DEVELOPMENT OF NICKEL-CATALYZED ASYMMETRIC REDUCTIVE CROSS-COUPLING REACTIONS

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To my family, gifted and gained

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ABSTRACT

Asymmetric reductive cross-electrophile coupling is a powerful method to forge C–C bonds and access enantioenriched small molecules, which can be further functionalized to access scaffolds present in natural products and bioactive pharmaceutical agents. However, an innate challenge of this methodology is identifying a chiral catalyst that achieves optimal cross-selectivity and stereocontrol. Herein, we report studies on the asymmetric cross-coupling of $C(sp^3)$ electrophiles, such as benzyl chlorides, α-chloroesters, and *N*-hydroxyphthalimide esters, with several classes of $C(sp^2)$ electrophiles.

We describe the asymmetric Ni-catalyzed reductive cross-coupling of (hetero)aryl iodides and benzyl chlorides to prepare enantioenriched 1,1-diarylalkanes. As part of these studies, a new chiral bi(oxazoline) ligand, 4-HeptylBiOX, was developed to obtain products in synthetically useful yield and enantioselectivity. This novel ligand is demonstrated to expand the substrate scope of these stereoconvergent reductive cross-couplings to include the asymmetric cross-coupling of α-chloroesters with aryl iodides, and sterically hindered *N*-hydroxyphthalimide esters with alkenyl bromides. Model studies have been initiated to study the application of these reactions toward the total synthesis of cylindrocyclophane natural products.

PUBLISHED CONTENT AND CONTRIBUTIONS

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

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   K.E.P. contributed to the reaction development, conducted experiments, and participated in preparation of the supporting data and writing of the manuscript.

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   K.E.P. contributed to the reaction development, conducted experiments, and participated in preparation of the supporting data and writing of the manuscript.

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LIST OF ABBREVIATIONS

$[\alpha]_D$	angle of optical rotation of plane-polarized light
Å	angstrom(s)
Ac	acetyl
acac	acetylacetonate
alk	alkyl
^{t}Am	*tert*-amyl
APCI	atmospheric pressure chemical ionization
app	apparent
aq	aqueous
Ar	aryl
atm	atmosphere(s)
bathophen	bathophenanthroline
BBN	borabicyclo[3.3.1]nonane
BHT	2,6-di-*tert*-butyl-4-methylphenol ("butylated hydroxytoluene")
BiOX	bi(oxazoline)
BINAP	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
BINOL	1,1'-bi(2-naphthol)
Bn	benzyl
Boc	*tert*-butoxycarbonyl
BOX	bis(oxazoline)
bp	boiling point
br	broad

Bu	butyl
^{i}Bu	*iso*-butyl
^{n}Bu	butyl or *norm*-butyl
^{s}Bu	*sec*-butyl
^{t}Bu	*tert*-butyl
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
CAM	cerium ammonium molybdate
cat.	catalyst
Cbz	benzyloxycarbonyl
cf.	consult or compare to (Latin: *confer*)
cis	on the same side
cm^{-1}	wavenumber(s)
cod	1,5-cyclooctadiene
conc.	concentrated
conv.	conversion
Cp	cyclopentadienyl
Cy	cyclohexyl
Cyp	cyclopentyl

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
DIPEA	*N*,*N*-diisopropylethylamine
DIBAL	diisobutylaluminum hydride
DFT	density functional theory
DKR	dynamic kinetic resolution
DMA	*N*,*N*-dimethylacetamide
DMAP	4-(dimethylamino)pyridine
DMBA	2,6-dimethylbenzoic acid
DME	1,2-dimethoxyethane
DMF	*N*,*N*-dimethylformamide
DMI	1,3-dimethyl-2-imidazolidinone
DMPU	*N*,*N*'-dimethylpropylene urea
DMSO	dimethylsulfoxide
dppb	1,4-bis(diphenylphosphino)butane
dppbz	1,2-bis(diphenylphosphino)benzene
dppf	1,1'-bis(diphenylphosphino)ferrocene

dppe	1,2-bis(diphenylphosphino)ethane
dr	diastereomeric ratio
dtbpy	4,4'-di-*tert*-butyl-2,2'-bipyridine
DYKAT	dynamic kinetic asymmetric transformation
E	methyl carboxylate (CO_2CH_3)
E^+	electrophile
E	trans (entgegen) olefin geometry
EDCI	*N*-(3-dimethylaminopropyl)-*N*'-ethylcarbodiimide hydrochloride
ee	enantiomeric excess
e.g.	for example (Latin: *exempli gratia*)
EI	electron impact
epi	epimeric
equiv	equivalent(s)
ESI	electrospray ionization
Et	ethyl
et al.	and others (Latin: *et alii*)
FAB	fast atom bombardment
g	gram(s)
GC	gas chromatography
h	hour(s)
^1H	proton
[H]	reduction
HC	homocoupling

hex	hexyl
HMDS	hexamethyldisilazane
HMPA	hexamethylphosphoramide
$h\nu$	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*)
in situ	in the reaction mixture
IPA	isopropanol
IR	infrared spectroscopy
J	coupling constant
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
LED	light-emitting diode
m	multiplet or meter(s)

M	molar or molecular ion
m	meta
μ	micro
m-CPBA	*meta*-chloroperbenzoic acid
Me	methyl
mg	milligram(s)
MHz	megahertz
min	minute(s)
mL	milliliter(s)
MM	mixed method
mol	mole(s)
MOM	methoxymethyl
mp	melting point
Ms	methanesulfonyl (mesyl)
MS	molecular sieves or mass spectrometry
m/*z*	mass-to-charge ratio
naph	naphthyl
nbd	norbornadiene
NBS	*N*-bromosuccinimide
ND	not determined
NHC	*N*-heterocyclic carbene
NHP	*N*-hydroxyphthalimide
nm	nanometer(s)

NMP	*N*-methyl-2-pyrrolidone
NMR	nuclear magnetic resonance
o	ortho
[O]	oxidation
p	para
Pc	phthalocyanine
Ph	phenyl
pH	hydrogen ion concentration in aqueous solution
phen	1,10-phenanthroline
PHOX	phosphinooxazoline
pin	pinacol
Piv	pivaloyl
pK_a	acid dissociation constant
Pr	propyl
^{i}Pr	isopropyl
^{n}Pr	propyl or *norm*-propyl
py	pyridine
PyBOX	pyridine-bis(oxazoline)
PyOx	pyridine-oxazoline
pyphos	(2-diphenylphosphino)ethylpyridine
q	quartet
quant.	quantitative
QuinOx	quinoline-oxazoline

R	alkyl group
R_L	large group
R	rectus
RCM	ring-closing metathesis
recry.	recrystallization
ref	reference
R_f	retention factor
rt	room temperature
s	singlet or seconds
S	sinister
sat.	saturated
SET	single-electron transfer
SFC	supercritical fluid chromatography
SM	starting material
t	triplet
TBAB	tetra-*n*-butylammonium bromide
TBAF	tetra-*n*-butylammonium fluoride
TBAI	tetra-*n*-butylammonium iodide
TBAT	tetra-*n*-butylammonium difluorotriphenylsilicate
TBS	*tert*-butyldimethylsilyl
TDAE	tetrakis(dimethylamino)ethylene
Tf	trifluoromethanesulfonyl
TFA	trifluoroacetic acid

temp	temperature
terpy	2,2′:6′,2″-terpyridine
THF	tetrahydrofuran
TIPS	triisopropylsilyl
TLC	thin layer chromatography
TMEDA	*N*,*N*,*N*’,*N*’-tetramethylethylenediamine
TMS	trimethylsilyl
TOF	time-of-flight
tol	toluene
trans	on the opposite side
Ts	*para*-toluenesulfonyl (tosyl)
UV	ultraviolet
vide infra	see below
v/v	volume per volume
w/v	weight per volume
X	anionic ligand or halide
xs	excess
Y	anionic ligand or halide
Z	cis (zusammen) olefin geometry

Chapter 1

Nickel Catalysis in Asymmetric Reductive Cross-Coupling

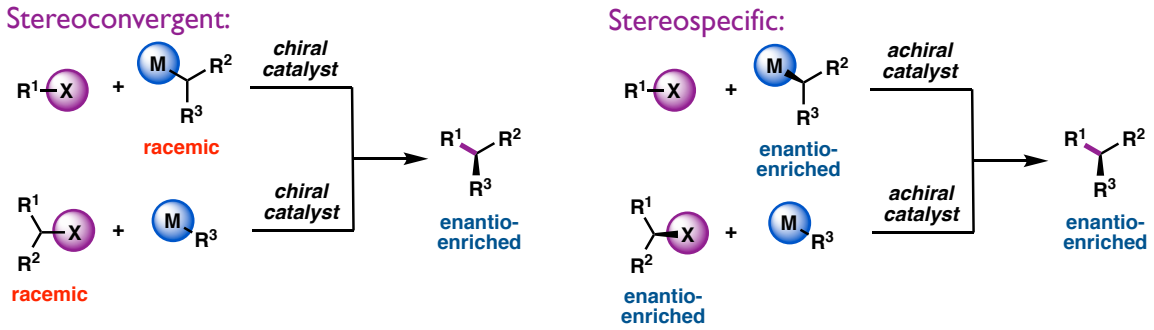
1.1 INTRODUCTION

Cross-coupling technology has become an incredibly powerful tool for forging C–C bonds in the synthesis of natural products and small molecules. An ongoing challenge for synthetic chemists is the stereocontrolled construction of these C–C bonds. Transition metal catalysis has opened up many new modes of reactivity for chemists that have redefined the synthetic strategies used for the preparation of enantioenriched molecules. In particular, the use of transition metal-catalyzed cross-coupling reactions, in which an organic electrophile (typically a halide or pseudo halide) is coupled to an organometallic reagent, has revolutionized organic chemistry.

These cross-coupling reactions, in which the stereogenic center is defined by the C–C bond forming event, can be organized in two categories, depending on the method in which the chiral information of the product is defined (Scheme 1.1).[1] In a *stereoconvergent* cross-coupling, one enantiomer of product is formed selectively from

an achiral and chiral racemic coupling partner, through the use of a chiral catalyst. In a *stereospecific* reaction, the stereochemistry of a chiral, enantioenriched coupling partner is transferred to the product with an achiral metal catalyst.

Scheme 1.1. *Strategies for enantioselective cross-coupling.*



While much focus has been placed on the use of palladium and other precious metals for these enantioselective cross-coupling reactions, processes involving alkyl coupling partners have been slow to develop due to the inherent challenges involved with Pd-catalyzed alkyl cross-coupling reactions. In these transformations, *sec*-alkyl organometallic reagents can be slow to undergo transmetalation,[2] while *sec*-alkyl electrophiles are often slow to undergo oxidative addition.[3] In either case, the resulting *sec*-alkyl Pd complex suffers from rapid β-hydride elimination.[4,5]

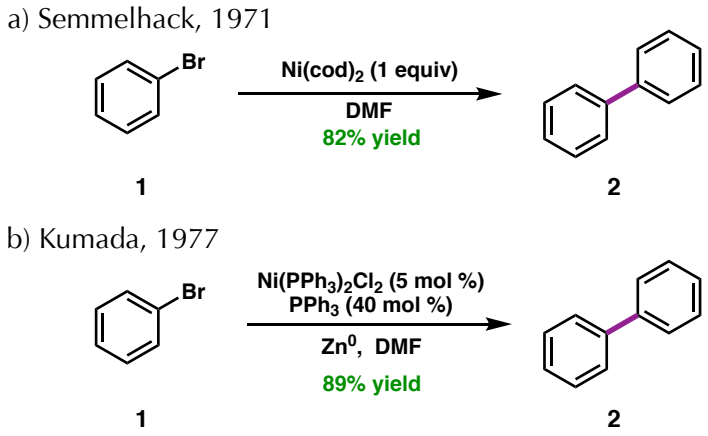
Due to these fundamental obstacles in reactivity, there has been much research into the alternative use of first-row transition metals for the enantioselective cross-coupling of alkyl substrates. In particular, the ability of nickel to engage in single electron processes makes it a desirable alternative to metals that proceed through polar, two electron mechanisms in the development of novel transformations.[4] Of these methods, reductive cross-coupling has recently emerged as a reliable and mild method to combine two electrophiles.

1.2 REDUCTIVE CROSS-COUPLING

1.2.1 Background and significance

In 1971, Semmelhack and coworkers reported the first reductive coupling of halide electrophiles using stoichiometric $Ni(cod)_2$ to form biaryl products (Scheme 1.2a).[6] Soon after, Kumada published the catalytic reductive homocoupling of aryl bromides using stoichiometric Zn as the chemical reductant (Scheme 1.2b).[7] Since then, renewed interest has led to the development of many catalytic reductive cross-couplings.

Scheme 1.2. *First reports of reductive homocoupling.*



Reductive cross-coupling offers many advantages over traditional redox-neutral transformations.[8–10] The mild nature of the reaction conditions allows for increased functional group tolerance and avoids racemization of newly formed stereogenic centers. Also, reductive coupling often utilizes halide electrophiles, from which many organometallic reagents are generated, rendering this approach more streamlined and efficient. Reductive cross-coupling is particularly advantageous for intramolecular coupling because it obviates the need to install both an electrophilic and organometallic functional group into the starting material.[11–14]

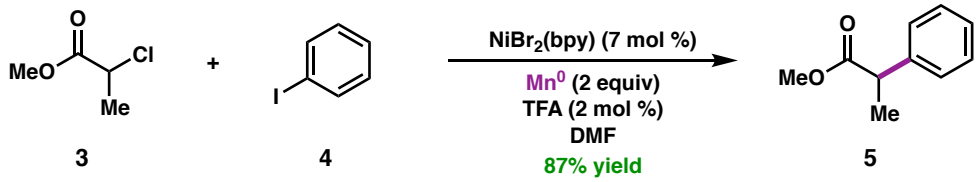
However, there are still many challenges associated with this new technology. The use of a stoichiometric amount of heterogeneous metal reductant renders these reactions sensitive to stirring and scale. Another major challenge in the development of reductive cross-coupling reactions is achieving cross-selectivity.[15,16] When employing two electrophilic coupling partners, there must be a way to differentiate them mechanistically to avoid undesired homocoupling. One strategy to address this is to leverage the hybridization of the electrophilic coupling partners. If differently-hybridized electrophiles react selectively with different oxidation states of Ni, then a careful sequencing of oxidative addition events could afford the desired cross-product, while minimizing the unwanted homo-coupled dimers. Optimization campaigns for these reactions require focus on this careful sequencing and the resultant product distribution.

1.2.2 Racemic $C(sp^3)$–$C(sp^2)$ bond formation

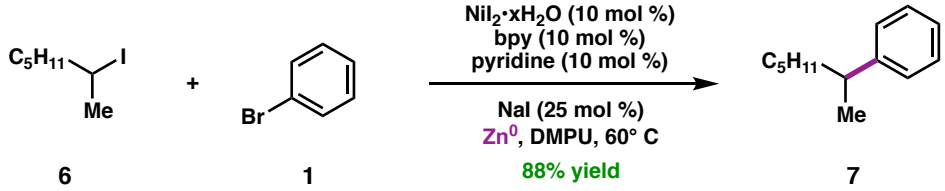
Since the first disclosure of Ni-mediated reductive homocoupling, there have been intensive efforts toward expanding this transformation to enable cross-selective couplings. In 2007, Durandetti and coworkers reported the first Ni-catalyzed reductive cross-coupling between α-chloroesters and aryl iodides with a chemical reductant (Scheme 1.3a).[17] Weix and coworkers followed that report in 2010 with the cross-coupling of *sec*-alkyl iodides and aryl halides, also utilizing a Ni(II) catalyst and bipyridine ligand (Scheme 1.3b).[18] Over the last 10 years, the labs of Weix,[15,19,20] Gong[21–27] and Molander[28,29] have greatly expanded the scope of this transformation, employing many different $C(sp^2)$ (aryl, alkenyl, acyl) and $C(sp^3)$ (activated and unactivated alkyl) coupling partners.

Scheme 1.3. *First reports of reductive cross-coupling using chemical reductants.*

a) Durandetti, 2007



b) Weix, 2010



1.3 STEREOCONVERGENT CROSS-ELECTROPHILE COUPLING

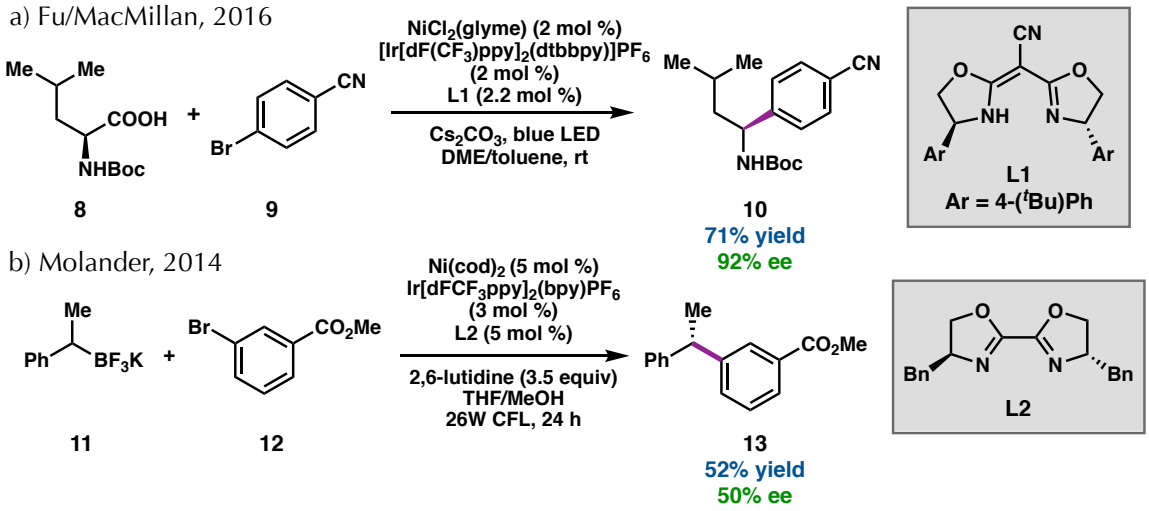
1.3.1 Strategic disconnection

Before the last decade, all examples of Ni-catalyzed asymmetric cross-coupling fell into the category of redox-neutral transformations. However, our group and others hypothesized that mechanisms active in stereoconvergent redox-neutral couplings could be leveraged toward the development of asymmetric reductive cross-couplings between two electrophilic partners. This effort requires control over the cross-selectivity of the reaction, as well as stereocontrol through an enantioconvergent transformation of the C(sp^3) electrophile.

Extensive methods development and mechanistic investigations by Fu and coworkers on the stereoconvergent cross-coupling of *sec*-alkyl electrophiles have demonstrated the feasibility of generating an alkyl radical through halide abstraction by a Ni(I) complex[30,31] and leveraging this species for asymmetric catalysis with a chiral ligand.[32] Beyond halide abstraction, there are several single electron processes that have been demonstrated to generate planar, prochiral radical intermediates that can be directed

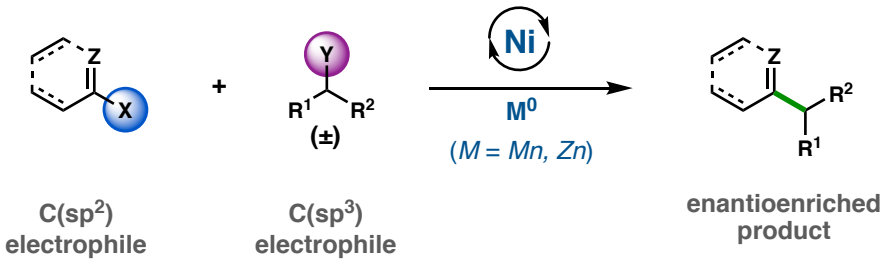
by chiral ligands for asymmetric catalysis. Decarboxylation and fragmentation of nucleophilic groups have been used for Ni-catalyzed photoredox dual catalysis (Molander,[33,34] Kozlowski,[35] Fu/MacMillan[36]) and reductive cross-electrophile (Reisman, Doyle[37]) stereoconvergent cross-couplings (Scheme 1.4).

Scheme 1.4. *Single electron chemistry in Ni-catalyzed cross-coupling.*



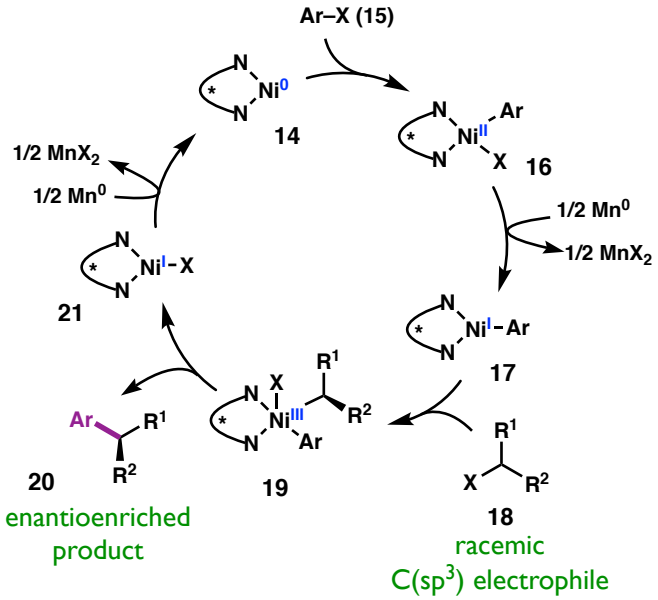
In order to achieve optimal cross-selectivity and enantiocontrol in reductive cross-couplings, our lab pairs C(sp^3) and C(sp^2)-hybridized electrophilic coupling partners for stereoconvergent reductive cross-coupling reaction development (Scheme 1.5). One of the advantages of a stereoconvergent approach is that after a single enantioselective preparation of a chiral ligand, many diverse enantioenriched product scaffolds can be readily accessed from racemic coupling partners. In a stereospecific approach, an enantioenriched coupling partner must be prepared beforehand for each corresponding desired product. However, it should be noted that achiral ligands are more often commercially available, and stereospecific reaction conditions can be easily adapted for diastereoselective transformations.[13,38–41]

Scheme 1.5. *General concept for stereoconvergent reductive cross-couplings.*



1.3.2 Mechanistic hypotheses

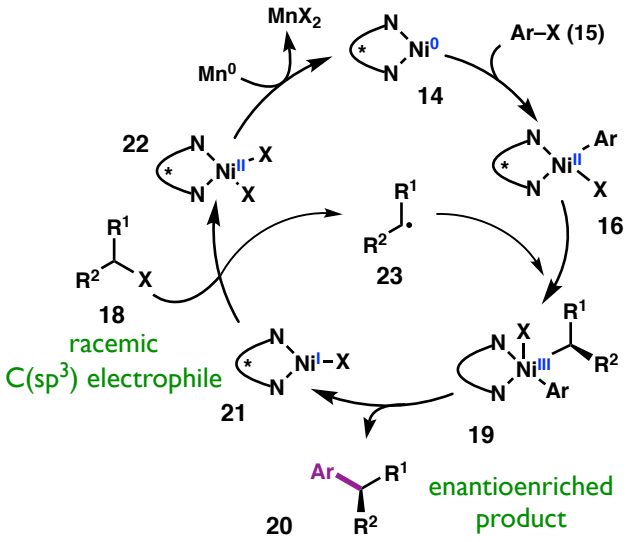
Figure 1.1. *Proposed sequential reduction mechanism.*



Mechanistic investigations into reductive cross-couplings have been conducted by several labs and can be primarily summarized by two related mechanistic hypotheses: a sequential reduction mechanism and a radical chain mechanism (Figure 1.1).[15,42,43] In a sequential reduction mechanism, we predict that the C(sp^2) electrophile undergoes concerted oxidative addition to Ni(0) species **14** to afford Ni(II)-aryl complex **16** (an aryl halide is shown as the C(sp^2) electrophile for clarity), which is then reduced by Mn^0 to a Ni(I)-aryl complex (**17**) (Figure 1.1).[44] **17** can then effect radical abstraction from

racemic *sec*-alkyl electrophile **18** to generate a prochiral radical, which undergoes radical addition with the metal center to give a Ni(III) intermediate (**19**).[30,31,45–47] Subsequent reductive elimination produces enantioenriched product **20** and a Ni(I)-halide complex (**21**), which can be reduced by Mn^0 to regenerate the Ni(0) catalyst and close the catalytic cycle.

Figure 1.2. *Proposed radical chain reaction mechanism.*



Our second mechanistic hypothesis involves a radical chain process (Figure 1.2). The $C(sp^2)$ electrophile undergoes oxidative addition to Ni(0) complex **14**, as before. This Ni(II) intermediate **16** then combines with a free *sec*-alkyl radical (**23**) to give Ni(III) complex **19**, which reductively eliminates to give enantioenriched product **20** and the Ni(I)-halide complex **21**. The resulting Ni(I)-halide complex can abstract a halide from the $C(sp^3)$ electrophile to generate long-lived *sec*-alkyl radical **23**.[48] The Ni(II)-dihalide (**22**) formed can be reduced by Mn^0 to regenerate the Ni(0) catalyst (**14**) and close the cycle.

The major difference between the sequential reduction and radical chain mechanism is the lifetime of the benzylic radical generated by halide abstraction, which is either short-lived and reacts via a radical-rebound process (sequential reduction mechanism), or long-lived and achieves cage escape (radical chain reaction mechanism). Mechanistic and computational data supports each mechanism in different systems, suggesting that the mechanism of Ni-catalyzed reductive cross-couplings may vary with different substrates, ligands, and reaction conditions. We can also imagine the two cycles working simultaneously for radicals of intermediate half-life. In these reactions, the enantiodetermining step could be radical combination with a Ni(II) complex to form the thermodynamically-preferred diastereomer of Ni(III), followed by facile reductive elimination. However, if radical combination to form a Ni(III) species is reversible, then reductive elimination through a Curtin-Hammett-type mechanism may be the enantiodetermining step.[35]

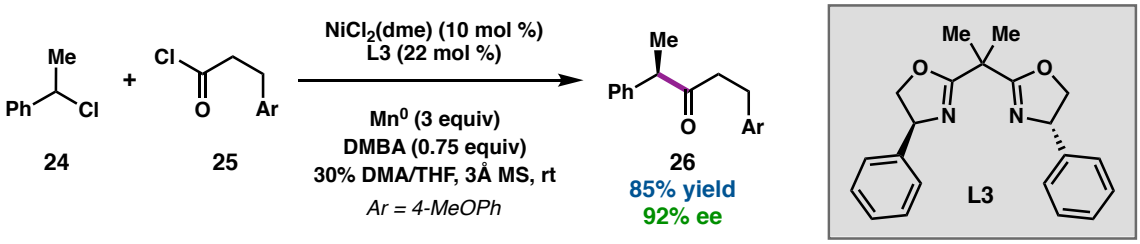
1.3.3 Stereoconvergent $C(sp^3)$–$C(sp^2)$ bond formation

With these general principles for cross-selectivity and enantioselectivity in mind, our lab aims to develop a number of general and highly selective Ni-catalyzed stereoconvergent reductive cross-coupling reactions. The first report of a Ni-catalyzed stereoconvergent reductive cross-coupling was published by our lab in 2013 (Scheme 1.6).[49] This report described the asymmetric cross-coupling of racemic benzyl chlorides and acyl chlorides using Mn^0 as a stoichiometric reductant, a Ni(II) catalyst, and a chiral bis(oxazoline) ligand. The mixed solvent system of DMA and THF provided the optimal balance of reactivity and selectivity; the highest ee's were observed in low yield in THF, while DMA provided higher conversion, though increased homocoupling. Importantly,

we found that the addition of dimethylbenzoic acid (DMBA) suppressed homocoupling of the C(sp^3) electrophile. While good functional group tolerance was observed for both coupling partners, we found that *o*-substituted benzyl chlorides were poor substrates, providing the products in low yield and ee.

Scheme 1.6. *First report of asymmetric reductive cross-coupling.*

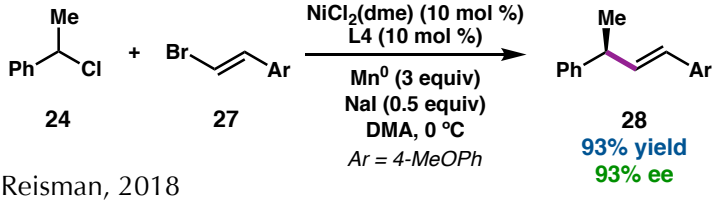
Reisman, 2013



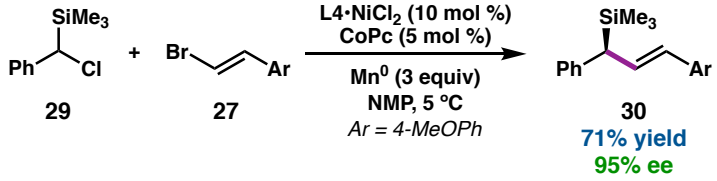
In 2014, we expanded the scope of the C(sp^2) coupling partner in the transformation to alkenyl bromides (Scheme 1.7a).[50] In DMA at 0 ºC, we identified chiral bis(oxazoline) **L4** as the optimal ligand for the reaction, giving the enantioenriched products bearing allylic stereogenic centers in excellent enantiomeric excess. We determined NaI to be an important additive in the reaction, improving the yield of **28** and decreasing the formation of the dibenzyl homodimer. NaI is known to enhance the reactivity in reductive cross-couplings, either through acceleration of electron transfer between Mn and Ni, or by *in situ* formation of iodide electrophiles.[51] In 2018, we were able to expand the scope of the benzyl chloride coupling partner to benzylic silanes,[52] extremely bulky electrophiles that required the addition of catalytic cobalt phthalocyanine (CoPc) to facilitate radical generation (Scheme 1.7b).[53]

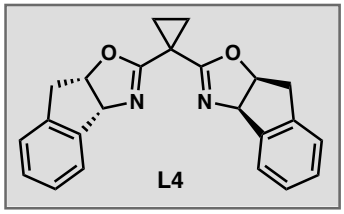
***Scheme 1.7**. Asymmetric reductive cross-coupling with alkenyl bromides.*

a) Reisman, 2014



b) Reisman, 2018

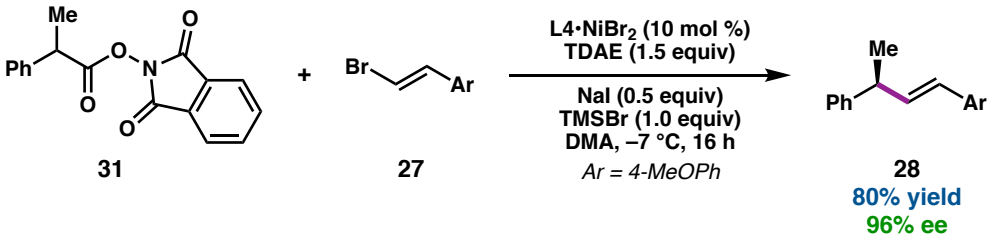




In 2017, we reported the use of a decarboxylative mechanism to generate a benzylic radical using *N*-hydroxyphthalimide (NHP) esters[54] for use in the asymmetric cross-coupling with alkenyl bromides (Scheme 1.8).[55] Interestingly, the organic reductant TDAE[56] was optimal in this reaction, with Mn^0 and Zn^0 providing the product in significantly lower yield. Intriguingly, we observed significant amounts of (*E*)-1-(2-chlorovinyl)-4-methoxybenzene when using a chloride-containing precatalyst or TMSCl as an additive, presumably due to a Ni-catalyzed halide exchange process.[57,58] This alkenyl chloride was inert in the cross-coupling reaction, and it was necessary to eliminate any source of chloride in the reaction to improve the yield.

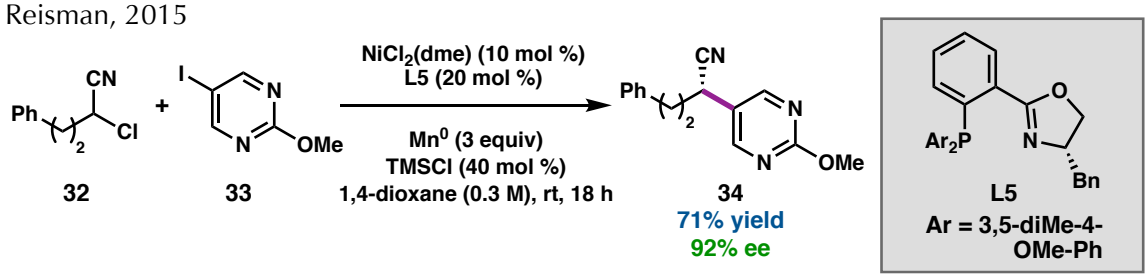
***Scheme 1.8**. Asymmetric reductive decarboxylative cross-coupling.*

Reisman, 2017 (Chapter 4)



While we had early success with benzyl chlorides as the C(sp^3) coupling partner, variation of the C(sp^3) electrophile has proven challenging and required the use of chiral ligands outside of the bis(oxazoline) family. In 2015, we published the Ni-catalyzed asymmetric reductive cross-coupling of α-chloronitriles and (hetero)aryl iodides (Scheme 1.9).[59] This reaction required a PHOX ligand and provided the highest yields and ee's of product in 1,4-dioxane with TMSCl as an additive, which has been proposed to activate the surface of the Mn.[15,60]

Scheme 1.9. *Asymmetric reductive cross-coupling with α-chloronitriles.*



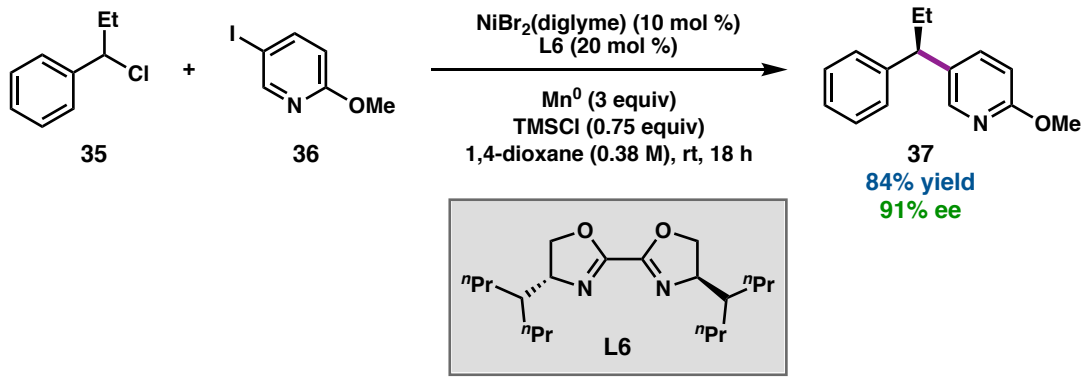
Interestingly, the asymmetric reductive cross-coupling of benzyl chlorides with aryl iodides proved to require significantly different reaction conditions from the corresponding reactions with alkenyl bromides, but similar conditions for the coupling of α-chloronitriles (Scheme 1.10a). This cross-coupling to access enantioenriched 1,1-diarylalkanes performed optimally in 1,4-dioxane with a novel bi(oxazoline) ligand bearing long alkyl chain substituents (**L6**).[61]

Invoking a similar stereoconvergent mechanism, Doyle and Sigman concurrently published the enantioselective reductive cross-coupling of racemic styrenyl aziridines with aryl iodides using **L6** developed by our lab (Scheme 1.10b).[37] Multivariate analysis of the effect of chiral bi(oxazoline) ligands on the reaction revealed ligand polarizability

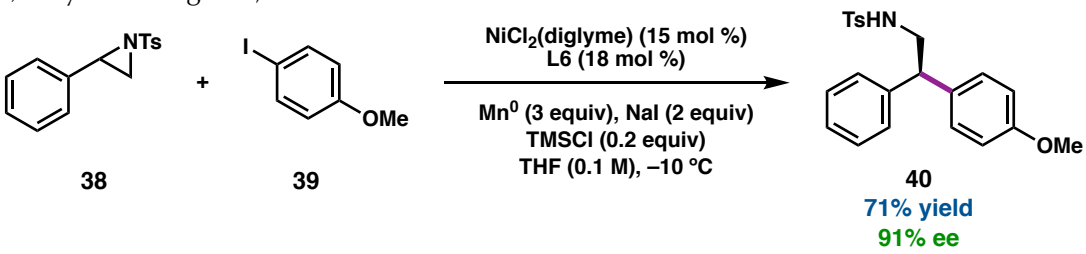
influences the enantioselectivity, suggesting the presence of noncovalent interactions, such as dispersion forces or CH–π interactions.

Scheme 1.10. *Asymmetric reductive cross-coupling with a novel BiOX ligand.*

a) Reisman, 2017 (Chapter 2)



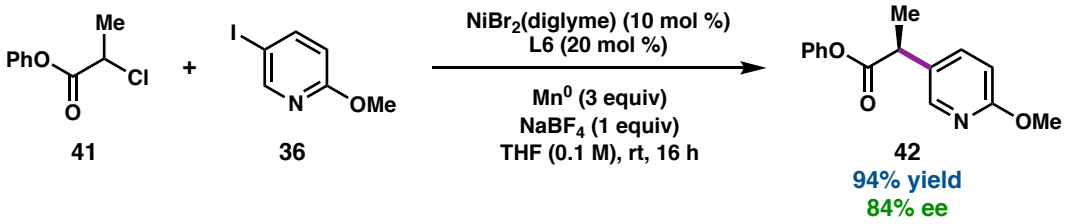
b) Doyle and Sigman, 2017



In an ongoing effort in our lab to expand the scope of the C(sp^3) coupling partner in this reaction, our lab is currently working on the development of the cross-coupling between α-chloroester substrates and (hetero)aryl iodides (Scheme 1.11). Toward this effort, we are collaborating with the Doyle and Sigman groups to identify the important features of the chiral bi(oxazoline) ligand in this system and direct the synthesis of novel alkyl-substituted bi(oxazoline) ligands.

Scheme 1.11. *Asymmetric reductive cross-coupling with α -chloroesters.*

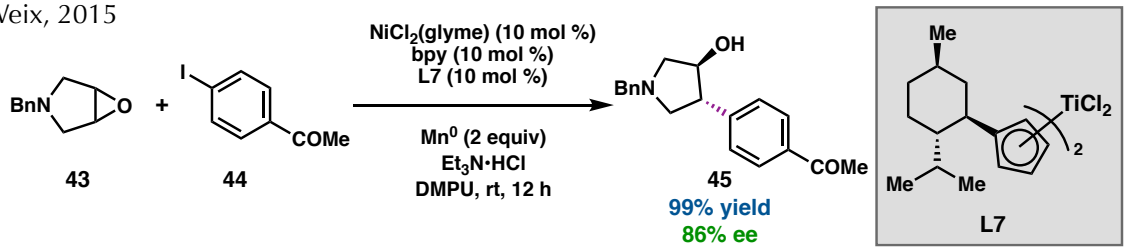
Reisman, unpublished (Chapter 3)



Outside of our lab's contributions to this field, the Weix group has published the enantioselective cross-coupling of *meso*-epoxides with aryl halides (Scheme 1.12).[42] In this transformation, a titanocene catalyst generates a chiral β-titanoxy carbon radical from the *meso*-epoxide, which can be intercepted by an Ar–Ni(II)bpy complex for reductive elimination from a Ni(III) species to give enantioenriched product.

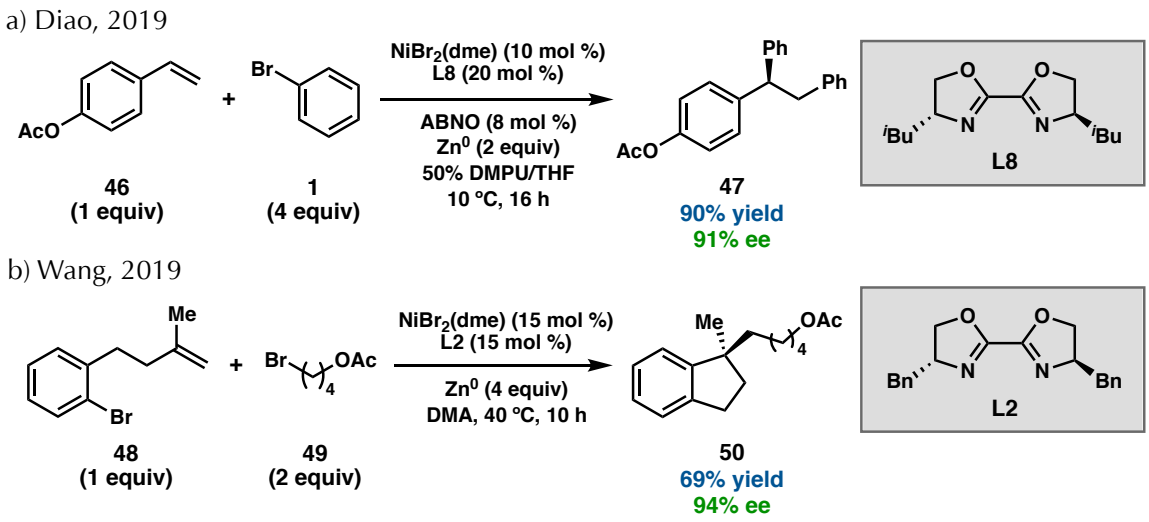
Scheme 1.12. *Reductive cross-coupling with Ni/Ti dual-catalysis.*

Weix, 2015



Recently, two reports of enantioselective Ni-catalyzed reductive cross-couplings with olefins have been reported. In 2019, Diao and coworkers disclosed the asymmetric reductive dicarbofunctionalization of styrenes utiliting a bi(oxazoline) ligand (**L8**) and Zn^0 as a stoichiometric reductant (Scheme 1.13a).[62] In this diarylation, a Ni(I)–aryl species is proposed to undergo radical addition across the olefin substrate to generate a Ni(I)–alkyl species. This complex can then undergo oxidative addition with a second equivalent of aryl halide and subsequent reductive elimination to form the enantioenriched product.

Scheme 1.13. *Enantioselective reductive cross-coupling with olefins.*



Soon after, Wang and coworkers published the asymmetric reductive arylalkylation of unactivated olefins to form enantioenriched benzene-fused cyclic products bearing quarternary centers using a chiral bi(oxazoline) ligand (**L2**) (Scheme 1.13b).[63] In this two-component coupling, an Ni(II)–aryl species can be reduced to Ni(I)–aryl, which could undergo 5-*exo*-trig cyclization with the pendent alkene. The resultant Ni(I)–alkyl species can then undergo oxidative addition with the alkyl bromide coupling partner to eventually furnish the final product.

1.4 CONCLUSION

While transition metal-catalyzed cross-coupling reactions remain an invaluable tool for the synthesis of natural products and other small molecules, the use of first-row transition metals has enabled the expansion of this methodology to allow for cross-electrophile couplings. The use of nickel in these reductive cross-couplings has enabled the development of mild reaction conditions that proceed to give the desired products in good yields with high levels of enantioselectivity. In particular, nickel-catalyzed

reductive cross-couplings have alleviated some of the challenges inherent to traditional, redox-neutral cross-coupling strategies. We anticipate that this field will continue to grow and revolutionize the way that carbon–carbon bonds are constructed in a stereoselective manner.

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Chapter 2

Nickel-Catalyzed Asymmetric Reductive Cross-Coupling to Access 1,1-Diarylalkanes[◊]

2.1 INTRODUCTION

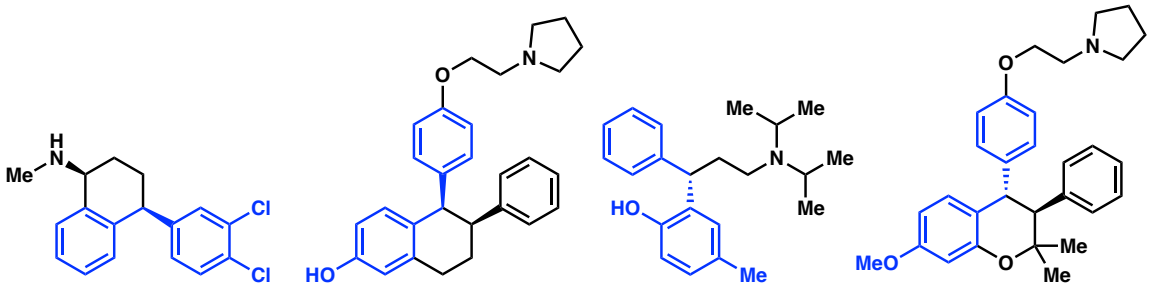
2.1.1 Background and significance

1,1-Diarylalkanes are a common pharmacophore, present in biologically active natural products as well as marketed drugs for a diverse range of applications (Figure 2.1). These products are active against cancer, osteoporosis, smallpox, tuberculosis, and insomnia and are present in natural products and pharmaceutical agents such as sertraline (**51**), lasofoxifene (**52**), and tolterodine (**53**), among others.[1–5] As such, methods for the enantioselective preparation of diarylalkanes have become a proving ground in

◊ Portions of this chapter have been reproduced from published studies (see reference **37**) and the supporting information found therein. The research presented in this chapter was completed in collaboration with Dr. Nathaniel Kadunce, a former graduate student in the Reisman group. Preliminary investigations discussed herein were conducted by Dr. Alan Cherney, a former graduate student in the Reisman lab.

asymmetric catalysis, with methods to afford these products being reported by many synthetic laboratories.[6–9] Enantioenriched 1,1-diarylalkanes have been prepared via Ni-catalyzed stereospecific,[1,10–15] as well as stereoconvergent,[16–18] cross-couplings. However, conditions for their preparation via asymmetric reductive cross-coupling remain elusive.

Figure 2.1. *Examples of bioactive chiral 1,1-diarylalkanes.*



Sertraline (51)
serotonin reuptake inhibitor used as antidepressant and anti-anxiety

Lasofoxifene (52)
non-steroidal selective estrogen receptor modulator (SERM) used for treatment of osteoporosis

Tolterodine (53)
antimuscarinic drug used to treat urinary incontinence

Ormeloxifene (54)
SERM, non-hormonal, non-steroidal oral contraceptive

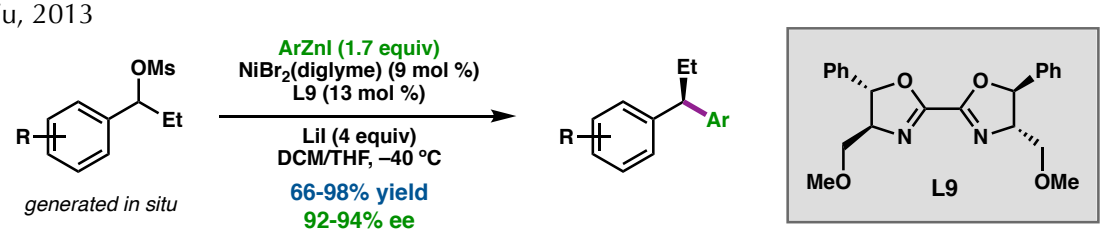
2.1.2 Previous Ni-catalyzed cross-coupling strategies

Due to the ubiquity of the 1,1-diarylalkane motif in bioactive molecules, significant effort has been devoted to the enantioselective synthesis of this substructure. As a complementary approach to methods such as asymmetric hydrogenation[19,20] and conjugate addition,[21–24] Ni-catalyzed stereospecific and stereoconvergent cross-coupling reactions have been developed (Scheme 2.1). In these strategies, redox-neutral couplings of a C(sp^3) benzyl electrophile and a nucleophilic organometallic C(sp^2) aryl partner are employed. For example, in 2013, Fu and coworkers reported the enantioselective Negishi coupling of benzyl mesylates with aryl zinc halides to furnish 1,1-diarylalkane products in good yields and high enantioselectivity.[16] In 2014, Jarvo and coworkers reported the

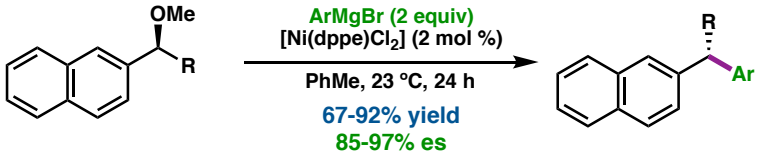
stereospecific Kumada-type coupling of enantioenriched benzyl ethers with aryl Grignard reagents using an achiral ligand.[10]

Scheme 2.1. *Examples of asymmetric cross-coupling strategies to access 1,1-diarylalkanes.*

a) Fu, 2013



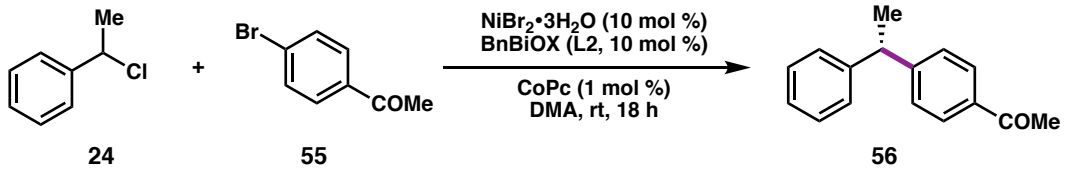
b) Jarvo, 2014



Efforts to prepare enantioenriched 1,1-diarylalkanes via asymmetric reductive coupling or Ni/Ir synergistic catalysis have proved challenging. In 2015, Weix reported a reductive cross-electrophile coupling between primary mesylates and aryl bromides;[25] this report contained a single enantioselective coupling of (1-chloroethyl)benzene (**24**) with 4-bromoacetophenone (**55**) using BnBiOX (**L2**) as the chiral ligand, which proceeded in both modest yield and ee (Scheme 2.2). Similarly, Molander reported that the coupling of (1-phenylethyl) potassium trifluoroborate (**11**) with methyl 3-bromobenzoate (**12**) proceeds in 50% ee, and coupling of more electron deficient arenes occurs with lower enantioselectivity.[18,26]

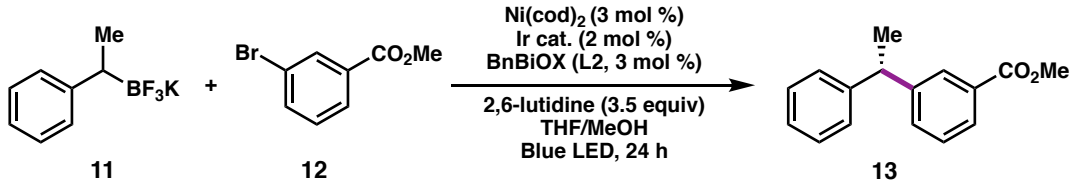
***Scheme 2.2**. Attempts to access enantioenriched 1,1-diarylalkanes.*

a) Weix, 2015



24 **55** **56**
41% yield
43% ee

b) Molander, 2014



11 **12** **13**
52% yield
50% ee

2.2 REACTION DEVELOPMENT

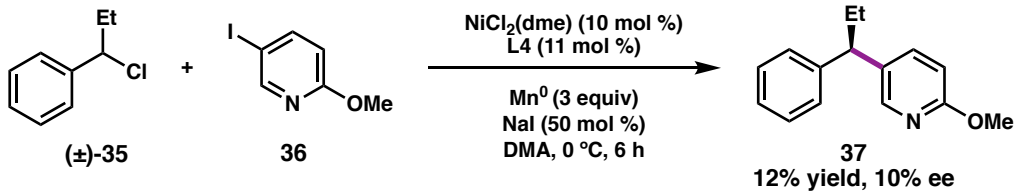
2.2.1 Application of previously developed conditions

Based on our previously disclosed research,[27,28] we hypothesized that we could develop conditions for the Ni-catalyzed asymmetric reductive cross-coupling of benzyl chlorides and aryl iodides to access heterocycle-containing products. However, a challenge in the development of such enantioselective reactions is that as one changes electrophile class (e.g. from alkenyl halides to aryl halides), or as one alters the ligand, the product yield and ee can decrease dramatically. Consistent with the challenges encountered by others, submission of a mixture of (1-chloropropyl)benzene (**35**) and 5-iodo-2-methoxypyridine (**36**) to the optimal conditions identified for the Ni-catalyzed asymmetric reductive cross-coupling of benzyl chlorides with alkenyl bromides provided **37** in only 12% yield and 10% ee (Scheme 2.3a). Similarly, use of the conditions developed for the reductive cross-coupling of heteroaryl iodides with α-chloronitriles failed to deliver detectable amounts of **37** (Scheme 2.3b). Despite these discouraging

preliminary results, we decided to focus our initial optimization efforts on reaction conditions similar to the precedent set by our lab for related transformations.

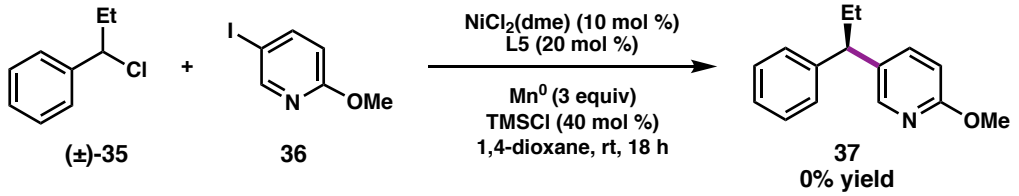
Scheme 2.3. *Application of previously developed cross-coupling conditions.*

a) Conditions for cross-coupling of benzyl chlorides with alkenyl bromides



(±)-35 36 37
12% yield, 10% ee

b) Conditions for cross-coupling of chloronitriles with heteroaryl iodides

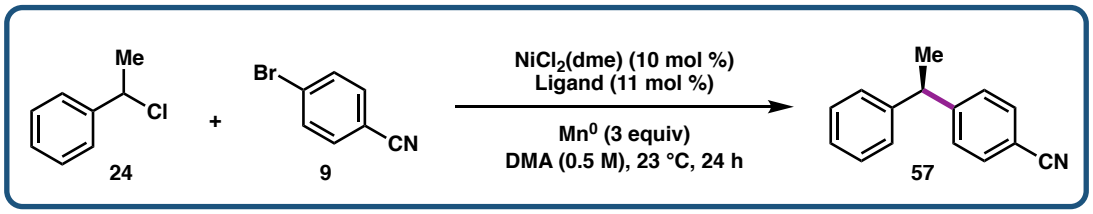


(±)-35 36 37
0% yield

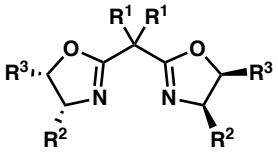
2.2.2 Initial optimization

We initiated studies focusing on the cross-coupling between benzyl chlorides and aryl iodides by screening a variety of chiral bidentate ligands under both sets of conditions shown in Scheme 2.3. Employing $NiCl_2$(dme) as the Ni source and Mn^0 as the superstoichiometric reductant, we investigated the cross-coupling of **9** and **24** in DMA at room temperature (Table 2.1). We observed poor chemoselectivity across a variety of chiral ligand classes, with the formation of homocoupled dimers of both coupling partners. Modest enantioselectivities were observed with both BOX (**L3**, 49% ee) and BiOX (**L2**, 33% ee) ligand scaffolds, suggesting promise for this enantioconvergent transformation. However, further optimization employing bis(oxazoline) ligand **L3** was unsuccessful. Other ligand scaffolds such as PyBOX (**L27)**, CyanoBOX (**L1)**, PyOx (**L28)**, QuinOx (**L29)**, and PHOX (**L30)** did not induce higher enantioselectivity.

***Table 2.1**. Initial ligand investigation with 4-bromobenzonitrile (**9**).*

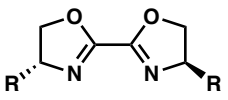


Bis(oxazoline) Ligand Scaffold



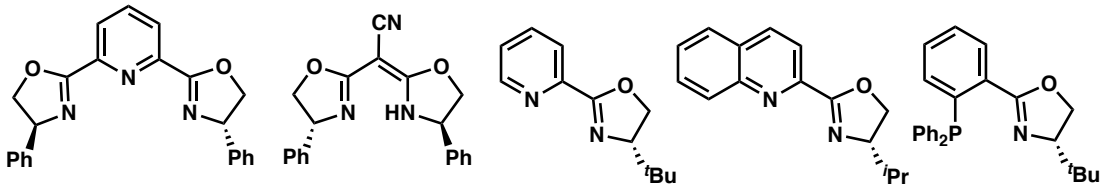
Ligand	R^1	R^2	R^3	% ee 57
L10	Me	^{i}Pr	H	19
L11	Me	^{t}Bu	H	0
L12	Me	Bn	H	1
L3	Me	Ph	H	49
L13	Me	Ph	Ph	14
L14	H	Ph	Ph	11
L15	H	Ph	H	1
L16	H	^{t}Bu	H	1
L17	H	indanyl		1
L18	Me	indanyl		3
L4	-CH_2CH_2-	indanyl		7

Bi(oxazoline) Ligand Scaffold



Ligand	R	% ee 57
L19	^{i}Pr	24
L20	^{t}Bu	8
L2	Bn	33
L21	Ph	1
L22	Cy	25
L23	^{s}Bu	23
L24	$CHPh_2$	3
L25	CH_2(1-naph)	20
L26	CH_2(2-naph)	29

Other Ligand Scaffolds



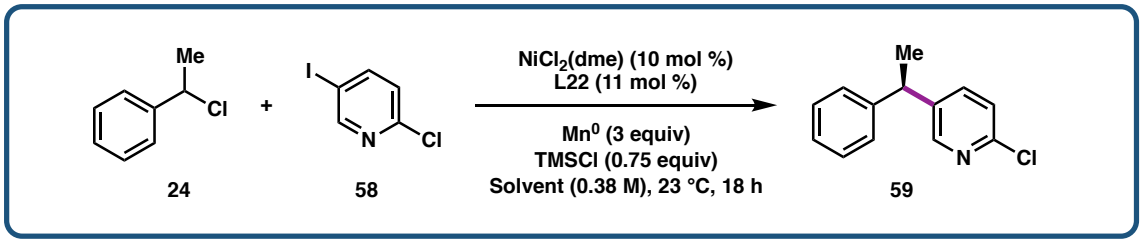
L27 3% ee | L1 39% ee | L28 14% ee | L29 8% ee | L30 12% ee

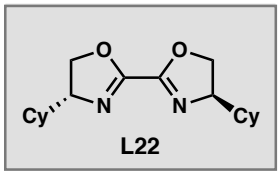
2.2.3 Application of 1,4-dioxane/TMSCl conditions

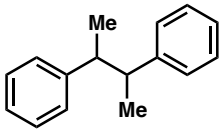
Given these results, we moved away from conditions similar to those shown in Scheme 2.3a in DMA, and focused instead on different chiral ligand classes in 1,4-dioxane with TMSCl as an activator, conditions more closely related to the cross-

coupling of heteroaryl iodides with α-chloronitriles (Scheme 2.3b). We explored several chiral bidentate ligand classes under these conditions and discovered that performing the reaction with bi(oxazoline) ligand **L22** in 1,4-dioxane with TMSCl as an activator[29,30] produced **59** in 74% yield and 74% ee (Table 2.2). Studying now the cross-coupling of (1-chloroethyl)benzene (**24**) and 2-chloro-5-iodopyridine (**58**), a solvent screen with **L22** confirmed 1,4-dioxane to give the highest level of yield and enantioselectivity with a clean reaction profile, delivering diminished amounts of homocoupled side product **60** (Table 2.2). Polar solvents, such as DMA and DMPU, gave product **59** in low to moderate enantioselectivity (Table 2.2).

Table 2.2. *Solvent investigation with bi(oxazoline) ligand (**L22**).*







60
rac and meso

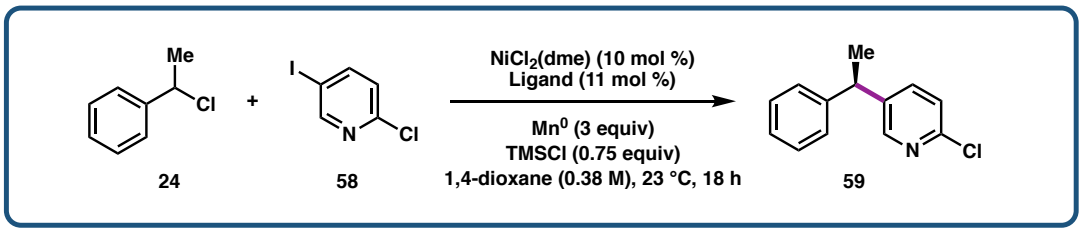
with 11 mol % CyBiOX (L22):

Solvent	Yield HC 60 (%)	Yield 59 (%)	ee 59 (%)
DMA	72	25	31
DMPU	33	60	49
THF	51	49	43
DME	41	54	55
MeCN	47	44	6
DCM	50	10	44
MeOH	77	13	73
1,4-Dioxane	26	74	74

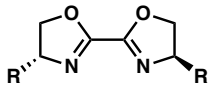
Encouraged by these results, we explored several more bi(oxazoline) ligand scaffolds bearing both aryl and alkyl substituents at room temperature (Table 2.3).[31] We

were surprised to observe that ligands bearing aryl substituents, such as phenyl (**L2**, **L21**, and **L24**) or naphthal (**L25** and **L26**), afforded poor yields of product in moderate ee. We note that BnBiOX (**L2**), the ligand used by used by Weix and Molander, perform poorly under these conditions. However, branched-alkyl ligands bearing groups such as cyclohexyl (**L22**), *sec*-butyl (**L23**), and *iso*-butyl (**L8**), furnished **59** in significantly improved yields and enantioselectivities over the aryl-substituted BiOX ligands (Table 2.3).

Table 2.3. *Bi(oxazoline) ligand investigation.*



Bi(oxazoline) Ligand Scaffold



Ligand	R	Yield HC 60 (%)	Yield 59 (%)	ee 59 (%)
L21	Ph	0	0	–
L24	$CHPh_2$	43	37	67
L25	CH_2-1-Nap	3	17	44
L26	CH_2-2-Nap	5	32	50

Ligand	R	Yield HC 60 (%)	Yield 59 (%)	ee 59 (%)
L2	Bn	54	39	44
L22	Cy	32	68	69
L23	*s*-Bu	0	35	76
L8	*i*-Bu	6	68	56

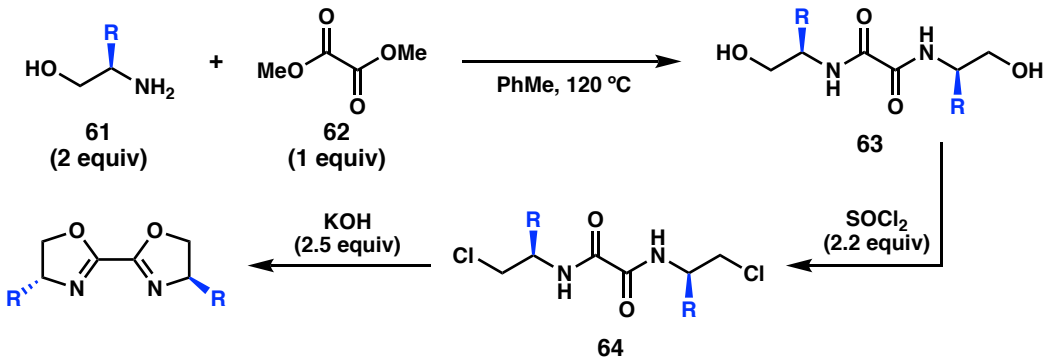
Our lab has had success employing chiral BOX ligands in the cross-coupling of various C(sp^3) electrophiles with alkenyl halides,[32–34] but these results, as well as results described in **Chapter 3**, suggest that while BOX ligands are optimal for an alkenyl halide coupling partner, BiOX ligands provide the best reactivity for the cross-coupling of aryl halides. Comparison of the BOX and BiOX structures reveals that the larger bite angle of the BiOX ligands directs the substituents on the oxazoline ring farther away from the

metal center, reducing steric encumbrance at the reaction site, creating a larger chiral cavity that can tolerate the larger steric profile of aryl halides (than a disubstituted *E*-alkenyl halide). While this larger bite angle might be responsible for increased reactivity, it is possible that the more distal substituents are less effective at transferring chiral information, resulting in moderate ee's.

2.2.4 Novel bi(oxazoline) ligand synthesis

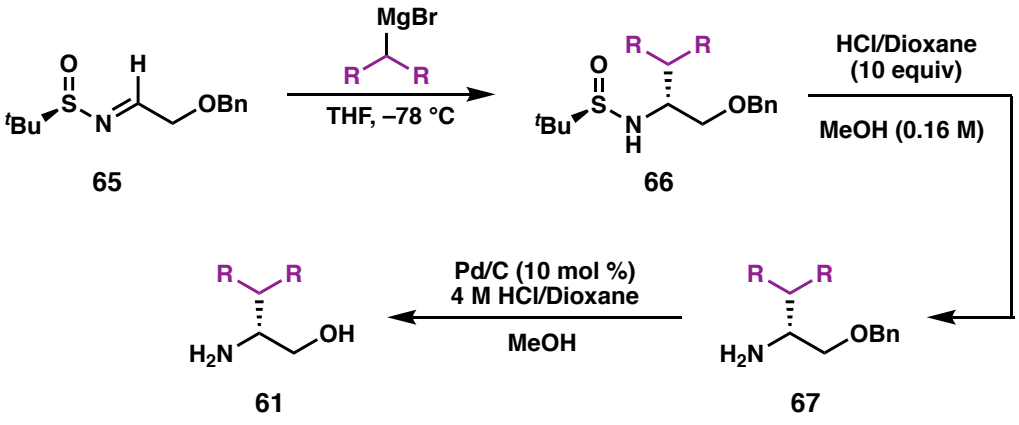
Given these exciting results, we aimed to incorporate several more alkyl groups onto the bi(oxazoline) scaffold in the hopes of improving the enantioselectivity of the cross-coupling. The usual method to synthesize bi(oxazoline) ligands is a four step sequence from the commercially available amino acid, or three steps from the amino alcohol (Scheme 2.4). However, we did not want to limit ourselves to alkyl groups found on commercially available amino acids and so developed an asymmetric route to introduce novel alkyl groups onto an amino alcohol backbone using Ellman's chiral auxiliary to perform diastereoselective Grignard additions of *sec*-alkyl reagents to access protected 1,2-amino alcohols.[35]

Scheme 2.4. *Bi(oxazoline) ligand synthesis from chiral amino alcohol.*



Known chiral sulfinimine **65** was synthesized in three steps from commercially available cis-2-butene-1,4-diol. From this compound, we were able to successfully perform several Grignard additions to introduce both cyclic and acyclic alkyl groups, such as cyclopentyl, cycloheptyl, 3-pentyl, and 4-heptyl, with high diastereoselectivity (Scheme 2.5). Cleavage of the chiral auxiliary with HCl/dioxane could be performed smoothly to furnish amine **67**. Finally, deprotection of the benzyl group was performed through a hydrogenolysis with Pd/C to access the desired amino alcohol (**61**), which could then taken through the three-step BiOX synthesis (Scheme 2.4). Condensation with dimethyl oxalate to give the polar diamide **63**, chlorination with thionyl chloride, and subsequent base-mediated cyclization provided the novel alkyl-substituted bi(oxazoline) ligands. Unfortunately, this route requires nine steps in the longest linear sequence and an early divergence point. Efforts to design a shorter synthesis of these ligands are ongoing in our laboratory.

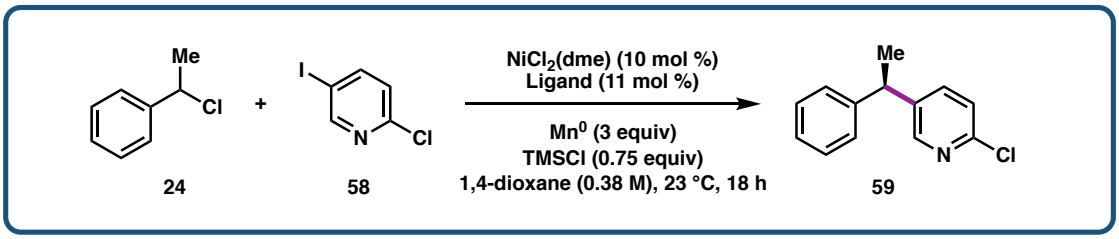
Scheme 2.5. *Synthesis of novel enantioenriched alkyl-substituted amino alcohols.*



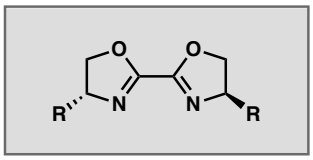
Gratifyingly, these novel branched-alkyl ligands performed well in the asymmetric reductive cross-coupling reaction, improving upon the yield and ee observed with CyBiOX (**L22**). CyPentyl (**L31**), CyHeptyl (**L32**), and 3-PentylBiOX (**L33**) gave

the desired product **59** in 75% ee and good yields with suppressed homocoupled product **60** (Table 2.4). We were pleased to observe that 4-HeptylBiOX (**L6**) provided the desired diarylalkane **59** in 81% yield with 80% ee, the highest yield and ee observed to that point.

Table 2.4. *Novel bi(oxazoline) ligand investigation.*



Bi(oxazoline) Ligand Scaffold



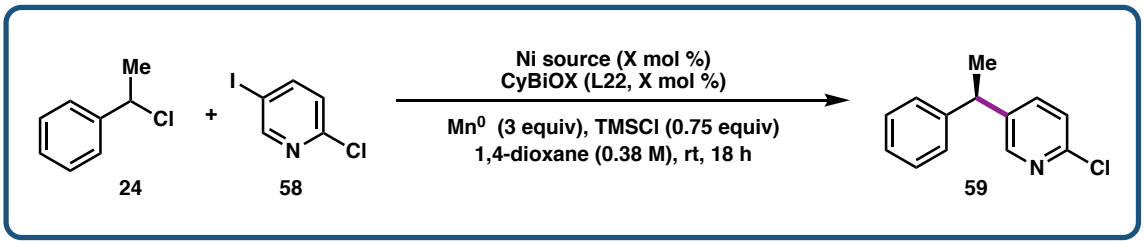
Ligand	R	Yield HC 60 (%)	Yield 59 (%)	ee 59 (%)
L31	Cy-Pentyl	15	81	75
L22	Cy-Hexyl	32	68	69
L32	Cy-Heptyl	28	72	75
L33	3-Pentyl	23	65	75
L6	4-Heptyl	16	81	80

2.2.5 Evaluation of remaining reaction parameters

With these promising ligand results in hand, we turned our attention to the optimization of the remaining reaction parameters. Due to the lengthy synthesis required to access noncommercial amino acid-derived branched ligands (such as **L6**), we chose to perform further reaction optimization using the analogous ligand, CyBiOX (**L22**), which can be readily accessed in four steps from the commercially available amino acid. A screen of Ni precatalysts revealed a significant improvement in yield and selectivity upon switching to $NiBr_2$(diglyme), the first time that a Ni source other than $NiCl_2$(dme) has been optimal in our hands (Table 2.5). Employing this Ni salt, we conducted a screen of metal/ligand ratios and catalyst loading. This survey revealed a remarkable tolerance for

variability in these parameters. However a catalyst loading of 10 mol % with a 2:1 ligand:metal ratio gave the most reproducible results and was chosen as the standard condition for further studies.

Table 2.5. *Evaluation of Ni sources and catalyst loadings.*



with 11 mol % CyBiOX (LXX):

Ni Source (10 mol %)	Yield HC 60 (%)	Yield 59 (%)	ee 59 (%)
$NiCl_2$(dme)	30	69	69
$Ni(OAc)_2 \cdot 4H_2O$	0	22	72
$Ni(BF_4)_2 \cdot 6H_2O$	5	0	-
$Ni(acac)_2$	30	69	69
$NiBr_2$(dme)	25	74	72
$NiBr_2$(diglyme)	20	81	74

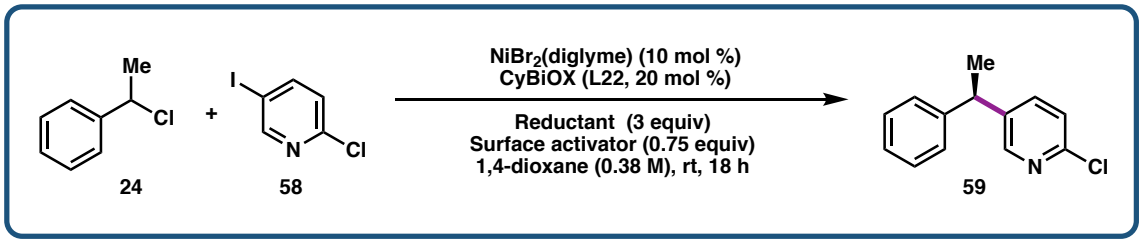
with $NiBr_2$(diglyme):

% Ni	M:L	Yield HC 60 (%)	Yield 59 (%)	ee 59 (%)
5%	1:1	15	71	75
5%	1:2	22	77	75
10%	1:1	16	68	74
10%	1:1.5	23	77	72
10%	1:2	25	75	74
10%	1:3	27	78	74
15%	1:1	29	71	71
15%	1:2	29	71	74

In a survey of reductants, Mn^0 emerged as the most efficacious in this series, with Zn^0 giving lower yield and selectivity (Table 2.6). The difference in reactivity may be attributed to the difference in reduction potential between the metals. However, the change in enantioselectivity is more difficult to rationalize. It is possible that the reductants favor different mechanisms, or one can imagine that the stoichiometric Lewis-acidic salt byproducts may exert significant influence over the course of the reaction. Poor yields were achieved employing the soluble organic reductant TDAE (entry 5),[36]

with lower selectivity. Other activating reagents in place of TMSCl, such as TFA or TfOH (entries 8 and 10),[29,30] resulted in minimal product formation with no enantioinduction, while TMSOTf and 4 M HCl/dioxane delivered **59** with moderate enantioselectivity, albeit in low yields (Table 2.6, entries 9 and 11).

Table 2.6. *Evaluation of reductants and activating reagents.*



with TMSCl:

Entry	Reductant	Yield (%)	ee (%)
1	Mn^0	83	72
2	Zn^0	20	30
3	Zn^0 + $MgCl_2$	6	0
4	In^0	0	-
5	TDAE	6	31
6	TDAE (-TMSCl)	6	43

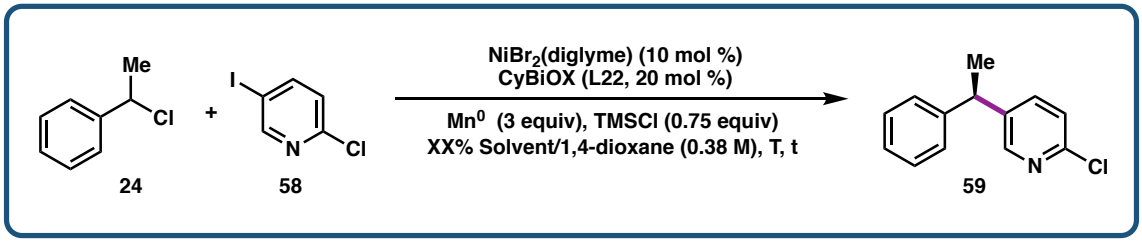
with Mn^0:

Entry	Surface activator	Yield (%)	ee (%)
7	TMSCl	74	74
8	TFA	3	0
9	TMSOTf	18	64
10	TfOH	1	3
11	4 M HCl/dioxane	4	60

Next, we screened the reaction at various temperatures. We observed a decrease in yield and ee with increasing temperature (Table 2.7, entries 2 and 3), with increased formation of homocoupled product **60**. Since the freezing point of 1,4-dioxane is 12 °C, it was necessary to employ a co-solvent to run the reaction at low temperature. DCM and DMA proved to be competent co-solvents at room temperature, and allowed us to explore the reactivity at 10 °C and 0 °C (Table 2.7). Regardless of the identity or ratio of co-solvent, the yield of **59** was greatly diminished at lower temperatures, even with allowing the reaction to run longer for 24 hours, with little benefit to the enantioinduction. The ee of **59** increased slightly to 76% with 30% DCM at both 10 °C and 0 °C, while only

resulting in approximately 25% yield of **59** (Table 2.7, entries 4 and 6). Increasing the ratio of DCM to 50% resulted in an increase in yield, but a decrease in ee (Table 2.7, entry 5). Finally, the use of DMA as a co-solvent resulted in a decrease in both yield and ee of **59** (Table 2.7, entry 7).

***Table 2.7**. Temperature investigation.*



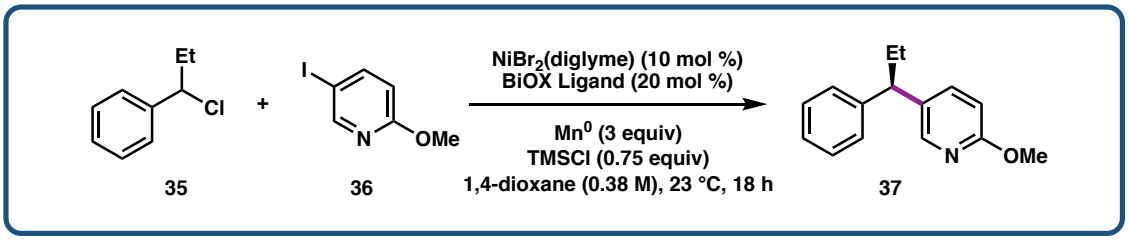
Entry	Solvent	T (°C)	t (h)	% Yield 59	% ee 59
1	–	23	18	74	70
2	–	40	18	65	62
3	–	60	18	56	55
4	30% DCM	10	24	23	76
5	50% DCM	10	24	52	55
6	30% DCM	0	24	27	78
7	30% DMA	0	24	28	53

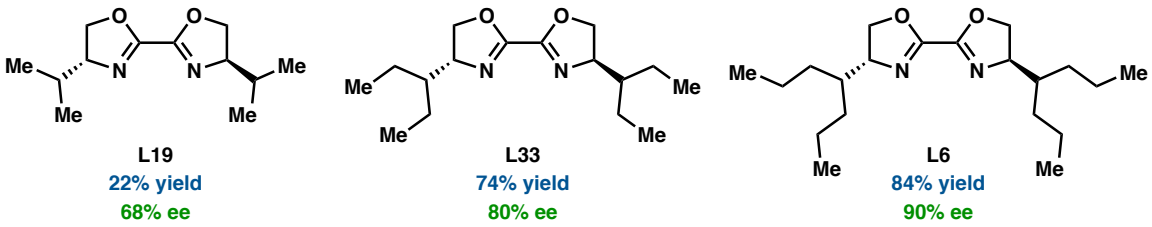
2.2.6 Investigation into sec-alkyl ligand effect

With optimized conditions in hand, we returned to the ligand effect on this reaction. The novel sec-alkyl bi(oxazoline) ligands that we synthesized provided a markedly improved effect on both the reactivity and selectivity of this reaction, suppressing homocoupling to favor the formation of the desired product, while also achieving the highest levels of enantioselectivity among various chiral ligand classes. Looking specifically at the cross-coupling of (1-chloropropyl)benzene (**35**) with 5-iodo-2-methoxypyridine (**36**) across a series of these acyclic *sec*-alkyl substituted BiOX ligands produces a fascinating trend in reactivity and selectivity (Table 2.8). As the

length of the alkyl chains increase incrementally by two methylenes from ^{i}Pr (**L19**) to 3-pentyl (**L33**) to 4-heptyl (**L6**), the enantioselectivity increases by 10% with each homologation. We observe a significant increase in yield from **L19** (22% yield) to **L33** (74% yield), and then a further 10% increase with **L6** (84% yield).

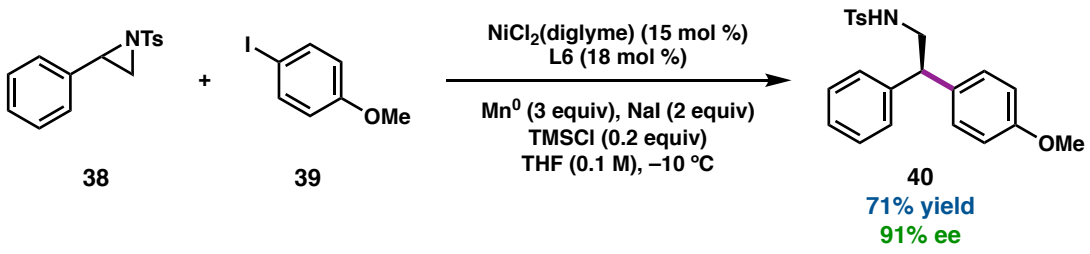
Table 2.8. *Sec-alkyl bi(oxazoline) ligand investigation.*





The effect of these longer alkyl groups on both the chemoselectivity and yield remains unclear at this stage. The hydrophobic alkyl chains could provide flexible, steric blocking, resulting in increased enantioinduction. During the development of this transformation,[37] the Doyle group at Princeton University reached out to us to request material of **L6**. Interestingly, **L6** was the optimal ligand in their stereoconvergent cross-coupling of racemic aziridines and aryl iodides (Scheme 2.6).[38]

Scheme 2.6. *Sigman and Doyle's reductive cross-coupling of racemic aziridines.*

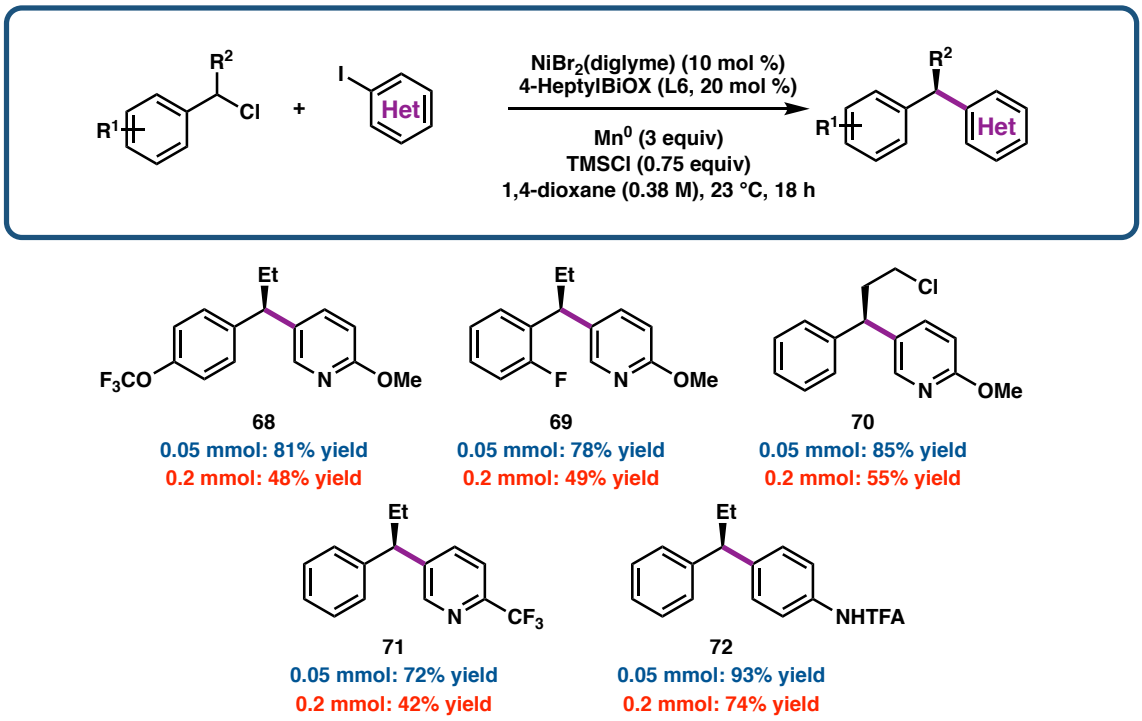


A collaboration between the Doyle and Sigman group at the University of Utah revealed parameters such as the minimum width of the ligand substituent (steric effects), electronic character, and polarizability of the ligand (presence of non-covalent interactions) were primarily responsible for the enantioselectivity of the reaction (Scheme 2.6). Our lab is currently collaborating with the Sigman group to apply their multivariate analysis tools to determine if the alkyl-substituents are inducing non-covalent interactions with the coupling partners, significantly altering the ligand bite angles, or influencing some other mechanistic parameter to produce the observed effects in our transformations.

2.2.7 Reproducibility issues on scale

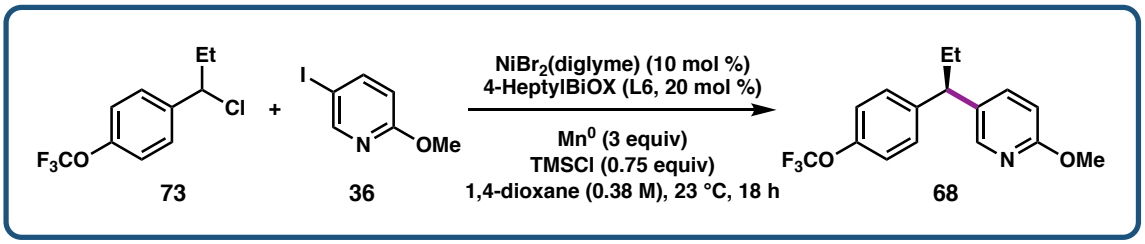
Finally, this reaction proved extremely sensitive to an increase in scale. When we increased the scale of the reaction from 0.05 mmol to 0.2 mmol, we observed a significant decrease in yield of the desired product, independent of reaction time, with no change in ee (Table 2.9). After exploring several variables, such as purity of substrates and reagents, vessel and stir bar size, stirring speed, concentration, catalyst loading, and activation of the reductant on 0.2 mmol scale, we discovered the method in which the reagents were added was essential to the success of the reaction.

***Table 2.9**. Reproducibility and conversion issues on 0.2 mmol scale.*



The reaction setup consists of the addition of solid reagents, including the Ni catalyst, ligand, and reductant, which are then dissolved in 1,4-dioxane. After several minutes of stirring, the aryl iodide (**36**), benzyl chloride (**73**), and lastly TMSCl are added. On scale, it was necessary to stir the reaction for 20 min before addition of the coupling partners and the activating reagent in order for the reaction to go to full conversion (Table 2.10, entries 2 and 3). Addition of the TMSCl before either coupling partner leads to reaction failure (Table 2.10, entry 4). Interestingly, this mirrors the setup of multiple reactions on the 0.05 mmol screening scale, which inherently requires more time for setup.

Table 2.10. *Effect of pre-stir of reagents on 0.2 mmol scale.*



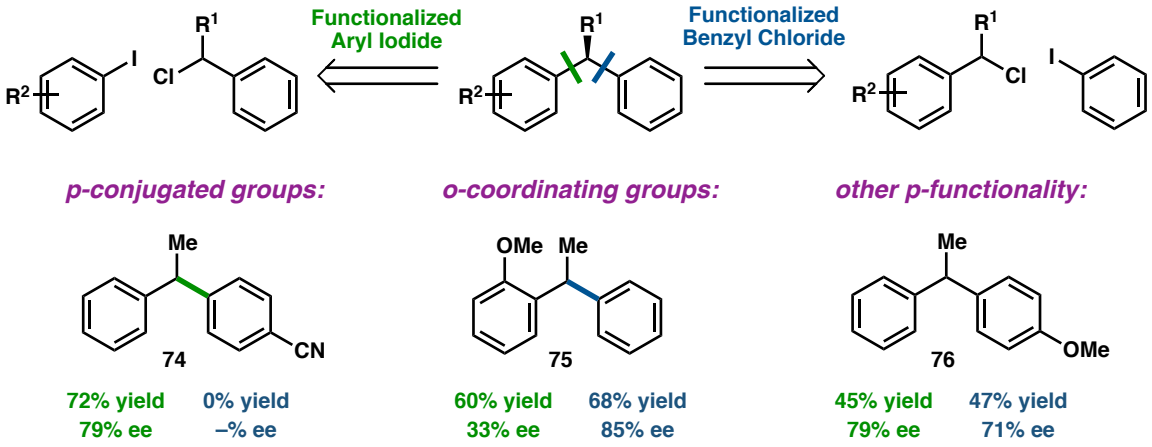
Entry	Pre-stir Conditions	% Yield 68	% ee 68
1	Control: Stir 2 min, then 36, 73, TMSCl	48	87
2	Stir 20 min, then 36, 73, TMSCl	76	87
3	36, stir 20 min, then 73, TMSCl	80	87
4	36, TMSCl, stir 20 min, then 73	0	—

2.3 SUBSTRATE SCOPE

Before investigating a wide range of substrates, we first sought to assess the strategy of functional group incorporation to access these pseudosymmetric products. That is, informed substrate selection in which substitution is introduced on either the benzyl component or the aryl partner depending on reaction tolerance, may allow us to prepare a variety of differently substituted mono-substituted 1,1-diarylalkane. This disconnection versatility is an advantage of this cross-coupling methodology, allowing us to leverage the ideal disconnection of the target. Therefore, we initially explored a short series of mono-substituted electrophiles to compare the functional group performance on each coupling partner. Benzyl chlorides bearing conjugated electron-withdrawing groups such as nitriles (**74**) underwent rampant decomposition, affording low yields and messy reaction profiles (Figure 2.2). Fortunately, these groups were well tolerated when incorporated via the aryl iodide partner. The opposite trend was observed with *ortho*-coordinating groups, such as *o*-methoxy **75**. These groups afforded good yields and high

ee's when installed on the benzyl chloride partner, but gave low enantioselectivity from the corresponding aryl iodide. Non-conjugated groups at the *para*- and *meta*-positions gave only slight and unpredictable variability between the two partners, as observed in the *para*-methoxy containing substrate **76**. Finally, non-coordinating *ortho*-substituents, such as methyl, performed poorly on both substrates (not shown).

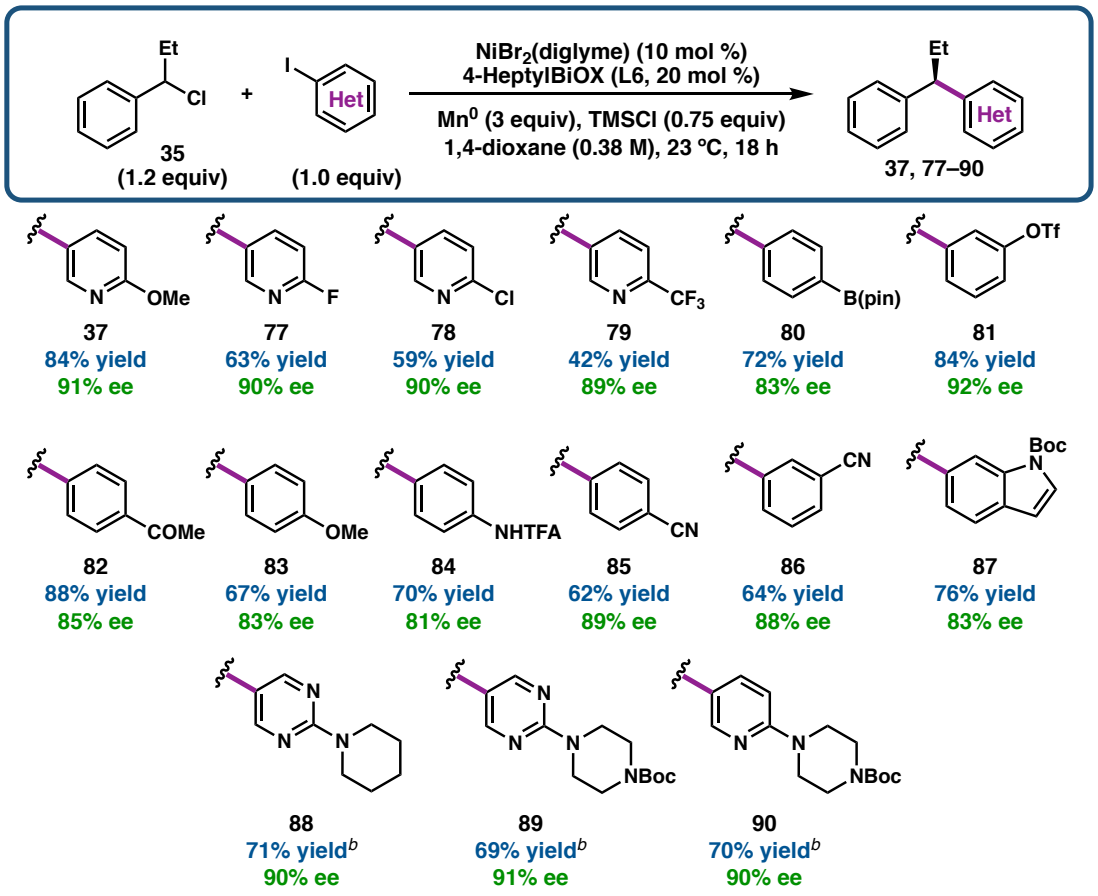
Figure 2.2. *Strategic disconnection of pseudosymmetric 1,1-diarylalkanes.*



With preliminary knowledge of substrate-dependent functional group tolerance, we evaluated the substrate scope of the aryl iodide coupling partner (Table 2.11). Pyridyl iodides bearing substitution at the 2-position couple smoothly (**37**, **77–79**, **90**), as do pyrimidines (**88**, **89**) and indoles (**87**). Non-heteroaryl iodides bearing either electron-rich (**83, 84**) or electron-poor (**81**, **82**, **85–86**) functional groups couple smoothly, although slightly lower ee is observed with more electron-rich arenes. It is notable that acidic protons are tolerated (**84**); no protodehalogenated byproducts observed. The cross-coupling is orthogonal to aryl boronates and triflates, affording **80** and **81** in excellent yields and providing handles for further derivatization. Interestingly, use of the

corresponding aryl bromide, instead of **36**, delivered **37** in only slightly reduced yield and comparable ee (72% yield, 89% ee).

Table 2.11. *Scope of (hetero)aryl iodides.*[a]

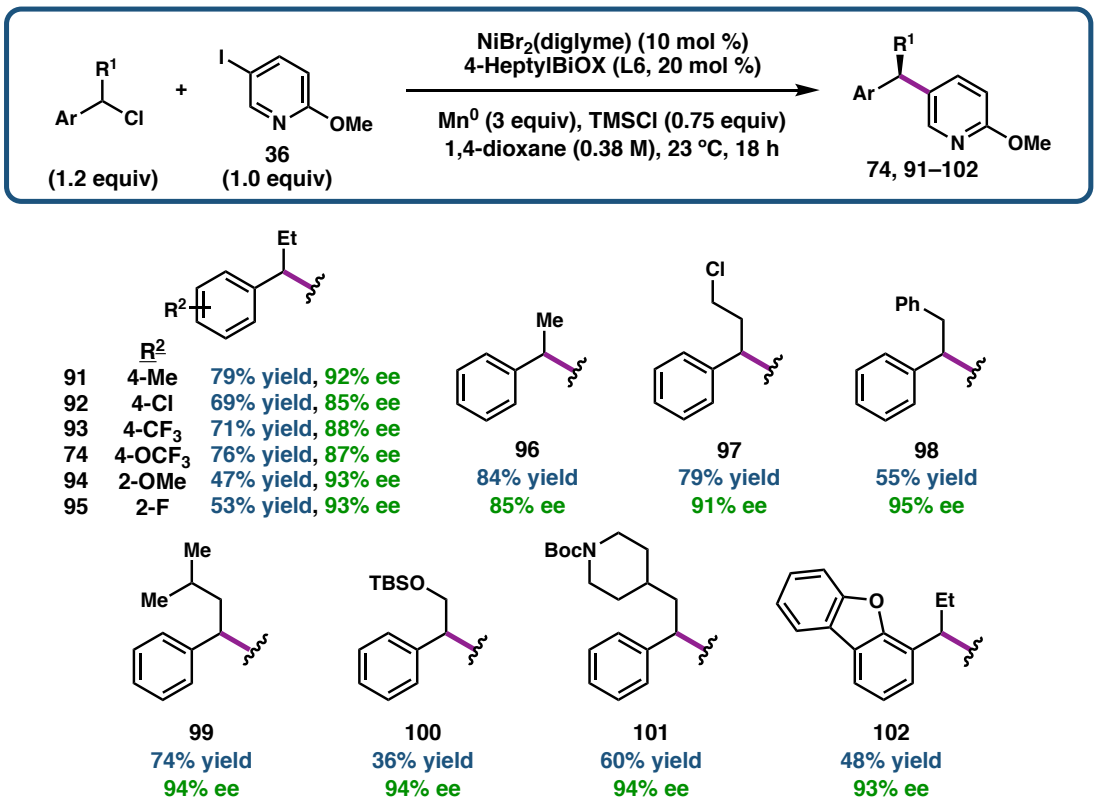


[a] Isolated yields, reactions conducted on 0.2 mmol scale under an N_2 atmosphere in a glovebox. % ee determined by SFC using a chiral stationary phase. [b] 2.4 equiv of 35 is used.

Next, we turned our attention to the scope of the benzyl chloride coupling partners (Table 2.12). Substrates with either electron-donating or -withdrawing substituents at the *para* position couple in comparable yields and enantioselectivity (**91**–**95**). In addition, *o*-substitution with either methoxy (**94**) or fluorine (**95**) is tolerated, although the products are formed in decreased yields. Substituents of varying steric encumbrance can be incorporated at the α-position of the benzyl halide (**96**–**101**). Of particular interest, good

chemoselectivity is observed for coupling of the benzyl chloride in preference to the primary chloride (**97**). *N*-Boc-piperidine (**101**) and dibenzofuran (**102**) groups are also tolerated, providing the products in serviceable yields and excellent ee. Employing the corresponding benzyl bromide in place of **35** increased formation of dibenzyl homocoupling product at the expense of **37** with slightly lower ee (8% yield, 81% ee).

Table 2.12. *Scope of benzyl chlorides.*[a]

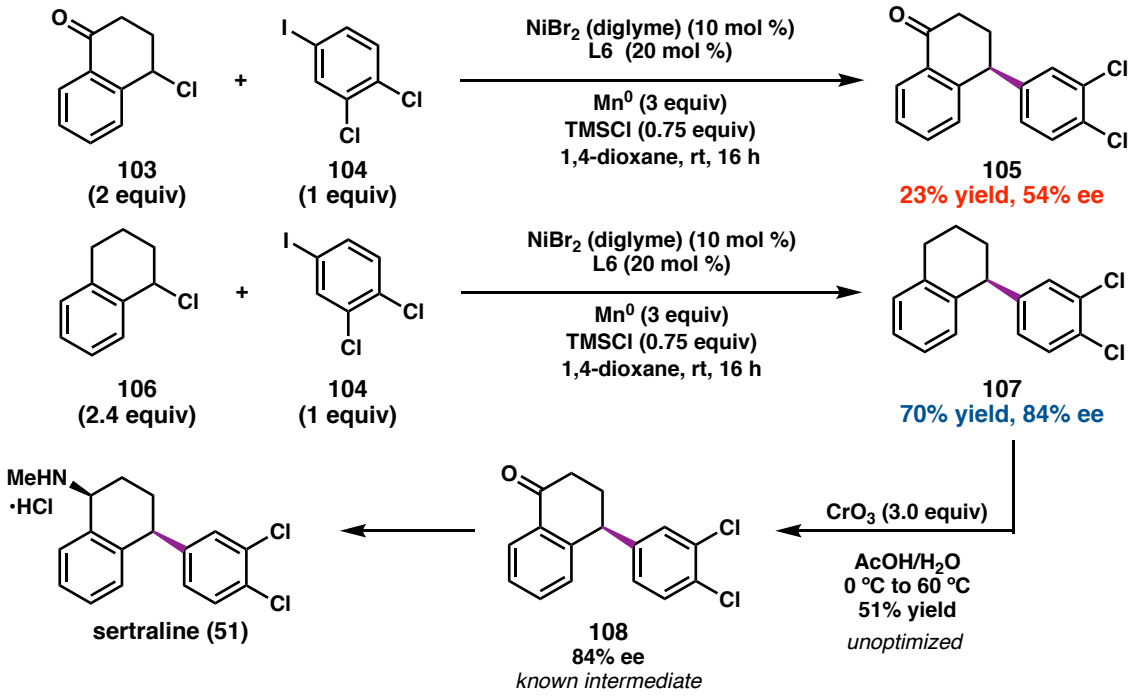


[a] Isolated yields, reactions conducted on 0.2 mmol scale under an N_2 atmosphere in a glovebox. % ee determined by SFC using a chiral stationary phase.

We were pleased to see the heterogeneous reaction performed well on a 2.0 mmol scale in a round bottom flask, producing pyridine **37** in 63% yield and 91% ee. To further demonstrate the potential synthetic utility of our method, we synthesized diarylalkane **107**, an intermediate in the synthesis of the commercial anti-depressant sertraline (Scheme 2.7).[39] Unfortunately, the cross-coupling of tetralone **103** with commercially

available iodobenzene **104** under our standard reaction conditions afforded product **105** in only 23% yield and 54% ee. This poor yield could be due to the instability of the benzyl chloride coupling partner, which was prone to decomposition into the corresponding naphthol. Fortunately, cross-coupling of 1-chloro-1,2,3,4-tetrahydronaphthalene (**106**) with **104** provides chiral tetrahydronaphthalene **107** in 70% yield, and 84% ee. Subsequent benzylic oxidation of **107** using 3 equiv of CrO_3 in $AcOH/H_2O$ afforded tetralone **108** in 51% yield (unoptimized) with no erosion of ee.[40] This oxidation suffered from both poor conversion, as well as the formation of over-oxidized side products. Tetralone **108** is a known intermediate in the synthesis of sertraline.[41–44]

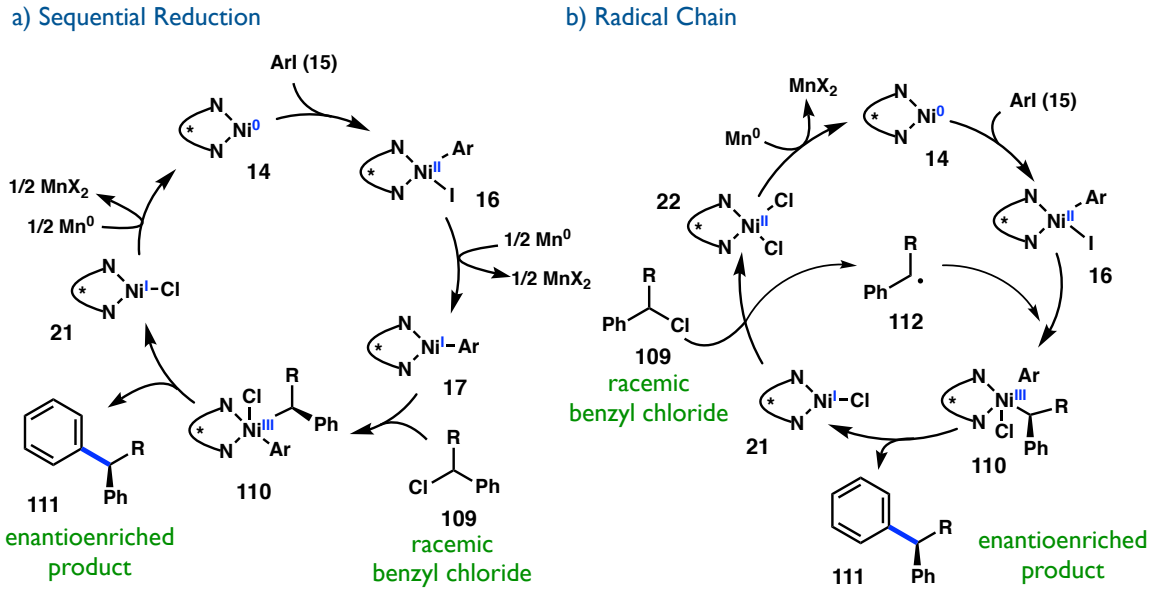
Scheme 2.7. *Synthesis of sertraline intermediate.*



2.4 MECHANISTIC STUDIES

Confident in the range and utility of the substrate scope, we next sought to probe the mechanism of this transformation. As described in **Chapter 1**, we hypothesize that asymmetric reductive cross-couplings of radical-stabilized C(sp^3) electrophiles may proceed through the intermediacy of prochiral radicals generated from a halide abstraction event. This can occur in either a sequential reduction mechanism, in which halide abstraction and radical addition occur rapidly in a radical rebound process (Figure 2.3a), or a radical chain reaction mechanism with a long-lived, cage escaped radical intermediate (Figure 2.3b).

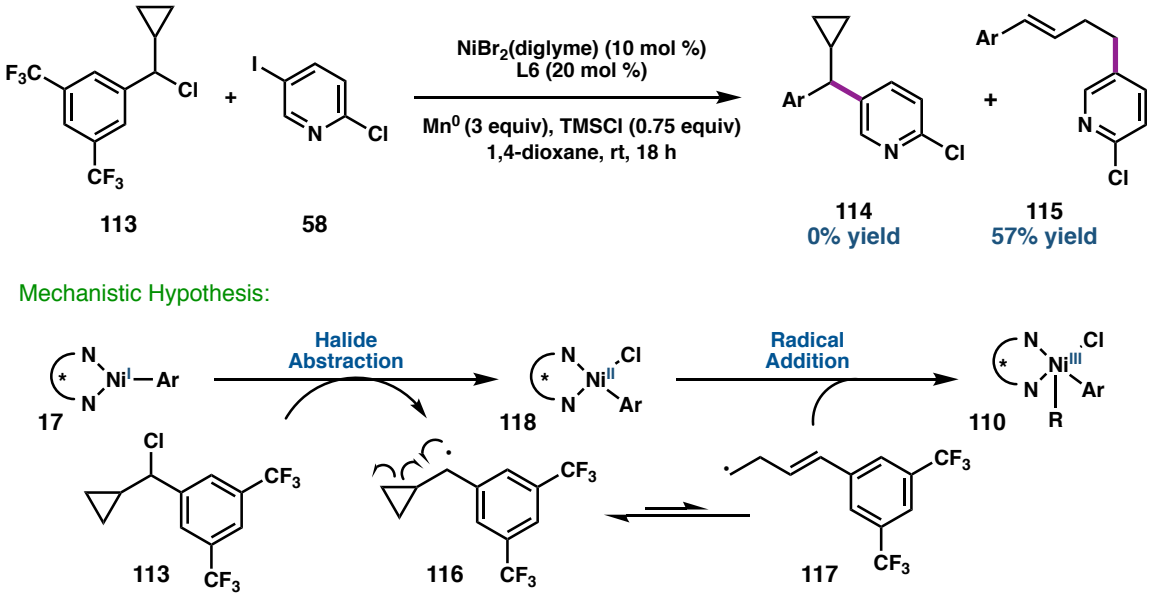
Figure 2.3. *Mechanistic hypotheses for the asymmetric reductive cross-coupling.*



In order to determine the presence and nature of benzylic radical intermediates in the reductive cross-coupling of benzyl chlorides and aryl halides, we conducted a series of mechanistic investigations. First, when cyclopropyl chloride **113** was subjected to the standard cross-coupling conditions, alkene **115** was obtained in 57% yield (Scheme 2.8).

We hypothesize that a cyclopropyl carbinyl radical (**116**) is generated from halide abstraction by Ni(I) species **17**. This benzylic radical can then reversibly open the cyclopropane to give a primary homoallylic radical,[45,46] which can be intercepted by Ni(II) species **118** to form Ni(III) **110**. Ideally, both **116** and **117** could add to the Ni(II) complex and a ratio of the unrearranged (**114**) and rearranged (**115**) products would form. Varying the Ni loading would then support one mechanistic hypothesis over the other depending on the behavior of the ratio of these products formed.[47] However, we were not able to observe the formation of **114**, likely due to steric interference of the cyclopropyl group, and thus cannot conclusively favor one mechanistic hypothesis. However, these findings are consistent with a mechanism that proceeds through a non-persistent alkyl radical, though we cannot rule out the possibility of a Ni-mediated cyclopropane opening pathway at this time.

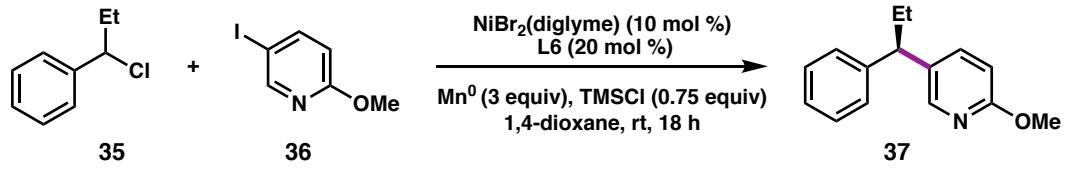
Scheme 2.8. *Radical clock studies.*



Next, the reaction was conducted in the presence of TEMPO, which has been used to trap carbon-centered radical species. However, no significant decrease in yield

was observed, and no TEMPO trapping adducts were detected (Scheme 2.9). A control experiment in which TEMPO was treated with Mn^0 and TMSCl in 1,4-dioxane indicated that TEMPO is stable under the reaction conditions, however we cannot rule out the possibility that reduction of TEMPO precludes trapping. Likewise, other known radical inhibitors, BHT and DHA, did not cause inhibition of the reaction at 50 mol % loading (Scheme 2.9). These findings suggest a non-persistent alkyl radical.

Scheme 2.9. *Radical inhibitor studies.*



35 36 37

Control: 84% yield, 90% ee
50 mol % BHT: 83% yield, 89% ee
50 mol % DHA: 78% yield, 88% ee
50 mol % TEMPO: 72% yield, 91% ee

Further studies of the mechanism are ongoing; it is unclear at this time whether the absolute stereochemistry is determined by addition to form a Ni(III) species or reductive elimination from Ni(III). Fu and coworkers have demonstrated that chiral Ni catalysts can promote stereoconvergent cross-couplings of racemic *sec*-alkyl electrophiles and organometallic reagents due to the stereoablative interaction of the *sec*-alkyl electrophile with Ni.[48–51] We can imagine that enantioinduction arises during either the oxidative addition of the C(sp^3) electrophile to generate the Ni(III) complex or, if oxidative addition is reversible, during reductive elimination.[18]

2.5 CONCLUSION

In conclusion, we have developed a Ni-catalyzed asymmetric reductive cross-coupling between (hetero)aryl iodides and benzyl chlorides. This transformation enables the synthesis of enantioenriched 1,1-diarylalkanes from simple organic halide starting materials. The reaction tolerates a wide range of functionality, including heterocyclic substrates. Key differences in the substrate scopes of the two partners highlight the advantage of this disconnection in synthetic planning, exploiting the pseudosymmetry of the products to select optimal coupling substrates. The success of this effort hinged on the development of a new chiral bi(oxazoline) ligand, 4-HeptylBiOX (**L6**), which provides 1,1-diarylalkanes with both improved yield and enantioselectivity relative to previously disclosed BiOX ligands.

2.6 EXPERIMENTAL SECTION

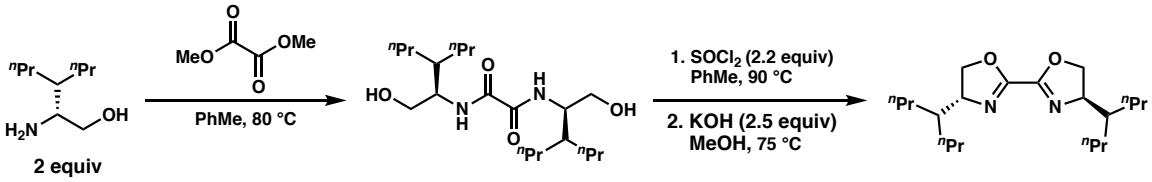
2.6.1 *Materials and Methods*

Unless otherwise stated, reactions were performed under a nitrogen atmosphere using freshly dried solvents. Methylene chloride (DCM), diethyl ether (Et_2O), tetrahydrofuran (THF), 1,4-dioxane and toluene (PhMe) were dried by passing through activated alumina columns. All other commercially obtained reagents were used as received unless specifically indicated. Aryl iodides were purchased from Sigma Aldrich, Combi-Blocks, or Astatech. Manganese powder (>99.9%) was purchased from Sigma Aldrich. $NiBr_2$(diglyme) was purchased from Strem. All reactions were monitored by thin-layer chromatography using EMD/Merck silica gel 60 F254 pre-coated plates (0.25 mm). Silica gel and basic alumina column chromatography was performed as described by Still et al. (W. C. Still, M. Kahn, A. Mitra, *J. Org. Chem*. **1978**, *43*, 2923.) using silica gel (particle size 0.032–0.063) purchased from Silicycle and aluminum oxide (activated, basic, Brockmann I, 58 Å pore size, powder) purchased from Sigma-Aldrich. ^1H and ^{13}C NMR were recorded on a Varian Inova 500 (at 500 MHz and 125 MHz respectively) or a Bruker Avance III HD with Prodigy cyroprobe (at 400 MHz and 101 MHz respectively). ^1H and ^{19}F NMR spectra were recorded on a Varian Inova 300 (at 300 MHz and 282 MHz, respectively). NMR data is reported relative to internal chloroform (^1H, δ = 7.26, ^{13}C, δ = 77.0) and C_6F_6 (^{19}F, δ = –164.9). Data for ^1H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicity and qualifier abbreviations are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm^{-1}). Analytical

SFC was performed with a Mettler SFC supercritical CO_2 analytical chromatography system with Chiralcel AD-H, OD-H, AS-H, OB-H, and IA columns (4.6 mm x 25 cm). SFC analysis performed at 100.0 bar and 40 ºC. HRMS were acquired using either an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI), atmospheric pressure chemical ionization (APCI), or mixed (MM) ionization mode. Low-temperature diffraction data (φ- and ω-scans) were collected on a Bruker AXS D8 VENTURE KAPPA diffractometer coupled to a PHOTON 100 CMOS detector or a PHOTON II CPAD detector with Cu-K_α radiation (λ = 1.54178 Å) from a $I_\mu S$ HB micro-focus sealed X-ray tube. All diffractometer manipulations, including data collection, integration, and scaling were carried out using the Bruker APEXII software. Absorption corrections were applied using SADABS. The structure was solved by intrinsic phasing using SHELXT and refined against F^2 on all data by full-matrix least squares with SHELXL-2014[3] using established refinement techniques. All non-hydrogen atoms were refined anisotropically. Unless otherwise noted, all hydrogen atoms were included into the model at geometrically calculated positions and refined using a riding model. The isotropic displacement parameters of all hydrogen atoms were fixed to 1.2 times the *U* value of the atoms they are linked to (1.5 times for methyl groups). Crystallographic data for **L6** and **84** can be obtained free of charge from The Cambridge Crystallographic Data Centre (CCDC) via www.ccdc.cam.ac.uk/data_request/cif under CCDC deposition number 1819175 and 1533022, respectively. Graphical representation of the structure with 50% probability thermal ellipsoids was generated using Mercury visualization software.

2.6.2 Ligand Synthesis

2.6.2.1 Preparation of (4R,4′R)-4,4′-diheptan-4-yl)-4,4′,5,5′-tetrahydro-2,2′bioxazole (L6, (R,R′)-4-HeptylBiOX)



(*R,R*)-4-HeptylBiOX (L6): The synthesis of this ligand was adapted from procedures described by Denmark and coworkers. (*R*)-2-amino-3-propylhexan-1-ol (2 equiv, 2.80 g, 17.6 mmol) and dimethyloxalate (1 equiv, 1.04 g, 8.80 mmol) were dissolved in PhMe (200 mL) and heated to 80 °C. The reaction was allowed to stir overnight with the diamide precipitating out of solution as a white solid. Reaction was cooled to room temperature and concentrated *in vacuo* to afford the crude diol as a sticky white solid (3.3 g, 8.86 mmol). The crude diol was dissolved in PhMe (60 mL) and heated to 70 °C whereupon thionyl chloride (1.4 mL, 19.2 mmol) was added. Reaction was stirred at 70 °C for 30 minutes then heated to 90 °C for 90 minutes. The reaction was cooled to room temperature and poured into 20% KOH solution cooled to 0 °C. The aqueous layer was separated and extracted (3x) with DCM and the combined organic layers were washed with 20% KOH solution, $NaHCO_3$ and brine. The organic layer was dried with Na_2SO_4, filtered through a pad of Celite, and concentrated under reduced pressure to afford the dichloride as a sticky brown solid. The crude dichloride (3.6 g, 8.8 mmol) was immediately dissolved in MeOH (90 mL) and KOH (1.23 g, 21.9 mmol) was added. The reaction was heated to reflux for 14 hours. The reaction was cooled to room temperature and concentrated to remove MeOH. The crude mixture was loaded directly onto a silica

gel column and eluted with 10–40% EtOAc/Hex. The pure ligand was obtained as an off-white solid (1.55 g, 53% over 3 steps, >99% ee).

$\mathbf{R_f}$ = 0.15 (silica gel, 20% EtOAc/Hex, UV).

$\mathbf{[\alpha]_D^{25}}$ = +119° (c = 1.0, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 4.47 – 4.33 (m, 2H), 4.18 – 4.11 (m, 1H), 1.65 (q, *J* = 6.2, 5.6 Hz, 1H), 1.48 – 1.12 (m, 7H), 0.95 – 0.86 (m, 5H).

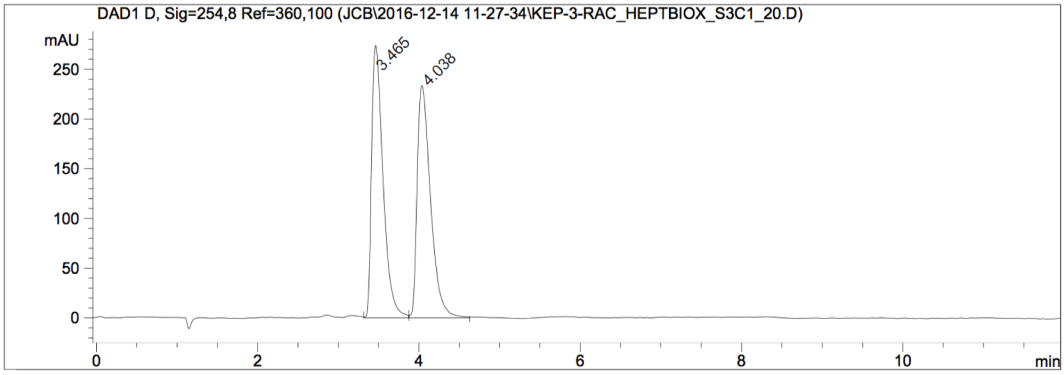
^{13}C NMR (101 MHz, $CDCl_3$): δ 154.6, 71.1, 70.0, 41.6, 32.5, 32.0, 20.3, 20.2, 14.6, 14.5.

FTIR (NaCl, thin film, cm^{-1}): 2955, 2926, 2870, 1620, 1456, 1378, 1120, 945.

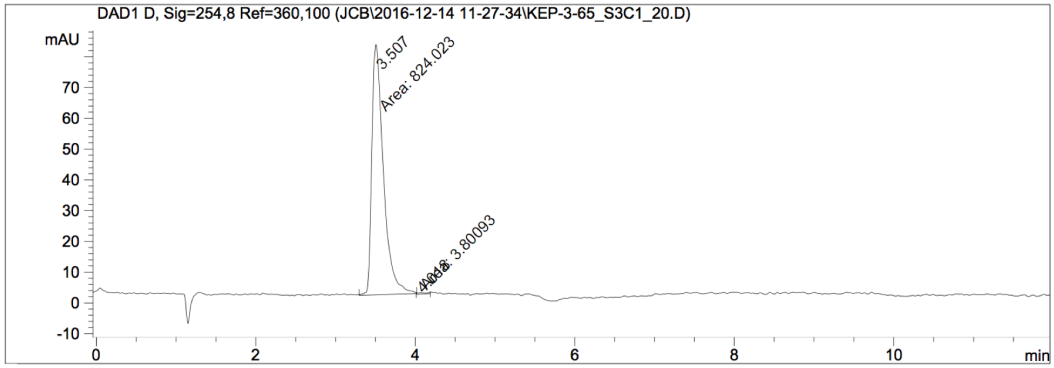
HRMS (ESI, *m/z*): calc'd for $C_{20}H_{37}N_2O_2^+$ $(M+H)^+$: 337.2850, found: 337.2847.

2.6.2.2 SFC Traces of rac-, (S,S)-, and (R,R)-4-HeptylBiOX

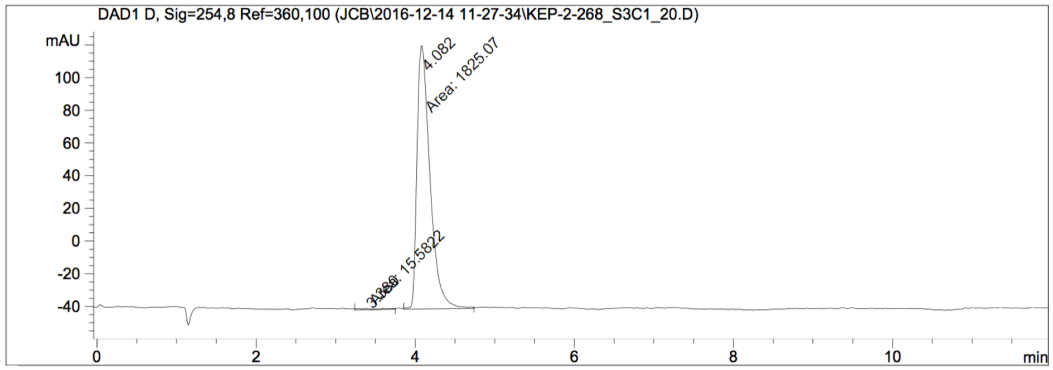
(IC, 2.5 mL/min, 20% IPA in CO_2, λ = 254 nm): t_R = 3.5 min, t_R = 4.0 min.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.465	VV	0.1518	2709.62598	273.04416	50.1608
2	4.038	VB	0.1788	2692.25098	233.04976	49.8392



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.507	MM	0.1687	824.02258	81.41270	99.5409
2	4.018	MM	0.0891	3.80093	5.68225e-1	0.4591



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.380	MM	0.2938	15.58221	8.83812e-1	0.8466
2	4.082	MM	0.1885	1825.06812	161.33264	99.1534

2.6.2.3 X-Ray crystal structure of (R,R)-4-HeptylBiOX

Suitable crystals of **L6** were grown by slow cooling in hexanes in the freezer for 4 weeks. Upon warming to room temperature, the crystals begin to dissolve in hexanes. The crystals also began to dissolve in Paratone oil, but were stable once they were removed from the oil. Compound **L6** crystallizes in the monoclinic space group $P2_1$ with three molecules in the asymmetric unit. Absolute configuration was determined by anomalous dispersion (Flack = 0.03(4)). The final R factor was refined to 3.63% with an average C–C bond e.s.d. value of 0.0022 Å. A second crystal was also analyzed by single-crystal X-ray diffraction, which was found to be in the same enantiomeric configuration (Flack = 0.05(4)). The second crystal was refined to a final R factor of 4.85% with an average C–C bond e.s.d. of 0.0032 Å. Taken together, we confirm the absolute stereochemistry of **L6** to be that of the R enantiomer.

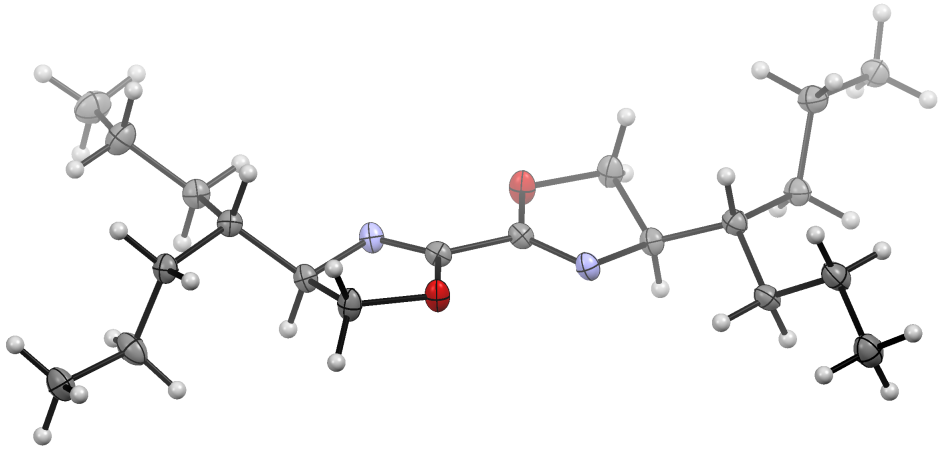
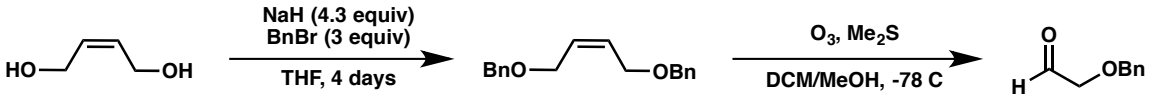


Table S2.1: Crystal data and structure refinement for **L6**.

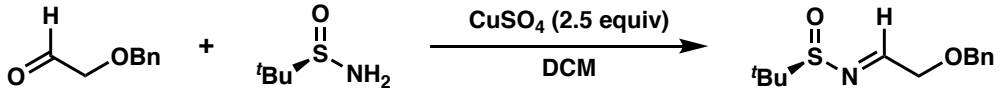
Identification code	KEP-3-236
Empirical formula	$C_{20}H_{36}N_2O_2$
Formula weight	336.51
Temperature	100 K
Wavelength	1.54178 Å

Crystal system	Monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 17.2695(12) Å	a= 90°.
	b = 8.4949(6) Å	b= 108.140(3)°.
	c = 21.7390(15) Å	g = 90°.
Volume	3030.7(4) $Å^3$	
Z	6	
Density (calculated)	1.106 Mg/m^3	
Absorption coefficient	0.549 mm^{-1}	
F(000)	1116	
Crystal size	0.22 x 0.16 x 0.04 mm^3	
Theta range for data collection	2.692 to 80.579°.	
Index ranges	-22<=h<=21, -10<=k<=10, -27<=l<=27	
Reflections collected	97605	
Independent reflections	12703 [R(int) = 0.0468]	
Completeness to theta = 67.679°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7543 and 0.6514	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	12703 / 1 / 661	
Goodness-of-fit on F^2	1.047	
Final R indices [I>2sigma(I)]	R1 = 0.0363, wR2 = 0.0969	
R indices (all data)	R1 = 0.0387, wR2 = 0.0991	
Absolute structure parameter	0.03(4)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.377 and -0.163 $e.Å^{-3}$	

2.6.2.4 Preparation of (R)-2-amino-3-propylhexan-1-ol



Benzyloxyacetaldehyde. Cis-1,4-dihydroxy-2-butene was benzyl protected under known literature procedure. The aldehyde was prepared following known literature procedure: (Z)-1,4-bis(benzyloxy)but-2-ene (1 equiv, 15 g, 56 mmol) was dissolved in 3:1 solution of DCM/MeOH (150 mL) and cooled to –78 °C. Ozone was bubbled through the reaction until the solution turned blue, signaling O_3 saturation. Reaction was sparged with O_2, then N_2 for 15 minutes. Dimethyl sulfide (12 equiv, 50 mL, 676 mmol) was added, and the reaction was allowed to warm to room temperature and stir for 14 hours. Reaction was concentrated under reduced pressure and purified by column chromatography (30% EtOAc/Hex) to afford the aldehyde as a yellow oil (16.6 g, 99% yield).



Preparation of (*R*)-2-amino-3-propylhexan-1-ol from benzyloxyacetaldehyde was based on the procedures described by Ellman and coworkers. 2-(benzyloxy)acetaldehyde (1 equiv, 16.6 g, 111 mmol) was dissolved in DCM (225 mL) at room temperature. (*R*)-(+)-*tert*-butylsulfinamide (1.1 equiv, 14.9 g, 123 mmol) and copper (II) sulfate (2.5 equiv, 44.1 g, 276 mmol) were added and the reaction was allowed to stir at room temperature for 36 hours. Reaction was filtered through a plug of Celite with DCM. The solution concentrated and purified by column chromatography (20% EtOAc/Hex) to afford imine product as a pale yellow oil (17.0 g, 61% yield).

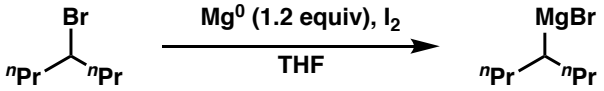
$\mathbf{R}_f$ = 0.23 (silica gel, 20% EtOAc/Hex, UV).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.13 (t, *J* = 3.2 Hz, 1H), 7.41 – 7.27 (m, 5H), 4.64 (d, *J* = 1.1 Hz, 2H), 4.41 (t, *J* = 3.1 Hz, 2H), 1.22 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 166.9, 137.3, 128.7, 128.2, 128.0, 73.4, 71.4, 57.1, 22.6.

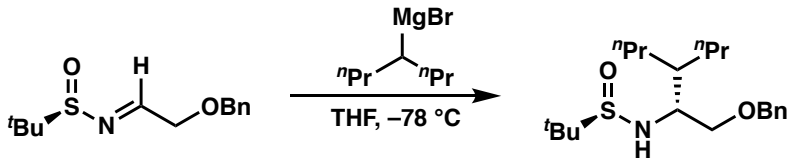
$[\alpha]_D^{25}$ = –221° (c = 1.0, $CHCl_3$).

HRMS (ESI, *m/z*): calc'd for $C_{13}H_{20}NO_2S^+$ $(M+H)^+$: 254.1209, found: 254.1214.



Grignard formation:

Magnesium (1.3 equiv, 4.00 g, 172 mmol) was activated by washing with minimal 1 M HCl, then washed with water, ethanol, and ether before transfer to a flame-dried 500 mL 3-neck flask, equipped with a reflux condenser and stir bar. The Mg^0 was stirred under vacuum overnight. THF (170 mL) and a fleck of I_2 was added and the stirring mixture was periodically heated to reflux with a heat gun over 20 minutes, until the brown solution turned dark, translucent gray. 4-Bromoheptane (1 equiv, 21 mL, 134 mmol) was added slowly, portion-wise, with manual heating to reflux in the intervals between additions. After addition of alkyl bromide, the reaction was stirred at 80 °C for 1 hour, then cooled to room temperature and titrated (0.36 M, 49% yield).



Sulfinamide (1 equiv, 7.33 g, 28.9 mmol) was dissolved in THF (260 mL) and cooled to –78 °C. Freshly prepared heptan-4-ylmagnesium bromide (1.6 equiv, 9.4 g, 46.2 mmol) was added via cannula. The reaction was stirred at –78 °C for 8 hours, then allowed to

stir overnight while the bath warmed slowly. The reaction mixture was quenched with water and Na_2SO_4 was added. The mixture was filtered through a plug of Celite and concentrated. The crude reaction was purified by silica gel chromatography (10% EtOAc/Hex to 30% EtOAc/Hex) to afford product (9.9 g, 97% yield, 97:3 d.r.).

R_f = 0.14 (silica gel, 20% EtOAc/Hex, UV).

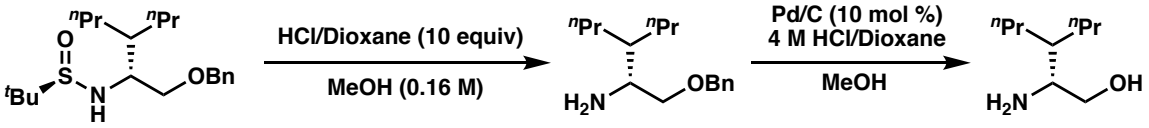
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 – 7.16 (m, 5H), 4.49 (d, *J* = 11.9 Hz, 1H), 4.41 (d, *J* = 11.9 Hz, 1H), 3.56 – 3.52 (m, 3H), 3.35 (dq, *J* = 7.3, 5.2 Hz, 1H), 1.63 (hept, *J* = 5.6, 5.1 Hz, 1H), 1.35 – 1.02 (m, 16H), 0.81 (td, *J* = 7.0, 4.9 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 137.8, 128.0, 127.5, 127.3, 72.7, 70.5, 57.3, 55.6, 38.7, 31.8, 31.6, 22.4, 22.4, 22.4, 22.3, 20.0, 19.9, 14.2, 14.1.

$[\alpha]_D^{25}$ = –38° (c = 6.7, $CHCl_3$).

FTIR (NaCl, thin film, cm^{-1}): 3216, 2065, 3032, 2960, 2871, 1720, 1455, 1363, 1073, 735.

HRMS (ESI, *m/z*): calc'd for $C_{20}H_{36}NO_2S^+$ $(M+H)^+$: 354.2461, found: 354.2469.



To a pale yellow solution of sulfinamine (1 equiv, 9.9 g, 28 mmol) in MeOH (175 mL) at room temperature, 4 M HCl/Dioxane (10 equiv, 70 mL) was added. The reaction was stirred for 1 hour and turned light amber. Reaction mixture was concentrated *in vacuo*. The crude oil was dissolved in minimal 50% EtOAc/Hex and loaded onto a silica gel column. 1 L of 50% EtOAc/Hex was eluted to remove sulfur impurities, then solvent

system was switched to 10% MeOH/DCM to elute brown product band from the top of the silica (6.2 g, 89% yield).

R_f = 0.17 (silica gel, 5% MeOH/DCM, Ninhydrin).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.53 (s, 3H), 7.43 – 7.23 (m, 5H), 4.70 – 4.43 (m, 2H), 3.68 (d, *J* = 5.5 Hz, 2H), 3.37 (s, 1H), 1.87 (q, *J* = 5.9 Hz, 1H), 1.58 (ddt, *J* = 12.9, 10.2, 4.6 Hz, 1H), 1.49 – 1.16 (m, 8H), 0.90 (td, *J* = 7.1, 3.0 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 137.9, 128.5, 127.8, 127.7, 73.4, 67.8, 54.0, 37.4, 31.6, 31.5, 20.2, 20.0, 14.3, 14.3.

$[\alpha]_D^{25}$ = +3° (c = 1.9, $CHCl_3$).

FTIR (NaCl, thin film, cm^{-1}): 2957, 2873, 1727, 1609, 1518, 1455, 1377, 1273, 1102, 737.

HRMS (ESI, *m/z*): calc'd for $C_{16}H_{28}NO^+$ $(M+H)^+$: 250.2165, found: 250.2166.

Pd/C (4.0 g) was added to the flask and dissolved in minimal EtOAc, then placed under N_2. Amine (1 equiv, 4.2 g, 16.8 mmol) was dissolved in MeOH (35 mL) and added to the reaction flask via cannula. 4 M HCl/Dioxane (35 mL) was added and the N_2 atmosphere was exchanged with H_2 and the reaction was allowed to stir 14 h under H_2. Upon completion, the reaction was sparged with argon and filtered through a pad of Celite with EtOAc. The filtrate was concentrated then dissolved in 250 mL EtOAc and added to 250 mL of 6 M NaOH. The organic layer was separated and extracted (x3) with EtOAc. The combined organic layers were dried, filtered, and concentrated under reduced pressure to afford pure amino alcohol (2.3 g, 86% yield).

R_f = 0.09 (silica gel, 5% MeOH/DCM, Ninhydrin).

^{1}H NMR (400 MHz, MeOD): δ 3.76 (dd, *J* = 11.6, 3.9 Hz, 1H), 3.57 (dd, *J* = 11.5, 8.4 Hz, 1H), 3.18 (ddd, *J* = 8.8, 5.3, 3.9 Hz, 1H), 1.91 (s, 3H), 1.67 (q, *J* = 5.5 Hz, 1H), 1.50 – 1.19 (m, 9H), 0.95 (td, *J* = 6.7, 3.9 Hz, 6H).

^{13}C NMR (101 MHz, MeOD): δ 61.0, 56.9, 39.0, 32.8, 32.4, 21.1, 21.1, 14.5, 14.5.

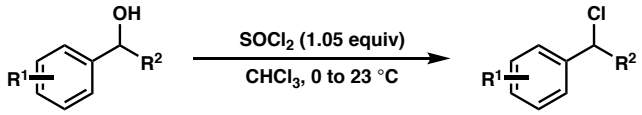
$[\alpha]_D^{25}$ = –11° (c = 2.1, $CHCl_3$).

FTIR (NaCl, thin film, cm^{-1}): 3283, 2957, 2922, 2345, 1570, 1466, 1378, 1051.

HRMS (ESI, *m/z*): calc'd for $C_9H_{22}NO^+$ $(M+H)^+$: 160.1696, found: 160.1701.

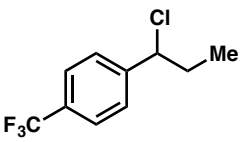
2.6.3 Substrate Synthesis

General Procedure 1: Benzyl Chloride Synthesis from Benzyl Alcohols



A flame-dried flask was charged with the benzyl alcohol substrate (1 equiv) and chloroform (0.30 M) and sealed with a rubber septum. This solution was cooled to 0 ºC in an ice bath and placed under a positive pressure of nitrogen. The flask was vented via a Teflon cannula into a saturated solution of $NaHCO_3$ to quench evolved SO_2 gas. To the cooled solution was slowly added thionyl chloride (1.05 equiv) via syringe. The reaction was allowed to stir overnight and the ice bath allowed to melt, unless otherwise noted. Reactions were then concentrated to typically afford the crude substrates as yellow oils containing a mixture of benzylic chloride and the styrenyl elimination product. Substrates were purified by column chromatography on silica gel in 100% hexanes to elute first the elimination product (strong staining by $KMnO_4$ and brightly fluorescent) followed by the desired chloride product (dimly fluorescent, no staining).

1-(1-chloropropyl)-4-(trifluoromethyl)benzene (119)



Prepared from 1-(4-(trifluoromethyl)phenyl)propan-1-ol (5.0 mmol, 1.02 g) following General Procedure 1 to yield 350 mg (31% yield, 1.57 mmol) as a mobile clear liquid. Benzyl chloride contained styrene elimination product and was used as 88% pure.

R_f= 0.6 (silica gel, hexane, UV)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 – 7.59 (m, 2H), 7.52 – 7.47 (m, 2H), 4.81 (dd, *J* = 7.8, 6.4 Hz, 1H), 2.23 – 1.98 (m, 2H), 1.01 (t, *J* = 7.3 Hz, 3H).

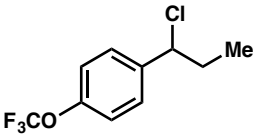
^{13}C NMR (101 MHz, $CDCl_3$): δ 145.7, 130.5 (q, *J* = 32.6 Hz), 127.5, 125.7 (q, *J* = 3.8 Hz), 124.1 (q, J = 272.2 Hz), 64.3, 33.3, 11.7.

^{19}F NMR (282 MHz, $CDCl_3$): δ –62.7

FTIR (NaCl, thin film, cm^{-1}): 2975, 1621, 1420, 1326, 1127, 1068, 849.

HRMS (EI+, m/z): calc'd for $C_{10}H_{10}ClF_3$ $[M+\bullet]^+$: 222.0423; found: 222.0408.

1-(1-chloropropyl)-4-(trifluoromethoxy)benzene (73)



Prepared from 1-(4-(trifluoromethoxy)phenyl)propan-1-ol (13.1 mmol, 2.88 g) following General Procedure 1 to yield 2.51 g (80% yield, 10.48 mmol) as a mobile clear liquid.

R_f= 0.6 (silica gel, hexane, UV)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 – 7.36 (m, 2H), 7.25 – 7.16 (m, 2H), 4.78 (dd, *J* = 7.9, 6.4 Hz, 1H), 2.20 – 1.99 (m, 2H), 1.00 (t, *J* = 7.3 Hz, 3H).

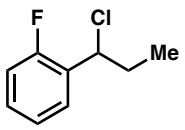
^{13}C NMR (101 MHz, $CDCl_3$): δ 149.0 (d, *J* = 1.9 Hz), 140.6, 128.6, 121.2, 120.6 (q, *J* = 257.3 Hz), 64.4, 33.4, 11.8.

^{19}F NMR (282 MHz, $CDCl_3$): δ –57.9

FTIR (NaCl, thin film, cm^{-1}): 2973, 1508, 1262, 1220, 1165

HRMS (FAB+, m/z): calc'd for $C_{10}H_{10}ClF_3O$ $[M+H]^+$: 239.0464; found: 239.0465.

1-(1-chloropropyl)-2-fluorobenzene (120)



Prepared from 1-(2-fluorophenyl)propan-1-ol (19.7 mmol, 3.03 g) following General Procedure 1 to yield 2.63 g (77% yield, 15.2 mmol) as a mobile clear liquid.

R_f= 0.6 (silica gel, hexane, UV)

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.51 (td, *J* = 7.6, 1.8 Hz, 1H), 7.32 – 7.25 (m, 1H), 7.17 (td, *J* = 7.6, 1.2 Hz, 1H), 7.04 (ddd, *J* = 10.3, 8.2, 1.2 Hz, 1H), 5.17 (dd, *J* = 8.0, 6.4 Hz, 1H), 2.24 – 2.02 (m, 2H), 1.03 (t, *J* = 7.3 Hz, 3H).

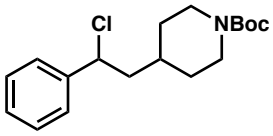
^{13}C NMR (101 MHz, $CDCl_3$): δ 159.65 (d, *J* = 247.5 Hz), 129.79 (d, *J* = 8.4 Hz), 128.94 (d, *J* = 13.0 Hz), 128.61 (d, *J* = 3.3 Hz), 124.57 (d, *J* = 3.7 Hz), 115.61 (d, *J* = 22.1 Hz), 57.61 (d, *J* = 3.7 Hz), 32.4, 11.6.

^{19}F NMR (282 MHz, $CDCl_3$): δ –118.6 (ddd, *J* = 10.3, 7.4, 5.1 Hz).

FTIR (NaCl, thin film, cm^{-1}): 3436, 3088, 2974, 2879, 1616, 1588, 1492, 1457, 1233, 1118, 755.

HRMS (EI+, m/z): calc'd for $C_9H_{10}ClF$ $[M+\bullet]^+$: 172.0455; found: 172.0445.

***tert*-butyl 4-(2-chloro-2-phenylethyl)piperidine-1-carboxylate (121)**



Prepared from *tert*-butyl 4-(2-hydroxy-2-phenylethyl)piperidine-1-carboxylate (6.2 mmol, 1.89 g) following General Procedure 1. The reaction was concentrated and loaded onto a silica plug. Elution with $CHCl_3$ delivered degradation products. Subsequent elution with 10% MeOH/DCM afforded the deprotected HCl salt as a tan solid 68% yield (4.22 mmol, 1.02 g). This product was not competent in the cross-coupling reaction. Reprotection with Boc_2O (1.05 equiv) in DCM with Et_3N (4 equiv) afforded the desired product containing 10% styrene and was used without further purification.

R_f= 0.3 (silica gel, 10% EtOAc/hexane, UV)

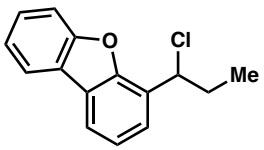
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 – 7.29 (m, 5H), 4.98 (dd, *J* = 9.2, 5.9 Hz, 1H), 4.10 (s, 3H), 2.69 (t, *J* = 12.8 Hz, 2H), 2.14 (ddd, *J* = 14.5, 9.3, 5.6 Hz, 1H), 1.90 (ddd, *J* = 14.0, 7.7, 5.9 Hz, 1H), 1.85 – 1.65 (m, 2H), 1.47 (s, 9H), 1.27 – 1.07 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 154.8, 141.7, 128.7, 128.4, 126.9, 79.4, 61.0, 46.6, 33.5, 28.5, 28.5, 27.4.

FTIR (NaCl, thin film, cm^{-1}): 3448, 2930, 1810, 1692, 1424, 1366, 1168, 698.

HRMS (FAB+, m/z): calc'd for $C_{18}H_{26}ClNO_2$ $[M+H]^+$: 324.1730; found: 324.1740.

4-(1-chloropropyl)dibenzo[*b*,*d*]furan (122)



Prepared from 1-(dibenzo[*b*,*d*]furan-4-yl)propan-1-ol (9.2 mmol, 2.08 g) following General Procedure 1 to yield 1.74 g (84% yield, 7.7 mmol) as a mobile clear liquid. Benzyl chloride contained styrene elimination product and was used as 78% pure.

R_f= 0.3 (silica gel, hexane, UV)

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.95 (dddd, *J* = 7.6, 2.6, 1.4, 0.7 Hz, 1H), 7.90 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.65 – 7.54 (m, 2H), 7.48 (ddd, *J* = 8.3, 7.3, 1.4 Hz, 1H), 7.40 – 7.32 (m, 2H), 5.50 (dd, *J* = 7.8, 6.5 Hz, 1H), 2.48 – 2.19 (m, 2H), 1.08 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 156.2, 153.1, 127.5, 126.0, 125.5, 124.6, 124.2, 123.2, 123.0, 120.9, 120.5, 112.0, 59.4, 32.2, 11.9.

FTIR (NaCl, thin film, cm^{-1}): 2971, 1588, 1451, 1424, 1326, 1272, 1189, 1108, 1055, 846, 749.

HRMS (FAB+, m/z): calc'd for $C_{15}H_{13}ClO$ $[M+H]^+$: 245.0733; found: 245.0731.

2.6.4 Enantioselective Reductive Cross-Coupling

2.6.4.1 General Procedures for Enantioselective Cross-Coupling of Benzyl Chlorides and (Hetero)aryl Iodides

General Procedure 2: Cross-Coupling on 0.05 mmol scale

On a bench-top, to a 1-dram vial was added a stir bar,* the appropriate ligand (20 mol %, 0.01 mmol), reductant (3 equiv, 0.15 mmol), and aryl iodide (1.0 equiv, 0.05 mmol). The vial was transferred into a N_2-filled glovebox and charged with $NiBr_2$(diglyme) (10 mol %, 0.005 mmol) and the appropriate solvent (0.14 mL, 0.36 M). Reaction was allowed to stir at 250 rpm for 20 minutes before addition of benzyl chloride (1.2 equiv, 0.06 mmol). After one minute of stirring, TMSCl (5 uL, 0.8 equiv) was added. The vial was sealed with a Teflon cap and removed from the glovebox. The mixture was stirred at 480 rpm over a period of 14 hours over which time the heterogeneous solution turned from dark gray to a light green, orange, or gray color (depending on substrate). The reaction was quenched by loading directly onto a short plug of basic alumina, eluting with 20% Et_2O/hexanes. The solution was concentrated to afford a clear oil. The crude residue was analyzed by chiral SFC and NMR. Dibenzyl ether was used as an internal NMR standard.

***Stir bar size is critically important to the success of the reaction**. The 2-dram sized (3 mm x 12 mm) stir bars are added to 1-dram vials in order to span the full diameter of the vial. Not all stir bars sold as 3 mm x 12 mm will be successful in every 1-dram vial. Manufacturing differences in stir bars and vials lead to certain stir bars fitting certain vials. To check for appropriate size: place the stir bar into the empty vial and shake it back and forth; a clinking noise will result if the stir bar is sufficiently small. If no clinking is heard, that stir bar will stick when Mn^0 is added and the reaction will result in no conversion. Vials should be placed on the stir plate such that the stir bar lies flat while stirring (completely centered or just off-center). Stir bars smaller than 3 mm x 12 mm will result in the Mn^0 settling on the outside perimeter of the vial and poor reaction conversion.

General Procedure 3: Cross-Coupling on 0.2 mmol scale

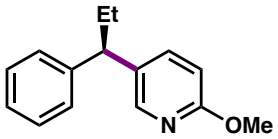
On the bench-top, a 20 mL scintillation vial was charged with a 1.0 x 1.9 cm cross stir bar, Mn^0 powder (3 equiv, 33 mg, 0.6 mmol), aryl iodide (*if solid*, 1 equiv, 0.2 mmol), and **L6** (0.2 equiv, 13.5 mg, 0.04 mmol). The vial was transferred into a N_2-filled glovebox and charged with $NiBr_2$(diglyme) (10 mol %, 7.1 mg, 0.02 mmol), 1,4-dioxane (0.56 mL, 0.36 M), and aryl iodide (*if liquid*, 1 equiv, 0.2 mmol). The reaction was allowed to stir at 250 rpm for **20 minutes** before addition of benzyl chloride (1.2 equiv, 0.24 mmol). After one minute of stirring, TMSCl (20 uL, 0.75 equiv) was added. The vial was sealed with a Teflon cap, taped, and removed from the glovebox. The mixture was stirred at 480 rpm over a period of 14 hours, over which time the heterogeneous solution turned from dark gray to a light green, deep red, or light gray color (depending on substrate). The reaction was quenched by loading directly onto a short plug of silica or basic alumina (if heteroatom present on arene), eluting with either 20% ethyl acetate/hexane or 20% Et_2O/hexane, respectively. The solution was concentrated to afford a clear oil. The oil was dissolved in DCM and dry loaded with Celite onto a silica gel or basic alumina column (if heteroatom present on arene) and eluted in a hexane/EtOAc or hexane/Et_2O gradient, respectively. The remaining benzyl homodimer could be collected in the first couple fractions, with biaryl homocoupled product being the most polar component. Reaction success is *critically dependent* on stirring. A stir bar too small for the reaction vessel will fail to suspend the Mn^0 powder and lead to low conversions. The reaction vessel should be sufficiently large (solvent height should be sufficiently low) to allow for even distribution of Mn^0 powder with vigorous stirring. *Short or no prestir before addition of benzyl chloride results in low yields on this scale.*

General Procedure 4: Cross-Coupling on 2.0 mmol scale

On the bench-top, a 100-mL flask with a 24/40 ground glass neck was charged with a large, 1.7 x 4.0 cm football-shaped stir bar, Mn^0 powder (3 equiv, 0.327 g, 6.0 mmol), and **L6** (0.2 equiv, 0.135 g, 0.4 mmol). The flask was transferred into a N_2-filled glovebox and charged with $NiBr_2$(diglyme) (10 mol %, 0.071 g, 0.2 mmol), 1,4-dioxane (5.6 mL, 0.36 M), and aryl iodide (1 equiv, 0.470 g, 2.0 mmol). Reaction was allowed to stir at 250 rpm for **30 minutes** before addition of benzyl chloride (1.2 equiv, 0.370 g, 2.4 mmol). After one minute of stirring, TMSCl (0.190 mL, 0.75 equiv) was added. The vial was sealed with a septum, taped, removed from the glovebox and a N_2 inlet needle inserted. The mixture was stirred at 1000 rpm over a period of 3 days, over which time the heterogeneous solution turned from green to dark gray. The reaction was quenched by loading directly onto a short plug of basic Alumina, eluting with 20% Et_2O/hexane. The solution was concentrated to afford a clear oil. The oil was dissolved in DCM and dry loaded with Celite onto a basic alumina column and eluted in a hexane/Et_2O gradient. Remaining benzyl homodimer could be collected in the first couple fractions, with biaryl homocoupled product being the most polar component. Reaction success is *critically dependent* on stirring. The stir bar was large enough and the correct shape to fit right along the bottom of the flask with minimal space between the stir bar and glass.

2.6.4.2 Characterization of Reaction Products

2-methoxy-5-(1-phenylpropyl)pyridine (37)



Prepared from 5-iodo-2-methoxypyridine (1 equiv, 47 mg, 0.2 mmol) and 1-(chloropropyl)benzene (1.2 equiv, 37 mg, 0.24 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **37** (38 mg, 84% yield) in 91% ee as a colorless oil.

$\mathbf{R}_f$ = 0.35 (silica gel, 10% EtOAc/Hex, UV).

Chiral SFC: (OJ-H, 2.5 mL/min, 4% IPA in CO_2, λ = 210 nm): t_R(minor) = 6.0 min, t_R(major) = 6.7 min.

$[\alpha]_D^{25}$ = +10.6° (c = 1.0, $CHCl_3$).

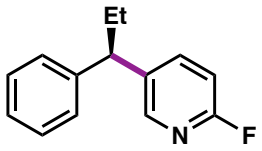
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (dt, *J* = 2.5, 0.7 Hz, 1H), 7.40 (ddd, *J* = 8.6, 2.5, 0.5 Hz, 1H), 7.33 – 7.24 (m, 2H), 7.24 – 7.14 (m, 3H), 6.66 (dd, *J* = 8.5, 0.7 Hz, 1H), 3.90 (s, 3H), 3.79 – 3.69 (m, 1H), 2.17 – 1.93 (m, 2H), 0.90 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 162.9, 145.8, 144.7, 138.4, 133.3, 128.6, 127.9, 126.4, 110.8, 53.5, 50.0, 28.5, 12.8.

FTIR (NaCl, thin film, cm^{-1}): 2963, 2874, 1605, 1572, 1492, 1392, 1287, 1262, 1028, 699.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{15}H_{17}NO$ $[M+H]^+$: 228.1383; found: 228.1379.

2-fluoro-5-(1-phenylpropyl)pyridine (77)



Prepared from 2-fluoro-5-iodopyridine (1 equiv, 45.0 mg, 0.2 mmol) and 1-(chloropropyl)benzene (1.2 equiv, 37 mg, 0.24 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **77** (27 mg, 63% yield) in 90% ee as a colorless oil.

$\mathbf{R}_f$ = 0.35 (silica gel, 10% EtOAc/Hex, UV).

Chiral SFC: (AD-H, 2.5 mL/min, 5% IPA in CO_2, λ = 254 nm): t_R(major) = 5.1 min, t_R(minor) = 5.6 min.

$[\alpha]_D^{25}$ = +3.3° (c = 1.0, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.14 – 8.04 (m, 1H), 7.57 (ddd, *J* = 8.7, 7.8, 2.6 Hz, 1H), 7.32 – 7.25 (m, 2H), 7.22 – 7.14 (m, 3H), 6.81 (dd, *J* = 8.5, 3.0 Hz, 1H), 3.79 (t, *J* = 7.8 Hz, 1H), 2.15 – 1.95 (m, 2H), 0.88 (t, *J* = 7.3 Hz, 3H).

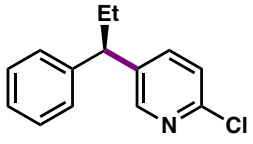
^{13}C NMR (101 MHz, $CDCl_3$): δ 162.41 (d, *J* = 237.3 Hz), 146.82 (d, *J* = 14.3 Hz), 143.7, 140.55 (d, *J* = 7.7 Hz), 138.28 (d, *J* = 4.6 Hz), 128.8, 127.9, 126.7, 109.38 (d, *J* = 37.4 Hz), 50.0, 50.0, 28.6, 12.7.

^{19}F NMR (282 MHz, $CDCl_3$): δ -71.9.

FTIR (NaCl, thin film, cm^{-1}): 2964, 2931, 2875, 1595, 1482, 1453, 1396, 1249, 700.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{14}H_{14}FN$ $[M+H]^+$: 216.1183; found: 216.1181.

2-chloro-5-(1-phenylpropyl)pyridine (78)



Prepared from 2-chloro-5-iodopyridine (1 equiv, 48.0 mg, 0.2 mmol) and 1-(chloropropyl)benzene (1.2 equiv, 37 mg, 0.24 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **78** (27 mg, 59% yield) in 90% ee as a colorless oil.

R_f = 0.4 (silica gel, 20% Et_2O/Hex, UV).

Chiral SFC: (AD-H, 2.5 mL/min, 8% IPA in CO_2, λ = 254 nm): t_R (major) = 6.3 min, t_R (minor) = 7.5 min.

$[\alpha]_D^{25}$ = –1.8° (c = 1.0, $CHCl_3$).

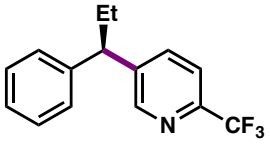
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (dt, *J* = 2.6, 0.6 Hz, 1H), 7.47 (ddd, *J* = 8.2, 2.5, 0.6 Hz, 1H), 7.35 – 7.27 (m, 2H), 7.24 – 7.16 (m, 4H), 3.80 (t, *J* = 7.8 Hz, 1H), 2.18 – 1.98 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 149.4, 149.3, 143.4, 139.6, 138.3, 128.9, 127.9, 126.8, 124.2, 50.1, 28.4, 12.7.

FTIR (NaCl, thin film, cm^{-1}): 2931, 2963, 2874, 1581, 1563, 1456, 1386, 1106, 1022, 700.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{14}H_{14}ClN$ $[M+H]^+$: 232.0888; found: 232.0888.

5-(1-phenylpropyl)-2-(trifluoromethyl)pyridine (79)



Prepared from 5-iodo-2-(trifluoromethyl)pyridine (1 equiv, 55.0 mg, 0.2 mmol) and 1-(chloropropyl)benzene (1.2 equiv, 37 mg, 0.24 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **79** (22 mg, 42% yield) in 89% ee as a colorless oil.

R_f = 0.27 (silica gel, 10% EtOAc/Hex, UV).

Chiral SFC: (AD-H, 2.5 mL/min, 5% IPA in CO_2, λ = 210 nm): t_R(major) = 3.2 min, t_R(minor) = 3.6 min.

$[\alpha]_D^{25}$ = +2.29° (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.64 (d, *J* = 2.1 Hz, 1H), 7.68 (ddt, *J* = 8.2, 2.3, 0.7 Hz, 1H), 7.59 (dd, *J* = 8.2, 0.8 Hz, 1H), 7.38 – 7.27 (m, 2H), 7.22 (td, *J* = 7.1, 1.1 Hz, 3H), 3.91 (t, *J* = 7.8 Hz, 1H), 2.26 – 2.01 (m, 2H), 0.93 (t, *J* = 7.3 Hz, 3H).

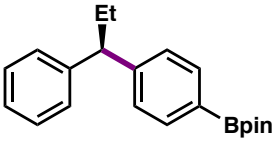
^{13}C NMR (101 MHz, $CDCl_3$): δ 150.0, 146.2 (q, *J* = 34.7 Hz), 144.0, 142.8, 136.4, 129.0, 127.9, 127.0, 121.7 (q, *J* = 273.2 Hz), 120.4 (q, *J* = 2.7 Hz), 50.7, 28.3, 12.7.

^{19}F NMR (282 MHz, $CDCl_3$): δ –67.8.

FTIR (NaCl, thin film, cm^{-1}): 2967, 2933, 2878, 1336, 1174, 1136, 1087, 1026, 700.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{15}H_{14}F_3N$ $[M+H]^+$: 266.1151; found: 266.1151.

4,4,5,5-tetramethyl-2-(4-(1-phenylpropyl)phenyl)-1,3,2-dioxaborolane (80)



Prepared from 2-(4-iodophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1 equiv, 66.0 mg, 0.2 mmol) and 1-(chloropropyl)benzene (1.2 equiv, 37 mg, 0.24 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **80** (47 mg, 72% yield) in 83% ee as a white solid.

R_f = 0.42 (silica gel, 10% EtOAc/Hex, UV).

Chiral SFC: (AD-H, 2.5 mL/min, 7% IPA in CO_2, λ = 254 nm): t_R(minor) = 6.2 min, t_R(major) = 6.9 min.

$[\alpha]_D^{25}$ = –3.3° (c = 1.0, $CHCl_3$).

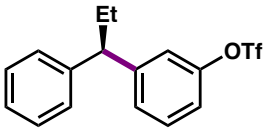
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 – 7.73 (m, 2H), 7.34 – 7.22 (m, 6H), 7.22 – 7.15 (m, 1H), 3.84 (t, *J* = 7.8 Hz, 1H), 2.11 (p, *J* = 7.4 Hz, 2H), 1.36 (s, 12H), 0.93 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 148.6, 145.0, 135.1, 128.5, 128.0, 127.6, 126.2, 83.8, 53.5, 28.5, 25.0, 25.0, 12.9.

FTIR (NaCl, thin film, cm^{-1}): 2976, 2930, 1611, 1399, 1390, 1359, 1320, 1144, 1091, 660.

HRMS (+ESI, *m/z*): calc'd for $C_{21}H_{27}BO_2$ [M+H]-H_2: 321.2026; found: 321.2020.

3-(1-phenylpropyl)phenyl trifluoromethanesulfonate (81)



Prepared from 3-iodophenyl trifluoromethanesulfonate (1 equiv, 70.0 mg, 0.2 mmol) and 1-(chloropropyl)benzene (1.2 equiv, 37 mg, 0.24 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **81** (58 mg, 84% yield) in 92% ee as a colorless oil.

R_f = 0.56 (silica gel, 10% EtOAc/Hex).

Chiral SFC: (OJ-H, 2.5 mL/min, 1% IPA in CO_2, λ = 254 nm): t_R(major) = 5.1 min, t_R(minor) = 5.8 min.

$[\alpha]_D^{25}$ = –5.6° (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 – 7.23 (m, 3H), 7.23 – 7.12 (m, 4H), 7.10 (t, *J* = 2.1 Hz, 1H), 7.04 (ddd, *J* = 8.2, 2.5, 1.1 Hz, 1H), 3.79 (t, *J* = 7.8 Hz, 1H), 2.03 (pd, *J* = 7.4, 2.5 Hz, 2H), 0.86 (t, *J* = 7.3 Hz, 3H).

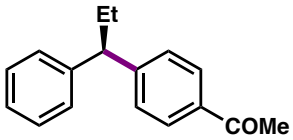
^{13}C NMR (101 MHz, $CDCl_3$): δ 149.8, 148.5, 143.8, 130.2, 128.8, 128.2, 128.0, 126.7, 120.8, 119.0, 52.9, 28.6, 12.7.

^{19}F NMR (282 MHz, $CDCl_3$): δ -72.9.

FTIR (NaCl, thin film, cm^{-1}): 2967, 2934, 1612, 1579, 1484, 1422, 1249, 1212, 1142, 1120, 852.

HRMS (FAB+, *m/z*): calc'd for $C_{16}H_{15}F_3O_3S$ $[(M+H) - H_2]^+$: 343.0616; found: 343.0624.

1-(4-(1-phenylpropyl)phenyl)ethan-1-one (82)



Prepared from 4-iodoacetophenone (1 equiv, 49.0 mg, 0.2 mmol) and 1-(chloropropyl)benzene (1.2 equiv, 37 mg, 0.24 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **82** (42 mg, 88% yield) in 85% ee as a white solid.

R_f = 0.18 (silica gel, 10% Et_2O/hexanes, UV).

Chiral SFC: (OJ-H, 2.5 mL/min, 10% IPA in CO_2, λ = 254 nm): t_R (minor) = 5.4 min, t_R (major) = 6.1 min.

$[\alpha]_D^{25}$ = –3.0° (c = 1.0, $CHCl_3$).

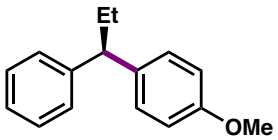
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 – 7.85 (m, 2H), 7.36 – 7.27 (m, 4H), 7.25 – 7.16 (m, 3H), 3.86 (t, *J* = 7.8 Hz, 1H), 2.56 (s, 3H), 2.19 – 2.01 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 197.9, 151.0, 144.2, 135.3, 128.7, 128.7, 128.2, 128.0, 126.5, 53.4, 28.4, 26.7, 12.8.

FTIR (NaCl, thin film, cm^{-1}): 2962, 2931, 2873, 1681, 1606, 1358, 1269, 700.

HRMS (FAB+, *m/z*): calc'd for $C_{17}H_{18}O$ $[M+H]^+$: 239.1436; found: 239.1446.

1-methoxy-4-(1-phenylpropyl)benzene (83)



Prepared from 4-iodoanisole (1 equiv, 47.0 mg, 0.2 mmol) and 1-(chloropropyl)benzene (1.2 equiv, 37 mg, 0.24 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **83** (30 mg, 67% yield) in 83% ee as a colorless oil.

R_f = 0.44 (silica gel, 10% Et_2O/hexanes, UV).

Chiral SFC: (OJ-H, 2.5 mL/min, 8% IPA in CO_2, λ = 235 nm): t_R(minor) = 7.9 min, t_R(major) = 9.9 min.

$[\alpha]_D^{25}$ = –3.7° (c = 1.0, $CHCl_3$).

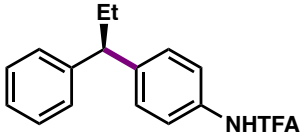
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 – 7.21 (m, 4H), 7.21 – 7.05 (m, 3H), 6.94 – 6.79 (m, 2H), 3.78 (m, 4H), 2.06 (p, *J* = 7.4 Hz, 2H), 0.91 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 157.9, 145.7, 137.5, 128.9, 128.5, 127.9, 126.0, 113.8, 55.3, 52.5, 28.9, 12.9.

FTIR (NaCl, thin film, cm^{-1}): 2960, 2931, 1610, 1507, 1452, 1248, 1178, 1037, 699.

HRMS (FAB+, *m/z*): calc'd for $C_{16}H_{18}O$ $[(M+H) - H_2]^+$: 225.1279; found: 225.1275.

2,2,2-trifluoro-*N*-(4-(1-phenylpropyl)phenyl)acetamide (84)



Prepared from 2,2,2-trifluoro-*N*-(4-iodophenyl)acetamide (1 equiv, 63.0 mg, 0.2 mmol) and 1-(chloropropyl)benzene (1.2 equiv, 37 mg, 0.24 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **84** (43 mg, 70% yield) in 81% ee as a white solid. Recrystallized by vapor diffusion of pentane into a saturated solution of **84** in DCM to give white needles.

R$_f$ = 0.52 (silica gel, 10:45:45 Et_2O/PhMe/Pentane, UV).

Chiral SFC: (OD-H, 2.5 mL/min, 10% IPA in CO_2, λ = 254 nm): t_R(minor) = 6.6 min, t_R(major) = 10.4 min.

[α]$_D^{25}$ = –5.9° (c = 1.0, $CHCl_3$).

m.p. = 73.3–73.8 ºC

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.91 (s, 1H), 7.50 – 7.45 (m, 2H), 7.33 – 7.24 (m, 4H), 7.24 – 7.16 (m, 3H), 3.80 (t, *J* = 7.8 Hz, 1H), 2.07 (pd, *J* = 7.4, 2.6 Hz, 2H), 0.90 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 154.84 (q, *J* = 37.4 Hz), 144.7, 143.7, 133.1, 128.9, 128.6, 127.9, 126.4, 120.7, 115.8 (q, *J* = 288.8 Hz) 52.8, 28.6, 12.8.

^{19}F NMR (282 MHz, $CDCl_3$): δ –75.7.

FTIR (NaCl, thin film, cm^{-1}): 3304, 2964, 1703, 1605, 1546, 1513, 1288, 1248, 1199, 1159, 699.

HRMS (FAB+, *m/z*): calc'd for $C_{17}H_{16}F_3NO$ $[M+H]^+$: 308.1262; found: 308.1266.

Compound **84** crystallizes in the monoclinic space group $P2_1$ with two molecules in the asymmetric unit. The coordinates for the hydrogen atoms bound to N1A and N1B were located in the difference Fourier synthesis and refined using a riding model. Absolute configuration was determined by anomalous dispersion (Flack = 0.05(7)).[6]

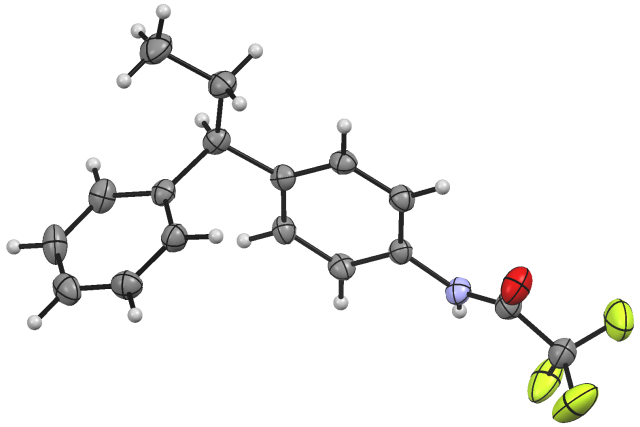
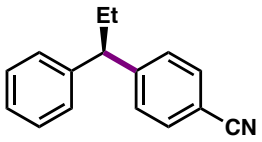


Table S2.2. Crystal data and structure refinement for 84.

Identification code	KEP-2-91	
Empirical formula	$C_{34}\ H_{32}\ F_6\ N_2\ O_2$	
Formula weight	614.61	
Temperature	200 K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 12.5921(3) Å	α= 90°.
	b = 5.30640(10) Å	β= 99.0020(10)°.
	c = 22.4242(5) Å	γ = 90°.
Volume	1479.90(6) $Å^3$	
Z	2	
Density (calculated)	1.379 Mg/m^3	
Absorption coefficient	0.949 mm^{-1}	
F(000)	640	
Crystal size	0.208 x 0.115 x 0.08 mm^3	
Theta range for data collection	3.554 to 79.473°.	
Index ranges	-15<=h<=15, -6<=k<=6, -28<=l<=27	
Reflections collected	20749	
Independent reflections	6253 [R(int) = 0.0455]	
Completeness to theta = 67.679°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7542 and 0.6425	

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6253 / 1 / 406
Goodness-of-fit on F^2	1.028
Final R indices [I>2sigma(I)]	R1 = 0.0390, wR2 = 0.0826
R indices (all data)	R1 = 0.0488, wR2 = 0.0872
Absolute structure parameter	0.05(7)
Extinction coefficient	0.0007(2)
Largest diff. peak and hole	0.154 and -0.161 e.$Å^{-3}$

4-(1-phenylpropyl)benzonitrile (85)



Prepared from 4-iodobenzonitrile (1 equiv, 46.0 mg, 0.2 mmol) and 1-(chloropropyl)benzene (1.2 equiv, 37 mg, 0.24 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **85** (27 mg, 62% yield) in 89% ee as a colorless oil.

$\mathbf{R}_f$ = 0.21 (silica gel, 10% Et_2O/Hex, UV).

Chiral SFC: (OB-H, 2.5 mL/min, 10% IPA in CO_2, λ = 235 nm): t_R(major) = 5.4 min, t_R(minor) = 7.2 min.

$\mathbf{[\alpha]_D^{25}}$ = –1.9° (c = 1.0, $CHCl_3$).

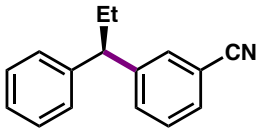
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (s, 5H), 7.39 – 7.27 (m, 4H), 7.25 – 7.16 (m, 3H), 3.84 (t, *J* = 7.8 Hz, 1H), 2.20 – 1.98 (m, 2H), 0.90 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 150.9, 143.6, 132.4, 128.8, 128.8, 128.0, 126.7, 119.1, 110.0, 53.4, 28.3, 12.7.

FTIR (NaCl, thin film, cm^{-1}): 2963, 2930, 2874, 2226, 1606, 1503, 1493, 1462, 1452, 699.

HRMS (FAB+, *m/z*): calc'd for $C_{16}H_{15}N$ $[M+\bullet]^+$: 221.1204; found: 221.1202.

3-(1-phenylpropyl)benzonitrile (86)



Prepared from 3-iodobenzonitrile (1 equiv, 46.0 mg, 0.2 mmol) and 1-(chloropropyl)benzene (1.2 equiv, 37 mg, 0.24 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **86** (28 mg, 64% yield) in 88% ee as a colorless oil.

$\mathbf{R}_f$ = 0.26 (silica gel, 10:45:45 Et_2O/PhMe/Pentane, UV).

Chiral SFC: (OJ-H, 2.5 mL/min, 8% IPA in CO_2, λ = 235 nm): t_R (major) = 5.8 min, t_R (minor) = 6.5 min.

$\mathbf{[\alpha]_D^{25}}$ = –10.6° (c = 1.0, $CHCl_3$).

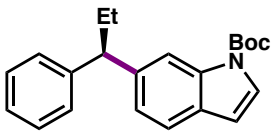
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 – 7.42 (m, 3H), 7.42 – 7.27 (m, 3H), 7.25 – 7.16 (m, 3H), 3.82 (t, *J* = 7.8 Hz, 1H), 2.18 – 1.95 (m, 2H), 0.90 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 146.8, 143.7, 132.7, 131.6, 130.0, 129.3, 128.8, 127.9, 126.8, 119.2, 112.5, 52.9, 28.4, 12.7.

FTIR (NaCl, thin film, cm^{-1}): 3062, 3028, 2964, 2931, 2875, 2229, 1598, 1582, 1482, 1452, 701, 692.

HRMS (FAB+, *m/z*): calc'd for $C_{16}H_{15}N$ [M+•]$^+$: 221.1204; found: 221.1203.

tert-butyl-6-(1-phenylpropyl)-1*H*-indole-1-carboxylate (87)



Prepared from *tert*-butyl 6-iodo-1*H*-indole-1-carboxylate (1 equiv, 69.0 mg, 0.2 mmol) and 1-(chloropropyl)benzene (1.2 equiv, 37 mg, 0.24 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **87** (51 mg, 76% yield) in 83% ee as a colorless oil.

R$_f$ = 0.37 (silica gel, 10% Et_2O/Hex, UV).

Chiral SFC: (AD-H, 2.5 mL/min, 5% IPA in CO_2, λ = 254 nm): t_R(minor) = 5.2 min, t_R(major) = 5.5 min.

[α]$_D^{25}$ = –6.2° (c = 1.0, $CHCl_3$).

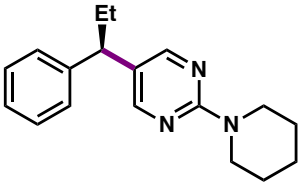
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.45 (dd, *J* = 8.1, 0.7 Hz, 1H), 7.36 – 7.23 (m, 5H), 7.21 – 7.09 (m, 2H), 6.50 (dd, *J* = 3.7, 0.8 Hz, 1H), 3.93 (t, *J* = 7.8 Hz, 1H), 2.22 – 2.08 (m, 2H), 1.66 (s, 9H), 0.93 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 145.8, 141.8, 128.9, 128.5, 128.0, 126.0, 125.8, 123.2, 120.8, 114.5, 107.2, 83.6, 53.8, 29.0, 28.4, 13.0.

FTIR (NaCl, thin film, cm^{-1}): 2971, 2930, 1734, 1437, 1378, 1343, 1254, 1147, 1129, 1024.

HRMS (FAB+, *m/z*): calc'd for $C_{22}H_{25}NO_2$ [M+H]$^+$: 335.1885; found: 335.1899.

5-(1-phenylpropyl)-2-(piperidin-1-yl)pyrimidine (88)



Prepared from 5-iodo-2-(piperidin-1-yl)pyrimidine (1 equiv, 58.0 mg, 0.2 mmol) and 1-(chloropropyl)benzene (2.4 equiv, 74 mg, 0.48 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **88** (40 mg, 71% yield) in 90% ee as a clear oil.

R$_f$ = 0.44 (silica gel, 10% EtOAc/hexane, UV).

Chiral SFC: (OB-H, 2.5 mL/min, 15% IPA in CO_2, λ = 254 nm): t_R(minor) = 5.1 min, t_R(major) = 7.7 min.

$[\alpha]_D^{25}$ = –9° (c = 1.0, $CHCl_3$).

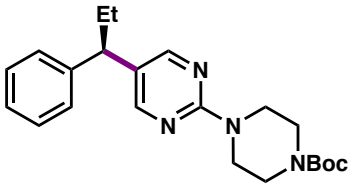
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (s, 2H), 7.33 – 7.24 (m, 2H), 7.23 – 7.13 (m, 3H), 3.80 – 3.68 (m, 4H), 3.60 (t, *J* = 7.8 Hz, 1H), 2.11 – 1.92 (m, 2H), 1.72 – 1.50 (m, 6H), 0.91 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 160.9, 157.3, 144.3, 128.7, 127.7, 126.4, 125.0, 48.1, 44.9, 28.3, 25.8, 25.0, 12.7.

FTIR (NaCl, thin film, cm^{-1}): 2931, 2852, 1599, 1537, 1505, 1462, 1446, 1364, 1271, 1255, 1022, 947.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{18}H_{23}N_3$ $[M+H]^+$: 282.1965; found: 282.1960.

***tert*-butyl-4-(5-(1-phenylpropyl)pyrimidin-2-yl)piperazine-1-carboxylate (89)**



Prepared from *tert*-butyl 4-(5-iodopyrimidin-2-yl)piperazine-1-carboxylate (1 equiv, 78.0 mg, 0.2 mmol) and 1-(chloropropyl)benzene (2.4 equiv, 74 mg, 0.48 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **89** (42 mg, 69% yield) in 91% ee as a clear oil.

R_f = 0.26 (silica gel, 10% EtOAc/hexane, UV).

Chiral SFC: (AD-H, 2.5 mL/min, 10% IPA in CO_2, λ = 254 nm): t_R(major) = 9.0 min, t_R(minor) = 10.1 min.

$[\alpha]_D^{25}$ = –7° (c = 1, $CHCl_3$).

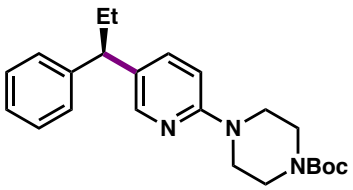
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.20 (s, 2H), 7.33 – 7.24 (m, 2H), 7.19 (d, *J* = 7.5 Hz, 3H), 3.75 (dd, *J* = 6.6, 4.0 Hz, 4H), 3.62 (t, *J* = 7.8 Hz, 1H), 3.47 (dd, *J* = 6.5, 4.0 Hz, 4H), 2.12 – 1.93 (m, 2H), 1.47 (s, 9H), 0.90 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 160.7, 157.3, 154.9, 144.1, 128.7, 127.7, 126.5, 126.3, 80.0, 48.0, 43.8, 28.5, 28.3, 12.7.

FTIR (NaCl, thin film, cm^{-1}): 2969, 2929, 2861, 1697, 1599, 1497, 1450, 1417, 1362, 1243, 1169, 1127, 998, 949.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{22}H_{30}N_4O_2$ $[M+H]^+$: 383.2442; found: 383.2433.

***tert*-butyl-4-(5-(1-phenylpropyl)pyridin-2-yl)piperazine-1-carboxylate (90)**



Prepared from *tert*-butyl 4-(5-iodopyridin-2-yl)piperazine-1-carboxylate (1 equiv, 78.0 mg, 0.2 mmol) and 1-(chloropropyl)benzene (2.4 equiv, 74 mg, 0.48 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **90** (65 mg, 85% yield) in 86% ee as a clear oil.

R_f = 0.36 (silica gel, 20% EtOAc/hexane, UV).

Chiral SFC: (OJ-H, 2.5 mL/min, 15% IPA in CO_2, λ = 235 nm): t_R(major) = 7.8 min, t_R(minor) = 8.7 min.

$[\alpha]_D^{25}$ = 1.4° (c = 1.0, $CHCl_3$).

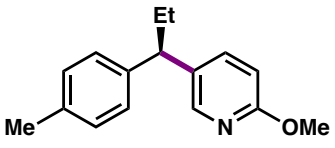
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (s, 2H), 7.34 – 7.23 (m, 2H), 7.23 – 7.13 (m, 3H), 3.85 – 3.66 (m, 4H), 3.60 (t, *J* = 7.8 Hz, 1H), 2.12 – 1.94 (m, 2H), 1.61 (dtt, *J* = 19.1, 7.5, 3.9 Hz, 6H), 0.91 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 160.5, 156.9, 144.0, 128.3, 127.4, 126.1, 124.7, 47.7, 44.6, 28.0, 25.5, 24.6, 12.4.

FTIR (NaCl, thin film, cm^{-1}): 2968, 2928, 2870, 2360, 2343, 1696, 1603, 1490, 1458, 1405, 1239, 1168, 1123, 99, 933.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{23}H_{31}N_3O_2$ $[M+H]^+$: 382.2489; found: 382.2483.

5-(1-(*p*-tolyl)propyl)-2-methoxypyridine (91)



Prepared from 2-methoxy-5-iodopyridine (1 equiv, 47.0 mg, 0.2 mmol) and 1-(1-chloropropyl)-4-methylbenzene (1.2 equiv, 40 mg, 0.24 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **91** (38 mg, 79% yield) in 92% ee as a colorless oil.

R_f = 0.32 (silica gel, 10% EtOAc/Hex, UV).

Chiral SFC: (OB-H, 2.5 mL/min, 5% IPA in CO_2, λ = 254 nm): t_R (major) = 5.3 min, t_R (minor) = 7.1 min.

$[\alpha]_D^{25}$ = +16.0° (c = 1.0, $CHCl_3$).

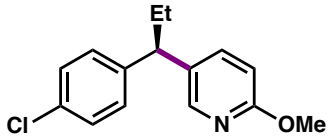
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (dt, *J* = 2.5, 0.7 Hz, 1H), 7.43 – 7.36 (m, 1H), 7.10 (s, 4H), 6.65 (dd, *J* = 8.5, 0.7 Hz, 1H), 3.90 (s, 3H), 3.70 (t, *J* = 7.8 Hz, 1H), 2.30 (s, 3H), 2.11 – 1.93 (m, 2H), 0.89 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 162.8, 145.7, 141.7, 138.3, 135.9, 133.5, 129.3, 127.7, 110.8, 53.4, 49.6, 28.5, 21.1, 12.8.

FTIR (NaCl, thin film, cm^{-1}): 2963, 2930, 2874, 1605, 1492, 1392, 1286, 1261, 1027, 820.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{16}H_{19}NO$ $[M+H]^+$: 242.1539; found: 242.1542.

5-(1-(4-chlorophenyl)propyl)-2-methoxypyridine (92)



Prepared from 2-methoxy-5-iodopyridine (1 equiv, 47.0 mg, 0.2 mmol) and 1-chloro-4-(1-chloropropyl)benzene (1.2 equiv, 45 mg, 0.24 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **92** (36 mg, 69% yield) in 85% ee as a colorless oil.

R_f = 0.24 (silica gel, 10% EtOAc/Hex, UV).

Chiral SFC: (OB-H, 2.5 mL/min, 5% IPA in CO_2, λ = 235 nm): t_R (minor) = 8.3 min, t_R (major) = 9.0 min.

$[\alpha]_D^{25}$ = 13.8° (c = 1.0, $CHCl_3$).

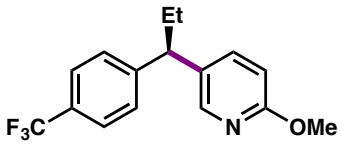
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (dt, *J* = 2.5, 0.7 Hz, 1H), 7.38 – 7.33 (m, 1H), 7.28 – 7.22 (m, 2H), 7.17 – 7.11 (m, 2H), 6.67 (dd, *J* = 8.6, 0.7 Hz, 1H), 3.90 (s, 3H), 3.71 (t, *J* = 7.8 Hz, 1H), 2.08 – 1.94 (m, 2H), 0.89 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 163.0, 145.8, 143.1, 138.2, 132.7, 132.1, 129.2, 128.8, 111.0, 53.5, 49.4, 28.4, 12.7.

FTIR (NaCl, thin film, cm^{-1}): 2964, 2932, 1605, 1572, 1489, 1461, 1392, 1291, 1262, 1027, 1014, 826.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{15}H_{16}ClNO$ $[M+H]^+$: 262.0993; found: 262.0995.

2-methoxy-5-(1-(4-(trifluoromethyl)phenyl)propyl)pyridine (93)



Prepared from 2-methoxy-5-iodopyridine (1 equiv, 47.0 mg, 0.2 mmol) and 1-(1-chloropropyl)-4-(trifluoromethyl)benzene (1.2 equiv, 53 mg, 0.24 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **93** (42 mg, 71% yield) in 88% ee as a colorless oil.

R_f = 0.31 (silica gel, 10% EtOAc/Hex, UV).

Chiral SFC: (AD-H, 2.5 mL/min, 2% IPA in CO_2, λ = 254 nm): t_R (minor) = 5.9 min, t_R (major) = 6.4 min.

$[\alpha]_D^{25}$ = 9.0° (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (dt, *J* = 2.5, 0.7 Hz, 1H), 7.61 – 7.48 (m, 2H), 7.37 (ddd, *J* = 8.6, 2.6, 0.5 Hz, 1H), 7.35 – 7.29 (m, 2H), 6.73 – 6.64 (m, 1H), 3.90 (s, 3H), 3.80 (t, *J* = 7.8 Hz, 1H), 2.13 – 1.99 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H).

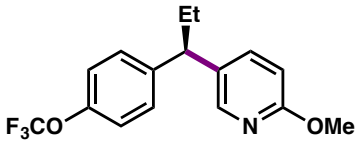
^{13}C NMR (101 MHz, $CDCl_3$): δ 163.1, 148.7, 145.9, 138.2, 132.2, 128.74 (q, *J* = 32.4 Hz), 128.2, 125.61 (q, *J* = 3.9 Hz), 124.3 (q, *J* = 271.7 Hz), 111.1, 53.5, 49.8, 28.3, 12.7.

^{19}F NMR (282 MHz, $CDCl_3$): δ –62.4.

FTIR (NaCl, thin film, cm^{-1}): 2967, 2937, 1618, 1605, 1493, 1325, 1289, 1165, 1122, 1068, 1018, 828.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{16}H_{16}F_3NO$ $[M+H]^+$: 296.1257; found: 296.1265.

2-methoxy-5-(1-(4-(trifluoromethoxy)phenyl)propyl)pyridine (74)



Prepared from 2-methoxy-5-iodopyridine (1 equiv, 47.0 mg, 0.2 mmol) and 1-(1-chloropropyl)-4-(trifluoromethoxy)benzene (1.2 equiv, 57 mg, 0.24 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **74** (47 mg, 76% yield) in 87% ee as a colorless oil.

R_f = 0.26 (silica gel, 10% EtOAc/Hex, UV).

Chiral SFC: (AD-H, 2.5 mL/min, 5% IPA in CO_2, λ = 245 nm): t_R (minor) = 3.0 min, t_R (major) = 3.3 min.

$[\alpha]_D^{25}$ = +10.0° (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (dt, *J* = 2.6, 0.7 Hz, 1H), 7.41 – 7.34 (m, 1H), 7.25 – 7.19 (m, 2H), 7.13 (ddt, *J* = 7.6, 2.1, 1.1 Hz, 2H), 6.68 (dd, *J* = 8.5, 0.7 Hz, 1H), 3.91 (s, 3H), 3.75 (t, *J* = 7.8 Hz, 1H), 2.11 – 1.94 (m, 2H), 0.90 (t, *J* = 7.3 Hz, 3H).

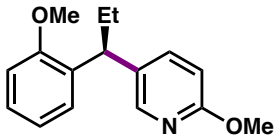
^{13}C NMR (101 MHz, $CDCl_3$): δ 163.0, 145.8, 143.4, 138.3, 132.6, 129.1, 128.2 (d, *J* = 62.1 Hz), 121.2, 120.6 (q, *J* = 257.7 Hz), 111.0, 53.5, 49.3, 28.5, 12.7.

^{19}F NMR (282 MHz, $CDCl_3$): δ –57.9.

FTIR (NaCl, thin film, cm^{-1}): 2967, 2935, 2877, 1605, 1508, 1493, 1259, 1222, 12264, 1027.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{16}H_{16}F_3NO_2$ $[M+H]^+$: 312.1206; found: 312.1198.

2-methoxy-5-(1-(2-methoxyphenyl)propyl)pyridine (94)



Prepared from 2-methoxy-5-iodopyridine (1 equiv, 47.0 mg, 0.2 mmol) and 1-(1-chloropropyl)-2-methoxybenzene (1.2 equiv, 44 mg, 0.24 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **94** (24 mg, 47% yield) in 93% ee as a colorless oil.

R_f = 0.24 (silica gel, 10% EtOAc/Hex, UV).

Chiral SFC: (OB-H, 2.5 mL/min, 5% IPA in CO_2, λ = 235 nm): t_R (minor) = 4.9 min, t_R (major) = 5.7 min.

$[\alpha]_D^{25}$ = –24.6° (c = 1.0, $CHCl_3$).

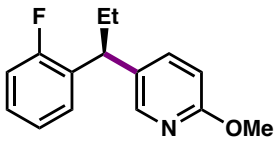
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (dt, *J* = 2.5, 0.7 Hz, 1H), 7.42 (ddd, *J* = 8.6, 2.5, 0.5 Hz, 1H), 7.23 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.17 (ddd, *J* = 8.2, 7.4, 1.7 Hz, 1H), 6.92 (td, *J* = 7.5, 1.2 Hz, 1H), 6.82 (dd, *J* = 8.2, 1.1 Hz, 1H), 6.66 – 6.60 (m, 1H), 4.18 (t, *J* = 7.8 Hz, 1H), 3.89 (s, 3H), 3.77 (s, 3H), 2.13 – 1.90 (m, 2H), 0.89 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 162.6, 157.1, 146.3, 138.5, 133.2, 133.1, 127.3, 127.2, 120.6, 110.7, 110.4, 55.5, 53.4, 42.2, 27.6, 12.8.

FTIR (NaCl, thin film, cm^{-1}): 2962, 2937, 1604, 1572, 1489, 1463, 1394, 1287, 1242, 1029, 753.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{16}H_{19}NO_2$ $[M+H]^+$: 258.1489; found: 258.1487.

2-methoxy-5-(1-(2-fluorophenyl)propyl)pyridine (95)



Prepared from 2-methoxy-5-iodopyridine (1 equiv, 47.0 mg, 0.2 mmol) and 1-(1-chloropropyl)-2-fluorobenzene (1.2 equiv, 41 mg, 0.24 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **95** (26 mg, 53% yield) in 93% ee as a colorless oil.

$\mathbf{R}_f$ = 0.30 (silica gel, 10% EtOAc/Hex, UV).

Chiral SFC: (AD-H, 2.5 mL/min, 10% IPA in CO_2, λ = 254 nm): t_R (major) = 2.8 min, t_R (minor) = 3.3 min.

$[\alpha]_D^{25}$ = +5.9° (c = 0.97, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 – 8.04 (m, 1H), 7.44 (dd, *J* = 8.6, 2.5 Hz, 1H), 7.29 – 7.20 (m, 1H), 7.17 (dddd, *J* = 8.1, 7.2, 5.2, 1.9 Hz, 1H), 7.09 (td, *J* = 7.5, 1.4 Hz, 1H), 6.99 (ddd, *J* = 10.5, 8.1, 1.4 Hz, 1H), 6.66 (dd, *J* = 8.6, 0.7 Hz, 1H), 4.09 (t, *J* = 7.9 Hz, 1H), 3.90 (s, 3H), 2.15 – 1.96 (m, 2H), 0.92 (t, *J* = 7.3 Hz, 3H).

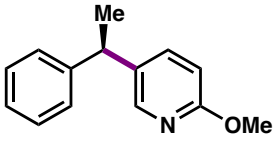
^{13}C NMR (101 MHz, $CDCl_3$): δ 162.9, 162.1, 159.6, 146.1, 138.4, 132.1, 131.6 (d, *J* = 14.3 Hz), 128.2 (dd, J = 40.4, 4.2), 124.3 (d, J = 3.54Hz), 115.7 (d, *J* = 22.7 Hz), 110.7, 53.5, 42.5, 27.6, 12.7.

^{19}F NMR (282 MHz, $CDCl_3$): δ –117.9.

FTIR (NaCl, thin film, cm^{-1}): 2965, 2943, 1605, 1572, 1492, 1455, 1394, 1289, 1262, 1027, 755.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{15}H_{16}FNO$ $[M+H]^+$: 246.1289; found: 246.1287.

2-methoxy-5-(1-phenylethyl)pyridine (96)



Prepared from 2-methoxy-5-iodopyridine (1 equiv, 47.0 mg, 0.2 mmol) and (1-chloroethyl)benzene (1.2 equiv, 34 mg, 0.24 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **96** (36 mg, 84% yield) in 85% ee as a colorless oil.

$\mathbf{R}_f$ = 0.35 (silica gel, 20% Et_2O/Hex, UV).

Chiral SFC: (OJ-H, 2.5 mL/min, 4% IPA in CO_2, λ = 254 nm): t_R (minor) = 5.7 min, t_R (major) = 6.3 min.

$[\alpha]_D^{25}$ = +3.5° (c = 1.0, $CHCl_3$).

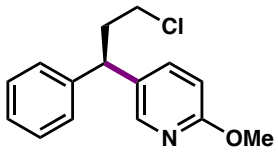
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.07 (dt, *J* = 2.5, 0.7 Hz, 1H), 7.38 (ddd, *J* = 8.6, 2.5, 0.5 Hz, 1H), 7.33 – 7.27 (m, 2H), 7.23 – 7.17 (m, 3H), 6.66 (dt, *J* = 8.5, 0.5 Hz, 1H), 4.10 (q, *J* = 7.2 Hz, 1H), 3.91 (s, 3H), 1.63 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 162.8, 145.8, 145.4, 138.3, 134.5, 128.6, 127.6, 126.4, 110.7, 53.5, 41.7, 21.8.

FTIR (NaCl, thin film, cm^{-1}): 3026, 2966, 2927, 1606, 1571, 1492, 1390, 1284, 1025, 831, 699.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{15}H_{15}NO$ $[M+H]^+$: 214.1226; found: 214.1220.

2-methoxy-5-(3-chloro-1-phenylpropyl)pyridine (97)



Prepared from 2-methoxy-5-iodopyridine (1 equiv, 47.0 mg, 0.2 mmol) and (1,3-dichloropropyl)benzene (1.2 equiv, 41.0 mg, 0.24 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **97** (41 mg, 79% yield) in 91% ee as a colorless oil.

R_f = 0.28 (silica gel, 10% EtOAc/Hex, UV).

Chiral SFC: (AD-H, 2.5 mL/min, 8% IPA in CO_2, λ = 210 nm): t_R (major) = 6.0 min, t_R (minor) = 7.2 min.

$[\alpha]_D^{25}$ = +4.2° (c = 1.0, $CHCl_3$).

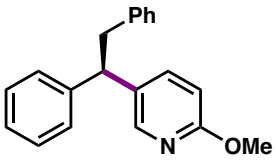
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (dt, *J* = 2.6, 0.7 Hz, 1H), 7.42 (ddd, *J* = 8.6, 2.6, 0.5 Hz, 1H), 7.34 – 7.27 (m, 2H), 7.25 – 7.18 (m, 3H), 6.68 (dd, *J* = 8.5, 0.7 Hz, 1H), 4.18 (t, *J* = 7.8 Hz, 1H), 3.91 (s, 3H), 3.45 (t, *J* = 6.5 Hz, 2H), 2.58 – 2.36 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 163.1, 145.8, 143.0, 138.4, 131.8, 128.9, 127.9, 126.9, 111.1, 53.5, 44.7, 43.0, 37.9.

FTIR (NaCl, thin film, cm^{-1}): 2945, 1719, 1605, 1572, 1489, 1453, 1394, 1291, 1028, 829, 753, 700.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{15}H_{16}ClNO$ $[M+H]^+$: 262.0993; found: 262.1003.

2-methoxy-5-(1,2-diphenylethyl)pyridine (98)



Prepared from 2-methoxy-5-iodopyridine (1 equiv, 47.0 mg, 0.2 mmol) and (1-chloro-1,2-diphenylethane (1.2 equiv, 52.0 mg, 0.24 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **98** (26 mg, 55% yield) in 95% ee as a colorless oil.

$\mathbf{R}_f$ = 0.32 (silica gel, 10% EtOAc/Hex, UV, $KMnO_4$).

Chiral SFC: (AD-H, 2.5 mL/min, 12% IPA in CO_2, λ = 280 nm): t_R (major) = 5.7 min, t_R (minor) = 6.6 min.

$[\alpha]_D^{25}$ = +37.9° (c = 0.865, $CHCl_3$).

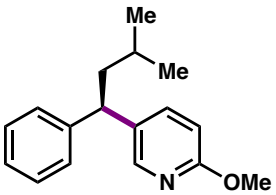
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.95 (dt, *J* = 2.5, 0.7 Hz, 1H), 7.38 (ddd, *J* = 8.5, 2.6, 0.5 Hz, 1H), 7.31 – 7.23 (m, 2H), 7.23 – 7.16 (m, 5H), 7.16 – 7.10 (m, 1H), 7.04 – 6.99 (m, 2H), 6.63 (dd, *J* = 8.5, 0.7 Hz, 1H), 4.18 (dd, *J* = 8.6, 7.2 Hz, 1H), 3.88 (s, 3H), 3.37 (dd, *J* = 13.6, 7.1 Hz, 1H), 3.29 (dd, *J* = 13.7, 8.6 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 162.8, 146.0, 144.1, 139.8, 138.6, 132.5, 129.2, 128.6, 128.3, 128.0, 126.6, 126.2, 110.7, 53.5, 50.0, 42.0.

FTIR (NaCl, thin film, cm^{-1}): 3027, 2943, 1606, 1571, 1492, 1453, 1393, 1291, 1029, 698.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{20}H_{19}NO$ $[M+H]^+$: 290.1539; found: 290.1527.

2-methoxy-5-(3-methyl-1-phenylbutyl)pyridine (99)



Prepared from 2-methoxy-5-iodopyridine (1 equiv, 47.0 mg, 0.2 mmol) and (1-chloro-3-methylbutyl)benzene (1.2 equiv, 44.0 mg, 0.24 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **99** (30 mg, 74% yield) in 94% ee as a colorless oil.

$\mathbf{R}_f$ = 0.32 (silica gel, 10% EtOAc/Hex, UV).

Chiral SFC: (AD-H, 2.5 mL/min, 5% IPA in CO_2, λ = 254 nm): t_R (major) = 4.9 min, t_R (minor) = 5.6 min.

$[\alpha]_D^{25}$ = +8.9° (c = 1.0, $CHCl_3$).

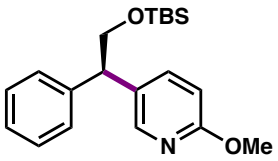
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.07 (dt, *J* = 2.6, 0.7 Hz, 1H), 7.42 (dd, *J* = 8.6, 2.5 Hz, 1H), 7.32 – 7.24 (m, 2H), 7.25 – 7.20 (m, 2H), 7.20 – 7.15 (m, 1H), 6.67 (dd, *J* = 8.5, 0.7 Hz, 1H), 3.97 (t, *J* = 8.0 Hz, 1H), 3.91 (s, 3H), 1.89 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 2H), 1.50 – 1.39 (m, 1H), 0.93 (d, *J* = 6.6 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 162.8, 145.8, 144.8, 138.4, 133.4, 128.7, 127.8, 126.4, 110.8, 53.5, 45.7, 44.9, 25.6, 22.8, 22.6.

FTIR (NaCl, thin film, cm^{-1}): 2955, 2868, 1605, 1572, 1489, 1466, 1452, 1393, 1286, 1259, 1029, 699.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{17}H_{21}NO$ $[M+H]^+$: 256.1696; found: 256.1697.

5-(2-((*tert*-butyldimethylsilyl)oxy)-1-phenylethyl)-2-methoxypyridine (100)



Prepared from 2-methoxy-5-iodopyridine (1 equiv, 47.0 mg, 0.2 mmol) and *tert*-butyl(2-chloro-2-phenylethoxy)dimethylsilane (1.2 equiv, 54.0 mg, 0.24 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **100** (25 mg, 36% yield) in 94% ee as a colorless oil.

R_f = 0.50 (silica gel, 10% EtOAc/hexanes).

Chiral SFC: (AD-H, 2.5 mL/min, 5% IPA in CO_2, λ = 235 nm): t_R (major) = 2.9 min, t_R (minor) = 3.3 min.

$[\alpha]_D^{25}$ = +5.9° (c = 1.0, $CHCl_3$).

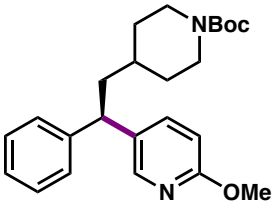
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, *J* = 2.5 Hz, 1H), 7.45 (dd, *J* = 8.6, 2.5 Hz, 1H), 7.33 – 7.25 (m, 3H), 7.25 – 7.17 (m, 3H), 6.67 (dd, *J* = 8.6, 0.7 Hz, 1H), 4.15 – 4.04 (m, 3H), 3.91 (s, 3H), 0.81 (s, 9H), -0.06 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 163.0, 146.6, 142.0, 139.2, 130.9, 128.5, 128.5, 126.7, 110.4, 66.6, 53.5, 50.5, 25.9, 18.3, -5.4.

FTIR (NaCl, thin film, cm^{-1}): 2952, 2928, 1606, 1492, 1289, 1257, 1105, 1030.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{20}H_{29}NO_2Si$ $[M+H]^+$: 344.2040; found: 344.2030.

tert-butyl-4-(2-(6-methoxypyridin-3-yl)-2-phenylethyl)piperidine-1-carboxylate (101)



Prepared from 2-methoxy-5-iodopyridine (1 equiv, 47.0 mg, 0.2 mmol) and *tert*-butyl 4-(2-chloro-2-phenylethyl)piperidine-1-carboxylate (1.2 equiv, 78.0 mg, 0.24 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **101** (48 mg, 60% yield) in 94% ee as a colorless oil.

R_f = 0.26 (silica gel, 10% EtOAc/Hexanes).

Chiral SFC: (AD-H, 2.5 mL/min, 15% IPA in CO_2, λ = 280 nm): t_R (major) = 7.6 min, t_R (minor) = 11.3 min.

$[\alpha]_D^{25}$ = +6.7° (c = 1.0, $CHCl_3$).

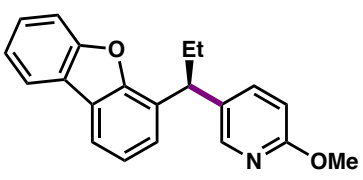
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (dd, *J* = 2.5, 0.7 Hz, 1H), 7.40 (dd, *J* = 8.6, 2.5 Hz, 1H), 7.33 – 7.23 (m, 2H), 7.24 – 7.15 (m, 3H), 6.66 (dd, *J* = 8.6, 0.7 Hz, 1H), 3.99 (t, *J* = 8.0 Hz, 2H), 3.89 (s, 3H), 2.56 (t, *J* = 12.2 Hz, 2H), 1.94 (ddd, *J* = 8.5, 6.7, 2.1 Hz, 2H), 1.69 (d, *J* = 12.9 Hz, 2H), 1.44 (s, 9H), 1.29 (dtd, *J* = 14.4, 7.4, 6.9, 3.8 Hz, 2H), 1.23 – 1.04 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 162.9, 154.9, 145.6, 144.4, 138.2, 132.9, 128.8, 127.7, 126.5, 111.0, 79.3, 53.4, 44.6, 42.5, 33.5, 32.3, 32.1, 28.6.

FTIR (NaCl, thin film, cm^{-1}): 2922, 1690, 1604, 1491, 1423, 1393, 1365, 1285, 1244, 1166, 1122, 1029.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{24}H_{32}N_2O_3$ $[M+H]^+$: 397.2486; found: 397.2473.

2-methoxy-5-(1-(dibenzo[*b,d*]furan-4-yl)propyl)pyridine (102)



Prepared from 2-methoxy-5-iodopyridine (1 equiv, 47.0 mg, 0.2 mmol) and 4-(1-chloropropyl)dibenzo[*b,d*]furan (1.2 equiv, 59.0 mg, 0.24 mmol) following General Procedure 3. The crude residue was purified by column chromatography to yield **102** (30 mg, 48% yield) in 93% ee as a colorless oil.

R_f = 0.31 (silica gel, 10% EtOAc/Hex, UV).

Chiral SFC: (OB-H, 2.5 mL/min, 10% IPA in CO_2, λ = 254 nm): t_R (minor) = 6.5 min, t_R (major) = 7.2 min.

$[\alpha]_D^{25}$ = –97.0° (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (dt, *J* = 2.5, 0.7 Hz, 1H), 7.92 (ddd, *J* = 7.7, 1.4, 0.7 Hz, 1H), 7.80 (dd, *J* = 7.3, 1.6 Hz, 1H), 7.62 – 7.54 (m, 2H), 7.45 (ddd, *J* = 8.3, 7.3, 1.4 Hz, 1H), 7.37 – 7.27 (m, 3H), 6.66 (dd, *J* = 8.5, 0.7 Hz, 1H), 4.42 (t, *J* = 7.9 Hz, 1H), 3.89 (s, 3H), 2.39 – 2.12 (m, 2H), 0.97 (t, *J* = 7.3 Hz, 3H).

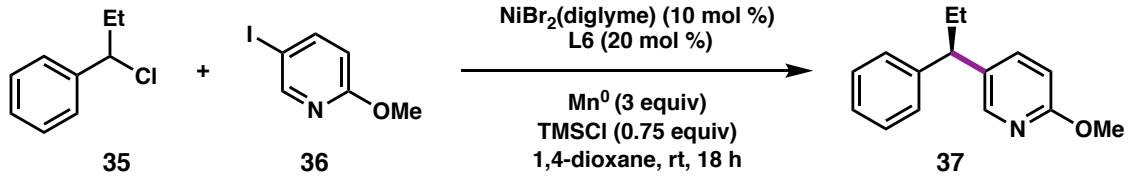
^{13}C NMR (101 MHz, $CDCl_3$): δ 162.9, 156.1, 154.3, 146.2, 138.5, 132.3, 128.8, 127.2, 125.3, 124.6, 124.3, 123.1, 122.8, 120.8, 118.8, 111.9, 110.7, 53.4, 44.2, 27.6, 12.9.

FTIR (NaCl, thin film, cm^{-1}): 2964, 1605, 1572, 1489, 1451, 1422, 1394, 1291, 1184, 1027, 828, 752.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{21}H_{19}NO_2$ $[M+H]^+$: 318.1489; found: 318.1486.

2.6.5 Mechanistic Experiments

2.6.5.1 Inhibitor Studies

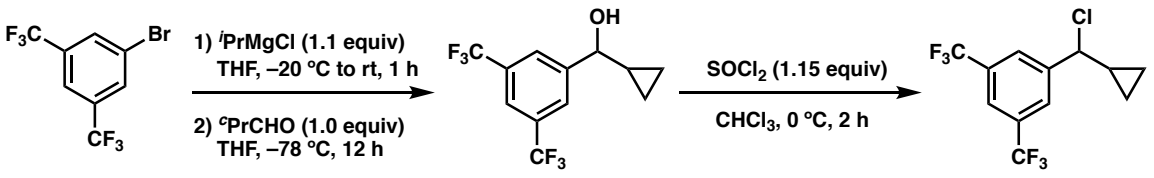


35 36 37

Control:	84% yield, 90% ee
50 mol % BHT:	83% yield, 89% ee
50 mol % DHA:	78% yield, 88% ee
50 mol % TEMPO:	72% yield, 91% ee

The experiment was conducted according to General Procedure 2 for cross-coupling, except that either BHT (0.025 mmol, 4.5 mg, 0.5 equiv), DHA (0.025 mmol, 5.5 mg, 0.5 equiv), or TEMPO (0.25 mmol, 3.9 mg, 0.5 equiv) were added prior to pumping into the glovebox. After 18 h, the reactions were light gray. The vials were opened and the reactions diluted with 20% Et_2O/hexanes and filtered through short basic alumina plugs. Analysis of the crude reaction mixture by ^1H NMR with 2,3,5,6-tetrachloronitrobenzene as a standard showed no inhibition.

2.6.5.2 Radical Clock Experiment



The aryl bromide (12 mmol, 2.07 mL, 1.0 equiv) was dissolved in 10 mL THF in a flame-dried round bottom flask and cooled to –20 ºC. ^{i}PrMgCl (13.2 mmol, 6.6 mL, 1.1 equiv) was added slowly and the reaction was warmed to 0 ºC for 1 hour. The aldehyde (12 mmol, 0.9 mL, 1.0 equiv) was dissolved in 30 mL dry THF in a flame-dried flask and

cooled to –78 ºC. The Grignard was added to the reaction flask slowly via cannula and the reaction was allowed to stir overnight, warming slowly to room temperature. The reaction was quenched with 30 mL sat. NH_4Cl and the aqueous layer was separated and extracted with 2 x 30 mL Et_2O. The combined organic layers were dried with Na_2SO_4, filtered and concentrated. The alcohol was purified by loading onto a silica plug and first eluting with hexane, then switching to Et_2O. Et_2O wash was concentrated to afford an off-white solid. (2.63 g, 77% yield).

R_f= 0.38 (silica gel, 20% EtOAc/hexanes, UV)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (dq, *J* = 1.3, 0.6 Hz, 2H), 7.80 (t, *J* = 1.4 Hz, 1H), 4.11 (dd, *J* = 8.6, 2.9 Hz, 1H), 2.11 (d, *J* = 2.9 Hz, 1H), 1.25 – 1.14 (m, 1H), 0.78 – 0.64 (m, 2H), 0.58 – 0.44 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 146.4, 131.69 (q, *J* = 33.2 Hz), 126.3, 123.5 (q, *J* = 273.8 Hz), 121.52 (t, *J* = 3.9 Hz), 19.8, 3.8, 3.6.

^{19}F NMR (282 MHz, $CDCl_3$): δ –62.8.

FTIR (NaCl, thin film, cm^{-1}): 3388, 1660, 1378, 1280, 1140, 1043, 901, 843, 683.

HRMS (EI+, m/z): calc'd for $C_{12}H_{10}F_6O$ $[M-F]^+$: 265.0652; found: 265.0658.

The alcohol (5.0 mmol, 1.42 g, 1 equiv) was dissolved in $CHCl_3$ (20 mL) in a flame-dried flask under N_2. The reaction was cooled to 0 ºC, then $SOCl_2$ (5.75 mmol, 0.42 mL, 1.15 equiv) was added. Reaction was allowed to stir for 2 hours, at which point monitoring by TLC showed the starting material was completely consumed. The reaction was concentrated and purified by silica gel chromatography (2% Et_2O/pentane) to afford the clean chloride as a clear oil (0.99 g, 65% yield). Care was taken to minimize exposure

to light or heat during reaction, concentration, and handling. The material was wrapped in foil and stored at –20 ºC.

R_f= 0.46 (silica gel, 5% EtOAc/hexanes, UV)

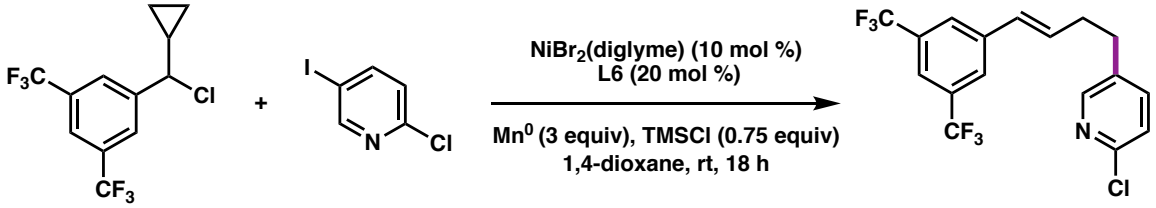
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.98 – 7.88 (m, 2H), 7.87 – 7.82 (m, 1H), 4.36 (d, *J* = 9.2 Hz, 1H), 1.64 – 1.44 (m, 1H), 0.91 (dddd, *J* = 8.9, 7.9, 5.9, 4.7 Hz, 1H), 0.78 (dddd, *J* = 8.7, 7.8, 5.9, 4.7 Hz, 1H), 0.66 (ddt, *J* = 9.5, 5.8, 4.8 Hz, 1H), 0.48 (ddt, *J* = 9.4, 5.7, 4.7 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 144.3, 132.10 (q, *J* = 33.4 Hz), 127.5, 123.2 (q, *J* = 272.6 Hz), 122.30 (dt, *J* = 7.5, 3.5 Hz), 66.6, 19.7, 6.8, 6.4.

^{19}F NMR (282 MHz, $CDCl_3$): δ –62.9.

FTIR (NaCl, thin film, cm^{-1}): 3433, 1627, 1466, 1375, 1279, 1177, 899, 682.

HRMS (EI+, m/z): calc'd for $C_{12}H_9ClF_6$ $[M-F]^+$: 283.0313; found: 283.0351.



113 **58** **57% yield** **115**

The cross coupling of radical clock substrate **113** was performed according to General Procedure 2, employing 2-chloro-5-iodopyridine (1 equiv, 12.0 mg, 0.05 mmol) and 1-(chloro(cyclopropyl)methyl)-3-(trifluoromethyl)benzene (1.2 equiv, 18.0 mg, 0.06 mmol). The crude reaction mixture contained the rearranged product **115** as the only cross-coupled product. No cyclopropyl peaks were remaining in the crude ^{1}H NMR. **115**

was reported as 57% yield after analysis of the crude reaction mixture by ^{1}H NMR with 2,3,5,6-tetrachloronitrobenzene as an internal standard.

R_f= 0.09 (silica gel, 5% Et_2O/10% PhMe/85% hexanes, UV)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.26 (dd, *J* = 2.5, 0.7 Hz, 1H), 7.71 (d, *J* = 4.2 Hz, 3H), 7.50 (dd, *J* = 8.1, 2.5 Hz, 1H), 7.27 (dd, *J* = 8.1, 0.7 Hz, 1H), 6.55 – 6.29 (m, 2H), 2.82 (dd, *J* = 8.5, 6.7 Hz, 2H), 2.58 (ddd, *J* = 9.3, 7.3, 6.1 Hz, 2H).

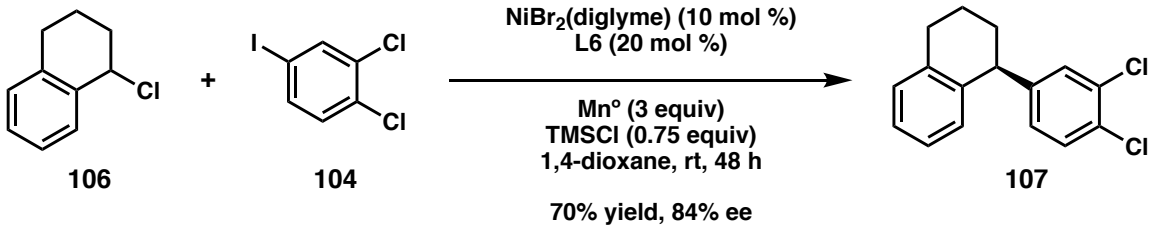
^{13}C NMR (101 MHz, $CDCl_3$): δ 149.7, 149.6, 139.3, 138.9, 135.4, 132.9, 132.02 (q, *J* = 33.1 Hz), 129.1, 126.11 – 125.87 (m), 124.2, 123.4 (q, *J* = 270.9 Hz), 120.81 (dt, *J* = 7.8, 3.9 Hz), 34.4, 31.8.

^{19}F NMR (282 MHz, $CDCl_3$): δ –63.0.

FTIR (NaCl, thin film, cm^{-1}): 2931, 2358, 1463, 1382, 1279, 1175, 1132.

HRMS (ESI-TOF, m/z): calc'd for $C_{17}H_{12}ClF_6N$ $[M+H]^+$: 380.0635; found: 380.0640.

2.6.6 Formal Synthesis of Sertraline



106 104 107

Prepared from 1,2-dichloro-4-iodobenzene (1 equiv, 55.0 mg, 0.2 mmol) and 1-chloro-1,2,3,4-tetrahydronaphthalene (2.4 equiv, 80.0 mg, 0.48 mmol) following General Procedure 3, stirring for 48 hours. The crude residue was purified by column chromatography to yield **107** (38 mg, 70% yield) in 84% ee as a colorless solid.

$\mathbf{R}_f$ = 0.26 (silica gel, 100% hexanes, UV).

Chiral SFC: (AD-H, 2.5 mL/min, 3% IPA in CO_2, λ = 235 nm): t_R (major) = 8.2 min, t_R (minor) = 10.6 min.

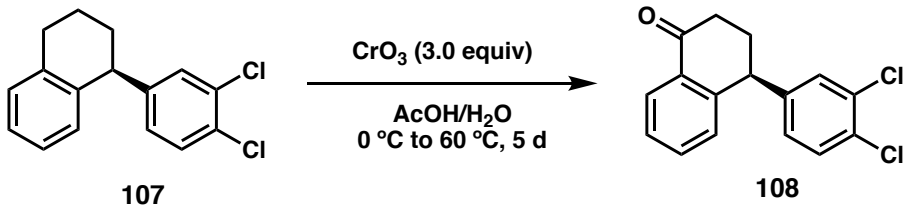
$[\alpha]_D^{25}$ = +10.0° (c = 1.0, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34 (d, *J* = 8.3 Hz, 1H), 7.19 (d, *J* = 2.1 Hz, 1H), 7.18 – 7.12 (m, 2H), 7.09 – 7.02 (m, 1H), 6.92 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.80 (dd, *J* = 7.7, 1.0 Hz, 1H), 4.11 – 4.05 (m, 1H), 2.98 – 2.78 (m, 2H), 2.20 – 2.10 (m, 1H), 1.92 – 1.70 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 148.0, 138.1, 137.7, 132.3, 130.8, 130.3, 130.1, 130.0, 129.3, 128.4, 126.5, 126.0, 45.0, 33.2, 29.7, 20.8.

FTIR (neat, cm^{-1}): 2358, 2325, 2330, 1480, 1458, 885, 667, 621.

HRMS (FAB+, *m/z*): calc'd for $C_{16}H_{14}Cl_2$ $[(M+H) - H_2]^+$: 275.0394; found: 275.0386.



107 **108**

107 (6.5 mg, 0.023 mmol, 1 equiv) was dissolved in 0.25 mL of AcOH in a 1-dram vial and cooled to 0 ºC. The ice bath was removed and CrO_3 (7 mg, 0.070 mmol, 3 equiv) was added as an 8:2 solution in AcOH/H_2O (0.7 M). The reaction was allowed to warm to room temperature slowly, then heated to 60 ºC for 5 days. The reaction was quenched with a few drops of EtOH and then carefully neutralized with sat. $NaHCO_3$ solution. The aqueous layer was separated and extracted three times with EtOAc. The combined organic layers were dried with Na_2SO_4, filtered, and concentrated. The crude residue was purified by column chromatography to yield **108** (3.5 mg, 51% yield) in 84% ee as a white solid.

$\mathbf{R_f}$ = 0.33 (silica gel, 20% EtOAc/Hex, UV).

Chiral SFC: (OJ-H, 2.5 mL/min, 20% IPA in CO_2, λ = 254 nm): t_R (major) = 3.7 min, t_R (minor) = 4.0 min.

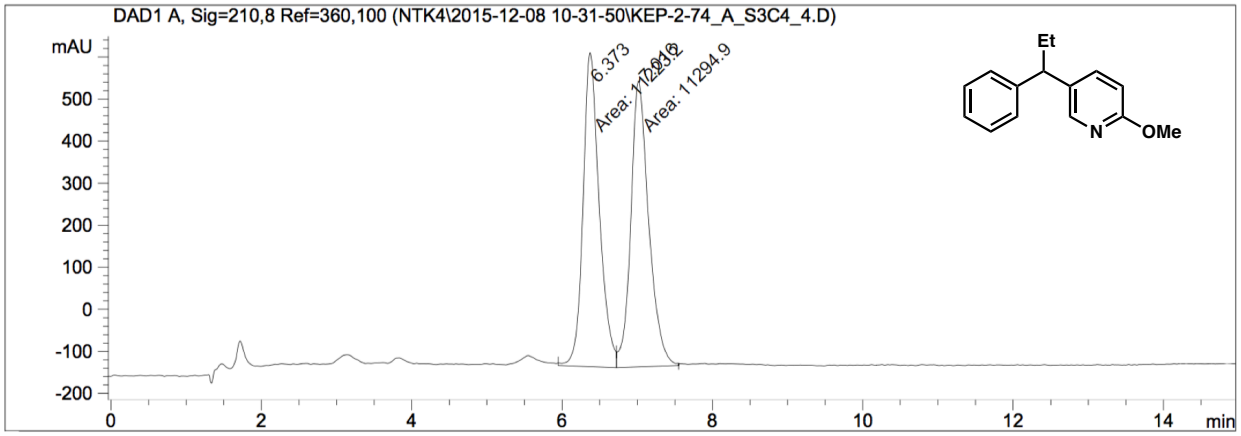
$\mathbf{[\alpha]_D^{25}}$ = +36.3° (c = 0.8, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.12 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.47 (td, *J* = 7.5, 1.5 Hz, 1H), 7.39 (dd, *J* = 8.2, 6.6 Hz, 2H), 7.22 (d, *J* = 2.1 Hz, 1H), 6.98 – 6.92 (m, 2H), 4.28 (dd, *J* = 8.2, 4.5 Hz, 1H), 2.77 – 2.60 (m, 2H), 2.48 (ddt, *J* = 13.4, 7.9, 4.6 Hz, 1H), 2.27 (dddd, *J* = 13.5, 9.3, 8.1, 4.5 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 197.6, 145.0, 144.1, 134.0, 132.9, 132.8, 131.1, 130.8, 130.7, 129.4, 128.1, 127.7, 127.5, 44.7, 36.7, 31.8.

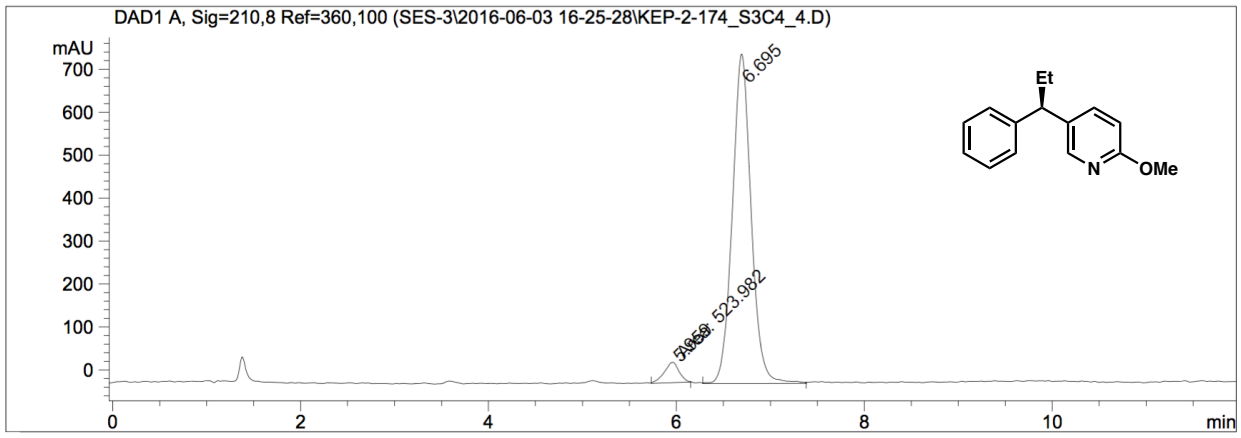
2.6.7 SFC Traces of Racemic and Enantioenriched Products

37 (Table 2.11): racemic



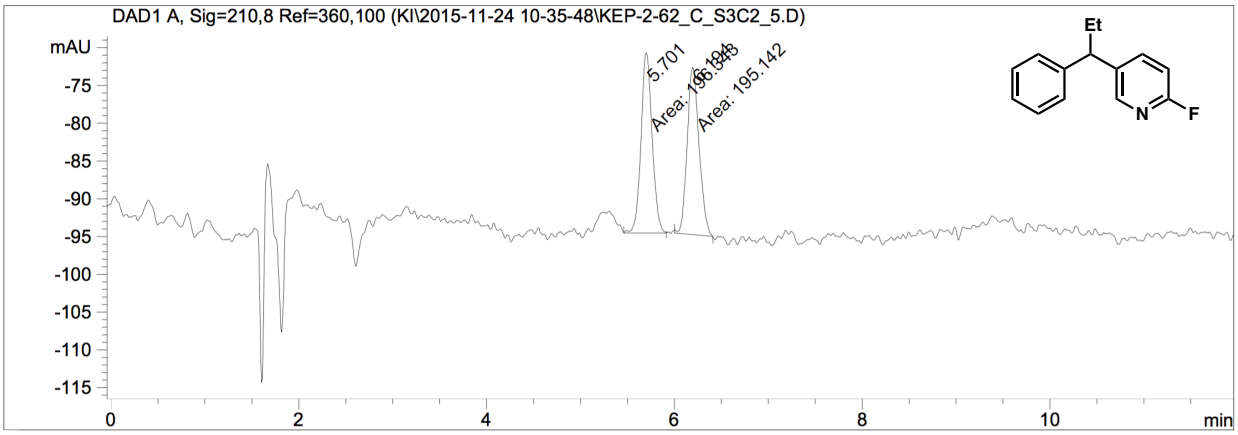
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.373	MM	0.2504	1.12232e4	746.91840	49.8408
2	7.016	MM	0.2768	1.12949e4	680.19781	50.1592

37 (Table 2.11): enantioenriched, 91% ee



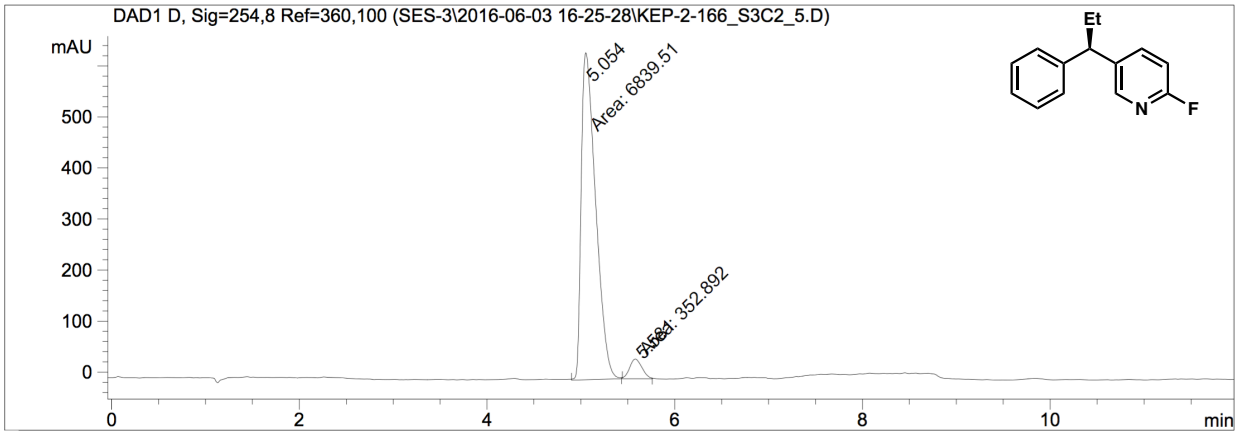
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.959	MM	0.1834	523.98187	47.63037	4.6799
2	6.695	VV	0.2104	1.06724e4	766.47681	95.3201

77 (Table 2.11): racemic



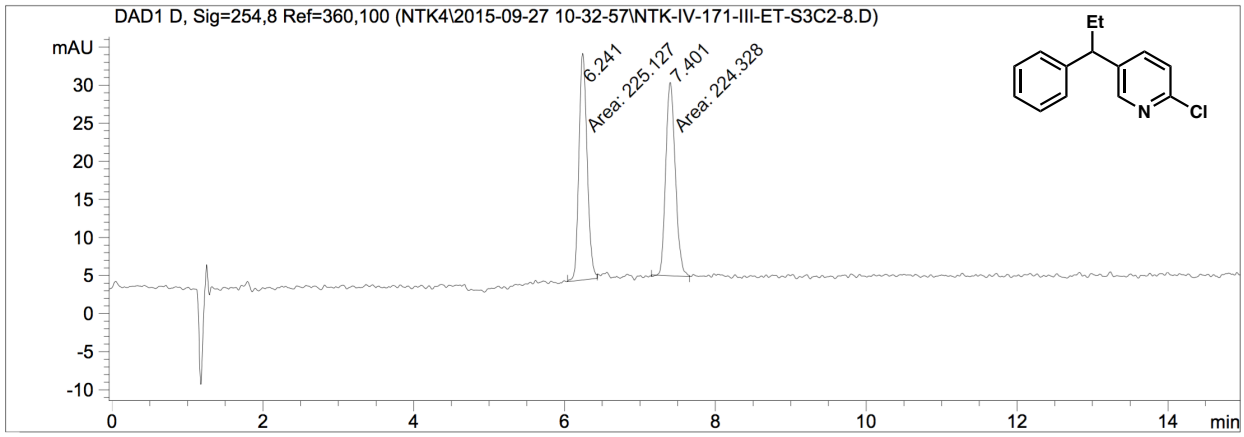
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.701	MM	0.1369	196.34299	23.90764	50.1534
2	6.194	MM	0.1463	195.14195	22.22900	49.8466

77 (Table 2.11): enantioenriched, 90% ee



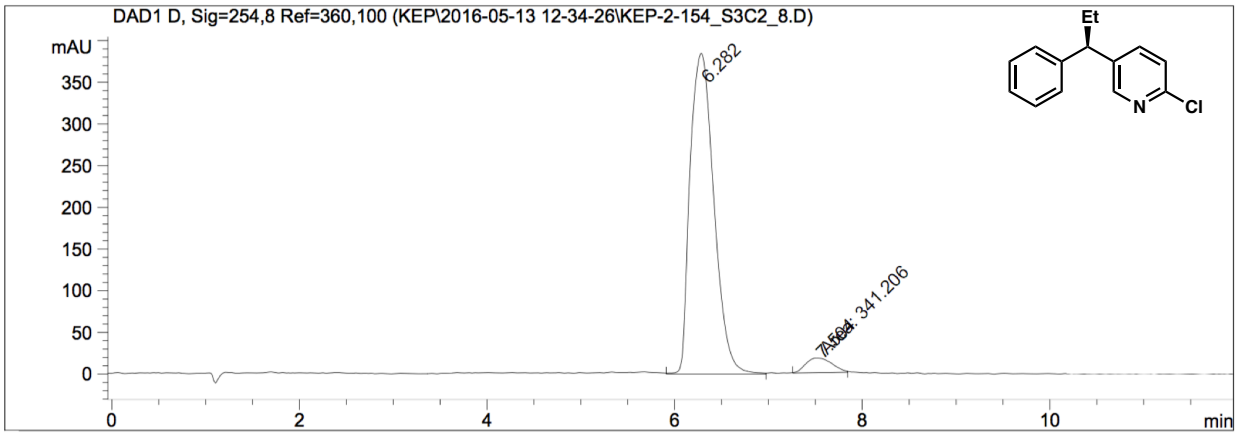
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.054	MM	0.1774	6839.51270	642.44238	95.0935
2	5.581	MM	0.1514	352.89209	38.86046	4.9065

78 (Table 2.11): racemic



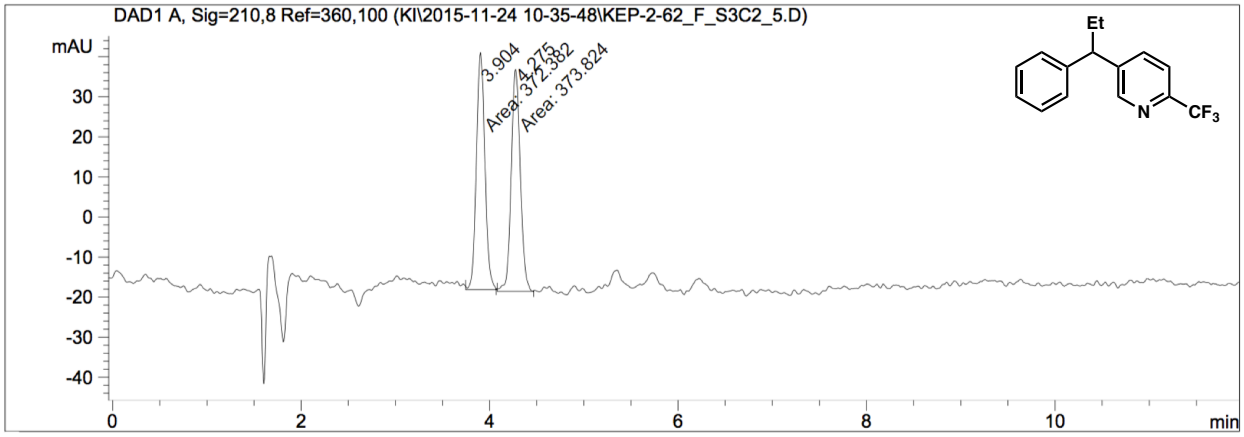
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.241	MM	0.1258	225.12733	29.83720	50.0889
2	7.401	MM	0.1469	224.32823	25.45803	49.9111

78 (Table 2.11): enantioenriched, 90% ee



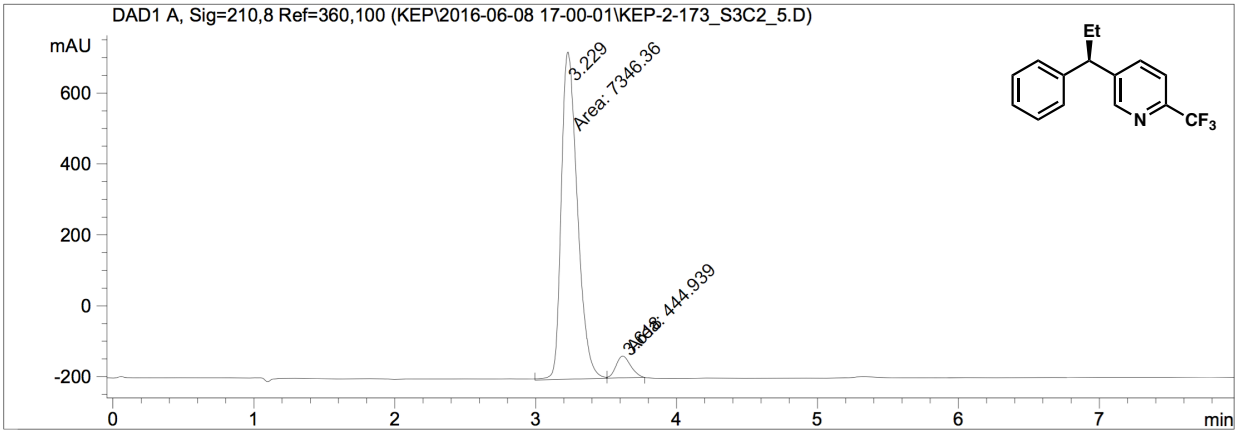
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.282	VV	0.2864	6799.51318	384.30942	95.2217
2	7.504	MM	0.3222	341.20612	17.64723	4.7783

79 (Table 2.11): racemic



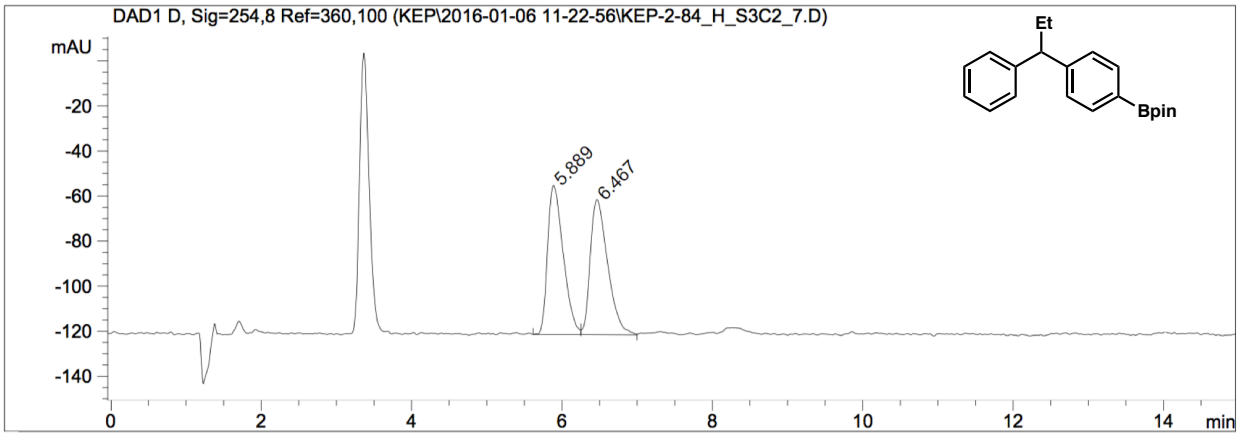
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.904	MM	0.1045	372.38202	59.37043	49.9034
2	4.275	MM	0.1119	373.82434	55.67645	50.0966

79 (Table 2.11): enantioenriched, 89% ee



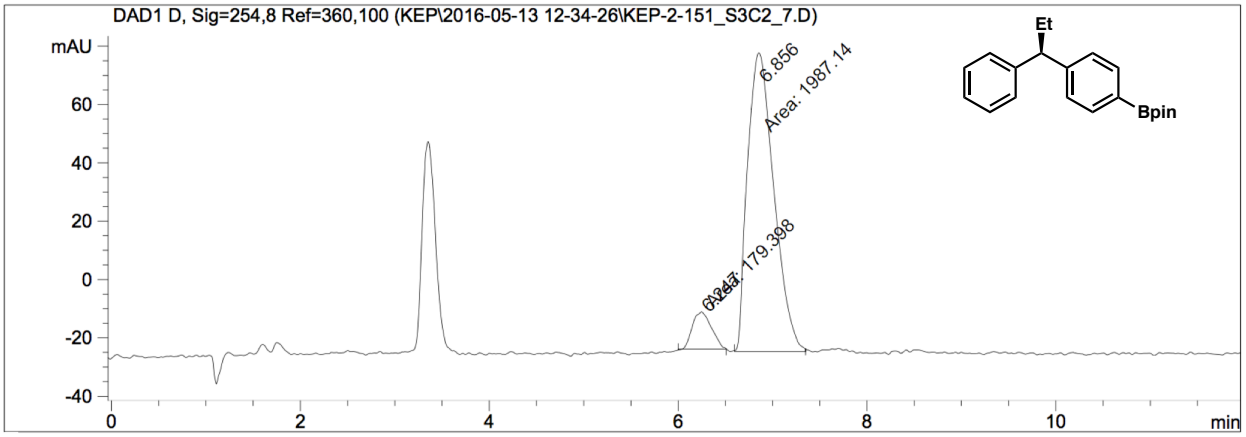
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.229	MM	0.1321	7346.35645	927.15521	94.2893
2	3.618	MM	0.1200	444.93854	61.81540	5.7107

80 (Table 2.11): racemic



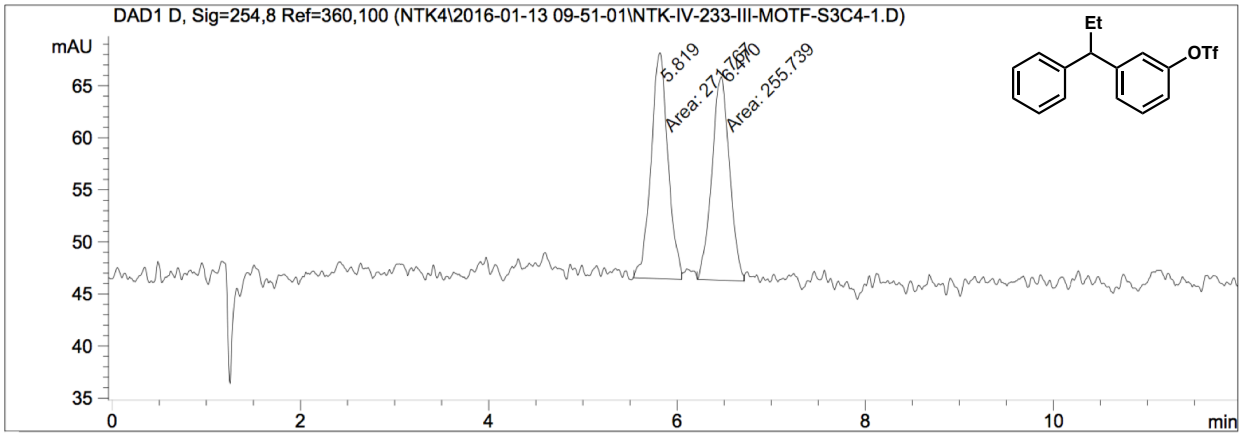
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.889	VV	0.2207	955.90326	66.10567	49.7597
2	6.467	VV	0.2441	965.13409	59.86779	50.2403

80 (Table 2.11): enantioenriched, 83% ee



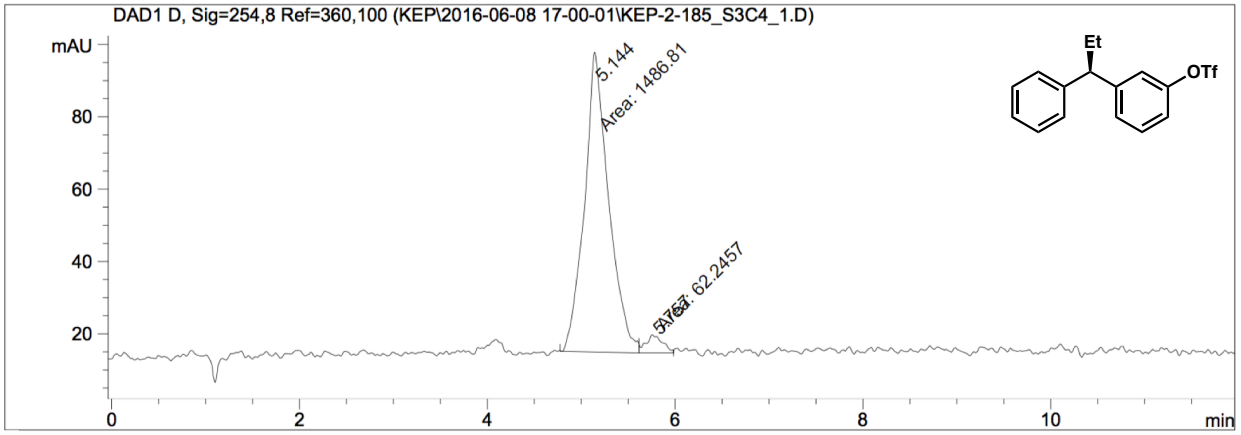
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.247	MM	0.2335	179.39758	12.80240	8.2804
2	6.856	MM	0.3232	1987.13965	102.47388	91.7196

81 (Table 2.11): racemic



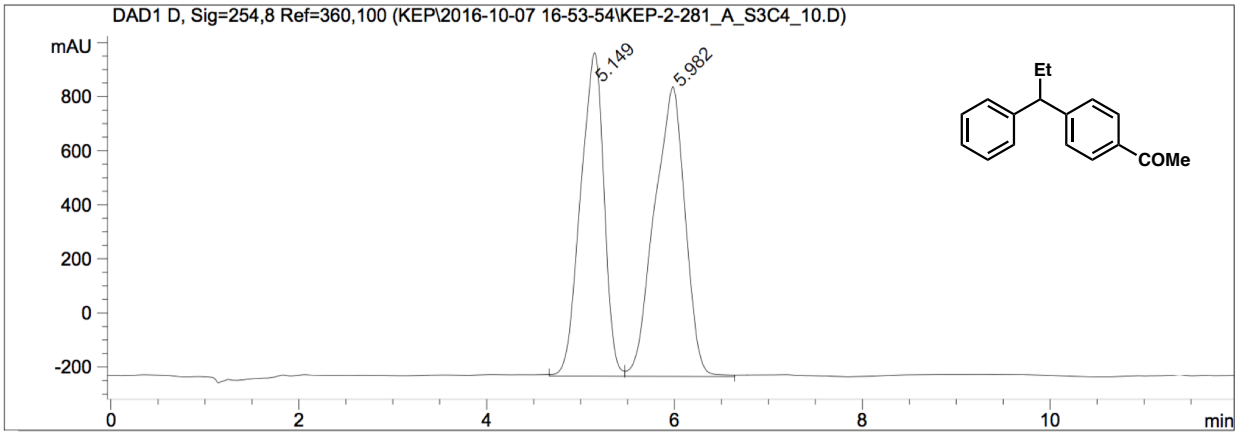
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.819	MM	0.2081	271.76694	21.76966	51.5192
2	6.470	MM	0.2176	255.73871	19.59052	48.4808

81 (Table 2.11): enantioenriched, 92% ee



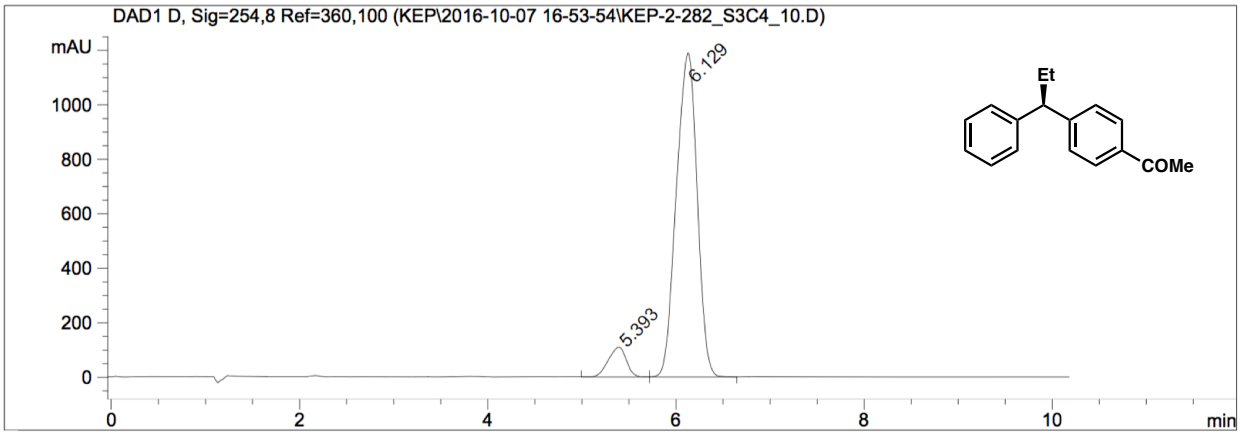
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.144	MM	0.2987	1486.80554	82.96041	95.9817
2	5.757	MM	0.2035	62.24570	5.09879	4.0183

82 (Table 2.11): racemic



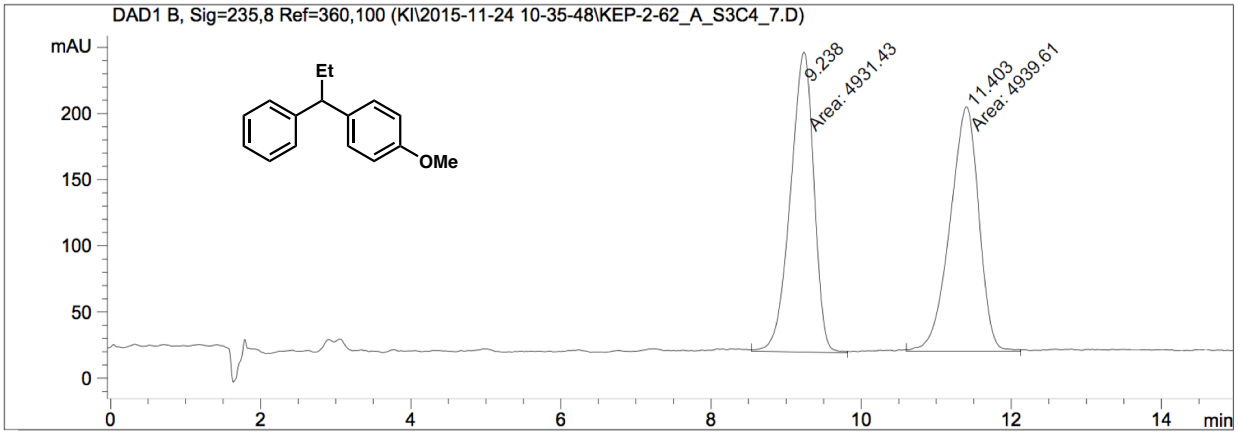
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.149	BV	0.2507	2.07723e4	1195.55908	46.0237
2	5.982	VV	0.3254	2.43617e4	1070.94434	53.9763

82 (Table 2.11): enantioenriched, 85% ee



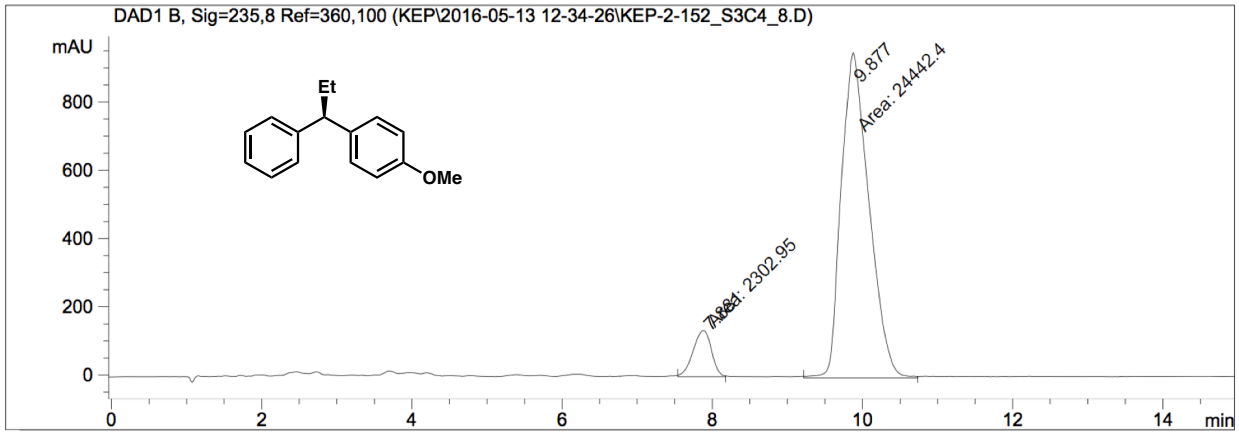
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.393	VV	0.2171	1477.27429	109.68082	7.4706
2	6.129	VV	0.2515	1.82972e4	1189.54590	92.5294

83 (Table 2.11): racemic



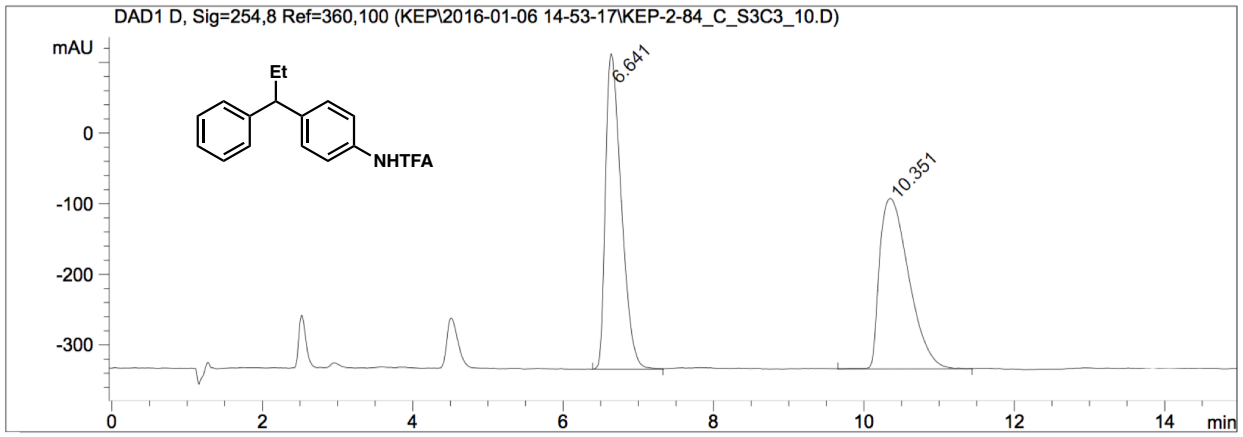
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.238	MM	0.3626	4931.42871	226.65631	49.9586
2	11.403	MM	0.4456	4939.61035	184.75740	50.0414

83 (Table 2.11): enantioenriched, 83% ee



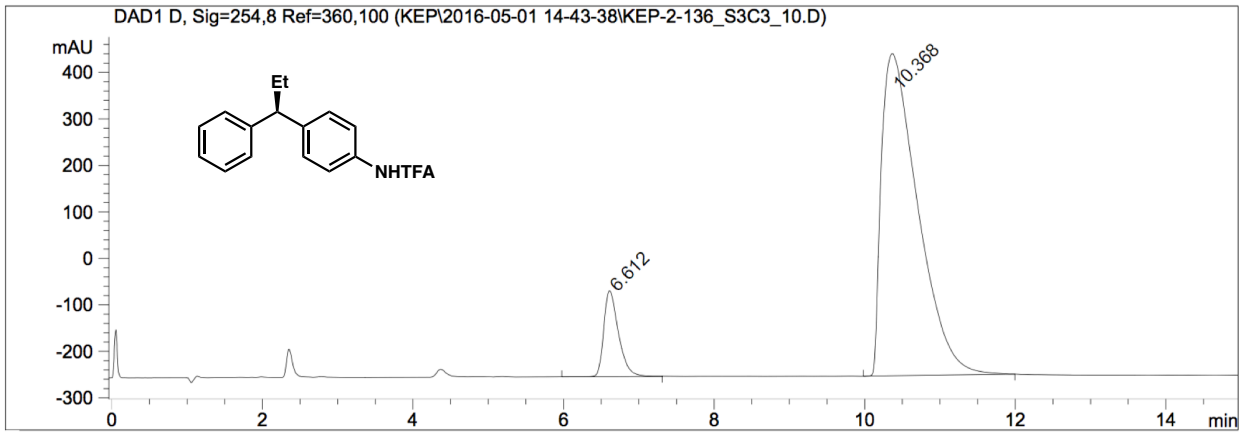
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.881	MM	0.2840	2302.95239	135.16910	8.6107
2	9.877	MM	0.4275	2.44424e4	952.97052	91.3893

84 (Table 2.11): racemic



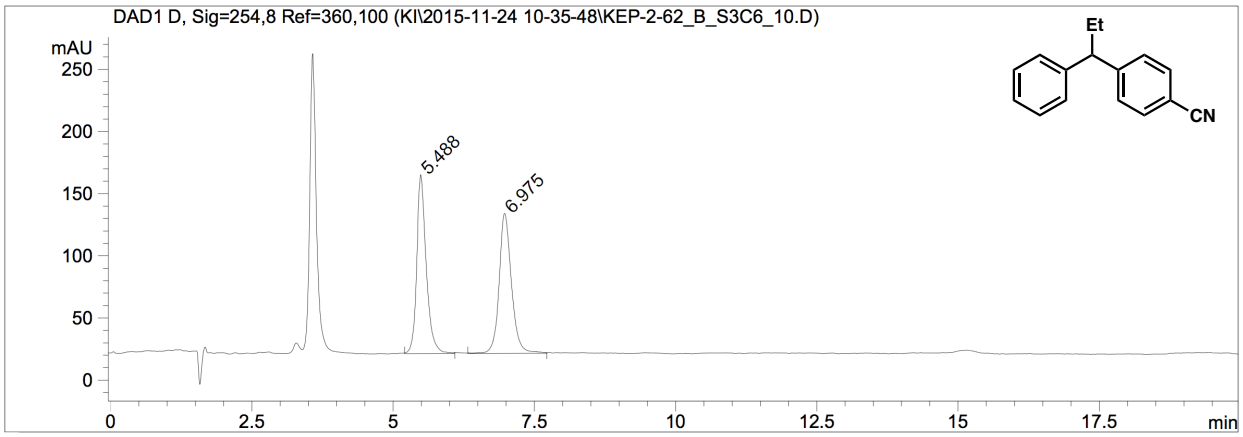
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.641	BV	0.2264	6517.64551	446.31766	49.9606
2	10.351	VB	0.4237	6527.92627	241.27650	50.0394

84 (Table 2.11): enantioenriched, 81% ee



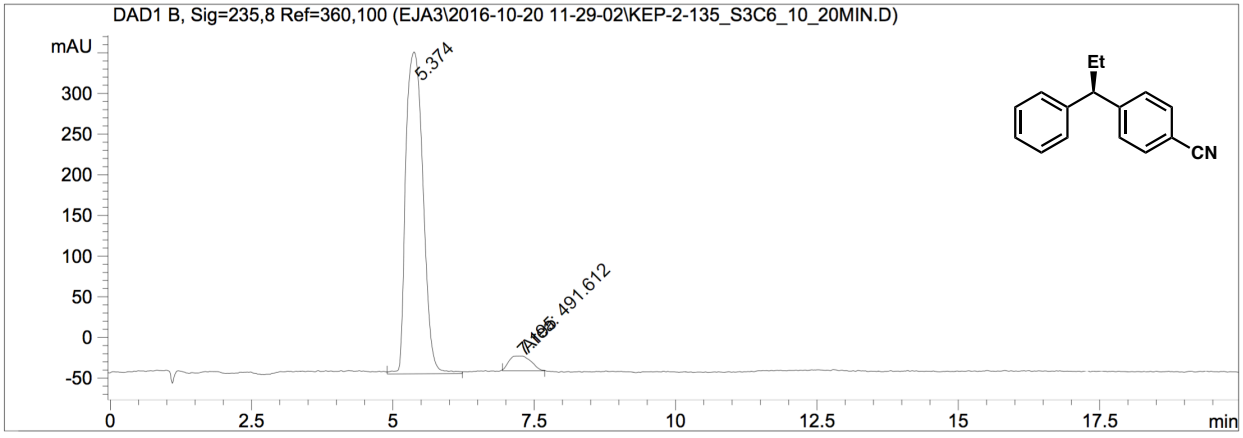
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.612	BB	0.2070	2511.82178	184.31891	9.7347
2	10.368	BBA	0.5081	2.32909e4	693.00104	90.2653

85 (Table 2.11): racemic



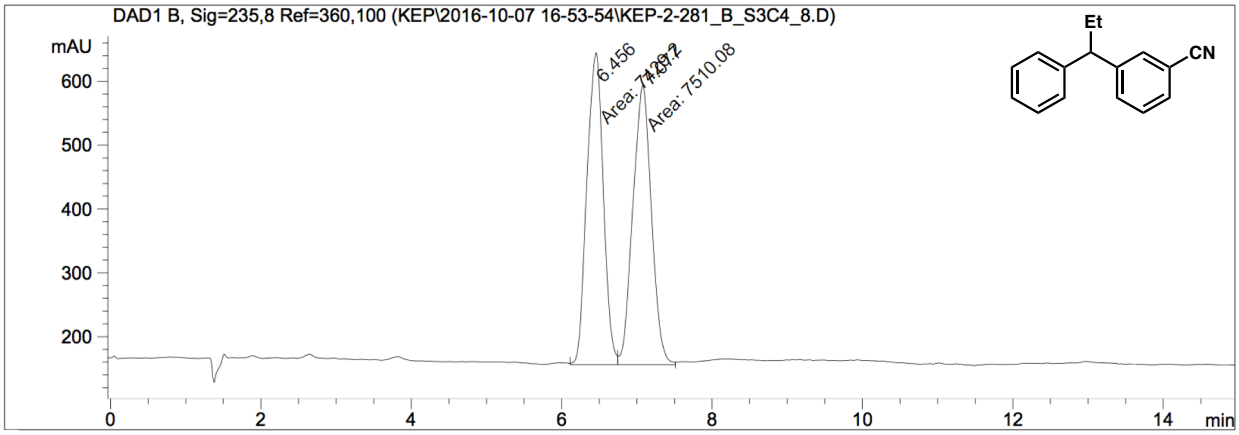
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.488	BB	0.1723	1681.73132	143.95172	49.4670
2	6.975	BB	0.2300	1717.97205	112.61301	50.5330

85 (Table 2.11): enantioenriched, 89% ee



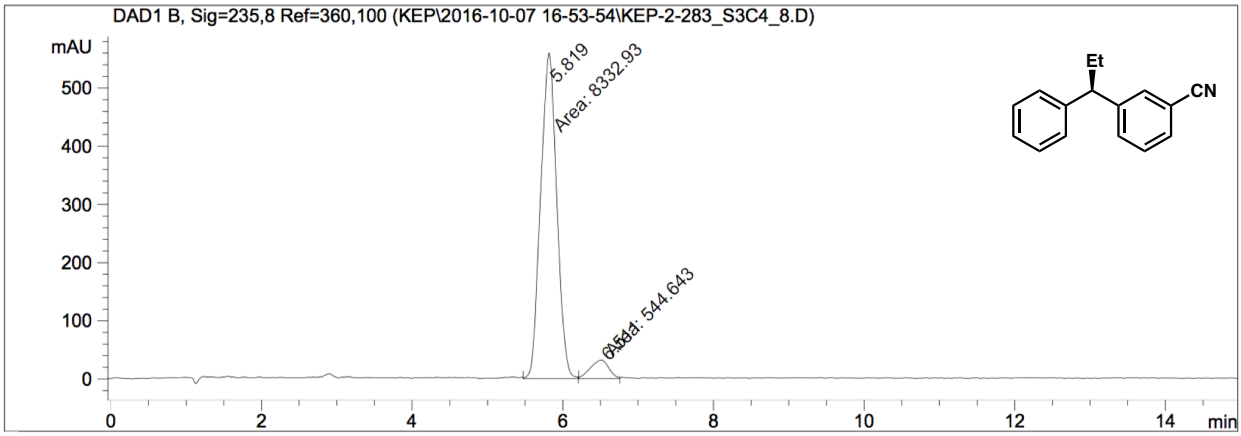
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.374	VB	0.3534	8457.98047	395.66473	94.5069
2	7.195	MM	0.4480	491.61188	18.28875	5.4931

86 (Table 2.11): racemic



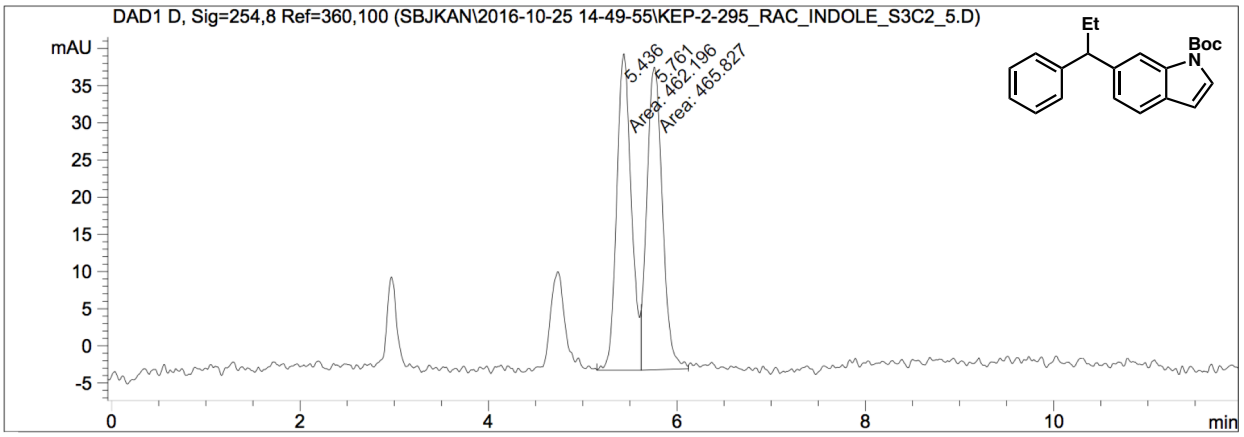
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.456	MM	0.2532	7429.20215	489.00641	49.7293
2	7.077	MM	0.2859	7510.07861	437.75015	50.2707

86 (Table 2.11): enantioenriched, 88% ee



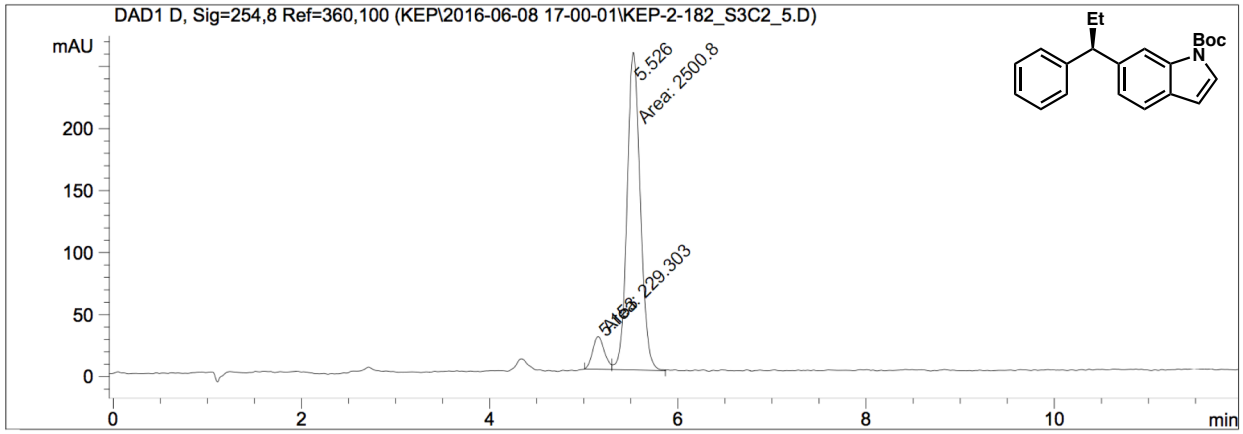
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.819	MM	0.2480	8332.93457	560.08173	93.8650
2	6.511	MM	0.2832	544.64307	32.05117	6.1350

87 (Table 2.11): racemic



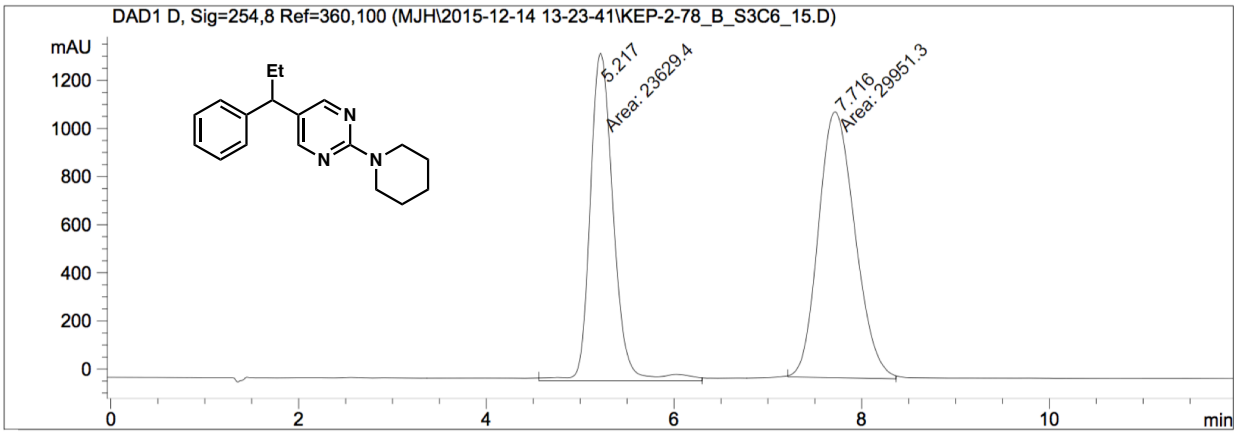
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.436	MM	0.1806	462.19641	42.65343	49.8044
2	5.761	MM	0.1903	465.82700	40.79035	50.1956

87 (Table 2.11): enantioenriched, 83% ee



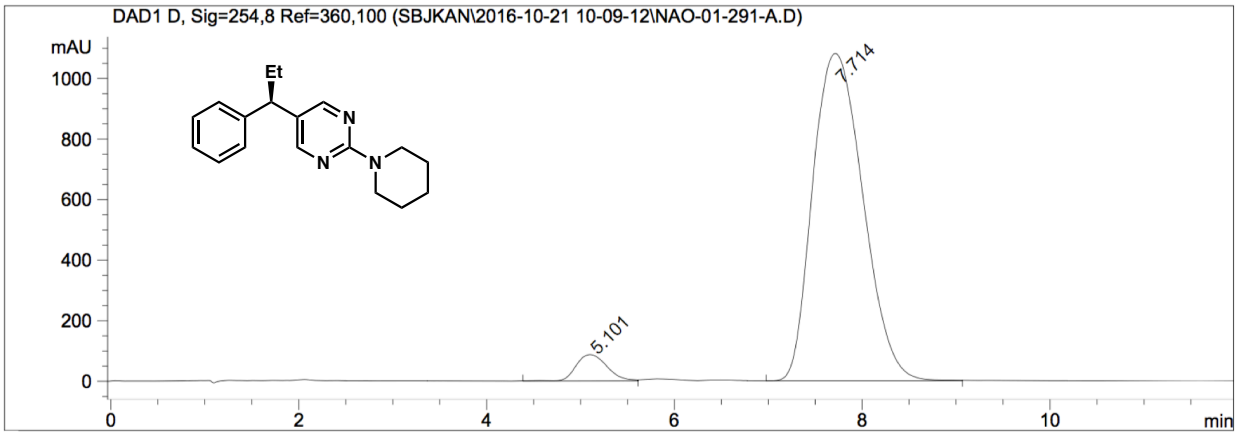
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.153	MM	0.1447	229.30257	26.41977	8.3991
2	5.526	MM	0.1625	2500.79614	256.55481	91.6009

88 (Table 2.11): racemic



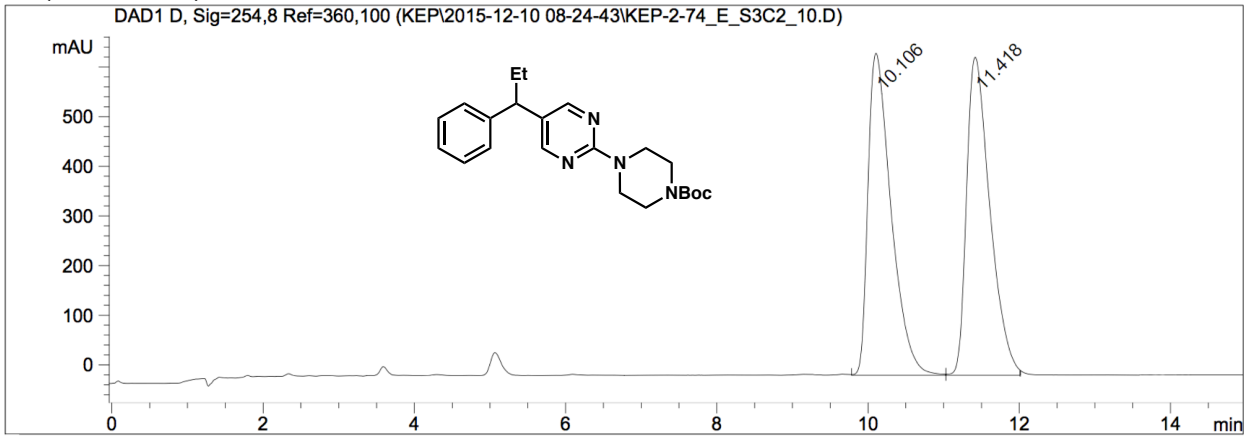
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.217	MM	0.2890	2.36294e4	1362.55078	44.1005
2	7.716	MM	0.4513	2.99513e4	1106.04492	55.8995

88 (Table 2.11): enantioenriched, 90% ee



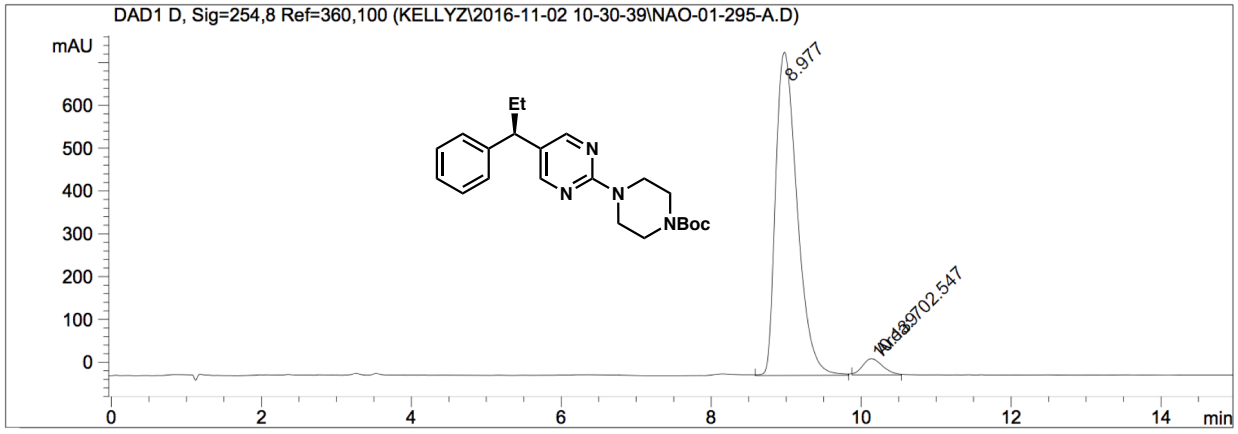
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.101	BV	0.3693	2020.01782	87.52279	4.7708
2	7.714	VB	0.6029	4.03216e4	1081.54956	95.2292

89 (Table 2.11): racemic



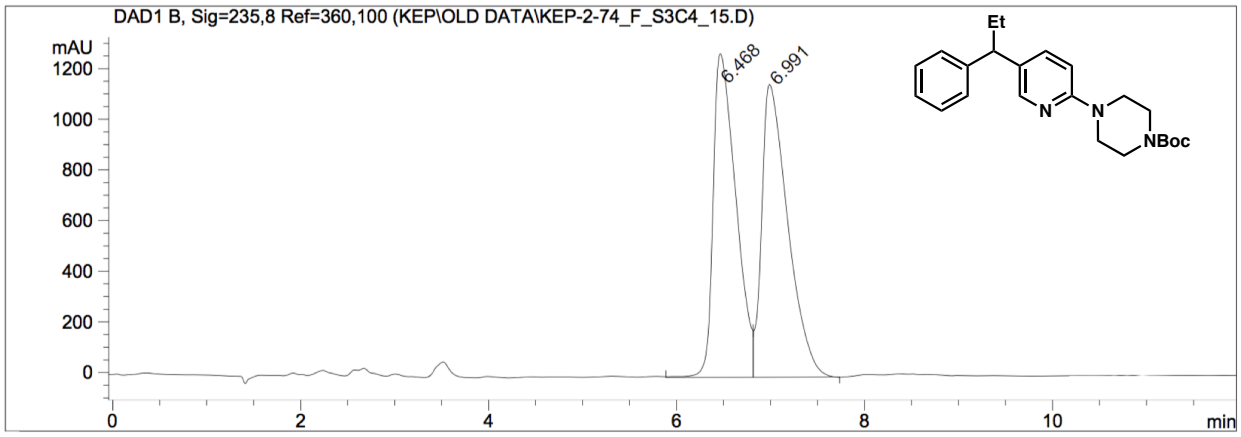
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.106	VV	0.3197	1.37647e4	648.30176	49.9751
2	11.418	VBA	0.3269	1.37784e4	640.60486	50.0249

89 (Table 2.11): enantioenriched, 91% ee



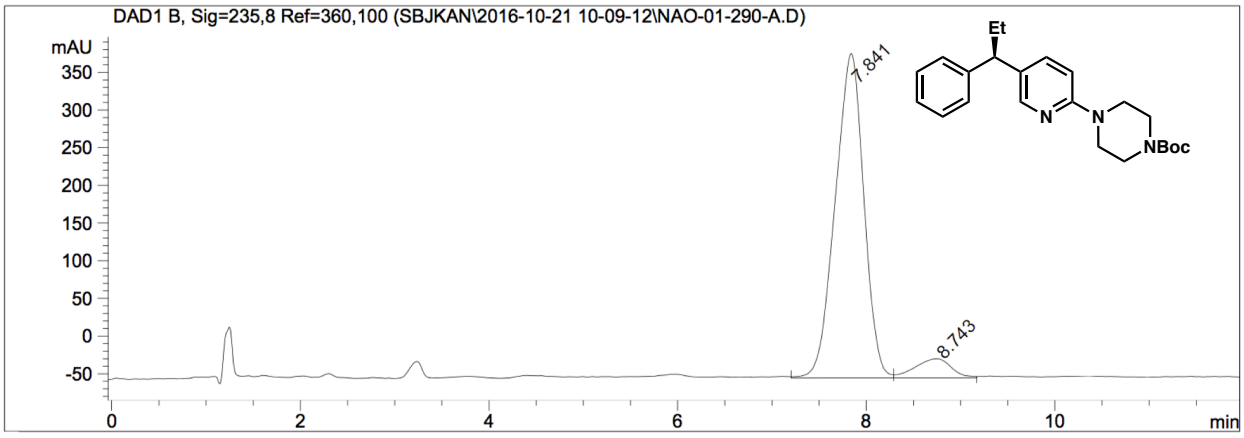
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.977	VV	0.3132	1.51019e4	755.54010	95.5548
2	10.139	MM	0.3080	702.54669	38.01196	4.4452

90 (Table 2.11): racemic



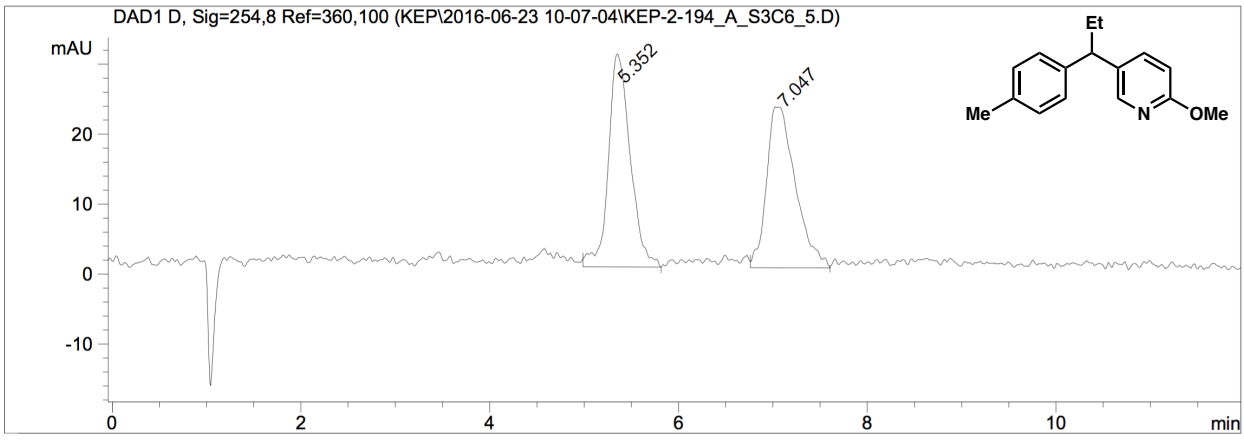
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.468	VV	0.2635	2.13999e4	1276.86255	48.9552
2	6.991	VV	0.2972	2.23133e4	1155.71497	51.0448

90 (Table 2.11): enantioenriched, 86% ee



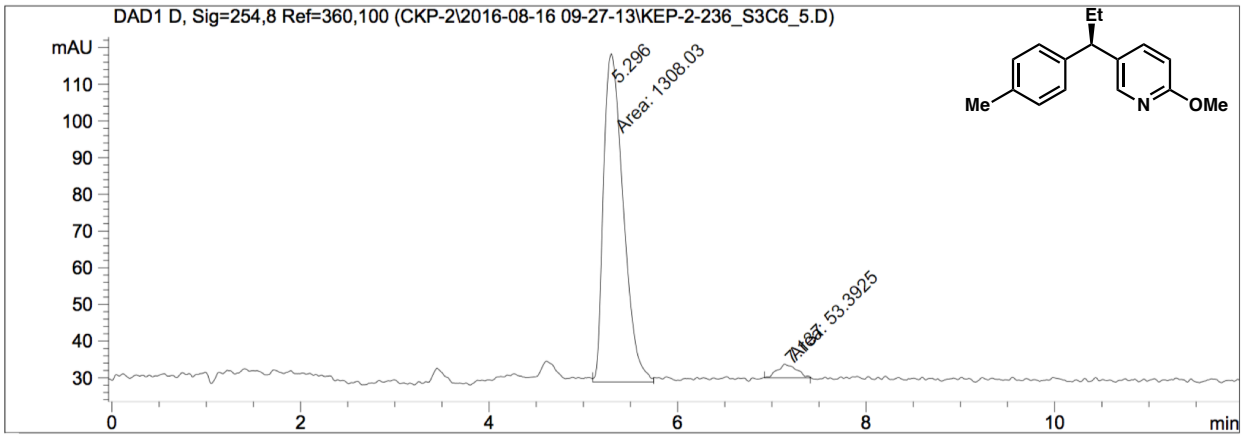
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.841	VV	0.3143	9084.12988	430.24960	93.1452
2	8.743	VV	0.3678	668.52216	25.34315	6.8548

91 (Table 2.12): racemic



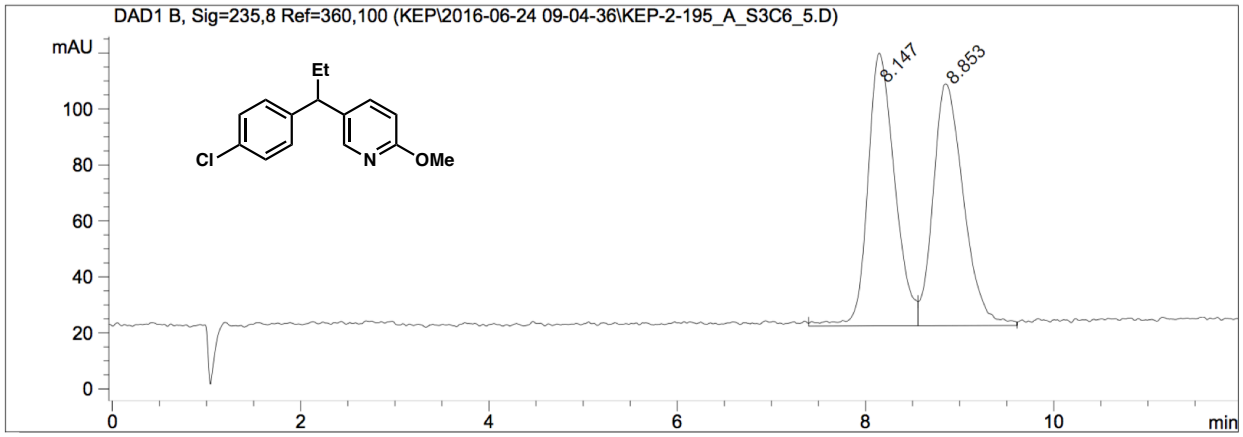
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.352	BV	0.2486	492.14969	30.44251	50.1656
2	7.047	VV	0.3051	488.90015	22.89762	49.8344

91 (Table 2.12): enantioenriched, 92% ee



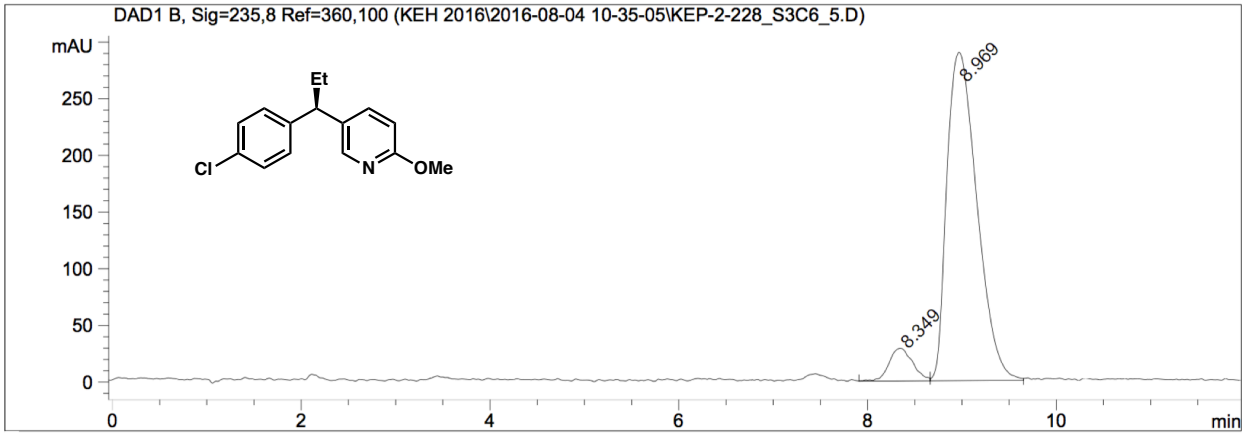
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.296	MM	0.2436	1308.03101	89.50471	96.0782
2	7.137	MM	0.2348	53.39251	3.78949	3.9218

92 (Table 2.12): racemic



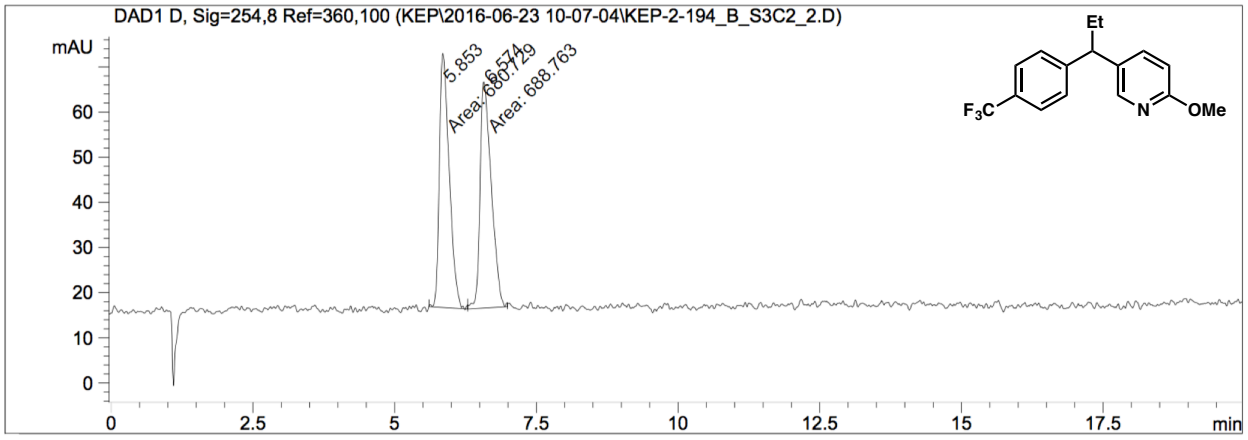
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.147	VV	0.3041	1937.56421	97.40051	50.0131
2	8.853	VV	0.3496	1936.54773	86.35545	49.9869

92 (Table 2.12): enantioenriched, 85% ee



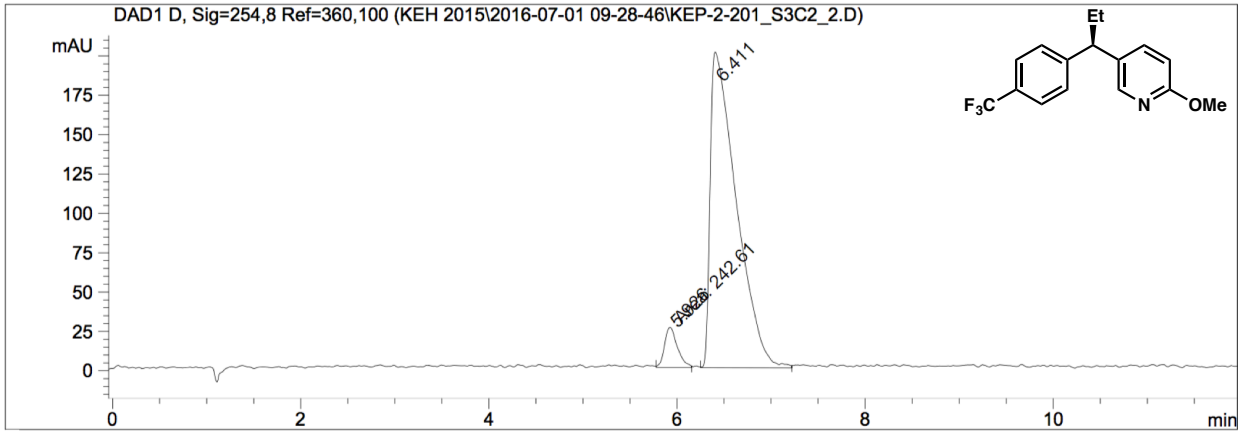
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.349	VV	0.2592	502.01791	28.81935	7.2551
2	8.969	VV	0.3586	6417.53760	289.55692	92.7449

93 (Table 2.12): racemic



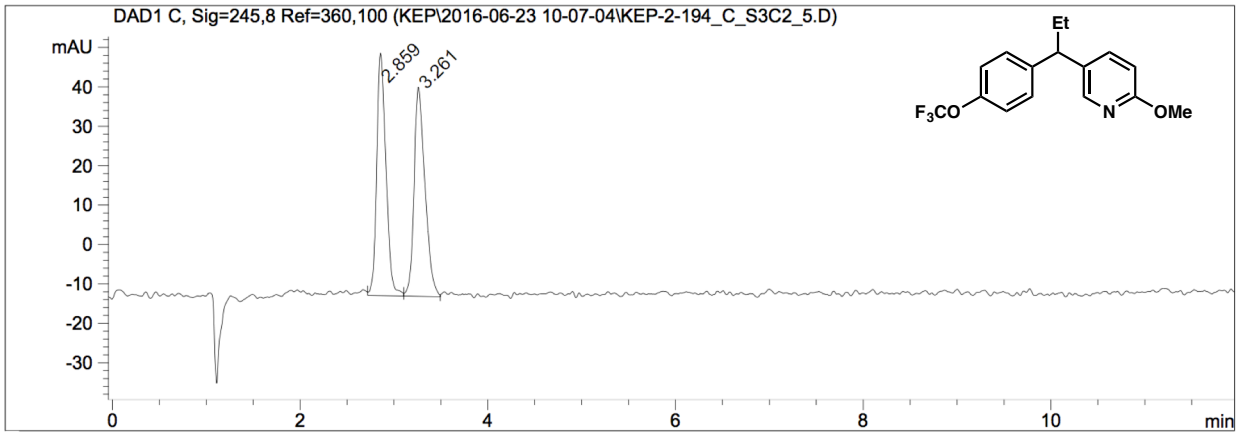
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.853	MM	0.2014	680.72894	56.33337	49.7067
2	6.574	MM	0.2290	688.76263	50.12506	50.2933

93 (Table 2.12): enantioenriched, 88% ee



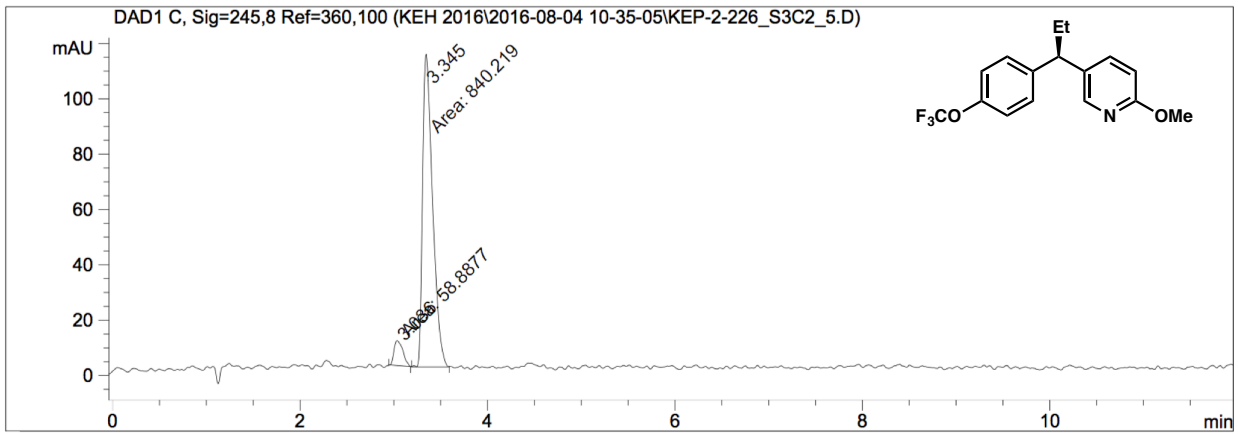
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.926	MM	0.1586	242.60960	25.49229	5.9009
2	6.411	VV	0.2976	3868.79395	200.08298	94.0991

74 (Table 2.12): racemic



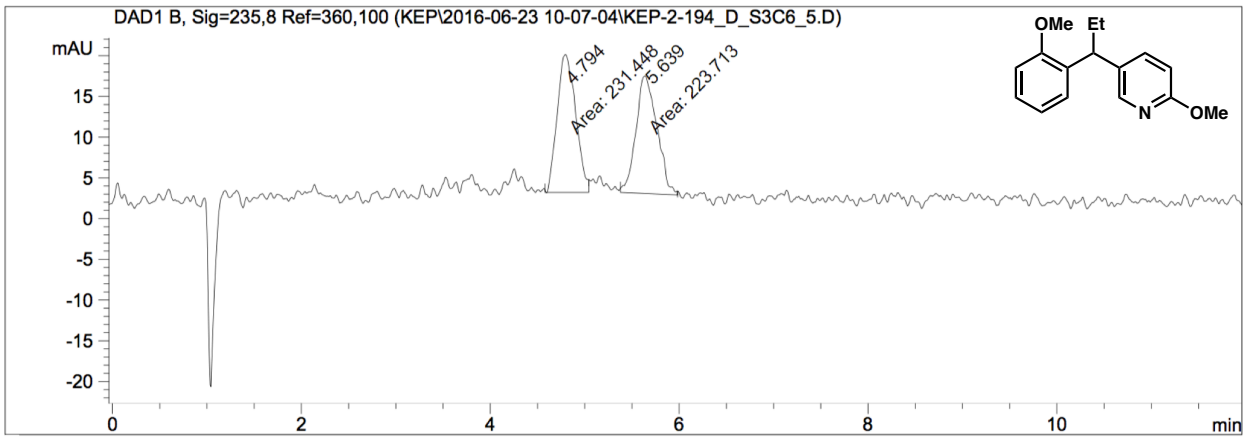
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.859	VV	0.1043	423.07886	61.46682	49.6391
2	3.261	VV	0.1230	429.23071	52.69527	50.3609

74 (Table 2.12): enantioenriched, 87% ee



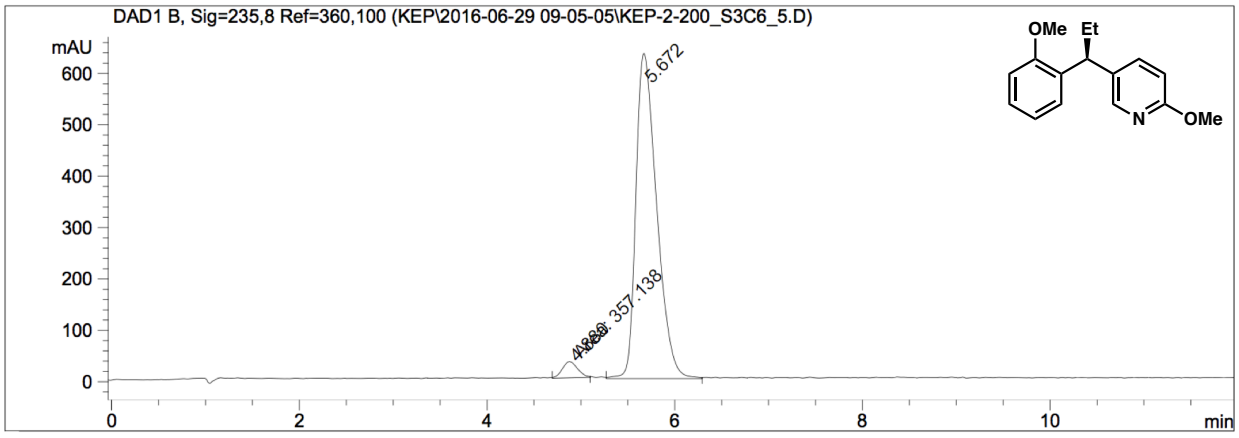
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.036	MM	0.1085	58.88769	9.04943	6.5496
2	3.345	MM	0.1231	840.21881	113.73206	93.4504

94 (Table 2.12): racemic



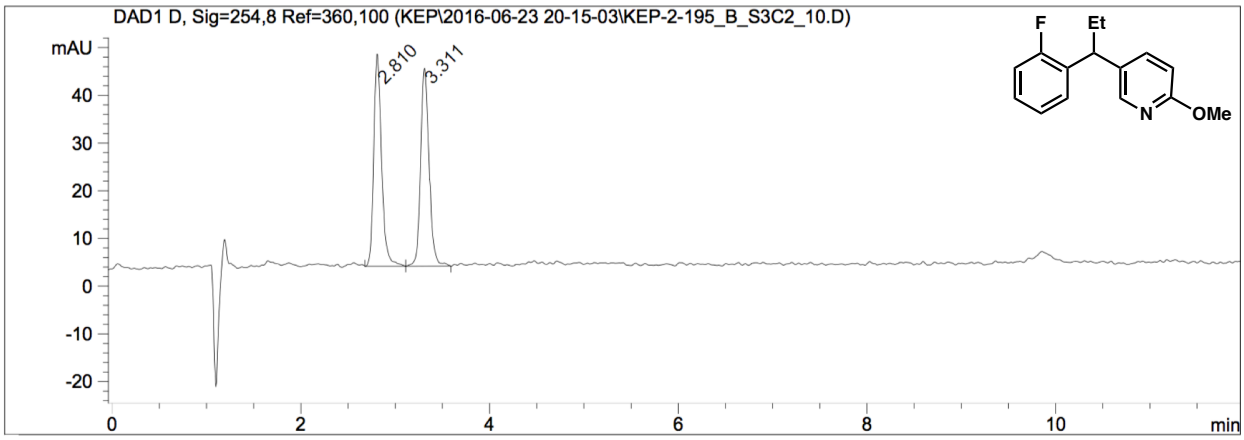
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.794	MM	0.2277	231.44783	16.93867	50.8497
2	5.639	MM	0.2590	223.71298	14.39786	49.1503

94 (Table 2.12): enantioenriched, 93% ee



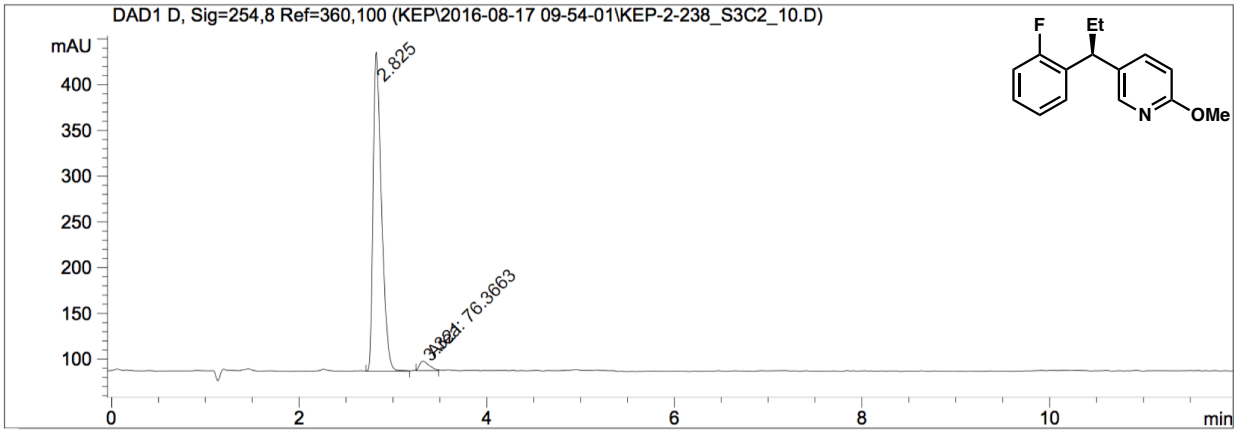
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.880	MM	0.1875	357.13812	31.74859	3.5278
2	5.672	VV	0.2402	9766.50586	632.42023	96.4722

95 (Table 2.12): racemic



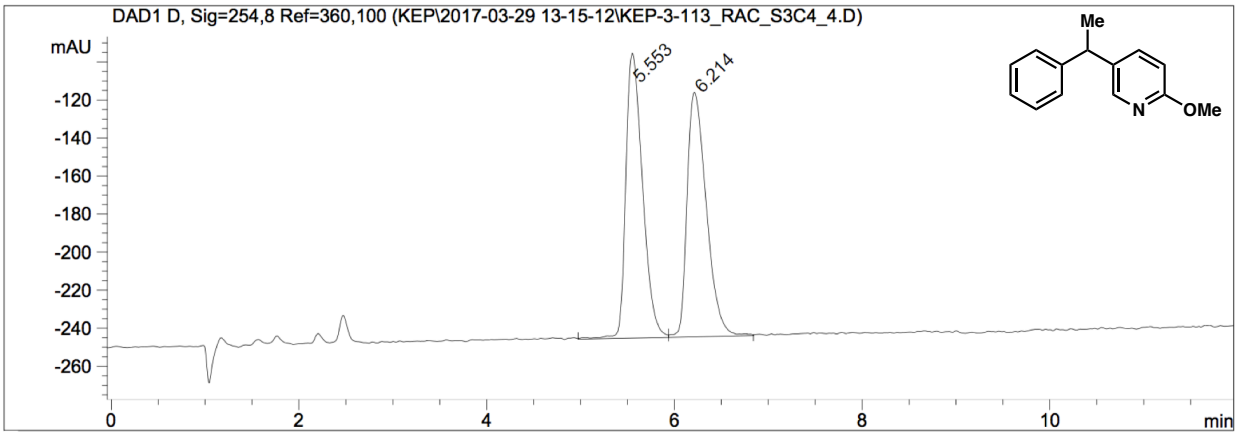
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.810	VV	0.0924	258.58182	44.11600	49.8675
2	3.311	VV	0.0972	259.95596	41.40617	50.1325

95 (Table 2.12): enantioenriched, 93% ee



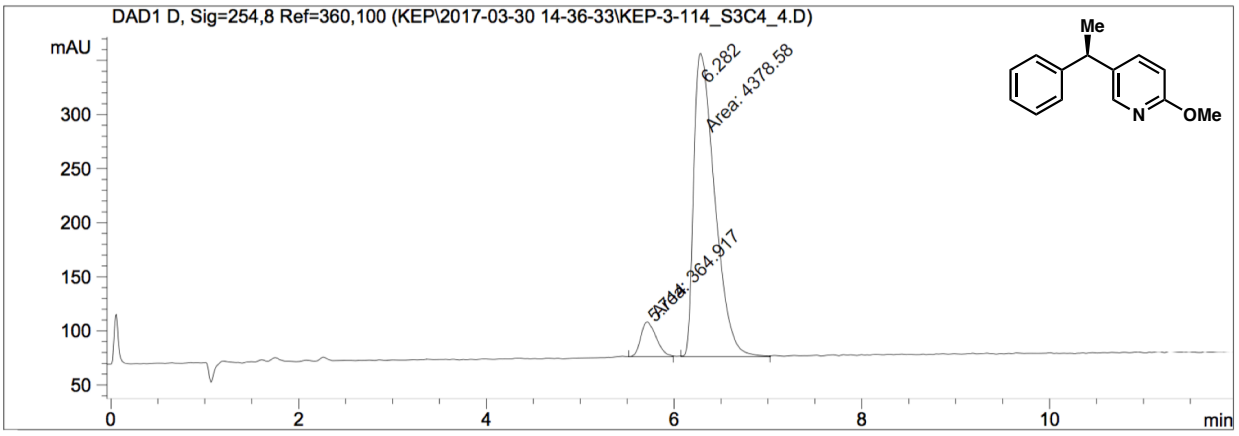
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.825	BV	0.0976	2180.79883	345.56207	96.6167
2	3.321	MM	0.1201	76.36634	10.59406	3.3833

96 (Table 2.12): racemic



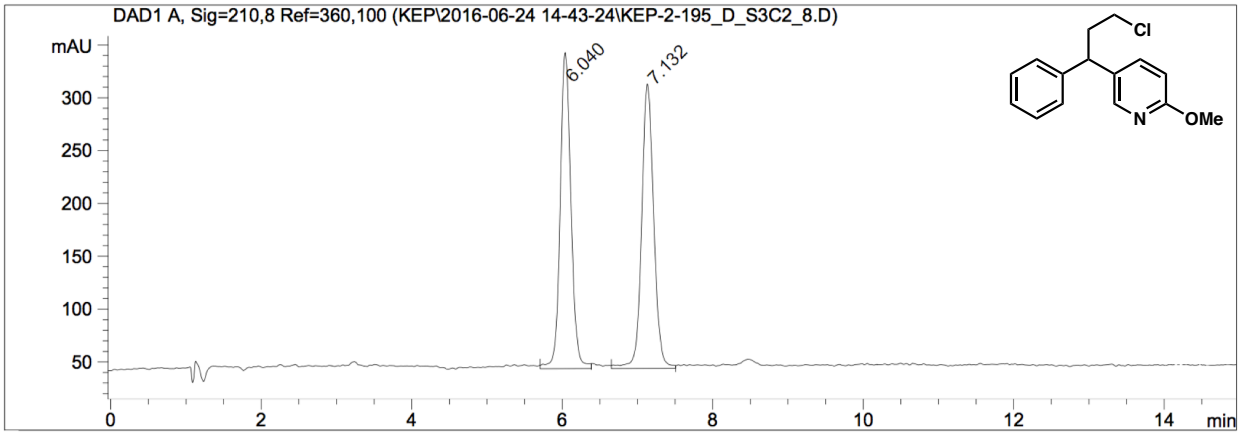
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.553	VV	0.1927	1857.50623	149.78943	50.2735
2	6.214	VB	0.2189	1837.29578	128.45862	49.7265

96 (Table 2.12): enantioenriched, 85% ee



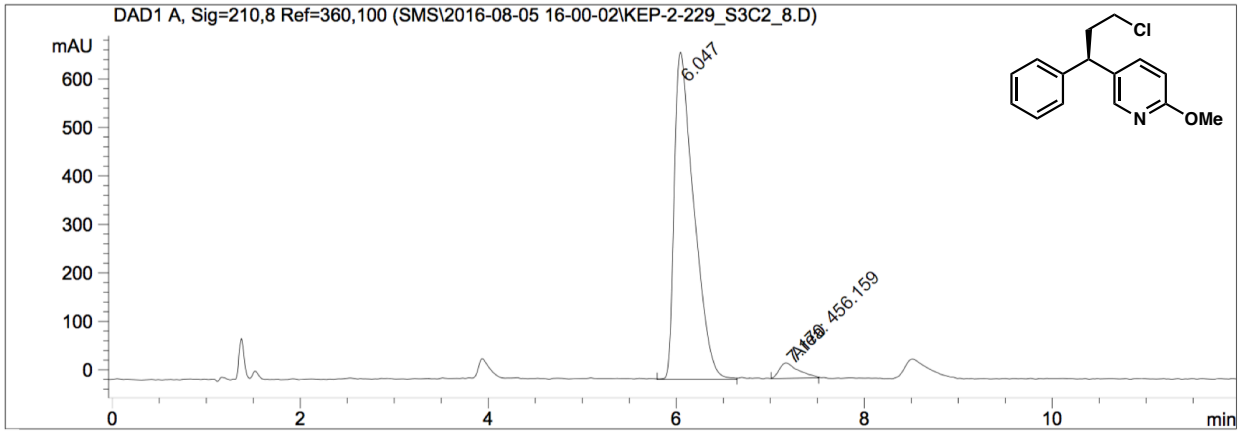
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.714	MM	0.1896	364.91733	32.08042	7.6930
2	6.282	MM	0.2601	4378.58398	280.57593	92.3070

97 (Table 2.12): racemic



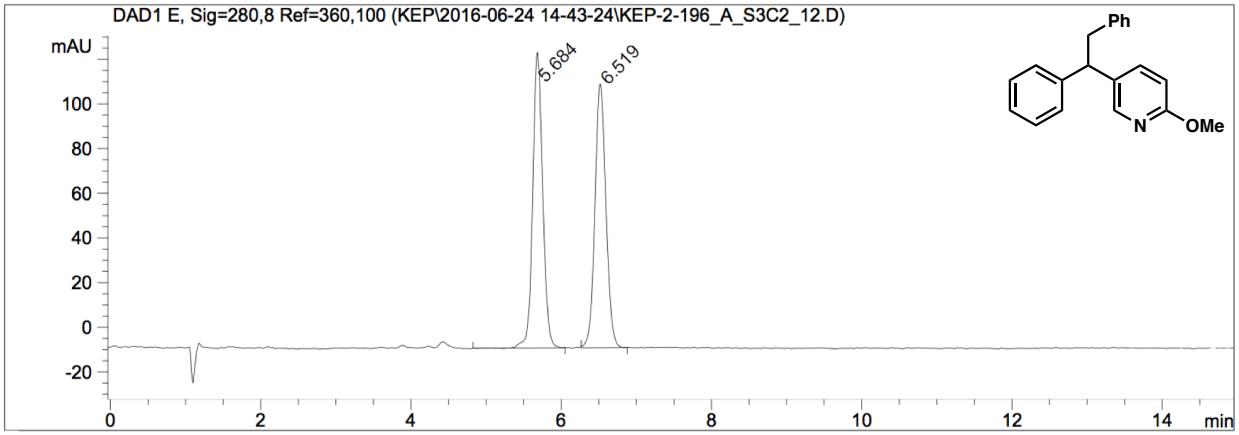
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.040	BB	0.1525	2986.70654	299.00430	49.6947
2	7.132	BV	0.1751	3023.40210	269.09836	50.3053

97 (Table 2.12): enantioenriched, 91% ee



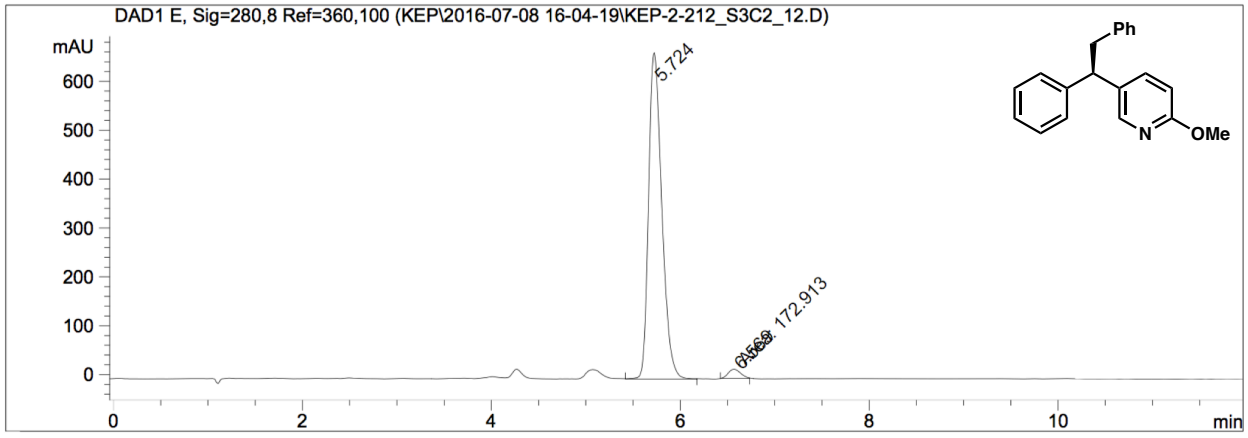
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.047	VV	0.2136	9809.45703	674.98010	95.5564
2	7.170	MM	0.2386	456.15921	31.86354	4.4436

98 (Table 2.12): racemic



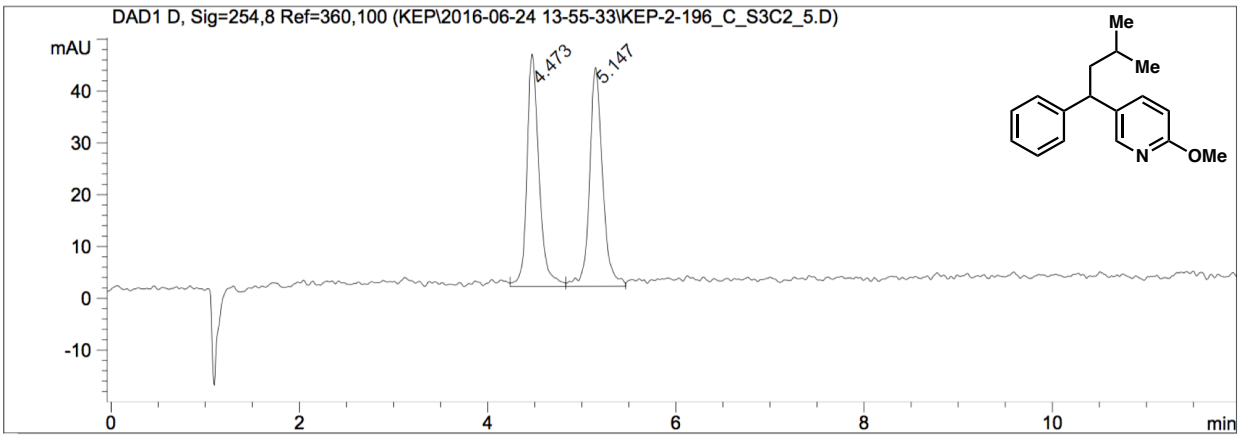
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.684	BB	0.1400	1223.06287	132.11612	50.4356
2	6.519	BB	0.1549	1201.93628	117.97483	49.5644

98 (Table 2.12): enantioenriched, 95% ee



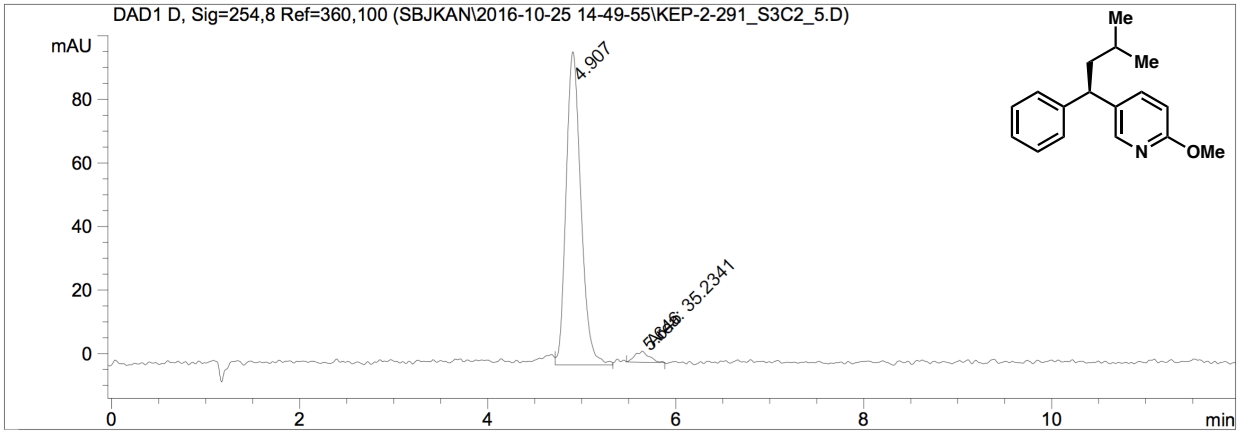
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.724	VB	0.1539	6510.68408	666.86530	97.4129
2	6.569	MM	0.1529	172.91284	18.84252	2.5871

99 (Table 2.12): racemic



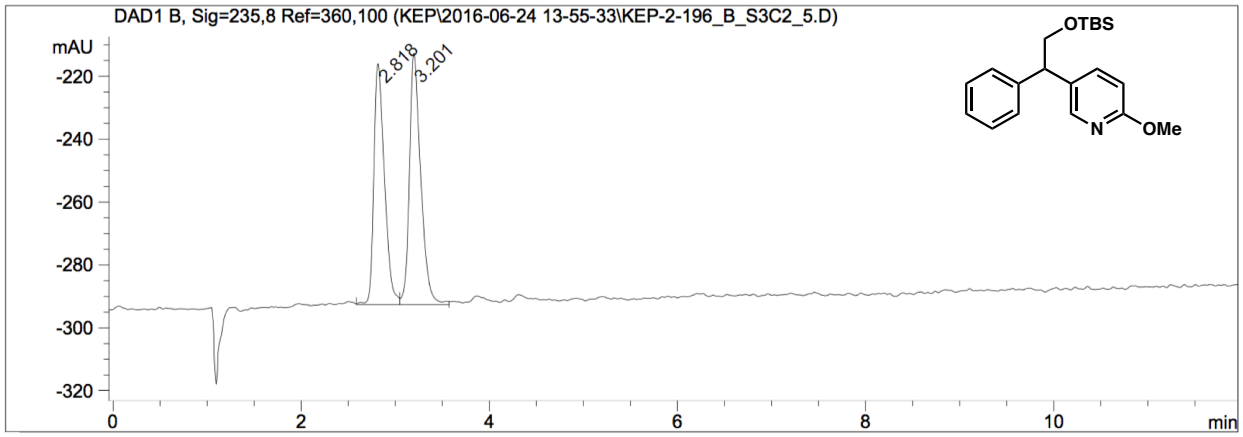
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.473	VV	0.1366	401.69574	44.82222	49.5490
2	5.147	VV	0.1451	409.00827	42.19704	50.4510

99 (Table 2.12): enantioenriched, 94% ee



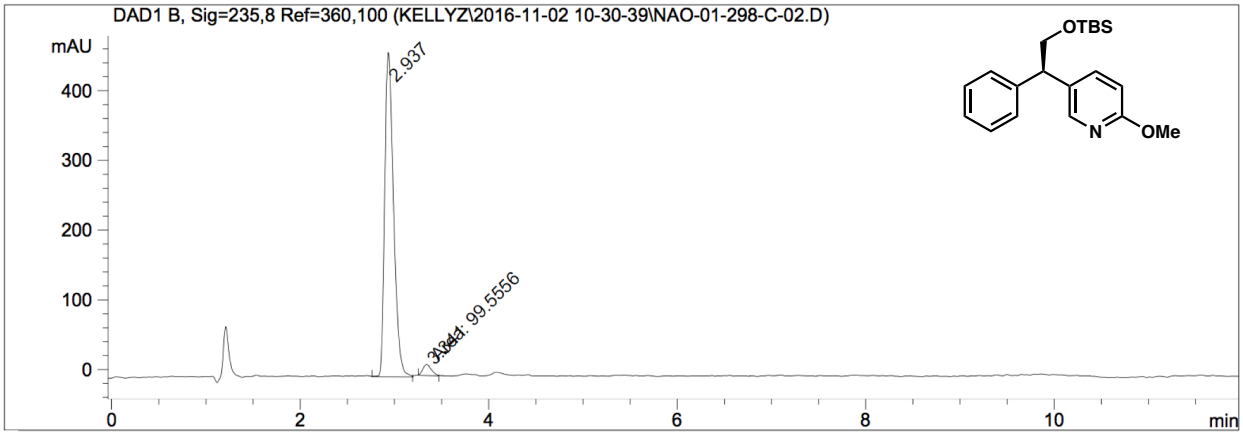
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.907	VV	0.1682	1080.82678	98.38535	96.8430
2	5.646	MM	0.1665	35.23412	3.52759	3.1570

100 (Table 2.12): racemic



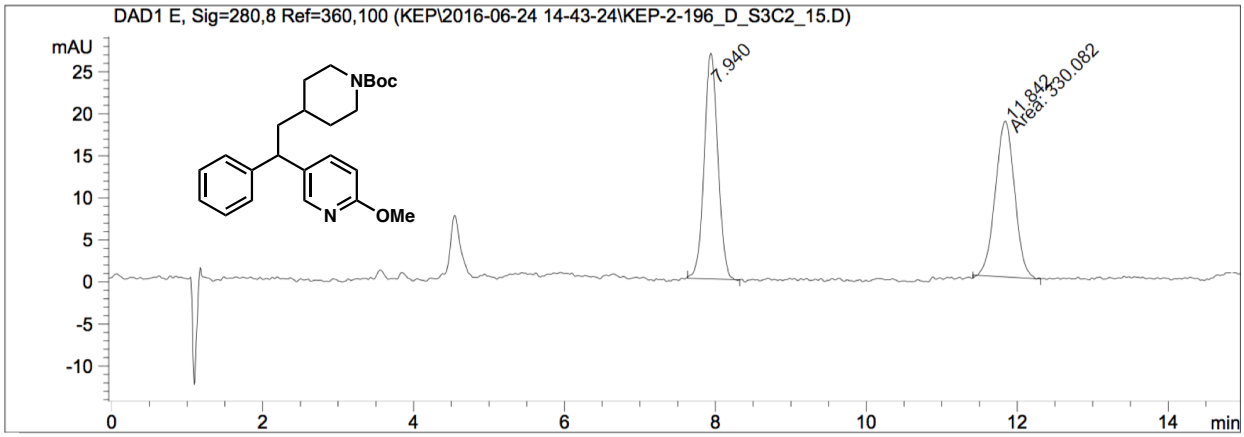
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.818	VV	0.1240	604.39984	76.62331	47.5039
2	3.201	VB	0.1257	667.91559	79.72723	52.4961

100 (Table 2.12): enantioenriched, 94% ee



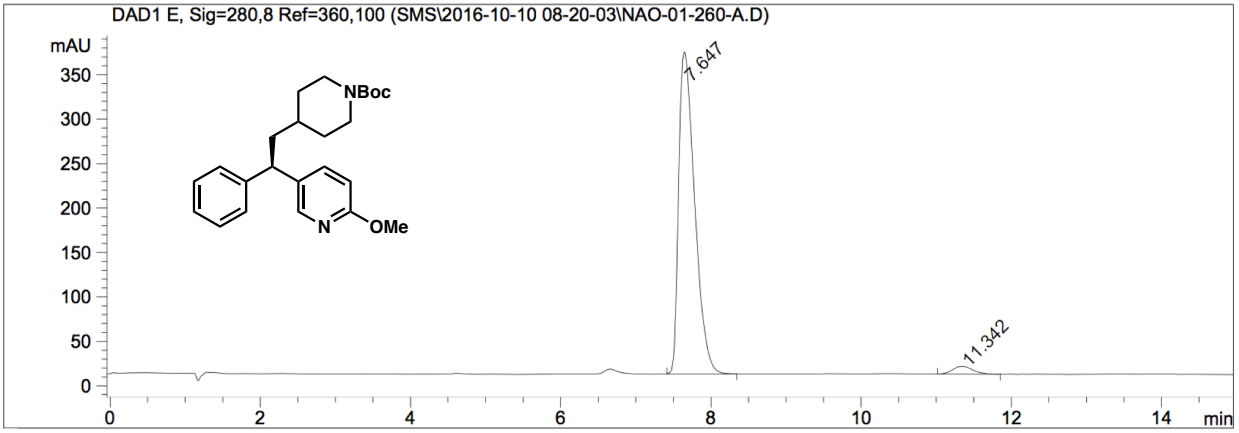
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.937	VV	0.1042	3032.79883	464.11722	96.8217
2	3.341	MM	0.1058	99.55560	15.68843	3.1783

101 (Table 2.12): racemic



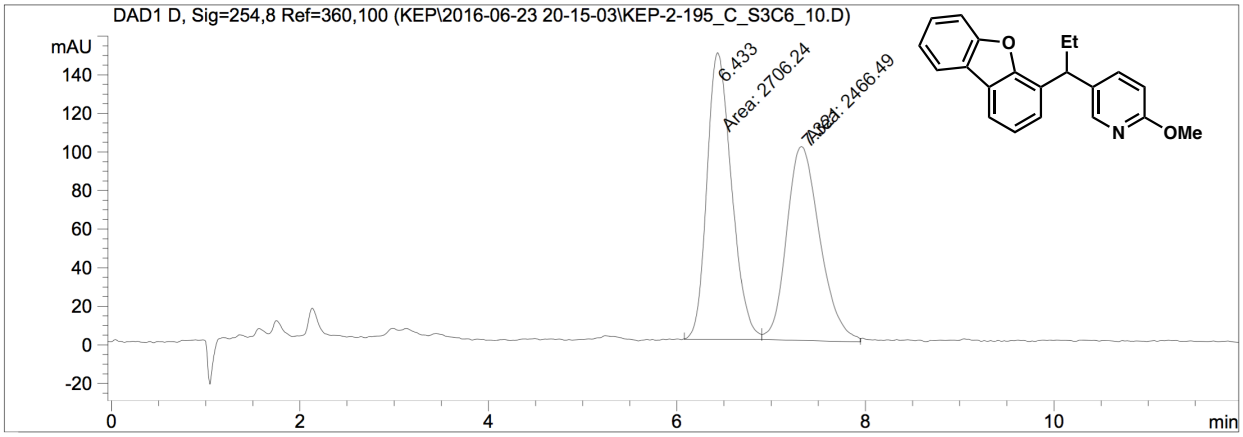
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.940	BB	0.1953	338.52716	26.80888	50.6315
2	11.842	MM	0.2963	330.08243	18.56997	49.3685

101 (Table 2.12): enantioenriched, 94% ee



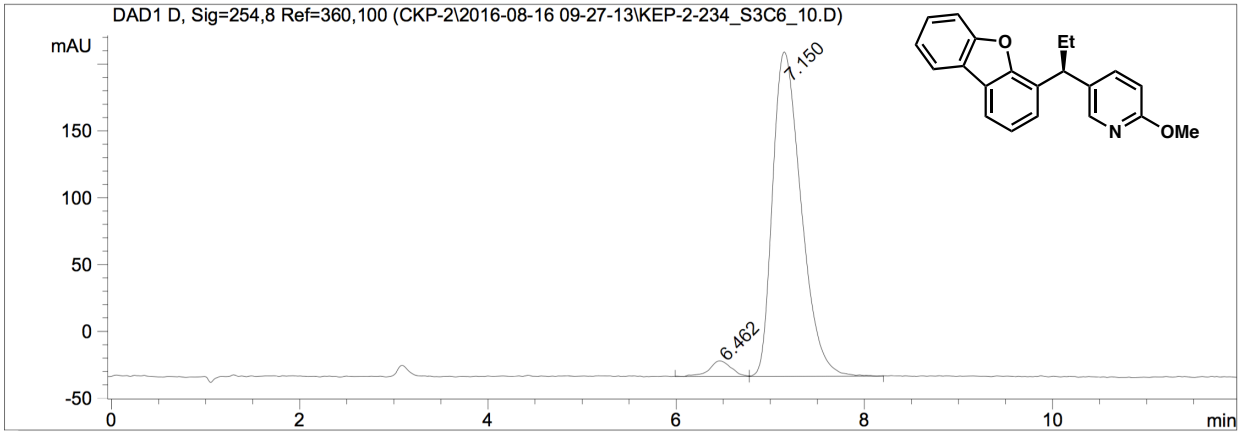
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.647	BB	0.2291	5372.29736	362.18082	97.0283
2	11.342	BB	0.2754	164.53700	8.91232	2.9717

102 (Table 2.12): racemic



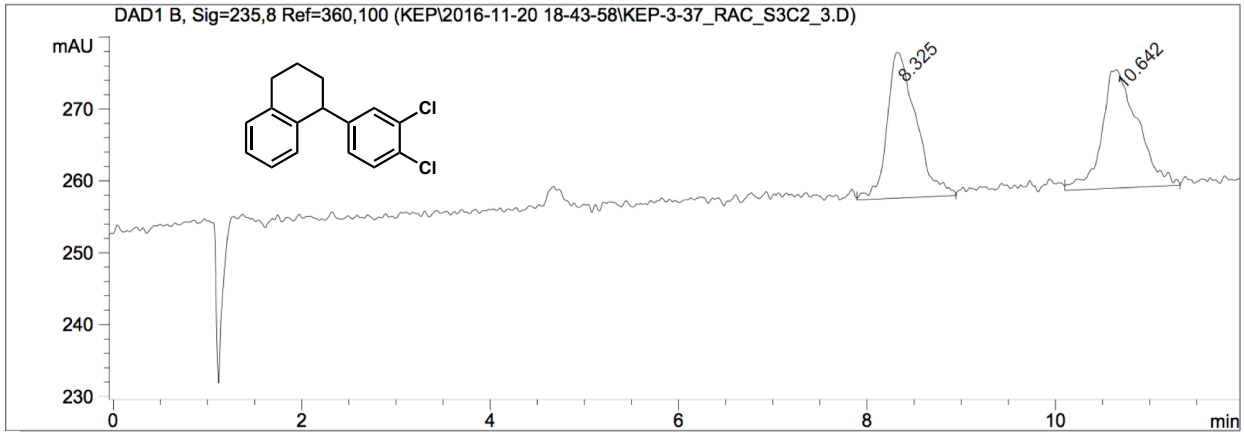
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.433	MM	0.3031	2706.24146	148.78586	52.3175
2	7.321	MM	0.4090	2466.48608	100.50787	47.6825

102 (Table 2.12): enantioenriched, 93% ee



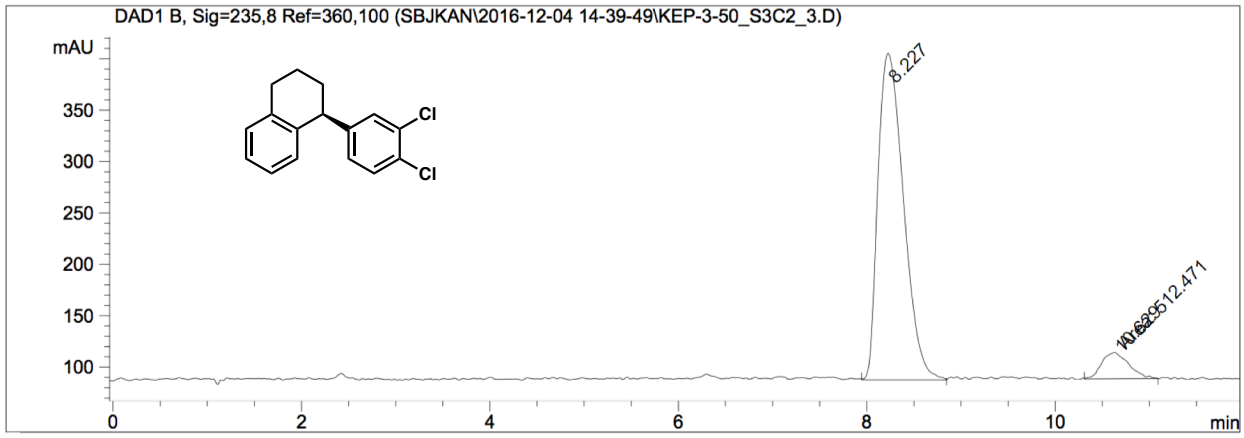
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.462	BV	0.2413	189.99944	11.70672	3.5725
2	7.150	VB	0.3266	5128.36816	242.62926	96.4275

107 (Scheme 2.7): racemic



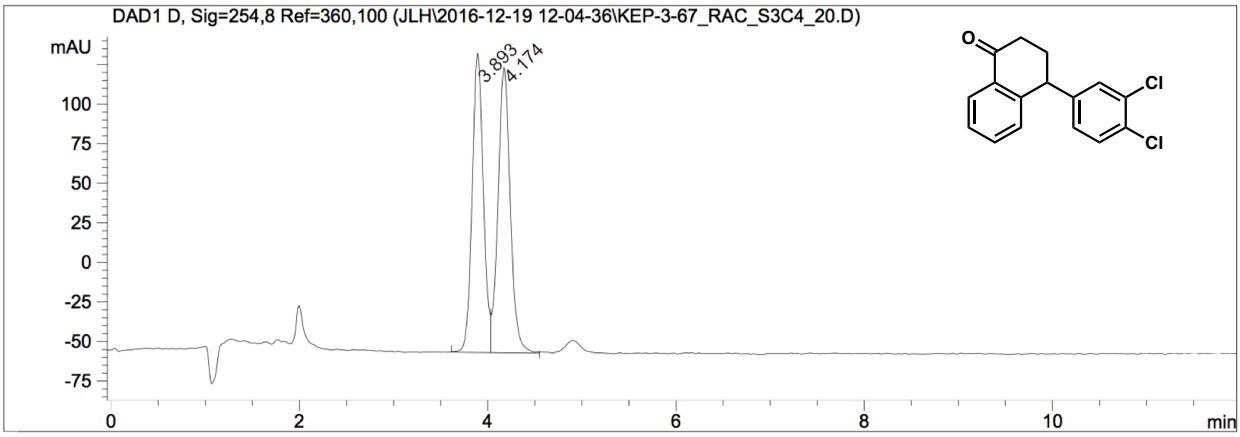
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.325	VV	0.3056	433.39096	20.25559	49.7137
2	10.642	VV	0.3314	438.38318	16.42403	50.2863

107 (Scheme 2.7): enantioenriched, 84% ee



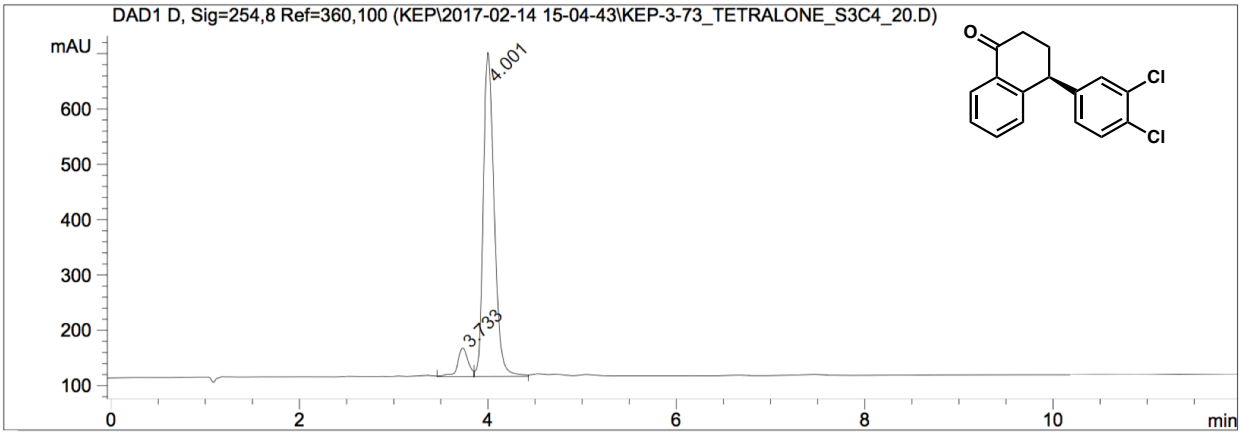
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.227	BV	0.3002	5989.72314	317.34003	92.1185
2	10.629	MM	0.3320	512.47150	25.72428	7.8815

108 (Scheme 2.7): racemic



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.893	BV	0.1280	1552.17676	188.69421	48.6803
2	4.174	VB	0.1381	1636.33215	179.92238	51.3197

108 (Scheme 2.7): enantioenriched, 84% ee



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.733	VV	0.1186	399.64880	51.48994	7.8135
2	4.001	VV	0.1262	4715.20508	583.70624	92.1865

2.7 NOTES AND REFERENCES

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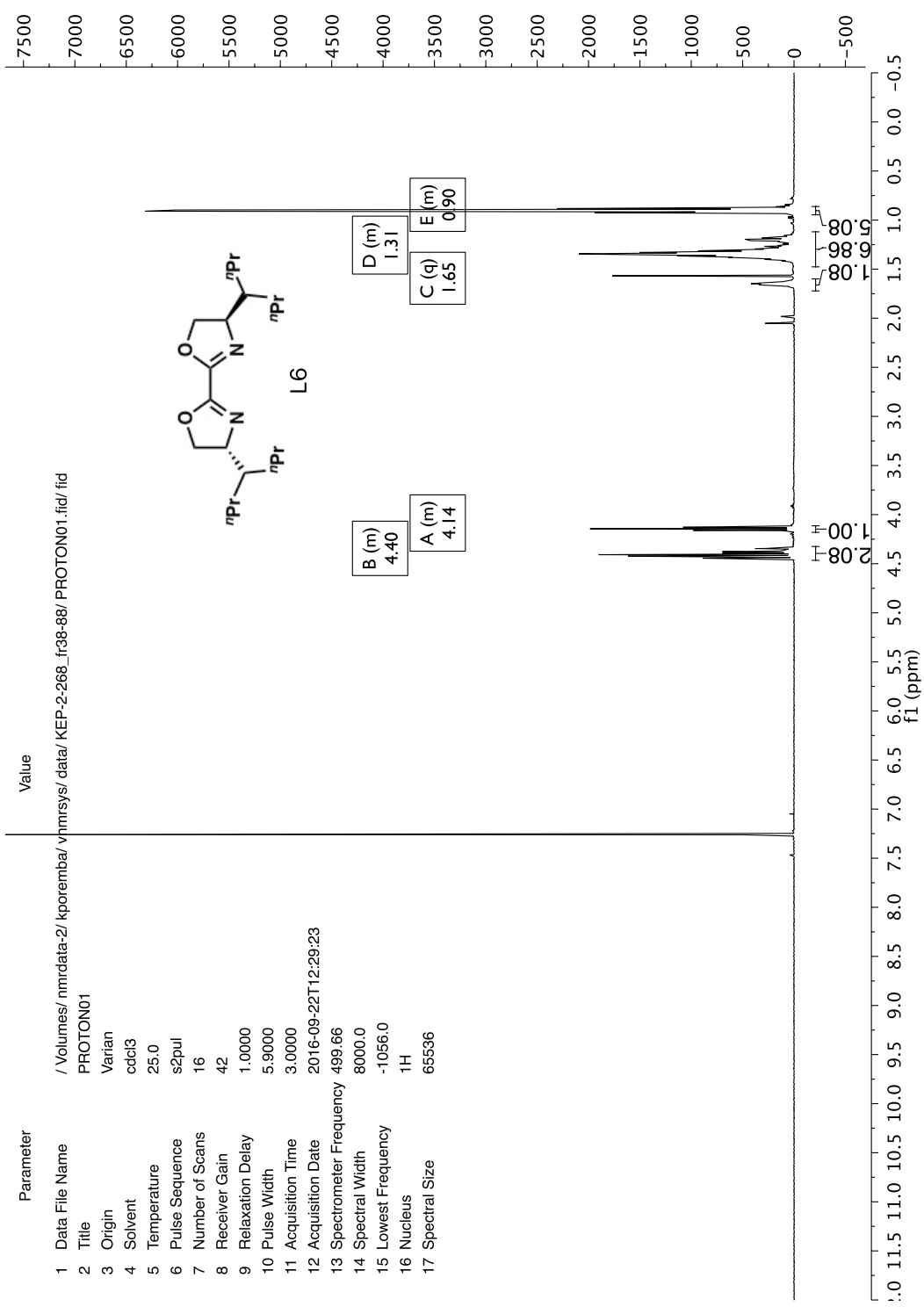
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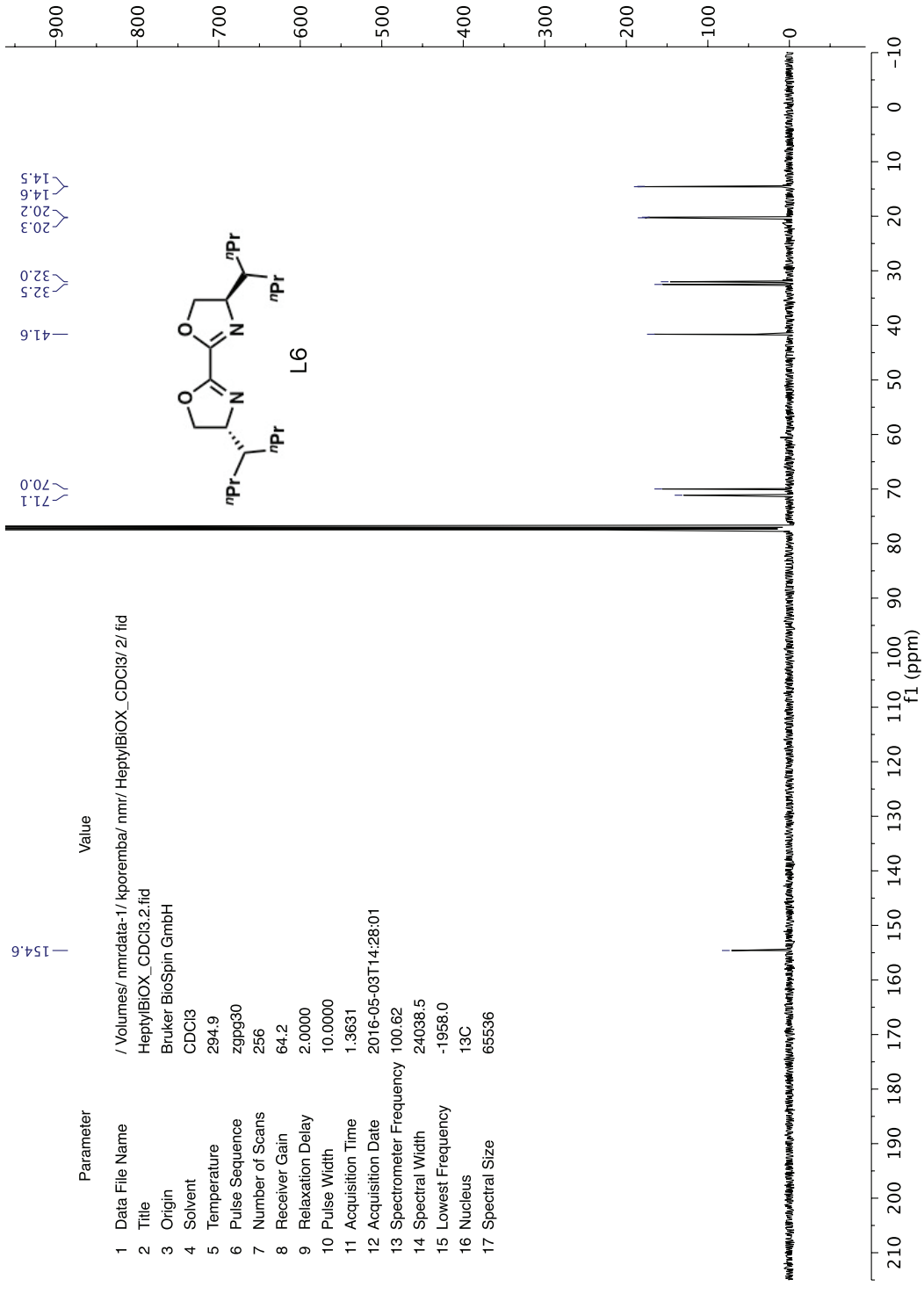
Appendix 1

Spectra Relevant to Chapter 2:

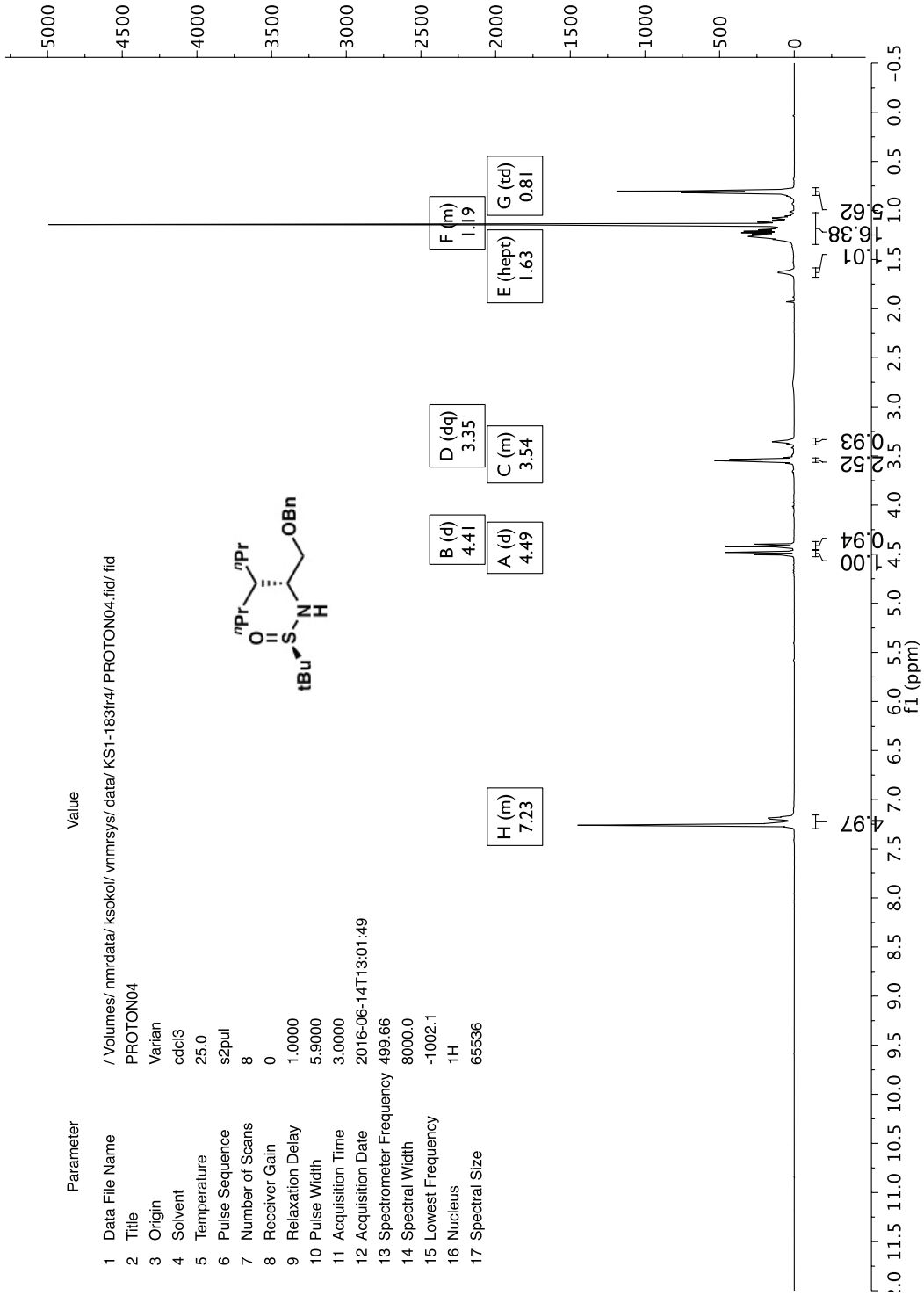
Nickel-Catalyzed Asymmetric Reductive Cross-Coupling to

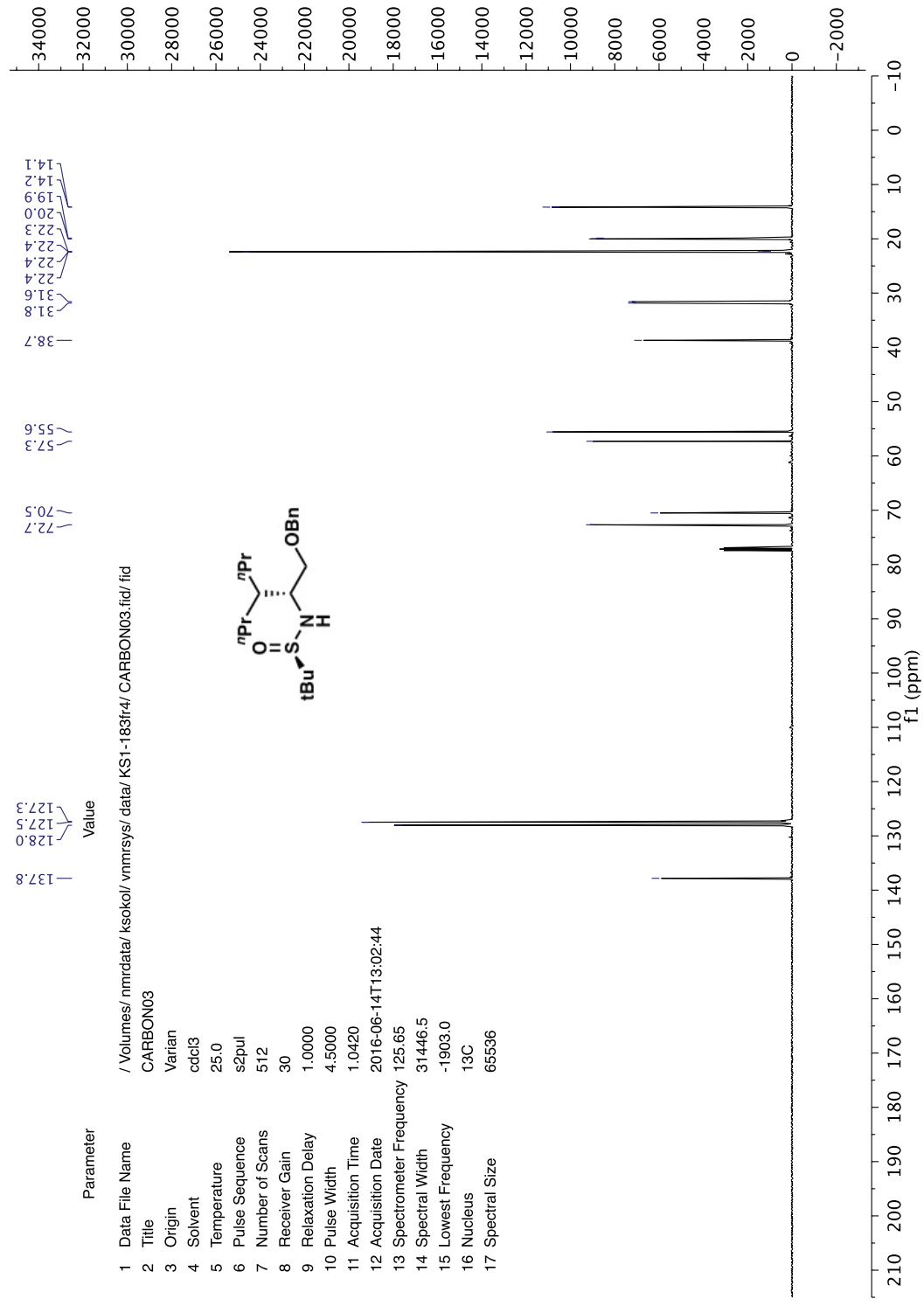
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14 Spectral Width 8000.0
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16 Nucleus 1H
17 Spectral Size 65536
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A (m) 4.14
D (m) 1.31
C (q) 1.65
E (m) 0.90
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1.00
5.08
6.86
1.08
f1 (ppm)

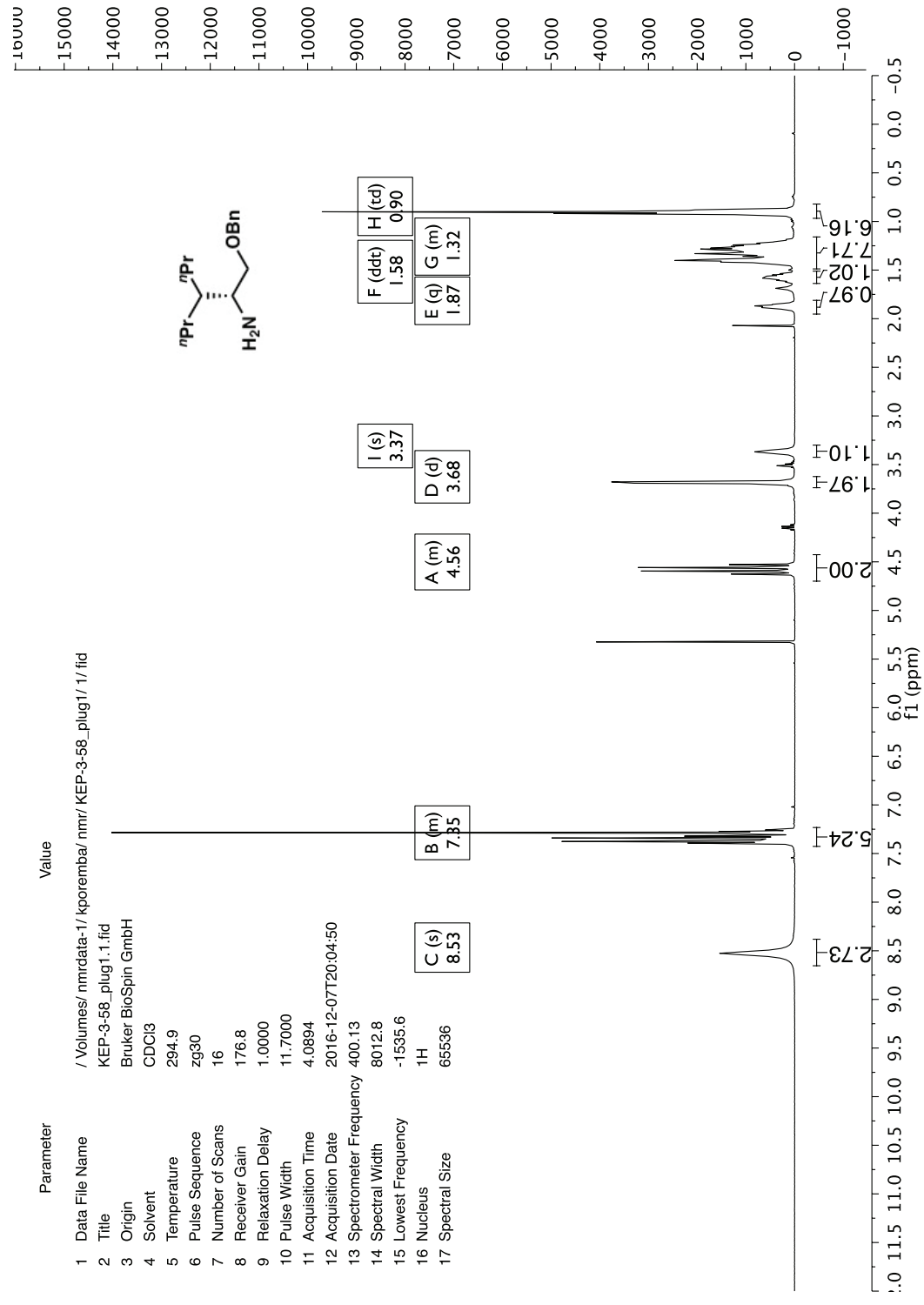


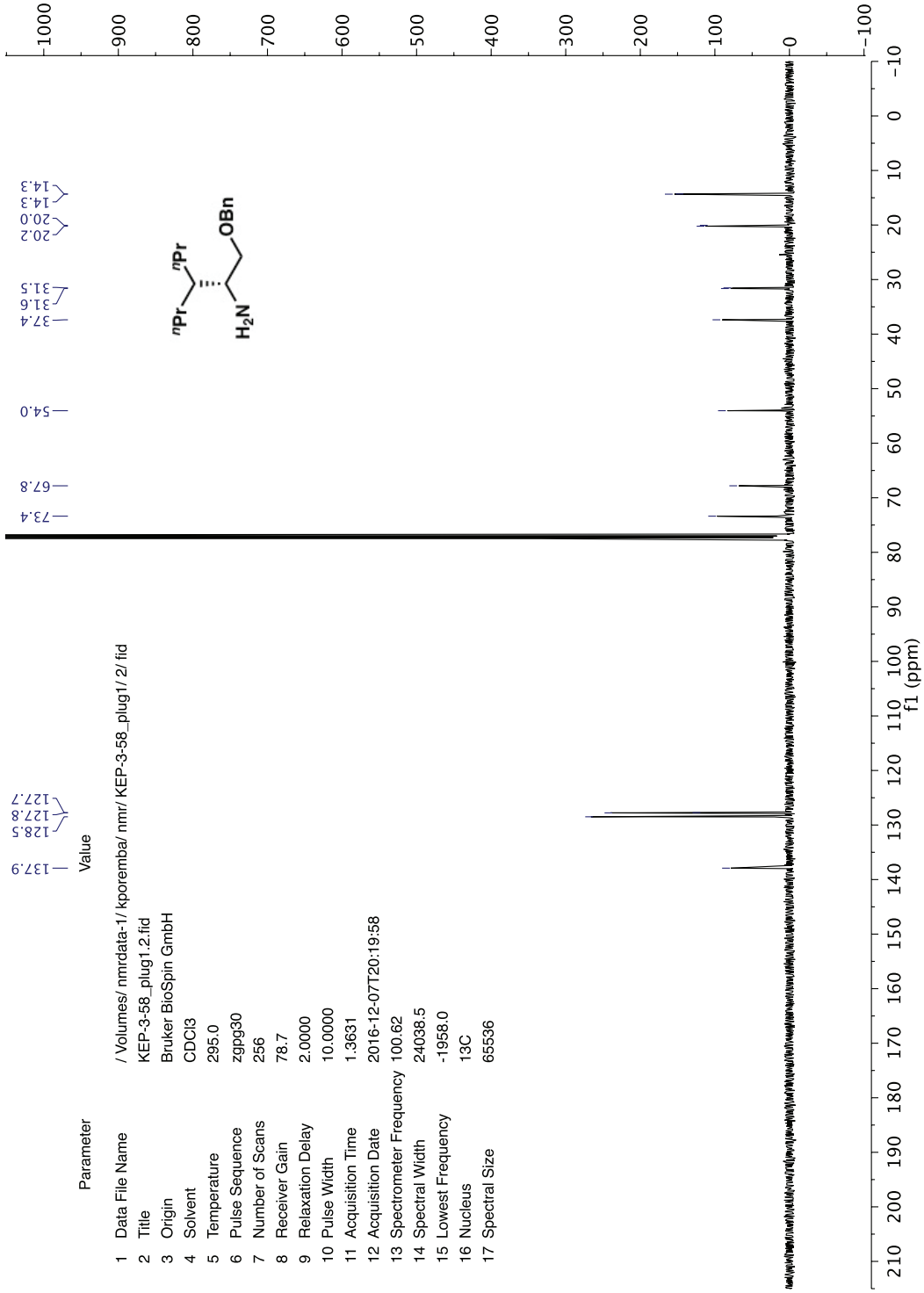
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16	Nucleus	13C
17	Spectral Size	65536


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B (d) 4.41
C (m) 3.54
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E (hept) 1.63
F (m) 1.19
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2.52
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1.01
6.38
3.62
f1 (ppm)

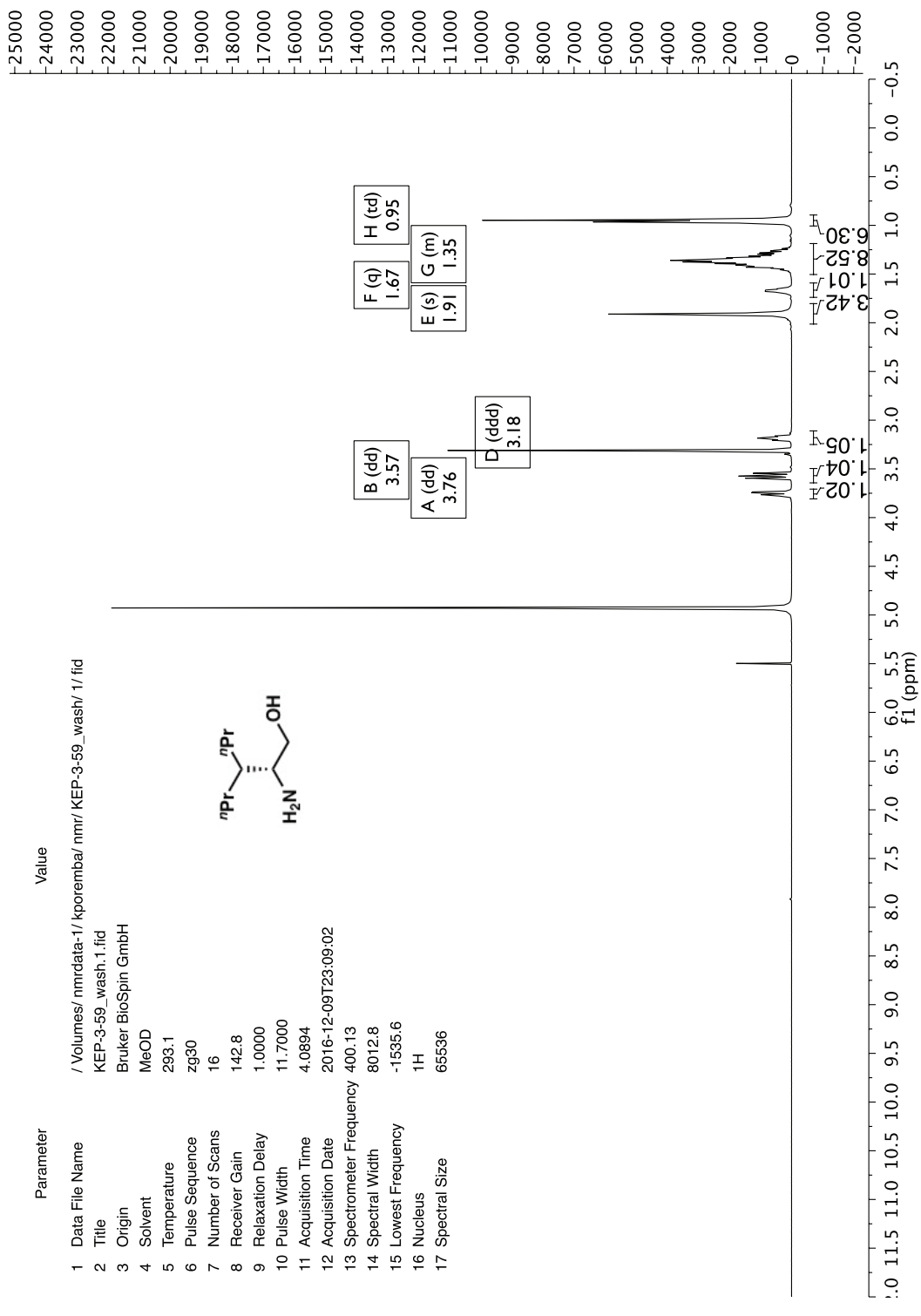


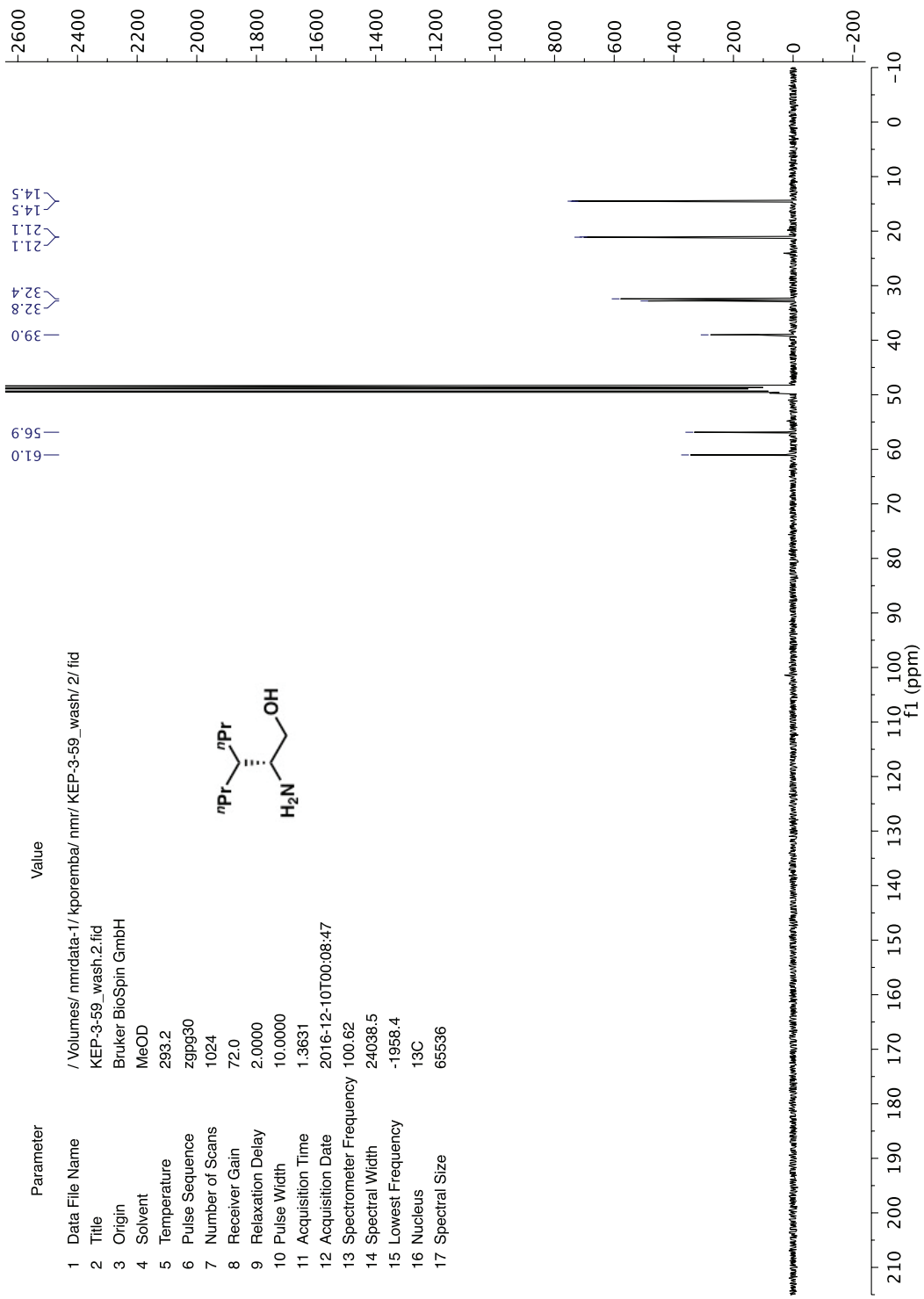
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16	Nucleus	13C
17	Spectral Size	65536


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B (m) 7.35
A (m) 4.56
D (d) 3.68
I (s) 3.37
F (ddt) 1.58
E (q) 1.87
G (m) 1.32
H (td) 0.90
2.73
5.24
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1.10
0.97
1.02
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nPr
OBn
H2N
f1 (ppm)

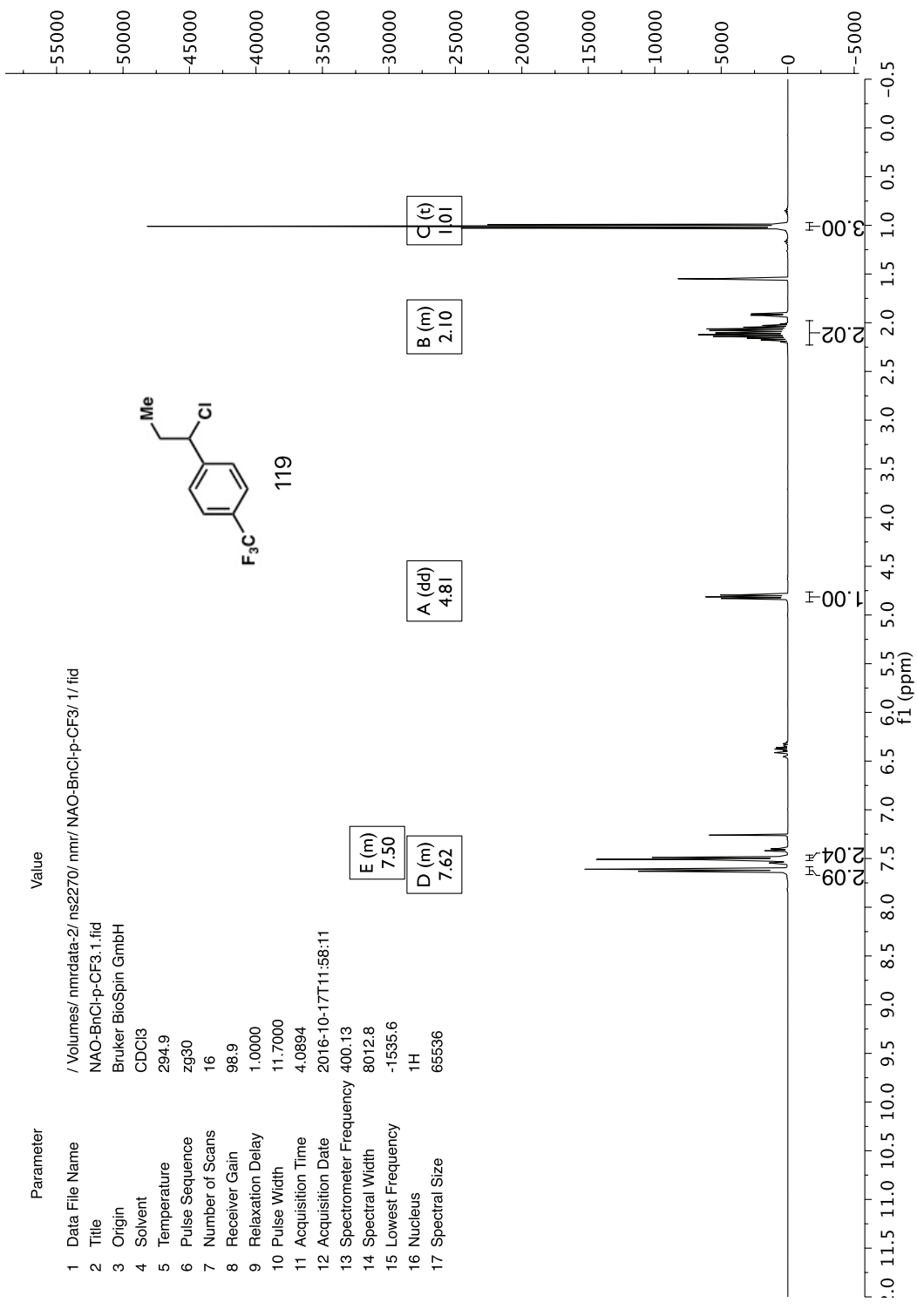


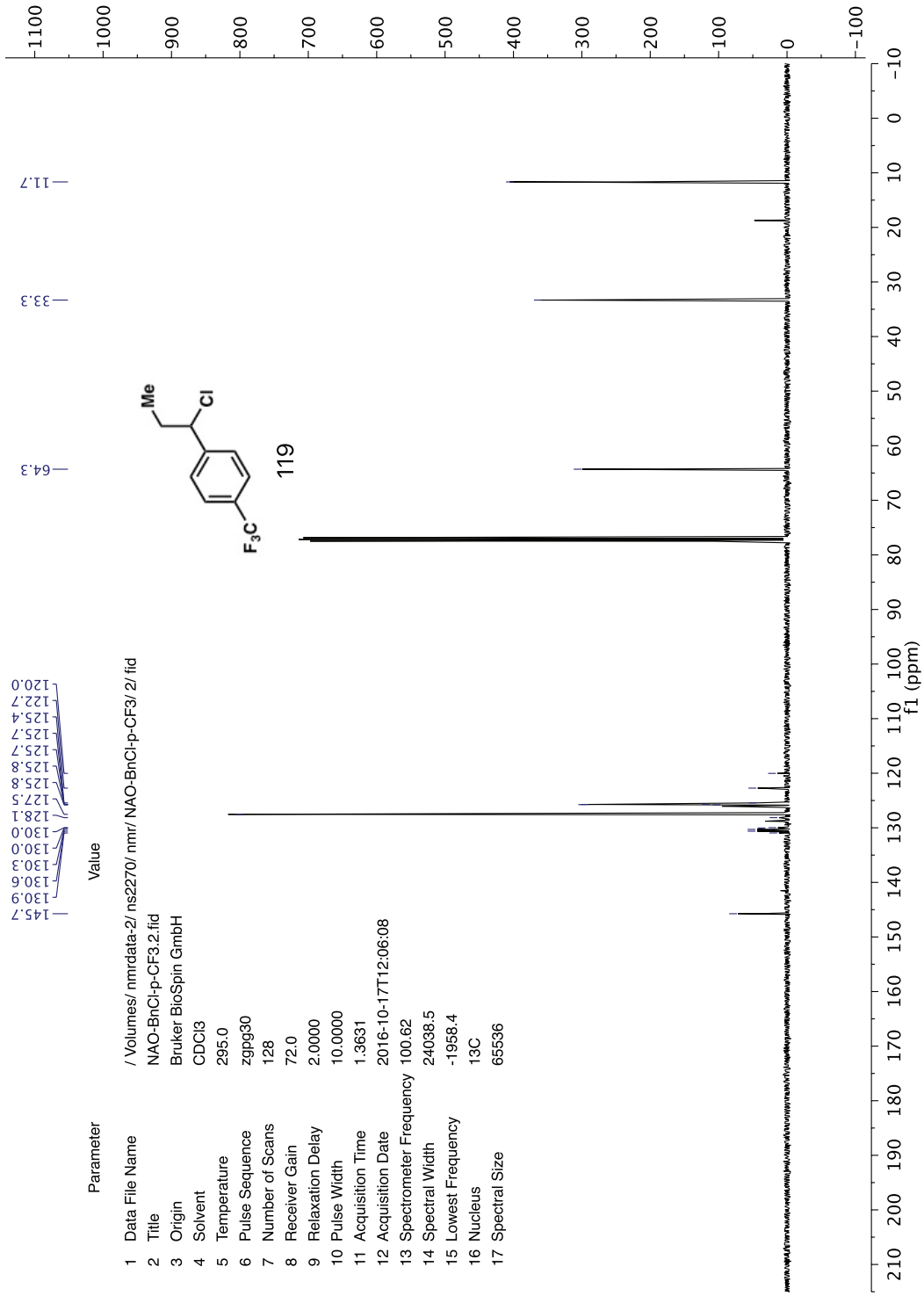
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15	Lowest Frequency	-1958.0
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17	Spectral Size	65536


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14 Spectral Width 8012.8
15 Lowest Frequency -1535.6
16 Nucleus 1H
17 Spectral Size 65536
nPr
nPr
H2N
OH
A (dd) 3.76
B (dd) 3.57
D (ddd) 3.18
E (s) 1.91
F (q) 1.67
G (m) 1.35
H (td) 0.95
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1.04
1.05
3.42
1.01
8.52
6.30
f1 (ppm)

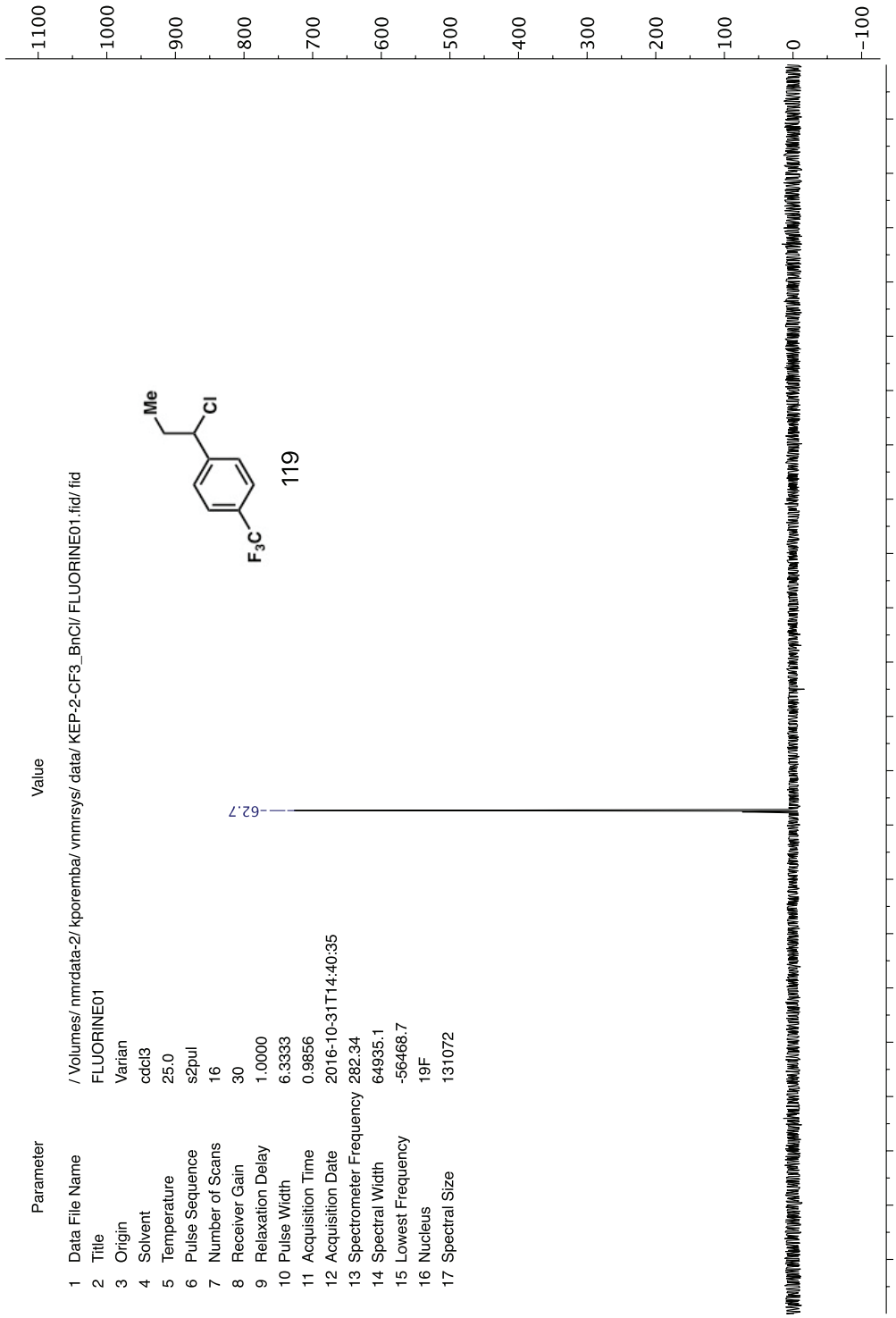


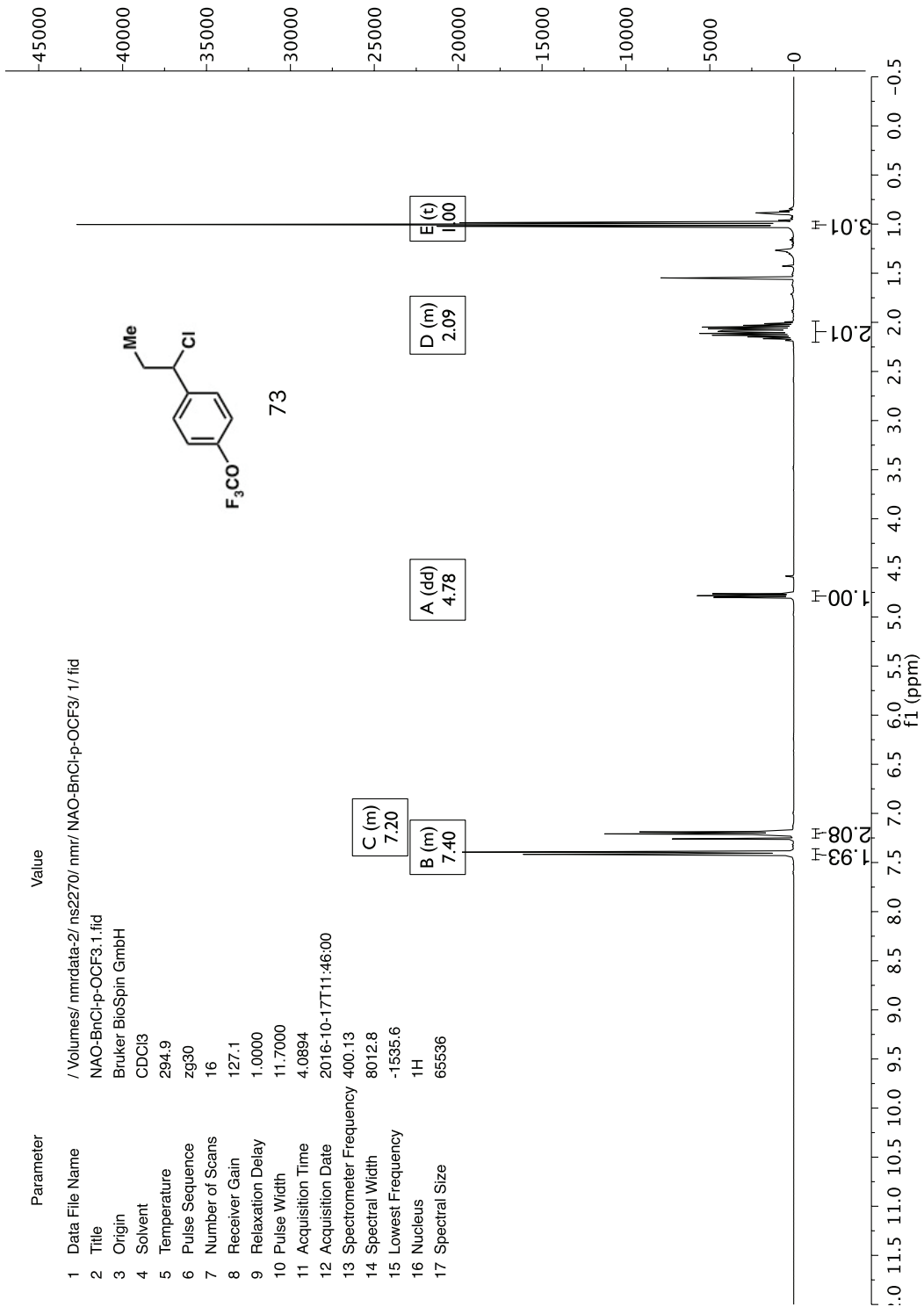
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17	Spectral Size	65536

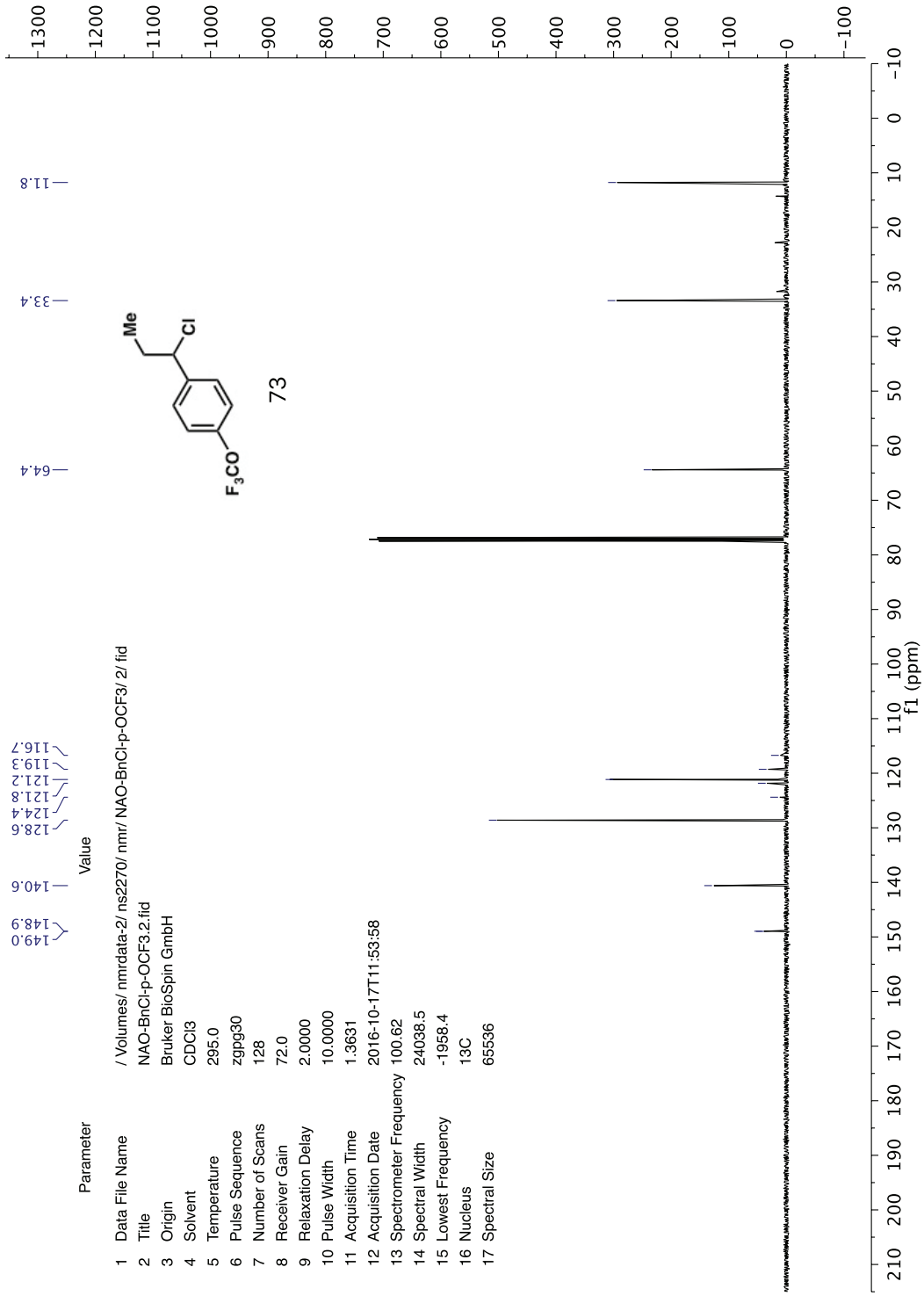

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16 Nucleus 1H
17 Spectral Size 65536
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Cl
F3C
119
A (dd) 4.81
B (m) 2.10
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E (m) 7.50
2.09
2.04
1.00
2.02
3.00
f1 (ppm)



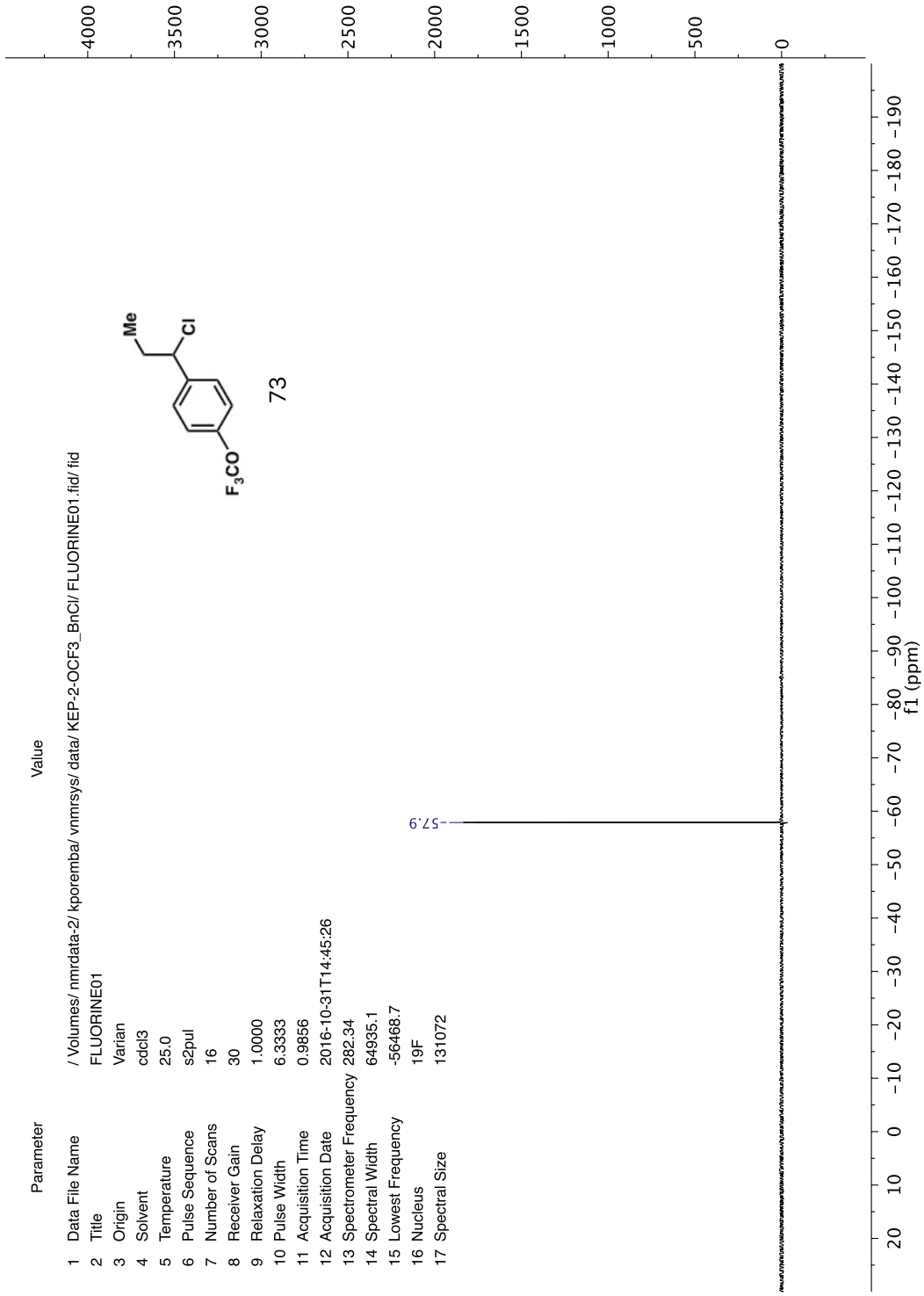
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11 Acquisition Time	1.3631
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14 Spectral Width	24038.5
15 Lowest Frequency	-1958.4
16 Nucleus	13C
17 Spectral Size	65536

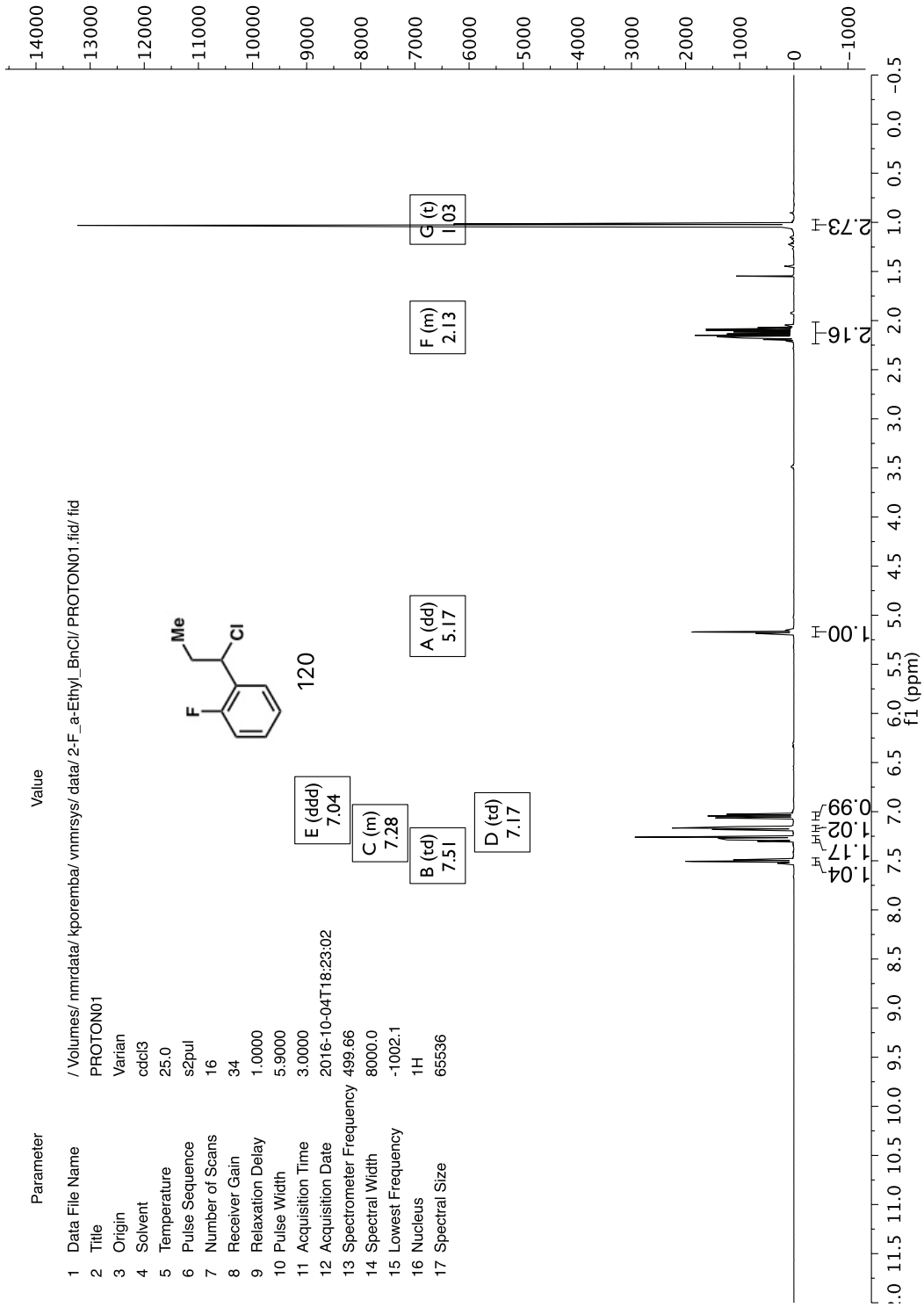

Parameter
Value
1 Data File Name / Volumes/ nmrdata-2/ kporemba/ vnmrsys/ data/ KEP-2-CF3_BnCl/ FLUORINE01.fid/ fid
2 Title FLUORINE01
3 Origin Varian
4 Solvent cdcl3
5 Temperature 25.0
6 Pulse Sequence s2pul
7 Number of Scans 16
8 Receiver Gain 30
9 Relaxation Delay 1.0000
10 Pulse Width 6.3333
11 Acquisition Time 0.9856
12 Acquisition Date 2016-10-31T14:40:35
13 Spectrometer Frequency 282.34
14 Spectral Width 64935.1
15 Lowest Frequency -56468.7
16 Nucleus 19F
17 Spectral Size 131072
Me
Cl
F3C
119
-62.7
f1 (ppm)

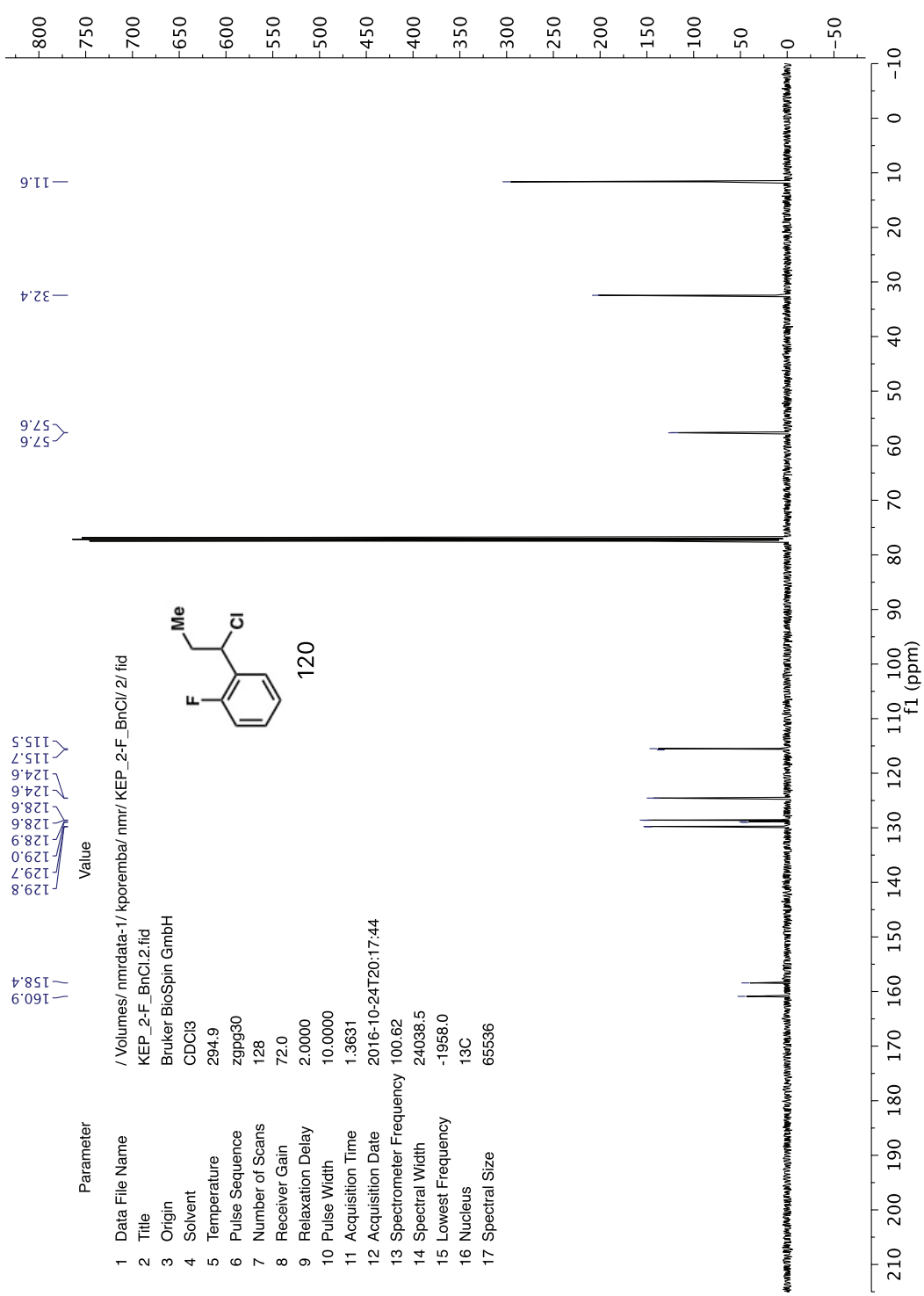

Parameter
Value
1 Data File Name / Volumes/ nmrdata-2/ ns2270/ nmr/ NAO-BnCl-p-OCF3/ 1/ fid
2 Title NAO-BnCl-p-OCF3.1.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 294.9
6 Pulse Sequence zg30
7 Number of Scans 16
8 Receiver Gain 127.1
9 Relaxation Delay 1.0000
10 Pulse Width 11.7000
11 Acquisition Time 4.0894
12 Acquisition Date 2016-10-17T11:46:00
13 Spectrometer Frequency 400.13
14 Spectral Width 8012.8
15 Lowest Frequency -1535.6
16 Nucleus 1H
17 Spectral Size 65536
Me
Cl
F3CO
73
A (dd) 4.78
B (m) 7.40
C (m) 7.20
D (m) 2.09
E (t) 1.00
1.93
2.08
1.00
2.01
3.01
f1 (ppm)

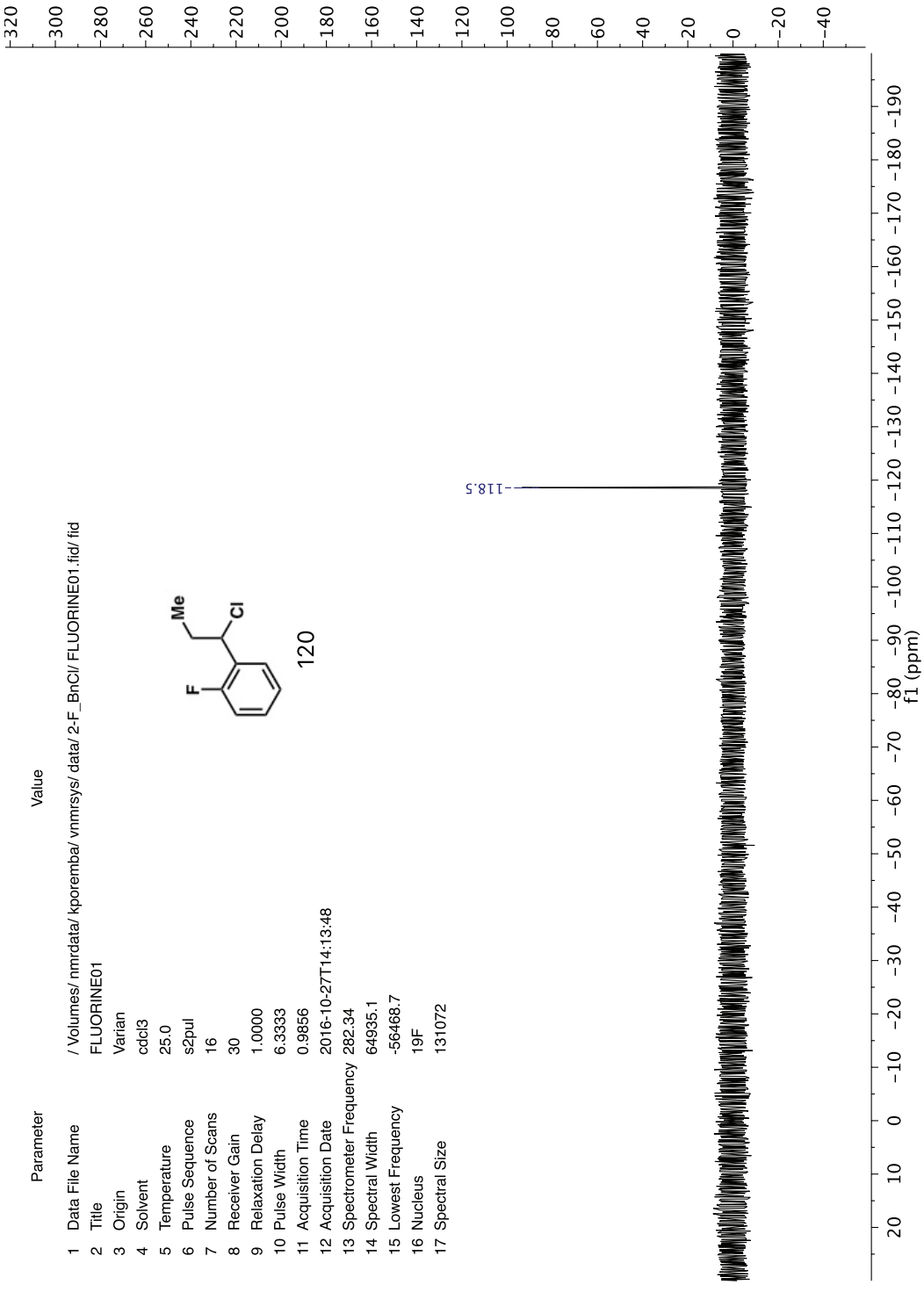


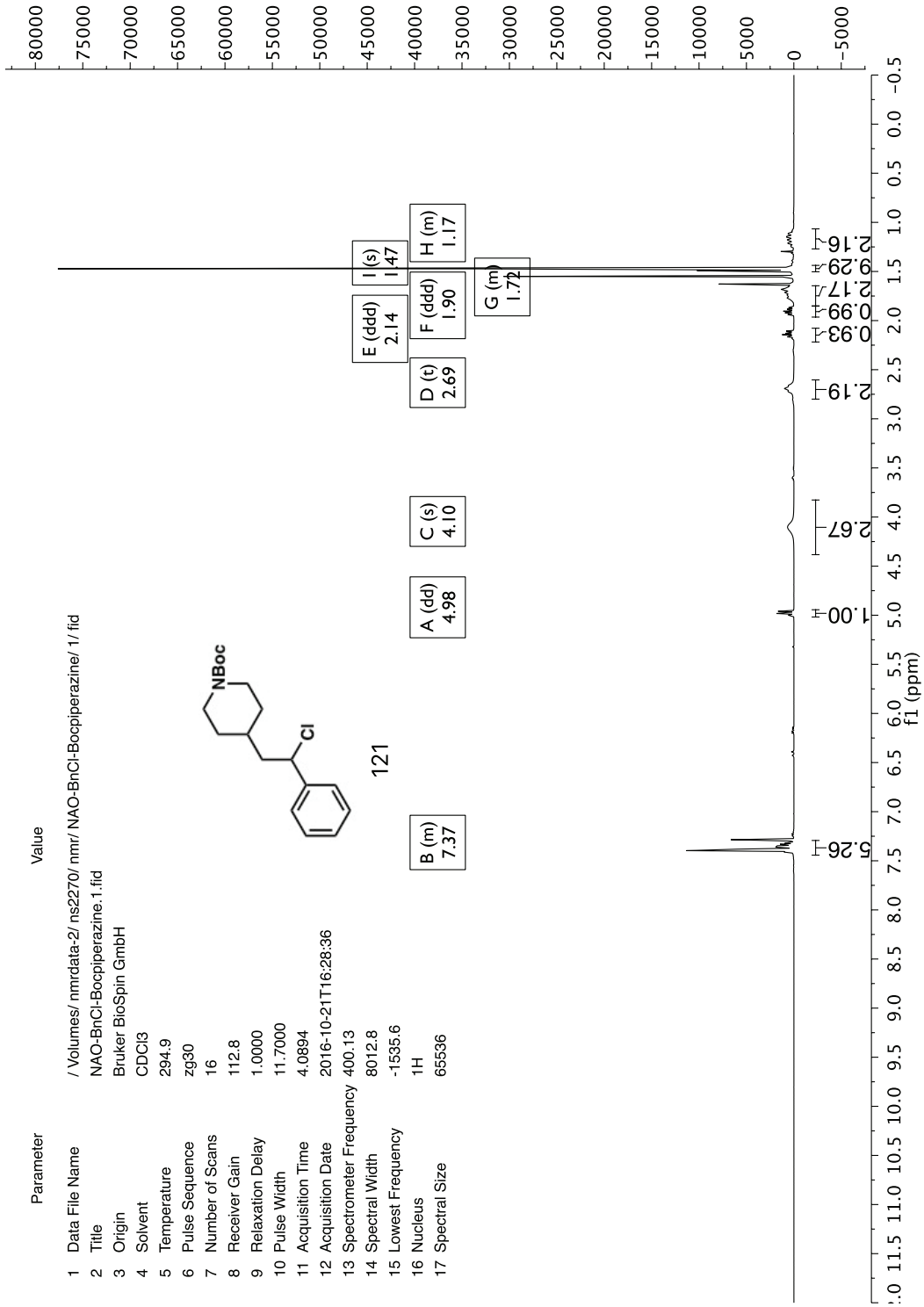
Parameter	Value
1 Data File Name	/ Volumes/ nmrdata-2/ ns2270/ nmr/ NAO-BnCl-p-OCF3/ 2/ fid
2 Title	NAO-BnCl-p-OCF3.2.fid
3 Origin	Bruker BioSpin GmbH
4 Solvent	CDCl3
5 Temperature	295.0
6 Pulse Sequence	zgpg30
7 Number of Scans	128
8 Receiver Gain	72.0
9 Relaxation Delay	2.0000
10 Pulse Width	10.0000
11 Acquisition Time	1.3631
12 Acquisition Date	2016-10-17T11:53:58
13 Spectrometer Frequency	100.62
14 Spectral Width	24038.5
15 Lowest Frequency	-1958.4
16 Nucleus	13C
17 Spectral Size	65536

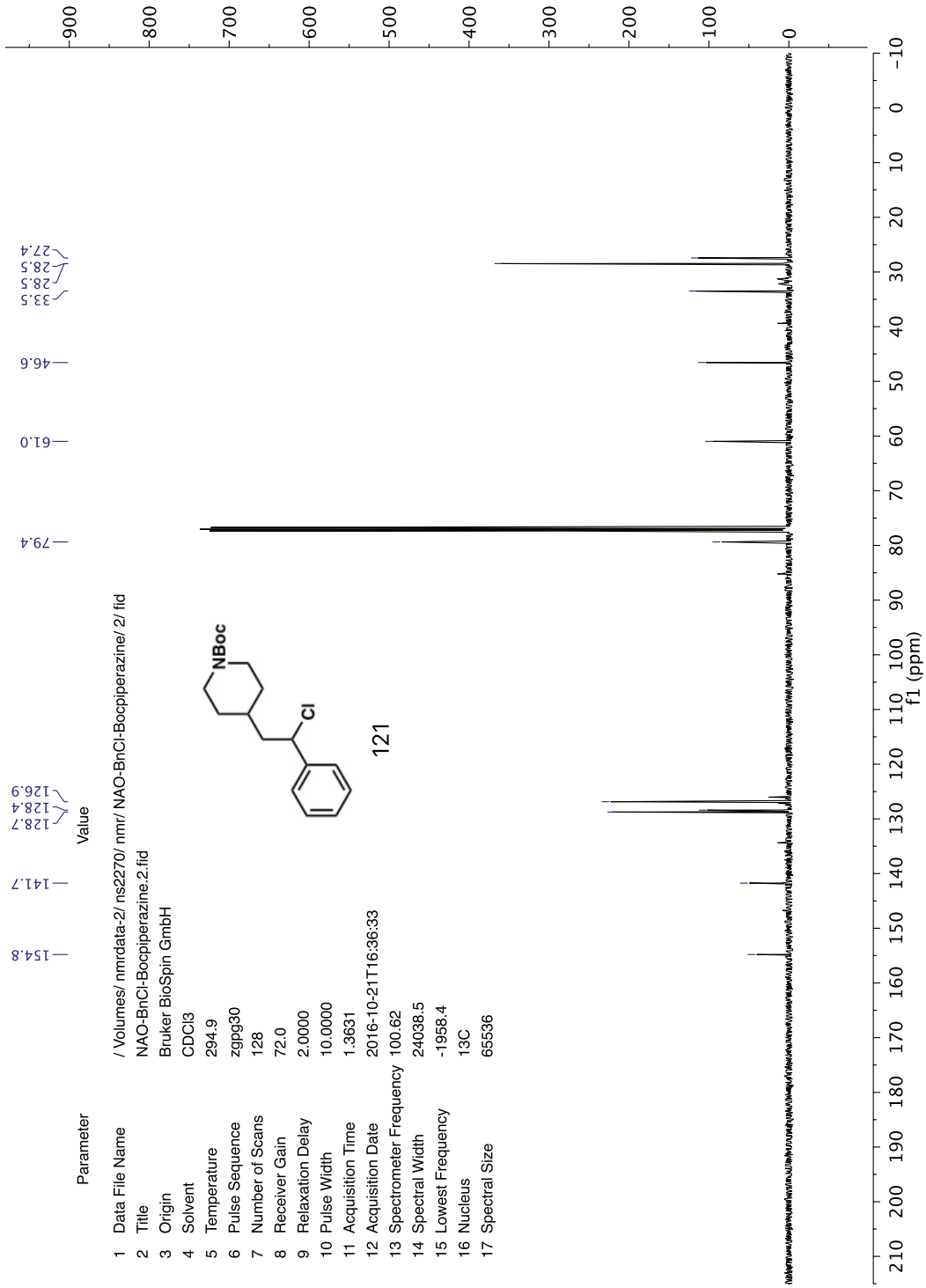

Parameter
Value
1 Data File Name / Volumes/ nmrdata-2/ kporemba/ vnmrsys/ data/ KEP-2-OCF3_BnCl/ FLUORINE01.fid/ fid
2 Title FLUORINE01
3 Origin Varian
4 Solvent cdcl3
5 Temperature 25.0
6 Pulse Sequence s2pul
7 Number of Scans 16
8 Receiver Gain 30
9 Relaxation Delay 1.0000
10 Pulse Width 6.3333
11 Acquisition Time 0.9856
12 Acquisition Date 2016-10-31T14:45:26
13 Spectrometer Frequency 282.34
14 Spectral Width 64935.1
15 Lowest Frequency -56468.7
16 Nucleus 19F
17 Spectral Size 131072
Me
Cl
F3CO
73
-57.9
4000
3500
3000
2500
2000
1500
1000
500
0
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)


Parameter
Value
1 Data File Name / Volumes/ nmrdata/ kporemba/ vnmrsys/ data/ 2-F_a-Ethyl_BnCl/ PROTON01.fid/ fid
2 Title PROTON01
3 Origin Varian
4 Solvent cdcl3
5 Temperature 25.0
6 Pulse Sequence s2pul
7 Number of Scans 16
8 Receiver Gain 34
9 Relaxation Delay 1.0000
10 Pulse Width 5.9000
11 Acquisition Time 3.0000
12 Acquisition Date 2016-10-04T18:23:02
13 Spectrometer Frequency 499.66
14 Spectral Width 8000.0
15 Lowest Frequency -1002.1
16 Nucleus 1H
17 Spectral Size 65536
Me
Cl
F
120
E (ddd) 7.04
C (m) 7.28
B (td) 7.51
D (td) 7.17
A (dd) 5.17
F (m) 2.13
G (t) 7.03
1.04
1.17
1.02
0.99
1.00
2.16
2.73
f1 (ppm)

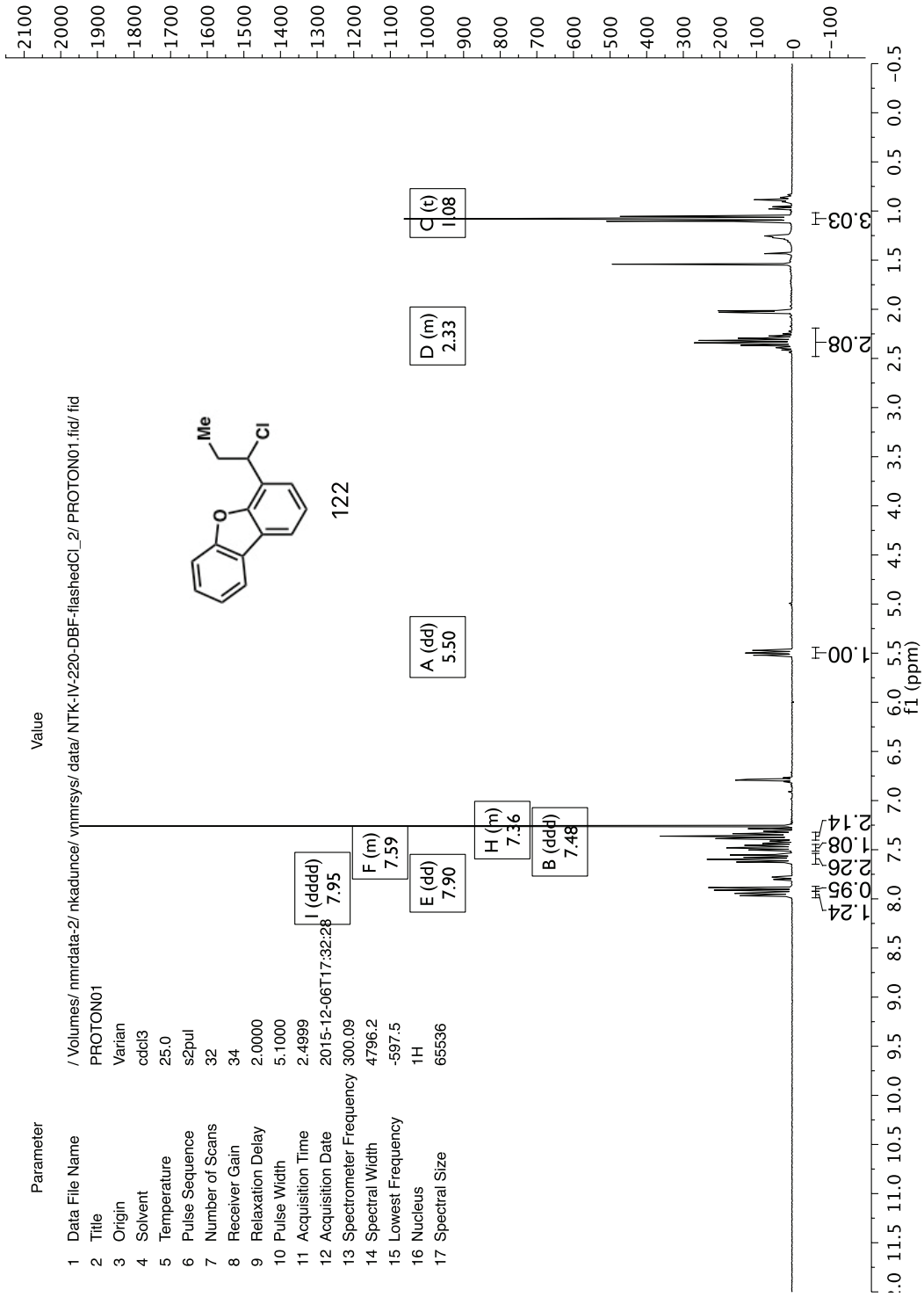

160.9
158.4
129.8
129.7
129.0
128.9
128.6
128.6
124.6
124.6
115.7
115.5
57.6
57.6
32.4
11.6
Me
Cl
F
120
Parameter Value
1 Data File Name / Volumes/ nmrdata-1/ kporemba/ nmr/ KEP_2-F_BnCl/ 2/ fid
2 Title KEP_2-F_BnCl.2.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 294.9
6 Pulse Sequence zgpg30
7 Number of Scans 128
8 Receiver Gain 72.0
9 Relaxation Delay 2.0000
10 Pulse Width 10.0000
11 Acquisition Time 1.3631
12 Acquisition Date 2016-10-24T20:17:44
13 Spectrometer Frequency 100.62
14 Spectral Width 24038.5
15 Lowest Frequency -1958.0
16 Nucleus 13C
17 Spectral Size 65536
f1 (ppm)

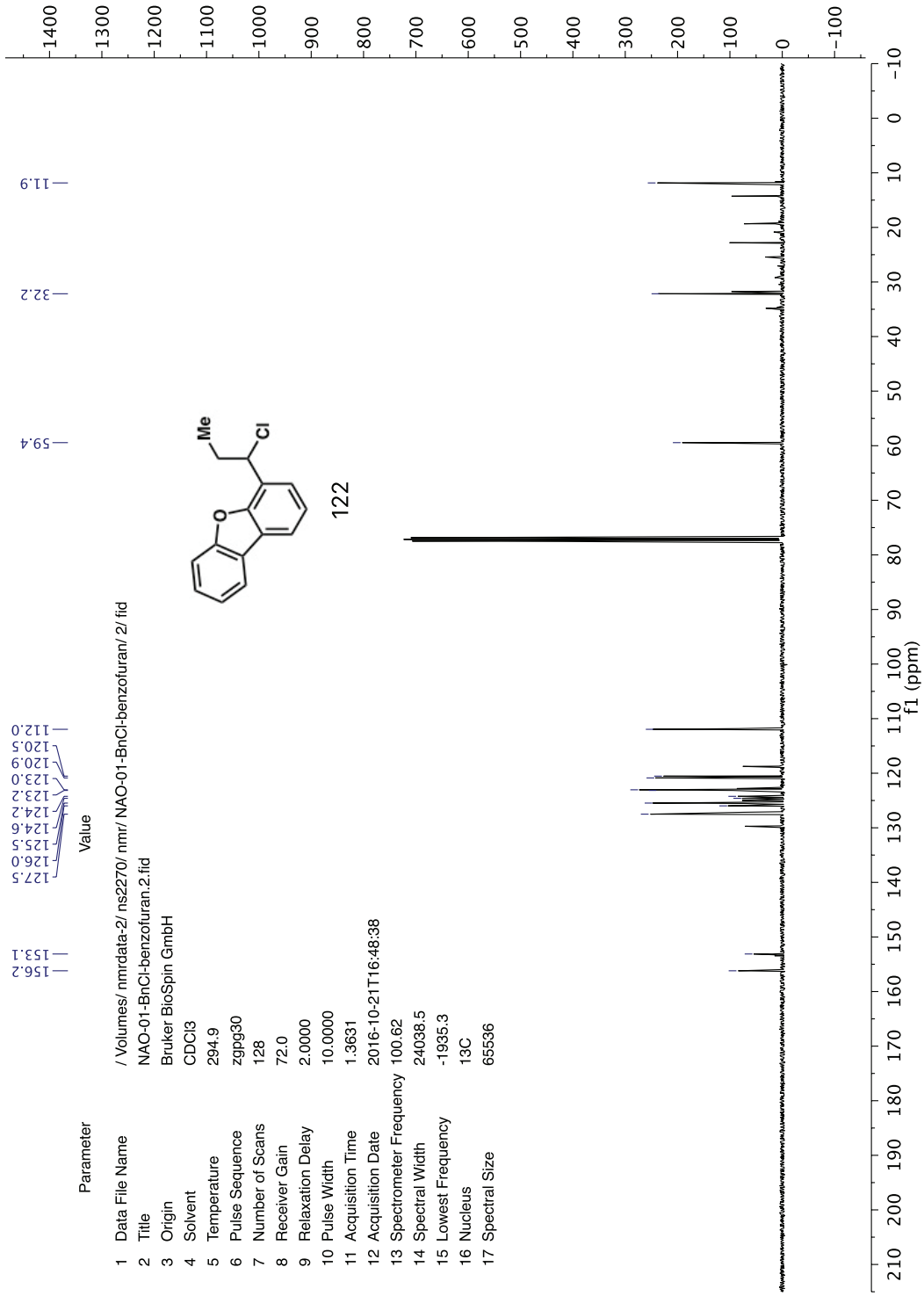

Parameter
Value
1 Data File Name / Volumes/ nmrdata/ kporemba/ vnmrsys/ data/ 2-F_BnCl/ FLUORINE01.fid/ fid
2 Title FLUORINE01
3 Origin Varian
4 Solvent cdcl3
5 Temperature 25.0
6 Pulse Sequence s2pul
7 Number of Scans 16
8 Receiver Gain 30
9 Relaxation Delay 1.0000
10 Pulse Width 6.3333
11 Acquisition Time 0.9856
12 Acquisition Date 2016-10-27T14:13:48
13 Spectrometer Frequency 282.34
14 Spectral Width 64935.1
15 Lowest Frequency -56468.7
16 Nucleus 19F
17 Spectral Size 131072
Me
Cl
F
120
-118.5
f1 (ppm)


Parameter
Value
1 Data File Name / Volumes/ nmrdata-2/ ns2270/ nmr/ NAO-BnCl-Bocpiperazine/ 1/ fid
2 Title NAO-BnCl-Bocpiperazine.1.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 294.9
6 Pulse Sequence zg30
7 Number of Scans 16
8 Receiver Gain 112.8
9 Relaxation Delay 1.0000
10 Pulse Width 11.7000
11 Acquisition Time 4.0894
12 Acquisition Date 2016-10-21T16:28:36
13 Spectrometer Frequency 400.13
14 Spectral Width 8012.8
15 Lowest Frequency -1535.6
16 Nucleus 1H
17 Spectral Size 65536
NBoc
Cl
121
B (m) 7.37
A (dd) 4.98
C (s) 4.10
D (t) 2.69
E (ddd) 2.14
F (ddd) 1.90
I (s) 1.47
G (m) 1.72
H (m) 1.17
5.26
1.00
2.67
2.19
0.93
0.99
2.17
9.29
2.16
f1 (ppm)

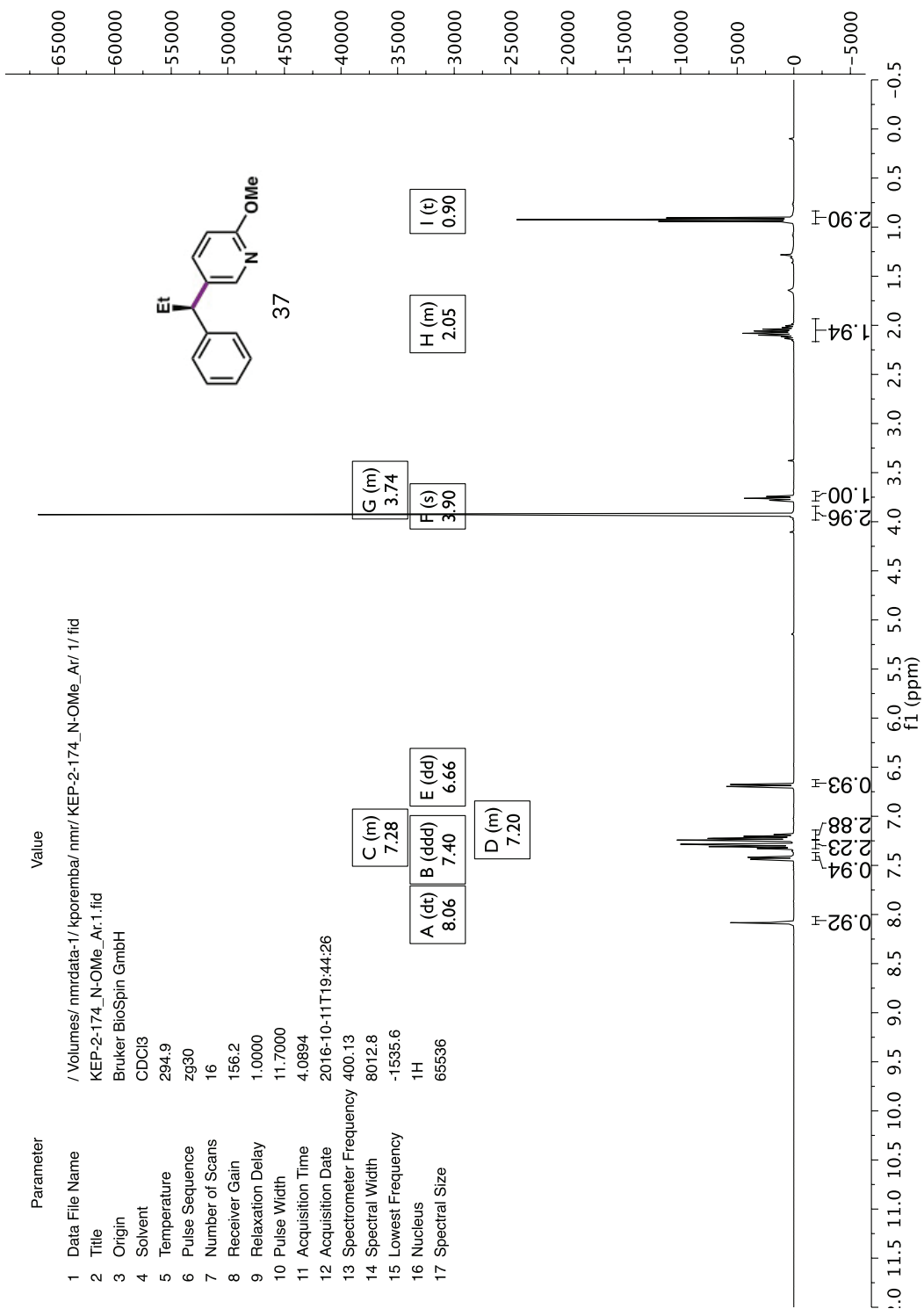


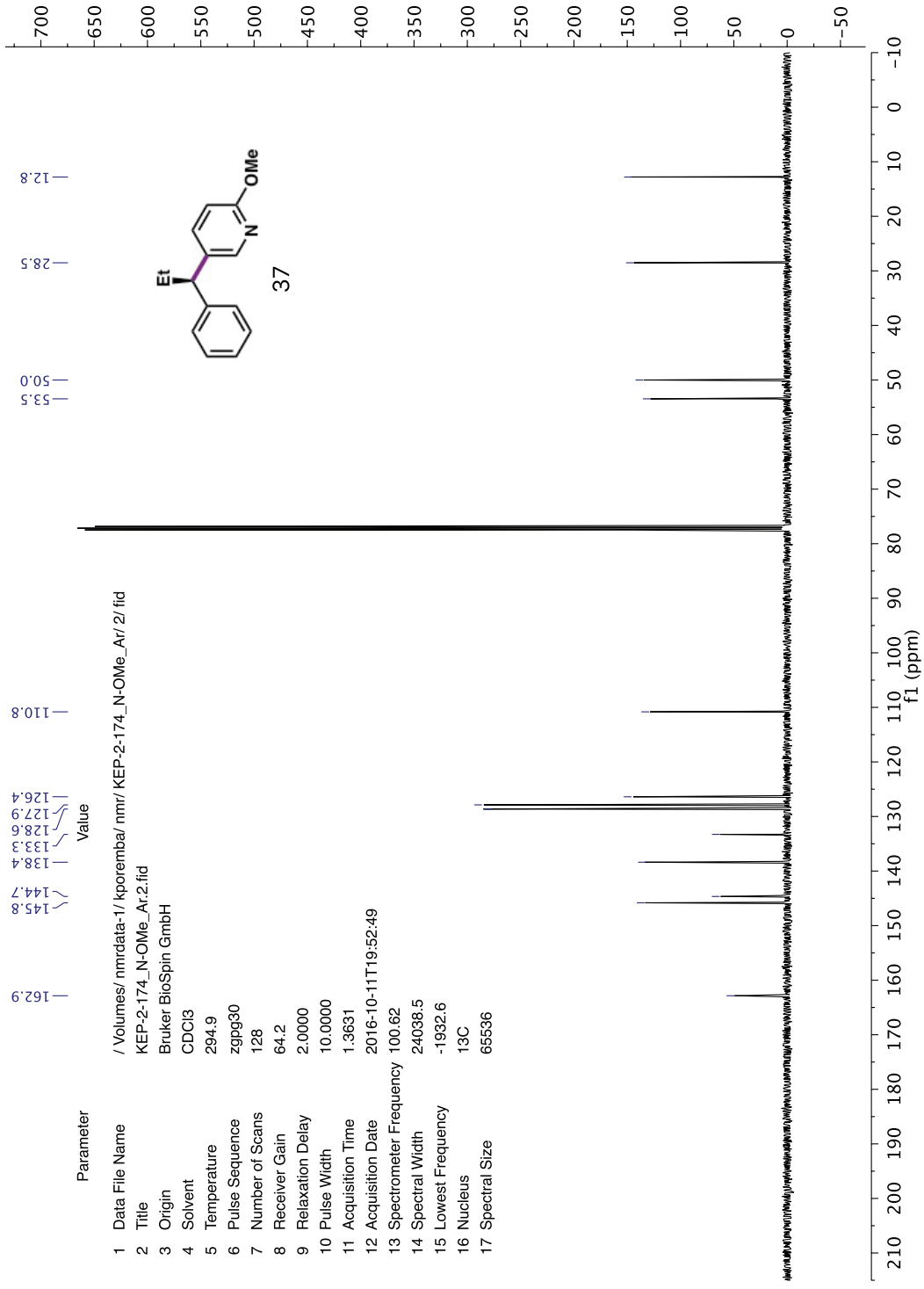
	Parameter	Value
1	Data File Name	/ Volumes/ nmrdata-2/ ns2270/ nmr/ NAO-BnCl-Bocpiperazine/ 2/ fid
2	Title	NAO-BnCl-Bocpiperazine.2.fid
3	Origin	Bruker BioSpin GmbH
4	Solvent	CDCl3
5	Temperature	294.9
6	Pulse Sequence	zgpg30
7	Number of Scans	128
8	Receiver Gain	72.0
9	Relaxation Delay	2.0000
10	Pulse Width	10.0000
11	Acquisition Time	1.3631
12	Acquisition Date	2016-10-21T16:36:33
13	Spectrometer Frequency	100.62
14	Spectral Width	24038.5
15	Lowest Frequency	-1958.4
16	Nucleus	13C
17	Spectral Size	65536


Parameter
Value
1 Data File Name / Volumes/ nmrdata-2/ nkaduncе/ vnmrsys/ data/ NTK-IV-220-DBF-flashedCl_2/ PROTON01.fid/ fid
2 Title PROTON01
3 Origin Varian
4 Solvent cdcl3
5 Temperature 25.0
6 Pulse Sequence s2pul
7 Number of Scans 32
8 Receiver Gain 34
9 Relaxation Delay 2.0000
10 Pulse Width 5.1000
11 Acquisition Time 2.4999
12 Acquisition Date 2015-12-06T17:32:28
13 Spectrometer Frequency 300.09
14 Spectral Width 4796.2
15 Lowest Frequency -597.5
16 Nucleus 1H
17 Spectral Size 65536
Me
Cl
O
122
I (dddd) 7.95
F (m) 7.59
E (dd) 7.90
H (m) 7.36
B (ddd) 7.48
A (dd) 5.50
D (m) 2.33
C (t) 1.08
3.03
2.08
1.00
2.14
1.08
2.26
0.95
1.24
f1 (ppm)

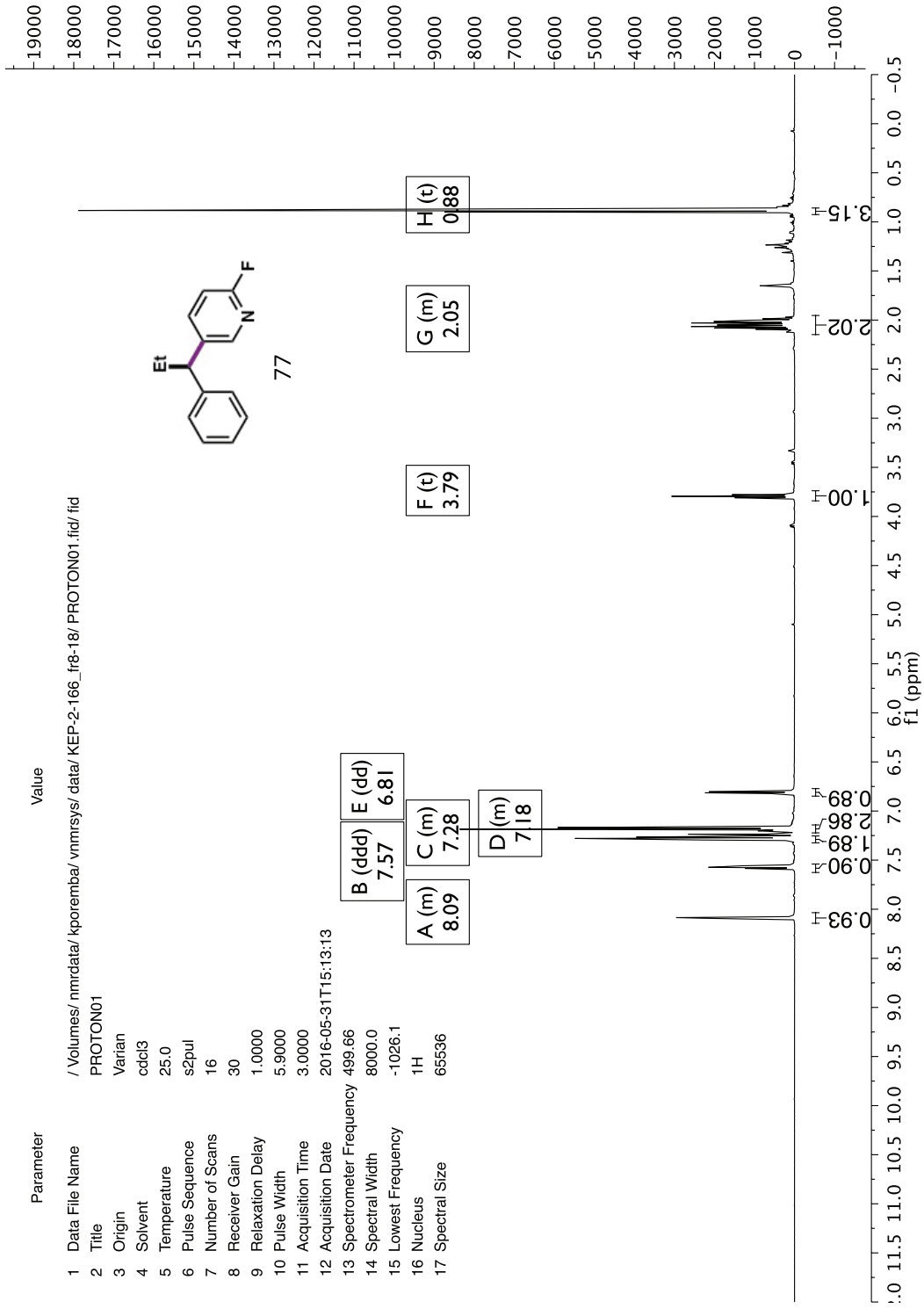


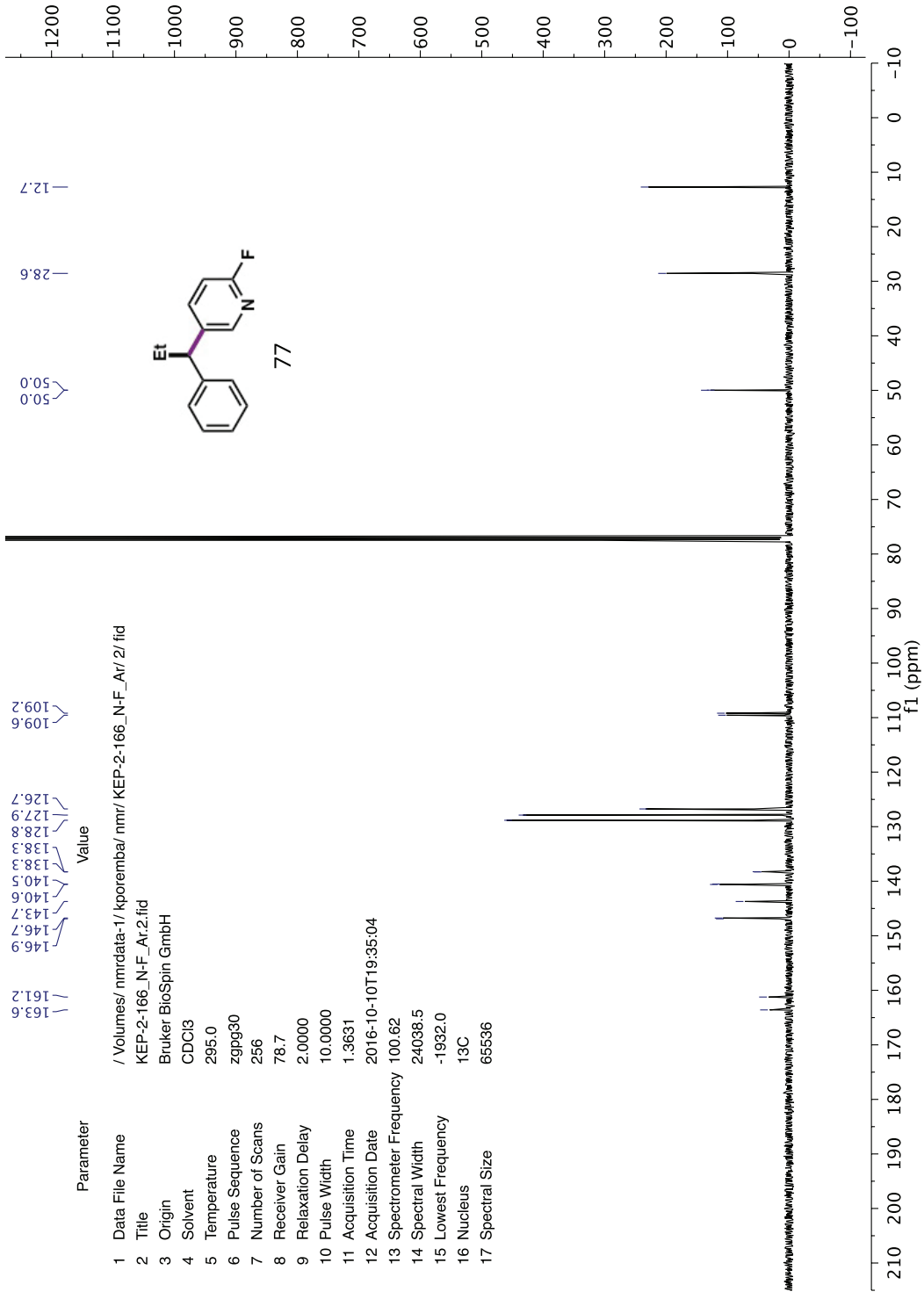
Parameter	Value
1 Data File Name	/ Volumes/ nmrdata-2/ ns2270/ nmr/ NAO-01-BnCl-benzofuran/ 2/ fid
2 Title	NAO-01-BnCl-benzofuran.2.fid
3 Origin	Bruker BioSpin GmbH
4 Solvent	CDCl3
5 Temperature	294.9
6 Pulse Sequence	zgpg30
7 Number of Scans	128
8 Receiver Gain	72.0
9 Relaxation Delay	2.0000
10 Pulse Width	10.0000
11 Acquisition Time	1.3631
12 Acquisition Date	2016-10-21T16:48:38
13 Spectrometer Frequency	100.62
14 Spectral Width	24038.5
15 Lowest Frequency	-1935.3
16 Nucleus	13C
17 Spectral Size	65536


Parameter
Value
1 Data File Name / Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-174_N-OMe_Ar/ 1/ fid
2 Title KEP-2-174_N-OMe_Ar.1.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 294.9
6 Pulse Sequence zg30
7 Number of Scans 16
8 Receiver Gain 156.2
9 Relaxation Delay 1.0000
10 Pulse Width 11.7000
11 Acquisition Time 4.0894
12 Acquisition Date 2016-10-11T19:44:26
13 Spectrometer Frequency 400.13
14 Spectral Width 8012.8
15 Lowest Frequency -1535.6
16 Nucleus 1H
17 Spectral Size 65536
A (dt) 8.06
B (ddd) 7.40
C (m) 7.28
D (m) 7.20
E (dd) 6.66
F (s) 3.90
G (m) 3.74
H (m) 2.05
I (t) 0.90
37
Et
OMe
N
0.92
2.88
2.23
0.94
0.93
1.00
2.96
1.94
2.90
f1 (ppm)

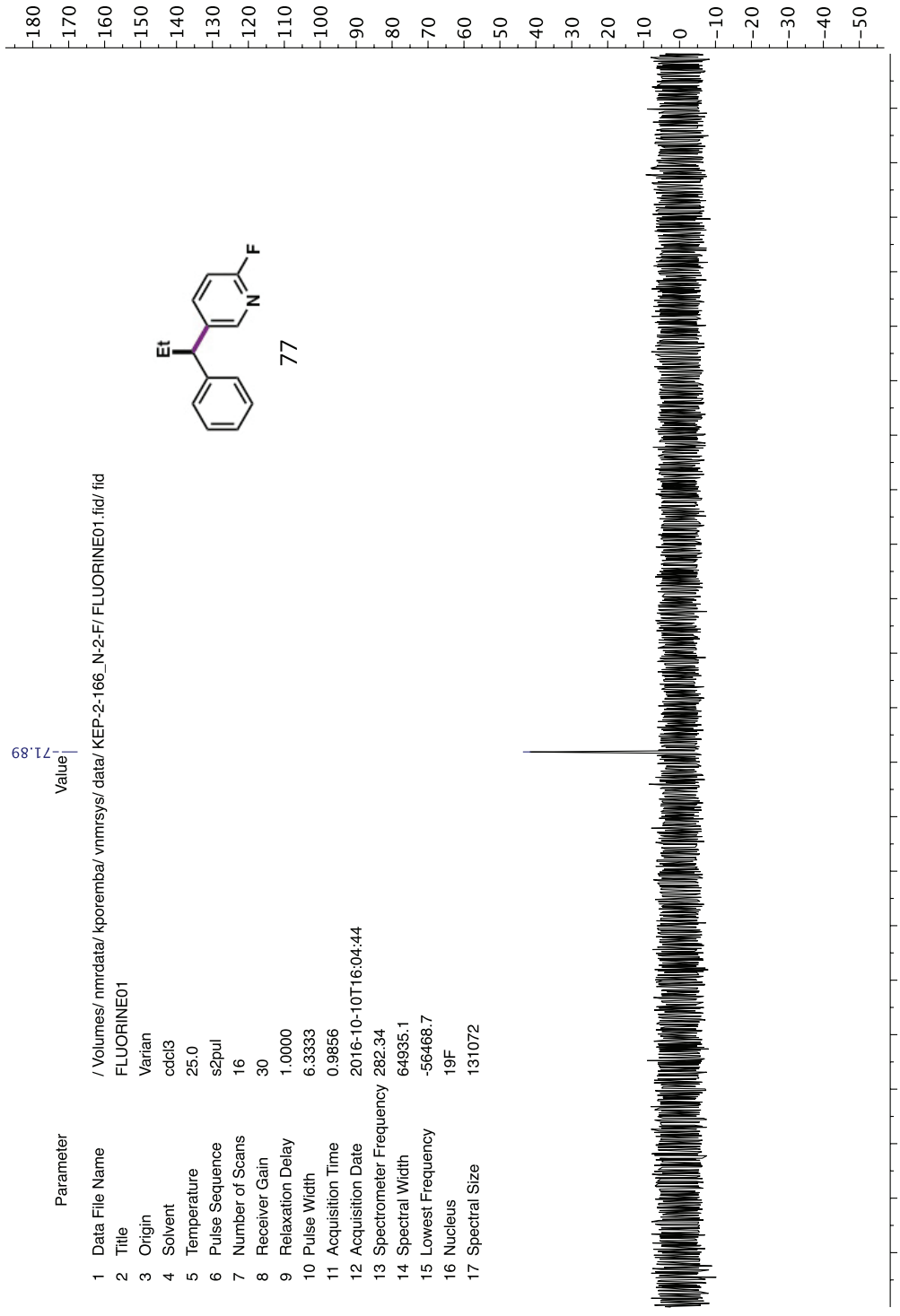


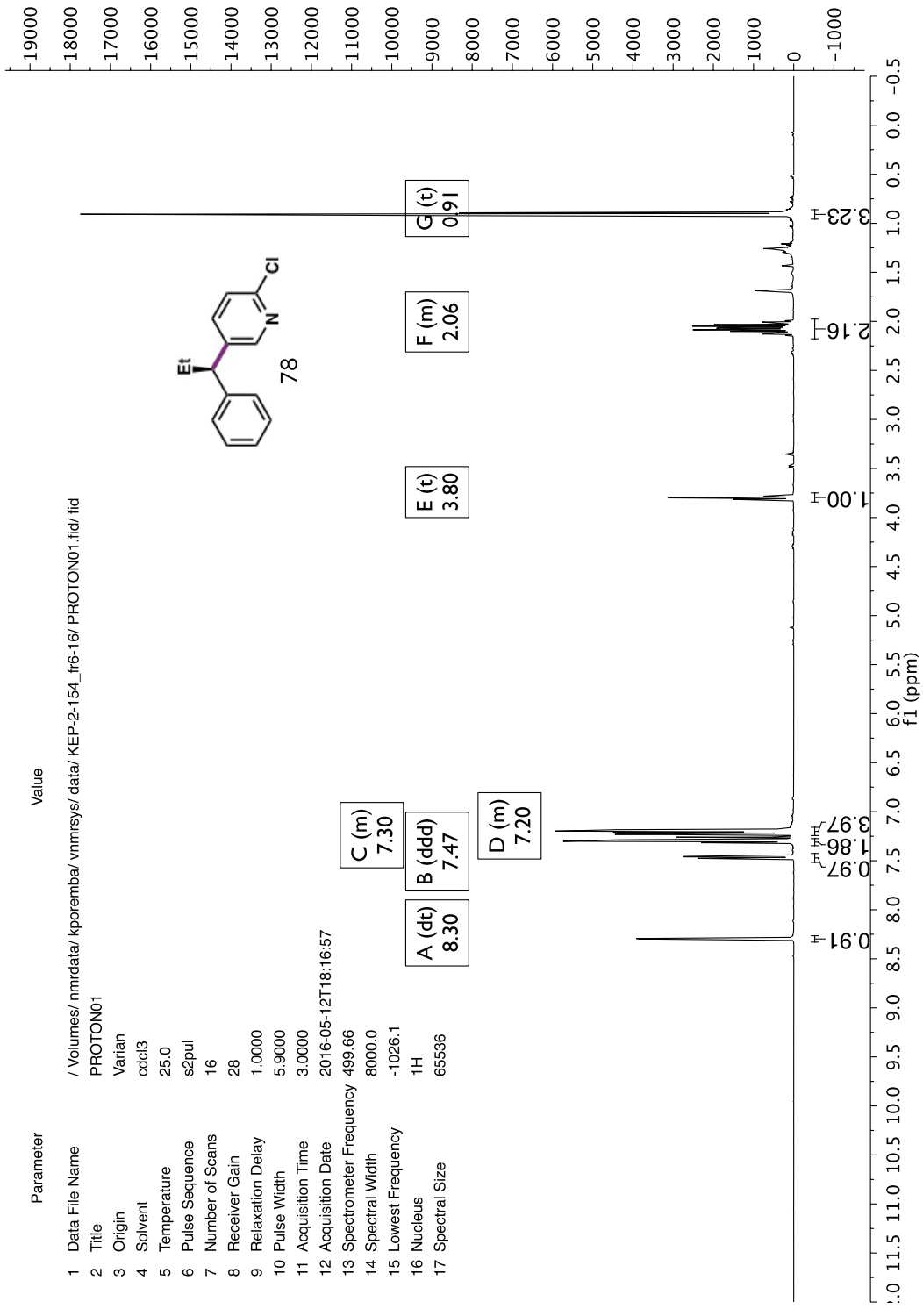
Parameter	Value
1 Data File Name	/ Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-174_N-OMe_Ar/ 2/ fid
2 Title	KEP-2-174_N-OMe_Ar.2.fid
3 Origin	Bruker BioSpin GmbH
4 Solvent	CDCl3
5 Temperature	294.9
6 Pulse Sequence	zgpg30
7 Number of Scans	128
8 Receiver Gain	64.2
9 Relaxation Delay	2.0000
10 Pulse Width	10.0000
11 Acquisition Time	1.3631
12 Acquisition Date	2016-10-11T19:52:49
13 Spectrometer Frequency	100.62
14 Spectral Width	24038.5
15 Lowest Frequency	-1932.6
16 Nucleus	13C
17 Spectral Size	65536

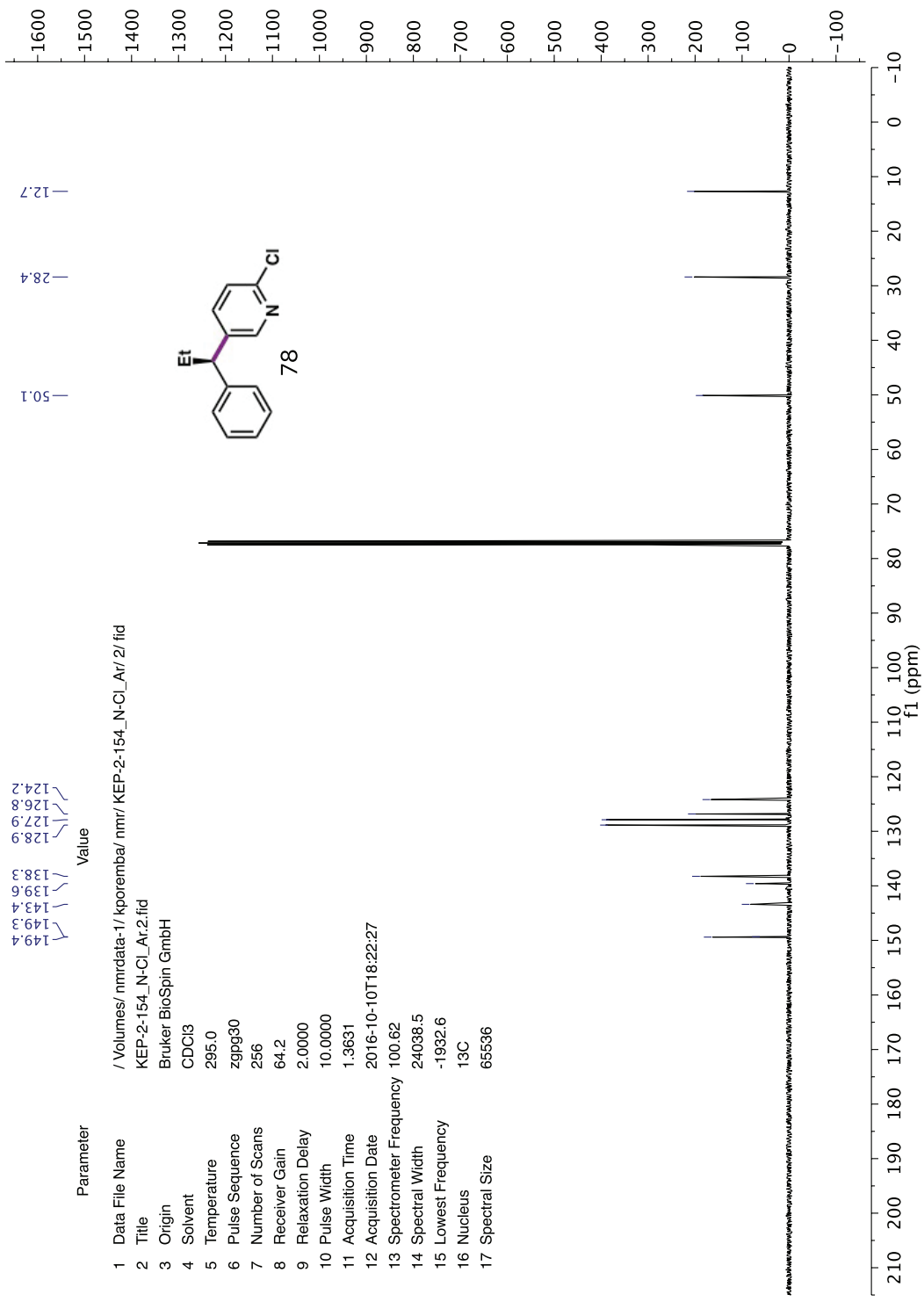

Parameter
Value
1 Data File Name / Volumes/ nmrdata/ kporemba/ vnmrsys/ data/ KEP-2-166_fr8-18/ PROTON01.fid/ fid
2 Title PROTON01
3 Origin Varian
4 Solvent cdcl3
5 Temperature 25.0
6 Pulse Sequence s2pul
7 Number of Scans 16
8 Receiver Gain 30
9 Relaxation Delay 1.0000
10 Pulse Width 5.9000
11 Acquisition Time 3.0000
12 Acquisition Date 2016-05-31T15:13:13
13 Spectrometer Frequency 499.66
14 Spectral Width 8000.0
15 Lowest Frequency -1026.1
16 Nucleus 1H
17 Spectral Size 65536
77
A (m) 8.09
B (ddd) 7.57
C (m) 7.28
D (m) 7.18
E (dd) 6.81
F (t) 3.79
G (m) 2.05
H (t) 0.88
0.93
0.90
1.89
2.86
0.89
1.00
2.02
3.15
f1 (ppm)



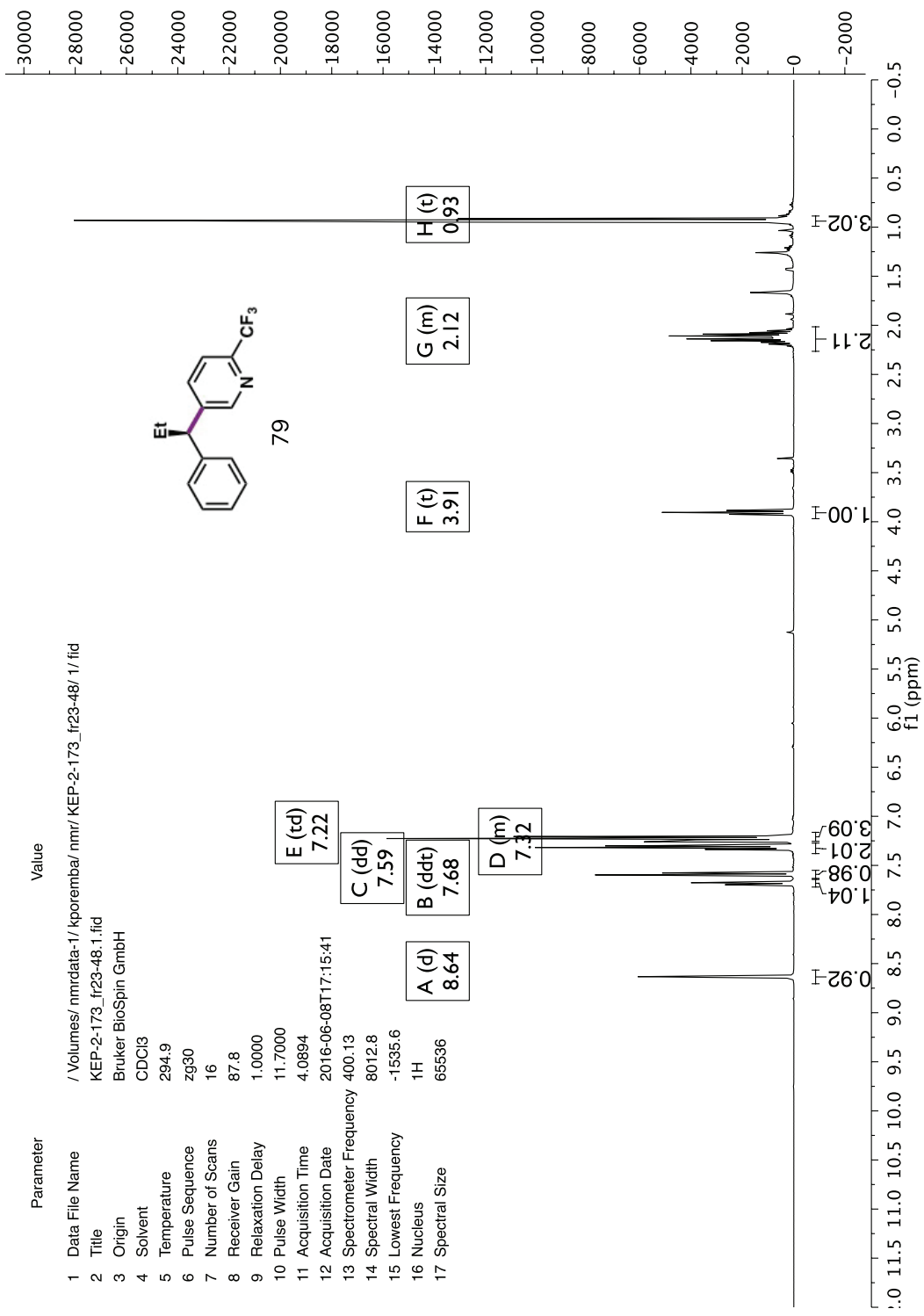
Parameter	Value
1 Data File Name	/ Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-166_N-F_Ar/ 2/ fid
2 Title	KEP-2-166_N-F_Ar.2.fid
3 Origin	Bruker BioSpin GmbH
4 Solvent	CDCl3
5 Temperature	295.0
6 Pulse Sequence	zgpg30
7 Number of Scans	256
8 Receiver Gain	78.7
9 Relaxation Delay	2.0000
10 Pulse Width	10.0000
11 Acquisition Time	1.3631
12 Acquisition Date	2016-10-10T19:35:04
13 Spectrometer Frequency	100.62
14 Spectral Width	24038.5
15 Lowest Frequency	-1932.0
16 Nucleus	13C
17 Spectral Size	65536

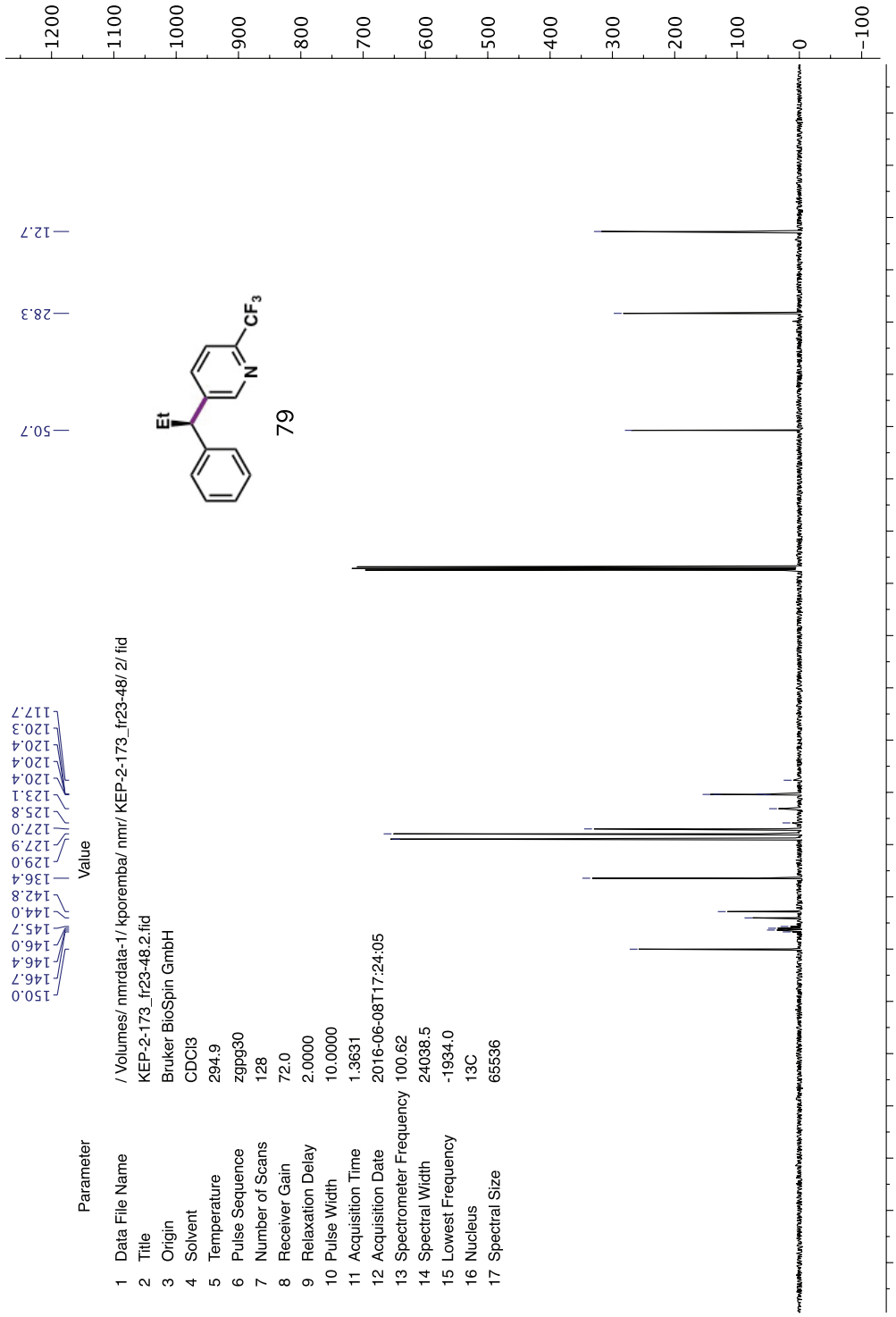

71.89
Value
Parameter
1 Data File Name / Volumes/ nmrdata/ kporemba/ vnmrsys/ data/ KEP-2-166_N-2-F/ FLUORINE01.fid/ fid
2 Title FLUORINE01
3 Origin Varian
4 Solvent cdcl3
5 Temperature 25.0
6 Pulse Sequence s2pul
7 Number of Scans 16
8 Receiver Gain 30
9 Relaxation Delay 1.0000
10 Pulse Width 6.3333
11 Acquisition Time 0.9856
12 Acquisition Date 2016-10-10T16:04:44
13 Spectrometer Frequency 282.34
14 Spectral Width 64935.1
15 Lowest Frequency -56468.7
16 Nucleus 19F
17 Spectral Size 131072
Et
N
F
77
f1 (ppm)

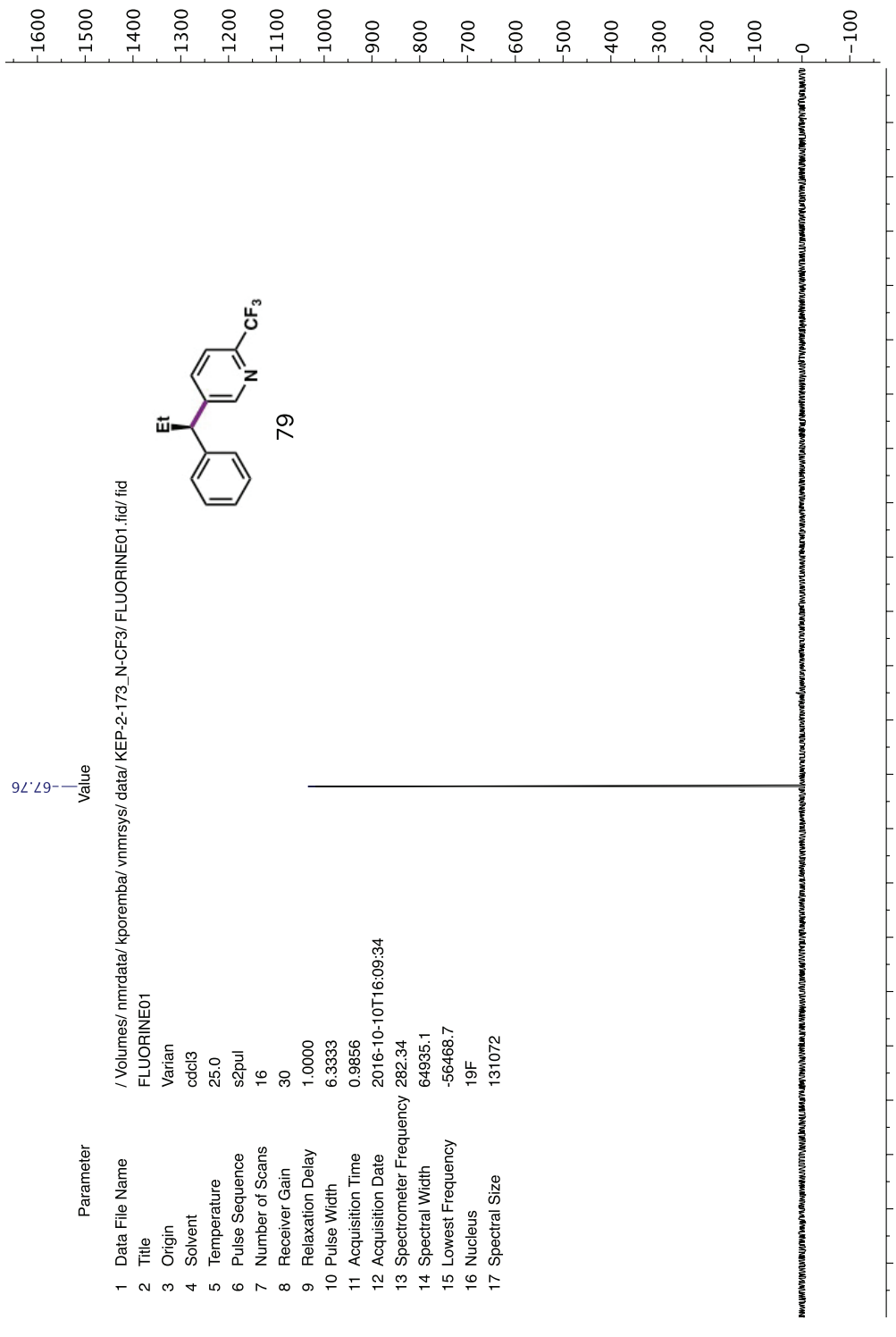

Parameter
Value
1 Data File Name / Volumes/ nmrdata/ kporemba/ vnmrsys/ data/ KEP-2-154_fr6-16/ PROTON01.fid/ fid
2 Title PROTON01
3 Origin Varian
4 Solvent cdcl3
5 Temperature 25.0
6 Pulse Sequence s2pul
7 Number of Scans 16
8 Receiver Gain 28
9 Relaxation Delay 1.0000
10 Pulse Width 5.9000
11 Acquisition Time 3.0000
12 Acquisition Date 2016-05-12T18:16:57
13 Spectrometer Frequency 499.66
14 Spectral Width 8000.0
15 Lowest Frequency -1026.1
16 Nucleus 1H
17 Spectral Size 65536
A (dt) 8.30
B (ddd) 7.47
C (m) 7.30
D (m) 7.20
E (t) 3.80
F (m) 2.06
G (t) 0.91
Et
Cl
N
78
0.91
3.97
1.86
0.97
1.00
2.16
3.23
f1 (ppm)



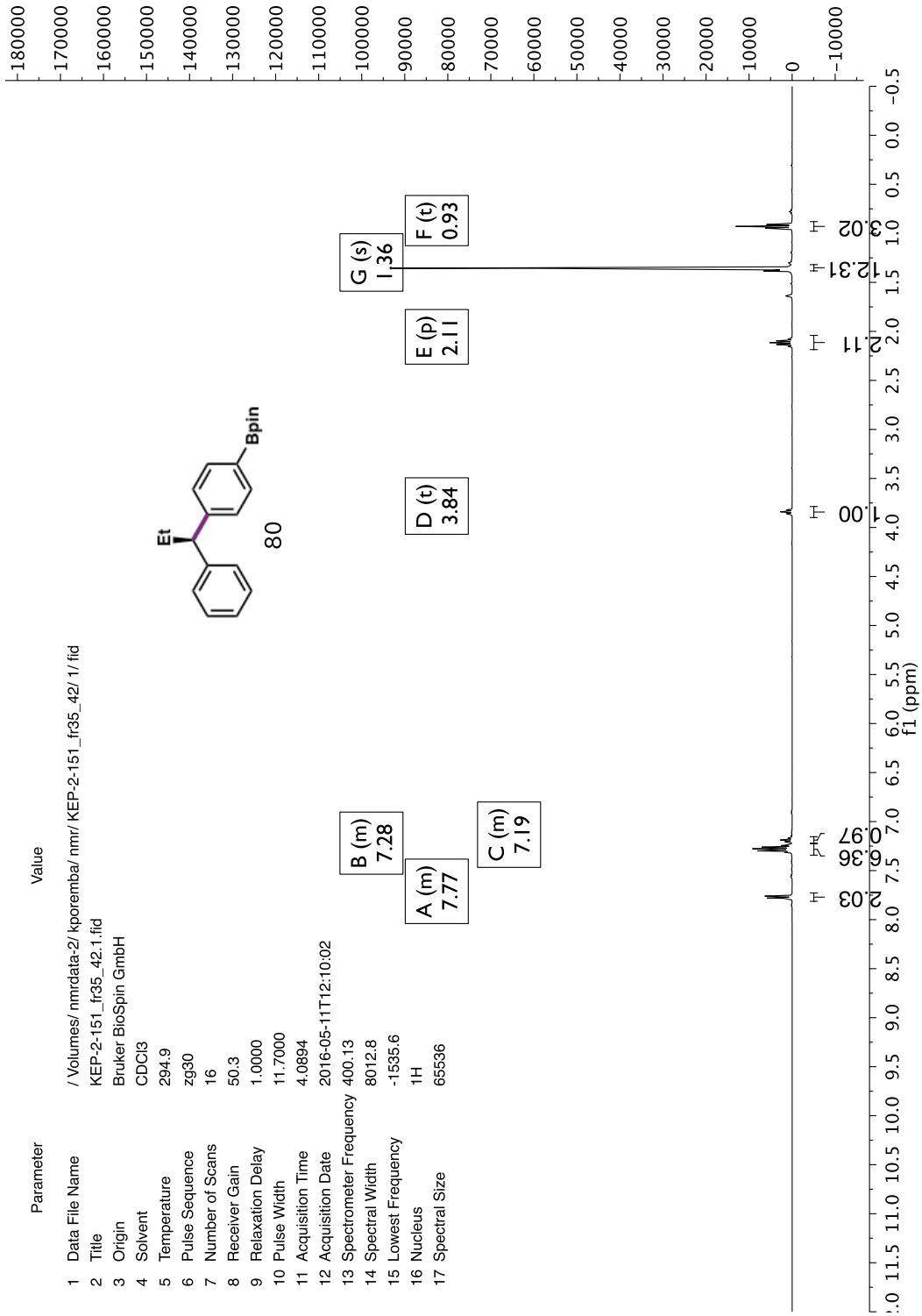
Parameter	Value
1 Data File Name	/ Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-154_N-Cl_Ar/ 2/ fid
2 Title	KEP-2-154_N-Cl_Ar.2.fid
3 Origin	Bruker BioSpin GmbH
4 Solvent	CDCl3
5 Temperature	295.0
6 Pulse Sequence	zgpg30
7 Number of Scans	256
8 Receiver Gain	64.2
9 Relaxation Delay	2.0000
10 Pulse Width	10.0000
11 Acquisition Time	1.3631
12 Acquisition Date	2016-10-10T18:22:27
13 Spectrometer Frequency	100.62
14 Spectral Width	24038.5
15 Lowest Frequency	-1932.6
16 Nucleus	13C
17 Spectral Size	65536

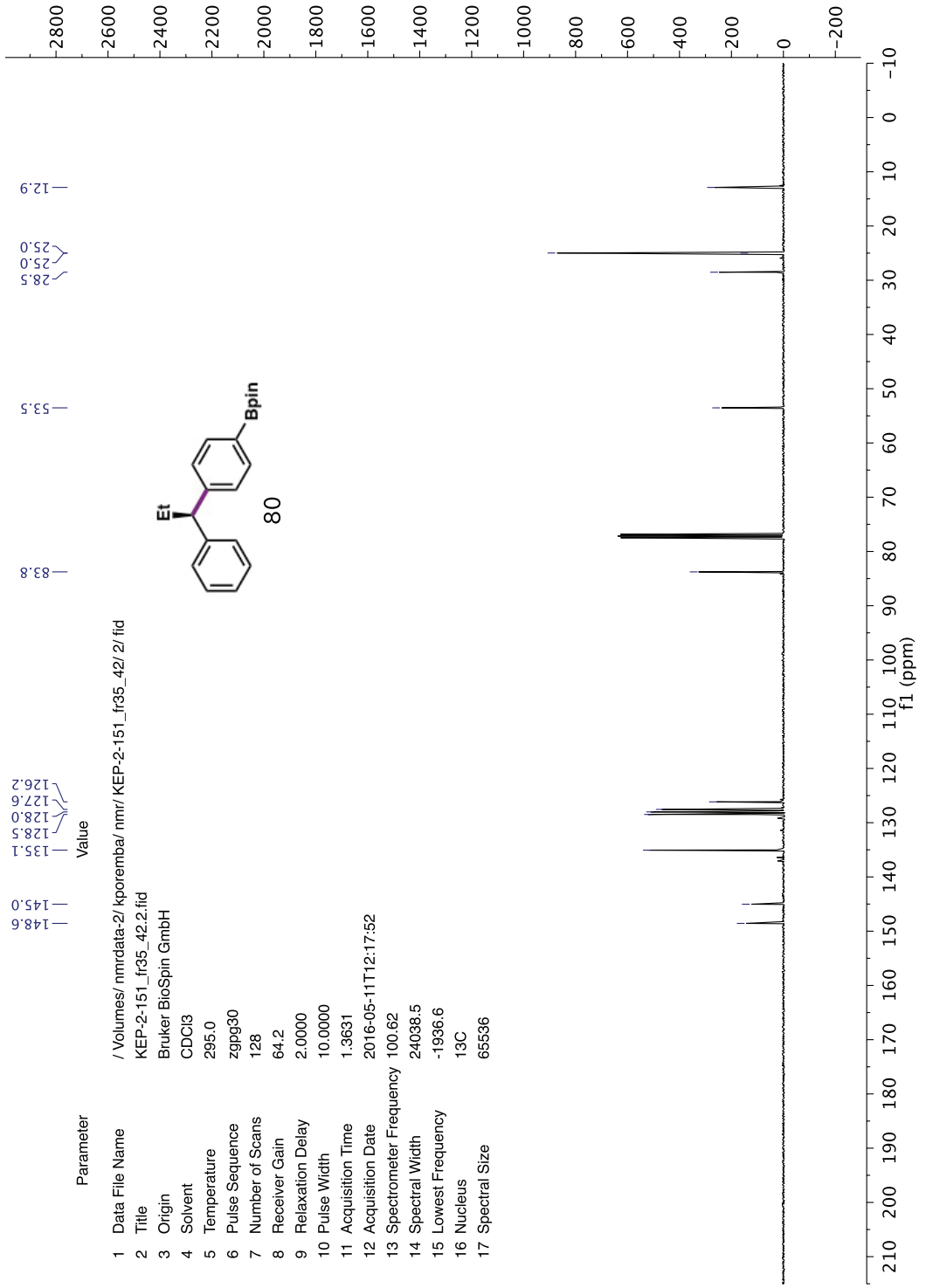

Parameter
Value
1 Data File Name / Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-173_fr23-48/ 1/ fid
2 Title KEP-2-173_fr23-48.1.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 294.9
6 Pulse Sequence zg30
7 Number of Scans 16
8 Receiver Gain 87.8
9 Relaxation Delay 1.0000
10 Pulse Width 11.7000
11 Acquisition Time 4.0894
12 Acquisition Date 2016-06-08T17:15:41
13 Spectrometer Frequency 400.13
14 Spectral Width 8012.8
15 Lowest Frequency -1535.6
16 Nucleus 1H
17 Spectral Size 65536
A (d) 8.64
B (ddt) 7.68
C (dd) 7.59
D (m) 7.32
E (td) 7.22
F (t) 3.91
G (m) 2.12
H (t) 0.93
79
Et
CF3
N
0.92
1.04
0.98
2.01
3.09
1.00
2.11
3.02
f1 (ppm)


79
Et
N
CF3
f1 (ppm)
Parameter Value
1 Data File Name / Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-173_fr23-48/ 2/ fid
2 Title KEP-2-173_fr23-48.2.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 294.9
6 Pulse Sequence zgpg30
7 Number of Scans 128
8 Receiver Gain 72.0
9 Relaxation Delay 2.0000
10 Pulse Width 10.0000
11 Acquisition Time 1.3631
12 Acquisition Date 2016-06-08T17:24:05
13 Spectrometer Frequency 100.62
14 Spectral Width 24038.5
15 Lowest Frequency -1934.0
16 Nucleus 13C
17 Spectral Size 65536

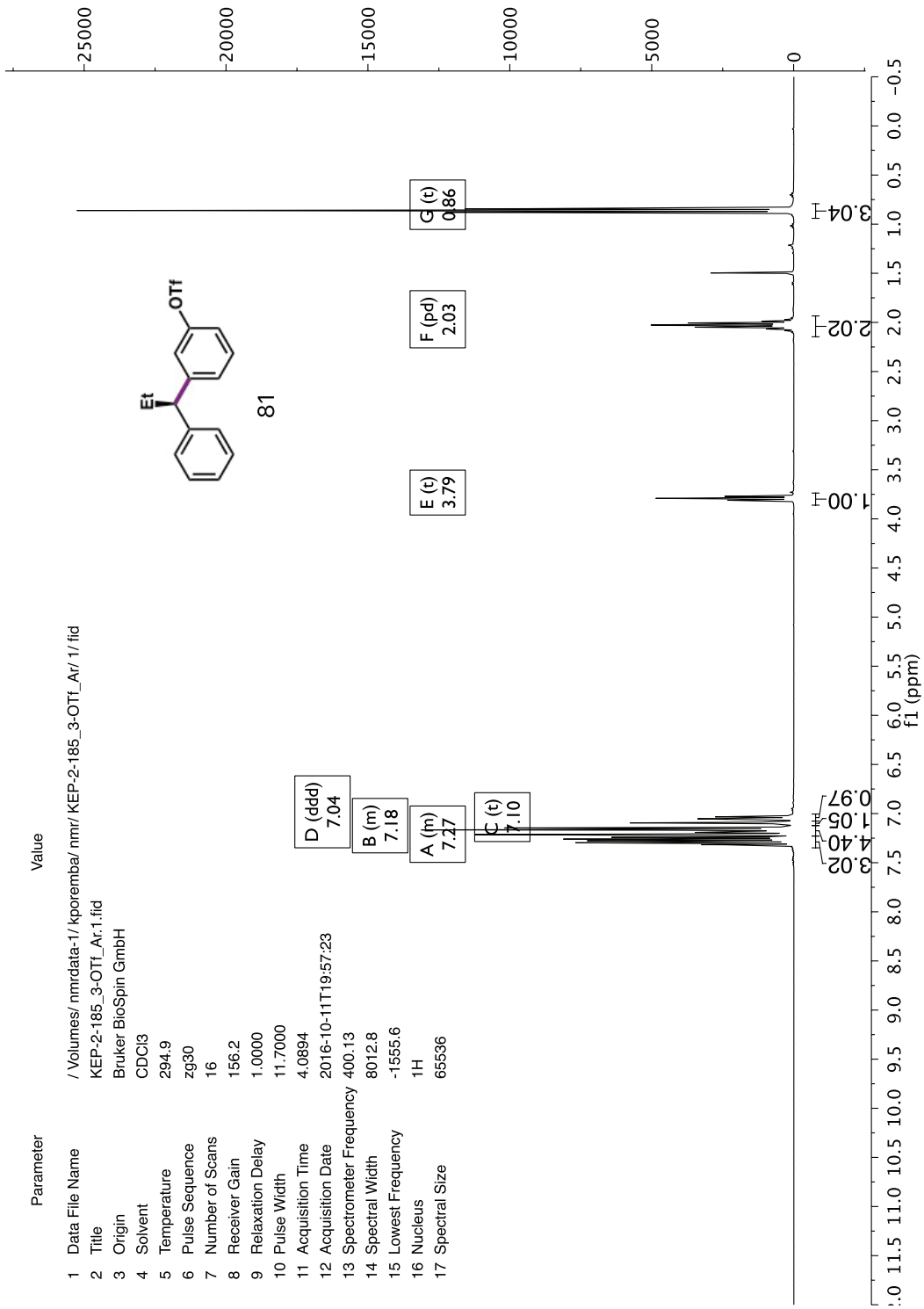


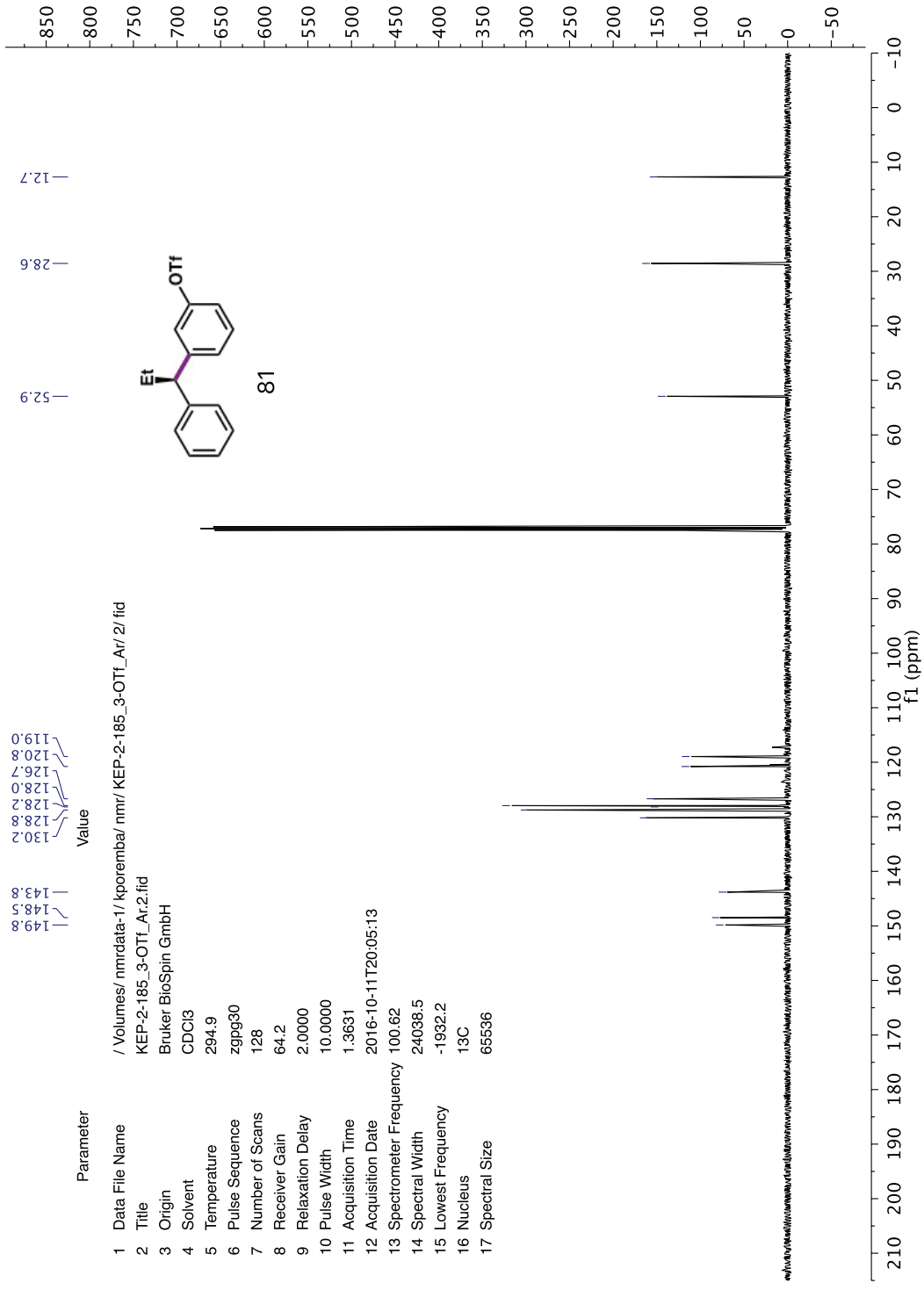
Parameter	Value
1 Data File Name	/ Volumes/ nmrdata/ kporemba/ vnmrsys/ data/ KEP-2-173_N-CF3/ FLUORINE01.fid/ fid
2 Title	FLUORINE01
3 Origin	Varian
4 Solvent	cdcl3
5 Temperature	25.0
6 Pulse Sequence	s2pul
7 Number of Scans	16
8 Receiver Gain	30
9 Relaxation Delay	1.0000
10 Pulse Width	6.3333
11 Acquisition Time	0.9856
12 Acquisition Date	2016-10-10T16:09:34
13 Spectrometer Frequency	282.34
14 Spectral Width	64935.1
15 Lowest Frequency	-56468.7
16 Nucleus	19F
17 Spectral Size	131072

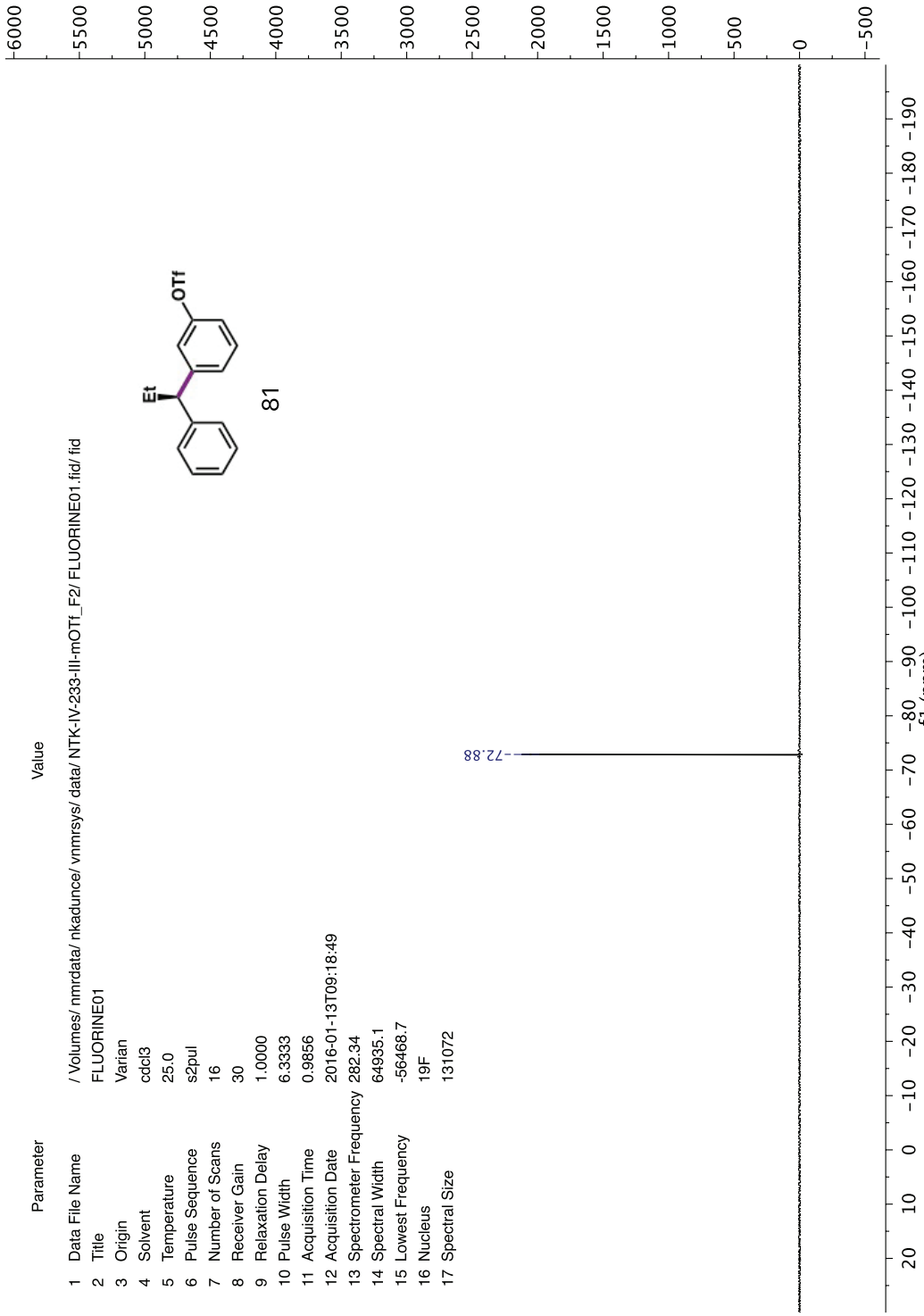

Parameter
Value
1 Data File Name / Volumes/ nmrdata-2/ kporemba/ nmr/ KEP-2-151_fr35_42/ 1/ fid
2 Title KEP-2-151_fr35_42.1.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 294.9
6 Pulse Sequence zg30
7 Number of Scans 16
8 Receiver Gain 50.3
9 Relaxation Delay 1.0000
10 Pulse Width 11.7000
11 Acquisition Time 4.0894
12 Acquisition Date 2016-05-11T12:10:02
13 Spectrometer Frequency 400.13
14 Spectral Width 8012.8
15 Lowest Frequency -1535.6
16 Nucleus 1H
17 Spectral Size 65536
Et
Bpin
80
A (m) 7.77
B (m) 7.28
C (m) 7.19
D (t) 3.84
E (p) 2.11
G (s) 1.36
F (t) 0.93
2.03
6.36
0.97
1.00
2.11
12.31
3.02
f1 (ppm)

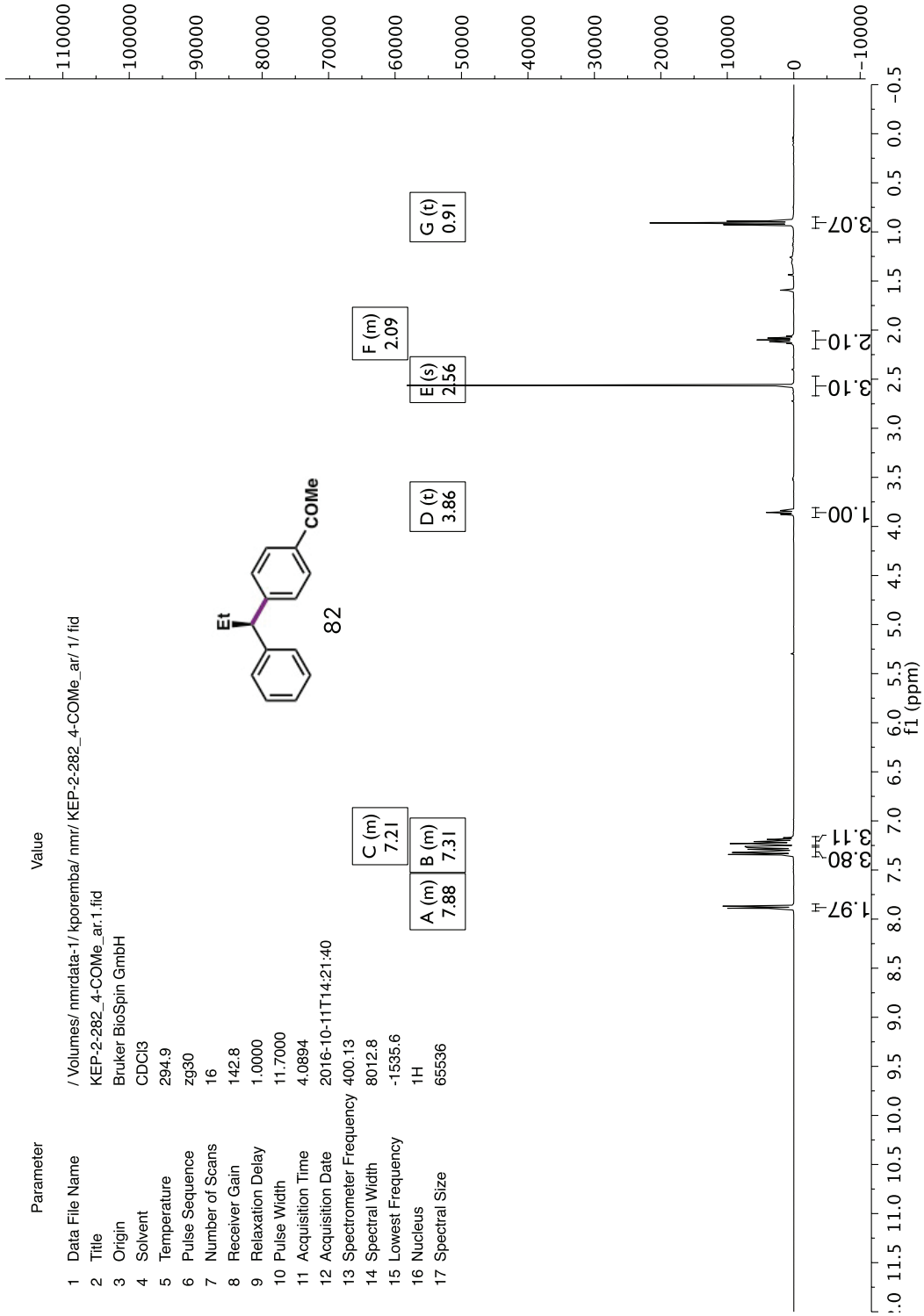


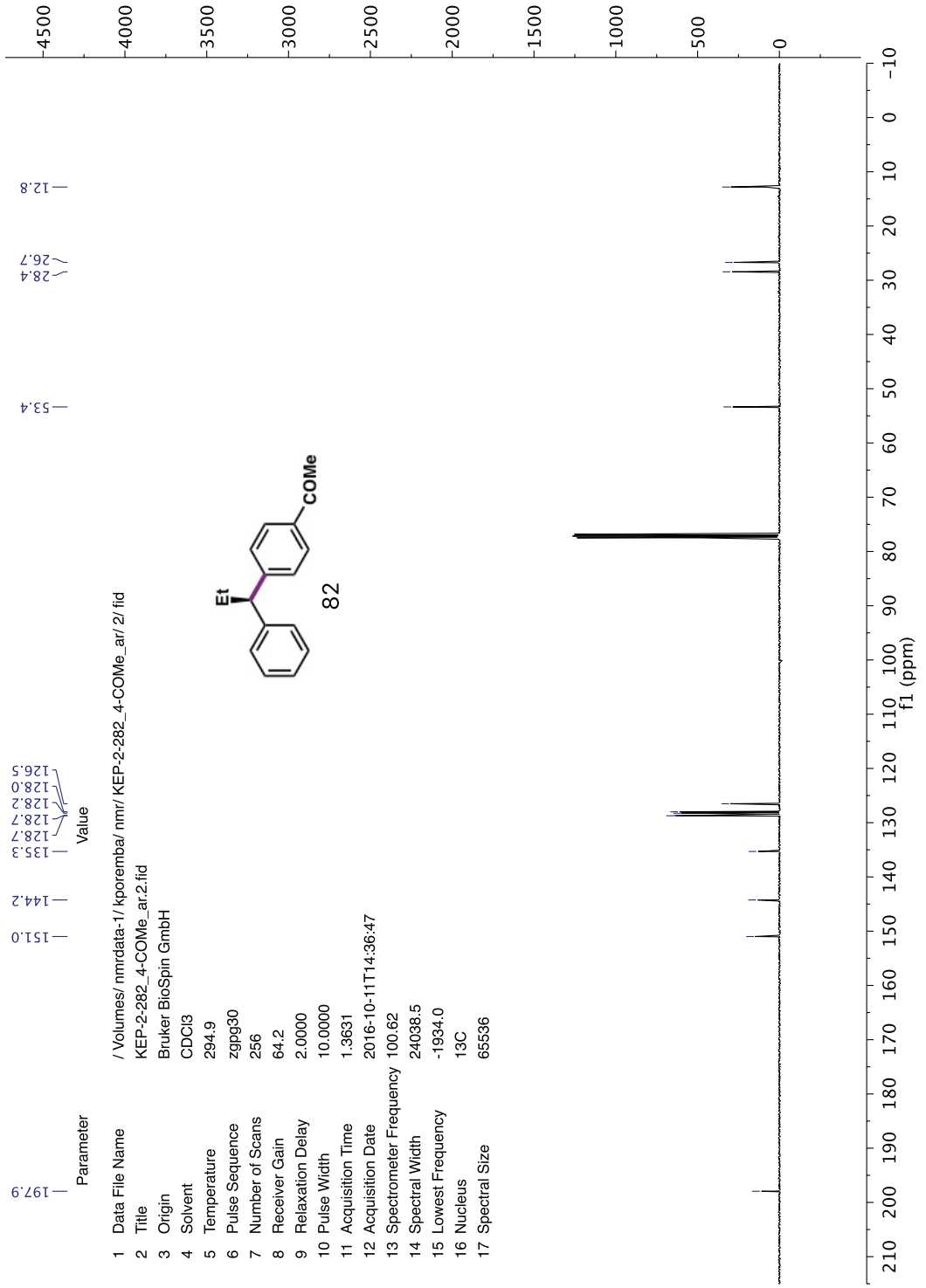
Parameter	Value
1 Data File Name	/ Volumes/ nmrdata-2/ kporemba/ nmr/ KEP-2-151_fr35_42/ 2/ fid
2 Title	KEP-2-151_fr35_42_2.fid
3 Origin	Bruker BioSpin GmbH
4 Solvent	CDCl3
5 Temperature	295.0
6 Pulse Sequence	zgpg30
7 Number of Scans	128
8 Receiver Gain	64.2
9 Relaxation Delay	2.0000
10 Pulse Width	10.0000
11 Acquisition Time	1.3631
12 Acquisition Date	2016-05-11T12:17:52
13 Spectrometer Frequency	100.62
14 Spectral Width	24038.5
15 Lowest Frequency	-1936.6
16 Nucleus	13C
17 Spectral Size	65536


Parameter
Value
1 Data File Name / Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-185_3-OTf_Ar/ 1/ fid
2 Title KEP-2-185_3-OTf_Ar.1.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 294.9
6 Pulse Sequence zg30
7 Number of Scans 16
8 Receiver Gain 156.2
9 Relaxation Delay 1.0000
10 Pulse Width 11.7000
11 Acquisition Time 4.0894
12 Acquisition Date 2016-10-11T19:57:23
13 Spectrometer Frequency 400.13
14 Spectral Width 8012.8
15 Lowest Frequency -1555.6
16 Nucleus 1H
17 Spectral Size 65536
OTf
Et
81
D (ddd) 7.04
B (m) 7.18
A (m) 7.27
C (t) 7.10
E (t) 3.79
F (pd) 2.03
G (t) 0.86
3.02
1.40
1.05
0.97
3.04
2.02
1.00
f1 (ppm)

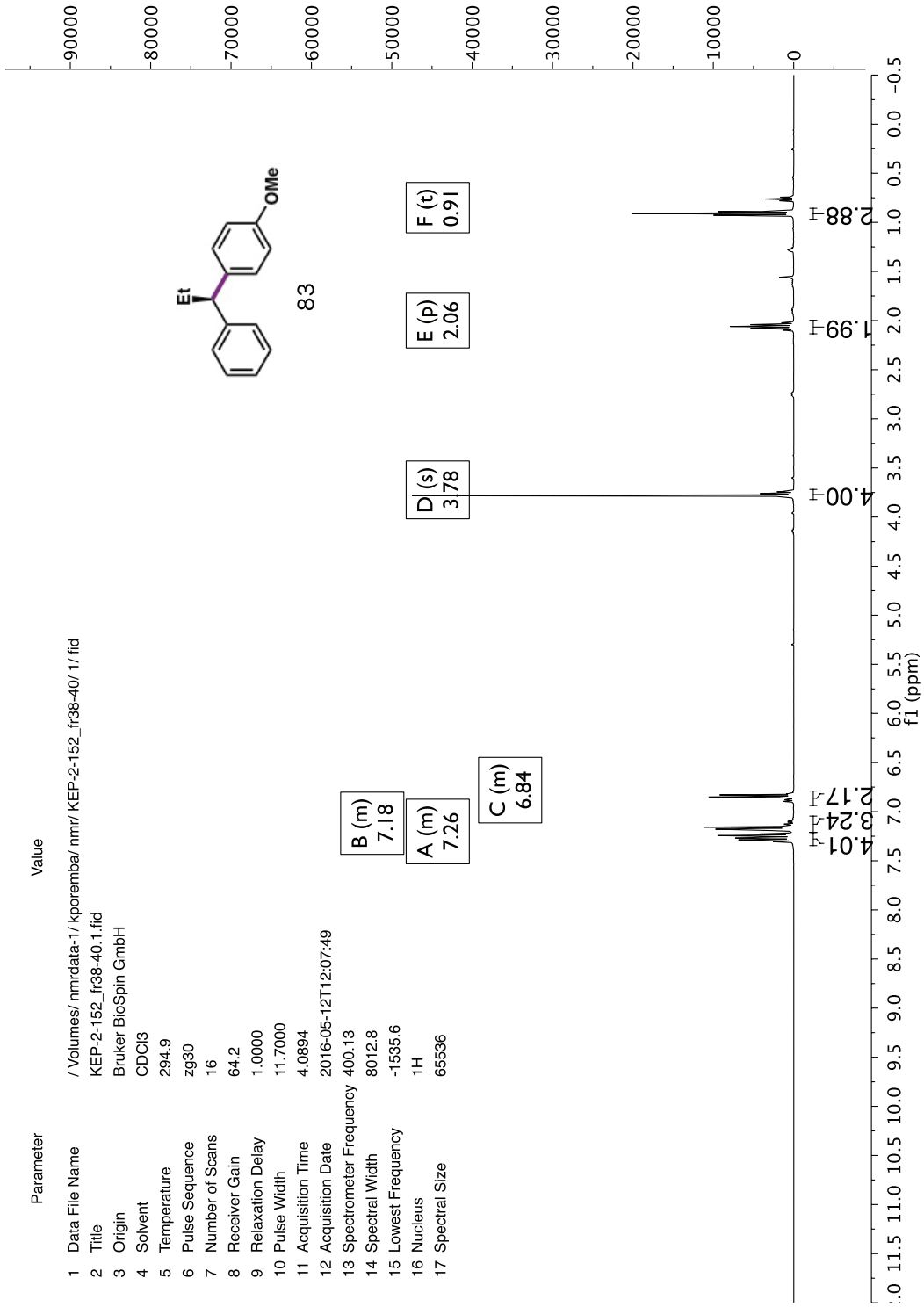

OTf
Et
81
f1 (ppm)
Parameter Value
1 Data File Name / Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-185_3-OTf_Ar/ 2/ fid
2 Title KEP-2-185_3-OTf_Ar.2.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 294.9
6 Pulse Sequence zgpg30
7 Number of Scans 128
8 Receiver Gain 64.2
9 Relaxation Delay 2.0000
10 Pulse Width 10.0000
11 Acquisition Time 1.3631
12 Acquisition Date 2016-10-11T20:05:13
13 Spectrometer Frequency 100.62
14 Spectral Width 24038.5
15 Lowest Frequency -1932.2
16 Nucleus 13C
17 Spectral Size 65536

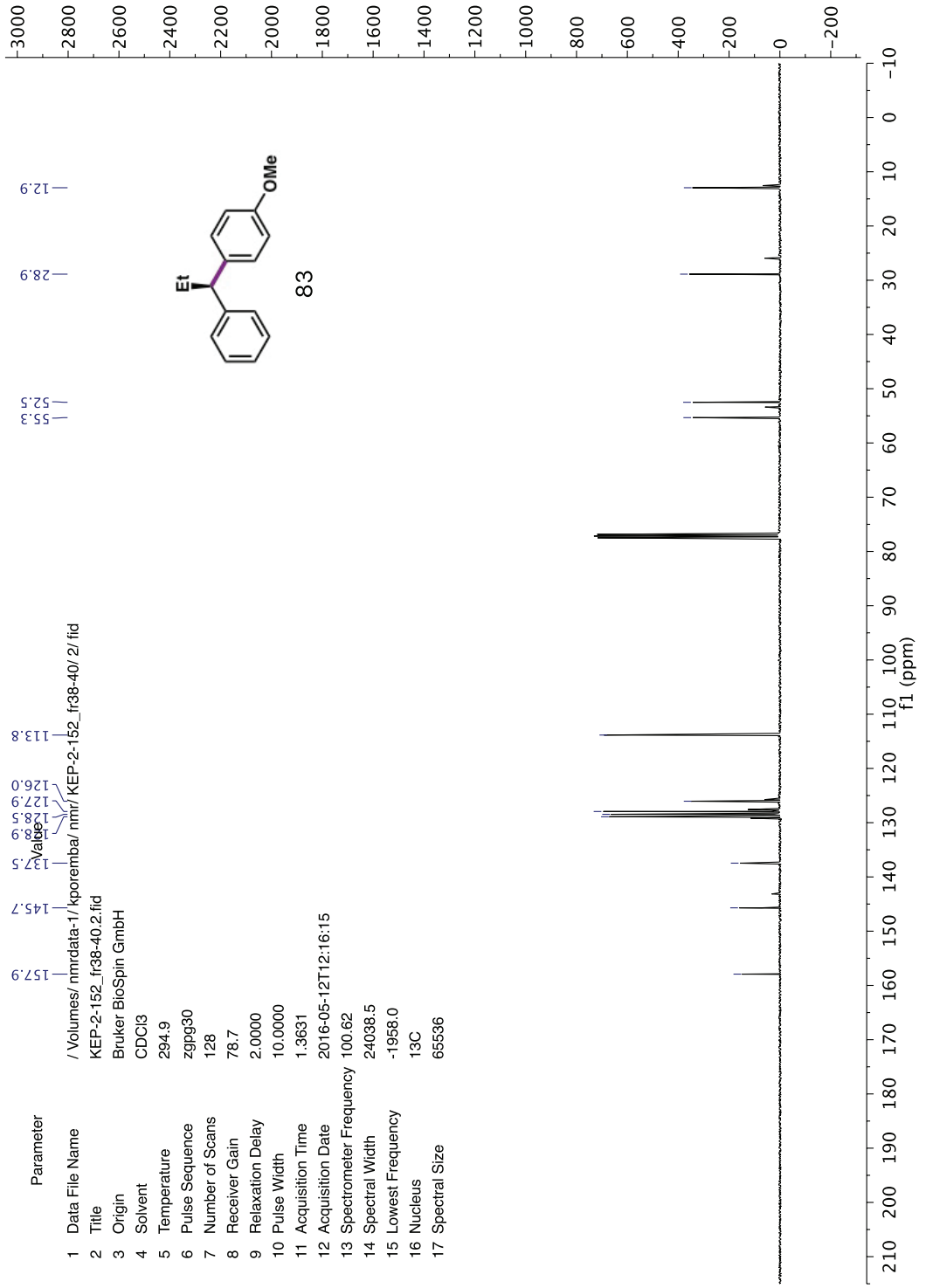

Parameter
Value
1 Data File Name / Volumes/ nmrdata/ nkadunce/ vnmrsys/ data/ NTK-IV-233-III-mOTf_F2/ FLUORINE01.fid/ fid
2 Title FLUORINE01
3 Origin Varian
4 Solvent cdcl3
5 Temperature 25.0
6 Pulse Sequence s2pul
7 Number of Scans 16
8 Receiver Gain 30
9 Relaxation Delay 1.0000
10 Pulse Width 6.3333
11 Acquisition Time 0.9856
12 Acquisition Date 2016-01-13T09:18:49
13 Spectrometer Frequency 282.34
14 Spectral Width 64935.1
15 Lowest Frequency -56468.7
16 Nucleus 19F
17 Spectral Size 131072
Et
OTf
81
-72.88
f1 (ppm)


Parameter
Value
1 Data File Name / Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-282_4-COMe_ar/ 1/ fid
2 Title KEP-2-282_4-COMe_ar.1.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 294.9
6 Pulse Sequence zg30
7 Number of Scans 16
8 Receiver Gain 142.8
9 Relaxation Delay 1.0000
10 Pulse Width 11.7000
11 Acquisition Time 4.0894
12 Acquisition Date 2016-10-11T14:21:40
13 Spectrometer Frequency 400.13
14 Spectral Width 8012.8
15 Lowest Frequency -1535.6
16 Nucleus 1H
17 Spectral Size 65536
Et
COMe
82
A (m) 7.88
B (m) 7.31
C (m) 7.21
D (t) 3.86
E (s) 2.56
F (m) 2.09
G (t) 0.91
1.97
3.80
3.11
1.00
3.10
2.10
3.07
f1 (ppm)

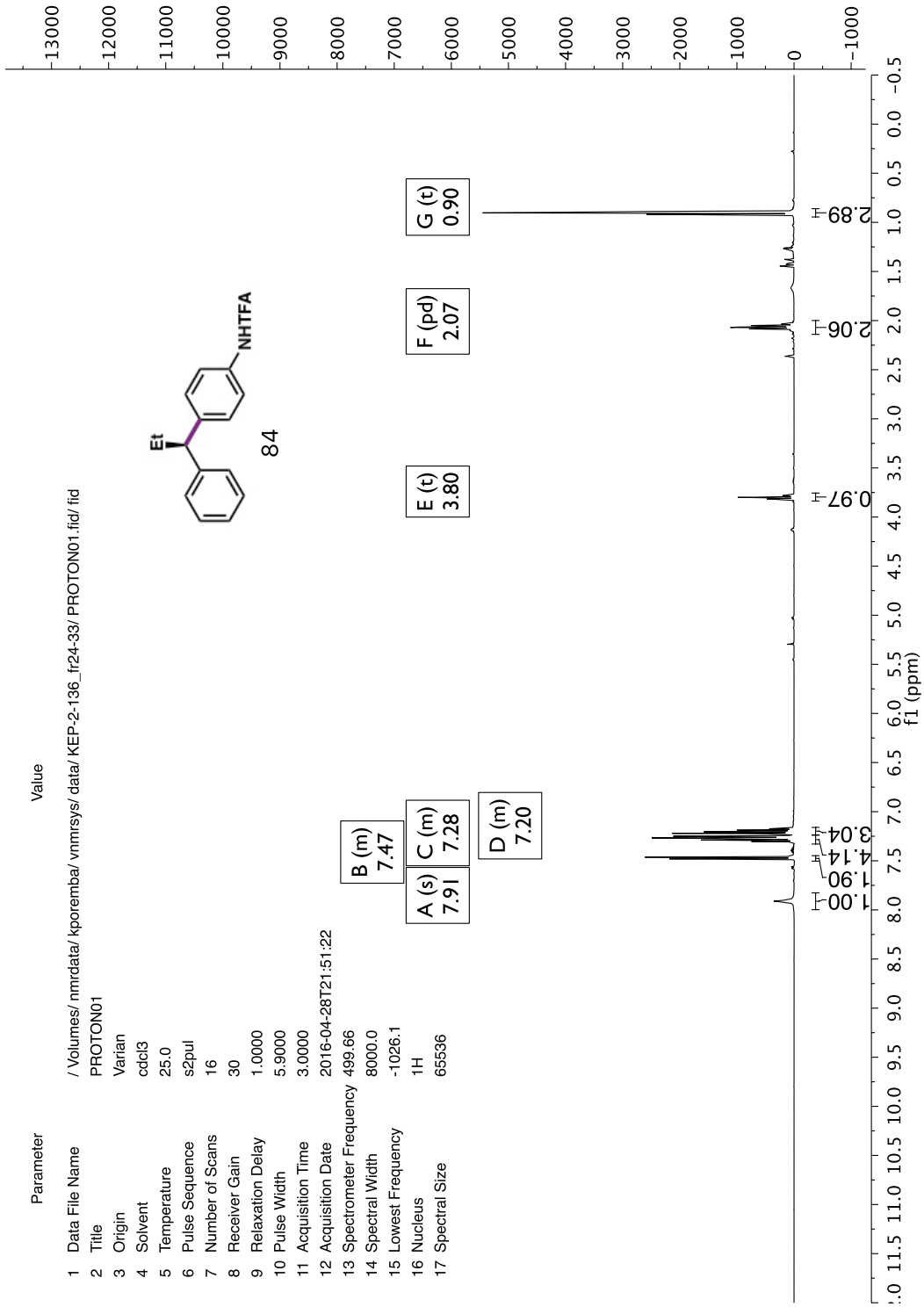


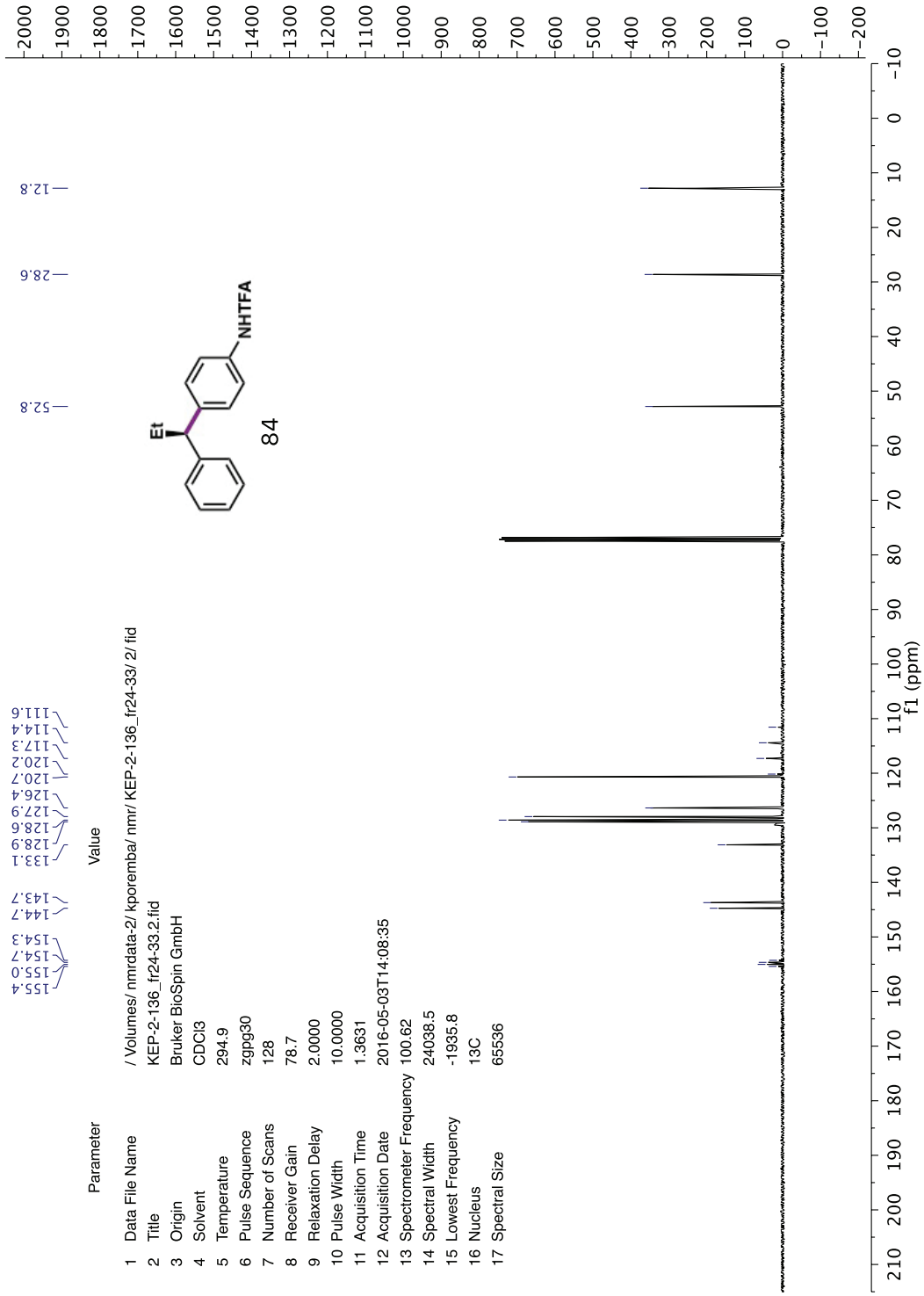
	Parameter	Value
1	Data File Name	/ Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-282_4-COMe_ar/ 2/ fid
2	Title	KEP-2-282_4-COMe_ar.2.fid
3	Origin	Bruker BioSpin GmbH
4	Solvent	CDCl3
5	Temperature	294.9
6	Pulse Sequence	zgpg30
7	Number of Scans	256
8	Receiver Gain	64.2
9	Relaxation Delay	2.0000
10	Pulse Width	10.0000
11	Acquisition Time	1.3631
12	Acquisition Date	2016-10-11T14:36:47
13	Spectrometer Frequency	100.62
14	Spectral Width	24038.5
15	Lowest Frequency	-1934.0
16	Nucleus	13C
17	Spectral Size	65536


Parameter
Value
1 Data File Name / Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-152_fr38-40/ 1/ fid
2 Title KEP-2-152_fr38-40.1.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 294.9
6 Pulse Sequence zg30
7 Number of Scans 16
8 Receiver Gain 64.2
9 Relaxation Delay 1.0000
10 Pulse Width 11.7000
11 Acquisition Time 4.0894
12 Acquisition Date 2016-05-12T12:07:49
13 Spectrometer Frequency 400.13
14 Spectral Width 8012.8
15 Lowest Frequency -1535.6
16 Nucleus 1H
17 Spectral Size 65536
Et
OMe
83
A (m) 7.26
B (m) 7.18
C (m) 6.84
D (s) 3.78
E (p) 2.06
F (t) 0.91
4.01
3.24
2.17
4.00
1.99
2.88
f1 (ppm)

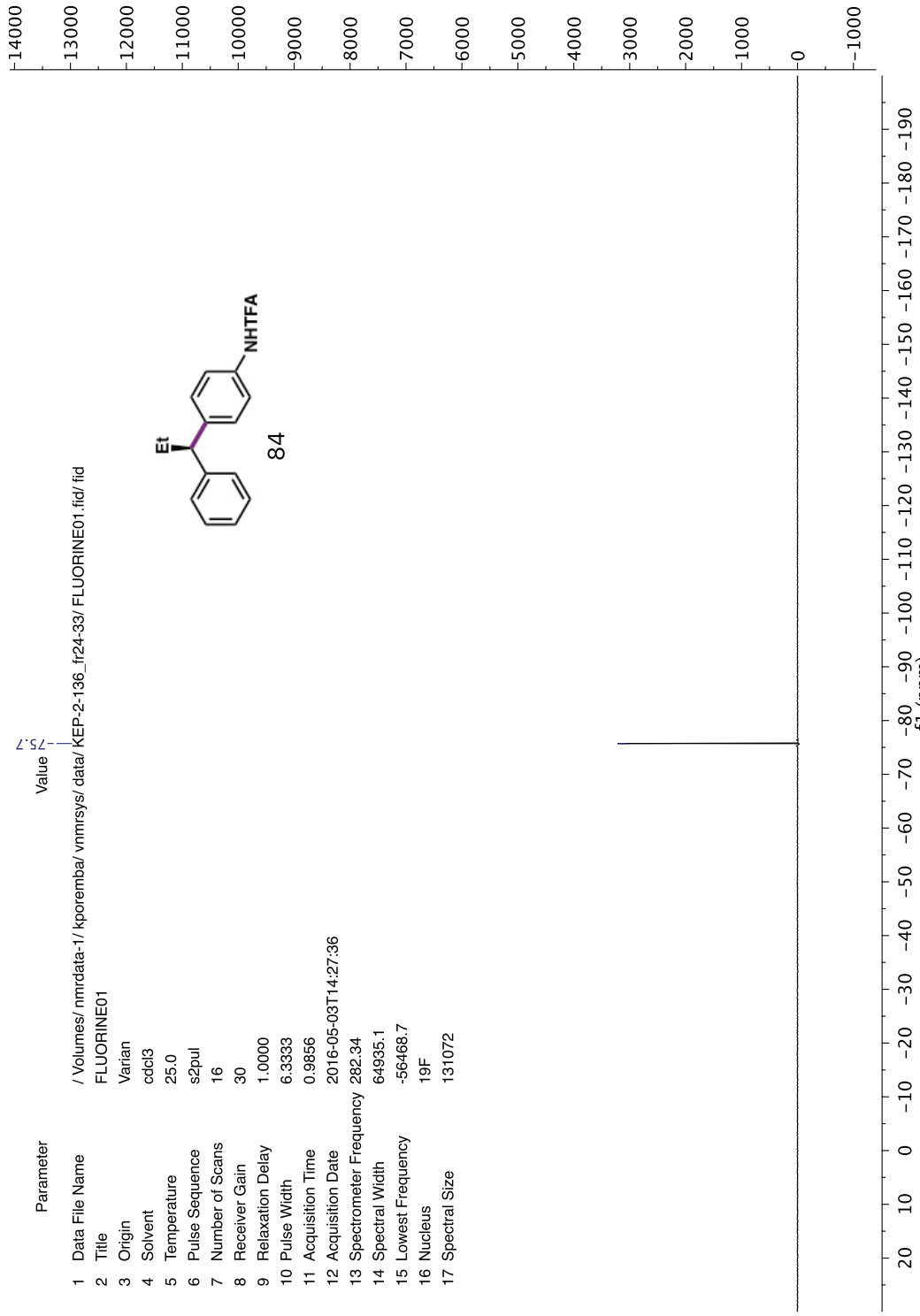


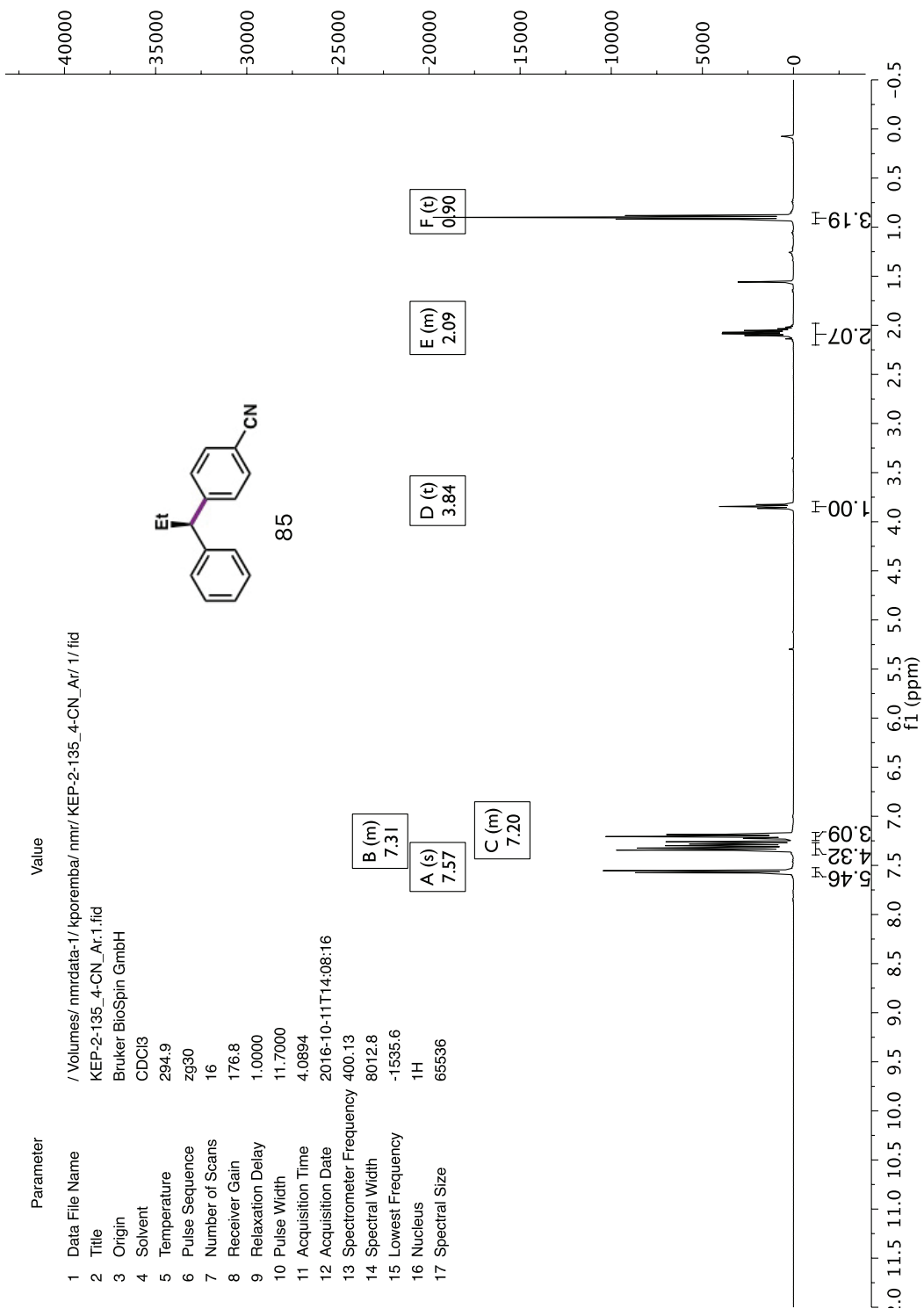
Parameter	Value
1 Data File Name	/ Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-152_fr38-40/ 2/ fid
2 Title	KEP-2-152_fr38-40.2.fid
3 Origin	Bruker BioSpin GmbH
4 Solvent	CDCl3
5 Temperature	294.9
6 Pulse Sequence	zgpg30
7 Number of Scans	128
8 Receiver Gain	78.7
9 Relaxation Delay	2.0000
10 Pulse Width	10.0000
11 Acquisition Time	1.3631
12 Acquisition Date	2016-05-12T12:16:15
13 Spectrometer Frequency	100.62
14 Spectral Width	24038.5
15 Lowest Frequency	-1958.0
16 Nucleus	13C
17 Spectral Size	65536

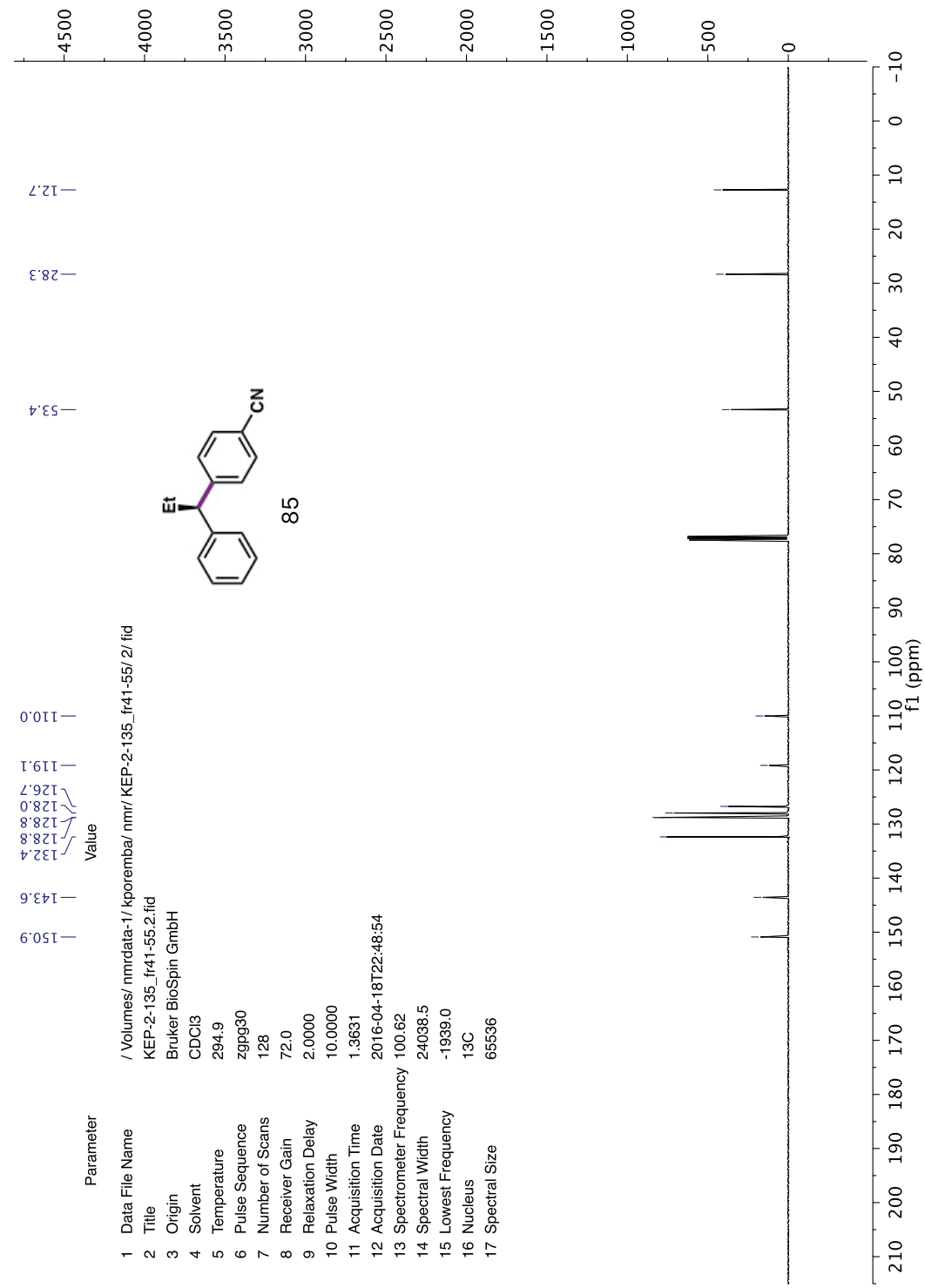

Parameter
Value
1 Data File Name / Volumes/ nmrdata/ kporemba/ vnmrsys/ data/ KEP-2-136_fr24-33/ PROTON01.fid/ fid
2 Title PROTON01
3 Origin Varian
4 Solvent cdcl3
5 Temperature 25.0
6 Pulse Sequence s2pul
7 Number of Scans 16
8 Receiver Gain 30
9 Relaxation Delay 1.0000
10 Pulse Width 5.9000
11 Acquisition Time 3.0000
12 Acquisition Date 2016-04-28T21:51:22
13 Spectrometer Frequency 499.66
14 Spectral Width 8000.0
15 Lowest Frequency -1026.1
16 Nucleus 1H
17 Spectral Size 65536
Et
NHTFA
84
A (s) 7.91
B (m) 7.47
C (m) 7.28
D (m) 7.20
E (t) 3.80
F (pd) 2.07
G (t) 0.90
1.00
1.90
4.14
3.04
0.97
2.06
2.89
f1 (ppm)



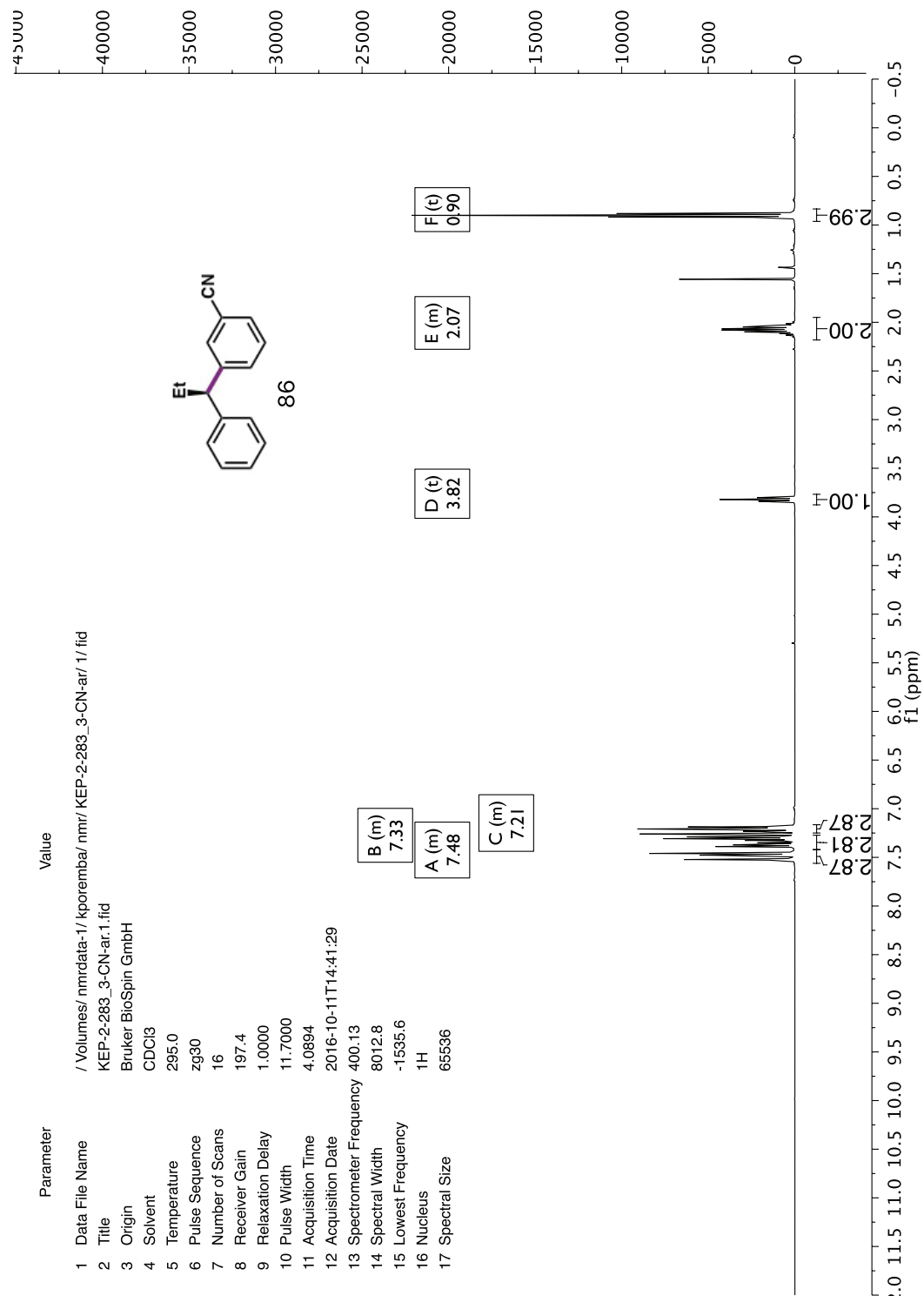
Parameter	Value
1 Data File Name	/ Volumes/ nmrdata-2/ kporemba/ nmr/ KEP-2-136_fr24-33/ 2/ fid
2 Title	KEP-2-136_fr24-33.2.fid
3 Origin	Bruker BioSpin GmbH
4 Solvent	CDCl3
5 Temperature	294.9
6 Pulse Sequence	zgpg30
7 Number of Scans	128
8 Receiver Gain	78.7
9 Relaxation Delay	2.0000
10 Pulse Width	10.0000
11 Acquisition Time	1.3631
12 Acquisition Date	2016-05-03T14:08:35
13 Spectrometer Frequency	100.62
14 Spectral Width	24038.5
15 Lowest Frequency	-1935.8
16 Nucleus	13C
17 Spectral Size	65536

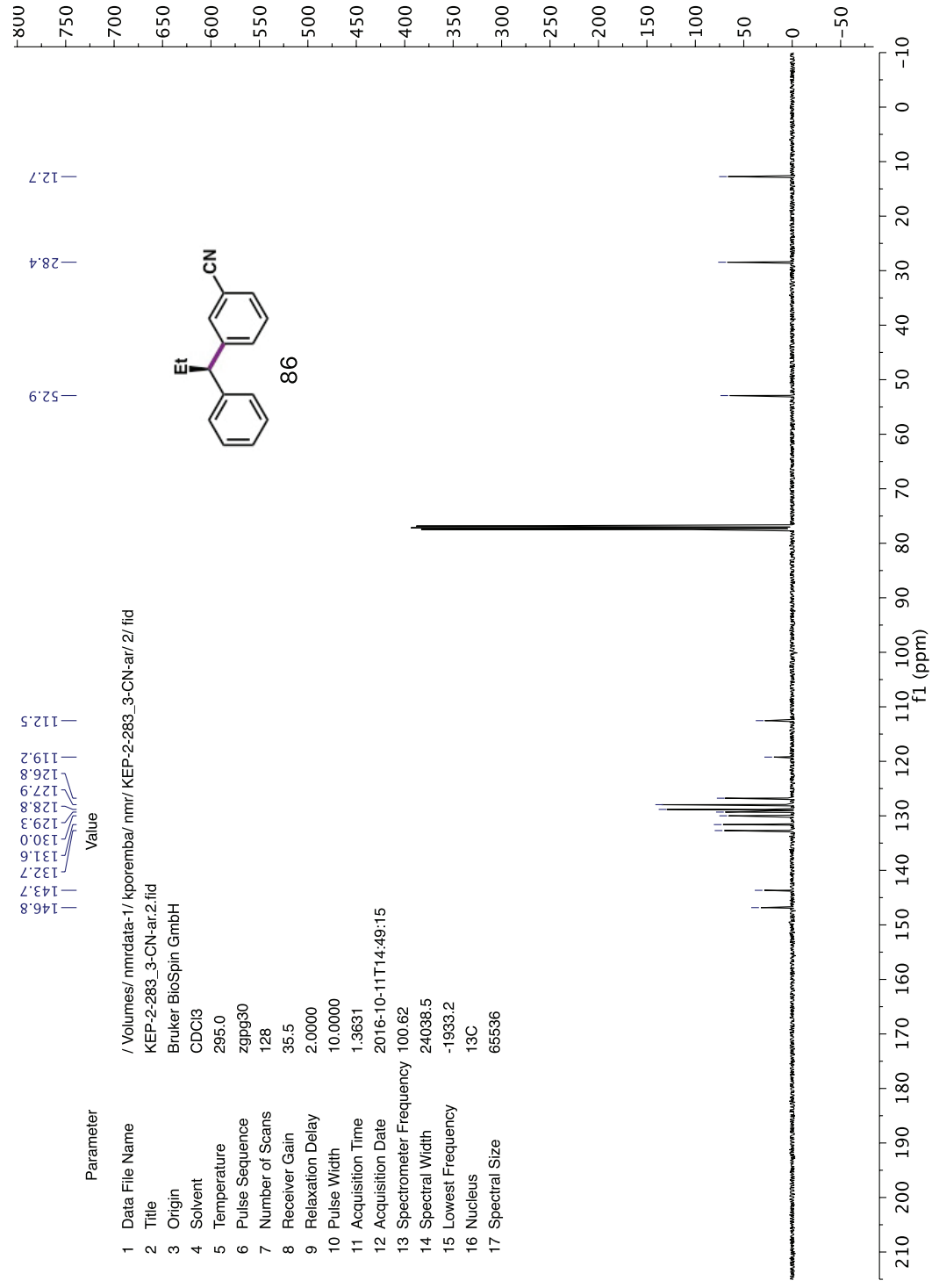

Value
-75.7
Parameter
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2 Title FLUORINE01
3 Origin Varian
4 Solvent cdcl3
5 Temperature 25.0
6 Pulse Sequence s2pul
7 Number of Scans 16
8 Receiver Gain 30
9 Relaxation Delay 1.0000
10 Pulse Width 6.3333
11 Acquisition Time 0.9856
12 Acquisition Date 2016-05-03T14:27:36
13 Spectrometer Frequency 282.34
14 Spectral Width 64935.1
15 Lowest Frequency -56468.7
16 Nucleus 19F
17 Spectral Size 131072
Et
NHTFA
84
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)


Parameter
Value
1 Data File Name / Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-135_4-CN_Ar/ 1/ fid
2 Title KEP-2-135_4-CN_Ar.1.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 294.9
6 Pulse Sequence zg30
7 Number of Scans 16
8 Receiver Gain 176.8
9 Relaxation Delay 1.0000
10 Pulse Width 11.7000
11 Acquisition Time 4.0894
12 Acquisition Date 2016-10-11T14:08:16
13 Spectrometer Frequency 400.13
14 Spectral Width 8012.8
15 Lowest Frequency -1535.6
16 Nucleus 1H
17 Spectral Size 65536
Et
CN
85
A (s) 7.57
B (m) 7.31
C (m) 7.20
D (t) 3.84
E (m) 2.09
F (t) 0.90
5.46
4.32
3.09
1.00
2.07
3.19
f1 (ppm)

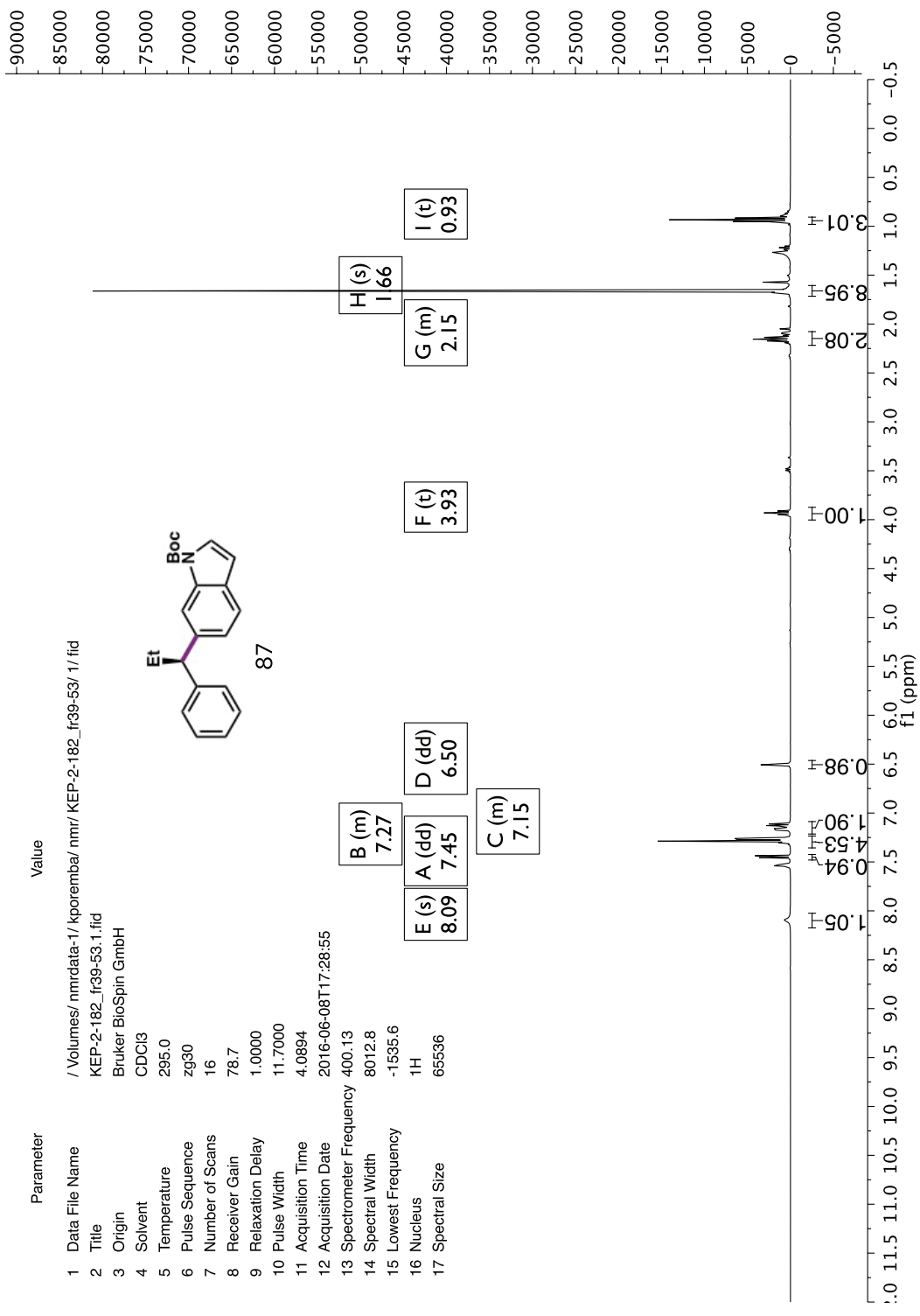


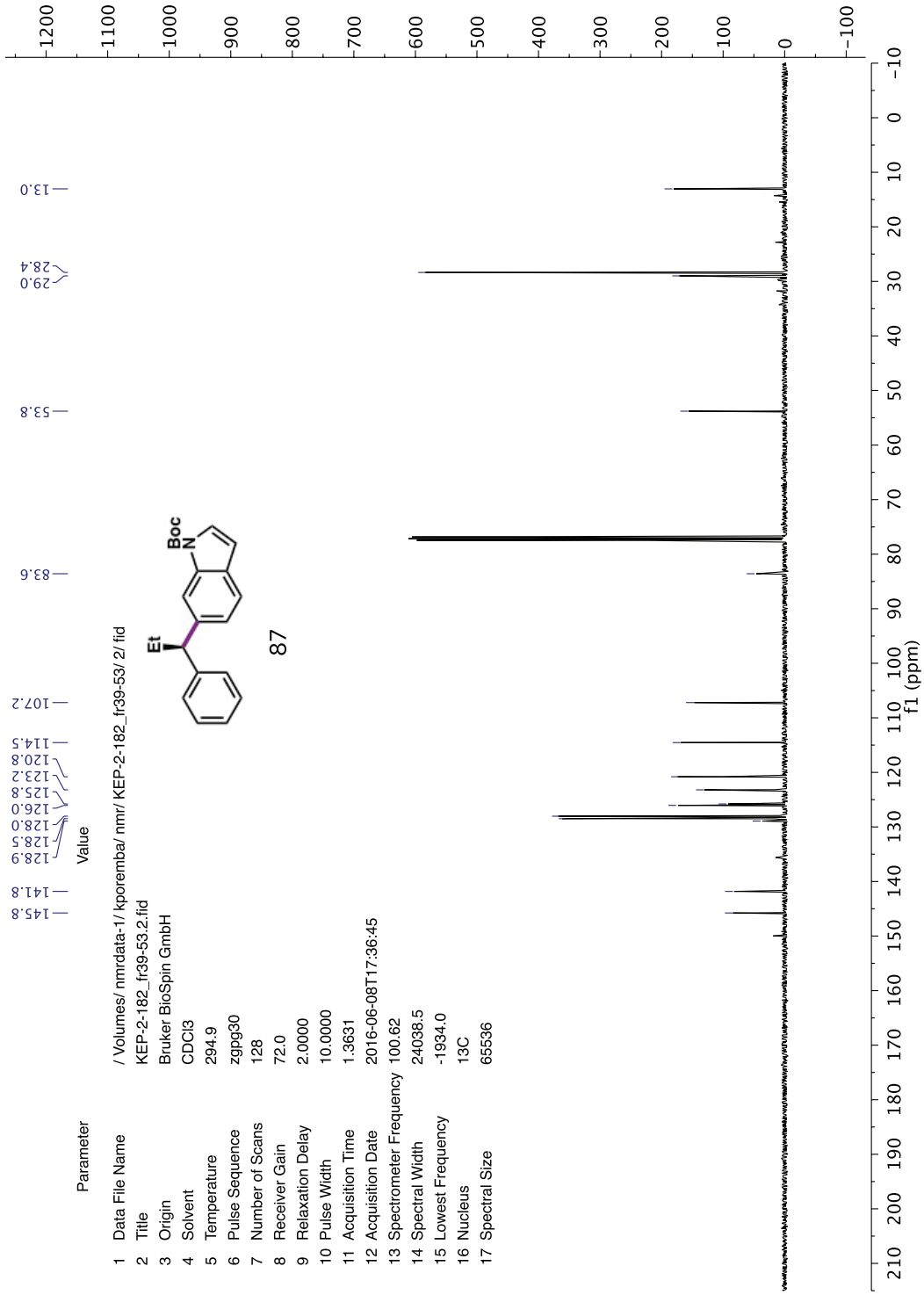
Parameter	Value
1 Data File Name	/ Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-135_fr41-55/ 2/ fid
2 Title	KEP-2-135_fr41-55.2.fid
3 Origin	Bruker BioSpin GmbH
4 Solvent	CDCl3
5 Temperature	294.9
6 Pulse Sequence	zgpg30
7 Number of Scans	128
8 Receiver Gain	72.0
9 Relaxation Delay	2.0000
10 Pulse Width	10.0000
11 Acquisition Time	1.3631
12 Acquisition Date	2016-04-18T22:48:54
13 Spectrometer Frequency	100.62
14 Spectral Width	24038.5
15 Lowest Frequency	-1939.0
16 Nucleus	13C
17 Spectral Size	65536


Parameter
Value
1 Data File Name / Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-283_3-CN-ar/ 1/ fid
2 Title KEP-2-283_3-CN-ar.1.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 295.0
6 Pulse Sequence zg30
7 Number of Scans 16
8 Receiver Gain 197.4
9 Relaxation Delay 1.0000
10 Pulse Width 11.7000
11 Acquisition Time 4.0894
12 Acquisition Date 2016-10-11T14:41:29
13 Spectrometer Frequency 400.13
14 Spectral Width 8012.8
15 Lowest Frequency -1535.6
16 Nucleus 1H
17 Spectral Size 65536
A (m) 7.48
B (m) 7.33
C (m) 7.21
D (t) 3.82
E (m) 2.07
F (t) 0.90
Et
CN
86
2.87
2.81
2.87
1.00
2.00
2.99
f1 (ppm)

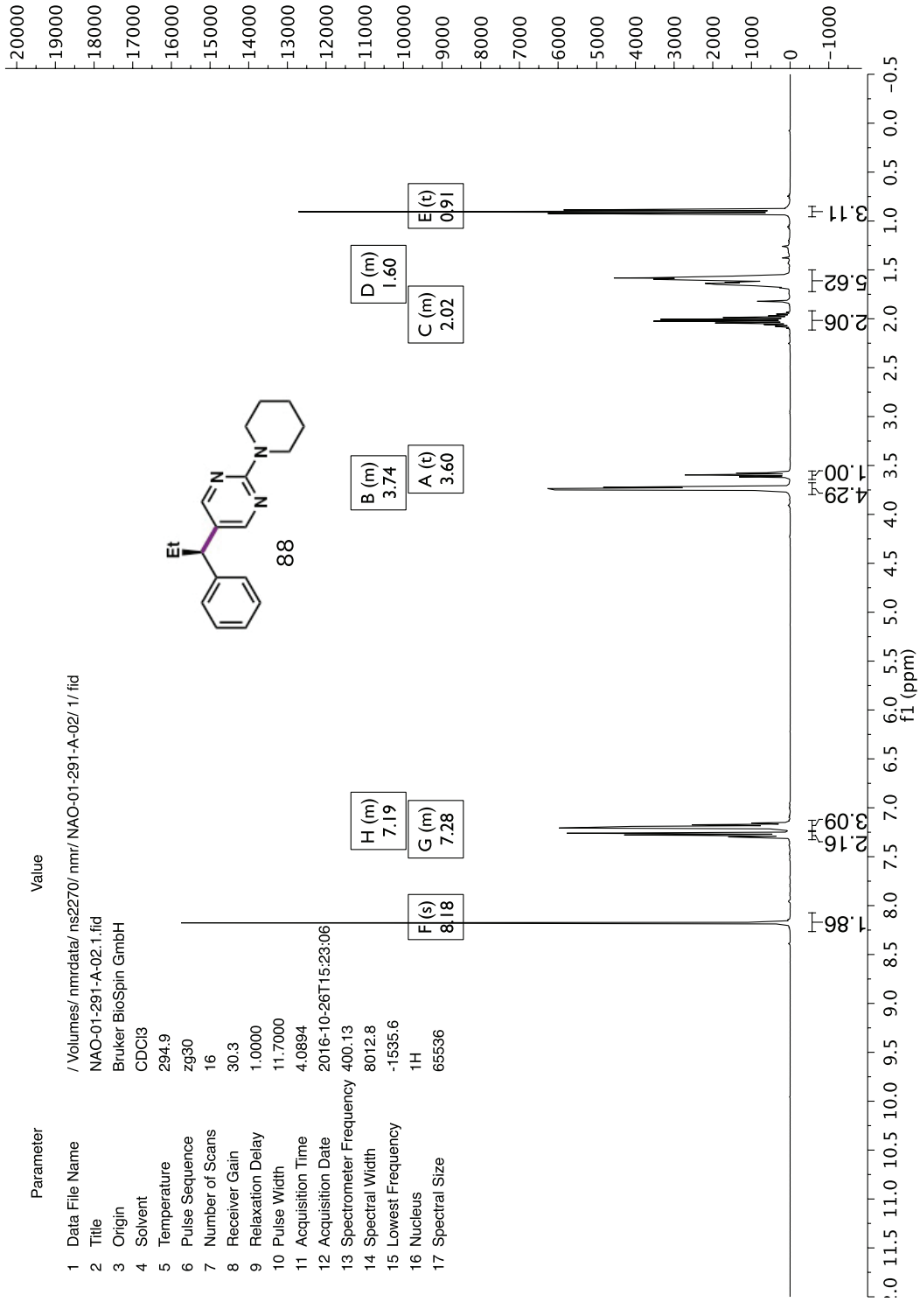


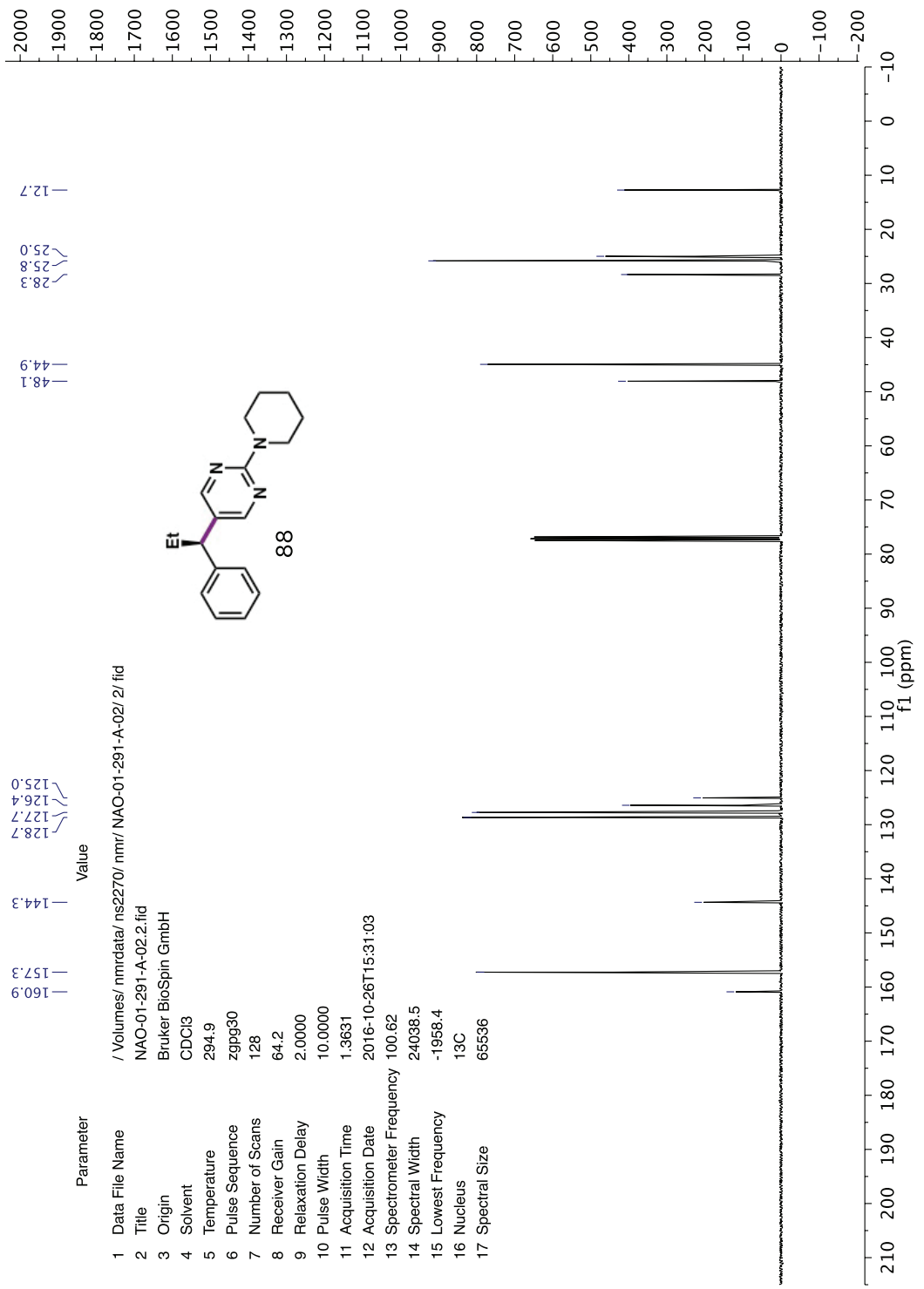
Parameter	Value
1 Data File Name	/ Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-283_3-CN-ar/ 2/ fid
2 Title	KEP-2-283_3-CN-ar.2.fid
3 Origin	Bruker BioSpin GmbH
4 Solvent	CDCl3
5 Temperature	295.0
6 Pulse Sequence	zgpg30
7 Number of Scans	128
8 Receiver Gain	35.5
9 Relaxation Delay	2.0000
10 Pulse Width	10.0000
11 Acquisition Time	1.3631
12 Acquisition Date	2016-10-11T14:49:15
13 Spectrometer Frequency	100.62
14 Spectral Width	24038.5
15 Lowest Frequency	-1933.2
16 Nucleus	13C
17 Spectral Size	65536

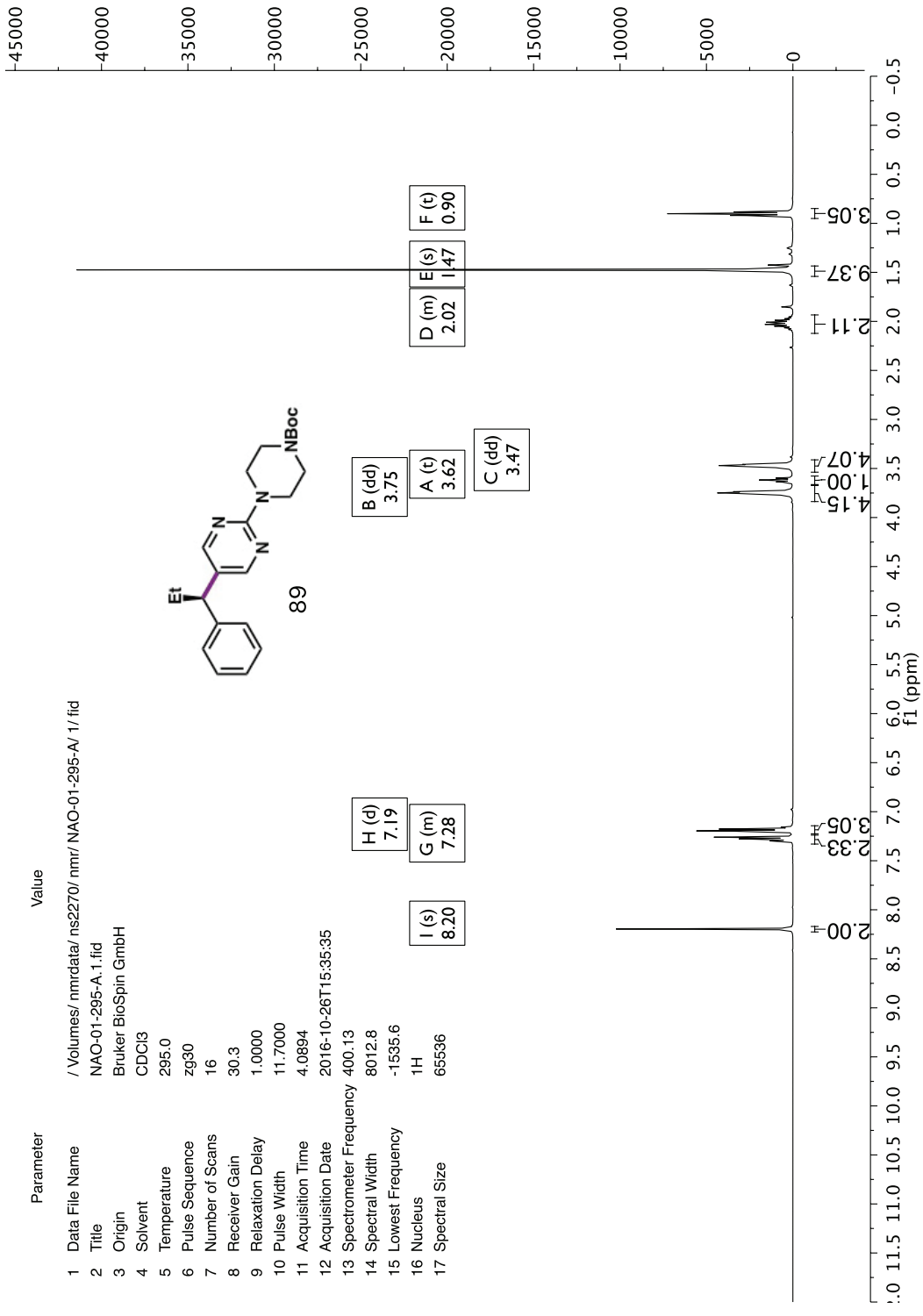

Parameter
Value
1 Data File Name / Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-182_fr39-53/ 1/ fid
2 Title KEP-2-182_fr39-53.1.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 295.0
6 Pulse Sequence zg30
7 Number of Scans 16
8 Receiver Gain 78.7
9 Relaxation Delay 1.0000
10 Pulse Width 11.7000
11 Acquisition Time 4.0894
12 Acquisition Date 2016-06-08T17:28:55
13 Spectrometer Frequency 400.13
14 Spectral Width 8012.8
15 Lowest Frequency -1535.6
16 Nucleus 1H
17 Spectral Size 65536
Et
Boc
N
87
E (s) 8.09
A (dd) 7.45
B (m) 7.27
C (m) 7.15
D (dd) 6.50
F (t) 3.93
G (m) 2.15
H (s) 1.66
I (t) 0.93
1.05
0.94
4.53
1.90
0.98
1.00
2.08
8.95
3.01
f1 (ppm)

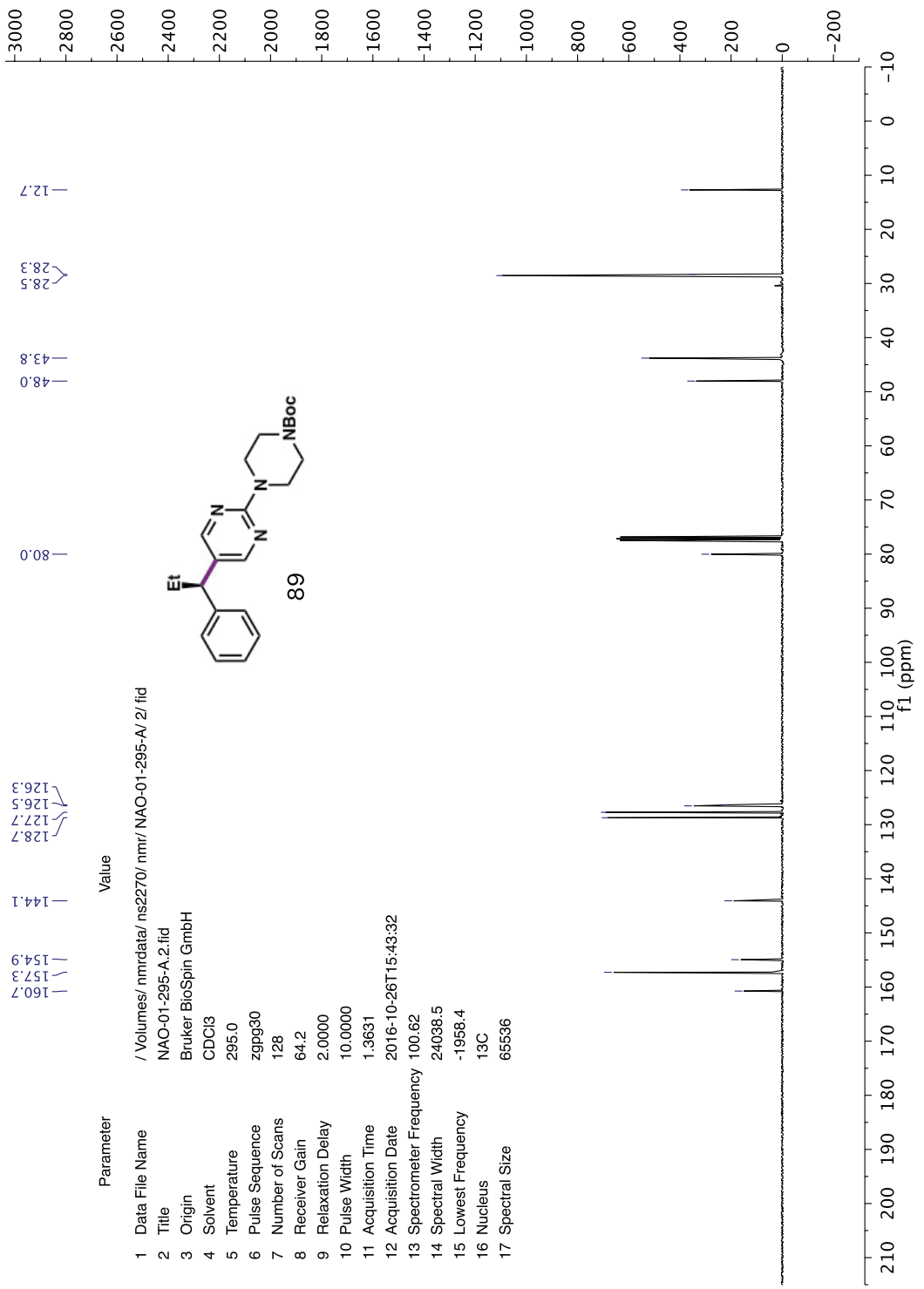


Parameter	Value
1 Data File Name	/ Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-182_fr39-53/ 2/ fid
2 Title	KEP-2-182_fr39-53.2.fid
3 Origin	Bruker BioSpin GmbH
4 Solvent	CDCl3
5 Temperature	294.9
6 Pulse Sequence	zgpg30
7 Number of Scans	128
8 Receiver Gain	72.0
9 Relaxation Delay	2.0000
10 Pulse Width	10.0000
11 Acquisition Time	1.3631
12 Acquisition Date	2016-06-08T17:36:45
13 Spectrometer Frequency	100.62
14 Spectral Width	24038.5
15 Lowest Frequency	-1934.0
16 Nucleus	13C
17 Spectral Size	65536

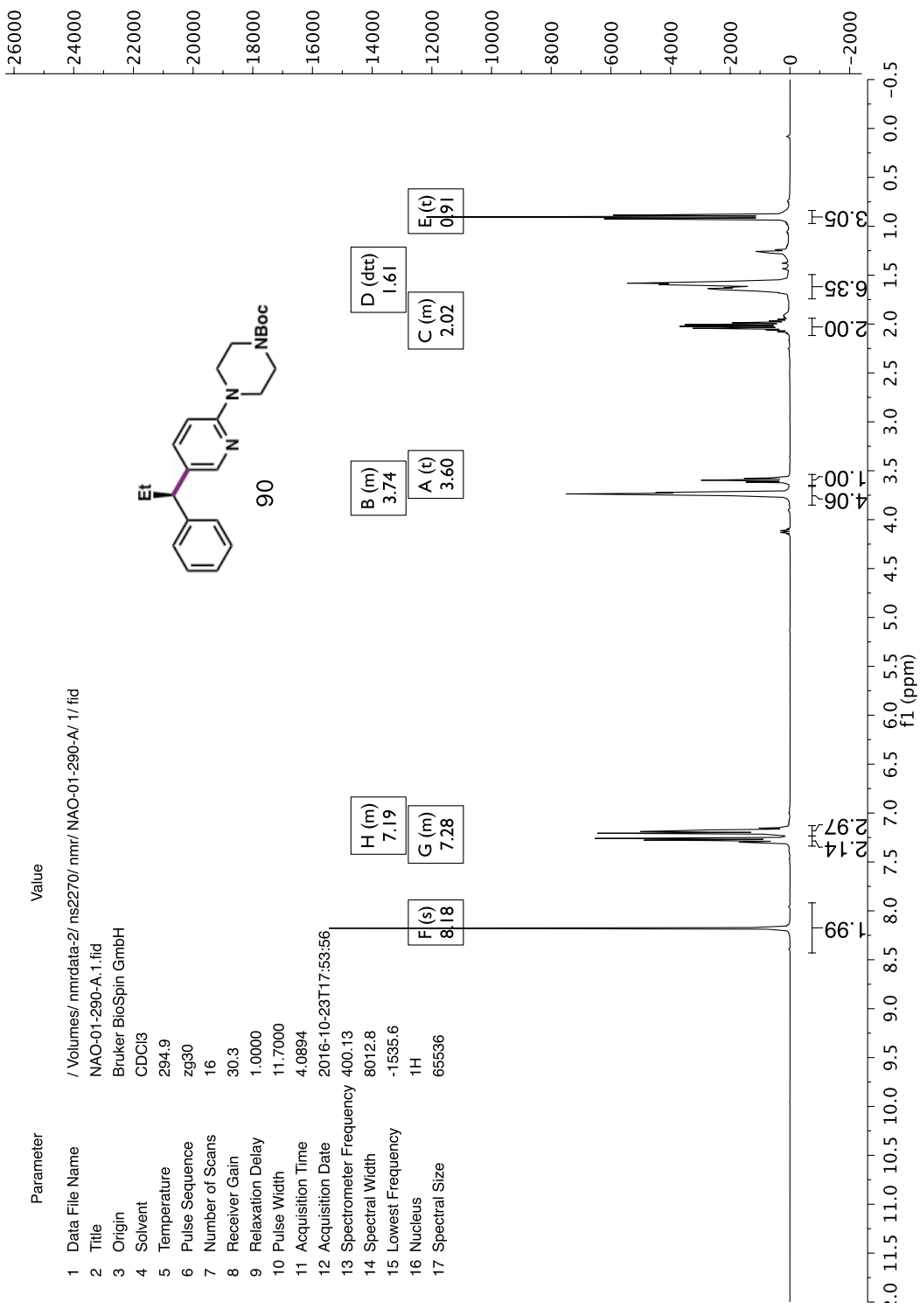

Parameter
Value
1 Data File Name / Volumes/ nmrdata/ ns2270/ nmr/ NAO-01-291-A-02/ 1/ fid
2 Title NAO-01-291-A-02.1.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 294.9
6 Pulse Sequence zg30
7 Number of Scans 16
8 Receiver Gain 30.3
9 Relaxation Delay 1.0000
10 Pulse Width 11.7000
11 Acquisition Time 4.0894
12 Acquisition Date 2016-10-26T15:23:06
13 Spectrometer Frequency 400.13
14 Spectral Width 8012.8
15 Lowest Frequency -1535.6
16 Nucleus 1H
17 Spectral Size 65536
F (s) 8.18
G (m) 7.28
H (m) 7.19
A (t) 3.60
B (m) 3.74
C (m) 2.02
D (m) 1.60
E (t) 0.91
Et
88
1.86
2.16
3.09
1.00
4.29
2.06
5.62
3.11
f1 (ppm)

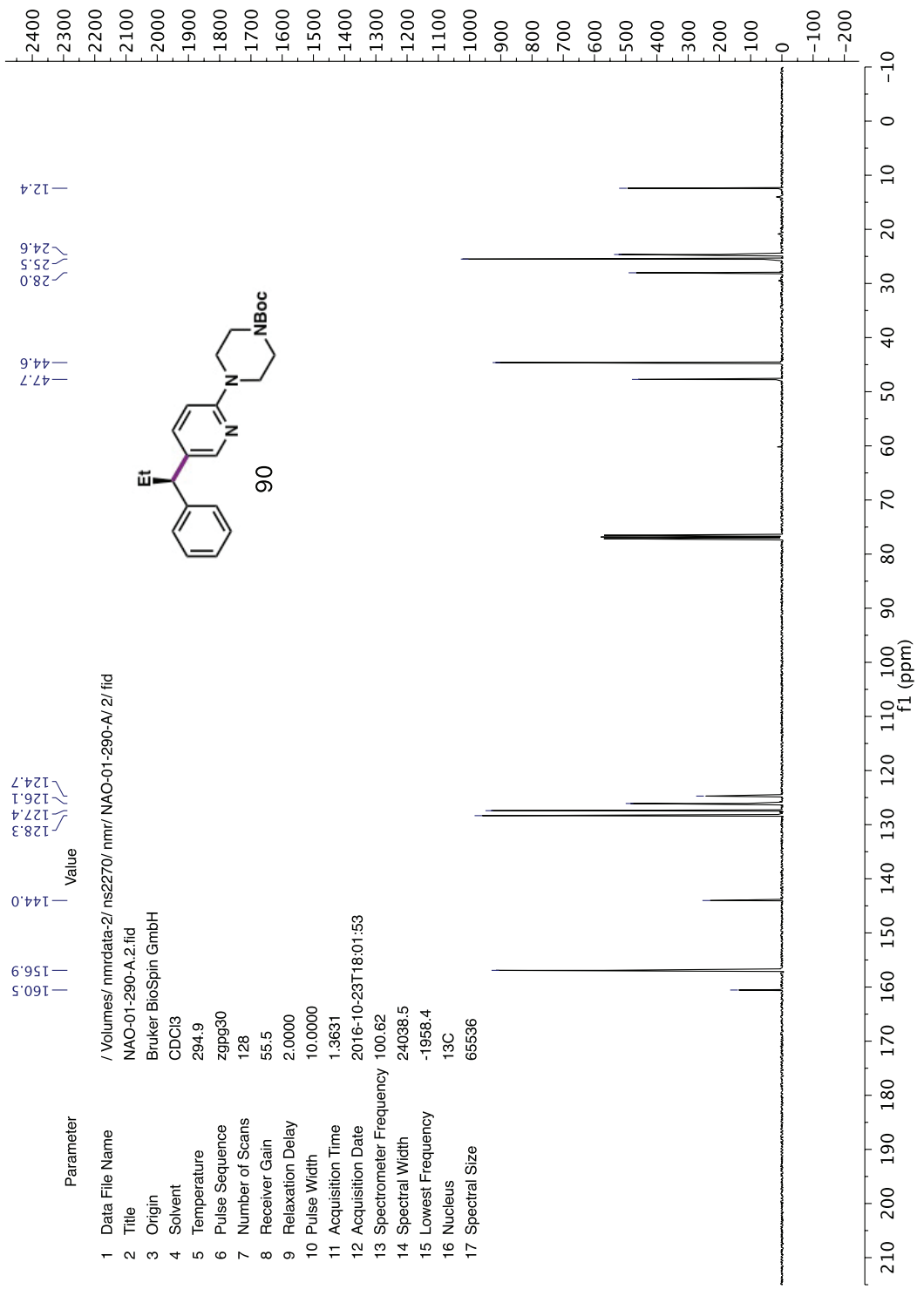

Et
88
f1 (ppm)
Parameter Value
1 Data File Name / Volumes/ nmrdata/ ns2270/ nmr/ NAO-01-291-A-02/ 2/ fid
2 Title NAO-01-291-A-02.2.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 294.9
6 Pulse Sequence zgpg30
7 Number of Scans 128
8 Receiver Gain 64.2
9 Relaxation Delay 2.0000
10 Pulse Width 10.0000
11 Acquisition Time 1.3631
12 Acquisition Date 2016-10-26T15:31:03
13 Spectrometer Frequency 100.62
14 Spectral Width 24038.5
15 Lowest Frequency -1958.4
16 Nucleus 13C
17 Spectral Size 65536

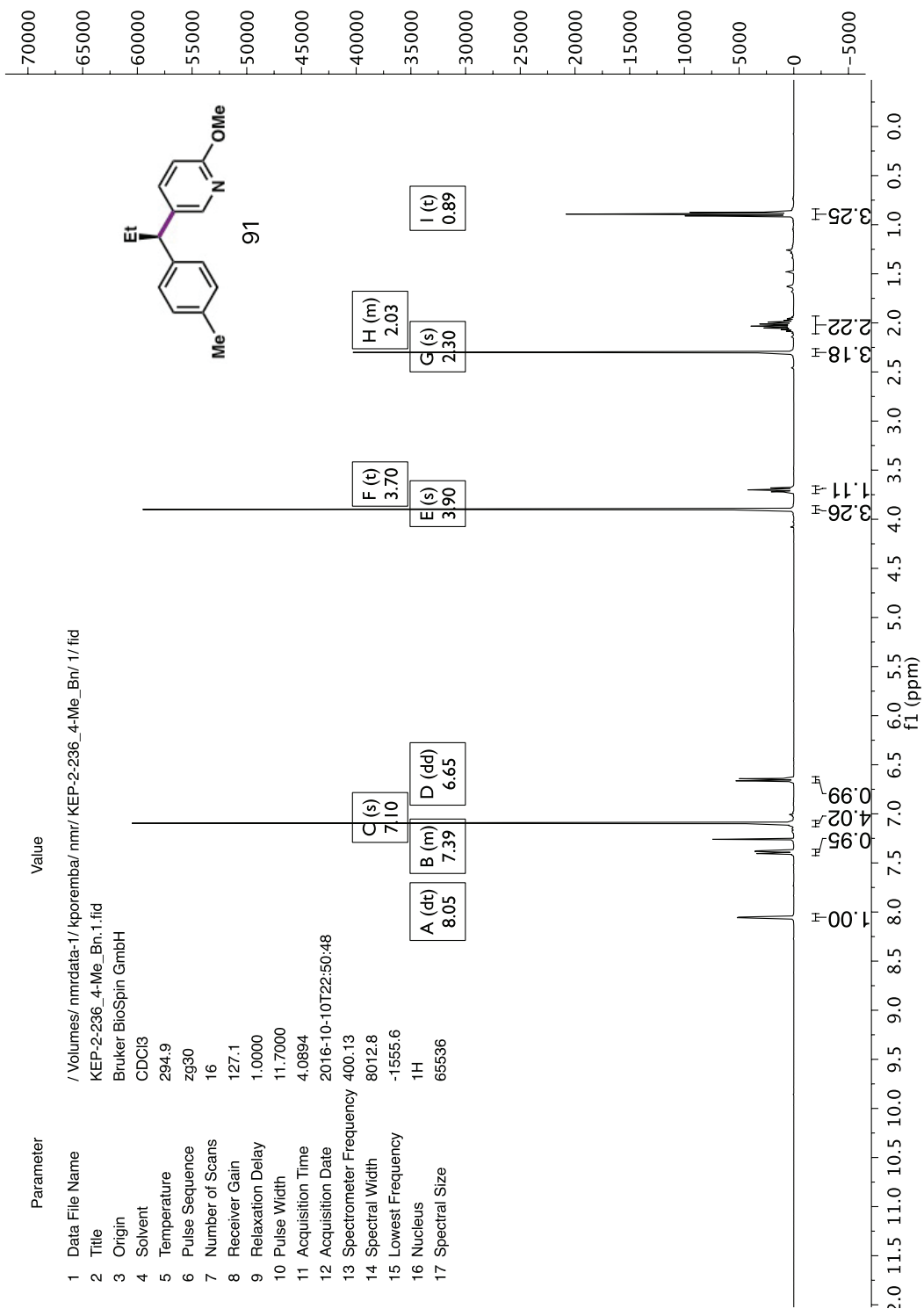

Parameter
Value
1 Data File Name / Volumes/ nmrdata/ ns2270/ nmr/ NAO-01-295-A/ 1/ fid
2 Title NAO-01-295-A.1.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 295.0
6 Pulse Sequence zg30
7 Number of Scans 16
8 Receiver Gain 30.3
9 Relaxation Delay 1.0000
10 Pulse Width 11.7000
11 Acquisition Time 4.0894
12 Acquisition Date 2016-10-26T15:35:35
13 Spectrometer Frequency 400.13
14 Spectral Width 8012.8
15 Lowest Frequency -1535.6
16 Nucleus 1H
17 Spectral Size 65536
Et
NBoc
89
I (s) 8.20
H (d) 7.19
G (m) 7.28
B (dd) 3.75
A (t) 3.62
C (dd) 3.47
D (m) 2.02
E (s) 1.47
F (t) 0.90
2.00
2.33
3.05
4.15
1.00
4.07
2.11
9.37
3.05
f1 (ppm)

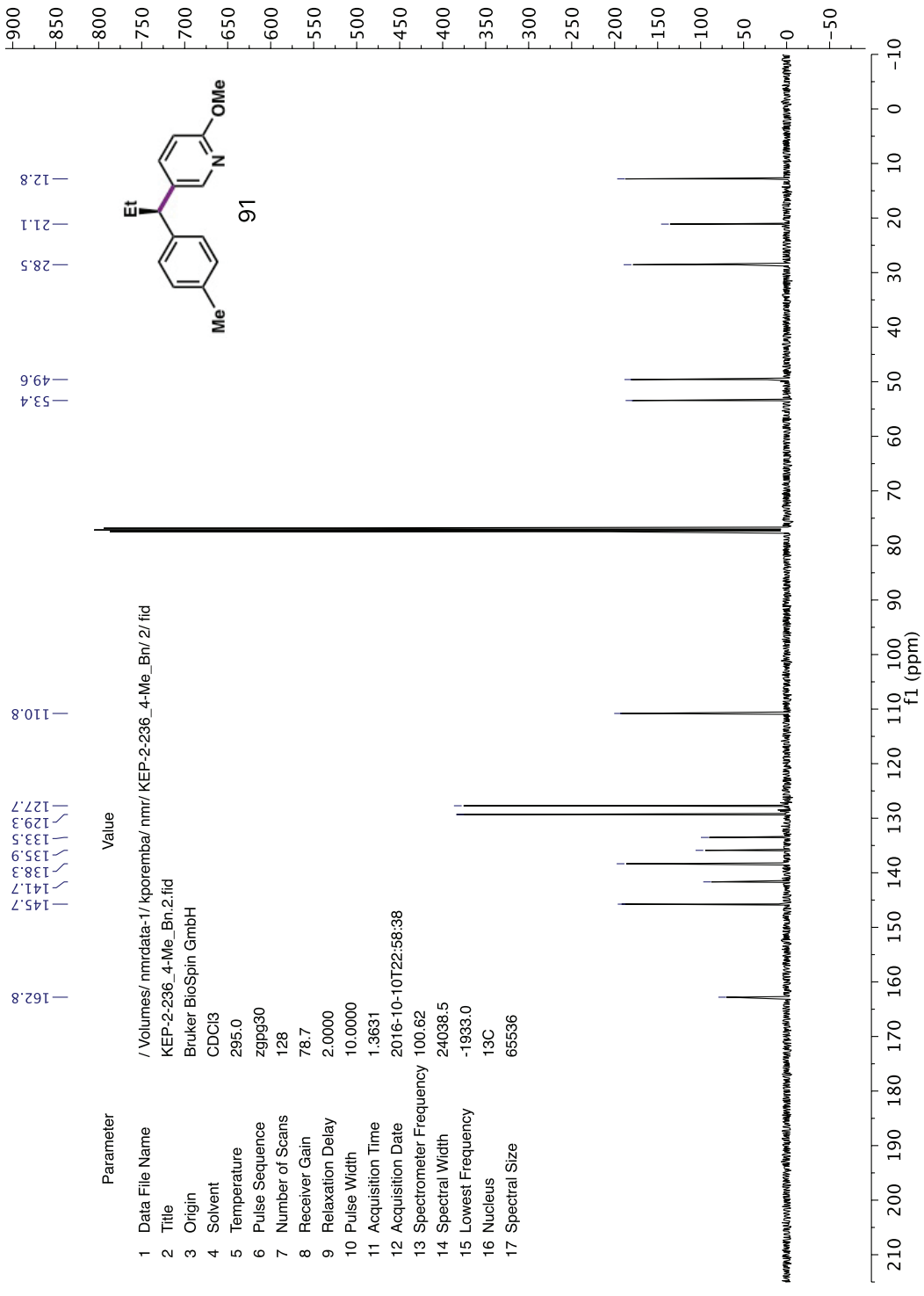


	Parameter	Value
1	Data File Name	/ Volumes/ nmrdata/ ns2270/ nmr/ NAO-01-295-A/ 2/ fid
2	Title	NAO-01-295-A.2.fid
3	Origin	Bruker BioSpin GmbH
4	Solvent	CDCl3
5	Temperature	295.0
6	Pulse Sequence	zgpg30
7	Number of Scans	128
8	Receiver Gain	64.2
9	Relaxation Delay	2.0000
10	Pulse Width	10.0000
11	Acquisition Time	1.3631
12	Acquisition Date	2016-10-26T15:43:32
13	Spectrometer Frequency	100.62
14	Spectral Width	24038.5
15	Lowest Frequency	-1958.4
16	Nucleus	13C
17	Spectral Size	65536

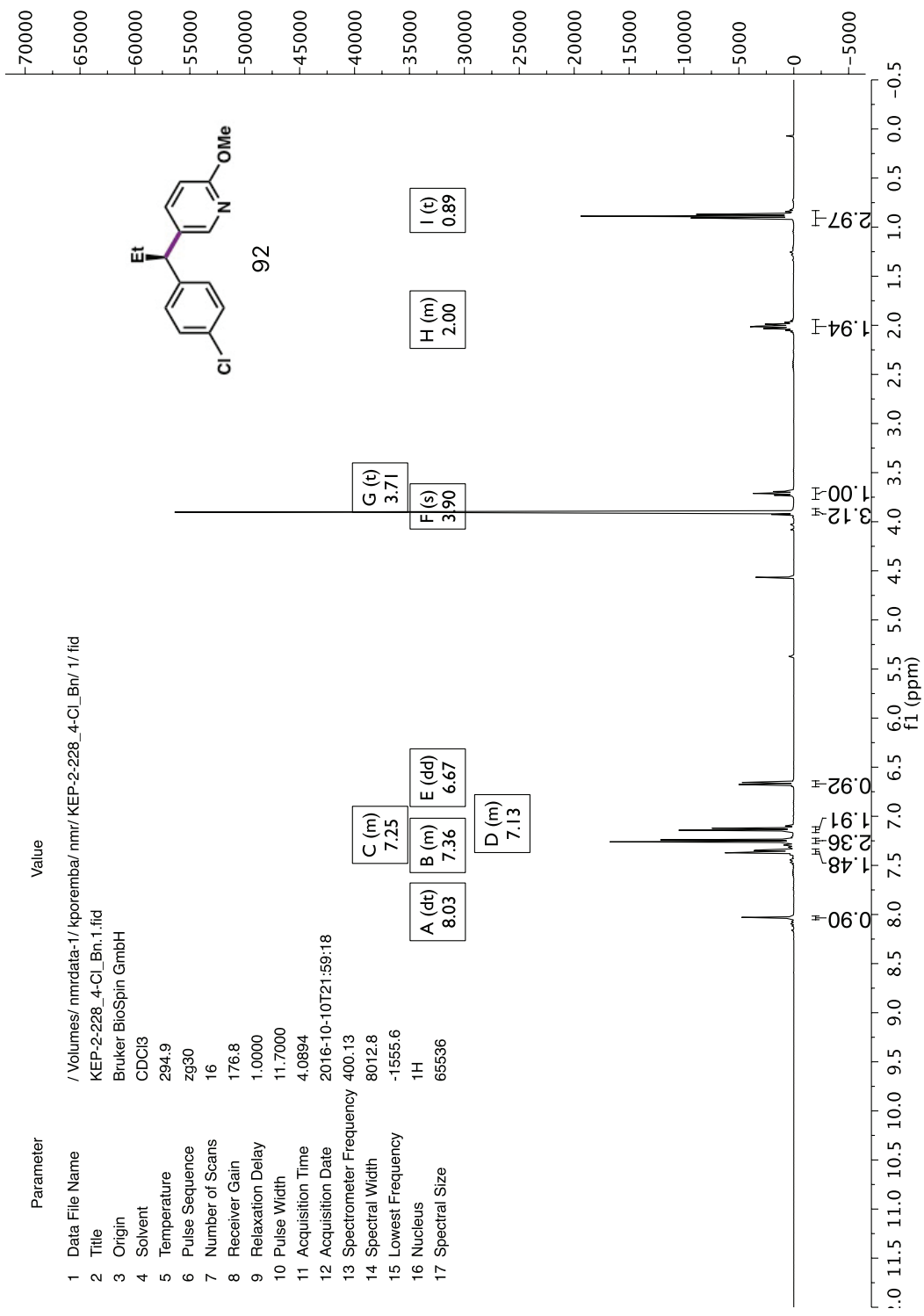

Parameter
Value
1 Data File Name / Volumes/ nmrdata-2/ ns2270/ nmr/ NAO-01-290-A/ 1/ fid
2 Title NAO-01-290-A.1.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 294.9
6 Pulse Sequence zg30
7 Number of Scans 16
8 Receiver Gain 30.3
9 Relaxation Delay 1.0000
10 Pulse Width 11.7000
11 Acquisition Time 4.0894
12 Acquisition Date 2016-10-23T17:53:56
13 Spectrometer Frequency 400.13
14 Spectral Width 8012.8
15 Lowest Frequency -1535.6
16 Nucleus 1H
17 Spectral Size 65536
Et
NBoc
90
F (s) 8.18
G (m) 7.28
H (m) 7.19
A (t) 3.60
B (m) 3.74
C (m) 2.02
D (dtt) 1.61
E (t) 0.91
1.99
2.14
2.97
1.00
4.06
2.00
6.35
3.05
f1 (ppm)

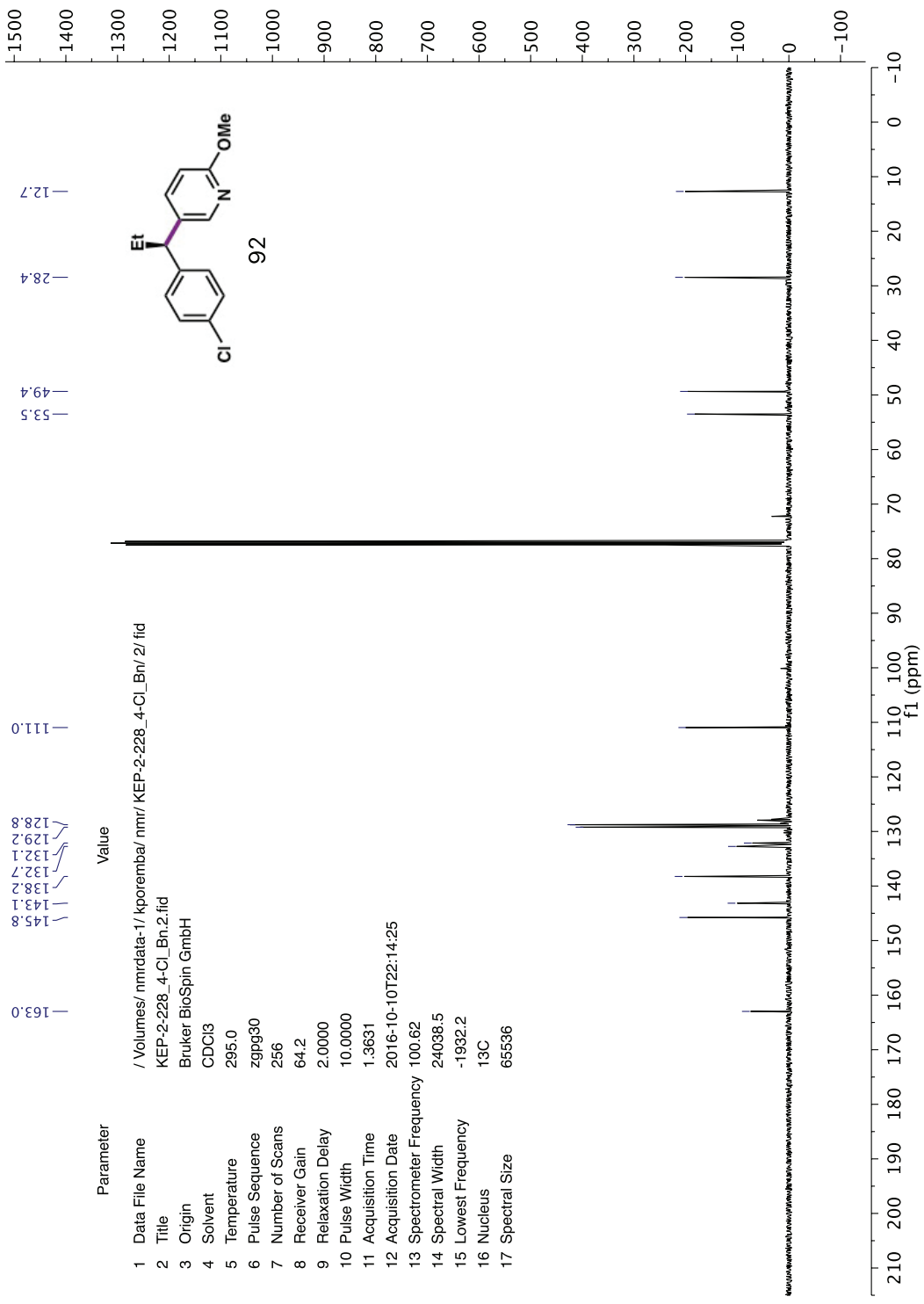

Parameter Value
1 Data File Name / Volumes/ nmrdata-2/ ns2270/ nmr/ NAO-01-290-A/ 2/ fid
2 Title NAO-01-290-A.2.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 294.9
6 Pulse Sequence zgpg30
7 Number of Scans 128
8 Receiver Gain 55.5
9 Relaxation Delay 2.0000
10 Pulse Width 10.0000
11 Acquisition Time 1.3631
12 Acquisition Date 2016-10-23T18:01:53
13 Spectrometer Frequency 100.62
14 Spectral Width 24038.5
15 Lowest Frequency -1958.4
16 Nucleus 13C
17 Spectral Size 65536
160.5
156.9
144.0
128.3
127.4
126.1
124.7
47.7
44.6
28.0
25.5
24.6
12.4
NBoc
Et
90
f1 (ppm)


Parameter
Value
1 Data File Name / Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-236_4-Me_Bn/ 1/ fid
2 Title KEP-2-236_4-Me_Bn.1.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 294.9
6 Pulse Sequence zg30
7 Number of Scans 16
8 Receiver Gain 127.1
9 Relaxation Delay 1.0000
10 Pulse Width 11.7000
11 Acquisition Time 4.0894
12 Acquisition Date 2016-10-10T22:50:48
13 Spectrometer Frequency 400.13
14 Spectral Width 8012.8
15 Lowest Frequency -1555.6
16 Nucleus 1H
17 Spectral Size 65536
A (dt) 8.05
B (m) 7.39
C (s) 7.10
D (dd) 6.65
E (s) 3.90
F (t) 3.70
G (s) 2.30
H (m) 2.03
I (t) 0.89
Et
OMe
Me
N
91
1.00
0.95
4.02
0.99
3.26
1.11
3.18
2.22
3.25
f1 (ppm)

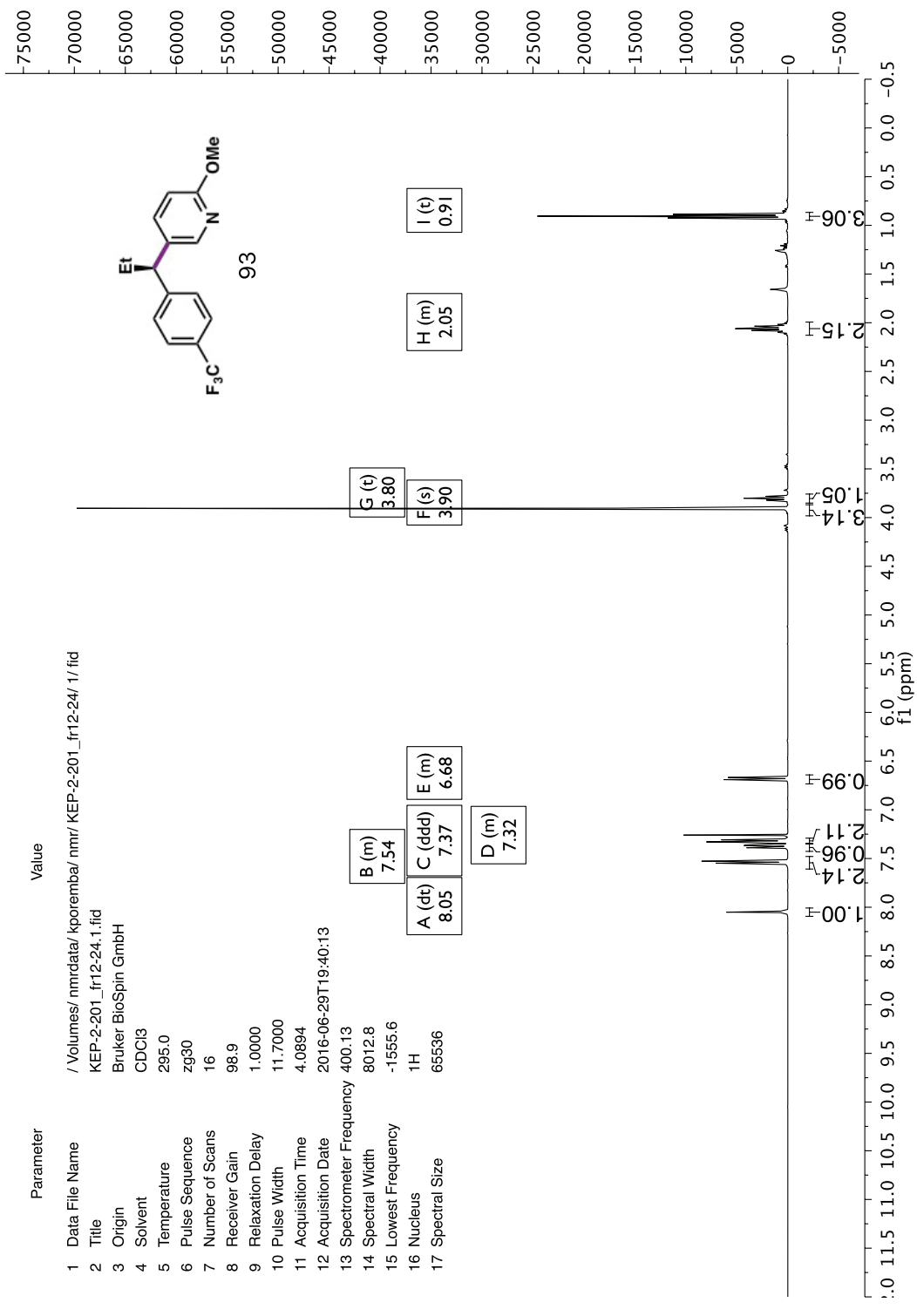


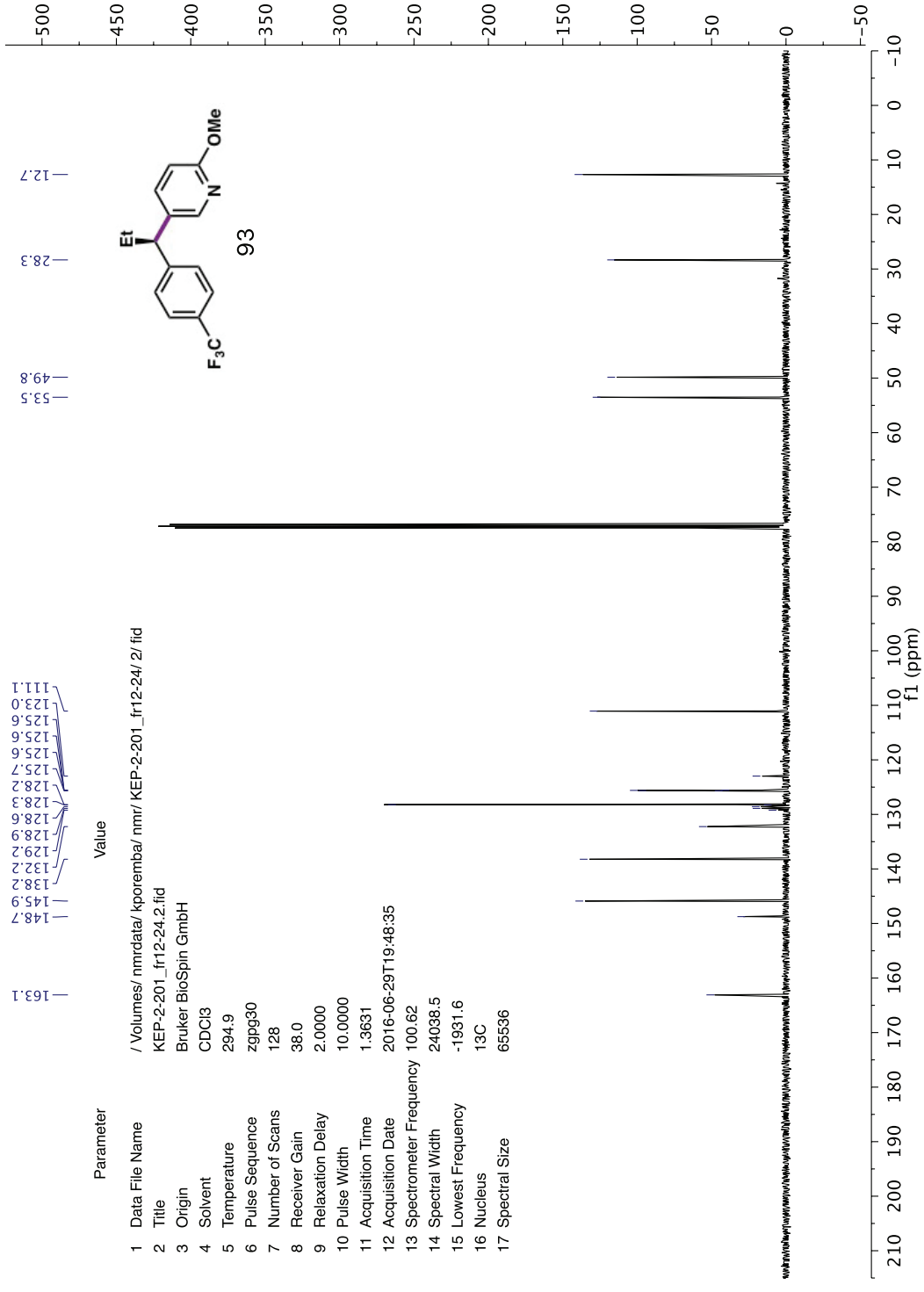
Parameter		Value
1	Data File Name	/ Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-236_4-Me_Bn/ 2/ fid
2	Title	KEP-2-236_4-Me_Bn.2.fid
3	Origin	Bruker BioSpin GmbH
4	Solvent	CDCl3
5	Temperature	295.0
6	Pulse Sequence	zgpg30
7	Number of Scans	128
8	Receiver Gain	78.7
9	Relaxation Delay	2.0000
10	Pulse Width	10.0000
11	Acquisition Time	1.3631
12	Acquisition Date	2016-10-10T22:58:38
13	Spectrometer Frequency	100.62
14	Spectral Width	24038.5
15	Lowest Frequency	-1933.0
16	Nucleus	13C
17	Spectral Size	65536

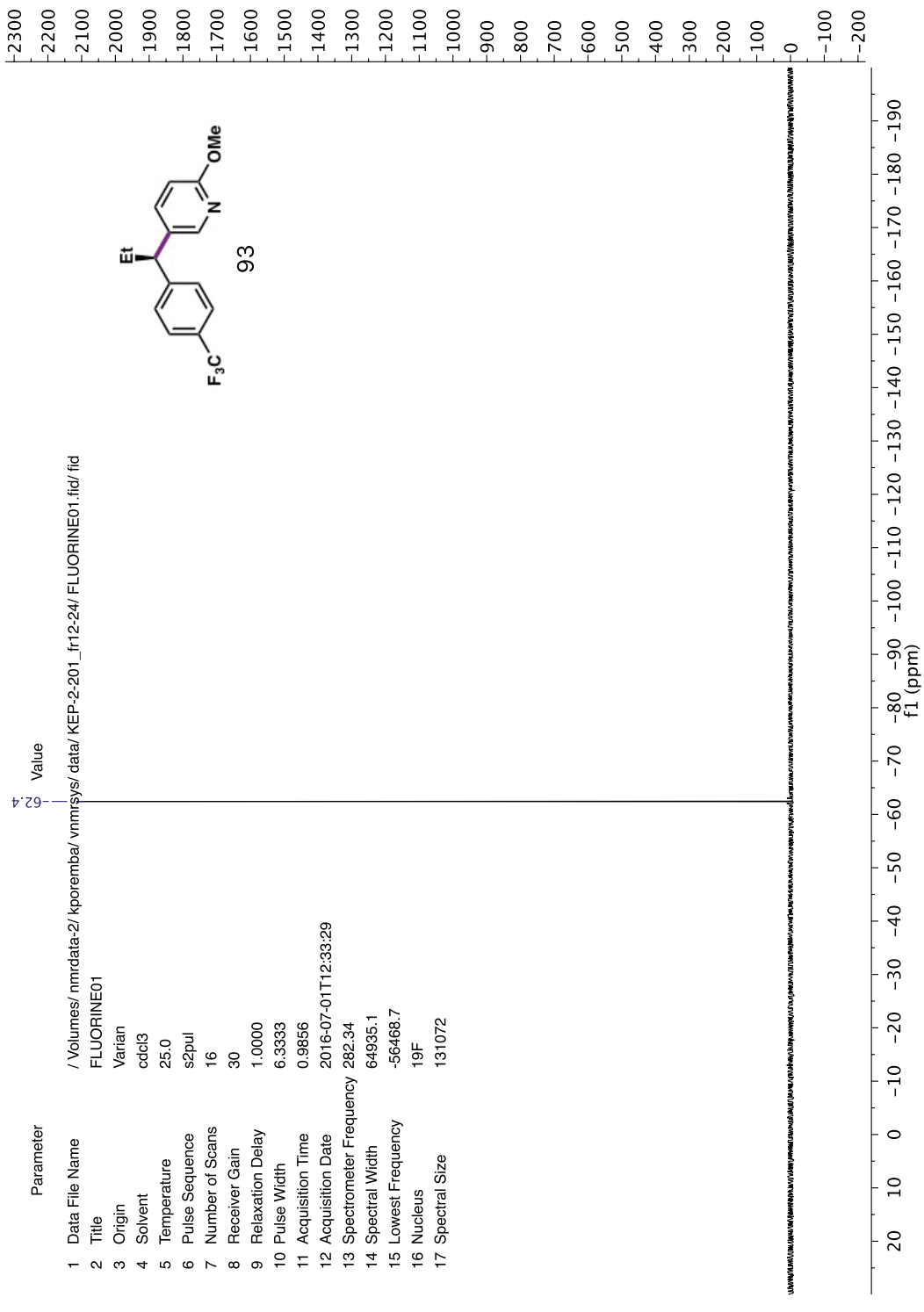

Parameter
Value
1 Data File Name / Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-228_4-Cl_Bn/ 1/ fid
2 Title KEP-2-228_4-Cl_Bn.1.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 294.9
6 Pulse Sequence zg30
7 Number of Scans 16
8 Receiver Gain 176.8
9 Relaxation Delay 1.0000
10 Pulse Width 11.7000
11 Acquisition Time 4.0894
12 Acquisition Date 2016-10-10T21:59:18
13 Spectrometer Frequency 400.13
14 Spectral Width 8012.8
15 Lowest Frequency -1555.6
16 Nucleus 1H
17 Spectral Size 65536
A (dt) 8.03
B (m) 7.36
C (m) 7.25
D (m) 7.13
E (dd) 6.67
F (s) 3.90
G (t) 3.71
H (m) 2.00
I (t) 0.89
92
Et
OMe
N
Cl
0.90
1.48
2.36
1.91
0.92
3.12
1.00
1.94
2.97
f1 (ppm)

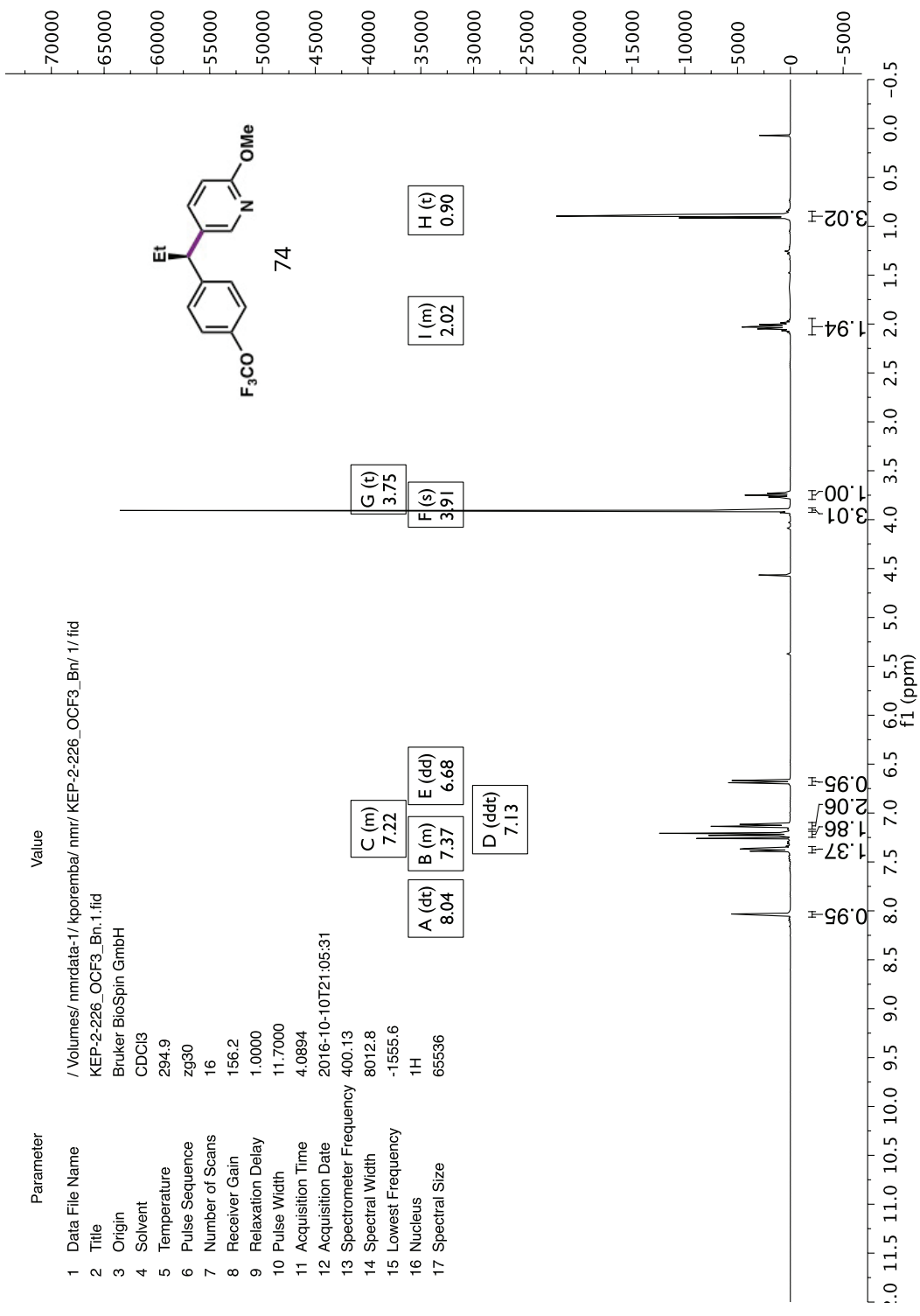


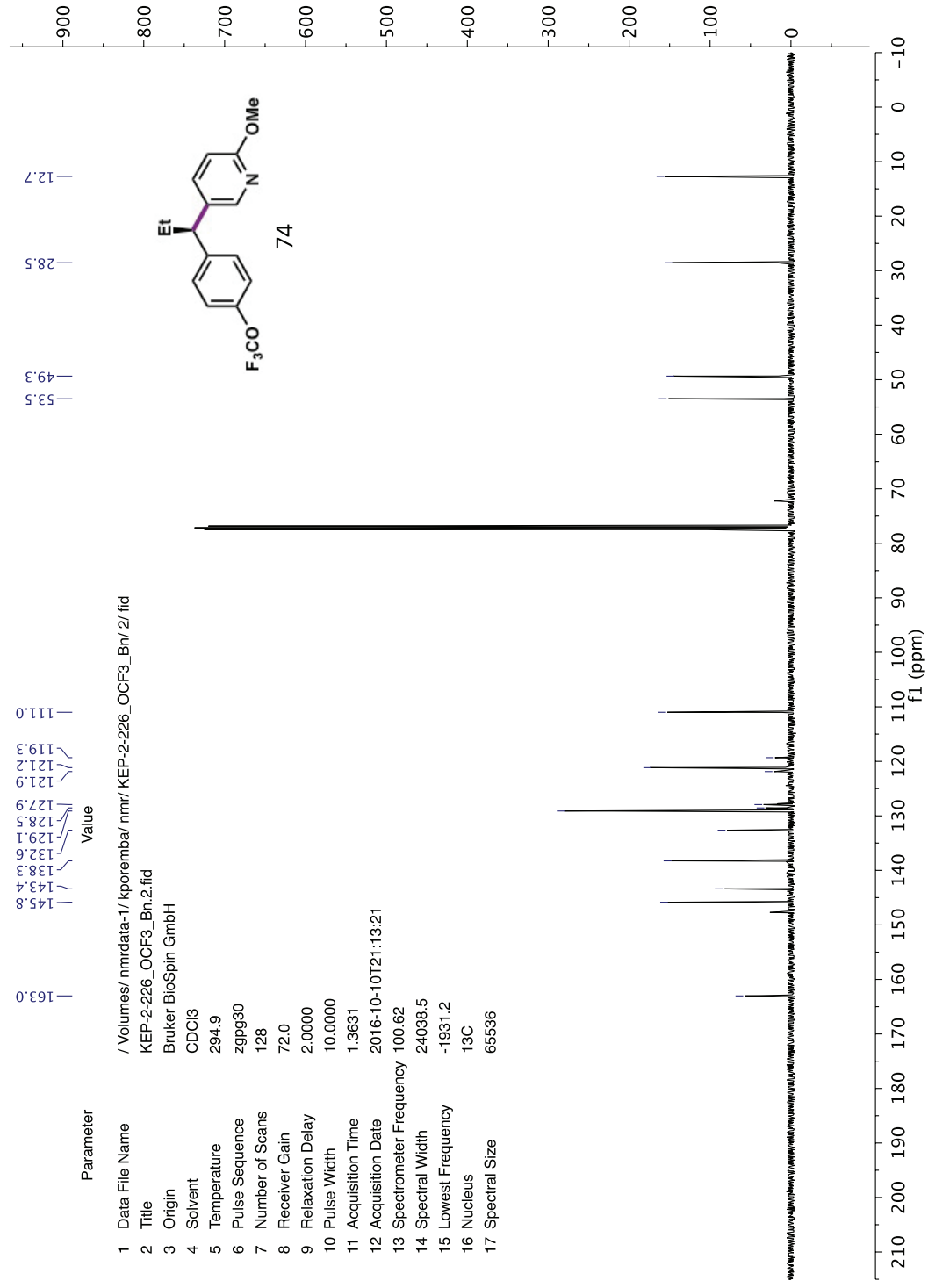
	Parameter	Value
1	Data File Name	/ Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-228_4-Cl_Bn/ 2/ fid
2	Title	KEP-2-228_4-Cl_Bn.2.fid
3	Origin	Bruker BioSpin GmbH
4	Solvent	CDCl3
5	Temperature	295.0
6	Pulse Sequence	zgpg30
7	Number of Scans	256
8	Receiver Gain	64.2
9	Relaxation Delay	2.0000
10	Pulse Width	10.0000
11	Acquisition Time	1.3631
12	Acquisition Date	2016-10-10T22:14:25
13	Spectrometer Frequency	100.62
14	Spectral Width	24038.5
15	Lowest Frequency	-1932.2
16	Nucleus	13C
17	Spectral Size	65536

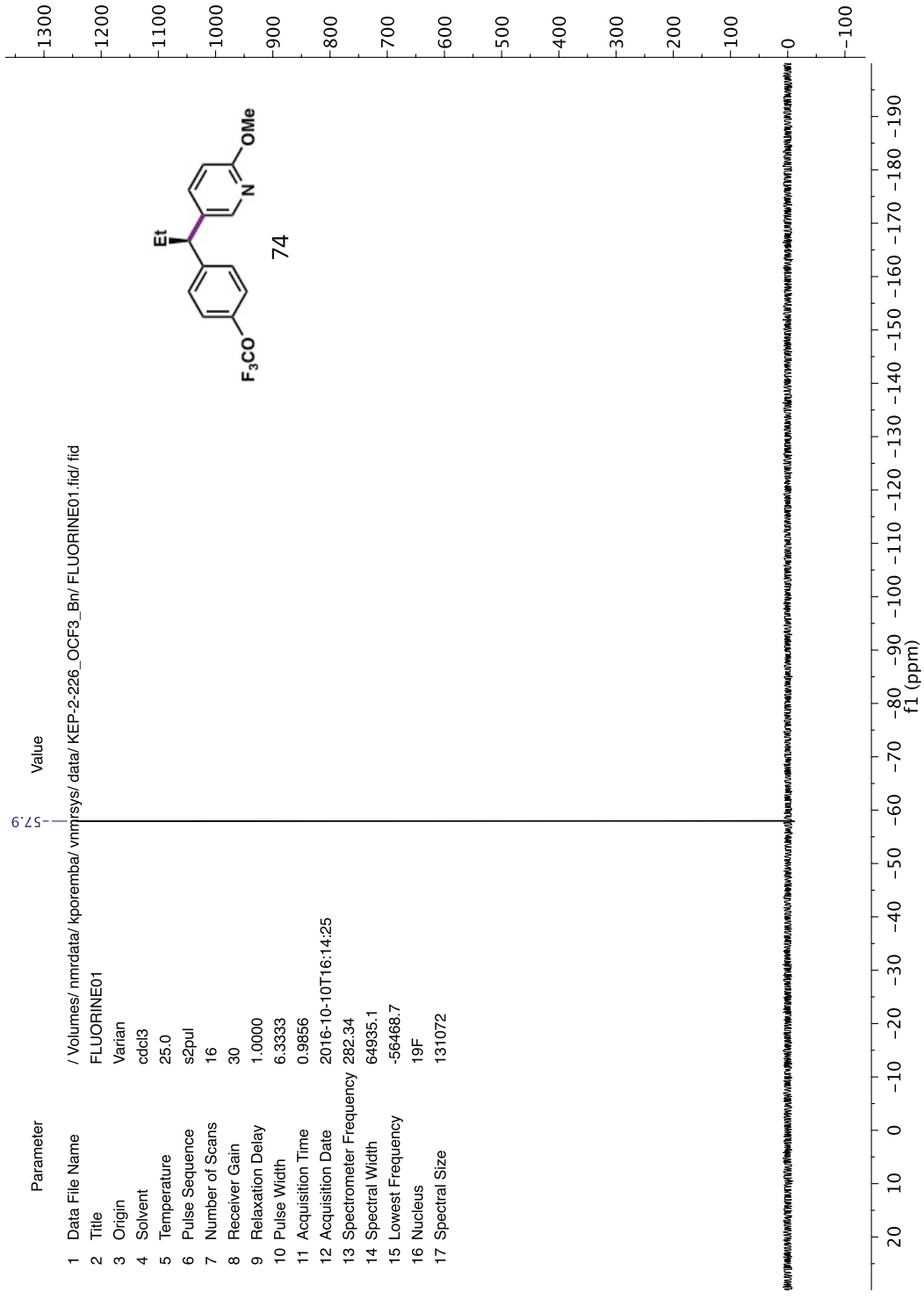

Parameter
Value
1 Data File Name / Volumes/ nmrdata/ kporemba/ nmr/ KEP-2-201_fr12-24/ 1/ fid
2 Title KEP-2-201_fr12-24.1.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 295.0
6 Pulse Sequence zg30
7 Number of Scans 16
8 Receiver Gain 98.9
9 Relaxation Delay 1.0000
10 Pulse Width 11.7000
11 Acquisition Time 4.0894
12 Acquisition Date 2016-06-29T19:40:13
13 Spectrometer Frequency 400.13
14 Spectral Width 8012.8
15 Lowest Frequency -1555.6
16 Nucleus 1H
17 Spectral Size 65536
A (dt) 8.05
B (m) 7.54
C (ddd) 7.37
D (m) 7.32
E (m) 6.68
F (s) 3.90
G (t) 3.80
H (m) 2.05
I (t) 0.91
Et
OMe
N
F_3C
93
1.00
2.14
0.96
2.11
0.99
3.14
1.05
2.15
3.06
f1 (ppm)


93
Et
OMe
N
F3C
f1 (ppm)
Parameter
Value
1 Data File Name / Volumes/ nmrdata/ kporemba/ nmr/ KEP-2-201_fr12-24/ 2/ fid
2 Title KEP-2-201_fr12-24.2.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 294.9
6 Pulse Sequence zgpg30
7 Number of Scans 128
8 Receiver Gain 38.0
9 Relaxation Delay 2.0000
10 Pulse Width 10.0000
11 Acquisition Time 1.3631
12 Acquisition Date 2016-06-29T19:48:35
13 Spectrometer Frequency 100.62
14 Spectral Width 24038.5
15 Lowest Frequency -1931.6
16 Nucleus 13C
17 Spectral Size 65536

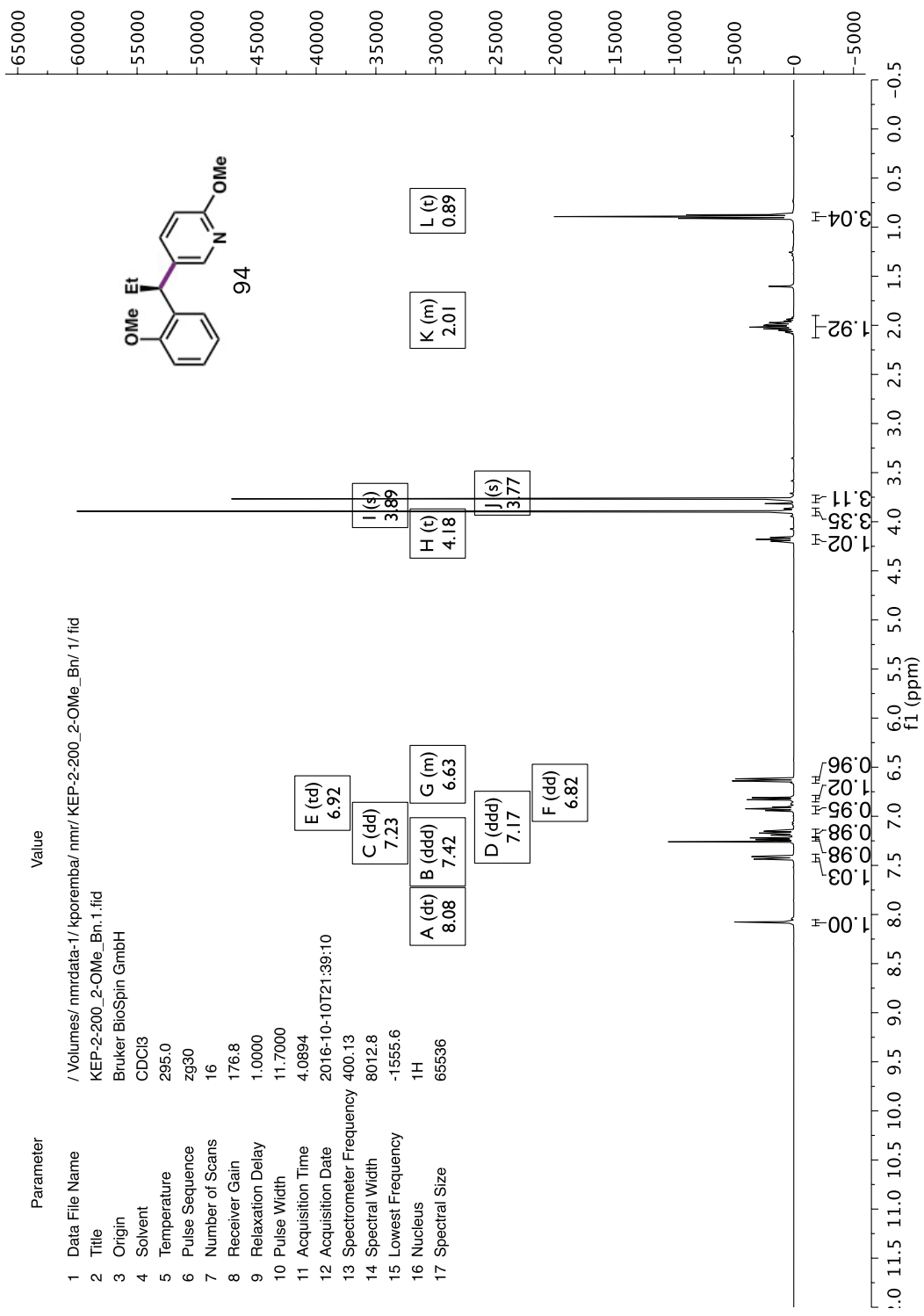

Parameter Value
1 Data File Name / Volumes/ nmrdata-2/ kporemba/ vnmrsys/ data/ KEP-2-201_fr12-24/ FLUORINE01.fid/ fid
2 Title FLUORINE01
3 Origin Varian
4 Solvent cdcl3
5 Temperature 25.0
6 Pulse Sequence s2pul
7 Number of Scans 16
8 Receiver Gain 30
9 Relaxation Delay 1.0000
10 Pulse Width 6.3333
11 Acquisition Time 0.9856
12 Acquisition Date 2016-07-01T12:33:29
13 Spectrometer Frequency 282.34
14 Spectral Width 64935.1
15 Lowest Frequency -56468.7
16 Nucleus 19F
17 Spectral Size 131072
-62.4
Et
OMe
N
F3C
93
f1 (ppm)

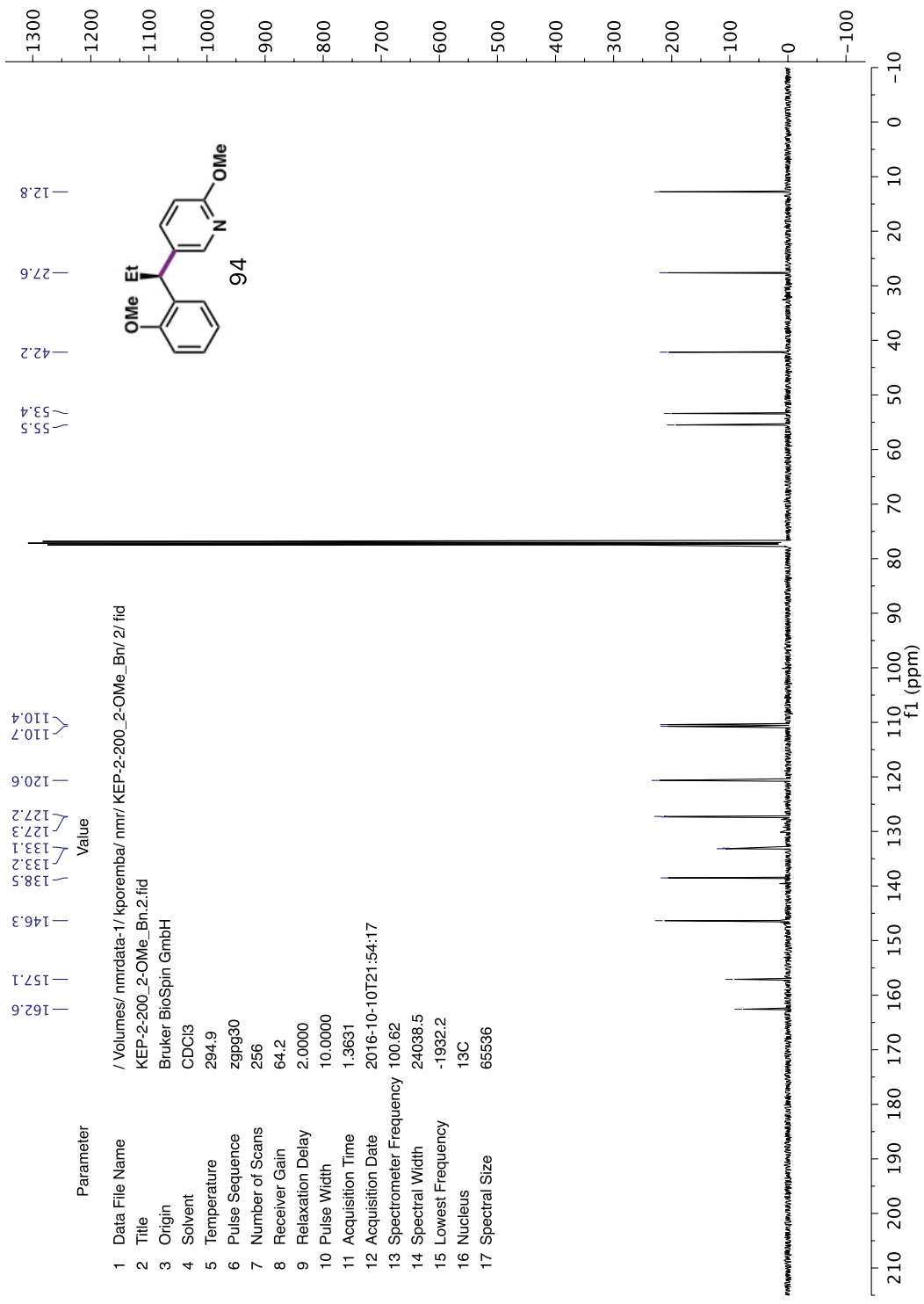

Parameter
Value
1 Data File Name / Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-226_OCF3_Bn/ 1/ fid
2 Title KEP-2-226_OCF3_Bn.1.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 294.9
6 Pulse Sequence zg30
7 Number of Scans 16
8 Receiver Gain 156.2
9 Relaxation Delay 1.0000
10 Pulse Width 11.7000
11 Acquisition Time 4.0894
12 Acquisition Date 2016-10-10T21:05:31
13 Spectrometer Frequency 400.13
14 Spectral Width 8012.8
15 Lowest Frequency -1555.6
16 Nucleus 1H
17 Spectral Size 65536
Et
OMe
N
F3CO
74
A (dt) 8.04
B (m) 7.37
C (m) 7.22
D (ddt) 7.13
E (dd) 6.68
F (s) 3.91
G (t) 3.75
I (m) 2.02
H (t) 0.90
0.95
1.37
1.86
2.06
0.95
1.94
3.01
1.00
3.02
f1 (ppm)


74
Et
OMe
N
F3CO
f1 (ppm)
12.7
28.5
49.3
53.5
111.0
119.3
121.2
121.9
127.9
128.5
129.1
132.6
138.3
143.4
145.8
163.0
Parameter Value
1 Data File Name / Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-226_OCF3_Bn/ 2/ fid
2 Title KEP-2-226_OCF3_Bn.2.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 294.9
6 Pulse Sequence zgpg30
7 Number of Scans 128
8 Receiver Gain 72.0
9 Relaxation Delay 2.0000
10 Pulse Width 10.0000
11 Acquisition Time 1.3631
12 Acquisition Date 2016-10-10T21:13:21
13 Spectrometer Frequency 100.62
14 Spectral Width 24038.5
15 Lowest Frequency -1931.2
16 Nucleus 13C
17 Spectral Size 65536

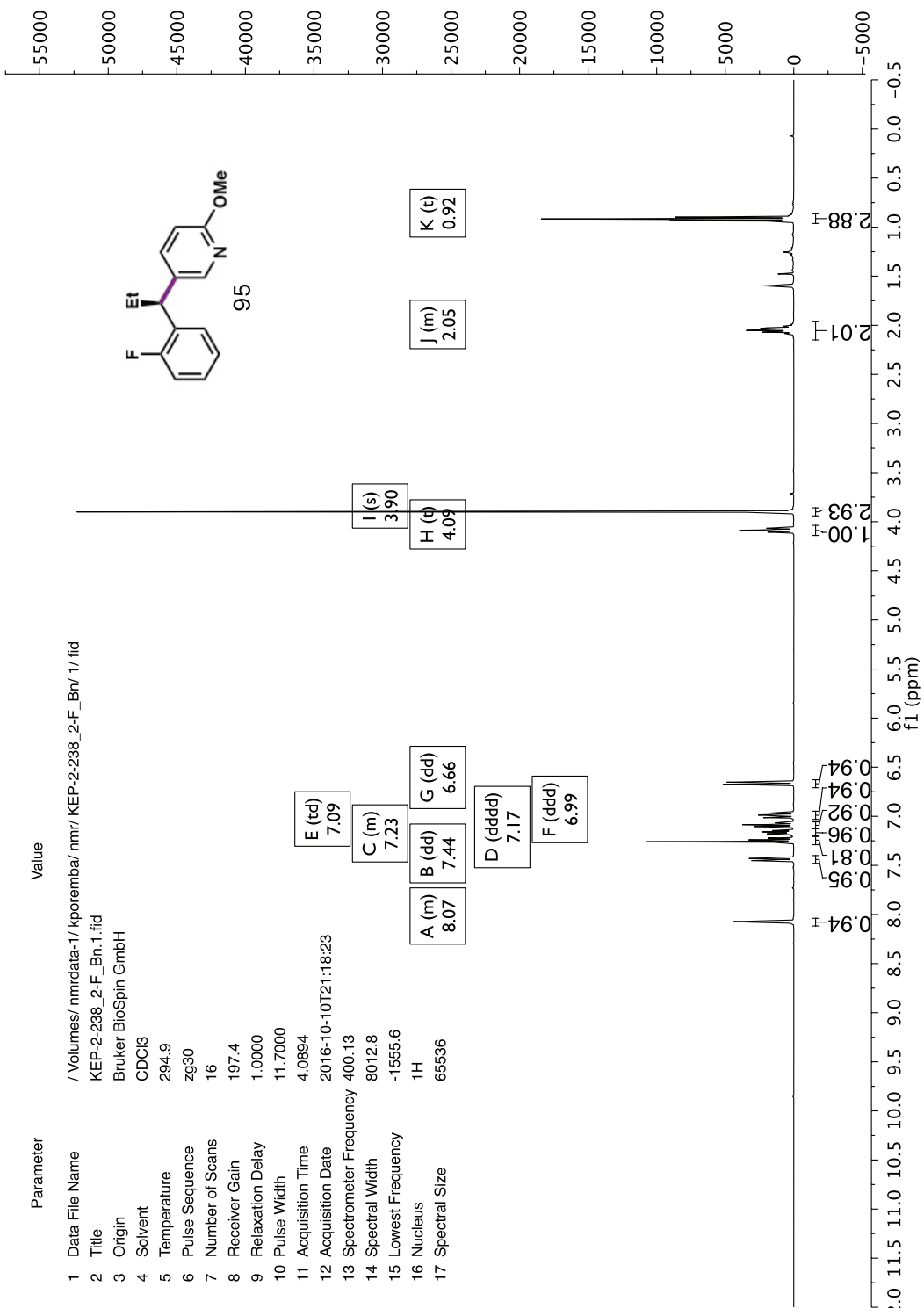


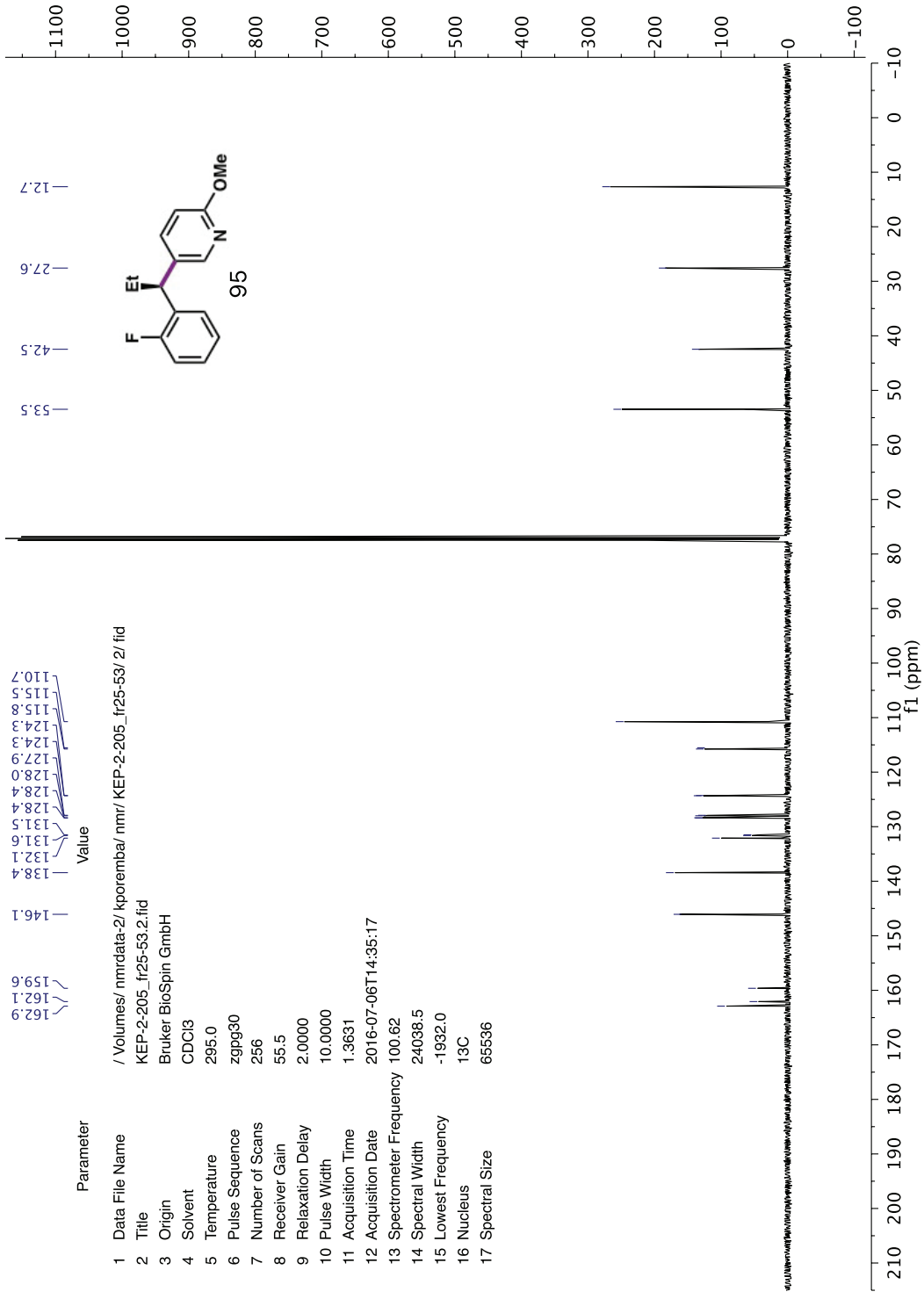
	Parameter	Value
1	Data File Name	/ Volumes/ nmrdata/ kporemba/ vnmrsys/ data/ KEP-2-226_OCF3_Bn/ FLUORINE01.fid/ fid
2	Title	FLUORINE01
3	Origin	Varian
4	Solvent	cdcl3
5	Temperature	25.0
6	Pulse Sequence	s2pul
7	Number of Scans	16
8	Receiver Gain	30
9	Relaxation Delay	1.0000
10	Pulse Width	6.3333
11	Acquisition Time	0.9856
12	Acquisition Date	2016-10-10T16:14:25
13	Spectrometer Frequency	282.34
14	Spectral Width	64935.1
15	Lowest Frequency	-56468.7
16	Nucleus	19F
17	Spectral Size	131072


Parameter
Value
1 Data File Name / Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-200_2-OMe_Bn/ 1/ fid
2 Title KEP-2-200_2-OMe_Bn.1.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 295.0
6 Pulse Sequence zg30
7 Number of Scans 16
8 Receiver Gain 176.8
9 Relaxation Delay 1.0000
10 Pulse Width 11.7000
11 Acquisition Time 4.0894
12 Acquisition Date 2016-10-10T21:39:10
13 Spectrometer Frequency 400.13
14 Spectral Width 8012.8
15 Lowest Frequency -1555.6
16 Nucleus 1H
17 Spectral Size 65536
OMe
Et
OMe
N
94
A (dt) 8.08
B (ddd) 7.42
C (dd) 7.23
D (ddd) 7.17
E (td) 6.92
F (dd) 6.82
G (m) 6.63
H (t) 4.18
I (s) 3.89
J (s) 3.77
K (m) 2.01
L (t) 0.89
1.00
1.03
0.98
0.98
0.95
1.02
0.96
3.11
3.35
1.02
1.92
3.04
f1 (ppm)

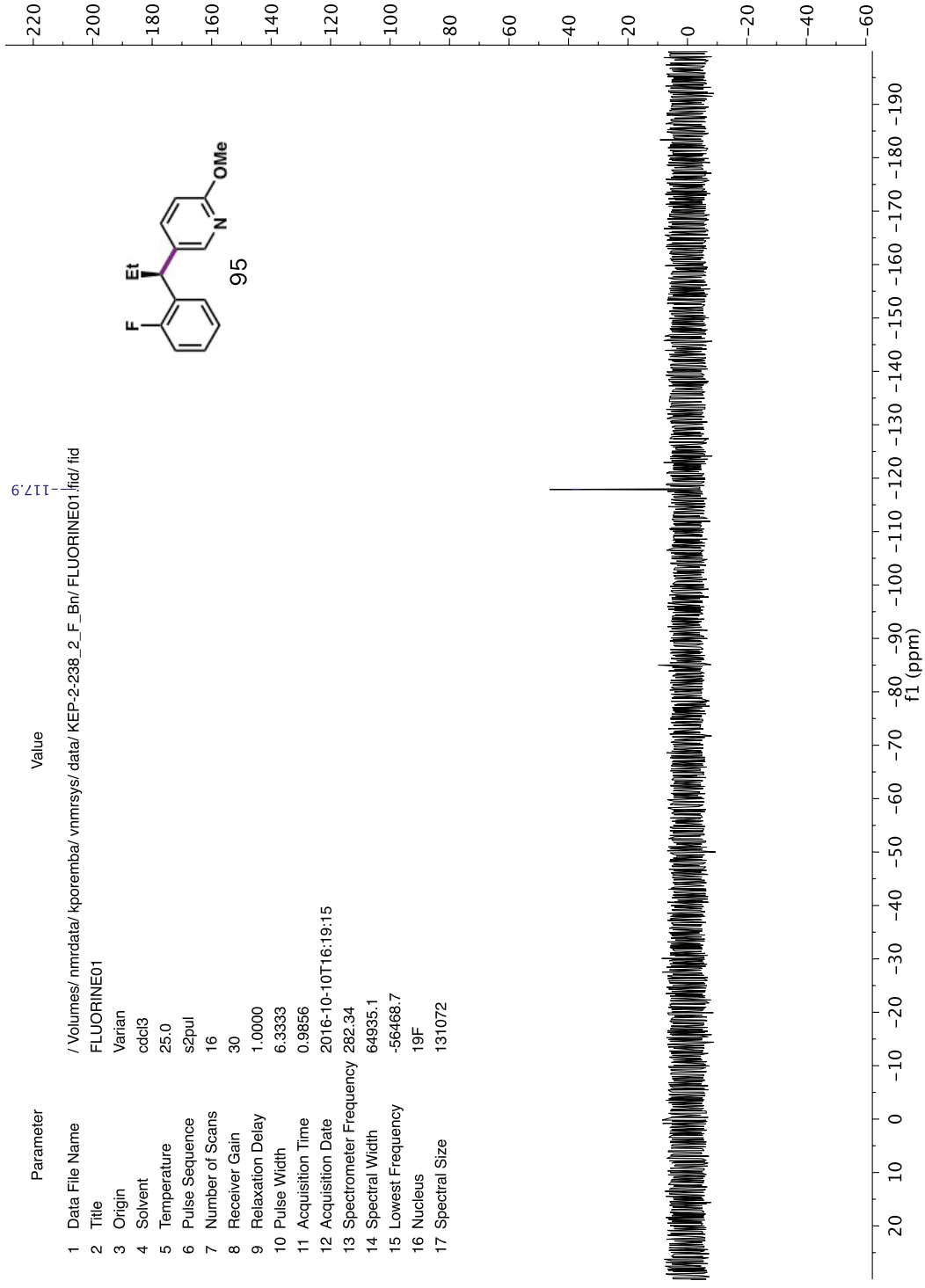


Parameter	Value
1 Data File Name	/ Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-200_2-OMe_Bn/ 2/ fid
2 Title	KEP-2-200_2-OMe_Bn.2.fid
3 Origin	Bruker BioSpin GmbH
4 Solvent	CDCl3
5 Temperature	294.9
6 Pulse Sequence	zgpg30
7 Number of Scans	256
8 Receiver Gain	64.2
9 Relaxation Delay	2.0000
10 Pulse Width	10.0000
11 Acquisition Time	1.3631
12 Acquisition Date	2016-10-10T21:54:17
13 Spectrometer Frequency	100.62
14 Spectral Width	24038.5
15 Lowest Frequency	-1932.2
16 Nucleus	13C
17 Spectral Size	65536

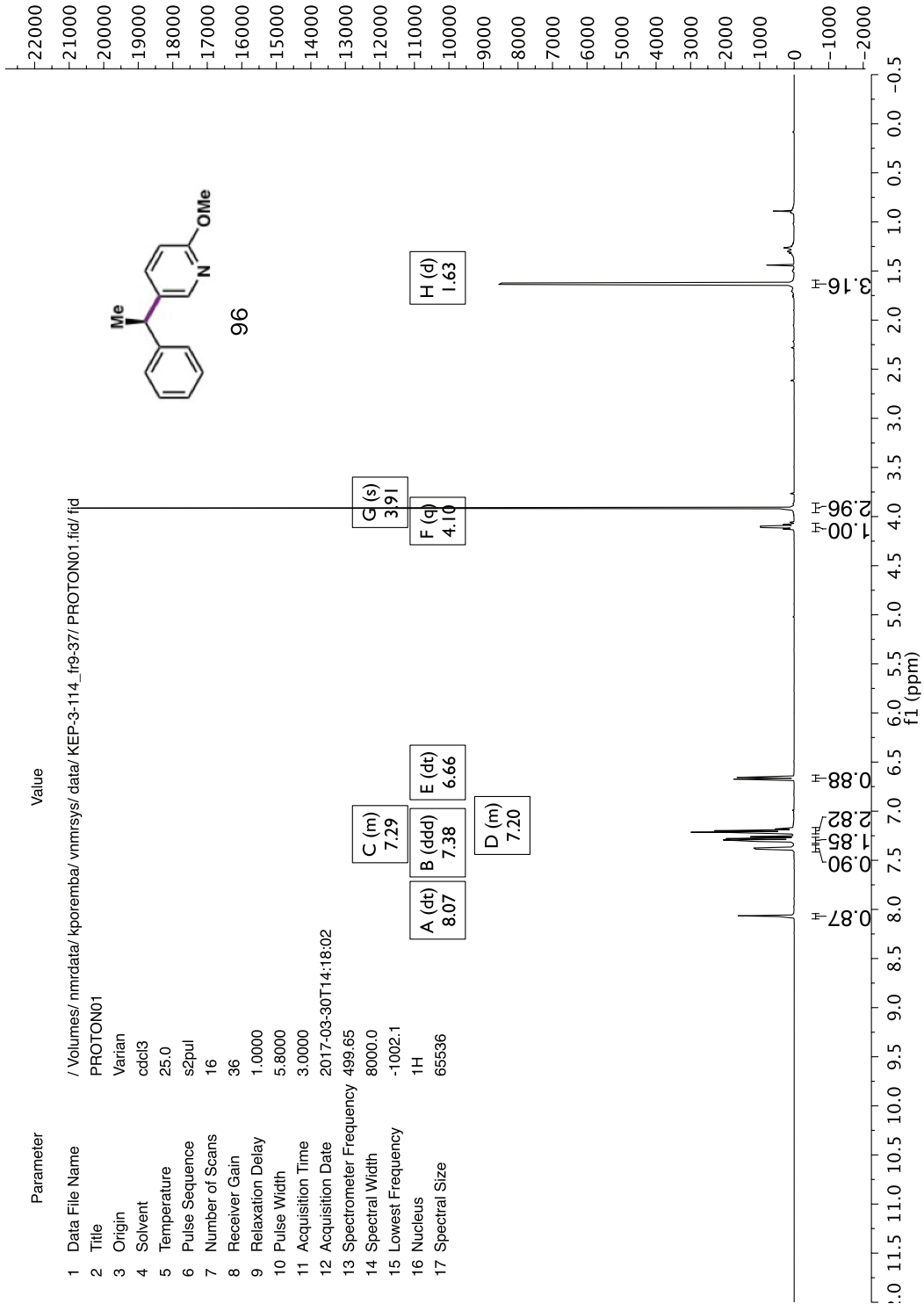

Parameter
Value
1 Data File Name / Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-238_2-F_Bn/ 1/ fid
2 Title KEP-2-238_2-F_Bn.1.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 294.9
6 Pulse Sequence zg30
7 Number of Scans 16
8 Receiver Gain 197.4
9 Relaxation Delay 1.0000
10 Pulse Width 11.7000
11 Acquisition Time 4.0894
12 Acquisition Date 2016-10-10T21:18:23
13 Spectrometer Frequency 400.13
14 Spectral Width 8012.8
15 Lowest Frequency -1555.6
16 Nucleus 1H
17 Spectral Size 65536
A (m) 8.07
B (dd) 7.44
C (m) 7.23
D (dddd) 7.17
E (td) 7.09
F (ddd) 6.99
G (dd) 6.66
H (t) 4.09
I (s) 3.90
J (m) 2.05
K (t) 0.92
F
Et
N
OMe
95
f1 (ppm)

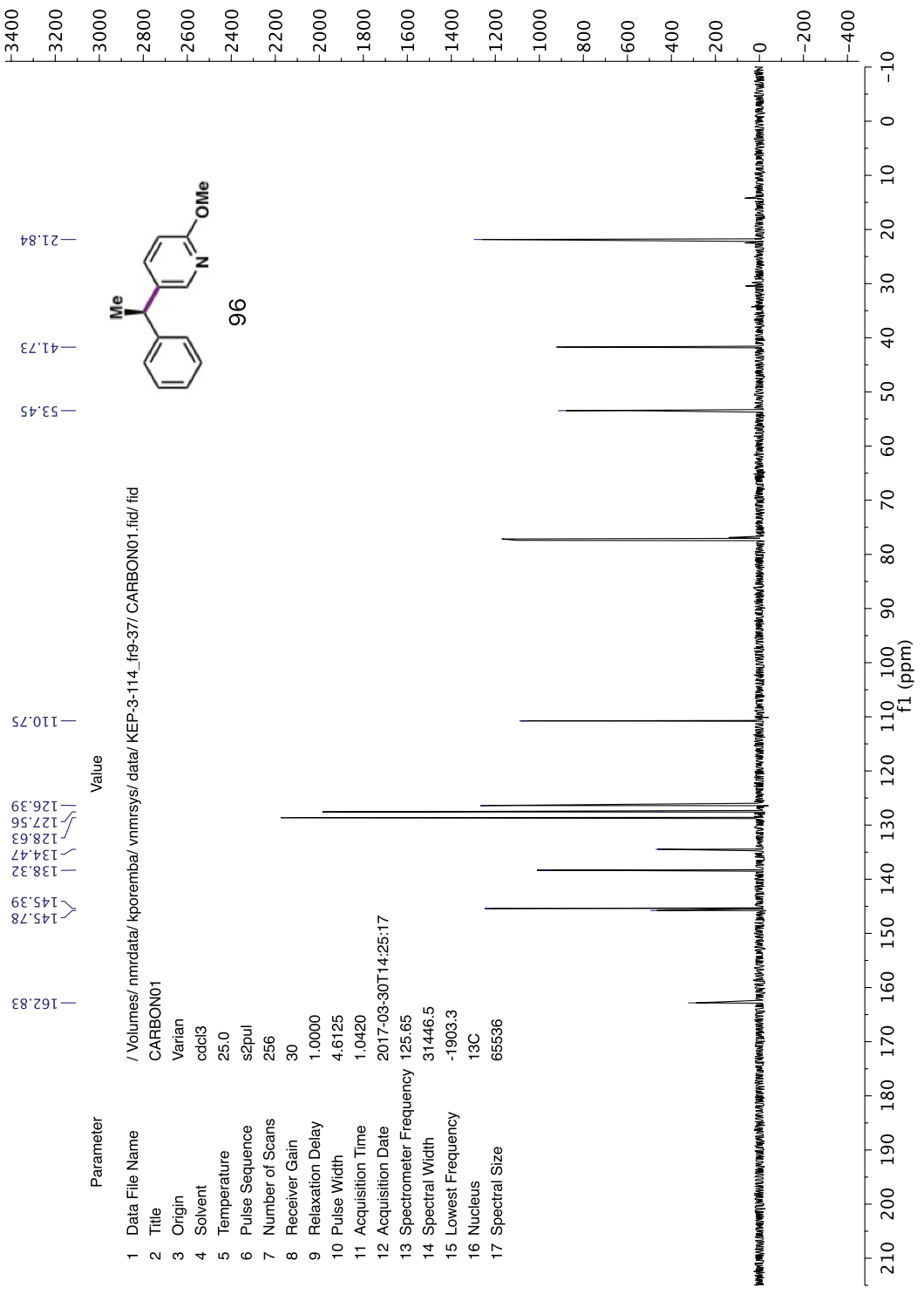


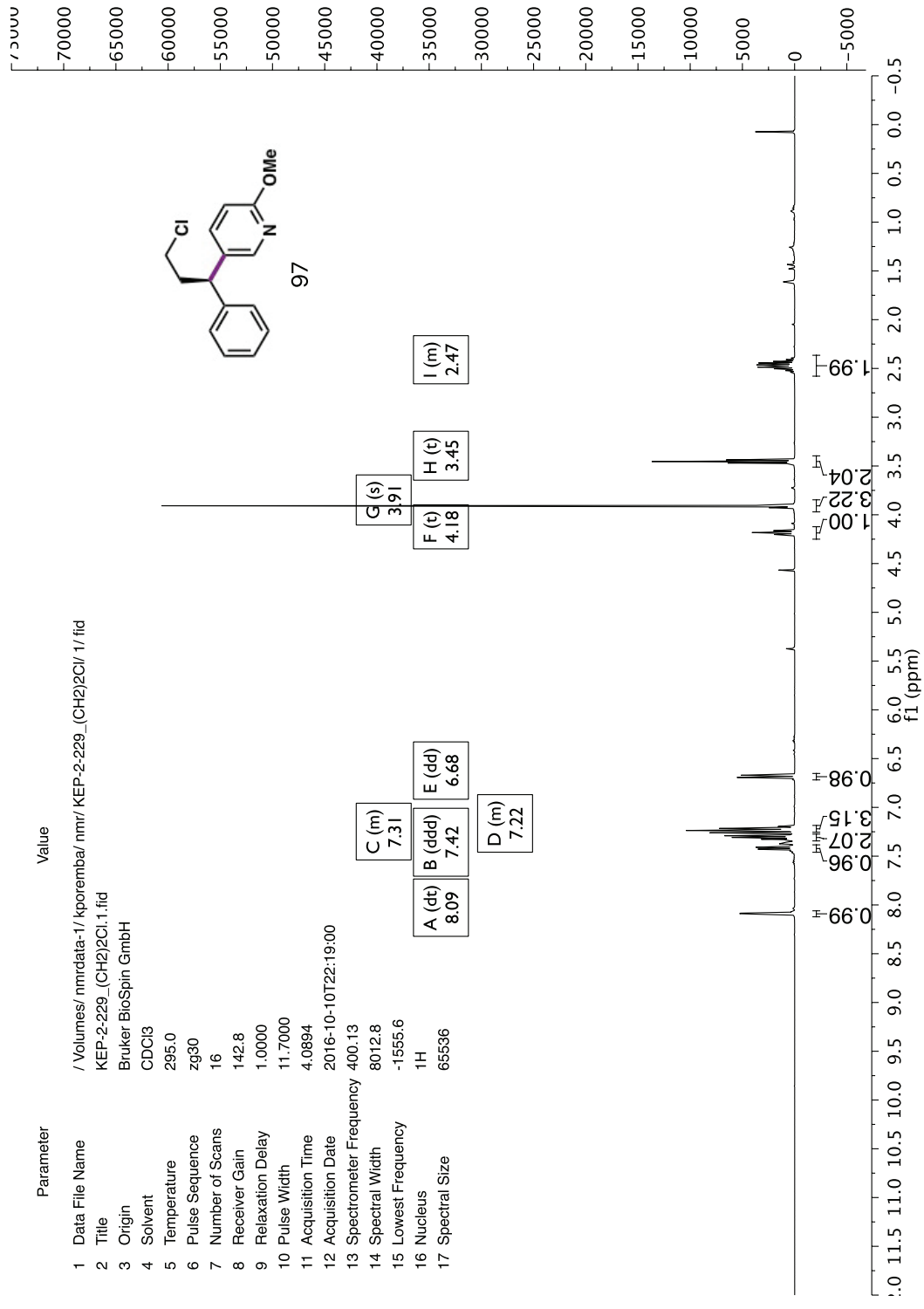
Parameter	Value
1 Data File Name	/ Volumes/ nmrdata-2/ kporemba/ nmr/ KEP-2-205_fr25-53/ 2/ fid
2 Title	KEP-2-205_fr25-53.2.fid
3 Origin	Bruker BioSpin GmbH
4 Solvent	CDCl3
5 Temperature	295.0
6 Pulse Sequence	zgpg30
7 Number of Scans	256
8 Receiver Gain	55.5
9 Relaxation Delay	2.0000
10 Pulse Width	10.0000
11 Acquisition Time	1.3631
12 Acquisition Date	2016-07-06T14:35:17
13 Spectrometer Frequency	100.62
14 Spectral Width	24038.5
15 Lowest Frequency	-1932.0
16 Nucleus	13C
17 Spectral Size	65536

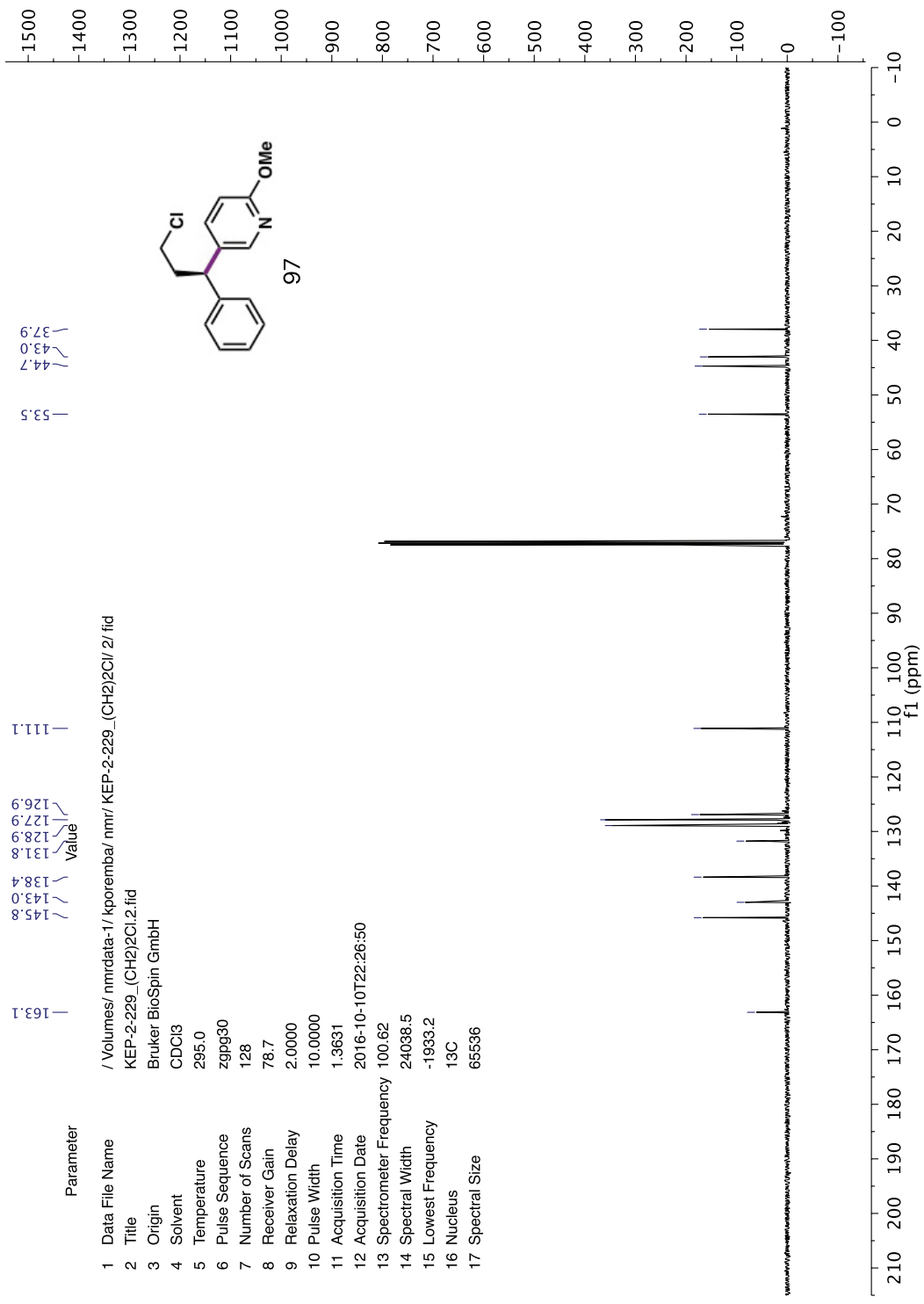


Parameter		Value
1	Data File Name	/ Volumes/ nmrdata/ kporemba/ vnmrsys/ data/ KEP-2-238_2_F_Bn/ FLUORINE01.fid/ fid
2	Title	FLUORINE01
3	Origin	Varian
4	Solvent	cdcl3
5	Temperature	25.0
6	Pulse Sequence	s2pul
7	Number of Scans	16
8	Receiver Gain	30
9	Relaxation Delay	1.0000
10	Pulse Width	6.3333
11	Acquisition Time	0.9856
12	Acquisition Date	2016-10-10T16:19:15
13	Spectrometer Frequency	282.34
14	Spectral Width	64935.1
15	Lowest Frequency	-56468.7
16	Nucleus	19F
17	Spectral Size	131072

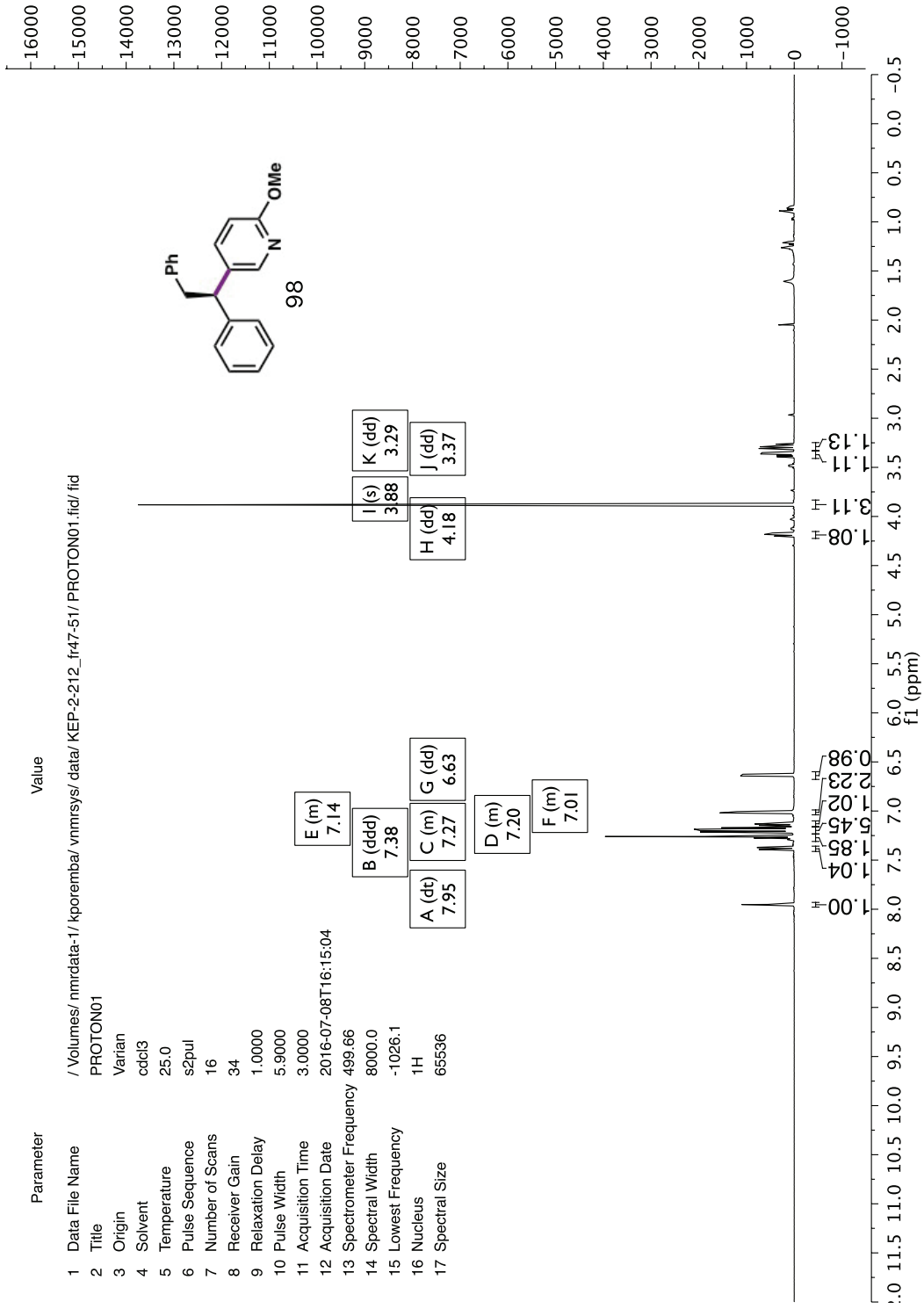

Parameter
Value
1 Data File Name / Volumes/ nmrdata/ kporemba/ vnmrsys/ data/ KEP-3-114_fr9-37/ PROTON01.fid/ fid
2 Title PROTON01
3 Origin Varian
4 Solvent cdcl3
5 Temperature 25.0
6 Pulse Sequence s2pul
7 Number of Scans 16
8 Receiver Gain 36
9 Relaxation Delay 1.0000
10 Pulse Width 5.8000
11 Acquisition Time 3.0000
12 Acquisition Date 2017-03-30T14:18:02
13 Spectrometer Frequency 499.65
14 Spectral Width 8000.0
15 Lowest Frequency -1002.1
16 Nucleus 1H
17 Spectral Size 65536
A (dt) 8.07
B (ddd) 7.38
C (m) 7.29
D (m) 7.20
E (dt) 6.66
F (q) 4.10
G (s) 3.91
H (d) 1.63
Me
OMe
N
96
0.87
0.90
1.85
2.82
0.88
2.96
1.00
3.16
f1 (ppm)

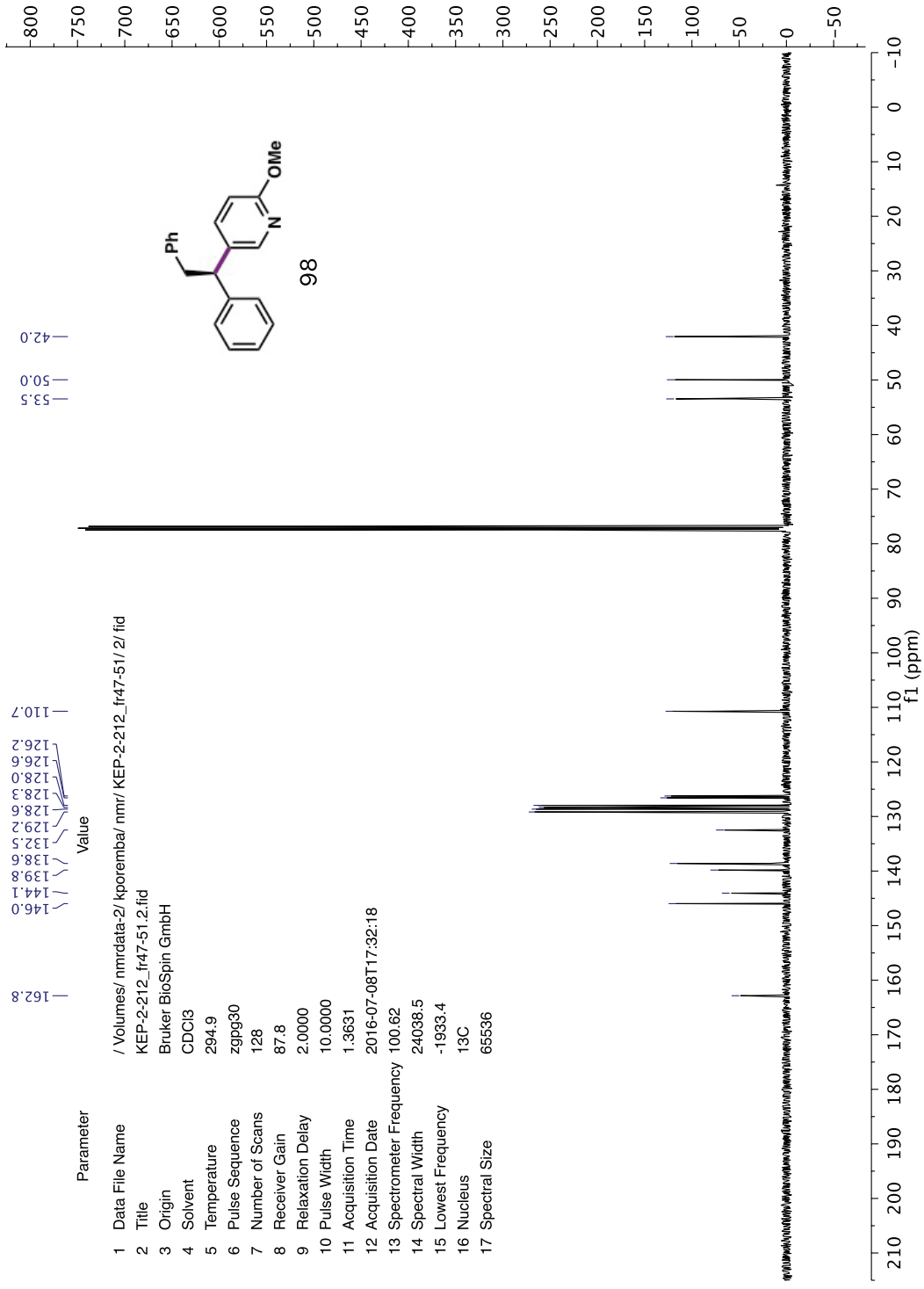

21.84
41.73
53.45
110.75
126.39
127.56
128.63
134.47
138.32
145.39
145.78
162.83
Me
OMe
N
96
Parameter Value
1 Data File Name / Volumes/ nmrdata/ kporemba/ vnmrsys/ data/ KEP-3-114_fr9-37/ CARBON01.fid/ fid
2 Title CARBON01
3 Origin Varian
4 Solvent cdcl3
5 Temperature 25.0
6 Pulse Sequence s2pul
7 Number of Scans 256
8 Receiver Gain 30
9 Relaxation Delay 1.0000
10 Pulse Width 4.6125
11 Acquisition Time 1.0420
12 Acquisition Date 2017-03-30T14:25:17
13 Spectrometer Frequency 125.65
14 Spectral Width 31446.5
15 Lowest Frequency -1903.3
16 Nucleus 13C
17 Spectral Size 65536
f1 (ppm)


Parameter
Value
1 Data File Name / Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-229_(CH2)2Cl/ 1/ fid
2 Title KEP-2-229_(CH2)2Cl.1.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 295.0
6 Pulse Sequence zg30
7 Number of Scans 16
8 Receiver Gain 142.8
9 Relaxation Delay 1.0000
10 Pulse Width 11.7000
11 Acquisition Time 4.0894
12 Acquisition Date 2016-10-10T22:19:00
13 Spectrometer Frequency 400.13
14 Spectral Width 8012.8
15 Lowest Frequency -1555.6
16 Nucleus 1H
17 Spectral Size 65536
A (dt) 8.09
B (ddd) 7.42
C (m) 7.31
D (m) 7.22
E (dd) 6.68
F (t) 4.18
G (s) 3.91
H (t) 3.45
I (m) 2.47
0.99
0.96
2.07
3.15
0.98
1.00
2.22
2.04
1.99
Cl
OMe
N
97
f1 (ppm)

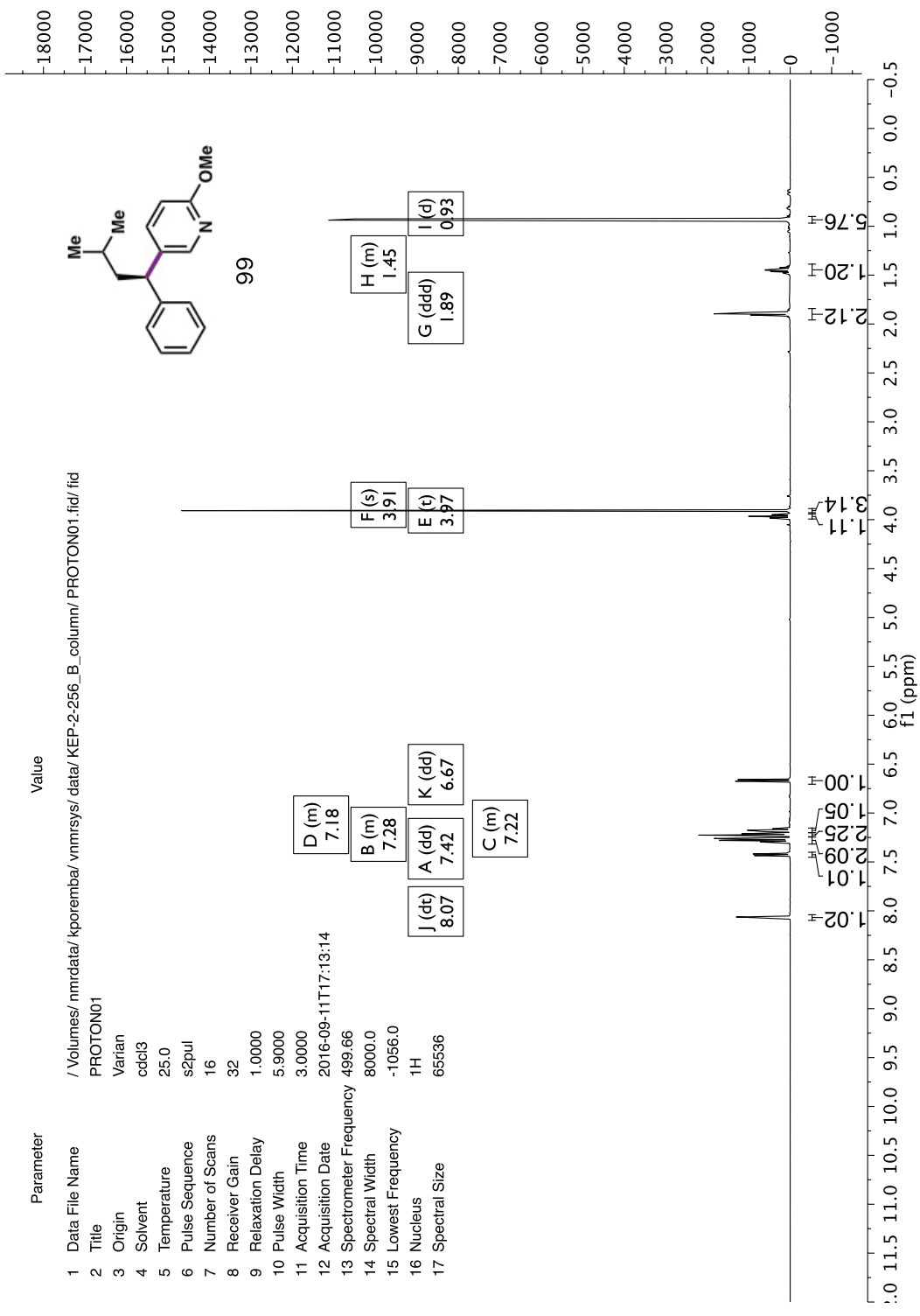


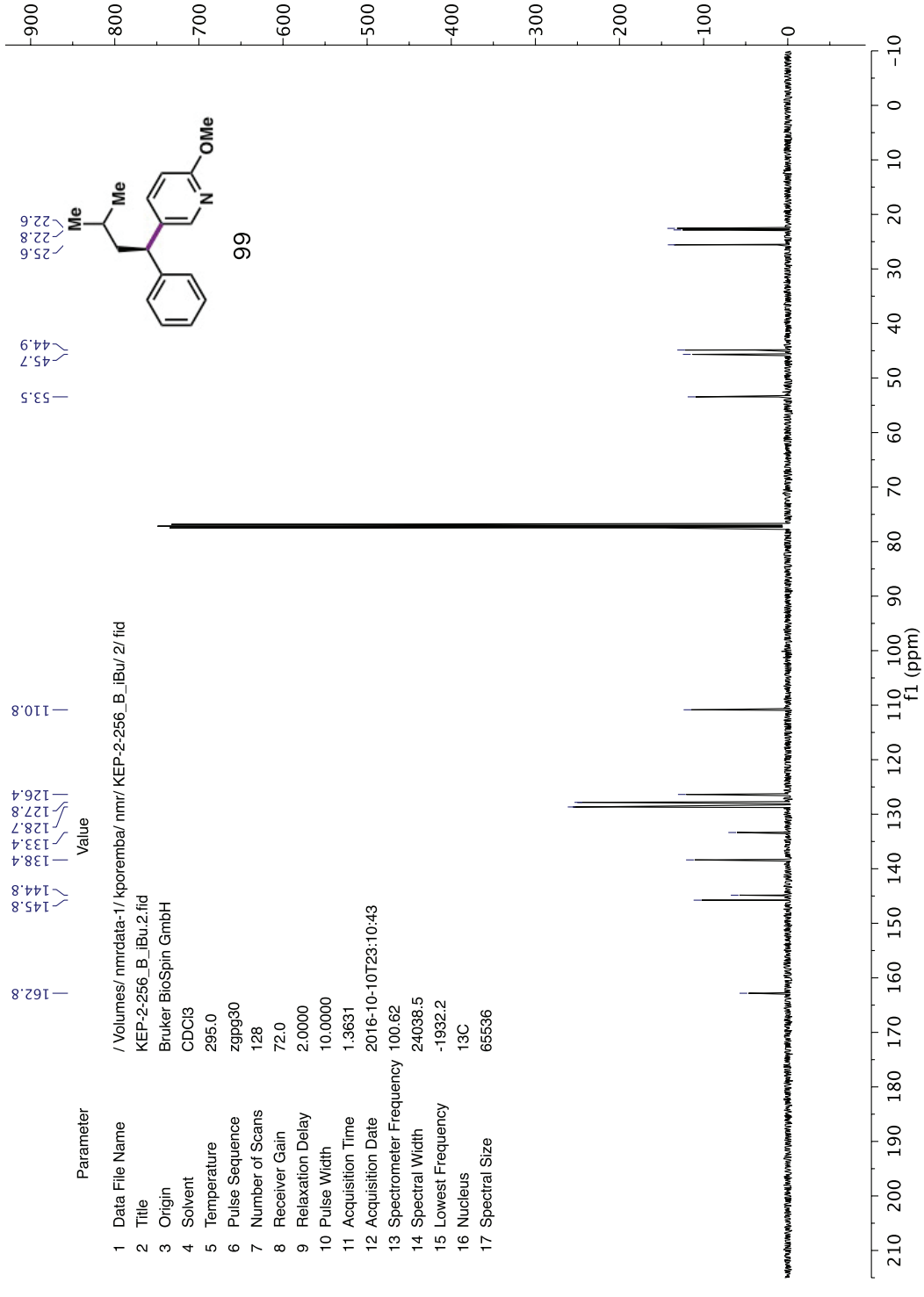
Parameter	Value
1 Data File Name	/ Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-229_(CH2)2Cl/ 2/ fid
2 Title	KEP-2-229_(CH2)2Cl.2.fid
3 Origin	Bruker BioSpin GmbH
4 Solvent	CDCl3
5 Temperature	295.0
6 Pulse Sequence	zgpg30
7 Number of Scans	128
8 Receiver Gain	78.7
9 Relaxation Delay	2.0000
10 Pulse Width	10.0000
11 Acquisition Time	1.3631
12 Acquisition Date	2016-10-10T22:26:50
13 Spectrometer Frequency	100.62
14 Spectral Width	24038.5
15 Lowest Frequency	-1933.2
16 Nucleus	13C
17 Spectral Size	65536

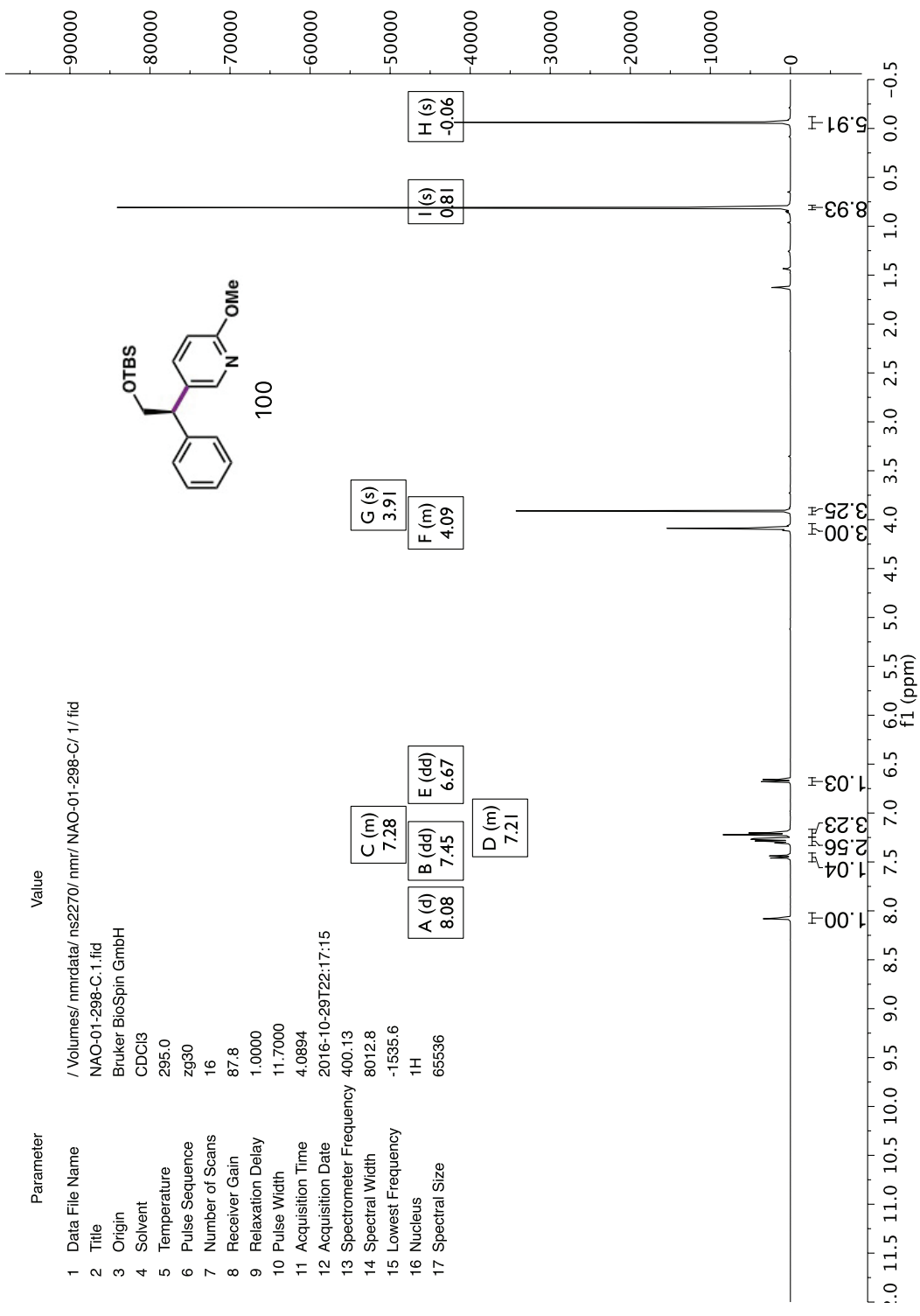

Parameter
Value
1 Data File Name / Volumes/ nmrdata-1/ kporemba/ vnmrsys/ data/ KEP-2-212_fr47-51/ PROTON01.fid/ fid
2 Title PROTON01
3 Origin Varian
4 Solvent cdcl3
5 Temperature 25.0
6 Pulse Sequence s2pul
7 Number of Scans 16
8 Receiver Gain 34
9 Relaxation Delay 1.0000
10 Pulse Width 5.9000
11 Acquisition Time 3.0000
12 Acquisition Date 2016-07-08T16:15:04
13 Spectrometer Frequency 499.66
14 Spectral Width 8000.0
15 Lowest Frequency -1026.1
16 Nucleus 1H
17 Spectral Size 65536
A (dt) 7.95
B (ddd) 7.38
C (m) 7.27
D (m) 7.20
E (m) 7.14
F (m) 7.01
G (dd) 6.63
H (dd) 4.18
I (s) 3.88
J (dd) 3.37
K (dd) 3.29
Ph
OMe
N
98
1.00
1.04
1.85
5.45
2.02
2.23
0.98
1.08
3.11
1.11
1.13
f1 (ppm)

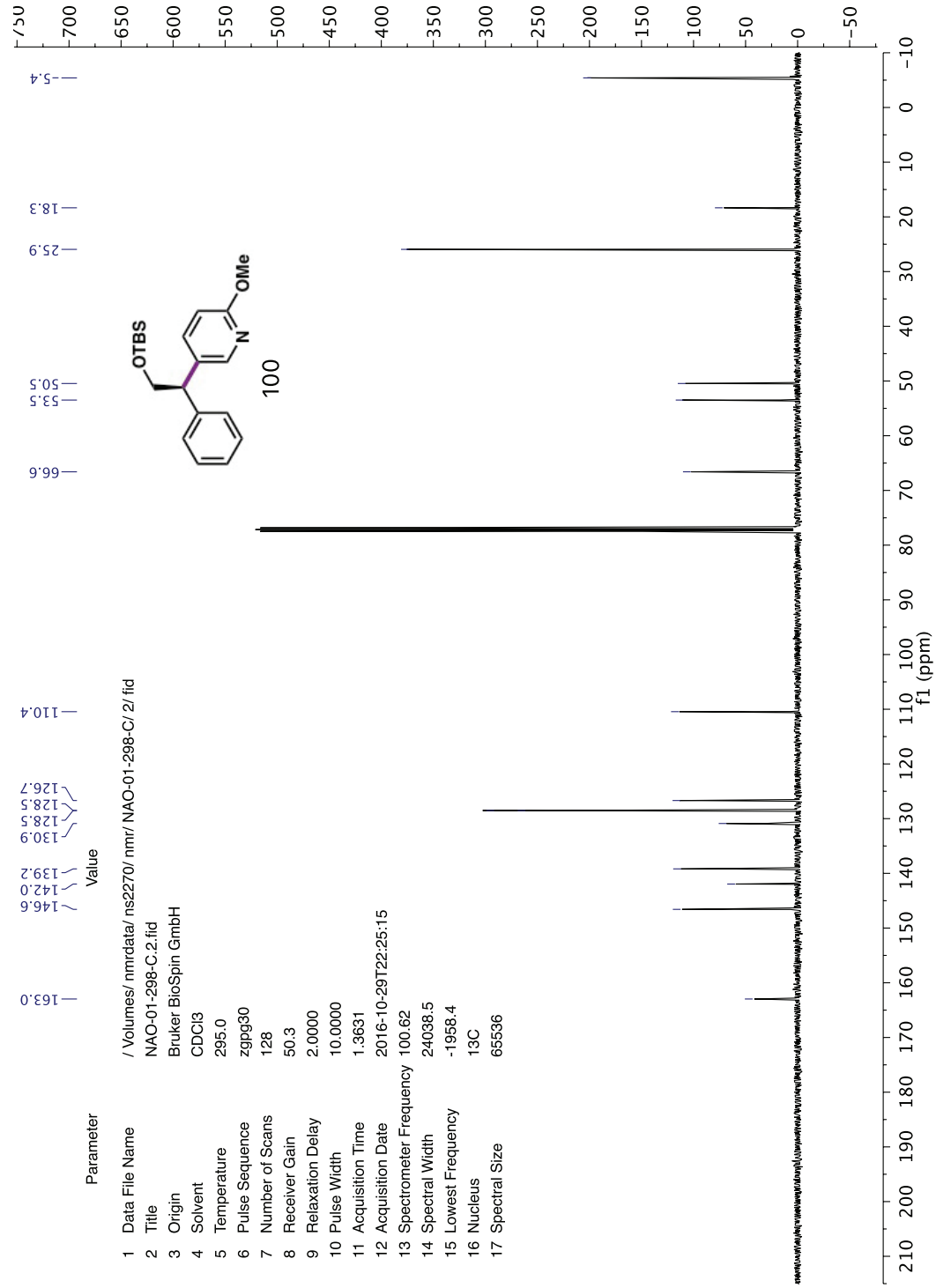


Parameter	Value
1 Data File Name	/ Volumes/ nmrdata-2/ kporemba/ nmr/ KEP-2-212_fr47-51/ 2/ fid
2 Title	KEP-2-212_fr47-51.2.fid
3 Origin	Bruker BioSpin GmbH
4 Solvent	CDCl3
5 Temperature	294.9
6 Pulse Sequence	zgpg30
7 Number of Scans	128
8 Receiver Gain	87.8
9 Relaxation Delay	2.0000
10 Pulse Width	10.0000
11 Acquisition Time	1.3631
12 Acquisition Date	2016-07-08T17:32:18
13 Spectrometer Frequency	100.62
14 Spectral Width	24038.5
15 Lowest Frequency	-1933.4
16 Nucleus	13C
17 Spectral Size	65536

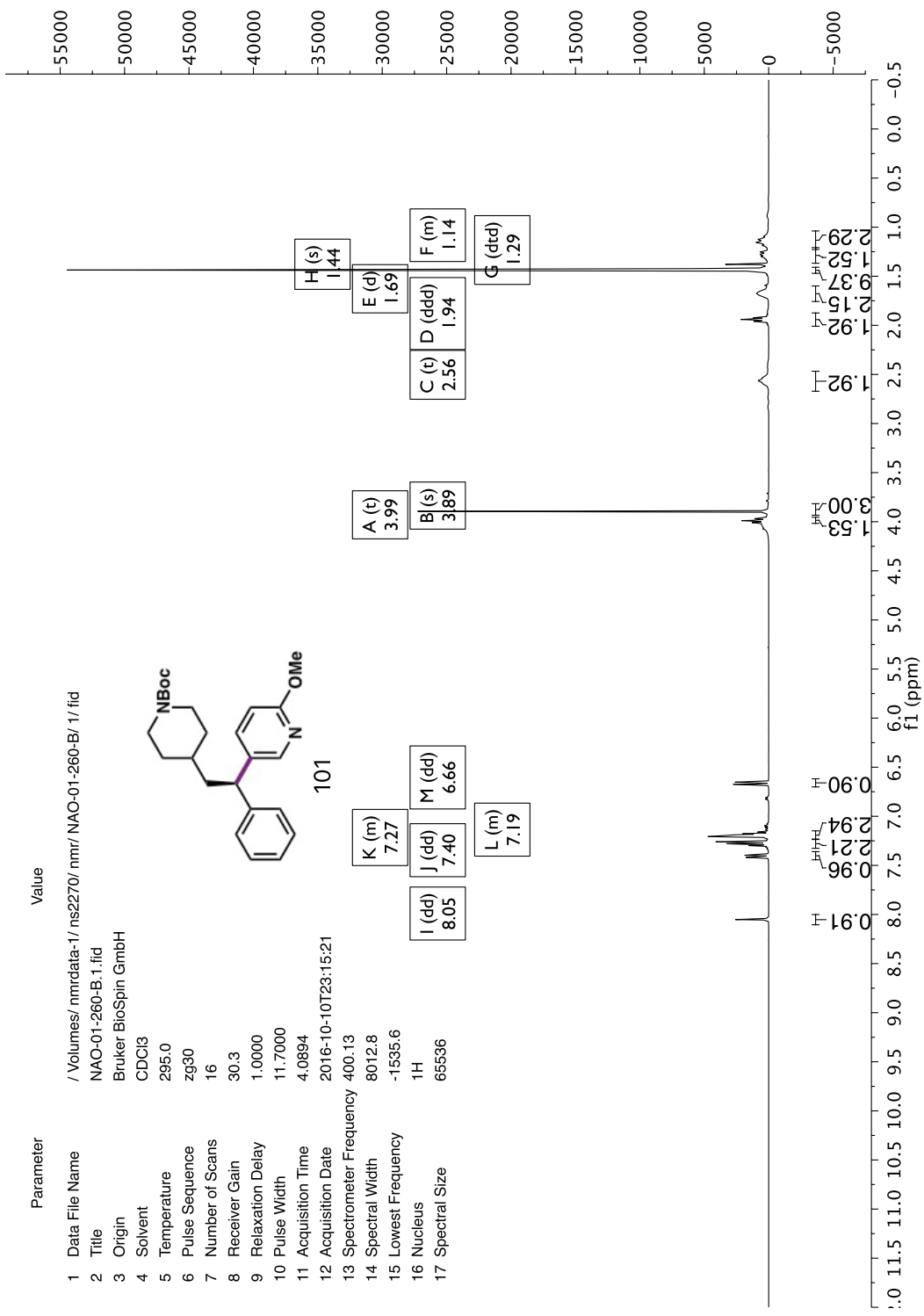

Parameter
Value
1 Data File Name / Volumes/ nmrdata/ kporemba/ vnmrsys/ data/ KEP-2-256_B_column/ PROTON01.fid/ fid
2 Title PROTON01
3 Origin Varian
4 Solvent cdcl3
5 Temperature 25.0
6 Pulse Sequence s2pul
7 Number of Scans 16
8 Receiver Gain 32
9 Relaxation Delay 1.0000
10 Pulse Width 5.9000
11 Acquisition Time 3.0000
12 Acquisition Date 2016-09-11T17:13:14
13 Spectrometer Frequency 499.66
14 Spectral Width 8000.0
15 Lowest Frequency -1056.0
16 Nucleus 1H
17 Spectral Size 65536
Me
Me
OMe
N
99
J (dt) 8.07
A (dd) 7.42
K (dd) 6.67
B (m) 7.28
D (m) 7.18
C (m) 7.22
F (s) 3.91
E (t) 3.97
H (m) 1.45
G (ddd) 1.89
I (d) 0.93
1.02
1.01
2.09
2.25
1.05
1.00
3.14
1.11
2.12
1.20
5.76
f1 (ppm)

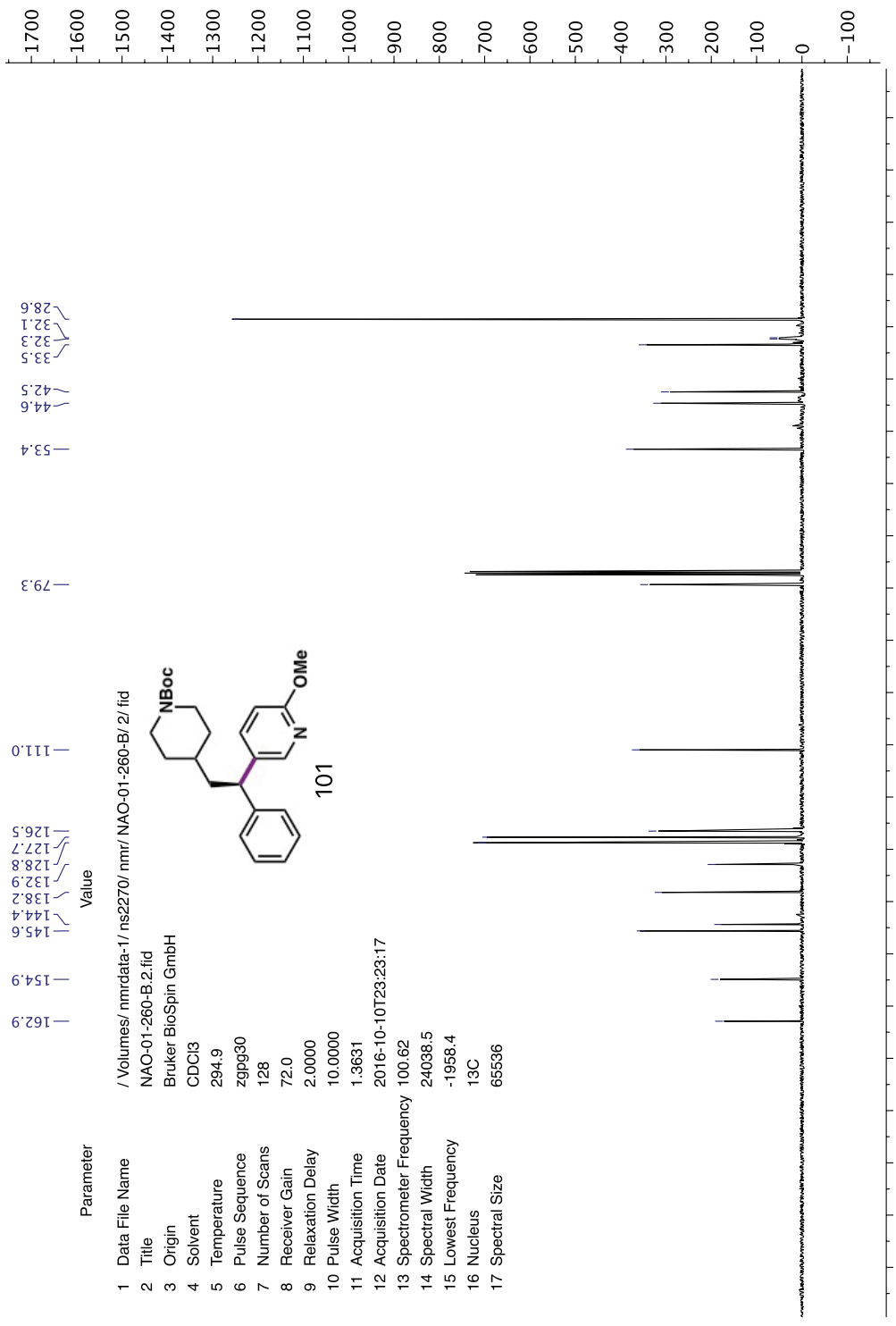

99
OMe
N
Me
Me
22.6
22.8
25.6
44.9
45.7
53.5
110.8
126.4
127.8
128.7
133.4
138.4
144.8
145.8
162.8
Parameter Value
1 Data File Name / Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-256_B_iBu/ 2/ fid
2 Title KEP-2-256_B_iBu.2.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 295.0
6 Pulse Sequence zgpg30
7 Number of Scans 128
8 Receiver Gain 72.0
9 Relaxation Delay 2.0000
10 Pulse Width 10.0000
11 Acquisition Time 1.3631
12 Acquisition Date 2016-10-10T23:10:43
13 Spectrometer Frequency 100.62
14 Spectral Width 24038.5
15 Lowest Frequency -1932.2
16 Nucleus 13C
17 Spectral Size 65536
f1 (ppm)


Parameter
Value
1 Data File Name / Volumes/ nmrdata/ ns2270/ nmr/ NAO-01-298-C/ 1/ fid
2 Title NAO-01-298-C.1.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 295.0
6 Pulse Sequence zg30
7 Number of Scans 16
8 Receiver Gain 87.8
9 Relaxation Delay 1.0000
10 Pulse Width 11.7000
11 Acquisition Time 4.0894
12 Acquisition Date 2016-10-29T22:17:15
13 Spectrometer Frequency 400.13
14 Spectral Width 8012.8
15 Lowest Frequency -1535.6
16 Nucleus 1H
17 Spectral Size 65536
OTBS
OMe
N
100
A (d) 8.08
B (dd) 7.45
C (m) 7.28
D (m) 7.21
E (dd) 6.67
F (m) 4.09
G (s) 3.91
H (s) -0.06
I (s) 0.81
1.00
1.04
2.56
3.23
1.03
3.00
3.25
8.93
5.91
f1 (ppm)

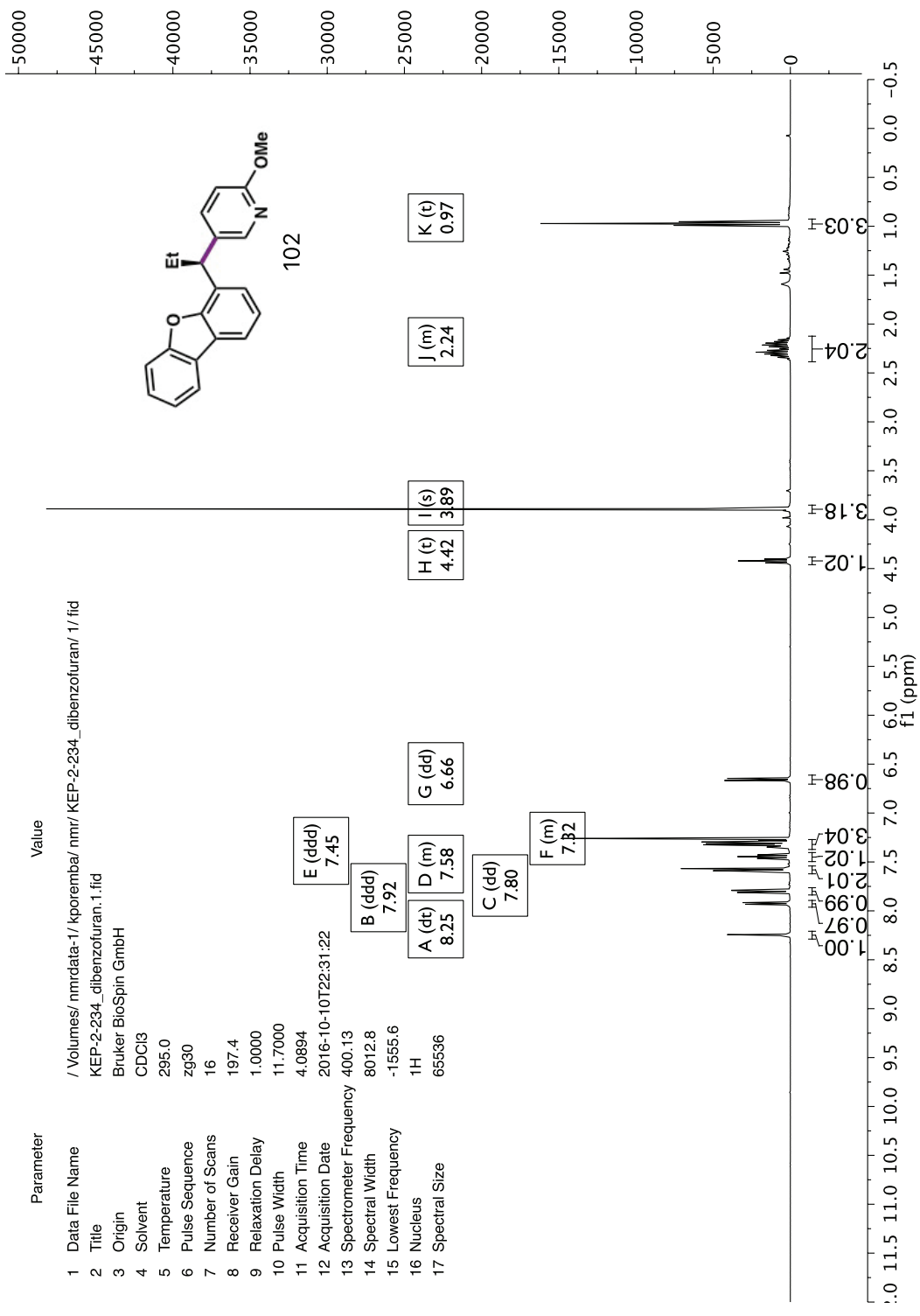


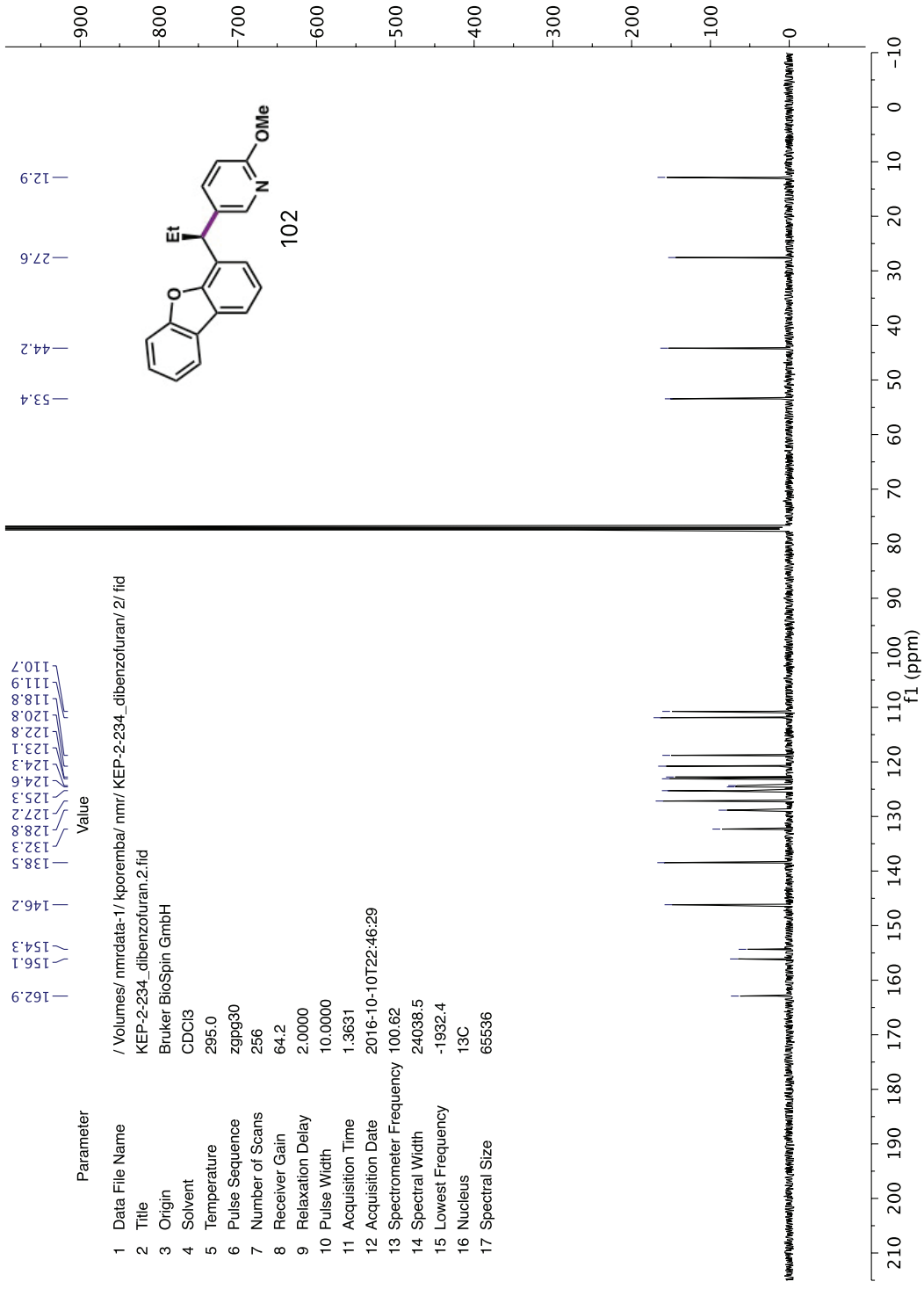
Parameter	Value
1 Data File Name	/ Volumes/ nmrdata/ ns2270/ nmr/ NAO-01-298-C/ 2/ fid
2 Title	NAO-01-298-C.2.fid
3 Origin	Bruker BioSpin GmbH
4 Solvent	CDCl3
5 Temperature	295.0
6 Pulse Sequence	zgpg30
7 Number of Scans	128
8 Receiver Gain	50.3
9 Relaxation Delay	2.0000
10 Pulse Width	10.0000
11 Acquisition Time	1.3631
12 Acquisition Date	2016-10-29T22:25:15
13 Spectrometer Frequency	100.62
14 Spectral Width	24038.5
15 Lowest Frequency	-1958.4
16 Nucleus	13C
17 Spectral Size	65536


Parameter
Value
1 Data File Name / Volumes/ nmrdata-1/ ns2270/ nmr/ NAO-01-260-B/ 1/ fid
2 Title NAO-01-260-B.1.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 295.0
6 Pulse Sequence zg30
7 Number of Scans 16
8 Receiver Gain 30.3
9 Relaxation Delay 1.0000
10 Pulse Width 11.7000
11 Acquisition Time 4.0894
12 Acquisition Date 2016-10-10T23:15:21
13 Spectrometer Frequency 400.13
14 Spectral Width 8012.8
15 Lowest Frequency -1535.6
16 Nucleus 1H
17 Spectral Size 65536
NBoc
OMe
N
101
A (t) 3.99
B (s) 3.89
C (t) 2.56
D (ddd) 1.94
E (d) 1.69
F (m) 1.14
G (dtd) 1.29
H (s) 1.44
I (dd) 8.05
J (dd) 7.40
K (m) 7.27
L (m) 7.19
M (dd) 6.66
0.91
0.96
2.21
2.94
0.90
3.00
1.53
1.92
2.15
9.37
2.52
2.29
f1 (ppm)

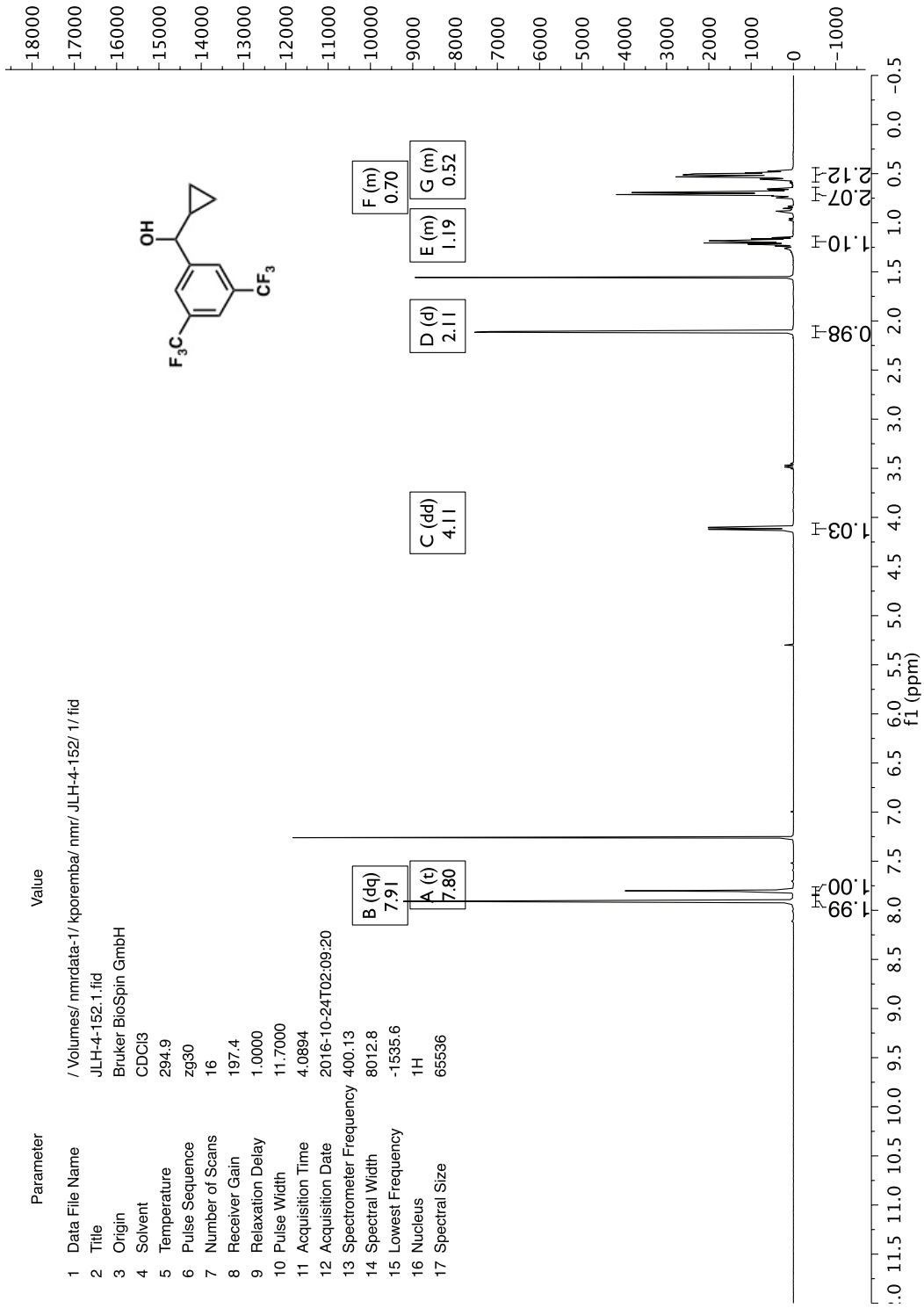


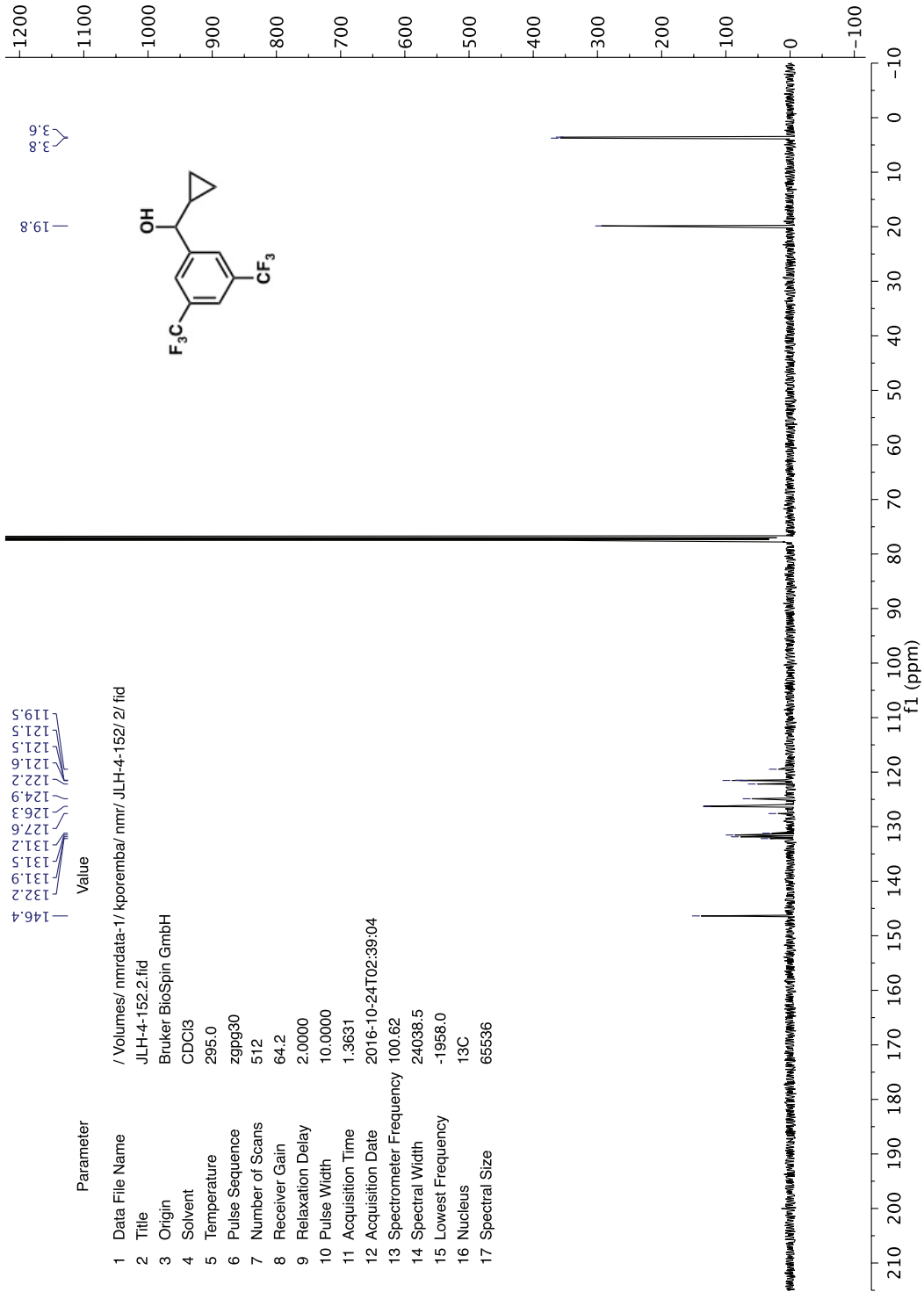
Parameter	Value
1 Data File Name	/ Volumes/ nmrdata-1/ ns2270/ nmr/ NAO-01-260-B/ 2/ fid
2 Title	NAO-01-260-B.2.fid
3 Origin	Bruker BioSpin GmbH
4 Solvent	CDCl3
5 Temperature	294.9
6 Pulse Sequence	zgpg30
7 Number of Scans	128
8 Receiver Gain	72.0
9 Relaxation Delay	2.0000
10 Pulse Width	10.0000
11 Acquisition Time	1.3631
12 Acquisition Date	2016-10-10T23:23:17
13 Spectrometer Frequency	100.62
14 Spectral Width	24038.5
15 Lowest Frequency	-1958.4
16 Nucleus	13C
17 Spectral Size	65536


Parameter
Value
1 Data File Name / Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-234_dibenzofuran/ 1/ fid
2 Title KEP-2-234_dibenzofuran.1.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 295.0
6 Pulse Sequence zg30
7 Number of Scans 16
8 Receiver Gain 197.4
9 Relaxation Delay 1.0000
10 Pulse Width 11.7000
11 Acquisition Time 4.0894
12 Acquisition Date 2016-10-10T22:31:22
13 Spectrometer Frequency 400.13
14 Spectral Width 8012.8
15 Lowest Frequency -1555.6
16 Nucleus 1H
17 Spectral Size 65536
102
A (dt) 8.25
B (ddd) 7.92
C (dd) 7.80
D (m) 7.58
E (ddd) 7.45
F (m) 7.32
G (dd) 6.66
H (t) 4.42
I (s) 3.89
J (m) 2.24
K (t) 0.97
f1 (ppm)

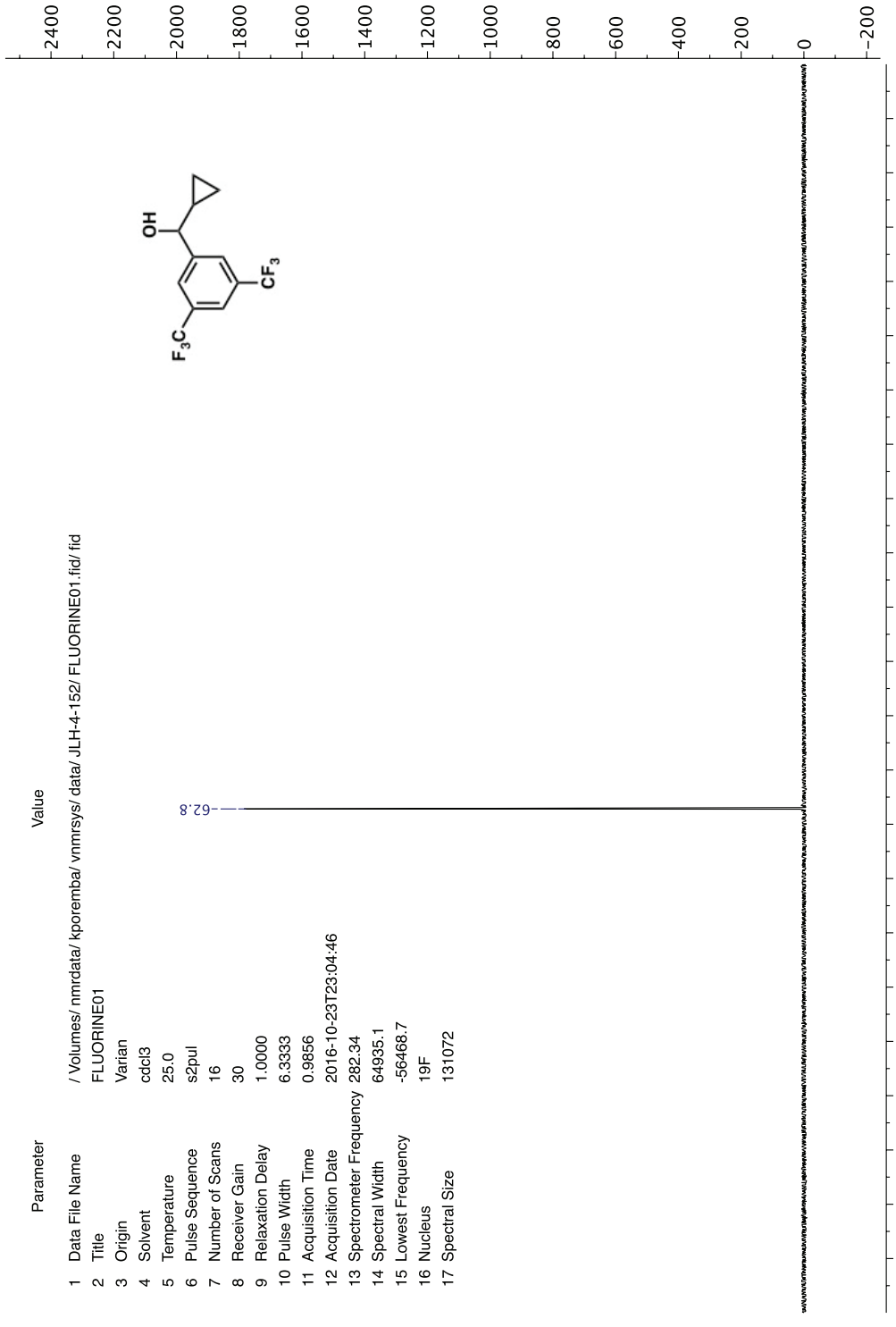


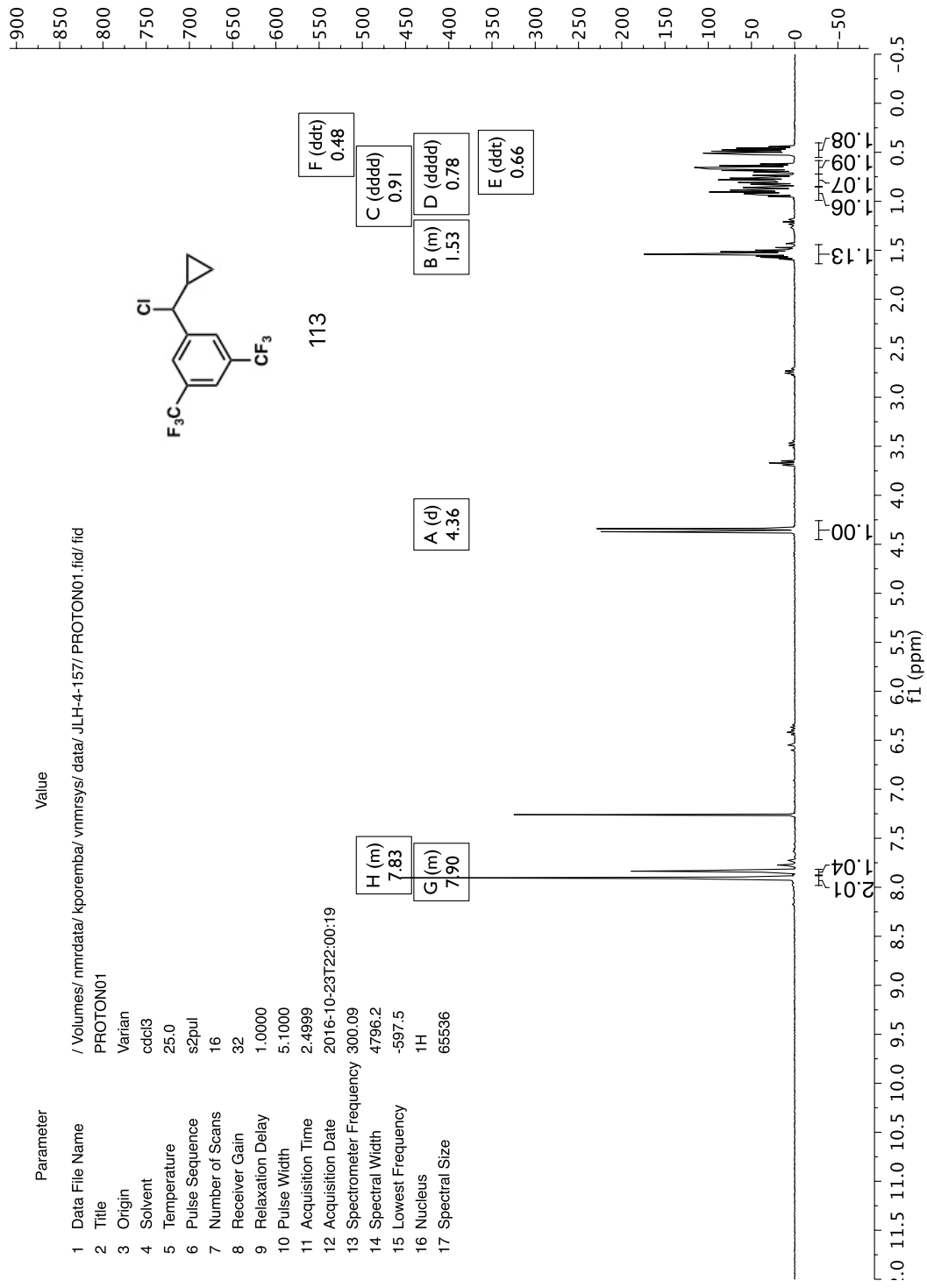
	Parameter	Value
1	Data File Name	/ Volumes/ nmrdata-1/ kporemba/ nmr/ KEP-2-234_dibenzofuran/ 2/ fid
2	Title	KEP-2-234_dibenzofuran.2.fid
3	Origin	Bruker BioSpin GmbH
4	Solvent	CDCl3
5	Temperature	295.0
6	Pulse Sequence	zgpg30
7	Number of Scans	256
8	Receiver Gain	64.2
9	Relaxation Delay	2.0000
10	Pulse Width	10.0000
11	Acquisition Time	1.3631
12	Acquisition Date	2016-10-10T22:46:29
13	Spectrometer Frequency	100.62
14	Spectral Width	24038.5
15	Lowest Frequency	-1932.4
16	Nucleus	13C
17	Spectral Size	65536

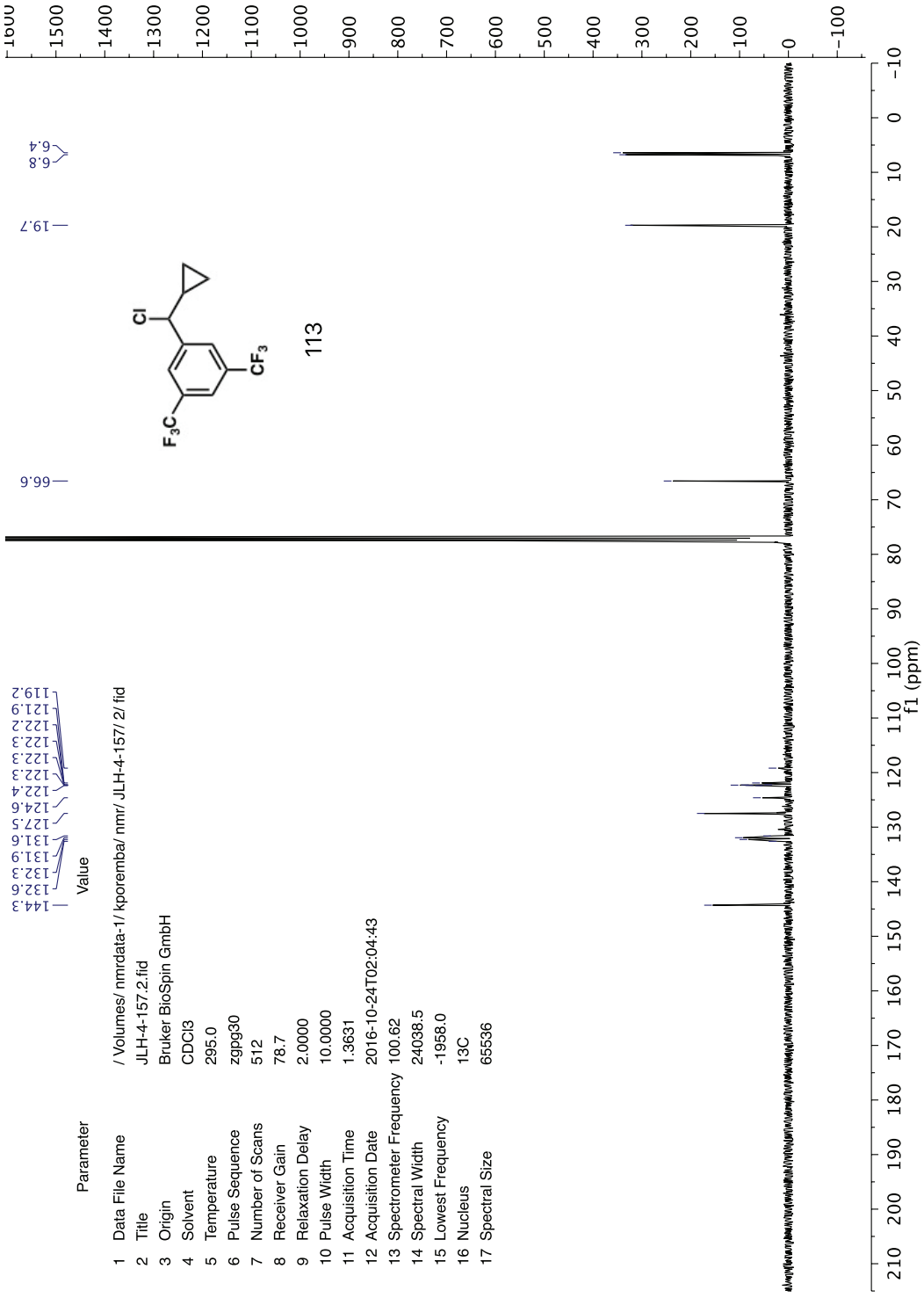

Parameter
Value
1 Data File Name / Volumes/ nmrdata-1/ kporemba/ nmr/ JLH-4-152/ 1/ fid
2 Title JLH-4-152.1.fid
3 Origin Bruker BioSpin GmbH
4 Solvent CDCl3
5 Temperature 294.9
6 Pulse Sequence zg30
7 Number of Scans 16
8 Receiver Gain 197.4
9 Relaxation Delay 1.0000
10 Pulse Width 11.7000
11 Acquisition Time 4.0894
12 Acquisition Date 2016-10-24T02:09:20
13 Spectrometer Frequency 400.13
14 Spectral Width 8012.8
15 Lowest Frequency -1535.6
16 Nucleus 1H
17 Spectral Size 65536
A (t) 7.80
B (dq) 7.91
C (dd) 4.11
D (d) 2.11
E (m) 1.19
F (m) 0.70
G (m) 0.52
OH
F_3C
CF_3
1.99
1.00
1.03
0.98
1.10
2.07
2.12
f1 (ppm)



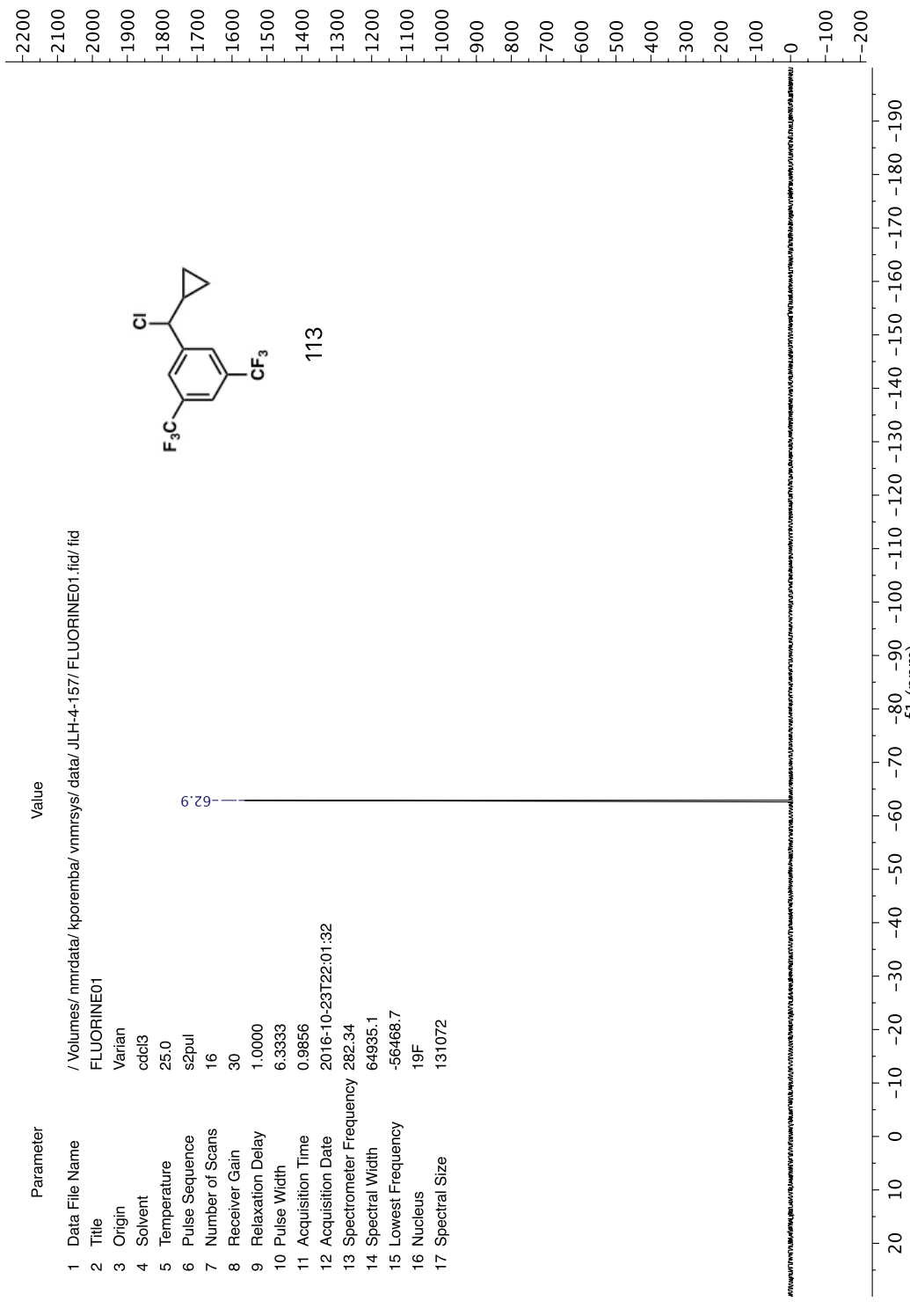
Parameter	Value
1 Data File Name	/ Volumes/ nmrdata-1/ kporemba/ nmr/ JLH-4-152/ 2/ fid
2 Title	JLH-4-152.2.fid
3 Origin	Bruker BioSpin GmbH
4 Solvent	CDCl3
5 Temperature	295.0
6 Pulse Sequence	zgpg30
7 Number of Scans	512
8 Receiver Gain	64.2
9 Relaxation Delay	2.0000
10 Pulse Width	10.0000
11 Acquisition Time	1.3631
12 Acquisition Date	2016-10-24T02:39:04
13 Spectrometer Frequency	100.62
14 Spectral Width	24038.5
15 Lowest Frequency	-1958.0
16 Nucleus	13C
17 Spectral Size	65536

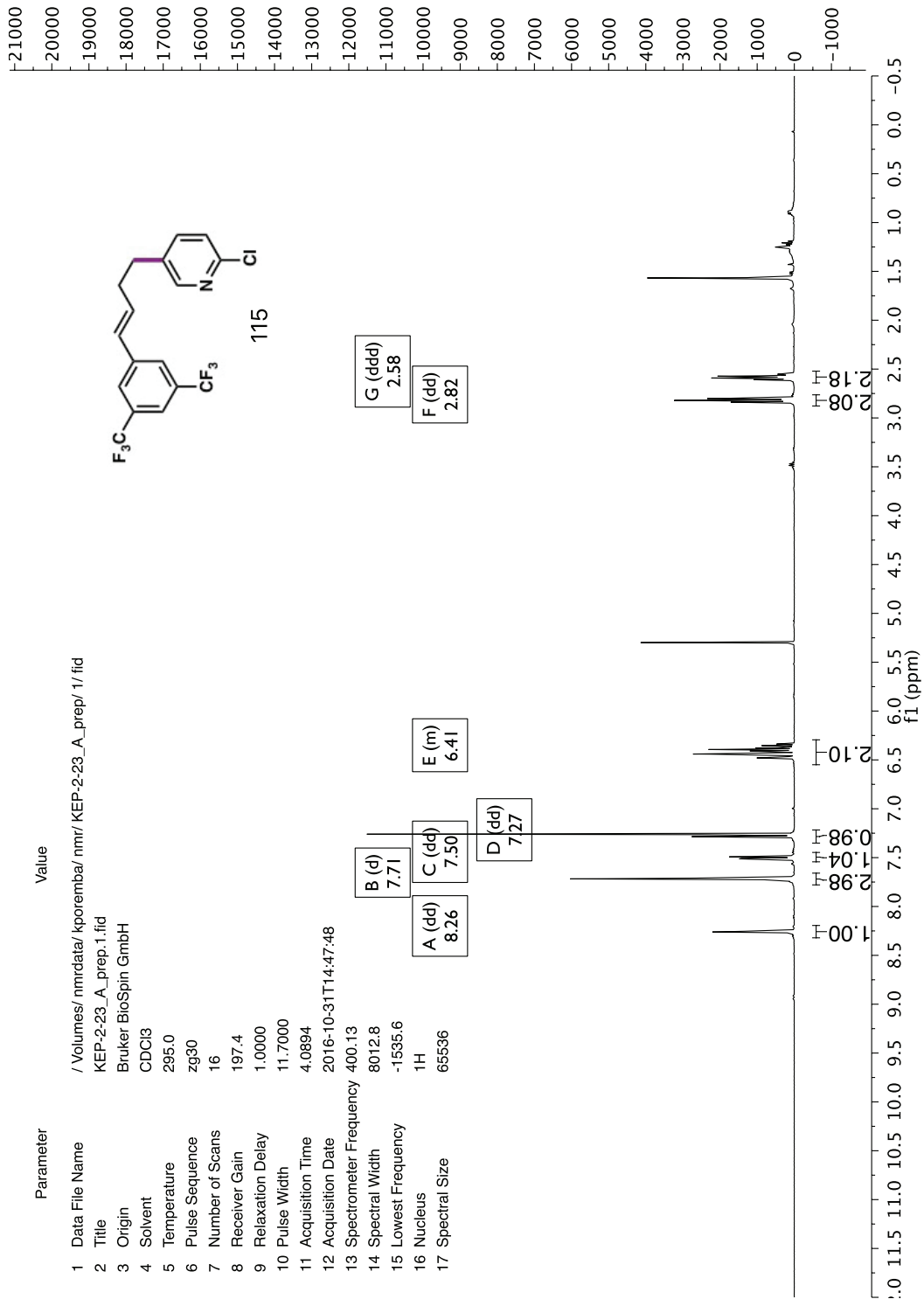

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16 Nucleus 19F
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CF3
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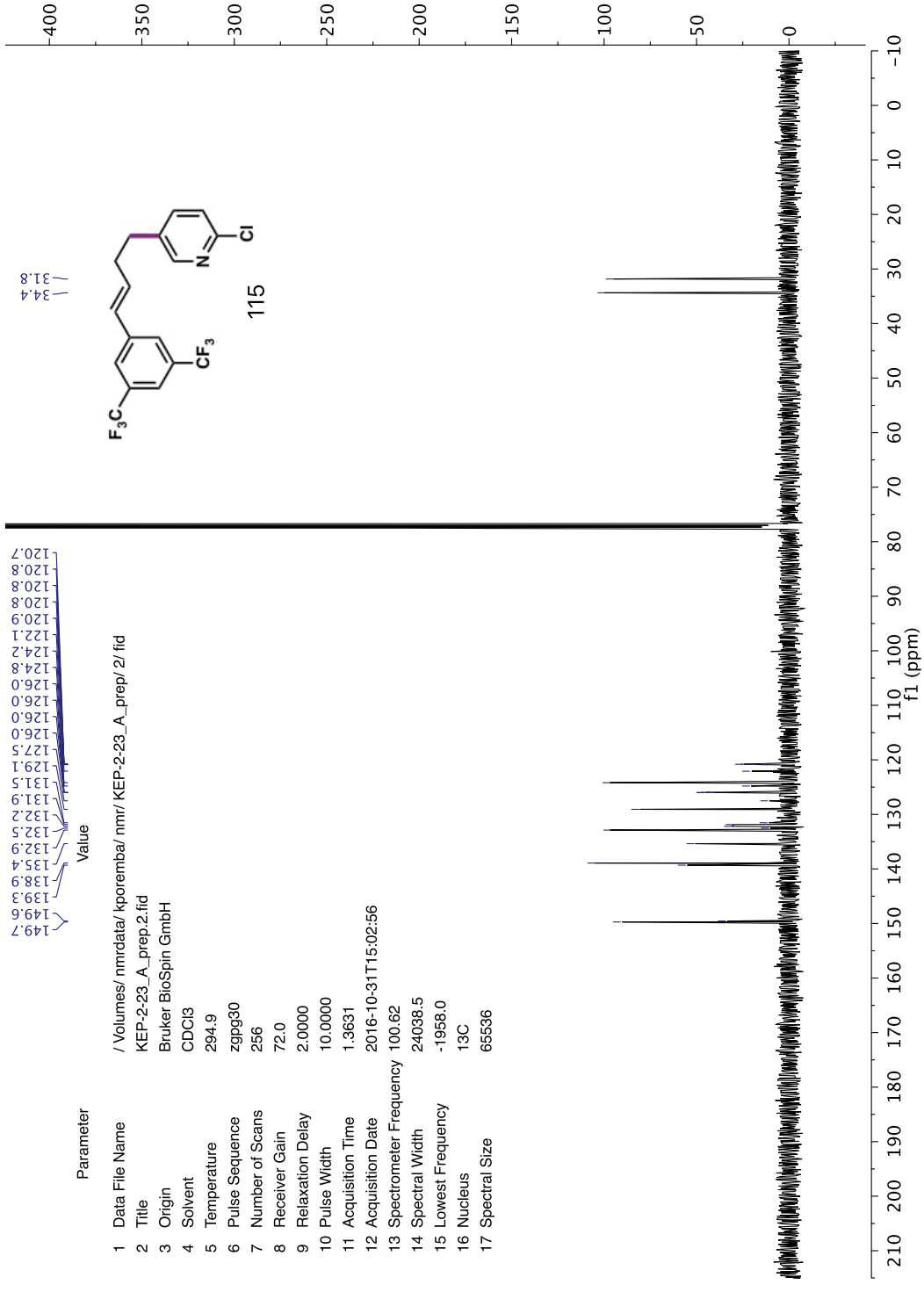

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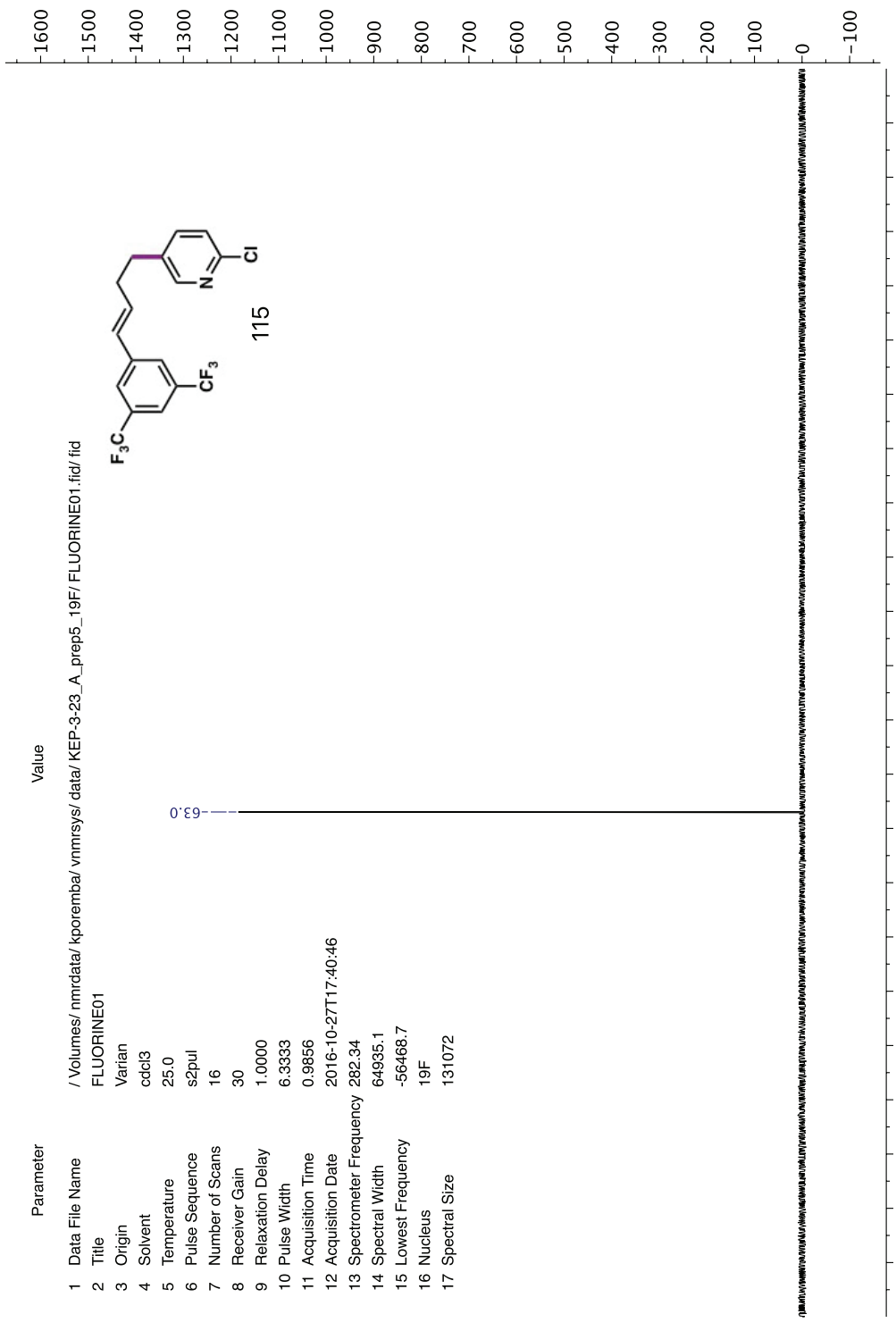


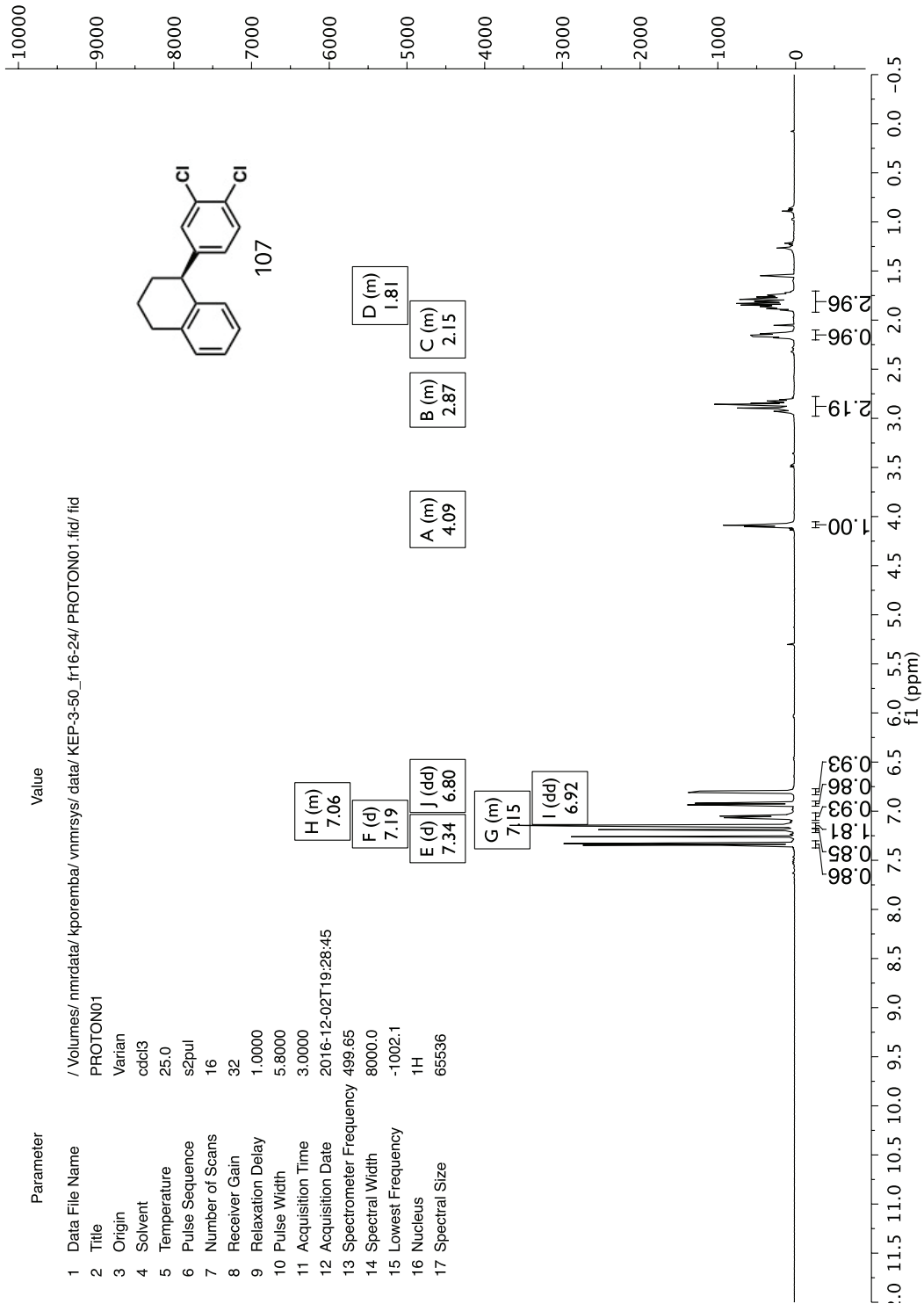
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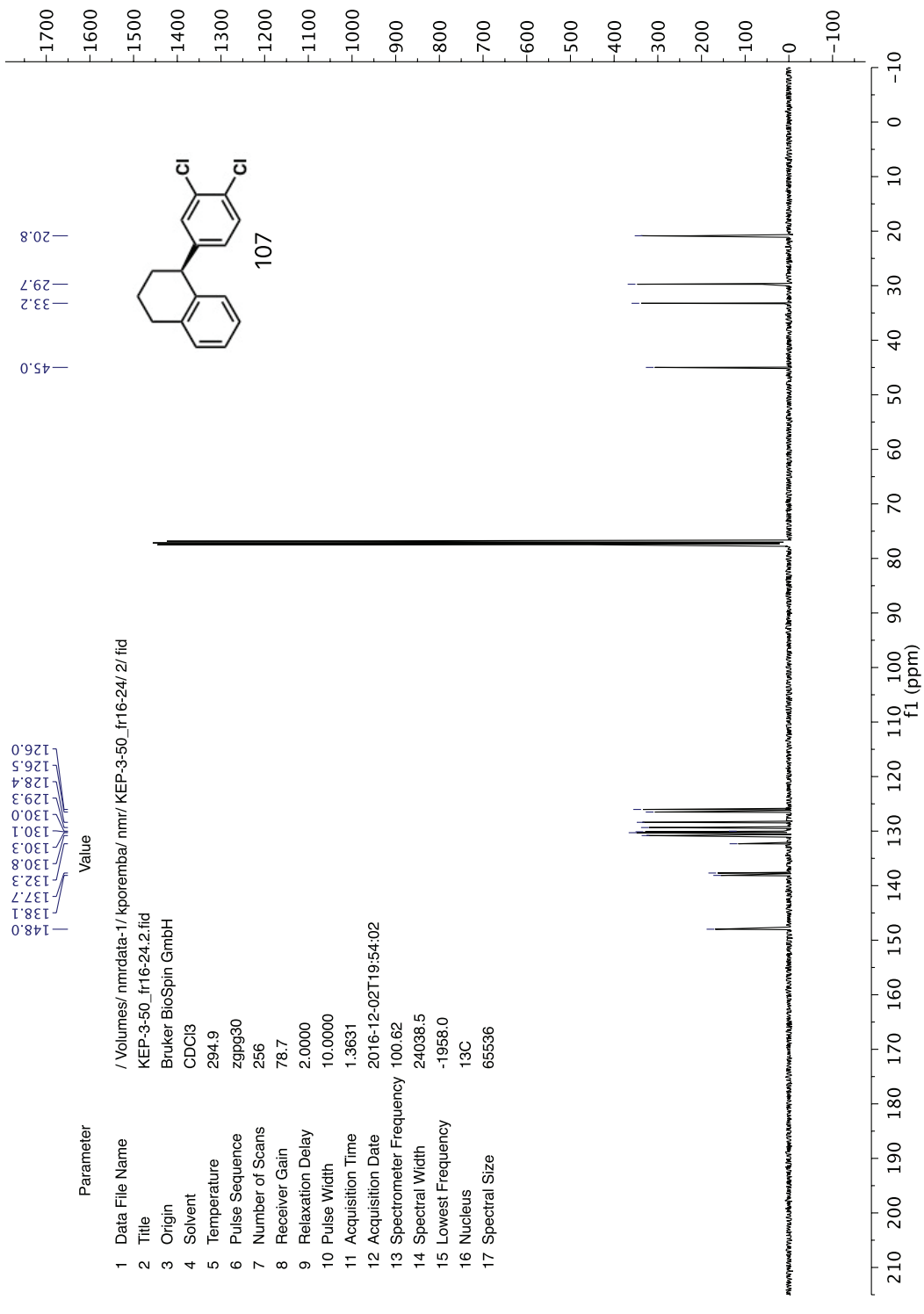

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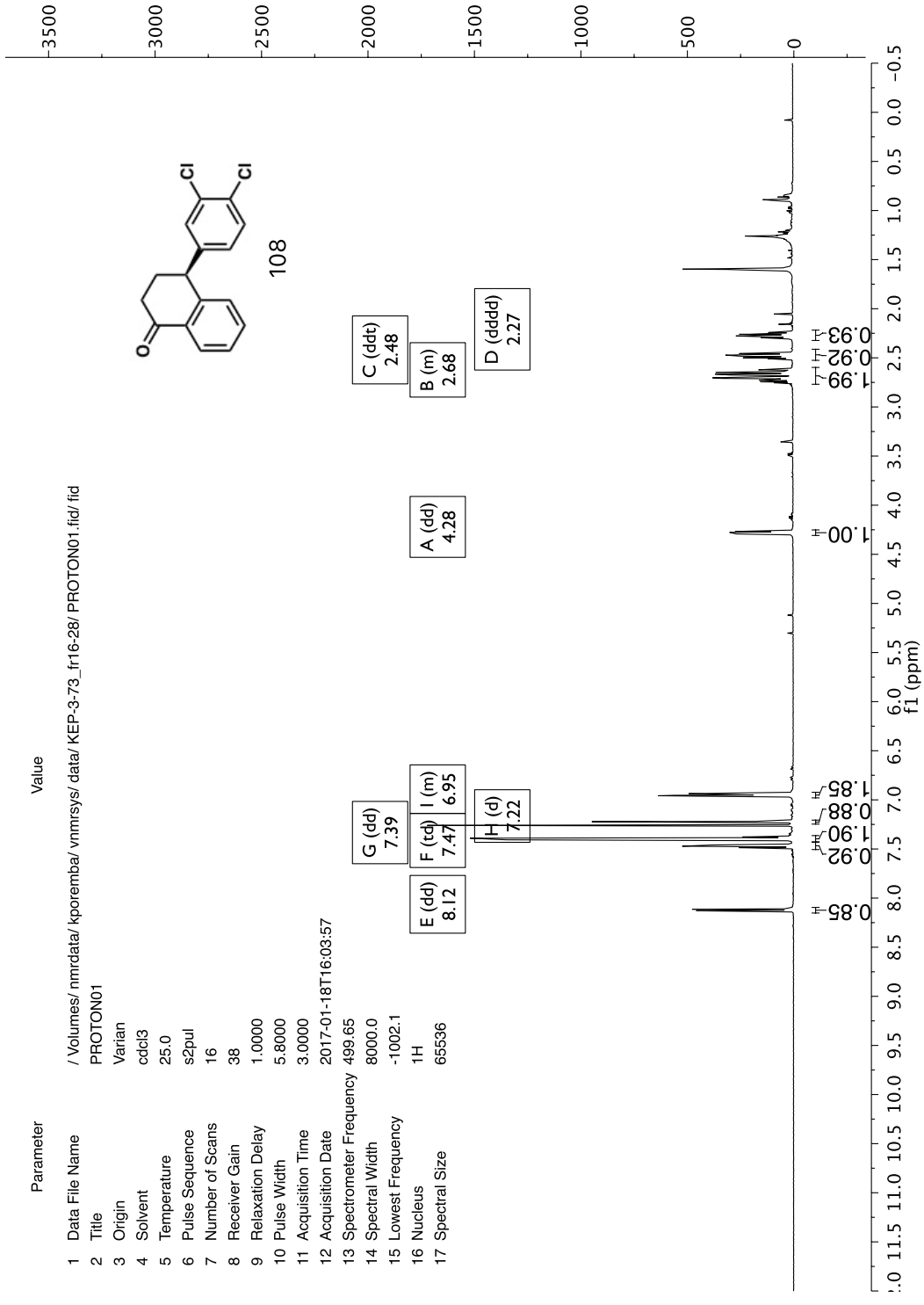

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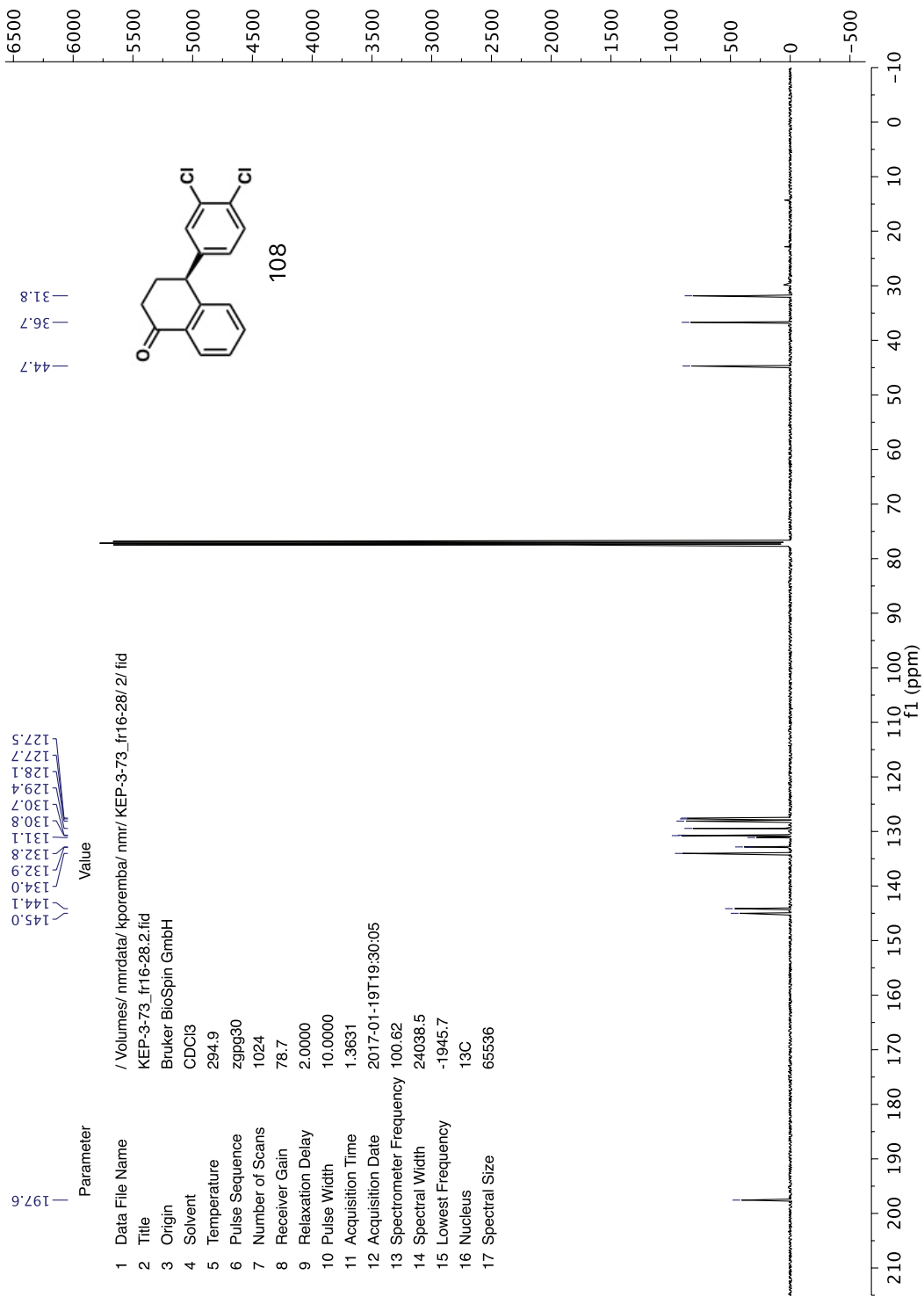

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f1 (ppm)


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D (m) 1.81
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f1 (ppm)



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f1 (ppm)


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Chapter 3

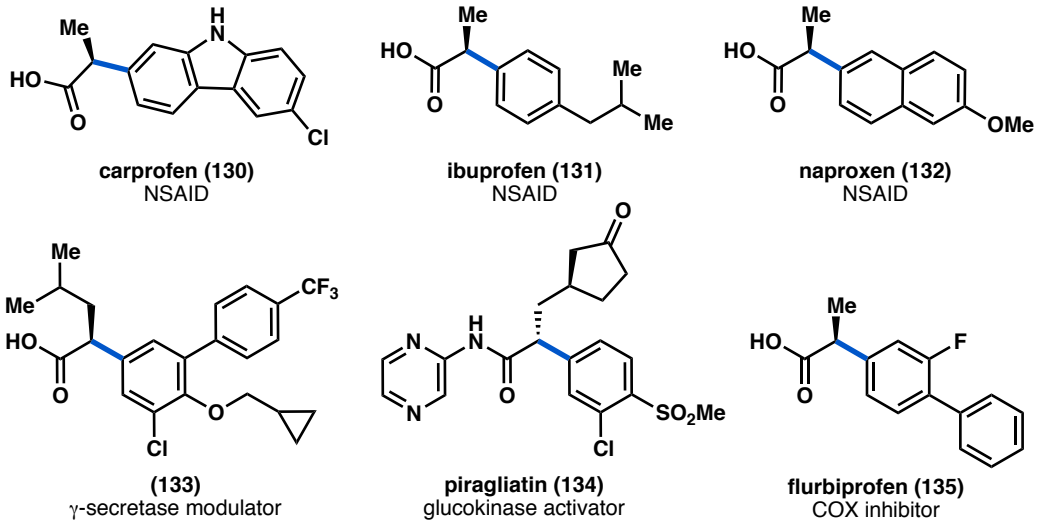
Nickel-Catalyzed Asymmetric Reductive Cross-Coupling of α-Chloroesters and Aryl Iodides

3.1 INTRODUCTION

Until recently, Ni-catalyzed asymmetric reductive cross-coupling was limited to benzyl chloride C(sp^3) electrophiles. In 2013, our group developed an asymmetric Ni-catalyzed reductive cross-coupling reaction between acid chlorides and benzyl chlorides to access α,α-disubstituted ketones.[1] Unfortunately, the conditions could not be applied to chloroformates or their derivatives to access α,α-disubstituted esters. This report was followed closely in 2014 with the cross-coupling of alkenyl bromides with benzyl chlorides.[2] In 2015, we expanded the scope of C(sp^3) electrophiles for this transformation to include α-chloronitriles.[3] We hypothesize that the successful coupling of a C(sp^3) electrophile is contingent upon radical stabilization by the α-substituent.[4] Based on this hypothesis, we could envision expanding this reactivity to include electrophiles with other radical-stabilizing α-substituents, such as α-halo carbonyl compounds. The

stereoconvergent cross-coupling of α-haloesters with C(sp^2) electrophiles, such as aryl iodides or alkenyl bromides, would allow us to access enantioenriched α,α-disubstituted esters, important motifs in both natural products and pharmaceuticals.[5]

Scheme 3.1. *Biologically active α-aryl carboxylic acid derivatives.*

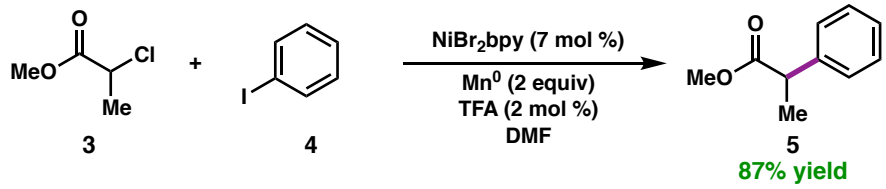


α-Functionalization of carbonyls has long been a challenge for synthetic chemists. Enantioenriched α,α-disubstituted carbonyl compounds are versatile synthetic intermediates and carboxylic acid derivatives containing α-aryl stereogenic centers are found in a number of biologically active compounds (Scheme 3.1).[5,6] Specifically, the nonsteroidal anti-inflammatory drugs (NSAIDs) are an FDA-approved class of molecules that contain an α-aryl carboxylic acid derivative. Often these compounds are synthesized in enantioenriched form by chiral resolution or through the use of chiral auxiliaries;[7–13] however, there has been much interest in developing catalytic, enantioselective alternatives to these processes.[14–19] A key challenge in this regard is identifying mild conditions under which the initially formed enantioenriched products are not racemized.[20]

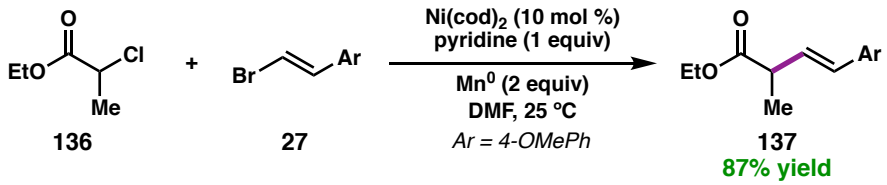
In recent years, several methods to access these compounds via Ni-catalysis have been disclosed.[21] Fu and coworkers have developed several asymmetric reactions to cross-couple α-halocarbonyl compounds with organometallic reagents.[22–26] In 2007, Durandetti reported the racemic reductive cross-coupling of α-chloroesters and aryl halides,[27,28] and in 2016, Gong disclosed the racemic reductive cross-coupling of α-chloroesters and -amides with alkenyl bromides (Scheme 3.2).[29] Drawing inspiration from these reports, we envisioned developing a Ni-catalyzed asymmetric reductive cross-electrophile coupling variant. While our lab's previous cross-coupling of α-chloronitriles generates enantioenriched products that can be derivatized to chiral α-aryl esters,[3] development of the cross-coupling with a different C(sp^3) electrophile may address the substrate limitations of the previous method. This alternative disconnection might broaden the scope of the C(sp^3) electrophile as well as enable the incorporation of more diverse aryl partners.

Scheme 3.2. *Ni-catalyzed reductive cross-coupling to access α-disubstituted carboxylic acid derivatives.*

a) Durandetti, 2007



b) Gong, 2016

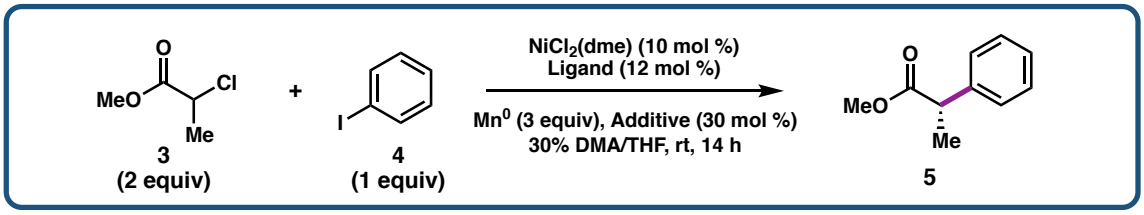


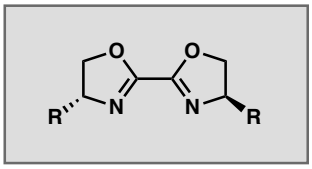
3.2 INITIAL EXPLORATION

3.2.1 Reaction Exploration

Our optimization efforts began with the arylation of methyl-2-chloropropionate (**3**), a commercially available substrate that was shown by Durandetti[27] to undergo Ni-catalyzed reductive coupling reactions. Exposure of a mixture of **3** and iodobenzene (**4**) to our standard conditions[1] using $NiCl_2$(dme) (10 mol %), Mn^0 as the reductant (3.0 equiv), in the presence of PhBOX (**L3**) failed to provide product. However, we discovered the use of bi(oxazoline) (BiOX) ligands provided more promising results,[30] with ^{i}PrBiOX **L19** delivering α-arylester **5** in 37% yield and 74% ee (Table 3.1, entry 3), perhaps due to the longer *N-N* distance tolerating the large steric profile of the aryl iodide coupling partner. Interestingly, use of the corresponding PhBiOX, **L21**, furnished the desired product in 26% yield, but with no enantiomeric excess (entry 1).

Table 3.1. *Preliminary bi(oxazoline) ligand screen.*[33]



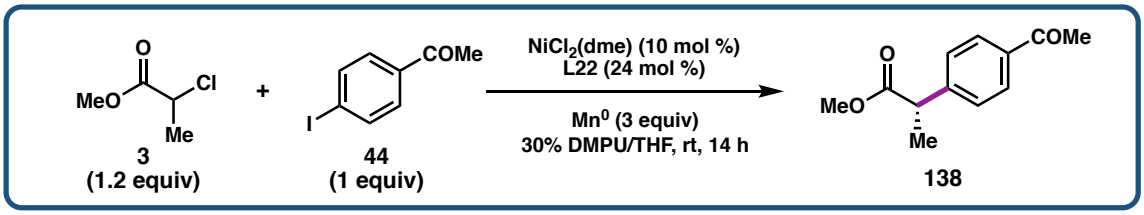


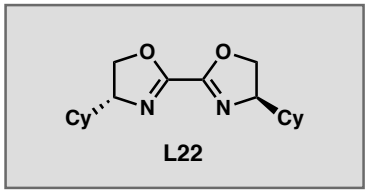
Ligand	R	Additive	Yield 5 (%)[a]	ee 5 (%)[b]
L21	Ph	—	26	0
L2	Bn	—	61	35
L19	^{i}Pr	—	37	74
L8	^{i}Bu	—	88	37
L19	^{i}Pr	TFA[c]	40	67
L19	^{i}Pr	TFA	73	76
L19	^{i}Pr	TMSCl	27	64

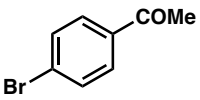
[a] Determined by GC using an internal standard. [b] Determined by GC using a chiral stationary phase. [c] 3 mol %.

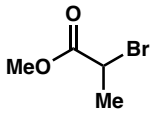
In these preliminary efforts to improve the yield, we determined that addition of co-catalytic trifluoroacetic acid (TFA) delivered arylation product **5** in 73% yield and 76% ee. The addition of TFA may serve to activate the Mn surface and improve reductive turnover of the catalyst, however additional studies are required to better understand the role it plays. Unfortunately, attempts to "pre-activate" the manganese surface by various acid washes delivered poor results, as well as other potential activators such as TMSCl.[31,32]

Table 3.2. *Investigation with a more functionalized aryl iodide.*[a]









Entry	Deviation	Yield 138 (%)[b]	ee 138 (%)[c]
1	L19	15	72
2	—	73	76
3	Zn^0	62	74
4	DMPU	40	65
5	THF	30	79
6	139 instead of 3	7	75
7	55 instead of 44	0	—
8	+ $NaBF_4$ (1 equiv)	78	76
9	+ NaI (0.5 equiv)	75	75

[a] Reactions conducted under inert atmosphere on 0.1 mmol scale. [b] Determined by ^1H NMR using an internal standard. [c] Determined by SFC using a chiral stationary phase.

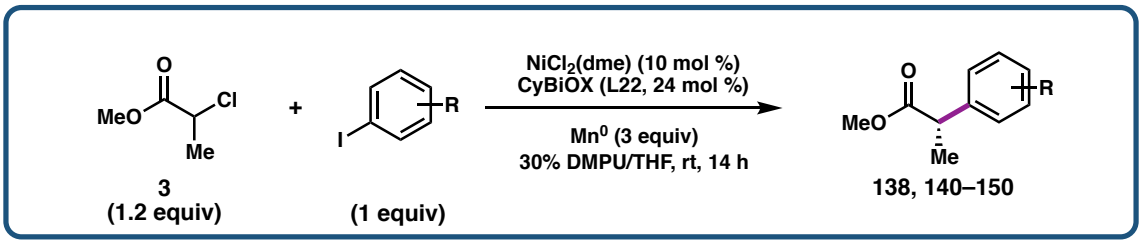
While these initial results were promising, we were disappointed to discover these conditions did not translate to functionalized aryl iodide coupling partners (Table 3.2, entry 1). Further exploration with aryl iodide **44** proved performing the reaction in a

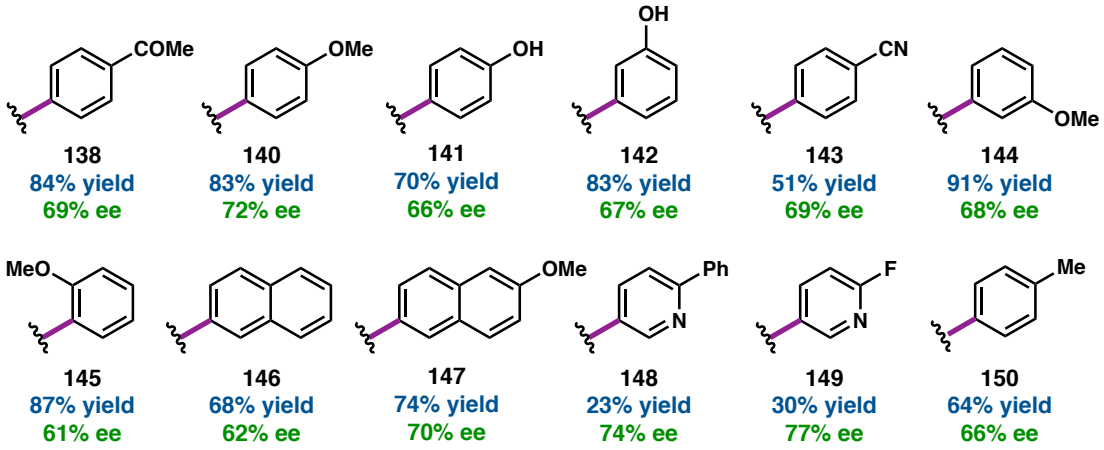
solvent mixture of 30% DMPU/THF with bi(oxazoline) ligand **L22**, without the addition of catalytic TFA, effected formation of the product **138** in 73% yield and 76% ee (Table 3.2, entry 2). Zn^0 was similarly effective as a reductant in this reaction, giving **138** in slightly diminished yield, but 74% ee (entry 3). Interestingly, the yield of the reaction decreased significantly when performed in either DMPU or THF alone, though the ee decreases about 10% in DMPU (entries 4 and 5). The corresponding α-bromo ester **139** and aryl bromide **55** were both inferior coupling partners, giving trace or no product, respectively (entries 6 and 7), presumably because of mismatched rates of oxidative addition. Addition of additives such as $NaBF_4$ or NaI, which have aided previous reductive cross-coupling reactions,[3,34] provided no change to the yield or ee (entries 8 and 9).

3.2.2 Initial Substrate Scope

After initial exploration of reaction parameters, we sought to determine the substrate scope of the reaction. Aryl iodides bearing a variety of functional groups and substitution patterns were tolerated in good yield, but in only moderate levels of ee (Table 3.3). Coupling of **3** with aryl iodides bearing electron-withdrawing substituents were well tolerated, including nitrile-containing **143**. Electron-donating substituents were similarly viable in this reaction, including phenols (**141** and **142**) and methoxy groups (**140**, **144**–**145**). Importantly, substitution at both the *meta* and *ortho* positions was well tolerated for the anisole substrates (**140**, **144**–**145**). Finally, initial results for 4-iodo-2-halo-pyridyl substrates exhibit especially promising ee's, albeit in poor yields (**148** and **149**).

Table 3.3. *Preliminary aryl iodide substrate scope.*[a]

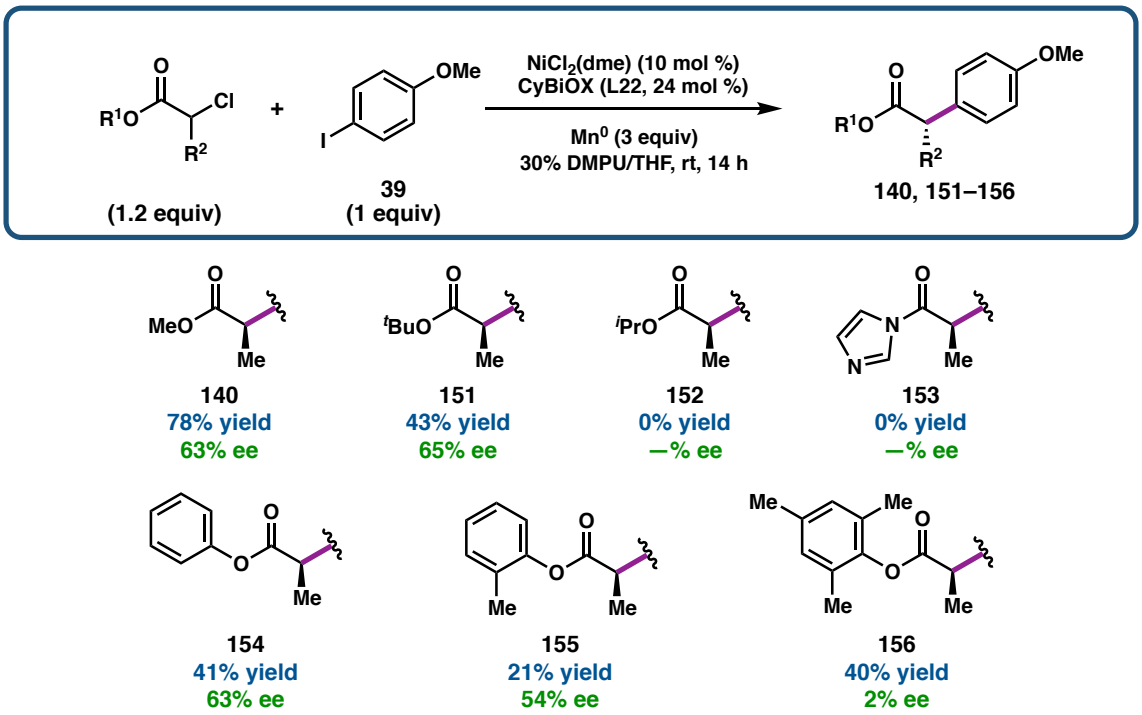




[a] NMR yields, reactions conducted on 0.2 mmol scale under a N_2 atmosphere. % ee determined by SFC using a chiral stationary phase.

Unfortunately, the substrate scope of the α-chloroester coupling partner was limited almost exclusively to methyl-2-chloropropionate (**3**, Table 3.4). Other ester groups, including alkyl and aryl derivatives, delivered the corresponding cross-coupled product in decreased yield and often with worse ee (**151**– **152**, **154–156**). Amide **153** did not afford any of the desired product. The C(sp^3) electrophile was also limited at R^2, only tolerating methyl-substitution.

***Table 3.4**. Preliminary α-chloroester substrate scope.*[a]



[a] NMR yields, reactions conducted on 0.2 mmol scale under a N_2 atmosphere. % ee determined by SFC using a chiral stationary phase.

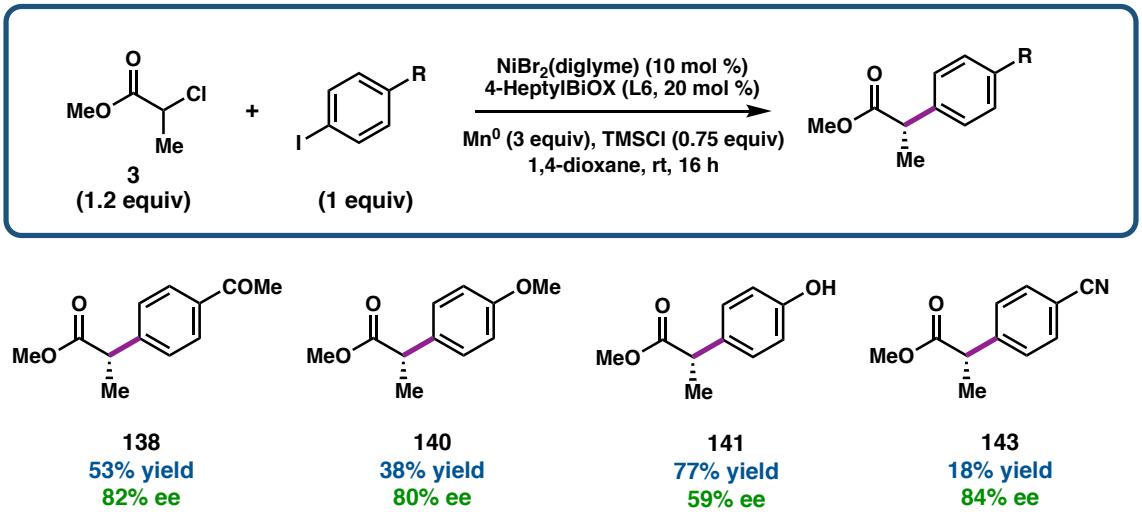
3.3 LIGAND EXPLORATION

3.3.1 Reaction Development

With significant limitations in both the substrate scope and enantioselectivity for this transformation, the development of this reaction was halted while the work described in **Chapter 2** was conducted. Upon the completion of that project, we sought to determine if the knowledge we gained in the development of the cross-coupling of benzyl chlorides and aryl iodides could be leveraged in the α-chloroester system, specifically how non-polar solvents with TMSCl and 4-HeptylBiOX (**L6**) would perform with this transformation. We were pleased to observe that upon subjection of **3** and **44** to $NiBr_2$(diglyme) (10 mol %), **L6** (20 mol %), Mn^0 as the reductant (3 equiv), TMSCl as an

additive (0.75 equiv), in 1,4-dioxane at room temperature (Table 3.5), **138** was formed in 82% ee, the highest ee we had observed in the cross-coupling of α-chloroesters to date by a significant margin. Similar results were observed with aryl iodide **39**, forming **140** in 80% ee, and 4-iodobenzonitrile, which gave **143** in 84% ee, again major increases from results with our previous conditions. While the yields of these three substrates decreased significantly, we felt confident that reinvestigation of this system would prove fruitful. Interestingly, the coupling of 4-iodophenol gave product **141** in reduced ee than previously observed, but in higher yield.

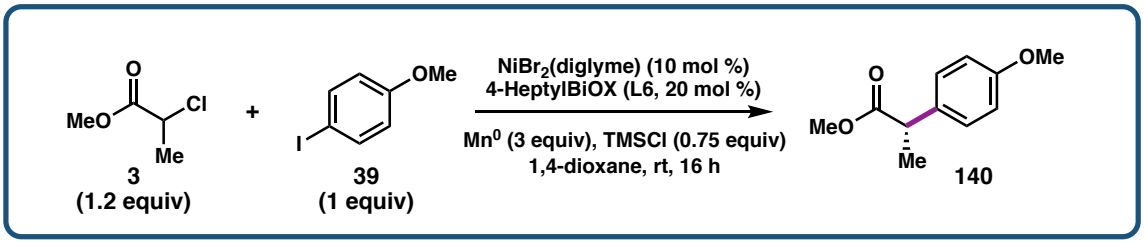
Table 3.5. *Application of 1,4-dioxane/TMSCl conditions.*

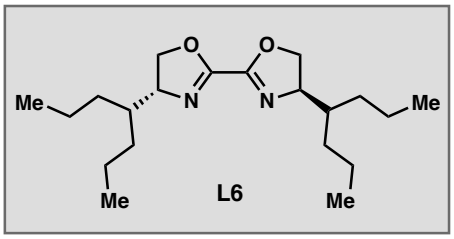


With these exciting results in hand, we renewed our investigation into the cross-coupling of **3** and **39**, starting from the conditions developed in **Chapter 2**. A screen of solvents revealed the yield of **140** increased to 60% in both THF and DMA, with little erosion of ee (Table 3.6, entries 2 and 3). However, while the yield increased to 75% when the reaction was performed in DMPU, the ee decreased significantly to 66% (entry 4). Addition of $NaBF_4$ to the reaction in 1,4-dioxane increased the yield of **140** from 28%

to 50% (entry 5), while increasing the equivalents of the aryl iodide coupling partner also improved the yield of **140** to 59% (entry 6). To our delight, increasing the equivalents of **39** in THF afforded **140** in 88% yield and 80% ee (entry 8). The combination of the addition of $NaBF_4$ with two equivalents of **39** in THF delivered **140** in 87% yield and 82% ee (entry 9).

***Table 3.6**. Investigation of reaction parameters with **L6**.*



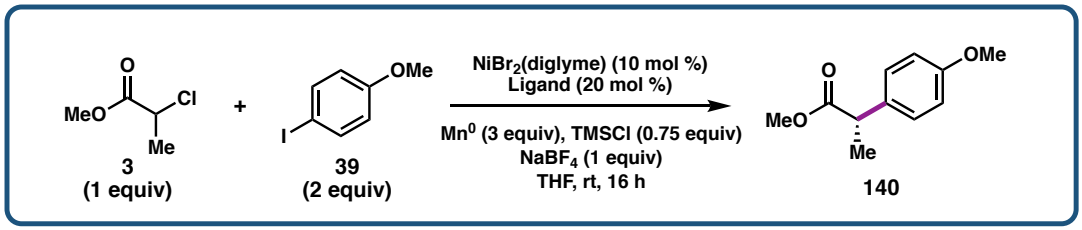


Entry	Solvent	Conditions	Yield 140 (%)	ee 140 (%)
1	1,4-dioxane	—	28	80
2	THF	—	59	75
3	DMA	—	60	77
4	DMPU	—	76	66
5	1,4-dioxane	+ $NaBF_4$ (1 equiv)	50	83
6	1,4-dioxane	2 equiv 39	59	82
7	THF	+ $NaBF_4$ (1 equiv)	59	81
8	THF	2 equiv 39	88	80
9	THF	+ $NaBF_4$, 2 equiv 39	87	82

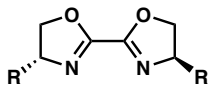
Performing the cross-coupling of methyl-2-chloropropionate (**3**) and 2 equiv of 4-iodoanisole (**39**), now in THF with both TMSCl and $NaBF_4$ as additives, we explored a series of bi(oxazoline) ligands (Table 3.7). Similar to results we observed in **Chapter 2**, aryl-substituted bi(oxazoline) ligands, such as **L21**, **L2**, and **L26** (entries 3-5), furnished the desired product in low yield and poor ee. Alkyl-substituted BiOX ligands, such as **L22** and **L19**, produced **140** in moderate yield and ee. Curiously, 4-HeptylBiOX was

significantly better than all other bi(oxazoline) ligand evaluated (entry 10), even compared to structurally similar **L33** (entry 9).

Table 3.7. *Bi(oxazoline) ligand screen in THF.*



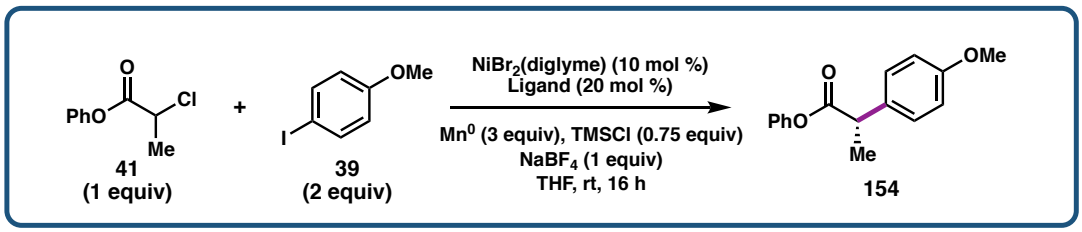
Bi(oxazoline) Ligand Scaffold



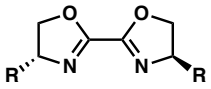
Entry	Ligand	R	Yield 140 (%)	ee 140 (%)
1	L22	Cy	40	64
2	L34	-CH_2Cy	41	32
3	L21	Ph	4	12
4	L2	Bn	41	29
5	L26	-CH_2-2-Nap	47	29
6	L19	^{i}Pr	33	66
7	L8	^{i}Bu	36	33
8	L20	^{t}Bu	3	21
9	L33	3-Pentyl	43	68
10	L6	4-Heptyl	87	82

At this time, a brief investigation into the substrate scope of the reaction in these updated reaction conditions revealed the surprising efficacy of phenyl-2-chloropropionate (**41**) as the C(sp^3) coupling partner (Table 3.8). An identical BiOX ligand screen was performed on the cross-coupling of **41** and **39** and we were pleased to observe a significant increase in yield across all ligands evaluated. Notably, *sec*-alkyl BiOX ligands **L33** and **L6** gave the product in nearly quantitative yield and 77% and 80% ee, respectively (entries 9-10).

Table 3.8. *Bi(oxazoline) ligand screen with phenyl-2-chloropropionate (**41**).*



Bi(oxazoline) Ligand Scaffold

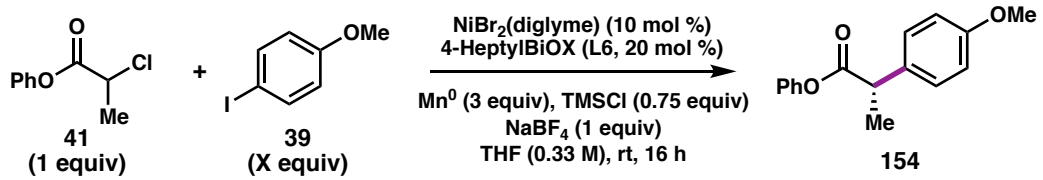


Entry	Ligand	R	Yield 154 (%)	ee 154 (%)
1	L22	Cy	80	70
2	L34	-CH_2Cy	81	35
3	L21	Ph	0	—
4	L2	Bn	58	30
5	L26	-CH_2-2-Nap	70	34

Entry	Ligand	R	Yield 154 (%)	ee 154 (%)
6	L19	^{i}Pr	72	74
7	L8	^{i}Bu	83	34
8	L20	^{t}Bu	7	21
9	L33	3-Pentyl	97	77
10	L6	4-Heptyl	99	80

Having successfully improved the yield of the coupling, we revisited the effect of equivalents of aryl iodide in the reaction. We were pleased to see that decreasing the equivalents of **39** from 2 to 1.5 afforded **154** in 93% yield and 82% ee (Scheme 3.3). However, lowering **39** to 1 equiv resulted in a decrease to 76% yield. Further reaction development was conducted with 1 equiv of the α-chloroester and 1.5 equiv of aryl iodide.

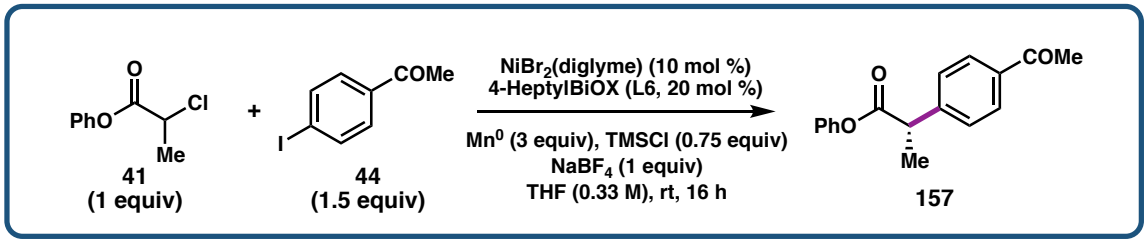
Scheme 3.3. *Equivalents of aryl iodide coupling partner.*



1.5 equiv 39: 93% yield, 82% ee
1.0 equiv 39: 76% yield, 82% ee

At this point in our optimization efforts, we chose to proceed with 4-iodoacetophenone (**44**), which, under the updated conditions, cross-coupled with **41** in only 67% yield and 85% ee. Intent on improving both the yield and enantioselectivity of this transformation, every reaction parameter was examined. Investigation of several Ni catalysts demonstrated $NiBr_2$(diglyme) was still the optimal catalyst in the reaction (Table 3.9, entry 1), but performed similarly to $NiBr_2$(glyme), $Ni(acac)_2$, and $Ni(cod)_2$ (entries 2, 4 and 5). Interestingly, anhydrous NiI_2, $NiCl_2$, and NiF_2 gave only a small amount of **157** in approximately 80% ee (entries 6-8), most likely due to solubility issues in THF.

Table 3.9. *Evaluation of reaction parameters.*



Catalyst Screen:

Entry	Catalyst	Yield 157 (%)	ee 157 (%)
1	$NiBr_2$(diglyme)	67	84
2	$NiBr_2$(glyme)	64	84
3	$NiCl_2$(glyme)	49	84
4	$Ni(acac)_2$	63	83
5	$Ni(cod)_2$	63	84
6	NiI_2	20	83
7	$NiCl_2$	13	79
8	NiF_2	19	81

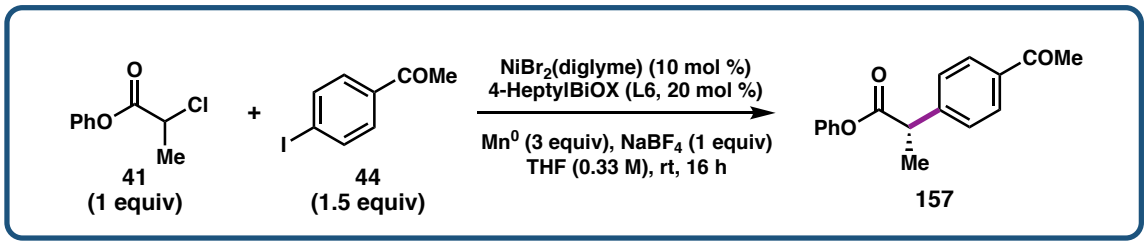
Additive Screen:

Entry	Conditions	Yield 157 (%)	ee 157 (%)
9	Control	67	85
10	–TMSCl	62	85
11	$–NaBF_4$	47	85
12	–TMSCl, $–NaBF_4$	59	84

We were interested to see if both TMSCl and $NaBF_4$ were necessary as additives for the reaction in THF. Control experiments removing one or both reagents

demonstrated that TMSCl was unnecessary (Table 3.9, entry 10), but the yield decreases in the absence of $NaBF_4$ (entries 11 and 12). The higher yields observed with $NaBF_4$ can be attributed to increased conversion, similar to results reported by Molander and coworkers in their reductive cross-couplings of heteroaromatic substrates.[35] Currently, it is unclear if the role of $NaBF_4$ is to act as a halide-scavenging agent, a mild Lewis acid, or simply an electrolyte.

Table 3.10. *Investigation of solvent and salt additive.*



Solvent:

Entry	Solvent	Yield 157 (%)	ee 157 (%)
1	THF	64	85
2	1,4-dioxane	53	84
3	DMPU	74	58
4	DMA	51	65
5	DMF	30	57

$^-BF_4$ Additive:

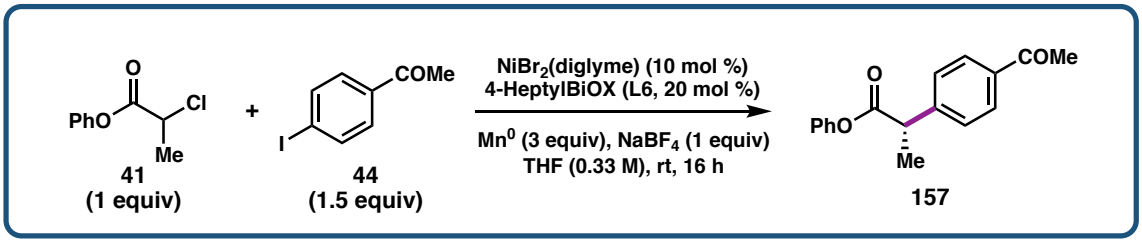
Entry	Additive	Yield 157 (%)	ee 157 (%)
6	$NaBF_4$	66	85
7	$LiBF_4$	77	73
8	KBF_4	50	84
9	$AgBF_4$	72	86

Conducting the reaction now without TMSCl, we reinvestigated solvent effect. While the same ee is achieved in THF as 1,4-dioxane (Table 3.10, entries 1 and 2), the yield of **157** decreases to 53% in 1,4-dioxane. Polar solvents such as DMPU, DMA and DMF give **157** with only moderate levels of enantioselectivity (entries 3–5). Looking closer at the role of $NaBF_4$ in the reaction, we evaluated a series of tetrafluoroborate salts (Table 3.10). While $LiBF_4$ gave **157** in higher yield (77%), the ee was reduced to 73%

(entry 7). $AgBF_4$ gave **157** in 72% yield and 86% ee (entry 9). Further investigation into the use of $AgBF_4$ is still needed on this system.

Next, we assessed catalyst and ligand loading and ratio (Table 3.11). Looking at 1:1, 1:2 and 1:3 ratios of Ni to **L6** at 5, 10 and 15 mol % Ni loading, we found that the optimal yield and ee was achieved at 10 mol % Ni and 20 mol % ligand (entry 4), which was the loading ratio we had been working with in previous screens. It is unclear why excess ligand is necessary for higher conversion, but one possibility is that the ligand is degraded during the course of the reaction. Unfortunately, we do not detect any remaining **L6** in the crude reaction mixtures.

Table 3.11. *Ni loading and concentration screens.*



Catalyst Loading:

Entry	Ni equiv	L equiv	Yield 157 (%)	ee 157 (%)
1	5%	5%	57	85
2	5%	10%	56	85
3	10%	10%	46	84
4	10%	20%	64	85
5	10%	30%	60	85
6	15%	15%	40	85
7	15%	30%	55	84

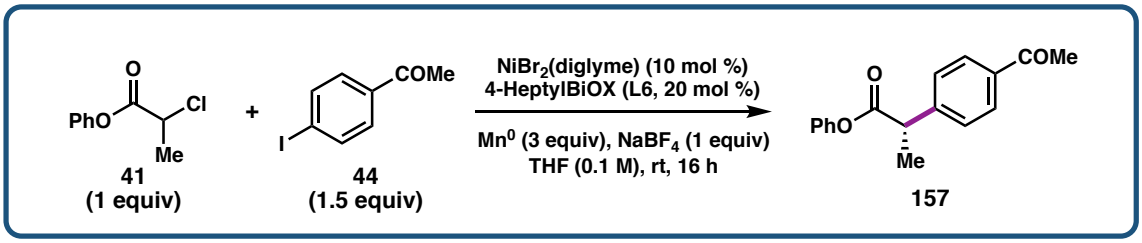
Concentration:

Entry	Concentration	Yield 157 (%)	ee 157 (%)
8	0.05 M	74	87
9	0.1 M	87	86
10	0.2 M	76	85
11	0.3 M	63	84
12	0.5 M	58	84
13	0.6 M	30	82
14	0.8 M	37	81
15	1.0 M	42	81

We then turned our attention toward determining the ideal concentration of the reaction (Table 3.11). Surveying the reaction at various molarities, we were delighted to

observe **157** was delivered in 87% yield at 0.1 M without any erosion of ee (entry 9). Presumably, the concentration of the reaction affects the rates of oxidative additive of each electrophile, changing the ratio of desired product to homocoupling products.

Table 3.12. *Temperature and dual solvent system exploration.*



Temperature:

Entry	Temperature (°C)	Yield 157 (%)	ee 157 (%)
1	10	72	87
2	23	72	86
3	40	80	86
4	60	61	85

Solvent:

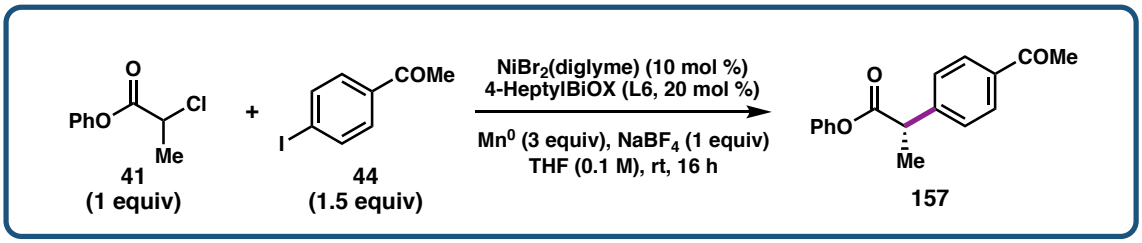
Entry	DMPU/THF	Yield 157 (%)	ee 157 (%)
6	0% DMPU	82	86
7	10% DMPU	84	82
8	20% DMPU	78	80
9	30% DMPU	62	76
10	40% DMPU	77	51

At this point in our optimization efforts, we hoped that lowering the reaction temperature would improve the ee, an effect our lab has observed previously.[2,36,37] Lowering the temperature to 10 ºC appeared to have no effect on the reaction (Table 3.12, entry 1). Further studies on lower temperatures are necessary to see if selectivity can increase without inhibiting product formation. Conversely, we also attempted increasing the reaction temperature to 40 and 60 ºC and observed a fluctuation in yield, but no change in ee (Table 3.12, entries 3 and 4). Now conducting the reaction at a more dilute concentration, we wondered if addition of a small amount of DMPU in THF could provide the synergistic effect we observed in our earliest optimization efforts (Table 3.2).

Unfortunately, the addition of any amount of DMPU in this system only resulted in a decrease in enantioselectivity (Table 3.12, entries 6-10).

Finally, we wanted to confirm that Mn^0 was still the optimal reductant in this transformation. When the reaction was performed with Mn^0, we observed product **157** forming in 82% yield and 86% ee with Mn^0 (Table 3.13, entry 1). Zn^0 provided identical ee, but lower 54% yield (entry 2). We did not observe product formation with TDAE acting as a terminal reductant (entry 3).

Table 3.13. *Evaluation of reductants.*

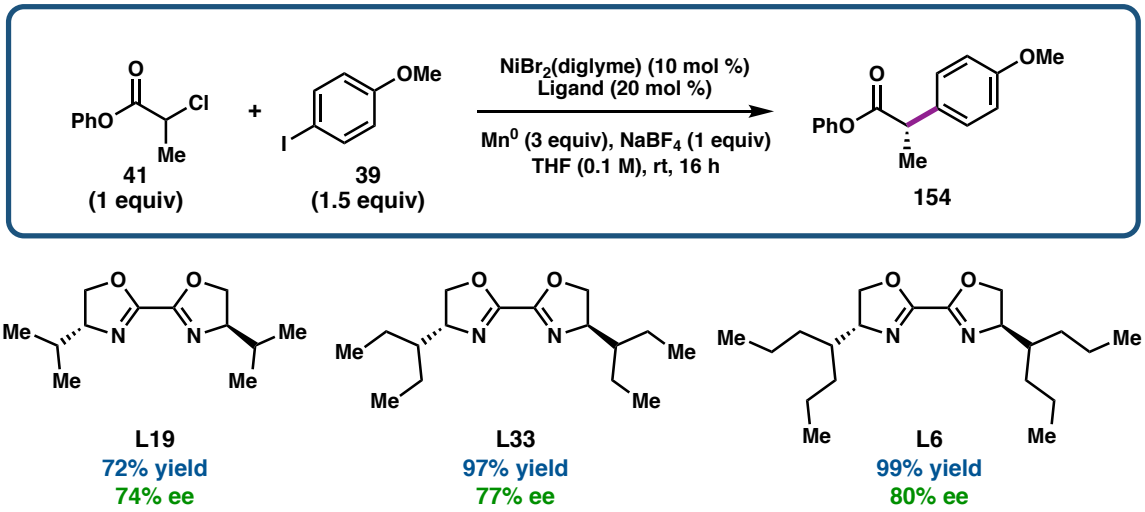


Entry	Reductant	Yield 157 (%)	ee 157 (%)
1	Mn	82	86
2	Zn	54	86
3	TDAE	0	—

3.3.2 Ligand Trends

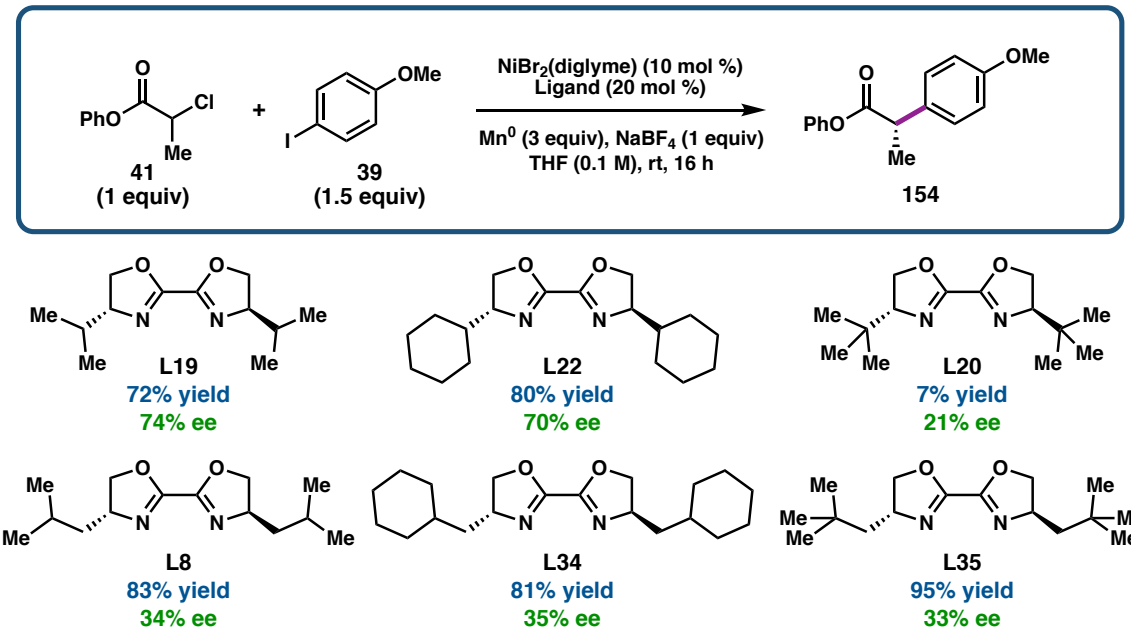
Having thoroughly explored several reaction parameters, we felt that in order to improve the selectivity, we needed to return to ligand design and more closely examine the effect of alkyl-substituted bi(oxazoline) ligands on this transformation. Interestingly, unlike the cross-coupling of benzyl chlorides and aryl iodides (**Chapter 2**), the ee of the desired product (**154**) does not change significantly as the length of the alkyl chains increase from ^{i}Pr (**L19**) to 4-Heptyl (**L6**, Table 3.14).

***Table 3.14**. Comparison of sec-alkyl substituted bi(oxazoline) ligands.*



However, upon closer inspection of the reactivity and selectivity trends across several alkyl-substituted ligands, it appears branching directly adjacent to the oxazoline core is crucial for selectivity (Table 3.15). While **154** is formed in 72% yield and 74% ee with **L19**, the corresponding ligand with a methylene unit separating the ^{i}Pr branching from the oxazoline (**L8**) gives **154** in still high 83% yield, but in only 34% ee. Similarly, **L22** produces **154** in 80% yield and 70% ee, but the addition of a methylene between the cyclohexyl group and the oxazoline (**L34**) decreases the ee of **154** to 35%, while still delivering the product in 81% yield. Finally, following this pattern, **L35** delivers **154** in 95% yield, but 33% ee. However, while the yield of **154** is consistently high amongst these alkyl-substituted ligands, **L20** with ^{t}Bu branching directly adjacent to the oxazoline proves to be too sterically hindered for productive reactivity. With these trends in mind, we must design and synthesize more alkyl-substituted BiOX ligands with sec-alkyl branching adjacent to the oxazoline, but with different branching scaffolds on the substituents, to try in this system.

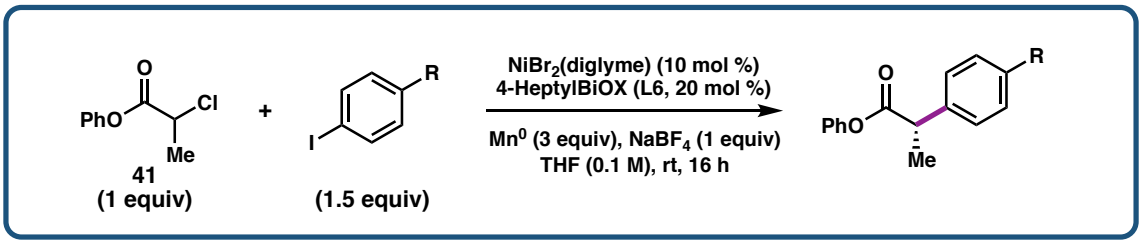
***Table 3.15**. Alkyl bi(oxazoline) ligand substitution effects on cross-coupling.*

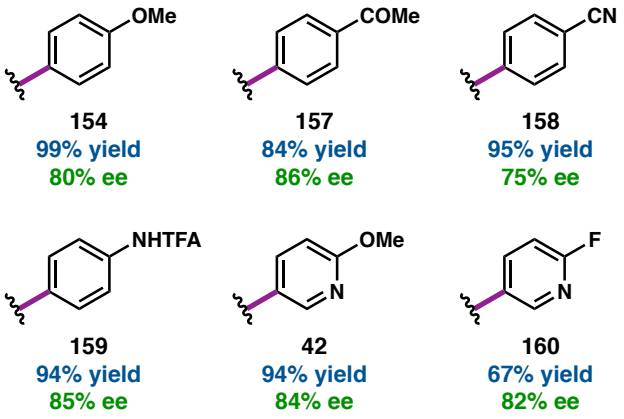


3.3.3 Improved Substrate Scope

Utilizing **L6** and running the cross-coupling of α-chloroesters and aryl iodides in THF with $NaBF_4$ as an additive has greatly expanded the substrate scope of the reaction. These seemingly subtle changes from the original DMPU/THF system have increased both the yields and ee of the cross-coupled products from several aryl iodides (Table 3.16). Substrates containing both electron-withdrawing and –donating groups are now coupling in up to 99% yield and 86% ee (Table 3.16). Notably, pyridine substrates **42** and **160** are now coupled in high yields, 94% and 67%, paving the way for further investigation into the use of (hetero)aryl iodides in this reaction. We look forward to full exploration of the functional groups tolerated in this reaction, as well as their substitution on the aryl iodide.

Table 3.16. *Current aryl iodide substrate scope.*[a]

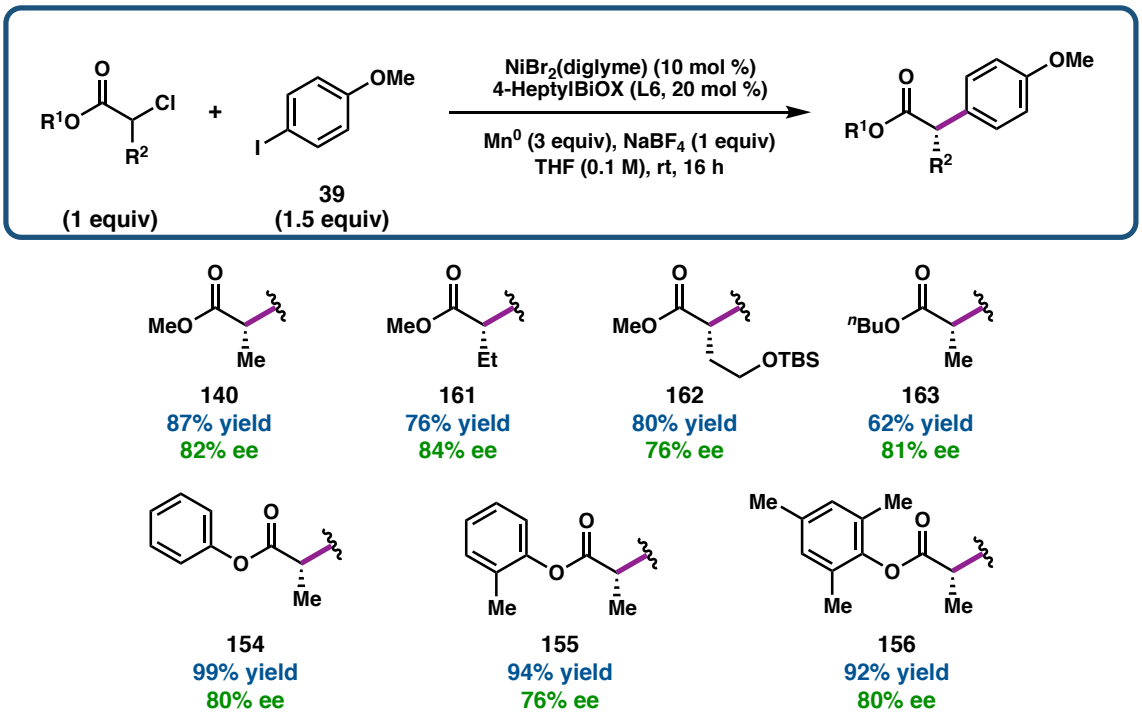




[a] NMR yields, reactions conducted on 0.05 mmol scale under a N_2 atmosphere. % ee determined by SFC using a chiral stationary phase.

More impressive, however, is the largely expanded tolerance of α-chloroester substrates in this transformation (Table 3.17). Before, methyl-2-chloropropionate (**3**) was the only effective C(sp^3) coupling partner. Now, several alkyl esters (**161**–**163**), as well as aryl esters (**154**–**156**) are tolerated in good to excellent yield and good ee. Moreover, groups larger than methyl are tolerated in the α-position, including ethyl (**161**) and silyloxyethyl (**162**). The promising expansion of the scope with more optimized conditions makes us hopeful for further substrate exploration and potential applications to the synthesis of bioactive targets.

***Table 3.17**. Current α-chloroester substrate scope.*[a]

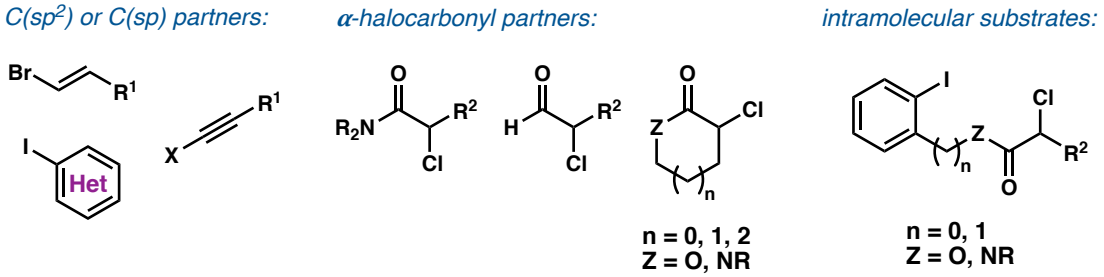


[a] NMR yields, reactions conducted on 0.05 mmol scale under a N_2 atmosphere. % ee determined by SFC using a chiral stationary phase.

3.3.4 Future Directions

In addition to novel ligand design and synthesis, we will seek to develop related reactions, including the cross-coupling of α-haloamides and α-haloaldehydes (Scheme 3.4). The latter substrates, which are prone to epimerization under mild conditions, will probe the mildness of the reaction conditions; given our success in preparing enantioenriched α-arylketones by Ni-catalyzed reductive coupling,[1] we are optimistic about this endeavor. The use of heteroaryl, vinyl, and alkynyl halides as coupling partners will also be investigated. As part of these studies, intramolecular reactions to make enantioenriched lactones and lactams will also be explored.

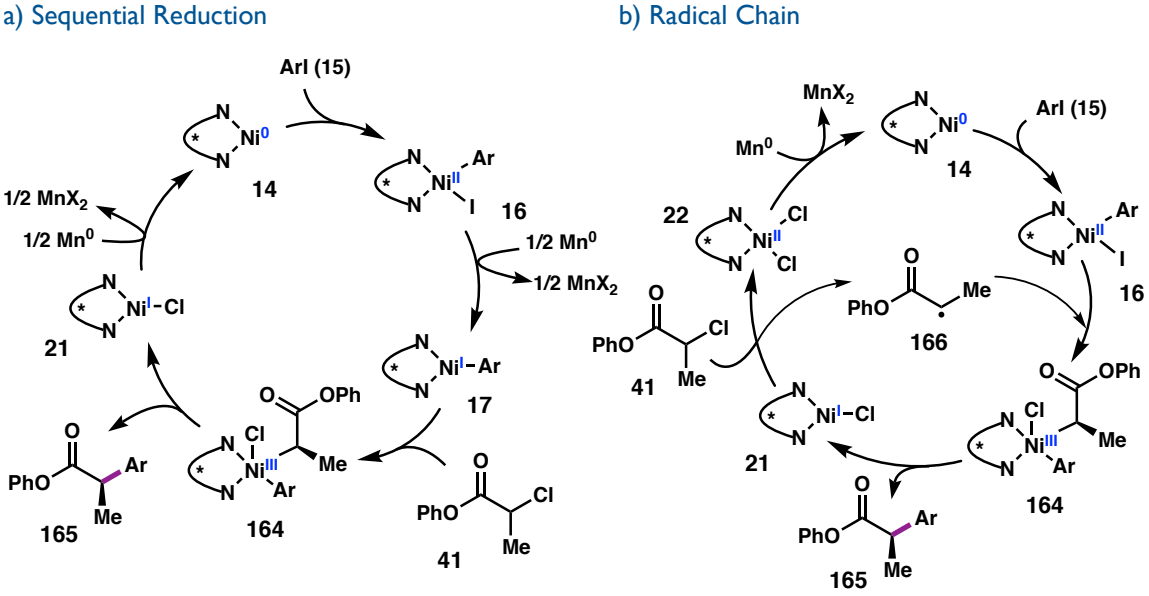
Scheme 3.4. *Further substrates for investigation.*



3.4 MECHANISTIC STUDIES

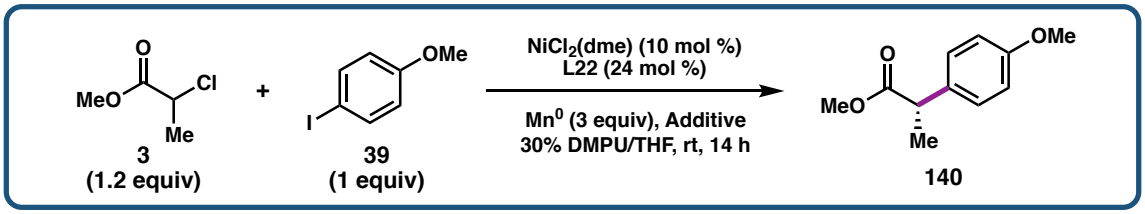
As described in **Chapter 1**, we hypothesize that asymmetric reductive cross-couplings of radical-stabilized C(sp^3) electrophiles may proceed through the intermediacy of prochiral radicals generated from a halide abstraction event. This can occur in either a sequential reduction mechanism, in which halide abstraction and radical addition occur rapidly in a radical rebound process (Figure 3.1a), or a radical chain reaction mechanism with a long-lived, cage escaped radical intermediate (Figure 3.1b).

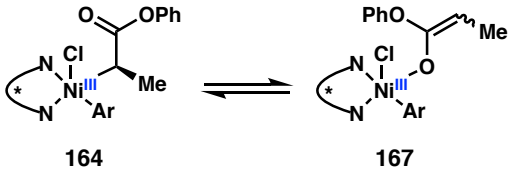
Figure 3.1. *Mechanistic hypotheses.*



A unique feature of the α-chloroester C(sp^3) electrophile is the ability of Ni to bind the substrate in an η^3 fashion. Competing carbon-bound and oxygen-bound Ni species (**167**, Table 3.18) could racemize a single diastereomer of Ni(III) complex **164** formed in an enantiodetermining oxidative addition step. We hypothesized that the addition of a Lewis acid could bind the carbonyl and favor a carbon-bound Ni species (**164**, Table 3.18). The reaction was treated with various Lewis acids to probe this phenomenon with an improvement in ee (Table 3.18). Unfortunately, these additives mostly inhibited reactivity and did not have a positive effect on the enantioselectivity.

Table 3.18. *Investigation of Lewis acids.*



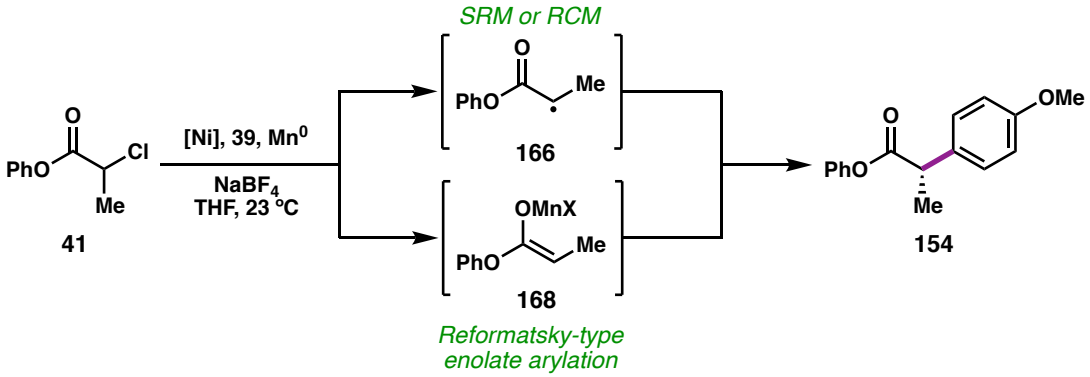


Entry	Additive	Yield 140 (%)	ee 140 (%)
1	none	41	69
2	$MnCl_2$	5	61
3	$ZnCl_2$	5	52
4	LiCl	2	47
5	$Sc(OTf)_3$	53	61
6	$Yb(OTf)_3$	13	45
7	$Zn(OTf)_2$	0	—

It is also possible that, rather than the sequential reduction mechanism or radical chain reaction mechanism hypothesized to be operative, the Ni-catalyzed reaction between **41** and an aryl iodide proceeds by a more conventional enolate arylation mechanism in which *in situ* formation of a manganese enolate is operative (Scheme

3.5).[38] If so, the steric and electronic profile of the metal enolate could potentially influence the reactivity and selectivity of the system.[39,40]

Scheme 3.5. *Possible Reformatsky-type enolate arylation mechanism.*



If this reaction proceeds by the formation of a manganese enolate, reduction of **41** by Mn^0 would provide enolate **168** (Scheme 3.5), which could undergo transmetalation with Ni(II) complex **16** to intercept a conventional enolate arylation mechanism. Thus, Mn^0 would not be required to turn over the catalyst, only to generate the enolate. In addition to determining the order in each component using kinetic analysis, it should be possible to distinguish between the Reformatsky-type mechanism and a radical chain reaction mechanism by stoichiometrically preparing the relevant manganese enolate.[41,42] If exposure of **168** to the standard reaction conditions in the absence of Mn^0 provides **154** in the same ee as the catalytic conditions, it would provide support for the Reformatsky-type mechanism. Alternatively, LNi(II)(Ph)I (**16**) could be prepared and treated with α-chloroester **41** in the presence and absence of Mn^0; if a radical chain reaction mechanism is operative, then addition of **16** to **41** would be expected to provide **154** in the absence of Mn^0.

3.5 CONCLUSION

In conclusion, the development of a Ni-catalyzed stereoconvergent reductive cross-coupling of α-chloroesters and aryl iodides to access enantioenriched α-arylpropionates is currently underway in our laboratory. Identification of a phenyl ester $C(sp^3)$ coupling partner suggests a promising substrate scope. Importantly, the enantioenriched α-arylated esters are stable and do not suffer from racemization under the mild reaction conditions. Further ligand synthesis is required to improve the enantioselectivity of the reaction.

3.6 EXPERIMENTAL SECTION

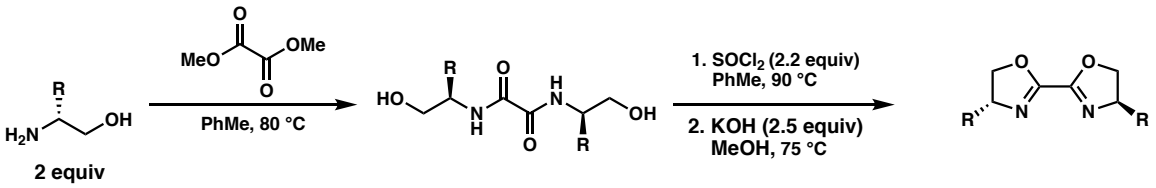
3.6.1 Materials and Methods

Unless otherwise stated, reactions were performed under a nitrogen atmosphere using freshly dried solvents. Methylene chloride (DCM), diethyl ether (Et_2O), tetrahydrofuran (THF), 1,4-dioxane and toluene (PhMe) were dried by passing through activated alumina columns. All other commercially obtained reagents were used as received unless specifically indicated. Aryl iodides were purchased from Sigma Aldrich, Combi-Blocks, or Astatech. Manganese powder (>99.9%) was purchased from Sigma Aldrich. $NiBr_2$(diglyme) was purchased from Strem. All reactions were monitored by thin-layer chromatography using EMD/Merck silica gel 60 F254 pre-coated plates (0.25 mm). Silica gel and basic alumina column chromatography was performed as described by Still et al. (W. C. Still, M. Kahn, A. Mitra, *J. Org. Chem*. **1978**, *43*, 2923.) using silica gel (particle size 0.032–0.063) purchased from Silicycle and aluminum oxide (activated, basic, Brockmann I, 58 Å pore size, powder) purchased from Sigma-Aldrich. ^1H and ^{13}C NMR were recorded on a Varian Inova 500 (at 500 MHz and 125 MHz respectively) or a Bruker Avance III HD with Prodigy cyroprobe (at 400 MHz and 101 MHz respectively). ^1H and ^{19}F NMR spectra were recorded on a Varian Inova 300 (at 300 MHz and 282 MHz, respectively). NMR data is reported relative to internal chloroform (^1H, δ = 7.26, ^{13}C, δ = 77.0) and C_6F_6 (^{19}F, δ = –164.9). Data for ^1H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicity and qualifier abbreviations are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm^{-1}). Analytical

SFC was performed with a Mettler SFC supercritical CO_2 analytical chromatography system with Chiralcel AD-H, OD-H, AS-H, OB-H, and IA columns (4.6 mm x 25 cm). SFC analysis performed at 100.0 bar and 40 ºC. HRMS were acquired using either an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI), atmospheric pressure chemical ionization (APCI), or mixed (MM) ionization mode.

3.6.2 Ligand Preparation

3.6.2.1 *General Procedure 1 for bi(oxazoline) ligand synthesis.*



Amino alcohol (2 equiv) and dimethyloxalate (1 equiv) were dissolved in PhMe (0.05 M) and heated to 80 °C. The reaction was allowed to stir overnight. Reaction was cooled to room temperature and concentrated *in vacuo* and placed under vacuum at room temperature for 3 h to remove all excess MeOH and afford the crude diol. The crude diol was dissolved in PhMe (0.15 M) and heated to 70 °C whereupon thionyl chloride (2.2 equiv) was added. Reaction was stirred at 70 °C for 30 minutes then heated to 90 °C for 90 minutes. The reaction was cooled to room temperature and poured into 20% KOH solution cooled to 0 °C. The aqueous layer was separated and extracted (3x) with DCM and the combined organic layers were washed with 20% KOH solution, $NaHCO_3$ and brine. The organic layer was dried with Na_2SO_4, filtered through a pad of Celite, and concentrated under reduced pressure to afford the dichloride. The crude dichloride was

immediately dissolved in MeOH (0.1 M) and KOH (2.5 equiv) was added. The reaction was heated to reflux for 14 hours. The reaction was cooled to room temperature and concentrated to remove MeOH. The crude mixture was purified by silica gel chromatography to afford pure ligand.

3.6.3 Substrate Preparation

3.6.3.1 *General Procedure 2 for preparation of aryl iodides.*[44]

To a flame-dried flask was added copper(I) iodide (0.05 equiv), followed by 1,4-dioxane and *N*,*N*'-DMEDA (0.10 equiv), then aryl bromide (1.0 equiv) and sodium iodide (2.0 equiv). The reaction was heated to 110 ºC for 24 h. Upon cooling to room temperature, the reaction was filtered over Celite and washed with DCM. The solution was concentrated to afford the aryl iodide as a light solid. Aryl iodides were employed in the coupling reactions without further purification. Purification by recrystallization was possible for all substrates, but was generally unnecessary.

3.6.3.2 *General Procedure 3 for preparation of α-chloroesters.*

To a solution of 2-chloropropionic acid chloride (1 equiv) was added alcohol (1 equiv) at 0 ºC in CH_2Cl_2 (0.65 M). Amine base (1.1 equiv) was added dropwise and HCl evolved. The reaction is gradually warmed to room temperature and stirred for 4 h. Water was added to quench the reaction and EtOAc was added for dilution. The organic layer was separated and the aqueous layer was extracted with EtOAc (3x), dried over Na_2SO_4,

and concentrated to yield pure product after filtration through silica with 10% EtOAc/hexanes.

3.6.4 Ni-Catalyzed Enantioselective Reductive Cross-Coupling

3.6.4.1 General Procedure 4: Reaction on 0.05 mmol scale.

On a bench-top, to a 1-dram vial were added a stir bar, **L6** (3.4 mg, 20 mol %, 0.01 mmol), Mn^0 (8.2 mg, 3 equiv, 0.15 mmol), and aryl iodide, if solid (1.5 equiv, 0.1 mmol). The vial was transferred into a N_2-filled glovebox and charged with $NiBr_2$(diglyme) (1.8 mg, 10 mol %, 0.005 mmol), $NaBF_4$ (5.4 mg, 0.5 equiv, 0.025 mmol) and anhydrous THF (0.5 mL, 0.1 M). Finally, the aryl iodide (if liquid) was added, followed by α-chloroester (1.0 equiv, 0.05 mmol) and the vial was sealed with a Teflon cap and removed from the glovebox. The mixture was stirred at 480 rpm over a period of 14 hours. The reaction was quenched by diluting with 1 mL of 20% EtOAc/hexanes and pushing through a short plug of silica with 20% EtOAc/hexanes into a scintillation vial (approximately 10 mL collected). The solution was concentrated and the crude reaction mixture was analyzed by ^{1}H NMR and chiral SFC.

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Chapter 4

Nickel-Catalyzed Asymmetric Reductive Cross-Coupling of N-Hydroxyphthalimide Esters and Alkenyl Bromides◊

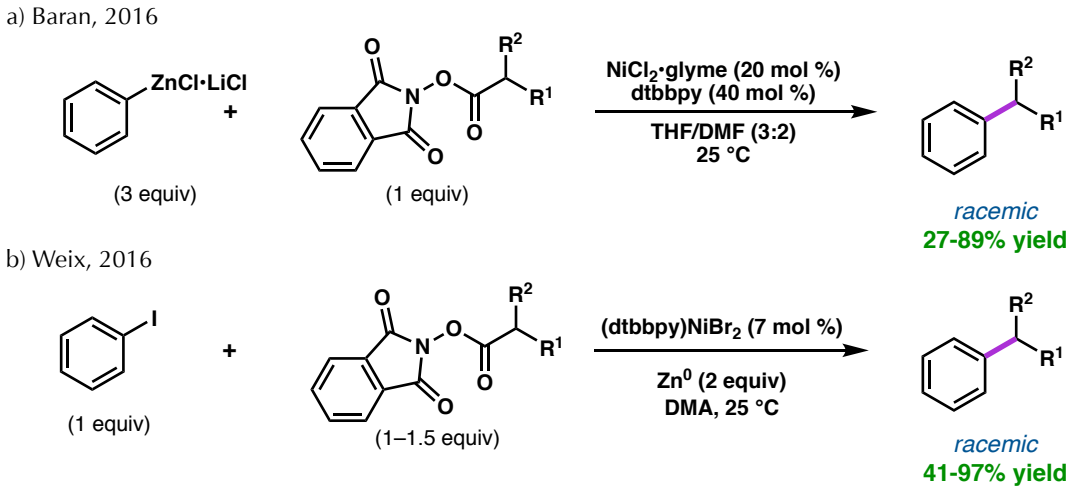
4.1 INTRODUCTION

As part of our efforts to develop asymmetric cross-coupling reactions that employ a variety of C(sp^3) electrophiles, we became interested in the coupling of redox-active *N*-hydroxyphthalimide (NHP) esters.[1,2] These electrophiles are prepared from the corresponding carboxylic acids, and have been recently demonstrated as C(sp^3) substrates for Ni-catalyzed Negishi,[3,4] Suzuki,[5] and reductive cross-coupling[6] reactions to generate racemic products (Scheme 4.1).[7,8] However, NHP esters have not been demonstrated as competent coupling partners in Ni-catalyzed *enantioselective* cross-coupling reactions. We recognized that the use of NHP esters might be advantageous for substrates in which

◊ Portions of this chapter have been reproduced from published studies (see reference **30**) and the supporting information found therein. The research presented in this chapter was completed in collaboration with Dr. Naoyuki Suzuki, then a postdoctoral scholar in the Reisman group, and Julie Hofstra, a graduate student in the Reisman group.

the corresponding alkyl chlorides are unstable or challenging to prepare. We recognize that many feedstock chemicals contain carboxylic acids, and finding a straightforward means of engaging carboxylic acid derivatives in asymmetric cross-coupling reactions would be of great use to the synthetic community.

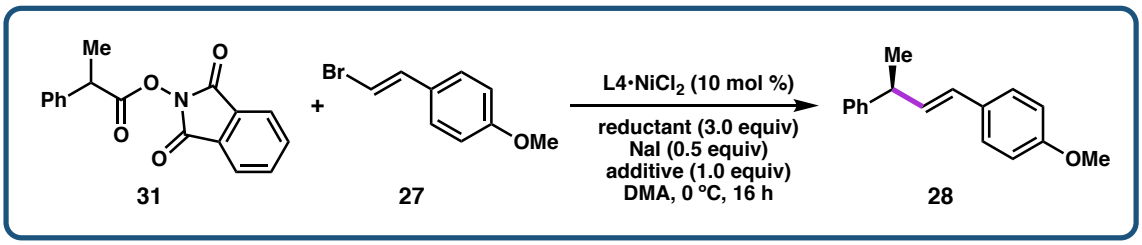
Scheme 4.1. *NHP esters in cross-coupling reactions.*

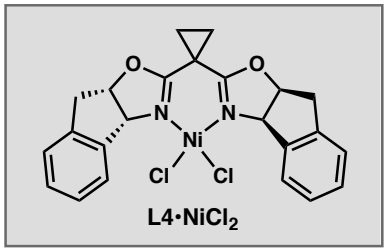


4.2 REACTION DEVELOPMENT

Our efforts began with NHP ester **31**, which is prepared in one step from commercially available 2-phenylpropanoic acid. Subjection of **31** and **27** to our optimal conditions developed for the reductive cross-coupling of alkenyl bromides and benzyl chlorides[9] provided only trace quantities of product (Table 4.1, entry 1), highlighting the challenges presented by this new C(sp^3)-electrophile. Slightly improved results could be obtained under the same conditions by adding 1.0 equiv TMSCl (Table 4.1, entry 2). An investigation of alternative reductants revealed that tetrakis(*N*,*N*-dimethylamino)ethylene (TDAE) substantially increased the reactivity, delivering **28** in 61% yield and 95% ee (Table 4.1, entries 2–4).[10]

Table 4.1. *Reductant investigation.*



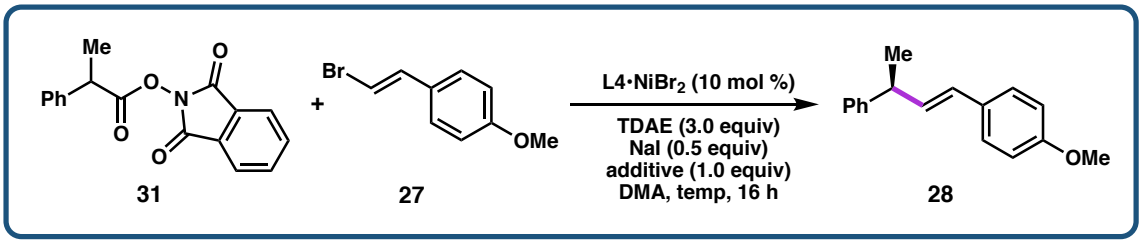


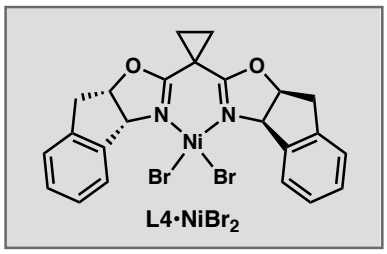
Entry	Reductant	Additive	% Yield 28	% ee 28
1	Mn^0	none	trace	—
2	Mn^0	TMSCl	27	90
3	Zn^0	TMSCl	38	64
4	TDAE	TMSCl	61	95

Monitoring the reaction progress at room temperature indicated that (*E*)-1-(2-chlorovinyl)-4-methoxybenzene was forming and accumulating under the reaction conditions, presumably through a Ni-catalyzed halide exchange process.[11,12] Since the alkenyl chloride does not readily engage in the cross-coupling reaction, we hypothesized that the yield of **28** could be improved by removing chloride from the reaction, thus preventing formation of this unproductive side product. Indeed, the use of TMSBr instead of TMSCl, and the use of **L4·NiBr$_2$** as the catalyst, furnished product **28** in 75% yield and 92% ee (Table 4.2, entry 2). By decreasing the reaction temperature to –7 °C, and using only 1.5 equivalents of TDAE, **28** could be obtained in 80% yield and 96% ee (Table 4.2, entry 4). Unfortunately, the reaction mixture freezes at temperatures lower than –7 ºC. Interestingly, in the coupling of (1-chloroethyl)benzene (**24**), TDAE provides the cross-coupled product in only 23% yield and 94% ee. Running the reaction under the optimal conditions, but omitting TMSBr, confirms that this additive is critical for obtaining high yields of **28** (Table 4.2, entry 3). The role of TMSBr under the optimal

conditions, which do not employ a metal reductant, is unclear. TMSCl has been proposed to activate Mn^0 or Zn^0.[13,14] We note that these optimal reaction conditions employ a 1:1 stoichiometry of the two electrophiles and only 10 mol % catalyst loading.

Table 4.2. *Additive and temperature investigation.*





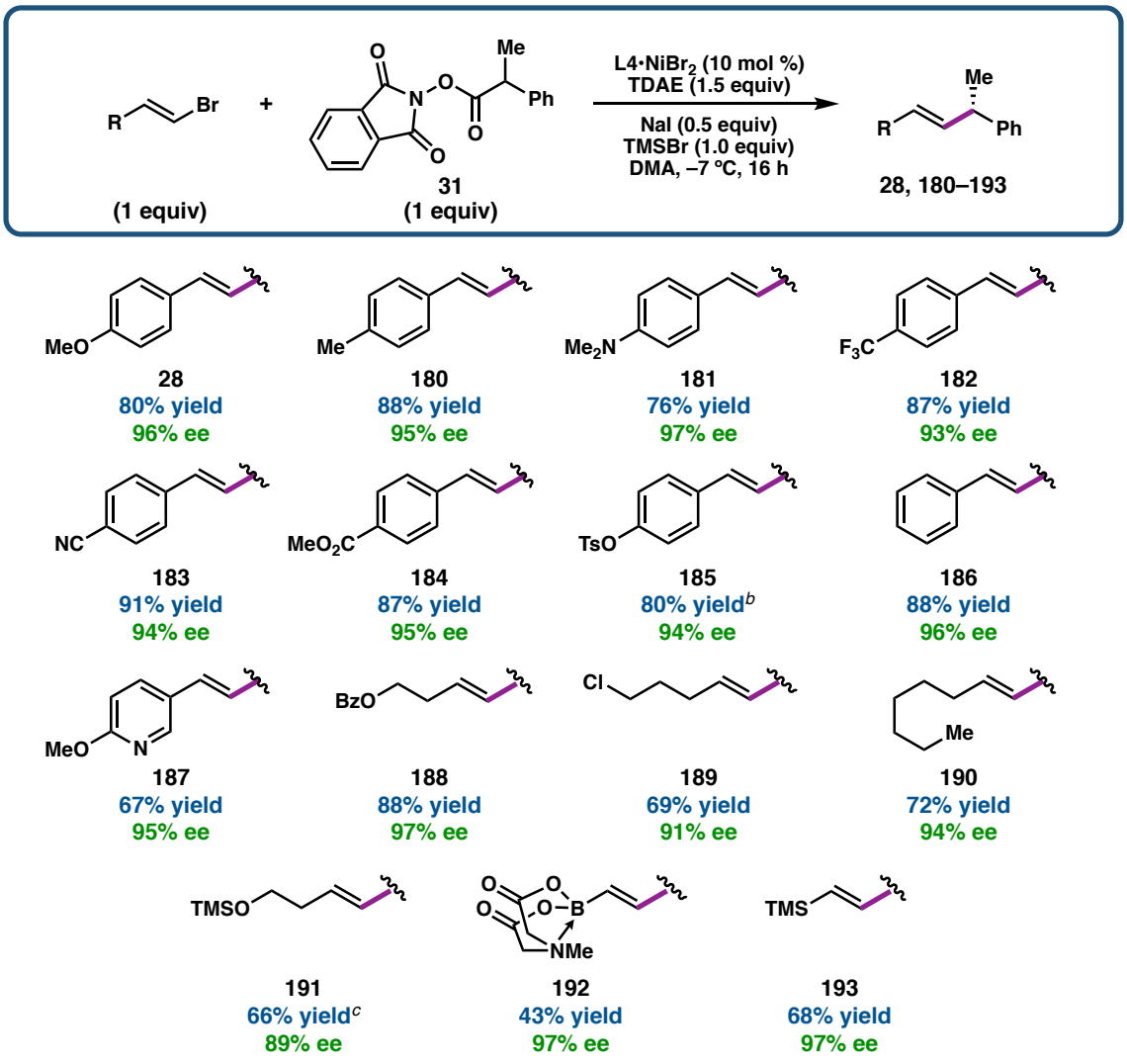
Entry	Additive	temp (°C)	% Yield 28	% ee 28
1	TMSCl	0	61	95
2	TMSBr	0	75	92
3	none	0	19	88
4	TMSBr	–7	80	96

4.3 SUBSTRATE SCOPE

To demonstrate the scope of the reaction, a series of (*E*)-alkenyl bromides was cross-coupled with NHP ester **31**, providing the corresponding products in uniformly good yield and high ee (Table 4.3). The reaction exhibits good tolerance of Lewis basic functional groups: for example, anilines (**181**), nitriles (**183**), and esters (**184**, **188**) can be incorporated into the substrate without detriment to the yield or enantioselectivity. A pyridine-containing alkenyl bromide also performs well, providing **187** in 67% yield and 95% ee. In addition, alkyl-substituted alkenyl bromides react smoothly, providing the corresponding products in good yield and ee (**188**–**191**). An alkenyl bromide possessing a free alcohol couples efficiently, although silylation occurs under the reaction conditions to give silyl ether **191**. The silyl ether can easily be cleaved with a mild acid workup; in

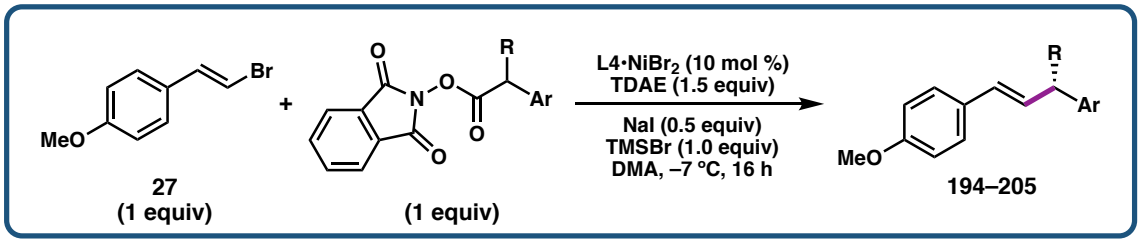
this case it was preserved in order to facilitate purification. It is notable that alkenyl MIDA-boronate **192** and alkenyl silane **193** can be prepared in 97% ee from commercially available vinyl bromides and could be used in further cross-couplings. To demonstrate that this method can be used preparatively, the coupling between **31** and **27** was conducted on 5.0 mmol scale, which delivered 918 mg (77% yield) of **28** in 91% ee.

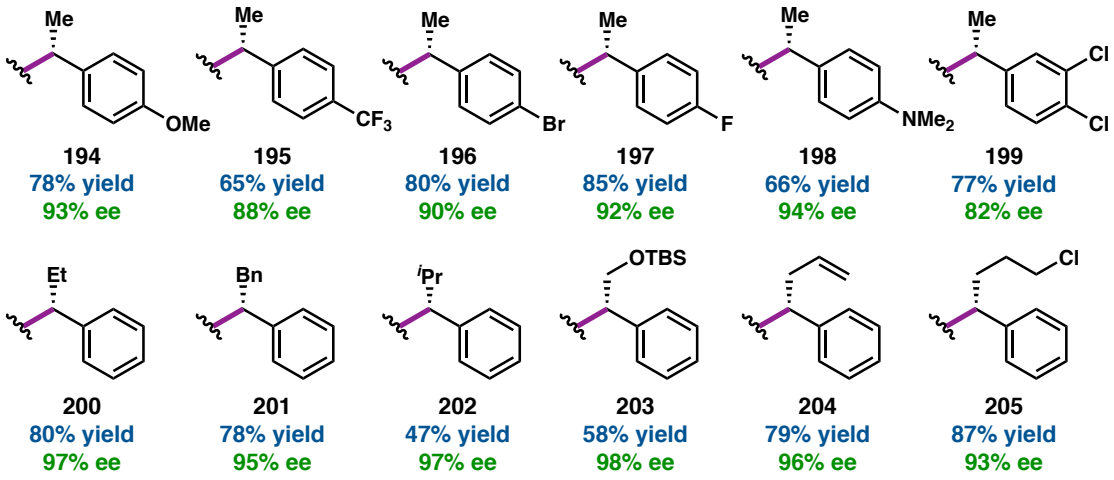
Table 4.3. *Alkenyl bromide substrate scope.*[a]



[a] Isolated yields, reactions conducted on 0.2 mmol scale under an N_2 atmosphere in a glovebox. % ee determined by SFC using a chiral stationary phase. [b] 1.5 equiv NHP ester used. [c] 2.0 equiv TMSBr used; the alcohol silylated under reaction conditions.

***Table 4.4**. NHP ester substrate scope.* [a]





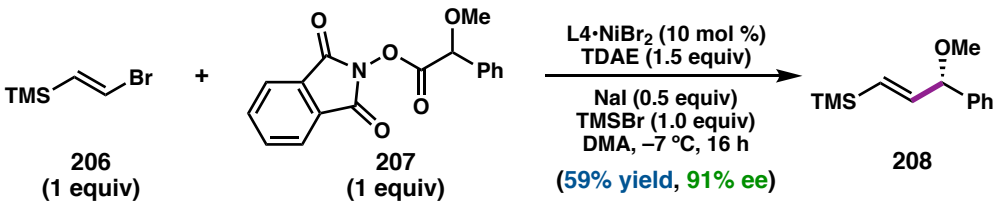
[a] Isolated yields, reactions conducted on 0.2 mmol scale under an N_2 atmosphere in a glovebox. % ee determined by SFC using a chiral stationary phase.

The reaction also exhibits broad scope for the NHP ester coupling partner, delivering good yields and high enantioselectivities for a range substrates bearing substitution on the arene or at the benzylic position (Table 4.4). In certain cases (e.g. **194**–**196**), the NHP esters cross-couple with improved yield relative to the corresponding benzyl chlorides (under the previously reported conditions).[9] Moreover, aniline **198** can be prepared in 66% yield and 94% ee; this compound could not be accessed via our previously reported benzylic chloride coupling due challenges in preparing and handling 4-(chloro(phenyl)methyl)-*N*,*N*-dimethylaniline under standard conditions. Higher substitution at the benzylic position is also tolerated (**200**–**205**), although the yield begins to decrease with larger groups (e.g. ^{i}Pr, **202**). Notable products include **203**, which

incorporates a siloxy group, **204**, containing an alkene, and **205**, which has an alkyl chloride. Perfect chemoselectivity for cross-coupling of the NHP ester over the primary alkyl chloride is observed.

Although the primary focus of this study was the cross-coupling of NHP esters with alkyl substituents at the benzylic position, we have also have begun to investigate substrates containing heteroatom substitution (Scheme 4.2). Reaction of α-methoxy ester **207** proceeds smoothly, furnishing allylic ether **208** in good yield and ee. This highlights an advantage of the NHP ester for certain C(sp^3) electrophiles, as the corresponding α-chloroether substrate is unstable and difficult to work with.

Scheme 4.2. *Reaction of α-methoxy NHP ester.*

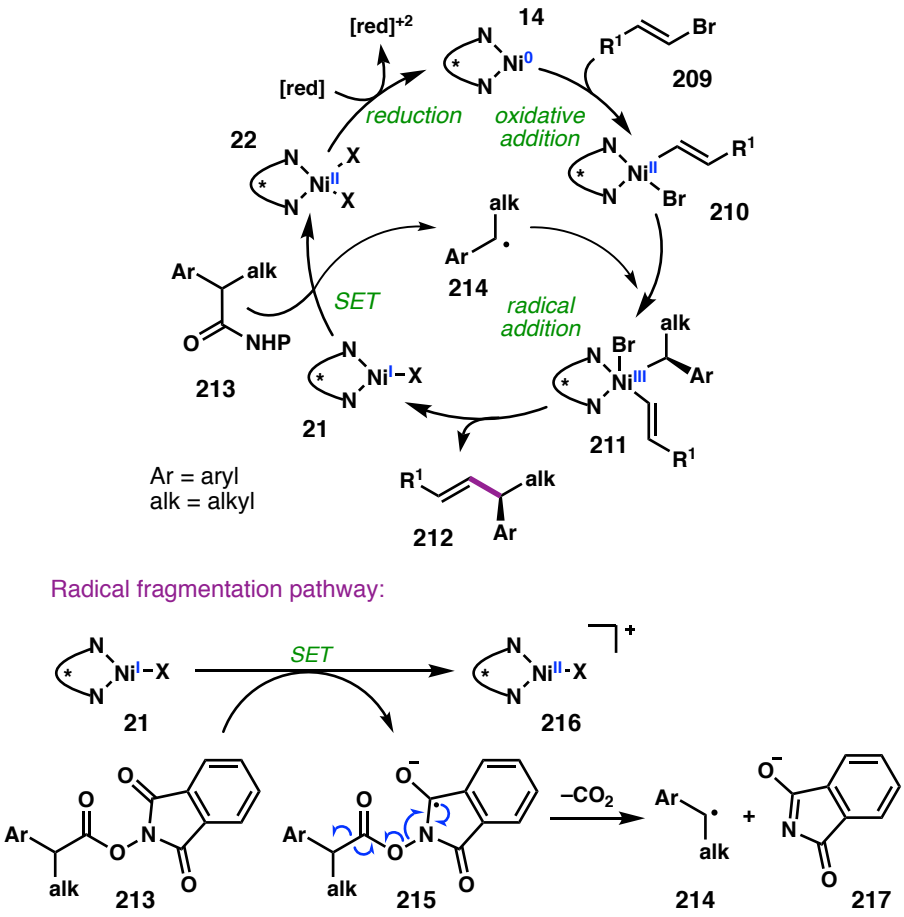


4.4 MECHANISTIC INVESTIGATIONS

We propose a catalytic cycle similar to the radical chain reaction mechanism described in **Chapter 2** for the cross-coupling of NHP esters and alkenyl bromides (Figure 4.1). Starting from a Ni(0) species (**14**), oxidative addition with alkenyl bromide **209** produces Ni(II)-alkenyl complex **210**. This can undergo radical addition with a benzylic radical (**214**) generated from single electron transfer (SET) with a Ni(I)-halide species (**21**), to form Ni(III) **211**. This Ni(III) complex can undergo reductive elimination to form the desired product **212** and a Ni(I) species, which can then undergo single-electron transfer (SET) with NHP ester substrate **213** to form Ni(II)-dihalide **22**. We hypothesize that this SET event results in the oxidation of Ni(I) species **21** to cationic

Ni(II) (**216**) and the reduction of phthalimide **213**. The resultant radical anionic species **215** could then decarboxylate to give the alkyl radical (**214**) and an equivalent of anionic phthalimide (**217**). We believe a role of TMSBr in the reaction could be to trap this stoichiometric phthalimide species to prevent reaction inhibition. Reduction of **22** regenerates **14** and closes the cycle.

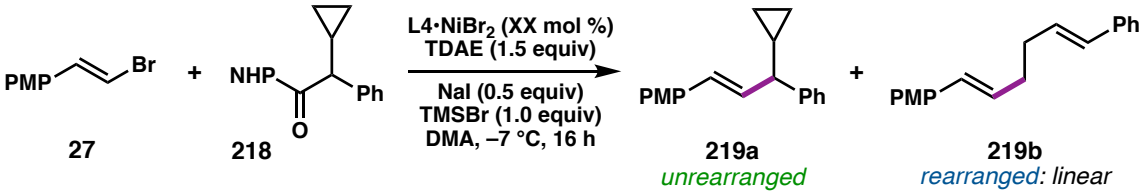
Figure 4.1. *Proposed catalytic cycle for reductive alkenylation of NHP esters.*



To probe for the intermediacy of a radical species, NHP ester **218** was prepared and subjected to the standard cross-coupling conditions (Scheme 4.3, 10 mol % **L4•NiBr$_2$**). A 42% combined yield of the coupled products **219a–c** was obtained. It has been shown that for phenyl substituted cyclopropyl carbonyl radicals, the ring opening is

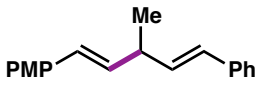
reversible and that the cyclopropane species is favored at lower temperatures.[15,16] The fact that **219b** and **219c** predominate, even though they derive from the minor equilibrium species, perhaps indicates that the rate of radical recombination with nickel is sensitive to the steric profile of the radical. When the catalyst loading of **L4•NiBr$_2$** was varied, the ratio of **219a** to total ring opened product (**219b** + **219c**) was found to increase at higher nickel concentrations. This Ni-dependent behavior suggests that the mechanism proceeds through a cage-escaped radical, which at higher concentrations of **L4•NiBr$_2$**, can competitively recombine with nickel before undergoing ring scission.[17]

Scheme 4.3. *Radical clock study.*



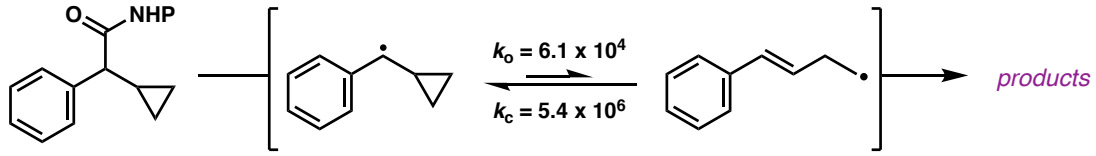
27 218 **219a** *unrearranged* **219b** *rearranged: linear*

Entry	L4•NiBr$_2$ mol %	Total Yield 219 (%)	Ratio 219a : [219b + 219c]
1	5	44	12 : 88
2	10	42	16 : 84
3	20	49	20 : 80



219c *rearranged: branched*

Mechanistic Hypothesis:



Further studies of the mechanism are ongoing; it is unclear at this time whether the absolute stereochemistry is set during the oxidative addition or reductive elimination[18] steps. We do note, however, that the products are formed in similar ee when using either the NHP esters under the conditions reported here or the benzyl chloride

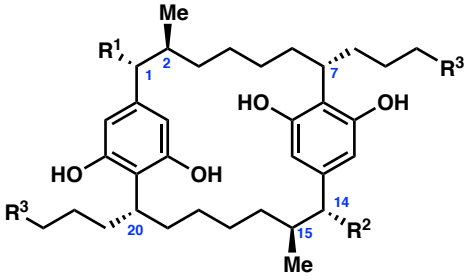
using the conditions reported previously,[9] which suggests that the reactions proceed through the same stereochemistry-determining step.

4.5 CYLINDROCYCLOPHANE NATURAL PRODUCTS

4.5.1 Background and significance

The cylindrocyclophanes are a family of cytotoxic natural products isolated from the photosynthetic cyanobacteria *Cylindrospermum licheniforme* Kützing (ATTC 29204).[19–21] Many of these natural products are C_2-symmetric, featuring a unique 22-membered, [7,7]-paracyclophane skeleton (Figure 4.2). Isotopic sodium acetate labeling studies revealed the polyketide origin of these paracyclophane natural products and the highly symmetric nature of the observed isotope patterns suggested a head-to-tail dimerization of a monomer unit.[19,20] Recently, Balskus and coworkers elucidated details of the biosynthesis through the use of genome-sequencing and *in vivo* and *in vitro* experiments.[22,23] The enzymatic reactions involved in the paracyclophane formation include an enantioselective chlorination of an unactivated C(sp^3)–H bond, followed by first an intermolecular stereospecific aromatic ring alkylation, then a second, intramolecular alkylation to complete the macrocyclization.[24]

Figure 4.2. *Cylindrocyclophanes A–F.*



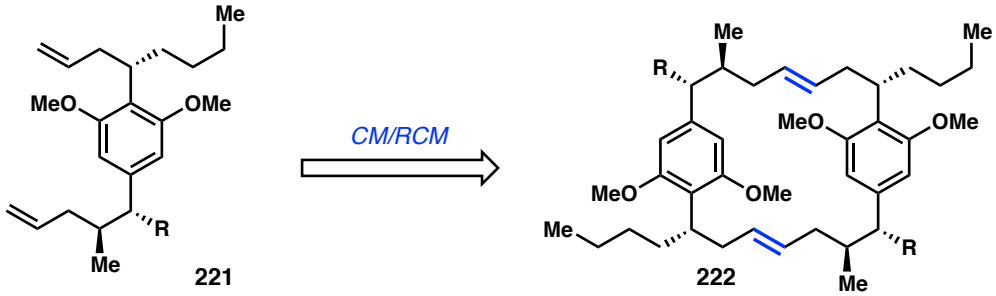
220A-F

	R^1	R^2	R^3
A	OH	OH	Me
B	OH	OAc	Me
C	OH	H	Me
D	OAc	OAc	Me
E	OAc	H	Me
F	H	H	Me
A_4	OH	OH	$CHCl_2$

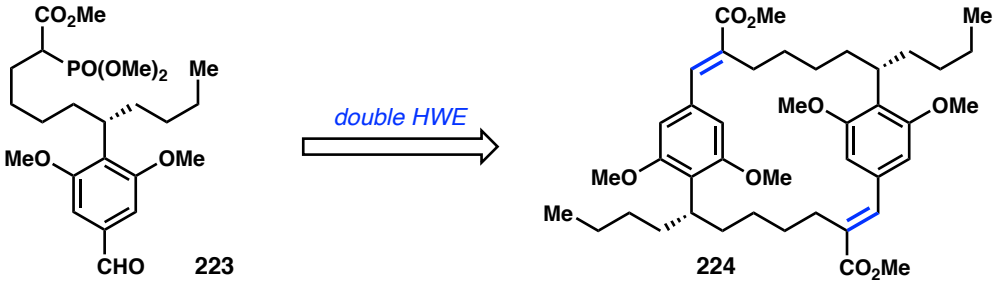
Initial reports found that several cylindrocyclophanes are cytotoxic against KB and LoVo tumor cells lines (IC_{50} = 2-10 μg/mL).[20] Orjala and coworkers determined that chlorinated cylindrocyclophanes inhibit the 20S proteasome, an important protein in the control of apoptosis, differentiation and proliferation in healthy and cancer cells.[25] It is believed the chloroalkyl moiety is important for inhibition of the proteasome, and that the presence of the hydroxyl groups at C1 and C14 contribute to binding.

Scheme 4.4. *Prior syntheses of the cylindrocyclophanes that employ head-to-tail cyclodimerization approaches.*

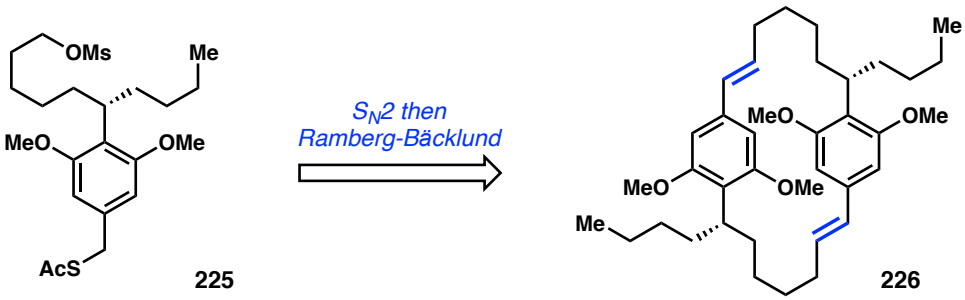
a) Smith (2000)



b) Hoye (2000)

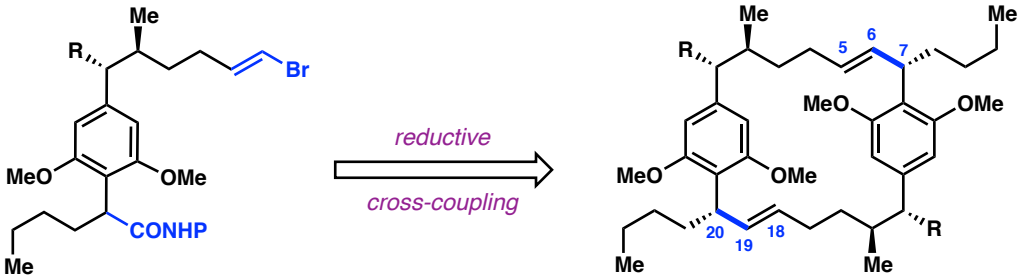


c) Nicolaou (2010)



Leveraging the C_2-symmetry of these molecules, previous synthetic approaches have employed head-to-tail cyclodimerization strategies (Scheme 4.4). In 2000, Smith and coworkers prepared cylindrocyclophane A and F by using a cross-metathesis/ring-closing metathesis (CM/RCM) reaction of diolefin **221** to form macrocycle **222** (Scheme 4.4a), which could be elaborated to either cylindrocyclophane A or F, depending on the oxidation pattern.[26,27] The same year, Hoye reported a synthesis of cylindrocyclophane A in which Masamune-Roush conditions for a double Horner-Wadsworth-Emmons dimerization were used to construct macrocycle **224** (Scheme 4.4b).[28] More recently, Nicolaou and coworkers reported the use of a Ramberg-Bäcklund olefination reaction to construct **226**, possessing the cylindrocyclophane core (Scheme 4.4c).[29]

Scheme 4.5. *Macrocyclization by a Ni-catalyzed reductive cross-coupling.*



R=H (227), R=OTMS (228) **R=H (229), R=OTMS (230)**

In considering an approach to the cylindrocyclophanes, we envisioned that the target compounds could be prepared from macrocycle **229** or **230**, possessing C5–C6 and C18–C19 unsaturation (Scheme 4.5). Macrocycle **229** would arise from a Ni-catalyzed double asymmetric reductive cross-coupling of the bis-electrophile **227**, in which the key C6–C7 and C19–C20 bonds would be formed while also setting the C7/C20 stereogenic centers. This strategic application of an asymmetric reductive cross-coupling is particularly well-suited for the preparation of the macrocyclic cylindrocyclophanes, since

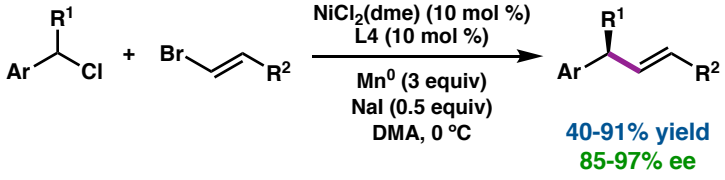
it obviates the need to prepare a dimerization substrate containing both an electrophile and a reactive organometallic functionality—as would be required for a conventional cross-coupling. Moreover, investigation of the key reductive alkenylation will advance the scope and deepen our understanding of these new and underexploited reductive cross-coupling transformations.

4.5.2 Preliminary studies

In 2014, our laboratory reported a Ni-catalyzed asymmetric reductive cross-coupling between alkenyl bromides and benzyl chlorides, which employ chiral BOX ligand **L4** and use Mn^0 as a stoichiometric reductant (Scheme 4.6a).[9] In 2017, the scope of this transformation was expanded through the use of *N*-hydroxyphthalimide (NHP) esters as the C(sp^3) electrophile, allowing for the incorporation of electron-rich functional groups on the arene (this chapter, Scheme 4.6b).[30] In the case of the NHP esters, the optimal conditions used tetrakisdimethylaminoethylene (TDAE) as the stoichiometric reductant and TMSBr as an activating agent.

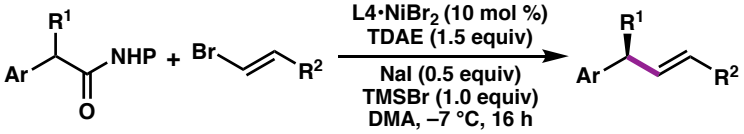
Scheme 4.6. *Asymmetric reductive cross-coupling reactions with alkenyl bromides.*

a) Reisman, 2014

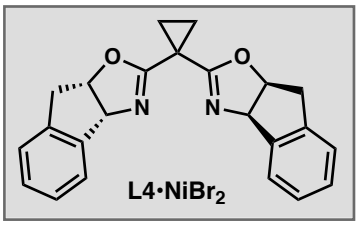


40-91% yield
85-97% ee

b) Reisman, 2017 (this chapter)



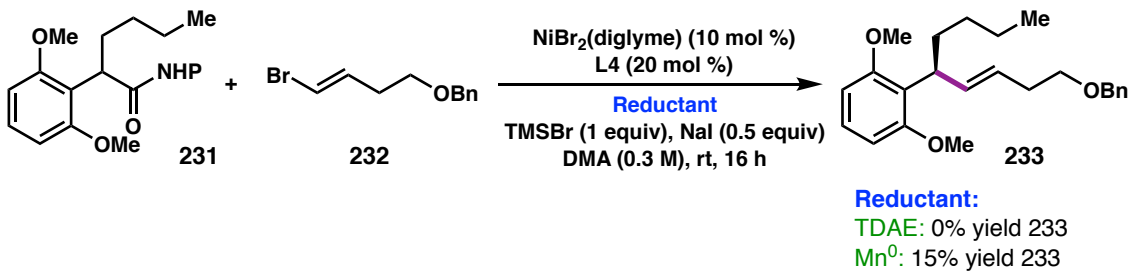
43-91% yield
82-98% ee



Based on this prior work, we envisioned preparing the cylindrocyclophane F macrocycle by a Ni-catalyzed asymmetric reductive dimerization/macrocyclization of NHP ester **227** (Scheme 4.5). Although the asymmetric reductive coupling of NHP esters tolerates electron-rich substrates, the *o*,*o*-disubstitution on the arene of the required substrate was expected to present a challenge to the established conditions and would require further reaction development.

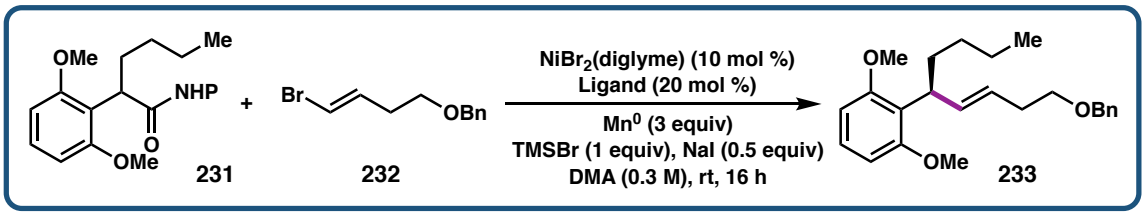
To first probe the feasibility of the intermolecular reductive cross-coupling, model substrates **231** and **232** were synthesized (Scheme 4.7). The benzylic NHP ester substrate **231** was selected over the corresponding benzylic chloride due to its improved stability; the corresponding benzylic chloride readily eliminates to give the styrene during isolation and purification. A mixture of **231** and **232** were subjected to conditions previously developed for asymmetric reductive alkenylation of NHP esters: $NiBr_2$(diglyme) as catalyst, ^{c}Pro-indaBOX (**L4**) as ligand, TDAE as the stoichiometric reductant, and TMSBr as an activating agent; however, no product formation was observed under these conditions. In contrast, when Mn^0 was used as the stoichiometric reductant, the product was formed in 15% yield. At this time, it is unclear why TDAE does not work, even though it was found to be optimal in our original report; we will continue to investigate the use of TDAE and related organic reductants in our future work.

Scheme 4.7. *Cross-coupling between model NHP ester and alkenyl bromide.*

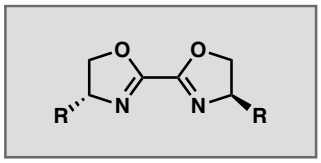


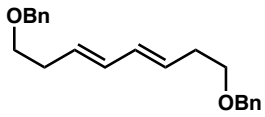
Following a survey of solvents including DMA, THF, and NMP, and several bis(oxazoline) (BOX) and bi(oxazoline) (BiOX) chiral ligands,[31] it was determined that DMA provided the most productive reactivity and **L6**, a new chiral ligand developed in our laboratory for diarylalkane formation (**Chapter 2**),[32] furnished the most promising enantioselectivity (Table 4.5). It is possible that the improved reactivity observed with the BiOX ligands results from the increased *N–N* distance, which provides better access to the nickel center for more sterically demanding coupling partners.

Table 4.5. *Ligand optimization of model cross-coupling.*



Bi(oxazoline) Ligand Scaffold





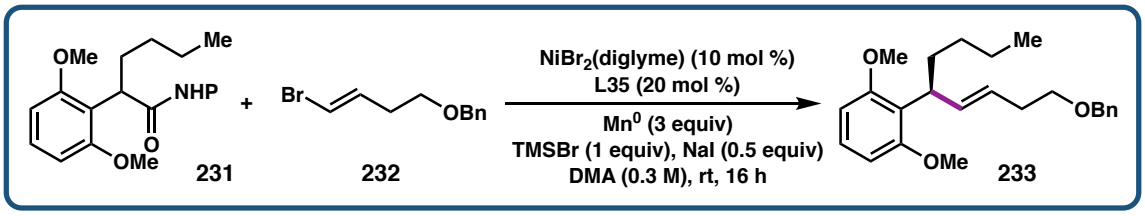
234

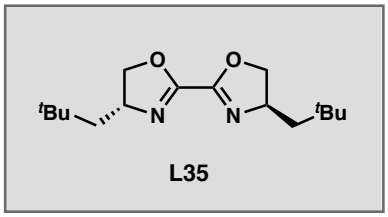
Ligand	R	Yield HC 234 (%)	Yield 233 (%)	ee 233 (%)
L21	Ph	59	8	7
L2	Bn	39	22	46
L8	^{i}Bu	70	28	65
L35	$CH_2{}^{t}$Bu	50	31	69
L19	^{i}Pr	51	30	63
L20	^{t}Bu	52	15	16
L22	CyHexyl	54	11	67
L6	4-Heptyl	35	24	86

The major side product in the reaction is diene **234**, resulting from homo-coupling of **232**. Although the homo-dimer derived from **231** was not isolated, NHP ester **231** was consumed under the conditions. While **L6** provides the most promising enantioselectivity, the initial screening of reaction parameters was conducted with **L35**, since it was more readily available at the time the screen was performed. The ee of **233**

improved slightly when the temperature was lowered to 0 °C, and the ratio of product **233** to dimer **234** improved (Table 4.6, entry 3). Use of Zn^0 as a reductant instead of Mn^0 gave comparable results. Interestingly, when 2.0 equivalents NHP ester **231** were employed, the yield almost doubled, giving **233** in 52% yield in 73% ee (Table 4.6, entry 6). This suggests that increasing the concentration of carbon-centered radical increases the productive cross-coupling.

***Table 4.6**. Optimization of model cross-coupling.*





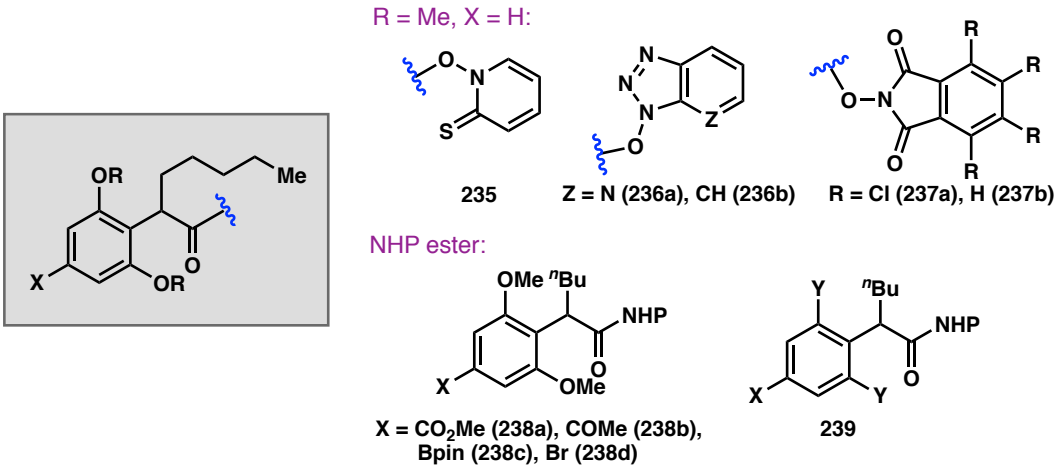
Entry	Deviation	Yield HC 234 (%)	Yield 233 (%)	ee 233 (%)
1	none	50	31	69
2	60 °C	16	12	76
3	0 °C	29	26	78
4	Zn	49	31	66
5	TDAE	0	0	—
6	2 equiv 231	21	52	73
7	2 equiv 232	36	26	67

4.5.3 Further development of substrate scope

Our efforts toward the cylindrocyclophanes will first focus on further improving the yield of the reductive alkenylation NHP ester **231**. Moving forward, we will reinvestigate chiral ligands, reductants, and additives while running the reaction at 0 °C, which showed improved ratios of product **233** to homo-dimer **234**. Our preliminary

studies determined that the yield increases when excess NHP ester is used, which could indicate that there is degradation of **231** through off-cycle non-productive pathways (see Figure 4.1 for proposed catalytic cycle). It is possible that tuning of the redox potential of the ester could improve the yield; thus, we will also investigate whether other redox-active esters (**235**, **236**, **237**) provide improved reactivity (Figure 4.3). In addition to tuning the redox potential of the ester, we will investigate whether substitution at the *para* position of the arene (e.g. **238**, X substituent) can be used to tune the stability of the radical; having a handle at the *para* position would also be helpful as we ultimately need to functionalize the arene here for elaboration to **227** (Figure 4.3). Similarly, different protecting groups at the *ortho* position will be evaluated for their effect on yield and selectivity (e.g. **239**, Y substituent).

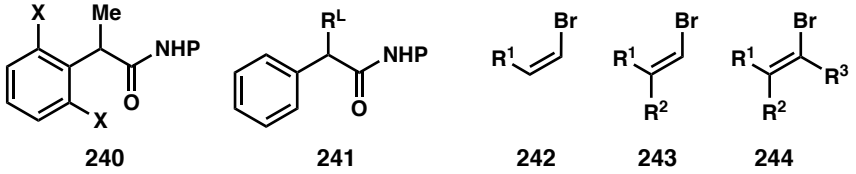
Figure 4.3. *Electronic tuning of NHP ester substrate.*



Given the promising levels of enantioselectivity obtained when using 4-HeptylBiOX (**L6**) under the initial screening conditions, we feel confident that appropriate conditions to deliver the product in high yield and enantioselectivity can be identified. Moreover, once optimal conditions have been identified for the cross-coupling

between **231** and **232**, we will investigate whether these conditions broaden the scope of the reductive alkenylation with respect to other challenging substrates. Of particular interest is improved reactivity with other NHP (or related) esters bearing *o*-substitution (**240**), or bulky substituents at the benzylic position (**241**) (Figure 4.4). In addition, we will investigate whether the newly identified conditions enable the cross-coupling of *Z*- and trisubstituted alkenyl bromides (**242** and **243**), substrates that fail to cross-couple under our first-generation conditions. Thus, in addition to solving the specific synthetic challenge presented by the cylindrocyclophanes, these studies will also serve to improve the generality of these asymmetric reductive alkenylation reactions.

Figure 4.4. *Expansion of substrate scope.*

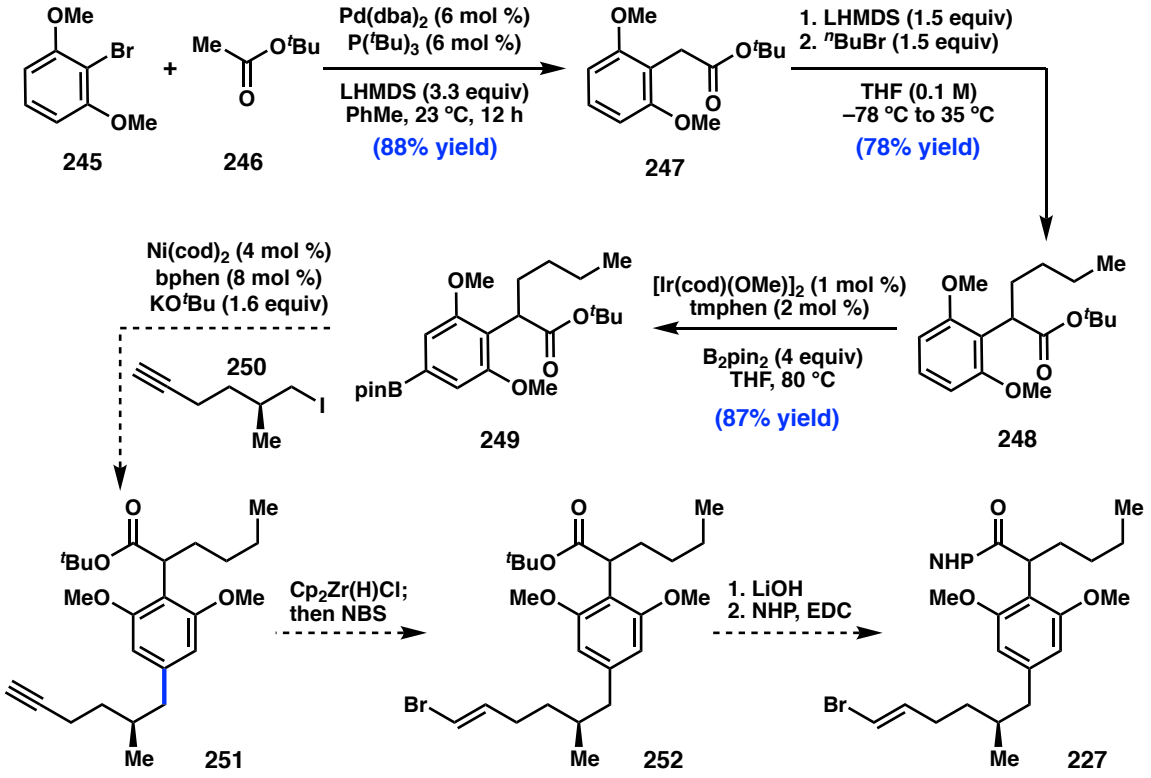


4.5.4 Synthesis of cylindrocyclophane F

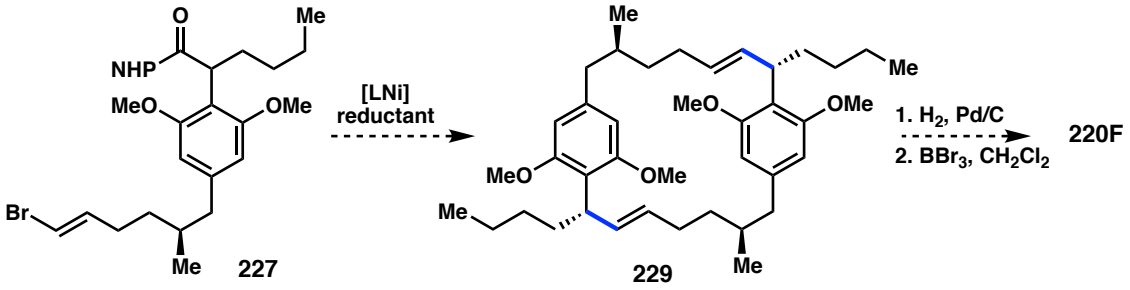
Having identified conditions for the Ni-catalyzed enantioselective cross-coupling between **231** and **232**, attention will turn to the synthesis of a bifunctional dimerization/macrocyclization substrate for the synthesis of cylindrocylophane F (Scheme 4.8). As part of our strategy design, we envisioned using aryl bromide **245** as a lynchpin unit, wherein cross-coupling chemistry could be employed to modularly join the fragments containing the NHP ester and alkenyl bromide functionalities. This approach would ultimately provide a flexible route that could be used to prepare additional cylindrocyclophane natural products. To this end, commercially available aryl bromide **245** was coupled to *tert*-butyl acetate (**246)** under Pd-catalyzed enolate arylation

conditions in 88% yield.[33] Ester **247** can be smoothly alkylated with 1-bromobutane to give **248** in 78% yield. Ester **248** is then submitted to Ir-catalyzed C–H borylation conditions,[34–36] and the resulting aryl pinacol boronate is formed in 87% yield. This pinacol boronate will then be coupled with alkyl iodide **250** using the Ni-catalyzed conditions developed by Fu and coworkers.[37,38] Preliminary experiments demonstrate we can cross-couple a simple alkyl iodide with **249** in good yield (not shown), demonstrating the feasibility of this transformation. Alkyne **250** can be prepared from commercially available hex-5-ynoic acid following a protocol developed by Paquette.[39] Finally, alkyne **251** will be converted to the alkenyl bromide, and the ester will be transesterified to give bis-electrophile **227**.

Scheme 4.8. *Synthesis of dimerization substrate* ***227***.[40]



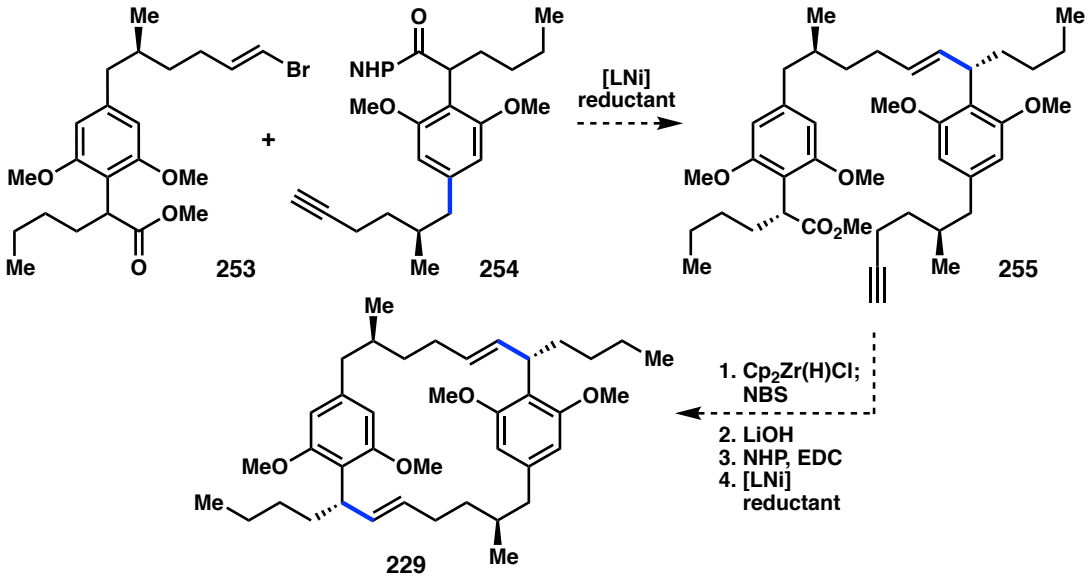
Scheme 4.9. *Ni-catalyzed dimerization to give cylindrocyclophane F (**220F**).*



Bis-electrophile **227** will be subjected to the Ni-catalyzed reductive alkenylation conditions developed on the model system (Scheme 4.9). A range of reaction concentrations will be explored in order to favor the formation of macrocycle **229** over competing linear dimerization reactions. Hydrogenation of **229** and demethylation under standard conditions will provide cylindrocyclophane F (**220F**).

4.5.5 Alternative strategies

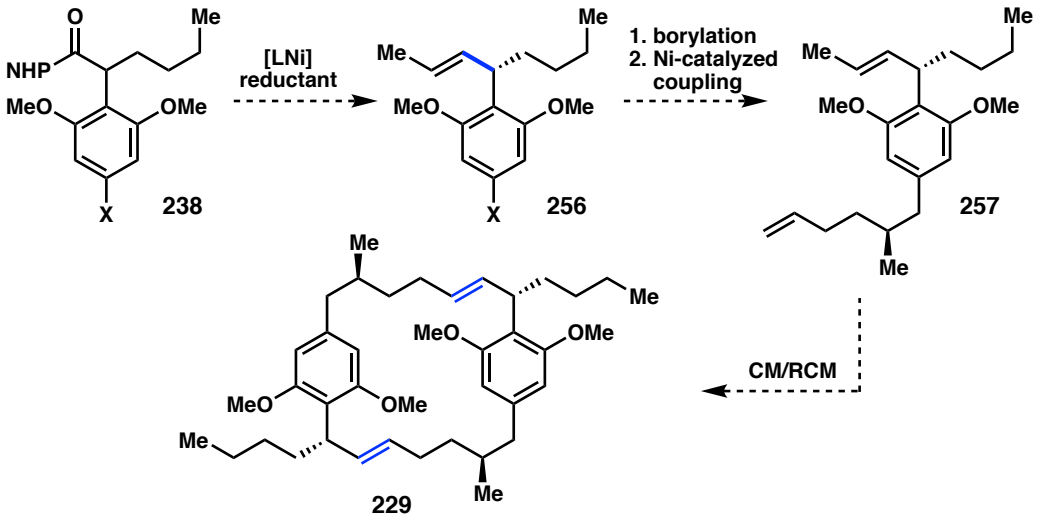
Scheme 4.10. *Sequential reductive coupling to access **229**.*



If the Ni-catalyzed asymmetric double reductive alkenylation strategy to form the cylindrocyclophanes proves problematic, two back-up strategies have been devised. The

first is a sequential coupling approach (Scheme 4.10), in which a Ni-catalyzed reductive coupling of vinyl bromide **253** with NHP ester **254** will provide **255**. Conversion of the alkyne to the alkenyl bromide, and conversion of the methyl ester to the NHP ester, will enable a second Ni-catalyzed reductive coupling to form the macrocycle and intercept diene **229**. Hydrogenation and demethylation would provide **220F**.

Scheme 4.11. *Macrocyclization through CM/RCM to access **229***.



The second back-up strategy will prepare the key fragment, **229**, using a Ni-catalyzed asymmetric reductive alkenylation of NHP ester **238** (Scheme 4.11). Ir-catalyzed borylation of arene **256** followed by Ni-catalyzed cross-coupling will provide diene **257**. Exposure of **257** to the CM/RCM conditions developed by Smith and coworkers should result in macrocycle formation, and hydrogenation and demethylation would complete the synthesis of **220F**. This route could prove necessary if our optimization studies of the Ni-catalyzed alkenylation reveal that electronic modulation of the NHP ester through *p*-substitution is required.

4.6 CONCLUSION

In summary, these results demonstrate that Ni-catalyzed reductive cross-coupling reactions of NHP esters can be rendered highly enantioselective, thus broadening the scope of $C(sp^3)$ electrophiles available for asymmetric C–C bond formation. In contrast to the related reductive cross-couplings of benzyl chlorides, optimal results are obtained when TDAE is used as the terminal reductant in place of Mn^0 or Zn^0, which are typical in these reactions. A preliminary result demonstrates that these conditions can be used to cross-couple α-alkoxy NHP esters and other substrates for which the corresponding benzylic chloride could be difficult to prepare or unstable. The ability to use both NHP esters and benzylic chlorides in asymmetric reductive alkenylation reactions allows users to select from either electrophile depending on factors such as commercial availability of the corresponding carboxylic acid or benzylic chloride starting material, and improves the overall scope of this transformation. The expansion of this technology to more challenging $C(sp^3)$ and $C(sp^2)$ electrophiles is the focus of ongoing work in our laboratory. We aim to prove the synthetic utility of this strategic disconnection in the total synthesis of cylindrocyclophane natural products.

4.7 EXPERIMENTAL SECTION

4.7.1 *Materials and methods*

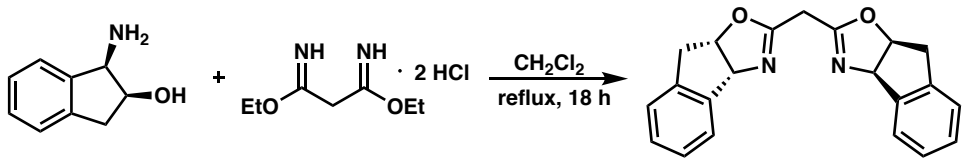
Unless otherwise stated, reactions were performed under a nitrogen atmosphere using freshly dried solvents. Methylene chloride (DCM), diethyl ether (Et_2O), tetrahydrofuran (THF), 1,4-dioxane and toluene (PhMe) were dried by passing through activated alumina columns. All other commercially obtained reagents were used as received unless specifically indicated. Aryl iodides were purchased from Sigma Aldrich, Combi-Blocks, or Astatech. Manganese powder (>99.9%) was purchased from Sigma Aldrich. $NiBr_2$(diglyme) was purchased from Strem. All reactions were monitored by thin-layer chromatography using EMD/Merck silica gel 60 F254 pre-coated plates (0.25 mm). Silica gel and basic alumina column chromatography was performed as described by Still et al. (W. C. Still, M. Kahn, A. Mitra, *J. Org. Chem*. **1978**, *43*, 2923.) using silica gel (particle size 0.032–0.063) purchased from Silicycle and aluminum oxide (activated, basic, Brockmann I, 58 Å pore size, powder) purchased from Sigma-Aldrich. ^1H and ^{13}C NMR were recorded on a Varian Inova 500 (at 500 MHz and 125 MHz respectively) or a Bruker Avance III HD with Prodigy cyroprobe (at 400 MHz and 101 MHz respectively). ^1H and ^{19}F NMR spectra were recorded on a Varian Inova 300 (at 300 MHz and 282 MHz, respectively). NMR data is reported relative to internal chloroform (^1H, δ = 7.26, ^{13}C, δ = 77.0) and C_6F_6 (^{19}F, δ = –164.9). Data for ^1H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicity and qualifier abbreviations are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm^{-1}). Analytical

SFC was performed with a Mettler SFC supercritical CO_2 analytical chromatography system with Chiralcel AD-H, OD-H, AS-H, OB-H, and IA columns (4.6 mm x 25 cm). SFC analysis performed at 100.0 bar and 40 ºC. HRMS were acquired using either an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI), atmospheric pressure chemical ionization (APCI), or mixed (MM) ionization mode.

4.7.2 *Ligand Synthesis*

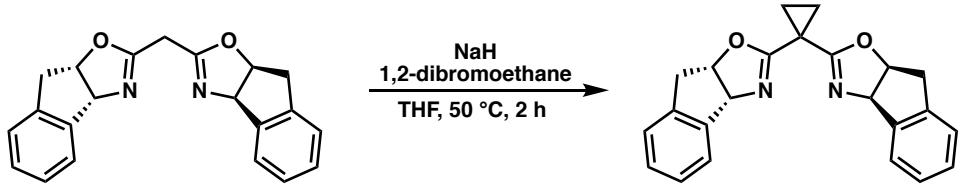
4.7.2.1 *Preparation of Ni(II) BOX Ligand Complex*

Bis((3a*R*,8a*S*)-3a,8a-dihydro-8*H*-indeno[1,2-*d*]oxazol-2-yl)methane (258)



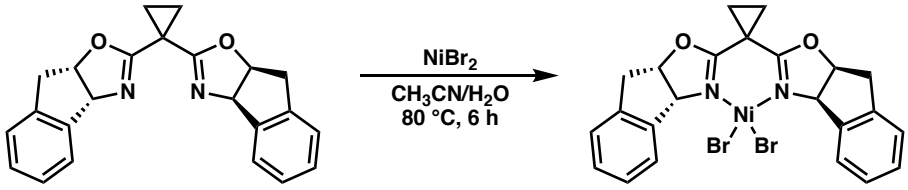
According to a procedure by Snyder and coworkers, the (1R,2S)-(+)-*cis*-1-amino-2-indanol (4.70 g, 31.5 mmol, 2.1 equiv) and diethyl malonimidate dihydrochloride (3.47 g, 15 mmol, 1 equiv) were added to a flame-dried 1 L round bottom flask fitted with a reflux condenser and a magnetic stirring rod, and put under an inert atmosphere (N_2). Then CH_2Cl_2 (360 mL) was added and the solution was heated at 45 °C for 18 hours. The reaction was cooled, then quenched with water (690 mL). The layers were separated, the aqueous layer was extracted with CH_2Cl_2 (4 x 180 mL), and the combined organic layers were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was purified by recrystallization from cooling hot ethanol to yield 3.30 g (67% yield) of **258** as a white solid. Spectral data matched those reported in literature.

(3a*R*,3a'*R*,8a*S*,8a'*S*)-2,2'-(Cyclopropane-1,1-diyl)bis(3a,8a-dihydro-8*H*-indeno[1,2-*d*]-oxazole) (L4)



According to a procedure by Sibi and coworkers, the bis(oxazoline) ligand **L4** (1.65 g, 5 mmol, 1 equiv) was added to a flame-dried 200 mL round bottom flask with a magnetic stir bar and put under an inert atmosphere (N_2). The compound was dissolved in THF (25 mL) and cooled to 0 °C before *dry* sodium hydride (60 wt % in mineral oil, 601 mg, 15 mmol, 3 equiv) was added in portions. *Note: Wet NaH resulted in saponification of the oxazoline, which could be removed by column chromatography (silica, 10% MeOH/CH_2Cl_2).* The solution was allowed to stir for 30 minutes before 1,2-dibromoethane (517 mL, mmol, 1.2 equiv) was added dropwise over the course of 10 minutes. The reaction was warmed to 50 °C and stirred for 2 hours. *Note: Aliquots could be monitored by ^1H NMR to ensure complete conversion of the starting material.* The reaction was quenched with aqueous NH_4Cl (25 mL) and extracted with CH_2Cl_2 (2 x 85 mL). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude material was purified by recrystallization from cooling hot ethanol to yield 1.46 g (82% yield) of **L4** as a light tan solid. Spectral data matched those reported in literature.

Nickel(II) bis(bromide) (3a*R*,3a'*R*,8a*S*,8a'*S*)-2,2'-(cyclopropane-1,1-diyl)bis(3a,8a-dihydro-8*H*-indeno[1,2-*d*]oxazole) (L4•$NiBr_2$)



Similar to a procedure reported by Evans and coworkers, the bis(oxazoline) ligand **L4** (1.07 g, 3.0 mmol, 1 equiv) and anhydrous nickel(II) bromide (655 mg, 3.0 mmol, 1 equiv) were added to a round bottom flask equipped with a magnetic stir bar and dissolved in a mixture of acetonitrile (CH_3CN, 65 mL) and water (0.75 mL). The solution was heated to 80 °C for 6 hours to afford a dark purple solution. The reaction was concentrated under reduced pressure and the obtained solid was saturated in CH_2Cl_2, filtered through a plug of cotton, dispensed into four 20 mL scintillation vials, and recrystallized by vapor diffusion (CH_2Cl_2/pentane) to afford dark purple crystals suitable for X-ray diffraction. For the isolation of **L4•$NiBr_2$**, the crystals were washed with hexane, which was added by pipet and subsequently removed. The crystals were removed with a spatula, transferred to a new vial, and crushed to provide a powder. The resulting complex was dried under vacuum to yield 1.6 g (91% yield) of **L4•$NiBr_2$** as a purple solid.

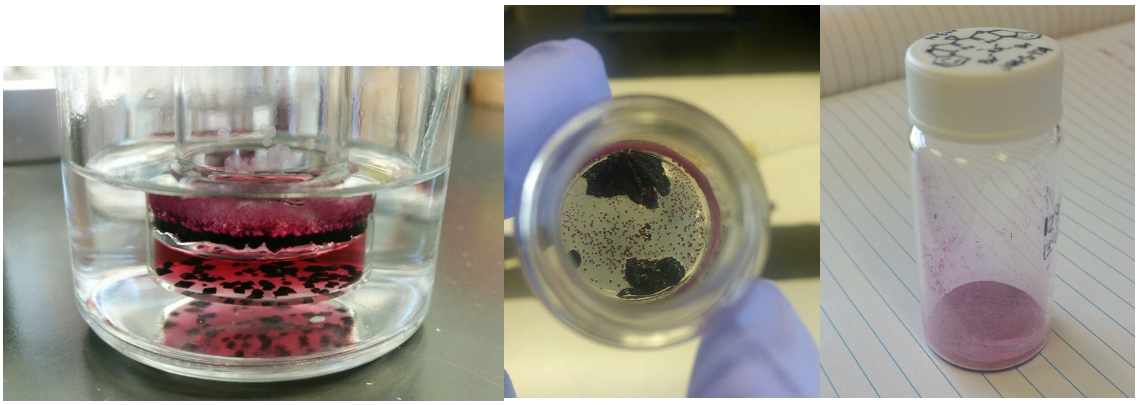
m.p. = >300 °C

^{1}H NMR (400 MHz, $CDCl_3$): δ 96.48 (s, 2H), 46.46 (s, 2H), 20.16 (d, *J* = 17.1 Hz, 2H), 11.67 – 10.85 (m, 6H), 10.55 (d, *J* = 16.6 Hz, 2H), 6.96 (s, 2H), 5.40 (s, 2H), -0.65 (s, 2H).

FTIR (NaCl, thin film, cm^{-1}): 3333, 2222, 1660, 1479, 1461, 1444, 1427, 1312, 1247, 1227, 1214, 1120, 1010, 911, 859, 758, 728.

EA: Anal. Calc'd. for **L4•NiBr$_2$**, $C_{23}H_{20}Br_2N_2NiO_2$ (%): C, 48.05; H, 3.51; N, 4.87. Found: C, 48.38;

H, 3.54; N, 4.84



(Left) Crystallized **L4•NiBr$_2$** following vapor diffusion. **(Center)** Large crystals of **L4•NiBr$_2$**. **(Right)** The powdered form of **L4•NiBr$_2$** after crushing the crystals with a spatula and drying under vacuum.

4.7.2.2 *X-Ray Structure Determination*

Low-temperature diffraction data (ϕ- and ω-scans) were collected on a Bruker AXS KAPPA APEXII diffractometer coupled to a CCD detector with Mo-$K\alpha$ radiation (λ = 0.71073 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. Absorption corrections were applied using SADABS. The structure was solved by intrinsic phasing using SHELXT and refined against F^2 on all data by full-matrix least squares with SHELXL-2014 using established refinement techniques. 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. Compound **L4•NiBr$_2$** crystallizes in the tetragonal space group $P4_1$ with one molecule in the asymmetric unit. The structure was solved as a merohedral twin with rotation around an axis 45° between a and b. The twin law was defined as the matrix (0.0, 1.0, 0.0, 1.0, 0.0, 0.0, 0.0, 0.0, -1.0). The BASF parameter [0.4980(14)] gave the twin ratio as 0.50:0.50. Absolute configuration was determined by anomalous dispersion (Flack = 0.011(2)). Crystallographic data for **L4•NiBr$_2$** can be obtained free of charge from The Cambridge Crystallographic Data Centre (CCDC) via www.ccdc.cam.ac.uk/data_request/cif under CCDC deposition number 1501744. Graphical representation of the structure with 50% probability thermal ellipsoids was generated using Mercury visualization software.

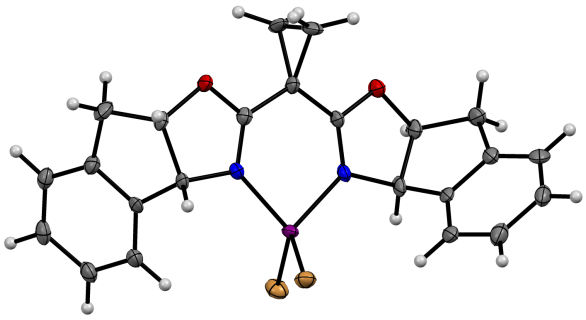


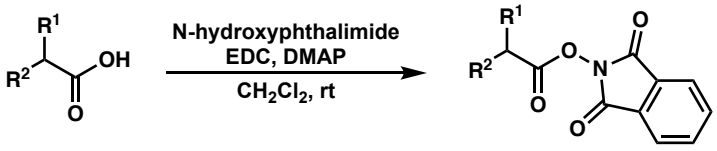
Table S4.1. Crystal data and structure refinement for L4•NiBr$_2$.

Identification code	JLH-3-168	
Empirical formula	$C_{23}H_{20}Br_2N_2NiO_2$	
Formula weight	574.94	
Temperature	100 K	
Wavelength	0.71073 Å	
Crystal system	Tetragonal	
Space group	$P4_1$	
Unit cell dimensions	a = 9.4823(6) Å	a= 90°.
	b = 9.4823(6) Å	b= 90°.
	c = 24.418(2) Å	g = 90°.
Volume	2195.5(3) Å^3	

Z	4
Density (calculated)	1.739 Mg/m^3
Absorption coefficient	4.546 mm^{-1}
F(000)	1144
Crystal size	0.31 x 0.27 x 0.14 mm^3
Theta range for data collection	0.834 to 38.918°.
Index ranges	-16<=h<=16, -16<=k<=16, -42<=l<=43
Reflections collected	113308
Independent reflections	12464 [R(int) = 0.0431]
Completeness to theta = 25.242°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7476 and 0.5466
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	12464 / 1 / 272
Goodness-of-fit on F^2	1.056
Final R indices [I>2sigma(I)]	R1 = 0.0470, wR2 = 0.1114
R indices (all data)	R1 = 0.0580, wR2 = 0.1168
Absolute structure parameter	0.011(2)
Extinction coefficient	n/a
Largest diff. peak and hole	2.381 and -1.019 $e.Å^{-3}$

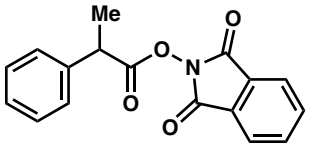
4.7.3 *Substrate Preparation*

4.7.3.1 *NHP Ester Synthesis*



General Procedure 1: To a round bottom flask equipped with a magnetic stir bar was added the carboxylic acid (1.0 equiv), N-hydroxyphthalimide (1.0 equiv), and 4-dimethylaminopyridine (DMAP, 0.10 equiv). The reagents were dissolved in CH_2Cl_2 (0.2 M) and the N-(3-dimethylaminopropyl)-N-ethylcarbodiimide (EDC, 1.1 equiv) was added. The reaction continued to stir overnight at room temperature. The crude reaction was concentrated to afford a thick oil, which was purified by column chromatography (silica, EtOAc/hexane or CH_2Cl_2) to afford the desired product.

1,3-dioxoisoindolin-2-yl 2-phenylpropanoate (259)



Prepared from 2-phenylpropanoic acid (5.0 g, 33.3 mmol) according to General Procedure 1. The crude residue was purified by filtering through a plug of silica with CH_2Cl_2 as the eluent to yield 8.7 g (88% yield) of **259** as a white solid.

R_f = 0.28 (silica gel, 20% EtOAc/hexane, UV).

m.p. = 62–64 °C

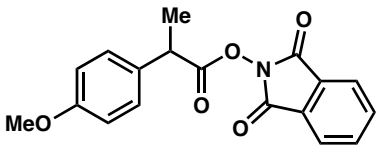
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, *J* = 5.5, 3.1 Hz, 2H), 7.76 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.43 – 7.37 (m, 4H), 7.37 – 7.30 (m, 1H), 4.13 (q, *J* = 7.2 Hz, 1H), 1.68 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 170.9, 161.9, 138.5, 134.9, 129.02, 128.98, 127.9, 127.7, 124.0, 43.1, 19.1.

FTIR (NaCl, thin film, cm^{-1}): 1810, 1785, 1743, 1466, 1453, 1358, 1186, 1123, 1043, 1028, 877, 695.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{17}H_{13}NO_4$ $[M+H]^+$: 296.0923; found: 296.0903.

1,3-dioxoisoindolin-2-yl 2-(4-methoxyphenyl)propanoate (260)



Prepared from 2-(4-methoxyphenyl)propanoic acid (500 mg, 2.77 mmol) according to General Procedure 1. The crude residue was purified by filtering through a plug of silica with 30% EtOAc/hexane as the eluent to yield 671 mg (74% yield) of **260** as a white solid.

R_f = 0.22 (silica gel, 20% EtOAc/hexane, UV).

m.p. = 91–92 °C

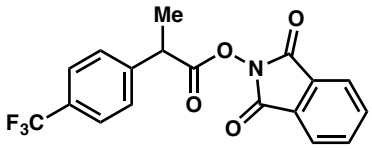
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.77 (dd, 2H), 7.33 (d, *J* = 8.7 Hz, 2H), 6.92 (d, *J* = 8.8 Hz, 2H), 4.08 (q, *J* = 7.2 Hz, 1H), 3.81 (s, 3H), 1.65 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 171.1, 162.0, 159.2, 134.9, 130.5, 129.0, 128.8, 124.0, 114.4, 55.4, 42.2, 19.2.

FTIR (NaCl, thin film, cm^{-1}): 1810, 1784, 1743, 1611, 1513, 1467, 1371, 1249, 1185, 1123, 1045, 1033, 878, 832, 696.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{18}H_{15}NO_5$ $[M+H]^+$: 326.1028; found: 326.1022.

1,3-dioxoisoindolin-2-yl 2-(4-(trifluoromethyl)phenyl)propanoate (261)



Prepared from 2-(4-(trifluoromethyl)phenyl)propanoic acid (200 mg, 0.92 mmol) according to General Procedure 1. The crude residue was purified by filtering through a plug of silica with 30% EtOAc/hexane as the eluent to yield 290 mg (87% yield) of **261** as a yellow solid.

R_f = 0.28 (silica gel, 20% EtOAc/hexane, UV).

m.p. = 76–77 °C

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (dd, *J* = 5.6, 3.2 Hz, 2H), 7.78 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.66 (d, *J* = 7.8 Hz, 2H), 7.54 (d, *J* = 8.1 Hz, 2H), 4.19 (q, *J* = 7.2 Hz, 1H), 1.69 (d, *J* = 7.2 Hz, 3H).

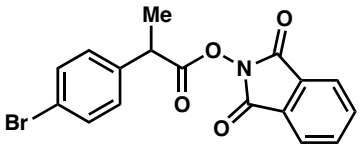
^{13}C NMR (101 MHz, $CDCl_3$): δ 170.3, 161.9, 142.4 (q, J_{C-F} = 1 Hz), 135.0, 130.2 (q, J_{C-F} = 33 Hz), 128.9, 128.2, 126.1 (q, J_{C-F} = 4 Hz). 124.14, 124.11 (q, J_{C-F} = 272 Hz), 43.0, 19.1.

^{19}F NMR (282 MHz, $CDCl_3$): δ -65.8.

FTIR (NaCl, thin film, cm^{-1}): 1813, 1788, 1746, 1620, 1468, 1421, 1359, 1326, 1186, 1168, 1125, 1079, 1067, 1048, 1017, 878, 842, 697.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{18}H_{12}F_3NO_4$ $[M+H]^+$: 364.0797; found: 364.0815.

1,3-dioxoisoindolin-2-yl 2-(4-bromophenyl)propanoate (262)



Prepared from 2-(4-bromophenyl)propanoic acid (1.0 g, 4.65 mmol) according to General Procedure 1. The crude residue was purified by filtering through a plug of silica with 20% EtOAc/hexane as the eluent to yield 511 mg (48% yield) of **262** as a light yellow solid.

R_f = 0.69 (silica gel, 20% EtOAc/hexane, UV).

m.p. = 77–78 °C

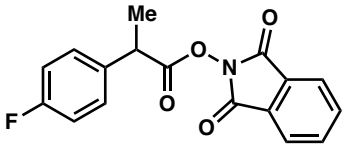
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.80 – 7.75 (m, 2H), 7.52 (d, *J* = 8.5 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 4.08 (q, *J* = 7.2 Hz, 1H), 1.65 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 170.5, 161.9, 137.4, 134.9, 132.2, 129.4, 129.0, 124.1, 122.0, 42.6, 19.0.

FTIR (NaCl, thin film, cm^{-1}): 1811, 1786, 1742, 1489, 1467, 1369, 1186, 1133, 1078, 1046, 1010, 877, 696.

LRMS (API-ES, *m/z*): calc'd for $C_{17}H_{12}BrNO_4$ $[M+H_2O]^+$: 391.0; found: 391.0.

1,3-dioxoisoindolin-2-yl 2-(4-fluorophenyl)propanoate (263)



Prepared from 2-(4-fluorophenyl)propanoic acid (500 mg, 2.92 mmol) according to General Procedure 1. The crude residue was purified by filtering through a plug of silica with 20% EtOAc/hexane as the eluent to yield 590 mg (63% yield) of **263** as a white solid.

R_f = 0.35 (silica gel, 20% EtOAc/hexane, UV).

m.p. = 108–110 °C

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (dd, *J* = 5.6, 3.1 Hz, 2H), 7.77 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.41 – 7.35 (m, 2H), 7.12 – 7.05 (m, 2H), 4.11 (q, *J* = 7.2 Hz, 1H), 1.66 (d, *J* = 7.2 Hz, 3H).

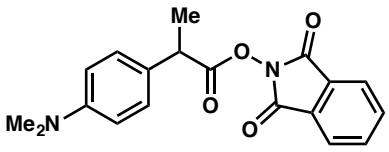
^{13}C NMR (101 MHz, $CDCl_3$): δ 170.78, 162.42 (d, $J_{C\text{-}F}$ = 246.4 Hz), 161.9, 134.9, 134.2 (d, $J_{C\text{-}F}$ = 3.3 Hz), 129.37 (d, $J_{C\text{-}F}$ = 8.3 Hz), 129.9, 124.1, 115.95 (d, $J_{C\text{-}F}$ = 21.5 Hz), 42.3, 19.2.

^{19}F NMR (282 MHz, $CDCl_3$): δ -117.64 (tt, $J_{F\text{-}H}$ = 8.4, 5.2 Hz).

FTIR (NaCl, thin film, cm^{-1}): 1811, 1785, 1739, 1605, 1509, 1467, 1360, 1225, 1186, 1120, 1045, 1016, 959, 877, 837, 783, 696.

HRMS (FAB, *m/z*): calc'd for $C_{17}H_{12}FNO_4$ $[M+H]^+$: 314.0823; found: 314.0859.

1,3-dioxoisoindolin-2-yl 2-(4-(dimethylamino)phenyl)propanoate (264)



Prepared from 2-(4-(dimethylamino)phenyl)propanoic acid (392 mg, 2.02 mmol) according to General Procedure 1, with the exception of no DMAP. The crude residue was purified column chromatography (silica, 20 to 50% EtOAc/hexane) to yield 640 mg (94% yield) of **264** as a yellow solid.

R_f = 0.54 (silica gel, 50% EtOAc/hexane, UV).

m.p. = 106–108 °C

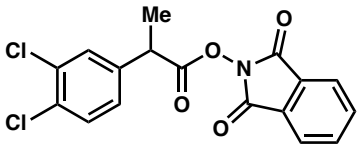
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (dd, *J* = 5.6, 3.1 Hz, 2H), 7.76 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.27 (d, *J* = 8.8 Hz, 2H), 6.75 (d, *J* = 8.8 Hz, 2H), 4.04 (q, *J* = 7.2 Hz, 1H), 2.95 (s, 6H), 1.64 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 171.4, 162.1, 150.2, 134.8, 129.1, 128.3, 126.0, 124.0, 112.8, 42.1, 40.6, 19.2.

FTIR (NaCl, thin film, cm^{-1}): 1809, 1784, 1743, 1615, 1523, 1467, 1356, 1186, 1134, 1081, 1044, 878, 819, 697.

HRMS (FAB, *m/z*): calc'd for $C_{19}H_{18}N_2O_4$ $[M+\cdot]^+$: 338.1267; found: 338.1272.

1,3-dioxoisoindolin-2-yl 2-(3,4-dichlorophenyl)propanoate (265)



Prepared from 2-(3,4-dichlorophenyl)propanoic acid (231 mg, 1.05 mmol) according to General Procedure 1, with the exception of no DMAP. The crude residue was purified by column chromatography (silica, 0 to 15% EtOAc/hexane) to yield 241 mg (63% yield) of **265** as a white solid.

R_f = 0.35 (silica gel, 20% EtOAc/hexane, UV).

m.p. = 103–105 °C

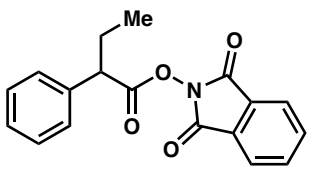
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.79 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.52 (d, *J* = 2.2 Hz, 1H), 7.47 (d, *J* = 8.3 Hz, 1H), 7.26 (dd, *J* = 8.3, 2.2 Hz, 1H), 4.08 (q, *J* = 7.2 Hz, 1H), 1.66 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 170.1, 161.9, 138.4, 135.0, 133.1, 132.2, 131.0, 129.9, 128.9, 127.1, 124.2, 42.3, 19.0.

FTIR (NaCl, thin film, cm^{-1}): 2341, 2359, 1785, 1743, 1426, 1186, 1135, 1049, 962, 878, 696.

HRMS (FAB, *m/z*): calc'd for $C_{17}H_{11}Cl_2NO_4$ $[M+H]^+$: 364.0143; found: 364.0131.

1,3-dioxoisoindolin-2-yl 2-phenylbutanoate (266)



Prepared from 2-phenylbutanoic acid (5.0 g, 30.5 mmol) according to General Procedure 1. The crude residue was purified by column chromatography (silica, 20% EtOAc/hexane) to yield 8.1 g (86% yield) of **266** as a white solid.

R_f = 0.31 (silica gel, 20% EtOAc/hexane, UV).

m.p. = 61–64 °C

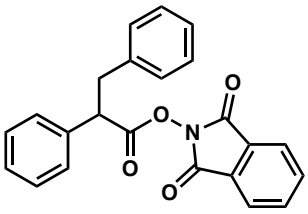
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (dd, *J* = 5.6, 3.1 Hz, 2H), 7.76 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.42 – 7.29 (m, 5H), 3.86 (t, *J* = 7.6 Hz, 1H), 2.31 – 2.18 (m, 1H), 2.03 – 1.90 (m, 1H), 1.04 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 170.4, 162.0, 136.9, 134.8, 129.0, 128.9, 128.2, 128.0, 124.0, 50.5, 27.3, 12.0.

FTIR (NaCl, thin film, cm^{-1}): 1811, 1786, 1744, 1467, 1455, 1360, 1186, 1128, 1080, 1058, 969, 877, 656.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{18}H_{15}NO_4$ $[M+H]^+$: 310.1079; found: 310.1061.

1,3-dioxoisoindolin-2-yl 2,3-diphenylpropanoate (267)



Prepared from 2,3-diphenylpropanoic acid (353 mg, 1.56 mmol) according to General Procedure 1. The crude residue was purified by column chromatography (silica, 20% EtOAc/hexane) to yield 542 mg (94% yield) of **267** as a white solid.

R_f = 0.28 (silica gel, 20% EtOAc/hexane, UV).

m.p. = 116–119 °C

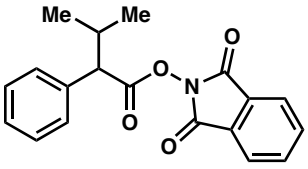
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.76 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.41 – 7.20 (m, 8H), 7.15 – 7.10 (m, 2H), 4.23 (t, *J* = 7.6 Hz, 1H), 3.56 (dd, *J* = 13.9, 7.5 Hz, 1H), 3.19 (dd, *J* = 13.9, 7.8 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 170.0, 161.8, 137.7, 136.4, 134.8, 129.2, 129.0, 128.9, 128.6, 128.3, 128.1, 126.9, 124.0, 50.9, 39.9.

FTIR (NaCl, thin film, cm^{-1}): 3030, 1810, 1784, 1744, 1496, 1467, 1454, 1359, 1186, 1134, 1080, 1068, 972, 877, 736, 695.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{23}H_{17}NO_4$ $[M+H]^+$: 372.1236; found: 372.1236.

1,3-dioxoisoindolin-2-yl 3-methyl-2-phenylbutanoate (268)



Prepared from 3-methyl-2-phenylbutanoic acid (300 mg, 1.68 mmol) according to General Procedure 1. The crude residue was purified by filtering through a plug of silica with 20%

EtOAc/hexane as the eluent to yield 509 mg (93% yield) of **268** as a white solid.

R_f = 0.34 (silica gel, 20% EtOAc/hexane, UV).

m.p. = 77–81 °C

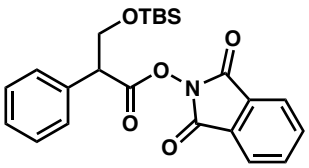
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (dd, *J* = 5.6, 3.1 Hz, 2H), 7.76 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.42 – 7.29 (m, 5H), 3.58 (d, *J* = 10.0 Hz, 1H), 2.51 – 2.37 (m, 1H), 1.23 (d, *J* = 6.6 Hz, 3H), 0.84 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 170.2, 162.0, 136.1, 134.8, 129.0, 128.8, 128.7, 128.0, 124.0, 56.7, 32.6, 21.3, 20.3.

FTIR (NaCl, thin film, cm^{-1}): 2966, 1811, 1786, 1745, 1468, 1455, 1375, 1311, 1186, 1132, 1080, 1060, 974, 889, 877, 786, 745, 696.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{19}H_{17}NO_4$ $[M+H]^+$: 324.1236; found: 324.1227.

1,3-dioxoisoindolin-2-yl 3-((*tert*-butyldimethylsilyl)oxy)-2-phenylpropanoate (269)



To a round bottom flask equipped with a stirring magnet was added tropic acid (830 mg, 5 mmol, 1 equiv), *tert*-butyldimethylsilyl chloride (1.1 g, 5.5 mmol, 1.1 equiv), dimethylaminopyridine (63 mg, 0.5 mmol, 0.1 equiv), and imidazole (682 mg, 10 mmol, 2 equiv). The reagents were dissolved in 15 mL of CH_2Cl_2 and stirred overnight at room temperature. The reaction was quenched with aq. NH_4Cl, extracted with Et_2O, dried with $MgSO_4$, filtered, and concentrated under reduced pressure to afford crude 3-((*tert*-butyldimethylsilyl)oxy)-2-phenylpropanoic acid. This crude material was used in the esterification step without purification, which was performed according to General Procedure 1. The crude residue was purified by column chromatography and dried under high vacuum (silica, 0 to 20% EtOAc/hexane) to yield 664 mg (31% yield) of **269** as a colorless oil.

R_f = 0.38 (silica gel, 20% EtOAc/hexane, UV).

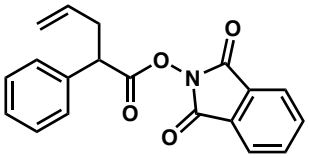
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (dd, *J* = 5.6, 3.1 Hz, 2H), 7.77 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.43 – 7.31 (m, 5H), 4.28 – 4.18 (m, 2H), 3.93 (dd, *J* = 8.6, 4.4 Hz, 1H), 0.89 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 169.0, 161.8, 134.8, 134.1, 129.1, 129.0, 128.5, 128.3, 124.0, 65.3, 52.2, 25.9, 18.4, -5.4, -5.6.

FTIR (NaCl, thin film, cm^{-1}): 2953, 2929, 2856, 1814, 1788, 1747, 1468, 1361, 1256, 1186, 1113, 1049, 1023, 877, 836, 780, 696.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{23}H_{27}NO_5Si$ $[M+H]^+$: 426.1737; found: 426.1708.

1,3-dioxoisoindolin-2-yl 2-phenylpent-4-enoate (270)



Prepared from 2-phenylpent-4-enoic acid (240 mg, 1.36 mmol) according to General Procedure 1. The crude residue was purified by column chromatography (silica, 0 to 20% EtOAc/hexane) to yield 295 mg (67% yield) of **270** as a white solid.

R$_f$ = 0.31 (silica gel, 20% EtOAc/hexane, UV).

m.p. = 68–69 °C

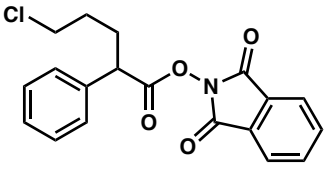
^{1}H NMR (400 MHz, CDCl$_3$): δ 7.85 (dd, *J* = 5.6, 3.1 Hz, 2H), 7.76 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.42 – 7.31 (m, 5H), 5.81 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1H), 5.16 (dq, *J* = 17.1, 1.5 Hz, 1H), 5.14 – 5.09 (m, 1H), 4.04 (dd, *J* = 8.0, 7.2 Hz, 1H), 3.00 – 2.90 (m, 1H), 2.68 (dtt, *J* = 14.3, 7.1, 1.3 Hz, 1H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 169.9, 161.9, 136.4, 134.9, 134.0, 129.02, 128.99, 128.2, 128.1, 124.0, 118.3, 48.8, 37.9.

FTIR (NaCl, thin film, cm^{-1}): 1811, 1785, 1743, 1467, 1359, 1186, 1133, 1080, 1068, 971, 877, 695.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{19}H_{15}NO_4$ $[M+H]^+$: 322.1079; found: 322.1063.

1,3-dioxoisoindolin-2-yl 5-chloro-2-phenylpentanoate (271)



Prepared from 5-chloro-2-phenylpentanoic acid (1.01 g, 4.75 mmol) according to General Procedure 1. The crude residue was purified by filtering through a plug of silica with 20% EtOAc/hexane as the eluent to yield 977 mg (58% yield) of **271** as a white solid.

R$_f$ = 0.25 (silica gel, 20% EtOAc/hexane, UV).

m.p. = 96–99 °C

^{1}H NMR (400 MHz, CDCl$_3$): δ 7.85 (dd, *J* = 5.6, 3.1 Hz, 2H), 7.77 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.42 – 7.31 (m, 5H), 3.97 (t, *J* = 7.7 Hz, 1H), 3.64 – 3.52 (m, 2H), 2.34 (dddd, *J* =

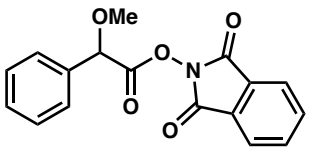
13.2, 10.4, 8.0, 5.1 Hz, 1H), 2.13 (dddd, *J* = 13.5, 10.3, 7.4, 5.5 Hz, 1H), 2.01 – 1.78 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 170.1, 161.9, 136.4, 134.9, 129.1, 129.0, 128.2, 128.1, 124.1, 48.2, 44.4, 31.2, 30.1.

FTIR (NaCl, thin film, cm^{-1}): 2960, 1811, 1786, 1744, 1494, 1455, 1468, 1361, 1186, 1134, 1081, 1045, 965, 878, 697.

HRMS (FAB, *m/z*): calc'd for $C_{19}H_{16}NO_4Cl$ $[M+H]^+$: 358.0846; found: 358.0872.

1,3-dioxoisoindolin-2-yl 2-methoxy-2-phenylacetate (207)



Prepared from 2-methoxy-2-phenylacetic acid (830 mg, 5.0 mmol) according to General Procedure 1. The crude residue was purified by column chromatography (silica, 10 to 30% EtOAc/hexane) to yield 1.16 g (74% yield) of **207** as a colorless oil. *Note: This compound will slowly decompose (solidifies/hydrolyzes) under ambient conditions over extended periods (~1 month).*

R_f = 0.22 (silica gel, 20% EtOAc/hexane, UV).

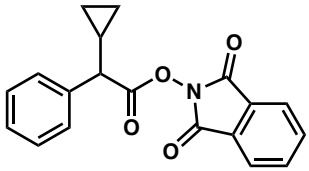
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.75 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.60 – 7.52 (m, 2H), 7.50 – 7.37 (m, 3H), 5.19 (s, 1H), 3.56 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 167.4, 161.6, 134.9, 134.4, 129.6, 129.0, 128.8, 127.6, 124.1, 81.0, 58.0.

FTIR (NaCl, thin film, cm^{-1}): 1818, 1789, 1745, 1468, 1359, 1186, 1079, 988, 969, 877, 696.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{17}H_{13}NO_5$ $[M+H]^+$: 312.0872; found: 312.0846.

1,3-dioxoisoindolin-2-yl 2-cyclopropyl-2-phenylacetate (218)



Prepared from 2-cyclopropyl-2-phenylacetic acid (50 mg, 0.28 mmol) according to General Procedure 1. The crude residue was purified by filtering through a plug of silica with 20% EtOAc/hexane as the eluent to yield 80 mg (89% yield) of **218** as a white solid.

R_f = 0.39 (silica gel, 50% EtOAc/hexane, UV).

m.p. = 92–93 °C

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.81 – 7.75 (m, 2H), 7.50 – 7.45 (m, 2H), 7.44 – 7.38 (m, 2H), 7.37 – 7.31 (m, 1H), 3.29 (d, *J* = 9.7 Hz, 1H), 1.53 (dtt, *J* = 9.7, 8.0, 4.9 Hz, 1H), 0.82 (dddd, *J* = 9.0, 8.1, 4.6, 2.9 Hz, 1H), 0.69 (dddd, *J* = 8.9, 8.0, 5.8, 4.8 Hz, 1H), 0.63 – 0.55 (m, 1H), 0.42 – 0.34 (m, 1H).

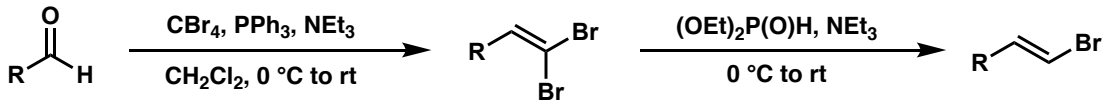
^{13}C NMR (101 MHz, $CDCl_3$): δ 170.0, 162.0, 136.8, 134.9, 129.1, 128.9, 128.1, 128.0, 124.1, 53.4, 14.6, 4.91, 4.90.

FTIR (NaCl, thin film, cm^{-1}): 1811, 1742, 1362, 1170, 1135, 1063, 974, 876.

HRMS (FAB, *m/z*): calc'd for $C_{19}H_{15}NO_4$ $[M+H]^+$: 322.1079; found: 322.1065.

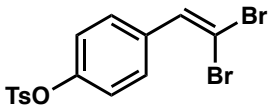
4.7.3.2 *Alkenyl Bromide Synthesis*

General Procedure 2: Alkenyl Bromides from Aldehydes



General Procedure 2, Part A: According to a procedure by Alexakis and coworkers, a flame dried round bottom flask equipped with a magnetic stir bar was put under an inert atmosphere (N_2) and charged with the tetrabromomethane (20 mmol, 2 equiv) and triphenylphosphine (40 mmol, 4 equiv). The flask was cooled to 0 °C and then CH_2Cl_2 (30 mL) was added, followed by the triethylamine (10 mmol, 1 equiv). The aldehyde (10 mmol, 1 equiv) was dissolved in CH_2Cl_2 (5 mL) and added dropwise to the reaction mixture. The reaction was allowed to warm to room temperature and continued to stir for 90 minutes. The reaction was removed from the stir plate and slowly added to a vigorously stirring solution of Et_2O (150 mL) and hexane (150 mL), filtered through a plug of silica gel, and concentrated under reduced pressure to afford the desired dibromoalkene.

4-(2,2-dibromovinyl)phenyl 4-methylbenzenesulfonate (272)



Prepared from 4-formylphenyl 4-methylbenzenesulfonate (5.14 g, 18.6 mmol) following General Procedure 2A. The crude residue was purified by filtering through a plug of silica to yield 6.2 g (77% yield) of **272** as a white solid.

$\mathbf{R}_f$ = 0.38 (silica gel, 10% EtOAc/hexane).

m.p. = 108–110 °C

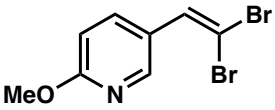
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 – 7.67 (m, 2H), 7.49 – 7.43 (m, 2H), 7.41 (s, 1H), 7.34 – 7.29 (m, 2H), 7.01 – 6.95 (m, 2H), 2.45 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 149.3, 145.7, 135.6, 134.2, 132.3, 129.9, 129.8, 128.6, 122.5, 90.8, 21.9.

FTIR (NaCl, thin film, cm^{-1}): 3081, 3065, 1929, 1910, 1596, 1500, 1495, 1406, 1379, 1360, 1271, 1178, 1160, 1094, 1018, 877, 832, 914, 781, 732, 706, 698, 658.

HRMS (FAB, m/z): calc'd for $C_{15}H_{12}Br_2O_3S$ $[M+H]^+$: 432.8932; found: 432.8915.

5-(2,2-dibromovinyl)-2-methoxypyridine (273)



Prepared from 6-methoxynicotinaldehyde (1.36 g, 10 mmol) following General Procedure 2A. The crude residue was purified by column chromatography (silica, 1% Et_2O/hexane to 10% Et_2O/hexane) to yield 570 mg (20% yield) of **273** as a yellow oil.

$\mathbf{R}_f$ = 0.48 (silica gel, 10% EtOAc/hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.25 (dt, J = 2.4, 0.6 Hz, 1H), 7.90 (ddd, J = 8.7, 2.5, 0.6 Hz, 1H), 7.37 (q, J = 0.6 Hz, 1H), 6.74 (dt, J = 8.7, 0.5 Hz, 2H), 3.94 (s, 3H).

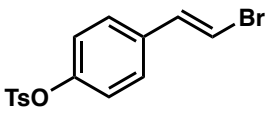
^{13}C NMR (126 MHz, $CDCl_3$): δ 163.8, 147.6, 137.8, 133.5, 124.9, 110.7, 89.3, 53.8.

FTIR (NaCl, thin film, cm^{-1}): 2982, 2946, 1603 1595, 1561, 1491, 1381, 1309, 1289, 1254, 1132, 1024, 1014, 867, 819, 751.

HRMS (ESI-TOF, m/z): calc'd for $C_8H_7NOBr_2$ $[M+H]^+$: 291.8973; found: 291.8967.

General Procedure 2, Part B: The dibromoalkene (1.7 mmol, 1 equiv) and diethyl phosphite (5.1 mmol, 3 equiv) were added to a vial with a magnetic stirring rod and put under an inert atmosphere (N_2). The solution was cooled to 0 °C and the triethylamine (5.1 mmol, 3 equiv) was added dropwise. The reaction was warmed to room temperature and stirred overnight. The reaction was quenched with water (5 mL) and extracted with CH_2Cl_2 (20 mL). The organic layer was washed with brine (5 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography (silica, ether/hexanes) to afford the vinyl bromide.

(*E*)-4-(2-bromovinyl)phenyl 4-methylbenzenesulfonate (274)



Prepared from **272** (4.32 g, 10 mmol) following General Procedure 2B. The crude residue was purified by column chromatography (silica, 5% EtOAc/hexane to 20% EtOAc/hexane) to yield 2.75 g (78% yield, 90:10 E:Z) of **274** as a white solid.

R_f = 0.34 (silica gel, 10% EtOAc/hexane).

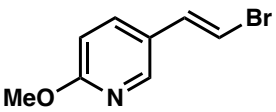
m.p. = 90–93 °C

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 – 7.67 (m, 2H), 7.34 – 7.28 (m, 2H), 7.23 – 7.17 (m, 2H), 7.03 (d, *J* = 14.0 Hz, 1H), 6.96 – 6.90 (m, 2H), 6.73 (d, *J* = 14.0 Hz, 1H), 2.44 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 149.3, 145.6, 135.9, 134.9, 132.3, 129.9, 128.6, 127.3, 122.9, 107.7, 21.9.

HRMS (FAB, m/z): calc'd for $C_{15}H_{13}BrO_3S$ $[M+\cdot]^+$: 353.9748; found: 353.9733.

(*E*)-5-(2-bromovinyl)-2-methoxypyridine (275)



Prepared from **273** (500 mg, 1.7 mmol) following General Procedure 2B. The crude residue was purified by column chromatography (silica, 2% Et_2O/hexane to 5% Et_2O/hexane) to yield 314 mg (86% yield, 96:4 E:Z) of **275** as a white solid.

R_f = 0.46 (silica gel, 10% EtOAc/hexane).

m.p. = 53–56 °C

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.05 (d, *J* = 2.5 Hz, 1H), 7.54 (ddd, *J* = 8.7, 2.5, 0.4 Hz, 1H), 7.02 (dq, *J* = 14.0, 0.5 Hz, 1H), 6.70 (dt, *J* = 8.7, 0.6 Hz, 1H), 6.65 (d, *J* = 14.0 Hz, 1H), 3.93 (s, 3H).

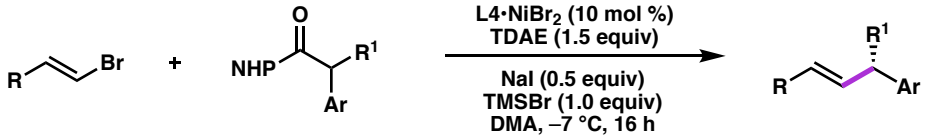
^{13}C NMR (126 MHz, $CDCl_3$): δ 164.0, 145.3, 135.3, 133.5, 125.5, 111.4, 105.5, 53.7.

FTIR (NaCl, thin film, cm^{-1}): 3061, 2943, 1613, 1598, 1562, 1490, 1385, 1303, 1285, 1258, 1238, 1026, 1015, 947, 837, 790.

HRMS (ESI-TOF, m/z): calc'd for C_8H_8NOBr $[M+H]^+$: 213.9868; found: 213.9858.

4.7.4 *Enantioselective Reductive Cross-Coupling*

4.7.4.1 *General Procedures for Enantioselective Cross-Coupling of N-Hydroxyphthalimide Esters with Alkenyl Bromides*



General Procedure 3: Cross-Coupling on 0.2 mmol scale

On a bench-top, a 1 dram vial equipped with a stir bar was charged with the vinyl bromide (if air stable, 0.2 mmol, 1 equiv), NHP ester (0.2 mmol, 1 equiv), **L4•NiBr$_2$** (11.5 mg, 0.02 mmol, 0.10 equiv), and sodium iodide (15.0 mg, 0.1 mmol, 0.5 equiv). The vial was then brought into the glovebox and charged with the vinyl bromide (if air sensitive, 0.2 mmol, 1 equiv) and DMA (0.2 mL, 1.0 M). The vial was then cooled to –7 °C and the reagents were stirred at 250 rpm until dissolved. *Note: The recirculating Julabo LH45 chiller was set to –10 °C however an external thermometer in the glovebox read the temperature as –7 °C.* The tetrakis(dimethyl-amino)ethylene (TDAE, 0.3 mmol, 70 μl, 1.5 equiv) was added and stirred for 10 minutes before the trimethylsilyl bromide (TMSBr, 0.2 mmol, 26 μL, 1 equiv) was added. The vial was sealed with a screw cap and stirred under nitrogen at –7 °C for 16 hours (overnight) in temperature controlled well plates in the glovebox. *Note: Monitoring the reaction kinetics for product **28** revealed that the reaction went to >90% conversion after 1 hour, however we choose to run these reactions overnight to ensure full conversion.* As the reaction proceeds, the TDAE salts begin to precipitate, forming an orange slurry. The crude reaction was quenched with 0.5 mL of 1 M HCl, diluted with water (5 mL), and extracted with diethyl ether (3 x 10 mL). *Note: In order to efficiently remove all of the viscous reaction contents from the vial, we*

found it useful to fill the vial ¾ full with an extraction solvent (2.5 mL each time: first HCl/water, then Et_2O, water, Et_2O 3x), screw on a Teflon cap, and shake the vial vigorously with the stir bar still inside. The contents could then be easily poured into a separatory funnel. The combined organic layers were washed with brine (5 mL), dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography.



Reaction Setup: (Left) The computer console sets the chiller to –10.0 °C, while actual temperature reading is –7.1 °C; stir plate set at 250 rpm and reads 255.7 rpm. **(Center)** Reactions conducted on 0.2 mmol scale and stirred in the temperature controlled glovebox stir plates. **(Right)** Conducting the reaction on the benchtop on a 5 mmol scale under a balloon of nitrogen; a cryocool is used to cool the reaction to –5 °C.

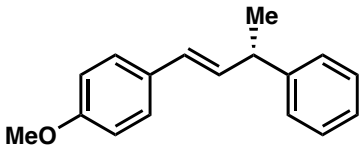
General Procedure 4: Cross-Coupling on 5.0 mmol scale

On a bench-top to a 25 mL round bottom flask equipped with a stir bar was added vinyl bromide **27** (1.065 g, 5 mmol, 1 equiv), NHP ester **31** (1.476 g, 5 mmol, 1 equiv), **L4•NiBr$_2$** (0.29 g, 0.5 mmol, 0.10 equiv), and sodium iodide (0.37 g, 2.5 mmol, 0.5 equiv). The flask was sealed with a rubber septum, purged with nitrogen, and the reagents

were dissolved in DMA (5.0 mL, 1.0 M). The flask was cooled to –5 °C by submerging it in an isopropanol bath cooled with a Thermo Scientific EK90 Immersion Cooler. *Note: We found that TDAE will begin to freeze at temperatures lower than –8 °C with this setup.* The tetrakis(dimethylamino)ethylene (TDAE, 1.74 mL, 7.5 mmol, 1.5 equiv) was added and stirred for 10 minutes before the trimethylsilyl bromide (TMSBr, 0.66 mL, 5.0 mmol, 1 equiv) was added. The flask was stirred under a balloon of nitrogen at –5 °C for 16 hours. As the reaction proceeds, the TDAE salts begin to precipitate, forming an orange slurry. The crude reaction was quenched with 1 M HCl (30 mL), and extracted with diethyl ether (3 x 20 mL). The combined organic layers were washed with water (2 x 20 mL) and brine (20 mL), dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography (silica gel, 10 to 20% toluene/hexane) to yield **28** (918 mg, 77% yield) in 91% ee as a colorless oil.

4.7.4.2 *Characterization of Reaction Products*

(*S*,*E*)-1-methoxy-4-(3-phenylbut-1-en-1-yl)benzene (28)



Prepared from (*E*)-1-(2-bromovinyl)-4-methoxybenzene (43 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 2-phenylpropanoate (59 mg, 0.2 mmol) according to General Procedure 3. The crude residue was purified by column chromatography (silica gel, 10 to 20% toluene/hexane) to yield **28** (39 mg, 80% yield) in 96% ee as a colorless oil. Spectral data matched those reported in literature.

$\mathbf{R}_f$ = 0.59 (silica gel, 10% EtOAc/hexane, UV).

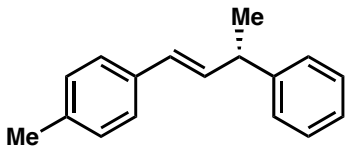
Chiral SFC: (OB-H, 2.5 mL/min, 20% IPA in CO_2, λ = 254 nm): t_R (major) = 7.1 min, t_R (minor) = 8.4 min.

$\mathbf{[\alpha]_D^{25}}$ = –34° (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 – 7.27 (m, 6H), 7.25 – 7.20 (m, 1H), 6.85 (d, *J* = 8.8 Hz, 2H), 6.38 (d, *J* = 16.2 Hz, 1H), 6.27 (dd, *J* = 15.9, 6.7 Hz, 1H), 3.81 (s, 3H), 3.70 – 3.58 (m, 1H), 1.48 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 158.9, 146.0, 133.3, 130.5, 128.6, 128.0, 127.42, 127.36, 126.3, 114.0, 55.4, 42.7, 21.5.

(*S*,*E*)-1-methyl-4-(3-phenylbut-1-en-1-yl)benzene (180)



Prepared from (*E*)-1-(2-bromovinyl)-4-methylbenzene (39 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 2-phenylpropanoate (59 mg, 0.2 mmol) according to General Procedure 3. The crude residue was purified by column chromatography (10% $AgNO_3$ silica gel, 0 to 2% Et_2O/hexane) to yield **180** (39 mg, 88% yield) in 95% ee as a colorless oil. Spectral data matched those reported in literature.

$\mathbf{R}_f$ = 0.26 (silica gel, hexane, UV).

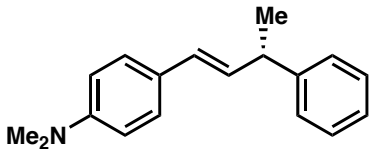
Chiral SFC: (OJ-H, 2.5 mL/min, 7% IPA in CO_2, λ = 254 nm): t_R (minor) = 8.0 min, t_R (major) = 10.0 min.

$\mathbf{[\alpha]_D^{25}}$ = –41° (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 – 7.30 (m, 6H), 7.30 – 7.24 (m, 1H), 7.16 (d, *J* = 8.0 Hz, 2H), 6.52 – 6.34 (m, 2H), 3.74 – 3.64 (m, 1H), 2.38 (s, 3H), 1.53 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 145.9, 136.9, 134.9, 134.3, 129.3, 128.6, 128.5, 127.5, 126.3, 126.2, 42.7, 21.5, 21.3.

(*S*,*E*)-*N*,*N*-dimethyl-4-(3-phenylbut-1-en-1-yl)aniline (181)



Prepared from (*E*)-4-(2-bromovinyl)-*N*,*N*-dimethylaniline (45 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 2-phenylpropanoate (59 mg, 0.2 mmol) according to General Procedure 3. The crude residue was purified by column chromatography (silica gel, 5% Et_2O/hexane) to yield **181** (38 mg, 76% yield) in 97% ee as a white solid. Spectral data matched those reported in literature.

R_f = 0.21 (silica gel, 5% Et_2O/hexane, UV).

m.p. = 65–67 °C

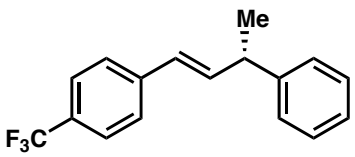
Chiral SFC: (OB-H, 2.5 mL/min, 35% IPA in CO_2, λ = 254 nm): t_R (major) = 6.0 min, t_R (minor) = 9.0 min.

$[\alpha]_D^{25}$ = –56° (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 – 7.29 (m, 6H), 7.29 – 7.23 (m, 1H), 6.73 (d, *J* = 8.8 Hz, 2H), 6.40 (d, *J* = 15.9 Hz, 1H), 6.24 (dd, *J* = 15.8, 6.8 Hz, 1H), 3.72 – 3.62 (m, 1H), 3.00 (s, 6H), 1.51 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 149.9, 146.4, 131.2, 128.5, 128.4, 127.5, 127.1, 126.4, 126.1, 112.7, 42.7, 40.8, 21.6.

(*S*,*E*)-1-(3-phenylbut-1-en-1-yl)-4-(trifluoromethyl)benzene (182)



Prepared from (*E*)-1-(2-bromovinyl)-4-(trifluoromethyl)benzene (50 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 2-phenylpropanoate (59 mg, 0.2 mmol) according to General Procedure 3. The crude residue was purified by column chromatography (silica gel, hexane) to yield **182** (48 mg, 87% yield) in 93% ee as a colorless oil. Spectral data matched those reported in literature.

R_f = 0.32 (silica gel, hexane, UV).

Chiral SFC: (OJ-H, 2.5 mL/min, 3% IPA in CO_2, λ = 254 nm): t_R (minor) = 6.3 min, t_R (major) = 7.3 min.

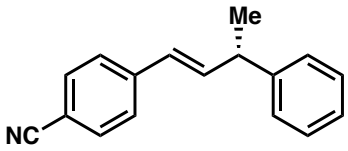
$[\alpha]_D^{25}$ = –27° (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, *J* = 8.6 Hz, 2H), 7.46 (d, *J* = 8.2 Hz, 2H), 7.40 – 7.33 (m, 2H), 7.33 – 7.23 (m, 3H), 6.52 (dd, *J* = 15.9, 6.2 Hz, 1H), 6.45 (d, *J* = 16.0 Hz, 1H), 3.74 – 3.64 (m, 1H), 1.51 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 145.2, 141.2 (q, J_{C-F} = 1 Hz), 138.1, 129.0 (q, J_{C-F} = 32 Hz), 128.7, 127.5, 127.4, 126.6, 126.4, 125.6 (q, J_{C-F} = 4 Hz), 124.4 (q, J_{C-F} = 272 Hz), 42.8, 21.2.

^{19}F NMR (282 MHz, $CDCl_3$): δ –65.6.

(*S*,*E*)-4-(3-phenylbut-1-en-1-yl)benzonitrile (183)



Prepared from methyl (*E*)-4-(2-bromovinyl)benzonitrile (42 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 2-phenylpropanoate (59 mg, 0.2 mmol) according to General Procedure 3. The crude residue was purified by column chromatography (silica gel, 0 to 3% Et_2O/hexane) to yield **183** (42 mg, 91% yield) in 94% ee as a colorless oil.

R_f = 0.42 (silica gel, 10% EtOAc/hexane, UV).

Chiral SFC: (OB-H, 2.5 mL/min, 10% IPA in CO_2, λ = 254 nm): t_R (minor) = 9.5 min, t_R (major) = 10.1 min.

$[\alpha]_D^{25}$ = –51° (c = 1.0, $CHCl_3$).

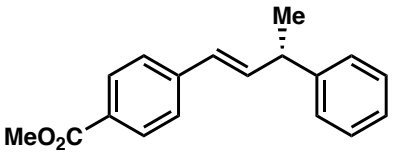
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, *J* = 8.5 Hz, 2H), 7.40 (d, *J* = 8.3 Hz, 2H), 7.36 – 7.30 (m, 2H), 7.28 – 7.19 (m, 3H), 6.52 (dd, *J* = 15.9, 6.7 Hz, 1H), 6.40 (d, *J* = 16.0 Hz, 1H), 3.72 – 3.61 (m, 1H), 1.48 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 144.7, 142.1, 139.5, 132.4, 128.7, 127.3, 127.2, 126.7, 126.6, 119.2, 110.2, 42.8, 21.0.

FTIR (NaCl, thin film, cm^{-1}): 3027, 2967, 2872, 2225, 1646, 1604, 1504, 1493, 1452, 1412, 1176, 1013, 970, 866, 819, 763, 701.

HRMS (FAB, *m/z*): calc'd for $C_{17}H_{15}N$ $[M+H]^+$: 234.1283; found: 234.1265.

Methyl (*S*,*E*)-4-(3-phenylbut-1-en-1-yl)benzoate (184)



Prepared from methyl (*E*)-4-(2-bromovinyl)benzoate (48 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 2-phenylpropanoate (59 mg, 0.2 mmol) according to General Procedure 3. The crude residue was purified by column chromatography (silica gel, 5% Et_2O/hexane) to yield **184** (46 mg, 87% yield) in 95% ee as a colorless oil.

$\mathbf{R_f}$ = 0.19 (silica gel, 5% Et_2O/hexane, UV).

Chiral SFC: (OB-H, 2.5 mL/min, 20% IPA in CO_2, λ = 254 nm): t_R (minor) = 8.2 min, t_R (major) = 11.6 min.

$\mathbf{[\alpha]_D^{25}}$ = –44° (c = 1.0, $CHCl_3$).

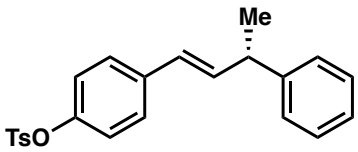
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 8.3 Hz, 2H), 7.37 – 7.30 (m, 2H), 7.30 – 7.20 (m, 3H), 6.53 (dd, *J* = 15.9, 6.5 Hz, 1H), 6.44 (d, *J* = 16.1 Hz, 1H), 3.91 (s, 3H), 3.72 – 3.62 (m, 1H), 1.49 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 167.1, 145.2, 142.2, 138.2, 130.0, 128.7, 128.6, 127.9, 127.4, 126.5, 126.1, 52.2, 42.8, 21.2.

FTIR (NaCl, thin film, cm^{-1}): 3025, 2963, 1718, 1605, 1492, 1433, 1411, 1276, 1177, 1108, 1015, 968, 759, 698.

LRMS (GC-MS, *m/z*): calc'd for $C_{18}H_{18}O_2$ $[M]^+$: 266.1; found: 266.1.

(*S*,*E*)-4-(3-phenylbut-1-en-1-yl)phenyl 4-methylbenzenesulfonate (185)



Prepared from (*E*)-4-(2-bromovinyl)phenyl 4-methylbenzenesulfonate (71 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 2-phenylpropanoate (89 mg, 0.3 mmol) according to General Procedure 3 with the exception that 1.5 equiv NHP ester was used instead of 1.0 equiv. *Note: The addition of excess NHP ester ensured full consumption of the vinyl bromide, which we found to be inseparable from the product when it remained in the crude reaction.* The crude residue was purified by column chromatography (silica gel, hexane to 5% Et_2O/hexane) to yield **185** (61 mg, 80% yield) in 94% ee as a colorless oil.

$\mathbf{R_f}$ = 0.39 (silica gel, 10% EtOAc/hexane, UV).

Chiral SFC: (OJ-H, 2.5 mL/min, 15% IPA in CO_2, λ = 254 nm): t_R (minor) = 12.2 min,

t_R (major) = 13.7 min.

$[\alpha]_D^{25}$ = –24° (c = 1.0, $CHCl_3$).

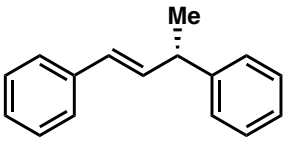
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, *J* = 8.4 Hz, 2H), 7.36 – 7.28 (m, 4H), 7.28 – 7.20 (m, 5H), 6.90 (d, *J* = 8.7 Hz, 2H), 6.39 – 6.30 (m, 2H), 3.69 – 3.58 (m, 1H), 2.45 (s, 3H), 1.46 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 148.5, 145.4, 145.3, 136.7, 136.5, 132.4, 129.8, 128.6, 127.3, 127.2, 126.4, 122.5, 42.7, 21.8, 21.2.

FTIR (NaCl, thin film, cm^{-1}): 3061, 3028, 2966, 2928, 2872, 1647, 1599, 1504, 1453, 1372, 1307, 1296, 1198, 1176, 1152, 1093, 1016, 969, 867, 841, 815, 763, 735, 700, 661.

HRMS (FAB, *m/z*): calc'd for $C_{23}H_{22}O_3S$ $[M+\cdot]^+$: 378.1290; found: 378.1283.

(*S*,*E*)-but-1-ene-1,3-diyldibenzene (186)



Prepared from (*E*)-(2-bromovinyl)benzene (37 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 2-phenylpropanoate (59 mg, 0.2 mmol) according to General Procedure 3. The crude residue was purified by column chromatography (silica gel, hexane) to yield **186** (37 mg, 88% yield) in 96% ee as a colorless oil.

R_f = 0.48 (silica gel, hexane, UV).

Chiral SFC: (OJ-H, 2.5 mL/min, 5% IPA in CO_2, λ = 254 nm): t_R (minor) = 9.8 min, t_R (major) = 10.9 min.

$[\alpha]_D^{25}$ = –35° (c = 1.0, $CHCl_3$).

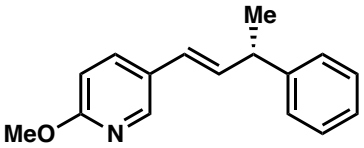
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 – 7.29 (m, 8H), 7.29 – 7.21 (m, 2H), 6.51 – 6.38 (m, 2H), 3.73 – 3.65 (m, 1H), 1.52 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 145.7, 137.7, 135.3, 128.6 (3C), 127.4, 127.2, 126.35, 126.27, 42.7, 21.4.

FTIR (NaCl, thin film, cm^{-1}): 3080, 3058, 3024, 2964, 2928, 2871, 1599, 1492, 1448, 1371, 1010, 964, 742, 692.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{16}H_{16}$ $[M–H_2+H]^+$: 207.1174; found: 207.1155.

(*S*,*E*)-2-methoxy-5-(3-phenylbut-1-en-1-yl)pyridine (187)



Prepared from (*E*)-5-(2-bromovinyl)-2-methoxypyridine (43 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 2-phenylpropanoate (59 mg, 0.2 mmol) according to General Procedure 3. The crude residue was purified by column chromatography (silica gel, 5% Et_2O/hexane) to yield **187** (32 mg, 67% yield) in 95% ee as a colorless oil.

R_f = 0.53 (silica gel, 10% EtOAc/hexane, UV).

Chiral SFC: (OB-H, 2.5 mL/min, 15% IPA in CO_2, λ = 280 nm): t_R (major) = 5.0 min, t_R (minor) = 6.9 min.

$[\alpha]_D^{25}$ = –33° (c = 1.0, $CHCl_3$).

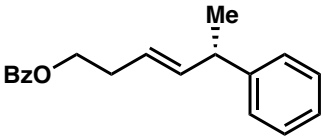
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, *J* = 2.4 Hz, 1H), 7.62 (dd, *J* = 8.7, 2.5 Hz, 1H), 7.35 – 7.28 (m, 2H), 7.28 – 7.18 (m, 3H), 6.67 (d, *J* = 8.6 Hz, 1H), 6.33 (d, *J* = 16.1 Hz, 1H), 6.26 (dd, *J* = 15.9, 6.3 Hz, 1H), 3.91 (s, 3H), 3.66 – 3.57 (m, 1H), 1.45 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 163.4, 145.6, 145.3, 135.5, 134.7, 128.7, 127.4, 126.8, 126.4, 124.7, 110.9, 53.6, 42.8, 21.3.

FTIR (NaCl, thin film, cm^{-1}): 2965, 1601, 1493, 1384, 1286, 1026, 962, 822, 762, 699.

HRMS (FAB, *m/z*): calc'd for $C_{16}H_{17}NO$ $[M+H]^+$: 240.1388; found: 240.1398.

(*S*,*E*)-5-phenylhex-3-en-1-yl benzoate (188)



Prepared from (*E*)-4-bromobut-3-en-1-yl benzoate (51 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 2-phenylpropanoate (59 mg, 0.2 mmol) according to General Procedure 3. The crude residue was purified by column chromatography (silica gel, 5% Et_2O/hexane) to yield **188** (49 mg, 88% yield) in 97% ee as a colorless oil. Spectral data matched those reported in literature.

R_f = 0.24 (silica gel, 5% Et_2O/hexane, UV).

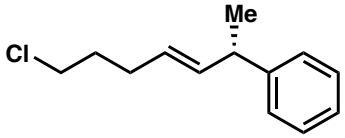
Chiral SFC: (OJ-H, 2.5 mL/min, 10% IPA in CO_2, λ = 254 nm): t_R (major) = 5.2 min, t_R (minor) = 6.1 min.

$[\alpha]_D^{25}$ = +5° (c =1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 – 8.00 (m, 2H), 7.59 – 7.53 (m, 1H), 7.46 – 7.40 (m, 2H), 7.29 – 7.23 (m, 2H), 7.22 – 7.15 (m, 3H), 5.77 (ddt, *J* = 15.4, 6.8, 1.3 Hz, 1H), 5.52 (dtd, *J* = 15.2, 6.8, 1.3 Hz, 1H), 4.36 (td, *J* = 6.7, 1.4 Hz, 2H), 3.50 – 3.42 (m, 1H), 2.54 – 2.46 (m, 2H), 1.35 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 166.7, 146.0, 138.3, 133.0, 130.5, 129.7, 128.5, 128.4, 127.3, 126.2, 124.3, 64.4, 42.4, 32.2, 21.4.

(*S*,*E*)-(7-chlorohept-3-en-2-yl)benzene (189)



Prepared from (*E*)-1-bromo-5-chloropent-1-ene (37 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 2-phenylpropanoate (59 mg, 0.2 mmol) according to General Procedure 3. The crude residue was purified by column chromatography (silica gel, hexane) to yield **189** (29 mg, 69% yield) in 91% ee as a colorless oil.

R_f = 0.29 (silica gel, hexane, UV/CAM).

Chiral SFC: (OD-H, 2.5 mL/min, 1% IPA in CO_2, λ = 210 nm): t_R (minor) = 5.4 min, t_R (major) = 6.0 min.

$[\alpha]_D^{25}$ = +9° (c =1.0, $CHCl_3$).

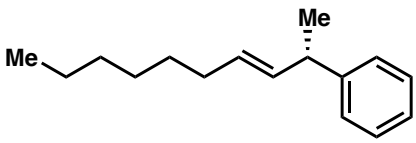
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 – 7.29 (m, 2H), 7.25 – 7.18 (m, 3H), 5.69 (ddt, *J* = 15.3, 6.8, 1.4 Hz, 1H), 5.43 (dtd, *J* = 15.1, 6.8, 1.1 Hz, 1H), 3.54 (t, *J* = 6.7 Hz, 2H), 3.50 – 3.40 (m, 1H), 2.23 – 2.16 (m, 2H), 1.90 – 1.82 (m, 2H), 1.36 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 146.3, 136.7, 128.5, 127.24, 127.17, 126.1, 44.6, 42.4, 32.4, 29.7, 21.6.

FTIR (NaCl, thin film, cm^{-1}): 3025, 2962, 2929, 2871, 1601, 1492, 1450, 1371, 1297, 1017, 969, 759, 698.

HRMS (FAB, *m/z*): calc'd for $C_{13}H_{17}Cl$ $[M–H_2+H]^+$: 207.0940; found: 207.0910.

(*S*,*E*)-dec-3-en-2-ylbenzene (190)



Prepared from (*E*)-1-bromooct-1-ene (38 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 2-phenylpropanoate (59 mg, 0.2 mmol) according to

General Procedure 3. The crude residue was purified by column chromatography (silica gel, hexane) to yield **190** (31 mg, 72% yield) in 94% ee as a colorless oil.

R_f = 0.59 (silica gel, hexane, UV/CAM).

Chiral SFC: (OJ-H, 2.5 mL/min, 1% IPA in CO_2, λ = 210 nm): t_R (minor) = 3.9 min, t_R (major) = 4.5 min.

$[\alpha]_D^{25}$ = +4° (c = 0.9, $CHCl_3$).

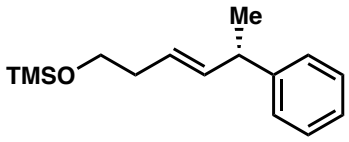
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 – 7.27 (m, 2H), 7.25 – 7.15 (m, 3H), 5.60 (ddt, *J* = 15.3, 6.6, 1.4 Hz, 1H), 5.46 (dtd, *J* = 15.1, 6.6, 1.2 Hz, 1H), 3.47 – 3.38 (m, 1H), 2.06 – 1.97 (m, 2H), 1.40 – 1.22 (m, 11H), 0.95 – 0.83 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 146.7, 135.0, 129.5, 128.4, 127.3, 126.0, 42.4, 32.7, 31.9, 29.6, 29.0, 22.8, 21.7, 14.3.

FTIR (NaCl, thin film, cm^{-1}): 3025, 2959, 2925, 2854, 1492, 1451, 1371, 1016, 965, 758, 697.

LRMS (GC-MS, *m/z*): calc'd for $C_{16}H_{24}$ $[M]^+$: 216.2; found: 216.2.

(*S*,*E*)-trimethyl((5-phenylhex-3-en-1-yl)oxy)silane (191)



Prepared from (*E*)-4-bromobut-3-en-1-ol (30 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 2-phenylpropanoate (59 mg, 0.2 mmol) according to General Procedure 3 with the exception that 2.0 equiv TMSBr was used instead of 1.0 equiv. The reaction was quenched with water instead of 1 M HCl to prevent decomposition of the primary silyl ether. *Note: An acidic workup yielded a mixture of the silyl ether and alcohol product, however the alcohol was inseparable from the phthalimide byproduct.* The crude residue was purified by column chromatography (florisil, hexane to 1% Et_2O/hexane) to yield **191** (33 mg, 66% yield) as a colorless oil. *Note: The two enantiomers of the racemic silyl ether were inseparable by chiral SFC.*

R_f = 0.67 (silica gel, 10% EtOAc/hexane, UV/CAM).

$[\alpha]_D^{25}$ = +6° (c = 1.0, $CHCl_3$).

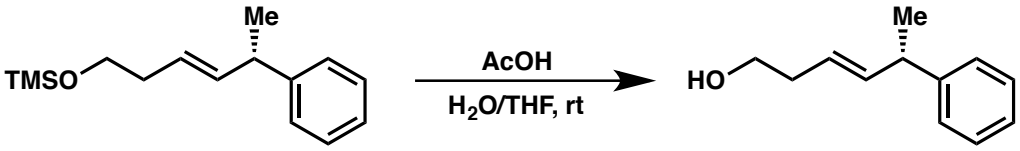
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 – 7.28 (m, 2H), 7.25 – 7.17 (m, 3H), 5.69 (ddt, *J* = 15.4, 6.7, 1.3 Hz, 1H), 5.47 (dtd, *J* = 15.3, 6.9, 1.4 Hz, 1H), 3.61 (t, *J* = 7.0 Hz, 2H), 3.49 – 3.40 (m, 1H), 2.28 (qt, *J* = 7.0, 1.1 Hz, 2H), 1.36 (d, *J* = 7.1 Hz, 3H), 0.13 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 146.3, 137.3, 128.5, 127.3, 126.1, 125.4, 62.7, 42.5, 36.2, 21.5, -0.3.

FTIR (NaCl, thin film, cm^{-1}): 2961, 2930, 2902, 2863, 1602, 1493, 1452, 1382, 1251, 1094, 968, 940, 876, 841, 758, 748, 699.

HRMS (FAB, *m/z*): calc'd for $C_{15}H_{24}OSi$ $[M+H]^+$: 249.1675; found: 249.1684.

(*S*,*E*)-5-phenylhex-3-en-1-ol (276)



Deprotection of Silyl Ether: Silyl ether **191** (33.0 mg, 0.132 mmol, 1 equiv) was dissolved in a solution of acetic acid (0.5 mL), water (0.5 mL), and THF (2.5 mL) in a 20 mL vial equipped with a magnetic stir bar and stirred at room temperature for 15 min. The reaction was slowly quenched with a solution of saturated $NaHCO_3$ until the pH was slightly basic (approx. 15 mL), extracted with Et_2O (3 x 10 mL), dried with $MgSO_4$, filtered, and concentrated under reduced pressure to yield **276** (22.6 mg, 97% yield) in 89% ee as a colorless oil. Spectral data matched those reported in literature.

R_f = 0.11 (silica gel, 10% EtOAc/hexane, UV/CAM).

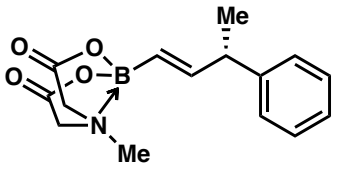
Chiral SFC: (OB-H, 2.5 mL/min, 3% IPA in CO_2, λ = 210 nm): t_R (minor) = 6.9 min, t_R (major) = 7.5 min.

$[\alpha]_D^{25}$ = +9° (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 – 7.27 (m, 2H), 7.25 – 7.16 (m, 3H), 5.76 (ddt, *J* = 15.4, 6.7, 1.4 Hz, 1H), 5.45 (dtd, *J* = 15.3, 7.0, 1.4 Hz, 1H), 3.65 (t, *J* = 6.3 Hz, 2H), 3.52 – 3.42 (m, 1H), 2.30 (q, *J* = 6.3 Hz, 2H), 1.54 (s, 1H), 1.37 (d, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 146.1, 138.8, 128.6, 127.2, 126.2, 124.8, 62.2, 42.5, 36.0, 21.6.

(*S*,*E*)-6-methyl-2-(3-phenylbut-1-en-1-yl)-1,3,6,2-dioxazaborocane-4,8-dione (192)



Prepared from *trans*-1-bromovinylboronic acid MIDA ester (52 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 2-phenylpropanoate (59 mg, 0.2 mmol) according to General Procedure 3. The crude residue was purified by column chromatography (silica gel, 10% EtOAc/hexane to 100% EtOAc) to yield **192** (25 mg, 43% yield) in 97% ee as a yellow solid. *Note: The ^{1}H NMR contains two minor impurities that were identified as DMA and methyliminodiacetic acid.*

R_f = 0.35 (silica gel, EtOAc, UV/$KMnO_4$).

m.p. = 144–146 °C

Chiral SFC: (OJ-H, 2.5 mL/min, 30% IPA in CO_2, λ = 210 nm): t_R (major) = 5.5 min, t_R (minor) = 10.2 min.

$[\alpha]_D^{25}$ = +0.5° ± 1.1° (c = 1.0, $CHCl_3$). *Note*: *This compound shows low optical rotation*.

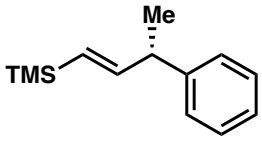
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 – 7.23 (m, 2H), 7.21 – 7.13 (m, 3H), 6.32 (dd, *J* = 17.7, 6.4 Hz, 1H), 5.38 (dd, *J* = 17.7, 1.5 Hz, 1H), 3.92 (dd, *J* = 16.7, 4.5 Hz, 2H), 3.59 (dd, *J* = 16.8, 13.9 Hz, 2H), 3.54 – 3.46 (m, 1H), 2.69 (s, 3H), 1.36 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 168.34, 168.27, 151.7, 145.3, 128.6, 127.4, 126.3, 61.53, 61.49, 47.0, 44.8, 20.8.

FTIR (NaCl, thin film, cm^{-1}): 2963, 1762, 1636, 1492, 1338, 1290, 1246, 1193, 1154, 1126, 1090, 1025, 1007, 956, 867, 761, 702.

HRMS (FAB, *m/z*): calc'd for $C_{15}H_{18}BNO_4$ $[M+H]^+$: 288.1407; found: 288.1414.

(*S*,*E*)-trimethyl(3-phenylbut-1-en-1-yl)silane (193)



Prepared from (*E*)-(2-bromovinyl)trimethylsilane (36 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 2-phenylpropanoate (59 mg, 0.2 mmol) according to General Procedure 3. Alkenyl bromide **206** is reported to be air sensitive, and was added to the reaction while inside the glovebox. The crude residue was purified by column chromatography (silica gel, hexane) to yield **193** (28 mg, 68% yield) in 97% ee as a colorless oil.

R_f = 0.65 (silica gel, hexane, UV/CAM).

Chiral SFC: (OJ-H, 2.5 mL/min, CO_2, λ = 210 nm): t_R (major) = 1.8 min, t_R (minor) = 2.0 min.

$[\alpha]_D^{25}$ = –2.4° ± 0.2° (c = 0.9, $CHCl_3$).

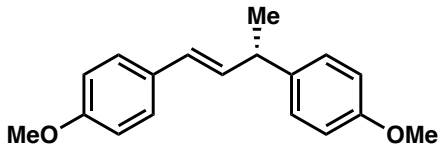
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 – 7.28 (m, 2H), 7.24 – 7.18 (m, 3H), 6.19 (dd, *J* = 18.6, 5.9 Hz, 1H), 5.68 (dd, *J* = 18.6, 1.6 Hz, 1H), 3.52 – 3.44 (m, 1H), 1.36 (d, *J* = 7.0 Hz, 3H), 0.06 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 150.8, 145.8, 128.5, 128.1, 127.5, 126.2, 45.6, 20.9, -1.0.

FTIR (NaCl, thin film, cm^{-1}): 3028, 2958, 1612, 1602, 1492, 1452, 1248, 1009, 987, 868, 837, 759, 698.

LRMS (GC-MS, *m/z*): calc'd for $C_{13}H_{20}Si$ $[M]^+$: 204.1; found: 204.1.

(*S*,*E*)-4,4'-(but-1-ene-1,3-diyl)bis(methoxybenzene) (194)



Prepared from (*E*)-1-(2-bromovinyl)-4-methoxybenzene (43 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 2-(4-methoxyphenyl)-propanoate (65 mg, 0.2 mmol) according to General Procedure 3. The crude residue was purified by column chromatography (silica gel, 10% toluene/hexane then 10% Et_2O/hexane) to yield **194** (42 mg, 78% yield) in 93% ee as a white solid. Spectral data matched those reported in literature.

R_f = 0.45 (silica gel, 10% EtOAc/hexane, UV).

m.p. = 51–59 °C

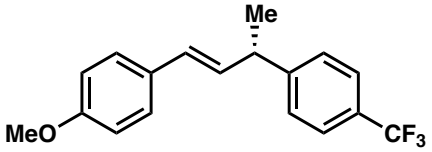
Chiral SFC: (AD-H, 2.5 mL/min, 20% IPA in CO_2, λ = 235 nm): t_R (major) = 7.0 min, t_R (minor) = 8.5 min.

$[\alpha]_D^{25}$ = –34° (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (d, *J* = 8.7 Hz, 2H), 7.22 (d, *J* = 8.5 Hz, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 6.37 (d, *J* = 16.0 Hz, 1H), 6.25 (dd, *J* = 15.9, 6.6 Hz, 1H), 3.82 (s, 3H), 3.81 (s, 3H), 3.65 – 3.55 (m, 1H), 1.46 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 158.9, 158.0, 138.1, 133.6, 130.5, 128.3, 127.7, 127.3, 114.0, 113.9, 55.4 (2C), 41.8, 21.6.

(*S*,*E*)-1-methoxy-4-(3-(4-(trifluoromethyl)phenyl)but-1-en-1-yl)benzene (195)



Prepared from (*E*)-1-(2-bromovinyl)-4-methoxybenzene (43 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 2-(4-(trifluoromethyl)-phenyl)propanoate (73 mg, 0.2 mmol) according to General Procedure 3. The crude residue was purified by column chromatography (silica gel, 5% toluene/hexane) to yield **195** (40 mg, 65% yield) in 88% ee as a white solid.

R_f = 0.48 (silica gel, 10% EtOAc/hexane, UV).

m.p. = 67–70 °C

Chiral SFC: (OB-H, 2.5 mL/min, 5% IPA in CO_2, λ = 254 nm): t_R (major) = 6.5 min, t_R (minor) = 7.5 min.

$[\alpha]_D^{25}$ = –39° (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, *J* = 8.1 Hz, 2H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.7 Hz, 2H), 6.85 (d, *J* = 8.8 Hz, 2H), 6.38 (d, *J* = 16.0 Hz, 1H), 6.21 (dd, *J* = 15.9, 6.8 Hz, 1H), 3.81 (s, 3H), 3.73 – 3.64 (m, 1H), 1.48 (d, *J* = 7.0 Hz, 3H).

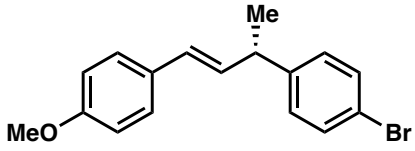
^{13}C NMR (101 MHz, $CDCl_3$): δ 159.1, 150.1 (q, $J_{C\text{-}F}$ = 1.4 Hz), 132.0, 130.1, 128.8, 128.6 (q, $J_{C\text{-}F}$ = 32.3 Hz), 127.8, 127.4, 125.5 (q, $J_{C\text{-}F}$ = 3.8 Hz), 124.5 (q, $J_{C\text{-}F}$ = 271.9 Hz), 114.1, 55.4, 42.6, 21.3.

^{19}F NMR (282 MHz, $CDCl_3$): δ –65.4.

FTIR (NaCl, thin film, cm^{-1}): 2965, 1608, 1512, 1252, 1174, 1164, 1122, 1069, 1036, 1016, 967, 840, 818.

HRMS (EI, *m/z*): calc'd for $C_{18}H_{17}F_3O$ $[M+\cdot]^+$: 306.1232; found: 306.1241.

(*S*,*E*)-1-bromo-4-(4-(4-methoxyphenyl)but-3-en-2-yl)benzene (196)



Prepared from (*E*)-1-(2-bromovinyl)-4-methoxybenzene (43 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 2-(4-bromophenyl)-propanoate (75 mg, 0.2 mmol) according to General Procedure 3. The crude residue was purified by column chromatography (silica gel, 5 to 10% toluene/hexane) to yield **196** (51 mg, 80% yield) in 90% ee as a white solid. Spectral data matched those reported in literature.

R_f = 0.59 (silica gel, 10% EtOAc/hexane, UV).

m.p. = 74–76 °C

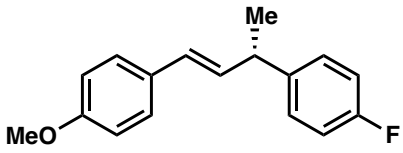
Chiral SFC: (OB-H, 2.5 mL/min, 35% IPA in CO_2, λ = 254 nm): t_R (major) = 5.3 min, t_R (minor) = 8.5 min.

$[\alpha]_D^{25}$ = –32° (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, *J* = 8.5 Hz, 2H), 7.30 (d, *J* = 8.6 Hz, 2H), 7.16 (d, *J* = 8.3 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 6.36 (d, *J* = 16.0 Hz, 1H), 6.20 (dd, *J* = 15.9, 6.7 Hz, 1H), 3.81 (s, 3H), 3.64 – 3.55 (m, 1H), 1.45 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 159.0, 145.0, 132.5, 131.6, 130.2, 129.2, 128.4, 127.4, 120.0, 114.0, 55.4, 42.1, 21.3.

(*S*,*E*)-1-fluoro-4-(4-(4-methoxyphenyl)but-3-en-2-yl)benzene (197)



Prepared from (*E*)-1-(2-bromovinyl)-4-methoxybenzene (43 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 2-(4-fluorophenyl)-propanoate (63 mg, 0.2 mmol) according to General Procedure 3. The crude residue was purified by column chromatography (silica gel, 5 to 30% toluene/hexane) to yield **197** (44 mg, 85% yield) in 92% ee as a colorless oil. Spectral data matched those reported in literature.

R_f = 0.70 (silica gel, 10% EtOAc/hexane, UV).

Chiral SFC: (OB-H, 2.5 mL/min, 15% IPA in CO_2, λ = 280 nm): t_R (major) = 5.9 min, t_R (minor) = 8.3 min.

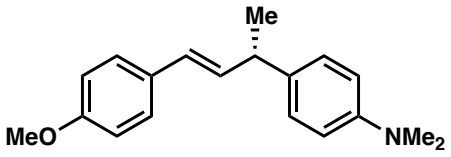
$[\alpha]_D^{25}$ = –29° (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 – 7.28 (m, 2H), 7.28 – 7.20 (m, 2H), 7.06 – 6.98 (m, 2H), 6.89 – 6.83 (m, 2H), 6.40 – 6.32 (m, 1H), 6.23 (dd, *J* = 15.9, 6.7 Hz, 1H), 3.81 (s, 3H), 3.67 – 3.58 (m, 1H), 1.46 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 161.5 (d, $J_{C\text{-}F}$ = 243.7 Hz), 159.0, 141.6 (d, $J_{C\text{-}F}$ = 3.1 Hz), 133.0, 130.3, 128.8 (d, $J_{C\text{-}F}$ = 7.8 Hz), 128.1, 127.4, 115.3 (d, $J_{C\text{-}F}$ = 21.2 Hz), 114.1, 55.4, 41.9, 21.6.

^{19}F NMR (282 MHz, $CDCl_3$): δ -123.56 (tt, $J_{F\text{-}H}$ = 8.9, 5.4 Hz).

(*S*,*E*)-4-(4-(4-methoxyphenyl)but-3-en-2-yl)-*N*,*N*-dimethylaniline (198)



Prepared from (*E*)-1-(2-bromovinyl)-4-methoxybenzene (43 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 2-(4-(dimethyl-amino)phenyl)propanoate (68 mg, 0.2 mmol) according to General Procedure 3. The reaction was quenched with water instead of 1 M HCl. The crude residue was purified by column chromatography (silica gel, hexane to 10% Et_2O/hexane) to yield **198** (37 mg, 66% yield) in 94% ee as a white solid.

R_f = 0.28 (silica gel, 10% EtOAc/hexane, UV).

m.p. = 72–75 °C

Chiral SFC: (AD-H, 2.5 mL/min, 20% IPA in CO_2, λ = 280 nm): t_R (major) = 8.2 min, t_R (minor) = 10.6 min.

$[\alpha]_D^{25}$ = –29° (c = 1.1, $CHCl_3$).

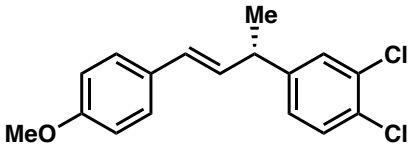
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29 (d, *J* = 8.7 Hz, 2H), 7.15 (d, *J* = 8.5 Hz, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 6.73 (d, *J* = 8.7 Hz, 2H), 6.34 (dd, *J* = 16.2, 0.8 Hz, 1H), 6.23 (dd, *J* = 15.9, 6.6 Hz, 1H), 3.80 (s, 3H), 3.58 – 3.50 (m, 1H), 2.93 (s, 6H), 1.42 (d, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 158.8, 149.3, 134.1, 130.7, 128.0, 127.3, 114.0, 113.1, 55.4, 41.6, 41.0, 21.5.

FTIR (NaCl, thin film, cm^{-1}): 2958, 1608, 1518, 1509, 1456, 1341, 1249, 1173, 1034, 966, 948, 815.

HRMS (FAB, *m/z*): calc'd for $C_{19}H_{23}NO$ $[M+\cdot]^+$: 281.1780; found: 281.1774.

(*S*,*E*)-1,2-dichloro-4-(4-(4-methoxyphenyl)but-3-en-2-yl)benzene (199)



Prepared from (*E*)-1-(2-bromovinyl)-4-methoxybenzene (43 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 2-(3,4-dichlorophenyl)-propanoate (73 mg, 0.2 mmol) according to General Procedure 3. The crude residue was purified by column chromatography (silica gel, hexane to 5% Et_2O/hexane) to yield **199** (48 mg, 77% yield) in 82% ee as a colorless oil.

R_f = 0.51 (silica gel, 10% EtOAc/hexane, UV).

Chiral SFC: (OB-H, 2.5 mL/min, 25% IPA in CO_2, λ = 280 nm): t_R (major) = 6.5 min, t_R (minor) = 9.0 min.

$[\alpha]_D^{25}$ = –26° (c = 1.1, $CHCl_3$).

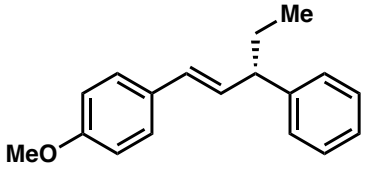
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (d, *J* = 8.3 Hz, 1H), 7.35 (d, *J* = 2.1 Hz, 1H), 7.32 – 7.27 (m, 2H), 7.10 (ddd, *J* = 8.2, 2.1, 0.6 Hz, 1H), 6.87 – 6.82 (m, 2H), 6.35 (dd, *J* = 15.9, 1.3 Hz, 1H), 6.15 (dd, *J* = 15.9, 6.8 Hz, 1H), 3.81 (s, 3H), 3.62 – 3.53 (m, 1H), 1.43 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 159.2, 146.3, 132.4, 131.7, 130.5, 130.1, 130.0, 129.4, 128.9, 127.4, 127.0, 114.1, 55.4, 41.9, 21.2.

FTIR (NaCl, thin film, cm^{-1}): 2964, 1607, 1511, 1466, 1299, 1250, 1174, 1106, 1030, 967, 815.

HRMS (FAB, *m/z*): calc'd for $C_{17}H_{16}Cl_2O$ $[M+\cdot]^+$: 306.0578; found: 306.0582.

(*S*,*E*)-1-methoxy-4-(3-phenylpent-1-en-1-yl)benzene (200)



Prepared from (*E*)-1-(2-bromovinyl)-4-methoxybenzene (43 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 2-phenylbutanoate (62 mg, 0.2 mmol) according to General Procedure 3. The crude residue was purified by column chromatography (silica gel, 10 to 20% toluene/hexane) to yield **200** (40 mg, 80% yield) in 97% ee as a colorless oil. Spectral data matched those reported in literature.

R_f = 0.59 (silica gel, 10% EtOAc/hexane, UV).

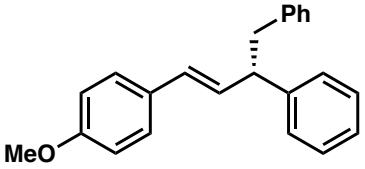
Chiral SFC: (OB-H, 2.5 mL/min, 15% IPA in CO_2, λ = 254 nm): t_R (minor) = 8.0 min, t_R (major) = 9.9 min.

$[\alpha]_D^{25}$ = –46° (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 – 7.19 (m, 7H), 6.84 (d, *J* = 8.8 Hz, 2H), 6.37 (d, *J* = 15.8 Hz, 1H), 6.21 (dd, *J* = 15.8, 7.8 Hz, 1H), 3.80 (s, 3H), 3.35 – 3.26 (m, 1H), 1.90 – 1.78 (m, 2H), 0.93 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 158.9, 144.9, 132.2, 130.6, 128.9, 128.6, 127.8, 127.3, 126.2, 114.0, 55.4, 51.1, 29.0, 12.5.

(*S*,*E*)-(4-(4-methoxyphenyl)but-3-ene-1,2-diyl)dibenzene (201)



Prepared from (*E*)-1-(2-bromovinyl)-4-methoxybenzene (43 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 2,3-diphenylpropanoate (74 mg, 0.2 mmol) according to General Procedure 3. The crude residue was purified by column chromatography (silica gel, 10% toluene/hexane then 10% Et_2O/hexane) to yield **201** (49 mg, 78% yield) in 95% ee as a white solid. Spectral data matched those reported in literature.

R_f = 0.48 (silica gel, 10% EtOAc/hexane, UV).

m.p. = 72–73 °C

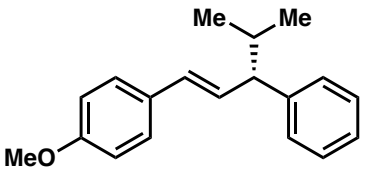
Chiral SFC: (AS-H, 2.5 mL/min, 10% IPA in CO_2, λ = 254 nm): t_R (minor) = 6.0 min, t_R (major) = 6.5 min.

$[\alpha]_D^{25}$ = +19° (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 – 7.13 (m, 10H), 7.10 (d, *J* = 8.8 Hz, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 6.30 (dd, *J* = 15.9, 6.3 Hz, 1H), 6.25 (d, *J* = 15.9 Hz, 1H), 3.80 (s, 3H), 3.78 – 3.67 (m, 1H), 3.19 – 3.06 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 158.9, 144.1, 140.2, 131.3, 130.4, 129.53, 129.49, 128.5, 128.2, 128.0, 127.4, 126.4, 126.0, 114.0, 55.4, 51.0, 42.9.

(*S*,*E*)-1-methoxy-4-(4-methyl-3-phenylpent-1-en-1-yl)benzene (202)



Prepared from (*E*)-1-(2-bromovinyl)-4-methoxybenzene (43 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 3-methyl-2-phenylbutanoate (65 mg, 0.2 mmol) according to General Procedure 3. The crude residue was purified by column chromatography (silica gel, 10 to 20% toluene/hexane) to yield **202** (25 mg, 47% yield) in 97% ee as a white solid.

R_f = 0.58 (silica gel, 10% EtOAc/hexane, UV).

m.p. = 67–68 °C

Chiral SFC: (AS-H, 2.5 mL/min, 10% IPA in CO_2, λ = 254 nm): t_R (minor) = 4.8 min, t_R (major) = 6.1 min.

$[\alpha]_D^{25}$ = –39° (c = 1.0, $CHCl_3$).

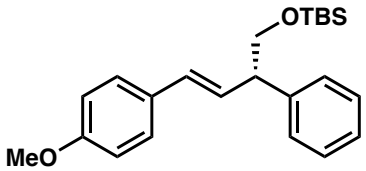
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 – 7.28 (m, 4H), 7.26 – 7.17 (m, 3H), 6.84 (d, *J* = 8.8 Hz, 2H), 6.36 (d, *J* = 15.7 Hz, 1H), 6.26 (dd, *J* = 15.7, 8.8 Hz, 1H), 3.80 (s, 3H), 3.04 (t, *J* = 8.8 Hz, 1H), 2.14 – 1.96 (m, 1H), 1.02 (d, *J* = 6.7 Hz, 3H), 0.82 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 158.9, 144.7, 131.2, 130.6, 129.8, 128.5, 128.1, 127.3, 126.1, 114.0, 57.8, 55.4, 33.4, 21.3, 21.1.

FTIR (NaCl, thin film, cm^{-1}): 2953, 1600, 1509, 1450, 1251, 1027, 966, 838, 701.

LRMS (GC-MS, *m/z*): calc'd for $C_{19}H_{22}O$ $[M]^+$: 266.2; found: 266.1.

(*S*,*E*)-*tert*-butyl((4-(4-methoxyphenyl)-2-phenylbut-3-en-1-yl)oxy)dimethylsilane (203)



Prepared from (*E*)-1-(2-bromovinyl)-4-methoxybenzene (43 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 3-((*tert*-butyldimethylsilyl)oxy)-2-phenylpropanoate (74 mg, 0.2 mmol) according to General Procedure 3. The crude residue was purified by column chromatography (silica gel, 10% toluene/hexane then 10% Et_2O/hexane) to yield **203** (43 mg, 58% yield) in 98% ee as a colorless oil.

R_f = 0.55 (silica gel, 10% EtOAc/hexane, UV).

Chiral SFC: (OJ-H, 2.5 mL/min, 10% IPA in CO_2, λ = 254 nm): t_R (major) = 3.4 min, t_R (minor) = 5.8 min.

$[\alpha]_D^{25}$ = –14° (c = 1.0, $CHCl_3$).

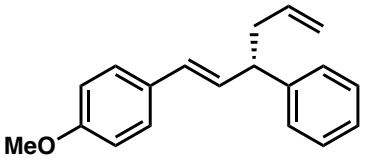
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.29 (m, 6H), 7.28 – 7.23 (m, 1H), 6.87 (d, *J* = 8.8 Hz, 2H), 6.44 (d, *J* = 16.0 Hz, 1H), 6.34 (dd, *J* = 15.9, 7.2 Hz, 1H), 3.98 – 3.89 (m, 2H), 3.83 (s, 3H), 3.70 – 3.63 (m, 1H), 0.89 (s, 9H), 0.02 (s, 3H), 0.01 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 159.0, 142.3, 130.7, 130.5, 128.8, 128.45, 128.42, 127.4, 126.6, 114.0, 67.5, 55.4, 51.8, 26.0, 18.4, -5.2, -5.3.

FTIR (NaCl, thin film, cm^{-1}): 2953, 2928, 2892, 2855, 1607, 1511, 1463, 1250, 1174, 1106, 1036, 836, 775, 699.

HRMS (FAB, *m/z*): calc'd for $C_{23}H_{32}O_2Si$ $[M–H_2+H]^+$: 367.2093; found: 367.2081.

(*S*,*E*)-1-methoxy-4-(3-phenylhexa-1,5-dien-1-yl)benzene (204)



Prepared from (*E*)-1-(2-bromovinyl)-4-methoxybenzene (43 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 2-phenylpent-4-enoate (53 mg, 0.2 mmol) according to General Procedure 3. The crude residue was purified by column chromatography (silica gel, 5 to 20% toluene/hexane) to yield **204** (42 mg, 79% yield) in 96% ee as a colorless oil.

R_f = 0.55 (silica gel, 10% EtOAc/hexane, UV).

Chiral SFC: (OJ-H, 2.5 mL/min, 10% IPA in CO_2, λ = 254 nm): t_R (minor) = 7.8 min, t_R (major) = 8.5 min.

$[\alpha]_D^{25}$ = –19° (c =1.0, $CHCl_3$).

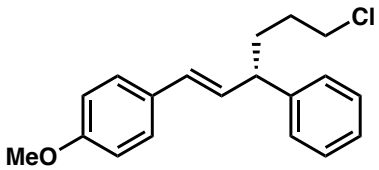
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 – 7.14 (m, 7H), 6.78 (d, *J* = 8.8 Hz, 2H), 6.30 (d, *J* = 15.9 Hz, 1H), 6.18 (dd, *J* = 15.8, 7.5 Hz, 1H), 5.73 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1H), 5.01 (ddt, *J* = 17.0, 2.0, 1.5 Hz, 1H), 4.95 (ddt, *J* = 10.2, 2.1, 1.0 Hz, 1H), 3.74 (s, 3H), 3.50 – 3.42 (m, 1H), 2.57 – 2.51 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 159.0, 144.2, 136.8, 131.5, 130.4, 129.2, 128.6, 127.8, 127.4, 126.4, 116.4, 114.0, 55.4, 49.1, 40.4.

FTIR (NaCl, thin film, cm^{-1}): 3025, 2913, 2834, 1606, 1509, 1246, 1173, 1032, 963, 911, 756, 698.

HRMS (EI, *m/z*): calc'd for $C_{19}H_{20}O$ $[M+\cdot]^+$: 264.1514; found: 264.1521.

(*S*,*E*)-1-(6-chloro-3-phenylhex-1-en-1-yl)-4-methoxybenzene (205)



Prepared from (*E*)-1-(2-bromovinyl)-4-methoxybenzene (43 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 5-chloro-2-phenylpentanoate (72 mg, 0.2 mmol) according to General Procedure 3. The crude residue was purified by column chromatography (silica gel, 5% Et_2O/hexane) to yield **205** (52 mg, 87% yield) in 93% ee as a colorless oil.

R_f = 0.53 (silica gel, 10% EtOAc/hexane, UV).

Chiral SFC: (AS-H, 2.5 mL/min, 15% IPA in CO_2, λ = 254 nm): t_R (minor) = 3.7 min, t_R

(major) = 4.7 min.

$[\alpha]_D^{25}$ = –21° (c = 1.0, $CHCl_3$).

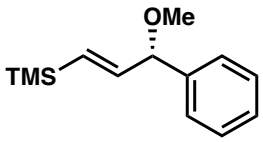
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 – 7.21 (m, 7H), 6.85 (d, *J* = 8.8 Hz, 2H), 6.38 (d, *J* = 15.8 Hz, 1H), 6.20 (dd, *J* = 15.8, 7.9 Hz, 1H), 3.81 (s, 3H), 3.56 (t, *J* = 6.5 Hz, 2H), 3.46 – 3.38 (m, 1H), 2.02 – 1.92 (m, 2H), 1.92 – 1.69 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 159.0, 144.2, 131.5, 130.2, 129.2, 128.7, 127.7, 127.4, 126.5, 114.0, 55.4, 48.7, 45.2, 33.2, 30.8.

FTIR (NaCl, thin film, cm^{-1}): 2915, 1605, 1491, 1438, 1509, 1246, 1173, 1031, 964.

HRMS (FAB, *m/z*): calc'd for $C_{19}H_{21}ClO$ $[M+\cdot]^+$: 300.1281; found: 300.1274.

(*S*,*E*)-(3-methoxy-3-phenylprop-1-en-1-yl)trimethylsilane (208)



Prepared from (*E*)-(2-bromovinyl)trimethylsilane (36 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 2-methoxy-2-phenylacetate (62 mg, 0.2 mmol) according to General Procedure 3. The crude residue was purified by column chromatography (silica gel, 0 to 3% Et_2O/hexane) to yield **208** (26 mg, 59% yield) in 91% ee as a colorless oil.

R_f = 0.62 (silica gel, 10% EtOAc/hexane, UV/CAM).

Chiral SFC: (OD-H, 2.5 mL/min, 1% IPA in CO_2, λ = 210 nm): t_R (minor) = 2.6 min, t_R (major) = 5.9 min.

$[\alpha]_D^{25}$ = +8° (c = 0.6, $CHCl_3$).

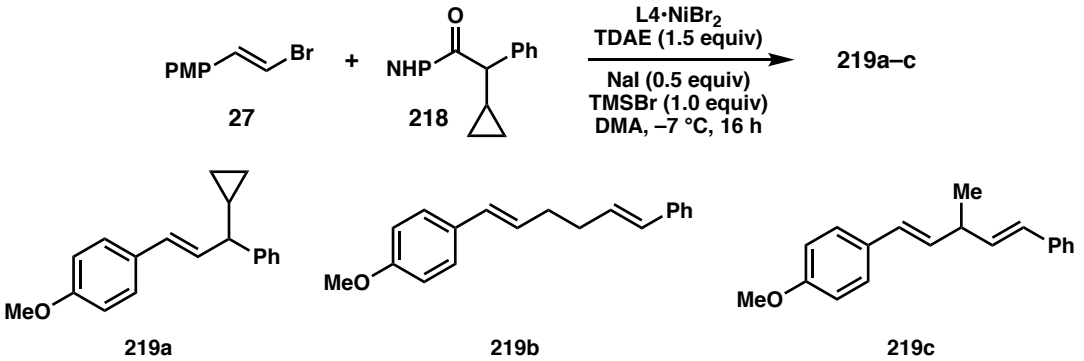
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 – 7.27 (m, 5H), 6.10 (dd, *J* = 18.6, 5.9 Hz, 1H), 5.93 (dd, *J* = 18.6, 1.2 Hz, 1H), 4.61 (d, *J* = 5.8 Hz, 1H), 3.32 (s, 3H), 0.07 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 145.7, 140.9, 131.9, 128.6, 127.7, 127.1, 86.6, 56.6, -1.2.

FTIR (NaCl, thin film, cm^{-1}): 2955, 2820, 1453, 1248, 1100, 990, 863, 838, 760, 699.

HRMS (FAB, *m/z*): calc'd for $C_{13}H_{20}OSi$ $[M–H_2+H]^+$: 219.1205; found: 219.1191.

4.7.5 Radical Clock Investigation



Prepared from (*E*)-1-(2-bromovinyl)-4-methoxybenzene (**27**, 43 mg, 0.2 mmol) and 1,3-dioxoisoindolin-2-yl 2-cyclopropyl-2-phenylacetate (**218**, 64 mg, 0.2 mmol) according to General Procedure 3. The crude residue was purified by column chromatography (silica gel, hexane to 30% toluene/hexane) to yield a mixture of **219a–c** (22 mg, 42% yield) as a colorless oil. The reaction was repeated with 5 mol % and 20 mol % of **L4•NiBr$_2$**, yielding a mixture of **219a–c** in 44% and 49% yield, respectively. Three products are confirmed by GC-MS (extract ion *m/z* = 264). Distinct ^{1}H/^{13}C signals and coupling correlations are confirmed by ^{1}H, ^{13}C, COSY, HSQC, and HMBC NMR spectroscopy.

NMR data for **219a–c** with 20 mol % **L4•NiBr$_2$**:

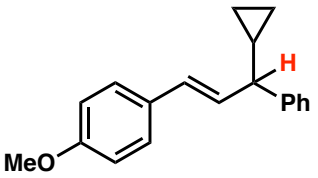
^{1}H NMR (400 MHz, CDCl$_3$): δ 7.42 – 7.18 (m, 7H), 6.86 (dq, *J* = 8.9, 2.5 Hz, 2H), 6.49 – 6.36 (m, 1.8H), 6.34 – 6.08 (m, 1.82H), 3.81 (s, 3H), 3.20 (qt, *J* = 6.9, 1.3 Hz, 0.1H, *11c*), 2.76 (ddd, *J* = 8.6, 6.9, 1.2 Hz, 0.2H, *11a*), 2.49 – 2.31 (m, 2.8H, *11b*), 1.31 (d, *J* = 6.9 Hz, 0.3H, *11c*), 1.23 – 1.13 (m, 0.2H, *11a*), 0.68 (dddd, *J* = 9.1, 8.0, 5.3, 4.1 Hz, 0.2H, *11a*), 0.56 (dddd, *J* = 9.4, 8.0, 5.2, 4.1 Hz, 0.2H, *11a*), 0.40 – 0.31 (m, 0.2H, *11a*), 0.28 (dtd, *J* = 9.3, 5.2, 4.2 Hz, 0.2H, *11a*).

^{13}C NMR (101 MHz, CDCl$_3$): δ 158.9, 158.8, 144.6, 137.9, 137.8, 134.7, 132.2, 131.2, 130.7, 130.5, 130.4, 130.3, 129.8, 129.0, 128.7, 128.6, 128.5, 128.3, 128.0, 127.9, 127.4, 127.3, 127.2, 127.1, 127.0, 126.4, 126.2, 126.1, 114.03, 114.02, 55.4, 53.2, 40.2, 33.2, 33.0, 20.5, 16.4, 4.9, 4.4.

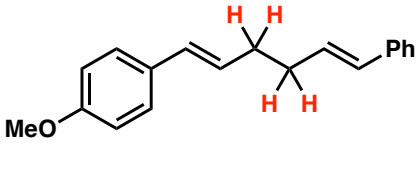
FTIR (NaCl, thin film, cm^{-1}): 3026, 2931, 2837, 1607, 1511, 1252, 1176, 1034, 966, 800, 692.

LRMS (GC-MS, *m/z*): calc'd for $C_{19}H_{20}O$ $[M]^+$: 264.2; found: 3 products, 264.1, 264.1, 264.2.

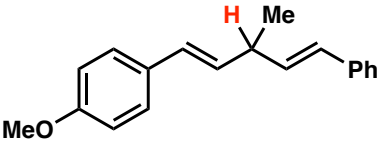
Ratios of **219a–c** were determined by ^{1}H NMR analysis:



219a

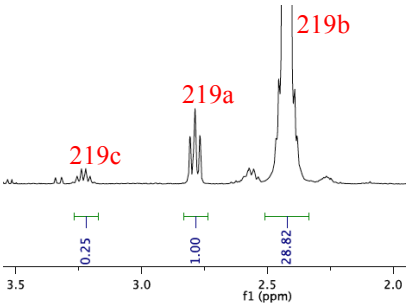


219b

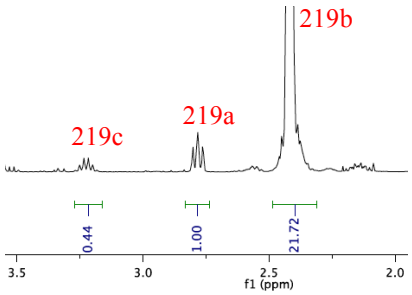


219c

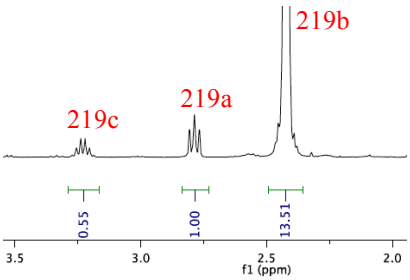
5 mol % **L4•NiBr$_2$**:



10 mol % **L4•NiBr$_2$**:



20 mol % **L4•NiBr$_2$**:



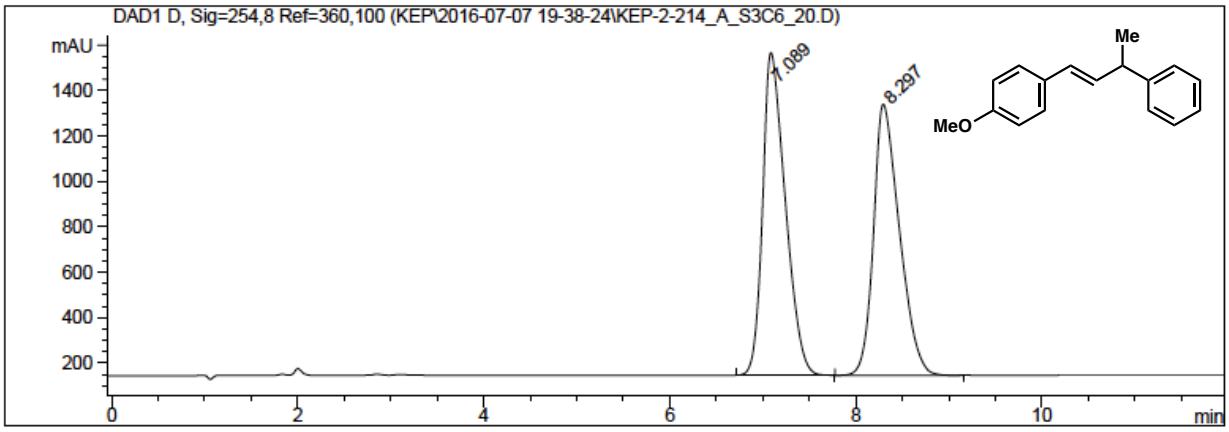
Integration of **219b** was divided by four to account for the contribution of four protons in the multiplet

NMR Integrations

Nickel Catalyst	Cyclopropane (219a)	Linear (219b)	Branched (219c)	Ring Closed Total	Ring Open Total
5%	1.00	7.21	0.25	1.00	7.46
10%	1.00	5.43	0.44	1.00	5.87
20%	1.00	3.38	0.55	1.00	3.93

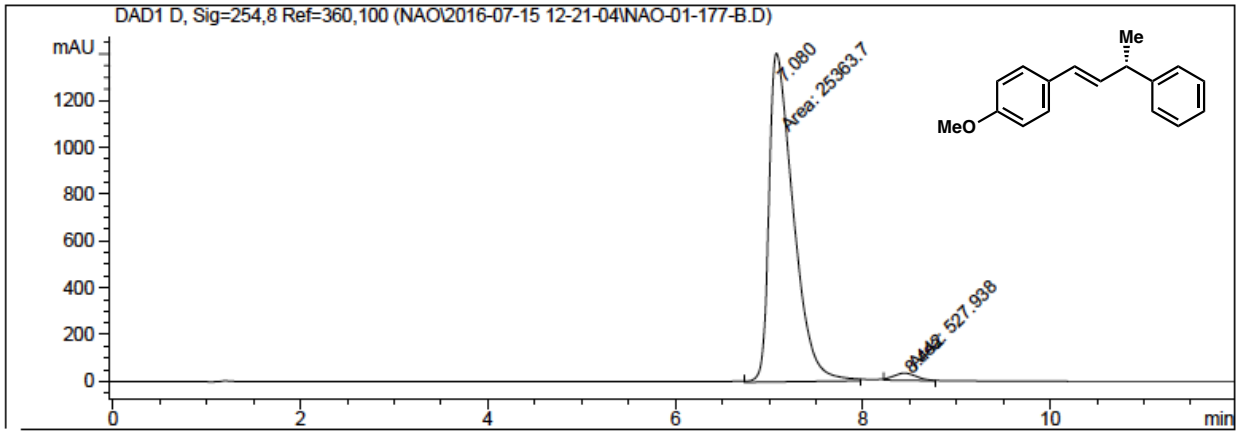
4.7.6 *SFC Traces of Racemic and Enantioenriched Products*

28 (Table 4.3): racemic



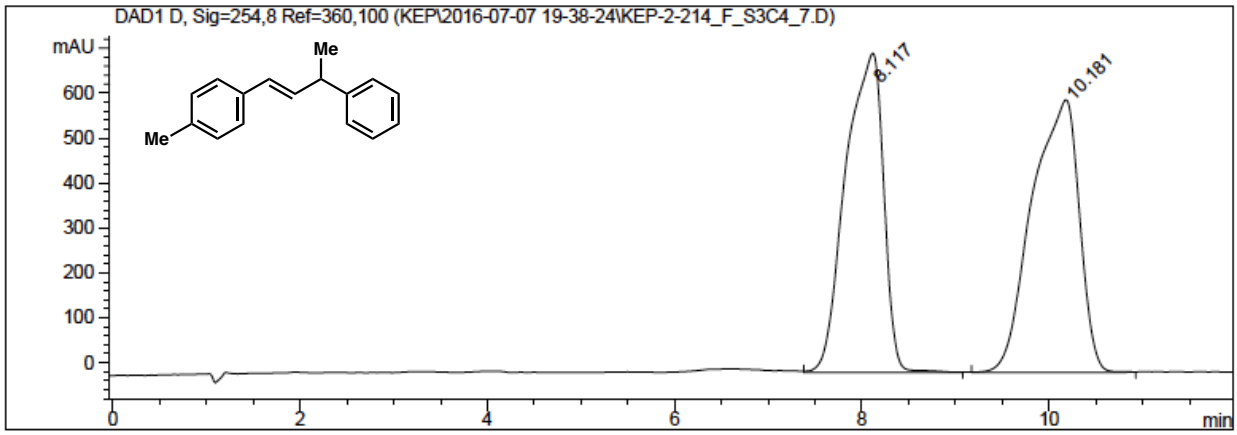
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.089	BV	0.2581	2.40965e4	1419.46216	50.9929
2	8.297	VB	0.2903	2.31582e4	1193.77161	49.0071

28 (Table 4.3): enantioenriched, 96% ee



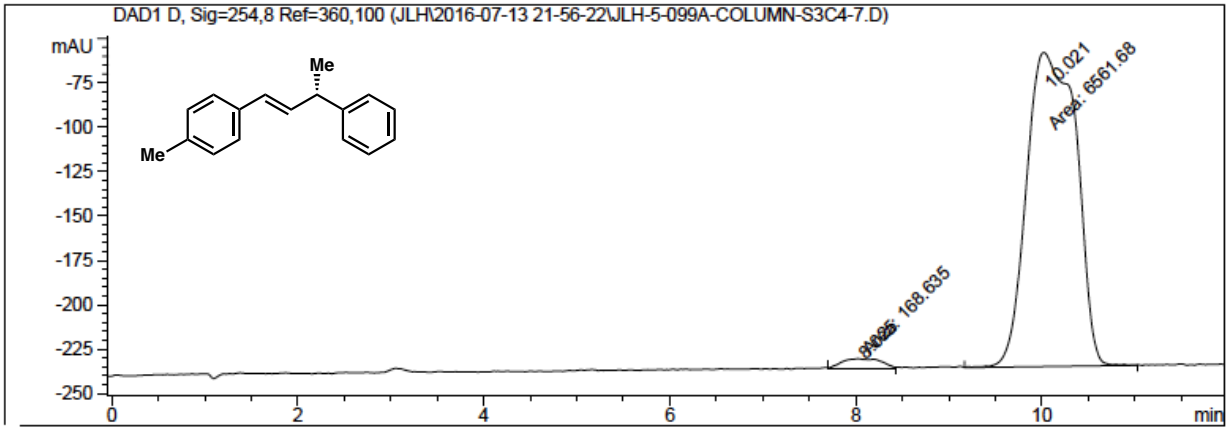
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.080	MM	0.3005	2.53637e4	1406.71533	97.9610
2	8.442	MM	0.2816	527.93842	31.25150	2.0390

180 (Table 4.3): racemic



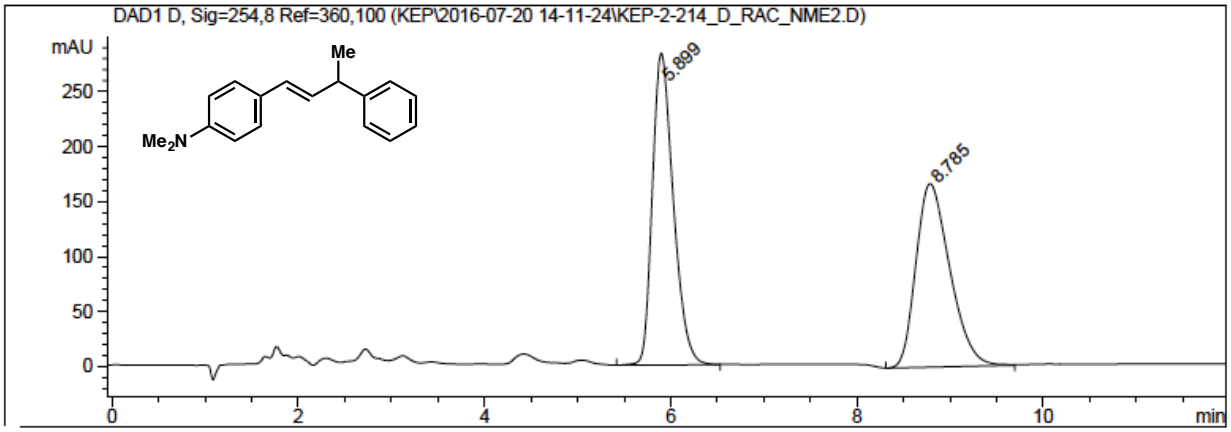
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.117	VB	0.3807	2.00095e4	710.31079	48.4555
2	10.181	BV	0.4692	2.12851e4	606.82129	51.5445

180 (Table 4.3): enantioenriched, 95% ee



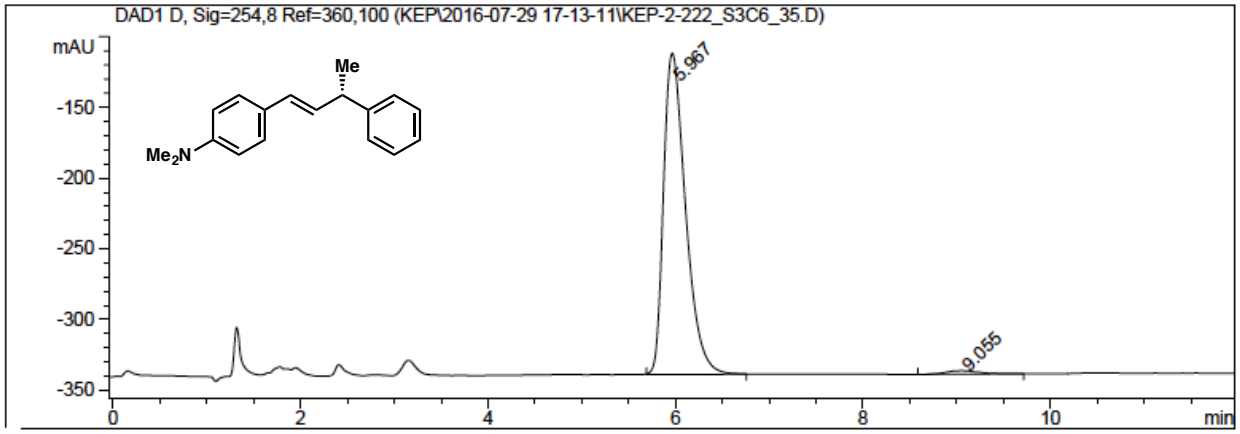
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.025	MM	0.4882	168.63531	5.75649	2.5056
2	10.021	MM	0.6182	6561.67920	176.91377	97.4944

181 (Table 4.3): racemic



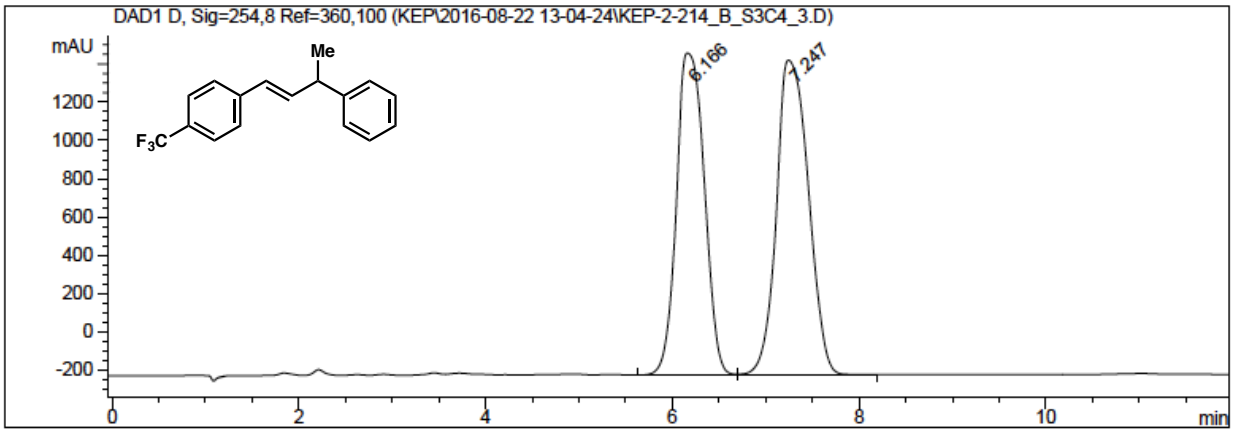
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.899	VB	0.2423	4429.97607	283.53226	51.2284
2	8.785	BB	0.3949	4217.52539	166.83267	48.7716

181 (Table 4.3): enantioenriched, 97% ee



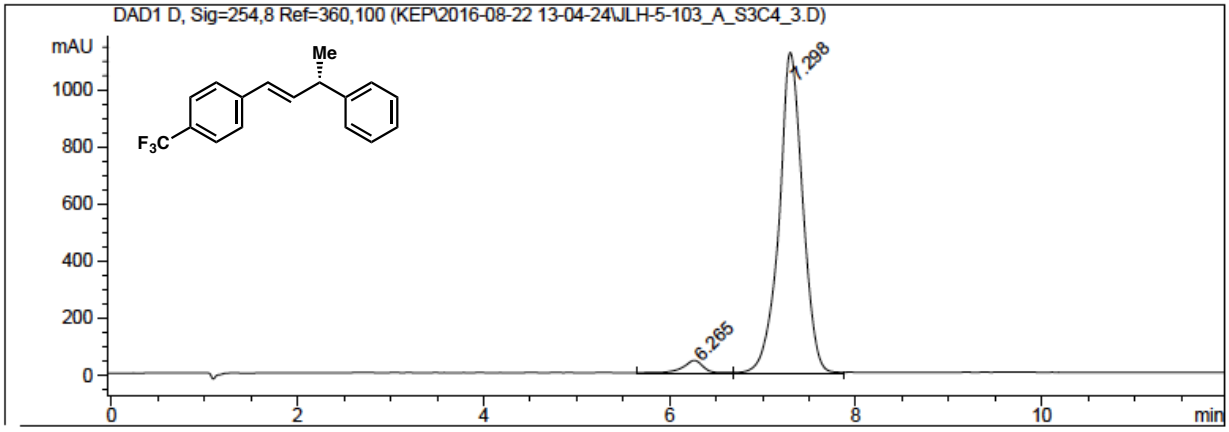
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.967	BB	0.2505	3707.96924	227.13380	98.4506
2	9.055	BB	0.2926	58.35402	2.46108	1.5494

182 (Table 4.3): racemic



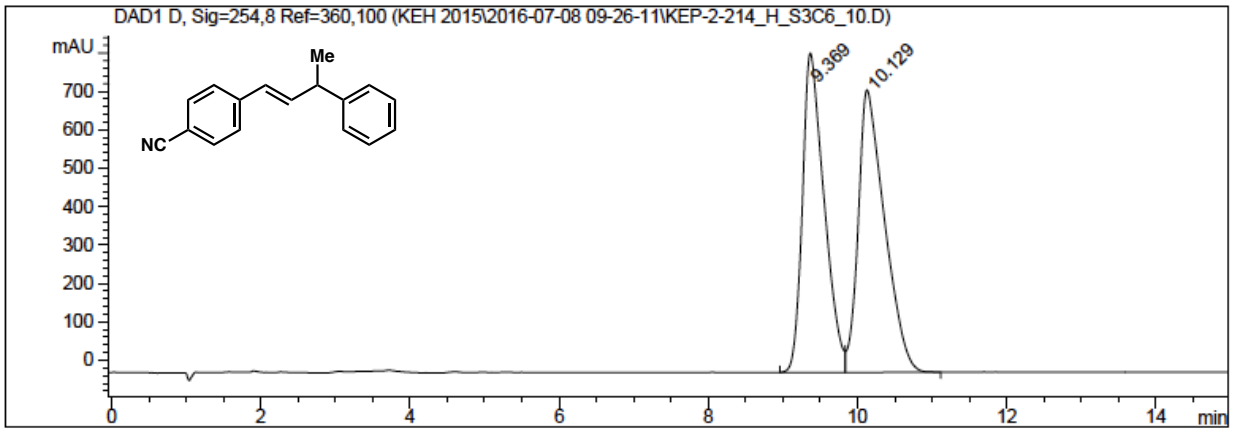
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.166	VV	0.3308	3.50747e4	1685.07422	47.1051
2	7.247	VB	0.3749	3.93858e4	1647.52795	52.8949

182 (Table 4.3): enantioenriched, 93% ee



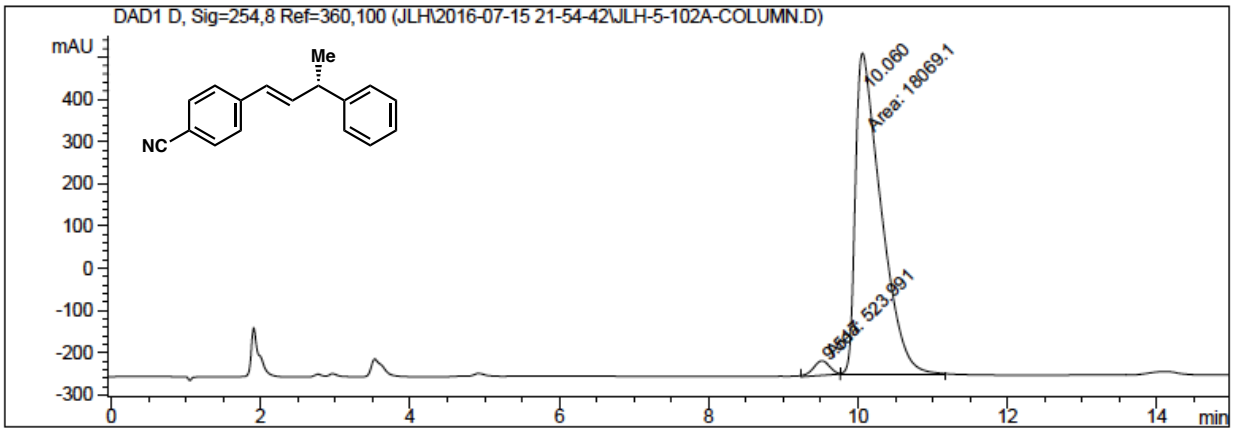
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.265	VV	0.2265	687.93018	43.98362	3.3472
2	7.298	VV	0.2624	1.98645e4	1122.81396	96.6528

183 (Table 4.3): racemic



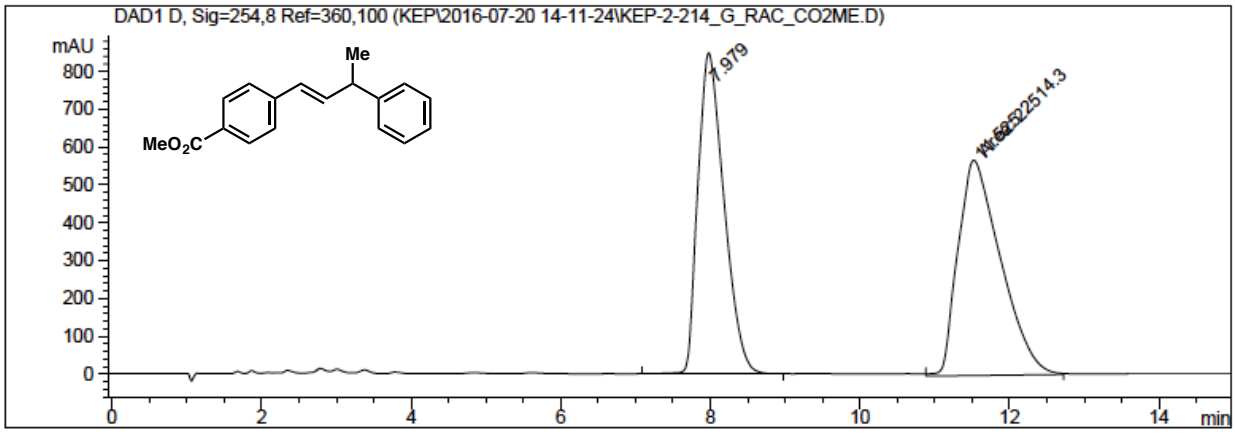
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.369	BV	0.2960	1.68057e4	830.62769	48.1897
2	10.129	VB	0.3508	1.80684e4	734.99915	51.8103

183 (Table 4.3): enantioenriched, 94% ee



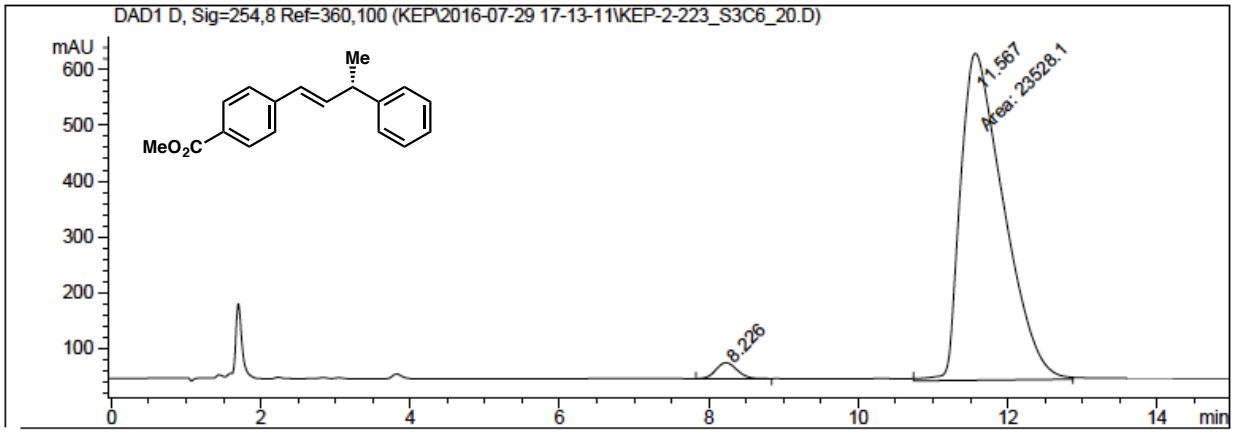
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.517	MM	0.2532	523.99091	34.49692	2.8182
2	10.060	MM	0.3962	1.80691e4	760.05249	97.1818

184 (Table 4.3): racemic



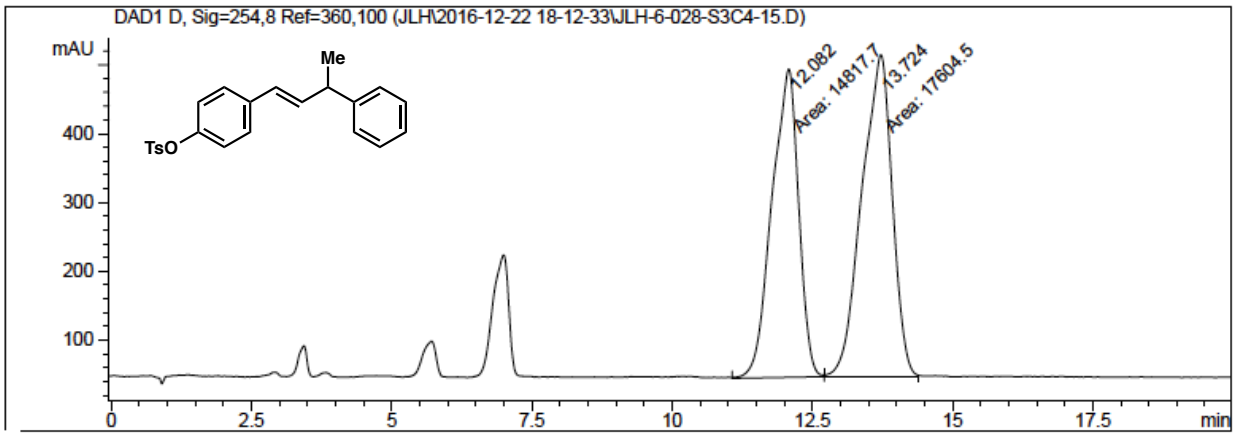
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.979	BB	0.3869	2.05724e4	848.34802	47.7466
2	11.525	MM	0.6592	2.25143e4	569.27423	52.2534

184 (Table 4.3): enantioenriched, 95% ee



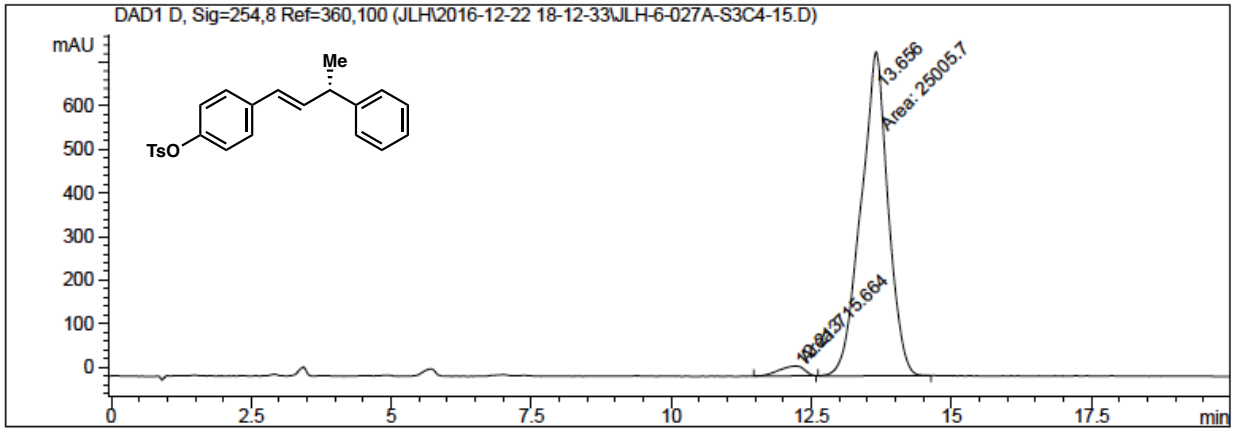
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.226	BB	0.3069	568.03058	28.69778	2.3574
2	11.567	MM	0.6679	2.35281e4	587.09686	97.6426

185 (Table 4.3): racemic



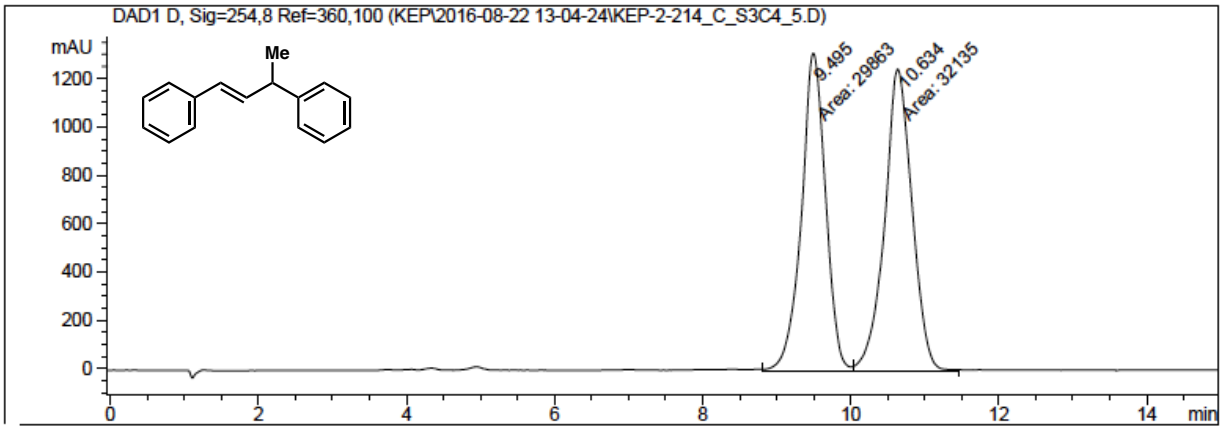
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.082	MM	0.5513	1.48177e4	447.97232	45.7023
2	13.724	MM	0.6275	1.76045e4	467.56030	54.2977

185 (Table 4.3): enantioenriched, 94% ee



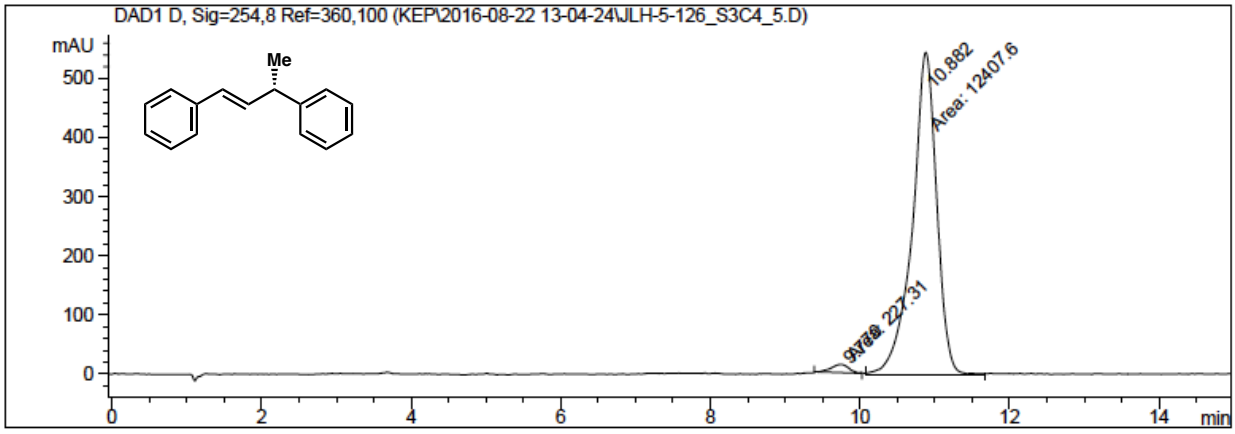
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.213	MM	0.5201	715.66412	22.93249	2.7824
2	13.656	MM	0.5598	2.50057e4	744.50916	97.2176

186 (Table 4.3): racemic



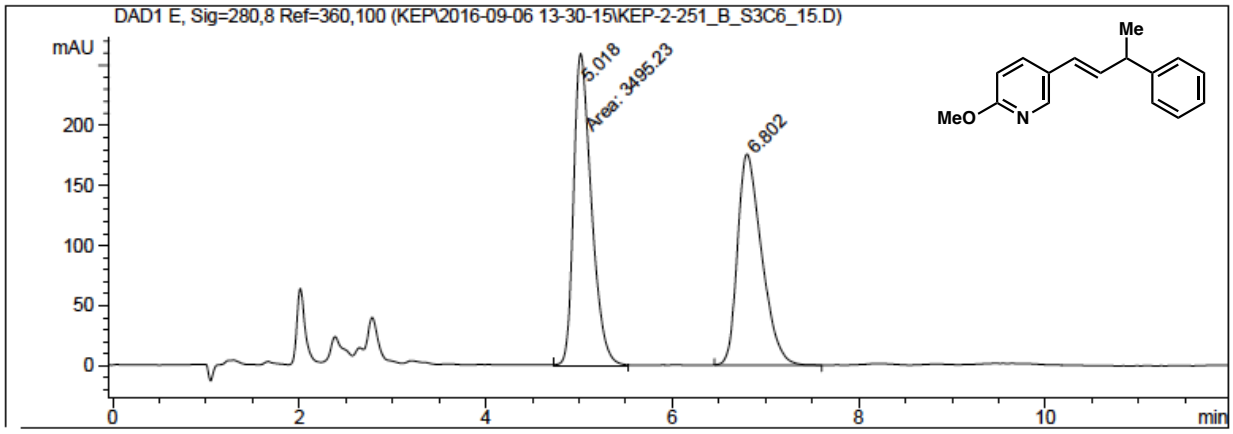
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.495	MM	0.3786	2.98630e4	1314.49744	48.1677
2	10.634	MM	0.4290	3.21350e4	1248.56421	51.8323

186 (Table 4.3): enantioenriched, 96% ee



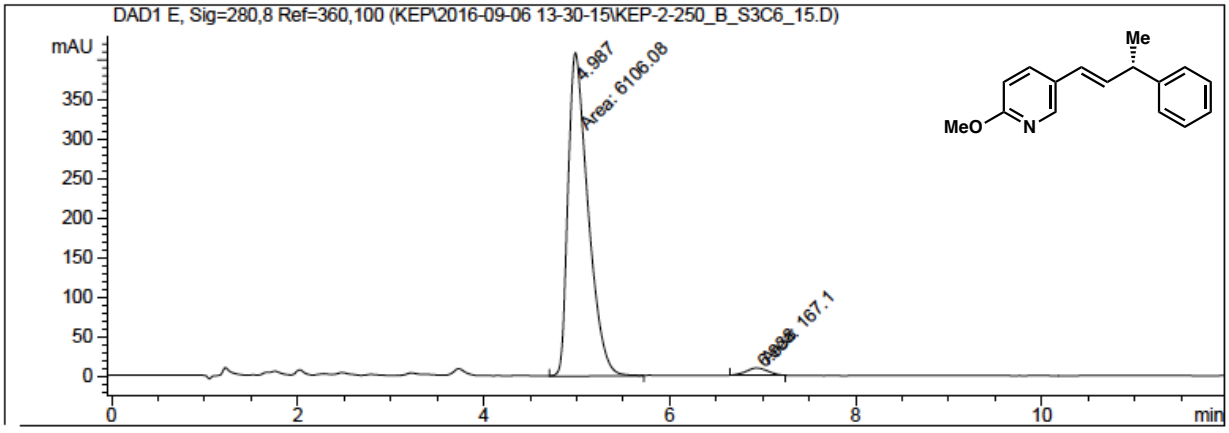
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.770	MM	0.2725	227.31046	13.90100	1.7991
2	10.882	MM	0.3782	1.24076e4	546.85577	98.2009

187 (Table 4.3): racemic



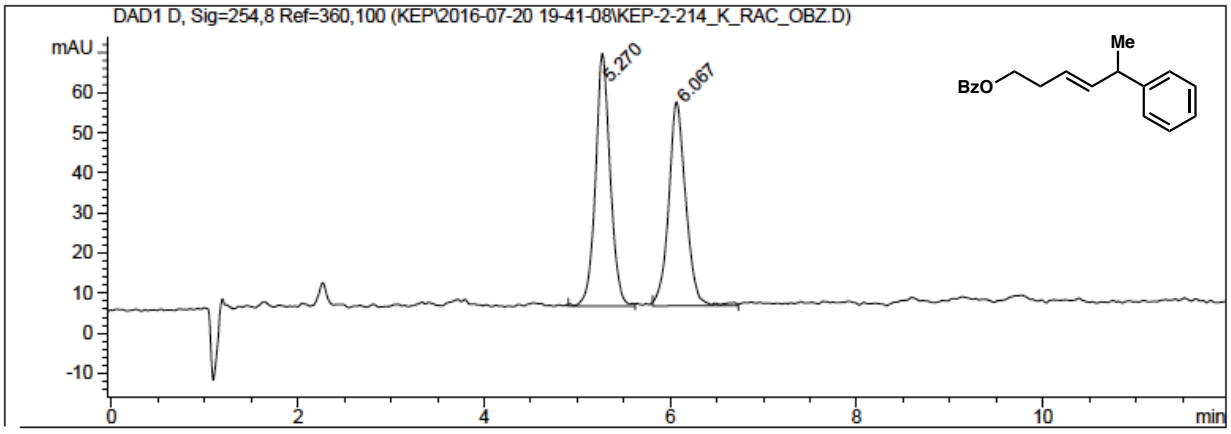
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.018	MM	0.2233	3495.22925	260.81982	52.4318
2	6.802	BB	0.2747	3171.01147	175.57878	47.5682

187 (Table 4.3): enantioenriched, 95% ee



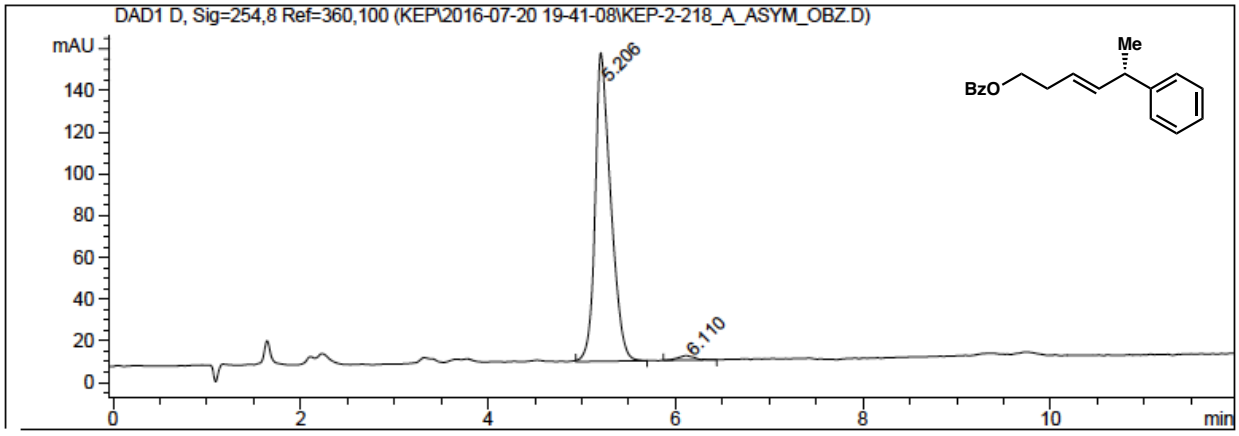
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.987	MM	0.2488	6106.07617	408.96854	97.3363
2	6.938	MM	0.2866	167.10007	9.71596	2.6637

188 (Table 4.3): racemic



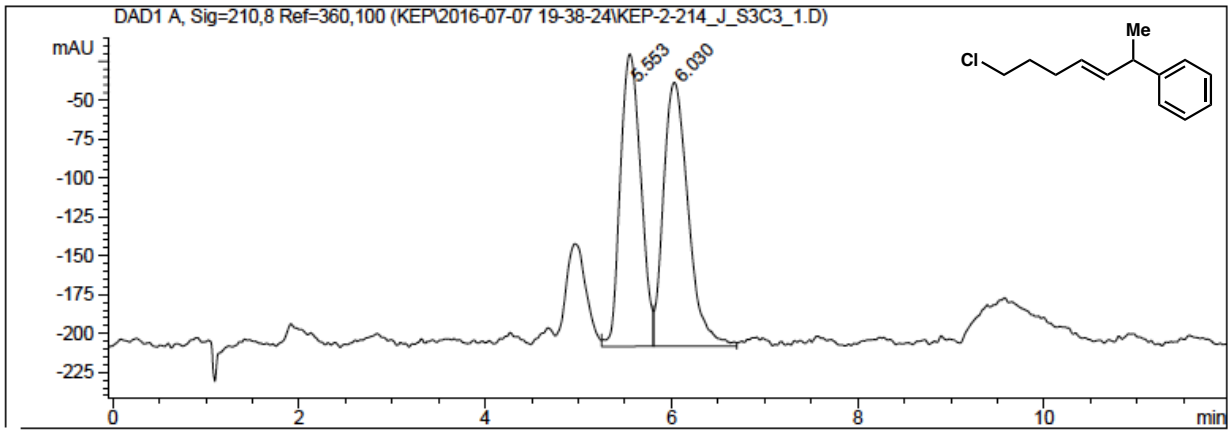
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.270	BB	0.1643	692.65100	62.99958	51.5795
2	6.067	BB	0.1892	650.22839	50.83070	48.4205

188 (Table 4.3): enantioenriched, 97% ee



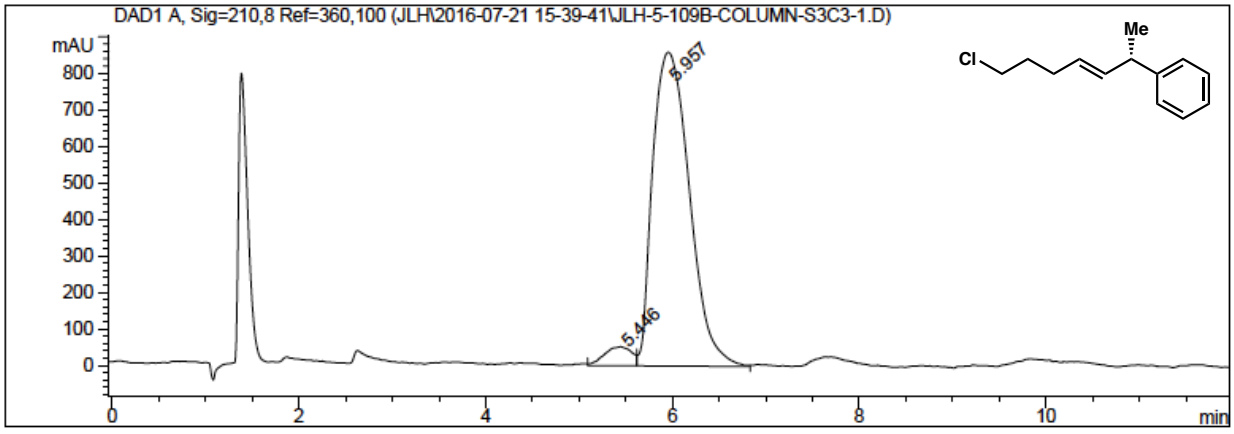
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.206	BB	0.1708	1710.15393	148.02460	98.4760
2	6.110	BB	0.1607	26.46575	2.19494	1.5240

189 (Table 4.3): racemic



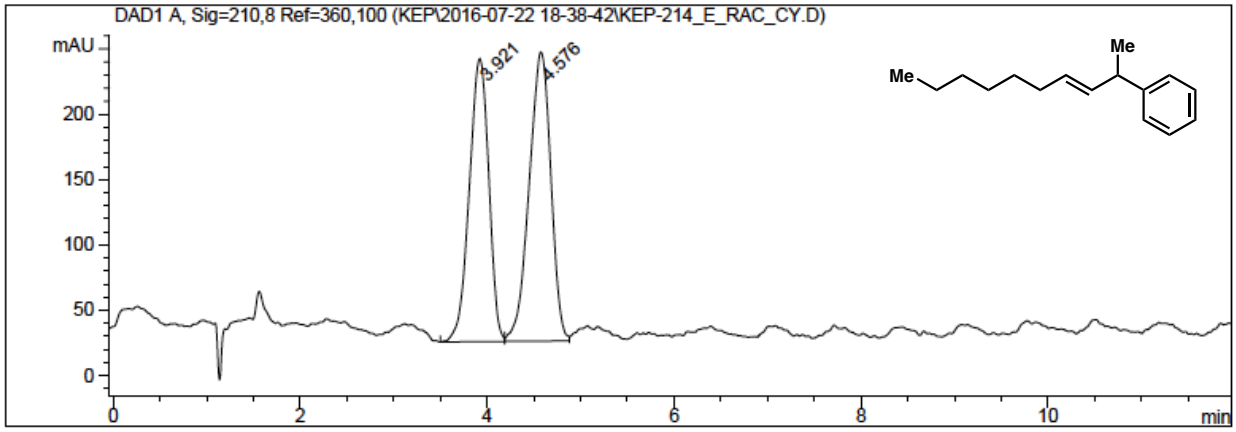
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.553	VV	0.2466	2879.10791	188.09062	47.7991
2	6.030	VV	0.2922	3144.24927	169.66949	52.2009

189 (Table 4.3): enantioenriched, 91% ee



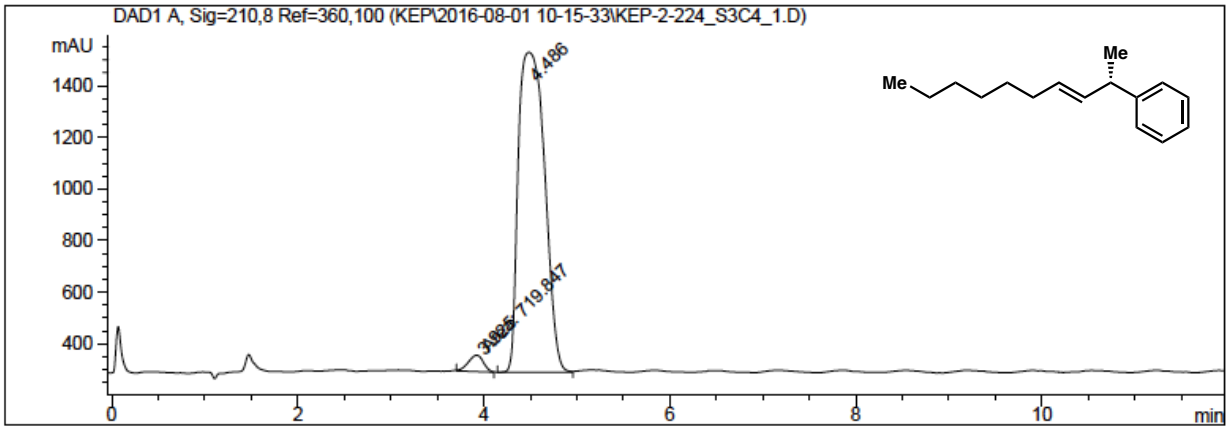
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.446	VV	0.2528	1053.08008	51.88251	4.2859
2	5.957	VV	0.4514	2.35179e4	858.91888	95.7141

190 (Table 4.3): racemic



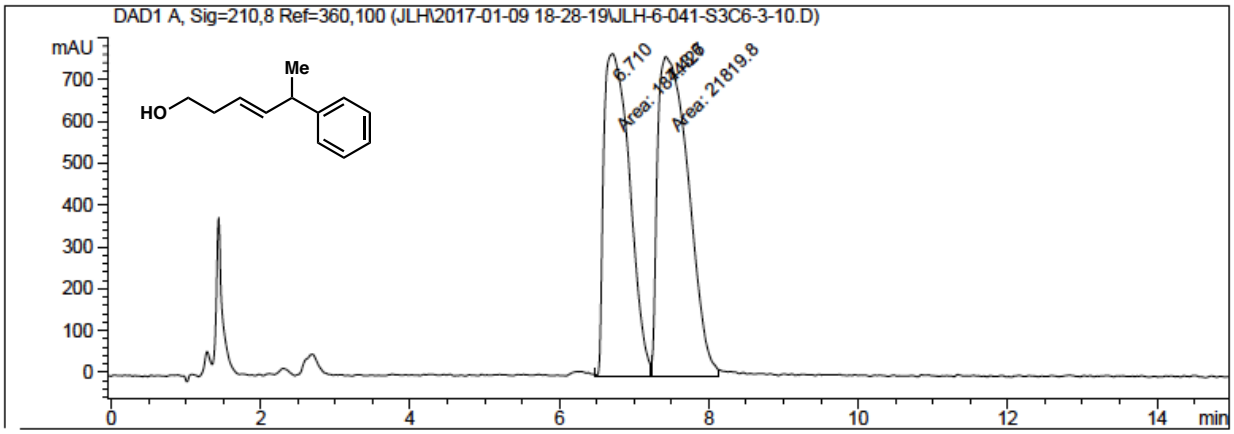
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.921	VV	0.2294	3145.27051	216.62386	46.8268
2	4.576	VV	0.2603	3571.54810	221.25337	53.1732

190 (Table 4.3): enantioenriched, 94% ee



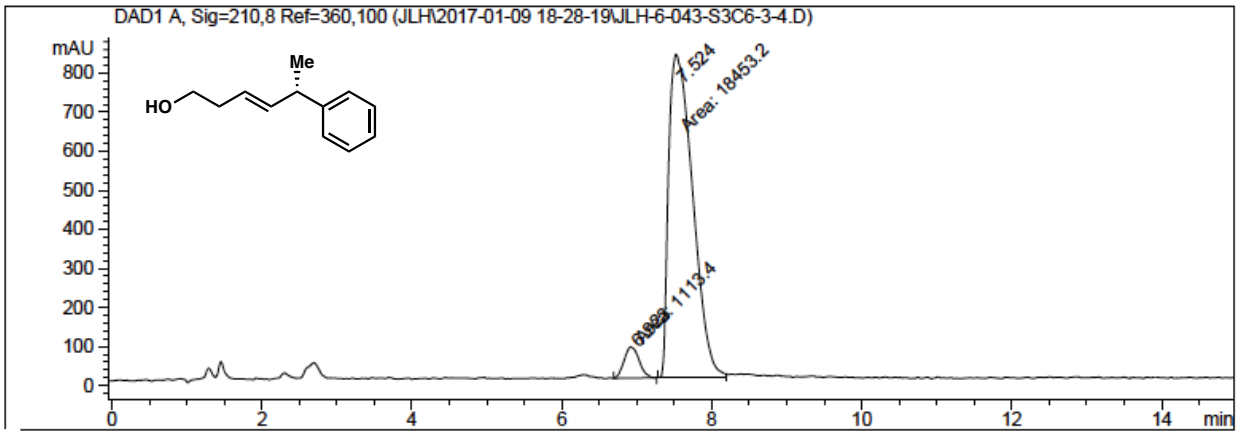
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.925	MM	0.1890	719.84717	63.47777	2.8630
2	4.486	VV	0.3261	2.44231e4	1238.09705	97.1370

276 (de-silylated 191, Table 4.3): racemic



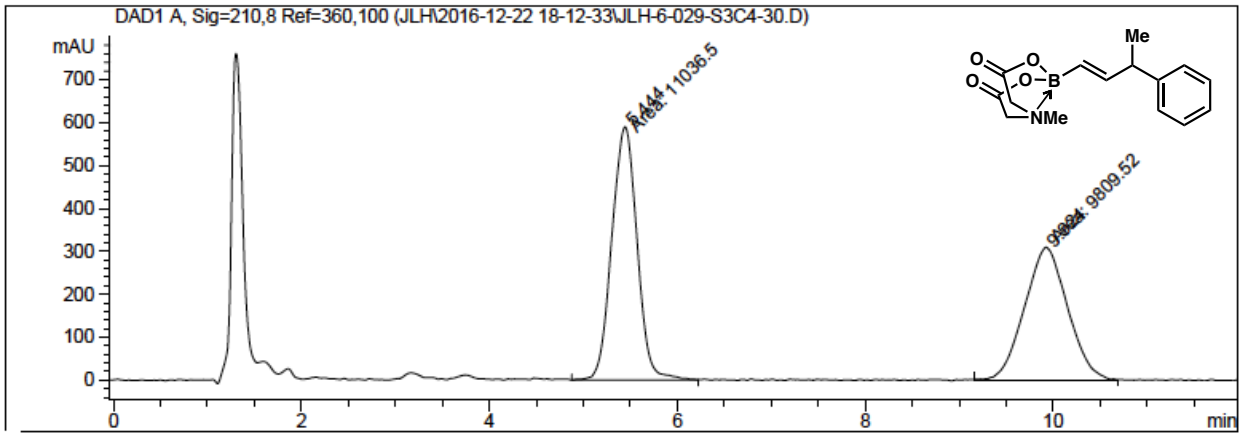
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.710	MM	0.3992	1.84436e4	770.06226	45.8074
2	7.427	MM	0.4761	2.18198e4	763.80591	54.1926

276 (de-silylated 191, Table 4.3): enantioenriched, 89% ee



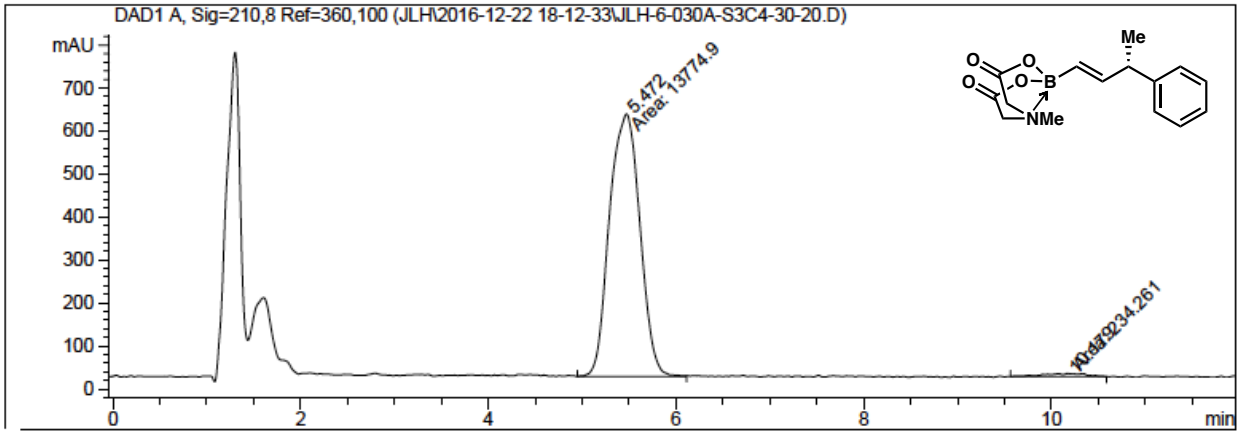
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.923	MM	0.2309	1113.40063	80.37251	5.6903
2	7.524	MM	0.3711	1.84532e4	828.86755	94.3097

192 (Table 4.3): racemic



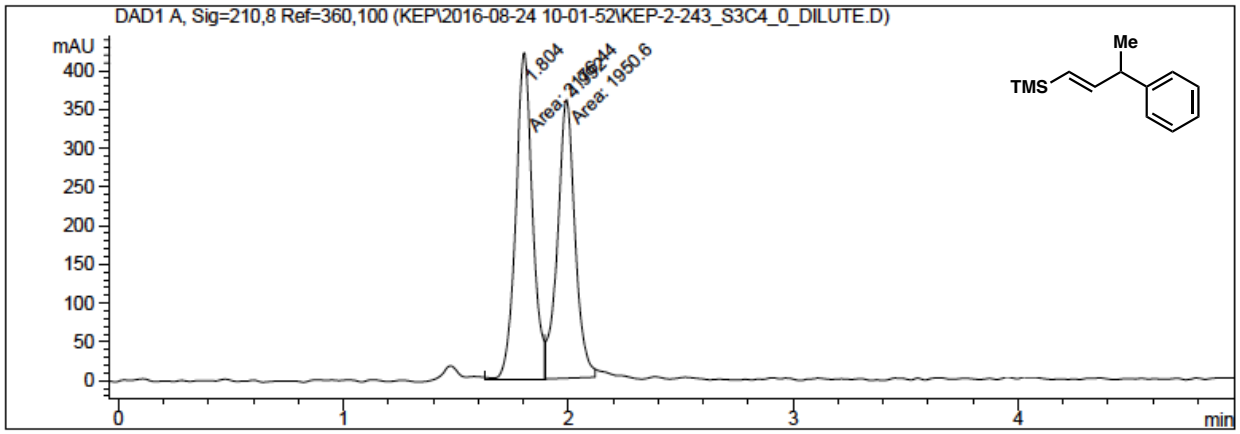
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.444	MM	0.3119	1.10365e4	589.78003	52.9429
2	9.924	MM	0.5290	9809.52246	309.03564	47.0571

192 (Table 4.3): enantioenriched, 97% ee



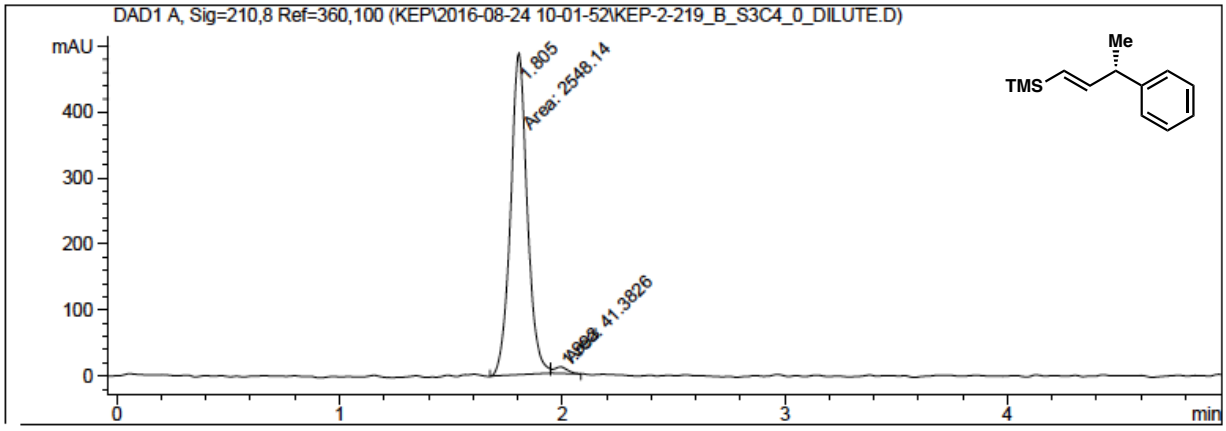
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.472	MM	0.3758	1.37749e4	610.96771	98.3278
2	10.179	MM	0.5146	234.26103	7.58734	1.6722

193 (Table 4.3): racemic



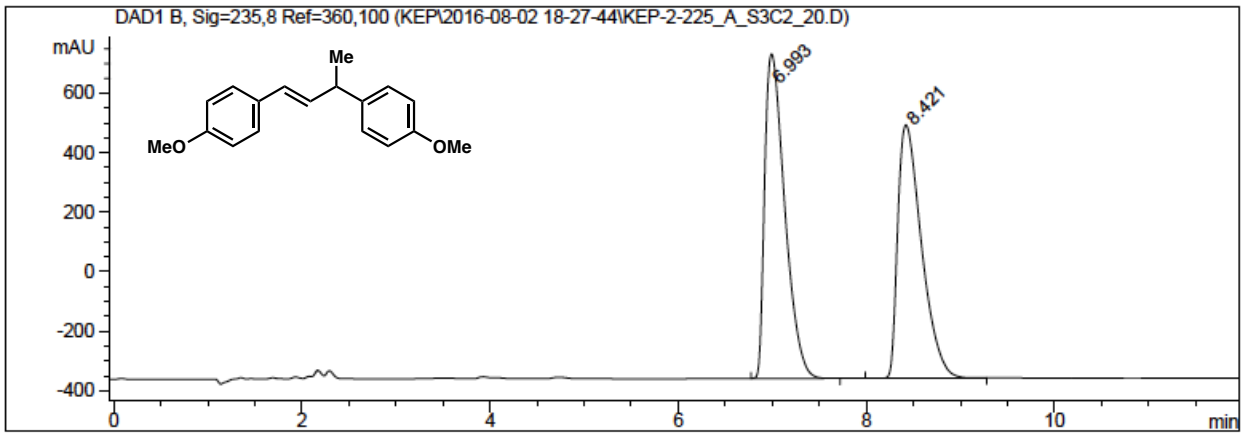
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.804	MM	0.0852	2176.43945	425.78909	52.7360
2	1.992	MM	0.0896	1950.60413	362.93353	47.2640

193 (Table 4.3): enantioenriched, 97% ee



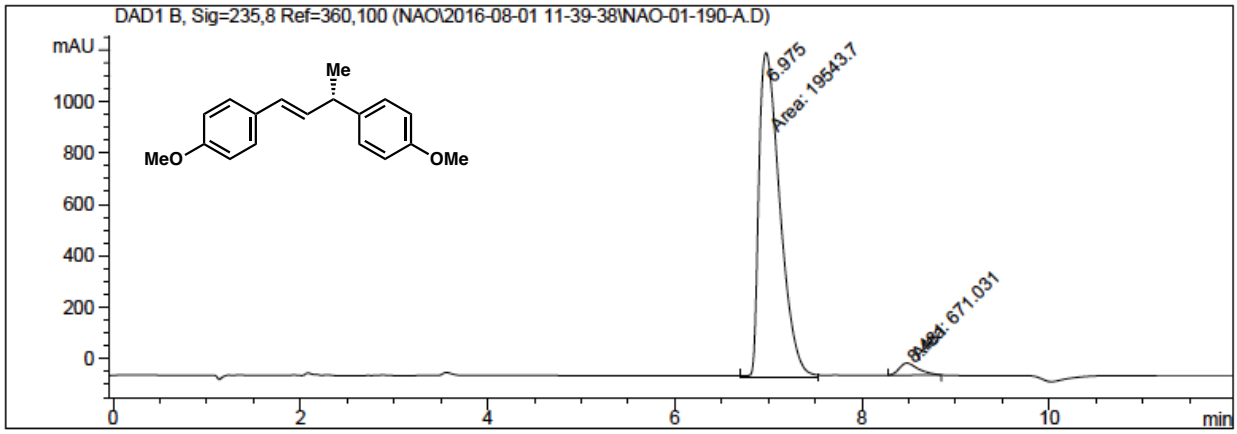
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.805	MM	0.0863	2548.14233	492.12225	98.4019
2	1.993	MM	0.0681	41.38256	10.12810	1.5981

194 (Table 4.4): racemic



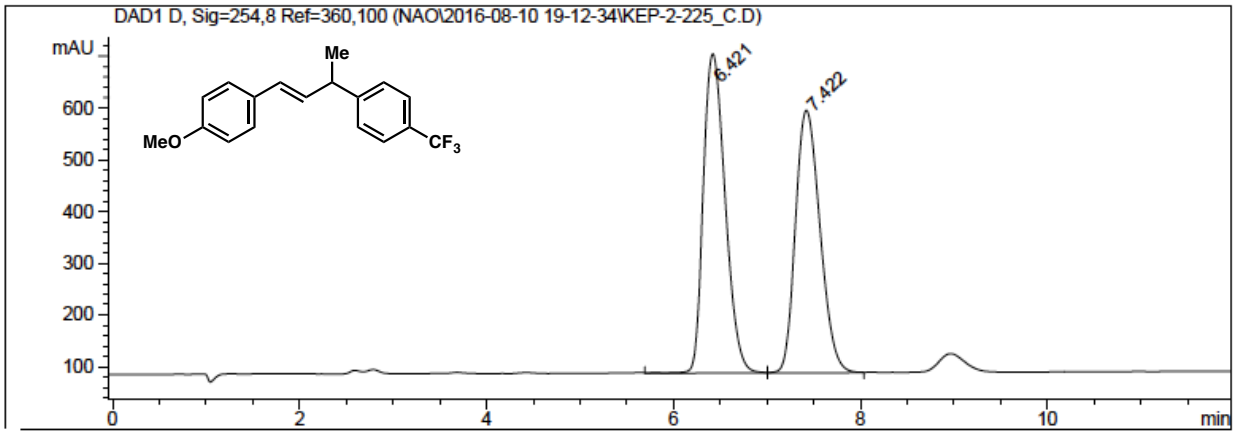
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.993	BB	0.2288	1.61745e4	1091.89661	51.9859
2	8.421	BB	0.2727	1.49387e4	851.43549	48.0141

194 (Table 4.4): enantioenriched, 93% ee



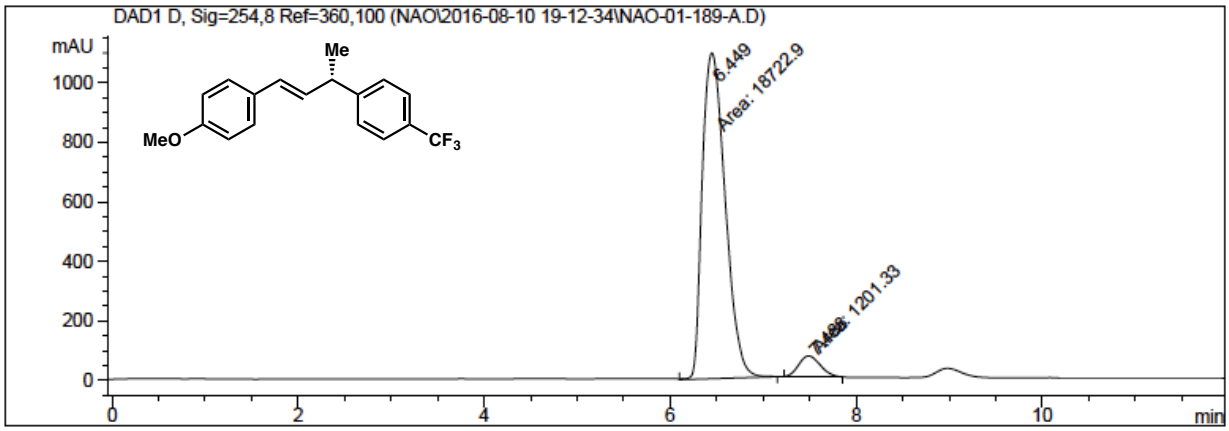
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.975	MM	0.2585	1.95437e4	1260.21631	96.6805
2	8.481	MM	0.2361	671.03094	47.35995	3.3195

195 (Table 4.4): racemic



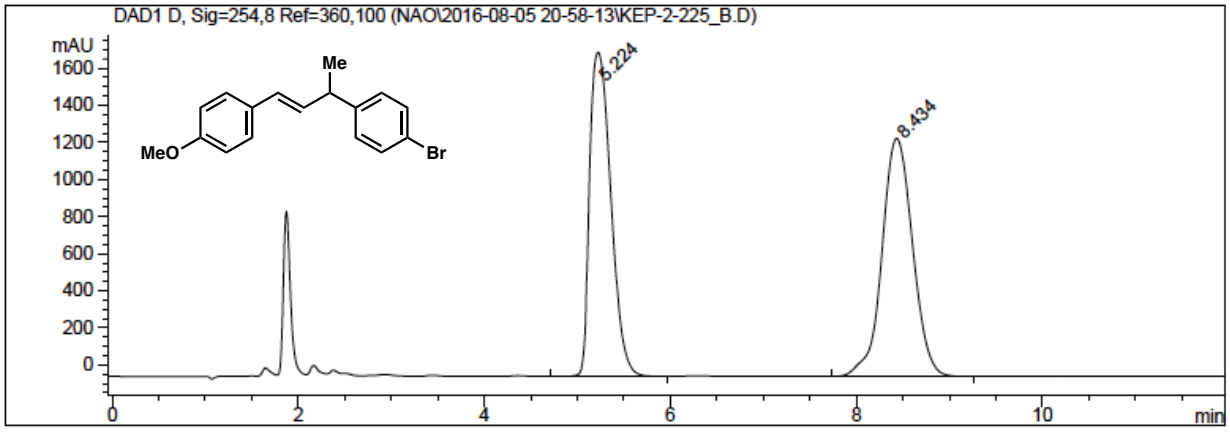
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.421	VV	0.2579	1.00441e4	616.96472	51.9654
2	7.422	VV	0.2894	9284.33398	507.48148	48.0346

195 (Table 4.4): enantioenriched, 88% ee



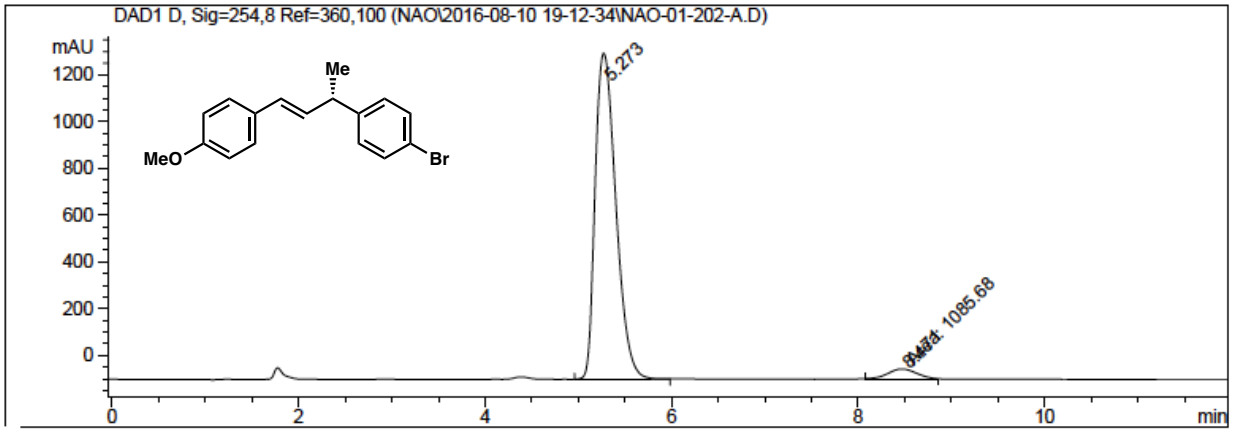
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.449	MM	0.2851	1.87229e4	1094.68372	93.9705
2	7.488	MM	0.2774	1201.33252	72.18948	6.0295

196 (Table 4.4): racemic



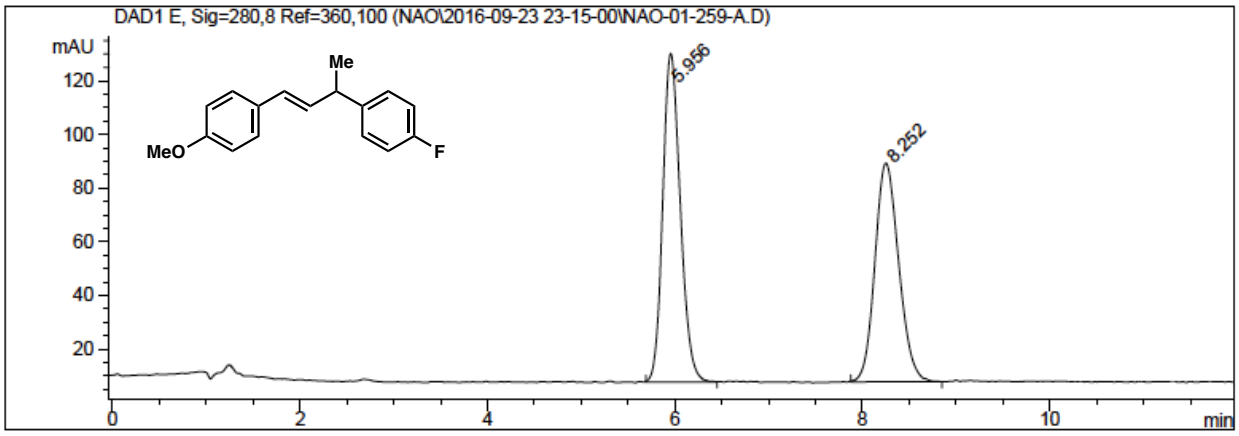
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.224	VV	0.2570	2.77188e4	1747.68750	48.5460
2	8.434	BB	0.3592	2.93793e4	1282.85803	51.4540

196 (Table 4.4): enantioenriched, 90% ee



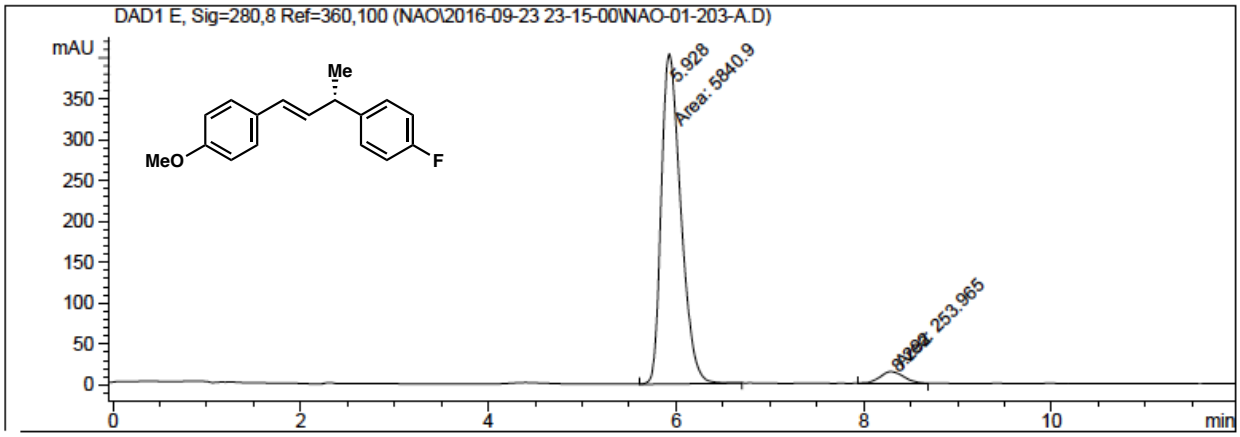
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.273	BB	0.2445	2.15843e4	1395.44788	95.2109
2	8.471	MM	0.3931	1085.67932	46.02574	4.7891

197 (Table 4.4): racemic



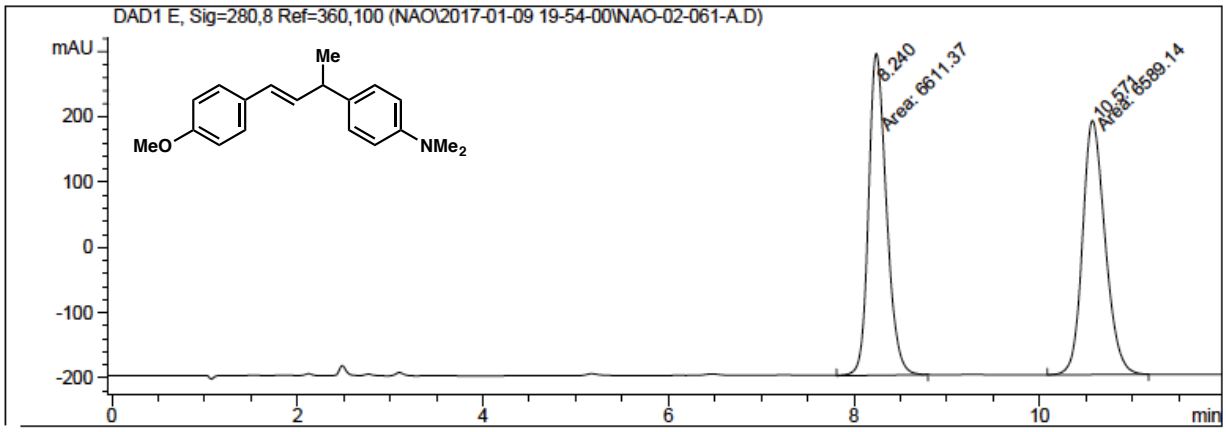
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.956	BB	0.2041	1597.30237	122.49622	52.5502
2	8.252	BB	0.2744	1442.27039	81.53059	47.4498

197 (Table 4.4): enantioenriched, 92% ee



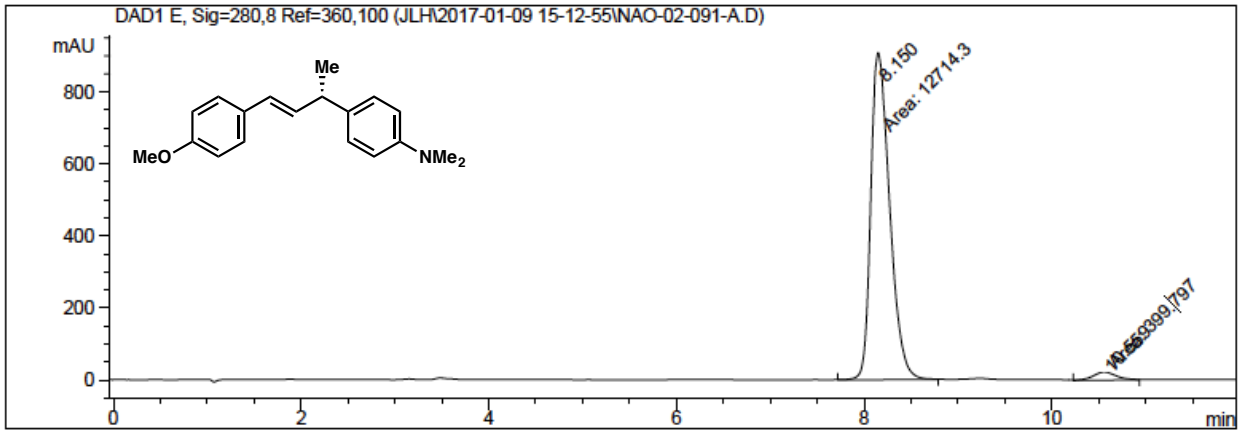
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.928	MM	0.2410	5840.89600	403.93130	95.8331
2	8.292	MM	0.2929	253.96486	14.45295	4.1669

198 (Table 4.4): racemic



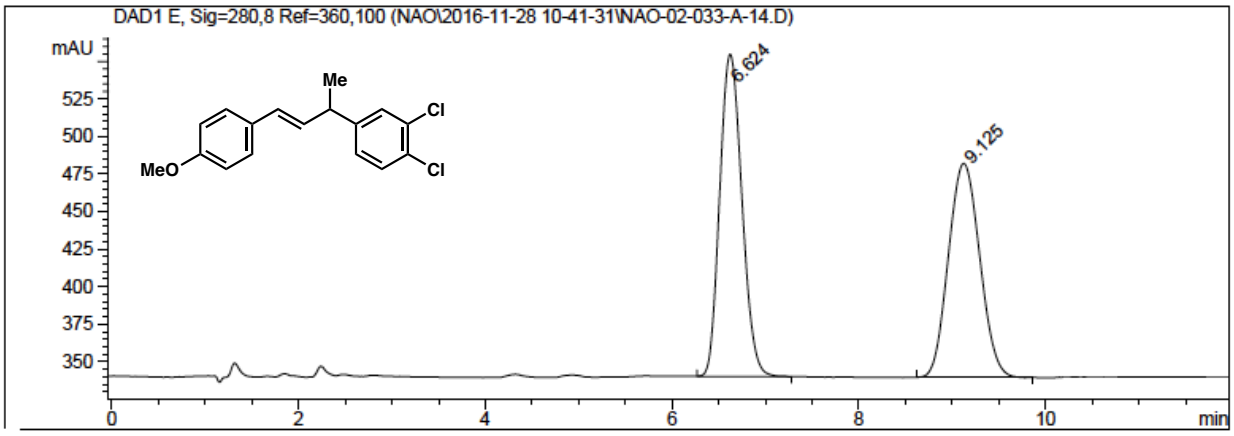
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.240	MM	0.2233	6611.36621	493.52872	50.0842
2	10.571	MM	0.2819	6589.13770	389.54446	49.9158

198 (Table 4.4): enantioenriched, 94% ee



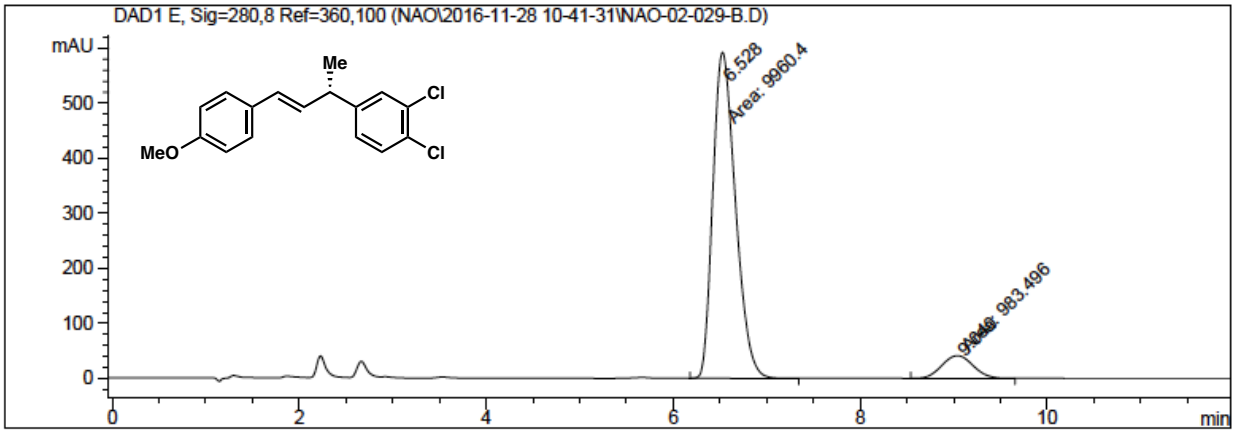
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.150	MM	0.2330	1.27143e4	909.57269	96.9514
2	10.559	MM	0.2917	399.79657	22.84231	3.0486

199 (Table 4.4): racemic



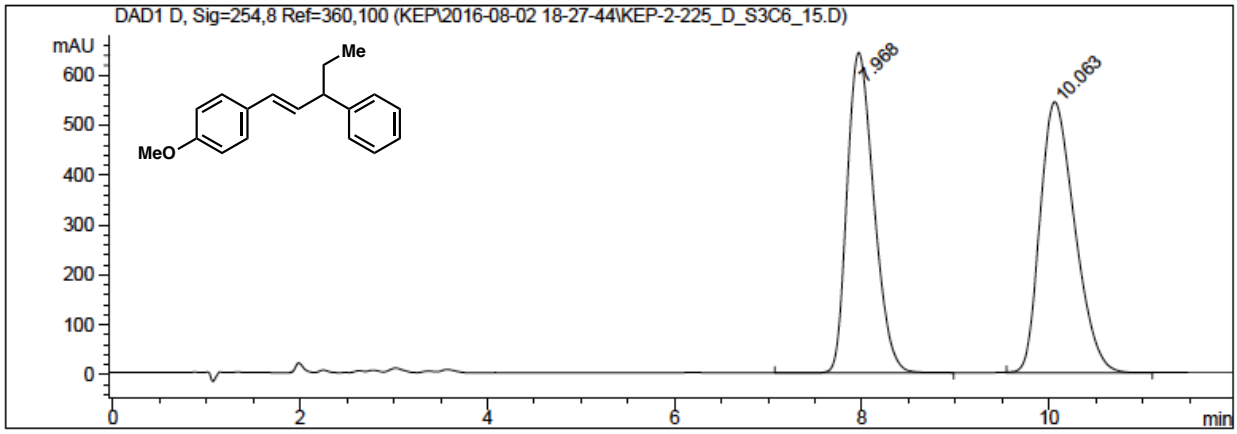
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.624	BB	0.2651	3551.33887	214.60269	51.6981
2	9.125	BB	0.3717	3318.03833	142.47495	48.3019

199 (Table 4.4): enantioenriched, 82% ee



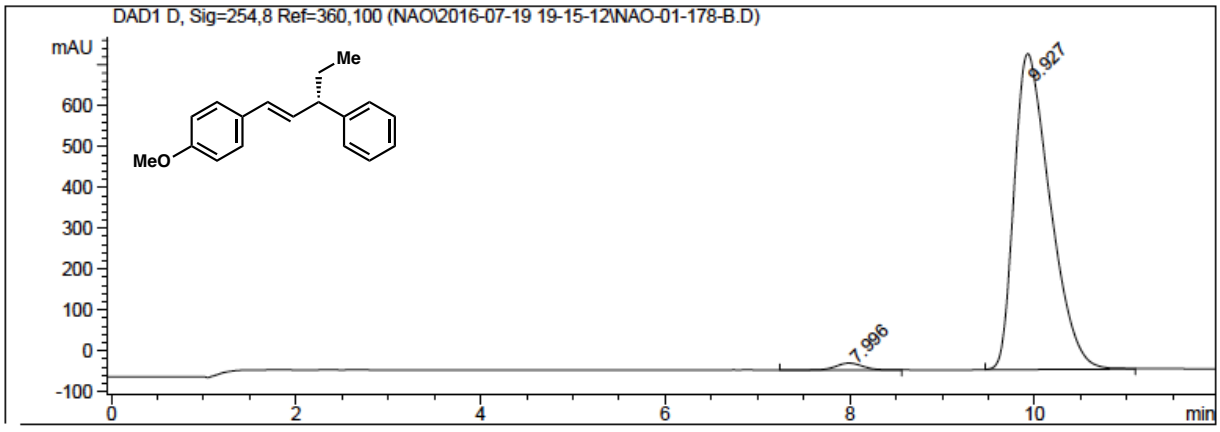
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.528	MM	0.2800	9960.39941	592.94763	91.0133
2	9.040	MM	0.3921	983.49628	41.80441	8.9867

200 (Table 4.4): racemic



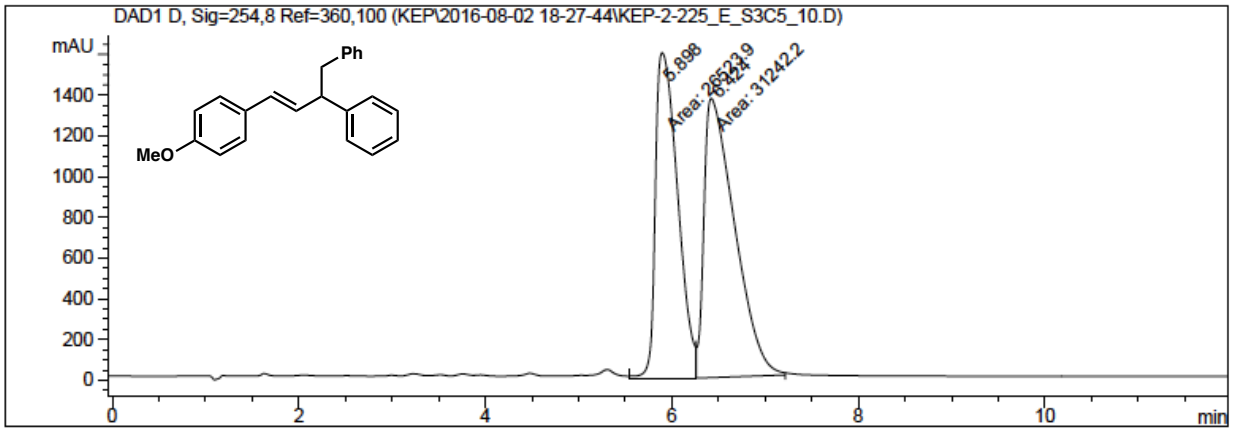
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.968	VB	0.3120	1.27647e4	642.02454	47.6750
2	10.063	BB	0.4049	1.40097e4	543.13721	52.3250

200 (Table 4.4): enantioenriched, 97% ee



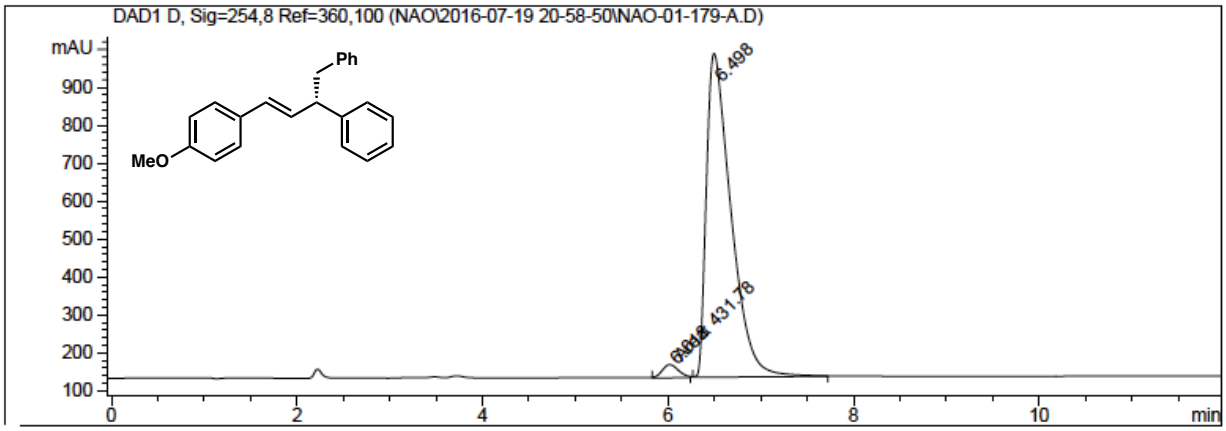
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.996	VB	0.3205	362.21658	17.28073	1.7024
2	9.927	BB	0.4153	2.09143e4	773.92688	98.2976

201 (Table 4.4): racemic



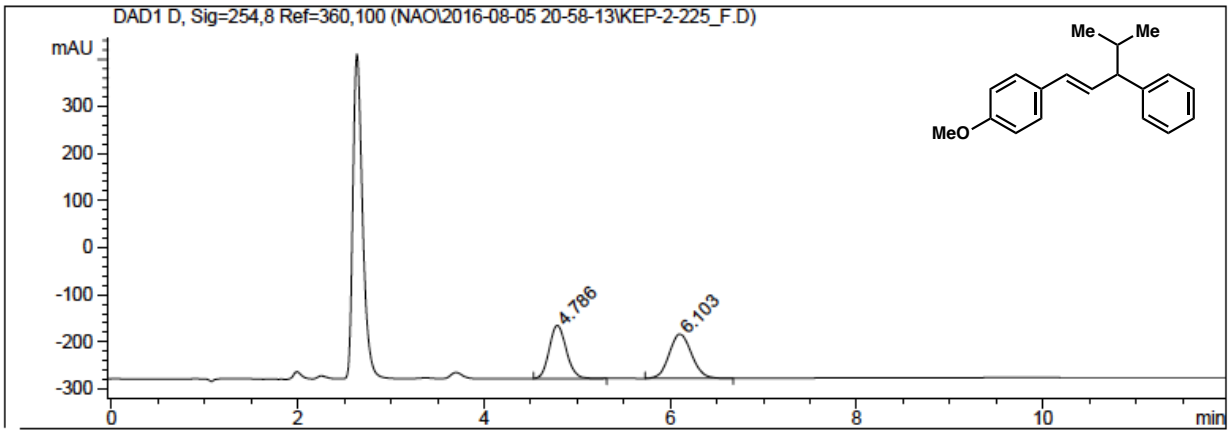
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.898	MM	0.2764	2.65239e4	1599.41284	45.9160
2	6.424	MM	0.3797	3.12422e4	1371.19714	54.0840

201 (Table 4.4): enantioenriched, 95% ee



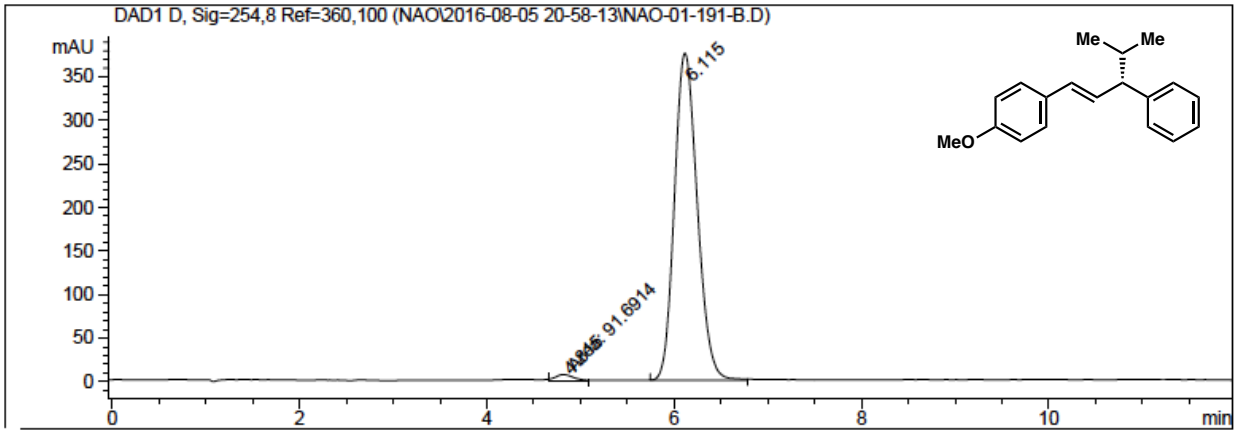
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.018	MM	0.2059	431.78006	34.94782	2.6714
2	6.498	VB	0.2791	1.57314e4	853.40881	97.3286

202 (Table 4.4): racemic



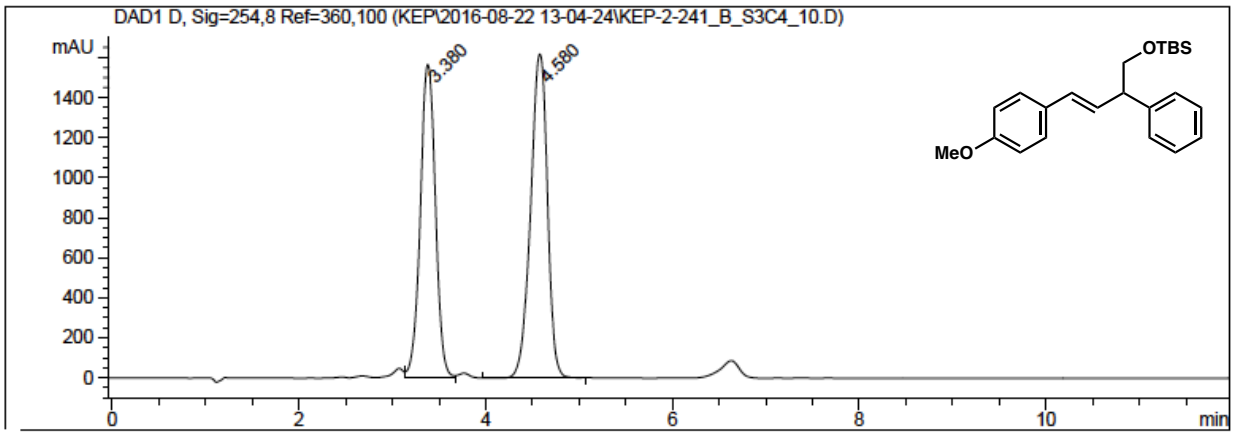
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.786	BB	0.2004	1430.79492	112.47615	47.8299
2	6.103	BB	0.2619	1560.63074	93.89527	52.1701

202 (Table 4.4): enantioenriched, 97% ee



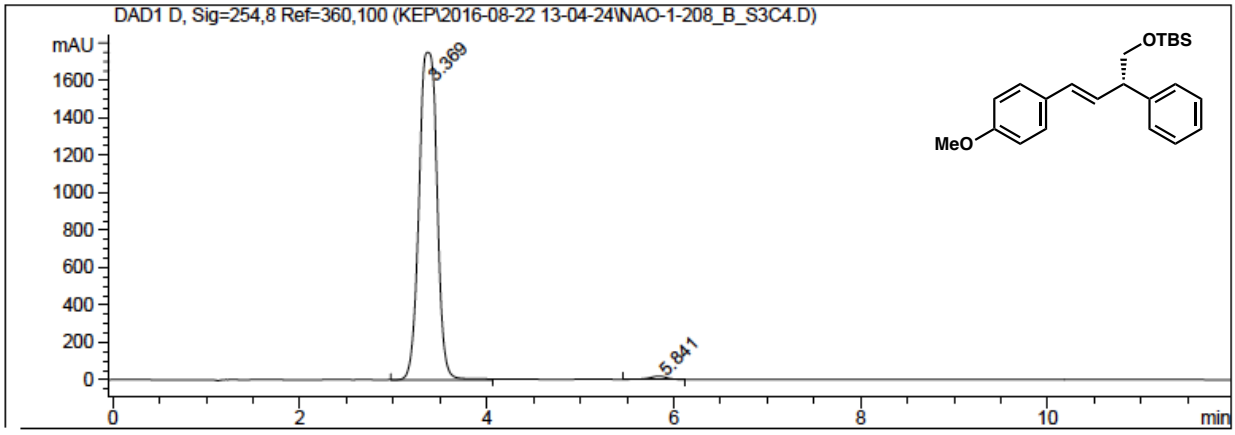
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.815	MM	0.2214	91.69138	6.90323	1.4194
2	6.115	BB	0.2659	6368.25781	375.46719	98.5806

203 (Table 4.4): racemic



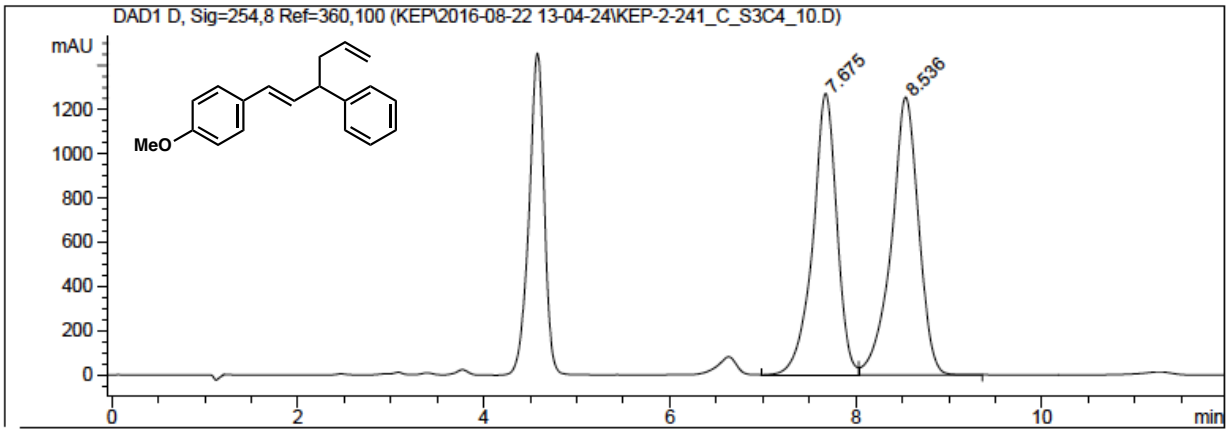
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.380	VV	0.1763	1.77440e4	1565.27930	46.6268
2	4.580	VB	0.1945	2.03113e4	1617.50305	53.3732

203 (Table 4.4): enantioenriched, 98% ee



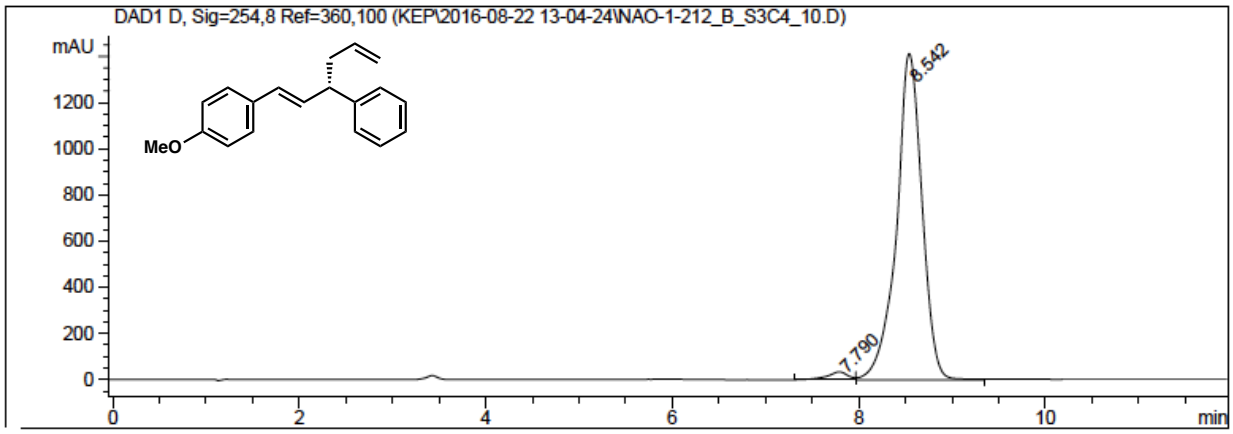
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.369	VV	0.2126	2.34730e4	1748.39075	98.8511
2	5.841	BV	0.2029	272.82288	19.07364	1.1489

204 (Table 4.4): racemic



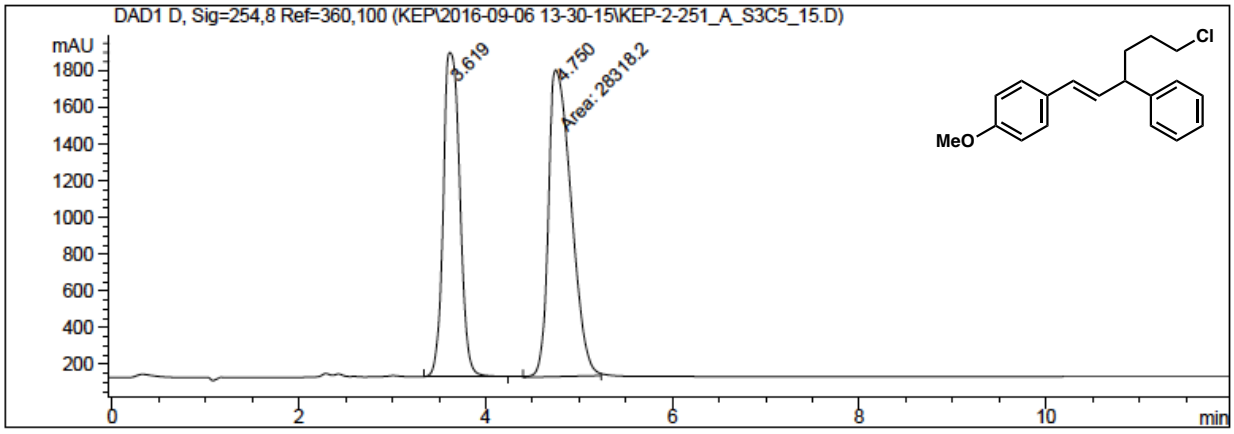
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.675	VV	0.2662	2.29359e4	1273.26990	47.2708
2	8.536	VB	0.3014	2.55844e4	1257.12512	52.7292

204 (Table 4.4): enantioenriched, 96% ee



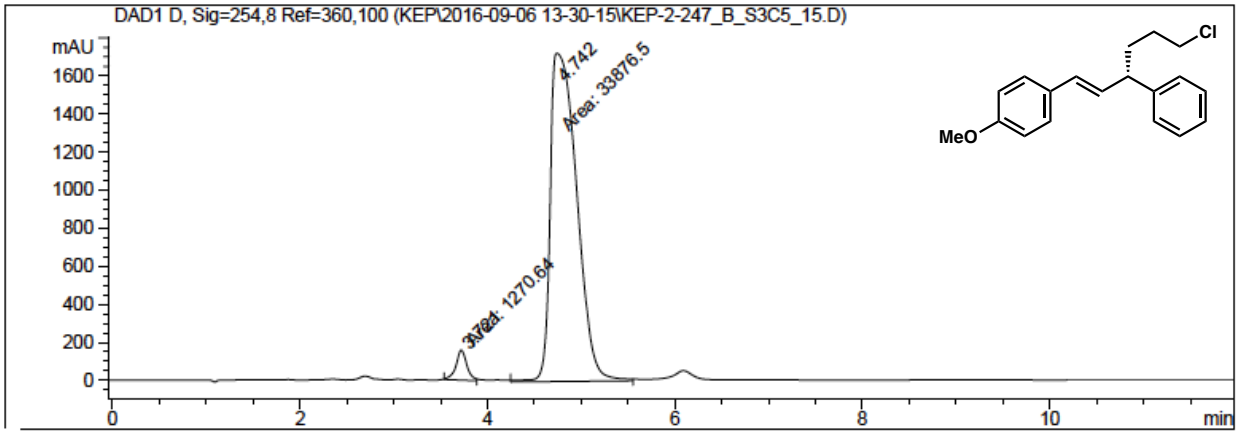
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.790	BV	0.2268	537.98590	34.33280	1.9596
2	8.542	VB	0.2824	2.69158e4	1411.98352	98.0404

205 (Table 4.4): racemic



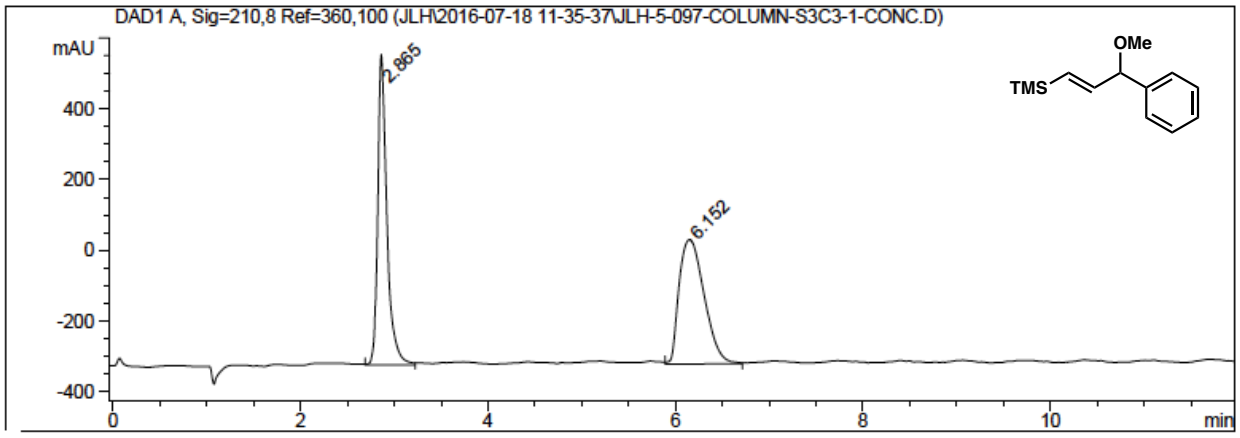
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.619	BV	0.1967	2.19414e4	1769.60486	43.6562
2	4.750	MM	0.2819	2.83182e4	1673.98267	56.3438

205 (Table 4.4): enantioenriched, 93% ee



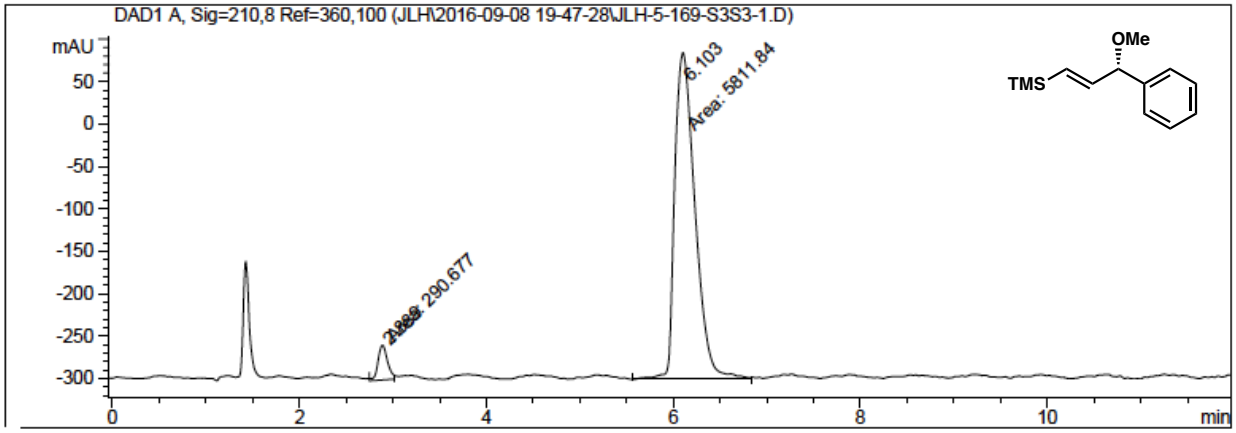
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.721	MM	0.1339	1270.64075	158.21689	3.6152
2	4.742	MM	0.3274	3.38765e4	1724.49841	96.3848

208 (Scheme 4.2): racemic



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.865	VV	0.1036	5942.20703	870.57599	47.5931
2	6.152	VV	0.2969	6543.22803	351.95050	52.4069

208 (Scheme 4.2): enantioenriched, 91% ee



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.889	MM	0.1180	290.67731	41.05857	4.7632
2	6.103	MM	0.2515	5811.83789	385.08493	95.2368

4.8 NOTES AND REFERENCES

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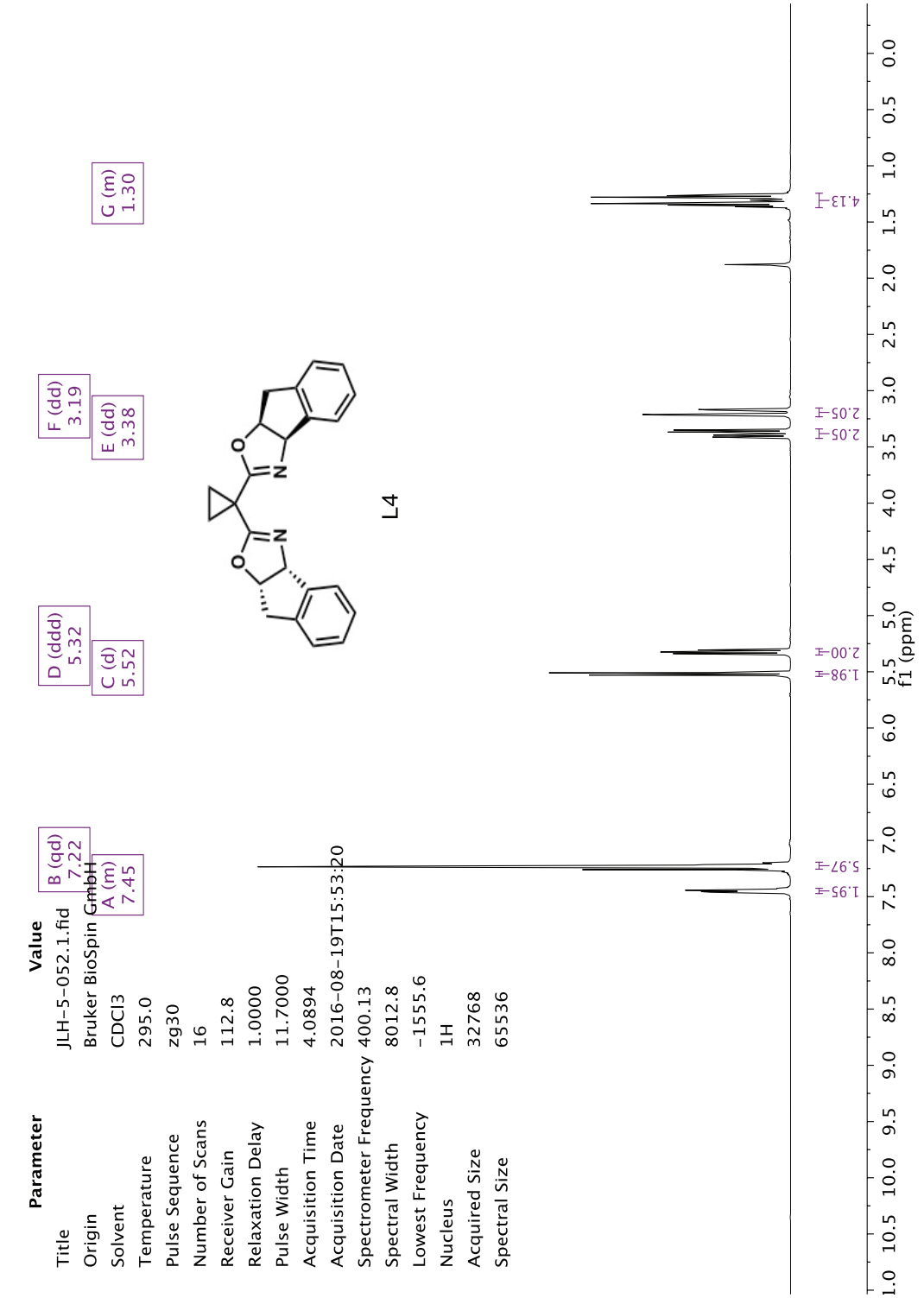
(40) This work was conducted in collaboration with Dr. Chris Lavoie, a postdoctoral scholar, and Sara Dibrell, a graduate student in the Reisman lab.

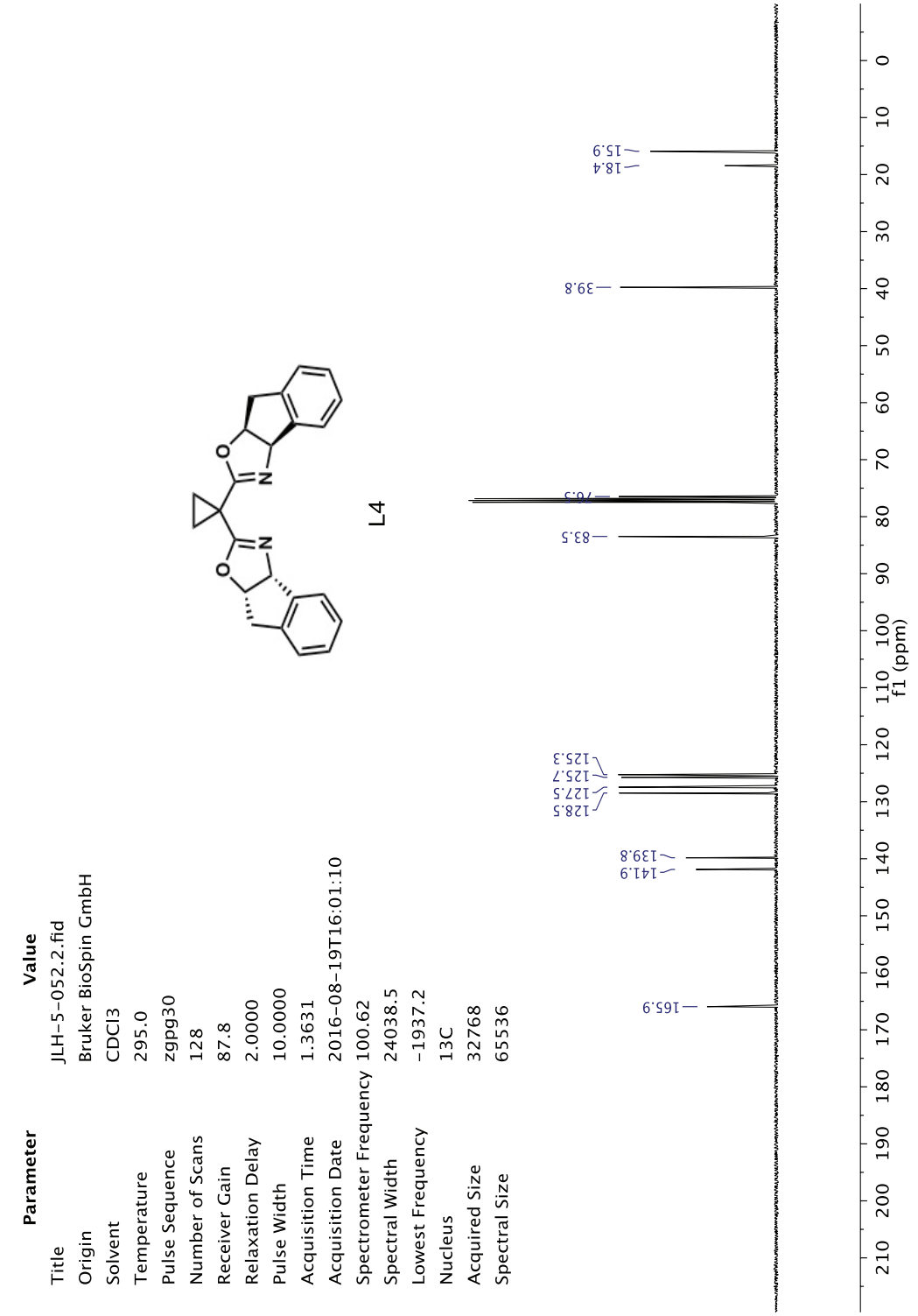
Appendix 2

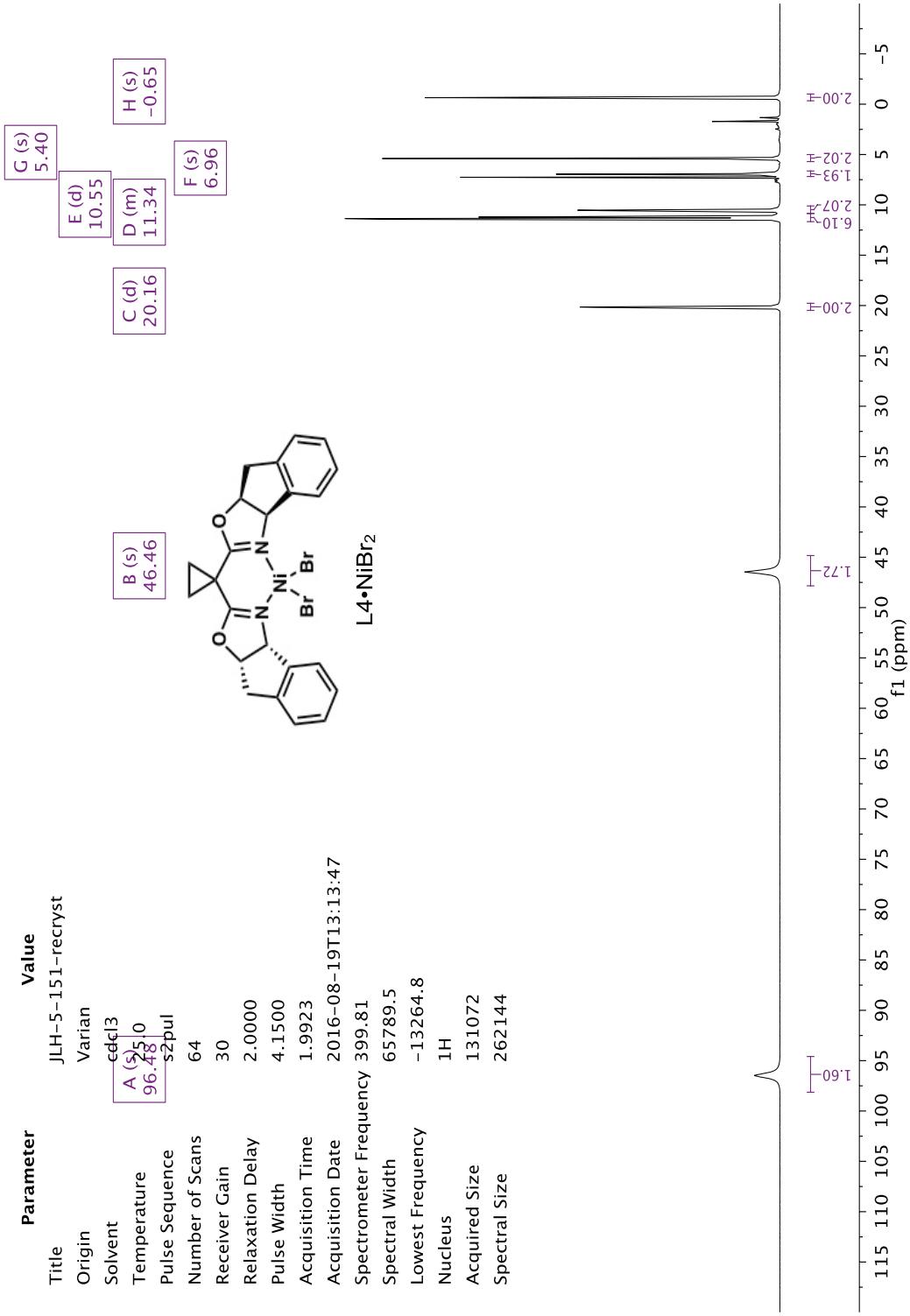
Spectra Relevant to Chapter 4:

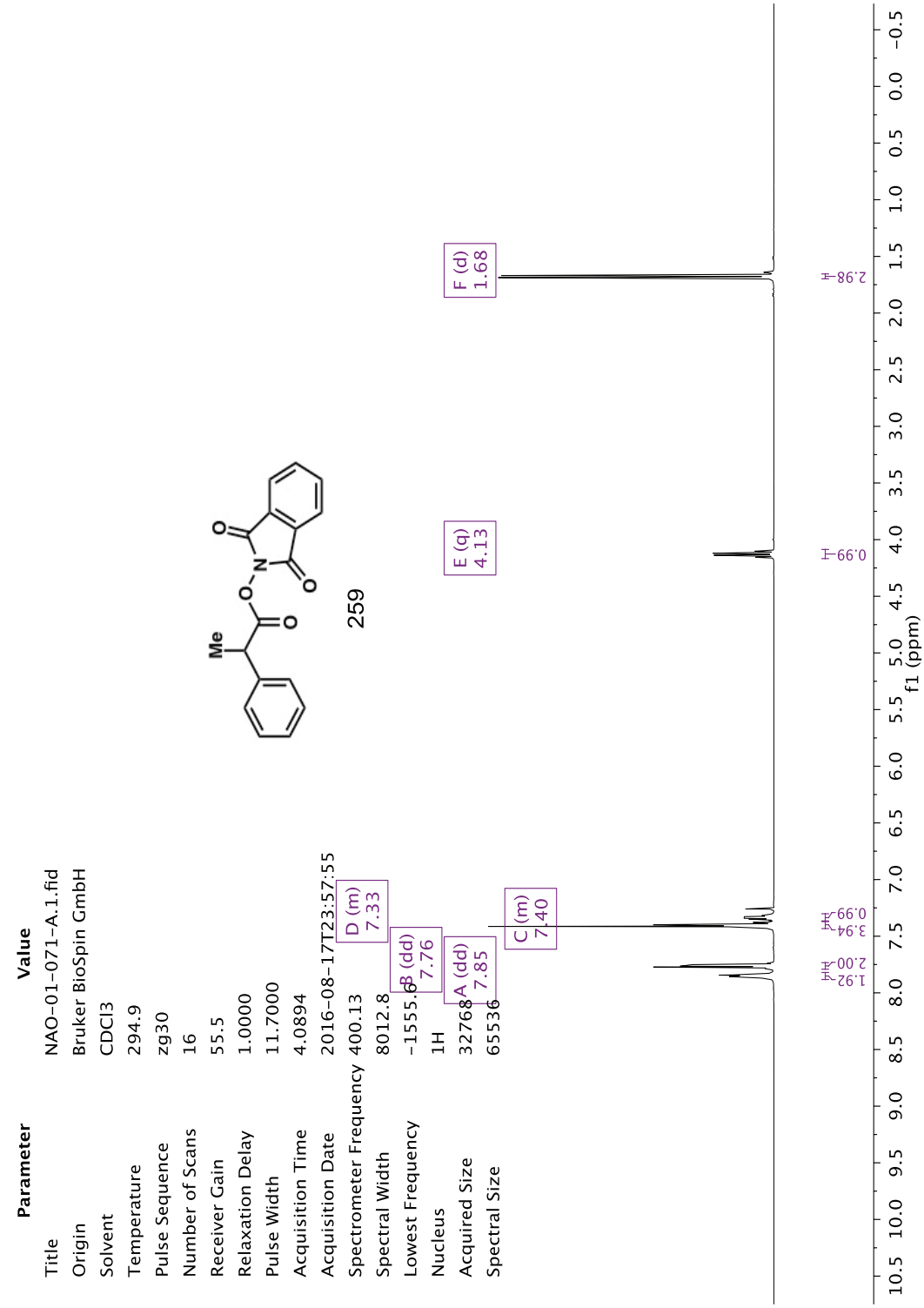
Nickel-Catalyzed Asymmetric Reductive Cross-Coupling of

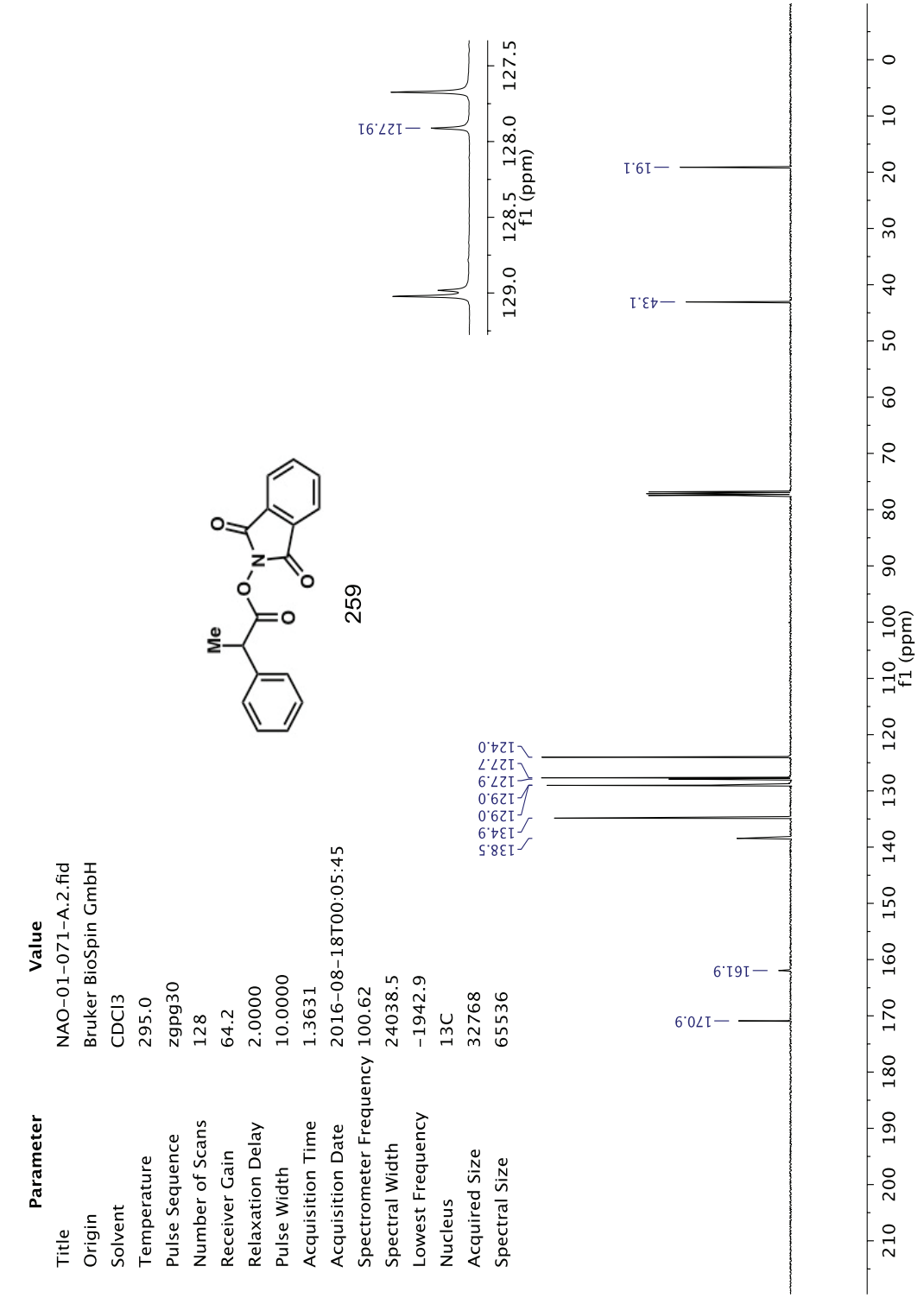
N-Hydroxyphthalimide Esters with Alkenyl Bromides

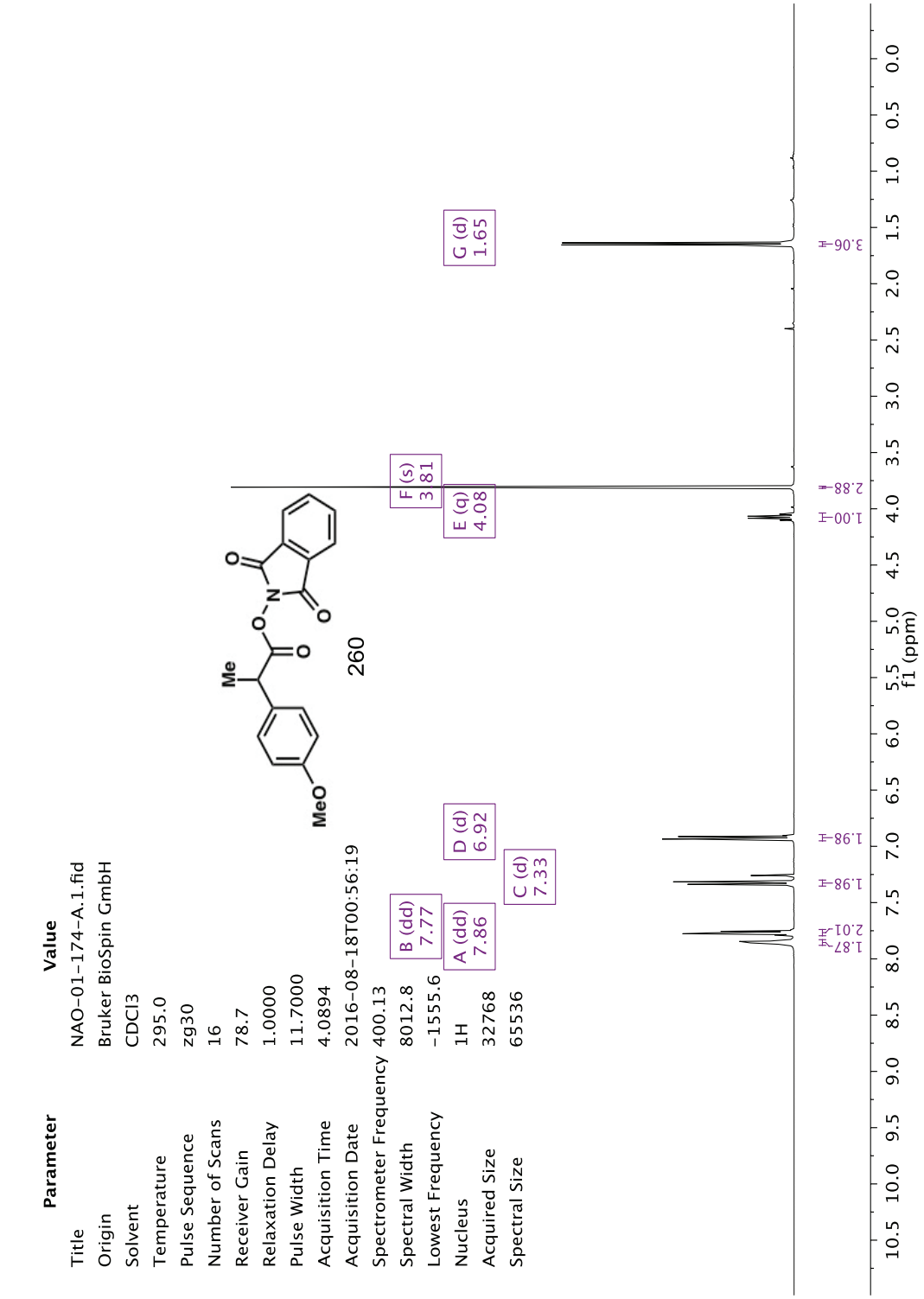

Parameter
Value
Title JLH-5-052.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 112.8
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2016-08-19T15:53:20
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1555.6
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
B (qd) 7.22
A (m) 7.45
D (ddd) 5.32
C (d) 5.52
F (dd) 3.19
E (dd) 3.38
G (m) 1.30
L4
1.95
5.97
1.98
2.00
2.05
2.05
4.13
f1 (ppm)

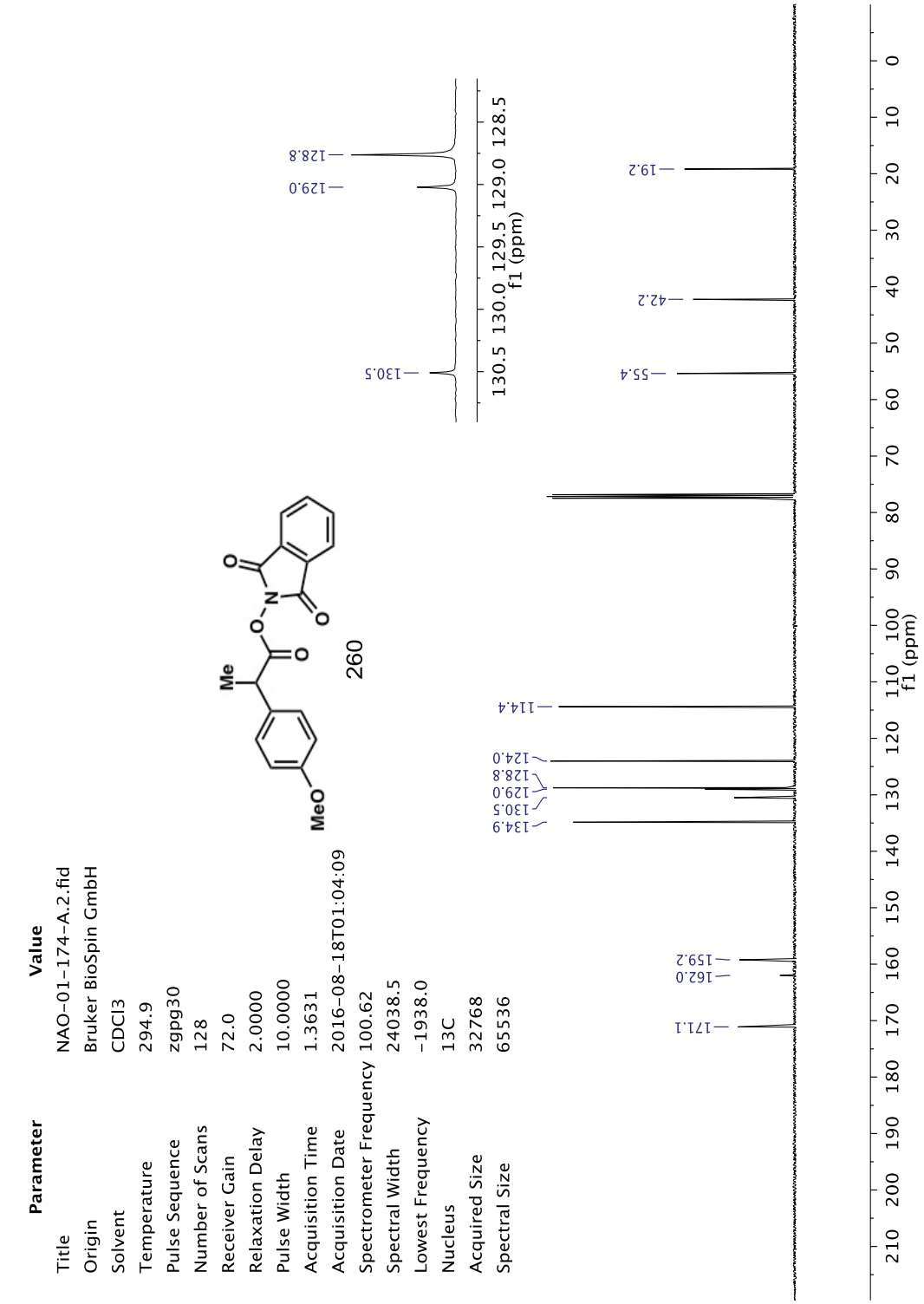

L4
Parameter Value
Title JLH-5-052.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 87.8
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-08-19T16:01:10
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1937.2
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
165.9
141.9
139.8
128.5
127.5
125.7
125.3
83.5
76.5
39.8
18.4
15.9
f1 (ppm)

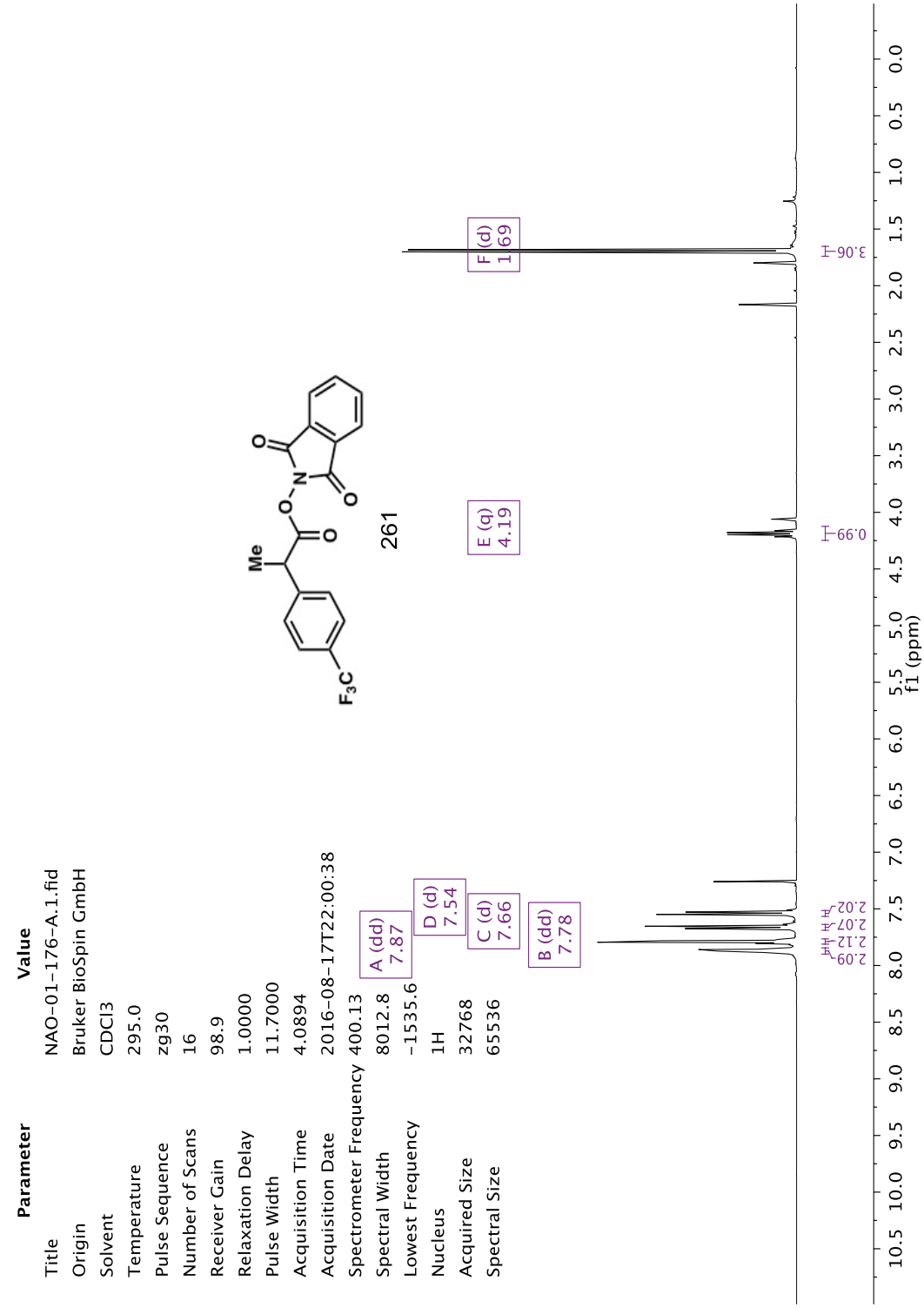

A (s) 25.10
96.48
B (s) 46.46
C (d) 20.16
D (m) 11.34
E (d) 10.55
F (s) 6.96
G (s) 5.40
H (s) -0.65
L4•NiBr2
Br
Br
Ni
N
N
O
O
Parameter Value
Title JLH-5-151-recryst
Origin Varian
Solvent cdcl3
Temperature 25.0
Pulse Sequence s2pul
Number of Scans 64
Receiver Gain 30
Relaxation Delay 2.0000
Pulse Width 4.1500
Acquisition Time 1.9923
Acquisition Date 2016-08-19T13:13:47
Spectrometer Frequency 399.81
Spectral Width 65789.5
Lowest Frequency -13264.8
Nucleus 1H
Acquired Size 131072
Spectral Size 262144
1.60
1.72
2.00
6.10
2.07
1.93
2.02
2.00
115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 -5
f1 (ppm)

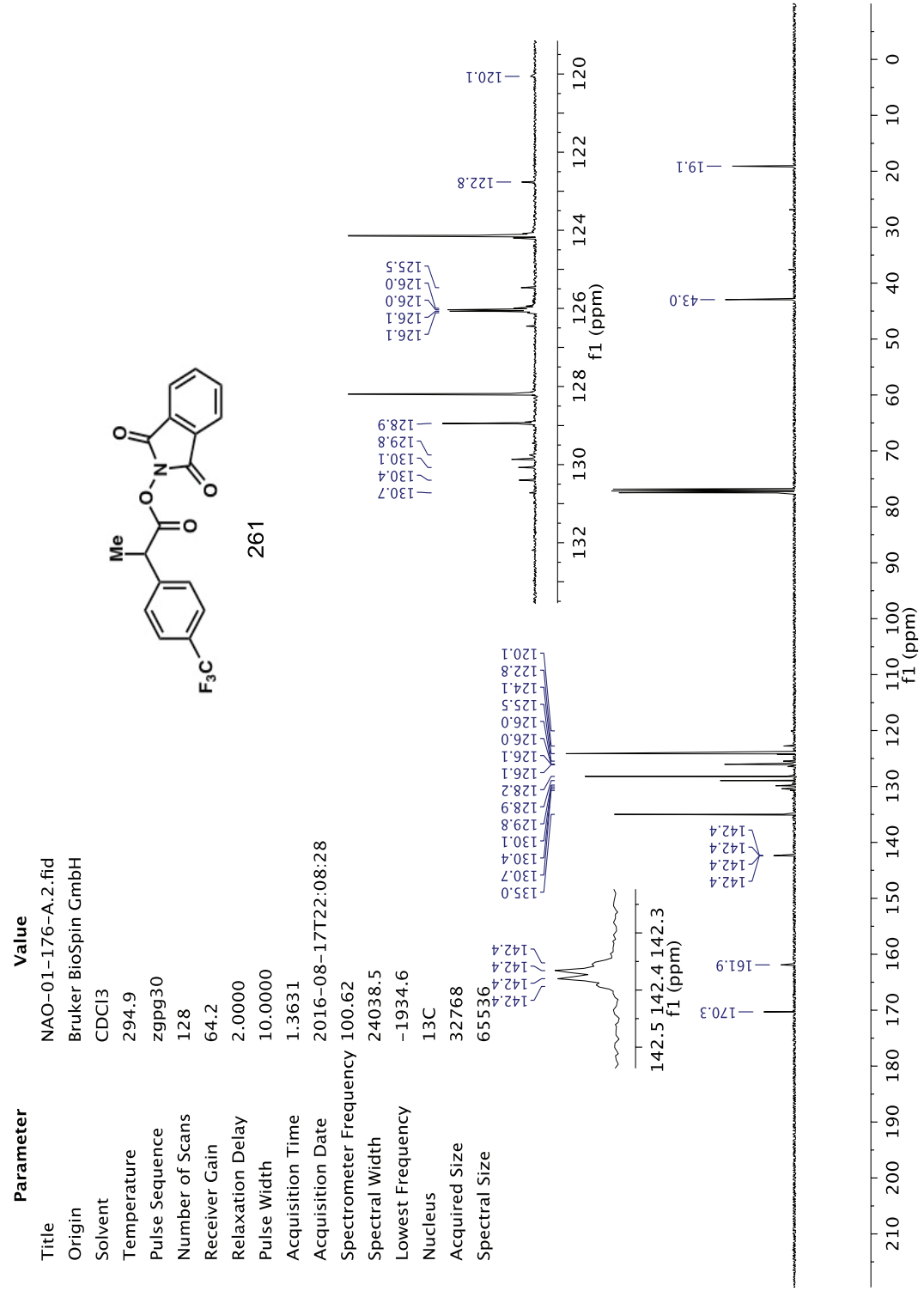

Parameter Value
Title NAO-01-071-A.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 55.5
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2016-08-17T23:57:55
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1555.6
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
Me
259
D (m) 7.33
B (dd) 7.76
A (dd) 7.85
C (m) 7.40
E (q) 4.13
F (d) 1.68
1.92
2.00
3.94
0.99
0.99
2.98
f1 (ppm)


Parameter Value
Title NAO-01-071-A.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-08-18T00:05:45
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1942.9
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
259
170.9
161.9
138.5
134.9
129.0
129.0
127.9
127.7
124.0
43.1
19.1
127.91
f1 (ppm)

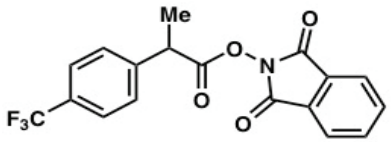

Parameter Value
Title NAO-01-174-A.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 78.7
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2016-08-18T00:56:19
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1555.6
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
Me
MeO
260
A (dd) 7.86
B (dd) 7.77
C (d) 7.33
D (d) 6.92
E (q) 4.08
F (s) 3.81
G (d) 1.65
1.87
2.01
1.98
1.98
1.98
2.88
1.00
3.06
f1 (ppm)


Parameter Value
Title NAO-01-174-A.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-08-18T01:04:09
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1938.0
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
MeO
260
171.1
162.0
159.2
134.9
130.5
129.0
128.8
124.0
114.4
55.4
42.2
19.2
130.5
129.0
128.8
130.5 130.0 129.5 129.0 128.5
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

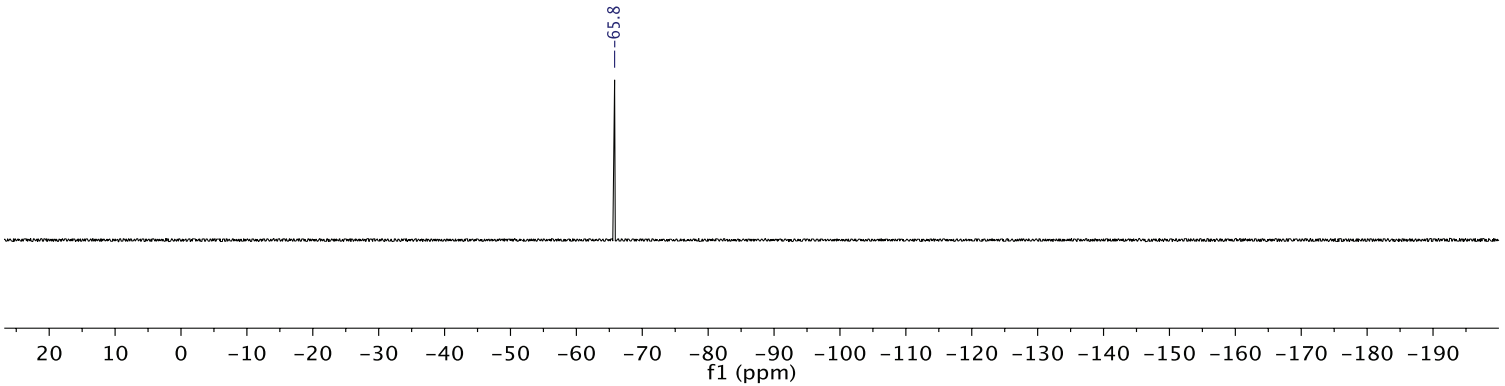

Parameter Value
Title NAO-01-176-A.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 98.9
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2016-08-17T22:00:38
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1535.6
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
261
A (dd) 7.87
B (dd) 7.78
C (d) 7.66
D (d) 7.54
E (q) 4.19
F (d) 1.69
2.09
2.12
2.07
2.02
0.99
3.06
f1 (ppm)


Parameter Value
Title NAO-01-176-A.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-08-17T22:08:28
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1934.6
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
261
Me
O
N
O
F3C
f1 (ppm)

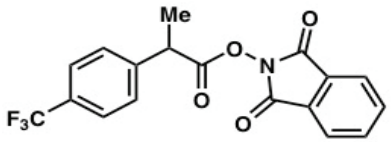
Parameter	Value
Title	NAO-01-176A
Origin	Varian
Solvent	"cdcl3"
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2016-08-31T23:19:24
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-58259.3
Nucleus	19F
Acquired Size	64000
Spectral Size	131072



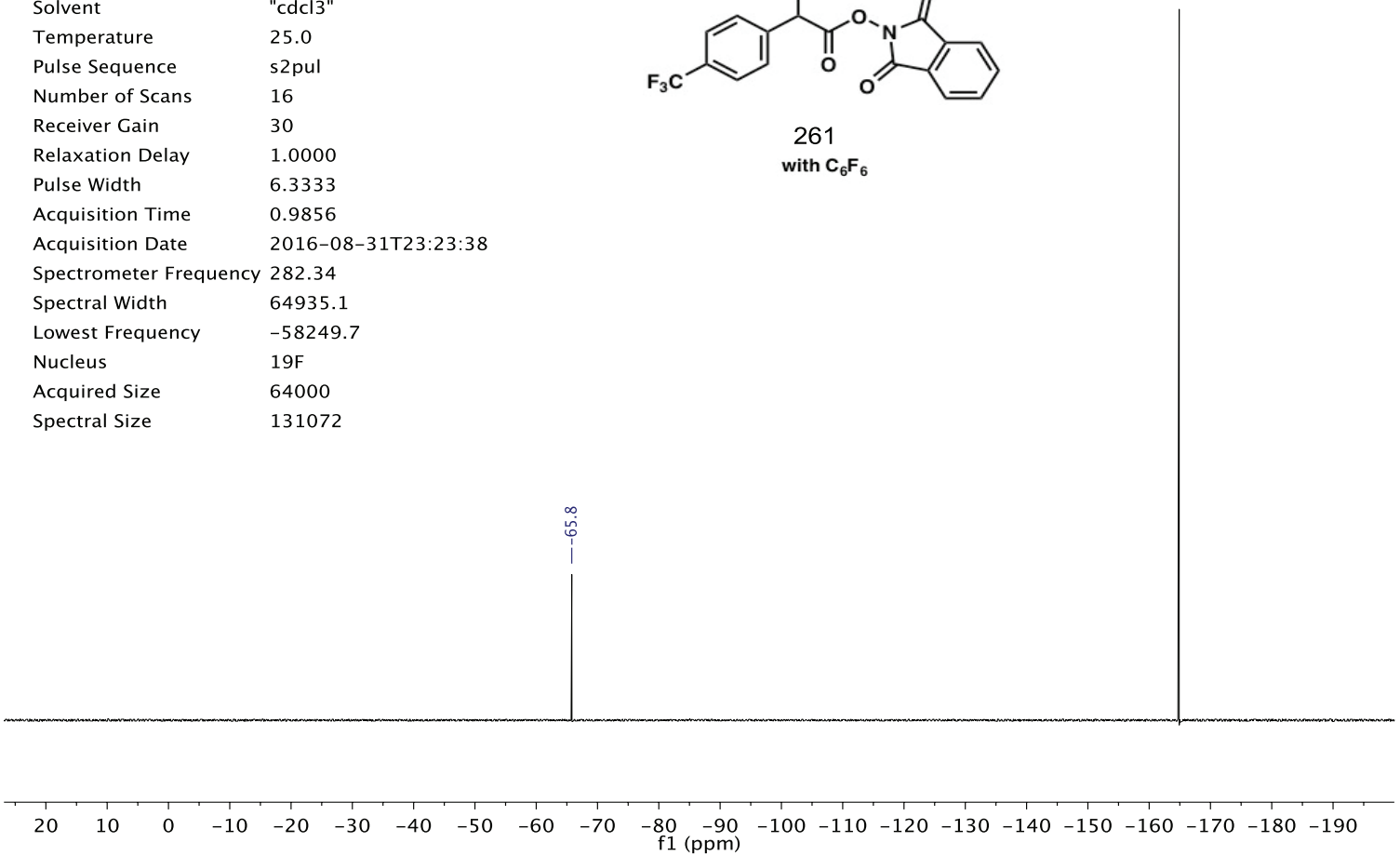
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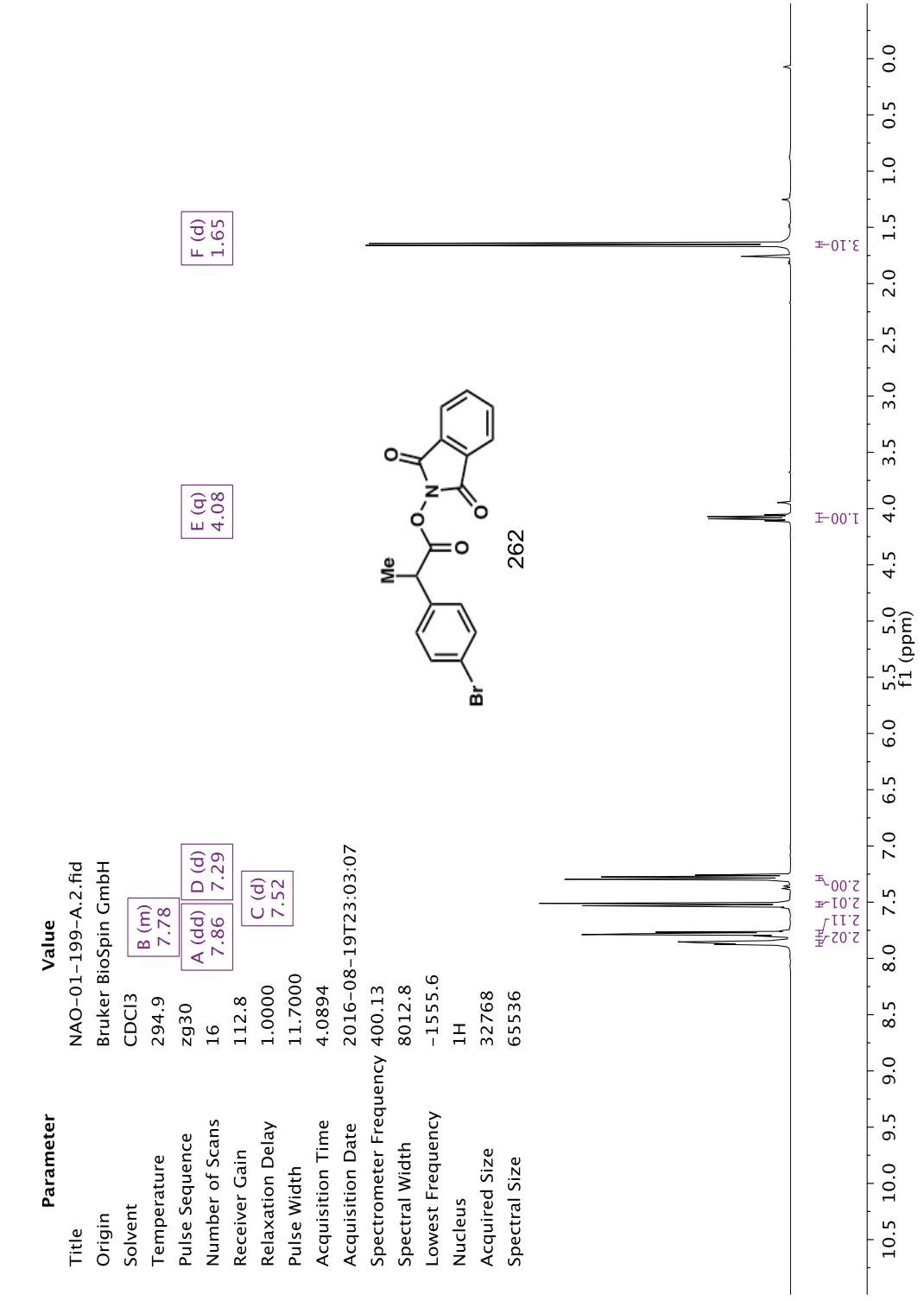


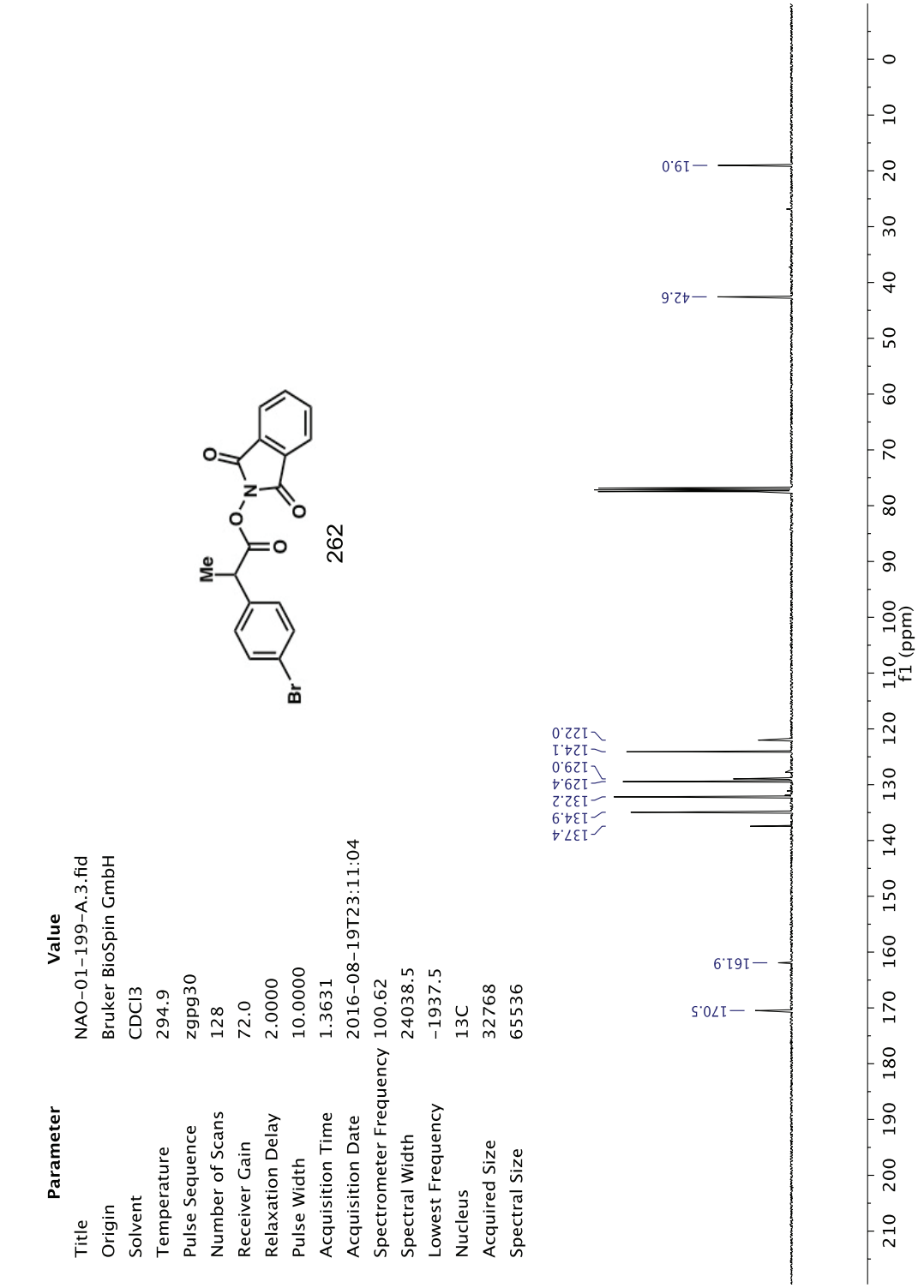
Parameter	Value
Title	NAO-01-176A-C6F6
Origin	Varian
Solvent	"cdcl3"
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2016-08-31T23:23:38
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-58249.7
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

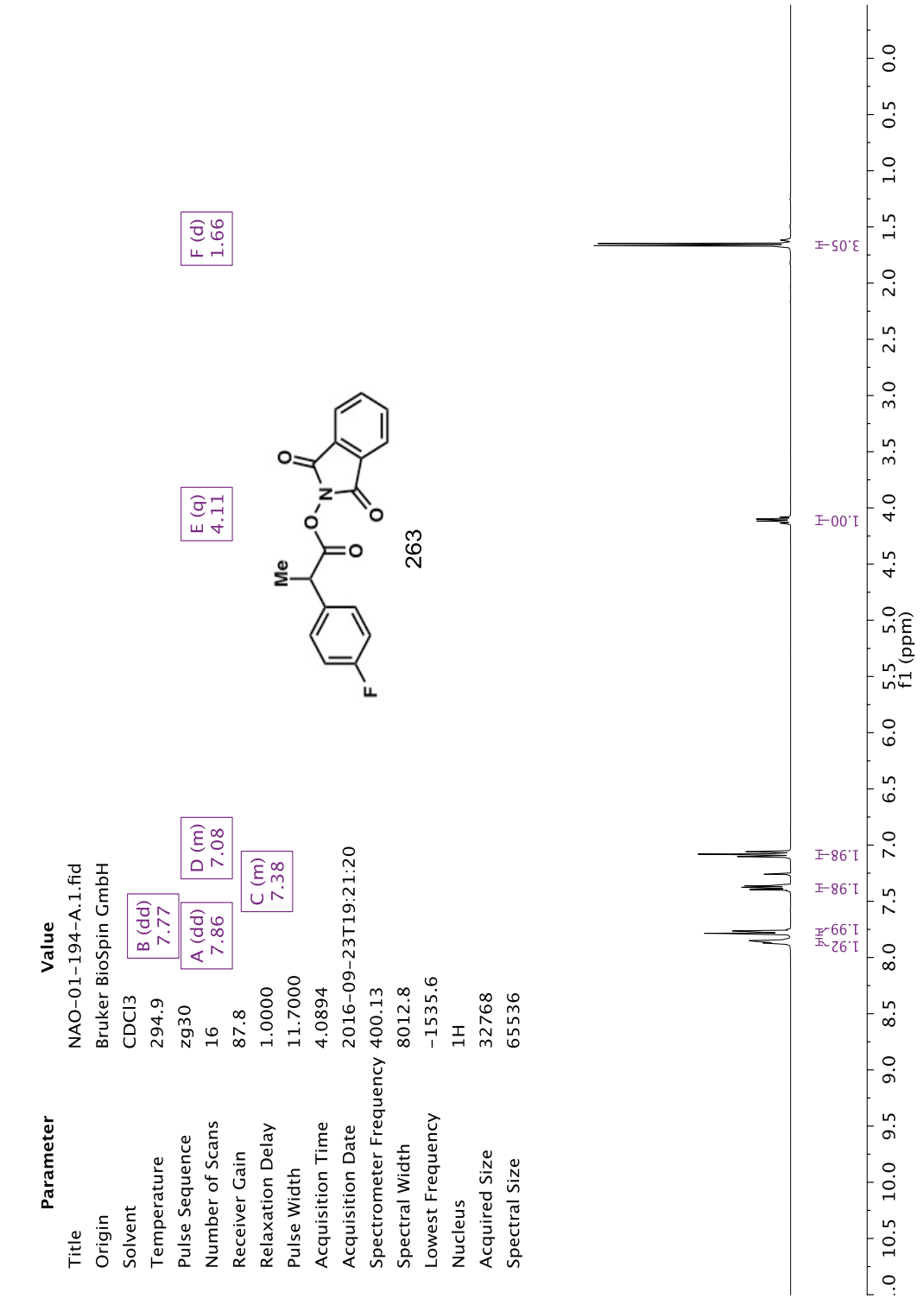


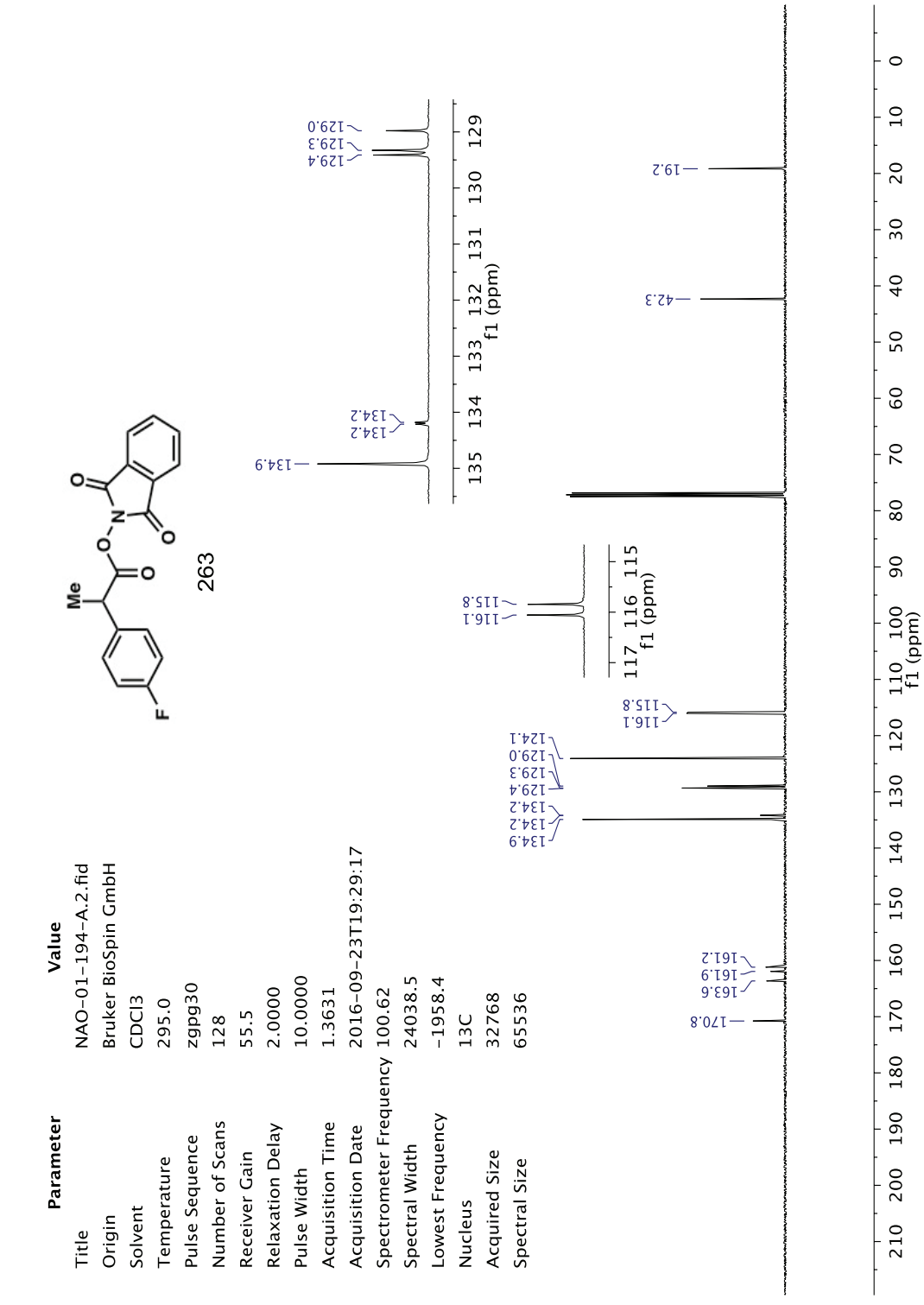
261
with C_6F_6



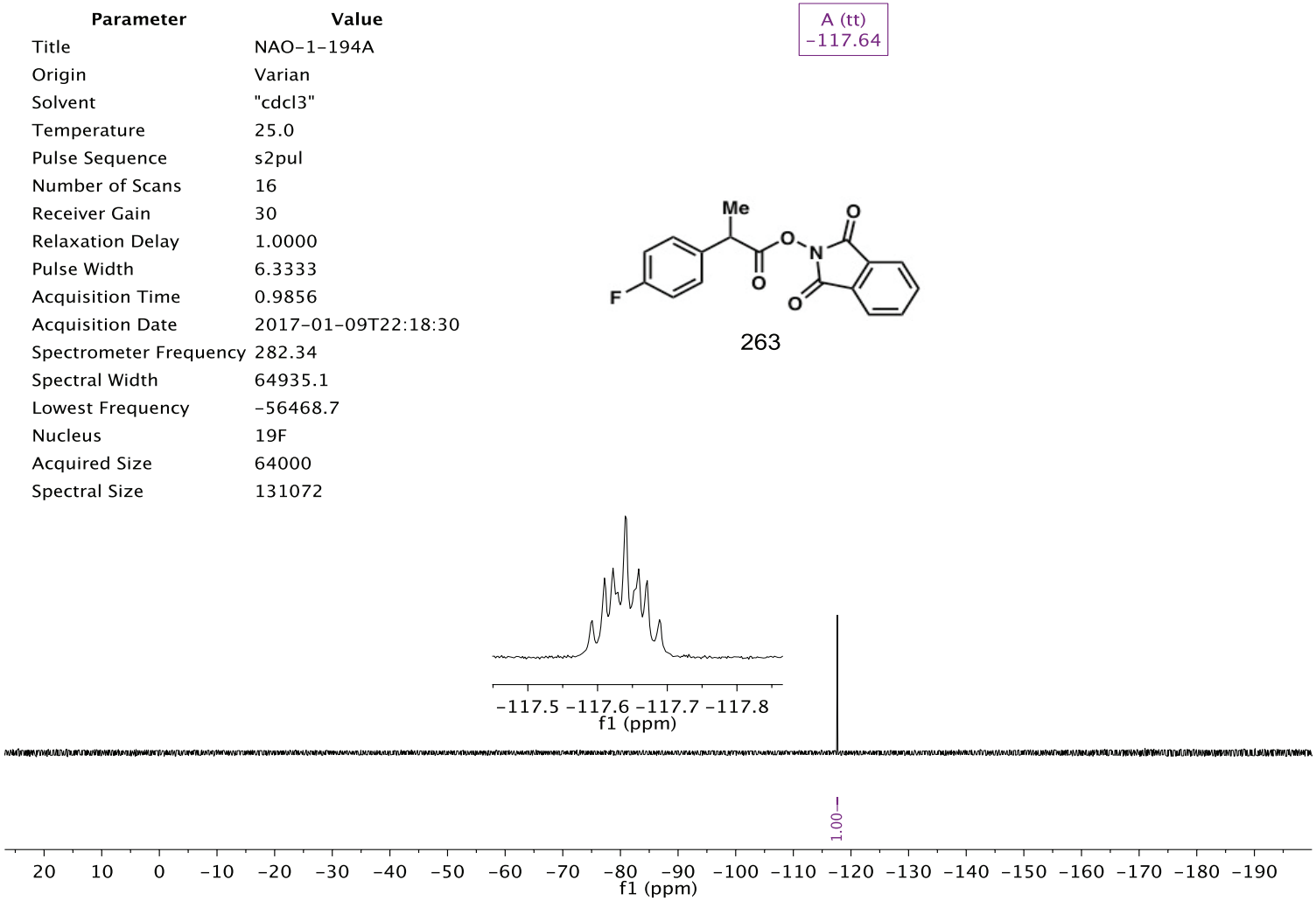

Parameter Value
Title NAO-01-199-A.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 112.8
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2016-08-19T23:03:07
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1555.6
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
B (m) 7.78
A (dd) 7.86
D (d) 7.29
C (d) 7.52
E (q) 4.08
F (d) 1.65
Me
Br
262
2.02
2.11
2.01
2.00
1.00
3.10
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


Parameter Value
Title NAO-01-199-A.3.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-08-19T23:11:04
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1937.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
262
Me
Br
O
N
O
O
O
170.5
161.9
137.4
134.9
132.2
129.4
129.0
124.1
122.0
42.6
19.0
f1 (ppm)

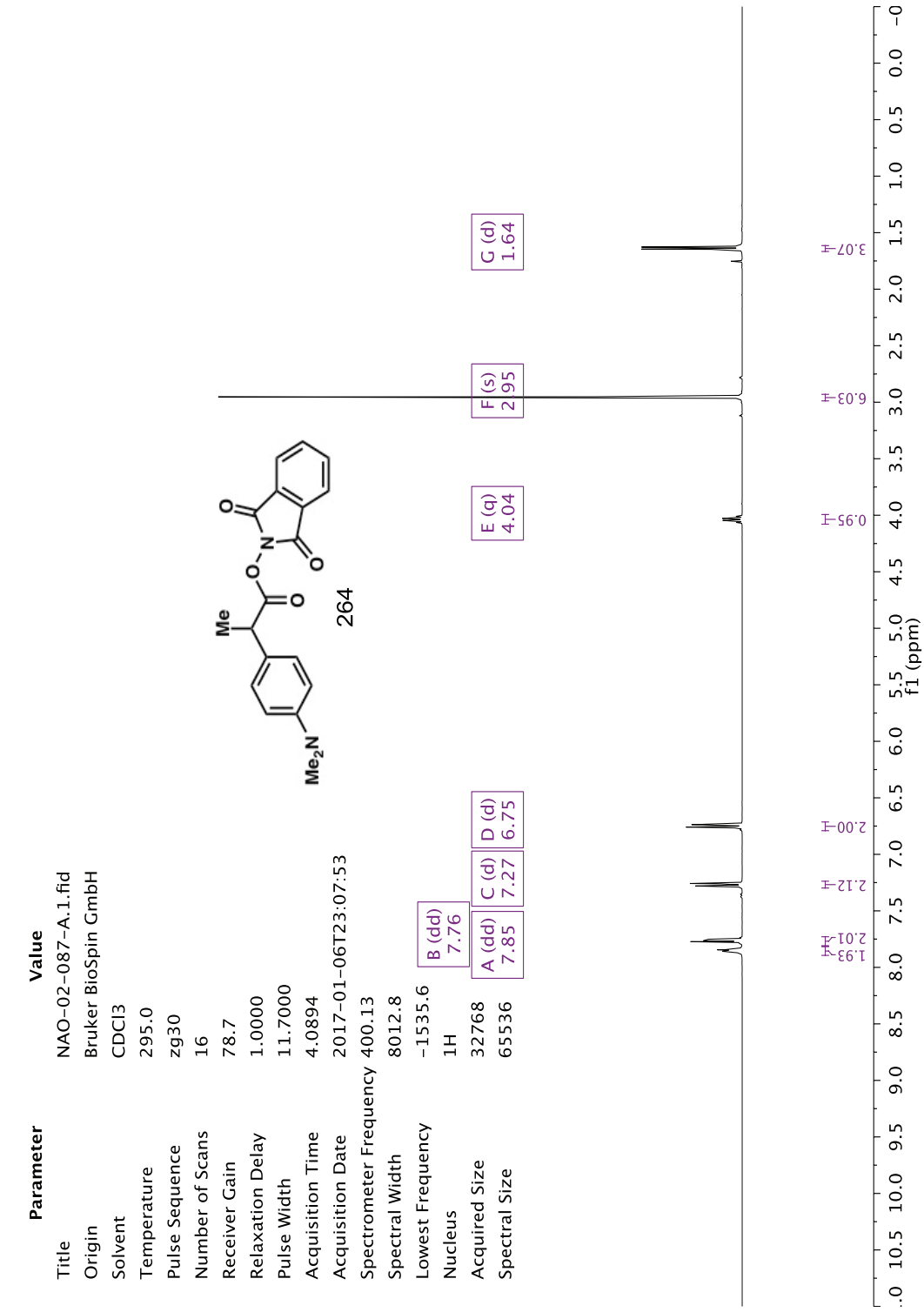

Parameter
Value
Title
NAO-01-194-A.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
87.8
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2016-09-23T19:21:20
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1535.6
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
B (dd) 7.77
A (dd) 7.86
D (m) 7.08
C (m) 7.38
E (q) 4.11
F (d) 1.66
Me
263
1.92
1.99
1.98
1.98
1.00
3.05
f1 (ppm)


263
Me
O
N
O
F
Parameter Value
Title NAO-01-194-A.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 55.5
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-09-23T19:29:17
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1958.4
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
170.8
163.6
161.9
161.2
134.9
134.2
134.2
129.4
129.3
129.0
124.1
116.1
115.8
116.1
115.8
42.3
19.2
f1 (ppm)

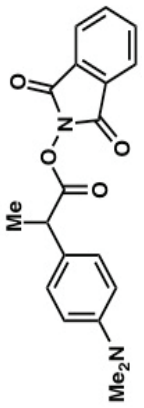
Parameter	Value
Title	NAO-1-194A
Origin	Varian
Solvent	"cdcl3"
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2017-01-09T22:18:30
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56468.7
Nucleus	19F
Acquired Size	64000
Spectral Size	131072



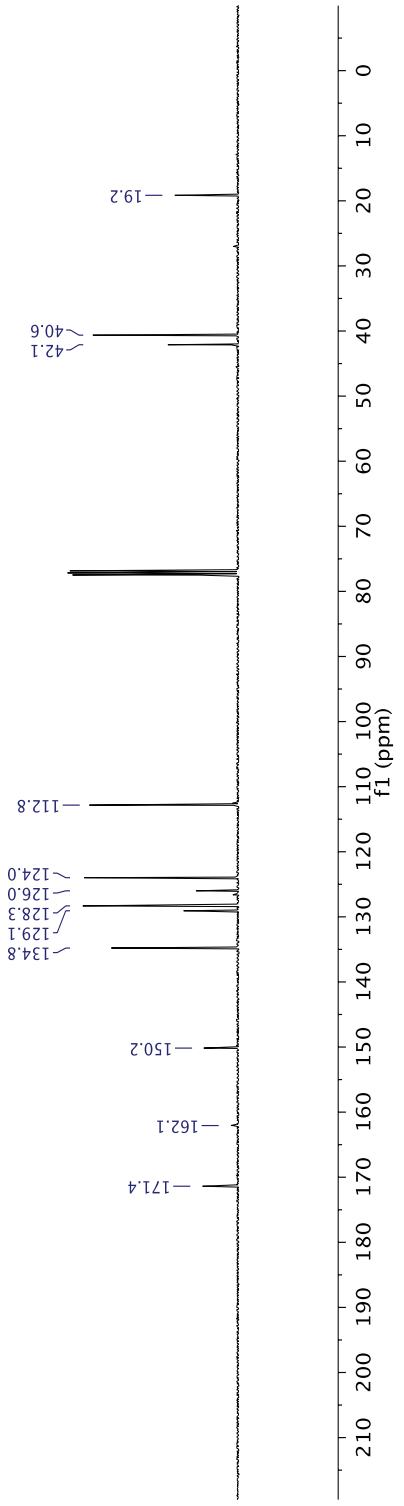
Parameter Value
Title NAO-1-194A-C6F6
Origin Varian
Solvent "cdcl3"
Temperature 25.0
Pulse Sequence s2pul
Number of Scans 16
Receiver Gain 30
Relaxation Delay 1.0000
Pulse Width 6.3333
Acquisition Time 0.9856
Acquisition Date 2017-01-09T22:35:50
Spectrometer Frequency 282.34
Spectral Width 64935.1
Lowest Frequency -56468.7
Nucleus 19F
Acquired Size 64000
Spectral Size 131072
A (tt)
-117.64
Me
263
with C_6F_6
1.00
-117.5 -117.6 -117.7 -117.8
f1 (ppm)
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

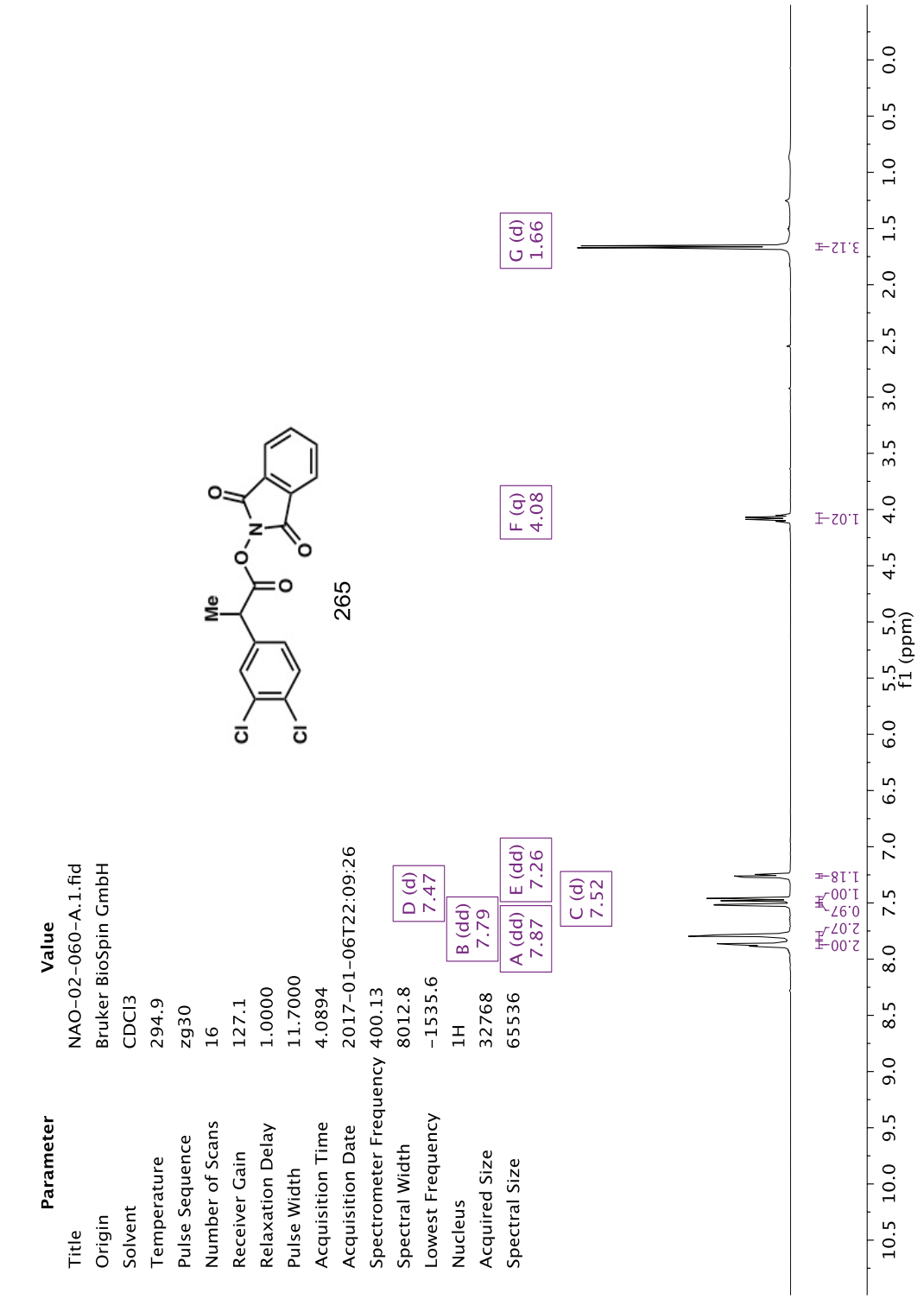

Parameter
Value
Title
NAO-02-087-A.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.0
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
78.7
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2017-01-06T23:07:53
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1535.6
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
264
Me
Me2N
A (dd) 7.85
B (dd) 7.76
C (d) 7.27
D (d) 6.75
E (q) 4.04
F (s) 2.95
G (d) 1.64
1.93
2.01
2.12
2.00
0.95
6.03
3.07
f1 (ppm)

Parameter	Value
Title	NAO-02-087-A.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	294.9
Pulse Sequence	zgpg30
Number of Scans	128
Receiver Gain	78.7
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2017-01-06T23:15:50
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1958.4
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

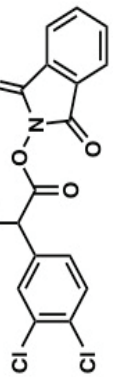


264

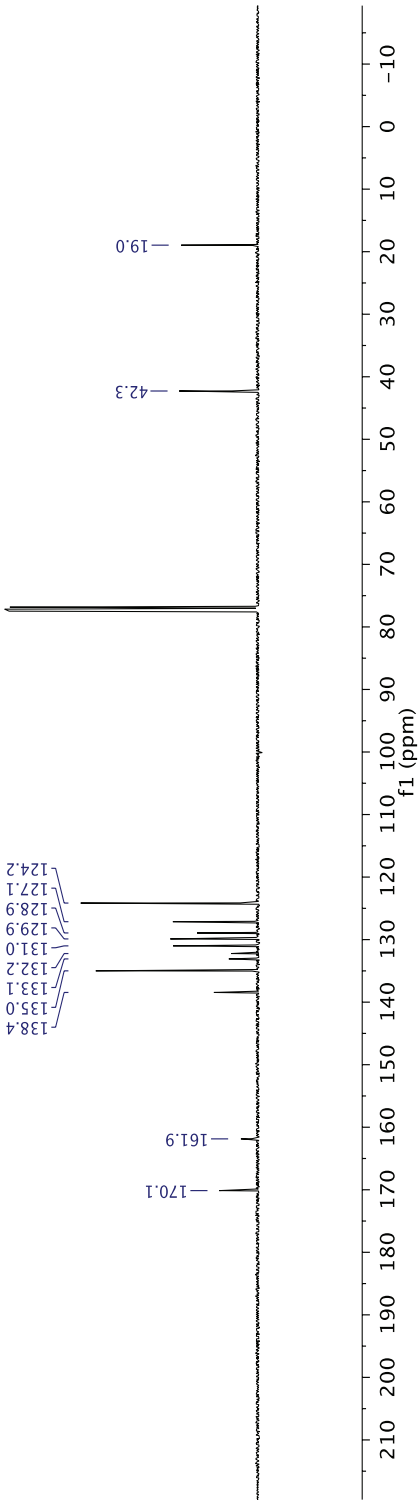


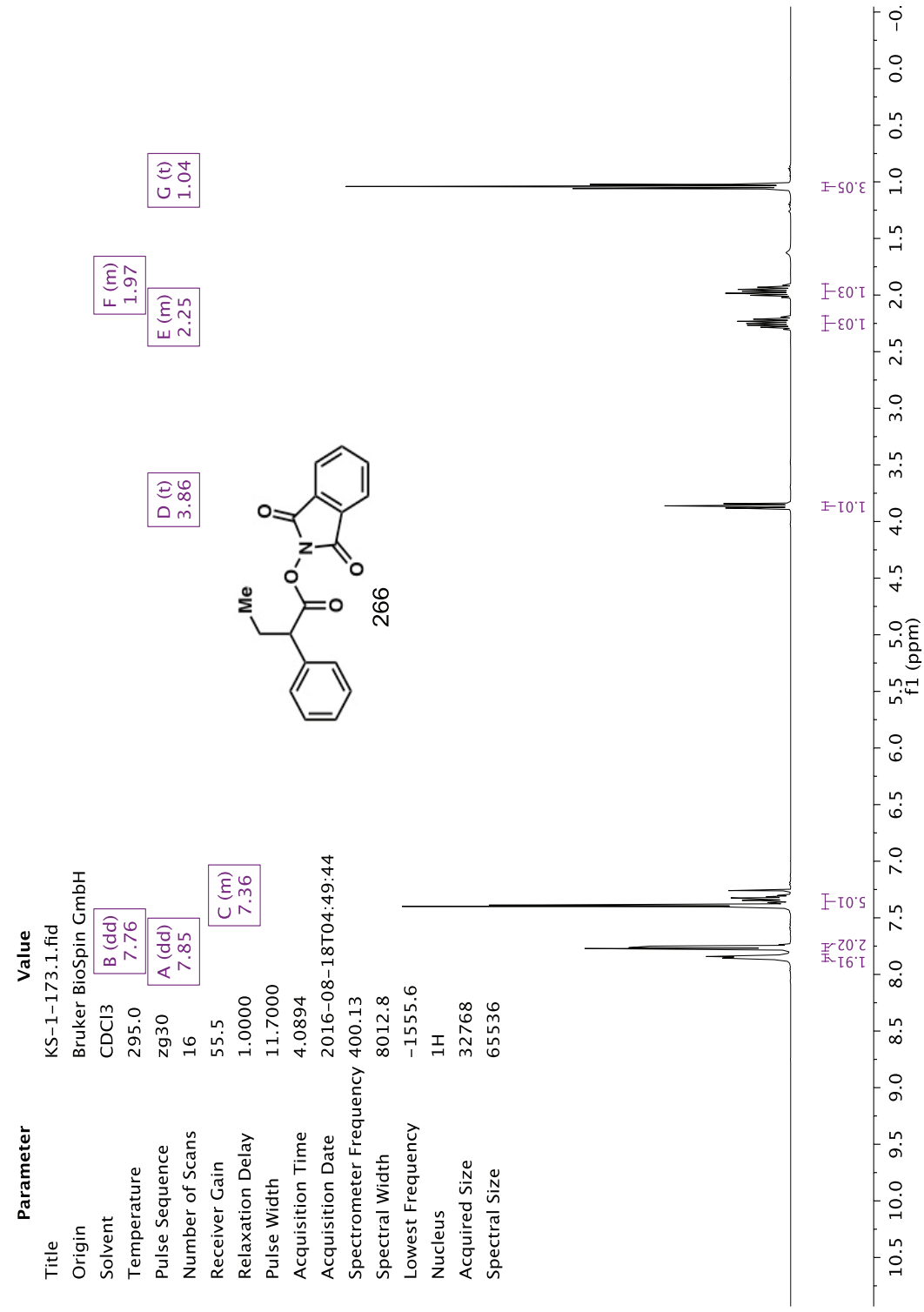

Parameter Value
Title NAO-02-060-A.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 127.1
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2017-01-06T22:09:26
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1535.6
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
Me
Cl
Cl
265
A (dd) 7.87
B (dd) 7.79
C (d) 7.52
D (d) 7.47
E (dd) 7.26
F (q) 4.08
G (d) 1.66
2.00
2.07
0.97
1.00
1.18
1.02
3.12
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

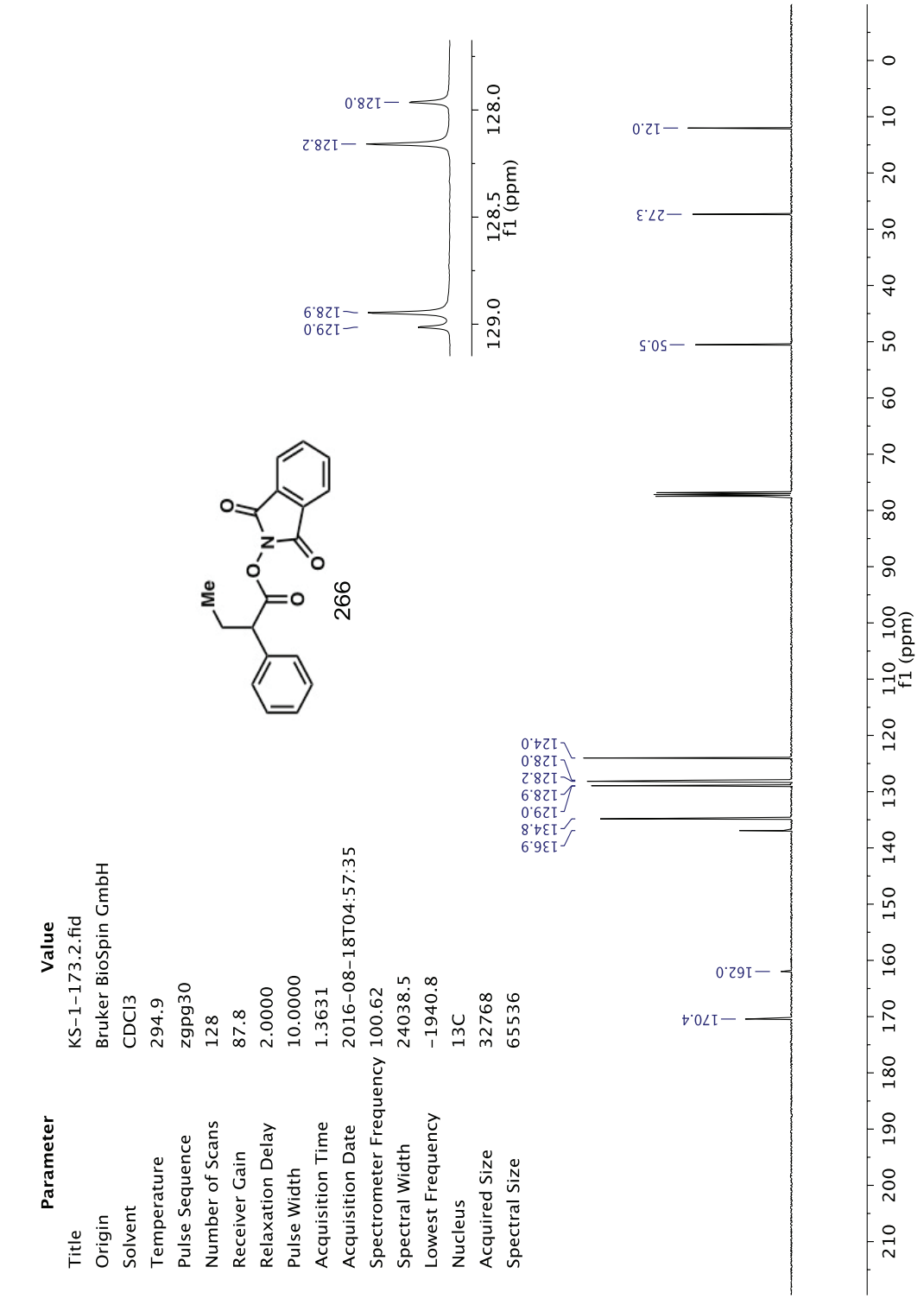
Parameter	Value
Title	NAO-02-060-A.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	294.9
Pulse Sequence	zgpg30
Number of Scans	128
Receiver Gain	64.2
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2017-01-06T22:17:23
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1958.4
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

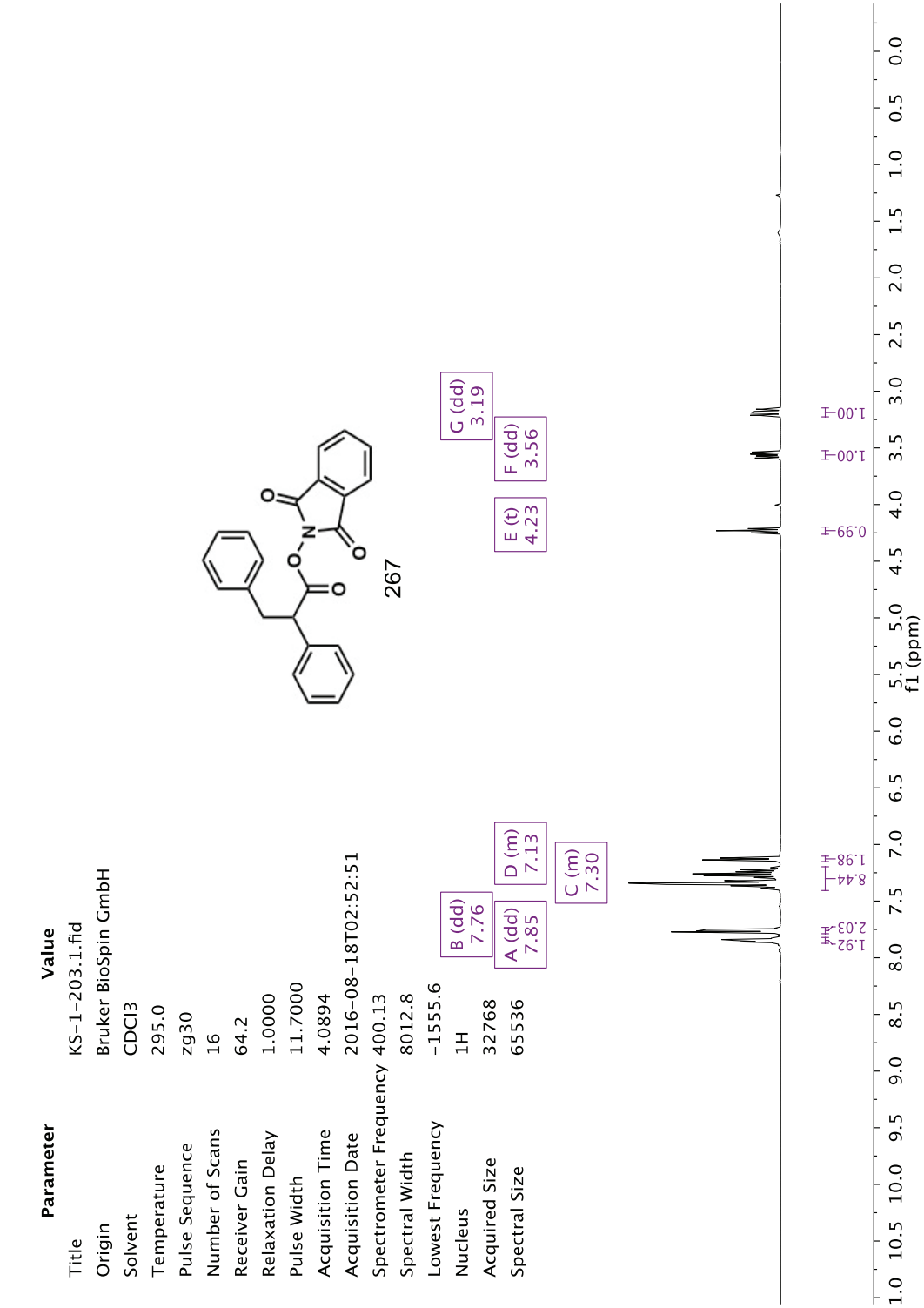


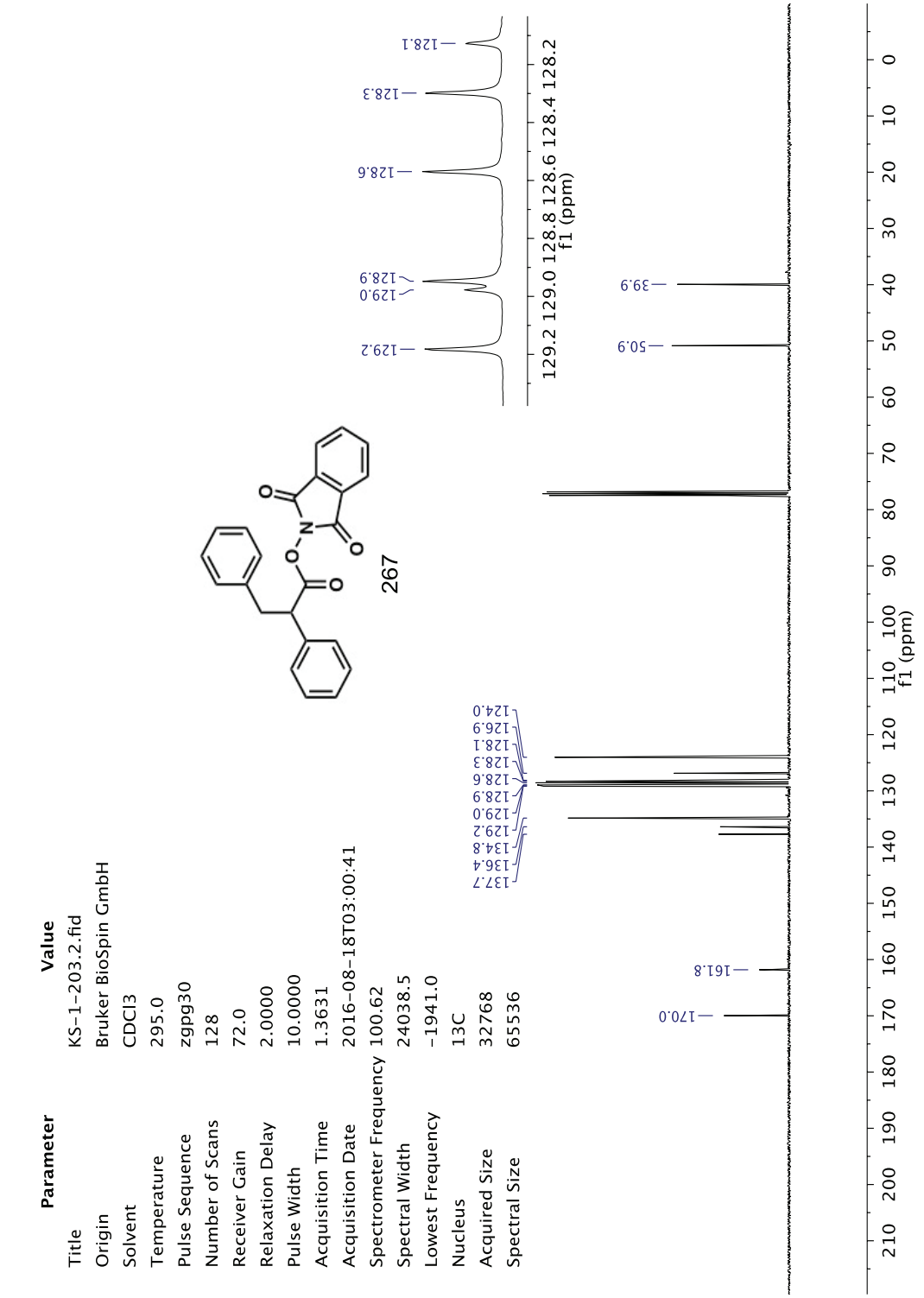
265

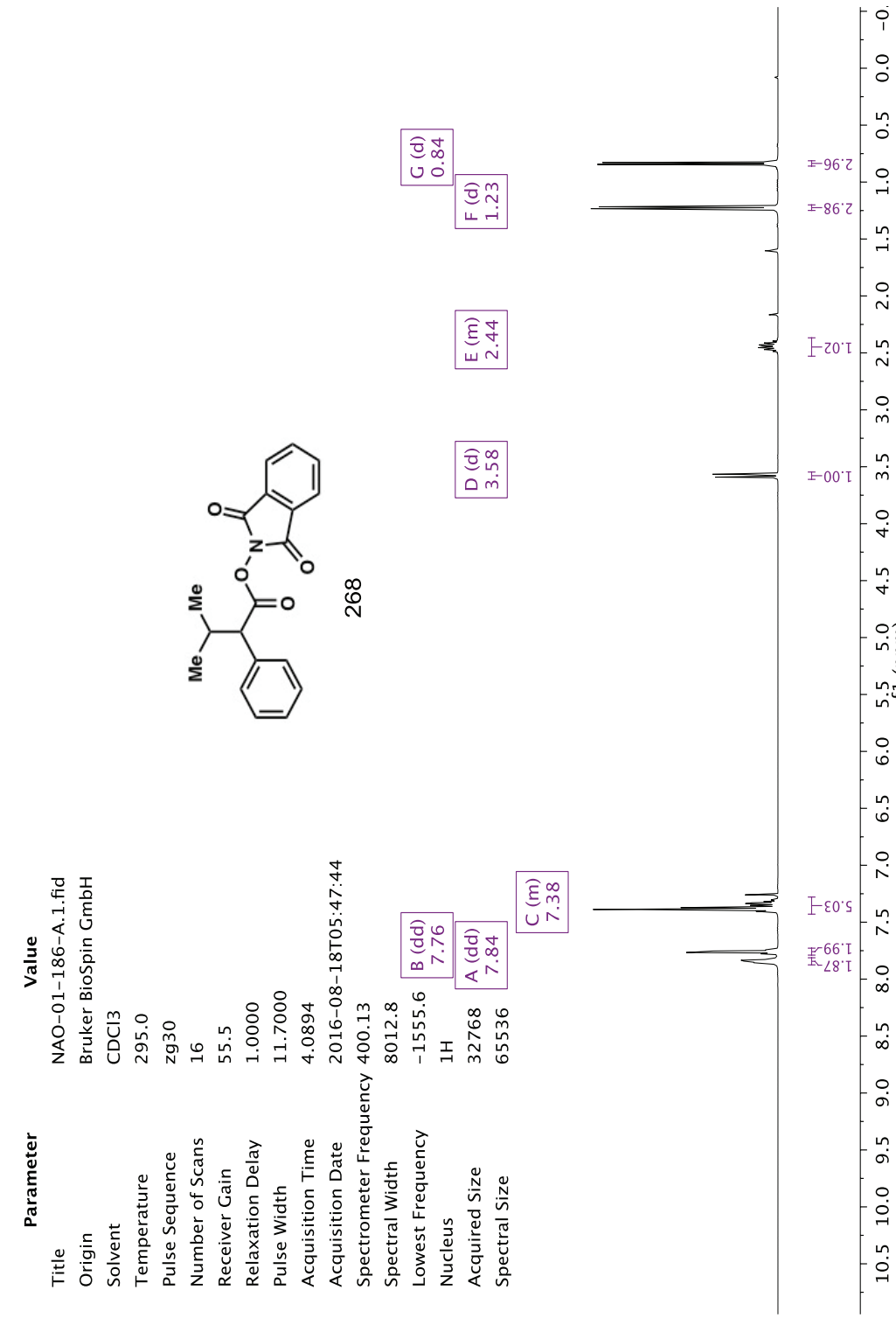


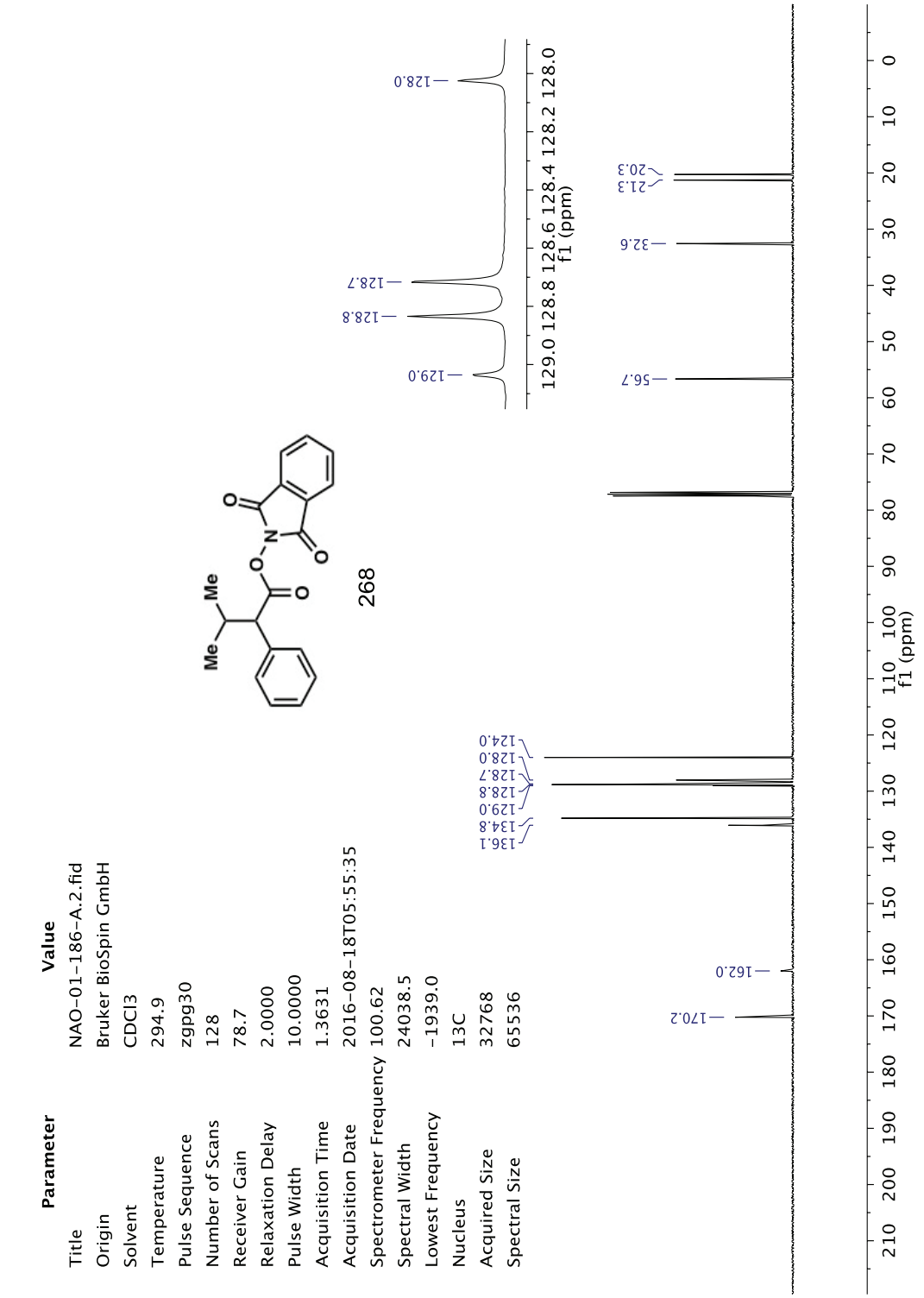

Parameter Value
Title KS-1-173.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 55.5
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2016-08-18T04:49:44
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1555.6
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
B (dd) 7.76
A (dd) 7.85
C (m) 7.36
D (t) 3.86
F (m) 1.97
E (m) 2.25
G (t) 1.04
Me
266
1.91
2.02
5.01
1.01
1.03
1.03
3.05
f1 (ppm)

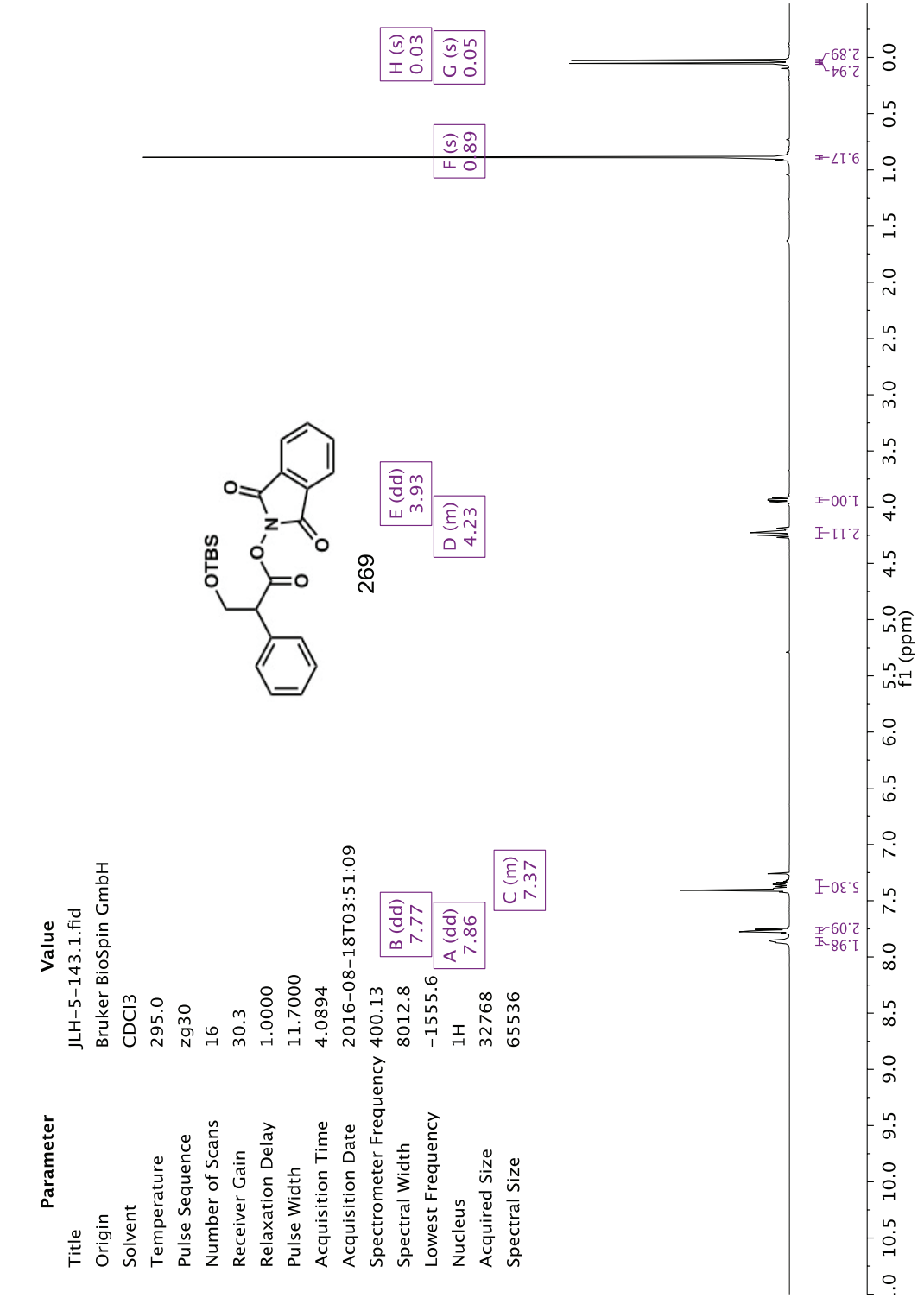

Parameter Value
Title KS-1-173.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 87.8
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-08-18T04:57:35
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1940.8
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
266
170.4
162.0
136.9
134.8
129.0
128.9
128.2
128.0
124.0
50.5
27.3
12.0
f1 (ppm)

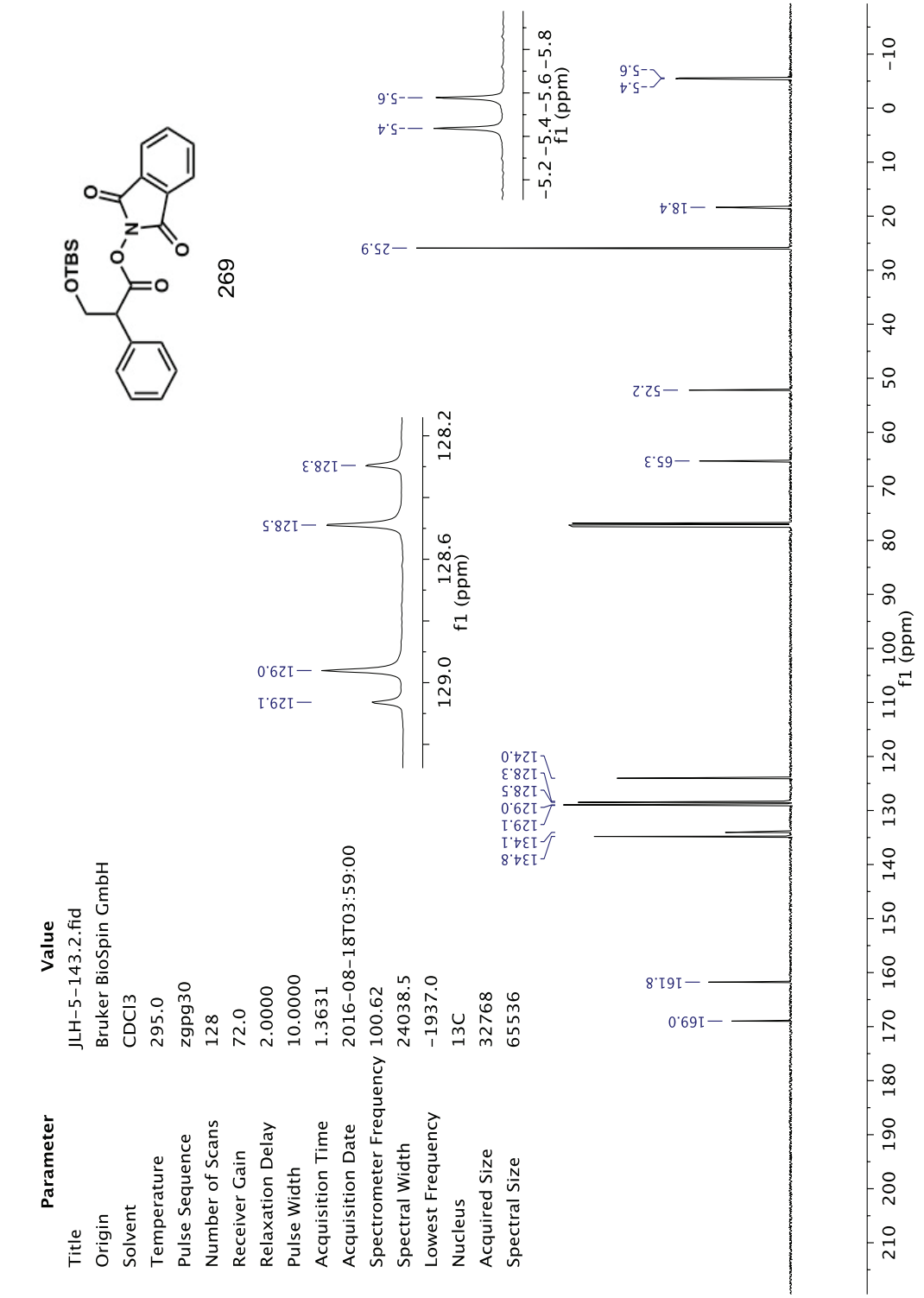

Parameter Value
Title KS-1-203.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 64.2
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2016-08-18T02:52:51
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1555.6
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
267
A (dd) 7.85
B (dd) 7.76
C (m) 7.30
D (m) 7.13
E (t) 4.23
F (dd) 3.56
G (dd) 3.19
1.92
2.03
8.44
1.98
0.99
1.00
1.00
f1 (ppm)

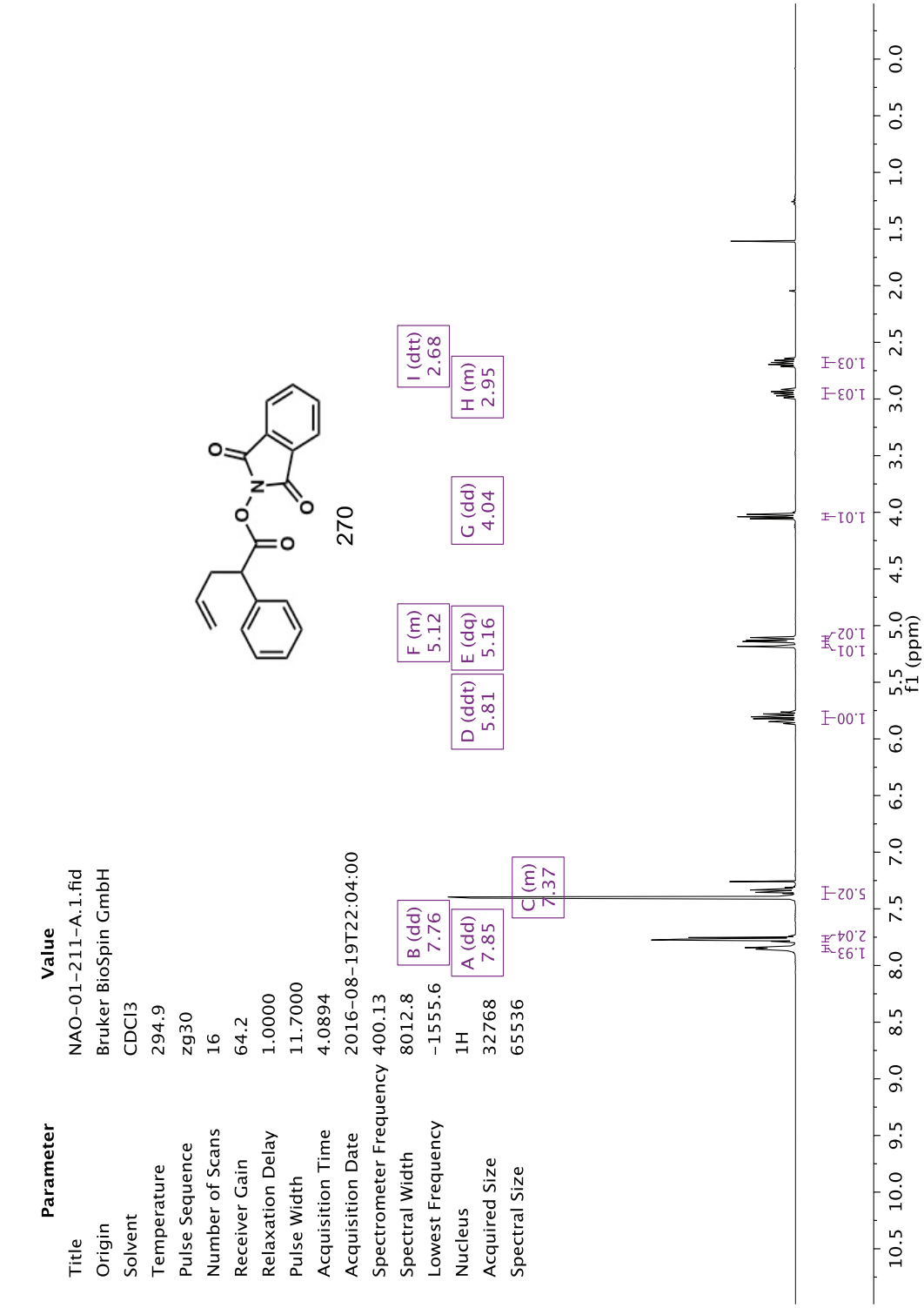

Parameter Value
Title KS-1-203.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-08-18T03:00:41
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1941.0
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
267
170.0
161.8
137.7
136.4
134.8
129.2
129.0
128.9
128.6
128.3
128.1
126.9
124.0
129.2
129.0
128.9
128.6
128.3
128.1
50.9
39.9
f1 (ppm)
129.2 129.0 128.8 128.6 128.4 128.2
f1 (ppm)

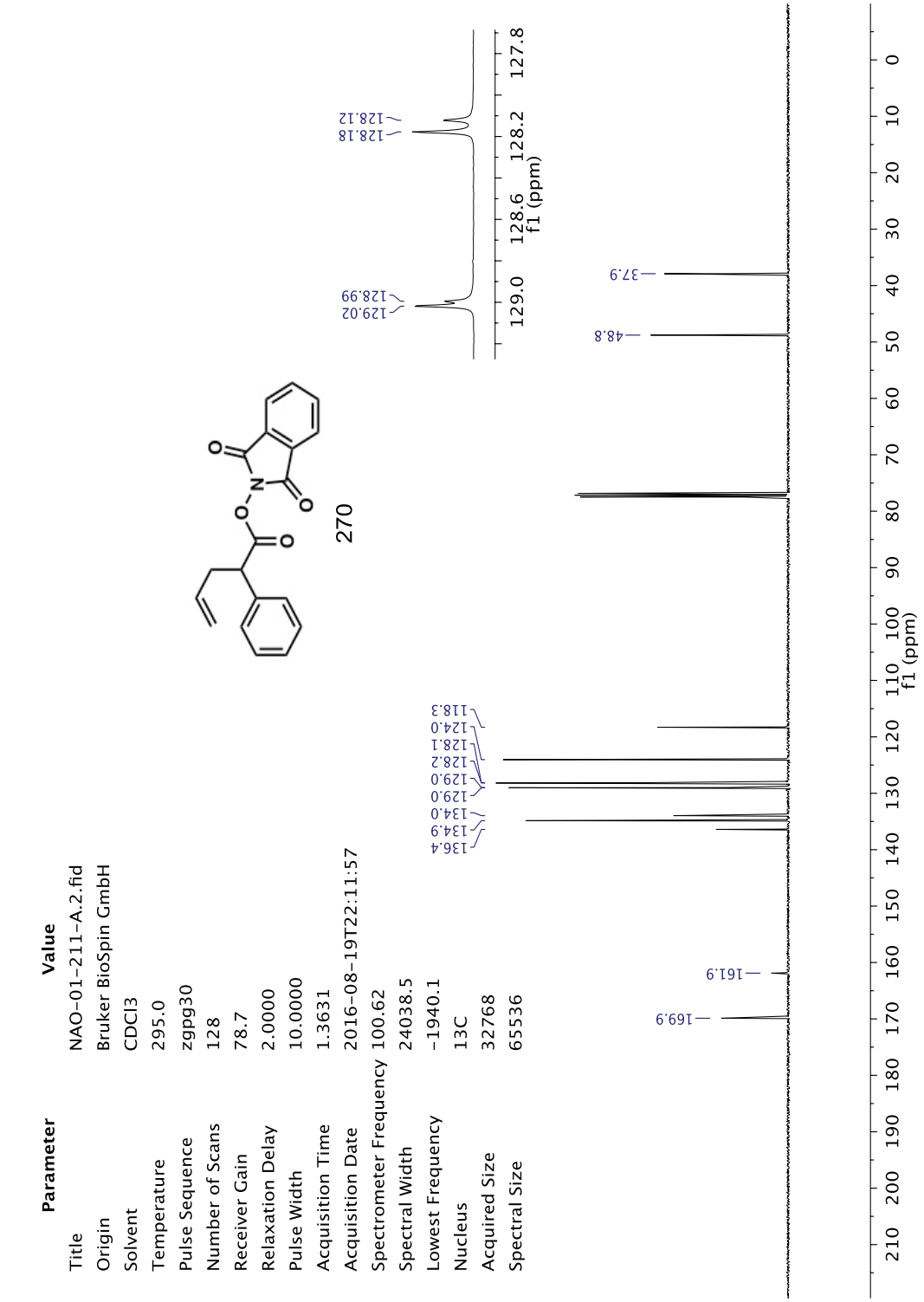

Parameter Value
Title NAO-01-186-A.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 55.5
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2016-08-18T05:47:44
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1555.6
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
268
A (dd) 7.84
B (dd) 7.76
C (m) 7.38
D (d) 3.58
E (m) 2.44
F (d) 1.23
G (d) 0.84
1.87
1.99
5.03
1.00
1.02
2.98
2.96
f1 (ppm)

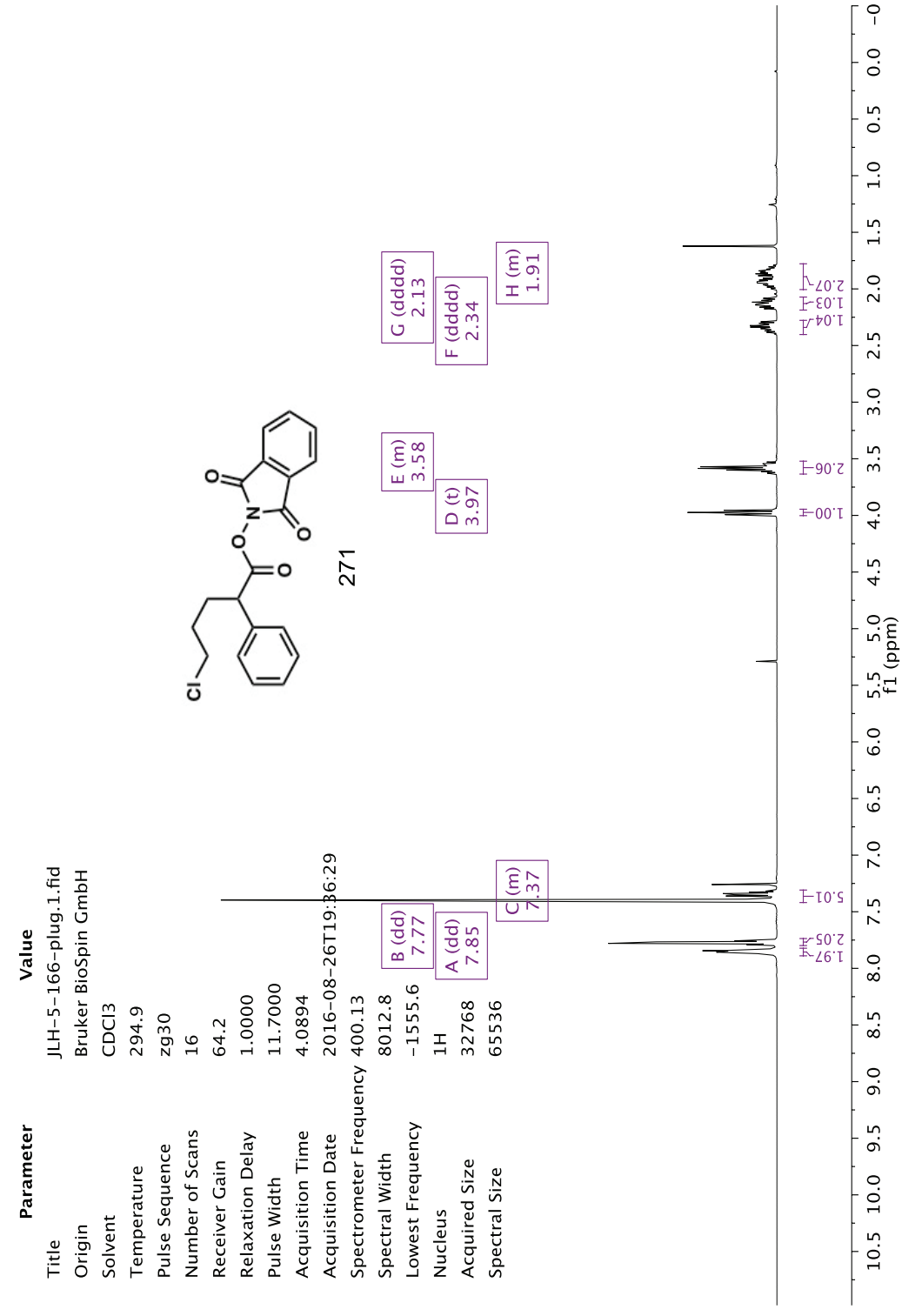

Parameter Value
Title NAO-01-186-A.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 78.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-08-18T05:55:35
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1939.0
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
Me
O
O
N
O
O
O
268
170.2
162.0
136.1
134.8
129.0
128.8
128.7
128.0
124.0
56.7
32.6
21.3
20.3
129.0
128.8
128.7
128.0
129.0 128.8 128.6 128.4 128.2 128.0
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

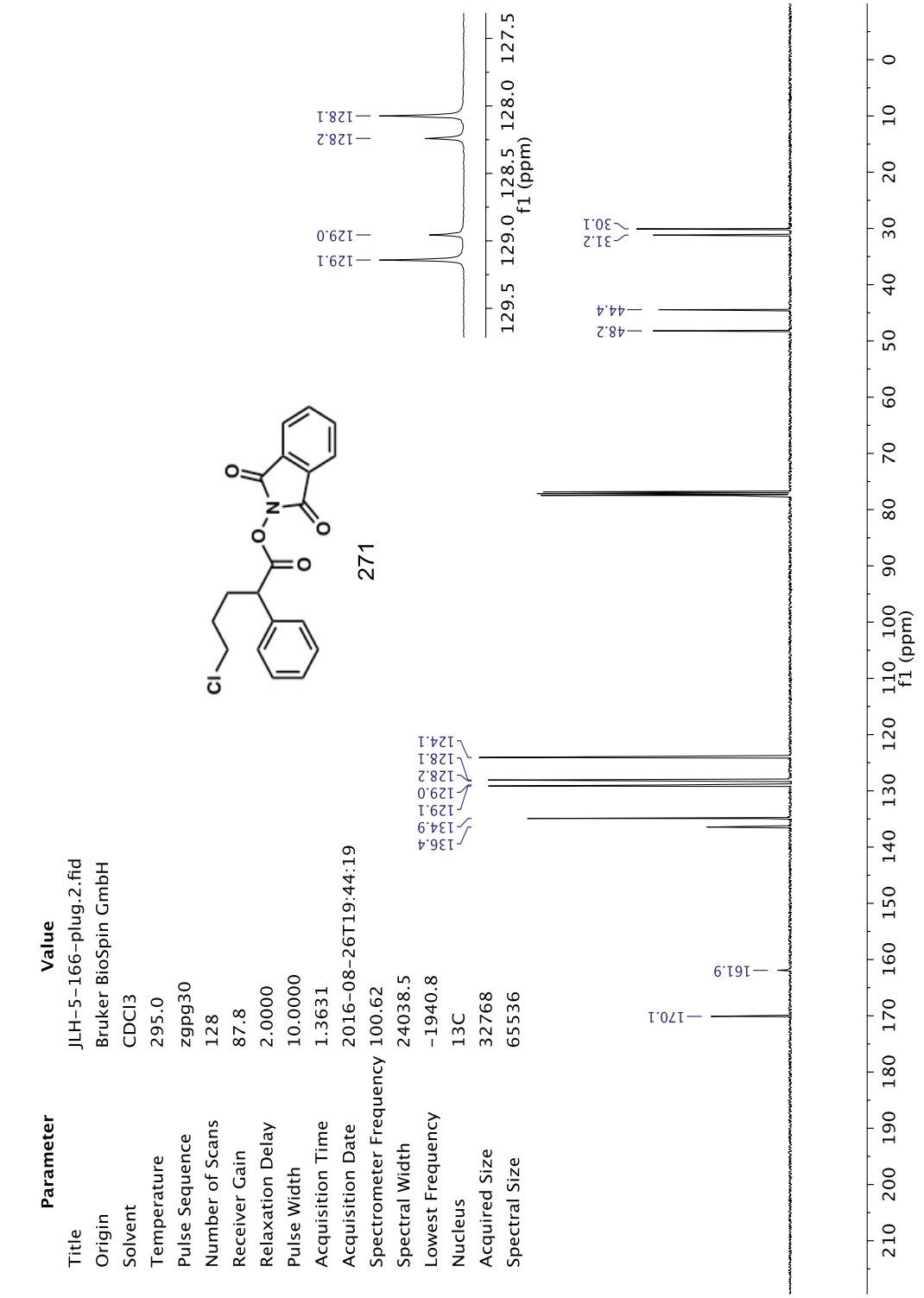

Parameter Value
Title JLH-5-143.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 30.3
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2016-08-18T03:51:09
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1555.6
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
OTBS
269
A (dd) 7.86
B (dd) 7.77
C (m) 7.37
D (m) 4.23
E (dd) 3.93
F (s) 0.89
G (s) 0.05
H (s) 0.03
1.98
2.09
5.30
2.11
1.00
9.17
2.94
2.89
f1 (ppm)

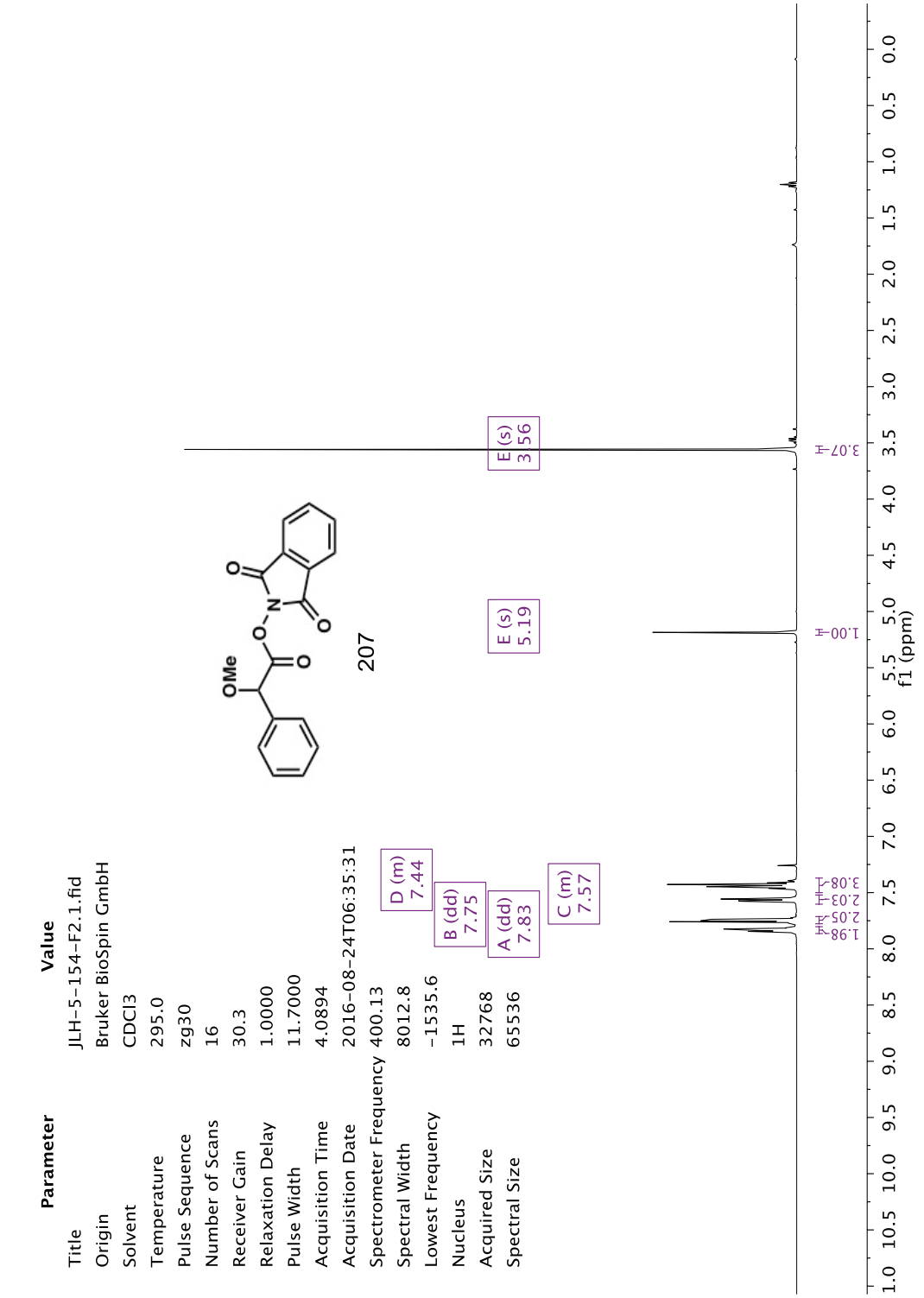

OTBS
O
N
O
O
O
O
269
Parameter Value
Title JLH-5-143.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-08-18T03:59:00
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1937.0
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
169.0
161.8
134.8
134.1
129.1
129.0
128.5
128.3
124.0
25.9
18.4
-5.4
-5.6
52.2
65.3
129.1
129.0
128.5
128.3
129.0
128.6
128.2
f1 (ppm)
-5.2 -5.4 -5.6 -5.8
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

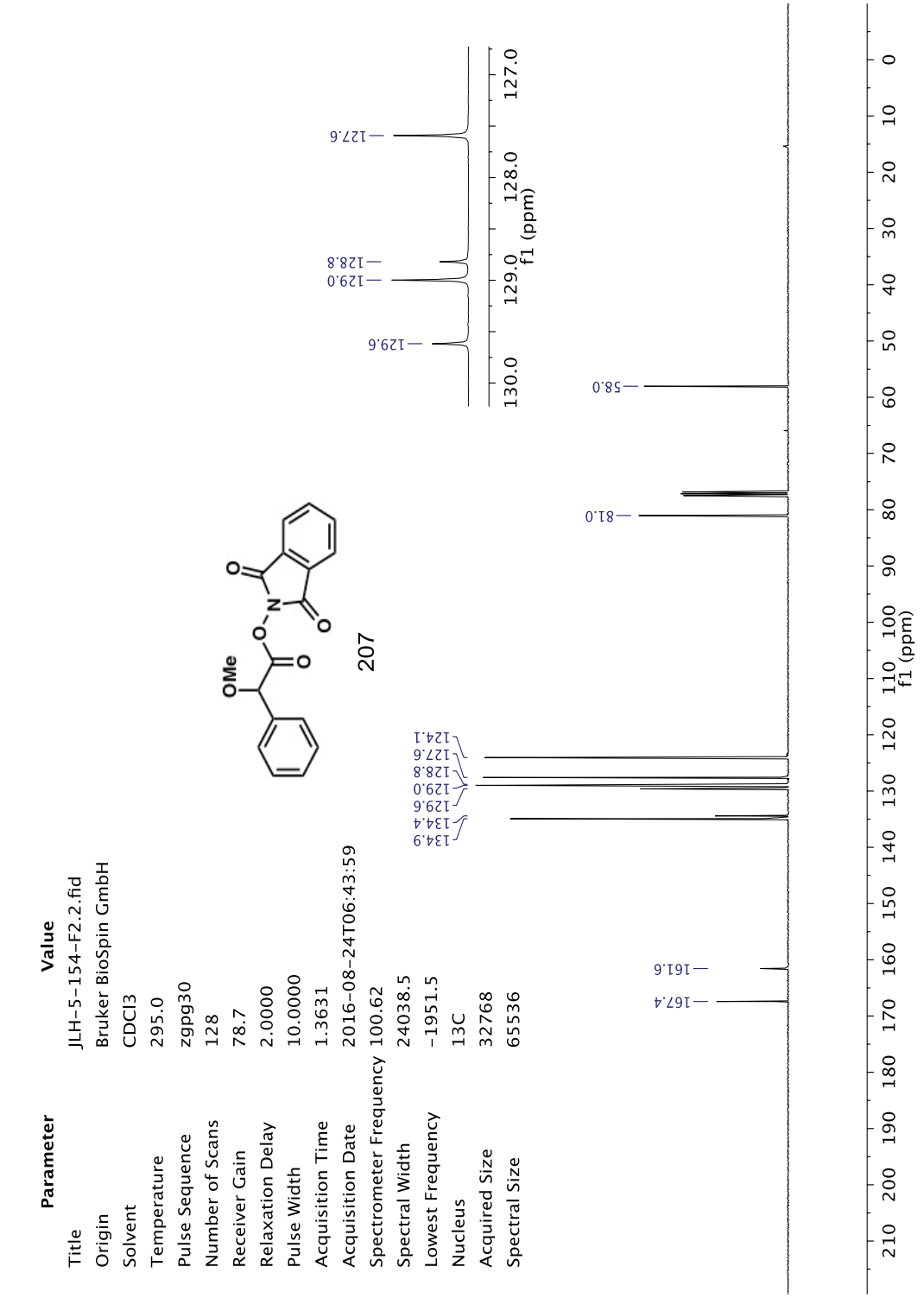

Parameter Value
Title NAO-01-211-A.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 64.2
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2016-08-19T22:04:00
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1555.6
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
270
A (dd) 7.85
B (dd) 7.76
C (m) 7.37
D (ddt) 5.81
E (dq) 5.16
F (m) 5.12
G (dd) 4.04
H (m) 2.95
I (dtt) 2.68
1.93
2.04
5.02
1.00
1.01
1.02
1.01
1.03
1.03
f1 (ppm)

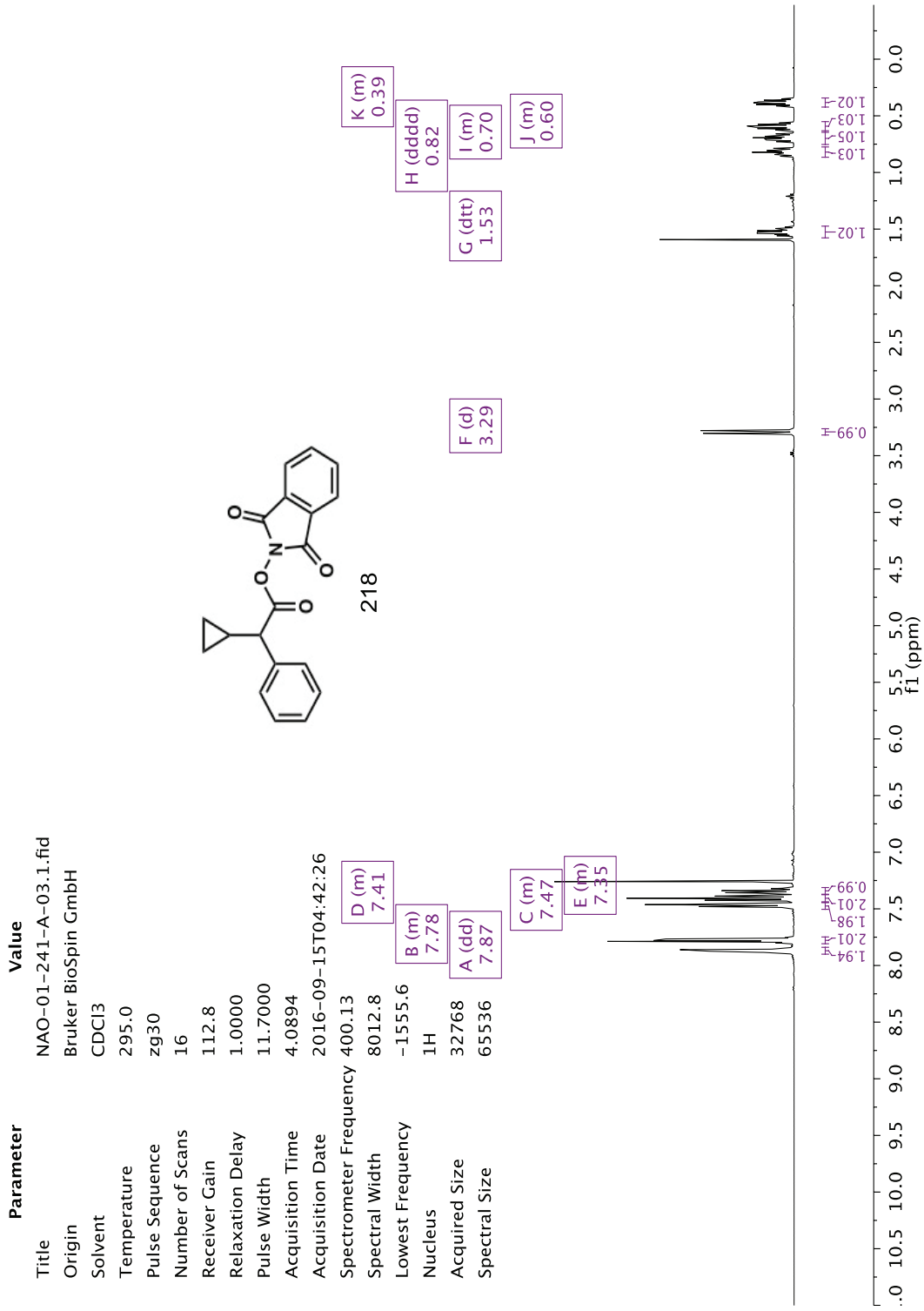

Parameter Value
Title NAO-01-211-A.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 78.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-08-19T22:11:57
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1940.1
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
270
169.9
161.9
136.4
134.9
134.0
129.0
129.0
128.2
128.1
124.0
118.3
129.02
128.99
128.18
128.12
48.8
37.9
f1 (ppm)
f1 (ppm)

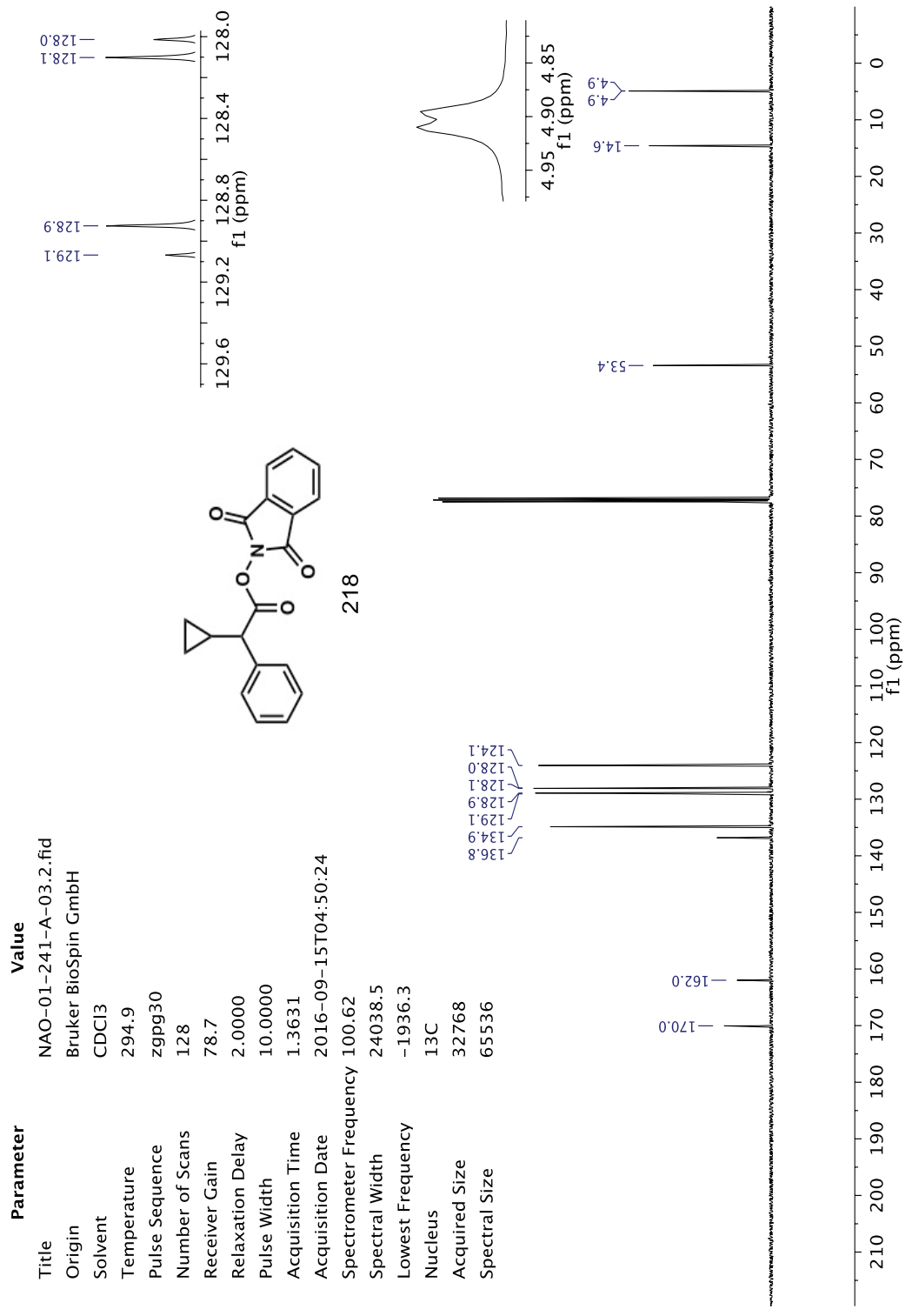

Parameter Value
Title JLH-5-166-plug.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 64.2
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2016-08-26T19:36:29
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1555.6
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
271
A (dd) 7.85
B (dd) 7.77
C (m) 7.37
D (t) 3.97
E (m) 3.58
F (dddd) 2.34
G (dddd) 2.13
H (m) 1.91
1.97
2.05
5.01
1.00
2.06
1.04
1.03
2.07
f1 (ppm)

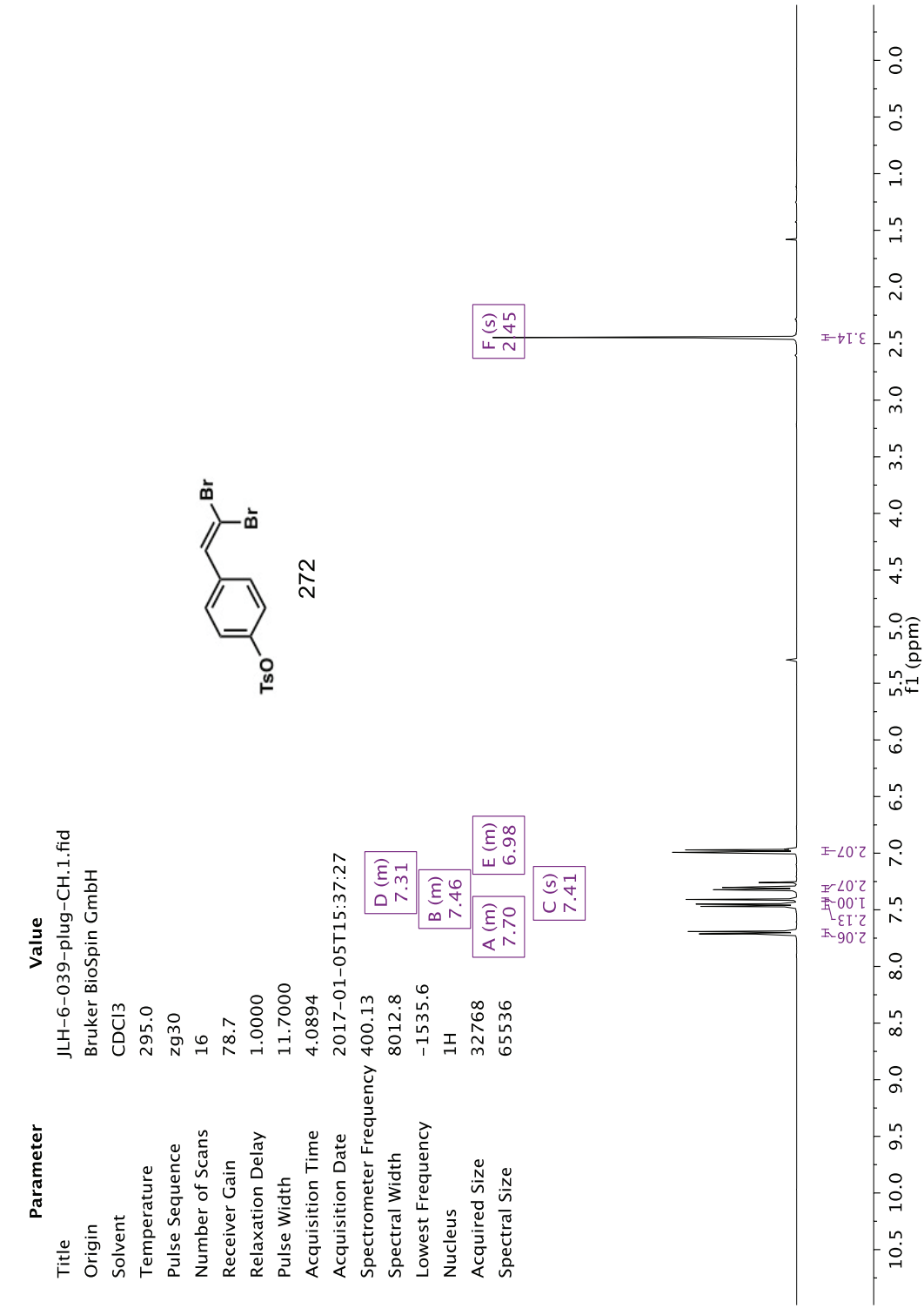

Parameter
Value
Title
JLH-5-166-plug.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.0
Pulse Sequence
zgpg30
Number of Scans
128
Receiver Gain
87.8
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2016-08-26T19:44:19
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1940.8
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
271
170.1
161.9
136.4
134.9
129.1
129.0
128.2
128.1
124.1
48.2
44.4
31.2
30.1
129.1
129.0
128.2
128.1
129.5 129.0 128.5 128.0 127.5
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

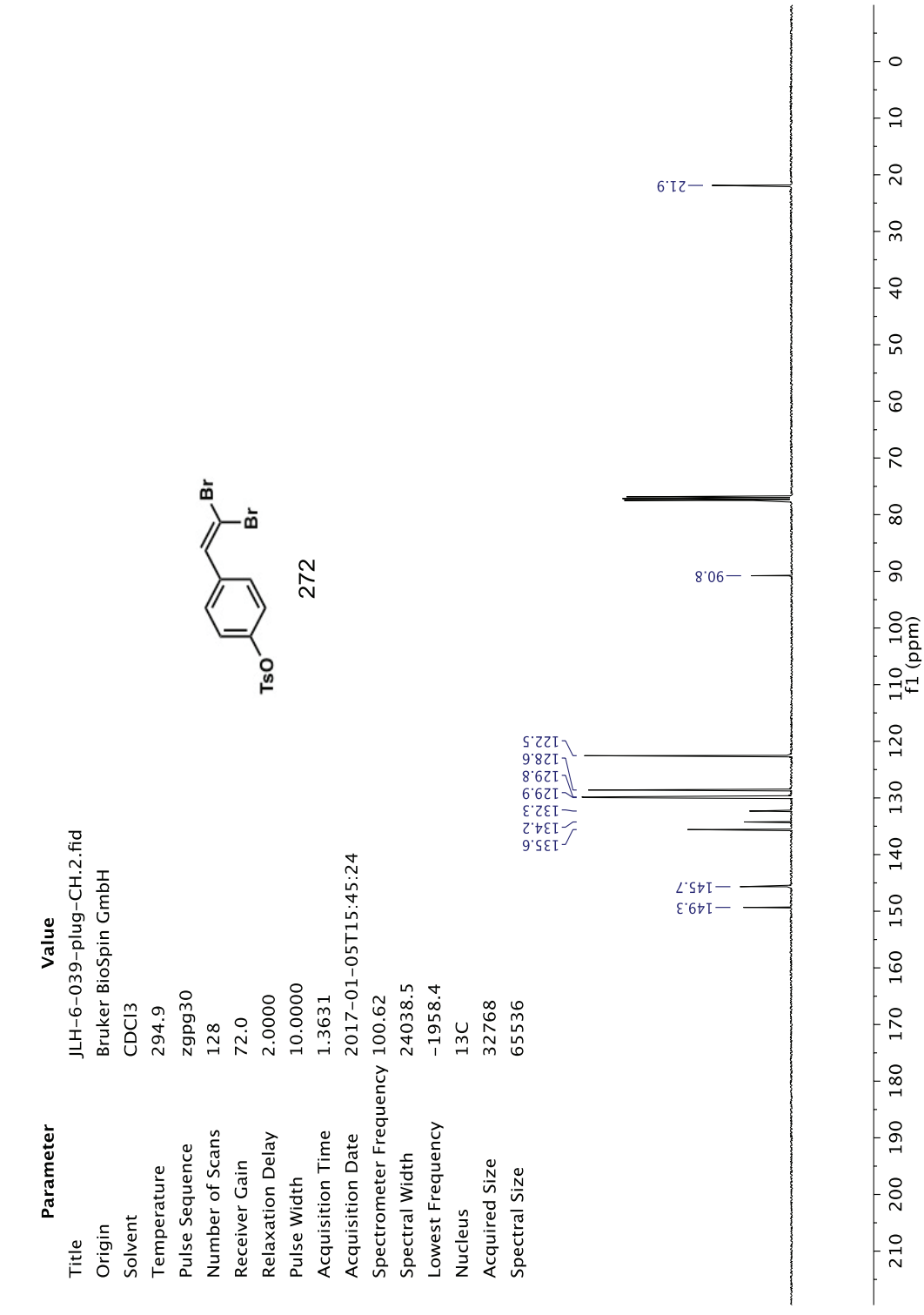

Parameter
Value
Title
JLH-5-154-F2.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.0
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
30.3
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2016-08-24T06:35:31
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1535.6
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
OMe
207
A (dd) 7.83
B (dd) 7.75
C (m) 7.57
D (m) 7.44
E (s) 5.19
E (s) 3.56
1.98
2.05
3.08
1.00
3.07
f1 (ppm)


Parameter
Value
Title JLH-5-154-F2.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 78.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-08-24T06:43:59
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1951.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OMe
207
167.4
161.6
134.9
134.4
129.6
129.0
128.8
127.6
124.1
81.0
58.0
f1 (ppm)

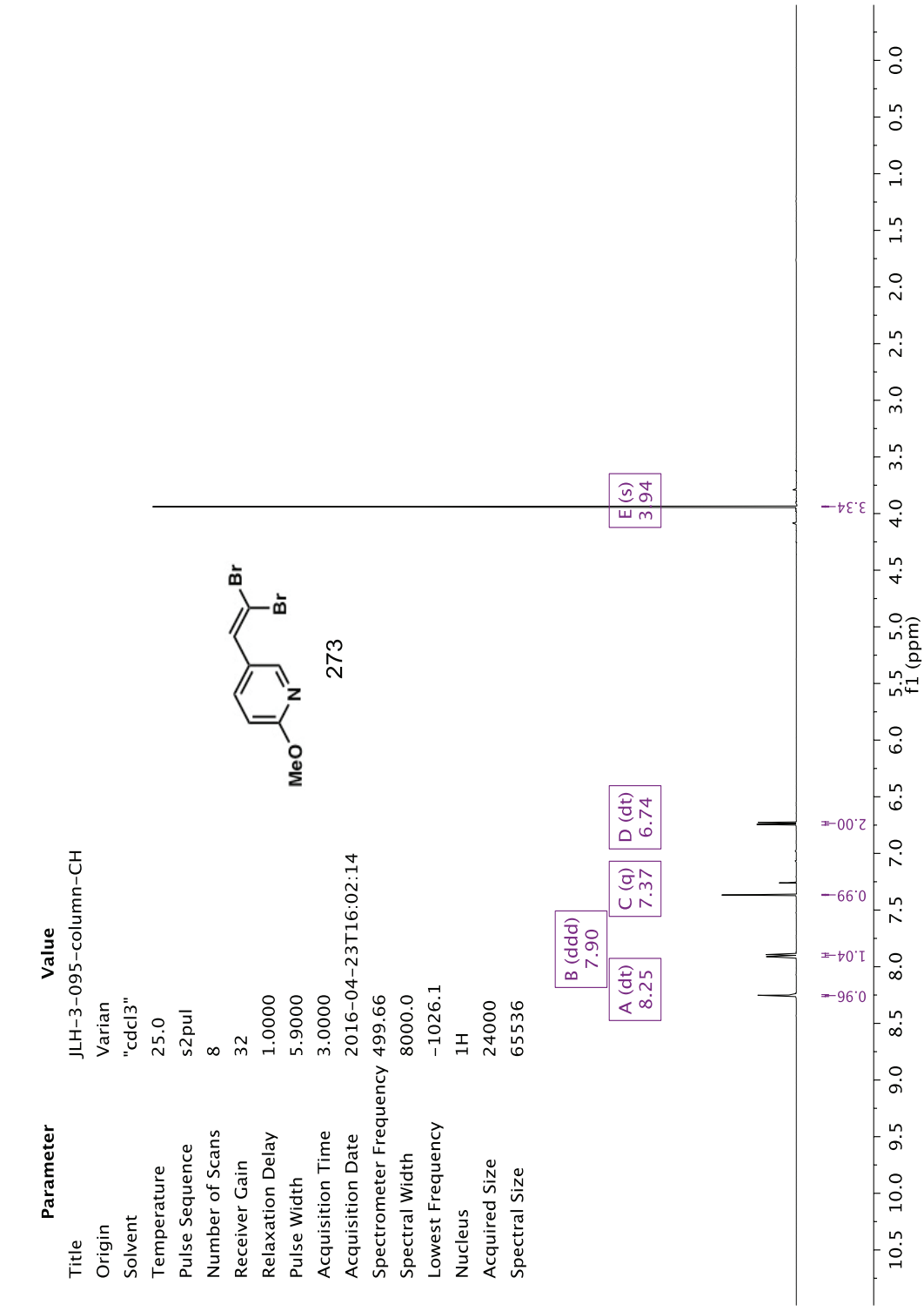

Parameter Value
Title NAO-01-241-A-03.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 112.8
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2016-09-15T04:42:26
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1555.6
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
218
A (dd) 7.87
B (m) 7.78
C (m) 7.47
D (m) 7.41
E (m) 7.35
F (d) 3.29
G (dtt) 1.53
H (dddd) 0.82
I (m) 0.70
J (m) 0.60
K (m) 0.39
1.94
2.01
1.98
2.01
0.99
0.99
1.02
1.03
1.05
1.03
1.02
f1 (ppm)

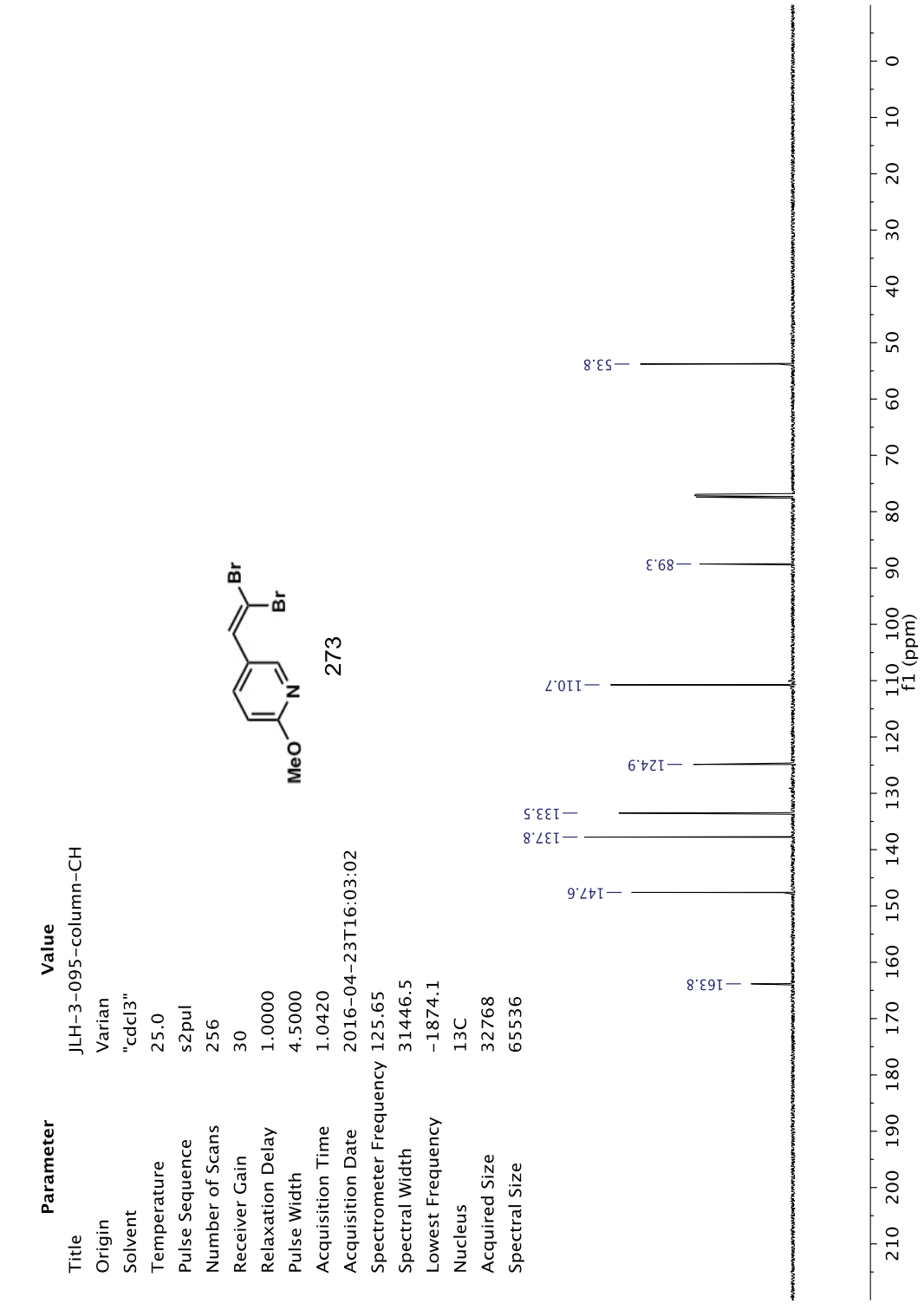

Parameter
Value
Title
NAO-01-241-A-03.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zgpg30
Number of Scans
128
Receiver Gain
78.7
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2016-09-15T04:50:24
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1936.3
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
218
170.0
162.0
136.8
134.9
129.1
128.9
128.1
128.0
124.1
53.4
14.6
4.9
4.9
129.1
128.9
128.1
128.0
f1 (ppm)
4.95 4.90 4.85
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

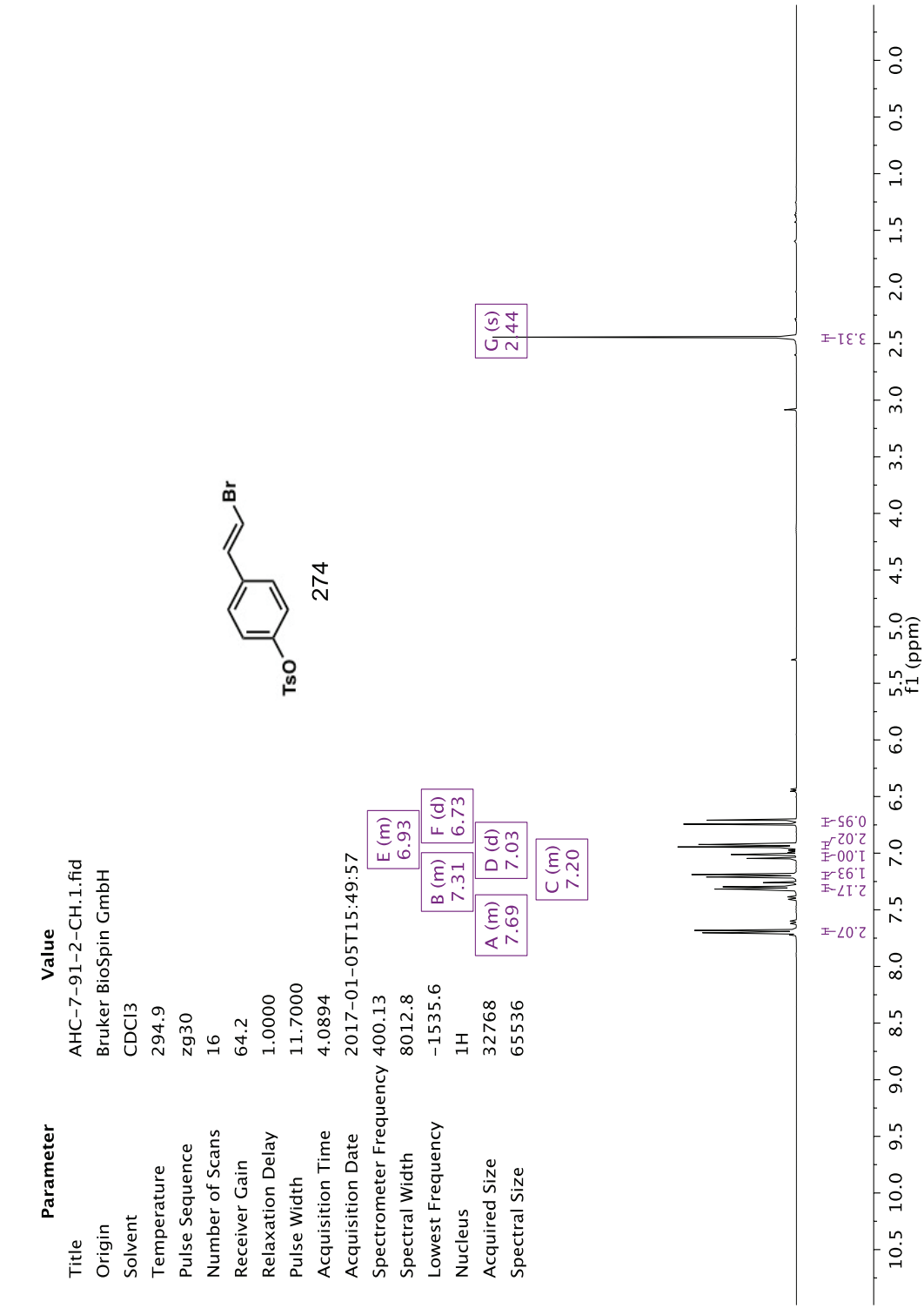

Parameter
Value
Title
JLH-6-039-plug-CH.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.0
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
78.7
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2017-01-05T15:37:27
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1535.6
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
Br
Br
TsO
272
A (m) 7.70
B (m) 7.46
C (s) 7.41
D (m) 7.31
E (m) 6.98
F (s) 2.45
2.06
2.13
1.00
2.07
2.07
3.14
f1 (ppm)

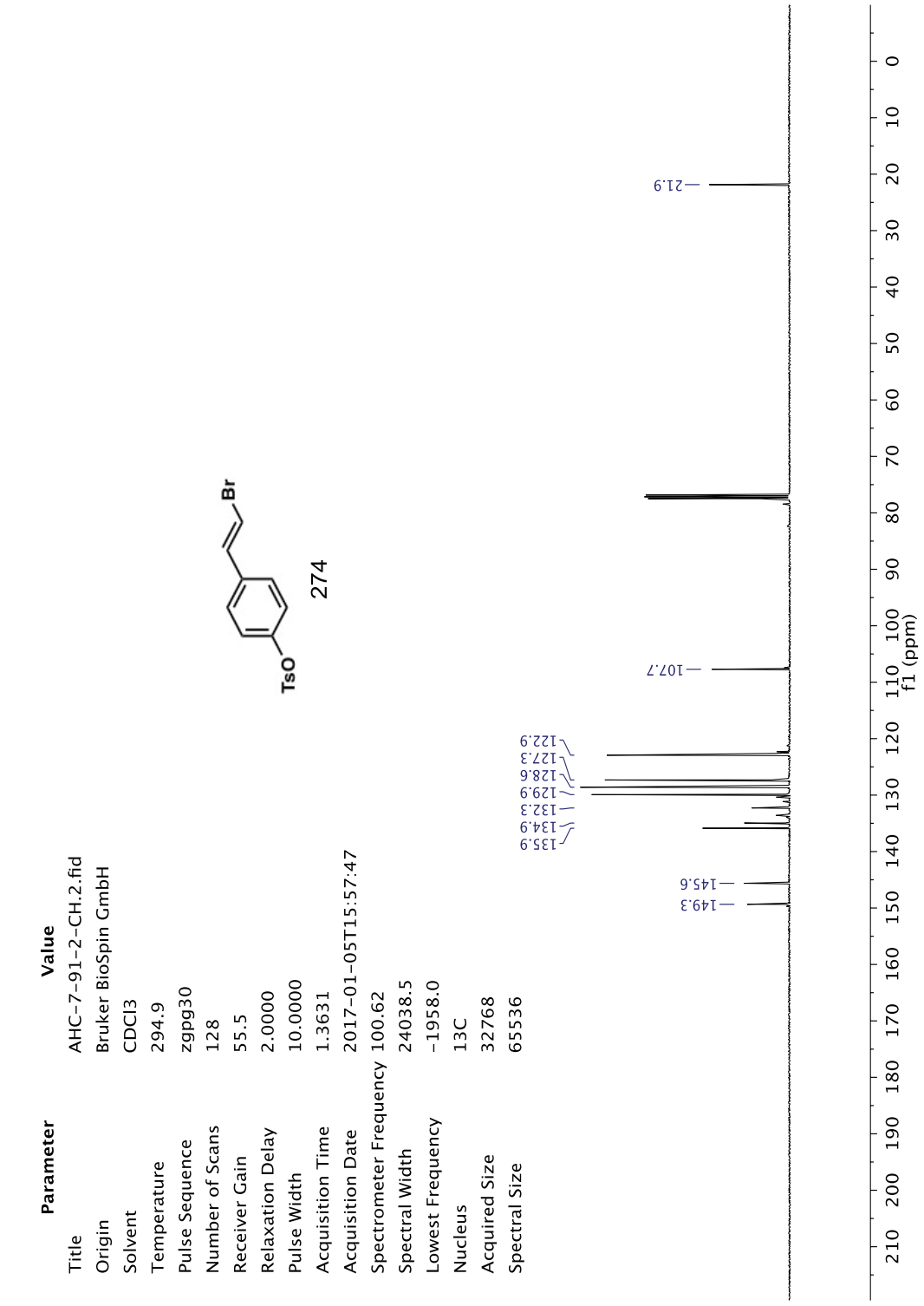


Parameter	Value
Title	JLH-6-039-plug-CH.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	294.9
Pulse Sequence	zgpg30
Number of Scans	128
Receiver Gain	72.0
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2017-01-05T15:45:24
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1958.4
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

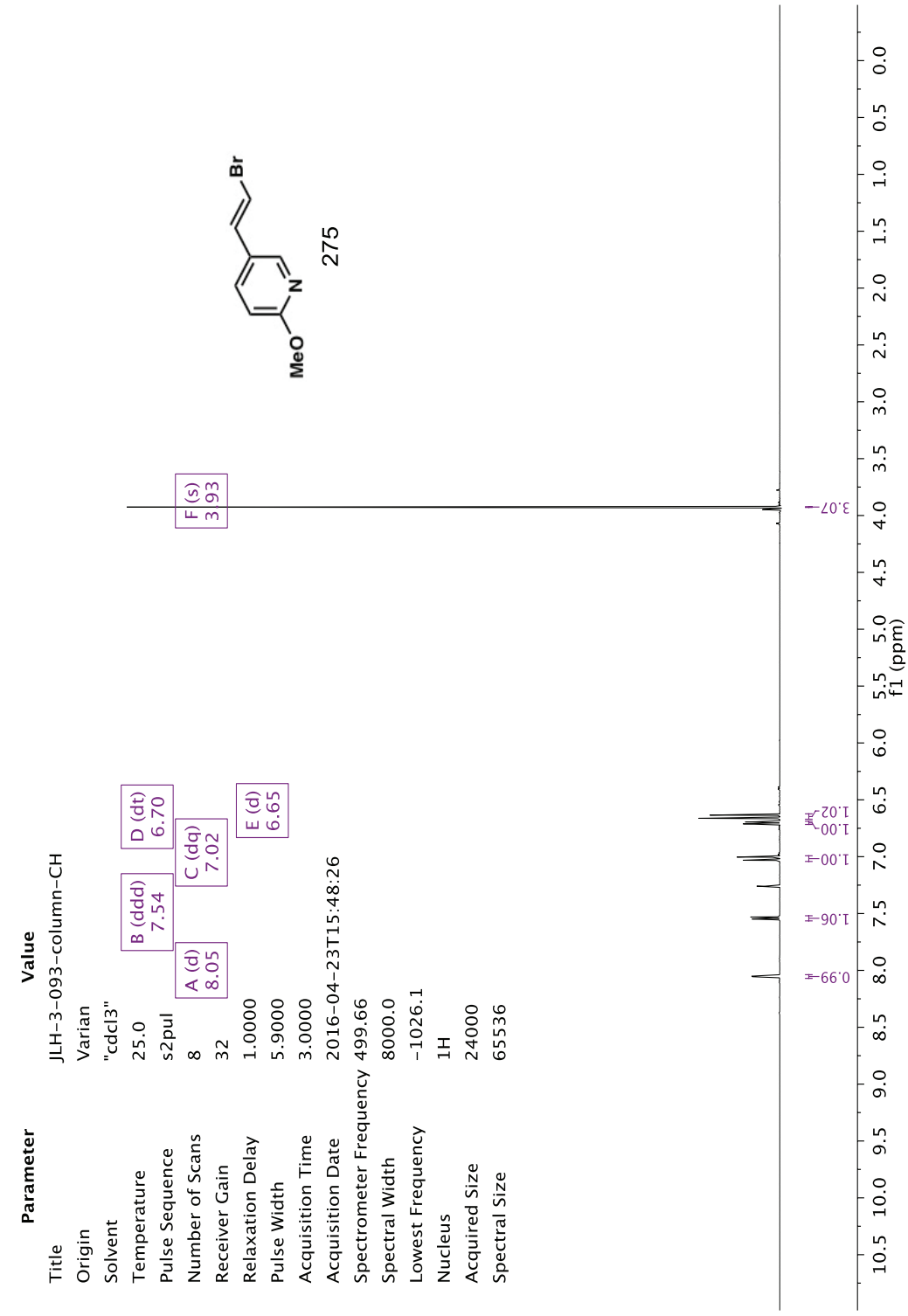

Parameter
Value
Title
JLH-3-095-column-CH
Origin
Varian
Solvent
"cdcl3"
Temperature
25.0
Pulse Sequence
s2pul
Number of Scans
8
Receiver Gain
32
Relaxation Delay
1.0000
Pulse Width
5.9000
Acquisition Time
3.0000
Acquisition Date
2016-04-23T16:02:14
Spectrometer Frequency
499.66
Spectral Width
8000.0
Lowest Frequency
-1026.1
Nucleus
1H
Acquired Size
24000
Spectral Size
65536
Br
Br
MeO
N
273
B (ddd)
7.90
A (dt)
8.25
C (q)
7.37
D (dt)
6.74
E (s)
3.94
0.96
1.04
0.99
2.00
3.34
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

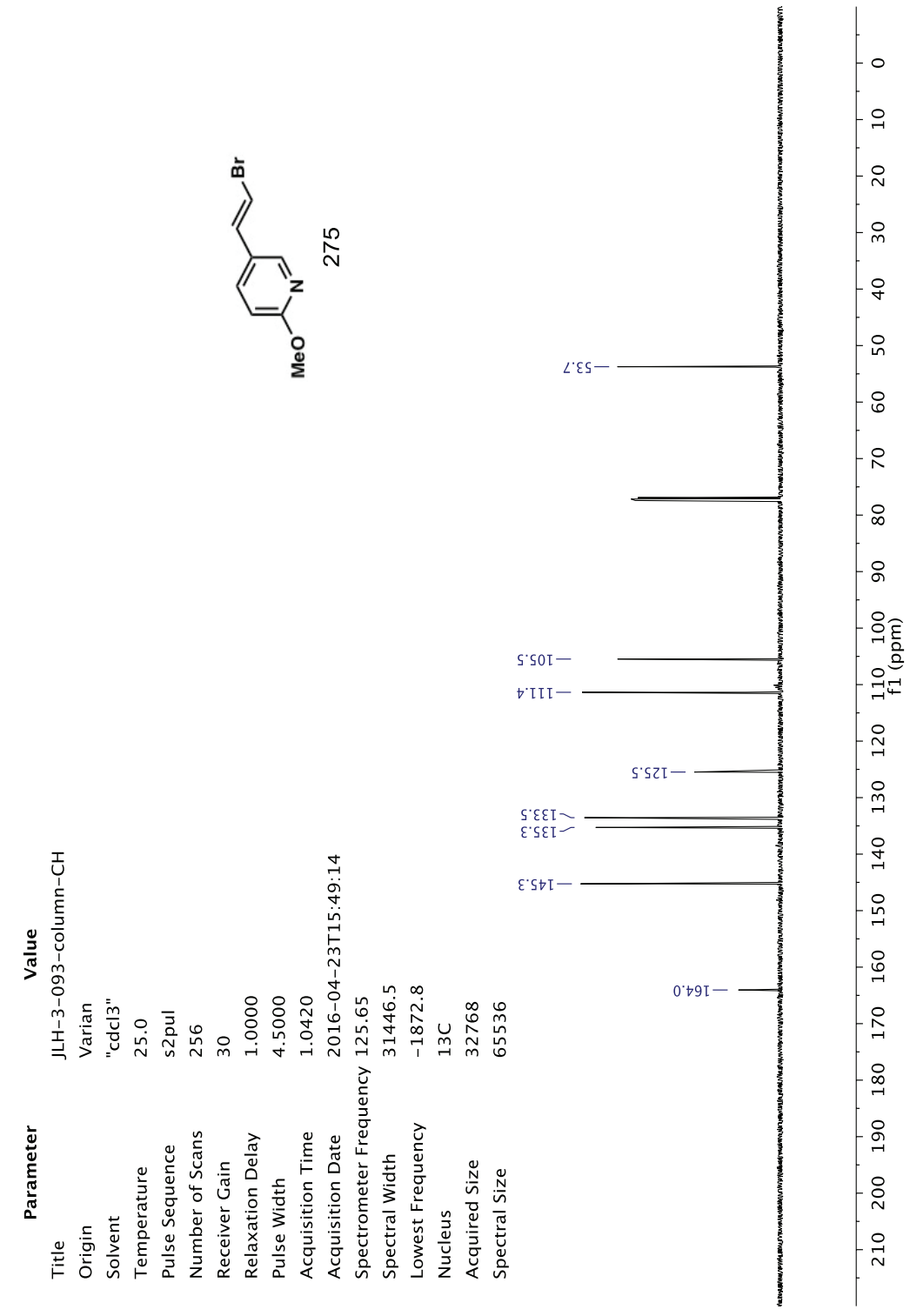

Parameter Value
Title JLH-3-095-column-CH
Origin Varian
Solvent "cdcl3"
Temperature 25.0
Pulse Sequence s2pul
Number of Scans 256
Receiver Gain 30
Relaxation Delay 1.0000
Pulse Width 4.5000
Acquisition Time 1.0420
Acquisition Date 2016-04-23T16:03:02
Spectrometer Frequency 125.65
Spectral Width 31446.5
Lowest Frequency -1874.1
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Br
Br
N
MeO
273
163.8
147.6
137.8
133.5
124.9
110.7
89.3
53.8
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Parameter
Value
Title
AHC-7-91-2-CH.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
64.2
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2017-01-05T15:49:57
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1535.6
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
Br
TsO
274
A (m) 7.69
B (m) 7.31
C (m) 7.20
D (d) 7.03
E (m) 6.93
F (d) 6.73
G (s) 2.44
2.07
2.17
1.93
1.00
2.02
0.95
3.31
f1 (ppm)

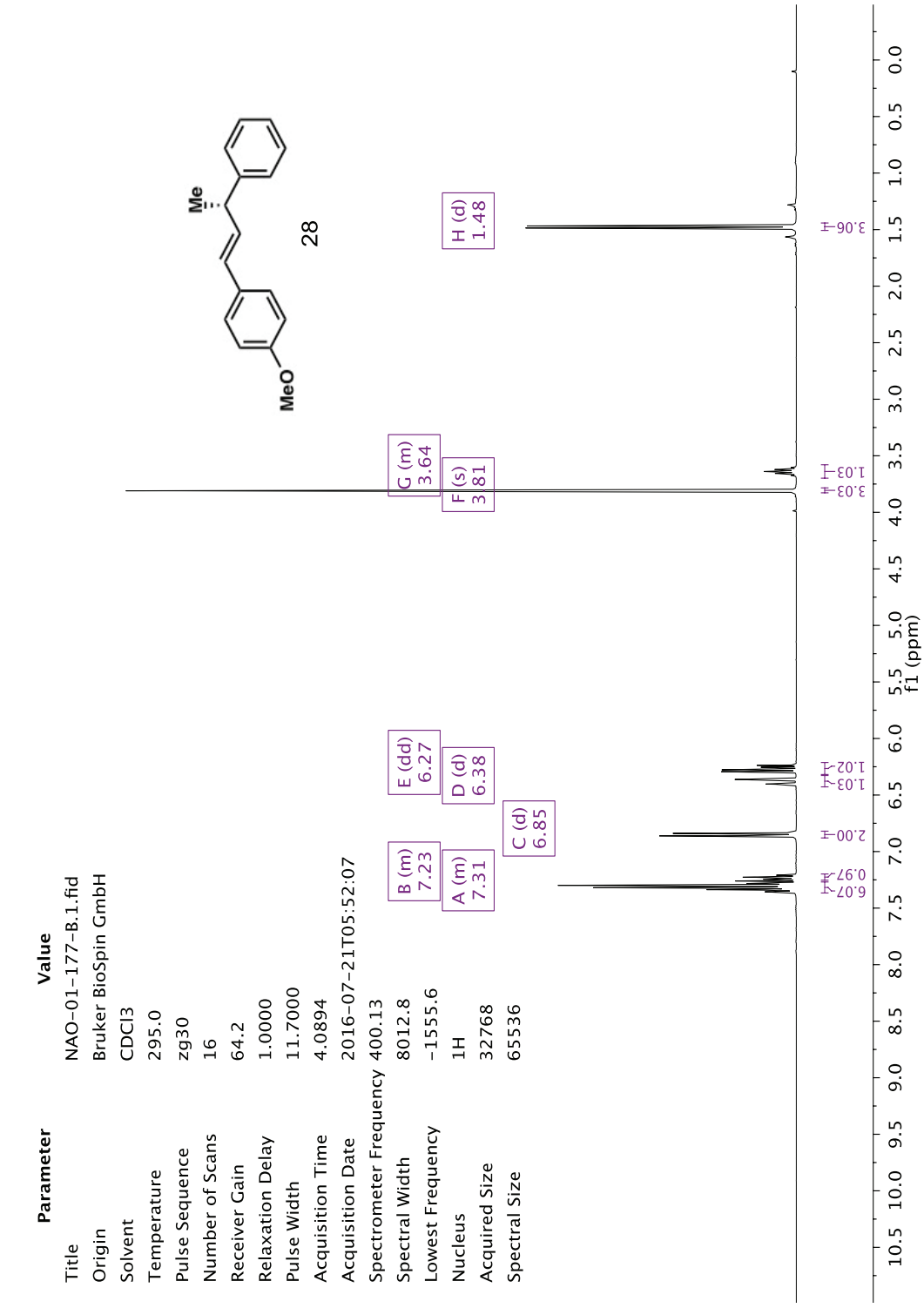


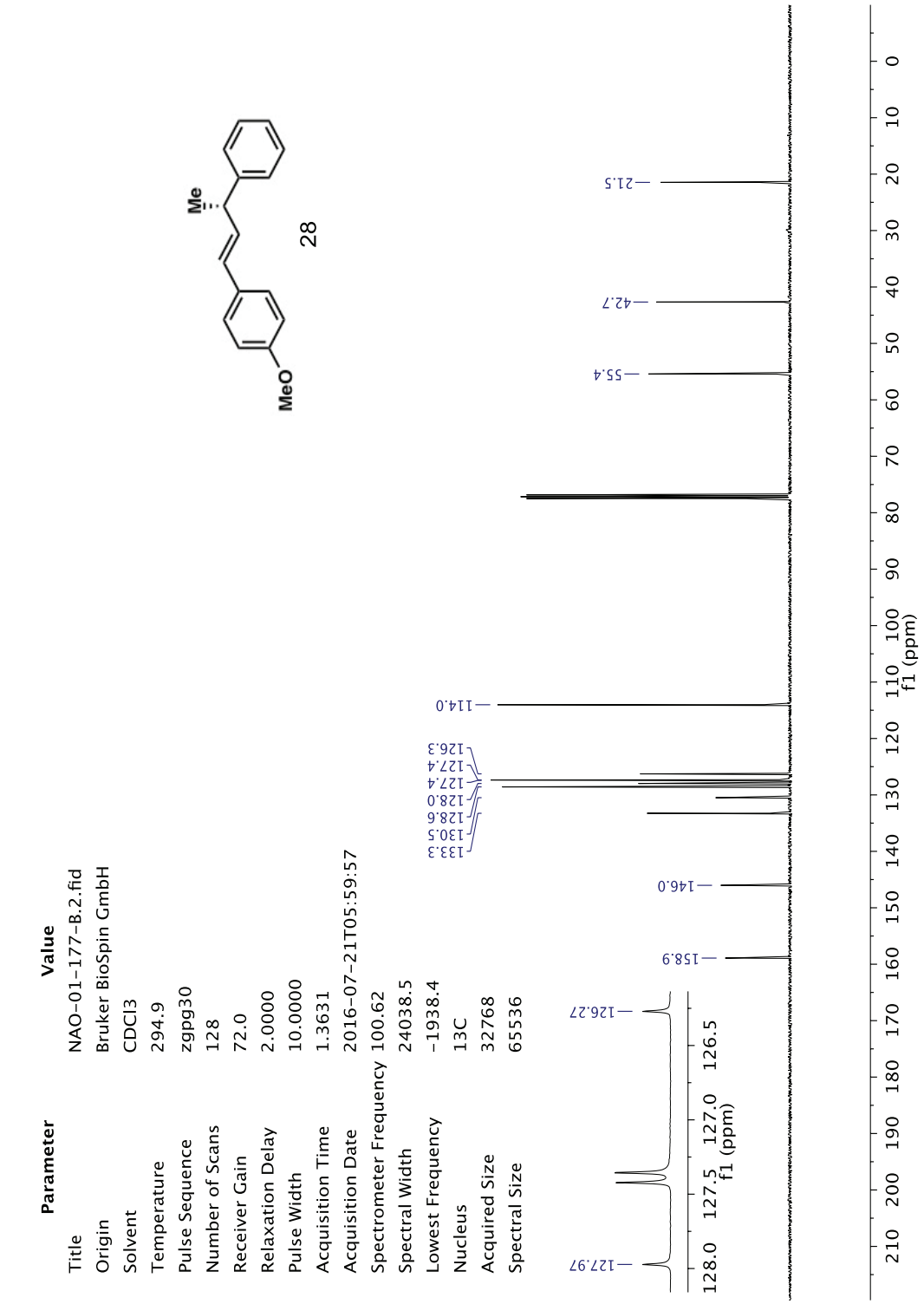
Parameter	Value
Title	AHC-7-91-2-CH.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	294.9
Pulse Sequence	zgpg30
Number of Scans	128
Receiver Gain	55.5
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2017-01-05T15:57:47
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1958.0
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

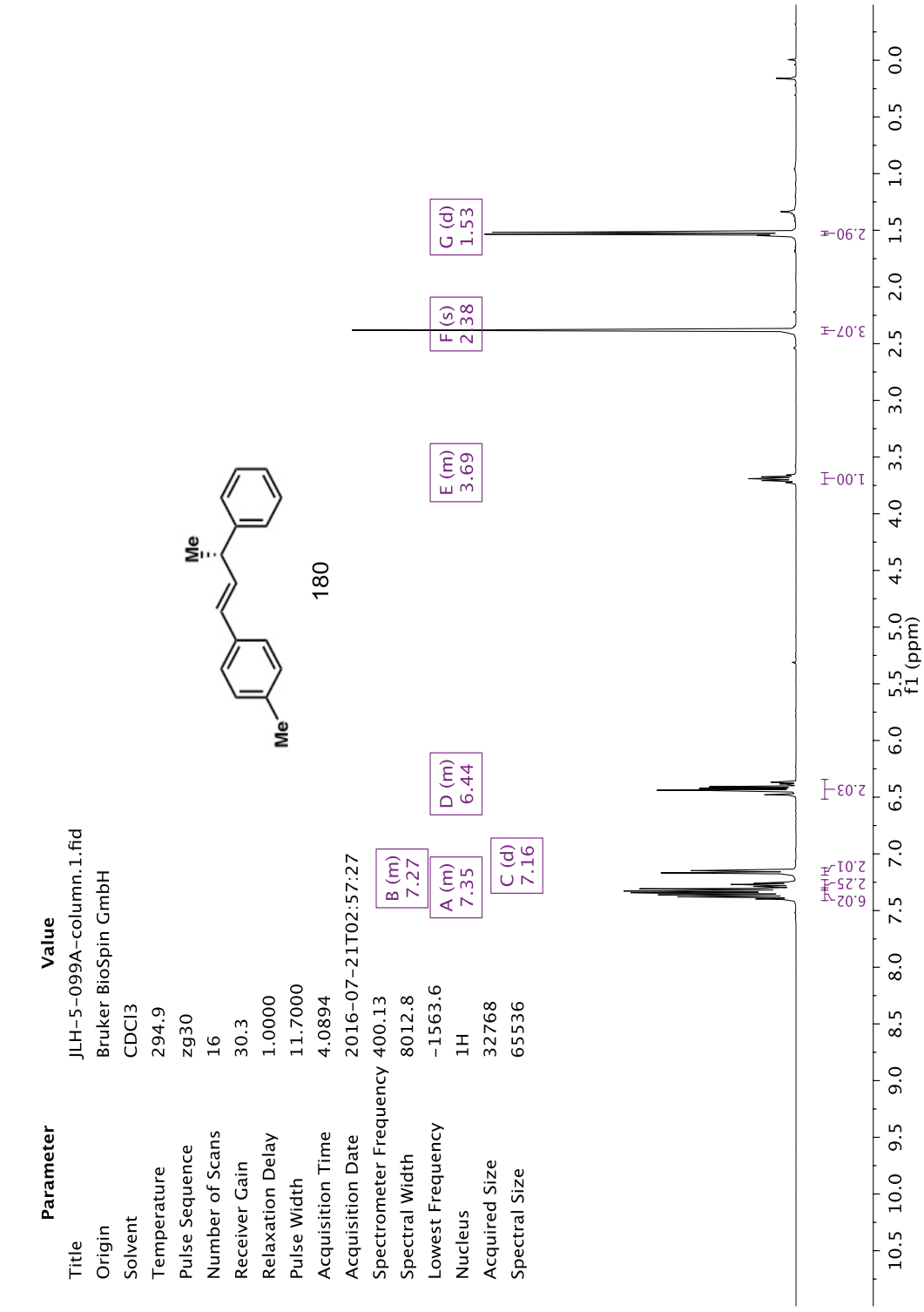

Parameter
Value
Title
JLH-3-093-column-CH
Origin
Varian
Solvent
"cdcl3"
Temperature
25.0
Pulse Sequence
s2pul
Number of Scans
8
Receiver Gain
32
Relaxation Delay
1.0000
Pulse Width
5.9000
Acquisition Time
3.0000
Acquisition Date
2016-04-23T15:48:26
Spectrometer Frequency
499.66
Spectral Width
8000.0
Lowest Frequency
-1026.1
Nucleus
1H
Acquired Size
24000
Spectral Size
65536
A (d) 8.05
B (ddd) 7.54
C (dq) 7.02
D (dt) 6.70
E (d) 6.65
F (s) 3.93
Br
N
MeO
275
0.99
1.06
1.00
1.00
1.02
3.07
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)



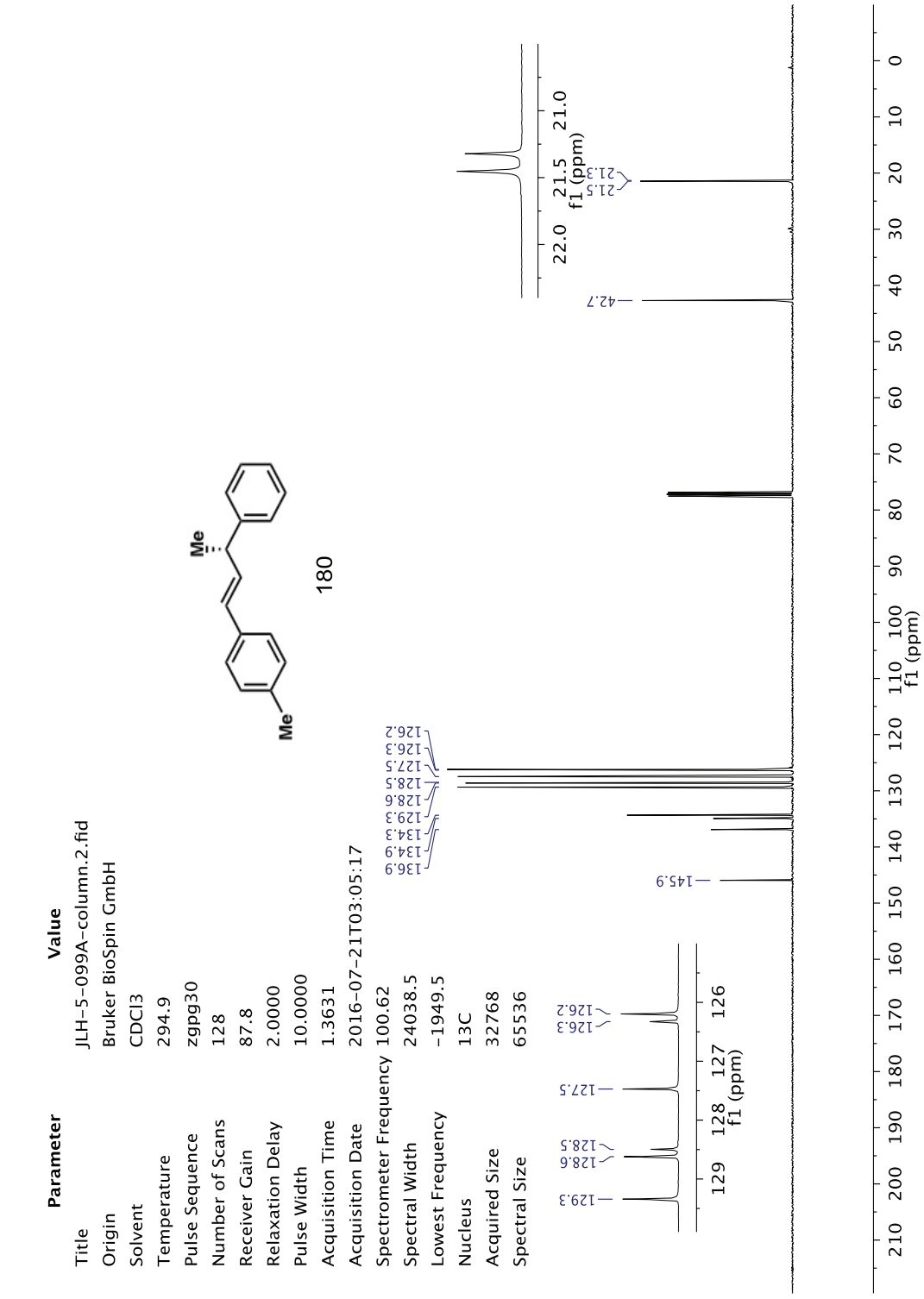
Parameter	Value
Title	JLH-3-093-column-CH
Origin	Varian
Solvent	"cdcl3"
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	256
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	4.5000
Acquisition Time	1.0420
Acquisition Date	2016-04-23T15:49:14
Spectrometer Frequency	125.65
Spectral Width	31446.5
Lowest Frequency	-1872.8
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

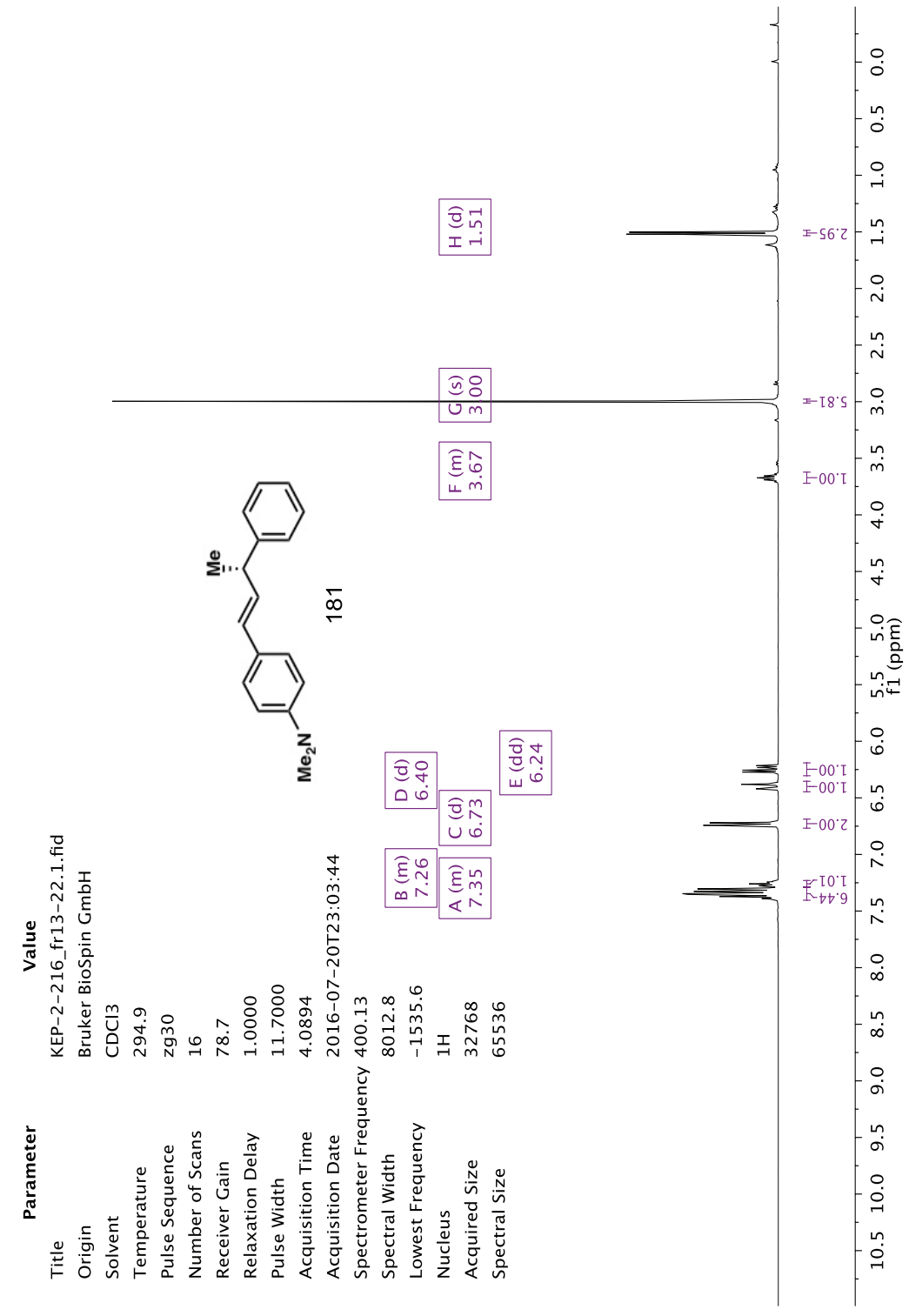

Parameter Value
Title NAO-01-177-B.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 64.2
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2016-07-21T05:52:07
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1555.6
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
Me
MeO
28
A (m) 7.31
B (m) 7.23
C (d) 6.85
D (d) 6.38
E (dd) 6.27
F (s) 3.81
G (m) 3.64
H (d) 1.48
6.07
0.97
2.00
1.03
1.02
1.03
3.03
1.03
3.06
f1 (ppm)

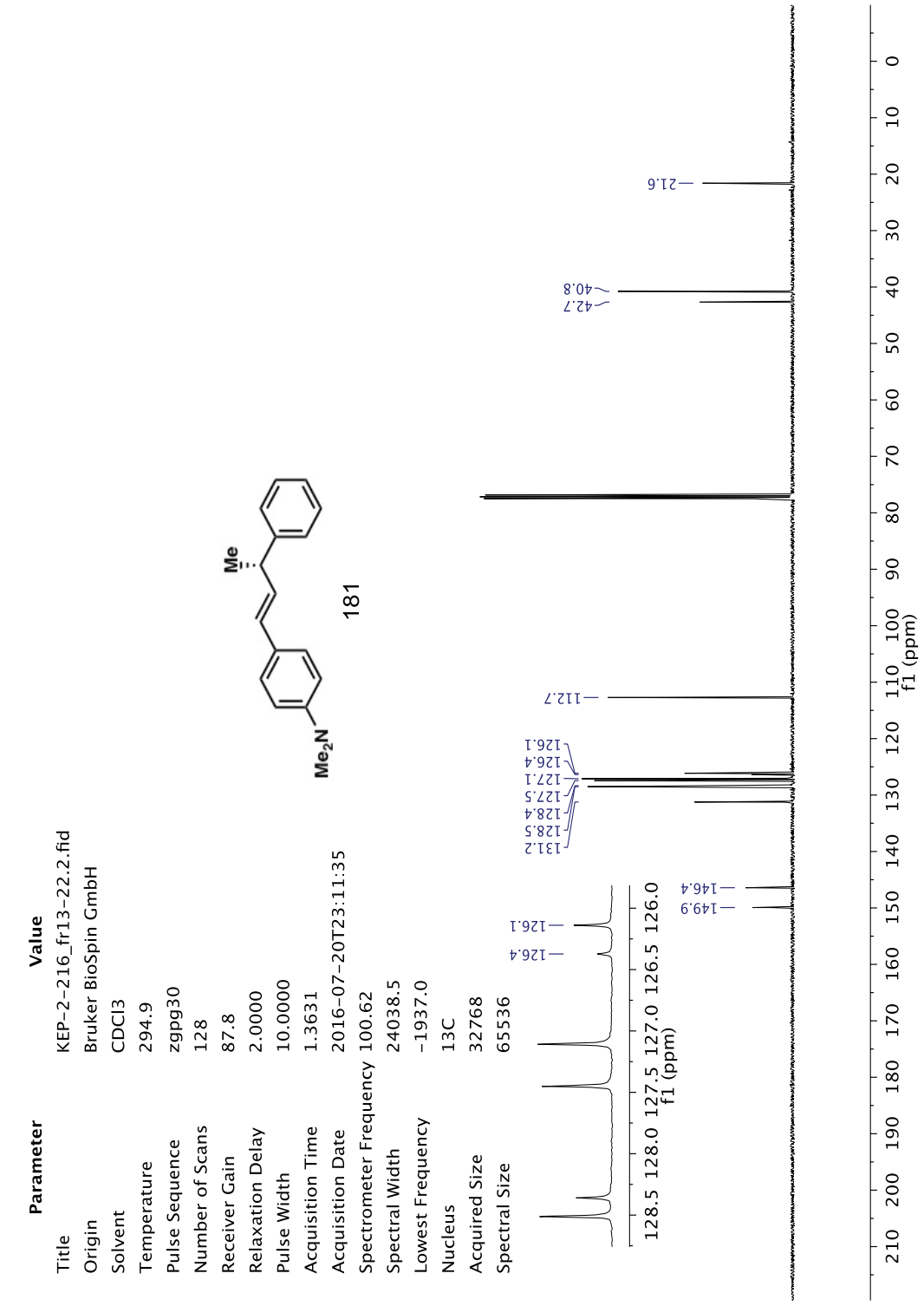

Parameter Value
Title NAO-01-177-B.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-07-21T05:59:57
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1938.4
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
MeO
28
21.5
42.7
55.4
114.0
126.3
127.4
127.4
128.0
128.6
130.5
133.3
146.0
158.9
126.27
127.97
f1 (ppm)

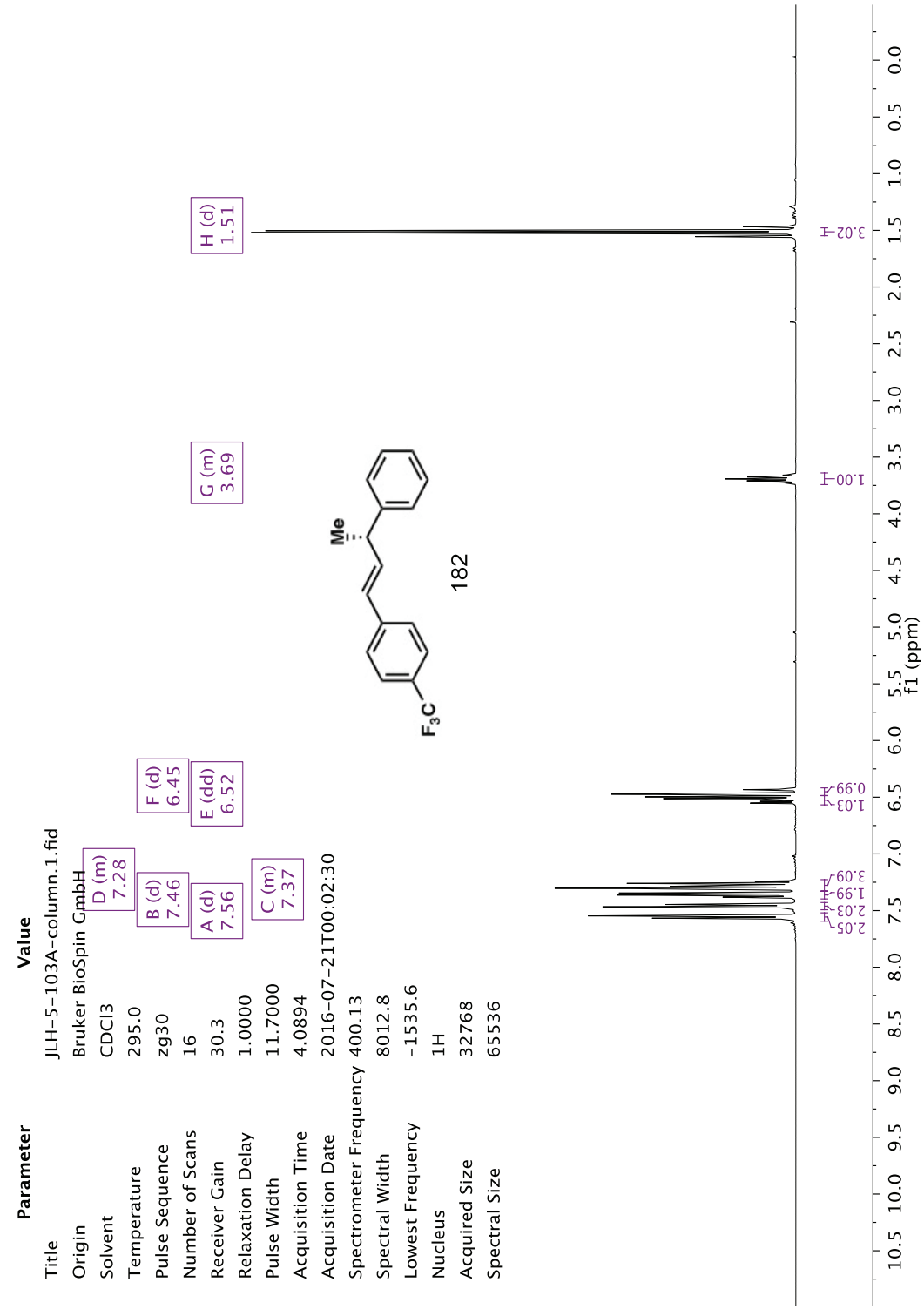


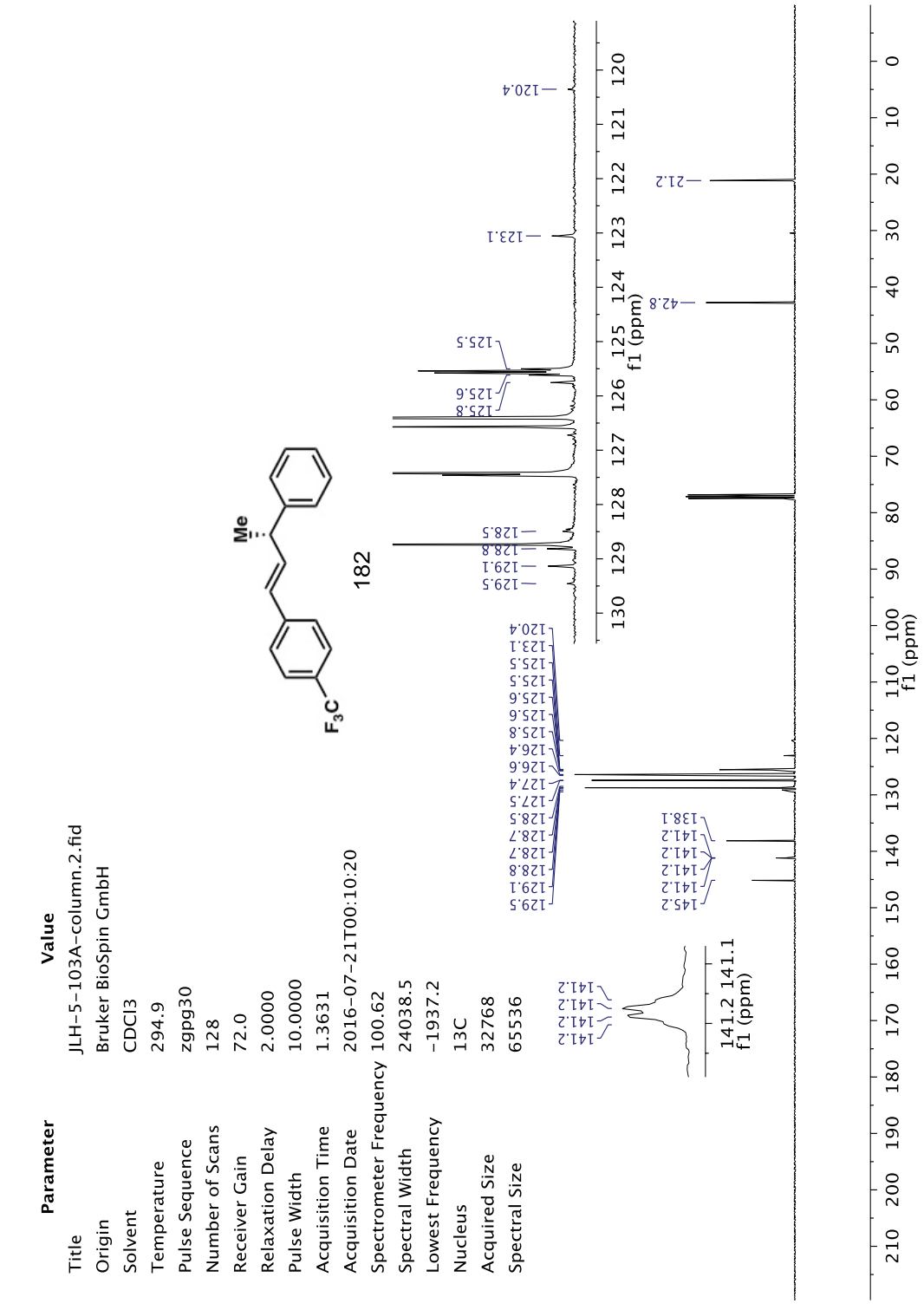
Parameter	Value
Title	JLH-5-099A-column.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	294.9
Pulse Sequence	zg30
Number of Scans	16
Receiver Gain	30.3
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2016-07-21T02:57:27
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1563.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536


Parameter Value
Title JLH-5-099A-column.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 87.8
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-07-21T03:05:17
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1949.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
Me
180
136.9
134.9
134.3
129.3
128.6
128.5
127.5
126.3
126.2
145.9
42.7
21.5
21.3
f1 (ppm)


Parameter
Value
Title
KEP-2-216_fr13-22.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
78.7
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2016-07-20T23:03:44
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1535.6
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
Me
Me2N
181
A (m) 7.35
B (m) 7.26
C (d) 6.73
D (d) 6.40
E (dd) 6.24
F (m) 3.67
G (s) 3.00
H (d) 1.51
6.44
1.01
2.00
1.00
1.00
1.00
5.81
2.95
f1 (ppm)


Parameter Value
Title KEP-2-216_fr13-22.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 87.8
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-07-20T23:11:35
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1937.0
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
Me2N
181
126.4
126.1
128.5 128.0 127.5 127.0 126.5 126.0
f1 (ppm)
146.4
149.9
131.2
128.5
128.4
127.5
127.1
126.4
126.1
112.7
42.7
40.8
21.6
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

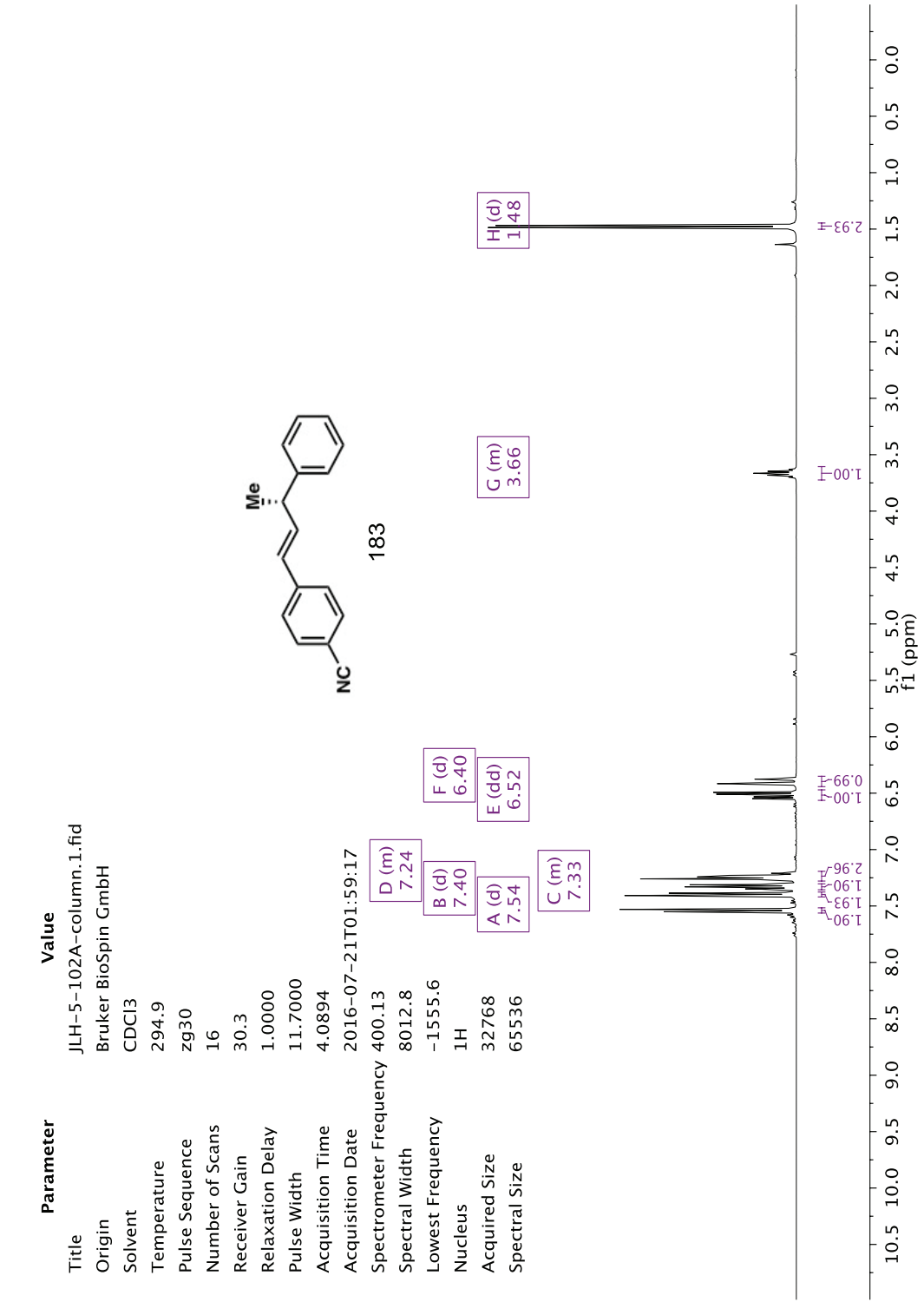

Parameter
Value
Title
JLH-5-103A-column.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.0
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
30.3
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2016-07-21T00:02:30
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1535.6
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
A (d) 7.56
B (d) 7.46
C (m) 7.37
D (m) 7.28
E (dd) 6.52
F (d) 6.45
G (m) 3.69
H (d) 1.51
Me
F3C
182
2.05
1.99
2.03
3.09
1.03
0.99
1.00
3.02
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

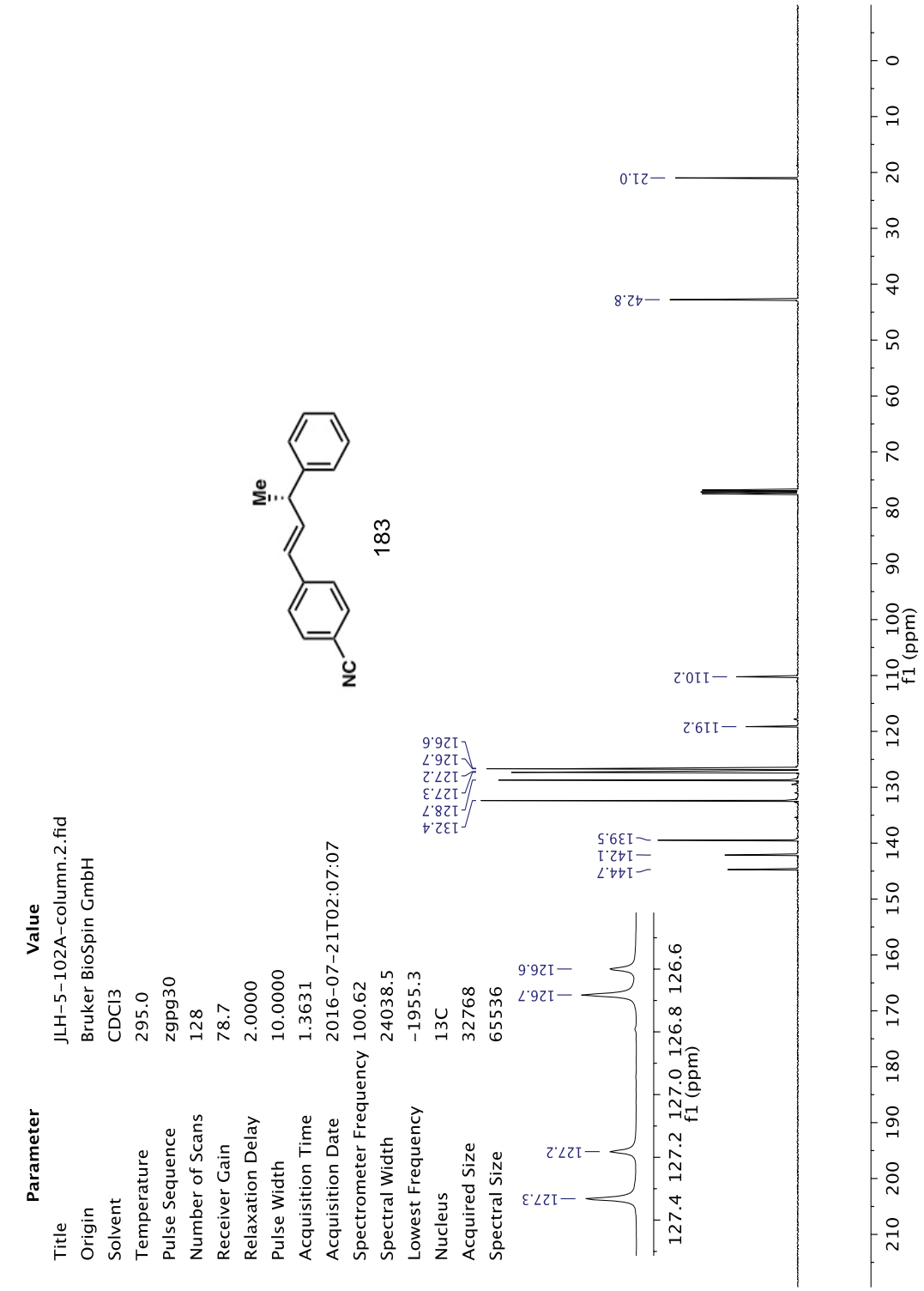

Parameter
Value
Title
JLH-5-103A-column.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zgpg30
Number of Scans
128
Receiver Gain
72.0
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2016-07-21T00:10:20
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1937.2
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Me
F3C
182
f1 (ppm)

Parameter	Value
Title	JLH-5-103A
Origin	Varian
Solvent	"cdcl3"
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2016-08-31T23:36:19
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-58252.6
Nucleus	19F
Acquired Size	64000
Spectral Size	131072
Absolute Reference	

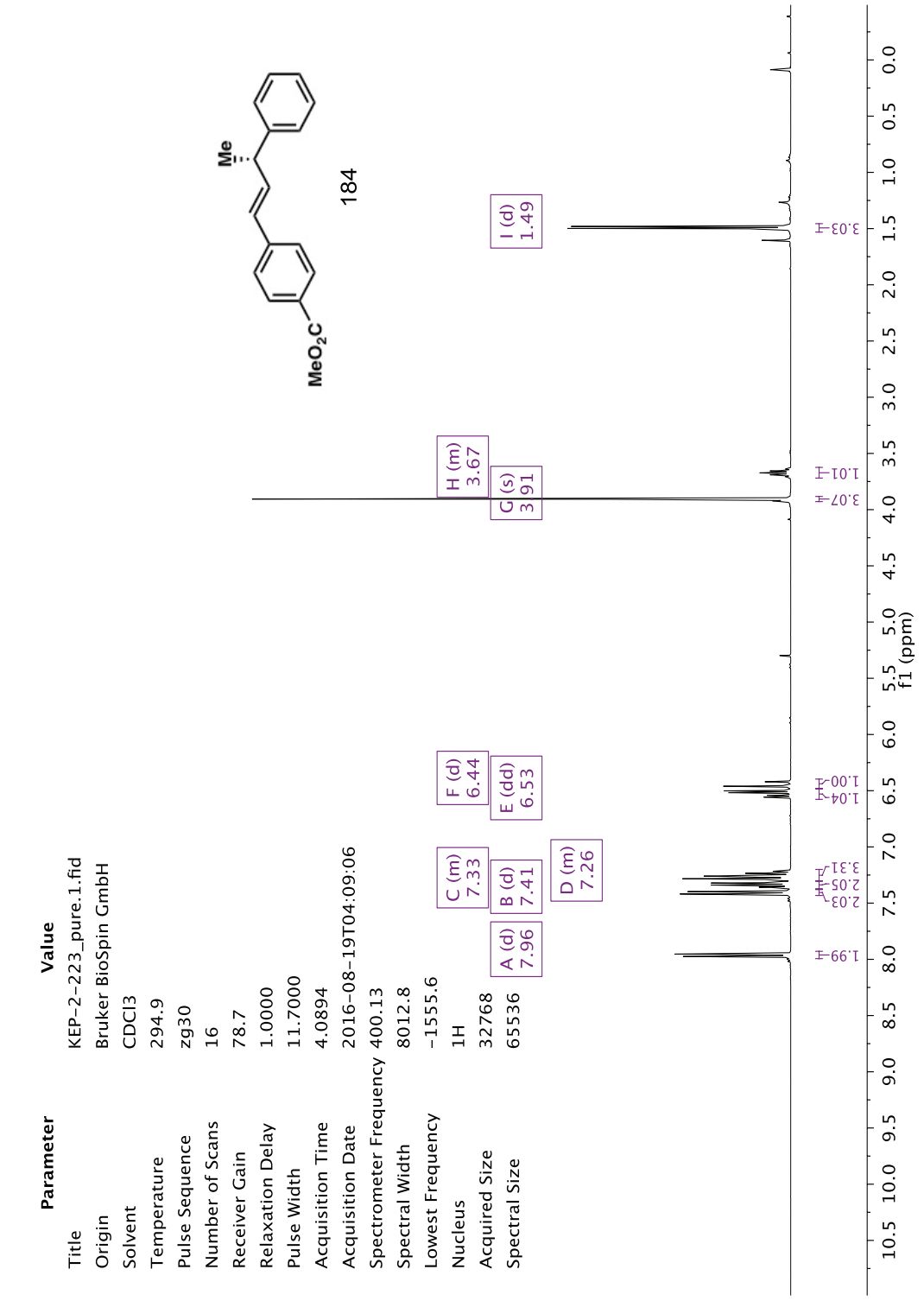
182

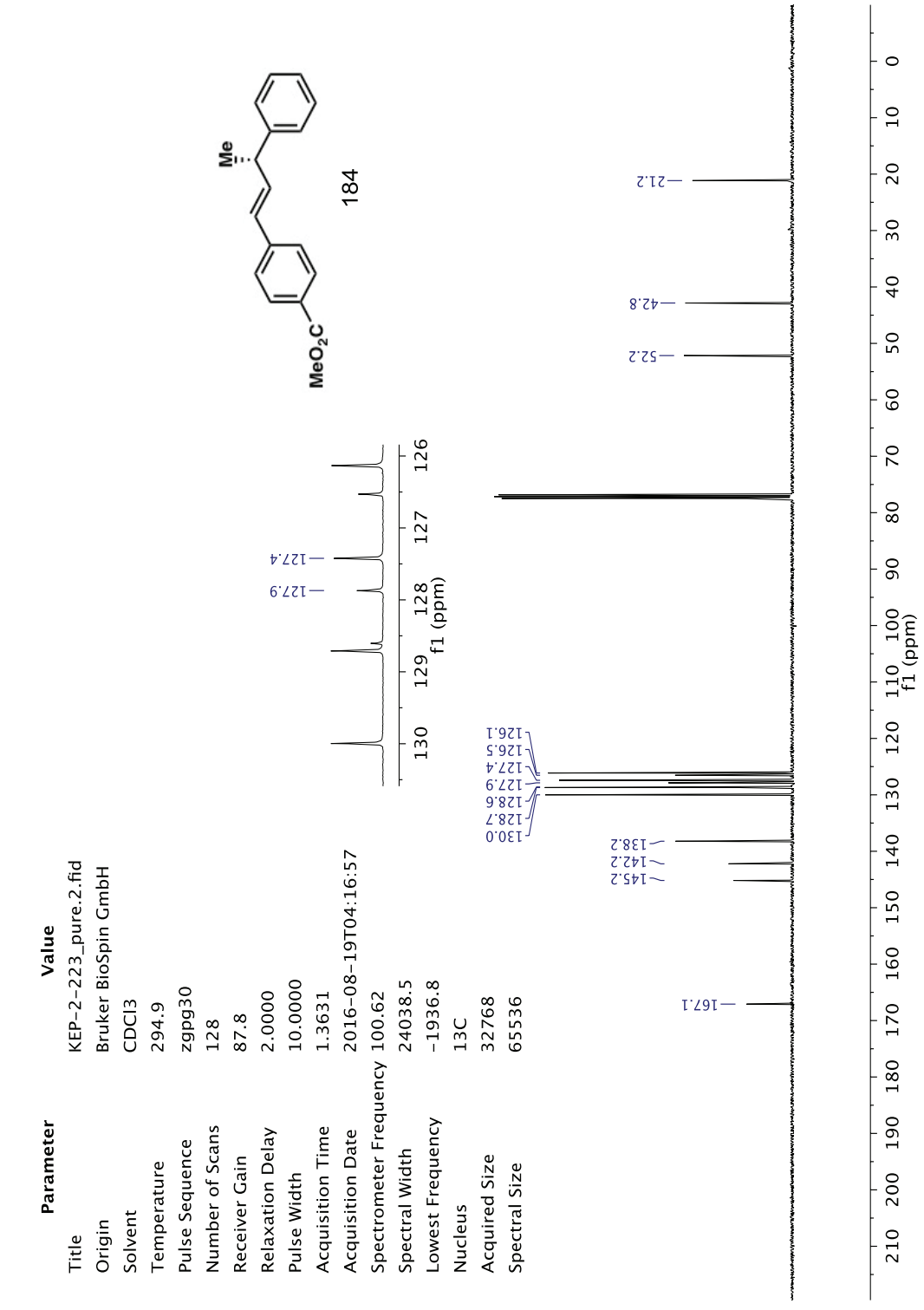
Parameter Value
Title JLH-5-103A-C6F6
Origin Varian
Solvent "cdcl3"
Temperature 25.0
Pulse Sequence s2pul
Number of Scans 16
Receiver Gain 30
Relaxation Delay 1.0000
Pulse Width 6.3333
Acquisition Time 0.9856
Acquisition Date 2016-08-31T23:40:31
Spectrometer Frequency 282.34
Spectral Width 64935.1
Lowest Frequency -58228.3
Nucleus 19F
Acquired Size 64000
Spectral Size 131072
-65.6
Me
F3C
182
with C6F6
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)


Parameter
Value
Title
JLH-5-102A-column.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
30.3
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2016-07-21T01:59:17
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1555.6
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
Me
NC
183
A (d) 7.54
B (d) 7.40
C (m) 7.33
D (m) 7.24
E (dd) 6.52
F (d) 6.40
G (m) 3.66
H (d) 1.48
1.90
1.93
2.96
1.90
1.00
0.99
1.00
2.93
f1 (ppm)

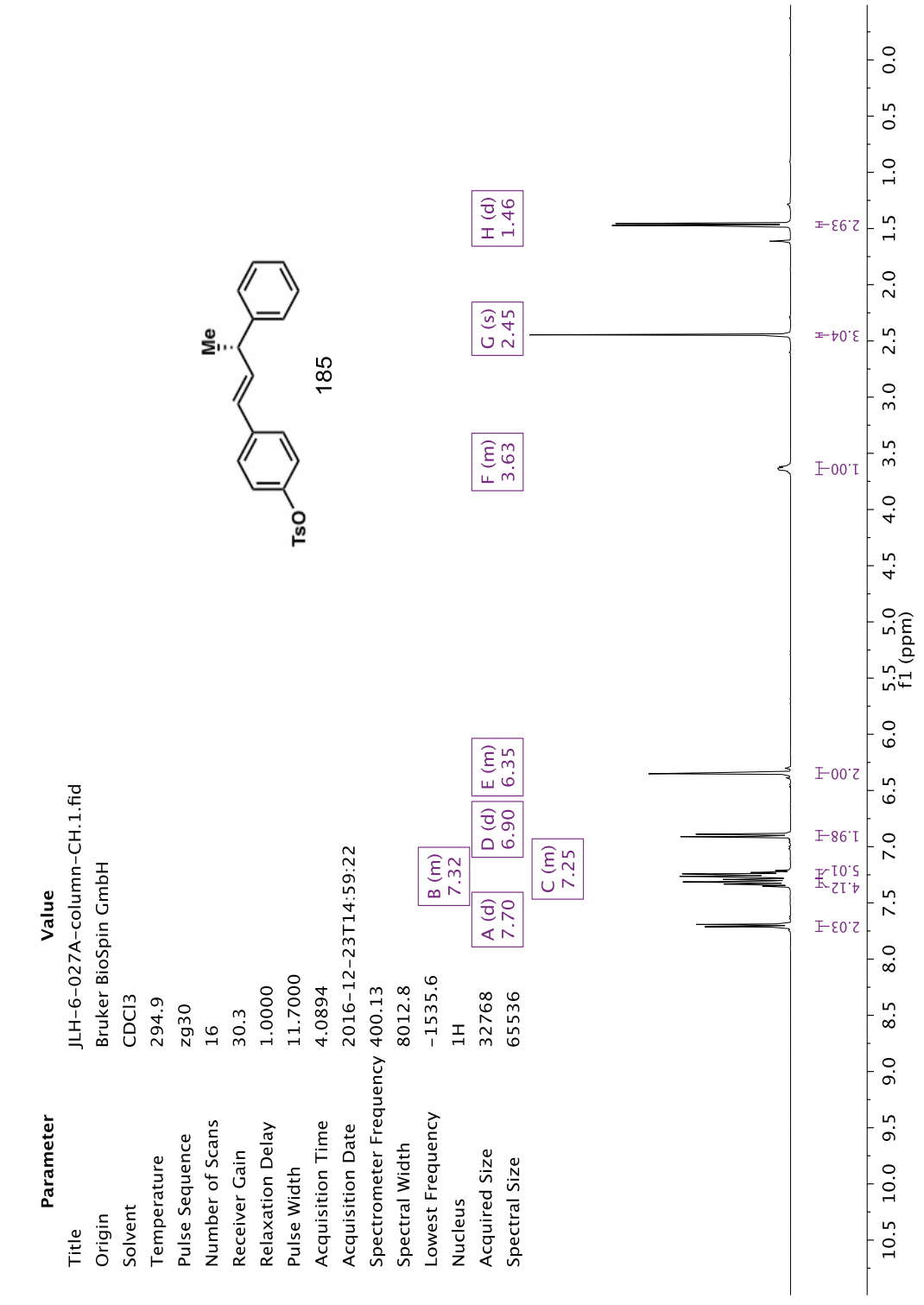

Me
NC
183
Parameter Value
Title JLH-5-102A-column.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 78.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-07-21T02:07:07
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1955.3
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
f1 (ppm)

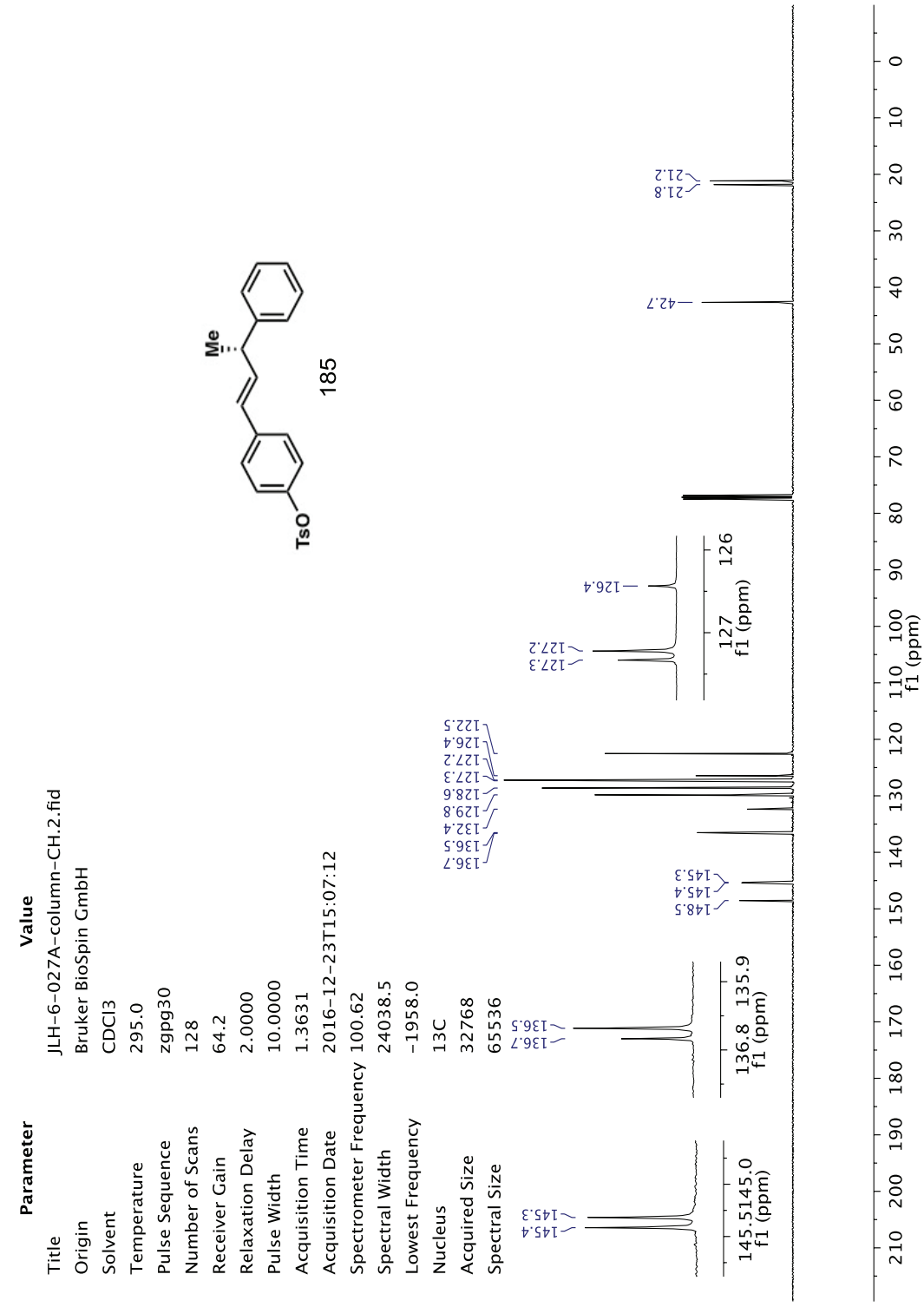
v

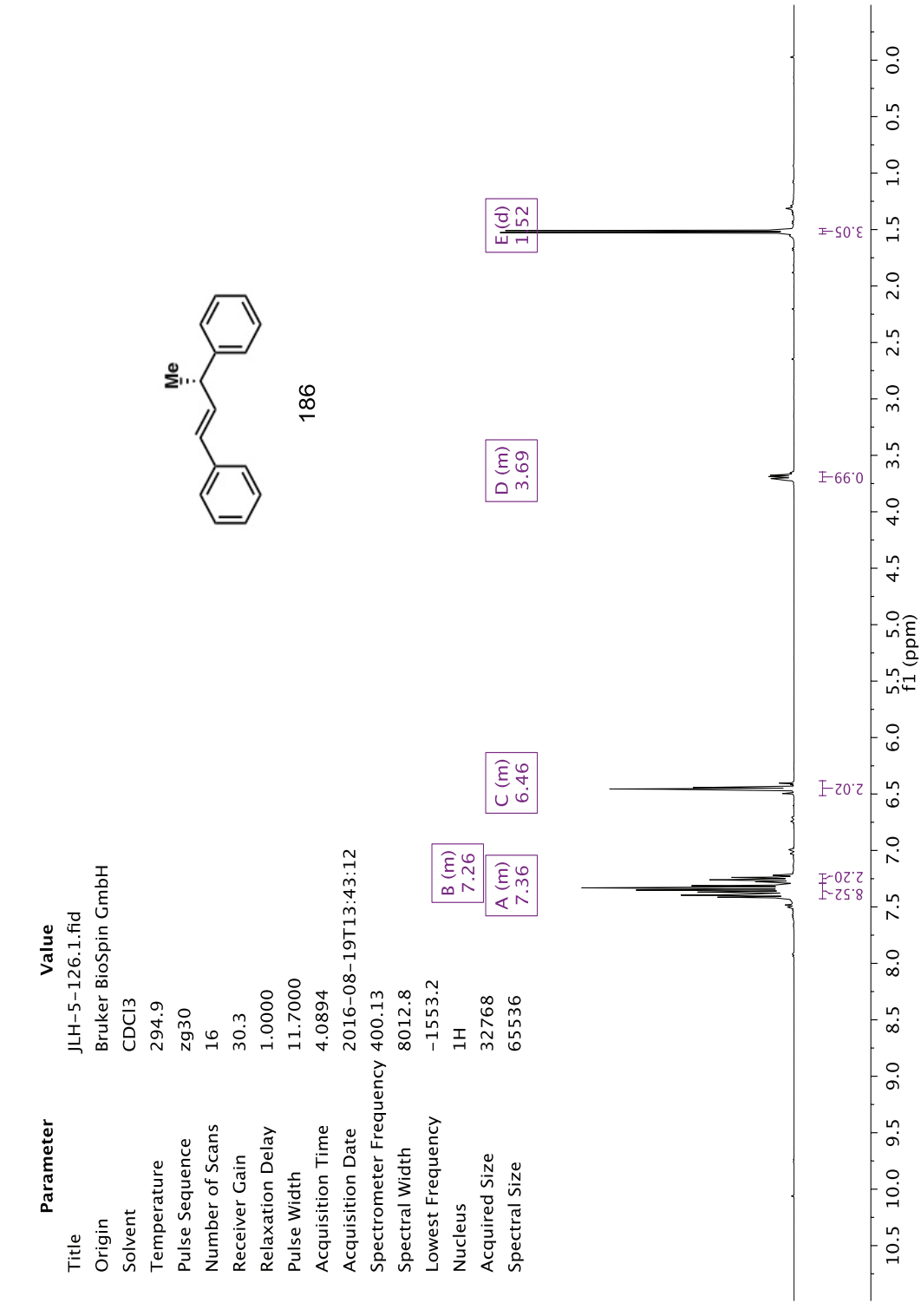

Parameter Value
Title KEP-2-223_pure.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 78.7
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2016-08-19T04:09:06
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1555.6
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
Me
MeO2C
184
A (d) 7.96
B (d) 7.41
C (m) 7.33
D (m) 7.26
E (dd) 6.53
F (d) 6.44
G (s) 3.91
H (m) 3.67
I (d) 1.49
1.99
2.03
2.05
3.31
1.04
1.00
3.07
1.01
3.03
f1 (ppm)



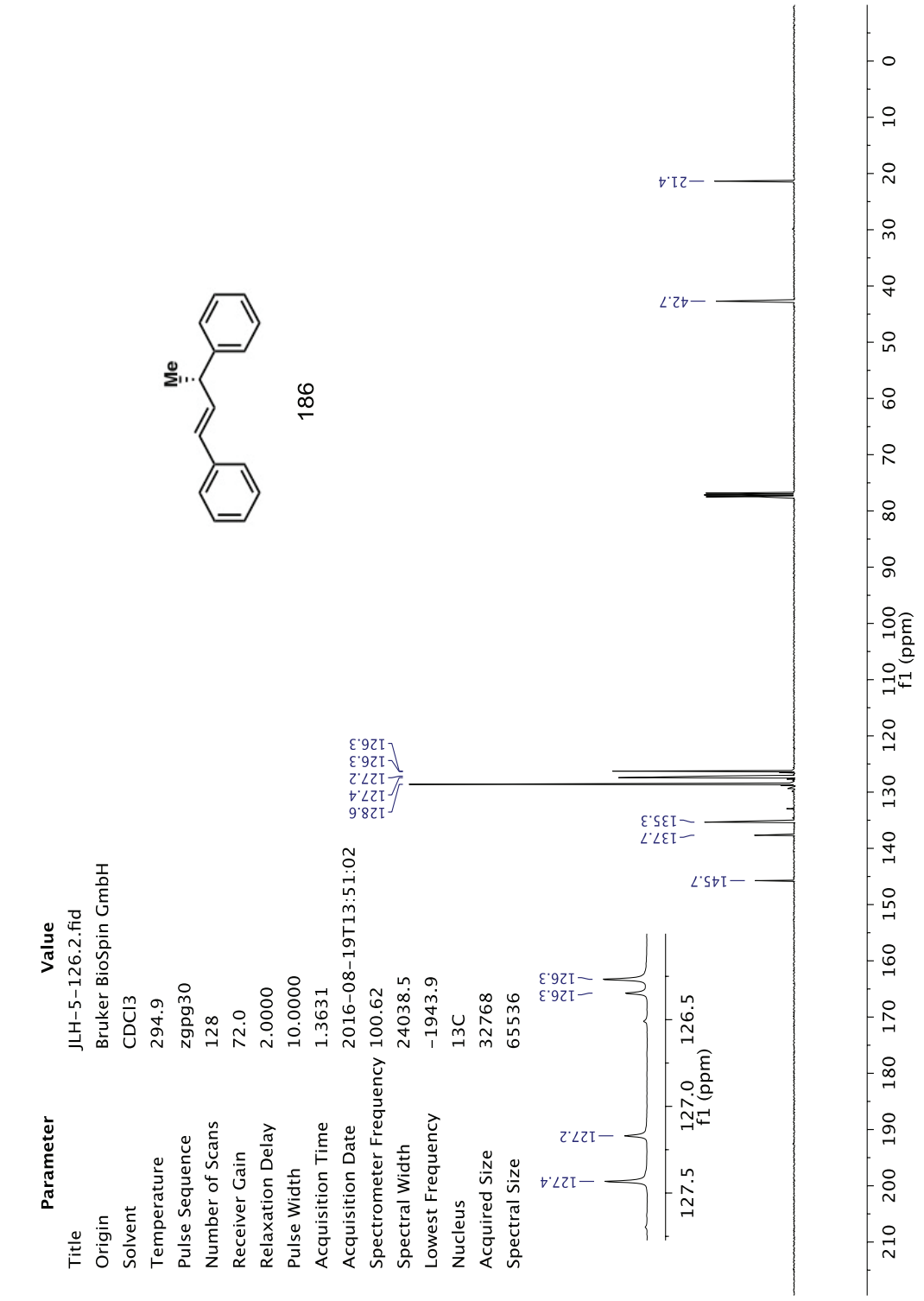
Parameter	Value
Title	KEP-2-223_pure.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	294.9
Pulse Sequence	zgpg30
Number of Scans	128
Receiver Gain	87.8
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2016-08-19T04:16:57
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1936.8
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

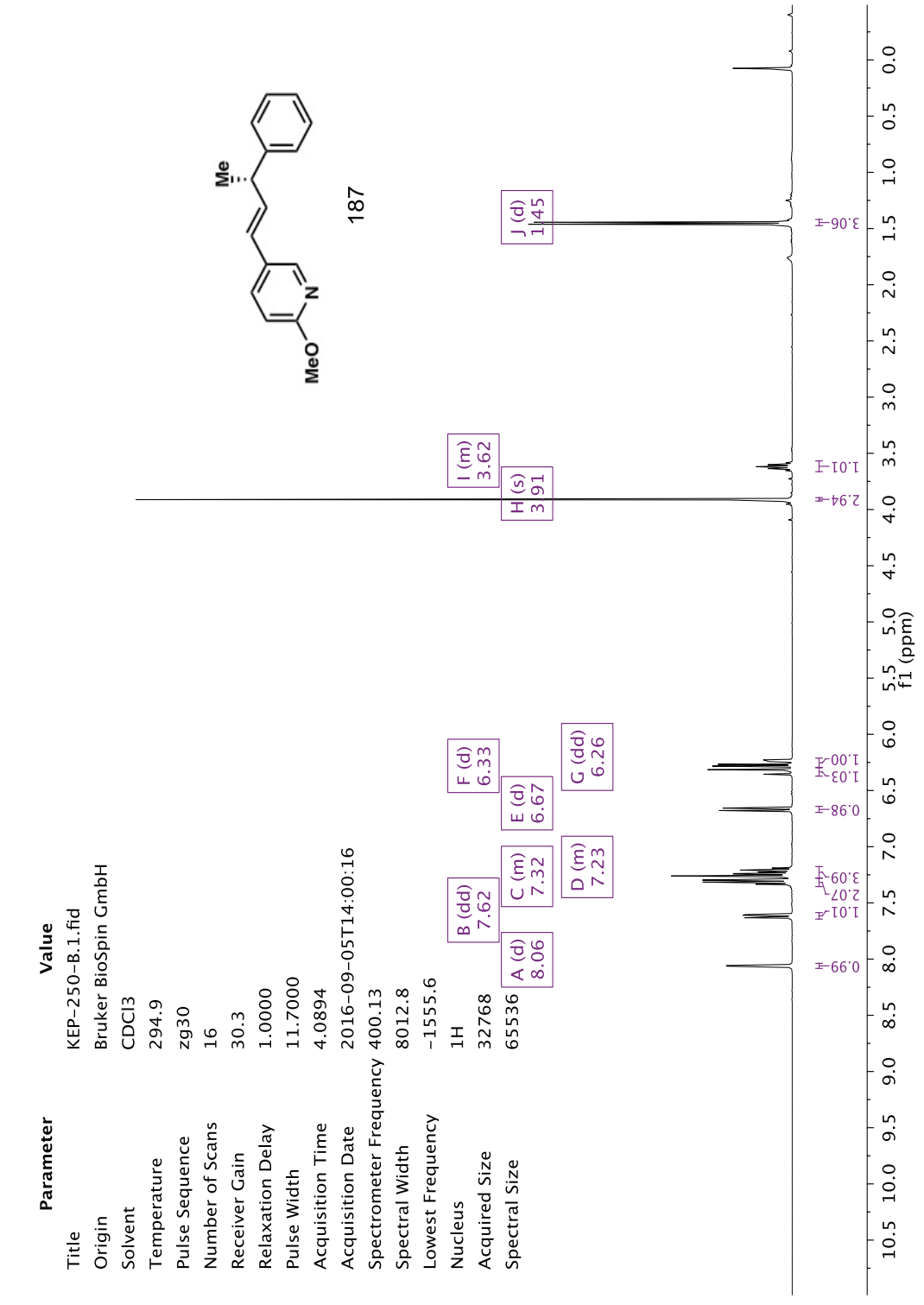

Parameter
Value
Title
JLH-6-027A-column-CH.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
30.3
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2016-12-23T14:59:22
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1535.6
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
Me
TsO
185
A (d) 7.70
B (m) 7.32
C (m) 7.25
D (d) 6.90
E (m) 6.35
F (m) 3.63
G (s) 2.45
H (d) 1.46
2.03
4.12
5.01
1.98
2.00
1.00
3.04
2.93
f1 (ppm)

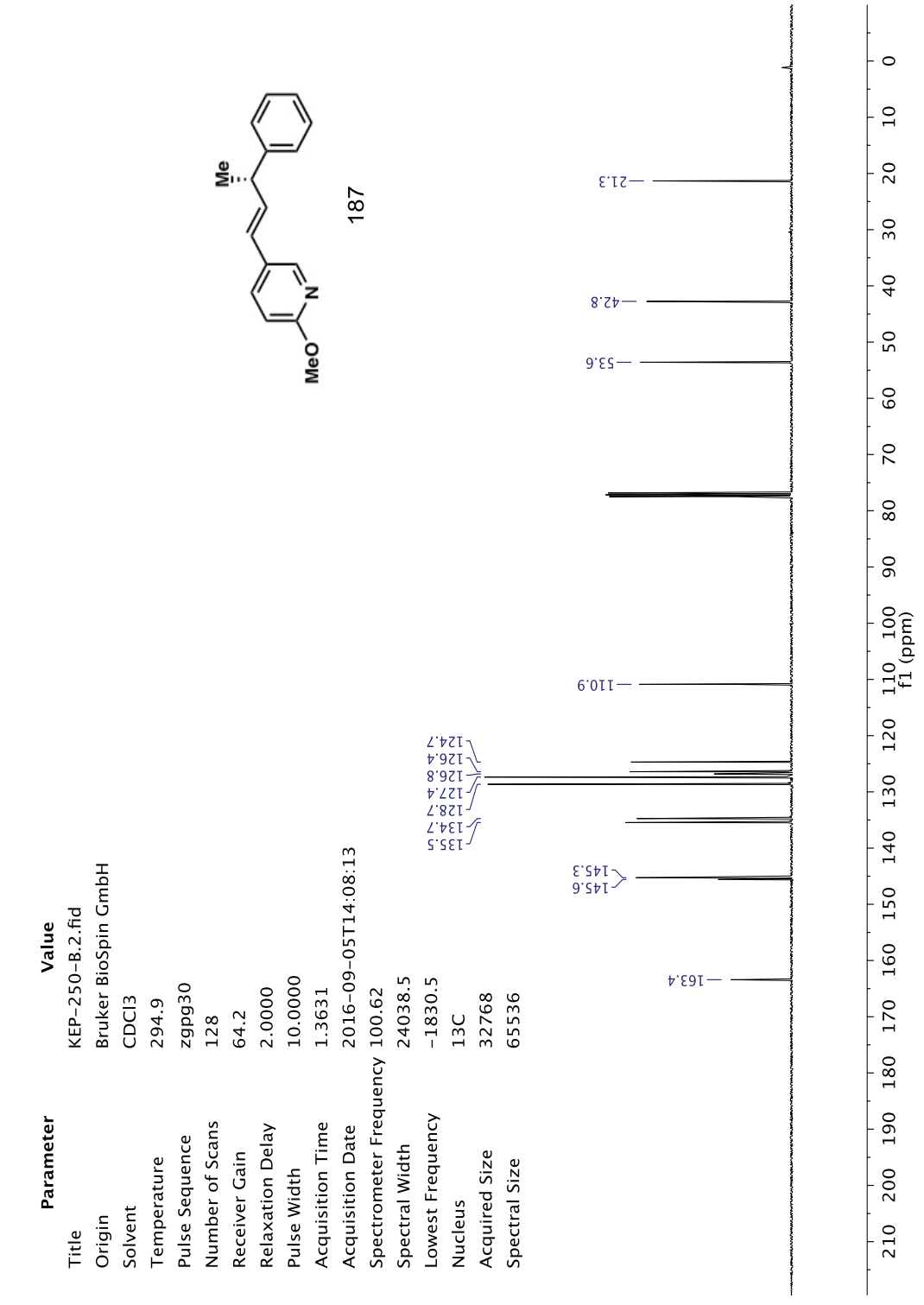

Parameter
Value
Title
JLH-6-027A-column-CH.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.0
Pulse Sequence
zgpg30
Number of Scans
128
Receiver Gain
64.2
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2016-12-23T15:07:12
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1958.0
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Me
TsO
185
145.4
145.3
136.7
136.5
148.5
145.4
145.3
136.7
136.5
132.4
129.8
128.6
127.3
127.2
126.4
122.5
127.3
127.2
126.4
42.7
21.8
21.2
145.5145.0
f1 (ppm)
136.8 135.9
f1 (ppm)
127
f1 (ppm)
126
f1 (ppm)

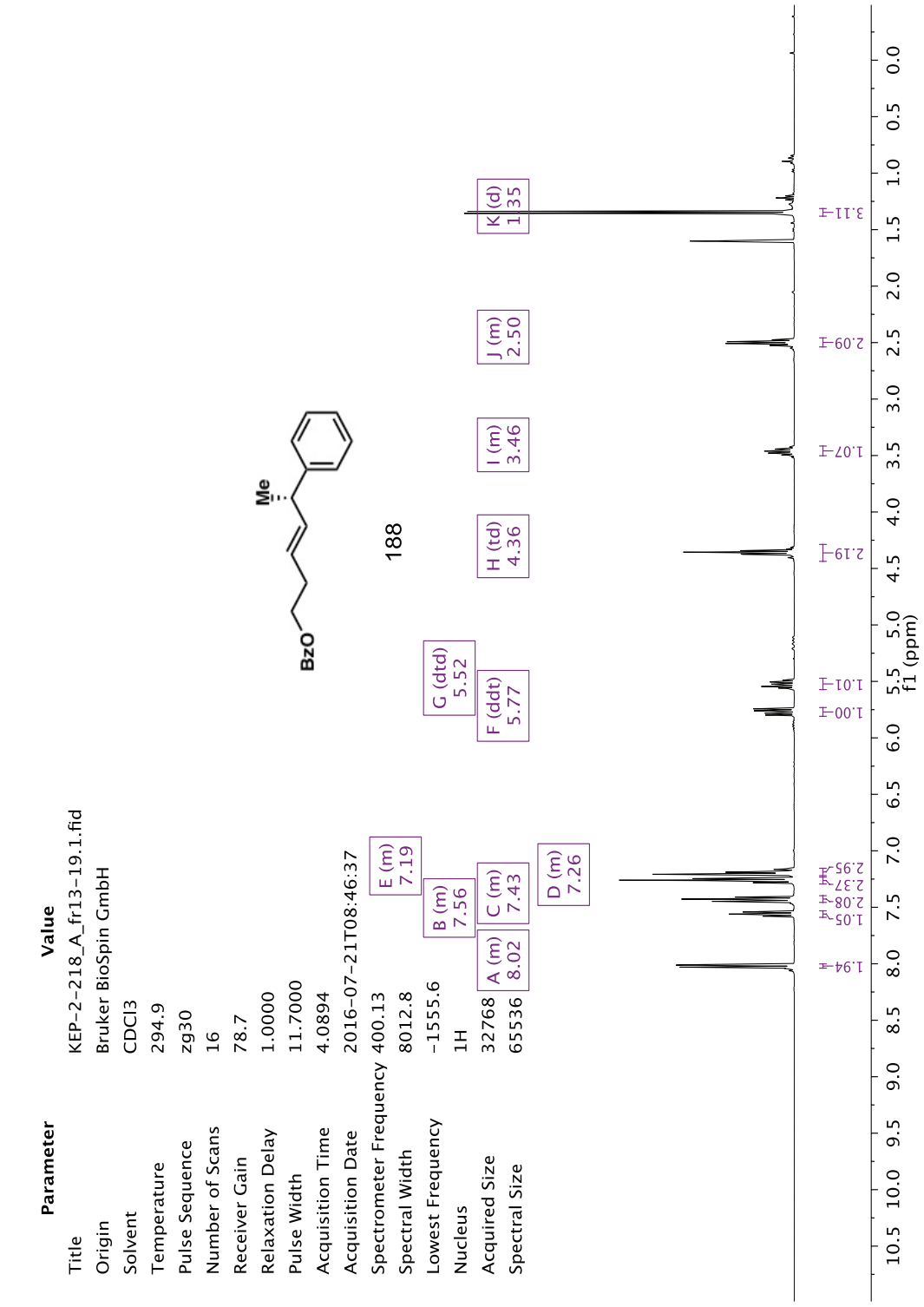


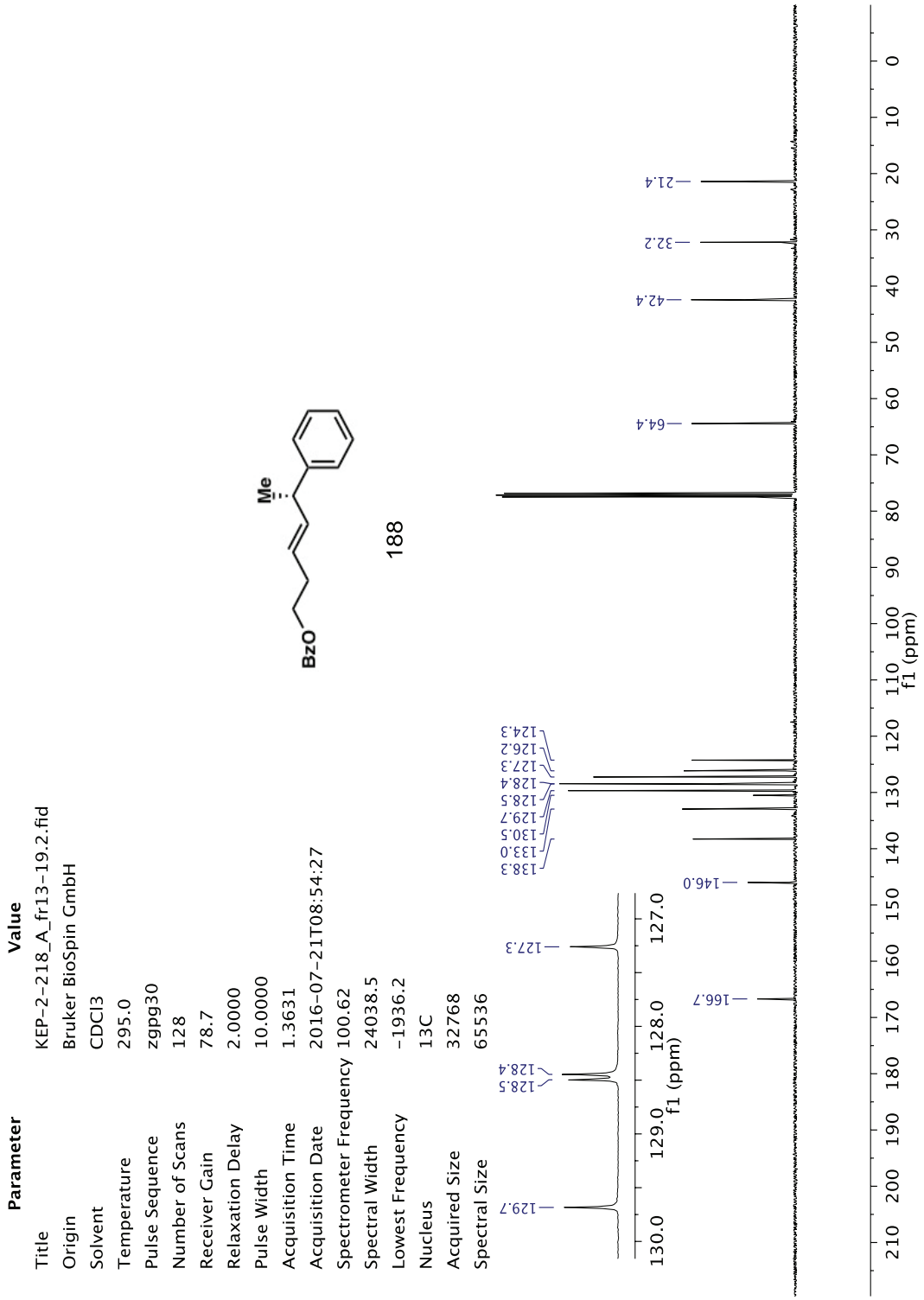
Parameter	Value
Title	JLH-5-126.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	294.9
Pulse Sequence	zg30
Number of Scans	16
Receiver Gain	30.3
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2016-08-19T13:43:12
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1553.2
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

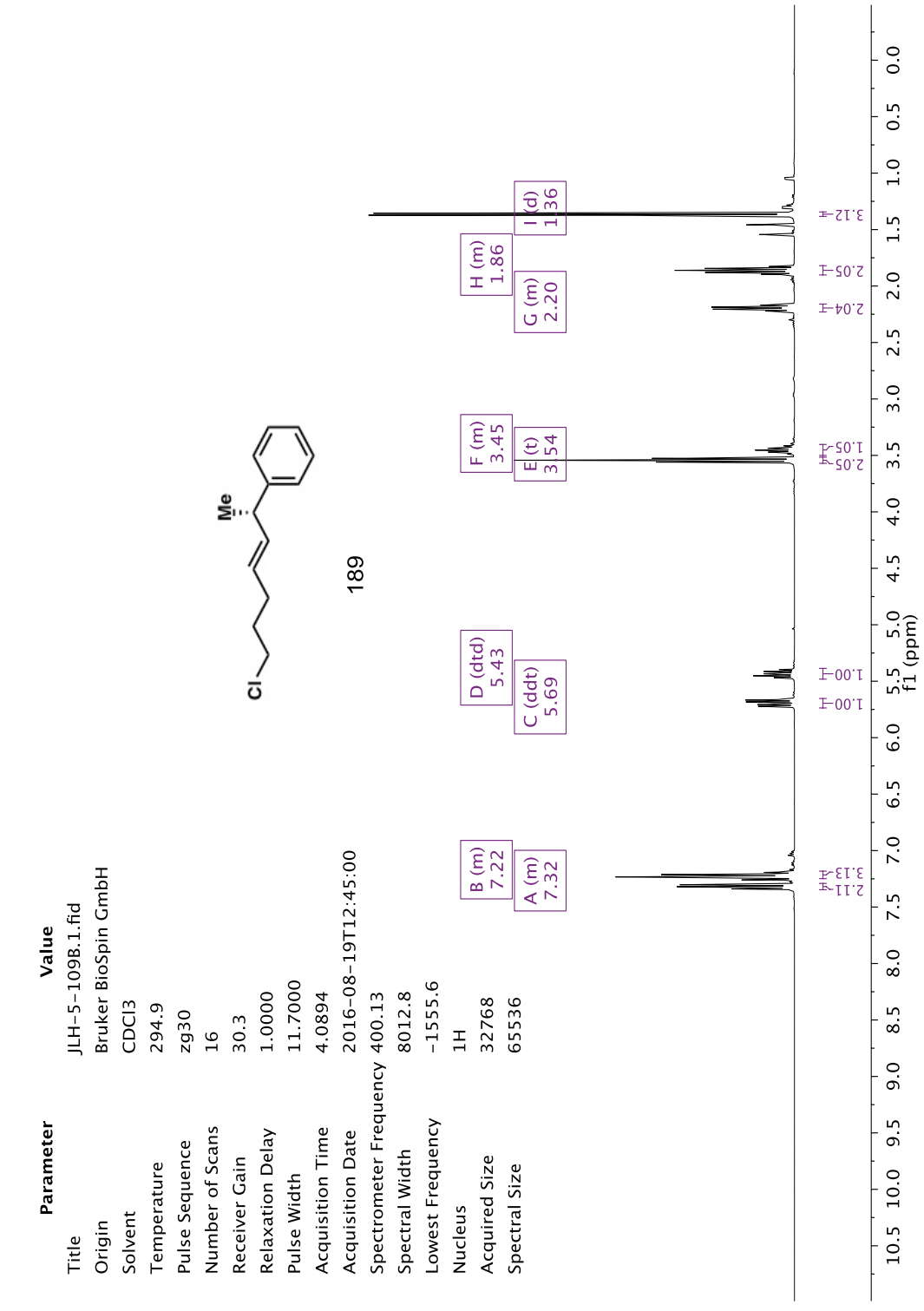

Me
186
Parameter Value
Title JLH-5-126.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-08-19T13:51:02
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1943.9
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
145.7
137.7
135.3
128.6
127.4
127.2
126.3
126.3
42.7
21.4
f1 (ppm)

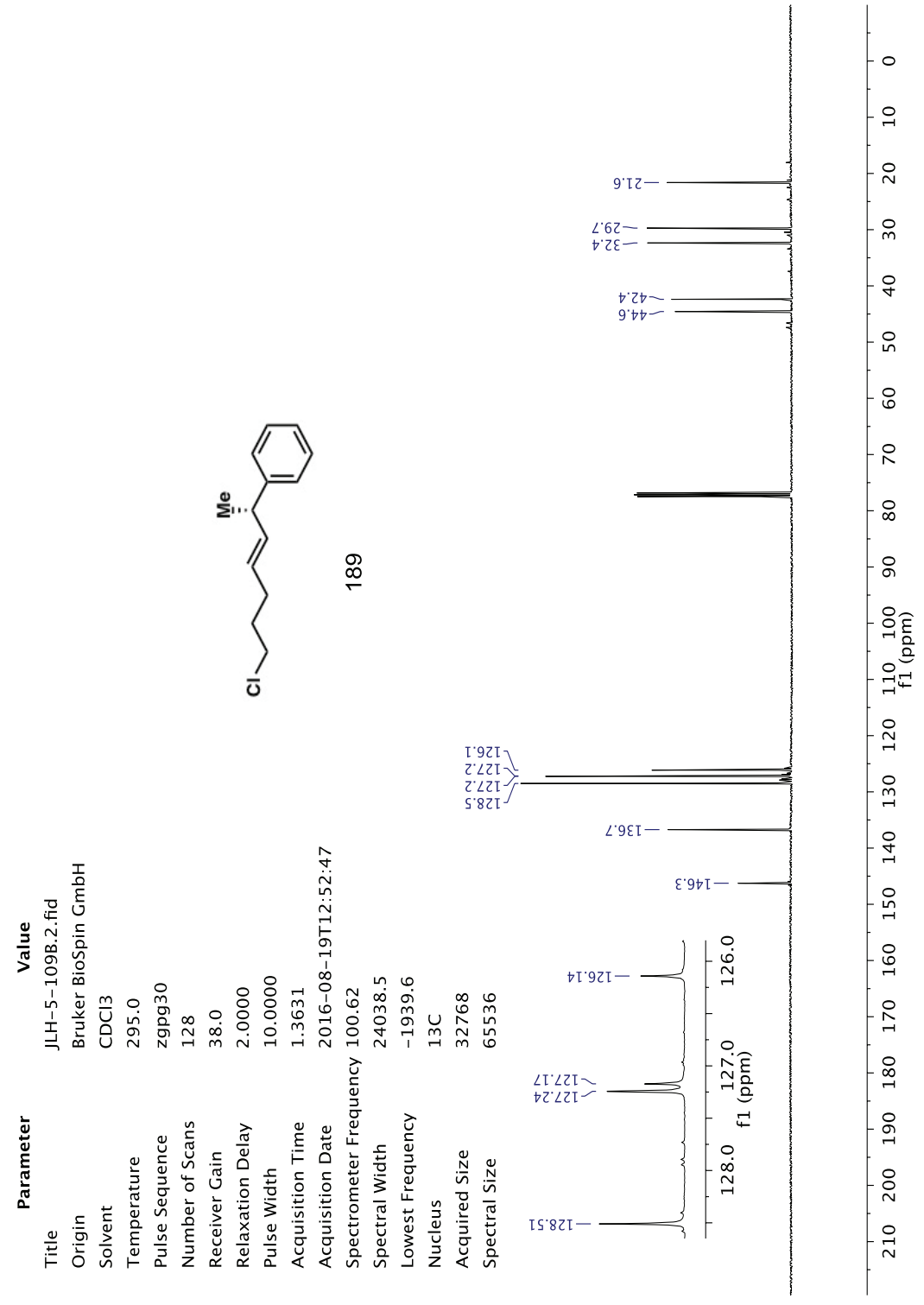

Parameter
Value
Title KEP-250-B.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 30.3
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2016-09-05T14:00:16
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1555.6
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
Me
MeO
N
187
A (d) 8.06
B (dd) 7.62
C (m) 7.32
D (m) 7.23
E (d) 6.67
F (d) 6.33
G (dd) 6.26
H (s) 3.91
I (m) 3.62
J (d) 1.45
0.99
1.01
2.07
3.09
0.98
1.03
1.00
2.94
1.01
3.06
f1 (ppm)

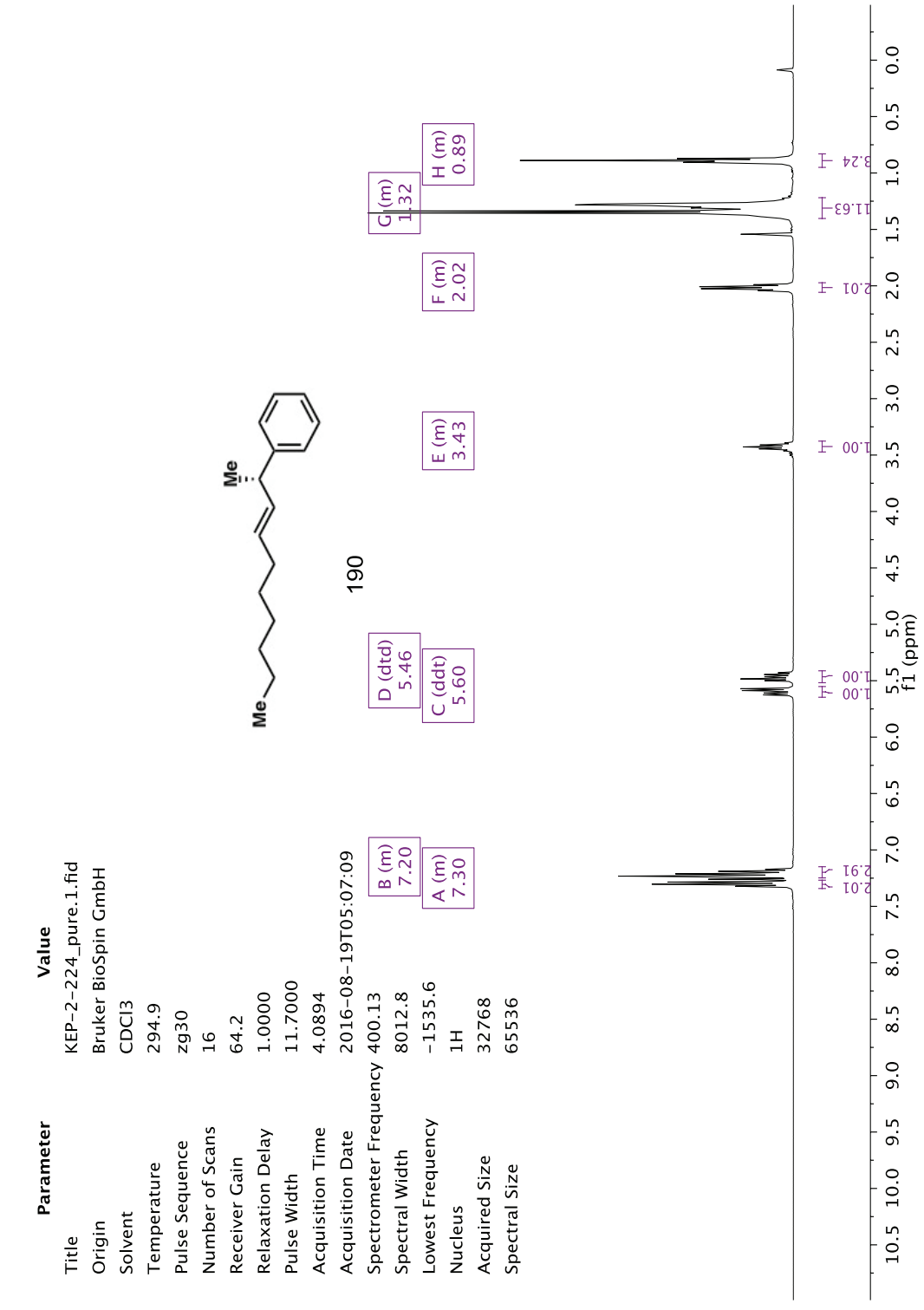

Me
N
MeO
187
Parameter Value
Title KEP-250-B.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 64.2
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-09-05T14:08:13
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1830.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
163.4
145.6
145.3
135.5
134.7
128.7
127.4
126.8
126.4
124.7
110.9
53.6
42.8
21.3
f1 (ppm)

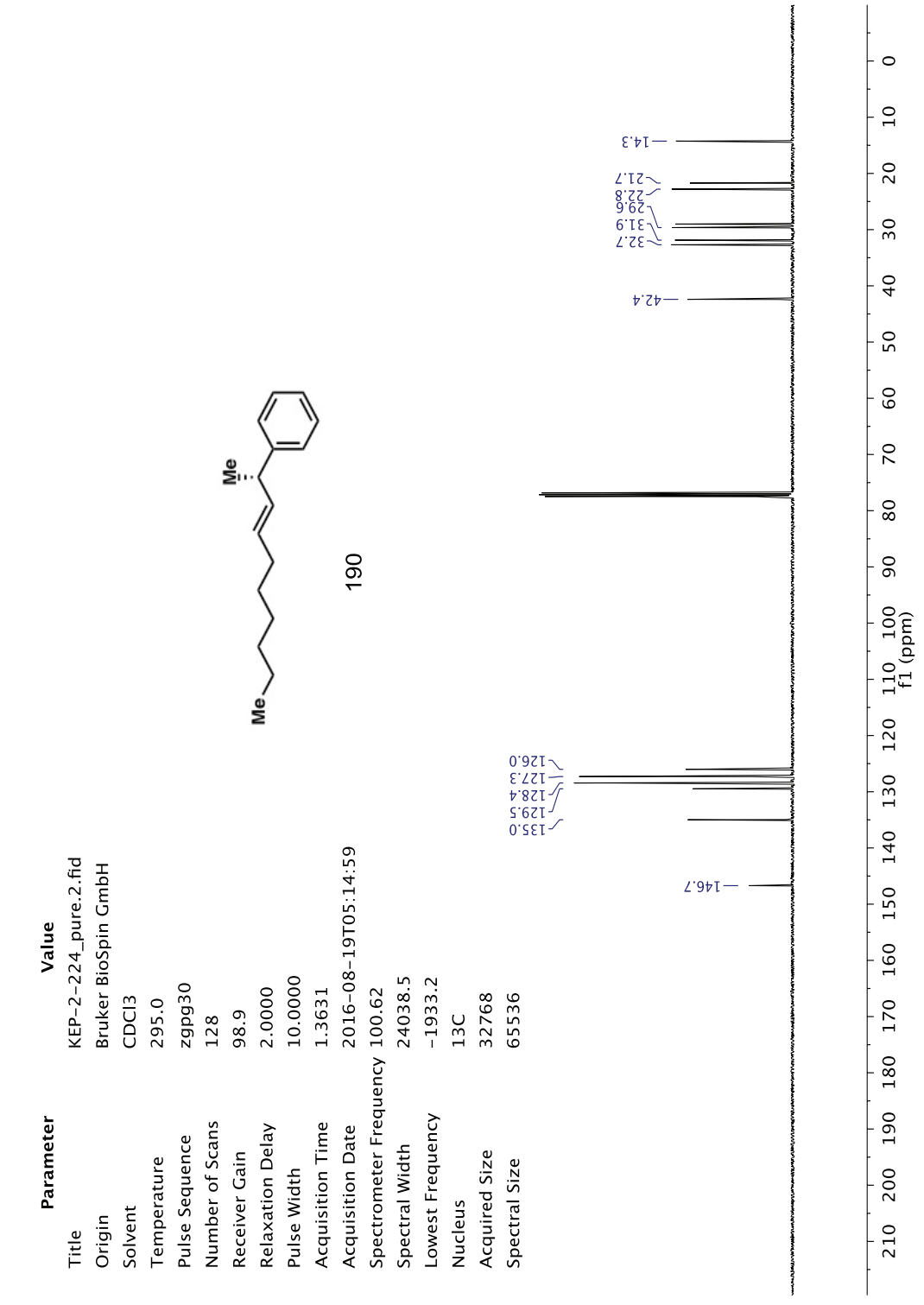

Parameter
Value
Title KEP-2-218_A_fr13-19.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 78.7
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2016-07-21T08:46:37
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1555.6
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
Me
BzO
188
A (m) 8.02
B (m) 7.56
C (m) 7.43
D (m) 7.26
E (m) 7.19
F (ddt) 5.77
G (dtd) 5.52
H (td) 4.36
I (m) 3.46
J (m) 2.50
K (d) 1.35
1.94
1.05
2.08
2.37
2.95
1.00
1.01
2.19
1.07
2.09
3.11
f1 (ppm)

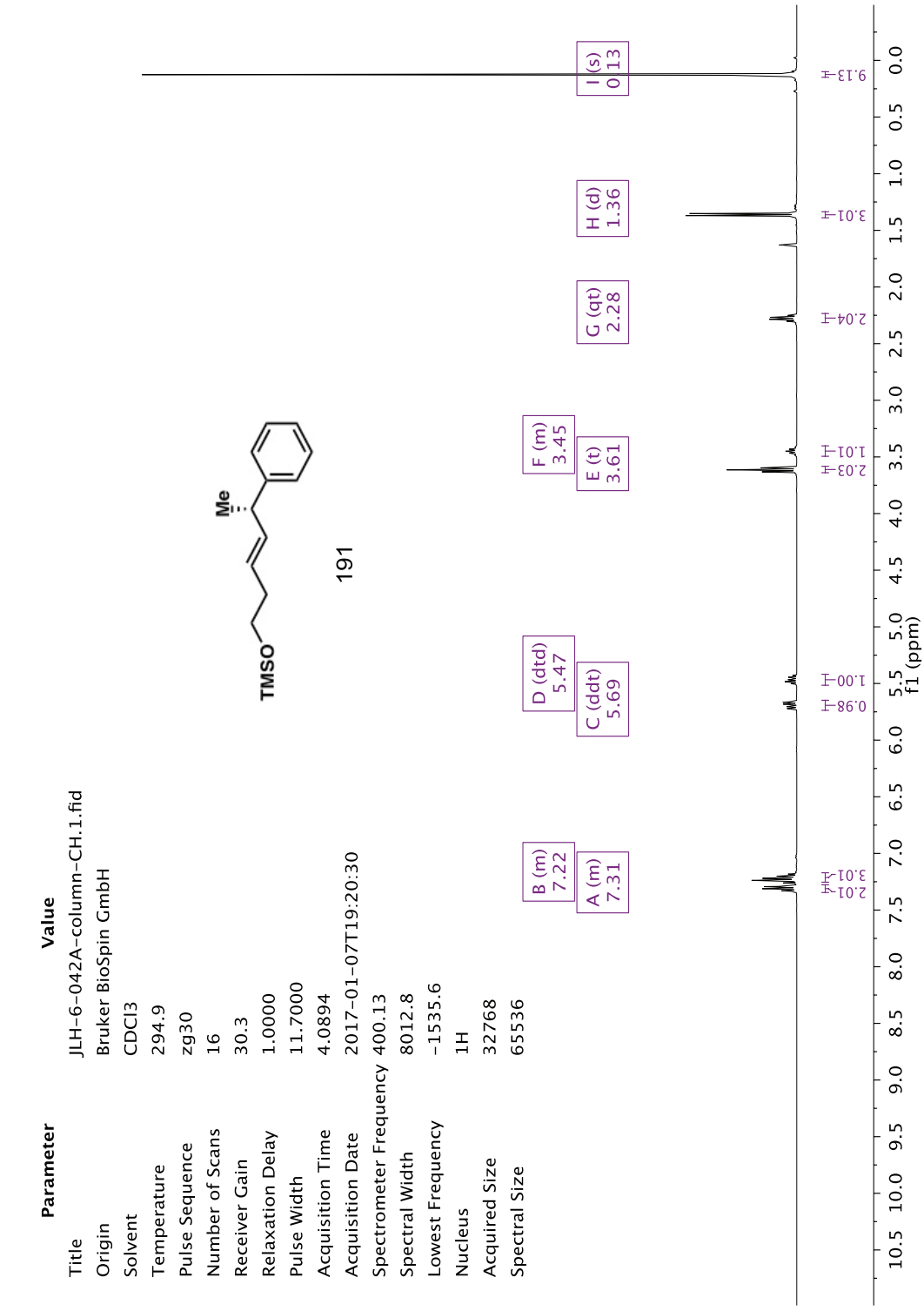

Parameter
Value
Title
KEP-2-218_A_fr13-19.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.0
Pulse Sequence
zgpg30
Number of Scans
128
Receiver Gain
78.7
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2016-07-21T08:54:27
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1936.2
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Me
BzO
188
166.7
146.0
138.3
133.0
130.5
129.7
128.5
128.4
127.3
126.2
124.3
64.4
42.4
32.2
21.4
f1 (ppm)

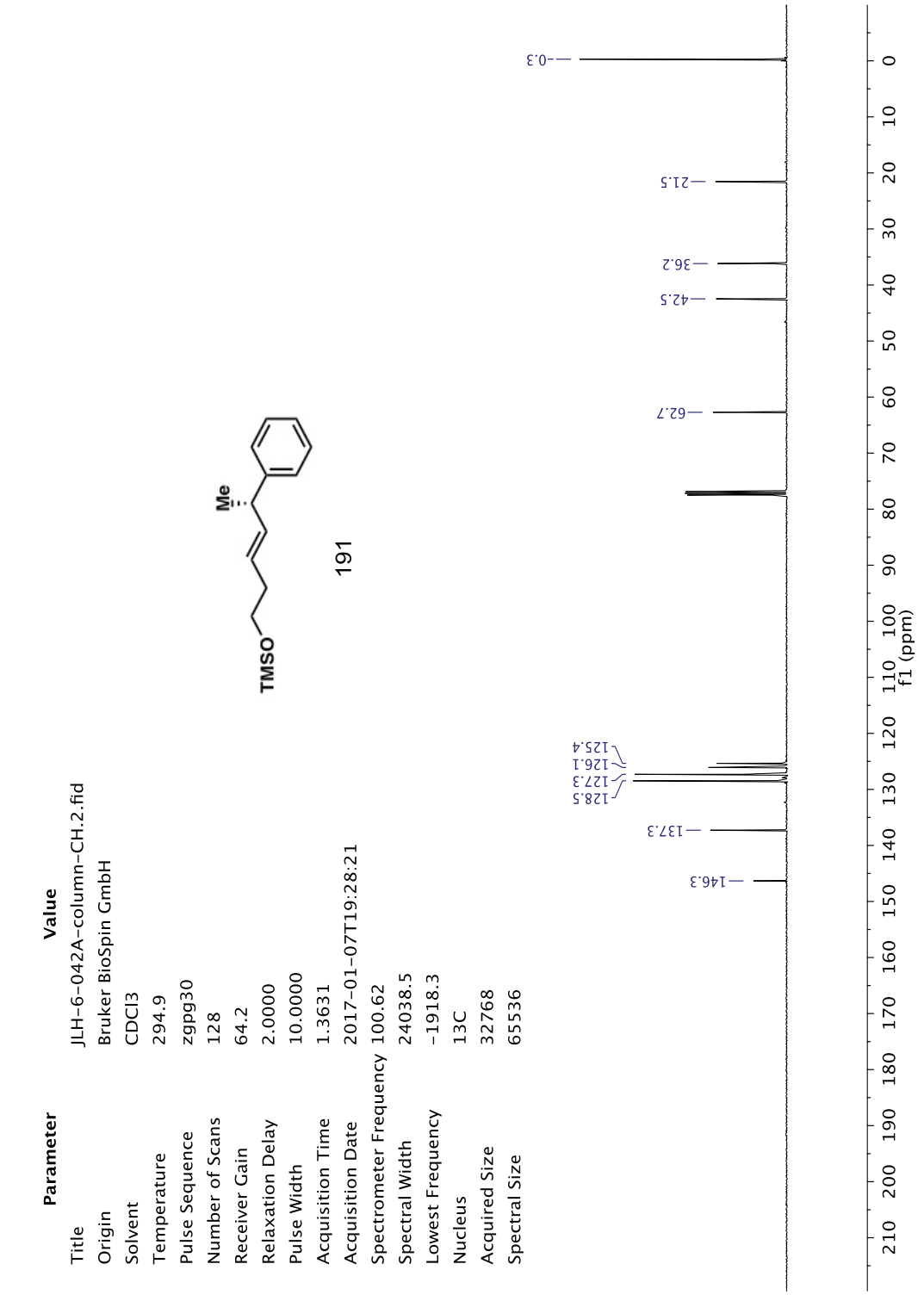

Parameter Value
Title JLH-5-109B.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 30.3
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2016-08-19T12:45:00
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1555.6
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
Me
Cl
189
A (m) 7.32
B (m) 7.22
C (ddt) 5.69
D (dtd) 5.43
E (t) 3.54
F (m) 3.45
G (m) 2.20
H (m) 1.86
I (d) 1.36
2.11
3.13
1.00
1.00
2.05
1.05
3.12
2.05
2.04
f1 (ppm)

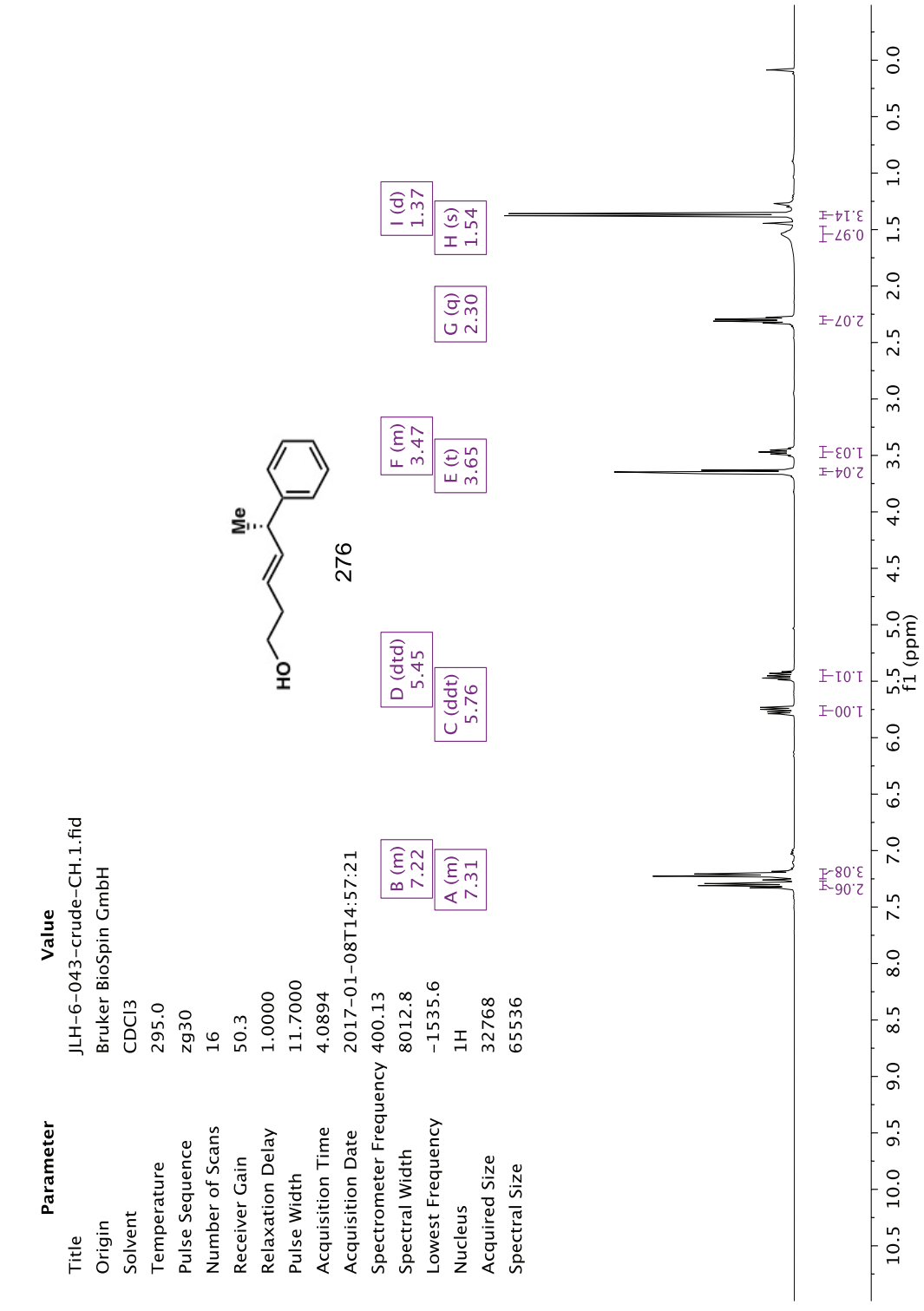

Parameter Value
Title JLH-5-109B.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 38.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-08-19T12:52:47
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1939.6
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
Cl
189
128.51
127.24
127.17
126.14
146.3
136.7
128.5
127.2
127.2
126.1
44.6
42.4
32.4
29.7
21.6
f1 (ppm)

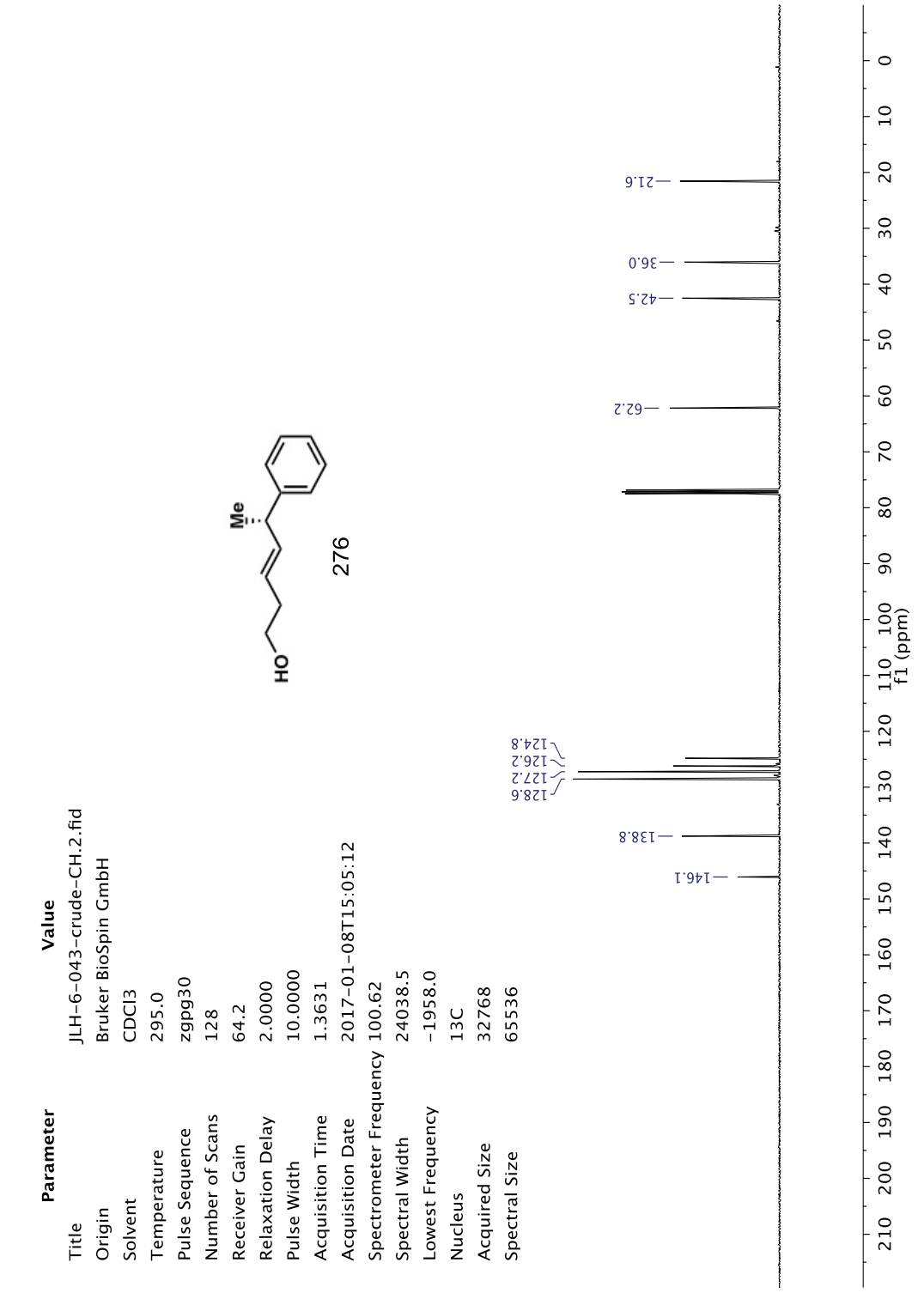

Parameter
Value
Title
KEP-2-224_pure.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
64.2
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2016-08-19T05:07:09
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1535.6
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
Me
Me
190
A (m) 7.30
B (m) 7.20
C (ddt) 5.60
D (dtd) 5.46
E (m) 3.43
F (m) 2.02
G (m) 1.32
H (m) 0.89
2.91
2.01
1.00
1.00
1.00
2.01
11.63
8.24
f1 (ppm)

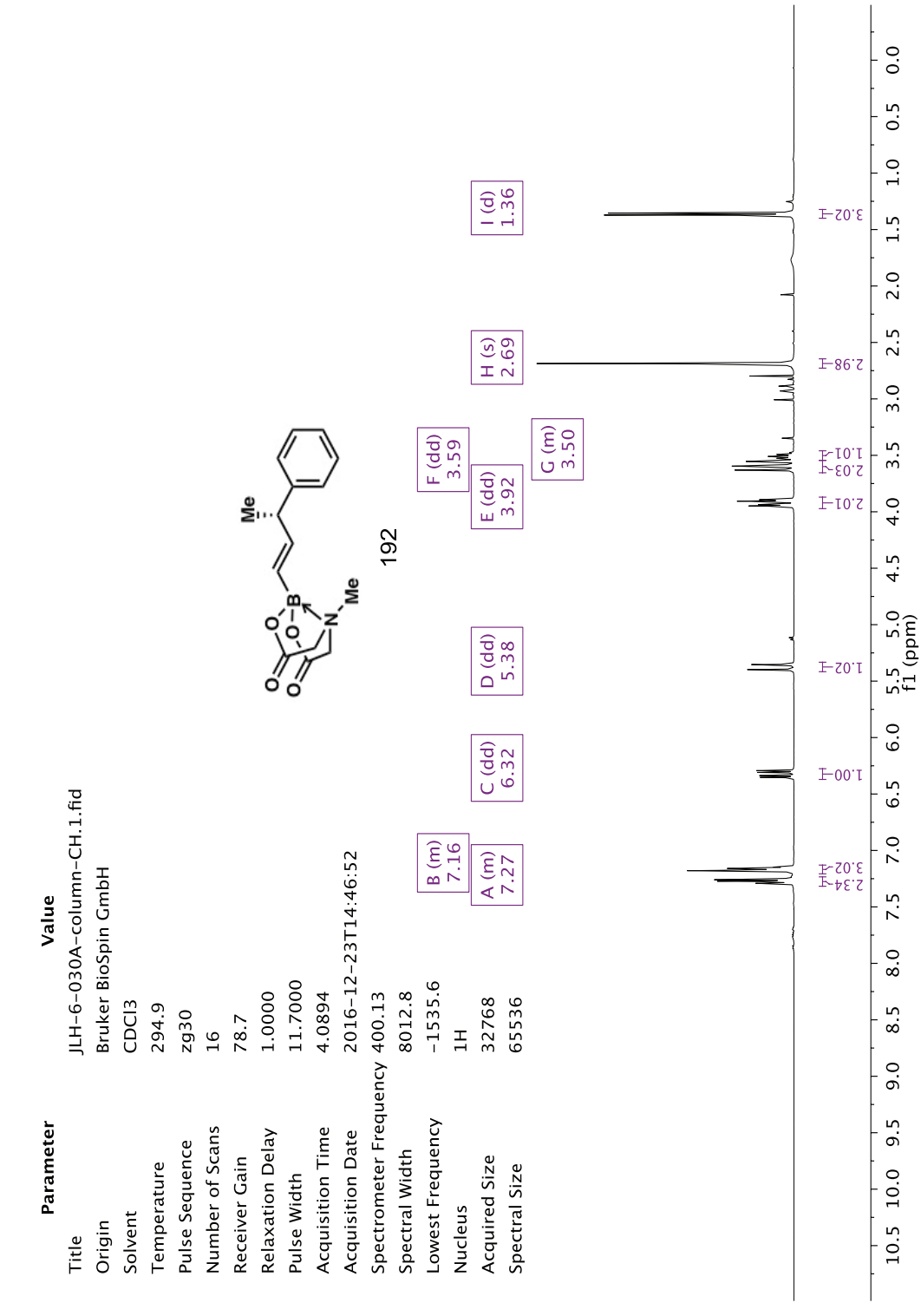

Parameter Value
Title KEP-2-224_pure.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 98.9
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-08-19T05:14:59
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1933.2
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
Me
190
146.7
135.0
129.5
128.4
127.3
126.0
42.4
32.7
31.9
29.6
22.8
21.7
14.3
f1 (ppm)

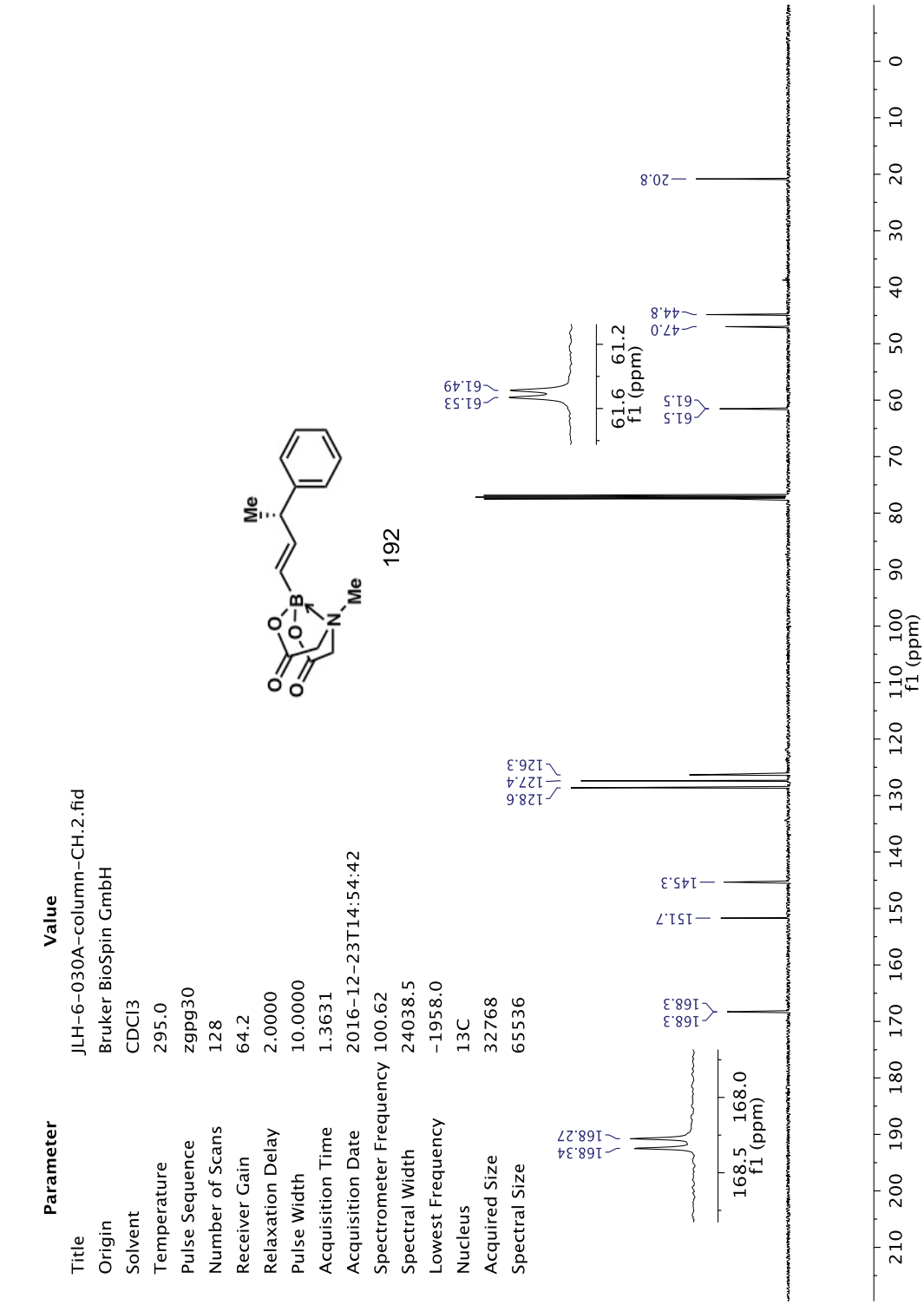

Parameter
Value
Title
JLH-6-042A-column-CH.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
30.3
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2017-01-07T19:20:30
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1535.6
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
Me
TMSO
191
A (m) 7.31
B (m) 7.22
C (ddt) 5.69
D (dtd) 5.47
E (t) 3.61
F (m) 3.45
G (qt) 2.28
H (d) 1.36
I (s) 0 13
2.01
3.01
0.98
1.00
2.03
1.01
2.04
3.01
9.13
f1 (ppm)

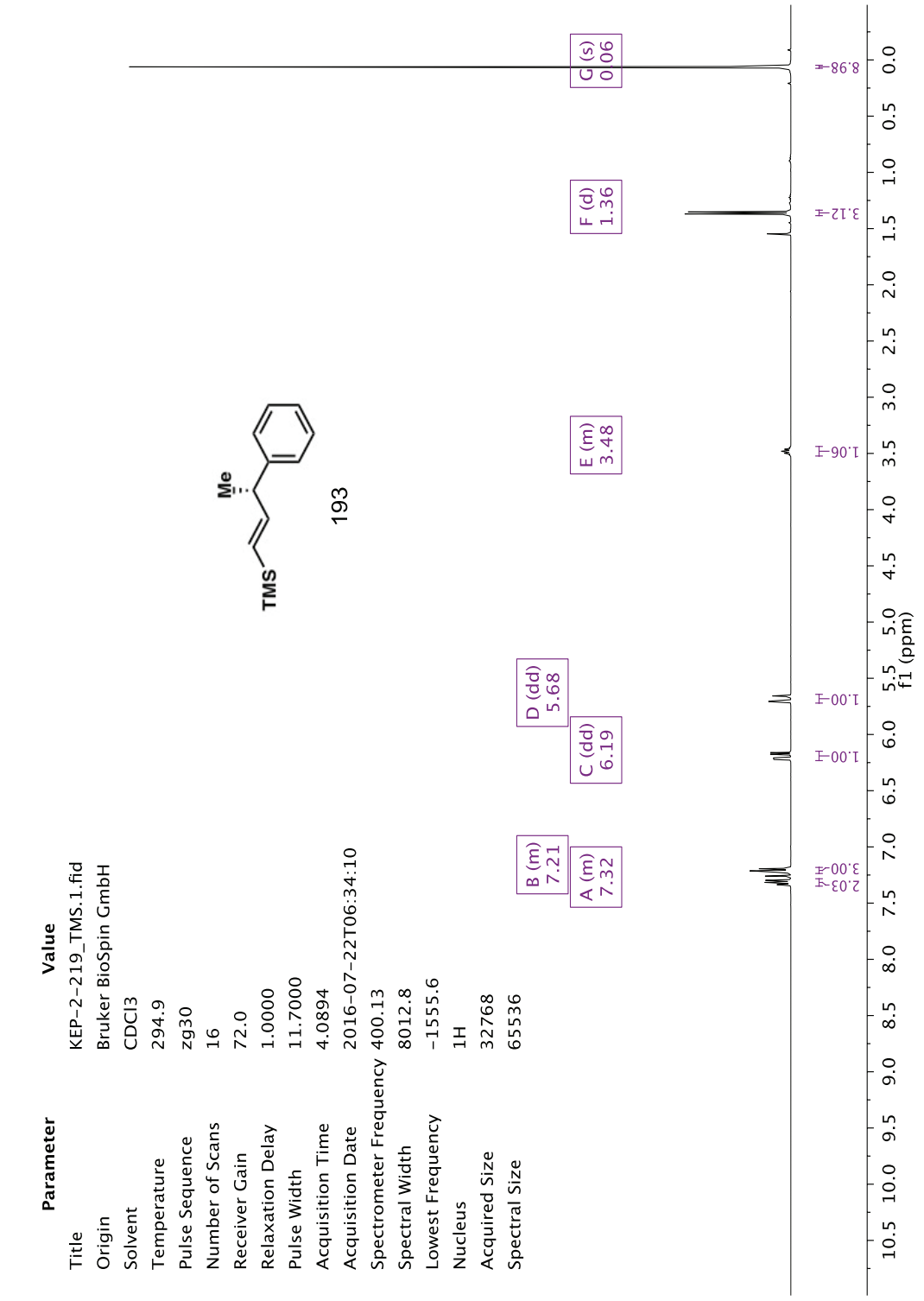

Parameter
Value
Title
JLH-6-042A-column-CH.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zgpg30
Number of Scans
128
Receiver Gain
64.2
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2017-01-07T19:28:21
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1918.3
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Me
TMSO
191
-0.3
21.5
36.2
42.5
62.7
128.5
127.3
126.1
125.4
137.3
146.3
f1 (ppm)

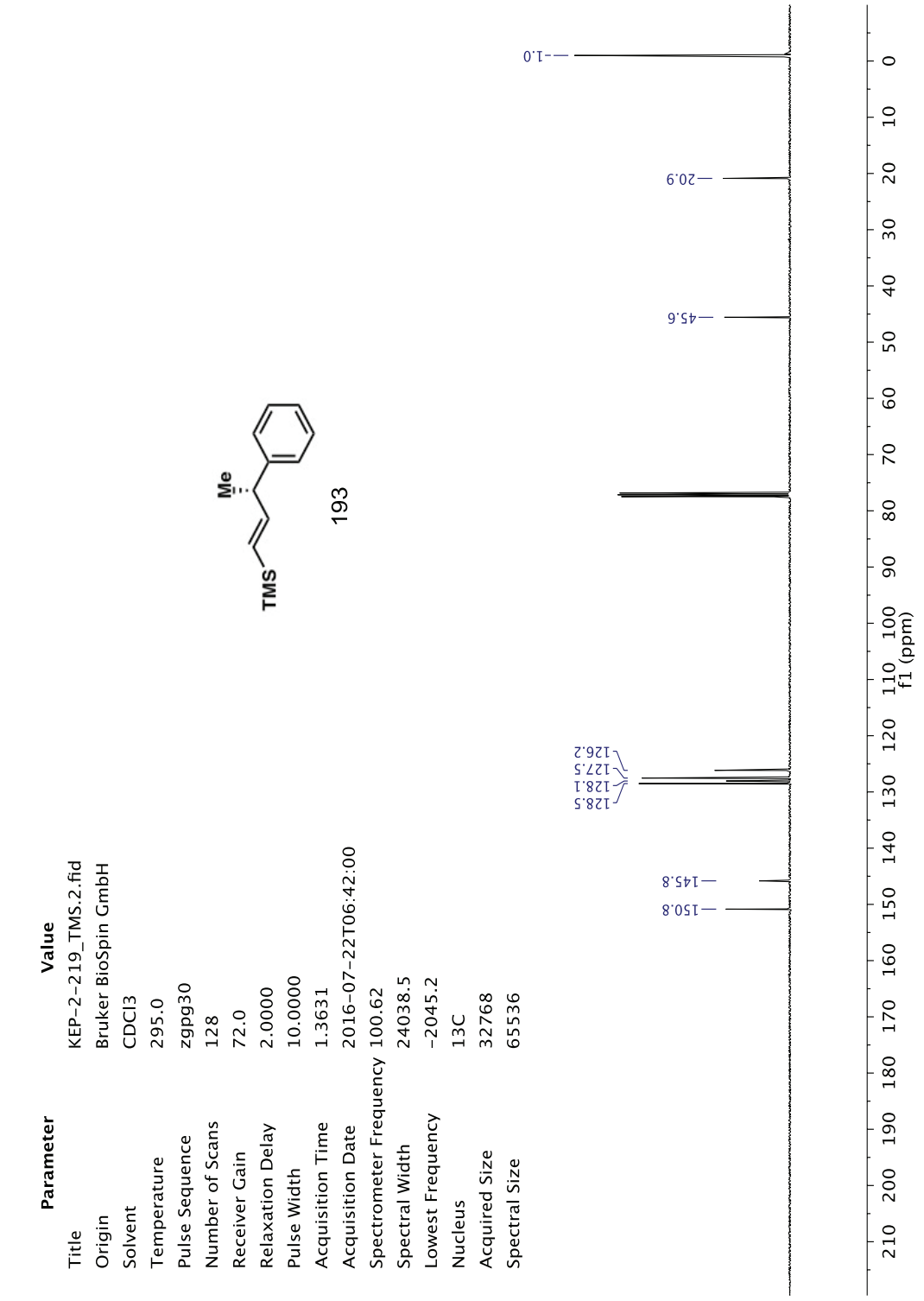

Parameter
Value
Title
JLH-6-043-crude-CH.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.0
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
50.3
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2017-01-08T14:57:21
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1535.6
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
Me
HO
276
A (m) 7.31
B (m) 7.22
C (ddt) 5.76
D (dtd) 5.45
E (t) 3.65
F (m) 3.47
G (q) 2.30
H (s) 1.54
I (d) 1.37
2.06
3.08
1.00
1.01
2.04
1.03
2.07
0.97
3.14
f1 (ppm)

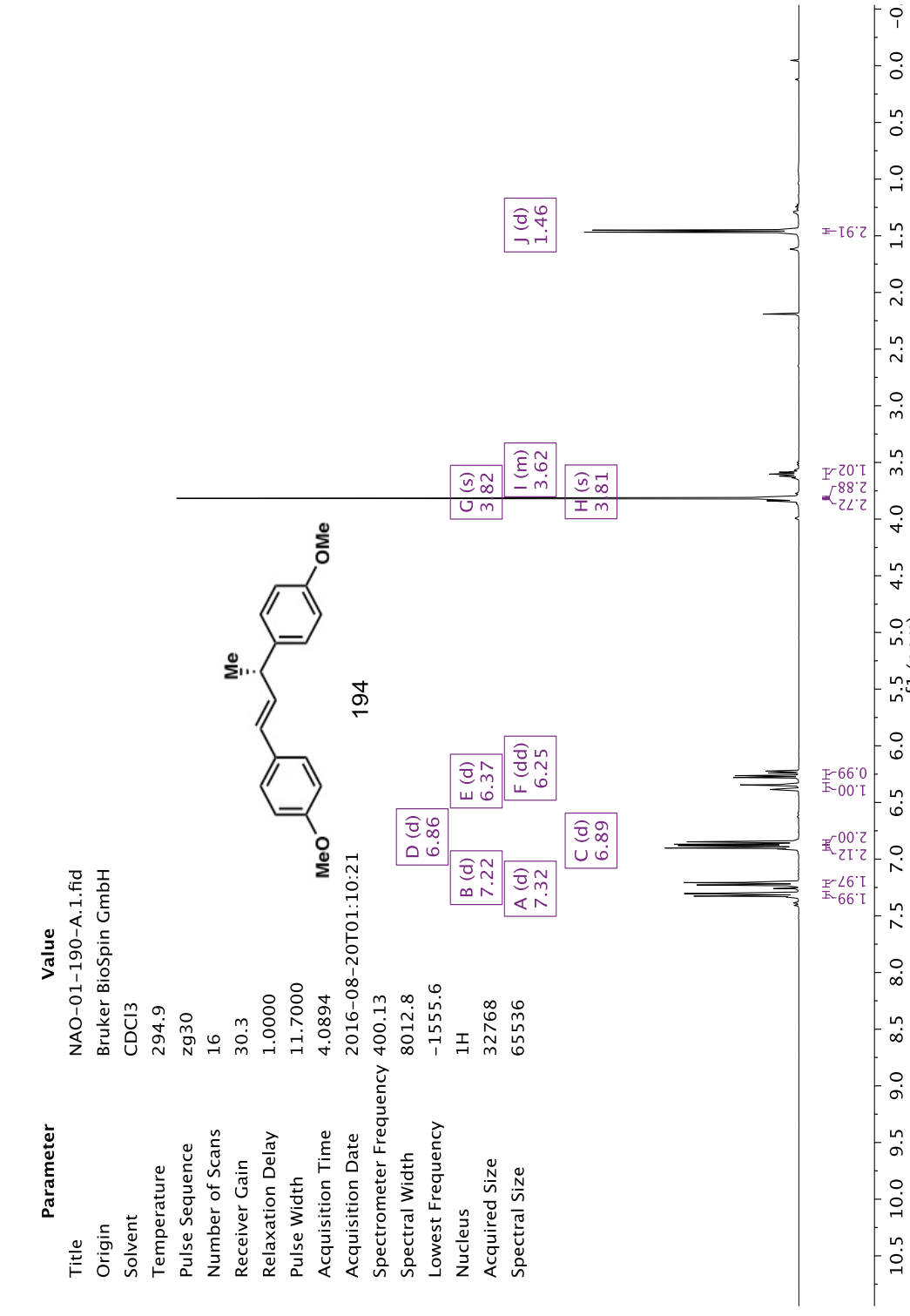

Parameter
Value
Title
JLH-6-043-crude-CH.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.0
Pulse Sequence
zgpg30
Number of Scans
128
Receiver Gain
64.2
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2017-01-08T15:05:12
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1958.0
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Me
HO
276
146.1
138.8
128.6
127.2
126.2
124.8
62.2
42.5
36.0
21.6
f1 (ppm)

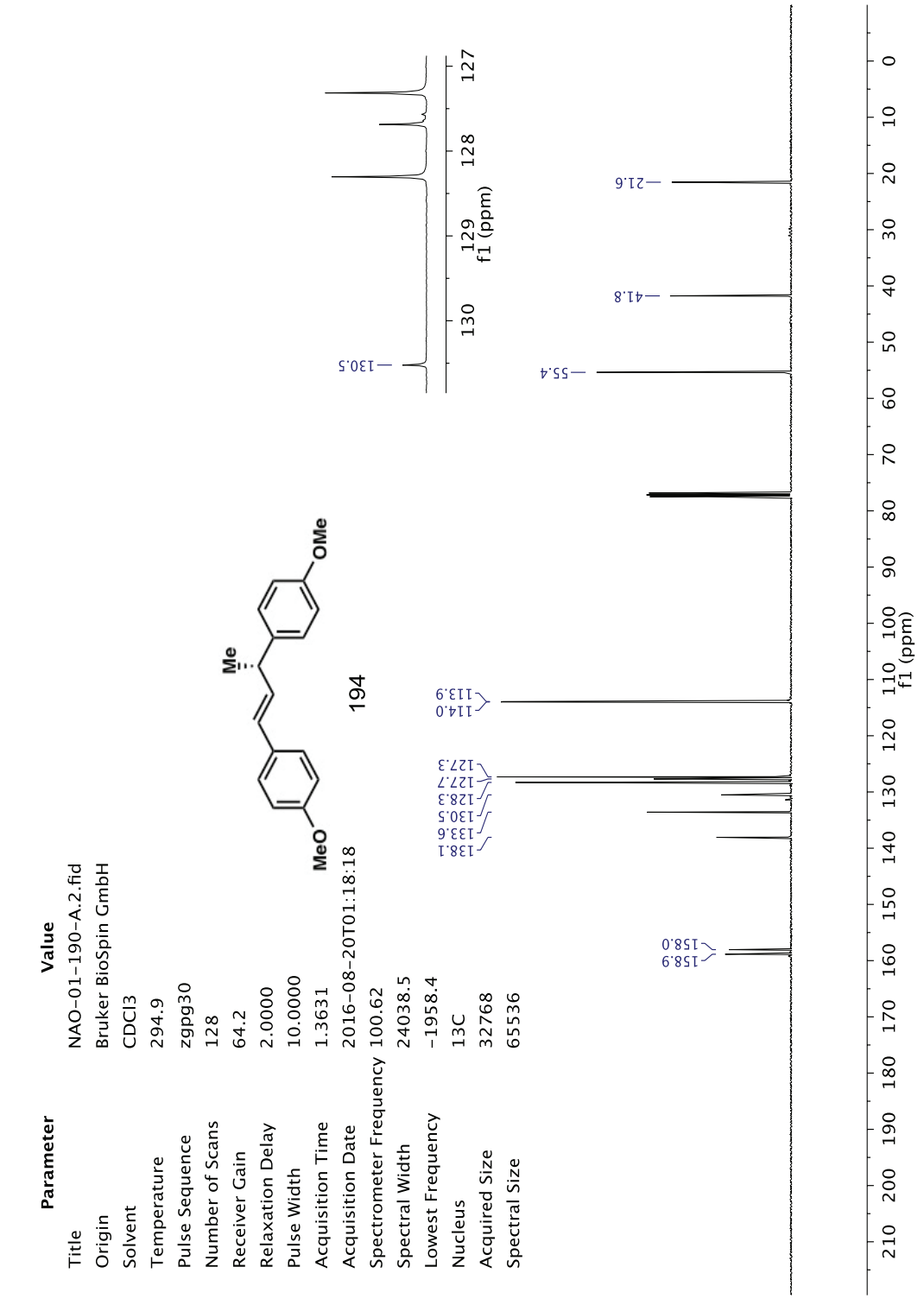

Parameter
Value
Title
JLH-6-030A-column-CH.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
78.7
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2016-12-23T14:46:52
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1535.6
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
192
Me
Me
A (m) 7.27
B (m) 7.16
C (dd) 6.32
D (dd) 5.38
E (dd) 3.92
F (dd) 3.59
G (m) 3.50
H (s) 2.69
I (d) 1.36
2.34
3.02
1.00
1.02
2.01
2.03
1.01
2.98
3.02
f1 (ppm)

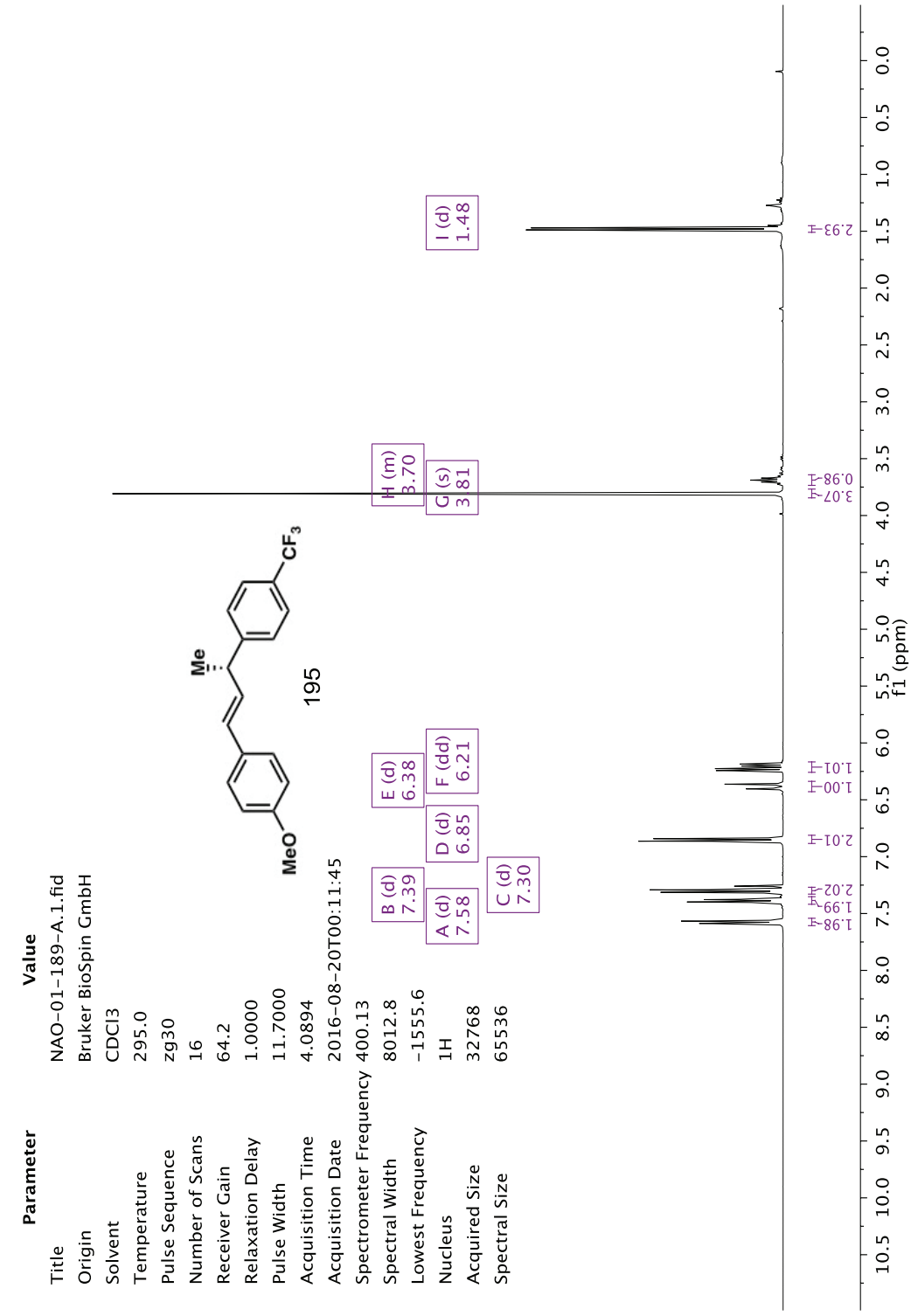

Parameter
Value
Title
JLH-6-030A-column-CH.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.0
Pulse Sequence
zgpg30
Number of Scans
128
Receiver Gain
64.2
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2016-12-23T14:54:42
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1958.0
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
192
Me
Me
N
B
O
O
O
O
168.34
168.27
168.3
168.3
151.7
145.3
128.6
127.4
126.3
61.53
61.49
61.5
61.5
47.0
44.8
20.8
168.5 168.0
f1 (ppm)
61.6 61.2
f1 (ppm)
f1 (ppm)

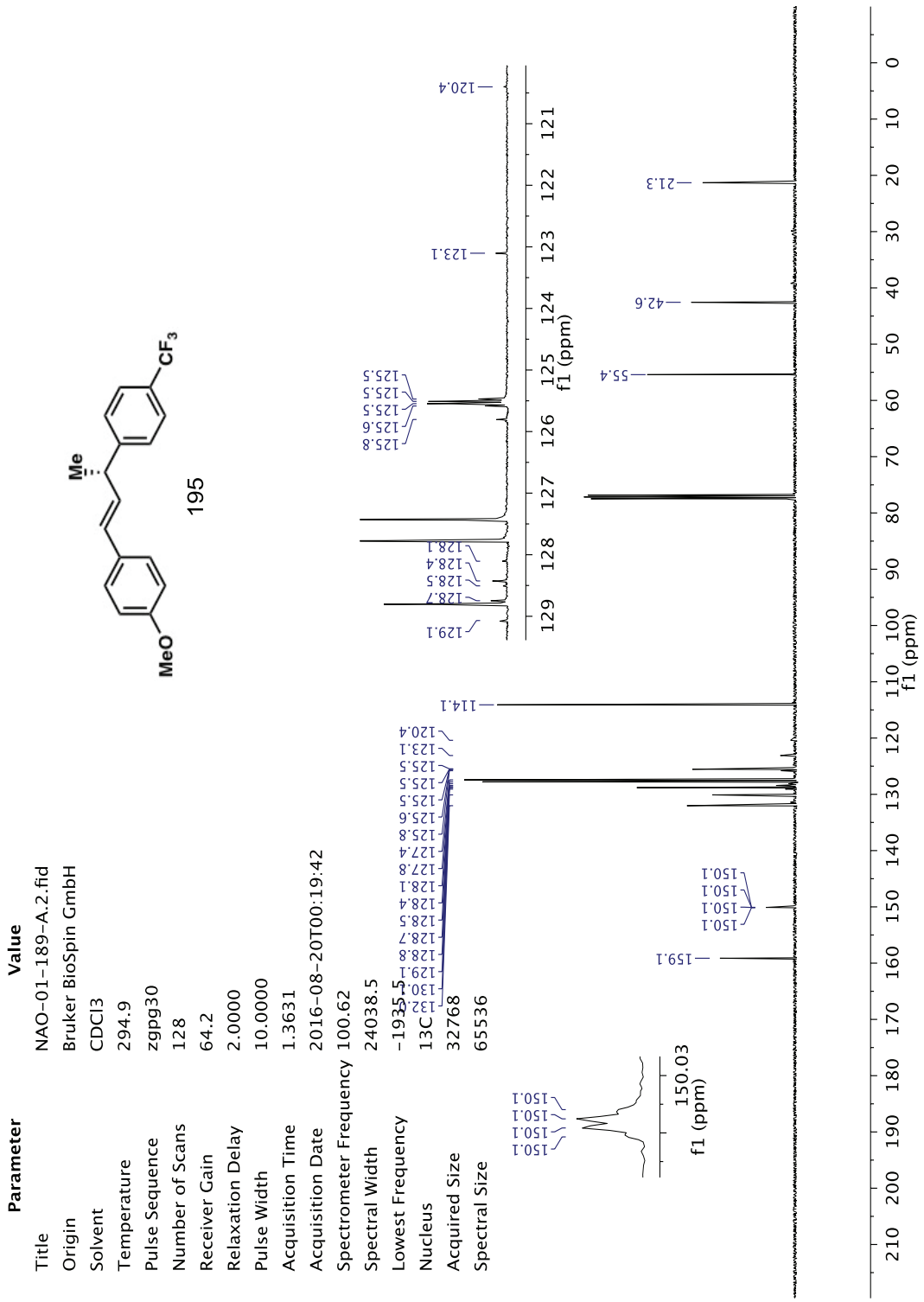

Parameter
Value
Title
KEP-2-219_TMS.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
72.0
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2016-07-22T06:34:10
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1555.6
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
Me
TMS
193
A (m) 7.32
B (m) 7.21
C (dd) 6.19
D (dd) 5.68
E (m) 3.48
F (d) 1.36
G (s) 0.06
2.03
3.00
1.00
1.00
1.06
3.12
8.98
f1 (ppm)


Parameter
Value
Title
KEP-2-219_TMS.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.0
Pulse Sequence
zgpg30
Number of Scans
128
Receiver Gain
72.0
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2016-07-22T06:42:00
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-2045.2
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Me
TMS
193
150.8
145.8
128.5
128.1
127.5
126.2
45.6
20.9
1.0
f1 (ppm)


Parameter
Value
Title
NAO-01-190-A.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
30.3
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2016-08-20T01:10:21
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1555.6
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
Me
OMe
MeO
194
A (d) 7.32
B (d) 7.22
C (d) 6.89
D (d) 6.86
E (d) 6.37
F (dd) 6.25
G (s) 3.82
H (s) 3.81
I (m) 3.62
J (d) 1.46
1.99
1.97
2.12
2.00
1.00
0.99
2.72
2.88
1.02
2.91
f1 (ppm)


Parameter
Value
Title
NAO-01-190-A.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zgpg30
Number of Scans
128
Receiver Gain
64.2
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2016-08-20T01:18:18
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1958.4
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Me
OMe
MeO
194
158.9
158.0
138.1
133.6
130.5
128.3
127.7
127.3
114.0
113.9
55.4
41.8
21.6
130.5
f1 (ppm)
f1 (ppm)

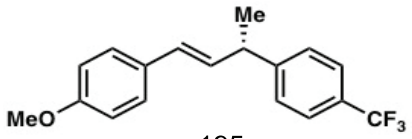

Parameter Value
Title NAO-01-189-A.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 64.2
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2016-08-20T00:11:45
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1555.6
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
Me
MeO
CF3
195
A (d) 7.58
B (d) 7.39
C (d) 7.30
D (d) 6.85
E (d) 6.38
F (dd) 6.21
H (m) 3.70
G (s) 3.81
I (d) 1.48
1.98
1.99
2.02
2.01
1.00
1.01
3.07
0.98
2.93
f1 (ppm)



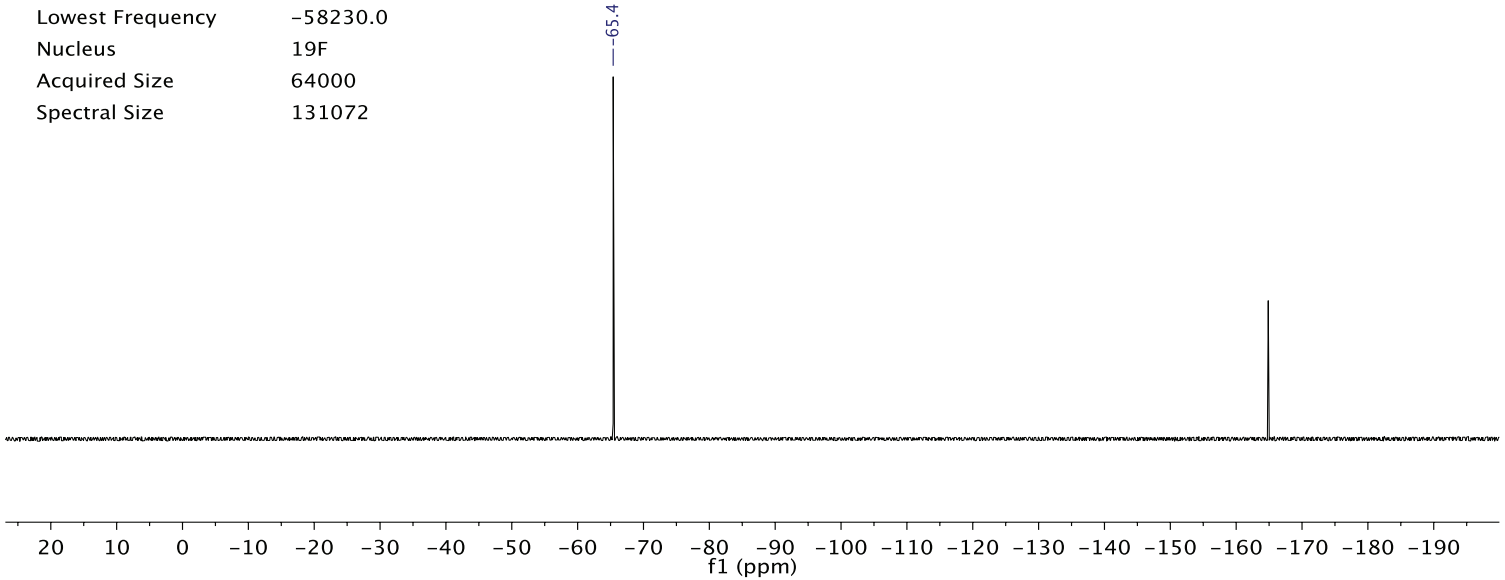
Parameter	Value
Title	NAO-01-189-A.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	294.9
Pulse Sequence	zgpg30
Number of Scans	128
Receiver Gain	64.2
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2016-08-20T00:19:42
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1935.5
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

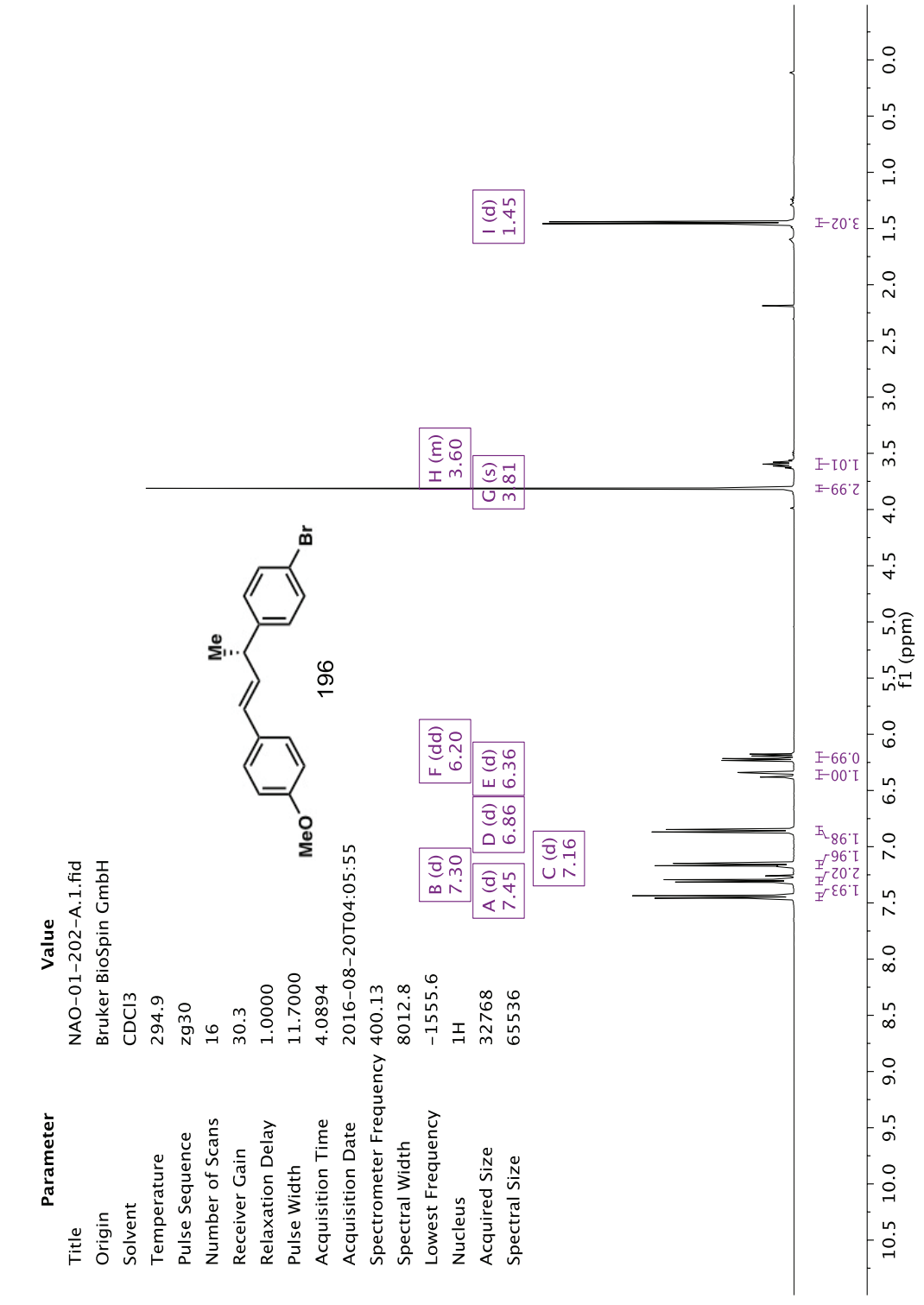
Parameter	Value
Title	NAO-01-189A
Origin	Varian
Solvent	"cdcl3"
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2016-08-31T23:27:51
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-57338.6
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

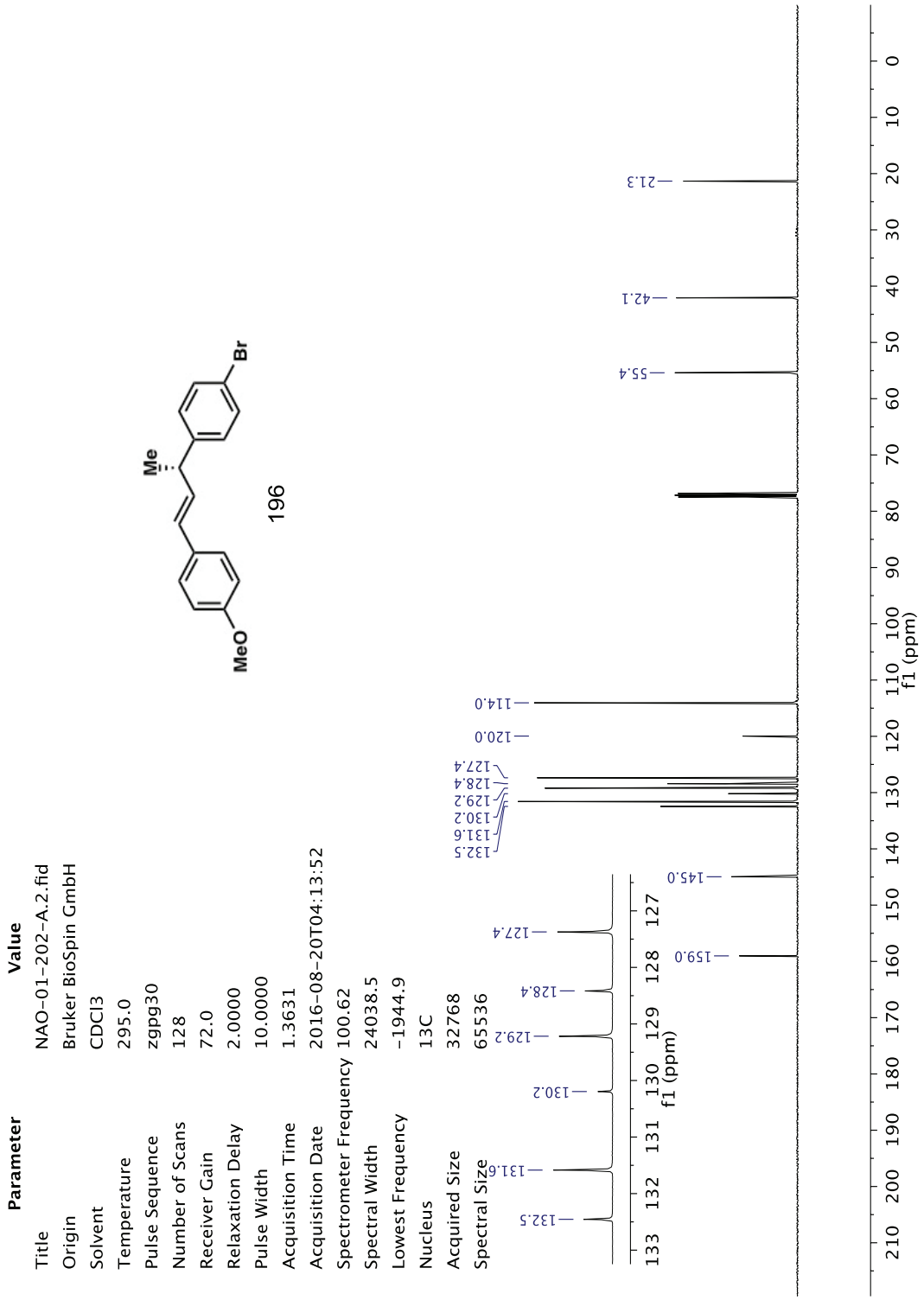
Parameter	Value
Title	NAO-01-189A-C6F6
Origin	Varian
Solvent	"cdcl3"
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2016-08-31T23:32:04
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-58230.0
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

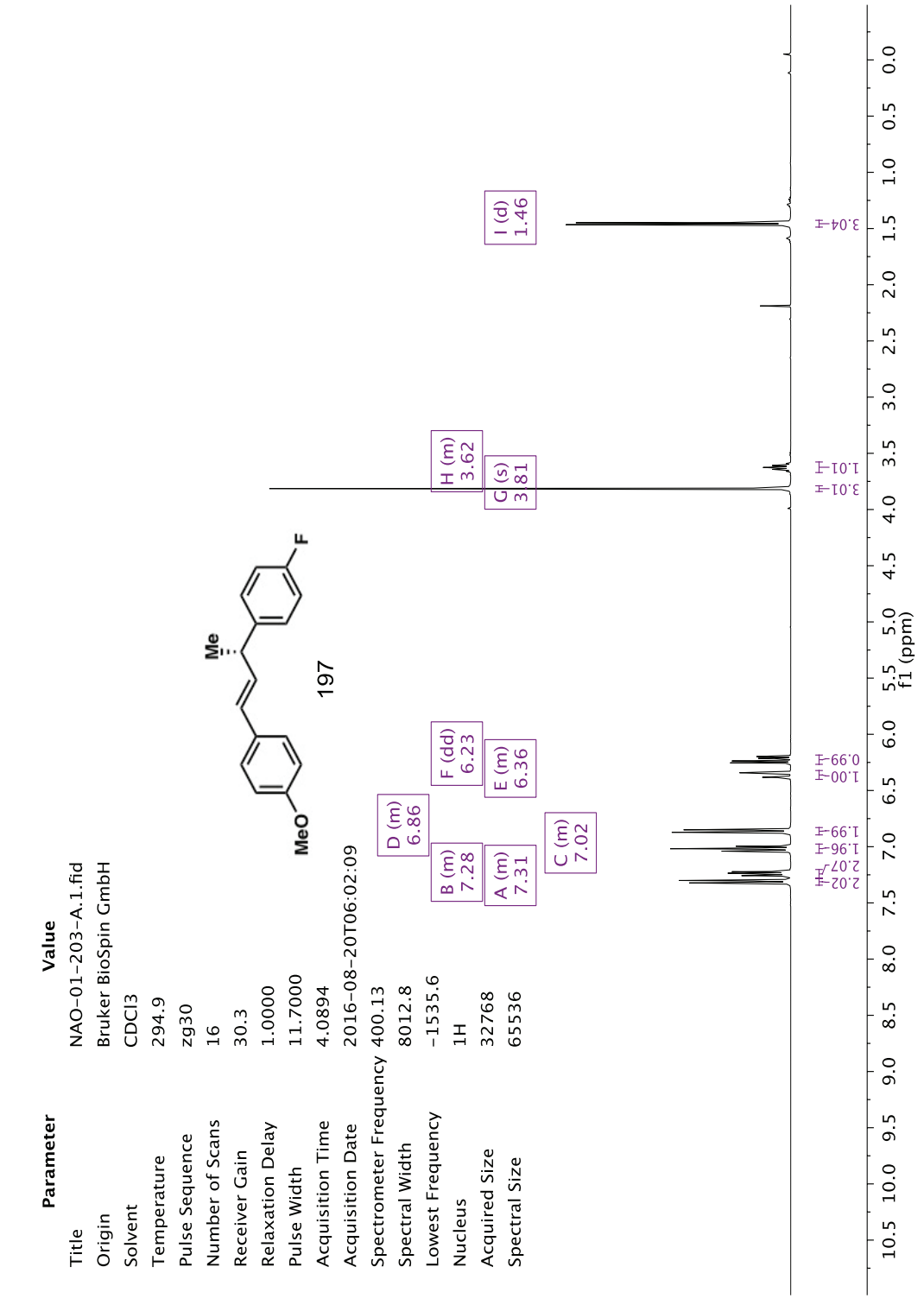


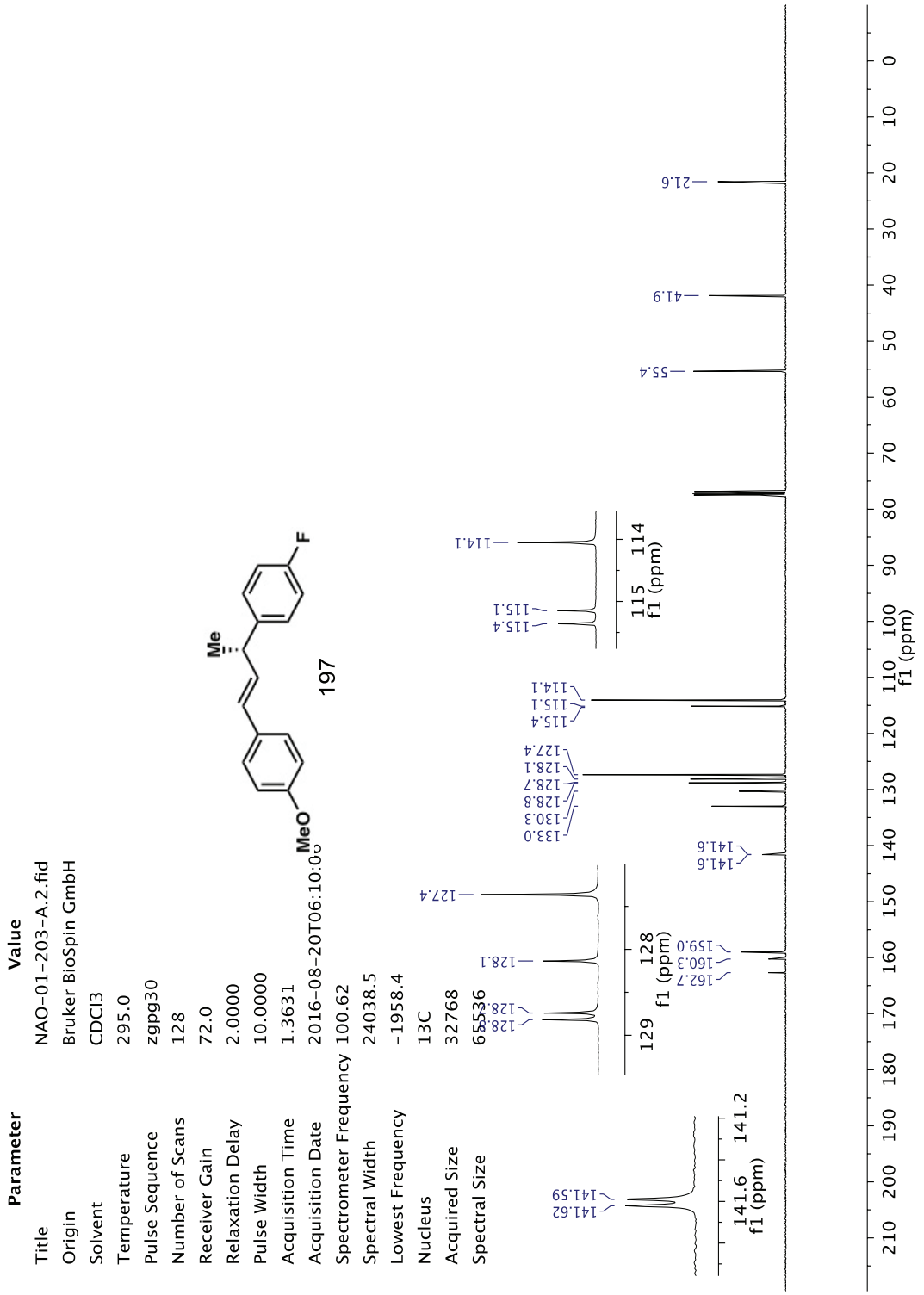
195
with C_6F_6




Parameter Value
Title NAO-01-202-A.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 294.9
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 30.3
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2016-08-20T04:05:55
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1555.6
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
Me
Br
MeO
196
A (d) 7.45
B (d) 7.30
C (d) 7.16
D (d) 6.86
E (d) 6.36
F (dd) 6.20
G (s) 3.81
H (m) 3.60
I (d) 1.45
1.93
2.02
1.96
1.98
1.00
0.99
2.99
1.01
3.02
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

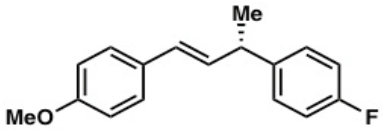

Parameter Value
Title NAO-01-202-A.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-08-20T04:13:52
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1944.9
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
Br
MeO
196
f1 (ppm)


Parameter
Value
Title
NAO-01-203-A.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
30.3
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2016-08-20T06:02:09
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1535.6
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
Me
MeO
F
197
A (m) 7.31
B (m) 7.28
C (m) 7.02
D (m) 6.86
E (m) 6.36
F (dd) 6.23
G (s) 3.81
H (m) 3.62
I (d) 1.46
2.02
2.07
1.96
1.99
1.00
0.99
3.01
1.01
3.04
f1 (ppm)

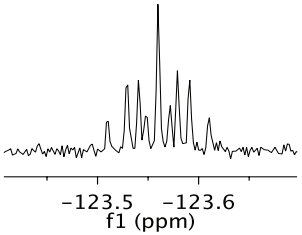

Parameter Value
Title NAO-01-203-A.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-08-20T06:10:0
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1958.4
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
F
MeO
197
f1 (ppm)

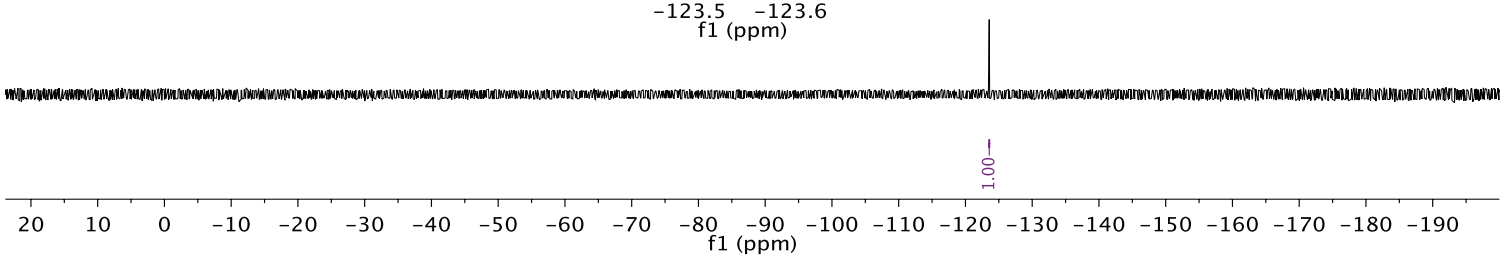
Parameter	Value
Title	JLH-6-040B
Origin	Varian
Solvent	"cdcl3"
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2017-01-09T23:50:23
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56468.7
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

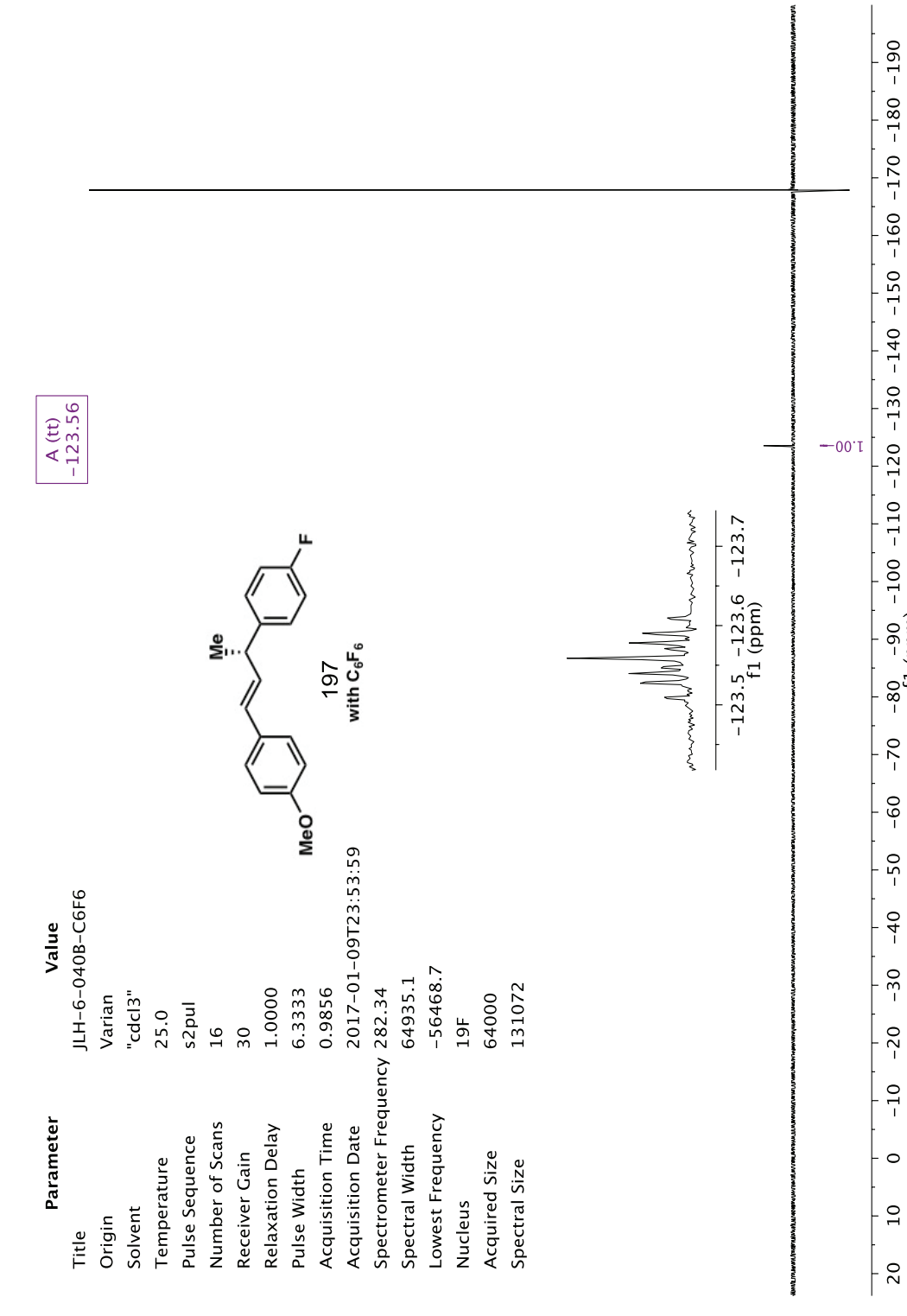
A (tt)
-123.56



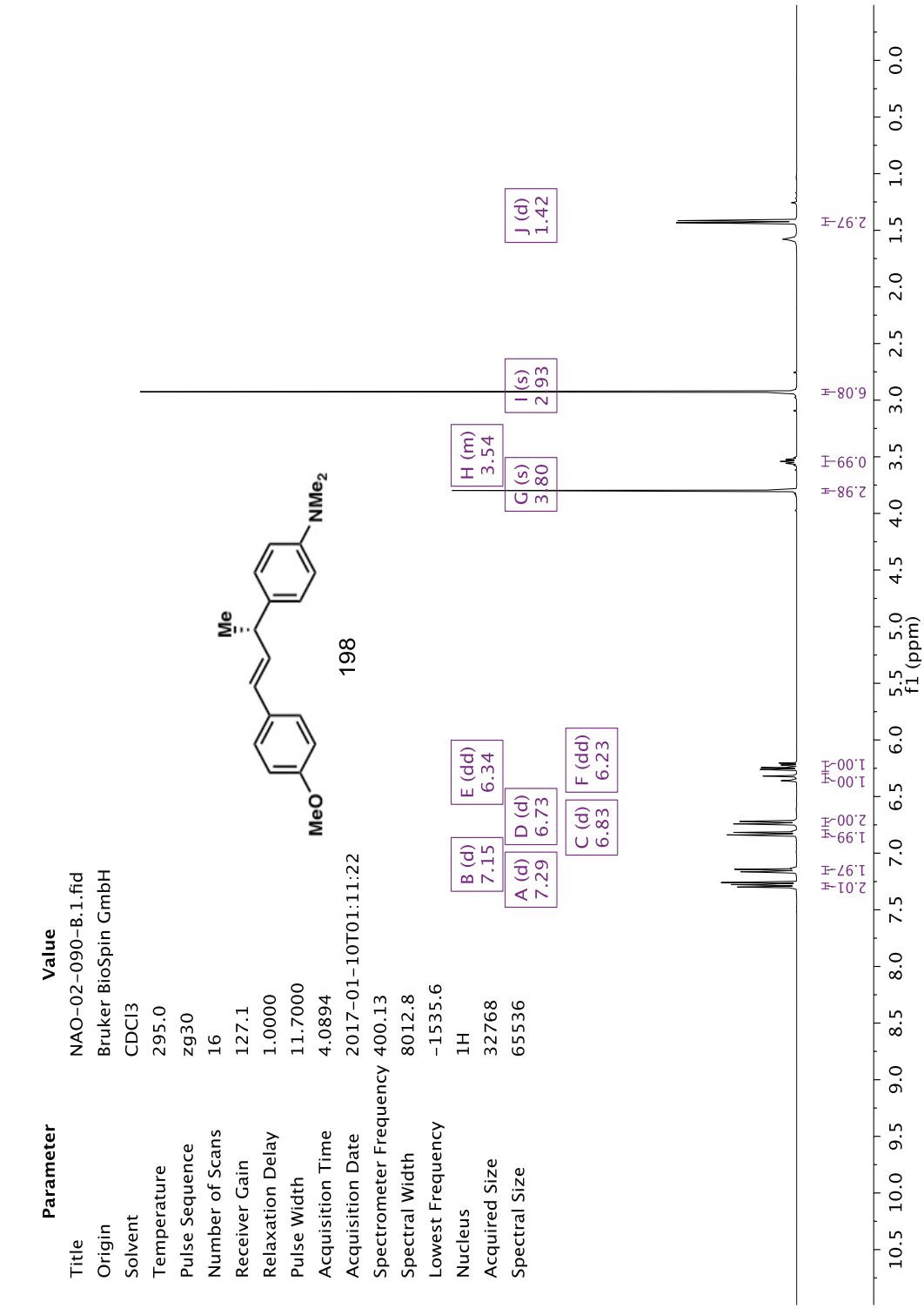
197



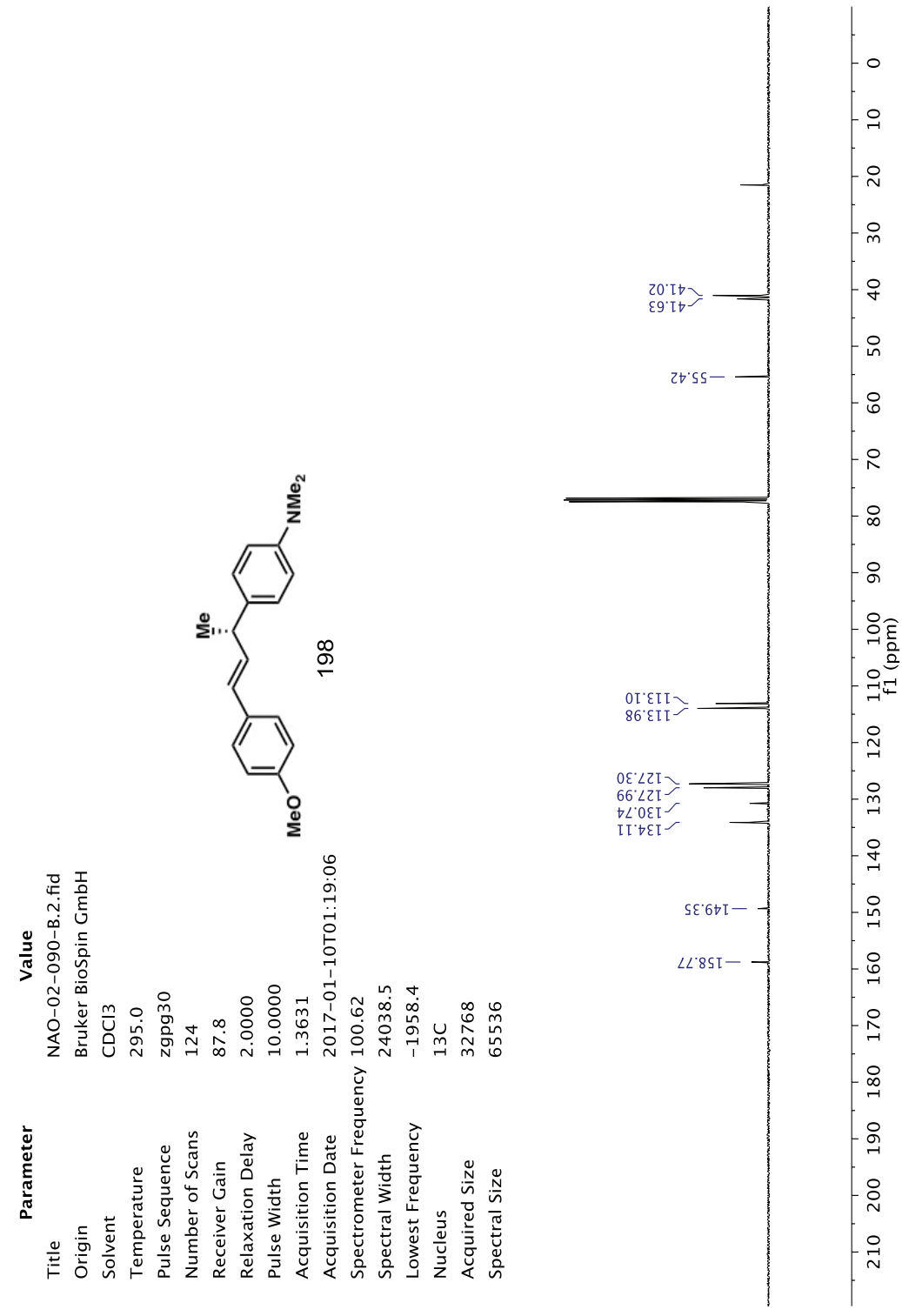


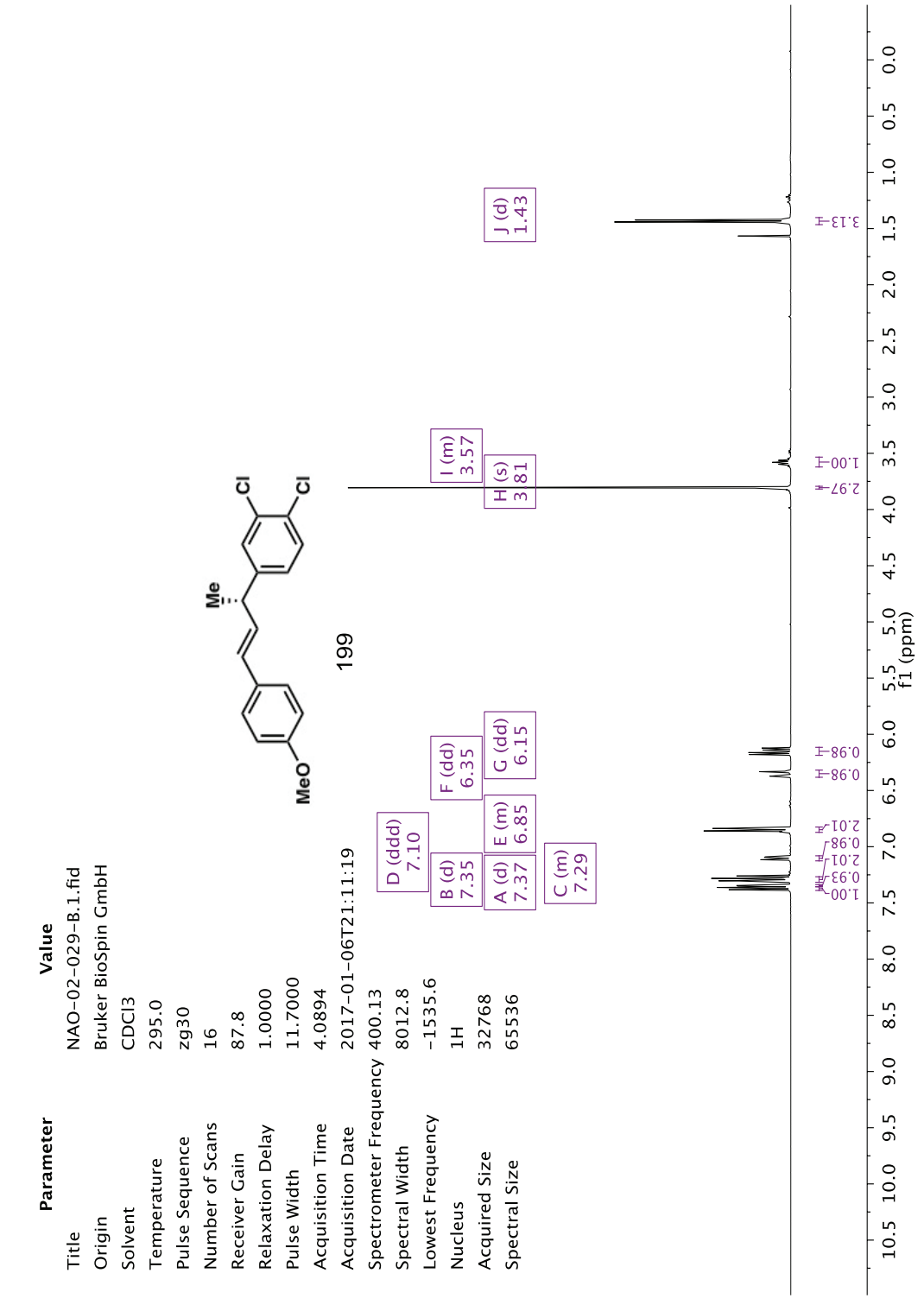


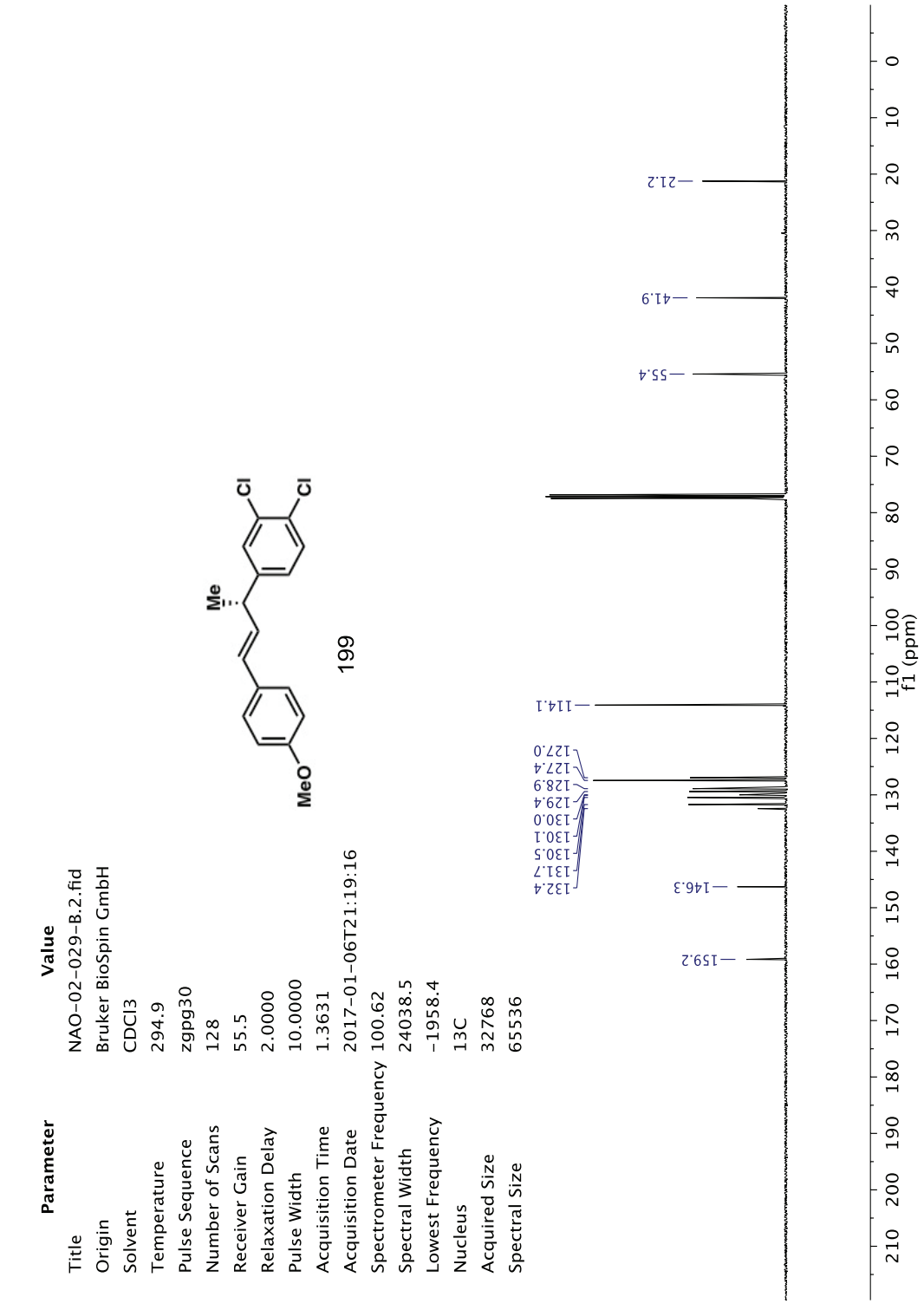
Parameter	Value
Title	JLH-6-040B-C6F6
Origin	Varian
Solvent	"cdcl3"
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2017-01-09T23:53:59
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56468.7
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

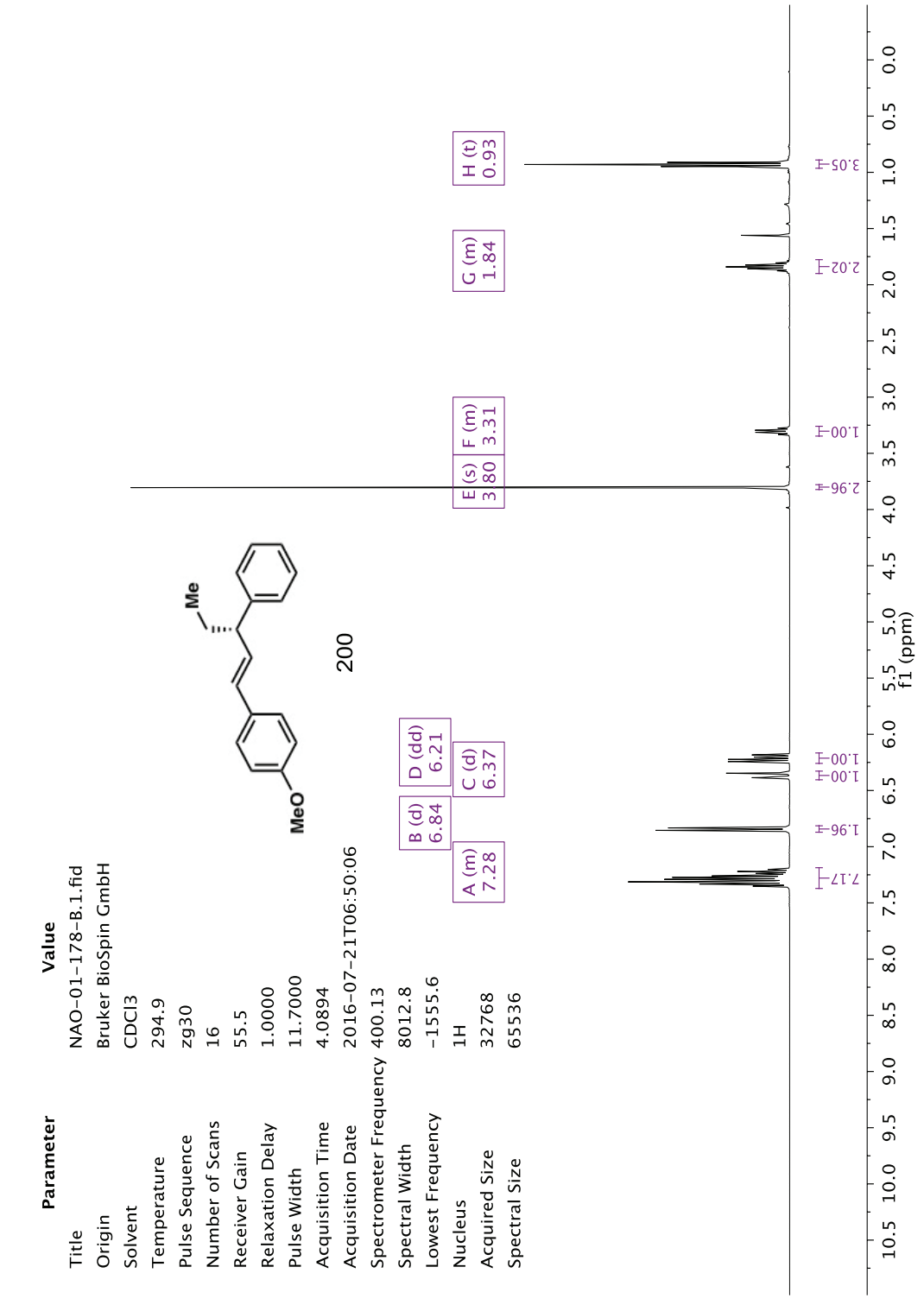

Parameter
Value
Title
NAO-02-090-B.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.0
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
127.1
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2017-01-10T01:11:22
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1535.6
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
198
Me
NMe2
MeO
A (d) 7.29
B (d) 7.15
C (d) 6.83
D (d) 6.73
E (dd) 6.34
F (dd) 6.23
G (s) 3.80
H (m) 3.54
I (s) 2.93
J (d) 1.42
2.01
1.97
1.99
2.00
1.00
1.00
2.98
0.99
6.08
2.97
f1 (ppm)

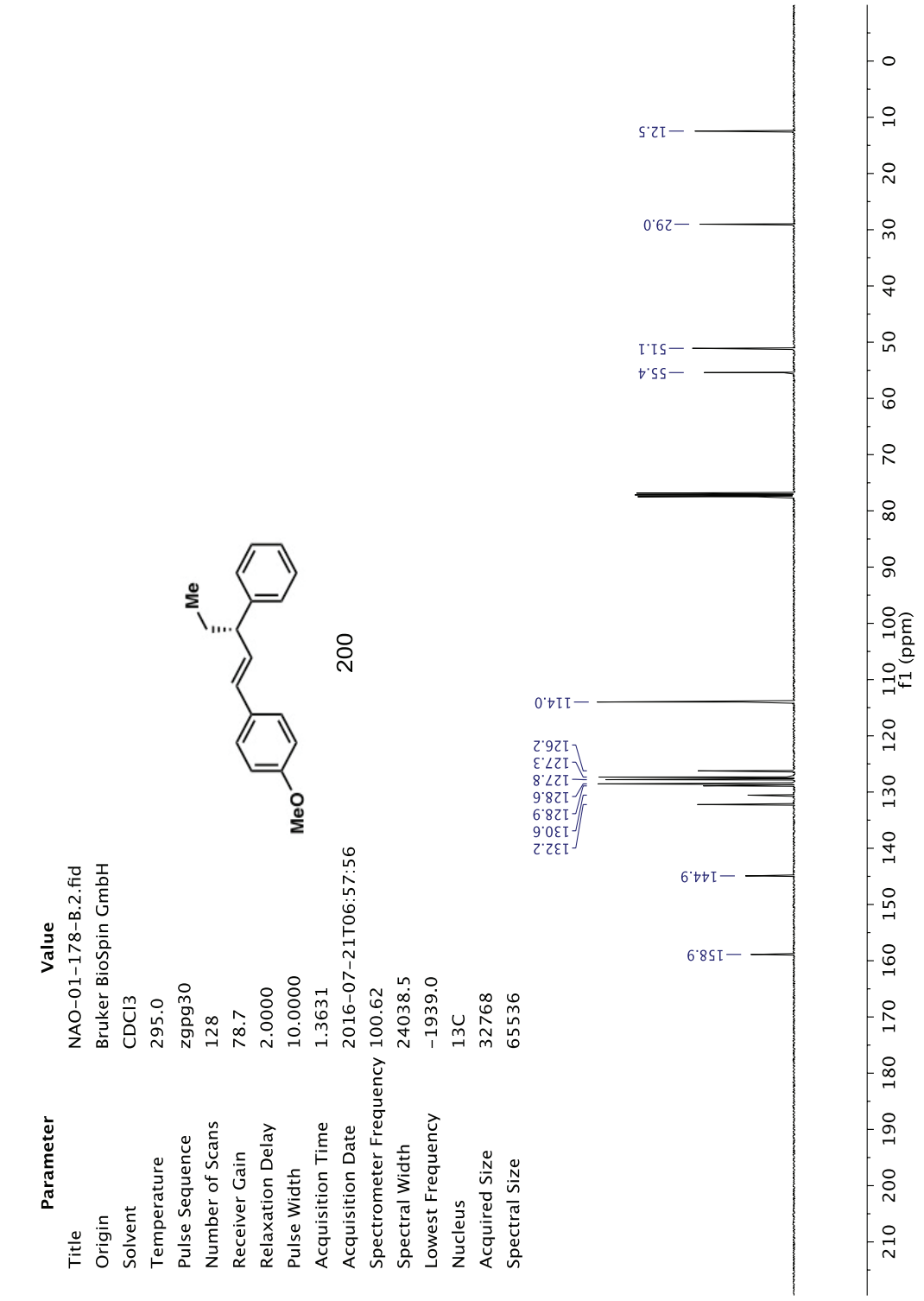
Parameter	Value
Title	NAO-02-090-B.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	zgpg30
Number of Scans	124
Receiver Gain	87.8
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2017-01-10T01:19:06
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1958.4
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

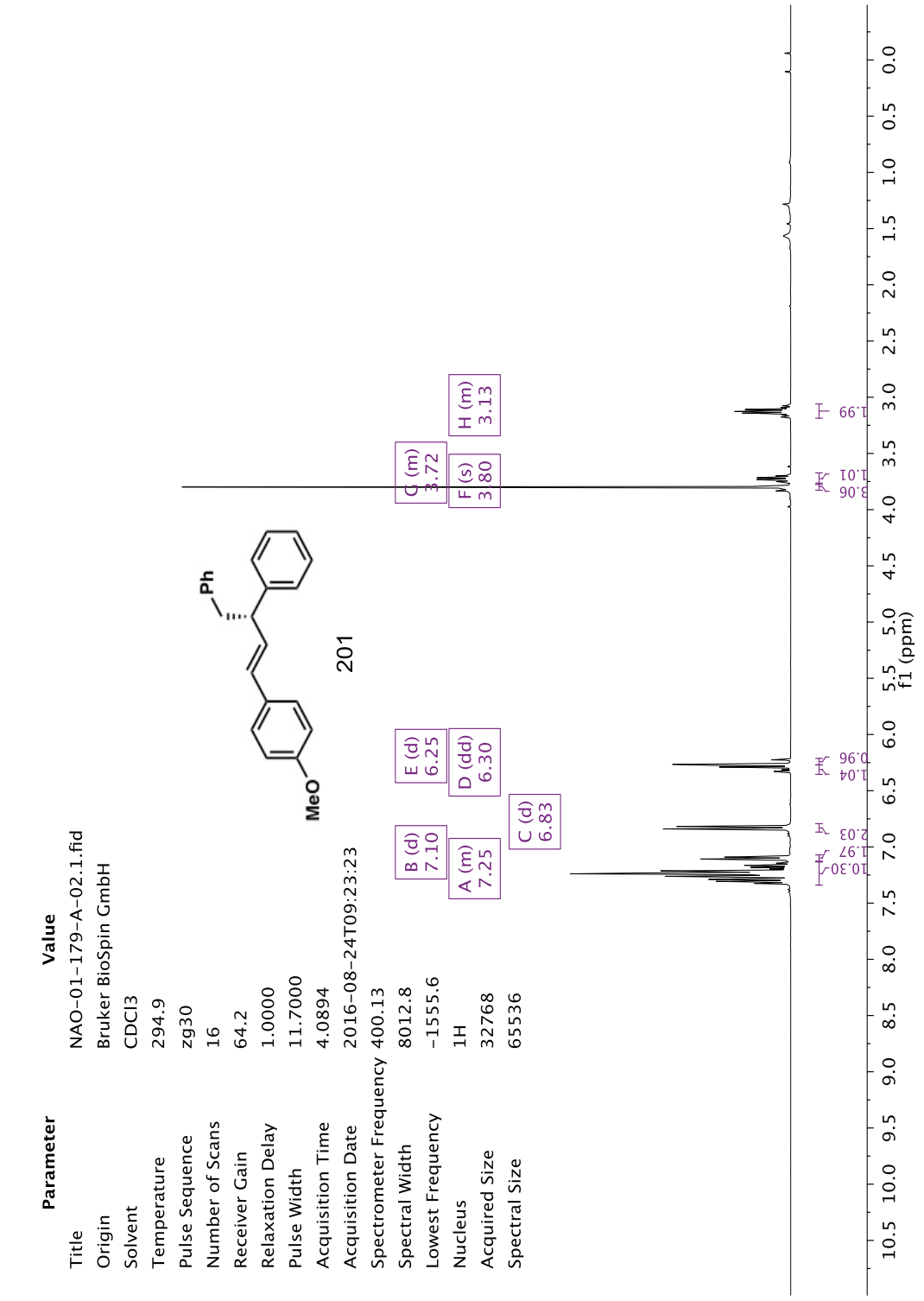


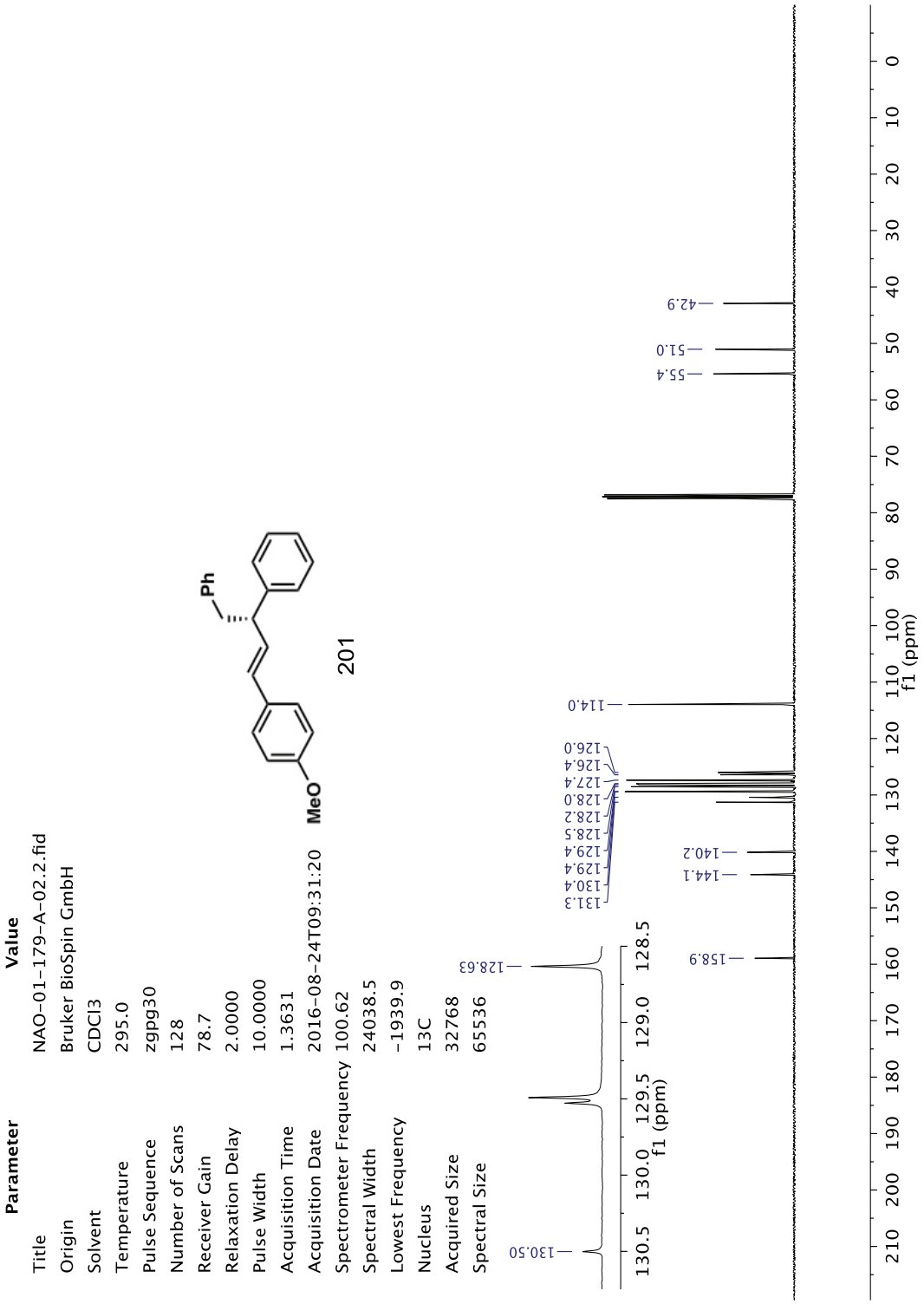

Parameter
Value
Title
NAO-02-029-B.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.0
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
87.8
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2017-01-06T21:11:19
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1535.6
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
Me
MeO
Cl
Cl
199
A (d) 7.37
B (d) 7.35
C (m) 7.29
D (ddd) 7.10
E (m) 6.85
F (dd) 6.35
G (dd) 6.15
H (s) 3.81
I (m) 3.57
J (d) 1.43
1.00
0.93
2.01
0.98
2.01
0.98
0.98
2.97
1.00
3.13
f1 (ppm)

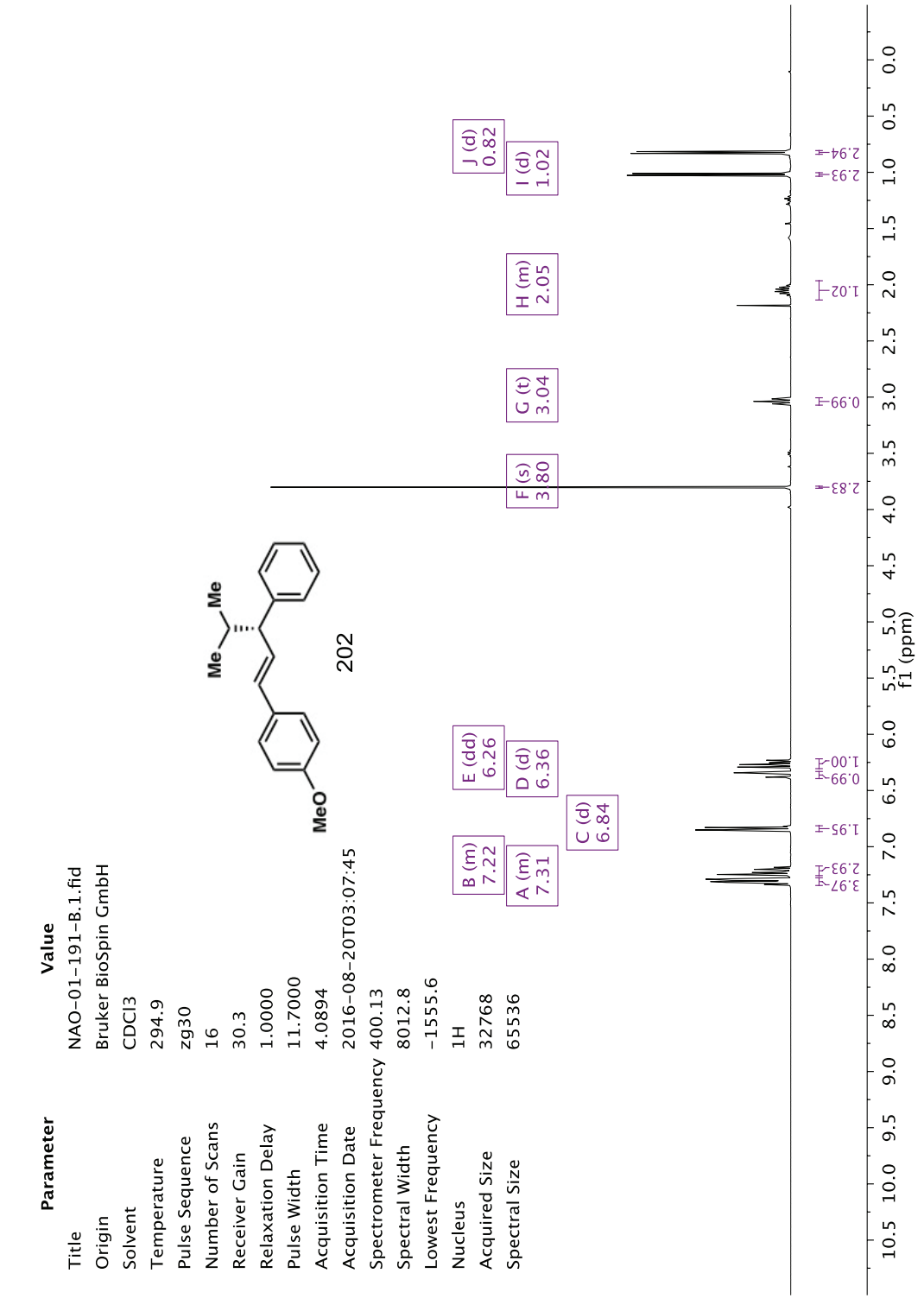

Parameter
Value
Title
NAO-02-029-B.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zgpg30
Number of Scans
128
Receiver Gain
55.5
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2017-01-06T21:19:16
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1958.4
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Me
Cl
Cl
MeO
199
159.2
146.3
132.4
131.7
130.5
130.1
130.0
129.4
128.9
127.4
127.0
114.1
55.4
41.9
21.2
f1 (ppm)

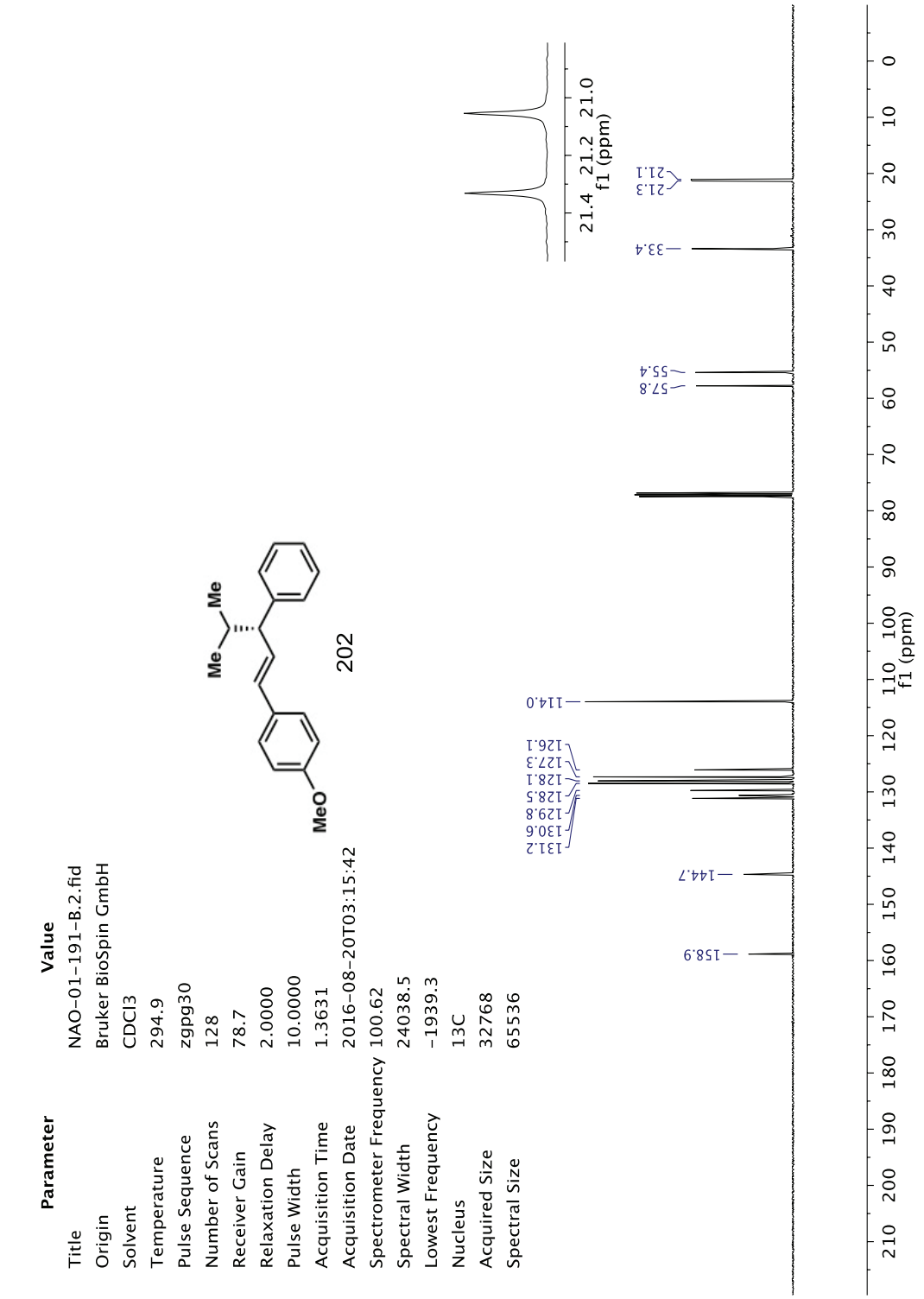

Parameter
Value
Title
NAO-01-178-B.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
55.5
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2016-07-21T06:50:06
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1555.6
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
Me
MeO
200
A (m) 7.28
B (d) 6.84
C (d) 6.37
D (dd) 6.21
E (s) 3.80
F (m) 3.31
G (m) 1.84
H (t) 0.93
7.17
1.96
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1.00
2.96
1.00
2.02
3.05
f1 (ppm)

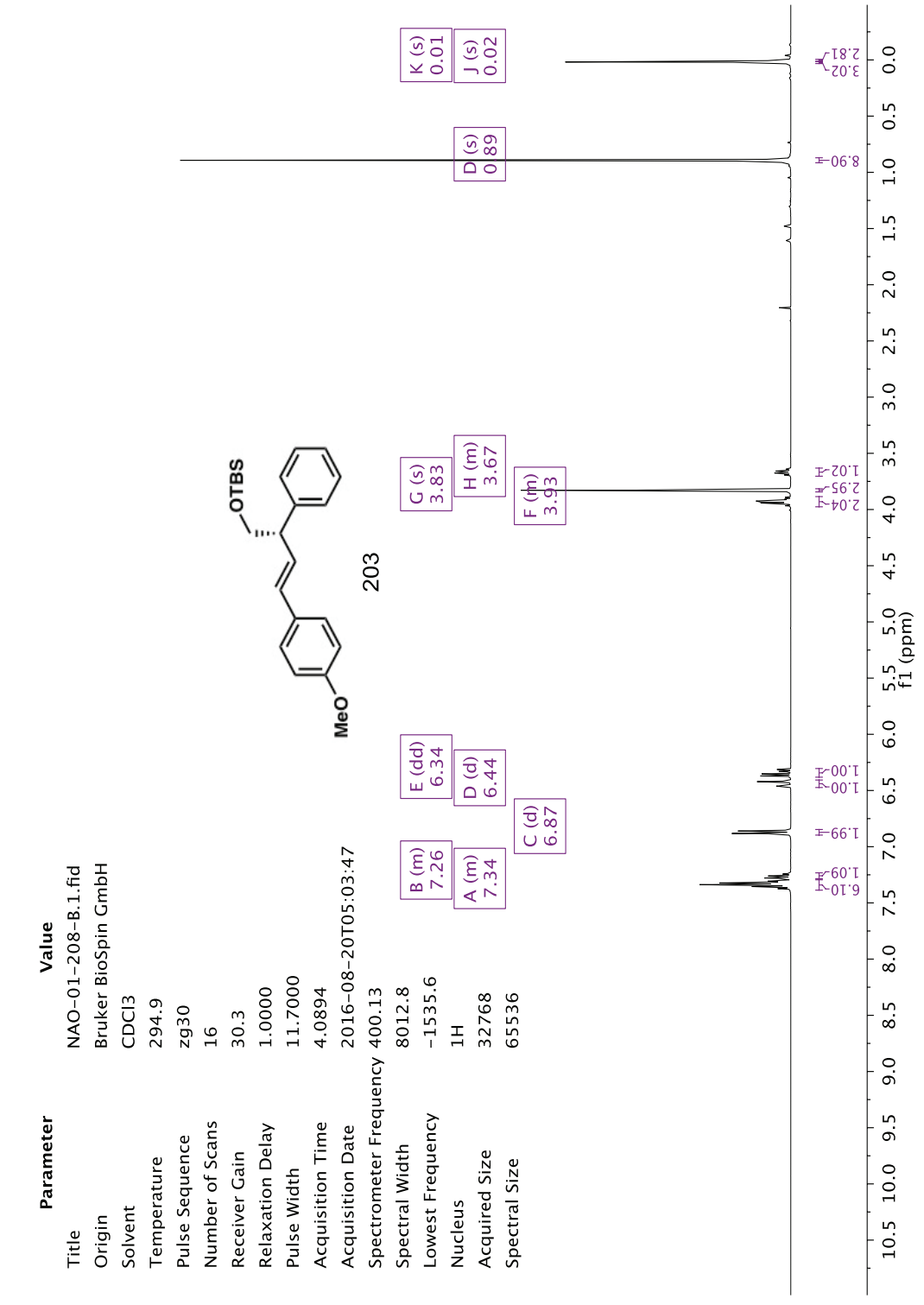

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Relaxation Delay
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Pulse Width
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Acquisition Time
1.3631
Acquisition Date
2016-07-21T06:57:56
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Spectral Width
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Lowest Frequency
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Nucleus
13C
Acquired Size
32768
Spectral Size
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Me
MeO
200
158.9
144.9
132.2
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127.8
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126.2
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29.0
12.5
f1 (ppm)

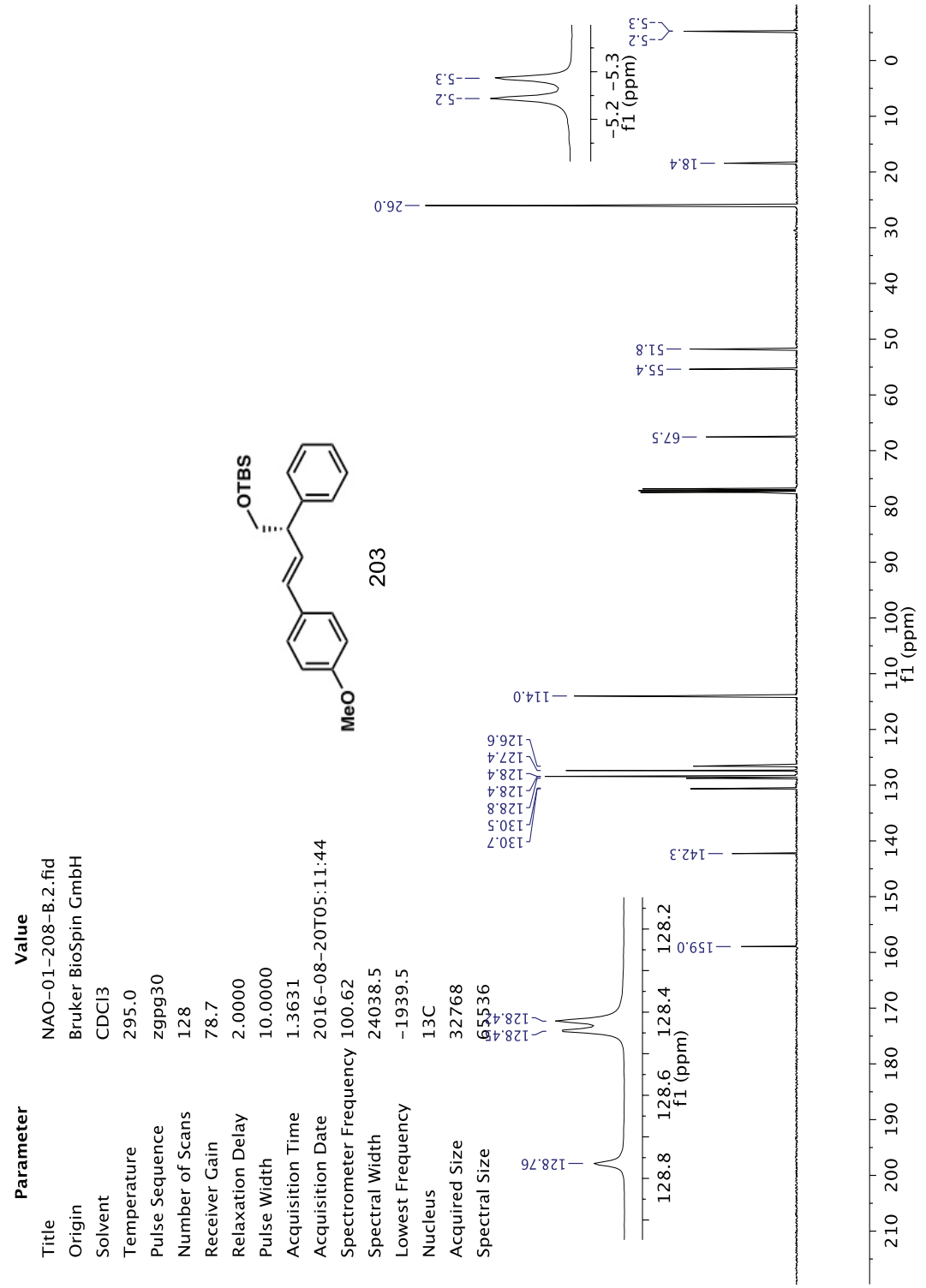

Parameter
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Bruker BioSpin GmbH
Solvent
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Temperature
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Pulse Sequence
zg30
Number of Scans
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Receiver Gain
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Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2016-08-24T09:23:23
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
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Nucleus
1H
Acquired Size
32768
Spectral Size
65536
Ph
MeO
201
A (m) 7.25
B (d) 7.10
C (d) 6.83
D (dd) 6.30
E (d) 6.25
F (s) 3.80
G (m) 3.72
H (m) 3.13
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2.03
1.04
0.96
8.06
1.01
1.99
f1 (ppm)

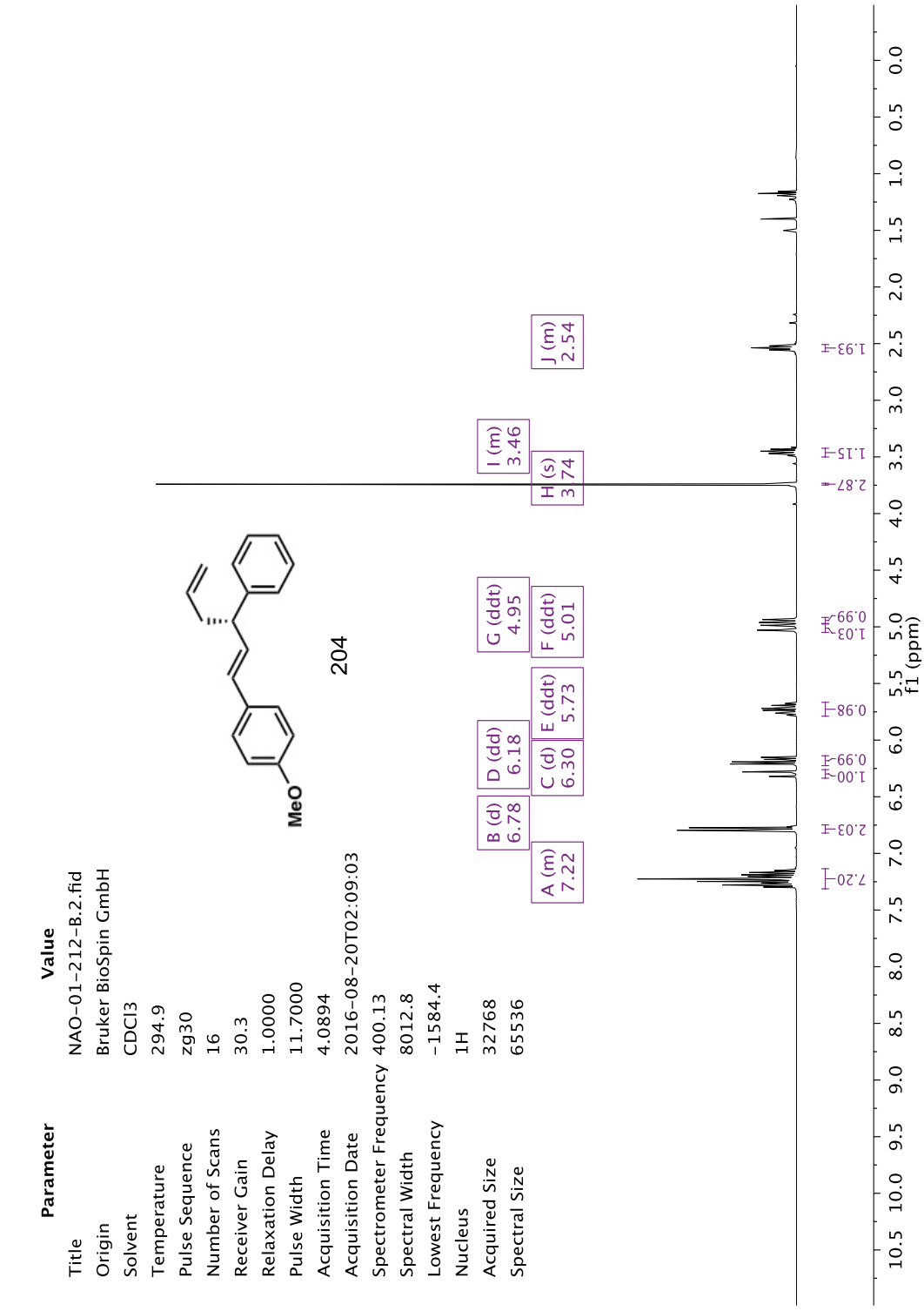

Parameter
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Solvent
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Temperature
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Pulse Sequence
zgpg30
Number of Scans
128
Receiver Gain
78.7
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2016-08-24T09:31:20
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1939.9
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Ph
MeO
201
130.50
128.63
114.0
126.0
126.4
127.4
128.0
128.2
128.5
129.4
129.4
130.4
131.3
140.2
144.1
158.9
55.4
51.0
42.9
130.5
130.0
129.5
129.0
128.5
f1 (ppm)
210
200
190
180
170
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100
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50
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20
10
0
f1 (ppm)

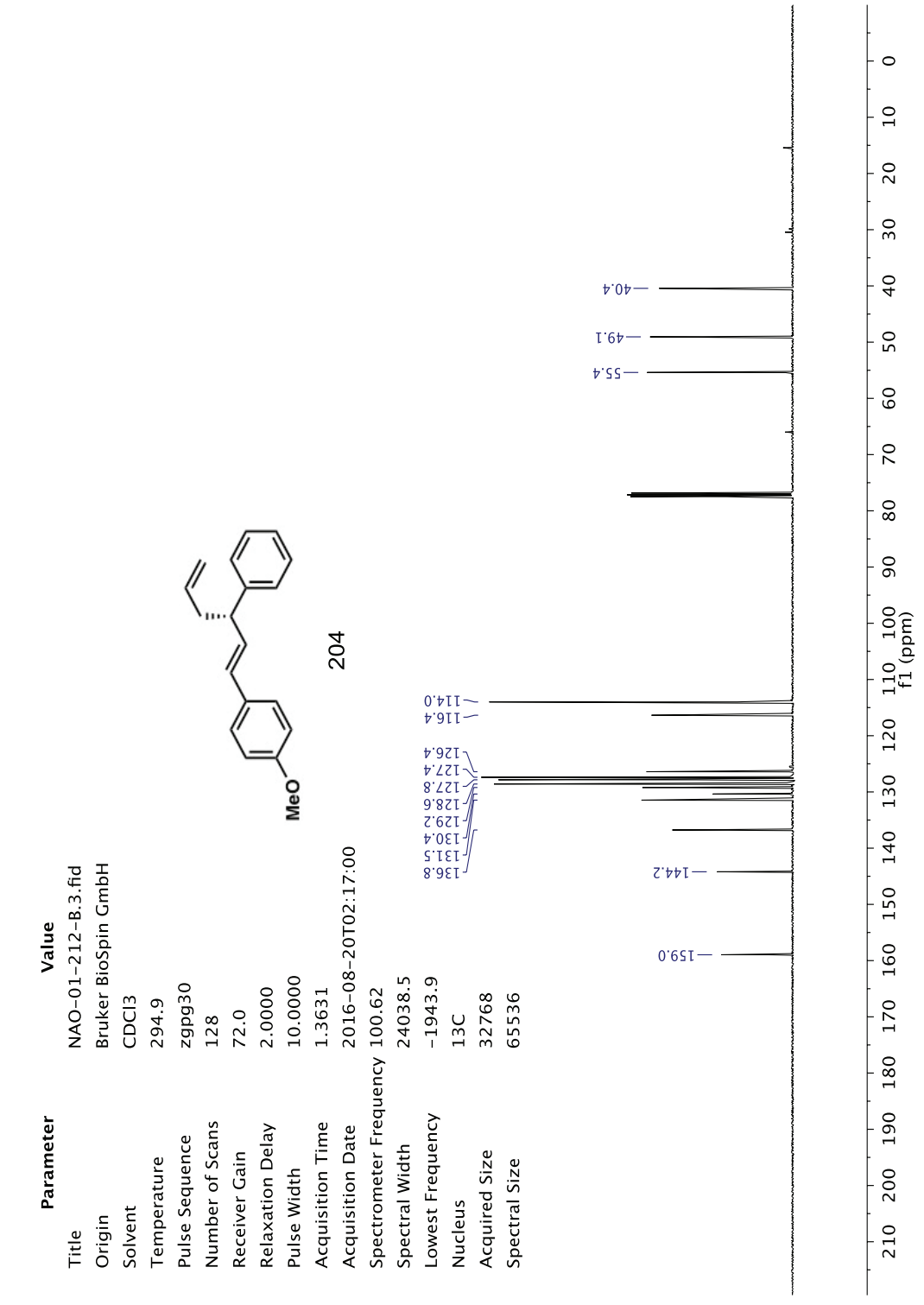

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Number of Scans 16
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Spectral Size 65536
Me
Me
MeO
202
A (m) 7.31
B (m) 7.22
C (d) 6.84
D (d) 6.36
E (dd) 6.26
F (s) 3.80
G (t) 3.04
H (m) 2.05
I (d) 1.02
J (d) 0.82
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2.93
1.95
0.99
1.00
2.83
0.99
1.02
2.93
2.94
f1 (ppm)

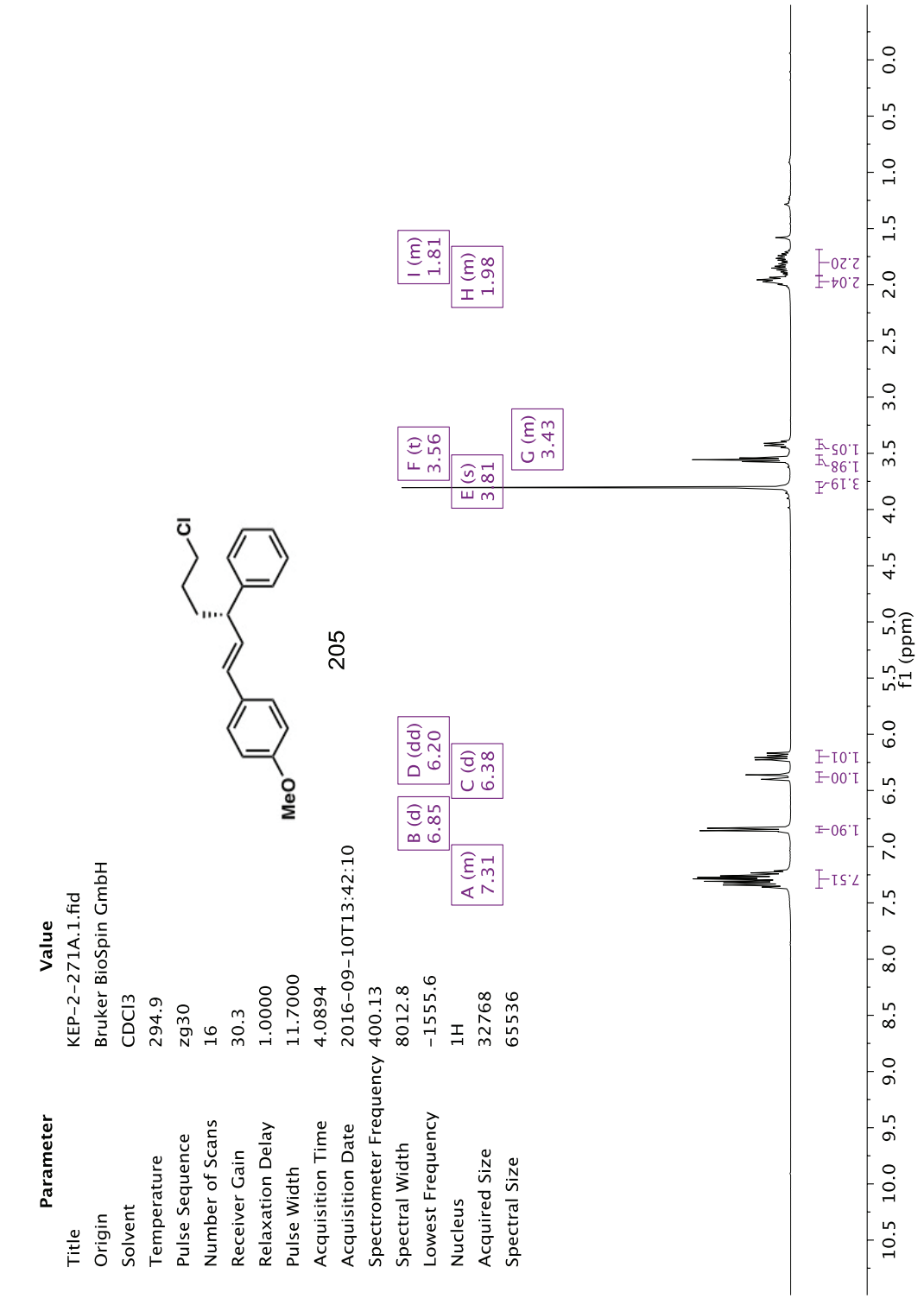

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Solvent CDCl3
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Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-08-20T03:15:42
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1939.3
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
Me
MeO
202
158.9
144.7
131.2
130.6
129.8
128.5
128.1
127.3
126.1
114.0
57.8
55.4
33.4
21.3
21.1
21.4 21.2 21.0
f1 (ppm)
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f1 (ppm)

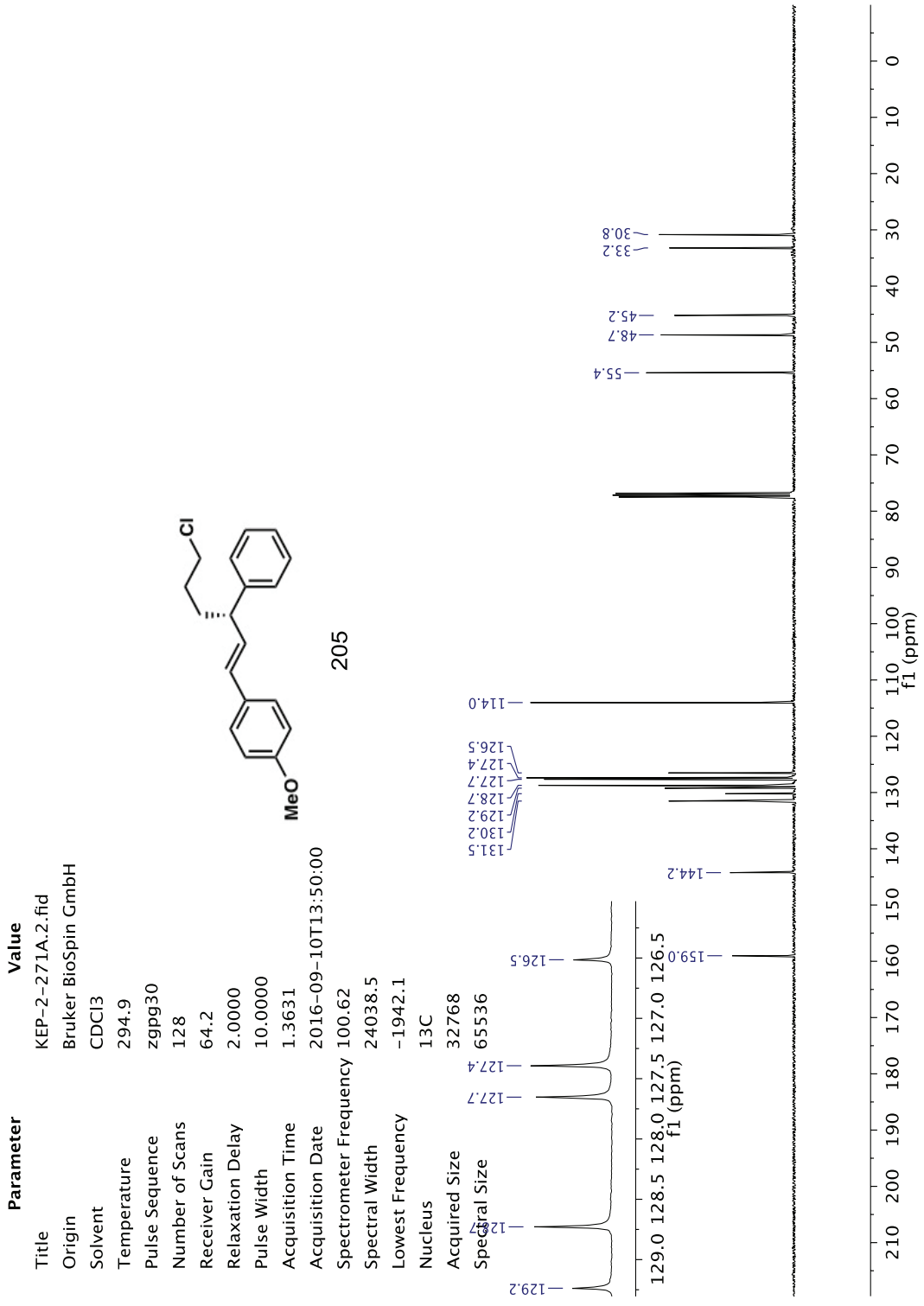

Parameter
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Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
30.3
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2016-08-20T05:03:47
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1535.6
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
OTBS
MeO
203
A (m) 7.34
B (m) 7.26
C (d) 6.87
D (d) 6.44
E (dd) 6.34
F (m) 3.93
G (s) 3.83
H (m) 3.67
D (s) 0.89
J (s) 0.02
K (s) 0.01
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1.99
1.00
2.04
2.95
1.02
8.90
3.02
2.81
f1 (ppm)

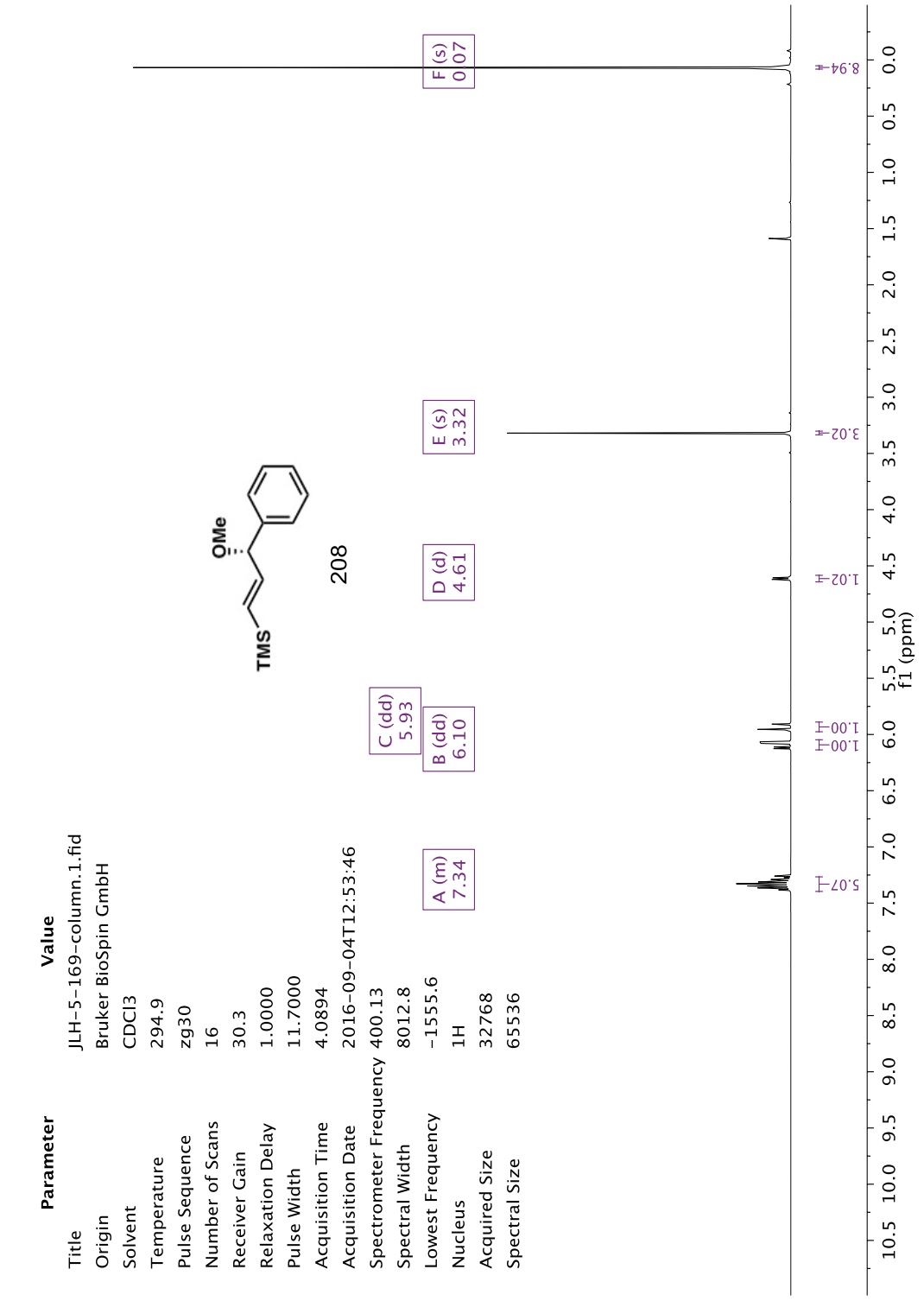

Parameter Value
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Temperature 295.0
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Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-08-20T05:11:44
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1939.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OTBS
MeO
203
159.0
142.3
130.7
130.5
128.8
128.4
128.4
127.4
126.6
114.0
67.5
55.4
51.8
26.0
18.4
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f1 (ppm)
-5.2 -5.3
f1 (ppm)
f1 (ppm)

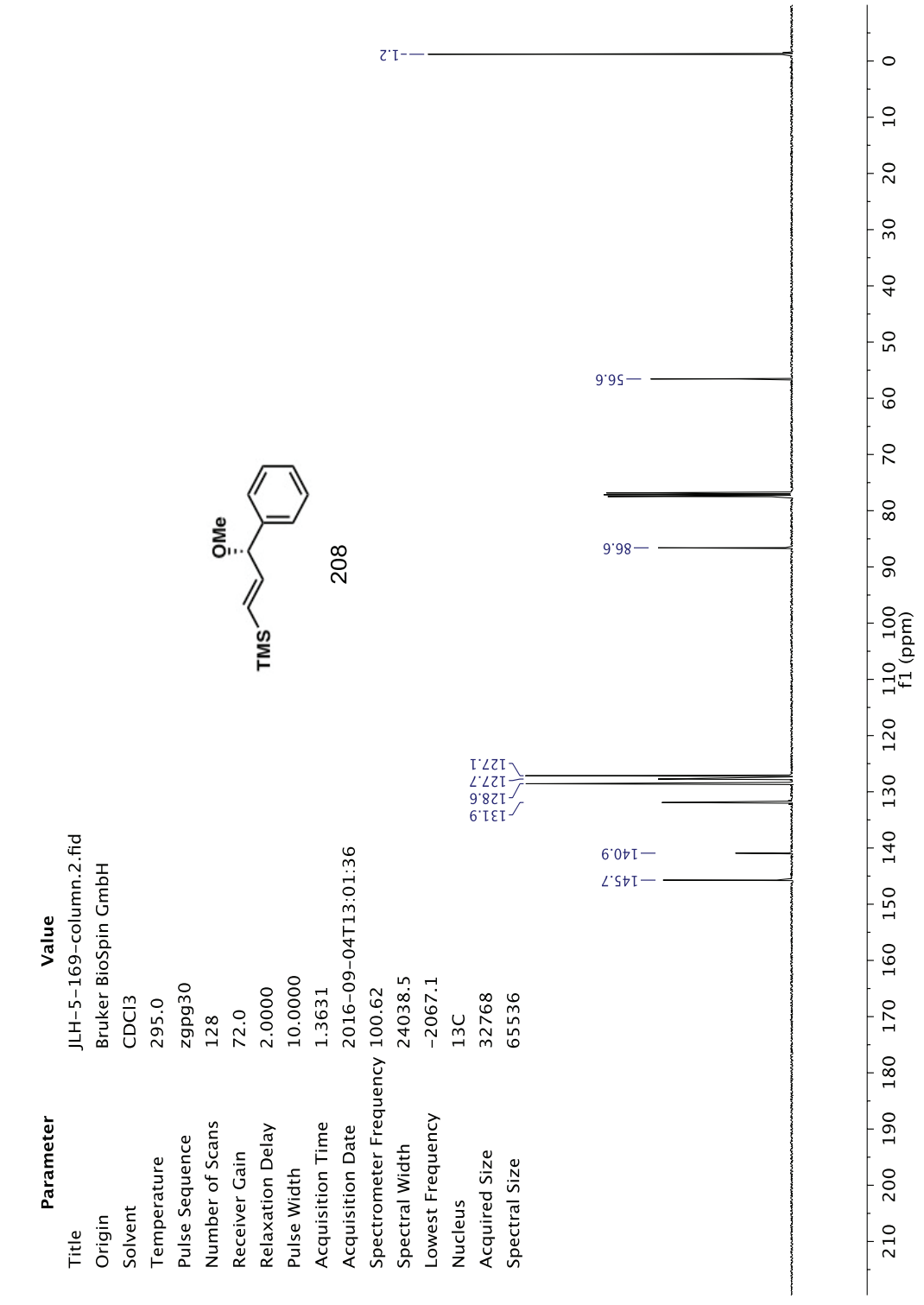

Parameter
Value
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Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
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Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
30.3
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2016-08-20T02:09:03
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1584.4
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
MeO
204
A (m) 7.22
B (d) 6.78
C (d) 6.30
D (dd) 6.18
E (ddt) 5.73
F (ddt) 5.01
G (ddt) 4.95
H (s) 3.74
I (m) 3.46
J (m) 2.54
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1.00
0.99
0.98
1.03
0.99
2.87
1.15
1.93
f1 (ppm)

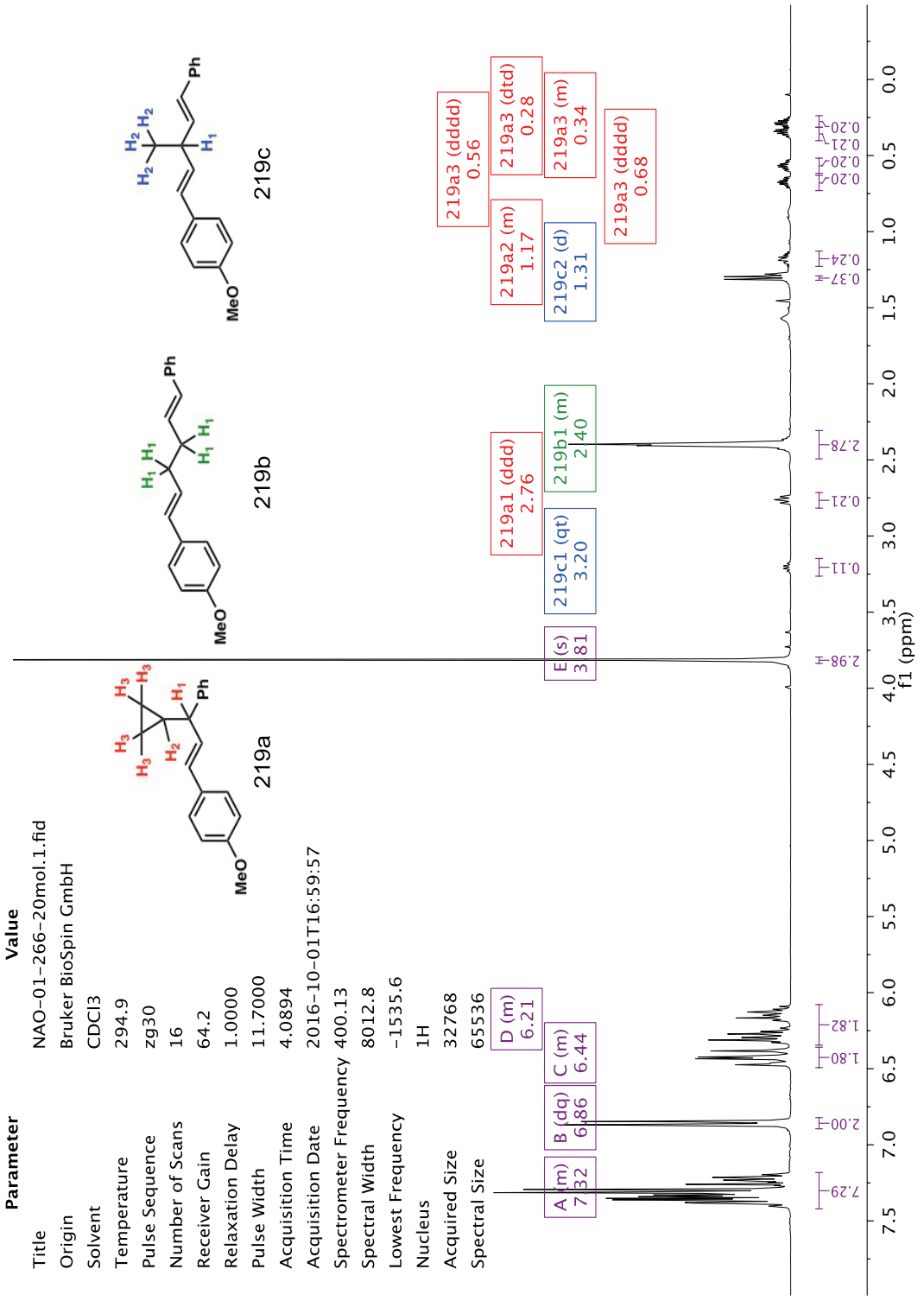

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Pulse Sequence
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Receiver Gain
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Relaxation Delay
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Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2016-08-20T02:17:00
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1943.9
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
MeO
204
159.0
144.2
136.8
131.5
130.4
129.2
128.6
127.8
127.4
126.4
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114.0
55.4
49.1
40.4
f1 (ppm)

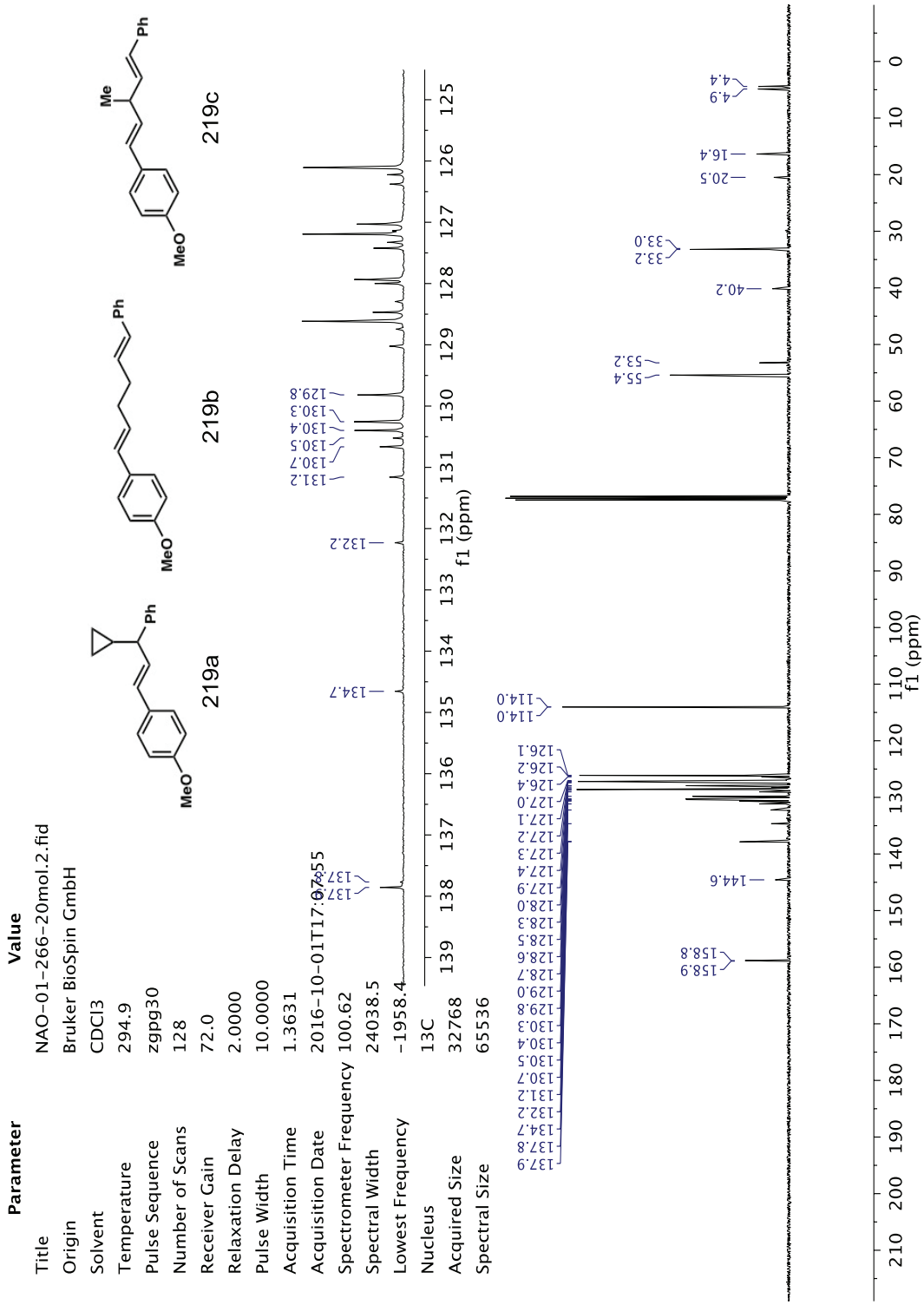

Parameter
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Solvent
CDCl3
Temperature
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Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
30.3
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2016-09-10T13:42:10
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
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Nucleus
1H
Acquired Size
32768
Spectral Size
65536
Cl
MeO
205
A (m) 7.31
B (d) 6.85
C (d) 6.38
D (dd) 6.20
E (s) 3.81
F (t) 3.56
G (m) 3.43
H (m) 1.98
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1.05
2.04
2.20
f1 (ppm)

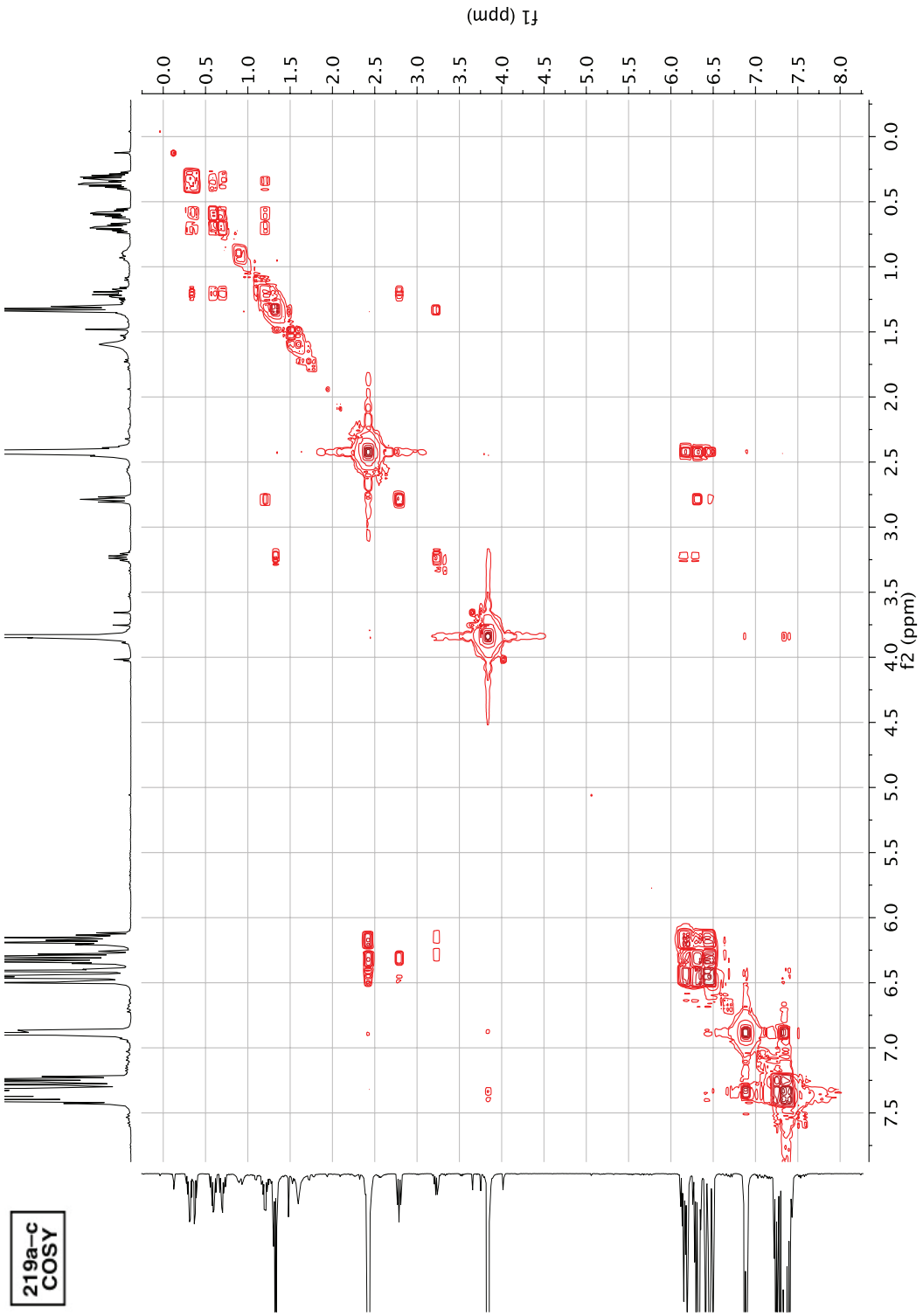

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Relaxation Delay 2.0000
Pulse Width 10.0000
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Acquisition Date 2016-09-10T13:50:00
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Spectral Width 24038.5
Lowest Frequency -1942.1
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Acquired Size 32768
Spectral Size 65536
Cl
MeO
205
159.0
144.2
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130.2
129.2
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127.7
127.4
126.5
114.0
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45.2
33.2
30.8
f1 (ppm)

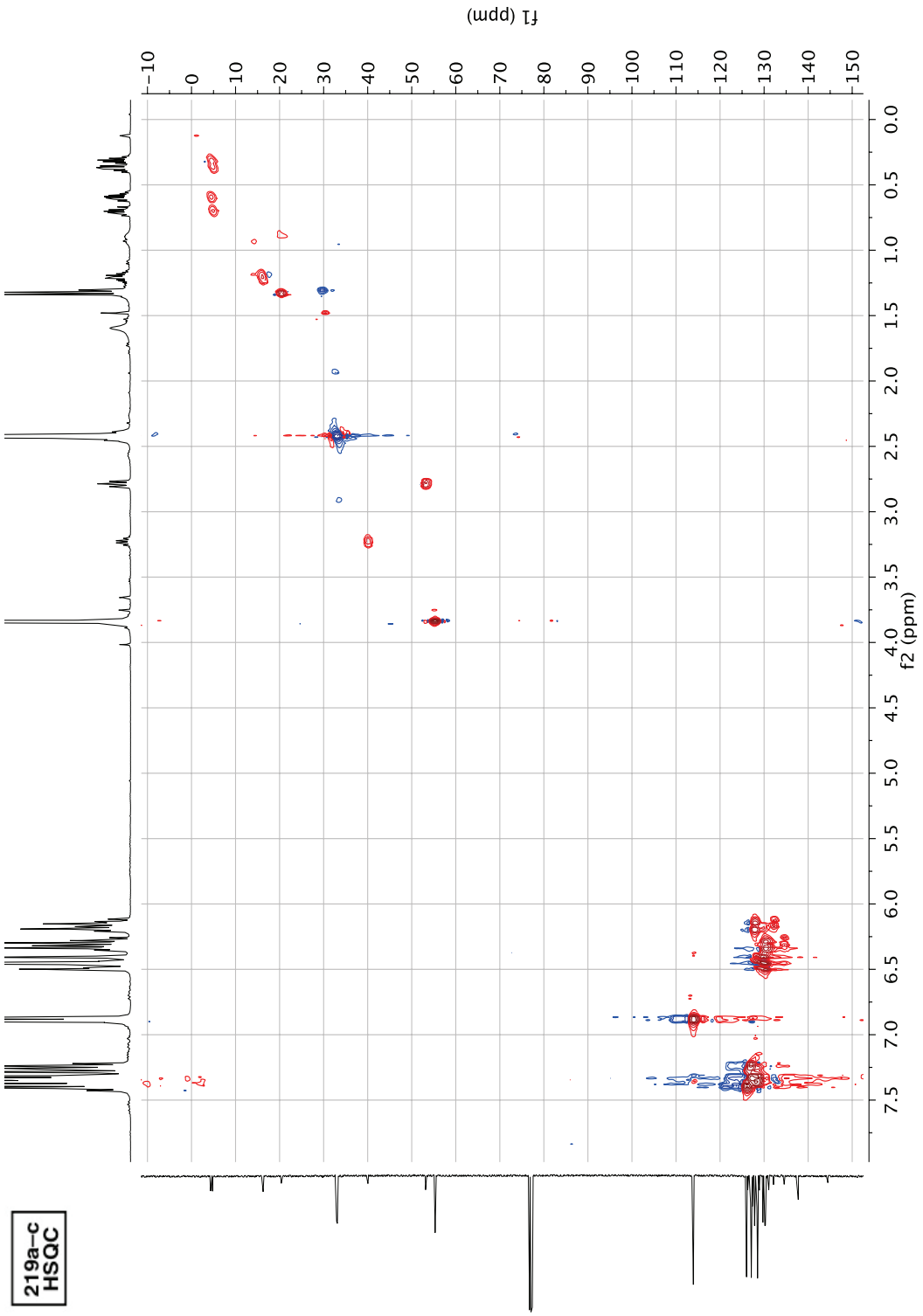

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Temperature 294.9
Pulse Sequence zg30
Number of Scans 16
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Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2016-09-04T12:53:46
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1555.6
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
OMe
TMS
208
A (m) 7.34
B (dd) 6.10
C (dd) 5.93
D (d) 4.61
E (s) 3.32
F (s) 9.07
5.07
1.00
1.00
1.02
3.02
8.94
f1 (ppm)

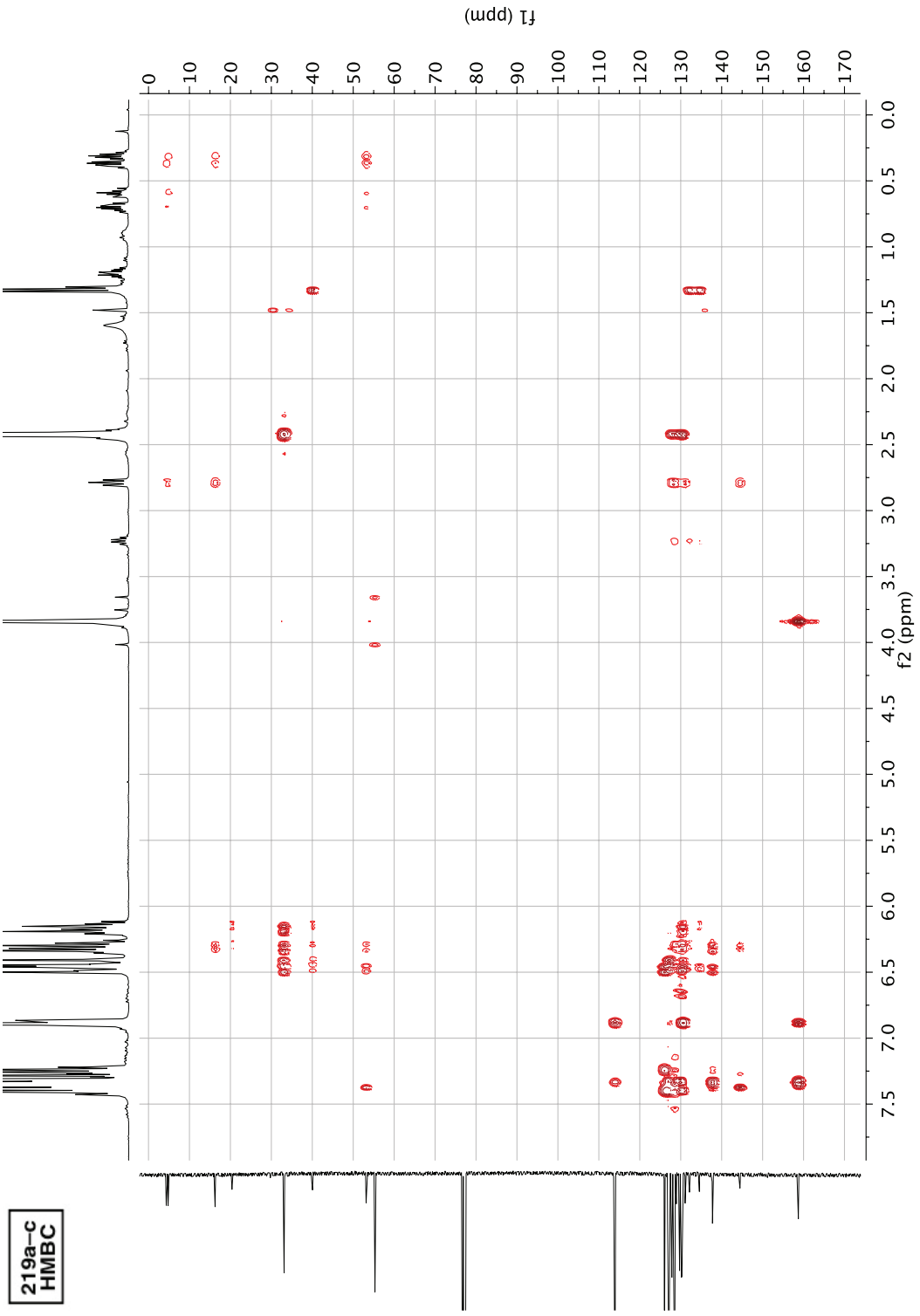

Parameter Value
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Solvent CDCl3
Temperature 295.0
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Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2016-09-04T13:01:36
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -2067.1
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OMe
TMS
208
-1.2
56.6
86.6
127.1
127.7
128.6
131.9
140.9
145.7
f1 (ppm)


Parameter
Value
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Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
64.2
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2016-10-01T16:59:57
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1535.6
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
219a
219b
219c
MeO
Ph
A (m) 7.32
B (dq) 6.86
C (m) 6.44
D (m) 6.21
E (s) 3.81
219c1 (qt) 3.20
219a1 (ddd) 2.76
219b1 (m) 2.40
219c2 (d) 1.31
219a2 (m) 1.17
219a3 (dddd) 0.56
219a3 (dddd) 0.68
219a3 (dtd) 0.28
219a3 (m) 0.34
7.29
2.00
1.80
1.82
2.98
0.11
0.21
2.78
0.37
0.24
0.20
0.20
0.21
0.20
f1 (ppm)


Parameter
Value
Title
NAO-01-266-20mol.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
294.9
Pulse Sequence
zgpg30
Number of Scans
128
Receiver Gain
72.0
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2016-10-01T17:07:55
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
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Nucleus
13C
Acquired Size
32768
Spectral Size
65536
MeO
Ph
219a
MeO
Ph
219b
MeO
Me
Ph
219c
f1 (ppm)
f1 (ppm)


219a–c
COSY
f1 (ppm)
f2 (ppm)


f1 (ppm)
-10
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
f2 (ppm)
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
219a–c
HSQC


219a–c
HMBC
f1 (ppm)
f2 (ppm)

Chapter 5

Nickel-Catalyzed Conversion of Enol Triflates to Alkenyl Halides◊

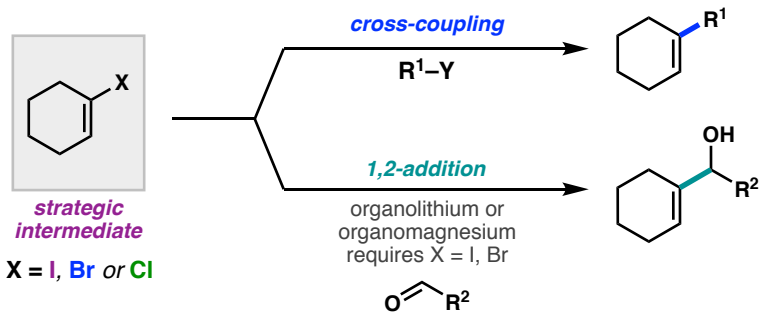
5.1 INTRODUCTION

Alkenyl halides are versatile functional groups that can be used in a variety of carbon–carbon and carbon–heteroatom bond-forming reactions.[1] For example, alkenyl halides are commonly employed as substrates in transition metal-catalyzed cross-coupling reactions or are converted to nucleophiles via metal-halogen exchange for 1,2-additions to carbonyl compounds (Scheme 5.1).[2] These transformations render alkenyl halides as indispensable functional group handles for synthetic disconnections. Furthermore, the alkenyl halide moiety appears in some natural products and bioactive molecules.[3,4]

◊ Portions of this chapter have been reproduced from a manuscript in preparation and the supporting information found therein. This work was conducted with Julie Hofstra and Alex Shimozono, graduate students in the Reisman lab.

While acyclic alkenyl halides are easily prepared from the corresponding alkyne[5–9] or aldehyde,[10,11] most cyclic alkenyl halides are synthesized from the corresponding ketone. The most direct method is the Barton reaction (and variations thereof),[12–17] which proceeds through an intermediate hydrazine (Scheme 5.2a). These reactions are notoriously capricious: the formation of the requisite hydrazone can be challenging on sterically encumbered substrates and the halogenation step often produces mixtures of alkenyl halide isomers or dihalide side products.[11]

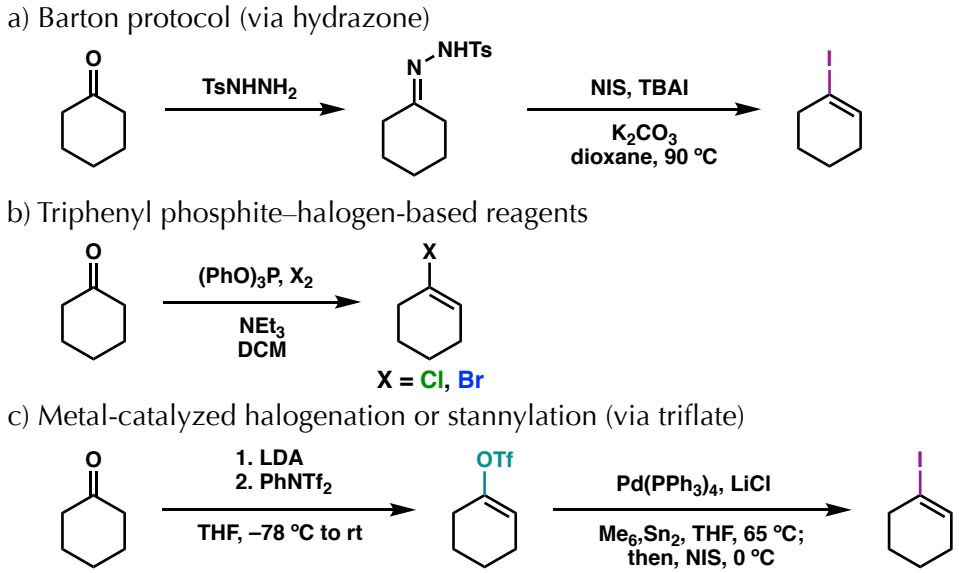
Scheme 5.1. *Synthetic utility of alkenyl halides.*



As a result, enol triflates, which can be prepared directly from cyclic ketones under either kinetic or thermodynamic control, have emerged as attractive "pseudohalides" for transition metal-catalyzed cross-coupling processes. Unfortunately, enol triflates cannot be directly converted to the corresponding alkenyllithium or -magnesium species commonly employed in 1,2-addition reactions. In cases where the Barton procedure to prepare the alkenyl halide is poor yielding, a multistep alternative is frequently employed: 1) conversion of the ketone to enol triflate, 2) conversion of the triflate to the alkenyl stannane, and 3) conversion of the stannane to the alkenyl halide[18] (Scheme 5.2c). Direct, mild methods to convert enol triflates to alkenyl halides, without

proceeding through organostannane intermediates, can streamline the preparation of these valuable intermediates.

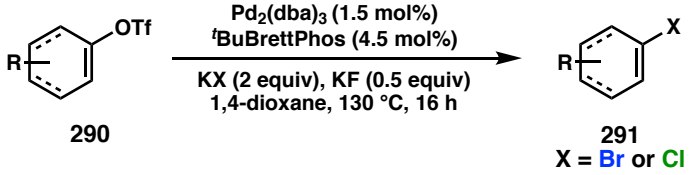
Scheme 5.2. *Methods to access alkenyl halides from ketones.*



Indeed, Buchwald has reported a Pd-catalyzed reaction to convert alkenyl triflates to alkenyl bromides and chlorides[19,20] (Scheme 5.3a); however, there are no examples of alkenyl iodide formation, and the reaction requires an expensive ligand, temperatures greater than 100 °C, or additives such as fluoride salts or $^{i}Bu_3Al$. These additives limit the functional group compatibility, particularly with common groups such as silyl ethers. More recently, Hayashi reported a Ru-catalyzed method to convert enol triflates to iodides, bromides, or chlorides that proceeds at ambient temperature (Scheme 5.3b); however, the requisite ruthenium catalyst is not commercially available and only three examples of alkenyl iodide formation are reported.[21,22]

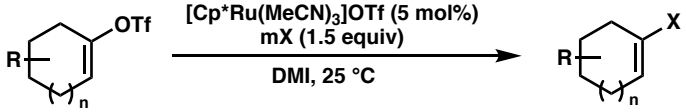
Scheme 5.3. *Alkenyl triflate-halide exchange reactions.*

a) Buchwald, 2011



290 **291**
X = Br or Cl

b) Hayashi, 2012

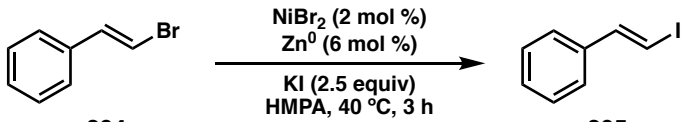


292 **293**
X = I, Br, Cl

During our investigations of Ni-catalyzed asymmetric reductive coupling reactions of alkenyl bromides (**Chapter 4**),[23,24] we observed an off-pathway halide exchange process that generated alkenyl chlorides and iodides. Whereas Ni-catalyzed aryl[25,26] and alkenyl halide exchange processes have been reported and extensively investigated (Scheme 5.4),[24,25,27,28] the corresponding reactions of enol triflates have not been developed.[29,30] Having observed promising reactivity with enol triflates,[31] we hypothesized that the appropriate Ni catalyst and inexpensive halide salts might enable the direct conversion of alkenyl triflates to alkenyl halides under mild conditions.

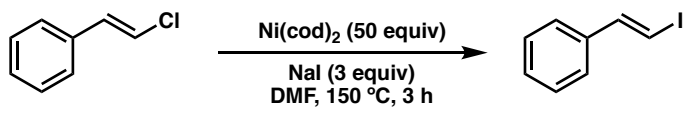
Scheme 5.4. *Ni-catalyzed alkenyl halide-halide exchange reactions.*

a) Kochi, 1978



294 **295**
95% yield

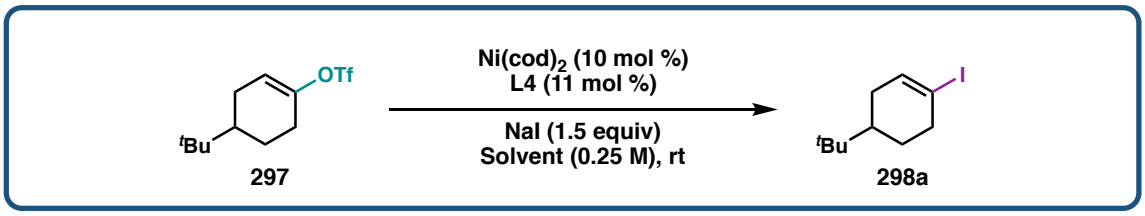
b) Brandsma, 1994

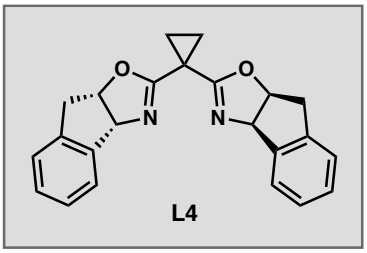


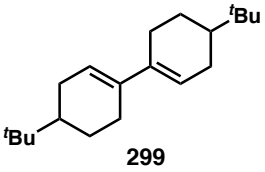
296 **295**
61% yield
80:20 E:Z

5.2 REACTION DEVELOPMENT

Table 5.1. *Initial solvent screen.*







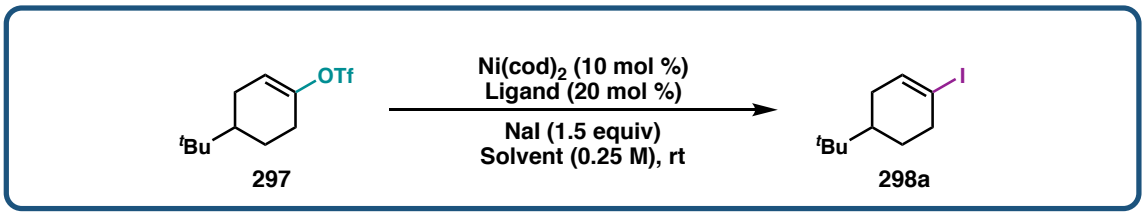
Entry	Solvent	L4	Yield 298a (%)	SM 297 (%)	HC 299 (%)
1	NMP	+	51	7	0
2	DMA	+	78	0	6
3	THF	+	71	0	0
4	MeCN	+	37	47	0
5	NMP	–	85	11	0
6	DMA	–	63	0	0
7	THF	–	9	80	0
8	MeCN	–	2	85	0

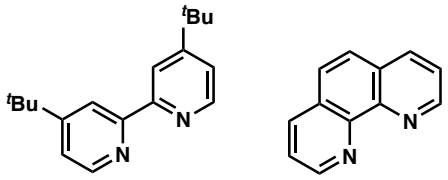
Our reaction development began with enol triflate **297**, prepared in one step from 4-*tert*-butylcyclohexanone, with the goal of identifying general conditions that could provide the alkenyl iodide, bromide, or chloride simply by changing the halide salt. We first explored reaction conditions similar to the asymmetric reductive cross-coupling reaction of alkenyl bromides that our lab previously developed where we first observed halide exchange side-products.[24] When **297** was subjected to $Ni(cod)_2$, **L4**, and NaI (1.5 equiv) in NMP, we obtained 51% yield of our desired alkenyl iodide **298a** (Table 5.1, entry 1), but poor recovery of starting material. A short solvent screen of DMA, THF and MeCN suggested promising reactivity across a range of solvents (Table 5.1, entries 2-4). Surprisingly, **298a** was formed in better yield (85% yield) in NMP without the addition of **L4** (Table 5.1, entry 5). However, poor conversion to alkenyl iodide **298a** was observed

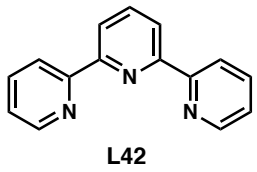
in solvents such as THF and MeCN without the chiral bis(oxazoline) ligand (Table 5.1, entries 7-8).

In an effort to optimize the reaction towards less polar solvents and away from costly chiral ligands, several achiral ligands were evaluated in THF (Table 5.2). While ligands such as **L41** provided comparable yield in THF (52% yield, Table 5.2, entry 4) to the reaction in DMA in the absence of ligand (63% yield, Table 5.2, entry 1), the reaction conversion was poor in THF. Other achiral ligands, such as substituted **L40** and **L42**, provided the desired product in low yield (Table 5.2, entries 3 and 5).

Table 5.2. *Evaluation of ligand effects on reaction.*





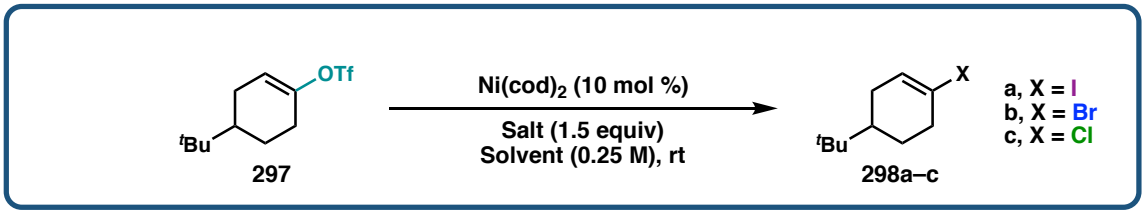


Entry	Solvent	Ligand	Yield 298a (%)	SM 297 (%)
1	DMA	—	63	0
2	THF	—	9	80
3	THF	L40	18	54
4	THF	L41	52	39
5	THF	L42	0	94

With these results in hand, we turned towards investigation of a mixed solvent system with DMA and THF (Table 5.3). While the yield of **298a** in DMA without an exogenous ligand was moderate, conversion of the starting enol triflate **297** to decomposition products prohibited further improvement in DMA (Table 5.1, entry 6). Interestingly, the addition of small quantities of THF to DMA significantly improved the

conversion of starting enol triflate **297** and yield of **298a** over either of the single solvent systems (Table 5.3, entries 1 and 8). Evaluation of several different ratios of DMA in THF revealed optimal yield and conversion occurs in approximately 20-30% DMA/THF, giving alkenyl iodide **298a** in 71% yield and some recovered starting material (Table 5.3, entries 3-4). While higher yield was observed at 40% DMA/THF, the high conversion of starting material to decomposition products discouraged further optimization in the mixed solvent system (Table 5.3, entry 5).

Table 5.3. *Evaluation of solvent and halide source.*



with NaI:

Entry	Solvent	Yield 298a (%)	SM 297 (%)
1	THF	5	91
2	10% DMA/THF	49	28
3	20% DMA/THF	71	26
4	30% DMA/THF	71	11
5	40% DMA/THF	78	4
6	50% DMA/THF	62	0
7	80% DMA/THF	54	5
8	DMA	55	0

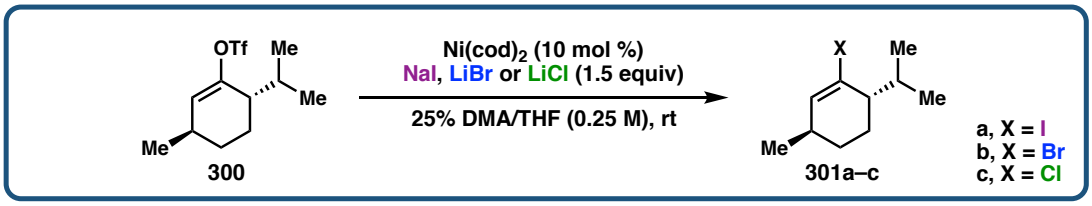
with 25% DMA/THF:

Entry	Salt	Yield 298 (%)	SM 297 (%)
9	LiI	47	0
10	LiBr	77	0
11	LiCl	83	0
12	NaI	82	9
13	NaBr	46	58
14	NaCl	0	96
15	KI	3	92
16	KBr	0	100
17	KCl	0	100

Next, we investigated halide salts for the iodination, bromination and chlorination reactions. Potassium salts provided poor results for all halides (Table 5.3, entries 15-17), while sodium salts provided poor yields for bromination and chlorination (Table 5.3, entries 12-14). Lithium salts worked well for the bromination and chlorination reaction

(Table 5.3, entries 10 and 11), while the sodium salt was optimal for the iodination (Table 5.3, entry 12).

Table 5.4. *Optimization of Ni-catalyzed exchange reaction conditions.*[a]



Entry	Deviation	Yield 301a (%)[b]	Yield 301b (%)[b]	Yield 301c (%)[b]	Entry	Deviation	Yield 301a (%)[b]	Yield 301b (%)[b]	Yield 301c (%)[b]
1	none	74	74	74	7	DMF	34	74	70
2	dtbbpy (0.2 equiv)	14	10	4	8	MeCN	4	52	7
3	TMEDA (0.2 equiv)	0	0	0	9	10% DMA/THF	68	68	77
4	dppf (0.2 equiv)	0	0	0	10	$^{n}Bu_4NX$ salt	71	84	80
5	DMA	72	75	70	11	5 mol % $Ni(cod)_2$	68	83	77
6	THF	35	75	61	12	10 mol % $Ni(cod)_2$	70	55	67

[a] Reactions conducted on 0.1 mmol scale under an inert atmosphere. [b] Determined by ^{1}H NMR vs 1,2,4,5-tetrachloronitrobenzene as an internal standard.

After initial reaction exploration, we found that evaluation of enol triflate **300**, prepared in one step from menthone, corroborated the results of extensive optimization efforts. Ultimately, we discovered that addition of the alkenyl triflate to a mixture of 10 mol % $Ni(cod)_2$ and 1.5 equiv of halide salt (either NaI, LiBr, or LiCl) in 1:3 DMA/THF at 23 °C provided the respective alkenyl halides in good yields (Table 5.4, entry 1). Ancillary ligands such as dtbbpy, TMEDA, and dppf inhibited the reaction, resulting in lower yields of alkenyl halide (Table 5.4, entries 2-4).

The alkenyl iodide formation proved most sensitive to the solvent: for example, while the bromination and chlorination work comparably well in both THF and DMA, the yield of the alkenyl iodide is significantly better in DMA than THF (Table 5.4, entries 5 and 6). Due to improved physical properties of the reaction mixture and work-up, a 1:3

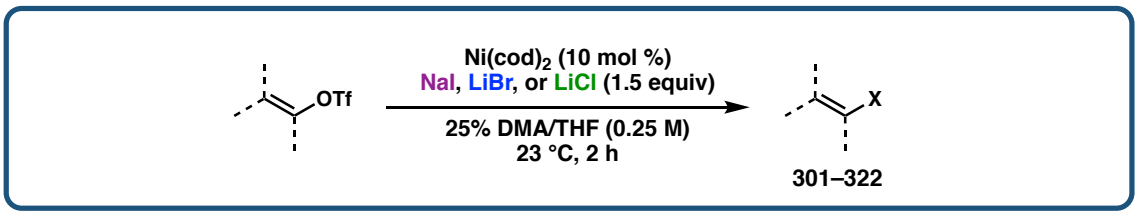
mixture of DMA and THF was selected as the optimal solvent system. Under these conditions, use of tetrabutylammonium salts provided all three halogenation products in comparably excellent yields (entry 10). At higher Ni loading, the yields of **301a–c** decreased due to increased homodimerization of the alkene (entry 12).

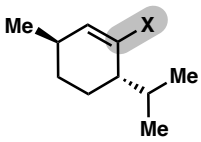
5.3 SUBSTRATE SCOPE

Having identified optimal reaction conditions, the substrate scope of the Ni-catalyzed halogenation reaction was investigated (Table 5.5). The halide exchange was found to be compatible with a variety of common functional groups, including amines (**303**), carbamates (**304**, **312**), pyridines (**317**), alkenes (**309**, **311**), esters (**316**), ketals (**305**, **320**), and enones (**310**). Dienyl bromides and chlorides could also be prepared in good yields; the yields of the corresponding iodides were typically lower (**309, 320**). Chemoselective halogenation of the alkenyl triflate was observed in preference to aryl triflates (**317**, **321**), aryl chlorides (**308**, **318**), and aryl boronates (**319**); however, competitive halide exchange was observed in the presence of aryl bromides and iodides.

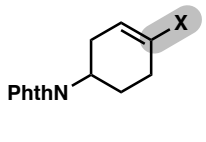
Although the Ni-catalyzed halogenation exhibits good functional group tolerance, the iodination, bromination, and chlorination did not perform equally well on all substrates. With the exception of the 1-arylvinyl triflates, the formation of the alkenyl chlorides proceeded with the most consistently high yields across different substrate classes. For example, 1-arylvinyl triflates (**316**–**319**, Table 5.5) provided the corresponding bromides and iodides in good yields; however, in the presence of chloride salts, elimination of the triflate to give the aryl acetylenes outcompeted chlorination.[32] For the non-styrenyl triflates, the yield of alkenyl iodide was most substrate-dependent. For example, cyclopentenyl triflates (**321**, **322**) were poor substrates for alkenyl iodide

***Table 5.5**. Alkenyl triflate substrate scope.*[a]

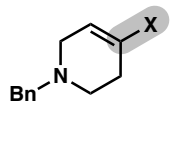




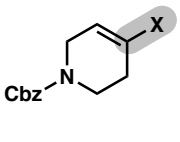
301a (I): 73%[b]
301b (Br): 80%
301c (Cl): 72%



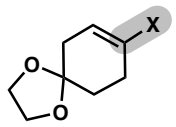
302a (I): 50%
302b (Br): 71%
302c (Cl): 92%



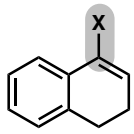
303a (I): 69%
303b (Br): 79%
303c (Cl): 80%



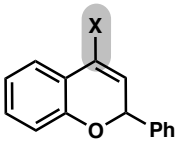
304a (I): 60%
304b (Br): 91%
304c (Cl): 86%



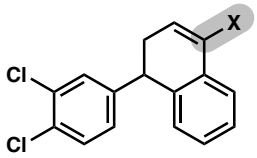
305a (I): 55%[c]
305b (Br): 73%
305c (Cl): 83%



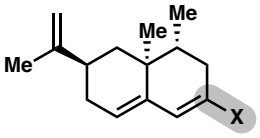
306a (I): 49%
306b (Br): 77%
306c (Cl): 80%



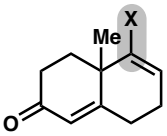
307a (I): 35%[d,e]
307b (Br): 75%
307c (Cl): 66%



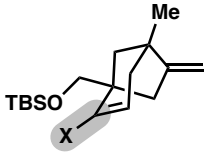
308a (I): 52%
308b (Br): 78%
308c (Cl): 75%



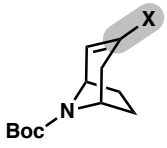
309a (I): 54%[c]
309b (Br): 82%
309c (Cl): 85%



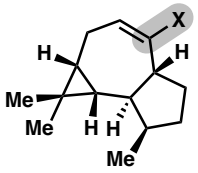
310a (I): 53%[c]
310b (Br): 78%
310c (Cl): 90%



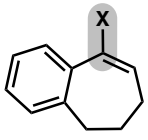
311a (I): 83%
311b (Br): 78%[d]
311c (Cl): 82%[d]



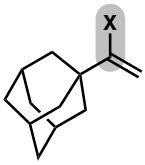
312a (I): 53%[c]
312b (Br): 65%
312c (Cl): 84%



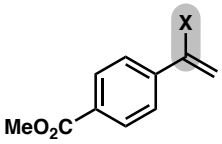
313a (I): 75%
313b (Br): 88%
313c (Cl): 88%



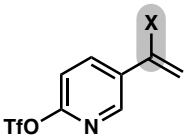
314a (I): 80%
314b (Br): 73%
314c (Cl): 71%



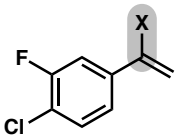
315a (I): 84%
315b (Br): 78%
315c (Cl): 78%



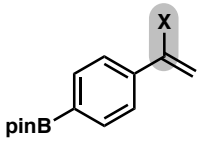
316a (I): 64%
316b (Br): 90%



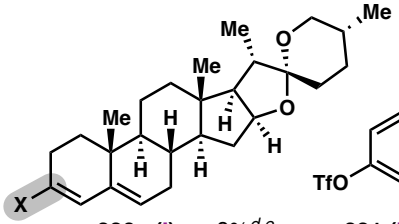
317a (I): 54%
317b (Br): 80%



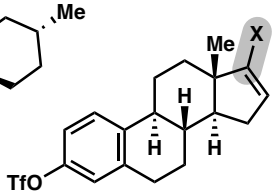
318a (I): 69%
318b (Br): 73%



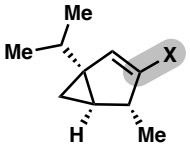
319a (I): 68%
319b (Br): 64%



320a (I): 9%[d,e]
320b (Br): 75%
320c (Cl): 97%



321 (I): 5%[d,e]
321b (Br): 59%
321c (Cl): 83%



322a (I): 3%[d,e]
322b (Br): 38%[f]
322c (Cl): 78%

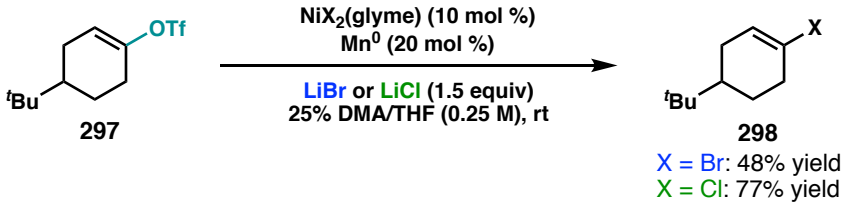
[a] Isolated yields, reactions conducted on 0.3 mmol scale under an N_2 atmosphere. [b] 0.5 mmol scale. [c] Enol nonaflate used. [d] 0.1 mmol scale. [e] Determined by ^{1}H NMR vs 1,2,4,5-tetrachloronitrobenzene as an internal standard. [f] 5 mol % $Ni(cod)_2$.

formation, but gave good yields of the alkenyl chlorides. The alkenyl iodide formation typically worked best for unactivated cyclohexenyl and cycloheptenyl triflates. For several substrates, alkenyl iodide formation from the enol triflate was poor yielding; however, use of the corresponding enol nonaflate resulted in significantly higher yields of the iodide (**305a**, **309a**, **310a**, **312a**). The iodination of **300** could be conducted on gram scale to give alkenyl iodide **301a** in 72% yield.

5.4 APPLICATION OF NICKEL (II) CATALYSTS

Due to the relative bench stability and cost effectiveness of Ni(II) precatalysts compared to $Ni(cod)_2$, we investigated the use of Ni(II) salts with *in situ* reduction by Mn^0 or Zn^0 in the presence and absence of 1,5-cyclooctadiene (cod). Initial attempts to use NiX_2(glyme) and Mn^0 in the bromination and chlorination of **297** proved inferior to the corresponding $Ni(cod)_2$ conditions (Scheme 5.5). Unfortunately, the heterogeneous nature of these conditions rendered these transformations sensitive to reaction set up and stirring. Further optimization of Ni(II) precatalysts would prove more fruitful, but were discovered after extensive development of the Ni(0) precatalyst transformation.

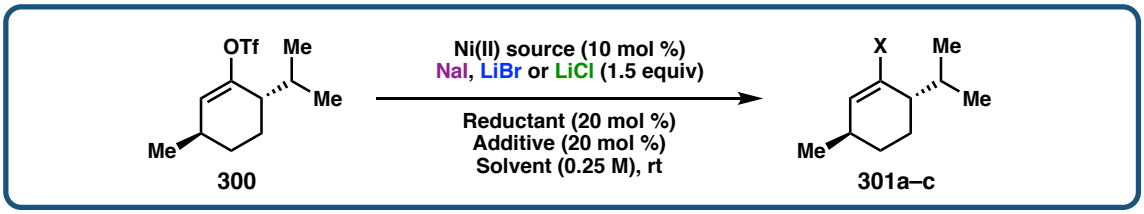
Scheme 5.5. *Initial attempts at use of Ni(II) precatalysts.*



We next turned our attention to the use of NiX_2 catalysts, as there is no commercially available NiX_2(glyme) iodide equivalent. Recognizing the potential utility of 1,5-cyclooctadiene (cod) as a ligand in the transformation, both Mn^0 and Zn^0 were

screened as reductants in the presence and absence of exogenous cod (Table 5.6). While moderate reactivity was observed for the bromination and chlorination reactions with NiX_2 salts (Table 5.6, entries 2-3), inconsistent results across all three halogenation reactions were discouraging for further optimization efforts (entries 1-4). Other Ni(II) catalysts, such as $Ni(acac)_2$ and $Ni(OTf)_2$, did not display any reactivity (entries 6 and 8). Finally, the use of NiX_2(glyme) with Zn^0 and exogenous cod gave bromide **301b** and chloride **301c** in excellent 87% yields (Table 5.6, entry 9). Gratifyingly, $Ni(OAc)_2$•$4H_2O$ provided similar yields for the bromination and chlorination, and a promising 33% yield of iodide **301a** (Table 5.6, entry 10).

Table 5.6. *Initial exploration of Ni(II) precatalyst conditions.*

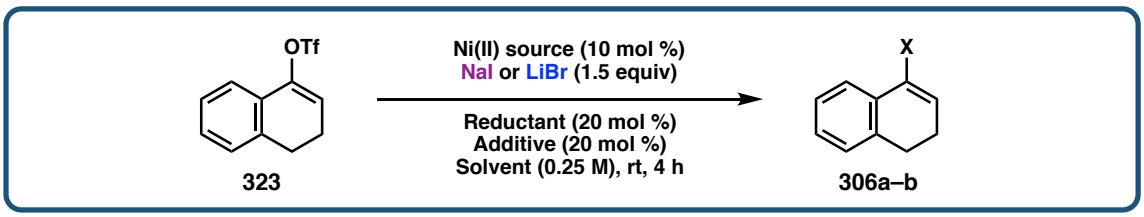


Entry	Ni source	reductant	additive	solvent	Yield 301a (%)	Yield 301b (%)	Yield 301c (%)
1	NiX_2	Mn^0	none	DMA/THF	0	0	0
2	NiX_2	Mn^0	COD	DMA/THF	4	41	63
3	NiX_2	Zn^0	none	DMA/THF	4	37	57
4	NiX_2	Zn^0	COD	DMA/THF	25	86	0
5	NiX_2	Zn^0	COD	DMA	62	83	0
6	$Ni(acac)_2$	Zn^0	none	DMA/THF	0	0	0
7	$Ni(acac)_2$	DIBAL	none	DMA/THF	3	5	0
8	$Ni(OTf)_2$	Zn^0	none	DMA/THF	0	0	0
9	NiX_2(dme)	Zn^0	COD	DMA/THF	—	87	87
10	$Ni(OAc)_2$•$4H_2O$	Zn^0	COD	DMA/THF	33	95	94

After observing promising reactivity with $Ni(OAc)_2$•$4H_2O$, we screened a number of Ni(II) catalysts with Zn^0 as a reductant, with cod, and in exclusively DMA, for the

iodination and bromination reaction (Table 5.7, entries 2-4). Unfortunately, the iodination under these conditions gave only trace amount of product. However, after evaluation of a number of additives, we discovered the addition of 20 mol % DMAP, as well as extending the reaction time, increased the yield of the iodination to 95% (Table 5.7, entry 6)

Table 5.7. *Optimization of Ni(II) precatalyst conditions.*

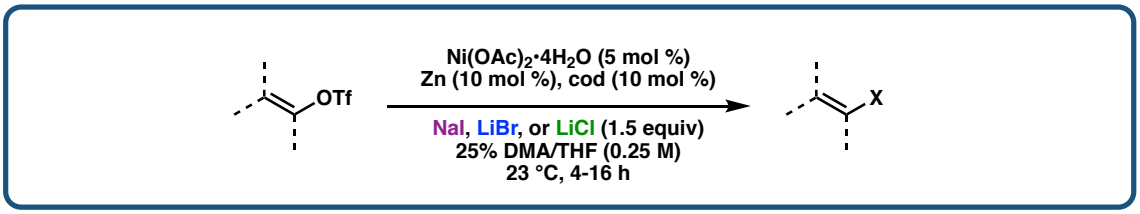


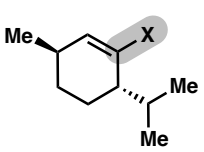
Entry	Ni source	reductant	additive	solvent	Yield 306a (%)	Yield 306b (%)
1	$Ni(acac)_2$	Zn^0	COD	DMA/THF	4	91
2	$Ni(acac)_2$	Zn^0	COD	DMA	4	97
3	$Ni(OTf)_2$	Zn^0	COD	DMA	5	0
4	$Ni(OAc)_2{\cdot}4H_2O$	Zn^0	COD	DMA	0	39
5	$Ni(OAc)_2{\cdot}4H_2O$	Zn^0	COD	DMA/THF	33	95
6	$Ni(OAc)_2{\cdot}4H_2O$	Zn^0	COD + DMAP	DMA/THF	95*	95

*reaction run 24 h

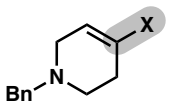
With optimized Ni(II) reaction conditions in hand, we explored the substrate scope under these conditions. Gratifyingly, the yields of the iodination, bromination, and chlorination of several substrates increased significantly over their corresponding Ni(0) results (Table 5.8). While $Ni(OAc)_2{\cdot}4H_2O$ is an inexpensive catalyst, we were pleased to see the yields of our halogenation reaction remained high even at lower Ni loading (5 mol %). Notably, substrates such as ketal **305** and tropinone-derivative **312** improved remarkably under these new reaction conditions.

***Table 5.8**. Substrate scope under Ni(II) precatalyst conditions.*[a]

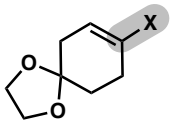




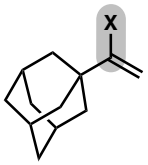
301a (I): 98%[b]
301b (Br): 78%
301c (Cl): 73%



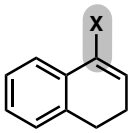
303a (I): 95%[b]
303b (Br): 92%
303c (Cl): 90%



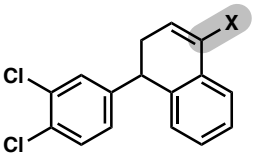
305a (I): 81%[b]
305b (Br): 94%
305c (Cl): 88%



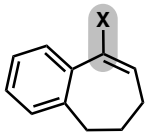
315a (I): 82%[b]
315b (Br): 90%
315c (Cl): 86%



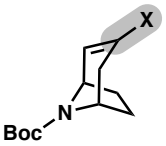
306a (I): 95%[b]
306b (Br): 96%
306c (Cl): 93%



308a (I): 80%[b]
308b (Br): 94%
308c (Cl): 87%



314a (I): 95%[b]
314b (Br): 94%
314c (Cl): 91%



312a (I): 55%[b]
312b (Br): 98%
312c (Cl): 98%

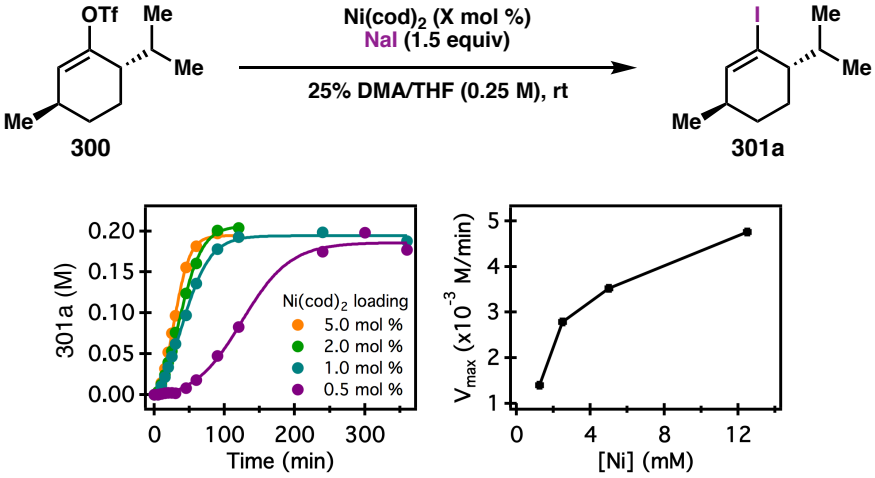
[a] Isolated yields, reactions conducted on 0.3 mmol scale under an N_2 atmosphere. [b] $Ni(OAc)_2 \cdot 4H_2O$ (10 mol %), Zn^0 (20 mol %), cod (20 mol %), DMAP (20 mol %). Determined by ^1H NMR vs 1,2,4,5-tetrachloronitrobenzene as an internal standard.

5.5 MECHANISTIC INVESTIGATIONS

To better understand the Ni-catalyzed halogenation of enol triflates, and the iodination in particular, a series of mechanistic experiments were performed on our initial Ni(0) system. The iodination of **300** exhibits an induction period at low $Ni(cod)_2$ loadings (e.g. 0.5 mol %, 1 mol %) (Figure 5.1). Addition of exogenous 1,5-cyclooctadiene (cod) inhibits the rate of the reaction, which suggests ligand dissociation could be the source of the induction period. Plotting V_{max} vs. [Ni] revealed that the reaction has a positive-order dependence on [Ni] that negatively deviates from first order at higher [Ni], suggesting the formation of dimeric (or higher order) off-cycle species at higher [Ni].[33] No change in the rate of iodination of **300** is observed when the amount of NaI is increased beyond 1 equiv. Although 10 mol % $Ni(cod)_2$ was used in Table 5.5 because it proved most robust

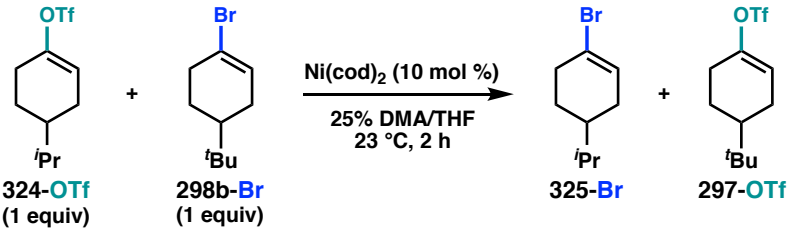
over a broad range of substrates, for highly reactive substrates, lower catalyst loadings can be beneficial to reduce formation of homodimers.

Figure 5.1. *Kinetic analysis.*



A crossover experiment was designed to evaluate the reversibility of alkenyl halide formation: treatment of a 1:1 mixture of **324** and **298b** with $Ni(cod)_2$ (10 mol %) in 1:3 DMA/THF at 23 °C resulted in complete recovery of **297** and **298b**, without detection of crossover products **297** or **325** (Scheme 5.6). Addition of 0.1 or 1.0 equiv LiBr resulted in conversion of **324** to **325** in 10% and 90% yield, respectively;[34] no **297** was detected at any point in either reaction. Monitoring the reaction by ^1H NMR confirms that no oxidative addition of **324** occurs in the absence of halide salt. Upon addition of a metal halide salt, conversion of **300** to the alkenyl halide (**301a–c**) was observed concomitantly with the formation of a Ni(I)–X species. The same Ni(I)–X species were detected upon mixing **301a–c** and $Ni(cod)_2$ (5 mol %).[35,36]

***Scheme 5.6**. Crossover experiment.*[a]



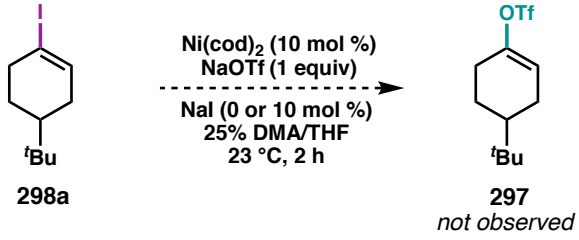
324-OTf (1 equiv) + **298b-Br (1 equiv)** → **325-Br** + **297-OTf**

	324-OTf (%)[b]	298b-Br (%)[b]	325-Br (%)[b]	297-OTf (%)[b]
no change	100	100	0	0
w/ LiBr (0.1 equiv)	90	100	10	0
w/ LiBr (1.0 equiv)	0	100	90	0

[a] Reactions conducted on 0.2 mmol scale under an inert atmosphere. [b] Determined by GC analysis vs undecane as an internal standard.

Similarly, subjection of alkenyl iodide **298a** to $Ni(cod)_2$ (10 mol %) and metal triflate salts (e.g. NaOTf) did not result in enol triflate formation (Scheme 5.7). Taken together, these results suggest that oxidative addition of the alkenyl triflate is irreversible, or that halide exchange for triflate in the oxidative addition complex is rapid and irreversible. In either scenario, the irreversible consumption of the enol triflate enables the reaction to proceed in good yield to the respective alkenyl halides. This is in contrast to Ni-catalyzed halide exchange reactions, which are thermodynamically driven equilibrium processes.[26] For example, an 85:15 mixture of **298b:298a** is obtained after 2 hours for both the Ni-catalyzed reactions of **298b** with LiI, or **298a** with LiBr.

***Scheme 5.7**. Attempts to observe halide-triflate exchange.*



298a → **297** *not observed*

5.6 CONCLUSION

In conclusion, two methods for a mild, Ni-catalyzed halogenation of alkenyl triflates have been developed. By modifying the halide salt, we observe that alkenyl iodides, bromides, or chlorides can be obtained using simple, commercially available catalysts, in a homogeneous or heterogeneous reaction. This reaction proceeds at room temperature and exhibits good functional group tolerance.

5.7 EXPERIMENTAL SECTION

5.7.1 *Materials and Methods*

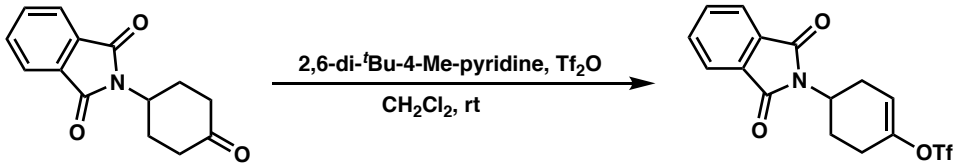
Unless otherwise stated, reactions were performed under a N_2 atmosphere using freshly dried solvents. Tetrahydrofuran (THF) and methylene chloride (CH_2Cl_2) were dried by passing through activated alumina columns. Diisopropylamine (*i*-Pr_2NH) was distilled over calcium hydride prior to use. Anhydrous dimethylacetamide (DMA), sodium iodide (NaI), lithium bromide (LiBr), and lithium chloride (LiCl) were purchased from Aldrich and stored under N_2. $Ni(cod)_2$ was purchased from Strem and stored in the glovebox at –20 °C. 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, CAM, or $KMnO_4$ staining. Flash column chromatography was performed as described by Still et al.[1] using silica gel (230-400 mesh, Silicycle). Purified compounds were dried on a high vacuum line (0.2 torr) to remove trace solvent. 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 cyroprobe (at 400 MHz and 101 MHz, respectively), a Varian 400 MR (at 400 MHz and 101 MHz, respectively), or a Varian Inova 500 (at 500 MHz and 126 MHz, respectively). ^1H and ^{19}F NMR spectra were also recorded on a Varian Inova 300 (at 300 MHz and 282 MHz, respectively). NMR data is reported relative to internal $CHCl_3$ (^1H, $\delta = 7.26$), $CDCl_3$ (^{13}C, $\delta = 77.0$), CD_3CN (^1H, $\delta = 1.94$), CD_3CN (^{13}C, $\delta = 1.32$), and C_6F_6 (^{19}F, $\delta = -161.64$). Data for ^1H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicity and qualifier abbreviations are as follows: s = singlet, d =

doublet, t = triplet, q = quartet, m = multiplet, br = broad. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm^{-1}). HRMS were acquired from the Caltech Mass Spectral Facility using fast-atom bombardment (FAB), electrospray ionization (ESI-TOF), or electron impact (EI).

5.7.2 *Substrate Preparation*

5.7.2.1 Enol Triflates

4-(1,3-dioxoisoindolin-2-yl)cyclohex-1-en-1-yl trifluoromethanesulfonate (326)



To a round bottom flask was added 2-(4-oxocyclohexyl)isoindoline-1,3-dione (730 mg, 3.0 mmol, 1.0 equiv), 2,6-di-tert-butyl-4-methylpyridine (924 mg, 4.5 mmol, 1.5 equiv), CH_2Cl_2 (10 mL), and trifluoromethanesulfonic anhydride (757 μL, 4.5 mmol, 1.5 equiv) sequentially. The reaction was stirred at room temperature overnight, then diluted with hexanes and filtered over a plug of Celite. The Celite was washed with CH_2Cl_2. The organic filtrate was washed with H_2O and brine, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried with $MgSO_4$, filtered, and concentrated. The product was purified by column chromatography (silica, 30% EtOAc/hexanes) to yield 752 mg (67% yield) of **326** as a white solid.

$\mathbf{R_f}$ = 0.30 (silica, 30% Et_2O/hexanes, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.77 – 7.66 (m, 2H), 5.78 (dt, *J* = 5.9, 2.3 Hz, 1H), 4.43 (dddd, *J* = 12.7, 10.8, 5.5, 3.1 Hz, 1H), 3.07 (dddt, *J* =

17.3, 10.7, 4.3, 2.3 Hz, 1H), 2.81 – 2.68 (m, 1H), 2.68 – 2.54 (m, 1H), 2.52 – 2.40 (m, 1H), 2.39 – 2.26 (m, 1H), 1.92 (dddd, J = 12.5, 5.9, 3.8, 1.8 Hz, 1H).

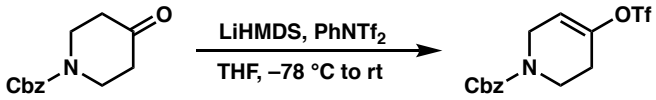
^{13}C NMR (101 MHz, $CDCl_3$): δ 168.2, 148.2, 134.3, 131.9, 123.4, 118.6 (q, J_{C-F} = 320.2 Hz), 116.9, 45.6, 27.7, 26.7, 26.1.

^{19}F NMR (282 MHz, $CDCl_3$): δ –73.7.

FTIR (NaCl, thin film, cm^{-1}): 1704, 1698, 1418, 1385, 1249, 1196, 1139, 1112, 876, 718.

HRMS (TOF-ESI, *m/z*): calc'd for $C_{15}H_{13}F_3O_5NS$ $[M+H]^+$: 376.0467; found: 376.0467.

Benzyl 4-(((trifluoromethyl)sulfonyl)oxy)-3,6-dihydropyridine-1(2*H*)-carboxylate (327)



Benzyl 4-oxopiperidine-1-carboxylate (1.17 g, 5.0 mmol, 1.0 equiv) was added to a round-bottom flask and placed under an atmosphere of N_2. THF (25 mL) was added and the reaction was cooled to –78 °C. LiHMDS (5.5 mL, 1 M in THF, 5.5 mmol, 1.1 equiv) was added dropwise and allowed to stir for 30 minutes before N-phenyl-bis(trifluoromethanesulfonimide) (1.88 g, 5.25 mmol, 1.05 equiv) was added in one portion. The reaction was allowed to reach room temperature and stir overnight. The reaction was then quenched with saturated aq. NH_4Cl (50 mL) and extracted with Et_2O (2 x 50 mL). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated. The product was purified by column chromatography (silica, 20% Et_2O/hexanes) to yield 901 mg (49% yield) of **327** as a colorless oil.

R_f = 0.30 (silica, 30% Et_2O/hexanes, $KMnO_4$).

^{1}H NMR (400 MHz, d_3-MeCN, 65 °C): δ 7.39 (s, 1H), 7.38 (s, 2H), 7.37 – 7.30 (m, 1H), 5.91 – 5.85 (m, 1H), 5.18 – 5.14 (m, 2H), 4.14 – 4.06 (m, 2H), 3.69 (t, J = 5.8 Hz, 2H), 2.47 (ttt, J = 5.7, 2.8, 1.3 Hz, 2H).

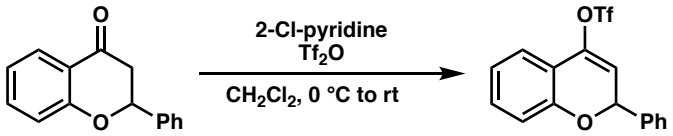
^{13}C NMR (101 MHz, d_3-MeCN, 65 °C): δ 156.2, 148.4, 138.5, 129.7, 129.2, 129.0, 117.4, 68.3, 43.1, 41.9, 29.0.

^{19}F NMR (282 MHz, $CDCl_3$): δ -71.7.

FTIR (NaCl, thin film, cm^{-1}): 3035, 2953, 1714, 1418, 1366, 1281, 1211, 1142, 1116, 1065, 872, 766, 698, 611.

HRMS (TOF-ESI, *m/z*): calc'd for $C_{14}H_{14}F_3NO_5S$ $[M+H]^+$: 366.0623; found: 366.0613.

2-phenyl-2*H*-chromen-4-yl trifluoromethanesulfonate (328)



To a flame dried, N_2-filled round bottom flask was added 2-phenylchroman-4-one (500 mg, 2.9 mmol, 1.0 equiv), 2-chloropyridine (304 mg, 2.7 mmol, 1.2 equiv), and CH_2Cl_2 (8 mL). The reaction was cooled to 0 °C before trifluoromethanesulfonic anhydride (0.45 mL, 2.7 mmol, 1.2 equiv) was added. The reaction was allowed to reach room temperature and continued to stir overnight. The reaction was then cooled to 0 °C, saturated aq. $NaHCO_3$ was slowly added until gas evolution ceased, and then H_2O (25 mL) was added. The crude mixture was extracted with CH_2Cl_2 (2 x 50 mL). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated. The product was purified by column chromatography (silica, 4% EtOAc/hexanes) to yield 421 mg (53% yield) of **328** as a pale solid.

R_f = 0.60 (silica, 10% Et_2O/hexanes, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 – 7.44 (m, 2H), 7.44 – 7.35 (m, 3H), 7.30 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.26 (td, *J* = 8.1, 7.7, 1.6 Hz, 1H), 6.99 (td, *J* = 7.6, 1.1 Hz, 1H), 6.86 (dd, *J* = 8.1, 1.0 Hz, 1H), 6.12 (d, *J* = 3.8 Hz, 1H), 5.85 (d, *J* = 3.8 Hz, 1H).

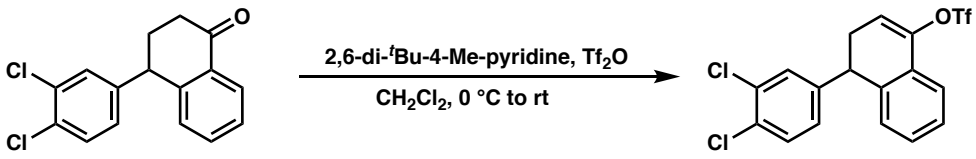
^{13}C NMR (101 MHz, $CDCl_3$): δ 153.9, 143.2, 138.8, 131.9, 129.2, 129.0, 127.1, 121.70, 121.67, 118.5 (q, J_{C-F} = 320.5 Hz), 116.6, 116.4, 113.1, 77.4.

^{19}F NMR (282 MHz, $CDCl_3$): δ -73.4.

FTIR (NaCl, thin film, cm^{-1}): 3068, 3036, 1667, 1607, 1485, 1455, 1428, 1354, 1248, 1222, 1139, 1032, 935, 883, 858, 758, 698.

HRMS (FAB, *m/z*): calc'd for $C_{16}H_{11}F_3O_4S$ $[M+\cdot]^+$: 356.0330; found: 356.0304.

4-(3,4-dichlorophenyl)-3,4-dihydronaphthalen-1-yl trifluoromethanesulfonate (329)



To a round bottom flask was added 4-(3,4-dichlorophenyl)-3,4-dihydronaphthalen-1(2*H*)-one (1.46 g, 5.0 mmol, 1.0 equiv), 2,6-di-*tert*-butyl-4-methylpyridine (1.13 g, 5.5 mmol, 1.1 equiv), and CH_2Cl_2 (15 mL). The reaction was cooled to 0 °C before trifluoromethanesulfonic anhydride (1.0 mL, 6.0 mmol, 1.2 equiv) was added. The reaction was allowed to reach room temperature and stirred for 30 minutes before being concentrated. The reaction mixture was then suspended in hexanes, filtered over a plug of Celite, and eluted with additional hexanes. The solution was concentrated and the product was purified by column chromatography (silica, 2% Et_2O/hexanes) to yield 2.09 g (99% yield) of **329** as a colorless oil.

R_f = 0.23 (silica, hexanes, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.39 (d, *J* = 8.3 Hz, 1H), 7.35 (tdd, *J* = 7.7, 1.4, 0.6 Hz, 1H), 7.32 – 7.26 (m, 2H), 7.03 (ddd, *J* = 8.3, 2.2, 0.5 Hz, 1H), 6.94 – 6.89 (m, 1H), 5.97 (t, *J* = 4.8 Hz, 1H), 4.18 (t, *J* = 7.9 Hz, 1H), 2.89 (ddd, *J* = 17.4, 7.4, 4.8 Hz, 1H), 2.72 (ddd, *J* = 17.3, 8.6, 4.9 Hz, 1H).

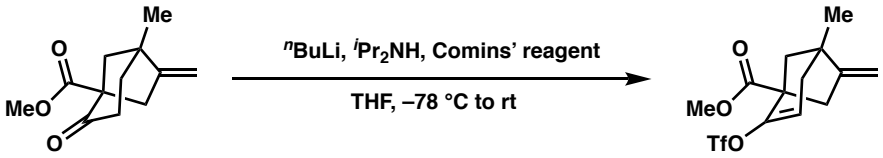
^{13}C NMR (101 MHz, $CDCl_3$): δ 146.2, 143.2, 137.4, 132.8, 131.2, 130.8, 130.3, 130.0, 128.7, 128.4, 127.9, 127.7, 121.9, 118.7 (q, $J_{C\text{-}F}$ = 320.4 Hz), 116.0, 42.4, 30.8.

^{19}F NMR (282 MHz, $CDCl_3$): δ -73.5.

FTIR (NaCl, thin film, cm^{-1}): 1658, 1470, 1422, 1249, 1213, 1140, 1066, 1019, 895, 765, 612.

HRMS (EI, *m/z*): calc'd for $C_{17}H_{11}Cl_2F_3O_3S$ $[M+\cdot]^+$: 421.9758; found: 421.9755.

methyl (1*s*,5*r*)-5-methyl-6-methylene-2-(((trifluoromethyl)sulfonyl)oxy)bicyclo[3.2.1] oct-2-ene-1-carboxylate (330)



To a flame dried, N_2 filled round bottom flask was added methyl (1*s*,5*r*)-5-methyl-6-methylene-2-oxobicyclo[3.2.1]octane-1-carboxylate (670 mg, 3.0 mmol, 1 equiv) and THF (15 mL). The reaction was cooled to –78 °C (dry ice/acetone) before LDA (0.75M in THF, 4.8 mL, 3.6 mmol, 1.2 equiv) was added via cannula. The reaction mixture was stirred for 30 minutes before Comins' reagent (1M in THF, 3.45 mL, 3.45 mmol, 1.15 equiv) was added via cannula. After 1 hour, the reaction was quenched by addition of saturated aq. $NaHCO_3$ (20 mL) and warmed to room temperature. The crude mixture was extracted with Et_2O (3 x 15 mL) and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The product was purified by column chromatography (silica, 5% EtOAc/hexanes) to yield 865 mg (81% yield) of **330** as a clear oil.

R_f = 0.54 (silica, 10% EtOAc/hexanes, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.63 (dd, *J* = 4.9, 2.6 Hz, 1H), 5.02 (ddd, *J* = 2.5, 1.7, 0.8 Hz, 1H), 4.96 (dd, *J* = 3.0, 1.9 Hz, 1H), 3.76 (s, 3H), 3.11 – 2.92 (m, 2H), 2.37 (dd, *J* = 17.3, 2.7 Hz, 1H), 2.17 (ddd, *J* = 11.0, 2.7, 0.8 Hz, 1H), 2.11 – 2.02 (m, 1H), 1.96 (dd, *J* = 11.0, 1.5 Hz, 1H), 1.26 (s, 3H).

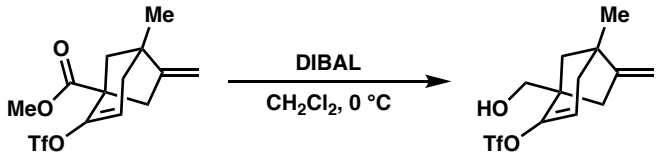
^{13}C NMR (101 MHz, $CDCl_3$): δ 171.1, 155.2, 149.6, 120.0 (q, $J_{C\text{-}F}$ = 319.9 Hz), 116.5, 107.7, 52.8, 52.6, 48.2, 44.7, 42.9, 41.9, 23.9.

^{19}F NMR (282 MHz, $CDCl_3$): δ –74.4.

FTIR (NaCl, thin film, cm^{-1}): 2959, 1744, 1420, 1299, 1249, 1209, 1142, 1071, 1029, 265, 623.

HRMS (FAB, *m/z*): calc'd for $C_{13}H_{15}F_3O_3S$ $[M+NH_4]^+$: 358.0931; found: 358.0924.

(1*r*,5*r*)-1-(hydroxymethyl)-5-methyl-6-methylenebicyclo[3.2.1]oct-2-en-2-yl trifluoromethanesulfonate (331)



To a flame dried, N_2 filled round bottom flask was added **330** (783 mg, 2.3 mmol, 1 equiv) and CH_2Cl_2 (23 mL). The reaction was cooled to 0 °C before DIBAL (1.23 mL, 6.9 mmol, 3 equiv) was added slowly. After 45 minutes, the reaction was quenched by addition of 1M HCl (6 mL) and warmed to room temperature. The crude mixture was diluted with water (20 mL) and extracted with CH_2Cl_2 (3 x 15 mL). The combined organic layers were washed with saturated aq. $NaHCO_3$ (30 mL), then brine (30 mL), and dried over $MgSO_4$, filtered and concentrated. The product was purified by column chromatography (silica, 10% to 20% EtOAc/hexanes) to yield 670 mg (93% yield) of **331** as a clear oil.

R_f = 0.36 (silica, 20% EtOAc/hexanes, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.61 (dd, *J* = 4.7, 2.7 Hz, 1H), 4.97 (ddd, *J* = 2.4, 1.4, 0.7 Hz, 1H), 4.94 (dd, *J* = 3.0, 1.7 Hz, 1H), 3.99 (dd, *J* = 11.3, 5.3 Hz, 1H), 3.59 (dd, *J* = 11.3, 5.7 Hz, 1H), 2.78 (ddt, *J* = 15.8, 3.2, 1.7 Hz, 1H), 2.41 – 2.29 (m, 2H), 2.08 – 1.98 (m, 2H), 1.74 – 1.67 (m, 2H), 1.25 (s, 3H).

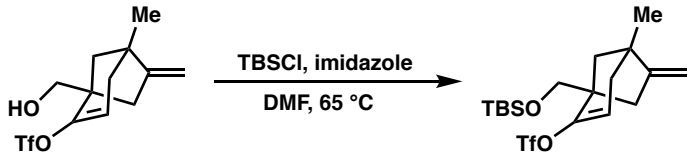
^{13}C NMR (101 MHz, $CDCl_3$): δ 156.6, 153.1, 118.7 (q, J_{C-F} = 319.8 Hz), 117.2, 107.1, 64.5, 48.4, 47.4, 44.3, 43.1, 42.3, 24.4.

^{19}F NMR (282 MHz, $CDCl_3$): δ –74.2.

FTIR (NaCl, thin film, cm^{-1}): 3390 (br), 3076, 2959, 2880, 1668, 1416, 1211, 1142, 1030, 871, 621.

HRMS (FAB, *m/z*): calc'd for $C_{11}H_{11}F_3O_3S$ $[M+H]^+$: 330.0981; found: 330.0981.

(1*r*,5*r*)-1-(((*tert*-butyldimethylsilyl)oxy)methyl)-5-methyl-6-methylenebicyclo[3.2.1] oct-2-en-2-yl trifluoromethanesulfonate (332)



To a round bottom flask was added **331** (576 mg, 1.8 mmol, 1 equiv), imidazole (251 mg, 3.7 mmol, 2 equiv), DMF (18 mL), and TBSCl (333 mg, 2.2 mmol, 1.2) equiv). The reaction was heated to 65 °C for 12 hours, cooled to room temperature and quenched by addition of saturated aq. NH_4Cl (20 mL). The crude mixture was extracted with EtOAc (3 x 20 mL), then the combined organic layers were washed with saturated aq. $NaHCO_3$ (30 mL), then saturated aq. NH_4Cl (3 x 30 mL), dried over $MgSO_4$, filtered, and concentrated. The product was purified by column chromatography (silica, hexanes to 3% EtOAc/Hexanes) to yield 738 mg (94% yield) of **332** as a white solid.

$\mathbf{R}_f$ = 0.27 (silica, hexanes, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.55 (dd, *J* = 4.7, 2.7 Hz, 1H), 4.95 (ddd, *J* = 2.5, 1.5, 0.8 Hz, 1H), 4.92 (dd, *J* = 3.1, 1.7 Hz, 1H), 3.90 (d, *J* = 10.1 Hz, 1H), 3.51 (d, *J* = 10.1 Hz, 1H), 2.69 (ddt, *J* = 15.8, 3.1, 1.6 Hz, 1H), 2.43 – 2.35 (m, 1H), 2.32 (dd, *J* = 17.1, 2.7 Hz, 1H), 2.06 – 1.97 (m, 1H), 1.91 (dd, *J* = 11.0, 2.8 Hz, 1H), 1.69 (dd, *J* = 10.9, 1.5 Hz, 1H), 1.24 (s, 3H), 0.89 (s, 9H), 0.05 (s, 6H).

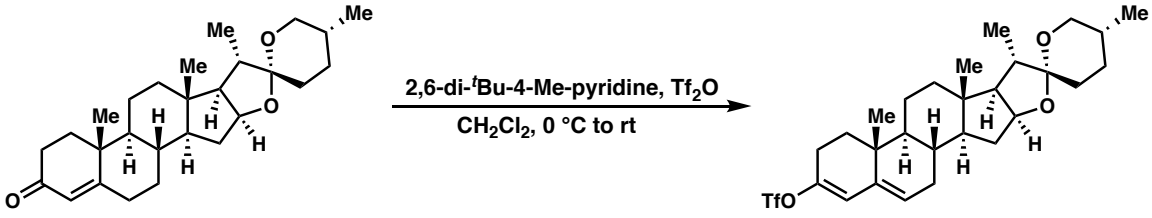
^{13}C NMR (101 MHz, $CDCl_3$): δ 157.3, 153.6, 120.1 (q, J_{C-F} = 319.3 Hz), 116.3, 106.7, 64.0, 48.4, 47.6, 43.8, 43.0, 42.4, 26.0, 24.5, 18.5, -5.5.

^{19}F NMR (282 MHz, $CDCl_3$): δ –74.4.

FTIR (NaCl, thin film, cm^{-1}): 3076, 2957, 2860, 1668, 1473, 1418, 1246, 1211, 1144, 1101, 1031, 874, 840, 778, 620.

HRMS (FAB, *m/z*): calc'd for $C_{18}H_{29}F_3O_4S$ $[M+H]^+$: 427.1581; found: 427.1568.

(5'*R*,6a*R*,6b*S*,8a*S*,8b*R*,9*S*,10*R*,11a*S*,12a*S*,12b*S*)-5',6a,8a,9-tetramethyl-1,3',4',5,5',6,6a,6b,-6',7,8,8a,8b,9,11a,12,12a,12b-octadecahydrospiro[naphtho[2',1':4,5]indeno[2,1-*b*]furan-10,2'-pyran]-4-yl trifluoromethanesulfonate (333)



To a round bottom flask was added (5'*R*,6a*R*,6b*S*,8a*S*,8b*R*,9*S*,10*R*,11a*S*,12a*S*,12b*S*)-5',6a,8a,9-tetramethyl-1,3',4',5,5',6,6a,6b,6',7,8,8a,8b,9,11a,12,12a,12b-octadecahydrospiro[naphtha[2',1':4-,5]indeno[2,1-*b*]furan-10,2'-pyran]-4(3*H*)-one (661 mg, 1.8 mmol, 1.0 equiv), 2,6-di-tert-butyl-4-methylpyridine (395 mg, 2.16 mmol, 1.2 equiv), and CH_2Cl_2 (5.0 mL). The reaction was cooled to 0 °C and trifluoromethanesulfonic anhydride (296 μL, 1.98 mmol, 1.1 equiv) was added. The reaction was stirred at room temperature overnight, then washed with saturated aq. $NaHCO_3$ (50 mL) and extracted with CH_2Cl_2 (2 x 100 mL). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated. The product was purified by column chromatography (silica, 5 to 10% Et_2O/hexanes) to yield 488 mg (50% yield) of **333** as a white solid.

$\mathbf{R_f}$ = 0.40 (silica, 10% Et_2O/hexanes, $KMnO_4$).

$[\boldsymbol{a}]_{\boldsymbol{D}}^{\mathbf{25}}$ = –125° (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.99 (d, *J* = 2.2 Hz, 1H), 5.57 (dd, *J* = 5.1, 2.9 Hz, 1H), 4.42 (ddd, *J* = 8.6, 7.5, 6.3 Hz, 1H), 3.47 (ddd, *J* = 10.8, 4.6, 2.0 Hz, 1H), 3.37 (t, *J* = 10.9 Hz, 1H), 2.63 – 2.48 (m, 1H), 2.40 – 2.30 (m, 1H), 2.23 (dt, *J* = 18.8, 5.2 Hz, 1H), 1.99 (ddd, *J* = 11.8, 7.5, 5.4 Hz, 1H), 1.95 – 1.51 (m, 11H), 1.51 – 1.39 (m, 2H), 1.32 (ddd, *J* = 13.7, 11.9, 6.4 Hz, 2H), 1.26 – 1.11 (m, 2H), 1.09 – 0.99 (m, 1H), 0.99 (s, 6H), 0.81 (s, 3H), 0.79 (d, *J* = 6.3 Hz, 3H).

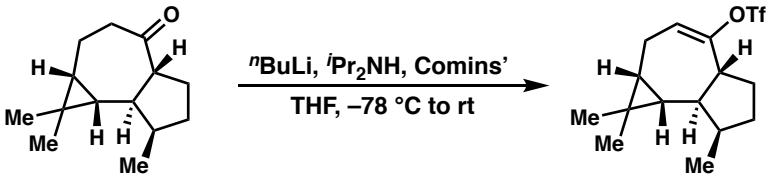
^{13}C NMR (101 MHz, $CDCl_3$): δ 147.1, 138.2, 128.1, 120.6, 118.7 (q, $J_{C\text{-}F}$ = 319.9 Hz), 109.5, 80.9, 67.0, 62.2, 56.6, 47.8, 41.8, 40.5, 39.8, 35.0, 33.9, 32.2, 31.9, 31.5, 31.3, 30.4, 28.9, 25.7, 21.2, 18.8, 17.3, 16.5, 14.7.

^{19}F NMR (282 MHz, $CDCl_3$): δ -73.8.

FTIR (NaCl, thin film, cm^{-1}): 3054, 2947, 2306, 1640, 1456, 1380, 1266, 1214, 1140, 1051, 919, 829, 740.

HRMS (FAB, *m/z*): calc'd for $C_{28}H_{40}F_3O_5S$ $[M+H]^+$: 545.2549; found: 545.2536.

(1a*R*,4a*R*,7*R*,7a*S*,7b*S*)-1,1,7-trimethyl-1a,2,4a,5,6,7,7a,7b-octahydro-1*H*-cyclopropa[*e*]azulen-4-yl trifluoromethanesulfonate (334)



To a round bottom flask was added diisopropyl amine (337 μL, 2.4 mmol, 1.2 equiv) and THF (6 mL). The solution was cooled to 0 °C, then *n*-butyllithium (960 μL, 2.5 M in hexanes, 2.4 mmol, 1.2 equiv) was added and stirred for 30 minutes before being cooled to –78 °C. (1a*R*,4a*R*,7*R*,7a*S*,7b*S*)-1,1,7-Trimethyldecahydro-4*H*-cyclopropa[*e*]azulen-4-one (412 mg, 2.0 mmol, 1.0 equiv) was added and stirred for 30 minutes before N-(5-chloro-2-pyridyl)bis(trifluoromethanesulfonimide) (942 mg, 2.4 mmol, 1.2 equiv) was added in one portion. The reaction was allowed to reach room temperature and stir overnight. The reaction was quenched with H_2O and extracted with Et_2O (2 x 50 mL). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated. The product was purified by column chromatography (silica, hexanes) to yield 386 mg (57% yield) of **334** as a colorless oil which solidified in the freezer.

$\mathbf{R}_f$ = 0.49 (silica, hexanes, $KMnO_4$).

$[\boldsymbol{a}]_D^{25}$ = –93° (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.74 (ddd, *J* = 9.3, 2.9, 2.1 Hz, 1H), 2.79 (tdd, *J* = 11.3, 5.4, 2.0 Hz, 1H), 2.29 (dddd, *J* = 17.3, 9.3, 7.0, 0.8 Hz, 1H), 2.24 – 2.11 (m, 1H), 2.11 – 1.90 (m, 3H), 1.70 (td, *J* = 11.7, 8.4 Hz, 1H), 1.56 – 1.41 (m, 1H), 1.24 (dtd, *J* = 13.1, 8.5, 4.3 Hz, 1H), 1.05 (d, *J* = 1.1 Hz, 6H), 0.97 (ddd, *J* = 10.1, 9.3, 7.0 Hz, 1H), 0.92 (d, *J* = 7.2 Hz, 3H), 0.65 (dd, *J* = 11.5, 9.2 Hz, 1H).

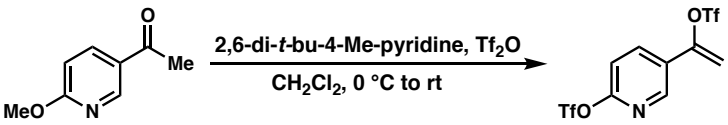
^{13}C NMR (101 MHz, $CDCl_3$): δ 154.6, 120.1, 118.7 (q, $J_{C\text{-}F}$ = 319.9 Hz), 48.0, 43.1, 34.4, 32.0, 29.8, 28.5, 25.7, 25.6, 20.3, 18.7, 18.0, 15.3.

^{19}F NMR (282 MHz, $CDCl_3$): δ -74.3.

FTIR (NaCl, thin film, cm^{-1}): 2957, 2872, 1672, 1457, 1415, 1246, 1208, 1145, 984, 941, 865.

HRMS (FAB, *m/z*): calc'd for $C_{15}H_{21}F_3O_3S$ $[M+\cdot]^+$: 338.1164; found: 338.1164.

1-(6-(((trifluoromethyl)sulfonyl)oxy)pyridin-3-yl)vinyl trifluoromethanesulfonate (335)

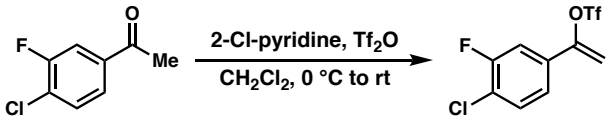


To a round bottom flask was added 1-(6-methoxypyridin-3-yl)ethan-1-one (756 mg, 5.0 mmol, 1.0 equiv), 2,6-di-tert-butyl-4-methylpyridine (2.26 g, 11 mmol, 2.2 equiv), and CH_2Cl_2 (15 mL). The reaction was cooled to 0 °C before trifluoromethanesulfonic anhydride (2.0 mL, 12.0 mmol, 2.4 equiv) was added. The reaction was allowed to reach room temperature and stir overnight. The reaction was then cooled to 0 °C and saturated aq. $NaHCO_3$ was added slowly until gas evolution ceased, then H_2O (25 mL) was added. The crude mixture was extracted with Et_2O (2 x 50 mL). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated. The product was purified by column chromatography (silica, 20% Et_2O/hexanes) to yield 544 mg (27% yield) of **335** as a light orange oil.

$\mathbf{R}_f$ = 0.33 (silica, 30% Et_2O/hexanes, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.59 (dd, *J* = 2.6, 0.7 Hz, 1H), 8.03 (dd, *J* = 8.6, 2.6 Hz, 1H), 7.30 – 7.23 (m, 1H), 5.75 (d, *J* = 4.5 Hz, 1H), 5.61 (d, *J* = 4.6 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 156.6, 149.0, 145.9, 138.0, 129.3, 118.7 (q, J_{C-F} = 320.6 Hz), 118.6 (q, J_{C-F} = 320.4 Hz), 115.4, 108.0.
^{19}F NMR (282 MHz, $CDCl_3$): δ -72.8, -73.3.
FTIR (NaCl, thin film, cm^{-1}): 1648, 1588, 1474, 1427, 1212, 1138, 943, 890, 819.
HRMS (TOF-ESI, *m/z*): calc'd for $C_9H_5F_6O_6NS_2$ $[M+H]^+$: 401.9541; found: 401.9551.

1-(4-chloro-3-fluorophenyl)vinyl trifluoromethanesulfonate (336)



To a flame dried, N_2 filled round bottom flask was added 1-(4-chloro-3-fluorophenyl)vinyl trifluoromethanesulfonate (500 mg, 2.9 mmol, 1.0 equiv), 2-chloropyridine (428 mg, 3.8 mmol, 1.3 equiv), and CH_2Cl_2 (10 mL). The reaction was cooled to 0 °C before trifluoromethanesulfonic anhydride (0.58 mL, 3.5 mmol, 1.2 equiv) was added. The reaction was allowed to reach room temperature and continued to stir overnight. The reaction was then cooled to 0 °C and saturated aq. $NaHCO_3$ was added slowly until gas evolution ceased, then H_2O (25 mL) was added. The crude mixture was extracted with CH_2Cl_2 (2 x 50 mL). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated. The product was purified by column chromatography (silica, hexanes) to yield 434 mg (49% yield) of **336** as a light yellow oil.

R_f = 0.31 (silica, hexanes, UV).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (dd, *J* = 8.4, 7.3 Hz, 1H), 7.32 (dd, *J* = 9.6, 2.1 Hz, 1H), 7.29 (ddd, *J* = 8.4, 2.1, 0.9 Hz, 1H), 5.64 (d, *J* = 4.3 Hz, 1H), 5.47 (d, *J* = 4.3 Hz, 1H).

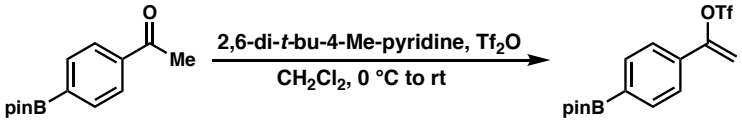
^{13}C NMR (101 MHz, $CDCl_3$): 158.3 (d, J_{C-F} = 250.3 Hz), 151.3 (d, J_{C-F} = 2.7 Hz), 132.6 (d, J_{C-F} = 7.2 Hz), 131.4, 123.5 (d, J_{C-F} = 17.7 Hz), 121.8 (d, J_{C-F} = 3.9 Hz), 118.6 (q, J_{C-F} = 320.3 Hz), 113.8 (d, J_{C-F} = 23.7 Hz), 106.0.

^{19}F NMR (282 MHz, $CDCl_3$): δ -73.5, -113.2 (dd, J_{F-H} = 9.3, 7.3 Hz).

FTIR (NaCl, thin film, cm^{-1}): 1647, 1575, 1492, 1423, 1296, 1244, 1216, 1141, 1080, 955, 916, 803, 607.

HRMS (FAB, *m/z*): calc'd for $C_9H_5ClF_4O_3S$ $[M+\cdot]^+$: 303.9584; found: 303.9592.

1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)vinyl trifluoromethanesulfonate (337)



To a round bottom flask was added 1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)ethan-1-one (984 mg, 4.0 mmol, 1.0 equiv), 2,6-di-tert-butyl-4-methylpyridine (904 mg, 4.4 mmol, 1.1 equiv), and CH_2Cl_2 (12 mL). The reaction was cooled to 0 °C before trifluoromethanesulfonic anhydride (808 μL, 4.8 mmol, 1.2 equiv) was added. The reaction was allowed to reach room temperature and continued to stir overnight. The reaction was concentrated and the product was purified by column chromatography (silica, 5% EtOAc/hexanes) to yield 742 mg (49% yield) of **337** as a blue oil.

R_f = 0.51 (silica, 10% Et_2O/hexanes, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 – 7.81 (m, 2H), 7.56 – 7.51 (m, 2H), 5.67 (d, J = 4.0 Hz, 1H), 5.41 (d, J = 4.0 Hz, 1H), 1.35 (s, 12H).

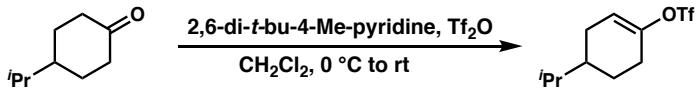
^{13}C NMR (101 MHz, $CDCl_3$): δ 153.6, 135.3, 134.4, 124.5, 118.6 (q, J_{C-F} = 320.2 Hz), 105.1, 84.3, 25.0. *(Note: carbon bonded to boron not observed.)*

^{19}F NMR (282 MHz, $CDCl_3$): δ -73.7.

FTIR (NaCl, thin film, cm^{-1}): 2981, 1646, 1612, 1423, 1402, 1362, 1225, 1143, 1096, 939, 829, 660, 605.

HRMS (FAB, *m/z*): calc'd for $C_{15}H_{15}BF_3O_5S$ $[M+\cdot]^+$: 378.0920; found: 378.0946.

4-isopropylcyclohex-1-en-1-yl trifluoromethanesulfonate (324)



To a flame dried, N_2-filled round bottom flask was added 4-isopropylcyclohexan-1-one (1.8 g, 12.5 mmol, 1.0 equiv), 2,6-ditertbutyl-4-methylpyridine (3.0 g, 14.4 mmol, 1.15 equiv), and CH_2Cl_2 (83 mL). The reaction was cooled to 0 °C before trifluoromethanesulfonic anhydride (2.3 mL, 2.7 mmol, 1.2 equiv) was added. The reaction was allowed to reach room temperature and continued to stir overnight. The reaction was then cooled to 0 °C, saturated aq. $NaHCO_3$ was slowly added until gas evolution ceased, and then H_2O (25 mL) was added. The crude mixture was extracted with CH_2Cl_2 (2 x 50 mL). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated. The product was purified by column chromatography (silica, hexanes) to yield 2.3 g (68% yield) of **324** as a clear oil.

$\mathbf{R_f}$ = 0.49 (silica, hexanes, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.74 (dt, *J* = 5.2, 2.6 Hz, 1H), 2.46 – 2.34 (m, 1H), 2.34 – 2.25 (m, 1H), 2.25 – 2.14 (m, 1H), 1.98 – 1.84 (m, 2H), 1.61 – 1.49 (m, 1H), 1.49 – 1.29 (m, 2H), 0.91 (d, *J* = 3.0 Hz, 3H), 0.90 (d, *J* = 3.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 149.4, 118.6 (q, J_{C-F} = 320.1 Hz), 118.3, 39.0, 31.7, 28.1, 27.4, 26.2, 20.0, 19.7.

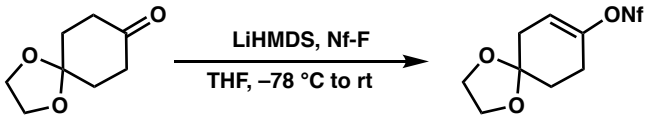
^{19}F NMR (282 MHz, $CDCl_3$): δ -73.9.

FTIR (NaCl, thin film, cm^{-1}): 2962, 2933, 2876, 1693, 1418, 1248, 1209, 1144, 1053, 1022, 879, 853, 615.

HRMS (EI, *m/z*): calc'd for $C_{10}H_{15}F_3O_3S$ $[M+\cdot]^+$: 272.0694; found: 272.0681.

5.7.2.2 Enol Nonaflates

1,4-dioxaspiro[4.5]dec-7-en-8-yl 1,1,2,2,3,3,4,4,4-nonafluorobutane-1-sulfonate (338)



1,4-dioxaspiro[4.5]decan-8-one (1.0 g, 6.4 mmol, 1.0 equiv) was added to a flame dried round-bottom flask and placed under an atmosphere of N_2. THF (13 mL) was added and the reaction was cooled to –78 °C. LiHMDS (8.3 mL, 1 M in THF, 5.5 mmol, 1.3 equiv) was added dropwise and allowed to stir for 30 minutes before perfluorobutanesulfonylfluoride (1.27 mL, 7.0 mmol, 1.1 equiv) was added in one portion. The reaction was allowed to reach room temperature and stir overnight. The reaction was then quenched with saturated aq. NH_4Cl (50 mL) and extracted with Et_2O (2 x 50 mL). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated. The product was purified by column chromatography (silica, 10% EtOAc/hexanes) to yield 1.3 g (45 % yield) of (**338**) as a colorless oil.

R_f = 0.66 (silica, 20% Et_2O/hexanes, anisaldehyde (blue)).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.68 (tt, *J* = 4.1, 1.4 Hz, 1H), 3.98 (p, *J* = 1.7 Hz, 4H), 2.54 (dtd, *J* = 6.6, 3.4, 2.6, 1.4 Hz, 2H), 2.41 (dt, *J* = 4.8, 2.6 Hz, 2H), 1.91 (t, *J* = 6.6 Hz, 2H).

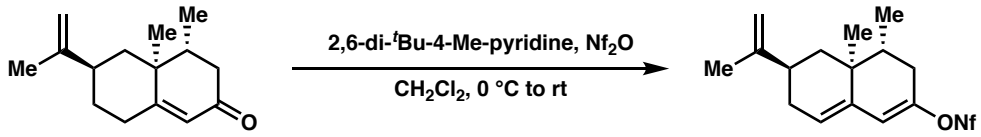
^{13}C NMR (101 MHz, $CDCl_3$): δ 148.4, 116.1, 106.3, 64.8, 34.3, 31.2, 26.6. (*Note: nonaflate carbons omitted due to low intensity resulting from C-F splitting*)

^{19}F NMR (282 MHz, $CDCl_3$): δ -80.55 (tt, *J* = 9.7, 2.3 Hz), -109.78 – -109.95 (m), -120.87 (dddd, *J* = 14.9, 9.8, 6.4, 2.4 Hz), -125.66 – -125.90 (m).

FTIR (NaCl, thin film, cm^{-1}): 2965, 2890, 1691, 1422, 1240, 1144, 1070, 883.

HRMS (EI, *m/z*): calc'd for $C_{12}H_{12}F_9O_5S$ $[M+H]^+$: 439.0261; found: 439.0276.

(4*R*,4a*S*,6*R*)-4,4a-dimethyl-6-(prop-1-en-2-yl)-3,4,4a,5,6,7-hexahydronaphthalen-2-yl 1,1,2,2,3,3,4,4,4-nonafluorobutane-1-sulfonate (339)



To a round bottom flask was added (4*S*,4a*R*,6*S*)-4,4a-dimethyl-6-(prop-1-en-2-yl)-4,4a,5,6,7,8-hexahydronaphthalen-2(3*H*)-one (174 mg, 0.8 mmol, 1.0 equiv), 2,6-di-tert-butyl-4-methylpyridine (312 mg, 0.9 mmol, 1.1 equiv), and CH_2Cl_2 (4 mL). The reaction was cooled to 0 °C before nonafluorobutanesulfonic anhydride (465 mg, 0.8 mmol, 1.0 equiv) was added. The reaction was allowed to reach room temperature and continued to stir for 2 hours. The reaction was diluted with hexanes, filtered, and concentrated. The product was purified by column chromatography (silica, hexanes) to yield 226 mg (56% yield) of (**339**) as a colorless oil.

R*f* = 0.22 (silica, hexanes, UV).

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$ = –66° (c = 0.5, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.04 (s, 1H), 5.63 (dd, *J* = 5.3, 2.7 Hz, 1H), 4.76 (pd, *J* = 1.9, 1.3 Hz, 2H), 2.50 – 2.36 (m, 1H), 2.36 – 2.29 (m, 3H), 2.26 (td, *J* = 5.4, 1.4 Hz, 1H), 1.98 (ddd, *J* = 18.9, 11.4, 2.3 Hz, 1H), 1.79 – 1.65 (m, 5H), 1.18 (t, *J* = 12.7 Hz, 1H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.93 (s, 3H).

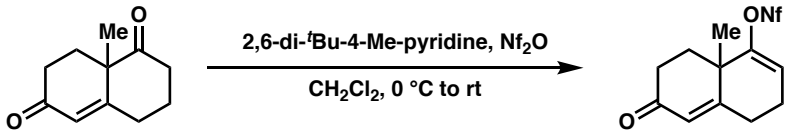
^{13}C NMR (101 MHz, $CDCl_3$): δ 149.6, 147.1, 138.5, 128.2, 120.5, 109.3, 39.7, 39.3, 37.1, 35.9, 34.3, 31.4, 30.3, 20.8, 17.3, 14.5. (*Note: nonaflate carbons omitted due to low intensity resulting from C-F splitting*)

^{19}F NMR (282 MHz, $CDCl_3$): δ -80.57 (tt, *J* = 9.8, 2.3 Hz), -109.77 – -109.94 (m), -120.90 (dddt, *J* = 15.8, 9.7, 6.3, 3.3 Hz), -125.69 – -125.92 (m).

FTIR (NaCl, thin film, cm^{-1}): 2969, 1644, 1416, 1238, 1142, 1058, 912.

HRMS (EI, *m/z*): calc'd for $C_{19}H_{20}F_9O_3S$ $[M-H]^+$: 499.0989; found: 499.0965.

8a-methyl-6-oxo-3,4,6,7,8,8a-hexahydronaphthalen-1-yl 1,1,2,2,3,3,4,4,4-nonafluorobutane-1-sulfonate (340)



To a round bottom flask was added 8a-methyl-3,4,8,8a-tetrahydronaphthalene-1,6(2*H*,7*H*)-dione (142 mg, 0.8 mmol, 1.0 equiv), 2,6-di-tert-butyl-4-methylpyridine (312 mg, 0.9 mmol, 1.1 equiv), and CH_2Cl_2 (4 mL). The reaction was cooled to 0 °C before nonafluorobutansulfonic anhydride (465 mg, 0.8 mmol, 1.0 equiv) was added. The reaction was allowed to reach room temperature and continued to stir for 2 hours. The reaction was diluted with hexanes, filtered, and concentrated. The product was purified by column chromatography (silica, 10% Et_2O/hexanes) to yield 270 mg (73% yield) of (**340**) as a white solid.

R_f = 0.32 (silica, 25% Et_2O/hexanes, UV).

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.15 (d, *J* = 2.3 Hz, 1H), 5.89 – 5.82 (m, 1H), 2.81 (ddd, *J* = 15.4, 7.3, 6.2 Hz, 1H), 2.74 – 2.35 (m, 5H), 2.07 (ddd, *J* = 13.6, 5.9, 1.6 Hz, 1H), 1.75 – 1.61 (m, 1H), 1.25 (s, 3H).

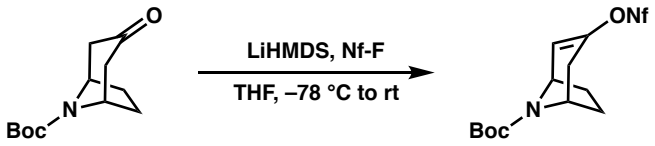
^{13}C NMR (101 MHz, $CDCl_3$): δ 213.0, 148.2, 136.4, 127.4, 119.4, 44.7, 35.2, 28.9, 25.1, 24.9, 22.7. (*Note: nonaflate carbons omitted due to low intensity resulting from C-F splitting*)

^{19}F NMR (282 MHz, $CDCl_3$): δ -80.57 (tt, *J* = 9.8, 2.3 Hz), -109.67 – -109.85 (m), -120.88 (dtd, *J* = 14.8, 7.1, 6.5, 4.2 Hz), -125.68 – -125.92 (m).

FTIR (NaCl, thin film, cm^{-1}): 2969, 2936, 1715, 1664, 1420, 1353, 1203, 1144, 1061, 880.

HRMS (EI, *m/z*): calc'd for $C_{15}H_{13}F_9O_4S$ $[M+\cdot]^+$: 460.0391; found: 460.0375.

tert-butyl (1*r*,5*s*)-3-(((perfluorobutyl)sulfonyl)oxy)-8-azabicyclo[3.2.1]oct-2-ene-8-carboxylate (341)



To a flame dried round-bottom flask under an inert atmosphere was added *tert*-butyl (1*R*,5*S*)-3-oxo-8-azabicyclo[3.2.1]octane-8-carboxylate (1.17 g, 5.0 mmol, 1.0 equiv). THF (9 mL) was added and the reaction was cooled to –78 °C. LiHMDS (5.5 mL, 1 M in THF, 5.5 mmol, 1.1 equiv) was added dropwise and allowed to stir for 30 minutes before perfluorobutanesulfonylfluoride (1.88 g, 5.25 mmol, 1.05 equiv) was added in one portion. The reaction was allowed to reach room temperature and stir overnight. The reaction was then quenched with saturated aq. NH_4Cl (50 mL) and extracted with Et_2O (2 x 50 mL). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated. The product was purified by column chromatography (silica, 10-20% Et_2O/hexanes) to yield 2.1 g (95% yield) of (**341**) as an off white solid.

R_f = 0.59 (silica, 75% Et_2O/hexanes, anisaldehyde (blue)).

^{1}H NMR (400 MHz, d_3-MeCN, 65 °C): δ 6.19 (ddd, *J* = 5.8, 1.9, 1.1 Hz, 1H), 4.53 – 4.45 (m, 1H), 4.44 – 4.36 (m, 1H), 3.08 – 2.95 (m, 1H), 2.23 (dddd, *J* = 13.6, 7.4, 6.3, 1.7 Hz, 1H), 2.16 (dt, *J* = 17.0, 1.2 Hz, 1H), 2.04 – 1.96 (m, 2H), 1.81 – 1.69 (m, 1H), 1.45 (s, 9H).

^{13}C NMR (101 MHz, d_3-MeCN, 65 °C): δ 154.9, 149.1, 125.3, 80.9, 53.6, 53.5, 37.6, 35.2, 30.4, 28.7. (*Note: nonaflate carbons omitted due to low intensity resulting from C-F splitting*)

^{19}F NMR (376 MHz, d_3-MeCN, 65 °C): δ -81.46 (tt, *J* = 9.7, 2.8 Hz), -109.99 (ddp, *J* = 16.8, 10.7, 2.7 Hz), -121.10 – -121.26 (m), -125.91 – -126.07 (m). (*Note: not standardized with internal C_6F_6*).

FTIR (NaCl, thin film, cm^{-1}): 3188, 3076, 2981, 1697, 1416, 1326, 1243, 1064, 875.

HRMS (EI, *m/z*): calc'd for $C_{16}H_{19}F_9O_5SN$ $[M+H]^+$: 508.0843; found: 508.0840.

5.7.3 Ni-Catalyzed Halogenation

5.7.3.1 General Procedures for Ni-Catalyzed Halogenation

General Procedure 1: Enol Triflate Halogenation on 0.1 mmol Scale

A 1-dram vial equipped with a stir bar was brought into a N_2-filled glovebox. The vial was charged with NaI, LiBr, or LiCl (0.15 mmol, 1.5 equiv) and $Ni(cod)_2$ (2.8 mg, 0.01 mmol, 0.1 equiv). Anhydrous DMA (0.1 mL) and THF (0.3 mL) were added, resulting in a clear yellow solution. Enol triflate (0.1 mmol, 1 equiv) was added neat, turning the reaction dark red (NaI) or aqua blue (LiBr or LiCl) over several minutes. The vial was sealed with a Teflon cap and brought out of the glovebox to stir on the bench (480 rpm) for two hours at room temperature. The reaction was quenched by eluting through a small plug of silica gel (5 cm of silica in a large glass pipette) with 40% Et_2O/pentane (10 mL collected). The crude reaction mixture was concentrated under reduced pressure and analyzed by NMR with tetrachloronitrobenzene as an external standard.

General Procedure 2: Enol Triflate Halogenation on 0.3 mmol Scale

A 2-dram vial was equipped with a stir bar and brought into a N_2-filled glovebox. The vial was charged with NaI, LiBr, or LiCl (0.45 mmol, 1.5 equiv) and $Ni(cod)_2$ (8.3 mg, 0.03 mmol, 0.1 equiv). Anhydrous DMA (0.3 mL) and THF (0.9 mL) were added, resulting in a clear yellow solution. Enol triflate (0.3 mmol, 1 equiv) was added in one portion, turning the reaction dark red (NaI) or aqua blue (LiBr or LiCl) over several minutes. The vial was sealed with Teflon cap and brought out of the glovebox. The reaction was allowed to stir on the bench (480 rpm) for two hours at room temperature. Reaction was quenched by addition of water and Et_2O. The organic layer was separated

and extracted with 2 x 10 mL Et_2O, then washed once with brine (20 mL). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude reaction was purified by silica gel chromatography to afford the desired product.

General Procedure 3: Enol Triflate Halogenation on 6.0 mmol Scale

A 100 mL Schlenk flask was equipped with a stir bar and brought into a N_2-filled glovebox. The vial was charged with NaI, LiBr, or LiCl (9.0 mmol, 1.5 equiv) and $Ni(cod)_2$ (166 mg, 0.6 mmol, 0.1 equiv). Anhydrous DMA (6 mL) and THF (18 mL) were added, resulting in a clear yellow solution. Enol triflate (6.0 mmol, 1 equiv) was added in one portion, turning the reaction dark red (NaI) or aqua blue (LiBr or LiCl) over several minutes. The Schlenk flask was sealed with a Kontes valve and brought out of the glovebox. The reaction was allowed to stir on the bench (480 rpm) for two hours at room temperature. Reaction was quenched by addition of water and Et_2O. The organic layer was separated and extracted with 2 x 200 mL Et_2O, then washed once with brine (400 mL). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude reaction was purified by silica gel chromatography to afford the desired product.

General Procedure 4: Enol Nonaflate Halogenation on 0.3 mmol Scale

A 2-dram vial was equipped with a stir bar and brought into a N_2-filled glovebox. The vial was charged with NaI, LiBr, or LiCl (0.45 mmol, 1.5 equiv) and $Ni(cod)_2$ (8.3 mg, 0.03 mmol, 0.1 equiv). Anhydrous DMA (0.3 mL) and THF (0.9 mL) were added,

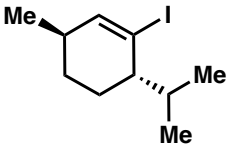
resulting in a clear yellow solution. Enol nonaflate (0.3 mmol, 1 equiv) was added in one portion, turning the reaction dark red (NaI) or aqua blue (LiBr or LiCl) over several minutes. The vial was sealed with Teflon cap and brought out of the glovebox. The reaction was allowed to stir on the bench (480 rpm) for two hours at room temperature. Reaction was quenched by addition of water and Et_2O. The organic layer was separated and extracted with 2 x 10 mL Et_2O, then washed once with brine (20 mL). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude reaction was purified by silica gel chromatography to afford the desired product.

General Procedure 5: Enol Triflate Halogenation on 0.1 mmol Scale with $Ni(OAc)_2$•$4H_2O$

A 1-dram vial was equipped with a stir bar and brought into a N_2-filled glovebox. The vial was charged with Zn^0 (0.01 mmol), $Ni(OAc)_2$•$4H_2O$ (0.005 mmol), 1,5-cyclooctadiene (cod) (0.01 mmol), anhydrous DMA (0.1 mL) and THF (0.3 mL). The reactions were stirred for 20 min at room temperature, then enol triflate (0.1 mmol, 1 equiv) was added. The vial was brought out of the glovebox to stir on the bench (480 rpm) for four to 24 hours at room temperature. Reactions were quenched by eluting through a small plug of silica gel (5 cm) in a large glass pipette with 40% Et_2O/pentane (10 mL collected). The crude reaction mixtures were concentrated under reduced pressure and analyzed by NMR with an internal standard (1,2,4,5-tetrachloronitrobenzene).

5.7.3.2 Characterization of Reaction Products

(3*R*,6*S*)-1-iodo-6-isopropyl-3-methylcyclohex-1-ene (301a)



Prepared from (3*R*,6*S*)-6-isopropyl-3-methylcyclohex-1-en-1-yl trifluoromethanesulfonate (143.2 mg, 0.3 mmol) and sodium iodide (112.5 mg, 0.75 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, pentane) to yield **301a** (96 mg, 73% yield) as a colorless oil.

$\mathbf{R}_f$ = 0.79 (silica, pentane, $KMnO_4$).

$\mathbf{[\alpha]_D^{25}}$ = –47° (c = 0.5, $CHCl_3$).

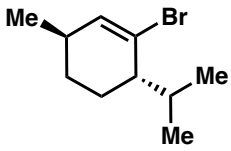
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.36 (d, *J* = 1.2 Hz, 1H), 2.35 – 2.14 (m, 3H), 1.89 – 1.79 (m, 1H), 1.68 (dddd, *J* = 13.3, 5.9, 4.5, 3.0 Hz, 1H), 1.54 – 1.42 (m, 1H), 1.18 (tdd, *J* = 13.1, 10.2, 3.1 Hz, 1H), 0.97 (d, *J* = 7.0 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.72 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 146.8, 109.2, 48.7, 35.7, 32.4, 30.9, 23.0, 21.5, 20.5, 15.1.

FTIR (NaCl, thin film, cm^{-1}): 2958, 2868, 1617, 1457, 1367, 1314, 944, 852, 782, 703.

HRMS (EI, *m/z*): calc'd for $C_{10}H_{17}I$ $[M+\cdot]^+$: 264.0375; found: 264.0392.

(3*R*,6*S*)-1-bromo-6-isopropyl-3-methylcyclohex-1-ene (301b)



Prepared from (3*R*,6*S*)-6-isopropyl-3-methylcyclohex-1-en-1-yl trifluoromethanesulfonate (85.9 mg, 0.3 mmol) and lithium bromide (39.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, pentane) to yield **301b** (52 mg, 80% yield) as a colorless oil.

$\mathbf{R}_f$ = 0.77 (silica, hexanes, $KMnO_4$).

$\mathbf{[\alpha]_D^{25}}$ = –26° (c = 1.0, $CHCl_3$).

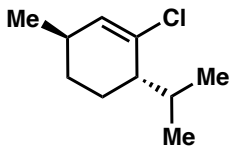
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.99 (td, *J* = 2.0, 1.0 Hz, 1H), 2.39 (ddt, *J* = 13.7, 6.8, 3.4 Hz, 1H), 2.32 (ddtd, *J* = 9.8, 5.8, 3.8, 1.8 Hz, 1H), 2.24 – 2.12 (m, 1H), 1.85 – 1.71 (m, 2H), 1.51 – 1.39 (m, 1H), 1.14 (tdd, *J* = 12.4, 10.1, 2.6 Hz, 1H), 0.98 (d, *J* = 7.1 Hz, 3H), 0.93 (d, *J* = 7.0 Hz, 3H), 0.75 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 137.8, 129.5, 47.0, 33.9, 30.8, 29.6, 23.2, 21.6, 20.3, 15.4.

FTIR (NaCl, thin film, cm^{-1}): 2959, 2930, 2870, 2854, 1634, 1458, 1387, 1318, 949, 851, 791.

HRMS (EI, *m/z*): calc'd for $C_{10}H_{17}Br$ $[M+\cdot]^+$: 216.0514; found: 216.0532.

(3*R*,6*S*)-1-chloro-6-isopropyl-3-methylcyclohex-1-ene (301c)



Prepared from (3*R*,6*S*)-6-isopropyl-3-methylcyclohex-1-en-1-yl trifluoromethanesulfonate (85.9 mg, 0.3 mmol) and lithium chloride (19.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, pentane) to yield **301c** (37 mg, 72% yield) as a colorless oil.

R_f = 0.87 (silica, hexanes, $KMnO_4$).

$[\alpha]_D^{25}$ = –11° (c = 0.5, $CHCl_3$).

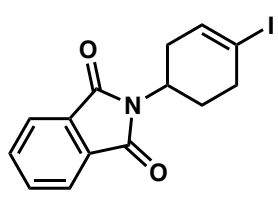
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.73 (td, *J* = 2.0, 1.0 Hz, 1H), 2.37 (m, 1H), 2.27 (ddtd, *J* = 9.7, 5.7, 3.8, 1.9 Hz, 1H), 2.23 – 2.14 (m, 1H), 1.84 – 1.71 (m, 2H), 1.48 – 1.35 (m, 1H), 1.16 – 1.04 (m, 1H), 0.98 (d, *J* = 7.0 Hz, 3H), 0.93 (d, *J* = 7.0 Hz, 3H), 0.76 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 136.5, 133.3, 45.8, 32.5, 30.8, 28.2, 22.8, 21.8, 20.3, 15.7.

FTIR (NaCl, thin film, cm^{-1}): 2960, 2870, 1642, 1454, 1368, 957, 851, 812, 727.

HRMS (EI, *m/z*): calc'd for $C_{10}H_{17}Cl$ $[M+\cdot]^+$: 172.1019; found: 172.1032.

2-(4-iodocyclohex-3-en-1-yl)isoindoline-1,3-dione (302a)



Prepared from 4-(1,3-dioxoisoindolin-2-yl)cyclohex-1-en-1-yl trifluoromethanesulfonate (113 mg, 0.3 mmol) and sodium iodide (67.5 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, 10 to 25% Et_2O/hexanes) to yield **302a** (53 mg, 50% yield) as a white solid.

R_f = 0.40 (silica, 30% Et_2O/hexanes, $KMnO_4$).

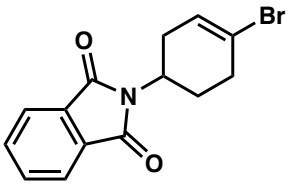
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (tt, *J* = 5.1, 2.4 Hz, 2H), 7.76 – 7.66 (m, 2H), 6.29 (dq, *J* = 5.7, 1.9 Hz, 1H), 4.44 (dqd, *J* = 11.5, 5.5, 3.1 Hz, 1H), 3.06 – 2.92 (m, 1H), 2.82 – 2.61 (m, 3H), 2.19 (dtd, *J* = 16.8, 5.7, 5.0, 3.0 Hz, 1H), 1.78 – 1.66 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 168.3, 135.5, 134.1, 132.0, 123.3, 95.1, 45.7, 39.9, 32.3, 28.9.

FTIR (NaCl, thin film, cm^{-1}): 1700, 1458, 1395, 1380, 1109, 990, 874, 716.

HRMS (FAB, *m/z*): calc'd for $C_{14}H_{12}NO_2I$ $[M+H]^+$: 353.9991; found: 353.9979.

2-(4-bromocyclohex-3-en-1-yl)isoindoline-1,3-dione (302b)



Prepared from 4-(1,3-dioxoisoindolin-2-yl)cyclohex-1-en-1-yl trifluoromethanesulfonate (113 mg, 0.3 mmol) and lithium bromide (39.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, 10 to 25% Et_2O/hexanes) to yield **302b** (65 mg, 71% yield) as a white solid.

$\mathbf{R}_f$ = 0.36 (silica, 30% Et_2O/hexanes, $KMnO_4$).

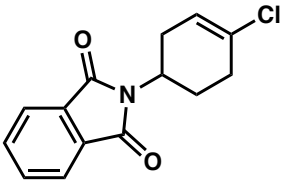
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 – 7.78 (m, 2H), 7.75 – 7.67 (m, 2H), 6.01 (dtd, *J* = 5.9, 2.3, 0.9 Hz, 1H), 4.42 (dddd, *J* = 12.6, 11.1, 5.5, 3.2 Hz, 1H), 3.01 – 2.89 (m, 1H), 2.79 – 2.63 (m, 2H), 2.63 – 2.51 (m, 1H), 2.25 – 2.14 (m, 1H), 1.88 – 1.76 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 168.3, 134.1, 132.0, 127.0, 123.3, 121.3, 46.0, 35.4, 30.4, 27.9.

FTIR (NaCl, thin film, cm^{-1}): 1695, 1464, 1396, 1111, 992, 919, 875, 717.

HRMS (TOF-ESI, *m/z*): calc'd for $C_{14}H_{12}NO_2Br$ $[M+H]^+$: 306.0130; found: 306.0121.

2-(4-chlorocyclohex-3-en-1-yl)isoindoline-1,3-dione (302c)



Prepared from 4-(1,3-dioxoisoindolin-2-yl)cyclohex-1-en-1-yl trifluoromethanesulfonate (113 mg, 0.3 mmol) and lithium chloride (19.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, 10 to 25% Et_2O/hexanes) to yield **302c** (72 mg, 92% yield) as a white solid.

$\mathbf{R}_f$ = 0.36 (silica, 30% Et_2O/hexanes, $KMnO_4$).

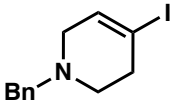
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85 – 7.79 (m, 2H), 7.74 – 7.68 (m, 2H), 5.80 (dtt, *J* = 5.9, 2.4, 0.7 Hz, 1H), 4.46 – 4.36 (m, 1H), 2.97 (dddt, *J* = 16.6, 11.0, 4.4, 2.3 Hz, 1H), 2.72 (tdd, *J* = 12.5, 11.8, 5.8 Hz, 1H), 2.66 – 2.55 (m, 1H), 2.49 – 2.40 (m, 1H), 2.27 – 2.18 (m, 1H), 1.90 – 1.82 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 168.3, 134.1, 132.0, 131.4, 123.3, 122.7, 46.2, 33.0, 29.1, 27.1.

FTIR (NaCl, thin film, cm^{-1}): 1700, 1465, 1378, 1112, 995, 920, 876, 717.

HRMS (FAB, *m/z*): calc'd for $C_{14}H_{12}NO_2Cl$ $[M+H]^+$: 262.0635; found: 262.0636.

1-benzyl-4-iodo-1,2,3,6-tetrahydropyridine (303a)



Prepared from 1-benzyl-1,2,3,6-tetrahydropyridin-4-yl trifluoromethanesulfonate (96 mg, 0.3 mmol) and sodium iodide (67.5 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, 10% Et_2O/hexanes) to yield **303a** (62 mg, 69% yield) as a light yellow oil.

R_f = 0.31 (silica, 10% Et_2O/hexanes, $KMnO_4$).

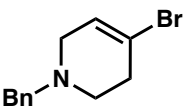
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 – 7.22 (m, 5H), 6.26 (td, *J* = 3.5, 1.7 Hz, 1H), 3.56 (s, 2H), 3.04 – 3.00 (m, 2H), 2.61 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 138.0, 135.3, 129.2, 128.5, 127.4, 93.2, 62.3, 55.7, 51.7, 39.8.

FTIR (NaCl, thin film, cm^{-1}): 2920, 2800, 2752, 1494, 1454, 1363, 1340, 1054, 960, 729, 698.

HRMS (FAB, *m/z*): calc'd for $C_{12}H_{14}IN$ $[M+H-H_2]^+$: 298.0093; found: 298.0081.

1-benzyl-4-bromo-1,2,3,6-tetrahydropyridine (303b)



Prepared from 1-benzyl-1,2,3,6-tetrahydropyridin-4-yl trifluoromethanesulfonate (96 mg, 0.3 mmol) and lithium bromide (39.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, 5% to 10 Et_2O/hexanes) to yield **303b** (60 mg, 79% yield) as a light yellow oil.

R_f = 0.60 (silica, 20% Et_2O/hexanes, $KMnO_4$).

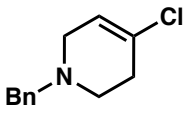
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 – 7.24 (m, 5H), 5.99 (tt, *J* = 3.5, 1.6 Hz, 1H), 3.59 (s, 2H), 3.01 (dt, *J* = 3.7, 2.8 Hz, 2H), 2.66 (td, *J* = 5.7, 0.6 Hz, 2H), 2.58 – 2.52 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 138.0, 129.1, 128.4, 127.4, 126.8, 119.9, 62.0, 54.1, 50.9, 35.8.

FTIR (NaCl, thin film, cm^{-1}): 3062, 3027, 2924, 2802, 2756, 1659, 1493, 1454, 1365, 1346, 1056, 995, 965, 822, 732, 698.

HRMS (TOF-ESI, *m/z*): calc'd for $C_{12}H_{14}BrN$ $[M+H]^+$: 252.0388; found: 252.0404.

1-benzyl-4-chloro-1,2,3,6-tetrahydropyridine (303c)



Prepared from 1-benzyl-1,2,3,6-tetrahydropyridin-4-yl trifluoromethanesulfonate (96 mg, 0.3 mmol) and lithium chloride (19.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, 5 to 10% Et_2O/hexanes) to yield **303c** (50 mg, 80% yield) as a light yellow oil.

R_f = 0.56 (silica, 20% Et_2O/hexanes, $KMnO_4$).

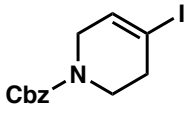
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 – 7.25 (m, 5H), 5.76 (tt, *J* = 3.5, 1.6 Hz, 1H), 3.60 (s, 2H), 3.03 (dt, *J* = 3.6, 2.8 Hz, 2H), 2.67 (t, *J* = 5.7 Hz, 2H), 2.43 (ttd, *J* = 5.7, 2.8, 1.5 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 138.1, 130.3, 129.1, 128.4, 127.4, 122.5, 62.0, 52.9, 50.2, 33.5.

FTIR (NaCl, thin film, cm^{-1}): 3062, 6027, 2925, 2801, 2759, 1666, 1494, 1454, 1365, 1350, 1059, 998, 972, 824, 735, 698.

HRMS (TOF-ESI, *m/z*): calc'd for $C_{12}H_{14}ClN$ $[M+H]^+$: 208.0893; found: 208.0881.

benzyl 4-iodo-3,6-dihydropyridine-1(2*H*)-carboxylate (304a)



Prepared from benzyl 4-(((trifluoromethyl)sulfonyl)oxy)-3,6-dihydropyridine-1(2*H*)-carboxylate (110 mg, 0.3 mmol) and sodium iodide (67.5 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, 10% Et_2O/hexanes) to yield **304a** (61 mg, 60% yield) as a colorless oil.

R_f = 0.25 (silica, 10% EtOAc/hexanes, $KMnO_4$).

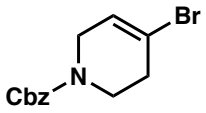
^{1}H NMR (400 MHz, d_3-MeCN, 65 °C): δ 7.61 – 7.11 (m, 5H), 6.38 – 6.30 (m, 1H), 5.13 (s, 2H), 3.97 (q, *J* = 3.0 Hz, 2H), 3.58 (t, *J* = 5.7 Hz, 2H), 2.69 – 2.49 (m, 2H).

^{13}C NMR (101 MHz, d_3-MeCN, 65 °C): δ 156.4, 138.6, 135.5, 129.7, 129.1, 128.9, 92.7, 68.1, 47.7, 43.7, 39.9.

FTIR (NaCl, thin film, cm^{-1}): 3032, 2932, 2838, 1704, 1428, 1361, 1335, 1273, 1231, 1108, 1044, 1027, 964, 697.

HRMS (TOF-ESI, *m/z*): calc'd for $C_{13}H_{14}INO_2$ $[M+H]^+$: 344.0148; found: 344.0154.

benzyl 4-bromo-3,6-dihydropyridine-1(2*H*)-carboxylate (304b)



Prepared from benzyl 4-(((trifluoromethyl)sulfonyl)oxy)-3,6-dihydropyridine-1(2*H*)-carboxylate (110 mg, 0.3 mmol) and lithium bromide (39.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, 10% Et_2O/hexanes) to yield **304b** (81 mg, 91% yield) as a colorless oil.

R_f = 0.36 (silica, 30% EtOAc/hexanes, $KMnO_4$).

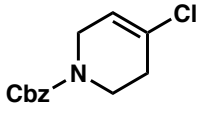
^{1}H NMR (400 MHz, d_3-MeCN, 65 °C): δ 7.38 (m, 4H), 7.33 (m, 1H), 6.06 (tt, *J* = 3.4, 1.7 Hz, 1H), 5.14 (s, 2H), 3.96 (q, *J* = 3.0 Hz, 2H), 3.63 (t, *J* = 5.8 Hz, 2H), 2.53 (ttd, *J* = 5.6, 2.7, 1.6 Hz, 2H).

^{13}C NMR (101 MHz, d_3-MeCN, 65 °C): δ 156.2, 138.5, 129.6, 129.1, 128.9, 127.1, 120.2, 68.0, 46.1, 43.0, 35.9.

FTIR (NaCl, thin film, cm^{-1}): 2934, 1698, 1428, 1361, 1336, 1274, 1230, 1111, 1027, 964, 757, 698.

HRMS (FAB, *m/z*): calc'd for $C_{13}H_{14}BrNO_2$ $[M+H]^+$: 296.0286; found: 296.0285.

benzyl 4-chloro-3,6-dihydropyridine-1(2*H*)-carboxylate (304c)



Prepared from benzyl 4-(((trifluoromethyl)sulfonyl)oxy)-3,6-dihydropyridine-1(2*H*)-carboxylate (110 mg, 0.3 mmol) and lithium chloride (19.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, 10% Et_2O/hexanes) to yield **304c** (65 mg, 86% yield) as a colorless oil.

R_f = 0.36 (silica, 30% EtOAc/hexanes, $KMnO_4$).

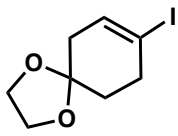
^{1}H NMR (400 MHz, d_3-MeCN, 65 °C): δ 7.41 – 7.36 (m, 4H), 7.36 – 7.31 (m, 1H), 5.84 (tt, *J* = 3.4, 1.6 Hz, 1H), 5.14 (s, 2H), 3.99 (q, *J* = 2.9 Hz, 2H), 3.64 (t, *J* = 5.8 Hz, 2H), 2.41 (ttd, *J* = 5.7, 2.7, 1.5 Hz, 2H).

^{13}C NMR (101 MHz, d_3-MeCN, 65 °C): δ 156.2, 138.5, 131.0, 129.7, 129.1, 128.9, 122.9, 68.0, 44.9, 42.4, 33.6.

FTIR (NaCl, thin film, cm^{-1}): 3033, 2940, 1698, 1497, 1428, 1362, 1276, 1233, 1112, 1049, 971, 813, 764, 699.

HRMS (TOF-ESI, *m/z*): calc'd for $C_{13}H_{14}ClNO_2$ $[M+H]^+$: 252.0791; found: 252.0807.

8-iodo-1,4-dioxaspiro[4.5]dec-7-ene (305a)



Prepared from 1,4-dioxaspiro[4.5]dec-7-en-8-yl 1,1,2,2,3,3,4,4,4-nonafluorobutane-1-sulfonate (131.4 mg, 0.3 mmol) and sodium iodide (67.5 mg, 0.45 mmol) according to General Procedure 4. The crude residue was purified by column chromatography (silica, 0.5% triethylamine/10% EtOAc/pentane) to yield **305a** (44 mg, 55% yield) as a colorless oil.

R_f = 0.45 (silica, 10% EtOAc/hexanes, $KMnO_4$).

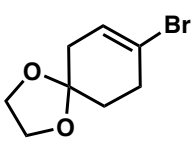
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.18 (tt, *J* = 3.9, 1.7 Hz, 1H), 3.97 (s, 4H), 2.70 (tq, *J* = 6.5, 2.2 Hz, 2H), 2.30 (dddd, *J* = 4.0, 3.3, 2.3, 1.2 Hz, 2H), 1.80 (tt, *J* = 6.5, 0.9 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 134.7, 106.1, 95.0, 64.6, 39.6, 38.7, 33.8.

FTIR (NaCl, thin film, cm^{-1}): 2882, 1651, 1429, 1366, 1252, 1114, 1059, 1022, 914, 860, 650.

HRMS (FAB, *m/z*): calc'd for $C_8H_{11}IO_2$ $[M+H]^+$: 266.9882; found: 266.9885.

8-bromo-1,4-dioxaspiro[4.5]dec-7-ene (305b)



Prepared from 1,4-dioxaspiro[4.5]dec-7-en-8-yl trifluoromethane-sulfonate (86.5 mg, 0.3 mmol) and lithium bromide (39.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, 10% Et_2O/pentane) to yield **305b** (48 mg, 73% yield) as a colorless oil.

R_f = 0.41 (silica, 10% EtOAc/hexanes, $KMnO_4$).

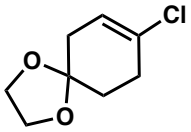
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.90 (tt, *J* = 4.0, 1.6 Hz, 1H), 3.97 (s, 4H), 2.62 (ttd, *J* = 6.5, 2.4, 1.6 Hz, 2H), 2.29 (dtt, *J* = 4.1, 2.4, 0.9 Hz, 2H), 1.84 (tt, *J* = 6.6, 0.9 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 126.2, 121.2, 106.4, 64.7, 37.7, 34.3, 32.8.

FTIR (NaCl, thin film, cm^{-1}): 2883, 1652, 1430, 1368, 1255, 1117, 1060, 1024, 929, 862, 654.

HRMS (EI, *m/z*): calc'd for $C_8H_{11}BrO_2$ $[M+\cdot]^+$: 217.9942; found: 217.9933.

8-chloro-1,4-dioxaspiro[4.5]dec-7-ene (305c)



Prepared from 1,4-dioxaspiro[4.5]dec-7-en-8-yl trifluoromethanesulfonate (**1e**, 86.5 mg, 0.3 mmol) and lithium chloride (19.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, 10% Et_2O/pentane) to yield **305c** (44 mg, 83% yield) as a colorless oil.

$\mathbf{R}_f$ = 0.38 (silica, 10% EtOAc/hexanes, $KMnO_4$).

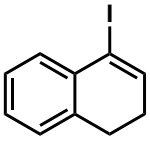
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.69 (tt, *J* = 4.1, 1.6 Hz, 1H), 3.98 (s, 4H), 2.51 (tq, *J* = 6.5, 2.0 Hz, 2H), 2.36 – 2.29 (m, 2H), 1.91 – 1.81 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 131.4, 121.8, 106.8, 64.7, 36.4, 32.0, 31.9.

FTIR (NaCl, thin film, cm^{-1}): 2933, 2884, 1659, 1433, 1370, 1336, 1251, 1203, 1119, 1062, 1028, 985, 944, 864, 666.

HRMS (TOF-ESI, *m/z*): calc'd for $C_8H_{11}ClO_2$ $[M+H]^+$: 175.0526; found: 175.0521.

4-iodo-1,2-dihydronaphthalene (306a)



Prepared from 3,4-dihydronaphthalen-1-yl trifluoromethanesulfonate (93.5 mg, 0.3 mmol) and sodium iodide (67.5 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, pentane) to yield **306a** (38 mg, 49% yield) as a colorless oil.

$\mathbf{R}_f$ = 0.65 (silica, hexanes, UV).

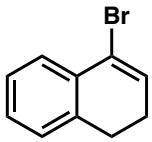
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.27 – 7.20 (m, 1H), 7.17 (td, *J* = 7.4, 1.4 Hz, 1H), 7.05 – 7.00 (m, 1H), 6.83 (t, *J* = 4.8 Hz, 1H), 2.85 (t, *J* = 8.0 Hz, 2H), 2.36 (ddd, *J* = 9.1, 7.4, 4.9 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 140.2, 135.9, 134.4, 130.9, 128.4, 127.4, 127.1, 98.1, 27.9, 27.2.

FTIR (NaCl, thin film, cm^{-1}): 3059, 2934, 2882, 2827, 1604, 1476, 1448, 1314, 1276, 938, 805, 756, 727.

HRMS (EI, *m/z*): calc'd for $C_{10}H_9I$ $[M+\cdot]^+$: 255.9749; found: 255.9744.

4-bromo-1,2-dihydronaphthalene (306b)



Prepared from 3,4-dihydronaphthalen-1-yl trifluoromethanesulfonate (93.5 mg, 0.3 mmol) and lithium bromide (39.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, pentane) to yield **306b** (48 mg, 77% yield) as a colorless oil.

R_f = 0.62 (silica, hexanes, UV).

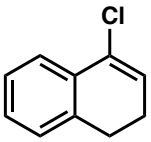
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.26 (td, *J* = 7.6, 1.5 Hz, 1H), 7.21 (td, *J* = 7.4, 1.5 Hz, 1H), 7.11 (dq, *J* = 7.8, 1.2 Hz, 1H), 6.46 (t, *J* = 4.8 Hz, 1H), 2.85 (t, *J* = 8.1 Hz, 2H), 2.38 (ddd, *J* = 9.1, 7.4, 4.9 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 136.4, 133.2, 130.8, 128.4, 127.4, 126.9, 126.6, 121.5, 27.7, 25.6.

FTIR (NaCl, thin film, cm^{-1}): 3059, 2937, 2884, 2831, 1690, 1615, 1479, 1450, 1316, 1169, 948, 809, 758, 730.

HRMS (EI, *m/z*): calc'd for $C_{10}H_9Br$ $[M+\cdot]^+$: 207.9888; found: 207.9876.

4-chloro-1,2-dihydronaphthalene (306c)



Prepared from 3,4-dihydronaphthalen-1-yl trifluoromethanesulfonate (93.5 mg, 0.3 mmol) and lithium chloride (19.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, pentane) to yield **306c** (39 mg, 80% yield) as a colorless oil.

R_f = 0.56 (silica, hexanes, $KMnO_4$).

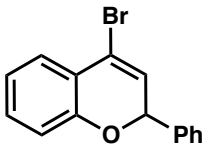
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.28 – 7.23 (m, 1H), 7.21 (td, *J* = 7.4, 1.6 Hz, 1H), 7.16 – 7.11 (m, 1H), 6.18 (t, *J* = 4.8 Hz, 1H), 2.84 (t, *J* = 8.0 Hz, 2H), 2.40 (ddd, *J* = 9.1, 7.5, 4.8 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 136.5, 132.5, 130.6, 128.3, 127.4, 126.8, 126.1, 124.2, 27.7, 24.3.

FTIR (NaCl, thin film, cm^{-1}): 3063, 2938, 2887, 2832, 1621, 1482, 1451, 1319, 1172, 964, 814, 760, 732.

HRMS (EI, *m/z*): calc'd for $C_{10}H_9Cl$ $[M+\cdot]^+$: 164.0393; found: 164.0382.

4-bromo-2-phenyl-2*H*-chromene (307b)



Prepared from 2-phenyl-2*H*-chromen-4-yl trifluoromethanesulfonate (107 mg, 0.3 mmol) and lithium bromide (39.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, 10% PhMe/hexanes) to yield **307b** (65 mg, 75% yield) as a yellow oil. *Note: This compound decomposes readily at room temperature.*

R_f = 0.69 (silica, 10% Et_2O/hexanes, $KMnO_4$).

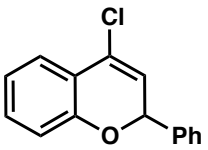
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (ddd, *J* = 7.7, 2.6, 1.5 Hz, 3H), 7.43 – 7.33 (m, 3H), 7.23 – 7.17 (m, 1H), 6.97 (td, *J* = 7.6, 1.2 Hz, 1H), 6.81 (dd, *J* = 8.1, 1.2 Hz, 1H), 6.21 (d, *J* = 3.7 Hz, 1H), 5.91 (d, *J* = 3.7 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 153.4, 139.6, 131.1, 128.9, 128.9, 127.2, 127.1, 126.5, 121.7, 121.1, 118.4, 116.2, 78.8.

FTIR (NaCl, thin film, cm^{-1}): 1645, 1605, 1478, 1464, 1450, 1374, 1223, 1116, 1062, 756, 697.

HRMS (FAB, *m/z*): calc'd for $C_{15}H_{11}BrO$ $[M+H-H_2]^+$: 284.9915; found: 284.9917.

4-chloro-2-phenyl-2*H*-chromene (307c)



Prepared from 2-phenyl-2*H*-chromen-4-yl trifluoromethanesulfonate (107 mg, 0.3 mmol) and lithium chloride (19.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, 10% PhMe/hexanes) to yield **307c** (48 mg, 66% yield) as a colorless oil. *Note: This compound decomposes readily at room temperature.*

R_f = 0.68 (silica, 10% Et_2O/hexanes, $KMnO_4$).

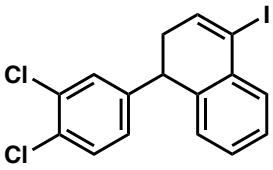
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 – 7.47 (m, 1H), 7.47 – 7.43 (m, 2H), 7.42 – 7.35 (m, 3H), 7.21 (ddd, *J* = 8.1, 7.4, 1.6 Hz, 1H), 6.98 (td, *J* = 7.6, 1.2 Hz, 1H), 6.84 (dd, *J* = 8.1, 1.1 Hz, 1H), 5.97 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 153.6, 139.8, 131.0, 128.9, 128.9, 128.3, 127.2, 124.7, 122.0, 121.6, 120.4, 116.2, 78.1.

FTIR (NaCl, thin film, cm^{-1}): 1634, 1605, 1481, 1451, 1328, 1224, 1118, 1064, 981, 914, 852, 754, 697.

HRMS (FAB, *m/z*): calc'd for $C_{15}H_{11}ClO$ $[M+\cdot]^+$: 242.0498; found: 242.0518.

4-iodo-1-(3,4-dichlorophenyl)-1,2-dihydronaphthalene (308a)



Prepared from 4-(3,4-dichlorophenyl)-3,4-dihydronaphthalen-1-yl trifluoromethanesulfonate (127.0 mg, 0.3 mmol) and sodium iodide (67.5 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, pentane) to yield **308a** (63 mg, 52% yield) as a white solid.

R_f = 0.44 (silica, hexanes, UV).

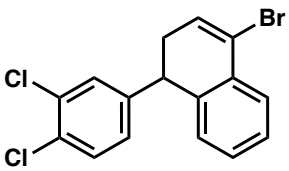
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.37 (d, *J* = 8.3 Hz, 1H), 7.33 – 7.26 (m, 2H), 7.17 (td, *J* = 7.5, 1.3 Hz, 1H), 6.98 (ddd, *J* = 8.3, 2.2, 0.5 Hz, 1H), 6.77 – 6.72 (m, 2H), 4.16 – 4.09 (m, 1H), 2.70 (ddd, *J* = 16.8, 7.0, 4.9 Hz, 1H), 2.59 (ddd, *J* = 16.8, 8.9, 4.8 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 143.6, 137.9, 136.8, 134.2, 132.6, 131.5, 130.9, 130.6, 130.3, 129.0, 127.9, 127.8, 127.6, 98.0, 43.1, 35.2.

FTIR (NaCl, thin film, cm^{-1}): 3059, 2932, 2876, 2827, 1603, 1561, 1470, 1447, 1396, 1132, 1030, 910, 862, 822, 879, 730.

HRMS (FAB, *m/z*): calc'd for $C_{16}H_{11}ICl_2$ $[M+\cdot]^+$: 399.9283; found: 399.9279.

4-bromo-1-(3,4-dichlorophenyl)-1,2-dihydronaphthalene (308b)



Prepared from 4-(3,4-dichlorophenyl)-3,4-dihydronaphthalen-1-yl trifluoromethanesulfonate (127.0 mg, 0.3 mmol) and lithium bromide (39.1 mg, 0.45 mmol) according to General Procedure

2. The crude residue was purified by column chromatography (silica, pentane) to yield **308b** (83 mg, 78% yield) as a white solid.

R_f = 0.35 (silica, hexanes, $KMnO_4$).

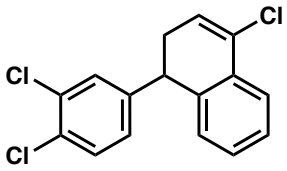
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.37 (d, *J* = 8.3 Hz, 1H), 7.31 (tdd, *J* = 7.7, 1.3, 0.6 Hz, 1H), 7.28 (d, *J* = 2.1 Hz, 1H), 7.20 (td, *J* = 7.5, 1.3 Hz, 1H), 7.00 (ddd, *J* = 8.3, 2.2, 0.5 Hz, 1H), 6.81 (dt, *J* = 7.4, 1.2 Hz, 1H), 6.38 (t, *J* = 4.8 Hz, 1H), 4.18 – 4.09 (m, 1H), 2.72 (ddd, *J* = 16.9, 7.1, 4.9 Hz, 1H), 2.60 (ddd, *J* = 16.9, 9.0, 4.8 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 143.7, 137.4, 133.0, 132.7, 130.9, 130.7, 130.4, 129.0, 128.7, 127.82, 127.75, 127.70, 127.2, 121.5, 43.0, 33.7.

FTIR (NaCl, thin film, cm^{-1}): 3062, 2879, 1618, 1468, 1448, 1397, 1132, 1030, 871, 822, 760.

HRMS (TOF-ESI, *m/z*): calc'd for $C_{16}H_{11}BrCl_2$ $[M+H]^+$: 352.9499; found: 352.9485.

4-chloro-1-(3,4-dichlorophenyl)-1,2-dihydronaphthalene (308c)



Prepared from 4-(3,4-dichlorophenyl)-3,4-dihydronaphthalen-1-yl trifluoromethanesulfonate (127.0 mg, 0.3 mmol) and lithium chloride (19.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, pentane) to yield **308c** (69 mg, 75% yield) as a white solid.

R_f = 0.55 (silica, hexanes, UV).

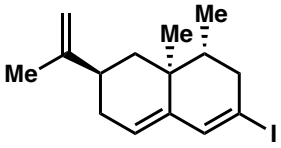
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.38 (d, *J* = 8.3 Hz, 1H), 7.33 (tdd, *J* = 7.7, 1.4, 0.6 Hz, 1H), 7.30 – 7.28 (m, 1H), 7.22 (td, *J* = 7.5, 1.4 Hz, 1H), 7.01 (ddd, *J* = 8.3, 2.2, 0.5 Hz, 1H), 6.85 (dt, *J* = 7.6, 1.2 Hz, 1H), 6.13 (t, *J* = 4.8 Hz, 1H), 4.17 – 4.09 (m, 1H), 2.76 (ddd, *J* = 17.0, 7.2, 4.9 Hz, 1H), 2.64 (ddd, *J* = 16.9, 9.0, 4.7 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 143.8, 137.4, 132.6, 132.3, 130.9, 130.7, 130.6, 130.3, 129.0, 127.8, 127.7, 127.6, 124.7, 124.0, 43.0, 32.5.

FTIR (NaCl, thin film, cm^{-1}): 3063, 2880, 1625, 1559, 1468, 1449, 1398, 1133, 1030, 980, 878, 814, 762, 735.

HRMS (TOF-ESI, *m/z*): calc'd for $C_{16}H_{11}Cl_3$ $[M+H]^+$: 309.0005; found: 309.0005.

(2*R*,8*R*,8a*S*)-6-iodo-8,8a-dimethyl-2-(prop-1-en-2-yl)-1,2,3,7,8,8a-hexahydronaphthalene (309a)



Prepared from (4*R*,4a*S*,6*R*)-4,4a-dimethyl-6-(prop-1-en-2-yl)-3,4,4a,5,6,7-hexahydronaphthalen-2-yl 1,1,2,2,3,3,4,4,4-nonafluorobutane-1-sulfonate (150 mg, 0.3 mmol) and sodium iodide (67.5 mg, 0.45 mmol) according to General Procedure 4. The crude residue was purified by column chromatography (silica, pentane) to yield **309a** (54 mg, 54% yield) as a colorless oil.

R_f = 0.63 (silica, hexanes, $KMnO_4$).

$[\alpha]_D^{25}$ = –155° (c = 1.0, $CHCl_3$).

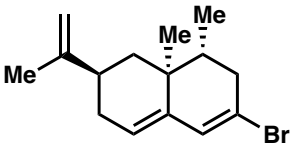
^{1}H NMR (500 MHz, $CDCl_3$): δ 6.58 (d, *J* = 2.4 Hz, 1H), 5.41 (dd, *J* = 5.4, 2.8 Hz, 1H), 4.80 – 4.70 (m, 2H), 2.54 (dd, *J* = 18.4, 5.2 Hz, 1H), 2.40 (dddd, *J* = 16.9, 8.5, 4.3, 2.4 Hz, 2H), 2.23 (dddd, *J* = 20.0, 6.8, 5.1, 2.3 Hz, 1H), 2.01 – 1.85 (m, 1H), 1.79 – 1.65 (m, 5H), 1.20 – 1.11 (m, 1H), 0.92 (d, *J* = 0.7 Hz, 3H), 0.86 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 150.0, 142.8, 139.1, 124.4, 109.0, 95.1, 46.1, 41.5, 40.0, 37.1, 35.5, 31.1, 20.8, 17.6, 14.2.

FTIR (NaCl, thin film, cm^{-1}): 3079, 2967, 2912, 1644, 1615, 1441, 1372, 1157, 888, 783.

HRMS (FAB, *m/z*): calc'd for $C_{15}H_{21}I$ $[M+H-H_2]^+$: 327.0610; found: 327.0598.

(2*R*,8*R*,8a*S*)-6-bromo-8,8a-dimethyl-2-(prop-1-en-2-yl)-1,2,3,7,8,8a-hexahydronaphthalene (309b)



Prepared from (4*R*,4a*S*,6*R*)-4,4a-dimethyl-6-(prop-1-en-2-yl)-3,4,4a,5,6,7-hexahydronaphthalen-2-yl trifluoromethane-sulfonate (105.1 mg, 0.3 mmol) and lithium bromide (39.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, pentane) to yield **309b** (55 mg, 82% yield) as a colorless oil which solidified in the freezer to give a white solid. *Note: This compound decomposes readily at room temperature.*

R_f = 0.57 (silica, hexanes, $KMnO_4$).

$[\alpha]_D^{25}$ = –172° (c = 1.0, $CHCl_3$).

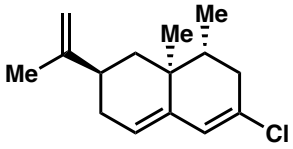
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.30 (d, *J* = 2.3 Hz, 1H), 5.45 (dd, *J* = 5.3, 2.8 Hz, 1H), 4.79 – 4.71 (m, 2H), 2.48 – 2.29 (m, 3H), 2.22 (dt, *J* = 18.6, 5.3 Hz, 1H), 1.99 – 1.87 (m, 1H), 1.75 (t, *J* = 1.1 Hz, 3H), 1.74 – 1.67 (m, 2H), 1.21 – 1.10 (m, 1H), 0.92 (d, *J* = 0.7 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 150.0, 141.7, 131.0, 124.3, 121.0, 109.0, 41.9, 40.8, 40.0, 37.2, 35.6, 31.2, 20.8, 17.6, 14.4.

FTIR (NaCl, thin film, cm^{-1}): 2959, 2914, 1643, 1620, 1442, 1376, 1349, 1154, 1005, 902, 888, 792, 632.

HRMS (FAB, *m/z*): calc'd for $C_{15}H_{21}Br$ $[M+H-H_2]^+$: 279.0748; found: 279.0744.

(2*R*,8*R*,8a*S*)-6-chloro-8,8a-dimethyl-2-(prop-1-en-2-yl)-1,2,3,7,8,8a-hexahydronaphthalene (309c)



Prepared from (4*R*,4a*S*,6*R*)-4,4a-dimethyl-6-(prop-1-en-2-yl)-3,4,4a,5,6,7-hexahydronaphthalen-2-yl trifluoromethanesulfonate (105.1 mg, 0.3 mmol) and lithium chloride (19.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, pentane) to yield **309c** (60 mg, 85% yield) as a colorless oil. *Note: This compound decomposes readily at room temperature.*

R_f = 0.63 (silica, hexanes, $KMnO_4$).

$[\alpha]_D^{25}$ = –165° (c = 1.0, $CHCl_3$).

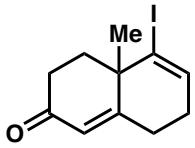
^{1}H NMR (500 MHz, $CDCl_3$): δ 6.09 (dt, *J* = 1.7, 0.9 Hz, 1H), 5.44 (ddd, *J* = 5.2, 2.1, 0.8 Hz, 1H), 4.75 (p, *J* = 1.1 Hz, 2H), 2.47 – 2.37 (m, 1H), 2.29 – 2.21 (m, 3H), 2.00 – 1.92 (m, 1H), 1.76 (t, *J* = 1.2 Hz, 3H), 1.75 – 1.71 (m, 1H), 1.71 (s, 1H), 1.17 (td, *J* = 12.7, 0.8 Hz, 1H), 0.93 – 0.90 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 150.0, 141.0, 130.5, 126.9, 124.0, 109.0, 40.0, 39.9, 39.5, 37.2, 35.7, 31.3, 20.8, 17.6, 14.5.

FTIR (NaCl, thin film, cm^{-1}): 3080, 2967, 2912, 1644, 1618, 1442, 1373, 1155, 1014, 888, 824, 635.

HRMS (EI, *m/z*): calc'd for $C_{15}H_{21}Cl$ $[M+\cdot]^+$: 236.1332; found: 236.1356.

5-iodo-4a-methyl-4,4a,7,8-tetrahydronaphthalen-2(3*H*)-one (310a)



Prepared from 8a-methyl-6-oxo-3,4,6,7,8,8a-hexahydronaphthalen-1-yl 1,1,2,2,3,3,4,4,4-nonafluorobutane-1-sulfonate (138 mg, 0.3 mmol) and sodium iodide (67.5 mg, 0.45 mmol) according to General Procedure 4. The crude residue was purified by column chromatography (silica, 5-10% Et_2O/hexanes) to yield **310a** (46 mg, 53% yield) as a colorless oil.

R_f = 0.24 (silica, 10% Et_2O/hexanes, $KMnO_4$).

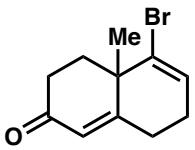
^{1}H NMR (500 MHz, $CDCl_3$): δ 6.68 (dt, *J* = 2.6, 0.8 Hz, 1H), 5.66 – 5.58 (m, 1H), 2.76 (ddd, *J* = 15.5, 7.3, 5.9 Hz, 1H), 2.72 (s, 2H), 2.63 – 2.53 (m, 1H), 2.49 – 2.40 (m, 1H), 2.36 (ddd, *J* = 15.5, 7.3, 6.7 Hz, 1H), 1.87 – 1.80 (m, 1H), 1.71 (dddd, *J* = 13.5, 11.5, 6.5, 0.8 Hz, 1H), 1.22 (d, *J* = 0.6 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 214.3, 140.3, 137.7, 123.7, 96.8, 44.3, 36.6, 35.4, 31.3, 24.2, 22.8.

FTIR (NaCl, thin film, cm^{-1}): 2926, 1711, 1443, 1322, 1047, 884.

HRMS (FAB, *m/z*): calc'd for $C_{11}H_{13}OI$ $[M+\cdot]^+$: 288.0011 found: 287.9997.

5-bromo-4a-methyl-4,4a,7,8-tetrahydronaphthalen-2(3*H*)-one (310b)



Prepared from 8a-methyl-6-oxo-3,4,6,7,8,8a-hexahydronaphthalen-1-yl trifluoromethanesulfonate (93.1 mg, 0.3 mmol) and lithium bromide (39.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, 5% Et_2O/hexanes) to yield **310b** (56 mg, 78% yield) as a colorless oil. *Note: This compound decomposes readily at room temperature.*

R_f = 0.24 (silica, 10% Et_2O/hexanes, $KMnO_4$).

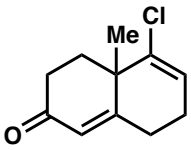
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.43 – 6.38 (m, 1H), 5.70 – 5.63 (m, 1H), 2.81 – 2.73 (m, 1H), 2.73 (s, 3H), 2.54 – 2.40 (m, 1H), 2.40 – 2.32 (m, 1H), 1.99 – 1.90 (m, 1H), 1.68 (dddd, *J* = 13.6, 12.2, 6.0, 0.7 Hz, 1H), 1.22 (d, *J* = 0.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 214.1, 139.4, 129.7, 123.6, 122.8, 44.4, 35.4, 32.4, 30.5, 24.4, 22.8.

FTIR (NaCl, thin film, cm^{-1}): 2930, 1713, 1611, 1445, 1348, 1048, 884, 750.

HRMS (FAB, *m/z*): calc'd for $C_{11}H_{13}OBr$ $[M+\cdot]^+$: 240.0150; found: 240.0153.

5-chloro-4a-methyl-4,4a,7,8-tetrahydronaphthalen-2(3*H*)-one (310c)



Prepared from 8a-methyl-6-oxo-3,4,6,7,8,8a-hexahydronaphthalen-1-yl trifluoromethanesulfonate (93.1 mg, 0.3 mmol) and lithium chloride (19.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, 5% Et_2O/hexanes) to yield **310c** (53 mg, 90% yield) as a colorless oil. *Note: This compound decomposes readily at room temperature.*

R_f = 0.13 (silica, 10% EtOAc/hexanes, $KMnO_4$).

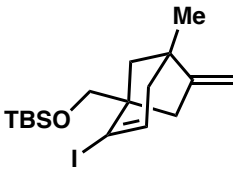
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.19 (dt, *J* = 2.4, 0.7 Hz, 1H), 5.68 – 5.63 (m, 1H), 2.77 (ddd, *J* = 15.4, 7.3, 5.9 Hz, 1H), 2.68 – 2.52 (m, 2H), 2.52 – 2.45 (m, 1H), 2.45 – 2.32 (m, 2H), 1.98 (dddd, *J* = 13.6, 5.7, 1.7, 0.6 Hz, 1H), 1.72 – 1.63 (m, 1H), 1.22 (d, *J* = 0.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 214.1, 138.8, 132.4, 125.6, 123.4, 44.6, 35.5, 30.1, 29.8, 24.5, 22.8.

FTIR (NaCl, thin film, cm^{-1}): 3549, 2938, 1714, 1682, 1652, 1446, 1424, 1253, 1155, 1080, 916, 733.

HRMS (EI, *m/z*): calc'd for $C_{11}H_{13}OCl$ $[M+\cdot]^+$: 196.0655; found: 196.0663.

***tert*-butyl(((1*r*,5*r*)-2-iodo-5-methyl-6-methylenebicyclo[3.2.1]oct-2-en-1-yl)methoxy)-dimethylsilane (311a)**



Prepared from (1*r*,5*r*)-1-(((*tert*-butyldimethylsilyl)oxy)methyl)-5-methyl-6-methylenebicyclo[3.2.1]oct-2-en-2-yl trifluoromethanesulfonate (128 mg, 0.3 mmol) and sodium iodide (67.5 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, pentane) to yield **311a** (101 mg, 83% yield) as a colorless oil.

R_f = 0.60 (silica, hexanes, $KMnO_4$).

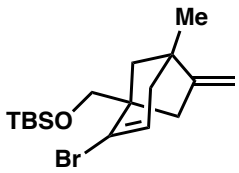
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.23 (dd, *J* = 4.8, 2.5 Hz, 1H), 4.90 (td, *J* = 1.8, 0.9 Hz, 1H), 4.88 (dd, *J* = 2.9, 1.9 Hz, 1H), 3.70 (d, *J* = 9.9 Hz, 1H), 3.49 (d, *J* = 9.9 Hz, 1H), 2.41 – 2.23 (m, 3H), 1.94 – 1.77 (m, 3H), 1.17 (s, 3H), 0.91 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 158.7, 137.8, 107.3, 106.1, 71.1, 50.0, 49.0, 46.8, 43.4, 43.3, 26.1, 24.9, 18.5, -5.1, -5.3.

FTIR (NaCl, thin film, cm^{-1}): 2954, 2929, 2857, 1655, 1471, 1464, 1251, 1156, 1097, 1007, 879, 851, 838, 808, 776.

HRMS (FAB, *m/z*): calc'd for $C_{17}H_{29}OISi$ $[M+H-H_2]^+$: 403.0955; found: 403.0969.

***tert*-butyl(((1*r*,5*r*)-2-bromo-5-methyl-6-methylenebicyclo[3.2.1]oct-2-en-1-yl)methoxy)-dimethylsilane (311b)**



Prepared from (1*r*,5*r*)-1-(((*tert*-butyldimethylsilyl)oxy)methyl)-5-methyl-6-methylenebicyclo[3.2.1]oct-2-en-2-yl trifluoromethanesulfonate (36 mg, 0.1 mmol) and lithium bromide (13.0 mg, 0.15 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, pentane) to yield **311b** (28 mg, 78% yield) as a colorless oil.

R_f = 0.58 (silica, hexanes, $KMnO_4$).

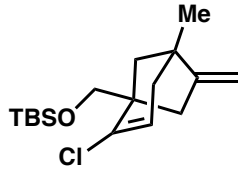
^{1}H NMR (500 MHz, $CDCl_3$): δ 5.86 (dd, *J* = 4.9, 2.5 Hz, 1H), 4.91 (t, *J* = 2.1 Hz, 1H), 4.89 – 4.86 (m, 1H), 3.82 (d, *J* = 9.9 Hz, 1H), 3.57 (d, *J* = 9.9 Hz, 1H), 2.50 – 2.43 (m, 1H), 2.42 – 2.36 (m, 1H), 2.24 (dd, *J* = 16.9, 2.5 Hz, 1H), 1.94 – 1.87 (m, 1H), 1.82 (d, *J* = 1.5 Hz, 2H), 1.19 (s, 3H), 0.90 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 158.8, 129.8, 128.7, 106.1, 67.2, 50.0, 47.3, 46.8, 43.7, 43.2, 26.1, 24.8, 18.5, -5.26, -5.33.

FTIR (NaCl, thin film, cm^{-1}): 2954, 2857, 1652, 1463, 1251, 1097, 1010, 880, 839, 811, 775

HRMS (FAB, *m/z*): calc'd for $C_{17}H_{29}OBrSi$ $[M+H-H_2]^+$: 357.1072; found: 357.1085.

***tert*-butyl(((1*r*,5*r*)-2-chloro-5-methyl-6-methylenebicyclo[3.2.1]oct-2-en-1-yl)methoxy)-dimethylsilane (311c)**



Prepared from (1*r*,5*r*)-1-(((*tert*-butyldimethylsilyl)oxy)methyl)-5-methyl-6-methylenebicyclo[3.2.1]oct-2-en-2-yl trifluoromethanesulfonate (36 mg, 0.1 mmol) and lithium chloride (6.4 mg, 0.15

mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, pentane) to yield **311c** (27 mg, 82% yield) as a colorless oil.

R_f = 0.56 (silica, hexanes, $KMnO_4$).

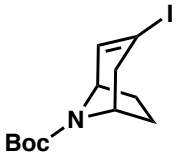
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.61 (dd, *J* = 4.8, 2.5 Hz, 1H), 4.89 (ddd, *J* = 7.2, 2.7, 1.8 Hz, 2H), 3.88 (d, *J* = 9.9 Hz, 1H), 3.59 (d, *J* = 9.9 Hz, 1H), 2.54 – 2.38 (m, 2H), 2.26 (dd, *J* = 16.9, 2.6 Hz, 1H), 1.97 – 1.88 (m, 1H), 1.84 – 1.73 (m, 2H), 1.20 (s, 3H), 0.90 (s, 9H), 0.06 (s, 3H), 0.06 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 158.9, 138.3, 124.0, 106.0, 65.4, 49.5, 47.2, 45.2, 43.9, 43.2, 26.0, 24.8, 18.5, -5.33, -5.34.

FTIR (NaCl, thin film, cm^{-1}): 2954, 2858, 1656, 1471, 1252, 1098, 880, 838, 812, 776

HRMS (TOF-ESI, *m/z*): calc'd for $C_{17}H_{29}OClSi$ $[M+H]^+$: 313.1754; found: 313.1732.

***tert*-butyl (1*r*,5*s*)-3-iodo-8-azabicyclo[3.2.1]oct-2-ene-8-carboxylate (312a)**



Prepared from *tert*-butyl (1*r*,5*s*)-3-(((perfluorobutyl)sulfonyl)oxy)-8-azabicyclo[3.2.1]oct-2-ene-8-carboxylate (152 mg, 0.3 mmol) and sodium iodide (67.5 mg, 0.45 mmol) according to General Procedure 4. The crude residue was purified by column chromatography (silica, 10% acetone/hexanes) to yield **312a** (53 mg, 53% yield) as a colorless oil.

R_f = 0.55 (silica, 30% Et_2O/hexanes, $KMnO_4$).

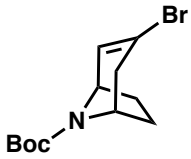
^{1}H NMR (400 MHz, d_3-MeCN, 65 °C): δ 6.70 – 6.65 (m, 1H), 4.23 (t, *J* = 5.6 Hz, 1H), 4.17 – 4.11 (m, 1H), 3.16 – 3.06 (m, 1H), 2.31 (dt, *J* = 17.5, 1.4 Hz, 1H), 2.26 – 2.12 (m, 1H), 1.98 – 1.81 (m, 2H), 1.76 (ddt, *J* = 15.6, 9.8, 3.8 Hz, 1H), 1.44 (d, *J* = 0.6 Hz, 9H).

^{13}C NMR (101 MHz, d_3-MeCN, 65 °C): δ 6.70 – 6.65 (m, 1H), 4.23 (t, *J* = 5.6 Hz, 1H), 4.17 – 4.11 (m, 1H), 3.16 – 3.06 (m, 1H), 2.31 (dt, *J* = 17.5, 1.4 Hz, 1H), 2.26 – 2.12 (m, 1H), 1.98 – 1.81 (m, 2H), 1.76 (ddt, *J* = 15.6, 9.8, 3.8 Hz, 1H), 1.44 (d, *J* = 0.6 Hz, 9H).

FTIR (NaCl, thin film, cm^{-1}): 2975, 1698, 1392, 1347, 1312, 1172, 1103, 1101, 973.

HRMS (FAB, *m/z*): calc'd for $C_{12}H_{18}INO_2$ $[M+H]^+$: 336.0461; found: 336.0454.

***tert*-butyl (1*r*,5*s*)-3-bromo-8-azabicyclo[3.2.1]oct-2-ene-8-carboxylate (312b)**



Prepared from *tert*-butyl (1*r*,5*s*)-3-(((trifluoromethyl)sulfonyl)oxy)-8-azabicyclo[3.2.1]oct-2-ene-8-carboxylate (107 mg, 0.3 mmol) and lithium bromide (39.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, 10 to 20% Et_2O/hexanes) to yield **312b** (56 mg, 65% yield) as a colorless oil.

R_f = 0.55 (silica, 30% Et_2O/hexanes, $KMnO_4$).

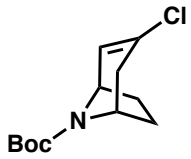
^{1}H NMR (400 MHz, d_3-MeCN, 65 °C): δ 6.38 (ddd, *J* = 5.5, 2.0, 1.4 Hz, 1H), 4.32 (td, *J* = 5.5, 1.2 Hz, 1H), 4.29 – 4.22 (m, 1H), 3.06 (ddt, *J* = 17.3, 4.3, 2.0 Hz, 1H), 2.26 – 2.13 (m, 2H), 1.99 – 1.85 (m, 2H), 1.74 (dddd, *J* = 12.9, 9.6, 6.7, 1.2 Hz, 1H), 1.45 (s, 9H).

^{13}C NMR (101 MHz, d_3-MeCN, 65 °C): δ 155.0, 135.7, 121.0, 80.5, 56.2, 54.8, 44.8, 35.0, 30.5, 28.8.

FTIR (NaCl, thin film, cm^{-1}): 2976, 1698, 1392, 1367, 1350, 1320, 1171, 1103, 1107, 975.

HRMS (FAB, *m/z*): calc'd for $C_{12}H_{18}BrNO_2$ $[M+H]^+$: 288.0599; found: 288.0593.

***tert*-butyl (1r,5*s*)-3-chloro-8-azabicyclo[3.2.1]oct-2-ene-8-carboxylate (312c)**



Prepared from *tert*-butyl (1*r*,5*s*)-3-(((trifluoromethyl)sulfonyl)oxy)-8-azabicyclo[3.2.1]oct-2-ene-8-carboxylate (107 mg, 0.3 mmol) and lithium chloride (19.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, 10 to 20% Et_2O/hexanes) to yield **312c** (61 mg, 84% yield) as a colorless oil.

R_f = 0.55 (silica, 30% Et_2O/hexanes, $KMnO_4$).

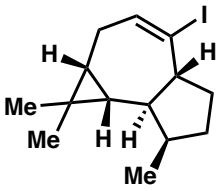
^{1}H NMR (400 MHz, d_3-MeCN, 65 °C): δ 6.16 (ddd, *J* = 5.6, 2.0, 1.3 Hz, 1H), 4.47 – 4.35 (m, 1H), 4.35 – 4.28 (m, 1H), 2.96 (ddt, *J* = 17.2, 3.9, 1.8 Hz, 1H), 2.26 – 2.14 (m, 1H), 2.09 (dt, *J* = 17.3, 1.4 Hz, 1H), 1.99 – 1.89 (m, 2H), 1.79 – 1.67 (m, 1H), 1.46 (s, 9H).

^{13}C NMR (101 MHz, d_3-MeCN, 65 °C): δ 154.9, 131.4, 80.4, 55.0, 53.9, 42.5, 35.1, 30.5, 28.8. (*Note: one carbon under solvent*).

FTIR (NaCl, thin film, cm^{-1}): 2976, 1694, 1638, 1392, 1323, 1256, 1168, 1103, 1015, 978, 888, 874, 775, 724.

HRMS (TOF-ESI, *m/z*): calc'd for $C_{12}H_{18}ClNO_2$ $[M+H]^+$: 244.1104; found: 244.1098.

(1a*R*,4a*R*,7*R*,7a*S*,7b*S*)-4-iodo-1,1,7-trimethyl-1a,2,4a,5,6,7,7a,7b-octahydro-1*H*-cyclopropa[*e*]azulene (313a)



Prepared from (1a*R*,4a*R*,7*R*,7a*S*,7b*S*)-1,1,7-trimethyl-1a,2,4a,5,6,7,7a,7b-octahydro-1*H*-cyclopropa[*e*]azulen-4-yl trifluoromethanesulfonate (101.5 mg, 0.3 mmol) and sodium iodide (67.5 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, pentane) to yield **313a** (48 mg, 75% yield) as a colorless oil.

$\mathbf{R}_f$ = 0.72 (silica, hexanes, $KMnO_4$).

$[\alpha]_D^{25}$ = –184° (c = 1.0, $CHCl_3$).

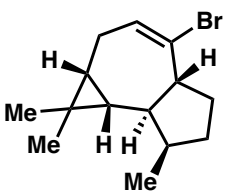
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.43 (ddd, *J* = 8.8, 3.6, 2.2 Hz, 1H), 2.77 (tdd, *J* = 11.3, 7.4, 3.3 Hz, 1H), 2.37 – 2.22 (m, 1H), 2.18 – 2.02 (m, 3H), 1.89 (dddd, *J* = 13.0, 9.8, 8.2, 3.1 Hz, 1H), 1.77 (td, *J* = 11.6, 8.4 Hz, 1H), 1.44 (dddd, *J* = 12.5, 11.4, 9.8, 8.8 Hz, 1H), 1.16 (dtd, *J* = 13.1, 8.7, 4.5 Hz, 1H), 1.03 (s, 3H), 1.02 (s, 3H), 0.97 – 0.87 (m, 4H), 0.60 (dd, *J* = 11.5, 9.3 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 138.5, 109.1, 56.7, 43.5, 36.6, 36.3, 30.9, 28.7, 26.8, 26.2, 25.8, 19.3, 18.3, 15.3.

FTIR (NaCl, thin film, cm^{-1}): 2953, 2866, 1455, 1376, 1216, 909, 723.

HRMS (FAB, *m/z*): calc'd for $C_{14}H_{21}I$ $[M+H-H_2]^+$: 315.0610; found: 315.0609.

(1a*R*,4a*R*,7*R*,7a*S*,7b*S*)-4-bromo-1,1,7-trimethyl-1a,2,4a,5,6,7,7a,7b-octahydro-1*H*-cyclopropa[*e*]azulene (313b)



Prepared from (1a*R*,4a*R*,7*R*,7a*S*,7b*S*)-1,1,7-trimethyl-1a,2,4a,5,6,7,7a,7b-octahydro-1*H*-cyclopropa[*e*]azulen-4-yl trifluoromethanesulfonate (101.5 mg, 0.3 mmol) and lithium bromide (39.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, pentane) to yield **313b** (73 mg, 88% yield) as a colorless oil.

R_f = 0.68 (silica, hexanes, $KMnO_4$).

$[\alpha]_D^{25}$ = –152° (c = 1.0, $CHCl_3$).

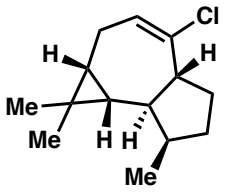
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.10 (ddd, *J* = 9.3, 3.3, 2.1 Hz, 1H), 2.77 (dddd, *J* = 18.2, 9.2, 3.7, 2.1 Hz, 1H), 2.29 – 2.10 (m, 3H), 2.04 – 1.85 (m, 2H), 1.76 (td, *J* = 11.7, 8.3 Hz, 1H), 1.46 (dddd, *J* = 12.6, 11.4, 9.8, 8.8 Hz, 1H), 1.18 (dtd, *J* = 13.1, 8.6, 4.3 Hz, 1H), 1.03 (d, *J* = 3.8 Hz, 6H), 0.97 – 0.88 (m, 4H), 0.60 (dd, *J* = 11.5, 9.3 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 130.8, 129.8, 53.7, 43.5, 35.5, 33.7, 31.3, 28.6, 26.0, 25.7, 24.5, 18.9, 18.2, 15.3.

FTIR (NaCl, thin film, cm^{-1}): 2953, 2867, 1633, 1455, 1376, 1251, 1064, 913, 860, 732.

HRMS (TOF-ESI, *m/z*): calc'd for $C_{14}H_{21}Br$ $[M+H-H_2]^+$: 267.0748; found: 267.0737.

(1a*R*,4a*R*,7*R*,7a*S*,7b*S*)-4-chloro-1,1,7-trimethyl-1a,2,4a,5,6,7,7a,7b-octahydro-1*H*-cyclopropa[*e*]azulene (313c)



Prepared from (1a*R*,4a*R*,7*R*,7a*S*,7b*S*)-1,1,7-trimethyl-1a,2,4a,5,6,7,7a,7b-octahydro-1*H*-cyclopropa[*e*]azulen-4-yl trifluoromethanesulfonate (101.5 mg, 0.3 mmol) and lithium chloride (19.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, pentane) to yield **313c** (40 mg, 88% yield) as a colorless oil.

R_f = 0.78 (silica, hexanes, $KMnO_4$).

$[\alpha]_D^{25}$ = –174° (c = 1.0, $CHCl_3$).

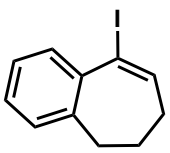
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.84 (ddd, *J* = 9.3, 3.3, 2.1 Hz, 1H), 2.68 (dddd, *J* = 18.1, 9.2, 3.8, 2.1 Hz, 1H), 2.26 – 2.09 (m, 3H), 2.01 (ddt, *J* = 16.8, 10.4, 3.6 Hz, 1H), 1.90 (dddd, *J* = 13.1, 9.9, 8.2, 3.1 Hz, 1H), 1.75 (td, *J* = 11.7, 8.3 Hz, 1H), 1.44 (dddd, *J* = 12.6, 11.3, 9.8, 8.8 Hz, 1H), 1.19 (dtd, *J* = 13.0, 8.6, 4.3 Hz, 1H), 1.04 (s, 3H), 1.03 (s, 3H), 0.95 – 0.87 (m, 4H), 0.60 (dd, *J* = 11.5, 9.3 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 138.6, 125.6, 51.9, 43.2, 35.0, 32.1, 31.6, 28.7, 26.1, 25.8, 23.0, 18.8, 18.1, 15.3.

FTIR (NaCl, thin film, cm^{-1}): 2952, 2866, 1453, 1376, 921, 748.

HRMS (EI, *m/z*): calc'd for $C_{14}H_{21}Cl$ $[M+\cdot]^+$: 224.1332; found: 224.1306.

9-iodo-6,7-dihydro-5*H*-benzo[7]annulene (314a)



Prepared from 6,7-dihydro-5*H*-benzo[7]annulen-9-yl trifluoromethanesulfonate (87.7 mg, 0.3 mmol) and sodium iodide (67.5 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, hexanes) to yield **314a** (65 mg, 80% yield) as a light yellow oil.

R_f = 0.66 (silica, hexanes, $KMnO_4$).

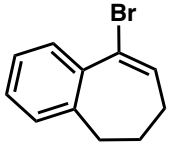
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.31 – 7.25 (m, 1H), 7.18 (td, *J* = 7.4, 1.4 Hz, 1H), 7.12 (dd, *J* = 7.6, 1.4 Hz, 1H), 6.95 (t, *J* = 7.5 Hz, 1H), 2.66 (t, *J* = 7.0 Hz, 2H), 2.14 (p, *J* = 7.1 Hz, 2H), 1.83 (q, *J* = 7.3 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 142.1, 141.3, 139.8, 131.1, 128.5, 128.2, 126.4, 95.8, 34.8, 32.6, 28.2.

FTIR (NaCl, thin film, cm^{-1}): 2928, 2854, 1478, 1447, 1195, 887, 763, 742, 662.

HRMS (FAB, *m/z*): calc'd for $C_{11}H_{11}I$ $[M+\cdot]^+$: 269.9906; found: 269.9910.

9-bromo-6,7-dihydro-5*H*-benzo[7]annulene (314b)



Prepared from 6,7-dihydro-5*H*-benzo[7]annulen-9-yl trifluoromethanesulfonate (87.7 mg, 0.3 mmol) and lithium bromide (39.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, hexanes) to yield **314b** (49 mg, 73% yield) as a light yellow oil.

R_f = 0.51 (silica, hexanes, $KMnO_4$).

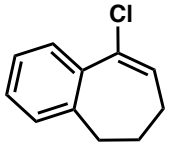
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.30 (td, *J* = 7.5, 1.6 Hz, 1H), 7.25 – 7.15 (m, 2H), 6.64 (t, *J* = 7.4 Hz, 1H), 2.68 (t, *J* = 6.9 Hz, 2H), 2.14 (p, *J* = 7.1 Hz, 2H), 1.92 (q, *J* = 7.0 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 140.7, 138.8, 133.3, 129.5, 128.7, 128.4, 126.4, 120.7, 34.3, 32.7, 26.9.

FTIR (NaCl, thin film, cm^{-1}): 3062, 2930, 2856, 1614, 1480, 1448, 1303, 1197, 897, 765, 745, 668.

HRMS (EI, *m/z*): calc'd for $C_{11}H_{11}Br$ $[M+\cdot]^+$: 222.0044; found: 222.0042.

9-chloro-6,7-dihydro-5*H*-benzo[7]annulene (314c)



Prepared from 6,7-dihydro-5*H*-benzo[7]annulen-9-yl trifluoromethanesulfonate (87.7 mg, 0.3 mmol) and lithium chloride (19.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, hexanes) to yield **314c** (38 mg, 71% yield) as a light yellow oil.

$\mathbf{R_f}$ = 0.54 (silica, hexanes, $KMnO_4$).

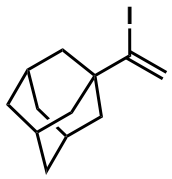
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.30 (td, *J* = 7.5, 1.7 Hz, 1H), 7.27 – 7.22 (m, 1H), 7.20 (dd, *J* = 7.5, 1.6 Hz, 1H), 6.40 (t, *J* = 7.1 Hz, 1H), 2.69 (t, *J* = 6.7 Hz, 2H), 2.17 – 2.09 (m, 2H), 1.99 (qd, *J* = 7.1, 0.9 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 141.1, 137.6, 130.7, 129.0, 128.9, 128.4, 128.3, 126.4, 33.8, 32.9, 26.0.

FTIR (NaCl, thin film, cm^{-1}): 3059, 2934, 2858, 1620, 1483, 1449, 1322, 1304, 1201, 1169, 916, 830, 766, 748, 676.

HRMS (EI, *m/z*): calc'd for $C_{11}H_{11}Cl$ $[M+\cdot]^+$: 178.0549; found: 178.0547.

(3*r*,5*r*,7*r*)-1-(1-iodovinyl)adamantane (315a)



Prepared from 1-((3*r*,5*r*,7*r*)-adamantan-1-yl)vinyl trifluoromethanesulfonate (93.0 mg, 0.3 mmol) and sodium iodide (67.5 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, pentane) to yield **315a** (72 mg, 84% yield) as a colorless oil.

$\mathbf{R_f}$ = 0.74 (silica, hexanes, $KMnO_4$).

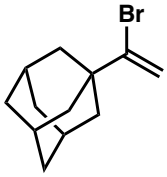
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.08 (d, *J* = 2.1 Hz, 1H), 5.80 (d, *J* = 2.1 Hz, 1H), 2.04 – 1.95 (m, 3H), 1.76 – 1.71 (m, 6H), 1.71 – 1.59 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 131.8, 122.8, 42.4, 41.8, 36.8, 28.7.

FTIR (NaCl, thin film, cm^{-1}): 2903, 2849, 1611, 1600, 1450, 1343, 1257, 1184, 1142, 1055, 894, 612.

HRMS (FAB, *m/z*): calc'd for $C_{12}H_{17}I$ $[M+H]^+$: 289.0454; found: 289.0447.

(3*r*,5*r*,7*r*)-1-(1-bromovinyl)adamantane (315b)



Prepared from 1-((3*r*,5*r*,7*r*)-adamantan-1-yl)vinyl trifluoromethanesulfonate (125 mg, 0.4 mmol) and lithium bromide (39.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, pentane) to yield **315b** (76 mg, 78% yield) as a colorless oil.

R_f = 0.81 (silica, hexanes, $KMnO_4$).

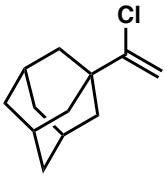
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.56 (d, *J* = 2.0 Hz, 1H), 5.42 (d, *J* = 2.0 Hz, 1H), 2.03 (q, *J* = 3.2 Hz, 3H), 1.82 – 1.76 (m, 6H), 1.74 – 1.61 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 148.1, 113.7, 41.4, 41.1, 36.7, 28.5.

FTIR (NaCl, thin film, cm^{-1}): 2905, 2850, 2678, 1622, 1453, 1344, 1152, 1057, 881, 716, 628.

HRMS (EI, *m/z*): calc'd for $C_{12}H_{17}Br$ $[M+\cdot]^+$: 240.0514; found: 240.0510.

(3*r*,5*r*,7*r*)-1-(1-chlorovinyl)adamantane (315c)



Prepared from 1-((3*r*,5*r*,7*r*)-adamantan-1-yl)vinyl trifluoromethanesulfonate (93.0 mg, 0.3 mmol) and lithium chloride (19.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, pentane) to yield **315c** (46 mg, 77% yield) as a colorless oil.

R_f = 0.84 (silica, hexanes, $KMnO_4$).

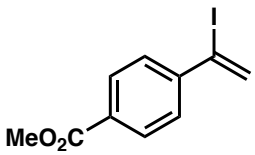
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.13 (d, *J* = 1.5 Hz, 1H), 5.09 (d, *J* = 1.5 Hz, 1H), 2.04 (q, *J* = 3.2 Hz, 3H), 1.79 (d, *J* = 3.0 Hz, 6H), 1.76 – 1.62 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 153.5, 109.1, 40.7, 40.2, 36.7, 28.4.

FTIR (NaCl, thin film, cm^{-1}): 2904, 2851, 1618, 1452, 1344, 1165, 162, 877, 734, 666.

HRMS (EI, *m/z*): calc'd for $C_{12}H_{17}Cl$ $[M+\cdot]^+$: 196.1019; found: 196.1040.

methyl 4-(1-iodovinyl)benzoate (316a)



Prepared from methyl 4-(1-(((trifluoromethyl)sulfonyl) oxy)vinyl)benzoate (93.1 mg, 0.3 mmol) and sodium iodide (67.5 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, 5 to 20% Et_2O/hexanes) to yield **316a** (56 mg, 64% yield) as a white solid. *Note: This compound slowly oxidizes to the α-iodo acetophenone under ambient conditions.*

R_f = 0.25 (silica, 10% Et_2O/hexanes, UV).

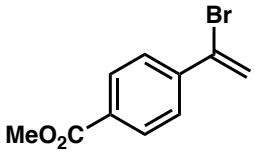
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.99 – 7.95 (m, 2H), 7.59 – 7.54 (m, 2H), 6.56 (d, *J* = 1.9 Hz, 1H), 6.17 (d, *J* = 1.9 Hz, 1H), 3.92 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 166.5, 145.8, 130.4, 129.6, 129.2, 128.2, 105.8, 52.4.

FTIR (NaCl, thin film, cm^{-1}): 2948, 1720, 1593, 1433, 1403, 1284, 1191, 1111, 1050, 902, 861, 777, 710.

HRMS (FAB, *m/z*): calc'd for $C_{10}H_8IO_2$ $[M+H]^+$: 288.9726; found: 288.9740.

methyl 4-(1-bromovinyl)benzoate (316b)



Prepared from methyl 4-(1-(((trifluoromethyl)sulfonyl) oxy)vinyl)benzoate (93.1 mg, 0.3 mmol) and lithium bromide (39.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, 1 to 2% Et_2O/hexanes) to yield **316b** (69 mg, 90% yield) as a white solid. *Note: This compound slowly oxidizes to the α-bromo acetophenone under ambient conditions.*

R_f = 0.47 (silica, 10% EtOAc/hexanes, $KMnO_4$).

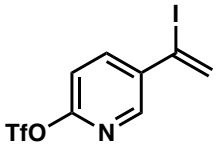
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 – 7.98 (m, 2H), 7.68 – 7.62 (m, 2H), 6.22 (d, *J* = 2.2 Hz, 1H), 5.88 (d, *J* = 2.2 Hz, 1H), 3.92 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 166.5, 142.7, 130.6, 129.9, 129.7, 127.4, 119.7, 52.4.

FTIR (NaCl, thin film, cm^{-1}): 3429, 2952, 1727, 1606, 1436, 1406, 1281, 1191, 1110, 1016, 860, 776, 710.

HRMS (TOF-ESI, *m/z*): calc'd for $C_{10}H_8BrO_2$ $[M+H]^+$: 240.9864; found: 240.9888.

5-(1-iodovinyl)pyridin-2-yl trifluoromethanesulfonate (317a)



Prepared from 1-(6-(((trifluoromethyl)sulfonyl)oxy)pyridin-3-yl)vinyl trifluoromethanesulfonate (120 mg, 0.3 mmol) and sodium iodide (67.5 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, 10% Et_2O/hexanes) to yield **317a** (62 mg, 54% yield) as a colorless oil. *Note: This compound slowly oxidizes to the α-iodo acetophenone under ambient conditions.*

R_f = 0.74 (silica, 30% EtOAc/hexanes, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.51 (dd, *J* = 2.6, 0.7 Hz, 1H), 8.00 (dd, *J* = 8.5, 2.6 Hz, 1H), 7.13 (dd, *J* = 8.5, 0.7 Hz, 1H), 6.58 (d, *J* = 2.2 Hz, 1H), 6.25 (d, *J* = 2.1 Hz, 1H).

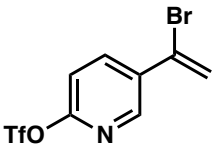
^{13}C NMR (101 MHz, $CDCl_3$): δ 155.6, 147.0, 141.0, 138.6, 130.9, 118.7 (q, J_{C-F} = 320.6 Hz), 114.6, 99.3.

^{19}F NMR (282 MHz, $CDCl_3$): δ -72.9.

FTIR (NaCl, thin film, cm^{-1}): 1604, 1579, 1469, 1428, 1370, 1215, 1171, 1137, 1020, 891, 842, 717, 647.

HRMS (TOF-ESI, *m/z*): calc'd for $C_8H_5F_3INO_3S$ $[M+H]^+$: 379.9065; found: 379.9076.

5-(1-bromovinyl)pyridin-2-yl trifluoromethanesulfonate (317b)



Prepared from 1-(6-(((trifluoromethyl)sulfonyl)oxy)pyridin-3-yl)vinyl trifluoromethanesulfonate (120 mg, 0.3 mmol) and lithium bromide (39.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, 10% Et_2O/hexanes) to yield **317b** (80 mg, 80% yield) as a colorless oil. *Note: This compound slowly oxidizes to the α-bromo acetophenone under ambient conditions.*

R_f = 0.70 (silica, 30% EtOAc/hexanes, UV).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.58 (dd, *J* = 2.6, 0.7 Hz, 1H), 8.08 (dd, *J* = 8.5, 2.6 Hz, 1H), 7.18 (dd, *J* = 8.5, 0.6 Hz, 1H), 6.24 (d, *J* = 2.6 Hz, 1H), 5.96 (d, *J* = 2.6 Hz, 1H).

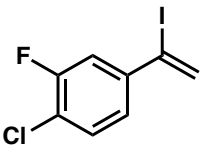
^{13}C NMR (126 MHz, $CDCl_3$): δ 155.8, 146.9, 140.1, 135.5, 124.9, 121.3, 118.7 (q, J_{C-F} = 320.7 Hz), 114.7.

^{19}F NMR (282 MHz, $CDCl_3$): δ -72.9.

FTIR (NaCl, thin film, cm^{-1}): 3105, 1615, 1582, 1470, 1426, 1370, 1215, 1173, 1137, 1020, 891, 621.

HRMS (TOF-ESI, *m/z*): calc'd for $C_8H_5F_3BrNO_3S$ $[M+H]^+$: 331.9204; found: 331.9195.

1-chloro-2-fluoro-4-(1-iodovinyl)benzene (318a)



Prepared from 1-(4-chloro-3-fluorophenyl)vinyl trifluoromethanesulfonate (91.4 mg, 0.3 mmol) and sodium iodide (67.5 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, pentane) to yield **318a** (58 mg, 69% yield) as a yellow oil. *Note: This compound slowly oxidizes to the α-iodo acetophenone derivative under ambient conditions.*

R_f = 0.57 (silica, hexanes, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 – 7.23 (m, 2H), 7.21 – 7.16 (m, 1H), 6.43 (d, *J* = 2.0 Hz, 1H), 6.06 (d, *J* = 2.0 Hz, 1H).

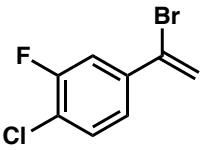
^{13}C NMR (101 MHz, $CDCl_3$): δ 157.5 (d, J_{C-F} = 249.4 Hz), 142.3 (d, J_{C-F} = 6.9 Hz), 130.3, 128.9, 124.4 (d, J_{C-F} = 3.5 Hz), 121.6 (d, J_{C-F} = 17.9 Hz), 116.5 (d, J_{C-F} = 22.8 Hz), 104.0 (d, J_{C-F} = 2.2 Hz).

^{19}F NMR (282 MHz, $CDCl_3$): δ -114.9 (dd, J_{F-H} = 10.1, 7.4 Hz).

FTIR (NaCl, thin film, cm^{-1}): 1598, 1484, 1414, 1402, 1285, 1244, 1070, 937, 901, 873, 818, 743, 733.

HRMS (EI, *m/z*): calc'd for C_8H_5ClFI $[M+\cdot]^+$: 281.9109; found: 281.9124.

1-bromo-2-fluoro-4-(1-iodovinyl)benzene (318b)



Prepared from 1-(4-chloro-3-fluorophenyl)vinyl trifluoromethanesulfonate (91.4 mg, 0.3 mmol) and lithium bromide (39.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, pentane) to yield **318b** (52 mg, 73% yield) as a yellow oil. *Note: This compound slowly oxidizes to the α-bromo acetophenone derivative under ambient conditions.*

R_f = 0.65 (silica, hexanes, UV).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41 – 7.35 (m, 2H), 7.32 (ddd, J = 8.4, 2.1, 0.7 Hz, 1H), 6.15 (d, J = 2.3 Hz, 1H), 5.83 (d, J = 2.3 Hz, 1H).

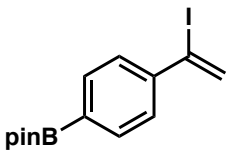
^{13}C NMR (126 MHz, $CDCl_3$): δ 157.6 (d, $J_{C\text{-}F}$ = 249.1 Hz), 139.0 (d, $J_{C\text{-}F}$ = 7.2 Hz), 130.3, 128.2 (d, $J_{C\text{-}F}$ = 2.3 Hz), 123.5 (d, $J_{C\text{-}F}$ = 3.8 Hz), 121.7 (d, $J_{C\text{-}F}$ = 18.0 Hz), 119.2, 115.7 (d, $J_{C\text{-}F}$ = 23.0 Hz).

^{19}F NMR (282 MHz, $CDCl_3$): δ -114.8 (m).

FTIR (NaCl, thin film, cm^{-1}): 1601, 1570, 1485, 1412, 1289, 1246, 1174, 1066, 937, 892, 875, 819, 738.

HRMS (EI, *m/z*): calc'd for C_8H_5ClFBr $[M+\cdot]^+$: 233.9247; found: 233.9228.

2-(4-(1-iodovinyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (319a)



Prepared from 1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)vinyl trifluoromethanesulfonate (113.5 mg, 0.3 mmol) and sodium iodide (68 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, 0 to 5% Et_2O/hexanes) to yield **319a** (72 mg, 68% yield) as a light yellow oil.

R_f = 0.53 (silica, 10% EtOAc/hexanes, $KMnO_4$).

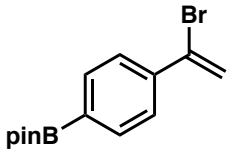
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 – 7.72 (m, 2H), 7.53 – 7.48 (m, 2H), 6.51 (d, J = 1.8 Hz, 1H), 6.11 (d, J = 1.7 Hz, 1H), 1.34 (s, 12H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 144.3, 134.8, 128.0, 127.5, 107.5, 84.1, 25.0. *(Note: carbon bonded to boron not observed.)*

FTIR (NaCl, thin film, cm^{-1}): 2978, 2930, 1607, 1398, 1360, 1324, 1269, 1210, 1144, 1092, 1018, 859, 841, 654.

HRMS (TOF-ESI, *m/z*): calc'd for $C_{14}H_{18}BIO_2$ $[M+H]^+$: 357.0523; found: 357.0527.

2-(4-(1-bromovinyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (319b)



Prepared from 1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)vinyl trifluoromethanesulfonate (113.5 mg, 0.3 mmol) and lithium bromide (39.1 mg, 0.45 mmol) according to General

Procedure 2. The crude residue was purified by column chromatography (silica, 0 to 5% Et_2O/hexanes) to yield **319b** (59 mg, 64% yield) as a light yellow oil which crystallized upon standing in the freezer.

R_f = 0.48 (silica, 10% Et_2O/hexanes, $KMnO_4$).

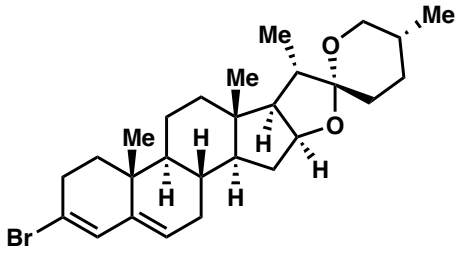
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 – 7.76 (m, 2H), 7.62 – 7.56 (m, 2H), 6.17 (d, *J* = 2.0 Hz, 1H), 5.81 (d, *J* = 2.0 Hz, 1H), 1.35 (s, 12H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 141.0, 134.8, 131.1, 126.6, 118.5, 84.1, 25.0. *(Note: carbon bonded to boron not observed.)*

FTIR (NaCl, thin film, cm^{-1}): 2979, 1607, 1507, 160, 1326, 1270, 1216, 1143, 1092, 1018, 859, 783, 656.

HRMS (TOF-ESI, *m/z*): calc'd for $C_{14}H_{18}BBrO_2$ $[M+H]^+$: 309.0661; found: 309.0670.

(5'*R*,6a*R*,6b*S*,8a*S*,8b*R*,9*S*,10*R*,11a*S*,12a*S*,12b*S*)-4-bromo-5',6a,8a,9-tetramethyl-1,3',4',5,5',6,6a,6b,6',7,8,8a,8b,9,11a,12,12a,12b-octadecahydrospiro[naphtho[2',1':4,5]indeno[2,1-*b*]furan-10,2'-pyran] (320b)



Prepared from (5'*R*,6a*R*,6b*S*,8a*S*,8b*R*,9*S*,10*R*,11a*S*,12a*S*,12b*S*)-5',6a,8a,9-tetramethyl-1,3',4',5,5',6,6a,6b,6',7,8,8a,8b,9,11a,12,12a,12b-octadecahydrospiro[naphtho-[2',1':4,5]indeno[2,1-*b*]furan-10,2'-pyran]-4-yl trifluoromethanesulfonate (163.4 mg, 0.3 mmol) and lithium bromide (39.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, 40% Et_2O/hexanes) to yield **320b** (107 mg, 75% yield) as a white solid.

R_f = 0.56 (silica, 10% Et_2O/hexanes, $KMnO_4$).

$[\alpha]_D^{25}$ = –176° (c = 1.0, $CHCl_3$).

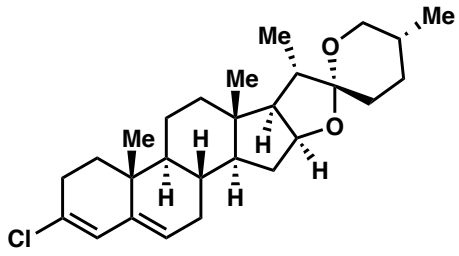
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.26 (d, *J* = 2.3 Hz, 1H), 5.39 (dd, *J* = 5.1, 2.9 Hz, 1H), 4.41 (ddd, *J* = 8.6, 7.5, 6.3 Hz, 1H), 3.47 (ddd, *J* = 10.9, 4.6, 2.0 Hz, 1H), 3.36 (t, *J* = 10.8 Hz, 1H), 2.67 – 2.53 (m, 1H), 2.46 (ddd, *J* = 18.4, 5.9, 1.6 Hz, 1H), 2.17 (dt, *J* = 18.7, 5.3 Hz, 1H), 1.98 (ddd, *J* = 11.8, 7.5, 5.4 Hz, 1H), 1.91 – 1.10 (m, 17H), 1.05 – 0.92 (m, 7H), 0.84 – 0.74 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 141.3, 131.2, 124.4, 120.9, 109.4, 80.9, 67.0, 62.2, 56.7, 48.0, 41.7, 40.5, 39.8, 35.6, 34.6, 33.2, 32.0, 31.9, 31.5, 31.3, 30.4, 28.9, 21.0, 19.1, 17.3, 16.5, 14.7.

FTIR (NaCl, thin film, cm^{-1}): 2949, 1616, 1455, 1377, 1241, 1173, 1051, 980, 899, 734.

HRMS (FAB, *m/z*): calc'd for $C_{27}H_{39}BrO_2$ $[M+H]^+$: 475.2035; found: 475.2049.

(5'*R*,6a*R*,6b*S*,8a*S*,8b*R*,9*S*,10*R*,11a*S*,12a*S*,12b*S*)-4-chloro-5',6a,8a,9-tetramethyl-1,3',4',5,5',6,6a,6b,6',7,8,8a,8b,9,11a,12,12a,12b-octadecahydrospiro[naphtho[2',1':4,5]indeno[2,1-*b*]furan-10,2'-pyran] (320c)



Prepared from (5'*R*,6a*R*,6b*S*,8a*S*,8b*R*,9*S*,10*R*,11a*S*,12a*S*,12b*S*)-5',6a,8a,9-tetramethyl-1,3',4',5,5',6,6a,6b,6',7,8,8a,8b,9,11a,12,12a,12b-octadecahydrospiro[naphtho[2',1':4,5]indeno[2,1-*b*]furan-10,2'-pyran]-4-yl trifluoromethanesulfonate (163.4 mg, 0.3 mmol) and lithium chloride (19.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, 40% Et_2O/hexanes) to yield **320c** (125 mg, 97% yield) as a white solid.

R_f = 0.57 (silica, 10% EtOAc/hexanes, $KMnO_4$).

$[\alpha]_D^{25}$ = –183° (c = 1.0, $CHCl_3$).

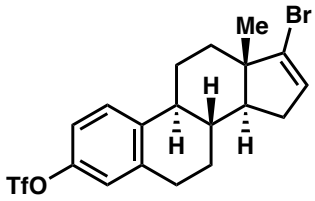
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.05 (d, *J* = 2.3 Hz, 1H), 5.38 (dd, *J* = 5.0, 2.9 Hz, 1H), 4.41 (ddd, *J* = 8.6, 7.6, 6.4 Hz, 1H), 3.47 (ddd, *J* = 10.9, 4.5, 2.0 Hz, 1H), 3.37 (t, *J* = 10.9 Hz, 1H), 2.50 (ddd, *J* = 17.8, 12.0, 5.8 Hz, 1H), 2.31 (ddd, *J* = 18.3, 5.9, 1.5 Hz, 1H), 2.19 (dt, *J* = 18.7, 5.3 Hz, 1H), 1.99 (ddd, *J* = 11.7, 7.5, 5.4 Hz, 1H), 1.93 – 1.50 (m, 11H), 1.50 – 1.39 (m, 2H), 1.31 (ddd, *J* = 13.5, 11.8, 6.3 Hz, 2H), 1.24 – 1.09 (m, 2H), 1.06 – 1.00 (m, 1H), 0.97 (t, *J* = 3.5 Hz, 6H), 0.84 – 0.75 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 140.6, 130.4, 127.1, 124.0, 109.4, 80.9, 67.0, 62.2, 56.7, 48.0, 41.7, 40.5, 39.8, 34.9, 34.7, 32.1, 31.9, 31.5, 31.4, 30.8, 30.4, 28.9, 21.1, 19.0, 17.3, 16.5, 14.7.

FTIR (NaCl, thin film, cm^{-1}): 2950, 2906, 1622, 1450, 1380, 1350, 1240, 1170, 1070, 1050, 981, 900, 868, 734.

HRMS (TOF-ESI, *m/z*): calc'd for $C_{27}H_{39}ClO_2$ $[M+H]^+$: 431.2717; found: 431.2716.

(8*R*,9*S*,13*S*,14*S*)-17-bromo-13-methyl-7,8,9,11,12,13,14,15-octahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl trifluoromethanesulfonate (321b)



Prepared from (8*R*,9*S*,13*S*,14*S*)-13-methyl-7,8,9,11,12,13,14,15-octahydro-6*H*-cyclopenta[*a*]phenanthrene-3,17-diylbis (trifluoromethanesulfonate) (160.3 mg, 0.3 mmol) and lithium bromide (39.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, 5% to 15% PhMe/hexanes) to yield **321b** (82 mg, 59% yield) as a colorless, tacky oil.

$\mathbf{R_f}$ = 0.38 (silica, 10% PhMe/hexanes, $KMnO_4$).

$\mathbf{[\alpha]_D^{25}}$ = 39° (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 (dd, *J* = 8.7, 1.1 Hz, 1H), 7.03 (dd, *J* = 8.6, 2.8 Hz, 1H), 6.99 (d, *J* = 2.6 Hz, 1H), 5.88 (dd, *J* = 3.3, 1.7 Hz, 1H), 2.97 – 2.91 (m, 2H), 2.45 – 2.36 (m, 1H), 2.36 – 2.29 (m, 1H), 2.25 (ddd, *J* = 14.8, 6.3, 3.2 Hz, 1H), 2.02 (ddd, *J* = 14.8, 11.1, 1.8 Hz, 1H), 1.99 – 1.93 (m, 1H), 1.90 (ddd, *J* = 12.3, 3.7, 2.1 Hz, 1H), 1.73 (td, *J* = 11.2, 6.2 Hz, 1H), 1.69 – 1.41 (m, 4H), 0.88 (s, 3H).

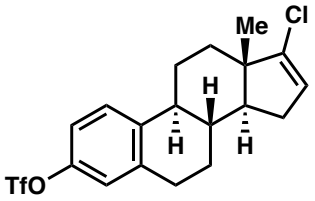
^{13}C NMR (101 MHz, $CDCl_3$): δ 147.7, 140.8, 139.5, 135.6, 129.1, 127.0, 121.3, 118.9 (q, $J_{C\text{-}F}$ = 320.7 Hz), 118.3, 54.9, 48.9, 44.4, 37.0, 34.6, 31.7, 29.5, 27.0, 26.2, 15.3.

^{19}F NMR (282 MHz, $CDCl_3$): δ -72.9.

FTIR (NaCl, thin film, cm^{-1}): 2932, 1592, 1490, 1422, 1247, 1210, 1142, 996, 919, 882, 846.

HRMS (FAB, *m/z*): calc'd for $C_{19}H_{20}BrF_3O_3S$ $[M+H-H_2]^+$: 465.0170; found: 465.0165.

(8*R*,9*S*,13*S*,14*S*)-17-chloro-13-methyl-7,8,9,11,12,13,14,15-octahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl trifluoromethanesulfonate (321c)



Prepared from (8*R*,9*S*,13*S*,14*S*)-13-methyl-7,8,9,11,12,13,14,15-octahydro-6*H*-cyclopenta[*a*]phenanthrene-3,17-diylbis (trifluoromethanesulfonate) (160.3 mg, 0.3 mmol) and lithium chloride (19.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, 1.5% EtOAc/hexanes) to yield **321c** (109 mg, 83% yield) as a colorless, tacky oil.

$\mathbf{R_f}$ = 0.67 (silica, 10% EtOAc/hexanes, $KMnO_4$).

$[\alpha]_D^{25}$ = +67° (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 (dd, *J* = 8.8, 1.2 Hz, 1H), 7.03 (dd, *J* = 8.6, 2.8 Hz, 1H), 7.00 – 6.94 (m, 1H), 5.67 (dd, *J* = 3.3, 1.7 Hz, 1H), 2.99 – 2.88 (m, 2H), 2.46 – 2.30 (m, 2H), 2.27 (ddd, *J* = 14.7, 6.3, 3.2 Hz, 1H), 2.05 (ddd, *J* = 14.8, 11.0, 1.8 Hz, 1H), 2.00 – 1.89 (m, 2H), 1.73 (td, *J* = 11.2, 6.3 Hz, 1H), 1.68 – 1.42 (m, 4H), 0.91 (s, 3H).

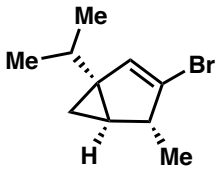
^{13}C NMR (101 MHz, $CDCl_3$): δ 147.7, 144.7, 140.9, 139.5, 127.0, 124.7, 121.3, 118.9 (q, $J_{C\text{-}F}$ = 320.7 Hz), 118.3, 55.1, 47.9, 44.5, 36.9, 33.8, 30.5, 29.5, 26.9, 26.1, 15.2.

^{19}F NMR (282 MHz, $CDCl_3$): δ -72.9.

FTIR (NaCl, thin film, cm^{-1}): 2934, 2859, 1598, 1490, 1417, 1248, 1211, 1142, 1007, 919, 851, 822, 701, 608.

HRMS (TOF-ESI, *m/z*): calc'd for $C_{19}H_{20}ClF_3O_3S$ $[M+H]^+$: 421.0852; found: 421.0845.

(1*S*,4*R*,5*R*)-3-bromo-1-isopropyl-4-methylbicyclo[3.1.0]hex-2-ene (322b)



Prepared from (1*S*,4*R*,5*R*)-1-isopropyl-4-methylbicyclo[3.1.0]hex-2-en-3-yl trifluoromethanesulfonate (85.3 mg, 0.3 mmol) and lithium bromide (39.1 mg, 0.45 mmol) according to General Procedure 2 with the exception of 5 mol % Ni used instead of 10 mol % Ni. The crude residue was purified by column chromatography (silica, pentane) to yield **322b** (27 mg, 42% yield, 92% purity by mass) as a colorless oil. Product was determined to be 92% pure by NMR (impurity is homocoupling product) therefore the yield is adjusted 42% x 0.92 = 38% yield.

R_f = 0.88 (silica, hexanes, $KMnO_4$).

$[\alpha]_D^{25}$ = –13° (c = 0.5, $CHCl_3$).

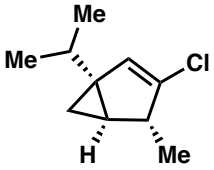
^{1}H NMR (500 MHz, $CDCl_3$): δ 5.93 (t, *J* = 1.3 Hz, 1H), 2.59 – 2.52 (m, 1H), 1.38 (p, *J* = 6.9 Hz, 1H), 1.15 – 1.11 (m, 4H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3H), 0.81 – 0.78 (m, 1H), 0.28 (t, *J* = 4.2 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 133.9, 123.9, 48.5, 40.9, 31.0, 26.5, 21.5, 20.9, 20.8, 20.8.

FTIR (NaCl, thin film, cm^{-1}): 2958, 2870, 1602, 1453, 1366, 1056, 973, 867, 832, 796, 754.

HRMS (EI, *m/z*): calc'd for $C_{10}H_{15}Br$ $[M+\cdot]^+$: 214.0357; found: 214.0358.

(1*S*,4*R*,5*R*)-3-chloro-1-isopropyl-4-methylbicyclo[3.1.0]hex-2-ene (322c)



Prepared from (1*S*,4*R*,5*R*)-1-isopropyl-4-methylbicyclo[3.1.0]hex-2-en-3-yl trifluoromethanesulfonate (85.3 mg, 0.3 mmol) and lithium chloride (19.1 mg, 0.45 mmol) according to General Procedure 2. The crude residue was purified by column chromatography (silica, pentane) to yield **322c** (40 mg, 78% yield) as a colorless oil.

R_f = 0.85 (silica, hexanes, $KMnO_4$).

$[\alpha]_D^{25}$ = +17° (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.75 (t, *J* = 1.3 Hz, 1H), 2.51 (tdd, *J* = 8.0, 6.0, 0.9 Hz, 1H), 1.36 (p, *J* = 6.8 Hz, 1H), 1.14 (d, *J* = 7.1 Hz, 3H), 1.12 – 1.06 (m, 1H), 0.99 (d, *J* = 6.9 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3H), 0.78 (dd, *J* = 7.8, 4.3 Hz, 1H), 0.27 (t, *J* = 4.2 Hz, 1H).

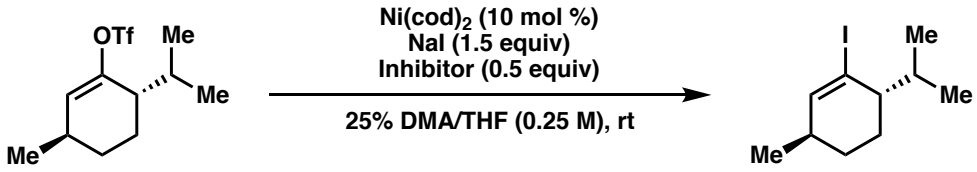
^{13}C NMR (101 MHz, $CDCl_3$): δ 134.6, 129.4, 46.8, 39.5, 31.1, 26.1, 21.6, 20.9, 20.8, 20.2.

FTIR (NaCl, thin film, cm^{-1}): 2956, 2924, 2854, 1458, 1364, 1057, 1026.

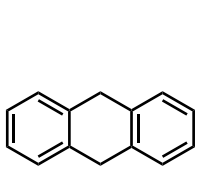
HRMS (EI, *m/z*): calc'd for $C_{10}H_{15}Cl$ $[M+\cdot]^+$: 170.0862; found: 170.0888.

5.7.4 Mechanistic Studies

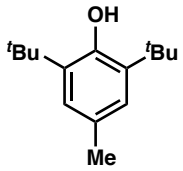
5.7.4.1 Radical Inhibitors



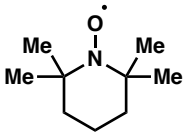
Four 1-dram vials were equipped with stir bars and brought into a N_2-filled glovebox. The vials were charged with NaI (0.15 mmol, 1.5 equiv) and $Ni(cod)_2$ (2.8 mg, 0.01 mmol, 0.1 equiv). Anhydrous DMA (0.1 mL) and THF (0.3 mL) were added, resulting in a clear yellow solution. DHA, BHT, TEMPO and Galvinoxyl were each added to one vial (0.5 equiv), then enol triflate **300** (0.1 mmol, 1 equiv) was added in one portion. The vials were sealed with a Teflon cap and brought out of the glovebox. The reactions were allowed to stir on the bench (480 rpm) for two hours at room temperature. Reactions were quenched by filtering through a plug of silica gel, eluting with 10 mL of 40% Et_2O/Hexanes, then concentrated under reduced pressure. An NMR standard (tetrachloronitrobenzene) was added to each vial for NMR analysis.



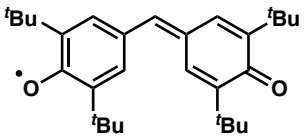
DHA
62% yield



BHT
67% yield

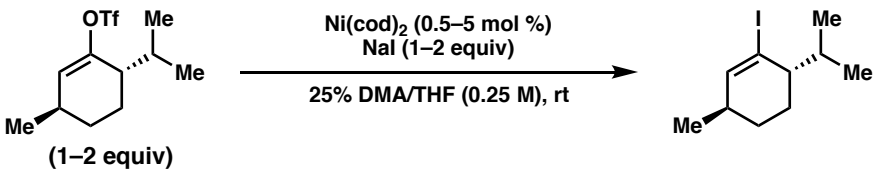


TEMPO
0% yield



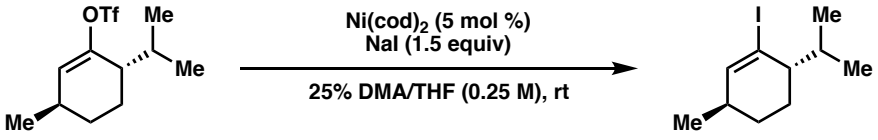
Galvinoxyl
5% yield

5.7.4.2 Kinetics



A 2-dram vial equipped with a stir bar was brought into a N_2-filled glovebox. The vial was charged with NaI and $Ni(cod)_2$. Anhydrous DMA (0.5 mL) and THF (1.5 mL) were added. Undecane (32 μL) was added as an internal analytical GC standard. Enol triflate (0.5 mmol, 1 equiv) was added neat. The vial was sealed with a Teflon cap and allowed to stir in the glovebox (480 rpm) at room temperature. Reaction aliquots (50 μL) were taken at various time points and were quenched by addition into 1 mL hexanes in a GC vial, giving an opaque white mixture. The reaction aliquots were analyzed by GC-FID.

5.7.4.3 EPR Studies



A 15 mL round-bottom flask equipped with a stir bar was brought into a N_2-filled glovebox. The vial was charged with NaI (1.2 mmol, 1.5 equiv) and $Ni(cod)_2$ (11.2 mg, 0.04 mmol, 0.05 equiv). Anhydrous DMA (0.8 mL) and THF (2.4 mL) were added. Enol triflate (0.8 mmol, 1 equiv) was added neat. The flask was sealed with a septum and allowed to stir in the glovebox (480 rpm) at room temperature. Aliquots (0.3 mL) were removed at various time points and added into EPR tubes, which were sealed and frozen at –78 ºC in a metal dewar filled with liquid nitrogen. The reaction aliquots were analyzed by EPR spectroscopy. An external standard of $CuSO_4$ in 1:9 ethylene glycol/H_2O was made and analyzed by EPR spectroscopy.

A single Ni(I) species is visible by EPR spectroscopy, which reaches a maximum concentration at 30 minutes. An additional broad Ni(II) species also forms as the reaction proceeds, which may indicate aggregate Ni species. In order to remove contribution from the broad Ni(II) signal, baseline corrections were applied using the 'msbackadj' command in MatLab.

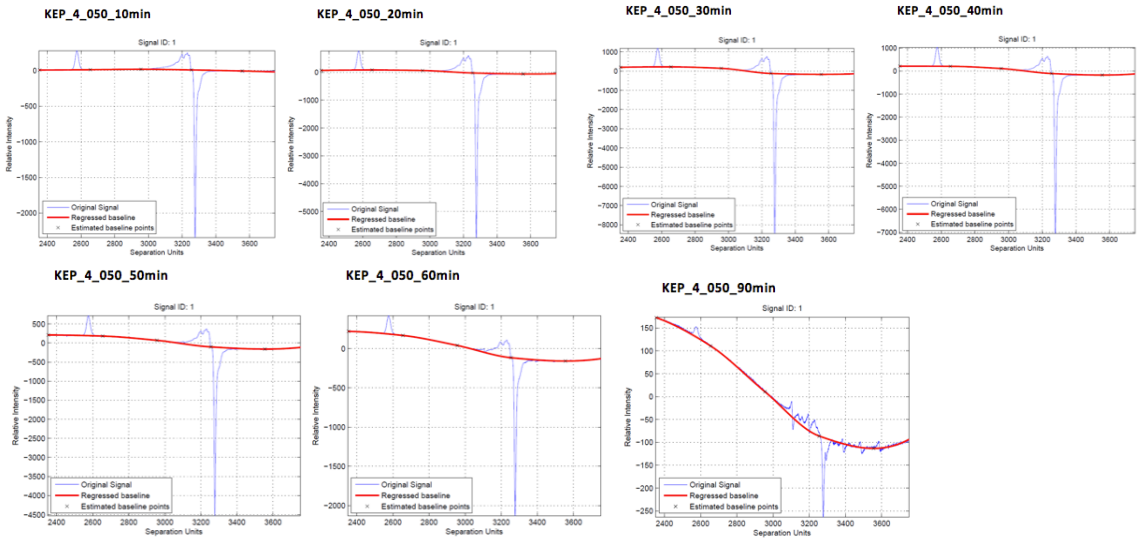


Figure S5.1: Baseline corrections of EPR spectra using MatLab.

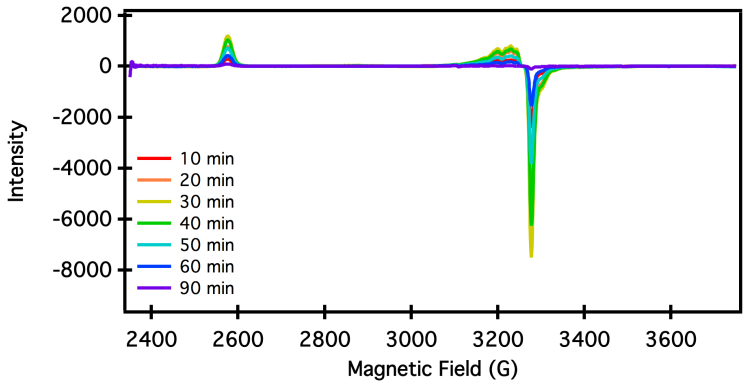


Figure S5.2: EPR spectra of the iodination of **300** at various time points.

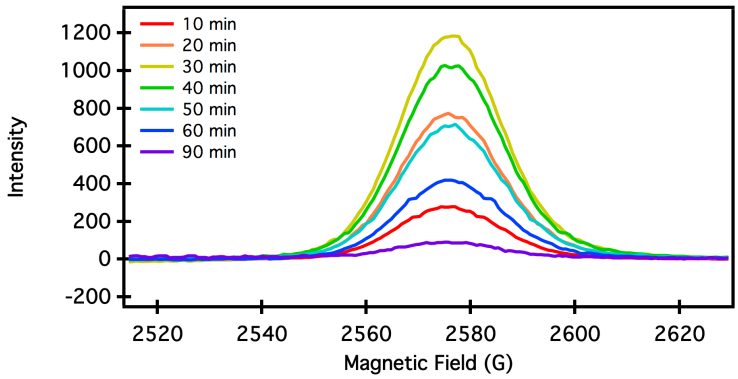


Figure S5.3: EPR spectra of the iodination of **300** at various time points (2520-2620 G region).

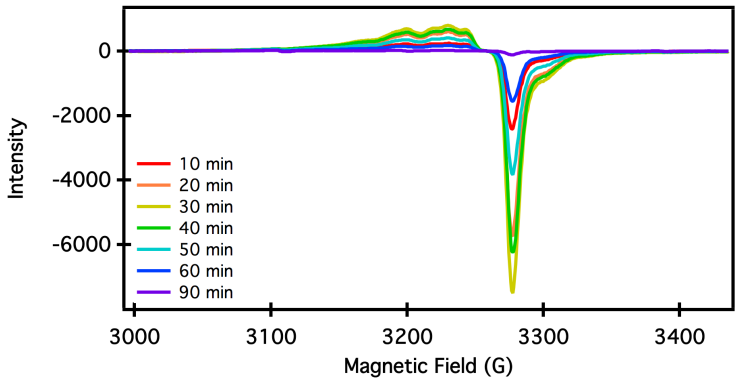


Figure S5.4: EPR spectra of the iodination of **300** at various time points (3000-3400 G region).

The spectra in **Figure S5.2** were processed by calculating the double integral. By comparison to the known concentration of $CuSO_4$ in **Figure S5.5**, the concentration of Ni(I) in the reaction was calculated to be <0.25 mM (i.e. less than 2% of all Ni added to the reaction, therefore indicating the Ni(I) species in this EPR spectrum is a trace Ni species).

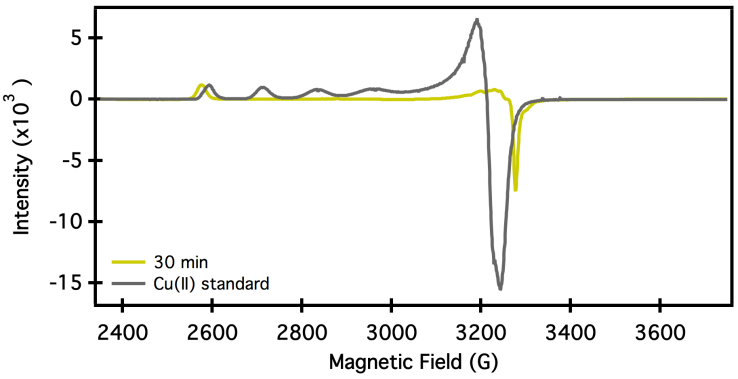


Figure S5.5: EPR spectra of the iodination of **300** at 30 minutes compared to 12.5 mM $CuSO_4$.

The halogenation of **300** was repeated with LiBr and LiCl to investigate the bromination and chlorination reactions. Time points were taken at 30 minutes and analyzed by EPR spectroscopy, demonstrating that the Ni(I) species observed does contain a halogen atom. The relative intensities of the spectra are I > Br > Cl.

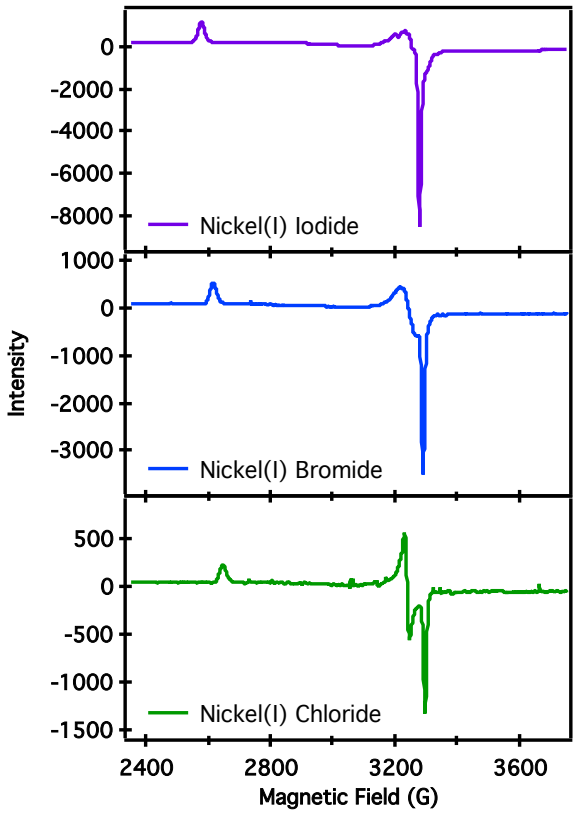
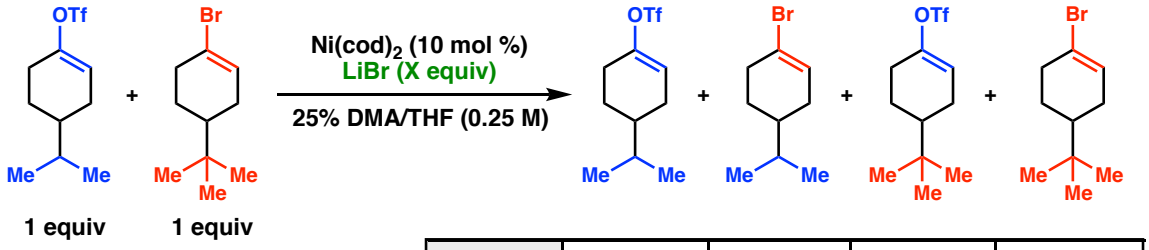


Figure S5.6: EPR spectra of the iodination, bromination, and chlorination of **300** at 30 minutes.

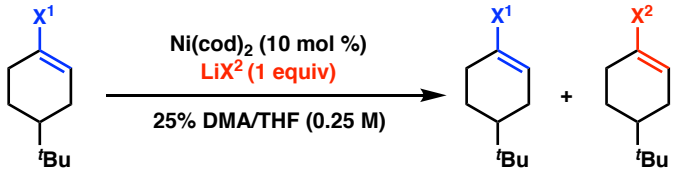
5.7.4.4 Crossover Experiments



0 equiv LiBr	100% recovered	0%	0%	100% recovered
0.1 equiv LiBr	90% recovered	10%	0%	100% recovered
1.0 equiv LiBr	0% recovered	90%	0%	100% recovered

A 2-dram vial equipped with a stir bar was brought into a N_2-filled glovebox. The vial was charged with LiBr (X equiv) and $Ni(cod)_2$ (5.5 mg, 0.02 mmol, 0.1 equiv). Anhydrous DMA (0.2 mL) and THF (0.6 mL) were added, resulting in a clear yellow solution. Undecane (13 µL) was added as an internal analytical GC standard. Enol triflate (0.2 mmol, 1 equiv) was added neat, followed by alkenyl bromide (0.2 mmol, 1 equiv). The vial was sealed with a Teflon cap and allowed to stir in the glovebox (480 rpm) at room temperature. Reaction aliquots (25 µL) were taken at time points and quenched by addition into 1 mL hexanes in a GC vial, giving an opaque white mixture. The reaction aliquots were analyzed by GC-FID against the internal standard.

5.7.4.5 Halide Competition



A 2-dram vial equipped with a stir bar was brought into a N_2-filled glovebox. The vial was charged with LiX^2 (0.5 mmol, 1 equiv) and $Ni(cod)_2$ (13.8 mg, 0.05 mmol, 0.1 equiv). Anhydrous DMA (0.5 mL) and THF (1.5 mL) were added. Undecane (32 µL) was added as an internal analytical GC standard. Alkenyl halide (RX^1) (0.5 mmol, 1 equiv) was added neat. The vial was sealed with a Teflon cap and allowed to stir in the glovebox (480 rpm) at room temperature. Reaction aliquots (50 µL) were taken at time points and quenched by addition into 1 mL hexanes in a GC vial, giving an opaque white mixture. The reaction aliquots were analyzed by GC-FID against the internal standard.

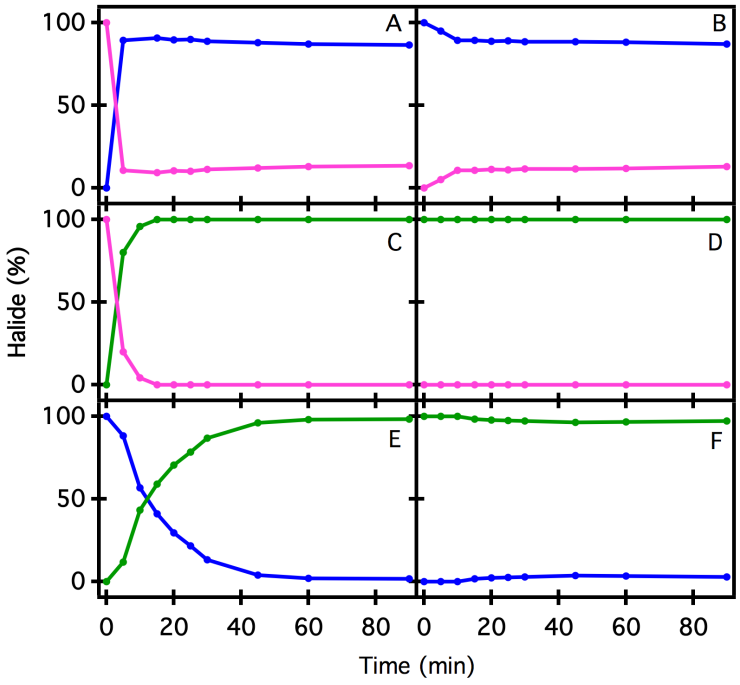


Figure S5.7: Ratios in terms of percentages for halide cross-over experiments: **A)** alkenyl iodide + LiBr, **B)** alkenyl bromide + LiI, **C)** alkenyl iodide + LiCl, **D)** alkenyl chloride + LiI, **E)** alkenyl bromide + LiCl, and **F)** alkenyl chloride + LiBr.

5.7.4.6 NMR Experiments

A 1-dram vial equipped with a stir bar was brought into a N_2-filled glovebox. The vial was charged with $Ni(cod)_2$ (5.5 mg, 0.02 mmol, 1.0 equiv). Deuterated DMA (0.2 mL) and deuterated THF (0.6 mL) were added and solubilized, affording a yellow solution. Trimethoxybenzene was added as an internal analytical NMR standard. Enol triflate **300** (5.7 mg, 0.02 mmol, 1 equiv) was added neat and the reaction was stirred for 10 seconds, then the mixture was transferred to a J Young NMR tube. NMR analysis was performed at 10, 70, and 130 min against the internal standard. No oxidative addition of the enol triflate was observed, however cod dissociation from $Ni(cod)_2$ was observed over time via NMR concomitant with the reaction turning brown in color.

5.8 NOTES AND REFERENCES

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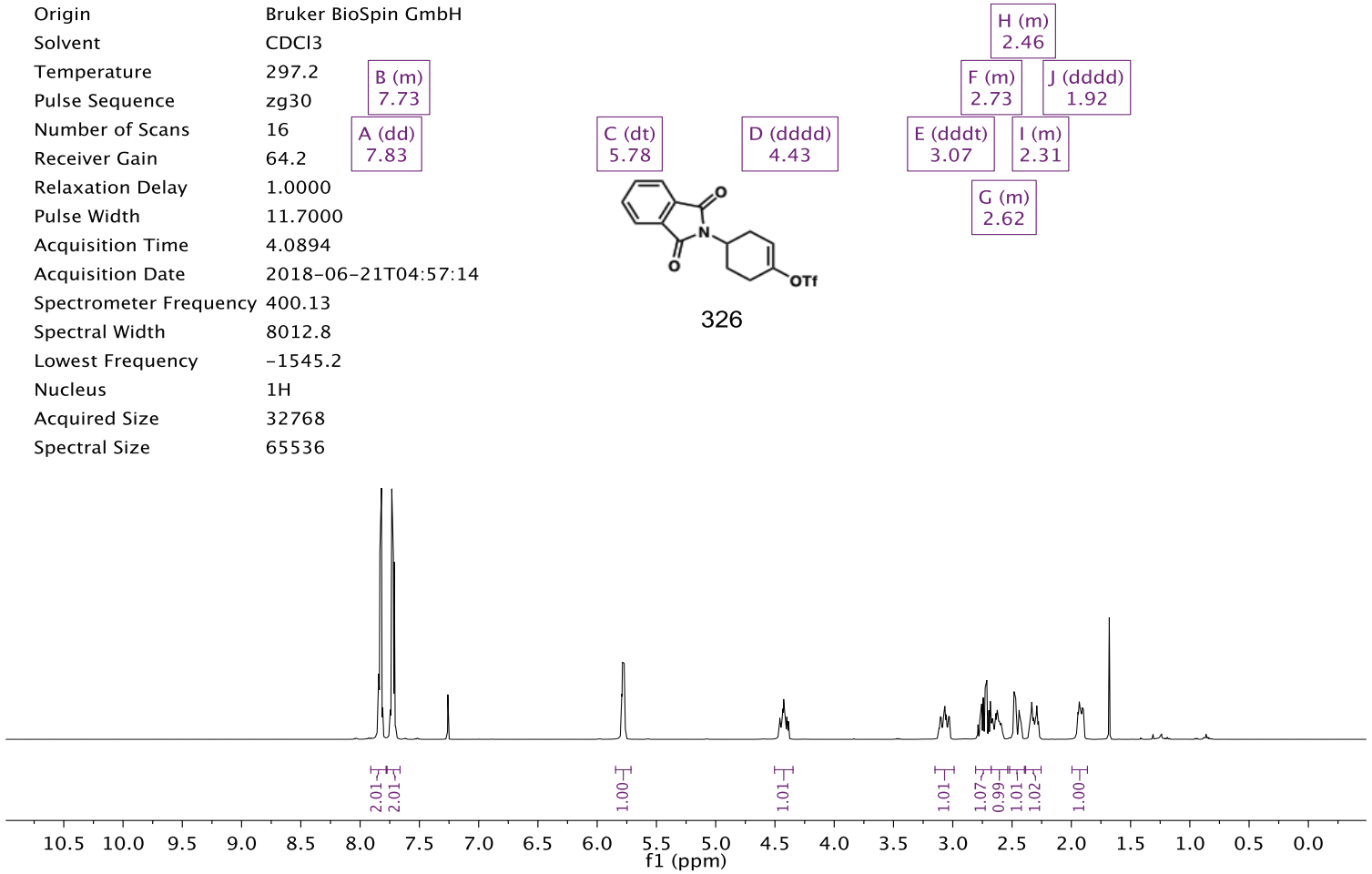
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Appendix 3

Spectra Relevant to Chapter 5:

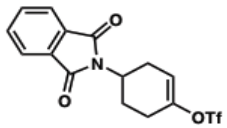
Nickel-Catalyzed Conversion of Enol Triflates to Alkenyl Halides

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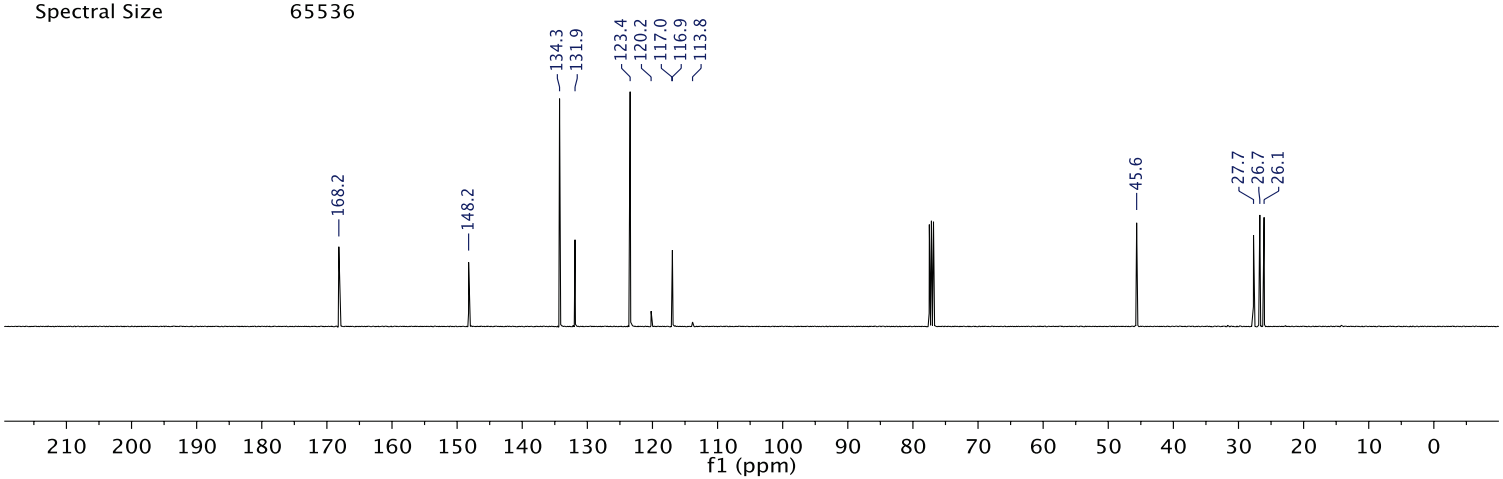


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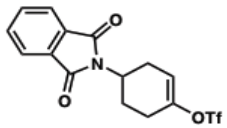
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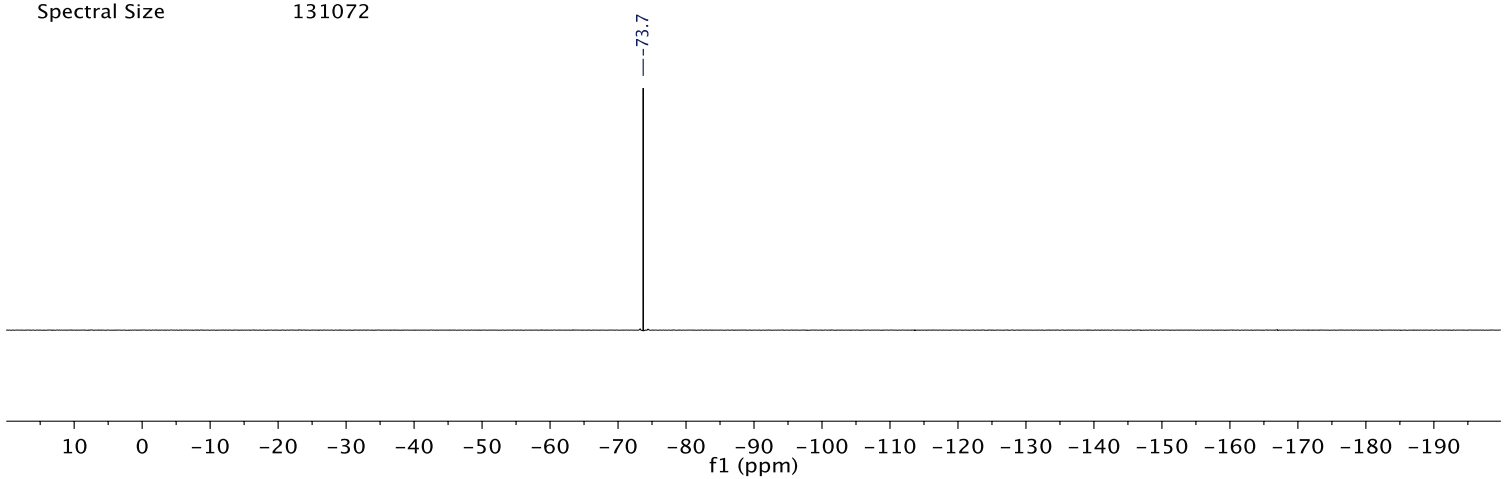
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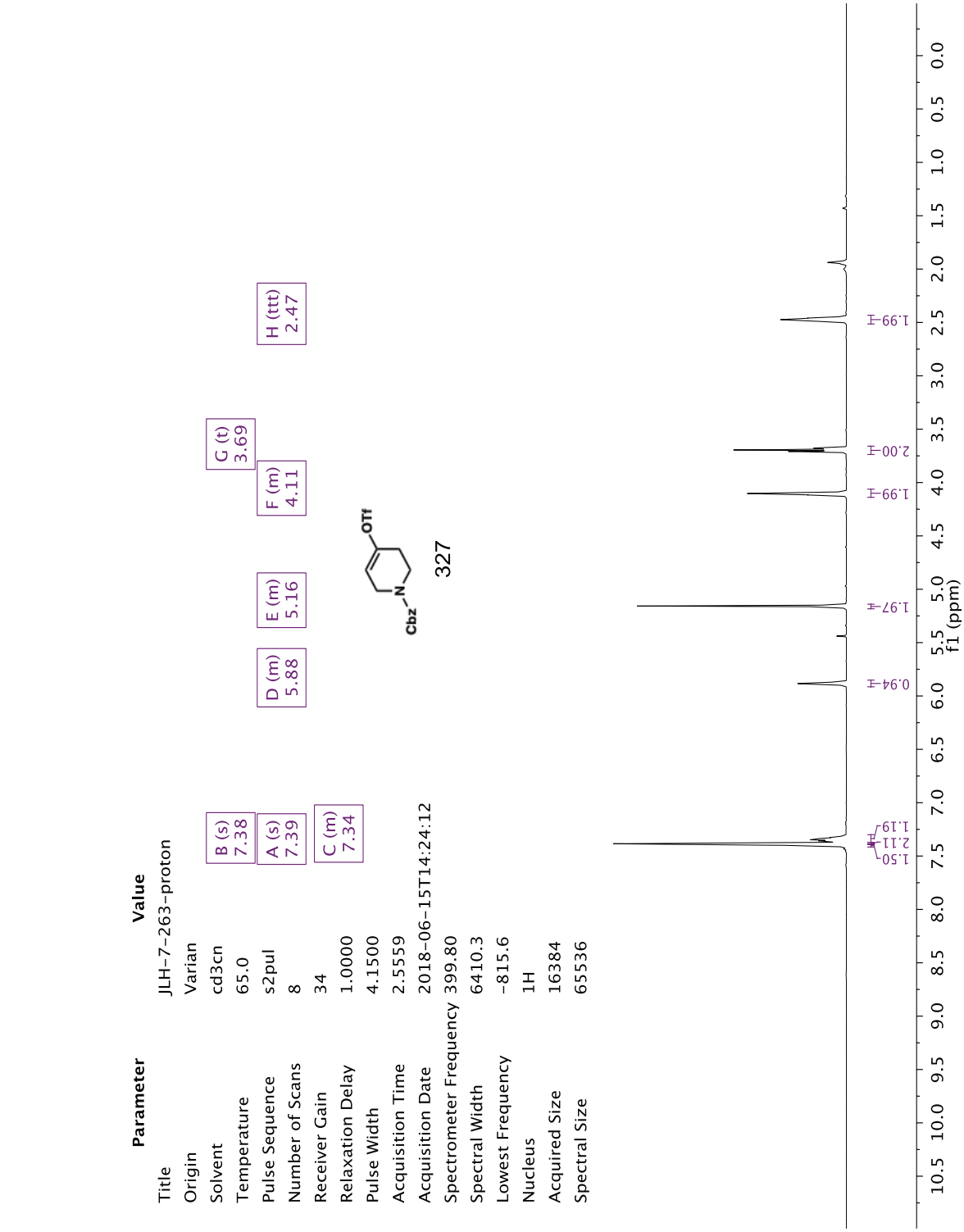
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326

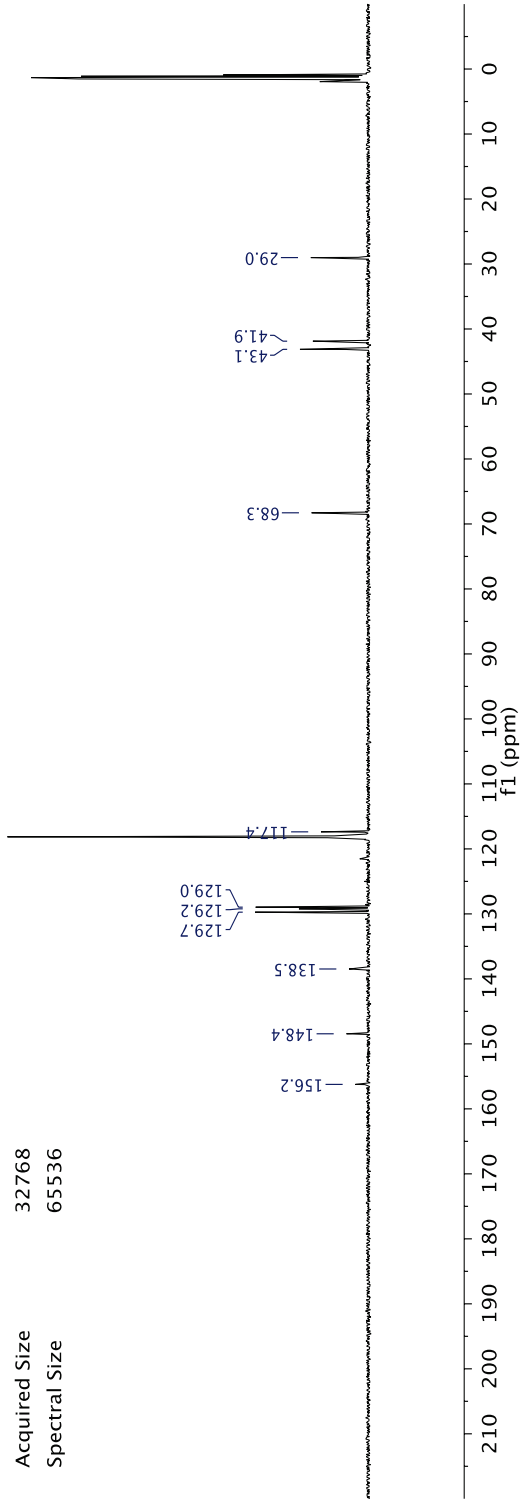


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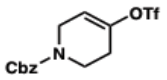

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D (m) 5.88
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OTf
Cbz
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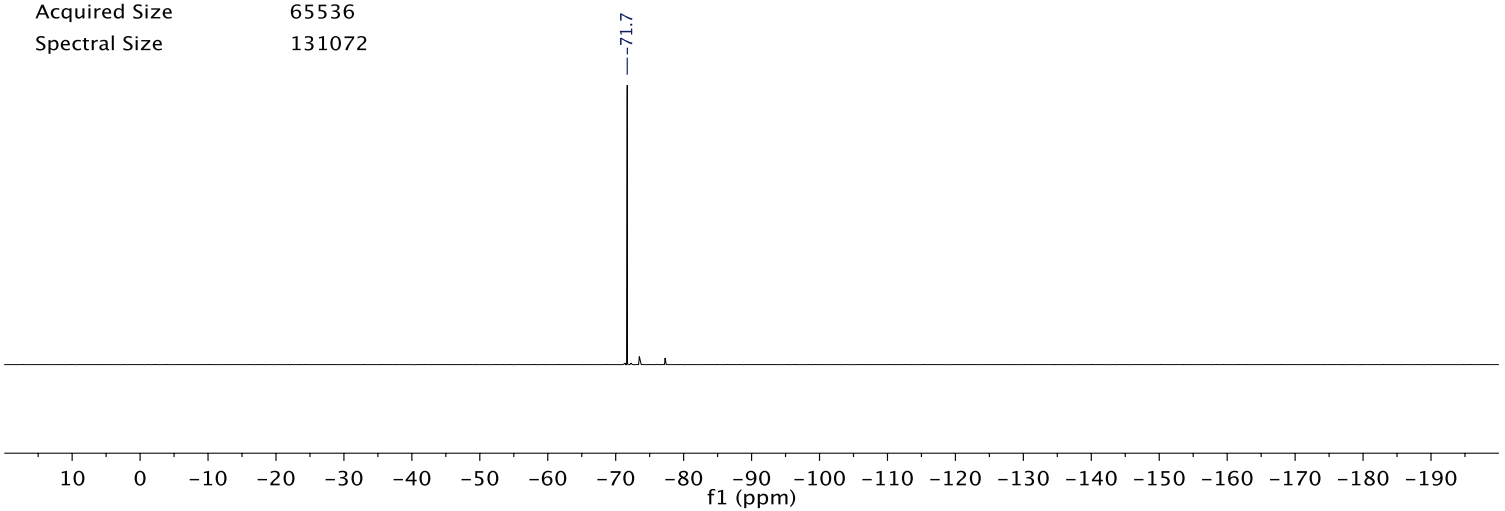
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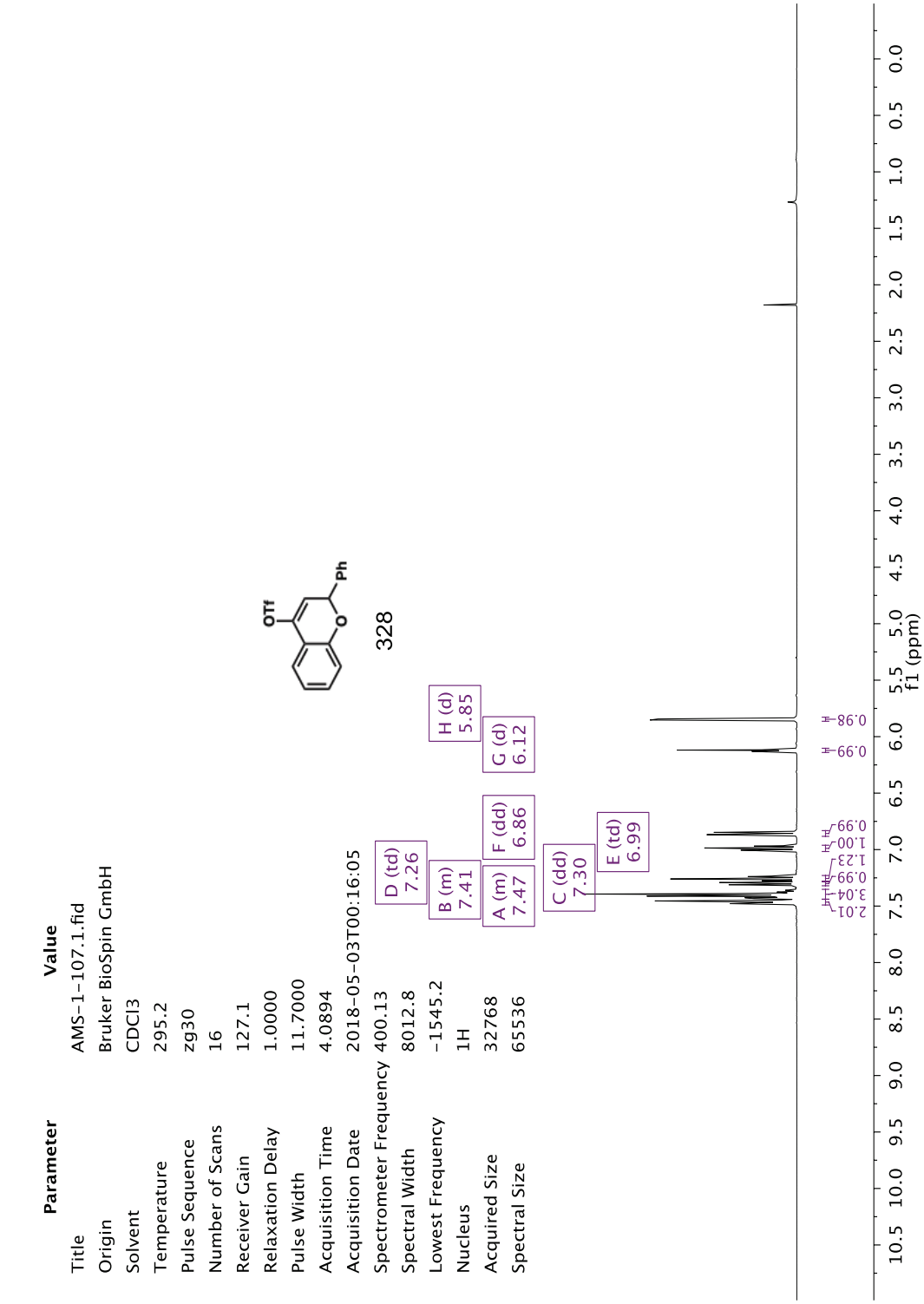
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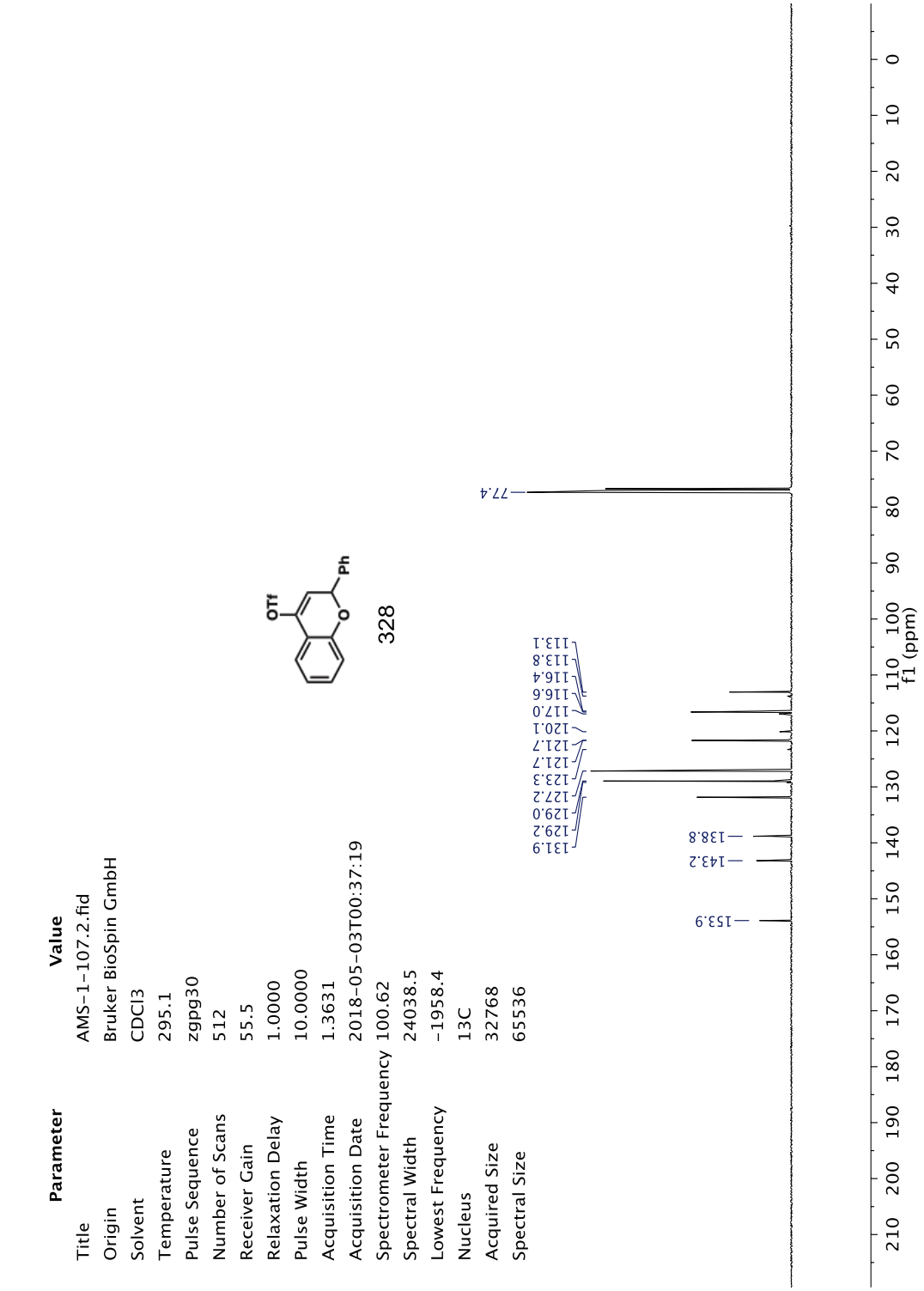


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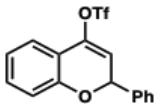
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OTf
Cbz
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f1 (ppm)


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OTf
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328
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C (dd) 7.30
D (td) 7.26
E (td) 6.99
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f1 (ppm)

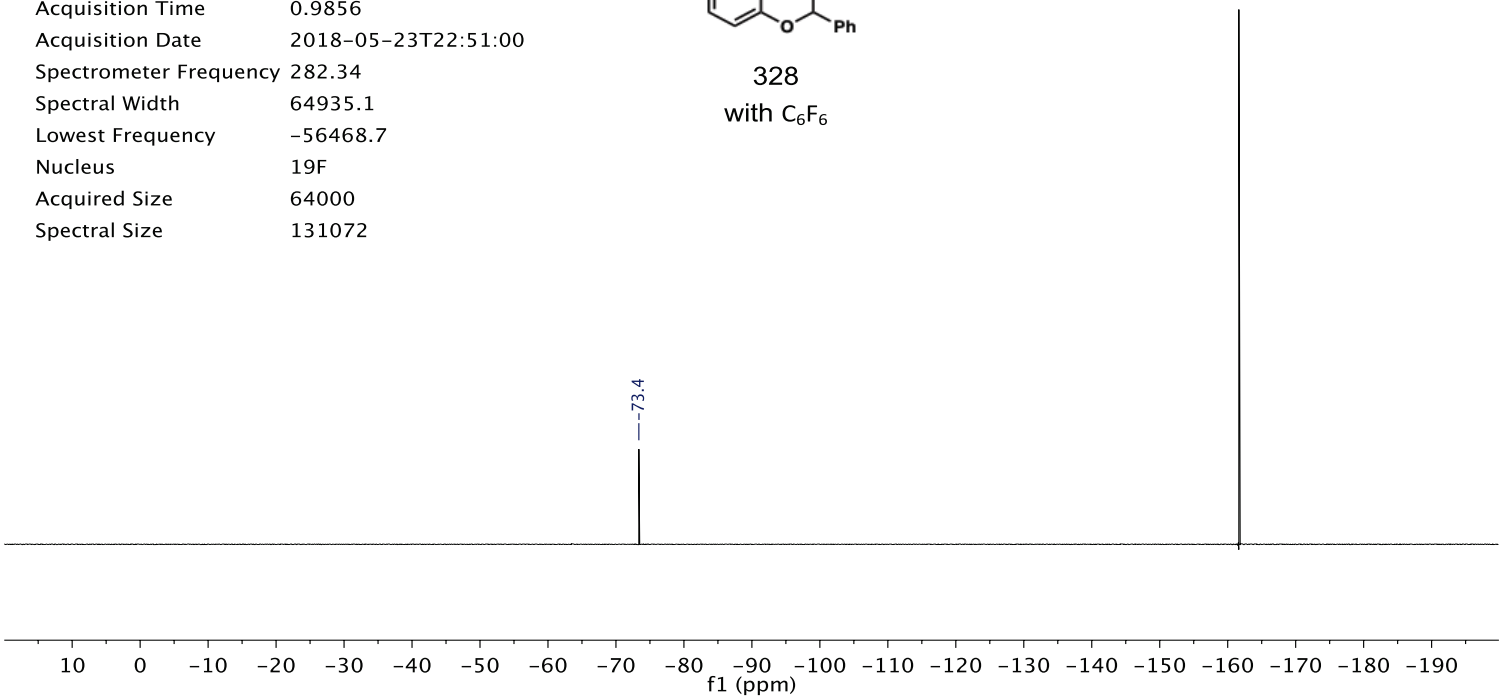

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OTf
Ph
O
328
77.4
153.9
143.2
138.8
131.9
129.2
129.0
127.2
123.3
121.7
121.7
120.1
117.0
116.6
116.4
113.8
113.1
f1 (ppm)

Parameter	Value
Title	AMS-1-107-F
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-05-03T23:05:28
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56468.7
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

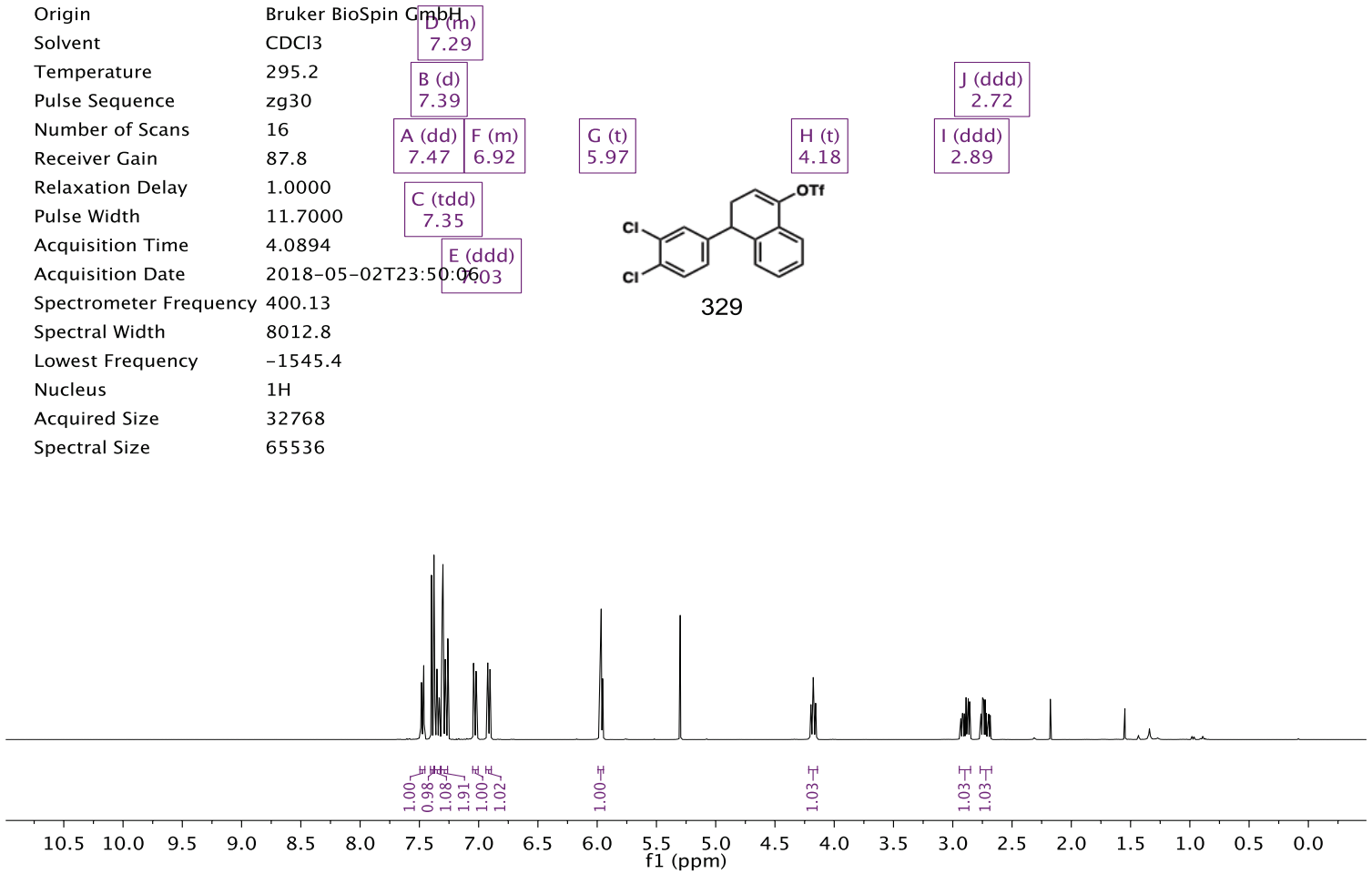
Parameter	Value
Title	AMS-1-107-F-C6F6
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-05-23T22:51:00
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56468.7
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

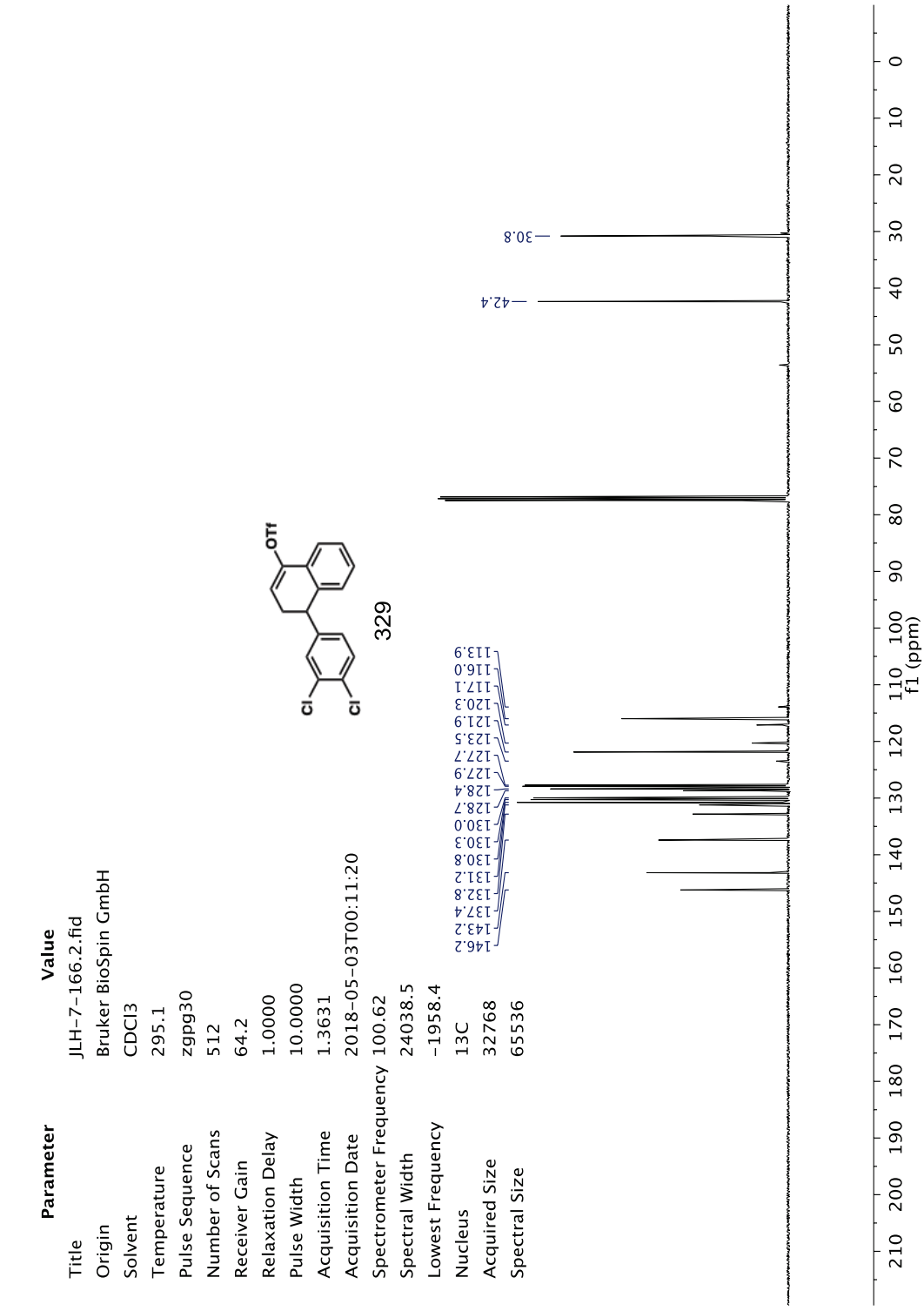


328
with C_6F_6



Parameter	Value
Title	JLH-7-166.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zg30
Number of Scans	16
Receiver Gain	87.8
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-05-02T23:50:06
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536




Parameter Value
Title JLH-7-166.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zgpg30
Number of Scans 512
Receiver Gain 64.2
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-05-03T00:11:20
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1958.4
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OTf
Cl
Cl
329
146.2
143.2
137.4
132.8
131.2
130.8
130.3
130.0
128.7
128.4
127.9
127.7
123.5
121.9
120.3
117.1
116.0
113.9
42.4
30.8
f1 (ppm)

Parameter	Value
Title	JLH-7-166-F
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-05-03T22:42:22
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56468.7
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

329

-73.5

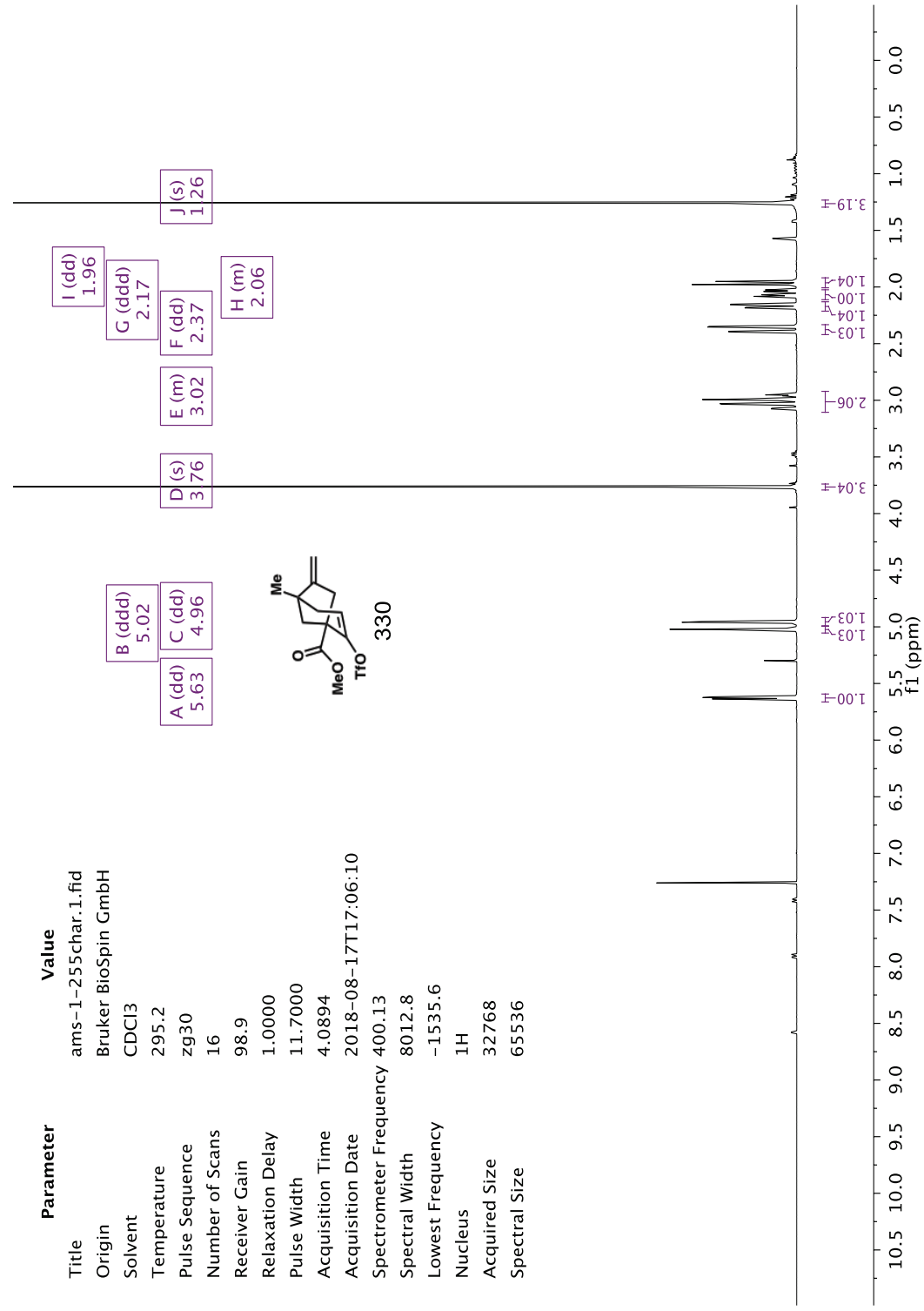
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

Parameter	Value
Title	JLH-7-166-F-C6F6
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-05-23T22:38:19
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56468.7
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

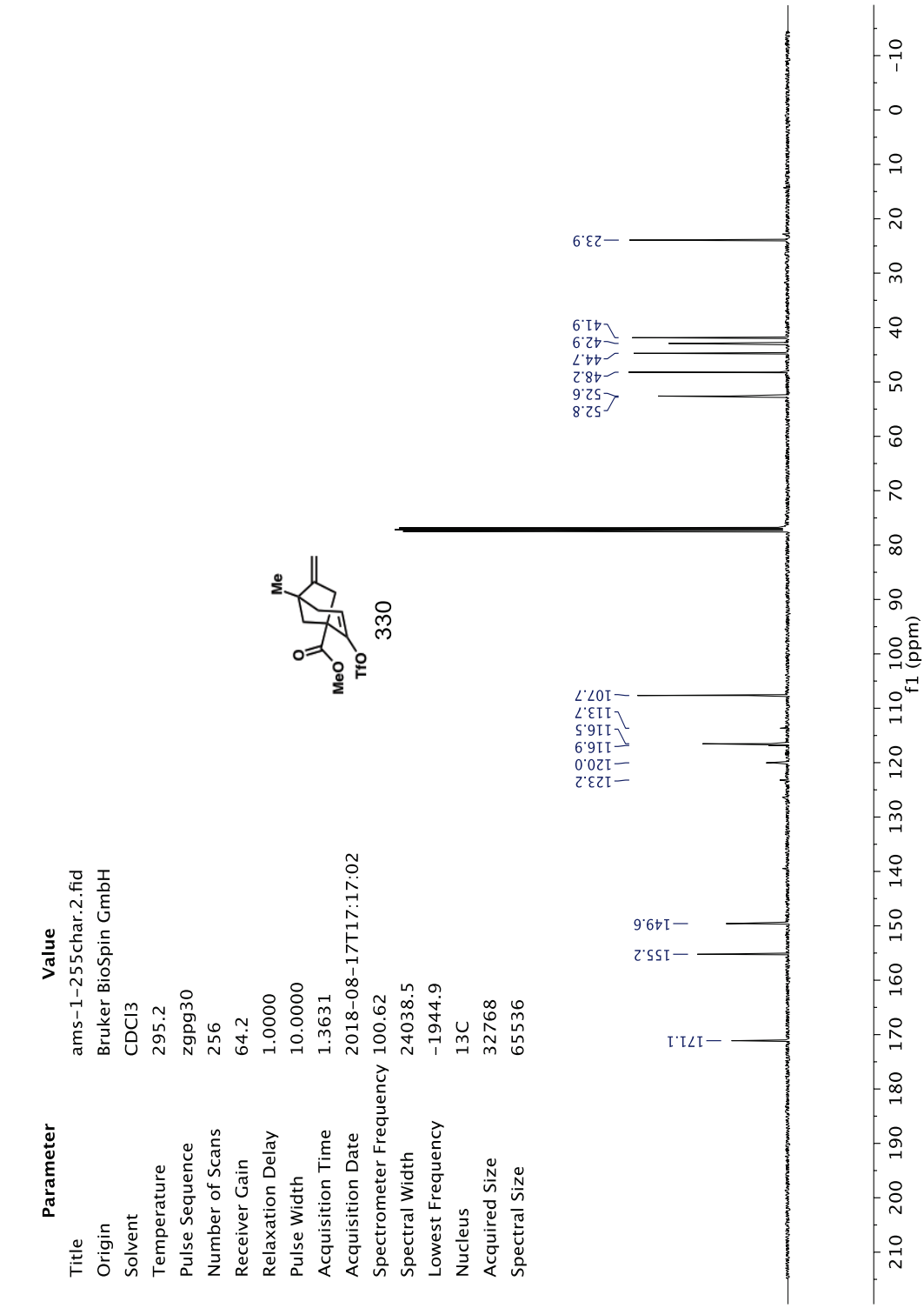
329
with C_6F_6

-73.5

10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)



Parameter	Value
Title	ams-1-255char.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zg30
Number of Scans	16
Receiver Gain	98.9
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-08-17T17:06:10
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1535.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536


Parameter Value
Title ams-1-255char.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zgpg30
Number of Scans 256
Receiver Gain 64.2
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-08-17T17:17:02
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1944.9
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
O
MeO
TfO
330
171.1
155.2
149.6
123.2
120.0
116.9
116.5
113.7
107.7
52.8
52.6
48.2
44.7
42.9
41.9
23.9
f1 (ppm)

Parameter	Value
Title	AMS-1-255-F
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-08-14T01:17:36
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56435.4
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

330

-74.4

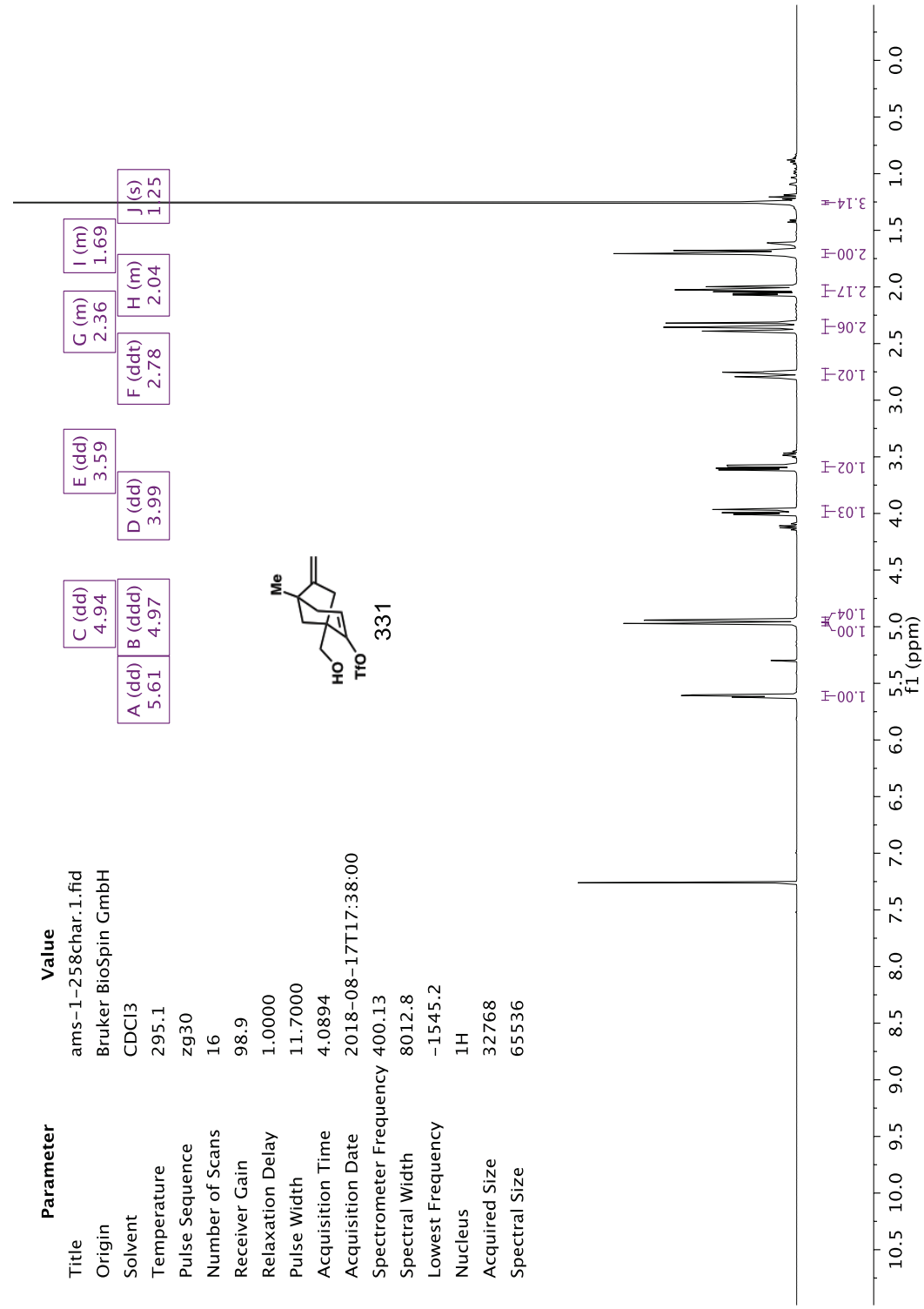
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

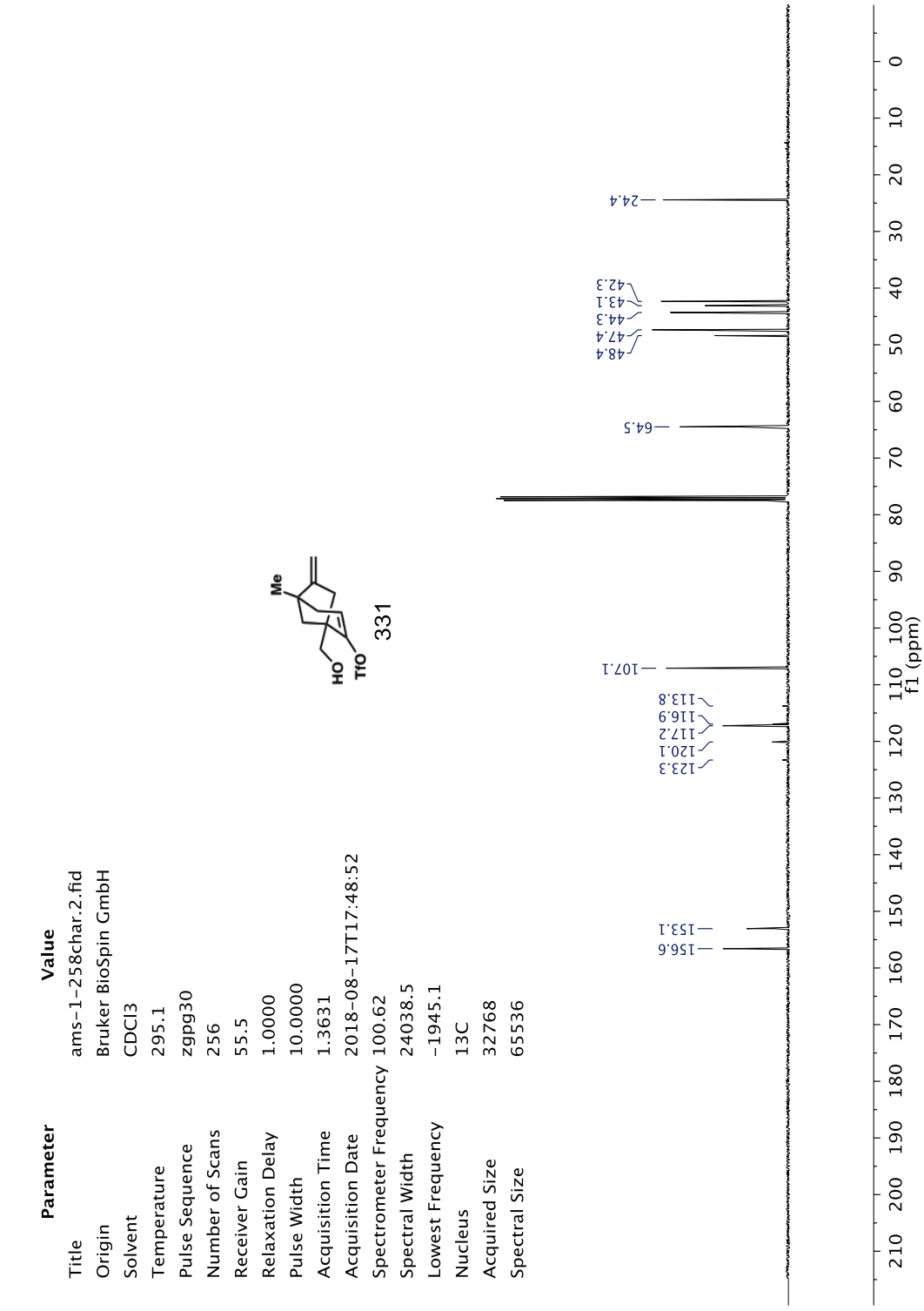
Parameter	Value
Title	AMS-1-255-F-std
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-09-23T19:52:39
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56435.1
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

330
with C_6F_6

-74.4

10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)


Parameter
Value
Title
ams-1-258char.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.1
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
98.9
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-08-17T17:38:00
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1545.2
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
A (dd) 5.61
B (ddd) 4.97
C (dd) 4.94
D (dd) 3.99
E (dd) 3.59
F (ddt) 2.78
G (m) 2.36
H (m) 2.04
I (m) 1.69
J (s) 125
Me
HO
TfO
331
1.00
1.04
1.00
1.03
1.02
1.02
2.06
2.17
2.00
3.14
f1 (ppm)


Parameter
Value
Title ams-1-258char.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zgpg30
Number of Scans 256
Receiver Gain 55.5
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-08-17T17:48:52
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1945.1
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
HO
TfO
331
156.6
153.1
123.3
120.1
117.2
116.9
113.8
107.1
64.5
48.4
47.4
44.3
43.1
42.3
24.4
f1 (ppm)

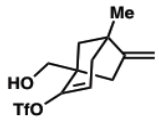
Parameter	Value
Title	AMS-1-258-F
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-08-19T23:06:01
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56444.7
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

331

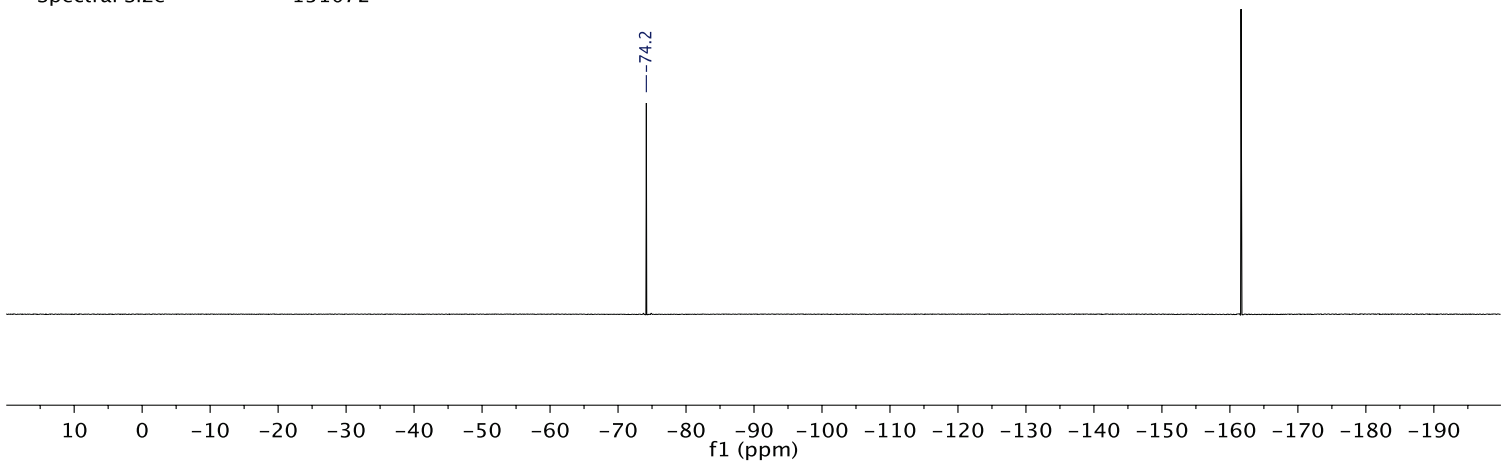
-74.2

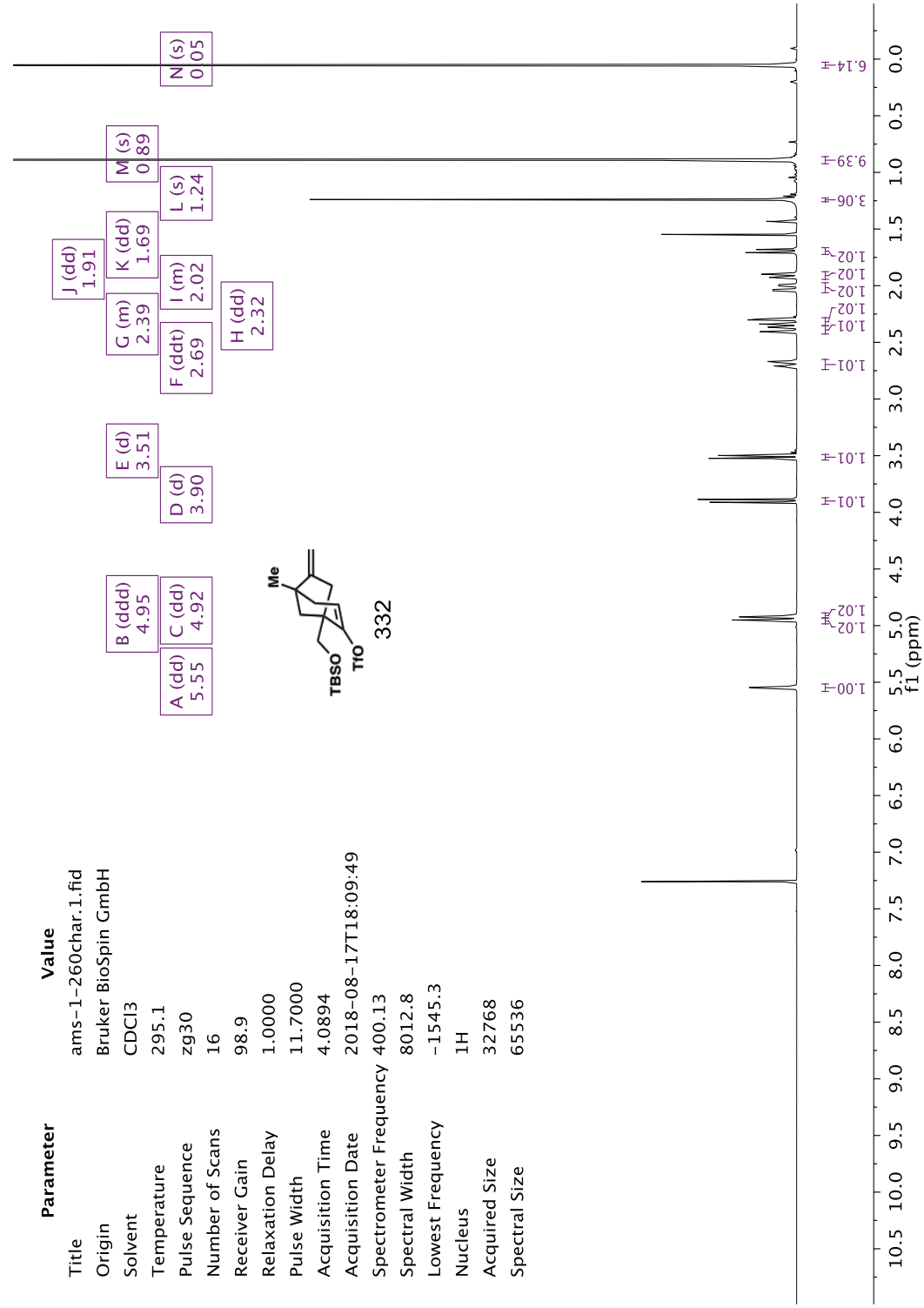
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

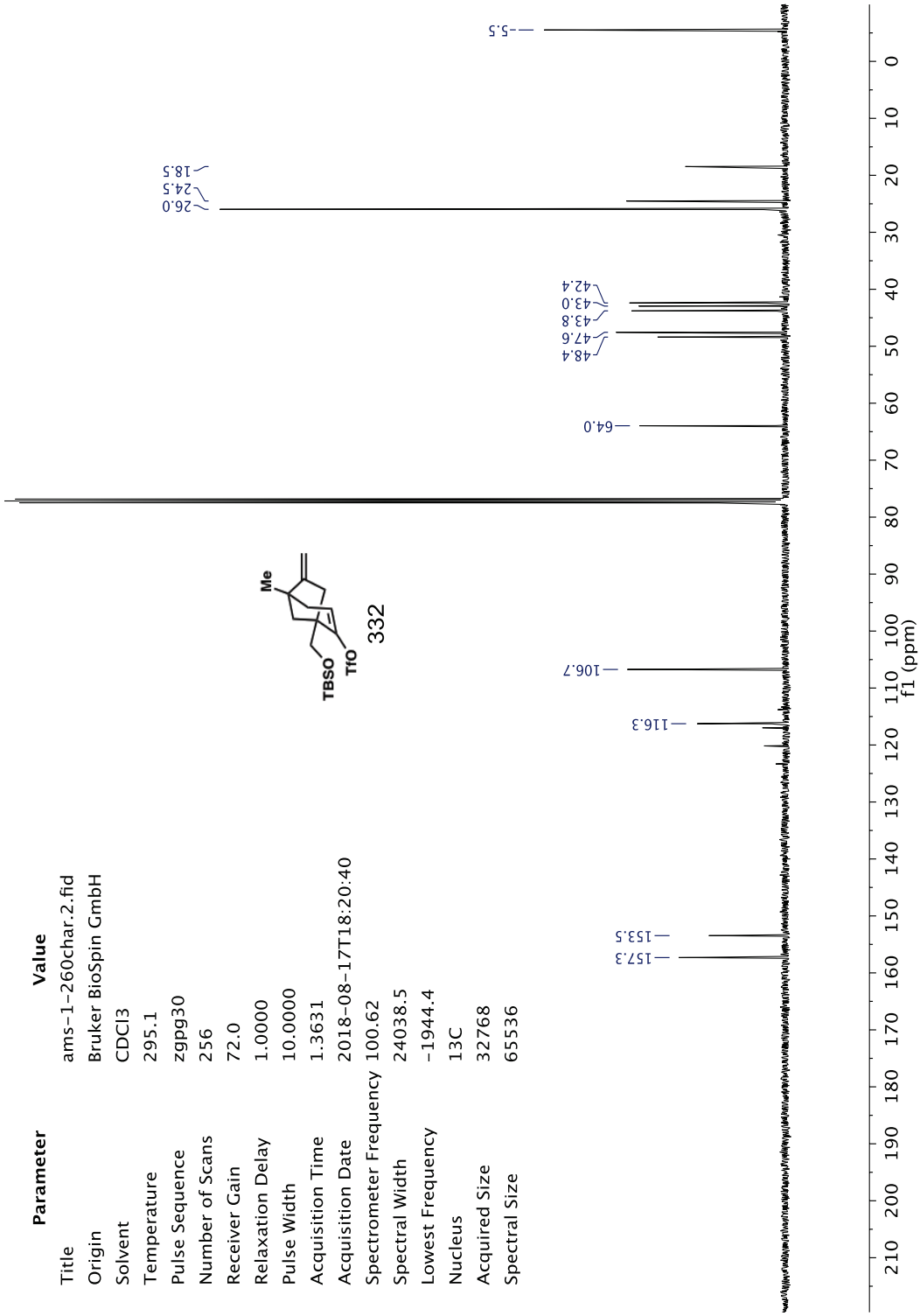
Parameter	Value
Title	AMS-1-258-F-C6F6
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-10-01T14:38:13
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56430.6
Nucleus	19F
Acquired Size	64000
Spectral Size	131072



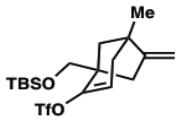
331
with C_6F_6



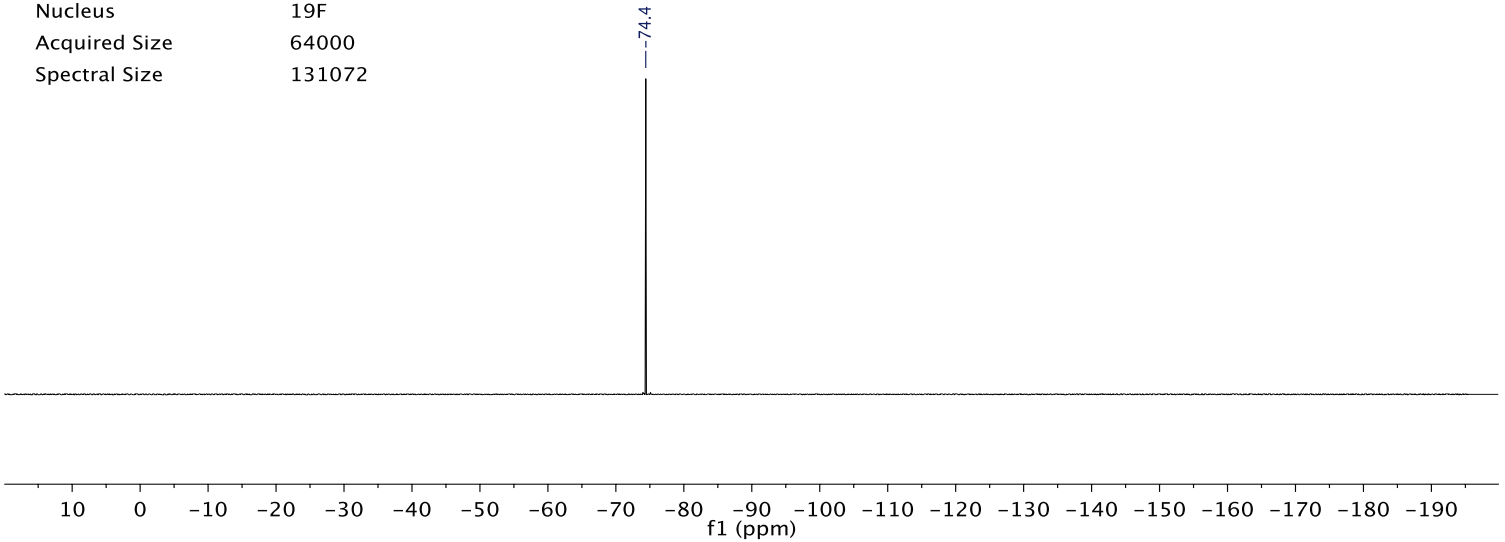

Parameter
Value
Title ams-1-260char.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 98.9
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-08-17T18:09:49
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1545.3
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
A (dd) 5.55
B (ddd) 4.95
C (dd) 4.92
D (d) 3.90
E (d) 3.51
F (ddt) 2.69
G (m) 2.39
H (dd) 2.32
I (m) 2.02
J (dd) 1.91
K (dd) 1.69
L (s) 1.24
M (s) 0.89
N (s) 0.05
Me
TBSO
TfO
332
f1 (ppm)


Parameter Value
Title ams-1-260char.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zgpg30
Number of Scans 256
Receiver Gain 72.0
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-08-17T18:20:40
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1944.4
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
TBSO
TfO
332
157.3
153.5
116.3
106.7
64.0
48.4
47.6
43.8
43.0
42.4
26.0
24.5
18.5
-5.5
f1 (ppm)

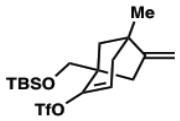
Parameter	Value
Title	AMS-1-260-F
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-08-19T23:14:03
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56449.5
Nucleus	19F
Acquired Size	64000
Spectral Size	131072



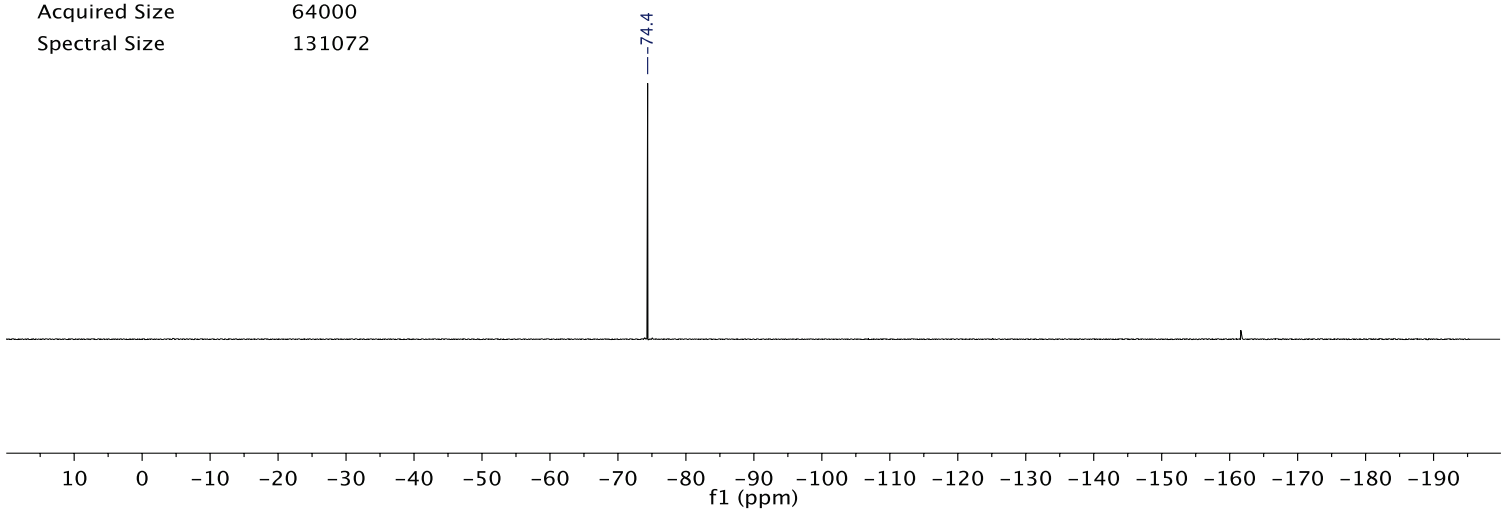
332

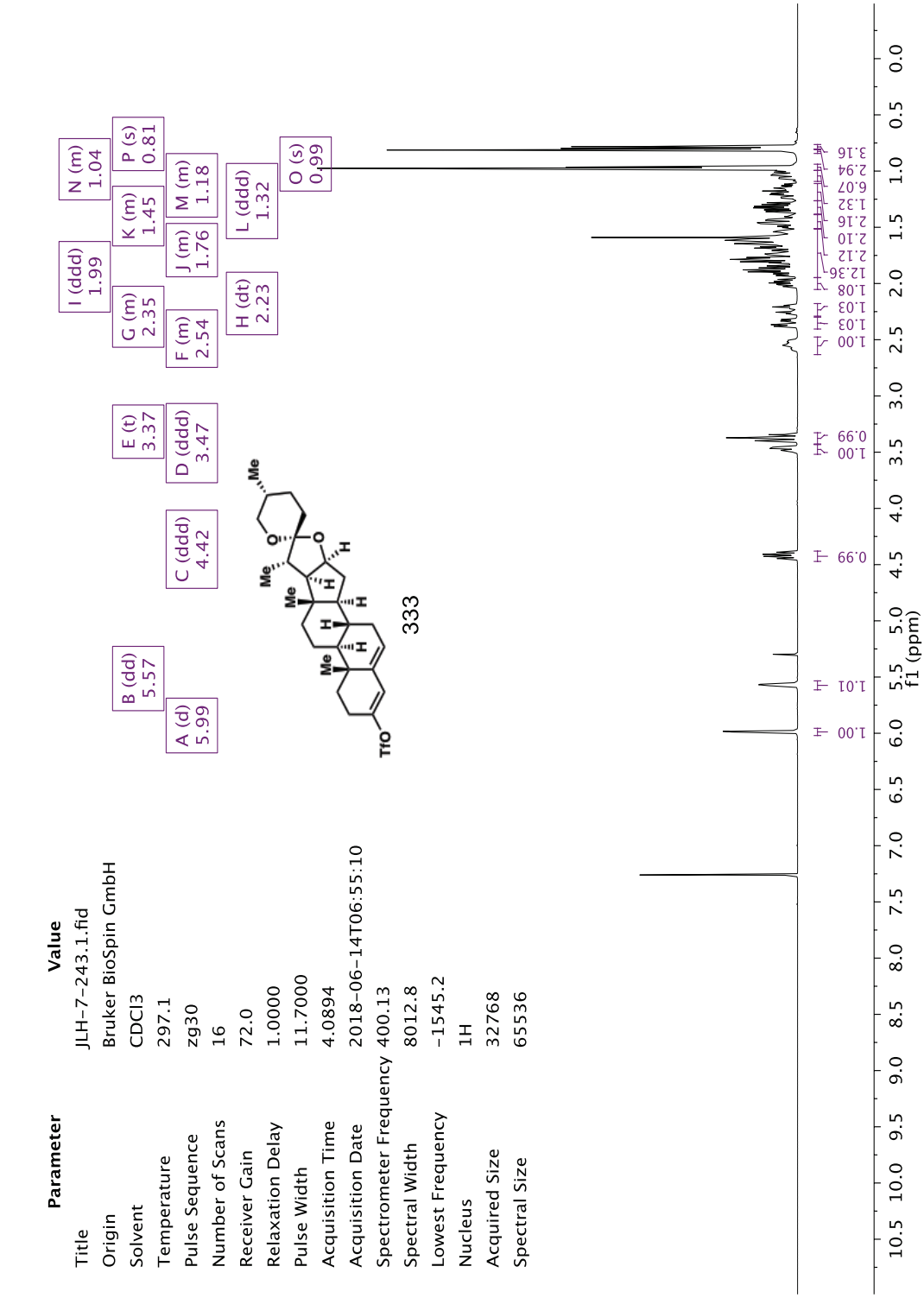


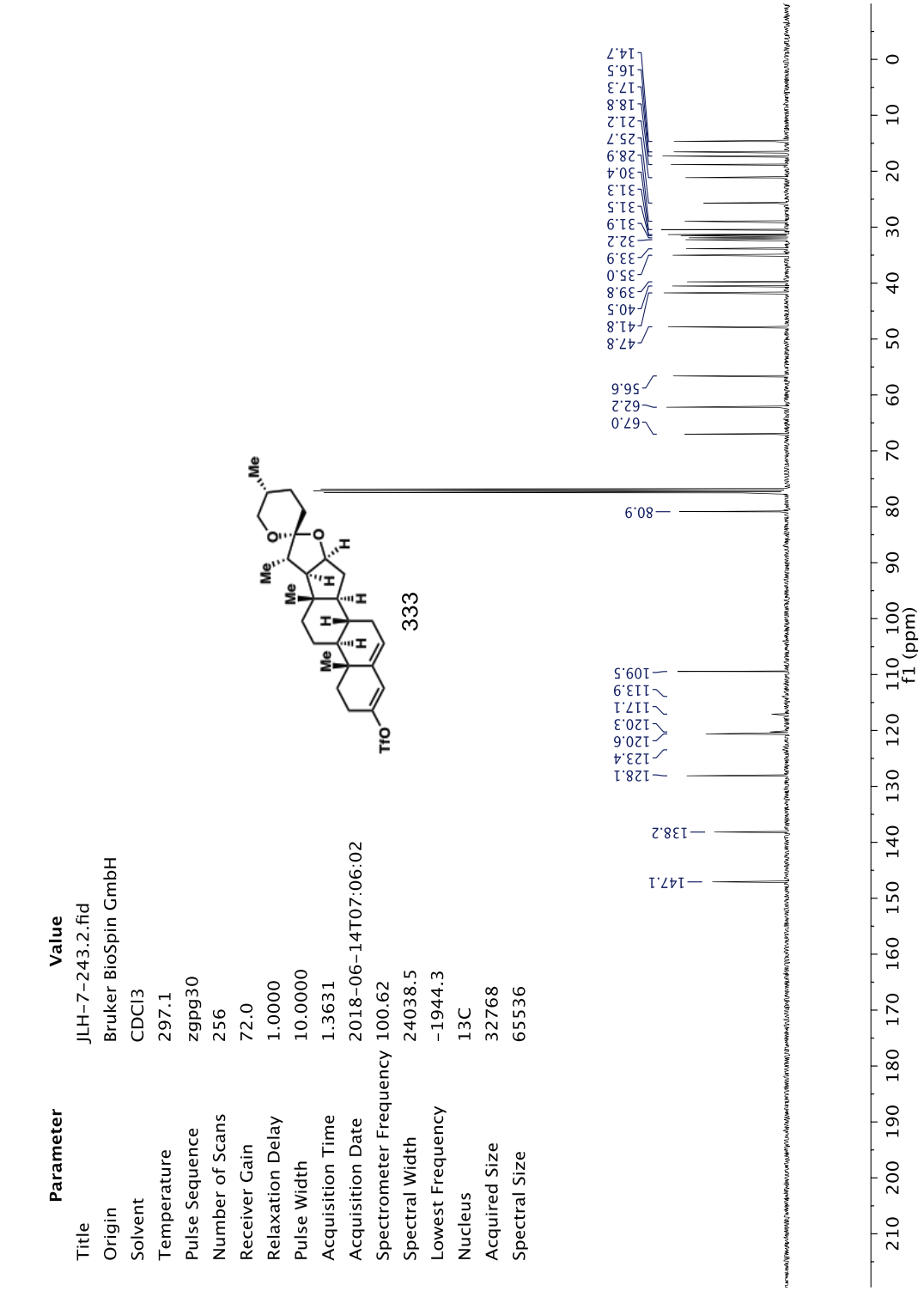
Parameter	Value
Title	AMS-1-260-F-std
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-09-23T20:01:28
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56442.2
Nucleus	19F
Acquired Size	64000
Spectral Size	131072



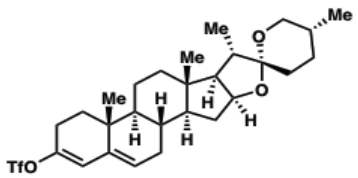
332
with C_6F_6



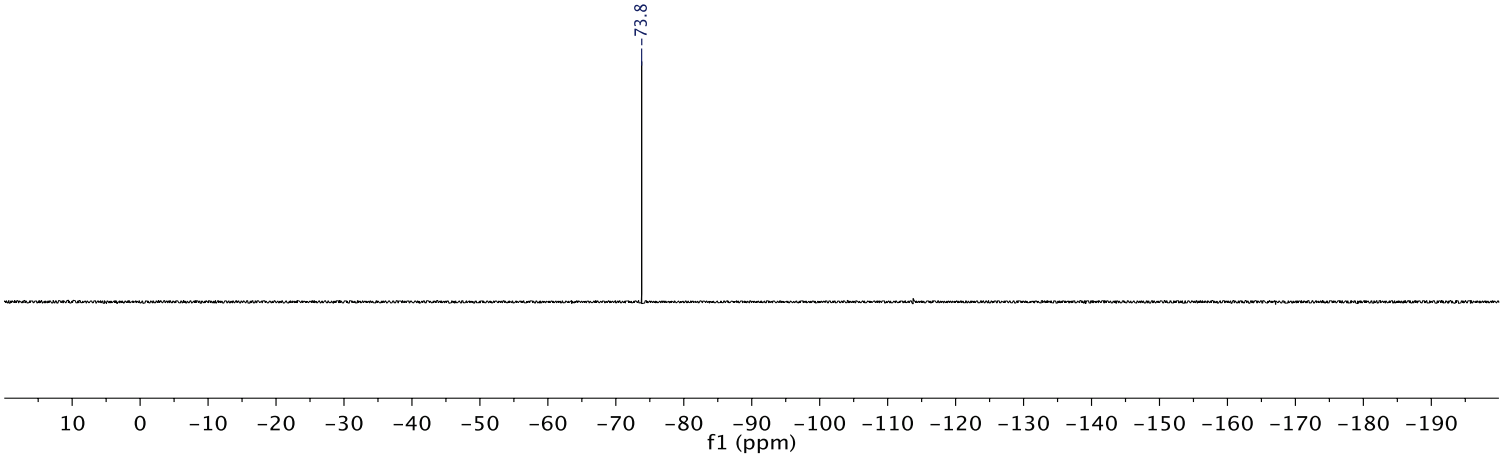

Parameter Value
Title JLH-7-243.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 297.1
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 72.0
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-06-14T06:55:10
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1545.2
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
A (d) 5.99
B (dd) 5.57
C (ddd) 4.42
D (ddd) 3.47
E (t) 3.37
F (m) 2.54
G (m) 2.35
H (dt) 2.23
I (ddd) 1.99
J (m) 1.76
K (m) 1.45
L (ddd) 1.32
M (m) 1.18
N (m) 1.04
O (s) 0.99
P (s) 0.81
333
TfO
f1 (ppm)


Parameter Value
Title JLH-7-243.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 297.1
Pulse Sequence zgpg30
Number of Scans 256
Receiver Gain 72.0
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-06-14T07:06:02
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1944.3
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
O
H
TfO
333
147.1
138.2
128.1
123.4
120.6
120.3
117.1
113.9
109.5
80.9
67.0
62.2
56.6
47.8
41.8
40.5
39.8
35.0
33.9
32.2
31.9
31.5
31.3
30.4
28.9
25.7
21.2
18.8
17.3
16.5
14.7
f1 (ppm)

Parameter	Value
Title	JLH-7-243-F
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-06-14T01:19:18
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56453.2
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

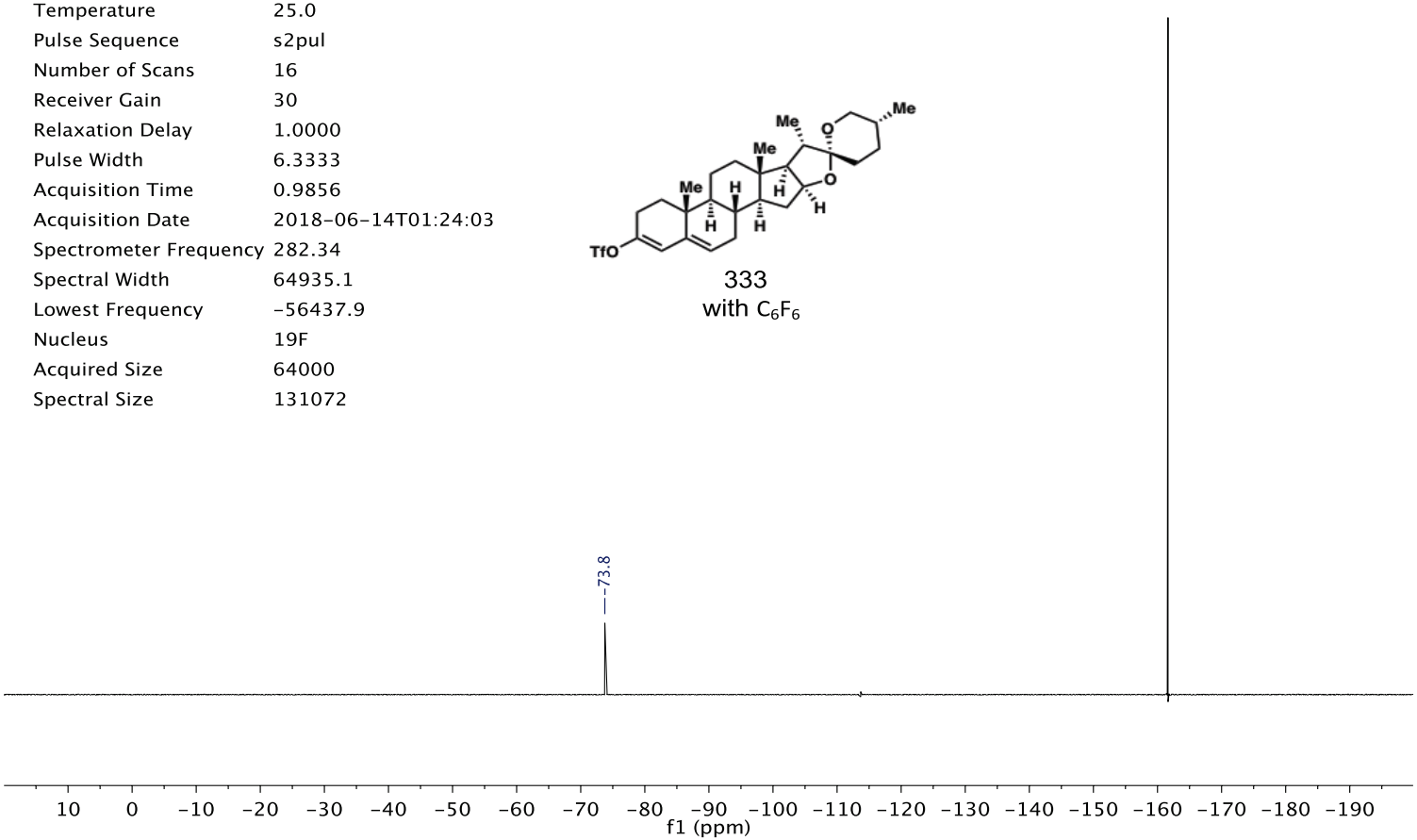


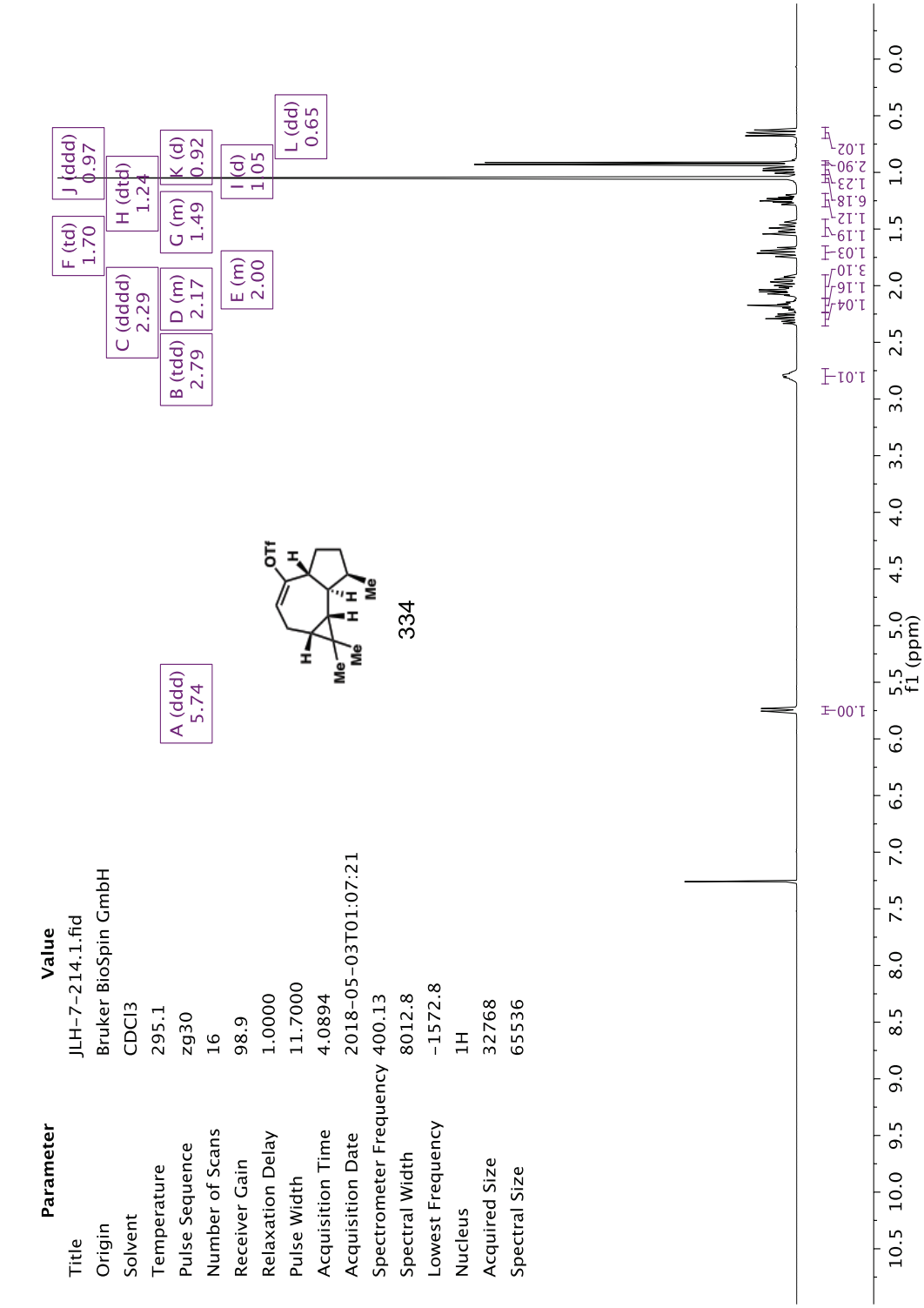
333

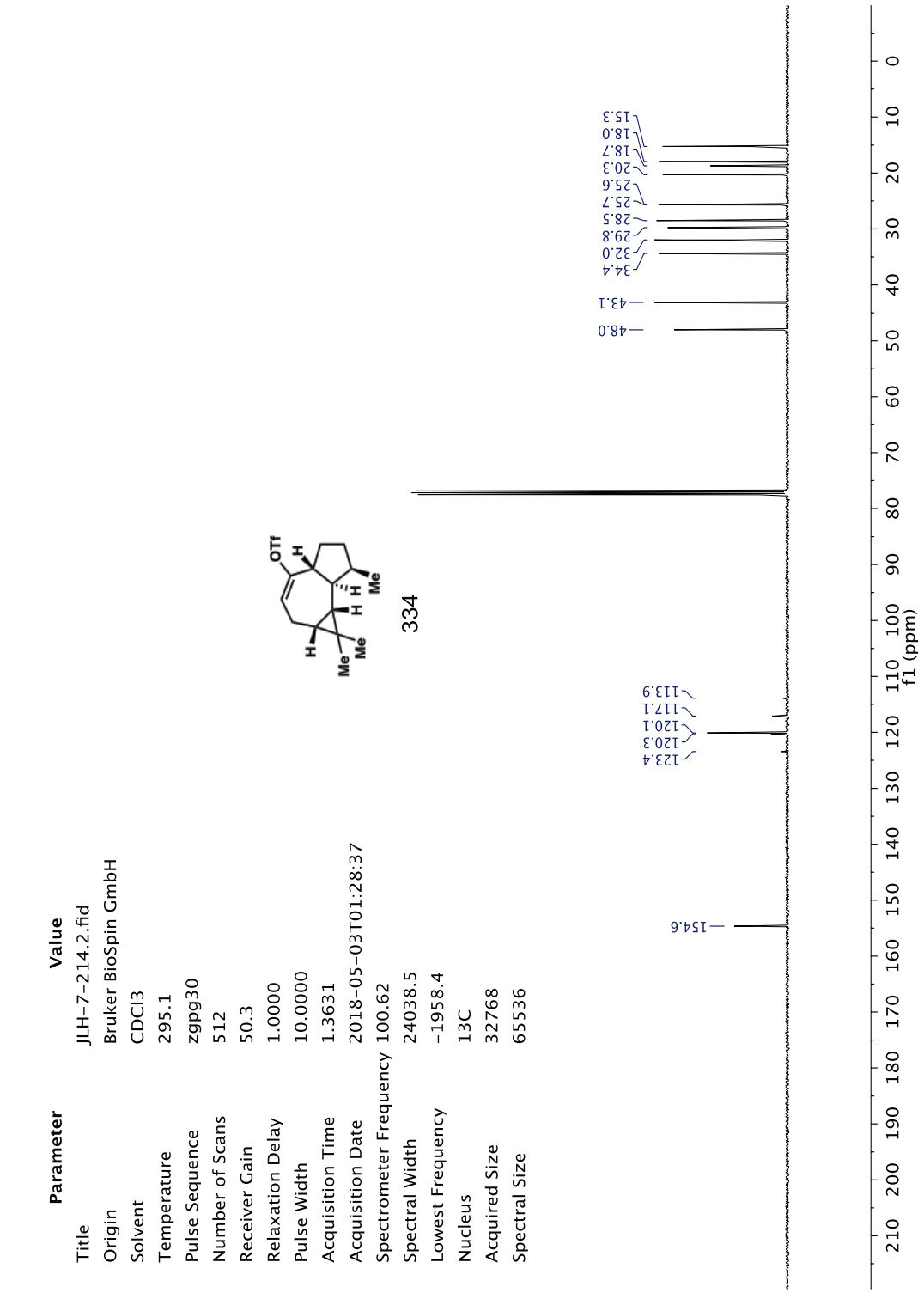


Parameter	Value
Title	JLH-7-243-F-C6F6
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-06-14T01:24:03
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56437.9
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

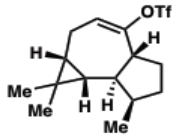
333
with C_6F_6



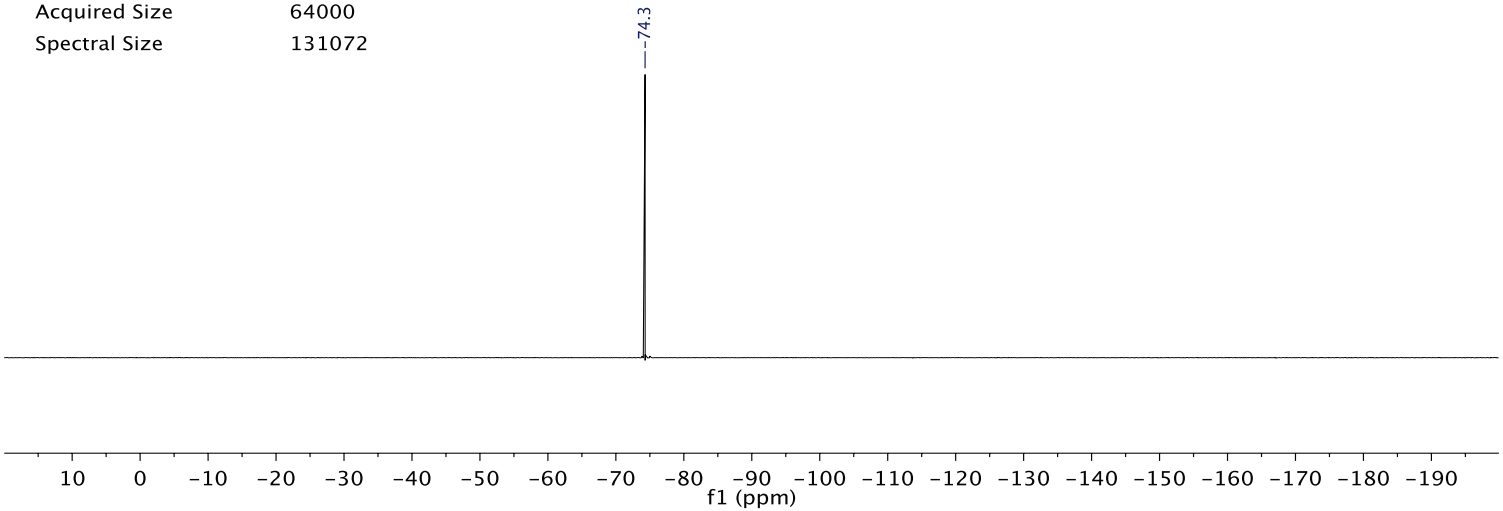

Parameter Value
Title JLH-7-214.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 98.9
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-05-03T01:07:21
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1572.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
A (ddd) 5.74
B (tdd) 2.79
C (dddd) 2.29
D (m) 2.17
E (m) 2.00
F (td) 1.70
G (m) 1.49
H (dtd) 1.24
I (d) 105
J (ddd) 0.97
K (d) 0.92
L (dd) 0.65
OTf
H
Me
Me
H
H
Me
334
1.00
1.01
1.04
1.16
3.10
1.03
1.19
1.12
6.18
1.23
2.90
1.02
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


Parameter Value
Title JLH-7-214.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zgpg30
Number of Scans 512
Receiver Gain 50.3
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-05-03T01:28:37
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1958.4
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OTf
H
Me
Me
Me
H
H
334
154.6
123.4
120.3
120.1
117.1
113.9
48.0
43.1
34.4
32.0
29.8
28.5
25.7
25.6
20.3
18.7
18.0
15.3
f1 (ppm)

Parameter	Value
Title	JLH-7-214-F
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-05-03T23:01:13
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56468.7
Nucleus	19F
Acquired Size	64000
Spectral Size	131072



334

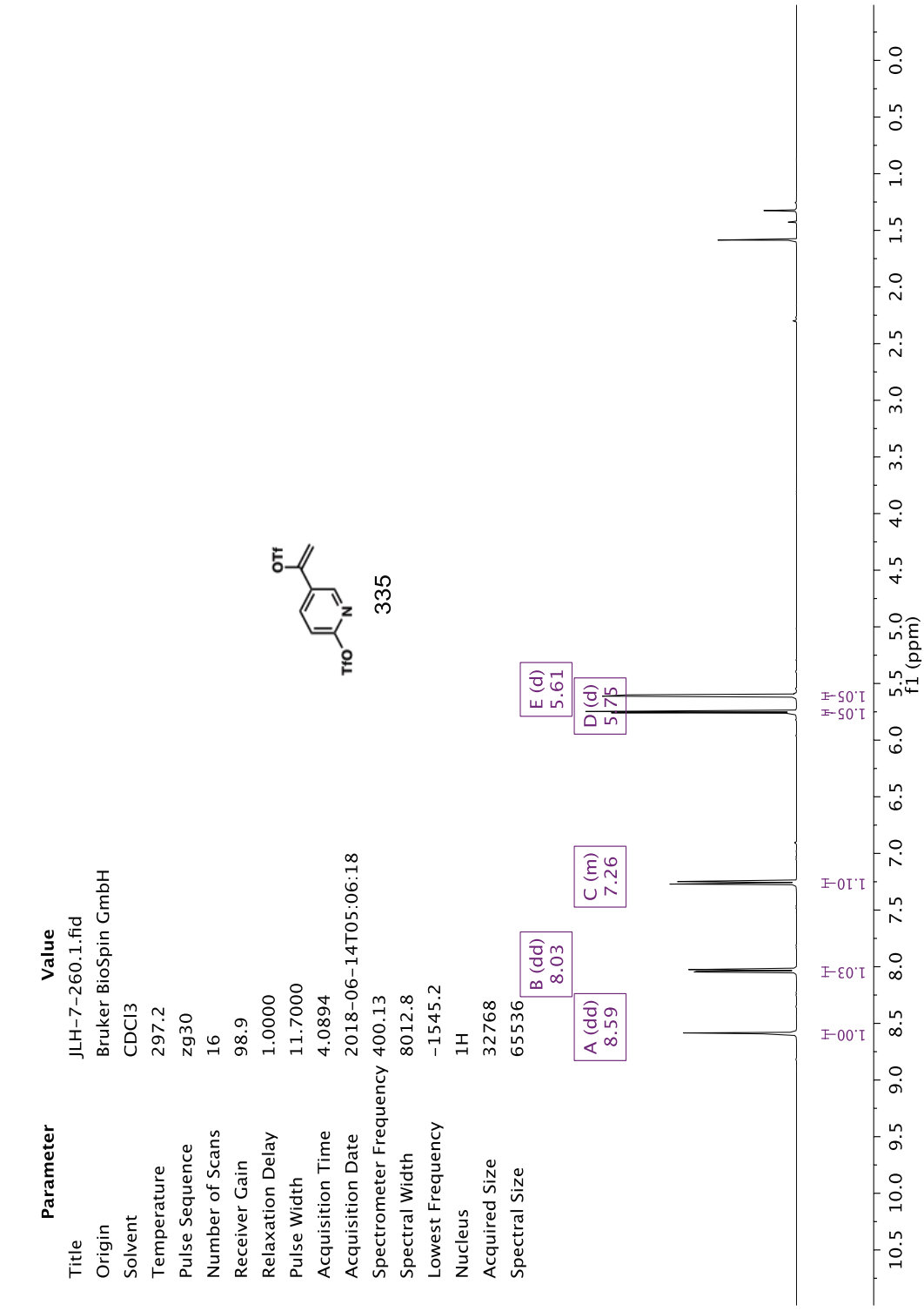


Parameter	Value
Title	JLH-7-214-F-C6F6
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-05-23T22:28:36
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56468.7
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

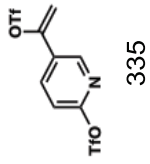
334
with C_6F_6

-74.3

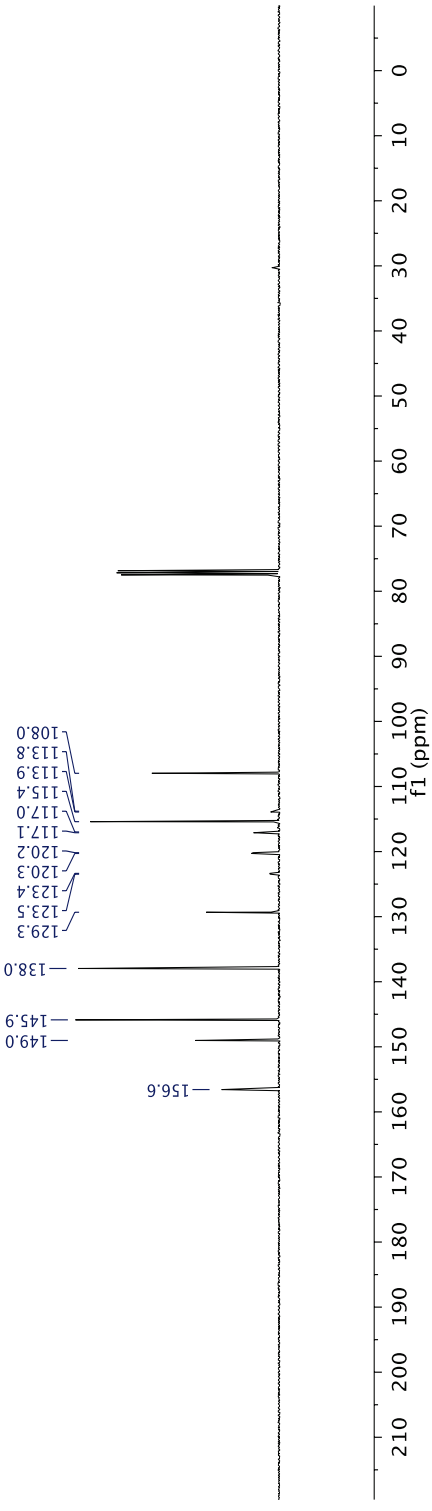
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)


Parameter
Value
Title
JLH-7-260.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
297.2
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
98.9
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-06-14T05:06:18
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1545.2
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
OTf
TfO
N
335
A (dd)
8.59
B (dd)
8.03
C (m)
7.26
D (d)
5.75
E (d)
5.61
1.00
1.03
1.10
1.05
1.05
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

Parameter	Value
Title	JLH-7-260.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	297.1
Pulse Sequence	zgpg30
Number of Scans	256
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-06-14T05:17:10
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1958.4
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

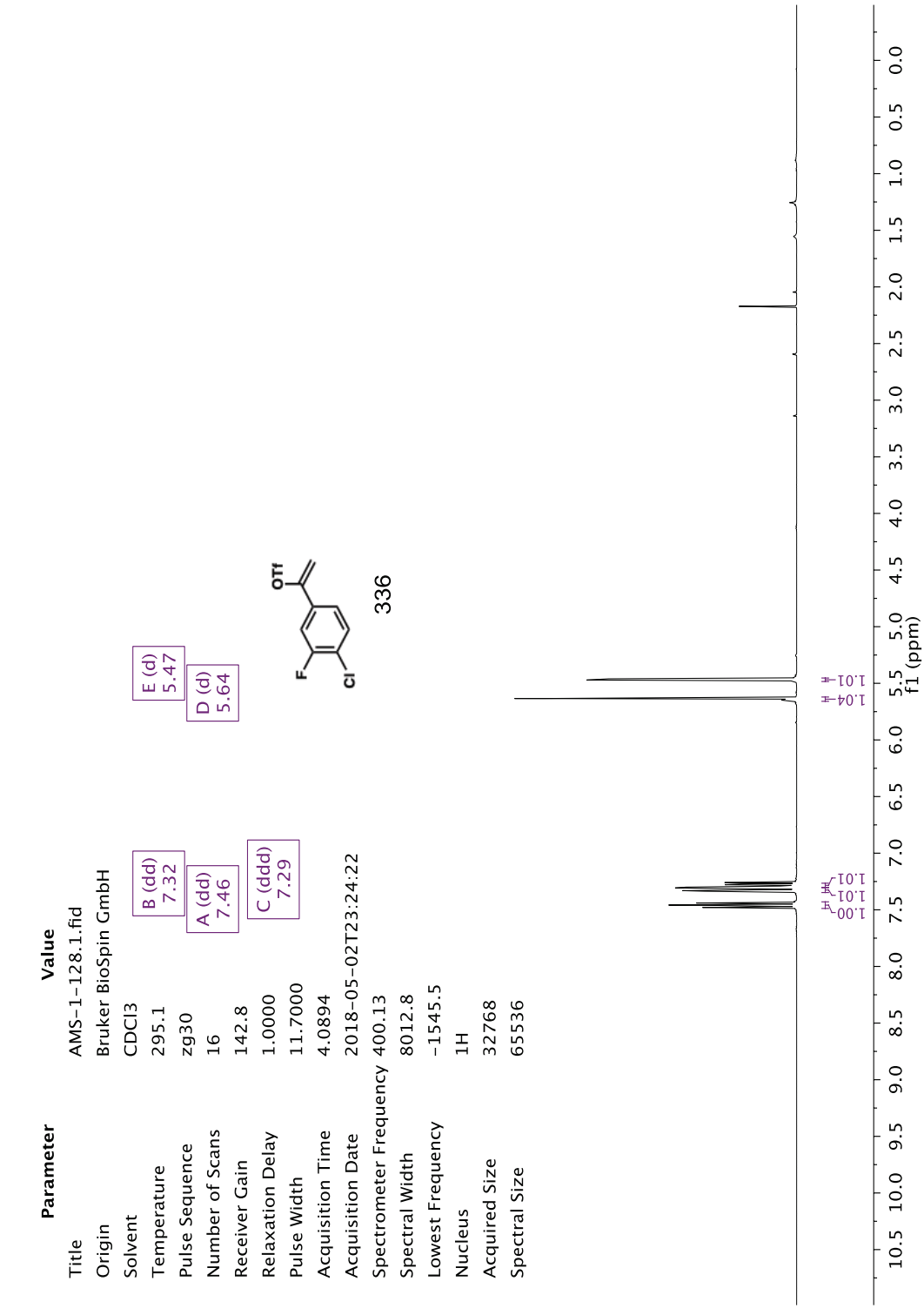


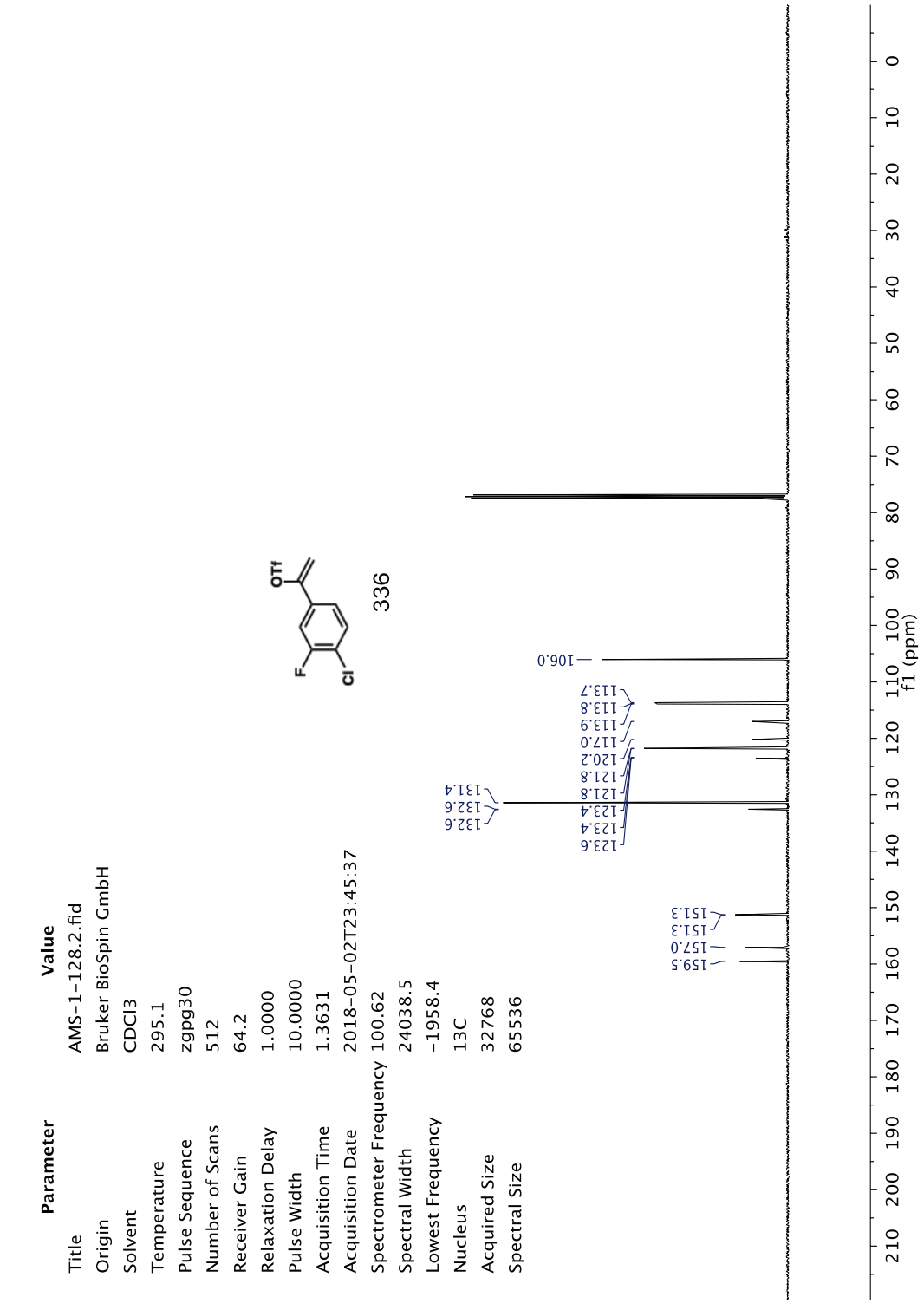
335



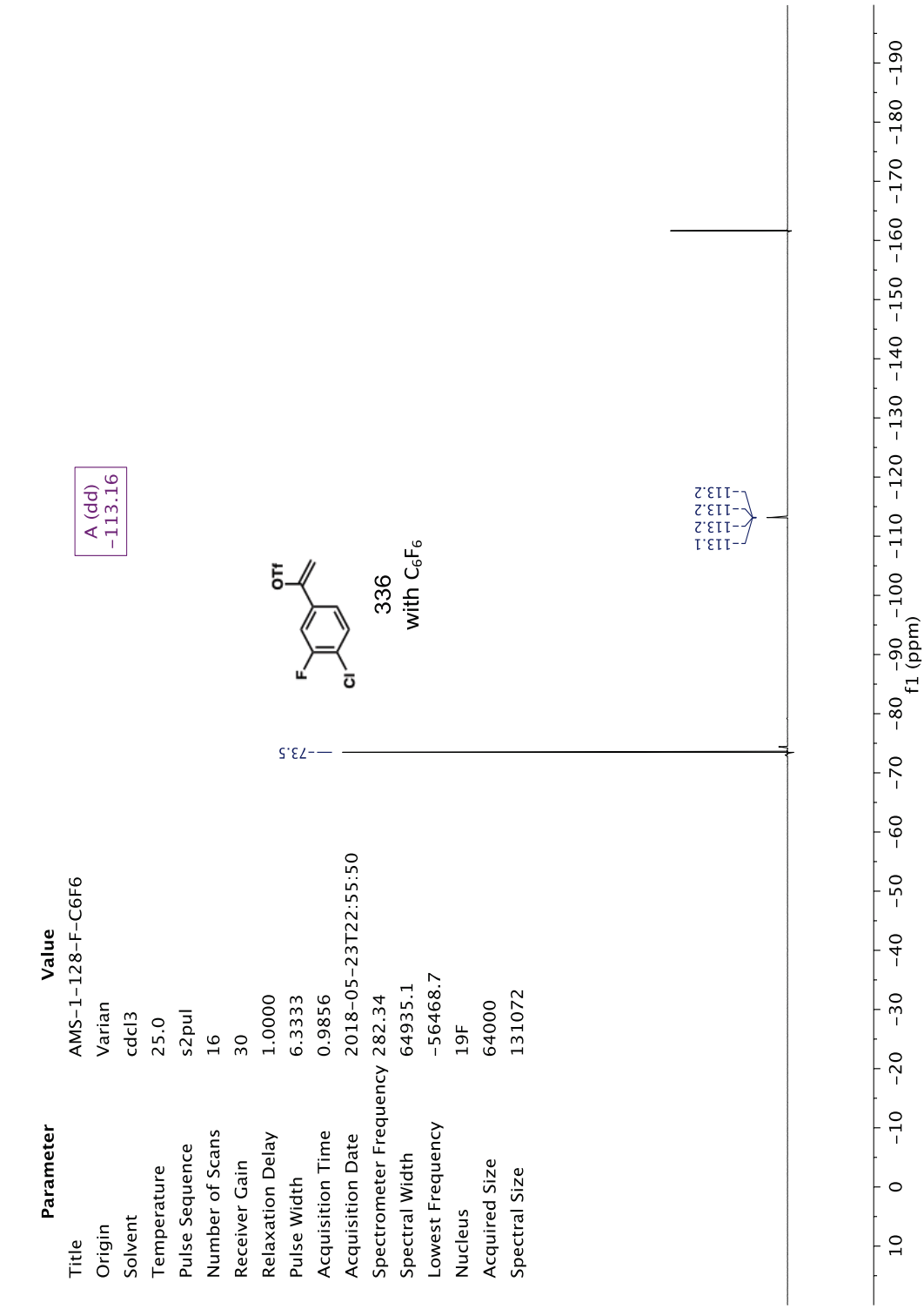
Parameter	Value
Title	JLH-7-260-F
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-06-14T01:00:14
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56431.2
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

Parameter Value
Title JLH-7-260-F-C6F6
Origin Varian
Solvent cdcl3
Temperature 25.0
Pulse Sequence s2pul
Number of Scans 16
Receiver Gain 30
Relaxation Delay 1.0000
Pulse Width 6.3333
Acquisition Time 0.9856
Acquisition Date 2018-06-14T01:04:23
Spectrometer Frequency 282.34
Spectral Width 64935.1
Lowest Frequency -56432.6
Nucleus 19F
Acquired Size 64000
Spectral Size 131072
OTf
TfO
N
335
with C_6F_6
-72.8
-73.3
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

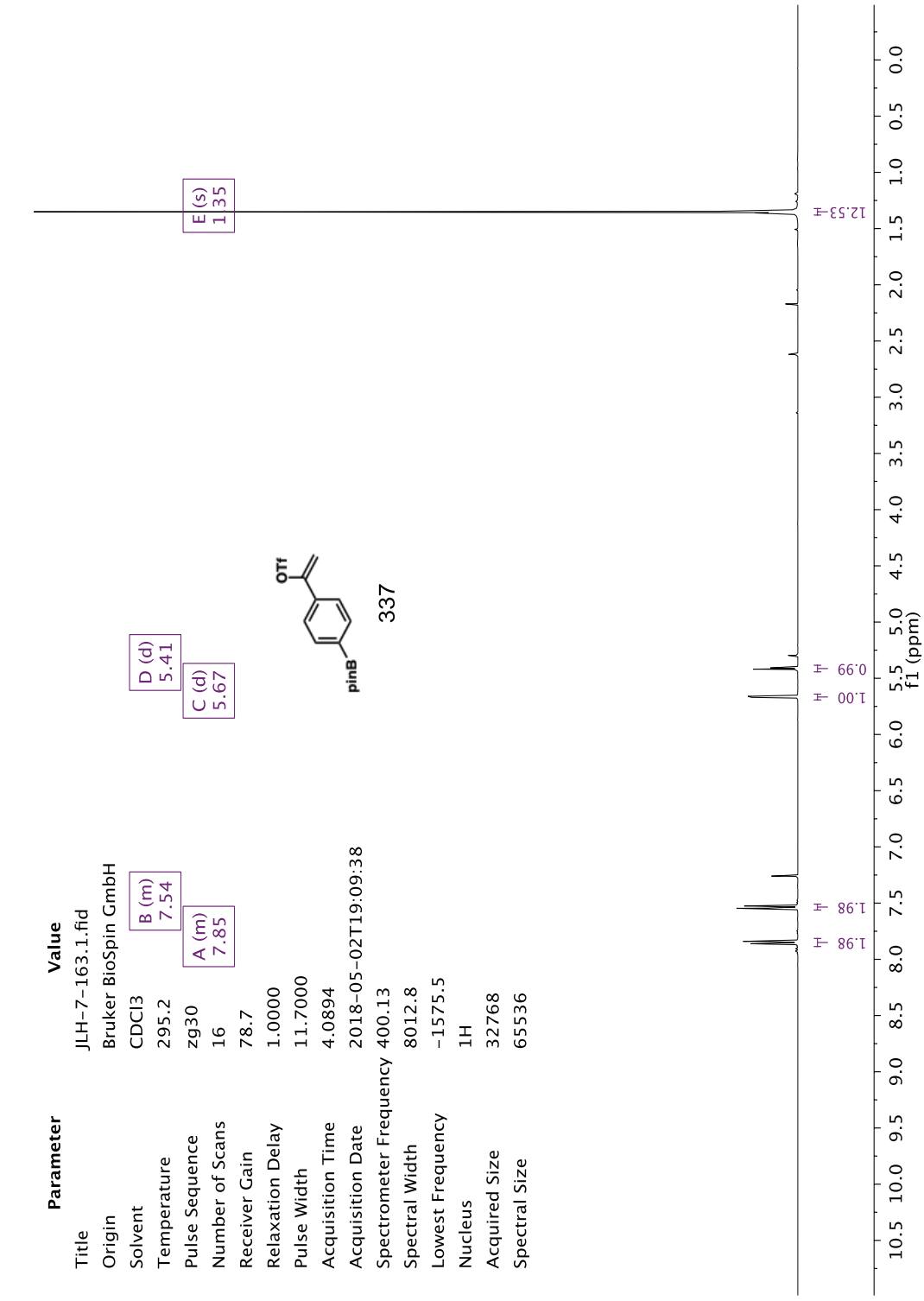

Parameter
Value
Title
AMS-1-128.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.1
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
142.8
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-05-02T23:24:22
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1545.5
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
B (dd) 7.32
A (dd) 7.46
C (ddd) 7.29
E (d) 5.47
D (d) 5.64
OTf
F
Cl
336
1.00
1.01
1.01
1.01
1.04
f1 (ppm)

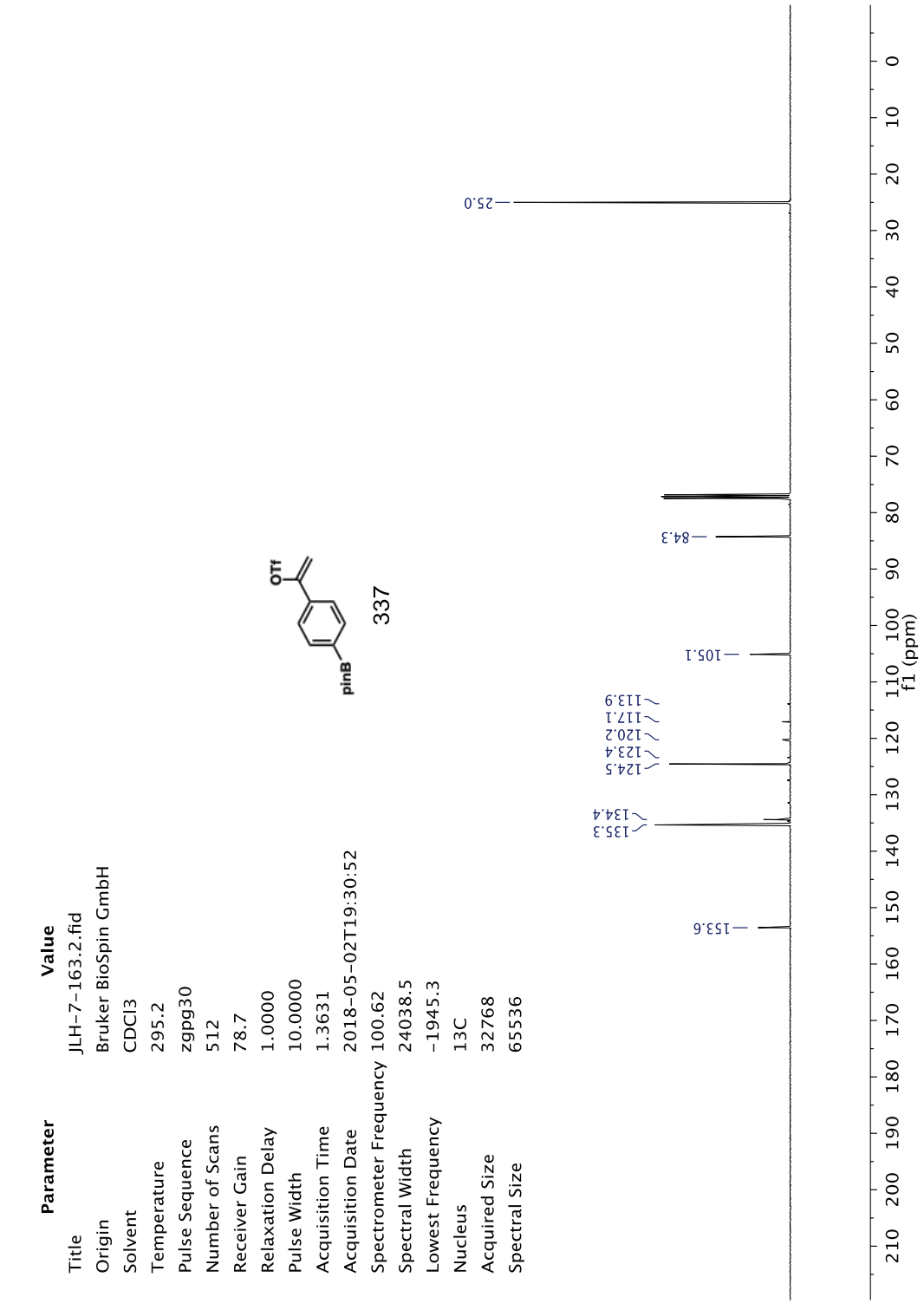

Parameter Value
Title AMS-1-128.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zgpg30
Number of Scans 512
Receiver Gain 64.2
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-05-02T23:45:37
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1958.4
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OTf
F
Cl
336
159.5
157.0
151.3
151.3
132.6
132.6
131.4
123.6
123.4
121.8
121.8
120.2
117.0
113.9
113.8
113.7
106.0
f1 (ppm)

Parameter Value
Title AMS-1-128-F
Origin Varian
Solvent cdcl3
Temperature 25.0
Pulse Sequence s2pul
Number of Scans 16
Receiver Gain 30
Relaxation Delay 1.0000
Pulse Width 6.3333
Acquisition Time 0.9856
Acquisition Date 2018-05-03T23:14:36
Spectrometer Frequency 282.34
Spectral Width 64935.1
Lowest Frequency -56468.7
Nucleus 19F
Acquired Size 64000
Spectral Size 131072
A (dd)
-113.16
OTf
F
Cl
336
-73.5
-113.1
-113.2
-113.2
-113.2
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)



Parameter	Value
Title	AMS-1-128-F-C6F6
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-05-23T22:55:50
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56468.7
Nucleus	19F
Acquired Size	64000
Spectral Size	131072


Parameter
Value
Title
JLH-7-163.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
78.7
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-05-02T19:09:38
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1575.5
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
A (m) 7.85
B (m) 7.54
C (d) 5.67
D (d) 5.41
E (s) 1.35
OTf
pinB
337
12.53
1.98
1.98
1.00
0.99
f1 (ppm)


Parameter Value
Title JLH-7-163.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zgpg30
Number of Scans 512
Receiver Gain 78.7
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-05-02T19:30:52
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1945.3
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OTf
pinB
337
153.6
135.3
134.4
124.5
123.4
120.2
117.1
113.9
105.1
84.3
25.0
f1 (ppm)

Parameter	Value
Title	JLH-7-163-F
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-05-03T23:10:20
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56468.7
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

337

-73.7

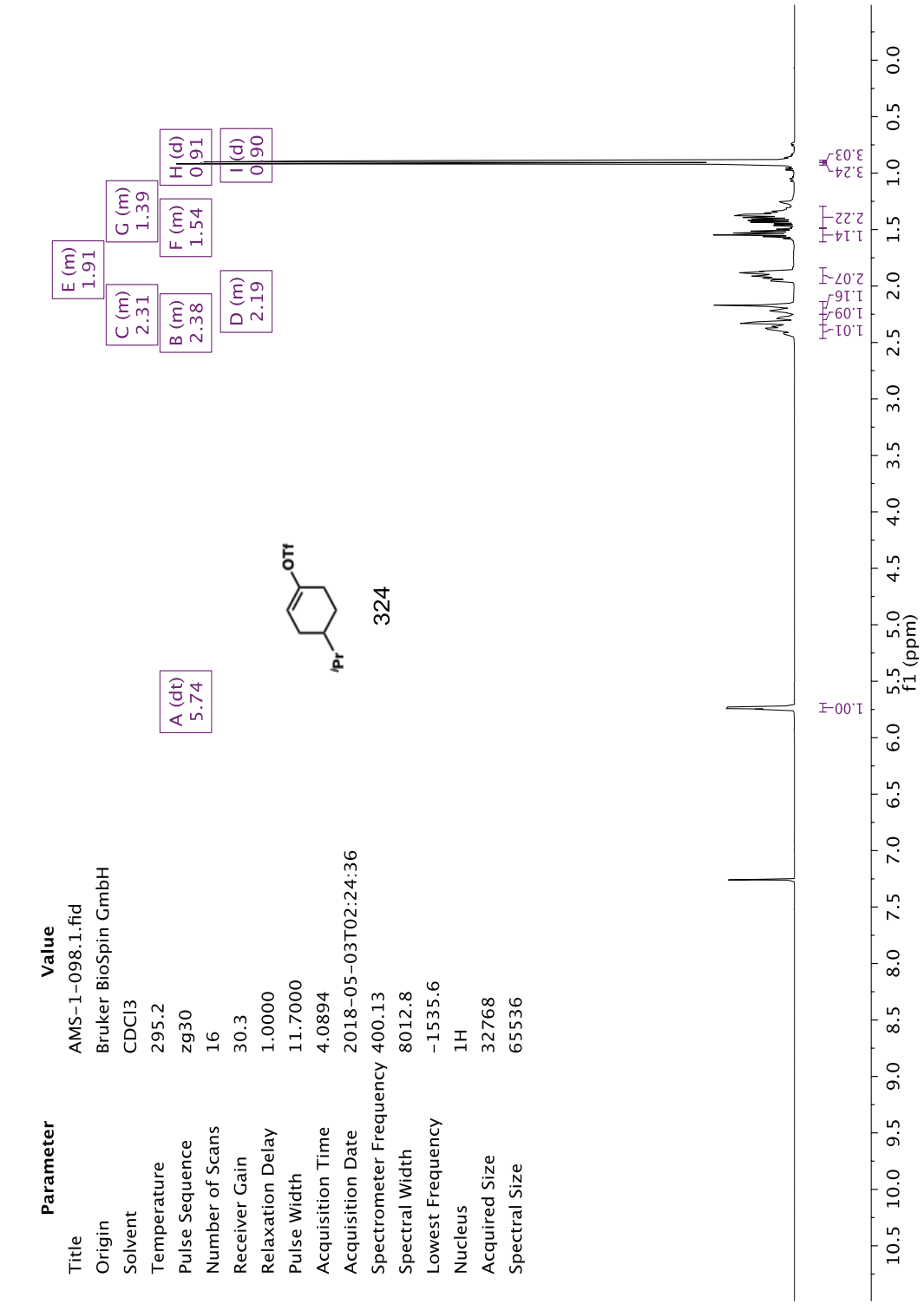
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

Parameter	Value
Title	JLH-7-163-F-C6F6
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-05-23T22:23:44
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56434.5
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

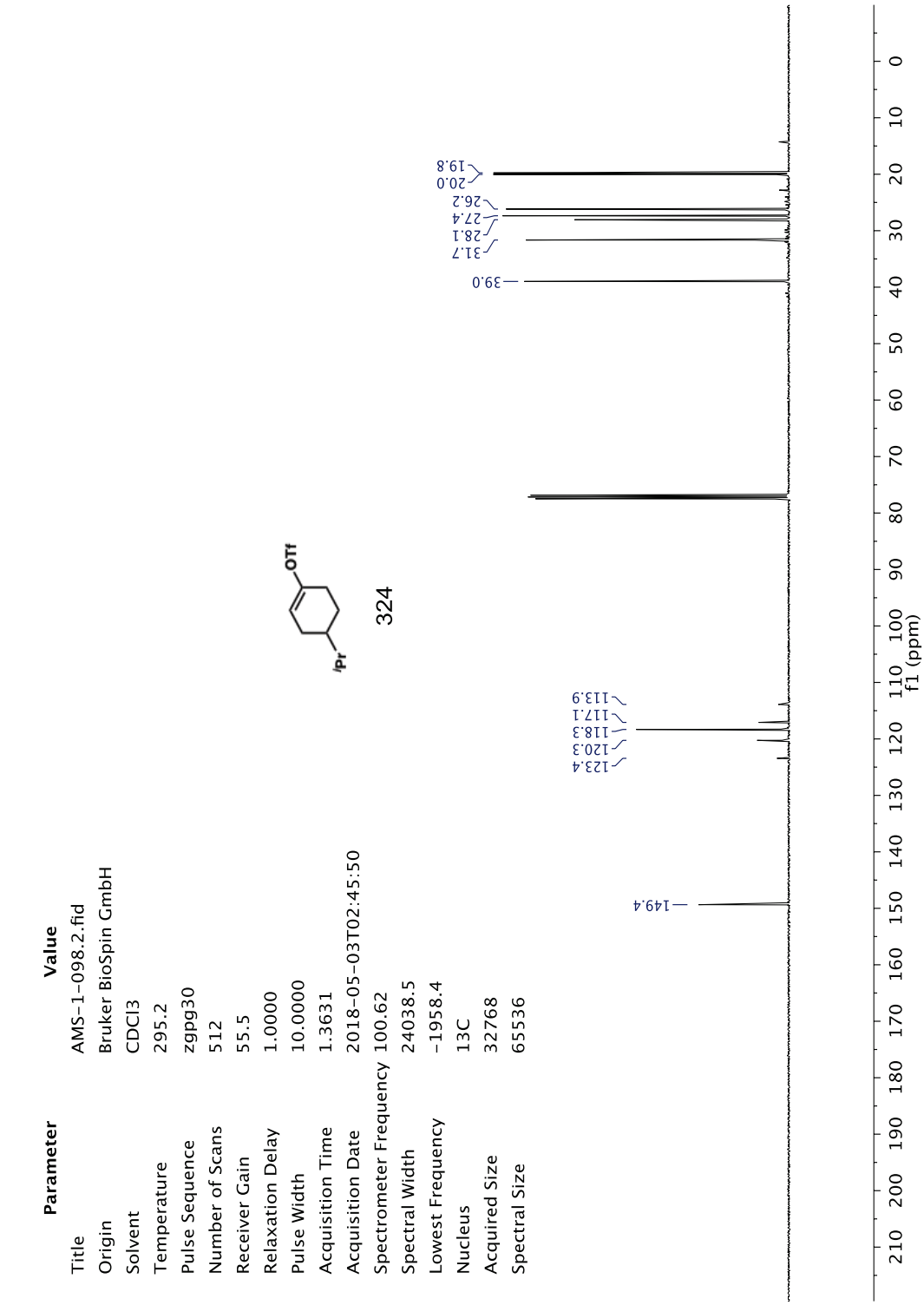
337
with C_6F_6

-73.7

10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)



Parameter	Value
Title	AMS-1-098.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zg30
Number of Scans	16
Receiver Gain	30.3
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-05-03T02:24:36
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1535.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536


Parameter Value
Title AMS-1-098.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zgpg30
Number of Scans 512
Receiver Gain 55.5
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-05-03T02:45:50
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1958.4
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
OTf
iPr
324
149.4
123.4
120.3
118.3
117.1
113.9
39.0
31.7
28.1
27.4
26.2
20.0
19.8
f1 (ppm)

Parameter	Value
Title	AMS-1-098-F
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-05-03T22:47:15
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56468.7
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

324

-73.9

10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

Parameter	Value
Title	AMS-1-098-F-C6F6
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-05-23T22:46:47
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56468.7
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

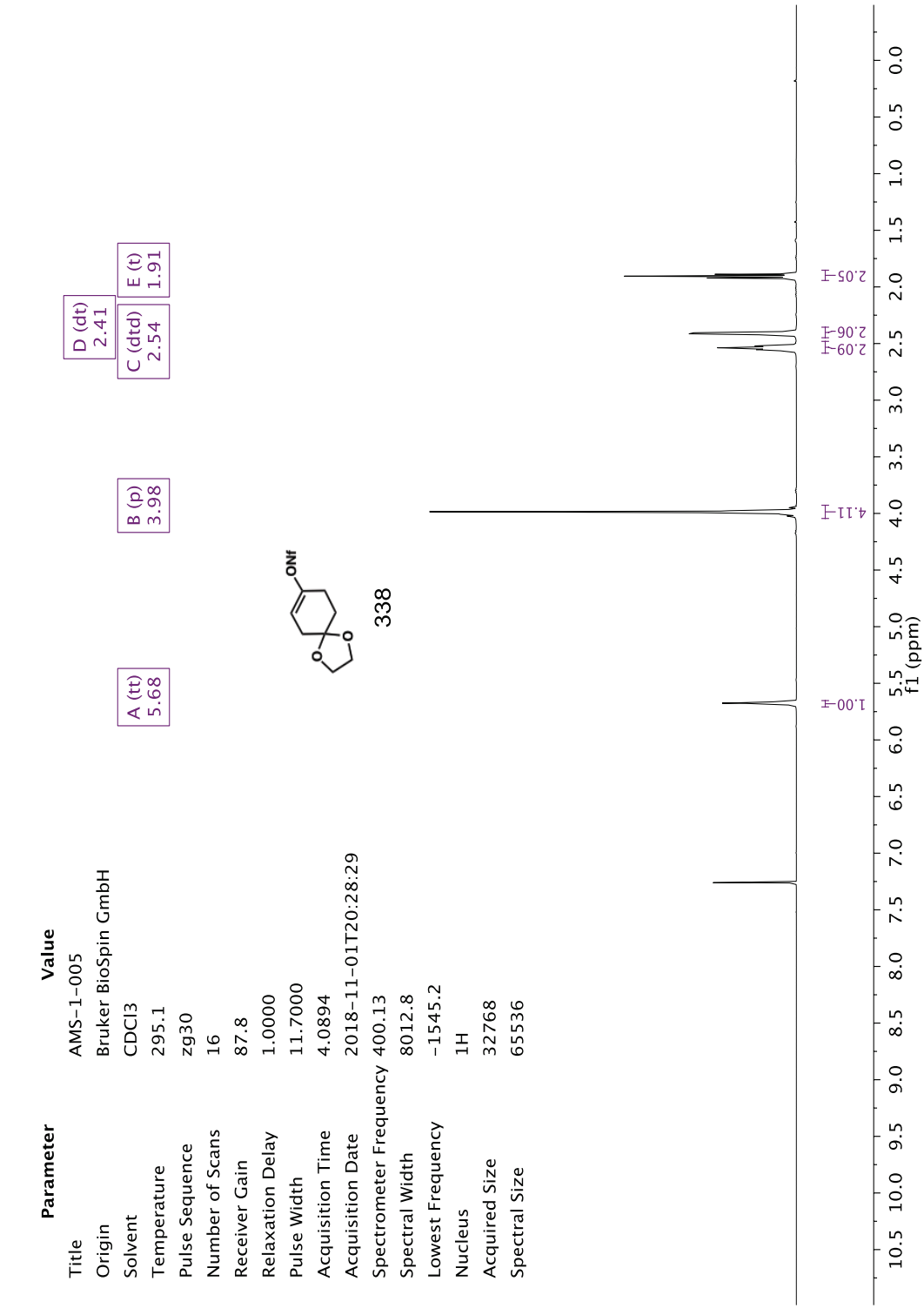
324

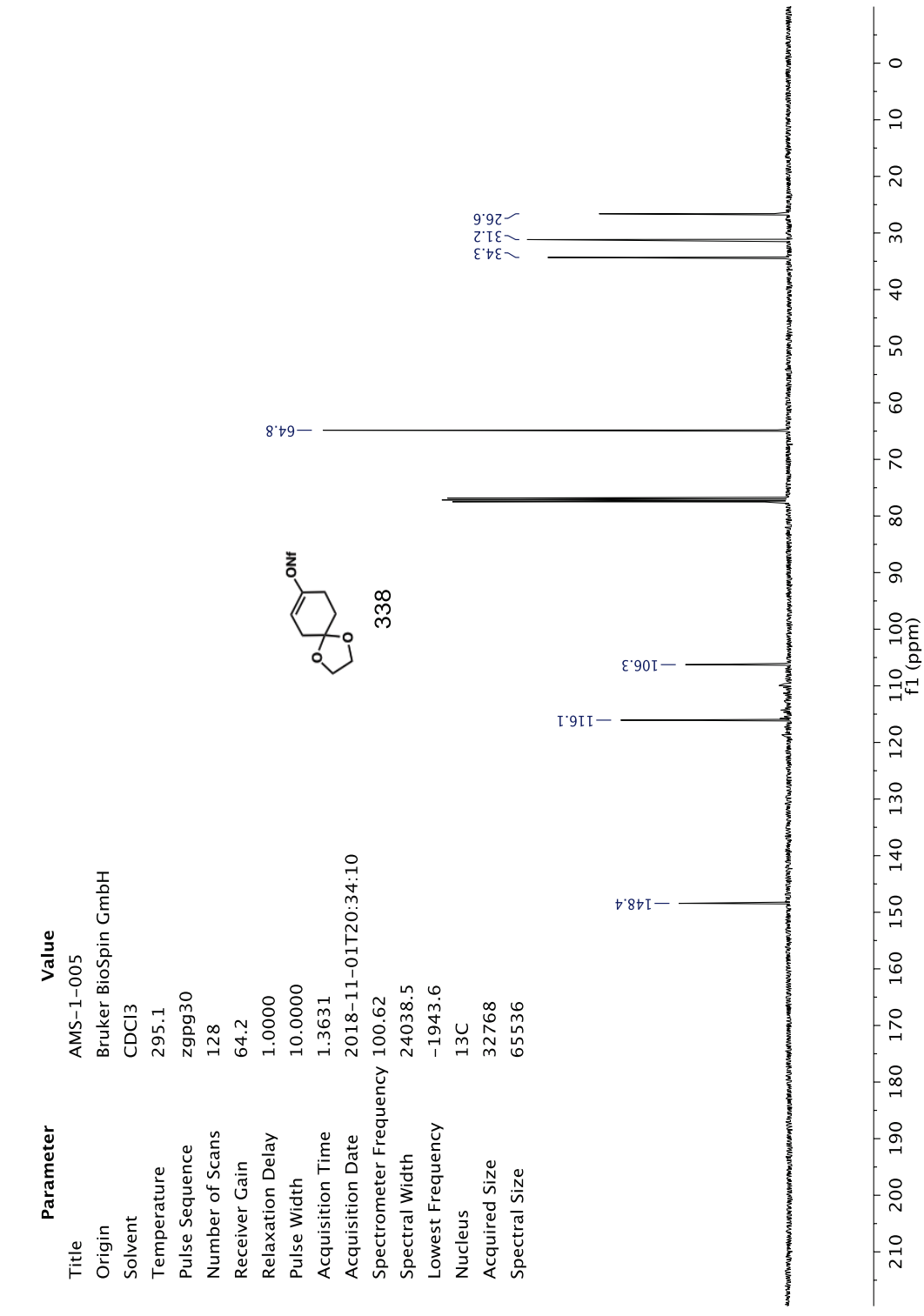
with C_6F_6

-73.9

10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190

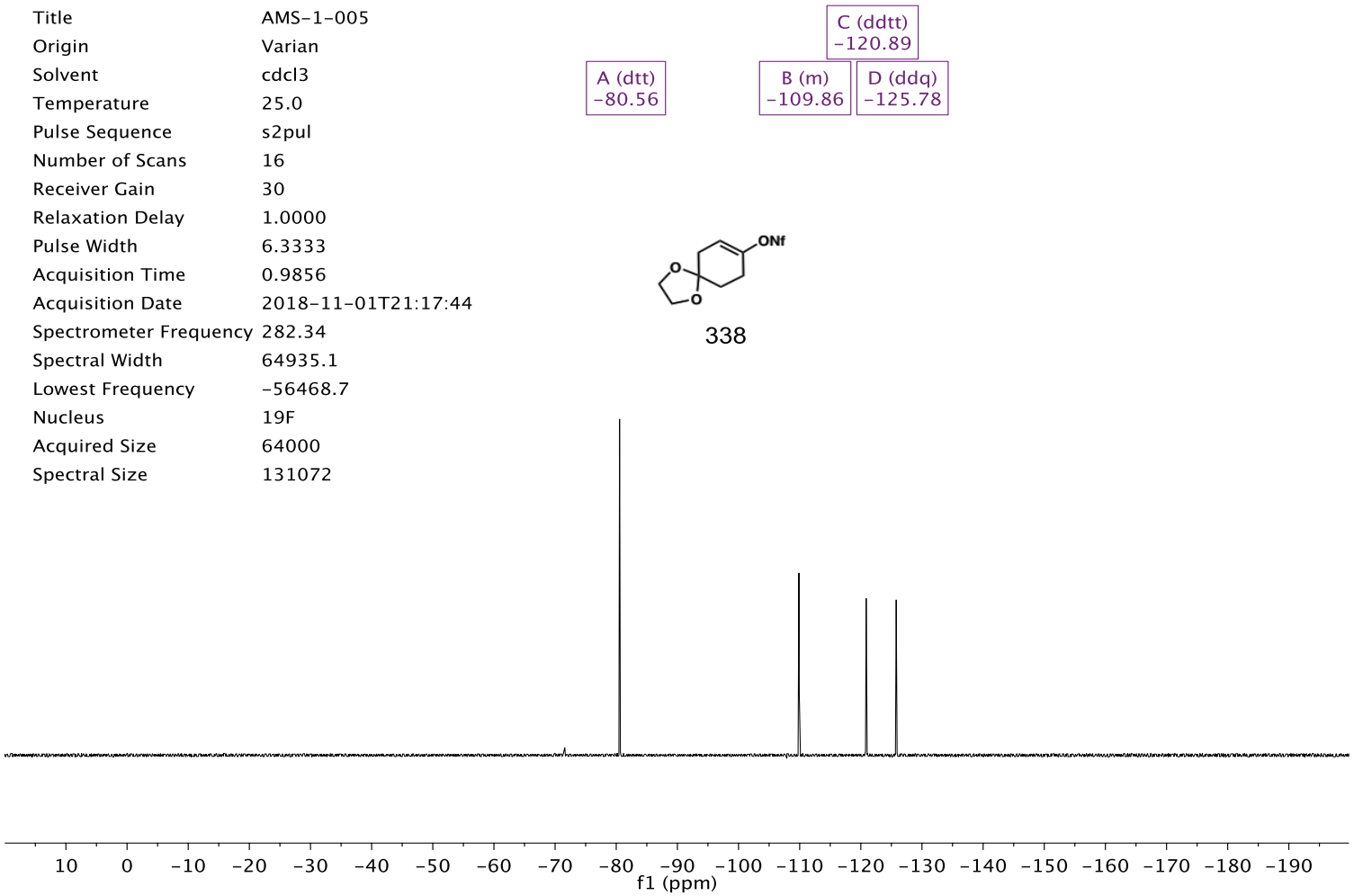
f1 (ppm)

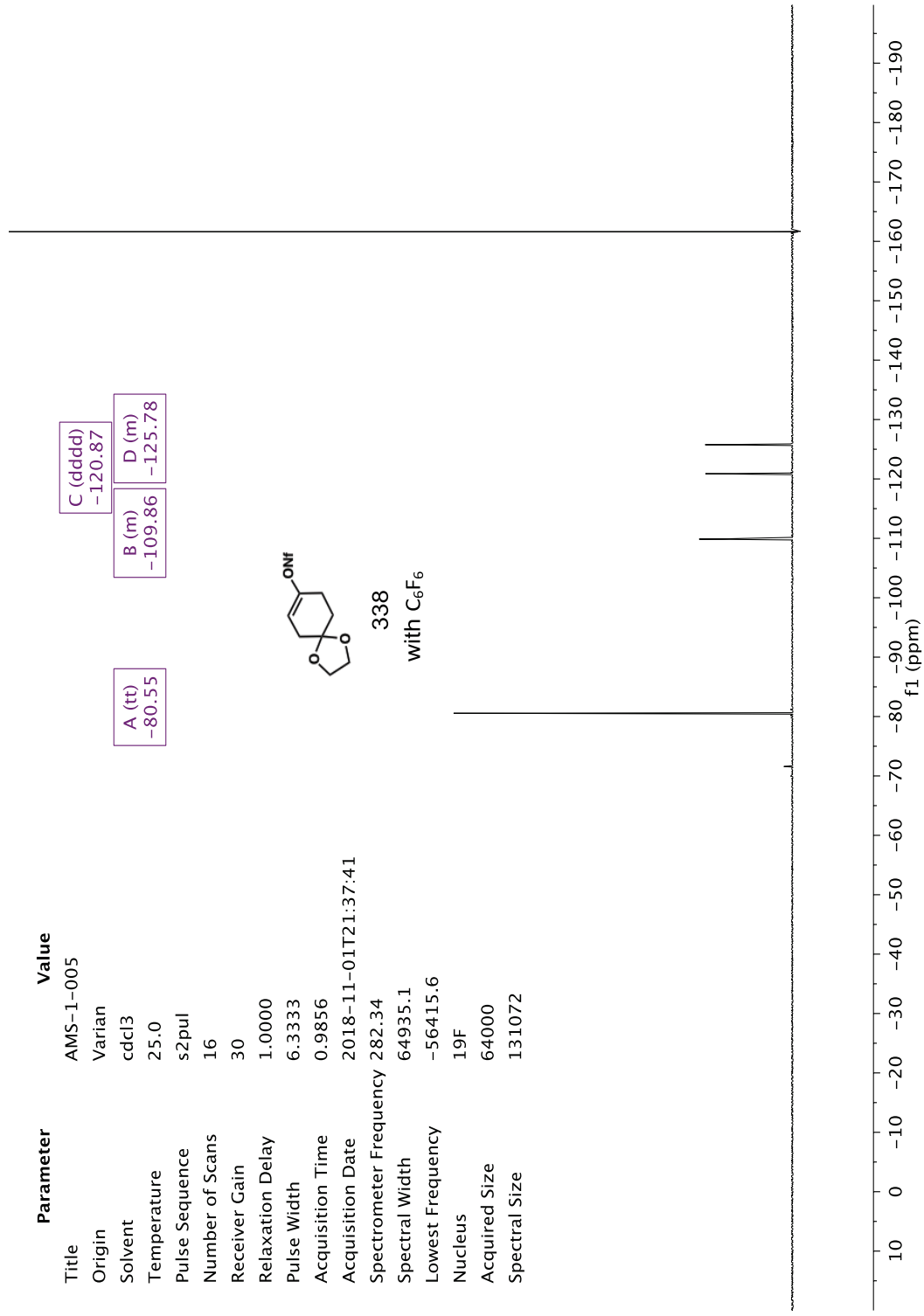

Parameter
Value
Title AMS-1-005
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 87.8
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-11-01T20:28:29
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1545.2
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
A (tt) 5.68
B (p) 3.98
C (dtd) 2.54
D (dt) 2.41
E (t) 1.91
ONf
338
1.00
4.11
2.09
2.06
2.05
f1 (ppm)



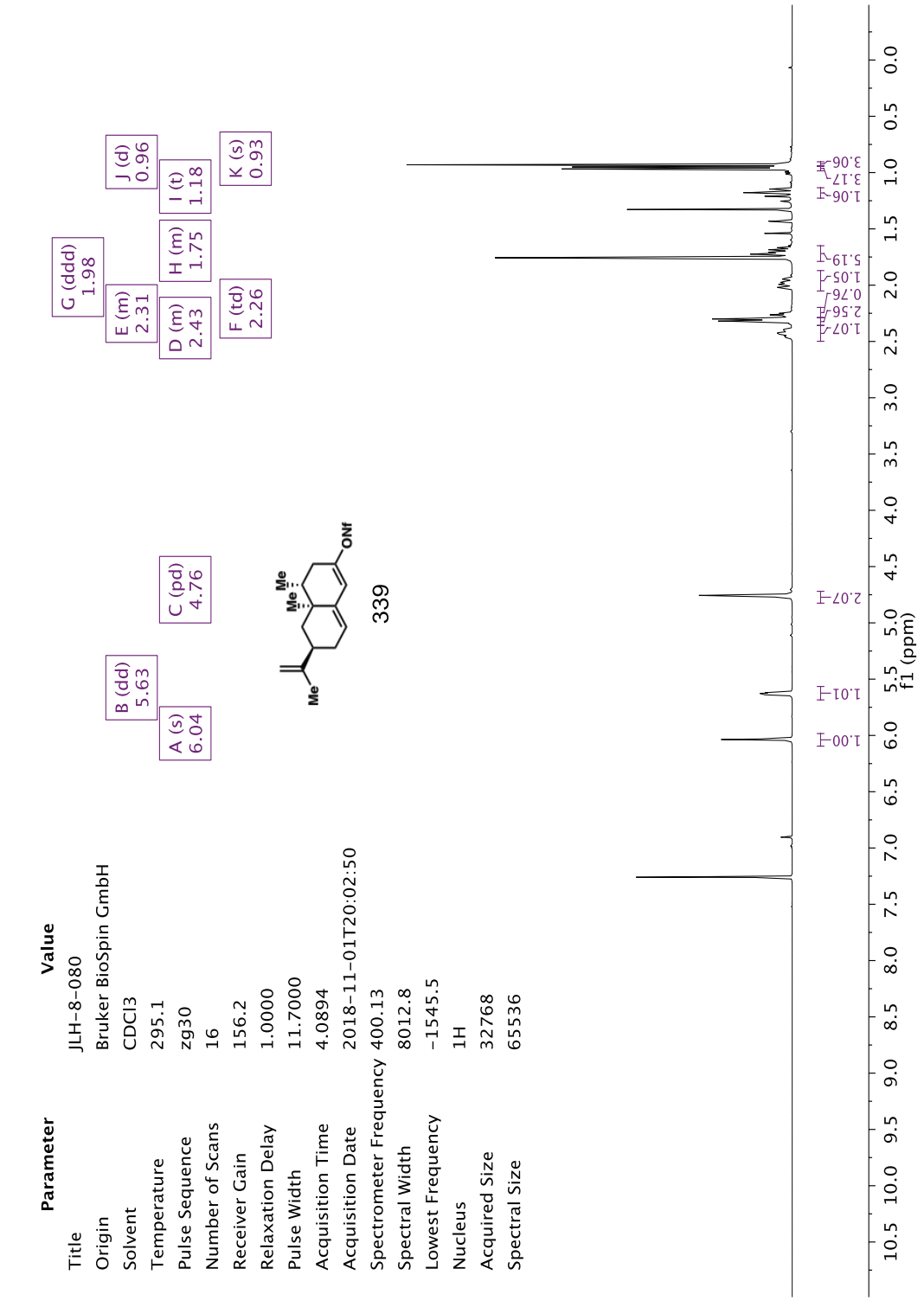
Parameter	Value
Title	AMS-1-005
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Number of Scans	128
Receiver Gain	64.2
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-11-01T20:34:10
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1943.6
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

Parameter	Value
Title	AMS-1-005
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-11-01T21:17:44
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56468.7
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

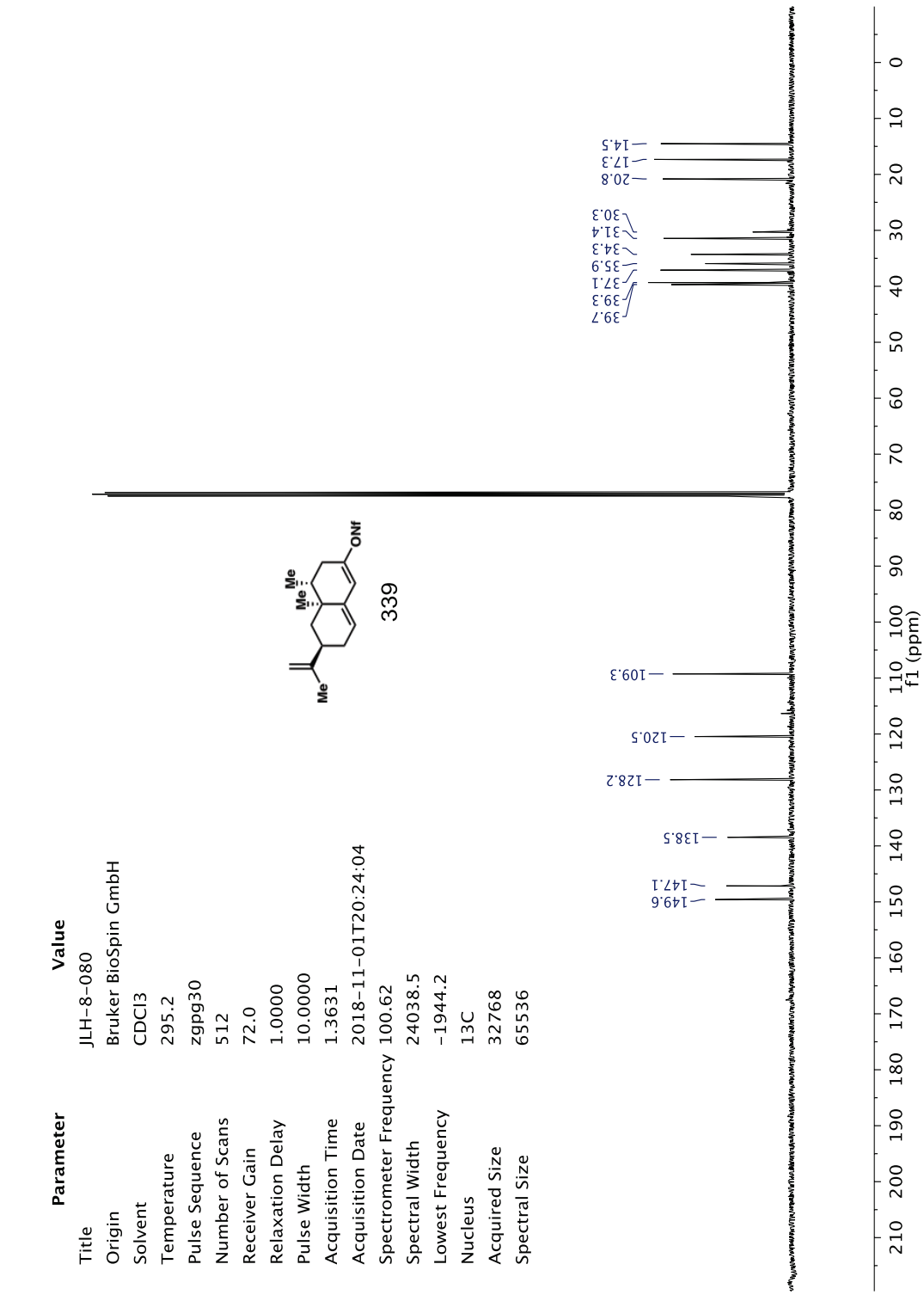




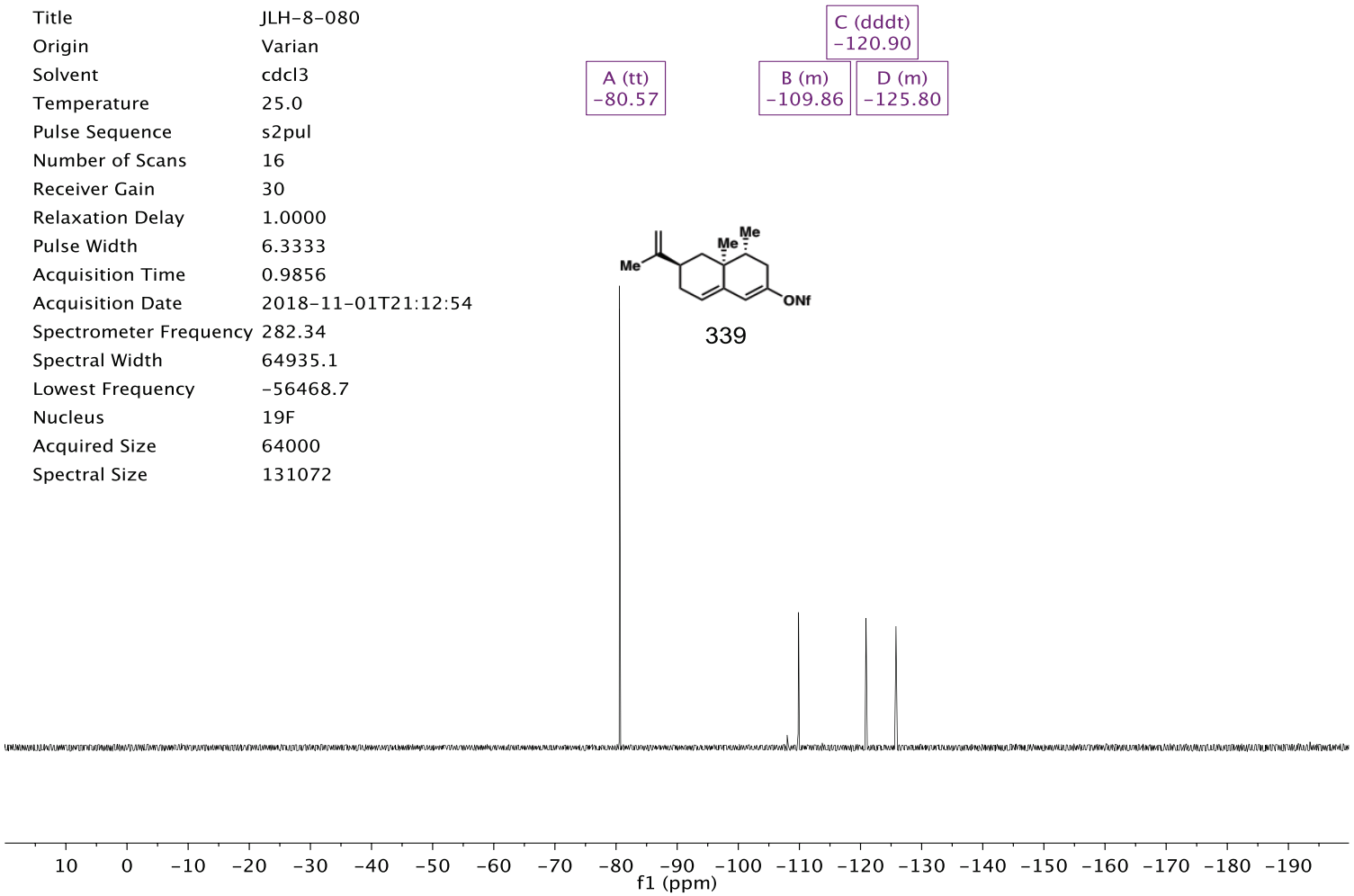
Parameter	Value
Title	AMS-1-005
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-11-01T21:37:41
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56415.6
Nucleus	19F
Acquired Size	64000
Spectral Size	131072


Parameter Value
Title JLH-8-080
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 156.2
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-11-01T20:02:50
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1545.5
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
A (s) 6.04
B (dd) 5.63
C (pd) 4.76
D (m) 2.43
E (m) 2.31
F (td) 2.26
G (ddd) 1.98
H (m) 1.75
I (t) 1.18
J (d) 0.96
K (s) 0.93
Me
Me
Me
ONf
339
1.00
1.01
2.07
1.07
2.56
0.76
1.05
5.19
1.06
3.17
3.06
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

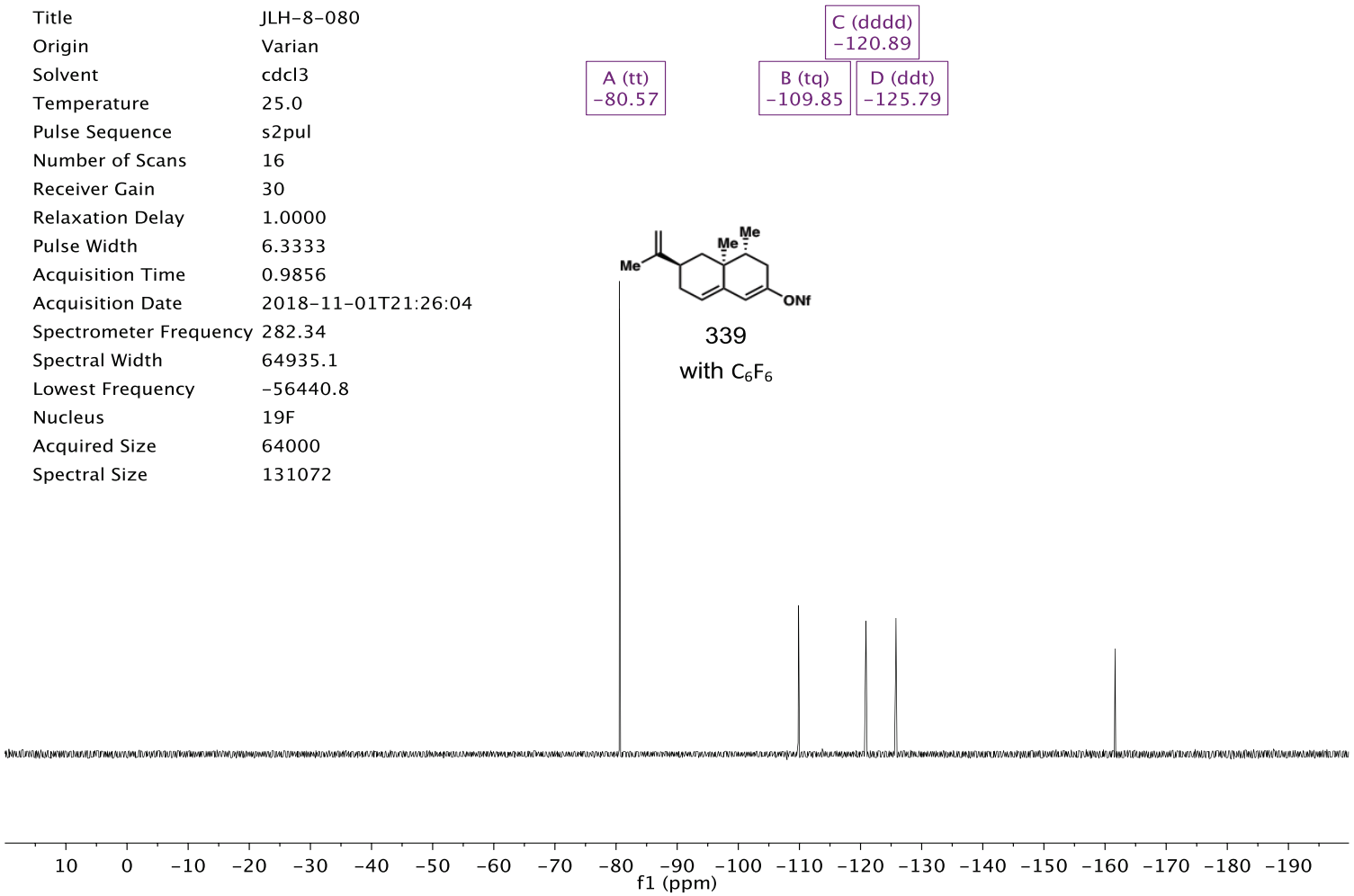
v

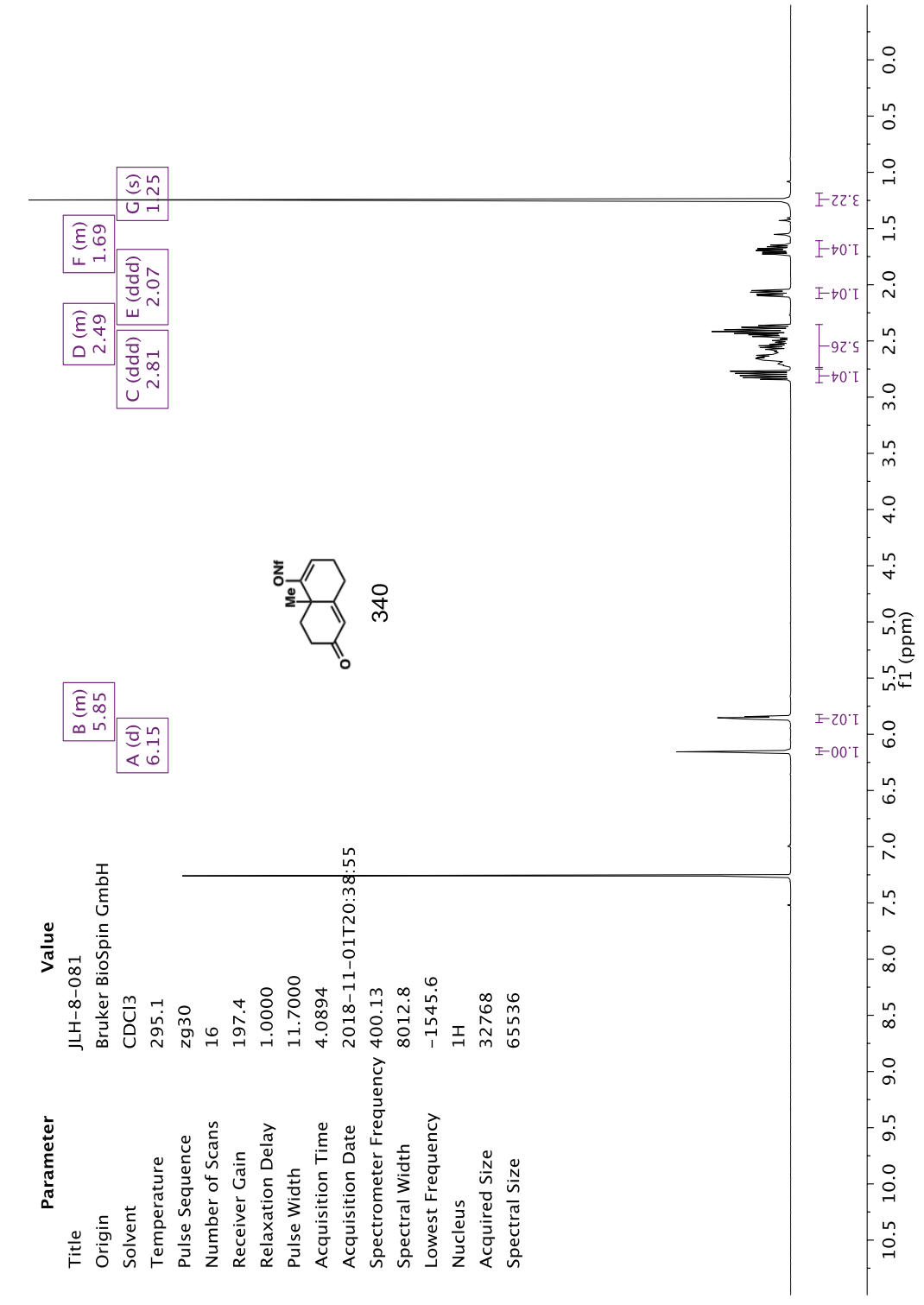

Parameter Value
Title JLH-8-080
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zgpg30
Number of Scans 512
Receiver Gain 72.0
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-11-01T20:24:04
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1944.2
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
Me
Me
ONf
339
149.6
147.1
138.5
128.2
120.5
109.3
39.7
39.3
37.1
35.9
34.3
31.4
30.3
20.8
17.3
14.5
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

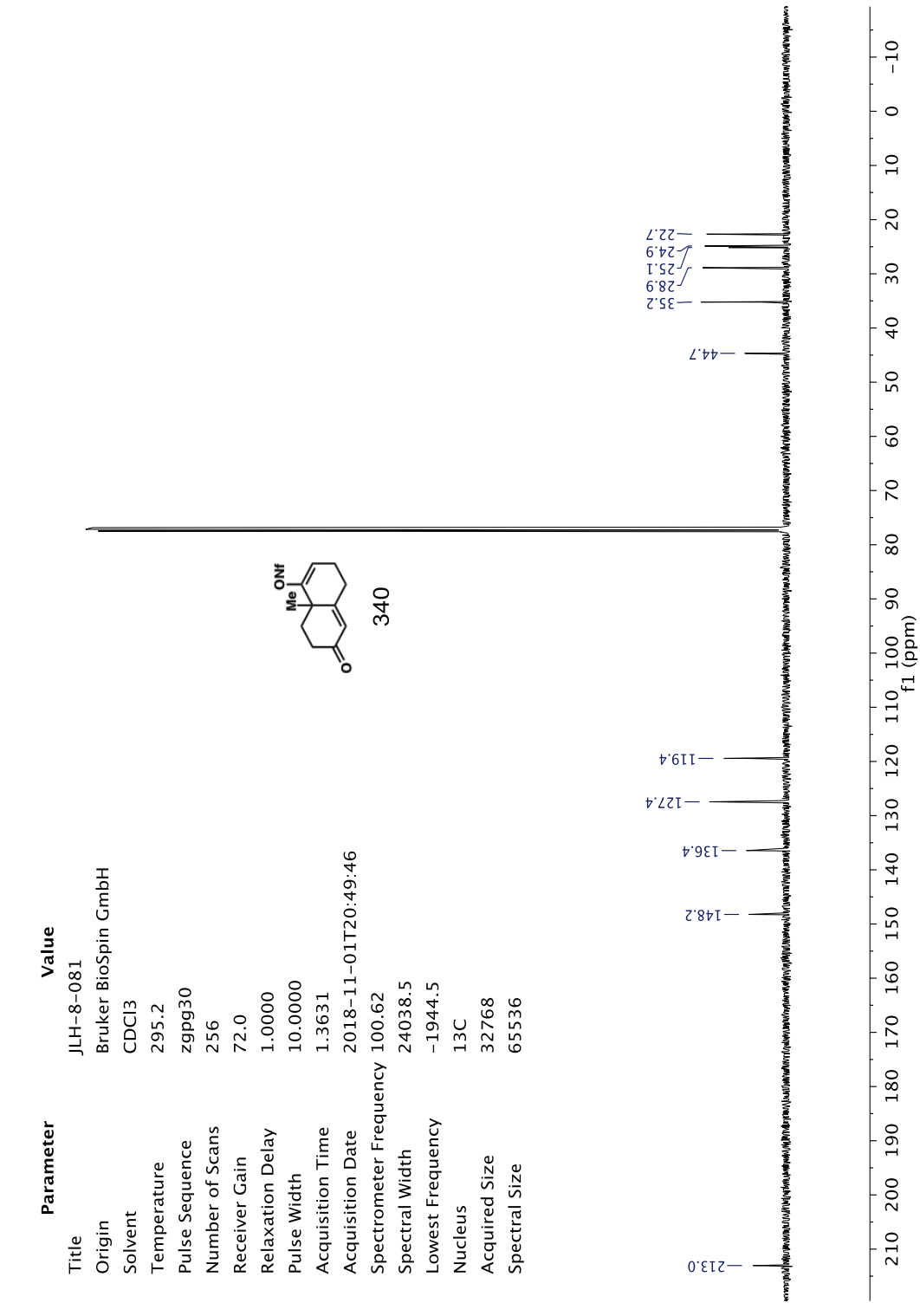
Parameter	Value
Title	JLH-8-080
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-11-01T21:12:54
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56468.7
Nucleus	19F
Acquired Size	64000
Spectral Size	131072



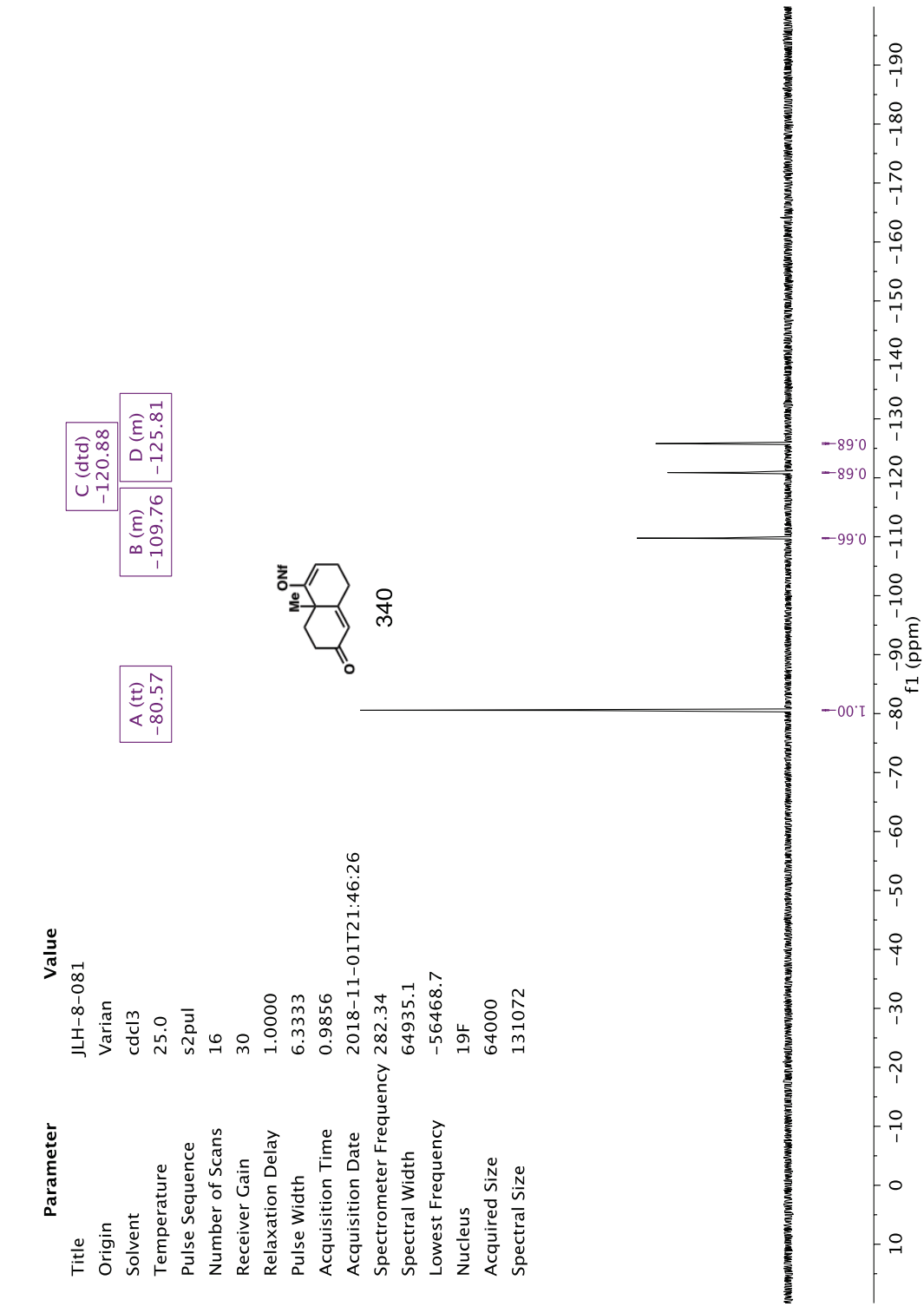
Parameter	Value
Title	JLH-8-080
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-11-01T21:26:04
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56440.8
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

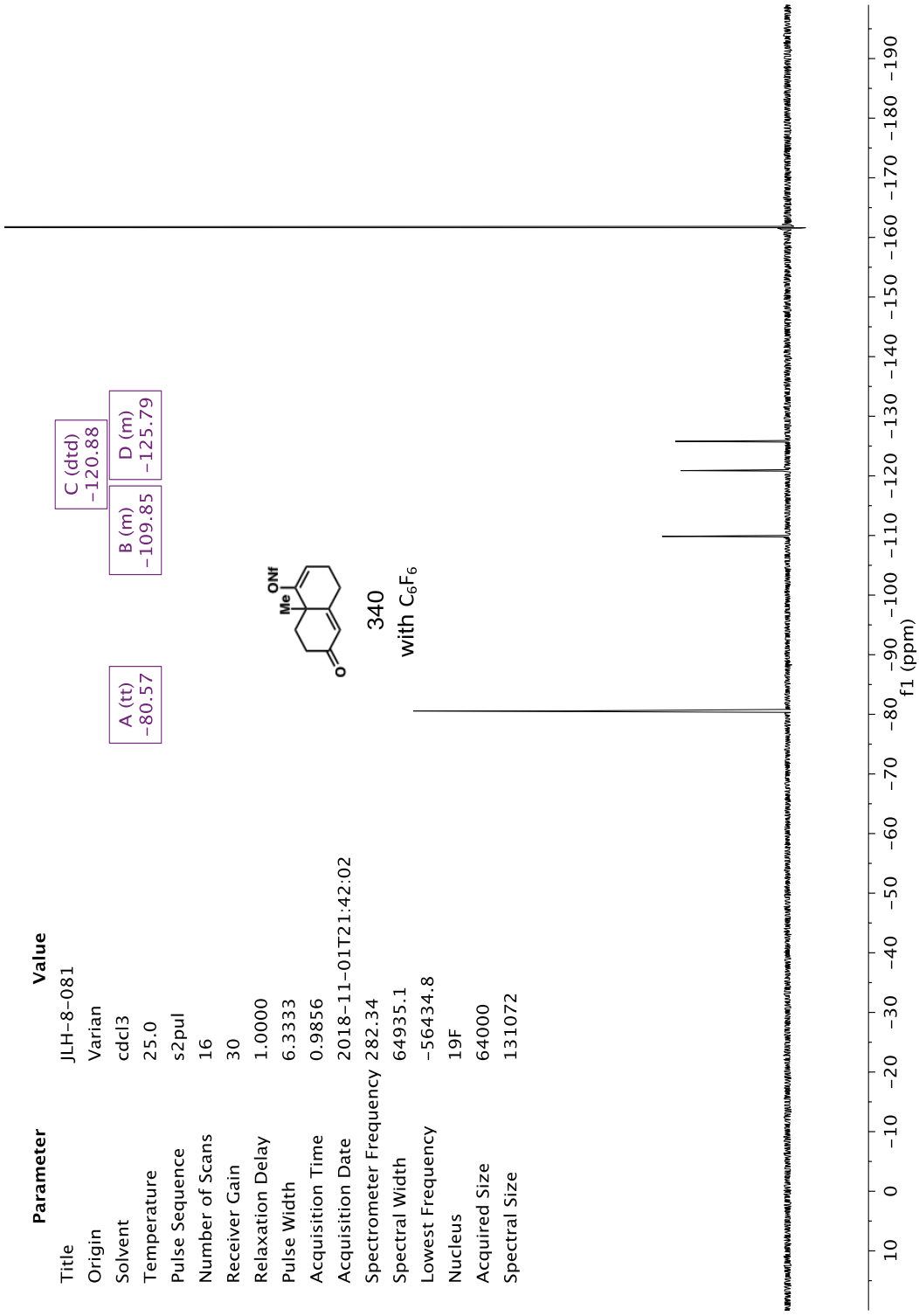



Parameter
Value
Title JLH-8-081
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 197.4
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-11-01T20:38:55
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1545.6
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
A (d) 6.15
B (m) 5.85
C (ddd) 2.81
D (m) 2.49
E (ddd) 2.07
F (m) 1.69
G (s) 1.25
ONf
Me
O
340
1.00
1.02
1.04
5.26
1.04
1.04
3.22
f1 (ppm)

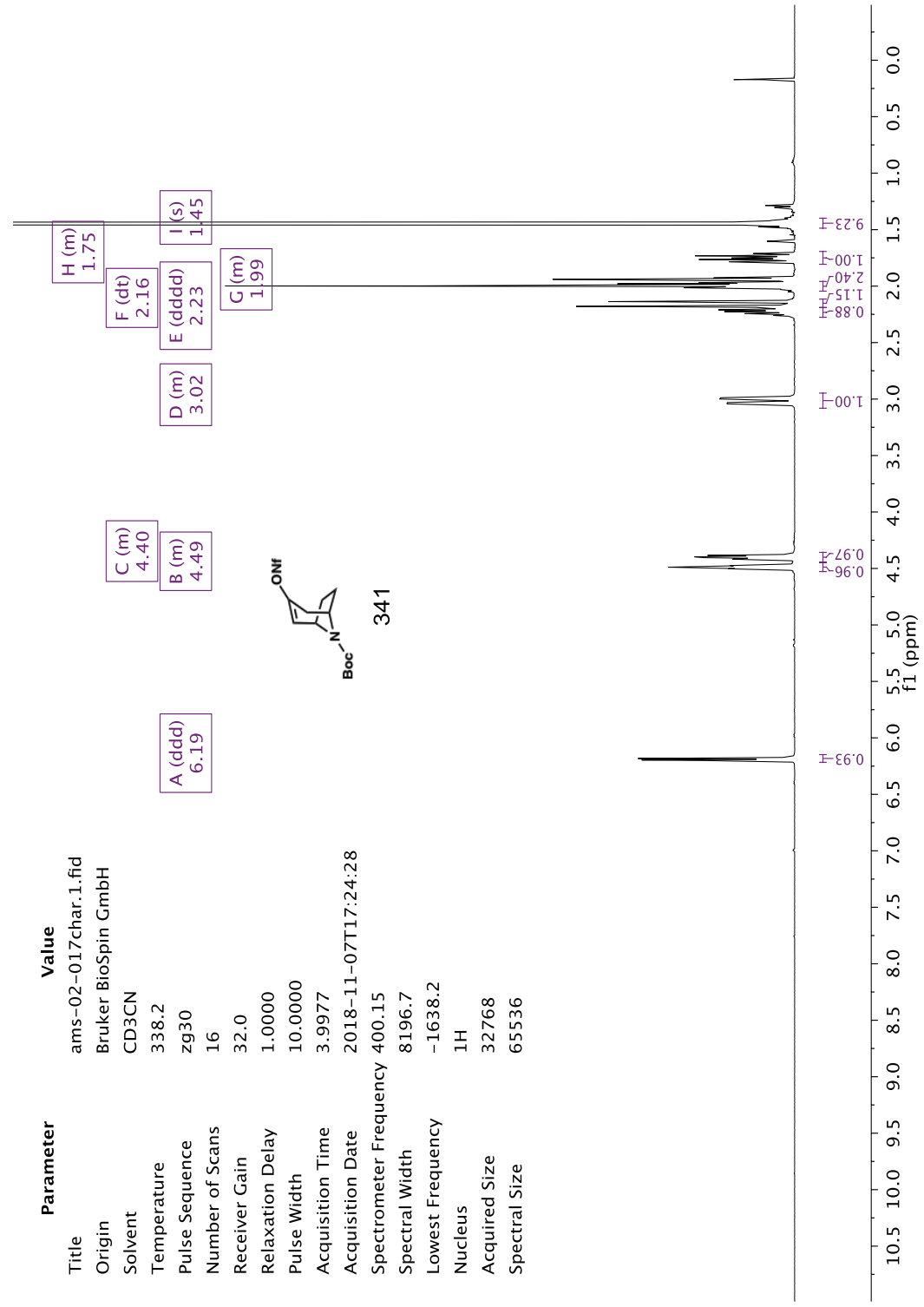


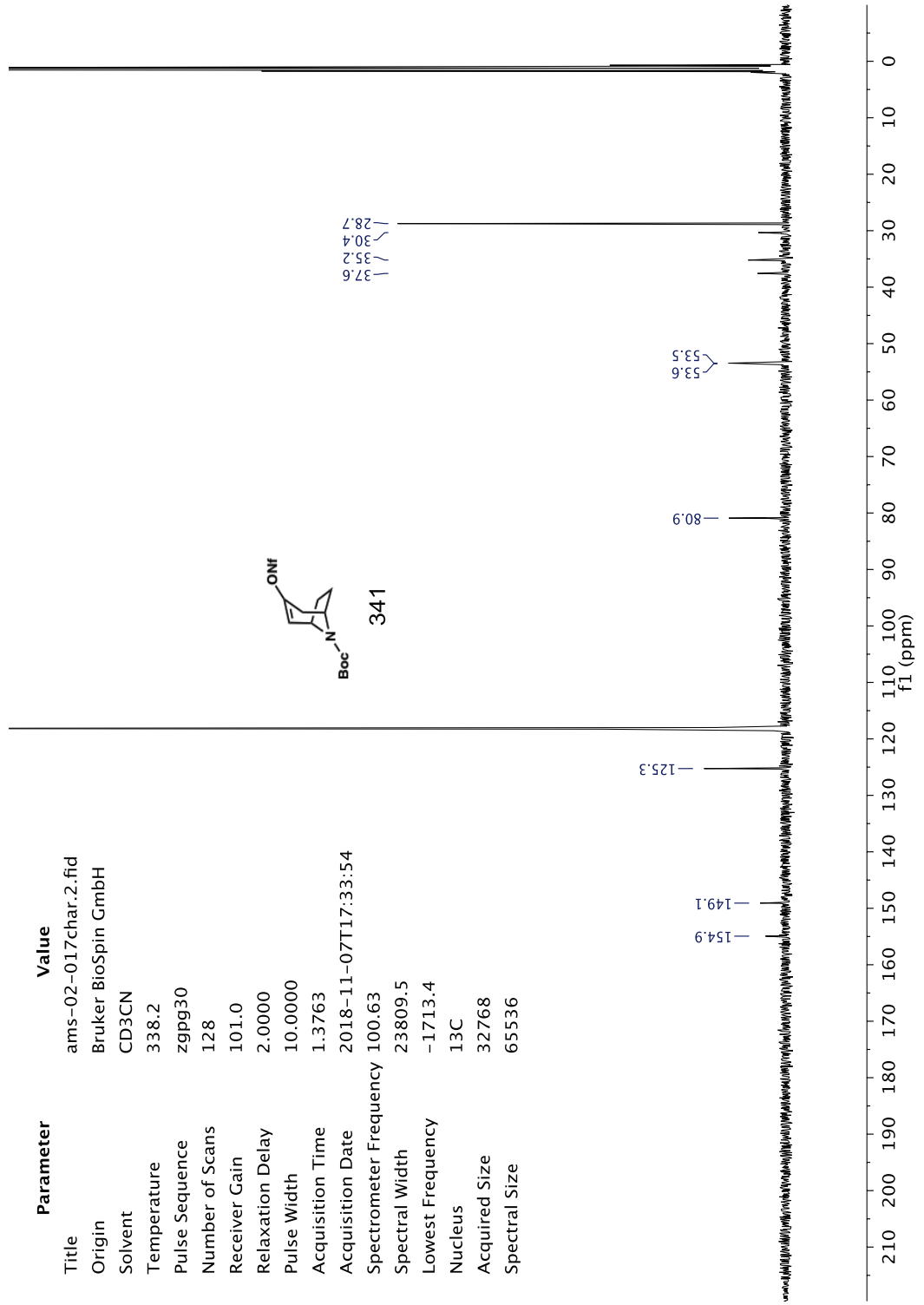
Parameter	Value
Title	JLH-8-081
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zgpg30
Number of Scans	256
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-11-01T20:49:46
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1944.5
Nucleus	13C
Acquired Size	32768
Spectral Size	65536


Parameter Value
Title JLH-8-081
Origin Varian
Solvent cdcl3
Temperature 25.0
Pulse Sequence s2pul
Number of Scans 16
Receiver Gain 30
Relaxation Delay 1.0000
Pulse Width 6.3333
Acquisition Time 0.9856
Acquisition Date 2018-11-01T21:46:26
Spectrometer Frequency 282.34
Spectral Width 64935.1
Lowest Frequency -56468.7
Nucleus 19F
Acquired Size 64000
Spectral Size 131072
A (tt) -80.57
B (m) -109.76
C (dtd) -120.88
D (m) -125.81
ONf
Me
O
340
1.00
0.66
0.89
0.89
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

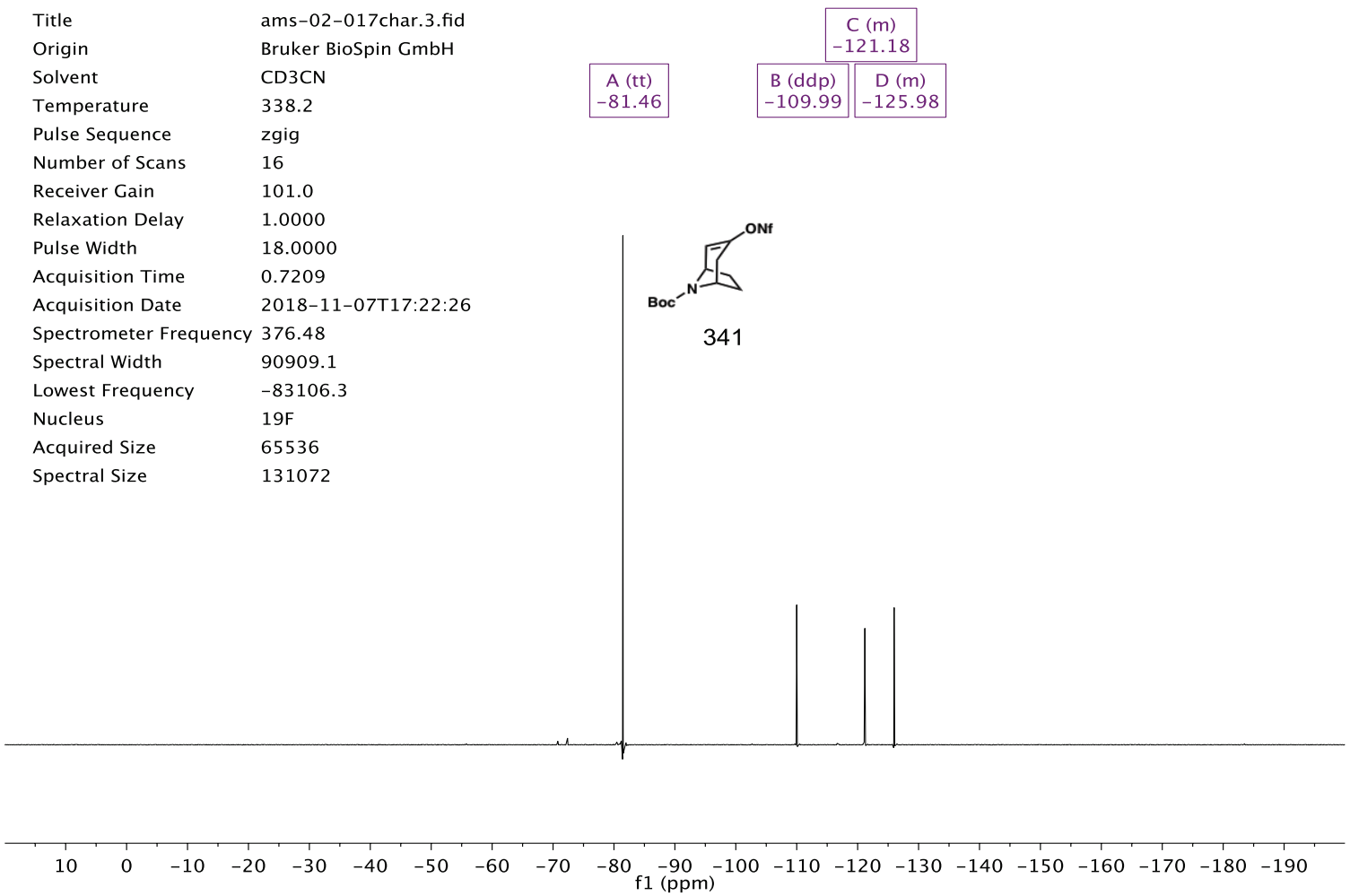


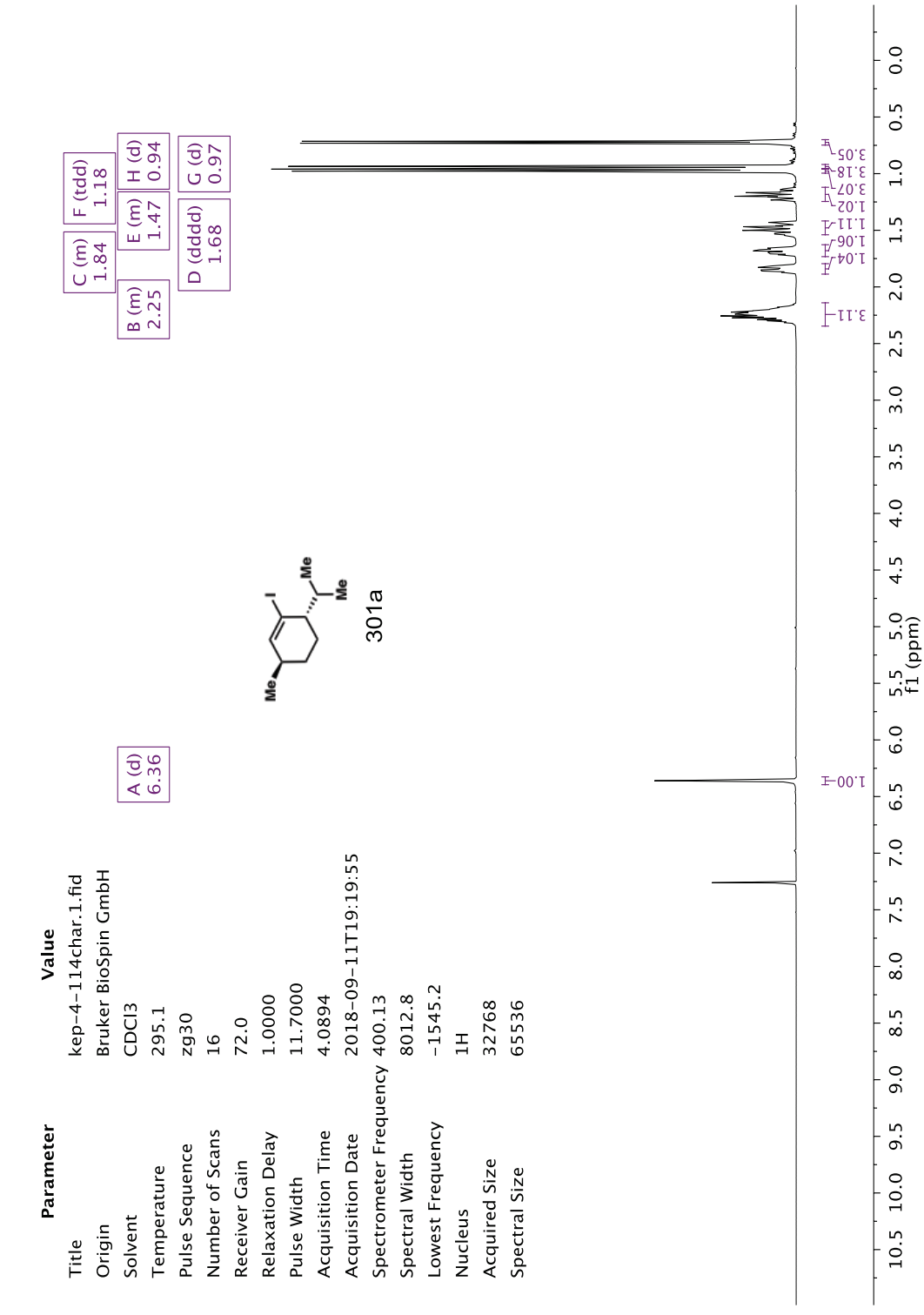
Parameter	Value
Title	JLH-8-081
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-11-01T21:42:02
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56434.8
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

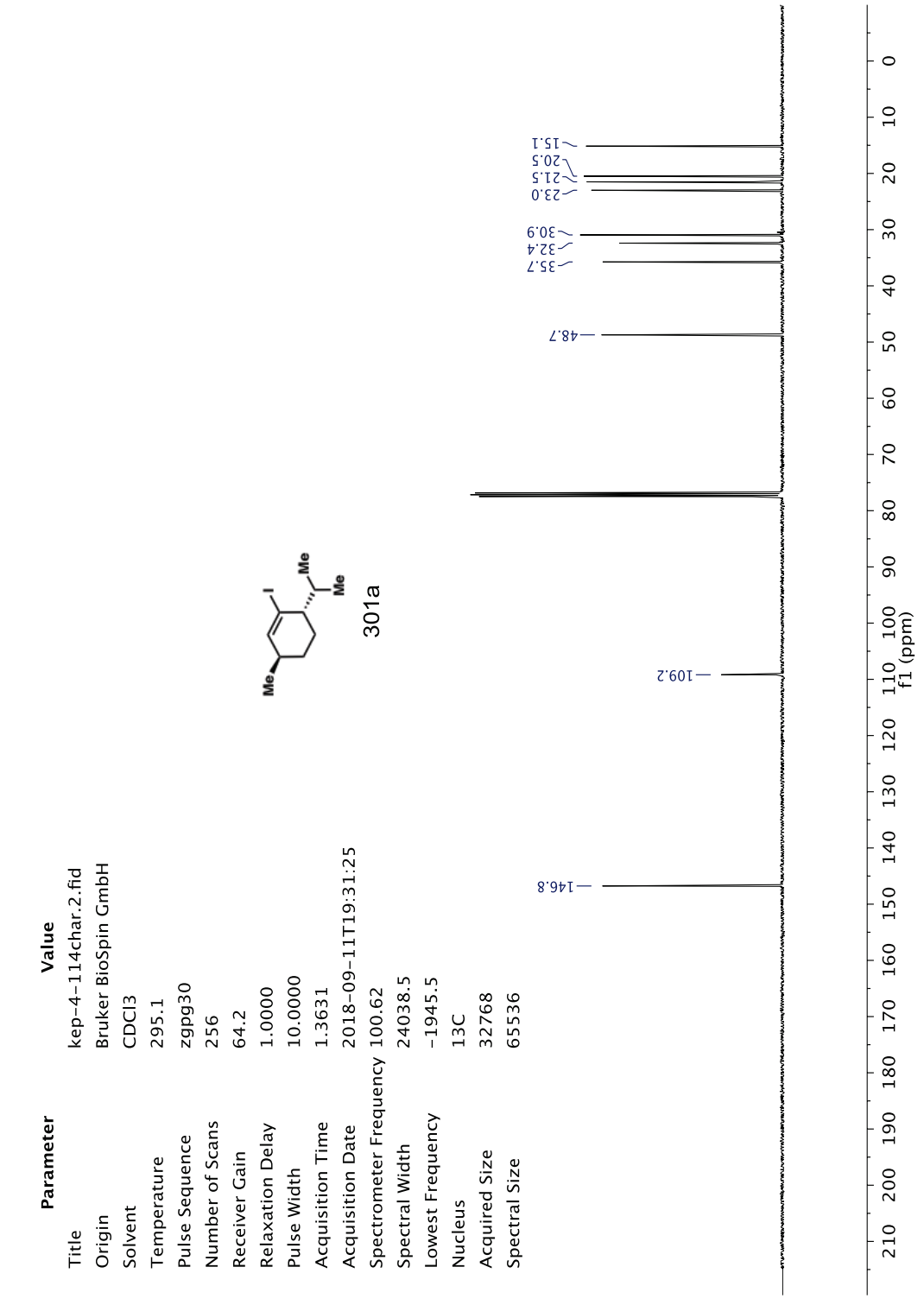

Parameter Value
Title ams-02-017char.1.fid
Origin Bruker BioSpin GmbH
Solvent CD3CN
Temperature 338.2
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 32.0
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 3.9977
Acquisition Date 2018-11-07T17:24:28
Spectrometer Frequency 400.15
Spectral Width 8196.7
Lowest Frequency -1638.2
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
A (ddd) 6.19
B (m) 4.49
C (m) 4.40
D (m) 3.02
E (dddd) 2.23
F (dt) 2.16
G (m) 1.99
H (m) 1.75
I (s) 1.45
ONf
Boc
N
341
0.93
0.96
0.97
1.00
0.88
1.15
2.40
1.00
9.23
f1 (ppm)

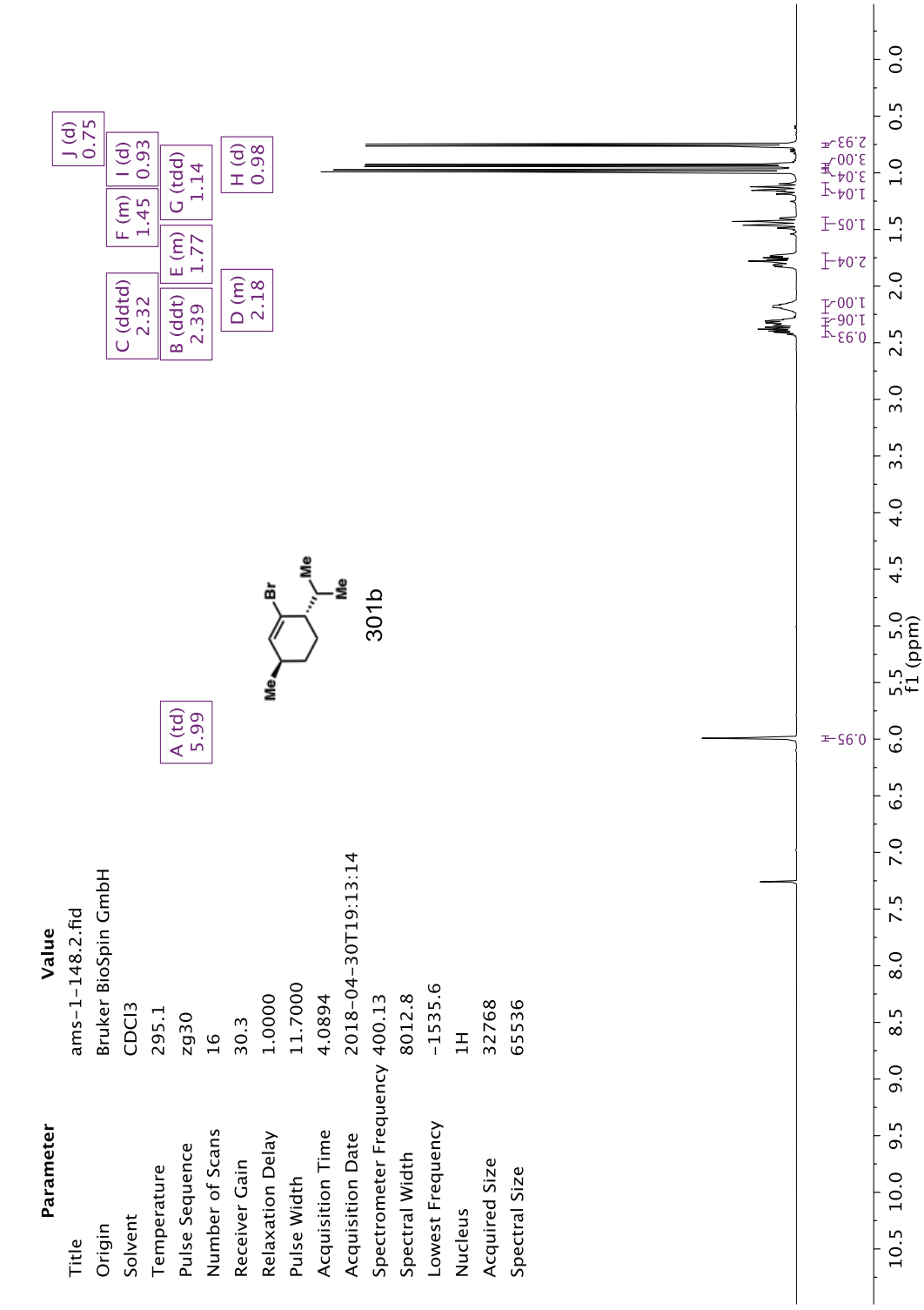

Parameter Value
Title ams-02-017char.2.fid
Origin Bruker BioSpin GmbH
Solvent CD3CN
Temperature 338.2
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 101.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3763
Acquisition Date 2018-11-07T17:33:54
Spectrometer Frequency 100.63
Spectral Width 23809.5
Lowest Frequency -1713.4
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
ONf
Boc
N
341
154.9
149.1
125.3
80.9
53.6
53.5
37.6
35.2
30.4
28.7
f1 (ppm)

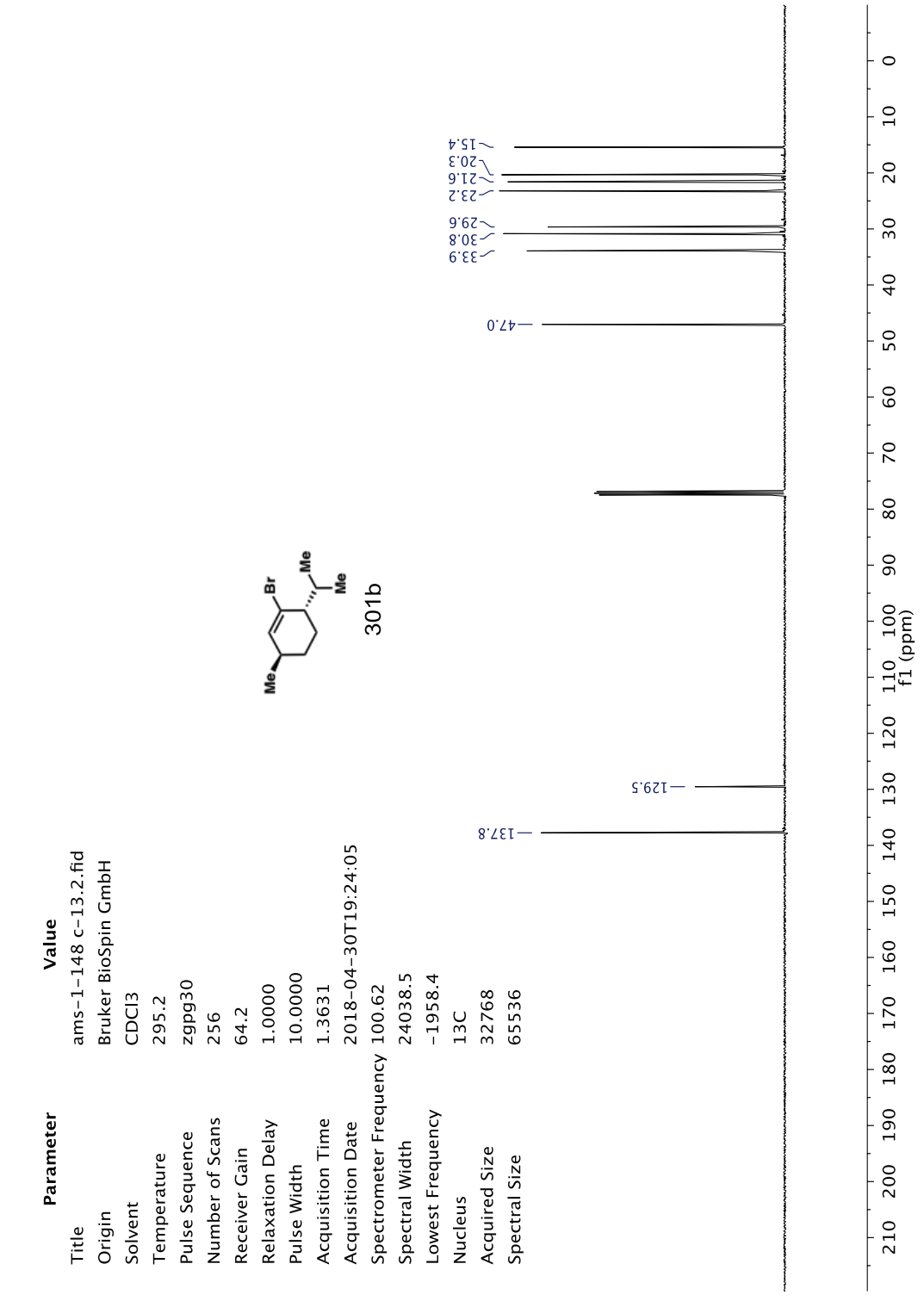
Parameter	Value
Title	ams-02-017char.3.fid
Origin	Bruker BioSpin GmbH
Solvent	CD3CN
Temperature	338.2
Pulse Sequence	zgig
Number of Scans	16
Receiver Gain	101.0
Relaxation Delay	1.0000
Pulse Width	18.0000
Acquisition Time	0.7209
Acquisition Date	2018-11-07T17:22:26
Spectrometer Frequency	376.48
Spectral Width	90909.1
Lowest Frequency	-83106.3
Nucleus	19F
Acquired Size	65536
Spectral Size	131072

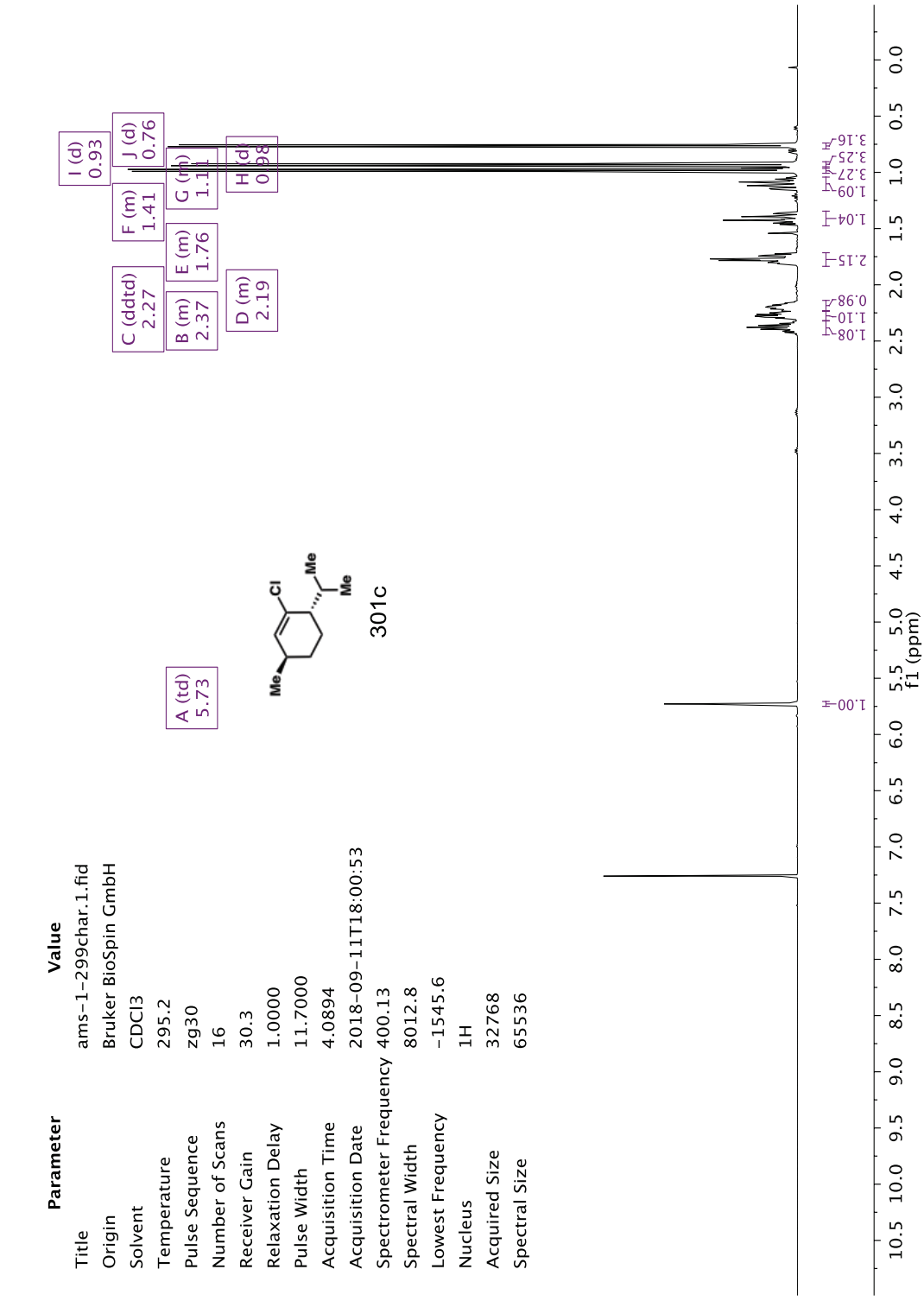



Parameter
Value
Title kep-4-114char.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 72.0
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-09-11T19:19:55
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1545.2
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
A (d) 6.36
B (m) 2.25
C (m) 1.84
D (dddd) 1.68
E (m) 1.47
F (tdd) 1.18
G (d) 0.97
H (d) 0.94
Me
Me
Me
301a
1.00
3.11
1.04
1.06
1.11
1.02
3.07
3.18
3.05
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

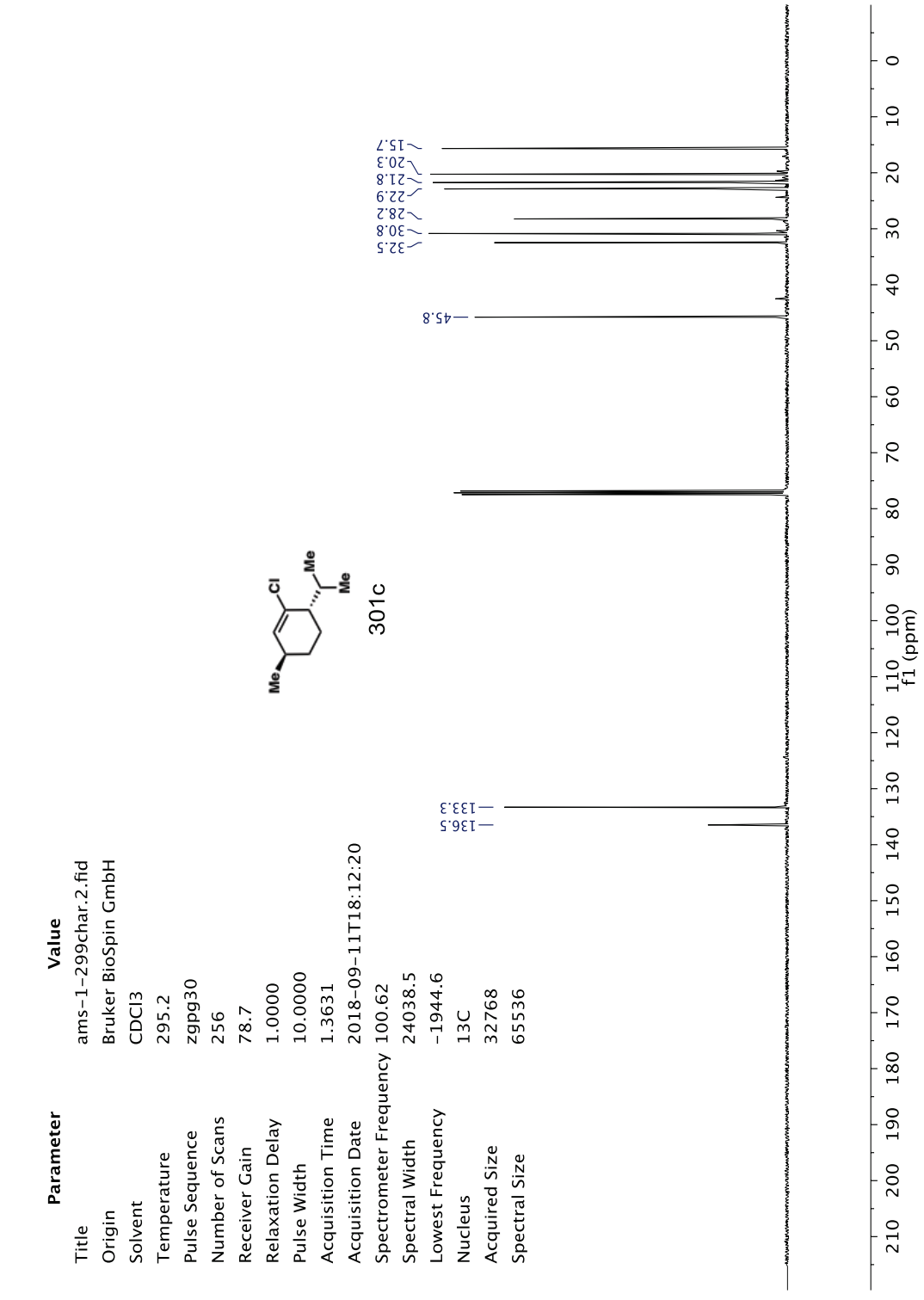

Parameter Value
Title kep-4-114char.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zgpg30
Number of Scans 256
Receiver Gain 64.2
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-09-11T19:31:25
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1945.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
I
Me
Me
Me
301a
146.8
109.2
48.7
35.7
32.4
30.9
23.0
21.5
20.5
15.1
f1 (ppm)

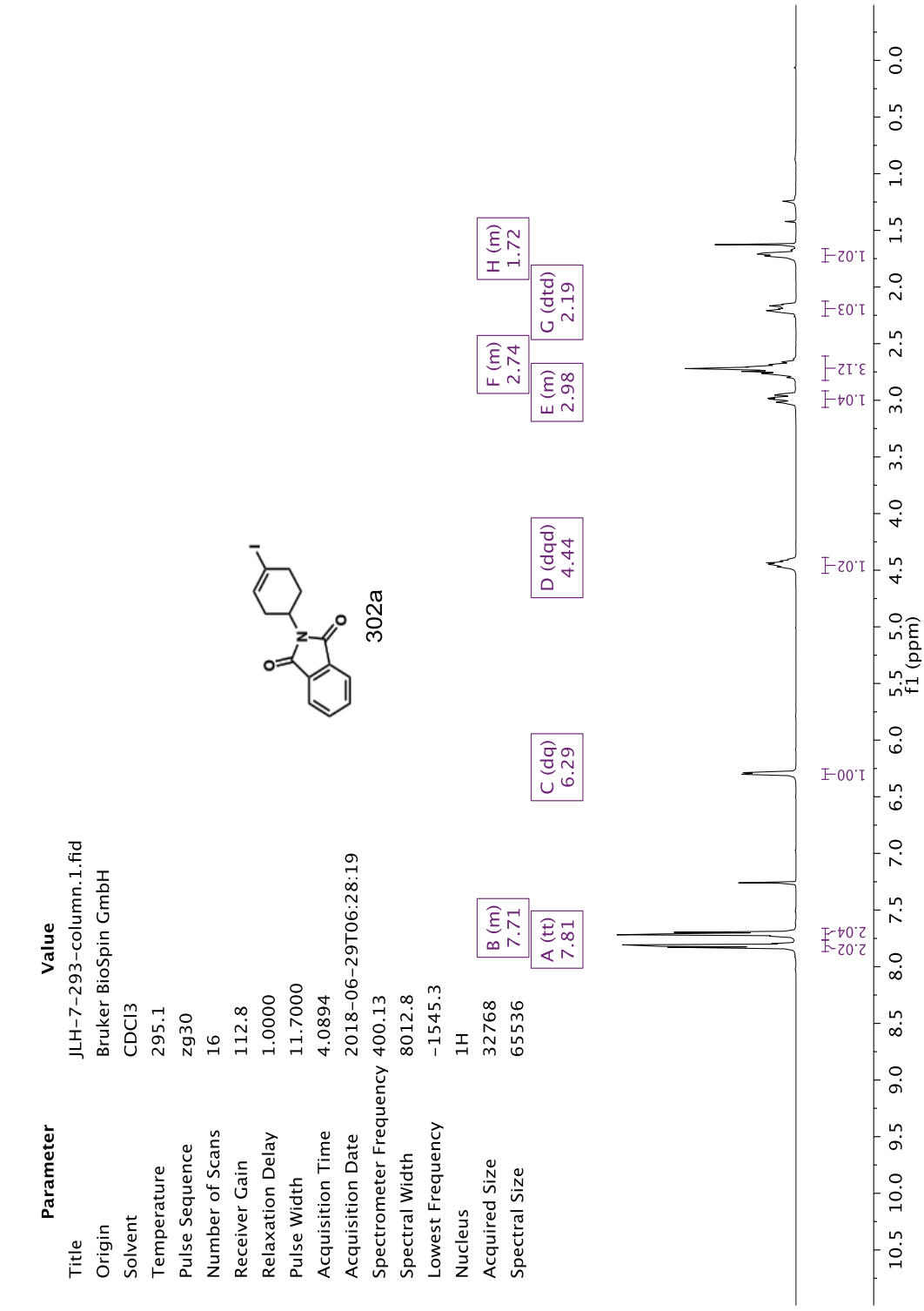

Parameter
Value
Title ams-1-148.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 30.3
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-04-30T19:13:14
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1535.6
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
A (td) 5.99
B (ddt) 2.39
C (ddtd) 2.32
D (m) 2.18
E (m) 1.77
F (m) 1.45
G (tdd) 1.14
H (d) 0.98
I (d) 0.93
J (d) 0.75
Br
Me
Me
Me
301b
0.95
0.93
1.06
1.00
2.04
1.05
1.04
3.04
3.00
2.93
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

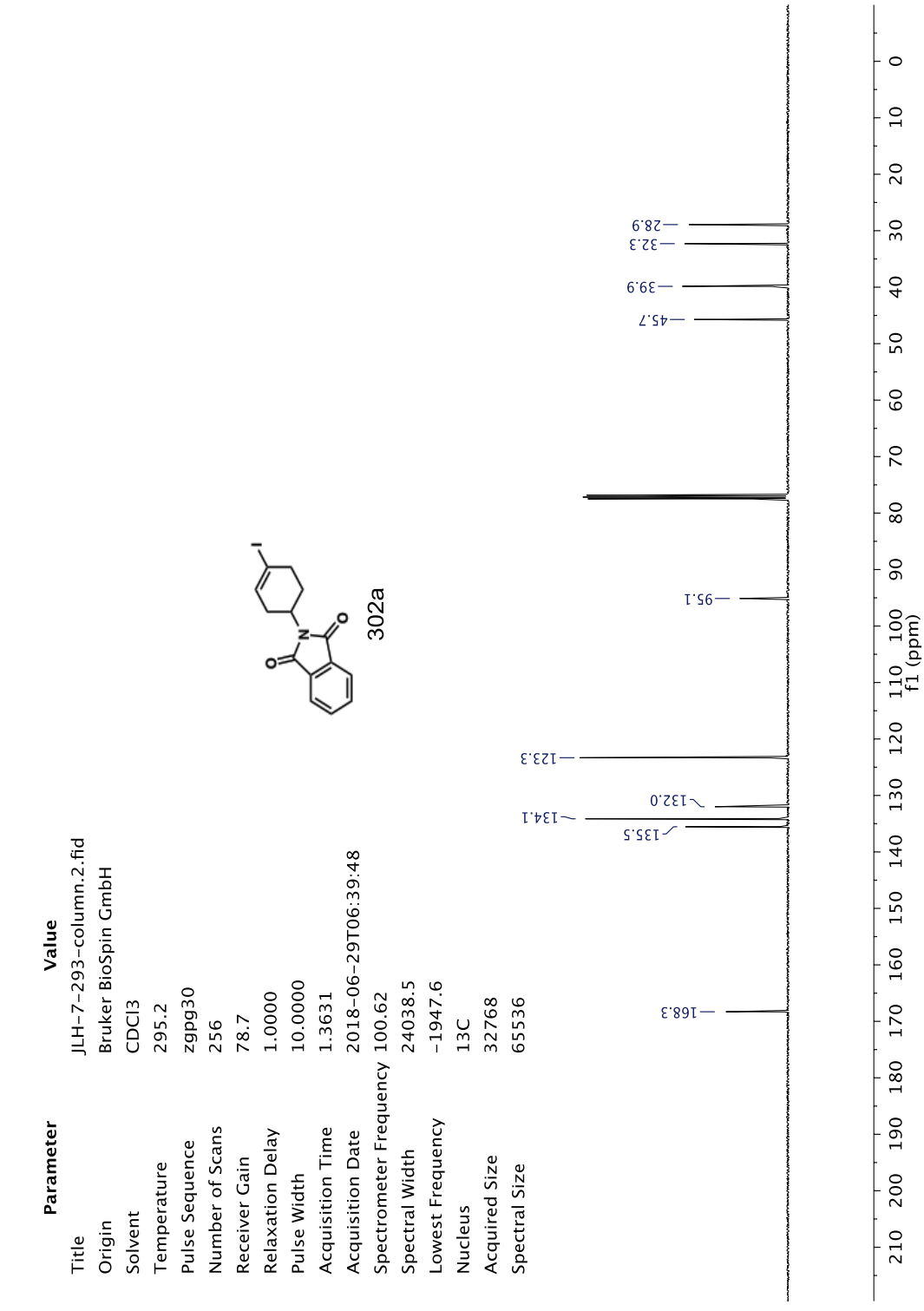

Parameter
Value
Title
ams-1-148 c-13.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
zgpg30
Number of Scans
256
Receiver Gain
64.2
Relaxation Delay
1.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-04-30T19:24:05
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1958.4
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Br
Me
Me
Me
301b
137.8
129.5
47.0
33.9
30.8
29.6
23.2
21.6
20.3
15.4
f1 (ppm)

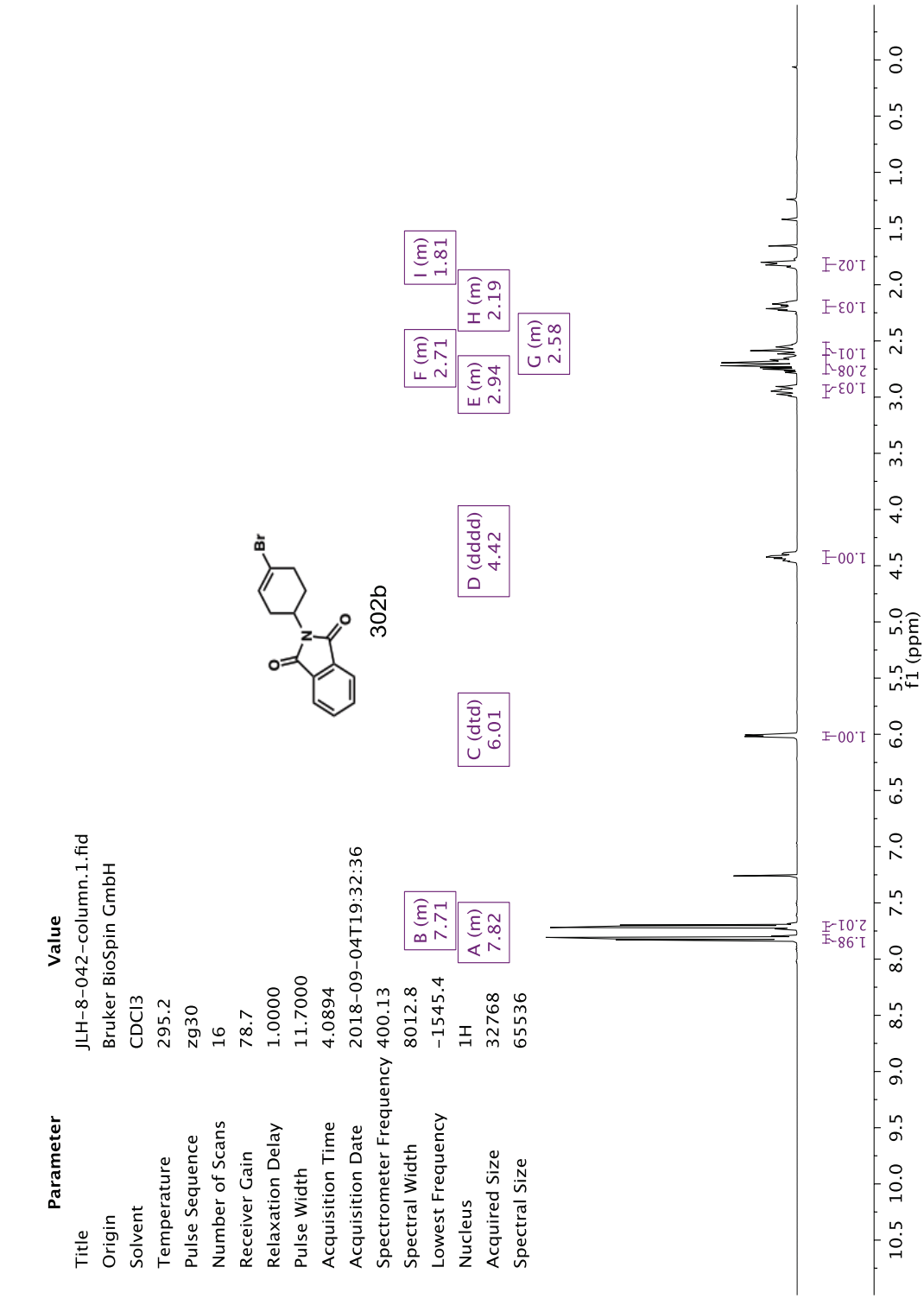


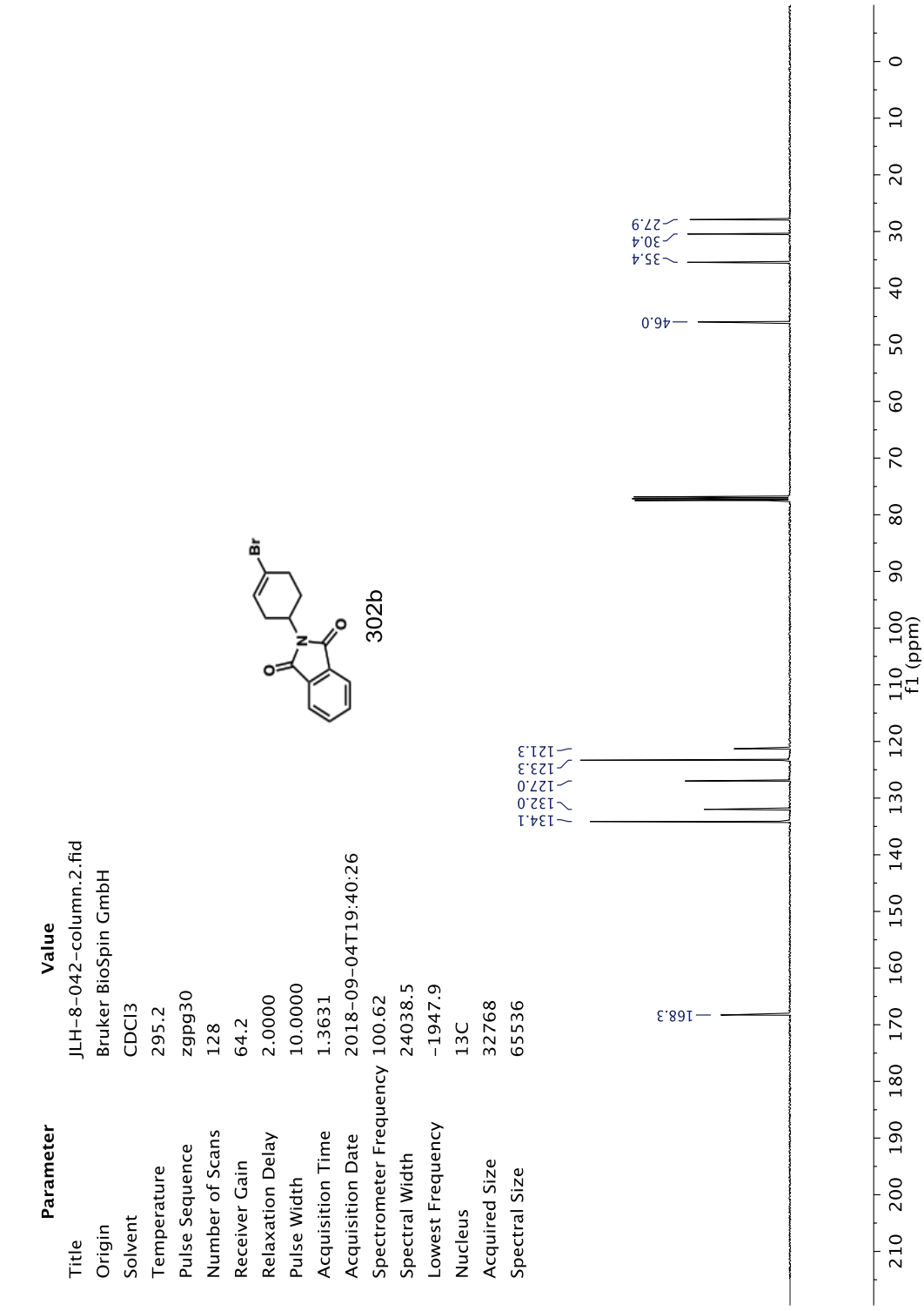
Parameter	Value
Title	ams-1-299char.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zg30
Number of Scans	16
Receiver Gain	30.3
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-09-11T18:00:53
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

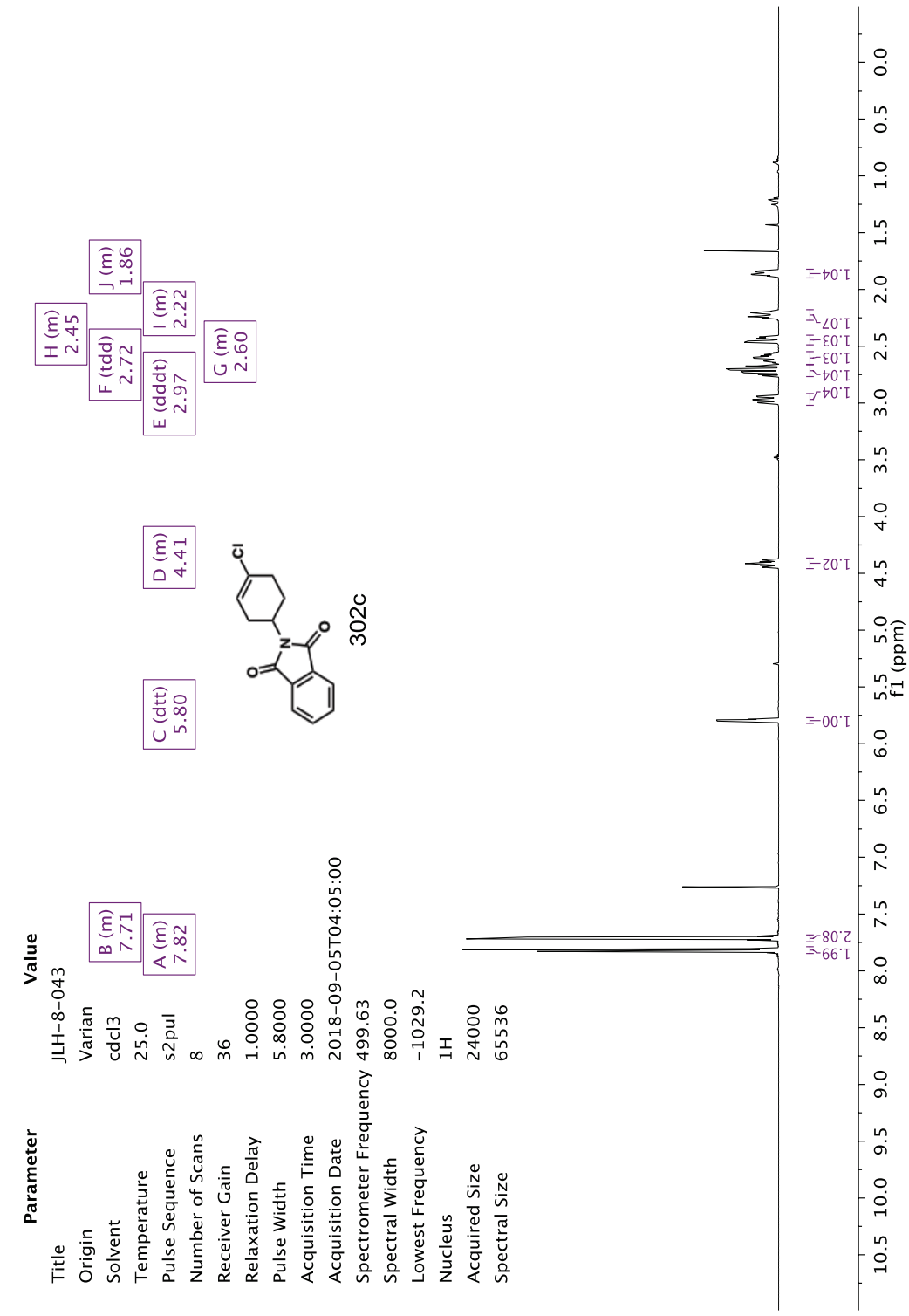

Parameter
Value
Title
ams-1-299char.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
zgpg30
Number of Scans
256
Receiver Gain
78.7
Relaxation Delay
1.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-09-11T18:12:20
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1944.6
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Cl
Me
Me
Me
301c
133.3
136.5
45.8
32.5
30.8
28.2
22.9
21.8
20.3
15.7
f1 (ppm)

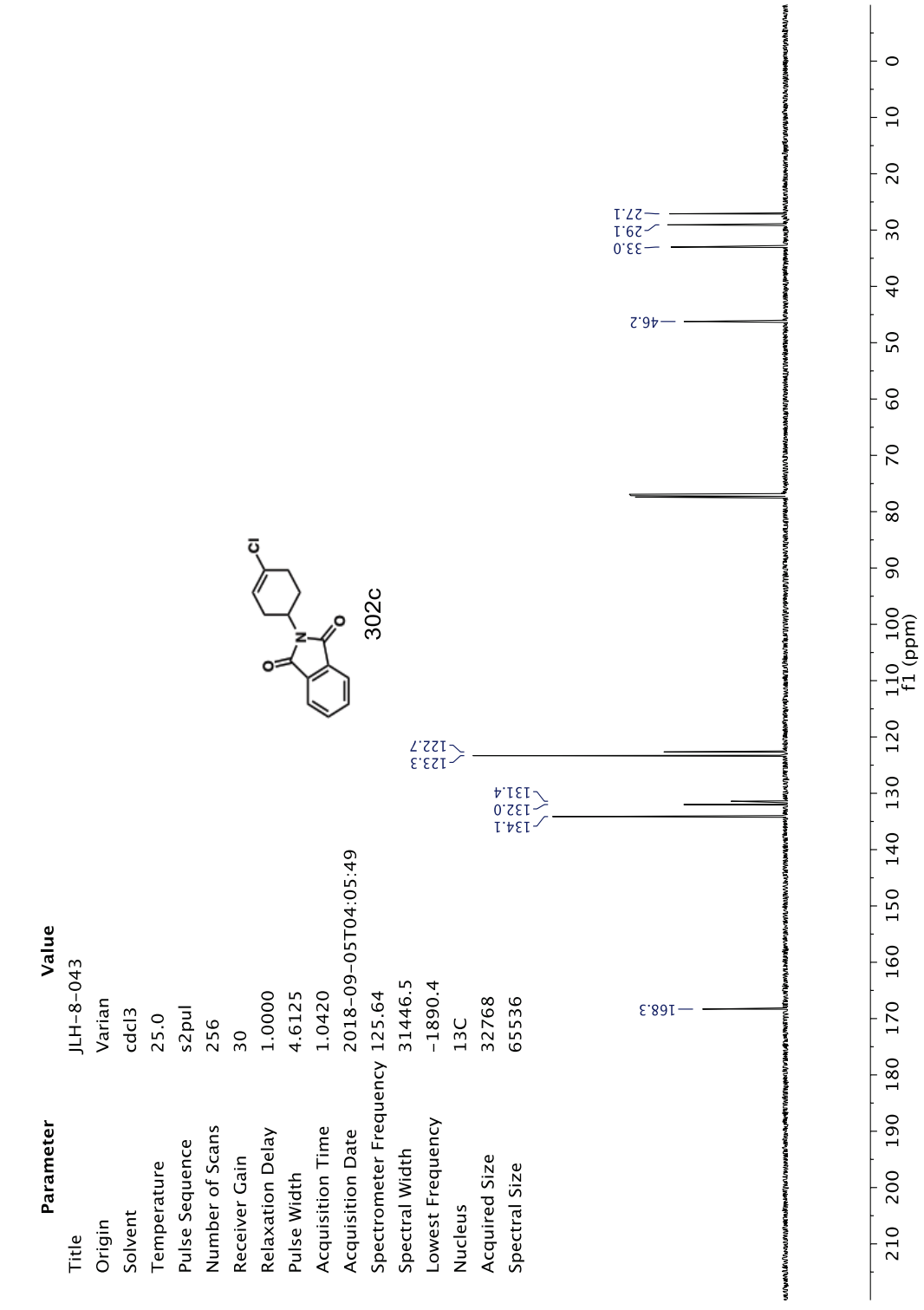

Parameter
Value
Title
JLH-7-293-column.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.1
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
112.8
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-06-29T06:28:19
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1545.3
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
302a
A (tt) 7.81
B (m) 7.71
C (dq) 6.29
D (dqd) 4.44
E (m) 2.98
F (m) 2.74
G (dtd) 2.19
H (m) 1.72
2.02
2.04
1.00
1.02
1.04
3.12
1.03
1.02
f1 (ppm)

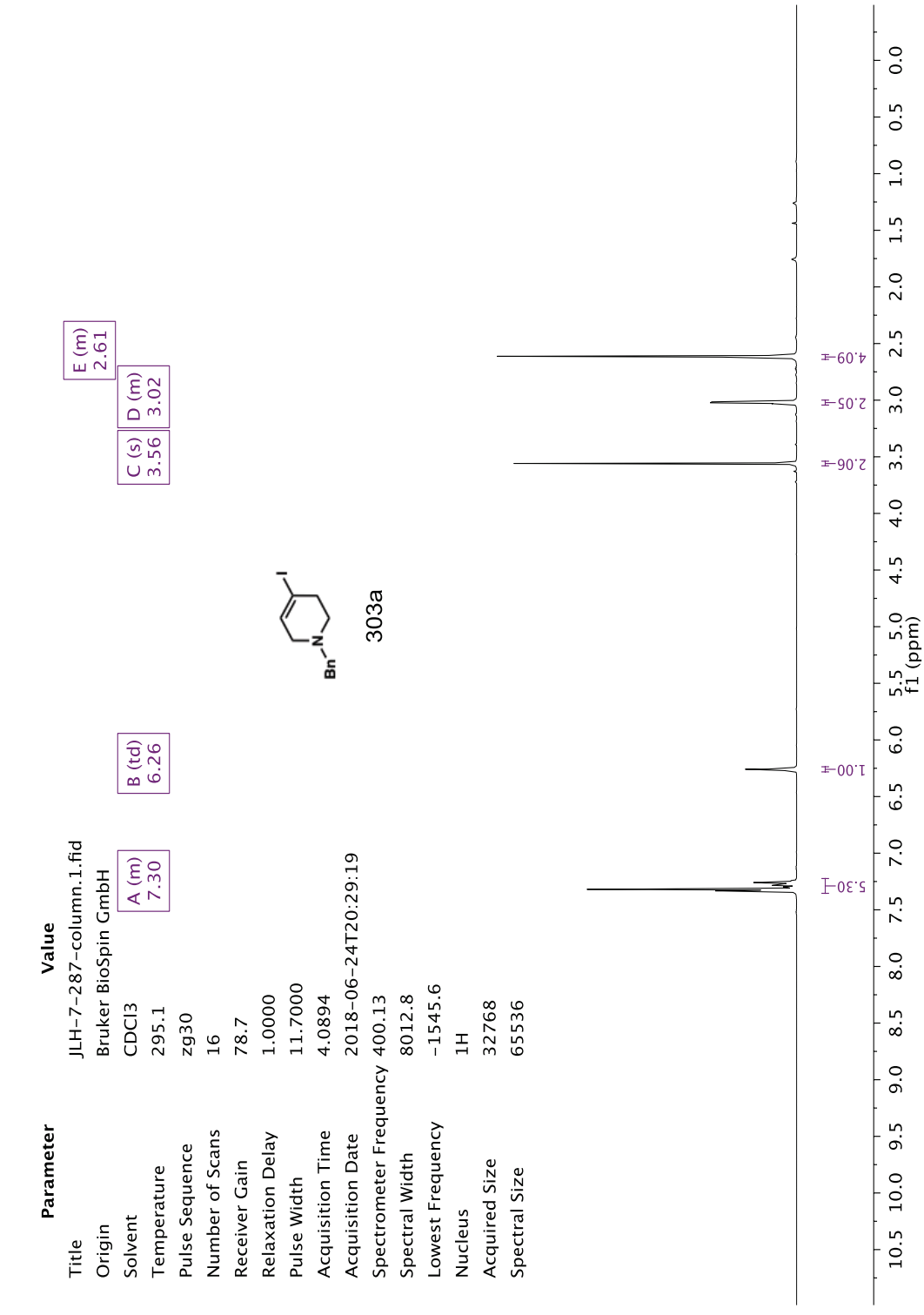

Parameter
Value
Title
JLH-7-293-column.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
zgpg30
Number of Scans
256
Receiver Gain
78.7
Relaxation Delay
1.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-06-29T06:39:48
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1947.6
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
302a
168.3
135.5
134.1
132.0
123.3
95.1
45.7
39.9
32.3
28.9
f1 (ppm)

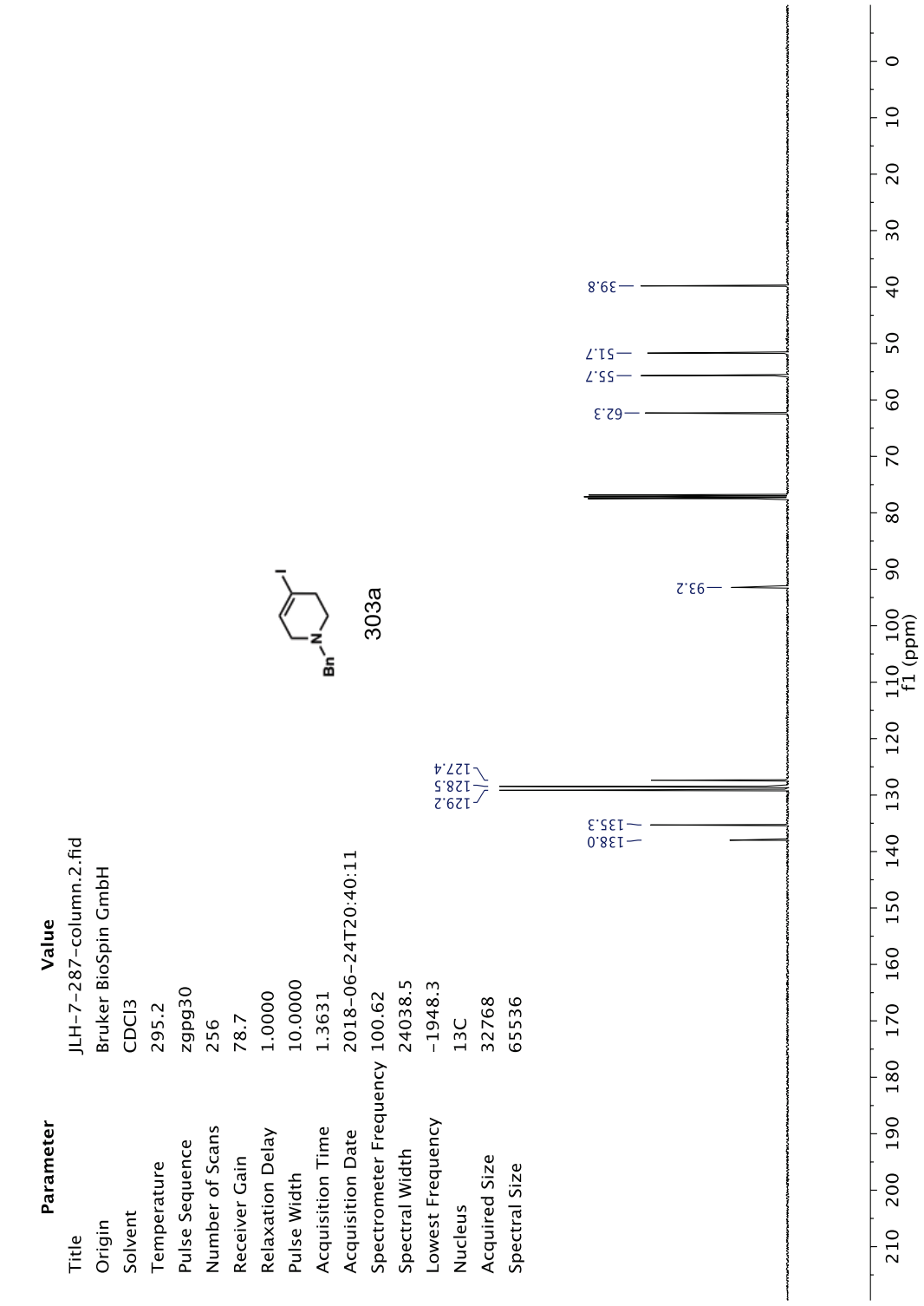

Parameter Value
Title JLH-8-042-column.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 78.7
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-09-04T19:32:36
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1545.4
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
Br
O
N
O
302b
B (m) 7.71
A (m) 7.82
C (dtd) 6.01
D (dddd) 4.42
F (m) 2.71
E (m) 2.94
G (m) 2.58
H (m) 2.19
I (m) 1.81
1.98
2.01
1.00
1.00
1.00
2.08
1.03
1.01
1.03
1.02
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

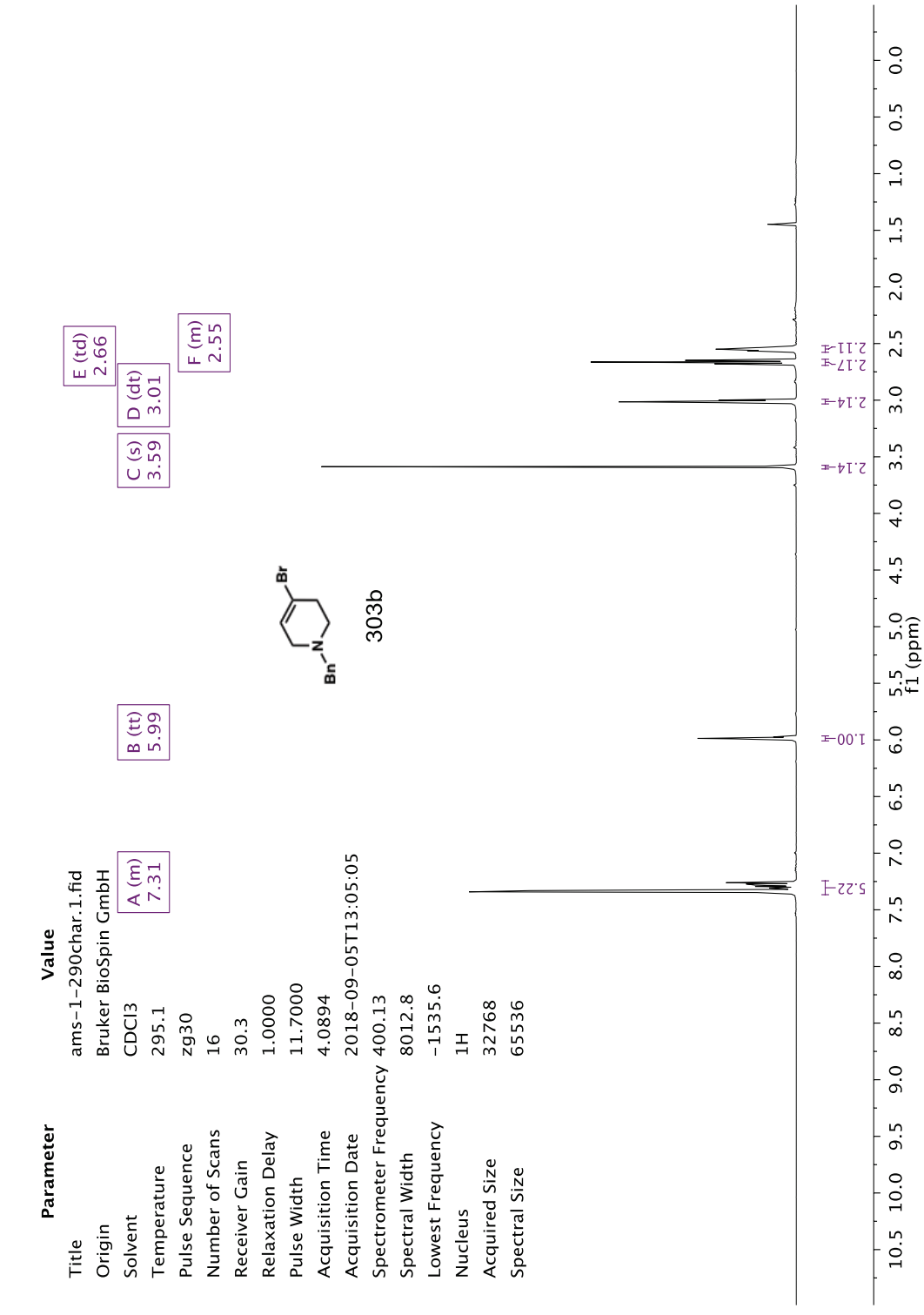

Parameter
Value
Title
JLH-8-042-column.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
zgpg30
Number of Scans
128
Receiver Gain
64.2
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-09-04T19:40:26
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1947.9
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Br
O
N
O
302b
168.3
134.1
132.0
127.0
123.3
121.3
46.0
35.4
30.4
27.9
f1 (ppm)

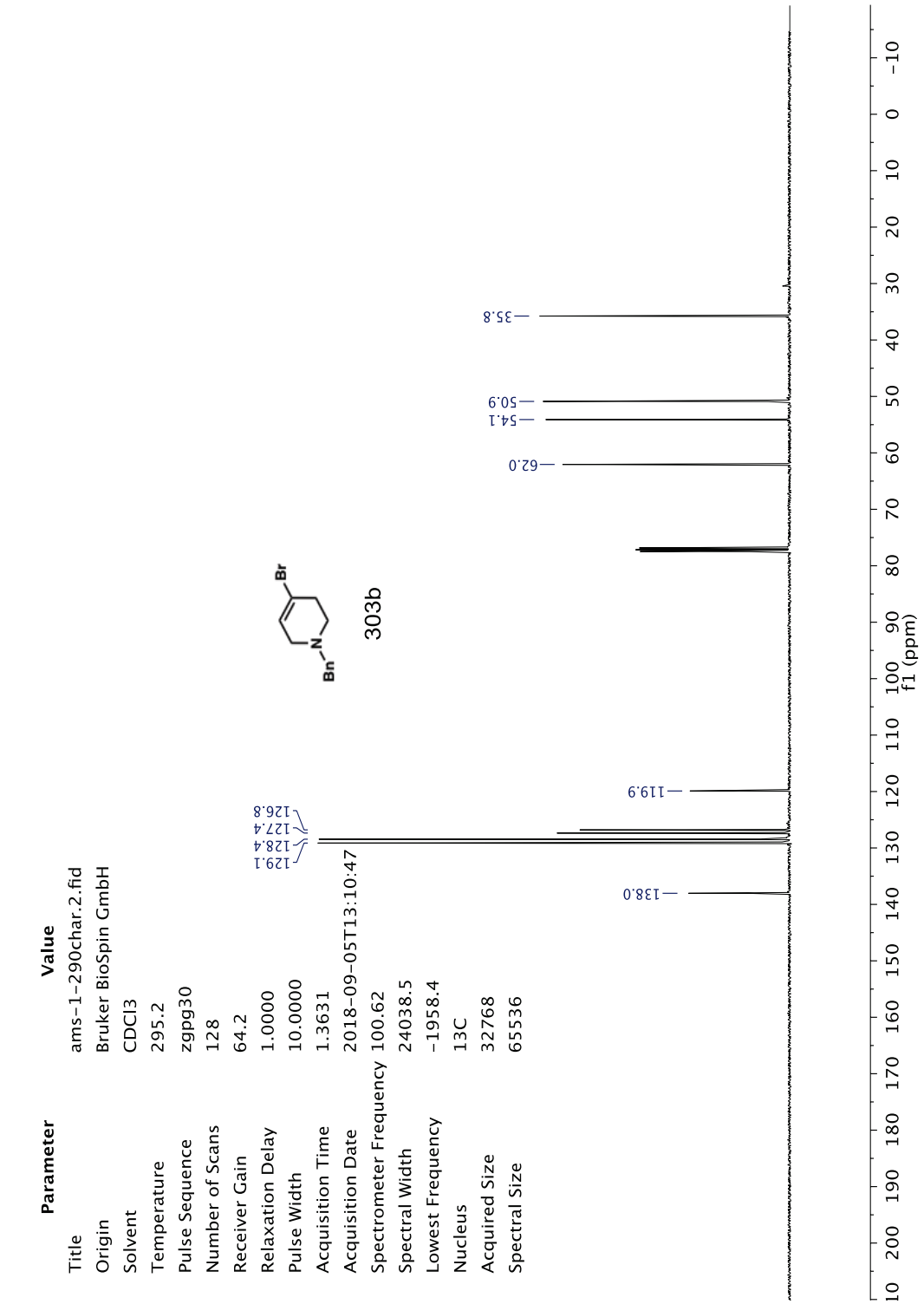

Parameter Value
Title JLH-8-043
Origin Varian
Solvent cdcl3
Temperature 25.0
Pulse Sequence s2pul
Number of Scans 8
Receiver Gain 36
Relaxation Delay 1.0000
Pulse Width 5.8000
Acquisition Time 3.0000
Acquisition Date 2018-09-05T04:05:00
Spectrometer Frequency 499.63
Spectral Width 8000.0
Lowest Frequency -1029.2
Nucleus 1H
Acquired Size 24000
Spectral Size 65536
A (m) 7.82
B (m) 7.71
C (dtt) 5.80
D (m) 4.41
E (dddt) 2.97
F (tdd) 2.72
G (m) 2.60
H (m) 2.45
I (m) 2.22
J (m) 1.86
Cl
O
N
O
302c
1.99
2.08
1.00
1.02
1.04
1.04
1.03
1.03
1.07
1.04
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

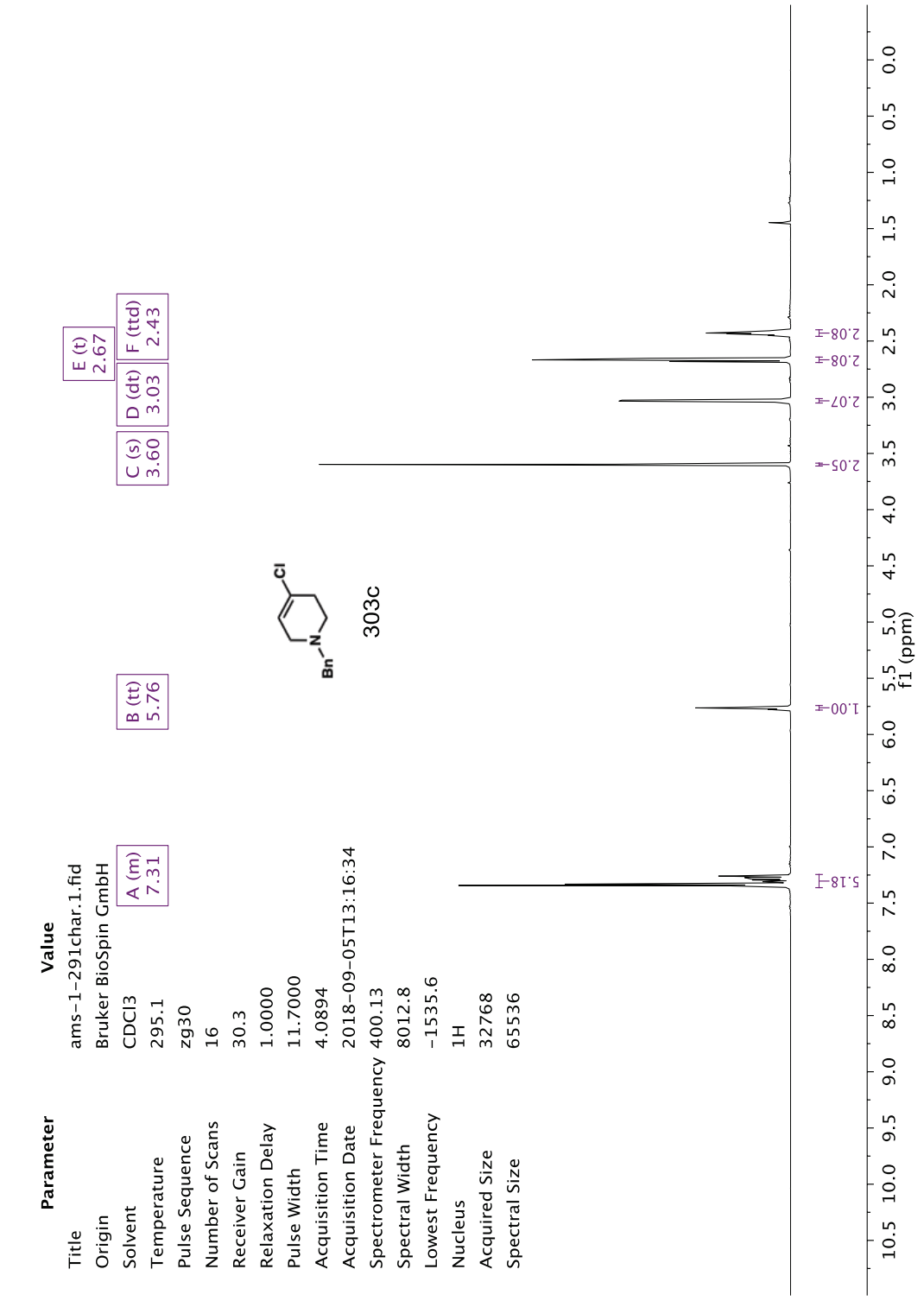

Parameter Value
Title JLH-8-043
Origin Varian
Solvent cdcl3
Temperature 25.0
Pulse Sequence s2pul
Number of Scans 256
Receiver Gain 30
Relaxation Delay 1.0000
Pulse Width 4.6125
Acquisition Time 1.0420
Acquisition Date 2018-09-05T04:05:49
Spectrometer Frequency 125.64
Spectral Width 31446.5
Lowest Frequency -1890.4
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Cl
O
N
O
302c
168.3
134.1
132.0
131.4
123.3
122.7
46.2
33.0
29.1
27.1
f1 (ppm)

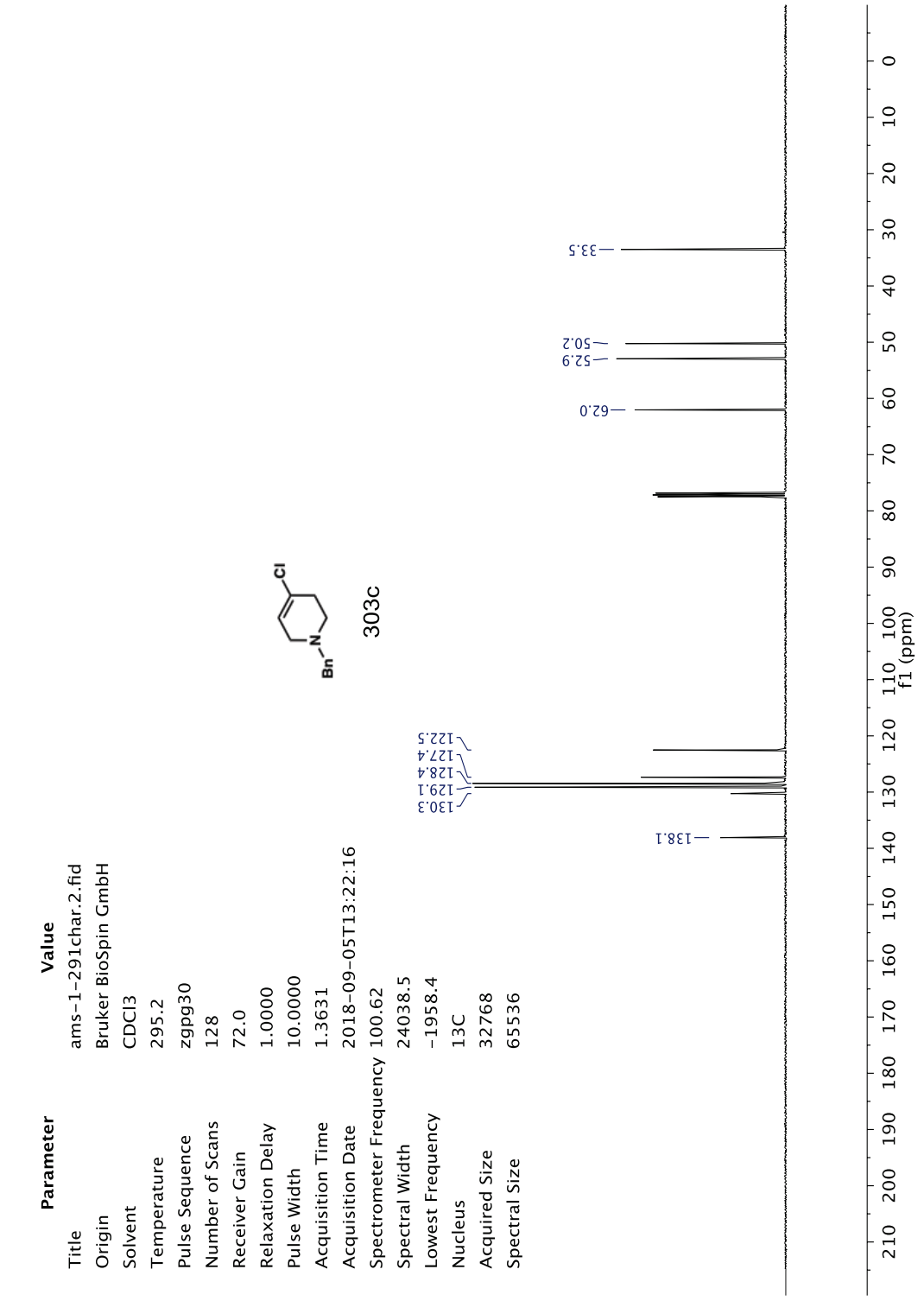

Parameter
Value
Title JLH-7-287-column.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 78.7
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-06-24T20:29:19
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1545.6
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
A (m) 7.30
B (td) 6.26
C (s) 3.56
D (m) 3.02
E (m) 2.61
Bn
303a
5.30
1.00
2.06
2.05
4.09
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

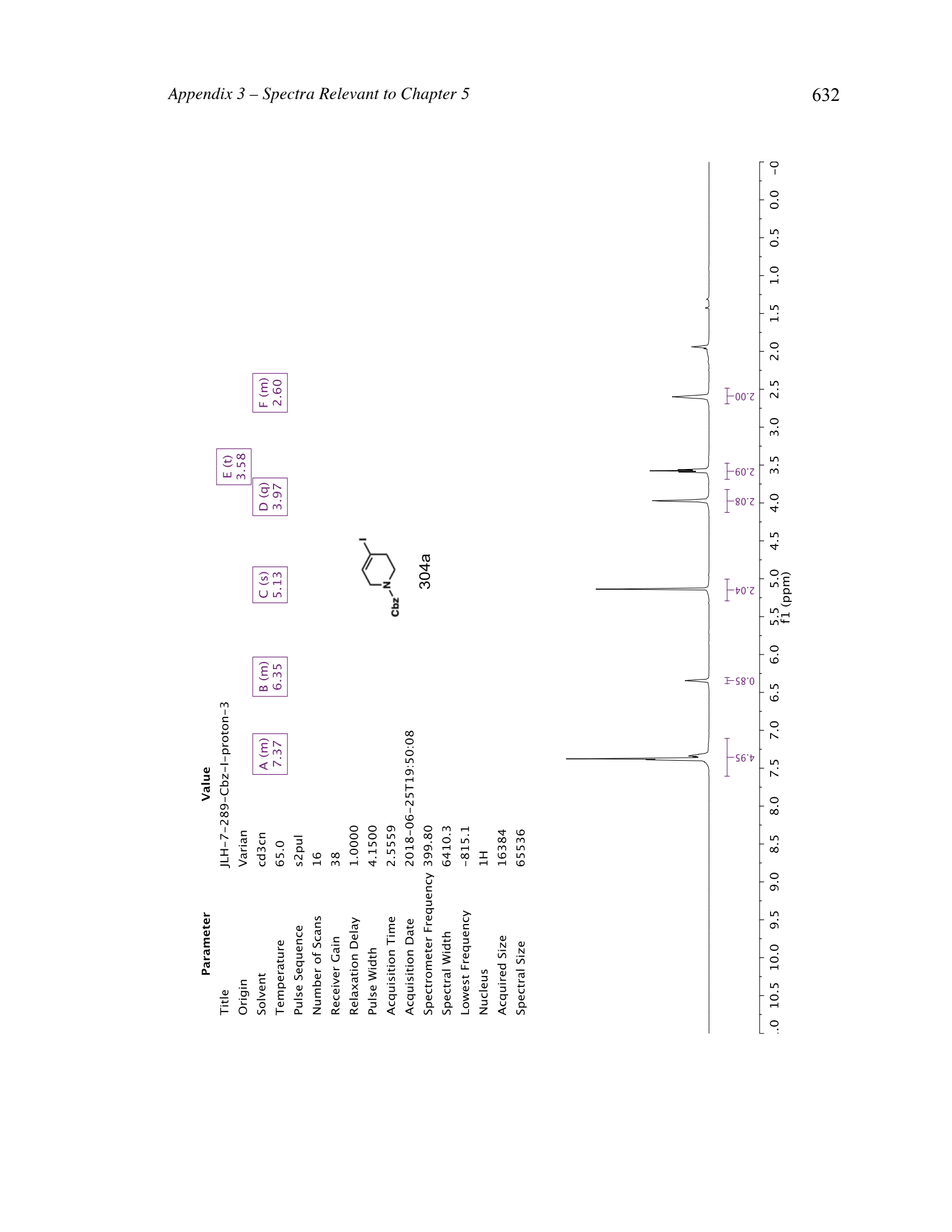

Parameter
Value
Title
JLH-7-287-column.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
zgpg30
Number of Scans
256
Receiver Gain
78.7
Relaxation Delay
1.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-06-24T20:40:11
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1948.3
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
303a
138.0
135.3
129.2
128.5
127.4
93.2
62.3
55.7
51.7
39.8
f1 (ppm)

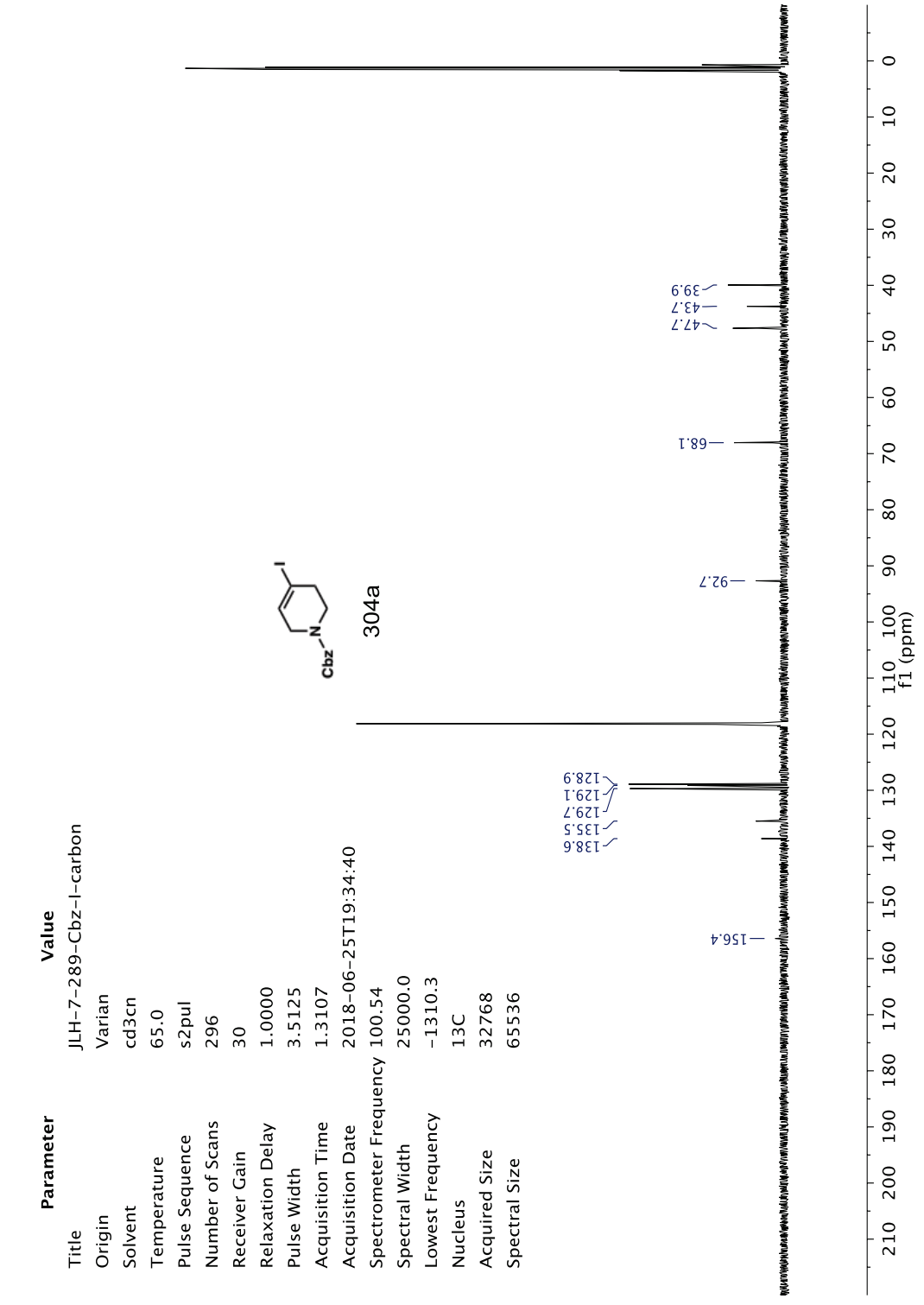

Parameter
Value
Title
ams-1-290char.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.1
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
30.3
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-09-05T13:05:05
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1535.6
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
A (m) 7.31
B (tt) 5.99
C (s) 3.59
D (dt) 3.01
E (td) 2.66
F (m) 2.55
303b
Br
N
Bn
5.22
1.00
2.14
2.14
2.14
2.17
2.11
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

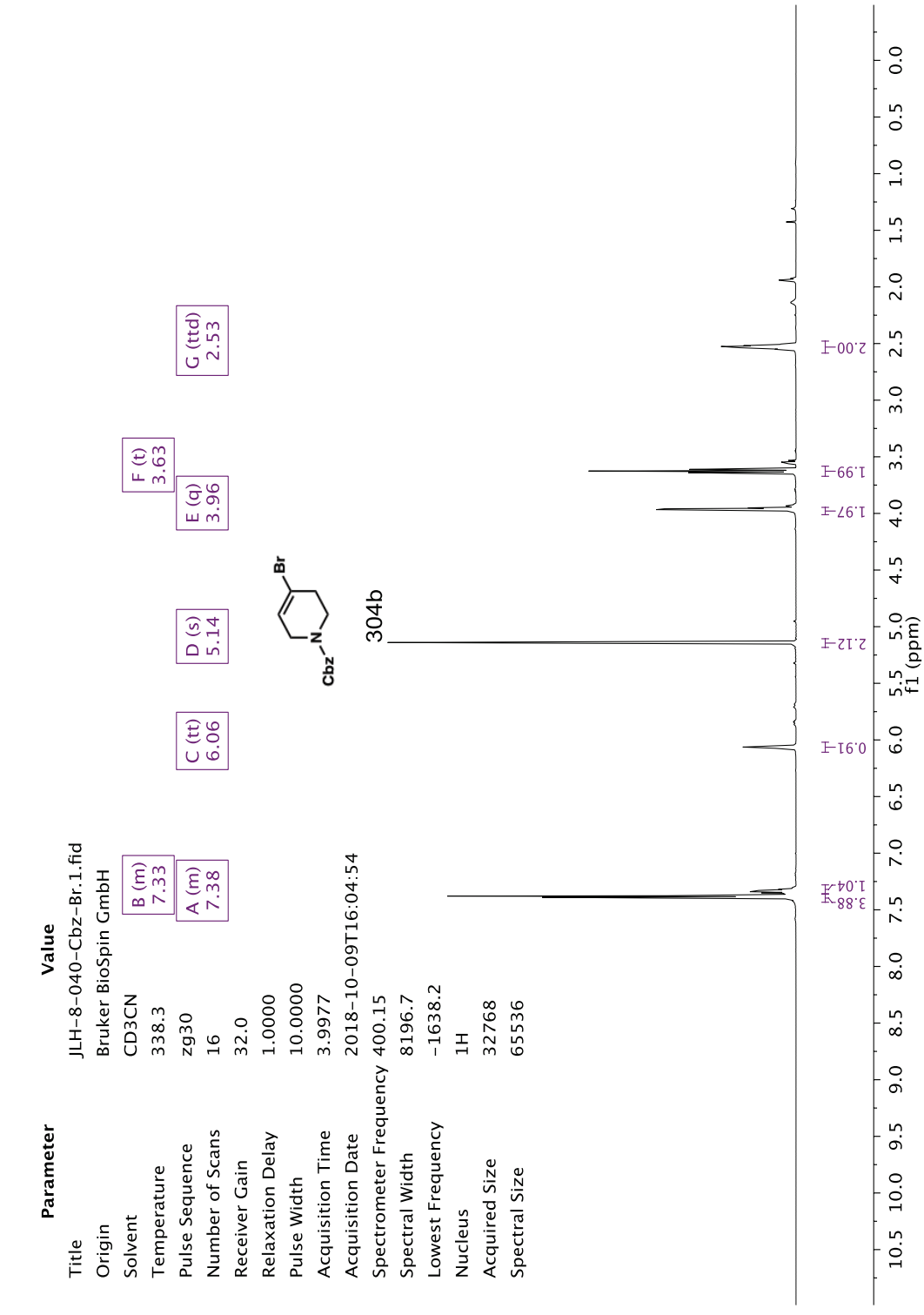

Parameter Value
Title ams-1-290char.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 64.2
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-09-05T13:10:47
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1958.4
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
138.0
129.1
128.4
127.4
126.8
119.9
62.0
54.1
50.9
35.8
Br
N
Bn
303b
f1 (ppm)

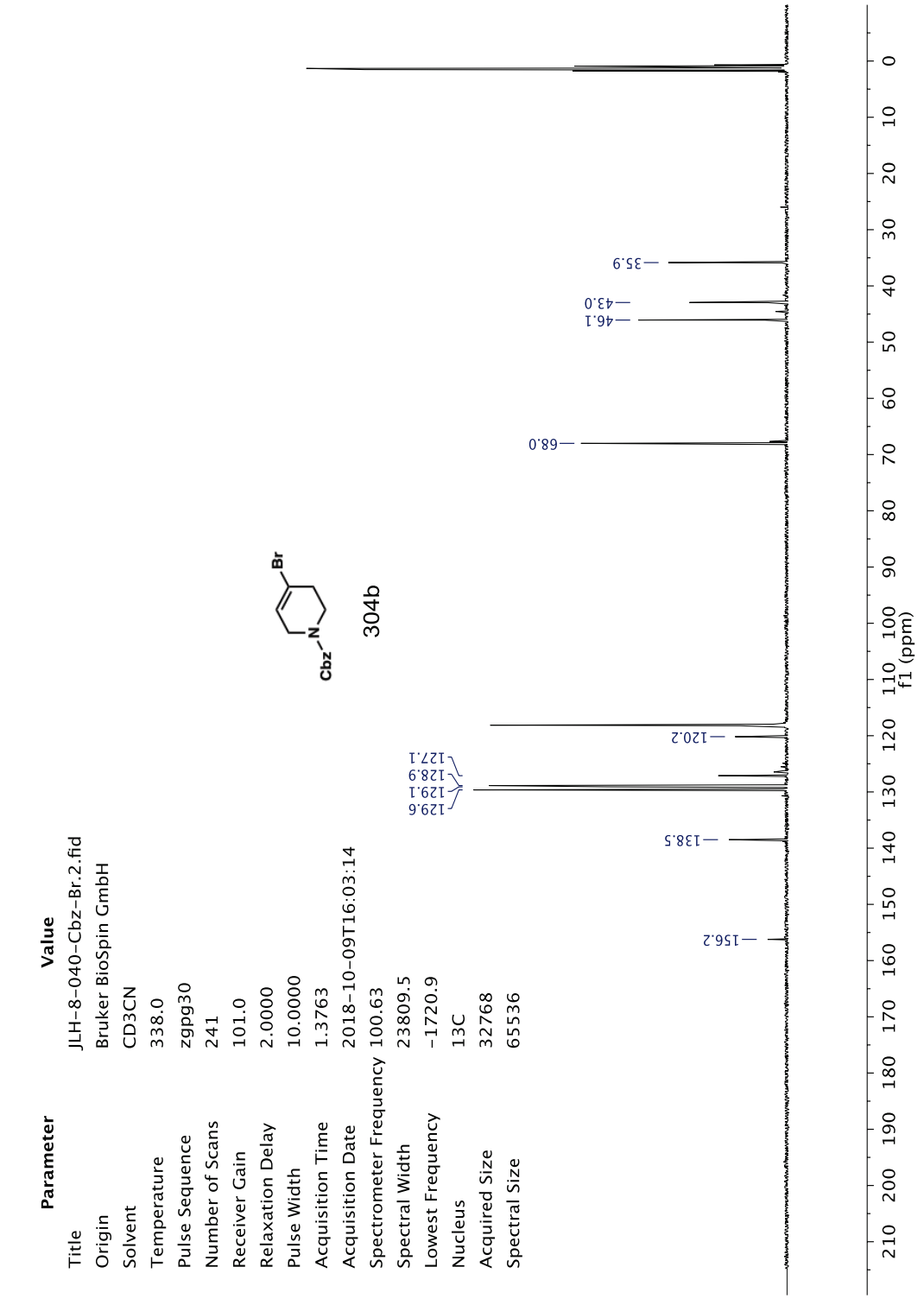

Parameter
Value
Title
ams-1-291char.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.1
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
30.3
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-09-05T13:16:34
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1535.6
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
A (m) 7.31
B (tt) 5.76
C (s) 3.60
D (dt) 3.03
E (t) 2.67
F (ttd) 2.43
Cl
N
Bn
303c
5.18
1.00
2.05
2.07
2.08
2.08
f1 (ppm)

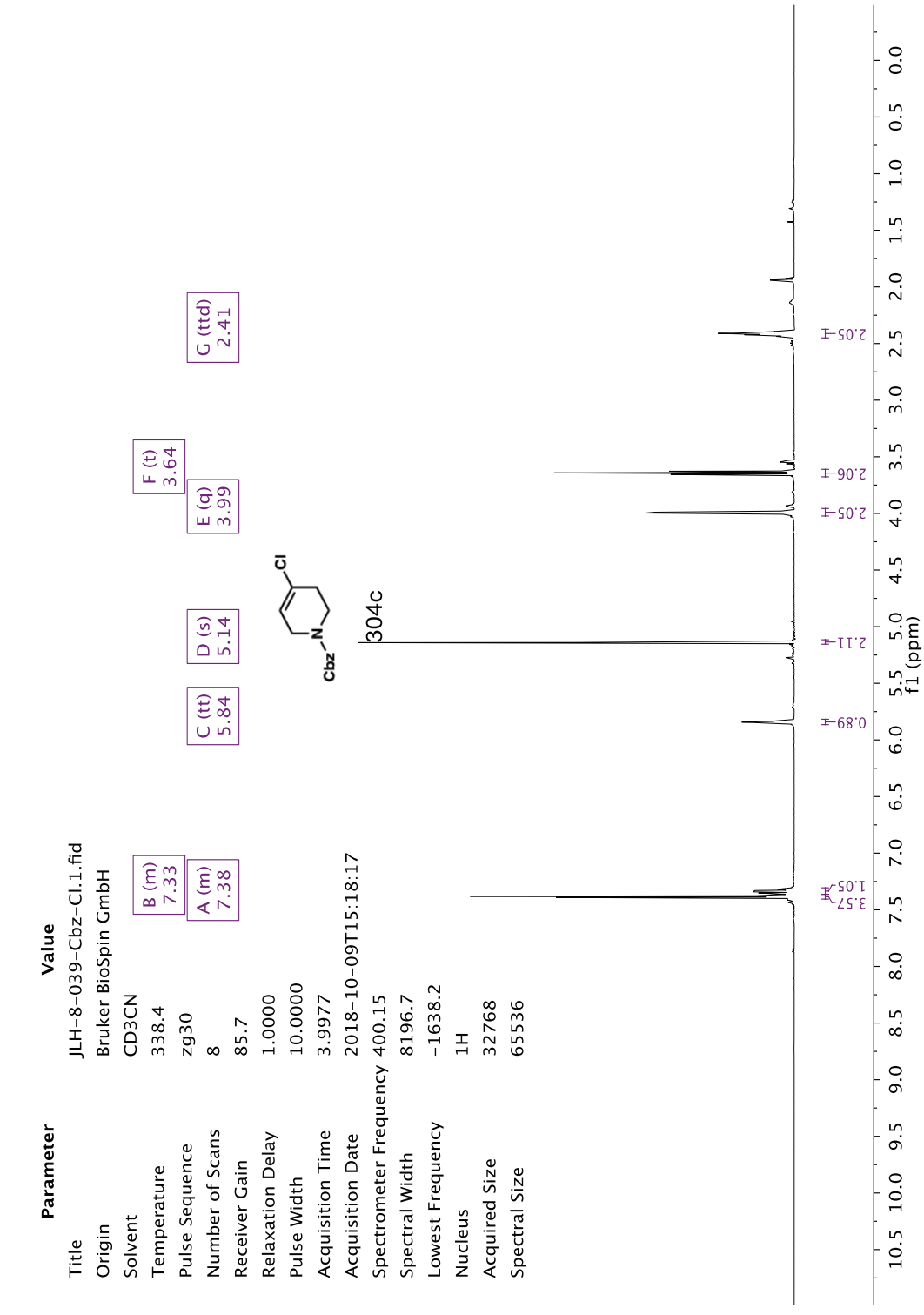

Parameter
Value
Title ams-1-291char.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 72.0
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-09-05T13:22:16
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1958.4
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Cl
N
Bn
303c
138.1
130.3
129.1
128.4
127.4
122.5
62.0
52.9
50.2
33.5
f1 (ppm)

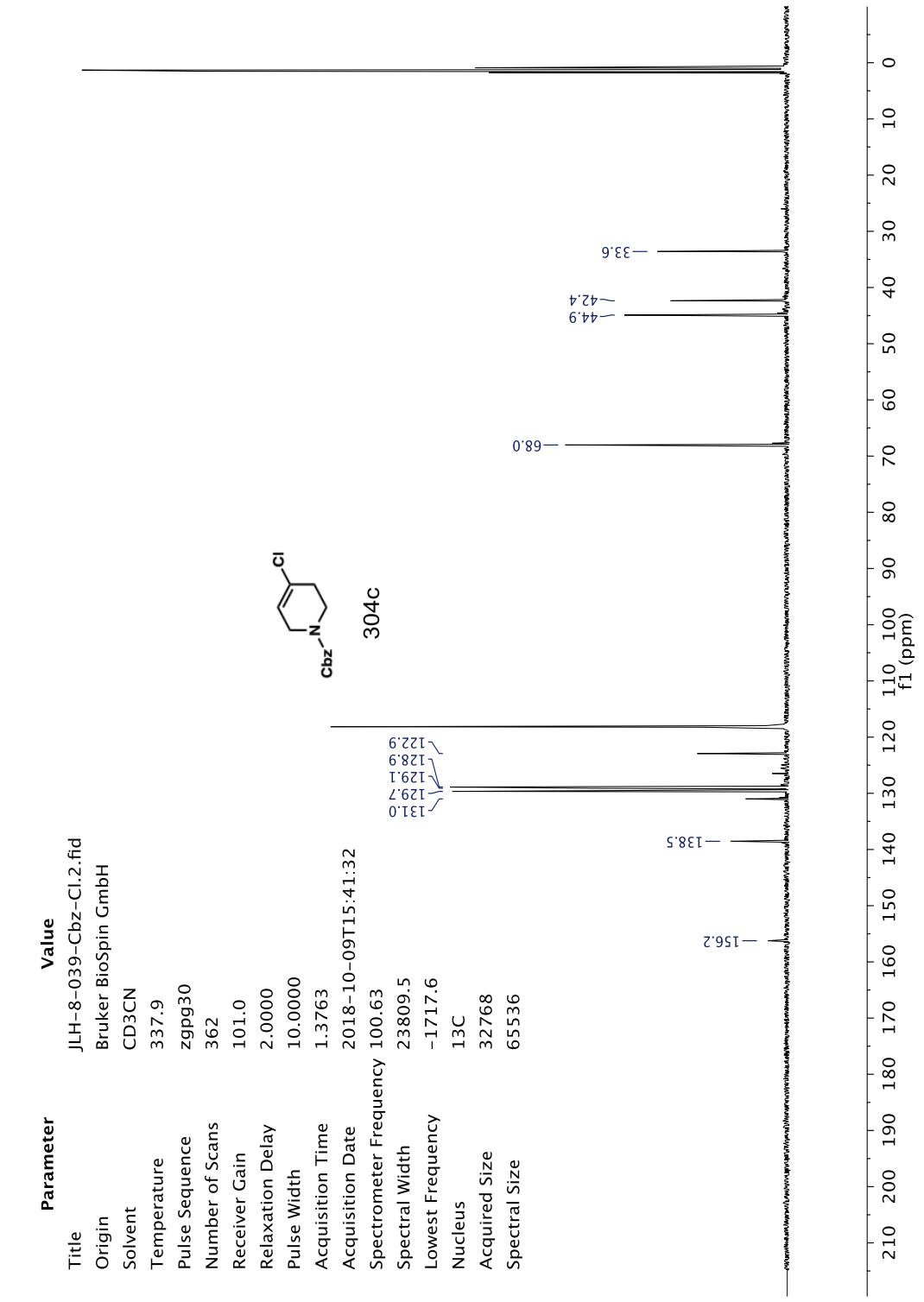

Parameter
Value
Title JLH-7-289-Cbz-I-proton-3
Origin Varian
Solvent cd3cn
Temperature 65.0
Pulse Sequence s2pul
Number of Scans 16
Receiver Gain 38
Relaxation Delay 1.0000
Pulse Width 4.1500
Acquisition Time 2.5559
Acquisition Date 2018-06-25T19:50:08
Spectrometer Frequency 399.80
Spectral Width 6410.3
Lowest Frequency -815.1
Nucleus 1H
Acquired Size 16384
Spectral Size 65536
A (m) 7.37
B (m) 6.35
C (s) 5.13
D (q) 3.97
E (t) 3.58
F (m) 2.60
Cbz
304a
4.95
0.85
2.04
2.08
2.09
2.00
f1 (ppm)

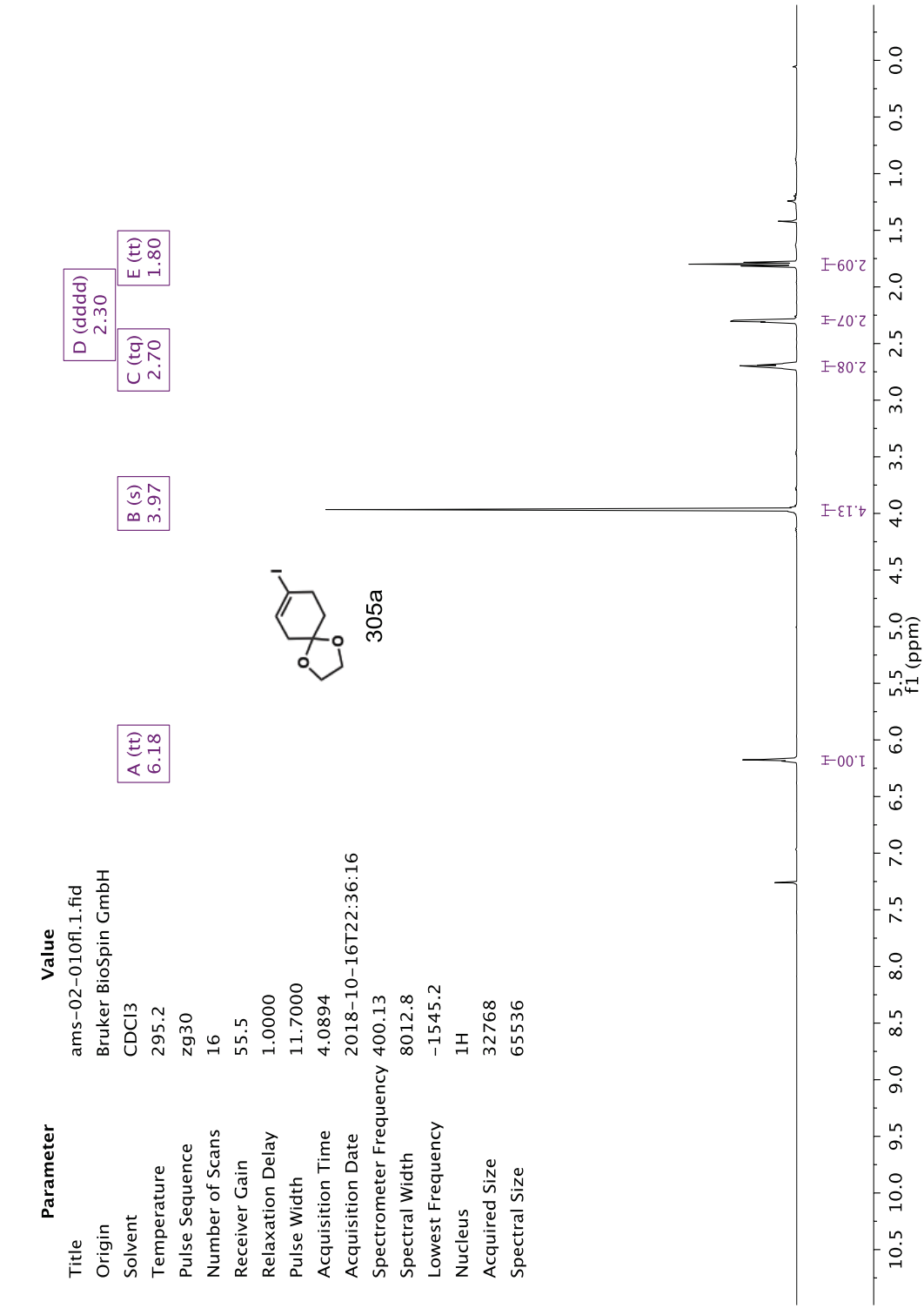

Parameter Value
Title JLH-7-289-Cbz-I-carbon
Origin Varian
Solvent cd3cn
Temperature 65.0
Pulse Sequence s2pul
Number of Scans 296
Receiver Gain 30
Relaxation Delay 1.0000
Pulse Width 3.5125
Acquisition Time 1.3107
Acquisition Date 2018-06-25T19:34:40
Spectrometer Frequency 100.54
Spectral Width 25000.0
Lowest Frequency -1310.3
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
304a
Cbz
156.4
138.6
135.5
129.7
129.1
128.9
92.7
68.1
47.7
43.7
39.9
f1 (ppm)

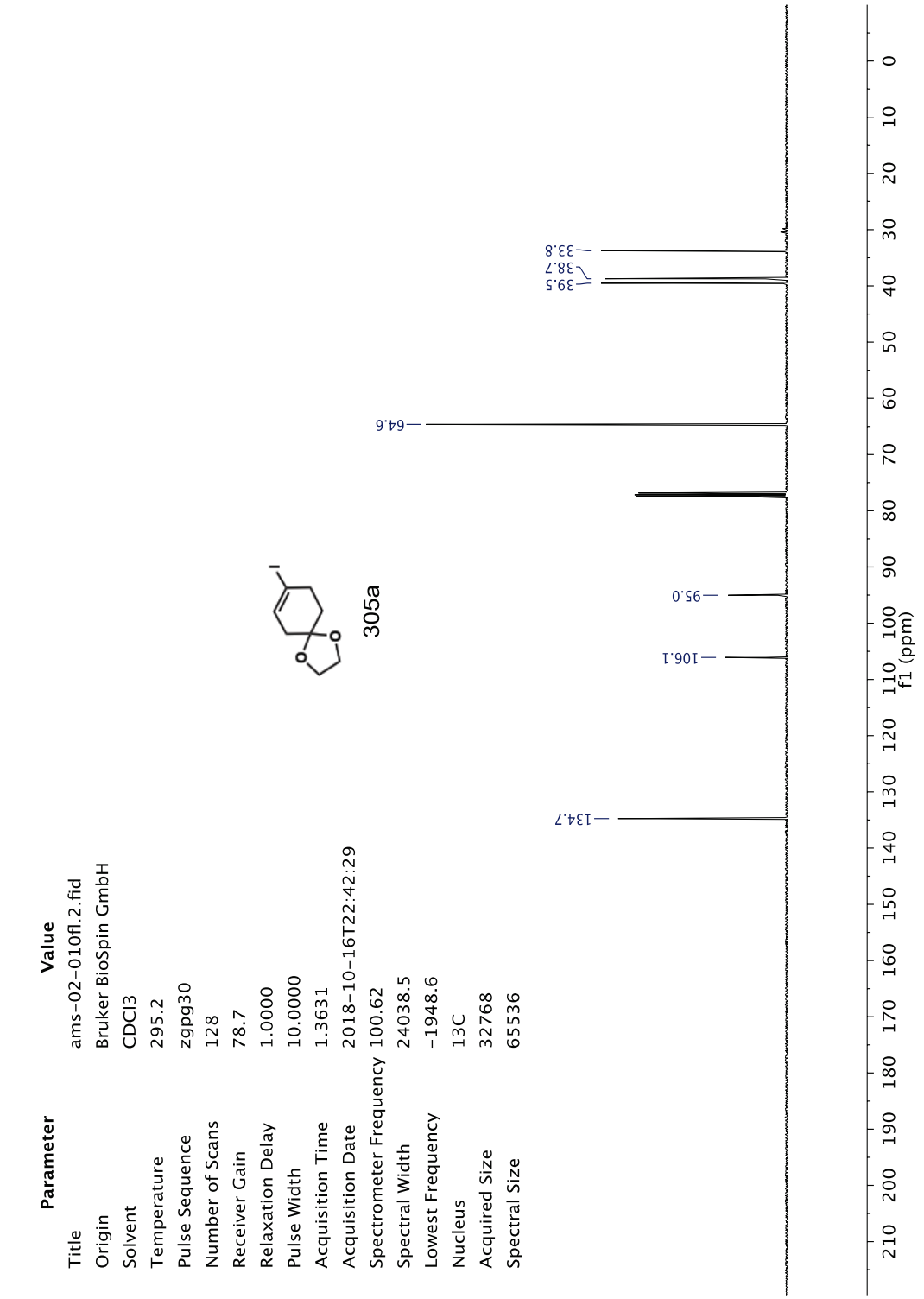

Parameter
Value
Title
JLH-8-040-Cbz-Br.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CD3CN
Temperature
338.3
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
32.0
Relaxation Delay
1.0000
Pulse Width
10.0000
Acquisition Time
3.9977
Acquisition Date
2018-10-09T16:04:54
Spectrometer Frequency
400.15
Spectral Width
8196.7
Lowest Frequency
-1638.2
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
B (m) 7.33
A (m) 7.38
C (tt) 6.06
D (s) 5.14
E (q) 3.96
F (t) 3.63
G (ttd) 2.53
Br
Cbz
N
304b
3.88
1.04
0.91
2.12
1.97
1.99
2.00
f1 (ppm)

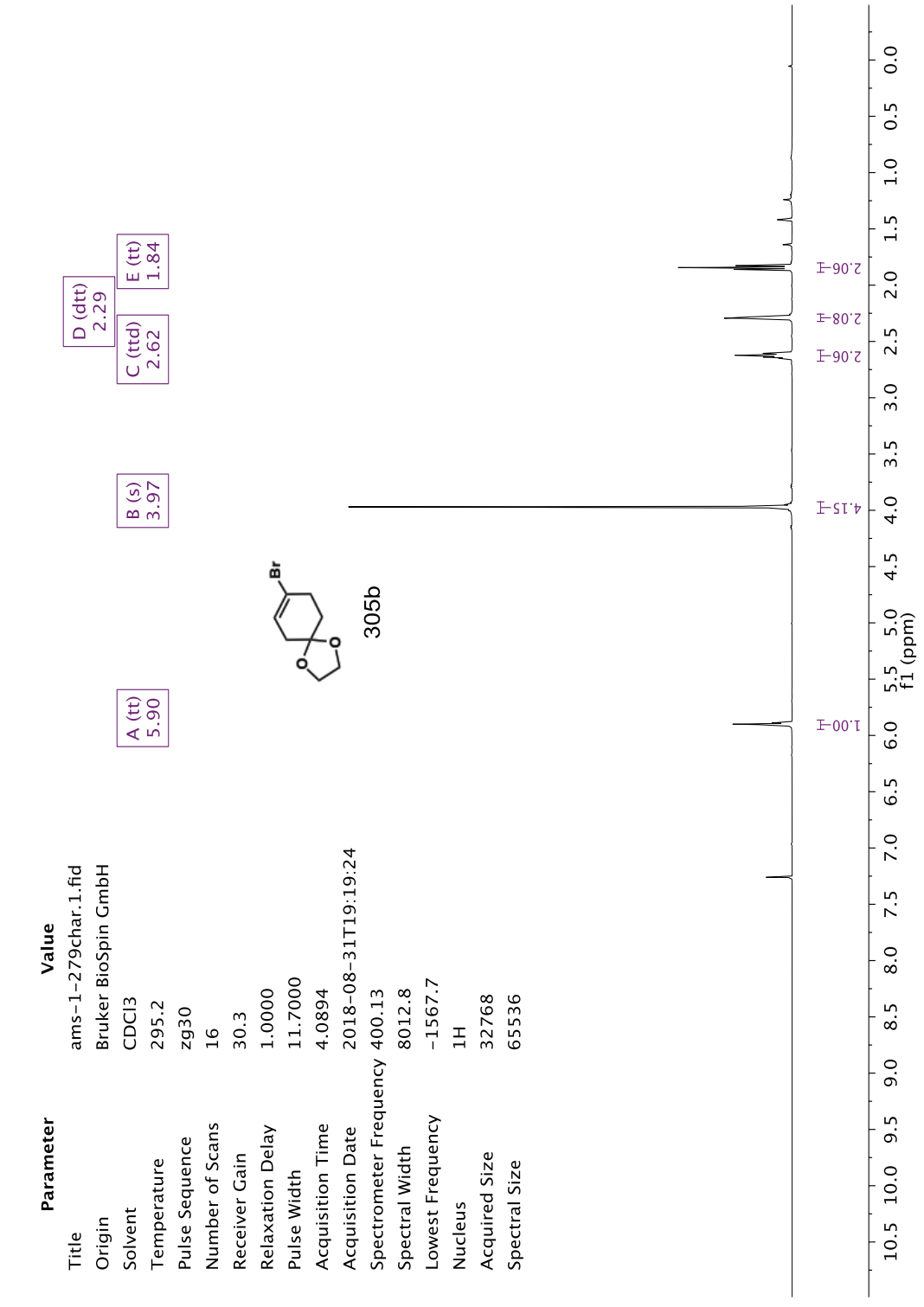

Parameter Value
Title JLH-8-040-Cbz-Br.2.fid
Origin Bruker BioSpin GmbH
Solvent CD3CN
Temperature 338.0
Pulse Sequence zgpg30
Number of Scans 241
Receiver Gain 101.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3763
Acquisition Date 2018-10-09T16:03:14
Spectrometer Frequency 100.63
Spectral Width 23809.5
Lowest Frequency -1720.9
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Br
N
Cbz
304b
156.2
138.5
129.6
129.1
128.9
127.1
120.2
68.0
46.1
43.0
35.9
f1 (ppm)

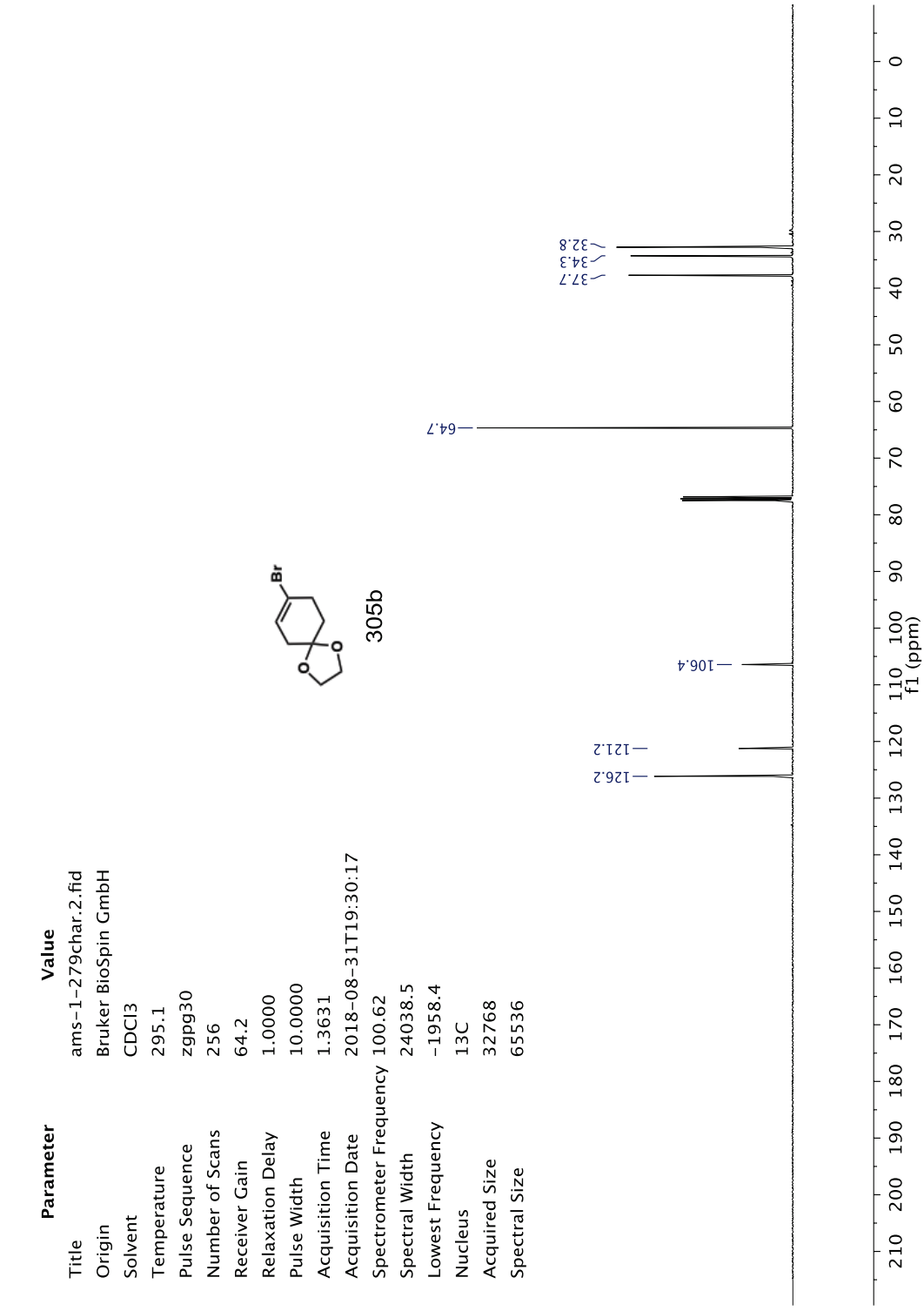

Parameter
Value
Title JLH-8-039-Cbz-Cl.1.fid
Origin Bruker BioSpin GmbH
Solvent CD3CN
Temperature 338.4
Pulse Sequence zg30
Number of Scans 8
Receiver Gain 85.7
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 3.9977
Acquisition Date 2018-10-09T15:18:17
Spectrometer Frequency 400.15
Spectral Width 8196.7
Lowest Frequency -1638.2
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
B (m) 7.33
A (m) 7.38
C (tt) 5.84
D (s) 5.14
E (q) 3.99
F (t) 3.64
G (ttd) 2.41
Cl
N
Cbz
304c
3.57
1.05
0.89
2.11
2.05
2.06
2.05
f1 (ppm)

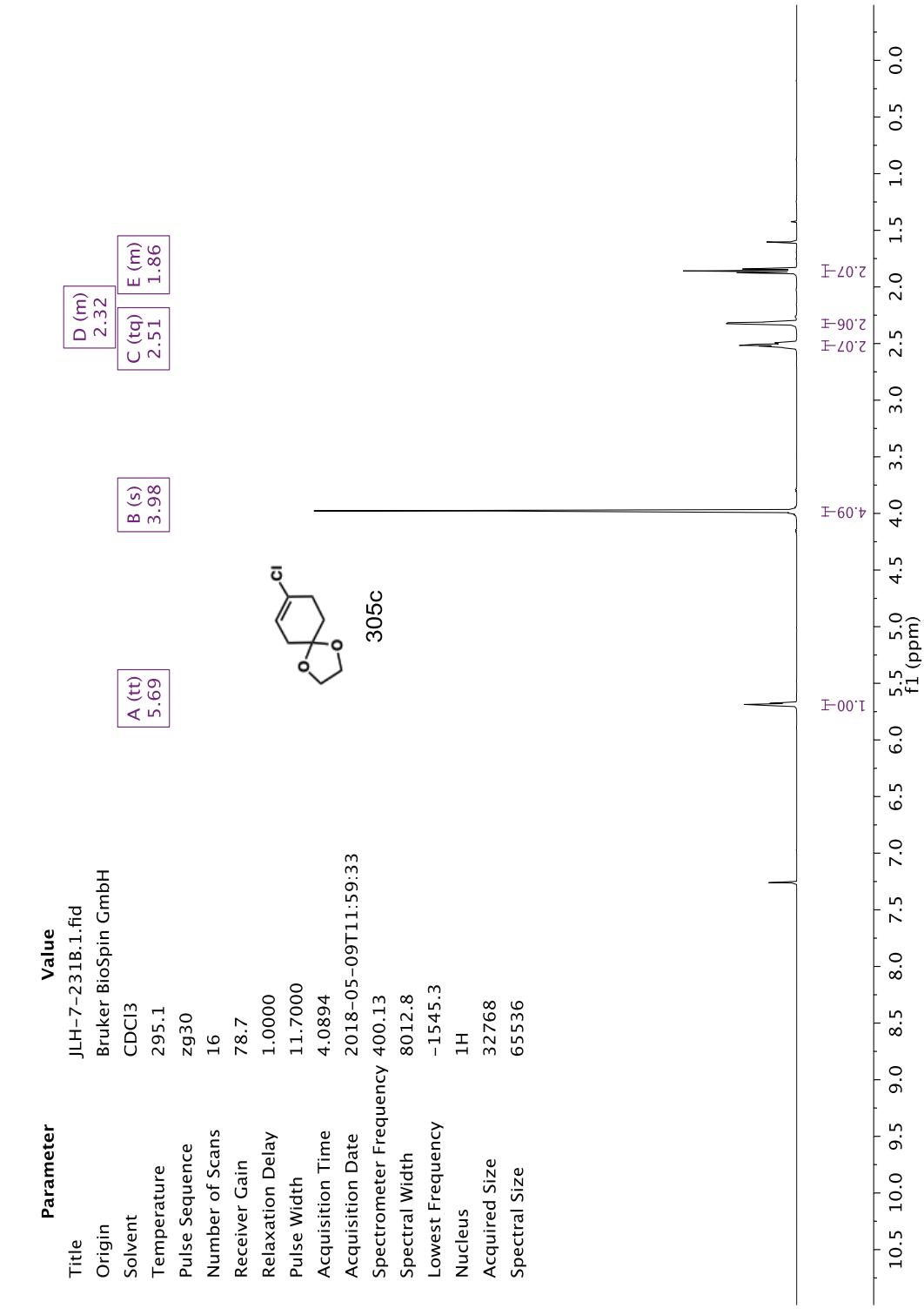

Parameter
Value
Title JLH-8-039-Cbz-Cl.2.fid
Origin Bruker BioSpin GmbH
Solvent CD3CN
Temperature 337.9
Pulse Sequence zgpg30
Number of Scans 362
Receiver Gain 101.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3763
Acquisition Date 2018-10-09T15:41:32
Spectrometer Frequency 100.63
Spectral Width 23809.5
Lowest Frequency -1717.6
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Cl
N
Cbz
304c
156.2
138.5
131.0
129.7
129.1
128.9
122.9
68.0
44.9
42.4
33.6
f1 (ppm)

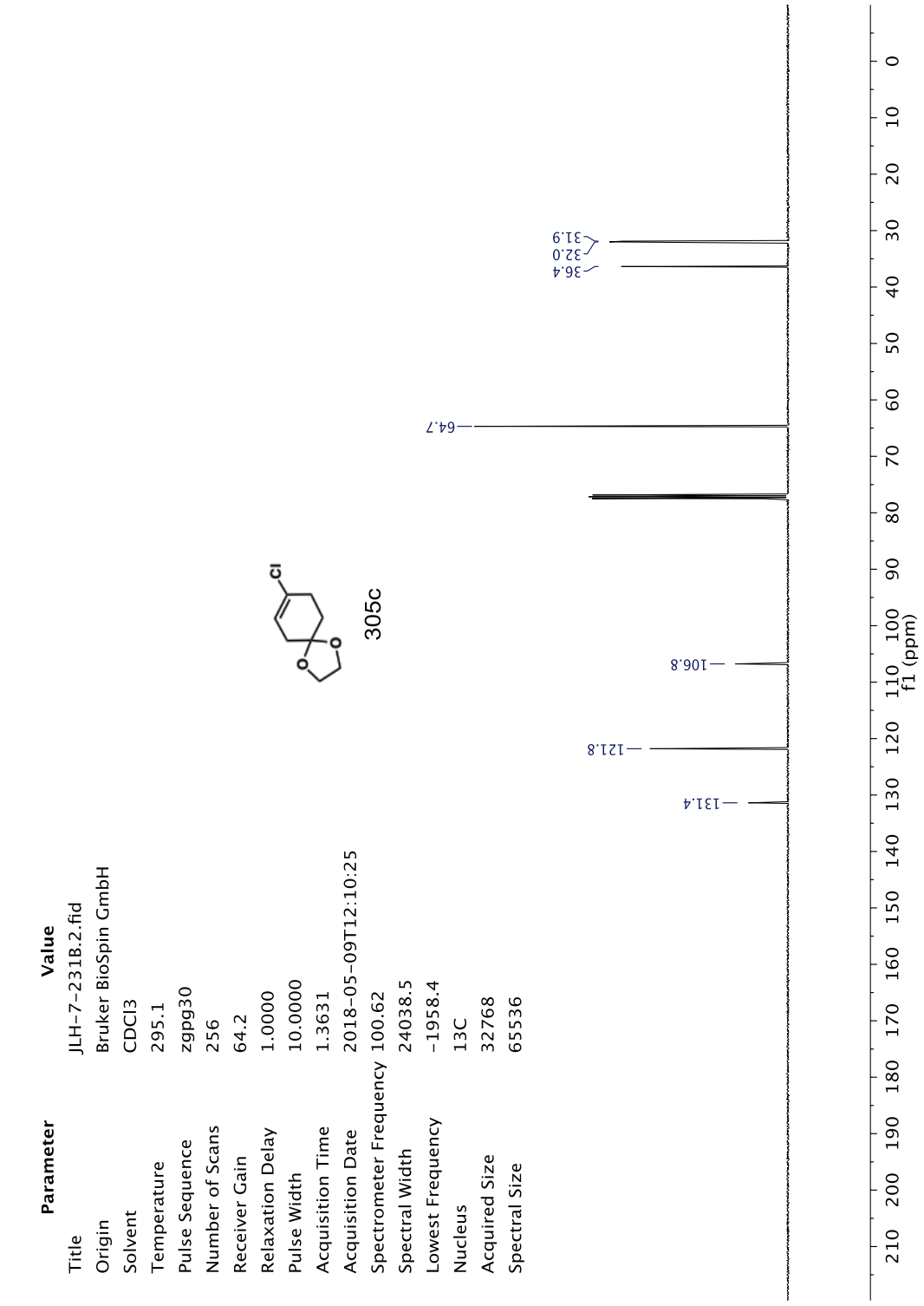

Parameter
Value
Title
ams-02-010fl.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
55.5
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-10-16T22:36:16
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1545.2
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
A (tt) 6.18
B (s) 3.97
C (tq) 2.70
D (dddd) 2.30
E (tt) 1.80
305a
1.00
4.13
2.08
2.07
2.09
f1 (ppm)

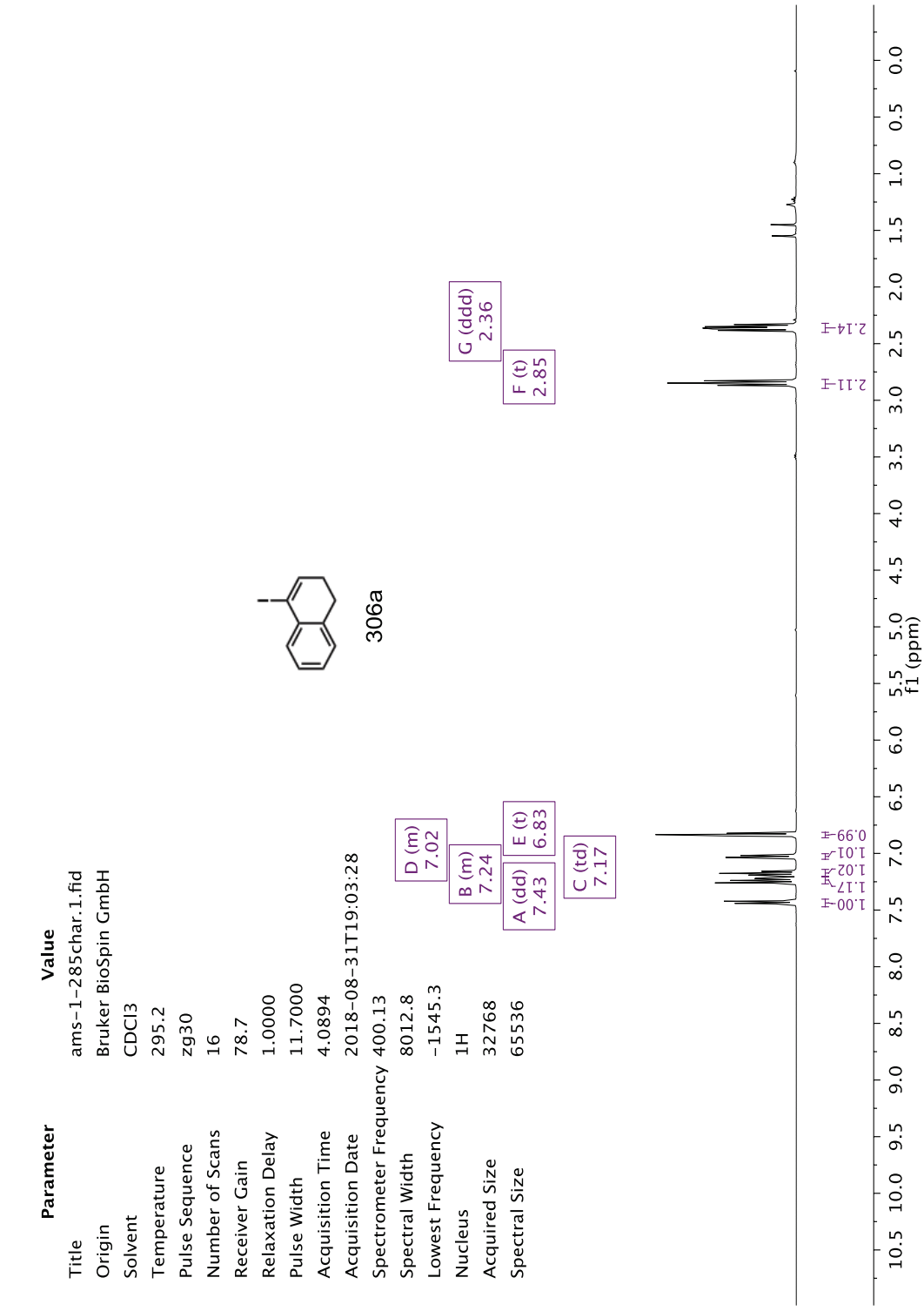

Parameter
Value
Title
ams-02-010fl.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
zgpg30
Number of Scans
128
Receiver Gain
78.7
Relaxation Delay
1.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-10-16T22:42:29
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1948.6
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
305a
134.7
106.1
95.0
64.6
39.5
38.7
33.8
f1 (ppm)

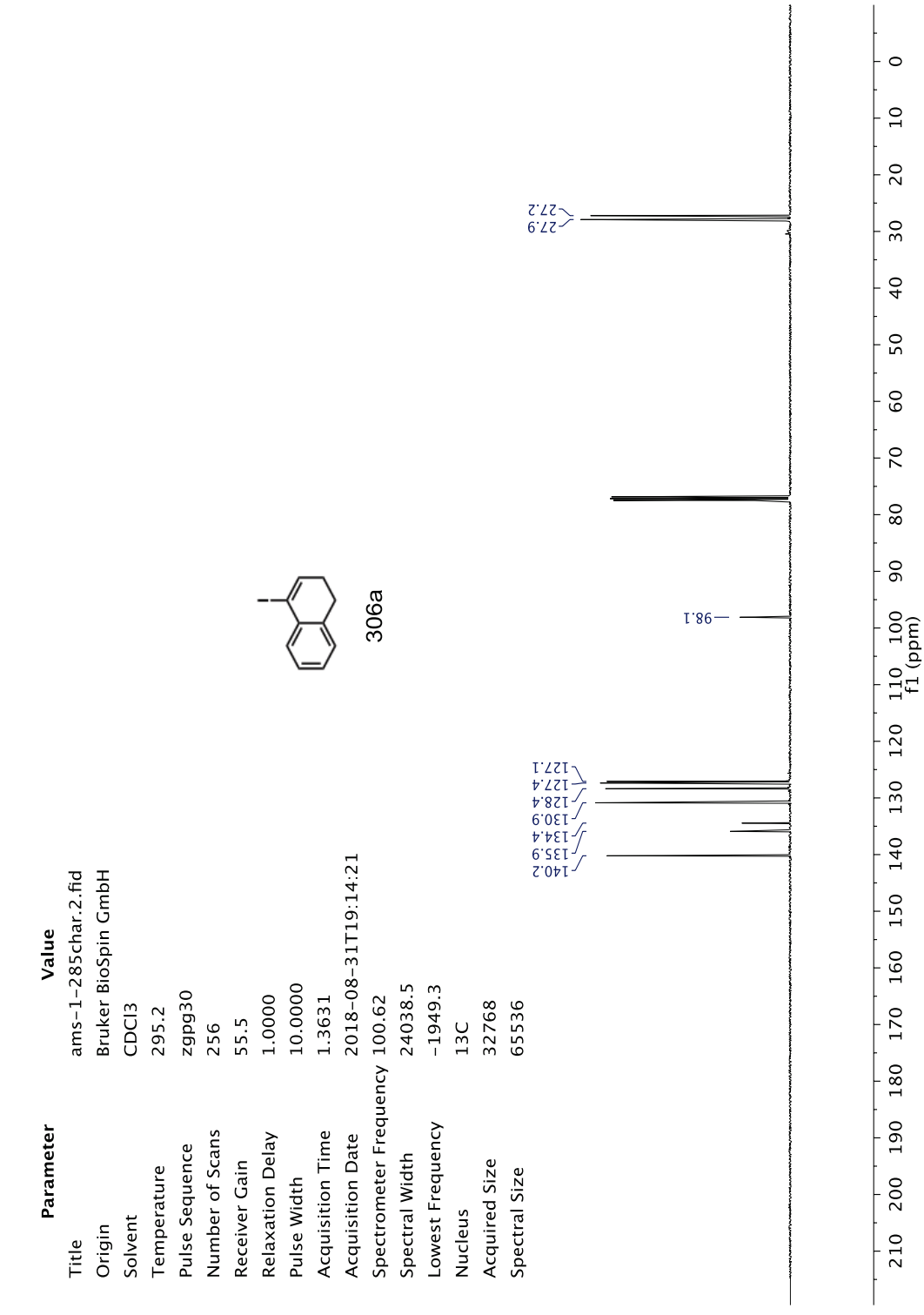

Parameter
Value
Title
ams-1-279char.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
30.3
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-08-31T19:19:24
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1567.7
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
A (tt)
5.90
B (s)
3.97
C (ttd)
2.62
D (dtt)
2.29
E (tt)
1.84
Br
O
O
305b
1.00
4.15
2.06
2.08
2.06
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

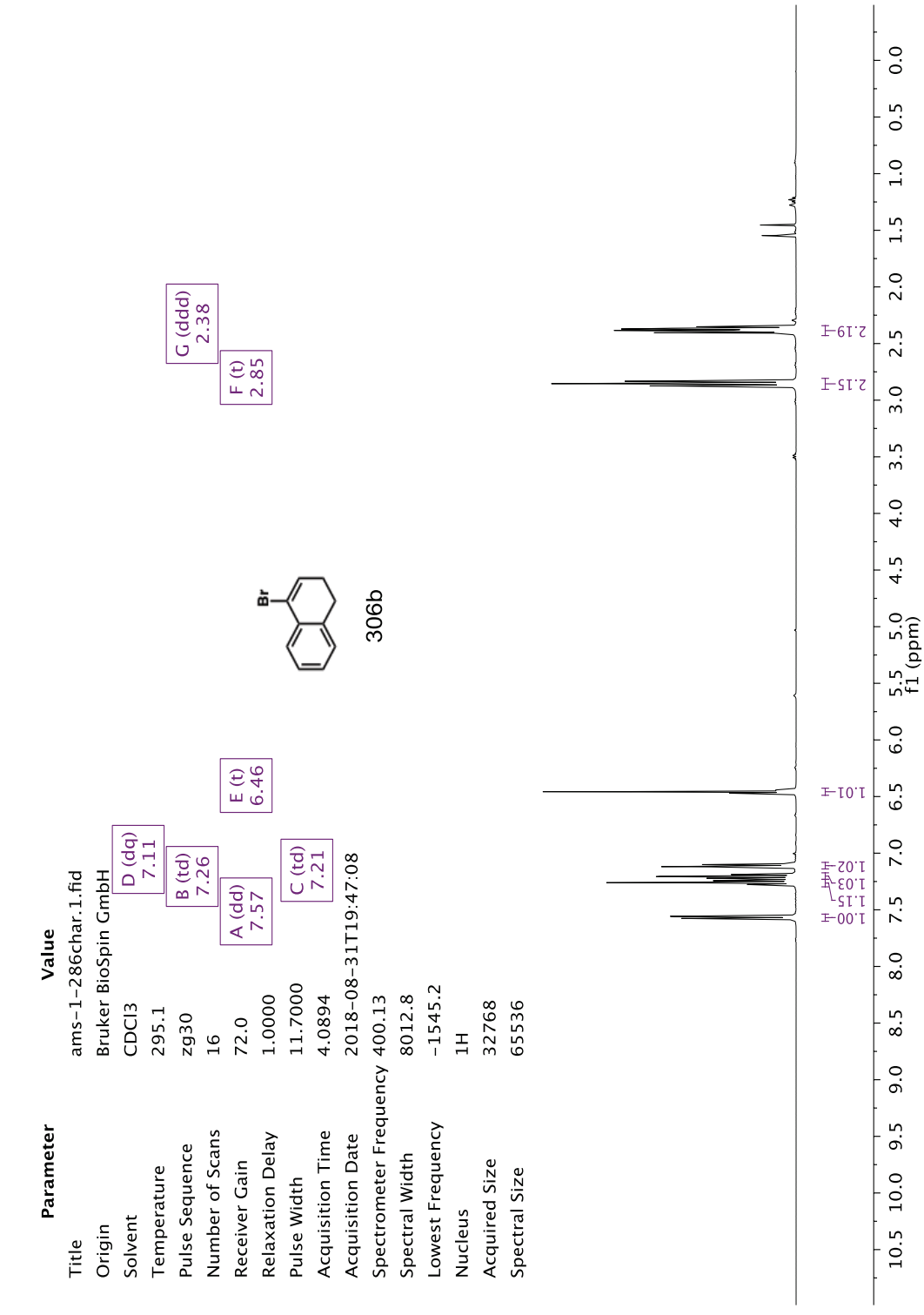

Parameter Value
Title ams-1-279char.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zgpg30
Number of Scans 256
Receiver Gain 64.2
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-08-31T19:30:17
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1958.4
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Br
O
O
305b
126.2
121.2
106.4
64.7
37.7
34.3
32.8
f1 (ppm)

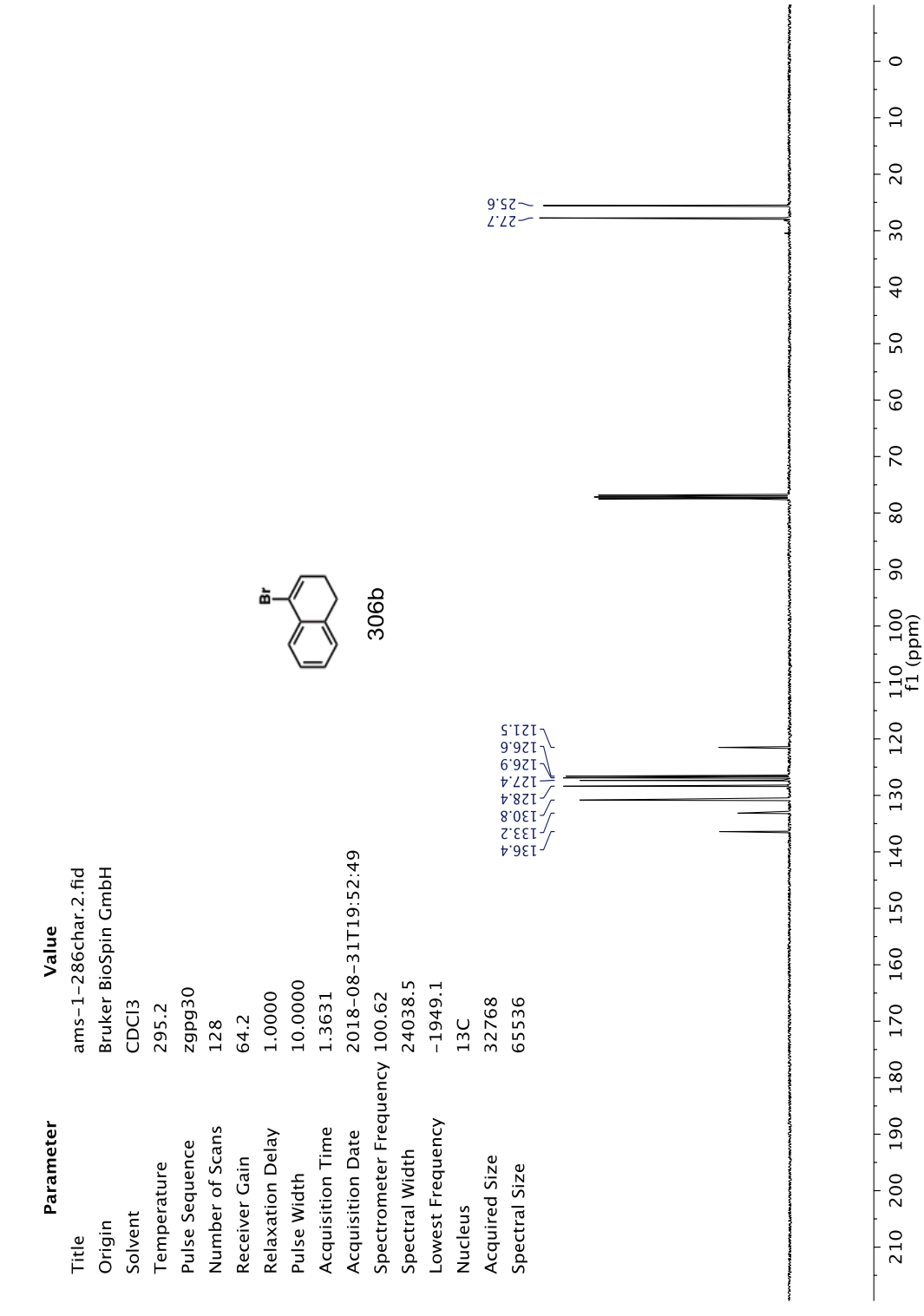

Parameter
Value
Title
JLH-7-231B.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.1
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
78.7
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-05-09T11:59:33
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1545.3
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
A (tt) 5.69
B (s) 3.98
C (tq) 2.51
D (m) 2.32
E (m) 1.86
Cl
O
O
305c
1.00
4.09
2.07
2.06
2.07
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

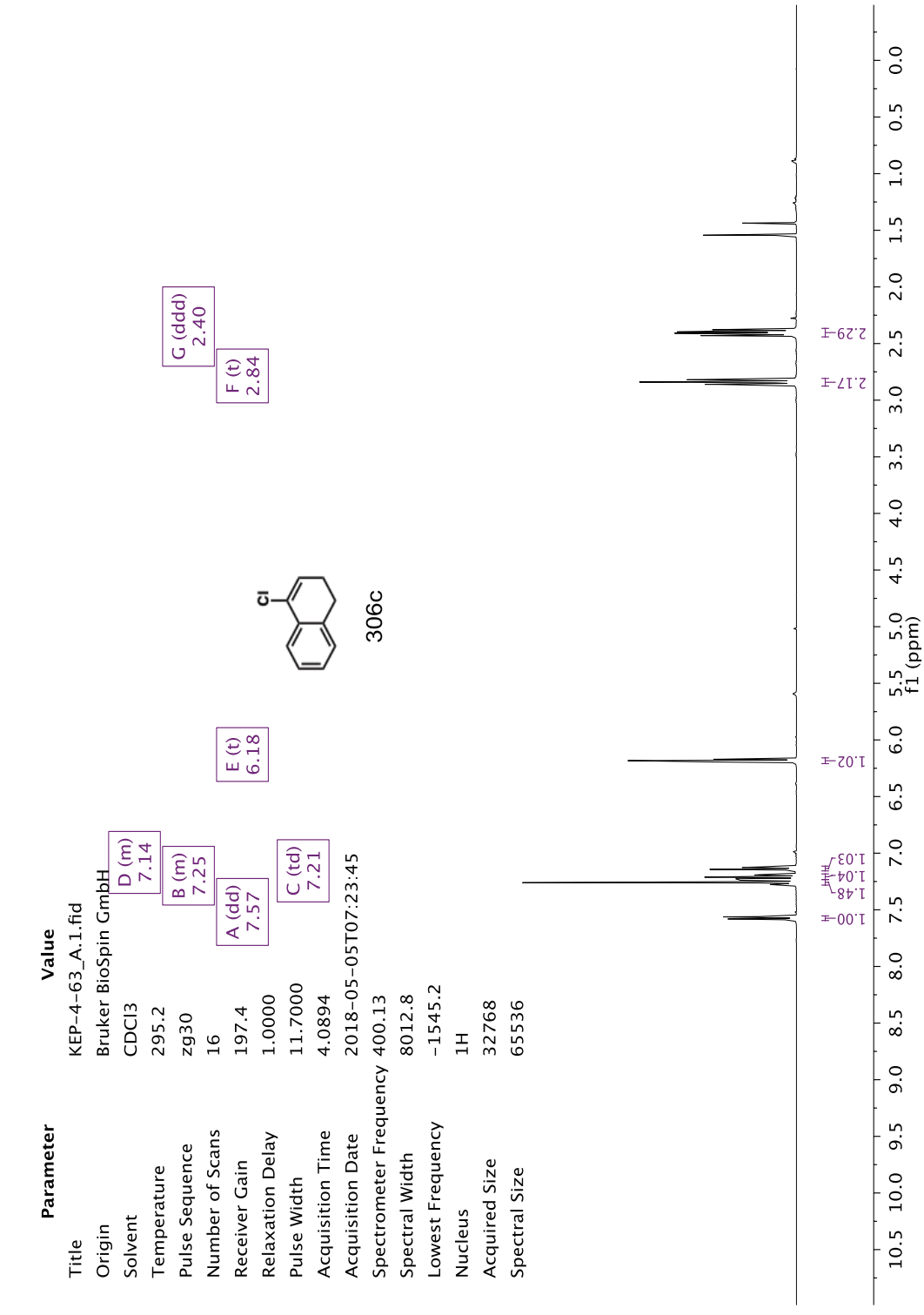

Parameter
Value
Title
JLH-7-231B.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.1
Pulse Sequence
zgpg30
Number of Scans
256
Receiver Gain
64.2
Relaxation Delay
1.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-05-09T12:10:25
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1958.4
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Cl
O
O
305c
131.4
121.8
106.8
64.7
36.4
32.0
31.9
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

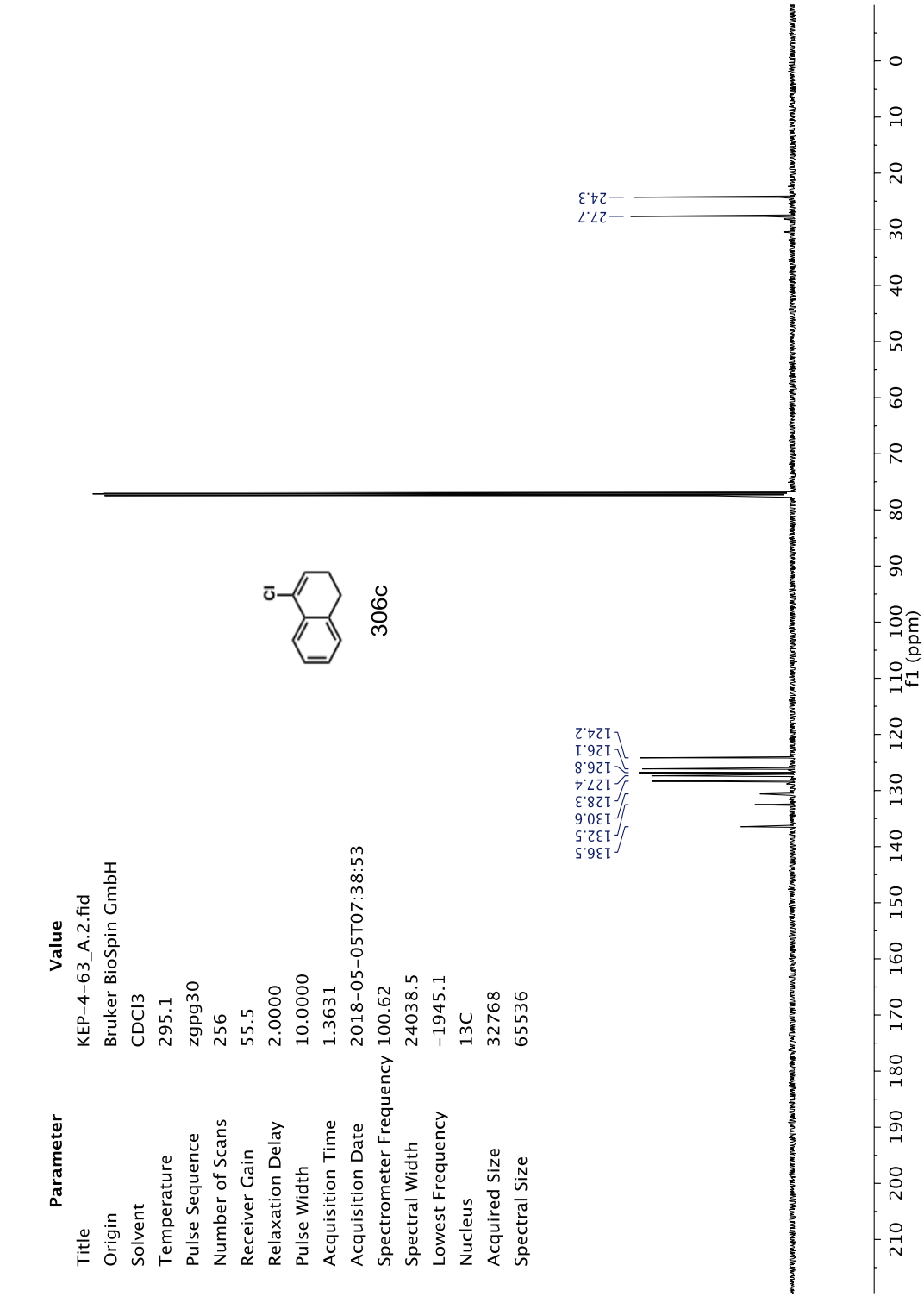

Parameter
Value
Title
ams-1-285char.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
78.7
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-08-31T19:03:28
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1545.3
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
306a
A (dd) 7.43
B (m) 7.24
C (td) 7.17
D (m) 7.02
E (t) 6.83
F (t) 2.85
G (dddd) 2.36
1.00
1.17
1.02
1.01
0.99
2.11
2.14
f1 (ppm)


Parameter
Value
Title
ams-1-285char.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
zgpg30
Number of Scans
256
Receiver Gain
55.5
Relaxation Delay
1.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-08-31T19:14:21
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1949.3
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
306a
140.2
135.9
134.4
130.9
128.4
127.4
127.1
98.1
27.9
27.2
f1 (ppm)

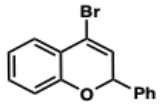

Parameter
Value
Title
ams-1-286char.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.1
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
72.0
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-08-31T19:47:08
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1545.2
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
A (dd) 7.57
B (td) 7.26
C (td) 7.21
D (dq) 7.11
E (t) 6.46
F (t) 2.85
G (ddd) 2.38
Br
306b
1.00
1.02
1.03
1.15
1.01
2.15
2.19
f1 (ppm)


Parameter
Value
Title
ams-1-286char.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
zgpg30
Number of Scans
128
Receiver Gain
64.2
Relaxation Delay
1.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-08-31T19:52:49
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1949.1
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Br
306b
27.7
25.6
136.4
133.2
130.8
128.4
127.4
126.9
126.6
121.5
f1 (ppm)

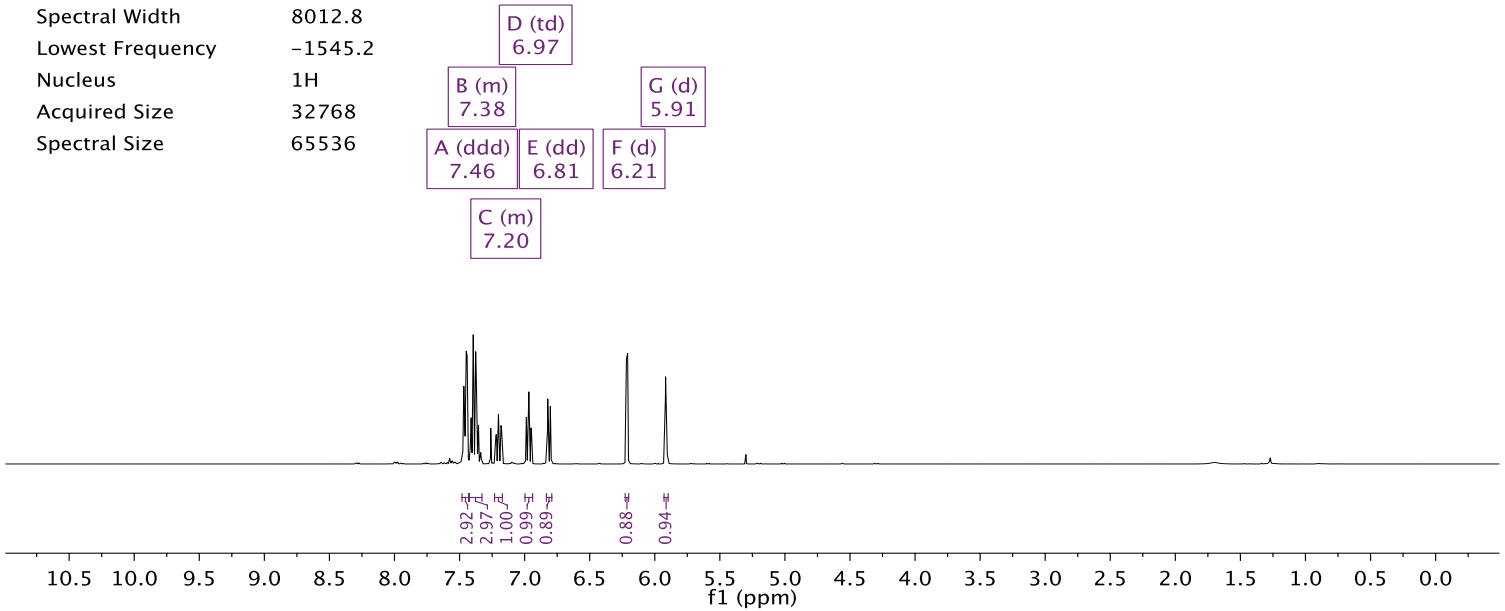

Parameter
Value
Title
KEP-4-63_A.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
197.4
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-05-05T07:23:45
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1545.2
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
A (dd) 7.57
B (m) 7.25
C (td) 7.21
D (m) 7.14
E (t) 6.18
F (t) 2.84
G (ddd) 2.40
Cl
306c
1.00
1.48
1.04
1.03
1.02
2.17
2.29
f1 (ppm)

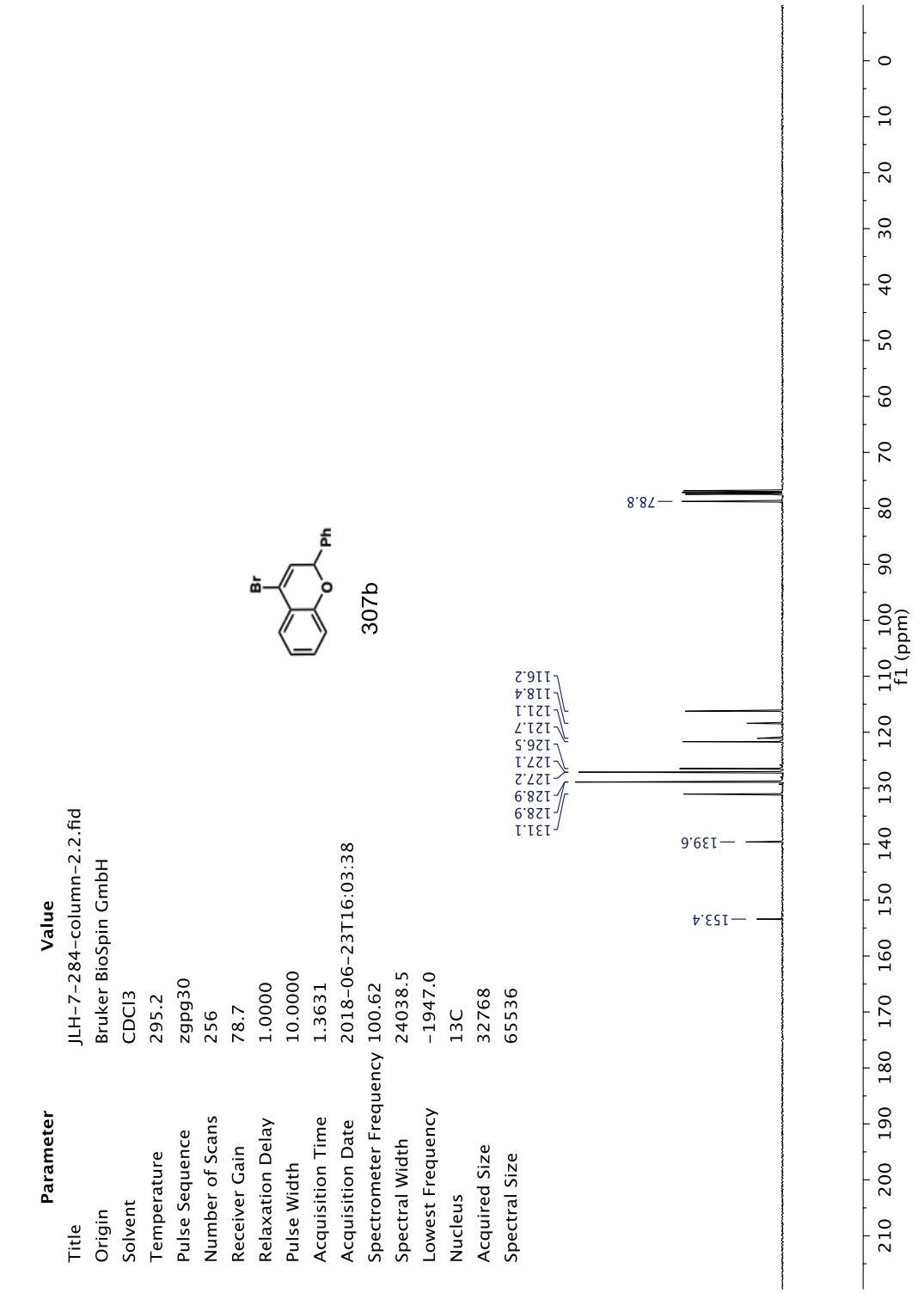

Parameter Value
Title KEP-4-63_A.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zgpg30
Number of Scans 256
Receiver Gain 55.5
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-05-05T07:38:53
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1945.1
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Cl
306c
27.7
24.3
136.5
132.5
130.6
128.3
127.4
126.8
126.1
124.2
f1 (ppm)

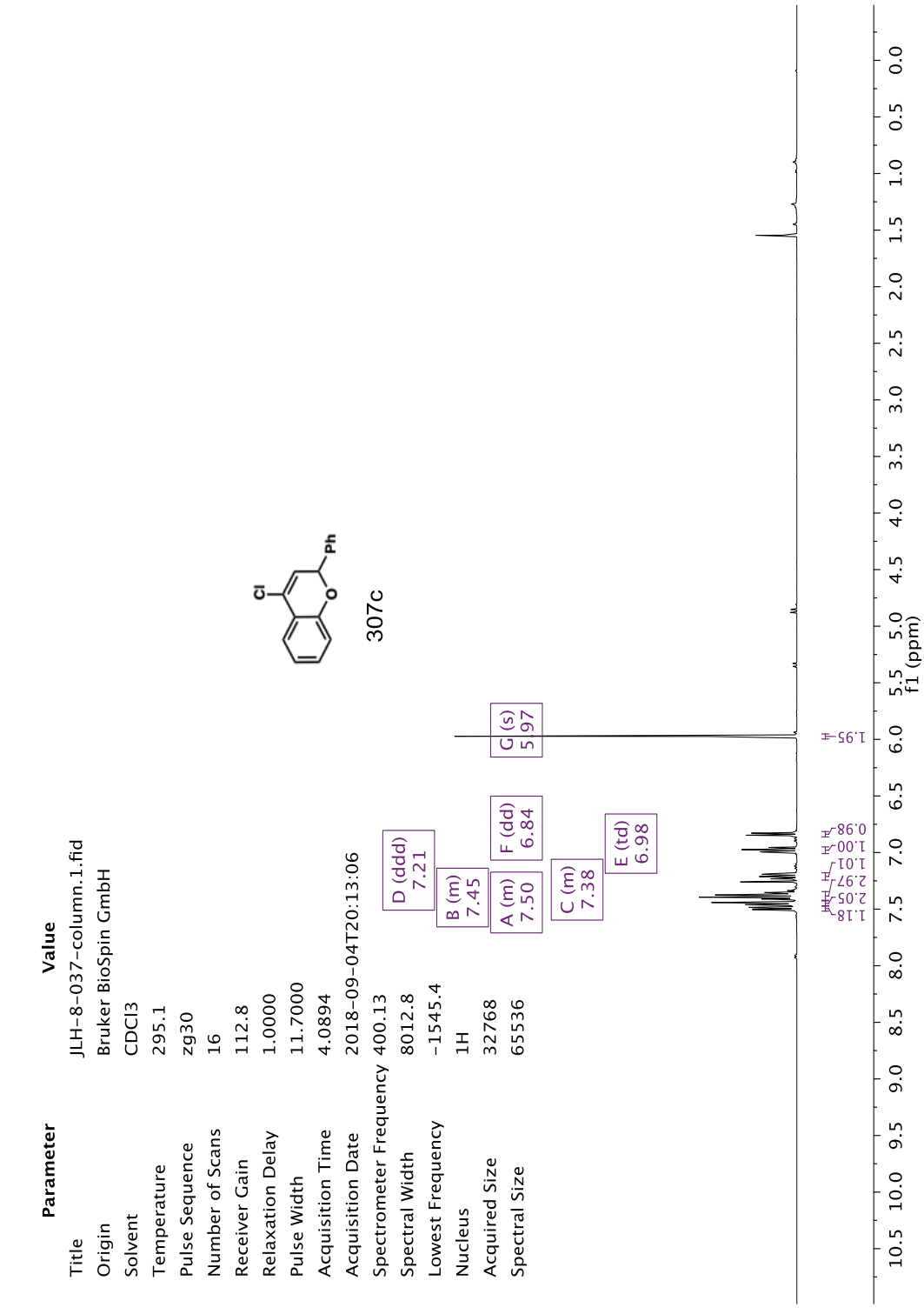
Parameter	Value
Title	JLH-7-284-column-2.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zg30
Number of Scans	16
Receiver Gain	98.9
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-06-23T15:52:10
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.2
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

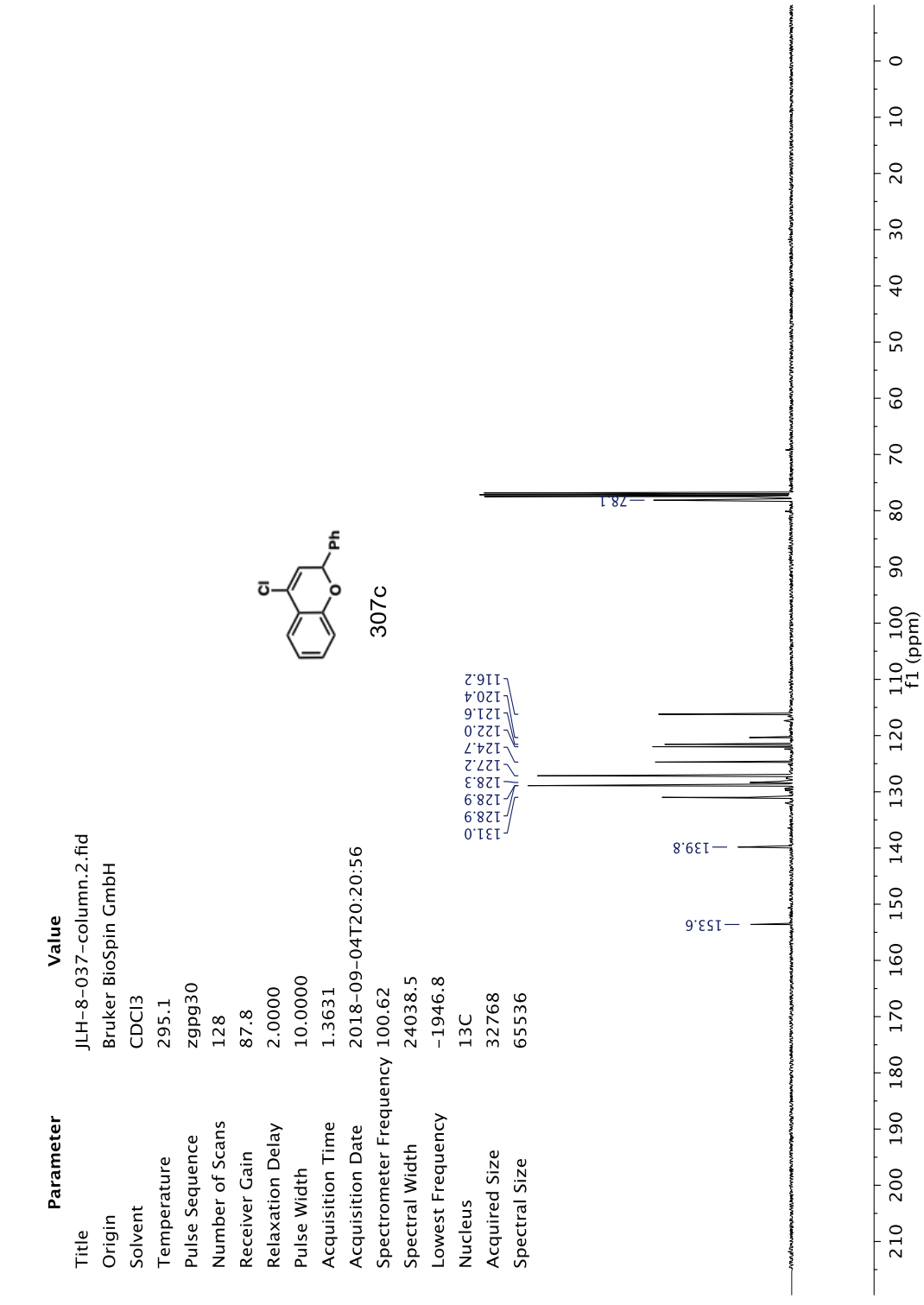


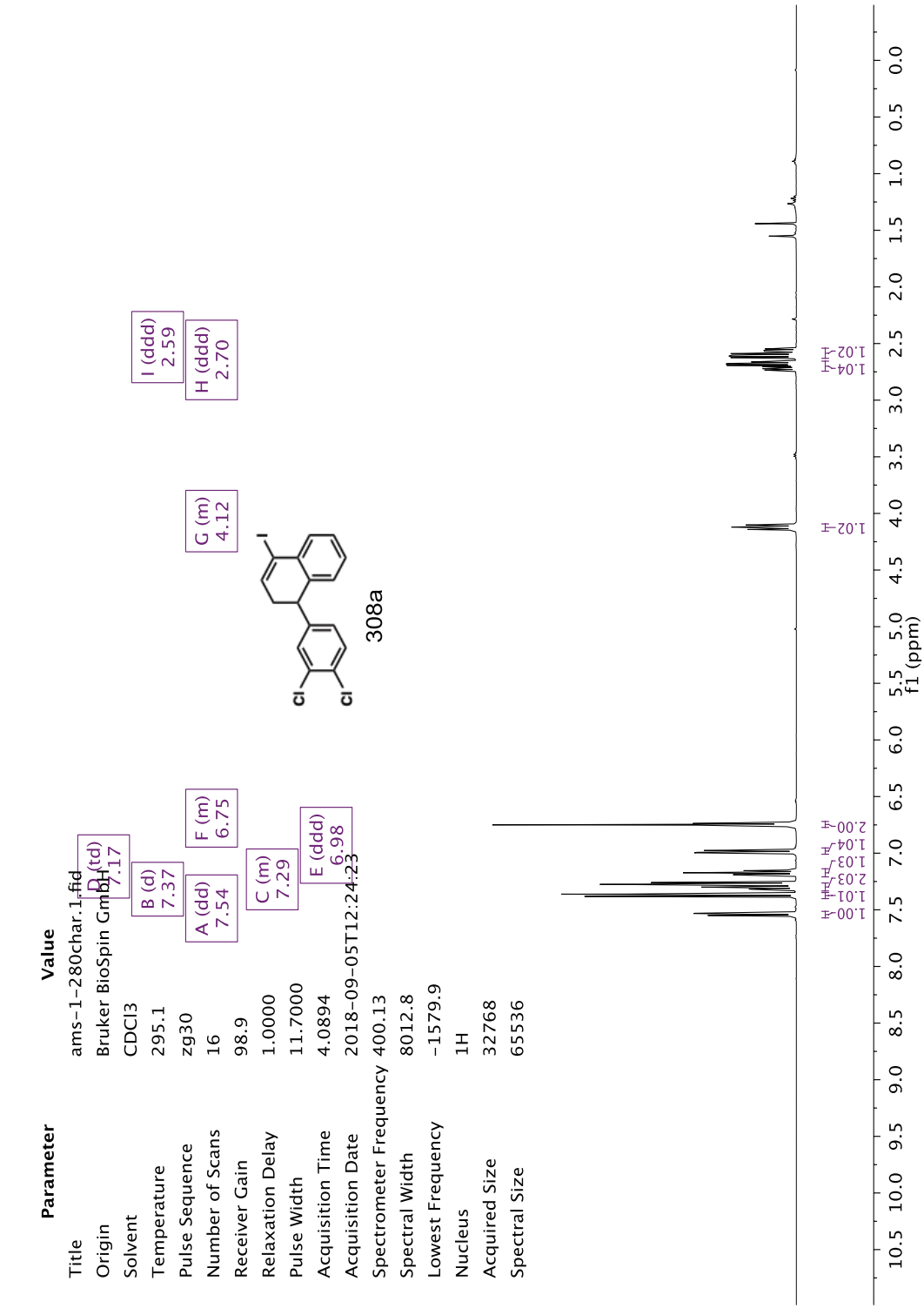
307b

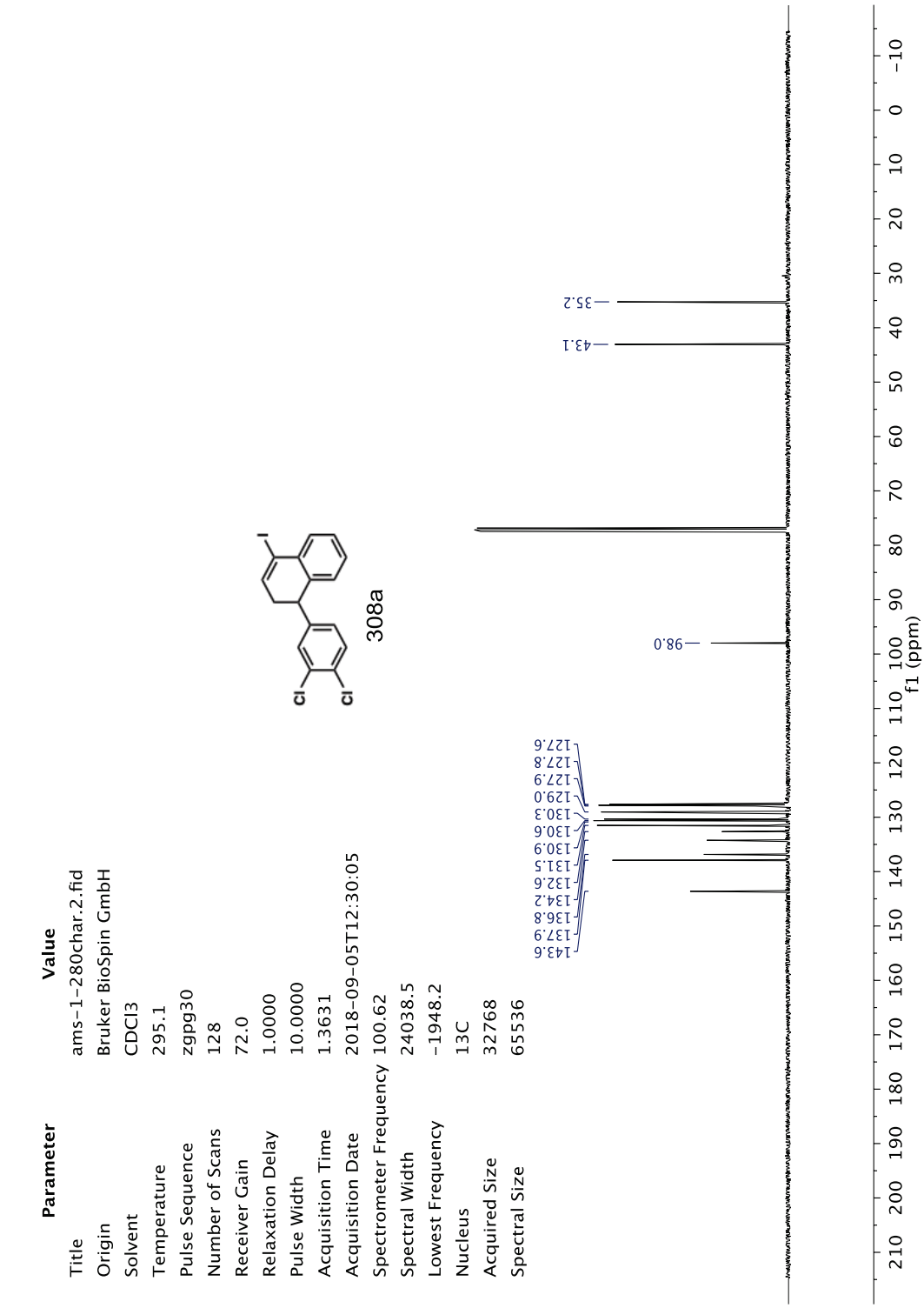


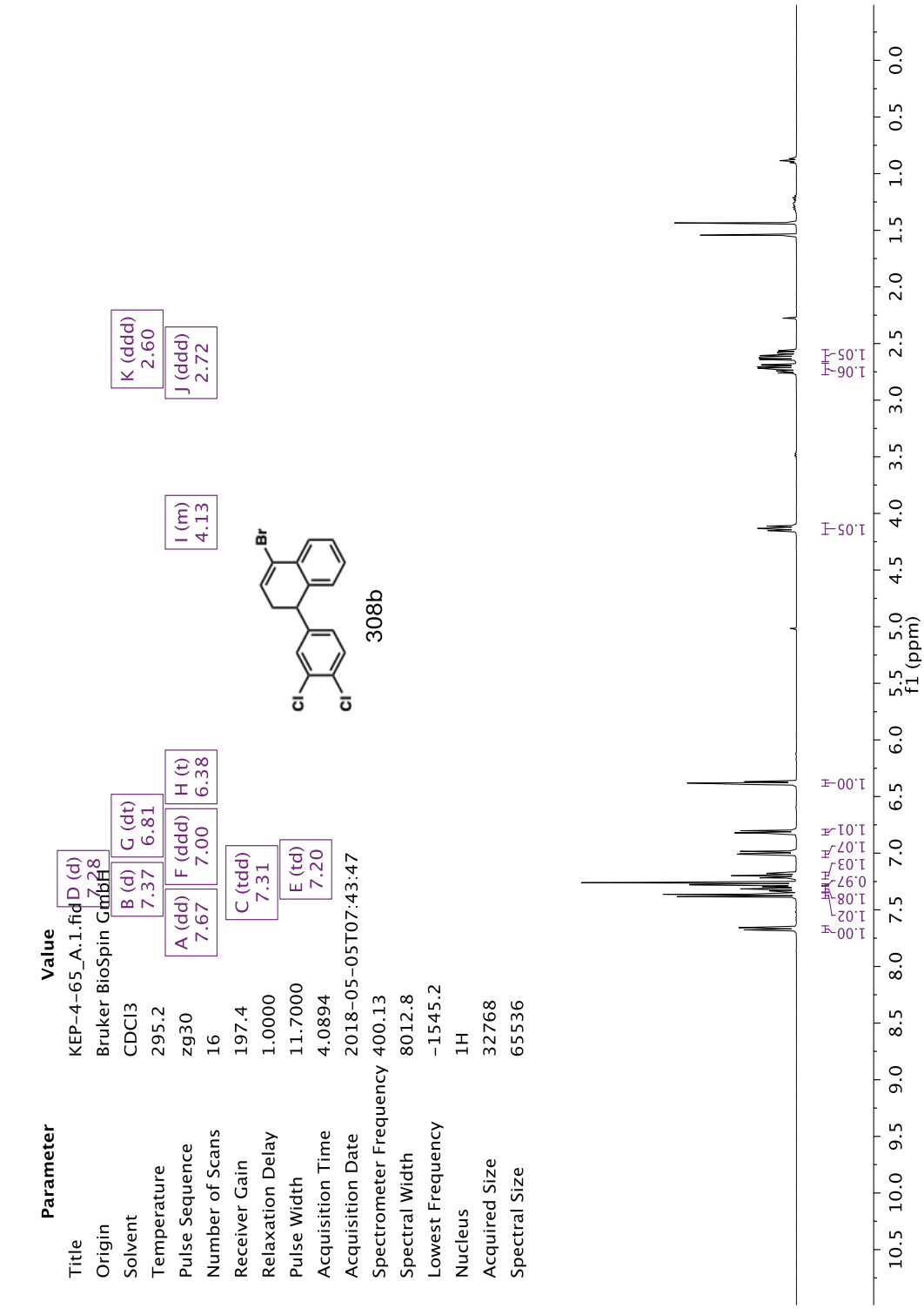

Parameter
Value
Title
JLH-7-284-column-2.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
zgpg30
Number of Scans
256
Receiver Gain
78.7
Relaxation Delay
1.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-06-23T16:03:38
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1947.0
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Br
Ph
O
307b
153.4
139.6
131.1
128.9
128.9
127.2
127.1
126.5
121.7
121.1
118.4
116.2
78.8
f1 (ppm)

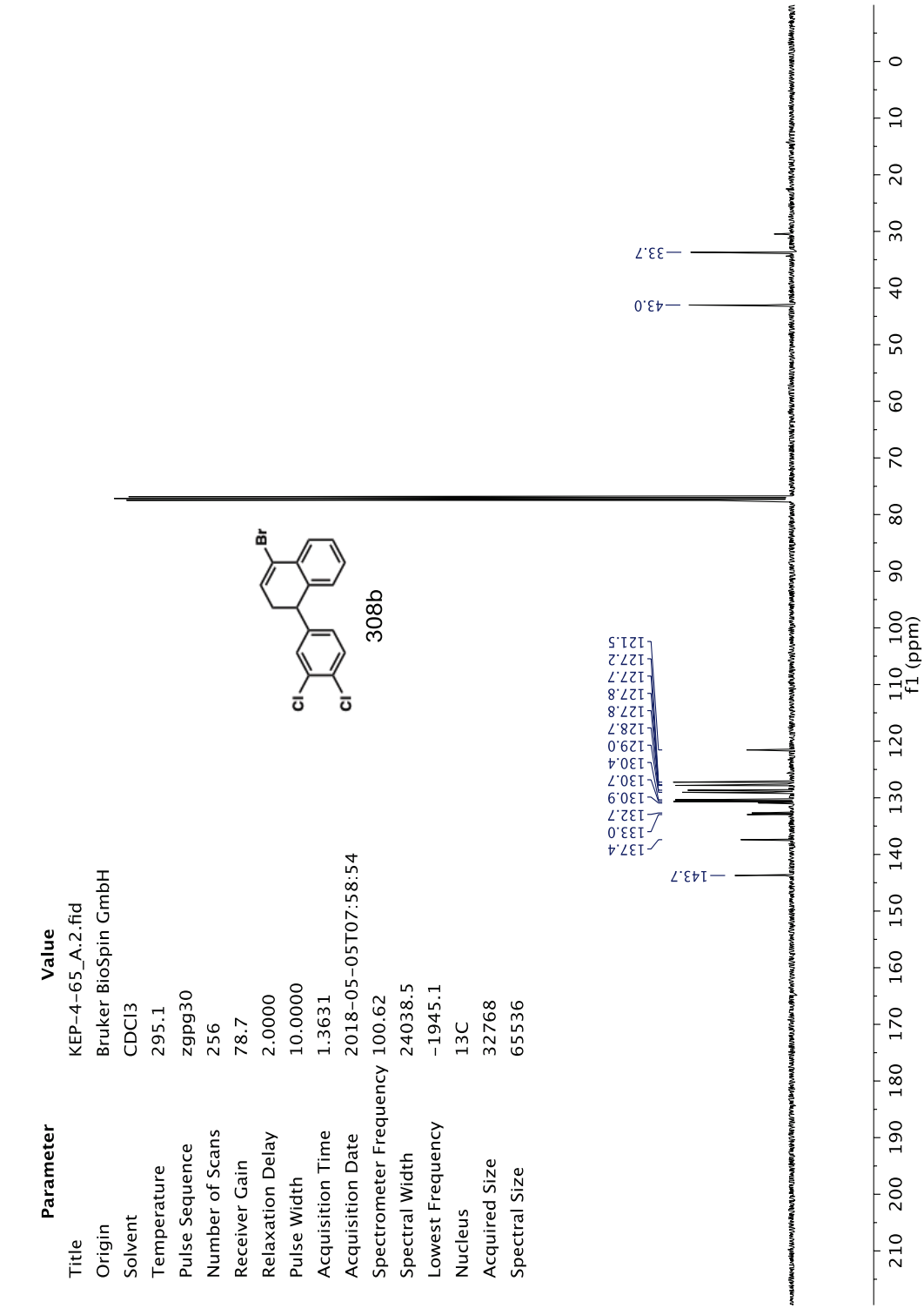

Parameter
Value
Title
JLH-8-037-column.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.1
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
112.8
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-09-04T20:13:06
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1545.4
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
Cl
Ph
O
307c
D (ddd) 7.21
B (m) 7.45
A (m) 7.50
F (dd) 6.84
C (m) 7.38
E (td) 6.98
G (s) 5.97
1.95
1.18
2.05
2.97
1.01
1.00
0.98
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

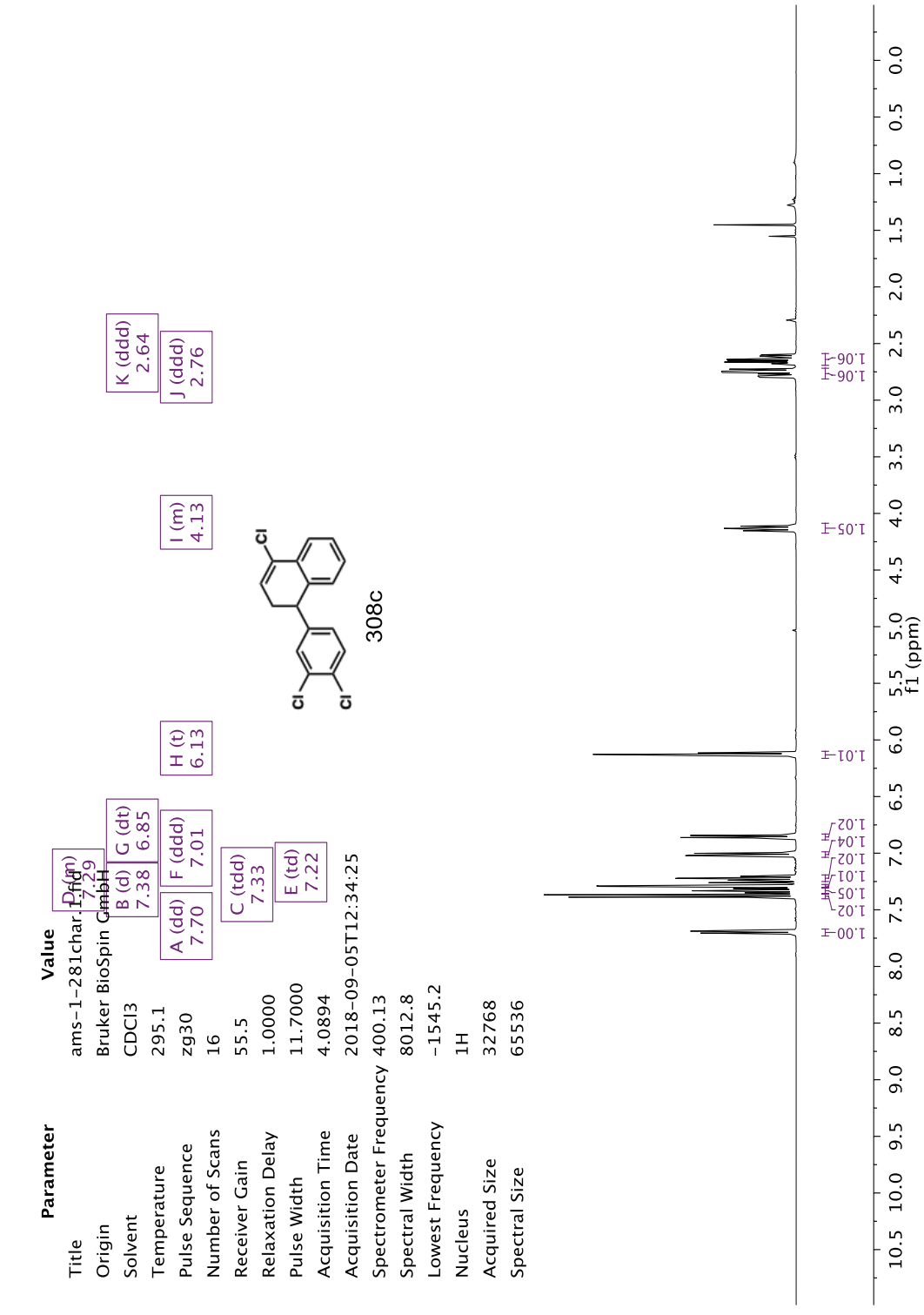

Parameter
Value
Title
JLH-8-037-column.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.1
Pulse Sequence
zgpg30
Number of Scans
128
Receiver Gain
87.8
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-09-04T20:20:56
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1946.8
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Cl
Ph
O
307c
153.6
139.8
131.0
128.9
128.9
128.3
127.2
124.7
122.0
121.6
120.4
116.2
78.1
f1 (ppm)

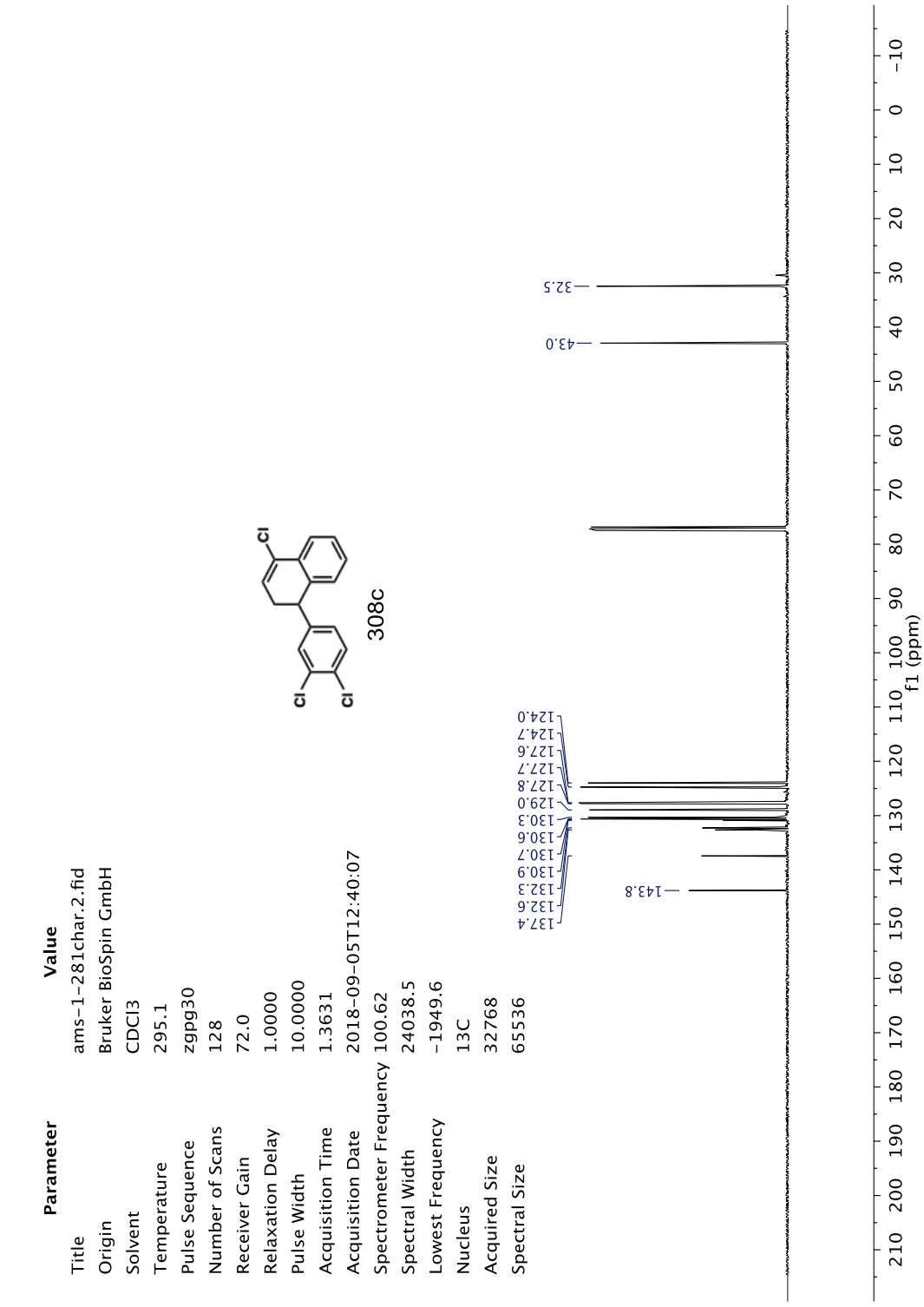

Parameter
Value
Title
ams-1-280char.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.1
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
98.9
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-09-05T12:24:23
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1579.9
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
D (td) 7.17
B (d) 7.37
A (dd) 7.54
F (m) 6.75
C (m) 7.29
E (ddd) 6.98
G (m) 4.12
I (ddd) 2.59
H (ddd) 2.70
Cl
Cl
I
308a
1.00
1.01
2.03
1.03
1.04
2.00
1.02
1.04
1.02
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

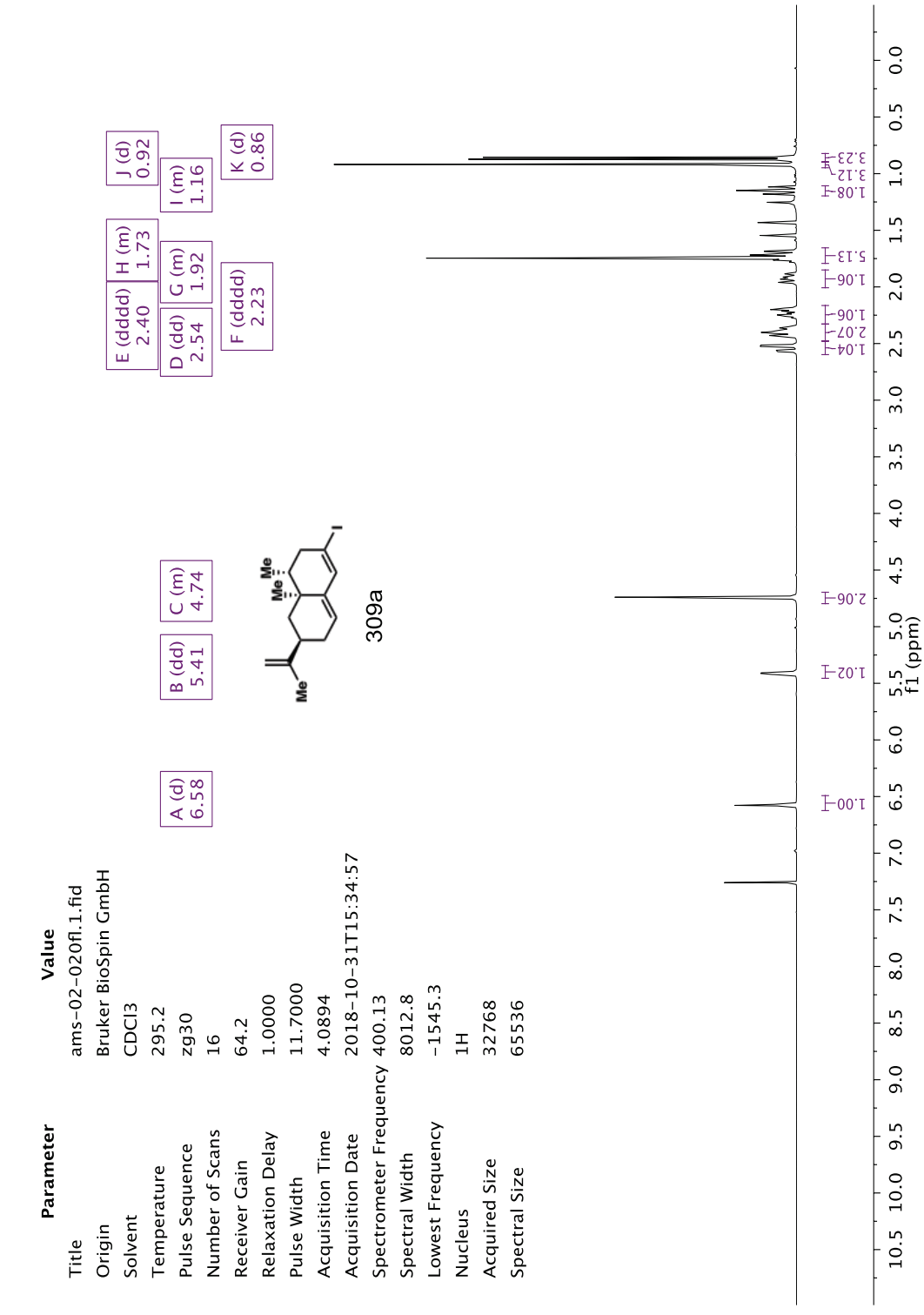

Parameter Value
Title ams-1-280char.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 72.0
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-09-05T12:30:05
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1948.2
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
308a
Cl
Cl
I
143.6
137.9
136.8
134.2
132.6
131.5
130.9
130.6
130.3
129.0
127.9
127.8
127.6
98.0
43.1
35.2
f1 (ppm)

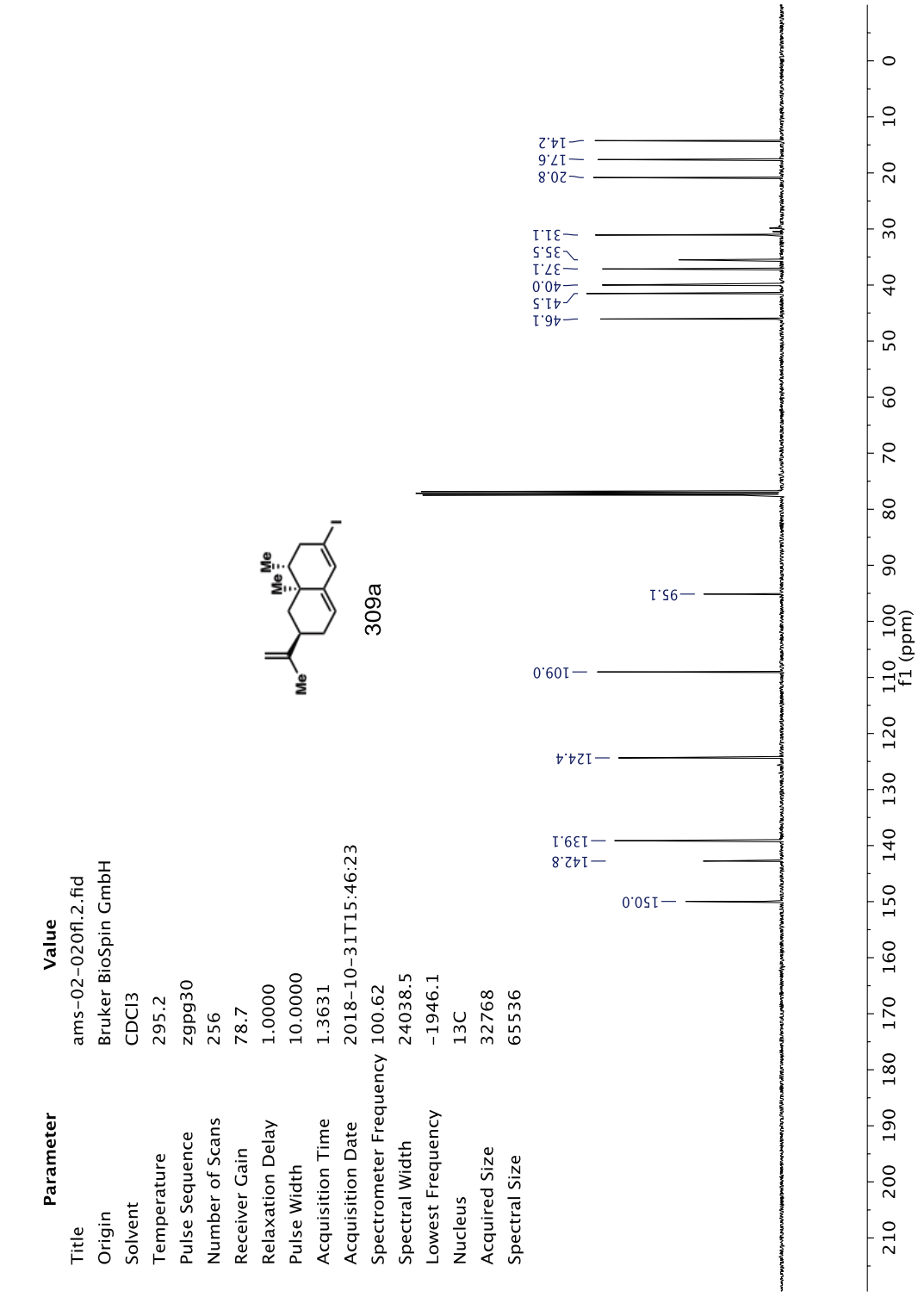

Parameter
Value
Title
KEP-4-65_A.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
197.4
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-05-05T07:43:47
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1545.2
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
D (d) 7.28
B (d) 7.37
G (dt) 6.81
A (dd) 7.67
F (ddd) 7.00
H (t) 6.38
C (tdd) 7.31
E (td) 7.20
I (m) 4.13
K (ddd) 2.60
J (ddd) 2.72
Br
Cl
Cl
308b
1.00
1.02
1.08
0.97
1.03
1.07
1.01
1.00
1.05
1.05
1.06
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

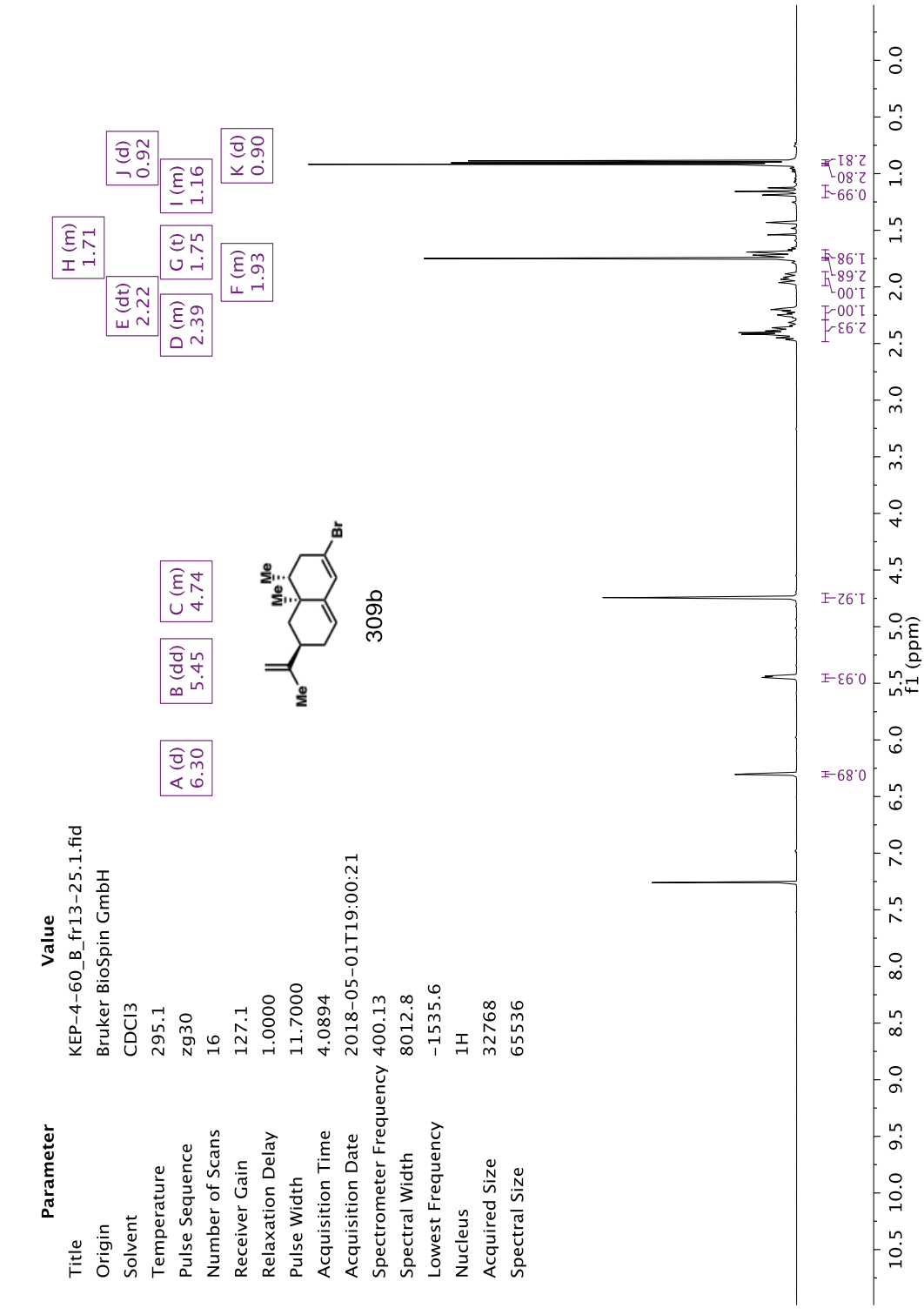

Parameter Value
Title KEP-4-65_A.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zgpg30
Number of Scans 256
Receiver Gain 78.7
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-05-05T07:58:54
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1945.1
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Br
Cl
Cl
308b
143.7
137.4
133.0
132.7
130.9
130.7
130.4
129.0
128.8
127.8
127.8
127.7
127.2
121.5
43.0
33.7
f1 (ppm)

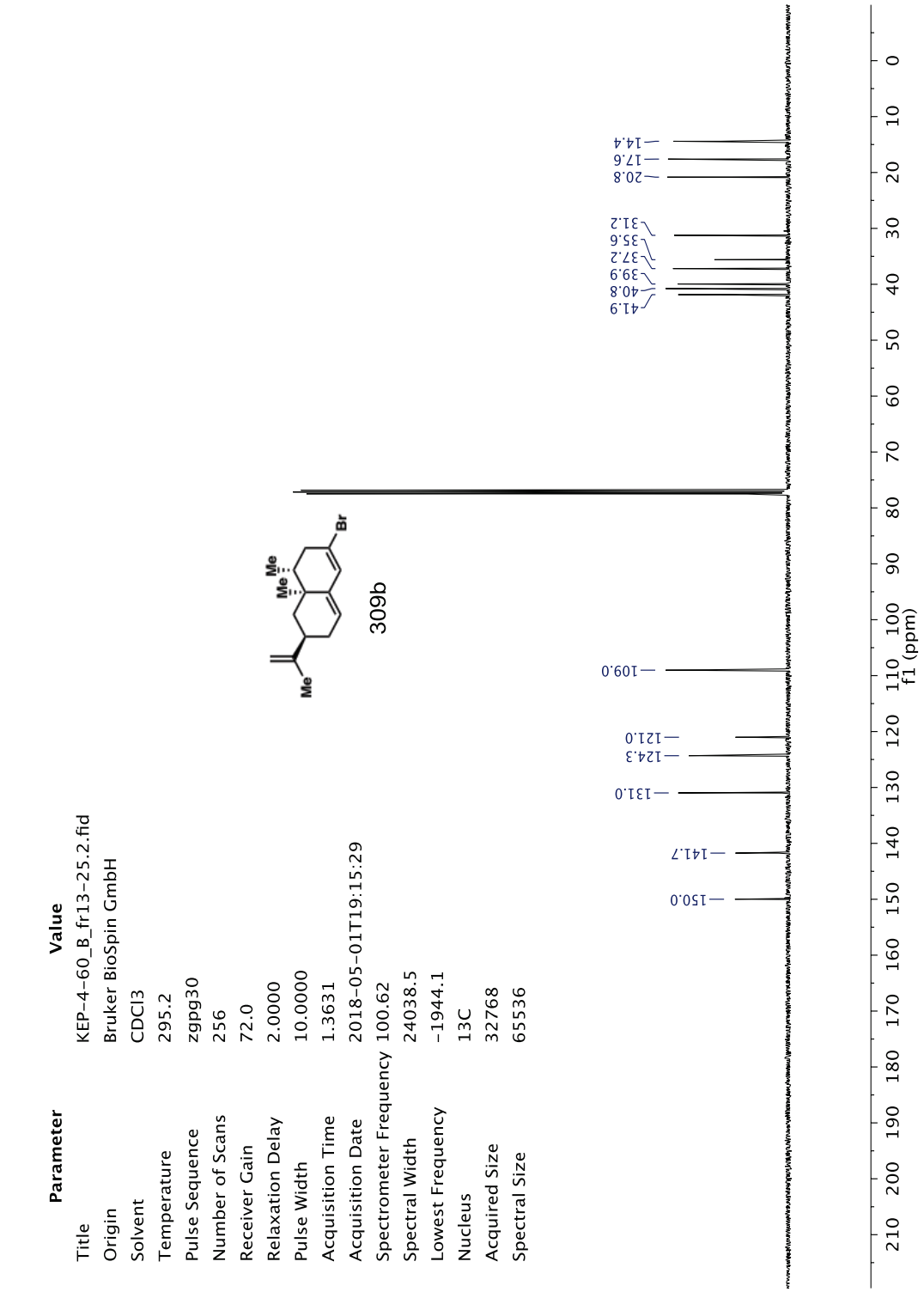

Parameter
Value
Title
ams-1-281char.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.1
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
55.5
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-09-05T12:34:25
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1545.2
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
D (m) 7.29
B (d) 7.38
G (dt) 6.85
A (dd) 7.70
F (ddd) 7.01
C (tdd) 7.33
E (td) 7.22
H (t) 6.13
I (m) 4.13
K (ddd) 2.64
J (ddd) 2.76
Cl
Cl
Cl
308c
1.00
1.02
1.05
1.01
1.02
1.04
1.02
1.01
1.05
1.02
1.01
1.05
1.06
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

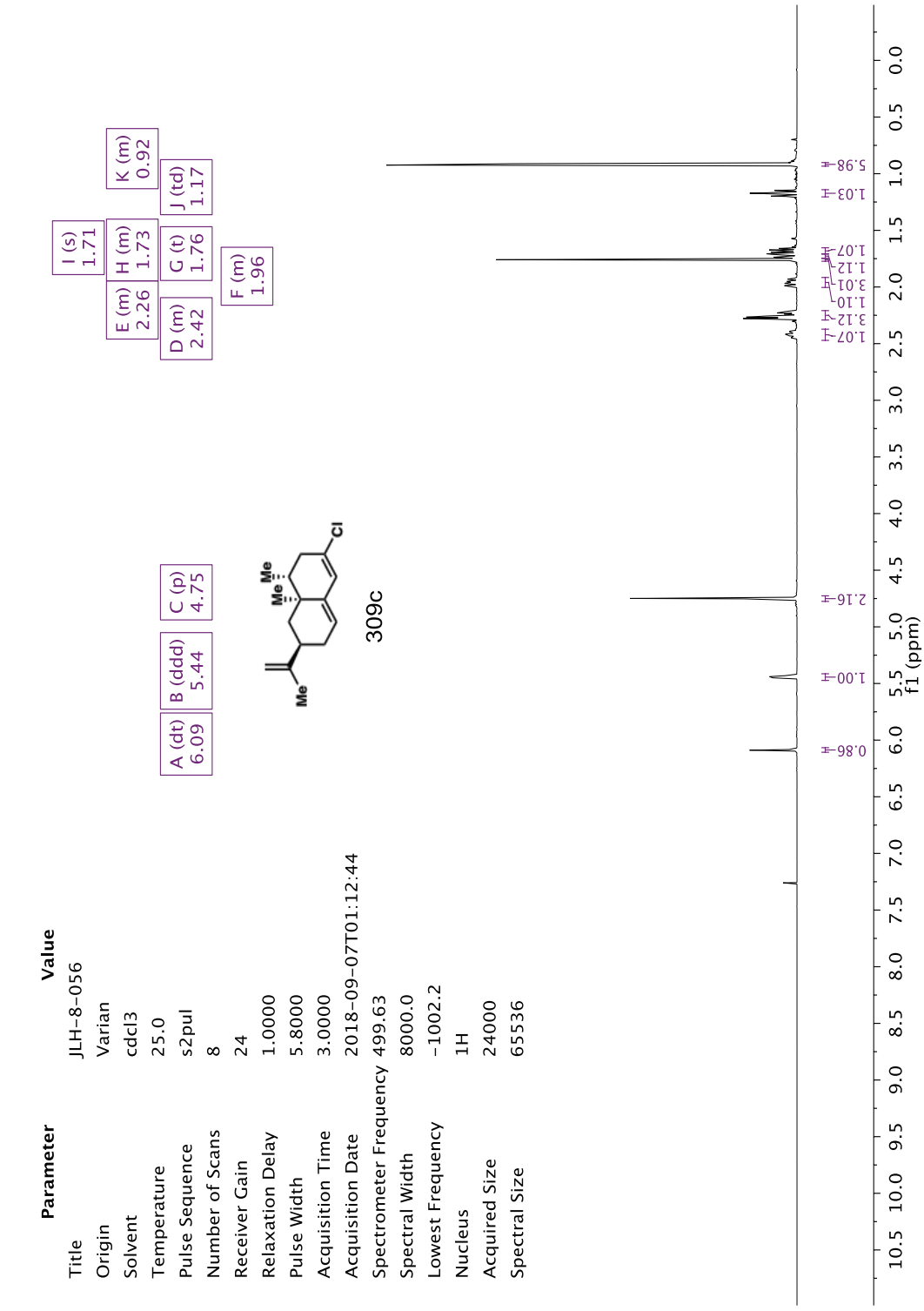

Parameter
Value
Title
ams-1-281char.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.1
Pulse Sequence
zgpg30
Number of Scans
128
Receiver Gain
72.0
Relaxation Delay
1.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-09-05T12:40:07
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1949.6
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Cl
Cl
Cl
308c
32.5
43.0
124.0
124.7
127.6
127.7
127.8
129.0
130.3
130.6
130.7
130.9
132.3
132.6
137.4
143.8
f1 (ppm)

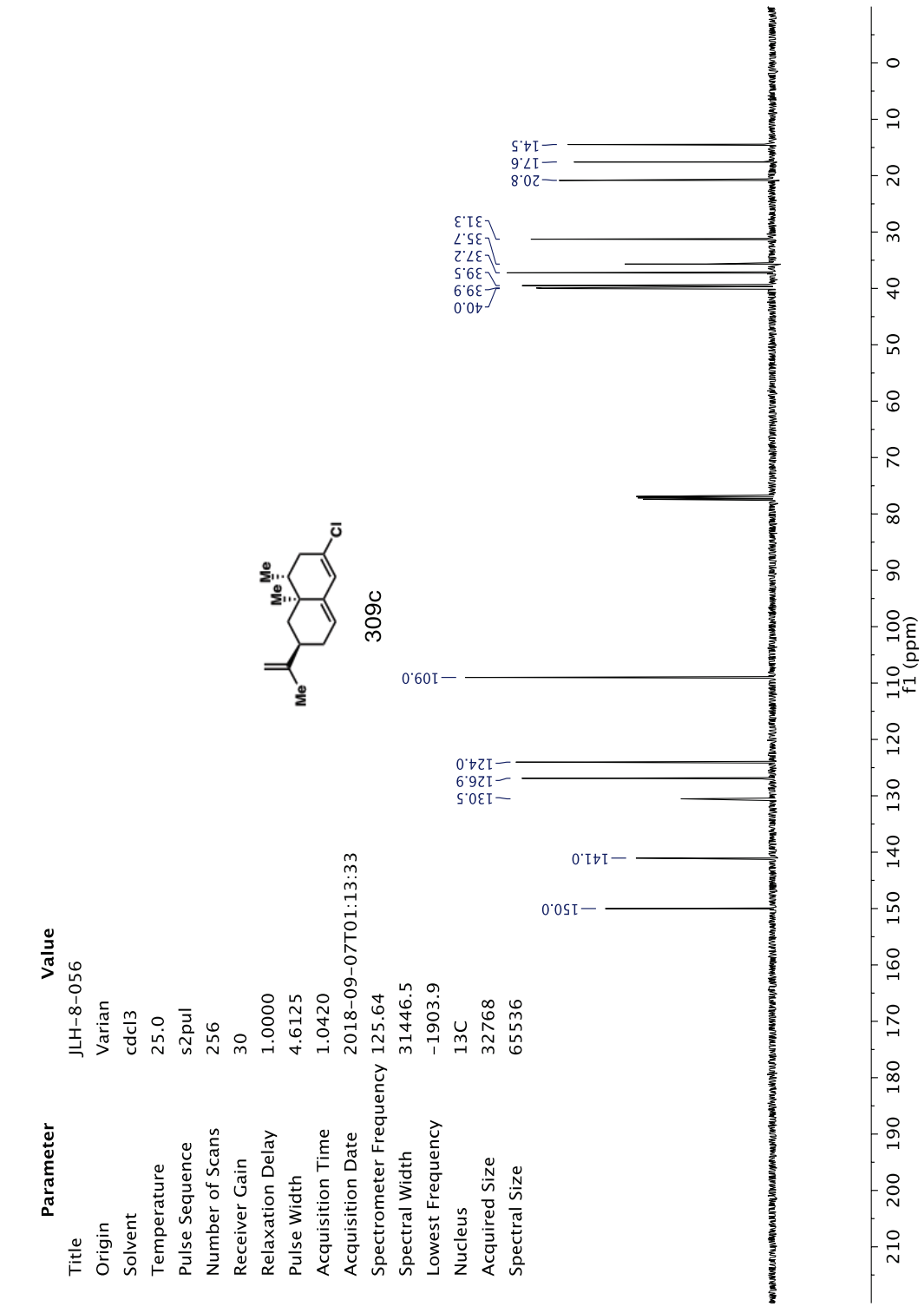

Parameter
Value
Title
ams-02-020fl.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
64.2
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-10-31T15:34:57
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1545.3
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
A (d) 6.58
B (dd) 5.41
C (m) 4.74
D (dd) 2.54
E (dddd) 2.40
F (dddd) 2.23
G (m) 1.92
H (m) 1.73
I (m) 1.16
J (d) 0.92
K (d) 0.86
Me
Me
Me
I
309a
1.00
1.02
2.06
1.04
2.07
1.06
1.06
5.13
1.08
3.12
3.23
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

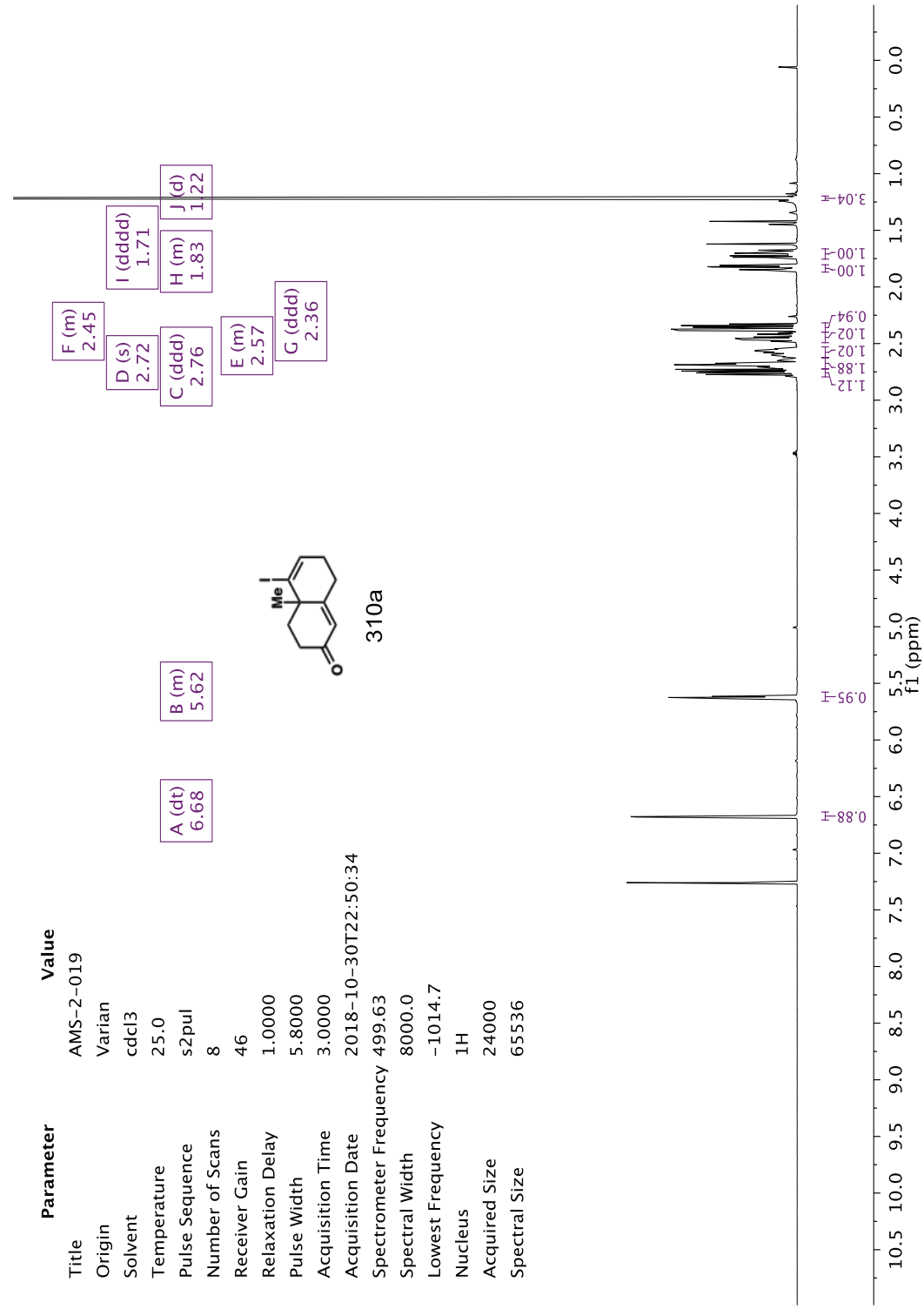

Parameter Value
Title ams-02-020fl.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zgpg30
Number of Scans 256
Receiver Gain 78.7
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-10-31T15:46:23
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1946.1
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
Me
Me
I
309a
150.0
142.8
139.1
124.4
109.0
95.1
46.1
41.5
40.0
37.1
35.5
31.1
20.8
17.6
14.2
f1 (ppm)


Parameter
Value
Title KEP-4-60_B_fr13-25.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 127.1
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-05-01T19:00:21
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1535.6
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
A (d) 6.30
B (dd) 5.45
C (m) 4.74
D (m) 2.39
E (dt) 2.22
F (m) 1.93
G (t) 1.75
H (m) 1.71
I (m) 1.16
J (d) 0.92
K (d) 0.90
Me
Me
Me
Br
309b
0.89
1.92
0.93
2.93
1.00
1.00
2.68
1.98
0.99
2.80
2.81
f1 (ppm)

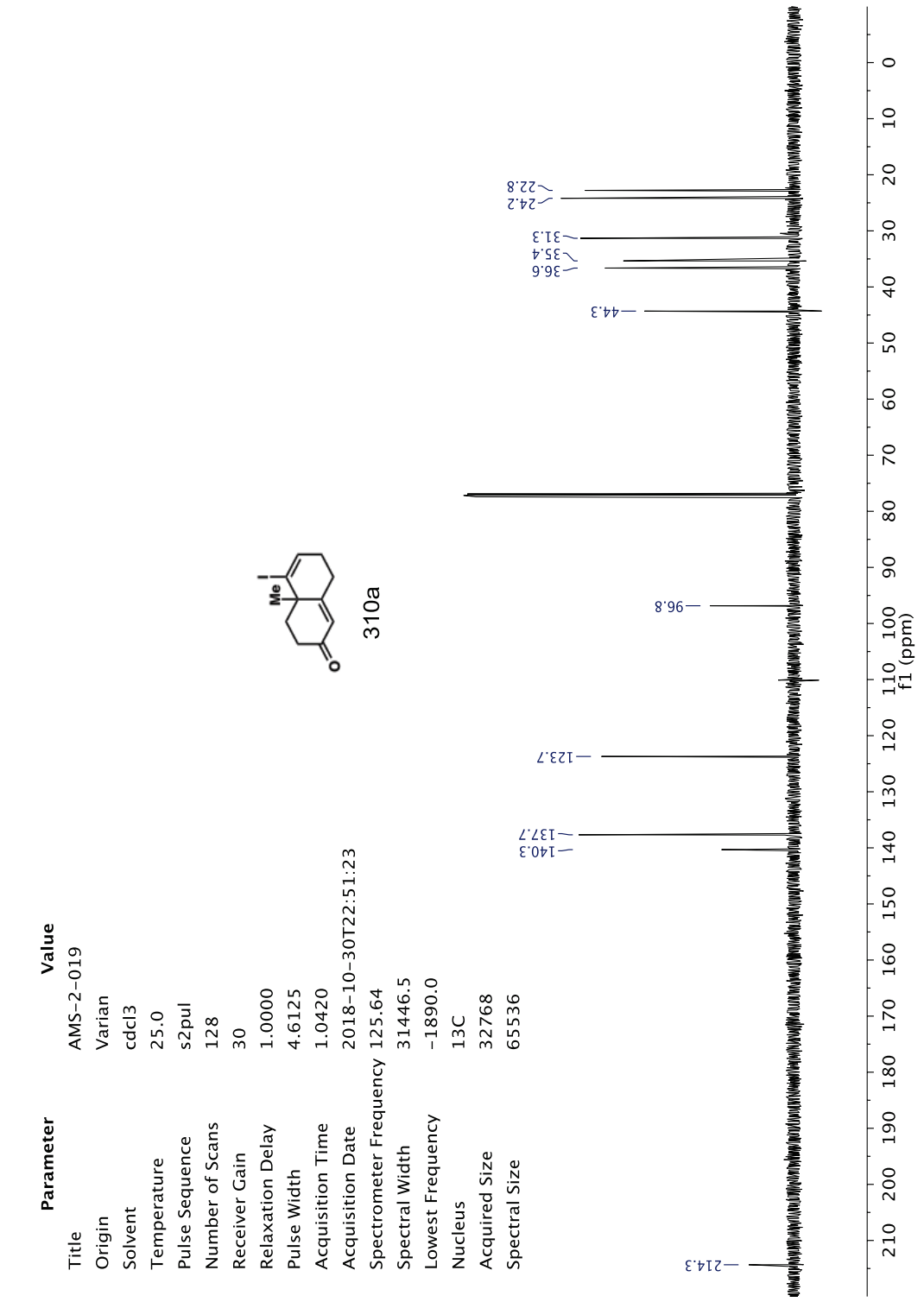

Parameter Value
Title KEP-4-60_B_fr13-25.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zgpg30
Number of Scans 256
Receiver Gain 72.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-05-01T19:15:29
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1944.1
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
Me
Me
Br
309b
150.0
141.7
131.0
124.3
121.0
109.0
41.9
40.8
39.9
37.2
35.6
31.2
20.8
17.6
14.4
f1 (ppm)

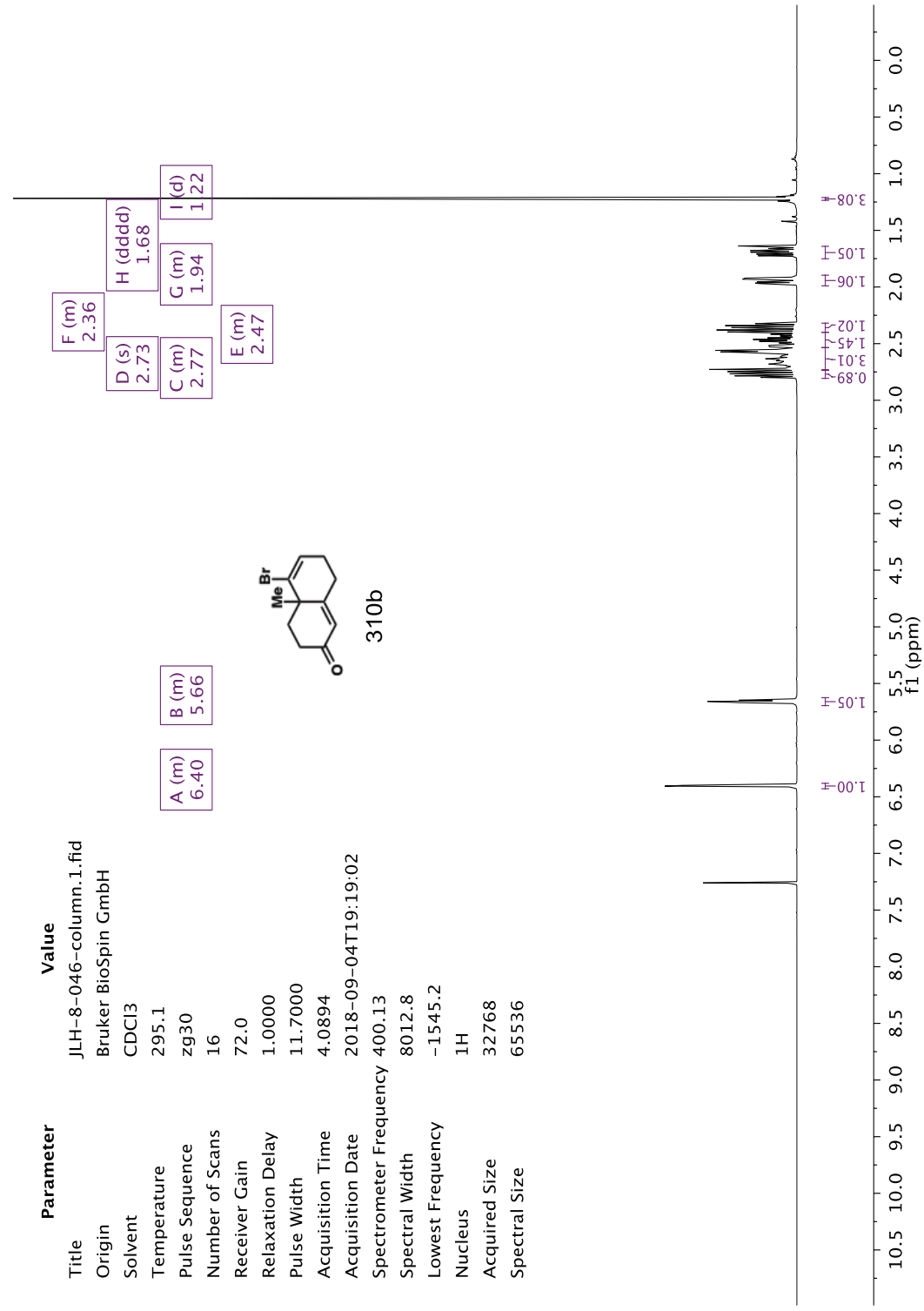

Parameter Value
Title JLH-8-056
Origin Varian
Solvent cdcl3
Temperature 25.0
Pulse Sequence s2pul
Number of Scans 8
Receiver Gain 24
Relaxation Delay 1.0000
Pulse Width 5.8000
Acquisition Time 3.0000
Acquisition Date 2018-09-07T01:12:44
Spectrometer Frequency 499.63
Spectral Width 8000.0
Lowest Frequency -1002.2
Nucleus 1H
Acquired Size 24000
Spectral Size 65536
A (dt) 6.09
B (ddd) 5.44
C (p) 4.75
D (m) 2.42
E (m) 2.26
F (m) 1.96
G (t) 1.76
H (m) 1.73
I (s) 1.71
J (td) 1.17
K (m) 0.92
Me
Me
Me
Cl
309c
0.86
1.00
2.16
1.07
3.12
1.10
3.01
1.12
1.07
1.03
5.98
f1 (ppm)


Parameter Value
Title JLH-8-056
Origin Varian
Solvent cdcl3
Temperature 25.0
Pulse Sequence s2pul
Number of Scans 256
Receiver Gain 30
Relaxation Delay 1.0000
Pulse Width 4.6125
Acquisition Time 1.0420
Acquisition Date 2018-09-07T01:13:33
Spectrometer Frequency 125.64
Spectral Width 31446.5
Lowest Frequency -1903.9
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
309c
Me
Me
Me
Cl
150.0
141.0
130.5
126.9
124.0
109.0
40.0
39.9
39.5
37.2
35.7
31.3
20.8
17.6
14.5
f1 (ppm)

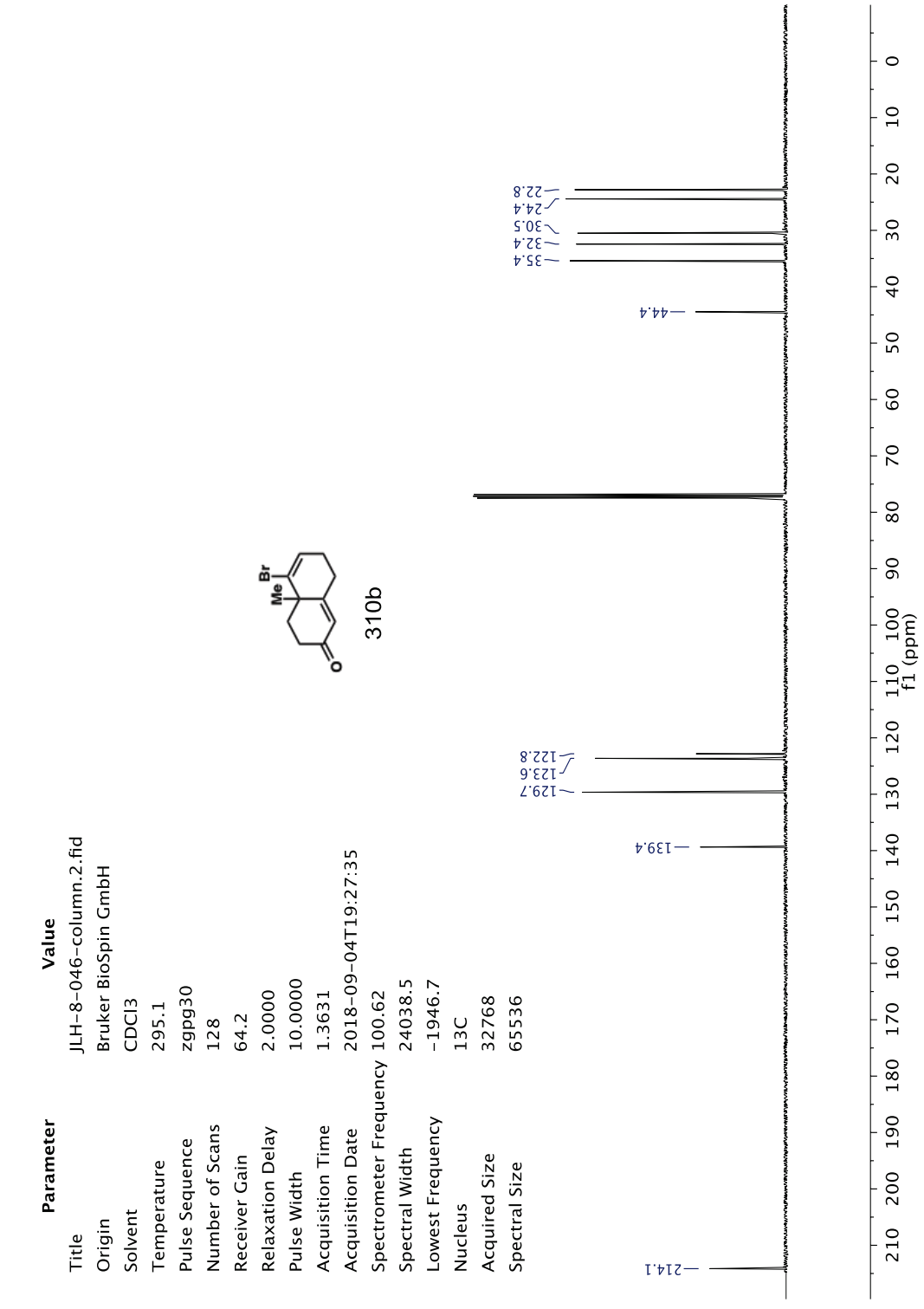


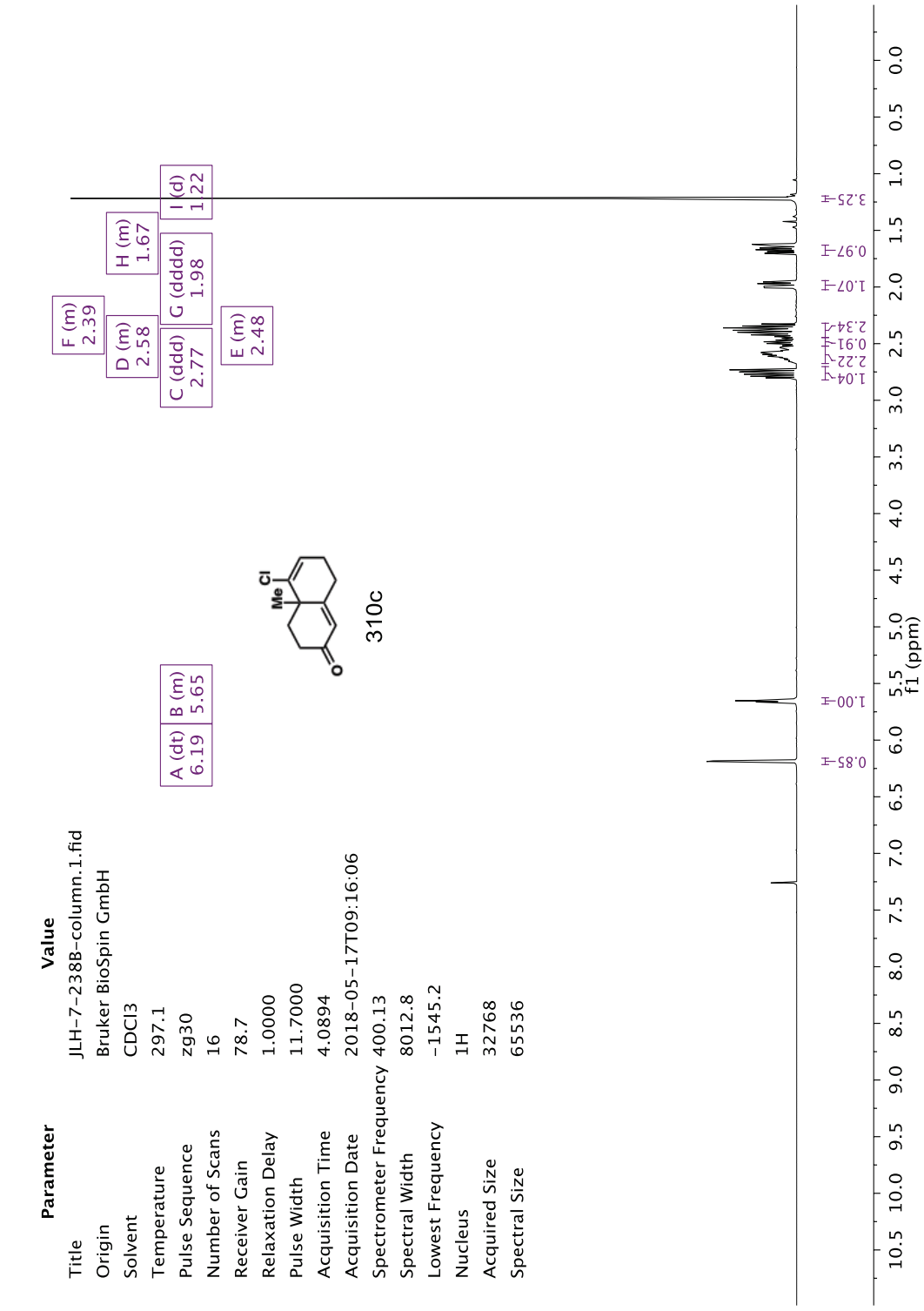
Parameter	Value
Title	AMS-2-019
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	8
Receiver Gain	46
Relaxation Delay	1.0000
Pulse Width	5.8000
Acquisition Time	3.0000
Acquisition Date	2018-10-30T22:50:34
Spectrometer Frequency	499.63
Spectral Width	8000.0
Lowest Frequency	-1014.7
Nucleus	1H
Acquired Size	24000
Spectral Size	65536


Parameter Value
Title AMS-2-019
Origin Varian
Solvent cdcl3
Temperature 25.0
Pulse Sequence s2pul
Number of Scans 128
Receiver Gain 30
Relaxation Delay 1.0000
Pulse Width 4.6125
Acquisition Time 1.0420
Acquisition Date 2018-10-30T22:51:23
Spectrometer Frequency 125.64
Spectral Width 31446.5
Lowest Frequency -1890.0
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
O
310a
214.3
140.3
137.7
123.7
96.8
44.3
36.6
35.4
31.3
24.2
22.8
f1 (ppm)

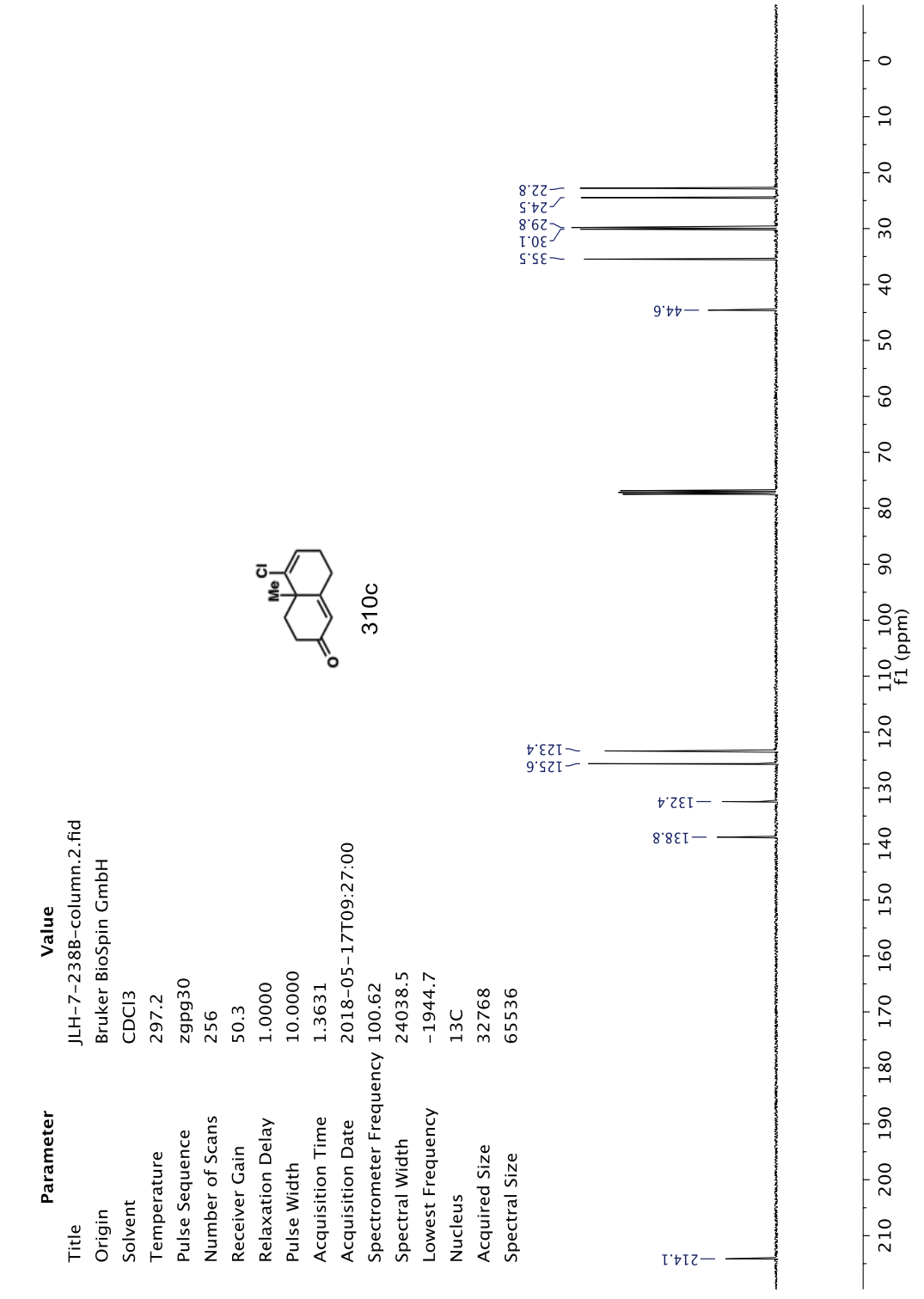


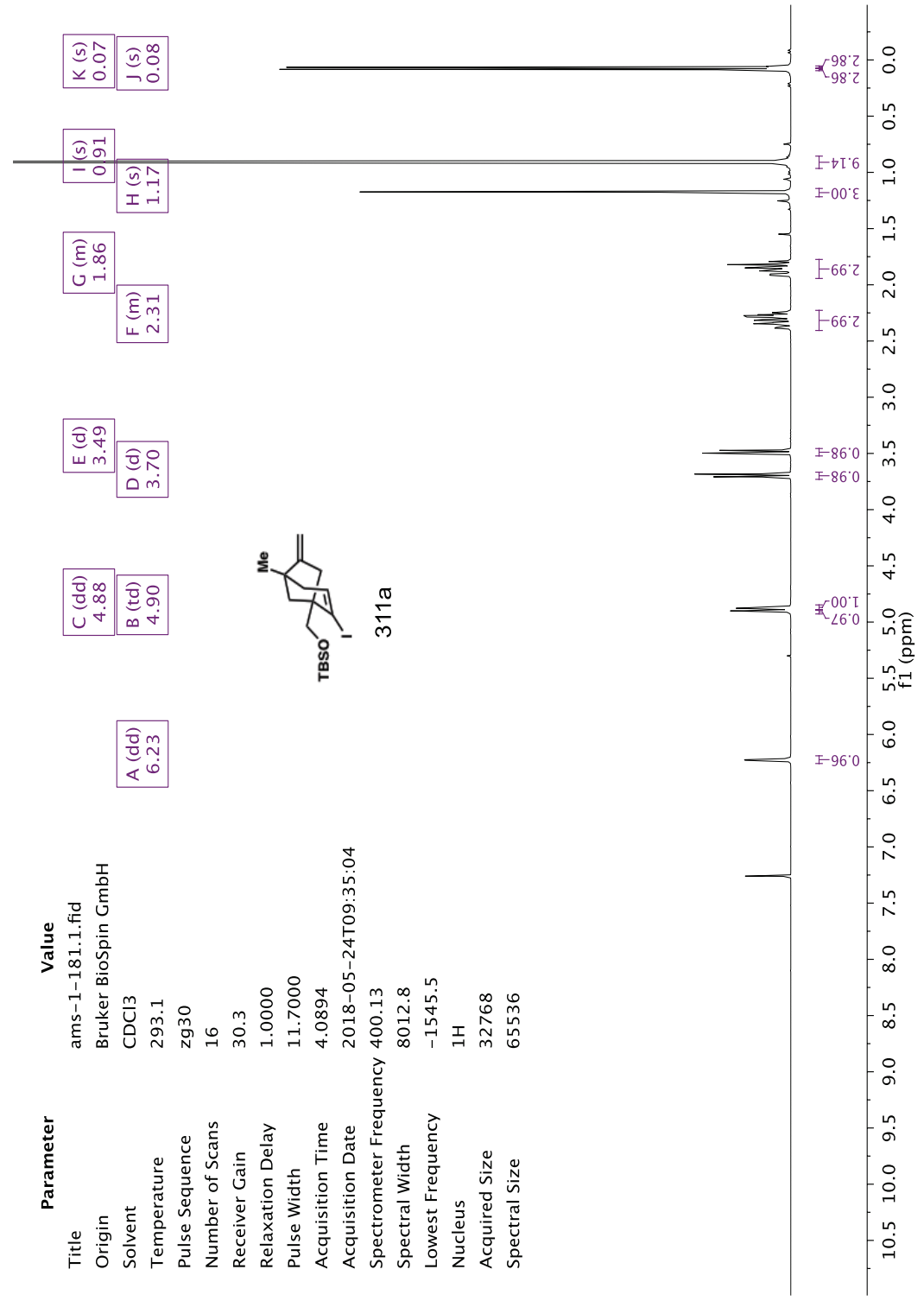
Parameter	Value
Title	JLH-8-046-column.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Number of Scans	16
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-09-04T19:19:02
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.2
Nucleus	1H
Acquired Size	32768
Spectral Size	65536


Parameter
Value
Title
JLH-8-046-column.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.1
Pulse Sequence
zgpg30
Number of Scans
128
Receiver Gain
64.2
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-09-04T19:27:35
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1946.7
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Br
Me
O
310b
214.1
139.4
129.7
123.6
122.8
44.4
35.4
32.4
30.5
24.4
22.8
f1 (ppm)

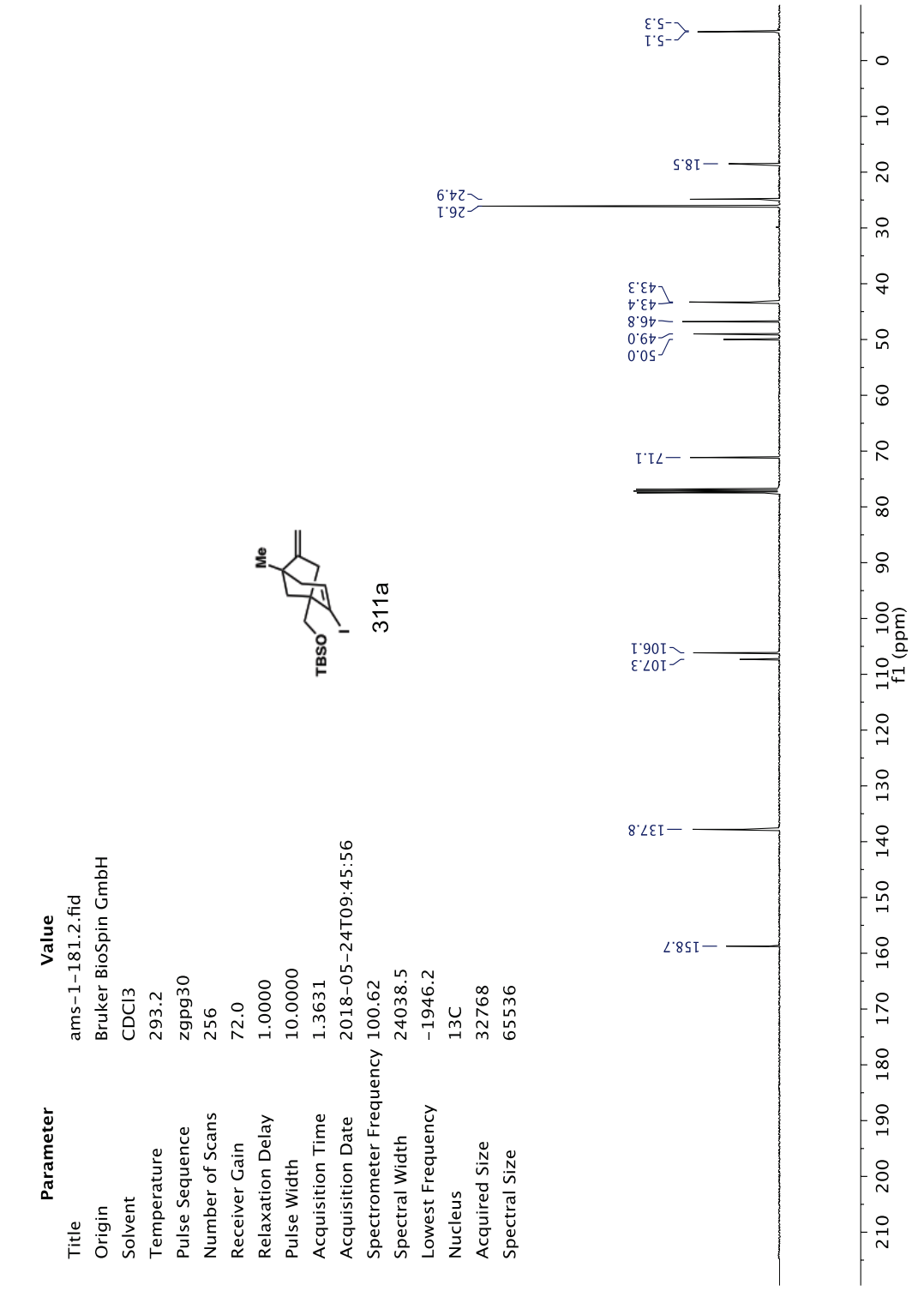


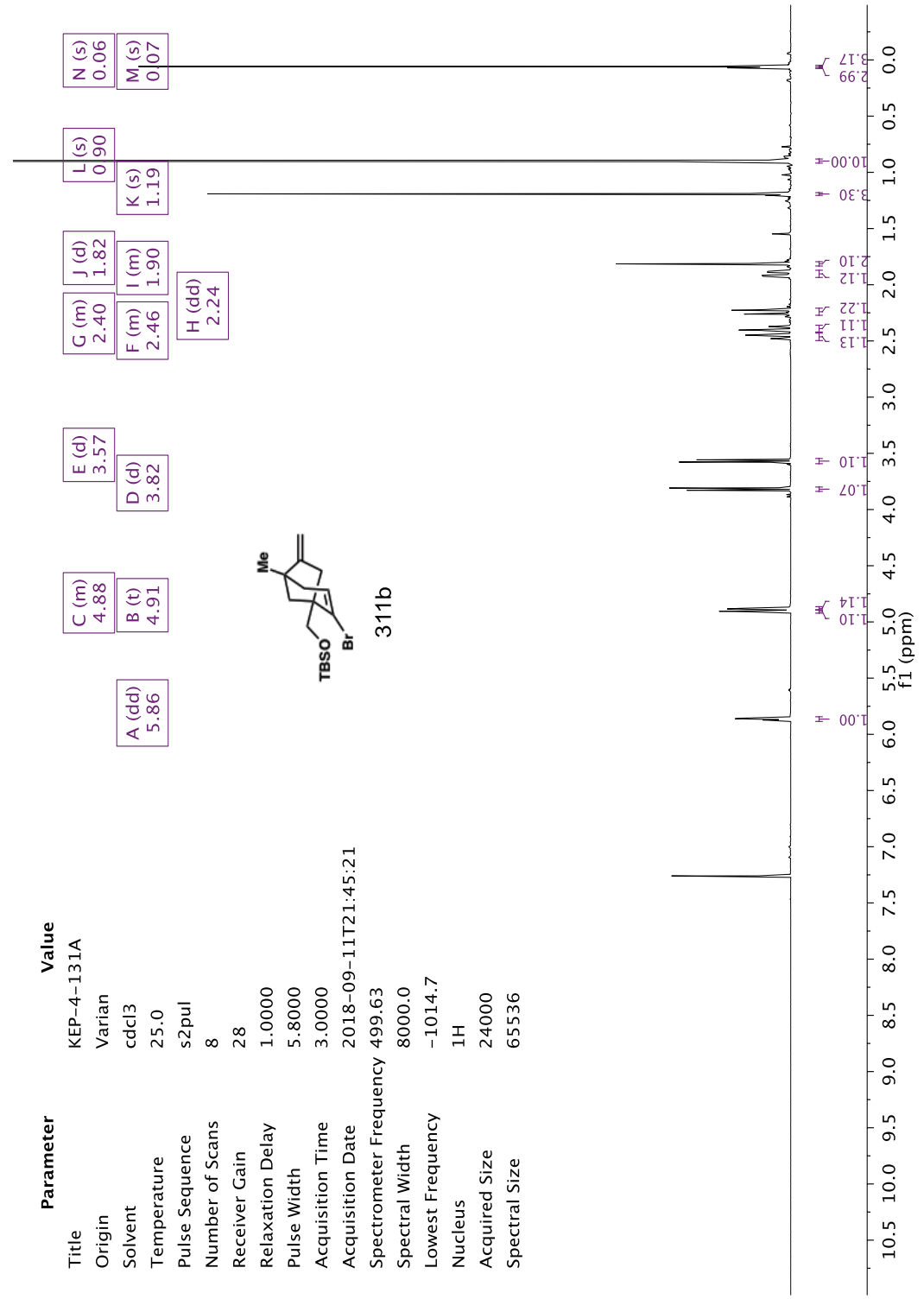
Parameter	Value
Title	JLH-7-238B-column.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	297.1
Pulse Sequence	zg30
Number of Scans	16
Receiver Gain	78.7
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-05-17T09:16:06
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.2
Nucleus	1H
Acquired Size	32768
Spectral Size	65536


Parameter
Value
Title
JLH-7-238B-column.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
297.2
Pulse Sequence
zgpg30
Number of Scans
256
Receiver Gain
50.3
Relaxation Delay
1.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-05-17T09:27:00
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1944.7
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Cl
Me
O
310c
214.1
138.8
132.4
125.6
123.4
44.6
35.5
30.1
29.8
24.5
22.8
f1 (ppm)

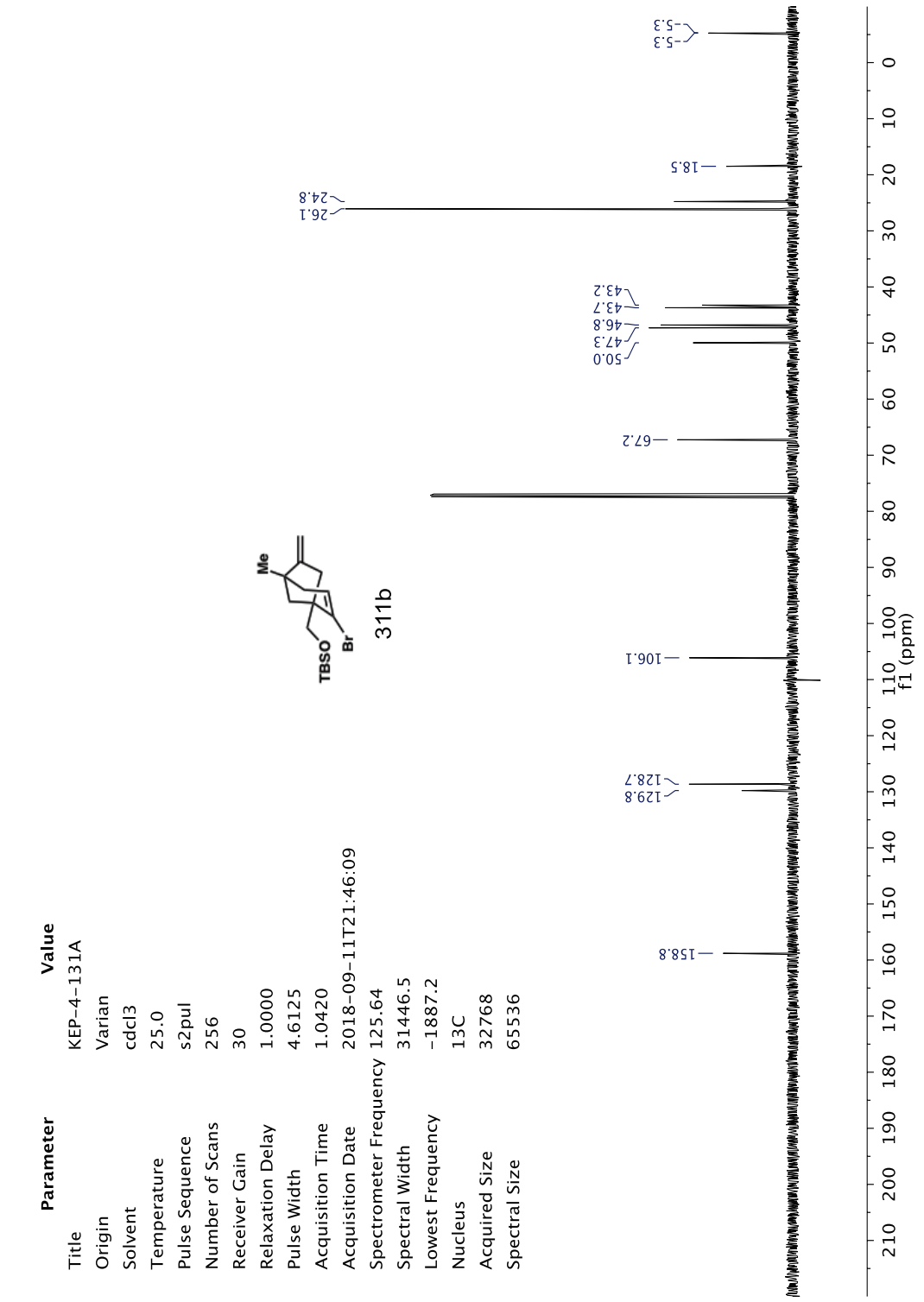


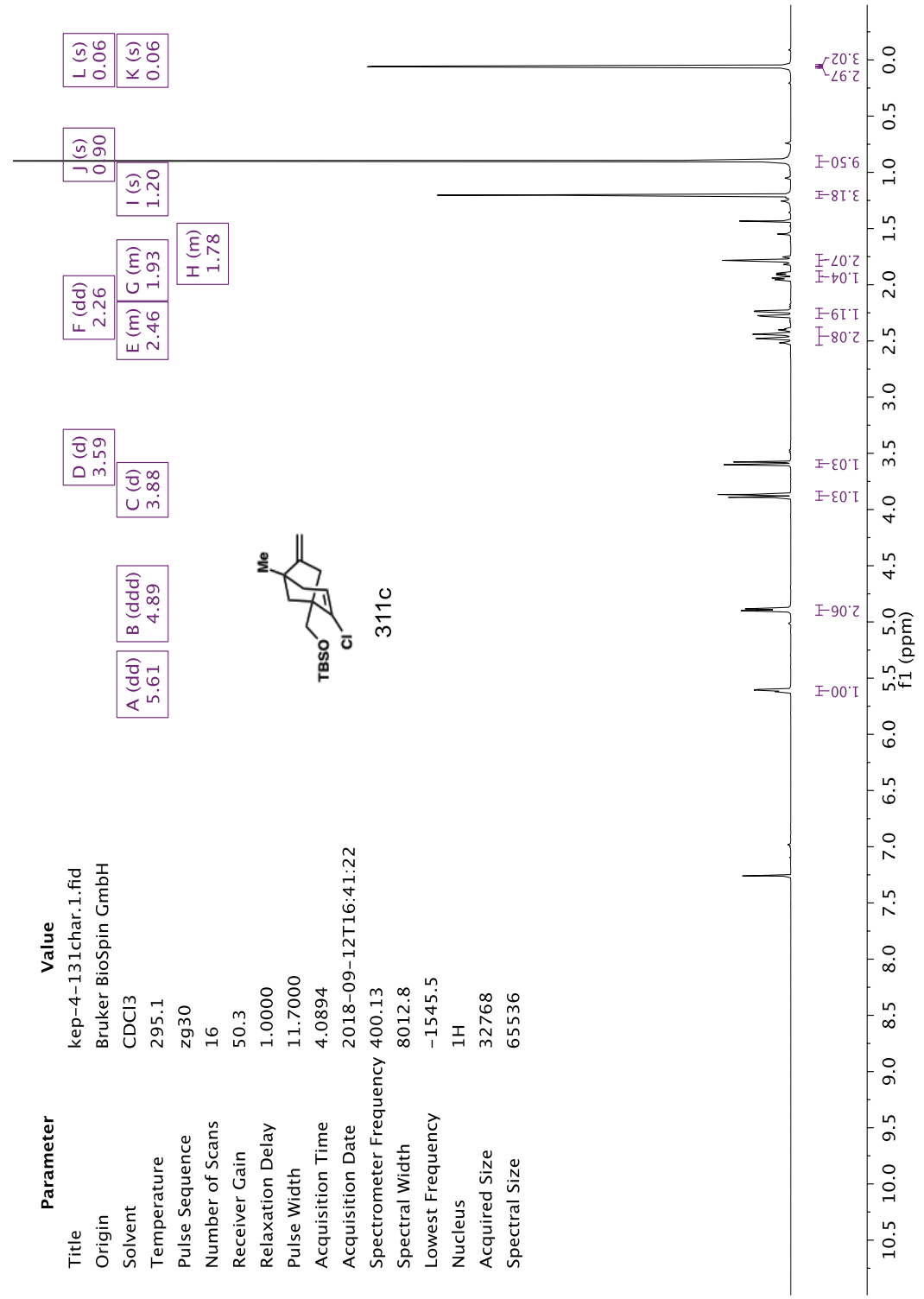
Parameter	Value
Title	ams-1-181.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	293.1
Pulse Sequence	zg30
Number of Scans	16
Receiver Gain	30.3
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-05-24T09:35:04
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.5
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

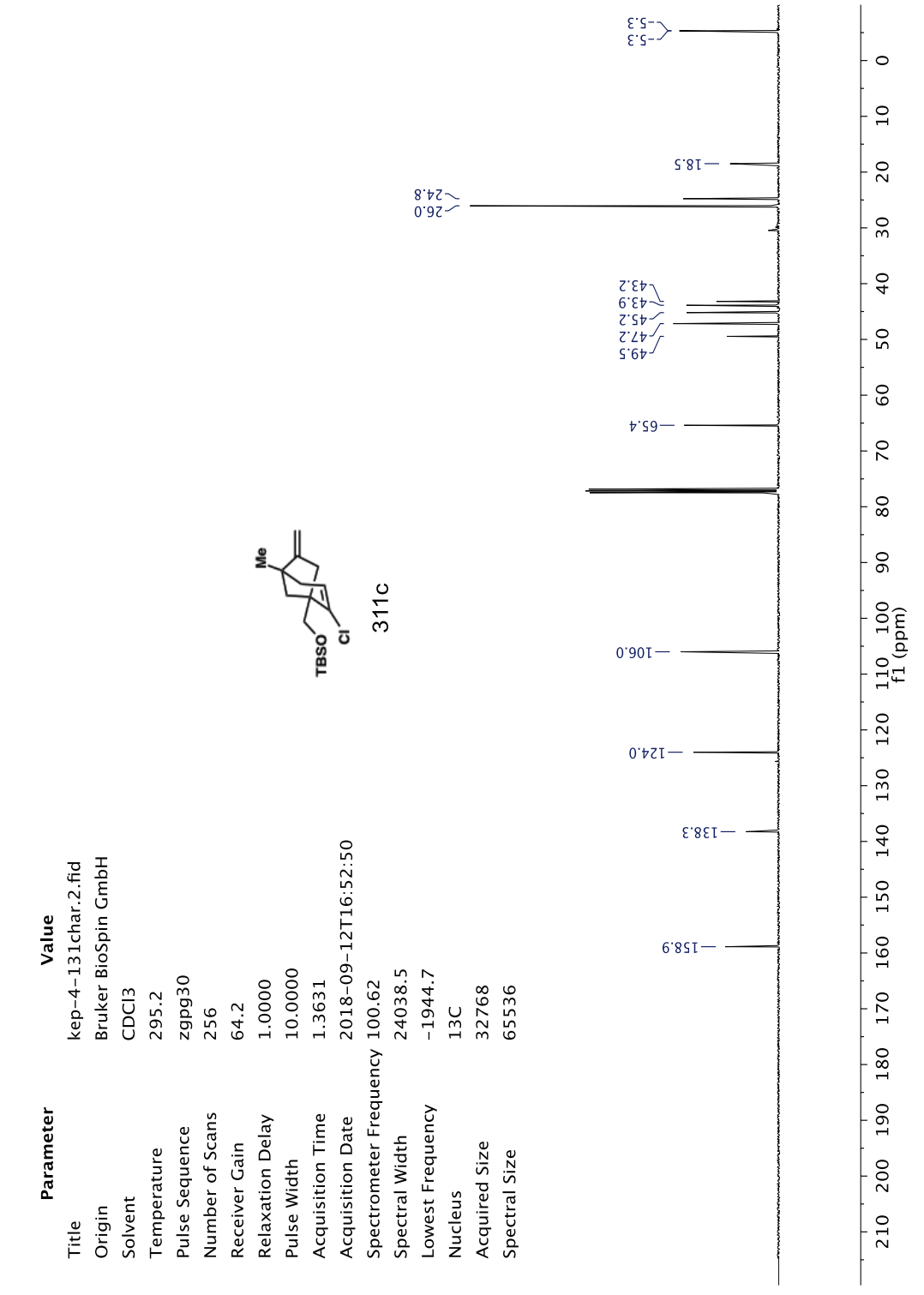

Parameter Value
Title ams-1-181.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 293.2
Pulse Sequence zgpg30
Number of Scans 256
Receiver Gain 72.0
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-05-24T09:45:56
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1946.2
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
TBSO
I
311a
158.7
137.8
107.3
106.1
71.1
50.0
49.0
46.8
43.4
43.3
26.1
24.9
18.5
-5.1
-5.3
f1 (ppm)

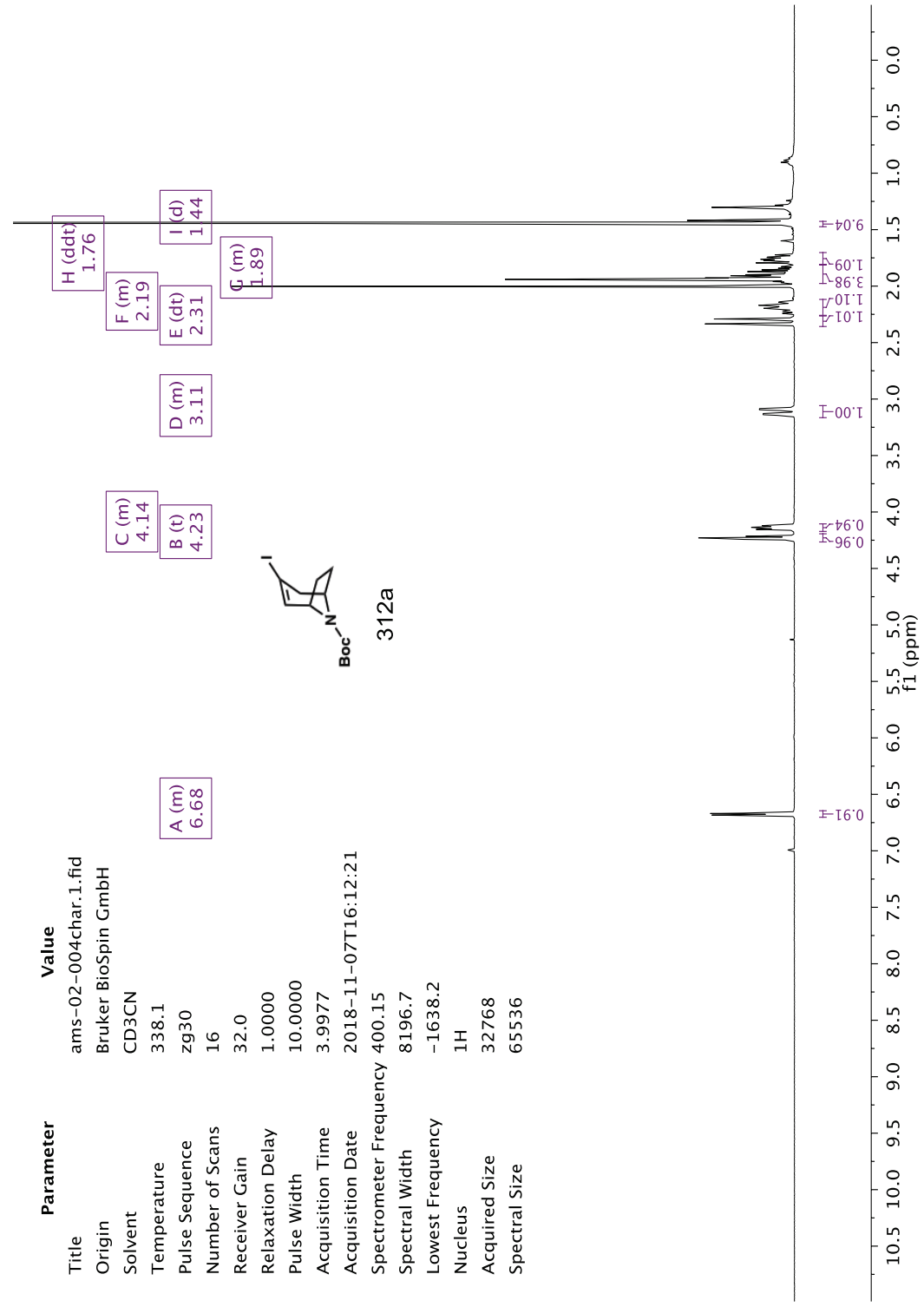


Parameter	Value
Title	KEP-4-131A
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	8
Receiver Gain	28
Relaxation Delay	1.0000
Pulse Width	5.8000
Acquisition Time	3.0000
Acquisition Date	2018-09-11T21:45:21
Spectrometer Frequency	499.63
Spectral Width	8000.0
Lowest Frequency	-1014.7
Nucleus	1H
Acquired Size	24000
Spectral Size	65536

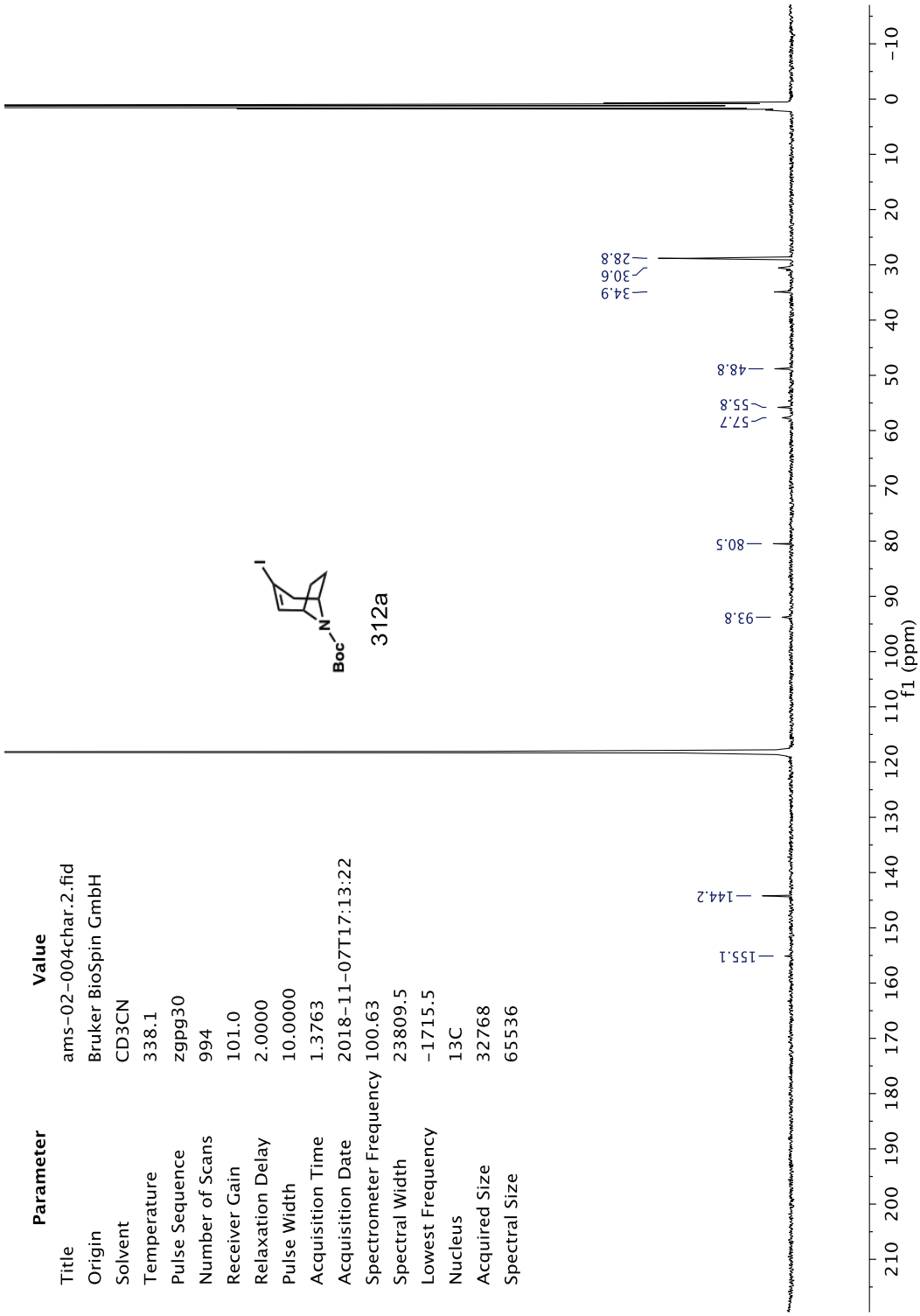

Parameter Value
Title KEP-4-131A
Origin Varian
Solvent cdcl3
Temperature 25.0
Pulse Sequence s2pul
Number of Scans 256
Receiver Gain 30
Relaxation Delay 1.0000
Pulse Width 4.6125
Acquisition Time 1.0420
Acquisition Date 2018-09-11T21:46:09
Spectrometer Frequency 125.64
Spectral Width 31446.5
Lowest Frequency -1887.2
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
TBSO
Br
311b
158.8
129.8
128.7
106.1
67.2
50.0
47.3
46.8
43.7
43.2
26.1
24.8
18.5
-5.3
-5.3
f1 (ppm)

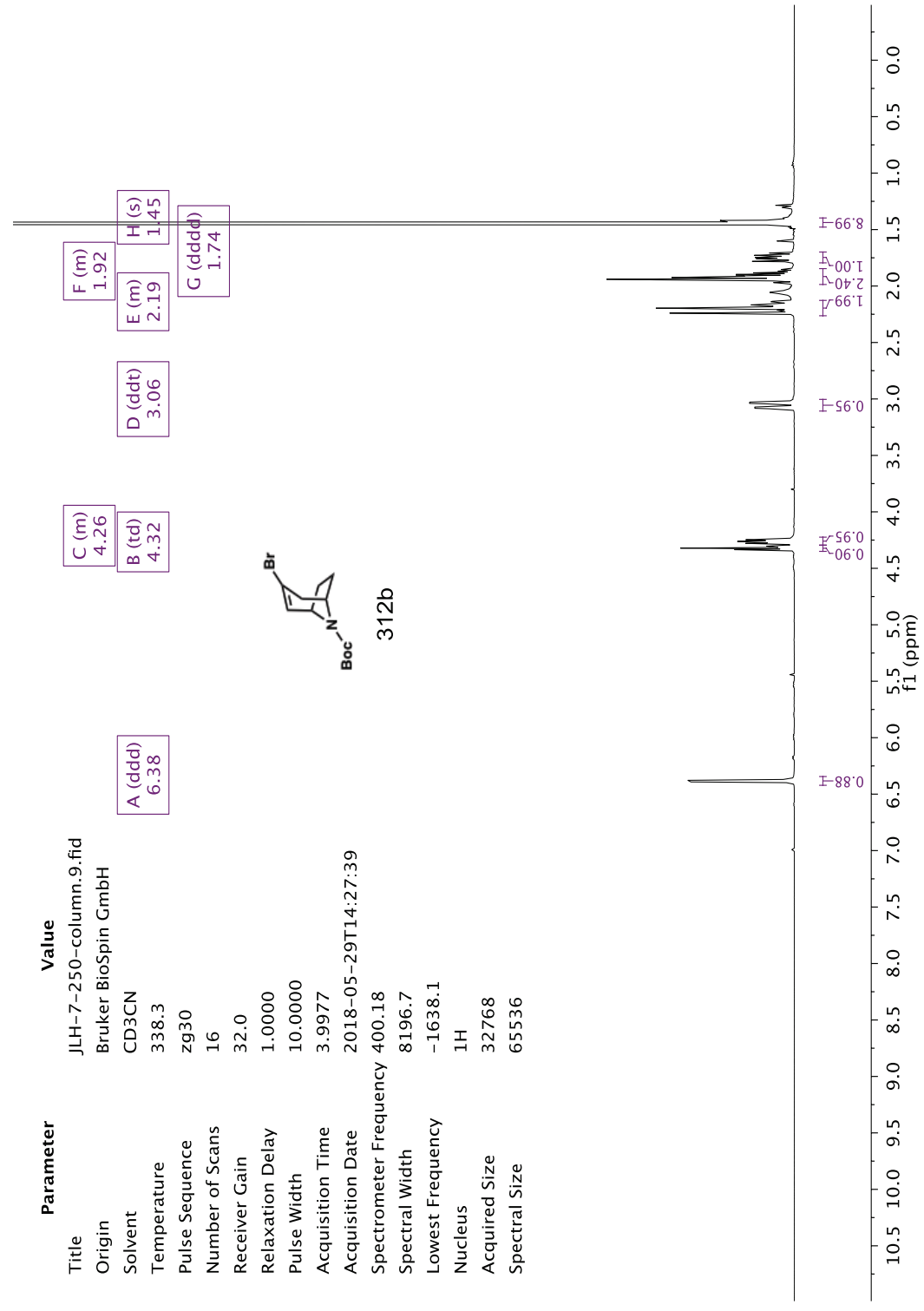

Parameter
Value
Title kep-4-131char.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 50.3
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-09-12T16:41:22
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1545.5
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
A (dd) 5.61
B (ddd) 4.89
C (d) 3.88
D (d) 3.59
E (m) 2.46
F (dd) 2.26
G (m) 1.93
H (m) 1.78
I (s) 1.20
J (s) 0.90
K (s) 0.06
L (s) 0.06
Me
TBSO
Cl
311c
f1 (ppm)


Parameter Value
Title kep-4-131char.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zgpg30
Number of Scans 256
Receiver Gain 64.2
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-09-12T16:52:50
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1944.7
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
TBSO
Cl
311c
158.9
138.3
124.0
106.0
65.4
49.5
47.2
45.2
43.9
43.2
26.0
24.8
18.5
-5.3
-5.3
f1 (ppm)

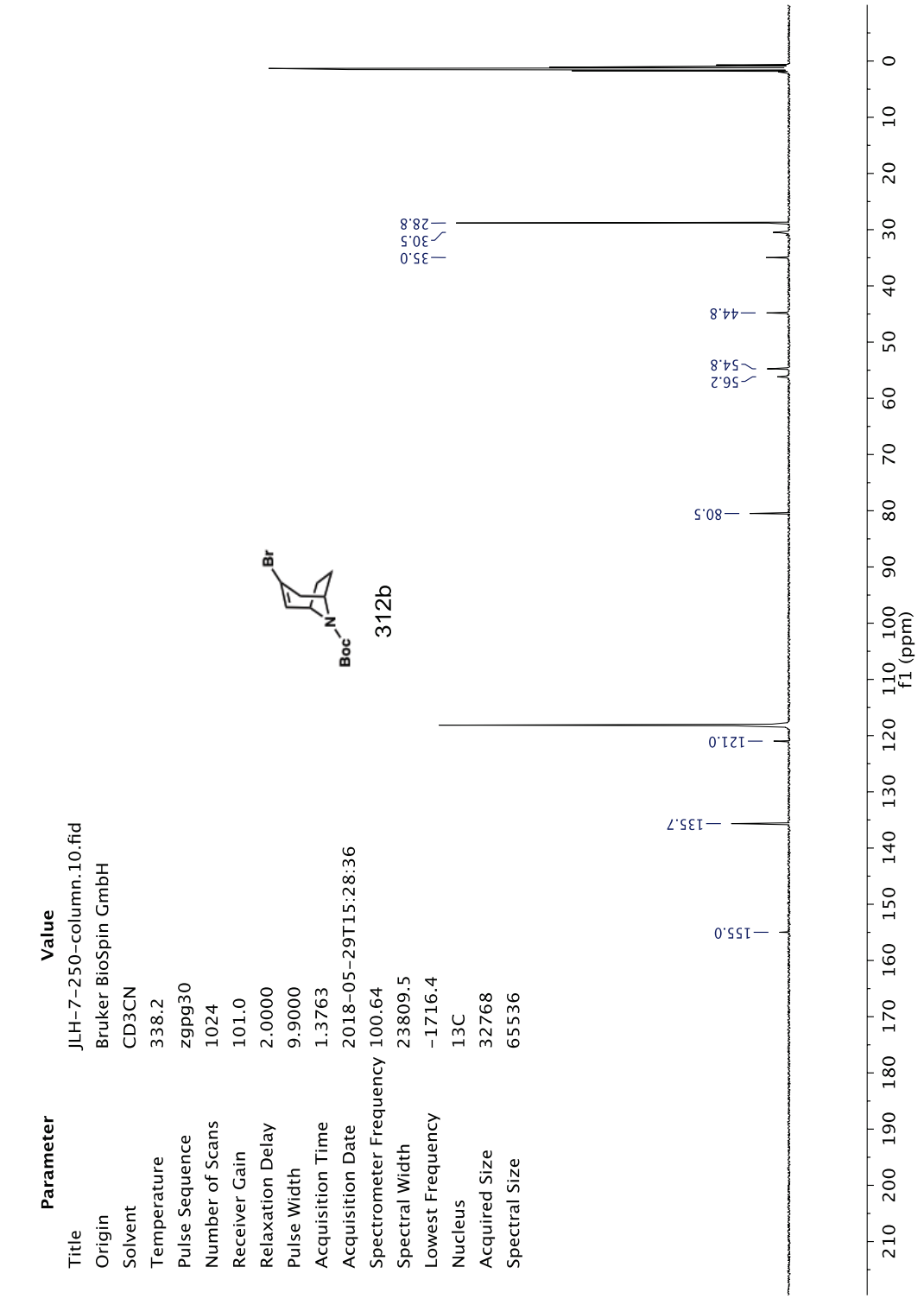


Parameter	Value
Title	ams-02-004char.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CD3CN
Temperature	338.1
Pulse Sequence	zg30
Number of Scans	16
Receiver Gain	32.0
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	3.9977
Acquisition Date	2018-11-07T16:12:21
Spectrometer Frequency	400.15
Spectral Width	8196.7
Lowest Frequency	-1638.2
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

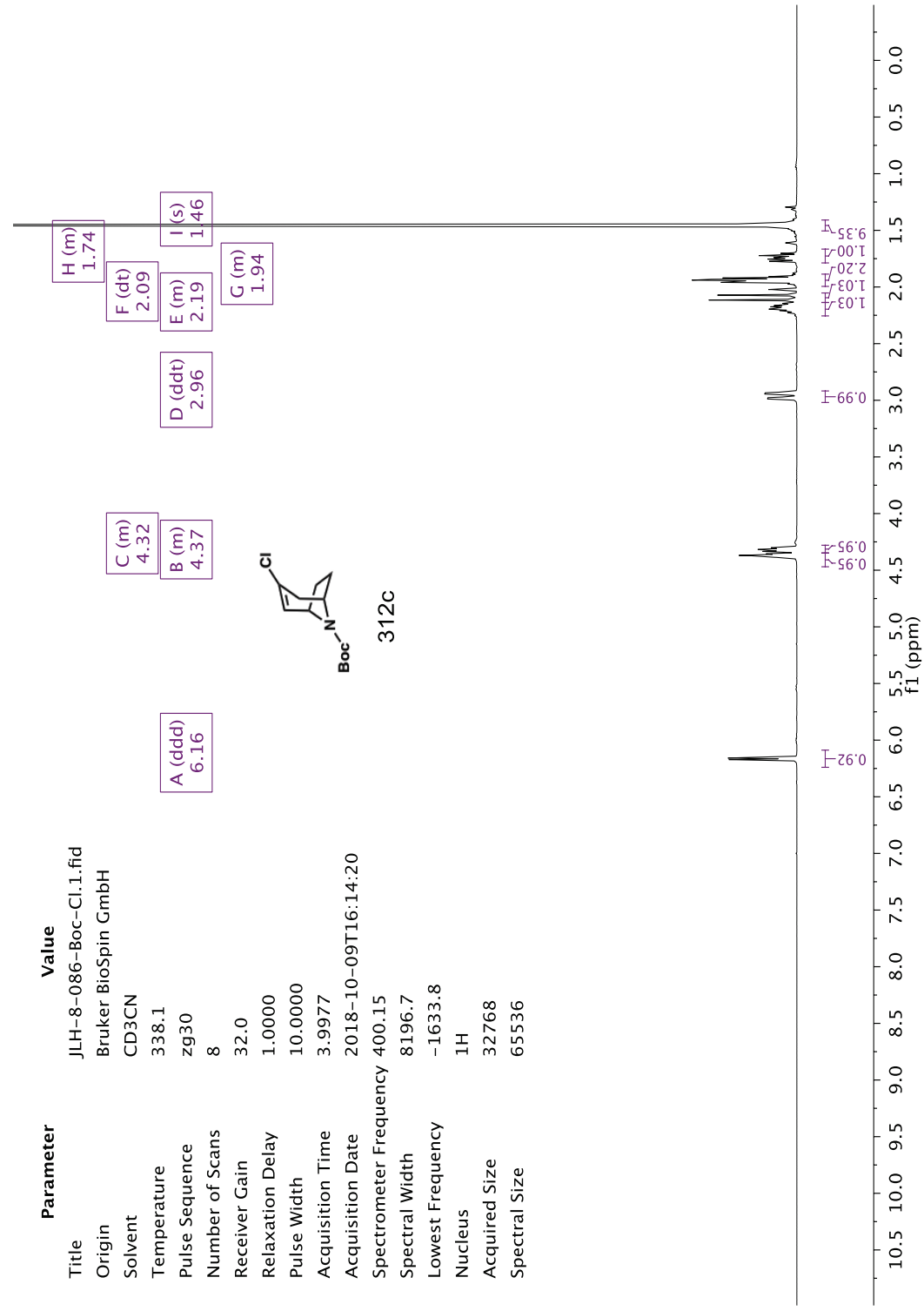

Parameter Value
Title ams-02-004char.2.fid
Origin Bruker BioSpin GmbH
Solvent CD3CN
Temperature 338.1
Pulse Sequence zgpg30
Number of Scans 994
Receiver Gain 101.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3763
Acquisition Date 2018-11-07T17:13:22
Spectrometer Frequency 100.63
Spectral Width 23809.5
Lowest Frequency -1715.5
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
155.1
144.2
93.8
80.5
57.7
55.8
48.8
34.9
30.6
28.8
I
N
Boc
312a
f1 (ppm)

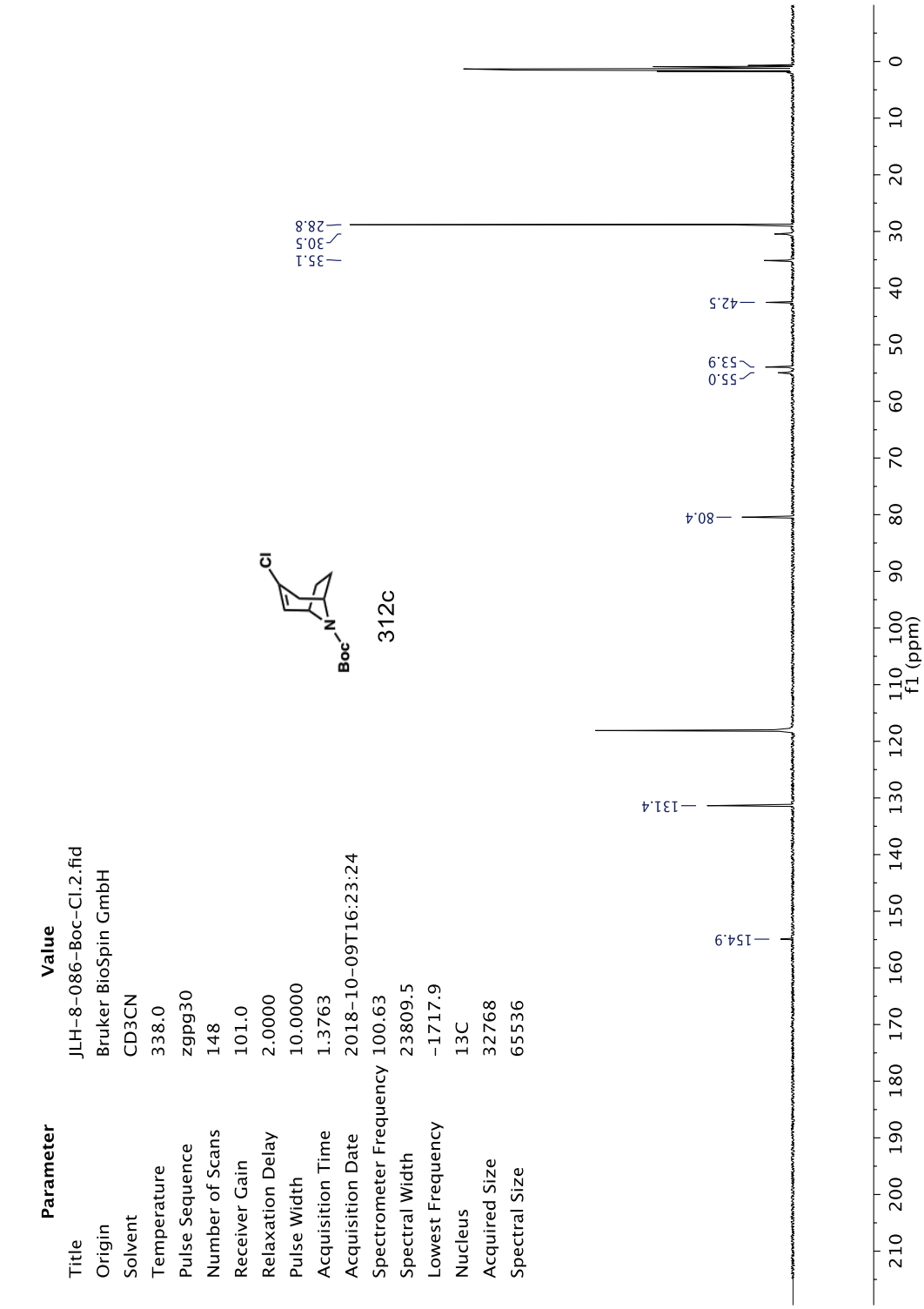


Parameter	Value
Title	JLH-7-250-column.9.fid
Origin	Bruker BioSpin GmbH
Solvent	CD3CN
Temperature	338.3
Pulse Sequence	zg30
Number of Scans	16
Receiver Gain	32.0
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	3.9977
Acquisition Date	2018-05-29T14:27:39
Spectrometer Frequency	400.18
Spectral Width	8196.7
Lowest Frequency	-1638.1
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

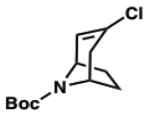


Parameter	Value
Title	JLH-7-250-column.10.fid
Origin	Bruker BioSpin GmbH
Solvent	CD3CN
Temperature	338.2
Pulse Sequence	zgpg30
Number of Scans	1024
Receiver Gain	101.0
Relaxation Delay	2.0000
Pulse Width	9.9000
Acquisition Time	1.3763
Acquisition Date	2018-05-29T15:28:36
Spectrometer Frequency	100.64
Spectral Width	23809.5
Lowest Frequency	-1716.4
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

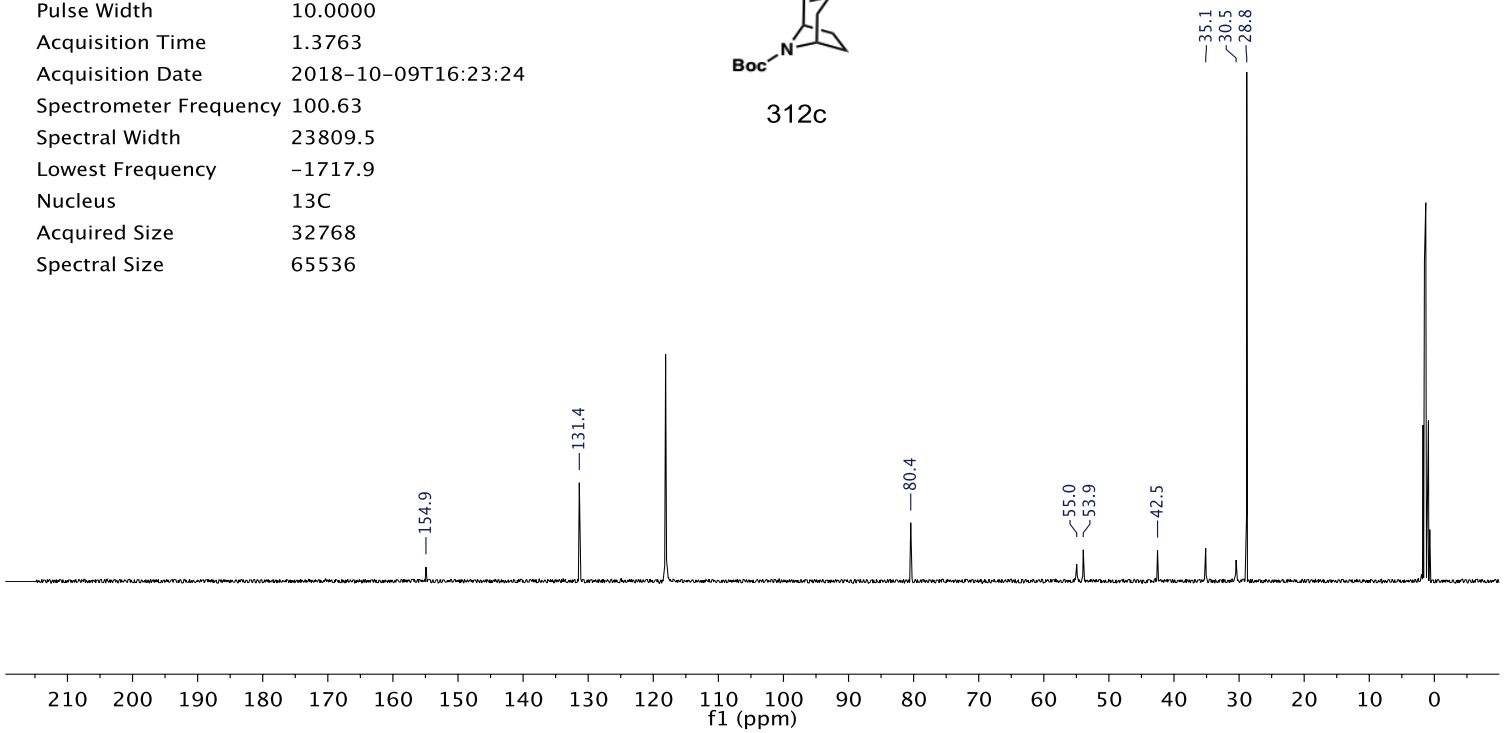

Parameter
Value
Title JLH-8-086-Boc-Cl.1.fid
Origin Bruker BioSpin GmbH
Solvent CD3CN
Temperature 338.1
Pulse Sequence zg30
Number of Scans 8
Receiver Gain 32.0
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 3.9977
Acquisition Date 2018-10-09T16:14:20
Spectrometer Frequency 400.15
Spectral Width 8196.7
Lowest Frequency -1633.8
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
A (ddd) 6.16
B (m) 4.37
C (m) 4.32
D (ddt) 2.96
E (m) 2.19
F (dt) 2.09
G (m) 1.94
H (m) 1.74
I (s) 1.46
Cl
N
Boc
312c
0.92
0.95
0.95
0.99
1.03
1.03
2.20
1.00
9.35
f1 (ppm)

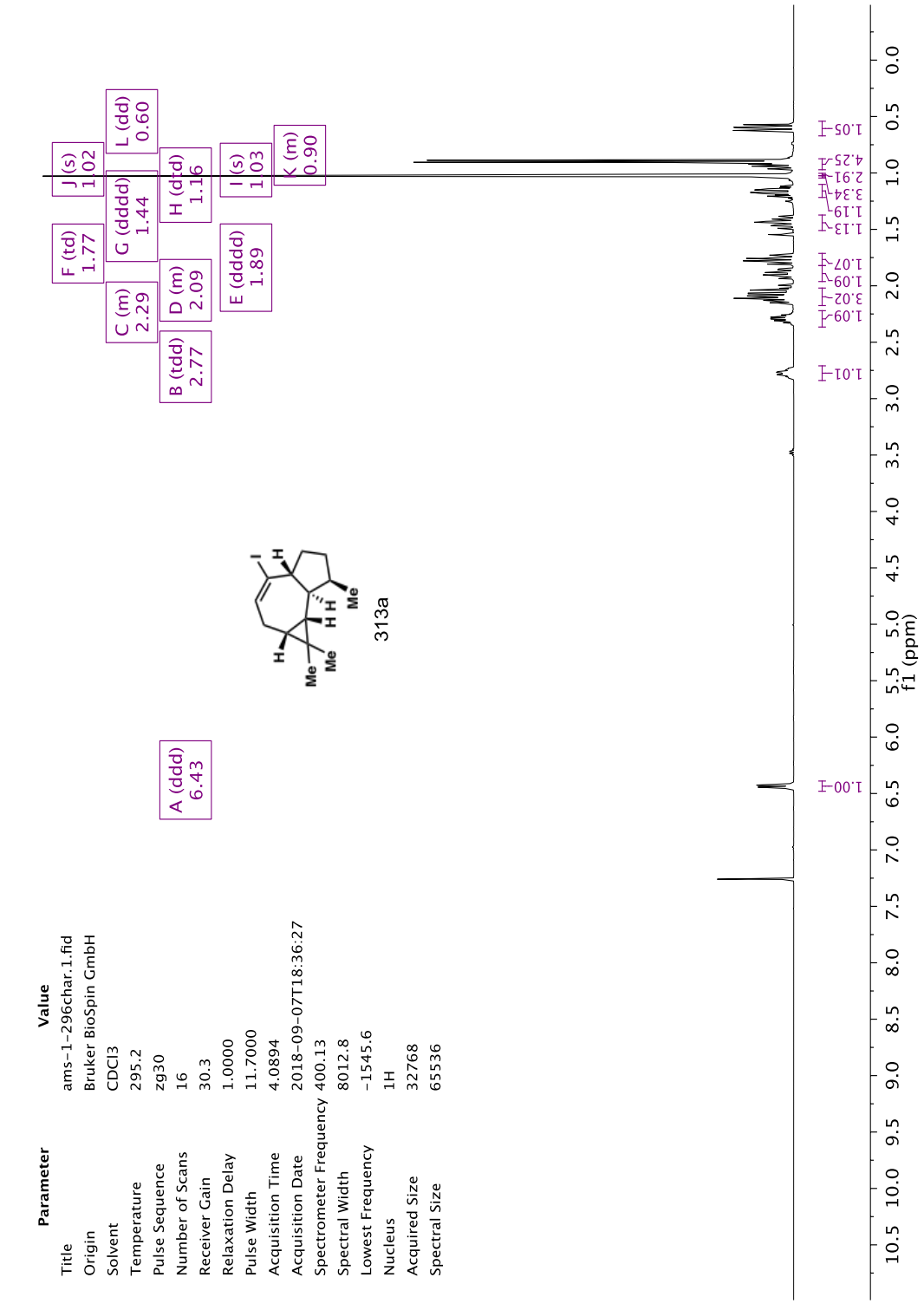

Parameter Value
Title JLH-8-086-Boc-Cl.2.fid
Origin Bruker BioSpin GmbH
Solvent CD3CN
Temperature 338.0
Pulse Sequence zgpg30
Number of Scans 148
Receiver Gain 101.0
Relaxation Delay 2.0000
Pulse Width 10.0000
Acquisition Time 1.3763
Acquisition Date 2018-10-09T16:23:24
Spectrometer Frequency 100.63
Spectral Width 23809.5
Lowest Frequency -1717.9
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Cl
N
Boc
312c
154.9
131.4
80.4
55.0
53.9
42.5
35.1
30.5
28.8
f1 (ppm)

Parameter	Value
Title	JLH-8-086-Boc-Cl.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CD3CN
Temperature	338.0
Pulse Sequence	zgpg30
Number of Scans	148
Receiver Gain	101.0
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.3763
Acquisition Date	2018-10-09T16:23:24
Spectrometer Frequency	100.63
Spectral Width	23809.5
Lowest Frequency	-1717.9
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

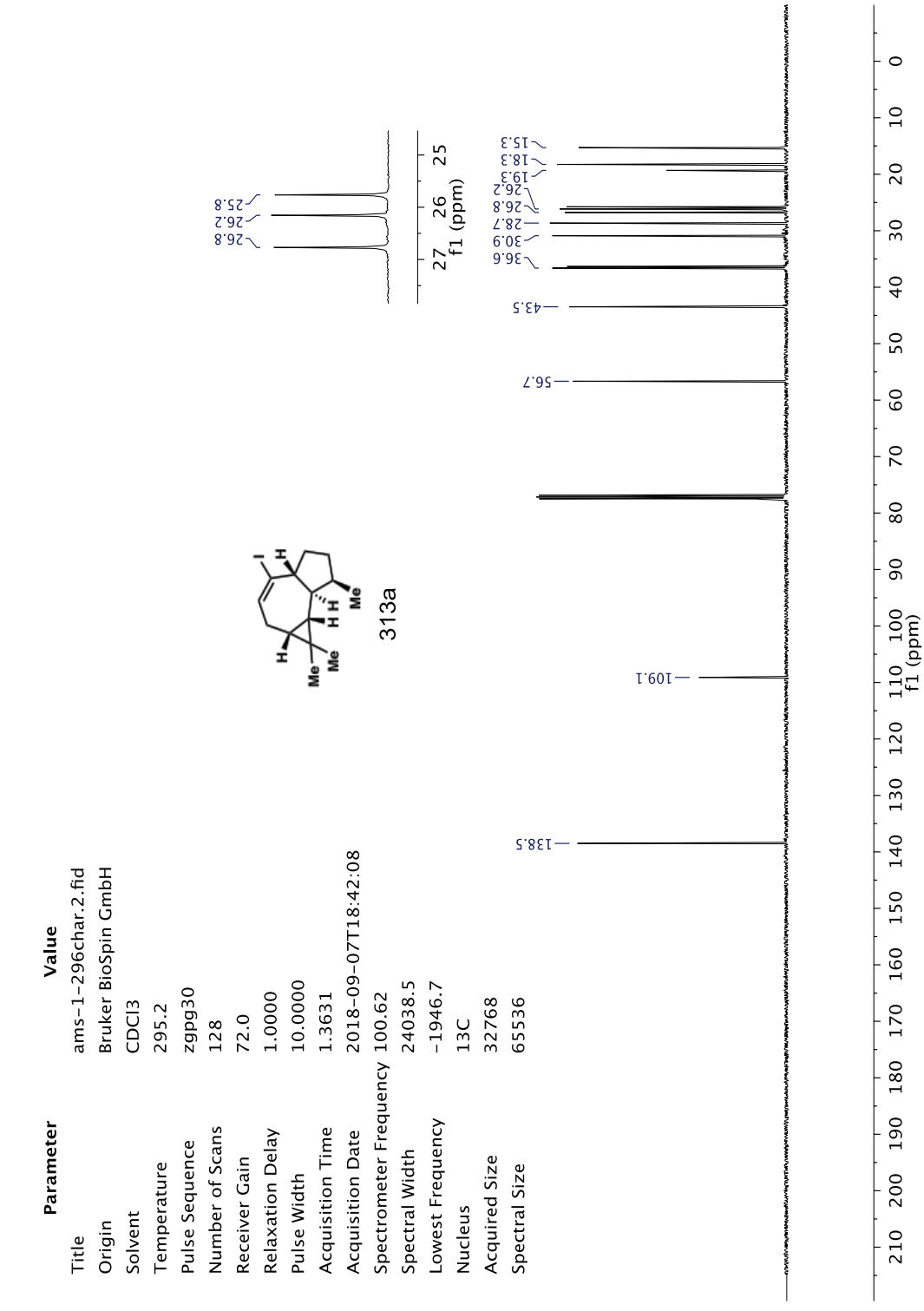


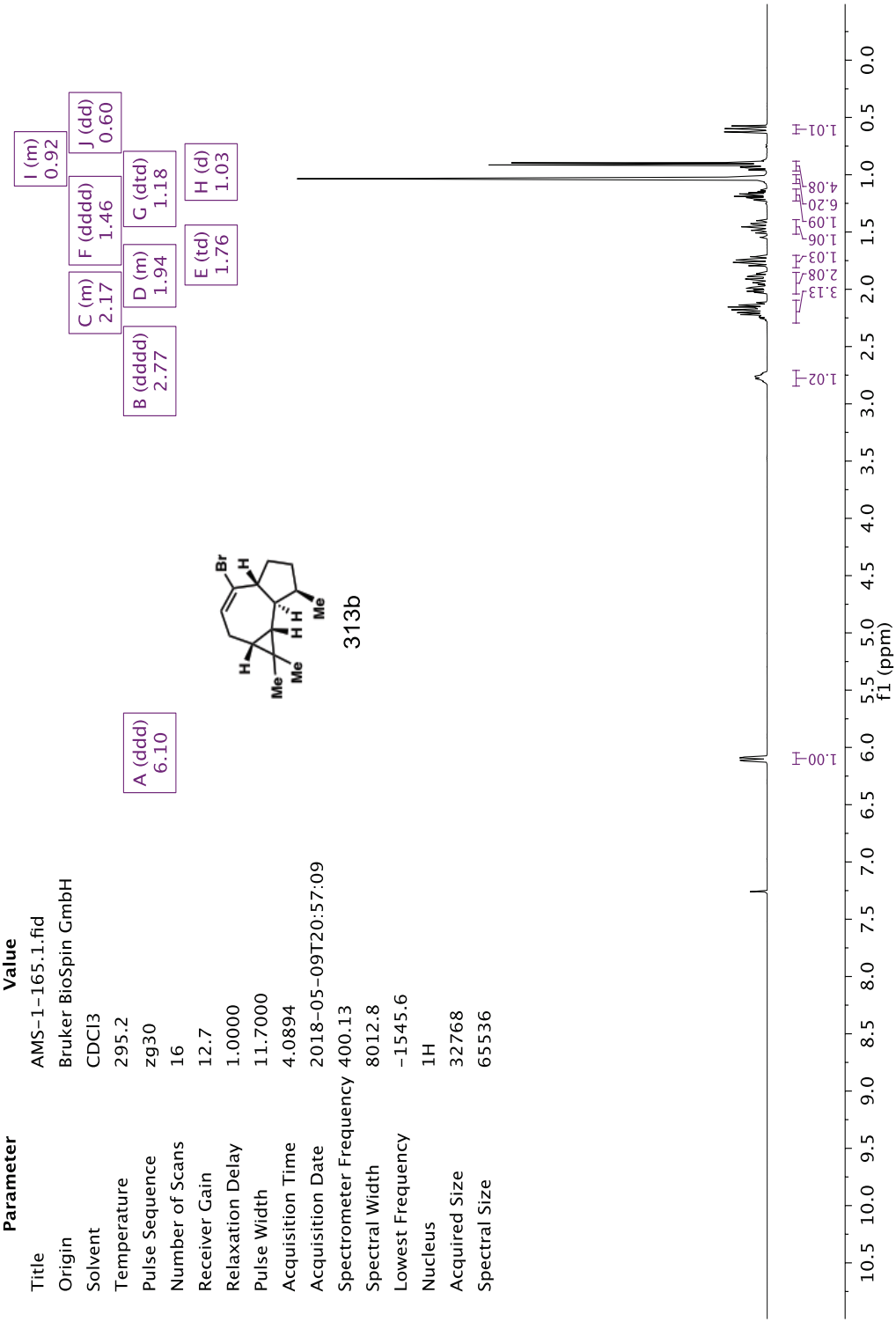
312c



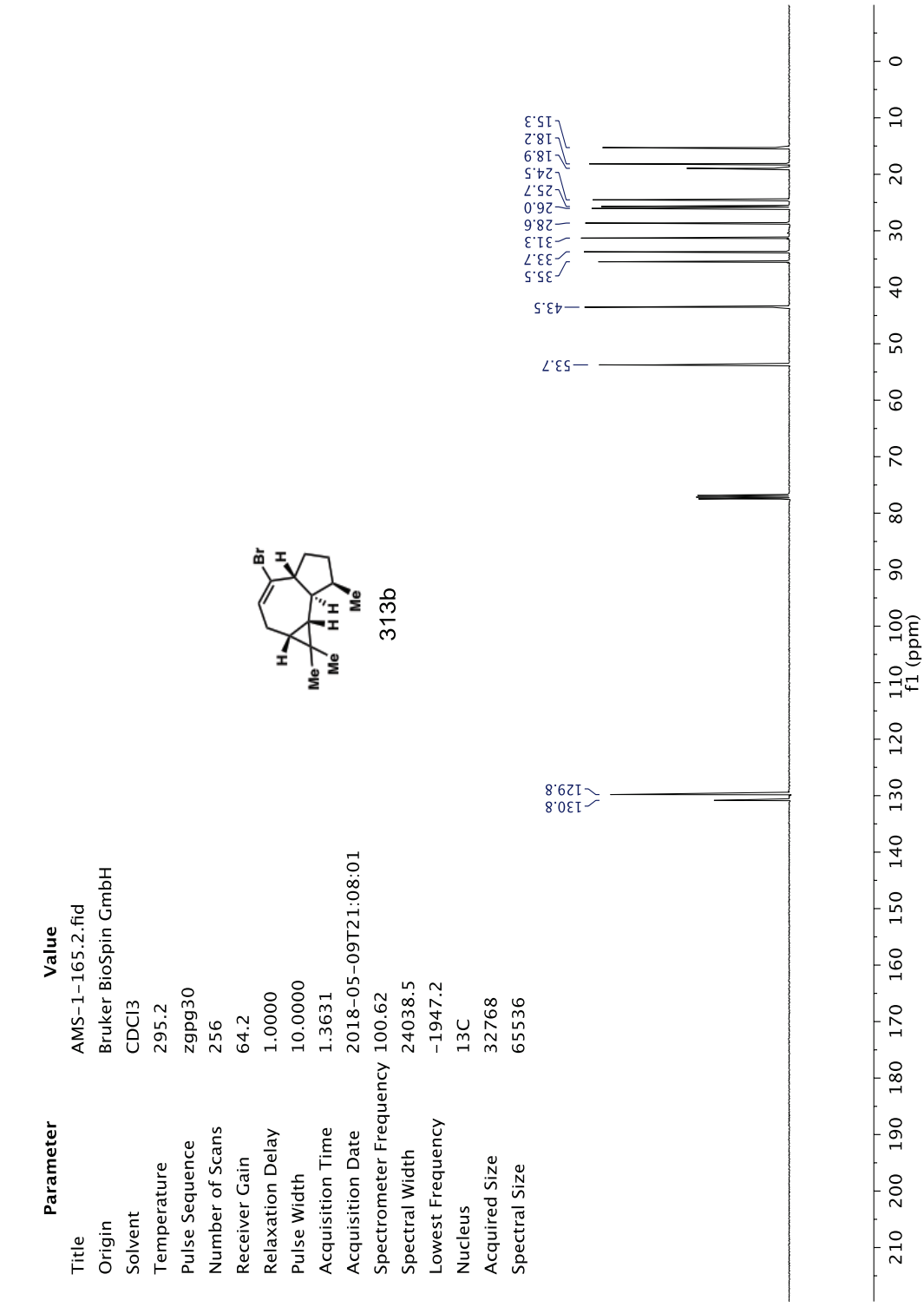


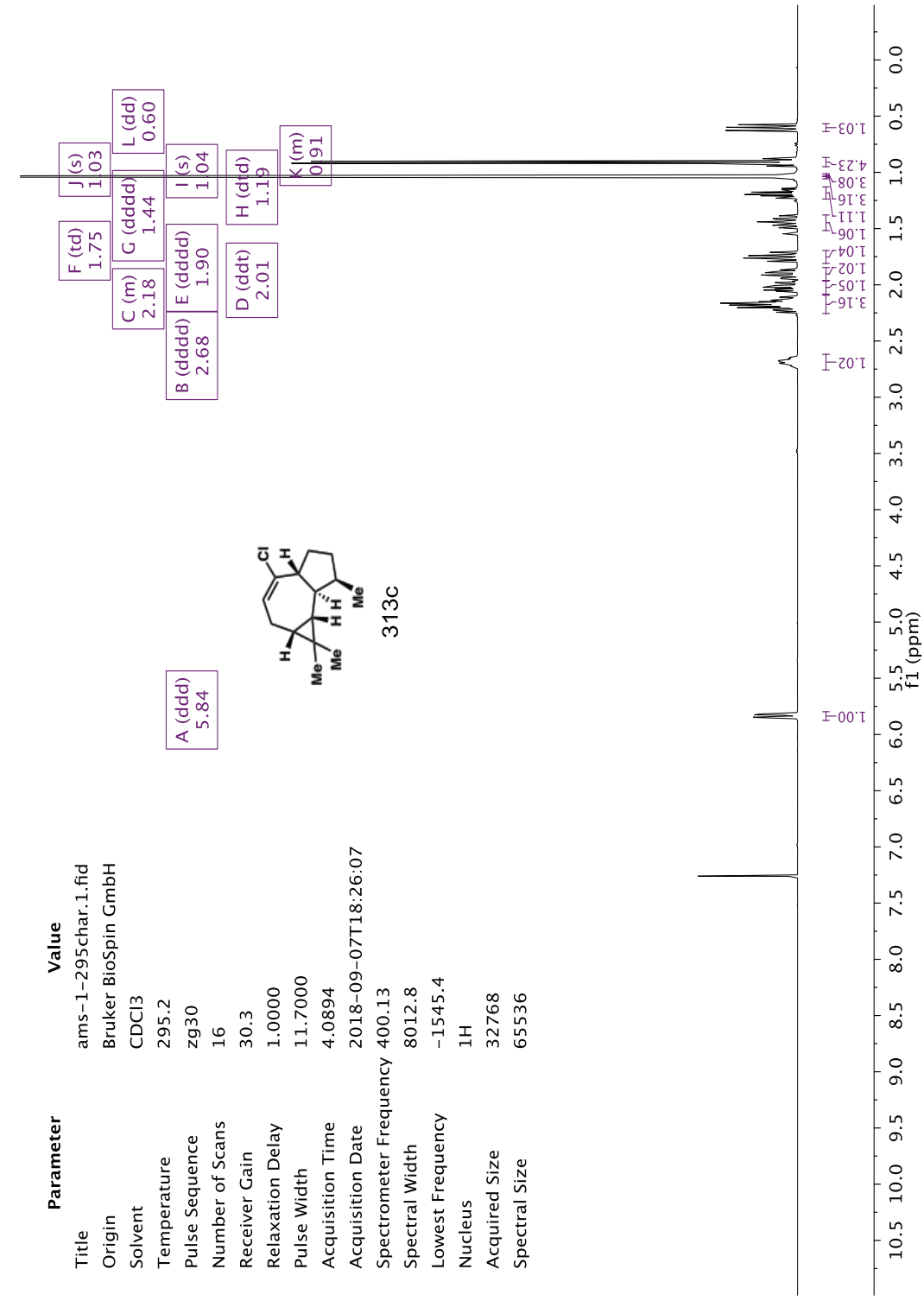
Parameter	Value
Title	ams-1-296char.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zg30
Number of Scans	16
Receiver Gain	30.3
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-09-07T18:36:27
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536


Parameter Value
Title ams-1-296char.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 72.0
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-09-07T18:42:08
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1946.7
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
313a
Me
Me
Me
H
H
H
I
138.5
109.1
56.7
43.5
36.6
30.9
28.7
26.8
26.2
19.3
18.3
15.3
26.8
26.2
25.8
f1 (ppm)
f1 (ppm)

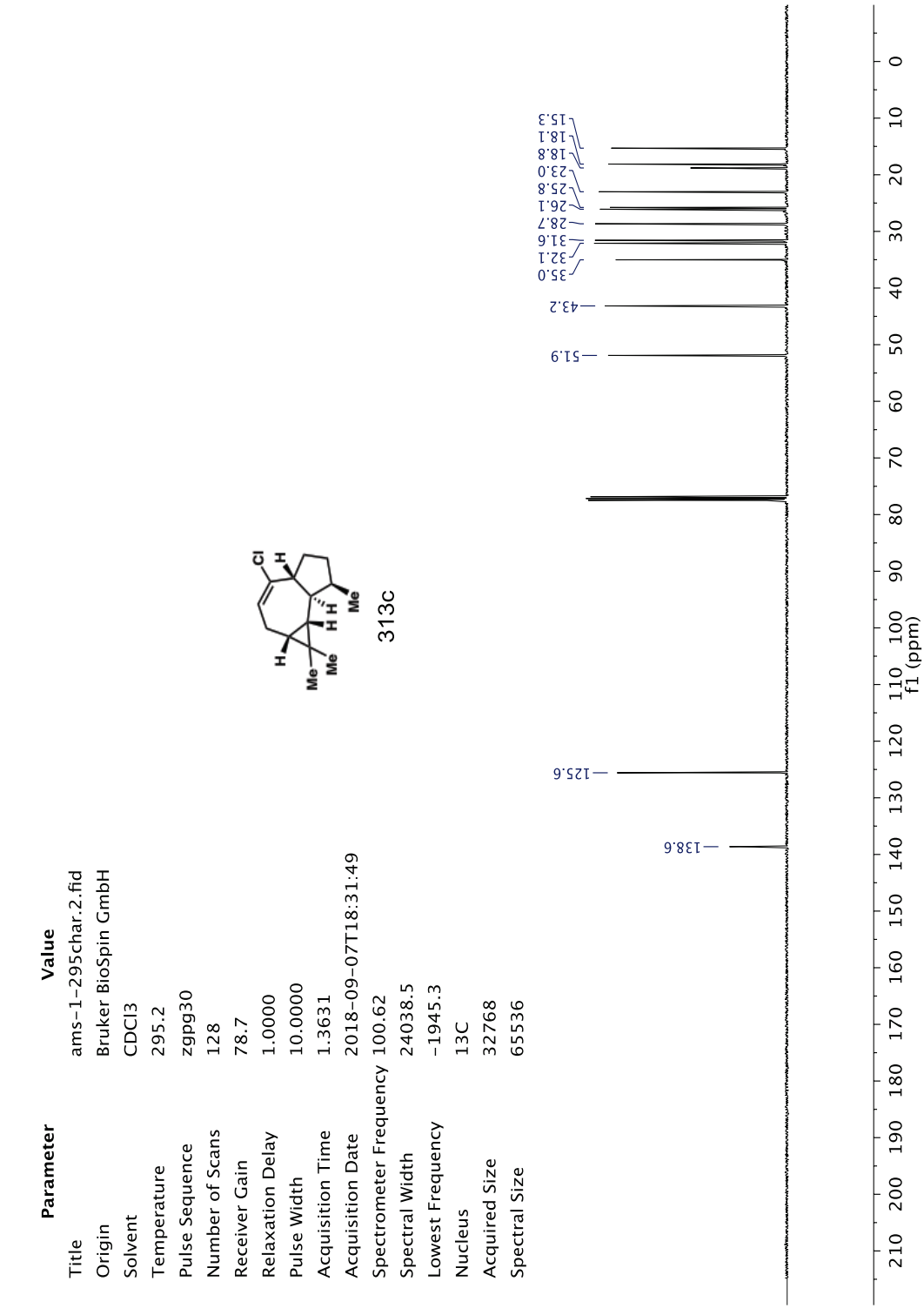


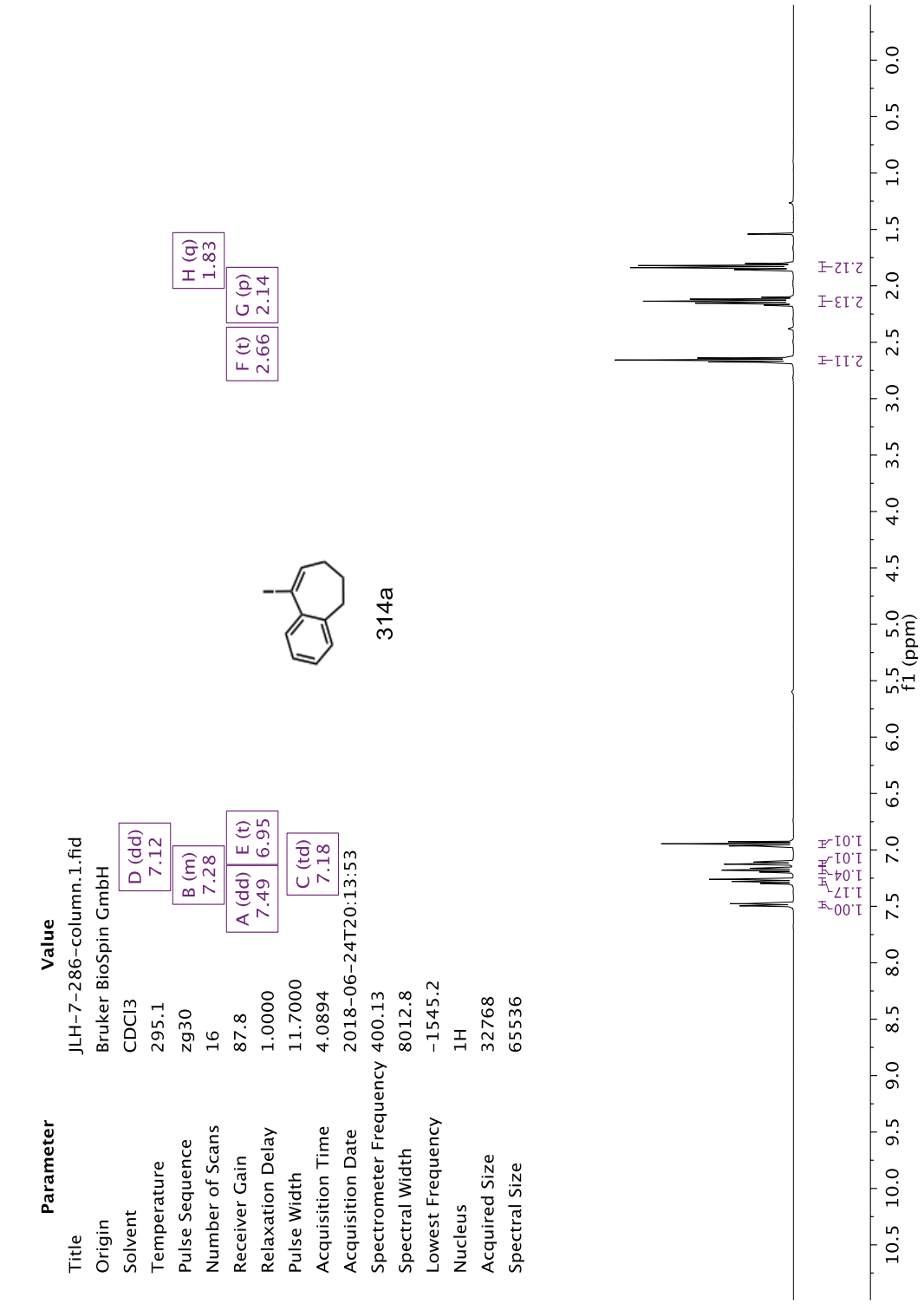
Parameter	Value
Title	AMS-1-165.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zg30
Number of Scans	16
Receiver Gain	12.7
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-05-09T20:57:09
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536


Parameter Value
Title AMS-1-165.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zgpg30
Number of Scans 256
Receiver Gain 64.2
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-05-09T21:08:01
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1947.2
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Br
H
H
Me
H H
Me
Me
313b
130.8
129.8
53.7
43.5
35.5
33.7
31.3
28.6
26.0
25.7
24.5
18.9
18.2
15.3
f1 (ppm)



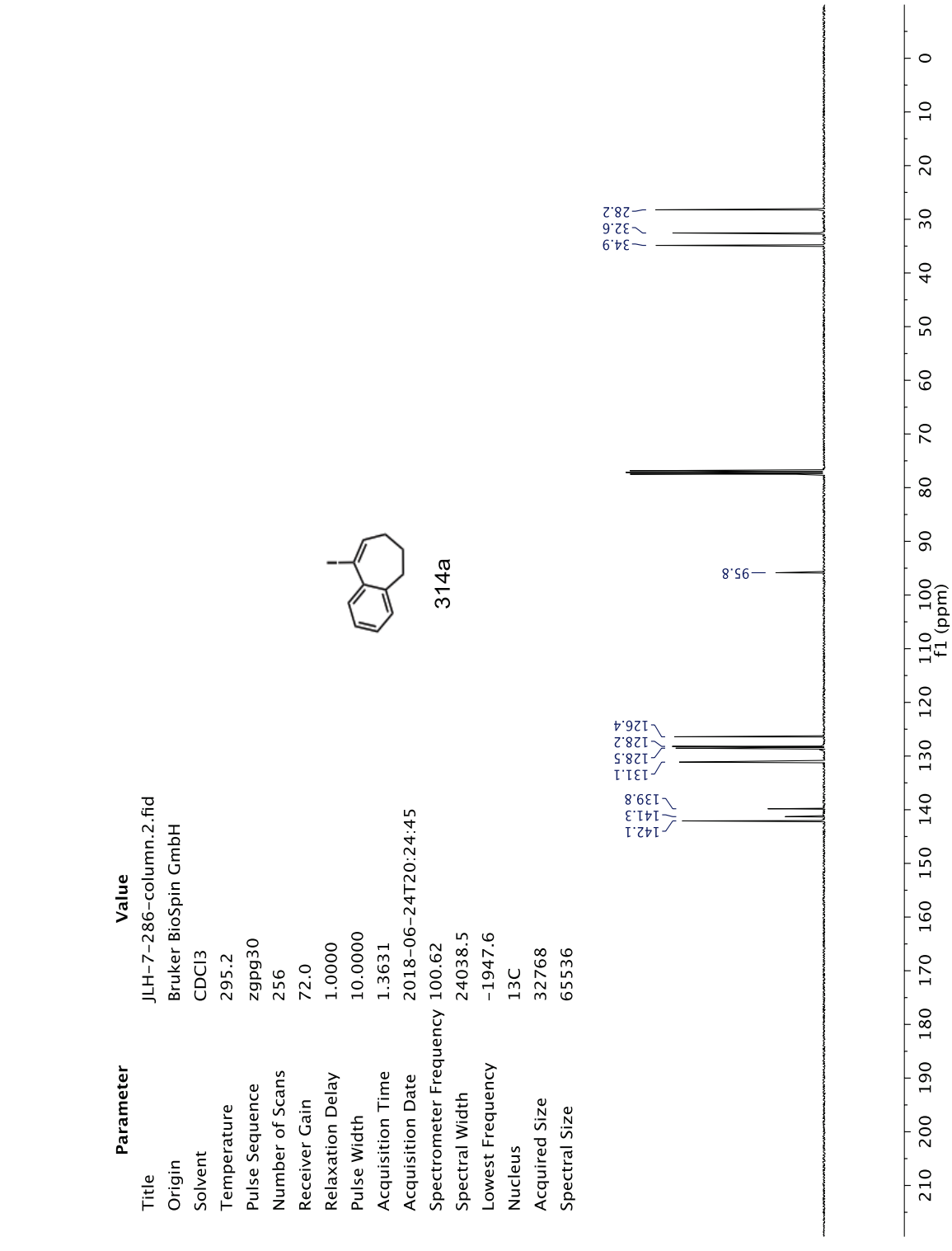
Parameter	Value
Title	ams-1-295char.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zg30
Number of Scans	16
Receiver Gain	30.3
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-09-07T18:26:07
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

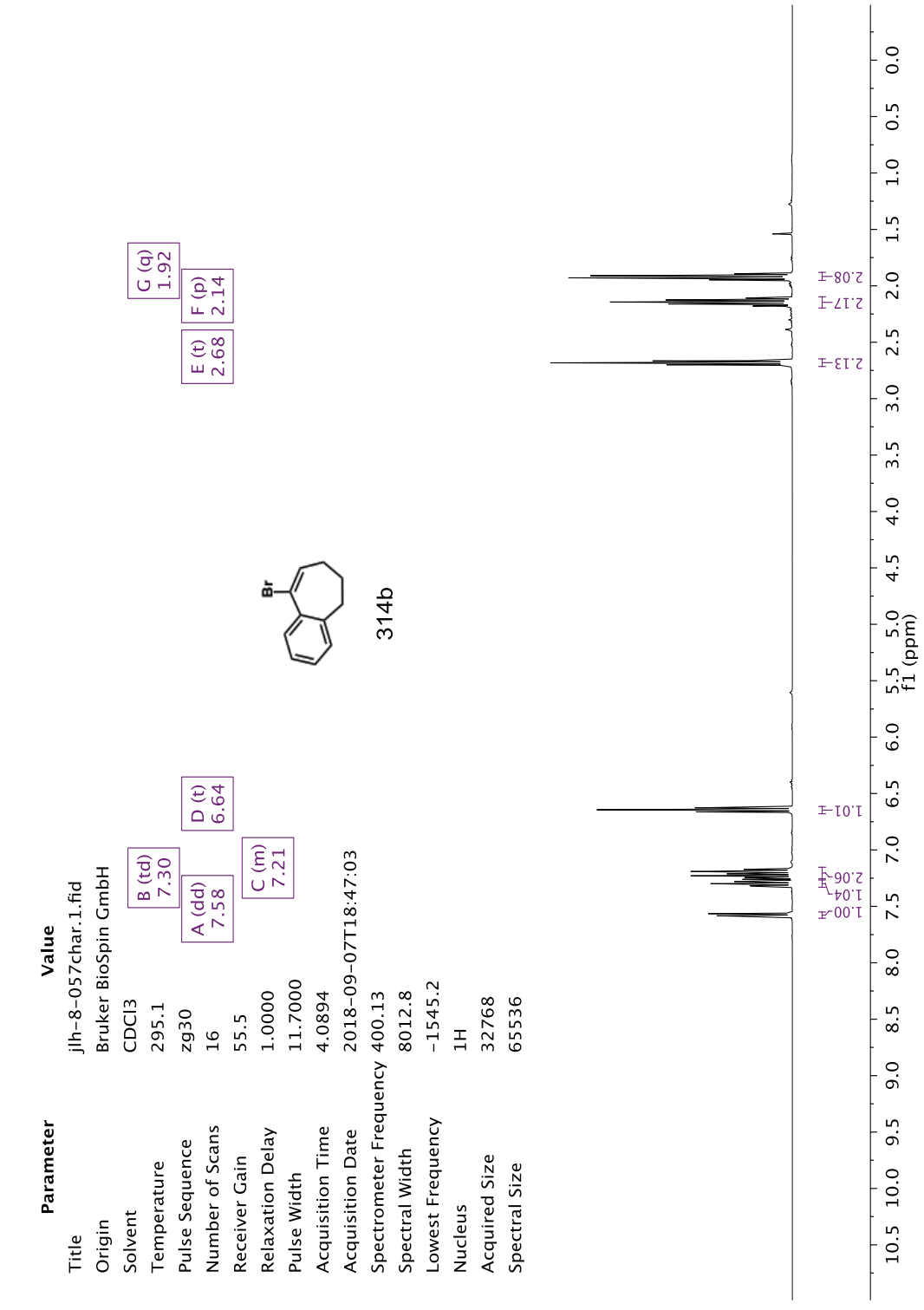

Parameter
Value
Title
ams-1-295char.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
zgpg30
Number of Scans
128
Receiver Gain
78.7
Relaxation Delay
1.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-09-07T18:31:49
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1945.3
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Cl
H
H
Me
H
Me
Me
313c
138.6
125.6
51.9
43.2
35.0
32.1
31.6
28.7
26.1
25.8
23.0
18.8
18.1
15.3
f1 (ppm)

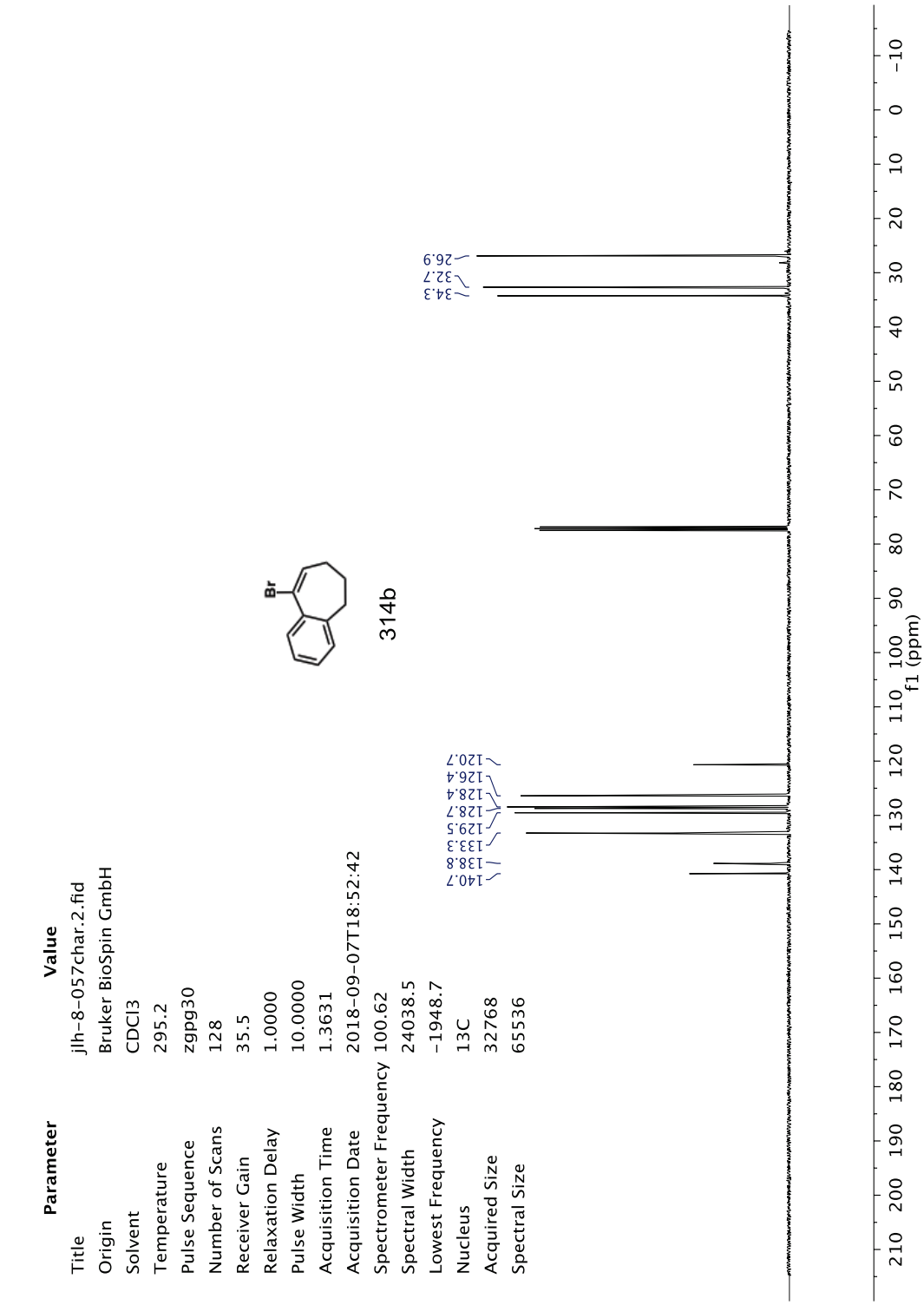

Parameter
Value
Title
JLH-7-286-column.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.1
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
87.8
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-06-24T20:13:53
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1545.2
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
A (dd) 7.49
E (t) 6.95
D (dd) 7.12
B (m) 7.28
C (td) 7.18
F (t) 2.66
G (p) 2.14
H (q) 1.83
314a
1.00
1.17
1.04
1.01
1.01
2.11
2.13
2.12
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

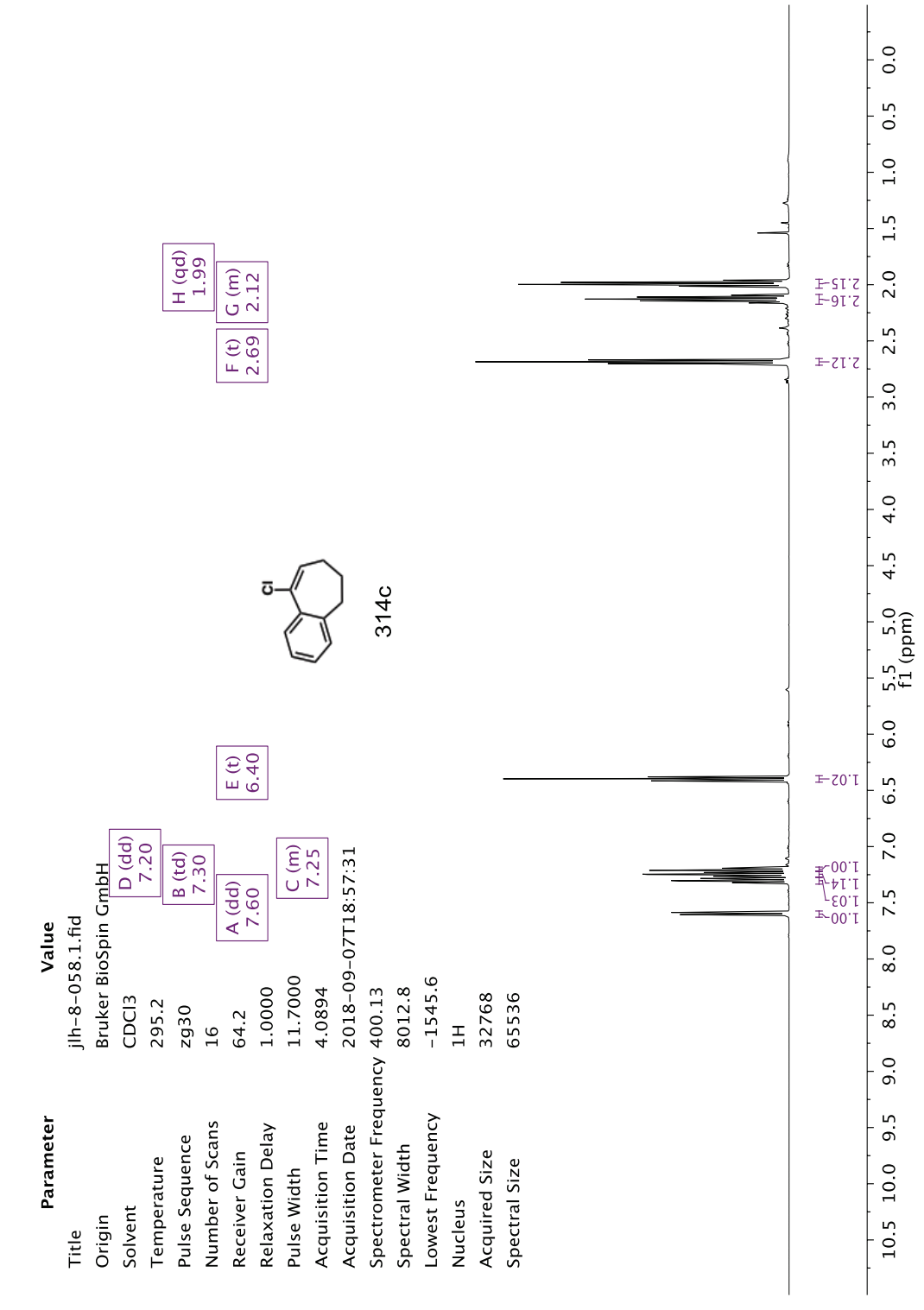
Parameter	Value
Title	JLH-7-286-column.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zgpg30
Number of Scans	256
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-06-24T20:24:45
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1947.6
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

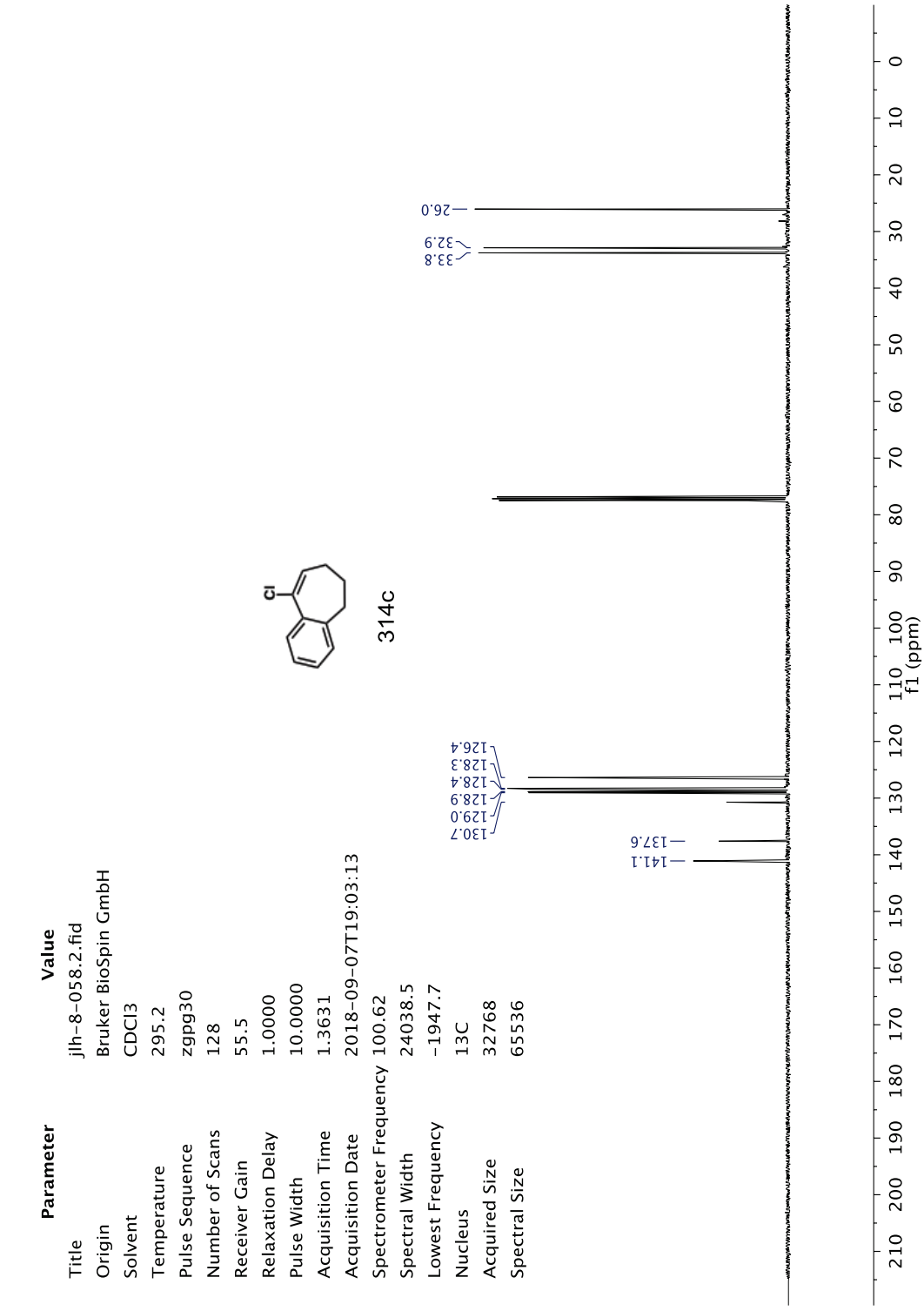
314a

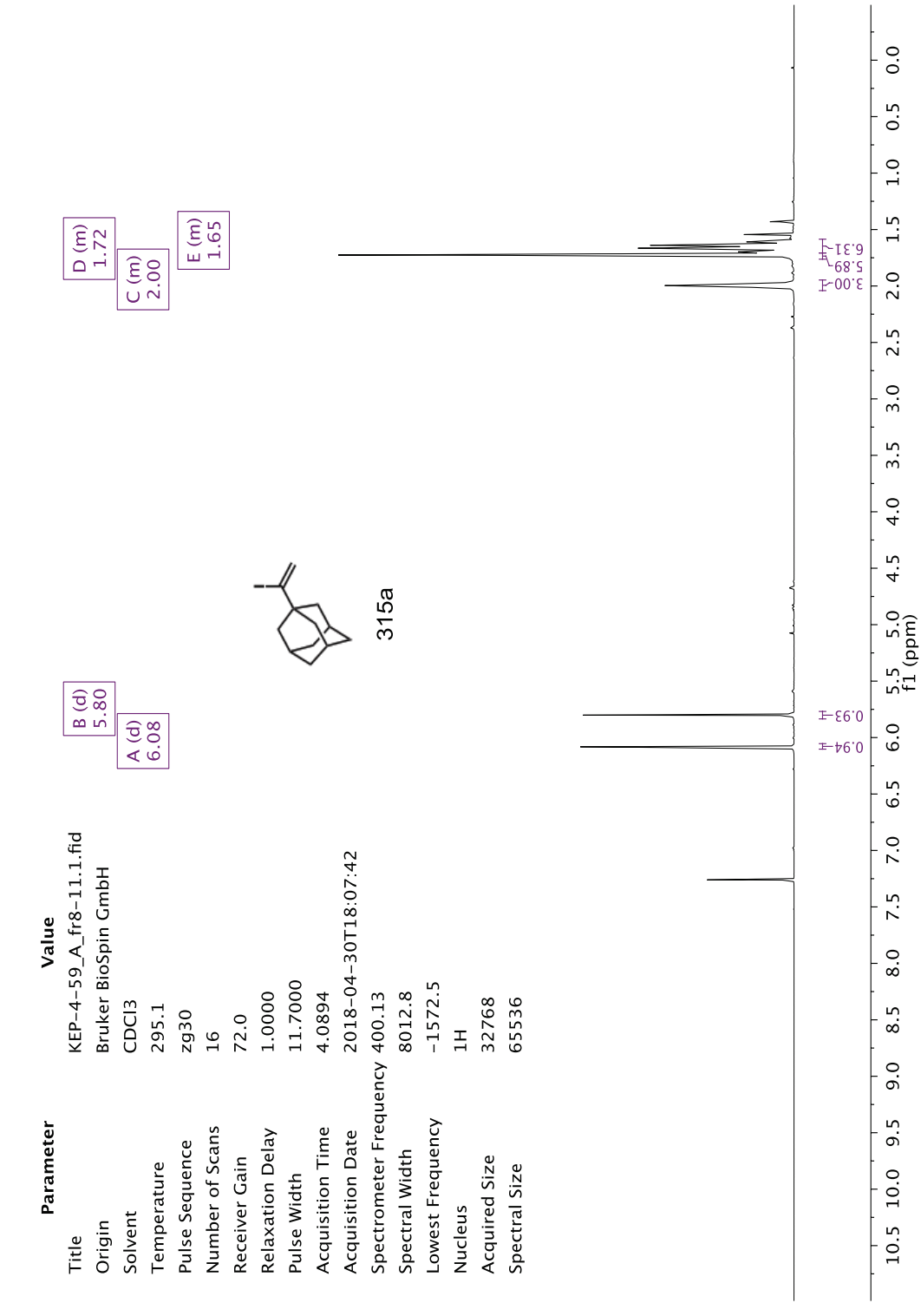



Parameter
Value
Title
jlh-8-057char.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.1
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
55.5
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-09-07T18:47:03
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1545.2
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
A (dd) 7.58
B (td) 7.30
C (m) 7.21
D (t) 6.64
E (t) 2.68
F (p) 2.14
G (q) 1.92
Br
314b
1.00
1.04
2.06
1.01
2.13
2.17
2.08
f1 (ppm)

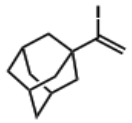

Parameter
Value
Title
jlh-8-057char.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
zgpg30
Number of Scans
128
Receiver Gain
35.5
Relaxation Delay
1.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-09-07T18:52:42
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1948.7
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Br
314b
34.3
32.7
26.9
140.7
138.8
133.3
129.5
128.7
128.4
126.4
120.7
f1 (ppm)


Parameter
Value
Title
jlh-8-058.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
64.2
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-09-07T18:57:31
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1545.6
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
D (dd) 7.20
B (td) 7.30
A (dd) 7.60
C (m) 7.25
E (t) 6.40
F (t) 2.69
G (m) 2.12
H (qd) 1.99
Cl
314c
1.00
1.14
1.03
1.00
1.02
2.12
2.16
2.15
f1 (ppm)

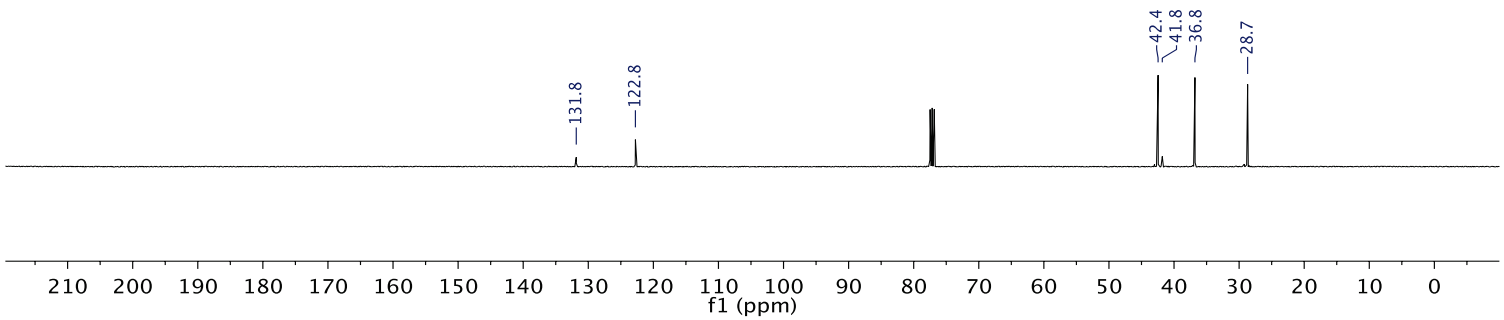

Parameter Value
Title jlh-8-058.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zgpg30
Number of Scans 128
Receiver Gain 55.5
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-09-07T19:03:13
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1947.7
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Cl
314c
141.1
137.6
130.7
129.0
128.9
128.4
128.3
126.4
33.8
32.9
26.0
f1 (ppm)

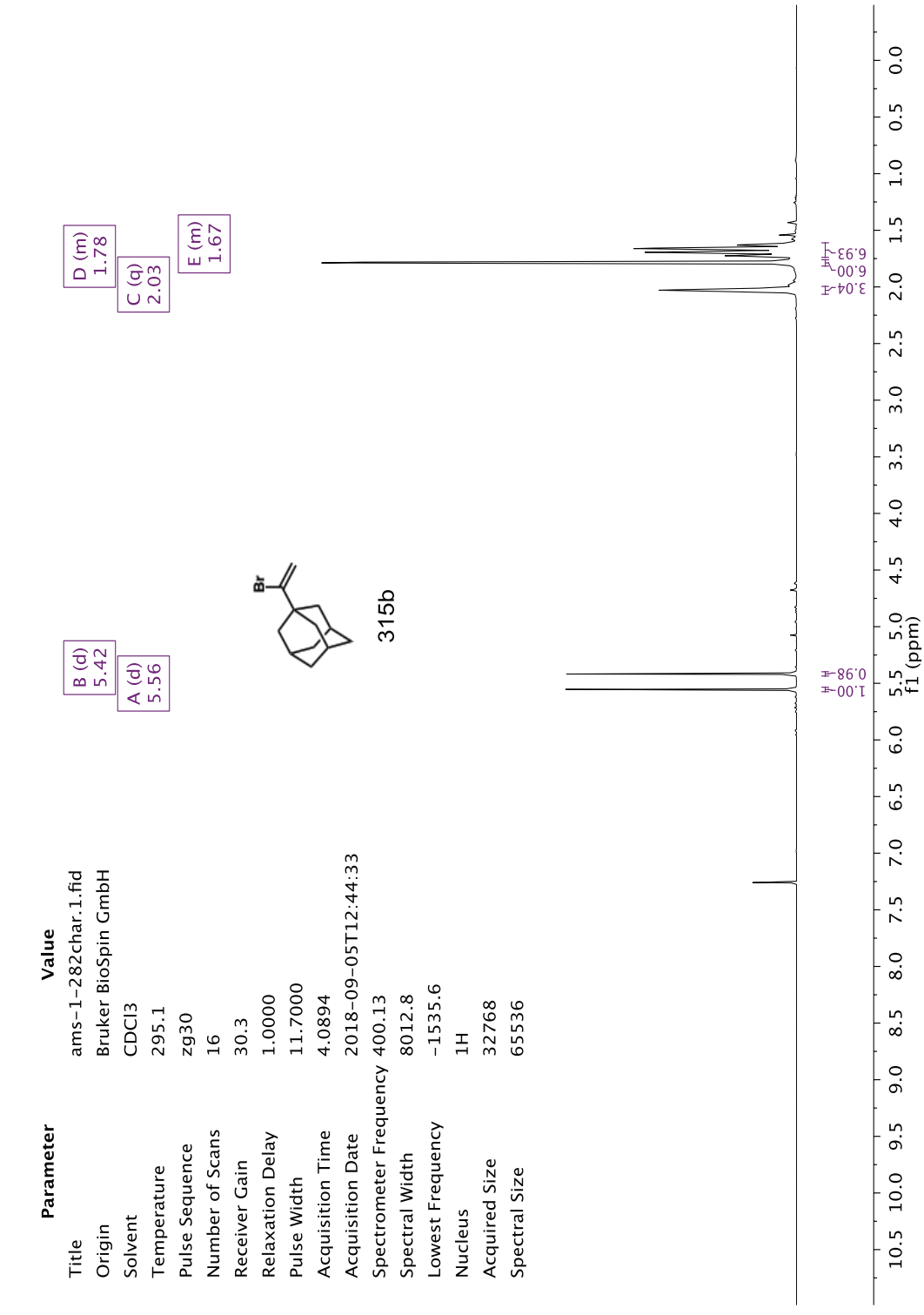

Parameter
Value
Title KEP-4-59_A_fr8-11.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 72.0
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-04-30T18:07:42
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1572.5
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
B (d) 5.80
A (d) 6.08
D (m) 1.72
C (m) 2.00
E (m) 1.65
315a
0.93
0.94
3.00
5.89
6.31
f1 (ppm)

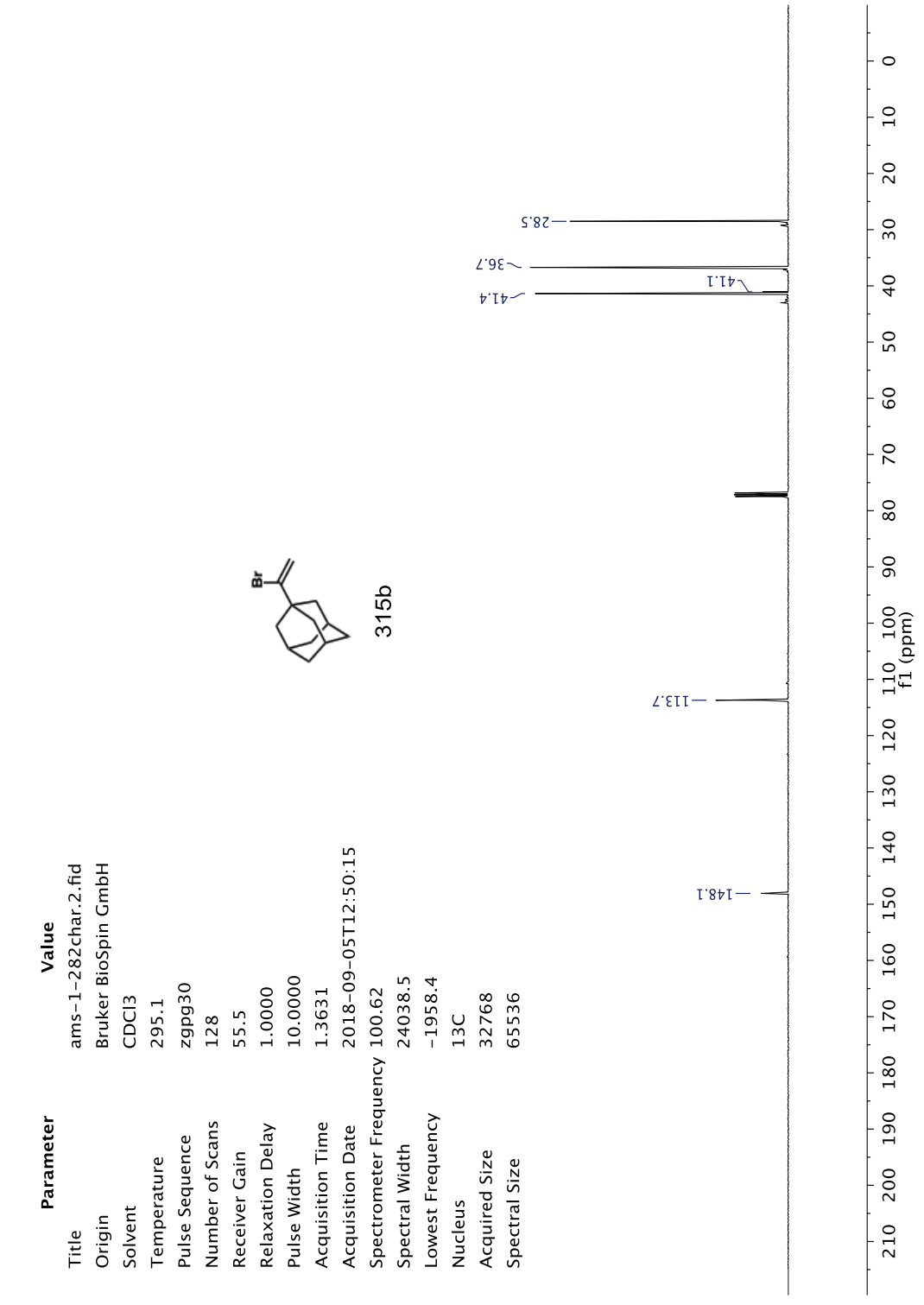
Parameter	Value
Title	KEP-4-59_A_fr8-11.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Number of Scans	128
Receiver Gain	72.0
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-04-30T18:15:32
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1958.0
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

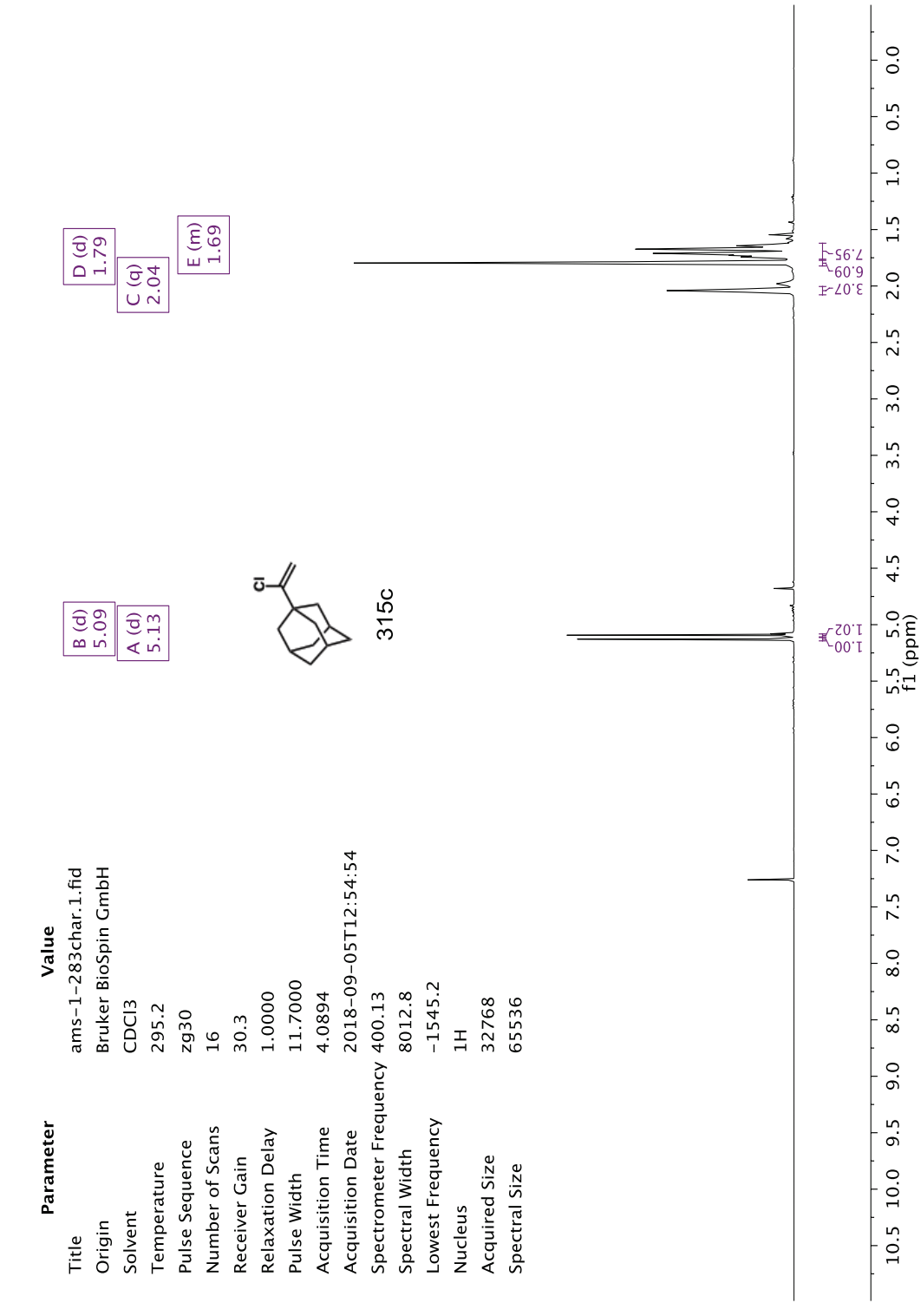


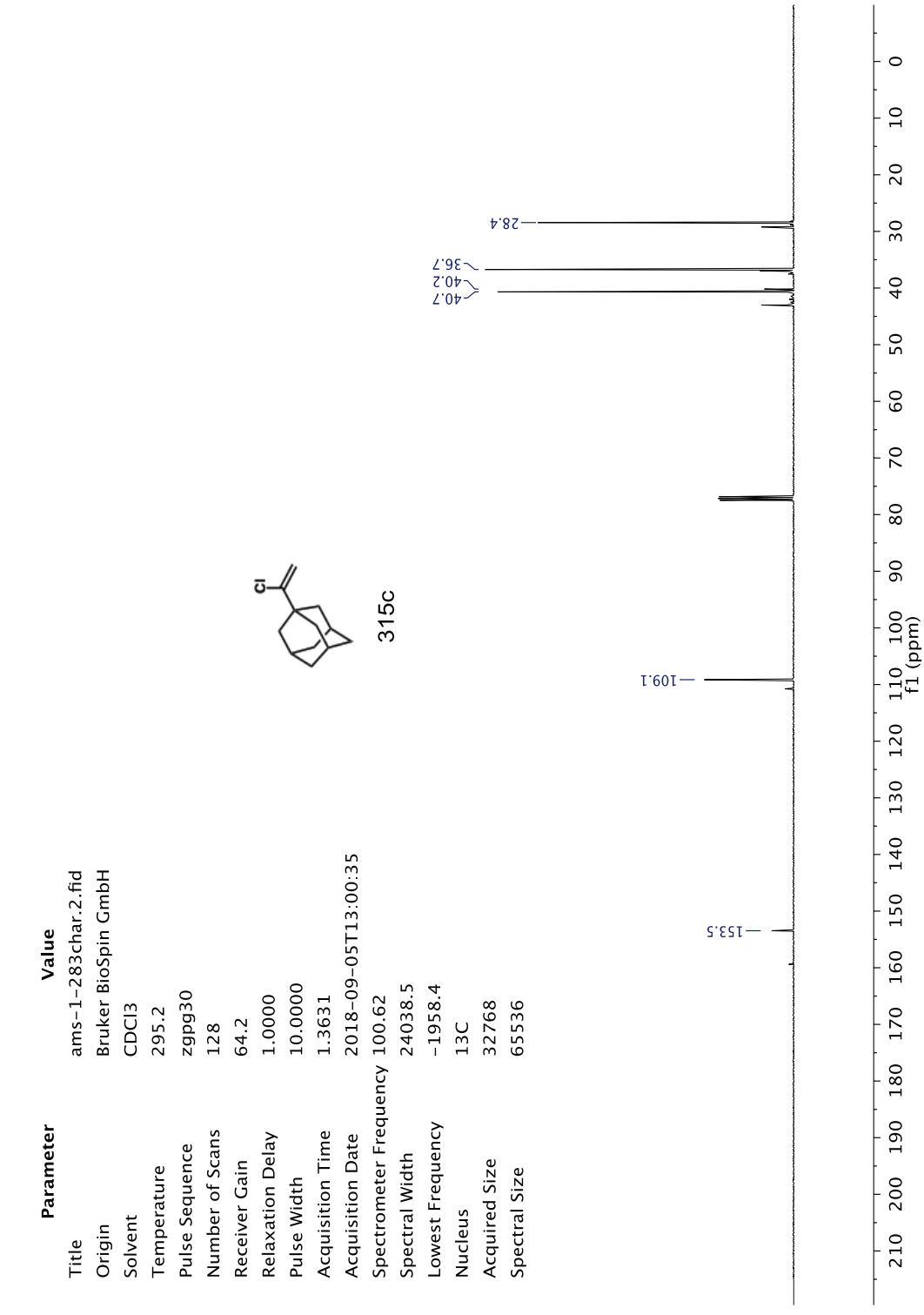
315a

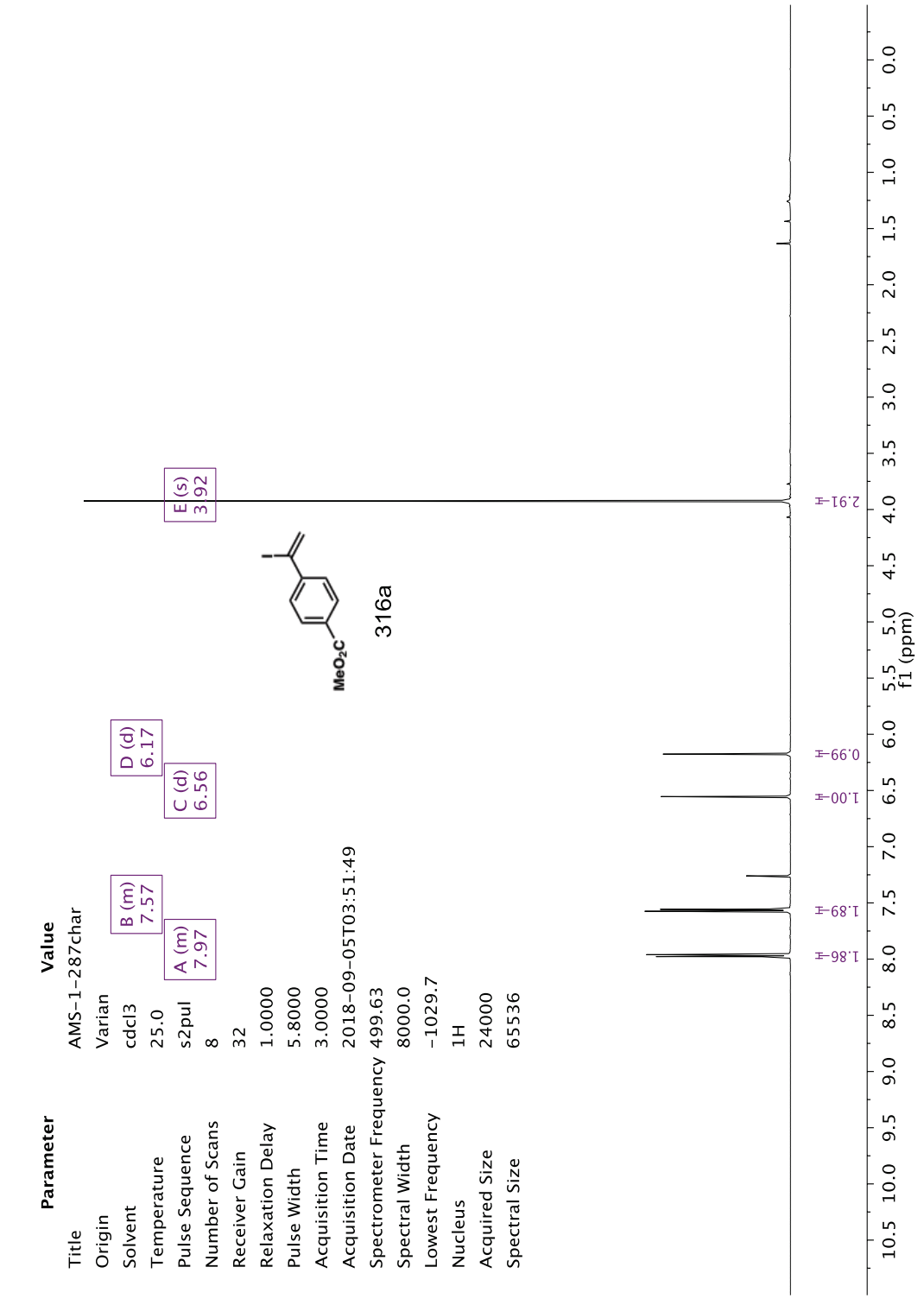



Parameter
Value
Title
ams-1-282char.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.1
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
30.3
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-09-05T12:44:33
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1535.6
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
B (d)
5.42
A (d)
5.56
D (m)
1.78
C (q)
2.03
E (m)
1.67
Br
315b
1.00
0.98
3.04
6.00
6.93
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


Parameter
Value
Title
ams-1-282char.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.1
Pulse Sequence
zgpg30
Number of Scans
128
Receiver Gain
55.5
Relaxation Delay
1.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-09-05T12:50:15
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1958.4
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Br
315b
148.1
113.7
41.4
36.7
41.1
28.5
f1 (ppm)

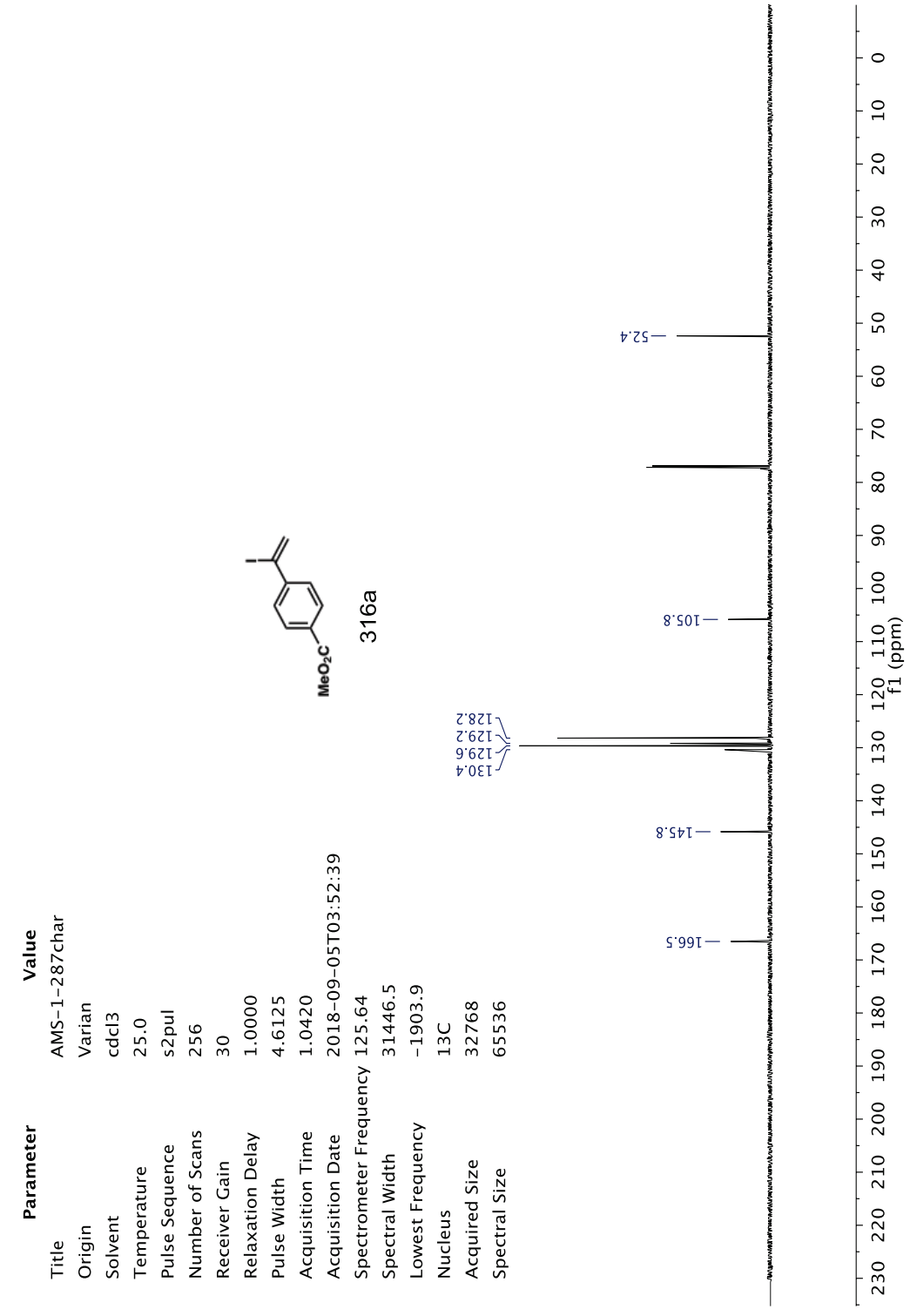

Parameter
Value
Title ams-1-283char.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 30.3
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-09-05T12:54:54
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1545.2
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
B (d) 5.09
A (d) 5.13
D (d) 1.79
C (q) 2.04
E (m) 1.69
Cl
315c
1.00
1.02
3.07
6.09
7.95
f1 (ppm)

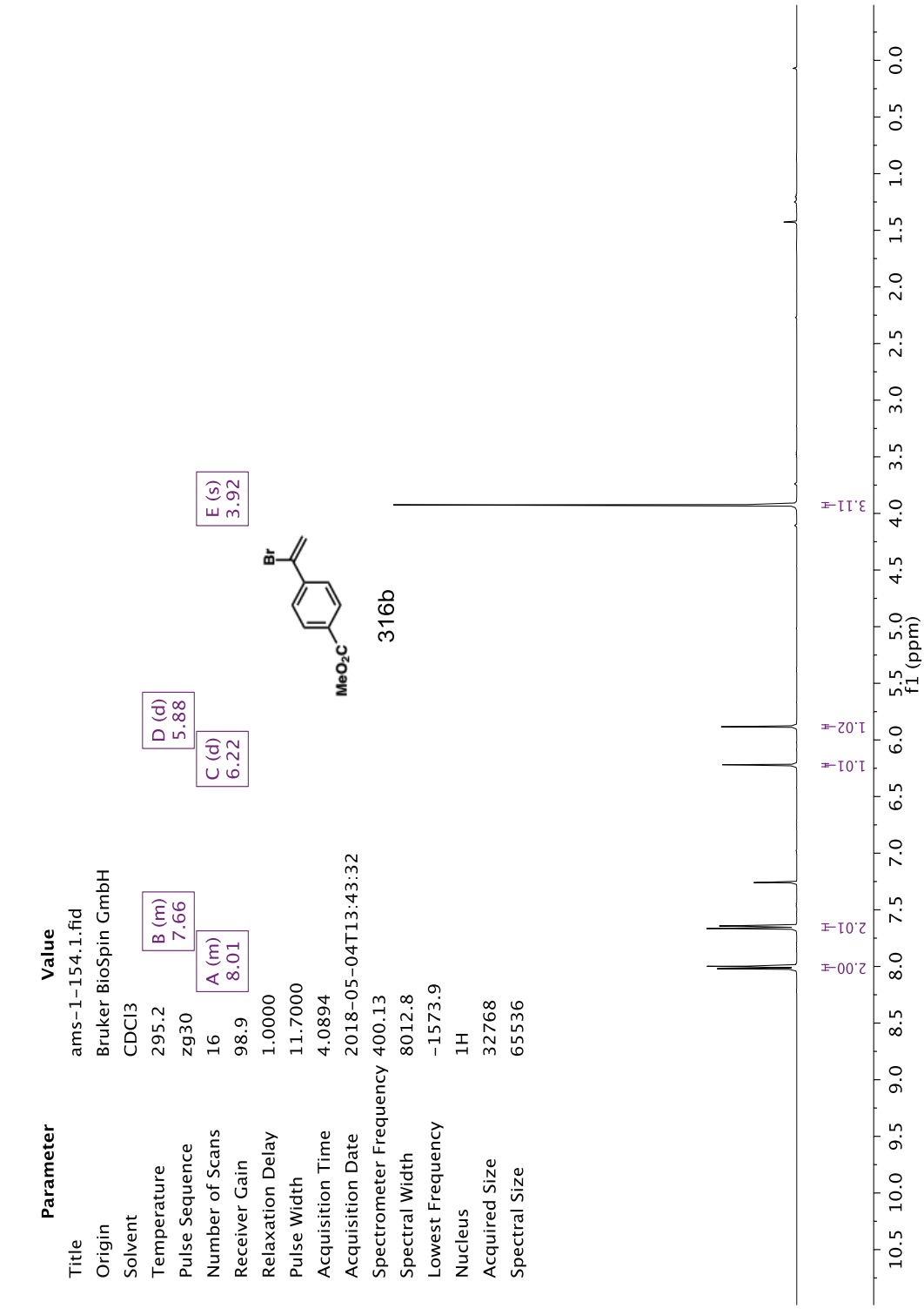

Parameter
Value
Title
ams-1-283char.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
zgpg30
Number of Scans
128
Receiver Gain
64.2
Relaxation Delay
1.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-09-05T13:00:35
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1958.4
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Cl
315c
153.5
109.1
40.7
40.2
36.7
28.4
f1 (ppm)

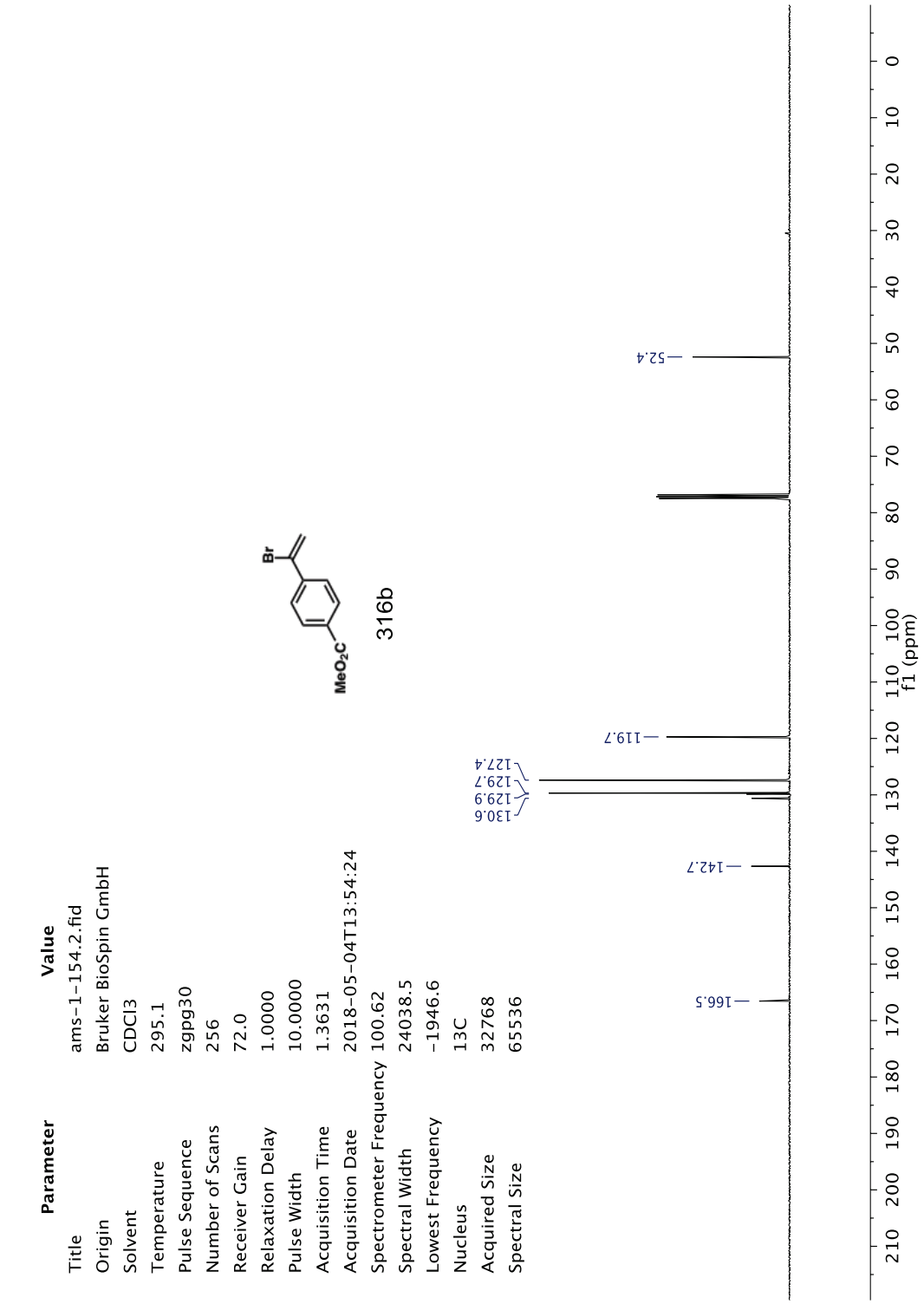

Parameter
Value
Title
AMS-1-287char
Origin
Varian
Solvent
cdcl3
Temperature
25.0
Pulse Sequence
s2pul
Number of Scans
8
Receiver Gain
32
Relaxation Delay
1.0000
Pulse Width
5.8000
Acquisition Time
3.0000
Acquisition Date
2018-09-05T03:51:49
Spectrometer Frequency
499.63
Spectral Width
8000.0
Lowest Frequency
-1029.7
Nucleus
1H
Acquired Size
24000
Spectral Size
65536
A (m) 7.97
B (m) 7.57
C (d) 6.56
D (d) 6.17
E (s) 3.92
MeO2C
316a
1.86
1.89
1.00
0.99
2.91
f1 (ppm)

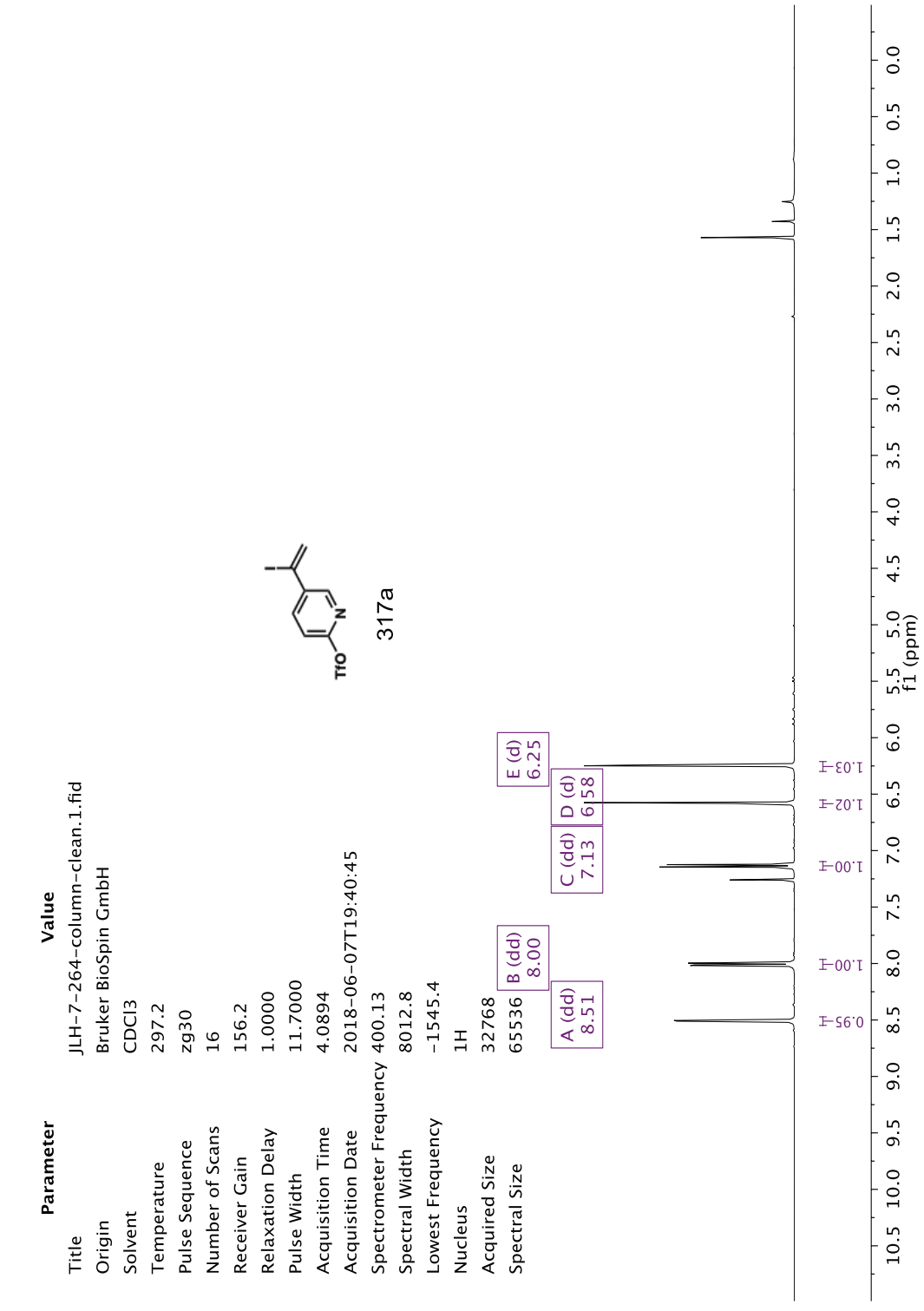
Parameter	Value
Title	AMS-1-287char
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	256
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	4.6125
Acquisition Time	1.0420
Acquisition Date	2018-09-05T03:52:39
Spectrometer Frequency	125.64
Spectral Width	31446.5
Lowest Frequency	-1903.9
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

316a

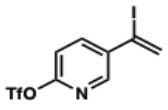



Parameter
Value
Title
ams-1-154.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
98.9
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-05-04T13:43:32
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1573.9
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
A (m) 8.01
B (m) 7.66
C (d) 6.22
D (d) 5.88
E (s) 3.92
Br
MeO2C
316b
2.00
2.01
1.01
1.02
3.11
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

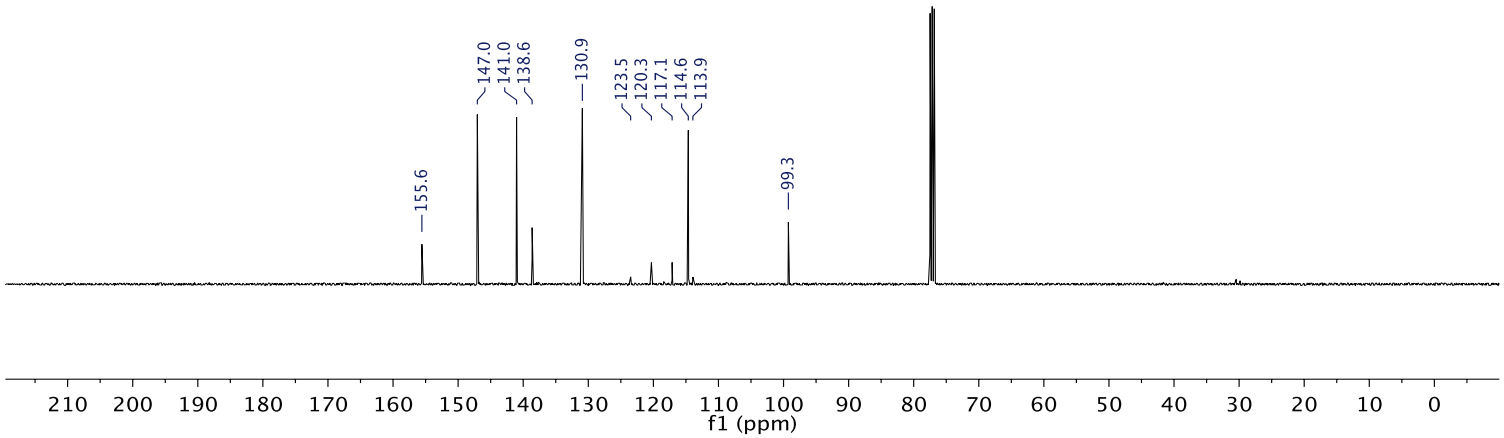

Parameter
Value
Title
ams-1-154.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.1
Pulse Sequence
zgpg30
Number of Scans
256
Receiver Gain
72.0
Relaxation Delay
1.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-05-04T13:54:24
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1946.6
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Br
MeO2C
316b
166.5
142.7
130.6
129.9
129.7
127.4
119.7
52.4
f1 (ppm)


Parameter
Value
Title
JLH-7-264-column-clean.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
297.2
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
156.2
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-06-07T19:40:45
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1545.4
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
TfO
N
317a
A (dd) 8.51
B (dd) 8.00
C (dd) 7.13
D (d) 6.58
E (d) 6.25
0.95
1.00
1.00
1.02
1.03
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

Parameter	Value
Title	JLH-7-264-column-clean.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	297.2
Pulse Sequence	zgpg30
Number of Scans	512
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-06-07T20:03:25
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1945.2
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



317a



Parameter	Value
Title	JLH-7-264-F
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-06-14T01:09:09
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56468.7
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

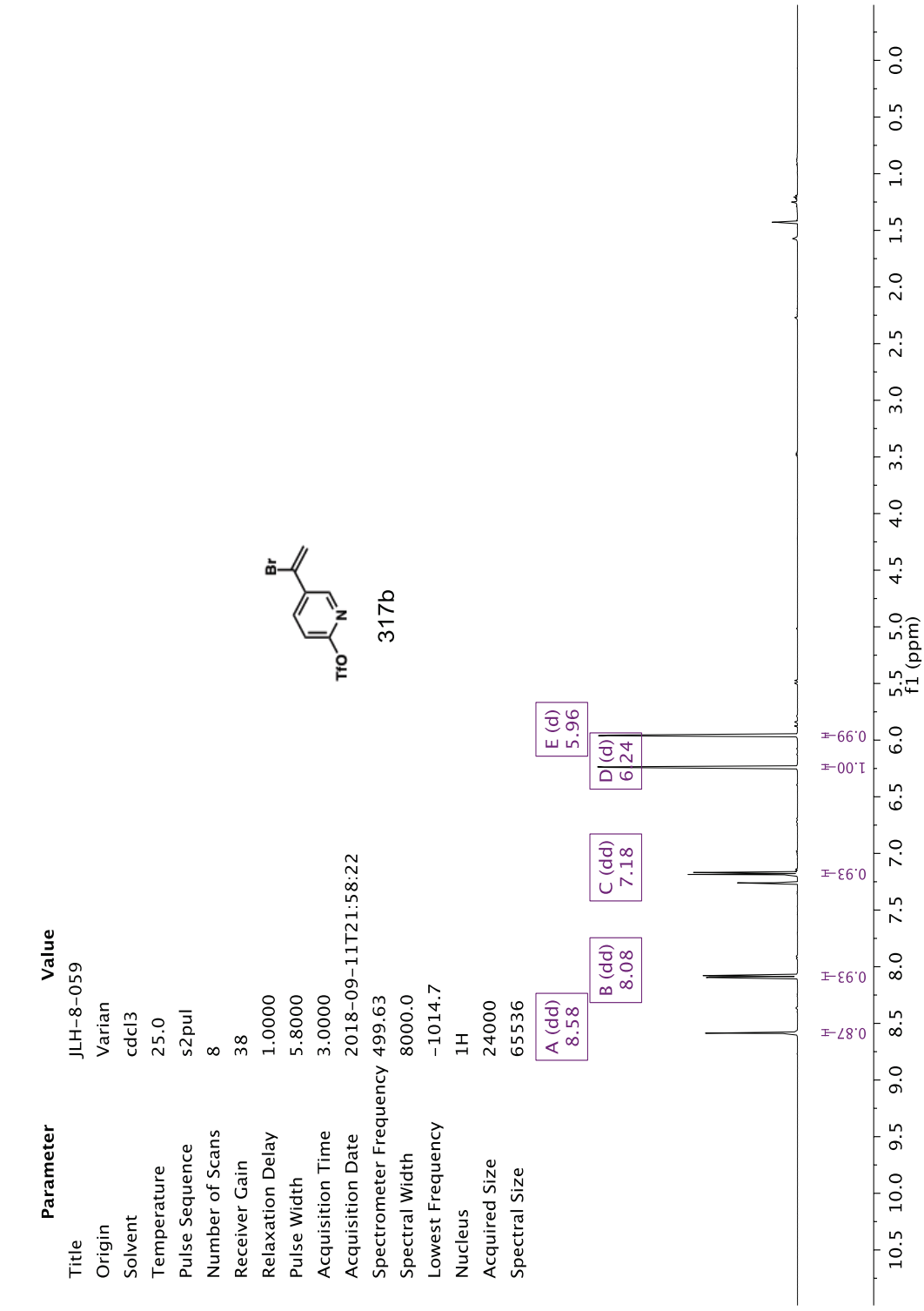
317a

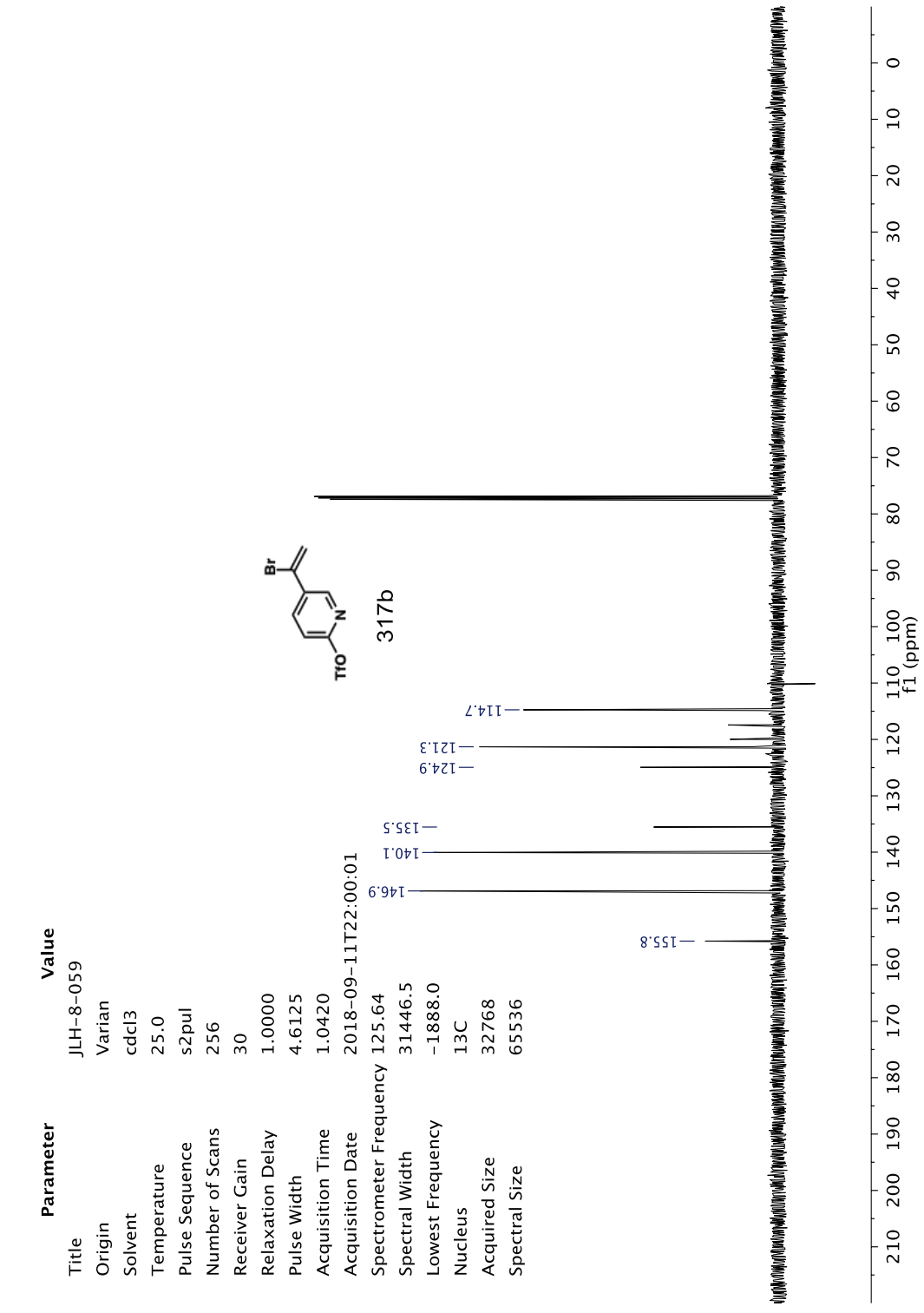
Parameter	Value
Title	JLH-7-264-F-C6F6
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-06-14T01:14:32
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56468.7
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

317a
with C_6F_6

-72.9

20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)


Parameter Value
Title JLH-8-059
Origin Varian
Solvent cdcl3
Temperature 25.0
Pulse Sequence s2pul
Number of Scans 8
Receiver Gain 38
Relaxation Delay 1.0000
Pulse Width 5.8000
Acquisition Time 3.0000
Acquisition Date 2018-09-11T21:58:22
Spectrometer Frequency 499.63
Spectral Width 8000.0
Lowest Frequency -1014.7
Nucleus 1H
Acquired Size 24000
Spectral Size 65536
Br
N
TfO
317b
A (dd) 8.58
B (dd) 8.08
C (dd) 7.18
D (dd) 6.24
E (d) 5.96
0.87
0.93
0.93
1.00
0.99
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


Parameter Value
Title JLH-8-059
Origin Varian
Solvent cdcl3
Temperature 25.0
Pulse Sequence s2pul
Number of Scans 256
Receiver Gain 30
Relaxation Delay 1.0000
Pulse Width 4.6125
Acquisition Time 1.0420
Acquisition Date 2018-09-11T22:00:01
Spectrometer Frequency 125.64
Spectral Width 31446.5
Lowest Frequency -1888.0
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
155.8
146.9
140.1
135.5
124.9
121.3
114.7
Br
N
TfO
317b
f1 (ppm)

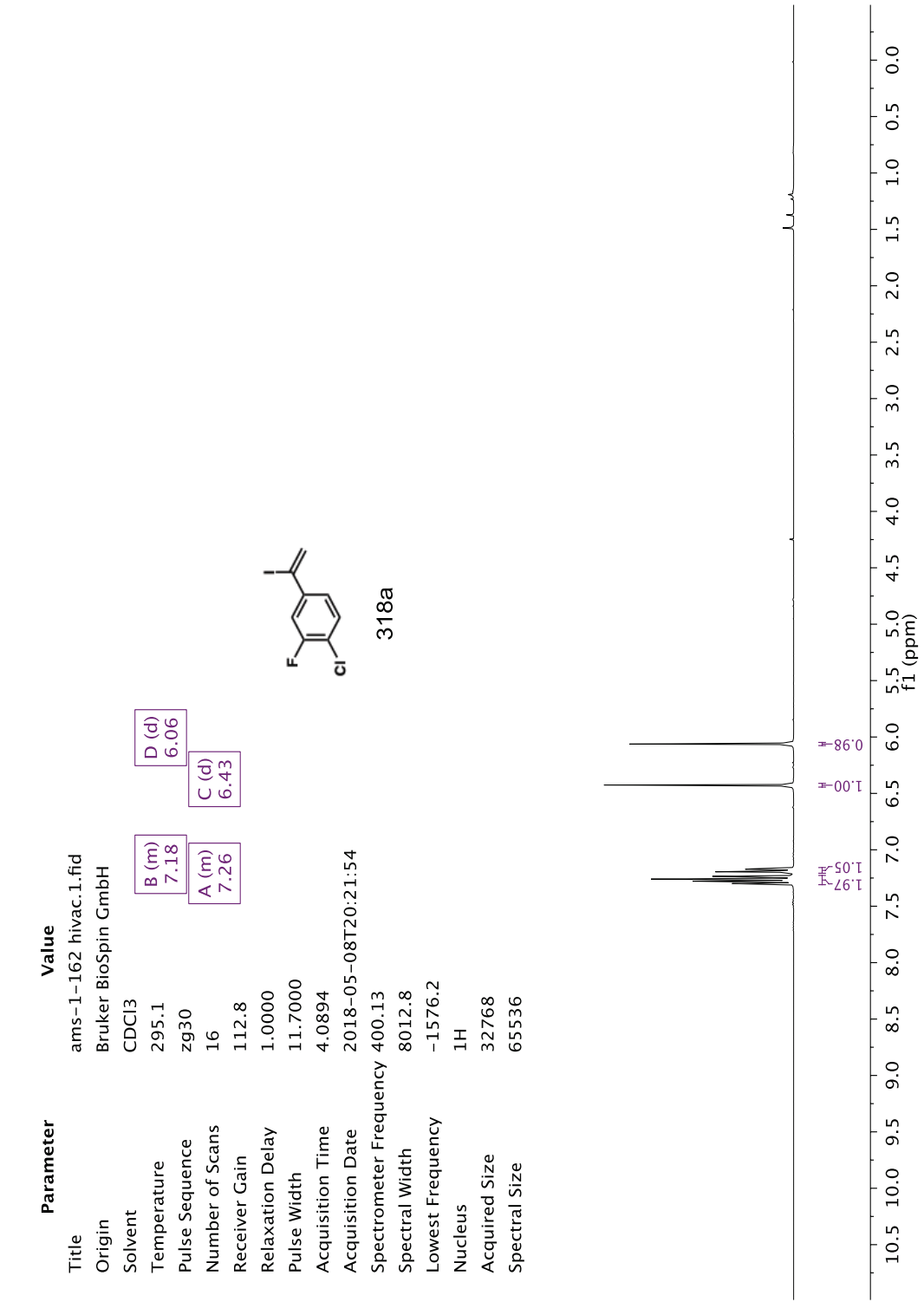
Parameter	Value
Title	JLH-8-059-F
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-09-11T21:25:01
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56435.1
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

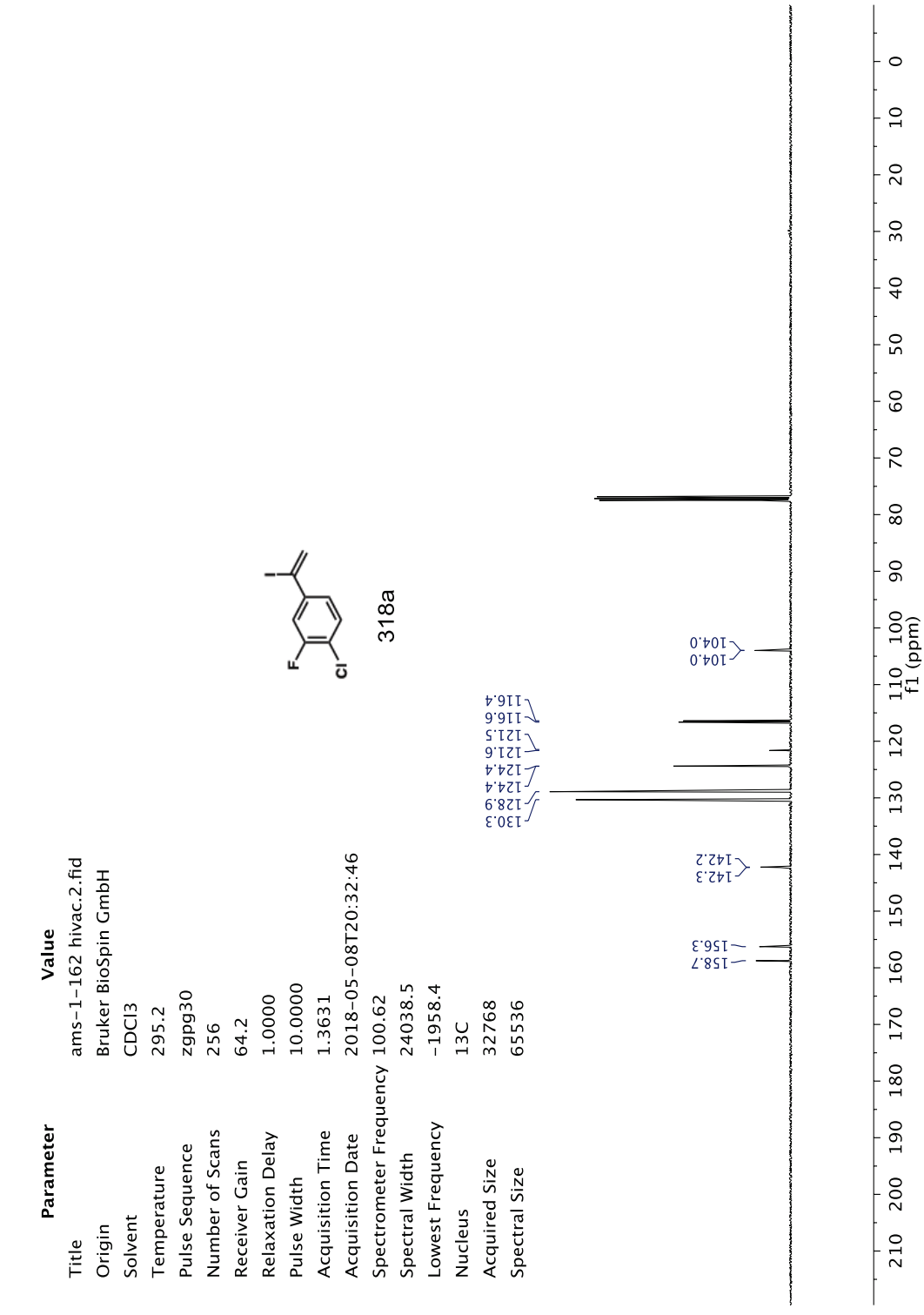
317b

-72.9

10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

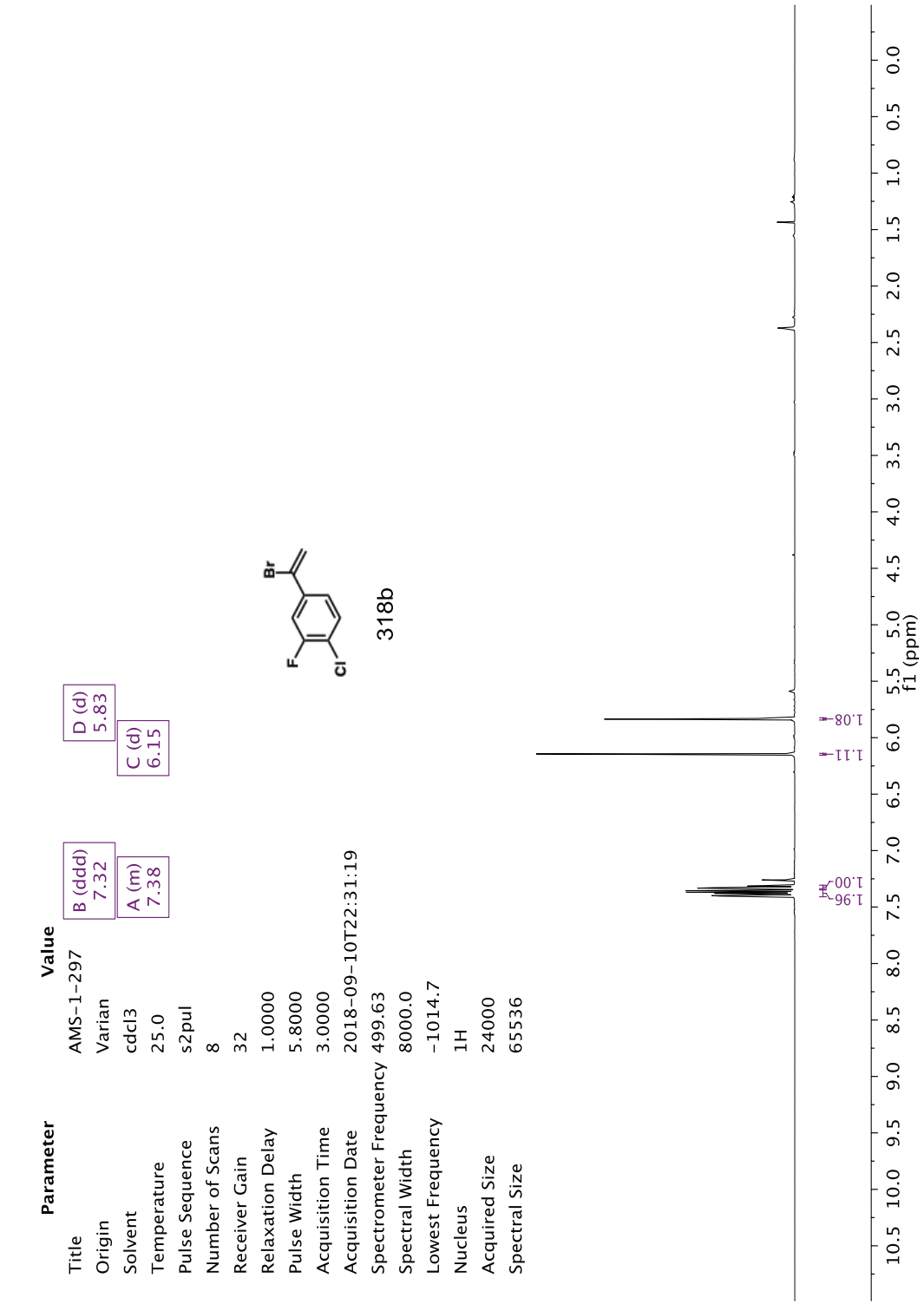
Parameter	Value
Title	JLH-8-059-F-C6F6
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-09-11T23:04:10
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56431.7
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

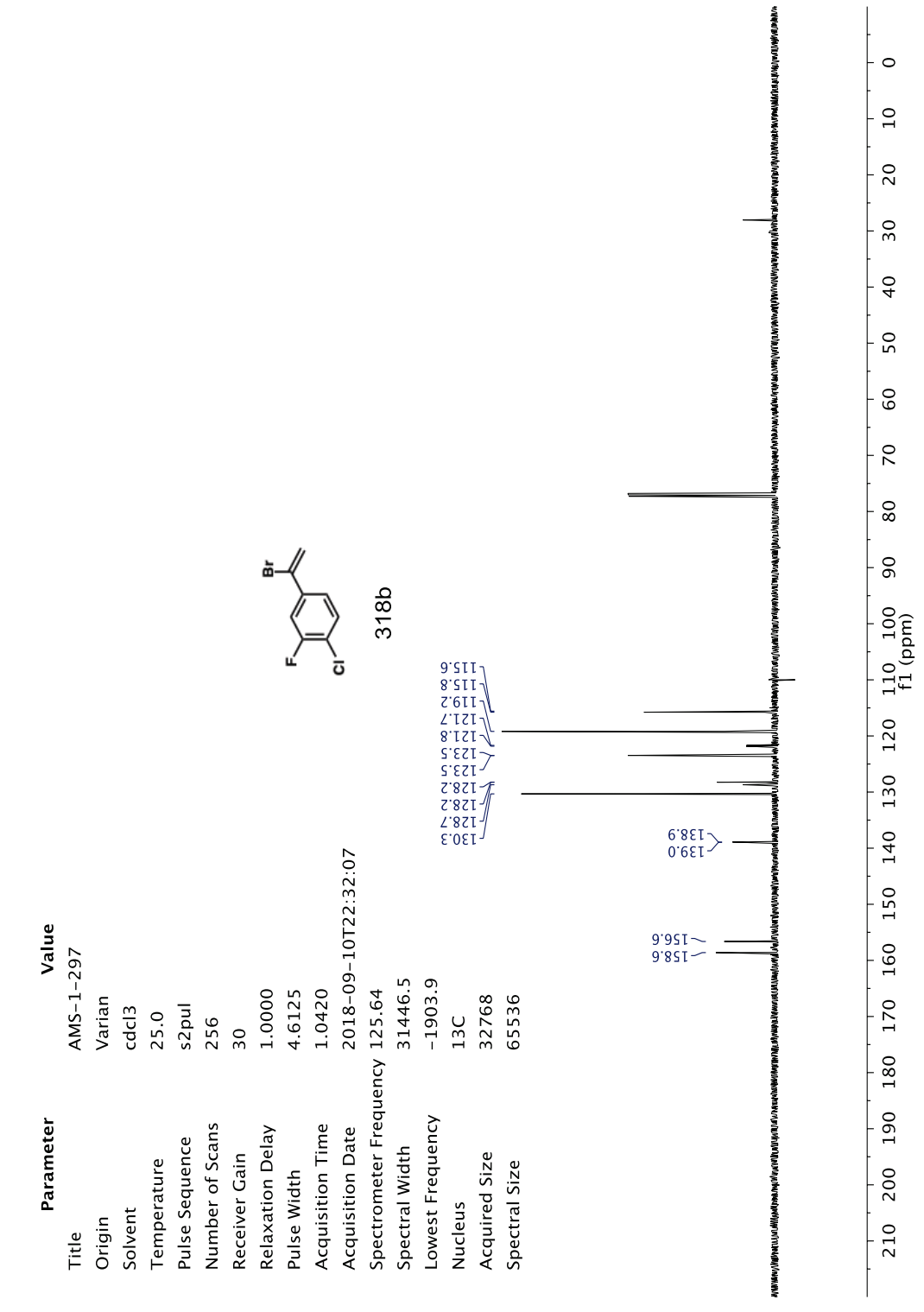

Parameter
Value
Title
ams-1-162 hivac.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.1
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
112.8
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-05-08T20:21:54
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1576.2
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
B (m) 7.18
A (m) 7.26
C (d) 6.43
D (d) 6.06
F
Cl
318a
1.97
1.05
1.00
0.98
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


Parameter
Value
Title
ams-1-162 hivac.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
zgpg30
Number of Scans
256
Receiver Gain
64.2
Relaxation Delay
1.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-05-08T20:32:46
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1958.4
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
F
Cl
318a
158.7
156.3
142.3
142.2
130.3
128.9
124.4
124.4
121.6
121.5
116.6
116.4
104.0
104.0
f1 (ppm)

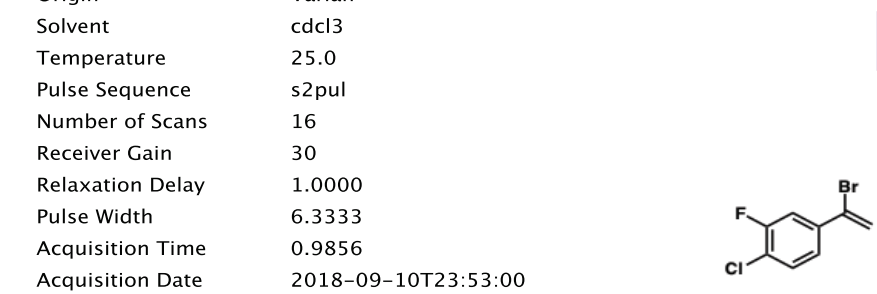
Parameter Value
Title AMS-1-162-F
Origin Varian
Solvent cdcl3
Temperature 25.0
Pulse Sequence s2pul
Number of Scans 16
Receiver Gain 30
Relaxation Delay 1.0000
Pulse Width 6.3333
Acquisition Time 0.9856
Acquisition Date 2018-06-14T02:05:22
Spectrometer Frequency 282.34
Spectral Width 64935.1
Lowest Frequency -56468.7
Nucleus 19F
Acquired Size 64000
Spectral Size 131072
A (dd)
-114.92
F
Cl
318a
1.00
-114.90
-115.00
-115.10
f1 (ppm)
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

Parameter	Value
Title	AMS-1-162-F-C6F6
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-06-14T02:10:13
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56468.7
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

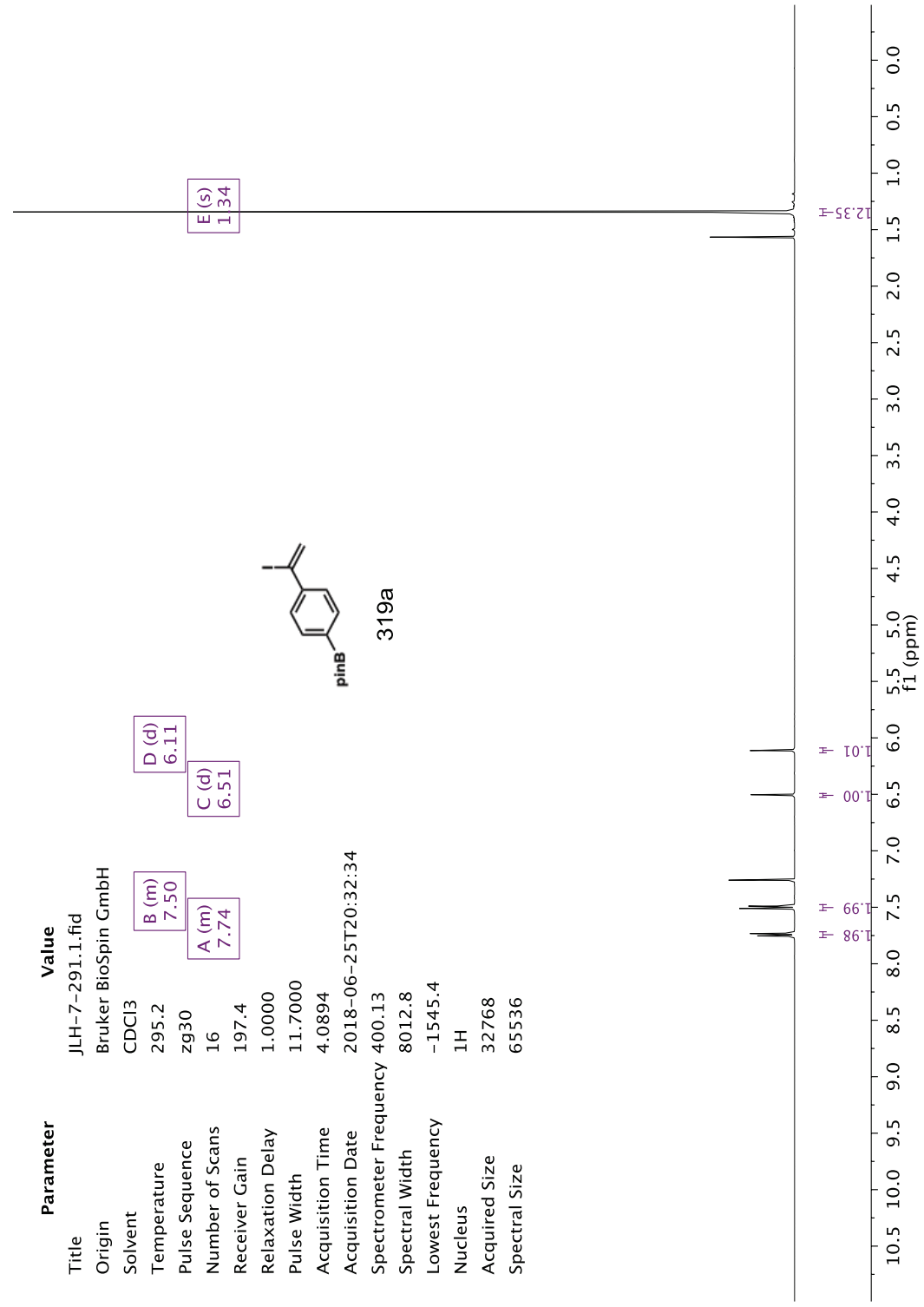

Parameter
Value
Title AMS-1-297
Origin Varian
Solvent cdcl3
Temperature 25.0
Pulse Sequence s2pul
Number of Scans 8
Receiver Gain 32
Relaxation Delay 1.0000
Pulse Width 5.8000
Acquisition Time 3.0000
Acquisition Date 2018-09-10T22:31:19
Spectrometer Frequency 499.63
Spectral Width 8000.0
Lowest Frequency -1014.7
Nucleus 1H
Acquired Size 24000
Spectral Size 65536
B (ddd) 7.32
A (m) 7.38
C (d) 6.15
D (d) 5.83
Br
F
Cl
318b
1.96
1.00
1.11
1.08
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

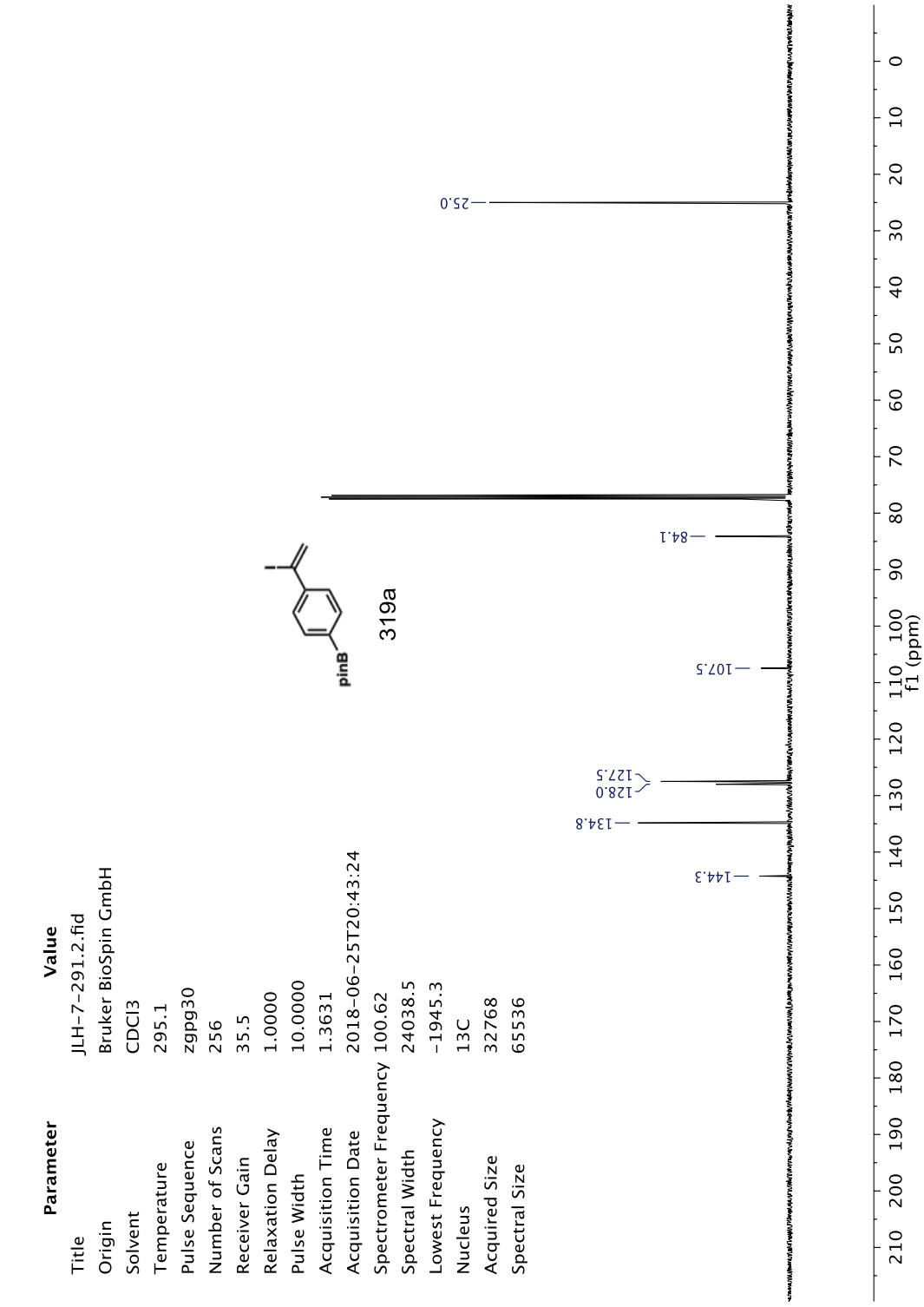

Parameter Value
Title AMS-1-297
Origin Varian
Solvent cdcl3
Temperature 25.0
Pulse Sequence s2pul
Number of Scans 256
Receiver Gain 30
Relaxation Delay 1.0000
Pulse Width 4.6125
Acquisition Time 1.0420
Acquisition Date 2018-09-10T22:32:07
Spectrometer Frequency 125.64
Spectral Width 31446.5
Lowest Frequency -1903.9
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Br
F
Cl
318b
158.6
156.6
139.0
138.9
130.3
128.7
128.2
128.2
123.5
123.5
121.8
121.7
119.2
115.8
115.6
f1 (ppm)

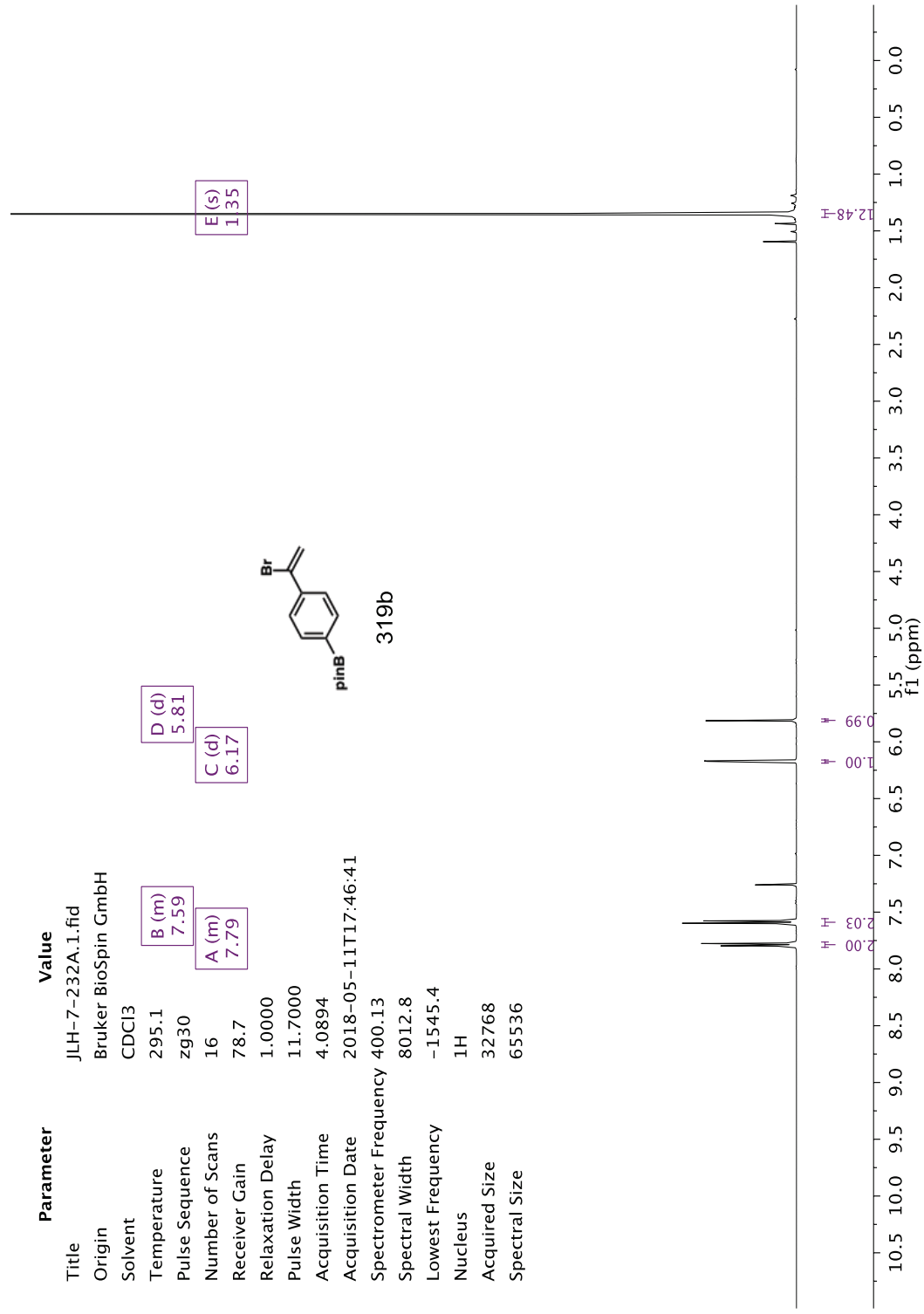
Parameter	Value
Title	AMS-1-297-F
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-09-10T23:53:00
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56450.9
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

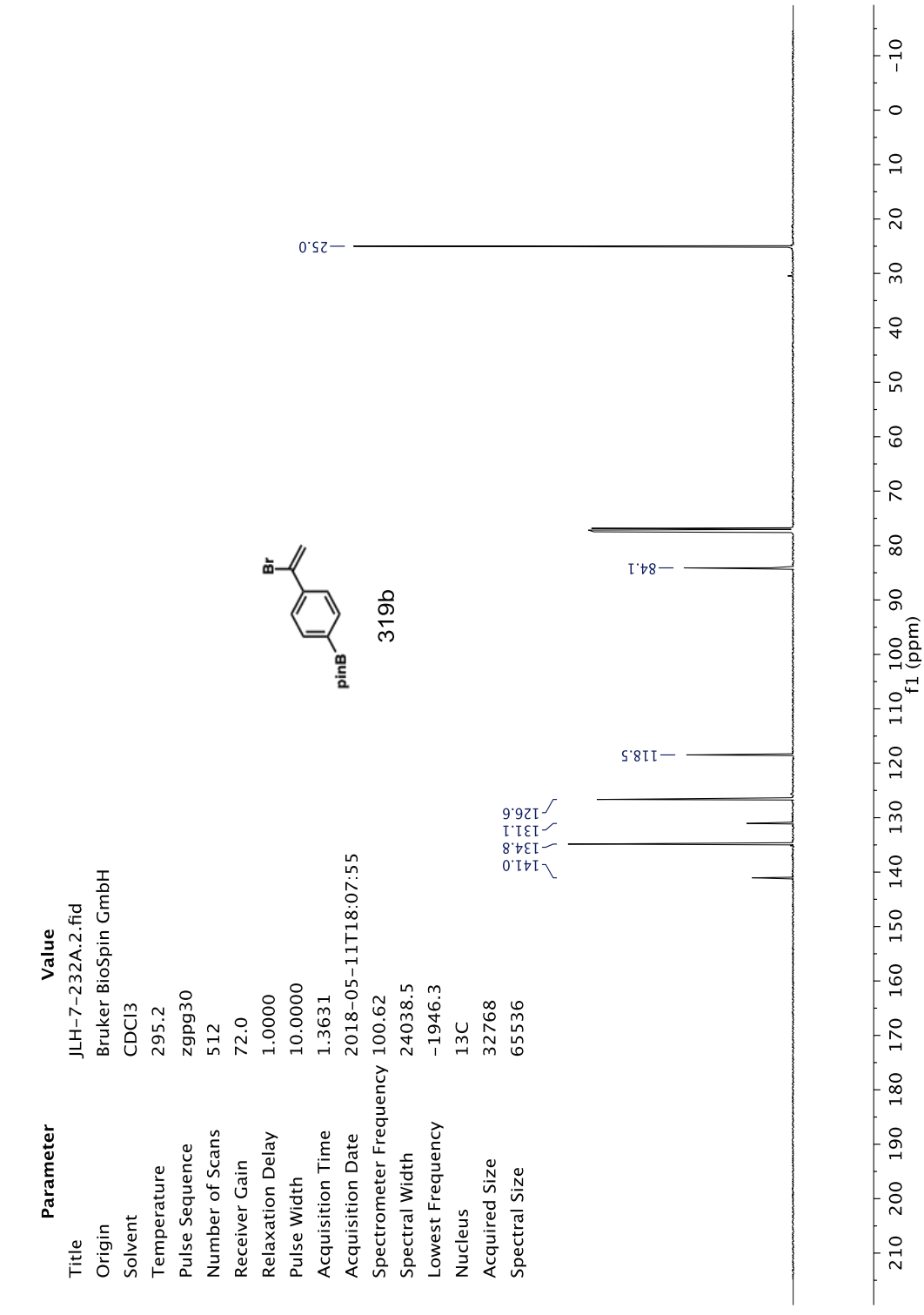


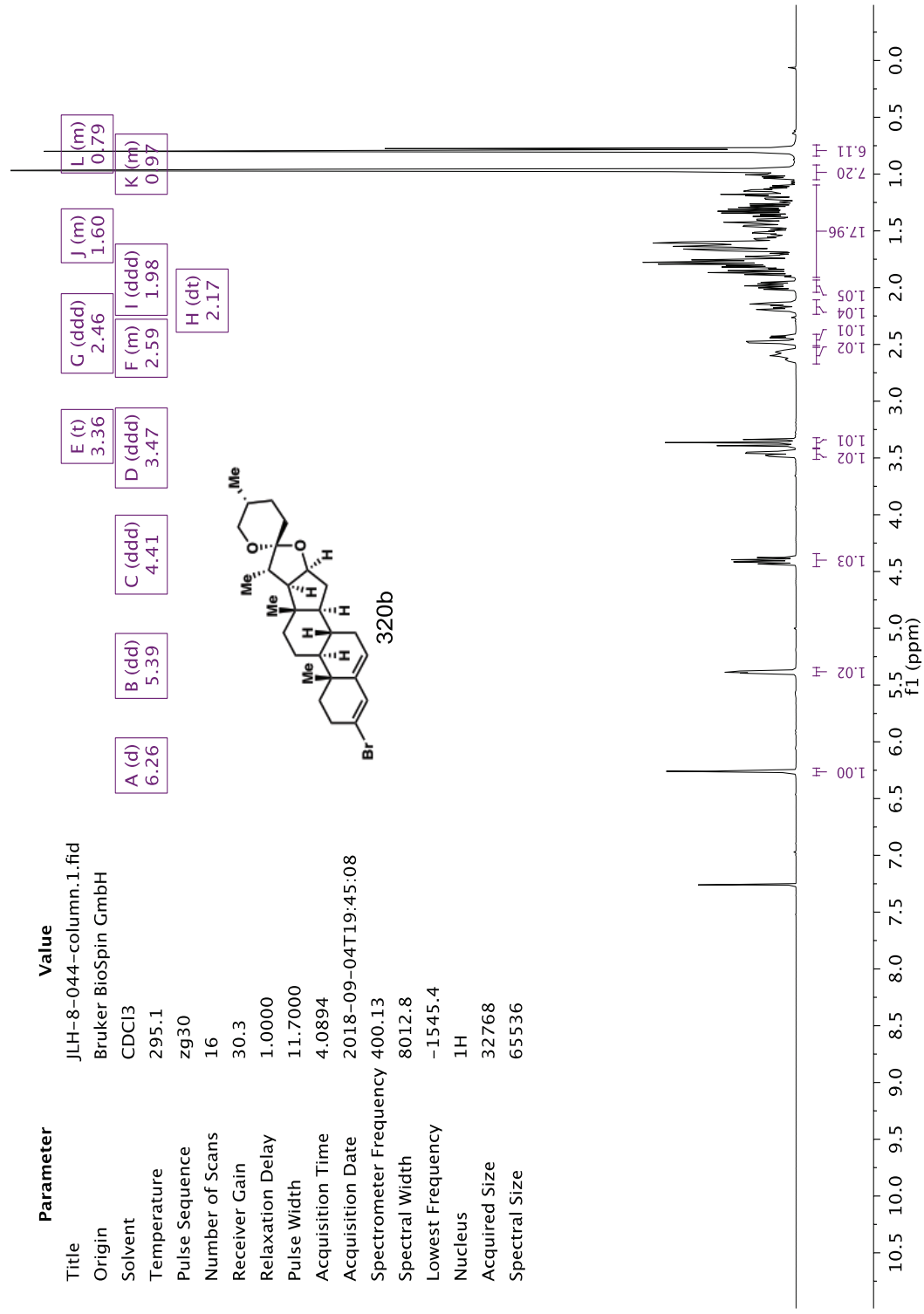
Parameter	Value
Title	AMS-1-297-F-C6F6
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-09-11T00:02:26
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56441.9
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

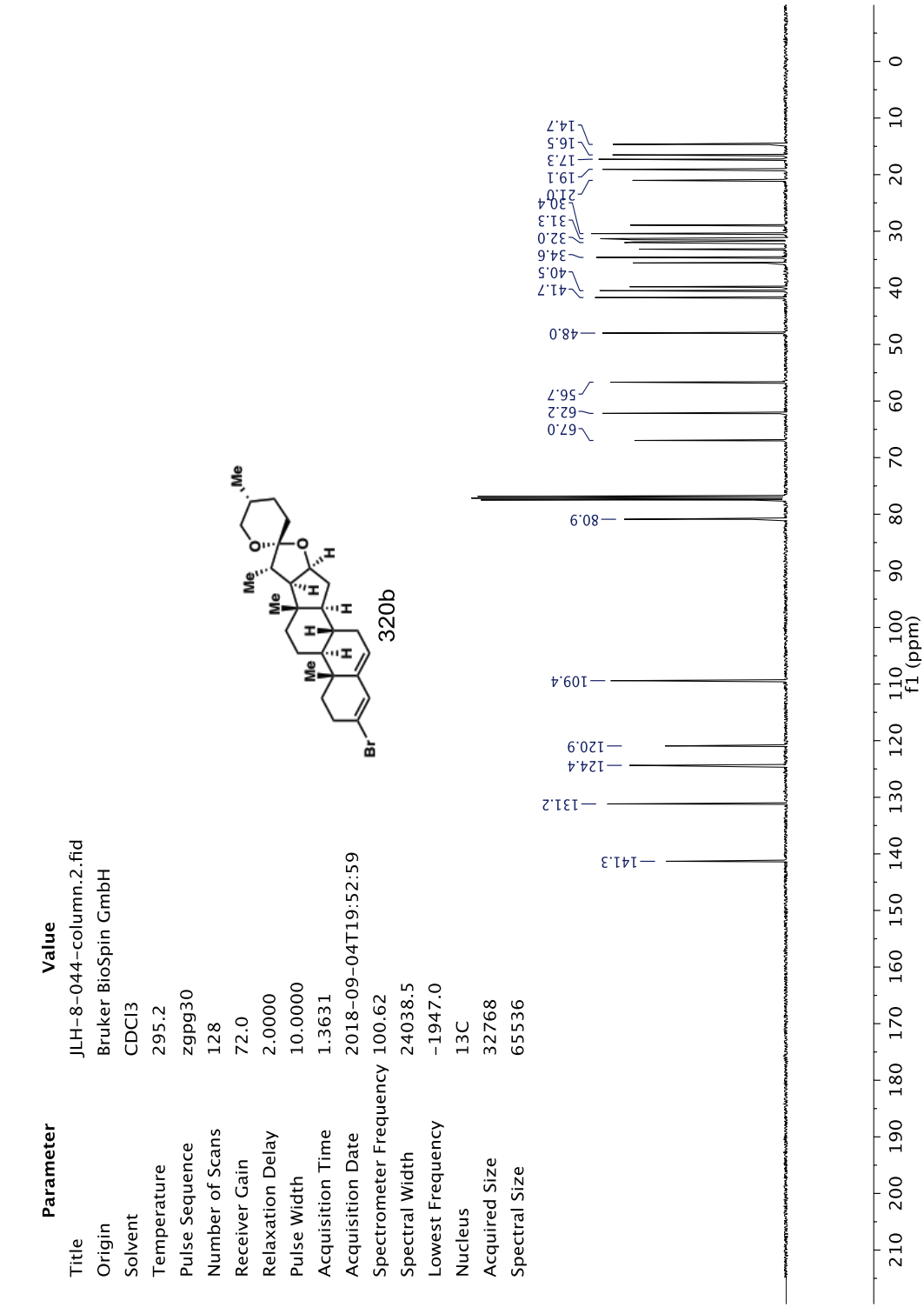

Parameter
Value
Title
JLH-7-291.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
197.4
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-06-25T20:32:34
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1545.4
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
A (m) 7.74
B (m) 7.50
C (d) 6.51
D (d) 6.11
E (s) 1.34
pinB
319a
12.35
1.99
1.98
1.00
1.01
f1 (ppm)

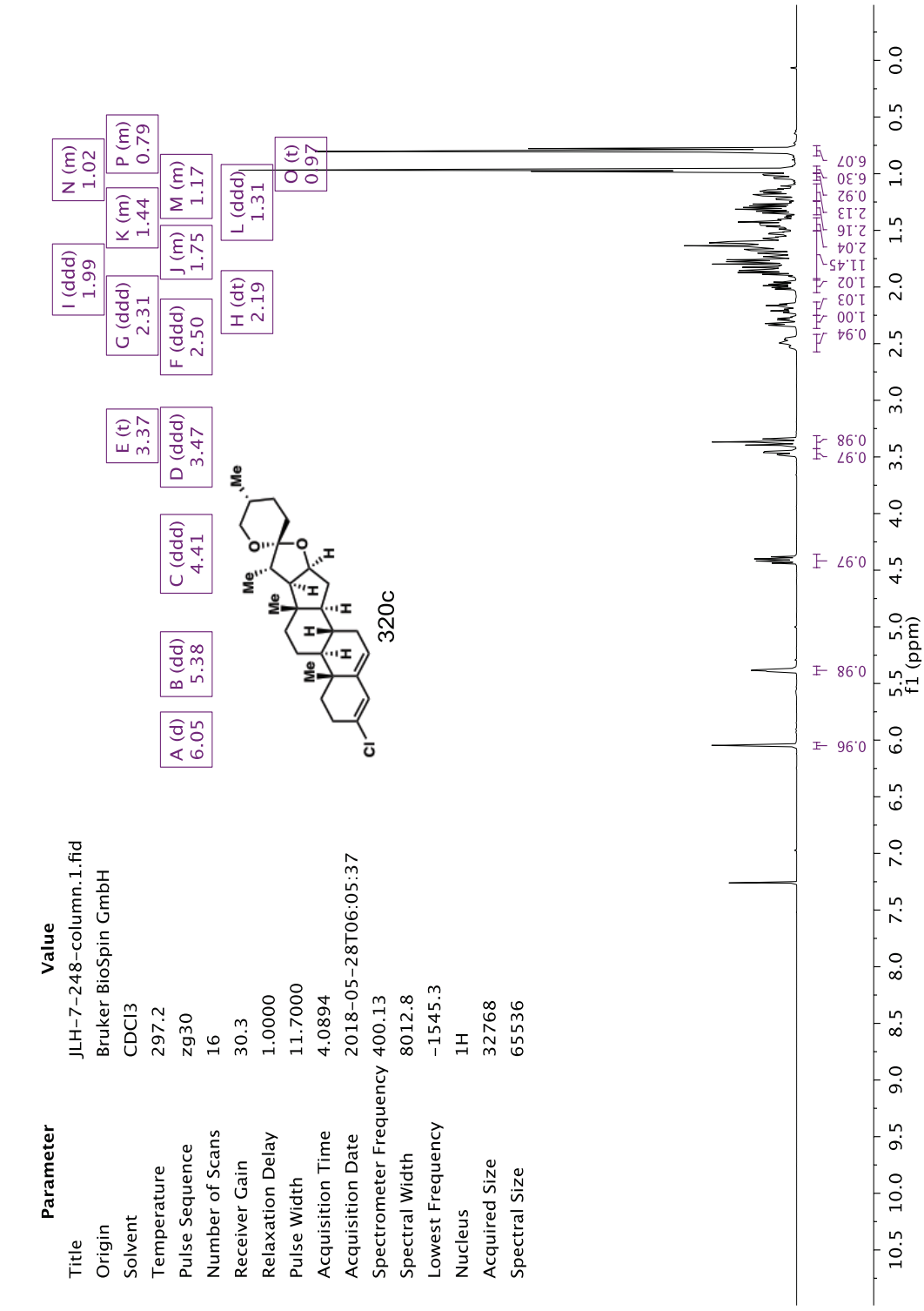

Parameter
Value
Title
JLH-7-291.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.1
Pulse Sequence
zgpg30
Number of Scans
256
Receiver Gain
35.5
Relaxation Delay
1.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-06-25T20:43:24
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1945.3
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
BpinB
319a
25.0
84.1
107.5
127.5
128.0
134.8
144.3
f1 (ppm)

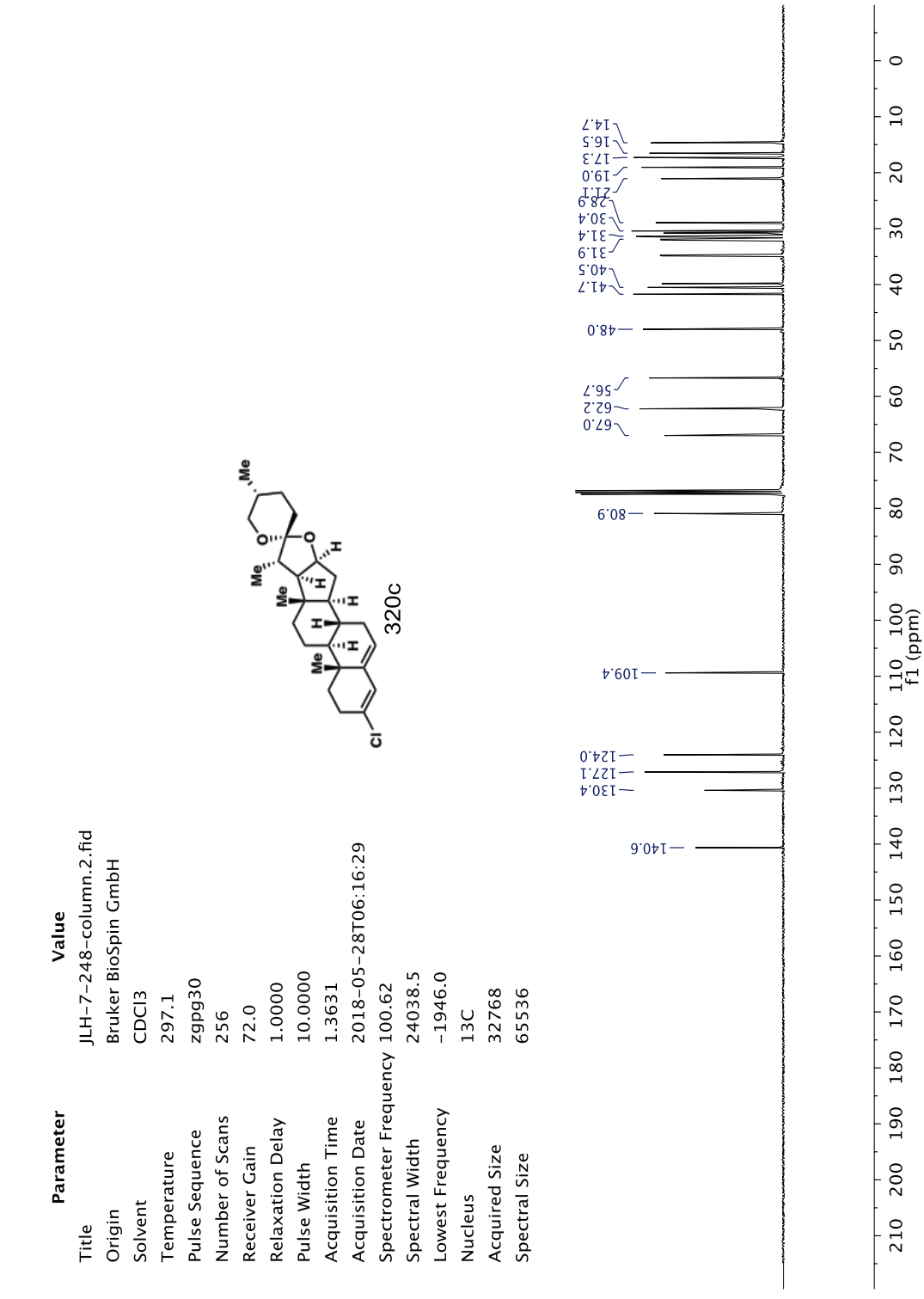

Parameter
Value
Title
JLH-7-232A.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.1
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
78.7
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-05-11T17:46:41
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1545.4
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
A (m) 7.79
B (m) 7.59
C (d) 6.17
D (d) 5.81
E (s) 1.35
Br
pinB
319b
12.48
2.03
2.00
1.00
0.99
f1 (ppm)

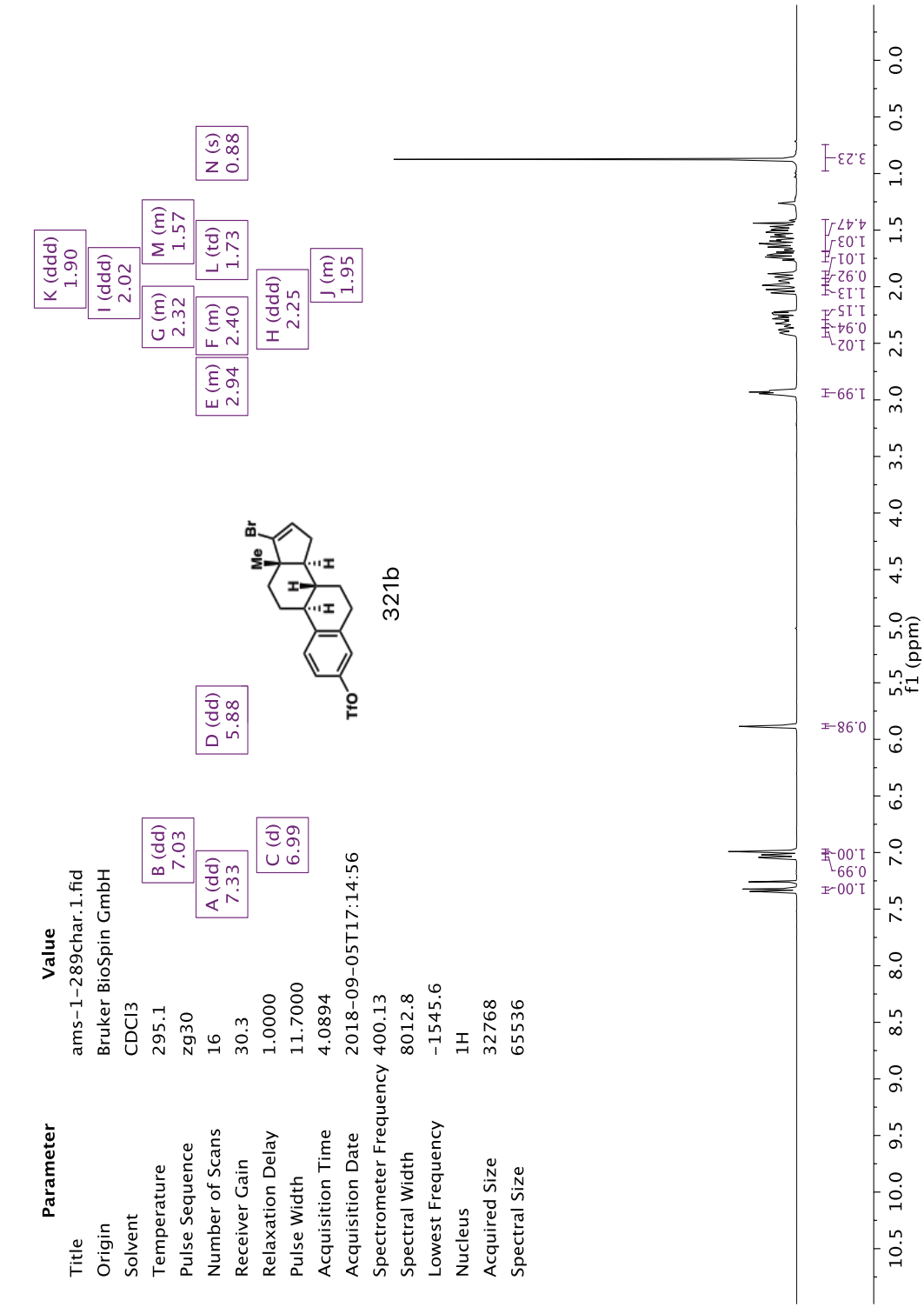

Parameter Value
Title JLH-7-232A.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zgpg30
Number of Scans 512
Receiver Gain 72.0
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-05-11T18:07:55
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1946.3
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
25.0
84.1
118.5
126.6
131.1
134.8
141.0
Br
pinB
319b
f1 (ppm)


Parameter
Value
Title JLH-8-044-column.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 30.3
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-09-04T19:45:08
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1545.4
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
A (d) 6.26
B (dd) 5.39
C (ddd) 4.41
D (ddd) 3.47
E (t) 3.36
F (m) 2.59
G (ddd) 2.46
H (dt) 2.17
I (ddd) 1.98
J (m) 1.60
K (m) 0.97
L (m) 0.79
Me
Me
Me
Me
H
H
H
H
H
O
O
Br
320b
1.00
1.02
1.03
1.02
1.01
1.02
1.01
1.04
1.05
17.96
7.20
6.11
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

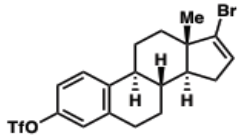

Parameter
Value
Title
JLH-8-044-column.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
zgpg30
Number of Scans
128
Receiver Gain
72.0
Relaxation Delay
2.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-09-04T19:52:59
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1947.0
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
320b
Me
O
H
Br
141.3
131.2
124.4
120.9
109.4
80.9
67.0
62.2
56.7
48.0
41.7
40.5
34.6
32.0
31.3
30.4
21.0
19.1
17.3
16.5
14.7
f1 (ppm)


Parameter
Value
Title JLH-7-248-column.1.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 297.2
Pulse Sequence zg30
Number of Scans 16
Receiver Gain 30.3
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 4.0894
Acquisition Date 2018-05-28T06:05:37
Spectrometer Frequency 400.13
Spectral Width 8012.8
Lowest Frequency -1545.3
Nucleus 1H
Acquired Size 32768
Spectral Size 65536
A (d) 6.05
B (dd) 5.38
C (ddd) 4.41
D (ddd) 3.47
E (t) 3.37
F (ddd) 2.50
G (ddd) 2.31
H (dt) 2.19
I (ddd) 1.99
J (m) 1.75
K (m) 1.44
L (ddd) 1.31
M (m) 1.17
N (m) 1.02
O (t) 0.97
P (m) 0.79
320c
f1 (ppm)

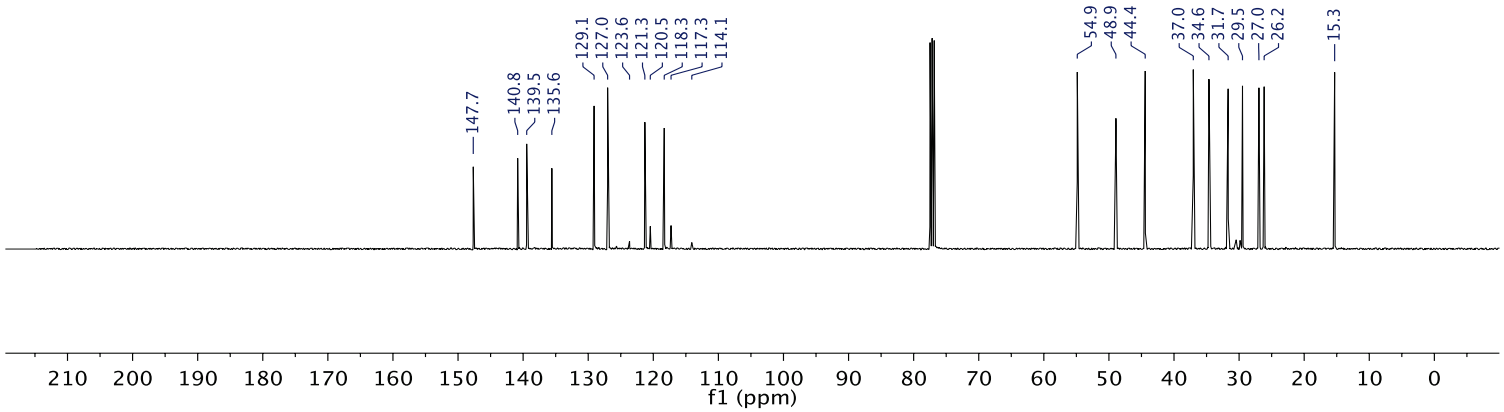

Parameter
Value
Title
JLH-7-248-column.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
297.1
Pulse Sequence
zgpg30
Number of Scans
256
Receiver Gain
72.0
Relaxation Delay
1.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-05-28T06:16:29
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1946.0
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Me
O
O
Me
Me
H
H
H
H
H
Me
Cl
320c
140.6
130.4
127.1
124.0
109.4
80.9
67.0
62.2
56.7
48.0
41.7
40.5
31.9
31.4
30.4
28.9
21.1
19.0
17.3
16.5
14.7
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Parameter
Value
Title
ams-1-289char.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.1
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
30.3
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-09-05T17:14:56
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1545.6
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
A (dd) 7.33
B (dd) 7.03
C (d) 6.99
D (dd) 5.88
E (m) 2.94
F (m) 2.40
G (m) 2.32
H (ddd) 2.25
I (ddd) 2.02
J (m) 1.95
K (ddd) 1.90
L (td) 1.73
M (m) 1.57
N (s) 0.88
Me
Br
TfO
321b
1.00
0.99
1.00
0.98
1.99
1.02
0.94
1.15
1.13
0.92
1.01
1.03
4.47
3.23
f1 (ppm)

Parameter	Value
Title	ams-1-289char.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zgpg30
Number of Scans	512
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-09-05T17:36:09
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1947.2
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



321b



Parameter	Value
Title	AMS-1-289-F
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-09-05T15:27:01
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56444.7
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

321b

-72.9

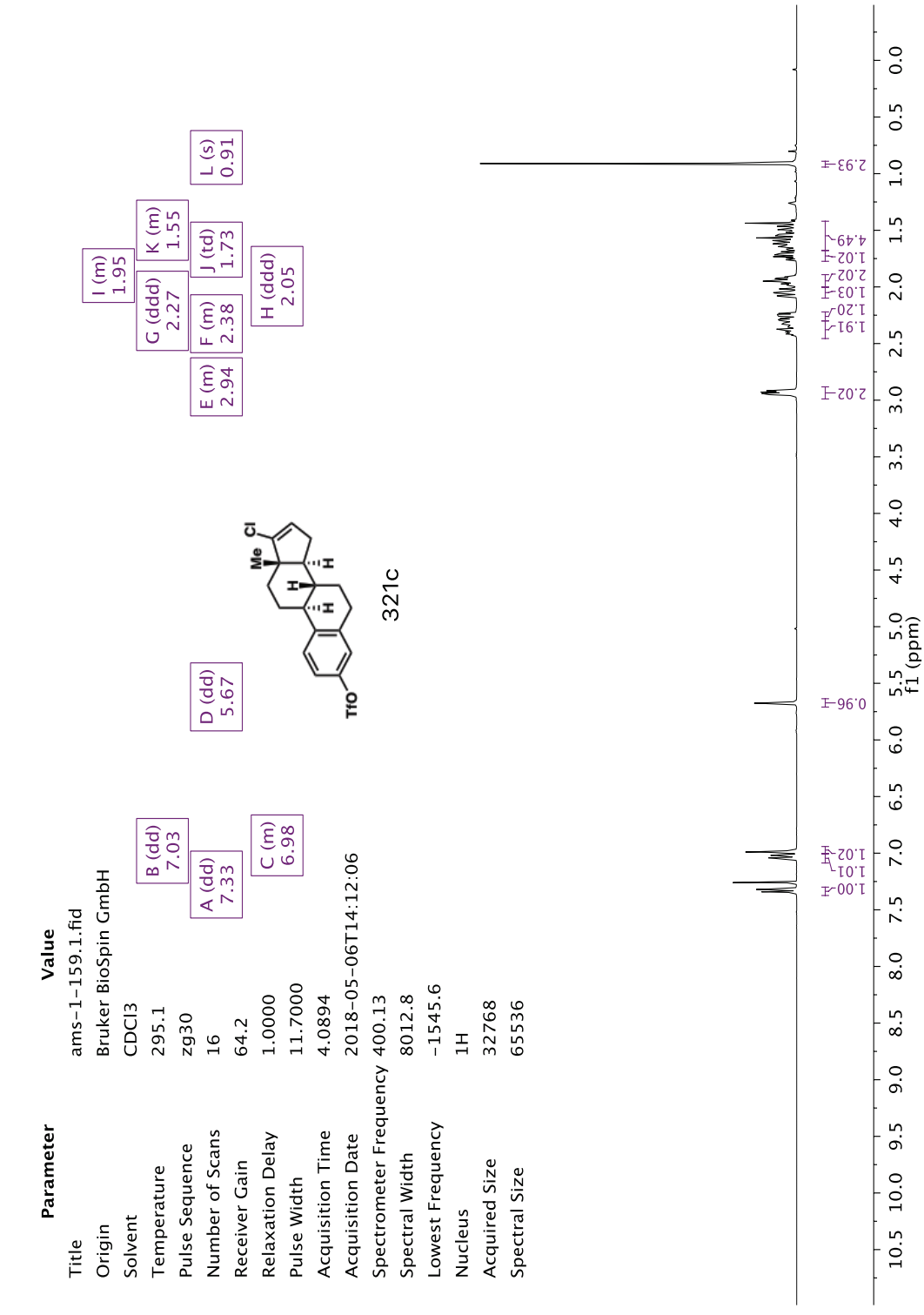
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

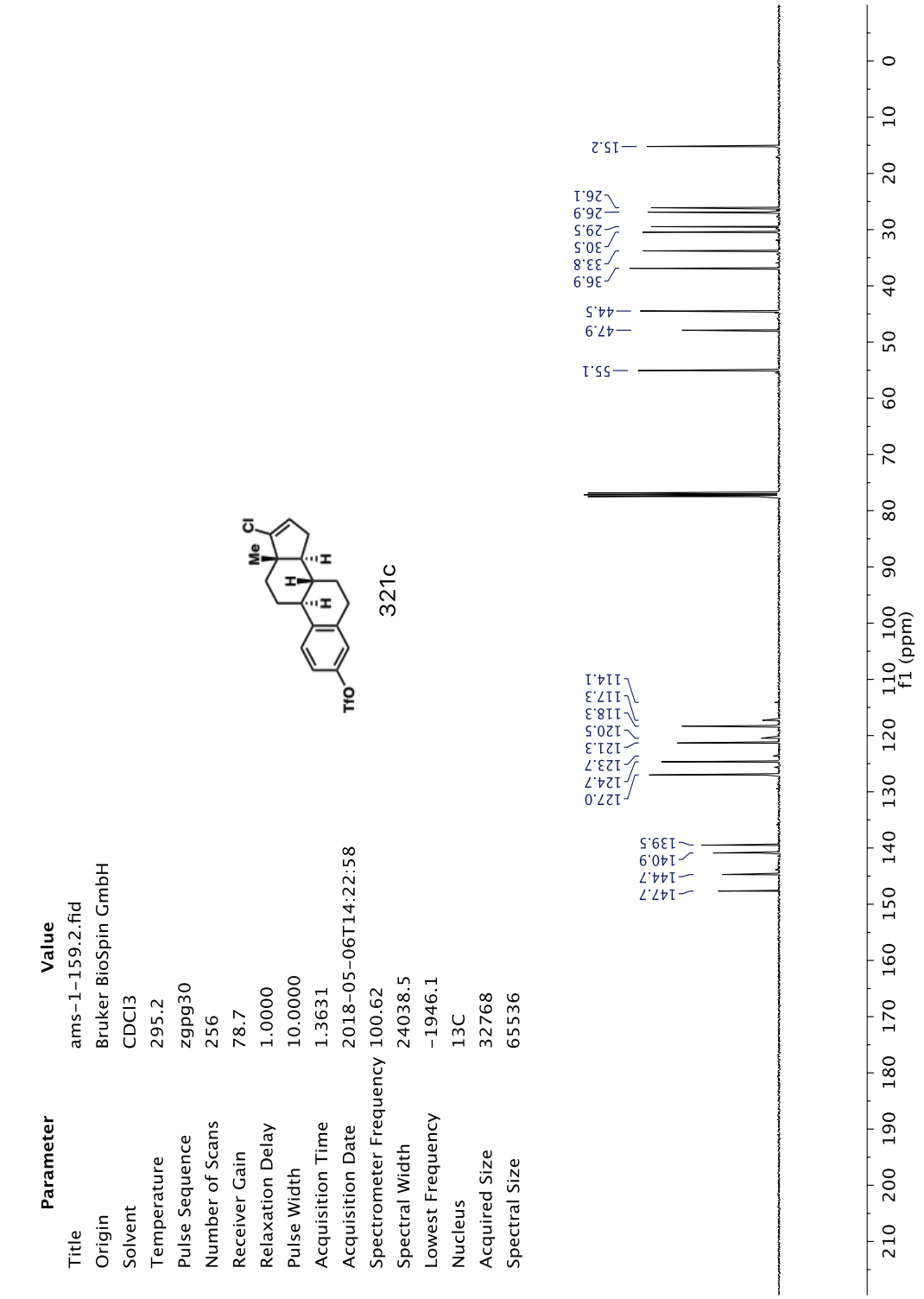
Parameter	Value
Title	AMS-1-289-F-std
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-09-10T23:58:01
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56442.5
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

321b
with C_6F_6

-72.9

10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)


Parameter
Value
Title
ams-1-159.1.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.1
Pulse Sequence
zg30
Number of Scans
16
Receiver Gain
64.2
Relaxation Delay
1.0000
Pulse Width
11.7000
Acquisition Time
4.0894
Acquisition Date
2018-05-06T14:12:06
Spectrometer Frequency
400.13
Spectral Width
8012.8
Lowest Frequency
-1545.6
Nucleus
1H
Acquired Size
32768
Spectral Size
65536
A (dd) 7.33
B (dd) 7.03
C (m) 6.98
D (dd) 5.67
E (m) 2.94
F (m) 2.38
G (ddd) 2.27
H (ddd) 2.05
I (m) 1.95
J (td) 1.73
K (m) 1.55
L (s) 0.91
Me
Cl
H
H
H
TIO
321c
1.00
1.01
1.02
0.96
2.02
1.91
1.20
1.03
2.02
1.02
4.49
2.93
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


Parameter
Value
Title
ams-1-159.2.fid
Origin
Bruker BioSpin GmbH
Solvent
CDCl3
Temperature
295.2
Pulse Sequence
zgpg30
Number of Scans
256
Receiver Gain
78.7
Relaxation Delay
1.0000
Pulse Width
10.0000
Acquisition Time
1.3631
Acquisition Date
2018-05-06T14:22:58
Spectrometer Frequency
100.62
Spectral Width
24038.5
Lowest Frequency
-1946.1
Nucleus
13C
Acquired Size
32768
Spectral Size
65536
Me
Cl
H
H
H
HO
321c
147.7
144.7
140.9
139.5
127.0
124.7
123.7
121.3
120.5
118.3
117.3
114.1
55.1
47.9
44.5
36.9
33.8
30.5
29.5
26.9
26.1
15.2
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

Parameter	Value
Title	AMS-1-159-F
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-06-14T01:56:19
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56468.7
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

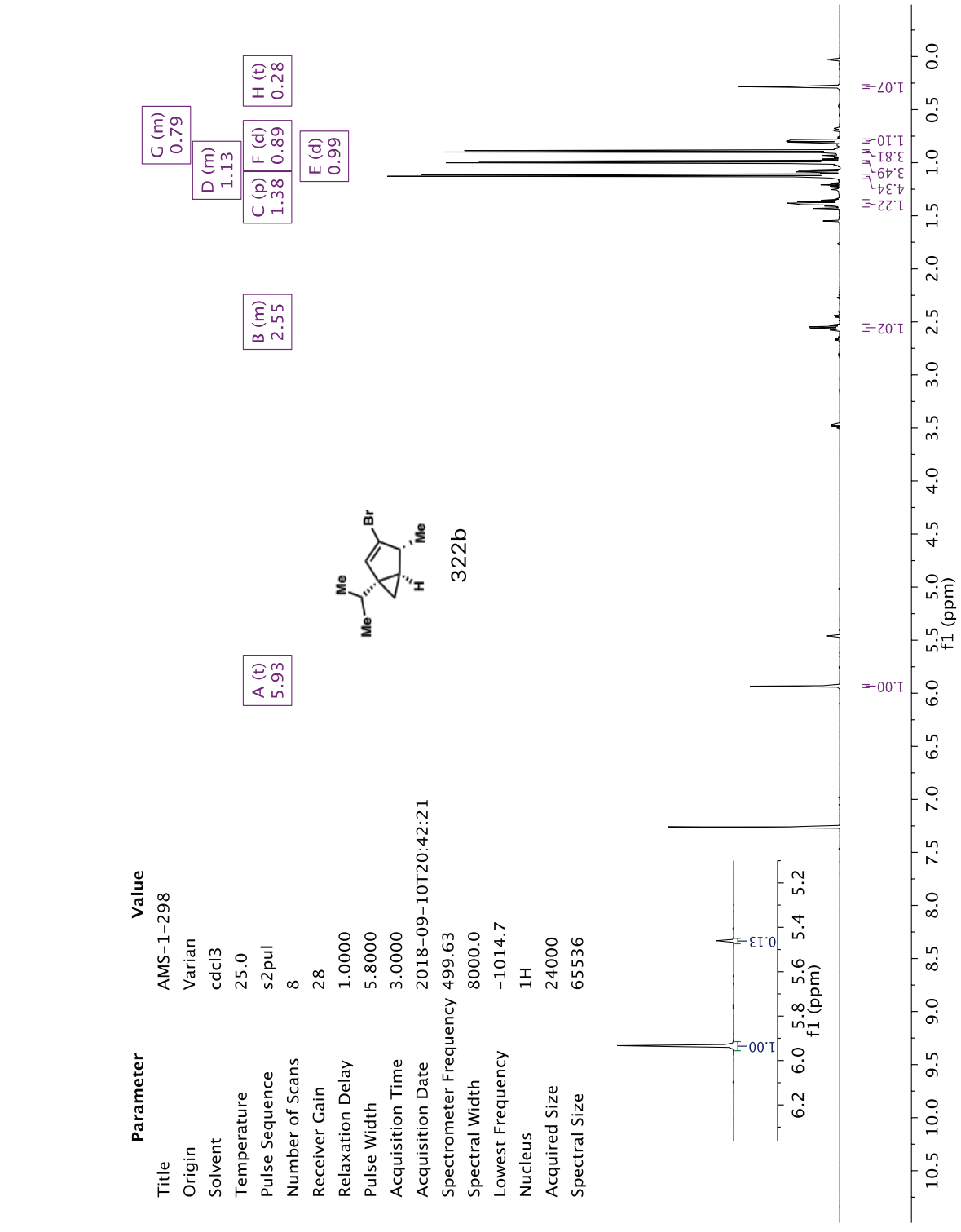
321c

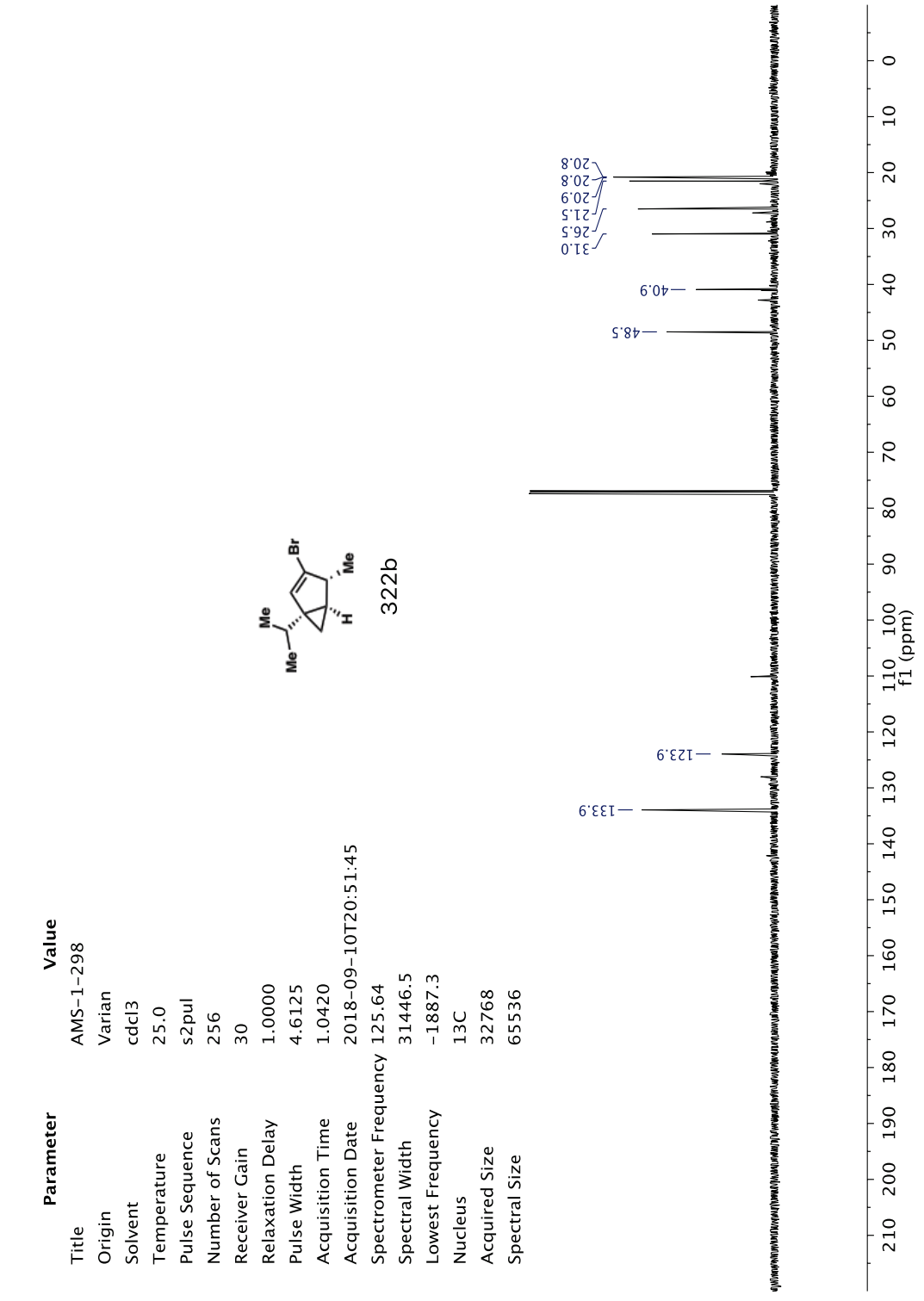
Parameter	Value
Title	AMS-1-159-F-C6F6
Origin	Varian
Solvent	cdcl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	6.3333
Acquisition Time	0.9856
Acquisition Date	2018-06-14T02:00:32
Spectrometer Frequency	282.34
Spectral Width	64935.1
Lowest Frequency	-56468.7
Nucleus	19F
Acquired Size	64000
Spectral Size	131072

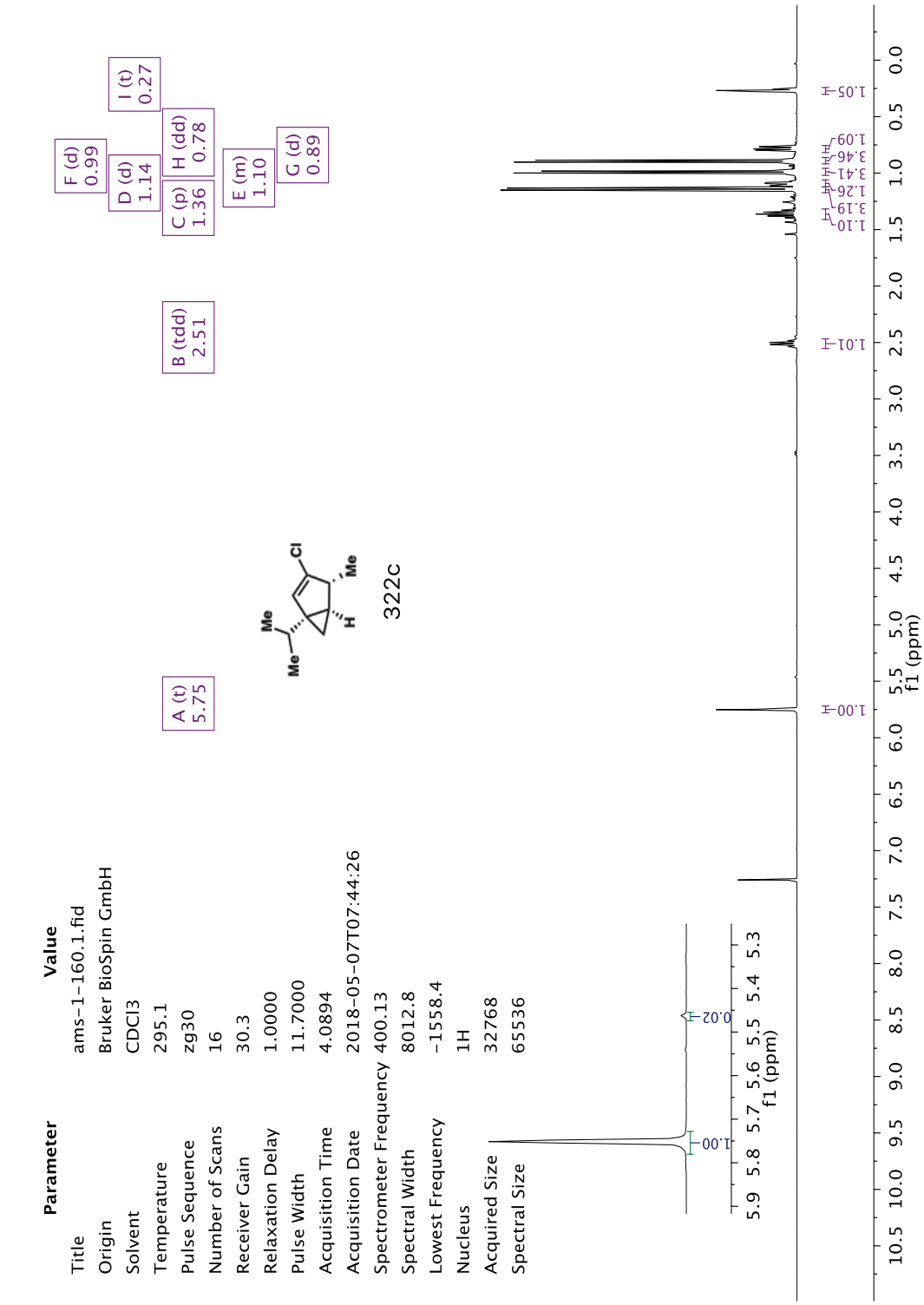
321c
with C_6F_6

-72.9

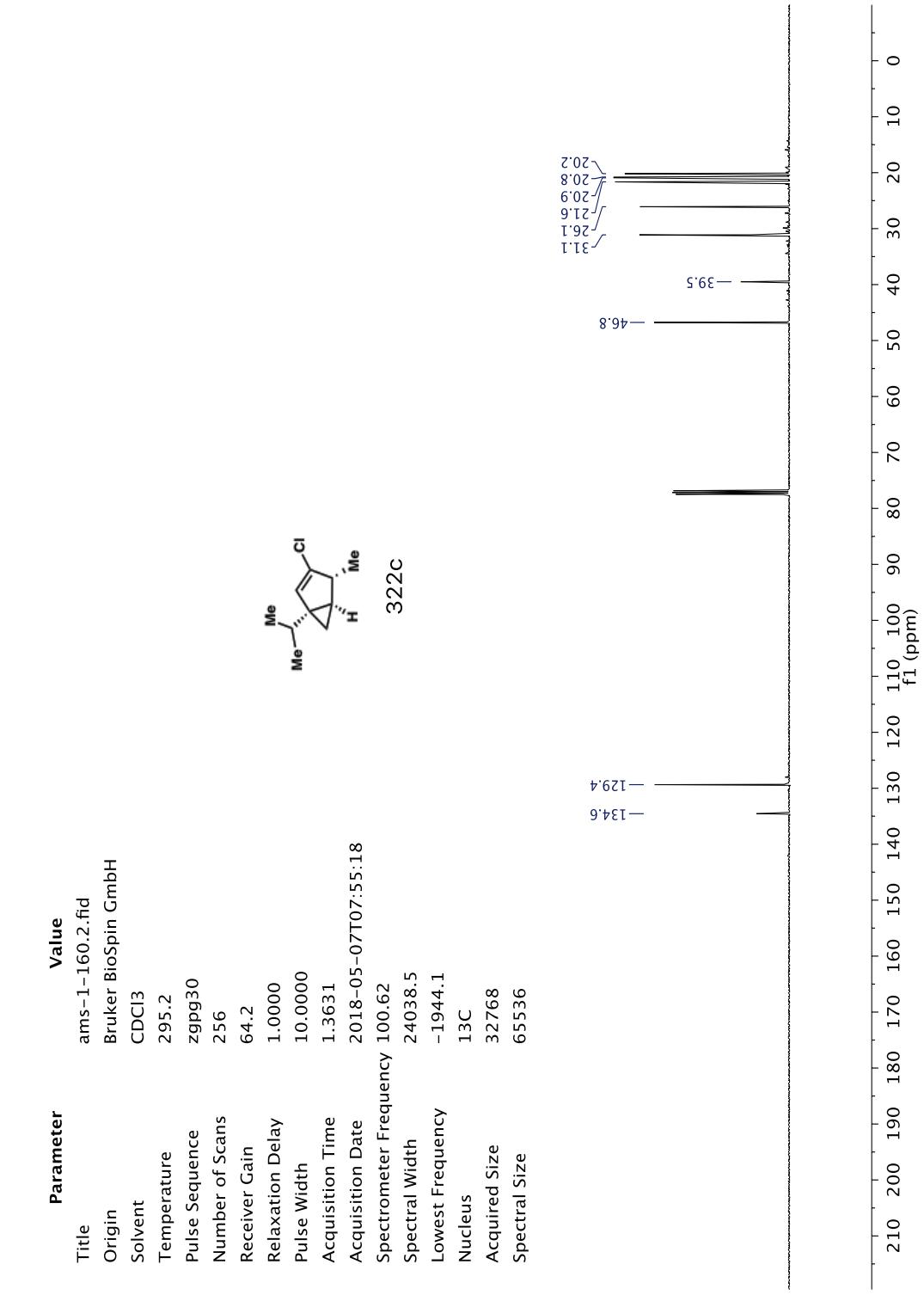
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)


Parameter Value
Title AMS-1-298
Origin Varian
Solvent cdcl3
Temperature 25.0
Pulse Sequence s2pul
Number of Scans 8
Receiver Gain 28
Relaxation Delay 1.0000
Pulse Width 5.8000
Acquisition Time 3.0000
Acquisition Date 2018-09-10T20:42:21
Spectrometer Frequency 499.63
Spectral Width 8000.0
Lowest Frequency -1014.7
Nucleus 1H
Acquired Size 24000
Spectral Size 65536
A (t) 5.93
B (m) 2.55
C (p) 1.38
D (m) 1.13
E (d) 0.99
F (d) 0.89
G (m) 0.79
H (t) 0.28
Me
Me
Br
Me
H
322b
1.00
0.13
1.00
1.02
1.22
4.34
3.49
3.81
1.10
1.07
f1 (ppm)


Parameter Value
Title AMS-1-298
Origin Varian
Solvent cdcl3
Temperature 25.0
Pulse Sequence s2pul
Number of Scans 256
Receiver Gain 30
Relaxation Delay 1.0000
Pulse Width 4.6125
Acquisition Time 1.0420
Acquisition Date 2018-09-10T20:51:45
Spectrometer Frequency 125.64
Spectral Width 31446.5
Lowest Frequency -1887.3
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
Me
Br
H
Me
322b
133.9
123.9
48.5
40.9
31.0
26.5
21.5
20.9
20.8
20.8
f1 (ppm)



Parameter	Value
Title	ams-1-160.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Number of Scans	16
Receiver Gain	30.3
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-05-07T07:44:26
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1558.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536


Parameter Value
Title ams-1-160.2.fid
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence zgpg30
Number of Scans 256
Receiver Gain 64.2
Relaxation Delay 1.0000
Pulse Width 10.0000
Acquisition Time 1.3631
Acquisition Date 2018-05-07T07:55:18
Spectrometer Frequency 100.62
Spectral Width 24038.5
Lowest Frequency -1944.1
Nucleus 13C
Acquired Size 32768
Spectral Size 65536
Me
Me
Cl
H
Me
322c
134.6
129.4
46.8
39.5
31.1
26.1
21.6
20.9
20.8
20.2
f1 (ppm)

ABOUT THE AUTHOR

Kelsey Elizabeth Poremba was born on December 23, 1991 to Dr. John Poremba, M.D., and Dr. Helen Poremba, M.D., in Biloxi, MS. As a military brat, she moved several times during her childhood, ultimately establishing roots in Bedford, NH. After graduating from Bedford High School in 2010, she attended the College of the Holy Cross where she was a Clare Boothe Luce Scholar. Her love for organic chemistry began when she studied under Professor Bianca R. Sculimbrene, eventually joining her research group. Kelsey's undergraduate research focused on the development of diastereoselective alkylations of unsaturated amides for the synthesis of peptide isosteres. She graduated summa cum laude in 2014 from Holy Cross with a B.A. in chemistry.

Kelsey drove across America that summer to join the lab of Professor Sarah E. Reisman at the California Institute of Technology to pursue a Ph.D. in organic chemistry. During her doctoral studies, Kelsey worked on the development of asymmetric nickel-catalyzed reductive cross-couplings and explored the application of these methods to natural product total synthesis. Following her graduation in June 2019, Kelsey will join the Discovery Process Chemistry group at Merck in Boston, MA. She is very much looking forward to openly cheering for the New England Patriots again. In her free time, Kelsey enjoys playing with dogs and spending time with friends.