Regulating Reactivity and Selectivity of a Dehydro-Diels–Alder Reaction of Vinyl Heteroarenes Informed by Mechanism and Application towards the Synthesis of Photovoltaic Materials

by

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Regulating Reactivity and Selectivity of a Dehydro-Diels–Alder Reaction of Vinyl Heteroarenes Informed by Mechanism and Application towards the Synthesis of Photovoltaic Materials

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Ring-fused heteroarenes are present in numerous natural products, FDA approved drugs, agrochemicals, and recently, organic solar cells able to achieve record breaking power conversion efficiencies. Access to these valuable compounds relies primarily on synthesis with dearomative cycloadditions of heteroarenes emerging as an efficient strategy. Many of these reactions require forceful conditions that utilize catalysts, acids and bases, or high temperatures to effect dearomatization. We have developed an intramolecular dearomative didehydro-Diels–Alder (DDDA) reaction which proceeds at temperatures as low as 60 °C with mild conditions, free of additives or catalysts. The adduct of the dearomative cycloaddition, which has been isolated and characterized, readily rearomatizes to either an isomerization product by way of a hydrogen migration or an oxidation product by way of a dehydrogenation.

To determine the substrate dependent factors that control the dearomative cycloaddition, kinetic studies were conducted with in situ reaction monitoring by ReactIR and afforded experimental Gibbs free energies of activation which correlated well with DFT calculations to reveal a highly asynchronous, concerted transition state. Aromaticity of the heteroarene, tether composition, and dispersion interactions were identified as substrate dependent factors that affect reactivity, establishing DFT calculations as a predictive tool in determining reactivity.

For the first time, the 1,4-cyclohexadienyl DA adduct was isolated, characterized, and confirmed as the product of the dearomative cycloaddition with divergent reactivity from the adduct leading to formation of either oxidation or isomerization products. These divergent mechanisms were investigated, and product selectivity was enhanced with control over the reaction parameters. Experiments utilizing deuterium oxide or increased exposure to air revealed the isomerization products were formed by an intermolecular, ionic proton transfer, while oxidation products were formed by an oxygen promoted dehydrogenation. Selectivity for either product was enhanced through reaction parameters such as temperature, solvent polarity, concentration, atmosphere, and additives.

Insight into the mechanisms of dearomatization and product formation allowed us to enhance the reactivity and product selectivity of the dearomative DDDA reaction for vinyl heteroarenes which was then applied towards the synthesis of ladder-type heteroarenes for organic photovoltaic materials. We expect these mechanistic findings to lend insight into other dearomative processes in the future.

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Δ	heat
$\Delta G^{\ddagger}$	Gibbs free energy of activation
$\Delta H^{\ddagger}$	enthalpy of activation
$\Delta S^{\ddagger}$	entropy of activation
^{1}H NMR	proton nuclear magnetic resonance
^{13}C NMR	carbon nuclear magnetic resonance
Å	angstrom
A	pre-exponential factor
a.u.	arbitrary units
Ac_2O	acetic anhydride
AcOH	acetic acid
A-D-A	acceptor-donor-acceptor
Avg	average
B	y-intercept
BDE	bond dissociation energy
BHT	di-t-butylhydroxytoluene
Boc	tert-butoxycarbonyl protecting group
Calc	calculated
Cat	catalyst
$CDCl_3$	chloroform-d
CFL	compact fluorescent light

Comp	computational
COSY	correlated spectroscopy
D_2O	deuterium oxide
DA	Diels–Alder
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCE	dichloroethane
DCM	dichloromethane
DDDA	didehydro-Diels–Alder
DFT	density-functional theory
DI	deionized
DIBAL	diisobutylaluminum hydride
DIPEA	*N*,*N*-diisopropylethylamine
Disp.	dispersion
DMAP	4-dimethylaminopyridine
DMF	*N*,*N*-dimethylformamide
dr	diastereomeric ratio
E_a	activation energy
EDCI	*N*-(3-Dimethylaminopropyl)-*N′*-ethylcarbodiimide hydrochloride
ee	enantiomeric excess
EI	electron ionization
er	enantiomeric ratio
ES	electron spray
ESI	electron spray ionization

Et_2O	diethyl ether
EtOAc	ethyl acetate
Exp	experimental
FTMS	Fourier transform ion cyclotron resonance mass spectrometer
h	Planck's constant
h	hours
H_2	molecular hydrogen
H_2O	water
Hex	n-hexane
HFIP	hexafluoroisopropanol
HMBC	heteronuclear multiple bond correlation
HRMS	high resolution mass spectroscopy
HSQC	heteronuclear single quantum correlation
HWE	Horner–Wadsworth–Emmons
IR	infrared
Isom	isomerization product
k	rate constant
k_B	Boltzmann constant
LDA	lithium diisopropylamide
$LiAlD_4$	lithium aluminum deuteride
$LiAlH_4$	lithium aluminum hydride
m	slope
mA	milliamps

MeCN	acetonitrile
min	minutes
MP	melting point
MS	mass spectroscopy
NICS	nucleus-independent chemical shifts
NMR	nuclear magnetic resonance
O_2	molecular oxygen
o-DCB	*o*-dichlorobenzene
OPV	organic photovoltaic
Oxid	oxidation product
PCE	power conversion efficiency
$PhNO_2$	nitrobenzene
ppm	parts per million
R	gas constant
R^2	R-squared
R_f	retention factor
rt	room temperature
SMD	solvation model based on density
T	temperature
$t_{1/2}$	half-life
TBA	tribromoacetic acid
TFE	tetrafluoroethanol
THF	tetrahydrofuran

TLC	thin layer chromatography
TOF	time of flight
tol	toluene
TS	transition state
UV	ultraviolet
μW	microwave

Acknowledgments

First, I would like to thank my family for their love and support during these past years of graduate school: my best friend and wife Carolyn who has motivated and encouraged me each day of my program, and our son Silas who has brought an incredible amount of joy to my life. My parents Norb and Kim, who raised me in love and wisdom. My father-in-law and mother-in-law Brian and Kelley who have loved me as their own. My sister Michelle as well as my brothers-in-law and sisters-in-law Calvin, Dan, Dave, Tim, Mallory, Caroline, and Audrey who have been my closest friends. Finally, my great-uncle Howard who has always supported me in my pursuit of education and science.

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1.0 Dearomative Cycloadditions of Vinylogous Heteroarenes

1.1 Valuable Synthetic Targets Containing Polycyclic Heteroarene Frameworks

Heteroarenes represent valuable scaffolds towards the synthesis of natural products, pharmaceuticals, pesticides, and other biologically active compounds.[1-5] Thiophenes as well as other sulfur based heteroarenes are especially valuable in medicinal chemistry as frameworks that are common in natural products and pharmaceuticals with therapeutic properties.[6-9] Marketed drugs with benzothiophene frameworks include the asthma medication Zileuton (**1.1**), osteoporosis treatment Raloxifene (**1.2**), and antifungal Sertaconazole (**1.3**).[10-12] Marketed drugs containing thiophene frameworks include the anti-psychotic Olanzapine (**1.4**), glaucoma treatment Dorzolamide (**1.5**), and antiplatelet Clopidogrel (**1.6**).[13-15]

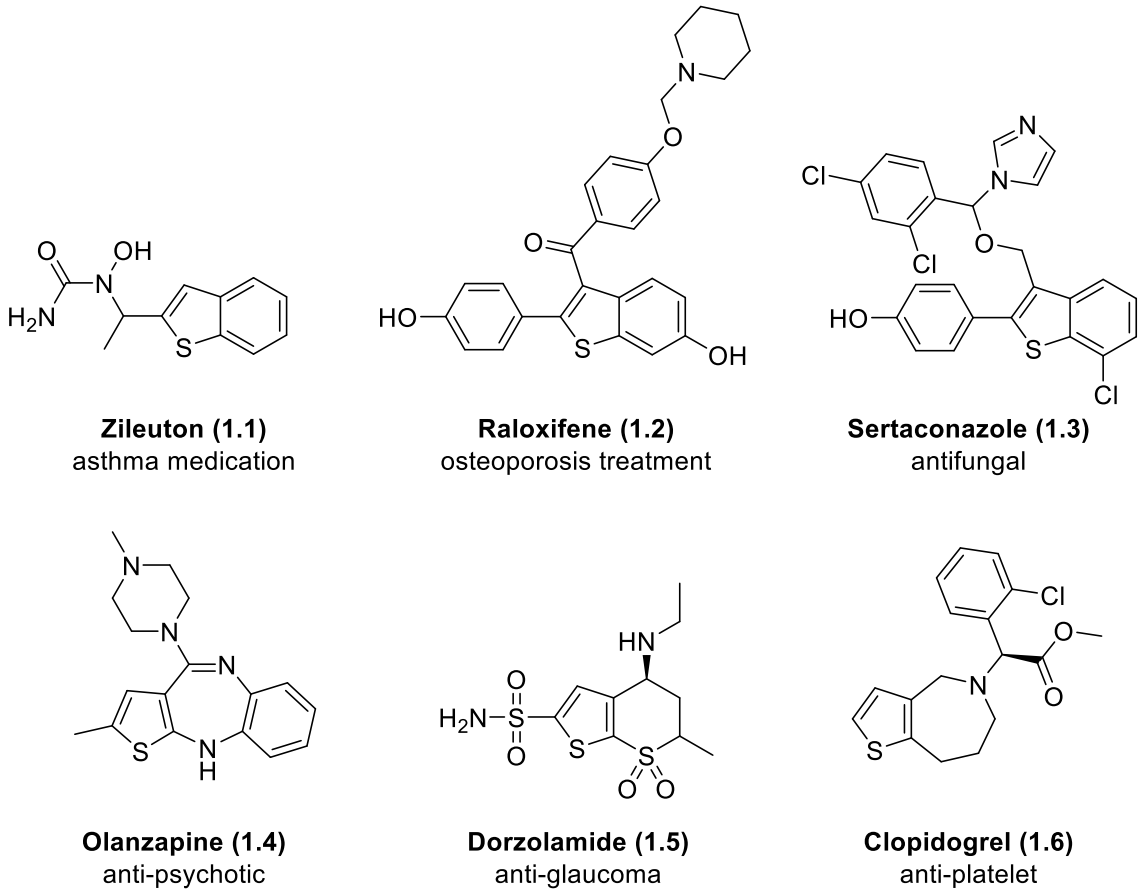
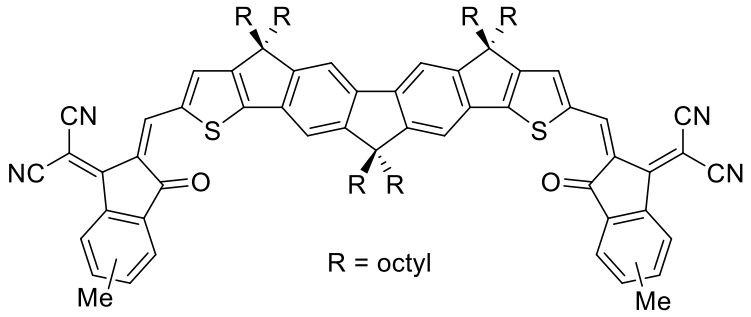
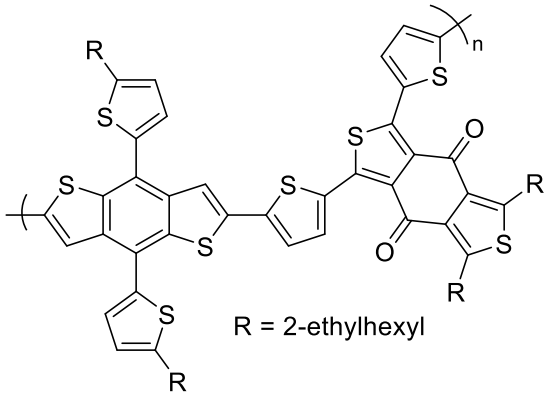


Figure 1.1. Marketed drugs containing heterocyclic frameworks of benzothiophenes or indoles

Recently, interest has grown in the application of heteroarenes towards ladder-type conjugated materials that have shown record breaking power conversion efficiencies (PCE) of greater than 17% in organic photovoltaic (OPV) solar-cells.[16] Sulfur based heteroarenes in particular have found increasing success in the application towards these materials. For example, a record-performing OPV solar-cell was achieved by blending Acceptor-Donor-Acceptor (A–D–A) molecules (**1.7**) and electron donor molecules (**1.8**) with conjugated polymers, incorporated into a tandem cell (Figure 1.2). The value and importance of heteroarenes and their derivatives continues to grow, and access to these compounds relies heavily upon synthesis. [17-20]



1.7
acceptor-donor-acceptor



1.8
donor

Figure 1.2. Ladder-type conjugated polycyclic structure utilized in OPV solar-cells achieving record-breaking PCE's of greater than 17%

1.2 Forcing Conditions Required in Dearomative Cycloaddition Processes

Dearomative cycloadditions are emerging as a valuable strategy to build complex polycyclic heteroarene compounds.[21-28] Various new approaches have been developed to effect these cycloadditions, affording products in high yields and high stereoselectivity. Still, forcing conditions are required to activate the aromatic π-system of the heteroarene for the dearomative cycloaddition. This synthetic toolbox includes reaction conditions such as acid catalysis, base

mediation, transition-metal catalysis, organocatalysis, photoredox catalysis, electrochemistry, and thermal conditions that utilize either high temperatures or highly reactive dienophiles. In the following section, we discuss recent examples with high yields and stereoselectivity that highlight several of the more prominent dearomative strategies.

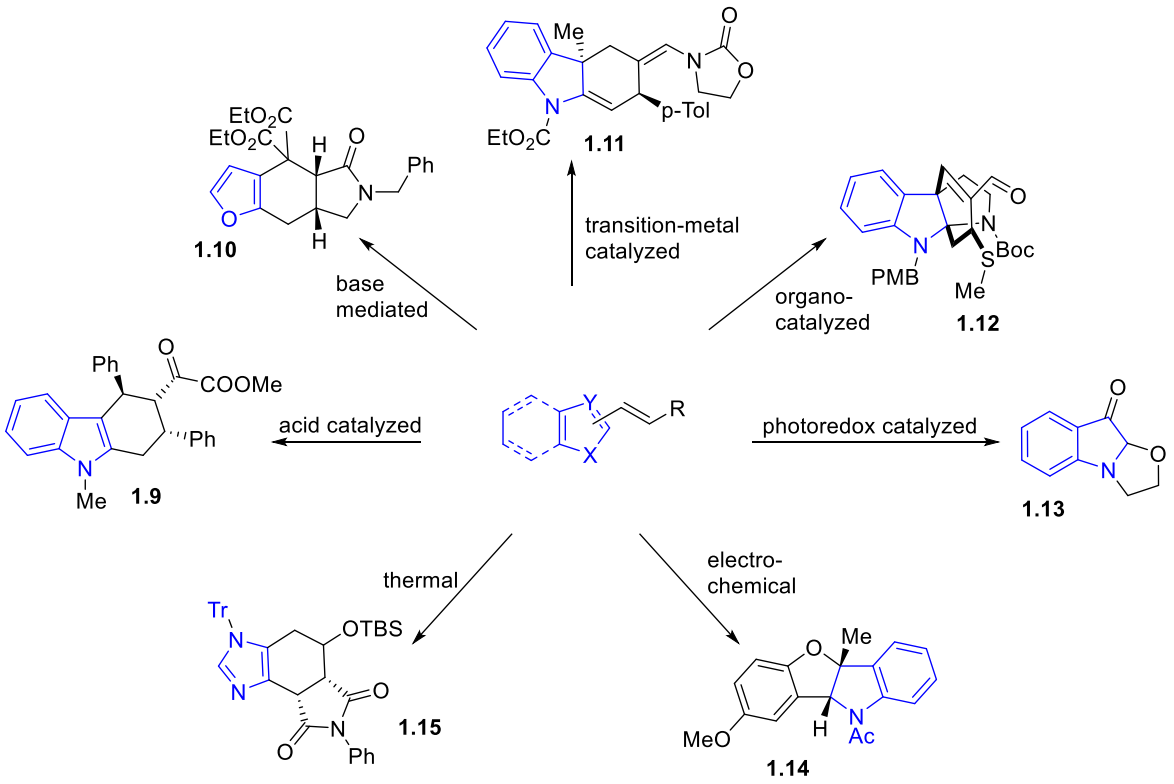
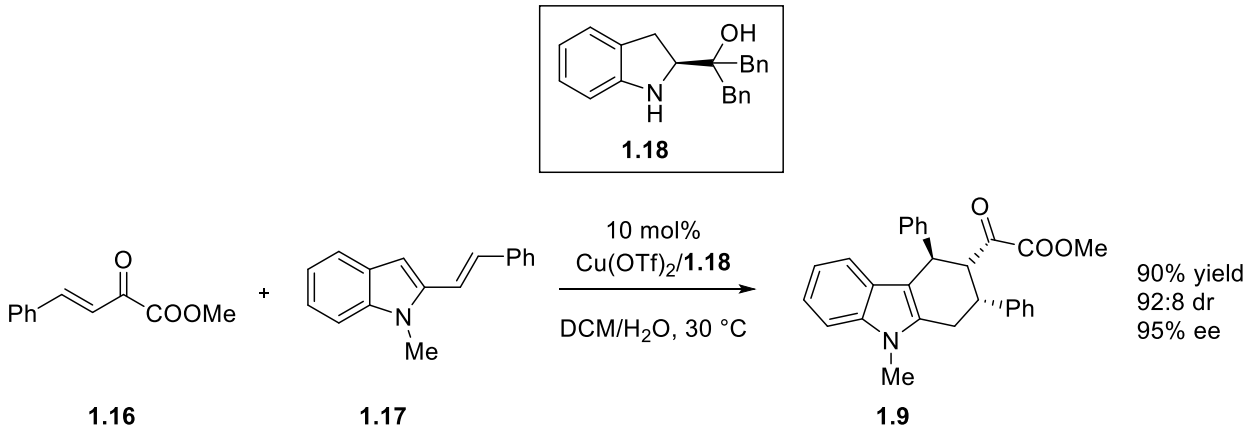


Figure 1.3. Synthetic toolbox of forcing conditions for dearomative cycloaddition processes

1.2.1 Acid Catalyzed Dearomative [4 +2] Cycloadditions of Vinyl Heteroarenes

Acid catalysis for dearomative cycloadditions of vinyl heteroarenes often utilizes transition-metals that act as a Lewis acid to coordinate with and activate the dienophile in the DA cycloaddition. Transition-metals equipped with chiral ligands control stereoselectivity and impart chirality into the new polycyclic product. Ouyang et al synthesized highly functionalized

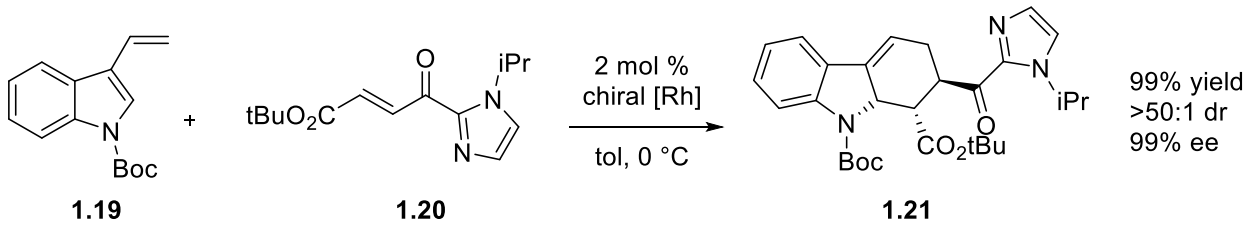
tetrahydrocarbazole **1.9** from 2-vinylindole **1.17** and β,γ-unsaturated α-ketoester **1.16** utilizing copper(II) triflate with chiral indolinylmethanol ligand **1.18** as the Lewis acid catalyst (Scheme 1.1).[29] Product was afforded in high yield of 90% good stereoselectivities with ee of 95% and dr 92:8. Based on product stereochemistry, the authors propose the reaction mechanism to be a concerted [4 + 2] cycloaddition. Whereas the initial cycloadduct and rearomatization process were not described, stereoselectivity in the product is attributed to a distorted octahedral transition state geometry of the copper complex coordinated to the β,γ-unsaturated α-ketoester **1.16** controlling both the facial and endo approach of 2-vinylindole **1.17**.



Scheme 1.1. Lewis acid catalyzed dearomative [4 +2] cycloaddition of a 2-vinylindole

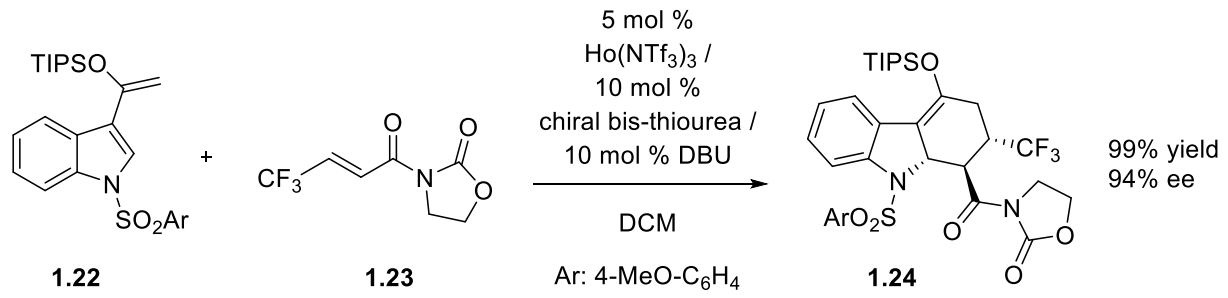
Huang et al demonstrated the use of chiral rhodium(III) as a Lewis acid in the preparation of hydrocarbazole **1.21** from 3-vinylindole **1.19** and α,β-unsaturated 2-acyl imidazole **1.20**.[30] The hydrocarbazole **1.21** was afforded in excellent yield (99%), regioselectivity (99:1), diastereoselectivity (>50:1), and enantioselectivity (99%) under optimized conditions. Based on product stereoselectivity, the authors propose that the chiral octahedral rhodium catalyst activates the 2-acyl imidazole dienophile **1.20** via bidentate coordination to the oxygen of the carbonyl and

the unsubstituted nitrogen of the imidazole, increasing reactivity towards the [4 + 2] cycloaddition reaction with the 3-vinylindole **1.19**. Phenylbenzoxazole ligands impart chirality, sterically directing the facial approach of vinylindole **1.19** with an endo attack. Steric clashing between the Boc group on the indole and the isopropyl group on the imidazole effect the observed regioselectivity.



Scheme 1.2. Chiral rhodium catalyst utilized as a Lewis acid in a dearomative [4 + 2] cycloaddition

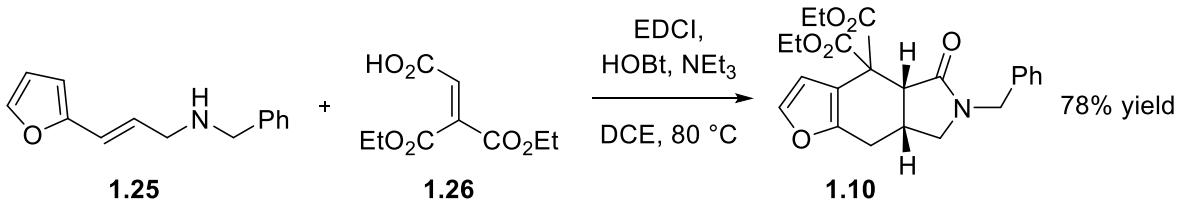
Lanthanide holmium has also been utilized as a chiral Lewis acid in catalytic and asymmetric dearomative cycloadditions. Harada et al synthesized substituted hydrocarbazole **1.24** from 3-vinylindole **1.22** and N-acyloxazolidinone **1.23**.[31] They were able to synthesize product **1.24** with three chiral stereogenic centers in 99% yield and 94% ee. The authors proposed that the [4 + 2] cycloaddition proceeds through an eight coordinate holmium(III) catalyst complex, a conclusion supported by mass spectroscopy analysis. The complex activates the N-acyloxazolidinone **1.23** by bidentate coordination to both carbonyl oxygens. The thiourea side chain and naphthyl ring of the chiral ligands create a steric barrier which directs a single approach of the 3-vinylindole **1.22** to the dienophile **1.23** to effect the observed regio- and stereochemistry in the product by facial attack of the 3-vinylindole **1.22** with endo approach to the dienophile **1.23**.



Scheme 1.3. Chiral holmium catalyst complex utilized as a Lewis acid in dearomative [4 + 2] cycloadditions

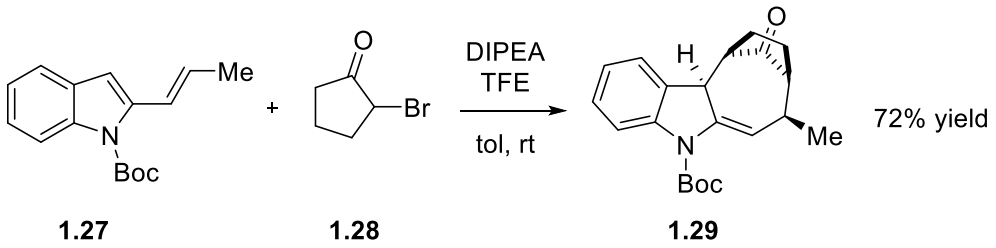
1.2.2 Base Mediated Dearomative Cycloadditions of Vinyl Heteroarenes

Dearomative cycloadditions of vinyl heteroarenes often utilizes basic conditions to initiate formation of a reactive dienophile from starting materials. Sugiura et al demonstrated such a reaction by reaction of 1,1,2-ethenetricarboxylic acid 1,1-diethyl ester **1.26** with E-3-(2-furyl)-2-propenylamine **1.25** under amide condensation conditions to afford cis-fused tricyclic compound **1.10** in moderate yield (78%).[32] This reaction proceeds through a sequential amide formation, [4 + 2] cycloaddition, and hydrogen migration. The initial cycloadducts could be isolated and characterized but were found to decompose at room temperature.



Scheme 1.4. Base mediated dearomative cycloaddition by sequential amide formation, [4 + 2] cycloaddition, and hydrogen-shift

Basic conditions were also used to mediate the dearomative [4 + 3] cycloaddition of 2-vinylindole **1.27** with α-bromoketone **1.28** by in situ generation of oxyallyl cations, as performed by Pirovano et al.[33] Cyclohepta[*b*]indole derivative **1.29** was synthesized 72% yield and complete diastereoselectivity. The highly reactive oxyallyl cations are generated from α-bromoketone **1.28** in the presence of *N,N*-diisopropylethylamine (DIPEA) as base and perfluorinated solvent tetrafluoroethanol (TFE). Complete regio- and diastereoselectivity is observed in the product **1.29** which the authors attribute to endo approach in the [4 + 3] cycloaddition which could proceed either by a concerted or fast stepwise process.

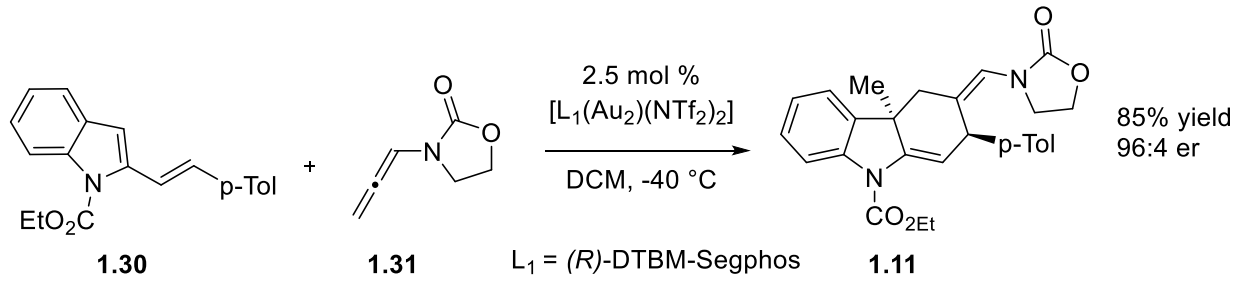


Scheme 1.5. Base generated oxyallyl cations as the dienophile for dearomative cycloadditions with vinylindoles

1.2.3 Transition-Metal Catalyzed Dearomative Cycloadditions of Vinyl Heteroarenes

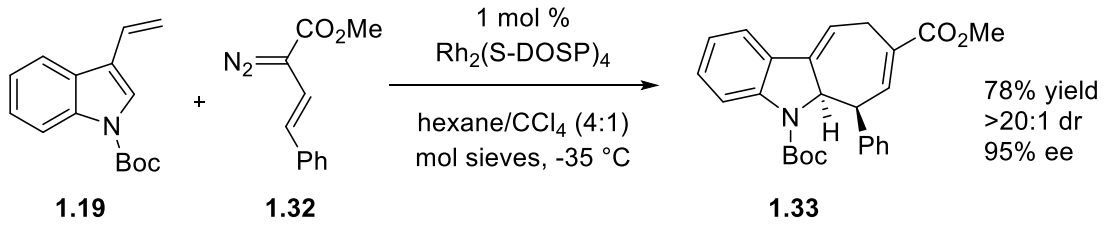
Transition-metals are used to effect dearomative cycloadditions with various types of dienophiles usually through stepwise mechanisms. Stereoselectivity can also be imparted to products with use of chiral ligands on the transition-metal catalysts. Rossi et al demonstrated gold-catalyzed synthesis of tetrahydrocarbazole **1.11** through dearomative [4 + 2] cycloadditions of substituted 2-vinylindole **1.30** with allenamide **1.31** in 85% yield and 96:4 enantiomeric ratio (er) with chiral Seg-Phos derivative ligands effecting stereoselectivity.[34] The [4 + 2] cycloaddition

proceeds via a stepwise mechanism as supported by the author's previous reports.[35] The chiral gold catalyst coordinates with the allene **1.31** to promote a stepwise cyclization with the 2-vinylindole **1.30** where steric interactions effect the observed stereoselectivity in the product **1.11**.



Scheme 1.6. Gold catalyzed dearomative cycloadditions between allenamides and vinylindoles.

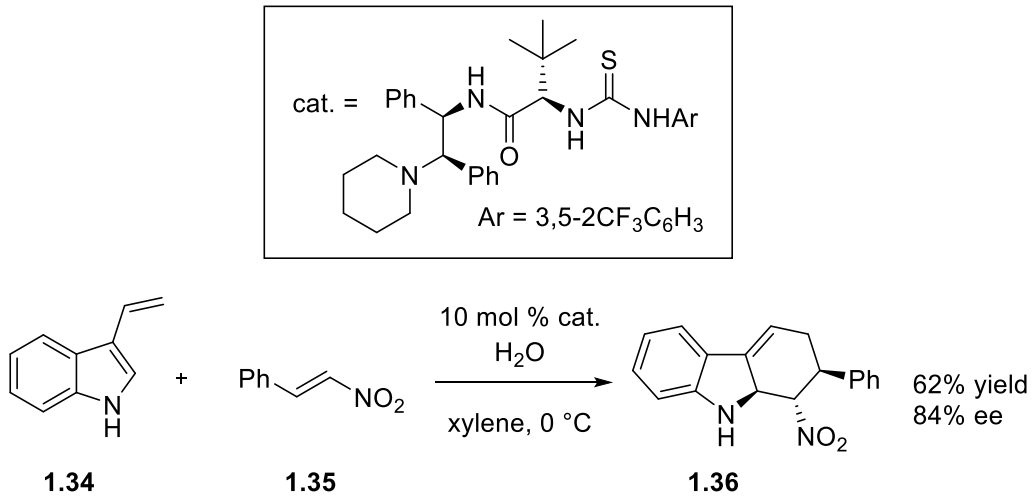
A chiral rhodium catalyst has been demonstrated to effect dearomative cycloadditions by Xu and coworkers.[36] Formal [4 + 3] cycloaddition of vinyindole **1.19** with vinyldiazoacetate **1.32** was effected with proline-derived dirhodium tetracarboxylate catalyst to access cyclohepta[*b*]indole **1.33** in 78% yield, >20:1 dr and 95% ee. The mechanism of the formal (4 + 3) cycloaddition proceeds by sequential asymmetric cyclopropanation of **1.32** and Cope rearrangement with the indole **1.19** promoted by the chiral rhodium catalyst which effects the observed enantioselectivity in the products **1.33** through the chiral ligands.



Scheme 1.7. Dirhodium chiral catalyst promoted dearomative cycloaddition of vinyindoles with vinyldiazoacetates

1.2.4 Organocatalyzed Dearomative Cycloadditions of Vinyl Heteroarenes

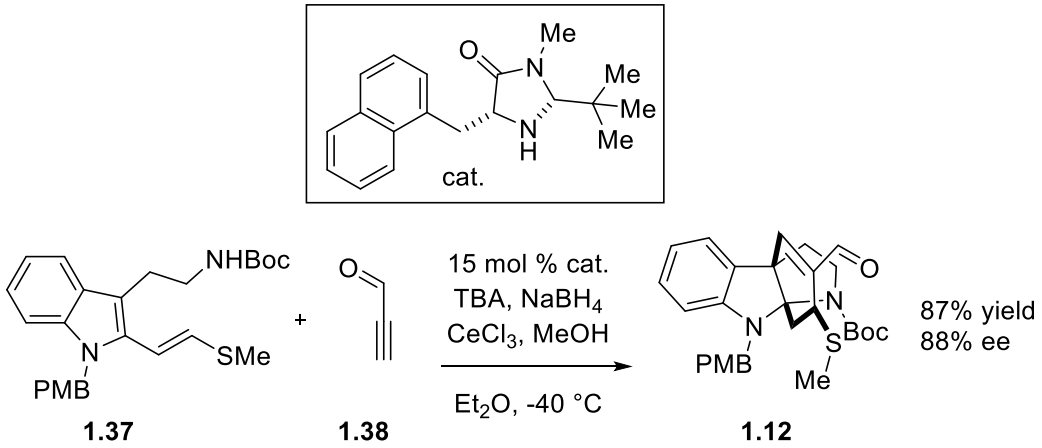
Organocatalyzed dearomative cycloadditions utilize specifically designed organic structures that activate starting materials for cycloaddition by reaction or interaction with Van der Waals forces.[37] Yang et al utilize organocatalysis in the synthesis of nitrohydrocarbazole **1.36** from 3-vinylindole **1.34** and nitroolefin **1.35**.[38] A chiral tertiary amine thiourea catalyst was used to effect the reaction in high yields (72%) and good ee (84%). Based upon control experiments and DFT calculations, the authors proposed that the thiourea catalyst promotes reactivity of the [4 + 2] cycloaddition via double hydrogen bonding nitroolefin **1.35.** This activates the dienophile for cycloaddition with the vinylindole **1.34** by an exo approach, enhancing the enantioselectivity of the reaction.



Scheme 1.8. Synthesis of nitrohydrocarbazoles via organocatalyzed dearomative cycloaddition reaction

Jones et al demonstrated a new organocatalytic DA and sequential amine cyclization affording tetracyclic carbazole frameworks **1.12** from propynal **1.38** and tryptamine derivative

1.37 in 87% yield and 88% ee in .[39] A chiral, secondary amine catalyst is utilized for a condensation reaction with the propynal **1.38** to afford an activated iminium ion which proceeds to the [4 + 2] cycloaddition with 2-vinylindole **1.37**. The authors propose, based upon the stereochemistry of the product, that steric interactions with the chiral catalyst increase selectivity for [4 + 2] cycloaddition in a regioselective manner to afford the DA adduct. Protonation of the enamine of the adduct facilitates an amine heterocyclization to deliver the product **1.12** and regenerate the organocatalyst.

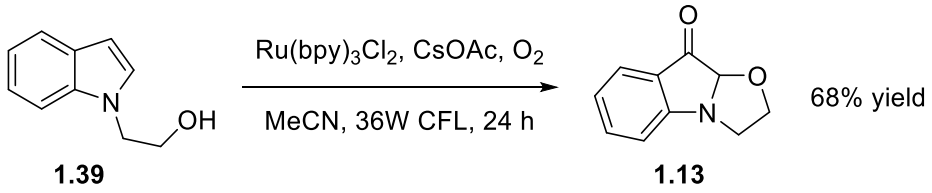


Scheme 1.9. Secondary amine organocatalyst utilized in the dearomative cycloaddition of propynal with 2-vinylindole

1.2.5 Photoredox Catalyzed Dearomative Cycloadditions of Heteroarenes

Reactions of heteroarenes as the two-carbon component of photoredox catalyzed dearomative cycloadditions are well studied and found to be initiated by a variety of means including photoactivated transition-metals, Lewis acids, electron donor-acceptor complexes, arenophiles, or generation of reactive radical intermediates.[24] Reactions of vinyl heteroarenes as the four-carbon component of a dearomative cycloaddition have yet to be explored to such an

extent. Zhang et al utilized photoactivated ruthenium catalyst to initiate intramolecular dearomative cycloaddition of indole-tethered alcohol **1.39** to afford oxazolo[3,2-α]indolone **1.13** in good yield (68%) in acetonitrile (MeCN) with light from a 36W compact fluorescent light (CFL) bulb.[40] Based upon experimental results and literature precedent, the authors propose that the photo-activated ruthenium(II) complex is used to effect a molecular oxygen induced single-electron oxidation of the indole **1.39** which undergoes cyclization via intramolecular nucleophilic attack.

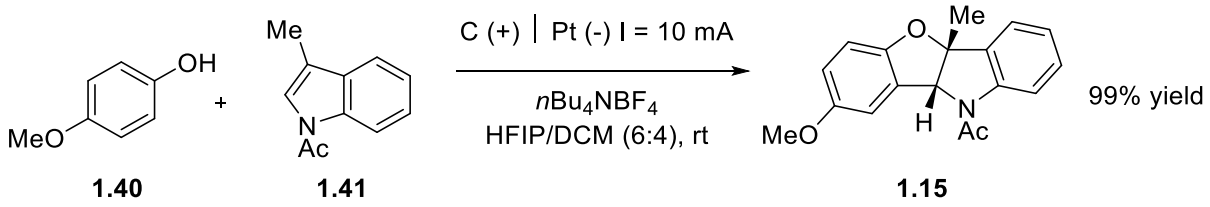


Scheme 1.10. Photoactivate ruthenium catalyst for dearomative cycloaddition to oxazolo[3,2-α]indolones

1.2.6 Electrochemical Dearomative Cycloadditions of Heteroarenes

Heteroarenes, which typically have electron-rich characteristics, are able to be anodically oxidized to the corresponding radical cation which may react by a radical coupling pathway or nucleophilic addition transformation.[25] These two reaction pathways are well studied for dearomative reactions of heteroarenes, yet reactions of vinyl heteroarenes as the four-carbon component of a dearomative cycloaddition have yet to be explored to such an extent. Liu et al demonstrated the dearomative, electrooxidative [3 + 2] annulation between phenol **1.40** and *N*-acetylindole (**1.41**) to afford benzofuroindoline **1.15** in up to 99% yield for 23 substrates in hexafluoroisopropanol (HFIP) and dichloromethane (DCM).[41] This [3 + 2] cyclization is accomplished through the single-electron-transfer oxidation of both the *p*-methoxylphenol (**1.40**)

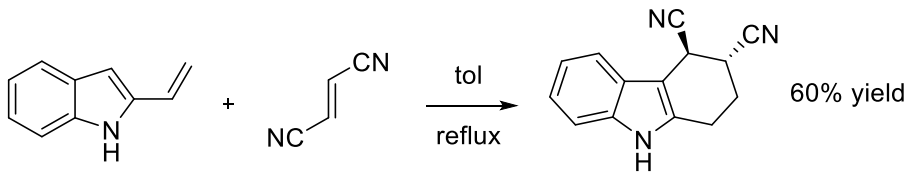
and the *N*-acetylindole (**1.41**) by the anode followed by cross-coupling of the two radical intermediates to generate the final product **1.15**.



Scheme 1.11. Electrochemical dearomative cycloaddition of phenols and *N*-acetylindoles to benzofuroindolines

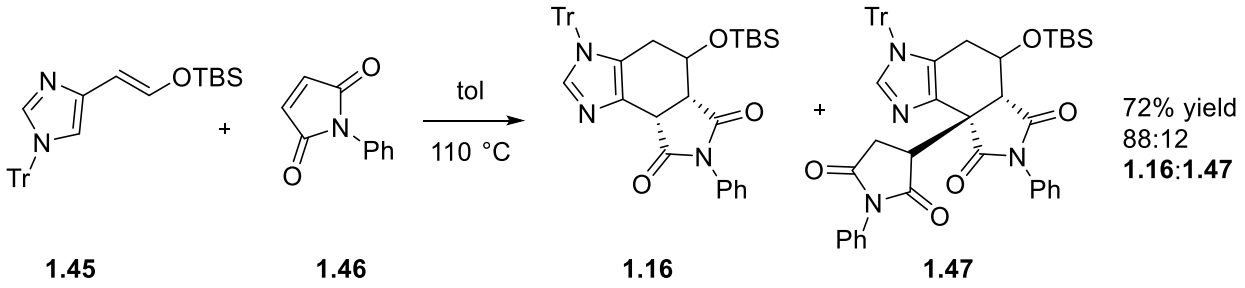
1.2.7 Thermal Dearomative Cycloadditions of Heteroarenes

Due to the lack of a catalyst or reagent to activate substrates for dearomative cycloadditions, thermal dearomative cycloadditions of vinyl heteroarenes typically require either highly reactive dienophiles or elevated temperatures to effect dearomatization. Mohamed et al effected the dearomative cycloaddition of 2-vinylindole **1.42** to carbazole derivative **1.44** with reactive dienophiles such as fumaronitrile **1.43**, dimethyl fumarate, *N*-phenylmaleimide, 1,4-naphthoquinone, and dimethyl acetylenedicarboxylate.[42] Carbazole derivative **1.44** was afforded under conditions of refluxing toluene in 60% yield. The authors do not report observing the DA adduct, nor do they explain how the isomerization product was formed.



Scheme 1.12. Thermal dearomative cycloaddition of 2-vinylindoles with highly reactive dienophiles

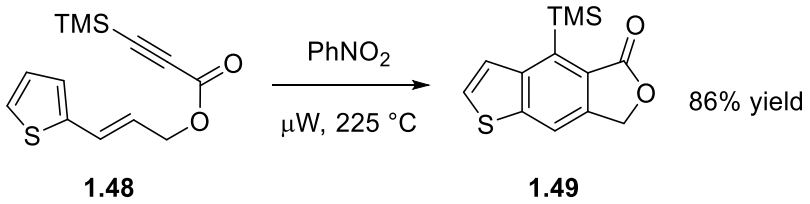
Cotterill et al also utilized a highly reactive dienophile in *N*-phenylmaleimide **1.46** to effect [4 + 2] dearomative cycloaddition with vinylimidazole **1.45** in refluxing toluene.[43] The DA adduct of the cycloaddition was observed and reported for several substrates. In most cases, adducts rapidly underwent a [1,3]-hydrogen migration to products **1.16.** A mechanism was not proposed for this migration, yet the product **1.16** was found to proceed into domino reactions affording trityl migration and even Michael addition with *N*-phenylmaleimide leading to formation of complex molecule **1.47**.



Scheme 1.13. Thermal dearomative cycloaddition of vinylimidazoles with highly reactive *N*-phenylmaleimide

Previous researchers from our lab have published dearomative cycloadditions of vinylogous heteroarenes under thermal conditions with elevated reaction temperatures via microwave heating.[44] Vinylogous furans, pyrroles, and thiophenes underwent intramolecular dearomative cycloadditions to afford either benzofurans, indoles, and benzothiophenes or the

corresponding dihydroaromatic products. Depicted in Scheme 1.14 is 2-vinylthiophene **1.48** reacting to afford benzothiophene **1.49** in 86% yield. In most reactions, temperatures of 225 °C were utilized with select cases proceeding at temperatures as low as 120 °C. Solvent selection afforded affected product selectivity with nitrobenzene increasing selectivity for fully aromatic products and dimethylformamide (DMF) increasing selectivity for dihydroaromatic products.



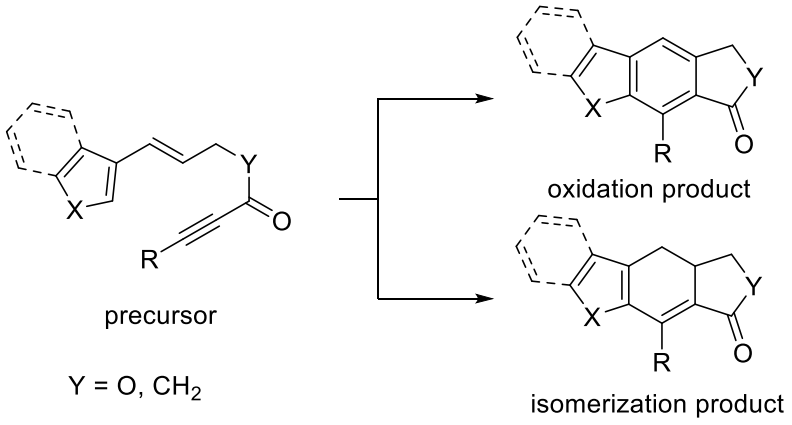
Scheme 1.14. Intramolecular, thermal dearomative cycloaddition of vinylogous furans, pyrroles, and thiophenes

1.2.8 Conclusions

Modern dearomative cycloadditions of vinyl heteroarenes have been employed through a variety of strategies to afford complex products in high yields and high stereoselectivity with efficient methods. The forcing conditions required to effect dearomatization often limit the substrate scope or cost efficiency of these reactions. Acid catalysis or base mediation strategies limit substrate functionality to that which is tolerant of these conditions. Transition-metal catalysis and organcatalysis strategies effect powerful stereochemical control that often require highly expensive catalysts and ligands to do so. Photoredox catalysis and electrochemical strategies are similarly powerful, yet literature examples for vinyl heteroarenes are currently lacking. Finally, thermal strategies often have a substrate scope limited by high temperatures or highly reactive dienophiles. Works utilizing these strategies ordinarily lack mechanistic analysis beyond proposed transition states based upon stereochemical outcomes.

1.3 Dearomative Didehydro-Diels–Alder Reaction for Vinyl Heteroarenes

The dearomative didehydro-Diels–Alder (DDDA) reaction for vinyl heteroarenes precursors affords access to both oxidation and isomerization products. Of all the dearomative cycloaddition strategies, the DDDA reaction is not limited by harsh reagents or expensive catalysts. Historically, the synthetic utility of this reaction has been limited by the low reactivity of the heteroarene precursors, requiring elevated reaction temperatures typically ≥130 °C, additives required to access oxidation products, and low afforded yields. Additionally, the mechanisms of the dearomative cycloaddition as well as the product formation mechanisms are not well understood.

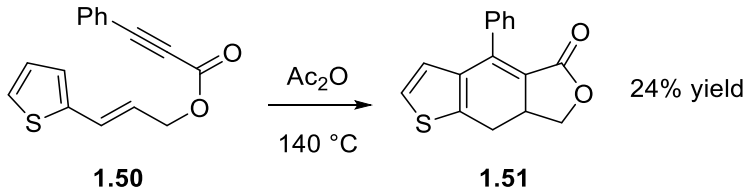


Scheme 1.15. Oxidation and isomerization products accessible via the dearomative DDDA reaction

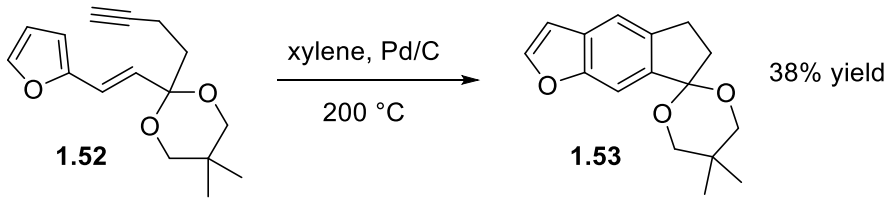
1.3.1 Dearomative Didehydro-Diels–Alder Reaction for Vinyl Heteroarenes

Klemm et al was the first to report the dearomative DDDA reaction for 2- and 3-vinylthiophenes under acidic conditions.[45] The 2-vinylthiophene **1.50** was refluxed in acetic anhydride to afford exclusively isomerization products **1.51** in relatively poor yield (24%). The

authors do not discuss the mechanisms by which the isomerization products are formed. Kanematsu et al reported dearomative DDDA reactions for 2-vinylfuran **1.52** as well as 2-vinylpyrroles.[46] Isomerization products were afforded in moderate yield (<59%) but the mechanisms by which they are formed from DA adduct is not discussed. Oxidation product **1.53** was accessed only by utilizing oxidative 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) or Pd/C additives and was afforded in low yield (38%, Scheme 1.53).

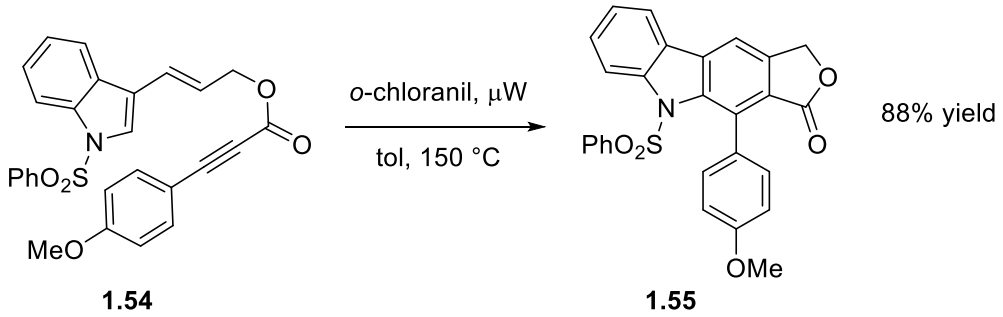


Scheme 1.16. First report of the dearomative DDDA reaction of vinyl heteroarenes



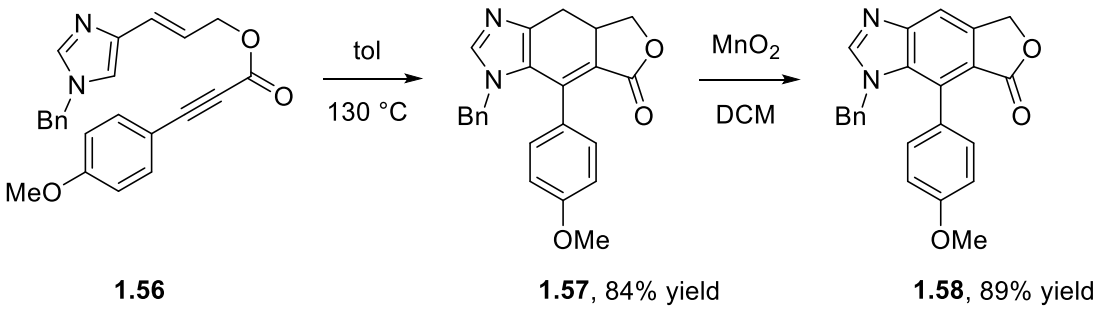
Scheme 1.17. Kanematsu's reported dearomative DDDA reaction for 2-vinylfurans and 2-vinylpyrroles

Hajbi et al effected the dearomative DDDA reaction of 3-vinylindoles **1.54** at 150 °C heated by microwave heating in toluene, protected from light and under inert atmosphere, to afford isomerization products in high yields (up to 99%). Oxidation product **1.55** was accessed only with utilization of *o*-chloranil as an oxidant in up to 88% yields.[47] Observation of DA adduct was not reported by the authors, nor was a mechanism proposed for formation of products from adduct.



Scheme 1.18. Dearomative DDDA reaction of 3-vinylindoles with improved yields up to 99%

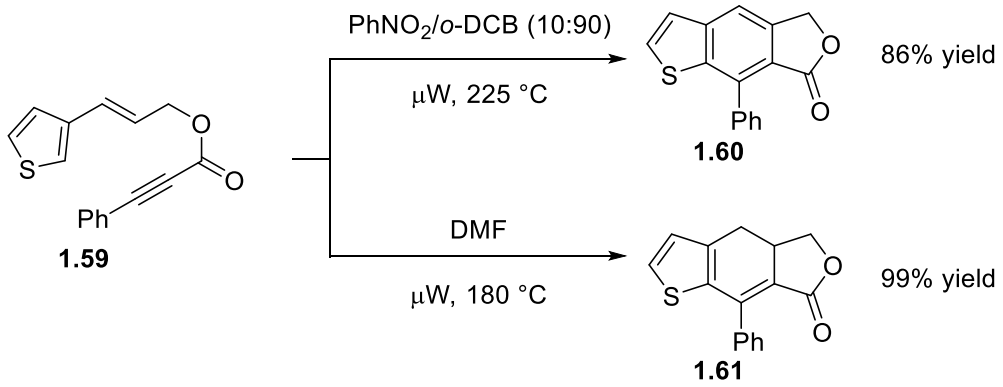
Dearomative DDDA reactions were demonstrated for 4-vinylimidazole **1.56** by Lima et al.[48] Isomerization product **1.57** was afforded by heating at 130 °C for 48 h in toluene in 84% yield. Oxidation product **1.58** was afforded upon reaction of isomerization product with oxidant manganese oxide in 89% yield. The authors do not report observation of DA adduct and do not discuss mechanisms for product formation.



Scheme 1.19. Dearomative DDDA reaction of 4-vinylimidazole precursors

As previously discussed, our research lab has published dearomative DDDA reactions of vinyl furans, pyrroles, and thiophene **1.59** which proceed under microwave heating temperatures of 225 °C with select cases proceeding at temperatures as low as 120 °C.[44] Selectivity for oxidation product **1.60** from 2-vinylthiophene **1.59** was enhanced in the presence of oxidant additive

nitrobenzene and afforded in 86% yield while selectivity for isomerization product **1.61** was enhanced by use of more polar solvents such as dimethylformamide (DMF) and afforded in 99% yield.



Scheme 1.20. Microwave assisted dearomative DDDA reaction with enhanced product selectivity

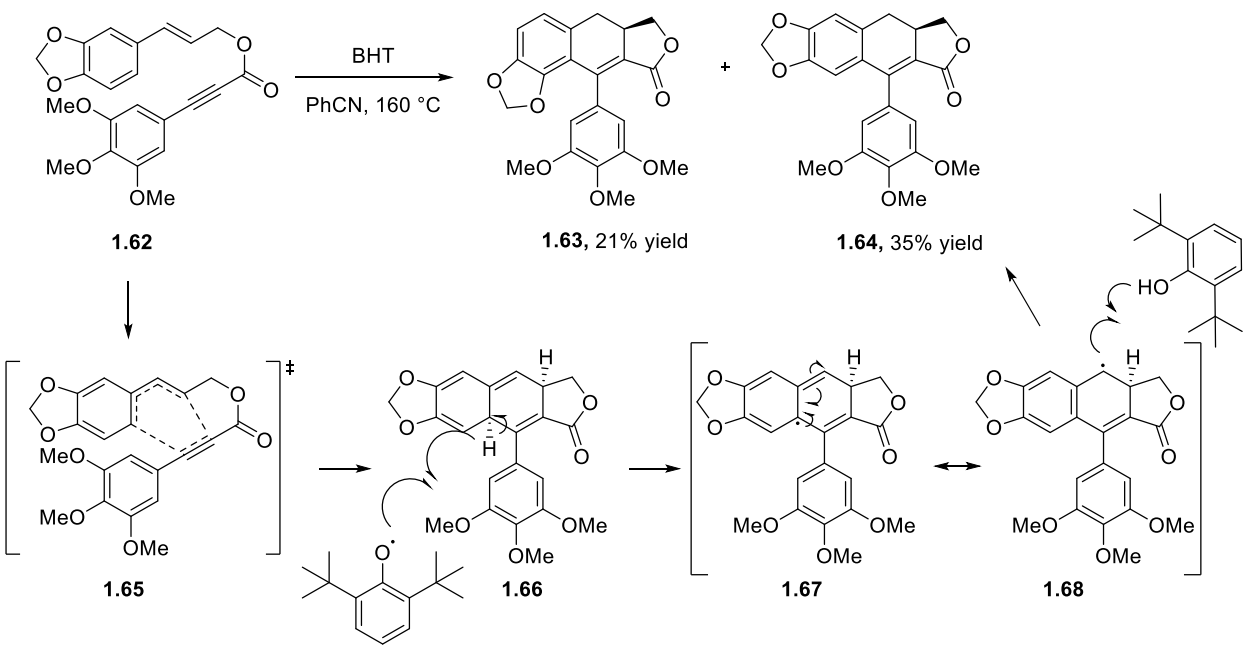
Literature examples have demonstrated use of the dearomative DDDA reaction offer a variety of heteroarenes with varied alkynyl tether compositions. Yet, overall, the utility of the reaction is often hindered by high temperatures above 130 °C, oxidizing additives required to afford oxidation product, and low yields. Furthermore, little is understood for the mechanisms of the dearomative cycloaddition and product formation steps as the DA adduct is rarely observed and has not been fully characterized.

1.3.2 Analogous Mechanistic Insight from Styryl Dearomative DDDA Reactions

There is a lack of literature on mechanistic studies of the dearomative DDDA reaction for vinyl heteroarenes, and as such, the mechanisms for the dearomative cycloaddition as well as

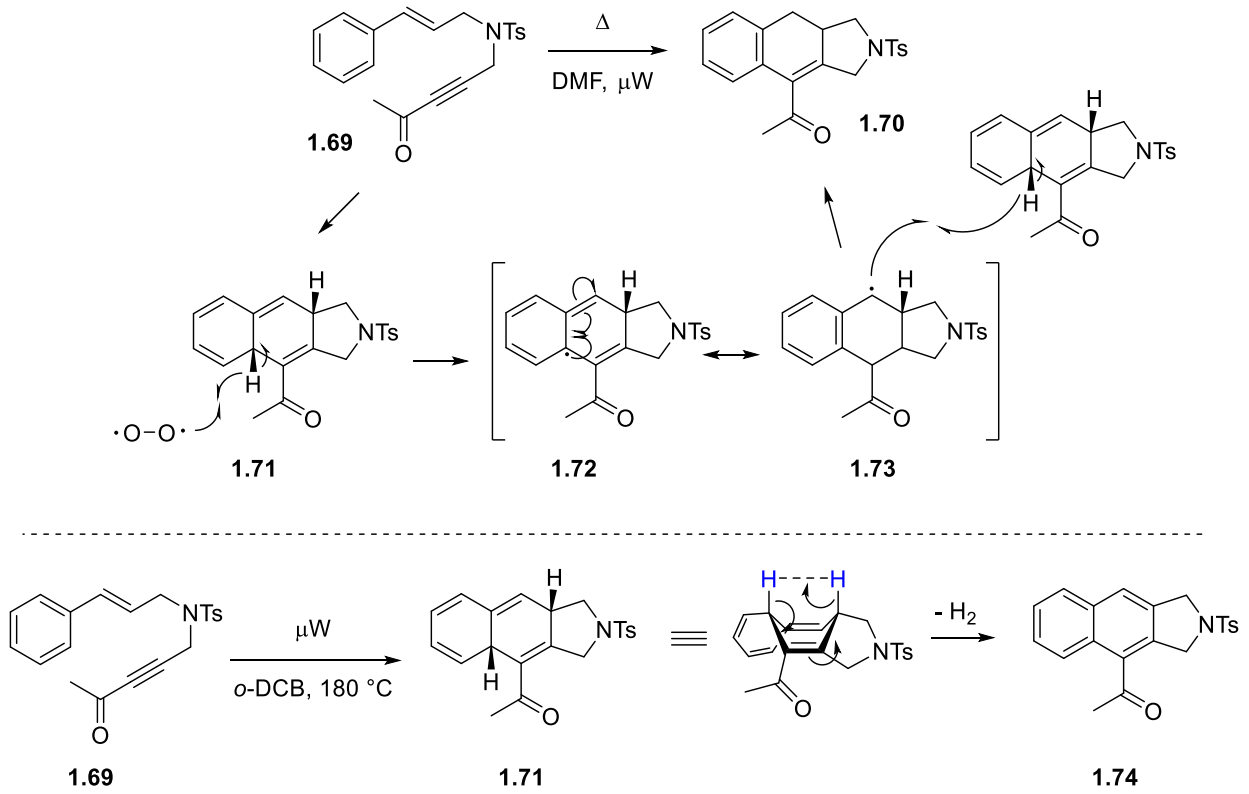
formation of oxidation and isomerization products are not well understood. The closest literature mechanistic studies are for the analogous intramolecular styryl dearomative DDDA reaction.

Andrus et al report the styryl **1.62** dearomative DDDA reaction at 160 °C for 2 h in benzonitrile solvent with 1.5 equivalents of di-t-butylhydroxytoluene (BHT) additive to afford isomerization products **1.63** and **1.64** in low yields (<56% combined).[49] DFT analysis of the dearomative cycloaddition identified an asynchronous concerted [4 + 2] Diels−Alder transition state **1.65** as the lower energy pathway in comparison to singlet-open-shell diradical pathways, and polar pathways. DFT analysis of isomerization product **1.64** formation identified the mechanism to be a BHT assisted [1,3]-formal hydrogen shift, where BHT initiates the hydrogen atom abstraction from the adduct **1.66** and subsequent addition to the newly formed radical **1.68**.



Scheme 1.21. Styryl dearomative DDDA reaction with DFT support for an asynchronous concerted [4 + 2] Diels−Alder cycloaddition

Kocsis et al from our research group also conducted intramolecular styryl **1.69** dearomative DDDA reactions to afford naphthalene (oxidation) **1.74** and dihydronapthalene (isomerization) **1.70** products under microwave heating.[50] Deuterium-labeled cross-over experiments supported isomerization product formation occurring via an intermolecular hydrogen atom abstraction and subsequent addition. Triplet oxygen initiates the reaction by hydrogen atom abstraction of the tris-allylic hydrogen in the DA adduct **1.71**. The newly formed radical **1.73** then abstracts the tris-allylic proton of another equivalent of adduct to afford the isomerization product **1.70**. Oxidation product formation **1.74** was proposed to occur by the concerted intramolecular elimination of hydrogen gas, made possible by the close proximity of the flagpole hydrogens in the boat-like conformation of the adduct **1.71**. The elimination of H_2 gas was supported by experiments that quantified the gas by analysis of the reaction headspace with gas chromatography and detection of the resonance for H_2 gas in the reaction solution by ^{1}H NMR.



Scheme 1.22. Styryl dearomative DDDA reaction afforded isomerization product via an intermolecular hydrogen atom abstraction and oxidation product via a concerted intramolecular elimination of hydrogen gas

Though these works are mechanistic analysis of the dearomative DDDA reaction, it is unclear to what extent these mechanisms are analogous to those for vinyl heteroarenes. Literature examples of the dearomative DDDA reaction for vinyl heteroarenes often afforded variable reactivity and product selectivity with changes in substrate. Further mechanistic studies are required to garner understanding of these reaction processes for vinyl heteroarenes.

1.4 Conclusions

Dearomative cycloadditions are emerging as efficient and effective strategies for accessing valuable, complex polycyclic heteroarene compounds. Yet, most strategies employ forcing conditions such as additives or catalysts to activate the aromatic π-system of the heteroarene for cycloaddition. Therefore, the substrate dependent factors that affect reactivity are often overlooked and understudied in lieu of these conditions. The thermal, intramolecular, dearomative DDDA reaction of vinyl heteroarenes exists as a potential alternative to dearomative reactions with forcing conditions, yet it is also plagued by high temperatures, low yields, and oxidants required to access fully aromatic products. These faults may be attributed to a lack of understanding for these reaction mechanisms as the DA adduct is not observed or fully characterized in literature examples. We propose that a mechanistic analysis of the dearomative DDDA reaction of vinyl heteroarenes would lead to increased synthetic utility and substrate scope for the reaction, as well as inform future dearomative processes.

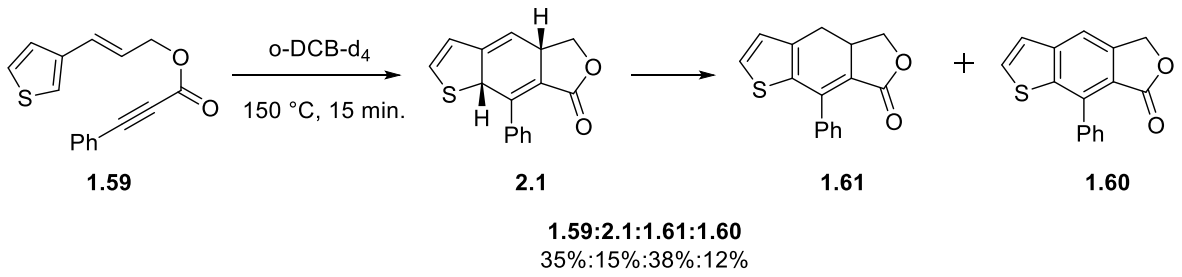
2.0 Synthesis, Isolation and Characterization of the DA Adduct

With changes in substrate affording variable reactivity and product selectivity for the dearomative DDDA reaction of vinylogous heteroarenes, we sought to investigate the mechanisms of the dearomative cycloaddition as well as product formation steps for these substrates. We proposed the DA adduct to be the intermediate between cycloaddition and formation of either oxidation or isomerization products. Isolation and characterization of this adduct provided insight into our mechanism study. Formation of products solely from the adduct was also confirmed.

This chapter is based on results presented in: Winkelbauer J. A.; Bober A. E.; Brummond K. M., Regulating Divergent Product Selectivity of the Dearomative Didehydro-Diels–Alder Reaction through Mechanistic Insight. Manuscript in preparation, submission expected 2021.

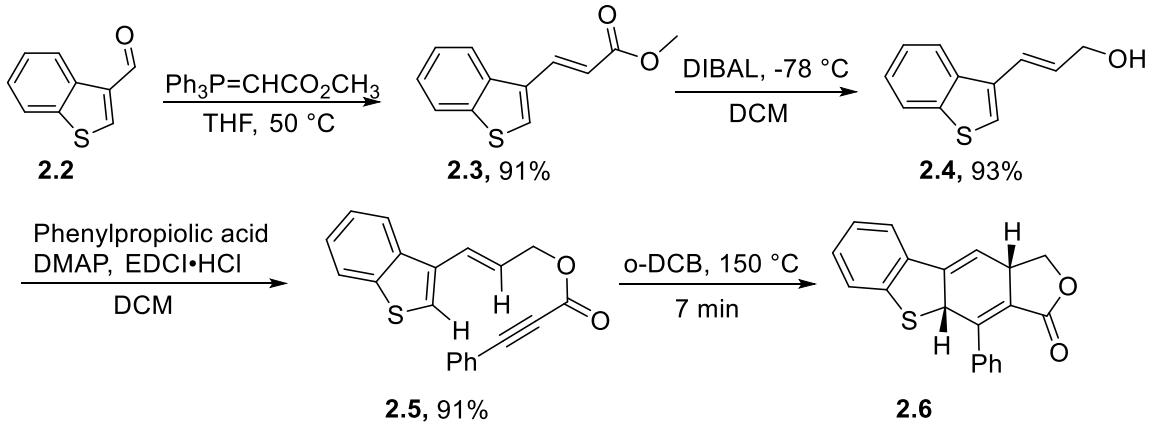
2.1 Synthesis and NMR Characterization of the DA Adduct

The proposed, and later confirmed, DA adduct was first observed in the dearomative DDDA reaction of the ester-tethered 3-thiophene precursor **1.59** when heated for 15 min at 150 °C in deuterated *o*-dichlorobenzene (*o*-DCB-d_4) which afforded a ratio of 35:15:38:12 (precursor **1.59**:adduct **2.1**:isomerization product **1.61**:oxidation product **1.60**) as observed by comparing integrative values of a crude ^{1}H NMR spectrum.



Scheme 2.1. Dearomative DDDA reaction of 1.59 to afford mixture of adduct and products

We hypothesized that a benzofused heteroarene may lead to a more persistent DA adduct due to stabilization afforded by the intact aromatic benzene. To test this hypothesis, dearomative DDDA precursor **2.5** was prepared. Horner–Wadsworth–Emmons (HWE) reaction of benzo[b]thiophene-3-carboxaldehyde **2.2** with methyl-(triphenylphosphoranylidene) acetate afforded (E)-3-(benzo[b]thiophen-3-yl)acrylate **2.3** in 91% yield. Reduction of the methyl ester **2.3** with diisobutylaluminum hydride (DIBAL) afforded allyl alcohol **2.4** in 93% yield. Alcohol **2.4** was subjected to a Steglich esterification with 4-dimethylaminopyridine (DMAP), *N*-(3-dimethylaminopropyl)-*N′*-ethylcarbodiimide hydrochloride (EDCI•HCl) and phenylpropiolic acid to afford the dearomative DDDA precursor **2.5** in 91% yield. Heating the DA precursor **2.5** for 7 min at 150 °C in *o*-DCB-d_4 afforded the DA adduct **2.6**. Trace amounts of oxidized product were also present evidenced by ^{1}H NMR of the crude material. The yield was not determined as adduct **2.6** converted to oxidized product during purification by silica-gel column chromatography.



Scheme 2.2. Synthesis of dearomative DDDA precursor **2.5** and adduct **2.6**

Structural confirmation of adduct **2.6** was accomplished with single (^{1}H and ^{13}C) and multi-dimensional (COSY, HSQC, and HMBC) NMR techniques. The most diagnostic data related to the two bis-allylic hydrogens (H_A and H_C) identified as the resonances at 5.45 and 3.60 ppm, each showing ^{5}J long-range couplings of 13.5 Hz. Durham and Studebaker have reported these long-range couplings as characteristic of 1,4-cyclohexadiene structures due to an adopted boat-like conformation with the bis-allylic hydrogens in axial positions (Figure 2.1).[51]

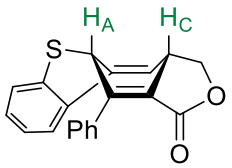
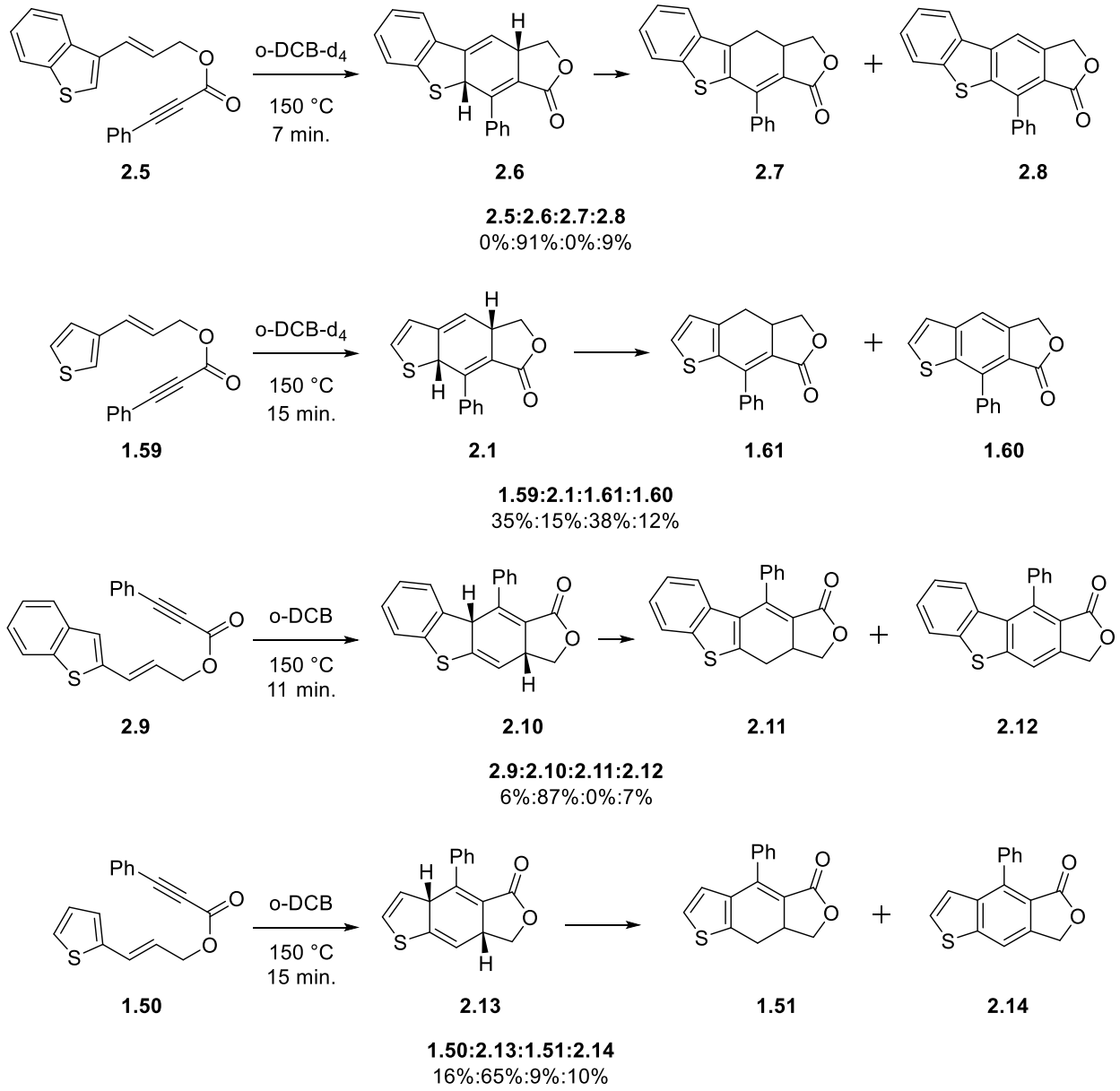


Figure 2.1. Boat-like conformation of the DA adduct **2.6** with bis-allylic hydrogens in flagpole positions

The coupling of the resonances at 5.45 and 3.60 ppm was confirmed by COSY NMR where the correlation was observed (see spectra in appendix B). HSQC NMR gave evidence that the resonances at 3.91 and 4.53 ppm are correlated to the same carbon with resonance at 68.6 ppm, and therefore, can be attributed to the methylene carbon. In HMBC NMR, the bis-allylic carbon

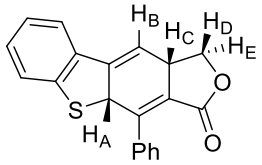
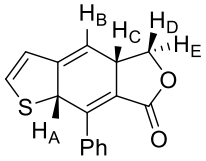
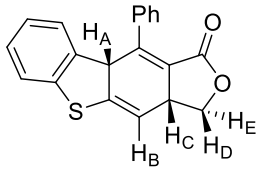
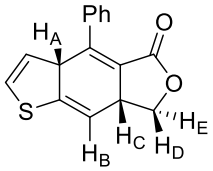
of proton H_A was observed to lack correlation to the methylene protons, indicative of the long spatial distance between these atoms.

DA precursors **1.59**, **2.9**, and **1.50** were synthesized by the same methodology and dearomative DDDA reactions were performed in order to characterize adduct for these substrates. 3-Vinylthiophene **1.59** heated for 15 min at 150 °C in *o*-DCB-d_4 afforded a ratio of 35:15:38:12 (**1.59**:**2.1**:**1.61**:**1.60**). 2-Vinylbenzothiophene **2.9** heated for 11 min at 150 °C in *o*-DCB afforded a ratio of 6:87:0:7 (**2.9**:**2.10**:**2.11**:**2.12).** 2-Vinylthiophene **1.50** heated for 15 min at 150 °C in *o*-DCB afforded a ratio of 16:65:9:10 (**1.50**:**2.13**:**1.51**:**2.14)**. These adducts were observed as mixtures with precursor, oxidation product and isomerization products, and therefore, were identified and characterized by analogy to **2.6**.



Scheme 2.3. Dearomative DDDA reactions with observation and characterization of DA adduct

Table 2.1. ^{1}H NMR characterization of the DA adducts in *o*-DCB by analogy to **2.6**

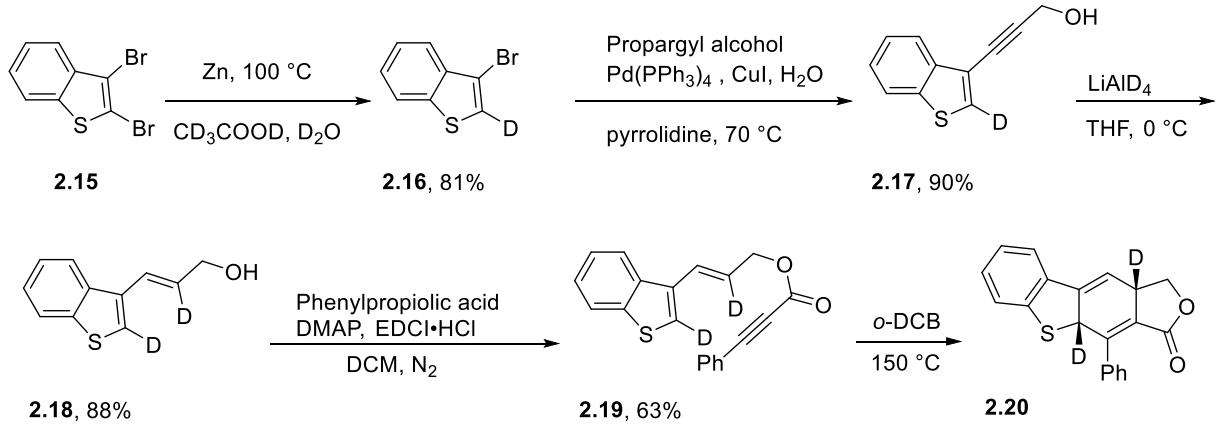
Adduct	Resonances	H_A	H_B	H_C	H_D	H_E
 **2.6**	δ (ppm)	5.46	5.93	3.64	3.91	4.53
	multiplicity	dd	dd	dddd	dd	dd
	J (Hz)	3.5, **13.5**	2.0, 3.5	2.0, 8.6, 10.4, **13.5**	8.2, 10.4	8.2, 8.6
 **2.1**	δ (ppm)	5.30	5.50	3.52	3.82	4.48
	multiplicity	dd	dd	dddd	dd	dd
	J (Hz)	3.8, **14.8**	2.1, 3.8	2.1, 8.9, 10.2, **14.8**	8.2, 10.2	8.2, 8.9
 **2.10**	δ (ppm)	4.74	5.59	3.56	3.82	4.50
	multiplicity	dd	dd	dddd	dd	dd
	J (Hz)	3.3, **13.4**	1.7, 3.4	1.7, 9.4, 9.4, **13.5**	8.6, 9.4	8.6, 9.4
 **2.13**	δ (ppm)	4.42	5.51	3.45	3.79	4.45
	multiplicity	dd	d	dddd	dd	t
	J (Hz)	3.4, **15.0**	3.4	1.9, 8.6, 9.6, **15.0**	8.7, 9.7	8.7

Thus, benzofused precursor **2.5** was successfully synthesized, and DA adduct **2.6** was attained and characterized by the heating of **2.5** for 7 min at 150 °C in *o*-DCB-d_4. Heating of precursors **1.59**, **2.9**, and **1.50** under comparable conditions resulted in mixtures of products and incomplete conversion of starting material as detailed above. Yet, it is still unclear whether this is due to higher stability of **2.6** in comparison to the other adducts or perhaps higher energy barriers for conversion of **2.6** to products.

2.2 Synthesis and Characterization of the Deuterated DA Adduct XX

We postulated that persistence of the DA adduct may be further enhanced with deuteriums at the bis-allylic positions because of the increased bond strength of C-D compared to C-H. And due to the unusual nature of observing a ^{5}J long-range coupling, we saw this as way to further confirm the structural assignment of the DA adduct **2.20** by ^{1}H NMR. To access this adduct, we first needed to prepare the dearomative DDDA precursor **2.19**.

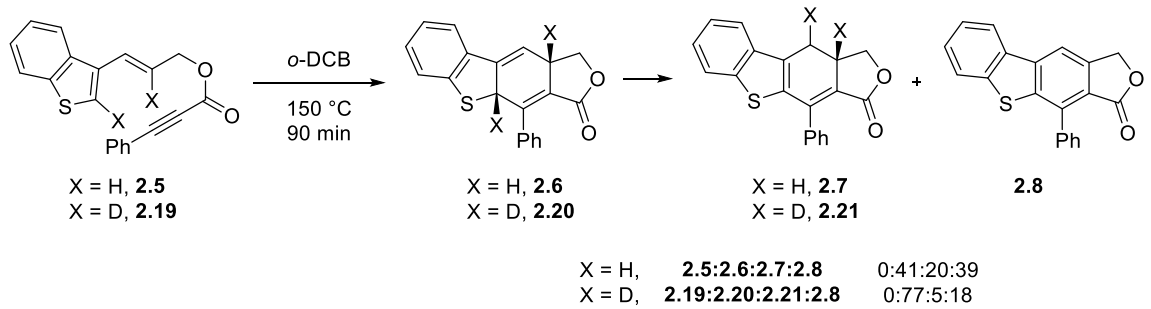
Towards the synthesis of **2.19**, dehalogenation of 2,3-dibromo-benzo[*b*]thiophene **2.15** with zinc powder and acetic acid-d_7 installed the first deuterium with generation of 3-bromobenzo[*b*]thiophene-2-d **2.16** in 81% yield. Sonogashira coupling of **2.16** with propargyl alcohol afforded the corresponding propargyl alcohol **2.17** in 90% yield. **2.17** was reduced by lithium aluminum deuteride ($LiAlD_4$) to the allyl alcohol **2.18** in 88% yield, installing the second deuterium. Allyl alcohol **2.18** was subjected to a Steglich esterification with DMAP, EDCI•HCl and phenylpropiolic acid to afford the dearomative DDDA precursor **2.19** in 63% yield. Finally, the dearomative DDDA reaction of **2.19** for 90 min at 150 °C in *o*-DCB afforded **2.20** with minimal amounts of isomerization and oxidization product present (77%:5%:18%). The yield was not determined as adduct **2.20** converted to oxidized product during purification by silica-gel column chromatography.



Scheme 2.4. Synthesis of dearomative DDDA precursor **2.19** and adduct **2.20**

As expected, the ^{1}H NMR of **2.20** lacked the corresponding bis-allylic proton resonances that appeared at 5.45 and 3.60 ppm for **2.6**. The appropriate coupling to neighboring protons was also non-existent in the ^{1}H NMR of **2.20**. This result aided in the confirmation of our NMR characterization.

Parallel dearomative DDDA reaction of **2.5** for 90 min at 150 °C in *o*-DCB afforded DA adduct **2.6** with a significant increase in the amounts of formed isomerization and oxidation products (41%:20%:39%, Scheme 2.5). Therefore, in parallel reactions, DA adduct **2.20** with deuterium at the bis-allylic positions existed as 77% of the product mixture in comparison to non-deuterated adduct **2.6** which existed as 41% of the product mixture. Deuteriums at the bis-allylic positions in the DA adduct did result in a more persistent adduct, likely due to increased bond strength of C-D compared to C-H. Therefore, the protons or deuteriums at the bis-allylic positions are likely involved in the rate determining step of product formation.



Scheme 2.5. Observed deuterium isotope effect from parallel reactions of **2.5** and **2.19**

2.3 Confirmation of Stereochemistry via the DP4 Probability Method

DFT computations were utilized in the characterization of the DA adduct to confirm the stereochemistry of the synthesized adduct. First, we predicted that the cycloaddition would proceed via a concerted transition state, and therefore, the bis-allylic protons (H_A and H_C) of the 1,4-cyclohexadiene would have cis stereochemistry rather than trans. Trans bis-allylic protons would be indicative of a possible cycloaddition via a stepwise mechanism. Second, we proposed that the isolated and characterized product had the 1,4-cyclohexadiene regiochemistry of the DA adduct, yet 1,3-cyclohexadienes afforded via isomerization of the adduct could have similar ^{1}H NMR spectra to that of was isolated.

DFT calculations with EDF2/6-31G* geometry optimizations were used to generate predictive ^{1}H and ^{13}C NMR spectra for the cis and trans 1,4-cyclohexadiene (**2.13** and **2.22**), the cis and trans 1,3-cyclohexadiene β to the ester (**2.23** and **2.24**), and the isomerization product (**2.7**). The DP4 probability method created by the Goodman group allowed us to compare these predictive ^{1}H and ^{13}C NMR spectra to the experimental spectra of our substrates and calculate the percent probability of a match.[52]

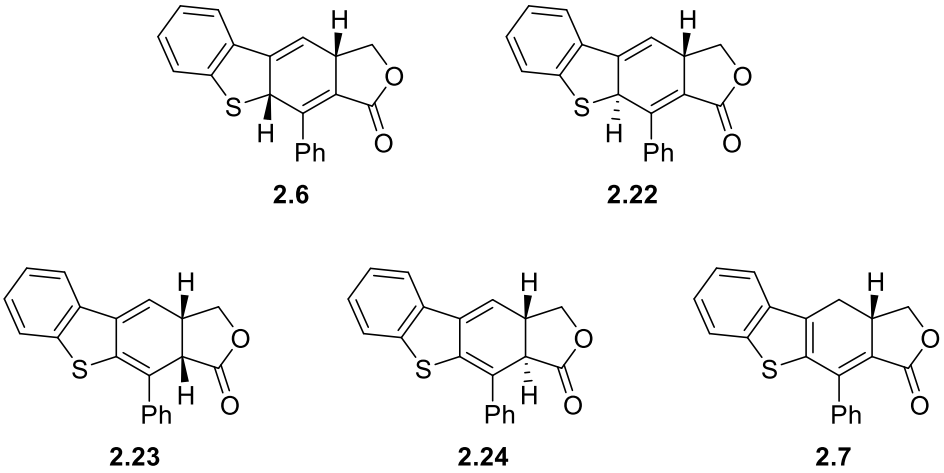


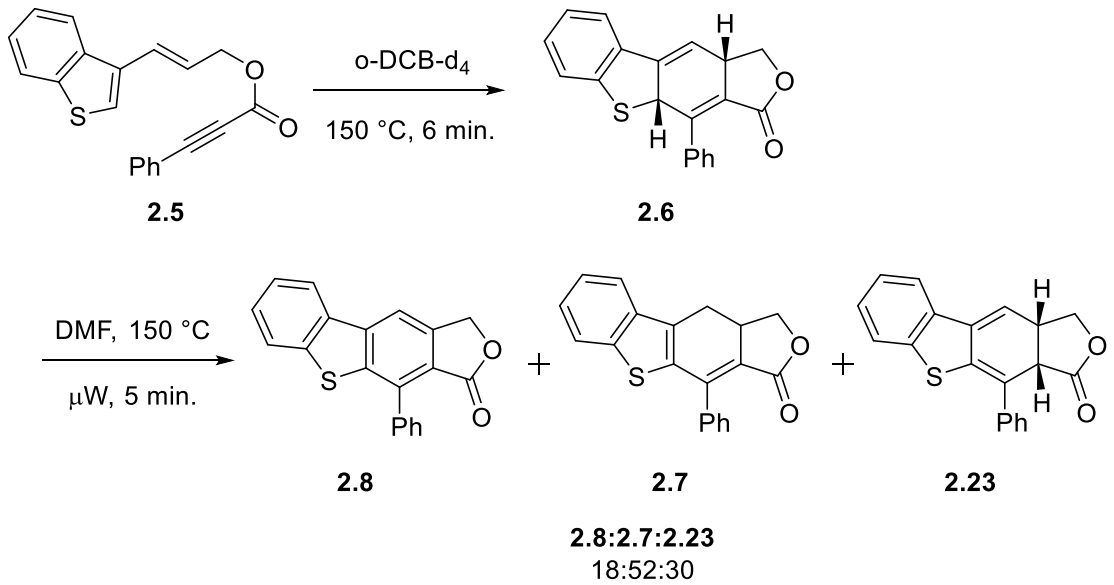
Figure 2.2. Possible regio- and steroisomers of the DA adduct analyzed by the DP4 probability method

The combined experimental ^{1}H and ^{13}C NMR's of our proposed cis-1,4-cyclohexadiene DA adduct had a 99.9% match to the Spartan predicted NMR's for **2.13**. This method also gave confirmation of the assignment for two isomerization products from the adduct, **2.23** and **2.7**, whose isolation and characterization are described in section 2.4.2.

2.4 Confirmation of the DA Adduct as the Common Intermediate to Formation of Oxidation Product, Isomerization Product, and Cis-Diene

With isolated DA adduct in hand, we proposed that the adduct was the common intermediate from which oxidation and isomerization products were formed and not just a newly characterized byproduct. To test our hypothesis, isolated DA adduct would be subjected to dearomative DDDA conditions in order to observe if oxidation and isomerization products would be generated from the adduct. **2.5** was heated for 6 min at 150 °C in *o*-DCB to generate **2.6** with

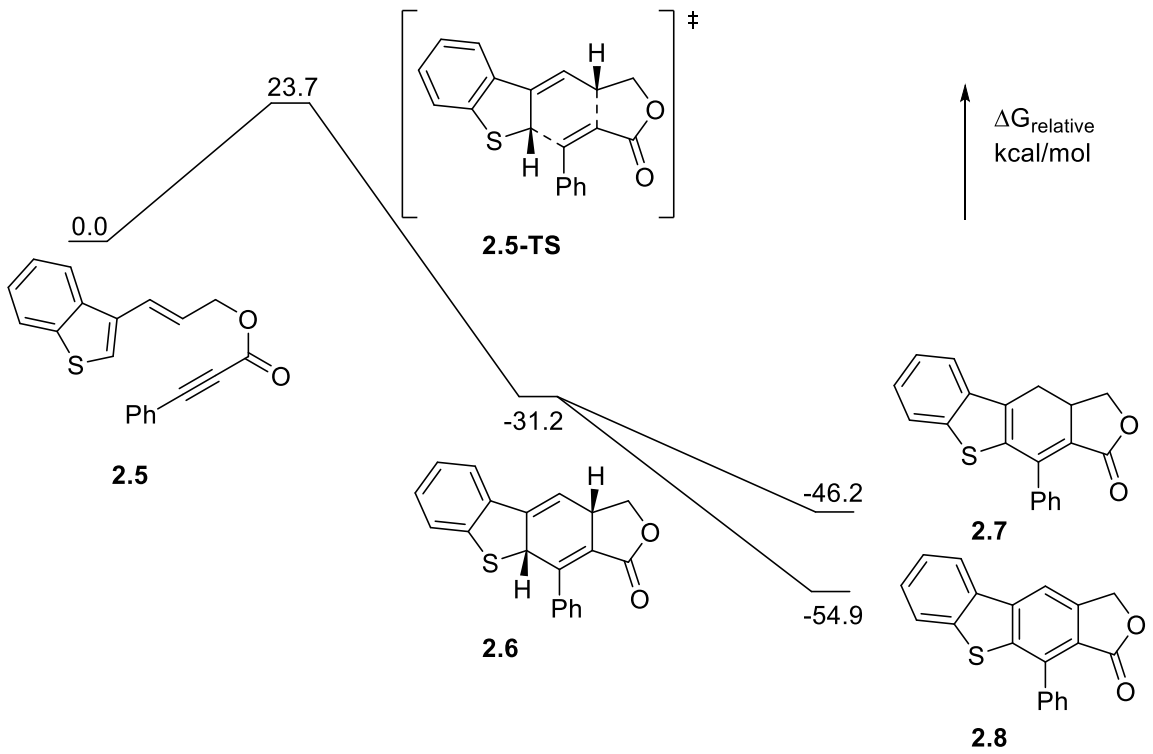
trace formation of **2.8**. The *o*-DCB solvent was removed by high-vacuum, and the adduct was dissolved in DMF before heated for 5 min at 150 °C in the microwave reactor. This reaction of isolated adduct resulted in the formation of **2.8**, **2.7**, and **2.23** in a ratio of 18:52:30 respectively (see ^{1}H NMR in experimental section). Therefore, the oxidation product, isomerization product, and the cis-diene were all found to be generated directly from isolated DA adduct rather than precursor.



Scheme 2.6. Formation of oxidation product, isomerization product, and 1,3-cyclohexadiene product from the DA adduct

To better understand the product ratios, we investigated the ground state energies for **2.5**, **2.6**, **2.8**, and **2.7** and analyzed the dearomative cycloaddition energy of activation. These calculations were performed by our collaborator Elena Kusevska from the Peng Liu research group. DFT calculations were performed at the M06/6-311+G(d,p)/SMD(DMF)//B3LYP/6-31G(d) level of theory. Results showed a relatively low Gibbs free energy of activation of 23.7

kcal/mol for the dearomative DA cycloaddition step with an exergonic formation of adduct at -31.2 kcal/mol relative to precursor. These ground state energies reveal a thermodynamic driving force towards adduct. Formation of oxidation product (-54.9 kcal/mol) and isomerization product (-46.2 kcal/mol) is also exergonic relative to precursor and suggests that product formation is irreversible.

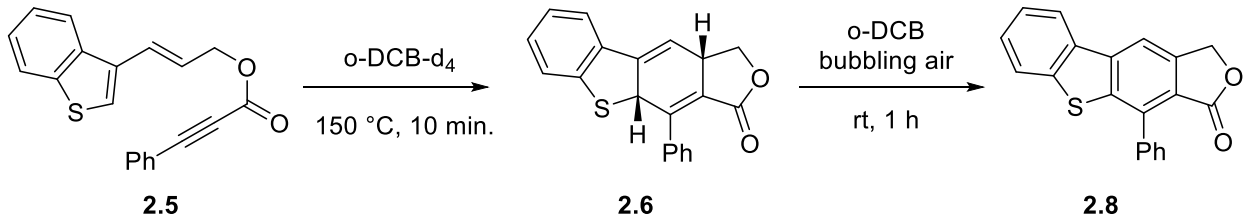


Scheme 2.7. DFT energy diagram for the dearomative DDDA reaction of **2.5** at the M06/6-311+G(d,p)/SMD(DMF)//B3LYP/6-31G(d) level of theory

2.4.1 No Evidence of Oxidation Product Formation from Isomerization Product

We propose that oxidation product forms directly from the DA adduct and is not a product from oxidation of the isomerization product. To test this hypothesis, we sought to effect the

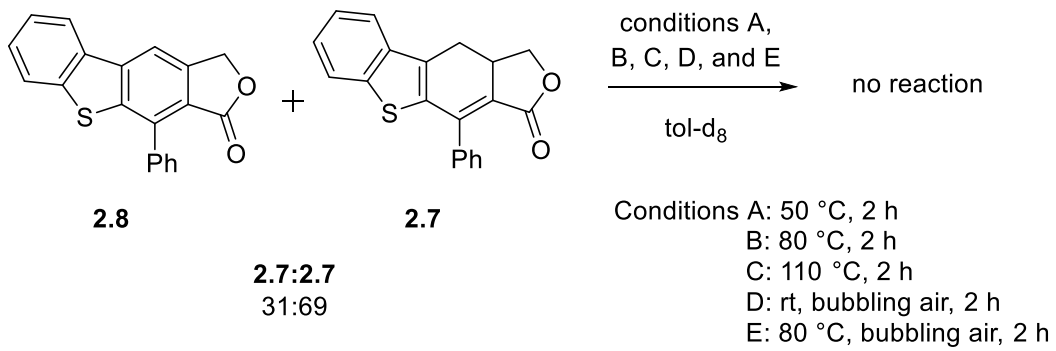
transformation of **2.6** to **2.8** with no formation of **2.7**. Additionally, we sought to subject **2.7** to those same reaction conditions in order to observe if there was any transformation of **2.7** to **2.8**. **2.5** was heated for 10 min at 150 °C in *o*-DCB to afford **2.6** with trace formation of **2.8**. The solution of **2.6** was allowed to cool to room temperature. Then, air was bubbled through the solution over the course of an hour affording **2.8** with trace amounts of **2.6** remaining (see ^{1}H NMR in experimental section). Thus, oxidation product forms readily from DA adduct at room temperature with an abundance of exposure to air and no evidence of isomerization product formation.



Scheme 2.8. Formation of oxidation product **2.8** from DA adduct **2.6** at rt with bubbling air

Additionally, a mixture of oxidation and isomerization products were subjected to conditions of bubbling air and heat in order to observe any transformation of isomerization product into oxidation product. Toluene-d_8 was chosen as a non-polar solvent that afforded trends of increased selectivity for oxidation product formation in dearomative DDDA reactions. A 31:69 mixture of **2.8**:**2.7** was dissolved in toluene-d_8 and subjected to heating via an oil bath at 50, 80 and 110 °C for 2 h increments. There was no observed change in the product ratios after any of the 2h increments (see ^{1}H NMR in experimental section). The solution was then subjected to bubbling air at room temperature for 2h, followed by bubbling air at 80 °C for 2h. There was also no observed change in the product ratios after either of the 2h increments with bubbling air. Therefore,

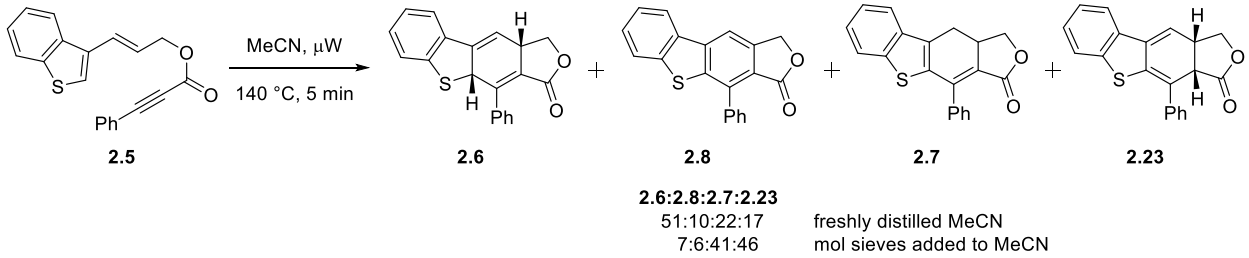
we propose that the isomerization product is a stable product that does not readily oxidize into oxidation product, but rather, oxidation is formed directly from the DA adduct.



Scheme 2.9. No conversion of isomerization product **2.7** to oxidation product **2.8** under thermal conditions with bubbling air

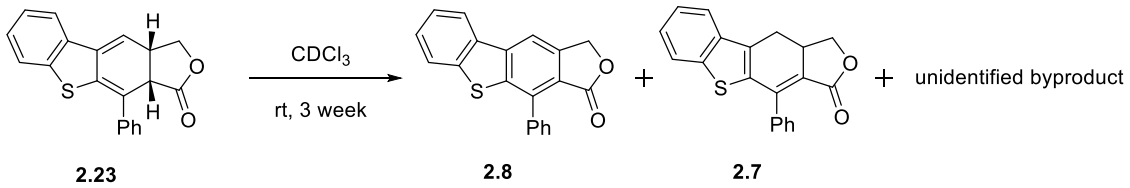
2.4.2 Cis-Diene as a Rarely Observed Byproduct that Converts to Oxidation and Isomerization Products

The cis-diene **2.23** is a byproduct of the dearomative DDDA reaction only found as a mixture with other products when polar solvents such as dimethylformamide or acetonitrile were used. Formation of cis-diene was observed when **2.5** was reacted for 5 min at 140 °C in freshly distilled acetonitrile using microwave heating to afford **2.6**:**2.8**:**2.7**:**2.23** in a ratio of 51:10:22:17 respectively. Repeating the reaction but with distilled acetonitrile solvent mixed with type 4Å mol sieves prior to the reaction afforded **2.6**:**2.8**:**2.7**:**2.23** in a ratio of 7:6:41:46. This enhanced selectivity for cis-diene and isomerization product in the presence of mol sieves suggests that the mol sieves are involved in the isomerization of the adduct to these products.



Scheme 2.10. Formation of cis-diene byproduct in acetonitrile with enhanced selectivity in the presence of mole sieves

Unlike the DA adduct, oxidation product, and isomerization product which have an equivalent R_f and are not separable by column chromatography, the cis-diene has a higher R_f and was isolated from the other products. Isolated cis-diene **2.23** dissolved in chloroform-d_1 at room temperature for 3 weeks afforded a mixture with a ratio of 25:34:29:12 (**2.23**:**2.8**:**2.7**:unidentified byproduct). Therefore, the cis-diene is considered an unstable byproduct of the dearomative DDDA reaction that converts to other products under the reaction conditions. Structural confirmation of the cis-diene was accomplished with single (^{1}H and ^{13}C) and multi-dimensional (COSY, HSQC, HMBC) NMR techniques as well as comparison to DFT predictive NMR via the DP4 probability method.



Scheme 2.11. Transformation of cis-diene into oxidation product, isomerization product, and unidentified byproduct

The resonances for the allylic protons observed at 3.75 and 3.85 ppm were confirmed by COSY NMR to be correlated to each other (see spectra in appendix B). HSQC NMR gave evidence

that the resonances at 4.63 and 4.54 ppm are correlated to the same carbon with resonance at 72.4 ppm, and therefore, can be attributed to the methylene carbon. In HMBC NMR, the resonance for the allylic proton α to the carbonyl is correlated to the carbonyl carbon, indicative of the short spatial distance between these atoms.

2.5 Conclusions

We established the DA adduct as the product of the dearomative cycloaddition step of the dearomative DDDA reaction and the pivotal intermediate on the reaction pathway to oxidation and isomerization product. This was accomplished by the synthesis and isolation of DA adduct **2.6** with structural confirmation by single and multidimensional NMR analysis, comparison to DFT predictive NMR through the DP4 probability method, and comparison to the synthesized adduct **2.20** with deuterium incorporation at the bis-allylic positions of the 1,4-cyclohexadiene. The DA adducts of precursors **1.59**, **2.9**, and **1.50** were synthesized and characterized by analogy, as the adducts were observed in mixtures of products. The oxidation product, isomerization product, and rarely observed cis-diene byproduct were established to be formed directly from DA adduct with no evidence for interconversion of isomerization product to oxidation product. This mechanistic understanding of the dearomative DDDA reaction is foundational to our efforts to enhance product selectivity and identify factors that control the reactivity of our substrates.

2.6 Experimental

2.6.1 General Methods

Unless otherwise indicated, all reactions were performed in flame-dried glassware under an air atmosphere and stirred with Teflon-coated magnetic stir bars. All commercially available compounds were purchased and used as received unless otherwise specified. Tetrahydrofuran (THF), diethyl ether (Et_2O), and dichloromethane (DCM) were purified by passing through alumina using a Sol-Tek ST-002 solvent purification system. Deuterated chloroform ($CDCl_3$) was dried over 4Å molecular sieves. Nitrogen gas was purchased from Matheson Tri Gas. Conventional heating was used for reactions that were monitored by ^{1}H NMR or performed open to the air. All microwave-mediated reactions were carried out using a Biotage Initiator Exp or Anton-Paar Monowave 300 microwave synthesizer. Purification of the compounds by flash column chromatography was performed using silica gel (40-63 μm particle size, 60 Å pore size). TLC analyses were performed on silica gel F_{254} glass plates (250 μm thickness). ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker Avance 300, 400, or 500 MHz spectrometers. Spectra were referenced to residual chloroform (7.26 ppm, ^{1}H; 77.16 ppm, ^{13}C) or *o*-dichlorobenzene (6.93 ppm, ^{1}H; 130.04 ^{13}C) unless otherwise specified. Chemical shifts are reported in ppm, multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), m (multiplet), and bs (broad singlet). Coupling constants, *J*, are reported in hertz (Hz). All NMR spectra were obtained at room temperature. IR spectra were obtained using a Nicolet Avatar E.S.P. 360 FT-IR. EI mass spectroscopy was performed on a Waters Micromass GCT high resolution mass spectrometer, while ES mass spectroscopy was performed on a Waters Q-TOF Ultima API, Micromass UK Limited high-resolution mass spectrometer.

2.6.2 Dearomative DDDA Reaction of 1.59 in *o*-DCB

Rxn 1. An oven-dried NMR tube was charged with dearomative DDDA precursor **1.59** (8 mg, 0.03 mmol) dissolved in *o*-DCB-d_4 (0.5 mL, 0.6 M) under an atmosphere of air. The NMR tube was sealed with a polypropylene cap and lowered into an oil bath preheated at 150 °C and heated for 15 min. The NMR tube was removed from the oil bath, rinsed with hexanes, and wiped with a ChemWipe before ^{1}H NMR was obtained. A 35:15:38:12 ratio of **1.59**:**2.1**:**1.61**:**1.60** was obtained. Ratios were determined by comparing the ^{1}H NMR resonances at 6.03 ppm (1H) for **1.59**, 5.50 ppm (1H) for **2.1**, 5.14 ppm (2H) for **1.60**, and 2.39 ppm (1H) for **1.61.**

2.6.3 Synthesis of the Dearomative DDDA Precursors

2.6.3.1 General Procedure A: Conversion of Carboxaldehyde to α,β-Unsaturated Ester

Prepared in the manner of Travas-Sejdic, et al.[53] A flame-dried, 2-necked, round-bottomed flask equipped with stir bar, condenser, septum, and nitrogen inlet needle, was charged with carboxaldehyde (1.0 equiv), THF (0.17 M), and methyl(triphenylphosphoranylidene) acetate (1.5 equiv), added in single portions by briefly removing the septum. The flask was placed in an oil bath and warmed to 60 °C. After 24 h, the reaction was judged complete evidenced by the disappearance of starting material by TLC. The stir bar was removed and the mixture was concentrated by rotary evaporation. The residue was purified by silica gel flash column chromatography.

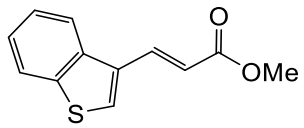
2.6.3.2 General Procedure B: Conversion of α,β-Unsaturated Ester to Allylic Alcohol

Prepared in the manner of Brummond, et al.[44] A flame-dried, single-necked, round-bottomed flask equipped with stir bar, septum, and nitrogen inlet needle was charged with the α,β-unsaturated ester (1.0 equiv) dissolved in dichloromethane (0.020 M) via syringe. The flask was placed in a dry ice/acetone bath (-78 °C). After 5 min, diisobutylaluminium hydride (DIBAL, 1.0 M in toluene, 3.5 equiv) was added dropwise via syringe, and the reaction mixture was maintained at -78 °C. After 1 h, the reaction was judged complete evidenced by the disappearance of starting material by TLC. Aqueous sodium potassium tartrate (1.2 M) was added and the mixture was vigorously stirred at rt for ca. 16 h. The solution was transferred to a separatory funnel, and the flask was rinsed with dichloromethane and transferred to the separatory funnel. The organic layer was separated, and the aqueous layer was extracted with dichloromethane (3x). The combined organic phase was washed with brine (1x), dried over magnesium sulfate, gravity filtered, and concentrated using rotary evaporation. The residue was purified by silica gel flash column chromatography.

2.6.3.3 General Procedure C: Conversion of Allylic Alcohol to Alkynoate

Prepared in the manner of Brummond, et al.[44] A flame-dried, single-necked, round-bottomed flask equipped with stir bar, septum, and nitrogen inlet, was charged with *N*,*N*-dimethylpyridin-4-amine (0.15 equiv) and phenylpropiolic acid (1.1 equiv) by briefly removing the septum. Allylic alcohol (1.0 equiv) was dissolved in dichloromethane (0.080 M) and added via syringe. *N*-(3-dimethylaminopropyl)-*N′*-ethylcarbodiimide hydrochloride (1.5 equiv) was added in one portion by briefly removing the septum and the resulting solution was maintained at rt. After 3 h, the reaction was judged complete evidenced by the disappearance of starting material by TLC.

The reaction mixture was transferred to a separatory funnel, and the flask was rinsed with dichloromethane and transferred to the separatory funnel. The solution was washed with deionized water and the aqueous layer was extracted with dichloromethane (3x). The combined organic layers were washed with brine (1x), dried over magnesium sulfate, gravity filtered, and concentrated using rotary evaporation. The residue was purified by silica gel flash column chromatography.



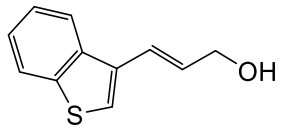
Methyl (*E*)-3-(benzo[*b*]thiophen-3-yl)acrylate (2.3). Follows General Procedure A. Benzo[*b*]thiophene-3-carboxaldehyde (1.0 g, 6.2 mmol), THF (36 mL), and methyl(triphenylphosphoranylidene) acetate (3.1 g, 9.3 mmol). The crude material was purified by flash column chromatography (20% EtOAc/Hex) to yield the title compound as a yellow solid (1.2 g, 91%). Compound **2.3** was previously prepared by Tay, et al.[54] Characterization data corresponds to the literature.

Data **2.3** previously characterized

^{1}H NMR (300 MHz, $CDCl_3$)

8.01 (d, J = 8.6 Hz, 1H), 7.97 (d, J = 16.4 Hz, 1H), 7.87 (d, J = 8.5 Hz, 1H), 7.75 (s, 1H), 7.46 (t, J = 7.0 Hz, 2H), 6.54 (d, J = 16.0 Hz, 1H) 3.84 (s, 3H) ppm. Water impurity at 1.56 ppm.

TLC R_f = 0.31 (10% EtOAc/Hex) [silica gel, UV]



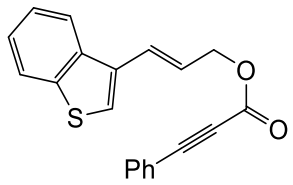
(*E*)-3-(benzo[*b*]thiophen-3-yl)prop-2-en-1-ol (2.4). Follows General Procedure B. **2.3** (1.2 g, 5.5 mmol), DCM (28 mL), DIBAL (19 mL, 19 mmol), aq sodium potassium tartrate solution (1.2 M, 30 mL). The crude material was purified by flash column chromatography (40% EtOAc/Hex) to yield the title compound as a light-yellow liquid (970 mg, 93%). Compound **2.4** was previously prepared by Wang, et al.[55] Characterization data corresponds to the literature.

Data **2.4** previously characterized

^{1}H NMR (300 MHz, $CDCl_3$)

7.91 (d, J = 8.0 Hz, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.44-7.35 (m , 3H), 6.91 (d, J = 16.0 Hz, 1H), 6.45 (dt, J = 5.7, 15.9 Hz, 1H), 4.37 (d, J = 5.2 Hz, 2H), 2.25 (s, 1H) ppm. DCM impurity at 5.30 ppm. EtOAC impurity at 2.05 ppm.

TLC R_f = 0.30 (40% EtOAc/Hex) [silica gel, UV]



(*E*)-3-(benzo[*b*]thiophen-3-yl)allyl 3-phenylpropiolate (2.5). Follows general procedure C: DMAP (13 mg, 0.10 mmol), **2.4** (100 mg, 0.53 mmol), phenylpropiolic acid (85 mg, 0.58 mmol), dichloromethane (10 mL), N-(3-dimethylaminopropyl)-N′-ethylcarbodiimide hydrochloride (150 mg, 0.79 mmol). The residue was purified by flash column chromatography (30% EtOAc/Hex) to yield the title compound as a yellow liquid (150 mg, 91%).

Data **2.5**

^{1}H NMR (400 MHz, $CDCl_3$)

7.93 (d, *J* = 8.1 Hz, 1H), 7.87 (d, *J* = 8.1, 1H), 7.61 (dd, *J* = 7.0, 1.5 Hz, 2H), 7.50 (s, 1H), 7.48-7.35 (m, 5H), 7.00 (d, *J* = 15.9 Hz, 1H), 6.42 (dt, *J* = 15.8, 6.7 Hz, 1H), 5.0 (d, *J* = 6.4, 2H) ppm. Water impurity at 1.58 ppm (<0.4%). Grease impurity at 0.10 ppm (<0.1%).

^{13}C NMR (100 MHz, $CDCl_3$)

153.9, 140.5, 137.5, 133.1 (2C), 132.8, 130.8, 128.7 (2C), 127.7, 124.7, 124.5, 123.8, 123.6, 123.0, 122.0, 119.6, 86.8, 80.6, 66.8 ppm

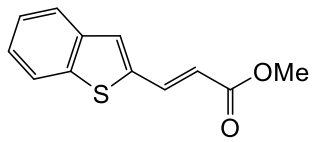
IR (thin film)

3057, 2220, 1709, 1490, 1425, 1379, 1285, 1169, 961 cm^{-1}

HRMS (FTMS + p ESI)

$[M + H]^+$ calcd for $C_{20}H_{15}O_2S$: 319.07928, found 319.07969

TLC R_f = 0.65 (40% EtOAc/Hex) [silica gel, UV]



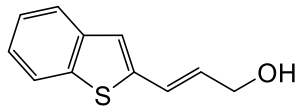
Methyl (*E*)-3-(benzo[*b*]thiophen-2-yl)acrylate (2.25). Follows General Procedure A. Benzo[*b*]thiophene-2-carboxaldehyde (550 mg, 3.4 mmol), THF (20 mL), and methyl(triphenylphosphoranylidene) acetate (1.7 g, 5.1 mmol). The material was purified by flash column chromatography (20% EtOAc/Hex) to yield the title compound as a yellow solid (720 mg, 97%). Compound **2.25** was previously prepared by Werner, et al.[56] Characterization data corresponds to the literature.

Data **2.25** previously characterized

^{1}H NMR (400 MHz, $CDCl_3$)

7.88 (d, J = 15.8 Hz, 1H), 7.81-7.73 (m, 2H), 7.45 (s, 1H), 7.40-7.32 (m, 2H), 6.30 (d, J = 15.7 Hz, 1H), 3.82 (s, 3H) ppm

TLC R_f = 0.29 (10% EtOAc/Hex) [silica gel, UV]



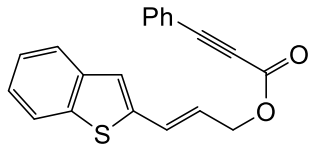
(*E*)-3-(benzo[*b*]thiophen-2-yl)prop-2-en-1-ol (2.26). Follows General Procedure B. **2.25** (710 mg, 3.3 mmol), DCM (30 mL), DIBAL (11 mL, 11 mmol), aq sodium potassium tartrate solution (1.2 M, 40 mL). The material was purified by flash column chromatography (40% EtOAc/Hex) to yield the title compound as a yellow solid (580 mg, 94%). Compound **2.26** was previously prepared by Shen, et al.[57] Characterization data corresponds to the literature.

Data **2.26** previously characterized

^{1}H NMR (400 MHz, $CDCl_3$)

7.78-7.65 (m, 2H), 7.34-7.27 (m, 2H), 7.14 (s, 1H), 6.85 (d, J = 15.7 Hz, 1H), 6.28 (dt, J = 15.6, 5.5 Hz, 1H), 4.34 (d, J = 5.5 Hz, 2H), 1.74 (s, 1H) ppm. EtOAc impurity at 2.05 ppm. Water impurity at 1.56 ppm.

TLC R_f = 0.30 (40% EtOAc/Hex) [silica gel, UV]



(*E*)-3-(benzo[*b*]thiophen-2-yl)allyl 3-phenylpropiolate (2.9). Follows General Procedure C: DMAP (39 mg, 0.32 mmol), **2.22** (300 mg, 1.6 mmol), phenylpropiolic acid (260 mg, 1.8 mmol), dichloromethane (24 mL), N-(3-dimethylaminopropyl)-N′-ethylcarbodiimide hydrochloride (460 mg, 2.4 mmol). The material was purified by flash column chromatography (30% EtOAc/Hex) to yield the title compound as a white solid (400 mg, 79%).

Data **2.9**

^{1}H NMR (400 MHz, $CDCl_3$)

7.79-7.68 (m, 2H), 7.61 (dd, J = 8.5, 1.6 Hz, 2H), 7.45 (t, J = 7.4 Hz, 1H), 7.38 (t, J = 7.9 Hz, 2H), 7.35-7.29 (m, 2H), 7.22 (s, 1H), 6.95 (d, J = 15.7 Hz, 1H), 6.24 (dt, J = 6.5, 15.6 Hz, 1H), 4.9 (dd, J = 6.5, 1.0 Hz, 2H) ppm. EtOAc impurity at 2.05 ppm (<0.4%). Water impurity at 1.56 ppm (<0.7%). Grease impurity at 1.26 ppm (<2.6%).

^{13}C NMR (100 MHz, $CDCl_3$)

153.9, 141.2, 140.0, 139.3, 133.2 (2C), 130.9, 128.9, 128.7 (2C), 125.2, 124.7, 124.3 (2C), 123.8, 122.4, 119.6, 87.0, 80.5, 66.0 ppm

IR (thin film)

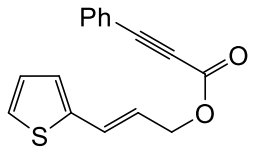
3405, 3063, 2947, 2221, 1696, 1643, 1488, 1444, 1374, 1284, 1171, 1097, 956, 728 cm^{-1}

HRMS (FTMS + p ESI)

$[M + H]^+$ calcd for $C_{20}H_{15}O_2S$: 319.0787, found 319.0798

TLC R_f = 0.66 (40% EtOAc/Hex) [silica gel, UV]

MP 107.0 – 109.3 °C



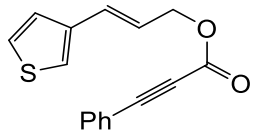
(*E*)-3-(thiophen-2-yl)allyl 3-phenylpropiolate (1.50). Prepared as described by Brummond, et al.[44] Follows General Procedure C: DMAP (97 mg, 0.79 mmol), (E)-3-(thiophen-2-yl)prop-2-en-1-ol (555 mg, 3.96 mmol), phenylpropiolic acid (636 mg, 4.35 mmol), dichloromethane (66 mL), N-(3-dimethylaminopropyl)-N′-ethylcarbodiimide hydrochloride (1.14 g, 5.94 mmol). The material was purified by flash column chromatography (30% EtOAc/Hex) to yield the title compound as a white solid (798 mg, 75%). Compound **1.50** was previously prepared by Brummond, et al.[44] Characterization data corresponds to the literature.

Data **1.50** previously characterized

^{1}H NMR (400 MHz, $CDCl_3$)

7.60 (d, *J* = 7.1 Hz, 2H), 7.46 (tt, *J* = 6.7, 1.4 Hz, 1H), 7.38 (tt, *J* = 6.8, 1.1 Hz, 2H), 7.21 (d, *J* = 4.9 Hz, 1H), 7.02 (d, *J* = 3.5 Hz, 1H), 6.98 (dd, *J* = 5.1, 3.6, 1H), 6.86 (d, *J* = 15.6 Hz, 1H), 6.16 (dt, *J* = 6.6, 15.6 Hz, 1H), 4.9 (dd, *J* = 6.7, 1.1 Hz, 2H) ppm. DCM impurity at 5.30 ppm (<1.6%). Water impurity at 1.54 ppm (<0.6%).

TLC R_f = 0.66 (40% EtOAc/Hex) [silica gel, UV]



(*E*)-3-(thiophen-3-yl)allyl 3-phenylpropiolate (1.59). Prepared as described by Brummond, et al.[44] Follows General Procedure C: DMAP (11 mg, 0.090 mmol), (E)-3-(thiophen-3-yl)prop-2-en-1-ol (85 mg, 0.61 mmol), phenylpropiolic acid (100 mg, 0.70 mmol), dichloromethane (5.0 mL), N-(3-dimethylaminopropyl)-N′-ethylcarbodiimide hydrochloride (170 g, 0.91 mmol). The material was purified by flash column chromatography (30% EtOAc/Hex) to yield the title compound as a clear yellow liquid (130 mg, 82%). Compound **1.59** was previously prepared by Brummond, et al.[44] Characterization data corresponds to the literature.

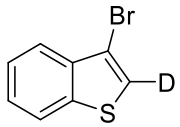
Data **1.59** previously characterized

^{1}H NMR (400 MHz, $CDCl_3$)

7.59 (d, *J* = 7 Hz, 2H), 7.45 (tt, *J* = 7.5, 1.3 Hz, 1H), 7.37 (t, *J* = 7.8 Hz, 2H), 7.29 (dd, *J* = 3.5, 5.0 Hz 1H), 7.23 (d, *J* = 4.2 Hz, 2H), 6.74 (d, *J* = 15.7, 1H), 6.19 (dt, *J* = 15.8, 6.7 Hz, 1H), 4.86 (dd, *J* = 6.7, 1.1 Hz, 2H) ppm. EtOAc impurity at 2.05

ppm (<0.4%). Grease impurity at 1.26 ppm (<0.3%).

TLC R_f = 0.70 (40% EtOAc/Hex) [silica gel, UV]



3-bromobenzo[*b*]thiophene-2-d (2.16). Follows procedure described by Gronowitz.[58] A 15 mL, two-necked, round-bottomed flask with stir bar, condenser, and septum, was charged with zinc powder (600 mg, 9.3 mmol, 3 equiv), acetic acid-d_7 (0.53 mL, 9.3 mmol, 3 equiv), and deionized water (5.0 mL, 0.60 M). The flask was lowered into a preheated oil bath at 100 °C. After 10 min, 2,3-dibromo-benzo[*b*]thiophene (900 mg, 3.1 mmol, 1 equiv) was added in one portion. After 3 h, the reaction showed complete consumption of starting material by GC. 2,3-dibromo-benzo[*b*] thiophene had a retention time of 12 min (185 °C) and product 3-bromobenzo[*b*]thiophene-2-d had a retention time of 9.8 min (150 °C) when the reaction solution is injected at a starting temperature of 80 °C with temperature ramping up to 300 °C at a rate of 15 °C per min. The column used was a Rtx-5 Crossbond (5% diphenyl – 95% dimethyl polysiloxane) 15 m, 0.25 mmID, 0.25 µm df. The solution was allowed to cool to rt and then transferred to a separatory funnel. The aqueous layer was extracted with diethyl ether (3 x 5 mL) and the combined organics were washed with brine, dried over magnesium sulfate, vacuum filtered, and concentrated using rotary evaporation to afford a light orange liquid. The material was purified by silica gel flash column chromatography (100% Hex) to afford the product as a light-yellow liquid (510 mg, 81%).

Data **2.16**

^{1}H NMR (300 MHz, $CDCl_3$)

8.00 (dd, *J* = 7.8, 0.5 Hz, 1H), 7.93 (dd, *J* = 8.2, 0.6 Hz, 1H), 7.57 (dt, *J* = 7.1, 1.1 Hz, 1H), 7.49 (dt, *J* = 7.6, 1.3 Hz, 1H) ppm. Water impurity at 1.56 ppm.

^{13}C NMR (75 MHz, $CDCl_3$)

138.4, 137.4, 125.2, 124.9, 123.2 (t, *J* = 28.9 Hz), 123.0, 122.6, 107.6 ppm

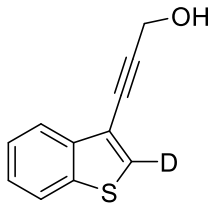
IR (thin film)

3106, 3056, 2924, 2852, 2320, 1557, 1480, 1454, 1419, 1302, 1247, 1162, 1072 cm^{-1}

HRMS (TOF MS ES+)

[M] calcd for $C_8H_4D_1SBr$: 212.9360, found 212.9230 and 214.9210

TLC R_f = 0.53 (100% Hex) [silica gel, UV]



3-(benzo[*b*]thiophen-3-yl-2-d)prop-2-yn-1-ol (2.17). Follows procedure described by Arsenyan, et al.[59] A flame-dried, 25 mL, two-necked, round-bottomed flask with stir bar, condenser, and septum, was flushed with nitrogen (3x) before charged with **2.16** (409 mg, 1.91 mmol, 1 equiv), propargyl alcohol (167 µL, 2.87 mmol, 1.5 equiv), tetrakis(triphenylphosphine) palladium(0) (22 mg, 0.020 mmol, 0.01 equiv), copper(I) iodide (15 mg, 0.08 mmol, 0.04 equiv), and deionized water (12 mL, 0.16 M) in one portion. The solution was degassed by bubbling N_2 through for 10

min. Pyrrolidine (240 µL, 2.88 mmol, 2 equiv) was added dropwise via syringe, and the solution was lowered into a preheated oil bath at 75 °C. The reaction was maintained overnight before the solution was allowed to cool to rt and transferred to a separatory funnel. The aqueous layer was extracted with diethyl ether (3 x 10 mL) and the combined organics were washed with brine, dried over magnesium sulfate, vacuum filtered, and concentrated using rotary evaporation to afford a dark orange liquid. The oil was purified by silica gel flash column chromatography (30% EtOAc/Hex) to afford the product as a dark yellow, orange oil (325 mg, 90%).

Data **2.17**

^{1}H NMR (500 MHz, $CDCl_3$)

7.97 (d, *J* = 7.5 Hz, 1H), 7.83 (d, *J* = 7.5 Hz, 1H), 7.40 (p, *J* = 7.3 Hz, 2H), 4.62 (s, 2H), 3.11 (s, 1H) ppm. DCM impurity at 5.27 ppm. EtOAc impurity at 4.14, 2.07, and 1.25 ppm.

^{13}C NMR (125 MHz, $CDCl_3$)

139.1, 138.7, 130.3 (t, *J* = 27.9 Hz), 125.0, 124.7, 122.9, 122.6, 117.5, 90.0, 79.3, 51.5 ppm

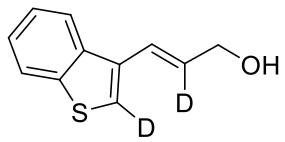
IR (thin film)

3943, 3593, 3431, 3054, 2986, 2305, 1631, 1421, 1265, 1016 cm^{-1}

HRMS (FTMS + p ESI)

$[M + H]^+$ calcd for $C_{11}H_8DOS$: 190.0431, found 190.0429

TLC R_f = 0.27 (30% EtOAc/Hex) [silica gel, UV]



(*E*)-3-(benzo[*b*]thiophen-3-yl-2-[^{2}H])prop-2-en-2-[^{2}H]-1-ol (2.18). Follows procedure by Kocsis, et al.[50] A flame-dried, 25 mL, two-necked, round-bottomed flask with stir bar, condenser, and septum, was charged with lithium aluminum deuteride (LAD, 114 mg, 2.72 mmol, 1.00 equiv). The apparatus was evacuated and filled with nitrogen (3 x). THF (7 mL, 0.370 M) was added via syringe and the solution was cooled in an ice-water bath. A separate flame-dried, 15-mL, round-bottomed flask with septum was charged with 3-(benzo[*b*]thiophen-3-yl-2-[^{2}H])prop-2-yn-1-ol (**3-2.17**, 515 mg, 2.72 mmol, 1.00 equiv) and the flask was evacuated and filled with nitrogen (3 x). THF (4.00 mL, 0.700 M) was added via syringe and the solution was cooled in an ice-water bath. The solution of **2.17** was cannulated dropwise to the lithium aluminum deuteride solution. Additional THF (1 mL) was used to transfer the last traces of **2.17** to the reaction flask. The reaction was maintained at 0 °C in an ice-water bath. After 1 h, the reaction showed no further change as observed by TLC but didn't show complete consumption of starting material. The reaction solution was cannulated dropwise into a separate flask charged with ice-water (10 mL), equipped with a stir bar, and placed in an ice bath. Vigorous bubbling occurred during the transfer process. The solution was allowed to warm to rt after removing from the ice bath. The solution was extracted with diethyl ether (3 x 10 mL) and the combined organics were washed with brine, dried over magnesium sulfate, vacuum filtered, and concentrated using rotary evaporation to afford a yellow liquid. The residue was purified by flash column chromatography (5% ethyl ether/dichloromethane) to afford the product as a yellow liquid (426 mg, 88%) and starting material **2.17** (40 mg).

Data **2.18**

^{1}H NMR (300 MHz, $CDCl_3$)

7.92 – 7.85 (m, 2H), 7.43 – 7.34 (m, 2H), 6.87 (s, 1H), 4.36 (s, 2H), 2.23 (s, 1H) ppm. DCM impurity at 5.30 ppm.

^{13}C NMR (100 MHz, $CDCl_3$)

140.3, 137.6, 133.2, 129.9 (t, J = 23.4), 124.5, 124.3, 122.9 (2C), 122.0 (t, J = 27.8), 121.9, 63.5 ppm

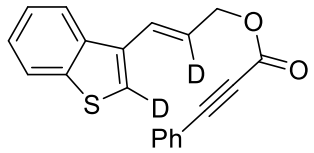
IR (thin film)

3600, 3405, 3054, 2927, 2306, 1423, 1265 cm^{-1}

HRMS (FTMS + p ESI)

$[MH – H_2O]^+$ calcd for $C_{11}H_7D_2S$: 175.0545, found 175.0542

TLC R_f = 0.21 (30% EtOAc/Hex) [silica gel, UV]



(*E*)-3-(benzo[*b*]thiophen-3-yl-2-d)allyl-2-d 3-phenylpropiolate (2.19). Follows General Procedure C: DMAP (108 mg, 0.882 mmol), **2.18** (424 mg, 2.21 mmol), phenylpropiolic acid (419 mg, 2.87 mmol), dichloromethane (16 mL), N-(3-dimethylaminopropyl)-N′-ethylcarbodiimide hydrochloride (634 mg, 3.31 mmol). The crude material was purified by flash column chromatography (20% EtOAc/Hex) to yield the title compound as a clear yellow liquid (254 mg, 63%).

Data **2.19**

^{1}H NMR (400 MHz, $CDCl_3$)

7.93 (d, *J* = 7.7 Hz, 1H), 7.87 (d, *J* = 7.7 Hz, 1H), 7.61 (m, 2H), 7.48 – 7.35 (m, 5H), 7.00 (s, 1H), 4.95 (s, 2H) ppm. DCM impurity at 5.30 ppm. EtOAc impurity at 4.14, 2.06, and 1.27 ppm.

^{13}C NMR (100 MHz, $CDCl_3$)

153.9, 140.4, 137.5, 133.1 (2C), 132.7, 130.8, 128.7 (2C), 127.6, 124.7, 124.5, 123.4 (t, *J* = 24.5 Hz), 123.4 (t, *J* = 22.2 Hz), 123.0, 122.0, 119.6, 86.8, 80.6, 66.7 ppm

IR (thin film)

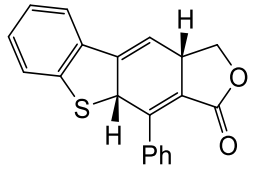
3055, 2218, 1704, 1490, 1422, 1375, 1265, 1170, 962 cm^{-1}

HRMS (FTMS + p ESI)

$[M+H]^+$ calcd for $C_{20}H_{13}D_2O_2S$: 321.09183, found 321.09261

TLC R_f = 0.65 (40% EtOAc/Hex) [silica gel, UV]

2.6.4 Synthesis of the Dearomative DDDA Adducts as Mixtures with Products



4-phenyl-4a,10a-dihydrobenzo[4,5]thieno[2,3-f]isobenzofuran-3(1H)-one (2.6) (Table 2.1, entry 1). An oven-dried NMR tube was charged with **2.5** (13 mg, 0.04 mmol) dissolved in o-dichlorobenzene (0.5 mL, 0.08 M). The NMR tube was sealed with a polypropylene cap and

lowered into a preheated oil bath at 150 °C. After 7 min, the NMR tube was removed from the oil bath, rinsed with hexanes, and wiped with a ChemWipe. A ratio of 91:9 (**2.6**:**2.8**) was afforded, and thus **2.6** was characterized as a mixture. Attempts to purify **2.6** by column chromatography led to conversion to products. The solution was analyzed by multi-dimensional NMR COSY, HSQC, and HMBC.

Data **2.6**

^{1}H NMR (400 MHz, o-DCB-d_4) ppm

7.34 – 7.25 (m, 5H), 7.19 (d, *J* = 7 Hz, 1H), 7.04 (dt, *J* = 1.3, 7.3 Hz, 1H), 6.98 – 6.91 (m, 2H), 5.93 (dd, *J* = 2.0, 3.5 Hz, 1H), 5.46 (dd, *J* = 3.5, 13.5 Hz, 1H), 4.53 (dd, *J* = 8.6 Hz, 1H), 3.91 (dd, *J* = 8.2, 10.4 Hz, 1H), 3.67 – 3.57 (m, 1H) ppm

^{13}C NMR (100 MHz, o-DCB-d_4)

166.2, 146.4, 143.5, 142.9, 136.2, 134.7, 129.5, 129.3, 129.0, 128.9, 128.2, 128.0, 124.8, 123.0, 122.4, 122.2, 114.8, 68.6, 55.5, 41.5 ppm

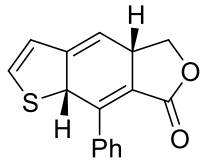
IR (thin film)

2978, 1756, 1455, 1354, 1223, 1060, 756, 700 cm^{-1}

HRMS (FTMS + p ESI)

$[M + H]^+$ calcd for $C_{20}H_{13}O_2S$: 317.06308, found 317.06243 indicative of formation of oxidation product **2.5** under ionization conditions. 319.07787 was also found in 8% relative abundance, which is the correct mass for **2.6**

TLC R_f = 0.44 (40% ethyl acetate/hexanes) [silica gel, UV]

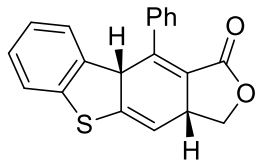


(4aS,8aR)-8-phenyl-4a,8a-dihydrothieno[2,3-f]isobenzofuran-7(5H)-one (2.1) (Table 2.1, entry 2). An oven-dried NMR tube was charged with dearomative DDDA precursor **1.59** (8 mg, 0.03 mmol) dissolved in *o*-DCB-d_4 (0.5 mL, 0.06 M) under an atmosphere of air. The NMR tube was sealed with a polypropylene cap and lowered into an oil bath preheated at 150 °C and heated for 15 min. The NMR tube was removed from the oil bath, rinsed with hexanes, and wiped with a ChemWipe before ^{1}H NMR was obtained. A 35:15:38:12 ratio of **1.59**:**2.1**:**1.61**:**1.60** was obtained. Ratios were determined by comparing the ^{1}H NMR resonances at 6.03 ppm (1H) for **1.59**, 5.50 ppm (1H) for **2.1**, 5.14 ppm (2H) for **1.60,** and 2.39 ppm (1H) for **1.61.** Characterization of **2.1** by analogy to **2.6** can be found in Table 2.1. Attempts to purify **2.1** by column chromatography led to conversion to products.

Data **2.1**

^{1}H NMR (400 MHz, o-DCB-d_4) ppm

5.50 (dd, *J* = 2.1, 3.8 Hz, 1H), 5.30 (dd, *J* = 3.8, 14.8 Hz, 1H), 4.48 (dd, *J* = 8.2, 8.9 Hz, 1H), 3.82 (dd, *J* = 8.2, 10.2 Hz, 1H), 3.57 – 3.47 (m, 1H) ppm. Resonances for aromatic protons overlapped with other resonances in the mixture and were not characterized.

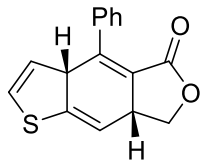


(3aR,9bS)-10-phenyl-3a,9b-dihydrobenzo[4,5]thieno[2,3-f]isobenzofuran-1(3H)-one (2.10) (Table 2.1, entry 3). An oven-dried NMR tube was charged with dearomative DDDA precursor **2.9** (10 mg, 0.03 mmol) dissolved in *o*-DCB (0.5 mL, 0.06 M) under an atmosphere of air. The NMR tube was sealed with a polypropylene cap and lowered into an oil bath preheated at 150 °C and heated for 11 min. The NMR tube was removed from the oil bath, rinsed with hexanes, and wiped with a ChemWipe before ^{1}H NMR was obtained. A 6:87:0:7 ratio of **2.9**:**2.10**:**2.11**:**2.12** was obtained. Ratios were determined by comparing the ^{1}H NMR resonances at 4.81 ppm (2H) for **2.9**, 5.59 ppm (1H) for **2.10**, and 5.12 ppm (2H) for **2.12.** Characterization of **2.10** by analogy to **2.6** can be found in Table 2.1. Attempts to purify **2.10** by column chromatography led to conversion to products.

Data **2.10**

^{1}H NMR (500 MHz, o-DCB) ppm

5.59 (dd, *J* = 1.7, 3.4 Hz, 1H), 4.74 (dd, *J* = 3.3, 13.4 Hz, 1H), 4.50 (dd, *J* = 8.6, 9.4 Hz, 1H), 3.82 (dd, *J* = 8.6, 9.4 Hz, 1H), 3.60 – 3.50 (m, 1H) ppm. Resonances for aromatic protons overlapped with other resonances in the mixture and were not characterized.

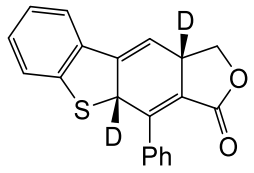


(3aR,7aR)-4-phenyl-7,7a-dihydrothieno[2,3-f]isobenzofuran-5(3aH)-one (2.13) (Table 2.1, entry 4). An oven-dried NMR tube was charged with dearomative DDDA precursor **1.50** (10 mg, 0.04 mmol) dissolved in *o*-DCB (0.5 mL, 0.07 M) under an atmosphere of air. The NMR tube was sealed with a polypropylene cap and lowered into an oil bath preheated at 150 °C and heated for 15 min. The NMR tube was removed from the oil bath, rinsed with hexanes, and wiped with a ChemWipe before ^{1}H NMR was obtained. A 16:65:9:10 ratio of **1.50**:**2.13**:**1.51**:**2.14** was obtained. Ratios were determined by comparing the ^{1}H NMR resonances at 4.74 ppm (2H) for **1.50**, 5.51 ppm (1H) for **2.13**, 5.10 ppm (2H) for **2.14,** and 2.51 ppm (1H) for **1.51.** Characterization of **2.13** by analogy to **2.6** can be found in Table 2.1. Attempts to purify **2.13** by column chromatography led to conversion to products.

Data **2.13**

^{1}H NMR (500 MHz, o-DCB) ppm

5.51 (dd, J = 3.4 Hz, 1H), 4.42 (dd, J = 3.4, 15.0 Hz, 1H), 4.45 (dd, J = 8.7 Hz, 1H), 3.79 (dd, J = 8.7, 8.9 Hz, 1H), 3.51 – 3.39 (m, 1H) ppm. Resonances for aromatic protons overlapped with other resonances in the mixture and were not characterized.



(4aR,10aS)-4-phenyl-4a,10a-dihydrobenzo[4,5]thieno[2,3-f]isobenzofuran-3(1H)-one-4a,10a-d2 (2.20). A 1-mL, flame-dried, microwave vial with stir bar was charged with precursor **2.19** (24 mg, 0.075 mmol) dissolved in o-DCB (0.50 mL, 0.15 M). The vial was sealed with a crimp cap with Teflon-lined septum, wrapped in parafilm at the top, and lowered into a pre-heated oil bath at 150 °C. After 90 min, the solution was allowed to cool to room temperature before transferred to an NMR tube for NMR analysis. Product ratios were determined by comparing the resonance integrations for starting material, adduct, oxidized product, and isomerized product from the ^{1}H NMR of the crude reaction solution using No-D spectroscopy. A 0:77:18:5 ratio of **2.19**:**2.20**:**2.8**:**2.21** was obtained. Ratios were determined by comparing the ^{1}H NMR resonances at 4.54 ppm (1H) for **2.20,** 5.21 ppm (2H) for **2.8,** and 3.09 ppm (1H) for **2.21**.

Data **2.20**

^{1}H NMR (500 MHz, o-DCB) ppm

5.95 (s, 1H), 4.54 (d, *J* = 8.9 Hz, 1H), 3.90 (d, *J* = 9.0 Hz, 1H) ppm. Resonances for aromatic protons overlapped with other resonances in the mixture and were not characterized.

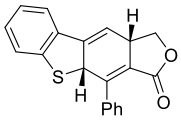
2.6.5 Deuterium Isotope Effect Observed in Parallel Reactions of 2.5 and 2.19

Rxn 1. A 1-mL, flame-dried, microwave vial with stir bar was charged with precursor **2.5** (20 mg, 0.063 mmol) dissolved in o-dichlorobenzene (0.50 mL, 0.13 M). The vial was sealed with a crimp cap with Teflon-lined septum, wrapped in parafilm at the top, and lowered into a pre-heated oil bath at 150 °C. After 90 min, the solution was allowed to cool to room temperature before transferred to an NMR tube for NMR analysis. Product ratios were determined by comparing the resonance integrations for starting material, adduct, oxidized product, and isomerized product from the ^{1}H NMR of the crude reaction solution using No-D spectroscopy. A 0:41:39:20 ratio of **2.5**, **2.6**, **2.8**, and **2.7** was obtained. Ratios were determined by comparing the ^{1}H NMR resonances at 5.45 ppm (1H) for **2.6,** 5.21 ppm (2H) for **2.8,** and 2.79 ppm (1H) for **2.7**.

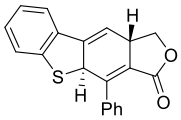
Rxn 2. A 1-mL, flame-dried, microwave vial with stir bar was charged with precursor **2.19** (24 mg, 0.075 mmol) dissolved in o-dichlorobenzene (0.50 mL, 0.15 M). The vial was sealed with a crimp cap with Teflon-lined septum, wrapped in parafilm at the top, and lowered into a pre-heated oil bath at 150 °C. After 90 min, the solution was allowed to cool to room temperature before transferred to an NMR tube for NMR analysis. Product ratios were determined by comparing the resonance integrations for starting material, adduct, oxidized product, and isomerized product from the ^{1}H NMR of the crude reaction solution using No-D spectroscopy. A 0:77:18:5 ratio of **2.19**, **2.20**, **2.8**, and **2.21** was obtained. Ratios were determined by comparing the ^{1}H NMR resonances at 4.53 ppm (1H) for **2.20,** 5.21 ppm (2H) for **2.8,** and 3.09 ppm (1H) for **2.21**.

2.6.6 DP4 Probability Measure Results and Analysis

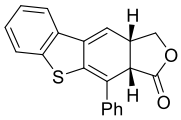
Table 2.2. Computational and experimental ^{13}C NMR resonances of the **2.6**, **2.22**, **2.23**, **2.24**, and **2.7**



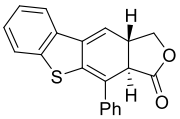
2.6



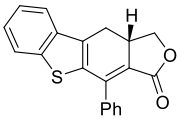
2.22



2.23



2.24



2.7

	Computational					Experimental		
Entry	**2.13**	**2.22**	**2.23**	**2.24**	**2.7**	**2.13**	**2.23**	**2.7**
1	42.70	44.52	39.88	41.50	27.09	41.59	39.00	26.57
2	56.64	54.86	45.92	42.12	37.81	55.64	45.32	37.06
3	67.37	69.00	72.08	66.73	70.29	68.69	72.35	71.27
4	113.59	115.86	116.46	113.91	119.71	114.87	116.22	119.51
5	121.73	121.28	121.52	121.36	122.34	122.32	121.16	122.53
6	122.04	123.61	122.65	122.73	123.25	122.51	121.81	123.05
7	122.78	124.65	124.31	124.79	125.33	123.16	122.43	125.03
8	124.69	125.03	124.84	127.85	125.41	124.88	125.05	125.99
9	127.91	127.72	127.80	127.85	127.53	128.10	127.74	128.10
10	127.91	127.72	127.80	128.30	127.53	128.32	127.74	128.10
11	128.58	129.84	127.86	128.93	130.01	129.03	127.99	129.35
12	128.58	130.27	128.89	128.93	131.37	129.15	128.77	129.35
13	129.66	130.27	128.89	129.04	131.37	129.41	128.77	129.58
14	129.70	130.86	129.37	131.63	131.63	129.66	129.84	132.94
15	134.02	132.26	133.05	132.48	133.75	134.80	133.73	134.27
16	135.58	135.61	134.77	135.74	136.35	136.34	133.78	137.75
17	143.33	141.15	141.24	138.71	140.68	142.97	139.33	139.05
18	145.85	144.65	141.42	141.78	141.71	143.62	140.68	142.12
19	148.06	145.79	142.73	144.24	145.74	146.50	140.94	143.51
20	165.94	166.14	175.88	169.31	166.30	166.28	176.68	167.95

Table 2.3. Computational and experimental ^{1}H NMR resonances of the **2.6**, **2.22**, **2.23**, **2.24**, and **2.7**

	Calculated					Experimental		
Entry	**2.13**	**2.22**	**2.23**	**2.24**	**2.7**	**2.13**	**2.23**	**2.7**
1	3.92	3.83	3.40	3.40	2.78	3.38	3.75	2.80
2	3.92	4.40	3.66	3.46	3.04	3.66	3.85	3.43
3	4.44	4.41	4.47	4.02	3.55	4.28	4.54	3.68
4	6.15	6.01	4.59	4.29	3.91	5.21	4.62	4.15
5	6.17	6.30	6.13	6.44	4.58	5.69	6.19	4.80
6	7.06	7.10	7.11	7.12	7.39	6.68	7.14	7.38
7	7.11	7.19	7.22	7.21	7.41	6.71	7.25	7.43
8	7.21	7.26	7.25	7.25	7.44	6.79	7.26	7.45
9	7.35	7.37	7.30	7.35	7.44	6.94	7.32	7.46
10	7.41	7.42	7.40	7.40	7.47	7.02	7.43	7.47
11	7.41	7.42	7.40	7.40	7.63	7.04	7.44	7.48
12	7.42	7.46	7.42	7.46	7.64	7.06	7.50	7.49
13	7.48	7.79	7.90	7.54	7.71	7.07	7.69	7.77
14	7.48	7.79	7.90	7.54	7.71	7.08	7.69	7.77

2.6.6.1 DP4 Analysis of the Experimental 2.6 NMR

Assignment of experimental NMR resonances of proposed **2.6** isomer to calculated NMR resonances of each considered isomer.

2.6 (atom, calc, exp):

C1 42.7 41.59
C10 127.91 128.1
C11 128.58 129.15
C12 128.58 129.03
C13 129.66 129.41
C14 129.7 129.66
C15 134.02 134.8
C16 135.58 136.34
C17 143.33 142.97
C18 145.85 143.62
C19 148.06 146.5
C2 56.64 55.64
C20 165.94 166.28
C3 67.37 68.69
C4 113.59 114.87
C5 121.73 122.32
C6 122.04 122.51
C7 122.78 123.16
C8 124.69 124.88
C9 127.91 128.32
H1 3.92 3.66
H10 7.41 7.04
H11 7.41 7.02
H12 7.42 7.06
H13 7.48 7.08
H14 7.48 7.07
H2 3.92 3.38
H3 4.44 4.28
H4 6.15 5.21
H5 6.17 5.69
H6 7.06 6.68
H7 7.11 6.71
H8 7.21 6.79
H9 7.35 6.94

2.22 (atom, calc, exp):

C1	44.52	41.59
C10	127.72	128.1
C11	129.84	129.03
C12	130.27	129.41
C13	130.27	129.15
C14	130.86	129.66
C15	132.26	134.8
C16	135.61	136.34
C17	141.15	142.97
C18	144.65	143.62
C19	145.79	146.5
C2	54.86	55.64
C20	166.14	166.28
C3	69.0	68.69
C4	115.86	114.87
C5	121.28	122.32
C6	123.61	122.51
C7	124.65	123.16
C8	125.03	124.88
C9	127.72	128.32
H1	3.83	3.38
H10	7.42	7.04
H11	7.42	7.02
H12	7.46	7.06
H13	7.79	7.08
H14	7.79	7.07
H2	4.4	3.66
H3	4.41	4.28
H4	6.01	5.21
H5	6.3	5.69
H6	7.1	6.68
H7	7.19	6.71
H8	7.26	6.79
H9	7.37	6.94

2.23 (atom, calc, exp):

C1	41.59	41.59
C10	122.78	129.66
C11	121.02	128.1
C12	122.75	129.41
C13	121.09	128.32
C14	122.63	129.15
C15	126.96	134.8
C16	135.31	142.97
C17	141.35	146.5
C18	134.69	136.34
C19	136.94	143.62
C2	47.55	55.64
C20	166.82	166.28
C3	70.96	68.69
C4	112.84	114.87
C5	115.31	122.32
C6	116.26	122.51
C7	120.4	124.88
C8	117.92	123.16
C9	121.41	129.03
H1	3.4	3.38
H10	7.4	7.04
H11	7.4	7.02
H12	7.42	7.06
H13	7.9	7.08
H14	7.9	7.07
H2	3.66	3.66
H3	4.47	4.28
H4	4.59	5.21
H5	6.13	5.69
H6	7.11	6.68
H7	7.22	6.71
H8	7.25	6.79
H9	7.3	6.94

2.24 (atom, calc, exp):

C1	41.5	41.59
C10	128.3	128.32
C11	128.93	129.15
C12	128.93	129.03
C13	129.04	129.41
C14	131.63	129.66
C15	132.48	134.8
C16	135.74	136.34
C17	138.71	142.97
C18	141.78	143.62
C19	144.24	146.5
C2	42.12	55.64
C20	169.31	166.28
C3	66.73	68.69
C4	113.91	114.87
C5	121.36	122.32
C6	122.73	122.51
C7	124.79	123.16
C8	127.85	128.1

C9 127.85 124.88
H1 3.4 3.38
H10 7.4 7.04
H11 7.4 7.02
H12 7.46 7.06
H13 7.54 7.08
H14 7.54 7.07
H2 3.46 3.66
H3 4.02 4.28
H4 4.29 5.21
H5 6.44 5.69
H6 7.12 6.68
H7 7.21 6.71
H8 7.25 6.79
H9 7.35 6.94

2.7

(atom, calc, exp):

C1 27.09 41.59
C10 127.53 128.1
C11 130.01 129.03
C12 131.37 129.41
C13 131.37 129.15
C14 131.63 129.66
C15 133.75 134.8
C16 136.35 136.34
C17 140.68 142.97
C18 141.71 143.62
C19 145.74 146.5
C2 37.81 55.64

Warning: Error = 17.8 ppm

C20 166.3 166.28
C3 70.29 68.69
C4 119.71 114.87
C5 122.34 122.32
C6 123.25 122.51
C7 125.33 123.16
C8 125.41 124.88
C9 127.53 128.32
H1 2.78 3.38
H10 7.47 7.02
H11 7.63 7.04
H12 7.64 7.06
H13 7.71 7.08
H14 7.71 7.07
H2 3.04 3.66
H3 3.55 4.28
H4 3.91 5.21
H5 4.58 5.69
H6 7.39 6.68
H7 7.41 6.71
H8 7.44 6.94
H9 7.44 6.79

The results show the probability that the experimental NMR spectrum corresponds to the indicated calculated NMR spectrum. The DP4 probability calculation uses the DP4-database2 version of the database and uses the t distribution.

Results of DP4 using both carbon and proton data:
2.6: 99.9%
2.22: 0.1%
2.23: 0.0%
2.24: 0.0%
2.7: 0.0%

Results of DP4 using the carbon data only:
2.6: 95.4%
2.22: 4.6%
2.23: 0.0%
2.24: 0.0%
2.7: 0.0%

Results of DP4 using the proton data only:
2.6: 97.1%
2.22: 2.6%
2.23: 0.3%
2.24: 0.1%
2.7: 0.0%

2.6.6.2 DP4 Analysis of the Experimental 2.23 NMR

Assignment of experimental NMR resonances of proposed **2.23** isomer to calculated NMR resonances of each considered isomer.

2.6 (atom, calc, exp):

C1 42.7 39.0
C10 127.91 127.74
C11 128.58 128.77
C12 128.58 127.99
C13 129.66 128.77
C14 129.7 129.84
C15 134.02 133.73
C16 135.58 133.78
C17 143.33 139.33
C18 145.85 140.68
C19 148.06 140.94
C2 56.64 45.32
C20 165.94 176.68
C3 67.37 72.35
C4 113.59 116.22
C5 121.73 121.16
C6 122.04 121.81
C7 122.78 122.43
C8 124.69 125.05
C9 127.91 127.74
H1 3.92 3.85
H10 7.41 7.44
H11 7.41 7.43

H12 7.42 7.5
H13 7.48 7.69
H14 7.48 7.69
H2 3.92 3.75
H3 4.44 4.54
H4 6.15 4.62
H5 6.17 6.19
H6 7.06 7.14
H7 7.11 7.25
H8 7.21 7.26
H9 7.35 7.32

2.22 (atom, calc, exp):
C1 44.52 39.0
C10 127.72 127.74
C11 129.84 127.99
C12 130.27 128.77
C13 130.27 128.77
C14 130.86 129.84
C15 132.26 133.73
C16 135.61 133.78
C17 141.15 139.33
C18 144.65 140.68
C19 145.79 140.94
C2 54.86 45.32
C20 166.14 176.68
C3 69.0 72.35
C4 115.86 116.22
C5 121.28 121.16
C6 123.61 121.81
C7 124.65 122.43
C8 125.03 125.05
C9 127.72 127.74
H1 3.83 3.75
H10 7.42 7.44
H11 7.42 7.43
H12 7.46 7.5
H13 7.79 7.69
H14 7.79 7.69
H2 4.4 3.85
H3 4.41 4.54
H4 6.01 4.62
H5 6.3 6.19
H6 7.1 7.14
H7 7.19 7.25
H8 7.26 7.26
H9 7.37 7.32

2.23 (atom, calc, exp):
C1 39.88 39.0
C10 127.8 127.74
C11 127.86 127.99
C12 128.89 128.77
C13 128.89 128.77
C14 129.37 129.84
C15 133.05 133.73
C16 134.77 133.78
C17 141.24 139.33
C18 141.42 140.68
C19 142.73 140.94
C2 45.92 45.32
C20 175.88 176.68
C3 72.08 72.35
C4 116.46 116.22
C5 121.52 121.16
C6 122.65 121.81
C7 124.31 122.43
C8 124.84 125.05
C9 127.8 127.74
H1 3.4 3.75
H10 7.4 7.44
H11 7.4 7.43
H12 7.42 7.5
H13 7.9 7.69
H14 7.9 7.69
H2 3.66 3.85
H3 4.47 4.54
H4 4.59 4.62
H5 6.13 6.19
H6 7.11 7.14
H7 7.22 7.25
H8 7.25 7.26
H9 7.3 7.32

2.24 (atom, calc, exp):
C1 41.5 39.0
C10 128.3 127.74
C11 128.93 128.77
C12 128.93 127.99
C13 129.04 128.77
C14 131.63 129.84
C15 132.48 133.73

C16 135.74 133.78
C17 138.71 139.33
C18 141.78 140.68
C19 144.24 140.94
C2 42.12 45.32
C20 169.31 176.68
C3 66.73 72.35
C4 113.91 116.22
C5 121.36 121.16
C6 122.73 121.81
C7 124.79 122.43
C8 127.85 127.74
C9 127.85 125.05
H1 3.4 3.75
H10 7.4 7.44
H11 7.4 7.43
H12 7.46 7.5
H13 7.54 7.69
H14 7.54 7.69
H2 3.46 3.85
H3 4.02 4.54
H4 4.29 4.62
H5 6.44 6.19
H6 7.12 7.14
H7 7.21 7.25
H8 7.25 7.26
H9 7.35 7.32

2.7 (atom, calc, exp):
C1 27.09 39.0
C10 127.53 127.74
C11 130.01 127.99
C12 131.37 128.77
C13 131.37 128.77
C14 131.63 129.84
C15 133.75 133.73
C16 136.35 133.78
C17 140.68 139.33
C18 141.71 140.68
C19 145.74 140.94
C2 37.81 45.32
C20 166.3 176.68
C3 70.29 72.35
C4 119.71 116.22
C5 122.34 121.16
C6 123.25 121.81
C7 125.33 122.43
C8 125.41 125.05
C9 127.53 127.74
H1 2.78 3.75
H10 7.47 7.43
H11 7.63 7.44
H12 7.64 7.5
H13 7.71 7.69
H14 7.71 7.69
H2 3.04 3.85
H3 3.55 4.54
H4 3.91 4.62
H5 4.58 6.19
H6 7.39 7.14
H7 7.41 7.25
H8 7.44 7.32
H9 7.44 7.26

The results show the probability that the experimental NMR spectrum corresponds to the indicated calculated NMR spectrum. The DP4 probability calculation uses the DP4-database2 version of the database and uses the t distribution.

Results of DP4 using both carbon and proton data:
2.6: 0.0%
2.22: 0.0%
2.23: 100.0%
2.24: 0.0%
2.7: 0.0%

Results of DP4 using the carbon data only:
2.6: 0.0%
2.22: 0.0%
2.23: 100.0%
2.24: 0.0%
2.7: 0.0%

Results of DP4 using the proton data only:
2.6: 0.0%
2.22: 0.0%
2.23: 71.9%
2.24: 28.1%
2.7: 0.0%

2.6.6.3 DP4 Analysis of the Experimental 2.7 NMR

Assignment of experimental NMR resonances of proposed **2.7** to calculated NMR resonances of each considered isomer.

2.6 (atom, calc, exp):

C1 42.7 26.57
Warning: Error = 16.1 ppm
C10 127.91 128.1
C11 128.58 129.35
C12 128.58 129.35
C13 129.66 129.58
C14 129.7 132.94
C15 134.02 134.27
C16 135.58 137.75
C17 143.33 139.05
C18 145.85 142.12
C19 148.06 143.51
C2 56.64 37.06
Warning: Error = 19.6 ppm
C20 165.94 167.95
C3 67.37 71.27
C4 113.59 119.51
C5 121.73 122.53
C6 122.04 123.05
C7 122.78 125.03
C8 124.69 125.99
C9 127.91 128.1
H1 3.92 3.43
H10 7.41 7.48
H11 7.41 7.47
H12 7.42 7.49
H13 7.48 7.77
H14 7.48 7.77
H2 3.92 2.8
H3 4.44 3.68
H4 6.15 4.15
H5 6.17 4.8
H6 7.06 7.38
H7 7.11 7.43
H8 7.21 7.45
H9 7.35 7.46

2.22 (atom, calc, exp):
C1 44.52 26.57
Warning: Error = 18.0 ppm
C10 127.72 128.1
C11 129.84 129.35
C12 130.27 129.58
C13 130.27 129.35
C14 130.86 132.94
C15 132.26 134.27
C16 135.61 137.75

C17 141.15 139.05
C18 144.65 142.12
C19 145.79 143.51
C2 54.86 37.06
Warning: Error = 17.8 ppm
C20 166.14 167.95
C3 69.0 71.27
C4 115.86 119.51
C5 121.28 122.53
C6 123.61 123.05
C7 124.65 125.03
C8 125.03 125.99
C9 127.72 128.1
H1 3.83 2.8
H10 7.42 7.48
H11 7.42 7.47
H12 7.46 7.49
H13 7.79 7.77
H14 7.79 7.77
H2 4.4 3.43
H3 4.41 3.68
H4 6.01 4.15
H5 6.3 4.8
H6 7.1 7.38
H7 7.19 7.43
H8 7.26 7.45
H9 7.37 7.46

2.23 (atom, calc, exp):
C1 41.59 26.57
Warning: Error = 15.0 ppm
C10 122.78 132.94
C11 121.02 128.1
C12 122.75 129.58
C13 121.09 128.1
C14 122.63 129.35
C15 126.96 134.27
C16 135.31 139.05
C17 141.35 143.51
C18 134.69 137.75
C19 136.94 142.12
C2 47.55 37.06
C20 166.82 167.95
C3 70.96 71.27
C4 112.84 119.51
C5 115.31 122.53
C6 116.26 123.05
C7 120.4 125.99
C8 117.92 125.03
C9 121.41 129.35
H1 3.4 2.8
H10 7.4 7.48
H11 7.4 7.47
H12 7.42 7.49
H13 7.9 7.77
H14 7.9 7.77
H2 3.66 3.43
H3 4.47 3.68
H4 4.59 4.15
H5 6.13 4.8
H6 7.11 7.38
H7 7.22 7.43
H8 7.25 7.45
H9 7.3 7.46

2.24 (atom, calc, exp):
C1 41.5 26.57
C10 128.3 128.1
C11 128.93 129.35
C12 128.93 129.35
C13 129.04 129.58
C14 131.63 132.94
C15 132.48 134.27
C16 135.74 137.75
C17 138.71 139.05
C18 141.78 142.12
C19 144.24 143.51
C2 42.12 37.06
C20 169.31 167.95
C3 66.73 71.27
C4 113.91 119.51
C5 121.36 122.53
C6 122.73 123.05
C7 124.79 125.03
C8 127.85 128.1
C9 127.85 125.99
H1 3.4 2.8
H10 7.4 7.48
H11 7.4 7.47
H12 7.46 7.49
H13 7.54 7.77
H14 7.54 7.77
H2 3.46 3.43

H3 4.02 3.68
H4 4.29 4.15
H5 6.44 4.8
H6 7.12 7.38
H7 7.21 7.43
H8 7.25 7.45
H9 7.35 7.46

2.7
(atom, calc, exp):
C1 27.09 26.57
C10 127.53 128.1
C11 130.01 129.35
C12 131.37 129.58
C13 131.37 129.35
C14 131.63 132.94
C15 133.75 134.27
C16 136.35 137.75
C17 140.68 139.05
C18 141.71 142.12
C19 145.74 143.51
C2 37.81 37.06
C20 166.3 167.95
C3 70.29 71.27
C4 119.71 119.51
C5 122.34 122.53
C6 123.25 123.05
C7 125.33 125.03
C8 125.41 125.99
C9 127.53 128.1
H1 2.78 2.8
H10 7.47 7.47
H11 7.63 7.48
H12 7.64 7.49
H13 7.71 7.77
H14 7.71 7.77
H2 3.04 3.43
H3 3.55 3.68
H4 3.91 4.15
H5 4.58 4.8
H6 7.39 7.38
H7 7.41 7.43
H8 7.44 7.46
H9 7.44 7.45

The results show the probability that the experimental NMR spectrum corresponds to the indicated calculated NMR spectrum. The DP4 probability calculation uses the DP4-database2 version of the database and uses the t distribution.

Results of DP4 using both carbon and proton data:
2.6: 0.0%
2.22: 0.0%
2.23: 0.0%
2.24: 0.0%
2.7: 100.0%

Results of DP4 using the carbon data only:
2.6: 0.0%
2.22: 0.0%
2.23: 0.0%
2.24: 0.0%
2.7: 100.0%

Results of DP4 using the proton data only:

2.6: 0.0%
2.22: 0.0%
2.23: 0.0%
2.24: 0.0%
2.7: 100.0%

2.6.6.4 Assignment of Spartan Calculated and Experimental ^{1}H and ^{13}C NMR Resonances

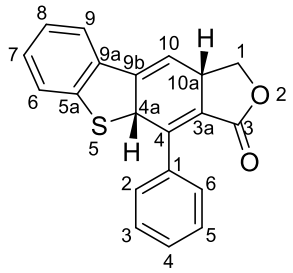


Table 2.4. Resonances for **2.6**

2.6		
	Calculated	Experimental
Carbons		
1	67.37	68.69
3	165.94	166.28
3a	122.04	122.51
4	148.06	146.50
4a	56.64	55.64
5a	143.33	142.97
6	122.78	123.16
7	129.66	129.41
8	124.69	124.88
9	121.73	122.32
9a	134.02	134.80
9b	145.85	143.62
10	113.59	114.87
10a	42.70	41.59
1'	135.58	136.34
2'	128.58	129.15
3'	127.91	128.10
4'	129.70	129.66
5'	127.91	128.32
6'	128.58	129.03
Protons		
6'-H	7.48	7.07
2'-H	7.48	7.08
4'-H	7.42	7.06
3'-H	7.41	7.02
5'-H	7.41	7.04
9-H	7.35	6.94
7-H	7.21	6.79
6-H	7.11	6.71
8-H	7.06	6.68
10-H	6.17	5.69
4a-H	6.15	5.21
1-Ha	4.44	4.28
1-Hb	3.92	3.66
10a-H	3.92	3.38

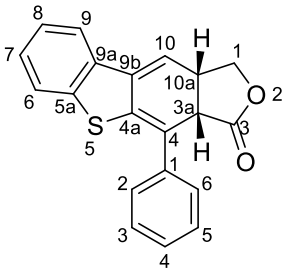


Table 2.5. Resonances for **2.23**

2.23		
	Calculated	Experimental
Carbons		
1	72.08	72.35
3	175.88	176.68
3a	45.92	45.32
4	124.31	122.43
4a	134.77	133.78
5a	141.24	140.94
6	122.65	121.81
7	129.37	129.84
8	124.84	125.05
9	121.52	121.16
9a	133.05	133.73
9b	142.73	140.68
10	116.46	116.22
10a	39.88	39.00
1'	141.42	139.33
2'	127.8	127.74
3'	128.89	128.77
4'	127.86	128.77
5'	128.89	127.99
6'	127.8	127.74
Protons		
2'-H	7.90	7.69
6'-H	7.90	7.69
9-H	7.42	7.50
3'-H	7.40	7.43
5'-H	7.40	7.44
4'-H	7.30	7.32
7-H	7.25	7.26
6-H	7.22	7.25
8-H	7.11	7.14
10-H	6.13	6.19
1-Hb	4.59	4.62
1-Ha	4.47	4.54
10a-H	3.66	3.85
3a-H	3.40	3.75

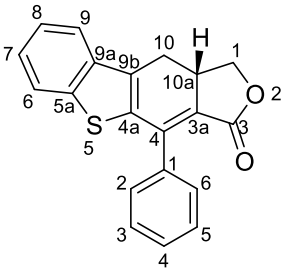


Table 2.6. Resonances for **2.7**

2.7		
	Calculated	Experimental
Carbons		
1	70.29	71.27
3	166.30	167.95
3a	119.71	119.51
4	145.74	143.51
4a	141.71	142.12
5a	140.68	139.05
6	123.25	123.05
7	125.33	125.03
8	125.41	125.99
9	122.34	122.53
9a	136.35	137.75
9b	131.63	132.94
10	27.09	26.57
10a	37.81	37.06
1'	133.75	134.27
2'	131.37	129.35
3'	127.53	128.10
4'	130.01	129.35
5'	127.53	128.10
6'	131.37	129.58
Protons		
6'-H	7.71	7.77
2'-H	7.71	7.77
6-H	7.64	7.49
9-H	7.63	7.48
4'-H	7.47	7.47
5'-H	7.44	7.45
3'-H	7.44	7.46
8-H	7.41	7.43
7-H	7.39	7.38
1-Hb	4.58	4.80
1-Ha	3.91	4.15
10a-H	3.55	3.68
10-Ha	3.04	3.43
10-Hb	2.78	2.80

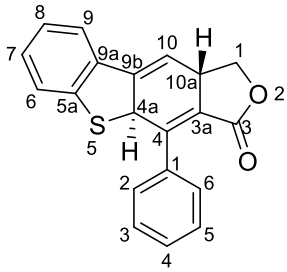


Table 2.7. Resonances for **2.22**

2.22	
	Calculated
Carbons	
1	69.00
3	166.14
3a	124.65
4	145.79
4a	54.86
5a	141.15
6	123.61
7	129.84
8	125.03
9	121.28
9a	135.61
9b	144.65
10	115.86
10a	44.52
1'	132.26
2'	130.27
3'	127.72
4'	130.86
5'	127.72
6'	130.27
Protons	
6'-H	7.79
2'-H	7.79
4'-H	7.46
5'-H	7.42
3'-H	7.42
9-H	7.37
7-H	7.26
6-H	7.19
8-H	7.10
4a-H	6.30
10-H	6.01
1-Hb	4.41
10a-H	4.40
1-Ha	3.83

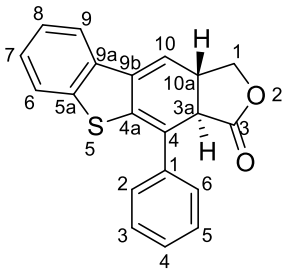


Table 2.8. Resonances for **2.24**

2.24	
	Calculated
Carbons	
1	66.73
3	169.31
3a	41.50
4	131.63
4a	138.71
5a	141.78
6	122.73
7	129.04
8	124.79
9	121.36
9a	132.48
9b	144.24
10	113.91
10a	42.12
1'	135.74
2'	128.93
3'	127.85
4'	128.30
5'	127.85
6'	128.93
Protons	
6'-H	7.54
2'-H	7.54
9-H	7.46
5'-H	7.40
3'-H	7.40
4'-H	7.35
7-H	7.25
6-H	7.21
8-H	7.12
10-H	6.44
1-Hb	4.29
1-Ha	4.02
3a-H	3.46
10a-H	3.40

2.6.7 Heating of 2.6 in DMF to Afford 2.8, 2.7, and 2.23

Rxn 1. An oven-dried NMR tube was charged with **2.5** (11 mg, 0.04 mmol) dissolved in o-DCB (0.5 mL, 0.08 M) under an atmosphere of air. The NMR tube was sealed with a polypropylene cap and lowered into a preheated oil bath at 150 °C. After 6 min, the reaction was paused for ^{1}H NMR analysis, and the NMR tube was rinsed with hexanes and wiped with a ChemWipe. **2.6** and **2.8** was afforded at a ratio of 95:5 as observed by No-D ^{1}H NMR. Ratios were determined by comparing the ^{1}H NMR resonance at 5.94 ppm (1H) for **2.6** to the resonance at 5.21 ppm (2H) for **2.8**. Solvent was removed under reduced pressure, and the crude residue was dissolved in DMF (0.5 mL). The solution was transferred to an oven-dried, 2-mL µW vial and capped with a Teflon-lined septum crimp cap. The vial was irradiated by microwave at 150 °C for 5 min. The solvent was removed by high vacuum and the crude residue was dissolved in chloroform-d. The solution was transferred to an oven-dried NMR tube and analyzed by ^{1}H NMR. A ratio of 18:52:30 (**2.8**:**2.7**:**2.23**) was afforded with residual DMF present. Ratios were determined by comparing the ^{1}H NMR resonance at 6.20 ppm (1H) for **2.23**, 5.45 ppm (2H) for **2.8**, and 3.40 ppm (1H) for **2.7**.

2.6.8 Under Aerobic Conditions, 2.6 Affords 2.8 at Room Temperature

Rxn 1. An oven-dried NMR tube was charged with **2.5** (20 mg, 0.06 mmol) dissolved in o-DCB (0.5 mL, 0.13 M) under an atmosphere of air. The NMR tube was sealed with a polypropylene cap and lowered into a preheated oil bath at 150 °C. After 10 min, the reaction was paused for ^{1}H NMR analysis, and the NMR tube was rinsed with hexanes and wiped with a ChemWipe. **2.6** and **2.8** was afforded at a ratio of 96:4 as observed by No-D ^{1}H NMR. Ratios were determined by comparing the ^{1}H NMR resonance at 3.90 ppm (1H) for **2.6** to the resonance at 5.21 ppm (2H) for

2.8. The solution was transferred to an oven-dried, 2-mL µW vial and capped with a Teflon-lined septum crimp cap and needle venting to the air. Air was bubbled through the solution. After 1 h, the solution was transferred to an oven-dried NMR tube for No-D ^{1}H NMR analysis. **2.8** was afforded exclusively**.**

2.6.9 Stability of 2.7 under Thermal and Aerobic Conditions

Rxn 1. An oven-dried NMR tube was charged with a mixture of **2.8** and **2.7** at a ratio of 31:69 (7 mg, 0.02 mmol) and mesitylene (1 µL, 0.01 µmol) dissolved in toluene-d_8 (0.5 mL, 0.13 M) under an atmosphere of air. Ratios were determined by comparing the ^{1}H NMR resonance at 4.51 ppm (2H) for **2.8** and 2.35 ppm (1H) for **2.7** to the resonance at 6.55 ppm (3H) for mesitylene. The NMR tube was sealed with a polypropylene cap and lowered into a preheated oil bath at 50 °C. After 2 h, the reaction was paused for ^{1}H NMR analysis, and the NMR tube was rinsed with hexanes and wiped with a ChemWipe. A ratio of 32:68 (**2.8:2.7**) was observed by crude ^{1}H NMR. The solution was lowered into a preheated oil bath at 80 °C. After 2 h, the reaction was paused for ^{1}H NMR analysis, and the NMR tube was rinsed with hexanes and wiped with a ChemWipe. A ratio of 32:68 (**2.8:2.7**) was observed by crude ^{1}H NMR. The solution was lowered into a preheated oil bath at 110 °C. After 2 h, the reaction was paused for ^{1}H NMR analysis, and the NMR tube was rinsed with hexanes and wiped with a ChemWipe. A ratio of 32:68 (**2.8:2.7**) was observed by crude ^{1}H NMR. The cap was removed, and air was bubbled through the solution at room temperature. After 2 h, the reaction was paused and a ratio of 32:68 (**2.8:2.7**) was observed by crude ^{1}H NMR analysis. The solution was lowered into a preheated oil bath at 80 °C and air was bubbled through the solution. After 2 h, the reaction was paused for ^{1}H NMR analysis, and the

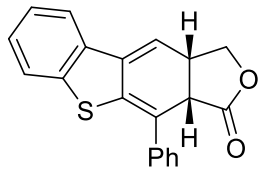
NMR tube was rinsed with hexanes and wiped with a ChemWipe. A ratio of 31:69 (**2.8:2.7**) was observed by crude ^{1}H NMR.

2.6.10 Heating of 2.5 in Acetonitrile to Afford 2.6, 2.23, 2.8, and 2.7

Rxn 1. An oven-dried, 0.5 mL microwave vial with stir bar was charged with **2.5** (12 mg, 0.04 mmol) dissolved in acetonitrile (0.5 mL 0.08 M). The vial was sealed with a Teflon-lined septum crimp cap and the solution was irradiated by microwave to 140 °C for 5 min. The solution was then transferred to a 25 mL round-bottom flask, and the solvent removed under reduced pressure to afford a yellow residue which was dissolved in chloroform-d under nitrogen. ^{1}H NMR in $CDCl_3$ showed a mixture of **2.8, 2.7, 2.6,** and **2.23** (10:22:51:17, respectively). Ratios were determined by comparing the ^{1}H NMR resonance at 6.28 ppm (1H) for **2.6**, 6.20 ppm (1H) for **2.23**, 5.45 ppm (2H) for **2.8**, and 3.44 ppm (1H) for **2.7**.

Rxn 2. An oven-dried, 0.5 mL microwave vial with stir bar was charged with **2.5** (11 mg, 0.03 mmol) dissolved in distilled acetonitrile that was stored over molecular sieves (type 4Å, 8-12 mesh beads, grade 514) which contained pulverized mole sieves that gave the solution a slight cloudy appearance. The vial was sealed with a Teflon-lined septum crimp cap and the solution was irradiated by microwave to 140 °C for 5 min. The solution was then transferred to a 25 mL round-bottom flask, and the solvent removed under reduced pressure to afford a yellow residue which was dissolved in chloroform-d under nitrogen. ^{1}H NMR in $CDCl_3$ showed a mixture of **2.8, 2.7, 2.6,** and **2.23** (6:41:7:46, respectively). Ratios were determined by comparing the ^{1}H NMR resonance at 6.28 ppm (1H) for **2.6**, 6.20 ppm (1H) for **2.23**, 5.45 ppm (2H) for **2.8**, and 3.44 ppm (1H) for **2.7**.

2.6.11 Synthesis of Cis-Diene



(3aS,10aS)-4-phenyl-3a,10a-dihydrobenzo[4,5]thieno[2,3-f]isobenzofuran-3(1H)-one (2.23). An oven-dried, 0.5 mL microwave vial with stir bar was charged with **2.5** (11 mg, 0.03 mmol) dissolved in distilled acetonitrile that was stored over molecular sieves (type 4Å, 8-12 mesh beads, grade 514) which contained pulverized mole sieves that gave the solution a slight cloudy appearance. The vial was sealed with a Teflon-lined septum crimp cap and the solution was irradiated by microwave to 140 °C for 5 min. The solution was then transferred to a 25 mL round-bottom flask, and the solvent removed under reduced pressure to afford a yellow residue. The residue was purified by silica gel flash column chromatography (100% DCM) to afford the product as a light-yellow solid (5 mg, 42%).

Data **2.23**

^{1}H NMR (600 MHz, $CDCl_3$)

7.69 (d, *J* = 7.8 Hz, 2H), 7.50 (d, *J* = 7.8 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 1H), 7.25 (q, *J* = 8.0, 14.3 Hz, 2H), 7.14 (dt, *J* = 1.9, 8.4 Hz, 1H), 6.19 (d, *J* = 3.7 Hz, 1H), 4.63 (dd, *J* = 5.7, 8.9 Hz, 1H), 4.54 (dd, *J* = 2.3, 9.1 Hz, 1H), 3.85 (m, 1H), 3.75 (d, *J* = 9.7 Hz, 1H) ppm. DCM impurity at 5.30 ppm. Water impurity at 1.56 ppm.

^{13}C NMR (125 MHz, $CDCl_3$)

176.7, 140.9, 140.7, 139.3, 133.8, 133.7, 129.8, 128.8 (2C), 128.0, 127.7 (2C), 125.1, 122.4, 121.8, 121.2, 116.2, 72.4, 45.3, 39.0 ppm

IR (thin film)

3482, 3060, 2908, 2252, 1765, 1589, 1494, 1449, 1372, 1197, 1151, 1090, 1028, 988, 909, 830, 764, 732, 697 cm^{-1}

HRMS (FTMS + p ESI)

$[M + H]^+$ calcd for $C_{20}H_{15}O_2S$: 319.07873, found 319.07817

317.06281 was also found in 50% relative abundance, indicative of formation of oxidation product **2.5** under ionization conditions

TLC R_f = 0.37 (100% DCM) [silica gel, UV]

2.6.12 Conversion of 2.23 to 2.8, 2.7, and Unknown at Room Temperature in $CDCl_3$

Rxn 1. An oven-dried NMR tube was charged with **2.23** (7 mg, 0.02 mmol) dissolved in $CDCl_3$ (0.5 mL, 0.04 M). The NMR tube was sealed with a polypropylene cap kept at room temperature for 3 weeks. The crude solution afforded a ratio of 25:34:29:12 (**2.23**:**2.8**:**2.7**:unknown). Ratios were determined by comparing the ^{1}H NMR resonance at 6.20 ppm (1H) for **2.23**, 5.45 ppm (2H) for **2.8**, 2.81 ppm (1H) for **2.7**, and 5.29 ppm for the unknown.

3.0 Factors that Determine Reactivity for the Dearomative DA Cycloaddition

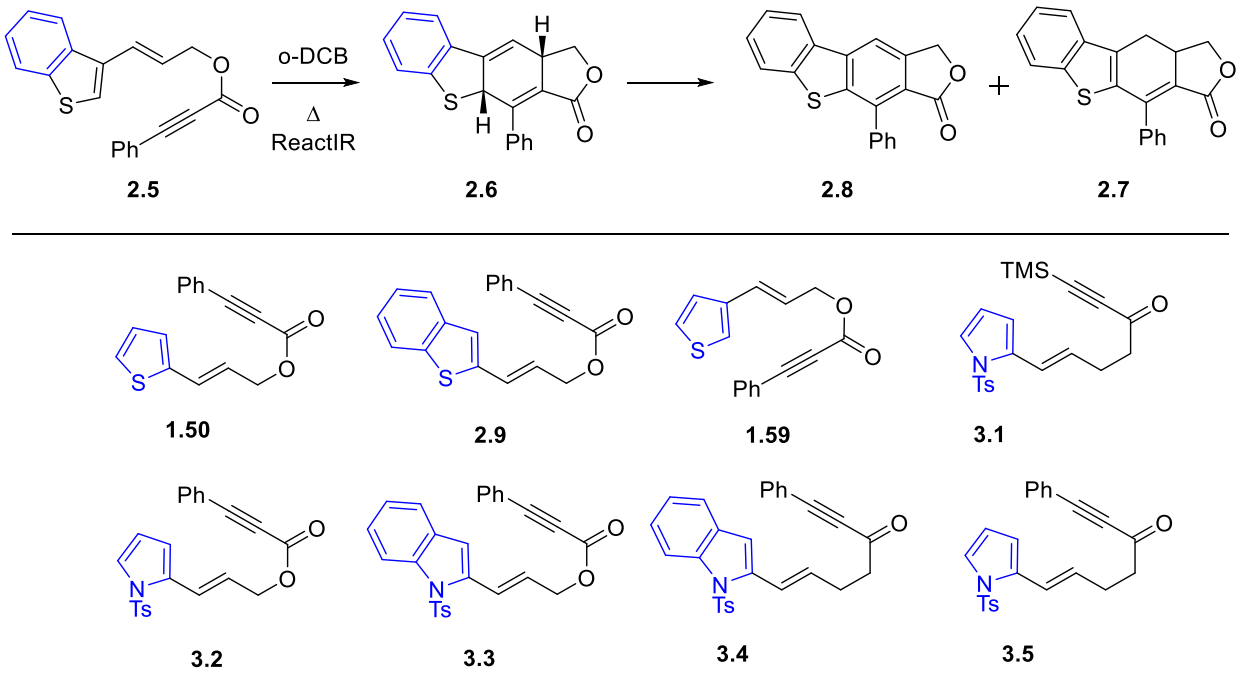
Having established the DA adduct as the result of the dearomative cycloaddition step and the intermediate to the oxidation and isomerization products, we were poised to investigate the substrate dependent factors that determine reactivity for the cycloaddition step. We launched a cooperative investigation utilizing reactivity data from experimental rate studies and computationally calculated energies from our collaboration with Professor Peng Liu's research group of the University of Pittsburgh. Correlation of our experimentally derived Gibbs free energies of activation with density functional theory (DFT) calculations provided insight into the mechanistic pathway of Dearomatization and the substrate dependent factors that determine reactivity.

This chapter is based on results presented in: Winkelbauer J. A.; Bober A. E.; Qi X.; Kusevska E.; Liu P.; Brummond K. M., Mechanisms and origin of reactivity of dearomative didehydro-Diels–Alder reactions of heteroarenes. Manuscript in preparation, submission expected 2021.

3.1 Determination of Reaction Rates and Half-Lives for Dearomative DDDA Precursors by In Situ Reaction Monitoring with ReactIR

To derive experimental reactivity data for the dearomative DDDA reaction, rate experiments monitored in situ by ReactIR were performed and the resulting data was evaluated to determine activation energy (E_a) and Gibbs free energies of activation ($\Delta G^{\ddagger}_{exp}$). Nine precursors

(**1.59**, **2.5**, **1.50**, **2.9**, **3.2**, **3.3**, **3.5**, **3.4**, and **3.1**) were selected based on results showing dearomative DDDA reactions that occurred in high yield and at a range of reaction temperatures. These precursors were selected to evaluate the impact of the heteroarene identity, tether functionality and position on the heteroarene, and group on the alkyne terminus on reactivity. Synthesis, ReactIR experiments, and determination of reaction rate constant and half-lives for the pyrrole and indole precursors were performed by Brummond Lab member Ashley Bober and are not described herein. Synthesis of the thiophene and benzothiophene precursors was performed by the same method as **2.5** described previously in chapter 2.1.



Scheme 3.1. Dearomative DDDA precursors selected for the reactivity study and analyzed by in situ ReactIR monitoring of reaction progress

A minimum of five separate experiments were conducted for each dearomative DDDA precursor with each experiment having a unique reaction temperature. The recorded temperature

is the internal temperature of the solution as measured by the ReactIR probe. For each series of reactions, the oil bath temperature was increased by an increment of 10 °C; however, the increase in the oil bath temperature did not translate to the internal reaction temperature. Thus, the actual temperature difference between each experiment in the series is between 5–15 °C. The consumption of starting material was measured by the disappearance of the absorption at ~1280 cm^{-1} which we propose may be the C-O bond stretching of the ester. Formation of oxidation and isomerization products was evidenced by the development of overlapping carbonyl absorptions at a higher frequency (~1760 cm^{-1}). The reaction was judged complete when the absorption at ~1280 cm^{-1} showed no change in intensity for at least 30 min. Complete disappearance of starting material was confirmed by TLC. A trend for the consumption of starting material was extracted using the iC IR 7.0 software and measured using peak height with a two-point baseline after solvent subtraction was applied. The trend data were exported to iC Kinetics 5.0 software, and the consumption of starting material vs. time data was plotted using GraphPad Prism 7.0. The half-lives and rate constants for each of the reactions were determined with GraphPad from a best-fit curve by plotting absorption intensity in arbitrary units relative to time in minutes (Figure 3.1). The data included by the best-fit curve contained 4-5 half-lives for each reaction. The selected reaction rate was first-order in substrate and an exponential one-phase decay nonlinear regression was applied to the data set, using a least square fit analysis. The half-lives and reaction rate constants for each experiment are reported in Table 3.1.

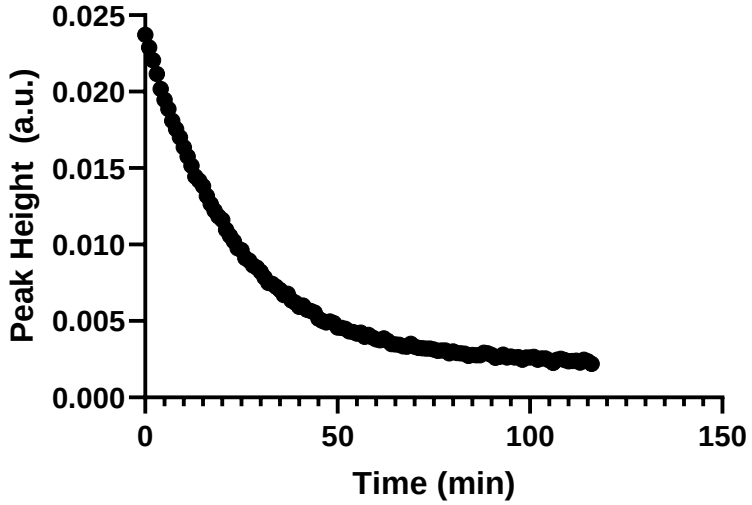
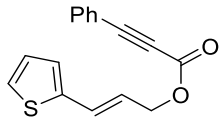
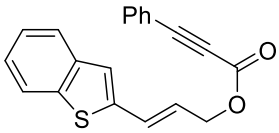
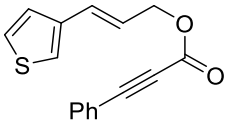
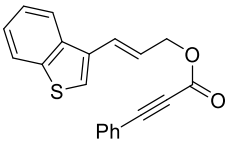


Figure 3.1. 1st order exponential decay of **2.5** at 90 °C

Table 3.1. Measured half-lives and rate constants for the dearomative DDDA reaction of the thiophene and benzothiophene precursors

Precursor	Entry	T (°C)	$t_{1/2}$ (min)	k (s^{-1})
 **1.50**	1	77	154	7.49E-05
	2	86	47	2.44E-04
	3	94	28	4.16E-04
	4	108	12	9.31E-04
	5	119	6	2.06E-03
 **2.9**	6	76	140	8.23E-05
	7	85	63	1.83E-04
	8	95	23	5.06E-04
	9	108	13	9.04E-04
	10	113	8	1.36E-03
 **1.59**	11	88	91	1.27E-04
	12	98	43	2.68E-04
	13	109	16	7.41E-04
	14	121	7	1.63E-03
	15	132	4	3.20E-03
 **2.5**	16	73	58	1.98E-04
	17	81	28	4.09E-04
	18	90	16	7.18E-04
	19	96	9	1.28E-03
	20	106	5	2.40E-03

T – temperature
$t_{1/2}$ – half-life
k – rate constant

3.2 Determination of Activation Energy and Pre-Exponential Factor via the Arrhenius Equation

To determine the DDDA activation energy (E_a) and pre-exponential factor (A) for each precursor, an Arrhenius plot was generated by plotting ln(k) against 1/T where k is the reaction rate constant in inverse seconds and T is the temperature in Kelvin.

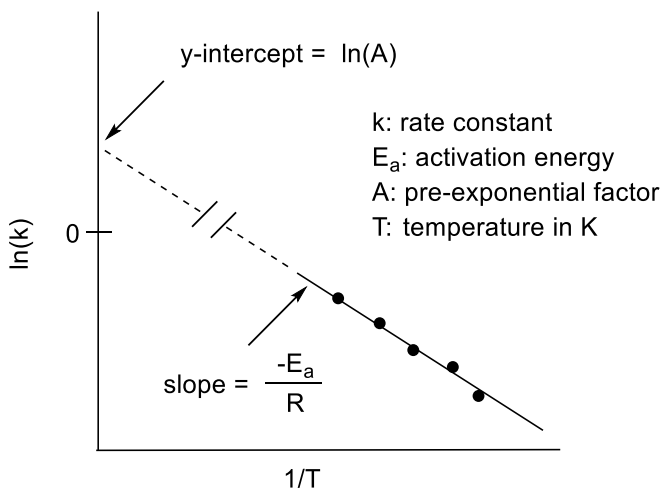


Figure 3.2. Representative Arrhenius plot and its relation to the Arrhenius equation

The Arrhenius plot afforded a trendline for the data with equation y = m • x + b (eq 3.1) where m is the slope of the line and b is the y-intercept. The trendline for the Arrhenius plot was generated by a linear regression analysis using the LINEST function in Microsoft Excel. The

LINEST function calculates a straight line that best fits our data by using the least squares method. The *const* value was set to TRUE so that the y-intercept would not be forced to equal zero. The *stats* value was set to TRUE so that the function output would include the linear regression statistics. The components of the trendline generated through the LINEST function include the slope, standard error for the slope, y-intercept, standard error for the y-intercept, R^2, and the y estimate standard error.

Equation 3.1. Arrhenius plot line equation

$$y = m \cdot x + b$$

where: $y = \ln(k)$; $m = \text{slope} = -E_a/R$; $x = 1/T$; $b = \text{y-intercept} = \ln(A)$

We related eq 3.1 to the linear form of the Arrhenius equation $\ln(k) = -E_a/(R \cdot T) + \ln(A)$ (eq 3.2) where E_a is the activation energy in kcal/mol, R is the gas constant 0.001987 kcal/(mol•K), and A is the pre-exponential factor for the reaction in inverse seconds.

Equation 3.2. Linear form of the Arrhenius equation

$$\ln(k) = -E_a/(R \cdot T) + \ln(A)$$

Equation 3.3. Activation energy

$$E_a = -m \cdot R$$

Equation 3.4. Pre-exponential value

$$A = e^b$$

Equation 3.5. Rate of reaction at 363 K

$$k_{363} = e^{(m \cdot (1/363) + b)}$$

The error for E_a was calculated by substituting the slope with the slope error value, and the error for A was calculated by substituting the y-intercept with the y-intercept error value.

Equation 3.6. Error for activation energy

$$E_{a\ error} = -m_{error} \bullet R$$

Equation 3.7. Error for pre-exponential value

$$A_{error} = e^{b\ error}$$

The activation energy, pre-exponential value, and the error for both were determined by these same methods for each dearomative DDDA precursor. Rate constants at 363 K were derived from the trendline as a means to compare rate constants across substrates. 363 K was chosen as a median temperature across all reaction temperatures.

Table 3.2. Arrhenius trendline components as derived from the LINEST function and the kinetic results derived from the trendline for each substrate

	1.50	**2.9**	**1.59**	**2.5**	**3.2**	**3.3**	**3.5**	**3.4**	**3.1**
Slope	-10229	-10016	-10881	-9886	-13397	-11653	-12837	-9248	-10028
Slope Standard Error	844	715	329	333	757	517	912	1025	837
Y-Intercept	20.0	19.4	21.2	20.1	31.0	26.4	28.0	18.1	18.2
Y-Intercept Standard Error	2.3	1.9	0.9	0.9	2.2	1.5	2.5	2.8	2.3
R^2	0.980	0.985	0.997	0.997	0.987	0.994	0.980	0.953	0.980
Y Estimate Standard Error	0.21	0.16	0.08	0.07	0.20	0.11	0.17	0.20	0.15
k_{363} (s^{-1})	2.68E-04	2.73E-04	1.51E-04	7.74E-04	2.70E-03	3.46E-03	6.33E-04	6.03E-04	8.39E-05
E_a (kcal/mol)	20.3	19.9	21.6	19.6	26.62	23.16	25.51	18.38	19.93
$E_{a\ error}$ (kcal/mol)	± 1.7	± 1.4	± 0.7	± 0.7	± 1.5	± 1.0	± 1.8	± 2.0	± 1.7
A (s^{-1})	4.63E+08	2.63E+08	1.57E+09	5.20E+08	2.88E+13	3.02E+11	1.44E+12	6.99E+07	8.34E+07
A_{error} (s^{-1})	± 9.8	± 7.0	± 2.4	± 2.5	± 9.1	± 4.5	± 12.6	± 17.0	± 10.3

3.3 Determination of Gibbs Free Energy of Activation, Enthalpy, and Entropy via the Eyring Equation

To determine the Gibbs free energy of activation, enthalpy, and entropy for each precursor, an Eyring plot was generated by plotting $\ln(k \bullet h/(k_B \bullet T))$ against 1/T where k is the rate of the reaction in inverse seconds, h is Planck's constant = 6.63×10^{-34} J • s, k_B is Boltzmann's constant = 1.38×10^{-23} J • K^{-1} and T is the temperature in Kelvin.

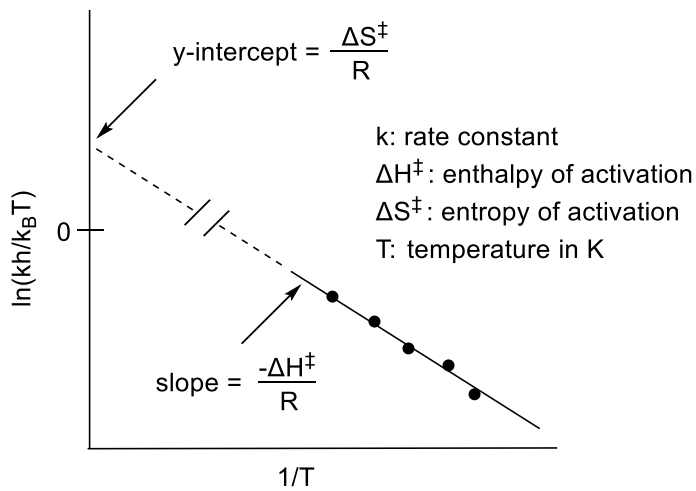


Figure 3.3. Representative Eyring plot and its relation to the Eyring equation

The Eyring plot affords a trendline for the data using the linear equation eq 3.8. Just as performed for the Arrhenius plots, the trendline for the Eyring plot was generated by a linear regression analysis using the LINEST function in Microsoft Excel. The LINEST function was set with the same parameters and output the same components of the trendline.

Equation 3.8. Eyring plot line equation

$$y = m \cdot x + b$$

where: $y = \ln(k \cdot h/(k_B \cdot T))$; m = slope = $-\Delta H^{\ddagger}/R$; $x = 1/T$; b = y-intercept = $\Delta S^{\ddagger}/R$

We related eq 3.8 to the linear form of the Eyring equation $\ln(k \cdot h/(k_B \cdot T)) = -\Delta H^{\ddagger}/(R \cdot T) + \Delta S^{\ddagger}/R$ (eq 3.9) where $\Delta H^{\ddagger}$ is the enthalpy of the reaction in kcal/mol, R is the gas constant 0.001987 kcal/(mol • K), and $\Delta S^{\ddagger}$ is entropy of the reaction in kcal/mol.

Equation 3.9. Linear form of the Eyring equation

$$\ln(k \cdot h/(k_B \cdot T)) = -\Delta H^{\ddagger}/RT + \Delta S^{\ddagger}/R$$

Equation 3.10. Enthalpy

$$\Delta H^{\ddagger} = -m \cdot R$$

Equation 3.11. Entropy

$$\Delta S^{\ddagger} = b \cdot R$$

Equation 3.12. Rate of reaction at 363 K

$$k_{363} = k_B \cdot T \cdot e^{(m \cdot (1/363) + b)} / h$$

The error for $\Delta H^{\ddagger}$ can be calculated by substituting the slope with the slope error, and the error for $\Delta S^{\ddagger}$ can be calculated by substituting the y-intercept with the y-intercept error.

Equation 3.13. Error for enthalpy

$$\Delta H^{\ddagger}_{error} = -m_{error} \cdot R$$

Equation 3.14. Error for entropy

$$\Delta S^{\ddagger}_{error} = b_{error} \cdot R$$

Gibbs free energy of activation can be calculated with the equation $\Delta G^{\ddagger} = \Delta H^{\ddagger} - \Delta S^{\ddagger}T$ (eq 3.15) at 363 K.

Equation 3.15. Gibbs free energy of activation

$$\Delta G^{\ddagger} = \Delta H^{\ddagger} - \Delta S^{\ddagger} \bullet T$$

The error for $\Delta G^{\ddagger}$ can be calculated by substituting $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ with the error for $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ at 363 K. Propagation of error through the result of a subtraction is done through quadrature.

Equation 3.16. Error for Gibbs free energy of activation

$$\Delta G^{\ddagger}_{error} = \Delta H^{\ddagger}_{error} - \Delta S^{\ddagger}_{error} \bullet T$$

Equation 3.17. Quadrature to calculate error for Gibbs free energy of activation

$$\Delta G^{\ddagger}_{error} = \sqrt{((\Delta H^{\ddagger}_{error})^2 + (\Delta S^{\ddagger}_{error} \bullet T)^2)}$$

The Gibbs free energy of activation, enthalpy, entropy, and the error for each were determined by these same methods for each dearomative DDDA precursor. Rate constants at 363 K as derived from the Eyring plot trendline remain unchanged and consistent to those derived from the Arrhenius plot trendline.

Table 3.3. Eyring trendline slope, y-intercept, and R^2 as derived from the LINEST function and the $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$, and $\Delta G^{\ddagger}$ values with their corresponding error

	1.50	**2.9**	**1.59**	**2.5**	**3.2**	**3.3**	**3.5**	**3.4**	**3.1**
Slope	-9859	-9649	-10499	-9524	-13053	-11309	-12475	-8882	-9668
Slope Standard Error	846	717	331	333	756	518	911	1027	837
Y-Intercept	-10.7	-11.3	-9.5	-10.6	0.4	-4.2	-2.7	-12.6	-12.4
Y-Intercept Standard Error	2.29	1.95	0.87	0.92	2.21	1.51	2.53	2.84	2.33
R^2	0.978	0.984	0.997	0.996	0.987	0.994	0.979	0.949	0.978
Y Estimate Standard Error	0.21	0.16	0.08	0.07	0.20	0.11	0.17	0.20	0.15
k_{363} (s^{-1})	2.68E-04	2.73E-04	1.51E-04	7.74E-04	1.65E-03	2.70E-03	3.46E-03	6.33E-04	6.03E-04
$\Delta H^{\ddagger}$ (kcal/mol)	19.6	19.2	20.9	18.9	25.9	22.5	24.8	17.7	19.2
$\Delta H^{\ddagger}_{error}$ (kcal/mol)	± 1.7	± 1.4	± 0.7	± 0.7	± 1.5	± 1.0	± 1.8	± 2.0	± 1.7
$\Delta S^{\ddagger}$ (kcal/mol)	-2.10E-02	-2.20E-02	-1.90E-02	-2.10E-02	7.75E-04	-8.28E-03	-5.27E-03	-2.50E-02	-2.47E-02
$\Delta S^{\ddagger}_{error}$ (kcal/mol)	± 4.60E-03	± 3.90E-03	±1.70E-03	±1.80E-03	± 4.39E-03	± 3.00E-03	± 5.04E-03	± 5.63E-03	± 4.63E-03
$\Delta G^{\ddagger}$ (kcal/mol)	27.3	27.3	27.7	26.6	25.7	25.5	26.7	26.7	28.2
$\Delta G^{\ddagger}_{error}$ (kcal/mol)	± 2.4	± 2.0	± 0.9	± 0.9	± 2.2	± 1.5	± 2.6	± 2.9	± 2.4

3.4 Analysis of Reactivity in Collaboration with DFT Computational Calculations

With experimental reactivity and rate data in hand, we sought to correlate our data with DFT computational calculations in order to derive the most likely mechanism of the dearomative cycloaddition step of the DDDA reaction, as well as determine which substrate dependent factors affect reactivity. All DFT computational calculations were performed by our collaborators Xiaotian Qi, Elena Kusevska, and Professor Peng Liu of the University of Pittsburgh.

3.4.1 Determination of the Dearomative Cycloaddition Mechanism

The thermal dearomative step of the DDDA reaction between the heterarenyl diene and the alkynyl dienophile is one that involves an initial [4 + 2] cycloaddition step to afford a 1,4-cyclohexadienyl intermediate. Mechanistically, the cycloaddition step may proceed via a concerted pathway with a six-membered, cyclic transition state or a stepwise pathway via a diradical intermediate (Figure 3.4).

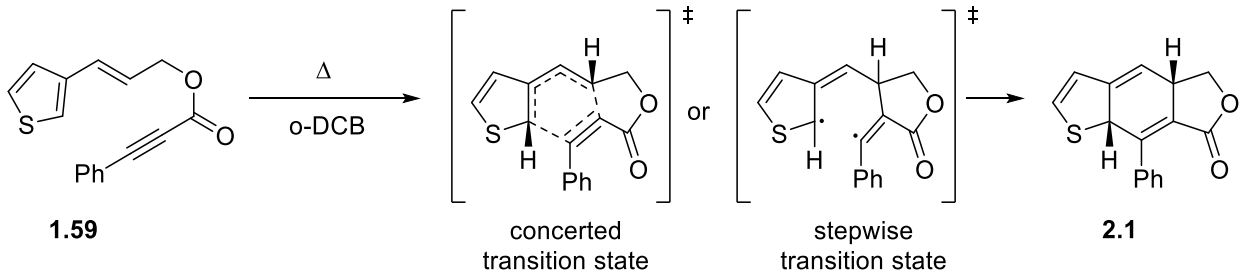


Figure 3.4. Proposed concerted and stepwise transition states as possible mechanisms for the dearomative cycloaddition step

We proposed that correlating the computed Gibbs free energies of activation ($\Delta G^{\ddagger}_{comp}$) for the concerted and stepwise transition states with experimentally derived $\Delta G^{\ddagger}_{exp}$ would help to elucidate the preferred mechanism. The $\Delta G^{\ddagger}_{comp}$ for both the stepwise and concerted reaction pathways were calculated for all nine DDDA precursors. M06-2X/6-311+G(d,p) single point energies were derived with both M06-2X/6-31+G(d) and B3LYP/6-31+G(d) structure optimization, and B3LYP/6-311+G(d,p) single point energies were derived with B3LYP/6-31+G(d) structure optimization. The SMD solvation model with o-DCB as the chosen solvent was used for the geometry optimizations as well as the single point energy calculations to match the experimental solvent. The computational Gibbs free energies of activation also include a thermal correction to 363 K which was the median experimental temperature. Example structure optimizations of **1.59** and the concerted and stepwise transition states with both M06-2X/6-31+G(d) and B3LYP/6-31+G(d) structure optimization are shown (Figure 3.5).

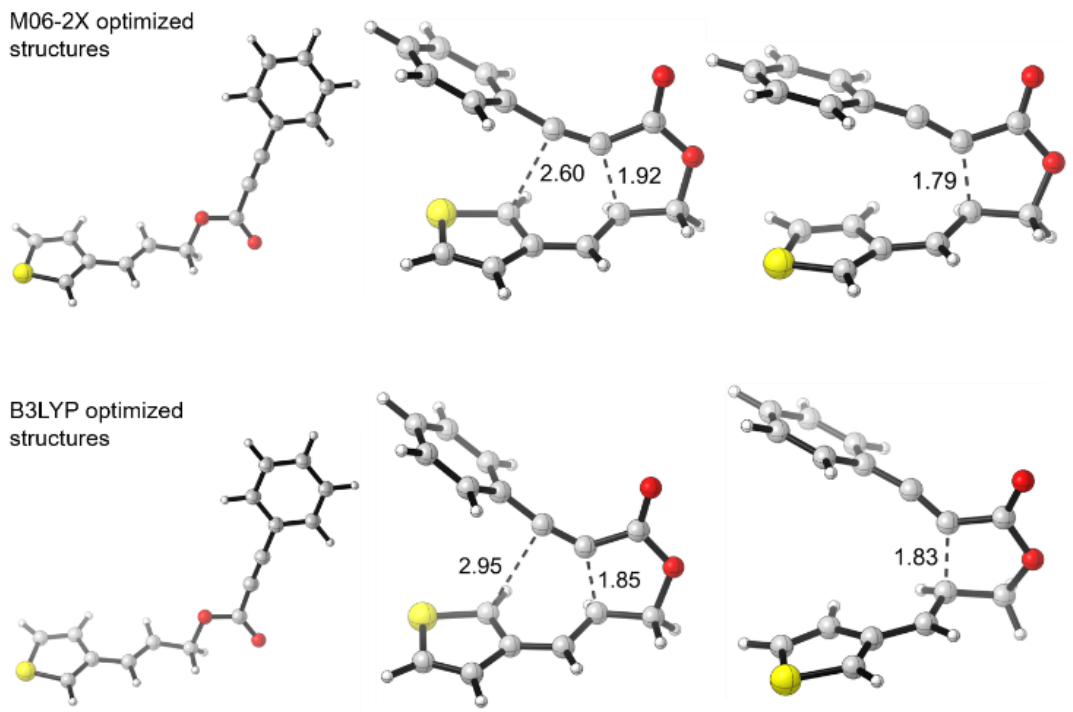


Figure 3.5. Structures of **1.59**, the concerted transition state¸ and the stepwise transition state for the cycloaddition step of the dearomative DDDA reaction with structures optimized by M06-2X/6-31+G(d) and B3LYP/6-31+G(d). Bond distances shown in angstroms.

The closed-shell transition state with the s-cis conformer of the vinyl heteroarene, utilized in the concerted pathway, was located for each dearomative DDDA precursor. The open-shell transition state with the s-trans conformer of the vinyl heteroarene, utilized in the stepwise pathway, was not able to be located for **1.50**, **2.9**, **3.5**, or **3.1** for the M06-2X/6-311+G(d,p) single point energies with M06-2X/6-31+G(d) geometry optimizations. The s-trans open-shell transition state was not able to be located for **3.4** at any of the attempted levels of theory. The s-cis open-shell transition state was also considered but could not be located at either level of theory for all precursors. For these cases where the transition states were not able to be located, the geometry would collapse to the s-cis closed-shell transition state, suggesting that they do not exist as

stationary points on the potential energy surfaces for the dearomative DDDA reactions. The Gibbs free energies of activation for all precursors are summarized in Table 3.4.

Table 3.4. DFT computationally derived Gibbs free energies of activation for the s-cis closed-shell and s-trans open-shell transition states

	1.50	**2.9**	**1.59**	**2.5**	**3.2**	**3.3**	**3.5**	**3.4**	**3.1**
experimental $\Delta G^{\ddagger}$ (kcal/mol)	27.3	27.3	27.7	26.6	25.7	25.5	26.7	26.7	28.2
$\Delta G^{\ddagger}$ s-cis closed-shell (kcal/mol)									
B3LYP/6-311+G(d,p)//B3LYP/6-31+G(d)	32.4	32.2	33.1	30.6	30.6	30.2	34.7	30.9	34.7
M06-2X/6-311+G(d,p)//M06-2X/6-31+G(d)	30.2	28.8	30.2	28.8	29.2	26.2	28.1	28.3	29.5
M06-2X/6-311+G(d,p)//B3LYP/6-31+G(d)	32.0	31.0	31.2	28.2	29.9	30.2	32.1	29.4	31.4
$\Delta G^{\ddagger}$ s-trans open-shell (kcal/mol)									
B3LYP/6-311+G(d,p)//B3LYP/6-31+G(d)	30.2	30.9	33.0	33.3	36.5	35.8	44.0	-	44.0
M06-2X/6-311+G(d,p)//M06-2X/6-31+G(d)	-	-	33.2	35.3	36.6	33.9	-	-	-
M06-2X/6-311+G(d,p)//B3LYP/6-31+G(d)	32.1	32.9	34.7	35.0	38.6	35.8	40.0	-	44.4

The mechanism of the dearomative cycloaddition was determined to be the concerted pathway due to the s-cis closed-shell transition state being lower in energy than the open-shell transition states for all precursors. Additionally, the concerted pathway had a smaller average deviation of computed activation energies from the experimentally derived activation free energies than the stepwise pathway at the M06-2X/6-311+G(d,p)//B3LYP/6-31+G(d) level of theory. The average deviations were 3.7 and 9.8 kcal/mol for the concerted and stepwise pathways, respectively. The closed-shell and open-shell transition states were compared with the M06-2X/6-311+G(d,p) single point energies and B3LYP/6-31+G(d) geometry optimizations as the M06-2X/6-311+G(d,p) single point energies include dispersion corrections that B3LYP/6-311+G(d,p) lacks, and several open-shell transition states were not able to be located with M06-2X/6-31+G(d) geometry optimizations.

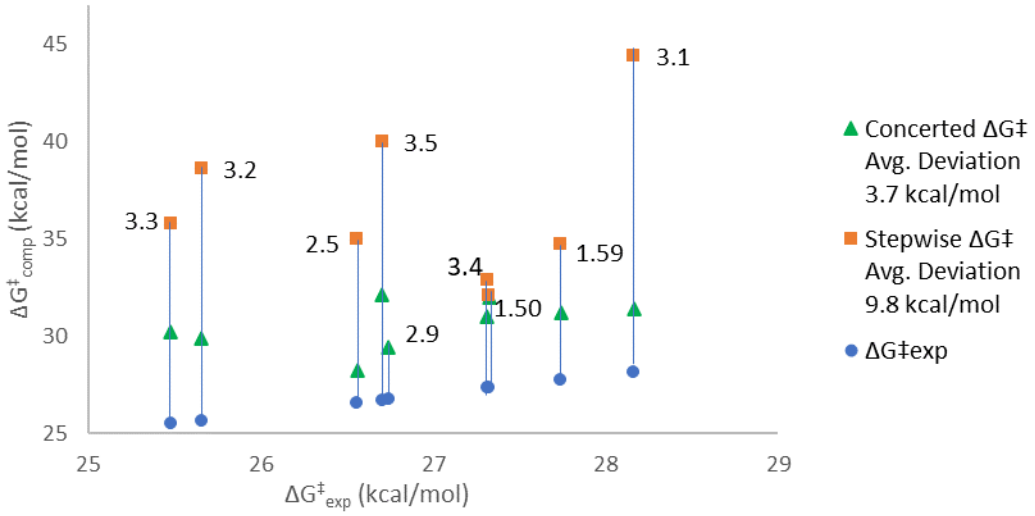


Figure 3.6. Average deviation of computational Gibbs free energies of activation from experimental energies for both the concerted and stepwise reaction pathways at the M06-2X/6-311+G(d,p)//B3LYP/6-31+G(d) level of theory

Analysis of the newly formed bond lengths in the concerted pathway for the dearomative cycloaddition step led to the discovery that the mechanism proceeds through an early and highly asynchronous concerted transition state. The degree of asynchronicity of the transition state was observed by the measurement of the newly forming bond lengths. These lengths were compared for both the M06-2X/6-31+G(d) and B3LYP/6-31+G(d) structure optimizations and are summarized in Table 3.5. Both levels of theory showed that the bond length for lactone formation was significantly shorter than the bond length between the heteroarene and the alkyne, indicative of the highly asynchronous concerted dearomative DDDA transition state (Figure 3.5). Overall, the M06-2X/6-31+G(d) level of theory showed a more synchronous TS structure with a difference in bond lengths of 0.53–0.81 Å compared to the B3LYP/6-31+G(d) level of theory which showed a difference in bond lengths of 0.88–1.32 Å. The B3LYP/6-31+G(d) level of theory lacks an accurate description for dispersion forces which may be responsible for the predicted longer bond forming distances between the heteroarene and the alkyne. The bond length differences found with the M06-2X/6-31+G(d) level of theory are comparable to the differences in bond length of ~0.8 Å found in the concerted asynchronous transitions state for the styryl Diels−Alder reactions.[49] This early transition state leads to less distortion of the heteroarene and a relatively small decrease of aromaticity from the precursor suggesting that substrate dependent factors such as aromaticity and electronic properties may have a reduced impact on reactivity.

Table 3.5. Newly forming bond lengths in the asynchronous, concerted transition state of the dearomative cycloaddition step

	1.50	**2.9**	**1.59**	**2.5**	**3.2**	**3.3**	**3.5**	**3.4**	**3.1**
1st formed bond length M06-2X/6-31+G(d) (Å)	1.88	1.94	1.92	1.94	1.88	1.95	1.92	1.98	1.95
2nd formed bond length M06-2X/6-31+G(d) (Å)	2.65	2.64	2.60	2.62	2.69	2.64	2.56	2.51	2.48
1st formed bond length B3LYP/6-31+G(d) (Å)	1.82	1.85	1.85	1.89	1.83	1.87	1.85	1.89	1.86
2nd formed bond length B3LYP/6-31+G(d) (Å)	3.14	3.14	2.95	2.94	3.15	3.08	2.97	2.93	2.74

3.4.2 Gibbs Free Energies of Activation at the M06-2X/6-311+G(d,p)//M06-2X/6-31+G(d) Level of Theory as the Most Accurate to Experimental Energies

With the asynchronous, concerted reaction pathway as the proposed mechanism for the dearomative cycloaddition, we then sought to evaluate which level of theory would afford computational Gibbs free energies of activation ($\Delta G^{\ddagger}_{comp}$) that would be the most accurate to experimental energies ($\Delta G^{\ddagger}_{exp}$) and thus the best predictive tool (Figure 3.7). The M06-2X/6-311+G(d,p)//M06-2X/6-31+G(d) level of theory provided the best agreement to experiments with an average overestimation from $\Delta G^{\ddagger}_{exp}$ of 2.0 kcal/mol and had a moderate correlation to $\Delta G^{\ddagger}_{exp}$ (R^2 = 0.48). The B3LYP/6-311+G(d,p)//B3LYP/6-31+G(d) level of theory provided a worse agreement to experiments with an average overestimation from $\Delta G^{\ddagger}_{exp}$ of 5.3 kcal/mol yet had significantly improved correlation to $\Delta G^{\ddagger}_{exp}$ (R^2 = 0.84) when **3.5** was removed as an outlier. The M06-2X/6-311+G(d,p)//B3LYP/6-31+G(d) level of theory provided an average overestimation from $\Delta G^{\ddagger}_{exp}$ of 3.7 kcal/mol and had a poor correlation to $\Delta G^{\ddagger}_{exp}$ (R^2 = 0.23). Overall, the M06-2X/6-311+G(d,p)//M06-2X/6-31+G(d) level of theory was established to be a more reliable level of theory for prediction of the absolute activation energies of the concerted dearomative cycloaddition. However, the B3LYP/6-311+G(d,p)//B3LYP/6-31+G(d) level of theory can still be used to predict the relative reactivity trend of different precursors.

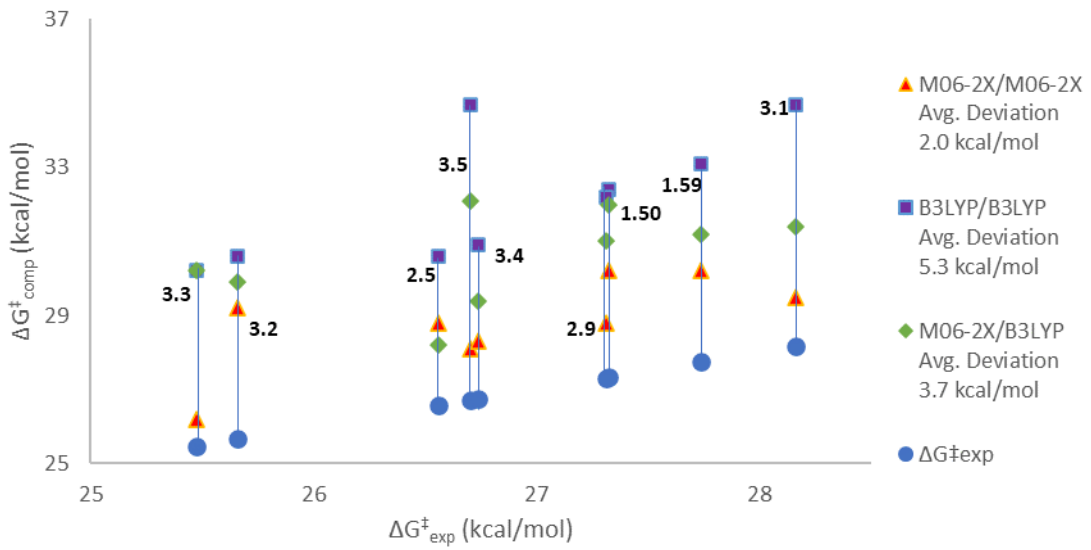
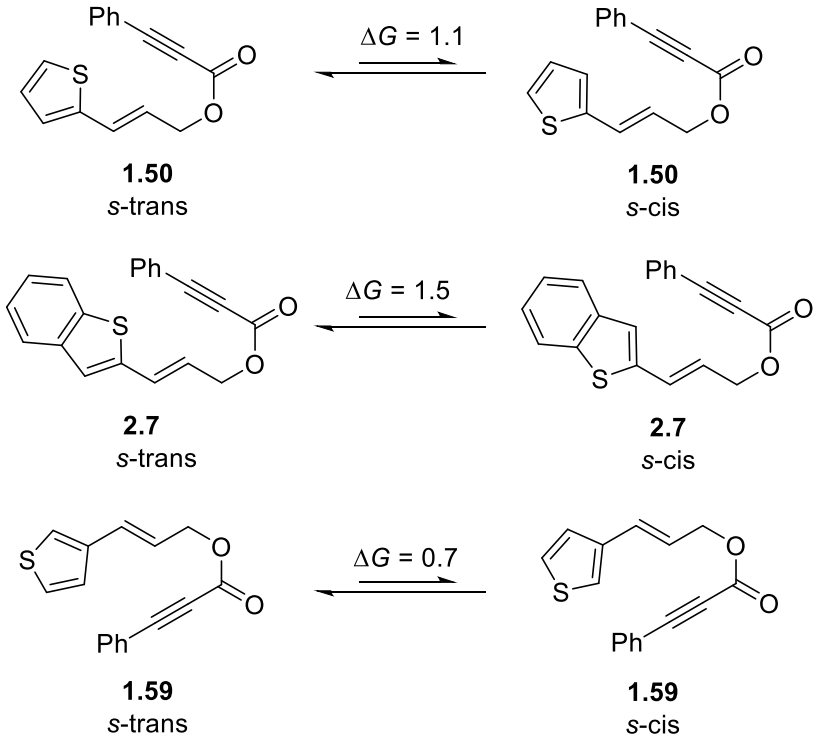


Figure 3.7. Comparison of different levels of theories used to calculate $\Delta G^{\ddagger}_{comp}$ and their accuracy to $\Delta G^{\ddagger}_{exp}$.

3.4.3 The Effect of Ground State Conformations on the Reactivity of the Dearomative Cycloaddition Step

We next sought to determine the substrate dependent factors that contribute to reactivity. The first to be evaluated was the energy required to access the reactive s-cis conformation of the vinyl heteroarene. M06-2X/6-31+G(d) geometry optimizations of the dearomative DDDA precursors were analyzed to determine the lowest energy rotamer for the precursors studied. Most afforded the *s*-cis rotamer as the lowest energy conformer in the ground state. The exceptions being **1.50**, **2.9**, and **1.59** for which the *s*-trans rotamer is 1.1, 1.5, and 0.7 kcal/mol more stable than the corresponding *s*-cis rotamer, respectively (Scheme 3.2). Therefore, the energy required to attain the reactive s-cis conformation from the unreactive s-trans does contribute to the overall energy barrier of the dearomative cycloaddition. This additional required energy is not present for the other dearomative DDDA precursors, thus **1.50**, **2.9**, and **1.59** have consequentially higher Gibbs free energies of activation than the other substrates.



Scheme 3.2. Rotational energy barriers required to attain the reactive *s*-cis conformer for precursors **1.50**, **2.9**, and **1.59**

3.4.4 Stabilizing Dispersion Interactions in the Dearomative Cycloaddition Transition States

Experimentally, the precursors with phenyl substitution on the terminus of the alkyne are more reactive than **3.1** with TMS substitution on the terminus of the alkyne. This result may be indicative of a π/π-stacking type interaction occurring between the heteroarene and the phenyl on the terminus of the alkyne. The relatively long forming C–C bond distances in the asynchronous, concerted transition state place the arene rings at a distance where the stacking would be possible. Cooperative dispersion interactions between dienes and dienophiles in the transition state have

been shown in previous studies by Houk et al to increase stabilization by up to 10 kcal/mol in Diels−Alder reactions.[60] To investigate these effects in our dearomative cycloaddition, London dispersion energies (ΔE_{disp}) between the heteroarene and the phenyl group in the transition state were calculated. The dispersion energy in the transition state for **3.1** (ΔE_{disp} = -12.9 kcal/mol) was found to be less stabilizing than that of **3.5** (ΔE_{disp} = -16.7 kcal/mol) by 3.8 kcal/mol. Though the calculated dispersion energies follow the reactivity trend, the lower reactivity of **3.1** may also be due to destabilizing steric interactions between the TMS group and the heteroarene rather than a lack of π-stabilizing interactions in the transition state.

Therefore, the dispersion interaction in the transition state of **2.9** was contrasted with an analogous concerted transition state of **2.9** containing a methyl substituted alkyne **2.9-Me** rather than the phenyl substitution (Figure 3.8). ΔE_{disp} between the highlighted heteroarene and phenyl moieties in the transition state of **2.9** was calculated to be –15.2 kcal/mol which was 4.2 kcal/mol higher than that of the analogous transition state with the methyl substituted alkyne (ΔE_{disp} = -11.0 kcal/mol). These results demonstrate the stabilizing dispersion interactions present between the heteroarene and the phenyl terminus of the alkyne.

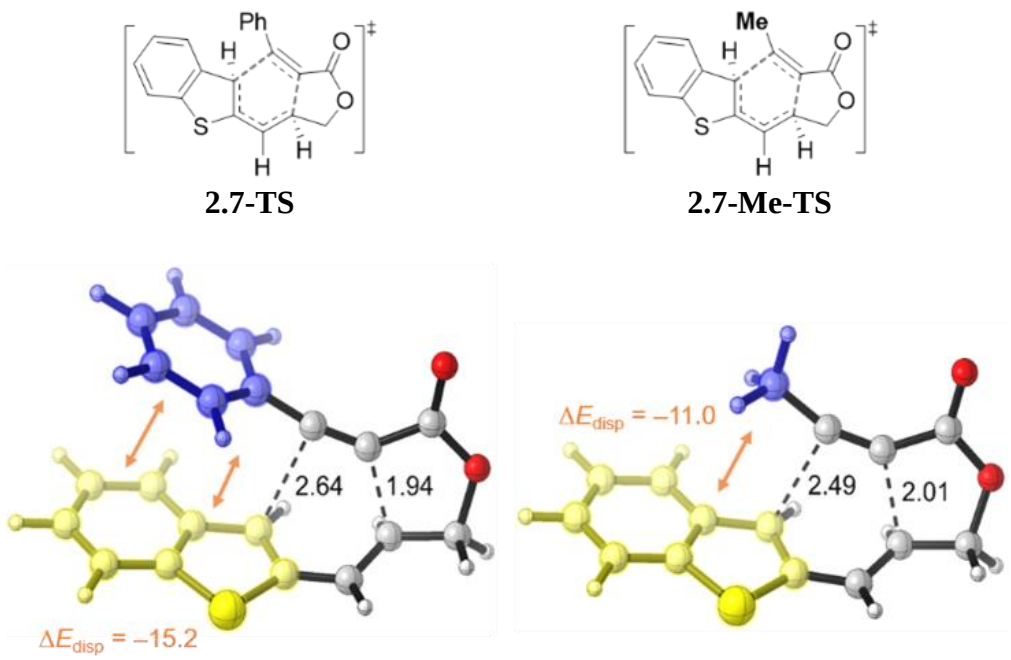


Figure 3.8. Dispersion effect on the stabilization of the concerted cycloaddition transition state

Optimized structures of transition states also show that there is a more favored π-π stacking interaction between the phenyl alkyne terminus and the benzo-fused heteroarenes in comparison to the non-benzo-fused heteroarenes. In each case, the benzo-fused precursors afforded transition states with greater stabilizing dispersion energies than their non-benzo-fused counterparts. **2.9**, **2.5**, **3.3**, and **3.4** (-15.2, -12.0, -21.1, and -21.3 kcal/mol) each had a dispersion stabilization energy that was lower than the non-benzo-fused **1.50**, **1.59**, **3.2**, and **3.5** (-11.0, -11.7, -16.1, and -16.7 kcal/mol) respectively. The presence of the benzene fused to the heteroarene likely affords an increase in the stabilizing π-π stacking interaction.

3.4.5 Effect of Heteroarene Aromaticity on Reactivity of the Dearomative Cycloaddition

To determine the effect that aromaticity of the heteroarene has on the reactivity of the dearomative cycloaddition, experimentally derived Gibbs free energies of activation were compared to the computationally derived aromaticity of the heteroarenes. Aromaticity was calculated using nucleus-independent chemicals shift (NICS) which is the negative of the magnetic shielding at a given point, using the NICS(1)zz method. The NICS(1)zz values were calculated by the placement of a ghost atom 1 Å above the heterocyclic ring for each precursor and their respective concerted transition state. These aromaticity calculations are summarized in Table 3.6. The NICS(1)zz values of the dearomative cycloaddition precursors are close to those of their respective transition states, indicative of a relatively small decrease of aromaticity of the heteroarene in the transition states. This is consistent with the proposed early, asynchronous transition state where the forming C-C bond between the heteroarene and the alkyne is longer than that of the forming lactone C-C bond.

Table 3.6. NICS(1)zz aromaticity of the heteroarene for the dearomative cycloaddition precursors and transition states

	1.50	**2.9**	**1.59**	**2.5**	**3.2**	**3.3**	**3.5**	**3.4**	**3.1**
experimental $\Delta G^{\ddagger}$ (kcal/mol)	27.3	27.3	27.7	26.6	25.7	25.5	26.7	26.7	28.2
experimental $\Delta G^{\ddagger}_{exp(s\text{-}cis)}$ (kcal/mol)	26.2	25.8	27.0	26.6	25.7	25.5	26.7	26.7	28.2
precursor NICS(1)zz (ppm) M06-2X/M06-2X	-27.8	-21.8	-28.8	-25.1	-25.1	-20.7	-25.8	-20.0	-25.5
transition state NICS(1)zz (ppm) M06-2X/M06-2X	-28.0	-20.8	-29.0	-22.8	-24.0	-17.9	-23.2	-16.3	-23.5

We then sought to isolate the contribution that heteroarene aromaticity had on the Gibbs free energy of activation to see the effect of aromaticity on reactivity. Tether composition affects the Gibbs free energy of activation due to the additional conformational mobility of a ketone-tethered precursor over that of an ester-tethered precursor. Therefore, only ester-tethered substrates were considered to eliminate this contribution in our analysis. As described previously, the ground state conformer for the precursors is the reactive s-cis conformation for all substrates except **2.9**, **1.50**, and **1.59** which have the s-trans conformation. Therefore, the $\Delta G^{\ddagger}_{exp}$ for **2.9**, **1.50**, and **1.59** was adjusted by subtracting the computed energy difference between the s-trans and s-cis conformers (1.5, 1.1, and 0.7 kcal/mol, respectively). These adjusted Gibbs free energies of activation, denoted as $\Delta G^{\ddagger}_{exp(s\text{-}cis)}$, are used in our comparison to reflect the reactivities of the reactive s-cis conformer of each precursor.

Therefore, the NICS(1)zz aromaticity of the heteroarene in the ester-tethered precursors and concerted transition states were plotted against the adjusted Gibbs free energies of activation, $\Delta G^{\ddagger}_{exp(s\text{-}cis)}$. The precursors afforded a correlation with $R^2 = 0.63$ for the trendline, and the transition states afforded a correlation with $R^2 = 0.56$ for the trendline (Figure 3.9). Aromaticity of the heteroarene in the precursor afforded a better correlation to the Gibbs free energy of activation than the aromaticity in the transition state, so that transition state calculations may not be necessary to use aromaticity as a predictive tool for reactivity. The positive correlation between aromaticity of the heteroarene and the Gibbs free energy of activation suggests that aromaticity is one of several influencing factors that control reactivity. For example, C3-substituted **1.59** (-28.8 ppm) and **2.5** (-25.1 ppm) are more aromatic than the corresponding C2-substituted **1.50** (-27.8 ppm) and **2.9** (-21.8 ppm). Consequentially, **1.59** and **2.5** (27.0 and 26.6 kcal/mol) have higher $\Delta G^{\ddagger}_{exp(s\text{-}cis)}$ than **1.50** and **2.9** (26.2 and 25.8 kcal/mol), respectively.

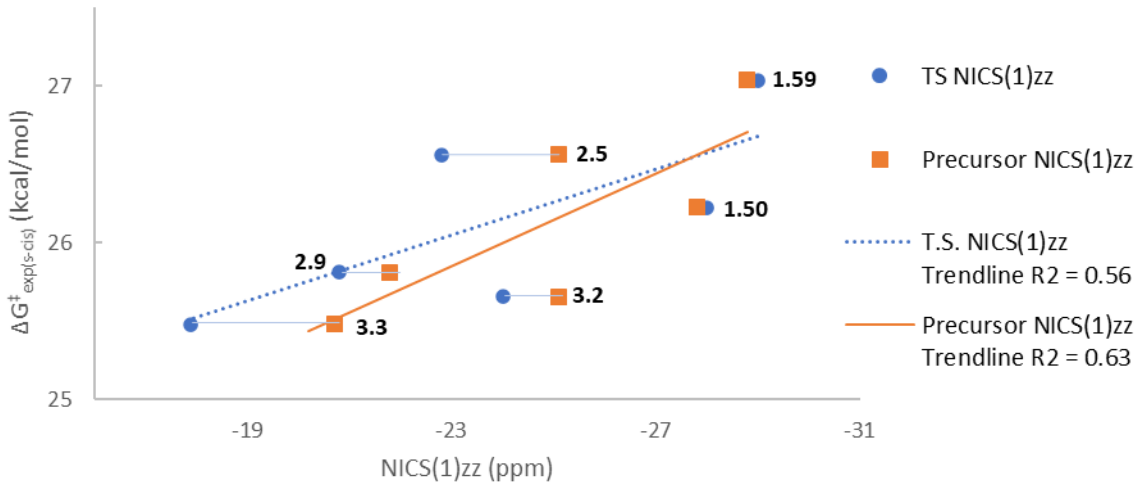


Figure 3.9. Correlation between $\Delta G^{\ddagger}_{exp(s\text{-}cis)}$, and both precursor and transition state $NICS(1)_{zz}$ aromaticity values for ester-tethered substrates

NICS(1)zz aromaticity of the heteroarene in the ester-tethered precursors and concerted transition states were plotted against the adjusted computational Gibbs free energies of activation, $\Delta G^{\ddagger}_{comp(s\text{-}cis)}$ as well, and afforded improved correlation. The precursors afforded a correlation with $R^2 = 0.88$ for the trendline, and the transition states afforded a correlation with $R^2 = 0.85$ for the trendline (Figure 3.10). The improved correlation for the computed Gibbs free energies of activation over the experimental energies is attributed to the lack of experimental error. As with experimental energies, aromaticity of the heteroarene in the precursor afforded a better correlation to the Gibbs free energy of activation than the aromaticity in the transition state. The positive correlation between aromaticity of the heteroarene and the computed Gibbs free energy of activation with improved correlation is in agreement with the correlation with experimental energies that aromaticity is one of several influencing factors that affects reactivity.

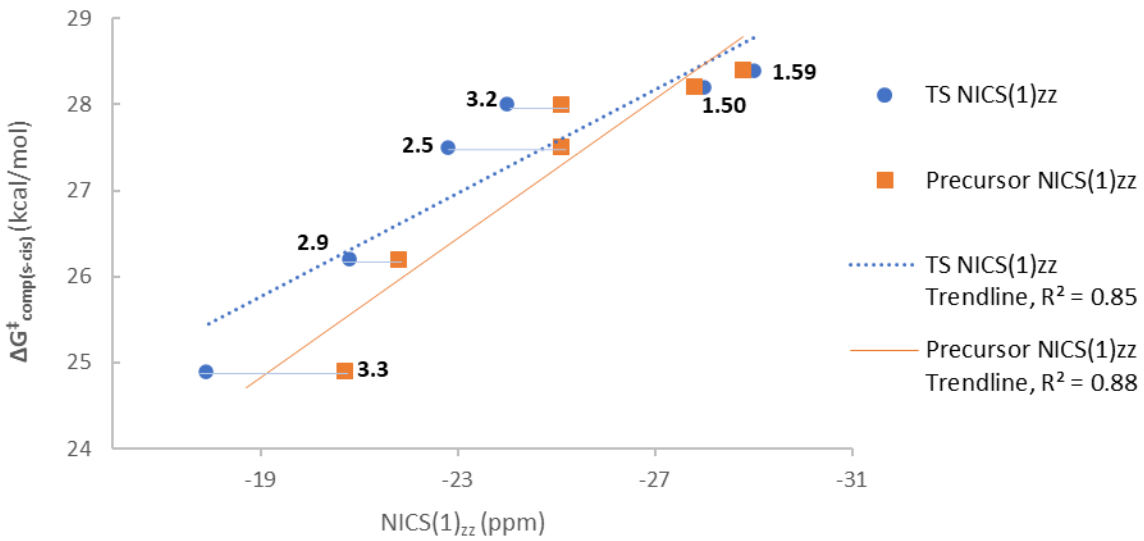


Figure 3.10. Correlation between the $\Delta G^{\ddagger}_{comp(s\text{-}cis)}$ at the M06-2X/M06-2X level of theory and the NICS(1)zz aromaticity calculation

However, the dearomative cycloaddition appears to lack sensitivity to the effect that the fused benzene ring has on the aromaticity of the heteroarene. Benzo-fused heteroarenes **2.9**, **2.5**, and **3.3** are less aromatic than their non-benzo-fused counterparts **1.50**, **1.59**, and **3.2**, yet the reaction rate of the dearomative cycloaddition for the benzo-fused heteroarenes is only accelerated by a factor of 1.02, 5.13, and 1.28-fold, respectively. This rate enhancement is relatively small when compared to the 400,000-fold rate enhancement observed in the Diels-Alder reaction between naphthalene and tetracyanoethylene over that of benzene and teracyanoethylene.[61] The lack of sensitivity to heteroarene aromaticity is consistent with the proposed early transition state that retains the aromaticity of the heteroarenes. Therefore, a broad range of heteroarenes with varied levels of aromaticity may be used as precursors for the dearomative DDDA reaction.

3.5 Conclusions

We established that the dearomative cycloaddition step of the dearomative DDDA reaction proceeds through a highly asynchronous, closed-shell, concerted transition state where the five-membered ring is formed to a greater degree than the six-membered ring. This was accomplished through a cooperative investigation incorporating experimentally derived kinetic data with computational DFT analysis to afford a deeper mechanistic understanding of the dearomative cycloaddition step and the substrate dependent factors that determine reactivity. Dearomative DDDA reactions were monitored in situ with ReactIR to afford kinetic reactivity data including Gibbs free energies of activation. These experimental energies were correlated with computational DFT calculated Gibbs free energies of activation. M06-2X/6-311+G(d,p)//M06-2X/6-31+G(d) level of theory afforded the most accurate computational energies of those tested while B3LYP/6-311+G(d,p)//B3LYP/6-31+G(d) level of theory had improved correlation to experimental energies and may be useful in the prediction of relative reactivity trends for different precursors. NICS(1)zz aromaticity calculations have a positive correlation with experimental Gibbs free energies of activation, yet the impacts on Gibbs free energies of activation are less than a few kcal/mol which is in agreement with the early transition state. Stabilizing dispersion interactions between the phenyl terminus of the alkyne and the heteroarenes were observed. The energy required to attain the reactive s-cis conformation of the vinyl heteroarene from the unreactive s-trans conformation was also found to contribute to the overall energy barrier of the dearomative cycloaddition. These results serve to benchmark DFT computation as a predictive tool in reactivity determination for the dearomative cycloaddition and to lend insight into the substrate dependent factors that control reactivity for this and other dearomative processes.

3.6 Experimental

3.6.1 General Methods

Unless otherwise indicated, all reactions were performed in flame-dried glassware under an air atmosphere and stirred with Teflon-coated magnetic stir bars. All commercially available compounds were purchased and used as received unless otherwise specified. Tetrahydrofuran (THF) was purified by passing through alumina using the Sol-Tek ST002 solvent purification system. Deuterated chloroform ($CDCl_3$) was passed over 3 Å molecular sieves. Nitrogen gas was purchased from Matheson Tri Gas. Purification of compounds by flash column chromatography was performed using silica gel (40-63 μm particle size, 60 Å pore size). TLC analyses were performed on silica gel F_{254} glass-backed plates (250 μm thickness). ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker Avance 300, 400, or 500 MHz spectrometers. Spectra were referenced to residual chloroform (7.26 ppm, ^{1}H; 77.16 ppm, ^{13}C). Chemical shifts (δ) are reported in ppm and multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), and m (multiplet). Coupling constants, J, are reported in hertz (Hz). All NMR spectra were obtained at room temperature. Compound characterization IR spectra were obtained using a Nicolet Avatar E.S.P. 360 FT-IR. ReactIR spectra were obtained using a Mettler Toledo ReactIR 45M with a silicone probe (SiComp, 9.5 x 1.5 mm AgX Fiber, Resistive Temperature Device). EI mass spectroscopy was performed on a Waters Micromass GCT high resolution mass spectrometer, while ES mass spectroscopy was performed on a Waters Q-TOF Ultima API, Micromass UK Limited high-resolution mass spectrometer.

3.6.2 Experimental Procedures for ReactIR

The dewar of the ReactIR 45M was filled with liquid nitrogen and the instrument was switched on 2 h prior to experiment. A 10 mL, 2-necked, heart-shaped flask equipped with a stir bar (flea sized) was fitted with the 9.5 mm silicone ReactIR probe via a 14/20 Teflon adapter. The tip of the probe was carefully positioned slightly above the stir bar through the center neck, and a 14/20 glass stopper was inserted into the side neck. The flask was clamped directly above a pre-heated oil-bath, while cautiously moving the fiber arm so as to avoid excessive bending. The iC IR 4.0 was used for data collection. The data collection frequency was set to 30 s, 1 min, or 3 min, depending upon predetermined reaction time and the temperature was monitored via the ReactIR probe. The alignment and clean steps were performed, and if necessary, the probe tip was cleaned by temporarily removing from the flask and gently wiping with an acetone soaked Kimwipe. A background scan in air was collected. The glass stopper was temporarily removed and o-dichlorobenzene (o-DCB, 1 mL) was added in a single portion via syringe–*the probe tip must be immersed in o-DCB*. The pre-heated oil bath was raised to the flask. Once the internal temperature reached equilibria as evidenced by the readout, the glass stopper was temporarily removed, and a solution of precursor (20 mg) diluted in o-DCB (0.5 mL) was added in a single portion via syringe. At this point, the reaction solution contained 20 mg of precursor dissolved in 1.5 mL (2.0 g) o-DCB affording a weight percent of 1.0%, well above the 0.1% detection limit of the ReactIR infrared absorber. The reaction progress was monitored by disappearance of starting material as observed by a decreasing peak height for a particular absorption attributed to the starting material–an absorption identified by the iC IR software to afford the best trend. Complete disappearance of starting material was confirmed by TLC. A trend for the consumption of starting material was extracted using the iC IR 7.0 software and measured using peak height with a two-point baseline

after solvent subtraction was applied. The trend data were exported to iC Kinetics 5.0 software, and the consumption of starting material vs. time data was plotted using GraphPad Prism 7.0. The reaction displayed first-order kinetics for the substrate. An exponential one-phase decay nonlinear regression was applied to the data set, using a least squares fit analysis.

3.6.3 ReactIR Data Output and Rate Calculations with GraphPad

As described in the experiment procedure, each ReactIR experiment began with a period where the probe recorded the absorption of background air or solvent during temperature equilibration, before starting material was added to the reaction vessel. All data recorded by the probe before the addition of starting material was considered irrelevant to the experiment. Therefore, the plots of consumption of starting material over time were set so that the introduction of starting material to the reaction has a time point of zero, and the probe recordings before that point were discarded and not displayed. Probe recordings after the point of five half-lives were also discarded and not displayed so as to eliminate error from the decomposition of products after the consumption of starting material was complete.

Plots of consumption of starting material over time are displayed as peak height vs. duration of the experiment. Peak height is recorded by the iC IR software with arbitrary units (a.u.). The GraphPad data output is displayed below the plot of consumption of starting material and represents the statistics for the one phase decay nonlinear regression. Y0 is the Y value when the time is zero. The plateau is the Y value at an infinite time. K is the rate constant expressed in inverse minutes. Tau is the reciprocal of K. The half-life is displayed as determined by ln(2)/K. The span is the difference between Y0 and the plateau. The 95% confidence interval is also displayed for the previous statistics. Statistics related to the goodness of the fit are given, including

the degrees of freedom, R^2 value, sum of squares, and the standard error of estimate (Sy.x). The only constraint imposed upon the one phase decay nonlinear regression is that the rate is greater than zero.

The data points for each ReactIR experiment and the corresponding plot and GraphPad output have been recorded and can be found in Appendix C.

3.6.4 Specifications for Measuring Half-Lives for DDDA Precursor

A minimum of five separate experiments were conducted for each DDDA precursor with each experiment having a unique reaction temperature. A significant improvement to the trendline fit was not observed beyond four data points for either the Eyring or Arrhenius plots. For example, Figure 3.11 shows an Eyring plot of **1.59** using five different reactions temperatures with an R^2 = 0.997 while Figure 3.12 shows a plot with four reactions with the same fit (R^2 = 0.997). The recorded temperature is the internal temperature of the solution as measured by the ReactIR probe. For each series of reactions, the oil bath temperature was increased by an increment of 10 °C; however, the increase in the oil bath temperature did not translate to the internal reaction temperature. Thus, the actual temperature difference between each experiment in the series is between 5–15 °C.

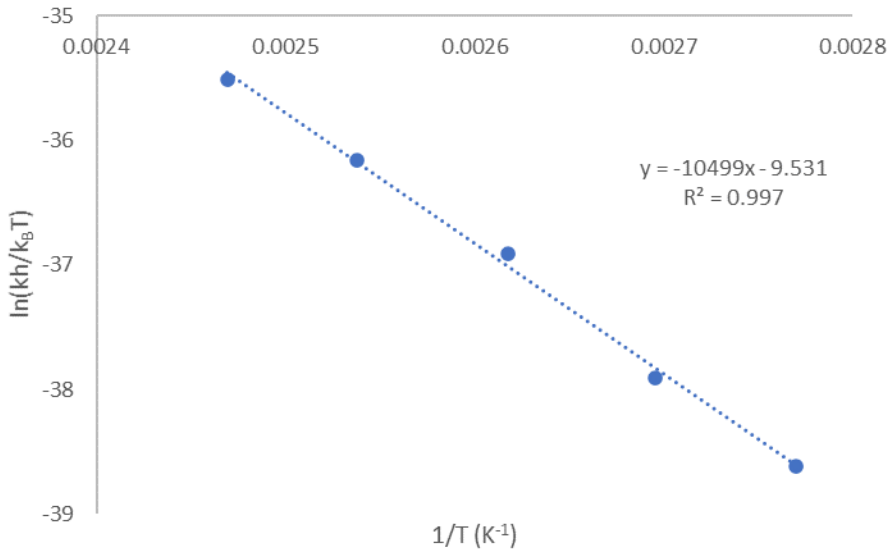


Figure 3.11. Eyring plot for the dearomative DDDA reaction of **1.59** using five different reaction temperatures

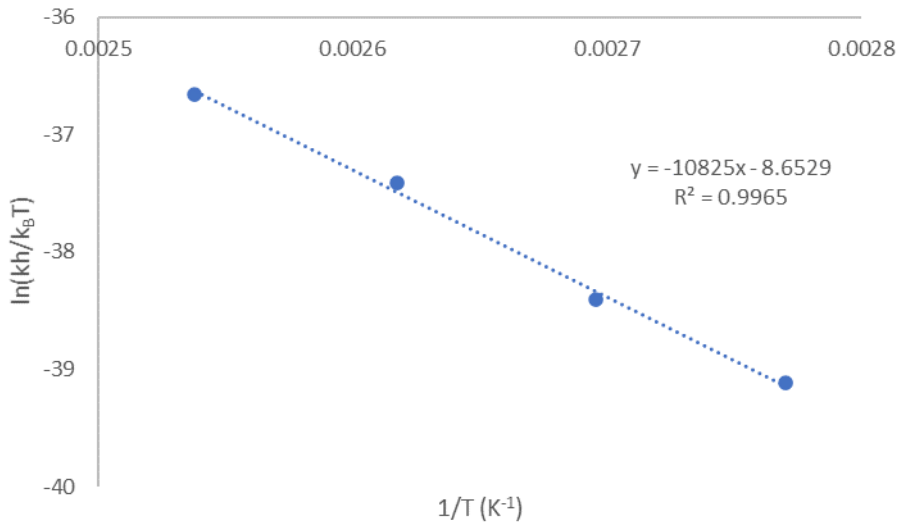


Figure 3.12. Eyring plot for the dearomative DDDA reaction of **1.59** using four different reaction temperatures

3.6.5 Arrhenius Plots

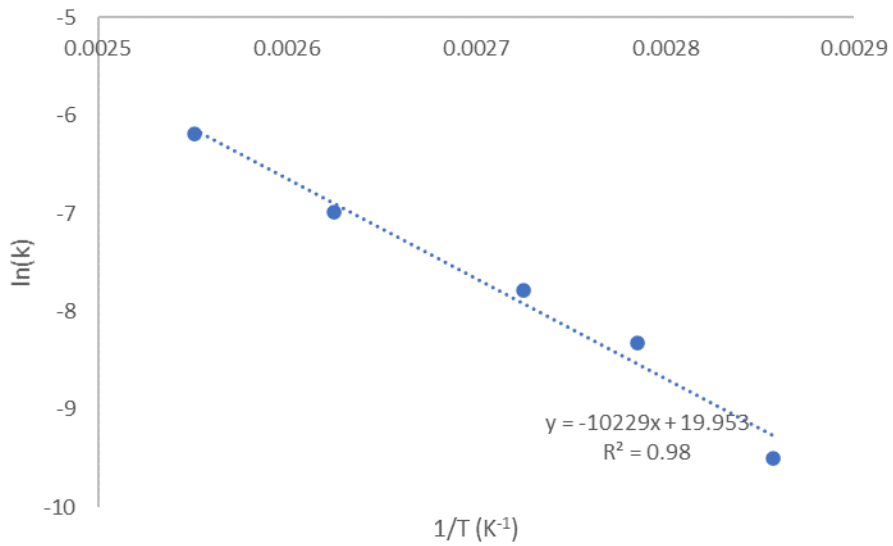


Figure 3.13. Arrhenius plot for the dearomative DDDA reaction of **1.50**

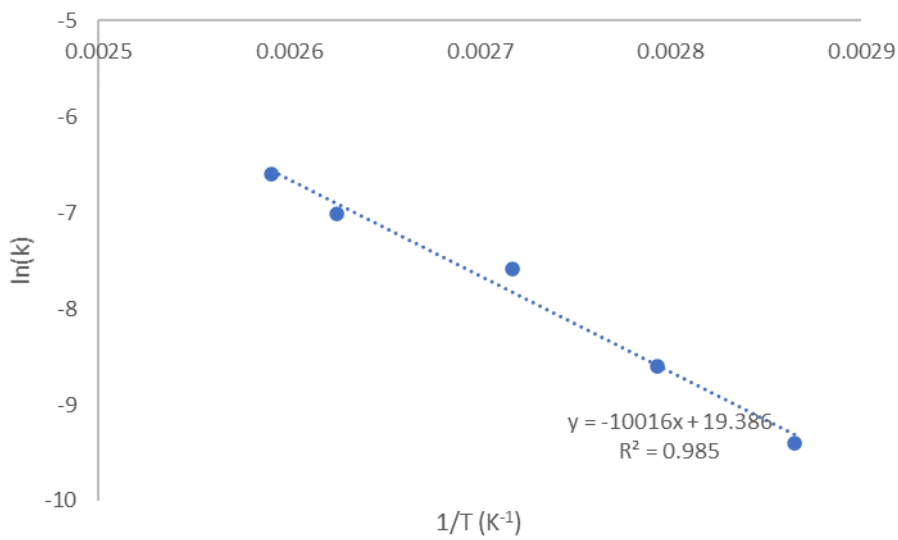


Figure 3.14. Arrhenius plot for the dearomative DDDA reaction of **2.9**

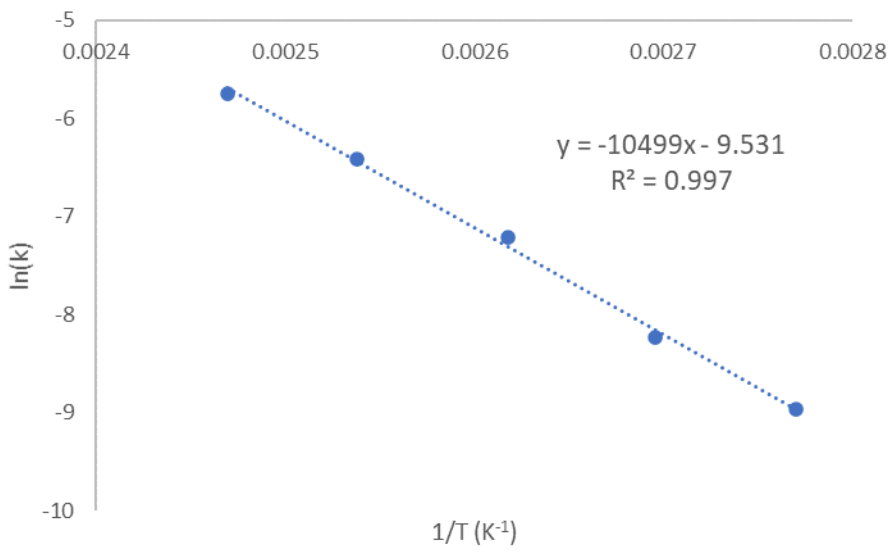


Figure 3.15. Arrhenius plot for the dearomative DDDA reaction of **1.59**

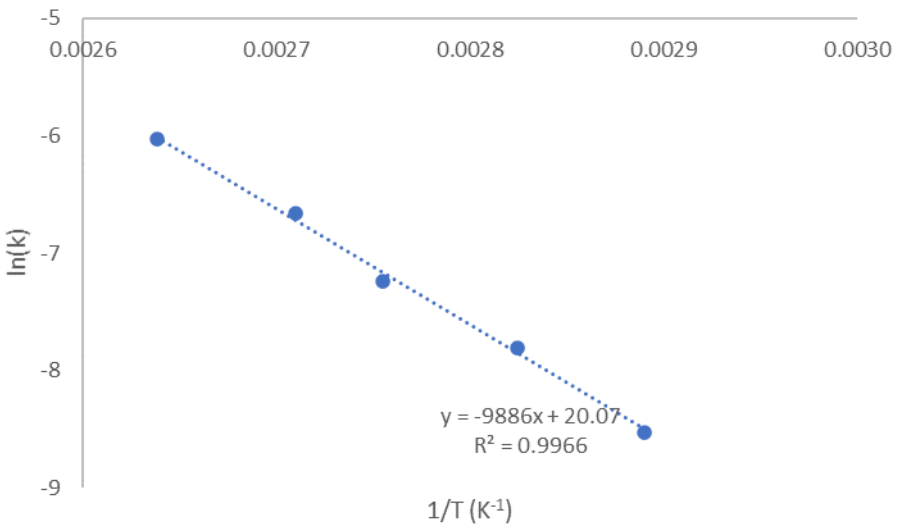


Figure 3.16. Arrhenius plot for the dearomative DDDA reaction of **2.5**

3.6.6 Eyring Plots

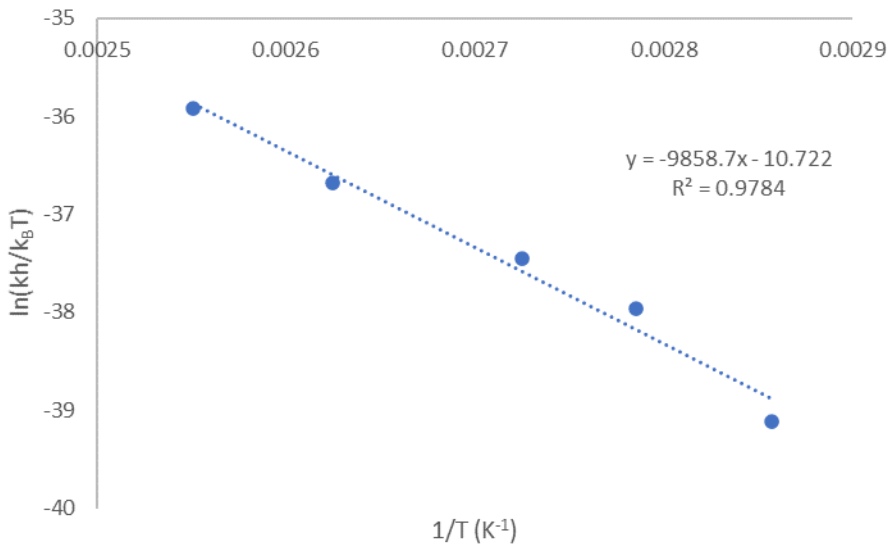


Figure 3.17. Eyring plot for the dearomative DDDA reaction of **1.50**

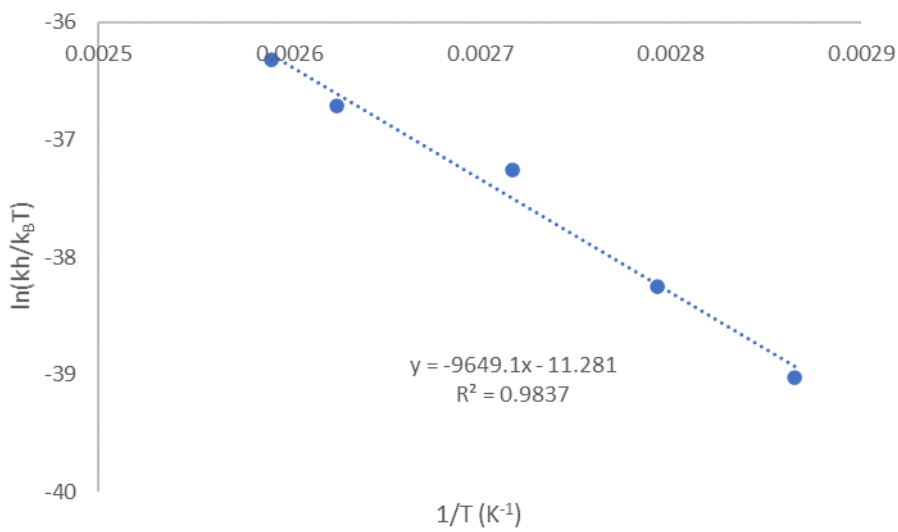


Figure 3.18. Eyring plot for the dearomative DDDA reaction of **2.9**

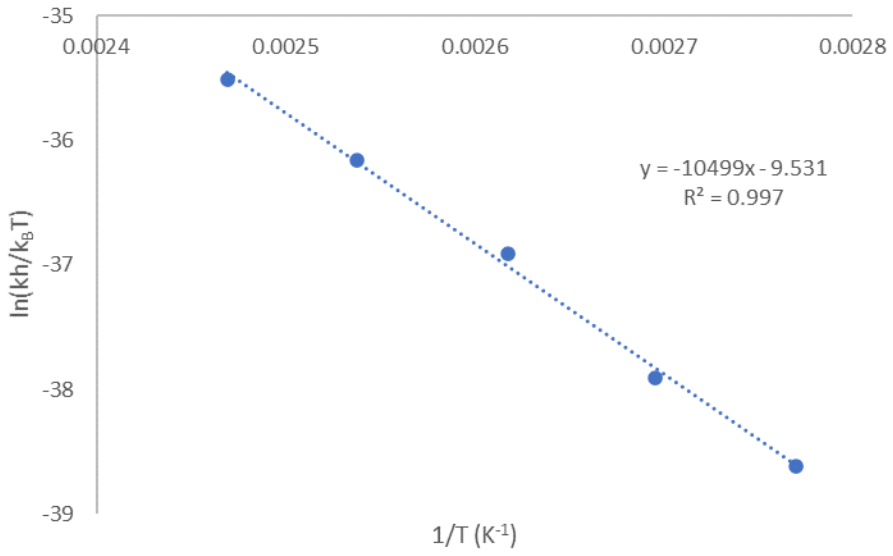


Figure 3.19. Eyring plot for the dearomative DDDA reaction of **1.59**

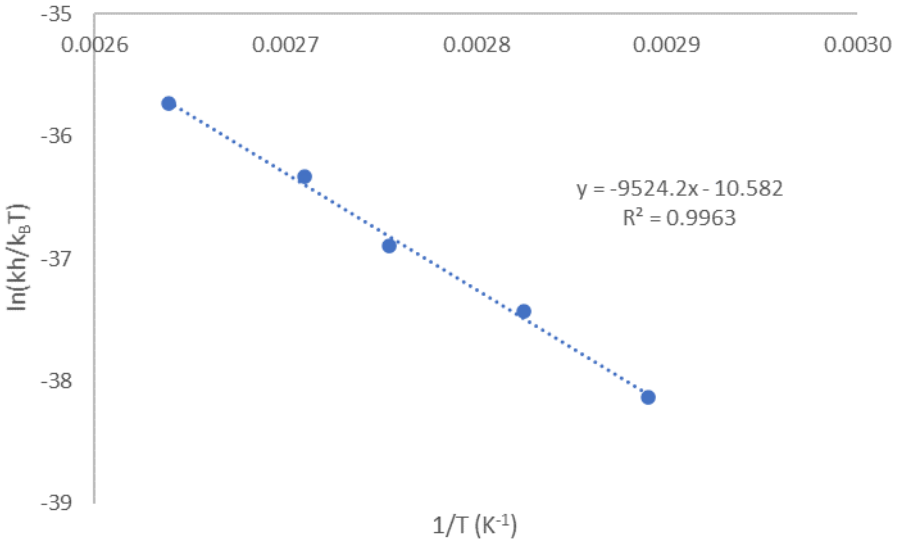


Figure 3.20. Eyring plot for the dearomative DDDA reaction of **2.5**

3.6.7 Correlation Plots between DFT Computational and Experimentally Derived Gibbs Free Energies of Activation

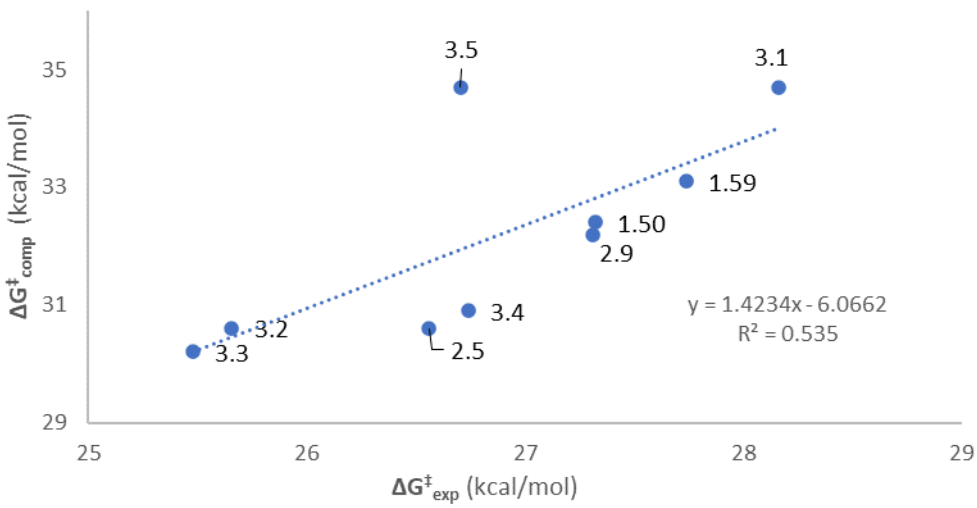


Figure 3.21. Correlation between the closed-shell transition state $\Delta G^{\ddagger}_{comp}$ with B3LYP/B3LYP level of theory and the $\Delta G^{\ddagger}_{exp}$ with **3.5** outlier

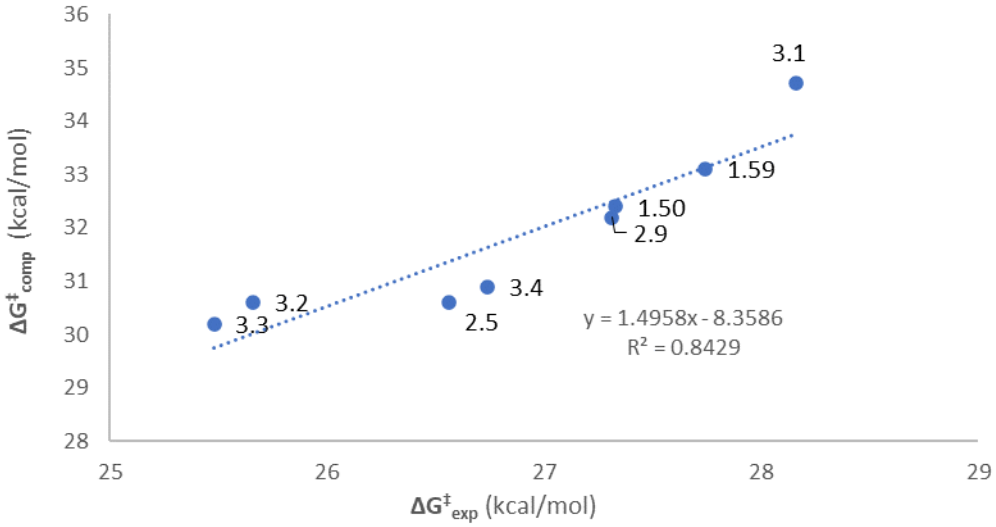


Figure 3.22. Correlation between the closed-shell transition state $\Delta G^{\ddagger}_{comp}$ with B3LYP/B3LYP level of theory and the $\Delta G^{\ddagger}_{exp}$ without **3.5** outlier

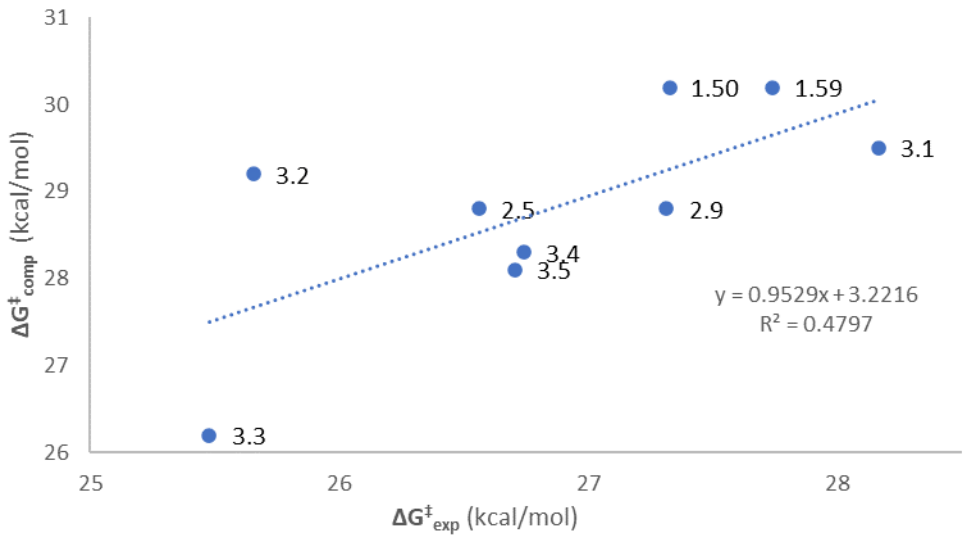


Figure 3.23. Correlation between the closed-shell transition state $\Delta G^{\ddagger}_{comp}$ with M06-2X/M06-2X level of theory and the $\Delta G^{\ddagger}_{exp}$

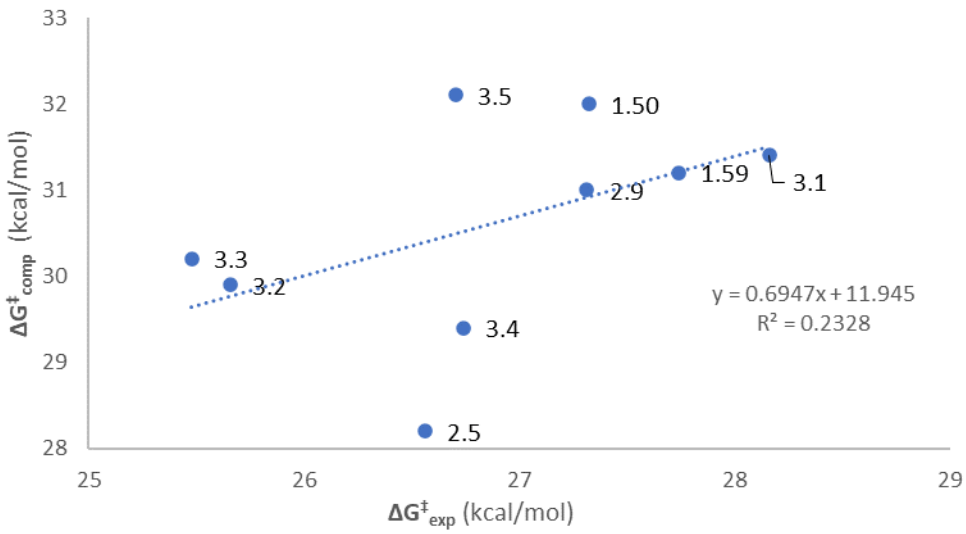


Figure 3.24. Correlation between the closed-shell transition state $\Delta G^{\ddagger}_{comp}$ with M06-2X/B3LYP level of theory and the $\Delta G^{\ddagger}_{exp}$

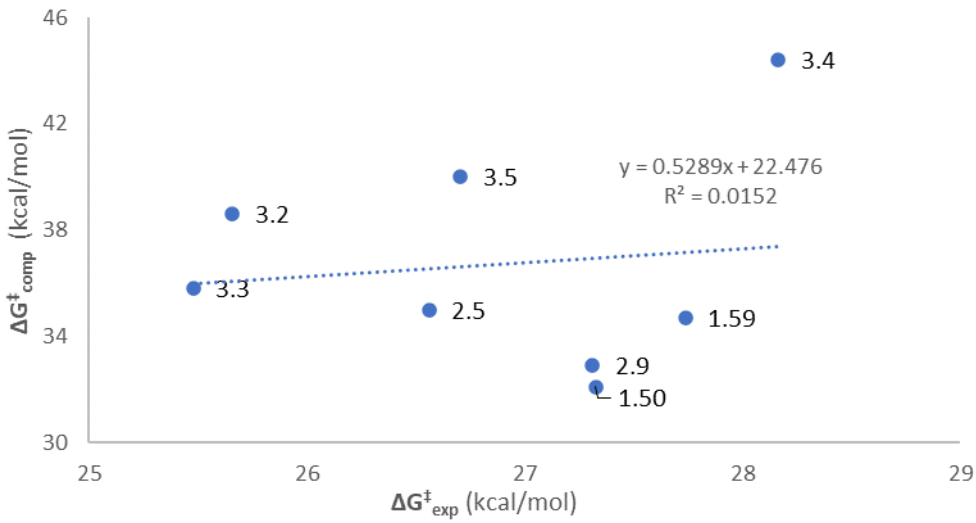


Figure 3.25. Correlation between the open-shell transition state $\Delta G^{\ddagger}_{comp}$ with M06-2X/B3LYP level of theory and the $\Delta G^{\ddagger}_{exp}$

4.0 Divergent Reactivity of the DA Adduct and Regulating the Selectivity for Oxidation or Isomerization Products

Having established the DA adduct to be on the pathway to both the oxidation and isomerization products, we were poised to investigate the mechanisms for their formation from adduct. We launched an investigation where dearomative DDDA conditions were systematically varied to identify how different reaction parameters affected product selectivity as a way to gain insight into the mechanisms of product formation. In turn, this information is used to regulate the dearomative DDDA reaction selectivity for either the oxidation or isomerization product.

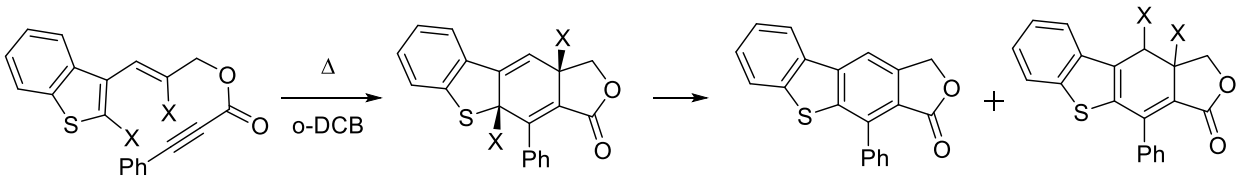
This chapter is based on results presented in: Winkelbauer J. A.; Bober A. E.; Brummond K. M., Regulating Divergent Product Selectivity of the Dearomative Didehydro-Diels–Alder Reaction through Mechanistic Insight. Manuscript in preparation, submission expected 2021.

4.1 Reaction Conditions that Affect Product Selectivity

The following effects of varied reaction conditions on the product selectivity of the dearomative DDDA reaction were observed as trends across multiple experiments and are herein reported with limited examples for direct comparison of the observed effects.

4.1.1 Temperature Effect on the Dearomative DDDA Reaction Product Selectivity

To determine the effect that temperature has on the product selectivity of the dearomative DDDA reaction of **2.5**, reaction temperatures were systematically varied, and product ratios were measured. Benzothiophene precursor **2.5** heated for 3 days at 60 °C in *o*-DCB afforded only **2.8.** The reaction progress and product ratios were monitored by ^{1}H NMR (see NMR overlay in experimental section). **2.19** for 2 h at 150 °C in *o*-DCB afforded a mixture of products with a 74:26 ratio of **2.8**:**2.21** along with a large quantity of adduct **2.20** remaining. Performing this same reaction at 180 °C resulted in an increased presence of isomerization product. Reaction of **2.19** heated for 2 h at 180 °C in *o*-DCB afforded a 45:55 ratio of products **2.8**:**2.21** with significantly less adduct **2.20** remaining. These three experiments demonstrate that reaction temperature has a significant impact on product ratios. Selectivity for the isomerization product increases at higher temperatures but a mixture of oxidation and isomerization products are afforded. The oxidation product is afforded exclusively at low temperature.

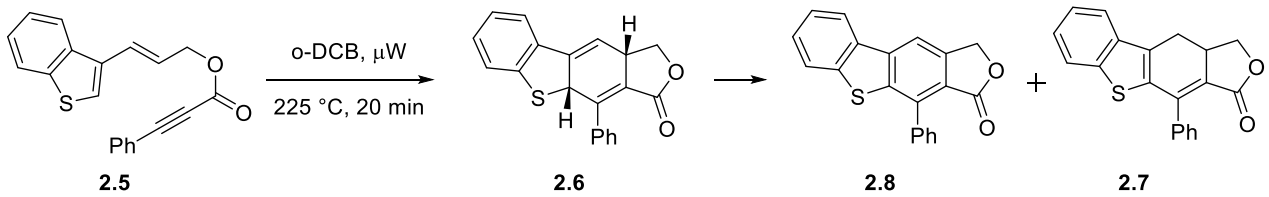


entry	precursor	T (°C)	t (h)	Ratio precursor	adduct	oxid.	isom.	Oxid:Isom
1	**2.5**	60	72	0	0	100	0	100:0
2	**2.19**	150	2	0	65	26	9	74:26
3	**2.19**	180	2	0	33	30	37	45:55

Scheme 4.1. Dearomative DDDA reactions of **2.5** with varied temperatures and affected product ratios

4.1.2 Concentration Effect on the Dearomative DDDA Reaction Product Selectivity

To determine the effect that reaction concentration has on the product selectivity of the dearomative DDDA reaction of 2.5, reaction concentrations were systematically varied, and product ratios were measured. DDDA precursor **2.5** was heated for 20 min at 225 °C in *o*-DCB via microwave heating at a concentration of 0.06 M affording a mixture of products with a 88:12 ratio of **2.8**:**2.7** and some adduct **2.6** remaining. Reaction of **2.5** heated for 20 min at 225 °C in *o*-DCB via microwave at a concentration of 0.12 M afforded a 77:23 ratio of products **2.8**:**2.7** with some adduct remaining. These two experiments demonstrate that product ratios vary with changes in reaction concentration. A doubling of the reaction concentration resulted in a modest increase in the isomerization product.



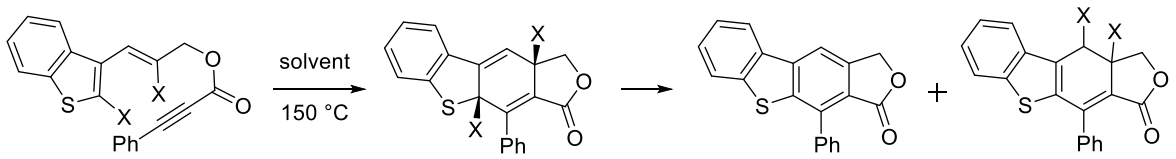
entry	concentration (M)	Ratio precursor	adduct	oxid.	isom.	Oxid:Isom
1	0.06	0	8	81	11	88:12
2	0.12	0	14	66	20	77:23

Scheme 4.2. Dearomative DDDA reaction of **2.5** with varied concentration and affected product ratios

4.1.3 Solvent Effect on the Dearomative DDDA Reaction Product Selectivity

To determine the effect that solvent has on the product selectivity of the dearomative DDDA reaction of **2.5**, reaction solvents with different dielectric constants (ε) were applied and product ratios were measured. **2.19** was heated for 2 h at 150 °C in *o*-DCB (ε = 9.9) and afforded

a mixture of products in a 74:26 ratio of **2.8**:**2.21** with considerable adduct **2.6** remaining. **2.5** heated for 3 h at 150 °C in DMF-d_7 (ε = 36.7) afforded a 23:77 ratio of **2.8**:**2.7** with no adduct remaining. Heating **2.5** in acetonitrile (ε = 37.5) for 5 min at 150 °C afforded a 7:93 ratio of **2.8**:**2.7** with a considerable amount of adduct remaining. These three experiments demonstrate that product ratios for the dearomative DDDA reaction of **2.5** vary with changes in solvent dielectric constant. Selectivity for the isomerization product shows a modest increase as the solvent dielectric constant is increased.



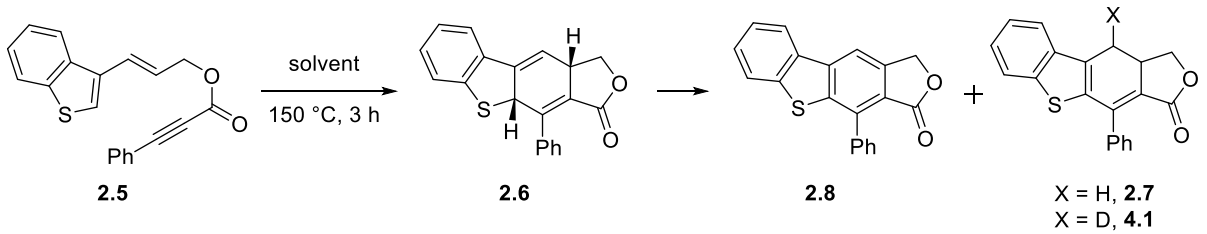
entry	precursor	t (min)	solvent	Ratio precursor	adduct	oxid.	isom.	Oxid:Isom
1	**2.19**	120	o-DCB	0	65	26	9	74:26
2	**2.5**	180	DMF-d_7	0	0	23	77	23:77
3	**2.5**	5	MeCN	0	45	4	51	7:93

Scheme 4.3. Dearomative DDDA reaction of **2.5** with varied solvent and affected product ratios

4.1.4 Water Additive Effect on the Dearomative DDDA Reaction Product Selectivity

To determine the effect that additives have on the product selectivity of the dearomative DDDA reaction of **2.5**, water was added to increase the dielectric constant of the reaction media and product ratios were measured. **2.5** heated for 3 h at 150 °C in DMF-d_7 afforded a mixture of products with a 23:77 ratio of **2.8**:**2.7**. Reaction of **2.5** heated for 3 h at 150 °C in D_2O/DMF-d_7 (10% v/v) afforded a 9:91 ratio of products **2.8**:**2.21**. These two experiments demonstrate that product ratios for the dearomative DDDA reaction of **2.5** vary with the presence of water.

Selectivity for the isomerization product shows a modest increase in the presence of water. The most striking observation is the isolation of isomerization product **4.1** with deuterium incorporation. This finding is discussed further in section 4.4.



entry	solvent	Ratio precursor	adduct	oxid.	isom.	Oxid:Isom
1	DMF-d_7	0	0	23	77	23:77
2	D_2O/DMF-d_7	0	0	9	91	9:91

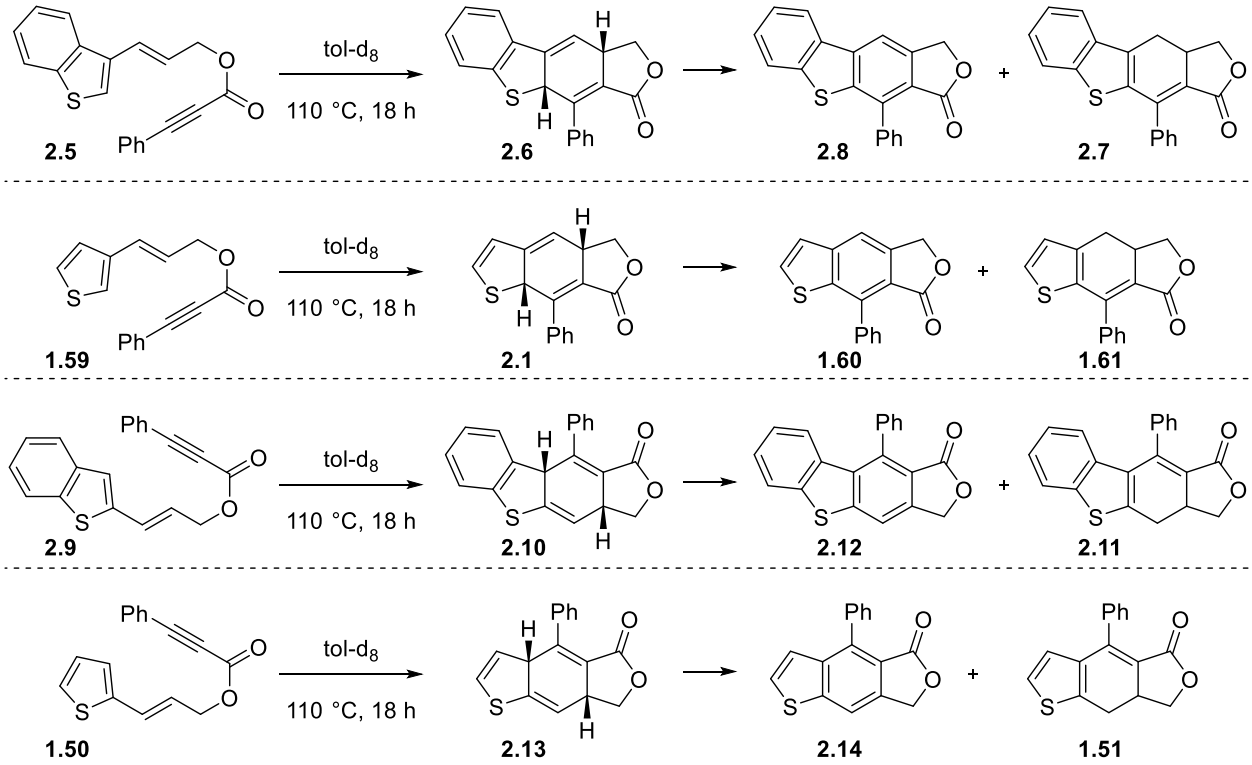
Scheme 4.4. Dearomative DDDA reaction of **2.5** with added water and affected product ratios

4.1.5 BHT Additive Effect on the Dearomative DDDA Reaction Product Selectivity

To determine the effect that a radical inhibitor has on the product selectivity of the dearomative cycloaddition of **2.5**, **1.59**, **2.9**, and **1.50**, 3,5-di-tert-4-butylhydroxytoluene (BHT) was added and product ratios were measured and compared to parallel reactions without BHT. Four separate reactions of precursors **2.5**, **1.59**, **2.9**, and **1.50** were heated for 18 h at 110 °C in toluene-d_8 within an NMR tube (entries 1, 3, 5, and 7, Table 4.1). Reactions were then performed under the same conditions but with 1 equivalent of added BHT (entries 2, 4, 6, and 8). Both sets of reactions were monitored at the 3, 8, and 18 h timepoints by pausing the reaction for ^{1}H NMR analysis of the crude solution. Yields and ratios were determined by comparing ^{1}H NMR resonances of substrates to a mesitylene internal standard. **2.5** showed complete selectivity for oxidation product under both sets of conditions (entries 1 and 2). **1.59**, **2.9**, and **1.50** all showed a

marked increase in isomerization product in the presence of BHT (compare entries 3–8). These four sets of experiments demonstrate that product ratios for the dearomative DDDA reaction of vary with the presence of BHT. Selectivity for the isomerization product shows a modest increase in the presence of BHT.

Table 4.1. Dearomative DDDA reaction of precursors with added BHT and affected product ratios



Entry	Precursor	Solvent/ Additive	Oxid:Isom	Yield (%)
1	**2.5**	Tol-d_8	100:0	94
2	**2.5**	Tol-d_8 BHT (1 equiv)	100:0	89
3	**1.59**	Tol-d_8	52:48	72
4	**1.59**	Tol-d_8 BHT (1 equiv)	29:71	84
5	**2.9**	Tol-d_8	76:24	97
6	**2.9**	Tol-d_8 BHT (1 equiv)	67:33	88
7	**1.50**	Tol-d_8	93:7	90
8	**1.50**	Tol-d_8 BHT (1 equiv)	67:33	83

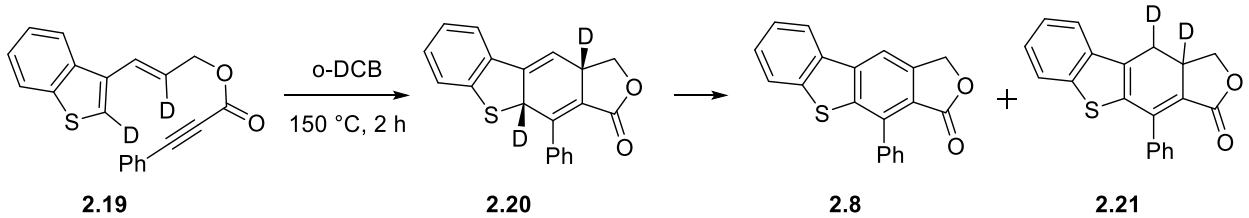
Additionally, the ratio of adduct observed at the 3 h timepoint was significantly increased for reactions that included BHT. Reaction of **2.5** showed an increase of adduct from 43% to 70% at the 3 h timepoint with BHT added (see experimental section 4.6.7). Reaction of **1.59** showed an increase from 5% to 12% with BHT added. Reaction of **2.9** showed an increase of adduct from 3% to 56% at the 3 h timepoint with BHT added, and reaction of **1.50** showed an increase from 2% to 32% with BHT added. These experiments demonstrate that BHT slows conversion of adduct to products as evidenced by an increased ratio of adduct at the 3 h timepoint.

The reactions of **2.5** in toluene-d_8 at 110 °C with and without BHT additive (entries 1 and 2, Table 4.1) afforded exclusively oxidation product **2.8**. To determine the effect of BHT additive on the product selectivity, these two reactions were repeated in *o*-DCB-d_4 at 150 °C. Reaction of **2.5** in *o*-DCB-d_4 at 150 °C without BHT additive afforded a ratio of 82:18 oxidation to isomerization product. Reaction of **2.5** in *o*-DCB-d_4 at 150 °C with 1 equivalent of BHT additive afforded a ratio of 77:23 oxidation to isomerization product. Presence of BHT additive afforded a small increase in formation of isomerization product under these conditions for **2.5** in comparison to the other precursors. It remains unclear as to why the addition of BHT had less of an impact on product selectivity for dearomative DDDA reaction of **2.5**.

4.1.6 Atmosphere Effect on the Dearomative DDDA Reaction Product Selectivity

To determine the effect that atmosphere has on the product selectivity of the dearomative cycloaddition of **2.5**, the reaction atmosphere was varied, and product ratios were measured. **2.19** heated for 2 h at 150 °C in *o*-DCB, sealed via a screw-top vial under air, afforded a mixture of products with a 65:26:9 ratio of **2.20:2.8**:**2.21**. A repeat of this reaction under an atmosphere of nitrogen afforded a mixture of products with a 82:12:6 ratio of **2.20**:**2.8**:**2.21.** Reaction of **2.19**

heated for 2 h at 150 °C in *o*-DCB, open to air via a 16-gauge needle, afforded a mixture of products with a 85:15 ratio of **2.8**:**2.21** and no remaining adduct present. Replacing the air atmosphere with one of nitrogen afforded an increased accumulation of adduct as conversion to oxidation product was slowed. Reaction that was open to air afforded an increase in the conversion of adduct to oxidation product. Selectivity for the oxidation product shows an atmosphere with increased exposure to air.



entry	atmosphere	Ratio precursor	adduct	oxid.	isom.	Oxid:Isom
1	air, sealed	0	65	26	9	74:26
2	N_2, sealed	0	82	12	6	67:33
3	air, open	0	0	85	15	85:15

Scheme 4.5. Dearomative DDDA reaction of **2.5** with air exposure and affected product ratios

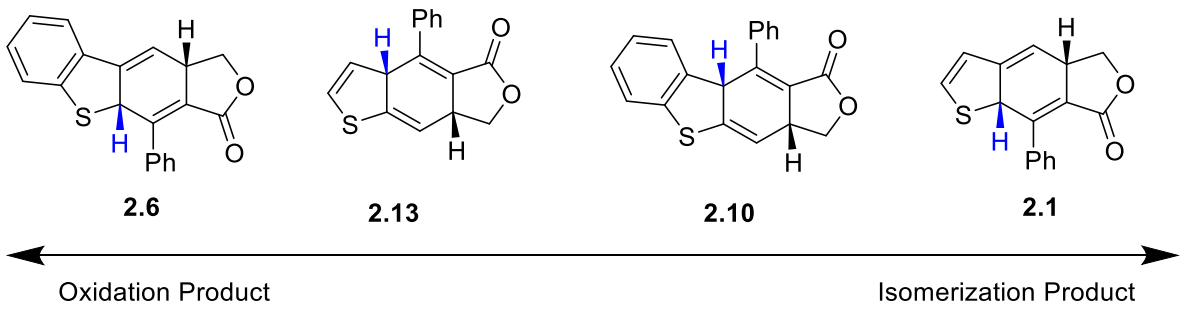
4.2 Substrate Identity Effect on the Dearomative DDDA Reaction Product Selectivity

To determine the effect that the tether attachment point has on the product selectivity of the dearomative cycloaddition, substrates **2.5**, **1.59**, **2.9**, and **1.50** were reacted under identical condition and product ratios were measured. In identical reactions, **2.5**, **1.59**, **2.9**, and **1.50** were heated for 18 h at 110 °C in toluene-d_8 (Table 4.1, entries 1, 3, 5, and 7). Reaction of **2.5** afforded a higher ratio of oxidation to isomerization products than **2.9**, yet reaction of **1.59** afforded a lower

ratio of oxidation to isomerization products than **1.50**. Tether position did not show a clear effect on product ratios for these precursors.

Comparison of the same set of reactions also showed the effect of heteroarene-fused benzene ring on the product selectivity. Reaction of **2.5** afforded a higher ratio of oxidation to isomerization products than **1.59**, yet reaction of **2.9** afforded a lower ratio of oxidation to isomerization products than **1.50**. The presence of a fused benzene ring did not show a clear effect on product ratios for these precursors.

Relative product selectivity based upon the ratio of oxidation to isomerization products was then compared to computational gas phase bond dissociation energies (BDE's) and acidities for the bisallylic hydrogen nearest the heteroarene in the adduct. These calculations were performed at the (u)M06-2X/6-311+g(d,p)//(u)M06-2X/6-31+g(d) level of theory by our collaborator Elena Kusevska from the Peng Liu research group. No correlation was found between the experimental product ratios and the calculated BDE's or acidities at this level of theory. These preliminary computational analyses are insufficient to predict experimental dearomative DDDA product ratios and therefore suggest that computational transition state analysis for the product formation steps would be necessary in order to use computational calculations as a predictive tool for determination of product selectivity.



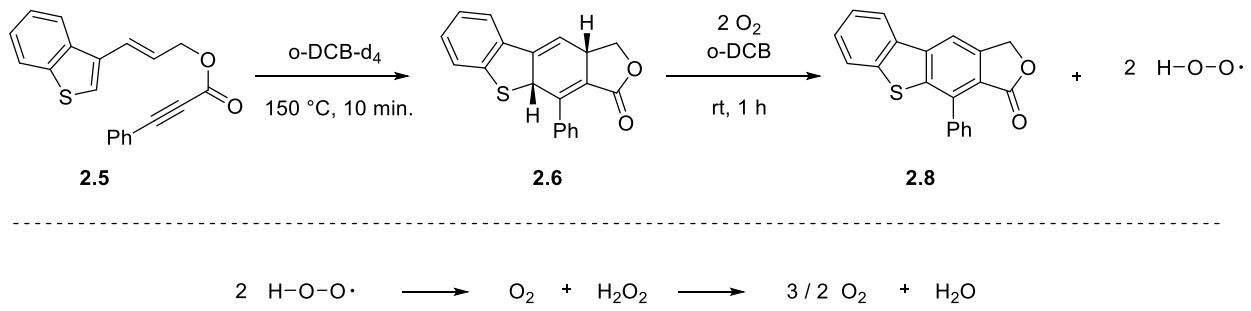
	2.6	> 2.13	> 2.10	> 2.1
Ratio Ox:Isom	100:0	93:7	76:24	52:48
BDE (kcal/mol)	58.8	52.0	55.1	56.3
Acidity (kcal/mol)	323.3	317.6	314.8	324.2

Figure 4.1. Ratio of oxidation product to isomerization product compared to computationally calculated BDE and acidity of the transferred proton of the Diels-Alder adduct

4.3 Evidence for Oxidation Product Formation via Dehydrogenation of Diels-Alder Adduct with Oxygen

As previously discussed, Diels-Alder adduct at room temperature, in *o*-DCB with air bubbled through for 1 h afforded complete selectivity for oxidation product (see section 2.4.1). Also, no evidence was observed for transformation of isomerization product into oxidation product under thermal conditions with or without enhanced exposure to air. These results support the hypothesis that formation of oxidation product is dependent on the presence of molecular oxygen. This is markedly different than the styrenyl dearomative DDDA reaction previously reported by Kocsis which afforded oxidation product and also detected evolved hydrogen gas in both aerobic and anaerobic conditions (see section 1.3.2).[50] The dearomative DDDA reaction of vinyl heteroarenes does not appear to involve release of hydrogen gas akin to the styrenyl dearomative DDDA reaction but rather produces oxidation product by an atmosphere dependent

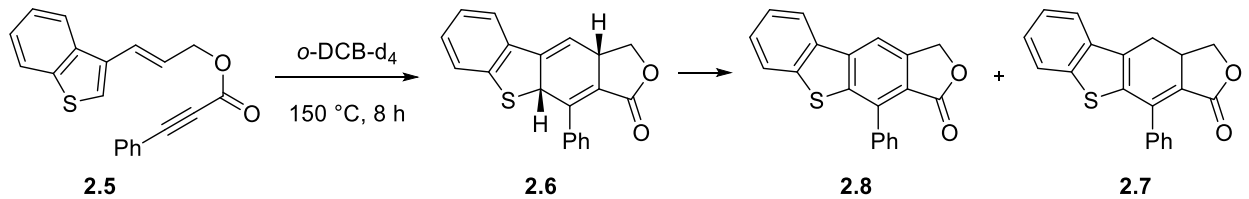
dehydrogenation pathway similar to that described by Hendry for the oxidation of 1,4-cyclohexadiene to benzene.[62] This pathway may be initiated by triplet molecular oxygen and then propagated by hydroperoxyl radicals which Hoffman and coworkers have found to be far more reactive.[63] These formed peroxides may then decompose into water and molecular oxygen.



Scheme 4.6. Formation of oxidation product through a oxygen mediated dehydrogenation

Reactions to monitor for the evolution of hydrogen gas as a product in the formation of oxidation product afforded no detection of H_2 gas. These experiments include seeking a detectable H_2 gas resonance in the ^{1}H NMR of reactions that afforded oxidation product, as well as seeking a detectable presence of H_2 gas in the headspace of a sealed vial reaction that afforded oxidation product. To check for the evolution of hydrogen gas as a product of oxidation product formation, ^{1}H NMR was analyzed for the reaction of **2.5** at 150 °C in *o*-DCB-d_4 after 3 and 8 hours (Scheme 4.7). After the reaction was completed, H_2 gas was bubbled through the solution for 2 min. and ^{1}H NMR was performed to observe the resonance for H_2 gas at 4.53 ppm. The solution was then bubbled through with argon gas far 2 min. and ^{1}H NMR was performed to observe the disappearance of the resonance for H_2 gas at 4.53 ppm. These experiments confirmed the ^{1}H NMR chemical shift for H_2 gas in *o*-DCB-d_4 to be 4.53 ppm. A resonance is observed at 4.53 ppm in the ^{1}H NMR at the 8 h timepoint, but the integration of that resonance remains consistent after

bubbling of argon gas through the solution, confirming the resonance to not be H_2 but rather a decomposition or unknown byproduct. The ^{1}H NMR for this reaction at the 3 h timepoint afforded a 17:65:18 ratio of **2.6:2.8:2.7**, but no resonance was observed for H_2 gas. This experiment was performed under the same reaction conditions in which H_2 gas was observed by ^{1}H NMR in dearomative DDDA reactions of styrene substrates.[50] The resonance for H_2 gas when bubbled through a solution of toluene-d_8 was observed to appear at 4.51 ppm by ^{1}H NMR. ^{1}H NMR was analyzed for the reaction of **2.5** at 110 °C in toluene-d_8 after 3, 8, and 18 hours, as well as the parallel reactions of **1.59**, **2.9**, and **1.50** (Table 4.1, see experimental section for NMR spectra). No H_2 gas was observed in the reaction solution by ^{1}H NMR for any substrate at any timepoint.



Scheme 4.7. Dearomative DDDA reaction of **2.5** in tol-d_8 at 150 °C for 3 h

To check the reaction headspace for evolved hydrogen gas, two sealed vial reactions were performed. **2.5**, sealed in a vial under air was heated for 90 min at 150 °C in *o*-DCB and afforded a 41:39:20 ratio of **2.6:2.8:2.7**. The vial was allowed to cool to room temperature and the headspace of the reaction was analyzed with no detection of hydrogen gas. The same experiment was repeated with precursor **2.19** and afforded a 77:18:5 ratio of **2.6:2.8:2.21**. No deuterium gas was detected in the reaction headspace for this reaction. For both reactions, the detection of evolved gas is inconclusive due to the limited amount of oxidation product that was formed. Yet, the formation of oxidation product was dramatically reduced in the sealed conditions with

comparison to the reaction with air bubbled through, presumably due to the limited amount of air available in the sealed vessel.

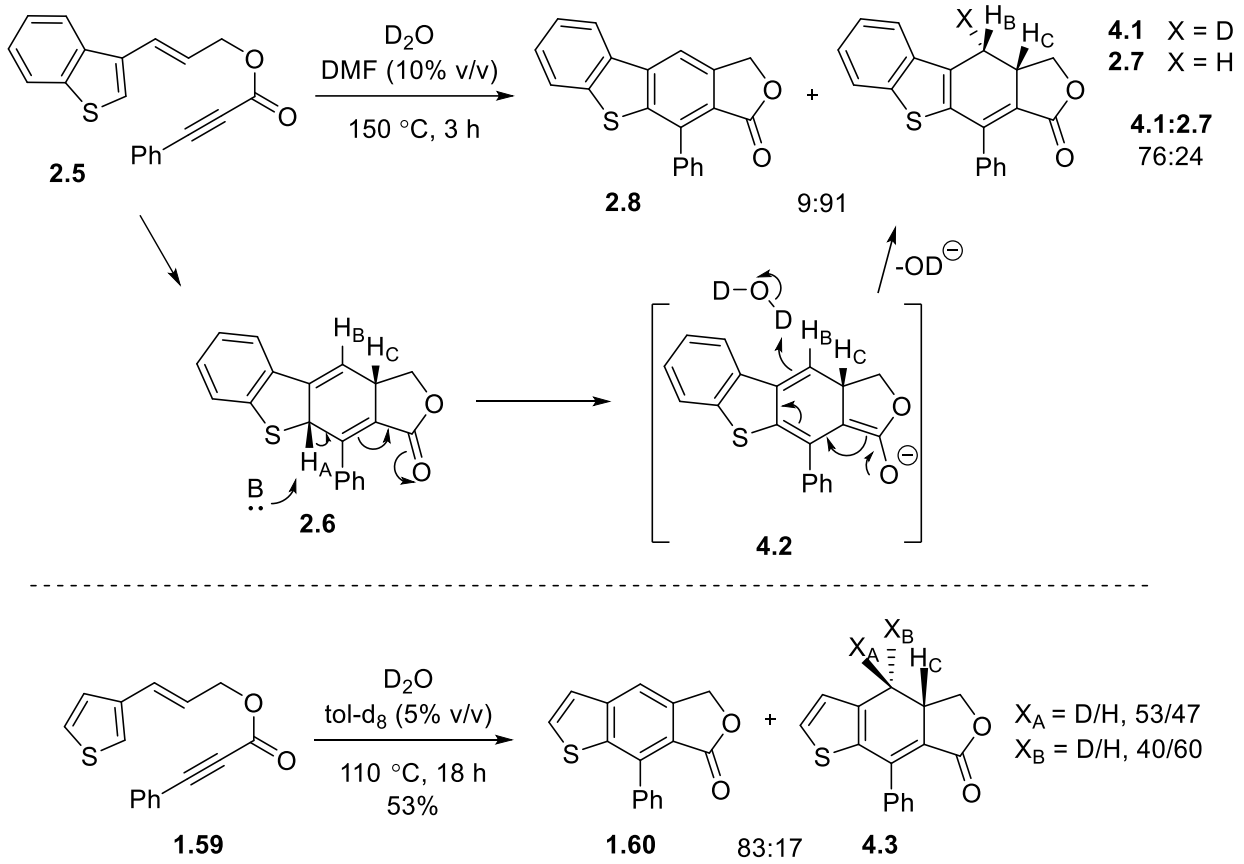
The higher ratio of oxidation product found when the reaction has an increased exposed to air is a result of the increased exposure to oxygen from the air. Likewise, reactions at lower temperatures, concentrations, and longer durations allow for increased exposure to air which affords a higher ratio of oxidation product. This mechanism differs from those of styrenyl precursors, which selectively provided oxidized product at elevated temperatures.[50] For most cases, the conversion of adduct to oxidation product is slowed in the presence of BHT and the ratio of oxidation product to isomerization product decreases which provides evidence that this transformation of adduct to oxidation product involves a radical process (see section 4.1.5). The presence of BHT in the reaction slows the dehydrogenation of adduct by acting as a radical scavenger for either oxygen in the solution or hydrogen atom abstracted adduct, thus slowing the formation of oxidation product.

4.4 Evidence for Isomerization Product Formation via Proton Transfer of Diels-Alder Adduct

Deuterium incorporation was observed when D_2O was introduced as an additive in dearomative DDDA reaction of **2.5**. Reaction of **2.5** heated for 3 h at 150 °C in D_2O/DMF (10% v/v) afforded predominantly isomerization product **4.1** with 76% deuterium incorporation at the X position as well as some **2.8** (91:9 respectively, Scheme 4.8). Deuterium incorporation was determined by comparing the integral intensities of resonances H_C at 3.70 ppm and H_A at 2.82

ppm. Product **4.1** was afforded as a single diastereomer and the stereochemistry shown was determined by the disappearance of the splitting for H_A (J^{AC} = 17.3 Hz).

We proposed that deuterium incorporation into isomerization product in the presence of D_2O would also occur with other precursors and in less nonpolar solvents. Dearomative DDDA reaction of **1.59** was performed in toluene with added D_2O rather than in DMF. Reaction of **1.59** heated for 18 h at 110 °C in D_2O/toluene (5% v/v) afforded a ratio of 83:17 of oxidation product to isomerization product in 53% yield. Deuterium incorporation was observed in the isomerization product and was determined by comparing the integral intensities of resonances X_A at 3.14 ppm, X_B at 2.70 ppm, and a methylene hydrogen of the lactone at 4.72 ppm. Product **4.3** was afforded as a mixture of diastereomers with overall deuterium incorporation of 53% at X_A and 40% at X_B.



Scheme 4.8. Mechanism of deuterium incorporation observed in dearomative Diels-Alder reactions with deuterium oxide present

The deuterium incorporation found in the isomerization product support formation of the product by an intermolecular, ionic proton transfer. Deuterium incorporation via a radical mechanism would be unlikely due to unfavorable generation of a hydroxyl radical. Deprotonation of the bis-allylic C–H_A of **2.6** affords the resonance-stabilized anion **4.2** that reacts with D_2O to afford **4.1**. The orbital alignment of bis-allylic hydrogen H_A with the π-orbitals of the adjacent α,β-unsaturated lactone enhances the acidity of the adduct. Selectivity for deuteration at the concave face is attributed to the steric incumbrance posed by H_C at the ring-fusion.

Enhanced selectivity for isomerization product was found in reactions with elevated temperatures and higher concentrations, likely due to increased intermolecular collisions necessary for the proton transfer. Reactions in solvents of higher polarity also afforded enhanced selectivity for isomerization product, most likely due to improved stabilization of an ionic intermediate. Finally, water, as an additive, acts as a more sterically accessible proton source for protonation of the ionic intermediate to afford enhanced selectivity for isomerization product.

4.5 Conclusions

We established that the dearomative DDDA reaction proceeds to either oxidation or isomerization products from the DA adduct via divergent mechanistic pathways with reaction conditions of temperature, concentration, solvent polarity, atmosphere, and mild additives as factors that control product selectivity. Reaction of DA adduct with bubbling air at room temperature supports the formation of oxidation product by an oxygen effected dehydrogenation of the adduct. Formation of isomerization product by an intermolecular, ionic proton transfer is supported by reactions where deuteron abstraction from D_2O affords deuterium incorporation into the isomerization product. Selectivity for the oxidation product was enhanced with reaction conditions of lower temperatures, non-polar solvents, lower concentrations, and increased exposure to air. Selectivity for the isomerization product was enhanced with conditions of higher temperatures, polar solvents, higher concentrations, water or BHT additives, and decreased exposure to air. Our mechanistic analysis of the dearomative DDDA reaction of heteroarenes has afforded improved understanding of its divergent mechanisms of reactivity and has allowed us to

determine the factors which control product selectivity. These findings enable us to enhance the scope and utility of this reaction for these and future substrates.

4.6 Experimental

4.6.1 General Methods

Unless otherwise indicated, all reactions were performed in flame-dried glassware under an air atmosphere and stirred with Teflon-coated magnetic stir bars. All commercially available compounds were purchased and used as received unless otherwise specified. Tetrahydrofuran (THF), diethyl ether (Et_2O), and dichloromethane (DCM) were purified by passing through alumina using a Sol-Tek ST-002 solvent purification system. Deuterated chloroform ($CDCl_3$) was dried over 4Å molecular sieves. Nitrogen gas was purchased from Matheson Tri Gas. Conventional heating was used for reactions that were monitored by ^{1}H NMR or performed open to the air. All microwave-mediated reactions were carried out using a Biotage Initiator Exp or Anton-Paar Monowave 300 microwave synthesizer. Purification of the compounds by flash column chromatography was performed using silica gel (40-63 μm particle size, 60 Å pore size). TLC analyses were performed on silica gel F_{254} glass plates (250 μm thickness). ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker Avance 300, 400, or 500 MHz spectrometers. Spectra were referenced to residual chloroform (7.26 ppm, ^{1}H; 77.16 ppm, ^{13}C) or *o*-dichlorobenzene (6.93 ppm, ^{1}H; 130.04 ^{13}C) unless otherwise specified. Chemical shifts are reported in ppm, multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), m (multiplet), and bs (broad singlet). Coupling constants, *J*, are reported in hertz (Hz). All NMR spectra were obtained at room

temperature. IR spectra were obtained using a Nicolet Avatar E.S.P. 360 FT-IR. EI mass spectroscopy was performed on a Waters Micromass GCT high resolution mass spectrometer, while ES mass spectroscopy was performed on a Waters Q-TOF Ultima API, Micromass UK Limited high-resolution mass spectrometer.

4.6.2 General Procedures for Dearomative DDDA Reactions

4.6.2.1 General Procedure D: Dearomative DDDA Reaction – Conventional Heating

An oven-dried NMR tube was charged with dearomative DDDA precursor (1 equiv) dissolved in solvent under an atmosphere of air. In some cases, butylated hydroxytoluene (BHT), deuterium oxide (D_2O), or water was added. In some cases, an internal standard of mesitylene was added to calculate an NMR yield. The NMR tube was sealed with a polypropylene cap and lowered into a preheated oil bath. Reaction progress was monitored by ^{1}H NMR by comparing the resonance integrations for starting material, adduct, oxidized product, and isomerized product at different time points. The reaction was paused for ^{1}H NMR analysis. The NMR tube was removed from the oil bath, rinsed with hexanes, and wiped with a ChemWipe. After obtaining an NMR spectrum, the tube was returned to the oil bath. Reaction time does not include the time required to obtain NMR spectrum at each time point (~15-20 min each). All yields are unoptimized.

4.6.2.2 General Procedure E: Dearomative DDDA Reaction – Microwave Heating

An oven-dried microwave vial equipped with a stir bar was charged with dearomative DDDA precursor (1 equiv) dissolved in solvent under an atmosphere of air. The vial was sealed with a Teflon-lined septum crimp cap and was heated in a Biotage Initiator Exp or Anton-Paar

Monowave 300 microwave synthesizer. The microwave parameters were set to variable power, constant temperature, fixed hold time set to on, and absorption set to "normal" for nonpolar solvents (o-DCB, DCE, $CDCl_3$) or "high" for polar solvents (acetonitrile, DMF). Product ratios were determined by comparing the resonance integrations for starting material, adduct, oxidized product, and isomerized product from the ^{1}H NMR of the reaction solution using No-D spectroscopy,[64] or by removing the solvent and re-dissolving in $CDCl_3$. Volatile solvents (DCE) were removed by rotary evaporation, o-DCB and $PhNO_2$ were removed by passing the reaction solution through a plug of silica gel with hexanes as eluent, and DMF was removed through aqueous extraction. All yields are unoptimized.

4.6.3 Experiments Showing the Effect of Temperature

Rxn 1. Follows General Procedure D. Precursor **2.5** (7 mg, 0.02 mmol) and mesitylene (3 µL, 0.02 mmol) in o-DCB-d_4 (0.5 mL, 0.04M) was heated at 60 °C for 66 h. A 0:0:100:0 ratio of **2.5**, **2.6**, **2.8**, and **2.7** was obtained in 58% NMR yield based upon the mesitylene internal standard. Ratios were determined by comparing the ^{1}H NMR resonances at 6.63 ppm (1H) for **2.5**, 5.46 ppm (1H) for **2.6,** and 5.21 ppm (2H) for **2.8** to the resonance at 6.64 ppm for mesitylene**.**

Table 4.2. Ratio of compounds in 4.6.3 – Rxn 1

Time (h)	**2.5**	**2.6**	**2.8**	**2.7**	Yield (%)
0	100	0	0	0	100
2	89	6	5	0	102
4	86	5	10	0	99
9	69	6	25	0	82
20	41	6	52	0	71
32	21	4	74	0	74
44	9	3	87	0	65
55	0	0	100	0	55

66	0	0	100	0	58

Rxn 2. A 1-mL screw-top flask with septum lid and stir bar was charged with precursor **2.19** (24 mg, 0.075 mmol) dissolved in o-dichlorobenzene (0.50 mL, 0.15 M) and sealed with a Teflon-lined septum screw cap under air. The solution was lowered into a pre-heated oil bath at 150 °C. After 2 h, the the solution was allowed to cool to room temperature, then transferred to an NMR tube for ^{1}H NMR analysis. Product ratios were determined by comparing the resonance integrations for starting material, adduct, oxidized product, and isomerized product from the ^{1}H NMR of the crude reaction solution using No-D spectroscopy. A 0:65:26:9 ratio of **2.19**, **2.20**, **2.8**, and **2.21** was obtained. Ratios were determined by comparing the ^{1}H NMR resonances at 4.56 ppm (1H) for **2.6,** 5.21 ppm (2H) for **2.8,** and 2.49 ppm (1H) for **2.7.** An unknown impurity identified by the resonance at 5.04 ppm exists in the starting material and persisted through the reaction to completion.

Rxn 3. Follows General Procedure D. Precursor **2.19** (22 mg, 0.069 mmol) in o-DCB (0.50 mL, 0.14 M) was heated at 180 °C for 120 min. A 0:33:30:37 ratio of **2.19**, **2.20**, **2.8**, and **2.21** was obtained. Ratios were determined by comparing the ^{1}H NMR resonances at 4.56 ppm (1H) for **2.6,** 5.21 ppm (2H) for **2.8,** and 2.49 ppm (1H) for **2.7.** An unknown impurity identified by the resonance at 5.04 ppm exists in the starting material and persisted through the reaction to completion.

4.6.4 Experiments Showing the Effect of Concentration

Rxn 1. Follows General Procedure E. Precursor **2.5** (19 mg, 0.060 mmol) in o-DCB (1.0 mL, 0.060 M) was heated at 225 °C for 20 min. A 0:8:81:11 ratio of **2.5**, **2.6**, **2.8**, and **2.7** was obtained. Ratios were determined by comparing the ^{1}H NMR resonances at 6.27 ppm (1H) for **2.6,** 5.44 ppm (2H) for **2.8,** and 2.79 ppm (1H) for **2.7**.

Rxn 2. Follows General Procedure E. Precursor **2.5** (39 mg, 0.12 mmol) in o-DCB (1.0 mL, 0.12 M) was heated at 225 °C for 20 min. A 0:14:66:20 ratio of **2.5**, **2.6**, **2.8**, and **2.7** was obtained. Ratios were determined by comparing the ^{1}H NMR resonances at 6.27 ppm (1H) for **2.6,** 5.44 ppm (2H) for **2.8,** and 2.79 ppm (1H) for **2.7**.

4.6.5 Experiments Showing the Effect of Solvent Polarity

Rxn 1. A 1-mL screw-top flask with septum lid and stir bar was charged with precursor **2.19** (24 mg, 0.075 mmol) dissolved in o-dichlorobenzene (0.50 mL, 0.15 M) and sealed with a Teflon-lined septum screw cap under air. The solution was lowered into a pre-heated oil bath at 150 °C. After 2 h, the the solution was allowed to cool to room temperature, then transferred to an NMR tube for ^{1}H NMR analysis. Product ratios were determined by comparing the resonance integrations for starting material, adduct, oxidized product, and isomerized product from the ^{1}H NMR of the crude reaction solution using No-D spectroscopy. A 0:65:26:9 ratio of **2.19**, **2.20**, **2.8**, and **2.21** was obtained. Ratios were determined by comparing the ^{1}H NMR resonances at 4.56 ppm (1H) for **2.6,** 5.21 ppm (2H) for **2.8,** and 2.49 ppm (1H) for **2.7.** An unknown impurity identified

by the resonance at 5.04 ppm exists in the starting material and persisted through the reaction to completion.

Rxn 2. Follows General Procedure D. Precursor **2.5** (10 mg, 0.031 mmol) in DMF-d_7 (0.50 mL, 0.060 M), sealed under an atmosphere of air, was heated at 150 °C for 180 min. A 0:0:23:77 ratio of **2.5**, **2.6**, **2.8**, and **2.7** was obtained in 60% isolated yield. Ratios were determined by comparing the ^{1}H NMR resonances at 5.46 ppm (2H) for **2.8,** and 4.84 ppm (1H) for **2.7.**

Rxn 3. Follows General Procedure D. Precursor **2.5** (6 mg, 0.02 mmol) in CH_3CN (0.5 mL, 0.04 M) was heated at 150 °C for 5 min. A 0:45:4:51 ratio of **2.5**, **2.6**, **2.8**, and **2.7** was obtained. Ratios were determined by comparing the ^{1}H NMR resonances at 6.20 ppm (1H) for **2.6,** 5.46 ppm (2H) for **2.8,** and 2.81 ppm (1H) for **2.7.**

4.6.6 Experiments Showing the Effect of Water Additive

Rxn 1. Follows General Procedure D. Precursor **2.5** (10 mg, 0.031 mmol) in DMF-d_7 (0.50 mL, 0.060 M), sealed under an atmosphere of air, was heated at 150 °C for 180 min. A 0:0:23:77 ratio of **2.5**, **2.6**, **2.8**, and **2.7** was obtained in 60% isolated yield. Ratios were determined by comparing the ^{1}H NMR resonances at 5.46 ppm (2H) for **2.8,** and 4.84 ppm (1H) for **2.7.**

Rxn 2. Follows General Procedure D. Precursor **2.5** (10 mg, 0.032 mmol) and D_2O (0.050 mL, 2.8 mmol) in DMF (0.45 mL, 0.60 M) was heated at 150 °C for 180 min. A 0:0:9:91 ratio of **2.5**, **2.6**, **2.8** and **4.1** was obtained in 50% yield. The isomerization product was observed to have 76%

deuterium incorporation. Ratios were determined by comparing the ^{1}H NMR resonances at 5.46 ppm (2H) for **2.8,** and 2.81 ppm (1H) for **2.7.**

4.6.7 Experiments Showing the Effect of BHT Additive

Rxn 1. Follows General Procedure D. Precursor **2.5** (6 mg, 0.02 mmol) and mesitylene (3 µL, 0.02 mmol) in toluene-d_8 (0.5 mL, 0.04M) was heated at 110 °C for 18 h. The experiment was paused briefly at the 3 h and 8 h time points for ^{1}H NMR analysis. A final ratio 0:0:100:0 of **2.5**, **2.6**, **2.8**, and **2.7** was obtained in 89% yield based on internal standard. Ratios were determined by comparing the ^{1}H NMR resonances at 6.07 ppm (1H) for **2.5**, 5.08 ppm (1H) for **2.6,** and 4.63 ppm (2H) for **2.8** to the resonance at 6.67 ppm for mesitylene.

Table 4.3. Ratio of compounds in 4.6.7 – Rxn 1

Time (h)	**2.5**	**2.6**	**2.8**	**2.7**	Yield (%)
3	0	43	57	0	100
8	0	0	100	0	91
18	0	0	100	0	94

Rxn 2. Follows General Procedure D. Precursor **2.5** (6 mg, 0.02 mmol), BHT (4 mg, 0.02 mmol), and mesitylene (3 µL, 0.02 mmol) in toluene-d_8 (0.5 mL, 0.04M) was heated at 110 °C for 18 h. The experiment was paused briefly at the 3 h and 8 h time points for ^{1}H NMR analysis. A final ratio 0:0:100:0 of **2.5**, **2.6**, **2.8**, and **2.7** was obtained in 96% yield based on internal standard. Ratios were determined by comparing the ^{1}H NMR resonances at 6.07 ppm (1H) for **2.5**, 5.08 ppm (1H) for **2.6,** and 4.63 ppm (2H) for **2.8** to the resonance at 6.67 ppm for mesitylene.

Table 4.4. Ratio of compounds in 4.6.7 – Rxn 2

Time (h)	**2.5**	**2.6**	**2.8**	**2.7**	Yield (%)
3	0	70	30	0	100
8	0	0	100	0	86
18	0	0	100	0	89

Rxn 3. Follows General Procedure D. Precursor **1.59** (6 mg, 0.02 mmol) and mesitylene (3 µL, 0.02 mmol) in toluene-d_8 (0.5 mL, 0.04M) was heated at 110 °C for 18 h. The experiment was paused briefly at the 3 h and 8 h time points for ^{1}H NMR analysis. A final ratio 5:0:49:46 of **1.59**, **2.1**, **1.60**, and **1.61** was obtained in 70% yield based on internal standard. Ratios were determined by comparing the ^{1}H NMR resonances at 5.84 ppm (1H) for **1.59**, 3.30 ppm (1H) for **2.1,** 4.56 ppm (2H) for **1.60,** and 3.24 ppm (1H) for **1.61** to the resonance at 6.67 ppm for mesitylene.

Table 4.5. Ratio of compounds in 4.6.7 – Rxn 3

Time (h)	**1.59**	**2.1**	**1.60**	**1.61**	Yield (%)
3	65	5	20	10	93
8	31	0	38	31	81
18	5	0	49	46	72

Rxn 4. Follows General Procedure D. Precursor **1.59** (6 mg, 0.02 mmol), BHT (4 mg, 0.02 mmol), and mesitylene (3 µL, 0.02 mmol) in toluene-d_8 (0.5 mL, 0.04M) was heated at 110 °C for 18 h. The experiment was paused briefly at the 3 h and 8 h time points for ^{1}H NMR analysis. A final ratio 0:0:29:71 of **1.59**, **2.1**, **1.60**, and **1.61** was obtained in 85% yield based on internal standard. Ratios were determined by comparing the ^{1}H NMR resonances at 5.84 ppm (1H) for **1.59**, 3.30 ppm (1H) for **2.1,** 4.56 ppm (2H) for **1.60,** and 3.24 ppm (1H) for **1.61** to the resonance at 6.67 ppm for mesitylene.

Table 4.6. Ratio of compounsd in 4.6.7 – Rxn 4

Time (h)	**1.59**	**2.1**	**1.60**	**1.61**	Yield (%)
3	58	12	7	23	101
8	23	0	17	60	93
18	0	0	29	71	84

Rxn 5. Follows General Procedure D. Precursor **2.9** (6 mg, 0.02 mmol) and mesitylene (3 µL, 0.02 mmol) in toluene-d_8 (0.5 mL, 0.04M) was heated at 110 °C for 18 h. The experiment was paused briefly at the 3 h and 8 h time points for ^{1}H NMR analysis. A final ratio 0:0:76:24 of **2.9**, **2.10**, **2.12**, and **2.11** was obtained in 97% yield based on internal standard. Ratios were determined by comparing the ^{1}H NMR resonances at 6.0 ppm (1H) for **2.9**, 5.08 ppm (1H) for **2.10,** 4.48 ppm (2H) for **2.12,** and 2.74 ppm (1H) for **2.11** to the resonance at 6.67 ppm for mesitylene.

Table 4.7. Ratio of compounds in 4.6.7 – Rxn 5

Time (h)	**2.9**	**2.10**	**2.12**	**2.11**	Yield (%)
3	14	3	72	11	127
8	0	0	76	24	95
18	0	0	76	24	97

Rxn 6. Follows General Procedure D. Precursor **2.9** (6 mg, 0.02 mmol), BHT (4 mg, 0.02 mmol), and mesitylene (3 µL, 0.02 mmol) in toluene-d_8 (0.5 mL, 0.04M) was heated at 110 °C for 18 h. The experiment was paused briefly at the 3 h and 8 h time points for ^{1}H NMR analysis. A final ratio 0:0:67:33 of **2.9**, **2.10**, **2.12**, and **2.11** was obtained in 91% yield based on internal standard. Ratios were determined by comparing the ^{1}H NMR resonances at 6.0 ppm (1H) for **2.9**, 5.08 ppm

(1H) for **2.10,** 4.47 ppm (2H) for **2.12,** and 2.90 ppm (1H) for **2.11** to the resonance at 6.67 ppm for mesitylene.

Table 4.8. Ratio of compounds in 4.6.7 – Rxn 6

Time (h)	**2.9**	**2.10**	**2.12**	**2.11**	Yield (%)
3	13	56	28	2	97
8	0	0	66	34	92
18	0	0	67	33	88

Rxn 7. Follows General Procedure D. Precursor **1.50** (6 mg, 0.02 mmol) and mesitylene (3 µL, 0.02 mmol) in toluene-d_8 (0.5 mL, 0.04M) was heated at 110 °C for 18 h. The experiment was paused briefly at the 3 h and 8 h time points for ^{1}H NMR analysis. A final ratio 0:0:93:7 of **1.50**, **2.13**, **2.14**, and **1.51** was obtained in 87% yield based on internal standard. Ratios were determined by comparing the ^{1}H NMR resonances at 5.93 ppm (1H) for **1.50**, 5.14 ppm (1H) for **2.13,** 4.47 ppm (2H) for **2.14,** and 3.17 ppm (1H) for **1.51** to the resonance at 6.67 ppm for mesitylene.

Table 4.9. Ratio of compounds in 4.6.7 – Rxn 7

Time (h)	**1.50**	**2.13**	**2.14**	**1.51**	Yield (%)
3	35	2	58	4	118
8	6	0	88	7	101
18	0	0	93	7	90

Rxn 8. Follows General Procedure D. Precursor **1.50** (6 mg, 0.02 mmol), BHT (4 mg, 0.02 mmol), and mesitylene (3 µL, 0.02 mmol) in toluene-d_8 (0.5 mL, 0.04M) was heated at 110 °C for 18 h. The experiment was paused briefly at the 3 h and 8 h time points for ^{1}H NMR analysis. A final ratio 0:0:70:30 of **1.50**, **2.13**, **2.14**, and **1.51** was obtained in 91% yield based on internal standard. Ratios were determined by comparing the ^{1}H NMR resonances at 5.90 ppm (1H) for **1.50**, 6.65

ppm (1H) for **2.13,** 4.48 ppm (2H) for **2.14,** and 3.15 ppm (1H) for **1.51** to the resonance at 6.67 ppm for mesitylene.

Table 4.10. Ratio of compounds in 4.6.7 – Rxn 8

Time (h)	**1.50**	**2.13**	**2.14**	**1.51**	Yield (%)
3	35	32	22	11	125
8	8	11	54	27	100
18	0	0	70	30	83

Rxn 9. Follows General Procedure D. Precursor **2.5** (10 mg, 0.03 mmol) and mesitylene (3 µL, 0.02 mmol) in *o*-DCB-d_4 (0.5 mL, 0.06M) was heated at 150 °C for 8 h. The experiment was paused briefly at the 3 h time point for ^{1}H NMR analysis. A final ratio 0:0:82:18 of **2.5**, **2.6**, **2.8**, and **2.7** was obtained in 93% yield based on internal standard. Ratios were determined by comparing the ^{1}H NMR resonances at 6.27 ppm (1H) for **2.5**, 5.94 ppm (1H) for **2.6,** 5.22 ppm (2H) for **2.8,** 3.31 ppm (1H) for **2.7** to the resonance at 6.63 ppm for mesitylene.

Table 4.11. Ratio of compounds in 4.6.7 – Rxn 9

Time (h)	**2.5**	**2.6**	**2.8**	**2.7**	Yield (%)
3	0	17	65	18	93
8	0	0	82	18	93

Rxn 10. Follows General Procedure D. Precursor **2.5** (10 mg, 0.03 mmol), BHT (7 mg, 0.03 mmol), and mesitylene (3 µL, 0.02 mmol) in *o*-DCB-d_4 (0.5 mL, 0.06M) was heated at 150 °C for 8 h. The experiment was paused briefly at the 3 h time point for ^{1}H NMR analysis. A final ratio 0:0:77:23 of **2.5**, **2.6**, **2.8**, and **2.7** was obtained in 53% yield based on internal standard. Ratios were determined by comparing the ^{1}H NMR resonances at 6.27 ppm (1H) for **2.5**, 5.94 ppm (1H) for **2.6,** 5.22 ppm (2H) for **2.8,** 3.31 ppm (1H) for **2.7** to the resonance at 6.63 ppm for mesitylene.

Table 4.12. Ratio of compounds in 4.6.7 – Rxn 10

Time (h)	**2.5**	**2.6**	**2.8**	**2.7**	Yield (%)
3	0	17	52	31	96
8	0	0	77	23	83

4.6.8 Experiments Showing the Effect of Atmosphere

Rxn 1. A 1-mL screw-top flask with septum lid and stir bar was charged with precursor **2.19** (24 mg, 0.075 mmol) dissolved in o-dichlorobenzene (0.50 mL, 0.15 M) and sealed with a Teflon-lined septum screw cap under air. The solution was lowered into a pre-heated oil bath at 150 °C. After 2 h, the the solution was allowed to cool to room temperature, then transferred to an NMR tube for ^{1}H NMR analysis. Product ratios were determined by comparing the resonance integrations for starting material, adduct, oxidized product, and isomerized product from the ^{1}H NMR of the crude reaction solution using No-D spectroscopy. A 0:65:26:9 ratio of **2.19**, **2.20**, **2.8**, and **2.21** was obtained. Ratios were determined by comparing the ^{1}H NMR resonances at 4.56 ppm (1H) for **2.6,** 5.21 ppm (2H) for **2.8,** and 2.49 ppm (1H) for **2.7.** An unknown impurity identified by the resonance at 5.04 ppm exists in the starting material and persisted through the reaction to completion.

Rxn 2. A 1-mL, screw-top vial with Teflon-lined septum screw cap and stir bar was charged with precursor **2.5** (23 mg, 0.072 mmol) dissolved in o-dichlorobenzene (0.50 mL, 0.14 M). The solution was degassed by bubbling N_2 through a needle into the solution and venting through an outlet needle. The vial was lowered into a preheated oil bath at 150 °C. After 2 h, the solution was

allowed to cool to rt before being transferred to an NMR tube for analysis. Product ratios were determined by comparing the resonance integrations for starting material, adduct, oxidized product, and isomerized product from the ^{1}H NMR of the reaction solution using No-D spectroscopy. A 0:82:12:6 ratio of **2.5**, **2.6**, **2.8**, and **2.7** was obtained. Ratios were determined by comparing the ^{1}H NMR resonances at 5.93 ppm (1H) for **2.6,** 5.21 ppm (2H) for **2.8,** and 2.49 ppm (1H) for **2.7.**

Rxn 3. A flame-dried, 5-mL, single-necked, pear-shaped flask equipped with a condenser, septum, and stir bar was charged with precursor **2.5** (23 mg, 0.072 mmol) dissolved in o-dichlorobenzene (0.50 mL, 0.14 M). A 16-gauge needle was inserted into the septum and left open to the air. The flask was lowered into a preheated oil bath at 150 °C. After 2 h, the solution was allowed to cool to room temperature before transferred to an NMR tube for NMR analysis. Product ratios were determined by comparing the resonance integrations for starting material, adduct, oxidized product, and isomerized product from the ^{1}H NMR of the reaction solution using No-D spectroscopy. A 0:0:85:15 ratio of **2.5**, **2.6**, **2.8**, and **2.7** was obtained. Ratios were determined by comparing the ^{1}H NMR resonances at 5.21 ppm (2H) for **2.8,** and 2.49 ppm (1H) for **2.7.**

4.6.9 Experiments as Evidence for Oxygen Mediated Dehydrogenation to Oxidation Product

Rxn 1. Follows General Procedure D. Precursor **2.5** (10 mg, 0.03 mmol) and mesitylene (3 µL, 0.02 mmol) in *o*-DCB-d_4 (0.5 mL, 0.06M) was heated at 150 °C for 8 h. The experiment was paused briefly at the 3 h time point for ^{1}H NMR analysis. A final ratio 0:0:82:18 of **2.5**, **2.6**, **2.8**, and **2.7** was obtained in 53% yield based on internal standard. Ratios were determined by

comparing the ^{1}H NMR resonances at 6.27 ppm (1H) for **2.5**, 5.94 ppm (1H) for **2.6,** 5.22 ppm (2H) for **2.8,** 3.31 ppm (1H) for **2.7** to the resonance at 6.63 ppm for mesitylene. After the reaction was completed, H_2 gas was bubbled through the solution for 2 min. and ^{1}H NMR was performed to observe the appearance of the resonance for H_2 gas at 4.53 ppm. The solution was then bubbled through with argon gas far 2 min. and ^{1}H NMR was performed to observe the disappearance of the resonance for H_2 gas at 4.53 ppm.

Table 4.13. Ratio of compounds in 4.6.9 – Rxn 1

Time (h)	**2.5**	**2.6**	**2.8**	**2.7**	Yield (%)
3	0	17	65	18	93
8	0	0	82	18	93

Rxn 2. A 1-mL, flame-dried, microwave vial with stir bar was charged with precursor **2.5** (20 mg, 0.063 mmol) dissolved in o-dichlorobenzene (0.50 mL, 0.13 M). The vial was sealed with a crimp cap with Teflon-lined septum, wrapped in parafilm at the top, and lowered into a pre-heated oil bath at 150 °C. After 90 min, the solution was allowed to cool to room temperature before transferred to an NMR tube for NMR analysis. Product ratios were determined by comparing the resonance integrations for starting material, adduct, oxidized product, and isomerized product from the ^{1}H NMR of the crude reaction solution using No-D spectroscopy. A 0:41:39:20 ratio of **2.5**, **2.6**, **2.8**, and **2.7** was obtained. Ratios were determined by comparing the ^{1}H NMR resonances at 5.45 ppm (1H) for **2.6,** 5.21 ppm (2H) for **2.8,** and 2.79 ppm (1H) for **2.7**.

Rxn 3. A 1-mL, flame-dried, microwave vial with stir bar was charged with precursor **2.19** (24 mg, 0.075 mmol) dissolved in o-dichlorobenzene (0.50 mL, 0.15 M). The vial was sealed with a

crimp cap with Teflon-lined septum, wrapped in parafilm at the top, and lowered into a pre-heated oil bath at 150 °C. After 90 min, the solution was allowed to cool to room temperature before transferred to an NMR tube for NMR analysis. Product ratios were determined by comparing the resonance integrations for starting material, adduct, oxidized product, and isomerized product from the ^{1}H NMR of the crude reaction solution using No-D spectroscopy. A 0:77:18:5 ratio of **2.19**, **2.20**, **2.8**, and **2.21** was obtained. Ratios were determined by comparing the ^{1}H NMR resonances at 4.53 ppm (1H) for **2.20,** 5.21 ppm (2H) for **2.8,** and 3.09 ppm (1H) for **2.21**.

4.6.10 Experiments as Evidence for Ionic Isomerization to Isomerization Product

Rxn 1. Follows General Procedure D. Precursor **2.5** (10 mg, 0.032 mmol) and D_2O (0.050 mL, 2.8 mmol) in DMF (0.45 mL, 0.60 M) was heated at 150 °C for 180 min. A 0:0:9:91 ratio of **2.5**, **2.6**, **2.8** and **4.1** was obtained in 50% yield. Ratios were determined by comparing the ^{1}H NMR resonances at 5.46 ppm (2H) for **2.8,** and 2.81 ppm (1H) for **2.7.** Deuterium incorporation was determined by comparing the integral intensities of resonances at 3.70 ppm and at 2.82 ppm. The isomerization product was observed to have 76% deuterium incorporation evidenced by the resonance at 2.82 ppm.

Rxn 2. A 2-mL, oven-dried microwave vial with stir bar was charged with **1.59** (15 mg, 0.06 mmol) in toluene (1207 µL) under an atmosphere of air. D_2O (64 µL, 3.2 mmol) was added via syringe to form a biphasic mixture. The vial was sealed with a Teflon-lined septum crimp cap and lowered into an oil bath preheated to 110 °C. After 18 h, the solution was allowed to cool to rt and concentrated by rotary evaporation. The residue was purified by silica gel flash column chromatography (40% EtOAc/Hex) to yield an 83:17 ratio of **1.60** to **4.3** (8 mg, 53%) with

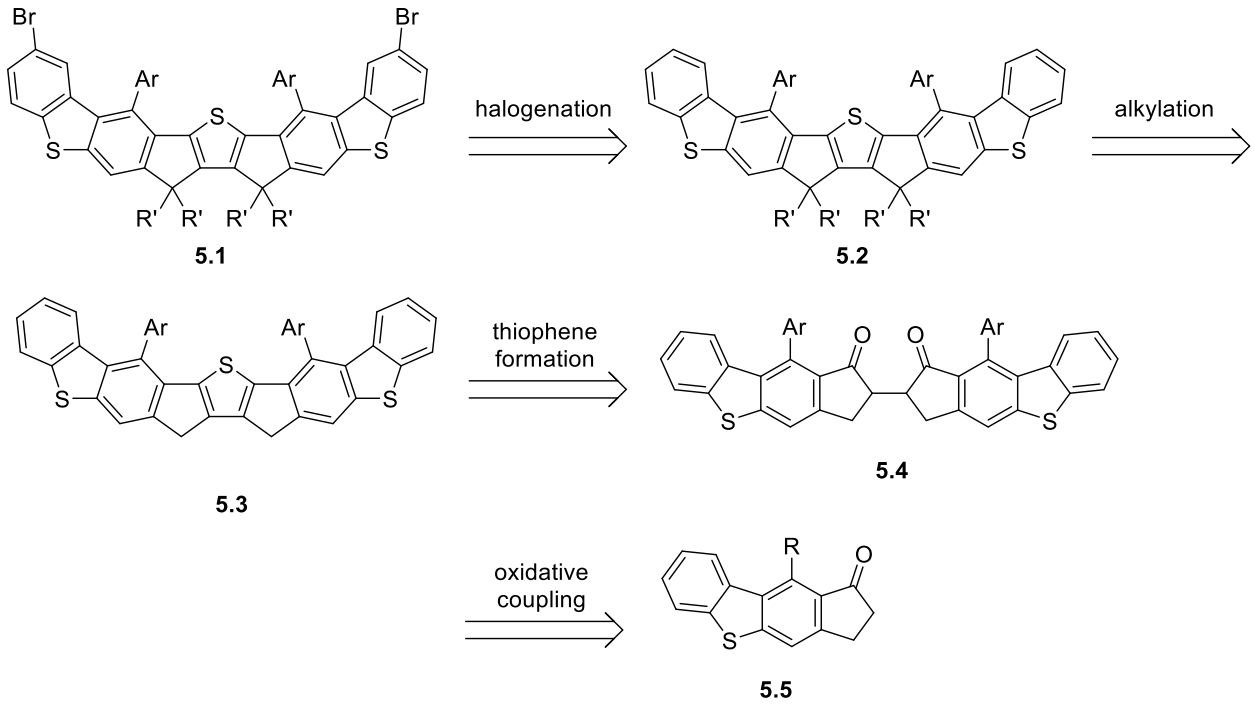
recovered starting material (4 mg, 27%). Deuterium incorporation was determined by comparing the integral intensities of resonances at 3.15 ppm, 2.70 ppm, and 4.72 ppm. The isomerization product was observed to have 53% deuterium incorporation evidenced by the resonance at 3.15 ppm and 40% for the proton at 2.70 ppm.

5.0 Application of the Dearomative DDDA Reaction Towards the Synthesis of Organic Solar Cell Materials

Recently, interest has grown in the application of heteroarenes towards ladder-type conjugated ring systems as materials for organic photovoltaic solar cells. Multi-fused ladder-type arenes have recently reached record-breaking power conversion efficiencies (PCE) in organic photovoltaic solar-cells.[16] We sought to apply our dearomative DDDA reaction to the generation of uniquely substituted ladder-type arenes.

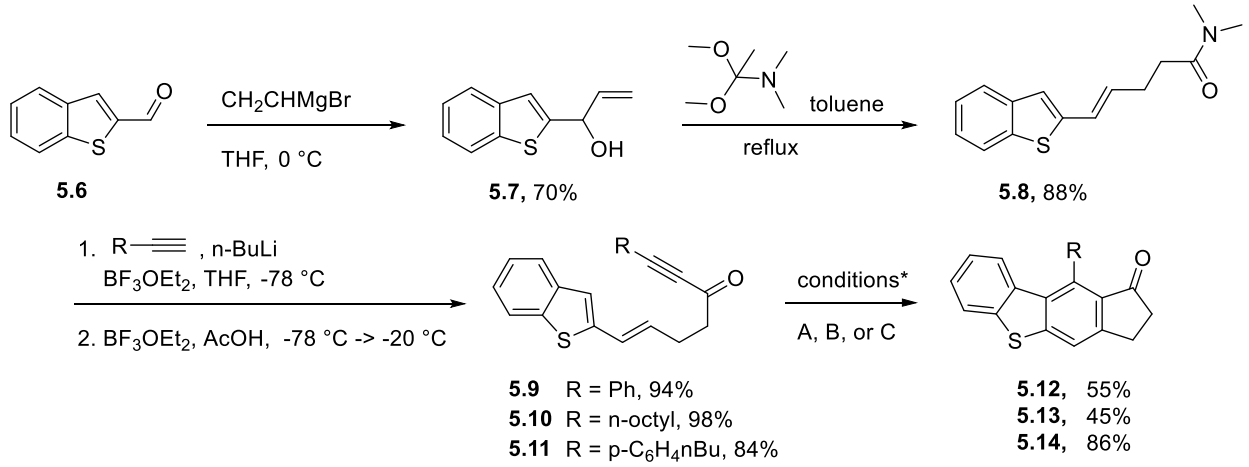
5.1 Synthesis of Dearomative DDDA Reaction Oxidation Product via Ketone-Tethered Precursors

We proposed accessing these ladder-type arenes for organic solar cells via the oxidation product of the dearomative DDDA reaction. Halogenation of the external benzene rings of the ladder-type arene would afford a handle for polymerization or functionalization. Dialkylation of the methylene carbons on the arene would increase solubility while formation of the ladder-type arene would be accomplished by thiophene formation via the 1,4-diketone. Synthesis of the 1,4-diketone would be accomplished by the oxidative coupling of oxidation product from the dearomative DDDA reaction of ketone-tethered precursor affording a 2-cyclopentenone rather than the lactone afforded from ester-tethered precursors.



Scheme 5.1. Retrosynthetic route for organic solar cell materials via the dearomative DDDA oxidation product

To this end, we set out to test the feasibility of the dearomative DDDA reaction as a way to access the oxidation product **5.5**. Benzo[*b*]thiophene-2-carbaldehyde **5.6** was subjected to Grignard reaction with vinyl magnesium bromide to afford allyl alcohol **5.7** in 70% yield. Reaction of allyl alcohol **5.7** to the Eschenmoser-Claisen rearrangement afforded the amide **5.8** in 88% yield. Reaction of amide **5.8** with the appropriate alkyne affords dearomative DDDA precursors **5.9** in 94% yield, **5.10** in 98% yield, and **5.11** in 86% yield.



* A = 1:1 nitrobenzene:*o*-DCB, sealed, under air, 225 °C, 3 min, to afford **5.12**; B = *o*-DCB, open to air, 150 °C, 48h, to afford **5.13**; C = *o*-DCB, open to air, 130 °C, 24h, to afford **5.14**

Scheme 5.2. Synthesis of dearomative DDDA reaction oxidation product via the ketone-tethered precursors

5.9 was heated via microwave irration for 3 min at 225 °C in 50% v/v nitrobenzene/*o*-DCB to afford exclusively the oxidation product **5.12** in 55% yield. The nitrobenzene was difficult to separate from **5.12** in the purification step, thus other conditions were employed for formation of **5.13** and **5.14**. Oxidation product **5.12** was extremely insoluble in a number of solvents, i.e., hexanes, acetonitrile, and methanol, thus, was not taken on to the oxidative coupling reaction. To access a more soluble oxidation product from the dearomative DDDA reaction, precursors **5.10** and **5.11** were prepared. **5.10** heated for 48 h at 150 °C in *o*-DCB, open to air, afforded oxidation product **5.13** in 45% yield. The nitrobenzene was difficult to separate from product **5.12** in purification, thus the slower conditions incorporating bubbled air were employed for formation of **5.13.** Precursor **5.11** heated for 24 h at 130 °C in *o*-DCB, open to air, afforded oxidation product **5.14** in 84% yield.

The synthesis of oxidation products **5.13** and **5.14** from the dearomative DDDA reaction was accomplished with complete selectivity. Enhanced selectivity for oxidation product was

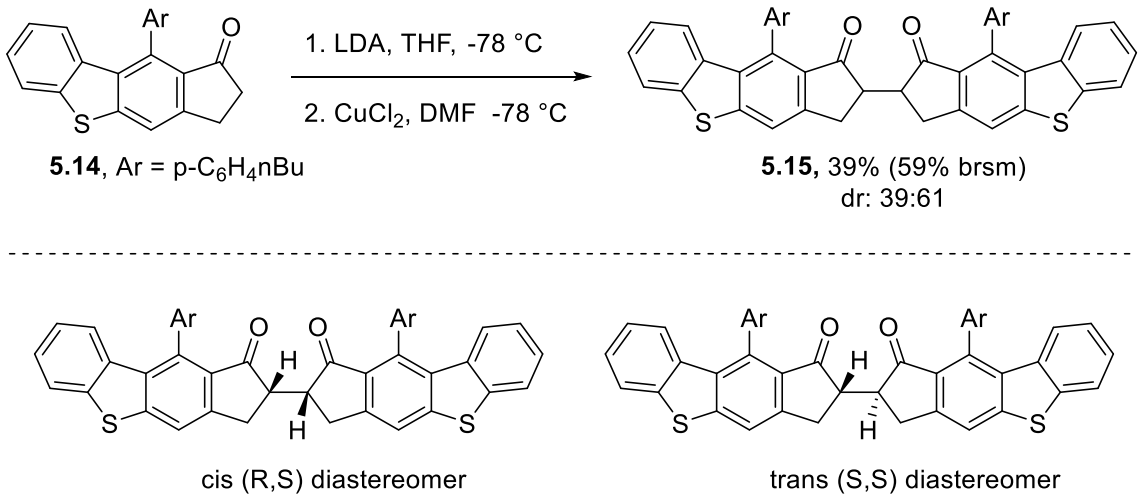
obtained through our new knowledge of the reaction conditions that affect product selectivity. Reaction conditions employed lower temperatures, a relatively non-polar solvent, and increased exposure to air via continuous bubbling through the reaction solution.

5.2 Progress Towards the Synthesis of Ladder-Type Arene Materials for Organic Solar Cells

With oxidation product in hand, our next steps were to apply our product of the dearomative DDDA reaction to the formation of a multi-fused ladder-type arene with conjugation across multiple rings. Oxidative coupling with phenyl substituted **5.12** and alkyl substituted **5.13** was unsuccessful as **5.12** proved insoluble in multiple solvents and reaction of **5.13** led to decomposition and retention of starting material. The insolubility of **5.12** may be due to favorable self-coordination because of strong intermolecular π-π dispersion interactions between aromatic rings. The decomposition of **5.13** under the basic reaction conditions may be due to competing deprotonation at the α position of the alkyl chain rather than desired deprotonation at the alpha position of the cyclopentenone. Evidence for the acidity of the protons at the α position of the alkyl chain can be observed in the ^{1}H NMR of **5.13** (see appendix B) where the resonance for those protons is shifted downfield to 3.8 ppm due to anisotropy effects from the nearby carbonyl. The resonance is also broadened, potentially due to tautomerization to the enol effecting an exchange broadening.

Oxidative coupling of **5.14** with LDA and $CuCl_2$ afforded **5.15** in 39% yield (59% based on recovered starting material, Scheme 5.3). Starting material **5.14** was recovered even when 5 equivalents of LDA and $CuCl_2$ were utilized. Optimization of this step would be vital to the make

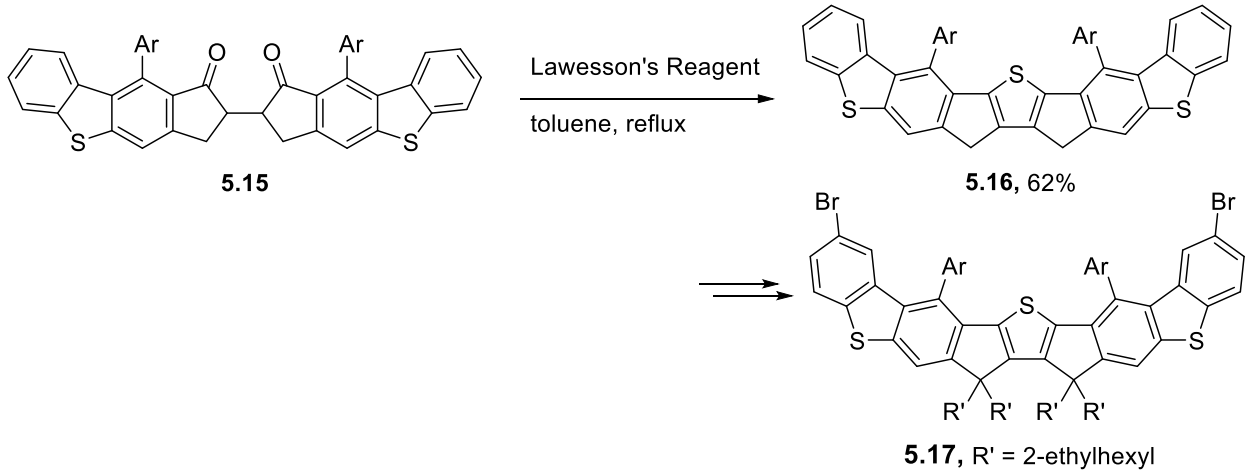
this synthetic route pragmatic. Cis and trans diastereomers of **5.15** for the protons α to the ketones (Scheme 5.3) were isolated and characterized separately as they were separable by flash column chromatography with an afforded diastereomeric ratio (dr) of 39:61. In literature, the diastereomer oxidative coupling products of 1-indanone are identified but not reported as separable, and they are instead characterized as a mixture.[65, 66] The cis (R,S) and trans (S,S) stereochemistry for the two diastereomers of **5.15** was not determined or assigned between the isolated products. Determination of stereochemistry may be possible in the future as the cis diastereomer is a meso compound, thus optically inactive, and should be distinguishable from the optically active trans diastereomer via polarimetry. Recrystallization of the isolated diastereomers has not been attempted, thus far, but may also possible as both were isolated as solids. Determination of stereochemistry could then be conducted via x-ray crystallography.



Scheme 5.3. Oxidative coupling of DA oxidation product with dr of 39:61

Reaction of **5.15** with Lawesson's reagent to afford the ladder-type arene **5.16** was performed separately for both diastereomers. The major diastereomer of **5.15** when reacted with

Lawesson's reagent in refluxing toluene afforded the ladder-type arene **5.16** in 62% yield (Scheme 5.4). The minor diastereomer of **5.15**, when reacted under the same conditions, did not afford any formation of product **5.16**, but 69% of the starting material **5.15** was recovered. It has yet to be determined as to why the minor diastereomer did not afford product under the same conditions that were successful for the major diastereomer. Recrystallization of **5.16** was attempted by dissolving in a minimal amount of dichloromethane, followed by dilution with n-heptane, and monitoring for crystal formation over the course of days at room temperature and at 0 °C in the laboratory freezer. All recrystallization attempts thus far have been unsuccessful.



Scheme 5.4. Synthesis of the polycyclic ladder-type arene with Lawesson's reagent

Future steps include alkylation of the methylene carbons to increase solubility of the product **5.17** followed by halogenation of the external benzene rings to provide handles for future functionalization or polymerization reactions. Once the feasibility of these future steps is established, Prof. Hutchison from the University of Pittsburgh will assist with a target selection process utilizing computational examination of a wide array of virtual compounds accessible using the proposed dearomative DDDA chemistry.

5.3 Conclusions

We established the dearomative DDDA reaction of vinyl heteroarenes as a key step in the synthesis of novel multi-ring ladder-type arenes which may be used as photovoltaic materials for organic solar cells. The ladder-type arene was successfully synthesized via oxidative coupling and thiophene formation from the oxidation product of the dearomative DDDA reaction. Oxidation product of the ketone-tethered precursor was generated selectively through mild manipulation of the reaction parameters as discovered in our studies. We hope that these novel, linearly fused ladder-type structures will enhance our understanding of photovoltaic materials and lead to improved efficiency in organic solar cells.

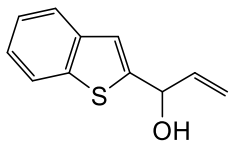
5.4 Experimental

5.4.1 General Methods

Unless otherwise indicated, all reactions were performed in flame-dried glassware under an air atmosphere and stirred with Teflon-coated magnetic stir bars. All commercially available compounds were purchased and used as received unless otherwise specified. Tetrahydrofuran (THF), diethyl ether (Et_2O), and dichloromethane (DCM) were purified by passing through alumina using a Sol-Tek ST-002 solvent purification system. Deuterated chloroform ($CDCl_3$) was dried over 4Å molecular sieves. Nitrogen gas was purchased from Matheson Tri Gas. Conventional heating was used for reactions that were monitored by ^{1}H NMR or performed open to the air. All microwave-mediated reactions were carried out using a Biotage Initiator Exp or Anton-Paar

Monowave 300 microwave synthesizer. Purification of the compounds by flash column chromatography was performed using silica gel (40-63 μm particle size, 60 Å pore size). TLC analyses were performed on silica gel F_{254} glass plates (250 μm thickness). ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker Avance 300, 400, or 500 MHz spectrometers. Spectra were referenced to residual chloroform (7.26 ppm, ^{1}H; 77.16 ppm, ^{13}C) or *o*-dichlorobenzene (6.93 ppm, ^{1}H; 130.04 ^{13}C) unless otherwise specified. Chemical shifts are reported in ppm, multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), m (multiplet), and bs (broad singlet). Coupling constants, *J*, are reported in hertz (Hz). All NMR spectra were obtained at room temperature. IR spectra were obtained using a Nicolet Avatar E.S.P. 360 FT-IR. EI mass spectroscopy was performed on a Waters Micromass GCT high resolution mass spectrometer, while ES mass spectroscopy was performed on a Waters Q-TOF Ultima API, Micromass UK Limited high-resolution mass spectrometer.

5.4.2 Synthesis of a Multi-Ring Ladder-Type Heteroarene



1-(benzo[b]thiophen-2-yl)prop-2-en-1-ol (5.7). A flame-dried, single-necked, 100-mL, round-bottomed flask equipped with a stir bar, septum, and a nitrogen inlet adaptor was charged with benzo[b]thiophene-2-carboxaldehyde (500 mg, 3.08 mmol) dissolved in THF (37.8 mL, 0.08 M) via syringe. The flask was placed in an ice/water bath (0 °C) and after 5 min, vinyl magnesium bromide (6.2 mL of a 1 M solution in THF, 6.16 mmol) was added dropwise by syringe. The solution was allowed to warm to rt over 1 h. After the complete disappearance of starting material

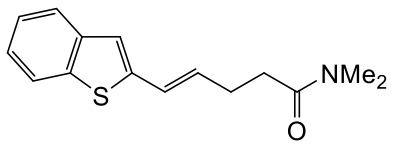
as observed by TLC, sat'd aqueous ammonium chloride (10.0 mL) was added to the flask all at once. The mixture was transferred to a separatory funnel, the layers separated, and the aqueous phase was extracted with ethyl acetate (10 mL x 3). The combined organic phase was washed with brine (10 mL), dried over magnesium sulfate, gravity filtered, and concentrated using rotary evaporation. The resulting brown oil was purified by flash column chromatography (20% ethyl acetate/hexanes) to yield the title compound as a yellow liquid (407 mg, 70%). Compound **5.7** was previously prepared by Wang et al.[67] Characterization data corresponds to the literature.

Data **5.7**

^{1}H NMR (300 MHz, $CDCl_3$)

7.82 (dd, J = 7.4, 1.6 Hz, 1H), 7.73 (dd, J = 6.4, 2.0 Hz, 1H), 7.37-7.27 (m, 2H), 7.21 (s, 1H), 6.23-6.12 (m, 1H), 5.54-5.43 (m, 2H), 5.31 (d, J = 10.4, 1H), 2.26 (t, J = 4.5 Hz, 1H) ppm. EtOAc impurity at 4.12, 2.05, and 1.25 ppm.

TLC R_f = 0.57 (40% ethyl acetate/hexanes) [silica gel, UV]



(E)-5-(benzo[b]thiophen-2-yl)-*N*,*N*-dimethylpent-4-enamide (5.8). A flame-dried, two-necked, 50-mL, round-bottomed flask equipped with a stir bar, septum, condenser, and a nitrogen inlet adaptor was charged with allyl alcohol **5.7** (780 mg, 4.10 mmol) dissolved in toluene (16.0 mL, 0.26 M) via syringe. *N*,*N*-dimethylacetamide dimethyl acetal (1.5 mL, 10.26 mmol) was added via syringe in one portion. The flask was placed in an oil bath at 115 °C, and the solution was heated to reflux for 2 h until the complete disappearance of starting material was observed by TLC. The

flask was removed from the oil bath and the solution was allowed to cool to rt. The solution was concentrated under rotary evaporation. The resulting oil was purified by flash column chromatography (80% ethyl acetate/hexanes) to yield the title compound as a light-yellow solid (935 mg, 88%).

Data **5.8**

^{1}H NMR (300 MHz, $CDCl_3$)

7.76-7.70 (m, 1H), 7.67-7.61 (m, 1H), 7.32-7.22 (m, 2H), 7.06 (s, 1H), 6.66 (d, *J* = 15.4 Hz, 1H), 6.19 (dt, *J* = 15.5, 6.8 Hz, 1H), 2.99 (d, *J* = 13.5 Hz, 6H), 2.63-2.45 (m, 4H) ppm. DCM impurity at 5.30 ppm.

^{13}C NMR (75 MHz, $CDCl_3$)

172.0, 142.9, 140.3, 138.7, 132.4, 124.8, 124.5, 124.4, 123.3, 122.2, 121.7, 37.3, 35.6, 32.9, 28.6 ppm

IR (thin film)

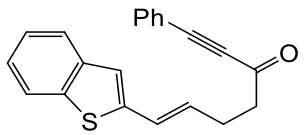
2926, 1777, 1643, 1494, 1401, 1264, 1141, 955, 749 cm^{-1}

HRMS (FTMS + p ESI)

$[M + H]^+$ Calcd for $C_{15}H_{18}ONS$ 260.1104; Found 260.1098

TLC R_f = 0.30 (80% ethyl acetate/hexanes) [silica gel, UV]

MP 88.0 – 91.6 °C



(E)-7-(benzo[b]thiophen-2-yl)-1-phenylhept-6-en-1-yn-3-one (5.9). A flame-dried, 25-mL, round-bottomed, single-necked flask equipped with stir bar, septum, and a nitrogen inlet adapter was charged with phenylacetylene (0.31 mL, 2.85 mmol) followed by THF (5.0 mL) via syringe. The flask was placed in a dry ice/acetone bath (-78 °C). After 10 min, n-butyllithium (1.58 mL of a 1.6 M solution in hexanes, 2.53 mmol) was added via syringe in one portion. After 5 min, boron trifluoride diethyl etherate (0.33 mL, 2.69 mmol) was added via syringe in one portion. After 15 min, amide **5.8** (410 mg, 1.58 mmol) diluted in THF (5 mL) was added in one portion via syringe. Upon disappearance of starting material as observed by TLC, a second portion of boron trifluoride diethyl etherate (0.33 mL, 2.53 mmol) was added followed by acetic acid (0.15 mL, 2.69 mmol), each were added via syringe in a single portion. The solution was allowed to warm in a brine/ice bath to -20 °C over the course of 1 h. Sat'd. aqueous ammonium chloride (8 mL) was added in one portion and the mixture was transferred to a separatory funnel. The aqueous layer was extracted with ethyl acetate (8 mL x 3). The combined organic layers were dried over magnesium sulfate, gravity filtered, and concentrated under rotary evaporation. The resulting brown oil was purified by flash column chromatography (20% ethyl acetate/hexanes) to yield the title compound as a brown oil (471 mg, 94%).

Data **5.9**

^{1}H NMR (300 MHz, $CDCl_3$)

7.73 (dd, *J* = 3.0, 6.6 Hz, 1H), 7.66 (dd, *J* = 2.4, 5.8 Hz, 1H), 7.59 (dt, *J* = 1.5, 7.0 Hz, 2H), 7.50-7.35 (m, 3H), 7.33-7.24 (m, 2H), 7.08 (s, 1H), 6.69 (d, *J* = 15.5 Hz, 1H), 6.7 (dt, *J* = 6.9, 15.6 Hz, 1H), 2.89 (t, *J* = 7.2 Hz, 2H), 2.67 (q, *J* = 7.5 Hz, 2H) ppm. Water impurity at 1.57 ppm.

^{13}C NMR (75 MHz, $CDCl_3$)

186.8, 142.6, 140.2, 138.8, 133.2 (2C), 130.9 (2C), 128.8 (2C), 125.3, 124.6, 124.5, 123.4, 122.3, 122.0, 120.0, 91.4, 87.9, 44.8, 27.4 ppm

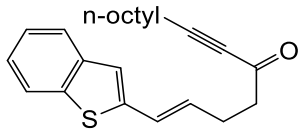
IR (thin film)

3403, 3058, 2925, 2200, 1708, 1671, 1582, 1449, 1320, 1272, 1098, 752, 696 cm^{-1}

HRMS (FTMS + p ESI)

$[M + H]^+$ Calcd for $C_{21}H_{17}OS$ 317.0994; Found 317.0986

TLC R_f = 0.77 (40% ethyl acetate/hexanes) [silica gel, UV]



(E)-1-(benzo[b]thiophen-2-yl)pentadec-1-en-6-yn-5-one (5.10). A flame-dried, 25-mL, round-bottomed, single-necked flask equipped with stir bar, septum, and a nitrogen needle inlet was charged with 1-decyne (0.38 mL, 2.03 mmol) followed by THF (3.8 mL) via syringe. The flask was placed in a dry ice/acetone bath (-78 °C). After 10 min, n-butyllithium (1.16 mL of a 1.6 M solution in hexanes, 1.80 mmol) was added via syringe in one portion. After 5 min, boron trifluoride diethyl etherate (0.24 mL, 1.91 mmol) was added via syringe in one portion. After 15 min, amide **5.8** (292 mg, 1.13 mmol) diluted in THF (3.8 mL) was added in one portion via syringe. Upon disappearance of starting material as observed by TLC, a second portion of boron trifluoride diethyl etherate (0.24 mL, 1.91 mmol) was added followed by acetic acid (0.12 mL, 1.91 mmol), each were added via syringe in a single portion. The solution was allowed to warm in a brine/ice bath to -20 °C over the course of 1 h. Sat'd. aqueous ammonium chloride (8 mL) was added in one portion and the mixture was transferred to a separatory funnel. The aqueous layer was extracted

with ethyl acetate (8 mL x 3). The combined organic layers were dried over magnesium sulfate, gravity filtered, and concentrated under rotary evaporation. The resulting oil was purified by flash column chromatography (20% ethyl acetate/hexanes) to yield the title compound as a yellow solid (388 mg, 98%).

Data **5.10**

^{1}H NMR (500 MHz, $CDCl_3$)

7.73 (dd, *J* = 1.1, 7.4 Hz, 1H), 7.65 (dd, *J* = 1.7, 6.7 Hz, 1H), 7.31-7.25 (m, 2H), 7.06 (s, 1H), 6.65 (d, *J* = 15.7 Hz, 1H), 6.13 (dt, *J* = 6.8, 15.4 Hz, 1H), 2.74 (t, *J* = 7.3 Hz, 2H), 2.59 (q, *J* = 6.9 Hz, 2H), 2.37 (t, *J* = 7.2 Hz, 2H), 1.58 (quint, *J* = 7.2 Hz, 2H), 1.40 (quint, *J* = 7.6 Hz, 2H), 1.32-1.25 (m, 9H), 0.89 (t, *J* = 6.6 Hz, 3H) ppm. EtOAc impurity at 4.12 and 2.05 ppm.

^{13}C NMR (125 MHz, $CDCl_3$)

187.0, 142.7, 140.3, 138.8, 131.1, 125.2, 124.6, 124.5, 123.4, 122.3, 121.9, 95.3, 81.0, 44.8, 31.9, 29.2, 29.1, 29.0, 27.9, 27.4, 22.8, 19.1, 14.2 ppm

IR (thin film)

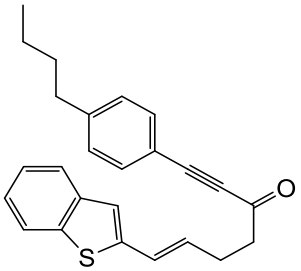
2924, 2855, 2210, 1671, 1434, 1307, 1238, 1155, 953, 808, 745, 724, 674 cm^{-1}

HRMS (FTMS + p ESI)

$[M + H]^+$ Calcd for $C_{23}H_{29}OS$ 353.1934; Found 353.1926

TLC R_f = 0.72 (40% ethyl acetate/hexanes) [silica gel, UV]

MP 35.9 – 37.1 °C



(E)-7-(benzo[b]thiophen-2-yl)-1-(4-butylphenyl)hept-6-en-1-yn-3-one (5.11). A flame-dried, 25-mL, round-bottomed, single-necked flask equipped with stir bar, septum, and a nitrogen inlet adapter was charged with 1-butyl-4-ethynylbenzene (0.36 mL, 2.08 mmol) followed by THF (4.5 mL) via syringe. The flask was placed in a dry ice/acetone bath (-78 °C). After 10 min, n-butyllithium (1.6 mL of a 1.6 M solution in hexanes, 1.85 mmol) was added via syringe in one portion. After 5 min, boron trifluoride diethyl etherate (0.24 mL, 1.97 mmol) was added via syringe in one portion. After 15 min, amide **5.8** (300 mg, 1.16 mmol) diluted in THF (4.5 mL) was added in one portion via syringe. Upon disappearance of starting material as observed by TLC, a second portion of boron trifluoride diethyl etherate (0.24 mL, 1.97 mmol) was added followed by acetic acid (0.12 mL, 1.97 mmol), each were added via syringe in a single portion. The solution was allowed to warm in a brine/ice bath to -20 °C over the course of 1 h. Sat'd. aqueous ammonium chloride (8 mL) was added in one portion and the mixture was transferred to a separatory funnel. The aqueous layer was extracted with ethyl acetate (8 mL x 3). The combined organic layers were dried over magnesium sulfate, gravity filtered, and concentrated under rotary evaporation. The resulting oil was purified by flash column chromatography (10% ethyl acetate/hexanes) to yield the title compound as a yellow liquid (361 mg, 84%).

Data **5.11**

^{1}H NMR (400 MHz, $CDCl_3$)

7.74 (dd, J = 1.7, 7.0 Hz, 1H), 7.66 (dd, J = 1.8, 6.4 Hz, 1H), 7.50 (d, J = 8.2 Hz, 2H), 7.32-7.24 (m, 2H), 7.20 (d, J = 8.1 Hz, 2H), 7.07 (s, 1H), 6.69 (d, J = 15.6 Hz, 1H), 6.17 (dt, J = 6.8, 15.4 Hz, 1H), 2.88 (t, J = 7.3 Hz, 2H), 2.66 (q, J = 7.9 Hz, 4H), 1.64-1.56 (m, 2H), 1.40-1.30 (m, 2H), 0.93 (t, J = 7.4 Hz, 3H) ppm

^{13}C NMR (100 MHz, $CDCl_3$)

186.9, 146.6, 142.7, 140.2, 138.8, 133.3 (2C), 131.0, 128.9 (2C), 125.3, 124.6, 124.5, 123.4, 122.3, 122.0, 117.0, 92.2, 87.7, 44.8, 35.9, 33.3, 27.4, 22.4, 14.0 ppm

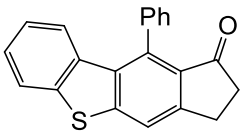
IR (thin film)

3402, 3057, 2926, 2859, 2200, 1709, 1671, 1581, 1449, 1321, 1272, 1099, 753, 695 cm^{-1}

HRMS (TOF MS ES+)

$[M + H]^+$ Calcd for $C_{25}H_{25}OS$ 373.1626; Found 373.1630

TLC R_f = 0.37 (10% ethyl acetate/hexanes) [silica gel, UV]



10-phenyl-2,3-dihydro-1H-benzo[b]indeno[5,6-d]thiophen-1-one (5.12). An oven-dried, 20-mL microwave vial with stir bar was charged with **5.9** (451 mg, 1.43 mmol) dissolved in a 1:1 solution of nitrobenzene : *o*-DCB (20 mL). The vial was sealed with a Teflon-lined septum crimp cap and the solution was heated to 225 °C in a Biotage Initiator microwave reactor for 3 min. The solution was then allowed to cool to room temperature before being transferred directly to a silica gel column for flash column chromatography (100% hexanes, followed by 100% ethyl acetate). The title compound was afforded as a red solid (246 mg, 55%).

Data **5.12**

^{1}H NMR (300 MHz, $CDCl_3$)

7.93 (s, 1H), 7.78 (d, *J* = 8.0 Hz 1H), 7.57 (t, *J* = 3.5 Hz, 3H), 7.38-7.31 (m 3H), 7.09-7.02 (m, 1H), 6.74 (d, *J* = 8.3 Hz, 1H), 3.29-3.22 (m, 2H), 2.76-2.70 (m, 2H) ppm. DCM impurity at 5.30 ppm. Impurities at 2.5 – 0.7 ppm.

^{13}C NMR (75 MHz, $CDCl_3$)

205.0, 152.5, 146.9, 139.6, 137.7, 137.3, 135.5, 133.4, 131.4, 129.0 (2C), 128.4 (2C), 128.2, 126.8, 125.4, 124.5, 122.7, 119.6, 37.6, 25.0 ppm

IR (thin film)

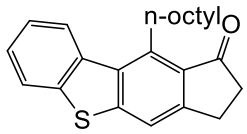
3064, 2859, 1703, 1580, 1494, 1428, 1323, 1237, 1183, 1117, 1032, 851, 739, 695, 520 cm^{-1}

HRMS (FTMS + p ESI)

$[M + H]^+$ Calcd for $C_{21}H_{15}OS$ 315.0838; Found 315.0834

TLC R_f = 0.54 (40% ethyl acetate/hexanes) [silica gel, UV]

MP Decomposes to black residue 258.2 – 261.3 °C



10-octyl-2,3-dihydro-1H-benzo[b]indeno[5,6-d]thiophen-1-one (5.13). An oven-dried single-necked, 5-mL, round-bottomed flask with stir bar, condenser, and septum was charged with **5.10** (20 mg, 0.06 mmol) dissolved in o-dichlorobenzene (0.5 mL). A 16-gauge needle was inserted into the septum and left open to the air. The flask was lowered into a preheated oil bath at 150 °C.

and stirred for 2 days. Upon disappearance of starting material as observed by TLC, the solution was allowed to cool to room temperature. The crude solution was transferred directly to a silica gel column and purified by flash column chromatography (80% dichloromethane/hexanes) to yield the title compound as an orange solid (9 mg, 45%).

Data **5.13**

^{1}H NMR (400 MHz, $CDCl_3$)

8.31 (dd, *J* = 1.5, 6.8 Hz, 1H), 7.84 (dd, *J* = 1.9, 6.8 Hz, 1H), 7.71 (s, 1H), 7.52-7.44 (m, 2H), 3.79 (bs, 2H), 3.15 (t, *J* = 6.0 Hz, 2H), 2.76 (t, *J* = 6.7 Hz, 2H), 1.79-1.70 (quint, *J* = 8.0 Hz, 2H), 1.62 (quint, *J* = 7.4 Hz, 2H), 1.45-1.25 (m, 9H), 0.89 (t, *J* = 7.0 Hz, 3H) ppm

^{13}C NMR (125 MHz, $CDCl_3$)

207.1, 153.1, 147.2, 142.2, 139.6, 135.7, 133.2, 131.1, 126.4, 125.3, 125.0, 123.1, 117.9, 37.9, 32.0, 30.2, 29.6, 29.4, 29.3, 27.8, 24.7, 22.8, 14.3 ppm

IR (thin film)

2923, 2854, 2211, 1699, 1583, 1449, 1325, 1226, 1143, 1081, 1035, 953, 856, 740 506 cm^{-1}

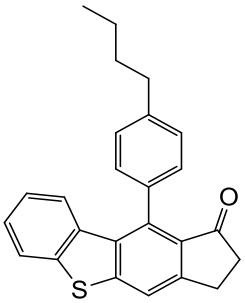
HRMS

(FTMS + p ESI)

$[M + H]^+$ Calcd for $C_{23}H_{27}OS$ 351.1777; Found 351.1770

TLC R_f = 0.48 (80% dichloromethane/hexanes) [silica gel, UV]

MP 87.5 – 89.5 °C



10-(4-butylphenyl)-2,3-dihydro-1H-benzo[b]indeno[5,6-d]thiophen-1-one (5.14). An oven-dried single-necked, 25-mL, round-bottomed flask with stir bar, condenser, and septum was charged with **5.11** (305 mg, 0.82 mmol) dissolved in o-dichlorobenzene (18.0 mL). A 16-gauge needle was inserted into the septum and left open to the air. The flask was lowered into a preheated oil bath at 130 °C and heated for 24 h. Upon disappearance of starting material as observed by TLC, the solution was allowed to cool to room temperature. The *o*-DCB solvent was removed by adding the solution to a silica gel plug and flushing the plug with hexanes. The crude product was then removed from the silica plug with ethyl acetate. The crude product dissolved in ethyl acetate was concentrated under rotary evaporation. The resulting crude solid was purified by flash column chromatography (10% ethyl acetate/hexanes) to yield the title compound as a yellow solid (260 mg, 86%).

Data **5.14**

^{1}H NMR (500 MHz, $CDCl_3$)

7.91 (s, 1H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.37 (d, *J* = 7.9 Hz, 2H), 7.34 (dt, *J* = 0.9, 7.3 Hz, 1H), 7.24 (d, *J* = 8.1 Hz, 2H), 7.04 (dt, *J* = 1.2, 7.8 Hz, 1H), 6.74 (d, *J* = 8.3 Hz, 1H), 3.25 (t, *J* = 6.0 Hz, 2H), 2.79 (t, *J* = 7.6 Hz, 2H), 2.74-2.71 (m, 2H), 1.79-1.72 (m, 2H), 1.50-1.42 (m, 2H), 1.00 (t, *J* = 7.3 Hz, 3H) ppm. Impurities at 2.9, 2.4, and 1.2 ppm.

^{13}C NMR (125 MHz, $CDCl_3$)

205.1, 152.5, 146.8, 142.7, 139.6, 138.1, 135.7, 134.5, 133.6, 131.5, 129.1 (2C), 128.1 (2C), 126.7, 125.5, 124.4, 122.7, 119.5, 37.6, 35.7, 33.6, 25.0, 22.5, 14.2 ppm

IR (thin film)

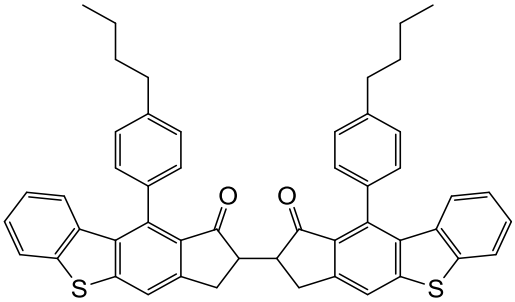
3055, 2926, 2858, 1709, 1580, 1432, 1321, 1182, 1117, 1030, 857, 774, 743 cm^{-1}

HRMS (TOF MS ES+)

$[M + H]^+$ Calcd for $C_{25}H_{23}OS$ 371.1470; Found 371.1448

TLC R_f = 0.16 (10% ethyl acetate/hexanes) [silica gel, UV]

MP 132.4 – 135.3 °C



10,10'-bis(4-butylphenyl)-2,2',3,3'-tetrahydro-1H,1'H-[2,2'-bibenzo[b]indeno[5,6-d]thiophene]-1,1'-dione (5.15). A flame-dried single-necked, 25-mL, round-bottomed flask with stir bar, septum, and a nitrogen inlet needle was charged with THF (1.7 mL), lowered into a dry ice/acetone bath, and cooled for 5 min. LDA (1.35 mL, 1 M in hexanes/THF) was added to the solution dropwise by syringe. **5.14** (100 mg, 0.27 mmol) dissolved in THF (2.0 mL), in a separate round-bottomed flask under nitrogen, was canulated to the LDA solution dropwise via syringe. The solution was maintained at -78 °C for 30 min. Copper(II) chloride (182 mg, 1.35 mmol) dissolved in distilled DMF (4.6 mL), in a separate round-bottomed flask under nitrogen, was canulated to the reaction solution dropwise via syringe. The solution was maintained at -78 °C for

an additional 1 h. The reaction solution was then cannulated to sat. aqueous ammonium chloride (15 mL) at room temperature, in a 50-mL round-bottomed flask, with septum under air. The aqueous layer was extracted with ethyl acetate (10 mL x 3). The combined organic layers were dried over magnesium sulfate, gravity filtered, and concentrated under rotary evaporation. The resulting crude residue was purified by flash column chromatography (60% dichloromethane/hexanes). Cis and trans diastereomers for the protons α to the ketones were isolated and characterized separately as they were separable by flash column chromatography. The afforded a dr of 39:61 (15 mg of the minor diastereomer and 24 mg of the major diastereomer) with both compounds yielded as a yellow solid (39 mg combined, 39% yield, 59% brsm).

Data **5.15** Minor Diastereomer

^{1}H NMR (400 MHz, $CDCl_3$)

7.89 (s, 2H), 7.79 (d, *J* = 8.3 Hz, 2H), 7.41-7.34 (m, 6H), 7.29 (dd, *J* = 1.6, 7.8 Hz, 2H), 7.19 (dd, *J* = 1.8, 7.6 Hz, 2H), 7.07 (dt, *J* = 0.9, 7.4 Hz, 2H), 6.81 (d, *J* = 8.3 Hz, 2H), 4.59 (q, *J* = 4.8 Hz, 2H), 3.88 (q, *J* = 7.8 Hz, 2H), 3.44-3.38 (m, 2H), 2.79 (t, *J* = 7.8 Hz, 4H), 1.79-1.71 (m, 4H), 1.51-1.41 (m, 4H), 1.00 (t, *J* = 7.3 Hz, 6H) ppm. Impurity of the major diastereomer present at 3.3 and 3.1 ppm. EtOAc impurity at 4.12 and 2.05 ppm. Water impurity at 1.55 ppm.

^{13}C NMR (100 MHz, $CDCl_3$)

197.3 (2C), 148.3 (2C), 147.5 (2C), 143.2 (2C), 139.5 (2C), 139.3 (2C), 135.3 (2C), 134.4 (2C), 133.6 (2C), 129.2 (2C), 129.1 (2C), 128.4 (2C), 128.3 (2C), 127.8 (2C), 127.1 (2C), 125.6 (2C), 124.7 (2C), 122.7 (2C), 119.1 (2C), 57.3 (2C), 36.7 (2C), 35.7 (2C), 33.7 (2C), 22.5 (2C), 14.2 (2C) ppm

IR (thin film)

3334, 3056, 2859, 1667, 1610, 1516, 1433, 1225, 1087, 1005, 954, 838, 743, 565 cm^{-1}

HRMS (FTMS + p ESI)

$[M + H]^+$ Calcd for $C_{50}H_{43}O_2S_2$ 739.2699; Found 739.2674

TLC R_f = 0.72 (80% dichloromethane/hexanes) [silica gel, UV]

MP 94.2 – 96.0 °C

Data **5.15** Major Diastereomer

^{1}H NMR (400 MHz, $CDCl_3$)

7.86 (s, 2H), 7.76 (d, *J* = 8.0 Hz, 2H), 7.36-7.30 (m, 6H), 7.27 (dd, *J* = 2.2, 6.6 Hz, 2H), 7.19 (dd, *J* = 2.2, 8.4 Hz, 2H), 7.02 (dt, *J* = 0.9, 7.2 Hz, 2H), 6.68 (d, *J* = 8.2 Hz, 2H), 3.52 (dd, *J* = 7.5, 16.8 Hz, 2H), 3.27 (dd, *J* = 4.6, 16.9 Hz, 2H), 3.18 (quint, *J* = 6.1 Hz, 2H), 2.76 (t, *J* = 7.7 Hz, 4H), 1.73 (quint, *J* = 7.4 Hz, 4H), 1.50-1.40 (m, 4H), 0.99 (t, *J* = 7.3 Hz, 6H) ppm. DCM impurity at 5.30 ppm. EtOAc impurity at 4.12 and 2.05 ppm.

^{13}C NMR (100 MHz, $CDCl_3$)

204.4 (2C), 150.6 (2C), 146.8 (2C), 142.7 (2C), 139.5 (2C), 138.1 (2C), 135.6 (2C), 134.4 (2C), 133.8 (2C), 131.2 (2C), 129.1 (2C), 129.1 (2C), 128.5 (2C), 128.0 (2C), 126.7 (2C), 125.5 (2C), 124.4 (2C), 122.7 (2C), 119.2 (2C), 49.6 (2C), 35.7 (2C), 33.6 (2C), 30.5 (2C), 22.5 (2C), 14.2 (2C) ppm

IR (thin film)

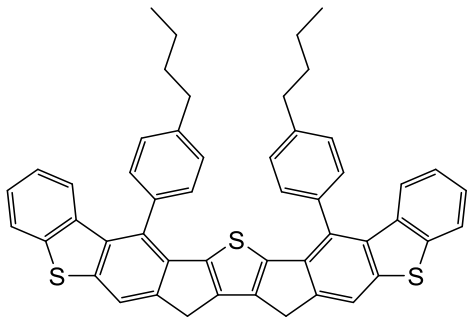
3334, 3056, 2859, 1667, 1610, 1516, 1433, 1225, 1087, 1005, 954, 838, 743, 565 cm^{-1}

HRMS (FTMS + p ESI)

$[M + H]^+$ Calcd for $C_{50}H_{43}O_2S_2$ 739.2699; Found 739.2675

TLC R_f = 0.66 (80% dichloromethane/hexanes) [silica gel, UV]

MP 94.0 – 96.6 °C



Tris-thiophene polycyclic ladder-type heteroarene (5.16). A flame-dried single-necked, 5-mL, round-bottomed flask with stir bar, septum, condenser and a nitrogen inlet needle was charged with the isolated major diastereomer of **5.15** (13 mg, 0.02 mmol) dissolved in THF (1.5 mL). Lawesson's reagent (14 mg, 0.04 mmol) was added to the solution all at once. The flask was lowered into a preheated oil bath at 110 °C and refluxed for 24 h. The solution was allowed to cool to room temperature, and the toluene was removed under rotary evaporation. The resulting crude residue was purified by flash column chromatography (20% ethyl acetate/hexanes) to yield the title compound as a brown solid (8 mg, 62% yield).

Data **5.16**

^{1}H NMR (400 MHz, $CDCl_3$)

7.85 (s, 2H), 7.77 (d, J = 7.9 Hz, 2H), 7.33 (d, J = 7.9 Hz, 4H), 7.30-7.25 (m, 6H), 7.01 (dt, J = 0.9, 7.2 Hz, 2H), 6.81 (d, J = 8.2 Hz, 2H), 3.77 (s, 4H), 2.87 (t, J = 7.6 Hz, 4H), 1.87-1.80 (m, 4H), 1.61-1.52 (m, 4H), 1.11 (t, J = 7.4 Hz, 6H) ppm. Grease impurity at 1.11 and 1.09 ppm.

^{13}C NMR (100 MHz, $CDCl_3$)

146.6 (2C), 144.4 (2C), 142.9 (2C), 140.8 (2C), 139.8 (2C), 137.3 (2C), 136.7 (2C), 136.1 (2C), 135.8 (2C), 132.5 (2C), 129.9 (2C), 129.4 (4C), 129.2 (4C), 125.7 (2C), 124.8 (2C), 123.8 (2C), 122.7 (2C), 118.3 (2C), 36.0 (2C), 33.9 (2C), 32.9 (2C), 22.7 (2C), 14.3 (2C) ppm

IR (thin film)

3055, 2857, 2926, 2857, 1713, 1586, 1510, 1461, 1298, 1260, 1111, 1069, 848, 746, 531 cm^{-1}

HRMS (FTMS + p ESI)

$[M + H]^+$ Calcd for $C_{50}H_{40}S_3$ 736.2287; Found 736.2276

TLC R_f = 0.52 (20% ethyl acetate/hexanes) [silica gel, UV]

MP Decomposes to black residue 175.9 – 179.8 °C

5.4.3 Reaction of the Minor Diastereomer of 5.15 with Lawesson's Reagent

A flame-dried single-necked, 5-mL, round-bottomed flask with stir bar, septum, condenser and a nitrogen inlet needle was charged with the isolated minor diastereomer of **5.15** (13 mg, 0.02 mmol) dissolved in THF (1.5 mL). Lawesson's reagent (14 mg, 0.04 mmol) was added to the solution all at once. The flask was lowered into a preheated oil bath at 110 °C and refluxed for 24 h. The solution was allowed to cool to room temperature, and the toluene was removed under

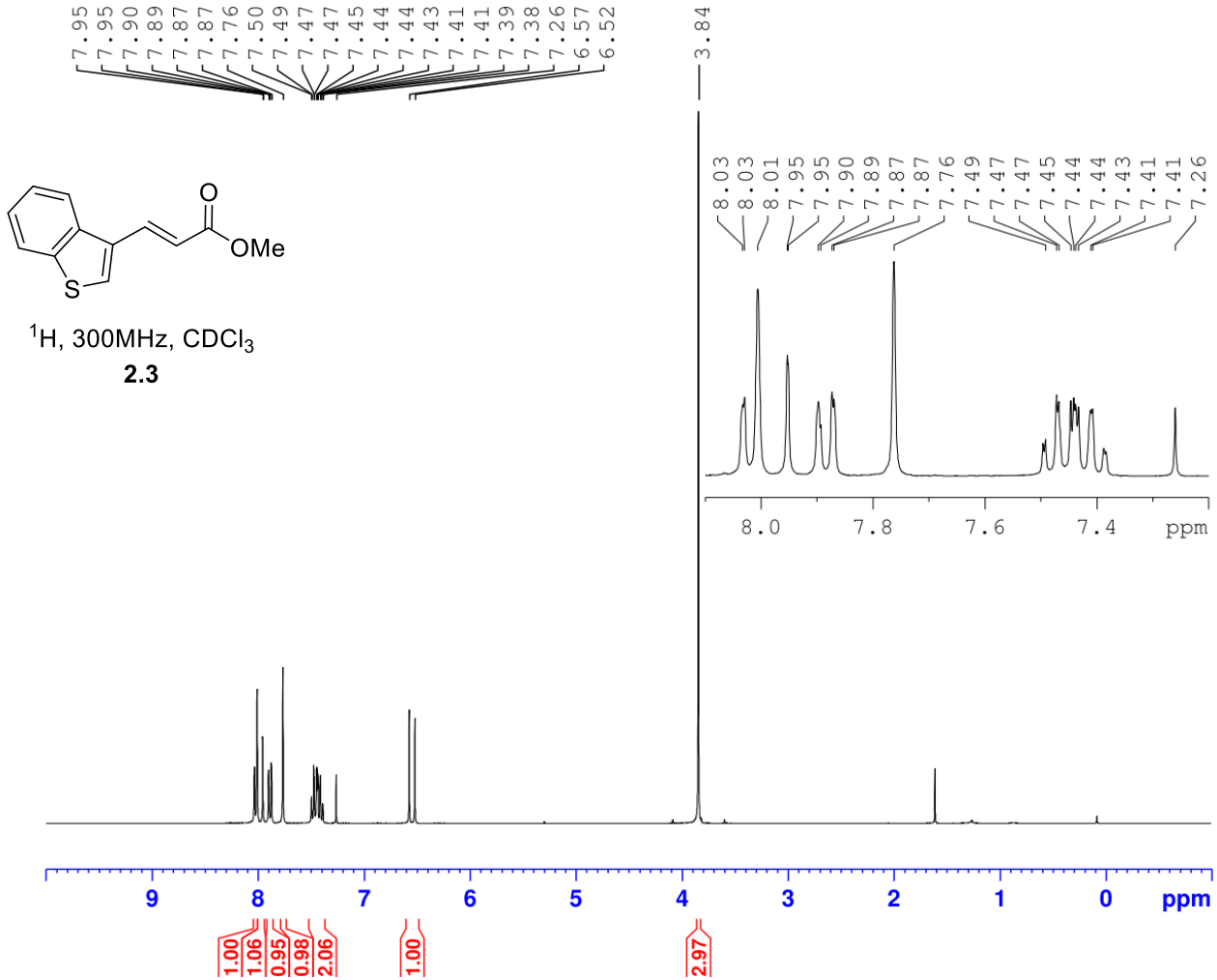
rotary evaporation. The resulting crude residue was purified by flash column chromatography (20% ethyl acetate/hexanes) and 69% of the starting material was recovered (9 mg) with no product formation.

Appendix A Compound Characterization Checklist

COMPOUND	IDENTITY														PURITY						COMPUTATIONAL DATA in SI*			AUTHOR REMARKS
Compound, structure, or table-entry number	New	Known	Weight and percentage yield	Physical state / mp range if cryst. solid	IR	UV-Vis	1H NMR	13C NMR	MS	MS Accurate mass (HRMS)	Optical rotation/ORD/CD	Enantiomeric/Diastereomeric ratio	X-ray [ORTEP and CIF in SI*]	Rf	Copy of 1H/13C NMR spectrum in SI*	Copy of chromatogram in SI*	Quant. GC, HPLC, electrophoresis	Elemental analysis	<>	Cartesian coordinates or Z-matrix	# of imaginary frequencies	Total energy	(* SI = Supporting Information)
2.3		X	X	X			X							X	X								
2.4		X	X	X			X							X	X								
2.5	X		X	X	X		X	X		X				X	X								
2.25		X	X	X			X							X	X								
2.26		X	X	X			X							X	X								
2.9	X		X	X	X		X	X		X				X	X								
1.50		X	X	X			X							X	X								
1.59		X	X	X			X							X	X								
2.16	X		X	X	X		X	X		X				X	X								
2.17	X		X	X	X		X	X		X				X	X								
2.18	X		X	X	X		X	X		X				X	X								
2.19	X		X	X	X		X	X		X				X	X								
2.6	X		X	X	X		X	X		X				X	X								

COMPOUND	IDENTITY														PURITY					COMPUTATIONAL DATA in SI*			AUTHOR REMARKS
Compound, structure, or table-entry number	New	Known	Weight and percentage yield	Physical state / mp range if cryst. solid	IR	UV-Vis	1H NMR	13C NMR	MS	MS Accurate mass (HRMS)	Optical rotation/ORD/CD	Enantiomeric/Diastereomeric ratio	X-ray [ORTEP and CIF in SI*]	Rf	Copy of 1H/13C NMR spectrum in SI*	Copy of chromatogram in SI*	Quant. GC, HPLC, electrophoresis	Elemental analysis	<>	Cartesian coordinates or Z-matrix	# of imaginary frequencies	Total energy	(* SI = Supporting Information)
2.23	X		X	X	X		X	X		X				X	X								
5.7		X	X	X			X							X	X								
5.8	X		X	X	X		X	X		X				X	X								
5.9	X		X	X	X		X	X		X				X	X								
5.10	X		X	X	X		X	X		X				X	X								
5.11	X		X	X	X		X	X		X				X	X								
5.12	X		X	X	X		X	X		X				X	X								
5.13	X		X	X	X		X	X		X				X	X								
5.14	X		X	X	X		X	X		X				X	X								
5.15	X		X	X	X		X	X		X				X	X								
5.16	X		X	X	X		X	X		X				X	X								

Appendix B ^{1}H and ^{13}C NMR Spectra of Synthetically Prepared Molecules



^{1}H, 300MHz, $CDCl_3$

2.3

```
Current Data Parameters
NAME          JAW-02-157
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20181008
Time               10.11
INSTRUM            spect
PROBHD   5 mm QNP  1H/1
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            6188.119 Hz
FIDRES         0.188846 Hz
AQ            2.6476543 sec
RG                   128
DW                80.800 usec
DE                  6.50 usec
TE                -923.4 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         300.2318540 MHz
NUC1                  1H
P1                12.71 usec
PLW1         18.19700050 W

F2 - Processing parameters
SI                 32768
SF          300.2300089 MHz
WDW                   EM
SSB      0
LB                 0.10 Hz
GB       0
PC                 1.00
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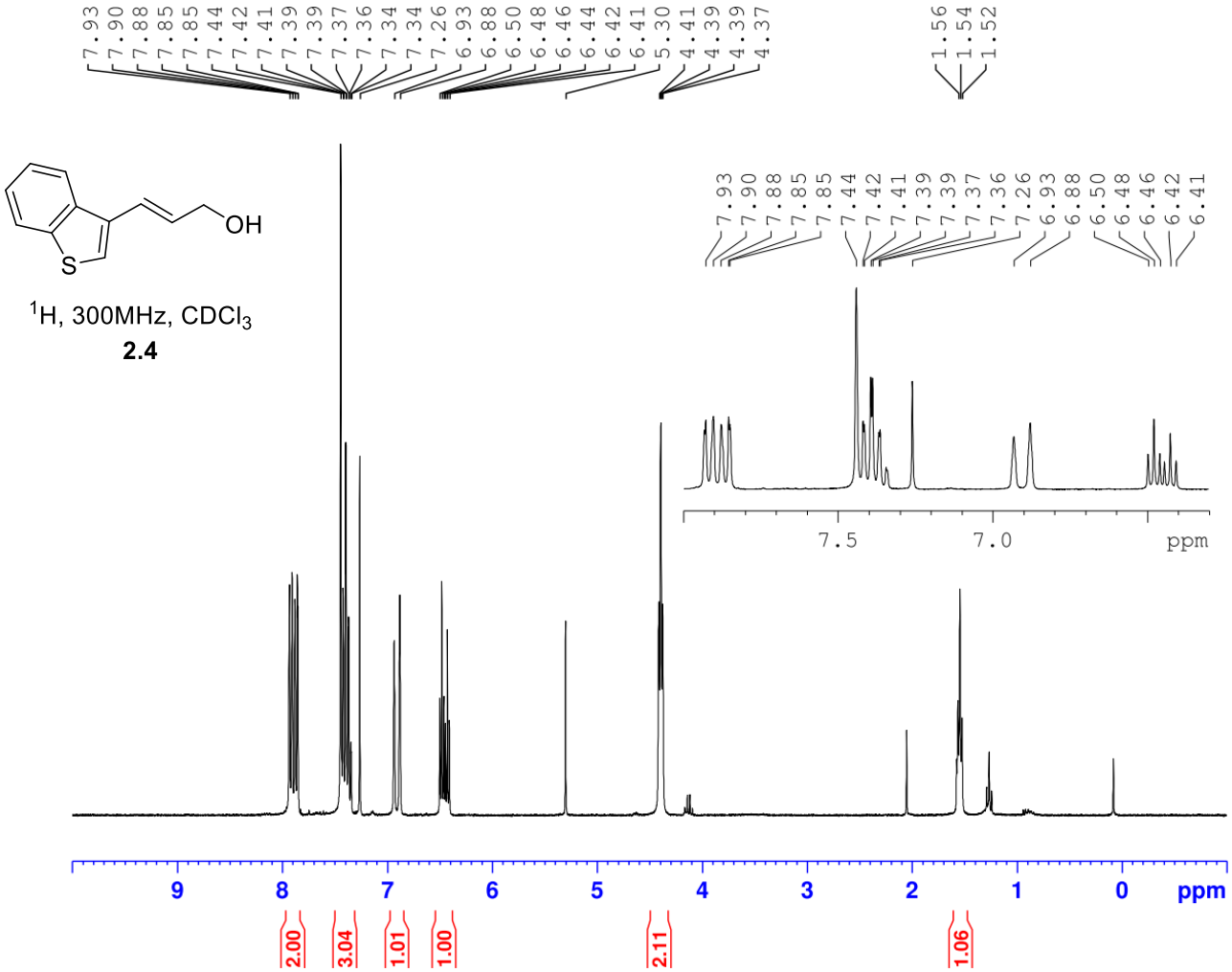


```
Current Data Parameters
NAME          JAW-02-158
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20181017
Time               11.19
INSTRUM            spect
PROBHD   5 mm QNP  1H/1
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             6188.119 Hz
FIDRES          0.188846 Hz
AQ             2.6476543 sec
RG                   322
DW                80.800 usec
DE                  6.50 usec
TE                -922.3 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         300.2318540 MHz
NUC1                  1H
P1                12.71 usec
PLW1         18.19700050 W

F2 - Processing parameters
SI                 32768
SF           300.2300086 MHz
WDW                   EM
SSB       0
LB                 0.10 Hz
GB        0
PC                 1.00
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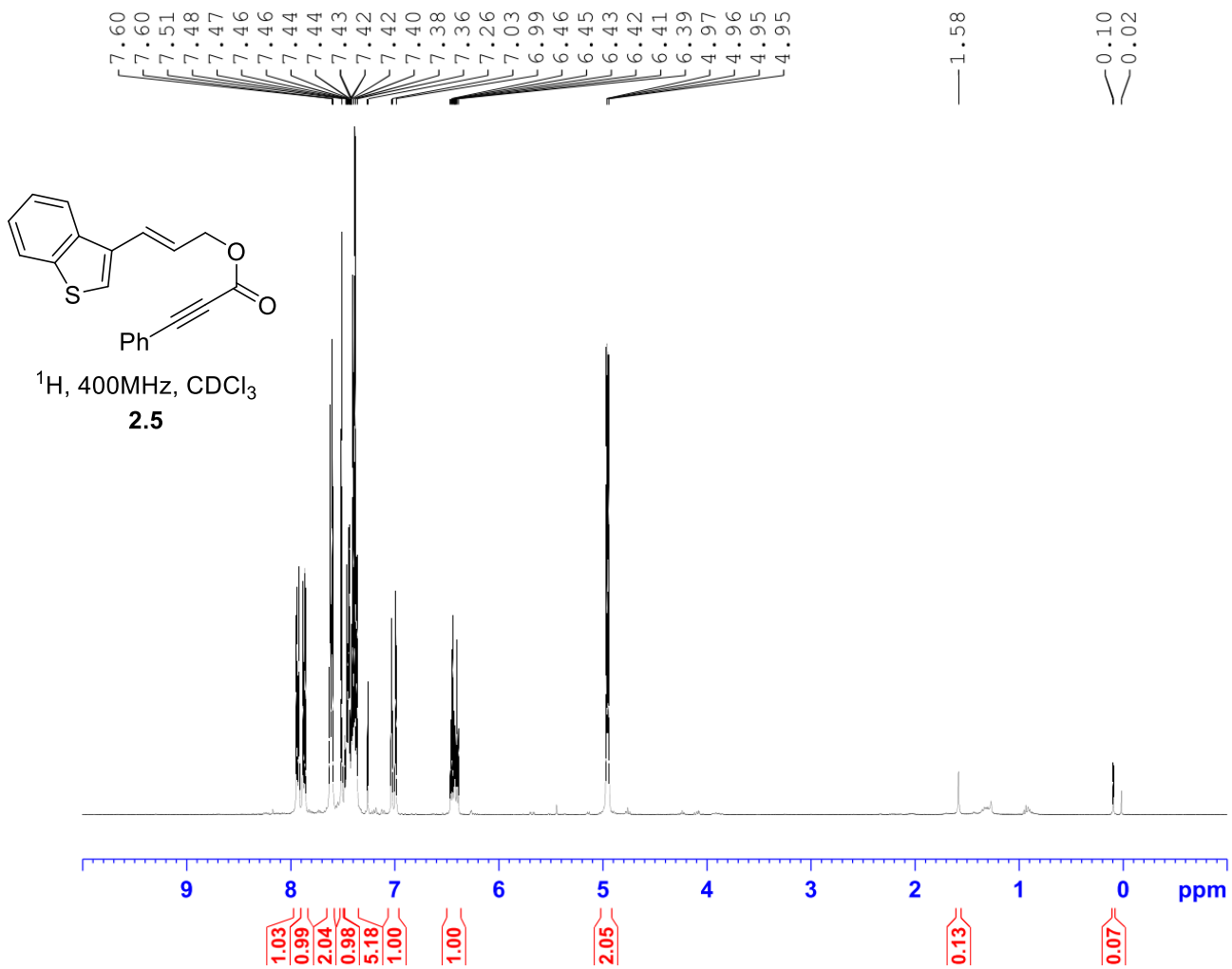


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Current Data Parameters
NAME          JAW-03-107
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210419
Time               9.00 h
INSTRUM           spect
PROBHD   Z108618_0240 (
PULPROG            zg30
TD                65536
SOLVENT           CDCl3
NS                   16
DS                    2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                  71.8
DW                62.400 usec
DE                 6.50 usec
TE                 92.2 K
D1           1.00000000 sec
TD0                   1
SFO1         400.1324708 MHz
NUC1                 1H
P0                 4.83 usec
P1                14.50 usec
PLW1         12.00000000 W

F2 - Processing parameters
SI                65536
SF          400.1300098 MHz
WDW                  EM
SSB      0
LB                0.30 Hz
GB       0
PC                1.00
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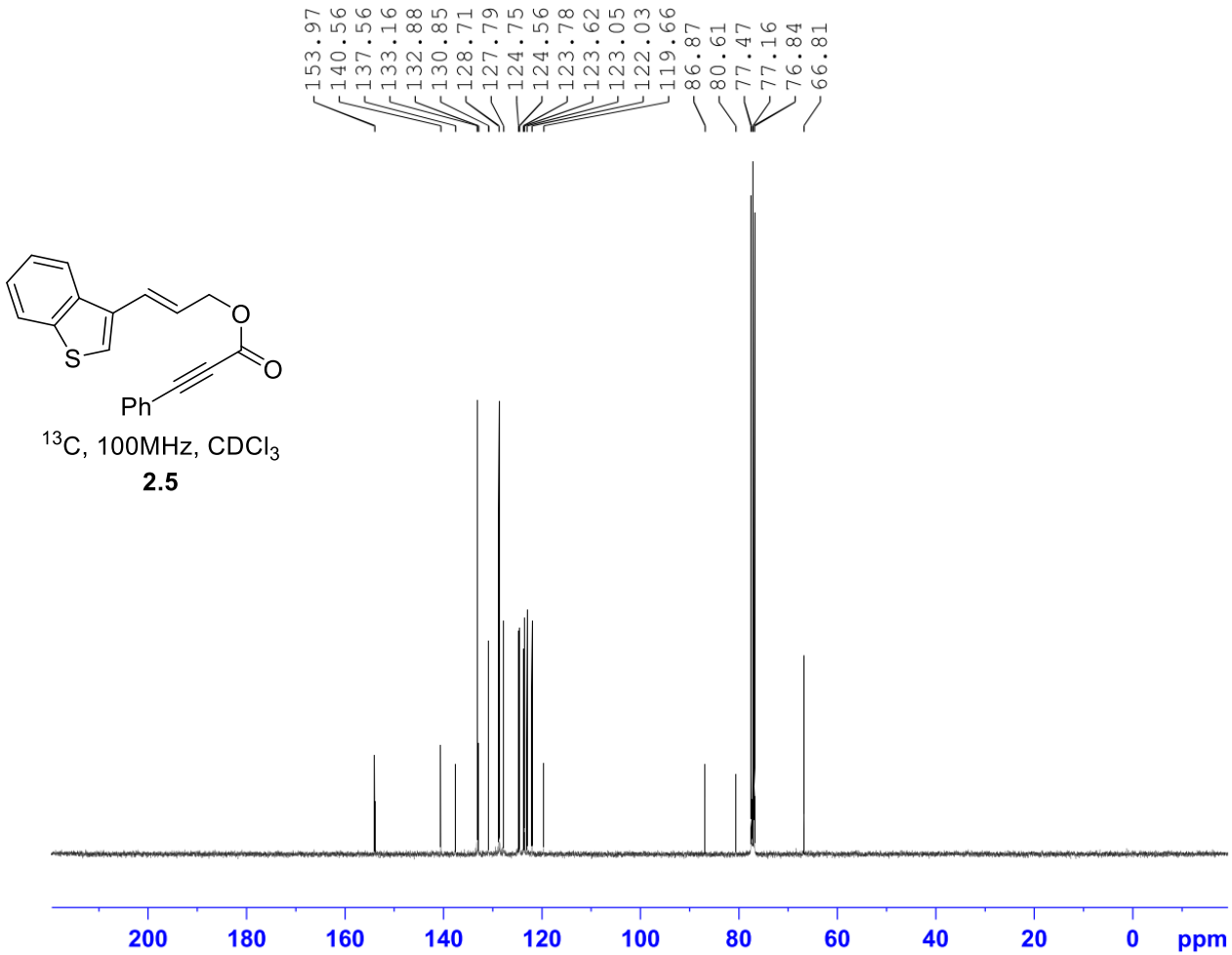


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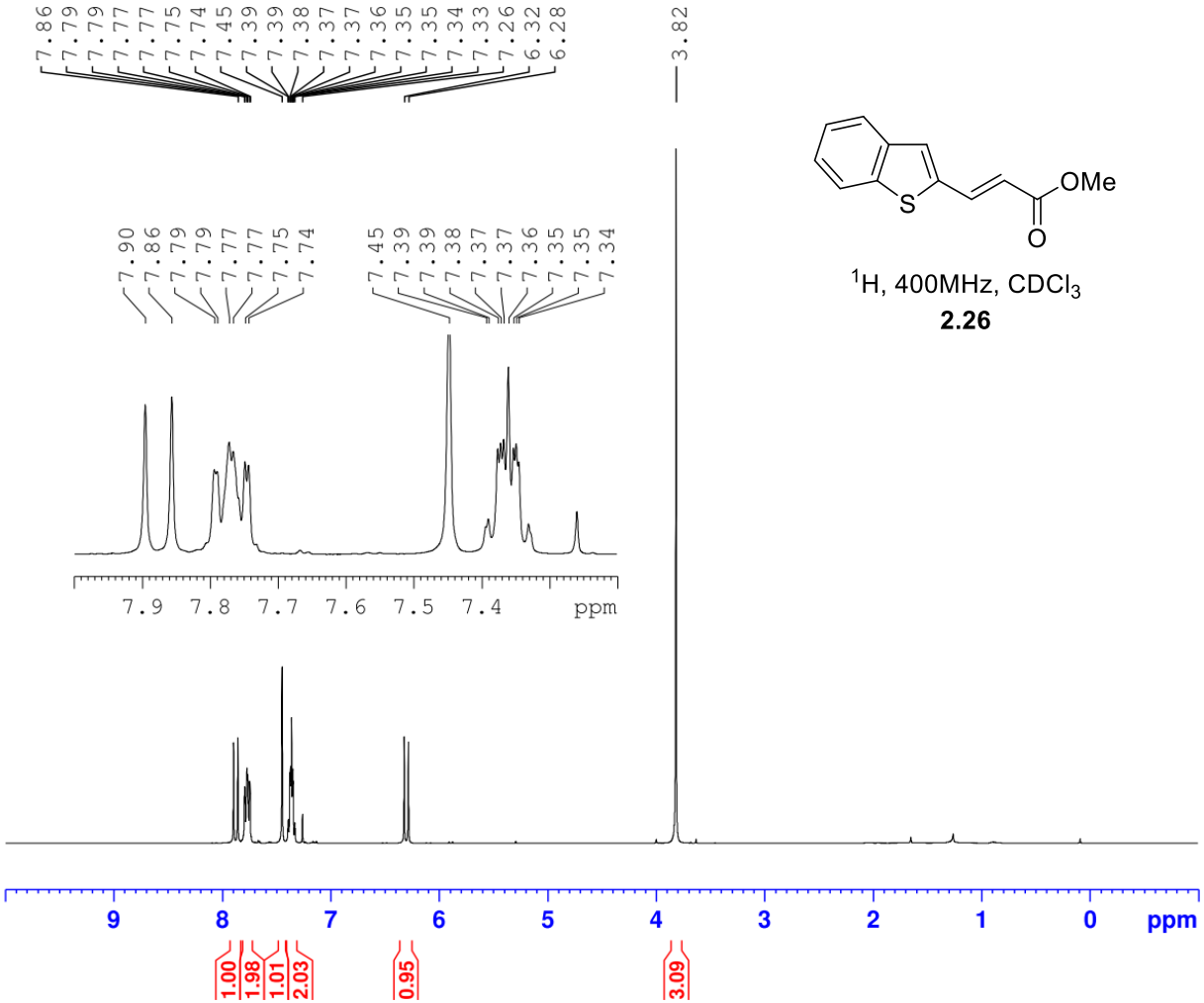
Current Data Parameters
NAME          JAW-03-107
EXPNO                  4
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210419
Time              21.05 h
INSTRUM           spect
PROBHD   Z108618_0240 (
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH            24038.461 Hz
FIDRES          0.733596 Hz
AQ             1.3631488 sec
RG                  203
DW                20.800 usec
DE                 6.50 usec
TE                 91.2 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                    1
SFO1         100.6228298 MHz
NUC1                 13C
P0                 3.33 usec
P1                10.00 usec
PLW1         56.13299942 W
SFO2         400.1316005 MHz
NUC2                  1H
CPDPRG[2         waltz65
PCPD2             90.00 usec
PLW2         12.00000000 W
PLW12         0.31147999 W
PLW13         0.15667000 W

F2 - Processing parameters
SI                32768
SF           100.6127586 MHz
WDW                  EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```



^{1}H, 400MHz, $CDCl_3$

2.26

```
Current Data Parameters
NAME          JAW-02-047
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180419
Time               14.18
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.122266 Hz
AQ             4.0894465 sec
RG                    57
DW                62.400 usec
DE                 6.50 usec
TE                1994.0 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         400.1324710 MHz
NUC1                  1H
P1                14.50 usec
PLW1         12.01700020 W

F2 - Processing parameters
SI                 65536
SF           400.1300101 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
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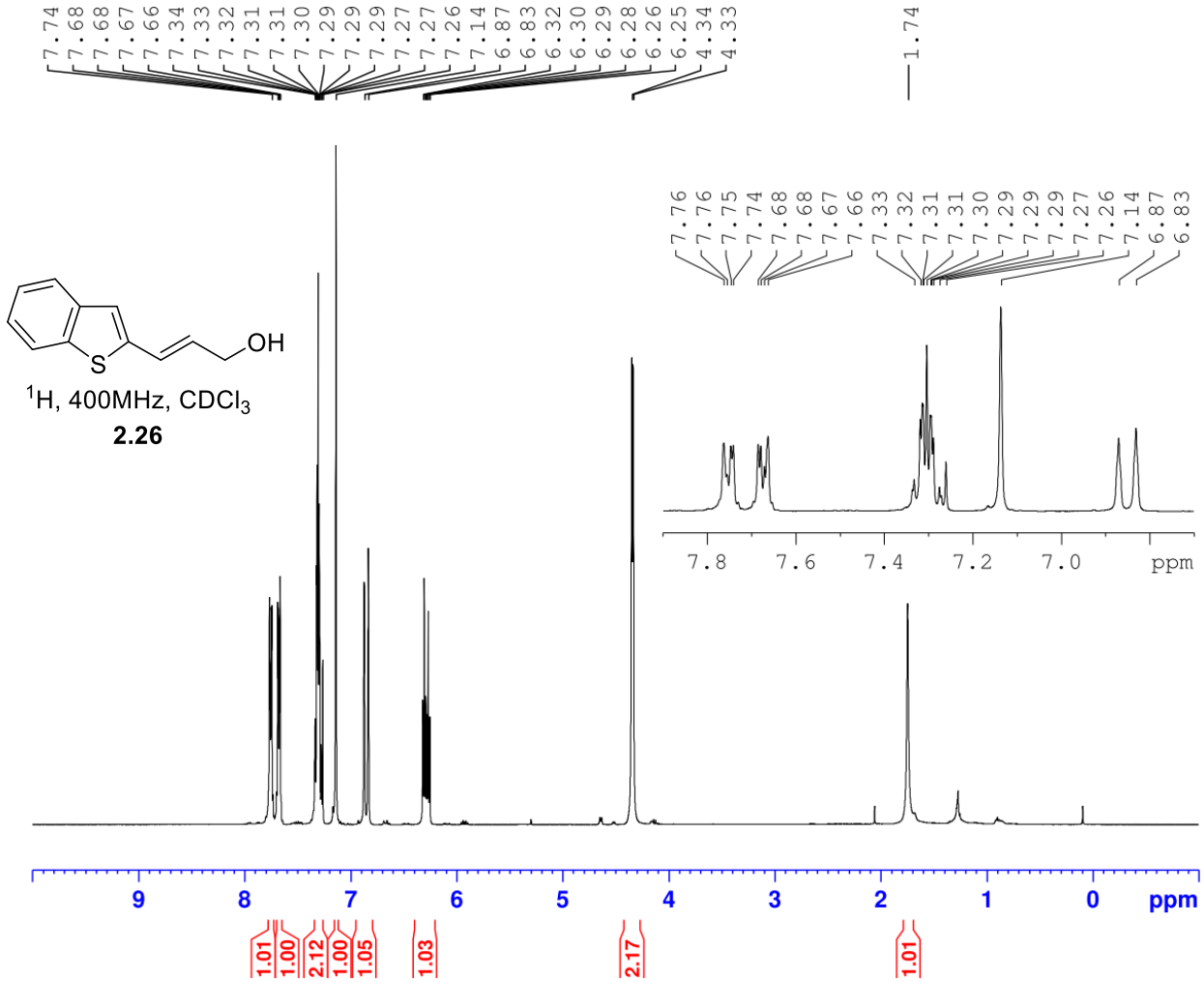

^{1}H, 400MHz, $CDCl_3$

2.26

```
Current Data Parameters
NAME          JAW-02-048
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180420
Time               13.36
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.122266 Hz
AQ             4.0894465 sec
RG                    64
DW                62.400 usec
DE                 6.50 usec
TE                2523.5 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         400.1324710 MHz
NUC1                  1H
P1                14.50 usec
PLW1         12.01700020 W

F2 - Processing parameters
SI                 65536
SF          400.1300103 MHz
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SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
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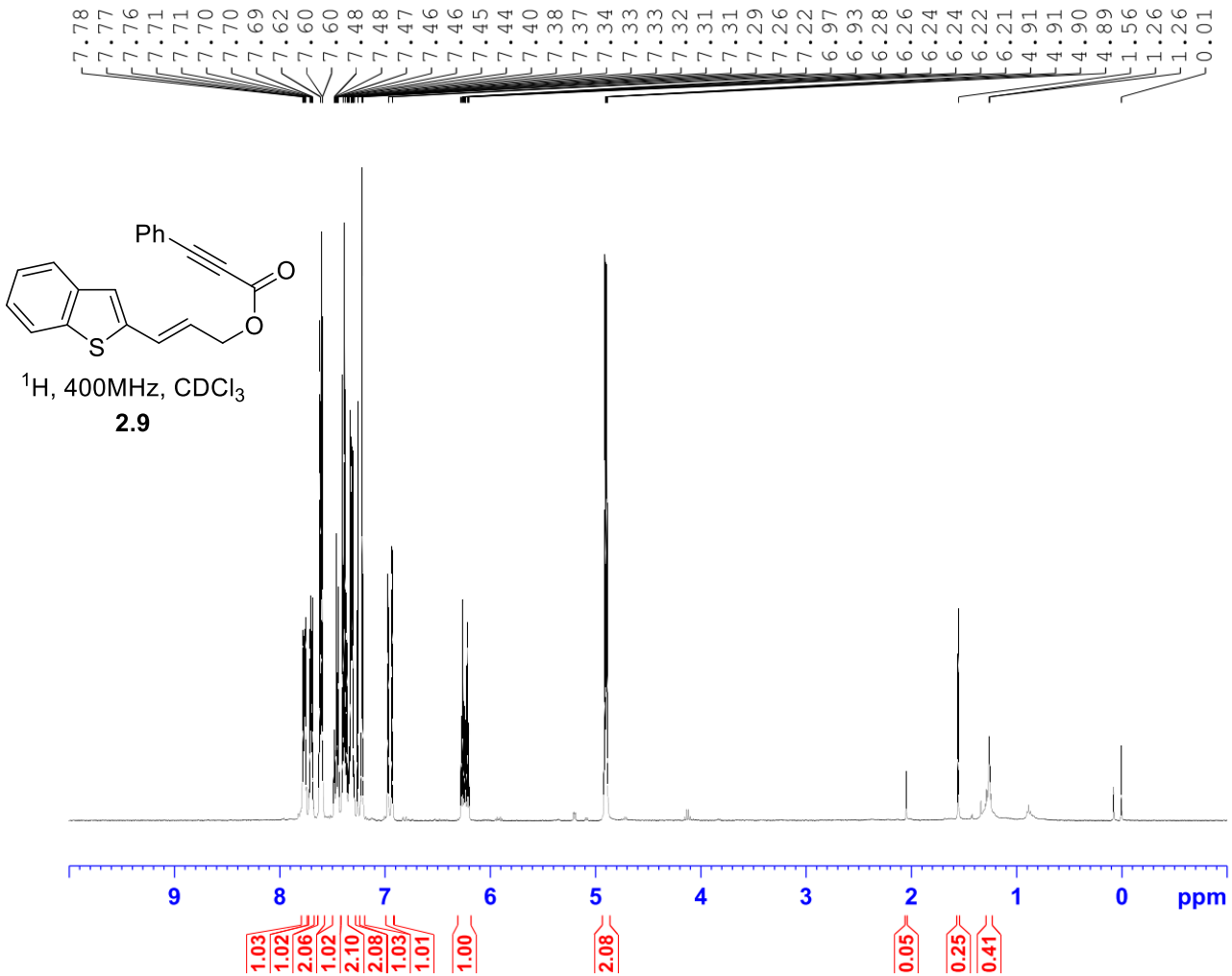


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Current Data Parameters
NAME          JAW-03-108
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210418
Time                2.20 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                   101
DW                62.400 usec
DE                 6.50 usec
TE                 91.1 K
D1           1.00000000 sec
TD0                    1
SFO1        400.1324708 MHz
NUC1                  1H
P0                 4.83 usec
P1                14.50 usec
PLW1        12.00000000 W

F2 - Processing parameters
SI                 65536
SF          400.1300099 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
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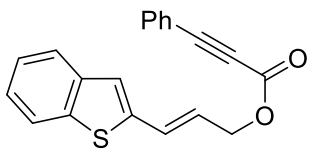
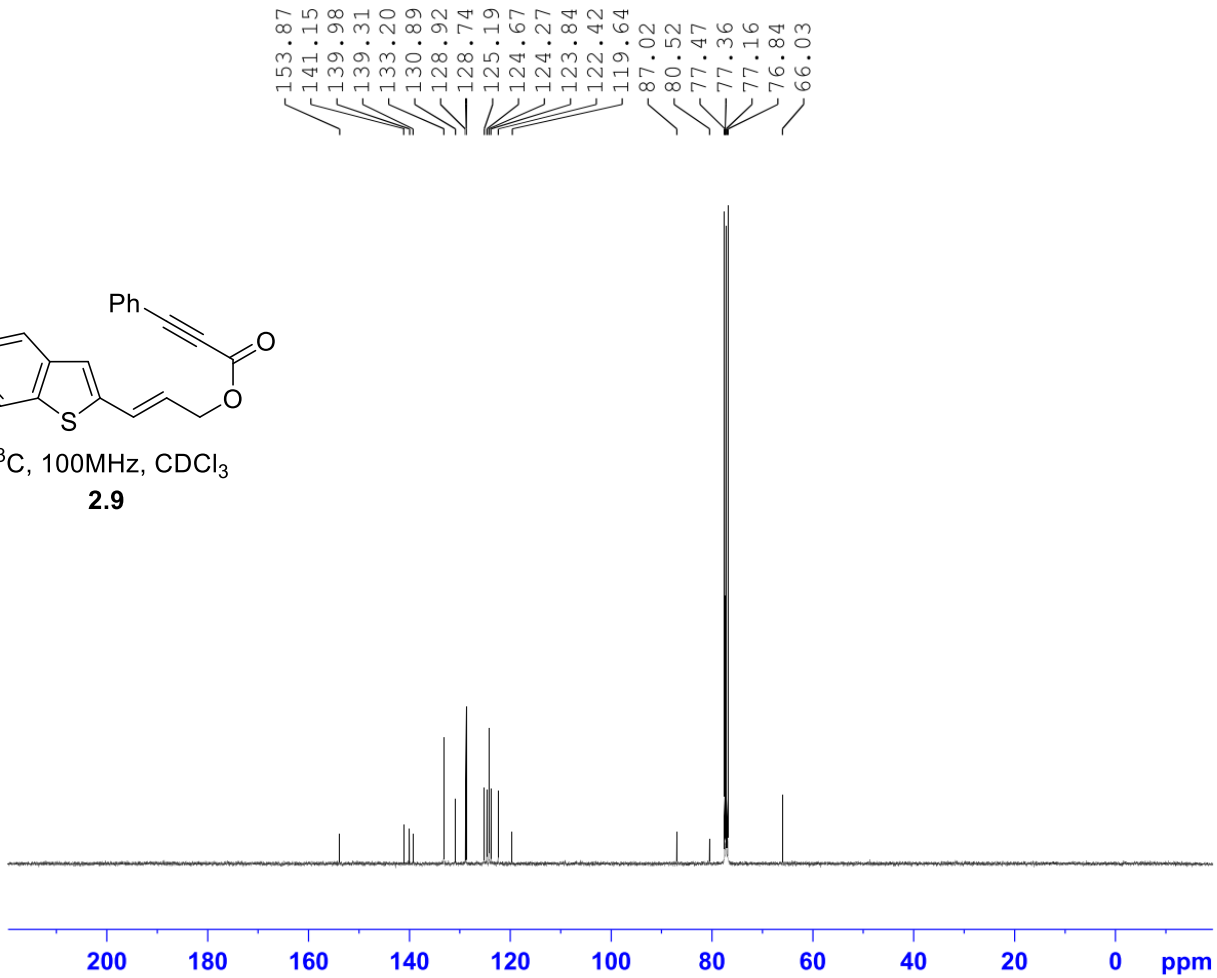


^{13}C, 100MHz, $CDCl_3$

2.9

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Current Data Parameters
NAME          JAW-03-108
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
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Time                3.20 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH            24038.461 Hz
FIDRES          0.733596 Hz
AQ             1.3631488 sec
RG                  203
DW                 20.800 usec
DE                  6.50 usec
TE                  91.1 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1
SFO1         100.6228298 MHz
NUC1                 13C
P0                  3.33 usec
P1                 10.00 usec
PLW1         56.13299942 W
SFO2         400.1316005 MHz
NUC2                  1H
CPDPRG[2         waltz65
PCPD2              90.00 usec
PLW2         12.00000000 W
PLW12         0.31147999 W
PLW13         0.15667000 W

F2 - Processing parameters
SI                 32768
SF           100.6127562 MHz
WDW                   EM
SSB       0
LB                  1.00 Hz
GB        0
PC                  1.40
```
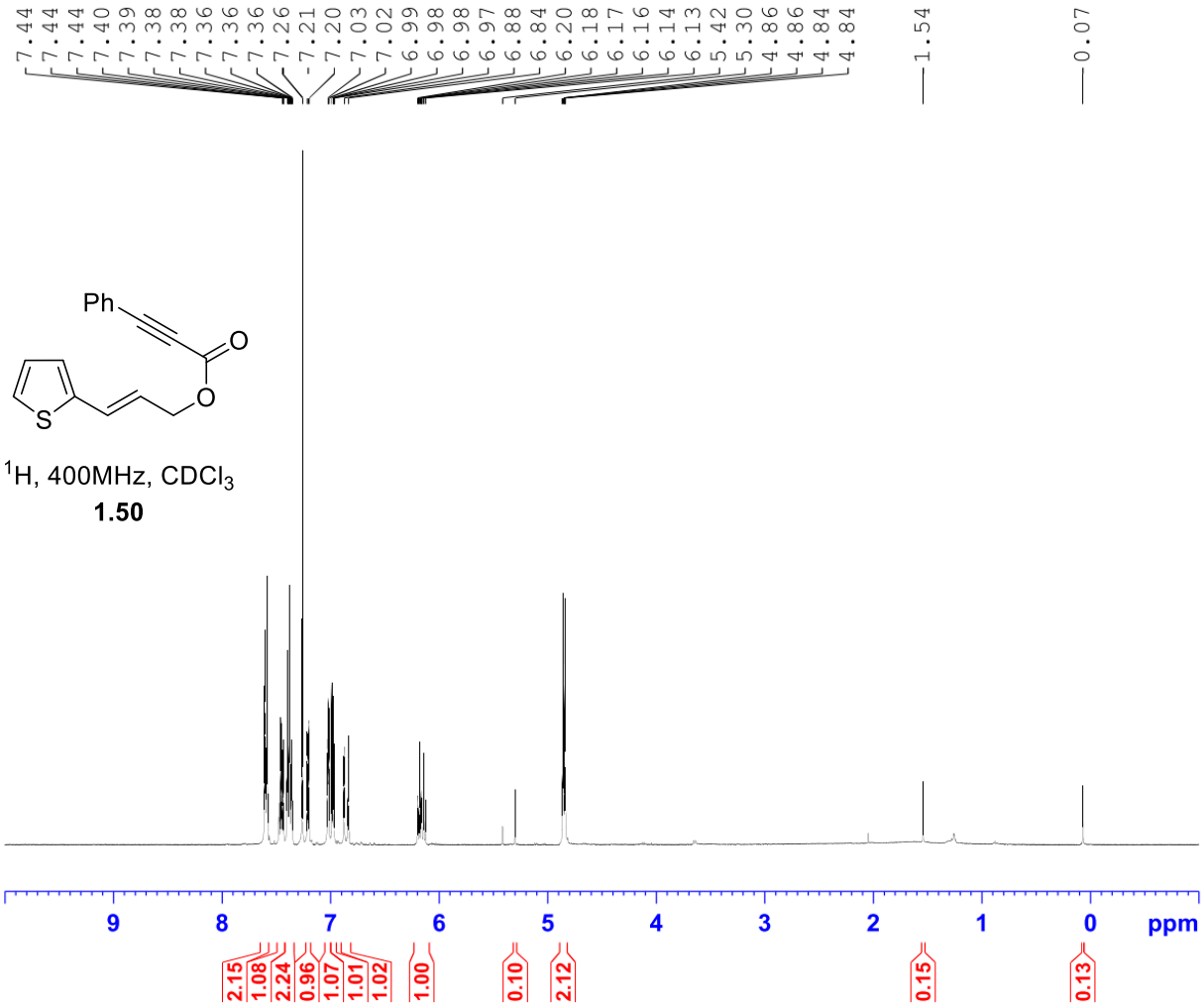
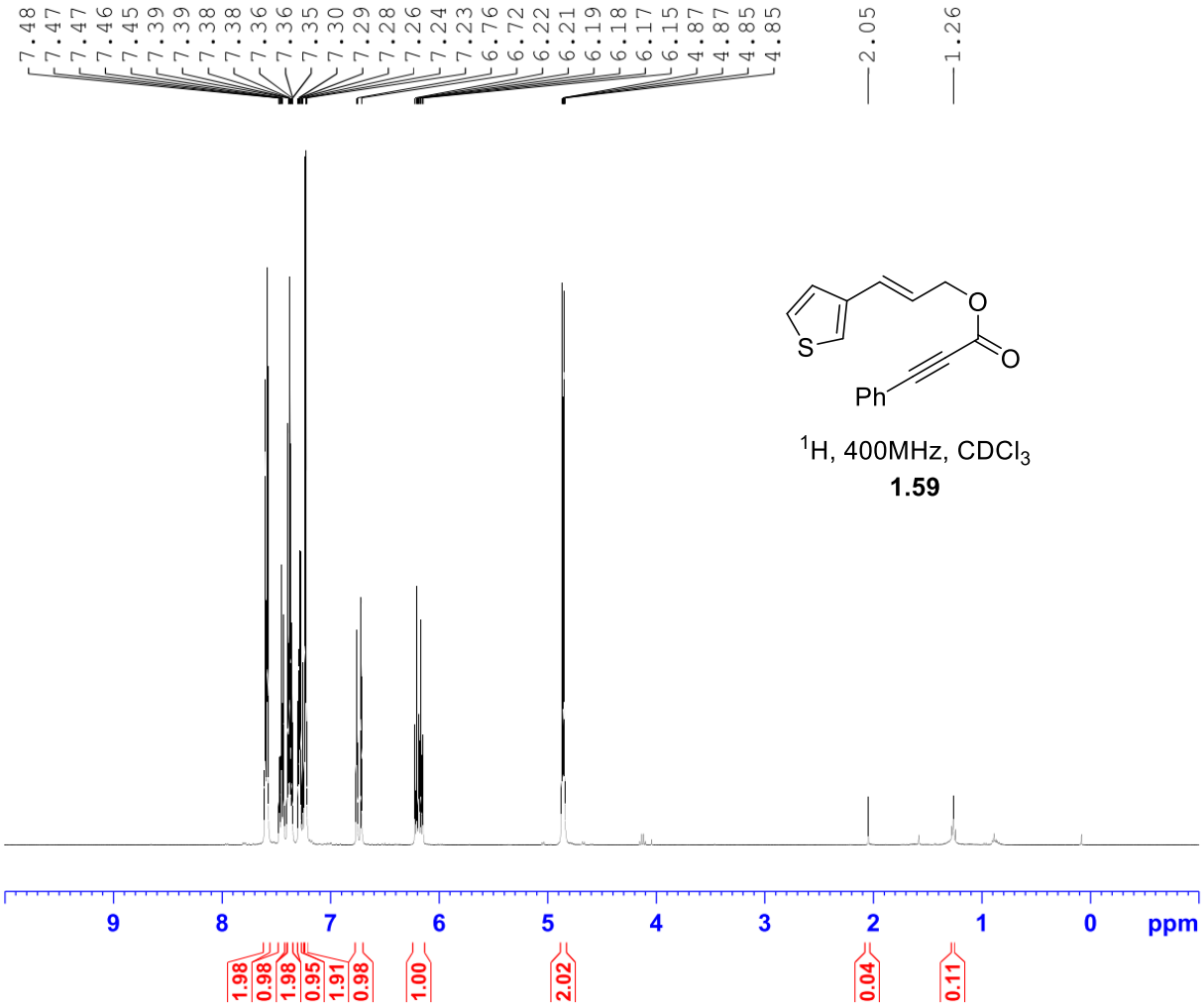
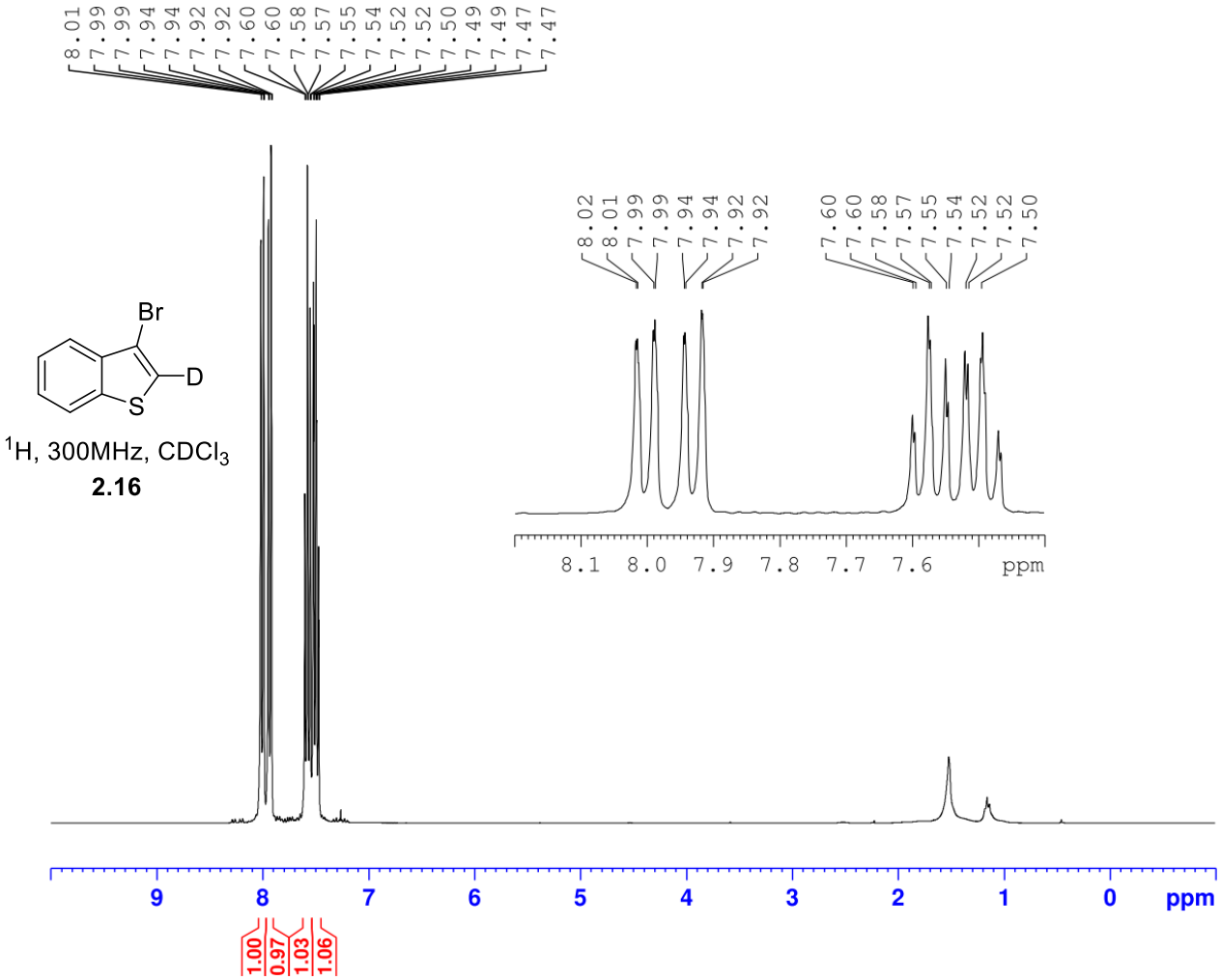



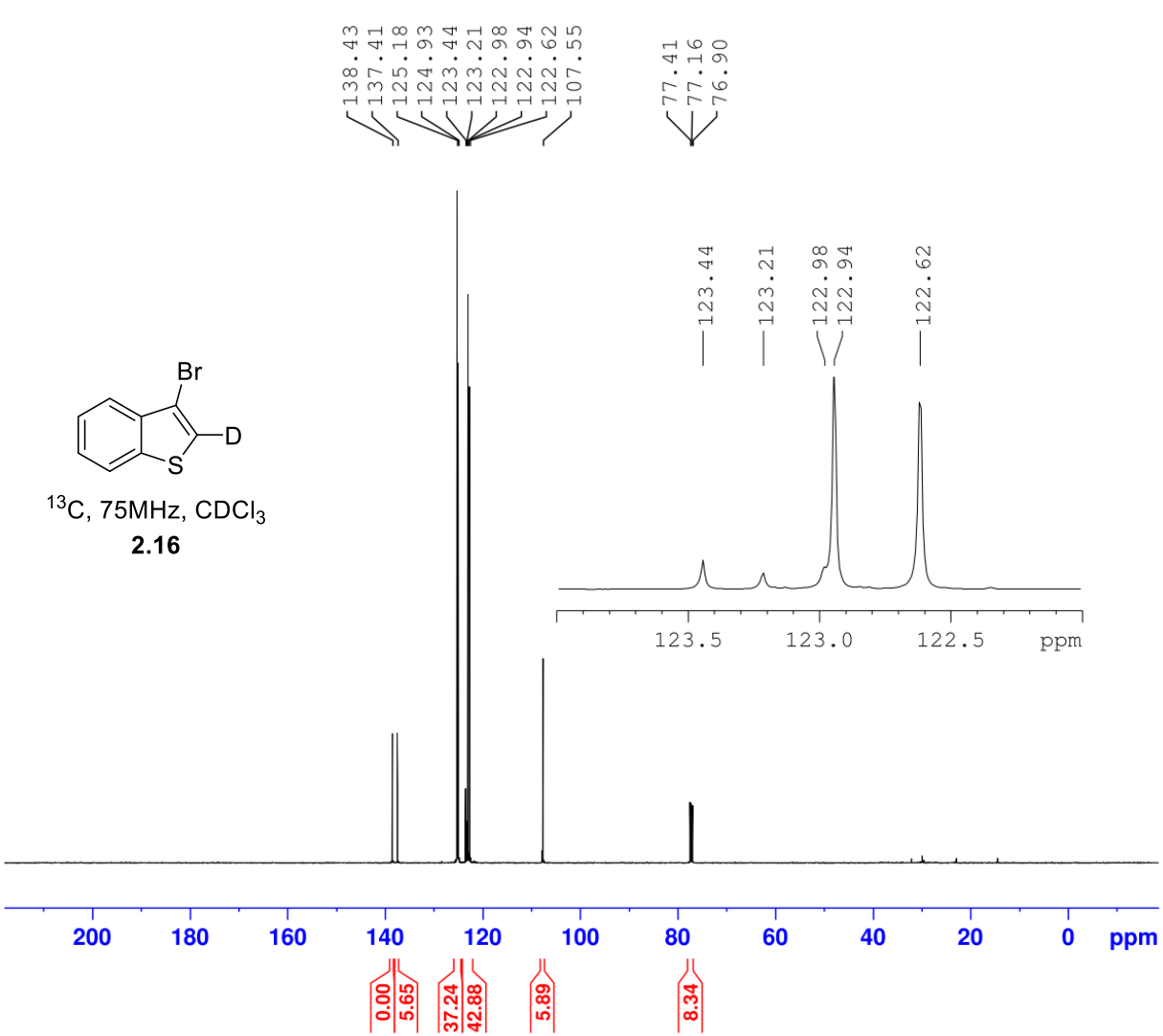

```
Current Data Parameters
NAME          JAW-02-036
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180404
Time               17.24
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.122266 Hz
AQ             4.0894465 sec
RG                   128
DW                62.400 usec
DE                 6.50 usec
TE               1833.9 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1        400.1324710 MHz
NUC1                  1H
P1                14.50 usec
PLW1        12.01700020 W

F2 - Processing parameters
SI                 65536
SF          400.1300103 MHz
WDW                   EM
SSB      0
LB                 0.30 Hz
GB       0
PC                 1.00
```



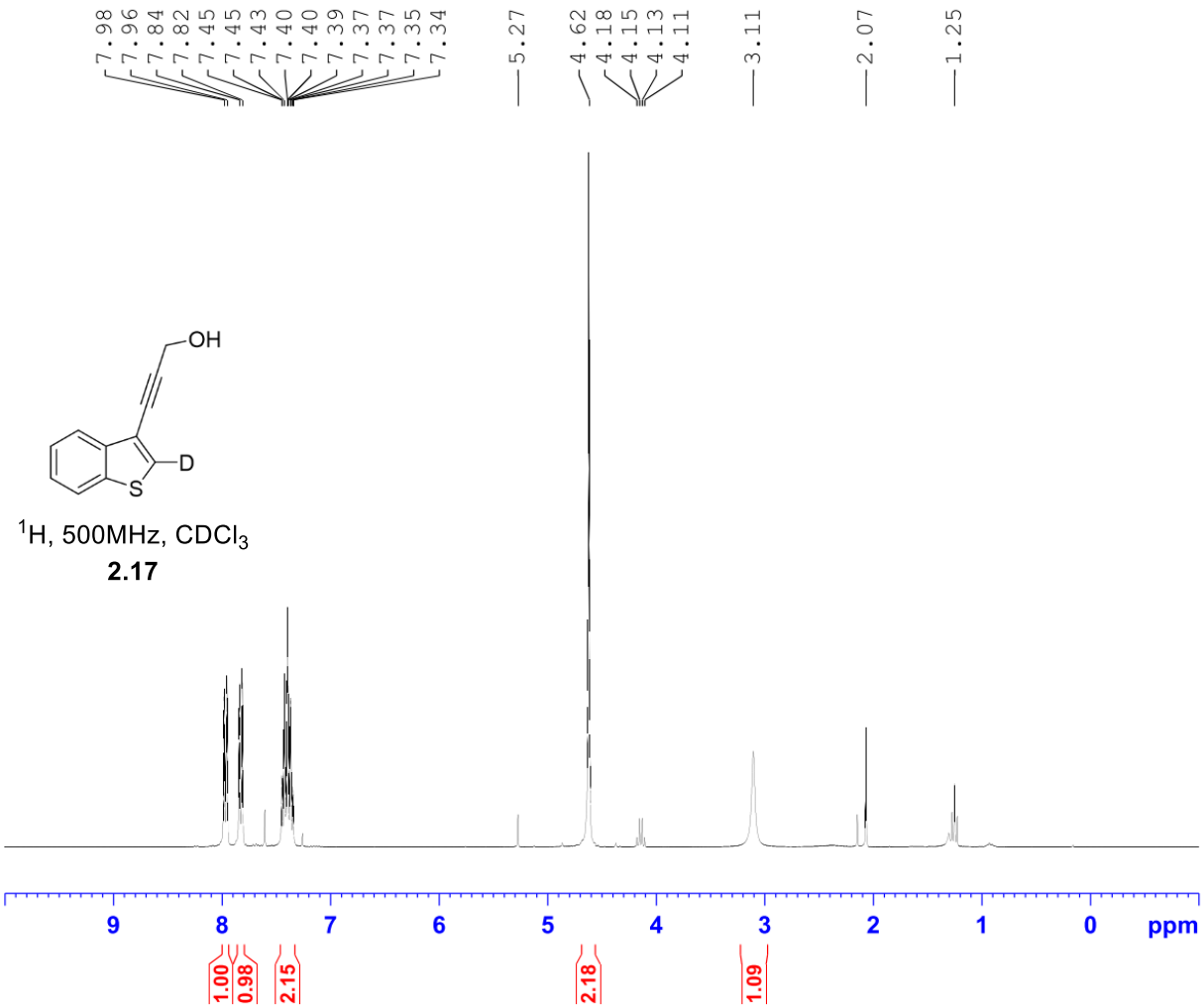

```
Current Data Parameters
NAME          JAW-01-085
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170308
Time              16.17
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG            zg30
TD                65536
SOLVENT           CDCl3
NS                   16
DS                    2
SWH            8012.820 Hz
FIDRES         0.122266 Hz
AQ           4.0894465 sec
RG                   64
DW               62.400 usec
DE                6.50 usec
TE               884.0 K
D1           1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1        400.1324710 MHz
NUC1                 1H
P1                13.75 usec
PLW1        12.01700020 W

F2 - Processing parameters
SI                65536
SF          400.1300099 MHz
WDW                  EM
SSB      0
LB                0.30 Hz
GB       0
PC                1.00
```



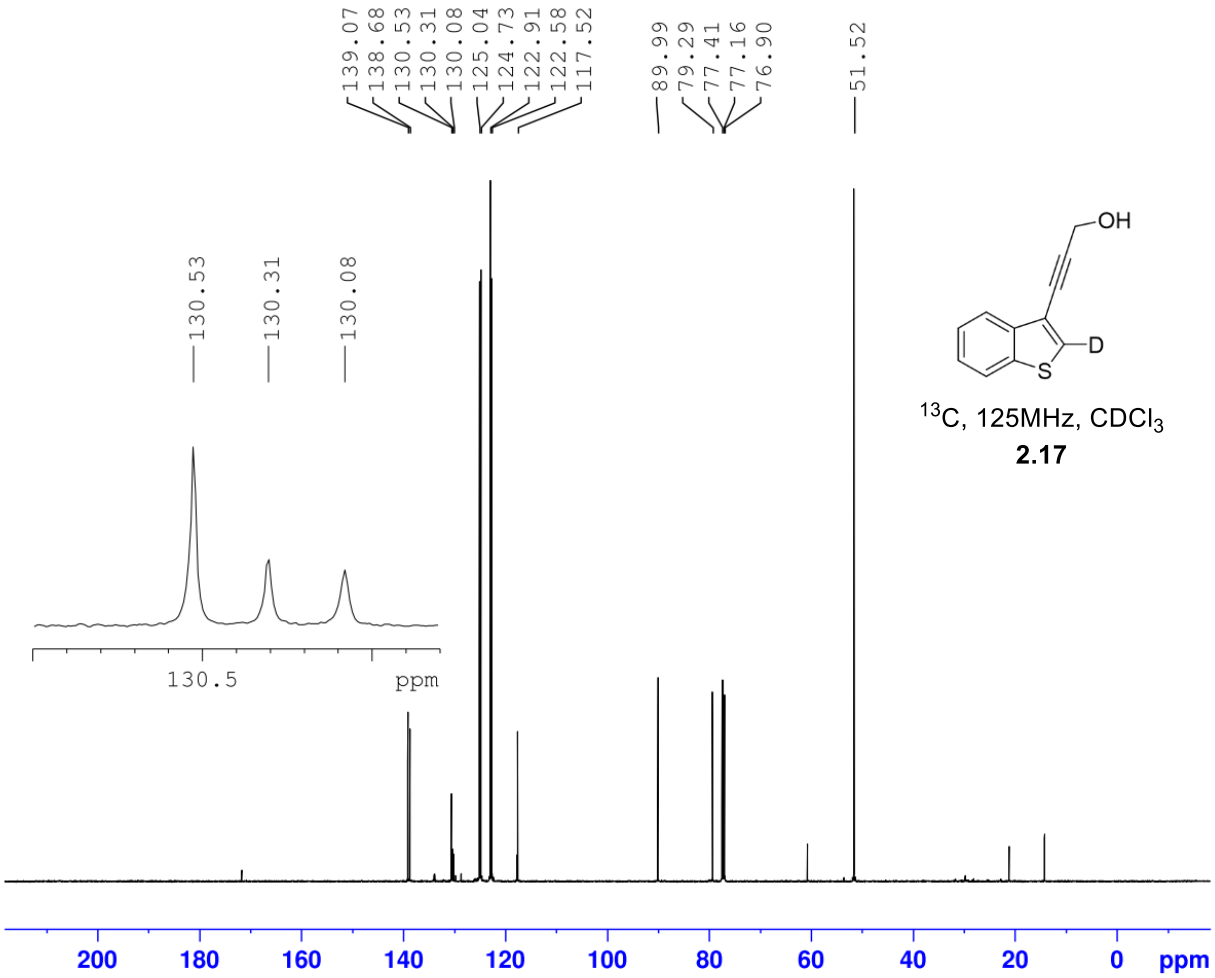

```
Current Data Parameters
NAME        JAW-01-128-A
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170717
Time               10.16
INSTRUM            spect
PROBHD   5 mm QNP  1H/1
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             6188.119 Hz
FIDRES          0.188846 Hz
AQ             2.6476543 sec
RG                  28.5
DW                80.800 usec
DE                  6.50 usec
TE                -925.4 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         300.2318540 MHz
NUC1                  1H
P1                 12.71 usec
PLW1         18.19700050 W

F2 - Processing parameters
SI                 32768
SF           300.2300080 MHz
WDW                   EM
SSB       0
LB                  0.10 Hz
GB        0
PC                  1.00
```




```
Current Data Parameters
NAME        JAW-01-128-A
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170715
Time                7.08
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    2
SWH            29761.904 Hz
FIDRES          0.454131 Hz
AQ             1.1010048 sec
RG                  203
DW                16.800 usec
DE                 6.50 usec
TE                300.3 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1         125.7779086 MHz
NUC1                  13C
P1                 10.50 usec
PLW1        110.00000000 W

======== CHANNEL f2 ========
SFO2         500.1620006 MHz
NUC2                   1H
CPDPRG[2         waltz16
PCPD2              80.00 usec
PLW2         18.00000000 W
PLW12         0.37195000 W
PLW13         0.23805000 W

F2 - Processing parameters
SI                 32768
SF          125.7653686 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```



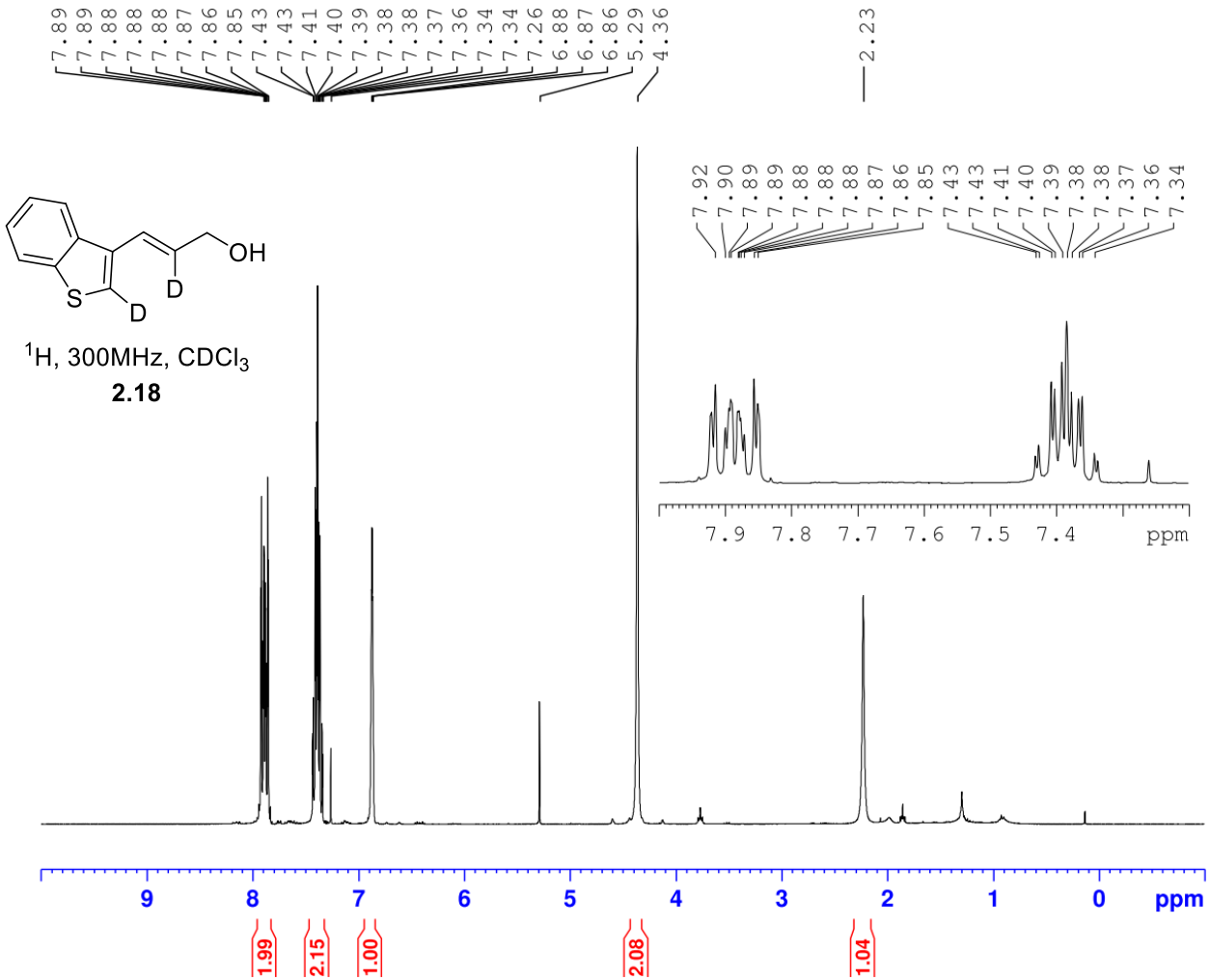

```
Current Data Parameters
NAME          JAW-01-138
EXPNO                  5
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170814
Time               10.04
INSTRUM            spect
PROBHD   5 mm QNP  1H/1
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             6188.119 Hz
FIDRES          0.188846 Hz
AQ            2.6476543 sec
RG                 40.3
DW                80.800 usec
DE                 6.50 usec
TE               -924.1 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1        300.2318540 MHz
NUC1                  1H
P1                12.71 usec
PLW1        18.19700050 W

F2 - Processing parameters
SI                 32768
SF          300.2300082 MHz
WDW                   EM
SSB       0
LB                 0.10 Hz
GB        0
PC                 1.00
```



^{13}C, 125MHz, $CDCl_3$

2.17

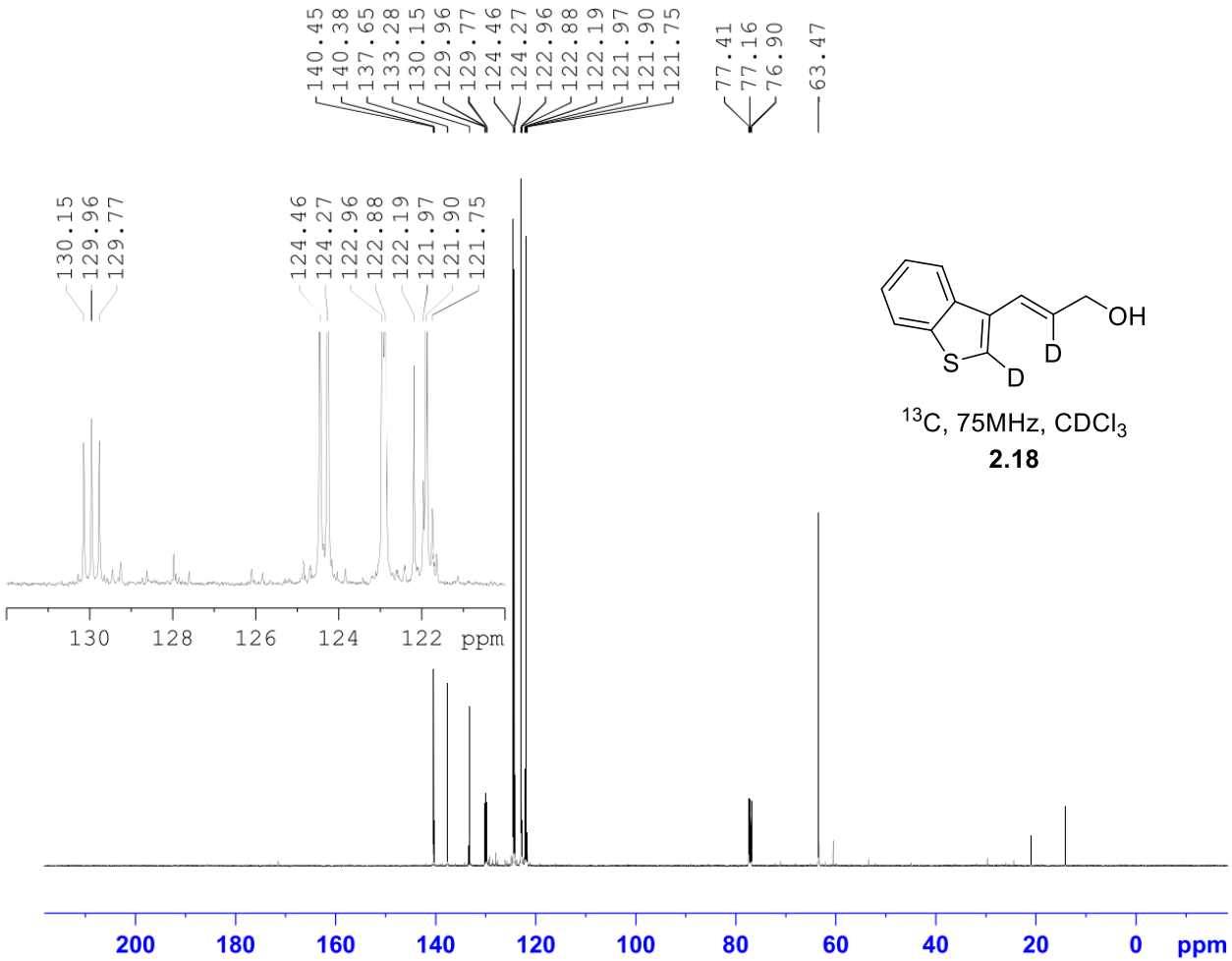
```
Current Data Parameters
NAME          JAW-01-132
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170722
Time               12.48
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    2
SWH            29761.904 Hz
FIDRES          0.454131 Hz
AQ             1.1010048 sec
RG                  203
DW                16.800 usec
DE                 6.50 usec
TE                299.8 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         125.7779086 MHz
NUC1                  13C
P1                 10.50 usec
PLW1        110.00000000 W

======== CHANNEL f2 ========
SFO2         500.1620006 MHz
NUC2                   1H
CPDPRG[2         waltz16
PCPD2              80.00 usec
PLW2         18.00000000 W
PLW12         0.37195000 W
PLW13         0.23805000 W

F2 - Processing parameters
SI                 32768
SF           125.7653415 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```



^{1}H, 300MHz, $CDCl_3$

2.18

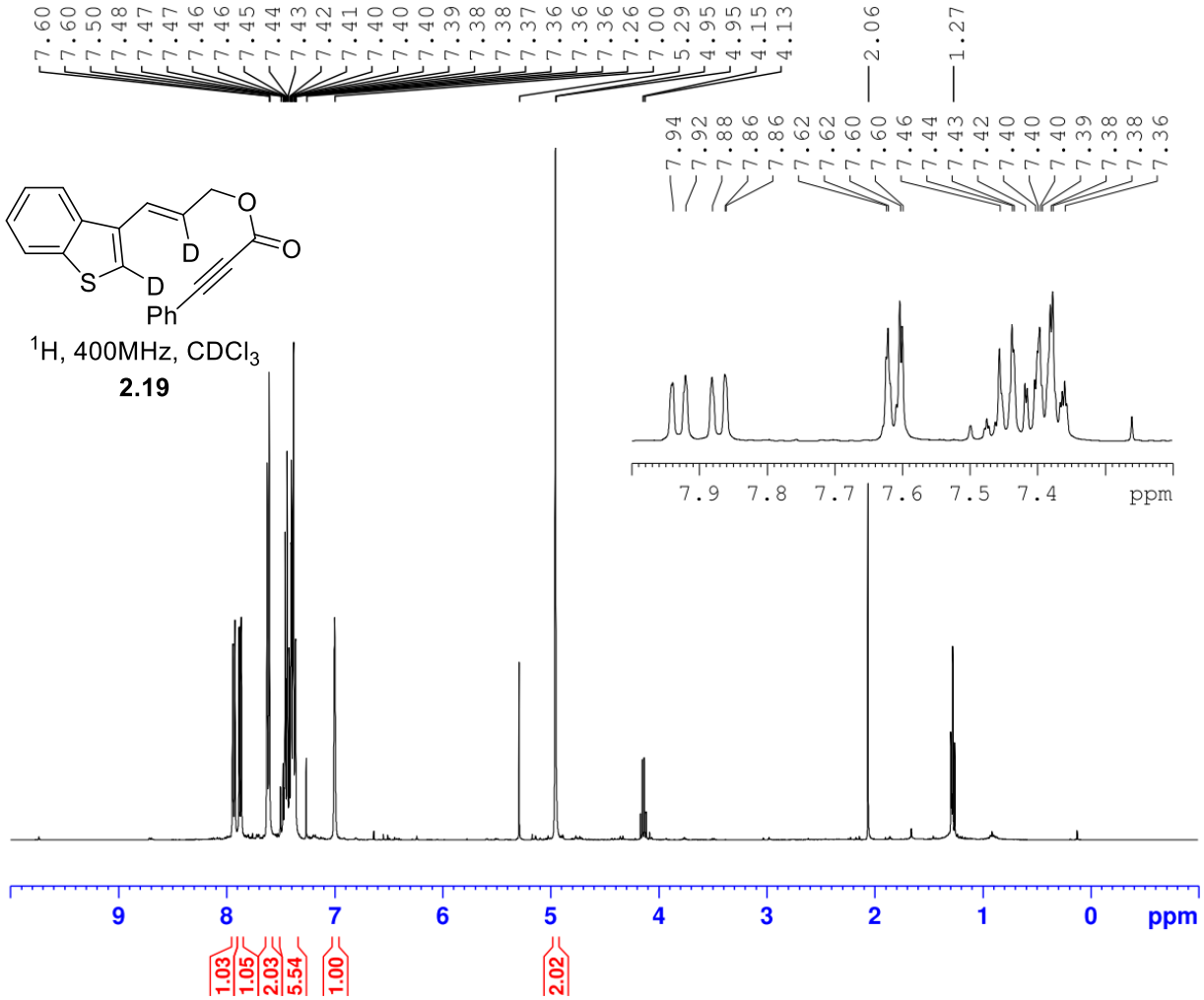
```
Current Data Parameters
NAME          JAW-01-140
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170823
Time                9.50
INSTRUM            spect
PROBHD   5 mm QNP  1H/1
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             6188.119 Hz
FIDRES          0.188846 Hz
AQ             2.6476543 sec
RG                    64
DW                80.800 usec
DE                  6.50 usec
TE                -924.2 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         300.2318540 MHz
NUC1                  1H
P1                 12.71 usec
PLW1         18.19700050 W

F2 - Processing parameters
SI                 32768
SF           300.2300083 MHz
WDW                   EM
SSB       0
LB                  0.10 Hz
GB        0
PC                  1.00
```



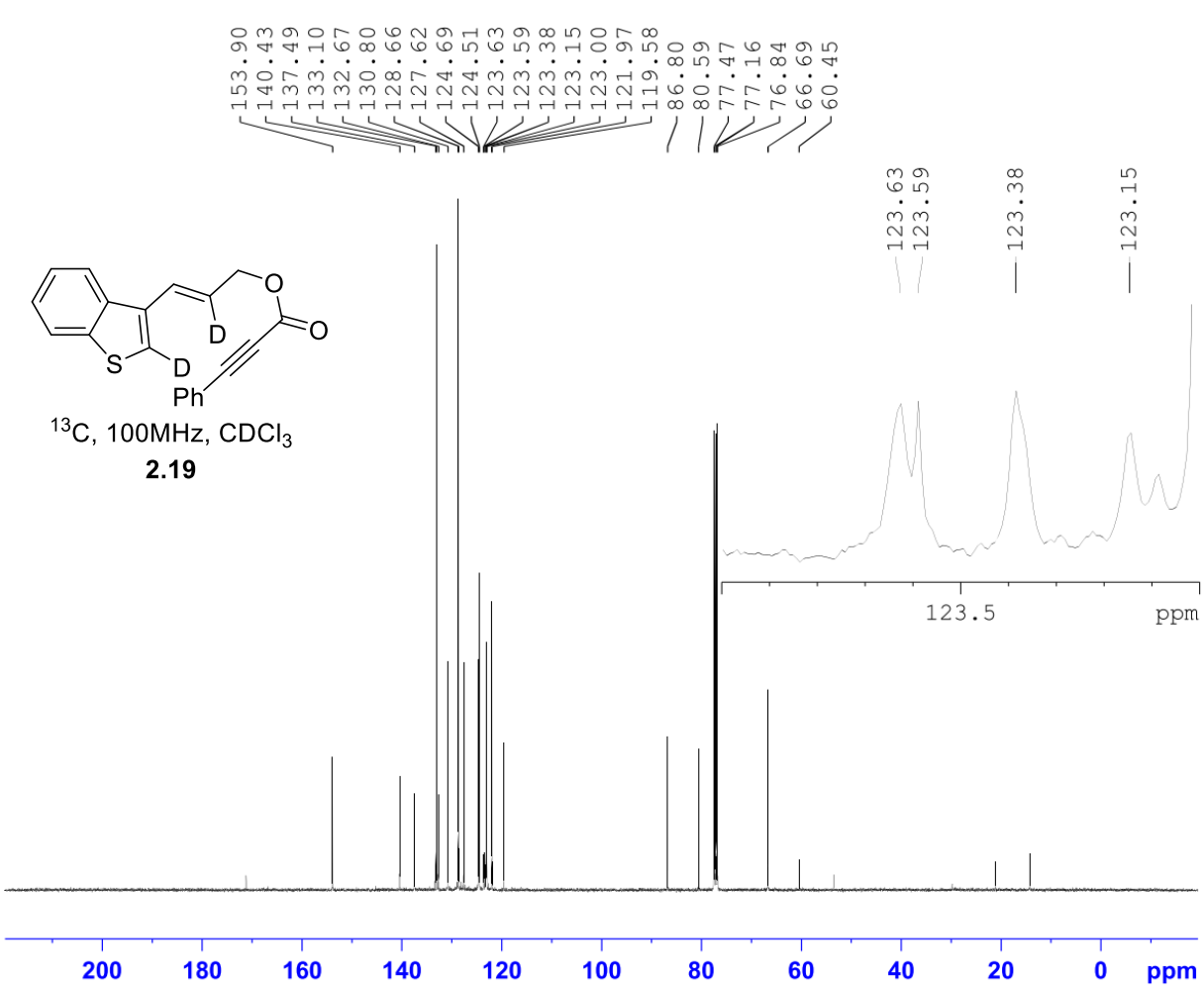
^{13}C, 75MHz, $CDCl_3$

2.18

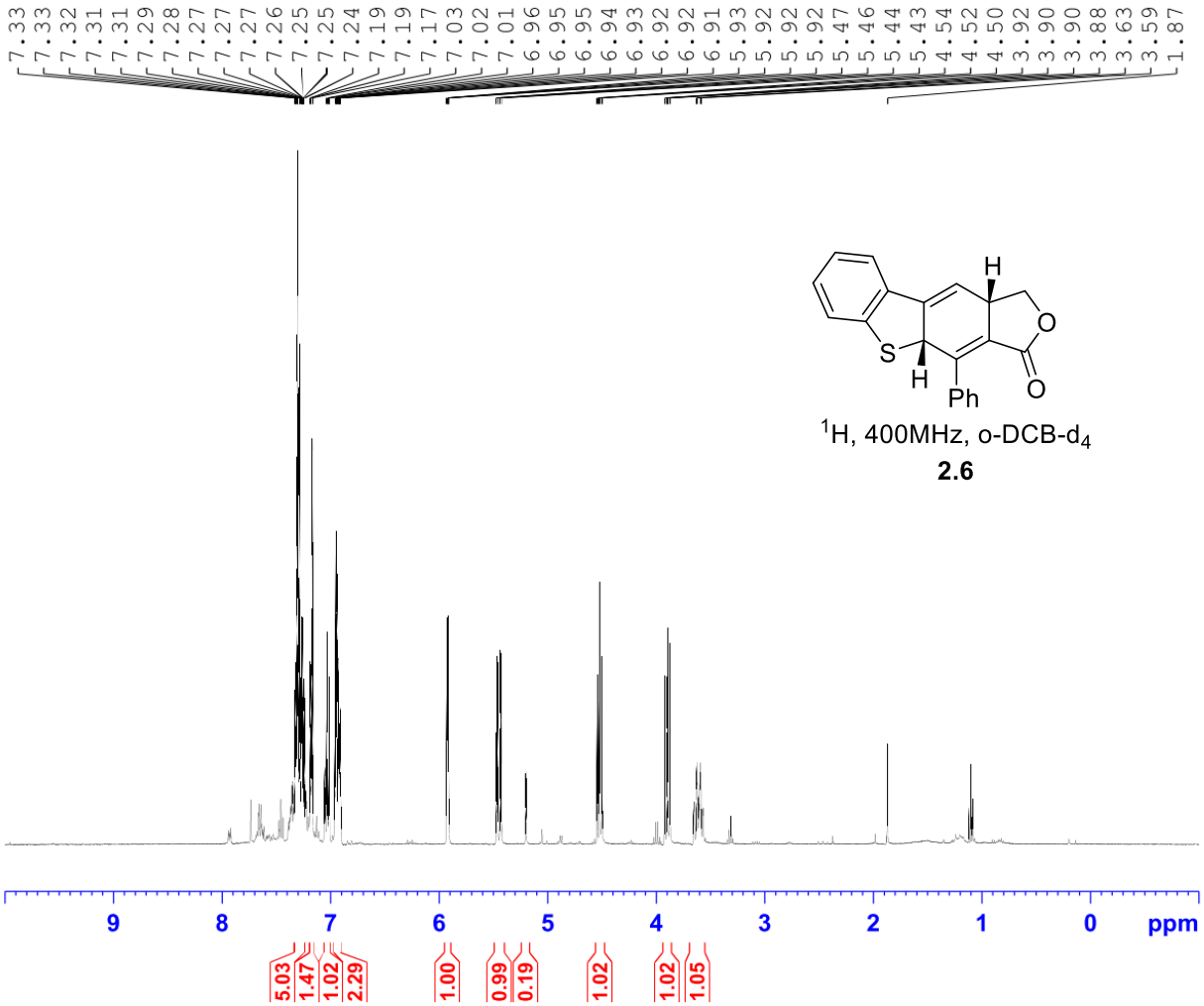
```
Current Data Parameters
NAME          JAW-01-140
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170830
Time                7.15
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    2
SWH            29761.904 Hz
FIDRES          0.454131 Hz
AQ             1.1010048 sec
RG                  203
DW                16.800 usec
DE                 6.50 usec
TE                298.5 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         125.7779086 MHz
NUC1                 13C
P1                10.50 usec
PLW1        110.00000000 W

======== CHANNEL f2 ========
SFO2         500.1620006 MHz
NUC2                  1H
CPDPRG[2         waltz16
PCPD2             80.00 usec
PLW2         18.00000000 W
PLW12         0.37195000 W
PLW13         0.23805000 W

F2 - Processing parameters
SI                 32768
SF           125.7653419 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```




```
Current Data Parameters
NAME          JAW-01-141
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170824
Time               17.04
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.122266 Hz
AQ             4.0894465 sec
RG                    32
DW                62.400 usec
DE                 6.50 usec
TE               -1899.1 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         400.1324710 MHz
NUC1                  1H
P1                13.75 usec
PLW1         12.01700020 W

F2 - Processing parameters
SI                 65536
SF           400.1300091 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



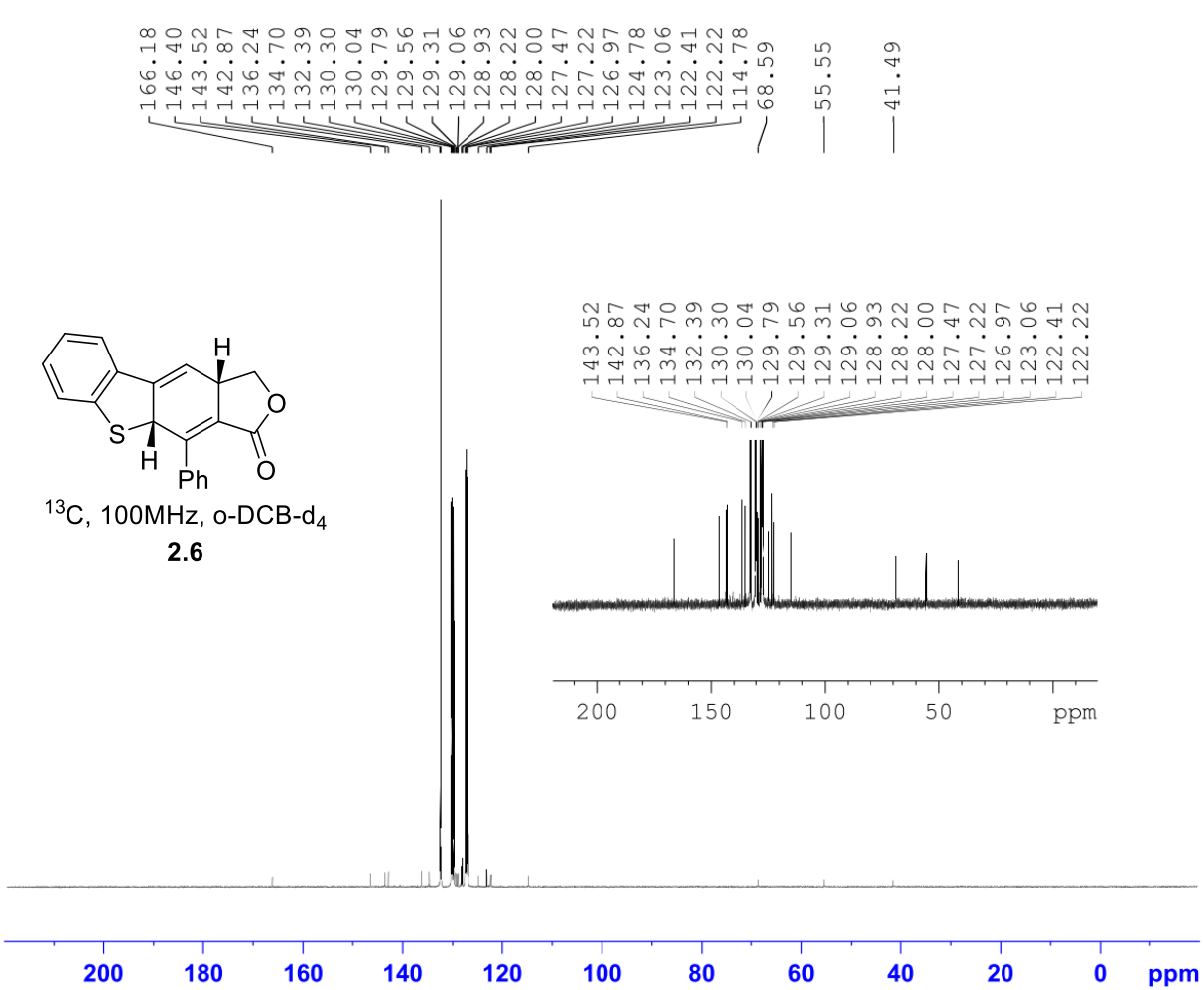

```
Current Data Parameters
NAME          JAW-01-141
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170824
Time               22.37
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ             1.3631488 sec
RG                  203
DW                20.800 usec
DE                 6.50 usec
TE              -2146.1 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         100.6228293 MHz
NUC1                  13C
P1                 10.00 usec
PLW1         56.13299942 W

======== CHANNEL f2 ========
SFO2         400.1316005 MHz
NUC2                   1H
CPDPRG[2          waltz16
PCPD2              90.00 usec
PLW2         12.01700020 W
PLW12         0.29076999 W
PLW13     0 W

F2 - Processing parameters
SI                 32768
SF           100.6127661 MHz
WDW                   EM
SSB       0
LB                  1.00 Hz
GB        0
PC                  1.40
```



^{1}H, 400MHz, o-DCB-d$_4$

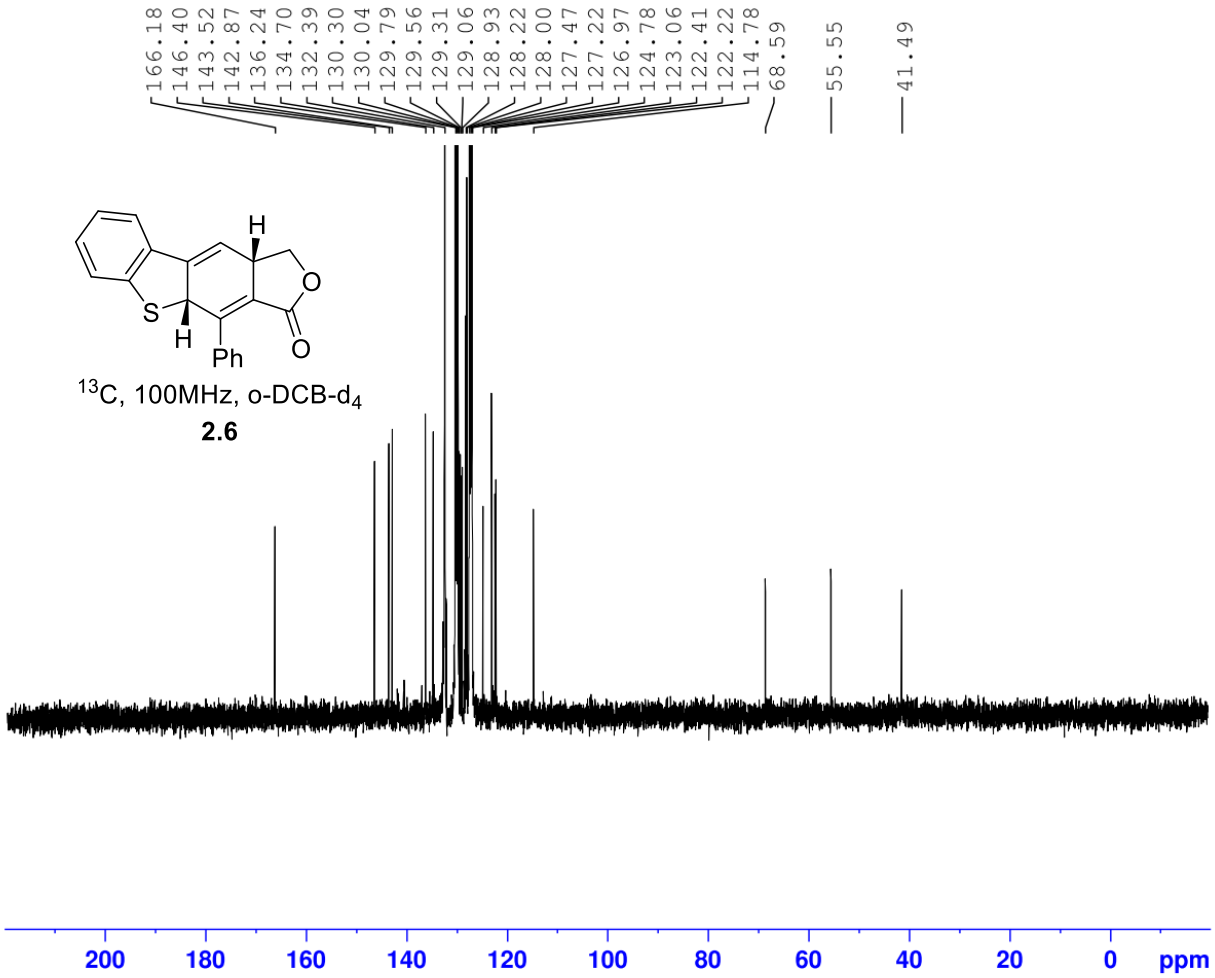
2.6

```
Current Data Parameters
NAME          JAW-01-164
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20171012
Time               15.39
INSTRUM            spect
PROBHD   5 mm PADUL 13C
PULPROG             zg30
TD                 65536
SOLVENT             C6D6
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ             3.9845889 sec
RG                   114
DW                60.800 usec
DE                 6.50 usec
TE                298.1 K
D1            2.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 9.31 usec
PL1               -3.90 dB
PL1W        21.64248466 W
SFO1        400.2324716 MHz

F2 - Processing parameters
SI                 32768
SF          400.2300984 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



BRUKER

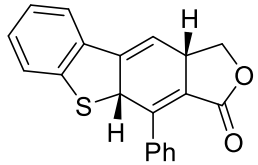
```
Current Data Parameters
NAME          JAW-01-164
EXPNO                  4
PROCNO                 1

F2 - Acquisition Parameters
Date_           20171012
Time               16.56
INSTRUM            spect
PROBHD   5 mm PADUL 13C
PULPROG           zgpg30
TD                 65536
SOLVENT             C6D6
NS                  1024
DS                     4
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ             1.3631488 sec
RG                   203
DW                20.800 usec
DE                 6.50 usec
TE                298.2 K
D1            3.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                 13C
P1                10.00 usec
PL1               -0.44 dB
PL1W        39.19395828 W
SFO1        100.6479773 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                  1H
PCPD2             90.00 usec
PL2               -3.90 dB
PL12              15.81 dB
PL13             120.00 dB
PL2W        21.64248466 W
PL12W        0.23137002 W
PL13W    0 W
SFO2        400.2316009 MHz

F2 - Processing parameters
SI                32768
SF          100.6379235 MHz
WDW                  EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```



^{13}C, 100MHz, o-DCB-d$_4$

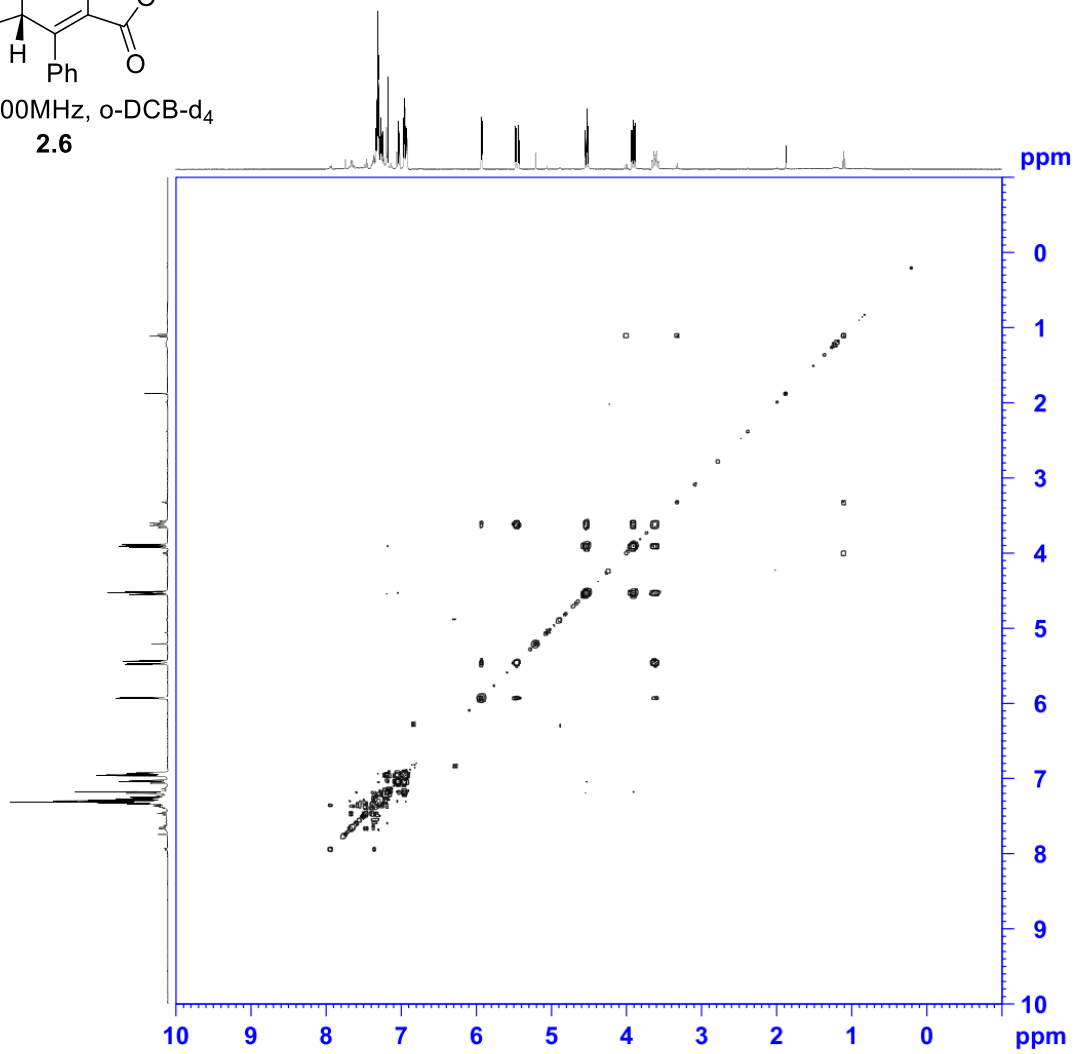
2.6

```
Current Data Parameters
NAME          JAW-01-164
EXPNO                  4
PROCNO                 1

F2 - Acquisition Parameters
Date_           20171012
Time               16.56
INSTRUM            spect
PROBHD   5 mm PADUL 13C
PULPROG          zgpg30
TD                65536
SOLVENT             C6D6
NS                  1024
DS                     4
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ             1.3631488 sec
RG                   203
DW                20.800 usec
DE                 6.50 usec
TE                298.2 K
D1            3.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                 13C
P1                10.00 usec
PL1               -0.44 dB
PL1W        39.19395828 W
SFO1        100.6479773 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                  1H
PCPD2             90.00 usec
PL2               -3.90 dB
PL12              15.81 dB
PL13             120.00 dB
PL2W        21.64248466 W
PL12W        0.23137002 W
PL13W    0 W
SFO2        400.2316009 MHz

F2 - Processing parameters
SI                32768
SF          100.6379235 MHz
WDW                  EM
SSB      0
LB                1.00 Hz
GB       0
PC                1.40
```

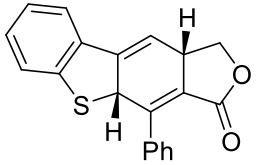


COSY, 500MHz, o-DCB-d_4

2.6

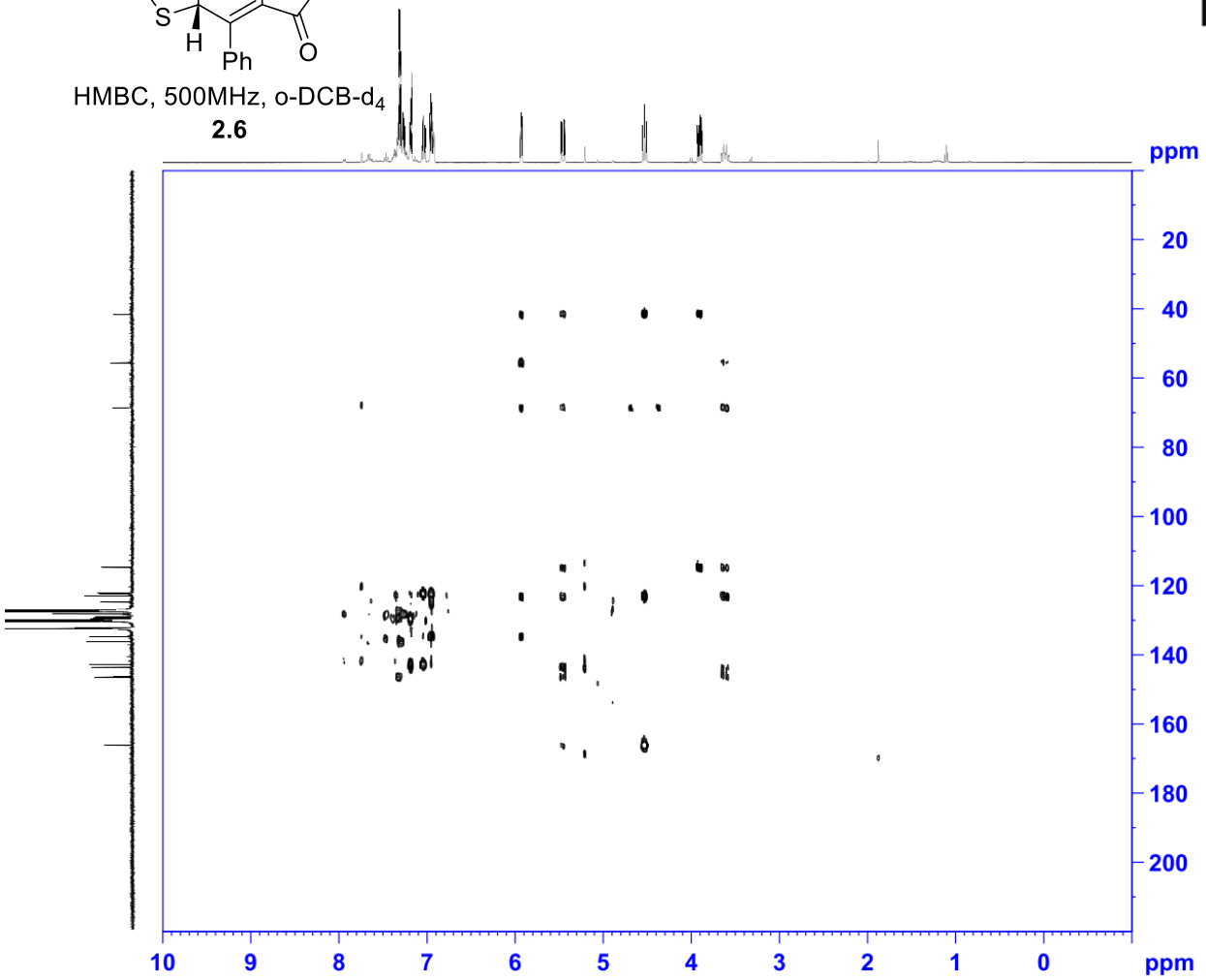



```
Current Data Parameters
NAME          JAW-01-164
EXPNO                  6
PROCNO                 1

F2 - Acquisition Parameters
Date_           20171012
Time               17.07
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG      cosygpppqf
TD                  2048
SOLVENT             C6D6
NS                     1
DS                     8
SWH            4504.504 Hz
FIDRES         2.199465 Hz
AQ            0.2273280 sec
RG                    64
DW              111.000 usec
DE                 6.50 usec
TE                296.3 K
D0           0.00000300 sec
D1           1.92586195 sec
D11          0.03000000 sec
D12          0.00002000 sec
D13          0.00000400 sec
D16          0.00020000 sec
IN0          0.00022200 sec

======== CHANNEL f1 ========
SFO1        500.1621512 MHz
NUC1                  1H
P0                11.50 usec
P1                11.50 usec
P17             2500.00 usec
PLW1         18.00000000 W
PLW10         3.52139997 W

====== GRADIENT CHANNEL =====
GPNAM[1]      SMSQ10.100
GPZ1               10.00 %
P16              1000.00 usec

F1 - Acquisition parameters
TD                   128
SFO1            500.1622 MHz
FIDRES         70.382881 Hz
SW                 9.006 ppm
FnMODE                QF

F2 - Processing parameters
SI                   1024
SF          500.1599890 MHz
WDW                 QSINE
SSB       0
LB        0 Hz
GB        0
PC                  1.40

F1 - Processing parameters
SI                   1024
MC2                    QF
SF          500.1599889 MHz
WDW                 QSINE
SSB       0
LB        0 Hz
GB        0
```

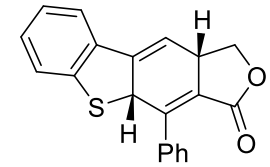


HMBC, 500MHz, o-DCB-d_4

2.6

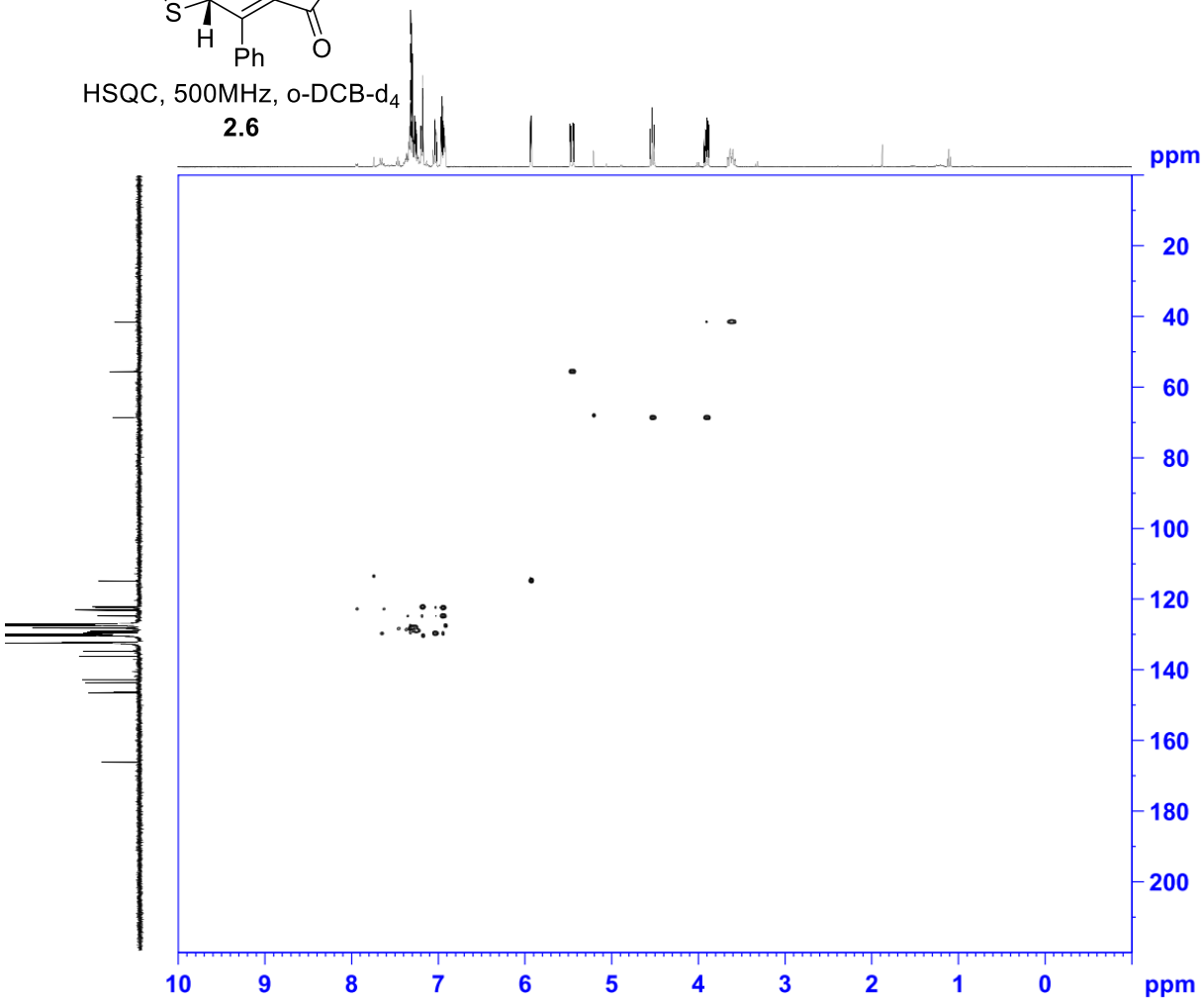



```
Current Data Parameters
NAME          JAW-01-164
EXPNO                  8
PROCNO                 1

F2 - Acquisition Parameters
Date_           20171012
Time                17.28
INSTRUM             spect
PROBHD   5 mm PABBO BB/
PULPROG    hmbcgplpndqf
TD                  2048
SOLVENT             C6D6
NS                     4
DS                    16
SWH            4504.504 Hz
FIDRES         2.199465 Hz
AQ            0.2273280 sec
RG                   203
DW              111.000 usec
DE                 6.50 usec
TE                296.9 K
CNST2       145.0000000
CNST13       10.0000000
D0           0.00000300 sec
D1           1.42995799 sec
D2           0.00344828 sec
D6           0.05000000 sec
D16          0.00020000 sec
IN0          0.00001790 sec

======== CHANNEL f1 ========
SFO1        500.1621512 MHz
NUC1                  1H
P1                 11.50 usec
P2                 23.00 usec
PLW1        18.00000000 W

======== CHANNEL f2 ========
SFO2        125.7778879 MHz
NUC2                 13C
P3                 10.50 usec
PLW2       110.00000000 W

====== GRADIENT CHANNEL =====
GPNAM[1]      SMSQ10.100
GPNAM[2]      SMSQ10.100
GPNAM[3]      SMSQ10.100
GPZ1               50.00 %
GPZ2               30.00 %
GPZ3               40.10 %
P16              1000.00 usec

F1 - Acquisition parameters
TD                   128
SFO1           125.7779 MHz
FIDRES       436.452515 Hz
SW              222.082 ppm
FnMODE                QF

F2 - Processing parameters
SI                   2048
SF          500.1599896 MHz
WDW                 SINE
SSB       0
LB        0 Hz
GB        0
PC                  1.40

F1 - Processing parameters
SI                   1024
MC2                    QF
SF          125.7653016 MHz
WDW                 SINE
SSB       0
LB        0 Hz
GB        0
```

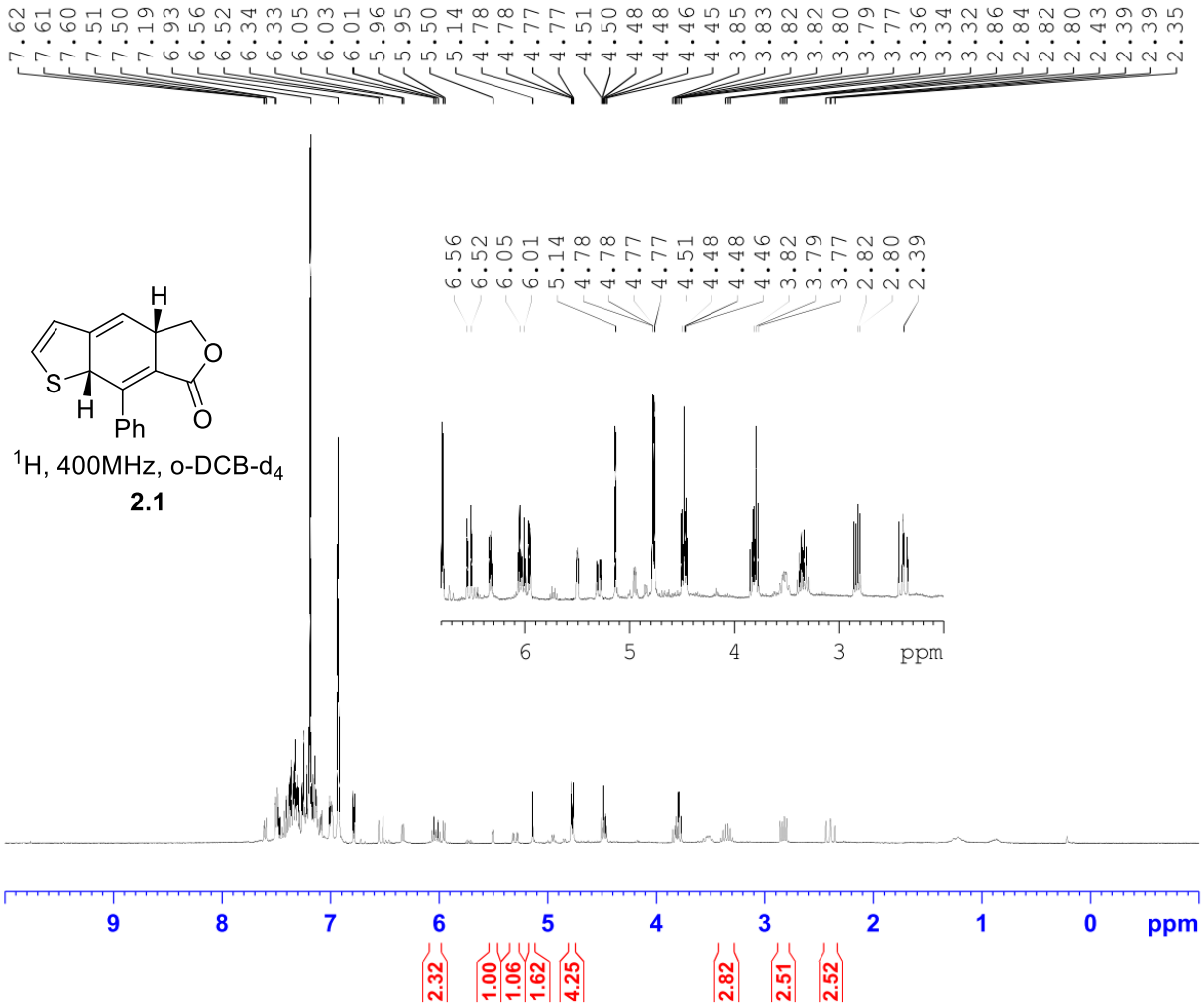


HSQC, 500MHz, o-DCB-d_4

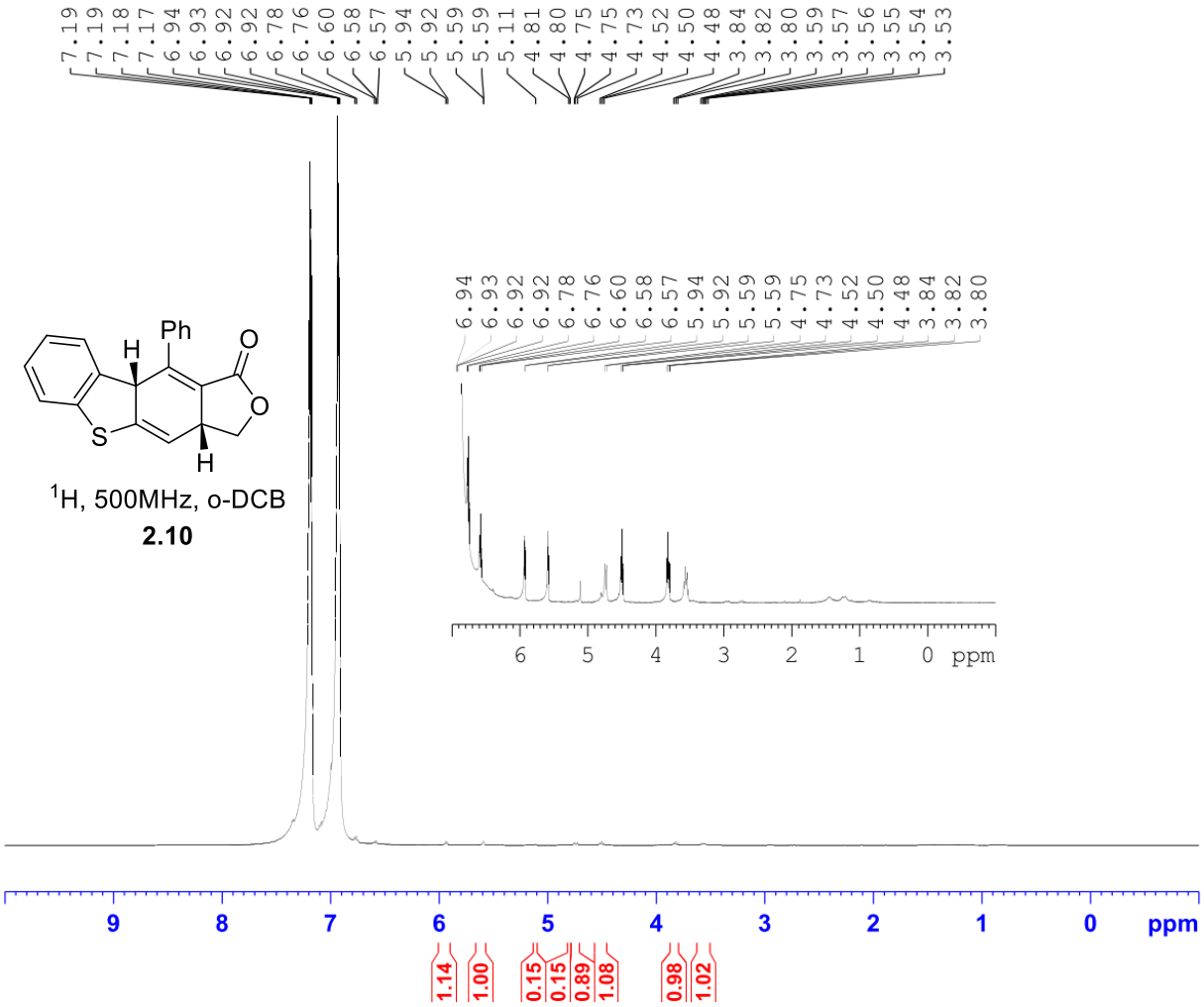
2.6



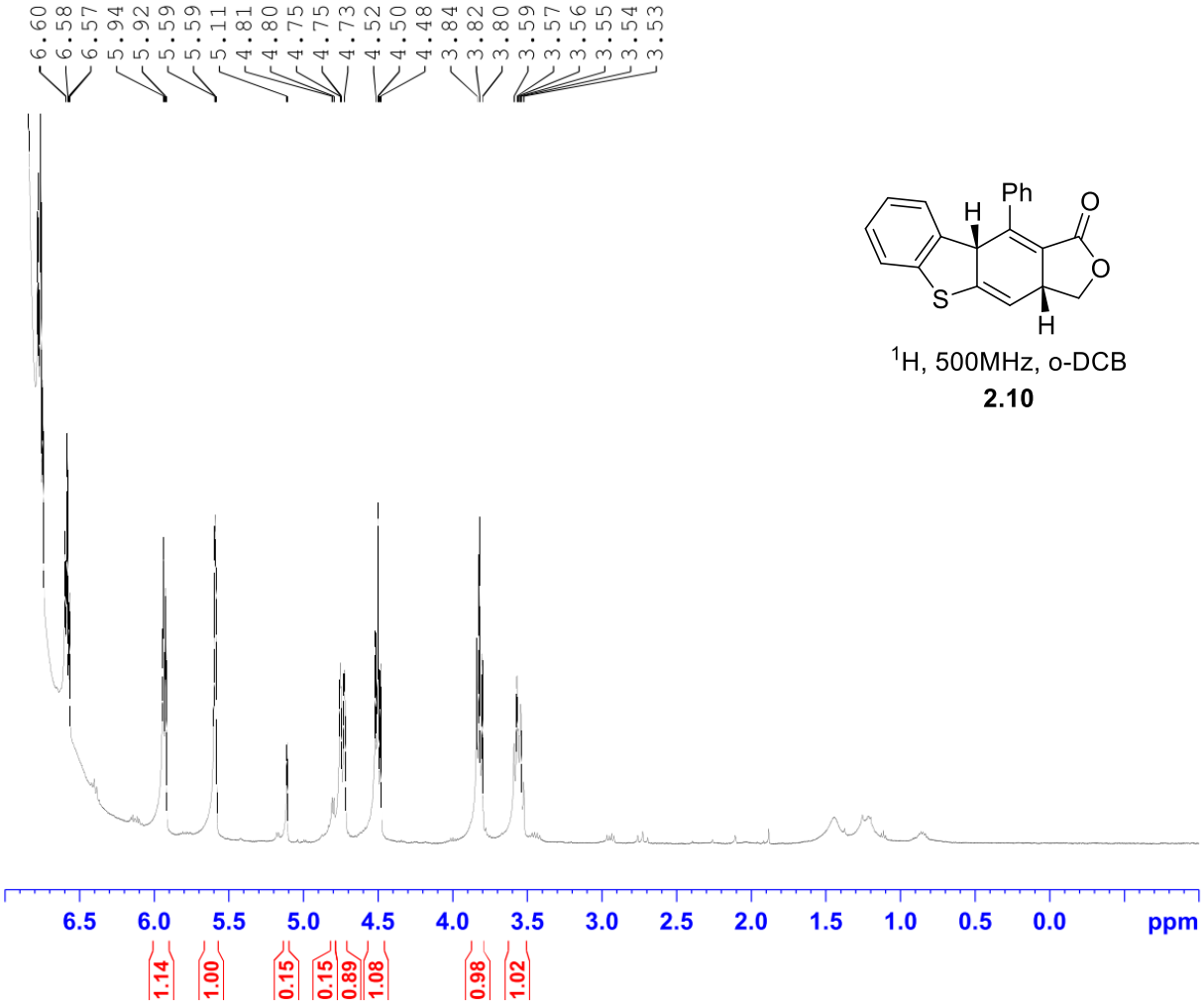

```
Current Data Parameters
NAME          JAW-01-164
EXPNO                  7
PROCNO                 1

F2 - Acquisition Parameters
Date_           20171012
Time                17.13
INSTRUM             spect
PROBHD    5 mm PABBO BB/
PULPROG     hsqcetgpsi2
TD                  1024
SOLVENT             C6D6
NS                     2
DS                    16
SWH            4504.504 Hz
FIDRES         4.398930 Hz
AQ           0.1136640 sec
RG                   203
DW               111.000 usec
DE                 6.50 usec
TE                296.3 K
CNST2       145.0000000
D0           0.00000300 sec
D1           1.46313596 sec
D4           0.00172414 sec
D11          0.03000000 sec
D16          0.00020000 sec
D24          0.00086207 sec
IN0          0.00002400 sec
ZGOPTNS

======== CHANNEL f1 ========
SFO1        500.1621512 MHz
NUC1                  1H
P1                11.50 usec
P2                23.00 usec
P28            1000.00 usec
PLW1        18.00000000 W

======== CHANNEL f2 ========
SFO2        125.7747618 MHz
NUC2                 13C
CPDPRG[2            garp
P3                10.50 usec
P4                21.00 usec
PCPD2             70.00 usec
PLW2       110.00000000 W
PLW12        2.47499990 W

====== GRADIENT CHANNEL =====
GPNAM[1]      SMSQ10.100
GPNAM[2]      SMSQ10.100
GPNAM[3]      SMSQ10.100
GPNAM[4]      SMSQ10.100
GPZ1              80.00 %
GPZ2              20.10 %
GPZ3              11.00 %
GPZ4              -5.00 %
P16            1000.00 usec
P19             600.00 usec

F1 - Acquisition parameters
TD                   256
SFO1           125.7748 MHz
FIDRES       162.760422 Hz
SW              165.640 ppm
FnMODE    Echo-Antiecho

F2 - Processing parameters
SI                  1024
SF          500.1599898 MHz
WDW                 QSINE
SSB                     2
LB        0 Hz
GB        0
PC                   1.40

F1 - Processing parameters
SI                  1024
MC2        echo-antiecho
SF          125.7653040 MHz
WDW                 QSINE
SSB                     2
LB        0 Hz
GB        0
```




```
Current Data Parameters
NAME          JAW-01-008
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20160617
Time               13.16
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT             C6D6
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.122266 Hz
AQ             4.0894465 sec
RG                   128
DW                62.400 usec
DE                 6.50 usec
TE                 95.6 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1        400.1324710 MHz
NUC1                  1H
P1                13.75 usec
PLW1        12.01700020 W

F2 - Processing parameters
SI                 65536
SF          400.1300900 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



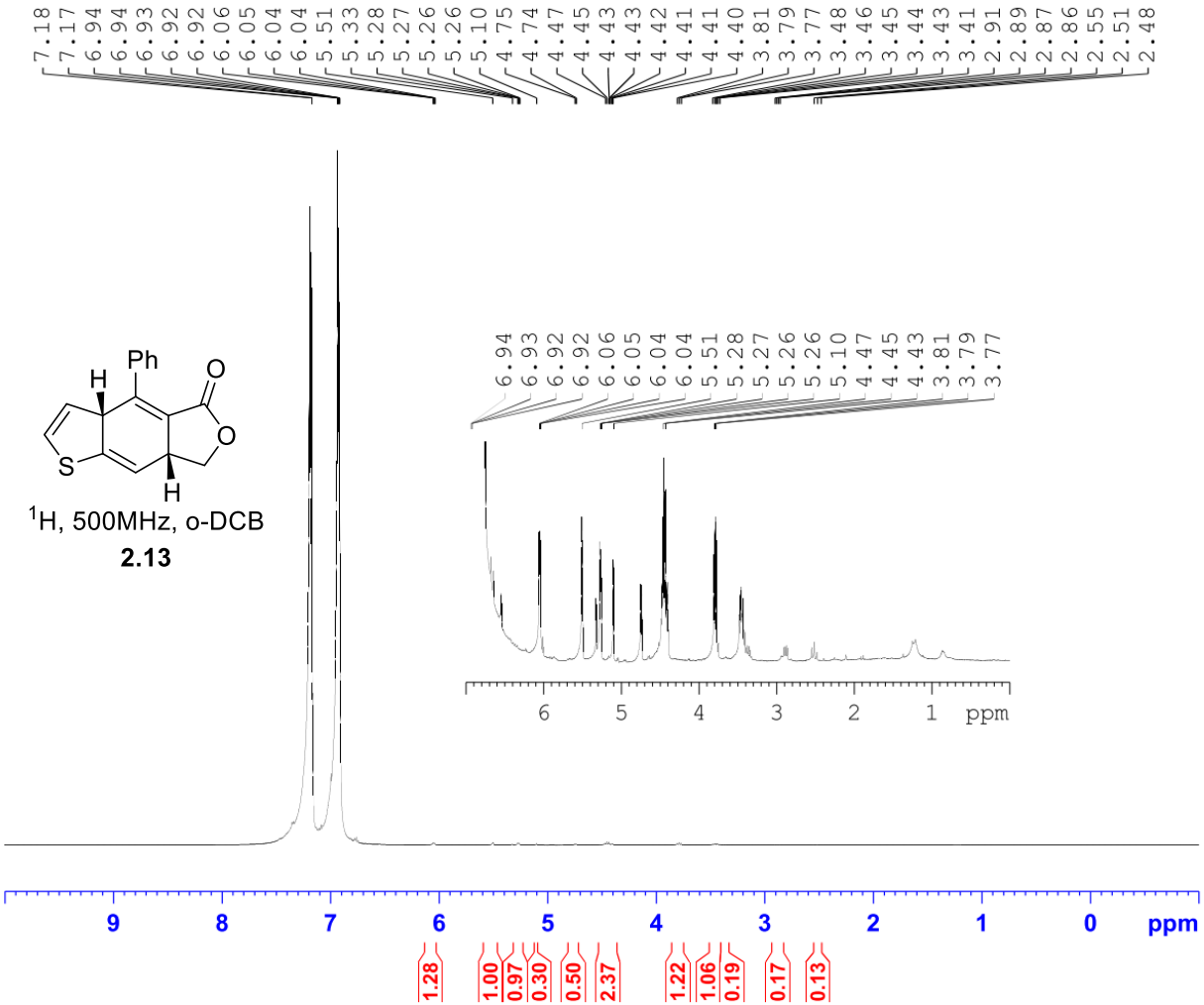

```
Current Data Parameters
NAME          JAW-02-115
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180817
Time               12.53
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT             None
NS                    32
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                   5.6
DW                50.000 usec
DE                 6.50 usec
TE                296.1 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                   1H
P1                 11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1598041 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```



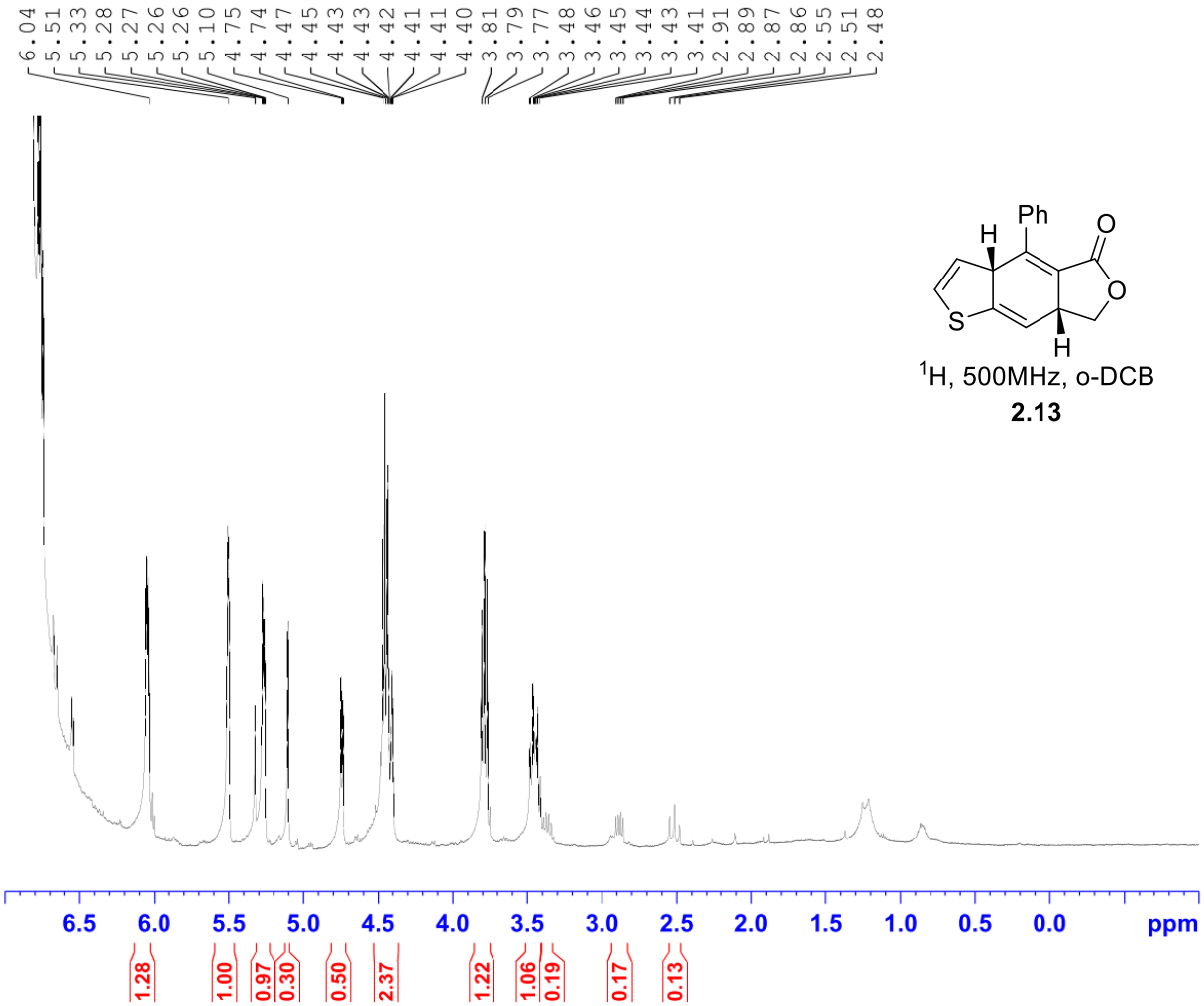
^{1}H, 500MHz, o-DCB

2.10

```
Current Data Parameters
NAME          JAW-02-115
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180817
Time               12.53
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT             None
NS                    32
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                   5.6
DW                50.000 usec
DE                 6.50 usec
TE                296.1 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                  1H
P1                11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1598041 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



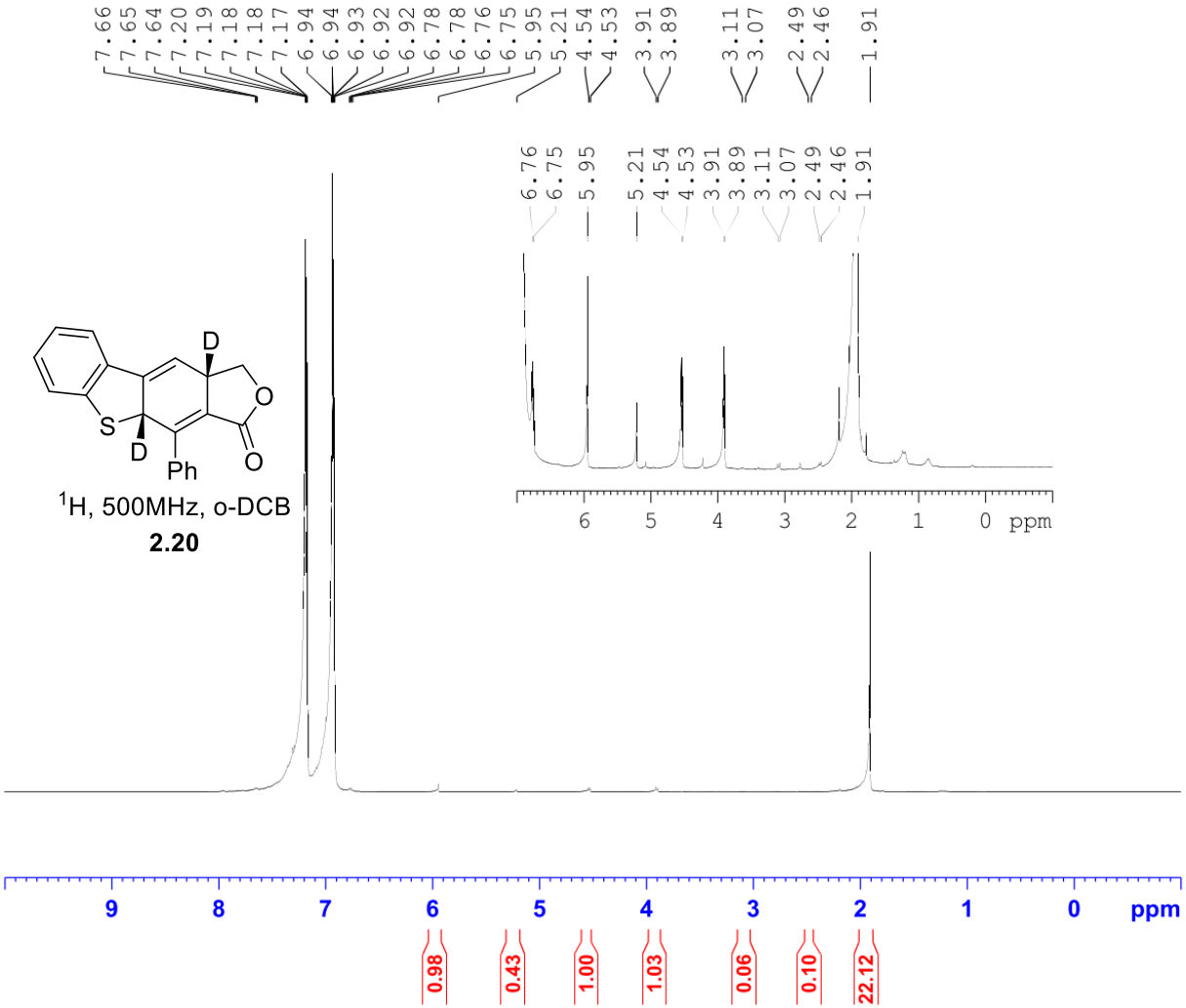

```
Current Data Parameters
NAME          JAW-02-114
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180823
Time               14.19
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT             None
NS                    32
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                   5.6
DW                50.000 usec
DE                 6.50 usec
TE                296.2 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                   1H
P1                 11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1598042 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



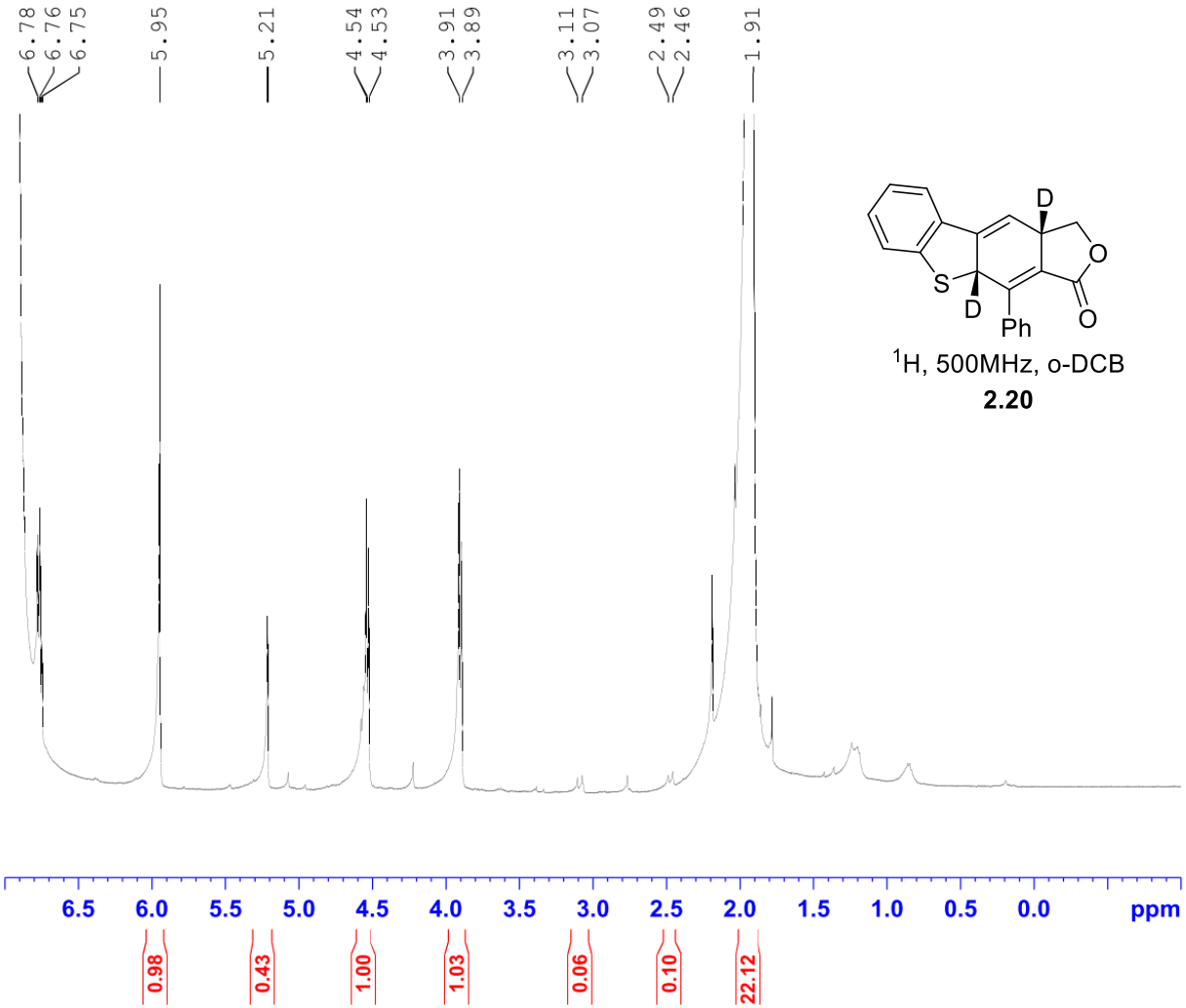
^{1}H, 500MHz, o-DCB

2.13

```
Current Data Parameters
NAME          JAW-02-114
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180823
Time               14.19
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT             None
NS                    32
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                   5.6
DW                50.000 usec
DE                 6.50 usec
TE                296.2 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                   1H
P1                 11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1598042 MHz
WDW                    EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```



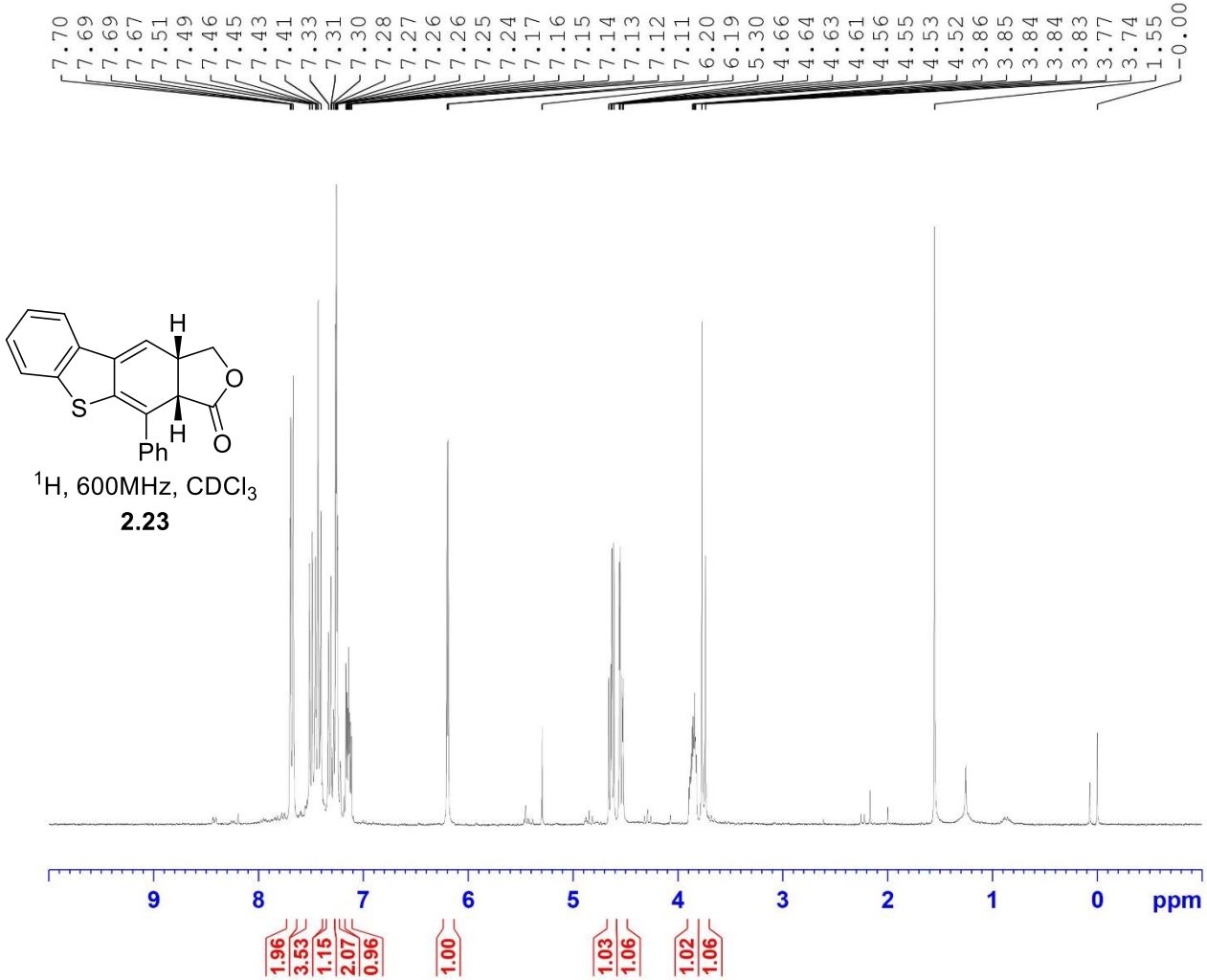

```
Current Data Parameters
NAME          JAW-01-126
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170621
Time              16.17
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG            zg30
TD                65536
SOLVENT            None
NS                   16
DS                    2
SWH           10000.000 Hz
FIDRES         0.152588 Hz
AQ            3.2767999 sec
RG                  5.6
DW               50.000 usec
DE                6.50 usec
TE                297.9 K
D1            1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1        500.1630887 MHz
NUC1                  1H
P1                11.50 usec
PLW1        18.00000000 W

F2 - Processing parameters
SI                65536
SF          500.1598314 MHz
WDW                  EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```



^{1}H, 500MHz, o-DCB

2.20

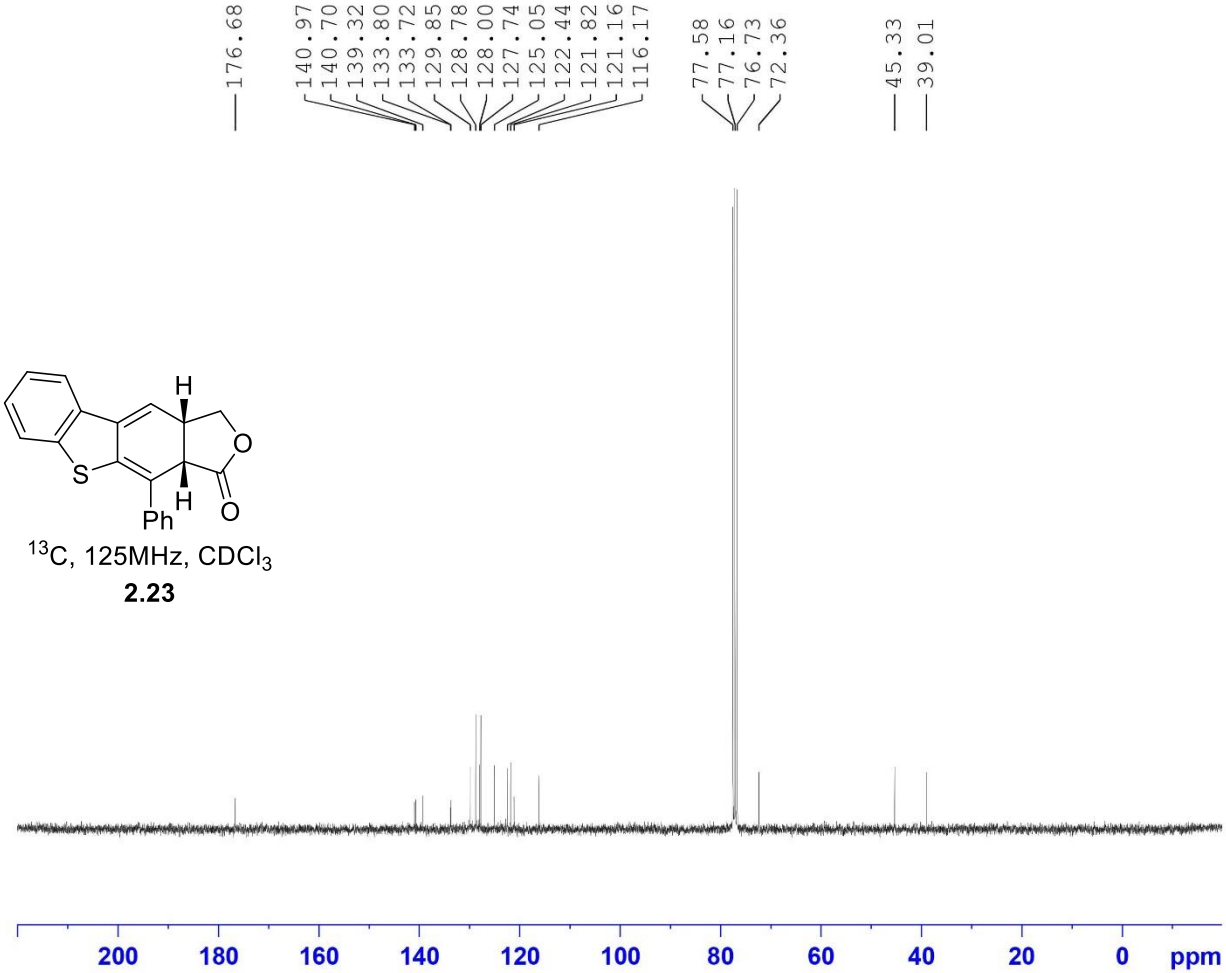
```
Current Data Parameters
NAME          JAW-01-126
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170621
Time              16.17
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG            zg30
TD                65536
SOLVENT            None
NS                   16
DS                    2
SWH           10000.000 Hz
FIDRES         0.152588 Hz
AQ            3.2767999 sec
RG                  5.6
DW               50.000 usec
DE                6.50 usec
TE               297.9 K
D1           1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1        500.1630887 MHz
NUC1                  1H
P1                11.50 usec
PLW1        18.00000000 W

F2 - Processing parameters
SI                65536
SF          500.1598314 MHz
WDW                  EM
SSB      0
LB                0.30 Hz
GB       0
PC                1.00
```



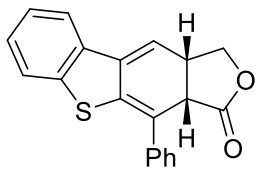

```
Current Data Parameters
NAME          JAW-03-112
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210428
Time              16.09 h
INSTRUM           spect
PROBHD   Z104275_0423 (
PULPROG            zg30
TD                32768
SOLVENT           CDCl3
NS                   16
DS                    2
SWH            6009.615 Hz
FIDRES         0.366798 Hz
AQ            2.7262976 sec
RG                  181
DW               83.200 usec
DE                 6.50 usec
TE                294.5 K
D1           1.00000000 sec
TD0                   1
SFO1        300.2318539 MHz
NUC1                 1H
P0                 4.67 usec
P1                14.00 usec
PLW1        17.16200066 W

F2 - Processing parameters
SI                65536
SF          300.2300080 MHz
WDW                  EM
SSB      0
LB                0.30 Hz
GB       0
PC                1.00
```

^{13}C, 125MHz, $CDCl_3$

2.23

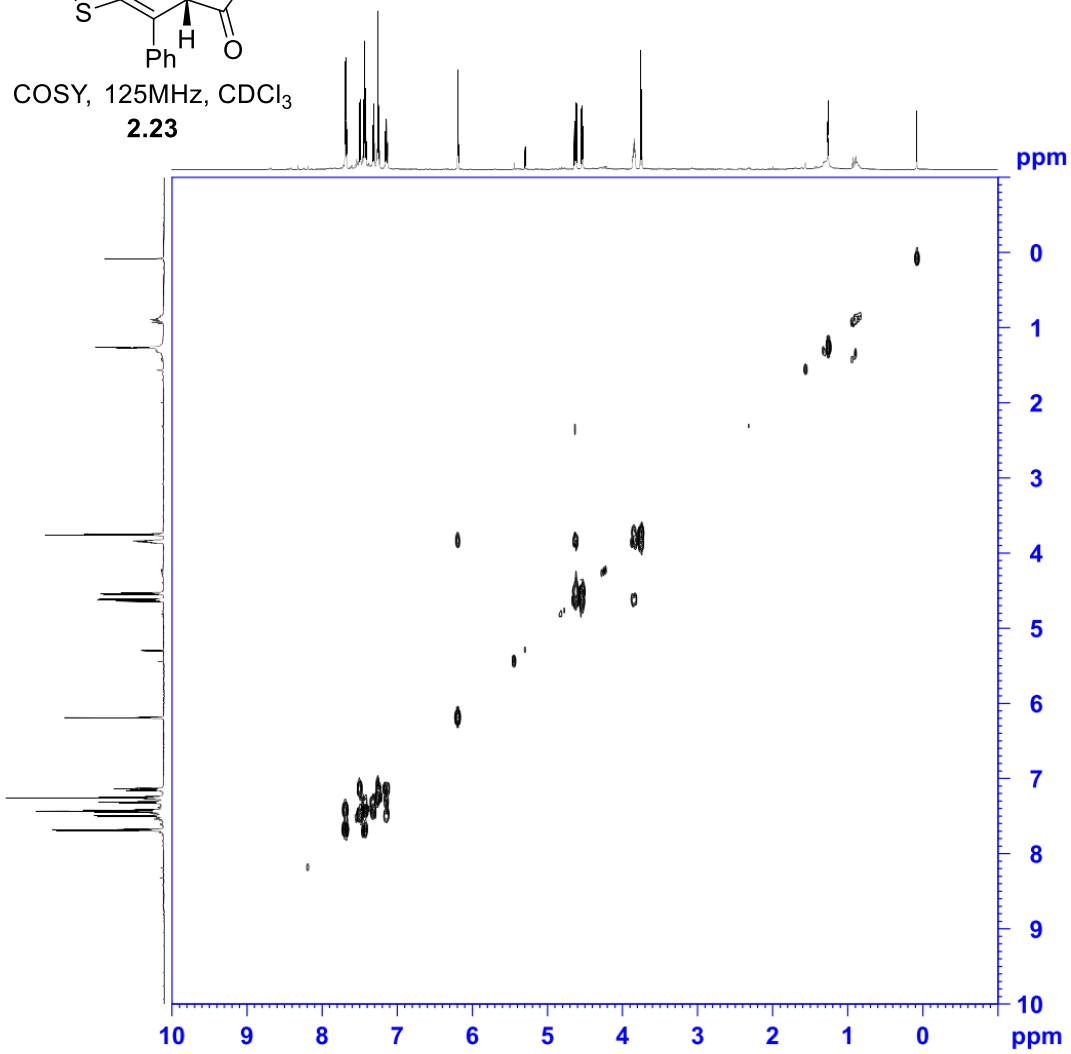



```
Current Data Parameters
NAME          JAW-03-112
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210428
Time              23.12 h
INSTRUM           spect
PROBHD   Z104275_0423 (
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           18115.941 Hz
FIDRES         0.552855 Hz
AQ            1.8087935 sec
RG                 1030
DW               27.600 usec
DE                6.50 usec
TE                294.8 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1         75.5004428 MHz
NUC1                 13C
P0                 3.33 usec
P1                10.00 usec
PLW1        39.28099823 W
SFO2        300.2312009 MHz
NUC2                  1H
CPDPRG[2         waltz65
PCPD2             90.00 usec
PLW2        17.16200066 W
PLW12        0.41528001 W
PLW13        0.20888001 W

F2 - Processing parameters
SI                32768
SF         75.4928834 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

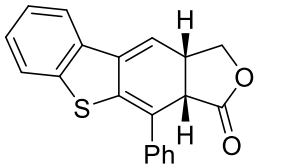


COSY, 125MHz, $CDCl_3$

2.23

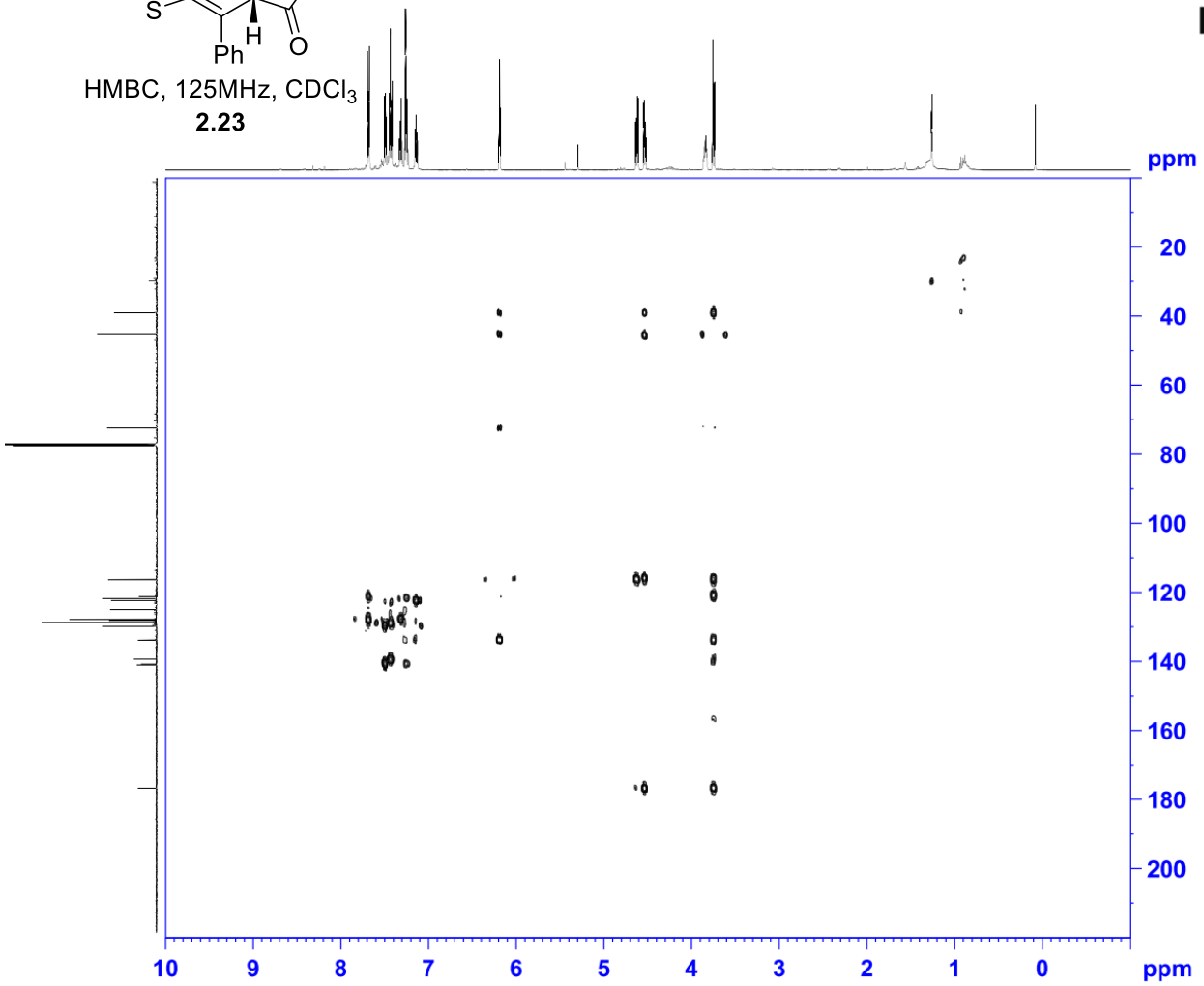



```
Current Data Parameters
NAME        JAW-02-179-b
EXPNO                   9
PROCNO                  1

F2 - Acquisition Parameters
Date_            20181214
Time               18.11
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG      cosygpppqf
TD                  2048
SOLVENT            CDCl3
NS                      6
DS                      8
SWH             6684.492 Hz
FIDRES          3.263912 Hz
AQ             0.1531904 sec
RG                    203
DW                 74.800 usec
DE                  6.50 usec
TE                 297.4 K
D0            0.00000300 sec
D1            2.00000000 sec
D11           0.03000000 sec
D12           0.00002000 sec
D13           0.00000400 sec
D16           0.00020000 sec
IN0           0.00014960 sec

======== CHANNEL f1 ========
SFO1         500.1630071 MHz
NUC1                  1H
P0                 11.50 usec
P1                 11.50 usec
P17              2500.00 usec
PLW1         18.00000000 W
PLW10         3.52139997 W

====== GRADIENT CHANNEL =====
GPNAM[1]      SMSQ10.100
GPZ1               10.00 %
P16              1000.00 usec

F1 - Acquisition parameters
TD                     32
SFO1              500.163 MHz
FIDRES        417.780762 Hz
SW                13.365 ppm
FnMODE                 QF

F2 - Processing parameters
SI                   1024
SF           500.1600127 MHz
WDW                 QSINE
SSB       0
LB        0 Hz
GB        0
PC                   1.40

F1 - Processing parameters
SI                   1024
MC2                    QF
SF           500.1600139 MHz
WDW                 QSINE
SSB       0
LB        0 Hz
GB        0
```

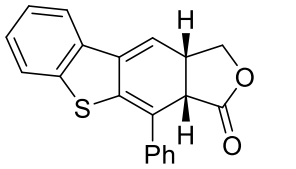


HMBC, 125MHz, $CDCl_3$

2.23

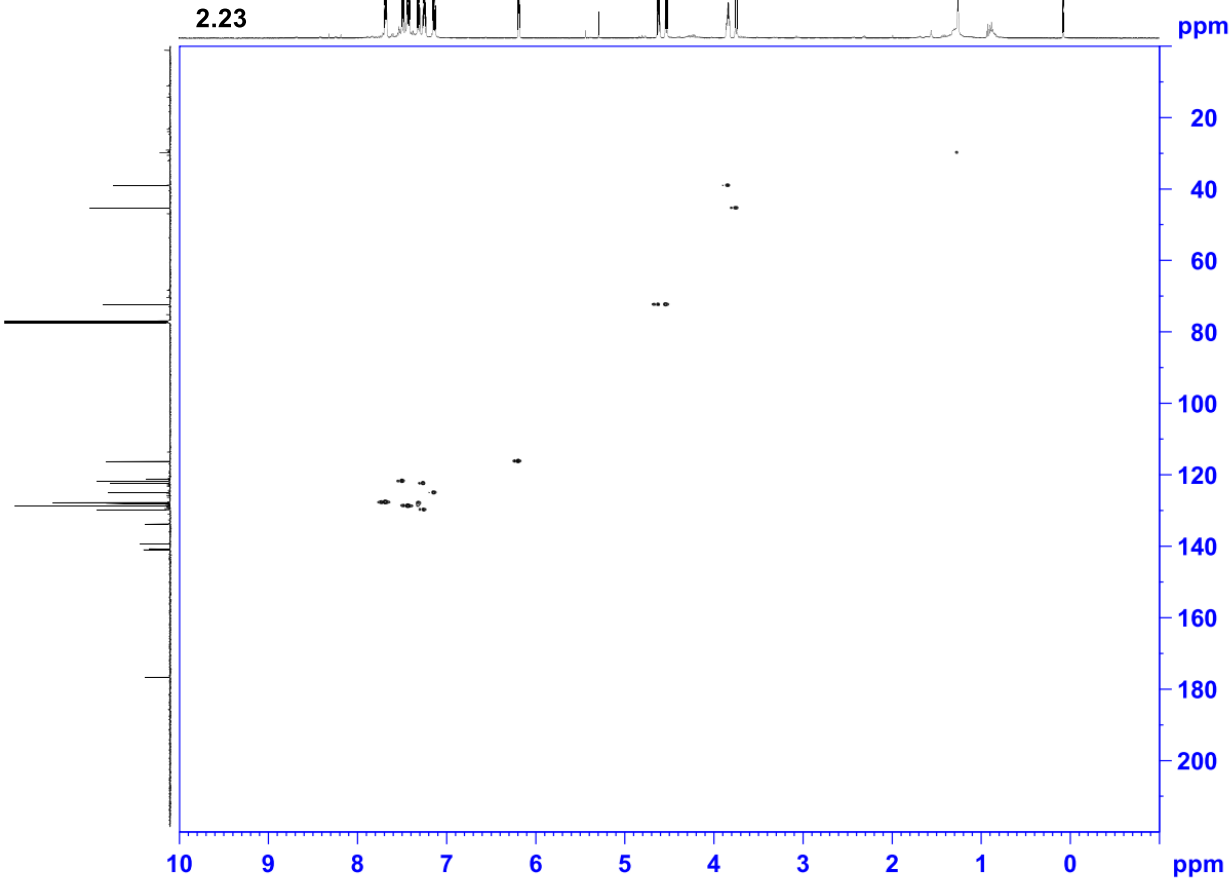



```
Current Data Parameters
NAME        JAW-02-179-b
EXPNO                   7
PROCNO                  1

F2 - Acquisition Parameters
Date_            20181214
Time                 17.52
INSTRUM              spect
PROBHD    5 mm PABBO BB/
PULPROG     hmbcgplpndqf
TD                   2048
SOLVENT             CDCl3
NS                      8
DS                      8
SWH              6510.417 Hz
FIDRES           3.178914 Hz
AQ             0.1572864 sec
RG                    203
DW                 76.800 usec
DE                  6.50 usec
TE                 297.3 K
CNST2        145.0000000
CNST13        10.0000000
D0            0.00000300 sec
D1            1.50000000 sec
D2            0.00344828 sec
D6            0.05000000 sec
D16           0.00020000 sec
IN0           0.00001790 sec

======== CHANNEL f1 ========
SFO1         500.1631510 MHz
NUC1                   1H
P1                  11.50 usec
P2                  23.00 usec
PLW1         18.00000000 W

======== CHANNEL f2 ========
SFO2         125.7778879 MHz
NUC2                  13C
P3                  10.50 usec
PLW2        110.00000000 W

====== GRADIENT CHANNEL =====
GPNAM[1]      SMSQ10.100
GPNAM[2]      SMSQ10.100
GPNAM[3]      SMSQ10.100
GPZ1                50.00 %
GPZ2                30.00 %
GPZ3                40.10 %
P16               1000.00 usec

F1 - Acquisition parameters
TD                     32
SFO1            125.7779 MHz
FIDRES       1745.810059 Hz
SW                222.082 ppm
FnMODE                  QF

F2 - Processing parameters
SI                   2048
SF           500.1600127 MHz
WDW                  SINE
SSB       0
LB        0 Hz
GB        0
PC                   1.40

F1 - Processing parameters
SI                   1024
MC2                     QF
SF           125.7653259 MHz
WDW                  SINE
SSB       0
LB        0 Hz
GB        0
```

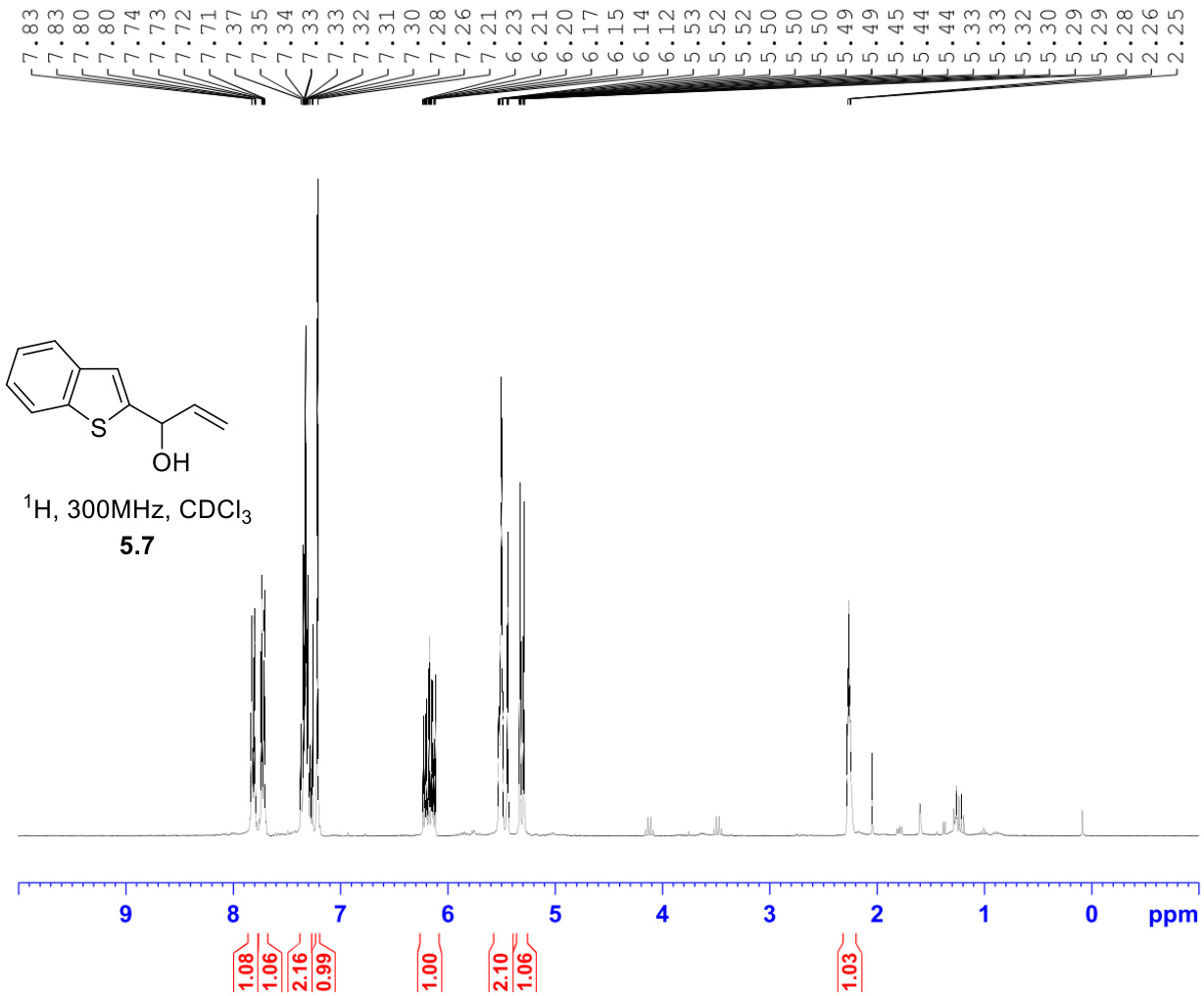


HSQC, 125MHz, $CDCl_3$

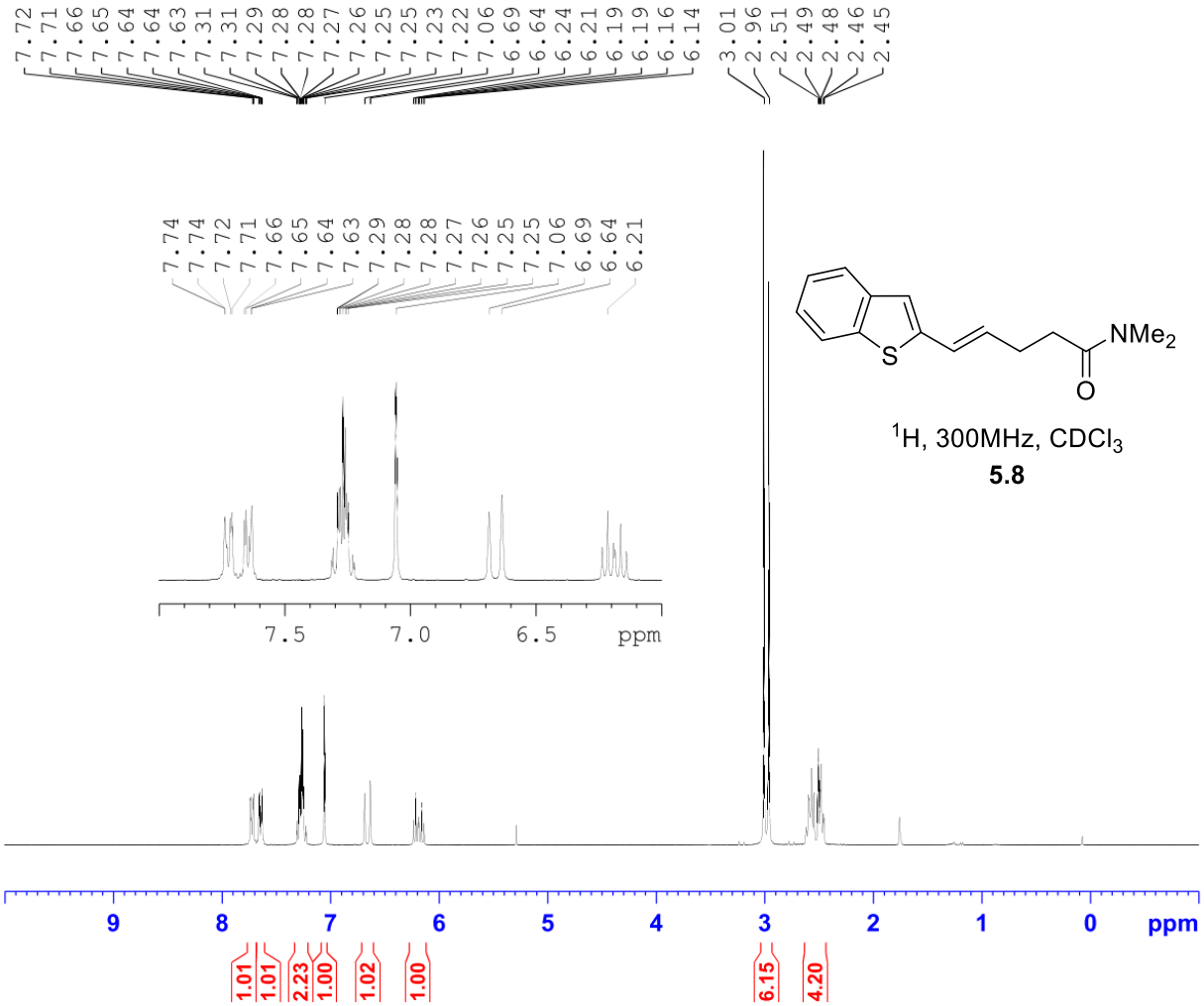
2.23




```
Current Data Parameters
NAME        JAW-02-179-b
EXPNO                   8
PROCNO                  1

F2 - Acquisition Parameters
Date_            20181214
Time                18.01
INSTRUM             spect
PROBHD   5 mm PABBO BB/
PULPROG  hsqcetgpsisp2.2
TD                    1024
SOLVENT             CDCl3
NS                      4
DS                     16
SWH             6009.615 Hz
FIDRES          5.868765 Hz
AQ              0.0851968 sec
RG                    203
DW                 83.200 usec
DE                  6.50 usec
TE                 297.4 K
CNST2        145.0000000
CNST17        -0.5000000
D0            0.00000300 sec
D1            2.00000000 sec
D4            0.00172414 sec
D11           0.03000000 sec
D16           0.00020000 sec
D24           0.00089000 sec
IN0           0.00002410 sec

======== CHANNEL f1 ========
SFO1         500.1623508 MHz
NUC1                    1H
P1                   11.50 usec
P2                   23.00 usec
P28                1000.00 usec
PLW1         18.00000000 W

======== CHANNEL f2 ========
SFO2         125.7741356 MHz
NUC2                    13C
CPDPRG[2 bi_p5m4sp_4sp.2
P3                   10.50 usec
P14                 500.00 usec
P24                2000.00 usec
P63                1500.00 usec
PLW0      0 W
PLW2       110.00000000 W
PLW12        2.47499990 W
SPNAM[3] Crp60,0.5,20.1
SPOAL3                0.500
SPOFFS3  0 Hz
SPW3         18.52899933 W
SPNAM[7]     Crp60comp.4
SPOAL7                0.500
SPOFFS7  0 Hz
SPW7         18.52899933 W
SPNAM[14 Crp32,1.5,20.2
SPOAL14               0.500
SPOFFS14 0 Hz
SPW14         7.90590000 W
SPNAM[31 Crp32,1.5,20.2
SPOAL31               0.500
SPOFFS31 0 Hz
SPW31         1.97650003 W

====== GRADIENT CHANNEL =====
GPNAM[1]      SMSQ10.100
GPNAM[2]      SMSQ10.100
GPNAM[3]      SMSQ10.100
GPNAM[4]      SMSQ10.100
GPZ1                 80.00 %
GPZ2                 20.10 %
GPZ3                 11.00 %
GPZ4                 -5.00 %
P16                1000.00 usec
P19                 600.00 usec

F1 - Acquisition parameters
TD                      64
SFO1             125.7741 MHz
FIDRES        648.340271 Hz
SW               164.954 ppm
FnMODE     Echo-Antiecho

F2 - Processing parameters
SI                    1024
SF           500.1600000 MHz
WDW                  QSINE
SSB                      2
LB        0 Hz
GB        0
PC                    1.40

F1 - Processing parameters
SI                    1024
MC2        echo-antiecho
SF           125.7653320 MHz
WDW                  QSINE
SSB                      2
LB        0 Hz
GB        0
```



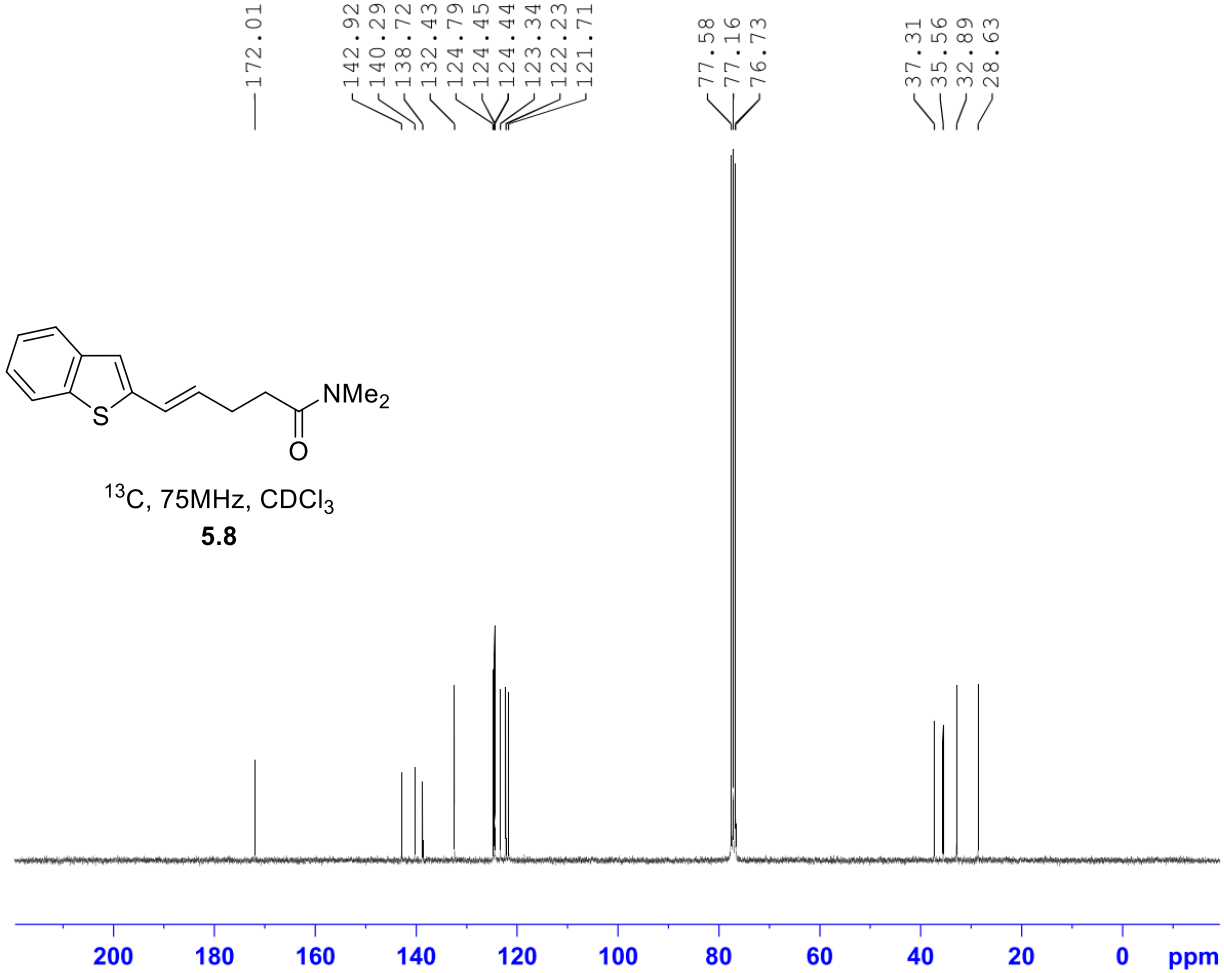

```
Current Data Parameters
NAME          JAW-02-142
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180922
Time               12.43
INSTRUM            spect
PROBHD   5 mm QNP  1H/1
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             6188.119 Hz
FIDRES          0.188846 Hz
AQ             2.6476543 sec
RG                   128
DW                80.800 usec
DE                  6.50 usec
TE                -923.3 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         300.2318540 MHz
NUC1                  1H
P1                12.71 usec
PLW1         18.19700050 W

F2 - Processing parameters
SI                 32768
SF           300.2300089 MHz
WDW                   EM
SSB       0
LB                 0.10 Hz
GB        0
PC                 1.00
```



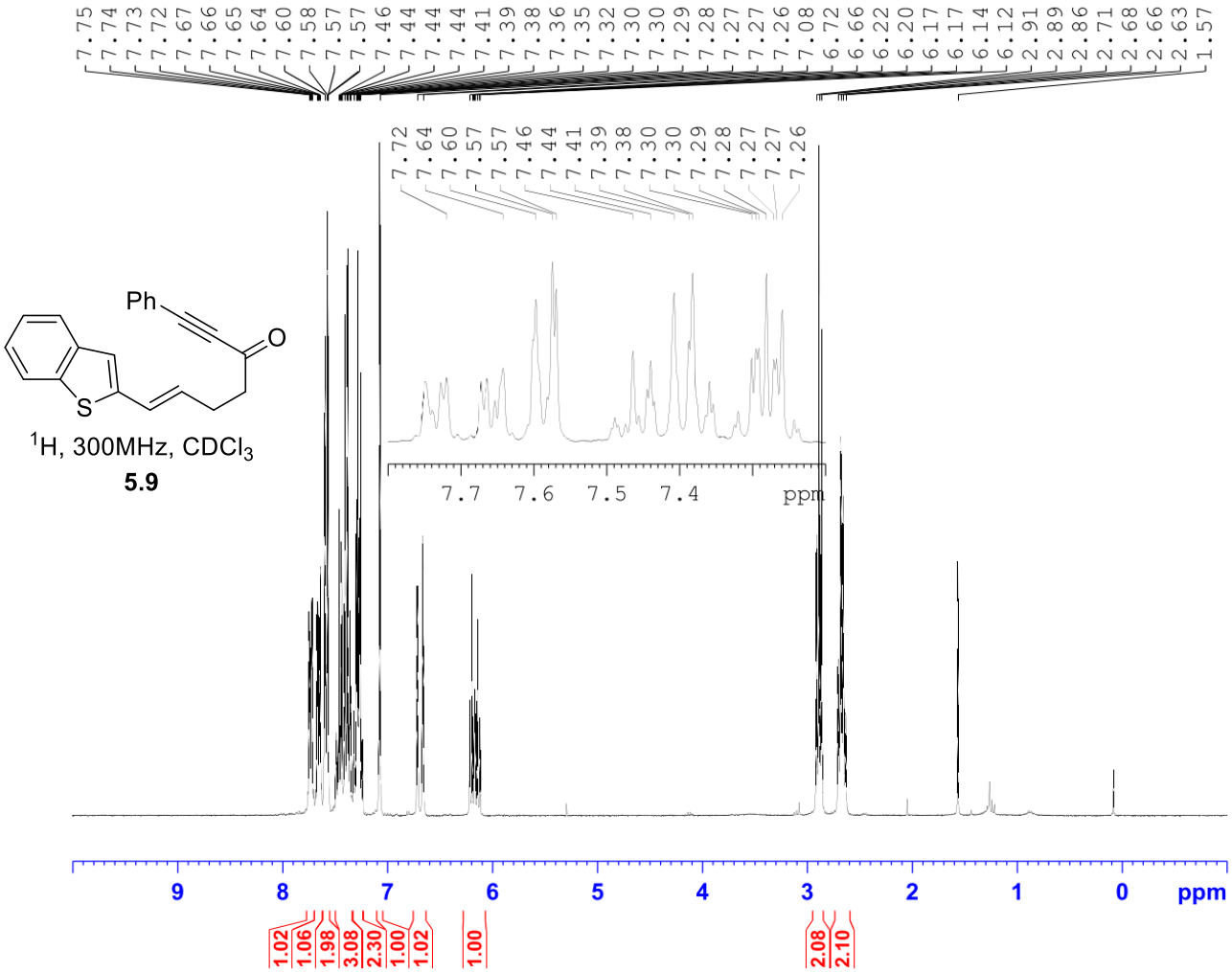
^{1}H, 300MHz, $CDCl_3$

5.8

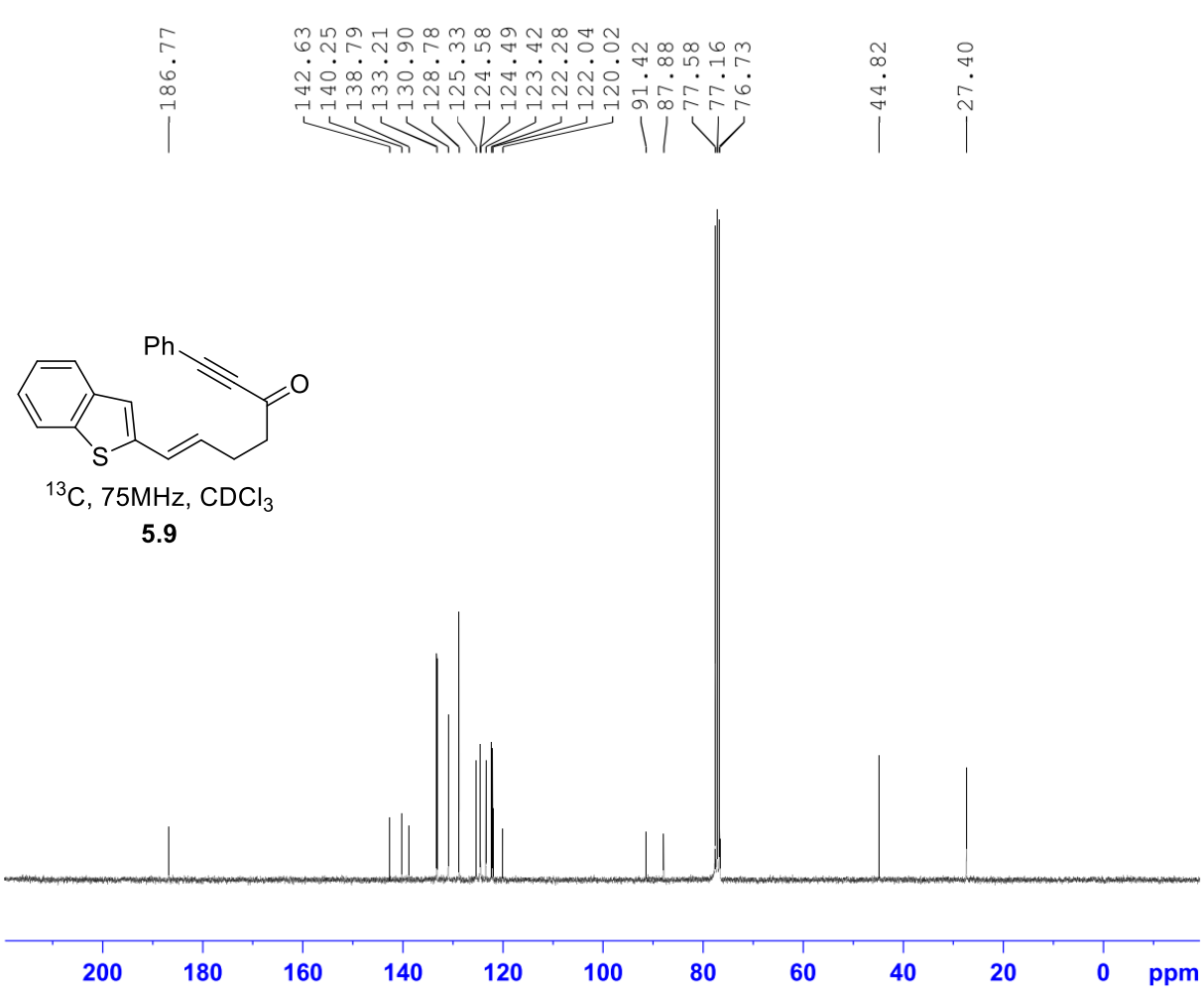
```
Current Data Parameters
NAME          JAW-02-148
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180923
Time               18.24
INSTRUM            spect
PROBHD   5 mm QNP  1H/1
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             6188.119 Hz
FIDRES          0.188846 Hz
AQ             2.6476543 sec
RG                   114
DW                80.800 usec
DE                  6.50 usec
TE                -923.0 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         300.2318540 MHz
NUC1                  1H
P1                12.71 usec
PLW1         18.19700050 W

F2 - Processing parameters
SI                 32768
SF           300.2300090 MHz
WDW                   EM
SSB       0
LB                 0.10 Hz
GB        0
PC                 1.00
```



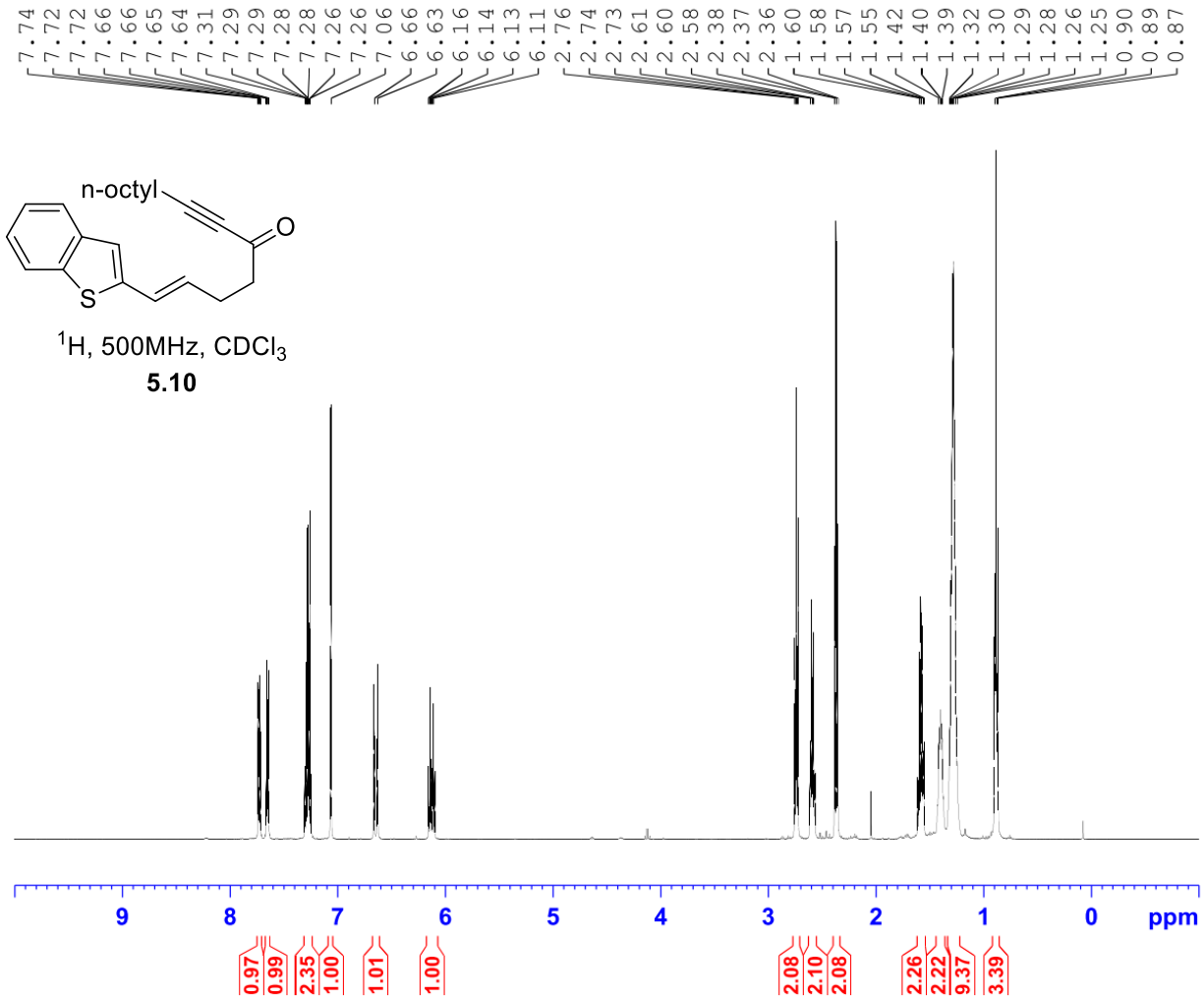

```
Current Data Parameters
NAME          JAW-02-148
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180923
Time               19.31
INSTRUM            spect
PROBHD   5 mm QNP  1H/1
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           18028.846 Hz
FIDRES         0.275098 Hz
AQ            1.8175317 sec
RG                  406
DW               27.733 usec
DE                6.50 usec
TE               -923.2 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1         75.5004428 MHz
NUC1                13C
P1                12.00 usec
PLW1        31.62299919 W

======== CHANNEL f2 ========
SFO2        300.2312009 MHz
NUC2                  1H
CPDPRG[2         waltz16
PCPD2             90.00 usec
PLW2        18.19700050 W
PLW12        0.36291999 W
PLW13        0.29396001 W

F2 - Processing parameters
SI                32768
SF         75.4928860 MHz
WDW                  EM
SSB       0
LB                1.00 Hz
GB        0
PC                 1.40
```



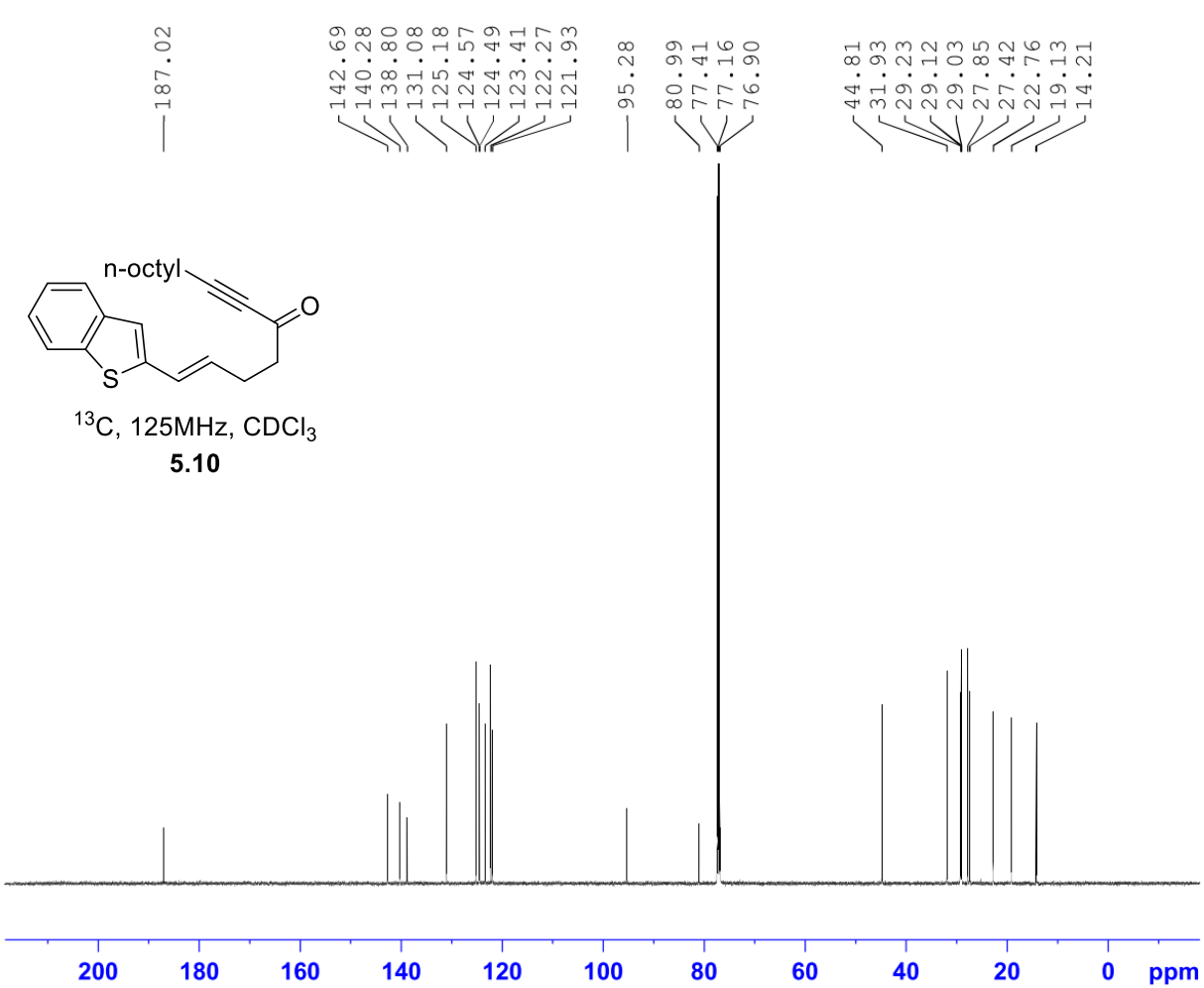

```
Current Data Parameters
NAME          JAW-02-150
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180924
Time               11.23
INSTRUM            spect
PROBHD   5 mm QNP  1H/1
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             6188.119 Hz
FIDRES          0.188846 Hz
AQ             2.6476543 sec
RG                   128
DW                80.800 usec
DE                  6.50 usec
TE                -923.1 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         300.2318540 MHz
NUC1                  1H
P1                 12.71 usec
PLW1         18.19700050 W

F2 - Processing parameters
SI                 32768
SF           300.2300091 MHz
WDW                   EM
SSB       0
LB                  0.10 Hz
GB        0
PC                  1.00
```




```
Current Data Parameters
NAME          JAW-02-150
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180924
Time               23.12
INSTRUM            spect
PROBHD   5 mm QNP  1H/1
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           18028.846 Hz
FIDRES         0.275098 Hz
AQ            1.8175317 sec
RG                  256
DW               27.733 usec
DE                6.50 usec
TE               -923.0 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1         75.5004428 MHz
NUC1                13C
P1               12.00 usec
PLW1        31.62299919 W

======== CHANNEL f2 ========
SFO2        300.2312009 MHz
NUC2                  1H
CPDPRG[2         waltz16
PCPD2            90.00 usec
PLW2        18.19700050 W
PLW12        0.36291999 W
PLW13        0.29396001 W

F2 - Processing parameters
SI                32768
SF           75.4928853 MHz
WDW                  EM
SSB       0
LB                1.00 Hz
GB        0
PC                 1.40
```



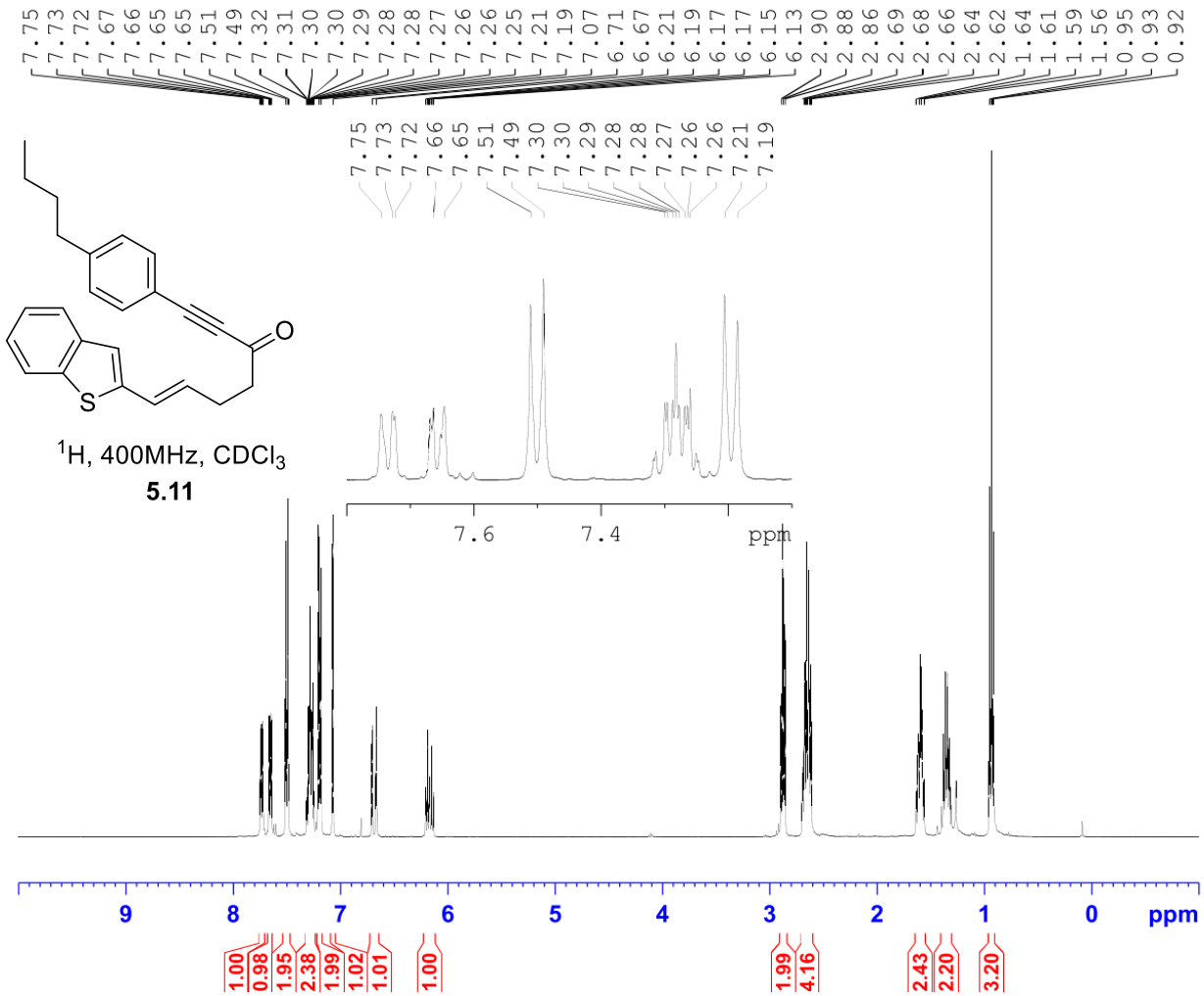

```
Current Data Parameters
NAME          JAW-02-166
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20181101
Time                3.10
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                    64
DW                50.000 usec
DE                 6.50 usec
TE                298.2 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                  1H
P1                11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1600120 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



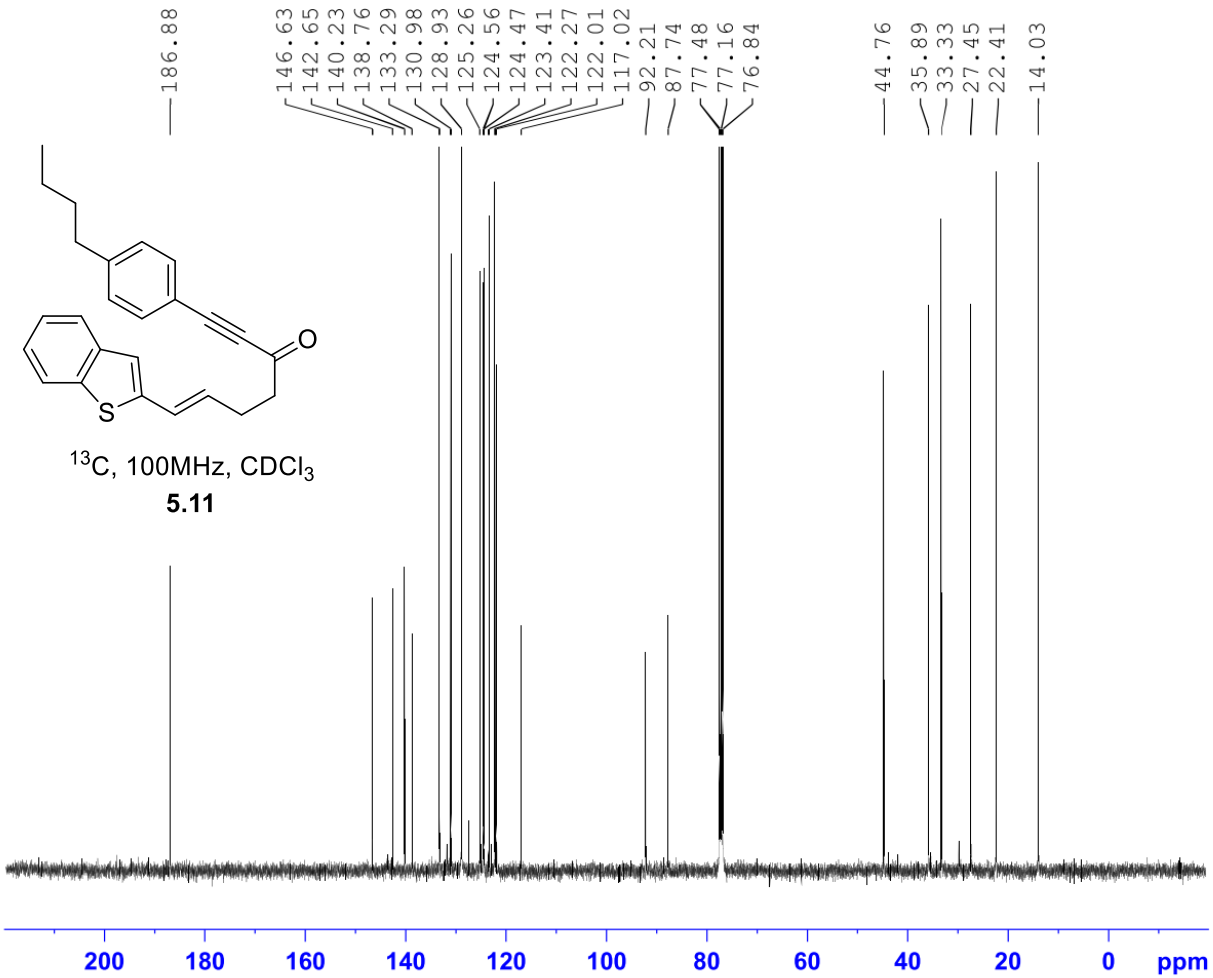
^{13}C, 125MHz, $CDCl_3$

5.10

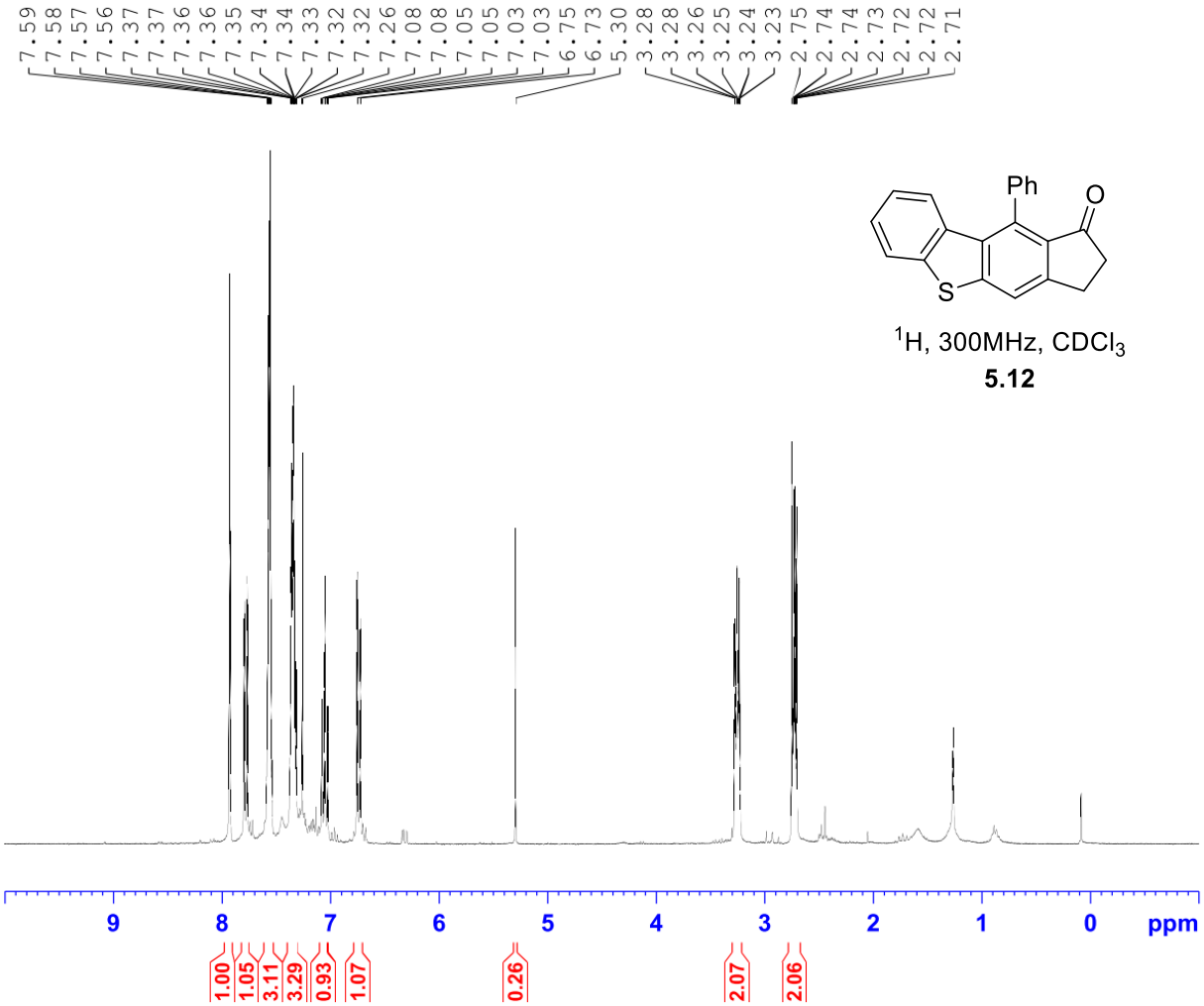
```
Current Data Parameters
NAME          JAW-02-166
EXPNO                 12
PROCNO                 1

F2 - Acquisition Parameters
Date_           20181101
Time                4.20
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    2
SWH            29761.904 Hz
FIDRES          0.454131 Hz
AQ             1.1010048 sec
RG                  203
DW                16.800 usec
DE                 6.50 usec
TE                299.1 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         125.7779086 MHz
NUC1                 13C
P1                 10.50 usec
PLW1        110.00000000 W

======== CHANNEL f2 ========
SFO2         500.1620006 MHz
NUC2                  1H
CPDPRG[2         waltz16
PCPD2             80.00 usec
PLW2         18.00000000 W
PLW12         0.37195000 W
PLW13         0.23805000 W

F2 - Processing parameters
SI                 32768
SF          125.7653145 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```



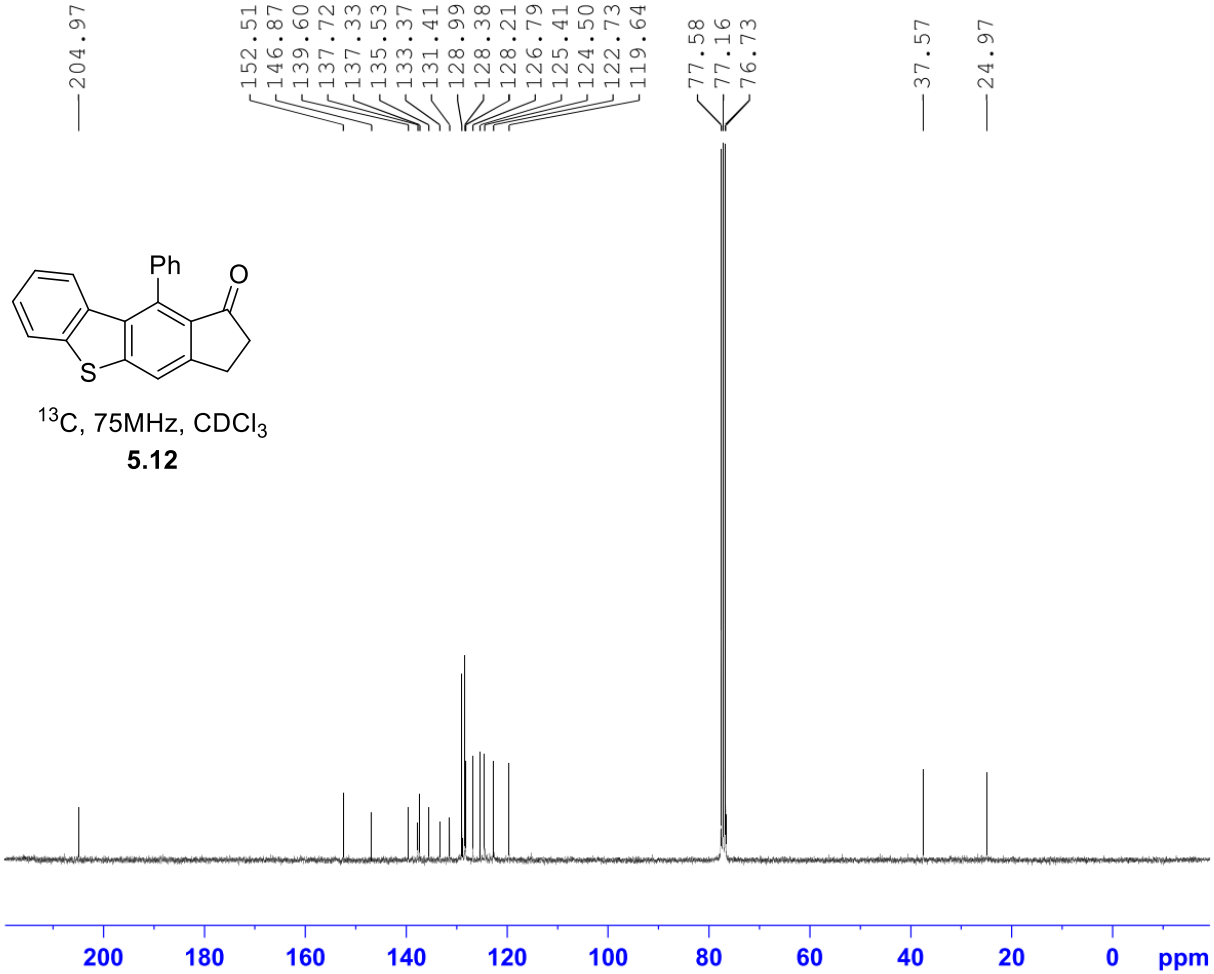

```
Current Data Parameters
NAME          JAW-03-028
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20190724
Time               12.58 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                    57
DW                62.400 usec
DE                 6.50 usec
TE                 88.6 K
D1           1.00000000 sec
TD0                    1
SFO1        400.1324708 MHz
NUC1                  1H
P0                 4.83 usec
P1                14.50 usec
PLW1        12.00000000 W

F2 - Processing parameters
SI                 65536
SF          400.1300097 MHz
WDW                   EM
SSB      0
LB                 0.30 Hz
GB       0
PC                 1.00
```




```
Current Data Parameters
NAME          JAW-03-028
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20190724
Time              22.11 h
INSTRUM           spect
PROBHD   Z108618_0240 (
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH            24038.461 Hz
FIDRES          0.733596 Hz
AQ             1.3631488 sec
RG                  203
DW                20.800 usec
DE                 6.50 usec
TE                 88.9 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1
SFO1         100.6228298 MHz
NUC1                 13C
P0                 3.33 usec
P1                10.00 usec
PLW1         56.13299942 W
SFO2         400.1316005 MHz
NUC2                  1H
CPDPRG[2         waltz65
PCPD2             90.00 usec
PLW2         12.00000000 W
PLW12         0.31147999 W
PLW13         0.15667000 W

F2 - Processing parameters
SI                32768
SF           100.6127587 MHz
WDW                  EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```



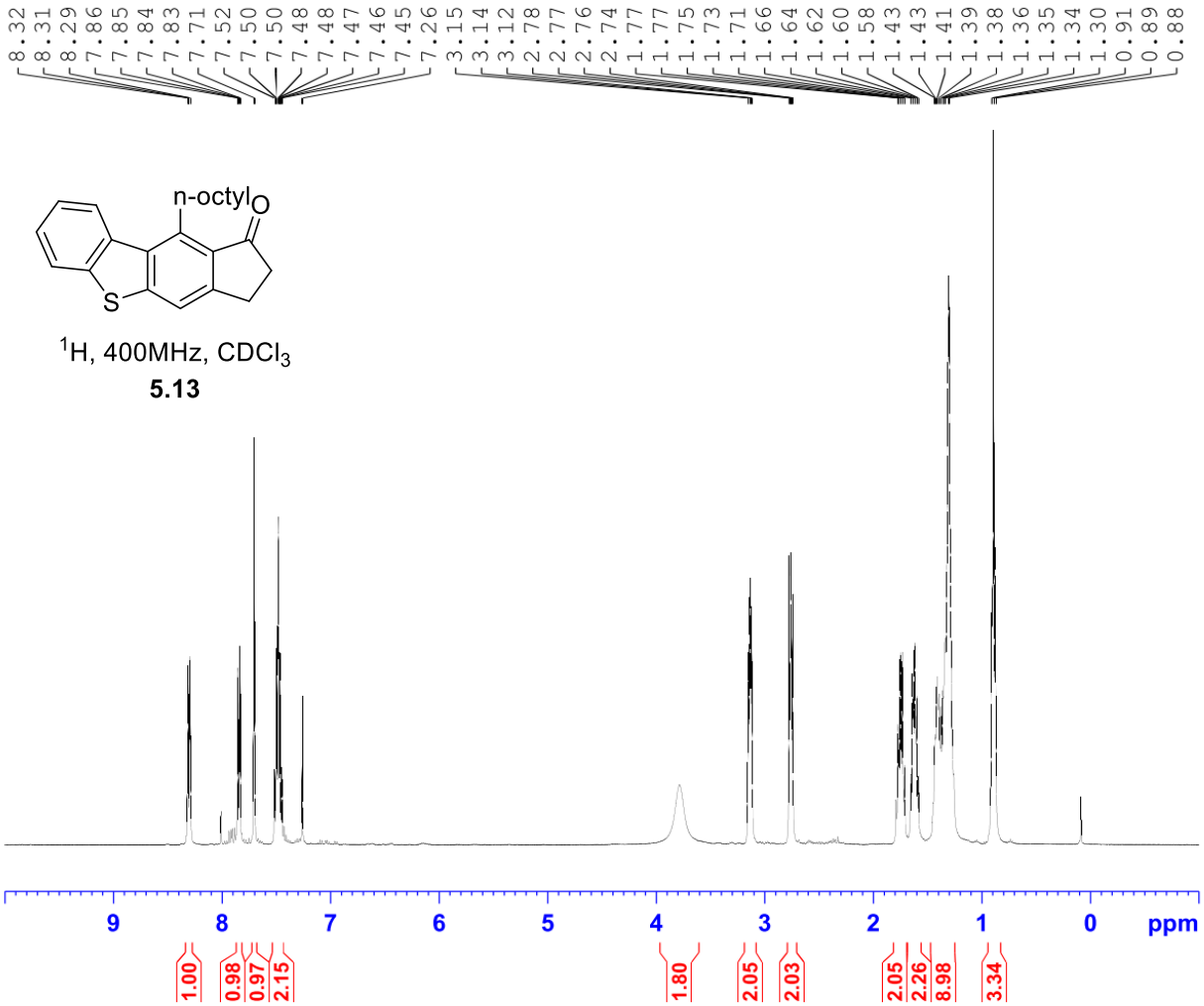

```
Current Data Parameters
NAME          JAW-02-152
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180924
Time               19.53
INSTRUM            spect
PROBHD   5 mm QNP  1H/1
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             6188.119 Hz
FIDRES          0.188846 Hz
AQ             2.6476543 sec
RG                   128
DW                80.800 usec
DE                  6.50 usec
TE                -923.0 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         300.2318540 MHz
NUC1                  1H
P1                 12.71 usec
PLW1         18.19700050 W

F2 - Processing parameters
SI                 32768
SF           300.2300086 MHz
WDW                   EM
SSB       0
LB                  0.10 Hz
GB        0
PC                  1.00
```



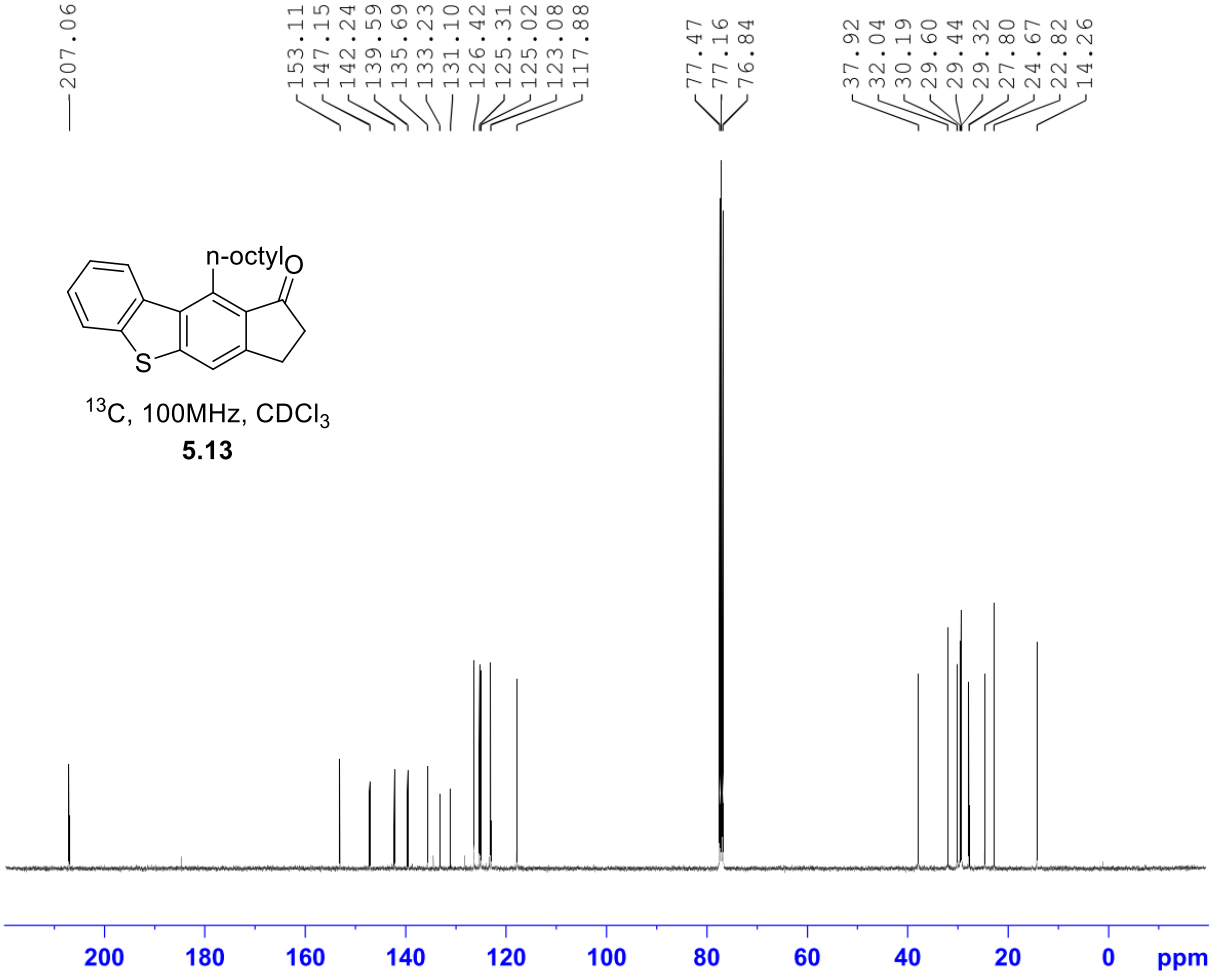
^{13}C, 75MHz, $CDCl_3$

5.12

```
Current Data Parameters
NAME          JAW-02-152
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180925
Time                5.39
INSTRUM            spect
PROBHD   5 mm QNP  1H/1
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           18028.846 Hz
FIDRES         0.275098 Hz
AQ            1.8175317 sec
RG                  256
DW               27.733 usec
DE                6.50 usec
TE               -921.5 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         75.5004428 MHz
NUC1                13C
P1               12.00 usec
PLW1        31.62299919 W

======== CHANNEL f2 ========
SFO2        300.2312009 MHz
NUC2                  1H
CPDPRG[2         waltz16
PCPD2             90.00 usec
PLW2        18.19700050 W
PLW12        0.36291999 W
PLW13        0.29396001 W

F2 - Processing parameters
SI                32768
SF         75.4928853 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```



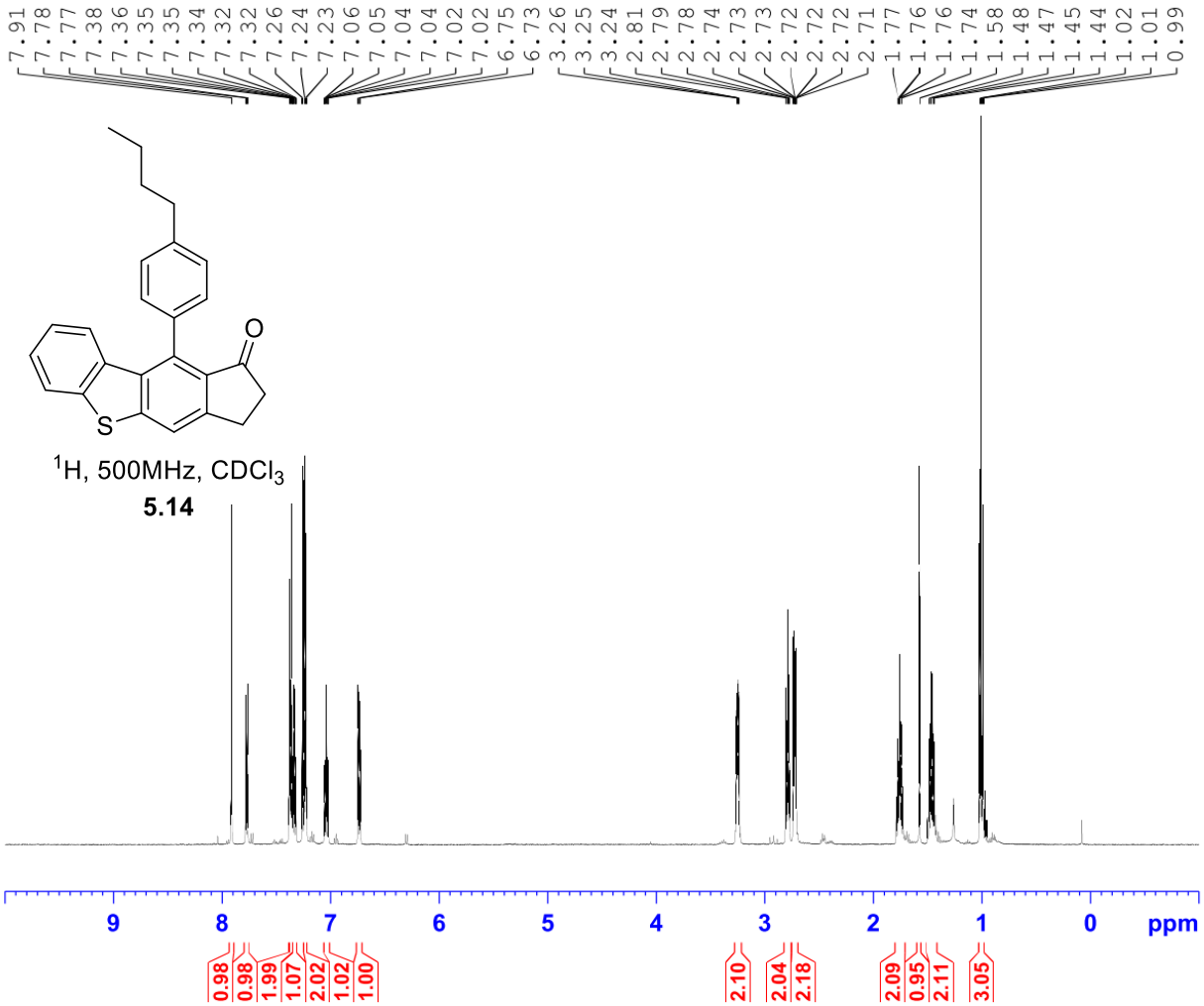

```
Current Data Parameters
NAME          JAW-02-174
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20181208
Time                6.52 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                    32
DW                62.400 usec
DE                 6.50 usec
TE                 88.3 K
D1           1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                 4.83 usec
P1                14.50 usec
PLW1         12.00000000 W

F2 - Processing parameters
SI                 65536
SF          400.1300099 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



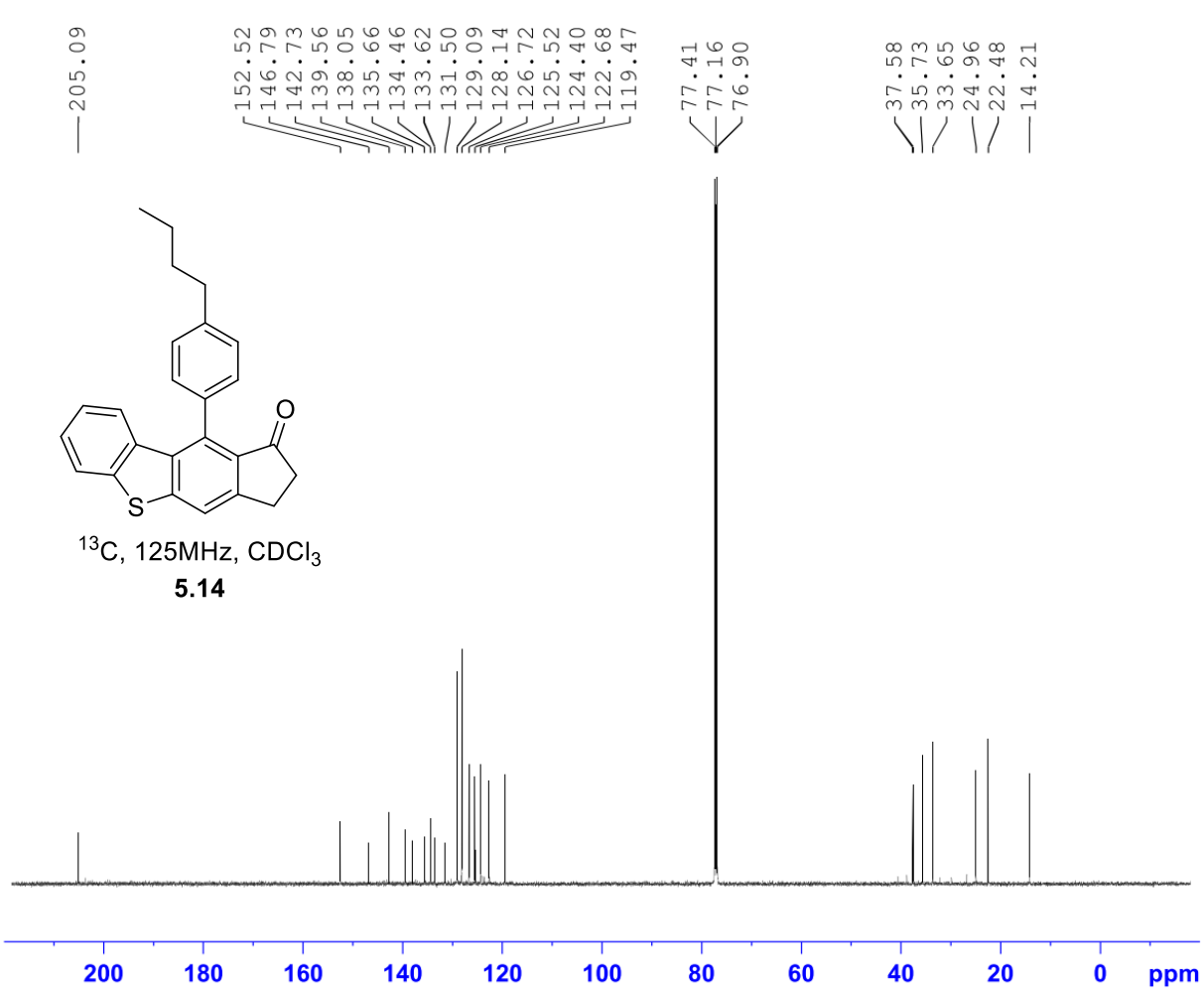
^{13}C, 100MHz, $CDCl_3$

5.13

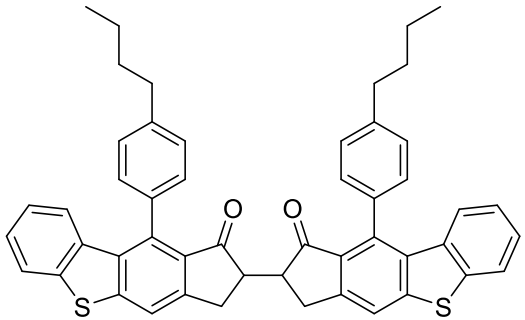
```
Current Data Parameters
NAME          JAW-02-174
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20181208
Time                7.52 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH            24038.461 Hz
FIDRES          0.733596 Hz
AQ             1.3631488 sec
RG                  203
DW                 20.800 usec
DE                  6.50 usec
TE                  88.3 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1
SFO1         100.6228298 MHz
NUC1                 13C
P0                  3.33 usec
P1                 10.00 usec
PLW1         56.13299942 W
SFO2         400.1316005 MHz
NUC2                  1H
CPDPRG[2         waltz65
PCPD2              90.00 usec
PLW2         12.00000000 W
PLW12         0.31147999 W
PLW13         0.15667000 W

F2 - Processing parameters
SI                 32768
SF           100.6127579 MHz
WDW                   EM
SSB       0
LB                  1.00 Hz
GB        0
PC                  1.40
```




```
Current Data Parameters
NAME          JAW-03-030
EXPNO                 20
PROCNO                 1

F2 - Acquisition Parameters
Date_           20190805
Time               15.48
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                   101
DW                50.000 usec
DE                  6.50 usec
TE                 295.8 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                  1H
P1                 11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1600122 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

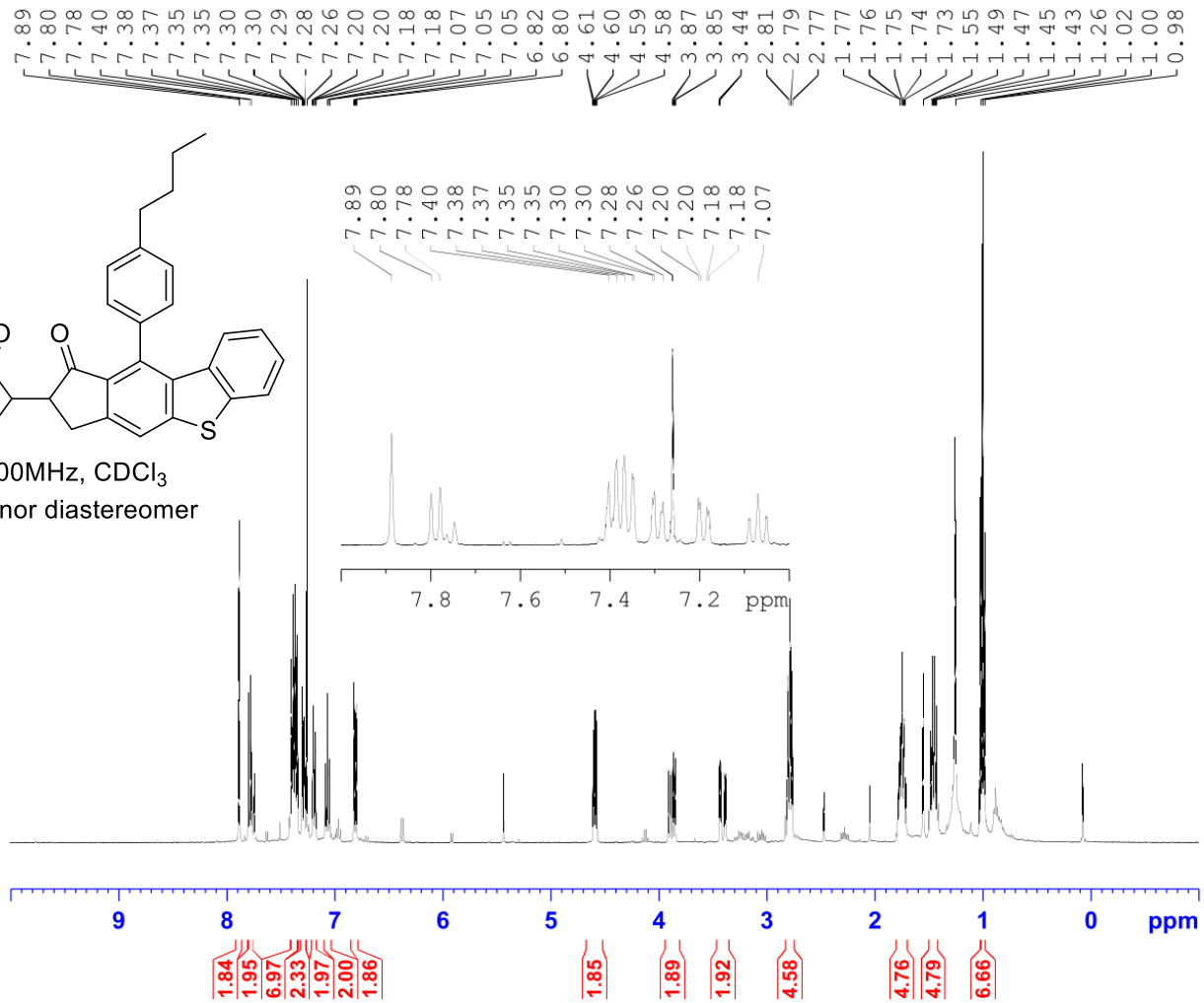



```
Current Data Parameters
NAME          JAW-03-030
EXPNO                 21
PROCNO                 1

F2 - Acquisition Parameters
Date_           20190806
Time                7.54
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1026
DS                    2
SWH           29761.904 Hz
FIDRES         0.454131 Hz
AQ            1.1010048 sec
RG                  203
DW               16.800 usec
DE                6.50 usec
TE                297.4 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1        125.7779086 MHz
NUC1                 13C
P1                10.50 usec
PLW1       110.00000000 W

======== CHANNEL f2 ========
SFO2        500.1620006 MHz
NUC2                  1H
CPDPRG[2         waltz16
PCPD2             80.00 usec
PLW2        18.00000000 W
PLW12        0.37195000 W
PLW13        0.23805000 W

F2 - Processing parameters
SI                32768
SF          125.7653168 MHz
WDW                  EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```



^{1}H, 400MHz, $CDCl_3$

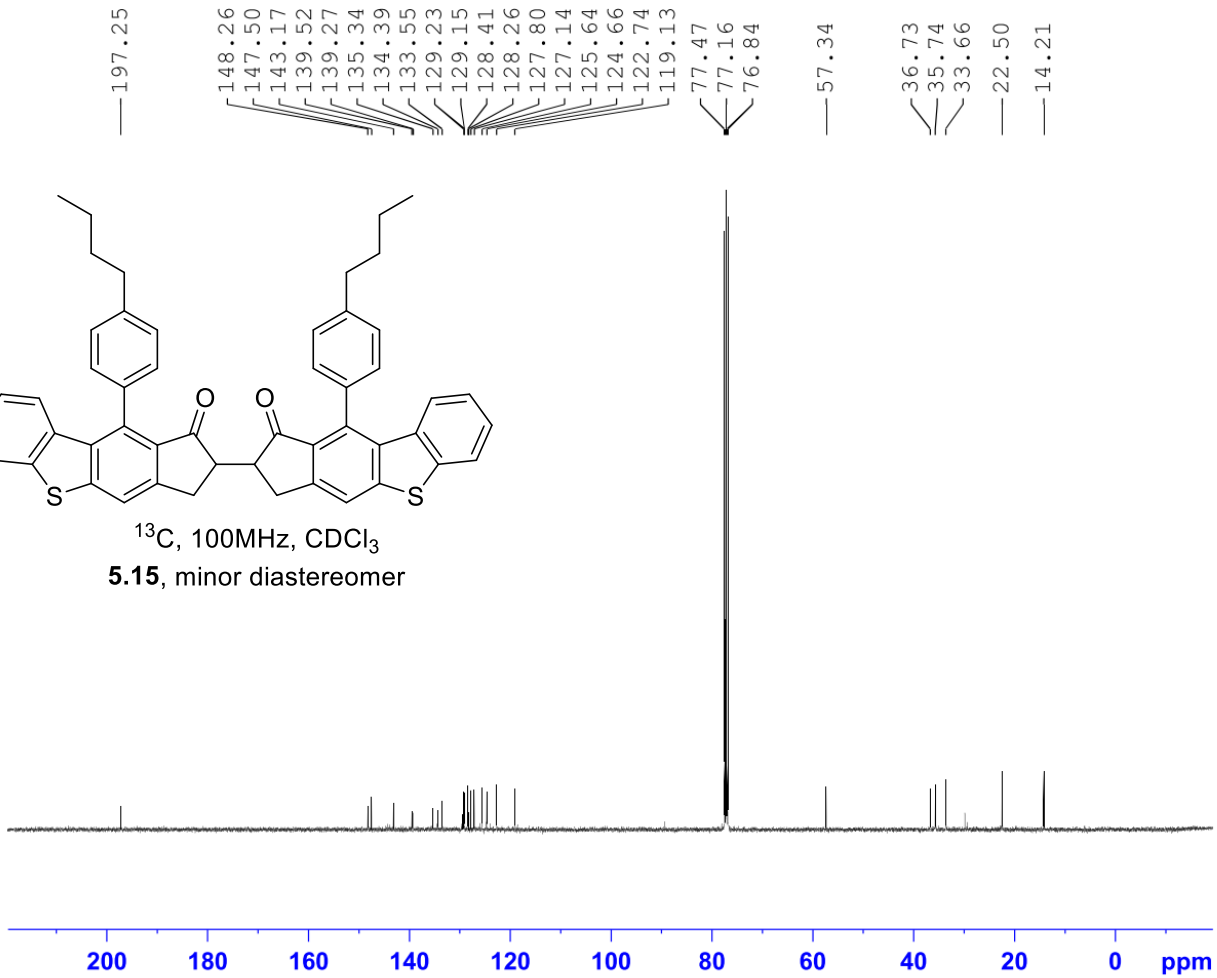
5.15, minor diastereomer



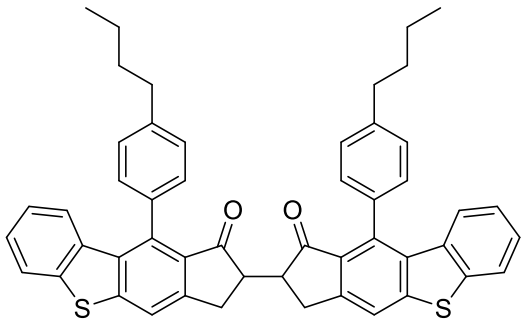

```
Current Data Parameters
NAME        JAW-03-061-A
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191030
Time               14.59 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                   101
DW                62.400 usec
DE                 6.50 usec
TE                 92.0 K
D1           1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                 4.83 usec
P1                14.50 usec
PLW1         12.00000000 W

F2 - Processing parameters
SI                 65536
SF          400.1300098 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

^{13}C, 100MHz, $CDCl_3$

5.15, minor diastereomer

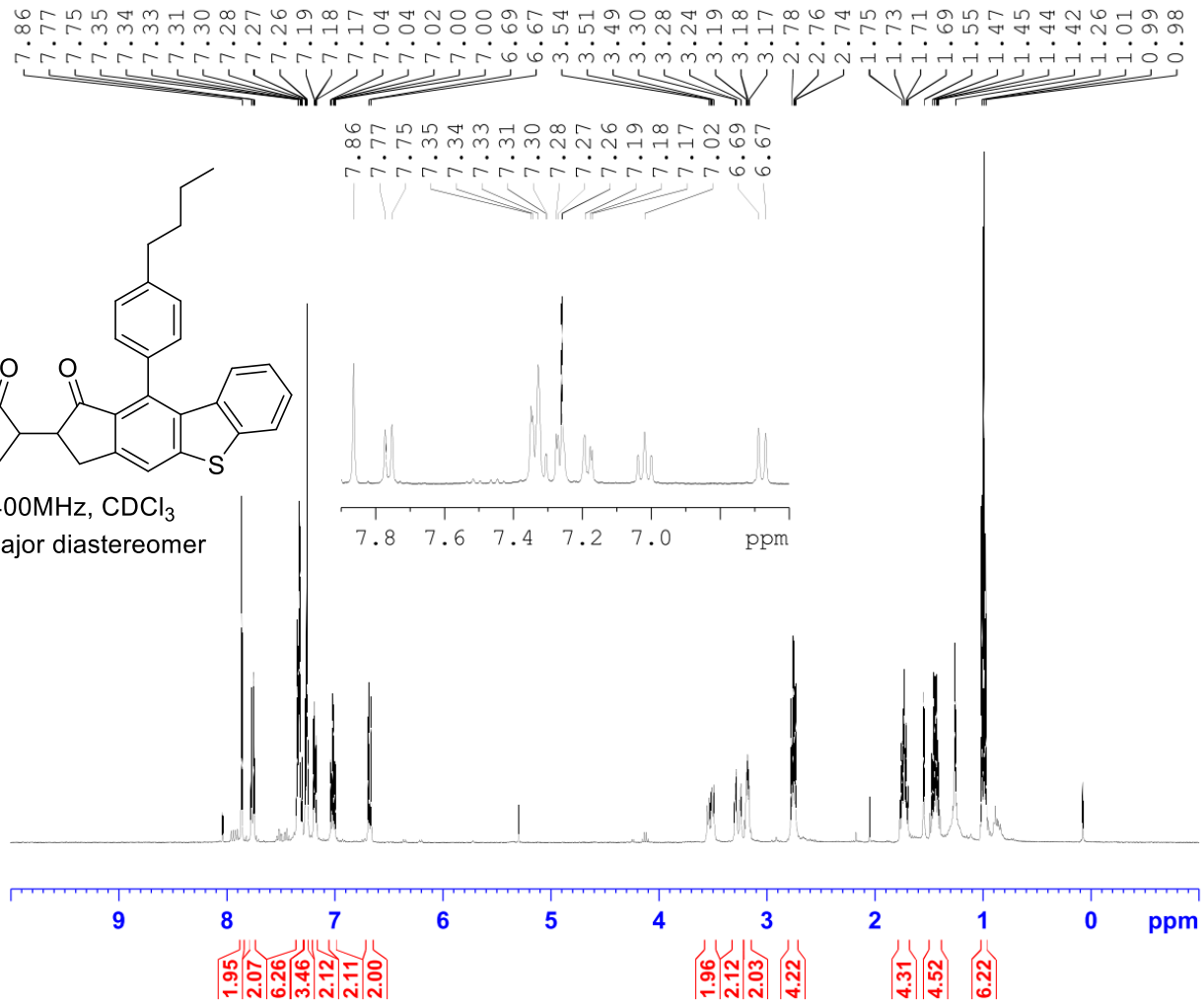



```
Current Data Parameters
NAME        JAW-03-061-A
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191031
Time                1.42 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH            24038.461 Hz
FIDRES          0.733596 Hz
AQ             1.3631488 sec
RG                  203
DW                 20.800 usec
DE                  6.50 usec
TE                  93.9 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1         100.6228298 MHz
NUC1                 13C
P0                  3.33 usec
P1                 10.00 usec
PLW1         56.13299942 W
SFO2         400.1316005 MHz
NUC2                  1H
CPDPRG[2         waltz65
PCPD2              90.00 usec
PLW2         12.00000000 W
PLW12         0.31147999 W
PLW13         0.15667000 W

F2 - Processing parameters
SI                 32768
SF           100.6127564 MHz
WDW                   EM
SSB       0
LB                  1.00 Hz
GB        0
PC                  1.40
```

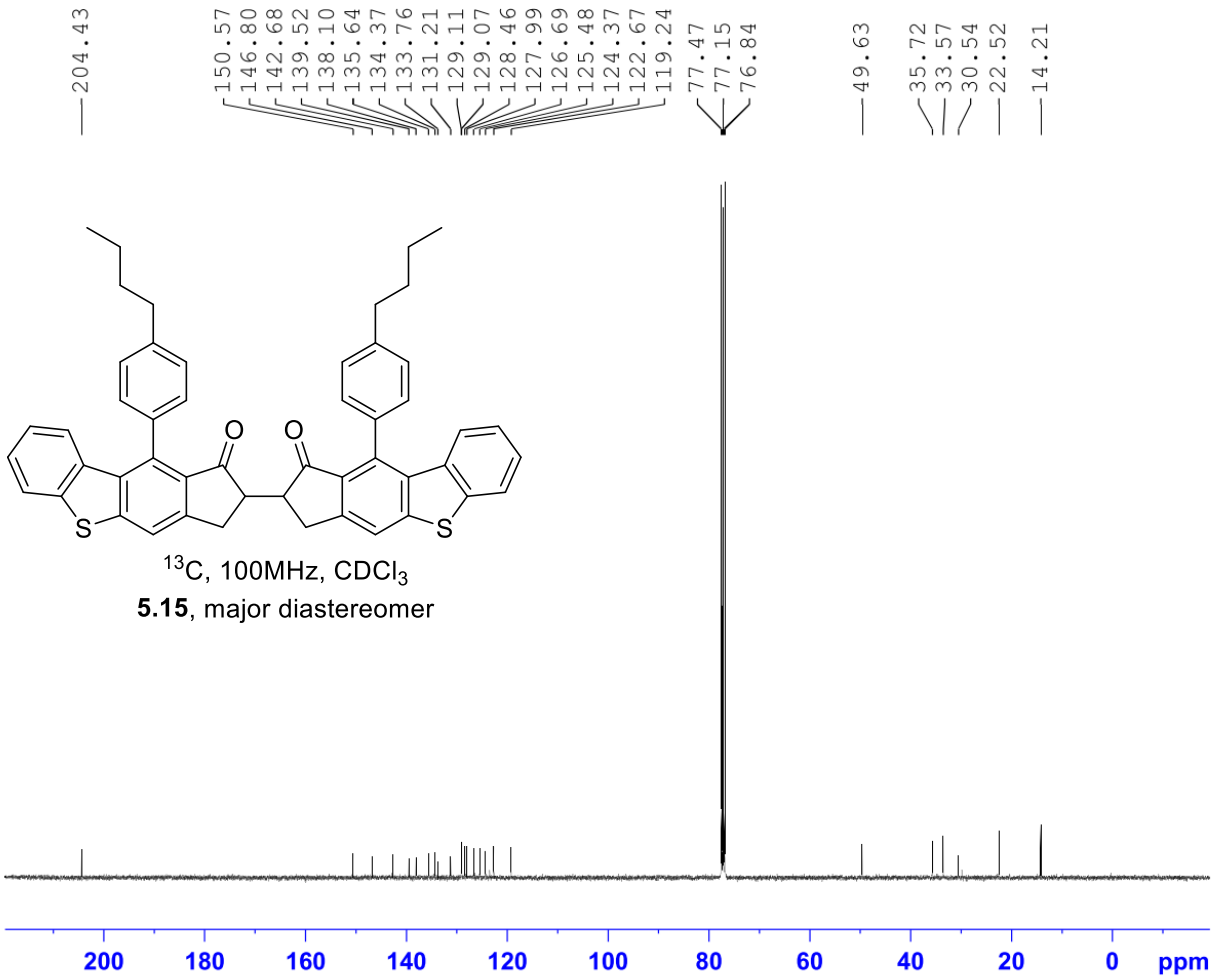


^{1}H, 400MHz, $CDCl_3$

5.15, major diastereomer



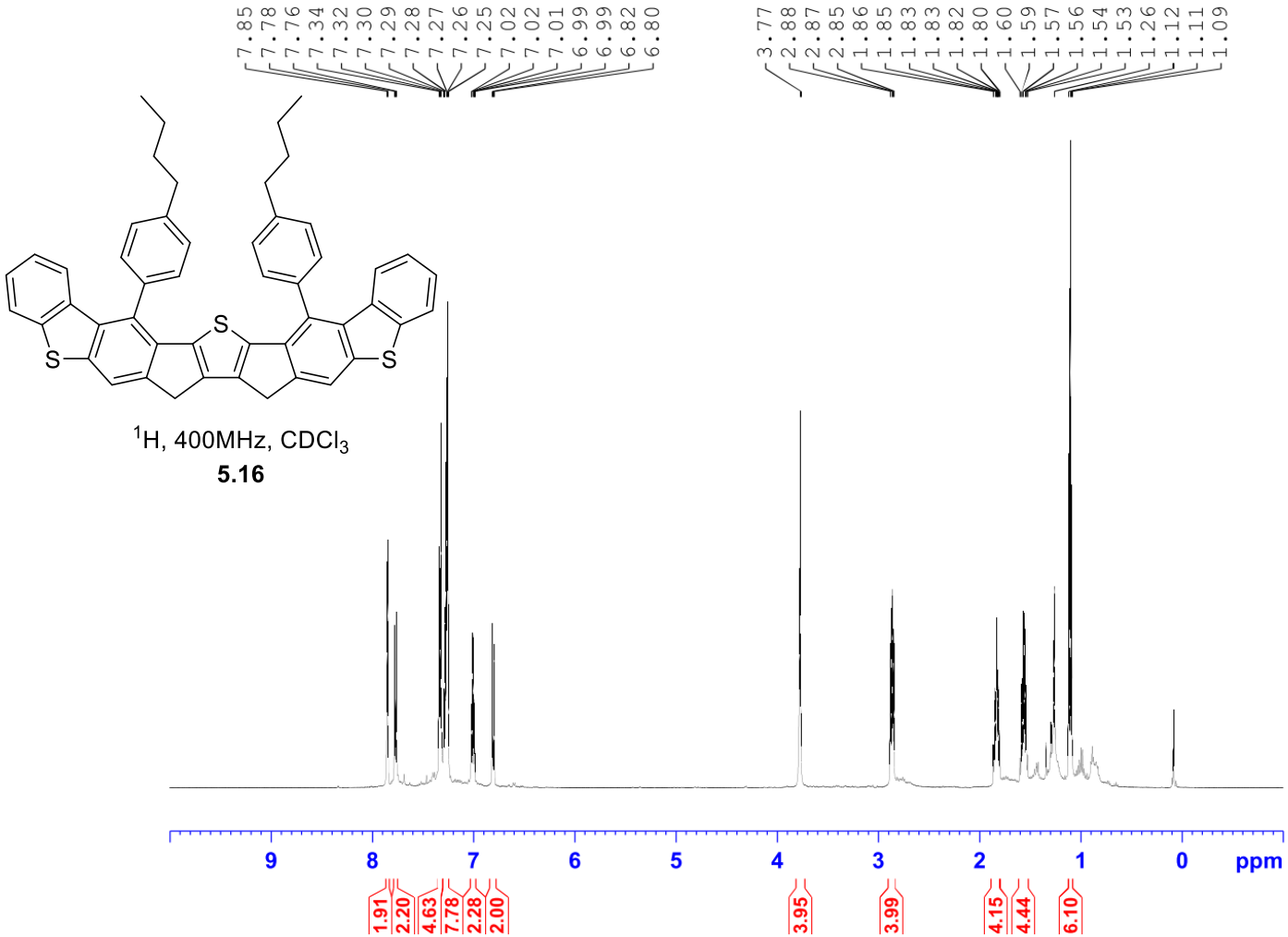

```
Current Data Parameters
NAME        JAW-03-061-B
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_           20191030
Time               14.06 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                   114
DW                62.400 usec
DE                 6.50 usec
TE                 93.2 K
D1           1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                 4.83 usec
P1                14.50 usec
PLW1         12.00000000 W

F2 - Processing parameters
SI                 65536
SF          400.1300098 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



^{13}C, 100MHz, $CDCl_3$

5.15, major diastereomer

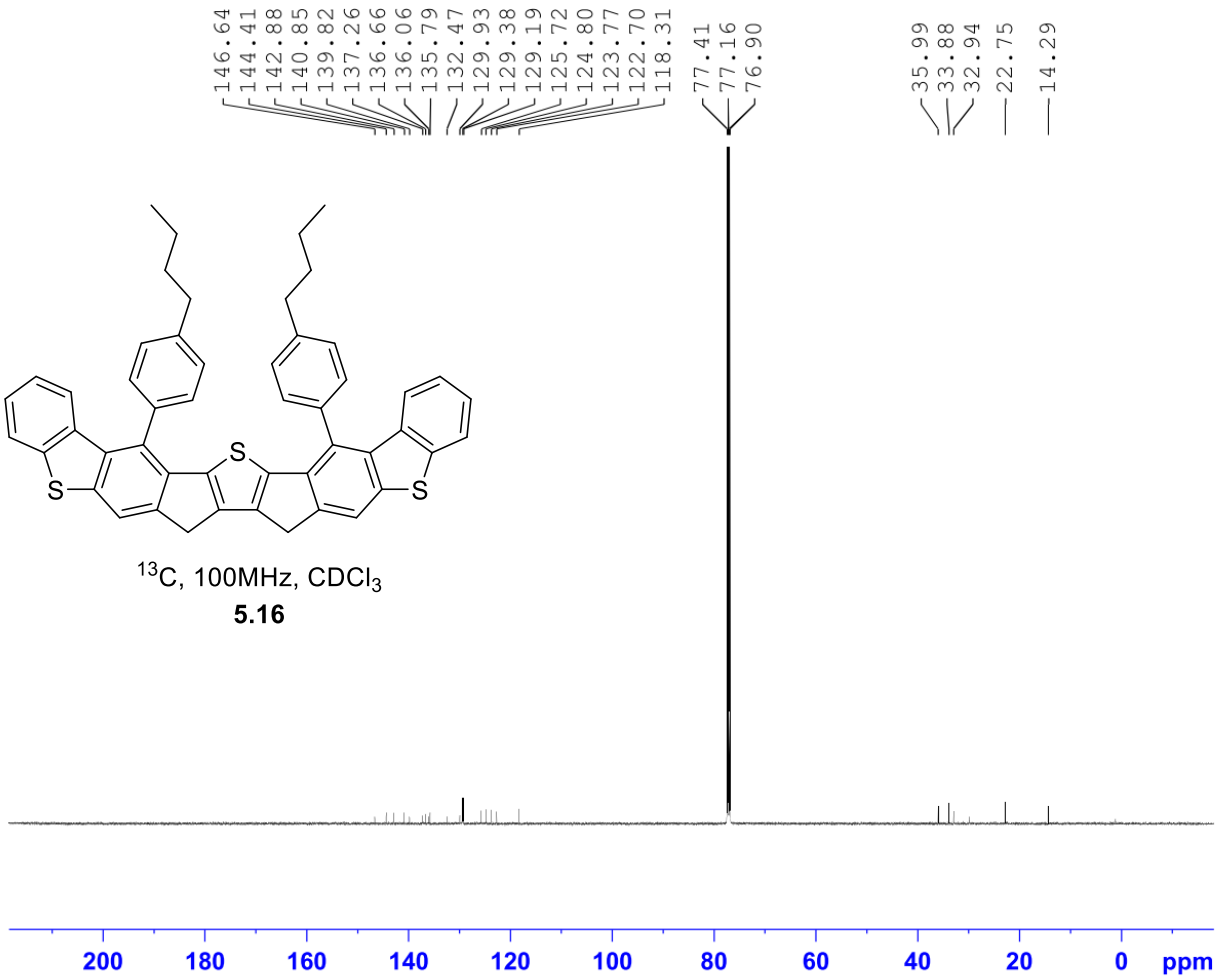
```
Current Data Parameters
NAME        JAW-03-061-B
EXPNO                   3
PROCNO                  1

F2 - Acquisition Parameters
Date_           20191030
Time              23.30 h
INSTRUM           spect
PROBHD   Z108618_0240 (
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH            24038.461 Hz
FIDRES          0.733596 Hz
AQ             1.3631488 sec
RG                  203
DW                20.800 usec
DE                 6.50 usec
TE                 93.0 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1         100.6228298 MHz
NUC1                13C
P0                 3.33 usec
P1                10.00 usec
PLW1         56.13299942 W
SFO2         400.1316005 MHz
NUC2                 1H
CPDPRG[2         waltz65
PCPD2             90.00 usec
PLW2         12.00000000 W
PLW12         0.31147999 W
PLW13         0.15667000 W

F2 - Processing parameters
SI                32768
SF           100.6127564 MHz
WDW                  EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```



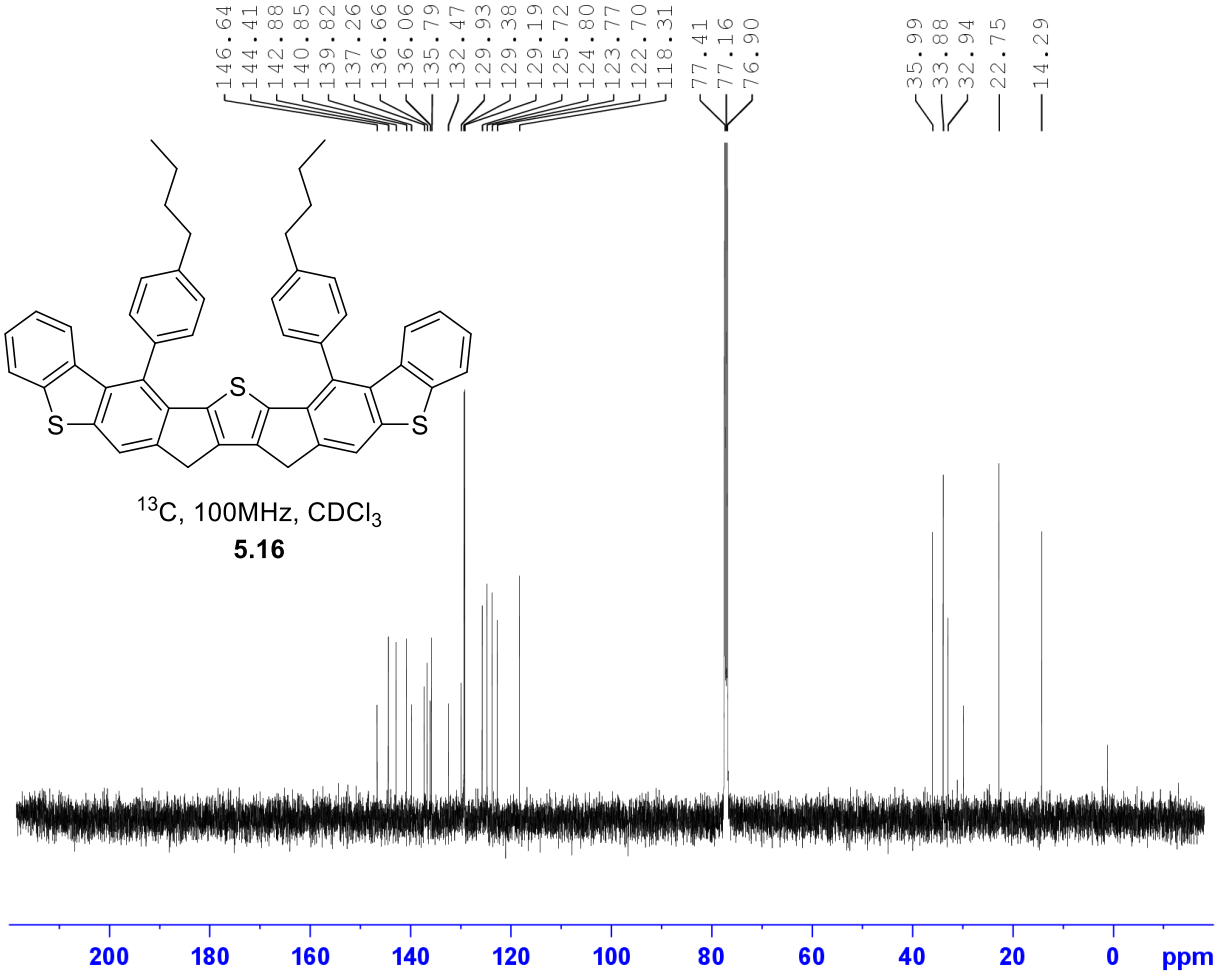

```
Current Data Parameters
NAME          JAW-03-074
EXPNO                  5
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191205
Time               14.23
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                  90.5
DW                50.000 usec
DE                 6.50 usec
TE                297.2 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                  1H
P1                11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1600122 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

^{13}C, 100MHz, $CDCl_3$

5.16



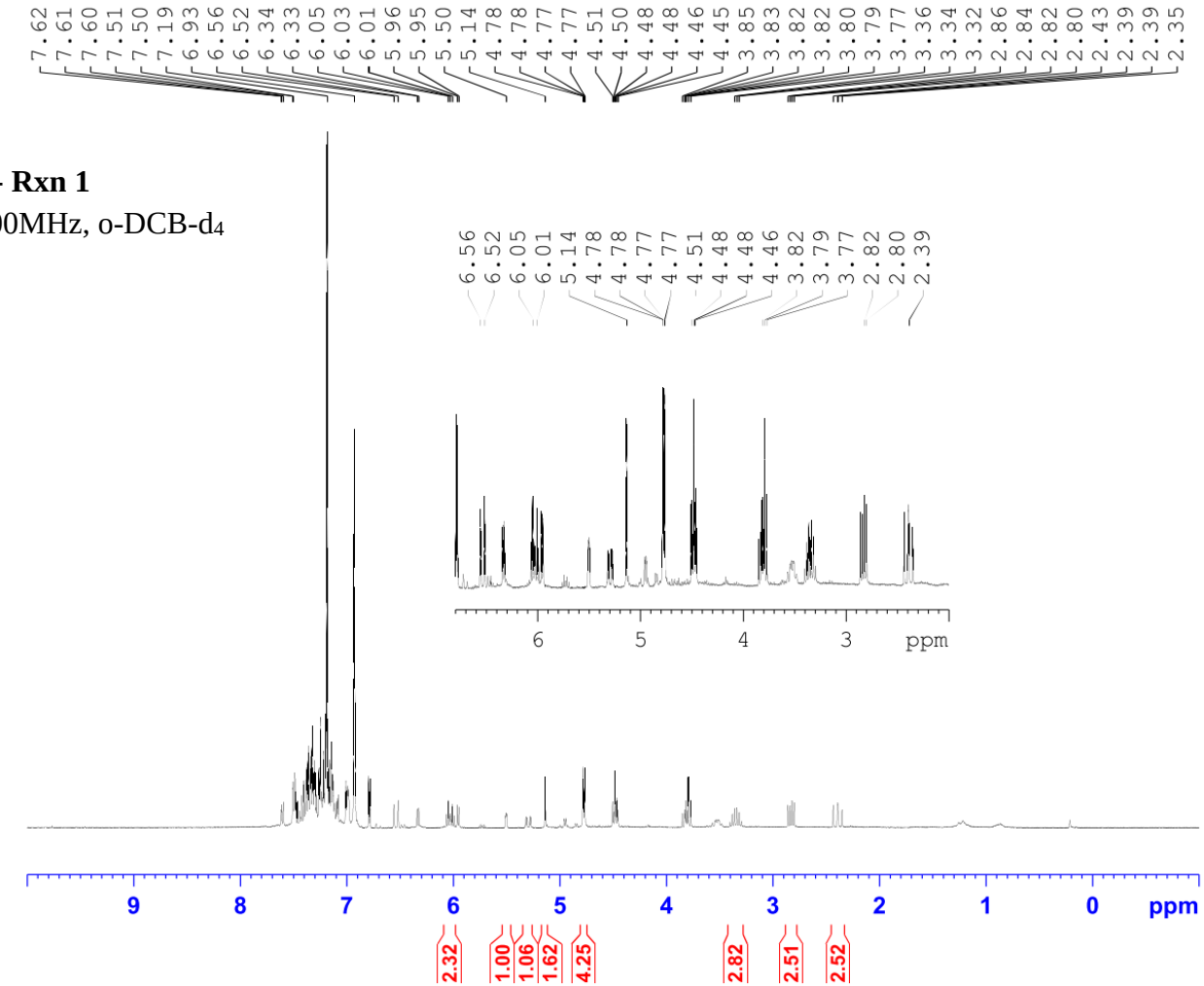

```
Current Data Parameters
NAME          JAW-03-054
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191011
Time                6.52
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 2048
DS                    2
SWH           29761.904 Hz
FIDRES         0.454131 Hz
AQ            1.1010048 sec
RG                  203
DW               16.800 usec
DE                6.50 usec
TE                298.5 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1        125.7779086 MHz
NUC1                 13C
P1                10.50 usec
PLW1       110.00000000 W

======== CHANNEL f2 ========
SFO2        500.1620006 MHz
NUC2                  1H
CPDPRG[2         waltz16
PCPD2             80.00 usec
PLW2        18.00000000 W
PLW12        0.37195000 W
PLW13        0.23805000 W

F2 - Processing parameters
SI                32768
SF          125.7653135 MHz
WDW                  EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```




```
Current Data Parameters
NAME          JAW-03-054
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191011
Time                6.52
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 2048
DS                    2
SWH           29761.904 Hz
FIDRES         0.454131 Hz
AQ            1.1010048 sec
RG                  203
DW               16.800 usec
DE                6.50 usec
TE                298.5 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1        125.7779086 MHz
NUC1                 13C
P1                10.50 usec
PLW1       110.00000000 W

======== CHANNEL f2 ========
SFO2        500.1620006 MHz
NUC2                  1H
CPDPRG[2         waltz16
PCPD2             80.00 usec
PLW2        18.00000000 W
PLW12        0.37195000 W
PLW13        0.23805000 W

F2 - Processing parameters
SI                 32768
SF          125.7653135 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

2.6.2 - Rxn 1

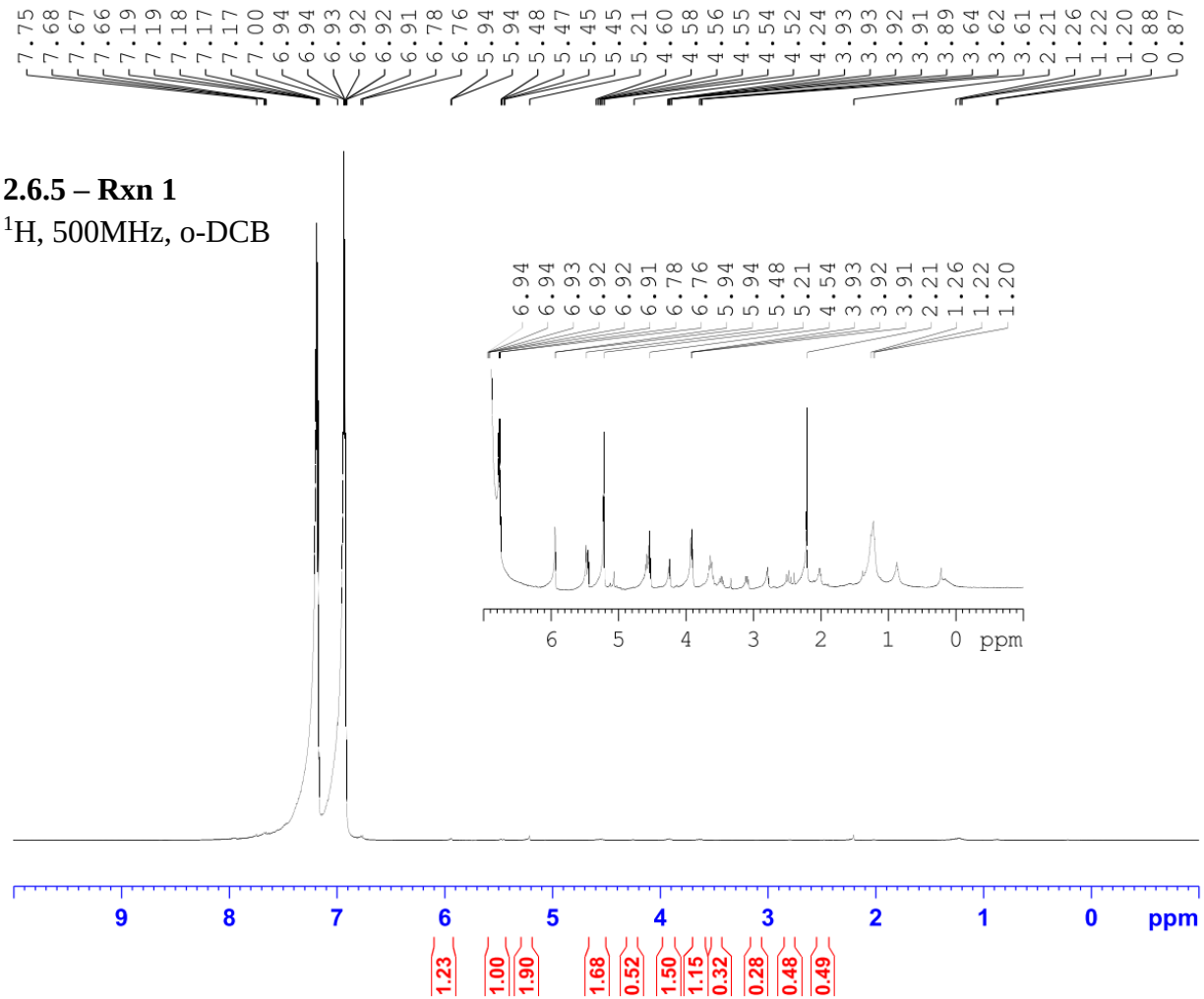
^{1}H, 400MHz, o-DCB-d$_4$




```
Current Data Parameters
NAME          JAW-01-008
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20160617
Time              13.16
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG            zg30
TD                65536
SOLVENT            C6D6
NS                    16
DS                     2
SWH            8012.820 Hz
FIDRES         0.122266 Hz
AQ           4.0894465 sec
RG                   128
DW              62.400 usec
DE                6.50 usec
TE                95.6 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1        400.1324710 MHz
NUC1                  1H
P1                13.75 usec
PLW1        12.01700020 W

F2 - Processing parameters
SI                65536
SF          400.1300900 MHz
WDW                  EM
SSB      0
LB                0.30 Hz
GB       0
PC                1.00
```

2.6.5 – Rxn 1

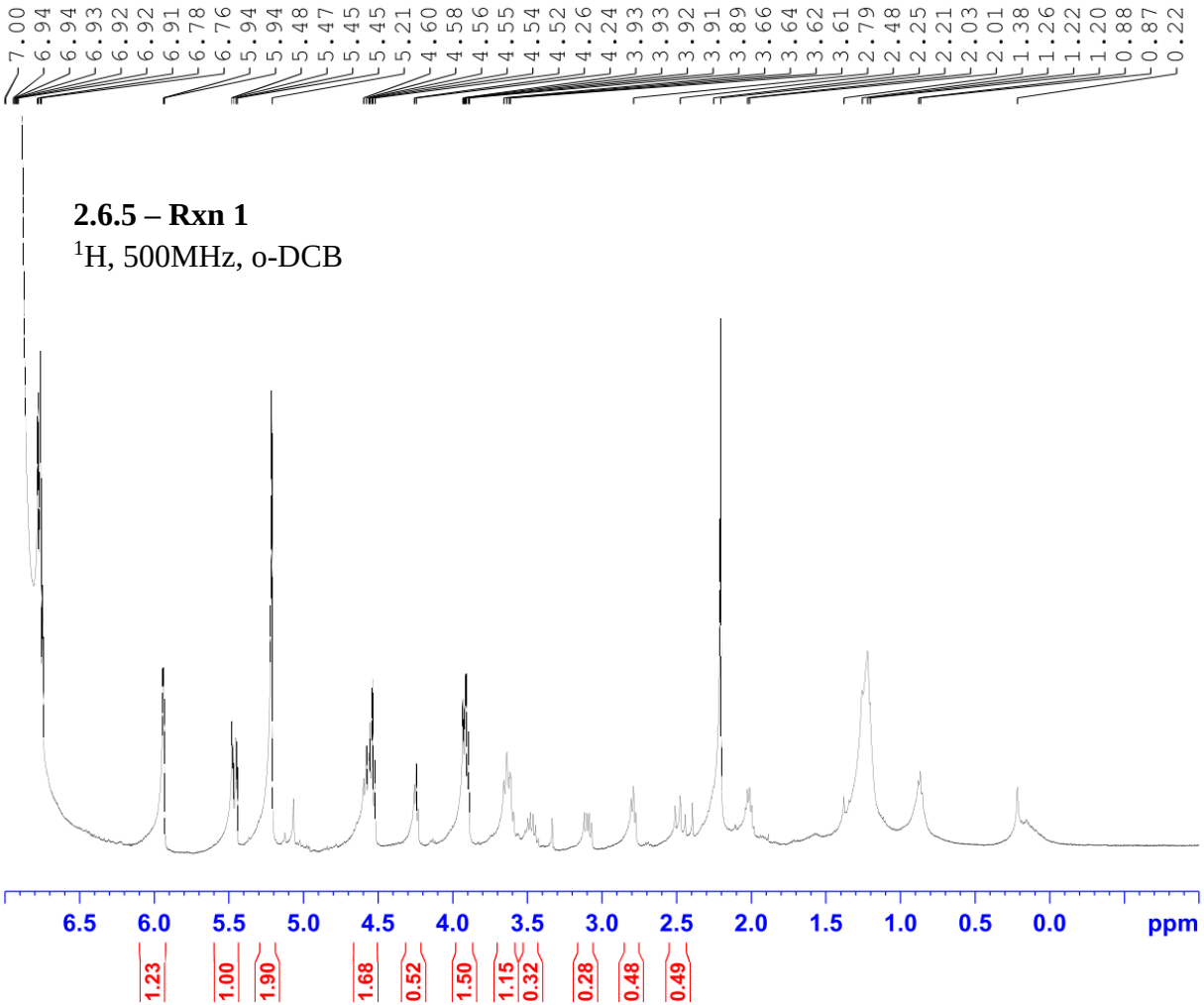
^{1}H, 500MHz, o-DCB




```
Current Data Parameters
NAME          JAW-01-124
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170621
Time              16.14
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG            zg30
TD                65536
SOLVENT            None
NS                   16
DS                    2
SWH           10000.000 Hz
FIDRES         0.152588 Hz
AQ            3.2767999 sec
RG                  5.6
DW               50.000 usec
DE                6.50 usec
TE                298.0 K
D1           1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1        500.1630887 MHz
NUC1                 1H
P1                11.50 usec
PLW1        18.00000000 W

F2 - Processing parameters
SI                65536
SF          500.1598169 MHz
WDW                  EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```

2.6.5 – Rxn 1

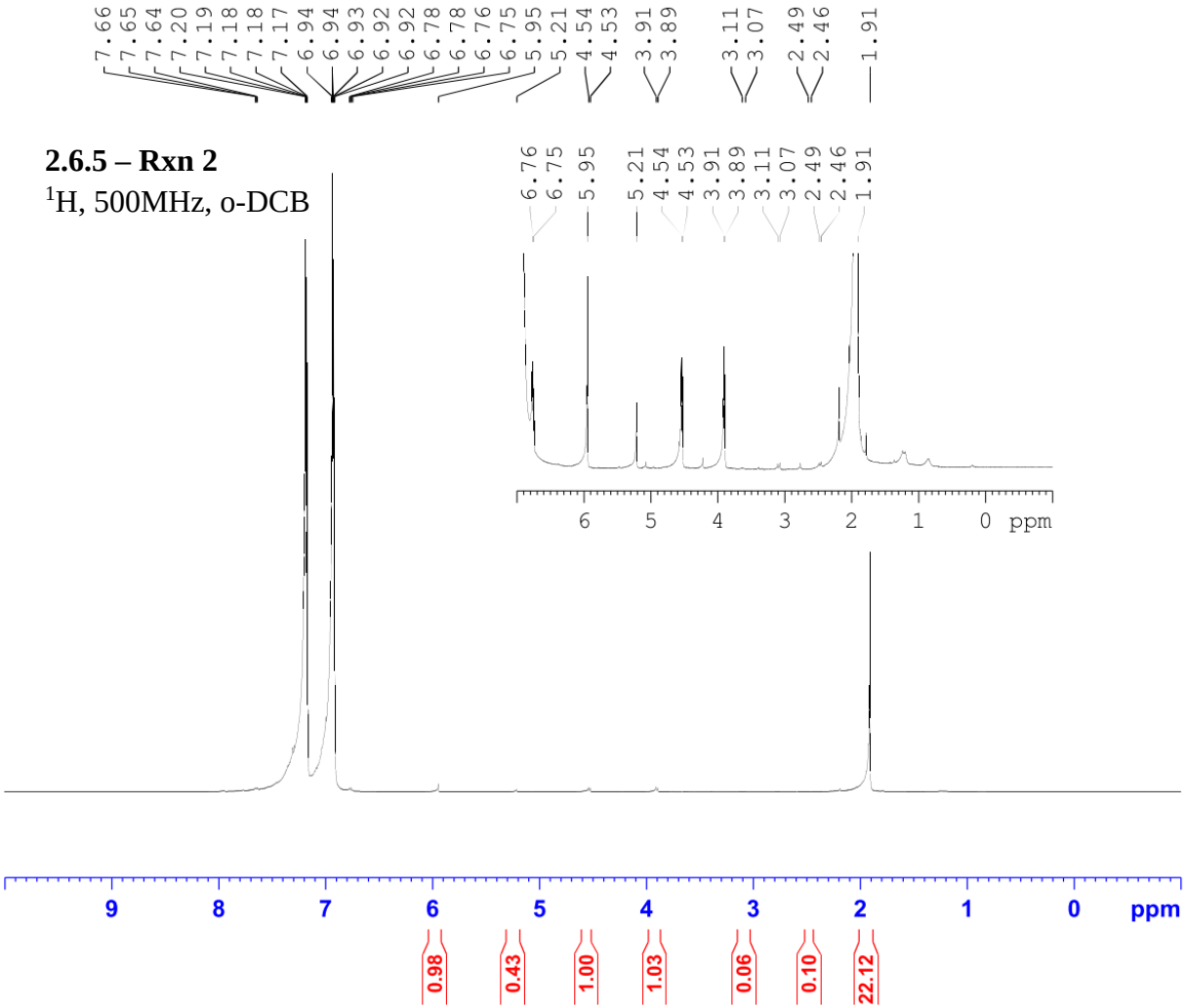
^{1}H, 500MHz, o-DCB




```
Current Data Parameters
NAME          JAW-01-124
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170621
Time              16.14
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG            zg30
TD                65536
SOLVENT            None
NS                   16
DS                    2
SWH           10000.000 Hz
FIDRES         0.152588 Hz
AQ            3.2767999 sec
RG                  5.6
DW               50.000 usec
DE                6.50 usec
TE               298.0 K
D1           1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1        500.1630887 MHz
NUC1                 1H
P1                11.50 usec
PLW1        18.00000000 W

F2 - Processing parameters
SI                65536
SF          500.1598169 MHz
WDW                  EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```

2.6.5 – Rxn 2

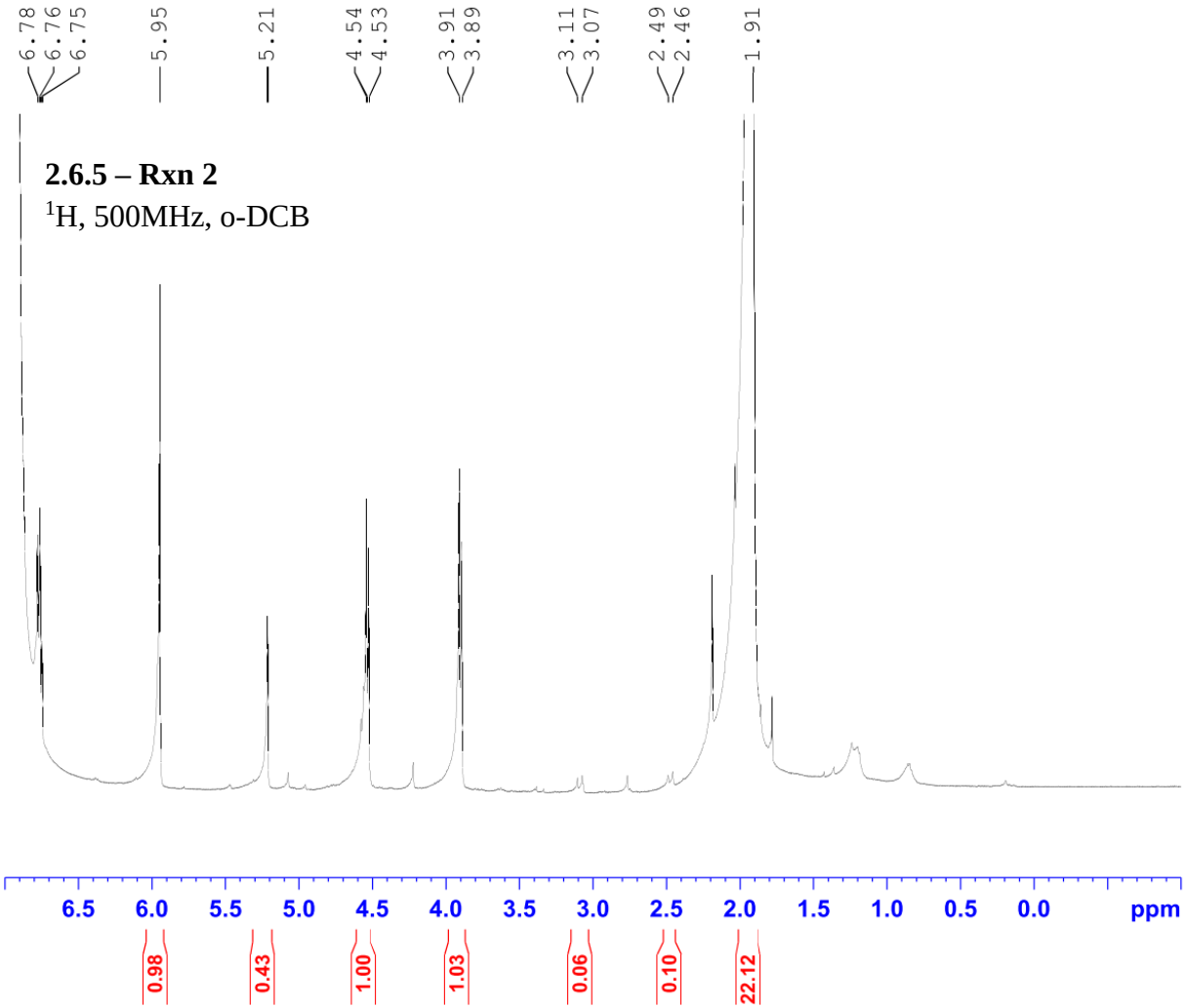
^{1}H, 500MHz, o-DCB




```
Current Data Parameters
NAME          JAW-01-126
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170621
Time              16.17
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG            zg30
TD                65536
SOLVENT            None
NS                   16
DS                    2
SWH           10000.000 Hz
FIDRES         0.152588 Hz
AQ            3.2767999 sec
RG                  5.6
DW               50.000 usec
DE                6.50 usec
TE               297.9 K
D1           1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1        500.1630887 MHz
NUC1                 1H
P1                11.50 usec
PLW1        18.00000000 W

F2 - Processing parameters
SI                65536
SF          500.1598314 MHz
WDW                  EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```

2.6.5 – Rxn 2

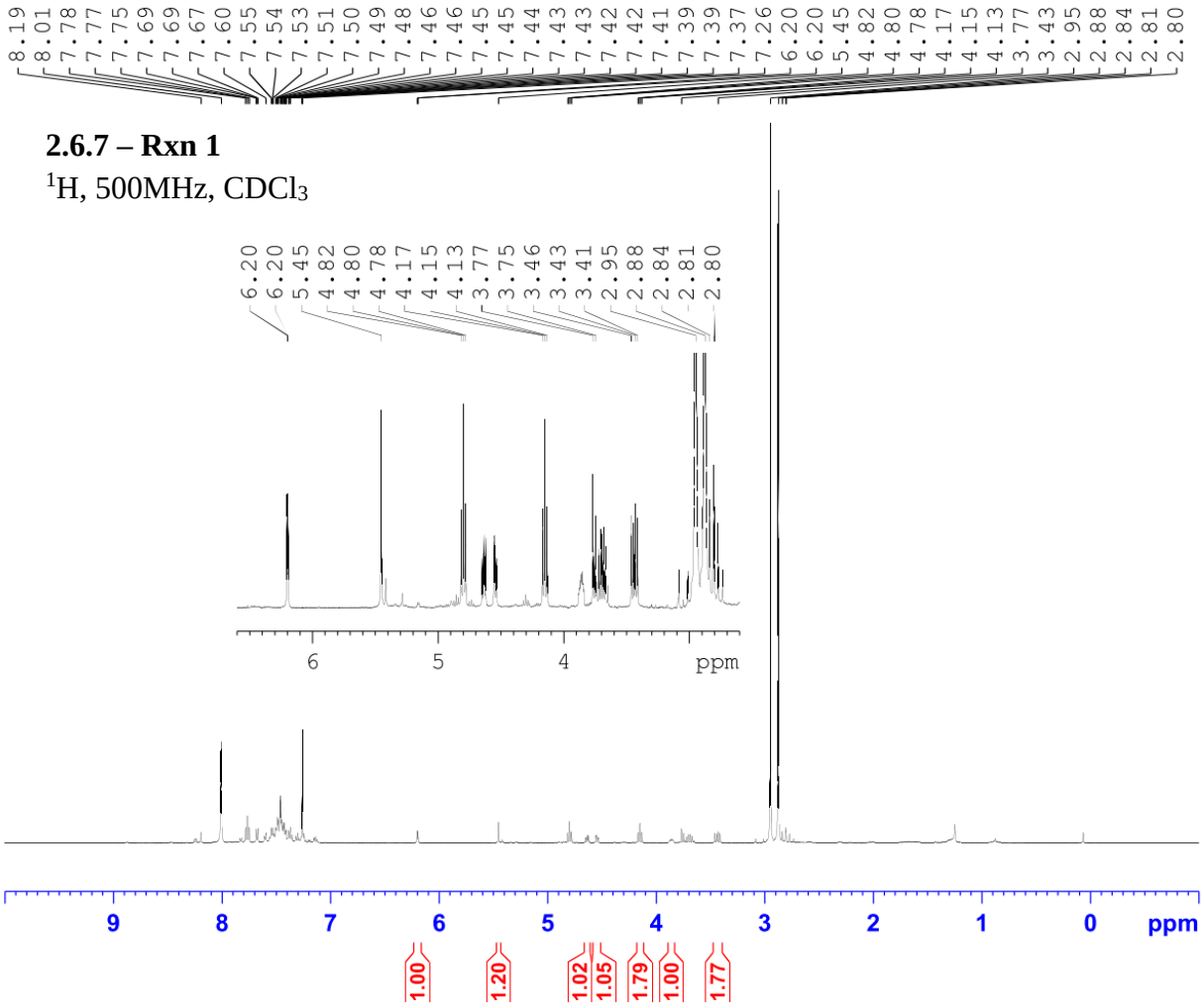
^{1}H, 500MHz, o-DCB




```
Current Data Parameters
NAME          JAW-01-126
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170621
Time              16.17
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG            zg30
TD                65536
SOLVENT            None
NS                   16
DS                    2
SWH           10000.000 Hz
FIDRES         0.152588 Hz
AQ            3.2767999 sec
RG                  5.6
DW               50.000 usec
DE                6.50 usec
TE               297.9 K
D1           1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1        500.1630887 MHz
NUC1                 1H
P1                11.50 usec
PLW1        18.00000000 W

F2 - Processing parameters
SI                65536
SF          500.1598314 MHz
WDW                  EM
SSB      0
LB                0.30 Hz
GB       0
PC                1.00
```

2.6.7 – Rxn 1

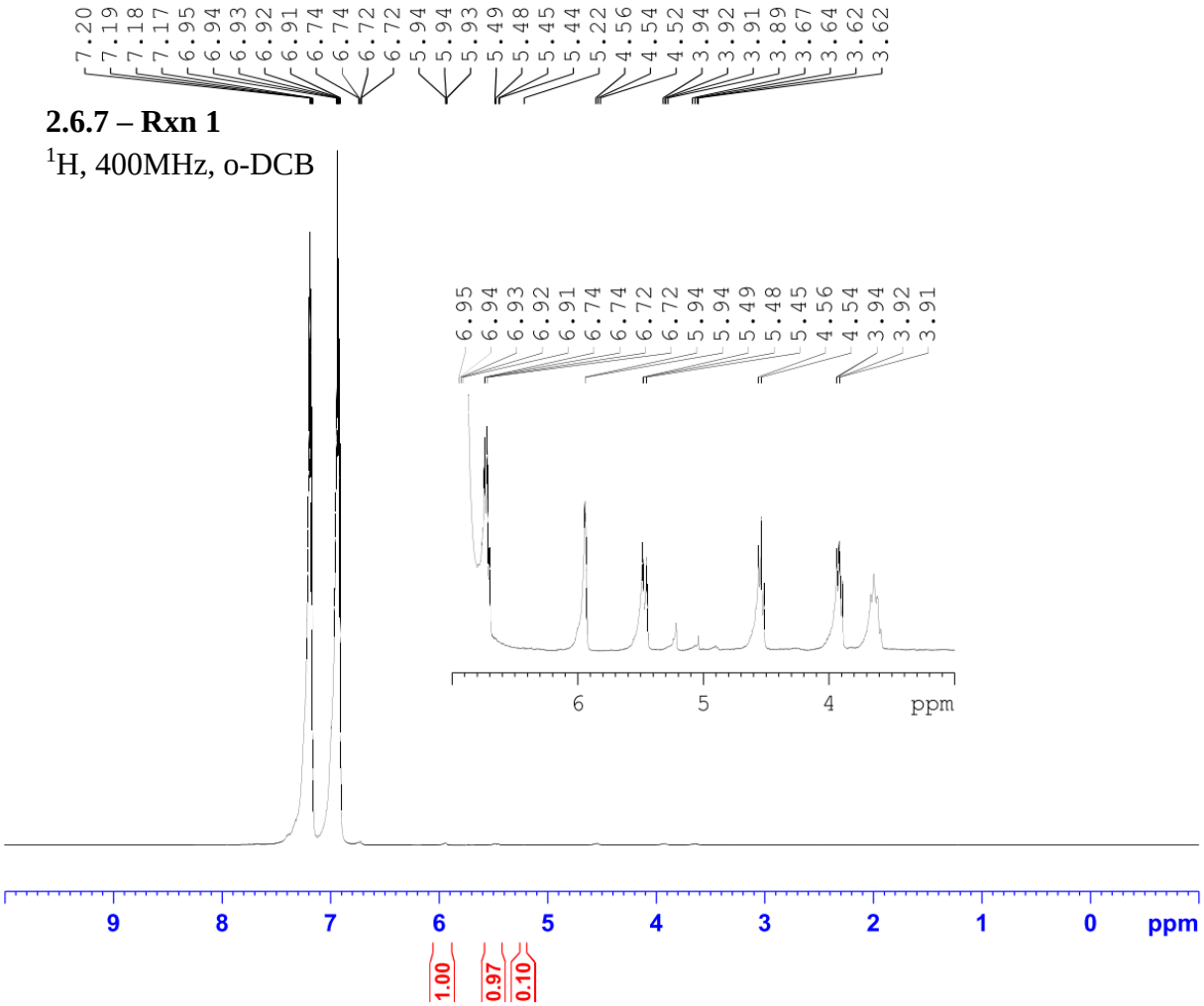
^{1}H, 500MHz, $CDCl_3$




```
Current Data Parameters
NAME          JAW-02-187
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20190124
Time               16.28
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                   101
DW                50.000 usec
DE                  6.50 usec
TE                 297.4 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                  1H
P1                 11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1600122 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

2.6.7 – Rxn 1

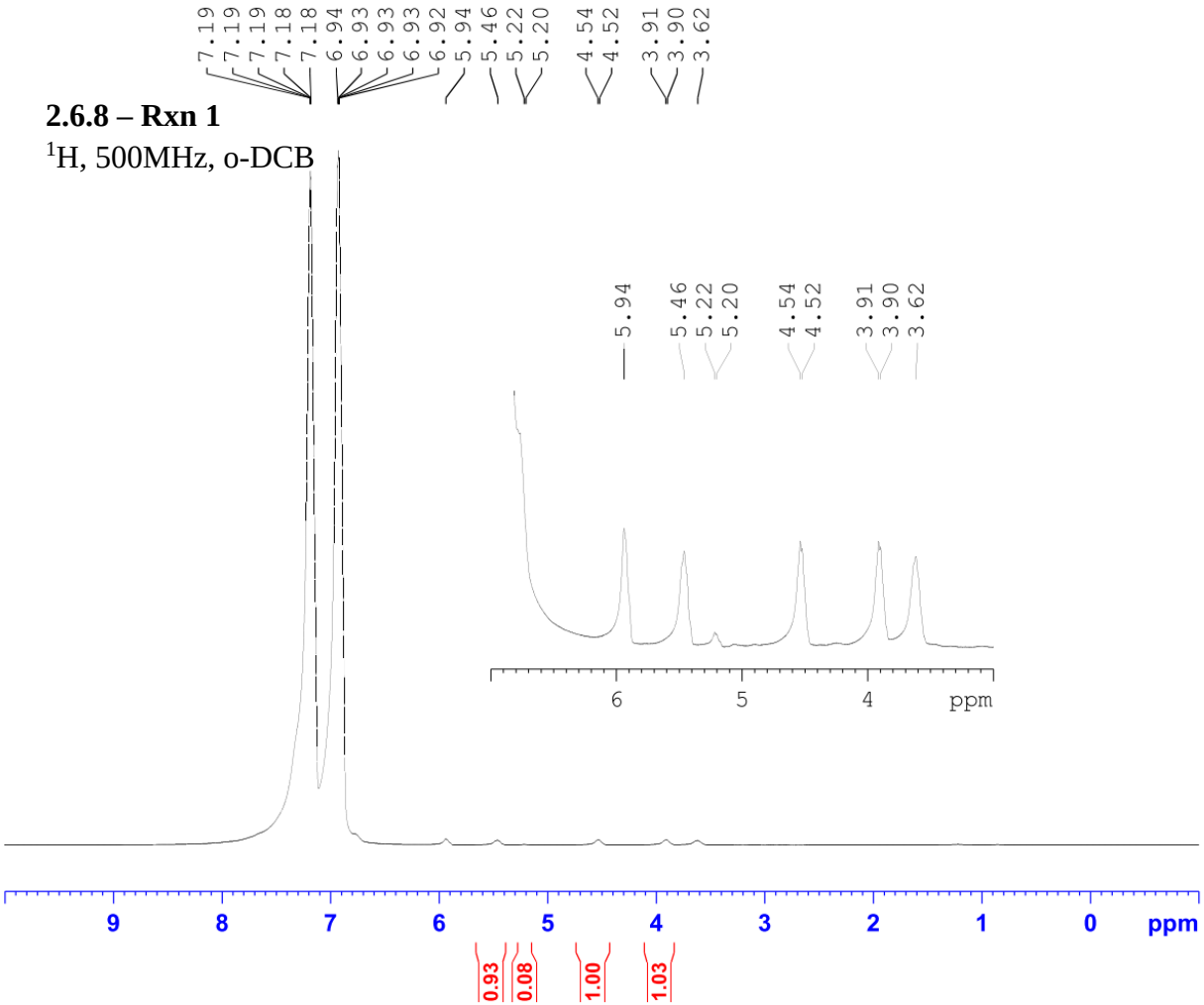
^{1}H, 400MHz, o-DCB




```
Current Data Parameters
NAME          JAW-02-187
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20190124
Time               14.52 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG             zg30
TD                 65536
SOLVENT             None
NS                    48
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                   5.6
DW                62.400 usec
DE                 6.50 usec
TE                 91.8 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                 4.83 usec
P1                14.50 usec
PLW1         12.00000000 W

F2 - Processing parameters
SI                 65536
SF          400.1295236 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

2.6.8 – Rxn 1

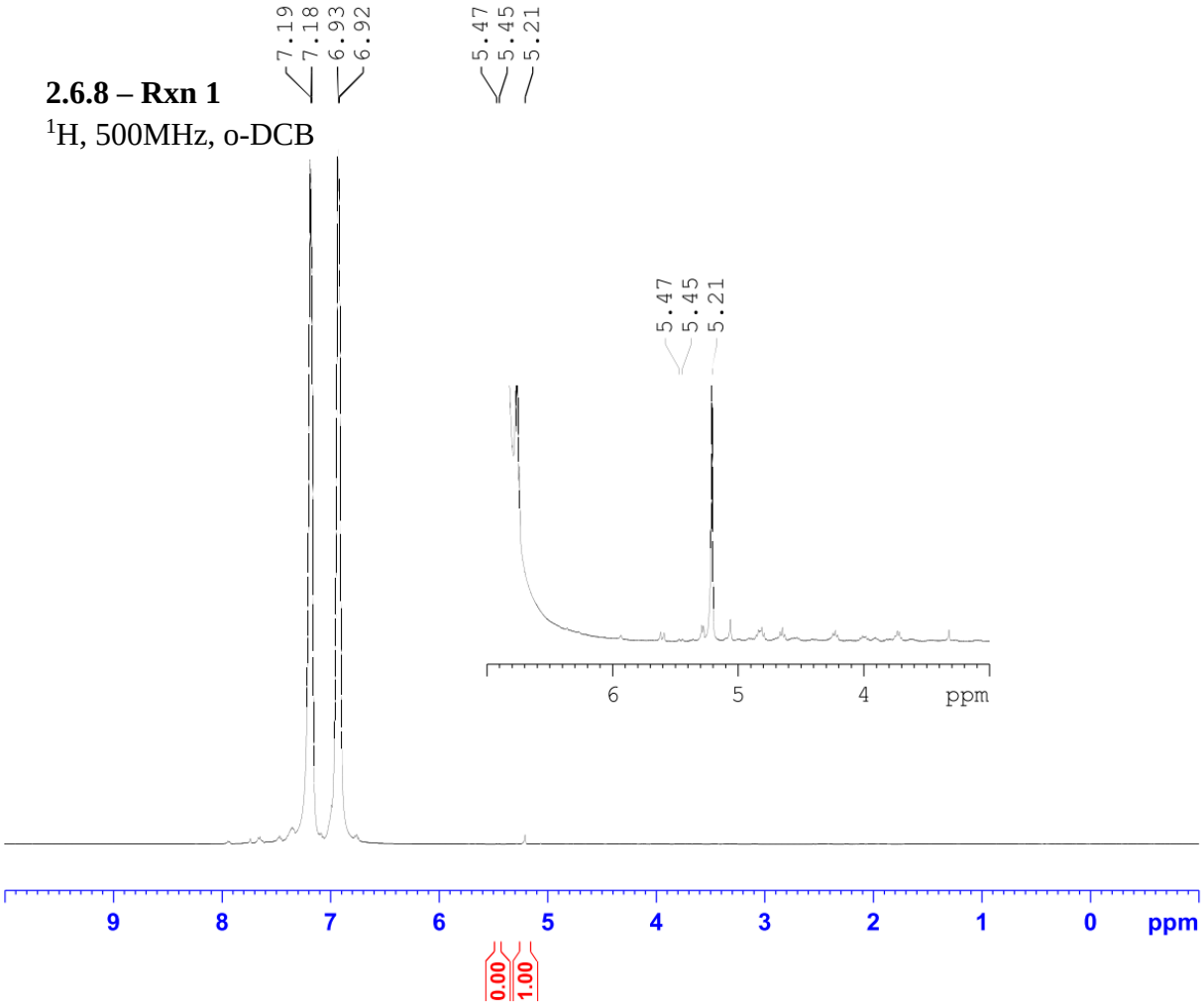
^{1}H, 500MHz, o-DCB




```
Current Data Parameters
NAME          JAW-02-183
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20181219
Time               14.19
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT             None
NS                    48
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                   5.6
DW                50.000 usec
DE                 6.50 usec
TE                297.3 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                   1H
P1                 11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1595369 MHz
WDW                    EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

2.6.8 – Rxn 1

^{1}H, 500MHz, o-DCB

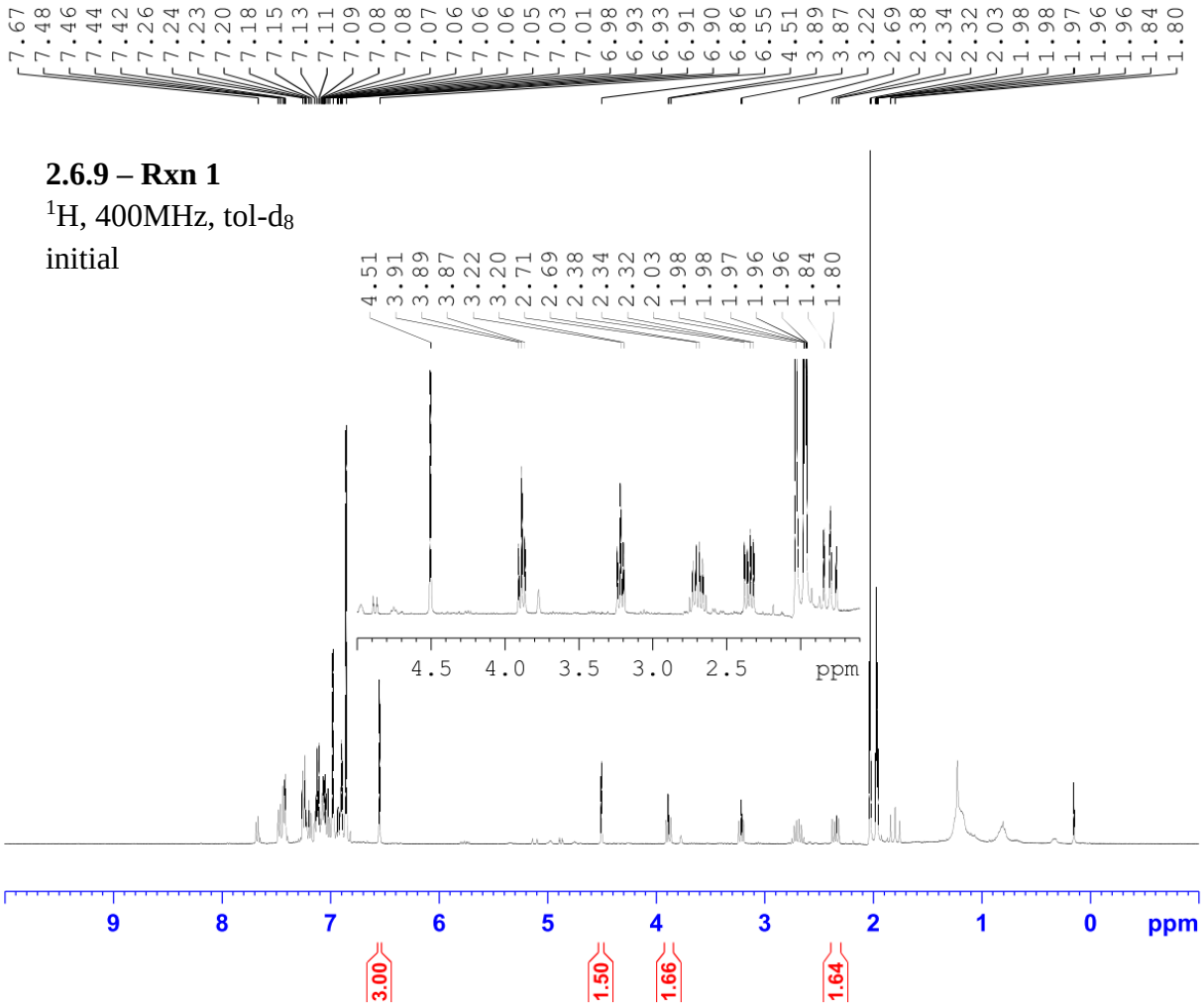



```
Current Data Parameters
NAME          JAW-02-183
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20181219
Time               16.58
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT             None
NS                    48
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                     5
DW                50.000 usec
DE                 6.50 usec
TE                297.3 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                  1H
P1                11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1598062 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

2.6.9 – Rxn 1

^{1}H, 400MHz, tol-d$_8$

initial

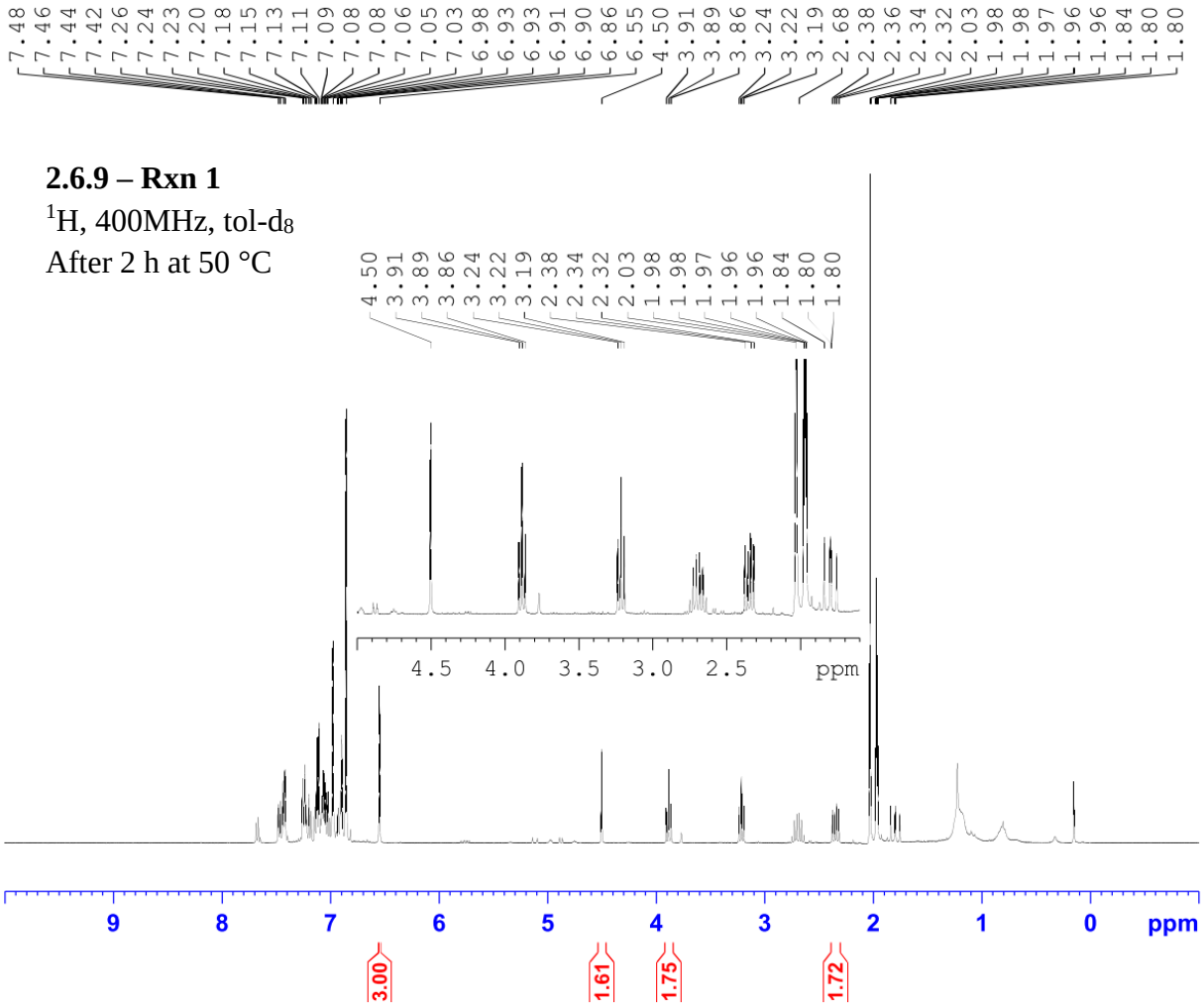



```
Current Data Parameters
NAME          JAW-03-097
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200227
Time               13.36 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG            zg30
TD                65536
SOLVENT             Tol
NS                   16
DS                    2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                  90.5
DW                62.400 usec
DE                 6.50 usec
TE                 91.3 K
D1           1.00000000 sec
TD0                   1
SFO1        400.1324708 MHz
NUC1                 1H
P0                 4.83 usec
P1                14.50 usec
PLW1        12.00000000 W

F2 - Processing parameters
SI                65536
SF          400.1300627 MHz
WDW                  EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```

2.6.9 – Rxn 1

^{1}H, 400MHz, tol-d_8

After 2 h at 50 °C

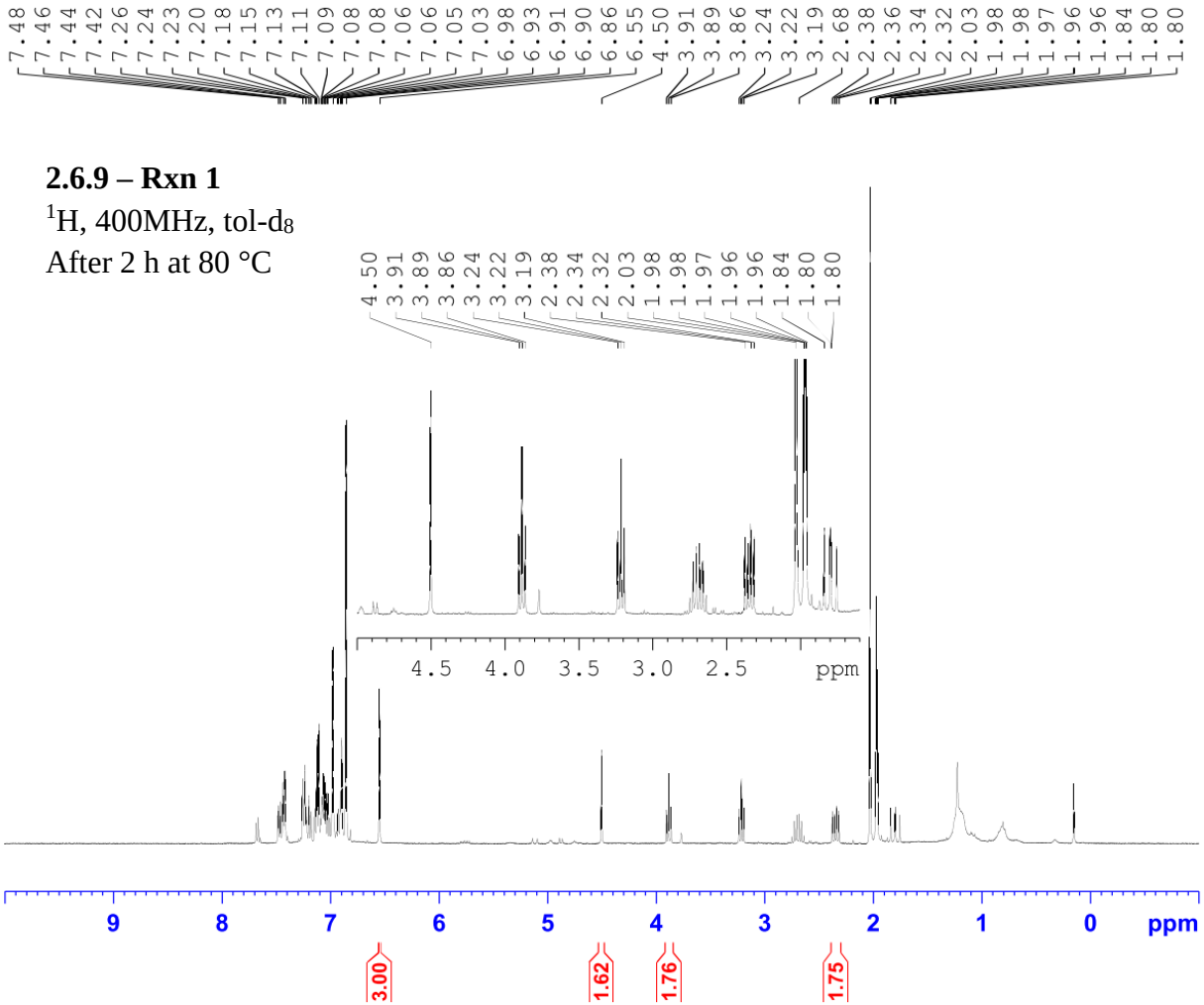



```
Current Data Parameters
NAME          JAW-03-097
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200227
Time               16.18 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                   101
DW                62.400 usec
DE                 6.50 usec
TE                 91.5 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                 4.83 usec
P1                14.50 usec
PLW1         12.00000000 W

F2 - Processing parameters
SI                 65536
SF          400.1300628 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

2.6.9 – Rxn 1

^{1}H, 400MHz, tol-d_8

After 2 h at 80 °C

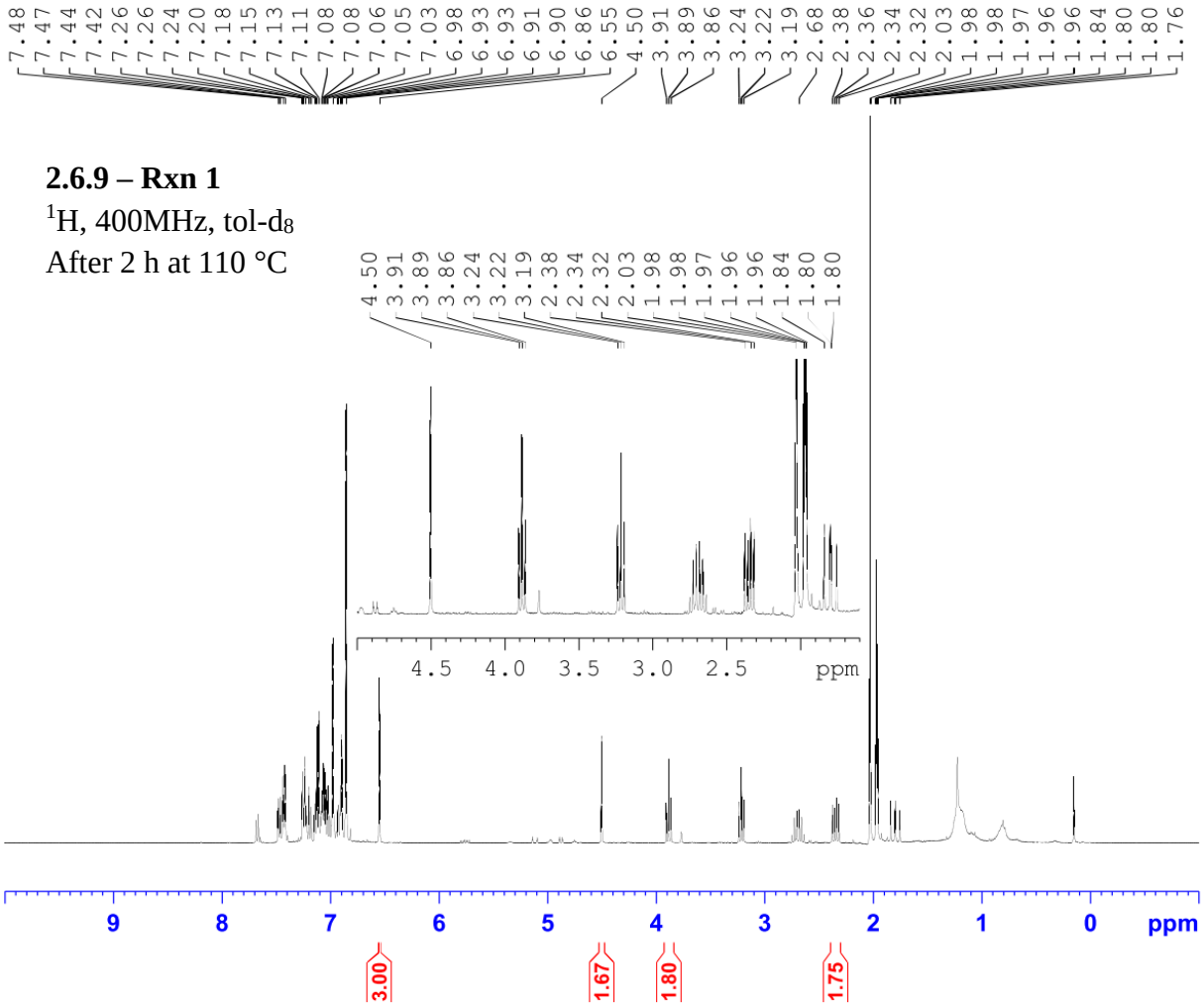



```
Current Data Parameters
NAME          JAW-03-097
EXPNO                  4
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200228
Time                8.52 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                   101
DW                62.400 usec
DE                 6.50 usec
TE                 92.2 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                  4.83 usec
P1                 14.50 usec
PLW1         12.00000000 W

F2 - Processing parameters
SI                 65536
SF          400.1300628 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

2.6.9 – Rxn 1

^{1}H, 400MHz, tol-d_8

After 2 h at 110 °C

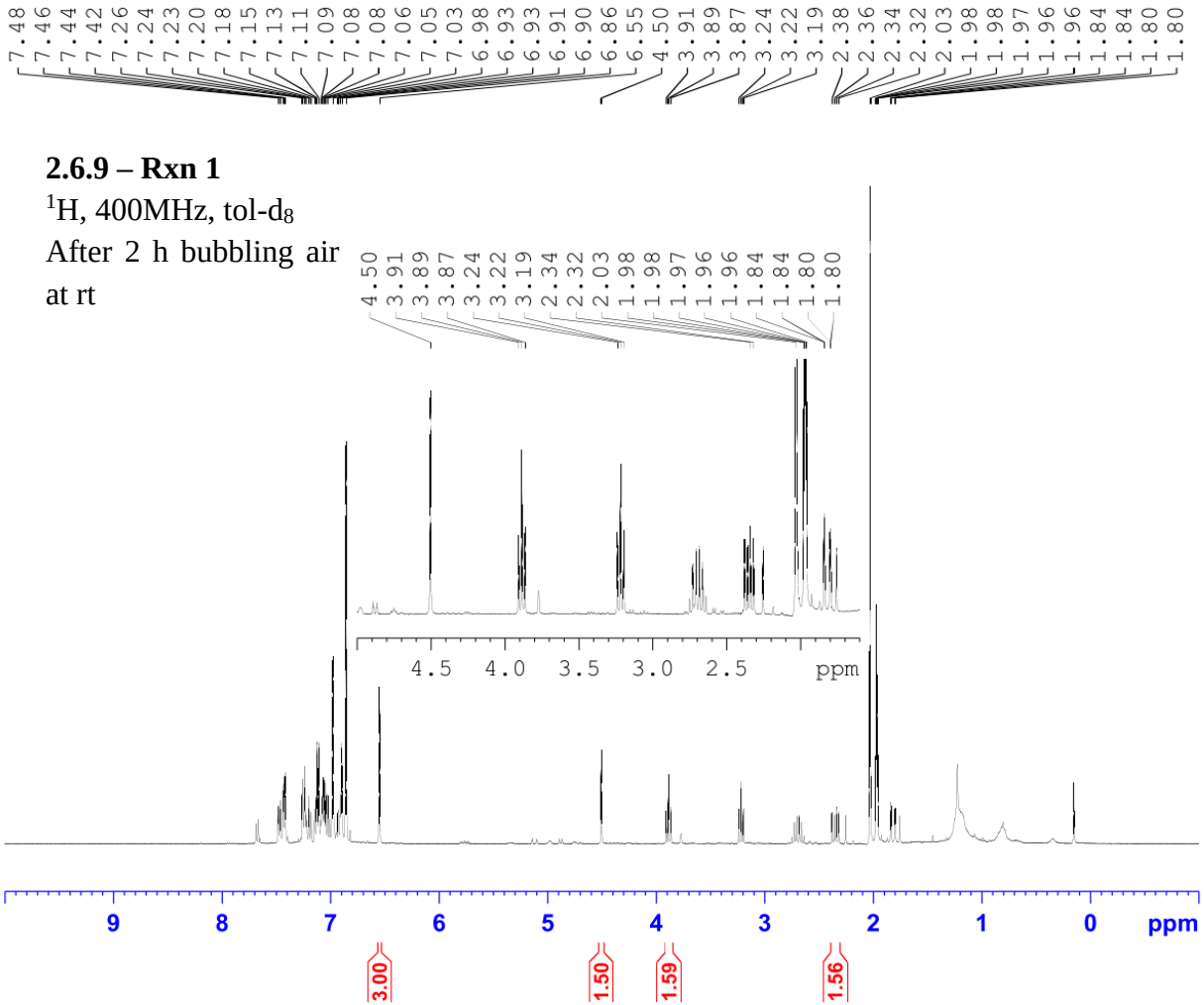



```
Current Data Parameters
NAME          JAW-03-097
EXPNO                  5
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200228
Time               11.35 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                  90.5
DW                62.400 usec
DE                 6.50 usec
TE                 91.8 K
D1           1.00000000 sec
TD0                    1
SFO1        400.1324708 MHz
NUC1                  1H
P0                 4.83 usec
P1                14.50 usec
PLW1         12.00000000 W

F2 - Processing parameters
SI                 65536
SF          400.1300628 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

2.6.9 – Rxn 1

^{1}H, 400MHz, tol-d_8

After 2 h bubbling air at rt

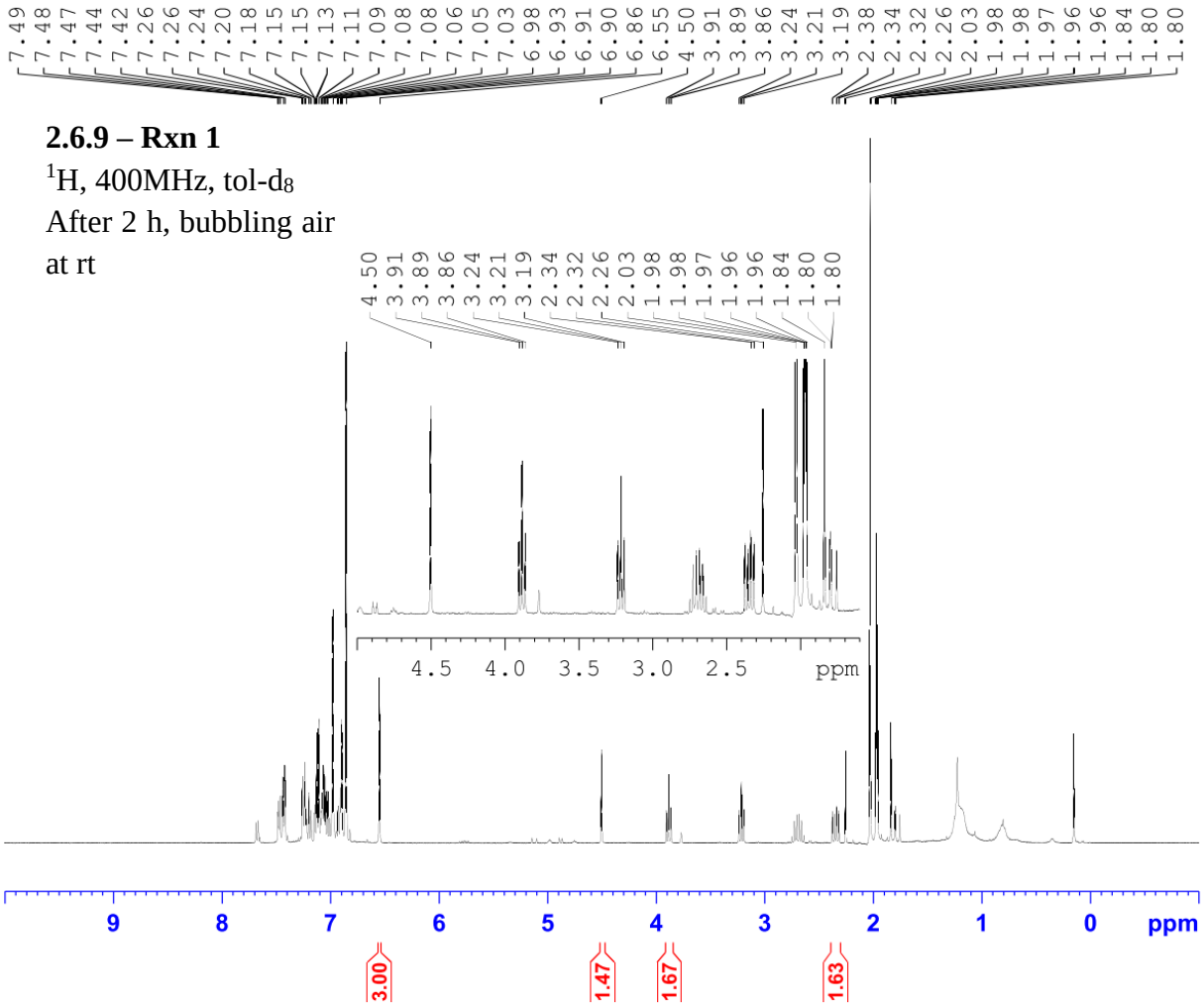



```
Current Data Parameters
NAME          JAW-03-097
EXPNO                  6
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200228
Time              16.17 h
INSTRUM           spect
PROBHD   Z108618_0240 (
PULPROG            zg30
TD                65536
SOLVENT             Tol
NS                   16
DS                    2
SWH            8012.820 Hz
FIDRES         0.244532 Hz
AQ            4.0894465 sec
RG                 90.5
DW               62.400 usec
DE                6.50 usec
TE                92.0 K
D1           1.00000000 sec
TD0                   1
SFO1        400.1324708 MHz
NUC1                 1H
P0                 4.83 usec
P1                14.50 usec
PLW1         12.00000000 W

F2 - Processing parameters
SI                65536
SF          400.1300627 MHz
WDW                  EM
SSB      0
LB                0.30 Hz
GB       0
PC                1.00
```

2.6.9 – Rxn 1

^{1}H, 400MHz, tol-d_8

After 2 h, bubbling air at rt

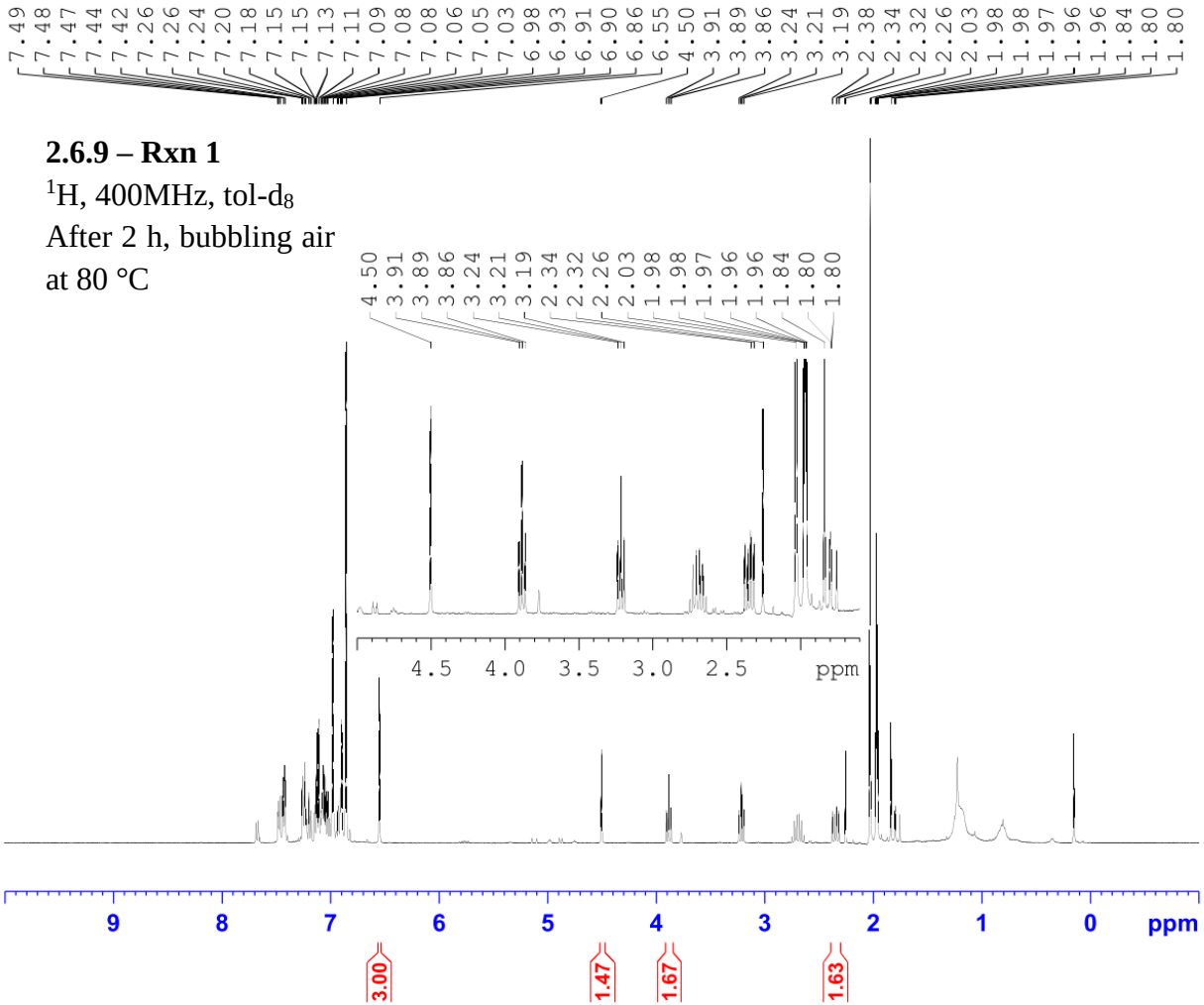



```
Current Data Parameters
NAME          JAW-03-097
EXPNO                  8
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200229
Time               13.43 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG            zg30
TD                65536
SOLVENT             Tol
NS                   16
DS                    2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                   101
DW                62.400 usec
DE                 6.50 usec
TE                 92.3 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                 4.83 usec
P1                14.50 usec
PLW1         12.00000000 W

F2 - Processing parameters
SI                65536
SF          400.1300627 MHz
WDW                  EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```

2.6.9 – Rxn 1

^{1}H, 400MHz, tol-d_8

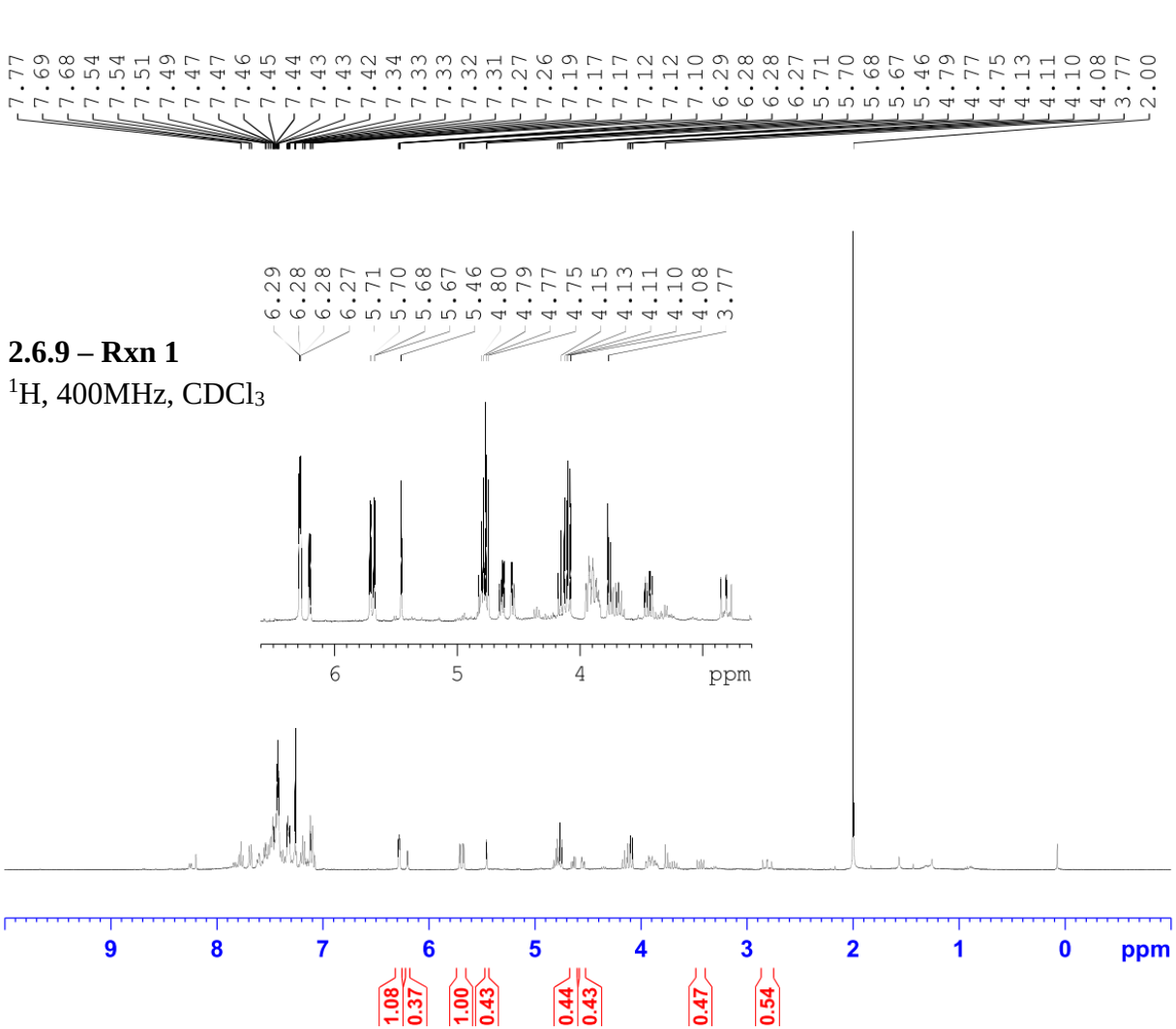
After 2 h, bubbling air at 80 °C




```
Current Data Parameters
NAME          JAW-03-097
EXPNO                  8
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200229
Time               13.43 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                   101
DW                62.400 usec
DE                 6.50 usec
TE                 92.3 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                 4.83 usec
P1                14.50 usec
PLW1         12.00000000 W

F2 - Processing parameters
SI                 65536
SF          400.1300627 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

2.6.9 – Rxn 1

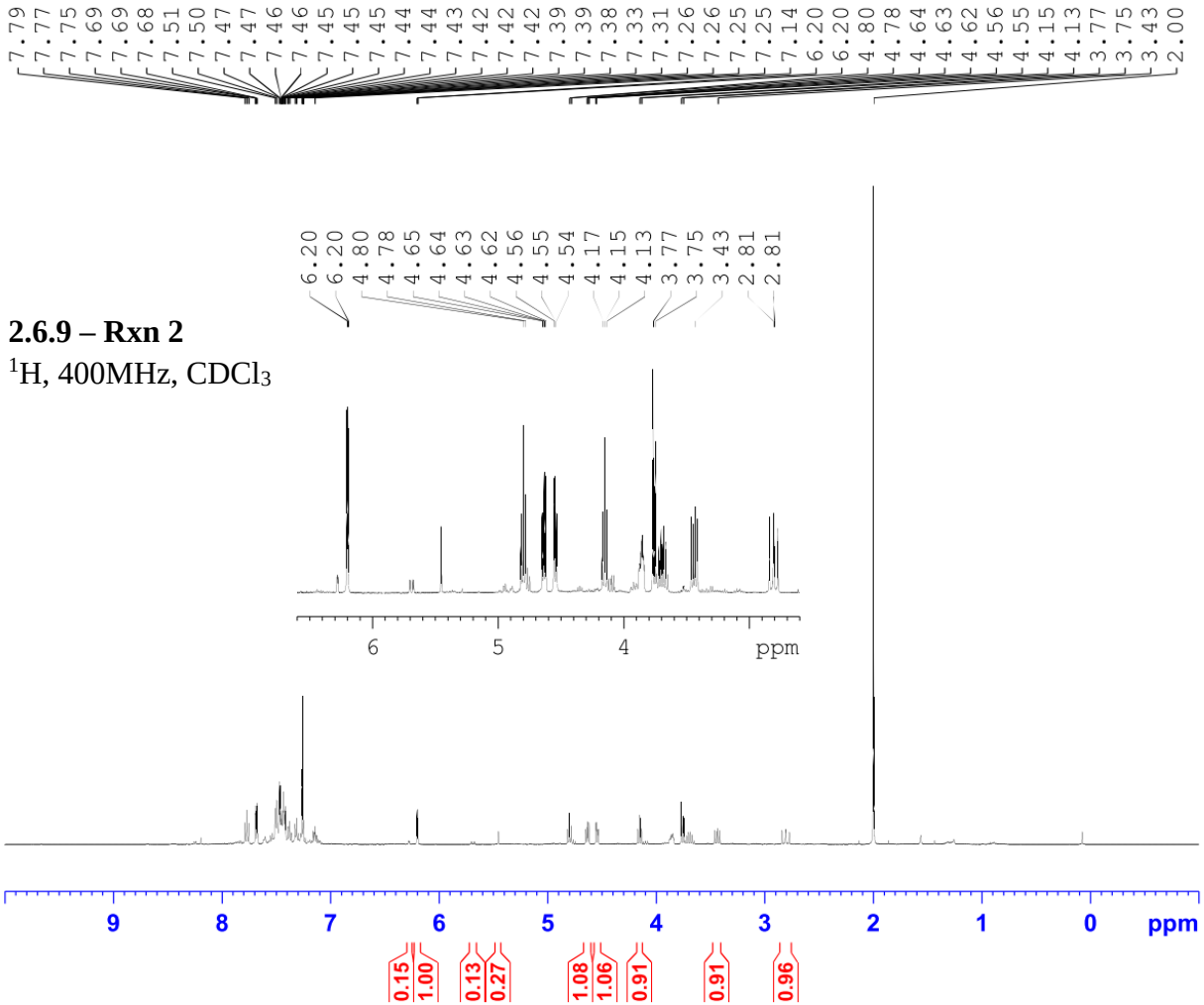
^{1}H, 400MHz, $CDCl_3$




```
Current Data Parameters
NAME          JAW-02-179
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20181213
Time               12.04 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                   101
DW                62.400 usec
DE                 6.50 usec
TE                 90.5 K
D1           1.00000000 sec
TD0                    1
SFO1        400.1324708 MHz
NUC1                  1H
P0                 4.83 usec
P1                14.50 usec
PLW1        12.00000000 W

F2 - Processing parameters
SI                 65536
SF          400.1300099 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

2.6.9 – Rxn 2

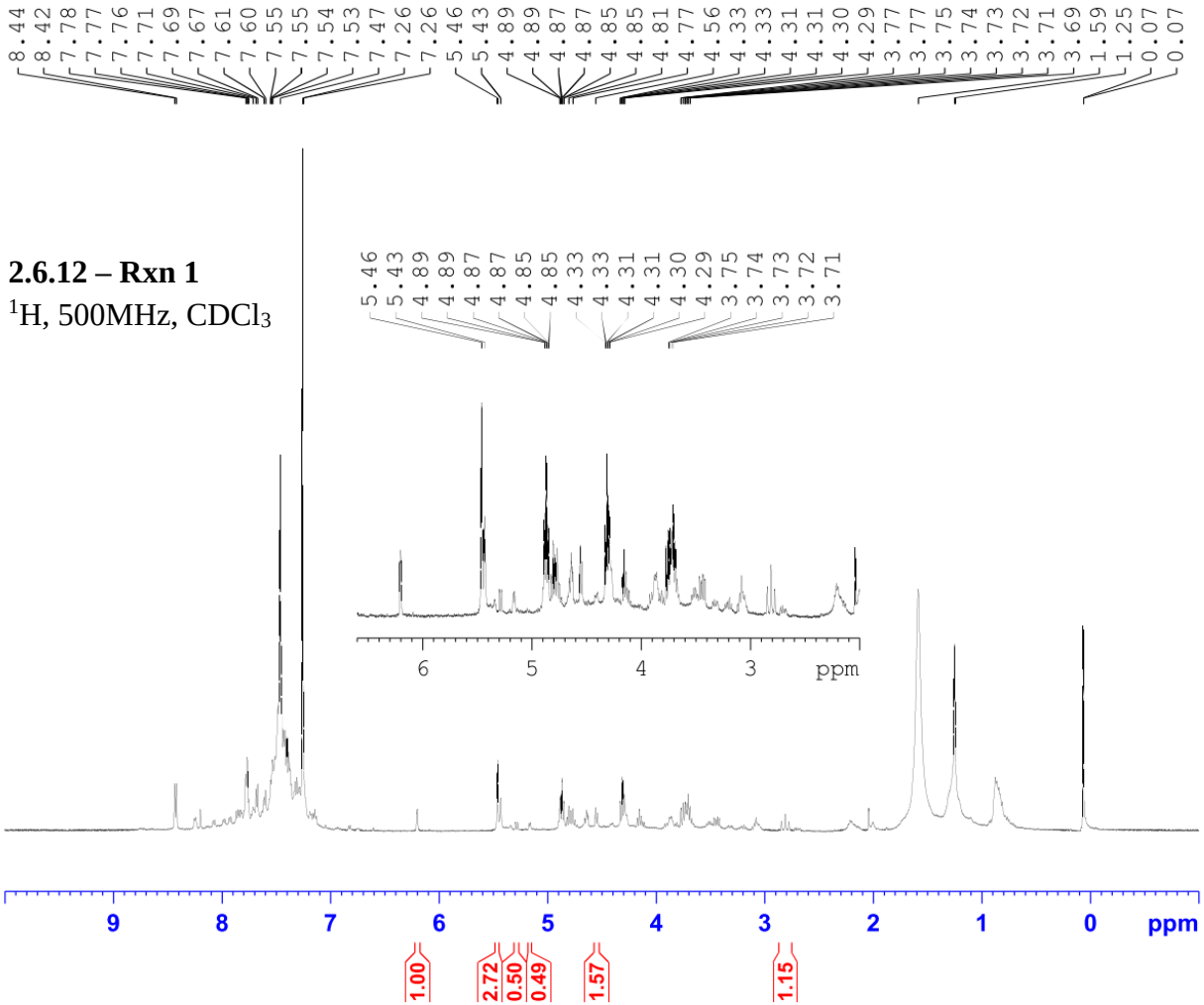
^{1}H, 400MHz, $CDCl_3$




```
Current Data Parameters
NAME        JAW-02-179-b
EXPNO                 30
PROCNO                 1

F2 - Acquisition Parameters
Date_           20181213
Time               15.26
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                   101
DW                50.000 usec
DE                  6.50 usec
TE                 297.6 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                   1H
P1                 11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1600122 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

2.6.12 – Rxn 1

^{1}H, 500MHz, $CDCl_3$

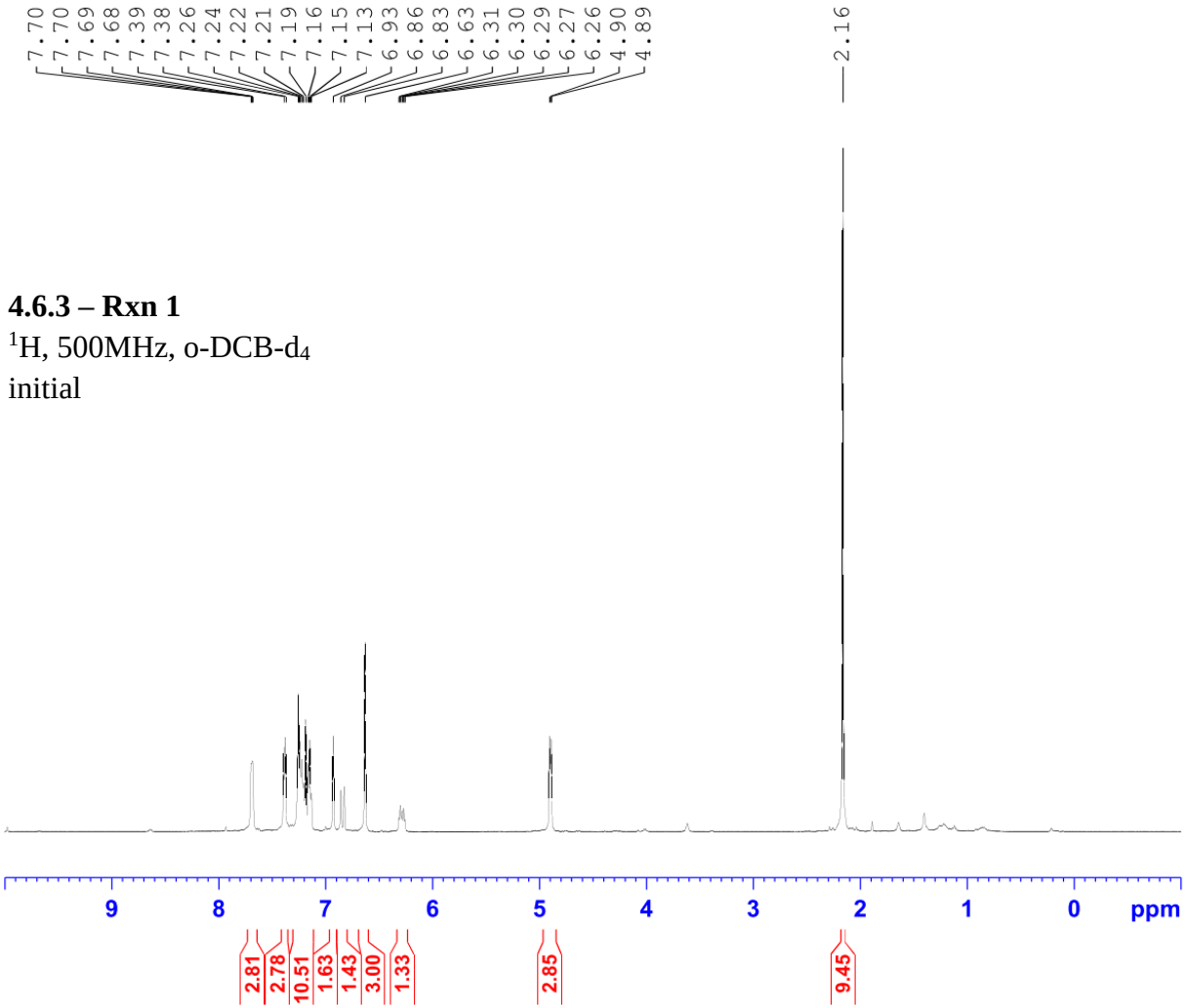



```
Current Data Parameters
NAME        JAW-02-110-a
EXPNO                 19
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180828
Time               14.31
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    32
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                   203
DW                50.000 usec
DE                 6.50 usec
TE                295.8 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                  1H
P1                11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1600133 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.3 – Rxn 1

^{1}H, 500MHz, o-DCB-d_4

initial

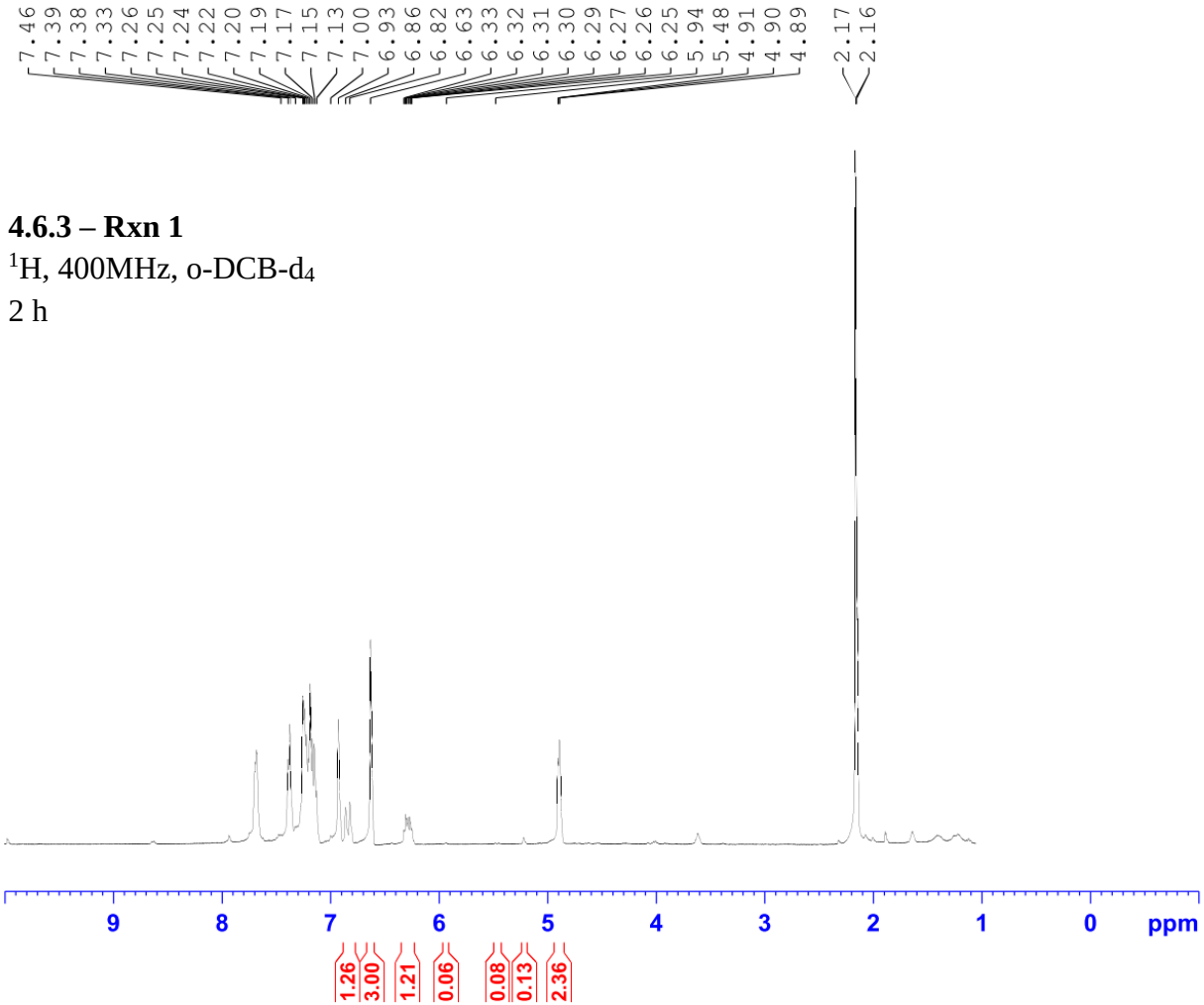



```
Current Data Parameters
NAME          JAW-01-155
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170921
Time               15.18
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT             C6D6
NS                    16
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                  90.5
DW                50.000 usec
DE                 6.50 usec
TE                297.1 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                  1H
P1                11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1601154 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.3 – Rxn 1

^{1}H, 400MHz, o-DCB-d$_4$

2 h

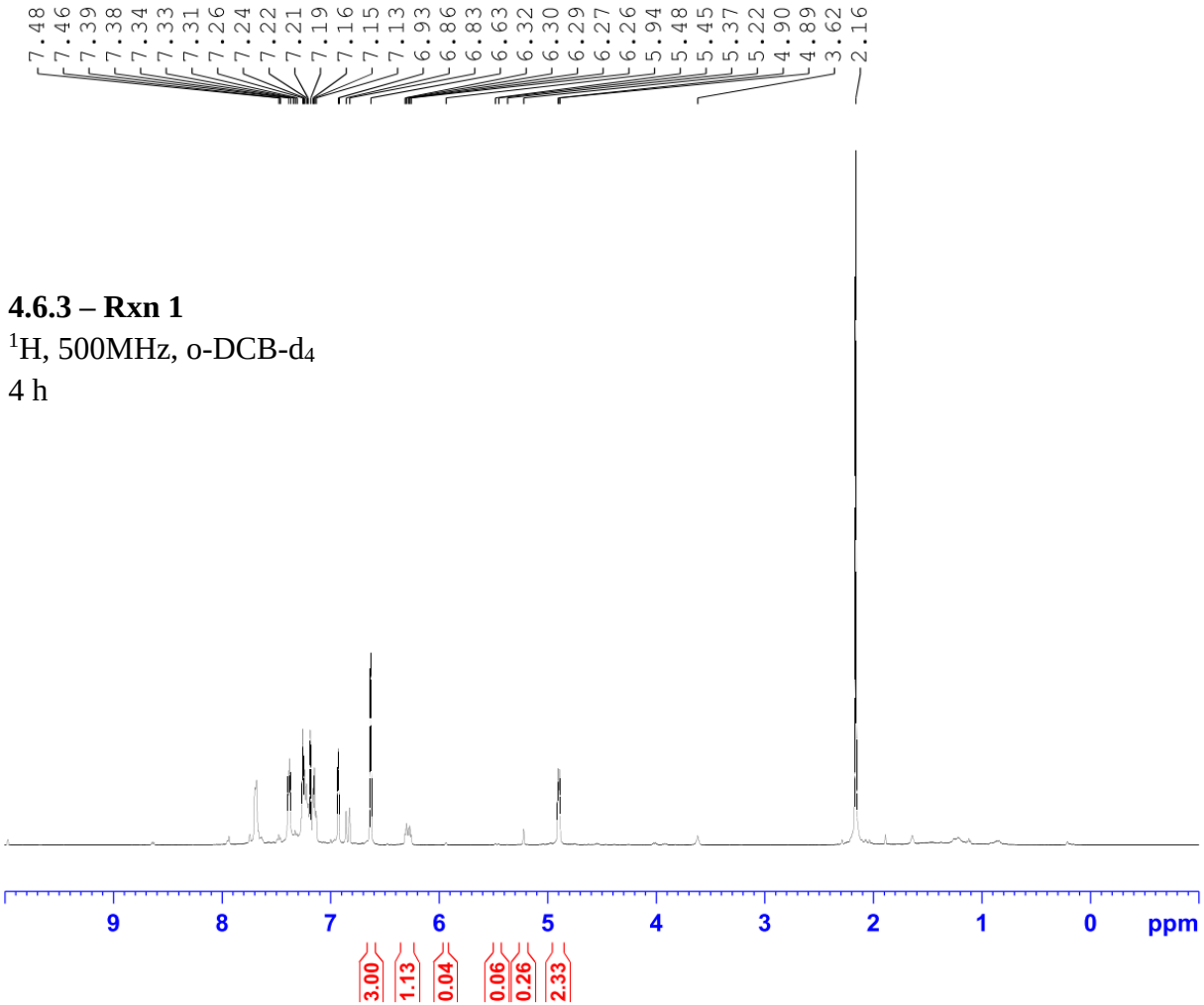



```
Current Data Parameters
NAME          JAW-01-155
EXPNO                 13
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170922
Time               13.23
INSTRUM            spect
PROBHD   5 mm PADUL 13C
PULPROG             zg30
TD                 65536
SOLVENT         oC6D4C12
NS                    32
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ             3.9845889 sec
RG                   128
DW                60.800 usec
DE                 6.50 usec
TE                298.0 K
D1            2.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                  9.31 usec
PL1                -3.90 dB
PL1W         21.64248466 W
SFO1         400.2324716 MHz

F2 - Processing parameters
SI                 32768
SF           400.2279381 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

4.6.3 – Rxn 1

^{1}H, 500MHz, o-DCB-d_4

4 h

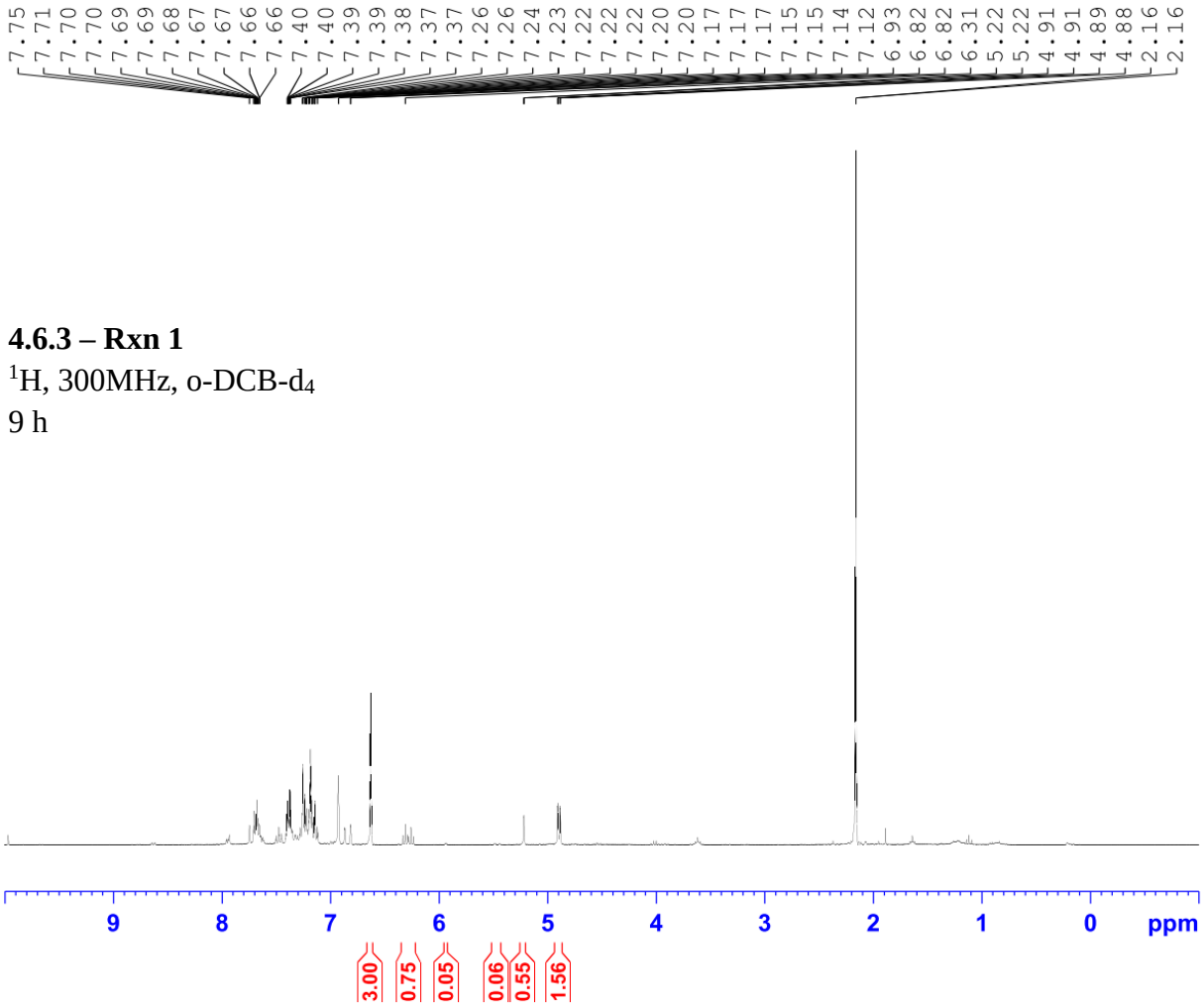



```
Current Data Parameters
NAME          JAW-01-155
EXPNO                 14
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170922
Time              16.57
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG            zg30
TD                65536
SOLVENT            C6D6
NS                    32
DS                     2
SWH           10000.000 Hz
FIDRES         0.152588 Hz
AQ            3.2767999 sec
RG                 90.5
DW               50.000 usec
DE                6.50 usec
TE               297.1 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1        500.1630887 MHz
NUC1                  1H
P1                11.50 usec
PLW1        18.00000000 W

F2 - Processing parameters
SI                65536
SF          500.1599834 MHz
WDW                   EM
SSB      0
LB                 0.30 Hz
GB       0
PC                 1.00
```

4.6.3 – Rxn 1

^{1}H, 300MHz, o-DCB-d$_4$

9 h

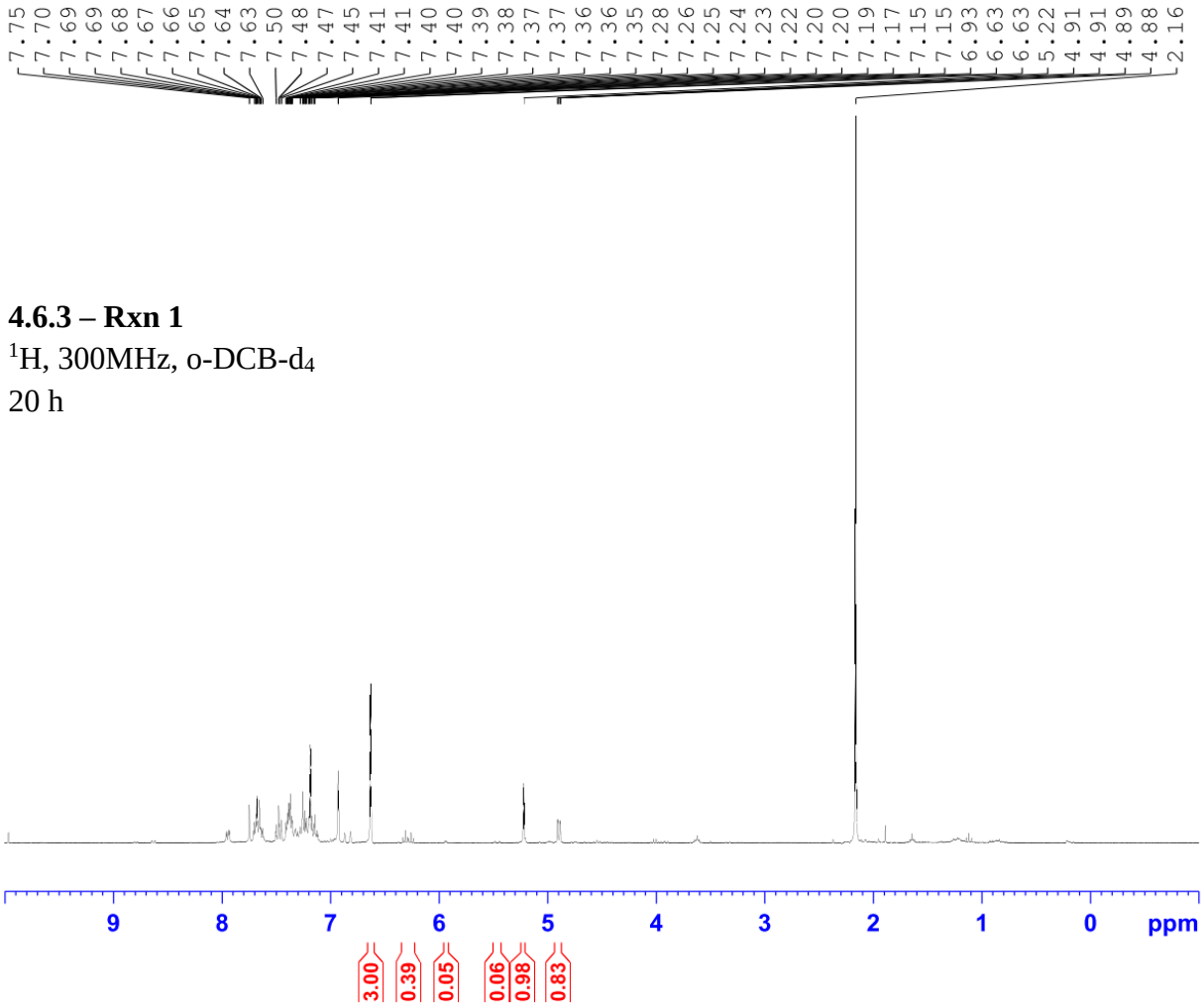



```
Current Data Parameters
NAME          JAW-01-155
EXPNO                 15
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170922
Time               23.20
INSTRUM            spect
PROBHD   5 mm QNP  1H/1
PULPROG             zg30
TD                 32768
SOLVENT             C6D6
NS                    92
DS                     2
SWH             6188.119 Hz
FIDRES          0.188846 Hz
AQ             2.6476543 sec
RG                   322
DW                80.800 usec
DE                  6.50 usec
TE                -925.2 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         300.2318540 MHz
NUC1                  1H
P1                12.71 usec
PLW1         18.19700050 W

F2 - Processing parameters
SI                 32768
SF           300.2300698 MHz
WDW                   EM
SSB       0
LB                 0.10 Hz
GB        0
PC                 1.00
```

4.6.3 – Rxn 1

^{1}H, 300MHz, o-DCB-d_4

20 h

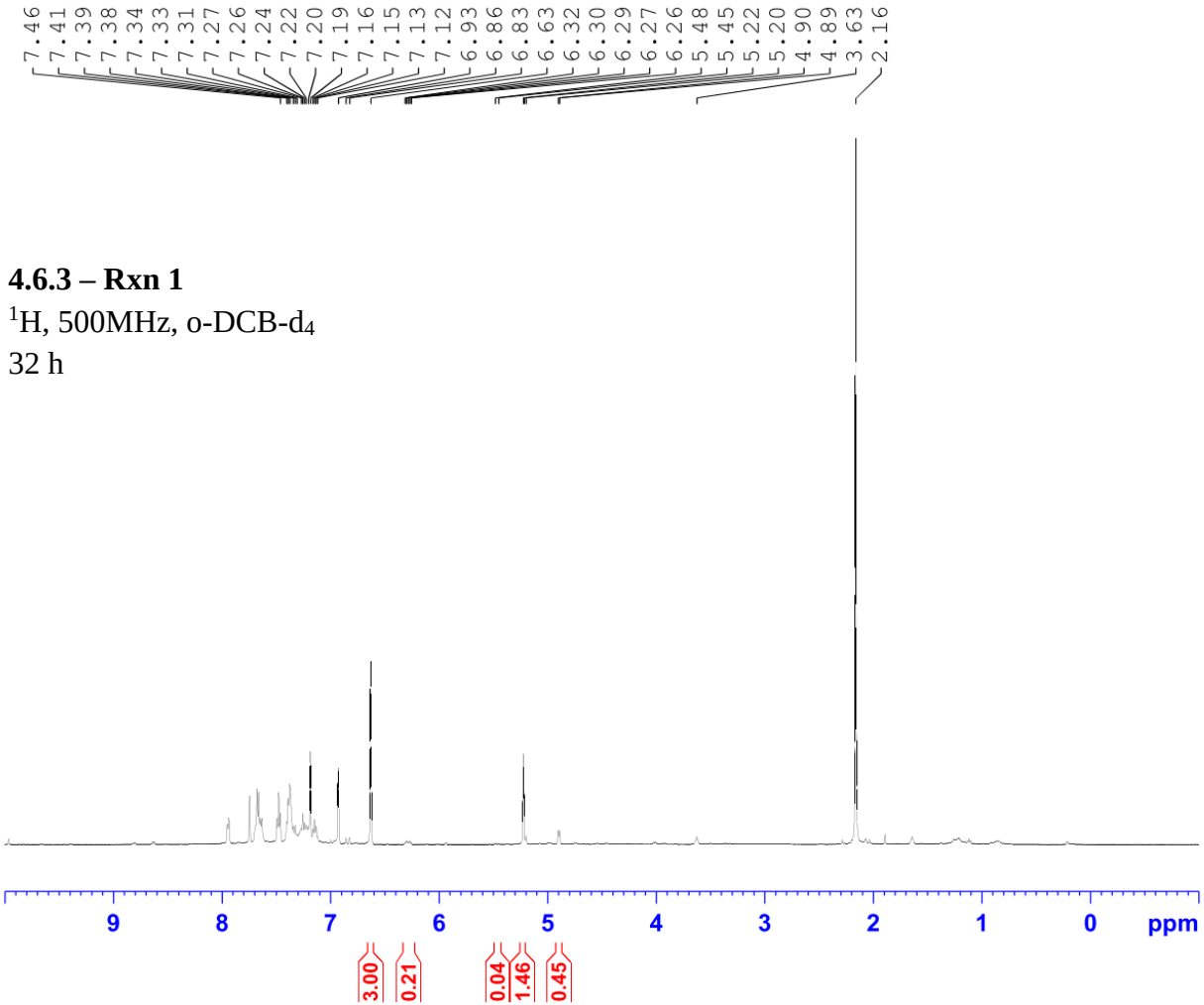



```
Current Data Parameters
NAME          JAW-01-155
EXPNO                 16
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170923
Time               10.45
INSTRUM            spect
PROBHD   5 mm QNP  1H/1
PULPROG             zg30
TD                 32768
SOLVENT             C6D6
NS                    64
DS                     2
SWH             6188.119 Hz
FIDRES          0.188846 Hz
AQ             2.6476543 sec
RG                   322
DW                80.800 usec
DE                  6.50 usec
TE                -923.5 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         300.2318540 MHz
NUC1                  1H
P1                 12.71 usec
PLW1         18.19700050 W

F2 - Processing parameters
SI                 32768
SF           300.2300692 MHz
WDW                   EM
SSB       0
LB                  0.10 Hz
GB        0
PC                  1.00
```

4.6.3 – Rxn 1

^{1}H, 500MHz, o-DCB-d$_4$

32 h

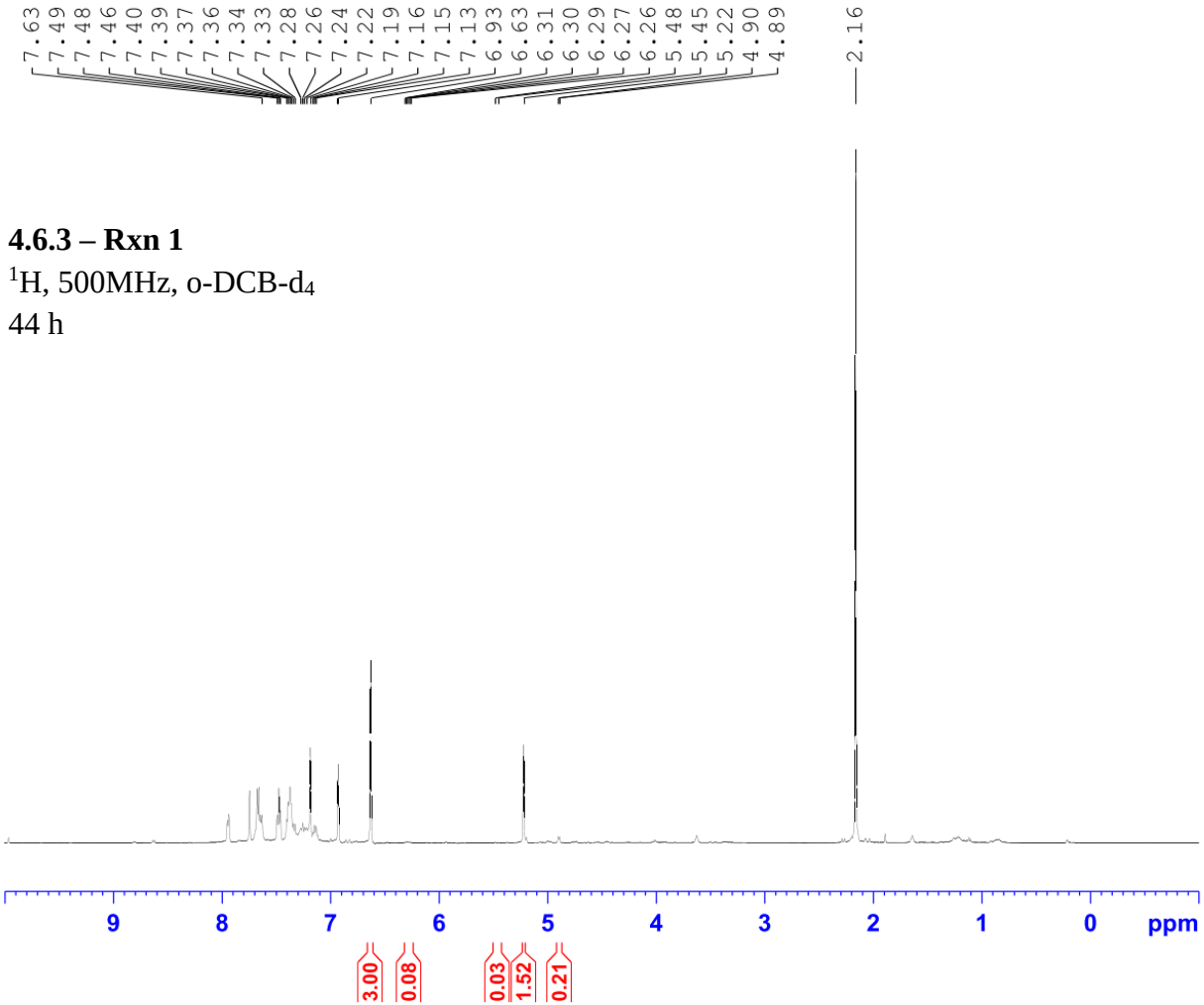



```
Current Data Parameters
NAME          JAW-01-155
EXPNO                 17
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170923
Time              23.05
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG            zg30
TD                65536
SOLVENT            C6D6
NS                    64
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                  90.5
DW                50.000 usec
DE                  6.50 usec
TE                 296.5 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                  1H
P1                 11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                65536
SF           500.1601163 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.3 – Rxn 1

^{1}H, 500MHz, o-DCB-d$_4$

44 h

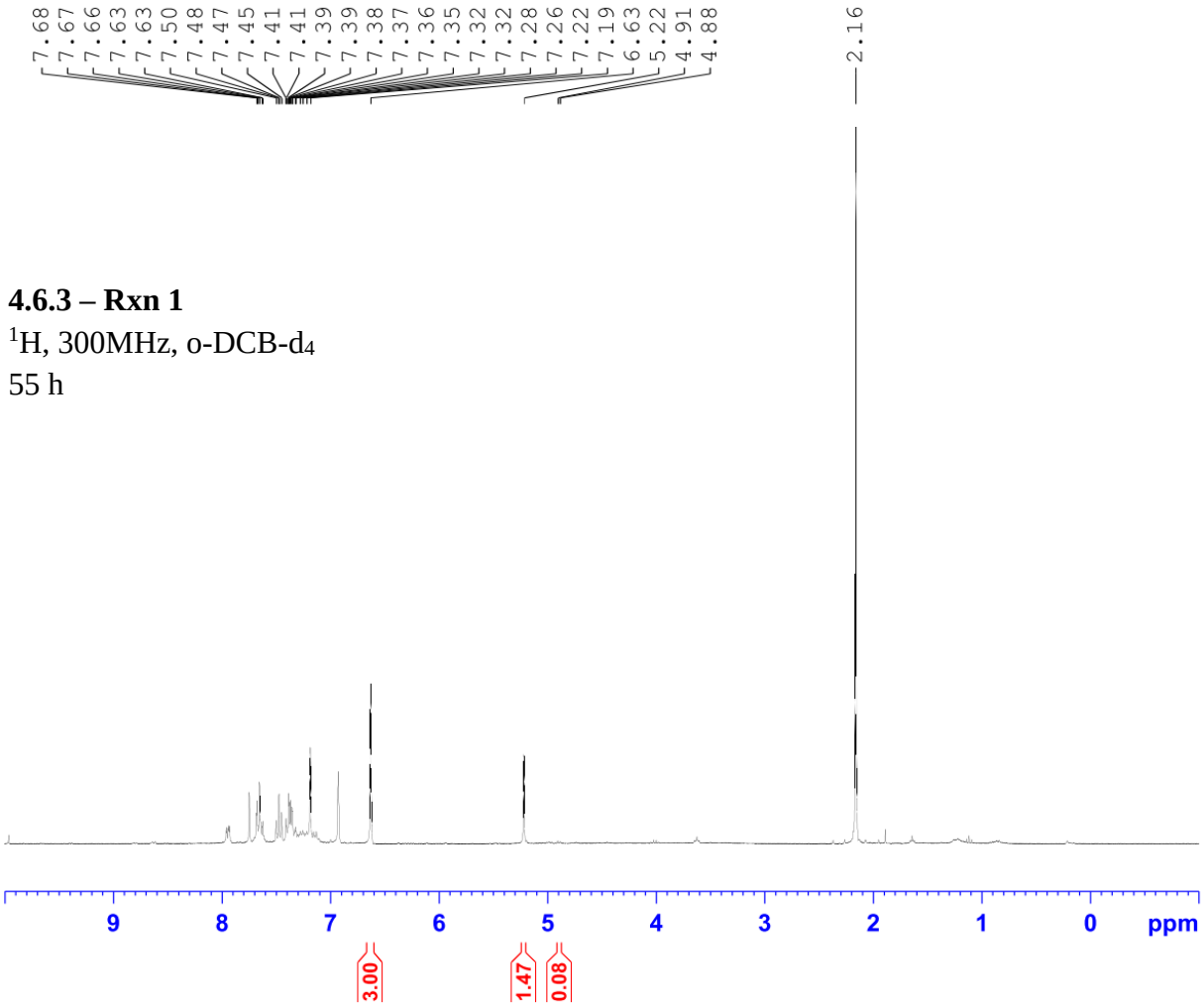



```
Current Data Parameters
NAME          JAW-01-155
EXPNO                 18
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170924
Time               11.04
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT             C6D6
NS                    64
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                  90.5
DW                50.000 usec
DE                 6.50 usec
TE                296.6 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                  1H
P1                11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1601138 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.3 – Rxn 1

^{1}H, 300MHz, o-DCB-d_4

55 h

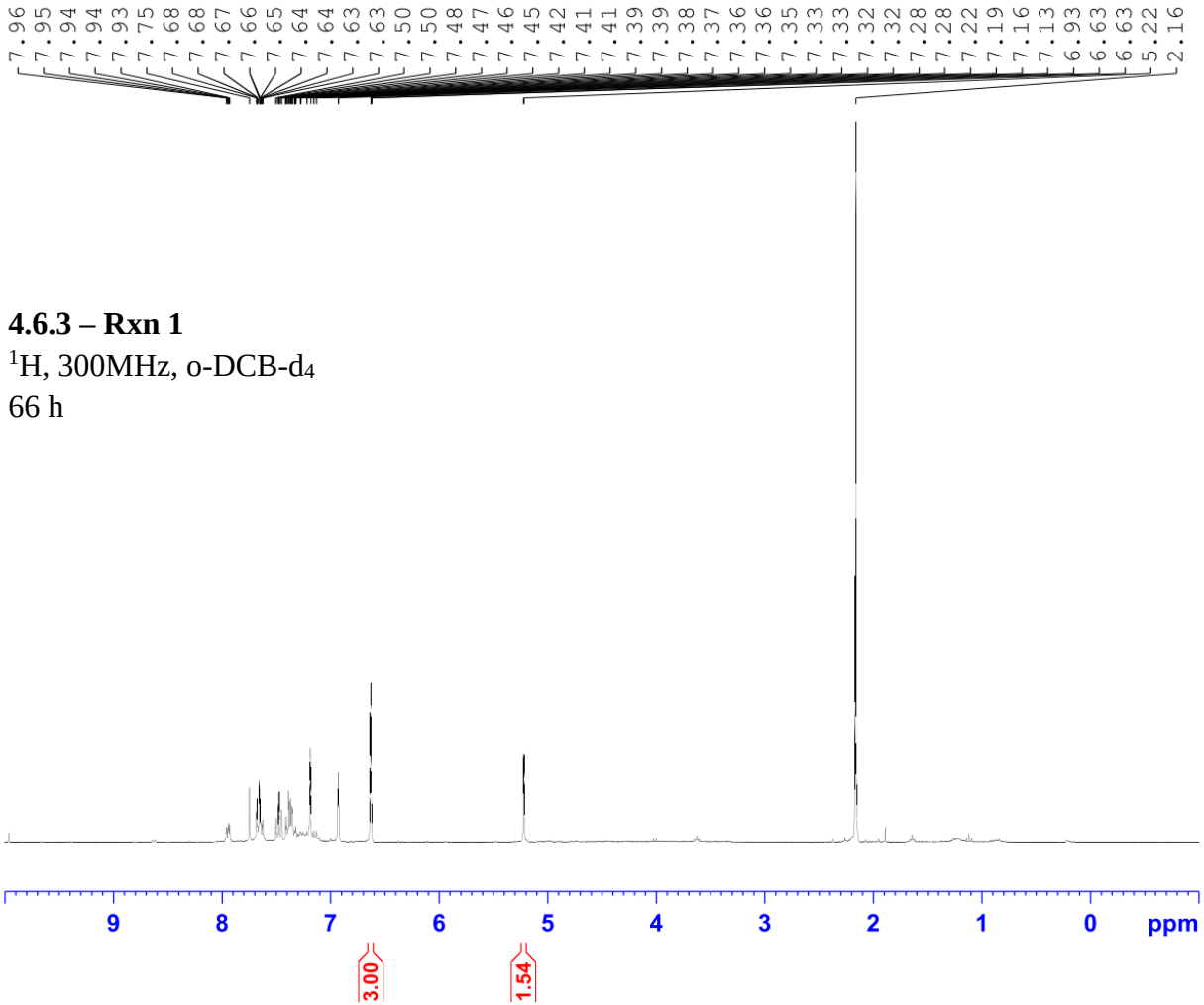



```
Current Data Parameters
NAME          JAW-01-155
EXPNO                 19
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170924
Time               22.55
INSTRUM            spect
PROBHD   5 mm QNP  1H/1
PULPROG             zg30
TD                 32768
SOLVENT             C6D6
NS                    64
DS                     2
SWH             6188.119 Hz
FIDRES          0.188846 Hz
AQ            2.6476543 sec
RG                  322
DW               80.800 usec
DE                 6.50 usec
TE               -924.2 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1        300.2318540 MHz
NUC1                  1H
P1                12.71 usec
PLW1        18.19700050 W

F2 - Processing parameters
SI                 32768
SF          300.2300693 MHz
WDW                   EM
SSB      0
LB                 0.10 Hz
GB       0
PC                 1.00
```

4.6.3 – Rxn 1

^{1}H, 300MHz, o-DCB-d$_4$

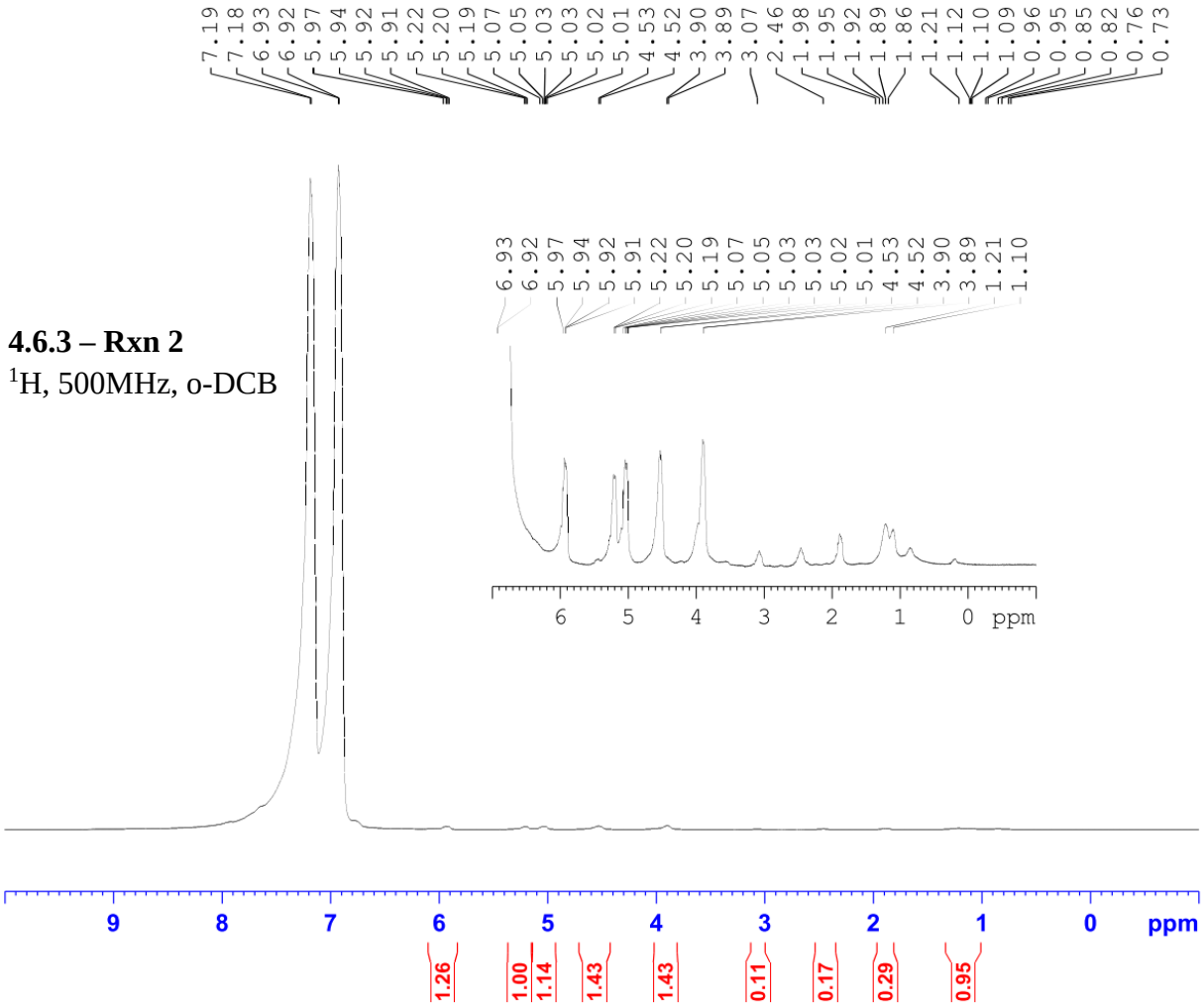
66 h




```
Current Data Parameters
NAME          JAW-01-155
EXPNO                 20
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170925
Time                9.57
INSTRUM            spect
PROBHD   5 mm QNP  1H/1
PULPROG             zg30
TD                 32768
SOLVENT             C6D6
NS                    64
DS                     2
SWH             6188.119 Hz
FIDRES          0.188846 Hz
AQ             2.6476543 sec
RG                   322
DW                80.800 usec
DE                  6.50 usec
TE                -925.0 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         300.2318540 MHz
NUC1                  1H
P1                 12.71 usec
PLW1         18.19700050 W

F2 - Processing parameters
SI                 32768
SF           300.2300688 MHz
WDW                   EM
SSB       0
LB                  0.10 Hz
GB        0
PC                  1.00
```

4.6.3 – Rxn 2

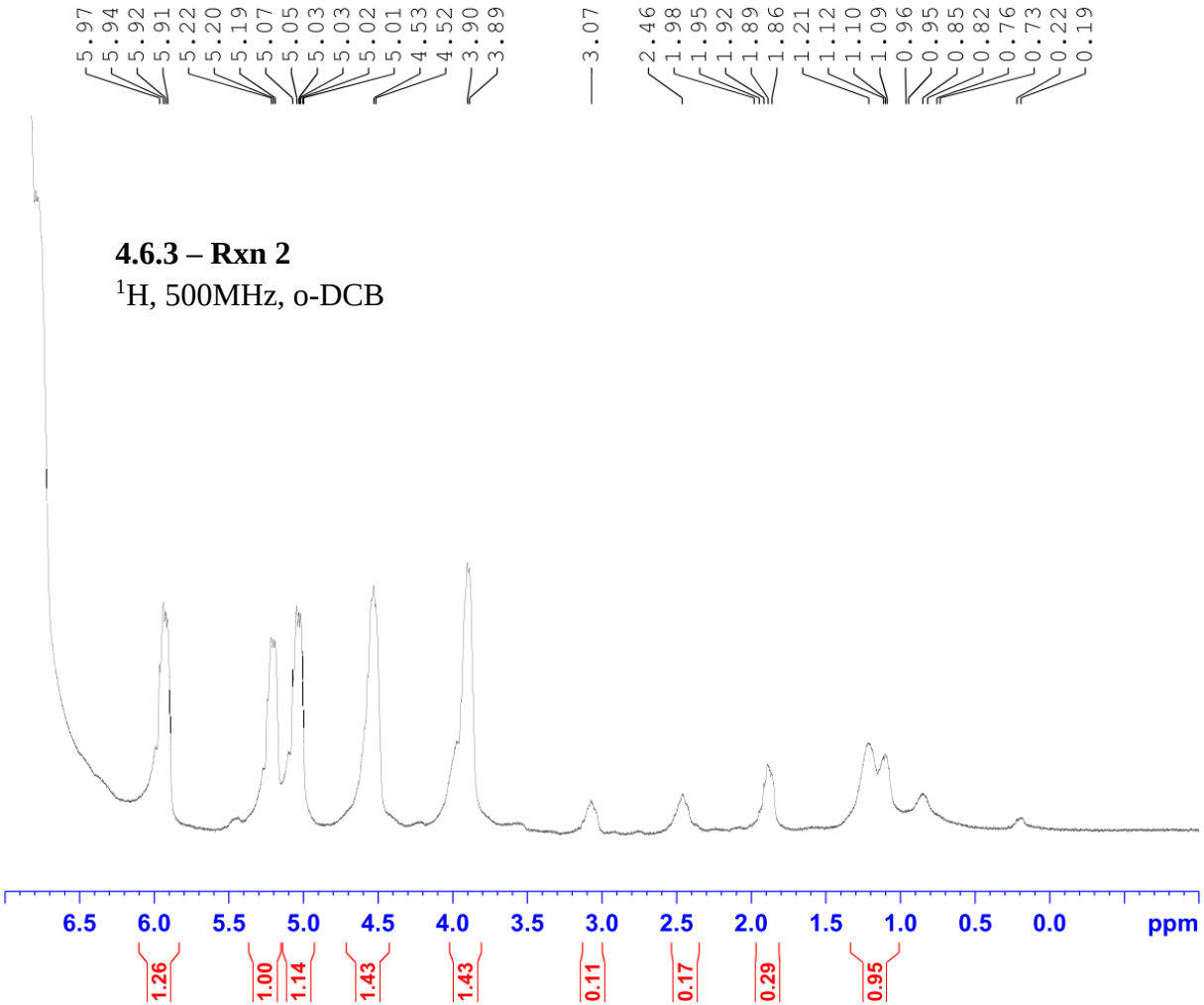
^{1}H, 500MHz, o-DCB




```
Current Data Parameters
NAME          JAW-01-143
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170831
Time               17.21
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT             None
NS                    16
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                  6.35
DW                50.000 usec
DE                  6.50 usec
TE                 296.1 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                  1H
P1                 11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1597941 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

4.6.3 – Rxn 2

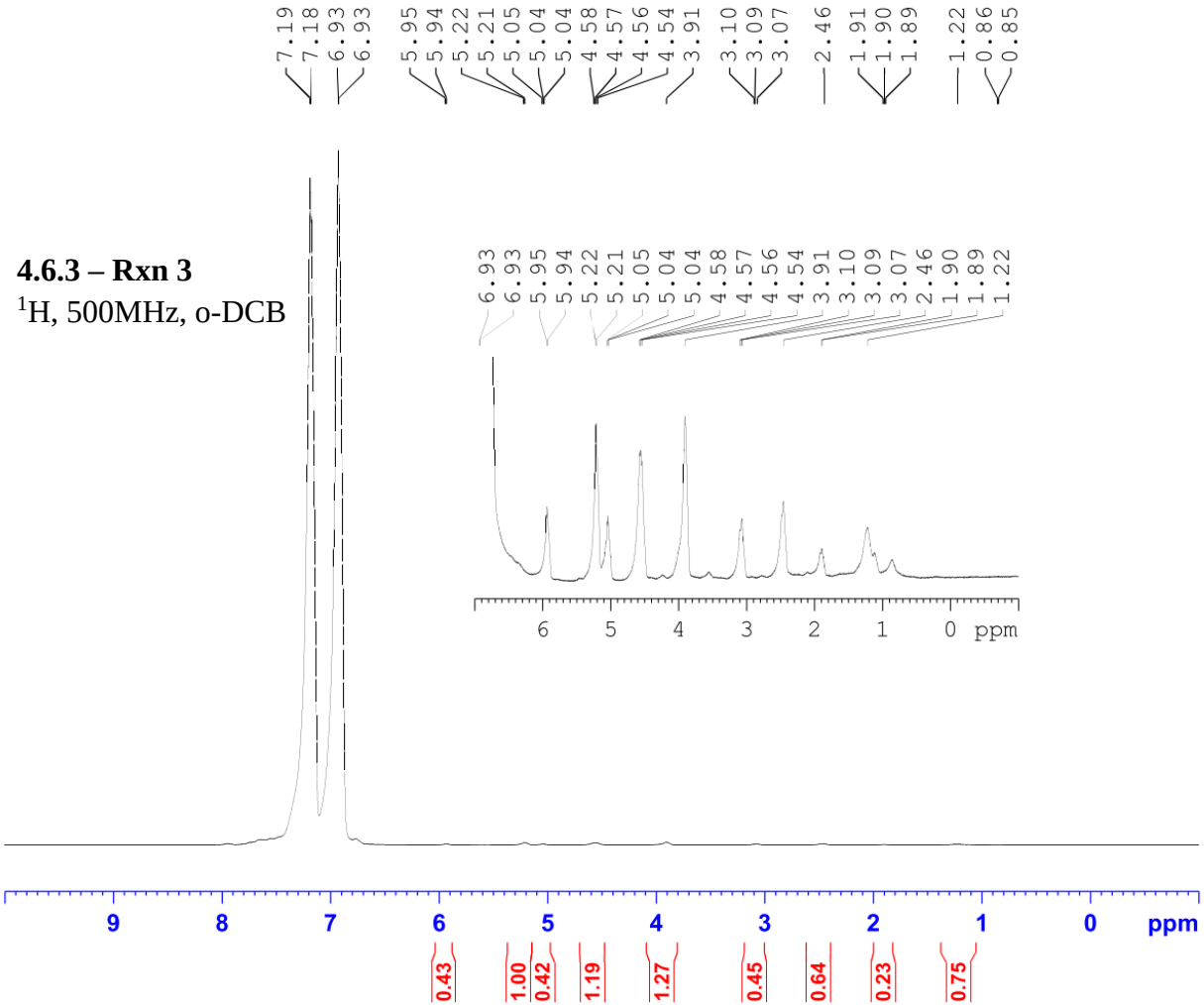
^{1}H, 500MHz, o-DCB




```
Current Data Parameters
NAME          JAW-01-143
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170831
Time               17.21
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT             None
NS                    16
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                  6.35
DW                50.000 usec
DE                  6.50 usec
TE                 296.1 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                  1H
P1                 11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1597941 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

4.6.3 – Rxn 3

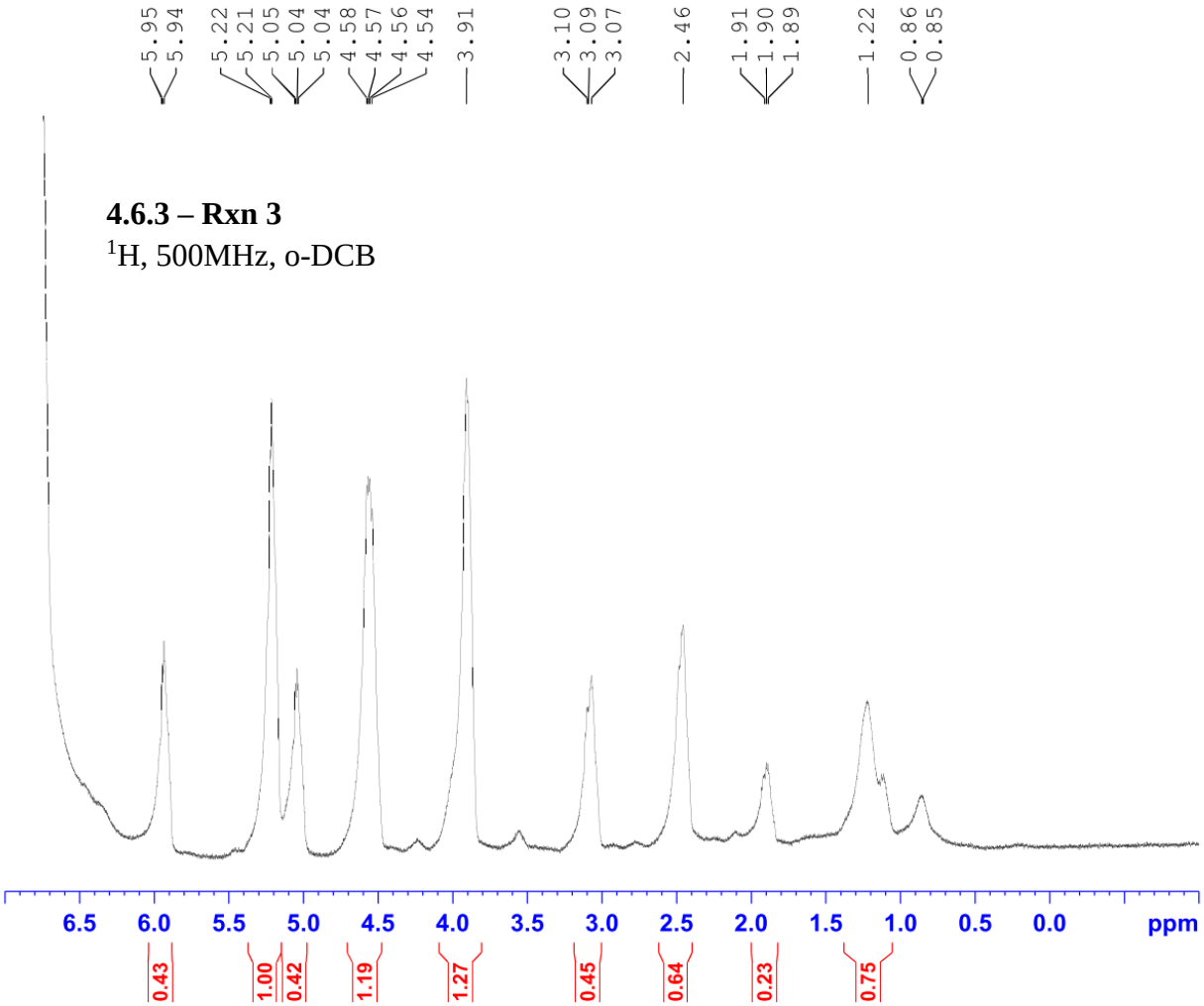
^{1}H, 500MHz, o-DCB




```
Current Data Parameters
NAME          JAW-01-144
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170901
Time               14.20
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT             None
NS                    16
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                  6.35
DW                50.000 usec
DE                 6.50 usec
TE                296.5 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                  1H
P1                11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1597306 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.3 – Rxn 3

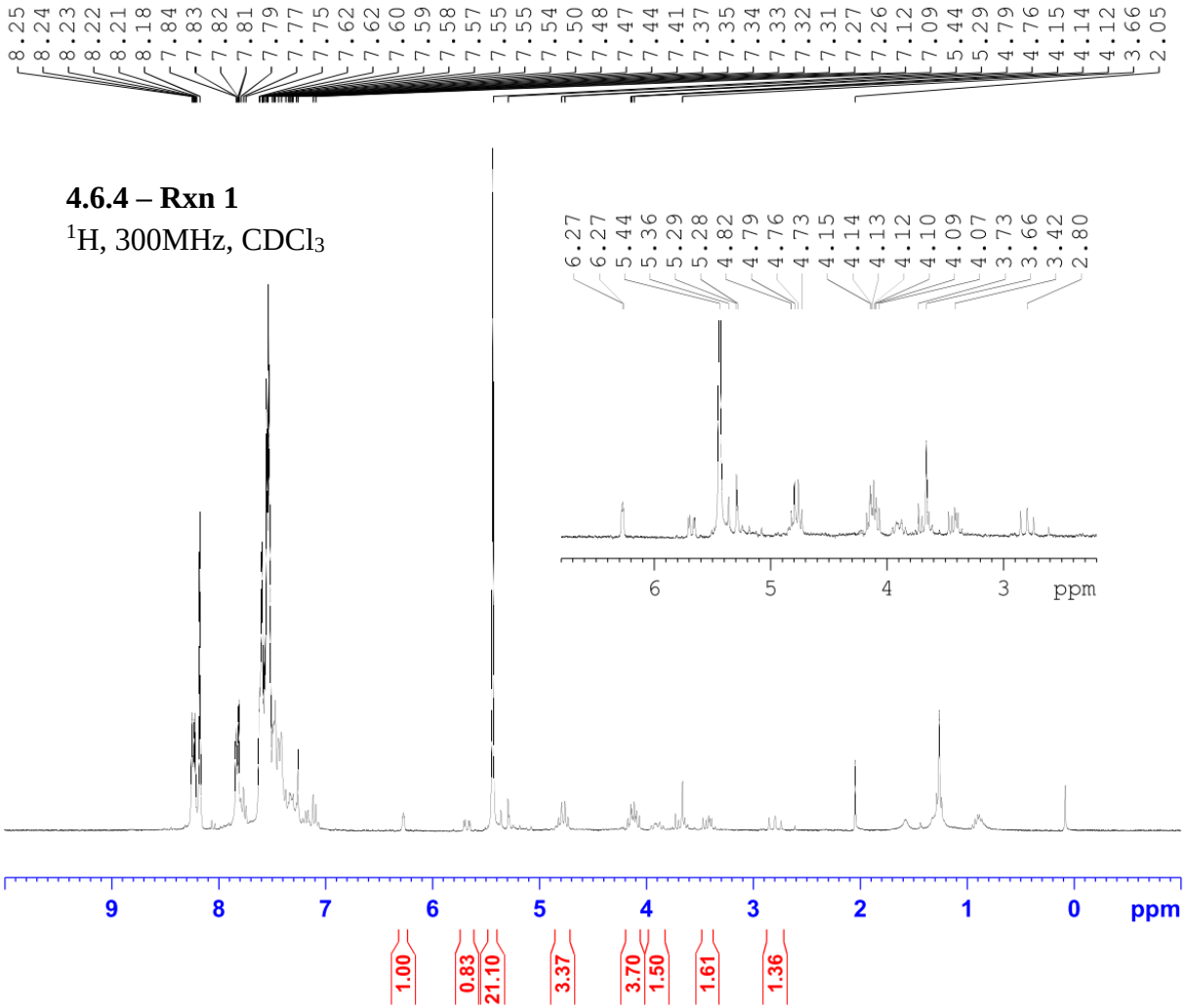
^{1}H, 500MHz, o-DCB




```
Current Data Parameters
NAME          JAW-01-144
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170901
Time               14.20
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT             None
NS                    16
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                  6.35
DW                50.000 usec
DE                 6.50 usec
TE                296.5 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                  1H
P1                11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1597306 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.4 – Rxn 1

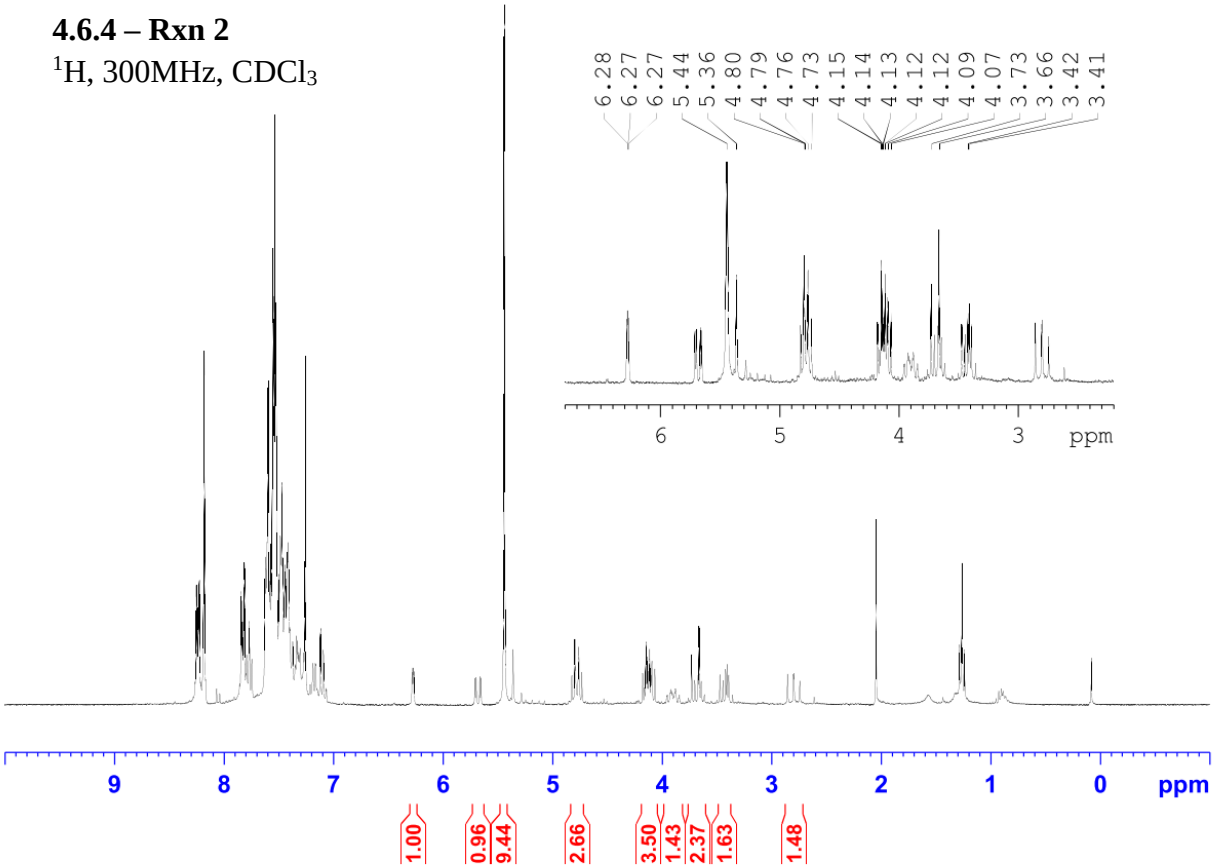
^{1}H, 300MHz, $CDCl_3$




```
Current Data Parameters
NAME          JAW-02-160
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20181022
Time               15.40
INSTRUM            spect
PROBHD   5 mm QNP  1H/1
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             6188.119 Hz
FIDRES          0.188846 Hz
AQ             2.6476543 sec
RG                   128
DW                80.800 usec
DE                  6.50 usec
TE                -925.3 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         300.2318540 MHz
NUC1                  1H
P1                 12.71 usec
PLW1         18.19700050 W

F2 - Processing parameters
SI                 32768
SF           300.2300086 MHz
WDW                   EM
SSB       0
LB                  0.10 Hz
GB        0
PC                  1.00
```

4.6.4 – Rxn 2

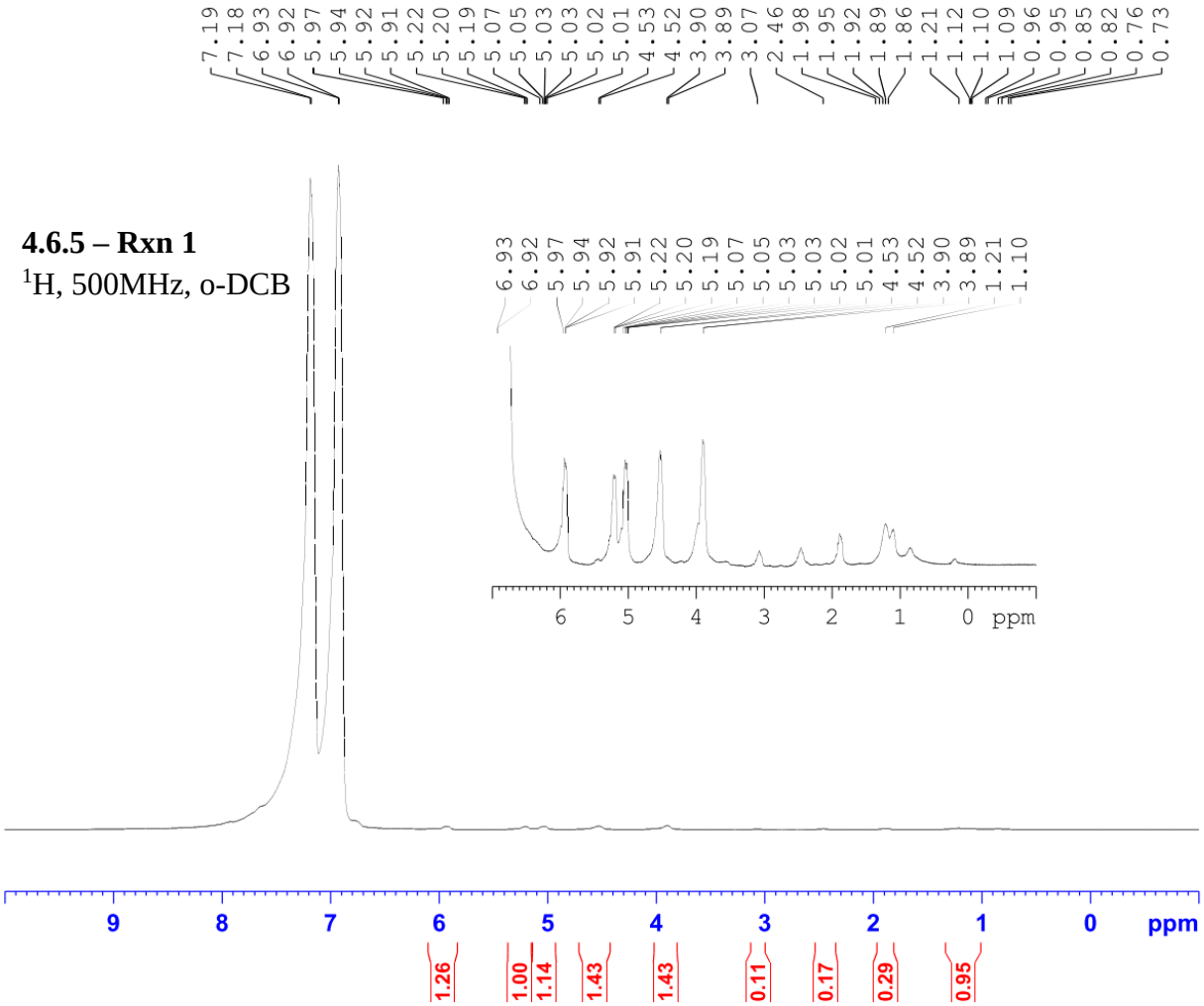
^{1}H, 300MHz, $CDCl_3$




```
Current Data Parameters
NAME          JAW-02-161
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20181022
Time              19.45
INSTRUM           spect
PROBHD   5 mm QNP  1H/1
PULPROG            zg30
TD                32768
SOLVENT           CDCl3
NS                   32
DS                    2
SWH            6188.119 Hz
FIDRES         0.188846 Hz
AQ            2.6476543 sec
RG                  144
DW               80.800 usec
DE                 6.50 usec
TE               -923.2 K
D1           1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1        300.2318540 MHz
NUC1                 1H
P1                12.71 usec
PLW1        18.19700050 W

F2 - Processing parameters
SI                32768
SF          300.2300086 MHz
WDW                  EM
SSB      0
LB                0.10 Hz
GB       0
PC                1.00
```

4.6.5 – Rxn 1

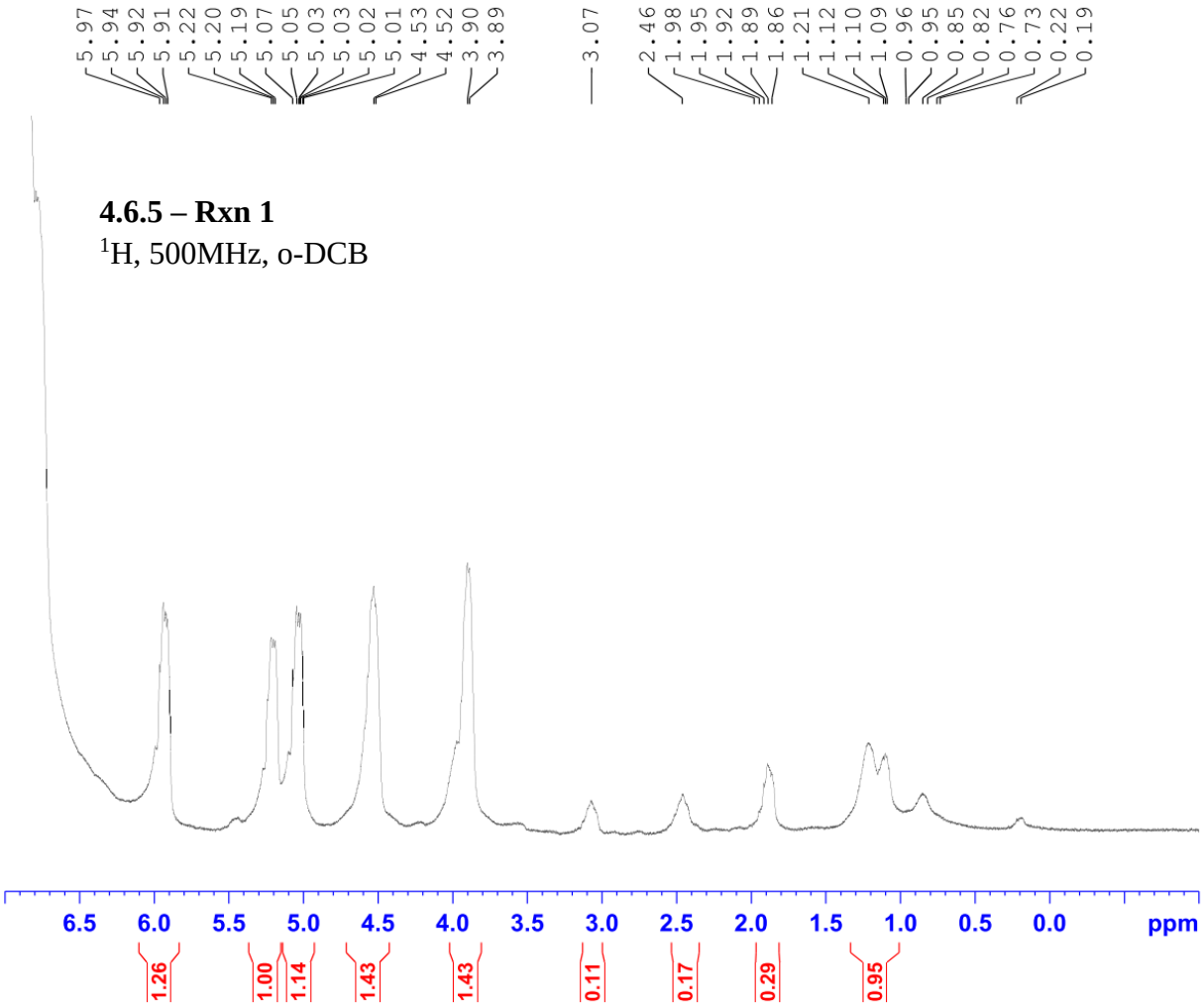
^{1}H, 500MHz, o-DCB



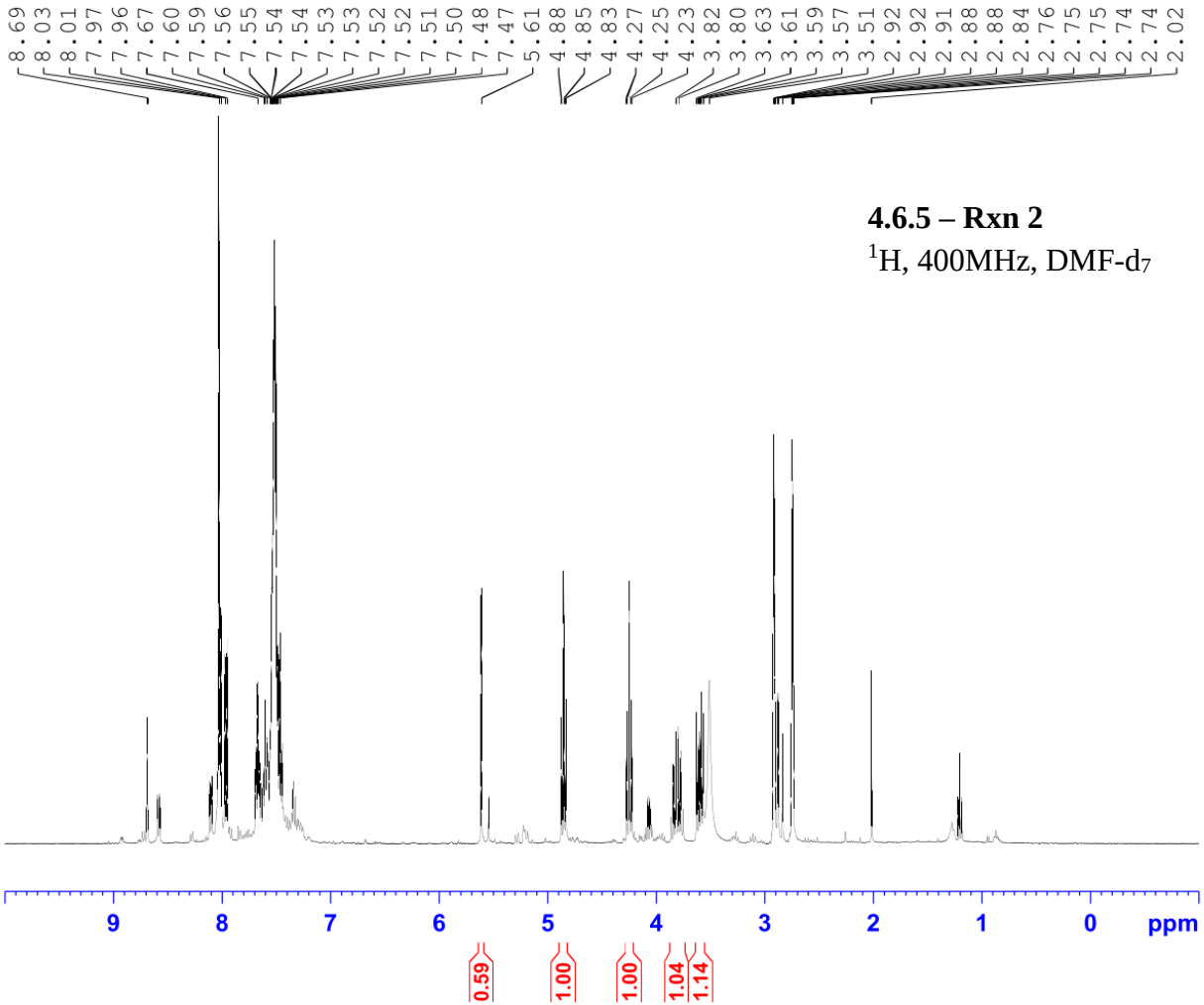

```
Current Data Parameters
NAME          JAW-01-143
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170831
Time               17.21
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT             None
NS                    16
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                  6.35
DW                50.000 usec
DE                 6.50 usec
TE                296.1 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                  1H
P1                11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1597941 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.5 – Rxn 1

^{1}H, 500MHz, o-DCB




```
Current Data Parameters
NAME          JAW-01-143
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170831
Time               17.21
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT             None
NS                    16
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                  6.35
DW                50.000 usec
DE                  6.50 usec
TE                 296.1 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                  1H
P1                 11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1597941 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```



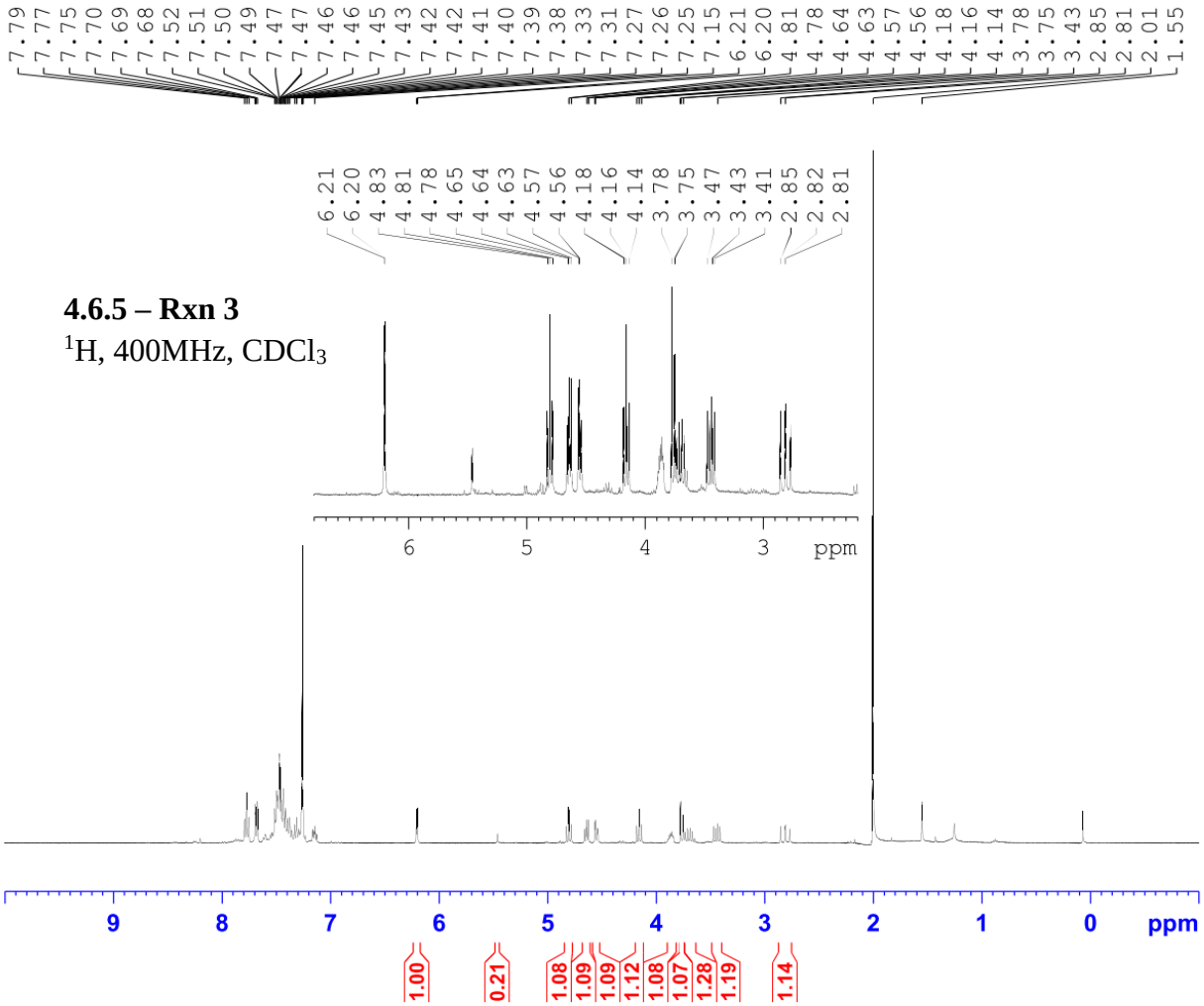
4.6.5 – Rxn 2

^{1}H, 400MHz, DMF-d_7

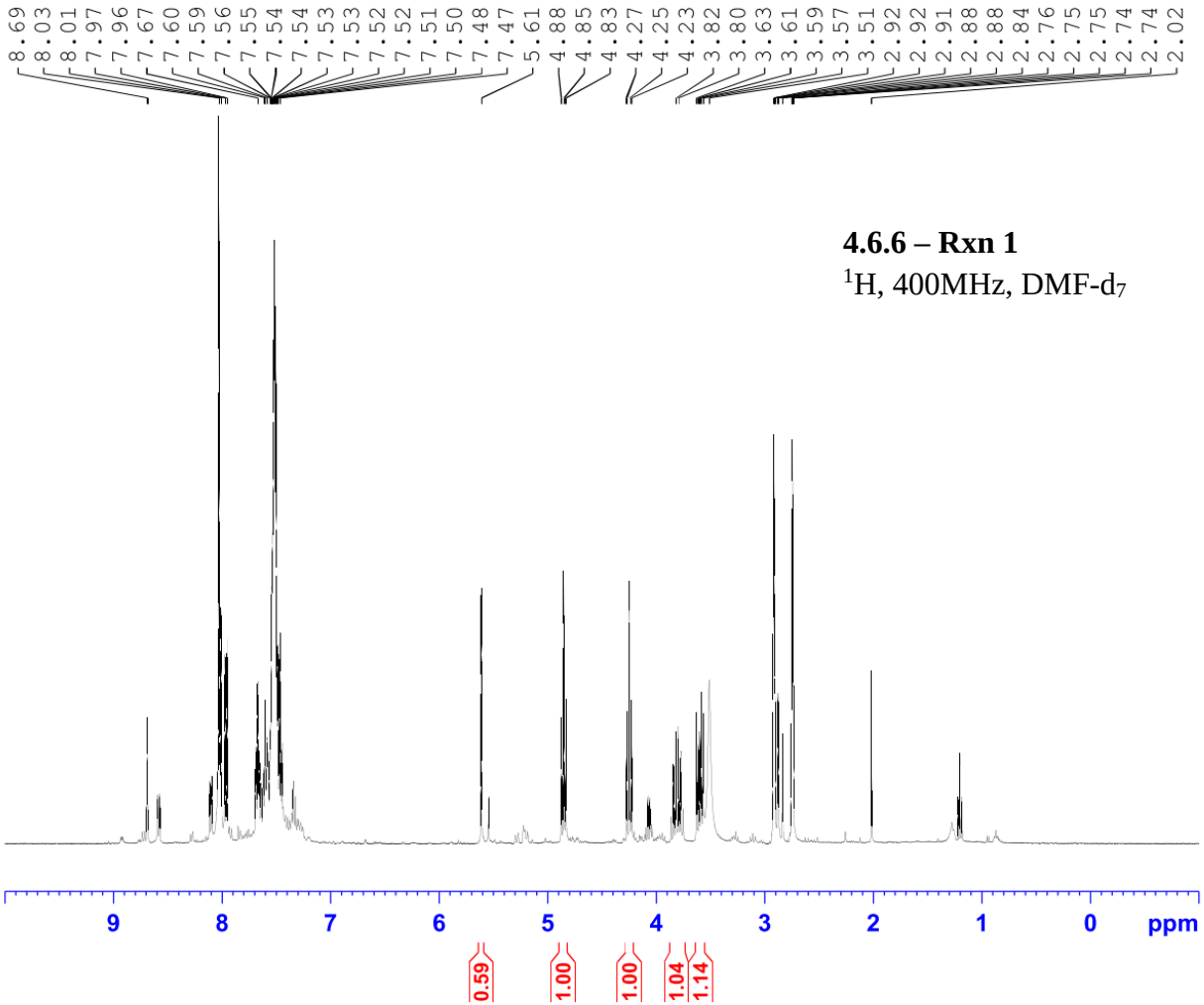
```
Current Data Parameters
NAME          JAW-01-174
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20171024
Time               17.24
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT              DMF
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.122266 Hz
AQ            4.0894465 sec
RG                 90.5
DW               62.400 usec
DE                6.50 usec
TE              -2372.0 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1        400.1324710 MHz
NUC1                  1H
P1                13.75 usec
PLW1        12.01700020 W

F2 - Processing parameters
SI                 65536
SF          400.1300735 MHz
WDW                   EM
SSB      0
LB                 0.30 Hz
GB       0
PC                 1.00
```

4.6.5 – Rxn 3

^{1}H, 400MHz, $CDCl_3$




```
Current Data Parameters
NAME          JAW-02-035
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180330
Time               16.02
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.122266 Hz
AQ             4.0894465 sec
RG                   128
DW                62.400 usec
DE                 6.50 usec
TE               2466.6 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         400.1324710 MHz
NUC1                  1H
P1                14.50 usec
PLW1         12.01700020 W

F2 - Processing parameters
SI                 65536
SF           400.1300101 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



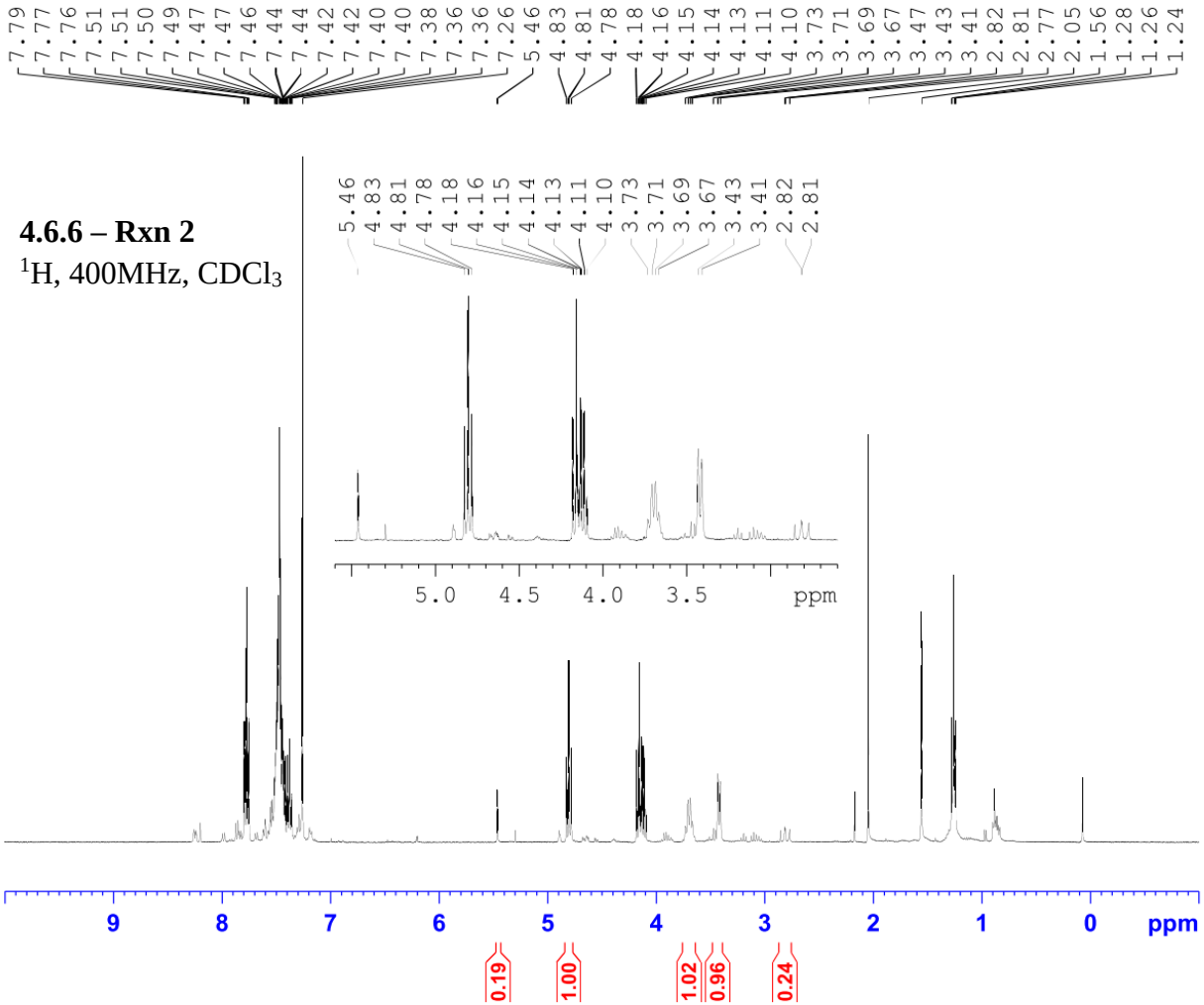
4.6.6 – Rxn 1

^{1}H, 400MHz, DMF-d_7

```
Current Data Parameters
NAME          JAW-01-174
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20171024
Time               17.24
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT              DMF
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.122266 Hz
AQ             4.0894465 sec
RG                  90.5
DW                62.400 usec
DE                 6.50 usec
TE              -2372.0 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1        400.1324710 MHz
NUC1                  1H
P1                13.75 usec
PLW1        12.01700020 W

F2 - Processing parameters
SI                 65536
SF          400.1300735 MHz
WDW                   EM
SSB      0
LB                 0.30 Hz
GB       0
PC                 1.00
```

4.6.6 – Rxn 2

^{1}H, 400MHz, $CDCl_3$

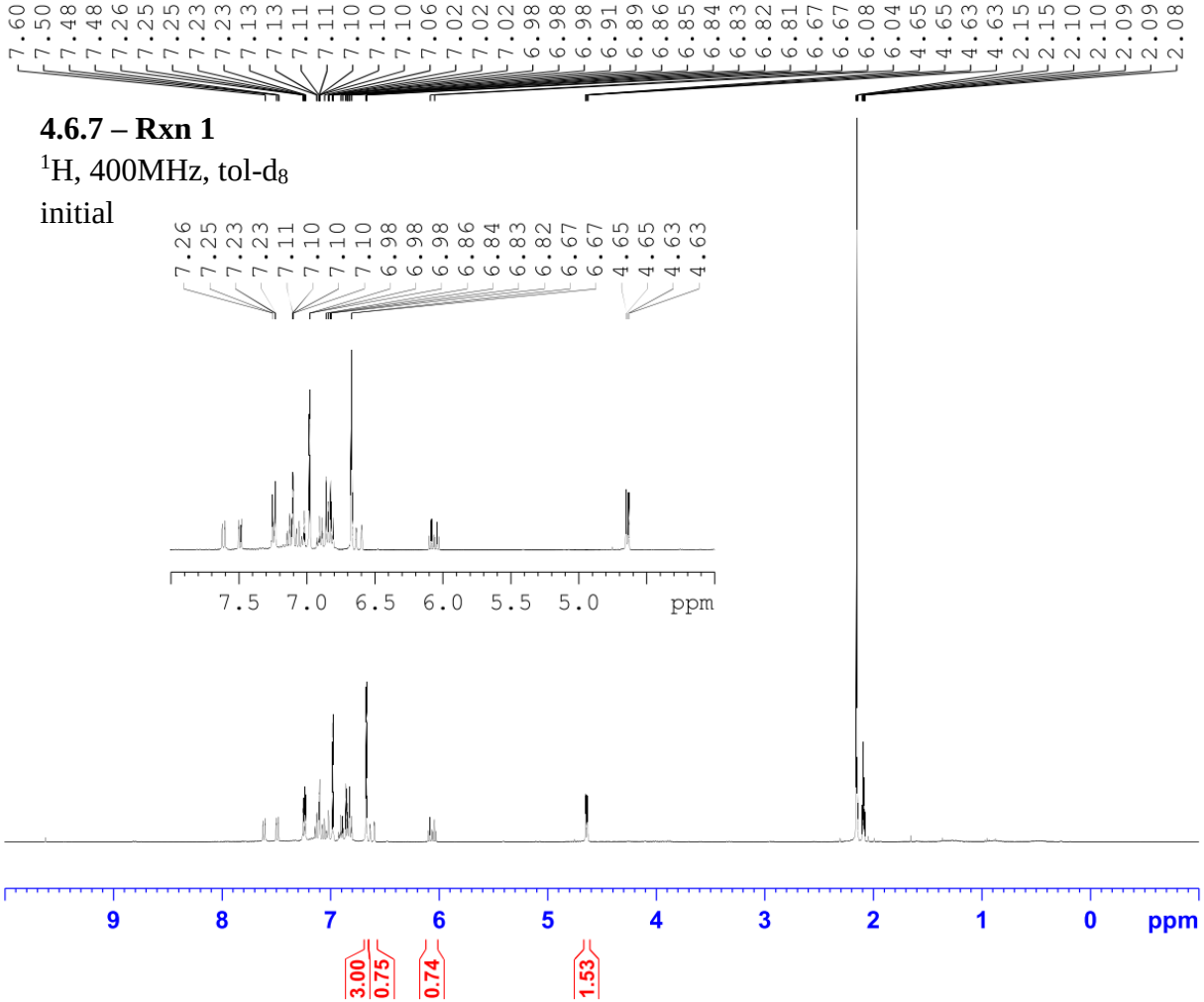



```
Current Data Parameters
NAME          JAW-01-173
EXPNO                  6
PROCNO                 1

F2 - Acquisition Parameters
Date_           20171025
Time               15.59
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.122266 Hz
AQ             4.0894465 sec
RG                   128
DW                62.400 usec
DE                  6.50 usec
TE               -2720.7 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         400.1324710 MHz
NUC1                  1H
P1                 13.75 usec
PLW1         12.01700020 W

F2 - Processing parameters
SI                 65536
SF           400.1300107 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

4.6.7 – Rxn 1

^{1}H, 400MHz, tol-d_8

initial

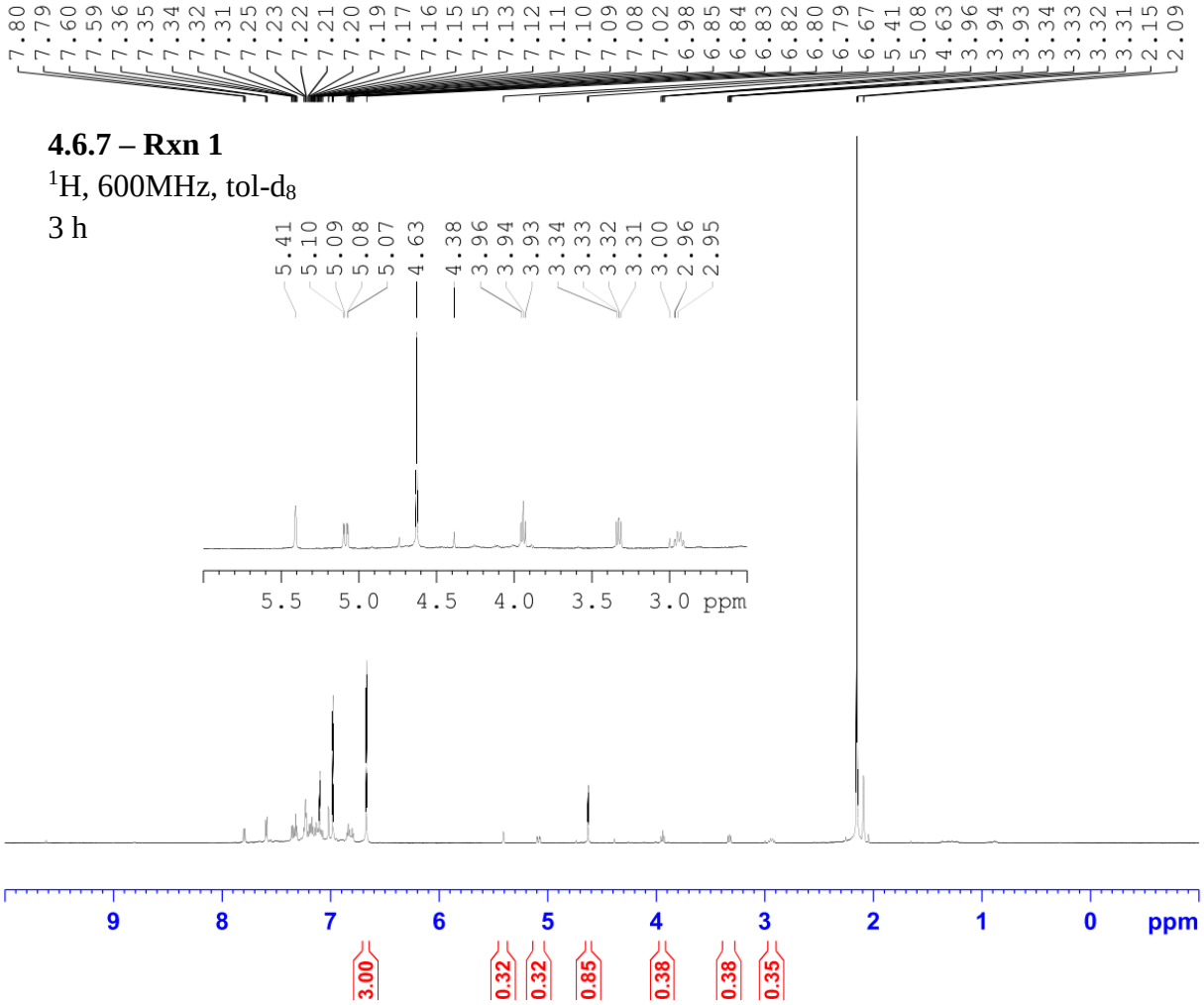



```
Current Data Parameters
NAME          JAW-03-070
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191121
Time               12.20
INSTRUM            spect
PROBHD   5 mm PADUL 13C
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ             3.9845889 sec
RG                   101
DW                60.800 usec
DE                 6.50 usec
TE                298.2 K
D1            2.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                  9.31 usec
PL1                -3.90 dB
PL1W         21.64248466 W
SFO1         400.2324716 MHz

F2 - Processing parameters
SI                 32768
SF          400.2300165 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.7 – Rxn 1

^{1}H, 600MHz, tol-d_8

3 h

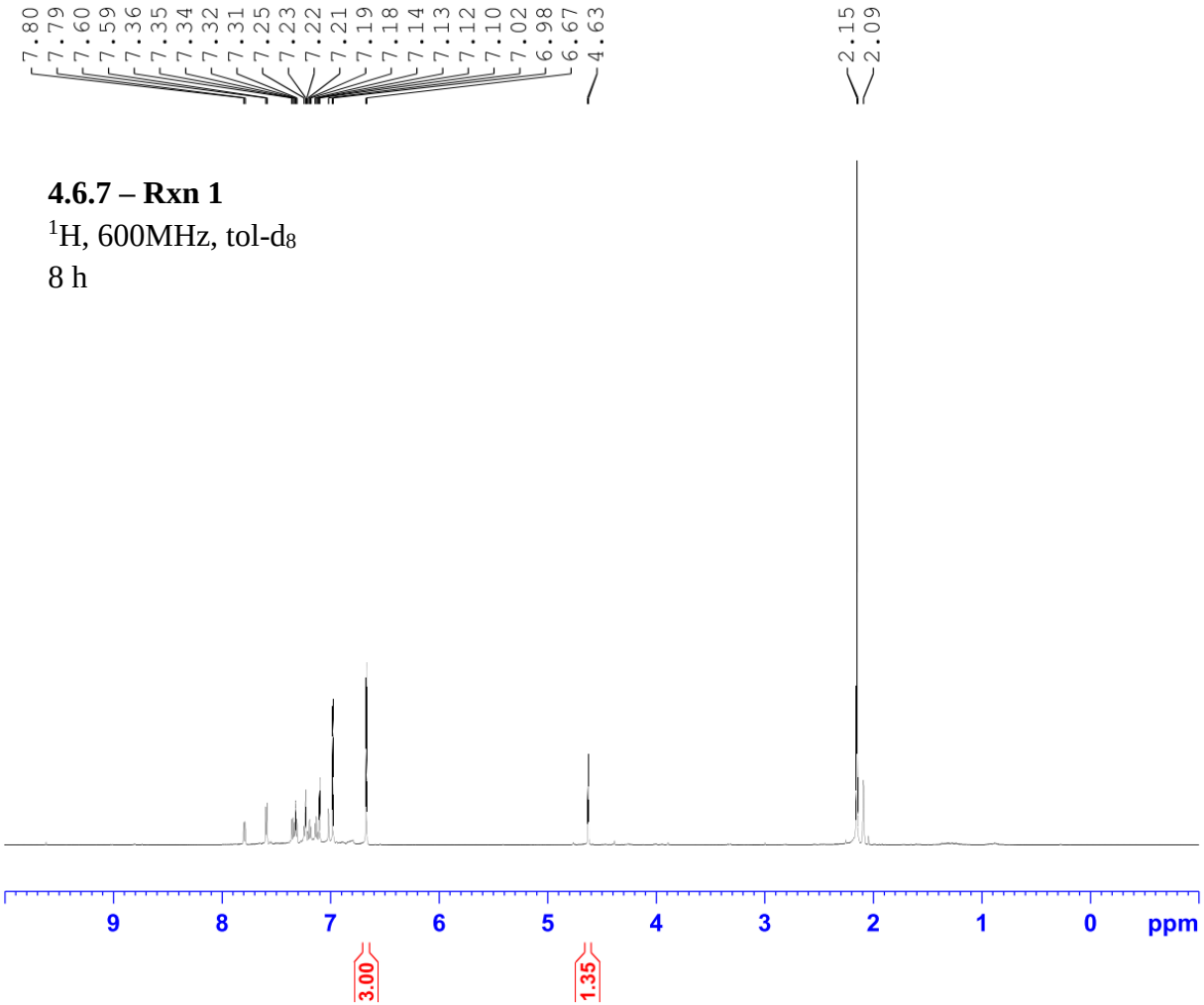



```
Current Data Parameters
NAME          JAW-03-070
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191121
Time               16.37
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH            12335.526 Hz
FIDRES          0.188225 Hz
AQ             2.6563926 sec
RG                    64
DW                40.533 usec
DE                  6.50 usec
TE                 295.2 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 10.86 usec
PL1                -2.00 dB
PL1W        19.70630455 W
SFO1        600.7137096 MHz

F2 - Processing parameters
SI                 32768
SF          600.7100223 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

4.6.7 – Rxn 1

^{1}H, 600MHz, tol-d_8

8 h

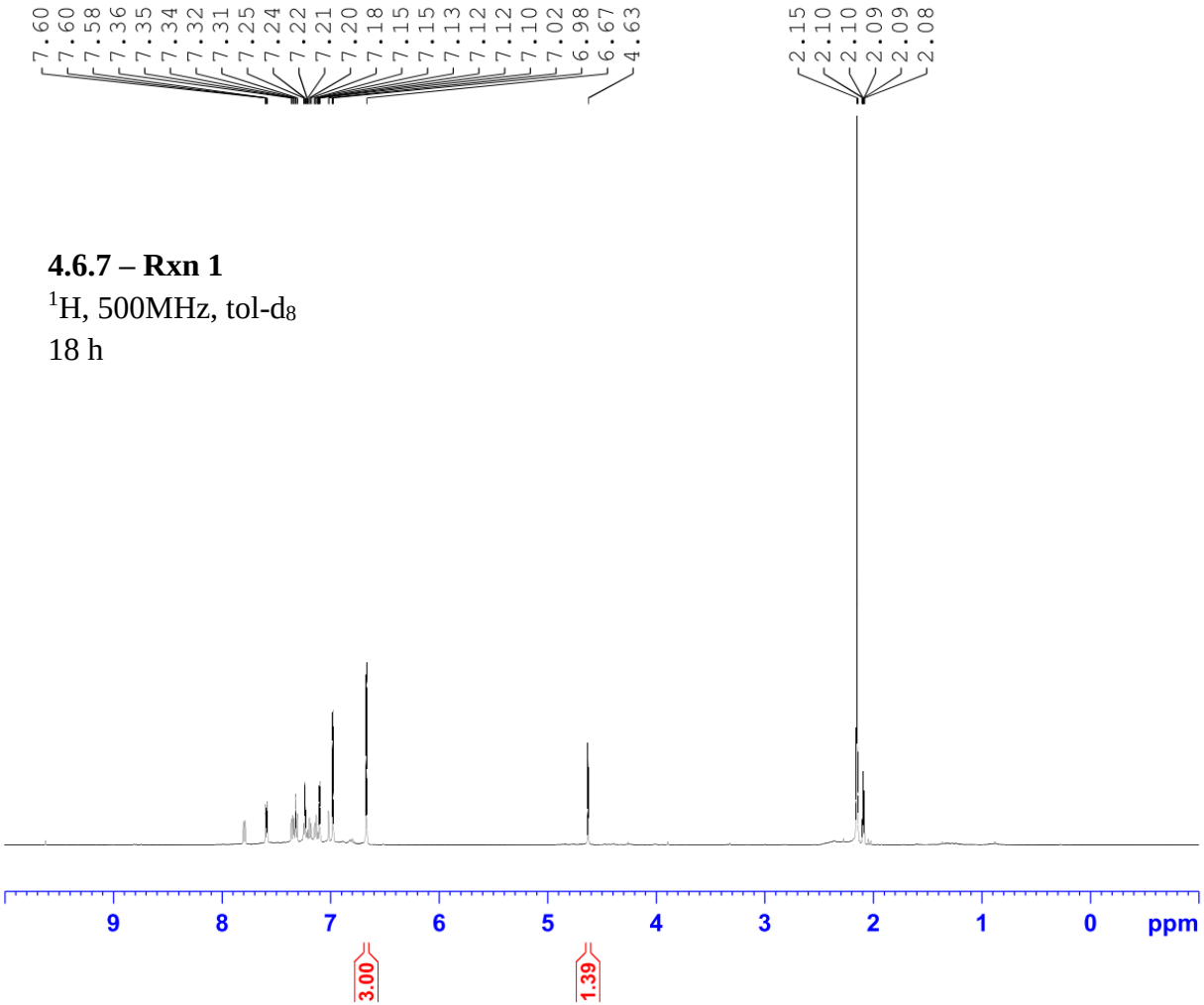



```
Current Data Parameters
NAME          JAW-03-070
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191121
Time               22.05
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH            12335.526 Hz
FIDRES          0.188225 Hz
AQ             2.6563926 sec
RG                   101
DW                40.533 usec
DE                  6.50 usec
TE                 295.1 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 10.86 usec
PL1                -2.00 dB
PL1W        19.70630455 W
SFO1        600.7137096 MHz

F2 - Processing parameters
SI                 32768
SF          600.7100224 MHz
WDW                   EM
SSB      0
LB                  0.30 Hz
GB       0
PC                  1.00
```

4.6.7 – Rxn 1

^{1}H, 500MHz, tol-d_8

18 h

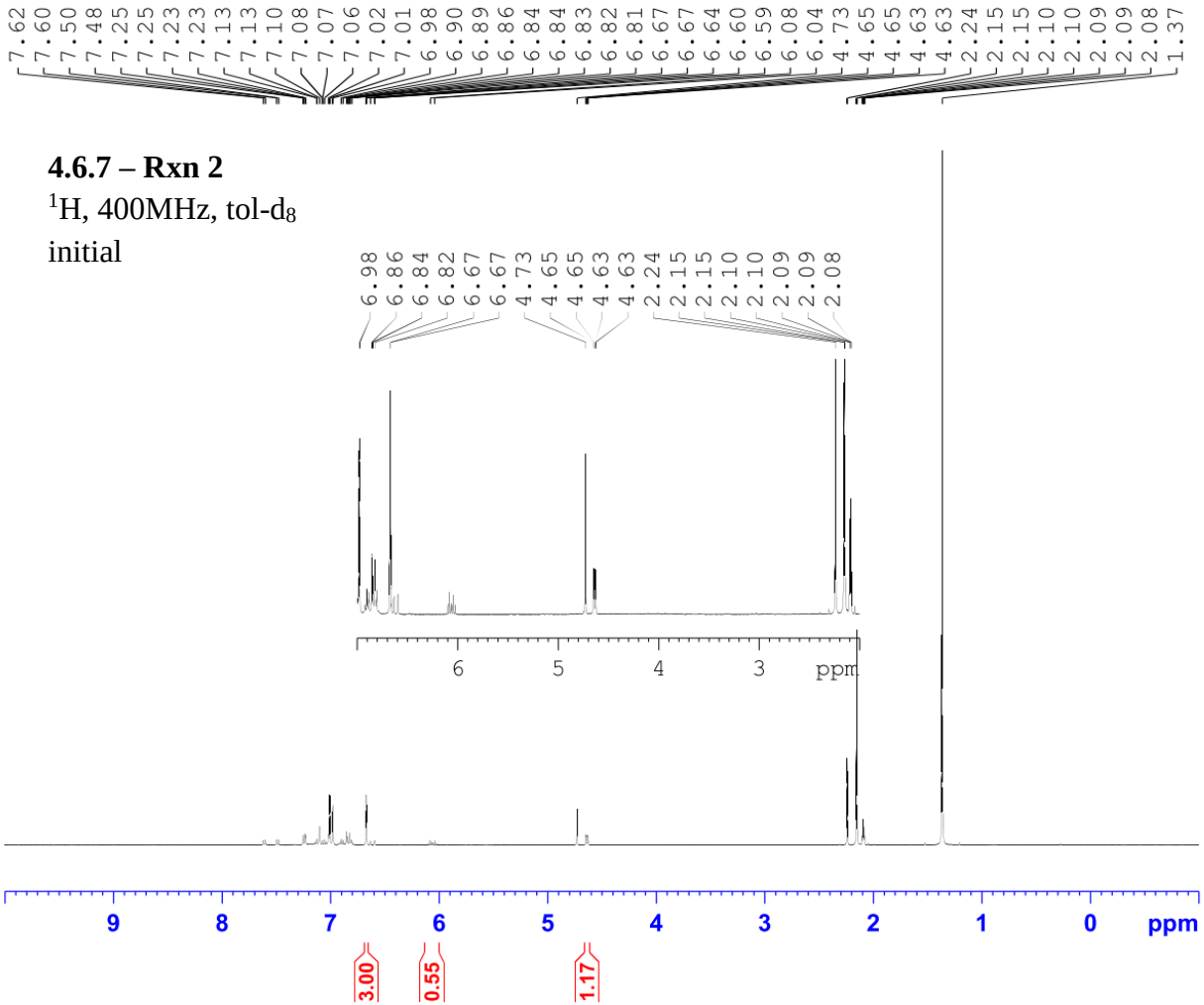



```
Current Data Parameters
NAME          JAW-03-070
EXPNO                  5
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191122
Time                9.29
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                  80.6
DW                50.000 usec
DE                 6.50 usec
TE                297.2 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                  1H
P1                11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1600172 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.7 – Rxn 2

^{1}H, 400MHz, tol-d_8

initial

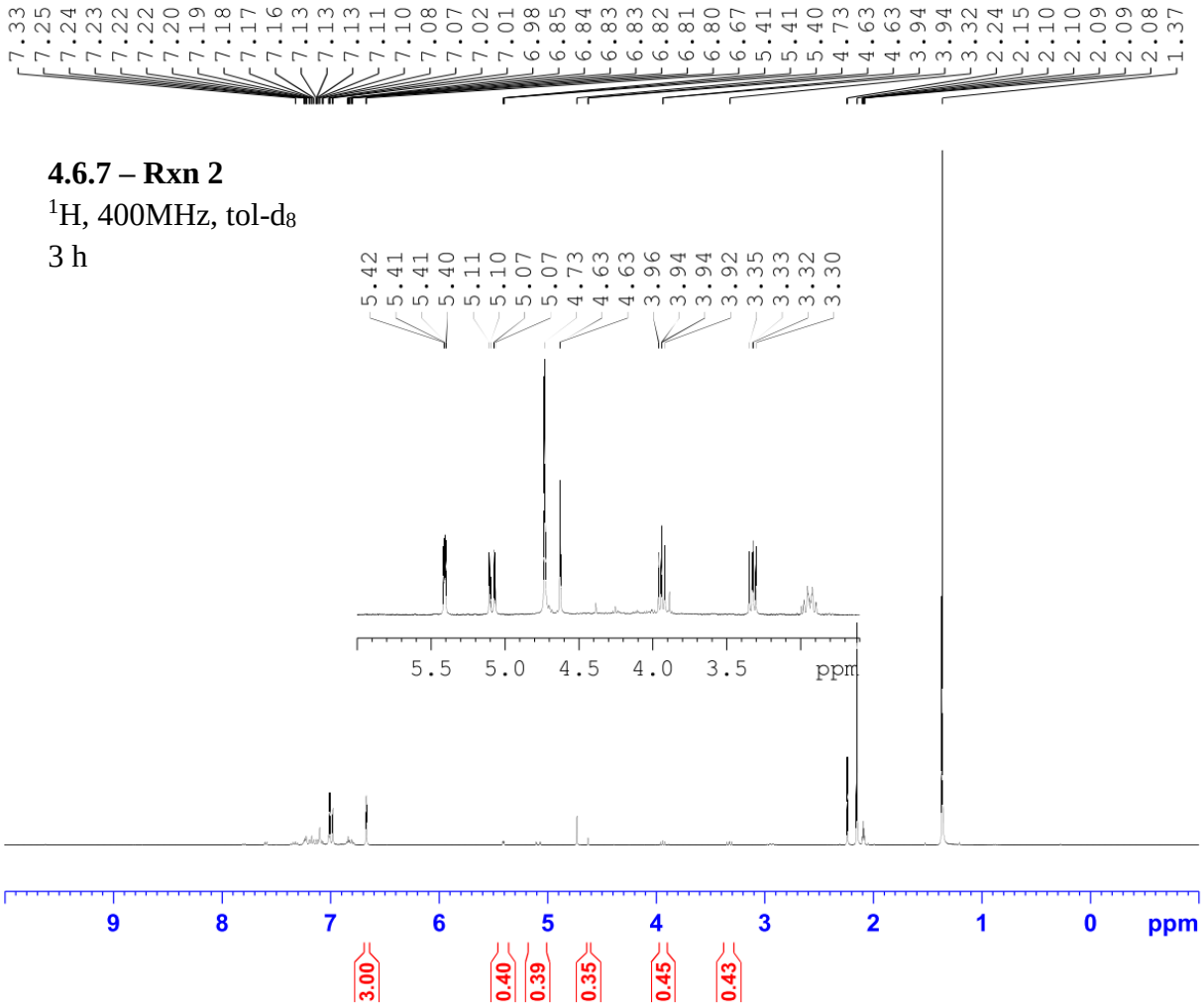



```
Current Data Parameters
NAME          JAW-03-078
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191230
Time               13.40 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                    57
DW                62.400 usec
DE                  6.50 usec
TE                  91.1 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                  4.83 usec
P1                 14.50 usec
PLW1         12.00000000 W

F2 - Processing parameters
SI                 65536
SF           400.1300139 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

4.6.7 – Rxn 2

^{1}H, 400MHz, tol-d_8

3 h

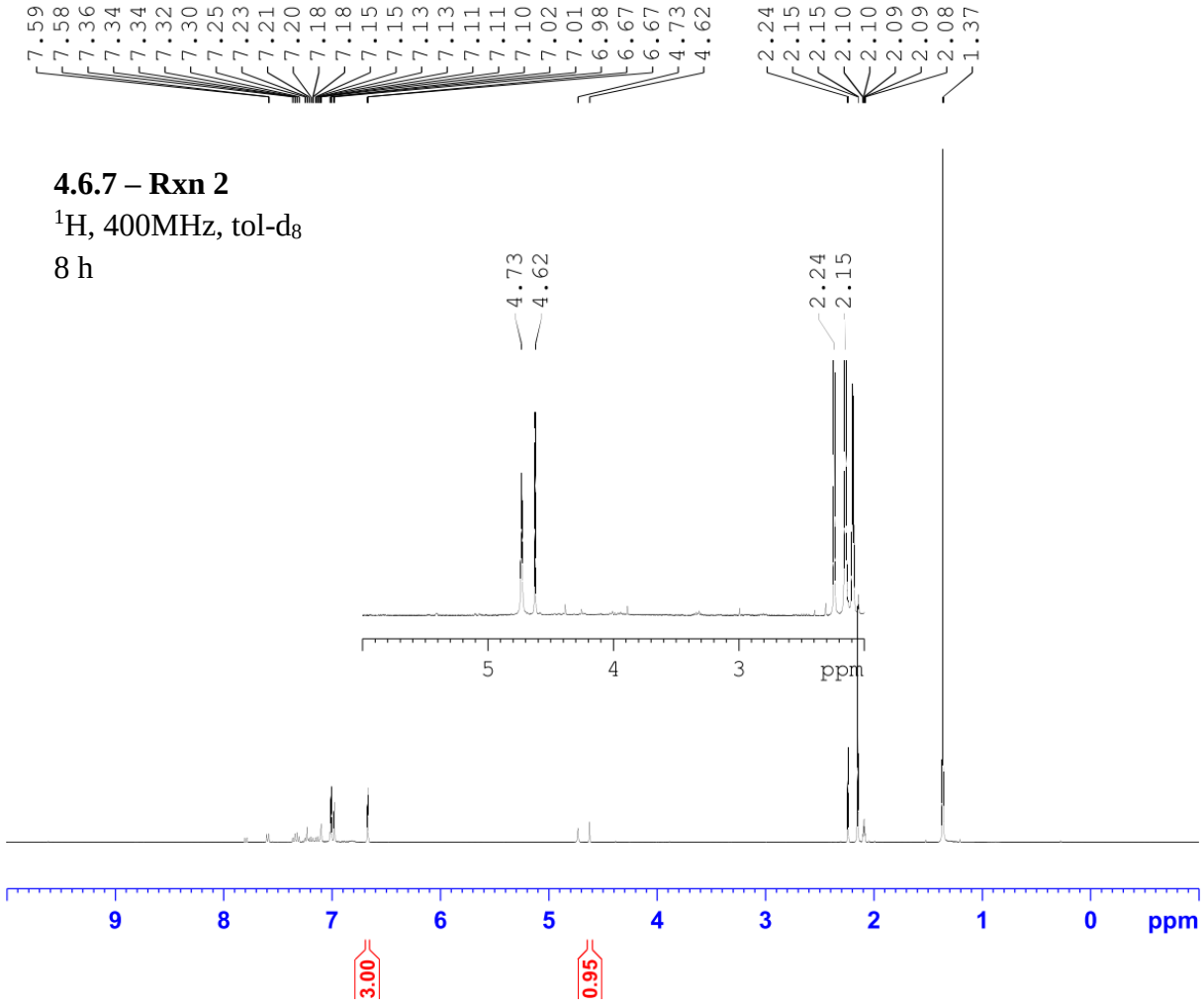



```
Current Data Parameters
NAME          JAW-03-078
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191230
Time               17.39 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                    57
DW                62.400 usec
DE                 6.50 usec
TE                 89.7 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                  4.83 usec
P1                 14.50 usec
PLW1         12.00000000 W

F2 - Processing parameters
SI                 65536
SF          400.1300140 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.7 – Rxn 2

^{1}H, 400MHz, tol-d_8

8 h

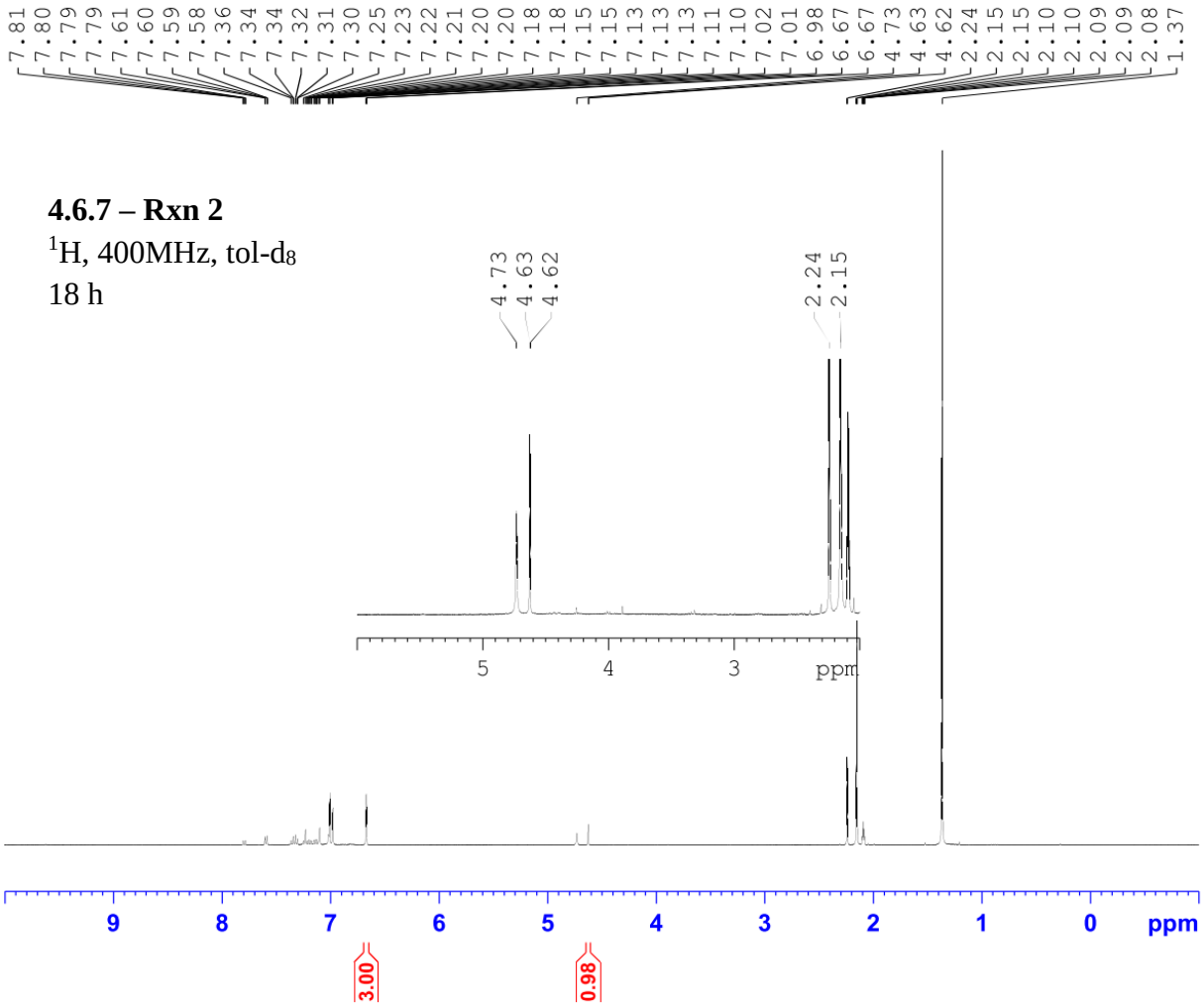



```
Current Data Parameters
NAME          JAW-03-078
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191230
Time               23.21 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                    64
DW                62.400 usec
DE                  6.50 usec
TE                  90.4 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                  4.83 usec
P1                 14.50 usec
PLW1         12.00000000 W

F2 - Processing parameters
SI                 65536
SF          400.1300141 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

4.6.7 – Rxn 2

^{1}H, 400MHz, tol-d_8

18 h

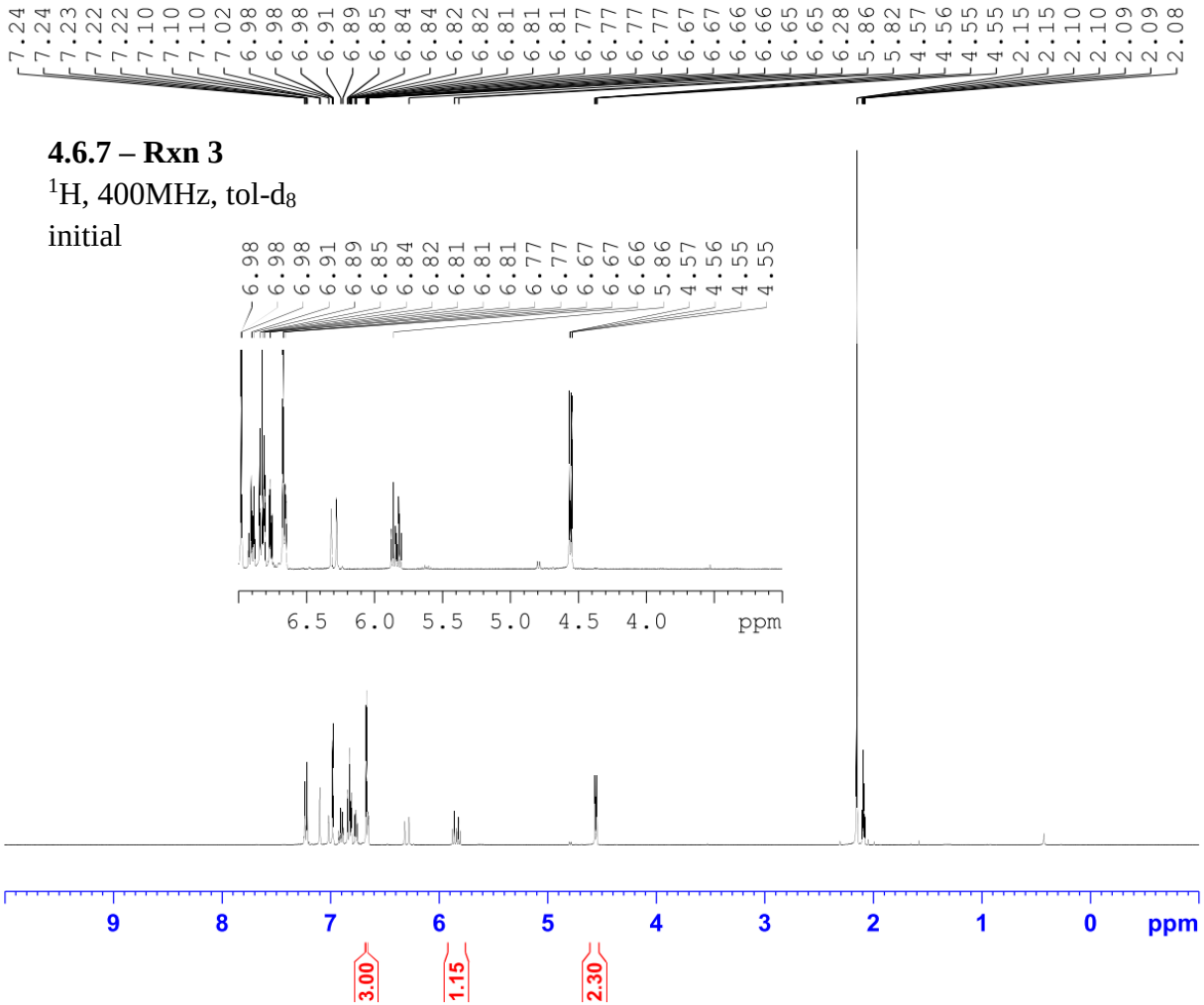



```
Current Data Parameters
NAME          JAW-03-078
EXPNO                  4
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191231
Time               10.51 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                    57
DW                62.400 usec
DE                 6.50 usec
TE                 91.3 K
D1           1.00000000 sec
TD0                    1
SFO1        400.1324708 MHz
NUC1                  1H
P0                 4.83 usec
P1                14.50 usec
PLW1        12.00000000 W

F2 - Processing parameters
SI                 65536
SF          400.1300141 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.7 – Rxn 3

^{1}H, 400MHz, tol-d_8

initial

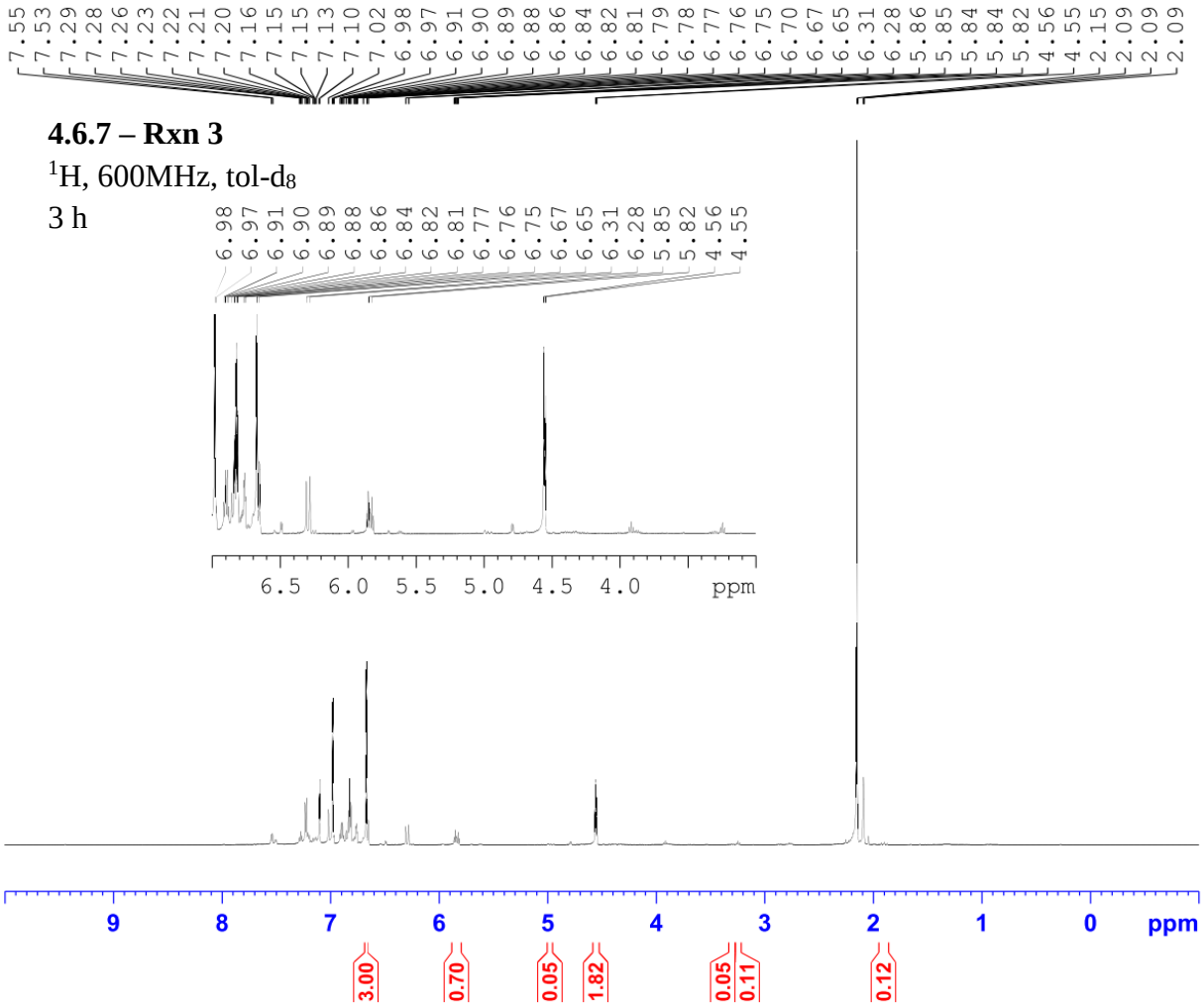



```
Current Data Parameters
NAME          JAW-03-072
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191121
Time               12.34
INSTRUM            spect
PROBHD   5 mm PADUL 13C
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ             3.9845889 sec
RG                   114
DW                60.800 usec
DE                 6.50 usec
TE                298.2 K
D1            2.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 9.31 usec
PL1               -3.90 dB
PL1W        21.64248466 W
SFO1        400.2324716 MHz

F2 - Processing parameters
SI                 32768
SF          400.2300165 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.7 – Rxn 3

^{1}H, 600MHz, tol-d_8

3 h

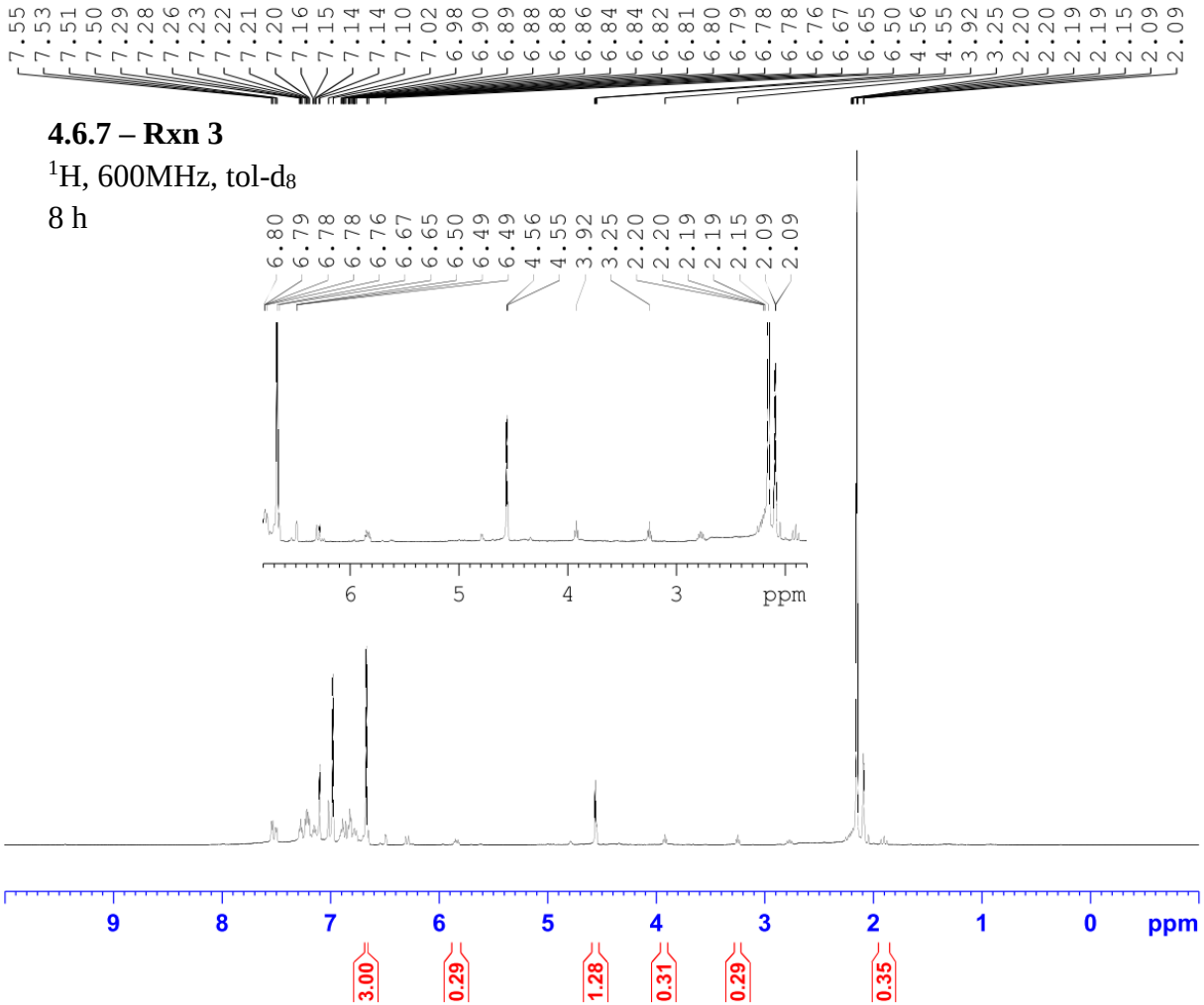



```
Current Data Parameters
NAME          JAW-03-072
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191121
Time               16.12
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH            12335.526 Hz
FIDRES          0.188225 Hz
AQ             2.6563926 sec
RG                   101
DW                40.533 usec
DE                  6.50 usec
TE                 295.2 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 10.86 usec
PL1                -2.00 dB
PL1W        19.70630455 W
SFO1        600.7137096 MHz

F2 - Processing parameters
SI                 32768
SF          600.7100218 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

4.6.7 – Rxn 3

^{1}H, 600MHz, tol-d_8

8 h

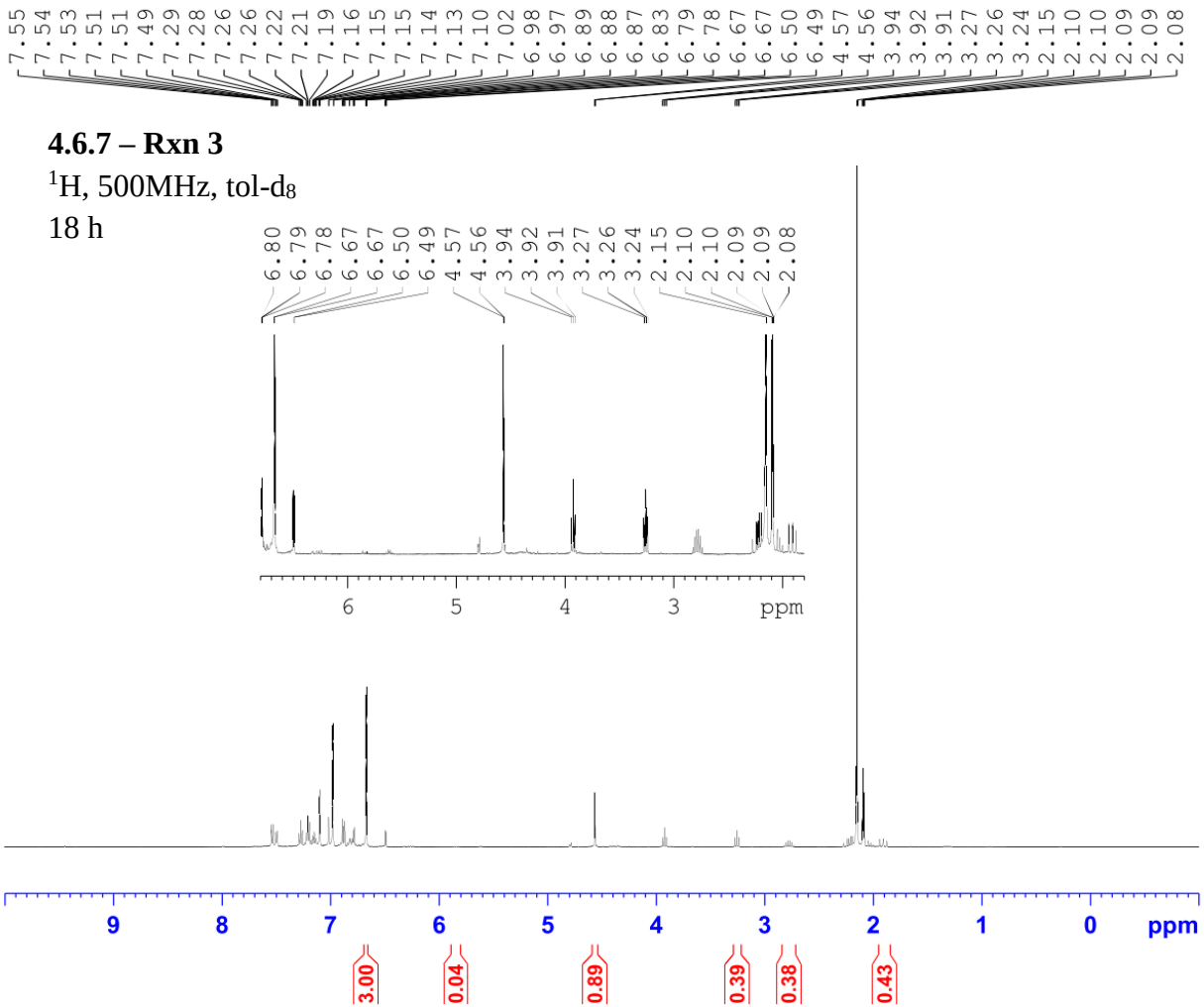



```
Current Data Parameters
NAME          JAW-03-072
EXPNO                  4
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191121
Time               22.29
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH            12335.526 Hz
FIDRES          0.188225 Hz
AQ             2.6563926 sec
RG                   101
DW                40.533 usec
DE                  6.50 usec
TE                 295.2 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 10.86 usec
PL1                -2.00 dB
PL1W        19.70630455 W
SFO1        600.7137096 MHz

F2 - Processing parameters
SI                 32768
SF          600.7100233 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

4.6.7 – Rxn 3

^{1}H, 500MHz, tol-d_8

18 h

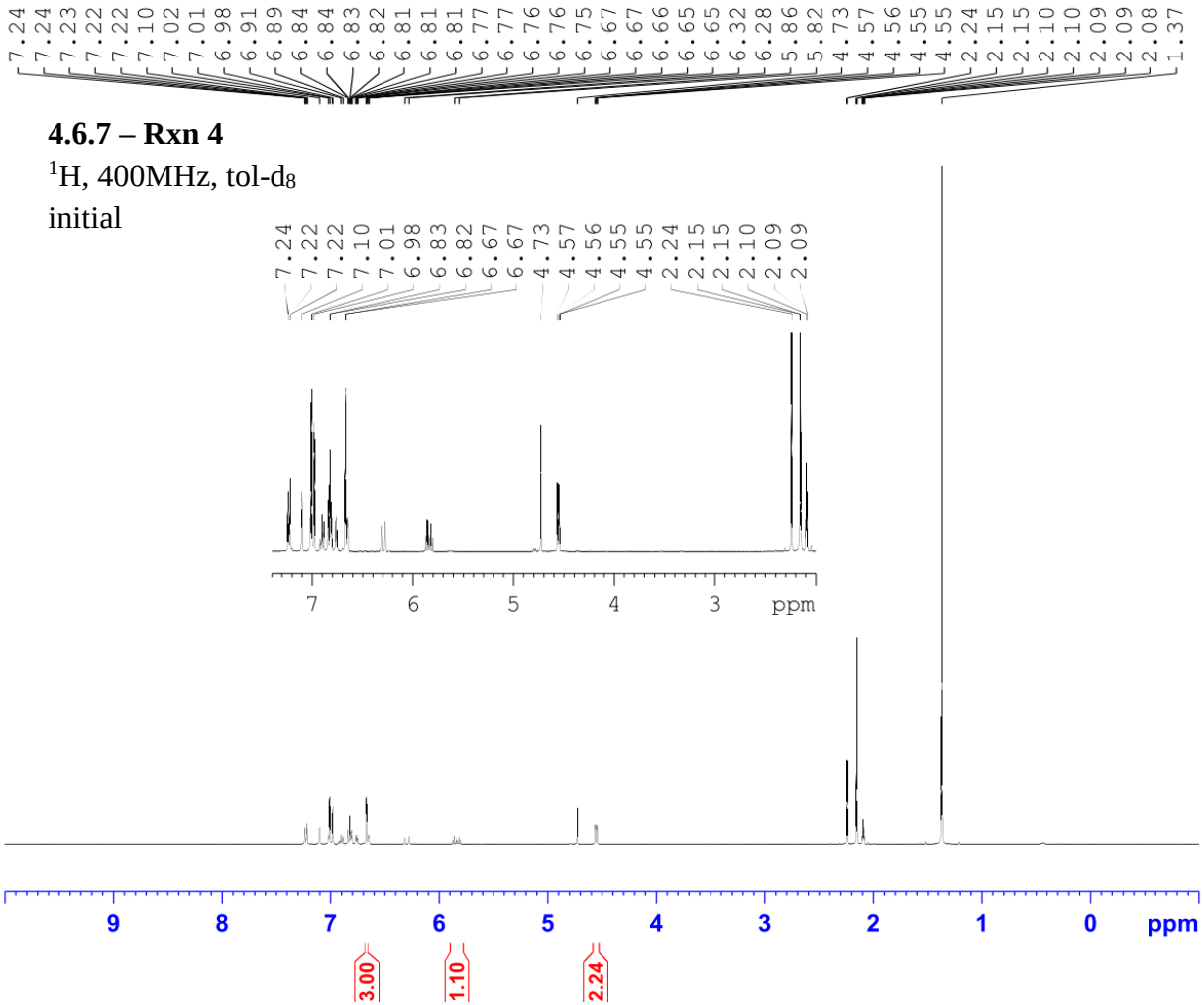



```
Current Data Parameters
NAME          JAW-03-072
EXPNO                  5
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191122
Time                9.50
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                  80.6
DW                50.000 usec
DE                 6.50 usec
TE                297.2 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                  1H
P1                11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1600174 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.7 – Rxn 4

^{1}H, 400MHz, tol-d_8

initial

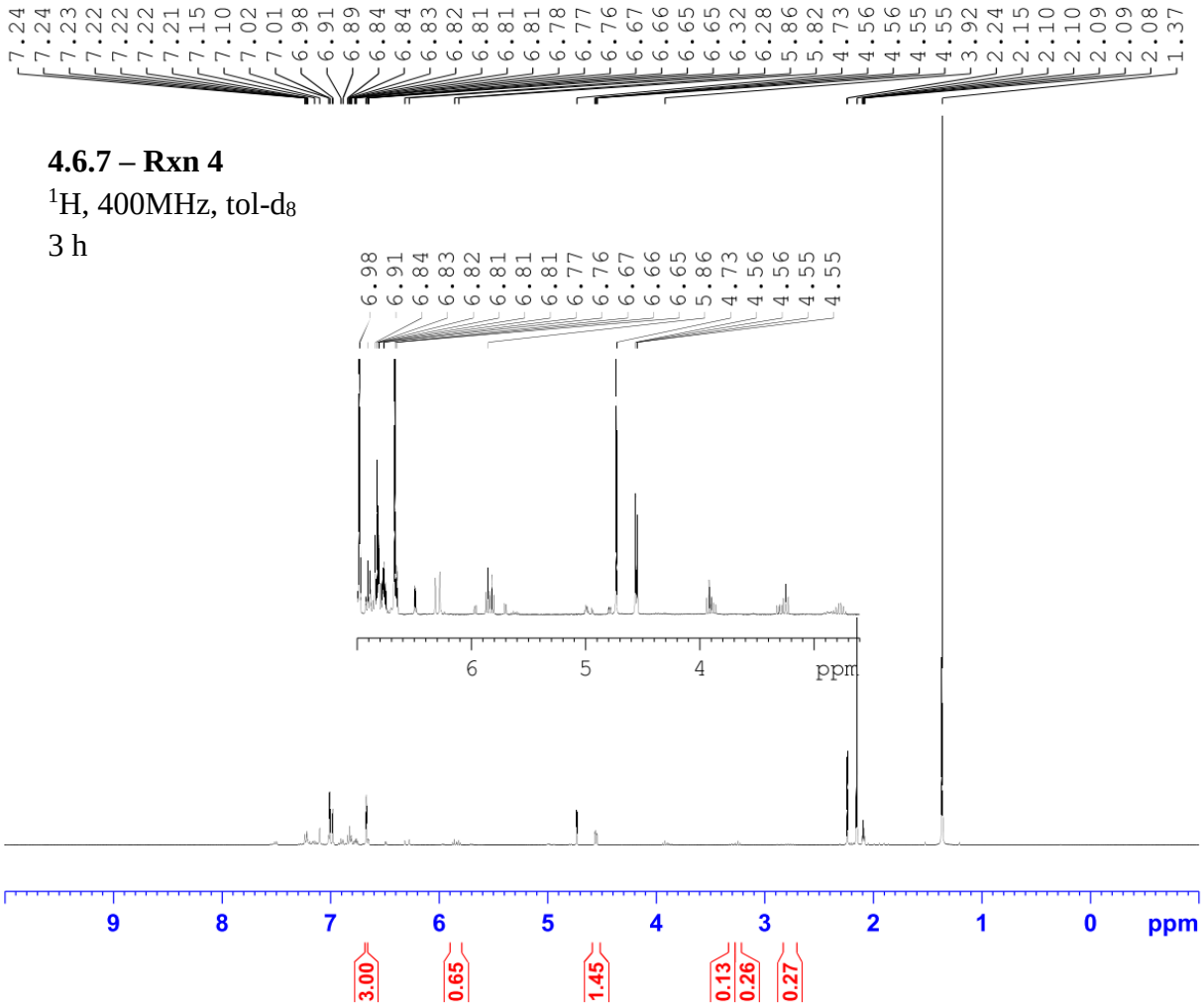



```
Current Data Parameters
NAME          JAW-03-080
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191230
Time               13.49 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                    57
DW                62.400 usec
DE                  6.50 usec
TE                  90.6 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                  4.83 usec
P1                 14.50 usec
PLW1         12.00000000 W

F2 - Processing parameters
SI                 65536
SF          400.1300139 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

4.6.7 – Rxn 4

^{1}H, 400MHz, tol-d_8

3 h

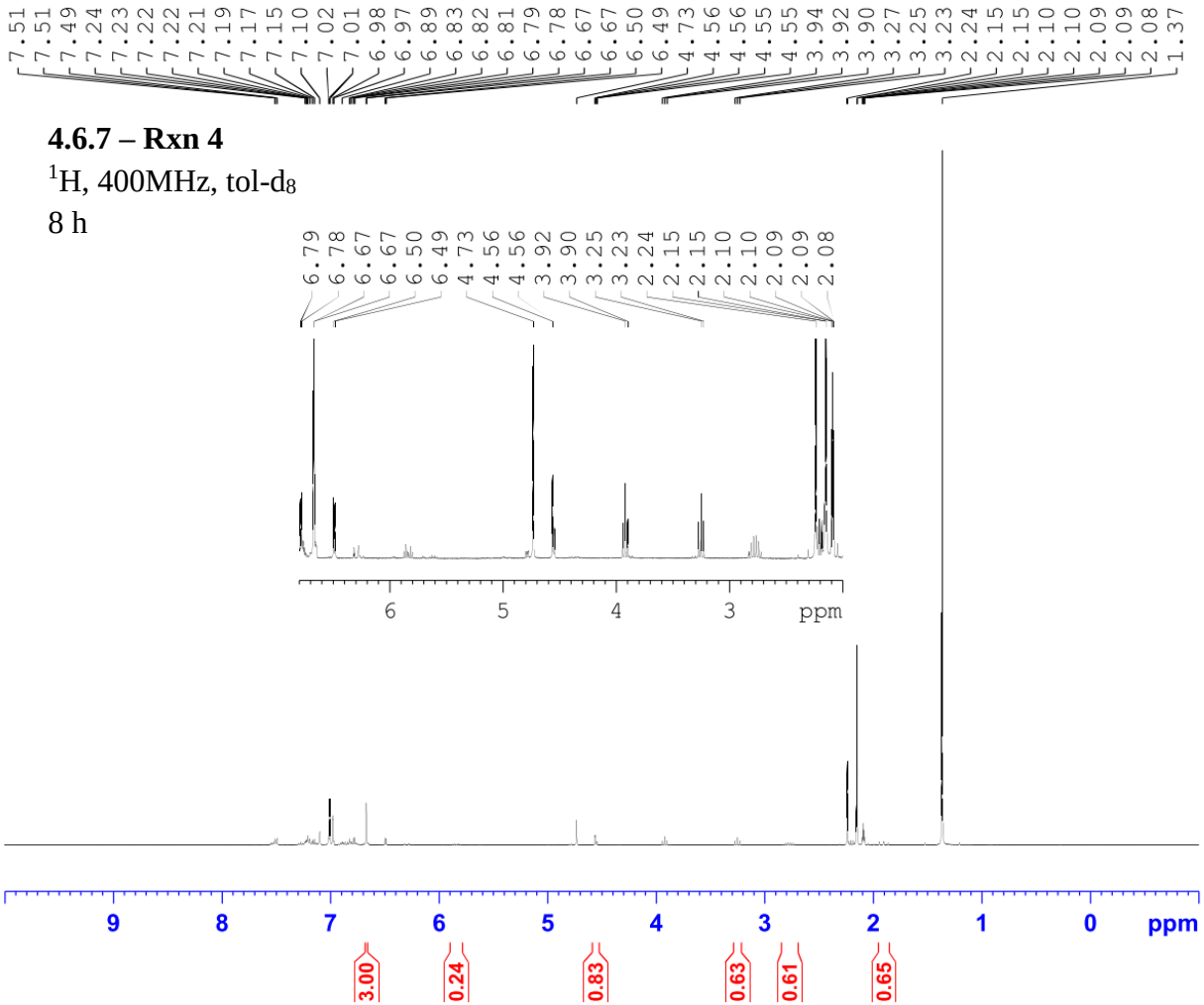



```
Current Data Parameters
NAME          JAW-03-080
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191230
Time               17.26 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                    57
DW                62.400 usec
DE                  6.50 usec
TE                  89.9 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                  4.83 usec
P1                 14.50 usec
PLW1         12.00000000 W

F2 - Processing parameters
SI                 65536
SF          400.1300140 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

4.6.7 – Rxn 4

^{1}H, 400MHz, tol-d_8

8 h

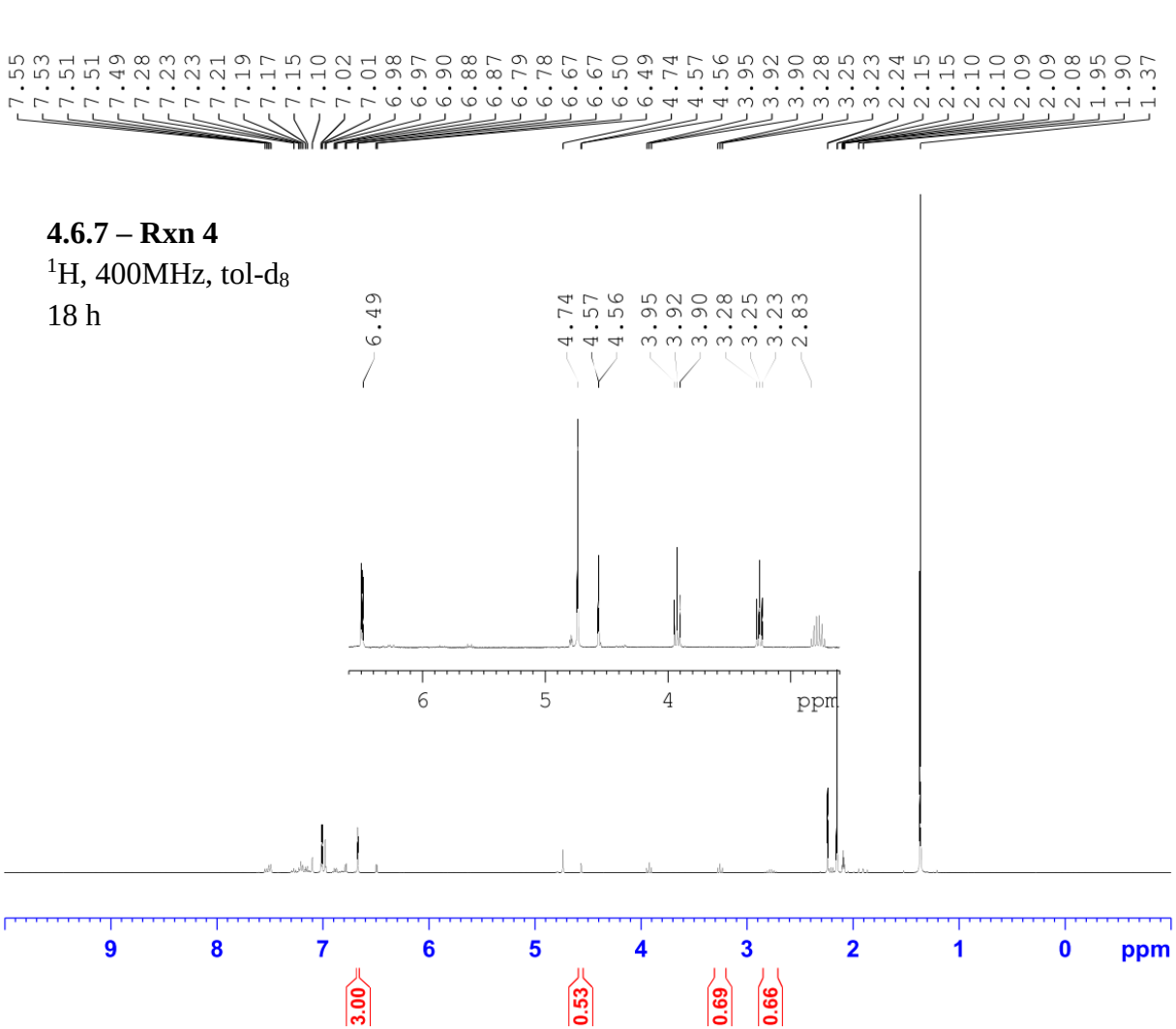



```
Current Data Parameters
NAME          JAW-03-080
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191230
Time               23.42 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                    57
DW                62.400 usec
DE                  6.50 usec
TE                  90.2 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                  4.83 usec
P1                 14.50 usec
PLW1         12.00000000 W

F2 - Processing parameters
SI                 65536
SF          400.1300140 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

4.6.7 – Rxn 4

^{1}H, 400MHz, tol-d_8

18 h

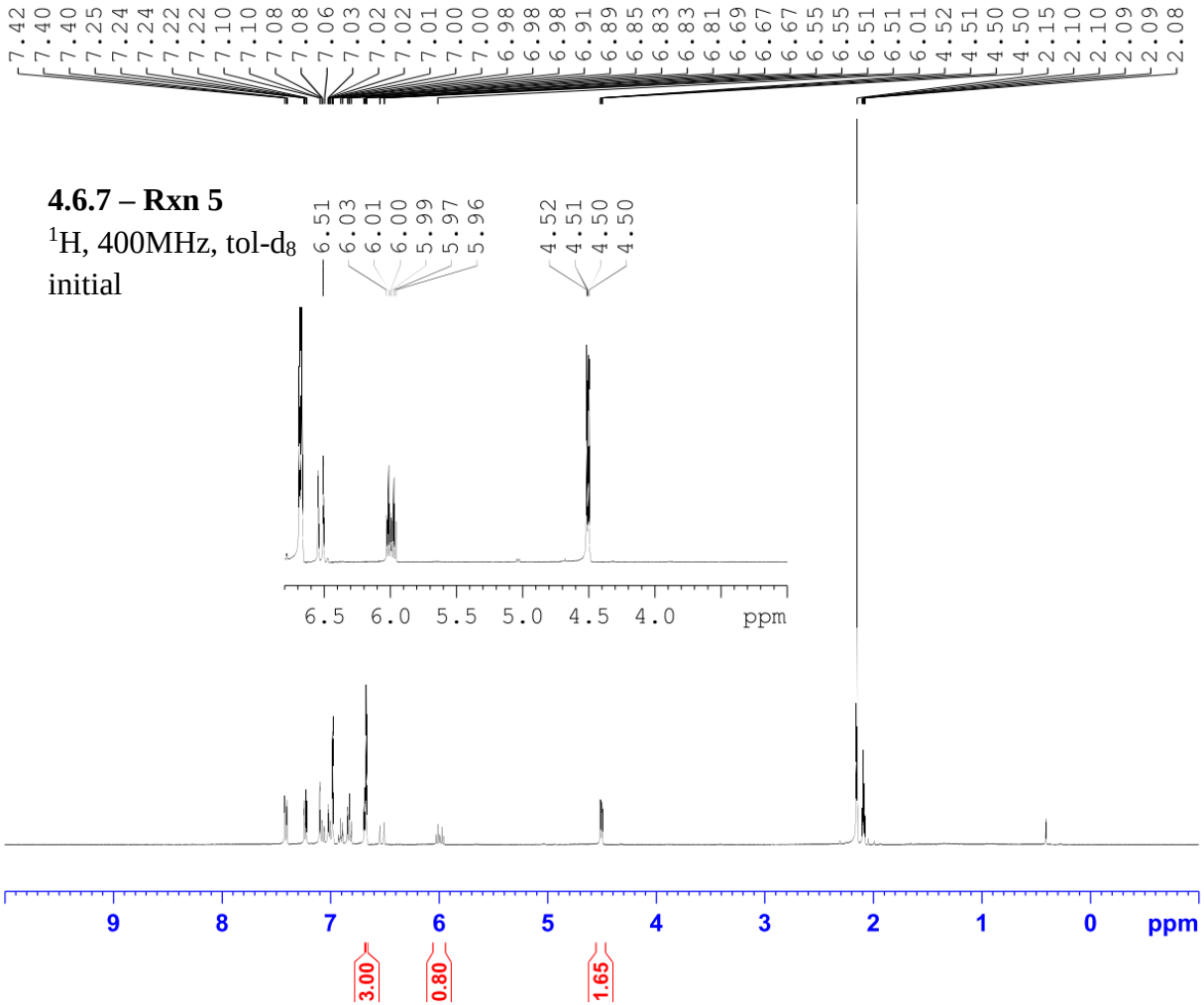



```
Current Data Parameters
NAME          JAW-03-080
EXPNO                  4
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191231
Time               11.09 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                    57
DW                62.400 usec
DE                  6.50 usec
TE                  91.1 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                  4.83 usec
P1                 14.50 usec
PLW1         12.00000000 W

F2 - Processing parameters
SI                 65536
SF          400.1300140 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

4.6.7 – Rxn 5

^{1}H, 400MHz, tol-d$_8$

initial

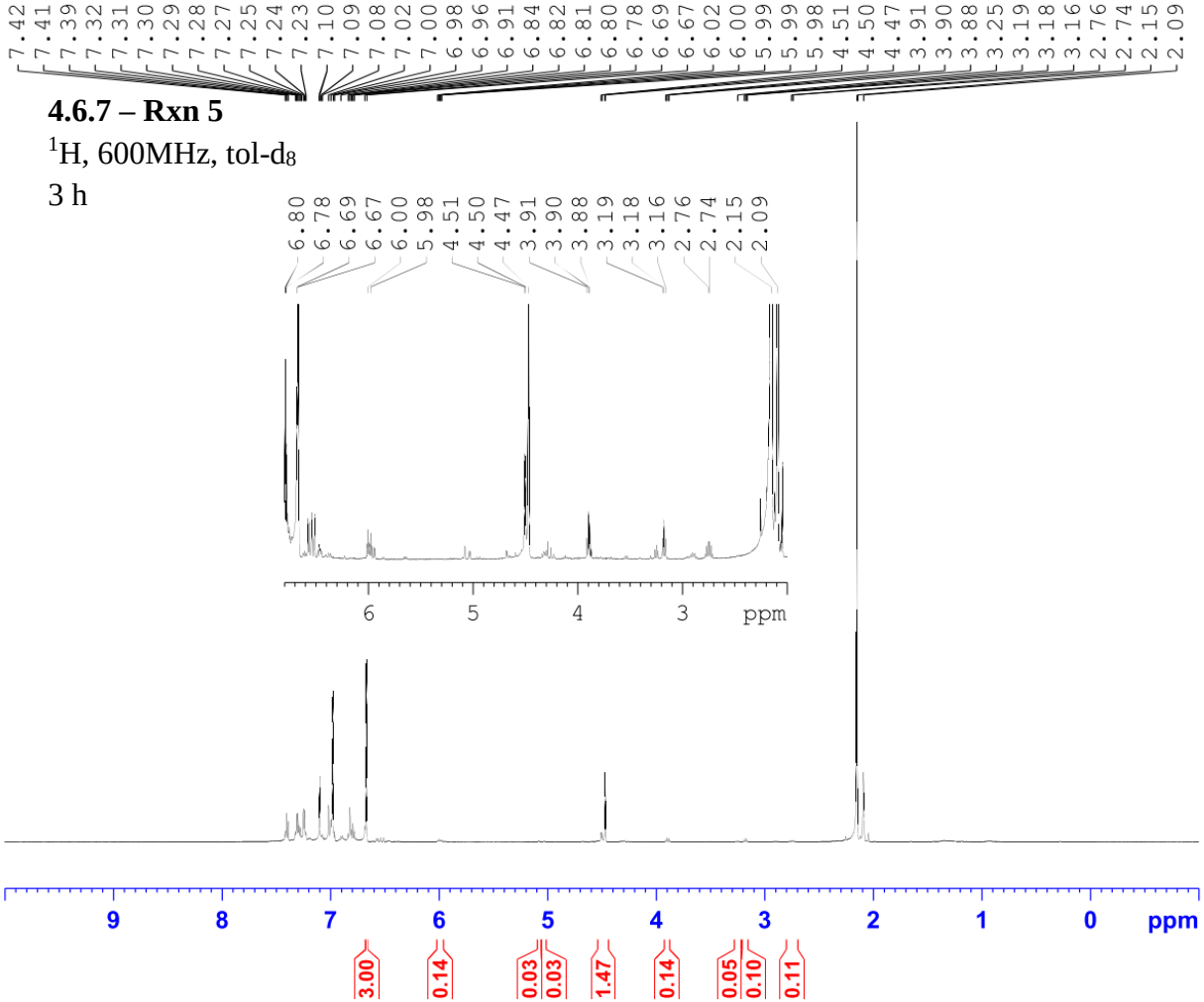



```
Current Data Parameters
NAME          JAW-03-071
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191121
Time               12.28
INSTRUM            spect
PROBHD   5 mm PADUL 13C
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ             3.9845889 sec
RG                   114
DW                60.800 usec
DE                 6.50 usec
TE                298.2 K
D1            2.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 9.31 usec
PL1               -3.90 dB
PL1W        21.64248466 W
SFO1        400.2324716 MHz

F2 - Processing parameters
SI                 32768
SF          400.2300166 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.7 – Rxn 5

^{1}H, 600MHz, tol-d_8

3 h

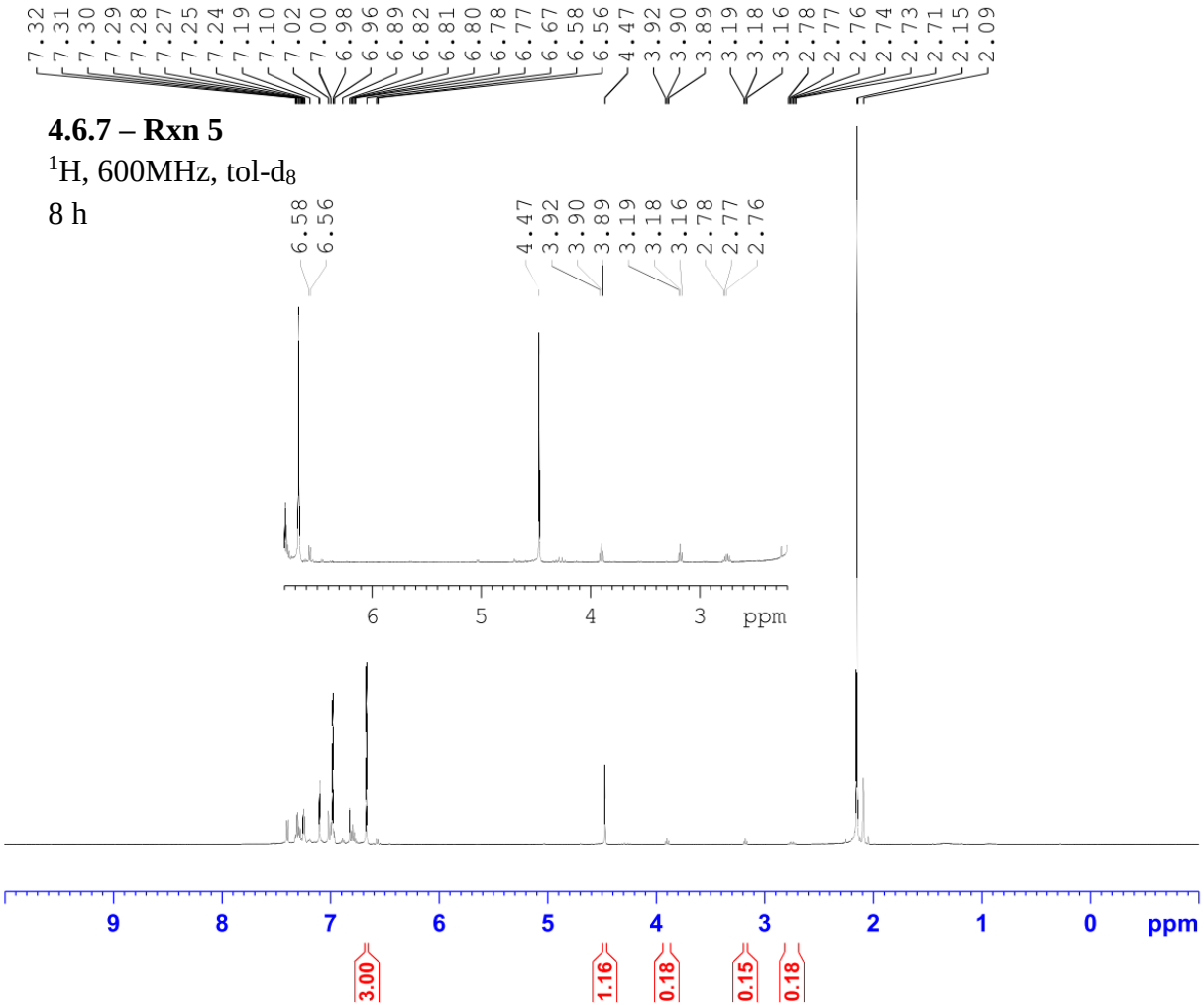



```
Current Data Parameters
NAME          JAW-03-071
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191121
Time               16.06
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH            12335.526 Hz
FIDRES          0.188225 Hz
AQ             2.6563926 sec
RG                  71.8
DW                40.533 usec
DE                 6.50 usec
TE                295.2 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 10.86 usec
PL1                -2.00 dB
PL1W        19.70630455 W
SFO1        600.7137096 MHz

F2 - Processing parameters
SI                 32768
SF          600.7100220 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.7 – Rxn 5

^{1}H, 600MHz, tol-d_8

8 h

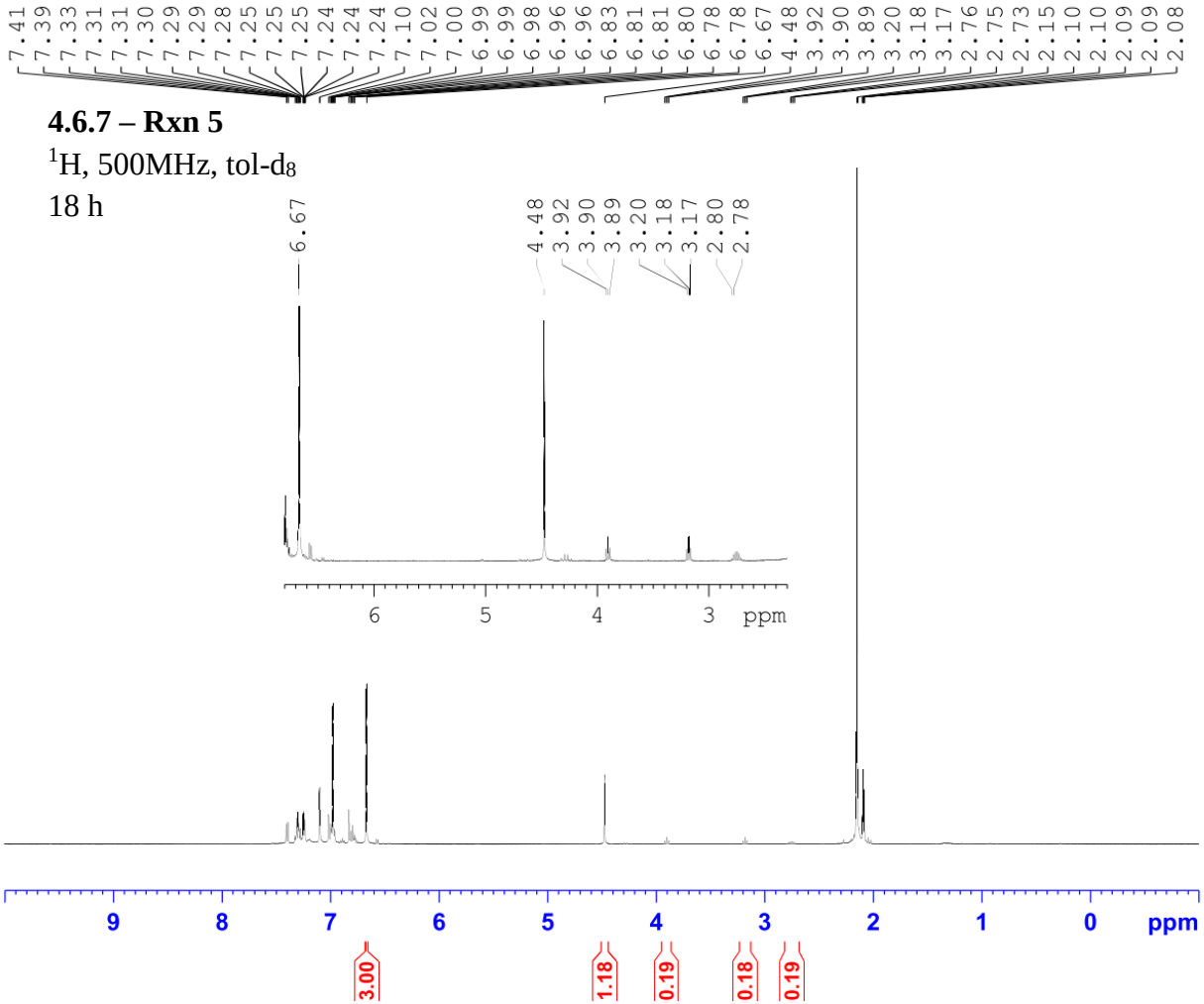



```
Current Data Parameters
NAME          JAW-03-071
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191121
Time               22.16
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH            12335.526 Hz
FIDRES          0.188225 Hz
AQ             2.6563926 sec
RG                  71.8
DW                40.533 usec
DE                  6.50 usec
TE                 295.1 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 10.86 usec
PL1                -2.00 dB
PL1W        19.70630455 W
SFO1        600.7137096 MHz

F2 - Processing parameters
SI                 32768
SF          600.7100217 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

4.6.7 – Rxn 5

^{1}H, 500MHz, tol-d_8

18 h

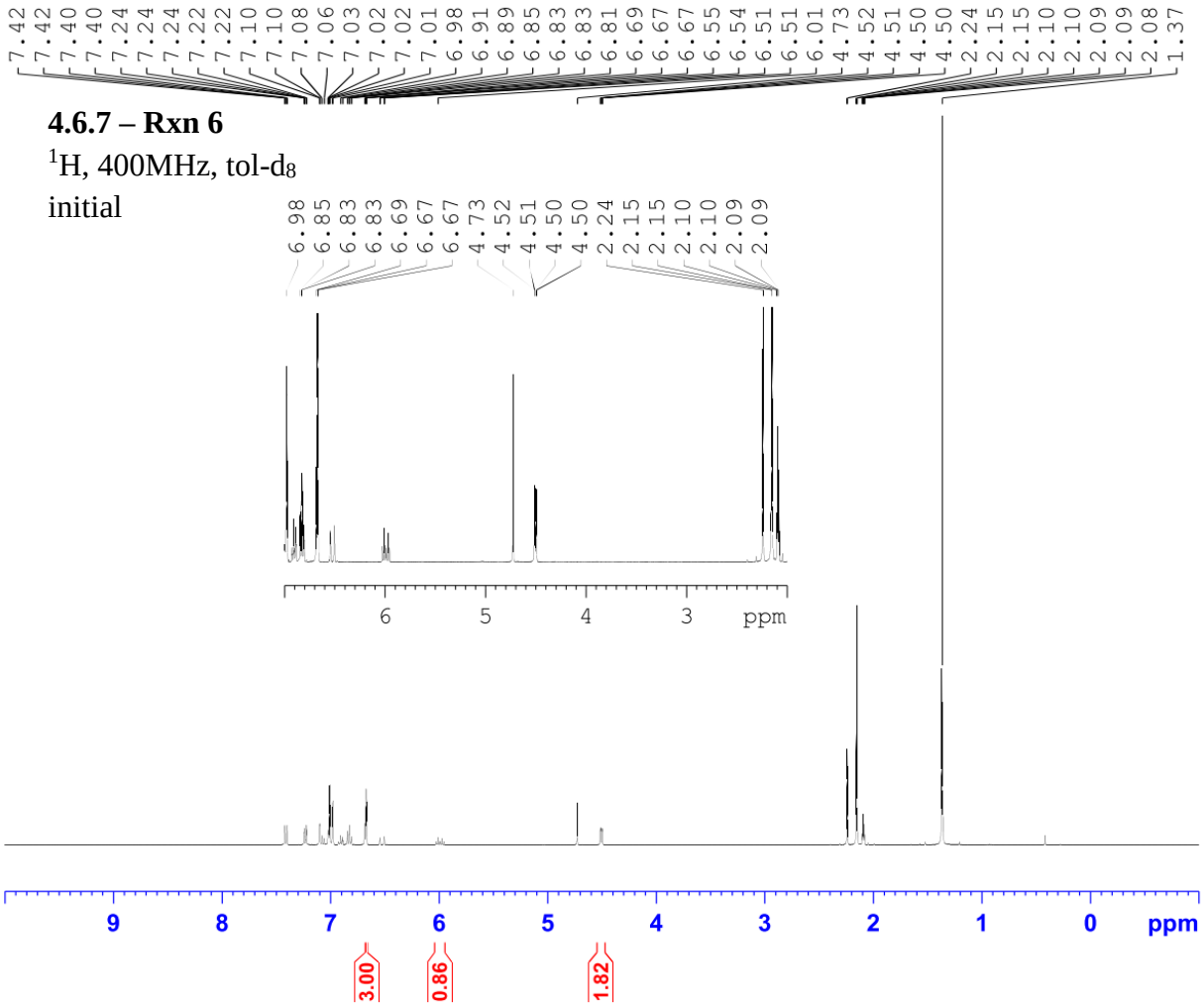



```
Current Data Parameters
NAME          JAW-03-071
EXPNO                  5
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191122
Time                9.40
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                  90.5
DW                50.000 usec
DE                 6.50 usec
TE                297.2 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                  1H
P1                11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1600174 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.7 – Rxn 6

^{1}H, 400MHz, tol-d_8

initial

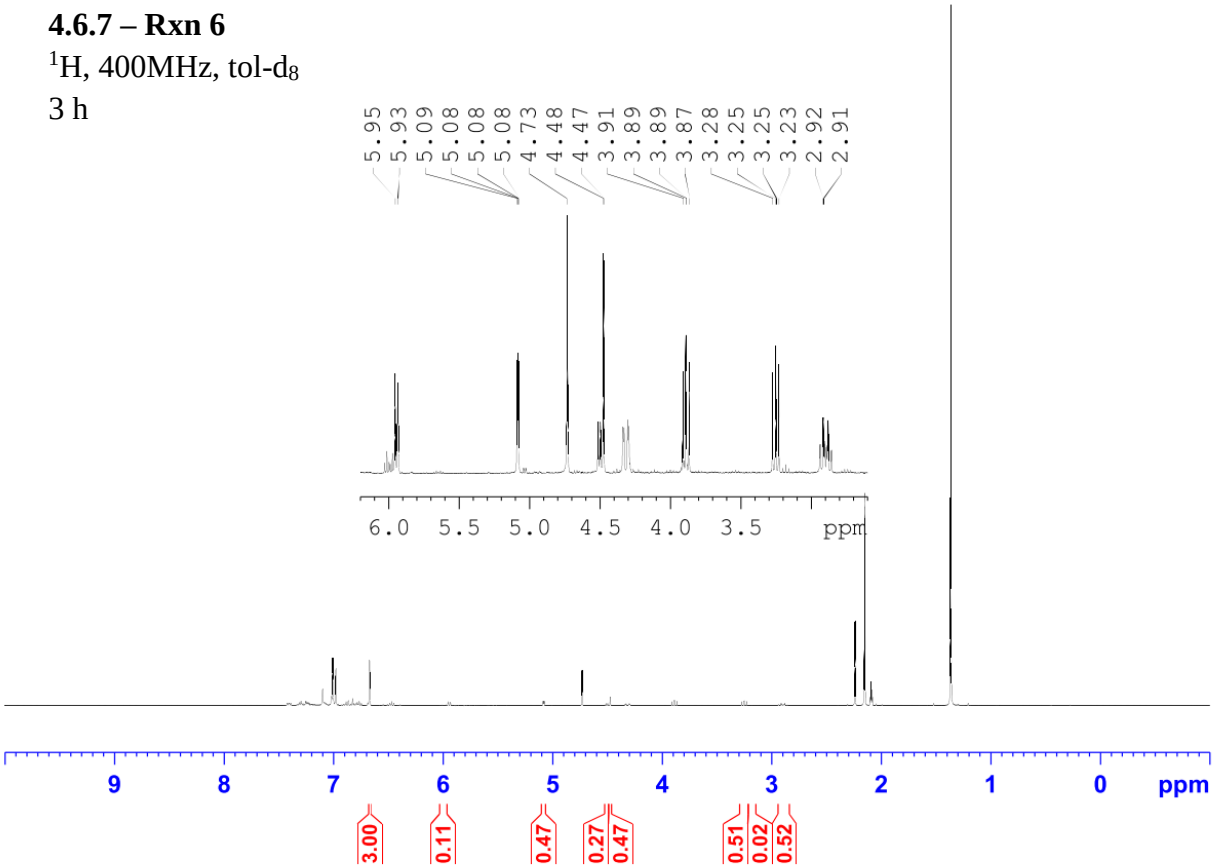



```
Current Data Parameters
NAME          JAW-03-079
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191230
Time               14.08 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                    64
DW                62.400 usec
DE                  6.50 usec
TE                  90.3 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                  4.83 usec
P1                 14.50 usec
PLW1         12.00000000 W

F2 - Processing parameters
SI                 65536
SF          400.1300139 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

4.6.7 – Rxn 6

^{1}H, 400MHz, tol-d_8

3 h

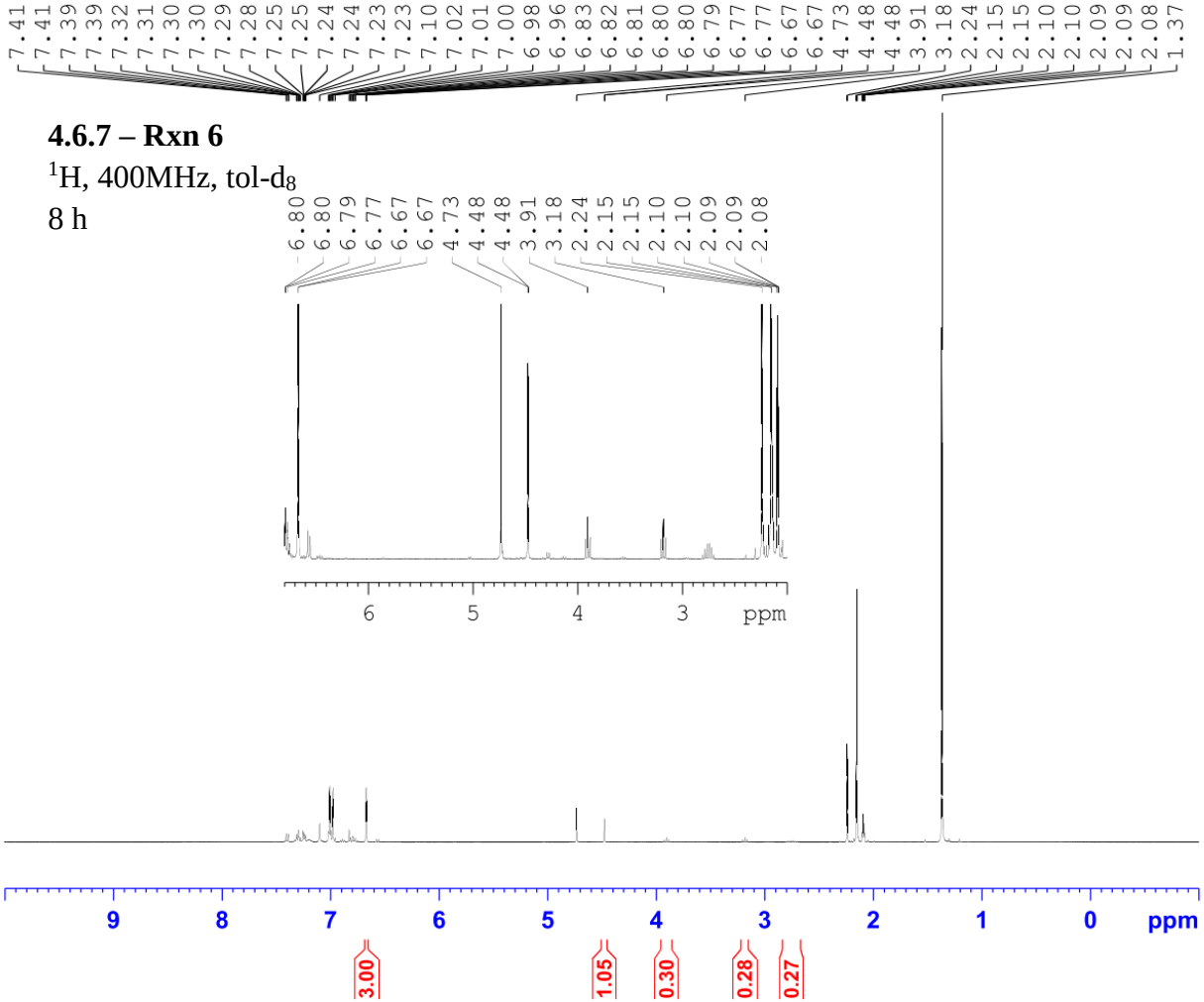



```
Current Data Parameters
NAME          JAW-03-079
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191230
Time               17.14 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                    64
DW                62.400 usec
DE                 6.50 usec
TE                 90.3 K
D1           1.00000000 sec
TD0                    1
SFO1        400.1324708 MHz
NUC1                  1H
P0                 4.83 usec
P1                14.50 usec
PLW1        12.00000000 W

F2 - Processing parameters
SI                 65536
SF          400.1300141 MHz
WDW                   EM
SSB      0
LB                 0.30 Hz
GB       0
PC                 1.00
```

4.6.7 – Rxn 6

^{1}H, 400MHz, tol-d_8

8 h

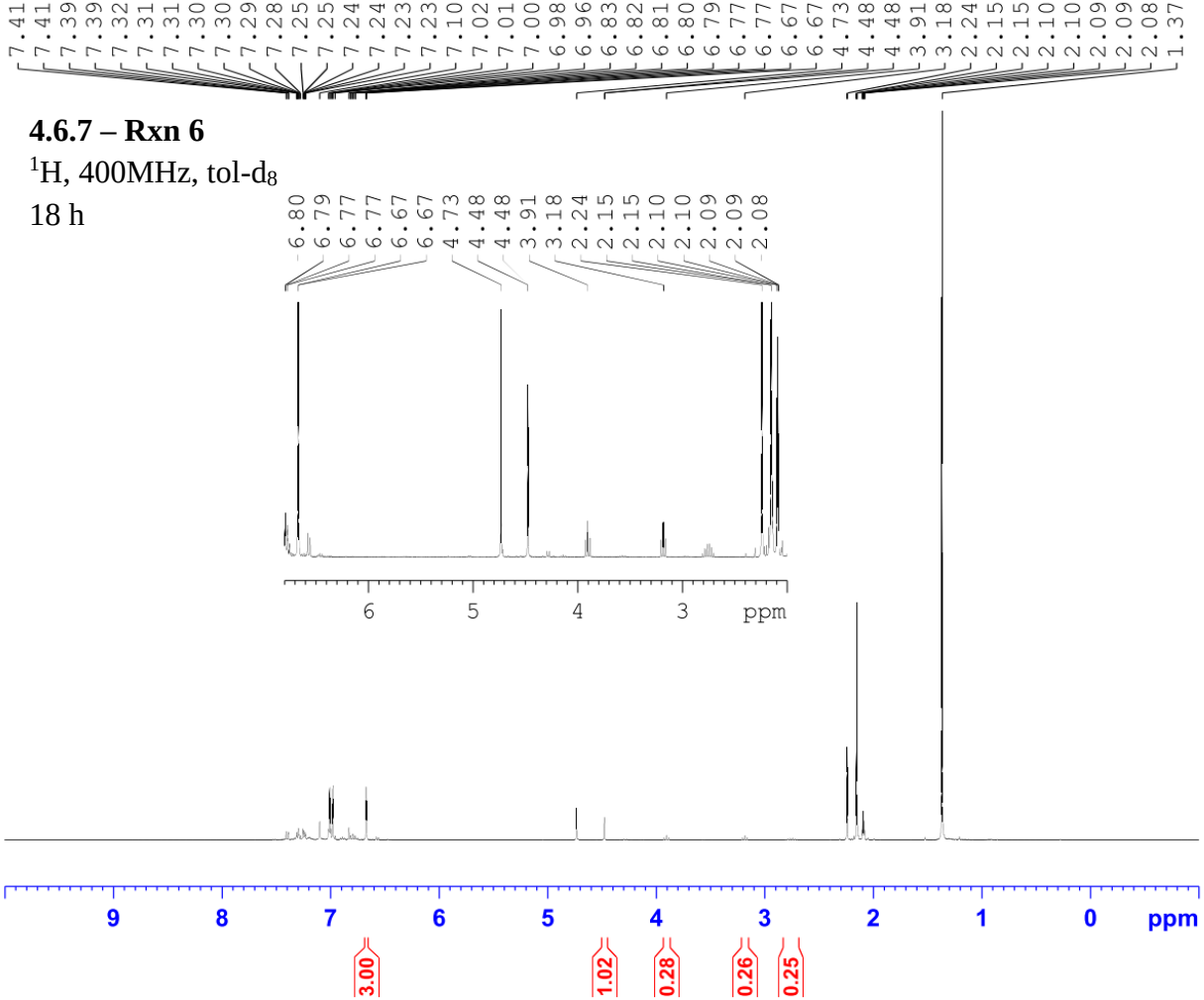



```
Current Data Parameters
NAME          JAW-03-079
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191230
Time               23.29 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG            zg30
TD                65536
SOLVENT             Tol
NS                   16
DS                    2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                   64
DW                62.400 usec
DE                 6.50 usec
TE                 90.2 K
D1           1.00000000 sec
TD0                   1
SFO1        400.1324708 MHz
NUC1                 1H
P0                 4.83 usec
P1                14.50 usec
PLW1        12.00000000 W

F2 - Processing parameters
SI                65536
SF          400.1300139 MHz
WDW                  EM
SSB      0
LB                0.30 Hz
GB       0
PC                1.00
```

4.6.7 – Rxn 6

^{1}H, 400MHz, tol-d$_8$

18 h

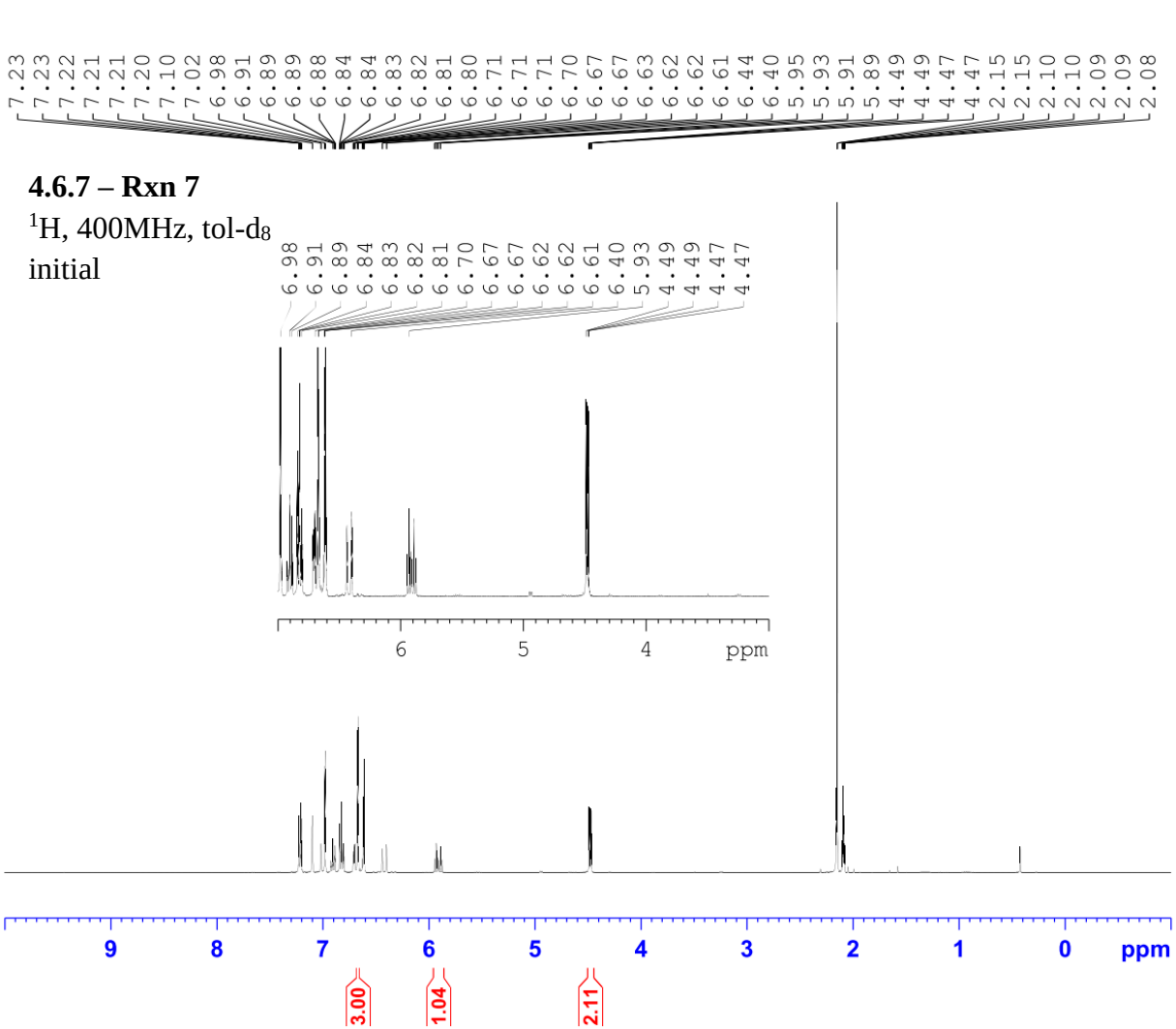



```
Current Data Parameters
NAME          JAW-03-079
EXPNO                  4
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191231
Time               10.59 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG            zg30
TD                65536
SOLVENT             Tol
NS                   16
DS                    2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                   64
DW                62.400 usec
DE                 6.50 usec
TE                 91.3 K
D1           1.00000000 sec
TD0                   1
SFO1        400.1324708 MHz
NUC1                 1H
P0                 4.83 usec
P1                14.50 usec
PLW1        12.00000000 W

F2 - Processing parameters
SI                65536
SF          400.1300138 MHz
WDW                  EM
SSB      0
LB                0.30 Hz
GB       0
PC                1.00
```

4.6.7 – Rxn 7

^{1}H, 400MHz, tol-d$_8$

initial

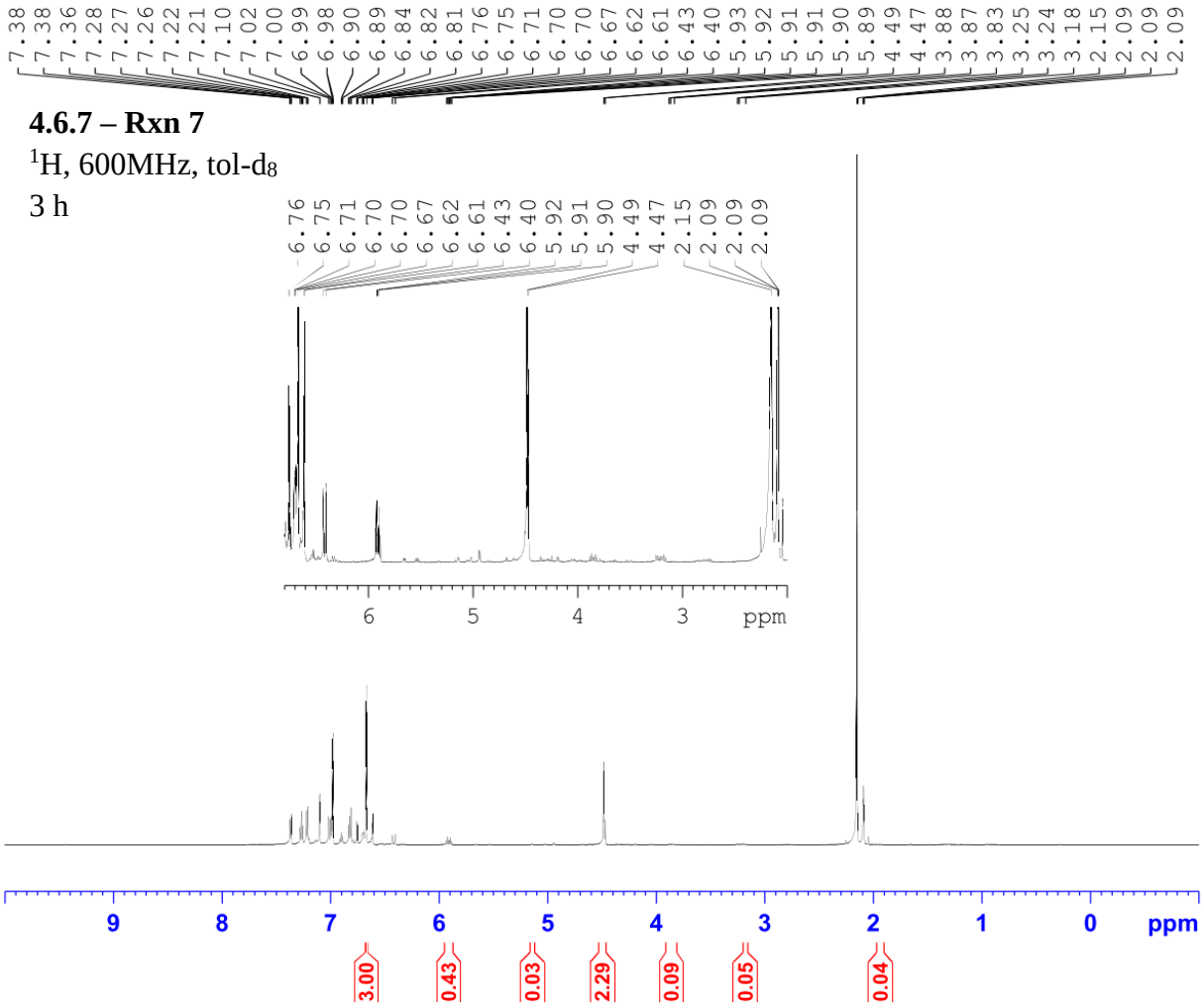



```
Current Data Parameters
NAME          JAW-03-073
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191121
Time               12.41
INSTRUM            spect
PROBHD   5 mm PADUL 13C
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ             3.9845889 sec
RG                   114
DW                60.800 usec
DE                 6.50 usec
TE                298.2 K
D1            2.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                  9.31 usec
PL1                -3.90 dB
PL1W        21.64248466 W
SFO1        400.2324716 MHz

F2 - Processing parameters
SI                 32768
SF          400.2300165 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

4.6.7 – Rxn 7

^{1}H, 600MHz, tol-d_8

3 h

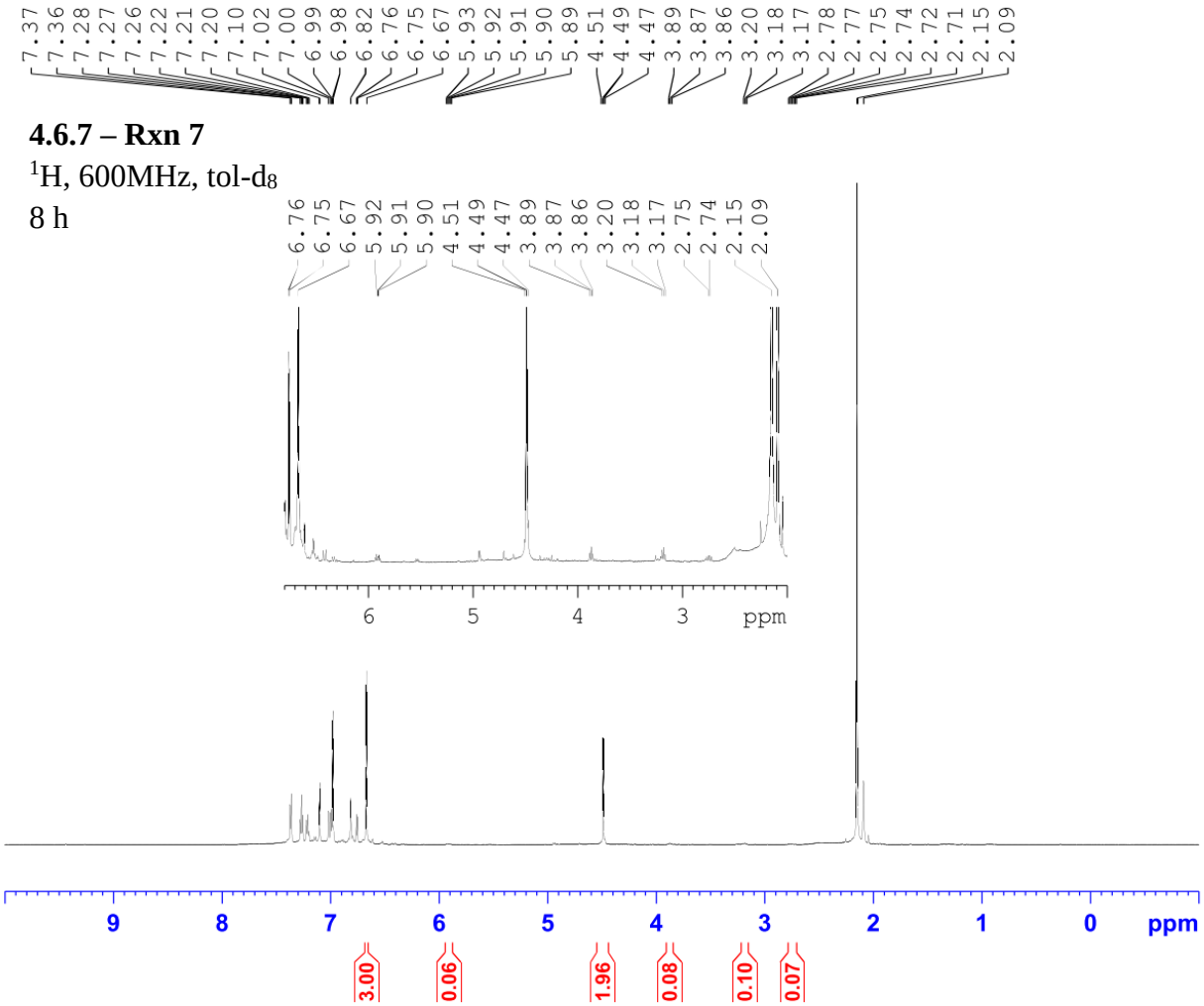



```
Current Data Parameters
NAME          JAW-03-073
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191121
Time               16.21
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH            12335.526 Hz
FIDRES          0.188225 Hz
AQ             2.6563926 sec
RG                   101
DW                40.533 usec
DE                  6.50 usec
TE                 295.2 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 10.86 usec
PL1                -2.00 dB
PL1W        19.70630455 W
SFO1        600.7137096 MHz

F2 - Processing parameters
SI                 32768
SF          600.7100217 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

4.6.7 – Rxn 7

^{1}H, 600MHz, tol-d$_8$

8 h

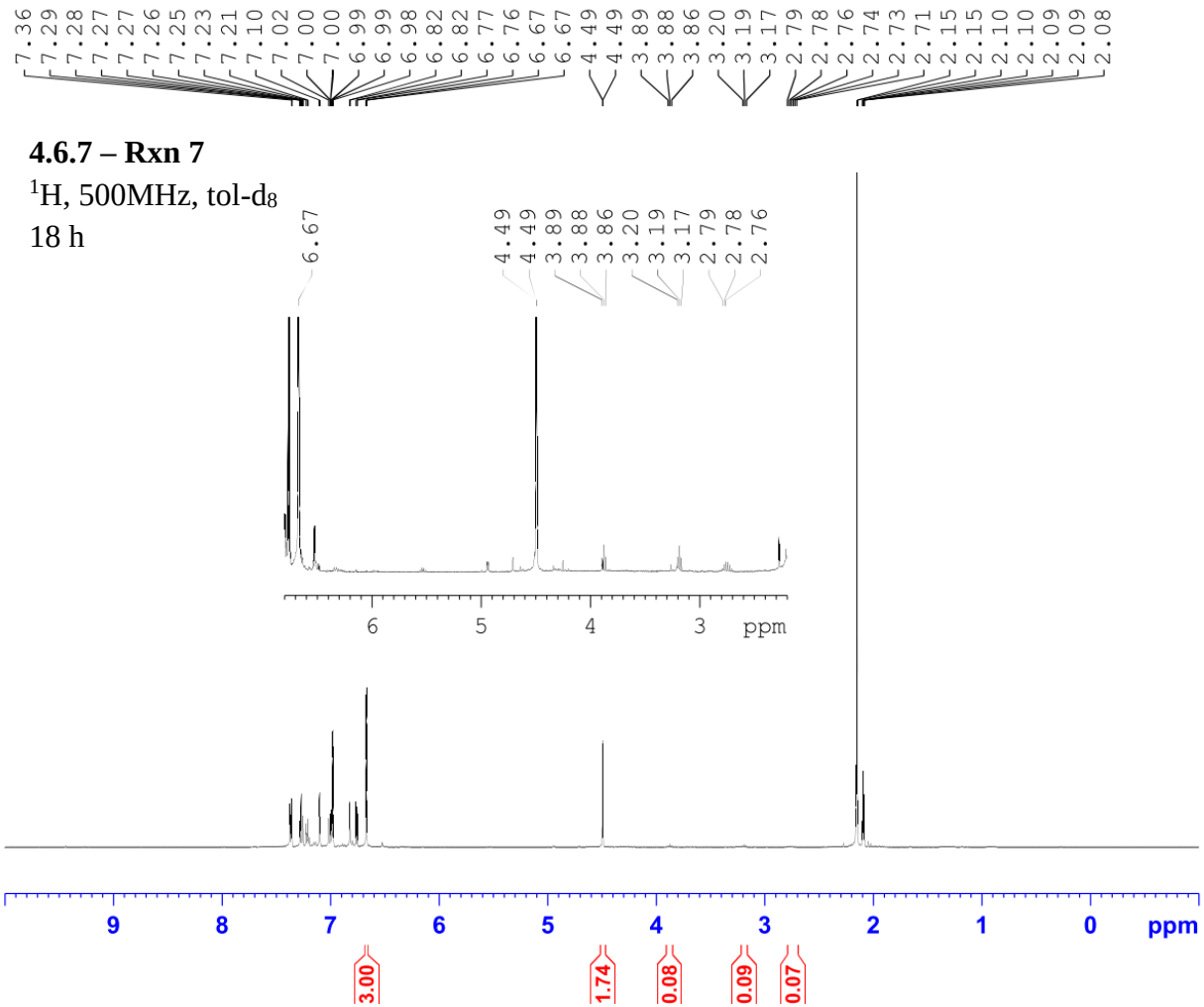



```
Current Data Parameters
NAME          JAW-03-073
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191121
Time               22.44
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH            12335.526 Hz
FIDRES          0.188225 Hz
AQ             2.6563926 sec
RG                   101
DW                40.533 usec
DE                  6.50 usec
TE                 295.3 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 10.86 usec
PL1                -2.00 dB
PL1W        19.70630455 W
SFO1        600.7137096 MHz

F2 - Processing parameters
SI                 32768
SF          600.7100219 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

4.6.7 – Rxn 7

^{1}H, 500MHz, tol-d$_8$

18 h

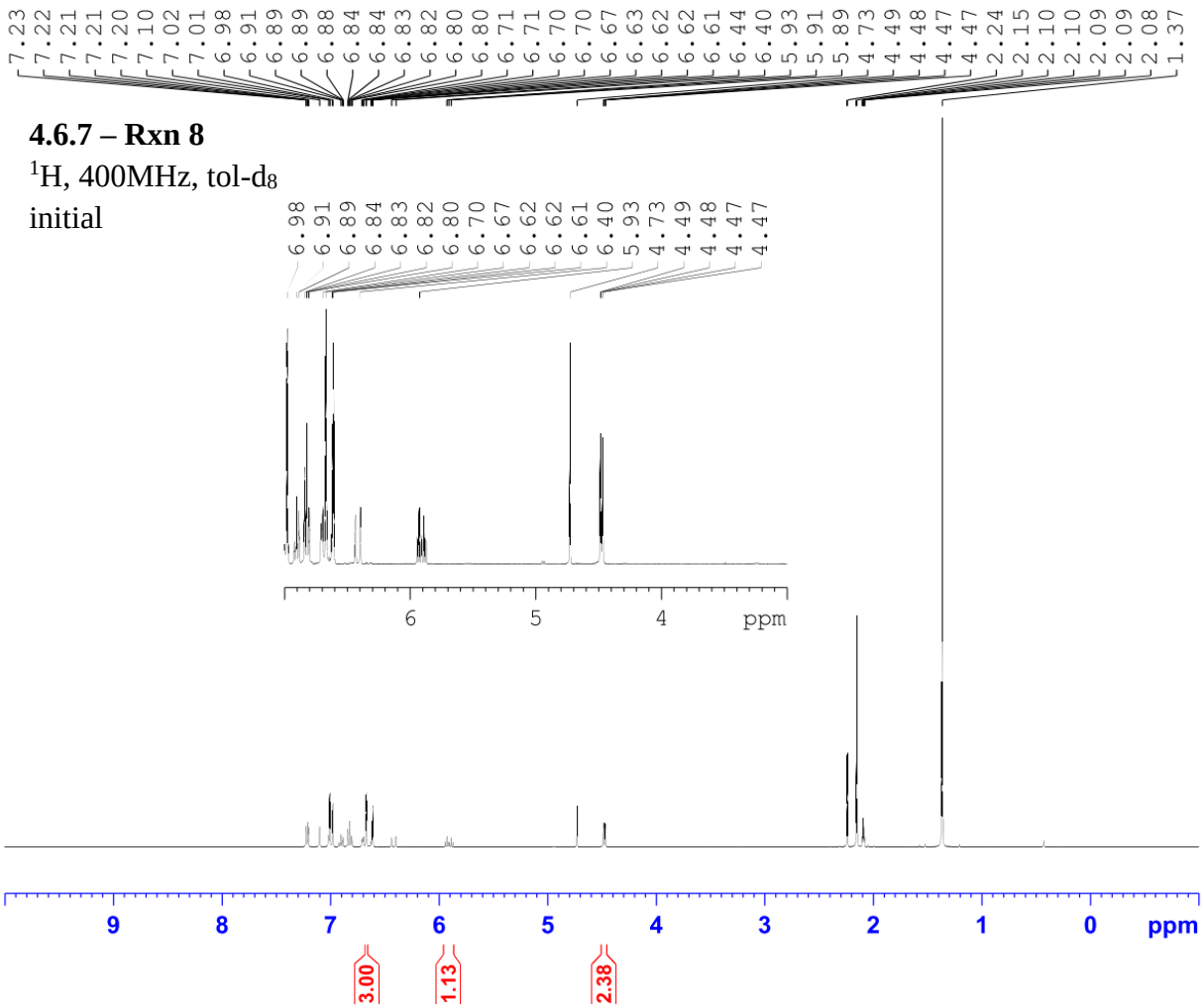



```
Current Data Parameters
NAME          JAW-03-073
EXPNO                  5
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191122
Time               10.00
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT              Tol
NS                    16
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                  80.6
DW                50.000 usec
DE                 6.50 usec
TE                297.3 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                  1H
P1                11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1600176 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.7 – Rxn 8

^{1}H, 400MHz, tol-d$_8$

initial

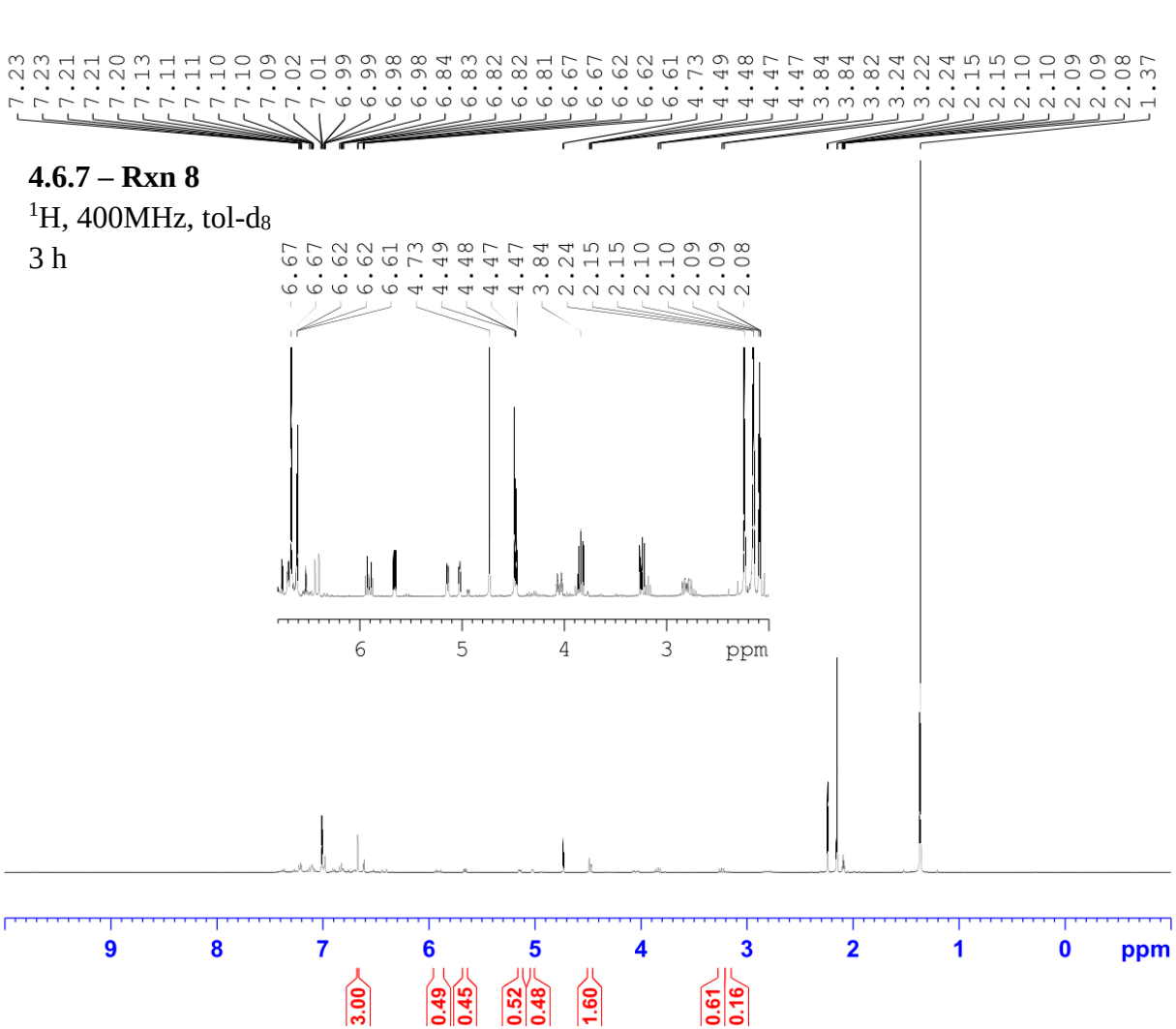



```
Current Data Parameters
NAME          JAW-03-081
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191230
Time               13.58 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG            zg30
TD                65536
SOLVENT             Tol
NS                   16
DS                    2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                   57
DW                62.400 usec
DE                 6.50 usec
TE                 90.2 K
D1           1.00000000 sec
TD0                   1
SFO1        400.1324708 MHz
NUC1                 1H
P0                 4.83 usec
P1                14.50 usec
PLW1        12.00000000 W

F2 - Processing parameters
SI                65536
SF          400.1300139 MHz
WDW                  EM
SSB      0
LB                0.30 Hz
GB       0
PC                1.00
```

4.6.7 – Rxn 8

^{1}H, 400MHz, tol-d_8

3 h

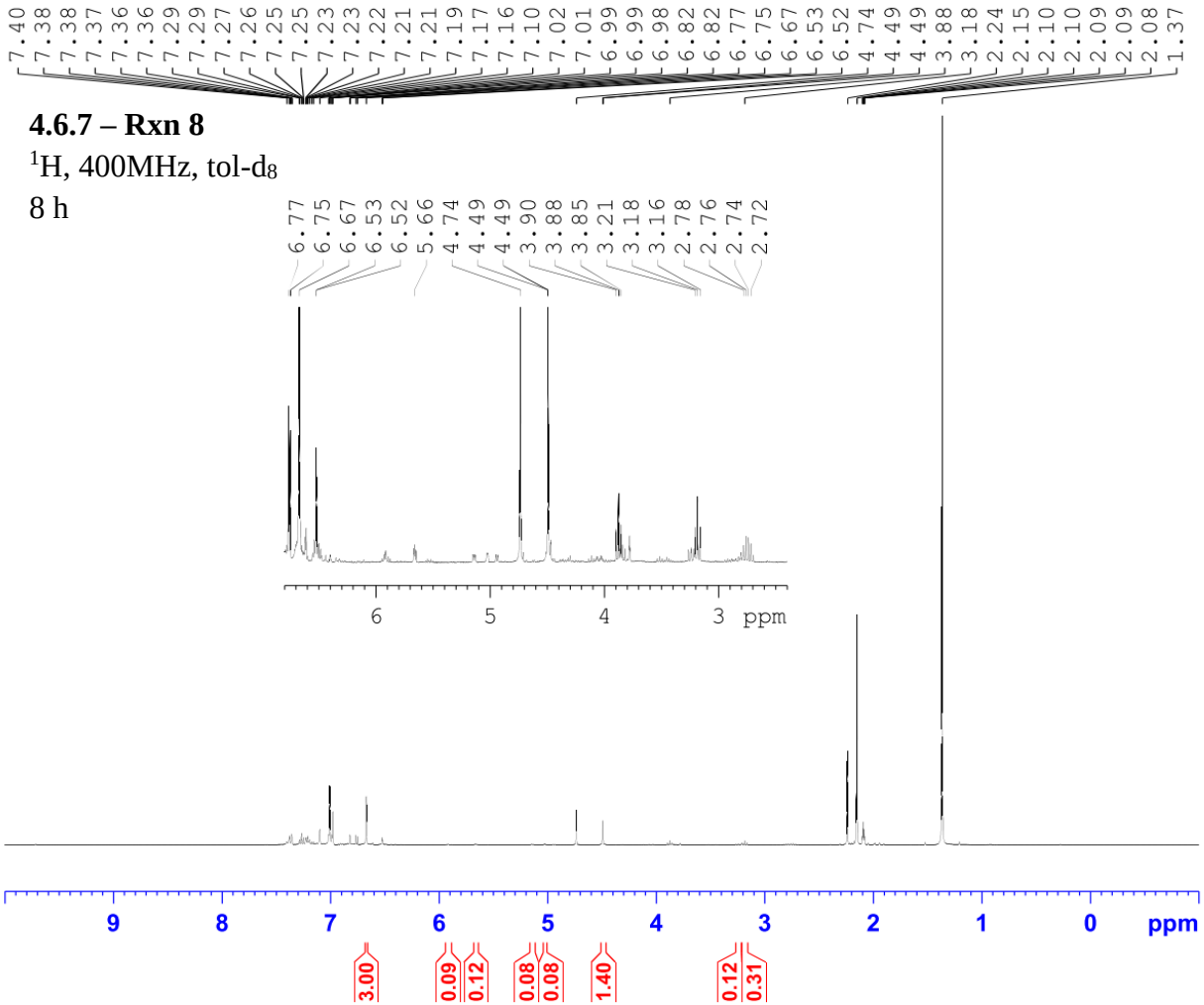



```
Current Data Parameters
NAME          JAW-03-081
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191230
Time               17.48 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG            zg30
TD                65536
SOLVENT             Tol
NS                   16
DS                    2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                   57
DW                62.400 usec
DE                 6.50 usec
TE                 90.1 K
D1           1.00000000 sec
TD0                   1
SFO1        400.1324708 MHz
NUC1                 1H
P0                 4.83 usec
P1                14.50 usec
PLW1        12.00000000 W

F2 - Processing parameters
SI                65536
SF          400.1300143 MHz
WDW                  EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```

4.6.7 – Rxn 8

^{1}H, 400MHz, tol-d_8

8 h

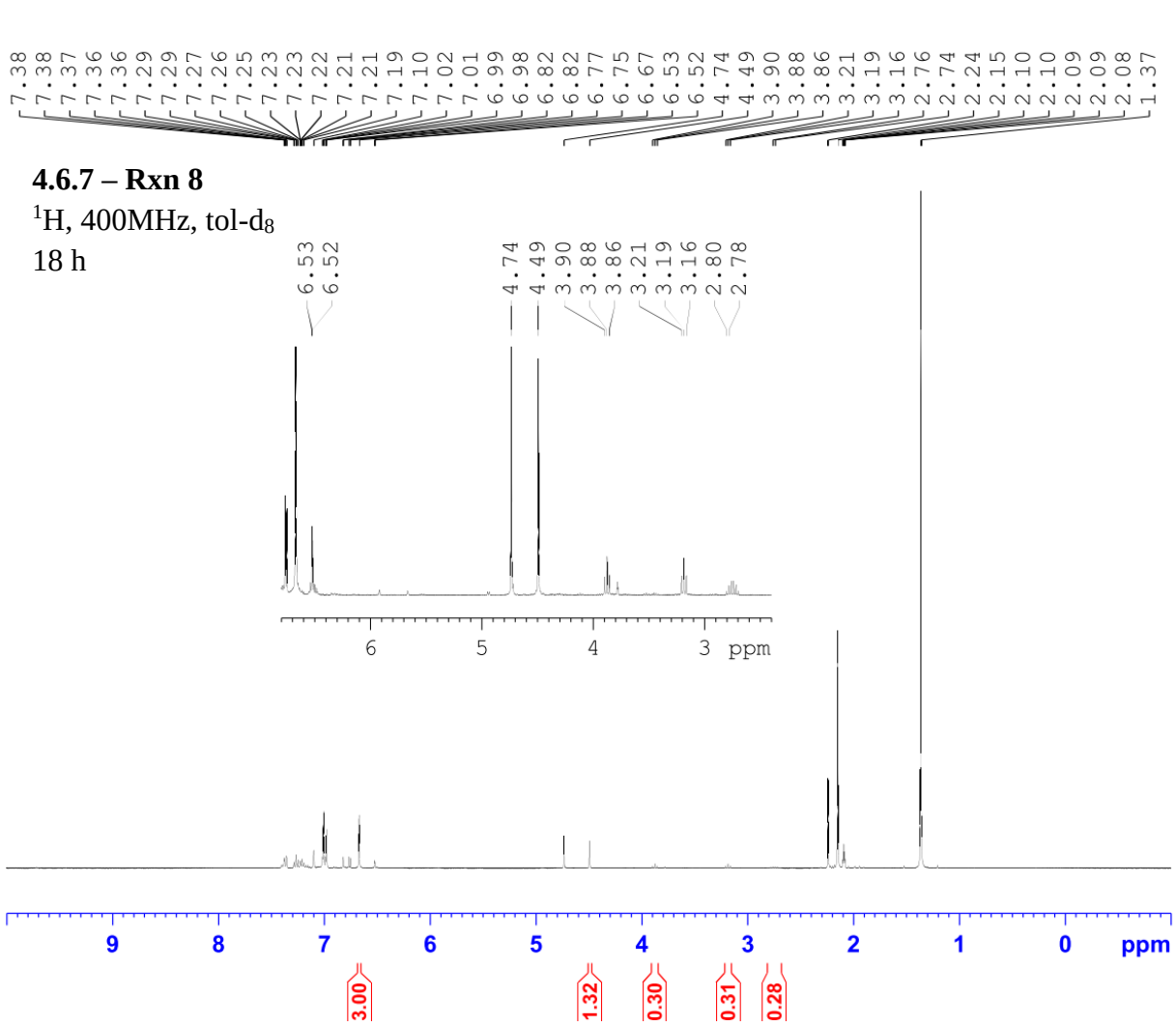



```
Current Data Parameters
NAME          JAW-03-081
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191230
Time               23.54 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG            zg30
TD                65536
SOLVENT             Tol
NS                   16
DS                    2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                   57
DW                62.400 usec
DE                 6.50 usec
TE                 90.2 K
D1           1.00000000 sec
TD0                   1
SFO1         400.1324708 MHz
NUC1                 1H
P0                 4.83 usec
P1                14.50 usec
PLW1         12.00000000 W

F2 - Processing parameters
SI                65536
SF          400.1300141 MHz
WDW                  EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```

4.6.7 – Rxn 8

^{1}H, 400MHz, tol-d_8

18 h

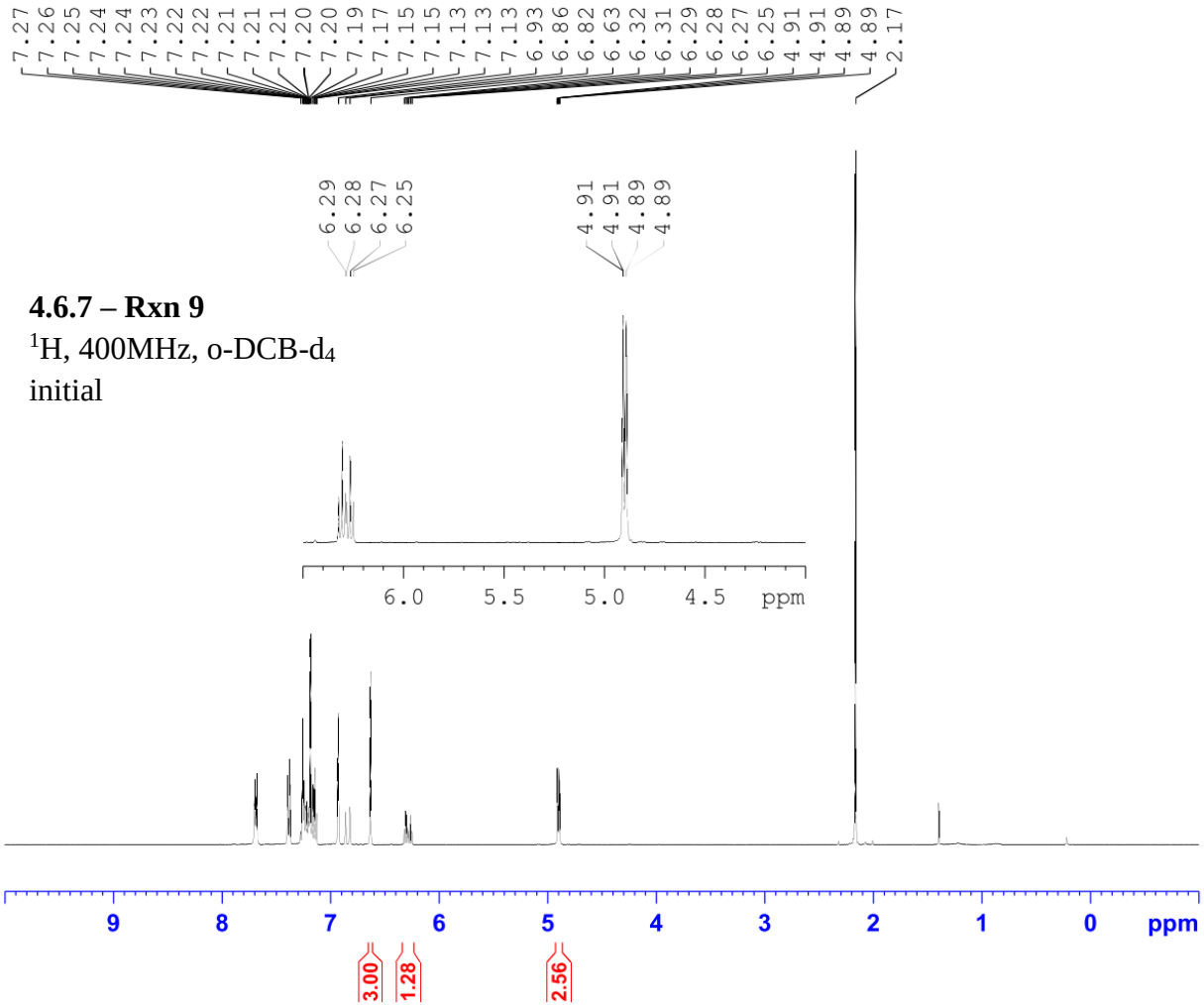



```
Current Data Parameters
NAME          JAW-03-081
EXPNO                  4
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191231
Time               11.23 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG            zg30
TD                65536
SOLVENT             Tol
NS                   16
DS                    2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                   57
DW                62.400 usec
DE                 6.50 usec
TE                 91.3 K
D1           1.00000000 sec
TD0                   1
SFO1         400.1324708 MHz
NUC1                 1H
P0                 4.83 usec
P1                14.50 usec
PLW1         12.00000000 W

F2 - Processing parameters
SI                65536
SF          400.1300139 MHz
WDW                  EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.7 – Rxn 9

^{1}H, 400MHz, o-DCB-d$_4$

initial

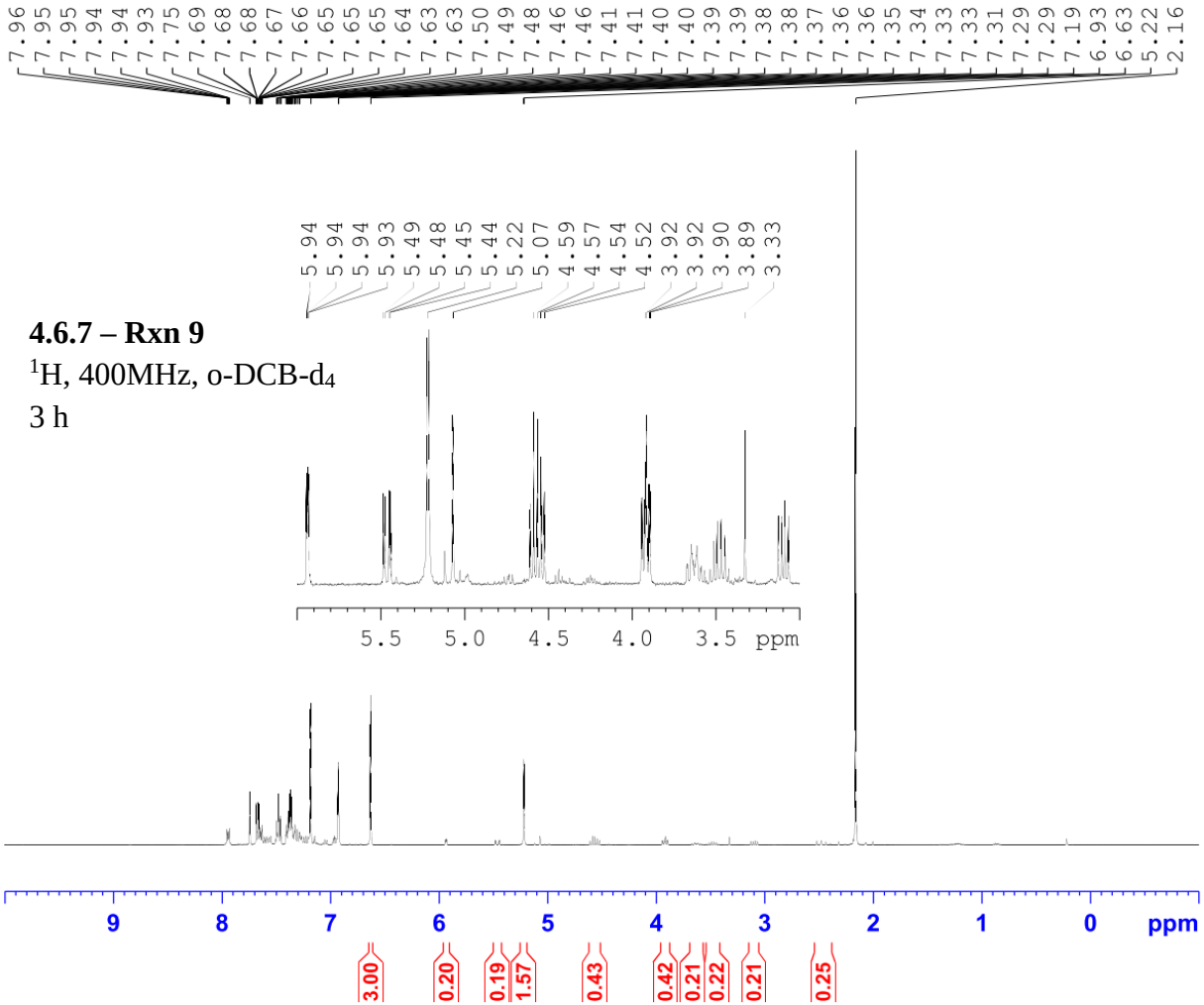



```
Current Data Parameters
NAME          JAW-03-109
EXPNO                  5
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210419
Time                9.36
INSTRUM            spect
PROBHD   5 mm PADUL 13C
PULPROG             zg30
TD                 65536
SOLVENT         oC6D4Cl2
NS                     16
DS                      2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ             3.9845889 sec
RG                    114
DW                 60.800 usec
DE                  6.50 usec
TE                 295.1 K
D1            2.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                  9.31 usec
PL1                -3.90 dB
PL1W         21.64248466 W
SFO1         400.2324716 MHz

F2 - Processing parameters
SI                 32768
SF          400.2300667 MHz
WDW                    EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

4.6.7 – Rxn 9

^{1}H, 400MHz, o-DCB-d$_4$

3 h

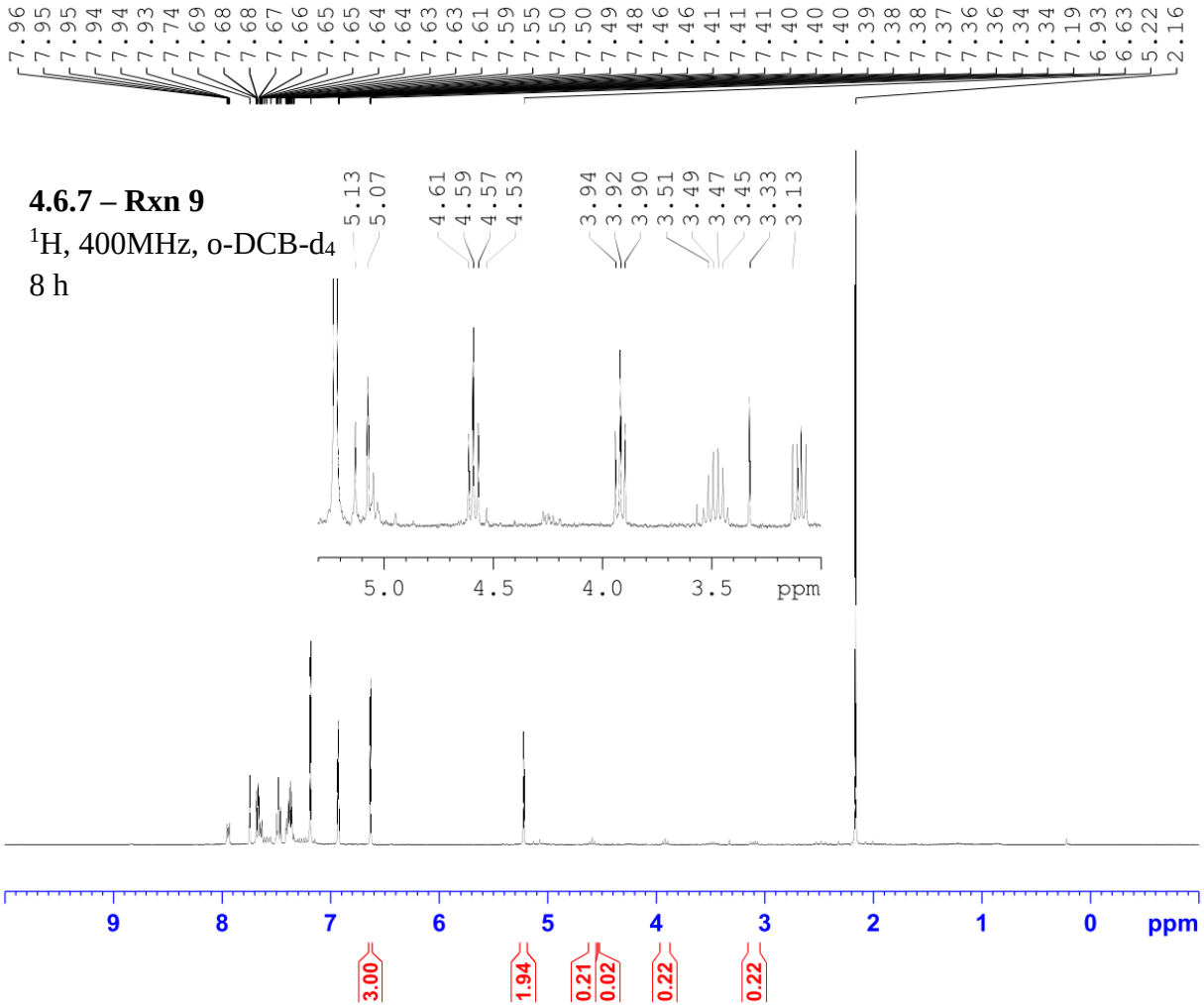



```
Current Data Parameters
NAME          JAW-03-109
EXPNO                  6
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210419
Time               12.55
INSTRUM            spect
PROBHD   5 mm PADUL 13C
PULPROG             zg30
TD                 65536
SOLVENT         oC6D4C12
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ             3.9845889 sec
RG                   114
DW                60.800 usec
DE                 6.50 usec
TE                295.1 K
D1            2.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                  9.31 usec
PL1                -3.90 dB
PL1W         21.64248466 W
SFO1         400.2324716 MHz

F2 - Processing parameters
SI                 32768
SF          400.2299657 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.7 – Rxn 9

^{1}H, 400MHz, o-DCB-d$_4$

8 h

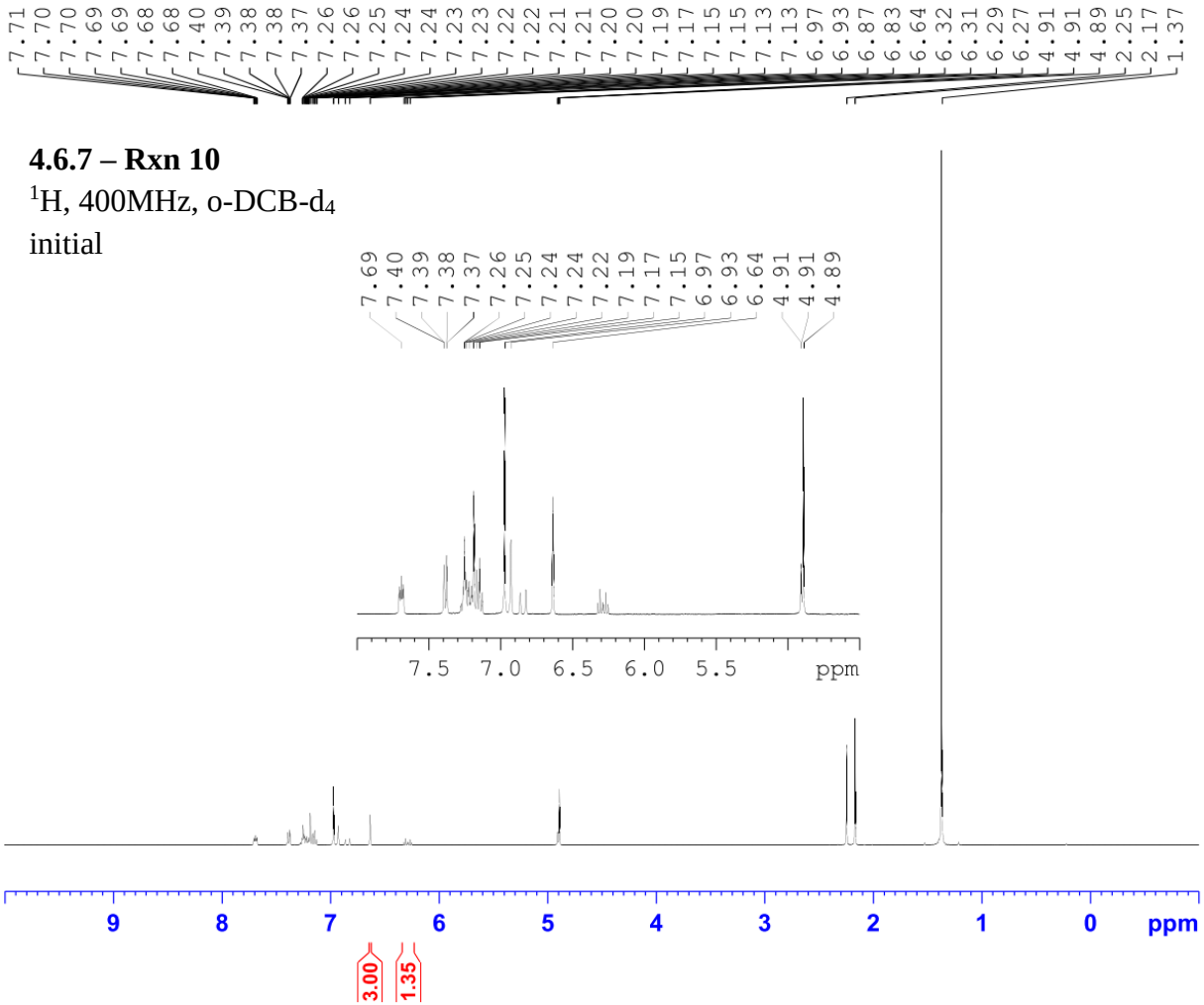



```
Current Data Parameters
NAME          JAW-03-109
EXPNO                  7
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210419
Time               22.30
INSTRUM            spect
PROBHD   5 mm PADUL 13C
PULPROG             zg30
TD                 65536
SOLVENT         oC6D4Cl2
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ             3.9845889 sec
RG                   114
DW                60.800 usec
DE                 6.50 usec
TE                295.4 K
D1            2.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                  9.31 usec
PL1                -3.90 dB
PL1W         21.64248466 W
SFO1         400.2324716 MHz

F2 - Processing parameters
SI                 32768
SF          400.2300665 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

4.6.7 – Rxn 10

^{1}H, 400MHz, o-DCB-d$_4$

initial

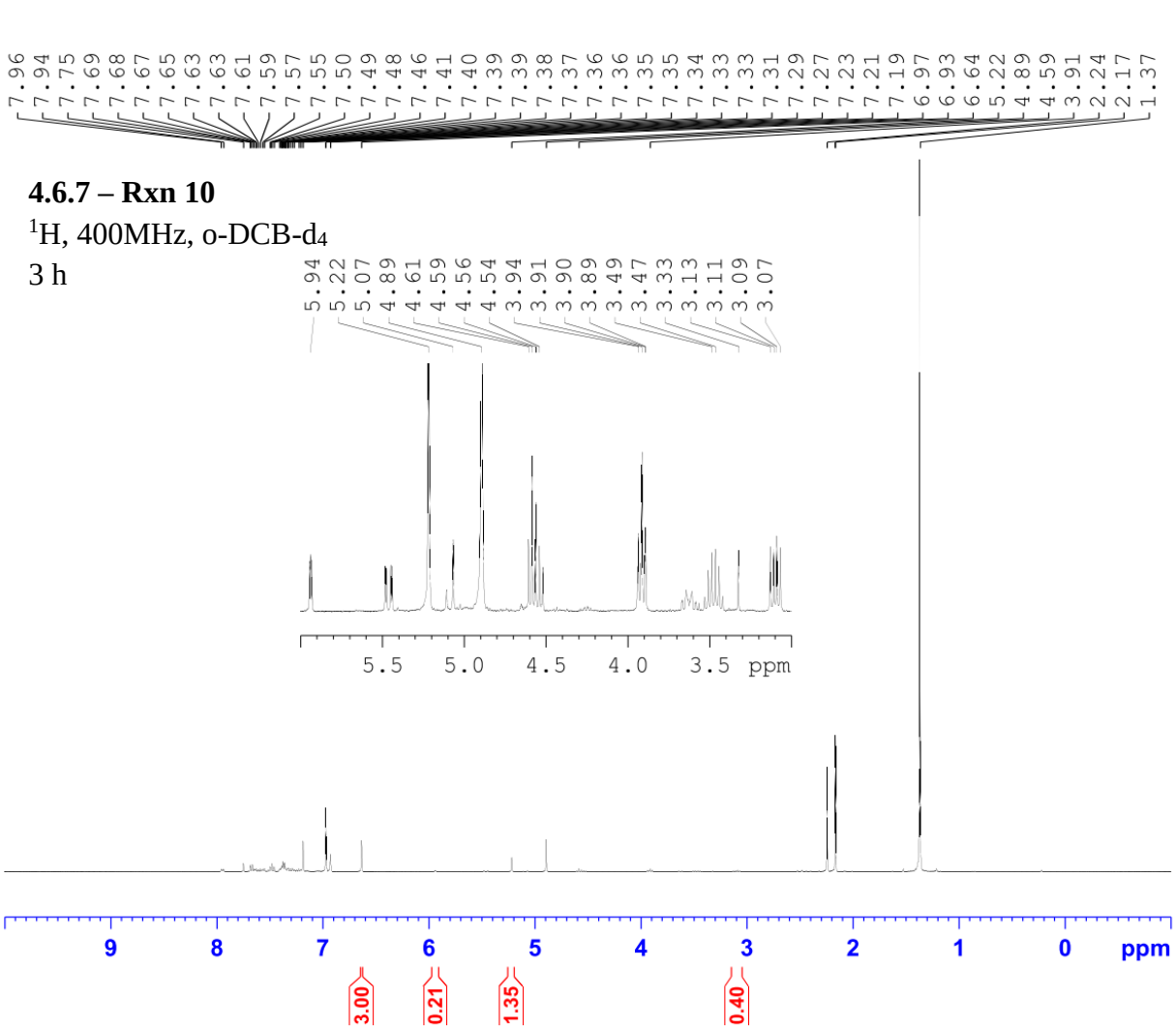



```
Current Data Parameters
NAME          JAW-03-110
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210421
Time                9.47
INSTRUM            spect
PROBHD   5 mm PADUL 13C
PULPROG             zg30
TD                 65536
SOLVENT         oC6D4Cl2
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ             3.9845889 sec
RG                  71.8
DW                60.800 usec
DE                 6.50 usec
TE                295.0 K
D1            2.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                  9.31 usec
PL1                -3.90 dB
PL1W        21.64248466 W
SFO1        400.2324716 MHz

F2 - Processing parameters
SI                 32768
SF          400.2299650 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.7 – Rxn 10

^{1}H, 400MHz, o-DCB-d$_4$

3 h

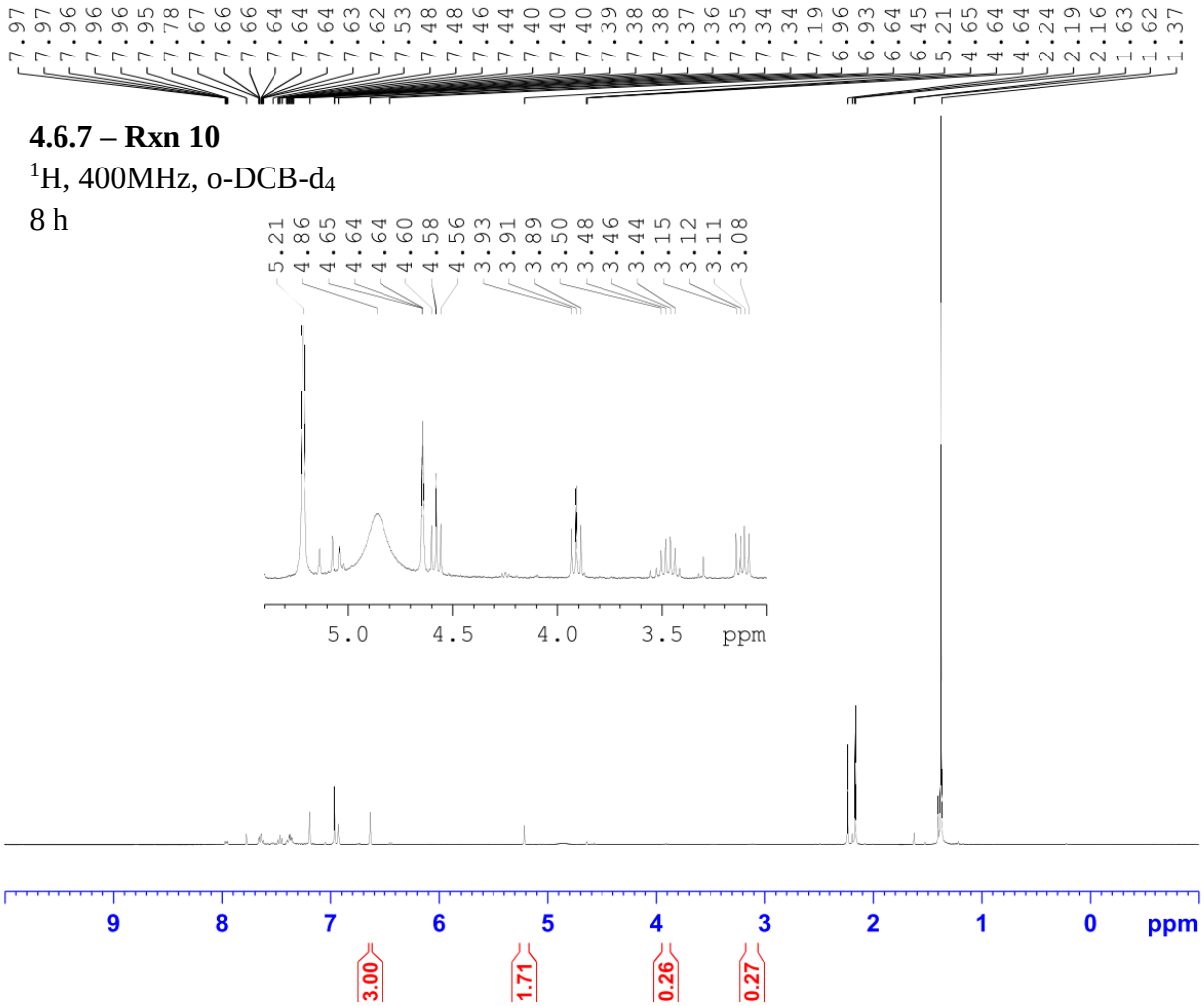



```
Current Data Parameters
NAME          JAW-03-110
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210421
Time               13.01
INSTRUM            spect
PROBHD   5 mm PADUL 13C
PULPROG             zg30
TD                 65536
SOLVENT         oC6D4Cl2
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ             3.9845889 sec
RG                  71.8
DW                60.800 usec
DE                 6.50 usec
TE                295.1 K
D1            2.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 9.31 usec
PL1               -3.90 dB
PL1W        21.64248466 W
SFO1        400.2324716 MHz

F2 - Processing parameters
SI                 32768
SF          400.2299652 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.7 – Rxn 10

^{1}H, 400MHz, o-DCB-d$_4$

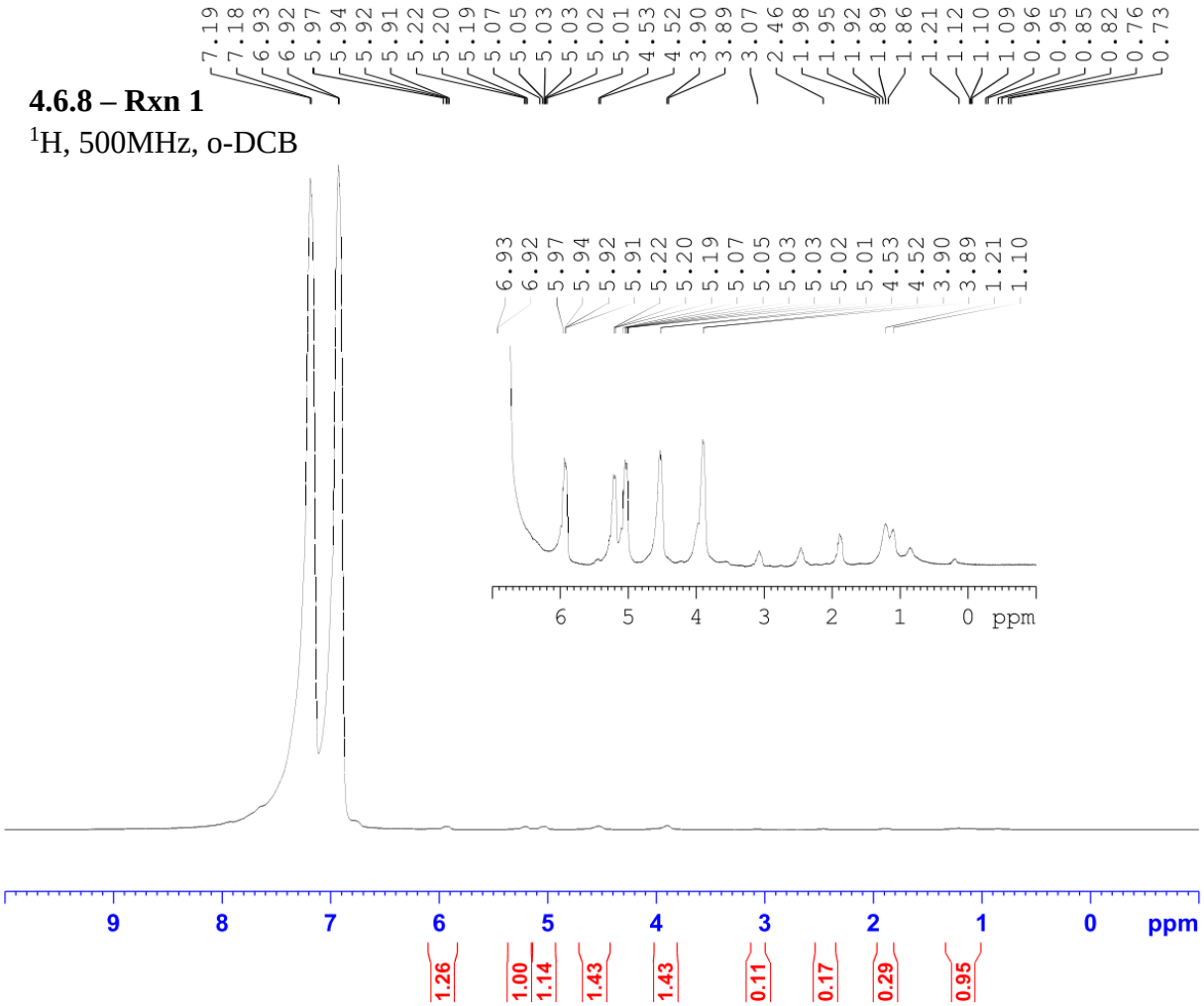
8 h




```
Current Data Parameters
NAME          JAW-03-110
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210422
Time                8.04
INSTRUM            spect
PROBHD   5 mm PADUL 13C
PULPROG             zg30
TD                 65536
SOLVENT         oC6D4Cl2
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ             3.9845889 sec
RG                  71.8
DW                60.800 usec
DE                 6.50 usec
TE                312.2 K
D1            2.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 9.31 usec
PL1               -3.90 dB
PL1W         21.64248466 W
SFO1         400.2324716 MHz

F2 - Processing parameters
SI                 32768
SF          400.2299629 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.8 – Rxn 1

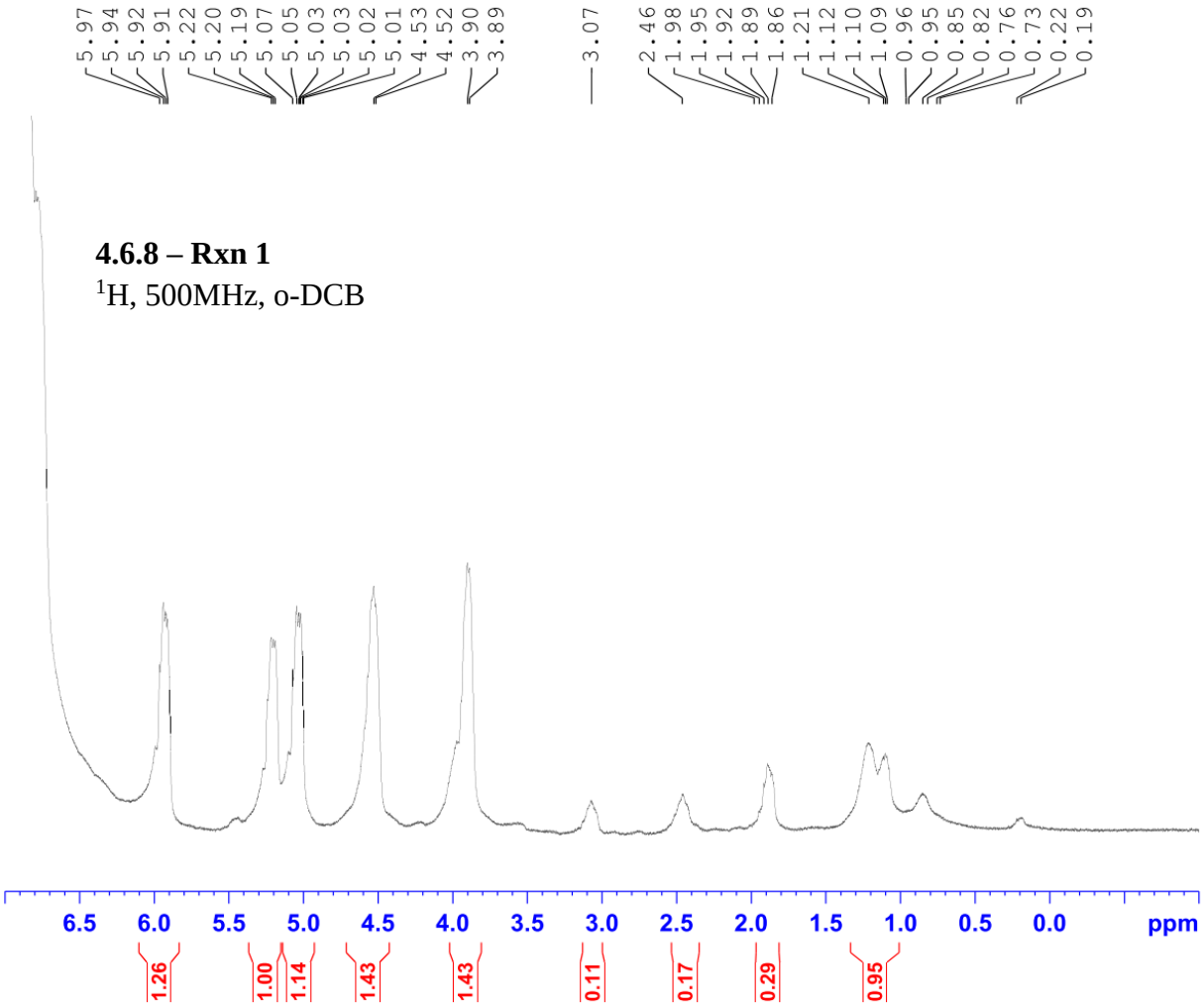
^{1}H, 500MHz, o-DCB




```
Current Data Parameters
NAME          JAW-01-143
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170831
Time               17.21
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT             None
NS                    16
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                  6.35
DW                50.000 usec
DE                 6.50 usec
TE                296.1 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                  1H
P1                11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1597941 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.8 – Rxn 1

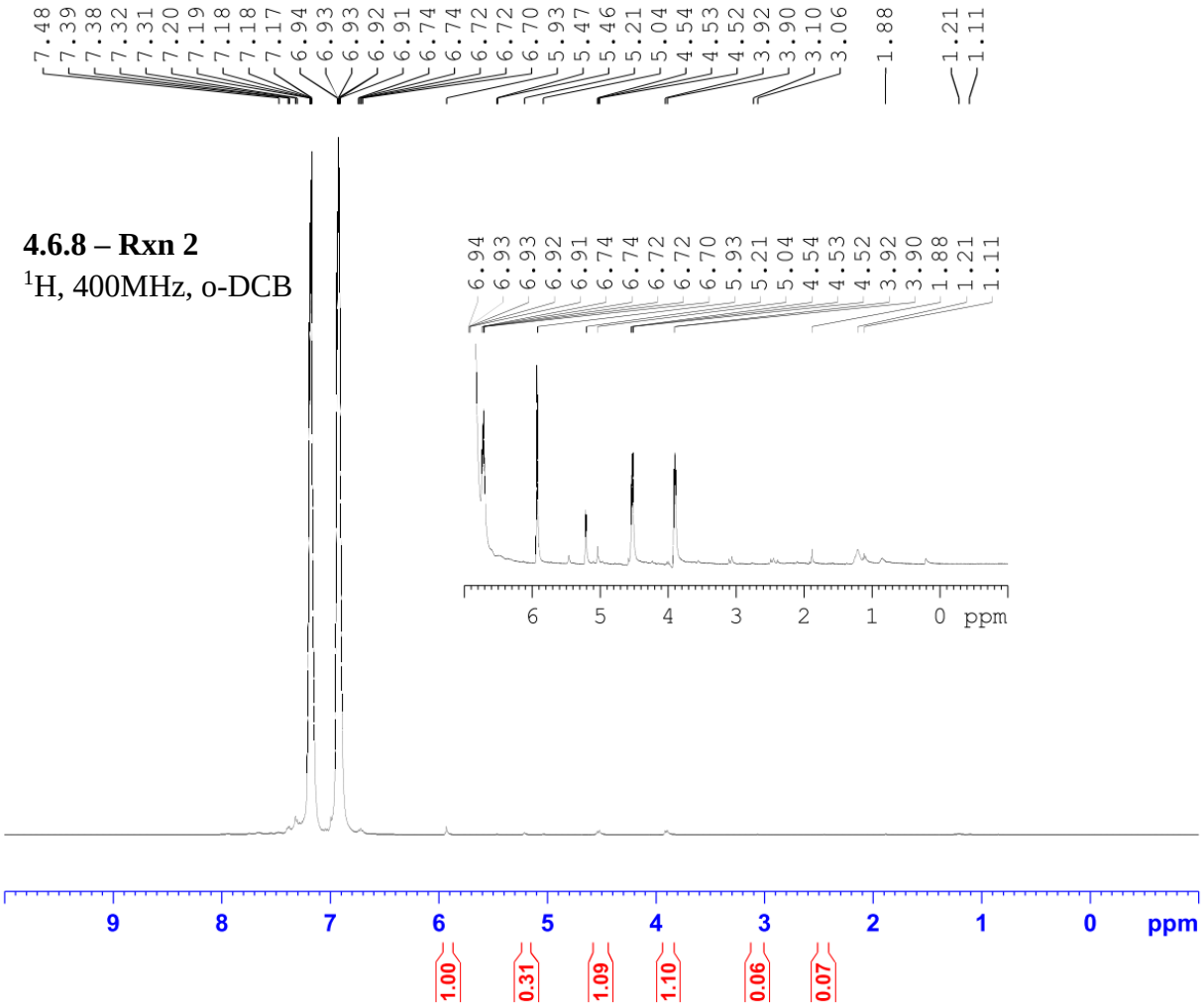
^{1}H, 500MHz, o-DCB



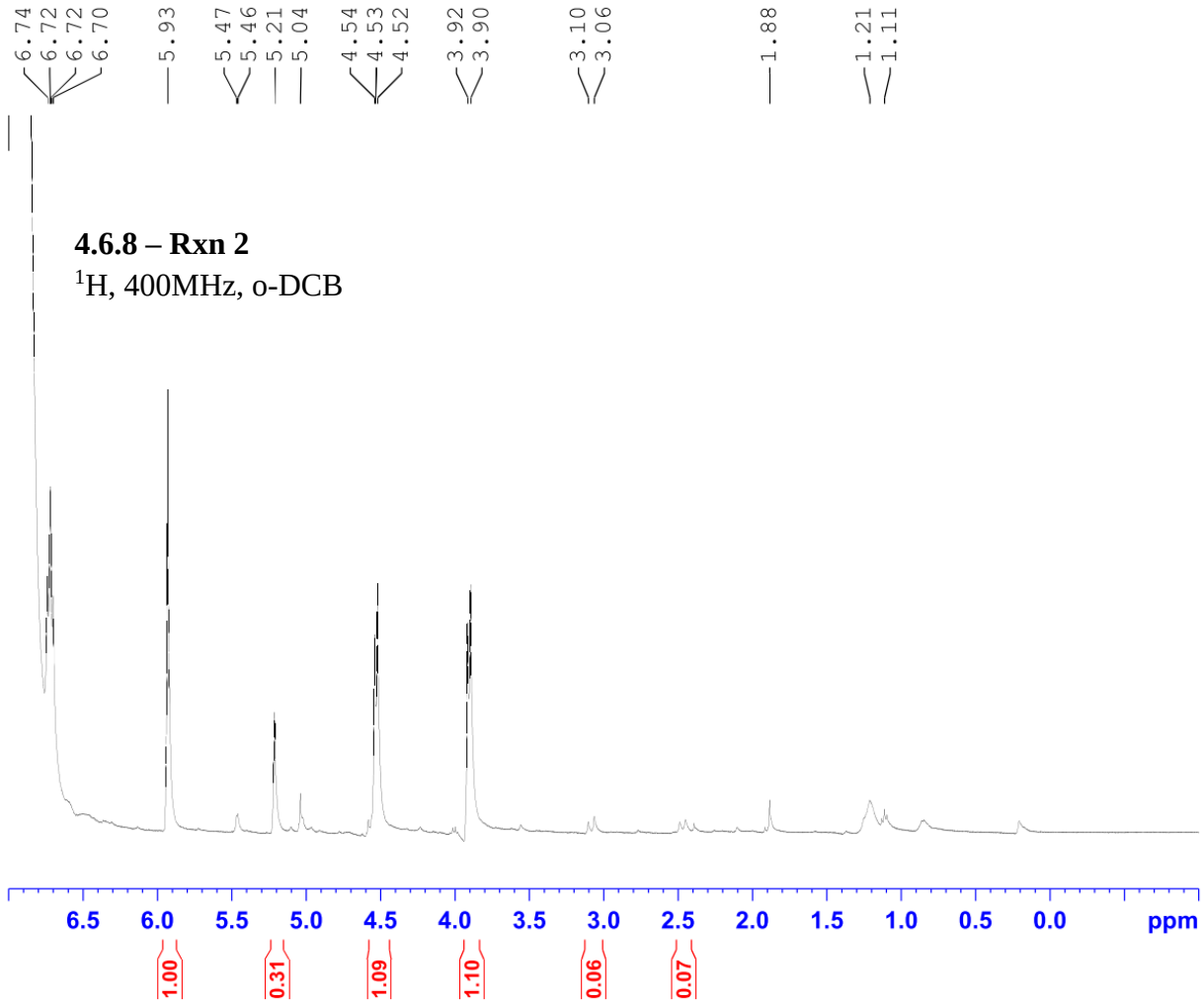

```
Current Data Parameters
NAME          JAW-01-143
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170831
Time               17.21
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT             None
NS                    16
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                  6.35
DW                50.000 usec
DE                  6.50 usec
TE                 296.1 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                  1H
P1                 11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1597941 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

4.6.8 – Rxn 2

^{1}H, 400MHz, o-DCB



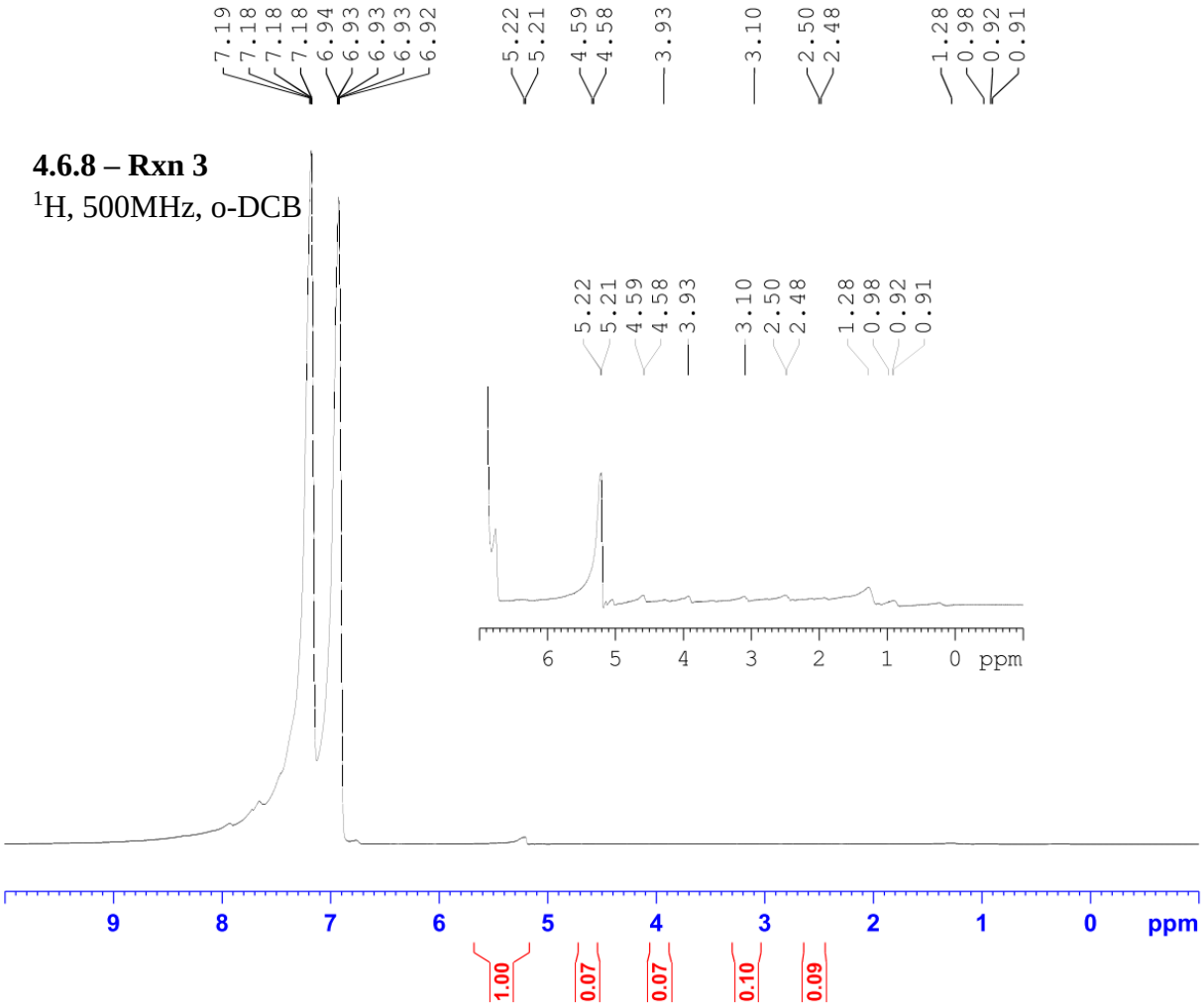

```
Current Data Parameters
NAME          JAW-01-149
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170913
Time               14.02
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    32
DS                     2
SWH             8012.820 Hz
FIDRES          0.122266 Hz
AQ             4.0894465 sec
RG                  6.35
DW                62.400 usec
DE                 6.50 usec
TE                3030.7 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         400.1324710 MHz
NUC1                  1H
P1                 13.75 usec
PLW1         12.01700020 W

F2 - Processing parameters
SI                 65536
SF           400.1305116 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```




```
Current Data Parameters
NAME          JAW-01-149
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170913
Time               14.02
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    32
DS                     2
SWH             8012.820 Hz
FIDRES          0.122266 Hz
AQ             4.0894465 sec
RG                  6.35
DW                62.400 usec
DE                 6.50 usec
TE                3030.7 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         400.1324710 MHz
NUC1                  1H
P1                 13.75 usec
PLW1         12.01700020 W

F2 - Processing parameters
SI                 65536
SF           400.1305116 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

4.6.8 – Rxn 3

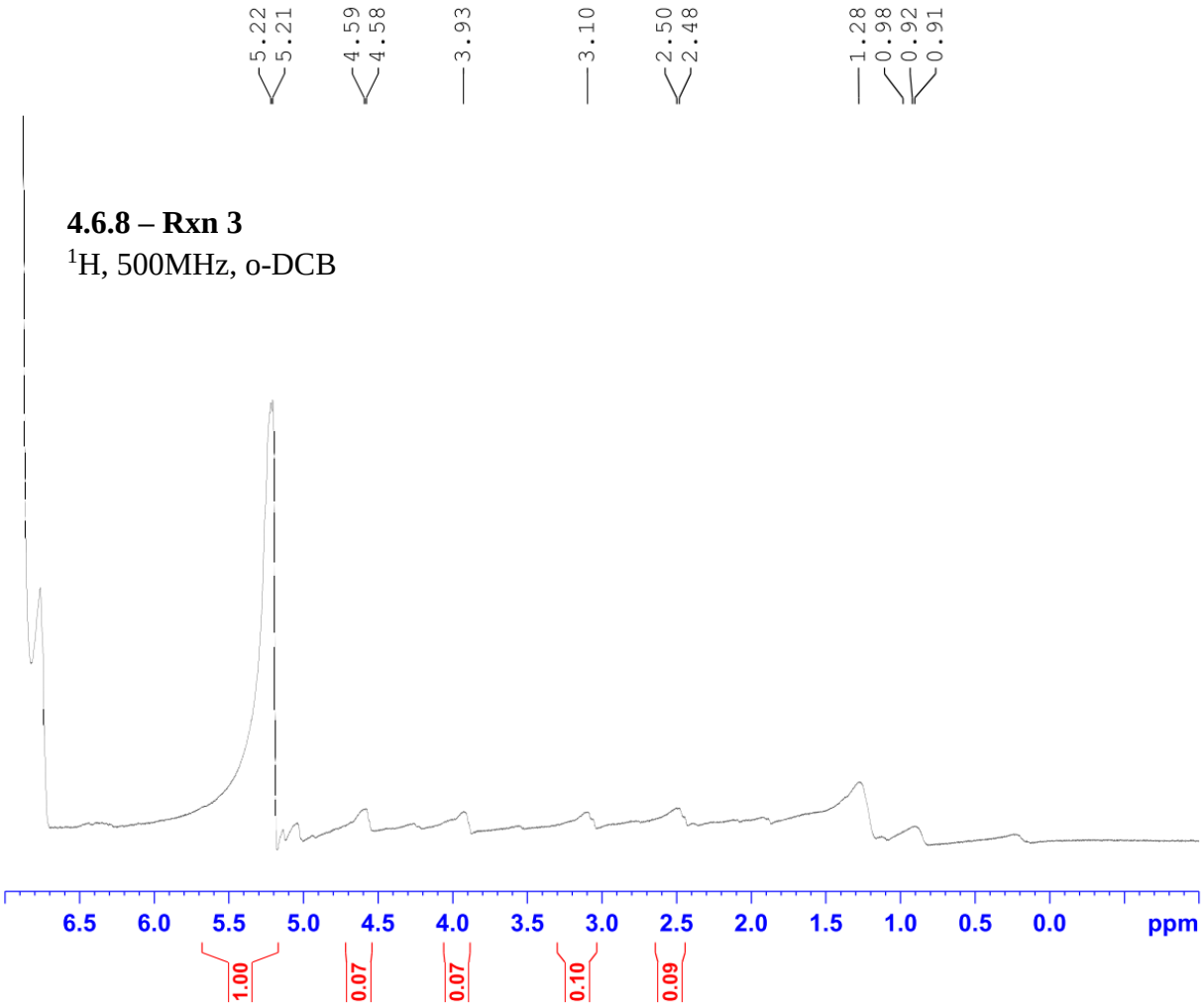
^{1}H, 500MHz, o-DCB




```
Current Data Parameters
NAME          JAW-01-150
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170914
Time               16.41
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT             None
NS                    32
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                   5.6
DW                50.000 usec
DE                 6.50 usec
TE                296.2 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                  1H
P1                11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1597985 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.8 – Rxn 3

^{1}H, 500MHz, o-DCB

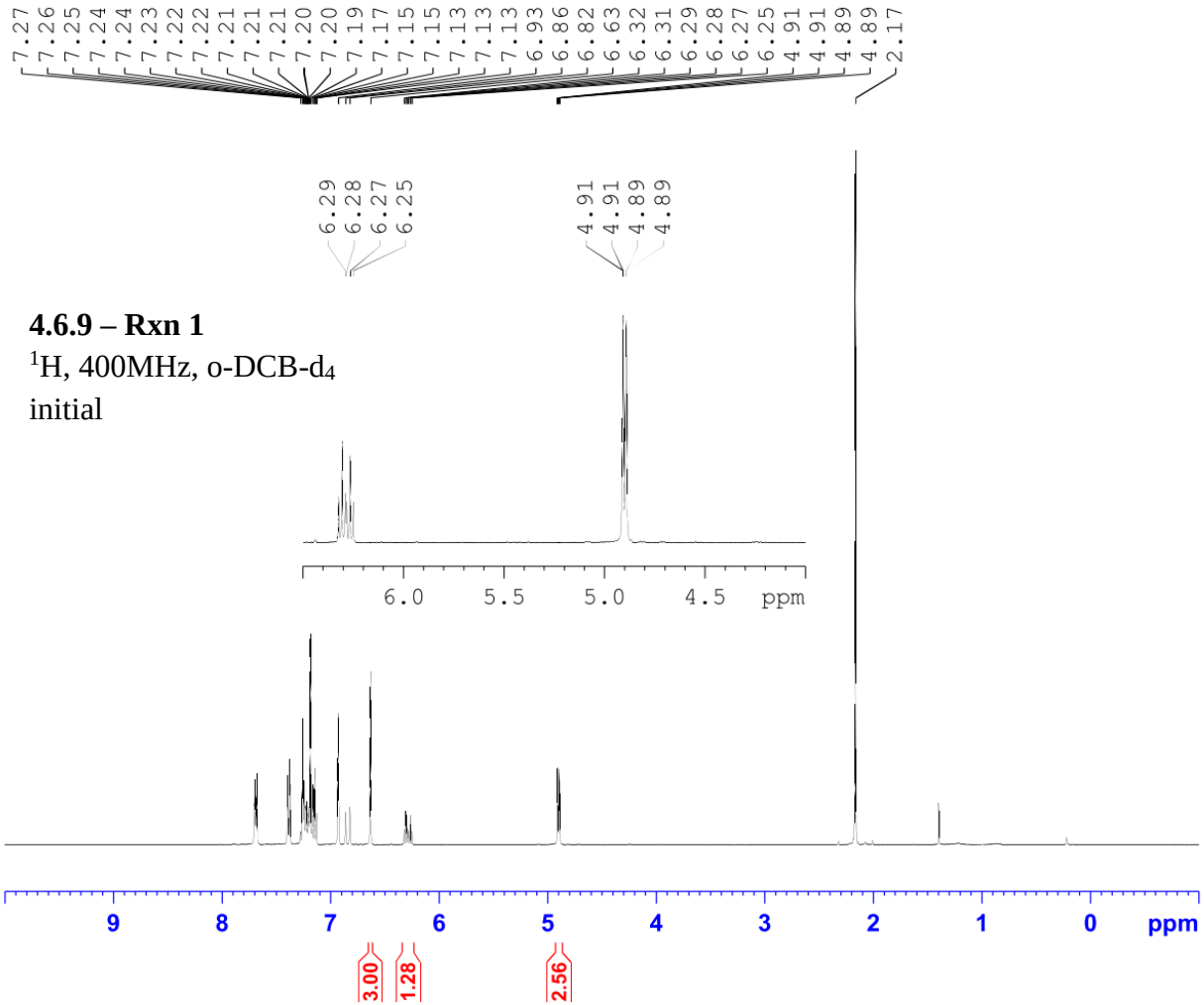



```
Current Data Parameters
NAME          JAW-01-150
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170914
Time               16.41
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT             None
NS                    32
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                   5.6
DW                50.000 usec
DE                 6.50 usec
TE                296.2 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                  1H
P1                11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1597985 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.9 – Rxn 1

^{1}H, 400MHz, o-DCB-d$_4$

initial

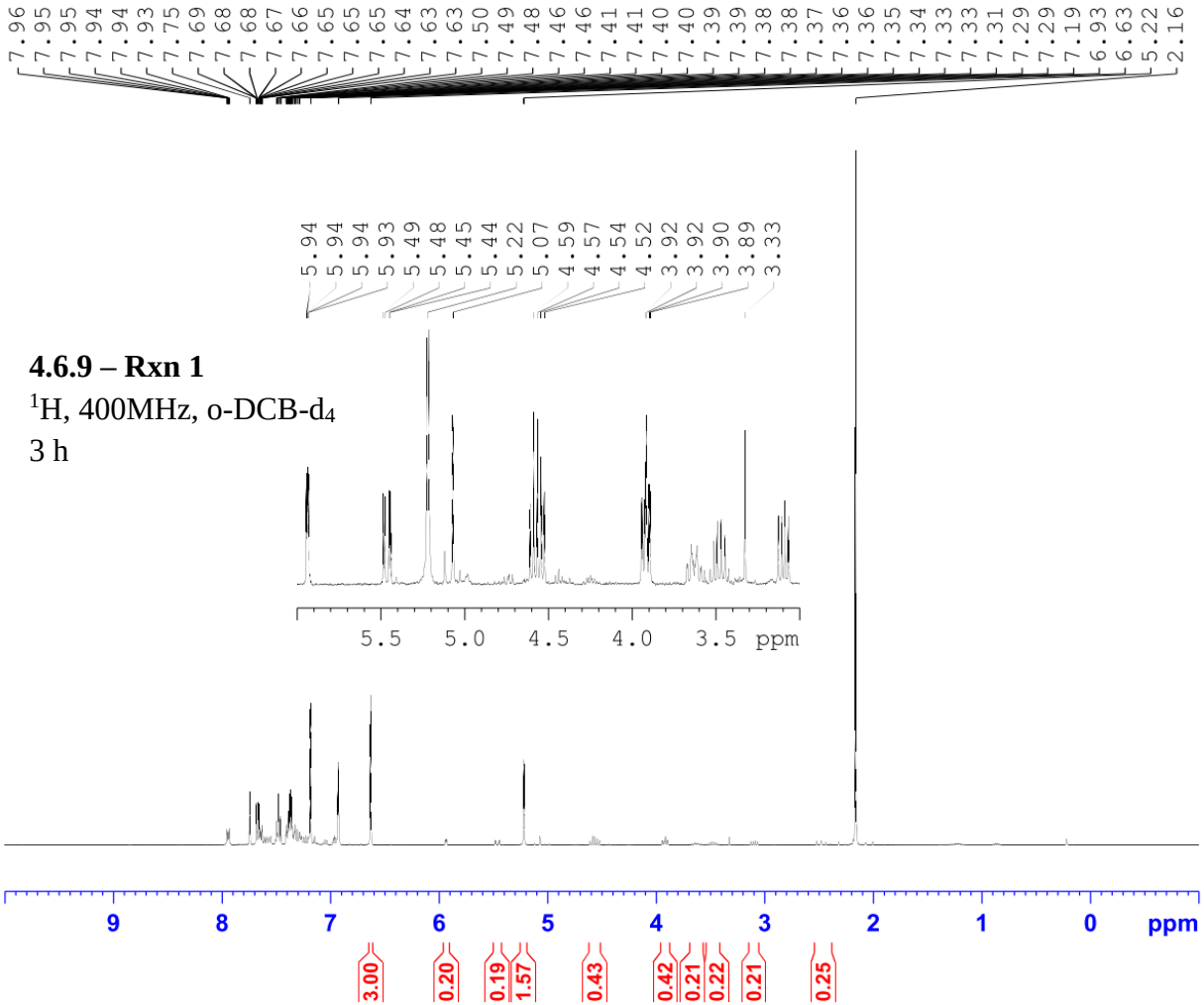



```
Current Data Parameters
NAME          JAW-03-109
EXPNO                  5
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210419
Time                9.36
INSTRUM            spect
PROBHD   5 mm PADUL 13C
PULPROG             zg30
TD                 65536
SOLVENT         oC6D4Cl2
NS                     16
DS                      2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ             3.9845889 sec
RG                    114
DW                 60.800 usec
DE                  6.50 usec
TE                 295.1 K
D1            2.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                  9.31 usec
PL1                -3.90 dB
PL1W         21.64248466 W
SFO1         400.2324716 MHz

F2 - Processing parameters
SI                 32768
SF          400.2300667 MHz
WDW                    EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

4.6.9 – Rxn 1

^{1}H, 400MHz, o-DCB-d$_4$

3 h

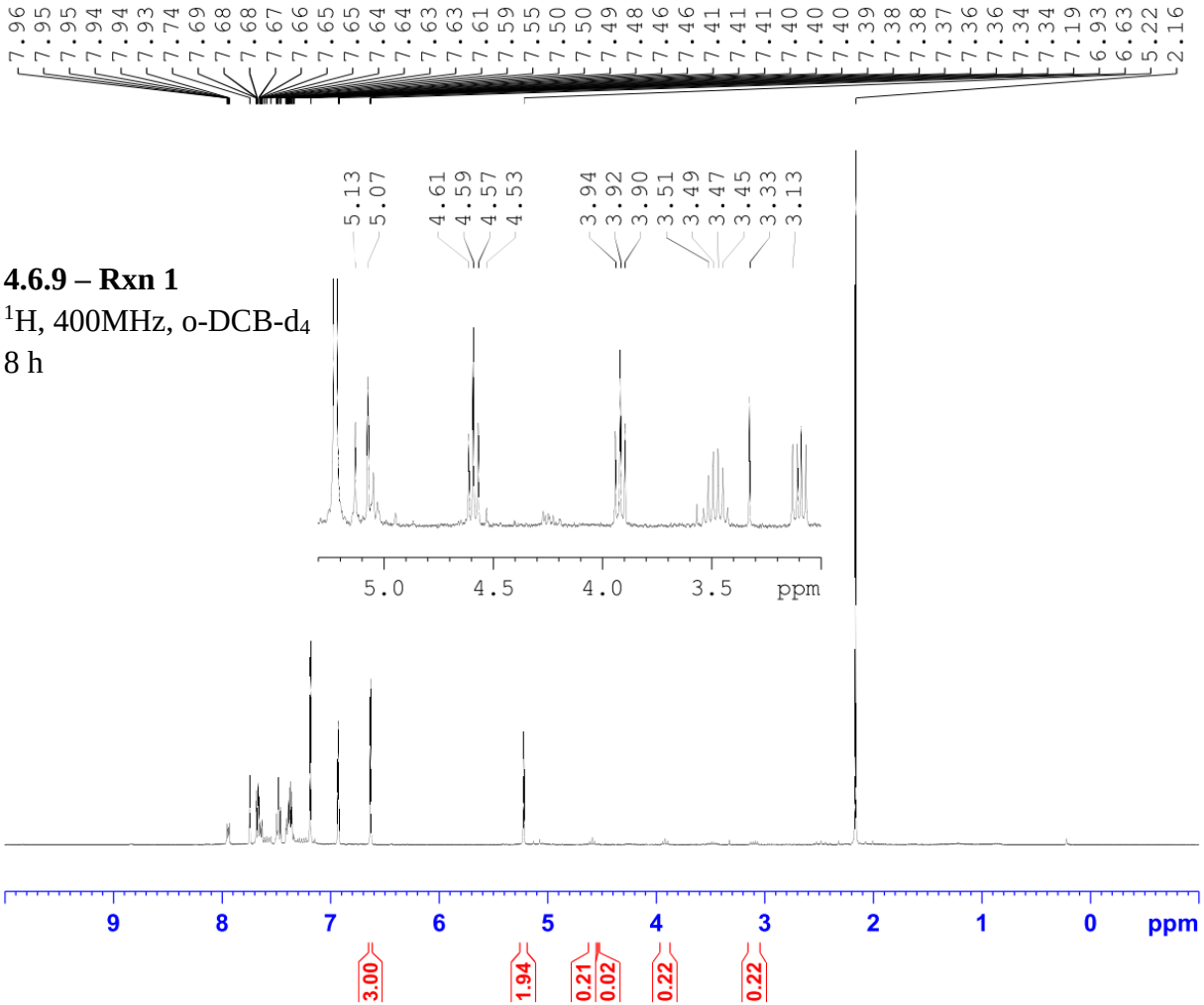



```
Current Data Parameters
NAME          JAW-03-109
EXPNO                  6
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210419
Time               12.55
INSTRUM            spect
PROBHD   5 mm PADUL 13C
PULPROG             zg30
TD                 65536
SOLVENT         oC6D4Cl2
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ             3.9845889 sec
RG                   114
DW                60.800 usec
DE                 6.50 usec
TE                295.1 K
D1            2.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                  9.31 usec
PL1                -3.90 dB
PL1W         21.64248466 W
SFO1         400.2324716 MHz

F2 - Processing parameters
SI                 32768
SF          400.2299657 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.9 – Rxn 1

^{1}H, 400MHz, o-DCB-d$_4$

8 h

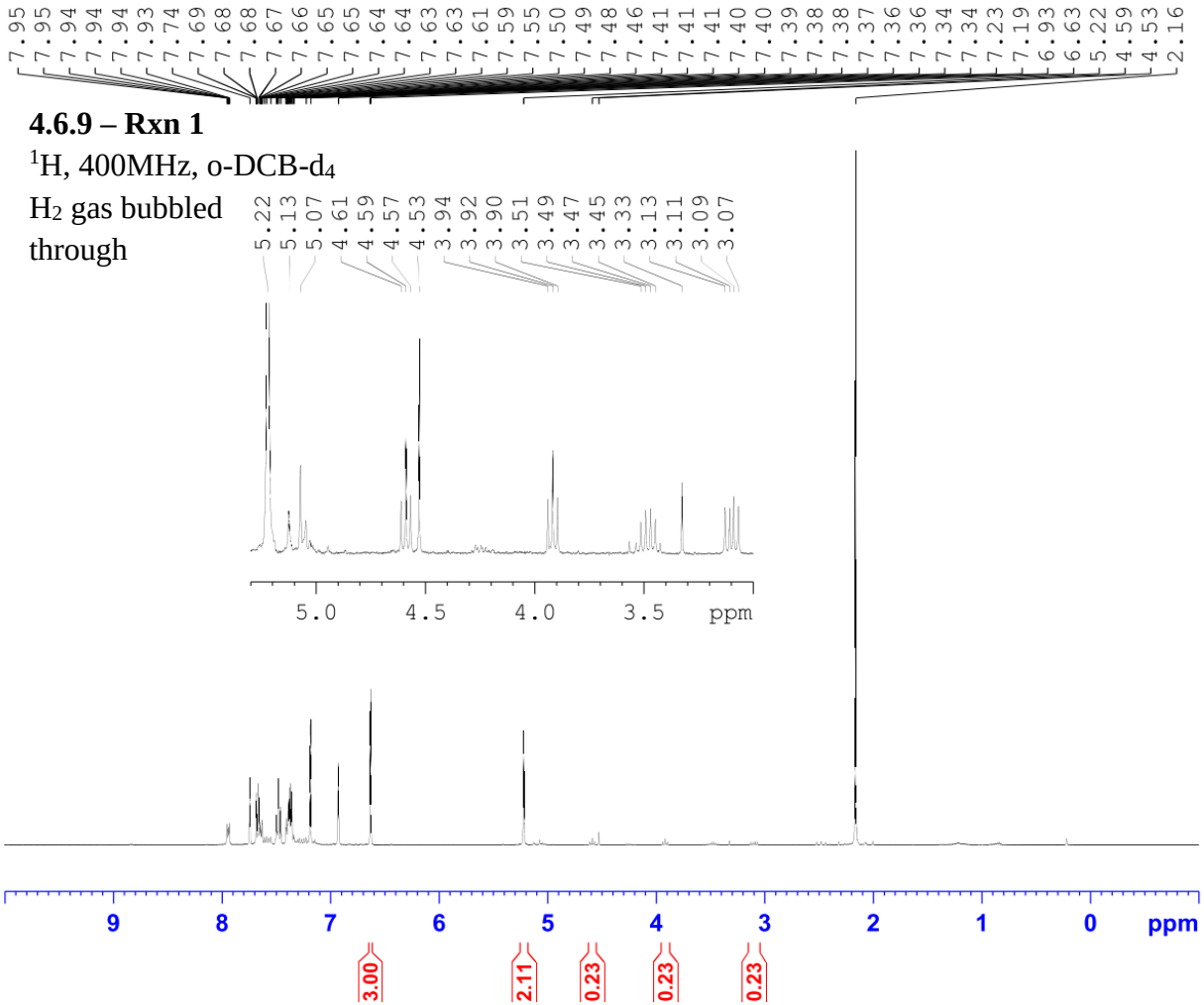



```
Current Data Parameters
NAME          JAW-03-109
EXPNO                  7
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210419
Time               22.30
INSTRUM            spect
PROBHD   5 mm PADUL 13C
PULPROG             zg30
TD                 65536
SOLVENT         oC6D4Cl2
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ             3.9845889 sec
RG                   114
DW                60.800 usec
DE                 6.50 usec
TE                295.4 K
D1            2.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                  9.31 usec
PL1                -3.90 dB
PL1W         21.64248466 W
SFO1         400.2324716 MHz

F2 - Processing parameters
SI                 32768
SF          400.2300665 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

4.6.9 – Rxn 1

^{1}H, 400MHz, o-DCB-d_4

H_2 gas bubbled through

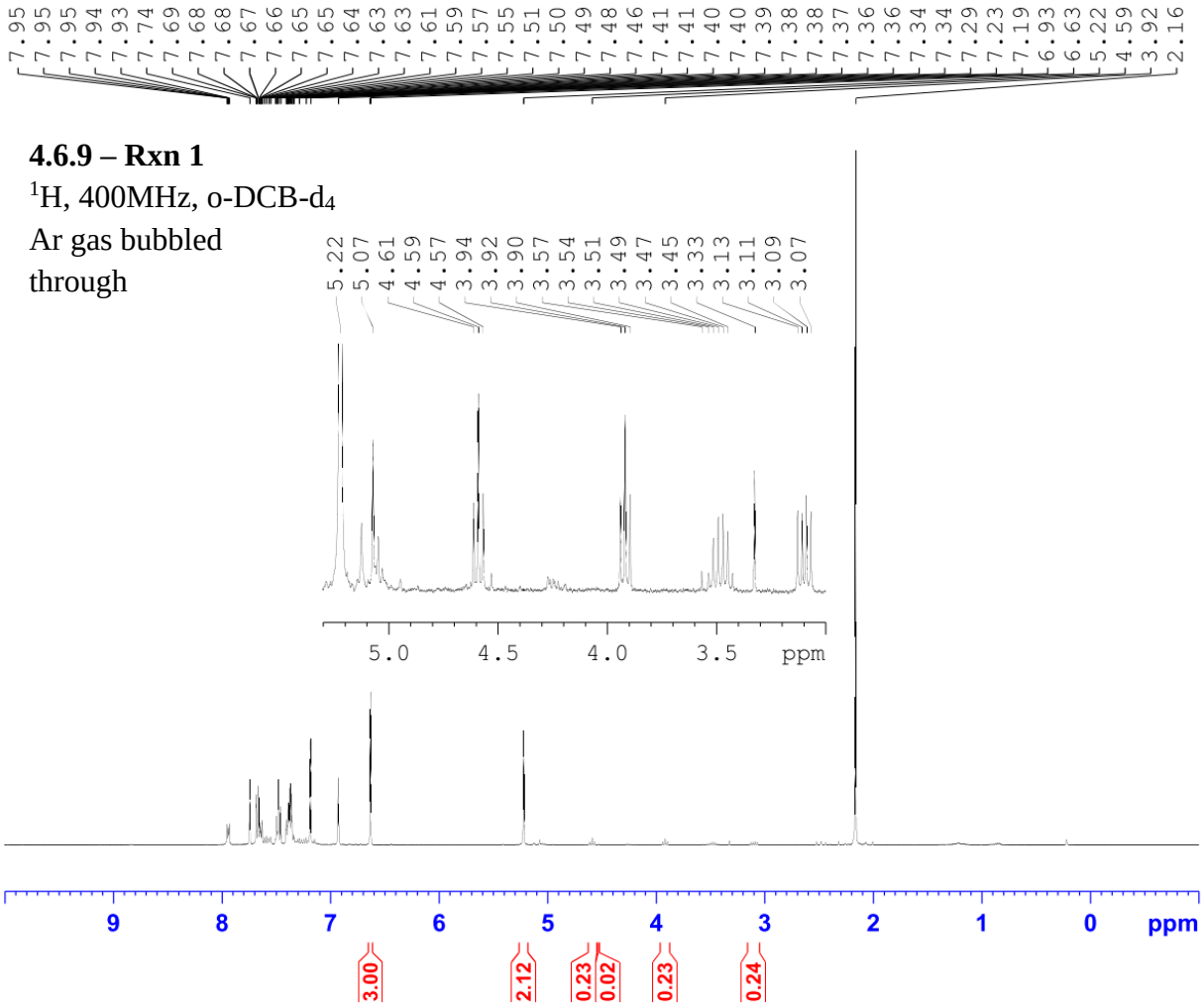



```
Current Data Parameters
NAME          JAW-03-109
EXPNO                  8
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210419
Time               22.46
INSTRUM            spect
PROBHD   5 mm PADUL 13C
PULPROG             zg30
TD                 65536
SOLVENT         oC6D4Cl2
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ             3.9845889 sec
RG                   114
DW                60.800 usec
DE                 6.50 usec
TE                295.3 K
D1            2.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                  9.31 usec
PL1                -3.90 dB
PL1W        21.64248466 W
SFO1        400.2324716 MHz

F2 - Processing parameters
SI                 32768
SF          400.2300666 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

4.6.9 – Rxn 1

^{1}H, 400MHz, o-DCB-d$_4$

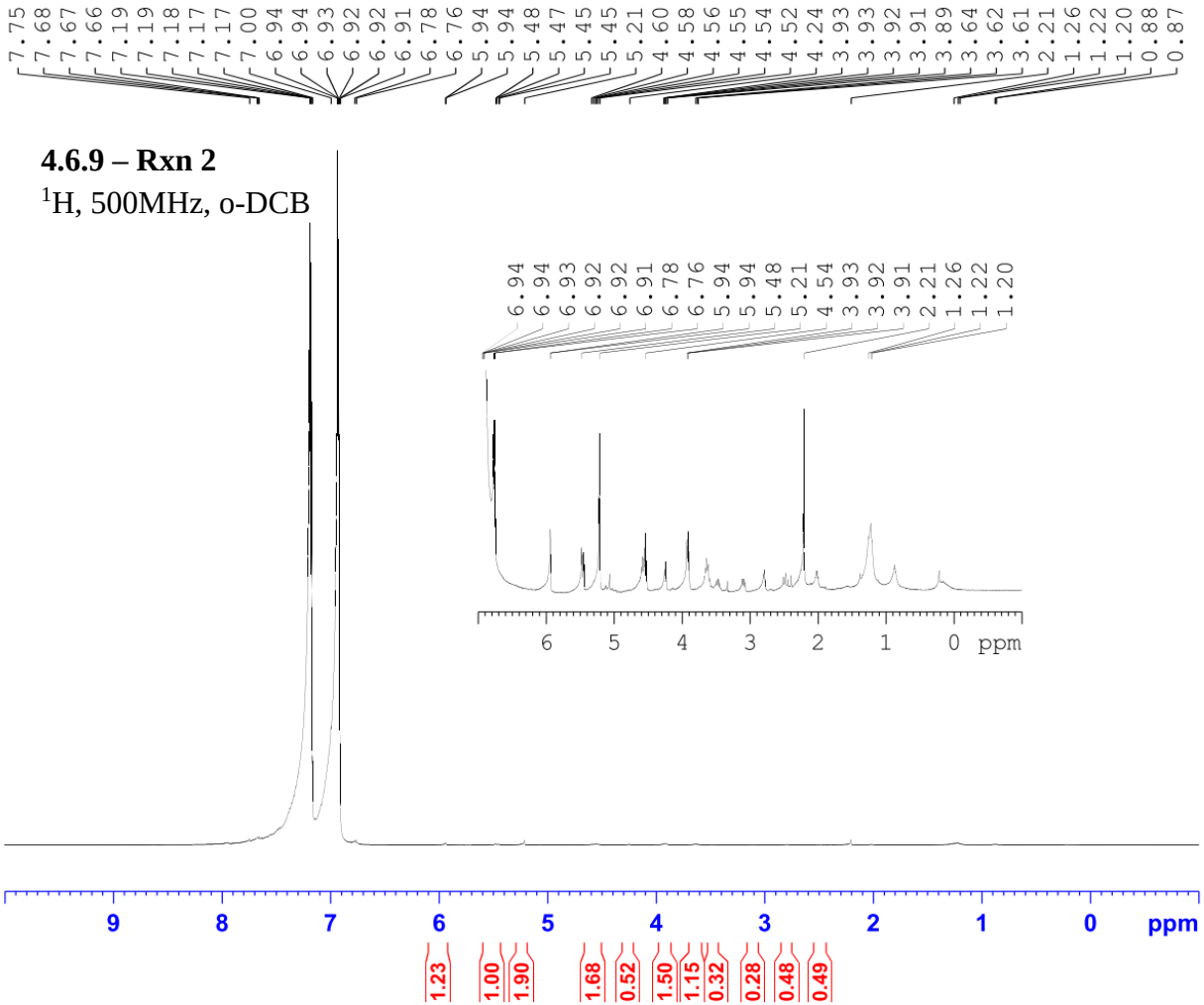
Ar gas bubbled through




```
Current Data Parameters
NAME          JAW-03-109
EXPNO                  9
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210419
Time               23.00
INSTRUM            spect
PROBHD   5 mm PADUL 13C
PULPROG             zg30
TD                 65536
SOLVENT         oC6D4Cl2
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ             3.9845889 sec
RG                   114
DW                60.800 usec
DE                 6.50 usec
TE                295.2 K
D1            2.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                  9.31 usec
PL1                -3.90 dB
PL1W         21.64248466 W
SFO1         400.2324716 MHz

F2 - Processing parameters
SI                 32768
SF          400.2300667 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

4.6.9 – Rxn 2

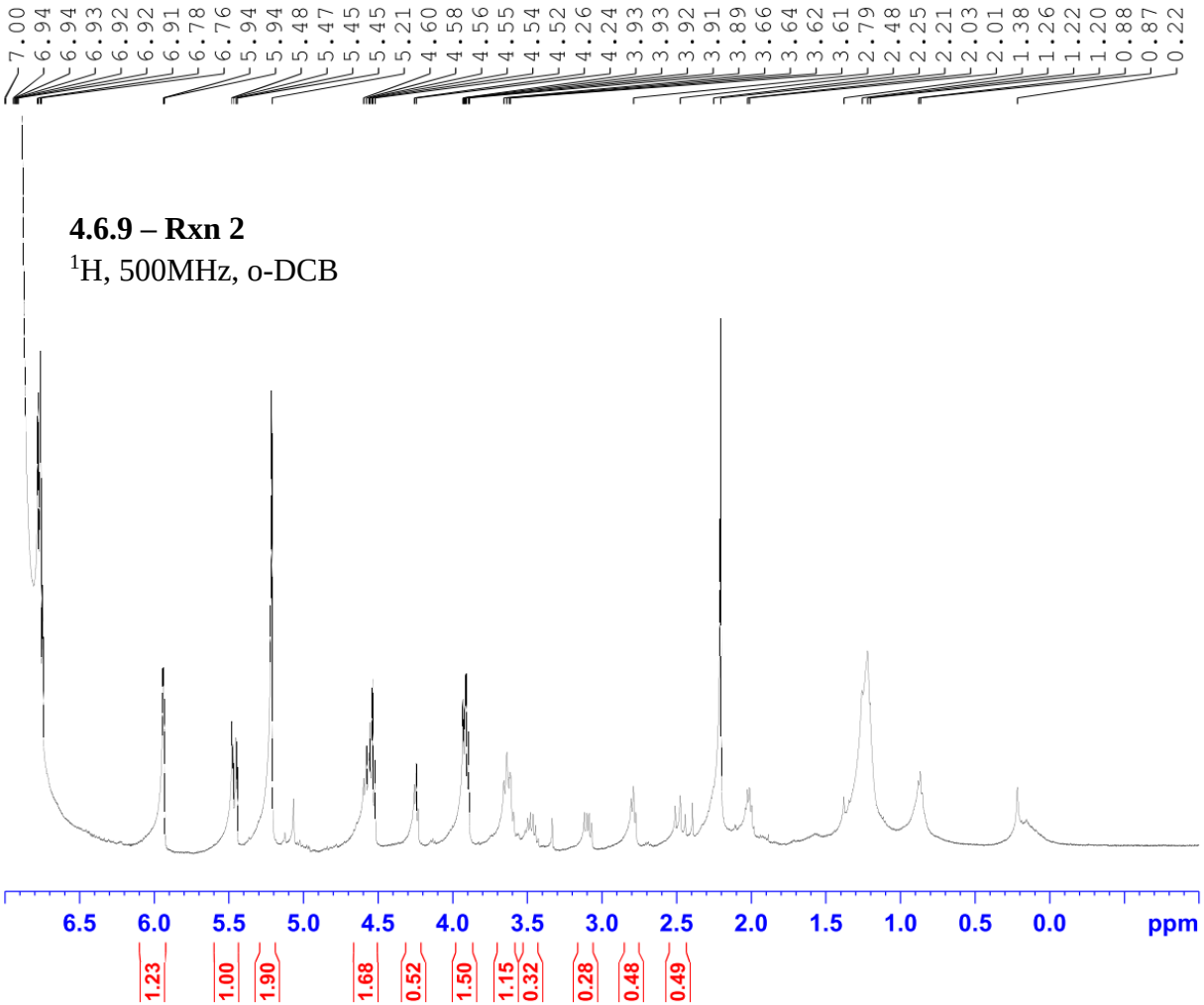
^{1}H, 500MHz, o-DCB




```
Current Data Parameters
NAME          JAW-01-124
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170621
Time              16.14
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG            zg30
TD                65536
SOLVENT            None
NS                   16
DS                    2
SWH           10000.000 Hz
FIDRES         0.152588 Hz
AQ            3.2767999 sec
RG                  5.6
DW               50.000 usec
DE                6.50 usec
TE                298.0 K
D1           1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1        500.1630887 MHz
NUC1                  1H
P1                11.50 usec
PLW1        18.00000000 W

F2 - Processing parameters
SI                65536
SF          500.1598169 MHz
WDW                  EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.9 – Rxn 2

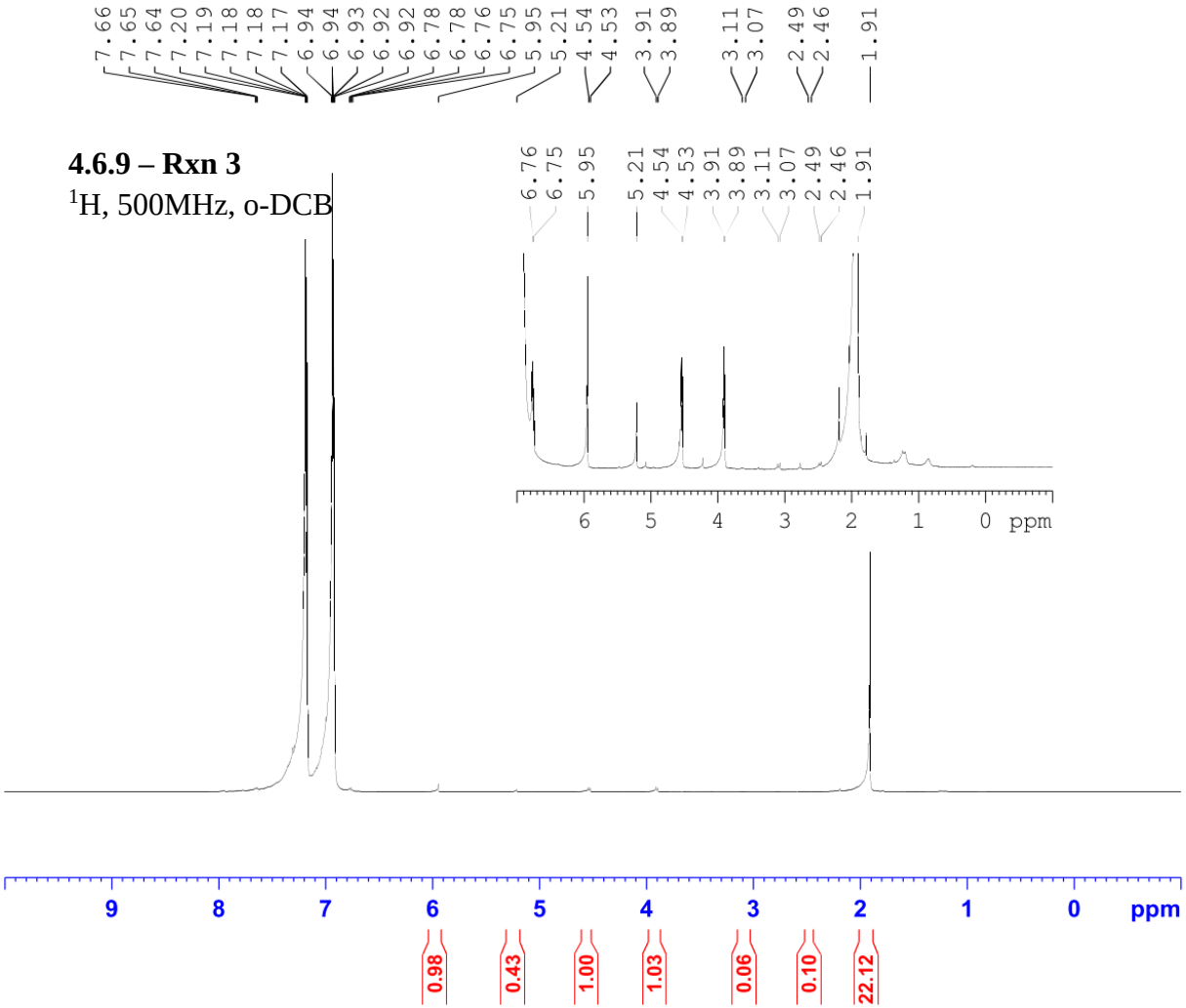
^{1}H, 500MHz, o-DCB



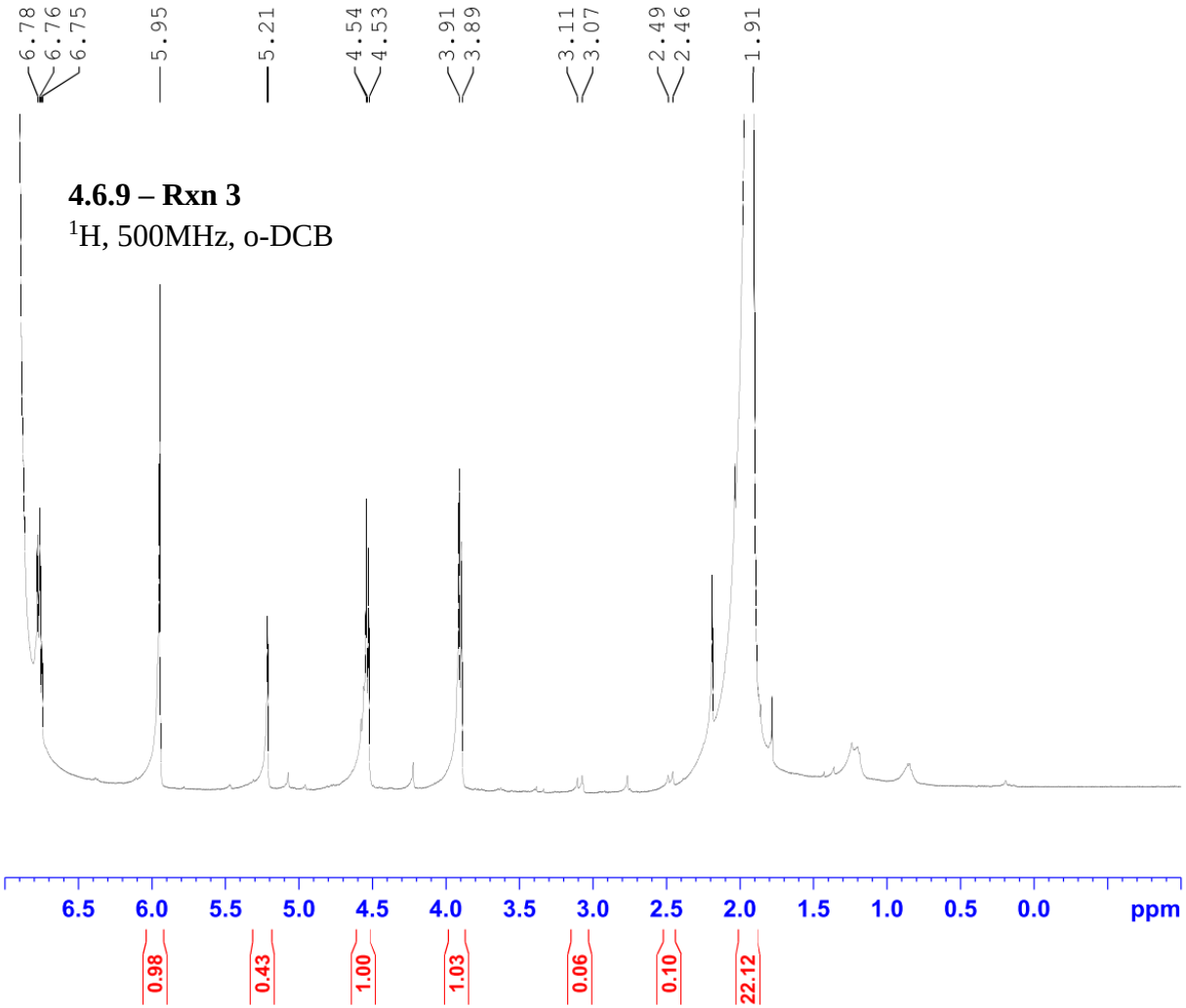

```
Current Data Parameters
NAME          JAW-01-124
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170621
Time               16.14
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT             None
NS                    16
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                   5.6
DW                50.000 usec
DE                 6.50 usec
TE                298.0 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                  1H
P1                11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1598169 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

4.6.9 – Rxn 3

^{1}H, 500MHz, o-DCB



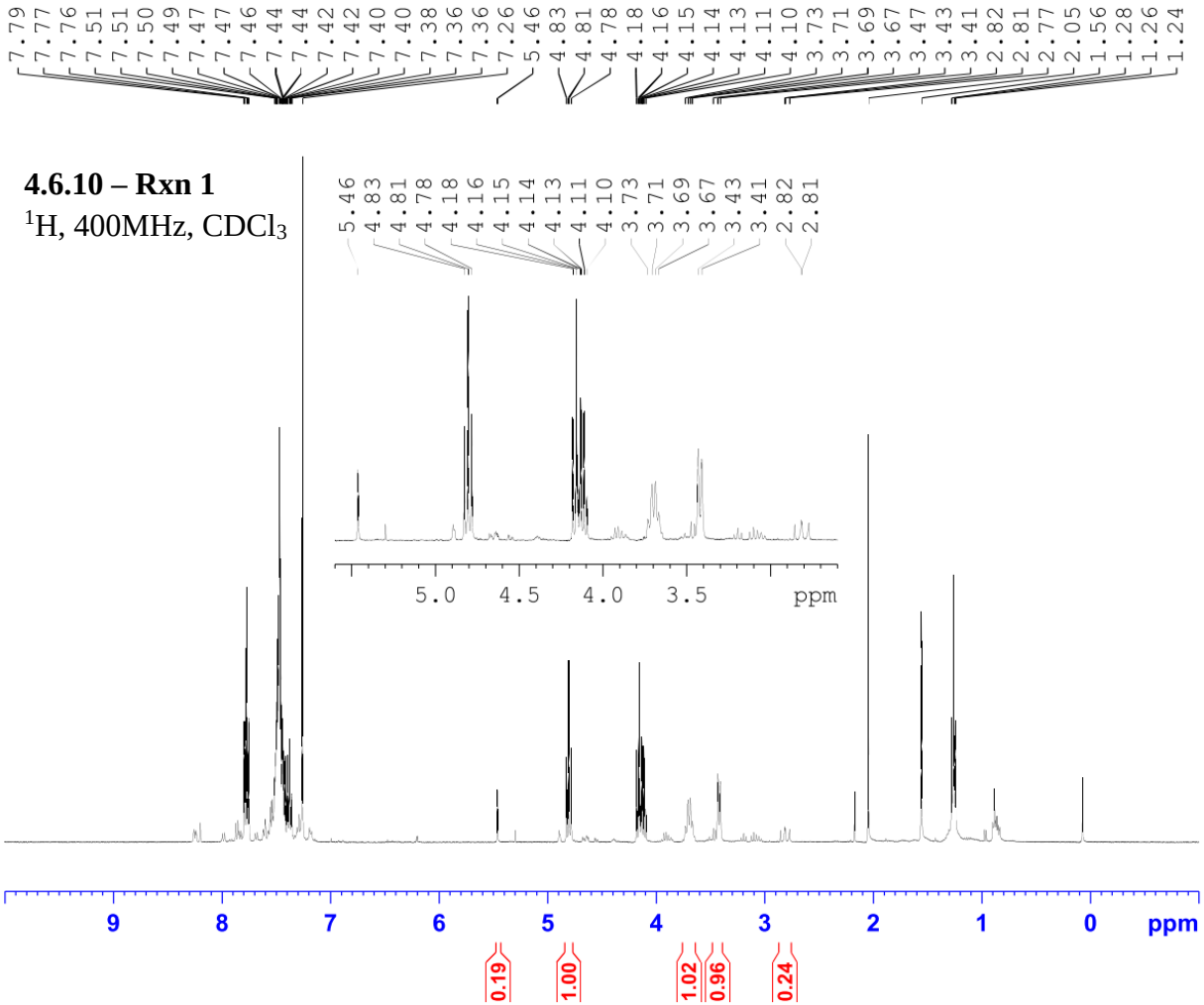

```
Current Data Parameters
NAME          JAW-01-126
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170621
Time              16.17
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG            zg30
TD                65536
SOLVENT            None
NS                   16
DS                    2
SWH           10000.000 Hz
FIDRES         0.152588 Hz
AQ            3.2767999 sec
RG                  5.6
DW               50.000 usec
DE                6.50 usec
TE               297.9 K
D1           1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1        500.1630887 MHz
NUC1                  1H
P1                11.50 usec
PLW1        18.00000000 W

F2 - Processing parameters
SI                65536
SF          500.1598314 MHz
WDW                  EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```




```
Current Data Parameters
NAME          JAW-01-126
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170621
Time              16.17
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG            zg30
TD                65536
SOLVENT            None
NS                   16
DS                    2
SWH           10000.000 Hz
FIDRES         0.152588 Hz
AQ            3.2767999 sec
RG                  5.6
DW               50.000 usec
DE                6.50 usec
TE               297.9 K
D1           1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1        500.1630887 MHz
NUC1                 1H
P1                11.50 usec
PLW1        18.00000000 W

F2 - Processing parameters
SI                65536
SF          500.1598314 MHz
WDW                  EM
SSB      0
LB                0.30 Hz
GB       0
PC                1.00
```

4.6.10 – Rxn 1

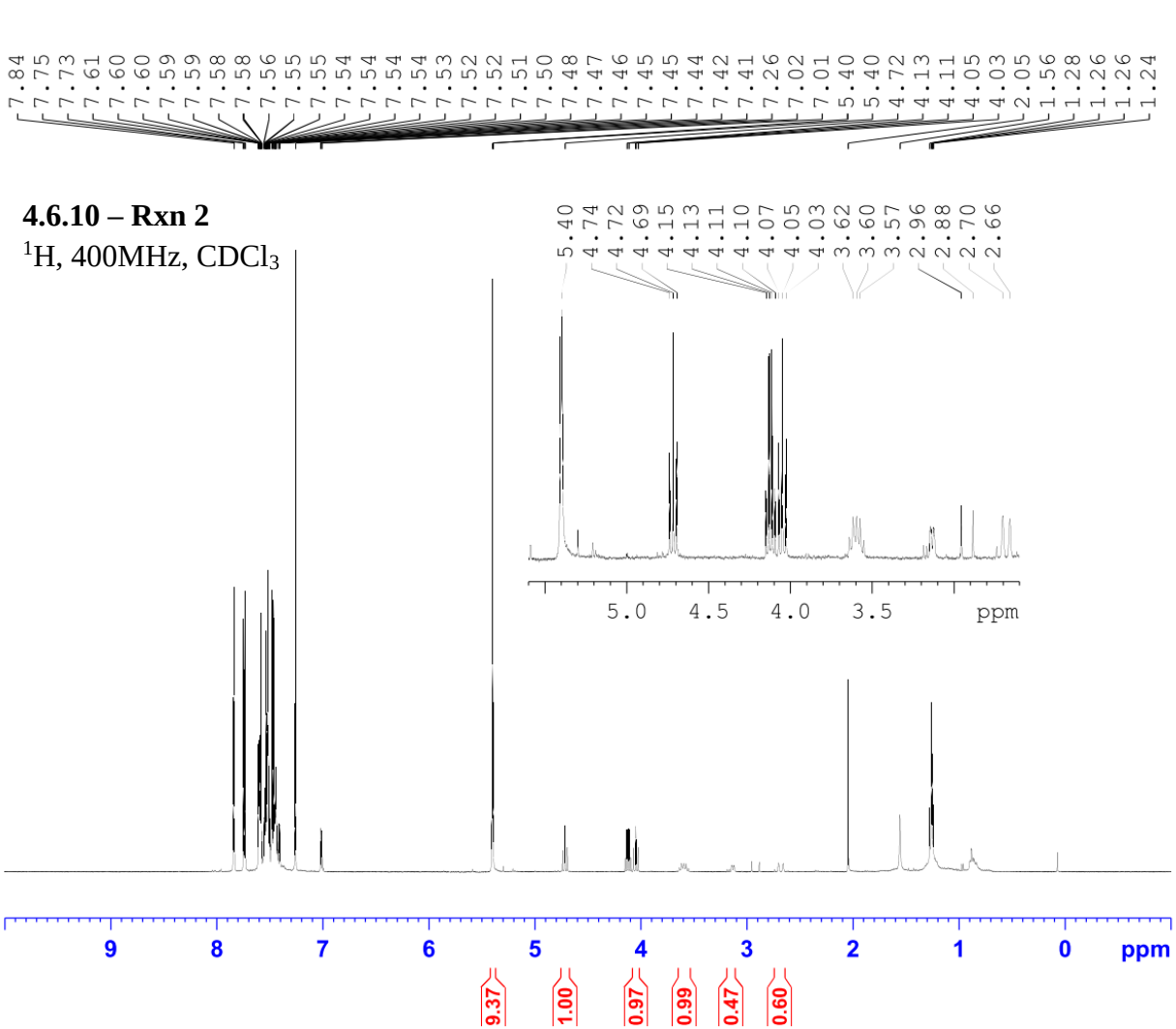
^{1}H, 400MHz, $CDCl_3$




```
Current Data Parameters
NAME          JAW-01-173
EXPNO                  6
PROCNO                 1

F2 - Acquisition Parameters
Date_           20171025
Time               15.59
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.122266 Hz
AQ             4.0894465 sec
RG                   128
DW                62.400 usec
DE                  6.50 usec
TE               -2720.7 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         400.1324710 MHz
NUC1                  1H
P1                 13.75 usec
PLW1         12.01700020 W

F2 - Processing parameters
SI                 65536
SF           400.1300107 MHz
WDW                   EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

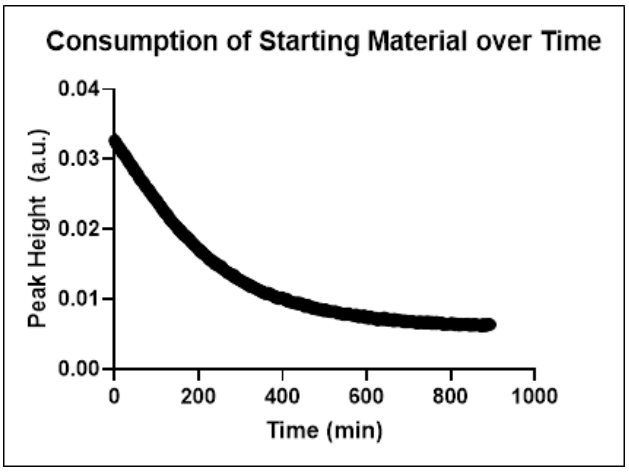
4.6.10 – Rxn 2

^{1}H, 400MHz, $CDCl_3$




```
Current Data Parameters
NAME        JAW-03-091-b
EXPNO                   1
PROCNO                  1

F2 - Acquisition Parameters
Date_            20200125
Time               14.14 h
INSTRUM            spect
PROBHD   Z108618_0240 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ             4.0894465 sec
RG                   128
DW                62.400 usec
DE                 6.50 usec
TE                 90.9 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                 4.83 usec
P1                14.50 usec
PLW1         12.00000000 W

F2 - Processing parameters
SI                 65536
SF          400.1300098 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

Appendix C ReactIR Data Output



Appendix Figure C.1. 1st order exponential decay of **1.50** at 77 °C

One phase decay	
Best-fit values	
Y0	0.03376
Plateau	0.005563
K	0.004494
Half Life	154.2
Tau	222.5
Span	0.02819
95% CI (profile likelihood)	
Y0	0.03366 to 0.03385
Plateau	0.005508 to 0.005618
K	0.004458 to 0.004530
Half Life	153.0 to 155.5
Tau	220.8 to 224.3
Goodness of Fit	
Degrees of Freedom	445
R squared	0.9989
Sum of Squares	2.63E-05
Sy.x	0.000243
Constraints	
K	K > 0

Number of points	
# of X values	448
# Y values analyzed	448

Time (min)	Peak at 1280 cm^{-1} (a.u.)
0.00	0.032722
2.00	0.03245
4.00	0.032253
6.00	0.032155
8.00	0.031902
10.00	0.031571
12.00	0.031564
14.00	0.031489
16.00	0.031219
18.00	0.030895
20.00	0.030791
22.00	0.030669
24.00	0.030673
26.00	0.030347
28.00	0.030256
30.00	0.030093
32.00	0.029786
34.00	0.029609
36.00	0.029368
38.00	0.029304
40.00	0.029074
42.00	0.028955
44.00	0.028845
46.00	0.028394
48.00	0.028365
50.00	0.028201
52.00	0.028152
54.00	0.027877

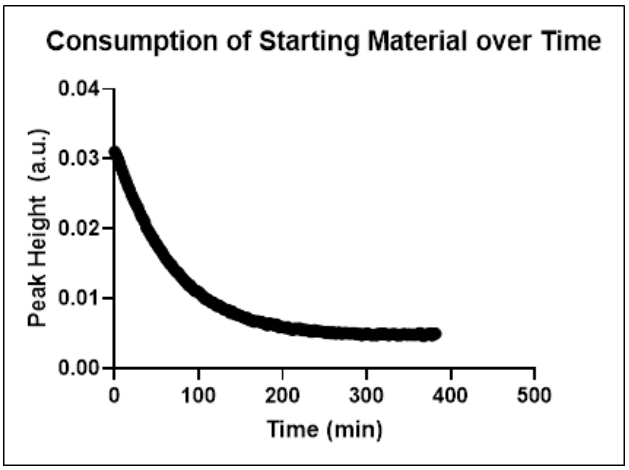
56.00	0.027773
58.00	0.027425
60.00	0.027183
62.00	0.027141
64.00	0.026852
66.00	0.026869
68.00	0.026757
70.00	0.02657
72.00	0.02629
74.00	0.026002
76.00	0.025977
78.00	0.025886
80.00	0.025762
82.00	0.025407
84.00	0.025473
86.00	0.025106
88.00	0.024981
90.00	0.024806
92.00	0.024654
94.00	0.024579
96.00	0.02427
98.00	0.024223
100.00	0.024181
102.00	0.023927
104.03	0.023725
106.00	0.023534
108.00	0.023368
110.00	0.023291
112.00	0.022954
114.00	0.022939
116.00	0.022691
118.00	0.022462
120.00	0.022429
122.00	0.022253
124.00	0.022156
126.00	0.022051
128.00	0.021865
130.00	0.021458
132.00	0.021459
134.05	0.021361
136.00	0.0211
138.00	0.02098
140.00	0.020878
142.00	0.020706
144.00	0.020515
146.00	0.020566
148.00	0.020451
150.00	0.020196
152.00	0.019963
154.00	0.019791
156.03	0.019923
158.00	0.01981
160.00	0.019524
162.00	0.019291
164.00	0.019325
166.00	0.019086
168.00	0.019166
170.00	0.018986
172.00	0.018797
174.05	0.018749
176.00	0.018684
178.00	0.018608
180.00	0.01828
182.00	0.018167
184.00	0.018141
186.00	0.017993
188.00	0.017856
190.00	0.017728
192.00	0.017643
194.00	0.017486
196.00	0.017354
198.00	0.017281
200.00	0.017145
202.00	0.016899
204.00	0.017012
206.00	0.016687
208.00	0.016823
210.05	0.016614
212.00	0.016459
214.00	0.016365
216.00	0.016415
218.00	0.016232
220.05	0.016063
222.00	0.015945
224.00	0.015684
226.00	0.015746
228.00	0.015706
230.00	0.015477
232.00	0.015351
234.00	0.015451

236.00	0.015356
238.00	0.015032
240.00	0.015209
242.00	0.014961
244.00	0.014941
246.00	0.014883
248.00	0.014795
250.00	0.014597
252.00	0.014516
254.00	0.014762
256.00	0.014466
258.00	0.014293
260.00	0.014233
262.00	0.01421
264.00	0.014038
266.00	0.013902
268.00	0.01378
270.00	0.01385
272.00	0.013676
274.00	0.013665
276.00	0.013559
278.00	0.013593
280.00	0.01338
282.00	0.013277
284.00	0.013492
286.00	0.013072
288.00	0.013197
290.00	0.01309
292.00	0.013016
294.00	0.012826
296.03	0.012867
298.00	0.012699
300.00	0.012728
302.00	0.012647
304.00	0.012521
306.00	0.012453
308.00	0.012376
310.00	0.01235
312.00	0.012252
314.02	0.01227
316.00	0.012057
318.00	0.012091
320.00	0.012084
322.00	0.011831
324.00	0.011955
326.00	0.011752
328.00	0.011771
330.00	0.011799
332.00	0.011729
334.00	0.01156
336.00	0.011644
338.00	0.011411
340.00	0.01137
342.00	0.011426
344.05	0.011363
346.00	0.011367
348.00	0.011092
350.00	0.01114
352.00	0.010993
354.00	0.011003
356.00	0.010977
358.00	0.010789
360.00	0.01082
362.00	0.010872
364.00	0.010836
366.00	0.010904
368.00	0.010767
370.00	0.010642
372.00	0.010757
374.00	0.010587
376.00	0.010552
378.00	0.010506
380.00	0.010453
382.00	0.010247
384.00	0.010299
386.00	0.01035
388.02	0.010141
390.03	0.010047
392.00	0.010217
394.00	0.010171
396.00	0.010267
398.00	0.010264
400.00	0.010113
402.00	0.010092
404.00	0.009947
406.00	0.009912
408.00	0.009894
410.00	0.010048
412.00	0.009694
414.00	0.009753

416.02	0.009607
418.00	0.009604
420.00	0.00964
422.00	0.009564
424.00	0.009507
426.00	0.009653
428.00	0.009463
430.00	0.009436
432.00	0.009372
434.00	0.009359
436.00	0.009501
438.00	0.009386
440.00	0.0093
442.00	0.009493
444.00	0.009247
446.00	0.009211
448.00	0.009329
450.00	0.009143
452.00	0.008936
454.00	0.008991
456.00	0.009015
458.00	0.009042
460.00	0.009152
462.00	0.009008
464.00	0.009009
466.00	0.008868
468.00	0.008749
470.00	0.008805
472.00	0.008674
474.00	0.008845
476.00	0.008692
478.00	0.008698
480.00	0.008722
482.00	0.008526
484.00	0.008618
486.00	0.008691
488.00	0.008563
490.00	0.008611
492.00	0.008574
494.00	0.008408
496.00	0.008435
498.00	0.008311
500.00	0.00843
502.00	0.00855
504.00	0.008341
506.00	0.008366
508.00	0.0083
510.00	0.008283
512.00	0.008264
514.00	0.008196
516.00	0.008232
518.00	0.008209
520.00	0.008199
522.00	0.008162
524.00	0.008238
526.00	0.008167
528.00	0.00817
530.05	0.008134
532.00	0.007947
534.00	0.00804
536.00	0.008099
538.00	0.008
540.00	0.007925
542.00	0.007979
544.00	0.00777
546.00	0.00793
548.00	0.00791
550.00	0.007796
552.00	0.007894
554.00	0.007877
556.00	0.007985
558.00	0.007904
560.00	0.007765
562.00	0.007749
564.00	0.007744
566.00	0.0077
568.00	0.007668
570.05	0.007691
572.00	0.007704
574.00	0.007819
576.00	0.00768
578.00	0.007605
580.00	0.007453
582.00	0.007544
584.00	0.007587
586.00	0.007693
588.00	0.007621
590.00	0.007499
592.00	0.007425
594.00	0.007684

596.00	0.007351
598.00	0.007486
600.00	0.007315
602.00	0.007447
604.00	0.007438
606.00	0.007244
608.00	0.007504
610.00	0.007459
612.00	0.007315
614.00	0.007292
616.00	0.007235
618.00	0.007283
620.00	0.007366
622.00	0.007125
624.00	0.007199
626.00	0.007022
628.05	0.007063
630.03	0.007219
632.00	0.007278
634.00	0.007213
636.00	0.007187
638.00	0.007041
640.00	0.007136
642.00	0.007381
644.00	0.007267
646.00	0.00717
648.00	0.007018
650.00	0.007024
652.00	0.007183
654.00	0.006962
656.00	0.006993
658.00	0.007107
660.00	0.006948
662.00	0.006888
664.00	0.006914
666.00	0.007167
668.00	0.006883
670.03	0.007048
672.00	0.006998
674.00	0.006903
676.05	0.006987
678.00	0.007013
680.00	0.006871
682.00	0.006942
684.00	0.006911
686.00	0.006855
688.00	0.006929
690.00	0.006715
692.00	0.006954
694.00	0.006896
696.00	0.006771
698.00	0.006713
700.00	0.006834
702.00	0.006819
704.00	0.006888
706.00	0.006801
708.00	0.006709
710.00	0.006858
712.00	0.006799
714.00	0.006758
716.05	0.006794
718.00	0.006599
720.00	0.006707
722.00	0.006615
724.00	0.006657
726.00	0.006808
728.02	0.006635
730.00	0.006718
732.00	0.006657
734.00	0.006779
736.00	0.006779
738.00	0.006556
740.00	0.00666
742.00	0.006638
744.00	0.006818
746.00	0.006658
748.00	0.006572
750.00	0.00661
752.00	0.006694
754.00	0.006797
756.00	0.006475
758.00	0.006571
760.00	0.006626
762.00	0.006596
764.00	0.00651
766.00	0.006748
768.00	0.006516
770.00	0.006582
772.00	0.006567
774.00	0.006563

776.00	0.006593
778.00	0.006648
780.00	0.006558
782.00	0.006342
784.00	0.006529
786.00	0.00659
788.00	0.006423
790.00	0.006437
792.00	0.006432
794.00	0.006432
796.00	0.006375
798.00	0.006499
800.00	0.006556
802.00	0.00645
804.00	0.006589
806.00	0.006672
808.00	0.0064
810.00	0.006301
812.00	0.00652
814.00	0.00642
816.00	0.006356
818.00	0.006435
820.00	0.006254
822.00	0.006371
824.00	0.006424
826.00	0.006355
828.05	0.006316
830.00	0.006431
832.00	0.006499
834.00	0.006371
836.00	0.006386
838.00	0.006343
840.00	0.006473
842.00	0.006311
844.00	0.006262
846.00	0.006393
848.00	0.006247
850.02	0.006308
852.00	0.006315
854.00	0.00629
856.05	0.006451
858.00	0.006234
860.00	0.006389
862.00	0.006424
864.00	0.006359
866.00	0.006348
868.00	0.006295
870.00	0.006214
872.00	0.006218
874.00	0.006119
876.00	0.006417
878.00	0.006176
880.00	0.006416
882.00	0.006413
884.00	0.00632
886.00	0.006231
888.00	0.006341
890.00	0.006437
892.00	0.006358
894.00	0.006375



Appendix Figure C.2. 1st order exponential decay of

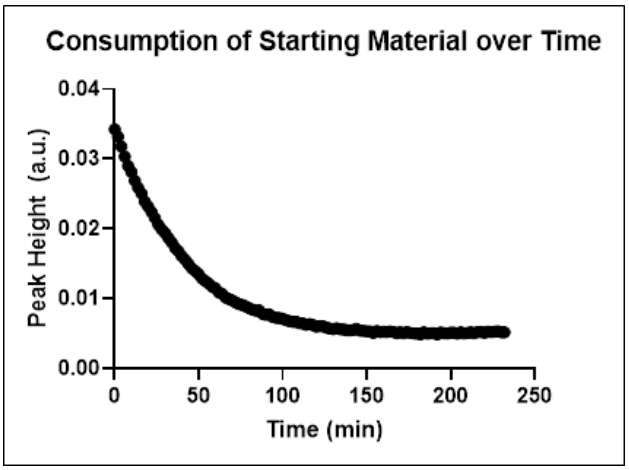
1.50 at 86 °C

One phase decay	
Best-fit values	
Y0	0.03177
Plateau	0.004558
K	0.01466
Half Life	47.28
Tau	68.21
Span	0.02722
95% CI (profile likelihood)	
Y0	0.03167 to 0.03187
Plateau	0.004521 to 0.004594
K	0.01456 to 0.01476
Half Life	46.95 to 47.61
Tau	67.73 to 68.69
Goodness of Fit	
Degrees of Freedom	189
R squared	0.9995
Sum of Squares	4.01E-06
Sy.x	0.000146
Constraints	
K	K > 0
Number of points	
# of X values	192
# Y values analyzed	192

Time (min)	Peak at 1280 cm^{-1} (a.u.)
0.00	0.031035
2.00	0.030557
4.03	0.030033
6.00	0.029388
8.00	0.028667
10.00	0.02801
12.00	0.027309
14.00	0.026761
16.00	0.02608
18.00	0.025594
20.00	0.024872
22.00	0.024389
24.00	0.023834
26.00	0.023392
28.00	0.022983
30.00	0.022267
32.00	0.021731
34.00	0.021401
36.00	0.020912
38.00	0.020136
40.00	0.019742
42.00	0.019346
44.00	0.018898
46.00	0.018662
48.05	0.018098
50.00	0.017825
52.00	0.017356
54.00	0.017052
56.00	0.016767
58.00	0.016322
60.00	0.015886
62.00	0.015591
64.00	0.015279
66.00	0.014909
68.00	0.014831
70.00	0.014329
72.00	0.014064
74.05	0.013794
76.00	0.013704
78.00	0.013306
80.00	0.013001
82.00	0.01275

84.00	0.012403
86.00	0.012267
88.00	0.011886
90.00	0.011915
92.00	0.011552
94.00	0.011288
96.00	0.011066
98.00	0.011081
100.00	0.010966
102.00	0.010674
104.03	0.010373
106.00	0.01024
108.00	0.009901
110.00	0.00993
112.00	0.009788
114.03	0.009526
116.00	0.009402
118.03	0.009412
120.00	0.009081
122.00	0.008929
124.00	0.009031
126.00	0.008887
128.00	0.008679
130.00	0.008461
132.00	0.008394
134.00	0.008397
136.00	0.00831
138.00	0.007902
140.00	0.008152
142.00	0.00793
144.03	0.007709
146.00	0.007707
148.00	0.007603
150.00	0.00751
152.00	0.007391
154.00	0.007295
156.00	0.007192
158.00	0.007256
160.00	0.006932
162.00	0.006911
164.00	0.006859
166.00	0.006667
168.00	0.006734
170.00	0.006754
172.00	0.00669
174.00	0.006613
176.00	0.0066
178.00	0.006455
180.00	0.006281
182.00	0.006186
184.00	0.00644
186.00	0.006343
188.00	0.00631
190.00	0.006144
192.00	0.00632
194.00	0.00618
196.00	0.00587
198.00	0.005906
200.00	0.005924
202.00	0.005841
204.00	0.005821
206.00	0.005924
208.00	0.005655
210.00	0.005629
212.00	0.005523
214.00	0.005733
216.00	0.005643
218.00	0.005656
220.00	0.005734
222.00	0.005558
224.03	0.005452
226.00	0.005554
228.05	0.005464
230.00	0.005469
232.00	0.00534
234.00	0.005258
236.00	0.005299
238.00	0.0055
240.00	0.005306
242.00	0.005323
244.03	0.005285
246.00	0.00528
248.00	0.005208
250.00	0.005169
252.00	0.005068
254.00	0.005185
256.00	0.005148
258.05	0.005024
260.00	0.005192
262.00	0.005017

264.02	0.004999
266.00	0.005123
268.00	0.005129
270.00	0.004944
272.00	0.005034
274.00	0.005042
276.00	0.005098
278.00	0.004974
280.00	0.005017
282.00	0.005051
284.03	0.00498
286.00	0.005042
288.00	0.004929
290.00	0.004873
292.00	0.004955
294.03	0.00474
296.00	0.00489
298.00	0.004855
300.00	0.004968
302.00	0.004964
304.00	0.004816
306.00	0.004773
308.00	0.00479
310.00	0.004849
312.00	0.004734
314.00	0.004963
316.00	0.004873
318.00	0.004943
320.00	0.004994
322.00	0.004883
324.00	0.004886
326.00	0.004747
328.00	0.00485
330.00	0.004893
332.00	0.004899
334.03	0.004928
336.00	0.00474
338.00	0.004828
340.00	0.00475
342.00	0.004844
344.00	0.004925
346.00	0.004887
348.00	0.004774
350.00	0.004873
352.00	0.004823
354.00	0.004852
356.00	0.004814
358.00	0.004857
360.00	0.004802
362.00	0.005
364.03	0.005043
366.00	0.004726
368.00	0.004607
370.00	0.004818
372.00	0.004903
374.00	0.004843
376.00	0.005033
378.00	0.004717
380.00	0.004909
382.00	0.004985

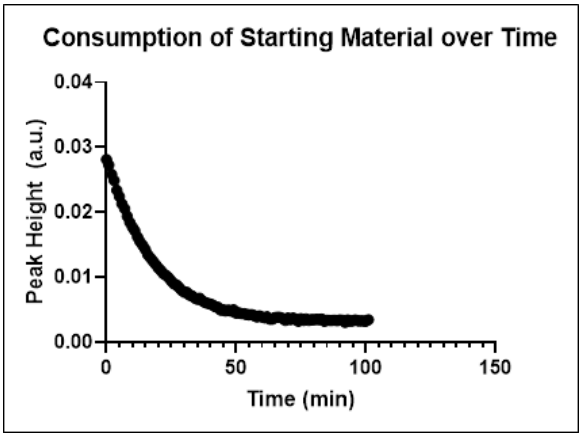


Appendix Figure C.3. 1st order exponential decay of **1.50** at 94 °C

One phase decay	
Best-fit values	
Y0	0.03477
Plateau	0.004734
K	0.02497
Half Life	27.76
Tau	40.05
Span	0.03004
95% CI (profile likelihood)	
Y0	0.03459 to 0.03496
Plateau	0.004667 to 0.004801
K	0.02467 to 0.02527
Half Life	27.43 to 28.10
Tau	39.58 to 40.53
Goodness of Fit	
Degrees of Freedom	114
R squared	0.9992
Sum of Squares	5.31E-06
Sy.x	0.000216
Constraints	
K	K > 0
Number of points	
# of X values	117
# Y values analyzed	117

Time (min)	Peak at 1280 cm^{-1} (a.u.)
0.00	0.034248
1.98	0.033186
4.00	0.031772
6.03	0.03035
8.00	0.029015
9.98	0.028162
12.00	0.026884
14.00	0.025893
15.98	0.025039
18.00	0.023881
19.98	0.023171
22.00	0.022385
24.00	0.021557
25.98	0.020585
28.00	0.019932
29.98	0.019433
32.00	0.018673
34.02	0.018048
35.98	0.017259
38.00	0.0168
39.98	0.016093
42.00	0.015552
44.00	0.01494
45.98	0.014317
48.00	0.013942
49.98	0.013515
52.00	0.012875
54.00	0.012504
55.98	0.012152
58.00	0.011704
59.98	0.011479
62.00	0.010891
63.98	0.0107
66.00	0.010164
68.00	0.009959
69.98	0.009765
72.00	0.009464
73.98	0.0092
76.00	0.00909
78.00	0.008889

79.98	0.008662
82.00	0.008428
83.98	0.008283
86.00	0.008307
88.00	0.007818
89.98	0.007676
92.00	0.00774
93.98	0.007369
96.00	0.007254
98.00	0.007208
99.98	0.007124
102.00	0.00692
103.98	0.006772
106.00	0.006694
108.00	0.006684
109.98	0.006499
112.00	0.006455
113.98	0.00624
115.98	0.006352
118.00	0.006215
119.98	0.00599
122.00	0.006034
124.00	0.006057
125.98	0.005848
128.00	0.005703
130.00	0.005621
131.98	0.005747
134.00	0.005618
135.98	0.005593
137.98	0.005496
140.00	0.005463
141.98	0.005514
144.00	0.005646
146.00	0.005433
147.98	0.005376
150.00	0.005312
152.00	0.005281
153.98	0.005091
156.00	0.005357
157.98	0.005219
160.00	0.005245
162.00	0.005221
164.02	0.005278
165.98	0.005215
168.00	0.005043
169.98	0.005173
171.98	0.005045
174.00	0.00521
175.98	0.005081
178.00	0.005001
180.00	0.004997
181.98	0.004882
184.00	0.005169
185.98	0.004977
188.00	0.005041
190.00	0.005048
191.98	0.00487
194.00	0.005134
196.03	0.005042
197.98	0.005009
200.00	0.005133
201.98	0.005116
204.00	0.004987
206.00	0.005192
207.98	0.005028
210.00	0.005082
211.98	0.005176
214.00	0.005059
216.00	0.00522
217.98	0.005213
220.00	0.005108
221.98	0.005234
223.98	0.005201
226.00	0.005264
227.98	0.005328
230.00	0.005169
232.00	0.00517

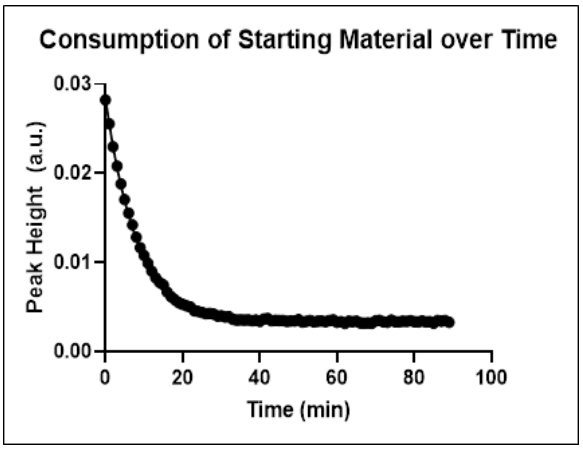


Appendix Figure C.4. 1st order exponential decay of **1.50** at 108 °C

One phase decay	
Best-fit values	
Y0	0.0286
Plateau	0.003099
K	0.05587
Half Life	12.41
Tau	17.9
Span	0.0255
95% CI (profile likelihood)	
Y0	0.02847 to 0.02873
Plateau	0.003051 to 0.003147
K	0.05532 to 0.05643
Half Life	12.28 to 12.53
Tau	17.72 to 18.08
Goodness of Fit	
Degrees of Freedom	99
R squared	0.9995
Sum of Squares	1.96E-06
Sy.x	0.000141
Constraints	
K	K > 0
Number of points	
# of X values	102
# Y values analyzed	102

Time (min)	Peak at 1280 cm^{-1} (a.u.)
0.00	0.028111
0.98	0.027245
2.03	0.025865
3.02	0.024898
4.02	0.023385
5.00	0.022425
5.98	0.021302
7.03	0.020561
8.03	0.019393
9.00	0.018437
10.00	0.0177
10.98	0.017149
12.00	0.01619
12.98	0.015489
14.00	0.014883
15.00	0.014237
15.98	0.013473
17.03	0.01294
18.00	0.012446
19.00	0.011945
20.00	0.011428
21.00	0.011025
21.98	0.010561
23.00	0.010291
24.00	0.00993
25.00	0.00942
26.00	0.008984
27.00	0.008805
27.98	0.00845
29.00	0.007968
30.00	0.007667
31.00	0.007692
32.00	0.007245
32.98	0.007144
34.00	0.006803
35.00	0.006614
35.98	0.006796
37.00	0.006348
38.00	0.006121
39.00	0.005997
40.02	0.005886
41.00	0.005721

41.98	0.005442
43.00	0.005393
44.00	0.004962
45.00	0.004969
45.98	0.004814
47.03	0.004945
48.03	0.004798
49.00	0.004973
49.98	0.0045
51.00	0.004528
51.98	0.004428
53.00	0.004379
54.00	0.004268
54.98	0.004215
56.00	0.004235
57.00	0.004087
58.00	0.003895
59.00	0.004057
59.98	0.003871
61.00	0.003739
61.98	0.003913
63.00	0.003551
64.00	0.003546
64.98	0.003783
66.00	0.003844
67.03	0.003813
68.00	0.003644
69.00	0.00336
70.03	0.003705
71.02	0.003485
72.02	0.003729
73.02	0.00348
74.00	0.003228
74.98	0.003627
76.00	0.003351
76.98	0.003586
78.00	0.003343
79.00	0.003474
79.98	0.00346
81.00	0.003522
82.02	0.003493
83.00	0.00356
84.00	0.00322
85.00	0.003394
86.00	0.003343
87.00	0.003366
88.00	0.003373
89.00	0.003332
89.98	0.003426
91.05	0.003377
92.03	0.003063
93.02	0.003422
94.02	0.003264
95.00	0.003267
95.98	0.003416
97.00	0.003285
98.00	0.003279
99.00	0.003274
99.98	0.003203
101.00	0.003445



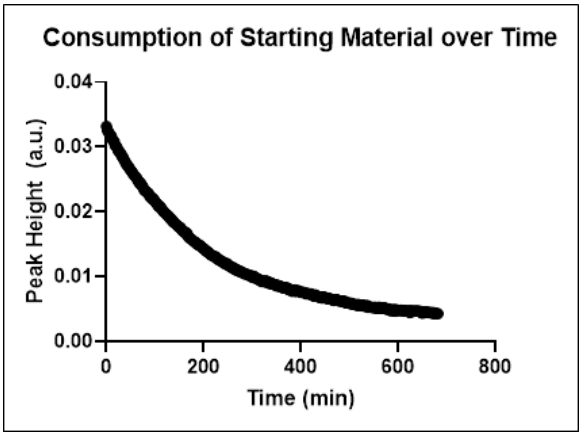
Appendix Figure C.5. 1st order exponential decay of **1.50** at 119 °C

One phase decay		
Best-fit values		
Y0		0.0285
Plateau		0.003339
K		0.1234
Half Life		5.619
Tau		8.107
Span		0.02516
95% CI (profile likelihood)		
Y0	0.02835 to 0.02866	
Plateau	0.003306 to 0.003372	
K	0.1221 to 0.1246	
Half Life	5.561 to 5.677	
Tau	8.023 to 8.191	
Goodness of Fit		
Degrees of Freedom		87
R squared		0.9994
Sum of Squares		1.35E-06
Sy.x		0.000125
Constraints		
K	K > 0	
Number of points		
# of X values		90
# Y values analyzed		90

Time (min)	Peak at 1279 cm^{-1} (a.u.)
0.00	0.028225
1.00	0.025561
1.98	0.022977
3.00	0.02081
4.00	0.018812
4.98	0.017063
6.00	0.015545
7.00	0.014214
8.00	0.012829
9.00	0.011662
10.00	0.010789
11.00	0.00992
11.98	0.009033
13.00	0.008295
14.00	0.007773
15.00	0.007498
15.98	0.006684
17.00	0.00617
18.00	0.005802
19.00	0.005489
19.98	0.00532
21.00	0.005131
22.00	0.005011
23.00	0.004581
23.98	0.004521
25.00	0.004393
26.00	0.004258
27.00	0.004285
28.00	0.004209
29.00	0.003982
30.00	0.004024
31.00	0.003888
32.00	0.003901
33.00	0.003619
34.00	0.003531
35.00	0.00355
36.00	0.003548
37.00	0.003568
38.00	0.003467
38.98	0.003525

40.00	0.003392
41.00	0.003654
42.00	0.003706
42.98	0.003458
44.00	0.003505
45.00	0.003499
46.00	0.003478
47.00	0.00339
47.98	0.003444
49.00	0.003446
50.00	0.003582
51.00	0.00331
51.98	0.00339
53.00	0.003481
54.00	0.003349
55.00	0.003424
55.98	0.003437
57.03	0.003366
58.00	0.003482
59.00	0.003558
59.98	0.003295
61.00	0.003355
62.00	0.00315
63.00	0.003421
63.98	0.003352
65.00	0.003409
66.00	0.003213
66.98	0.003194
68.00	0.003222
69.00	0.003176
70.00	0.003452
70.98	0.003524
72.00	0.003345
73.05	0.003292
74.00	0.003542
74.98	0.003368
76.00	0.003338
77.00	0.003424
78.00	0.003396
79.00	0.003453
80.00	0.003364
81.00	0.003348
82.00	0.003432
83.00	0.003339
83.98	0.003373
85.00	0.003181
86.00	0.003482
87.00	0.003404
87.98	0.003493
89.00	0.003286

2.7 76 °C



Appendix Figure C.6. 1st order exponential decay of **2.7** at 76 °C

One phase decay	
Best-fit values	
Y0	0.03299
Plateau	0.003348
K	0.004941
Half Life	140.3
Tau	202.4
Span	0.02964
95% CI (profile likelihood)	
Y0	0.03293 to 0.03304
Plateau	0.003303 to 0.003393
K	0.004914 to 0.004967
Half Life	139.5 to 141.1
Tau	201.3 to 203.5
Goodness of Fit	
Degrees of Freedom	339
R squared	0.9997
Sum of Squares	6.12E-06
Sy.x	0.000134
Constraints	
K	K > 0
Number of points	
# of X values	342
# Y values analyzed	342

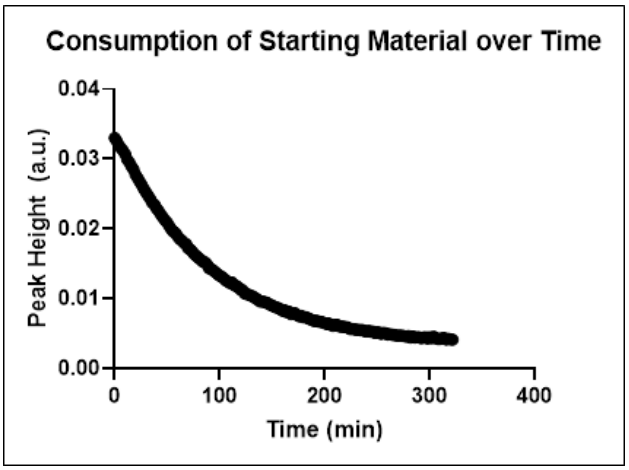
Time (min)	Peak at 1284 cm^{-1} (a.u.)
0.00	0.033199
2.00	0.032622
3.98	0.032326
6.00	0.032122
7.98	0.031736
10.00	0.031715
11.98	0.031259
14.00	0.030996
16.00	0.030836
17.98	0.030265
20.00	0.030113
21.98	0.029902
24.00	0.029465
25.98	0.029321
27.98	0.029146
30.03	0.028961
31.98	0.028549
34.00	0.028458
35.98	0.028082
38.00	0.027804
39.98	0.027531
42.00	0.027218
44.00	0.02711
45.98	0.026845
48.00	0.026624
49.98	0.026429
52.00	0.026195
54.00	0.026028
56.00	0.025695
57.98	0.025649
60.03	0.025391
62.00	0.025255
64.00	0.02491
66.00	0.024711
67.98	0.024427
70.00	0.024497
71.98	0.024174
74.00	0.023998

75.98	0.023712
78.00	0.023292
79.98	0.023342
82.00	0.023101
84.00	0.022921
85.98	0.022905
88.03	0.022556
89.98	0.022267
92.00	0.02228
93.98	0.021996
96.00	0.022064
98.00	0.021858
99.98	0.021577
102.00	0.021458
103.98	0.021232
106.00	0.020971
107.98	0.020773
110.00	0.020868
111.98	0.02065
114.00	0.020375
116.00	0.020225
118.00	0.019967
120.00	0.019848
121.98	0.019809
124.00	0.019544
125.98	0.019466
128.00	0.019316
130.02	0.019015
132.00	0.01893
134.00	0.018875
135.98	0.018547
138.00	0.018417
139.98	0.018305
142.00	0.018138
143.98	0.018172
146.00	0.017899
148.00	0.017691
150.00	0.017657
152.00	0.017598
153.98	0.017359
156.00	0.017085
158.03	0.017006
160.00	0.016961
161.98	0.016709
163.98	0.016774
166.00	0.016671
167.98	0.016212
170.03	0.016064
171.98	0.015919
174.00	0.015825
176.00	0.015669
177.98	0.015697
180.00	0.015419
182.03	0.015344
184.00	0.015239
185.98	0.015017
188.00	0.014983
190.00	0.014933
191.98	0.014778
194.00	0.014738
195.98	0.014592
198.00	0.014378
199.98	0.014315
202.00	0.014265
203.98	0.014049
206.03	0.013884
207.98	0.013773
210.03	0.013763
212.00	0.013588
213.98	0.013383
216.00	0.01333
217.98	0.013265
220.00	0.013167
222.00	0.013111
223.98	0.012997
226.00	0.013008
227.98	0.012712
230.00	0.01273
231.98	0.012598
234.00	0.012465
235.98	0.01241
237.98	0.0123
240.03	0.012266
241.98	0.012044
244.00	0.012092
245.98	0.01192
248.00	0.01202
250.00	0.011854
251.98	0.011654
254.00	0.011612

255.98	0.011626
258.00	0.011357
259.98	0.011356
262.00	0.011375
263.98	0.011111
266.00	0.011005
268.00	0.011045
269.98	0.011018
272.00	0.010856
273.98	0.010768
276.00	0.010821
278.00	0.010654
279.98	0.010696
282.00	0.010552
283.98	0.01041
286.00	0.010434
288.00	0.010382
289.98	0.010304
292.05	0.010216
293.98	0.010186
296.00	0.010192
298.03	0.009988
299.98	0.009966
302.00	0.00984
303.98	0.01004
306.00	0.0098
307.98	0.009744
310.00	0.009695
312.00	0.009662
313.98	0.009517
316.00	0.009353
317.98	0.009433
320.00	0.009205
322.00	0.009275
323.98	0.00928
326.00	0.009218
328.00	0.009347
329.98	0.009069
332.00	0.009204
333.98	0.00904
336.00	0.008897
338.00	0.009054
339.98	0.008937
342.00	0.008858
343.98	0.00884
346.00	0.008725
348.00	0.008754
349.98	0.008557
352.00	0.008659
354.00	0.008563
355.98	0.008575
358.00	0.008476
359.98	0.008399
362.05	0.008304
364.00	0.008248
365.98	0.008301
367.98	0.008316
370.00	0.008272
371.98	0.008257
374.00	0.007983
376.00	0.008075
378.00	0.007987
380.03	0.007962
382.00	0.007707
383.98	0.007827
385.98	0.007851
388.00	0.007948
389.98	0.007681
391.98	0.007793
394.00	0.007826
395.98	0.007777
398.03	0.007694
400.00	0.007538
401.98	0.007515
404.00	0.007583
405.98	0.007556
407.98	0.007556
410.00	0.007364
411.98	0.007442
414.00	0.007355
416.00	0.007301
417.98	0.007285
420.00	0.007362
421.98	0.007203
423.98	0.007142
426.03	0.006977
428.00	0.007014
430.00	0.007185
431.98	0.006967
433.98	0.006926

436.00	0.00691
437.98	0.006833
440.00	0.006827
442.00	0.006728
443.98	0.006719
446.00	0.006884
447.98	0.006798
450.03	0.006792
452.00	0.006628
453.98	0.006654
456.00	0.006697
457.98	0.006564
460.00	0.00658
462.00	0.006485
463.98	0.006436
466.00	0.006398
467.98	0.006326
470.00	0.006345
472.03	0.006362
473.98	0.006437
476.00	0.006311
477.98	0.006291
480.00	0.006205
481.98	0.006279
484.00	0.006237
485.98	0.006132
488.00	0.006094
490.05	0.00622
491.98	0.005999
494.00	0.005919
495.98	0.005951
498.00	0.005911
500.00	0.005903
502.03	0.005779
504.00	0.005886
505.98	0.005829
507.98	0.005724
510.00	0.005754
511.98	0.005704
514.00	0.005577
516.00	0.005577
517.98	0.00573
520.03	0.005511
521.98	0.005486
523.98	0.005561
526.00	0.005484
527.98	0.00563
530.00	0.00552
532.00	0.005426
533.98	0.00542
536.00	0.005557
537.98	0.005261
539.98	0.005364
542.00	0.00529
543.98	0.005332
546.00	0.00526
548.05	0.005205
549.98	0.005207
552.00	0.005287
553.98	0.005264
555.98	0.005096
558.00	0.005166
559.98	0.005244
562.00	0.005235
564.00	0.005116
566.03	0.00517
568.00	0.005098
569.98	0.005027
571.98	0.005211
574.00	0.005049
575.98	0.00498
577.98	0.005023
580.00	0.005013
581.98	0.004882
584.00	0.004707
586.00	0.004694
587.98	0.004908
589.98	0.004697
592.00	0.004915
593.98	0.004642
596.03	0.004872
598.00	0.004811
599.98	0.004849
601.98	0.004753
604.00	0.004772
605.98	0.004809
607.98	0.004868
610.00	0.004739
611.98	0.004645
613.98	0.004761

616.00	0.00471
617.98	0.004703
619.98	0.004634
622.00	0.004713
623.98	0.004444
626.00	0.004751
628.00	0.004579
629.98	0.004625
632.00	0.004713
634.00	0.004659
635.98	0.004669
638.00	0.004667
640.00	0.004672
641.98	0.004613
644.00	0.004688
645.98	0.004551
648.00	0.004387
650.00	0.004598
651.98	0.004371
653.98	0.004466
656.00	0.004567
657.98	0.004503
660.03	0.004515
662.00	0.004453
663.98	0.004425
666.03	0.004499
668.00	0.004375
669.98	0.004383
672.00	0.004451
673.98	0.004291
675.98	0.004381
678.00	0.004359
679.98	0.004228
682.00	0.00429



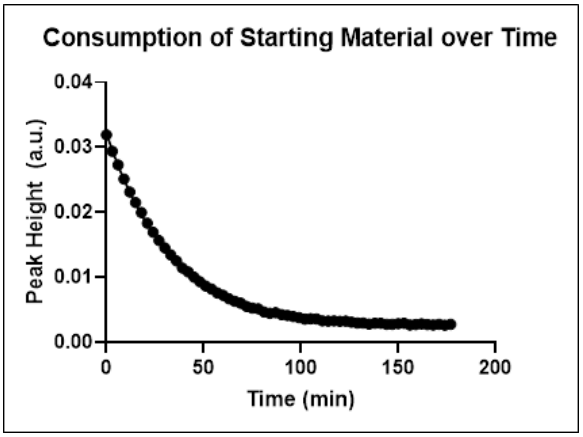
Appendix Figure C.7. 1st order exponential decay of **2.7** at 85 °C

One phase decay	
Best-fit values	
Y0	0.03369
Plateau	0.003168
K	0.011
Half Life	63.04
Tau	90.94
Span	0.03052
95% CI (profile likelihood)	
Y0	0.03361 to 0.03377
Plateau	0.003112 to 0.003223
K	0.01092 to 0.01107
Half Life	62.62 to 63.46
Tau	90.34 to 91.55
Goodness of Fit	
Degrees of Freedom	159
R squared	0.9998
Sum of Squares	2.39E-06
Sy.x	0.000123
Constraints	
K	K > 0
Number of points	
# of X values	162
# Y values analyzed	162

Time (min)	Peak at 1283 cm^{-1} (a.u.)
0.00	0.033009
1.98	0.032598
3.98	0.03201
5.98	0.03157
7.98	0.031221
10.03	0.030691
11.98	0.029961
13.98	0.029536
15.98	0.028947
17.98	0.028504
19.98	0.027753
22.00	0.027252
23.98	0.026743
25.98	0.026264
27.98	0.025693
29.98	0.025231
31.98	0.024761
33.98	0.024282
35.98	0.023732
38.00	0.023436
39.98	0.022905
41.98	0.022546
44.00	0.02201
45.98	0.021666
47.98	0.021204
49.98	0.020921
51.98	0.020405
53.98	0.019936
55.98	0.019585
57.98	0.01943
59.98	0.018936
61.98	0.018547
63.98	0.018334
66.00	0.017936
68.03	0.017825
69.98	0.017233
71.98	0.017099
73.98	0.016758
75.98	0.016345
78.02	0.016074

79.98	0.015815
82.00	0.015592
83.98	0.015288
86.00	0.015208
88.00	0.01487
89.98	0.014345
92.00	0.014228
93.98	0.01404
95.98	0.013779
98.03	0.013518
99.98	0.013291
101.98	0.013134
103.98	0.012922
105.98	0.012577
107.98	0.012456
109.98	0.01221
111.98	0.012305
114.00	0.01189
115.98	0.011804
117.98	0.011606
119.98	0.011282
121.98	0.0112
123.98	0.010728
125.98	0.010636
127.98	0.010535
129.98	0.010408
132.00	0.010268
133.98	0.010036
135.98	0.009926
138.00	0.009623
139.98	0.009575
141.98	0.009565
143.98	0.009461
145.98	0.009339
147.98	0.009117
150.00	0.009011
152.00	0.008816
153.98	0.00875
155.98	0.00866
157.98	0.008486
159.98	0.008264
161.98	0.008349
163.98	0.008037
165.98	0.008157
167.98	0.007787
169.98	0.007931
171.98	0.007913
173.98	0.007601
175.98	0.007464
177.98	0.007527
179.98	0.007328
181.98	0.007338
183.98	0.007202
185.98	0.007053
187.98	0.006966
189.98	0.006786
192.00	0.006849
193.98	0.006723
195.98	0.006698
197.98	0.006622
199.98	0.006488
202.03	0.006348
203.98	0.00645
205.98	0.006261
207.98	0.006089
209.98	0.006215
211.98	0.006235
213.98	0.006016
215.98	0.006017
217.98	0.005951
219.98	0.005904
221.98	0.005886
223.98	0.00565
225.98	0.005661
228.02	0.005623
229.98	0.005544
231.98	0.005505
233.98	0.005479
235.98	0.005501
237.98	0.005351
239.98	0.005284
242.05	0.005369
243.98	0.005261
245.98	0.005288
247.98	0.005082
249.98	0.005176
251.98	0.005134
253.98	0.004963
255.98	0.005094
257.98	0.005061

259.98	0.004851
261.98	0.004932
263.98	0.004803
265.98	0.004802
268.00	0.004723
269.98	0.004684
271.98	0.00471
274.00	0.004675
275.98	0.004602
278.00	0.004539
279.98	0.004641
281.98	0.004408
283.98	0.004597
285.98	0.004419
287.98	0.004482
290.00	0.004436
291.98	0.004304
293.98	0.004408
295.98	0.004497
297.98	0.004292
299.98	0.004489
301.98	0.004303
303.98	0.004541
306.00	0.00432
307.98	0.004209
309.98	0.004231
311.98	0.004314
313.98	0.004342
315.98	0.004127
317.98	0.004253
320.00	0.004161
321.98	0.004106

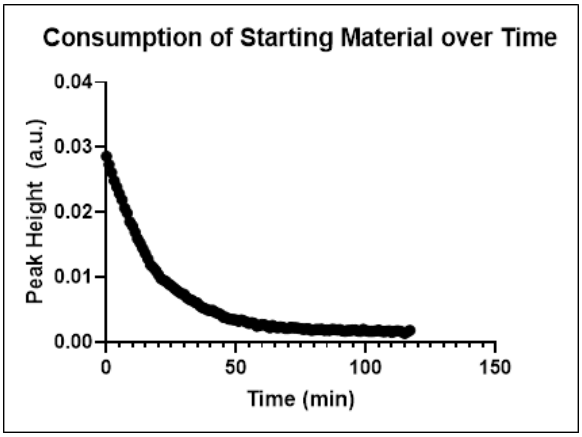


Appendix Figure C.8. 1st order exponential decay of **2.7** at 95 °C

One phase decay	
Best-fit values	
Y0	0.03221
Plateau	0.002406
K	0.03037
Half Life	22.82
Tau	32.92
Span	0.02981
95% CI (profile likelihood)	
Y0	0.03206 to 0.03237
Plateau	0.002343 to 0.002468
K	0.03005 to 0.03070
Half Life	22.58 to 23.06
Tau	32.58 to 33.27
Goodness of Fit	
Degrees of Freedom	57
R squared	0.9997
Sum of Squares	1.04E-06
Sy.x	0.000135
Constraints	
K	K > 0
Number of points	
# of X values	60
# Y values analyzed	60

Time (min)	Peak at 1282 cm^{-1} (a.u.)
0.00	0.031919
3.00	0.029384
6.00	0.027284
9.05	0.025112
12.00	0.023126
15.00	0.021493
18.00	0.019935
21.02	0.018321
24.00	0.016911
27.00	0.015649
30.00	0.014522
33.00	0.01344
36.00	0.012512
39.00	0.011429
42.00	0.010803
45.00	0.010028
48.00	0.009333
51.00	0.008663
54.02	0.00817
57.00	0.007591
60.00	0.007202
63.00	0.006693
66.00	0.006286
69.00	0.006001
72.00	0.005512
75.00	0.005254
78.02	0.00515
81.00	0.00466
84.02	0.004436
87.00	0.004542
90.00	0.004252
93.00	0.004111
96.00	0.003964
99.00	0.003792
102.00	0.003562
105.02	0.00363
108.00	0.003588
111.02	0.00328
114.00	0.003253
117.00	0.003287
120.00	0.003231
123.00	0.003257

126.00	0.003068
129.00	0.002956
132.00	0.002952
135.00	0.00279
138.00	0.002904
141.00	0.002908
144.02	0.002753
147.00	0.002752
150.00	0.002846
153.00	0.002901
156.00	0.002661
159.00	0.002708
162.00	0.002821
165.00	0.002708
168.00	0.002645
171.02	0.002765
174.00	0.00263
177.00	0.002749

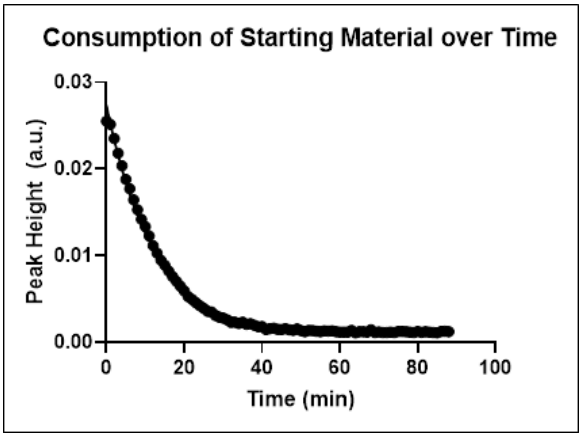


Appendix Figure C.9. 1st order exponential decay of **2.7** at 108 °C

One phase decay	
Best-fit values	
Y0	0.02904
Plateau	0.001611
K	0.05423
Half Life	12.78
Tau	18.44
Span	0.02743
95% CI (profile likelihood)	
Y0	0.02887 to 0.02922
Plateau	0.001554 to 0.001668
K	0.05359 to 0.05489
Half Life	12.63 to 12.93
Tau	18.22 to 18.66
Goodness of Fit	
Degrees of Freedom	115
R squared	0.9991
Sum of Squares	4.36E-06
Sy.x	0.000195
Constraints	
K	K > 0
Number of points	
# of X values	118
# Y values analyzed	118

Time (min)	Peak at 1281 cm^{-1} (a.u.)
0.00	0.028602
1.00	0.027335
2.00	0.026118
3.00	0.024847
4.00	0.023897
5.00	0.022861
6.00	0.021923
7.00	0.020644
8.00	0.019895
9.00	0.018544
10.02	0.01792
11.00	0.01696
12.00	0.0159
13.00	0.015234
14.02	0.014409
15.00	0.013616
16.05	0.012824
17.00	0.011898
18.00	0.011503
19.00	0.011062
20.00	0.010412
21.00	0.009796
22.00	0.009564
23.00	0.009362
24.00	0.008965
25.00	0.008715
26.00	0.008336
27.00	0.008
28.00	0.007724
29.00	0.007464
30.00	0.007378
31.00	0.006843
32.00	0.006584
33.00	0.006466
34.00	0.006138
35.00	0.006064
36.00	0.005577
37.00	0.005305
38.00	0.005179
39.02	0.004944
40.00	0.004882
41.00	0.004914

42.00	0.004591
43.00	0.004444
44.00	0.00427
45.00	0.003839
46.00	0.003838
47.00	0.003588
48.00	0.003527
49.00	0.003468
50.00	0.003428
51.00	0.003228
52.00	0.003409
53.00	0.003281
54.00	0.003069
55.00	0.002869
56.00	0.003011
57.00	0.002899
58.00	0.002447
59.00	0.00259
60.00	0.002729
61.00	0.002696
62.00	0.002457
63.00	0.002229
64.00	0.002577
65.00	0.002365
66.02	0.002201
67.02	0.002358
68.00	0.002277
69.00	0.002111
70.00	0.00211
71.02	0.002299
72.02	0.002225
73.00	0.002233
74.00	0.002164
75.00	0.002075
76.00	0.001979
77.00	0.00204
78.00	0.002037
79.00	0.001829
80.00	0.001879
81.00	0.001989
82.00	0.001961
83.00	0.002001
84.00	0.001822
85.00	0.00188
86.00	0.00181
87.00	0.001974
88.00	0.001942
89.00	0.00188
90.00	0.001964
91.00	0.001759
92.00	0.001678
93.00	0.001829
94.00	0.00179
95.00	0.001882
96.00	0.001891
97.00	0.001728
98.00	0.001696
99.00	0.001972
100.00	0.001793
101.00	0.001697
102.00	0.001667
103.00	0.001694
104.00	0.001743
105.00	0.001843
106.00	0.001683
107.00	0.00162
108.00	0.001668
109.00	0.001755
110.00	0.001528
111.00	0.001634
112.00	0.001744
113.00	0.001731
114.00	0.001567
115.00	0.001341
116.00	0.001588
117.00	0.00181

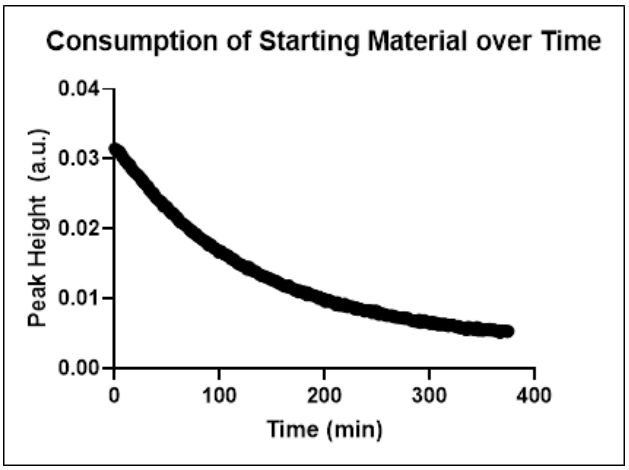


Appendix Figure C.10. 1st order exponential decay of **2.7** at 113 °C

One phase decay	
Best-fit values	
Y0	0.02738
Plateau	0.000936
K	0.0817
Half Life	8.484
Tau	12.24
Span	0.02644
95% CI (profile likelihood)	
Y0	0.02700 to 0.02776
Plateau	0.0008268 to 0.001044
K	0.07968 to 0.08377
Half Life	8.275 to 8.699
Tau	11.94 to 12.55
Goodness of Fit	
Degrees of Freedom	86
R squared	0.9968
Sum of Squares	1.08E-05
Sy.x	0.000354
Constraints	
K	K > 0
Number of points	
# of X values	89
# Y values analyzed	89

Time (min)	Peak at 1282 cm^{-1} (a.u.)
0.00	0.025508
1.00	0.025143
2.00	0.02351
3.02	0.021824
4.00	0.020361
5.00	0.018793
6.00	0.017703
7.00	0.01644
8.00	0.015294
9.00	0.014181
10.00	0.013328
11.00	0.012251
12.00	0.011137
13.03	0.010283
14.02	0.009464
15.00	0.008881
16.00	0.0082
17.00	0.007555
18.02	0.007011
19.00	0.006471
20.00	0.005905
21.03	0.005254
22.00	0.004937
23.00	0.004571
24.00	0.004219
25.00	0.003912
26.00	0.003556
27.00	0.003483
28.00	0.003077
29.00	0.002893
30.00	0.002776
31.00	0.002581
32.00	0.002291
33.00	0.002315
34.00	0.002157
35.00	0.00231
36.02	0.00205
37.00	0.002137
38.00	0.001968
39.00	0.00178
40.02	0.001804
41.00	0.001469

42.00	0.00157
43.00	0.001606
44.00	0.001488
45.00	0.001468
46.00	0.001558
47.00	0.001447
48.00	0.001352
49.02	0.001549
50.00	0.001344
51.00	0.00121
52.00	0.001358
53.02	0.001344
54.00	0.001251
55.00	0.001222
56.00	0.00131
57.00	0.001284
58.02	0.00131
59.00	0.001202
60.00	0.001164
61.00	0.001164
62.02	0.001173
63.00	0.001353
64.00	0.001075
65.00	0.001214
66.02	0.001201
67.00	0.001161
68.00	0.001438
69.00	0.001105
70.02	0.001181
71.00	0.001115
72.00	0.001106
73.00	0.001156
74.00	0.001106
75.00	0.001245
76.00	0.001244
77.00	0.001223
78.00	0.001164
79.00	0.00111
80.00	0.001235
81.00	0.001125
82.00	0.001223
83.00	0.001169
84.00	0.001113
85.00	0.001096
86.00	0.001238
87.00	0.001253
88.00	0.001208



Appendix Figure C.11. 1st order exponential decay of **1.59** at 88 °C

One phase decay		
Best-fit values		
Y0		0.03187
Plateau		0.003693
K		0.007641
Half Life		90.71
Tau		130.9
Span		0.02818
95% CI (profile likelihood)		
Y0	0.03182 to 0.03192	
Plateau	0.003638 to 0.003747	
K	0.007596 to 0.007687	
Half Life	90.17 to 91.26	
Tau	130.1 to 131.7	
Goodness of Fit		
Degrees of Freedom		373
R squared		0.9997
Sum of Squares		6.62E-06
Sy.x		0.000133
Constraints		
K	K > 0	
Number of points		
# of X values		376
# Y values analyzed		376

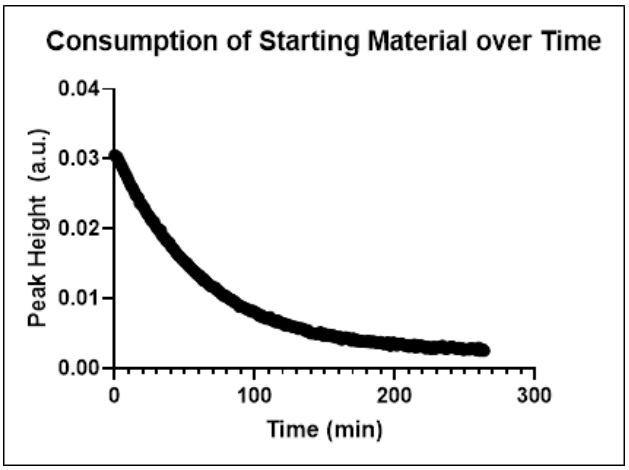
Time (min)	Peak at 1282 cm^{-1} (a.u.)
0.00	0.031504
1.00	0.03125
2.00	0.031245
3.02	0.031238
4.00	0.031081
5.00	0.031005
6.00	0.030752
7.00	0.030319
8.00	0.030284
9.00	0.02996
10.00	0.029698
11.00	0.029615
12.00	0.029526
13.00	0.02912
14.00	0.029186
15.00	0.029127
16.00	0.02854
17.00	0.028504
18.00	0.028173
19.00	0.028193
20.00	0.027951
21.00	0.027843
22.00	0.027692
23.00	0.027655
24.00	0.027303
25.00	0.027297
26.00	0.026828
27.00	0.026955
28.00	0.02649
29.00	0.02651
30.00	0.026235
31.00	0.026088
32.00	0.026042
33.00	0.025524
34.00	0.025442
35.05	0.025241
36.00	0.025029
37.00	0.025168
38.00	0.024837
39.00	0.024465

40.00	0.024379
41.00	0.024216
42.00	0.02413
43.00	0.023904
44.00	0.023893
45.00	0.023855
46.00	0.023228
47.05	0.023234
48.00	0.02314
49.00	0.023123
50.00	0.023153
51.00	0.022815
52.00	0.022541
53.00	0.022393
54.00	0.02216
55.00	0.022217
56.00	0.022254
57.00	0.021968
58.05	0.021776
59.00	0.021537
60.00	0.02162
61.00	0.021193
62.00	0.020953
63.00	0.020993
64.00	0.02078
65.00	0.020877
66.00	0.020662
67.00	0.0205
68.00	0.020413
69.00	0.020437
70.00	0.020152
71.00	0.019913
72.00	0.019775
73.00	0.019588
74.00	0.019708
75.00	0.019381
76.00	0.019287
77.00	0.019193
78.00	0.019238
79.00	0.018904
80.00	0.018826
81.00	0.01878
82.00	0.018579
83.00	0.018542
84.02	0.018466
85.00	0.018254
86.00	0.0182
87.02	0.018053
88.00	0.018112
89.00	0.017643
90.00	0.017629
91.00	0.017782
92.00	0.017702
93.00	0.017581
94.00	0.01726
95.00	0.017219
96.00	0.017193
97.00	0.017064
98.00	0.016921
99.00	0.016593
100.00	0.016835
101.00	0.016697
102.00	0.016755
103.00	0.016513
104.00	0.016361
105.00	0.016314
106.00	0.016227
107.00	0.016209
108.00	0.016182
109.00	0.015948
110.00	0.015949
111.00	0.015626
112.00	0.015639
113.00	0.015686
114.00	0.01561
115.00	0.015357
116.00	0.015252
117.00	0.015027
118.00	0.015054
119.00	0.014882
120.00	0.014871
121.00	0.014701
122.00	0.014785
123.00	0.014662
124.00	0.01457
125.00	0.014555
126.00	0.01416
127.00	0.014315
128.02	0.014542
129.00	0.014236

130.00	0.014237
131.00	0.014002
132.00	0.013886
133.00	0.013785
134.00	0.01385
135.00	0.013896
136.00	0.013652
137.00	0.013662
138.00	0.013397
139.03	0.013429
140.00	0.013213
141.00	0.013322
142.00	0.013179
143.00	0.013212
144.00	0.013038
145.00	0.013079
146.02	0.012872
147.00	0.01299
148.00	0.012823
149.00	0.012793
150.00	0.012594
151.00	0.012672
152.00	0.012559
153.02	0.01247
154.00	0.01247
155.00	0.012451
156.00	0.012166
157.00	0.012217
158.00	0.012147
159.00	0.012024
160.00	0.011846
161.00	0.011903
162.00	0.011718
163.00	0.01184
164.00	0.011658
165.00	0.011694
166.00	0.011882
167.00	0.011565
168.00	0.011495
169.00	0.011425
170.00	0.011435
171.00	0.011249
172.00	0.011127
173.00	0.01118
174.00	0.011182
175.00	0.010925
176.00	0.011181
177.00	0.011047
178.00	0.010999
179.00	0.01087
180.00	0.010765
181.03	0.010994
182.00	0.010794
183.00	0.010496
184.00	0.010874
185.00	0.010506
186.00	0.010646
187.00	0.010443
188.00	0.010484
189.03	0.010464
190.00	0.010499
191.00	0.010358
192.05	0.010292
193.00	0.010228
194.00	0.00998
195.00	0.010285
196.00	0.010019
197.00	0.010026
198.00	0.009979
199.00	0.010002
200.00	0.009554
201.00	0.009749
202.00	0.009574
203.02	0.009806
204.00	0.009599
205.00	0.009745
206.00	0.009586
207.00	0.009557
208.00	0.009487
209.00	0.00941
210.00	0.009067
211.00	0.009365
212.00	0.009479
213.00	0.009322
214.00	0.008959
215.00	0.009082
216.00	0.00918
217.00	0.009141
218.00	0.008916
219.00	0.009269

220.00	0.008952
221.00	0.008811
222.00	0.008771
223.00	0.008906
224.00	0.00881
225.00	0.008735
226.00	0.008868
227.00	0.008752
228.00	0.008664
229.00	0.008434
230.00	0.008737
231.00	0.008499
232.00	0.00838
233.00	0.00854
234.00	0.008443
235.00	0.008452
236.00	0.008367
237.00	0.008302
238.00	0.00816
239.00	0.008253
240.00	0.008214
241.00	0.008356
242.00	0.008311
243.00	0.008227
244.02	0.008257
245.00	0.007904
246.00	0.008255
247.00	0.008105
248.00	0.007986
249.00	0.008276
250.00	0.008149
251.00	0.00773
252.00	0.008001
253.00	0.007717
254.00	0.007812
255.00	0.007818
256.00	0.007732
257.00	0.007793
258.00	0.007681
259.00	0.007507
260.00	0.007577
261.00	0.00754
262.02	0.007535
263.00	0.007509
264.00	0.00762
265.00	0.007547
266.00	0.007366
267.00	0.007499
268.00	0.007283
269.02	0.007188
270.00	0.007282
271.00	0.007311
272.00	0.007269
273.00	0.007267
274.00	0.007223
275.00	0.007304
276.00	0.007083
277.00	0.00719
278.00	0.007205
279.00	0.007226
280.00	0.007096
281.00	0.006984
282.00	0.006858
283.00	0.006913
284.00	0.006812
285.00	0.006815
286.00	0.006694
287.00	0.006868
288.00	0.006754
289.00	0.00669
290.00	0.006976
291.00	0.006501
292.00	0.006801
293.00	0.006784
294.00	0.006603
295.00	0.006931
296.00	0.006645
297.02	0.006678
298.00	0.006591
299.03	0.00656
300.00	0.006382
301.00	0.006342
302.00	0.006663
303.00	0.006529
304.00	0.006343
305.00	0.006586
306.00	0.006508
307.02	0.006395
308.00	0.00617
309.00	0.006355

310.00	0.006411
311.00	0.006245
312.00	0.006233
313.00	0.006273
314.00	0.006429
315.00	0.006299
316.00	0.006155
317.00	0.006085
318.00	0.00605
319.00	0.006154
320.00	0.006255
321.00	0.006162
322.00	0.006257
323.03	0.006078
324.00	0.005996
325.00	0.005969
326.00	0.006005
327.00	0.006092
328.00	0.005786
329.00	0.005982
330.00	0.005775
331.00	0.005813
332.00	0.005825
333.05	0.005842
334.00	0.005501
335.00	0.005569
336.00	0.005548
337.00	0.00594
338.02	0.005785
339.00	0.005773
340.00	0.005645
341.00	0.005706
342.00	0.005512
343.00	0.005673
344.00	0.005695
345.00	0.005906
346.00	0.00541
347.00	0.005791
348.00	0.005447
349.00	0.005643
350.00	0.005592
351.00	0.005367
352.00	0.005538
353.00	0.005611
354.02	0.005546
355.00	0.00558
356.00	0.005448
357.00	0.005645
358.00	0.005491
359.00	0.005507
360.00	0.005433
361.00	0.005577
362.05	0.005428
363.00	0.005459
364.00	0.005353
365.00	0.005297
366.00	0.005443
367.05	0.005082
368.00	0.005298
369.03	0.005398
370.00	0.005374
371.00	0.005416
372.00	0.005355
373.00	0.005269
374.00	0.005232
375.00	0.005347



Appendix Figure C.12. 1st order exponential decay of **1.59** at 98 °C

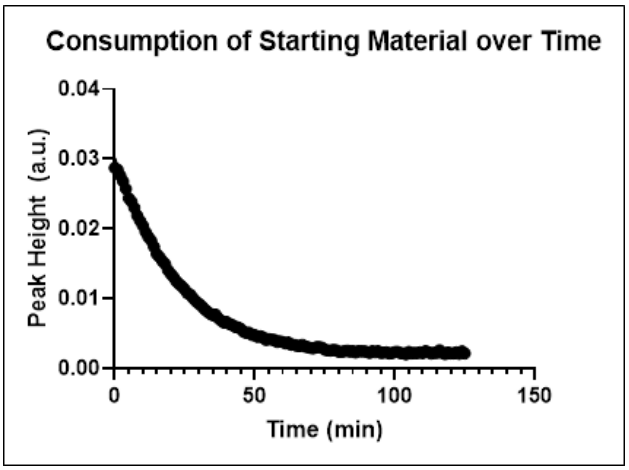
One phase decay	
Best-fit values	
Y0	0.03117
Plateau	0.00225
K	0.01605
Half Life	43.18
Tau	62.3
Span	0.02892
95% CI (profile likelihood)	
Y0	0.03110 to 0.03124
Plateau	0.002212 to 0.002288
K	0.01596 to 0.01614
Half Life	42.94 to 43.43
Tau	61.95 to 62.65
Goodness of Fit	
Degrees of Freedom	262
R squared	0.9997
Sum of Squares	4.83E-06
Sy.x	0.000136
Constraints	
K	K > 0
Number of points	
# of X values	265
# Y values analyzed	265

Time (min)	Peak at 1280 cm^{-1} (a.u.)
0.00	0.030556
1.00	0.030255
1.98	0.030322
3.00	0.029739
4.00	0.029364
5.00	0.028939
6.00	0.028546
7.00	0.028083
8.00	0.027759
9.00	0.027343
9.98	0.026919
11.00	0.026404
12.00	0.026025
13.00	0.025784
14.00	0.025304
15.00	0.024792
16.00	0.024678
17.00	0.024399
17.98	0.02364
19.00	0.023604
20.00	0.023238
21.00	0.023054
22.00	0.022565
23.00	0.0222
24.00	0.021931
25.00	0.021704
25.98	0.021234
27.00	0.021055
28.02	0.021054
28.98	0.020558
30.00	0.020108
31.00	0.020011
32.00	0.019605
33.00	0.019796
33.98	0.019033
35.00	0.0188
36.00	0.018643
36.98	0.018253
38.00	0.018113
39.00	0.018038

40.00	0.017555
41.00	0.017318
41.98	0.01719
43.00	0.016866
44.00	0.016543
44.98	0.016308
46.00	0.016082
47.00	0.015947
48.00	0.015666
49.00	0.015485
50.03	0.015236
51.00	0.015114
52.00	0.015019
52.98	0.014604
54.00	0.014488
55.00	0.014236
56.03	0.014031
57.00	0.013923
58.00	0.013568
59.00	0.013572
60.00	0.013235
61.00	0.013277
62.00	0.012931
63.00	0.012589
64.00	0.012784
65.00	0.012408
66.02	0.012333
67.00	0.01206
68.03	0.01181
69.00	0.011807
69.98	0.011754
71.00	0.011558
72.00	0.011599
73.02	0.01119
74.00	0.011162
75.00	0.010979
75.98	0.010709
77.00	0.010547
78.00	0.010356
79.00	0.010458
80.00	0.010285
81.00	0.010062
82.00	0.009952
83.00	0.009819
84.00	0.009817
85.00	0.009513
86.00	0.009537
86.98	0.00951
88.00	0.009166
89.00	0.008828
89.98	0.008906
91.00	0.008845
92.00	0.008765
92.98	0.008772
94.00	0.008482
95.00	0.008484
95.98	0.008381
97.00	0.008156
98.00	0.008285
99.00	0.008202
100.00	0.008104
101.00	0.007892
102.00	0.007885
103.00	0.007549
104.00	0.007483
105.00	0.0076
106.00	0.007299
107.00	0.007307
107.98	0.007206
109.00	0.007088
110.00	0.007172
111.00	0.007343
112.00	0.006942
112.98	0.006858
114.00	0.006797
115.00	0.006615
115.98	0.006846
117.00	0.00682
118.00	0.006561
118.98	0.006443
120.00	0.006483
121.00	0.006419
121.98	0.006133
123.00	0.006318
124.00	0.006068
125.00	0.006147
126.00	0.006085
127.00	0.005935
128.00	0.005903
129.00	0.005923

130.00	0.005871
131.00	0.005656
132.00	0.005732
133.00	0.005731
134.00	0.005718
135.00	0.005605
136.00	0.005373
137.02	0.005357
138.00	0.005477
138.98	0.005192
140.00	0.005011
141.00	0.005036
141.98	0.004919
143.00	0.004981
144.00	0.004916
145.00	0.005054
145.98	0.004986
147.00	0.005187
148.00	0.004817
149.00	0.004689
150.00	0.004939
151.00	0.004829
152.00	0.004661
153.00	0.004824
154.00	0.004738
155.00	0.004585
156.00	0.004757
157.00	0.004526
158.00	0.004522
159.00	0.004392
160.00	0.00448
161.00	0.004501
162.00	0.004102
163.00	0.004209
164.00	0.004347
165.00	0.004438
166.00	0.00425
167.00	0.004303
168.00	0.004233
169.00	0.003953
170.00	0.00429
171.00	0.004238
172.00	0.003913
173.00	0.004095
174.00	0.003974
175.00	0.003834
176.00	0.003961
177.02	0.003836
177.98	0.003856
179.00	0.00389
180.00	0.003775
181.00	0.003917
182.00	0.003851
183.00	0.003712
184.00	0.003896
185.00	0.003776
186.00	0.00382
187.00	0.003653
188.00	0.003707
189.00	0.003735
190.00	0.003771
191.00	0.003638
192.00	0.003474
193.00	0.003517
194.00	0.00358
195.00	0.003753
196.00	0.003361
197.00	0.003259
198.00	0.003527
199.00	0.003707
200.05	0.00349
201.00	0.003315
202.00	0.003316
203.00	0.003418
204.00	0.003536
205.00	0.00354
206.02	0.003431
207.00	0.003254
207.98	0.003247
209.00	0.00336
210.00	0.003096
210.98	0.003264
212.00	0.003249
213.00	0.003164
214.00	0.003412
214.98	0.003017
216.00	0.003301
217.00	0.003075
218.02	0.003245
219.00	0.003247

220.00	0.003202
221.00	0.003122
222.00	0.002864
223.00	0.003027
224.00	0.003086
225.00	0.002879
226.00	0.002786
227.03	0.003018
228.00	0.003078
229.00	0.002828
229.98	0.002865
231.00	0.003097
231.98	0.003007
233.00	0.002948
234.00	0.003247
235.00	0.002955
236.05	0.002853
237.00	0.002771
238.00	0.002984
239.00	0.002944
240.00	0.003085
241.00	0.003121
242.00	0.002934
243.00	0.002963
244.00	0.002812
245.00	0.002814
245.98	0.002941
247.00	0.002911
248.05	0.002868
249.00	0.00265
250.00	0.002701
250.98	0.002811
252.00	0.00277
253.00	0.002679
254.00	0.002851
255.00	0.002895
256.00	0.002786
257.00	0.002788
258.00	0.002605
259.00	0.002766
260.00	0.002993
261.00	0.002533
261.98	0.002722
263.00	0.002712
263.98	0.002532

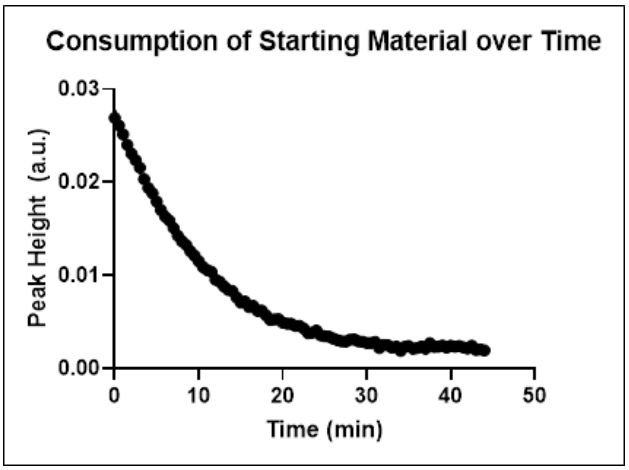


Appendix Figure C.13. 1st order exponential decay of **1.59** at 109 °C

One phase decay	
Best-fit values	
Y0	0.03019
Plateau	0.001863
K	0.04444
Half Life	15.6
Tau	22.5
Span	0.02832
95% CI (profile likelihood)	
Y0	0.02998 to 0.03039
Plateau	0.001788 to 0.001938
K	0.04383 to 0.04505
Half Life	15.39 to 15.82
Tau	22.20 to 22.82
Goodness of Fit	
Degrees of Freedom	123
R squared	0.9988
Sum of Squares	7.24E-06
Sy.x	0.000243
Constraints	
K	K > 0
Number of points	
# of X values	126
# Y values analyzed	126

Time (min)	Peak at 1281 cm^{-1} (a.u.)
0.00	0.028714
1.00	0.028493
2.00	0.027616
3.00	0.026768
4.00	0.025716
5.00	0.024385
6.00	0.023897
7.00	0.023004
8.02	0.02193
9.00	0.021179
10.00	0.020473
11.00	0.019551
12.00	0.018843
13.00	0.018305
14.00	0.017431
15.00	0.016394
16.00	0.015946
17.00	0.015399
18.00	0.014961
19.00	0.014088
20.00	0.013554
21.00	0.013094
22.00	0.012471
23.00	0.012097
24.00	0.01176
25.00	0.011323
26.00	0.010749
27.03	0.010576
28.00	0.010041
29.00	0.009629
30.00	0.009269
31.00	0.008939
32.00	0.008528
33.00	0.008135
34.00	0.007841
35.00	0.007607
36.00	0.007704
37.00	0.00719
38.00	0.006858
39.00	0.006547

40.00	0.00666
41.00	0.006349
42.00	0.006202
43.00	0.005952
44.00	0.005886
45.00	0.005682
46.00	0.005237
47.00	0.005084
48.00	0.005105
49.00	0.004782
50.00	0.004785
51.00	0.004533
52.00	0.004623
53.00	0.004458
54.00	0.004095
55.00	0.00423
56.00	0.004105
57.00	0.004082
58.00	0.003784
59.00	0.003877
60.00	0.003775
61.05	0.0036
62.00	0.003708
63.00	0.003398
64.00	0.003393
65.00	0.003241
66.00	0.003231
67.00	0.003394
68.00	0.003106
69.00	0.003051
70.00	0.002921
71.00	0.002891
72.00	0.003065
73.00	0.003063
74.00	0.002987
75.00	0.002672
76.00	0.002585
77.00	0.002548
78.00	0.002644
79.00	0.002633
80.00	0.002398
81.00	0.002392
82.00	0.002444
83.00	0.002565
84.00	0.002416
85.00	0.002476
86.00	0.002291
87.00	0.002474
88.00	0.002435
89.00	0.002448
90.00	0.002381
91.00	0.002212
92.00	0.002468
93.00	0.002306
94.00	0.002469
95.00	0.002212
96.00	0.002239
97.00	0.002315
98.00	0.002142
99.00	0.002167
100.00	0.002364
101.00	0.002374
102.00	0.00219
103.00	0.002147
104.00	0.002027
105.00	0.002367
106.00	0.002157
107.00	0.002214
108.00	0.002168
109.00	0.002301
110.00	0.002191
111.00	0.002492
112.00	0.002301
113.00	0.002106
114.00	0.002234
115.00	0.002218
116.00	0.002612
117.00	0.002219
118.00	0.00205
119.00	0.002287
120.00	0.002156
121.00	0.002143
122.00	0.002305
123.00	0.002089
124.00	0.002445
125.00	0.002149

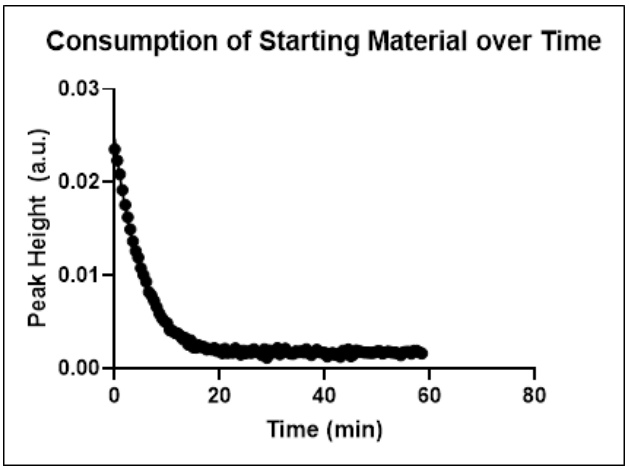


Appendix Figure C.14. 1st order exponential decay of **1.59** at 121 °C

One phase decay	
Best-fit values	
Y0	0.02781
Plateau	0.001448
K	0.09781
Half Life	7.087
Tau	10.22
Span	0.02636
95% CI (profile likelihood)	
Y0	0.02755 to 0.02807
Plateau	0.001309 to 0.001584
K	0.09565 to 0.09999
Half Life	6.932 to 7.247
Tau	10.00 to 10.45
Goodness of Fit	
Degrees of Freedom	86
R squared	0.9982
Sum of Squares	7.32E-06
Sy.x	0.000292
Constraints	
K	K > 0
Number of points	
# of X values	89
# Y values analyzed	89

Time (min)	Peak at 1280 cm^{-1} (a.u.)
0.00	0.026924
0.50	0.026095
1.00	0.025125
1.50	0.024022
2.00	0.023069
2.50	0.022365
3.00	0.021563
3.50	0.020341
4.00	0.019378
4.50	0.018806
5.00	0.017912
5.50	0.017023
6.00	0.016307
6.50	0.015899
7.00	0.015087
7.50	0.014255
8.00	0.013666
8.50	0.013252
9.02	0.012587
9.50	0.012114
10.00	0.011511
10.50	0.010878
11.00	0.010569
11.50	0.010383
12.00	0.009526
12.50	0.009319
13.00	0.008801
13.50	0.008427
14.00	0.008324
14.50	0.007632
15.00	0.007052
15.50	0.007184
16.00	0.006593
16.50	0.006702
17.00	0.006199
17.50	0.006204
18.00	0.005706
18.50	0.005201
19.00	0.00525
19.50	0.005287

20.00	0.004907
20.50	0.004804
21.00	0.004792
21.50	0.004571
22.00	0.00457
22.50	0.004278
23.00	0.003781
23.50	0.003828
24.00	0.004057
24.50	0.003561
25.00	0.003459
25.50	0.003411
26.00	0.003202
26.50	0.003049
27.00	0.002924
27.50	0.002879
28.00	0.003097
28.50	0.003111
29.00	0.002918
29.50	0.002854
30.00	0.002742
30.50	0.00274
31.00	0.002847
31.50	0.002195
32.00	0.002524
32.50	0.002496
33.00	0.002236
33.53	0.00233
34.03	0.001878
34.52	0.002311
34.98	0.002415
35.50	0.002108
36.00	0.002176
36.50	0.002342
37.00	0.002123
37.50	0.002721
38.00	0.002317
38.50	0.002333
39.00	0.00247
39.50	0.002247
40.00	0.002439
40.50	0.002337
41.00	0.002413
41.50	0.002254
42.00	0.002145
42.50	0.002443
43.00	0.00199
43.50	0.002027
44.00	0.001926

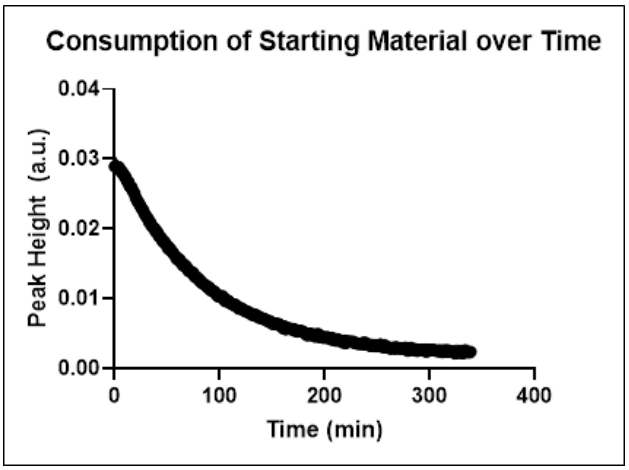


Appendix Figure C.15. 1st order exponential decay of **1.59** at 132 °C

One phase decay	
Best-fit values	
Y0	0.0247
Plateau	0.00161
K	0.1922
Half Life	3.607
Tau	5.203
Span	0.02309
95% CI (profile likelihood)	
Y0	0.02438 to 0.02501
Plateau	0.001546 to 0.001673
K	0.1880 to 0.1965
Half Life	3.528 to 3.687
Tau	5.090 to 5.319
Goodness of Fit	
Degrees of Freedom	115
R squared	0.9964
Sum of Squares	9.14E-06
Sy.x	0.000282
Constraints	
K	K > 0
Number of points	
# of X values	118
# Y values analyzed	118

Time (min)	Peak at 1278 cm^{-1} (a.u.)
0.00	0.023538
0.50	0.02234
1.00	0.020874
1.50	0.019154
2.00	0.017555
2.50	0.016225
3.00	0.01493
3.50	0.013653
4.00	0.01261
4.50	0.011902
5.00	0.010783
5.50	0.010039
6.00	0.009313
6.50	0.008212
7.00	0.007868
7.50	0.007276
8.00	0.006578
8.50	0.005908
9.00	0.005417
9.50	0.005062
10.00	0.004872
10.50	0.004124
11.03	0.00403
11.50	0.003822
12.00	0.003758
12.50	0.003505
13.00	0.003142
13.50	0.003273
14.00	0.002571
14.50	0.003006
15.00	0.002271
15.50	0.00223
16.00	0.00249
16.50	0.002282
17.02	0.002303
17.52	0.002035
18.02	0.002083
18.50	0.002036
19.00	0.002185
19.50	0.001867

20.00	0.001945
20.52	0.001649
21.00	0.002124
21.50	0.001659
22.00	0.001726
22.50	0.001677
23.00	0.00215
23.50	0.001863
24.00	0.00149
24.50	0.001901
25.00	0.001636
25.50	0.001843
26.00	0.001671
26.50	0.002074
27.00	0.001817
27.50	0.001699
28.00	0.001446
28.50	0.002064
29.00	0.001139
29.50	0.001933
30.00	0.001693
30.50	0.001761
31.00	0.002176
31.50	0.001502
32.00	0.001785
32.50	0.002141
33.00	0.001726
33.50	0.001592
34.00	0.001556
34.52	0.001828
35.00	0.001748
35.50	0.001836
36.00	0.001711
36.50	0.002061
37.00	0.001644
37.50	0.001432
38.00	0.001786
38.50	0.002002
39.00	0.001771
39.50	0.00168
40.00	0.001694
40.50	0.001282
41.00	0.001524
41.50	0.001651
42.00	0.001472
42.50	0.001545
43.00	0.001227
43.50	0.001906
44.00	0.001647
44.50	0.002046
45.00	0.001312
45.50	0.001495
46.00	0.001949
46.50	0.001842
47.00	0.001795
47.50	0.001711
48.00	0.001723
48.50	0.001688
49.00	0.001656
49.50	0.001719
50.00	0.001843
50.50	0.001834
51.00	0.001616
51.50	0.0017
52.00	0.0018
52.50	0.00177
53.00	0.001692
53.50	0.001713
54.00	0.001581
54.50	0.00141
55.00	0.001731
55.50	0.001783
56.00	0.00178
56.50	0.001583
57.00	0.001884
57.52	0.00189
58.02	0.001741
58.52	0.001607



Appendix Figure C.16. 1st order exponential decay of **2.5** at 73 °C

One phase decay	
Best-fit values	
Y0	0.03032
Plateau	0.001773
K	0.0119
Half Life	58.24
Tau	84.02
Span	0.02855
95% CI (profile likelihood)	
Y0	0.03024 to 0.03040
Plateau	0.001728 to 0.001818
K	0.01182 to 0.01198
Half Life	57.86 to 58.62
Tau	83.48 to 84.57
Goodness of Fit	
Degrees of Freedom	337
R squared	0.9995
Sum of Squares	9.81E-06
Sy.x	0.000171
Constraints	
K	K > 0
Number of points	
# of X values	340
# Y values analyzed	340

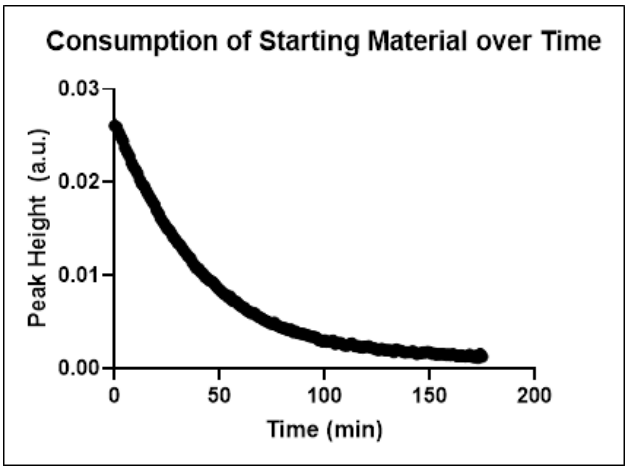
Time (min)	Peak at 1284 cm^{-1} (a.u.)
0.00	0.028924
1.00	0.028987
2.00	0.028907
3.00	0.028734
4.00	0.028824
5.02	0.028524
6.00	0.028188
7.00	0.028174
8.00	0.027901
9.00	0.027584
10.00	0.027516
11.00	0.02713
12.02	0.026757
13.02	0.026773
14.02	0.026156
15.05	0.025994
16.00	0.025993
17.00	0.025476
18.02	0.025279
19.00	0.025006
20.00	0.024444
21.00	0.024229
22.00	0.023857
23.00	0.023707
24.00	0.023427
25.02	0.023123
26.00	0.022842
27.00	0.02272
28.00	0.022283
29.00	0.022038
30.00	0.021763
31.02	0.021621
32.00	0.021351
33.00	0.020923
34.03	0.020904
35.03	0.020448
36.00	0.02031
37.00	0.020159
38.02	0.020042
39.03	0.019594

40.02	0.019644
41.00	0.01941
42.00	0.018921
43.00	0.018913
44.02	0.018736
45.00	0.018416
46.00	0.018108
47.00	0.018226
48.00	0.017988
49.00	0.017723
50.00	0.017504
51.02	0.01713
52.00	0.017286
53.00	0.017036
54.00	0.016813
55.00	0.016728
56.00	0.016382
57.02	0.016368
58.00	0.016085
59.00	0.015682
60.02	0.015792
61.00	0.015474
62.00	0.015582
63.02	0.015231
64.02	0.015016
65.00	0.014743
66.00	0.014925
67.00	0.014613
68.00	0.014602
69.00	0.014393
70.03	0.014002
71.00	0.013918
72.00	0.013942
73.00	0.01387
74.00	0.013637
75.00	0.013687
76.02	0.013157
77.00	0.0132
78.00	0.013059
79.02	0.013
80.00	0.012738
81.00	0.012545
82.02	0.012518
83.00	0.012258
84.02	0.012153
85.02	0.012143
86.00	0.011948
87.00	0.011895
88.05	0.011668
89.02	0.0116
90.02	0.011611
91.00	0.011286
92.00	0.011118
93.05	0.011229
94.00	0.011077
95.02	0.010968
96.00	0.010797
97.00	0.010652
98.00	0.01039
99.00	0.010278
100.00	0.010351
101.00	0.010298
102.02	0.01015
103.00	0.010348
104.00	0.009975
105.00	0.009652
106.00	0.009812
107.00	0.009654
108.02	0.009726
109.00	0.009407
110.00	0.009379
111.00	0.009269
112.00	0.0092
113.00	0.009229
114.02	0.008988
115.00	0.009138
116.00	0.008944
117.00	0.008873
118.03	0.008543
119.00	0.008697
120.00	0.008657
121.02	0.008581
122.00	0.008492
123.00	0.008333
124.00	0.008267
125.00	0.008163
126.00	0.008104
127.02	0.008071
128.03	0.008023
129.00	0.007977

130.00	0.007702
131.00	0.007799
132.00	0.007614
133.02	0.007757
134.02	0.007663
135.02	0.007526
136.00	0.00755
137.00	0.007275
138.00	0.007321
139.03	0.007305
140.03	0.00715
141.02	0.007093
142.00	0.007095
143.00	0.007028
144.05	0.006969
145.00	0.006908
146.00	0.00676
147.02	0.006675
148.00	0.006784
149.00	0.006695
150.00	0.006391
151.00	0.006476
152.00	0.006453
153.02	0.006432
154.00	0.006383
155.00	0.006279
156.02	0.006369
157.00	0.006249
158.02	0.006076
159.00	0.006095
160.02	0.005745
161.00	0.006005
162.00	0.005979
163.00	0.005591
164.00	0.005837
165.05	0.005714
166.00	0.00568
167.02	0.005674
168.00	0.005656
169.05	0.0055
170.05	0.00565
171.00	0.005417
172.00	0.005547
173.02	0.005338
174.00	0.005295
175.05	0.005353
176.00	0.005423
177.00	0.005391
178.03	0.005307
179.03	0.005304
180.00	0.005103
181.02	0.005117
182.00	0.005043
183.00	0.004752
184.00	0.004767
185.00	0.00499
186.00	0.004977
187.02	0.00477
188.03	0.004742
189.00	0.004895
190.00	0.004865
191.00	0.004535
192.00	0.004627
193.02	0.004901
194.00	0.004916
195.00	0.004507
196.00	0.004579
197.00	0.004451
198.00	0.004551
199.03	0.004395
200.05	0.004414
201.03	0.004395
202.00	0.004472
203.03	0.004453
204.03	0.004261
205.02	0.004172
206.00	0.004149
207.02	0.004369
208.00	0.004078
209.00	0.00407
210.00	0.004116
211.00	0.00394
212.02	0.004201
213.00	0.004134
214.00	0.004052
215.00	0.003942
216.00	0.003918
217.00	0.003729
218.00	0.003936
219.02	0.003975

220.00	0.003603
221.00	0.00386
222.00	0.003862
223.05	0.003848
224.00	0.003807
225.02	0.00383
226.00	0.003775
227.00	0.003841
228.00	0.003636
229.02	0.003538
230.00	0.003655
231.00	0.003557
232.07	0.003521
233.02	0.00353
234.00	0.003508
235.05	0.003492
236.00	0.003612
237.02	0.003671
238.00	0.003409
239.02	0.003682
240.03	0.003434
241.00	0.003308
242.00	0.003292
243.00	0.003399
244.00	0.00321
245.05	0.003375
246.00	0.003258
247.02	0.003349
248.00	0.003194
249.05	0.003364
250.00	0.003267
251.00	0.003189
252.00	0.003241
253.02	0.003463
254.02	0.003226
255.00	0.003037
256.00	0.003131
257.00	0.003334
258.00	0.002981
259.02	0.003017
260.02	0.003067
261.00	0.00318
262.00	0.002835
263.00	0.002859
264.00	0.002938
265.02	0.003051
266.00	0.002994
267.02	0.00282
268.00	0.00306
269.00	0.002982
270.05	0.002869
271.03	0.002906
272.00	0.002862
273.07	0.002928
274.07	0.002895
275.00	0.002902
276.00	0.002776
277.00	0.002969
278.00	0.00273
279.00	0.002531
280.02	0.002671
281.00	0.002872
282.00	0.002954
283.00	0.002788
284.00	0.002627
285.00	0.002716
286.00	0.002772
287.02	0.00269
288.02	0.002477
289.02	0.002585
290.00	0.002641
291.00	0.00261
292.00	0.002699
293.00	0.002569
294.03	0.002646
295.00	0.002606
296.00	0.002416
297.00	0.002716
298.00	0.002463
299.02	0.002608
300.00	0.002639
301.02	0.002521
302.00	0.002634
303.02	0.002688
304.00	0.002568
305.00	0.002476
306.02	0.002503
307.00	0.002568
308.00	0.002436
309.00	0.002509

310.02	0.002599
311.00	0.002556
312.00	0.002316
313.02	0.002504
314.00	0.002562
315.00	0.002606
316.00	0.002381
317.00	0.002576
318.00	0.002528
319.02	0.00252
320.00	0.002421
321.00	0.002393
322.00	0.002326
323.00	0.002412
324.00	0.002146
325.00	0.002279
326.02	0.002536
327.00	0.002212
328.00	0.002319
329.00	0.002419
330.03	0.002519
331.00	0.002176
332.00	0.002196
333.05	0.002437
334.02	0.002628
335.00	0.002355
336.00	0.002306
337.00	0.002296
338.00	0.002276
339.00	0.002381



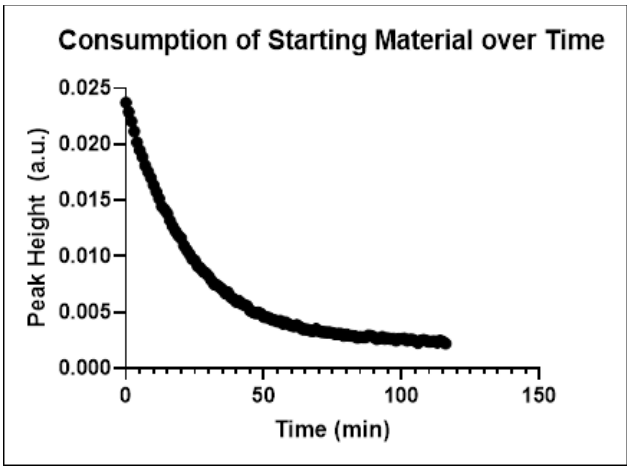
Appendix Figure C.17. 1st order exponential decay of **2.5** at 81 °C

One phase decay		
Best-fit values		
Y0		0.02687
Plateau		0.000859
K		0.02452
Half Life		28.27
Tau		40.78
Span		0.02601
95% CI (profile likelihood)		
Y0	0.02677 to 0.02697	
Plateau	0.0008063 to 0.0009120	
K	0.02431 to 0.02474	
Half Life	28.02 to 28.52	
Tau	40.43 to 41.14	
Goodness of Fit		
Degrees of Freedom		173
R squared		0.9995
Sum of Squares		4.24E-06
Sy.x		0.000157
Constraints		
K	K > 0	
Number of points		
# of X values		176
# Y values analyzed		176

Time (min)	Peak at 1284 cm^{-1} (a.u.)
0.00	0.026063
1.00	0.025905
2.00	0.025346
3.00	0.024838
4.00	0.024408
4.98	0.023693
6.00	0.023214
7.00	0.022796
8.00	0.022097
8.98	0.021673
10.00	0.021304
10.98	0.020942
12.00	0.020273
13.00	0.019779
14.00	0.019595
15.00	0.019105
15.98	0.018705
17.00	0.018285
18.00	0.017905
19.00	0.01757
20.00	0.016969
21.00	0.0166
21.98	0.016124
23.00	0.01573
24.00	0.015414
25.05	0.014987
25.98	0.014884
27.00	0.014521
27.98	0.014075
29.00	0.013839
30.00	0.013472
31.00	0.013302
32.00	0.012967
32.98	0.012637
34.00	0.012328
35.00	0.012017
36.00	0.011867
37.00	0.01135
38.00	0.011091
38.98	0.010743

40.00	0.010706
41.00	0.010348
42.00	0.010221
43.00	0.009808
44.00	0.009721
44.98	0.009473
46.00	0.009388
47.00	0.009202
48.00	0.008909
49.00	0.008632
50.00	0.008438
50.98	0.008228
52.00	0.007983
53.00	0.007921
54.00	0.007638
55.00	0.007745
55.98	0.007292
57.00	0.007217
58.02	0.007172
59.00	0.006854
59.98	0.006744
61.00	0.006541
61.98	0.006524
63.00	0.006182
64.00	0.006119
65.03	0.005917
66.00	0.005957
66.98	0.005891
68.00	0.005588
69.00	0.005487
70.00	0.005396
71.00	0.005181
72.00	0.005118
72.98	0.005001
74.00	0.00484
75.00	0.004776
76.00	0.004931
76.98	0.004666
78.00	0.004516
79.00	0.004441
80.00	0.004309
81.00	0.004329
81.98	0.004151
83.00	0.004117
83.98	0.004193
85.00	0.003882
86.00	0.003982
87.00	0.003803
88.00	0.003755
88.98	0.003706
90.00	0.00372
91.00	0.00358
92.00	0.003558
93.00	0.003425
93.98	0.003417
95.00	0.003386
96.00	0.003304
97.00	0.003028
98.00	0.003022
98.98	0.002888
100.00	0.003017
101.00	0.002857
102.00	0.00285
102.98	0.00289
104.00	0.002979
105.00	0.002617
106.00	0.002732
107.00	0.002729
107.98	0.002707
109.00	0.002484
109.98	0.002457
111.00	0.002465
112.00	0.002635
113.00	0.002687
114.00	0.002442
114.98	0.00237
116.00	0.00239
117.00	0.002255
118.00	0.002234
119.00	0.002341
120.00	0.002321
120.98	0.002383
122.00	0.002243
123.00	0.002172
124.00	0.002142
125.00	0.001986
126.00	0.001978
127.00	0.002112
128.00	0.002021
129.03	0.001933

130.03	0.001963
131.02	0.001974
132.00	0.001913
132.98	0.001725
134.00	0.002047
135.00	0.001952
136.00	0.001876
136.98	0.001828
138.00	0.001706
138.98	0.001733
140.00	0.001748
141.00	0.001756
142.00	0.00184
143.00	0.001668
143.98	0.001525
145.00	0.001635
146.00	0.001646
147.00	0.001728
148.00	0.001685
148.98	0.00178
150.00	0.001729
151.00	0.001567
152.00	0.001623
153.00	0.001482
153.98	0.001541
155.00	0.001522
156.00	0.001539
157.00	0.001503
158.00	0.001429
158.98	0.001501
160.00	0.001411
161.00	0.001542
162.00	0.001432
163.00	0.001314
163.98	0.001304
165.00	0.001401
166.00	0.001324
167.00	0.001293
168.00	0.001321
169.05	0.001485
170.05	0.001259
171.03	0.001201
172.00	0.001367
173.00	0.001112
174.00	0.001568
175.03	0.001255

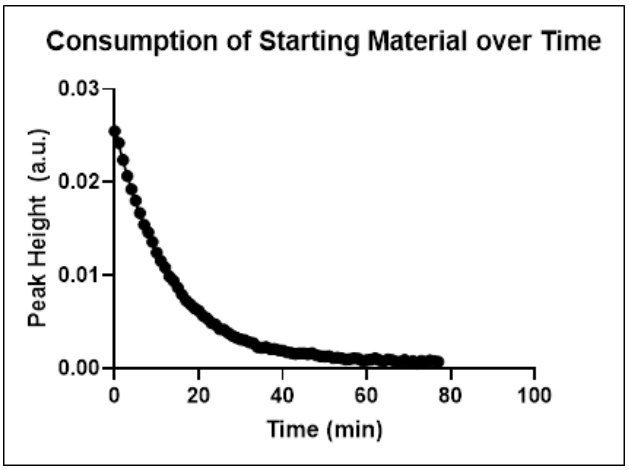


Appendix Figure C.18. 1st order exponential decay of **2.5** at 90 °C

One phase decay	
Best-fit values	
Y0	0.02381
Plateau	0.002239
K	0.04311
Half Life	16.08
Tau	23.2
Span	0.02157
95% CI (profile likelihood)	
Y0	0.02372 to 0.02389
Plateau	0.002203 to 0.002275
K	0.04276 to 0.04346
Half Life	15.95 to 16.21
Tau	23.01 to 23.39
Goodness of Fit	
Degrees of Freedom	114
R squared	0.9997
Sum of Squares	1.17E-06
Sy.x	0.000101
Constraints	
K	K > 0
Number of points	
# of X values	117
# Y values analyzed	117

Time (min)	Peak at 1283 cm^{-1} (a.u.)
0.00	0.023711
1.00	0.022877
2.00	0.022056
3.00	0.021157
4.05	0.020176
5.00	0.01947
6.02	0.018872
7.00	0.018086
8.00	0.017544
9.00	0.01702
10.00	0.016363
11.00	0.015767
12.00	0.015165
13.00	0.014443
14.02	0.014187
15.00	0.013813
16.00	0.013182
17.00	0.01266
18.00	0.012228
19.02	0.011834
20.00	0.011621
21.00	0.010968
22.00	0.010576
23.00	0.010214
24.00	0.009763
25.00	0.009641
26.00	0.009121
27.00	0.008957
28.00	0.008629
29.00	0.008498
30.00	0.008219
31.00	0.007844
32.00	0.0075
33.02	0.00742
34.00	0.007247
35.00	0.007021
36.00	0.006693
37.00	0.006789
38.00	0.006342
39.00	0.006203

40.00	0.005918
41.00	0.006018
42.00	0.00573
43.00	0.005654
44.00	0.005557
45.00	0.005166
46.00	0.005005
47.00	0.004908
48.02	0.004979
49.00	0.004862
50.00	0.004569
51.00	0.00456
52.00	0.004489
53.02	0.00433
54.00	0.004281
55.00	0.004186
56.00	0.004249
57.05	0.003973
58.00	0.004088
59.00	0.003935
60.00	0.003795
61.00	0.003737
62.00	0.003872
63.02	0.003691
64.00	0.003482
65.00	0.003463
66.00	0.00345
67.02	0.003352
68.00	0.003325
69.00	0.00351
70.00	0.003322
71.00	0.003242
72.00	0.003222
73.02	0.003201
74.00	0.003202
75.00	0.003127
76.00	0.003049
77.03	0.003069
78.00	0.003065
79.00	0.002895
80.00	0.003016
81.00	0.002916
82.00	0.002877
83.00	0.002872
84.00	0.002709
85.00	0.002778
86.02	0.00277
87.00	0.002752
88.00	0.002935
89.00	0.002892
90.00	0.002789
91.05	0.002591
92.05	0.002649
93.00	0.002811
94.00	0.002618
95.00	0.002674
96.02	0.002611
97.00	0.002639
98.02	0.002479
99.00	0.002621
100.00	0.002618
101.00	0.002646
102.00	0.002474
103.00	0.002545
104.00	0.002555
105.00	0.002429
106.00	0.002253
107.00	0.002471
108.00	0.002536
109.00	0.002443
110.02	0.002356
111.00	0.002388
112.00	0.002412
113.00	0.002277
114.00	0.002465
115.00	0.002361
116.00	0.00219

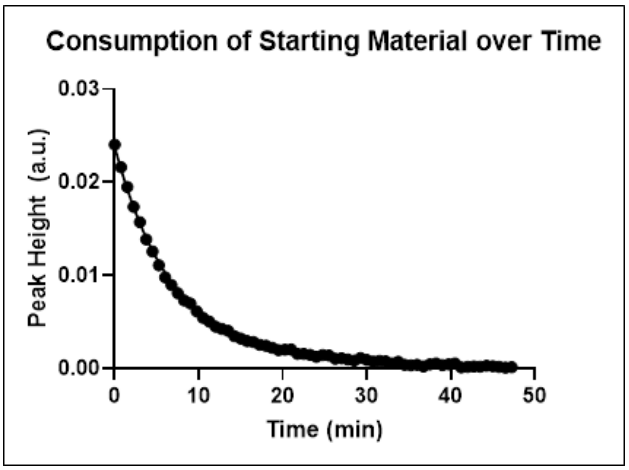


Appendix Figure C.19. 1st order exponential decay of **2.5** at 96 °C

One phase decay		
Best-fit values		
Y0		0.02592
Plateau		0.000674
K		0.0767
Half Life		9.037
Tau		13.04
Span		0.02524
95% CI (profile likelihood)		
Y0	0.02579 to 0.02605	
Plateau	0.0006280 to 0.0007205	
K	0.07594 to 0.07746	
Half Life	8.948 to 9.128	
Tau	12.91 to 13.17	
Goodness of Fit		
Degrees of Freedom		75
R squared		0.9996
Sum of Squares		1.12E-06
Sy.x		0.000122
Constraints		
K	K > 0	
Number of points		
# of X values		78
# Y values analyzed		78

Time (min)	Peak at 1284 cm^{-1} (a.u.)
0.00	0.025499
1.00	0.024202
2.00	0.022398
3.00	0.020664
4.00	0.019229
5.00	0.018014
6.00	0.016699
7.00	0.015436
8.00	0.014614
9.00	0.013596
10.00	0.01244
11.00	0.01154
12.00	0.010836
13.00	0.009895
14.00	0.009411
15.00	0.008691
16.00	0.007936
17.00	0.00728
18.00	0.006877
19.05	0.00646
20.03	0.006199
21.00	0.005658
22.00	0.005358
23.00	0.004892
24.00	0.004714
25.00	0.004208
26.02	0.004151
27.00	0.00382
28.00	0.003515
29.00	0.00328
30.05	0.003109
31.00	0.003036
32.00	0.002822
33.00	0.00272
34.00	0.002289
35.02	0.002223
36.02	0.002278
37.00	0.002075
38.00	0.002094
39.00	0.001962

40.00	0.001918
41.00	0.001745
42.00	0.001659
43.00	0.001573
44.00	0.001601
45.00	0.001603
46.00	0.001528
47.00	0.00163
48.05	0.001421
49.00	0.00131
50.00	0.001291
51.00	0.001313
52.00	0.001123
53.00	0.001152
54.00	0.001097
55.00	0.000953
56.02	0.001024
57.00	0.001099
58.00	0.001036
59.00	0.000824
60.03	0.00089
61.00	0.000945
62.00	0.001088
63.00	0.000894
64.00	0.000762
65.00	0.000957
66.02	0.000881
67.00	0.000701
68.00	0.000722
69.00	0.000913
70.00	0.000651
71.00	0.000799
72.00	0.000524
73.00	0.000821
74.00	0.000661
75.00	0.000868
76.02	0.000793
77.00	0.000702



Appendix Figure C.20. 1st order exponential decay of **2.5** at 106 °C

One phase decay	
Best-fit values	
Y0	0.02384
Plateau	0.00042
K	0.1441
Half Life	4.811
Tau	6.94
Span	0.02342
95% CI (profile likelihood)	
Y0	0.02357 to 0.02412
Plateau	0.0003323 to 0.0005065
K	0.1409 to 0.1474
Half Life	4.704 to 4.921
Tau	6.786 to 7.099
Goodness of Fit	
Degrees of Freedom	61
R squared	0.9985
Sum of Squares	3.11E-06
Sy.x	0.000226
Constraints	
K	K > 0
Number of points	
# of X values	64
# Y values analyzed	64

Time (min)	Peak at 1285 cm^{-1} (a.u.)
0.00	0.024033
0.75	0.021623
1.50	0.019497
2.25	0.017366
3.00	0.015722
3.75	0.013856
4.50	0.012562
5.25	0.011079
6.00	0.009786
6.77	0.008965
7.50	0.008086
8.27	0.007319
9.00	0.006981
9.75	0.006125
10.50	0.005443
11.25	0.005033
12.00	0.004476
12.75	0.004249
13.50	0.004032
14.25	0.00346
15.00	0.00322
15.75	0.002941
16.50	0.002827
17.25	0.002527
18.00	0.002439
18.75	0.002213
19.50	0.001967
20.25	0.002002
21.00	0.002048
21.77	0.001558
22.50	0.001558
23.25	0.001466
24.00	0.001235
24.75	0.001425
25.50	0.001394
26.27	0.001037
27.00	0.00108
27.75	0.000971
28.50	0.00083
29.25	0.001117

30.00	0.000903
30.75	0.000733
31.50	0.000804
32.25	0.000768
33.05	0.000529
33.75	0.000724
34.50	0.00039
35.25	0.000346
36.00	0.000379
36.75	0.000213
37.50	0.000433
38.25	0.000532
39.00	0.00037
39.75	0.000431
40.50	0.000546
41.25	0.000124
42.00	0.000173
42.75	0.000221
43.50	0.000192
44.25	0.000298
45.00	0.000245
45.75	0.000155
46.50	0.0000835
47.25	0.000129

Bibliography

1. Jampilek, J., Heterocycles in Medicinal Chemistry. *Molecules* **2019,** *24* (21).

2. Davison, E. K.; Sperry, J., Natural Products with Heteroatom-Rich Ring Systems. *Journal of Natural Products* **2017,** *80* (11), 3060-3079.

3. Ciufolini, M. A., Synthetic studies on heterocyclic natural products. *Il Farmaco* **2005,** *60* (8), 627-641.

4. Heravi, M. M.; Ahmadi, T.; Ghavidel, M.; Heidari, B.; Hamidi, H., Recent applications of the hetero Diels–Alder reaction in the total synthesis of natural products. *RSC Advances* **2015,** *5* (123), 101999-102075.

5. Eguchi, S., Recent Progress in the Synthesis of Heterocyclic Natural Products by the Staudinger/Intramolecular aza-Wittig Reaction. *ChemInform* **2005,** *36*.

6. Lahsasni, S.; Al-Hemyari, D. A. M.; Ghabbour, H. A.; Mabkhoot, Y. N.; Aleanizy, F. S.; Alothman, A. A.; Almarhoon, Z. M., Synthesis, Characterization, and Antibacterial and Anti-Inflammatory Activities of New Pyrimidine and Thiophene Derivatives. *Journal of Chemistry* **2018,** *2018*, 8536063.

7. Shah, R.; Verma, P. K., Therapeutic importance of synthetic thiophene. *Chemistry Central Journal* **2018,** *12* (1), 137.

8. Pathania, S.; Narang, R. K.; Rawal, R. K., Role of sulphur-heterocycles in medicinal chemistry: An update. *European Journal of Medicinal Chemistry* **2019,** *180*, 486-508.

9. Keri, R. S.; Chand, K.; Budagumpi, S.; Balappa Somappa, S.; Patil, S. A.; Nagaraja, B. M., An overview of benzo[b]thiophene-based medicinal chemistry. *European Journal of Medicinal Chemistry* **2017,** *138* (Supplement C), 1002-1033.

10. Khovidhunkit, W.; Shoback, D. M., CLinical effects of raloxifene hydrochloride in women. *Annals of Internal Medicine* **1999,** *130* (5), 431-439.

11. Berger, W.; De Chandt, M. T. M.; Cairns, C. B., Zileuton: clinical implications of 5-Lipoxygenase inhibition in severe airway disease. *International Journal of Clinical Practice* **2007,** *61* (4), 663-676.

12. Croxtall, J. D.; Plosker, G. L., Sertaconazole. *Drugs* **2009,** *69* (3), 339-359.

13. Tohen, M.; Vieta, E.; Calabrese, J.; Ketter, T. A.; Sachs, G.; Bowden, C.; Mitchell, P. B.; Centorrino, F.; Risser, R.; Baker, R. W.; Evans, A. R.; Beymer, K.; Dubé, S.; Tollefson, G. D.; Breier, A., Efficacy of Olanzapine and Olanzapine-Fluoxetine

Combination in the Treatment of Bipolar I Depression. *Archives of General Psychiatry* **2003,** *60* (11), 1079-1088.

14. Harris, A.; Arend, O.; Arend, S.; Martin, B., Effects of topical dorzolamide on retinal and retrobulbar hemodynamics. *Acta Ophthalmologica Scandinavica* **1996,** *74* (6), 569-572.

15. Gurbel, P. A.; Tantry, U. S., Clopidogrel resistance? *Thrombosis Research* **2007,** *120* (3), 311-321.

16. Meng, L.; Zhang, Y.; Wan, X.; Li, C.; Zhang, X.; Wang, Y.; Ke, X.; Xiao, Z.; Ding, L.; Xia, R.; Yip, H.-L.; Cao, Y.; Chen, Y., Organic and solution-processed tandem solar cells with 17.3% efficiency. *Science* **2018,** *361* (6407), 1094-1098.

17. Di Carlo Rasi, D.; Janssen, R. A. J., Advances in Solution-Processed Multijunction Organic Solar Cells. *Advanced Materials* **2019,** *31* (10), 1806499.

18. Chen, J.; Yang, K.; Zhou, X.; Guo, X., Ladder-Type Heteroarene-Based Organic Semiconductors. *Chemistry – An Asian Journal* **2018,** *13* (18), 2587-2600.

19. He, D.; Zhao, F.; Jiang, L.; Wang, C., A–D–A small molecule acceptors with ladder-type arenes for organic solar cells. *Journal of Materials Chemistry A* **2018,** *6* (19), 8839-8854.

20. Wu, J.-S.; Cheng, S.-W.; Cheng, Y.-J.; Hsu, C.-S., Donor–acceptor conjugated polymers based on multifused ladder-type arenes for organic solar cells. *Chemical Society Reviews* **2015,** *44* (5), 1113-1154.

21. Roche, S. P.; Porco Jr., J. A., Dearomatization Strategies in the Synthesis of Complex Natural Products. *Angewandte Chemie International Edition* **2011,** *50* (18), 4068-4093.

22. Wang, Z., Palladium-catalyzed asymmetric dearomative cyclization in natural product synthesis. *Organic & Biomolecular Chemistry* **2020,** *18* (23), 4354-4370.

23. Zi, W.; Zuo, Z.; Ma, D., Intramolecular Dearomative Oxidative Coupling of Indoles: A Unified Strategy for the Total Synthesis of Indoline Alkaloids. *Accounts of Chemical Research* **2015,** *48* (3), 702-711.

24. Okumura, M.; Sarlah, D., Visible-Light-Induced Dearomatizations. *European Journal of Organic Chemistry* **2020,** *2020* (10), 1259-1273.

25. Lv, S.; Zhang, G.; Chen, J.; Gao, W., Electrochemical Dearomatization: Evolution from Chemicals to Traceless Electrons. *Advanced Synthesis & Catalysis* **2020,** *362* (3), 462-477.

26. Zheng, L.; Hua, R., Recent Advances in Construction of Polycyclic Natural Product Scaffolds via One-Pot Reactions Involving Alkyne Annulation. *Frontiers in Chemistry* **2020,** *8*, 906.

27. Zhuo, C.-X.; Zhang, W.; You, S.-L., Catalytic Asymmetric Dearomatization Reactions. *Angewandte Chemie International Edition* **2012,** *51* (51), 12662-12686.

28. Ding, Q.; Zhou, X.; Fan, R., Recent advances in dearomatization of heteroaromatic compounds. *Organic & Biomolecular Chemistry* **2014,** *12* (27), 4807-4815.

29. Ouyang, B.; Yu, T.; Luo, R.; Lu, G., The asymmetric Cu(ii)–indolinylmethanol complex catalyzed Diels–Alder reaction of 2-vinylindoles with β,γ-unsaturated α-ketoesters: an efficient route to functionalized tetrahydrocarbazoles. *Organic & Biomolecular Chemistry* **2014,** *12* (24), 4172-4176.

30. Huang, Y.; Song, L.; Gong, L.; Meggers, E., Asymmetric Synthesis of Hydrocarbazoles Catalyzed by an Octahedral Chiral-at-Rhodium Lewis Acid. *Chemistry – An Asian Journal* **2015,** *10* (12), 2738-2743.

31. Harada, S.; Morikawa, T.; Nishida, A., Chiral Holmium Complex-Catalyzed Diels–Alder Reaction of Silyloxyvinylindoles: Stereoselective Synthesis of Hydrocarbazoles. *Organic Letters* **2013,** *15* (20), 5314-5317.

32. Sugiura, H.; Yamazaki, S.; Ogawa, A., Sequential Intramolecular Diels–Alder Reaction of 3-Heteroaryl-2-propenylamides of Ethenetricarboxylate. *Journal of Heterocyclic Chemistry* **2019,** *56* (9), 2592-2603.

33. Pirovano, V.; Brambilla, E.; Moretti, A.; Rizzato, S.; Abbiati, G.; Nava, D.; Rossi, E., Synthesis of Cyclohepta[b]indoles by (4 + 3) Cycloaddition of 2-Vinylindoles or 4H-Furo[3,2-b]indoles with Oxyallyl Cations. *The Journal of Organic Chemistry* **2020,** *85* (5), 3265-3276.

34. Pirovano, V.; Borri, M.; Abbiati, G.; Rizzato, S.; Rossi, E., Gold(I)-Catalyzed Enantioselective Synthesis of Tetrahydrocarbazoles through Dearomative [4+2] Cycloadditions of 3/2-Substituted 2/3-Vinylindoles. *Advanced Synthesis & Catalysis* **2017,** *359* (11), 1912-1918.

35. Pirovano, V.; Decataldo, L.; Rossi, E.; Vicente, R., Gold-catalyzed synthesis of tetrahydrocarbazole derivatives through an intermolecular cycloaddition of vinyl indoles and N-allenamides. *Chemical Communications* **2013,** *49* (34), 3594-3596.

36. Xu, G.; Chen, L.; Sun, J., Rhodium-Catalyzed Asymmetric Dearomative [4 + 3]-Cycloaddition of Vinylindoles with Vinyldiazoacetates: Access to Cyclohepta[b]indoles. *Organic Letters* **2018,** *20* (11), 3408-3412.

37. Tu, M.-S.; Chen, K.-W.; Wu, P.; Zhang, Y.-C.; Liu, X.-Q.; Shi, F., Advances in organocatalytic asymmetric reactions of vinylindoles: powerful access to enantioenriched indole derivatives. *Organic Chemistry Frontiers* **2021**.

38. Yang, X.; Zhou, Y.-H.; Yang, H.; Wang, S.-S.; Ouyang, Q.; Luo, Q.-L.; Guo, Q.-X., Asymmetric Diels–Alder Reaction of 3-Vinylindoles and Nitroolefins Promoted by Multiple Hydrogen Bonds. *Organic Letters* **2019,** *21* (4), 1161-1164.

39. Jones, S. B.; Simmons, B.; MacMillan, D. W. C., Nine-Step Enantioselective Total Synthesis of (+)-Minfiensine. *Journal of the American Chemical Society* **2009,** *131* (38), 13606-13607.

40. Zhang, M.; Duan, Y.; Li, W.; Cheng, Y.; Zhu, C., Visible-light-induced aerobic dearomative reaction of indole derivatives: access to heterocycle fused or spirocyclo indolones. *Chemical Communications* **2016,** *52* (26), 4761-4763.

41. Liu, K.; Tang, S.; Huang, P.; Lei, A., External oxidant-free electrooxidative [3 + 2] annulation between phenol and indole derivatives. *Nat Commun* **2017,** *8* (1), 775-775.

42. Mohamed, Y. A. M.; Inagaki, F.; Takahashi, R.; Mukai, C., A new procedure for the preparation of 2-vinylindoles and their [4+2] cycloaddition reaction. *Tetrahedron* **2011,** *67* (29), 5133-5141.

43. Cotterill, L. J.; Harrington, R. W.; Clegg, W.; Hall, M. J., Thermal 1,3-Trityl Migrations in Diels−Alder Domino Reactions of 1-Trityl-4-vinyl-1H-imidazoles. *The Journal of Organic Chemistry* **2010,** *75* (13), 4604-4607.

44. Bober, A. E.; Proto, J. T.; Brummond, K. M., Intramolecular Didehydro-Diels–Alder Reaction for the Synthesis of Benzo- and Dihydrobenzo-Fused Heterocycles. *Organic Letters* **2017,** *19* (7), 1500-1503.

45. Klemm, L. H.; Gopinath, K. W., Intramolecular diels-alder cyclization into the thiophene ring. *Journal of Heterocyclic Chemistry* **1965,** *2* (3), 225-227.

46. Hayakawa, K.; Yodo, M.; Ohsuki, S.; Kanematsu, K., Novel bicycloannulation via tandem vinylation and intramolecular Diels-Alder reaction of five-membered heterocycles: a new approach to construction of psoralen and azapsoralen. *Journal of the American Chemical Society* **1984,** *106* (22), 6735-6740.

47. Hajbi, Y.; Neagoie, C.; Biannic, B.; Chilloux, A.; Vedrenne, E.; Baldeyrou, B.; Bailly, C.; Mérour, J.-Y.; Rosca, S.; Routier, S.; Lansiaux, A., Synthesis and biological activities of new furo[3,4-b]carbazoles: Potential topoisomerase II inhibitors. *European Journal of Medicinal Chemistry* **2010,** *45* (11), 5428-5437.

48. Lima, H. M.; Sivappa, R.; Yousufuddin, M.; Lovely, C. J., Total Synthesis of 7′-Desmethylkealiiquinone, 4′-Desmethoxykealiiquinone, and 2-Deoxykealiiquinone. *The Journal of Organic Chemistry* **2014,** *79* (6), 2481-2490.

49. Saavedra, D. I.; Rencher, B. D.; Kwon, D.-H.; Smith, S. J.; Ess, D. H.; Andrus, M. B., Synthesis and Computational Studies Demonstrate the Utility of an Intramolecular Styryl Diels–Alder Reaction and Di-t-butylhydroxytoluene Assisted [1,3]-Shift to Construct Anticancer dl-Deoxypodophyllotoxin. *The Journal of Organic Chemistry* **2018,** *83* (4), 2018-2026.

50. Kocsis, L. S.; Kagalwala, H. N.; Mutto, S.; Godugu, B.; Bernhard, S.; Tantillo, D. J.; Brummond, K. M., Mechanistic Insight into the Dehydro-Diels–Alder Reaction of Styrene–Ynes. *The Journal of Organic Chemistry* **2015,** *80* (23), 11686-11698.

51. Durham, L. J.; Studebaker, J.; Perkins, M. J., Long-range coupling in the proton magnetic resonance spectra of 1,4-dihydrobenzenes. *Chemical Communications (London)* **1965,** (19), 456-457.

52. Smith, S. G.; Goodman, J. M., Assigning Stereochemistry to Single Diastereoisomers by GIAO NMR Calculation: The DP4 Probability. *Journal of the American Chemical Society* **2010,** *132* (37), 12946-12959.

53. Peng, H.; Soeller, C.; Travas-Sejdic, J., Novel Conducting Polymers for DNA Sensing. *Macromolecules* **2007,** *40* (4), 909-914.

54. Tay, D. W.; Jong, H.; Lim, Y. H.; Wu, W.; Chew, X.; Robins, E. G.; Johannes, C. W., Palladium-meta-Terarylphosphine Catalyst for the Mizoroki–Heck Reaction of (Hetero)Aryl Bromides and Functional Olefins. *The Journal of Organic Chemistry* **2015,** *80* (8), 4054-4063.

55. Yang, B.; Wang, Z.-X., Synthesis of Allylsilanes via Nickel-Catalyzed Cross-Coupling of Silicon Nucleophiles with Allyl Alcohols. *Organic Letters* **2019,** *21* (19), 7965-7969.

56. Werner, T.; Hoffmann, M.; Deshmukh, S., Phospholane-Catalyzed Wittig Reaction. *European Journal of Organic Chemistry* **2015,** *2015* (15), 3286-3295.

57. Guo, Y.; Shen, Z., Palladium-catalyzed allylic C–H oxidation under simple operation and mild conditions. *Organic & Biomolecular Chemistry* **2019,** *17* (12), 3103-3107.

58. Gronowitz, S.; Raznikiewicz, T., 3-Bromothiophene. *Organic Syntheses* **1964,** *44*, 9.

59. Paegle, E.; Belyakov, S.; Arsenyan, P., An Approach to the Selenobromination of Aryl(thienyl)alkynes: Access to 3-Bromobenzo[b]selenophenes and Selenophenothiophenes. *European Journal of Organic Chemistry* **2014,** *2014* (18), 3831-3840.

60. Dieckmann, A.; Houk, K. N., Elucidation of Strong Cooperative Effects Caused by Dispersion Interactions in a Recognition-Mediated Diels–Alder Reaction. *Journal of Chemical Theory and Computation* **2012,** *8* (12), 5064-5071.

61. Litvinov, G. G. I. V. D. K. E. A. K. L. N. P. E. A. B. D. B. K. I. A., Diels-Alder reaction between naphthalene and N-phenylmaleimide under ambient and high pressure conditions. *Arkivoc* **2005,** *2004* (12), 70-79.

62. Hendry, D. G.; Schuetzle, D., Reactions of hydroperoxy radicals. Liquid-phase oxidation of 1,4-cyclohexadiene. *Journal of the American Chemical Society* **1975,** *97* (24), 7123-7127.

63. Borden, W. T.; Hoffmann, R.; Stuyver, T.; Chen, B., Dioxygen: What Makes This Triplet Diradical Kinetically Persistent? *Journal of the American Chemical Society* **2017,** *139* (26), 9010-9018.

64. Hoye, T. R.; Eklov, B. M.; Ryba, T. D.; Voloshin, M.; Yao, L. J., No-D NMR (No-Deuterium Proton NMR) Spectroscopy: A Simple Yet Powerful Method for Analyzing Reaction and Reagent Solutions. *Org. Lett.* **2004,** *6* (6), 953-956.

65. Chen, C.-H.; Cheng, Y.-J.; Dubosc, M.; Hsieh, C.-H.; Chu, C.-C.; Hsu, C.-S., Alternating and Diblock Donor–Acceptor Conjugated Polymers Based on Diindeno[1,2-b:2′,1′-d]thiophene Structure: Synthesis, Characterization, and Photovoltaic Applications. *Chemistry – An Asian Journal* **2010,** *5* (12), 2483-2492.

66. Baierweck, P.; Simmross, U.; Müllen, K., Biindenyls, Biindenylides, and Diindeno-Fused Heterocycles from Oxidative Coupling of 1- and 2-Indanone. *Chemische Berichte* **1988,** *121* (12), 2195-2200.

67. Wang, G.; Gan, Y.; Liu, Y., Nickel-Catalyzed Direct Coupling of Allylic Alcohols with Organoboron Reagents. *Chinese Journal of Chemistry* **2018,** *36* (10), 916-920.