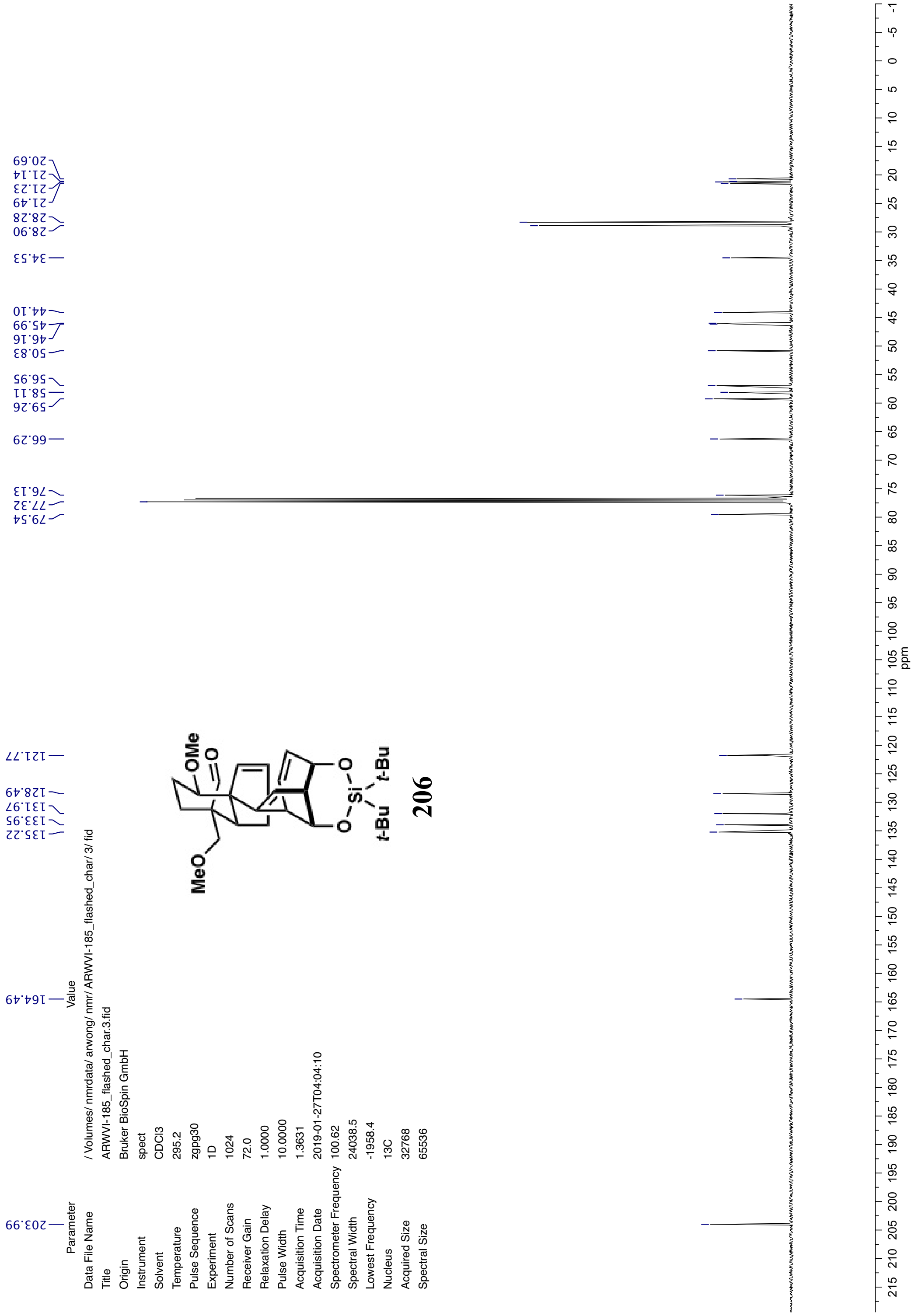
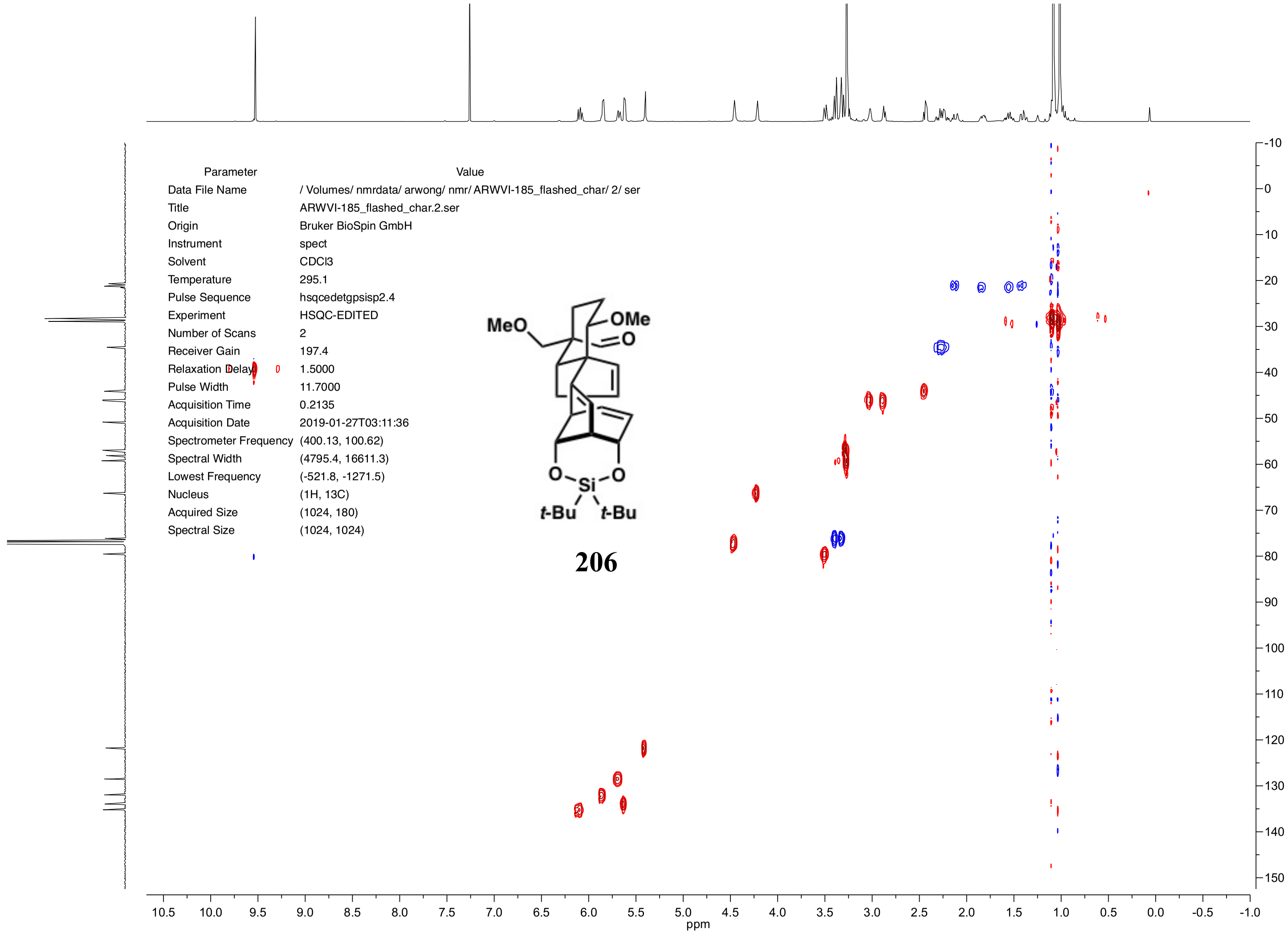




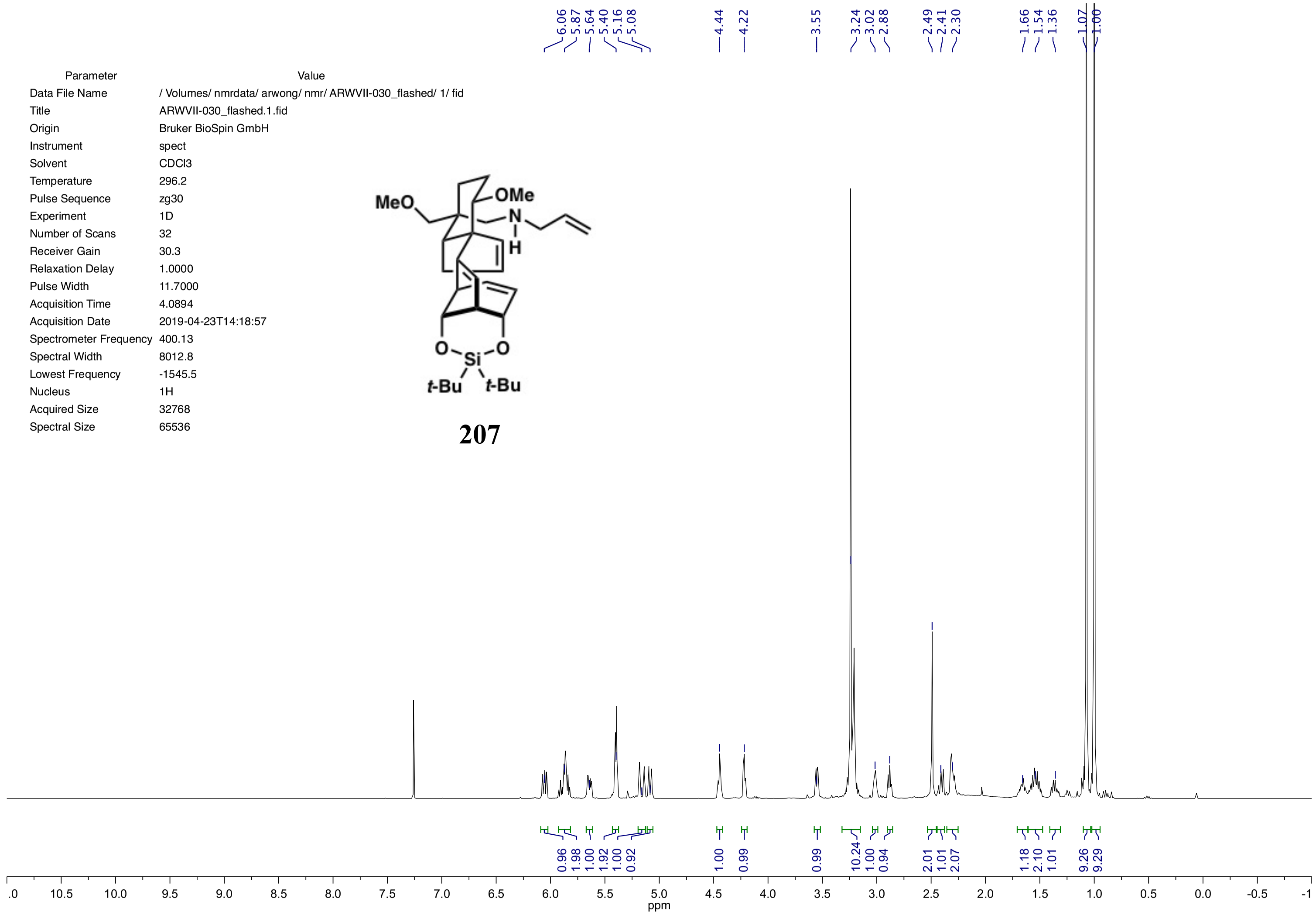
206

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-185_flashed_char/ 3/ fid
Title	ARWVI-185_flashed_char.3.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1024
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2019-01-27T04:04:10
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1958.4
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-185_flashed_char/ 2/ ser
Title	ARWVI-185_flashed_char.2.ser
Origin	Bruker BioSpin GmbH
Instrument	spect
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	2019-01-27T03:11:36
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(4795.4, 16611.3)
Lowest Frequency	(-521.8, -1271.5)
Nucleus	(1H, 13C)
Acquired Size	(1024, 180)
Spectral Size	(1024, 1024)

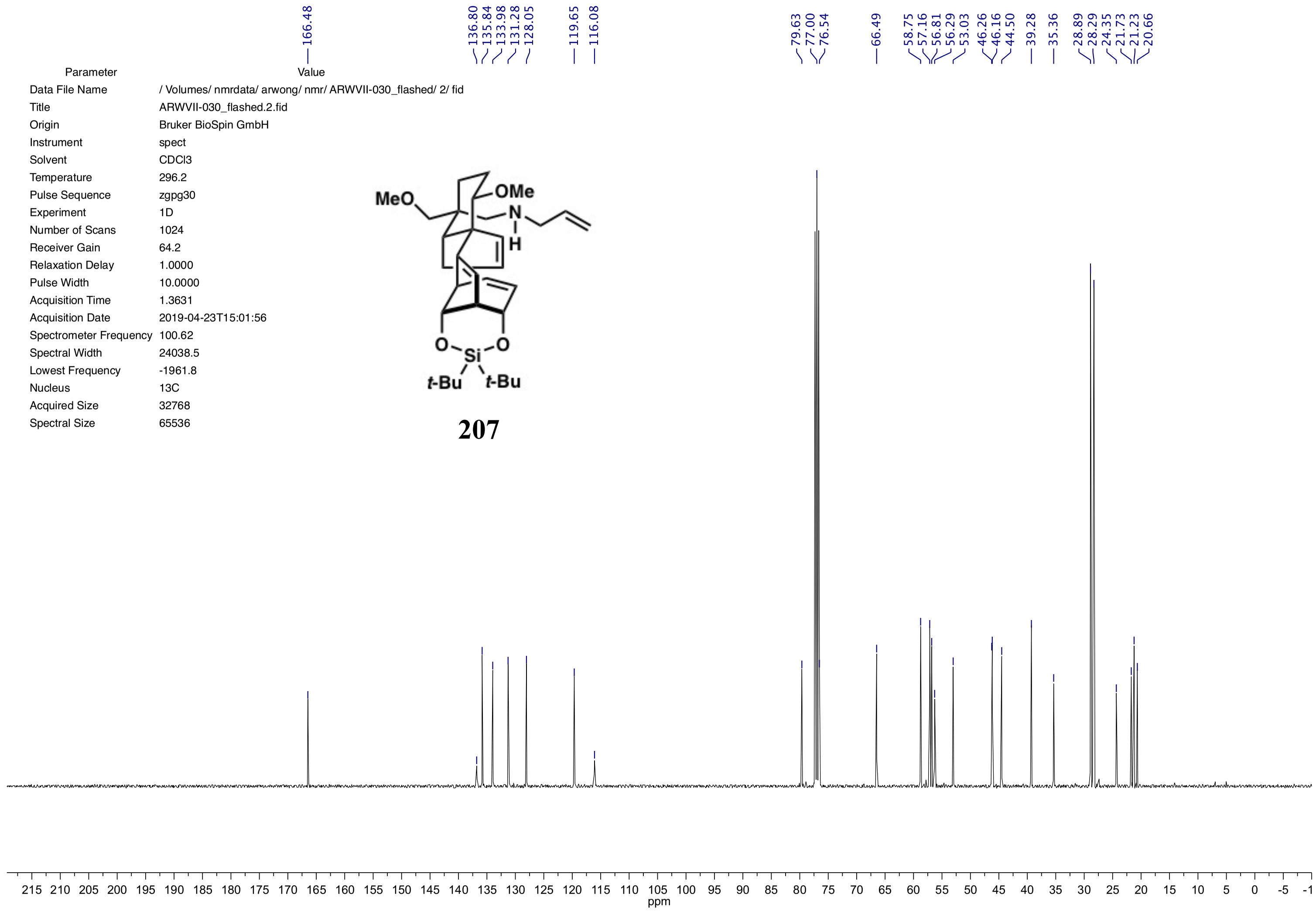
206



207

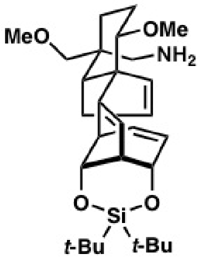
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVII-030_flashed/ 1/ fid
Title	ARWVII-030_flashed.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	296.2
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	30.3
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2019-04-23T14:18:57
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.5
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVII-030_flashed/ 2/ fid
Title	ARWVII-030_flashed.2.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	296.2
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	2019-04-23T15:01:56
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.8
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

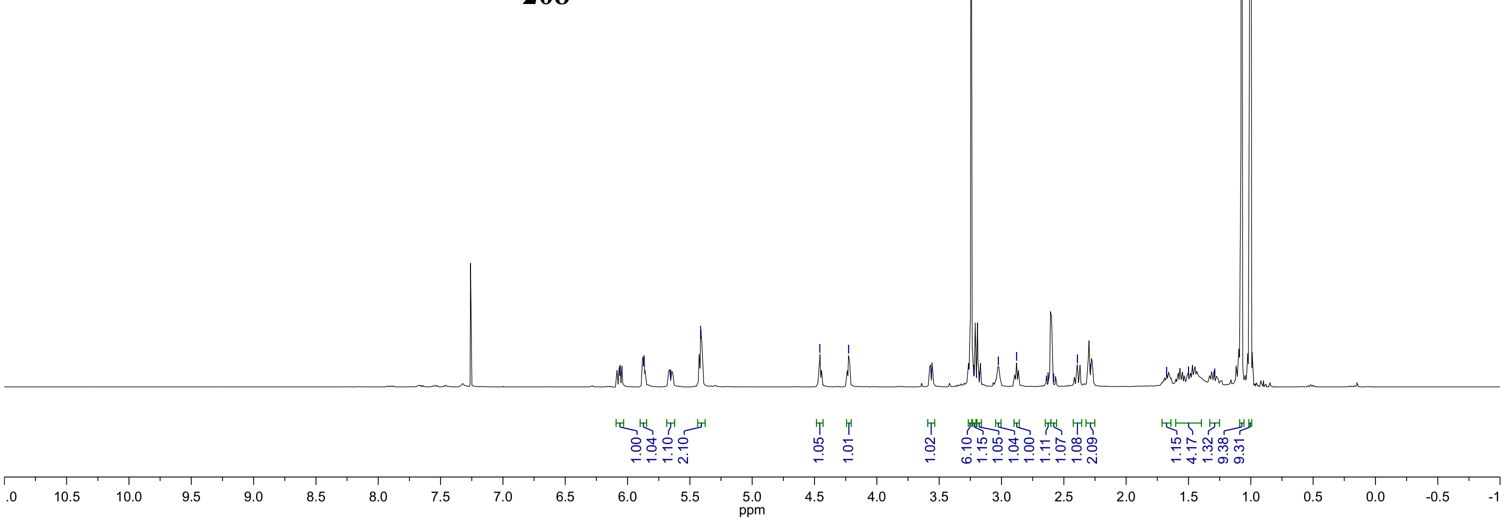


207

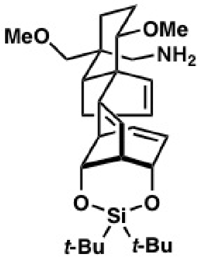
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-270_flashed_char/ 1/ fid
Title	ARWVI-270_flashed_char.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	64.2
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-12-11T01:00:34
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



208



Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-270_flashed_char/ 6/ fid
Title	ARWVI-270_flashed_char.6.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1024
Receiver Gain	78.7
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-12-11T03:29:33
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1962.2
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



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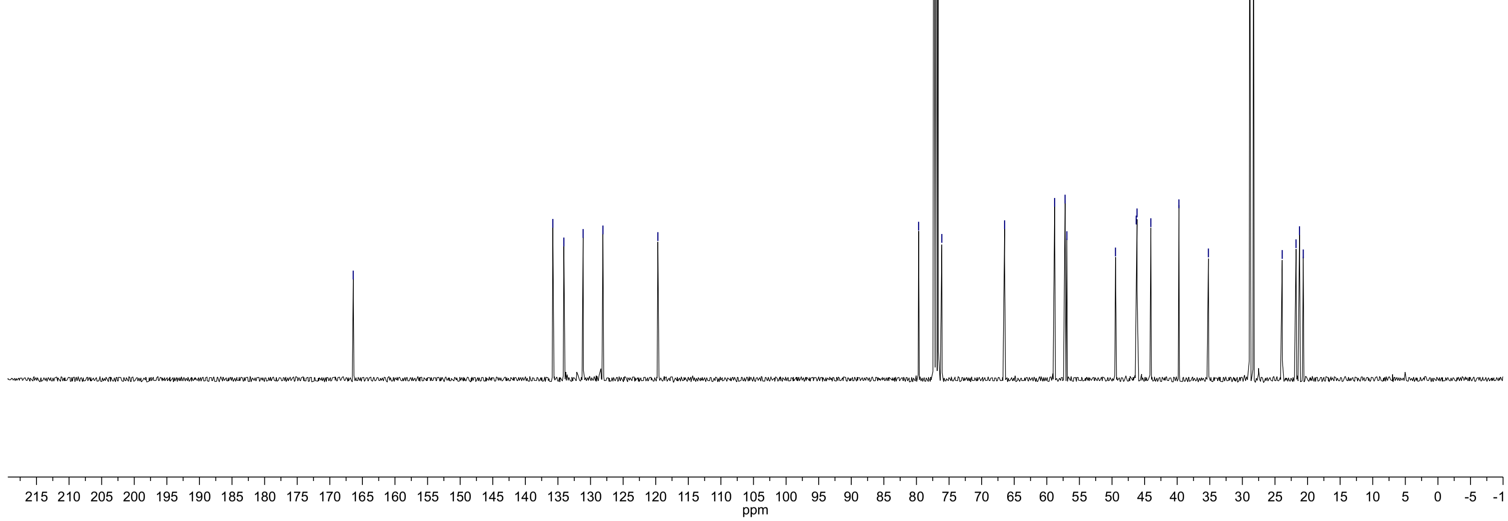
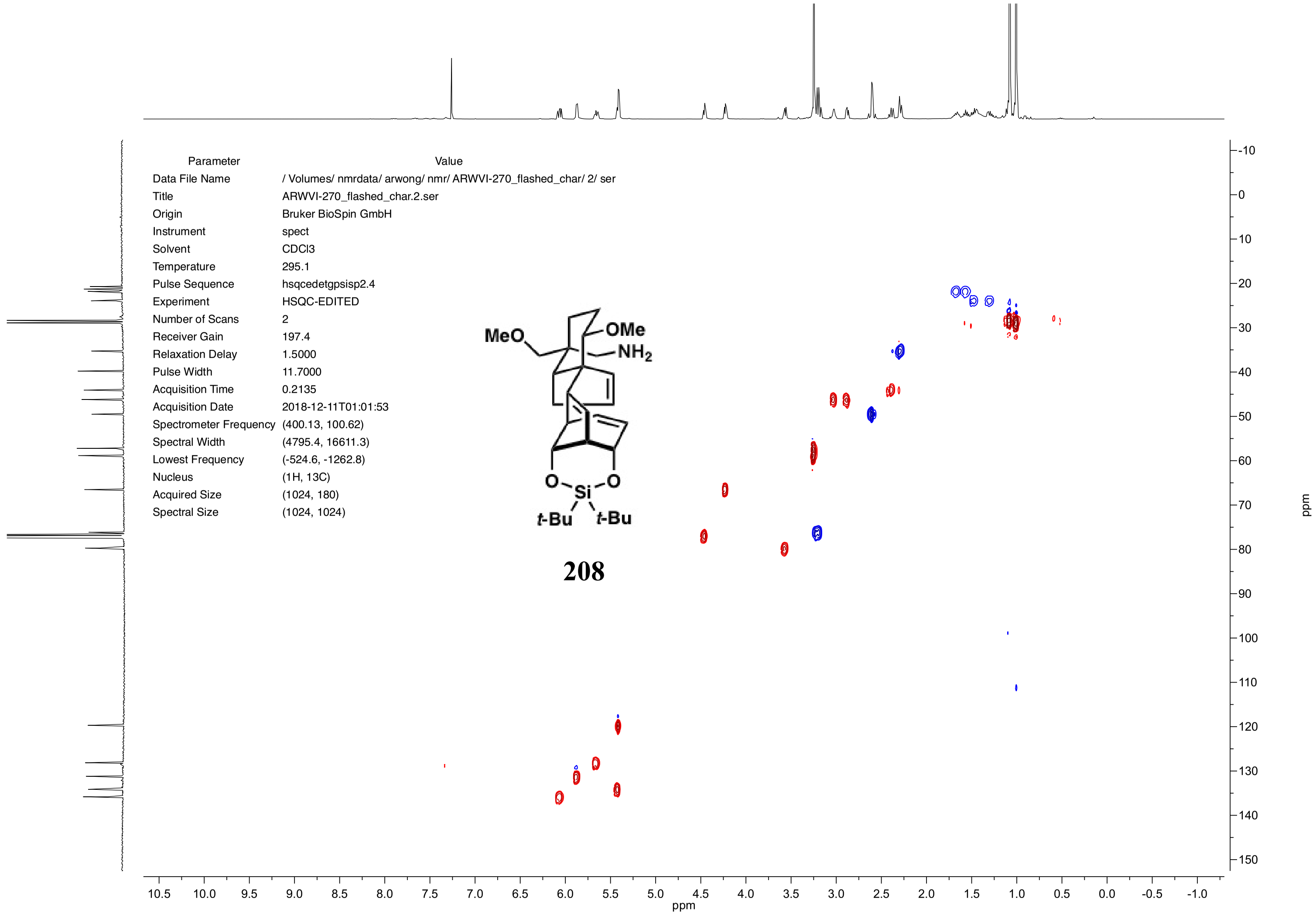
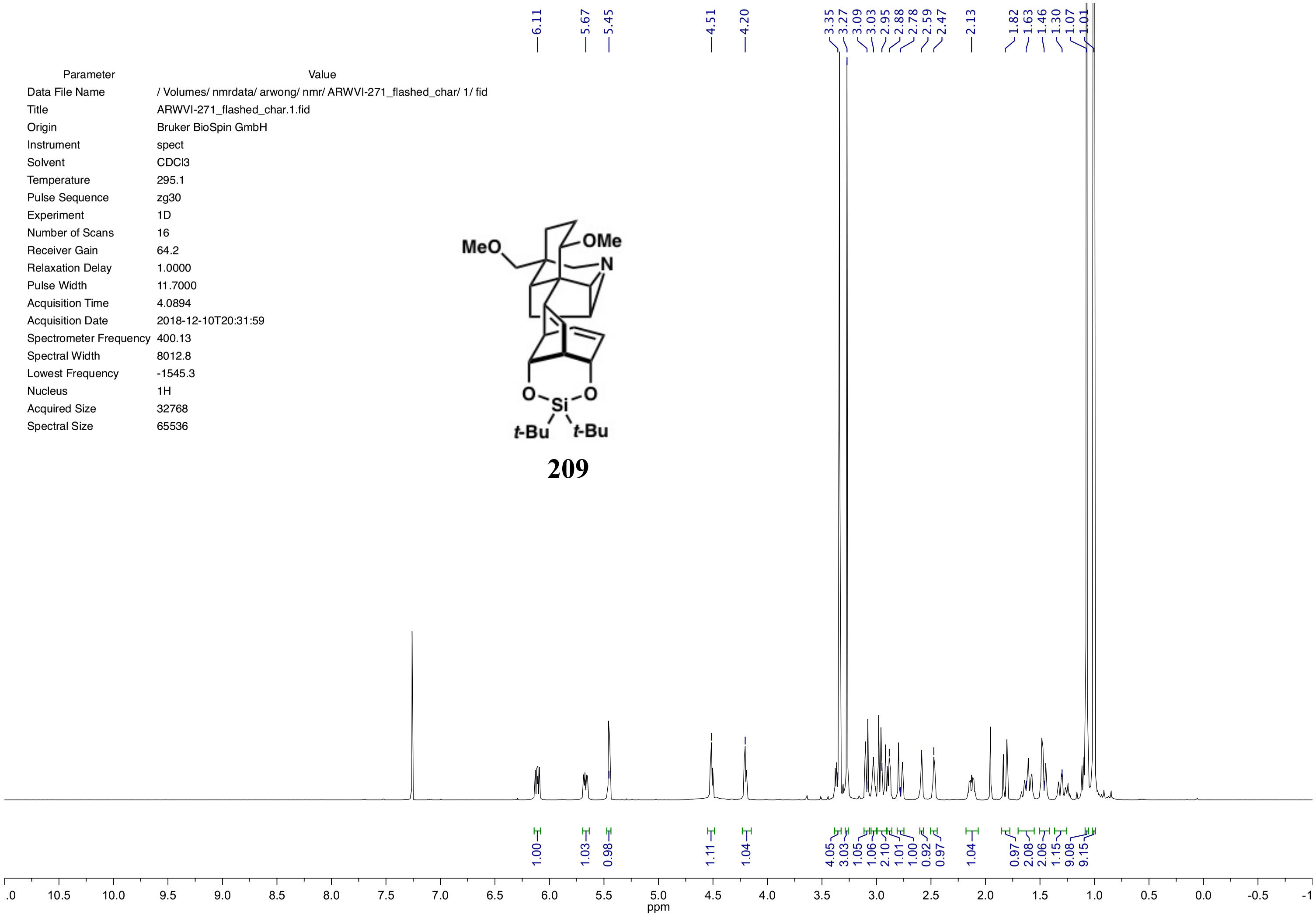




Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-270_flashed_char/ 2/ ser
Title	ARWVI-270_flashed_char.2.ser
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	hsqcedetgpsisp2.4
Experiment	HSQC-EDITED
Number of Scans	2
Receiver Gain	197.4
Relaxation Delay	1.5000
Pulse Width	11.7000
Acquisition Time	0.2135
Acquisition Date	2018-12-11T01:01:53
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(4795.4, 16611.3)
Lowest Frequency	(-524.6, -1262.8)
Nucleus	(1H, 13C)
Acquired Size	(1024, 180)
Spectral Size	(1024, 1024)

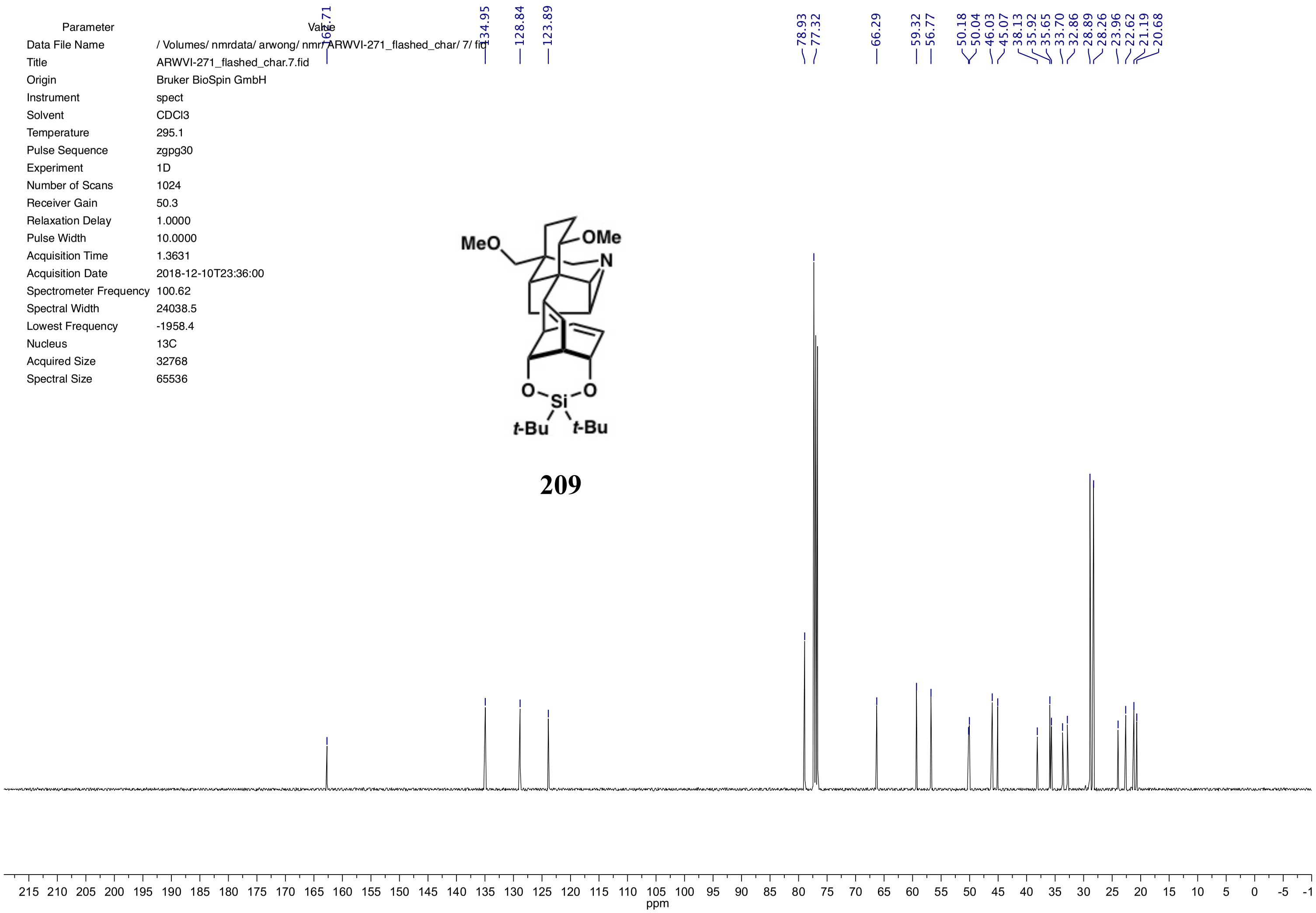
208



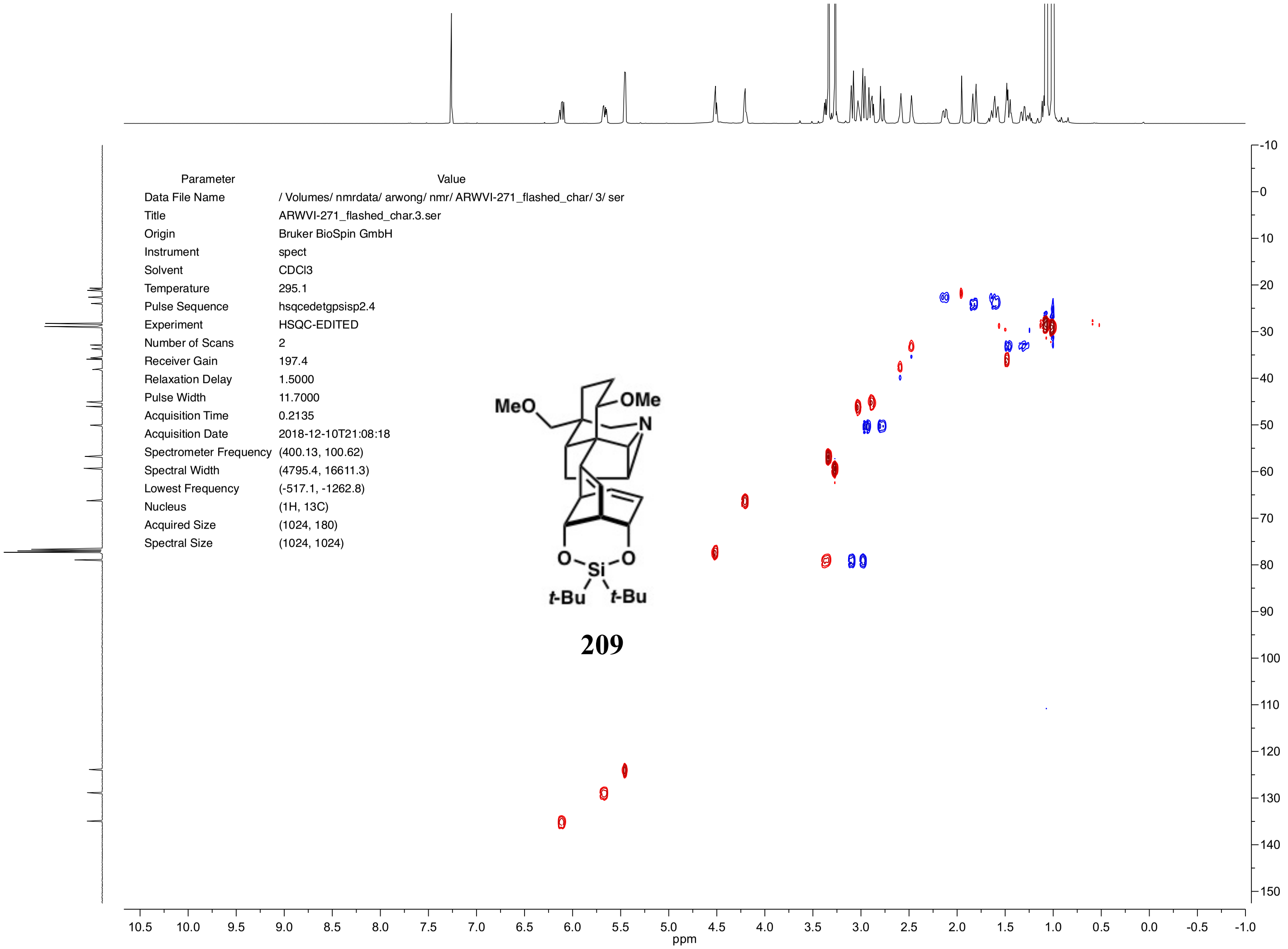
209

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-271_flashed_char/ 1/ fid
Title	ARWVI-271_flashed_char.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
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	2018-12-10T20:31:59
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.3
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-271_flashed_char/ 7/ fid
Title	ARWVI-271_flashed_char.7.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1024
Receiver Gain	50.3
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-12-10T23:36:00
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1958.4
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

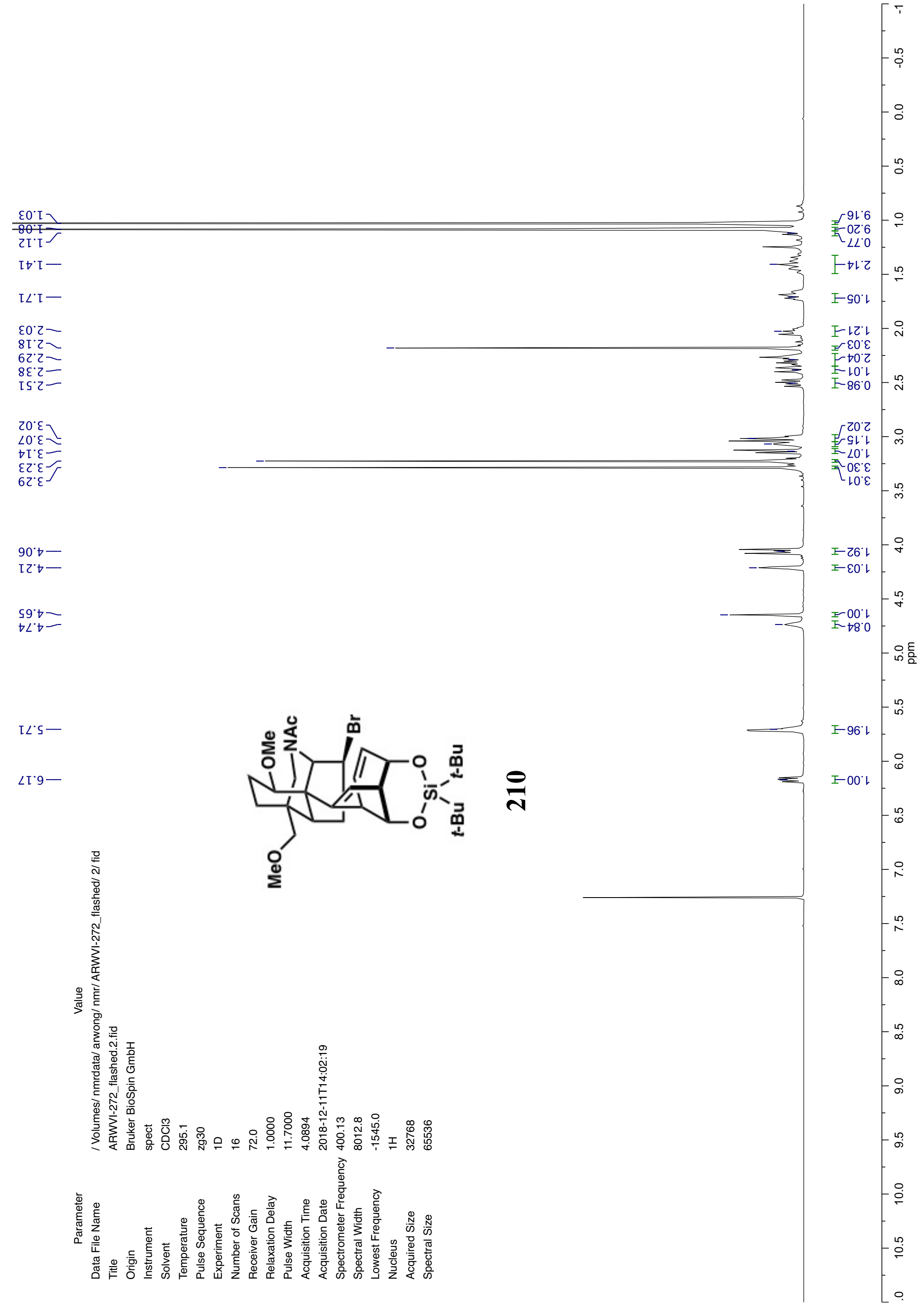


209



Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-271_flashed_char/ 3/ ser
Title	ARWVI-271_flashed_char.3.ser
Origin	Bruker BioSpin GmbH
Instrument	spect
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	2018-12-10T21:08:18
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(4795.4, 16611.3)
Lowest Frequency	(-517.1, -1262.8)
Nucleus	(1H, 13C)
Acquired Size	(1024, 180)
Spectral Size	(1024, 1024)

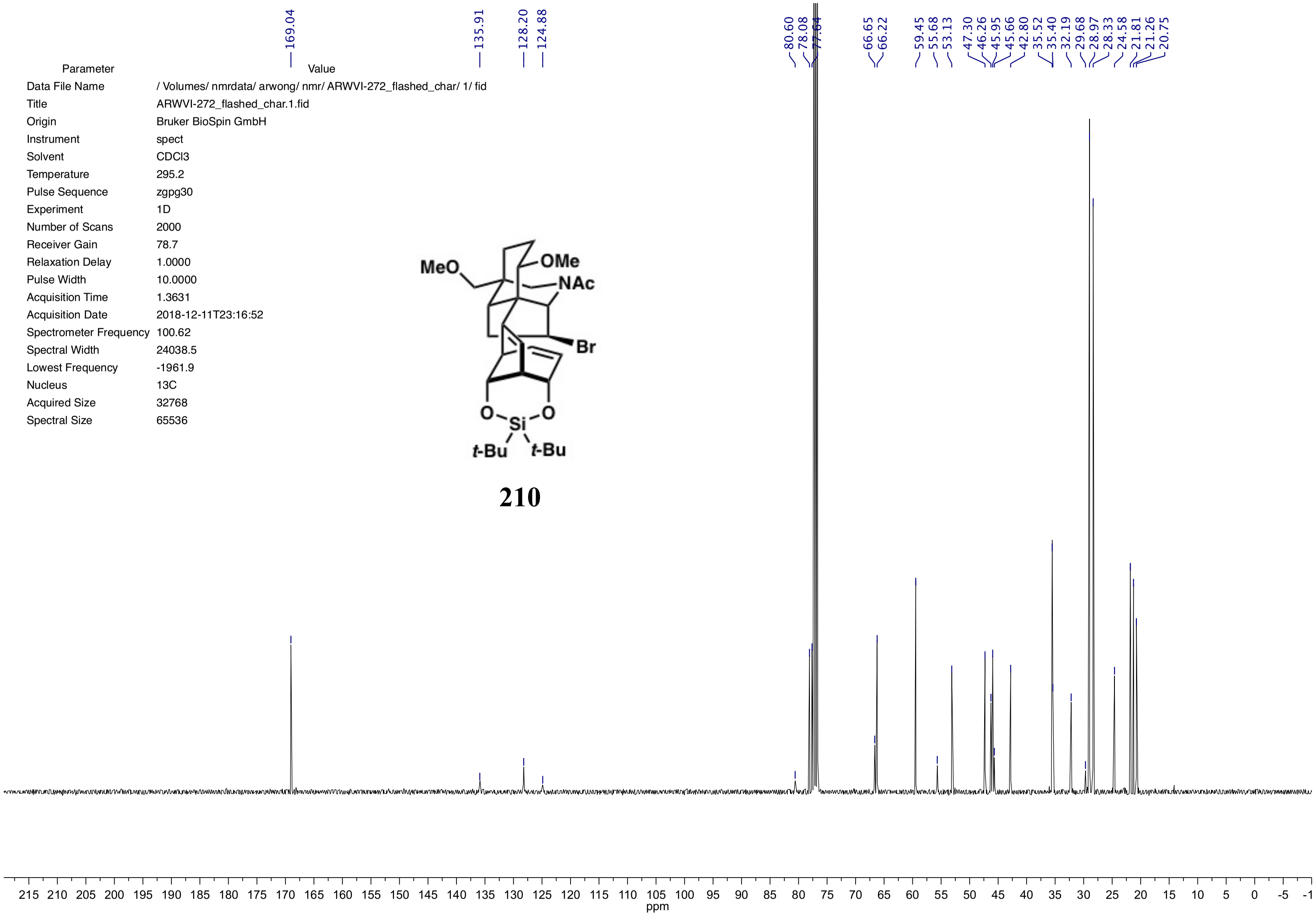
209



210

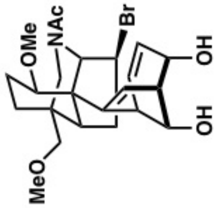
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-272_flashed/ 2/ fid
Title	ARWVI-272_flashed.2.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	16
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-12-11T14:02:19
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.0
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-272_flashed_char/ 1/ fid
Title	ARWVI-272_flashed_char.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	2000
Receiver Gain	78.7
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-12-11T23:16:52
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.9
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

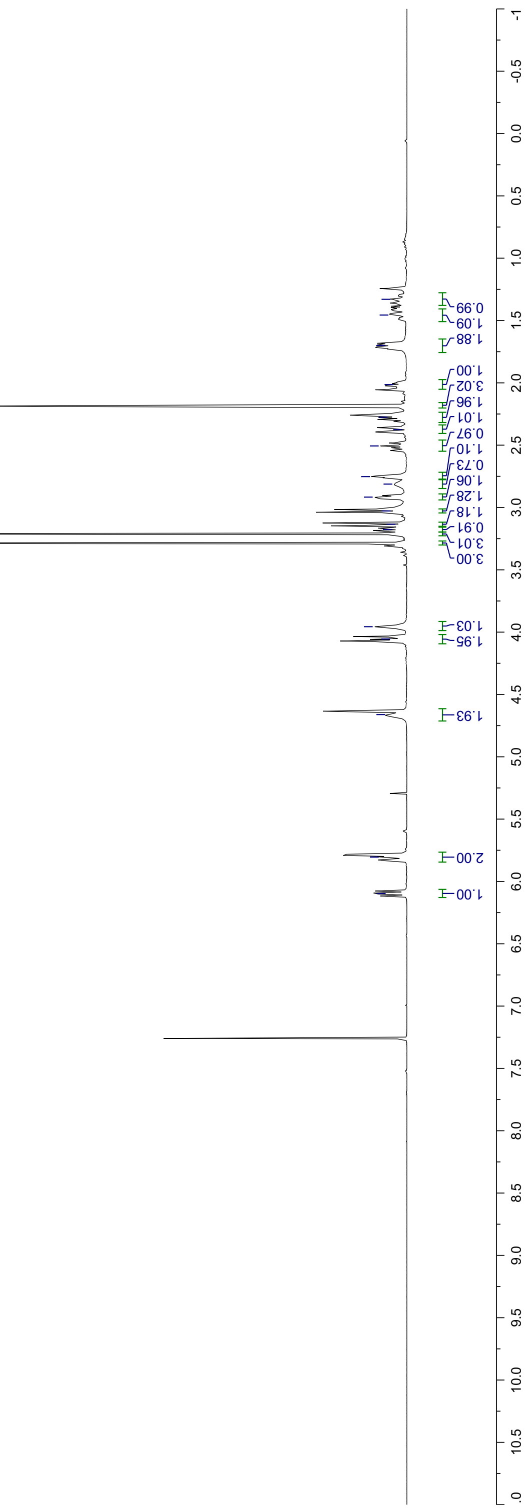


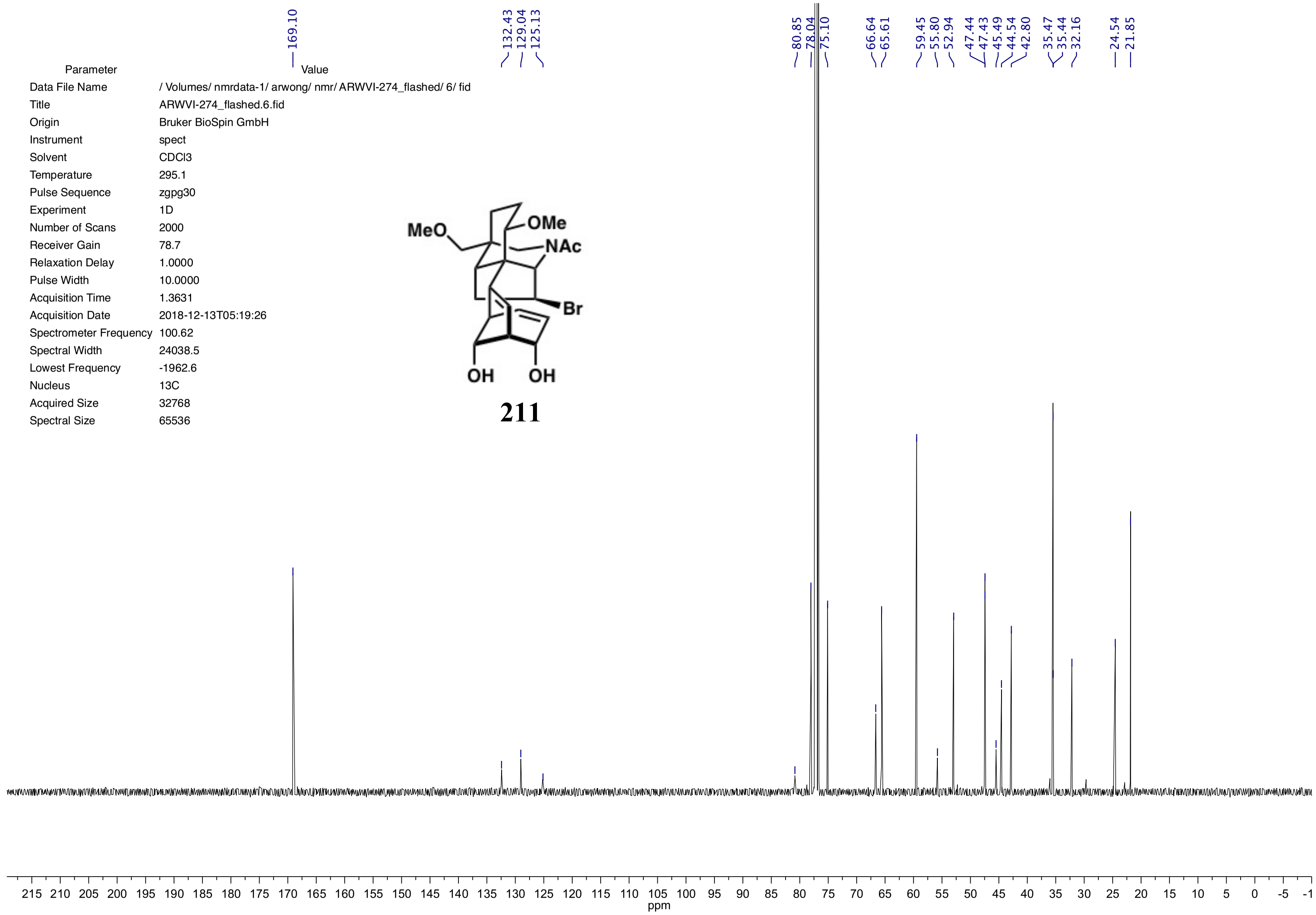
210

Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ arwong/ nmr/ ARWVI-274_flashed/ 1/ fid
Title	ARWVI-274_flashed.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
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	2018-12-13T02:10:44
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



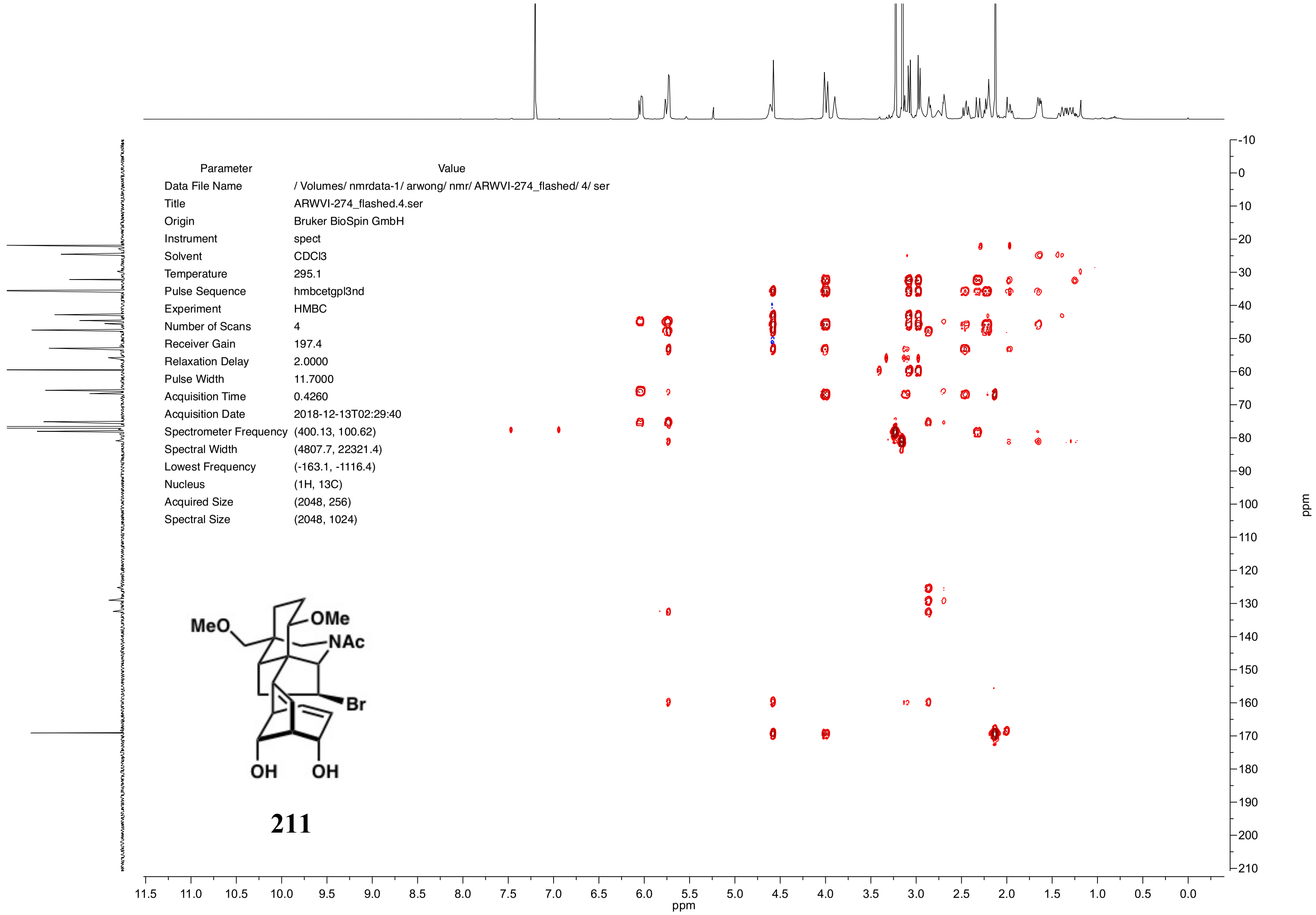
211





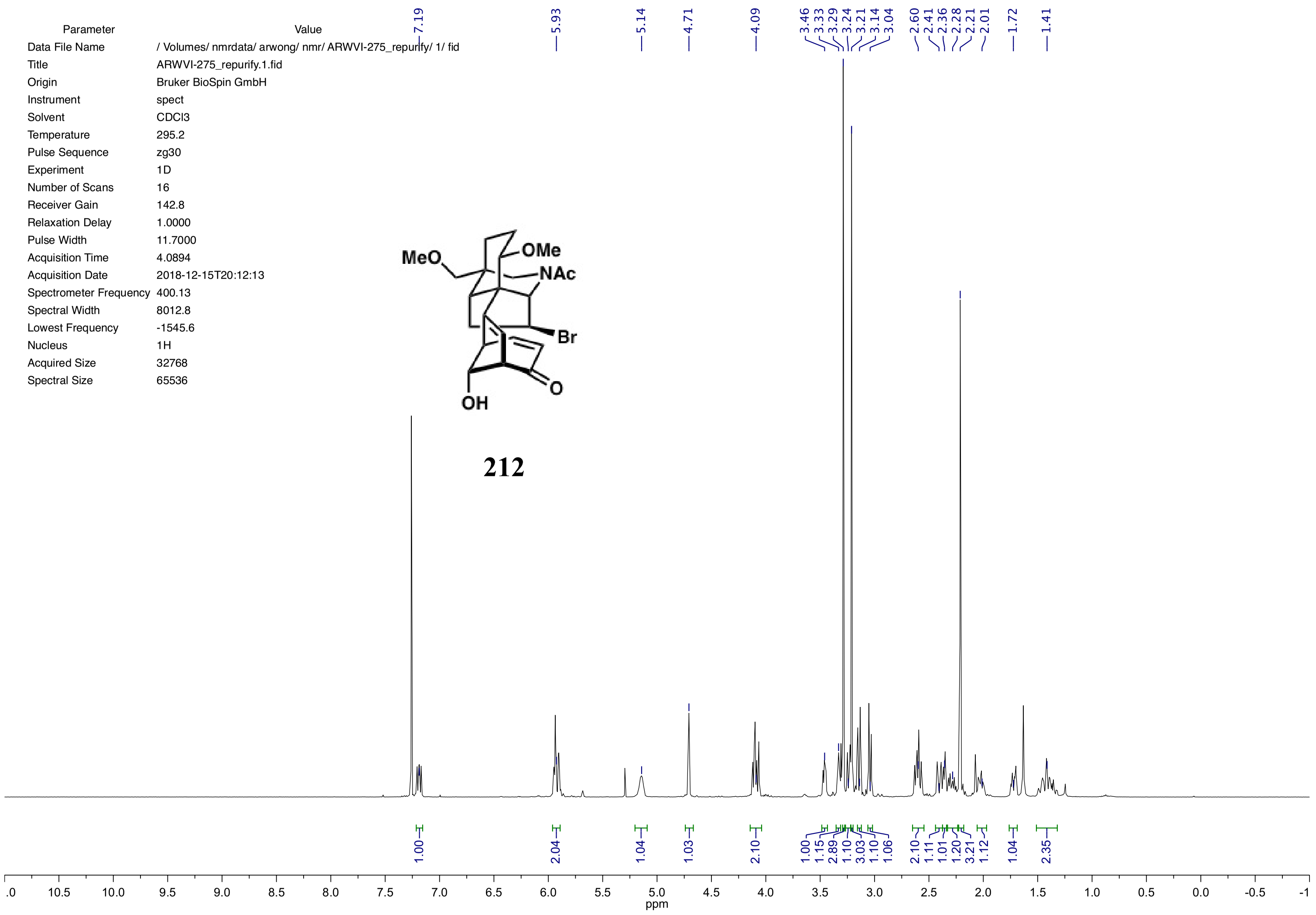
211

Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ arwong/ nmr/ ARWVI-274_flashed/ 6/ fid
Title	ARWVI-274_flashed.6.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	2000
Receiver Gain	78.7
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-12-13T05:19:26
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1962.6
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



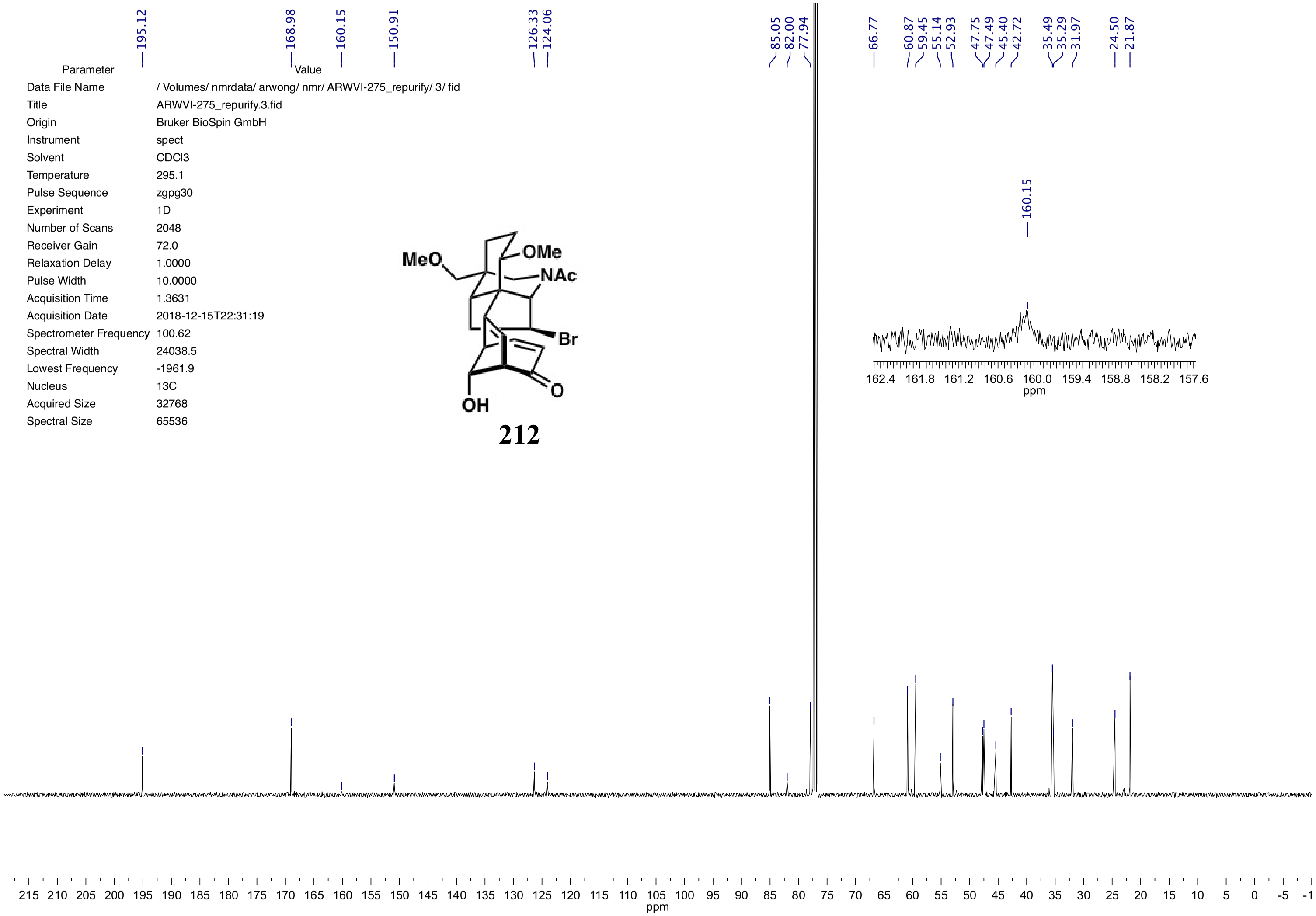
Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ arwong/ nmr/ ARWVI-274_flashed/ 4/ ser
Title	ARWVI-274_flashed.4.ser
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	hmbcetgpl3nd
Experiment	HMBC
Number of Scans	4
Receiver Gain	197.4
Relaxation Delay	2.0000
Pulse Width	11.7000
Acquisition Time	0.4260
Acquisition Date	2018-12-13T02:29:40
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(4807.7, 22321.4)
Lowest Frequency	(-163.1, -1116.4)
Nucleus	(1H, 13C)
Acquired Size	(2048, 256)
Spectral Size	(2048, 1024)

211



212

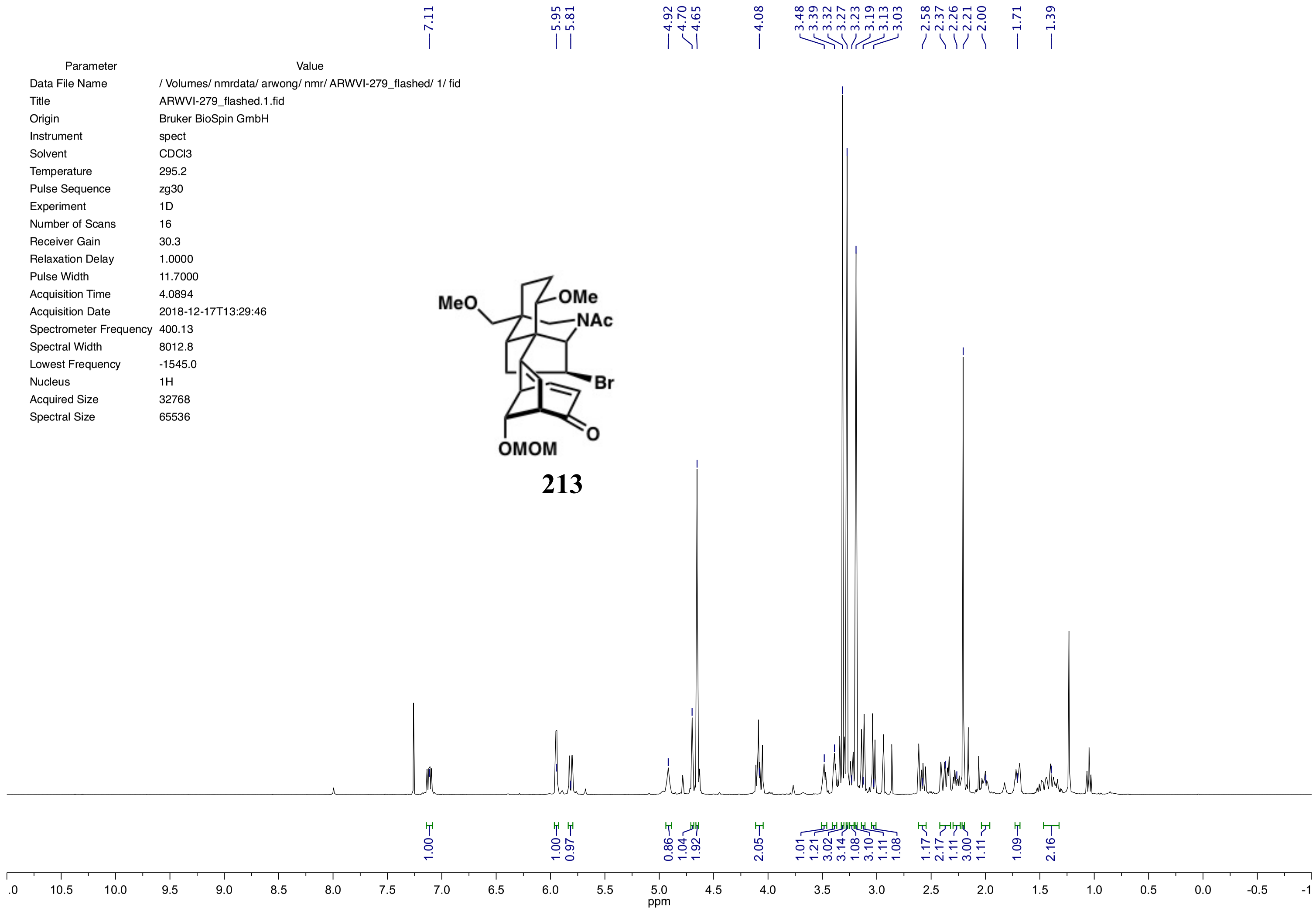
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-275_repurify/ 1/ fid
Title	ARWVI-275_repurify.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zg30
Experiment	1D
Number of Scans	16
Receiver Gain	142.8
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-12-15T20:12:13
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



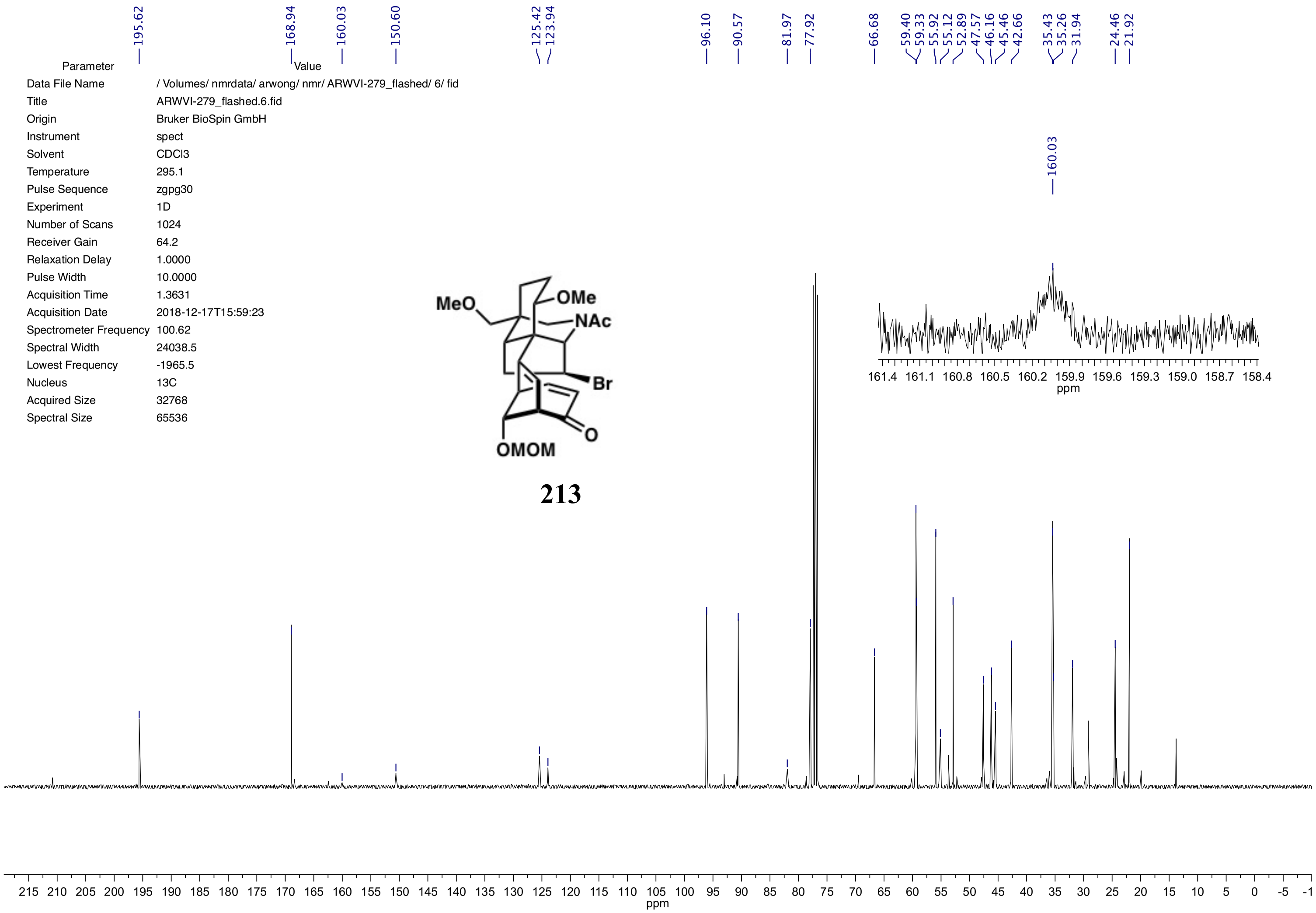
212

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-275_repurify/ 3/ fid
Title	ARWVI-275_repurify.3.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	2048
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-12-15T22:31:19
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.9
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-279_flashed/ 1/ fid
Title	ARWVI-279_flashed.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
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	2018-12-17T13:29:46
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.0
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



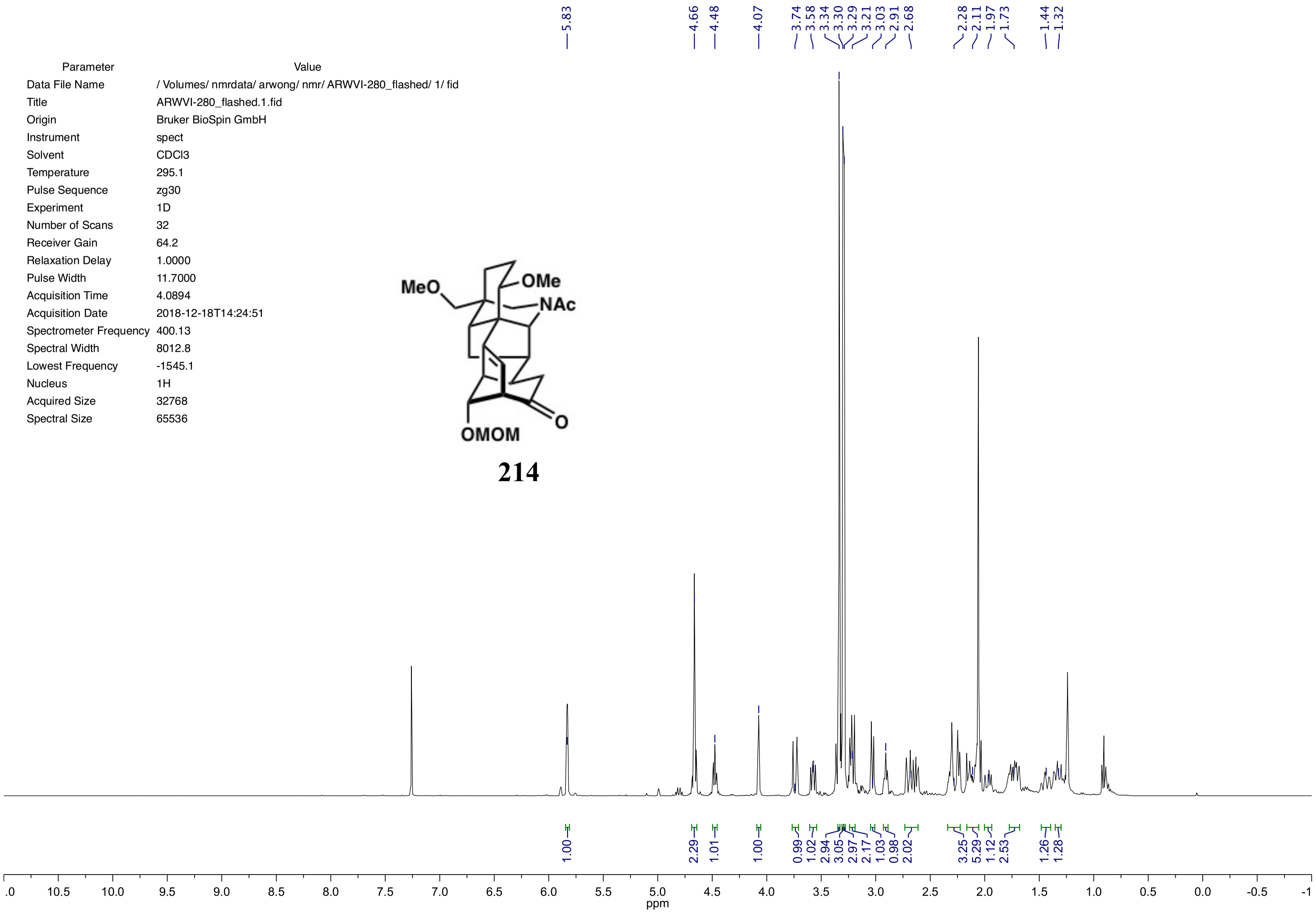
213



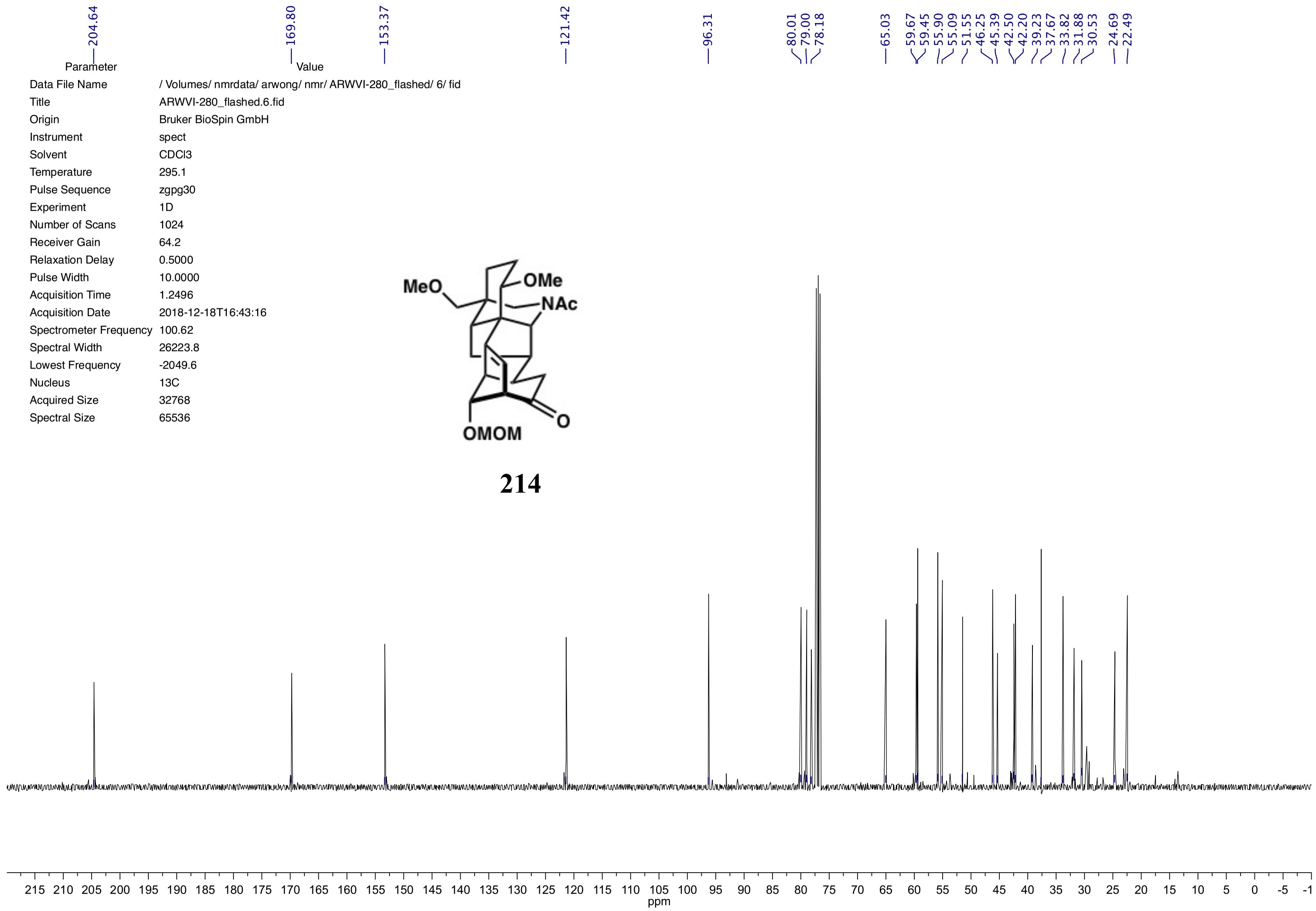
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-279_flashed/ 6/ fid
Title	ARWVI-279_flashed.6.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1024
Receiver Gain	64.2
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-12-17T15:59:23
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1965.5
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

213

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-280_flashed/ 1/ fid
Title	ARWVI-280_flashed.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	64.2
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-12-18T14:24:51
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.1
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

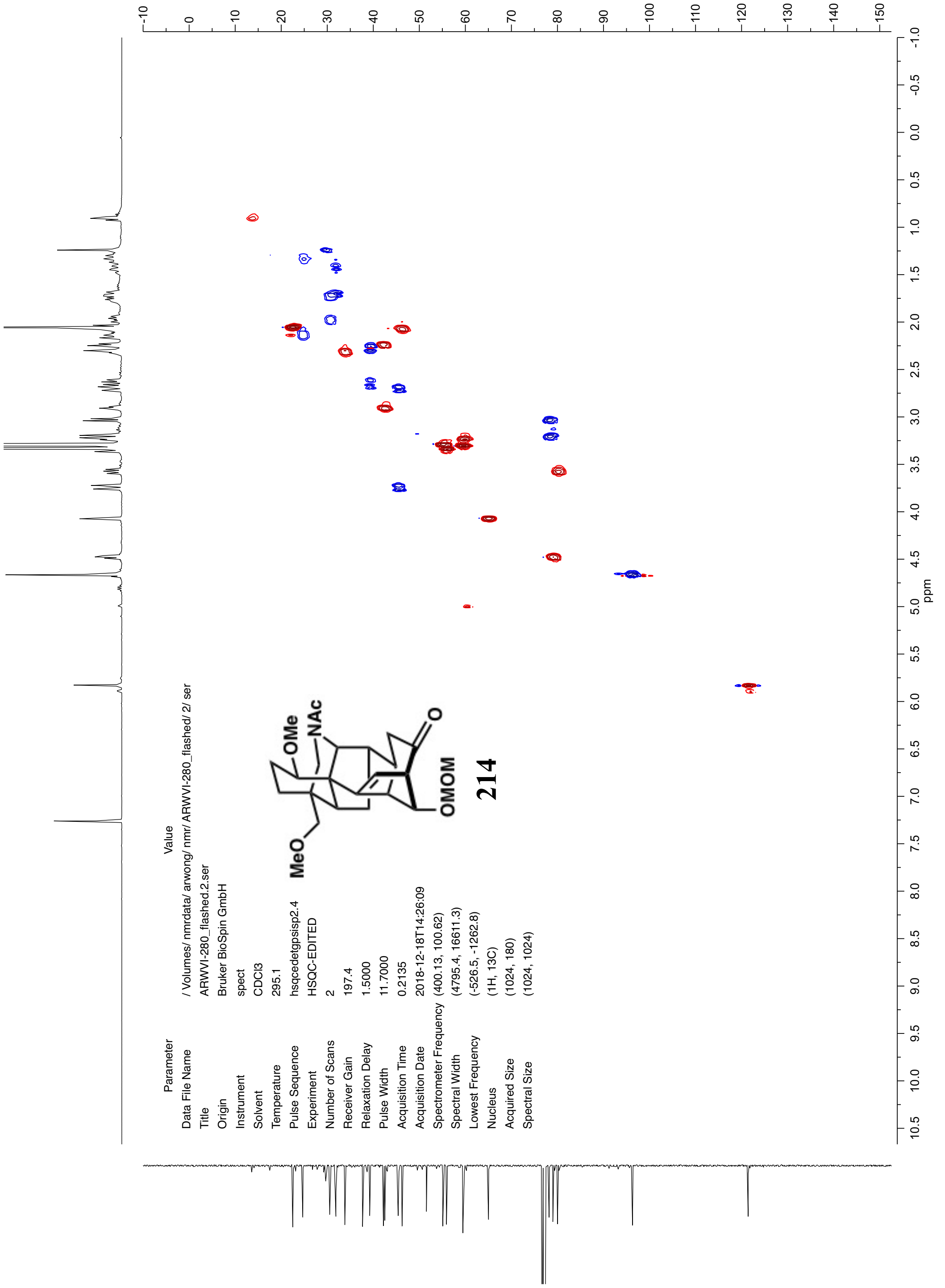


214



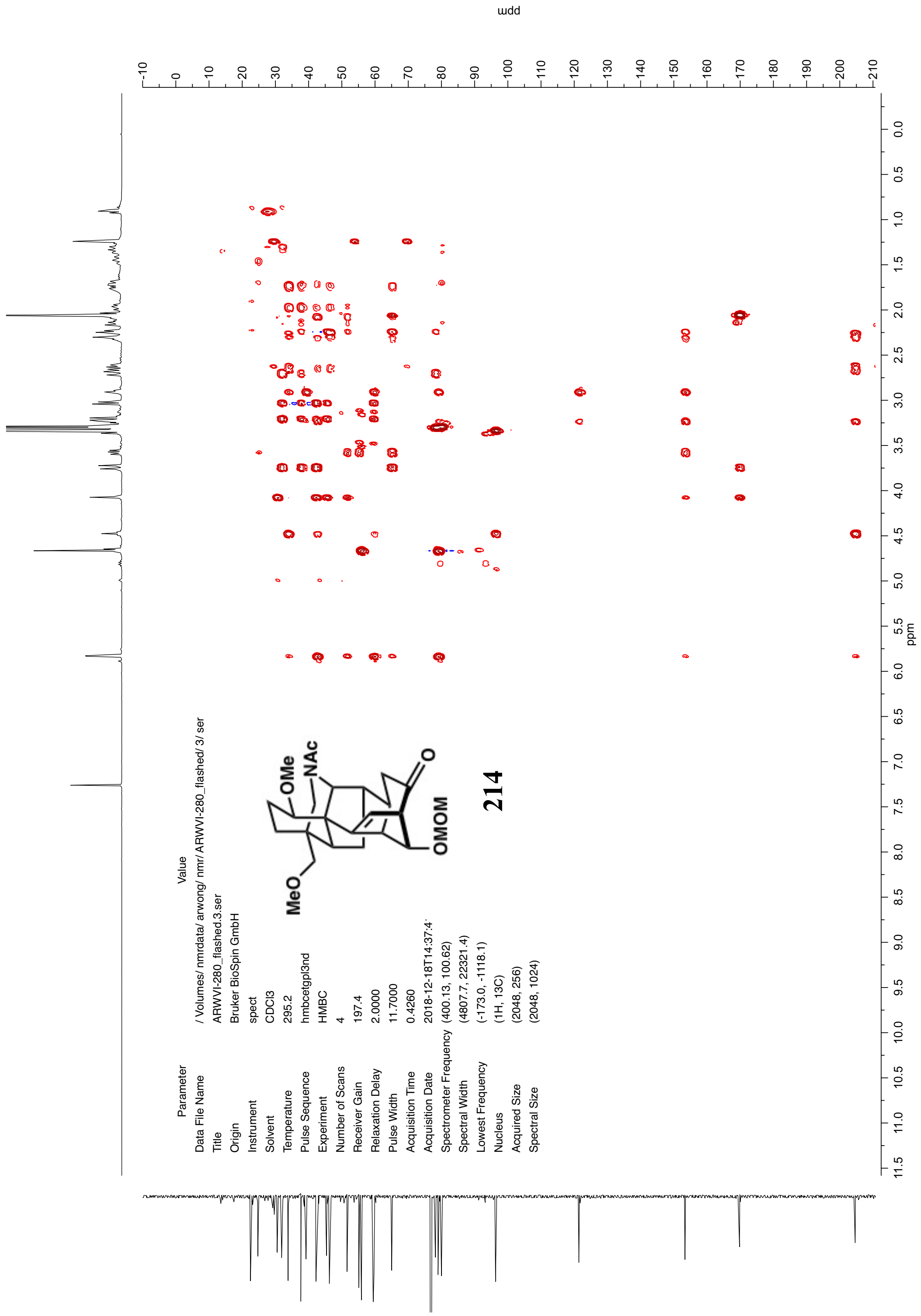
214

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-280_flashed/ 6/ fid
Title	ARWVI-280_flashed.6.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1024
Receiver Gain	64.2
Relaxation Delay	0.5000
Pulse Width	10.0000
Acquisition Time	1.2496
Acquisition Date	2018-12-18T16:43:16
Spectrometer Frequency	100.62
Spectral Width	26223.8
Lowest Frequency	-2049.6
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



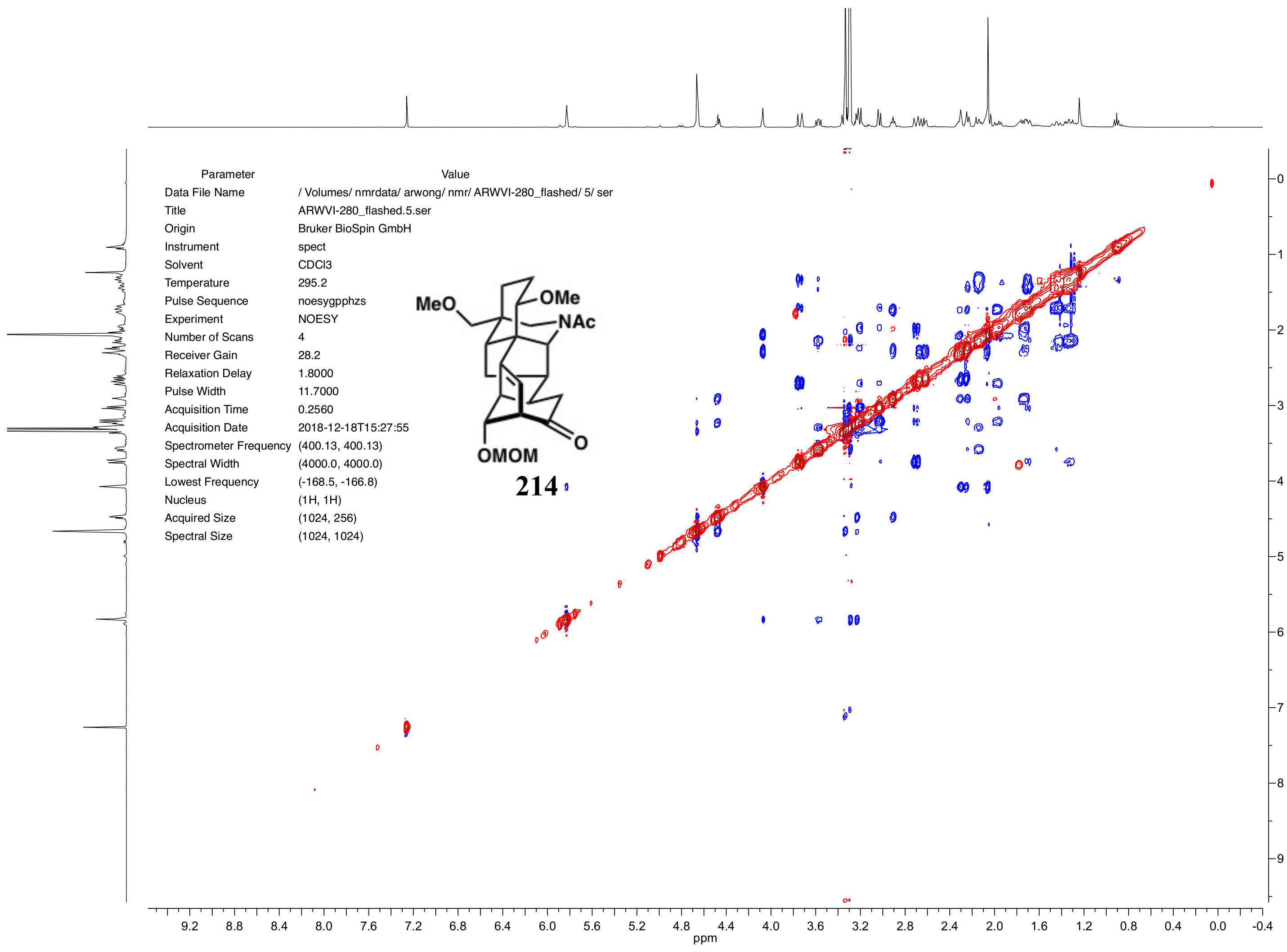
214

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-280_flashed/ 2/ ser
Title	ARWVI-280_flashed.2.ser
Origin	Bruker BioSpin GmbH
Instrument	spect
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	2018-12-18T14:26:09
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(4795.4, 16611.3)
Lowest Frequency	(-526.5, -1262.8)
Nucleus	(1H, 13C)
Acquired Size	(1024, 180)
Spectral Size	(1024, 1024)



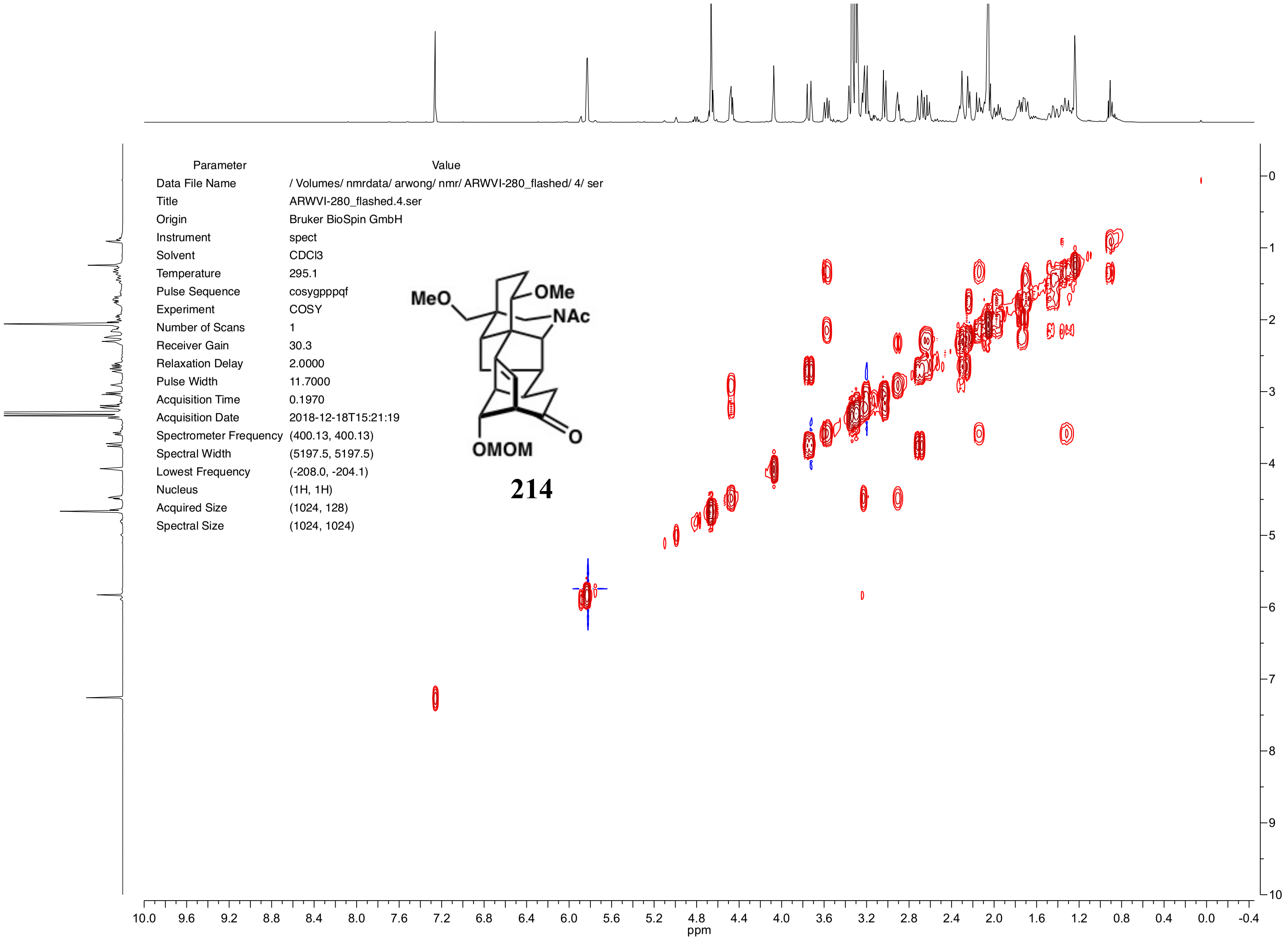
214

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-280_flashed/ 3/ ser
Title	ARWVI-280_flashed.3.ser
Origin	Bruker BioSpin GmbH
Instrument	spect
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	2018-12-18T14:37:4
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(4807.7, 22321.4)
Lowest Frequency	(-173.0, -1118.1)
Nucleus	(1H, 13C)
Acquired Size	(2048, 256)
Spectral Size	(2048, 1024)



Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-280_flashed/ 5/ ser
Title	ARWVI-280_flashed.5.ser
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
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	2018-12-18T15:27:55
Spectrometer Frequency	(400.13, 400.13)
Spectral Width	(4000.0, 4000.0)
Lowest Frequency	(-168.5, -166.8)
Nucleus	(1H, 1H)
Acquired Size	(1024, 256)
Spectral Size	(1024, 1024)

214

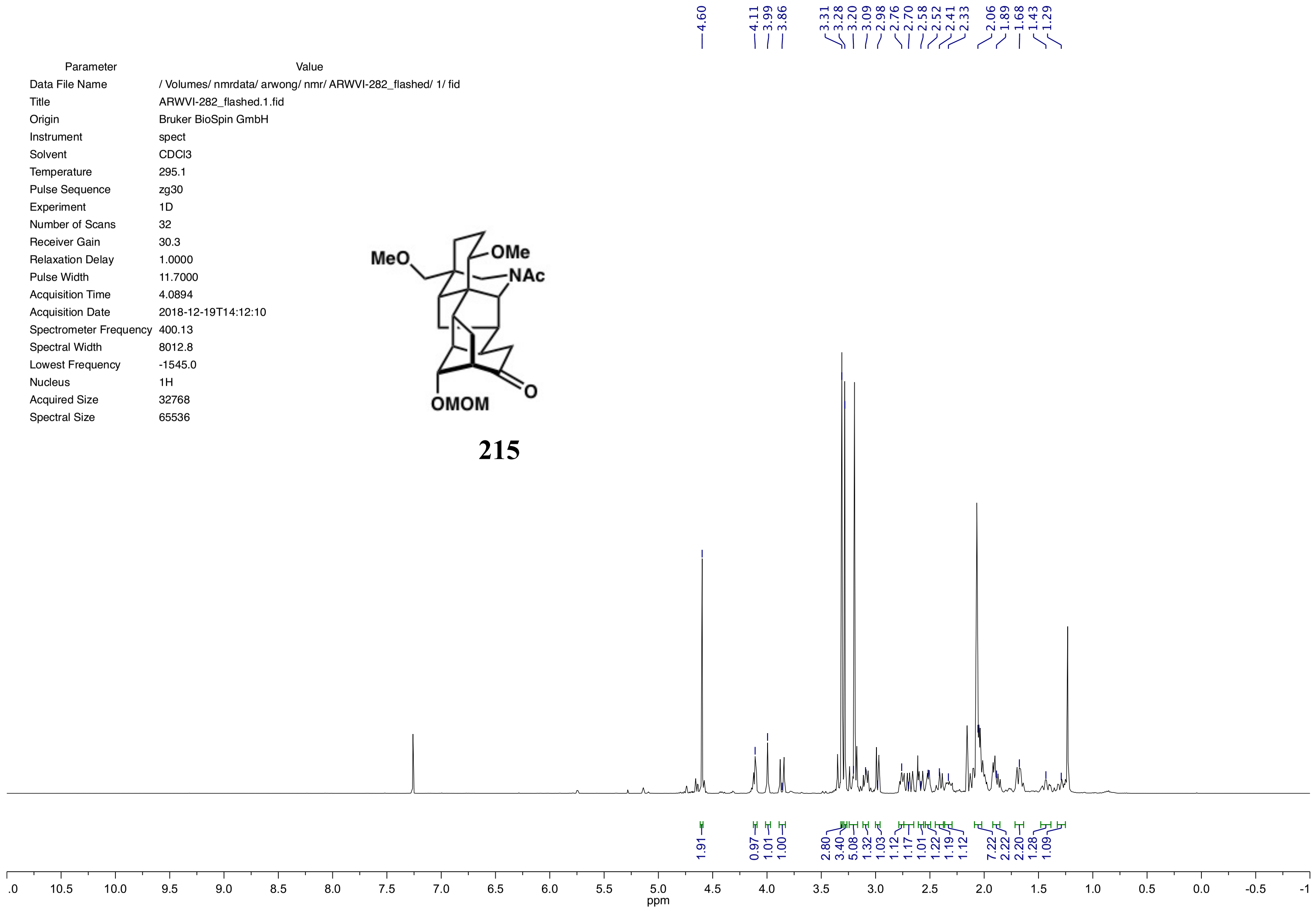


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-280_flashed/ 4/ ser
Title	ARWVI-280_flashed.4.ser
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	cosygpppqf
Experiment	COSY
Number of Scans	1
Receiver Gain	30.3
Relaxation Delay	2.0000
Pulse Width	11.7000
Acquisition Time	0.1970
Acquisition Date	2018-12-18T15:21:19
Spectrometer Frequency	(400.13, 400.13)
Spectral Width	(5197.5, 5197.5)
Lowest Frequency	(-208.0, -204.1)
Nucleus	(1H, 1H)
Acquired Size	(1024, 128)
Spectral Size	(1024, 1024)

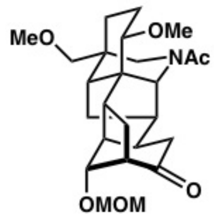
214

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-282_flashed/ 1/ fid
Title	ARWVI-282_flashed.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	30.3
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-12-19T14:12:10
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.0
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

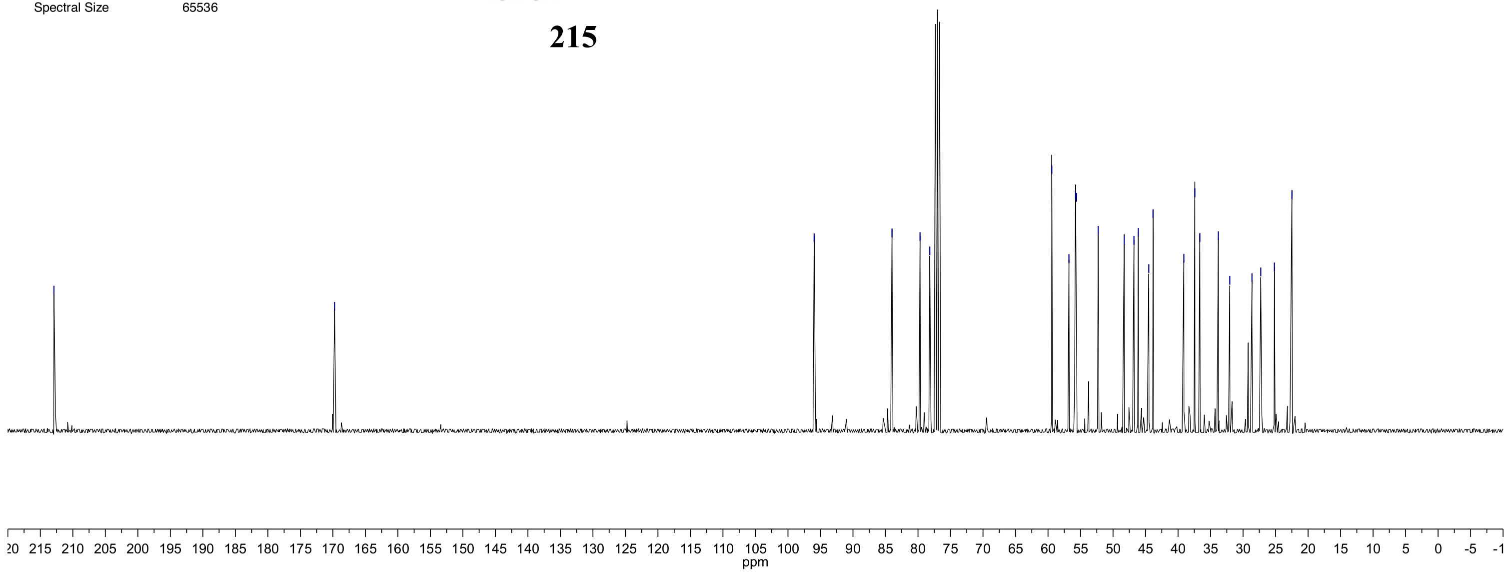
215

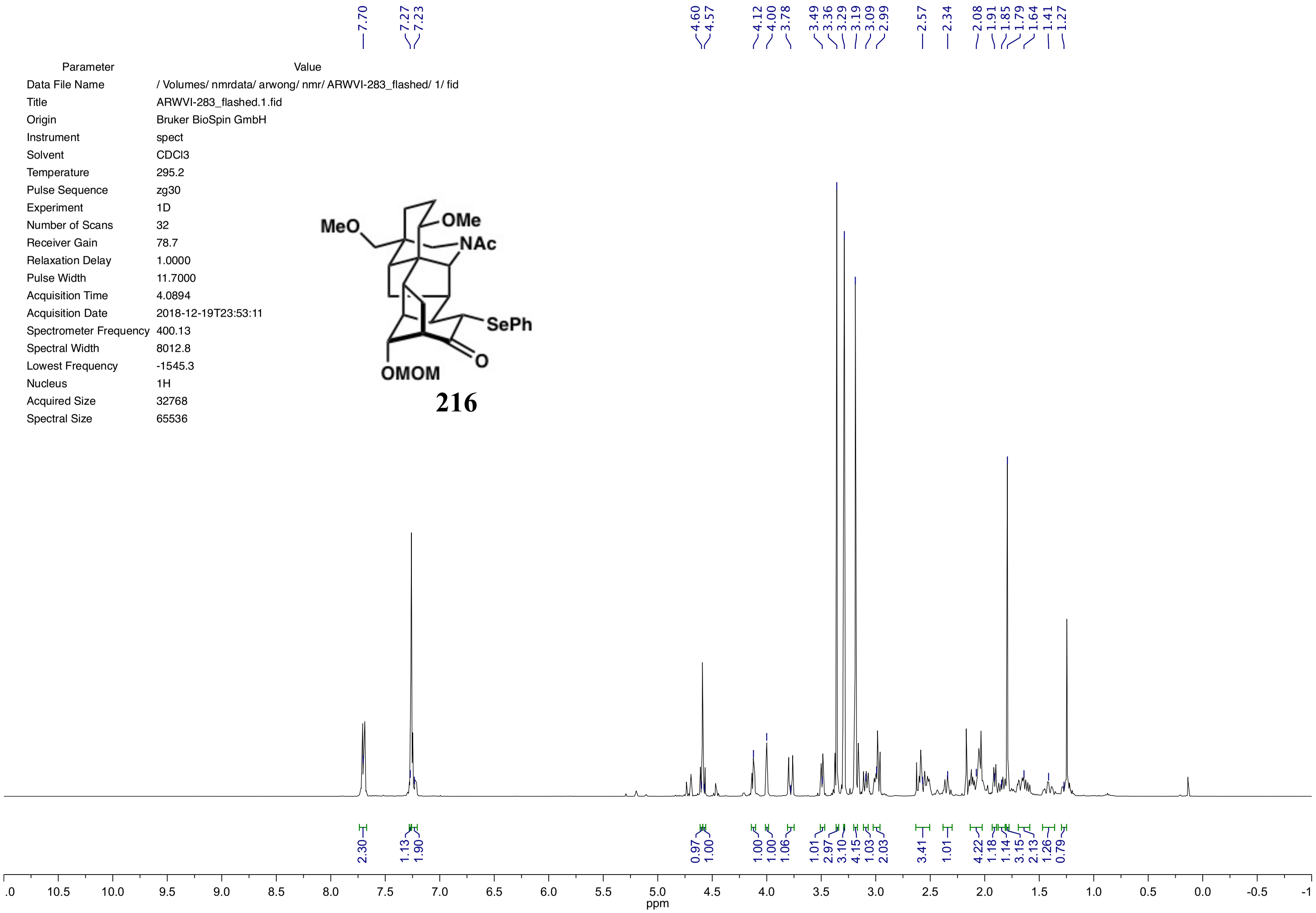


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-282_flashed/ 6/ fid
Title	ARWVI-282_flashed.6.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1024
Receiver Gain	55.5
Relaxation Delay	0.5000
Pulse Width	10.0000
Acquisition Time	1.2496
Acquisition Date	2018-12-19T16:31:04
Spectrometer Frequency	100.62
Spectral Width	26223.8
Lowest Frequency	-2051.1
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



215

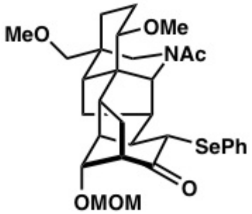




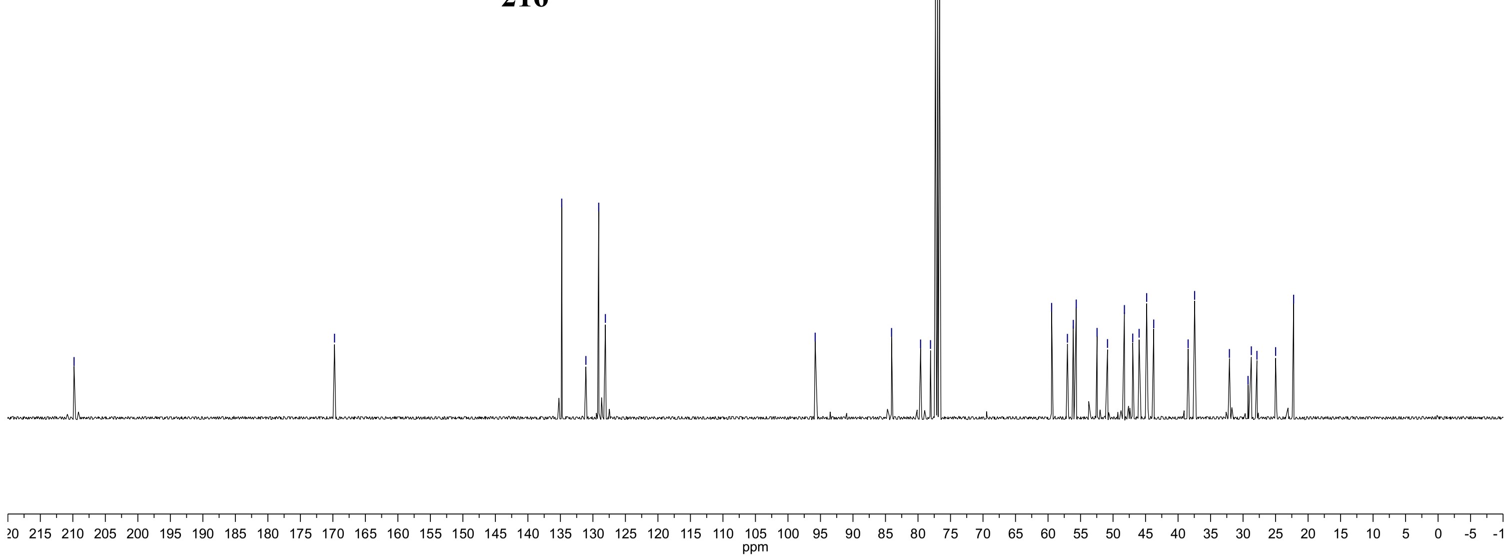
216

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-283_flashed/ 1/ fid
Title	ARWVI-283_flashed.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	78.7
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-12-19T23:53:11
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.3
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

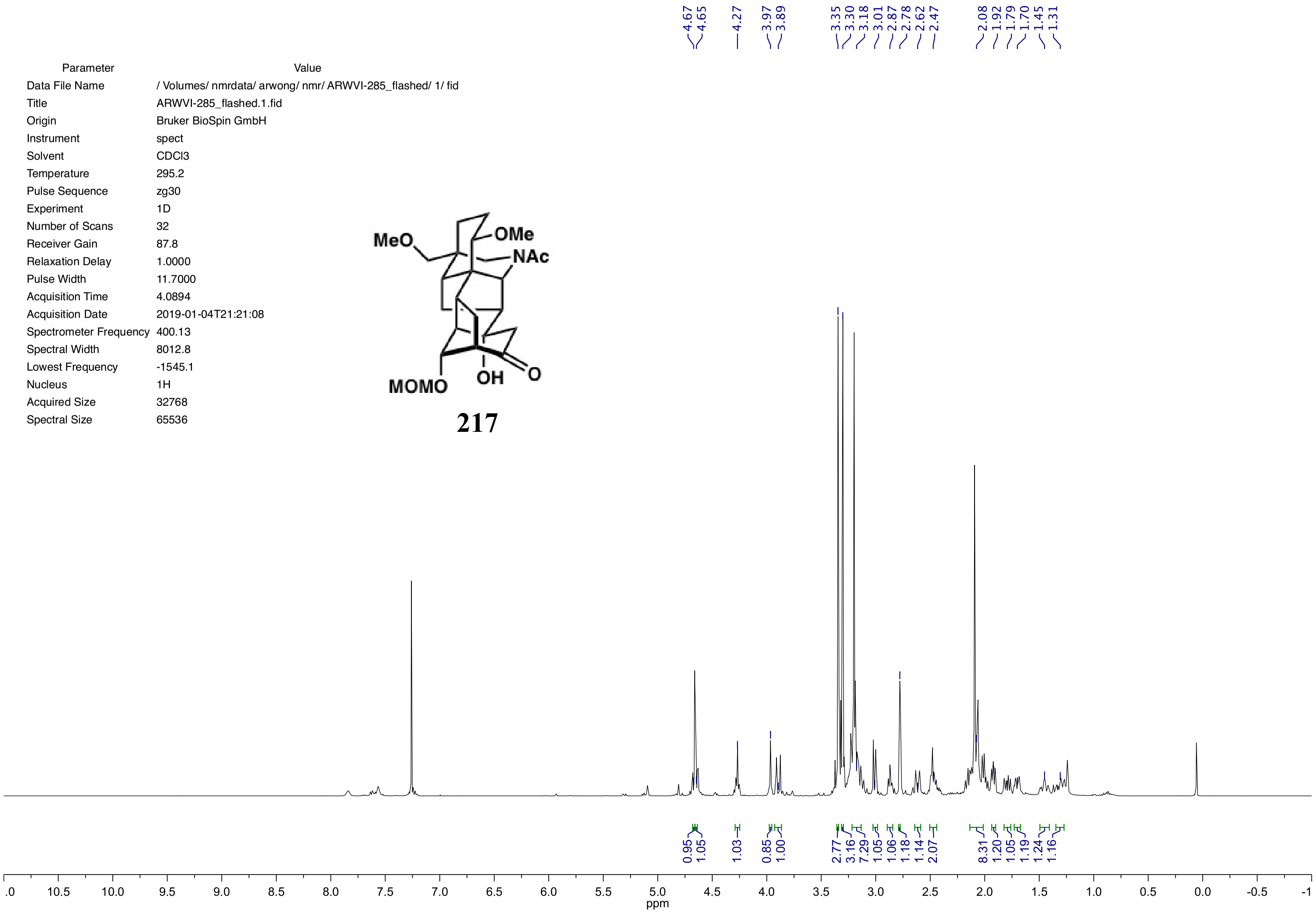
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-283_flashed/ 6/ fid
Title	ARWVI-283_flashed.6.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1600
Receiver Gain	78.7
Relaxation Delay	0.5000
Pulse Width	10.0000
Acquisition Time	1.2496
Acquisition Date	2018-12-20T02:29:13
Spectrometer Frequency	100.62
Spectral Width	26223.8
Lowest Frequency	-2049.3
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



216

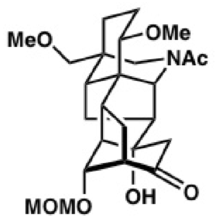


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-285_flashed/ 1/ fid
Title	ARWVI-285_flashed.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	87.8
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2019-01-04T21:21:08
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.1
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

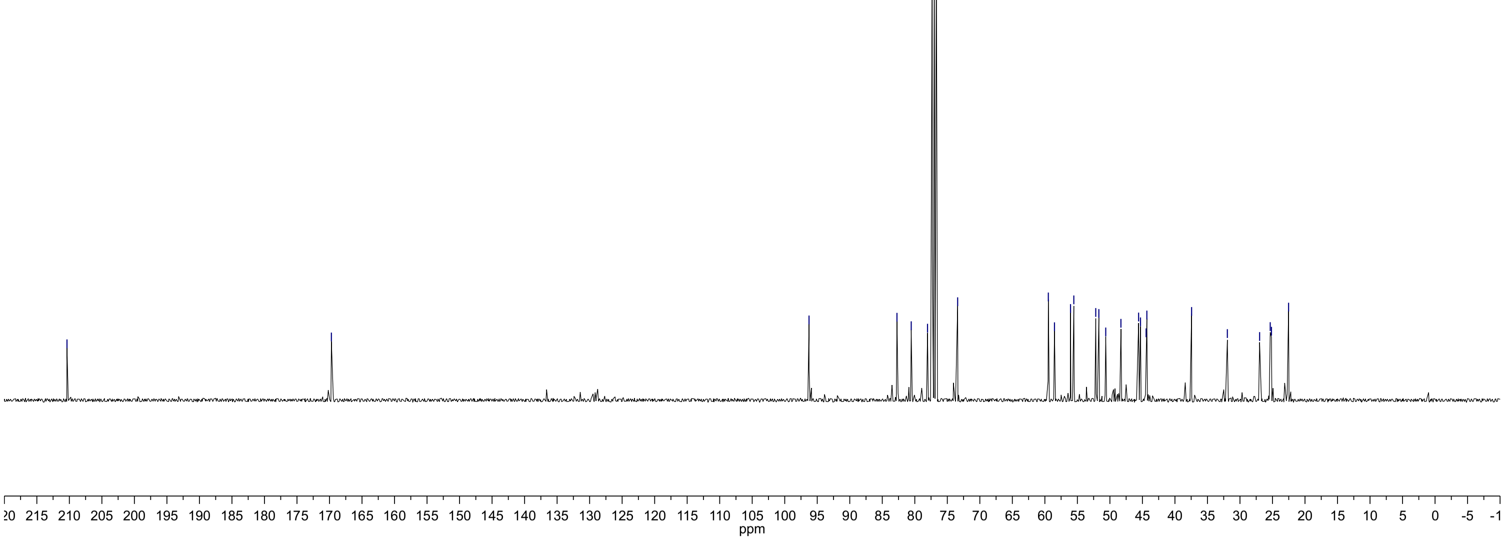


217

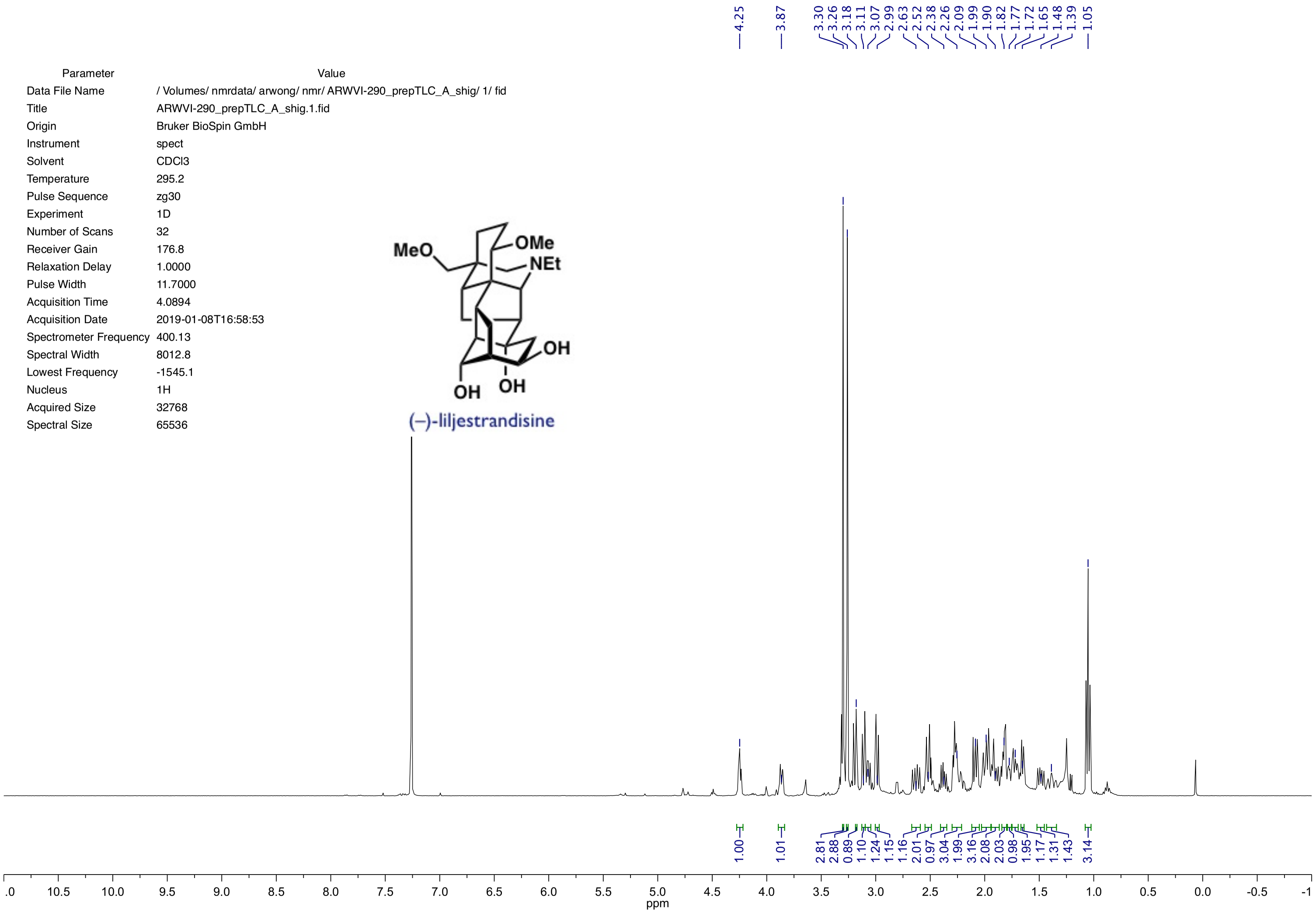
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-285_flashed/ 6/ fid
Title	ARWVI-285_flashed.6.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1500
Receiver Gain	72.0
Relaxation Delay	0.5000
Pulse Width	10.0000
Acquisition Time	1.2496
Acquisition Date	2019-01-04T23:54:05
Spectrometer Frequency	100.62
Spectral Width	26223.8
Lowest Frequency	-2048.9
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



217



Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-290_prepTLC_A_shig/ 1/ fid
Title	ARWVI-290_prepTLC_A_shig.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	176.8
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2019-01-08T16:58:53
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.1
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



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Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-290_prepTLC_A_shig/ 6/ fid
Title	ARWVI-290_prepTLC_A_shig.6.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	5000
Receiver Gain	72.0
Relaxation Delay	0.5000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2019-01-09T02:50:47
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.2
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

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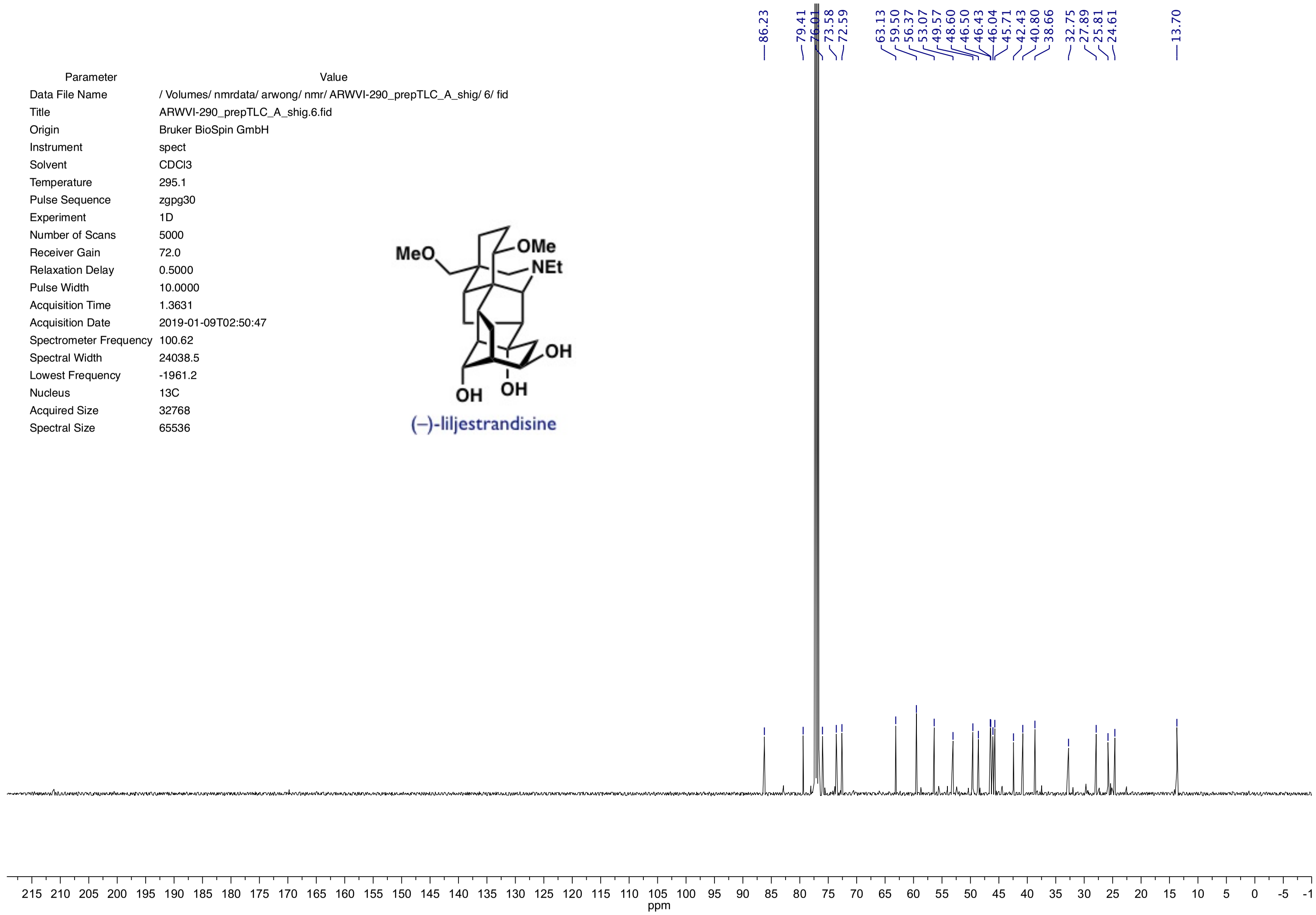

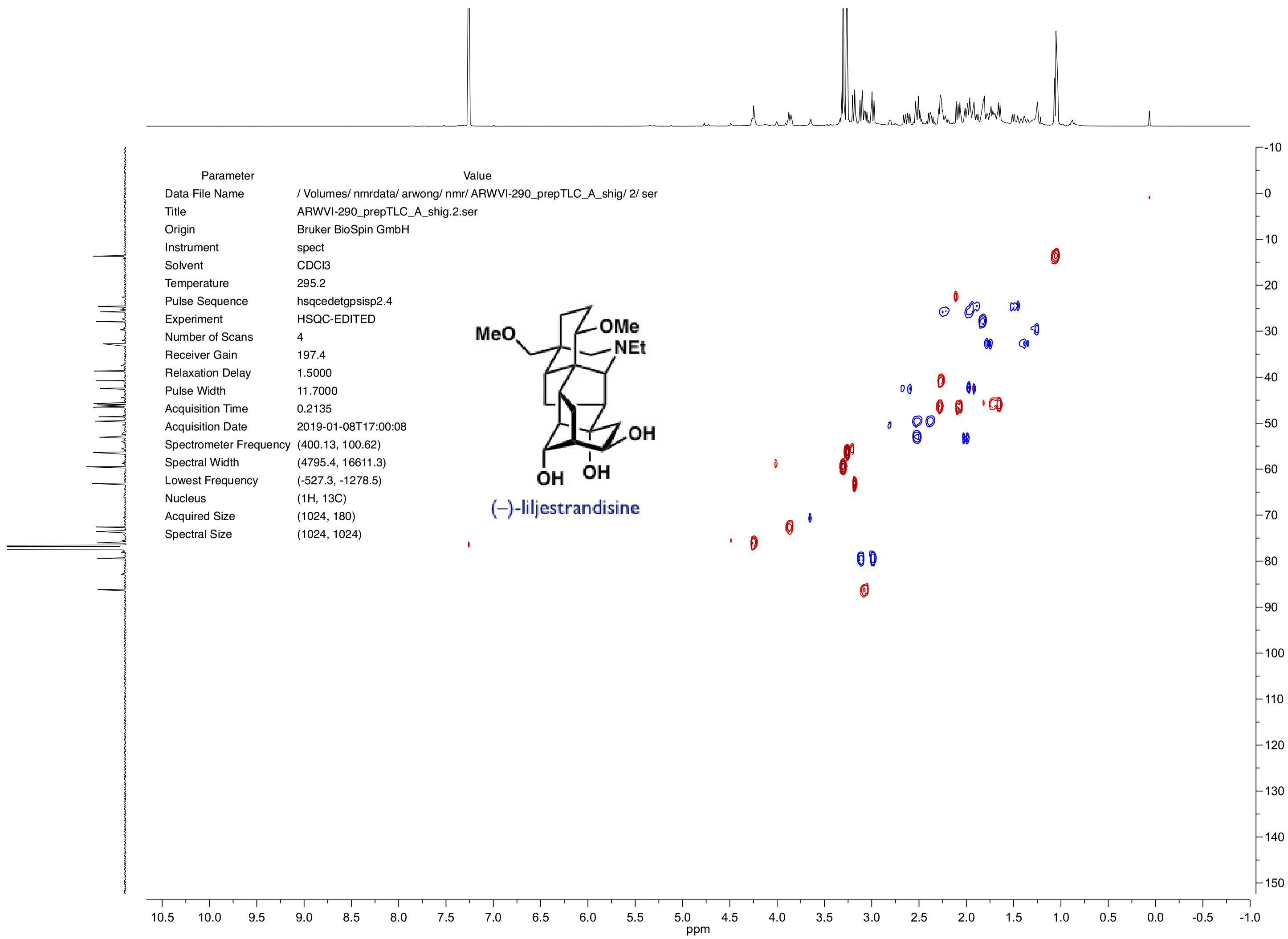

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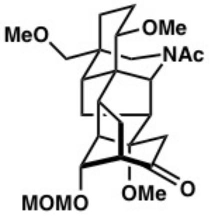
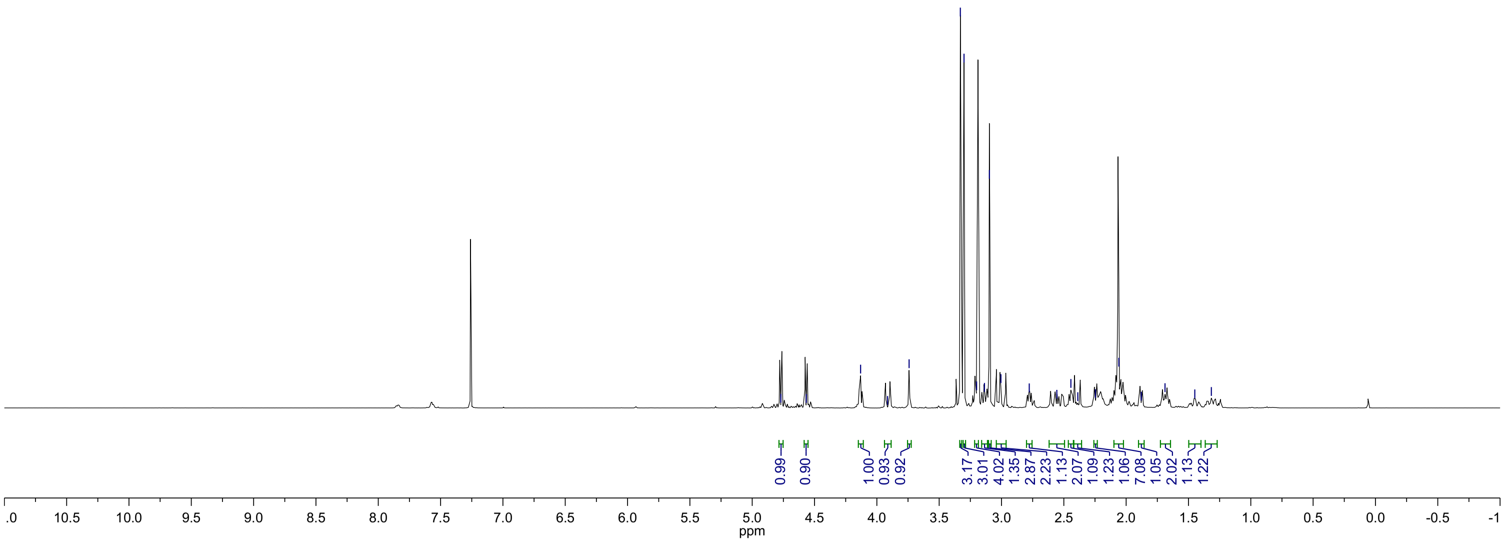
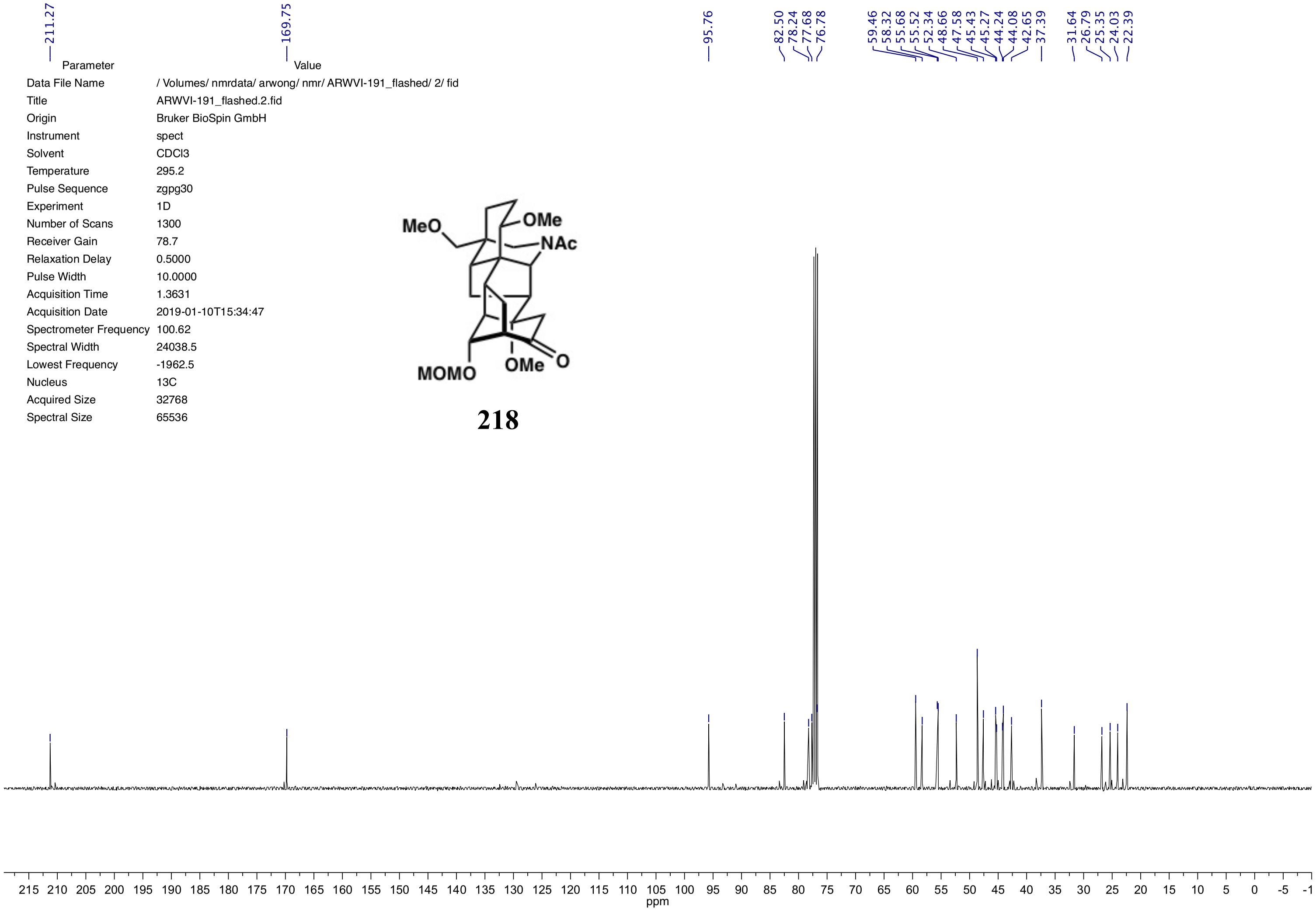
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-290_prepTLC_A_shig/ 2/ ser
Title	ARWVI-290_prepTLC_A_shig.2.ser
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	hsqcedetgpsisp2.4
Experiment	HSQC-EDITED
Number of Scans	4
Receiver Gain	197.4
Relaxation Delay	1.5000
Pulse Width	11.7000
Acquisition Time	0.2135
Acquisition Date	2019-01-08T17:00:08
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(4795.4, 16611.3)
Lowest Frequency	(-527.3, -1278.5)
Nucleus	(1H, 13C)
Acquired Size	(1024, 180)
Spectral Size	(1024, 1024)

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-191_flashed/ 1/ fid
Title	ARWVI-191_flashed.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	98.9
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2019-01-10T14:52:36
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



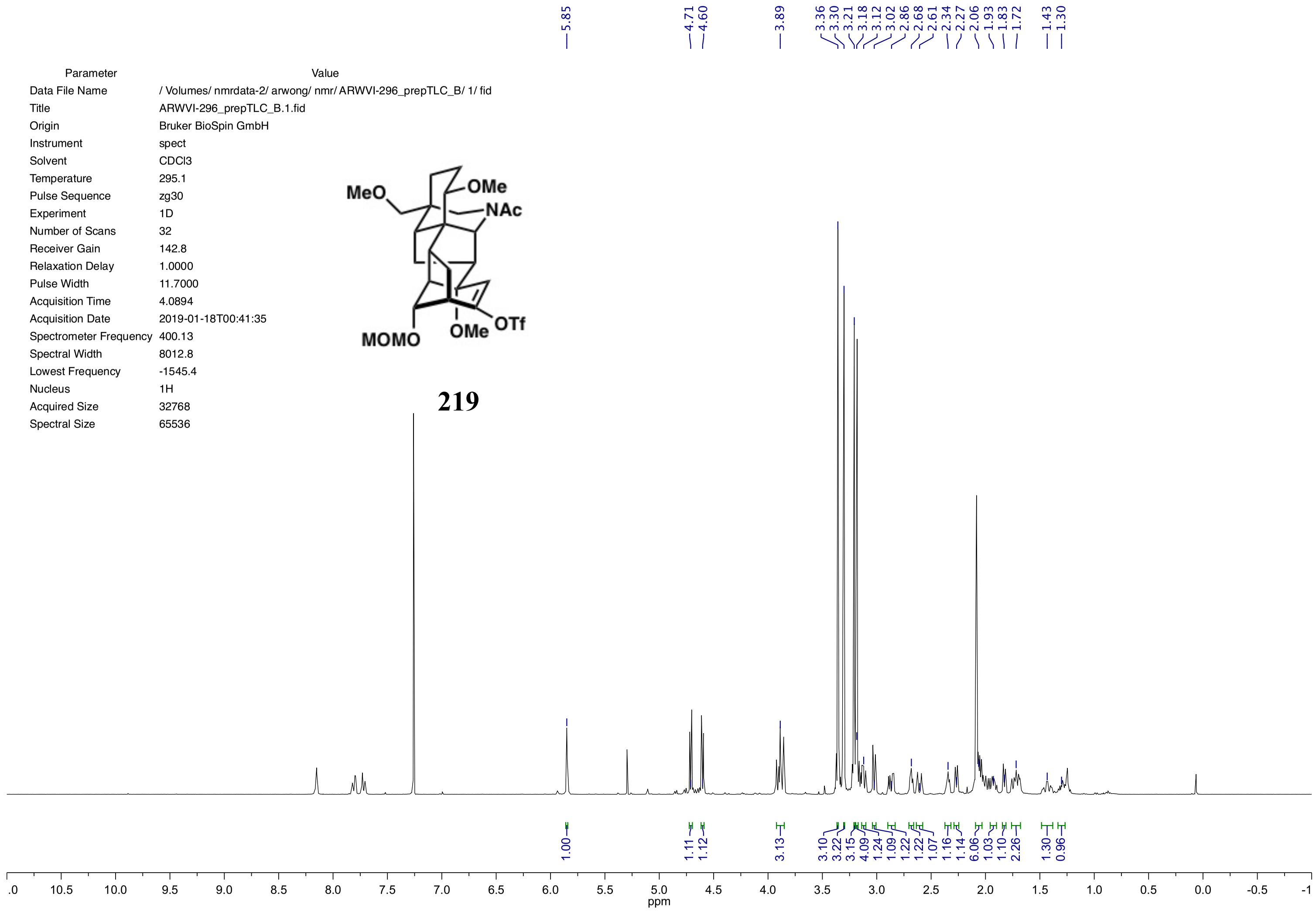
218





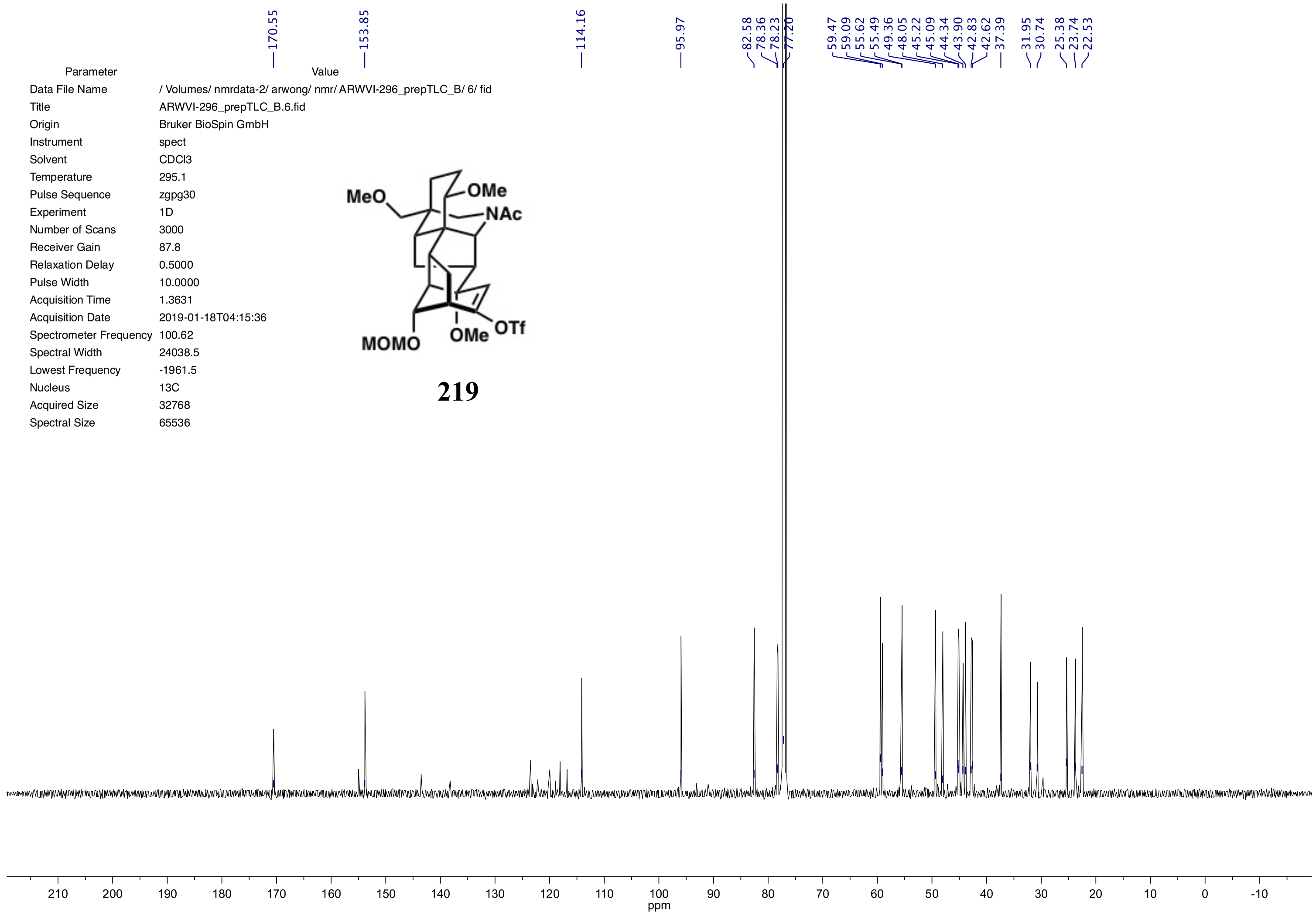
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-191_flashed/ 2/ fid
Title	ARWVI-191_flashed.2.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1300
Receiver Gain	78.7
Relaxation Delay	0.5000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2019-01-10T15:34:47
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1962.5
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

218



219

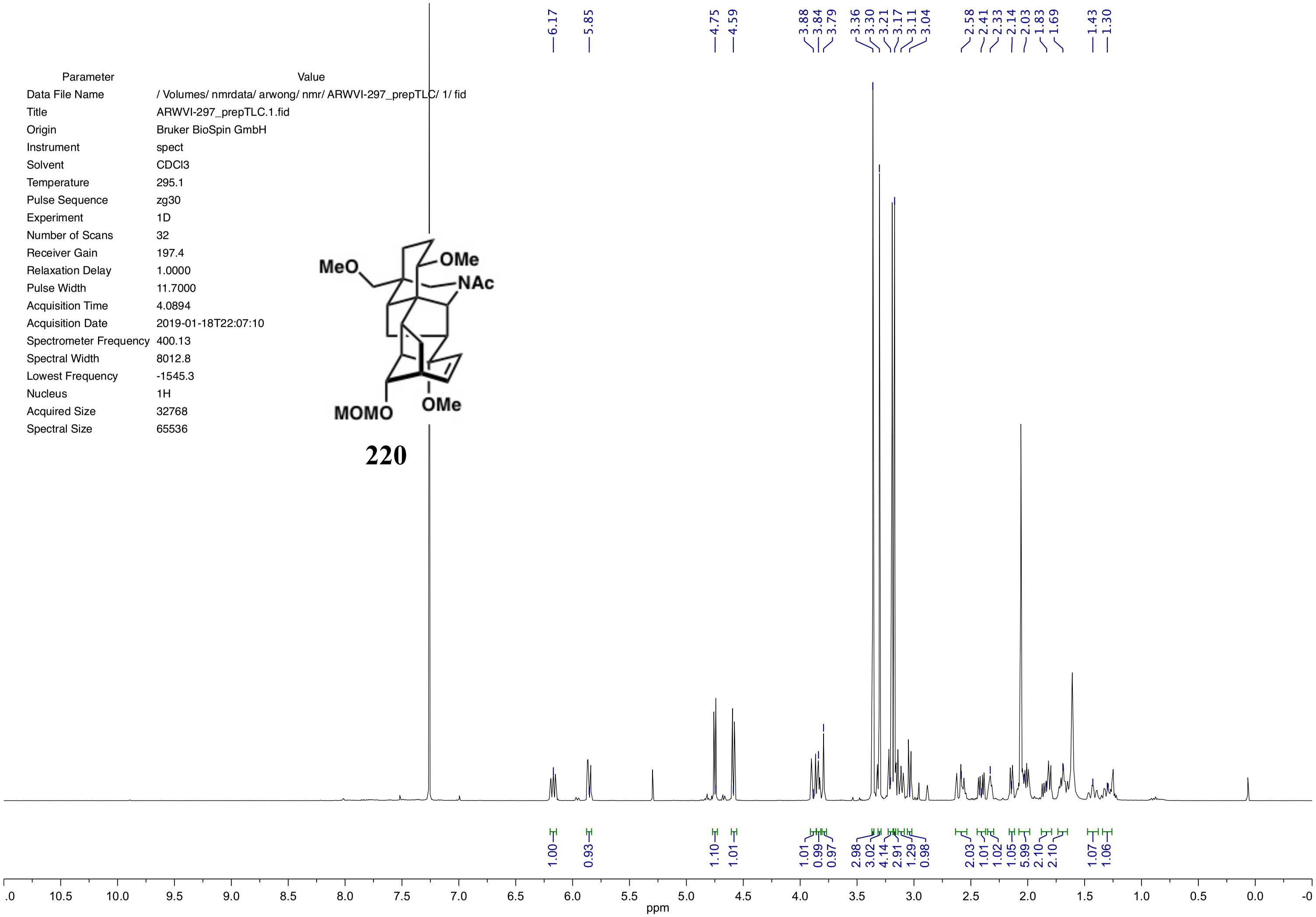
Parameter	Value
Data File Name	/ Volumes/ nmrdata-2/ arwong/ nmr/ ARWVI-296_prepTLC_B/ 1/ fid
Title	ARWVI-296_prepTLC_B.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	142.8
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2019-01-18T00:41:35
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



Parameter	Value
Data File Name	/ Volumes/ nmrdata-2/ arwong/ nmr/ ARWVI-296_prepTLC_B/ 6/ fid
Title	ARWVI-296_prepTLC_B.6.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	3000
Receiver Gain	87.8
Relaxation Delay	0.5000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2019-01-18T04:15:36
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.5
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

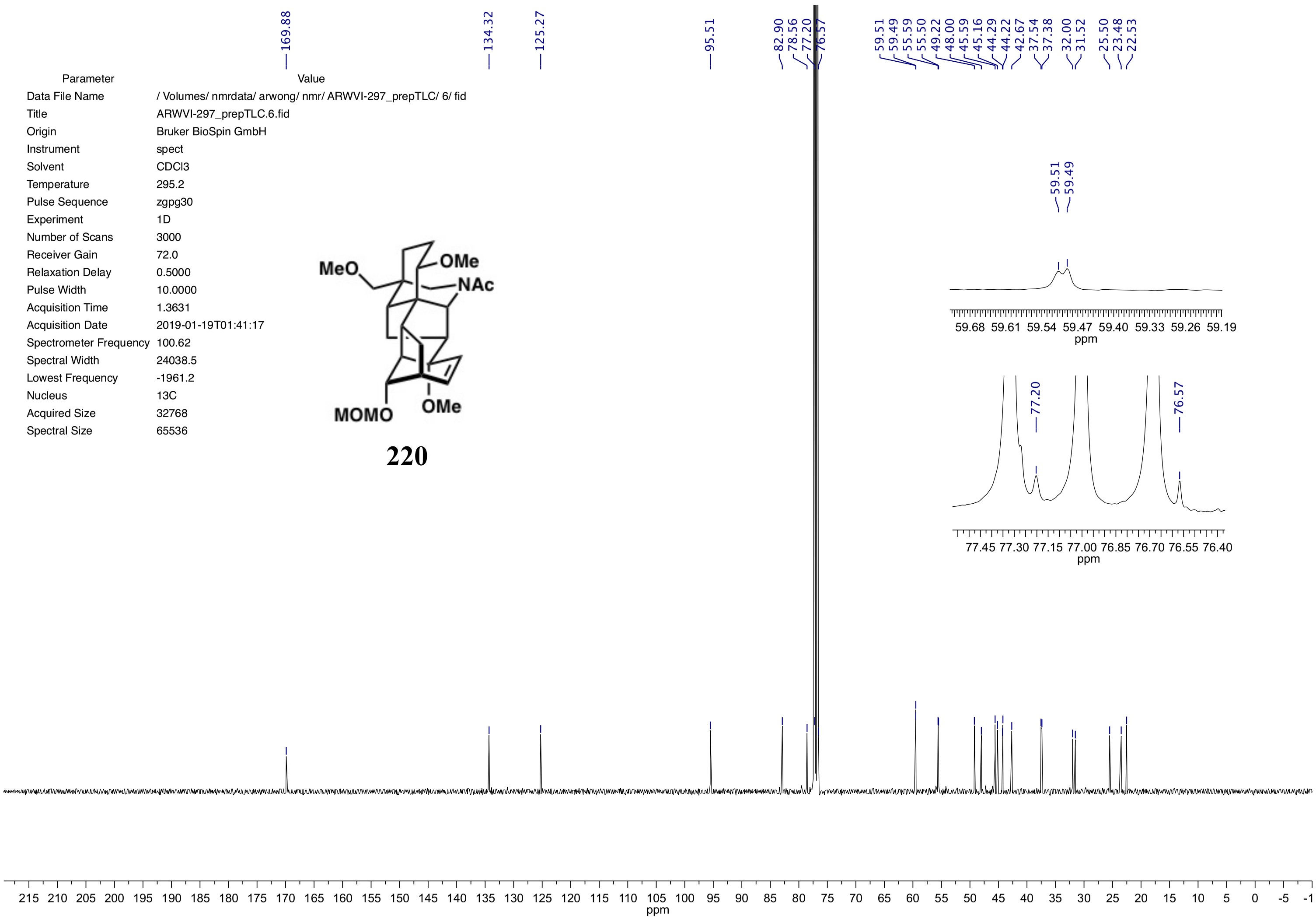
219

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-297_prepTLC/ 1/ fid
Title	ARWVI-297_prepTLC.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	197.4
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2019-01-18T22:07:10
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.3
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



220

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-297_prepTLC/ 6/ fid
Title	ARWVI-297_prepTLC.6.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	3000
Receiver Gain	72.0
Relaxation Delay	0.5000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2019-01-19T01:41:17
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.2
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



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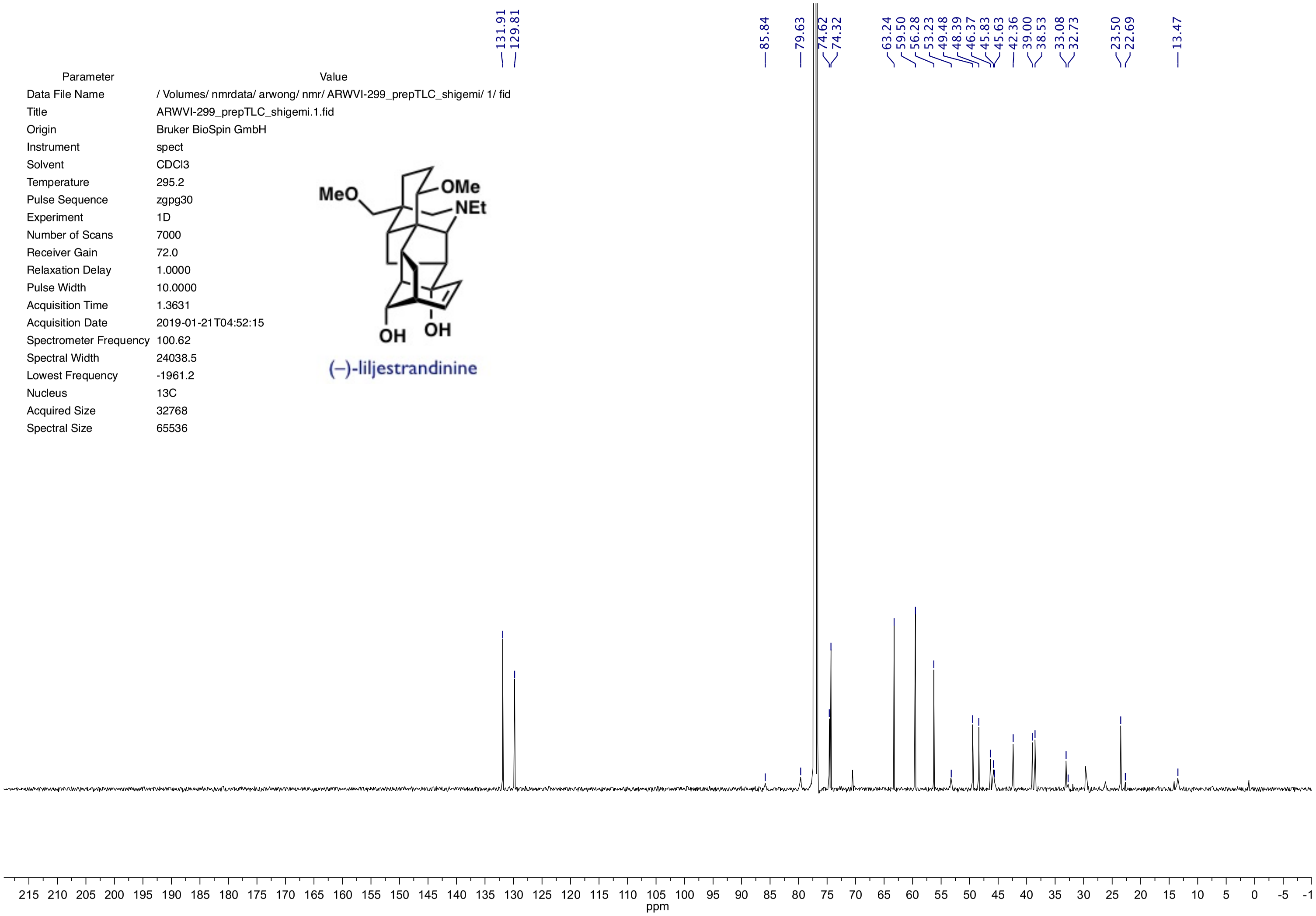

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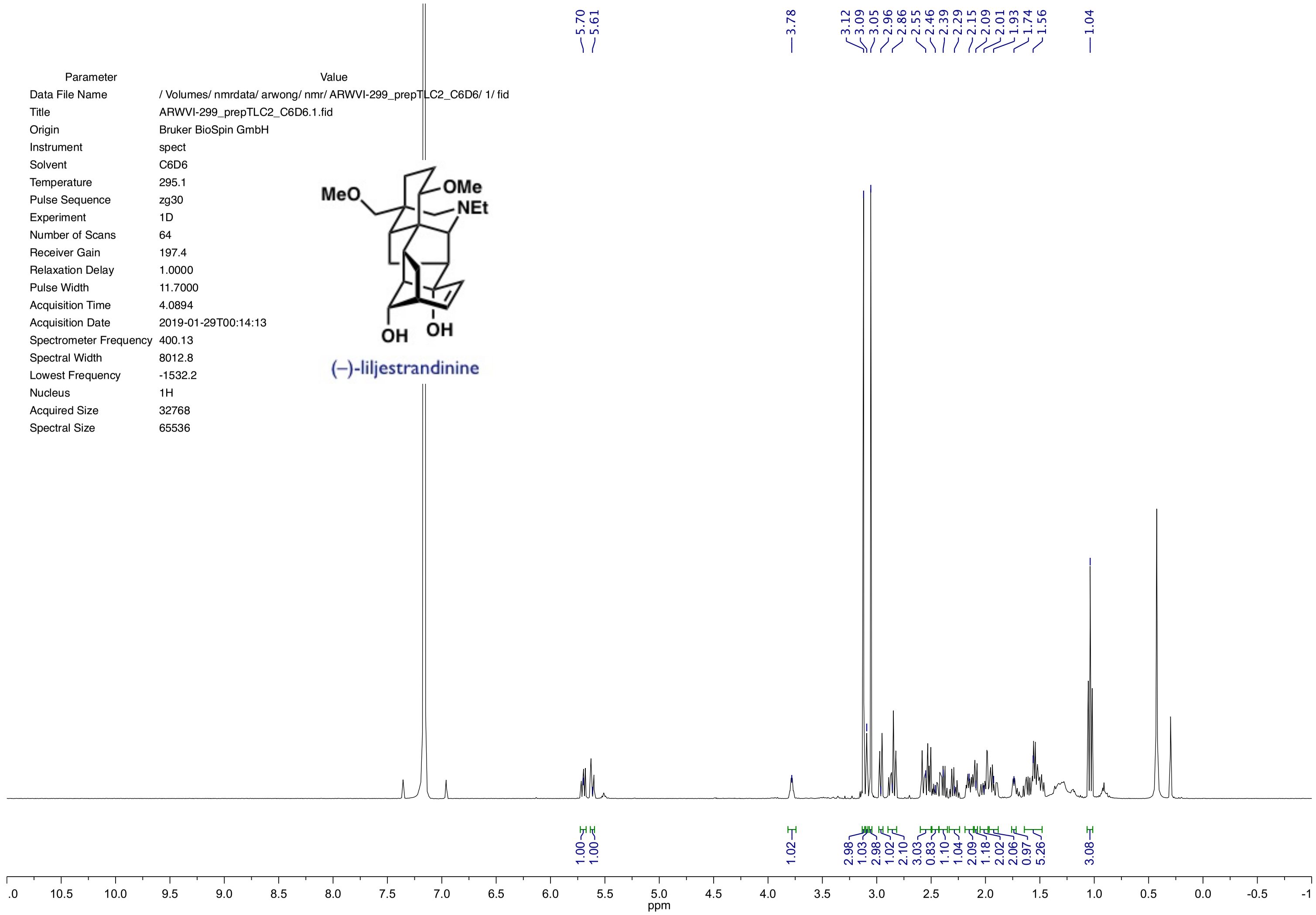
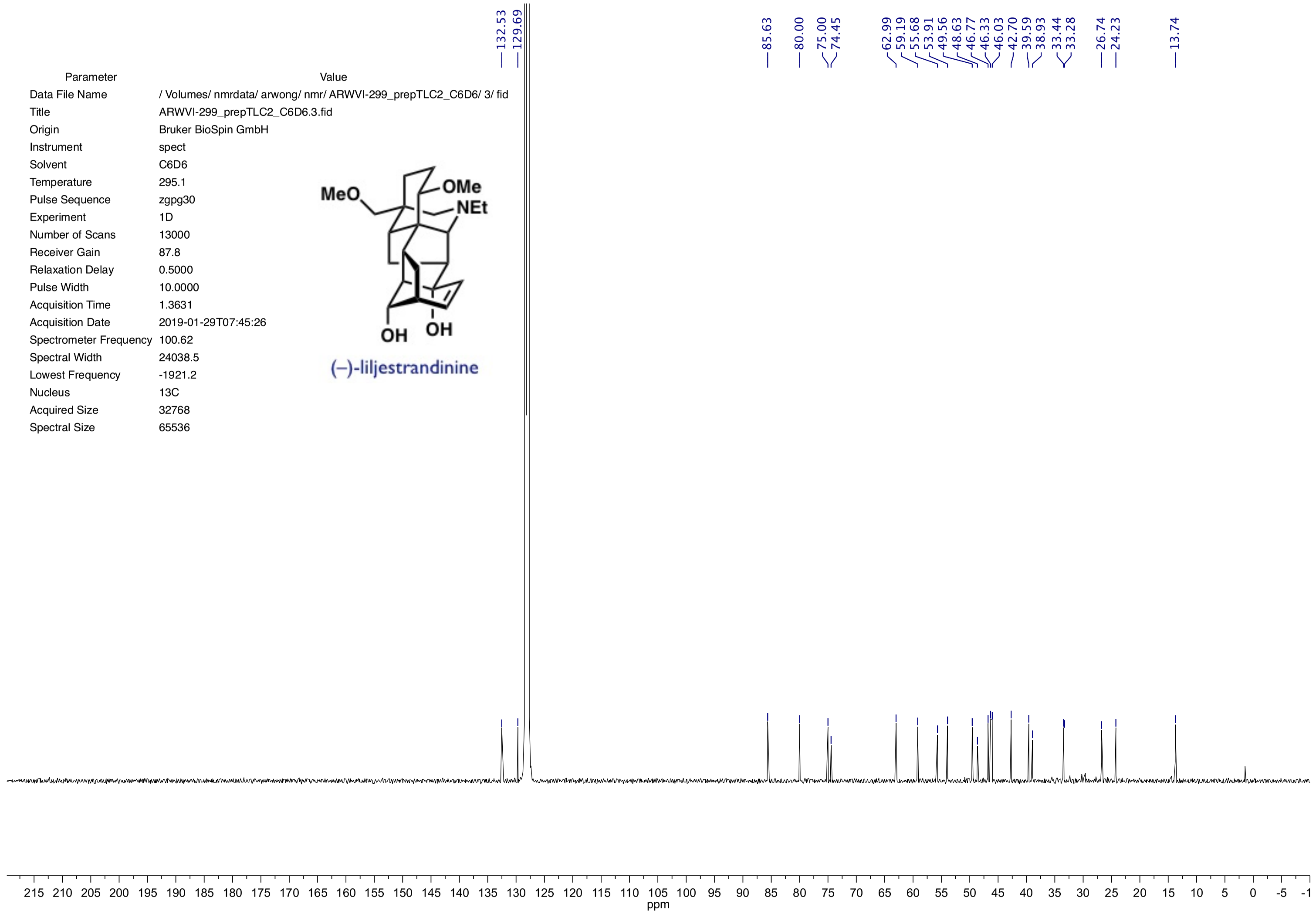
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-299_prepTLC_shigemi/ 1/ fid
Title	ARWVI-299_prepTLC_shigemi.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	7000
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2019-01-21T04:52:15
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.2
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-299_prepTLC2_C6D6/ 1/ fid
Title	ARWVI-299_prepTLC2_C6D6.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	C6D6
Temperature	295.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	64
Receiver Gain	197.4
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2019-01-29T00:14:13
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1532.2
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-299_prepTLC2_C6D6/ 3/ fid
Title	ARWVI-299_prepTLC2_C6D6.3.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	C6D6
Temperature	295.1
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	13000
Receiver Gain	87.8
Relaxation Delay	0.5000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2019-01-29T07:45:26
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1921.2
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

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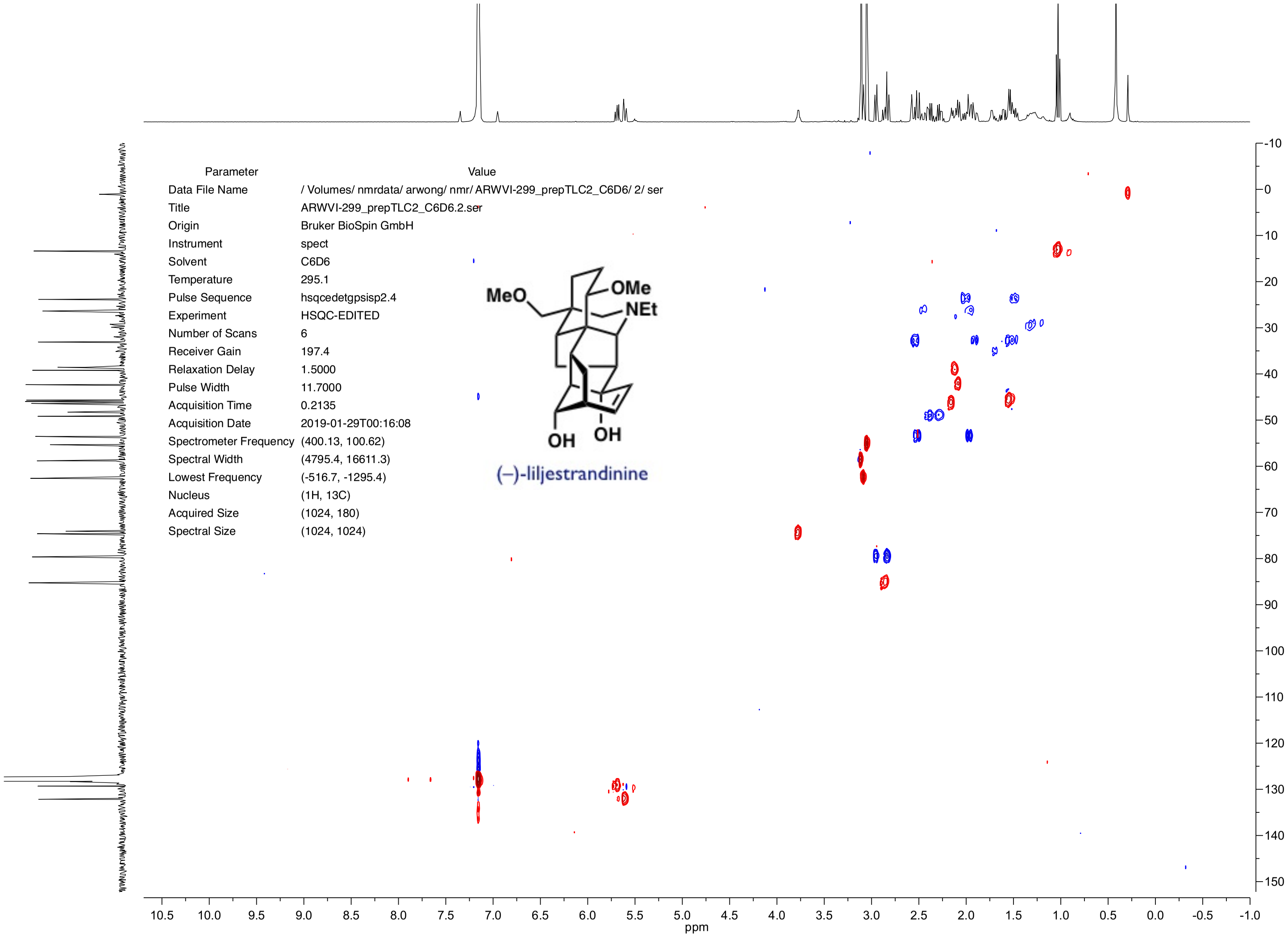

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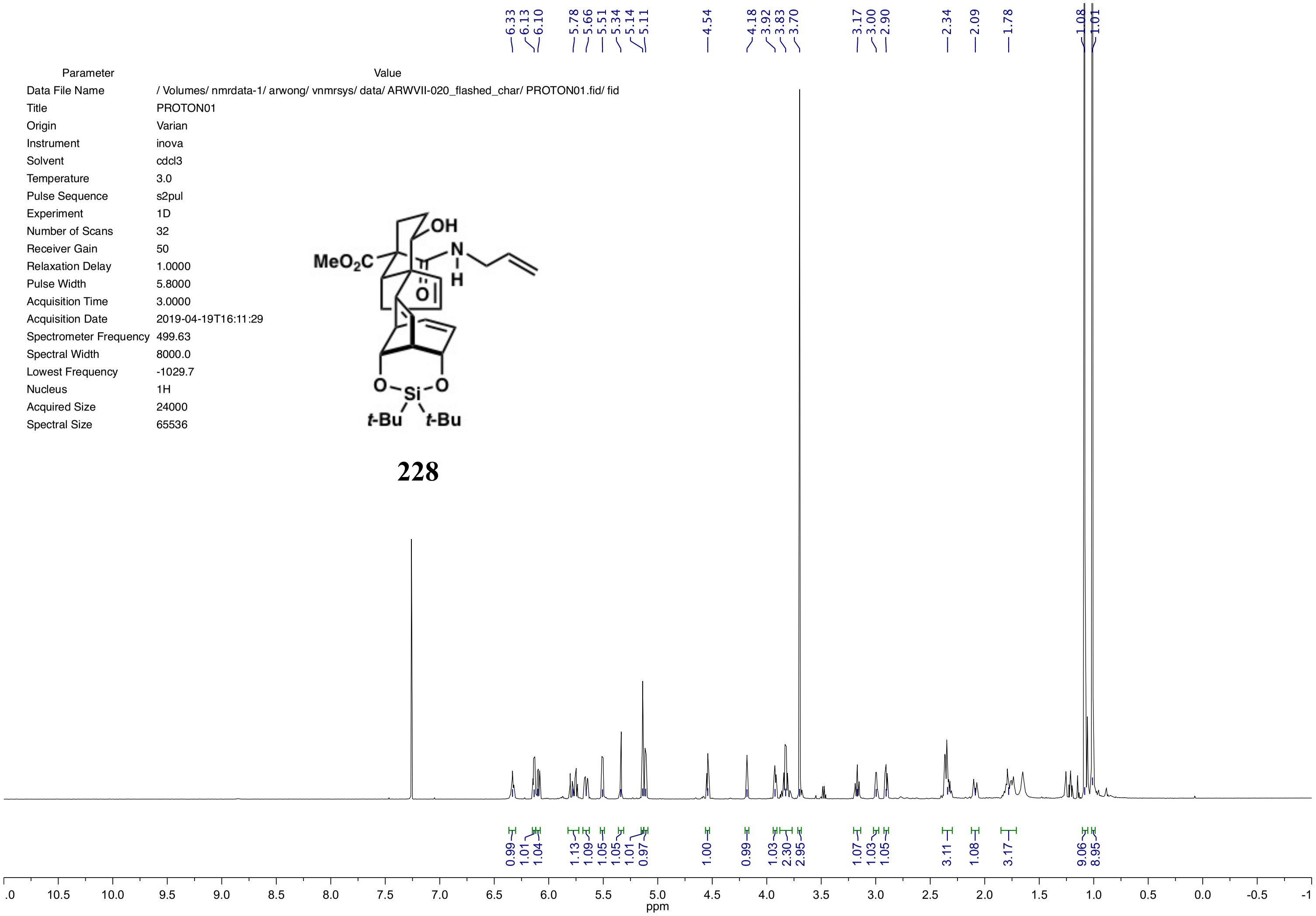
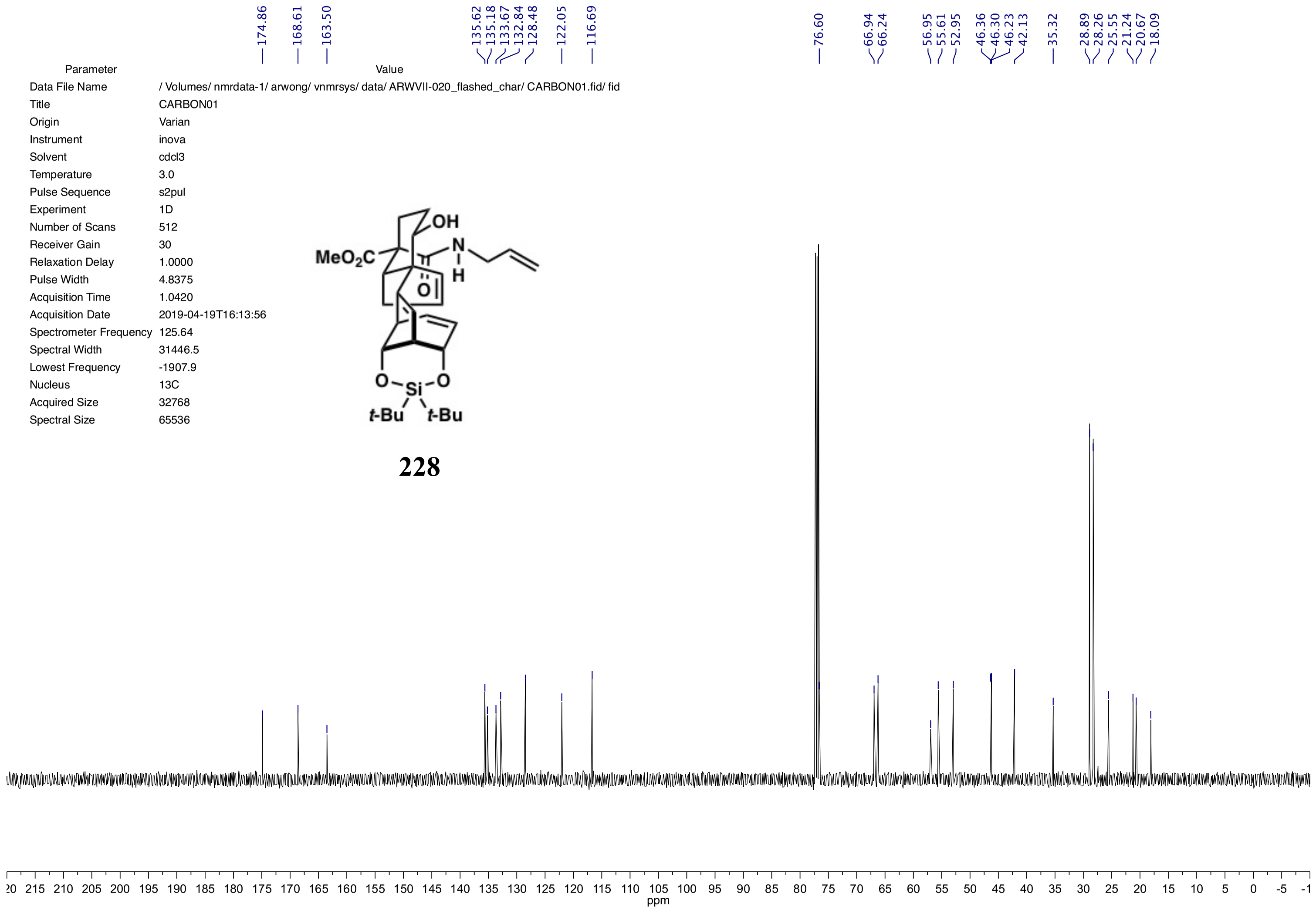
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVI-299_prepTLC2_C6D6/ 2/ ser
Title	ARWVI-299_prepTLC2_C6D6.2.ser
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	C6D6
Temperature	295.1
Pulse Sequence	hsqcedetgpsisp2.4
Experiment	HSQC-EDITED
Number of Scans	6
Receiver Gain	197.4
Relaxation Delay	1.5000
Pulse Width	11.7000
Acquisition Time	0.2135
Acquisition Date	2019-01-29T00:16:08
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(4795.4, 16611.3)
Lowest Frequency	(-516.7, -1295.4)
Nucleus	(1H, 13C)
Acquired Size	(1024, 180)
Spectral Size	(1024, 1024)



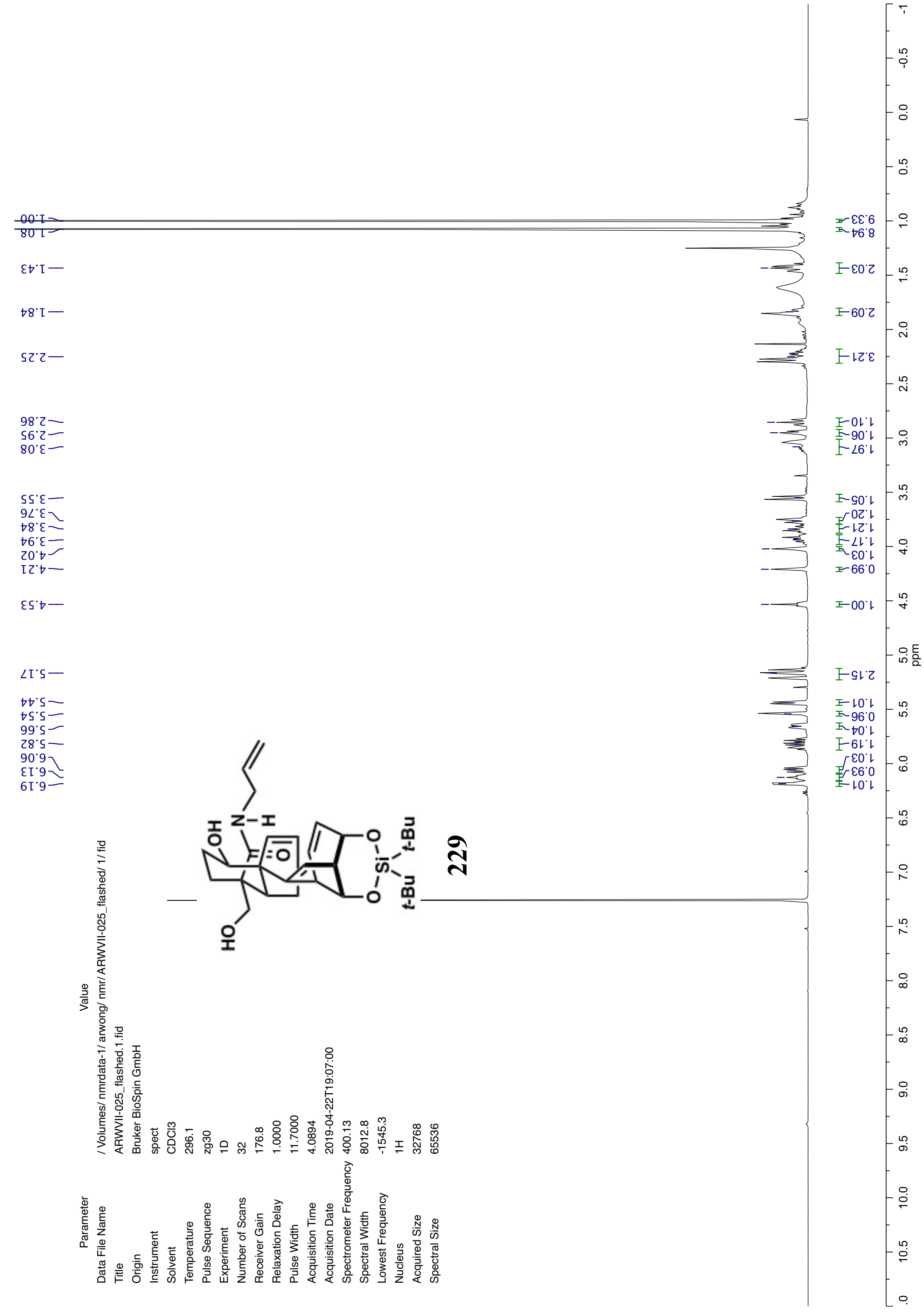
228

Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ arwong/ vnmrsys/ data/ ARWVII-020_flashed_char/ PROTON01.fid/ fid
Title	PROTON01
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	3.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	32
Receiver Gain	50
Relaxation Delay	1.0000
Pulse Width	5.8000
Acquisition Time	3.0000
Acquisition Date	2019-04-19T16:11:29
Spectrometer Frequency	499.63
Spectral Width	8000.0
Lowest Frequency	-1029.7
Nucleus	1H
Acquired Size	24000
Spectral Size	65536



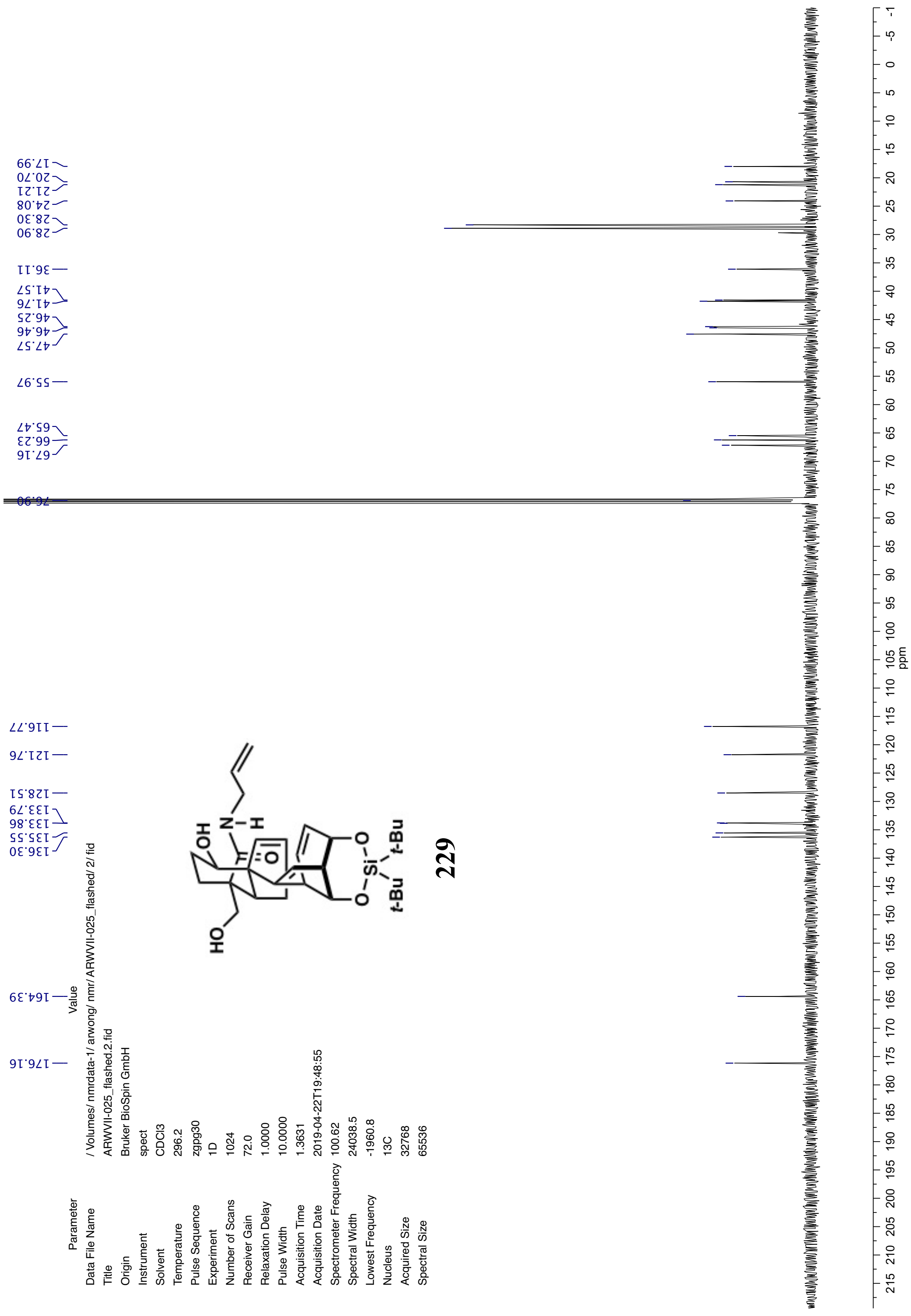
228

Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ arwong/ vnmrsys/ data/ ARWVII-020_flashed_char/ CARBON01.fid/ fid
Title	CARBON01
Origin	Varian
Instrument	inova
Solvent	cdcl3
Temperature	3.0
Pulse Sequence	s2pul
Experiment	1D
Number of Scans	512
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	4.8375
Acquisition Time	1.0420
Acquisition Date	2019-04-19T16:13:56
Spectrometer Frequency	125.64
Spectral Width	31446.5
Lowest Frequency	-1907.9
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



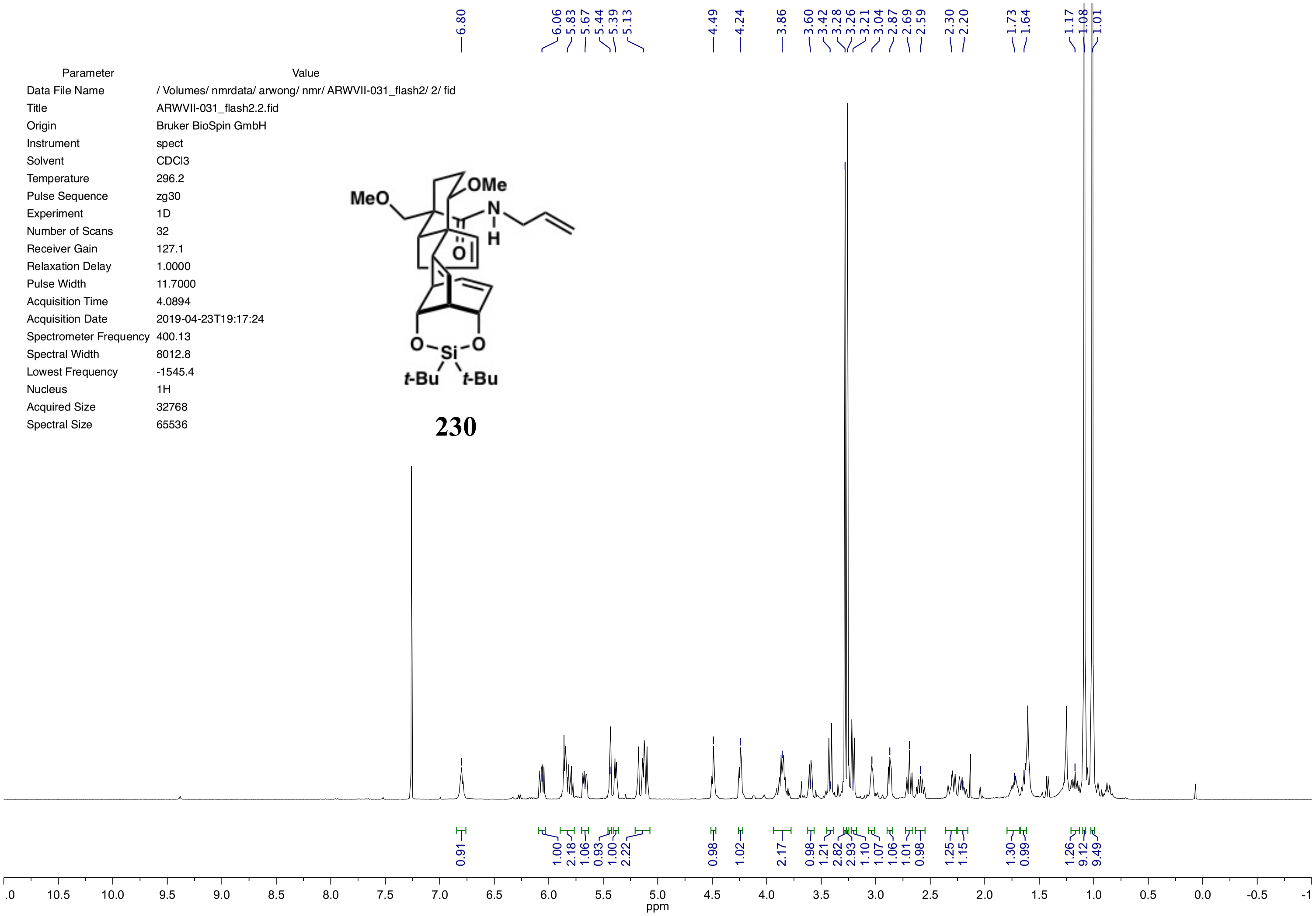
229

Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ arwong/ nmr/ ARWVII-025_flashed/ 1/ fid
Title	ARWVII-025_flashed.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	296.1
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	176.8
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2019-04-22T19:07:00
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.3
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



229

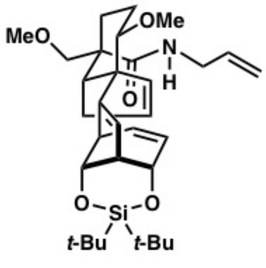
Parameter	Value
Data File Name	/Volumes/nmrdata-1/arwong/nmr/ARWVII-025_flashed/2/fid
Title	ARWVII-025_flashed.2.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	296.2
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1024
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2019-04-22T19:48:55
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1960.8
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



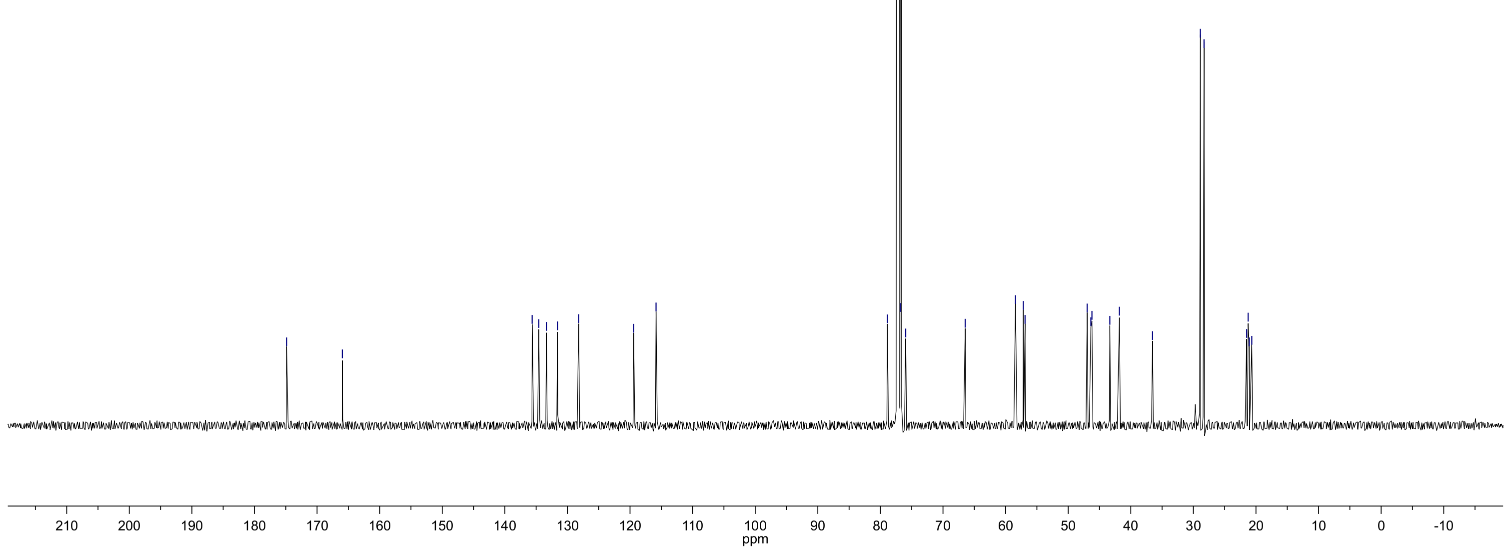
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVII-031_flash2/ 2/ fid
Title	ARWVII-031_flash2.2.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	296.2
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	127.1
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2019-04-23T19:17:24
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

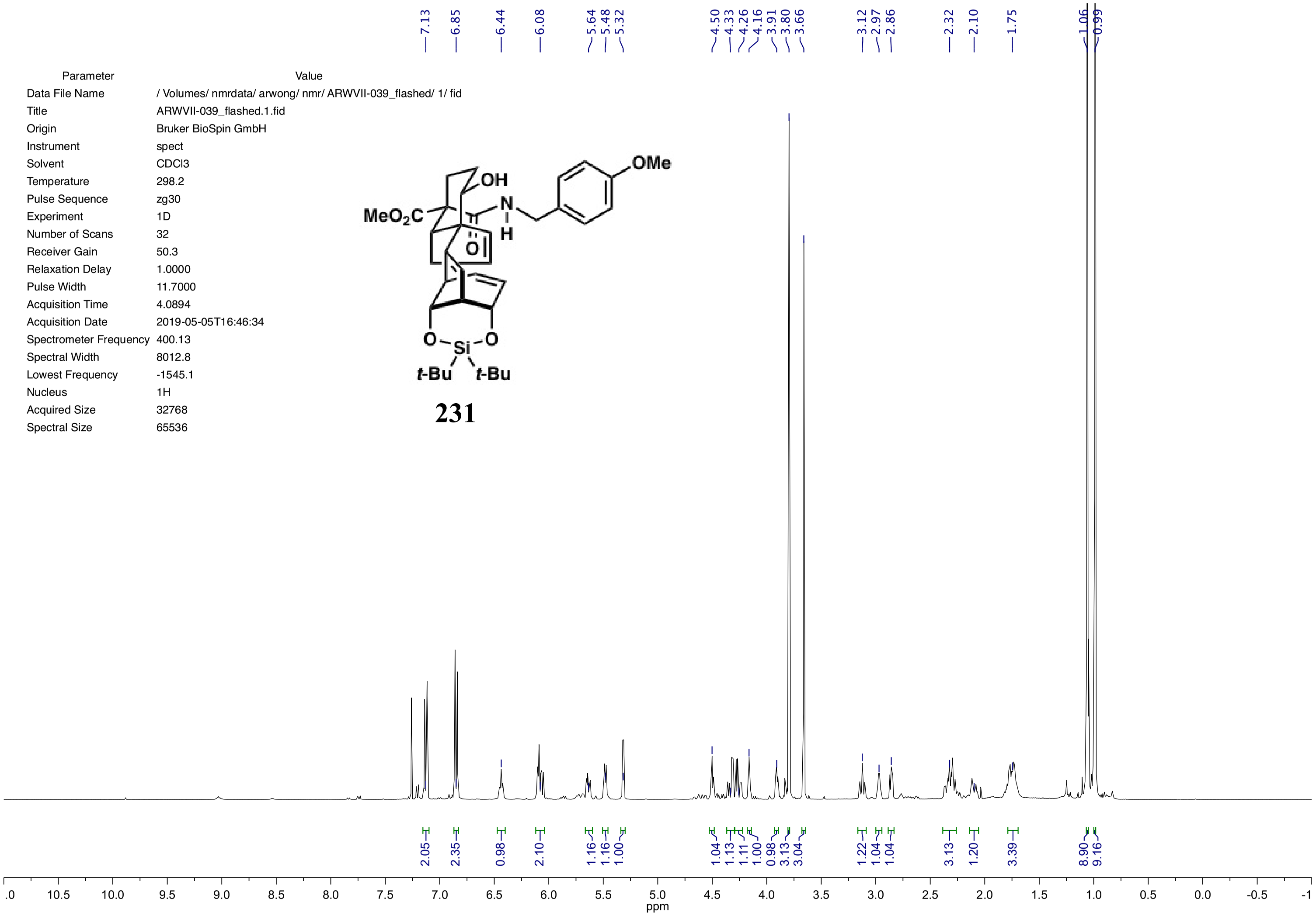
230

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVII-031_flash2/ 3/ fid
Title	ARWVII-031_flash2.3.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	296.1
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1024
Receiver Gain	87.8
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2019-04-23T19:59:55
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.0
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



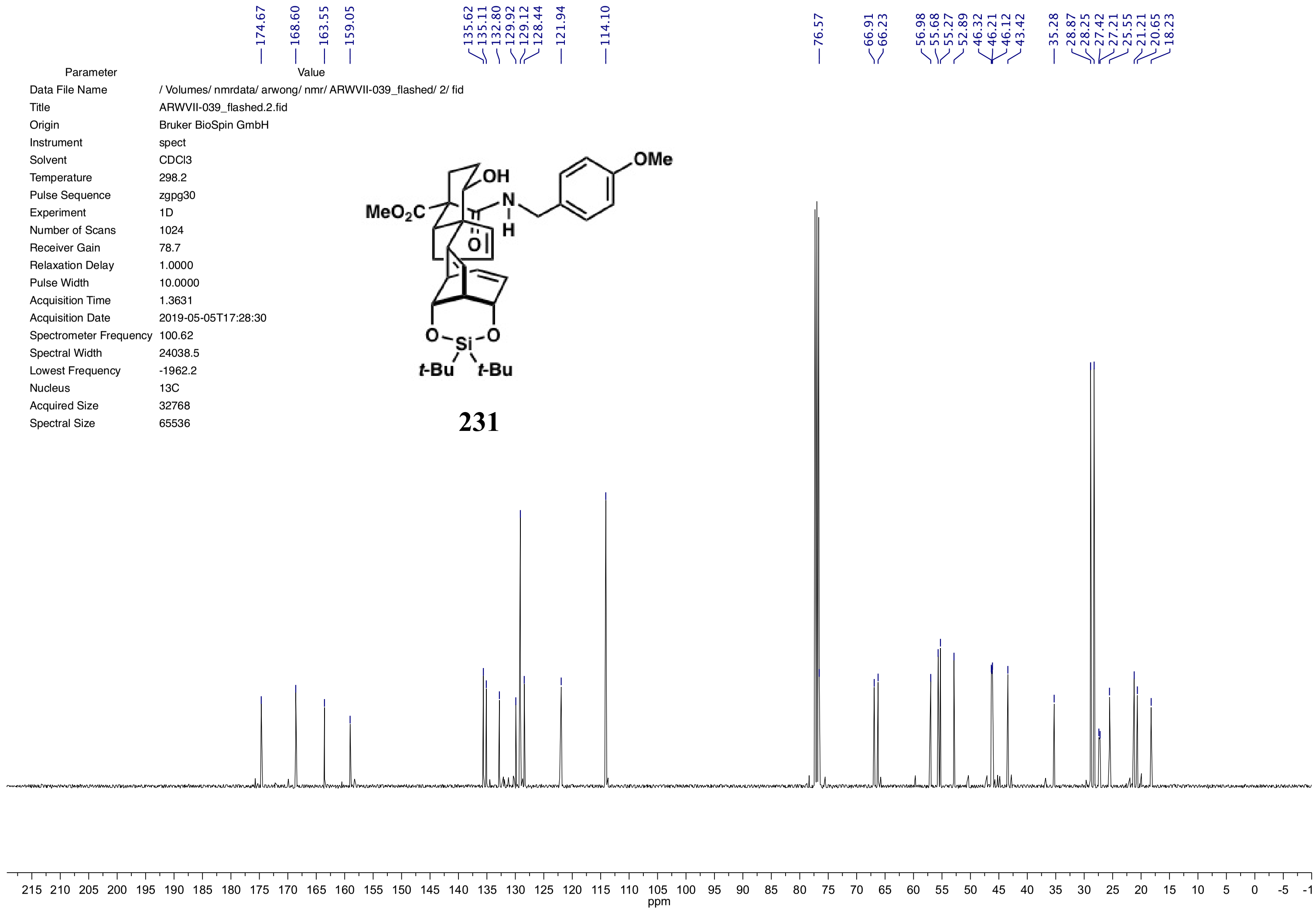
230





231

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVII-039_flashed/ 1/ fid
Title	ARWVII-039_flashed.1.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	298.2
Pulse Sequence	zg30
Experiment	1D
Number of Scans	32
Receiver Gain	50.3
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2019-05-05T16:46:34
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.1
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



231

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ arwong/ nmr/ ARWVII-039_flashed/ 2/ fid
Title	ARWVII-039_flashed.2.fid
Origin	Bruker BioSpin GmbH
Instrument	spect
Solvent	CDCl3
Temperature	298.2
Pulse Sequence	zgpg30
Experiment	1D
Number of Scans	1024
Receiver Gain	78.7
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2019-05-05T17:28:30
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1962.2
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

Appendix 4

X-Ray Crystallography Reports Relevant to Chapters 1–3:

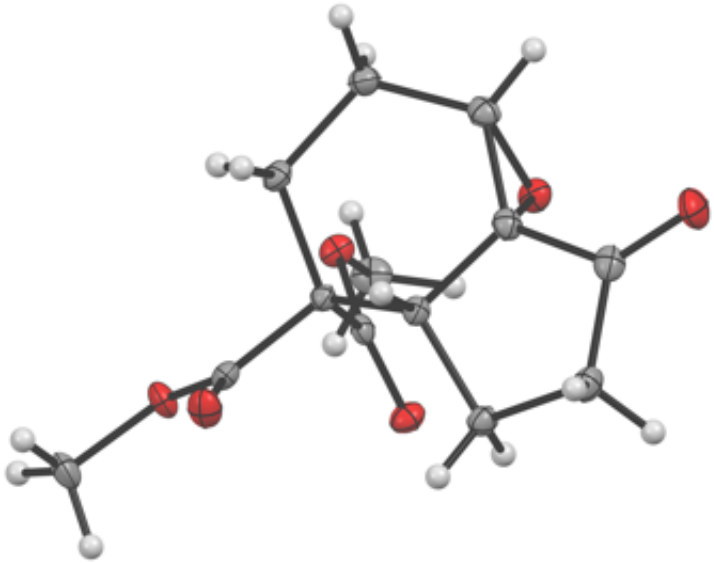
A4.1 STRUCTURAL DETERMINATION AND REFINEMENT DETAILS

Low-temperature diffraction data (ϕ- and ω-scans) were collected on a Bruker AXS D8 VENTURE KAPPA diffractometer coupled to either a PHOTON 100 CMOS detector with Mo-$K\alpha$ radiation (λ = 0.71073 Å) or a PHOTON II CPAD detector with either Mo-$K\alpha$ radiation (λ = 0.71073 Å) or Cu-$K\alpha$ radiation (λ = 1.54178 Å) from a fine-focus sealed X-ray tube. All diffractometer manipulations, including data collection integration, and scaling were carried out using the Bruker APEXII software.[1] Absorption corrections were applied using SADABS.[2] The structure was solved by intrinsic phasing using SHELXT[3] and refined against F^2 on all data by full-matrix least squares with SHELXL-2014[4] using established refinement techniques.[5] 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 and hydroxyl groups). Absolute configuration was determined by anomalous dispersion[6] and confirmed by Bayesian statistical analysis using the program PLATON.[7] Graphical representation of the structure with 50% probability thermal ellipsoids was generated using Mercury visualization software.

A4.2 CRYSTALLOGRAPHIC ANALYSIS OF 7

A4.2.1 Special Refinement Details

Figure A2.1 *Rendering of* ***7****.*



Compound **7** crystallizes in the orthorhombic space group *P*$2_12_12_1$ with one molecule in the asymmetric unit. Absolute configuration was determined by anomalous dispersion (Flack = 0.12(3)).[6] Bayesian statistics further confirm the absolute stereochemistry: P2(true) = 1.000, P3(true) = 1.000, P3(rac-twin) = $0.5\text{x}10^{-33}$, and P3(false) = $0.6\text{x}10^{-176}$.[7]

A4.2.2 Crystallographic Tables

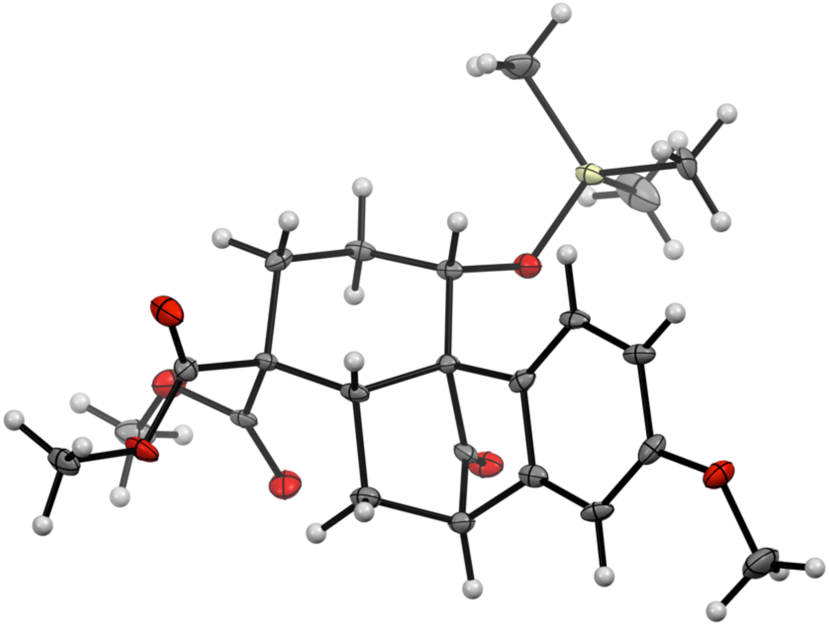
Table A4.1. Crystal data and structure refinement for **7**.

Identification code	V19114	
Empirical formula	$C_{13}H_{16}O_6$	
Formula weight	268.26	
Temperature	100 K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 6.0214(7) Å	α = 90°.
	b = 6.7387(7) Å	β = 90°.
	c = 29.463(3) Å	γ = 90°.
Volume	1195.5(2) $Å^3$	
Z	4	
Density (calculated)	1.490 Mg/m^3	
Absorption coefficient	1.005 mm^{-1}	
F(000)	568	
Crystal size	0.30 x 0.22 x 0.20 mm^3	
Theta range for data collection	3.000 to 79.174°.	
Index ranges	-7<=h<=7, -8<=k<=8, -36<=l<=37	
Reflections collected	23348	
Independent reflections	2581 [R(int) = 0.0403]	
Completeness to theta = 67.679°	99.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7542 and 0.6302	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2581 / 0 / 174	
Goodness-of-fit on F^2	1.083	
Final R indices [I>2sigma(I)]	R1 = 0.0261, wR2 = 0.0684	
R indices (all data)	R1 = 0.0261, wR2 = 0.0684	
Absolute structure parameter	0.12(3)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.267 and -0.179 e.$Å^{-3}$	

A4.3 CRYSTALLOGRAPHIC ANALYSIS OF 30

A4.3.1 Special Refinement Details

Figure A2.2 *Rendering of **30**.*



Compound **30** crystallizes in the orthorhombic space group *P*bca with one molecule in the asymmetric unit.

A4.3.2 Crystallographic Tables

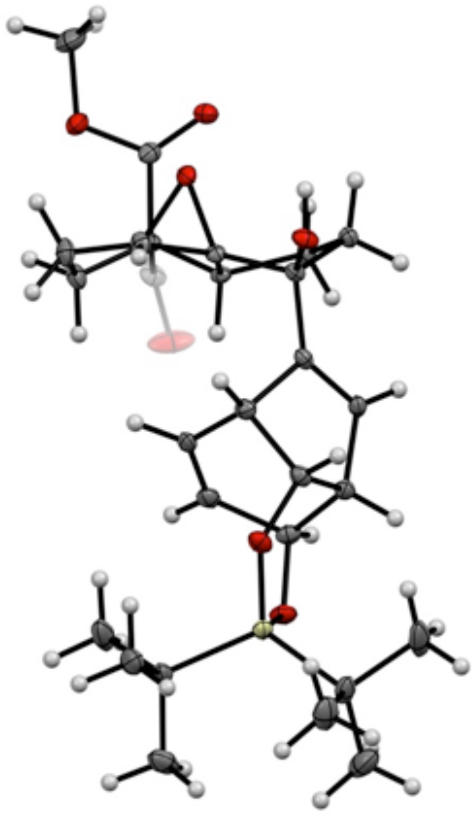
Table A4.2. Crystal data and structure refinement for **30**.

Identification code	P16149	
Empirical formula	$C_{23}H_{30}O_7Si$	
Formula weight	446.56	
Temperature	100 K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	Pbca	
Unit cell dimensions	a = 18.2041(15) Å	α = 90°.
	b = 12.7693(13) Å	β = 90°.
	c = 19.5076(18) Å	γ = 90°.
Volume	4534.6(7) $Å^3$	
Z	8	
Density (calculated)	1.308 Mg/m^3	
Absorption coefficient	0.145 mm^{-1}	
F(000)	1904	
Crystal size	0.188 x 0.151 x 0.05 mm^3	
Theta range for data collection	2.210 to 32.037°.	
Index ranges	-27<=h<=27, -17<=k<=18, -29<=l<=26	
Reflections collected	135898	
Independent reflections	7877 [R(int) = 0.0810]	
Completeness to theta = 26.000°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7468 and 0.6970	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	7877 / 0 / 287	
Goodness-of-fit on F^2	1.090	
Final R indices [I>2sigma(I)]	R1 = 0.0443, wR2 = 0.0997	
R indices (all data)	R1 = 0.0621, wR2 = 0.1053	
Extinction coefficient	0.0014(3)	
Largest diff. peak and hole	0.412 and -0.287 e.$Å^{-3}$	

A4.4 CRYSTALLOGRAPHIC ANALYSIS OF 75

A4.4.1 Special Refinement Details

Figure A2.3 *Rendering of **75**.*



Compound **75** crystallizes in the monoclinic space group $P12_11$ with two molecules in the asymmetric unit. Absolute configuration was determined by anomalous dispersion (Flack = 0.02(2)).[6]

A4.4.2 Crystallographic Tables

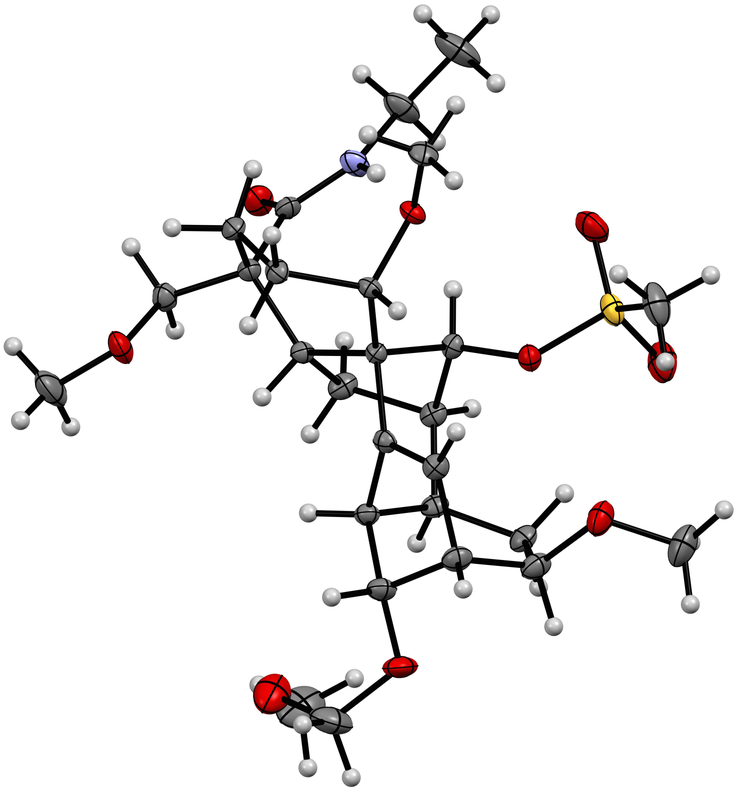
Table A4.3. Crystal data and structure refinement for **75**.

Identification code	P16421	
Empirical formula	$C_{29}H_{42}O_8Si$	
Formula weight	546.71	
Temperature	100 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 8.8034(13) Å	α = 90°.
	b = 24.957(4) Å	β = 101.552(5)°.
	c = 13.429(2) Å	γ = 90°.
Volume	2890.6(7) Å^3	
Z	4	
Density (calculated)	1.256 Mg/m^3	
Absorption coefficient	0.129 mm^{-1}	
F(000)	1176	
Crystal size	0.28 x 0.17 x 0.08 mm^3	
Theta range for data collection	2.361 to 30.544°.	
Index ranges	-12<=h<=12, -35<=k<=35, -19<=l<=19	
Reflections collected	130883	
Independent reflections	17688 [R(int) = 0.0665]	
Completeness to theta = 26.000°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7461 and 0.7071	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	17688 / 1 / 707	
Goodness-of-fit on F^2	1.036	
Final R indices [I>2sigma(I)]	R1 = 0.0394, wR2 = 0.0851	
R indices (all data)	R1 = 0.0512, wR2 = 0.0896	
Absolute structure parameter	0.02(2)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.295 and -0.229 e.Å^{-3}	

A4.5 CRYSTALLOGRAPHIC ANALYSIS OF 110

A4.5.1 Special Refinement Details

Figure A2.4 *Rendering of **110**.*



Compound **110** crystallizes in the triclinic space group *P*1 with one molecule in the asymmetric unit. Absolute configuration was determined by anomalous dispersion (Flack = 0.009(9)).[6]

A4.5.2 Crystallographic Tables

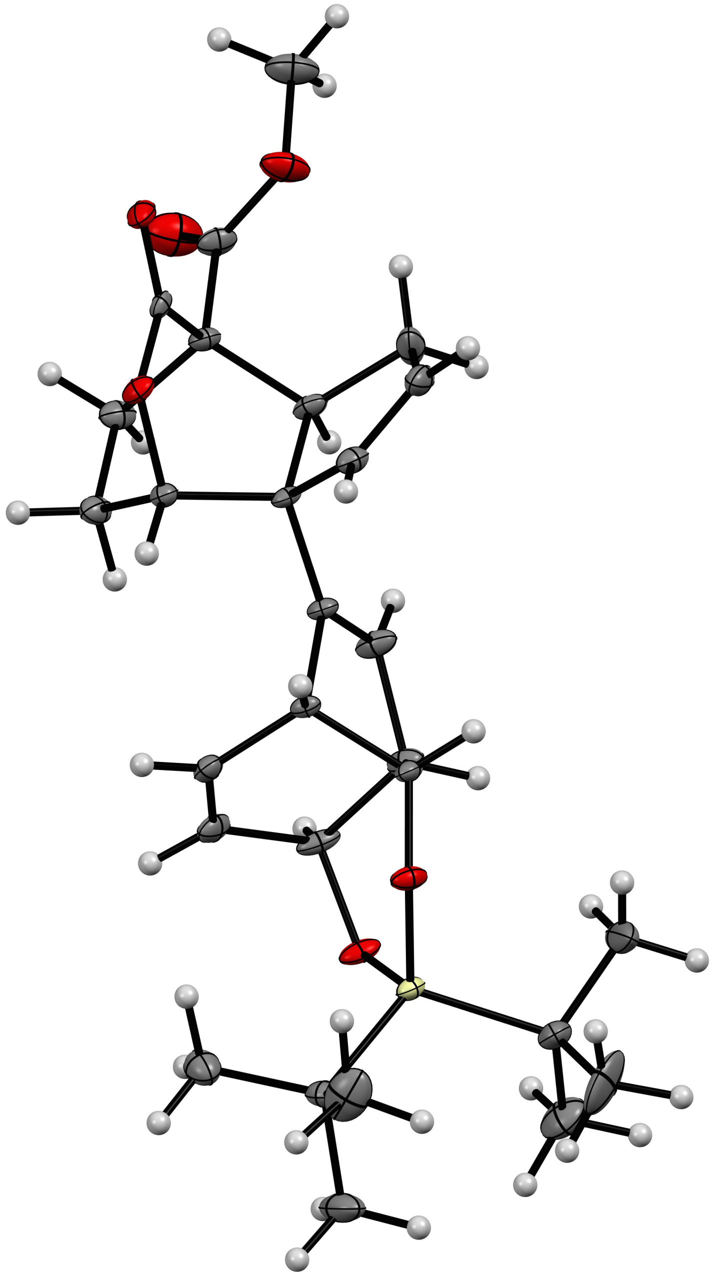
Table A4.4. *Crystal data and structure refinement for* ***110****.*

Identification code	P17327	
Empirical formula	$C_{27}H_{43}NO_9S$	
Formula weight	557.68	
Temperature	100 K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P1	
Unit cell dimensions	a = 8.3667(6) Å	α = 102.392(3)°.
	b = 9.4679(7) Å	β = 104.944(3)°.
	c = 9.6022(7) Å	γ = 91.127(3)°.
Volume	715.52(9) Å^3	
Z	1	
Density (calculated)	1.294 Mg/m^3	
Absorption coefficient	0.165 mm^{-1}	
F(000)	300	
Crystal size	0.24 x 0.23 x 0.22 mm^3	
Theta range for data collection	2.528 to 27.530°.	
Index ranges	-10<=h<=10, -12<=k<=12, -12<=l<=12	
Reflections collected	79773	
Independent reflections	6599 [R(int) = 0.0533]	
Completeness to theta = 26.000°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7456 and 0.6978	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6599 / 3 / 353	
Goodness-of-fit on F^2	1.051	
Final R indices [I>2sigma(I)]	R1 = 0.0249, wR2 = 0.0669	
R indices (all data)	R1 = 0.0264, wR2 = 0.0676	
Absolute structure parameter	0.009(9)	
Extinction coefficient	0.022(5)	
Largest diff. peak and hole	0.250 and -0.199 e.Å^{-3}	

A4.6 CRYSTALLOGRAPHIC ANALYSIS OF 119

A4.6.1 Special Refinement Details

Figure A2.5 *Rendering of **119**.*



Compound **119** crystallizes in the monoclinic space group $P12_11$ with two molecules in the asymmetric unit. Positional disorder of the methyl ester was not refined. Absolute configuration was determined by anomalous dispersion (Flack = –0.02(5)).[6]

A4.6.2 Crystallographic Tables

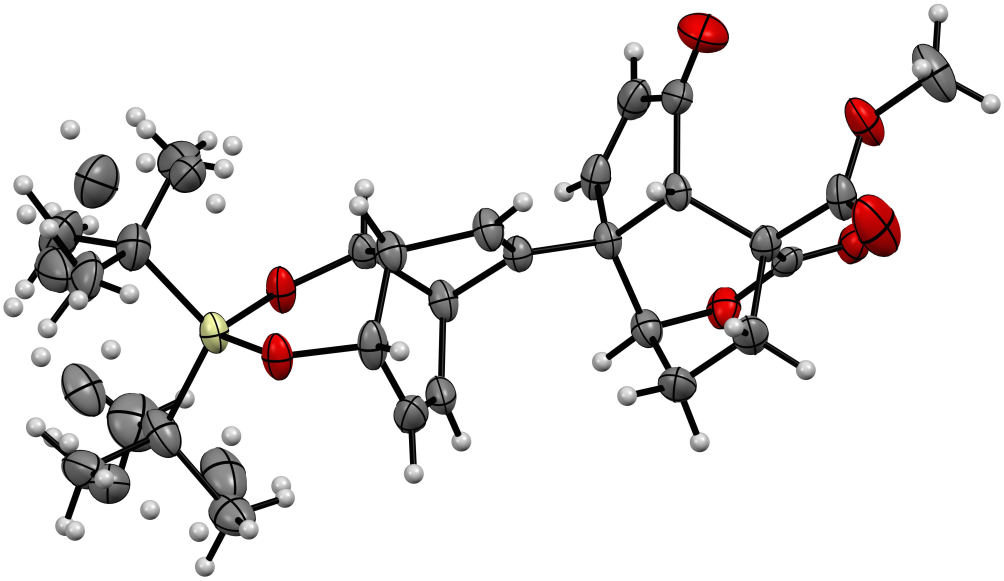
Table A4.5. *Crystal data and structure refinement for* ***119****.*

Identification code	P17564	
Empirical formula	$C_{28}H_{38}O_6Si$	
Formula weight	498.67	
Temperature	100 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 16.5088(10) Å	α = 90°.
	b = 8.7968(6) Å	β = 107.079(2)°.
	c = 18.4061(11) Å	γ = 90°.
Volume	2555.1(3) $Å^3$	
Z	4	
Density (calculated)	1.296 Mg/m^3	
Absorption coefficient	0.133 mm^{-1}	
F(000)	1072	
Crystal size	0.56 x 0.37 x 0.12 mm^3	
Theta range for data collection	2.296 to 27.617°.	
Index ranges	-21<=h<=21, -11<=k<=11, -23<=l<=23	
Reflections collected	38328	
Independent reflections	11787 [R(int) = 0.0572]	
Completeness to theta = 26.000°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7456 and 0.5556	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	11787 / 1 / 645	
Goodness-of-fit on F^2	1.025	
Final R indices [I>2sigma(I)]	R1 = 0.0599, wR2 = 0.1613	
R indices (all data)	R1 = 0.0716, wR2 = 0.1720	
Absolute structure parameter	-0.02(5)	
Extinction coefficient	n/a	
Largest diff. peak and hole	1.314 and -0.466 e.$Å^{-3}$	

A4.7 CRYSTALLOGRAPHIC ANALYSIS OF 137

A4.7.1 Special Refinement Details

Figure A2.6 *Rendering of* ***137****.*



Compound **137** crystallizes in the monoclinic space group $P12_11$ with one molecule in the asymmetric unit. Diffraction data was collected at 200 K. The *tert*-butyl groups were disordered over two positions (the first was 68% and 32% occupancy and the second was 75% and 25% occupancy). Disordered *tert*-butyl groups are omitted for clarity. Absolute configuration was determined by anomalous dispersion (Flack = 0.083(18)).[6] Bayesian statistics further confirm the absolute stereochemistry: P2(true) = 1.000, P3(true) = 1.000, P3(rac-twin) = 0.2x10^{-204}, and P3(false) = 0.0x10^{0}.[7]

A4.7.2 Crystallographic Tables

Table A4.6. *Crystal data and structure refinement for* ***137****.*

Identification code	V18223

Empirical formula	$C_{28}H_{36}O_7Si$	
Formula weight	512.66	
Temperature	200 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 8.4502(3) Å	α = 90°.
	b = 8.7388(3) Å	β = 99.3880(10)°.
	c = 18.0584(7) Å	γ = 90°.
Volume	1315.65(8) $Å^3$	
Z	2	
Density (calculated)	1.294 Mg/m^3	
Absorption coefficient	0.134 mm^{-1}	
F(000)	548	
Crystal size	0.29 x 0.17 x 0.09 mm^3	
Theta range for data collection	2.443 to 27.557°.	
Index ranges	-10<=h<=10, -11<=k<=11, -23<=l<=23	
Reflections collected	77934	
Independent reflections	5815 [R(int) = 0.1306]	
Completeness to theta = 26.000°	99.5 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7456 and 0.7210	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5815 / 187 / 395	
Goodness-of-fit on F^2	1.261	
Final R indices [I>2sigma(I)]	R1 = 0.0977, wR2 = 0.1034	
R indices (all data)	R1 = 0.1328, wR2 = 0.1070	
Absolute structure parameter	0.083(18)	
Extinction coefficient	0.0058(11)	
Largest diff. peak and hole	0.395 and -0.308 e.$Å^{-3}$	

A4.8 REFERENCES

(1) *APEX2, Version 2 User Manual, M86-E01078, Bruker Analytical X-ray Systems*, Madison, WI, **2006**.

(2) Sheldrick, G.M. *SADABS (version 2008/1): Program for Absorption Correction for Data from Area Detector Frames*, University of Göttingen, **2008**.

(3) Sheldrick, G. *Acta Crystallogr., Sect. A: Found. Crystallogr*. **2008**, *64*, 112.

(4) Sheldrick, G. M. *Acta Crystallogr., Sect. C: Struct. Chem.* **2015**, *C71*, 3.

(5) Müller, P. *Crystallogr. Rev.* **2009**, *15*, 57.

(6) Parsons, S.; Flack, H. D.; Wagner, T. *Acta Crystallogr., Sect. B: Struct. Sci. Cryst. Eng. Mater.* **2013**, *B69*, 249.

(7) Spek, A. L. *Acta Crystallogr., Sect. D: Struct. Biol.* **2009**, *D65*, 148.