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New Ventures in Amidine-Based Catalyst Design

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WASHINGTON UNIVERSITY IN ST. LOUIS

Department of Chemistry

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Kevin D. Moeller

New Ventures in Amidine-Based Catalyst Design

by

Nicholas A. Ahlemeyer

A dissertation presented to
The Graduate School
of Washington University in
partial fulfillment of the
requirements for the degree
of Doctor of Philosophy

December 2017
St. Louis, Missouri

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Table of Contents

List of Figures

List of Tables

List of Abbreviations

4-Cl-Bz	4-Chloro-benzoyl
ABC	Amidine-based catalyst
Ac	Acetyl
Ar	Aryl
BINAP	2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl
BINOL	[1,1'-Binaphthalene]-2,2'-diol
Boc	*tert*-Butyloxy carbonyl
Boc_2O	Di-*tert*-butyl decarbonate
BOX	Bis(oxazoline)
Bu	Butyl
t-Bu	*tert*-Butyl
t-BuOK	Potassium *tert*-butoxide
BTM	Benzotetramisole
Bz	Benzoyl
Cat	Catalyst
CF_3-PIP	2-Phenyl-6-(trifluoromethyl)-2,3-dihydroimidazo[1,2-*a*]pyridine
Cl-PIQ	7-Chloro-2-phenyl-1,2-dihydroimidazo[1,2-*a*]quinoline
DABCO	1,4-Diazabicyclo[2.2.2]octane
DBN	1,5-Diazabicyclo[4.3.0]non-5-ene
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DCC	*N*,*N'*-Dicyclohexylcarbodiimide
DCE	1,2-Dichloroethane
DDQ	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
DFT	Density functional theory
DHIP	2,3-Dihydroimidazo[1,2-*a*]pyridine
DHIT	3-Phenyl-5,6-dihydroimidazo[2,1-*b*]thiazole
DHPB	3,4-Dihydro-2*H*-benzo[4,5]thiazolo[3,2-*a*]pyrimidine
DHTP	3-Phenyl-6,7-dihydro-5*H*-thiazolo[3,2-*a*]pyrimidine
DIPEA	*N*,*N*-Diisopropylethylamine

DMA	*N*,*N*-Dimethylacetamide
DMAP	4-Dimethylaminopyridine
DMF	*N*,*N*-Dimethylformamide
DMSO	Dimethylsulfoxide
dr	Diastereomeric ratio
ee	Enantiomeric excess
er	Enantiomeric ratio
Et	Ethyl
EtOAc	Ethyl acetate
EtOH	Ethanol
EWG	Electron-withdrawing group
H-PIP	2-Phenyl-2,3-dihydroimidazo[1,2-*a*]pyridine
Hal	Halide
HBTM	Homobenzotetramisole
HPLC	High performance liquid chromatography
LiHMDS	Lithium bis(trimethylsilyl)amide
M	Metal
m-	*meta*
Me	Methyl
MeDuPhos	1,2-Bis(2,5-dimethylphospholan) benzene
MeOH	Methanol
Mes	Mesityl
MS	Molecular sieve
MsCl	Methanesulfonyl chloride
NBS	*N*-Bromosuccinimide
NHC	N-Heterocyclic carbene
NMI	*N*-Methylimidazole
o-	*ortho*
O(4-Cl-Bz)	4-Chlorobenzoate
OAc	Acetate
OBz	Benzoate

OPiv	Pivalate
p-	*para*
Ph	Phenyl
Piv	Pivaloyl
PPY	4-Pyrrolidinopyridine
PyBox	Pyridinediyl bis(oxazoline)
i-Pr	Isopropyl
i-PrOH	Isopropanol
SALEN	*N*,*N*′-Bis(3,5-di-tert-butylsalicylidene)-1,2-cyclohexanediamine
TADDOL	α,α,α,α-Tetraaryl-1,3-dioxolane-4,5- dimethanols
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
TMS	Tetramethylsilane

Acknowledgements

First, I would like to express my sincere gratitude to my advisor Professor Vladimir Birman for his patience, support, and guidance throughout the course of my Ph.D. at Washington University. His immense knowledge of organic synthesis and firsthand instruction in the lab shaped the chemist that I have become and made the work mentioned here possible. I greatly appreciate everything he has done for me.

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Finally, I would like to thank my parents and my sister for their encouragement in my education as well as in my life. Also, I am thankful to my daughter who has provided excitement in my life watching her learn and grow. I am also grateful to my grandfather Glennon Bodenschatz who was not able to see me attend graduate school but helped mold the person I have become.

Nicholas A. Ahlemeyer

Washington University in St. Louis

December 2017

To my grandfather

Glennon Bodenschatz

ABSTRACT OF THE DISSERTATION

New Ventures in Amidine-Based Catalyst Design.

for Arts & Sciences Graduate Students

by

Nicholas A. Ahlemeyer

Washington University in St. Louis, 2017

Professor Vladimir B. Birman, Chair

Two new cascade transformations of α,β-unsaturated thioesters catalyzed by amidine-based catalysts have been developed. First, a reagent-free transformation of *o*-formylaryl cinnamoyl thioesters catalyzed by HBTM-2 to produce 2-substituted thiochromenes achieved high enantioselectivities and yields while forming carbon dioxide as the only byproduct. Second, a highly diastereo- and enantioselective tandem rearrangement of less reactive enone thioesters into tricyclic thiochromanes in the presence of electron-rich amidine-based catalysts was developed. These catalysts were designed with the help of DFT calculations. H-PIP, the first chiral amidine-based catalyst synthesized in our group, performed the best overall in the thiochromane synthesis.

The second chapter of this thesis describes the design of chiral ligands using the Cl-PIQ structure as a building block. A new class of fused imidazoline ligands was synthesized from 2-chloro-3-quinolinecarboxaldehyde, and their efficacy was demonstrated by their performance in the asymmetric Henry reaction.

CHAPTER 1: Cascade Reactions of Thioesters[1]

1.1 Introduction.

Enantioselective acyl transfer catalysis has become an essential tool of asymmetric synthesis. Several types of Lewis bases, such as 4-amino-pyridines (e.g., DMAP, PPY), *N*-alkylimidazoles (e.g., NMI), N-heterocyclic carbenes (NHCs), and trialkylphosphines (e.g., PBu_3) are known to catalyze nucleophilic acyl substitution reactions by the mechanism called acyl transfer.[2] This mode of catalysis operates primarily under three basic pathways shown in Figure 1.1.[3] In the first pathway, activation of the carbonyl, the Lewis base catalyst (:Cat) attacks an acyl donor (**1.01**) to form a reactive ion pair (**1.02**) that can then react with a nucleophile (H-Y) to displace the catalyst and form the final product **1.03**. The second pathway, activation of the conjugate system, consists of the Lewis base catalyst (:Cat) attacking an acyl donor containing an α,β-unsaturated double bond (**1.04**) to form an ion pair intermediate (**1.05**) that is activated as either a Michael acceptor (Figure 1.1, **b**) or as a dienophile (Figure 1.1, **c**) which ultimately reacts with a nucleophile (H-Y) to turn over the catalyst. The final pathway, activation of the α-carbon, occurs when the initial cationic species undergoes deprotonation to form a zwitterionic, acylammonium enolate (**1.12)**, which can attack various electrophiles followed by displacement of the catalyst by a nucleophile. These basic catalytic pathways offer rich opportunities in enantioselective acyl transfer.

1. The results in this chapter were previously published. See reference 1.

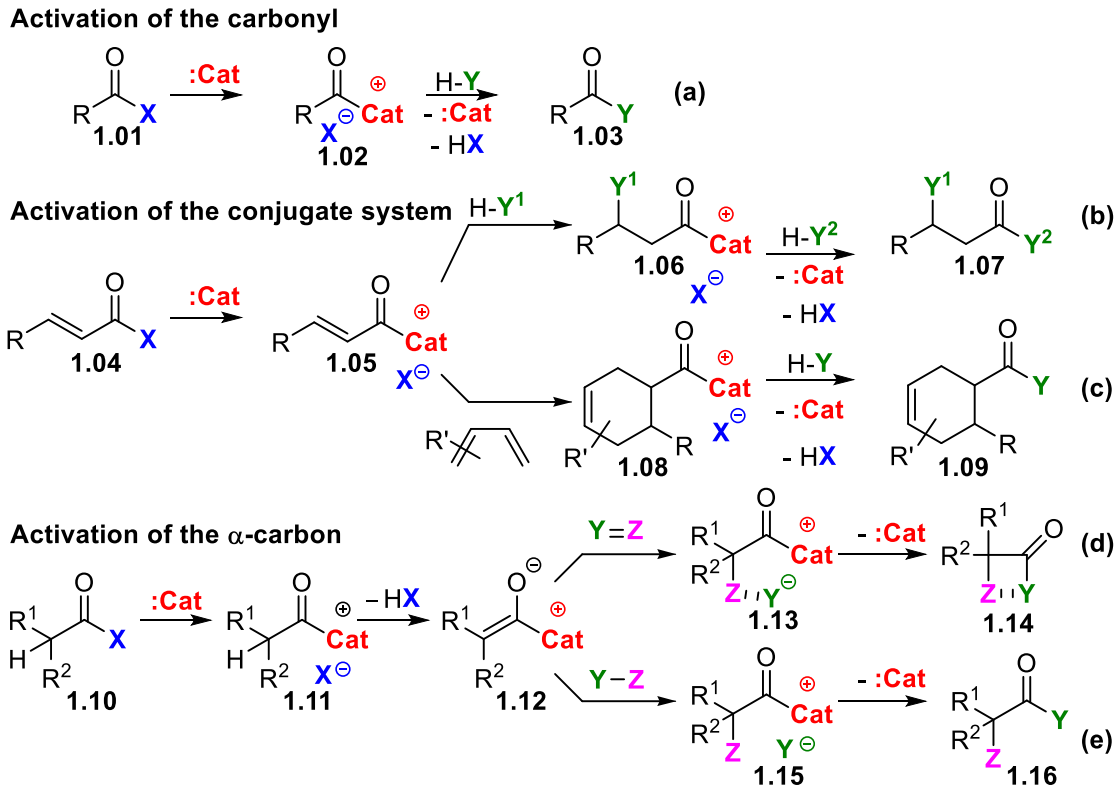


Figure 1.1: Basic catalytic pathways involving acyl transfer.

Many research groups have developed chiral variants of Lewis bases known to catalyze acyl transfer reactions. This approach was more difficult to implement than anticipated. Introducing chiral groups on the carbon next to the nucleophilic nitrogen in catalysts such as DMAP or NMI renders the catalyst inactive in acyl group transfer. Conversely, placing the chiral groups more remote from the nucleophilic nitrogen produces poor enantioselectivity in many cases. Some of the best enantioselective acyl transfer catalysts developed by other groups are shown in Figure 1.2.[4-13] Many of these catalysts still suffer from a limited substrate scope or work well for only specific reactions.

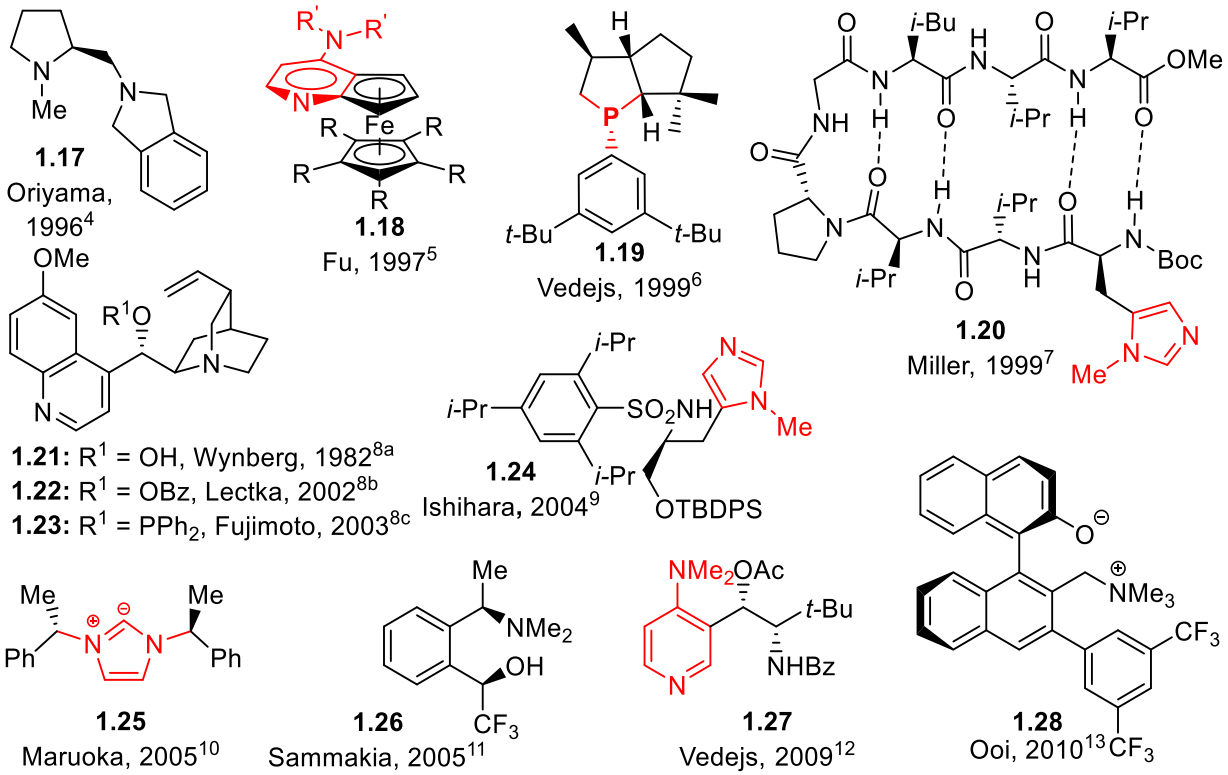


Figure 1.2: Best enantioselective acyl-transfer catalysts developed by other groups.

Our group took a different approach to designing enantioselective acyl transfer catalysts. Rather than preparing a chiral variant of a known Lewis base, we sought to discover a new class of Lewis bases that would have nucleophilicity toward acyl groups but would allow for synthetically easier introduction of chirality. This led us to develop amidine-based catalysts (ABCs) shown in Figure 1.3.[14] Although there were no prior reports of amidine catalysts for acyl transfer, simple resonance structures suggest the nitrogen atom would be highly nucleophilic and form resonance stabilized N-acylammonium intermediates. Additionally, the easily introduced chiral carbon adjacent to the nucleophilic nitrogen atom would allow for effective enantiofacial discrimination without creating too much steric encumbrance around the nitrogen. Subsequently, our group developed new generations of ABCs shown in Figure 1.3 eventually leading to the discovery of chiral isothioureas (ITUs) such as benzotetramisole (BTM) and the

homobenzotetramisole (HBTM, HBTM-2) catalysts. These chiral isothioureas containing a sulfur atom were the most active catalysts yet, which has been attributed to non-bonding S···O interactions with the acyl carbonyl.[14d]

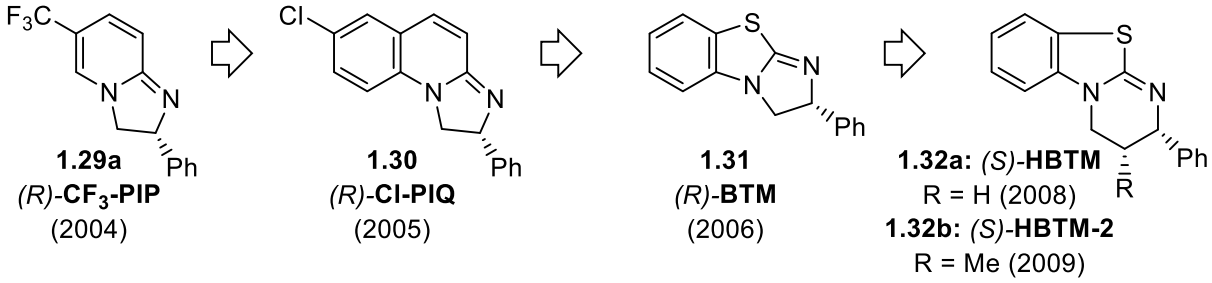


Figure 1.3: Evolution of amidine-based catalyst design in our group.

Our group focused on the development of reactions from pathway (**a**) in Figure 1.1, activation of the carbonyl.[15] For example, our early studies dealt with the non-enzymatic kinetic resolution of secondary alcohols by ABCs. Due to the π-stacking ability of the catalysts, ABCs were found to give good to excellent selectivity factors for benzylic, allylic, and propargylic alcohols as well as 2-phenylcycloalkanols shown in Figure 1.4.[15a] Pathways (**b**)-(**e**) have been explored by other groups.[16,17]

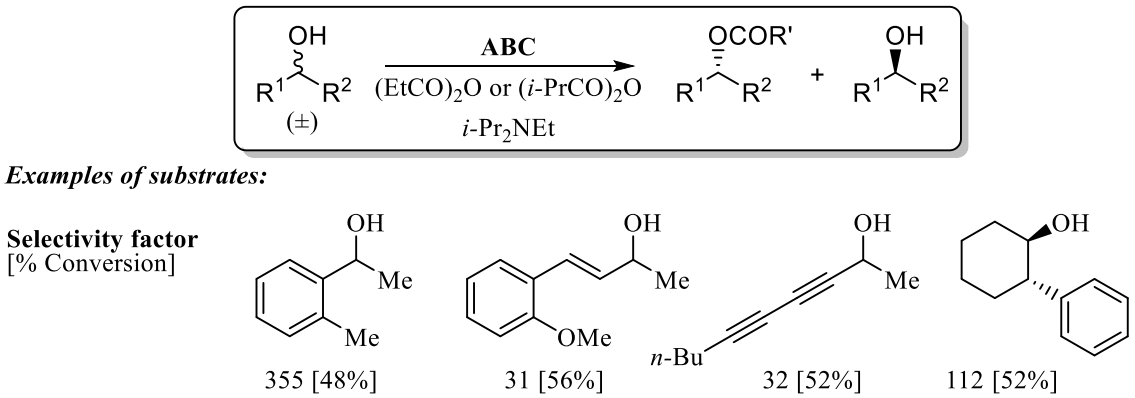


Figure 1.4: Representative examples of classes of alcohols resolved by ABCs.

1.2 Asymmetric synthesis of thiochromenes.

1.2.1 New acyl donors operating in a rearrangement mode.

One of the limitations of existing acyl transfer catalysts is the need to match the reactivity of acyl donors to the reactivity of the catalysts. These activated substrates in turn may be unstable to long term storage or may need to be formed in situ. An additional draw back to acyl transfer catalysis is that many processes are not atom economical. For example, if an acyl donor is viewed as two separate parts (Figure 1.5), the leaving group is simply lost in most acyl transfer processes.

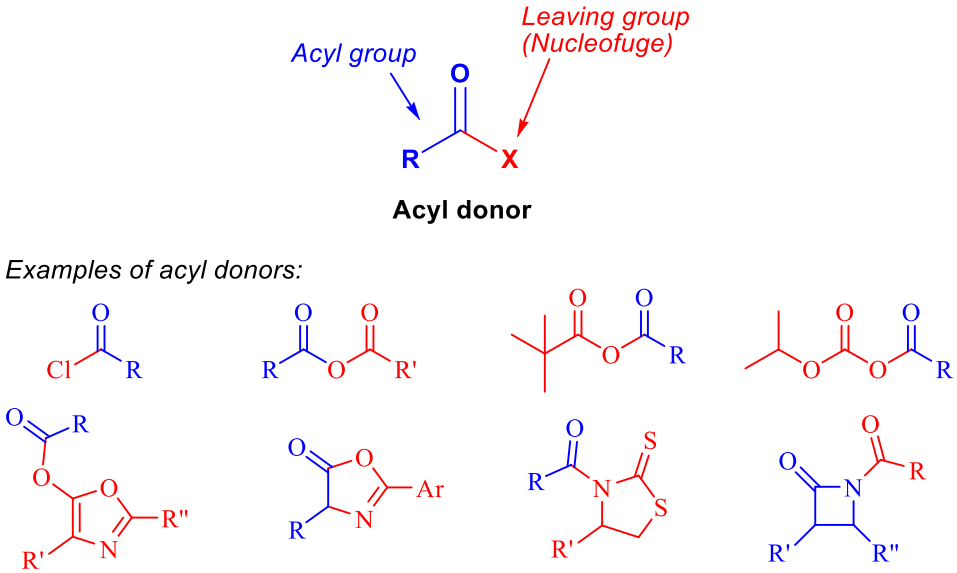


Figure 1.5: Parts of an acyl donor.

Our goal was to develop a new tandem reaction that consists of an acyl donor operating in a rearrangement mode. Before we began our studies, few reports of this type of acyl donor could be found in the literature. In 2009,[18a] Lupton disclosed an NHC (**1.34**) catalyzed rearrangement reaction where enol ester **1.33** underwent acyl transfer to free an enolate that performed a Michael addition followed by proton transfer and acylation of the enolate to form **1.35** and free the catalyst as shown in Figure 1.6. Later, Lupton developed an acyl transfer-Diels-Alder-lactonization

cascade[18b] also shown in Figure 1.6. During this process, an NHC catalyst (**1.37**) displaced enol ester **1.36** to free an anionic diene which underwent a Diels-Alder reaction followed by the formation of β-lactone **1.38**.

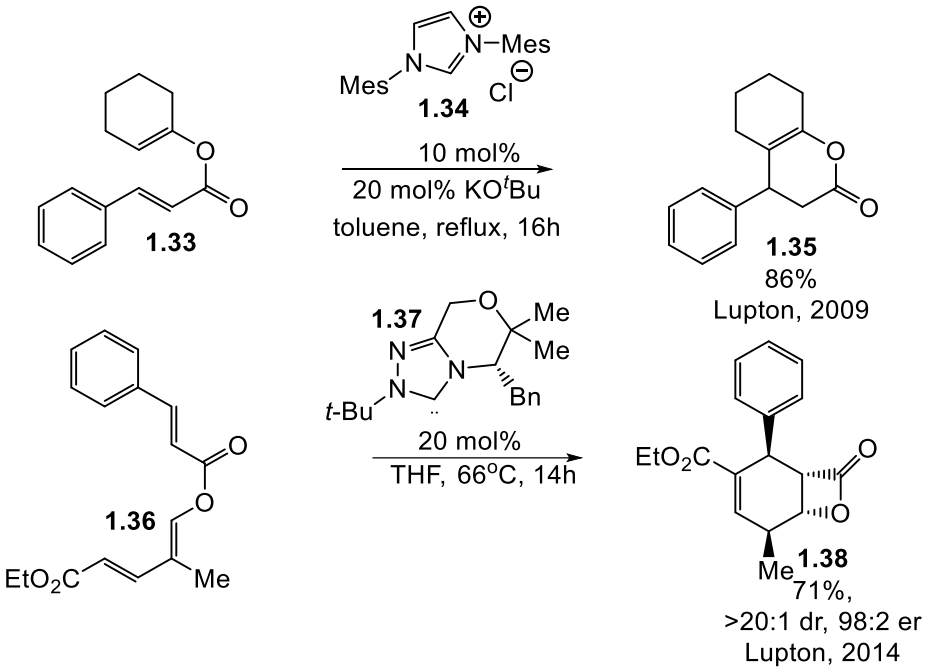


Figure 1.6: Acyl donors operating in a rearrangement mode.

We set out to accomplish a tandem transformation using α,β-unsaturated thioesters (**1.39**) as acyl donors (Figure 1.7). In the presence of a Lewis base catalyst, **1.39** was anticipated to undergo acyl transfer to form ion pair **1.40** and give rise to zwitterionic enolate **1.41** following sulfa-Michael addition. Enolate **1.41** can be considered a potential precursor to a variety of formal cycloadditions such as nucleophilic addition to an electrophile with subsequent displacement of the catalyst. Conceptually, the transformation of **1.39** into **1.41** can be thought of as its 1,3-rearrangement into the β-sulfenylketene **1.42**.

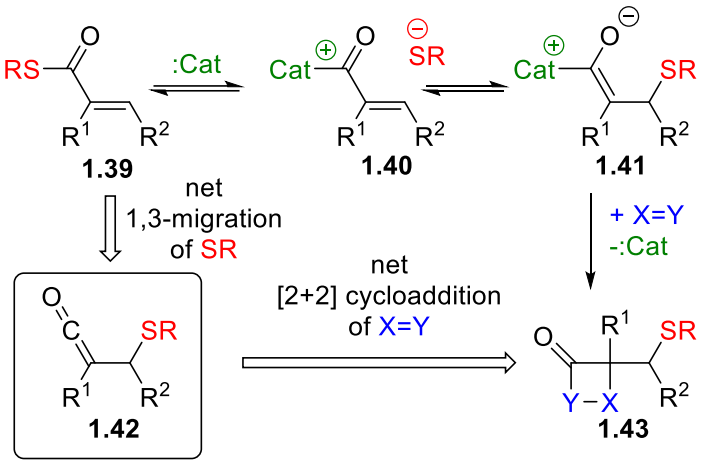


Figure 1.7: Proposed tandem transformation.

We envisioned experimentally that this type of tandem process could be achieved with thioester **1.44a** in the presence of an acyl transfer catalyst to produce thiochromene **1.45a** with carbon dioxide as the only byproduct (Figure 1.8).

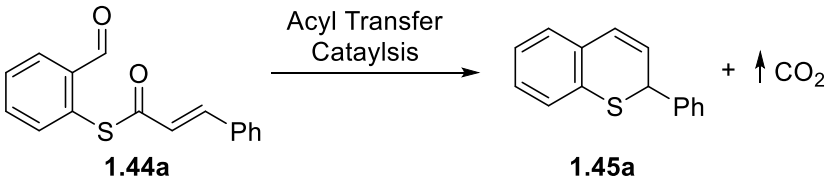


Figure 1.8: Proposed thiochromene synthesis.

1.2.2 Michael addition reactions catalyzed by isothioureas.

In 2013, Romo reported an isothiourea catalyzed Michael-Aldol-Lactonization cascade[19a] to form β-lactone fused cyclopentanes **1.48** shown in Figure 1.9. The process starts with the deprotonation of the acidic carbon of **1.46** followed by the C-C bond forming Michael addition to the α,β-unsaturated intermediate of (*S*)-HBTM and **1.47**. The resulting acyl ammonium enolate proceeds to do an intramolecular aldol on the methyl ketone forming an alkoxide which then displaces the catalyst to form **1.48**. In 2015, Matsubara reported an enantioselective net [4+3] cycloaddition to form 1,5-benzothiazepines **1.51**.[19b] In the presence of (*R*)-BTM, α,β-unsaturated

carbonic anhydrides (**1.50**) undergo sulfa-Michael addition followed by lactamization by 2-aminothiophenols (**1.49**) with excellent yields and enantioselectivities as shown in Figure 1.9. These Michael-additions catalyzed by isothiourea catalysts suggested that our proposed rearrangement could be highly enantioselective with isothiourea catalysis.

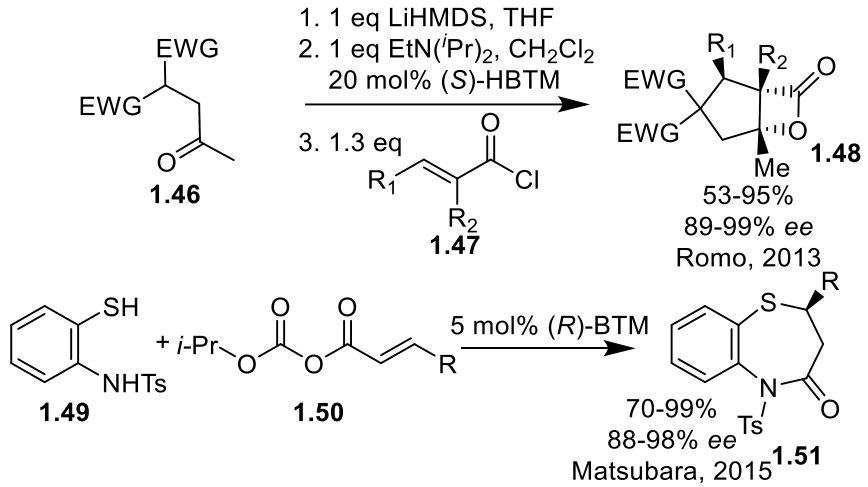


Figure 1.9: Michael additions catalyzed by isothioureas.

1.2.3 Previous asymmetric approaches to thiochromenes.

2-substituted thiochromenes and thiochromanes have drawn interest due to their potential in drug design and their occurrence as natural products (Figure 1.10).[20] Unfortunately, previously reported asymmetric catalytic methods produce thiochromenes with an undesirable electron-withdrawing group at C3 (Figure 1.11).[21] The iminium catalyzed process developed independently and concurrently by Wang and Cordova relies on an α,β-unsaturated aldehyde (**1.53**) as a handle for the chiral iminium catalyst for a sulfa-Michael-aldol condensation cascade bringing about a thiochromene with an aldehyde on C3 (**1.55**). A similar sulfa-Michael-Horner-Wadsworth-Emmons cascade reported by Mukherjee relies on hydrogen-bond donor catalyst **1.57** but leaves an ester on C3 (**1.58**) as well.

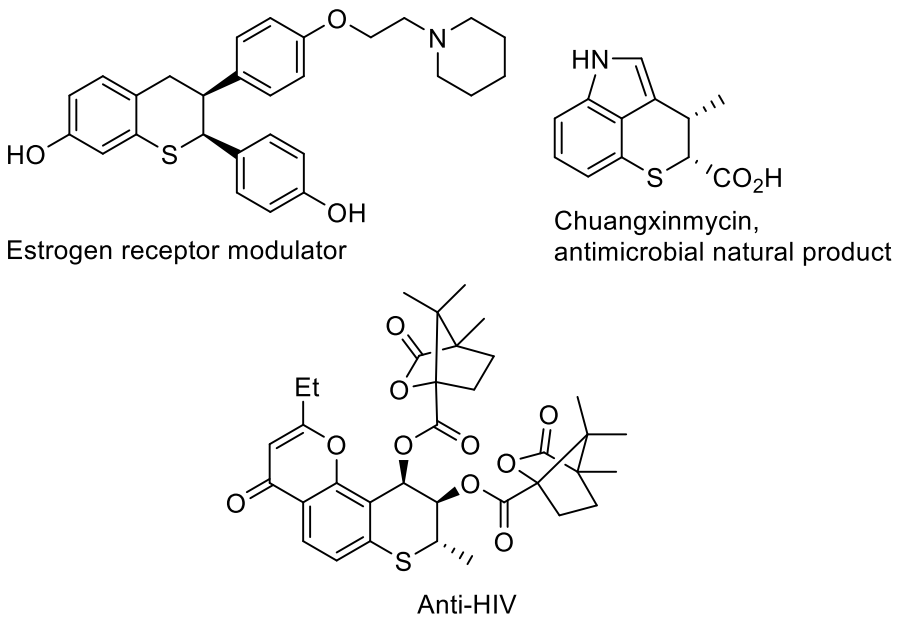


Figure 1.10: 2-substituted thiochromane derivatives.

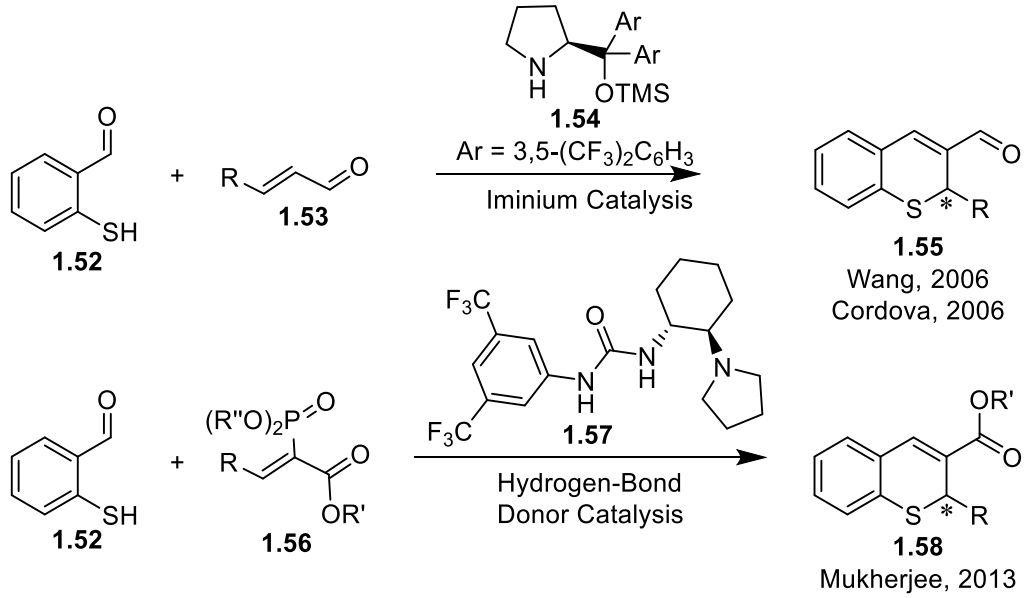


Figure 1.11: Asymmetric approaches to thiochromenes.

1.2.4 Our approach to thiochromenes.

Based on our long-standing interest in amidine-based catalysts (ABCs), we wanted to explore their ability to activate thioesters via nucleophilic acyl substitution.[1a] Taking this into account, we prepared thioester **1.44a** bearing an *o*-aldehyde group which would serve two purposes. First, the electron-withdrawing nature of the aldehyde would activate the thioacyl carbonyl beyond that of a simple phenyl thioester. Second and most importantly, the aldehyde would serve as an electrophile to trap the putative zwitterionic enolate **1.60a** and produce 2-phenylthiochromene **1.45a** with carbon dioxide as the only byproduct.

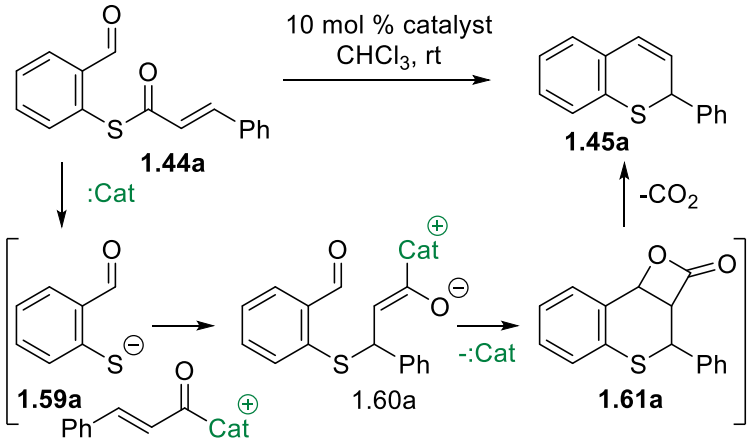


Figure 1.12: New synthesis of thiochromenes.

To our delight, this model substrate underwent the desired transformation into 2-phenylthiochromene (**1.45a**) in 94% yield when subjected to DHPB (**1.63a**)[22] (Figure 1.13). A further survey of achiral catalysts revealed other Lewis bases to be poorly suitable for this reaction due to slow reactions times and complex mixtures of products formed (Table 1.1).

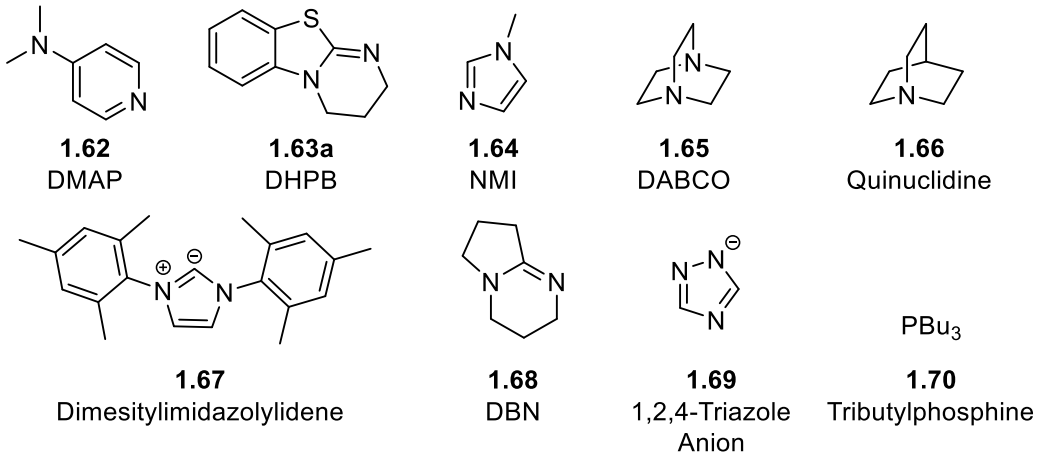
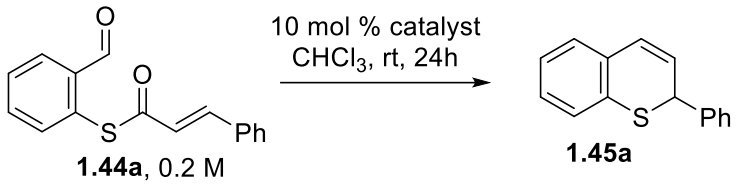


Figure 1.13: Achiral Lewis base catalysts.

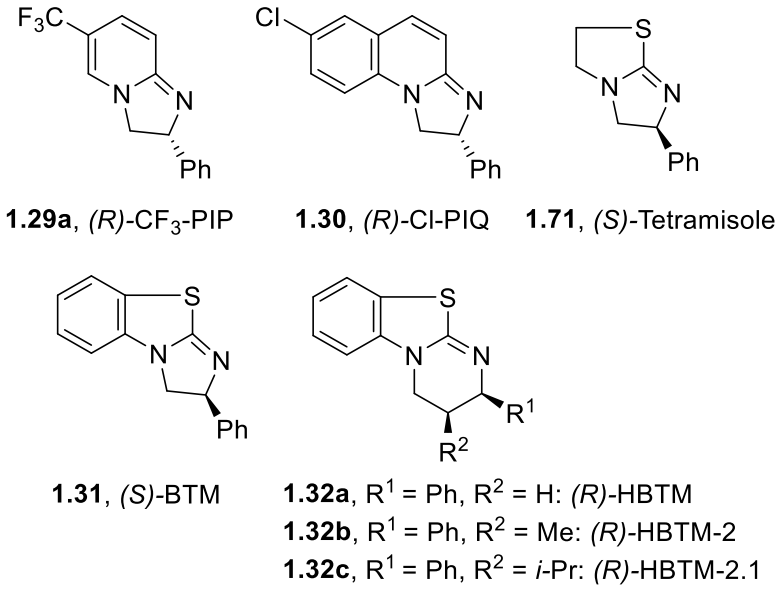
Table 1.1: Achiral catalyst survey.[a]



entry	catalyst	conversion, %	yield, %
1	**1.62**	80	44
2	**1.63a**	100	94
3	**1.64**	0	0
4	**1.65**	0	0
5	**1.66**	8	8
6	**1.67**	13	12
7	**1.68**	58	32
8	**1.69**	100	37
9	**1.70**	100	45

[a]Conditions: 0.2 M **1.44a**, 0.02 M catalyst, $CDCl_3$, rt.

Chiral ABCs were then screened for the enantioselective reaction. All the chiral ABCs shown in Figure 1.14 catalyzed this reaction with excellent enantioselectivity (Table 1.2). HBTM (**1.32a**)[14e] and its derivatives HBTM-2 (**1.32b**)[14f] and HBTM-2.1 (**1.32c**)[23] showed the best overall combination of catalytic activity and enantioselectivity (entries 7-9). Based on its availability in our lab, *(R)*-HBTM-2 (**1.32b**) was chosen for the ensuing study.



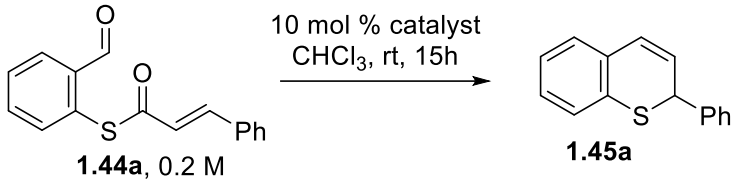
1.29a, *(R)*-CF_3-PIP **1.30**, *(R)*-Cl-PIQ **1.71**, *(S)*-Tetramisole

1.31, *(S)*-BTM

1.32a, R^1 = Ph, R^2 = H: *(R)*-HBTM
1.32b, R^1 = Ph, R^2 = Me: *(R)*-HBTM-2
1.32c, R^1 = Ph, R^2 = *i*-Pr: *(R)*-HBTM-2.1

Figure 1.14: Amidine-based catalysts.

Table 1.2: Chiral catalyst survey.[a]



entry	catalyst	yield, %	*ee*, %
1	*(R)*-**1.29a**	45	99 (*R*)
2	*(R)*-**1.30**	47	98 (*R*)
3	*(S)*-**1.71**	25	98 (*S*)
4	*(S)*-**1.31**	63	99 (*S*)
5	*(S)*-**1.32a**	98	>99 (*R*)
6	*(R)*-**1.32b**	99	>99 (*S*)
7	*(R)*-**1.32c**	99	>99 (*S*)

[a]Conditions: 0.2 M **1.44a**, 0.02 M catalyst, $CDCl_3$, rt.

A series of S-cinnamoyl derivatives of 2-mercaptobenzaldehyde (**1.44**) were prepared with a wide range of substituents and subjected to **1.32b** to produce 2-substituted thiochromenes (**1.45**) (Figure 1.15). A substrate with an *ortho* group produced an excellent yield and *ee* (**1.45c**). Although they affected the reaction rate, both electron-withdrawing and electron-donating groups on the aryl substituent R^1 gave excellent yields and *ee* values as well (**1.45d-h**). An additional *p*-aldehyde group in the substrate still allowed for a clean and enantioselective reaction (**1.45f**). Heterocyclic analogues also produced excellent enantioselectivity though the yields were somewhat lower (**1.45i, j**). Finally, a substrate with an alicyclic R^1 group produced a similar outstanding result (**1.45k**), which was somewhat surprising considering ABCs usually fail when the substituents are not π systems. Shown in Figure 1.16, the core of the thiochromene could also be modified with relative ease, but a steep drop in yield was observed when electron-withdrawing

groups were introduced. This was like due to a reduction of nucleophilicity in more stabilized thiolates (**1.45l-m** and **1.45p-q**).

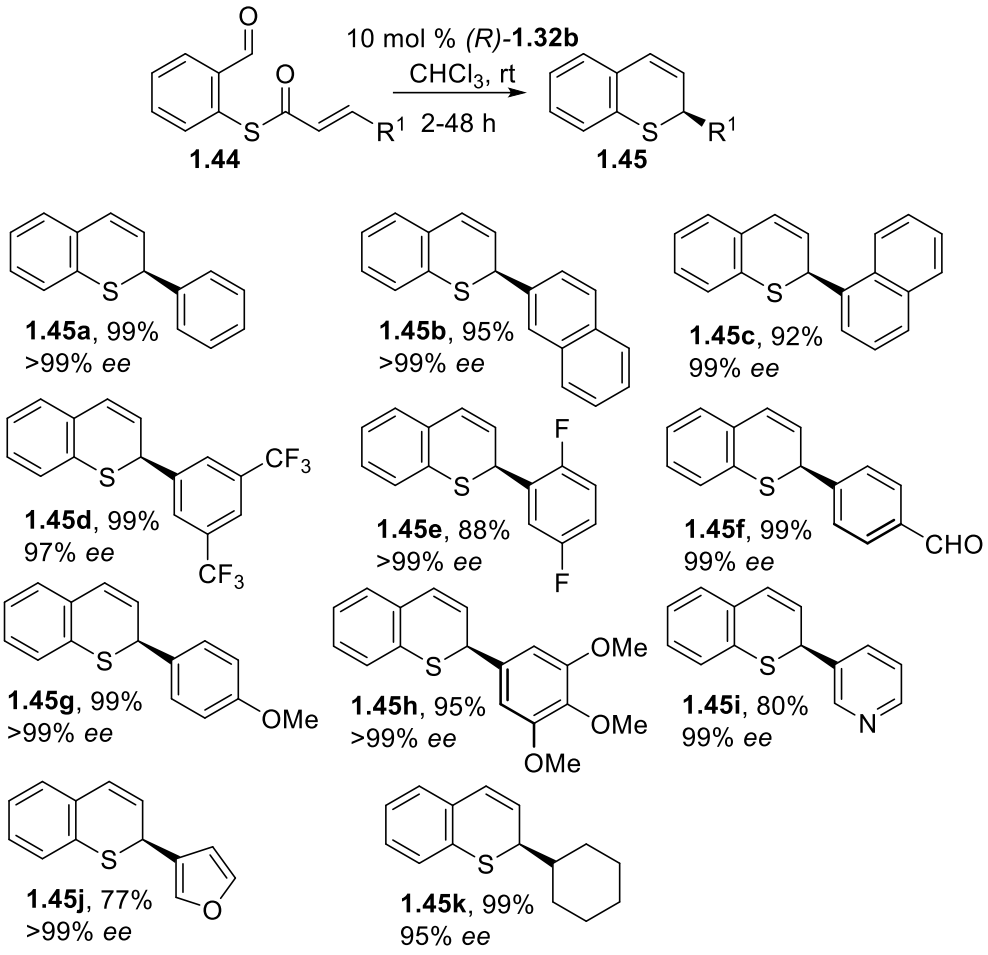


Figure 1.15: Substrate scope: variation of the side chain.

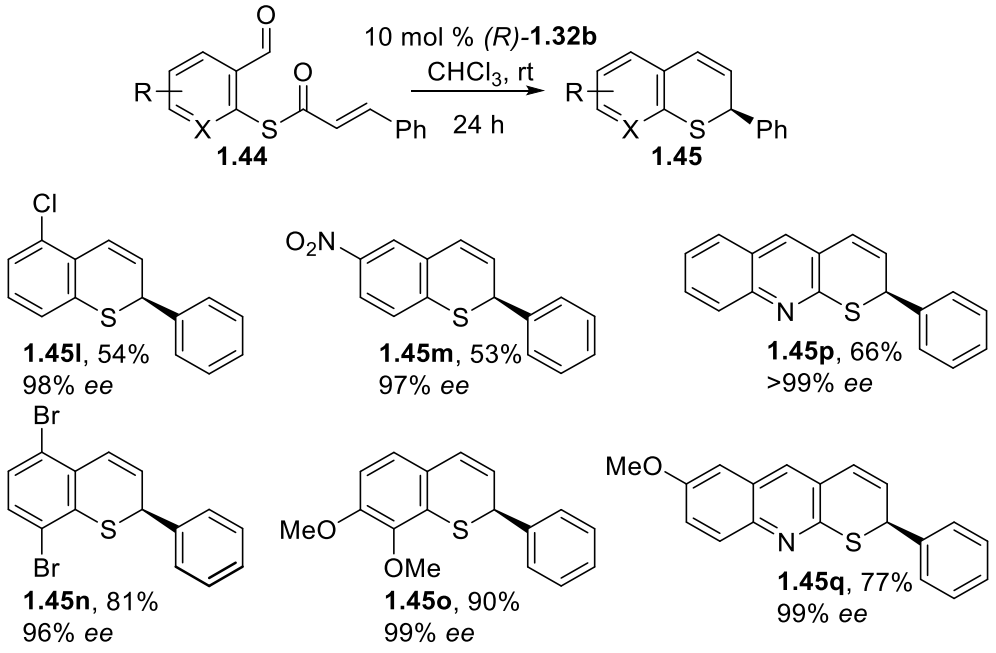


Figure 1.16: Substrate scope: variation of the thiochromene core.

To predict the absolute configuration at C2, we proposed the transition state model **1.72a** shown in Figure 1.17, where the conjugate addition of the thiolate proceeds from the opposite face of the phenyl group on the catalyst. An additional transition state model to consider would be to treat this as a hetero-Diels-Alder reaction with the C—S and C—C bonds forming in a concerted fashion (**1.72b**). **1.45q** was crystalline and its anomalous diffraction X-ray structure[24] (Figure 1.18) provided experimental verification of our prediction although this does not distinguish whether the absolute configuration arises from transition states **1.72a** or **1.72b**.

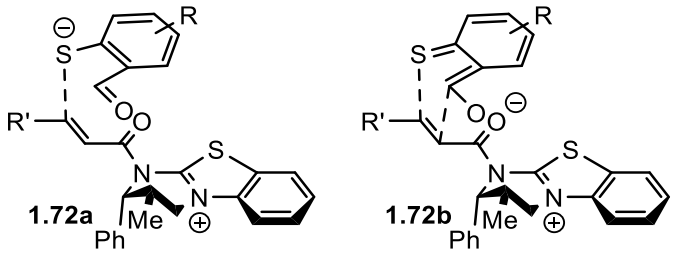


Figure 1.17: Transition state models.

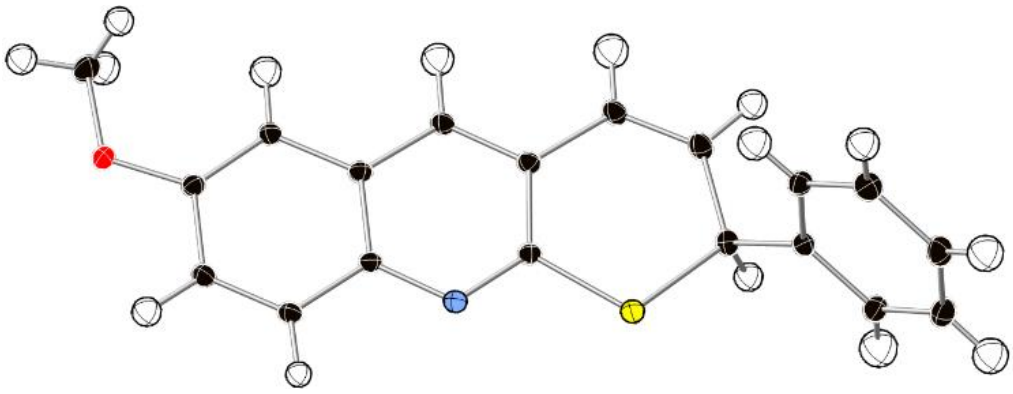


Figure 1.18: X-ray structure of **1.45q.** The absolute configuration was determined from the Flack parameters.[24]

Unfortunately, more challenging variations to **1.44** resulted in slow or no reaction (Figure 1.19). Replacing the aldehyde with a ketone (**1.73**) gave less than 5% conversion in 24 hours when subjected to DHPB. Substituting a fluorine in the α-position proceeded to form the desired 3-fluoro-2-phenyl thiochromene (**1.76**) but in a lousy 28% yield after 3 days. Although refluxing in benzene provided slightly higher conversions, the requirement of such forcing conditions would not lend itself to the development of an asymmetric version, our end goal.

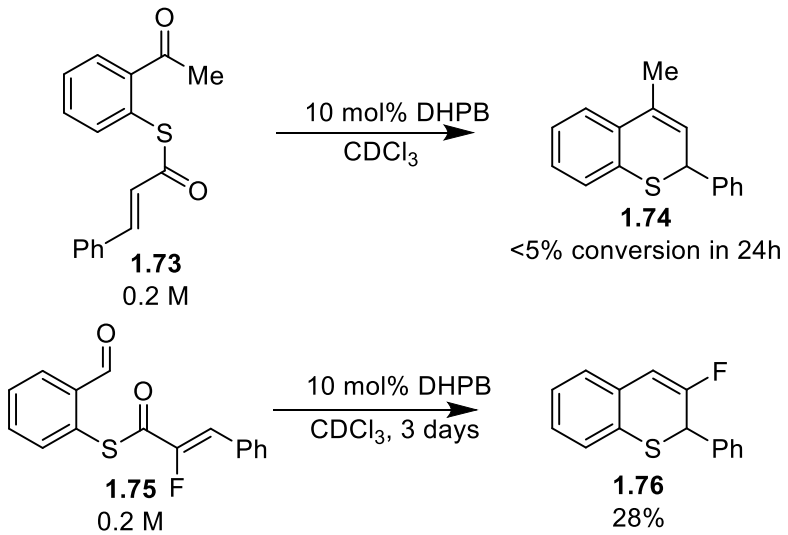


Figure 1.19: Problematic substrates in thiochromene synthesis.

Following the publication of our synthesis of thiochromenes, Mukherjee reported a sulfa-Michael/Julia-Kocienski approach to thiochromenes.[25] This iminium catalyzed method allowed thiochromenes (**1.45**) to be produced without an electron-withdrawing group at C3 like our method albeit with lower yields and more undesirable byproducts.

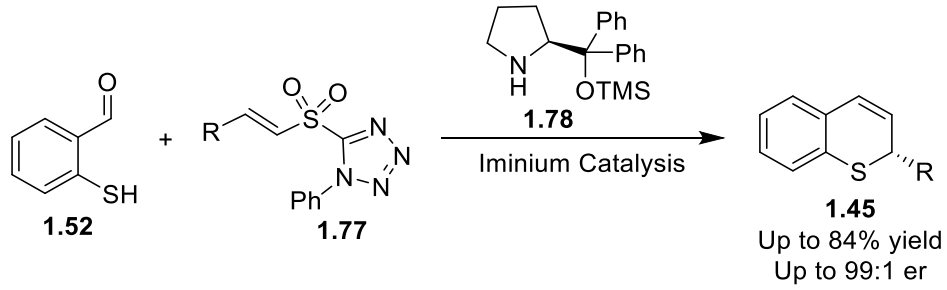


Figure 1.20: Mukherjee's approach to C3 unsubstituted thiochromenes.

1.2.5 Alternative mode of catalysis.

During the investigation of the thiochromene synthesis catalyzed by ABCs, an interesting observation was made. When **1.44a** was prepared by direct acylation of 2-mercaptobenzaldehyde (**1.52**) with cinnamoyl chloride, thiochromene **1.45a** formed as a byproduct comprising as much as 30% of the material. Follow up experiments showed an uncatalyzed form of the reaction can be promoted by the addition of one equivalent of 2-mercaptobenzaldehyde (**1.52**) and triethylamine as shown in Figure 1.21.

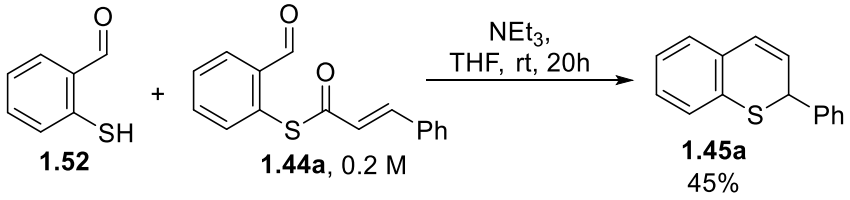


Figure 1.21: Thiolate promoted synthesis of thiochromenes.

Although this method gave only a 45% yield, this discovery suggests a different mode of catalysis could be exploited to perform the same transformation. Shown in Figure 1.22, we propose that the reaction is initiated by uncatalyzed thiolate addition to **1.44a** to form enolate **1.79a**, which can then undergo the aldol-lactonization cascade freeing additional thiolate for subsequent cycles.

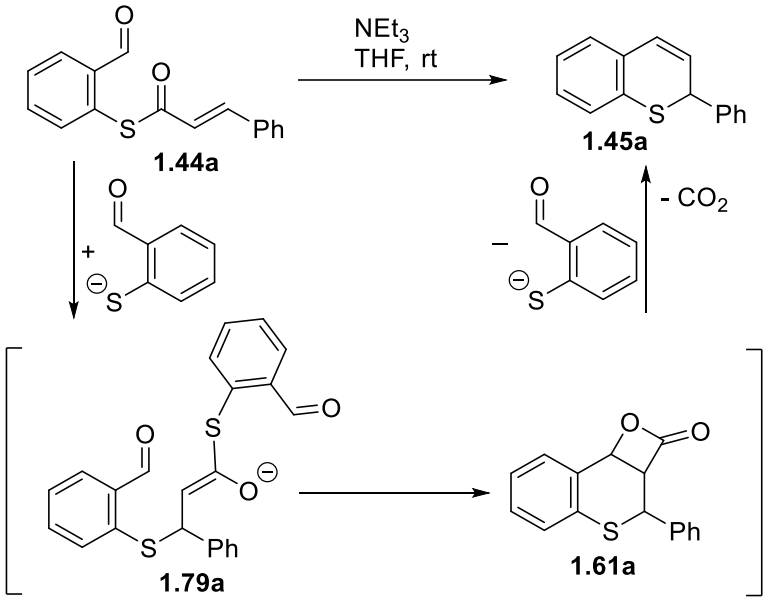


Figure 1.22: Proposed mechanism of thiolate promoted pathway.

Matsubara reported a similar thiol promoted reaction of α,β-unsaturated thioesters in the presence of a bifunctional thiourea catalyst (**1.82**) shown in Figure 1.23.[26] While the *ee* values were only modest, this mode of catalysis would reasonably apply for the 2-mercaptobenzaldehyde-promoted thiochromene synthesis.

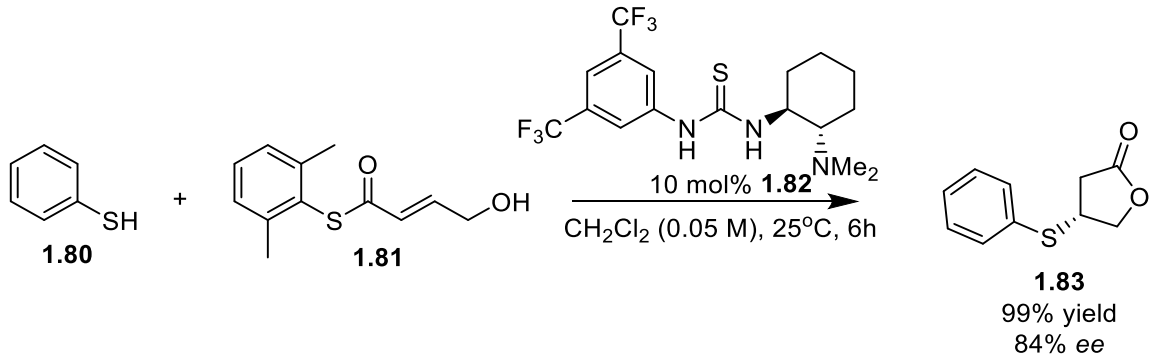


Figure 1.23: Thiol promoted reaction of ω-hydroxy-α,β-unsaturated thioesters.

1.3 Asymmetric synthesis of thiochromanes.

1.3.1 Shortcomings of DHPB.

Early in our enantioselective synthesis of 2-substituted thiochromenes, we realized enone substrate **1.84a** could be easily prepared via Wittig reaction of **1.44a**. After the encouraging results of the thiochromene synthesis, we set out to develop a related process that would proceed via a formal [4+2] cycloaddition (Figure 1.24).[1b] When the enone substrate **1.84a** was treated with DHPB **1.63**, the expected tricyclic ene-lactone **1.85a** formed with good diastereoselectivity. However, the reaction advanced excruciatingly slowly, reaching only 35% conversion after 5 days. With such low conversions, the asymmetric variant of this process was not promising, and the desired reaction was not observed after one week in the presence of the HBTM-2 (**1.32b**).

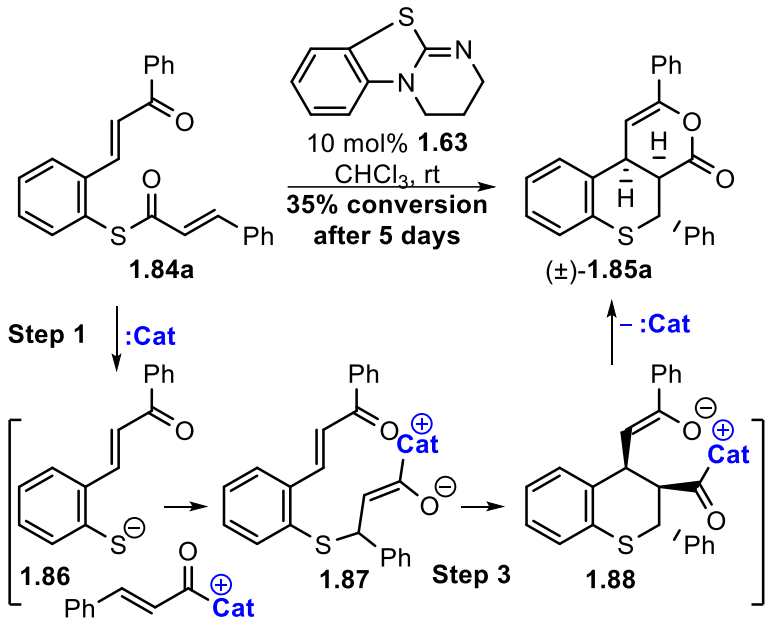


Figure 1.24: New tandem transformation.

1.3.2 Rational design of new catalysts using computational chemistry.

We hypothesized that two steps in the new tandem may be slowing the reaction to the point of impracticality: activation of the thioester (Figure1.24, Step 1) and the Michael addition of the zwitterionic enolate to the enone moiety (Figure 1.24, Step 3). Further corroborating our hypothesis, a highly activated, bis(trifluoromethyl) enone **1.84g** underwent clean conversion to ene-lactone **1.85g** in 48 h when subjected to DHPB (**1.63**) as shown in Figure 1.25. Fearing **1.85g** would be unstable to chromatography, it was treated with methanol for an additional 48 h to give methyl ester **1.89** in a 77% isolated yield based on **1.84g** with excellent diastereoselectivity.

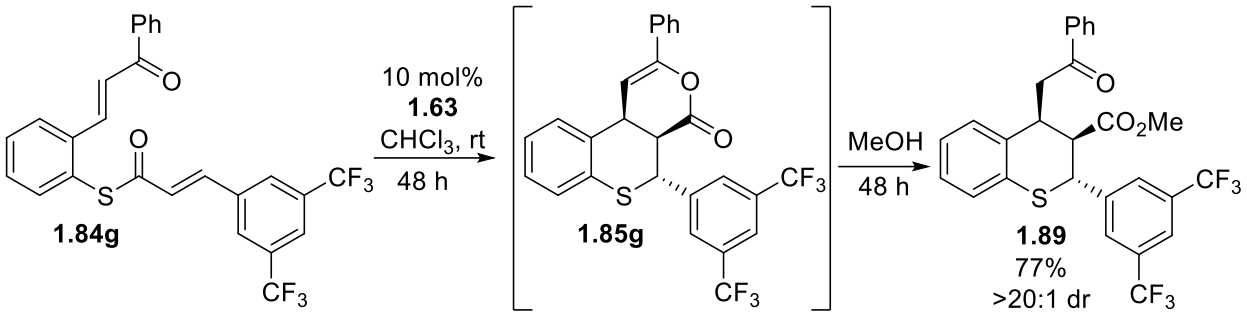


Figure 1.25: Successful rearrangement and methanolysis of activated enone **1.84g**.

This result suggested the acyl transfer step was likely the limiting step in our new tandem process. Rather than tailor make more activated enone substrates to overcome this limitation, we chose to design more active catalysts using DFT calculations. These new catalysts would hopefully be effective for a broader range of reactions and substrates. With the difficult acyl transfer step in mind, we computed the enthalpies of the isodesmic acyl transfer reaction between N-acetyl-DHPB cation (**1.90**) and several types of achiral ABCs (Figure 1.26).[27] As expected, adding electron-donating substituents to the benzene ring on DHPB (**1.63b-e**) gave strongly negative values. Bicyclic isothioureas **1.91a** and **1.92a** reported recently by Okamoto et al.[28] and their electron-rich derivatives (**1.91b-d**, **1.92b-d**) displayed considerably higher predicted Lewis basicities than DHPB itself while following the same trend of increasingly negative values with increasing electron-donating groups. Finally, the most negative enthalpy was calculated for DHIP **1.93**. This also happened to be the very first ABC that served as the starting point for designing this entire class of catalysts.

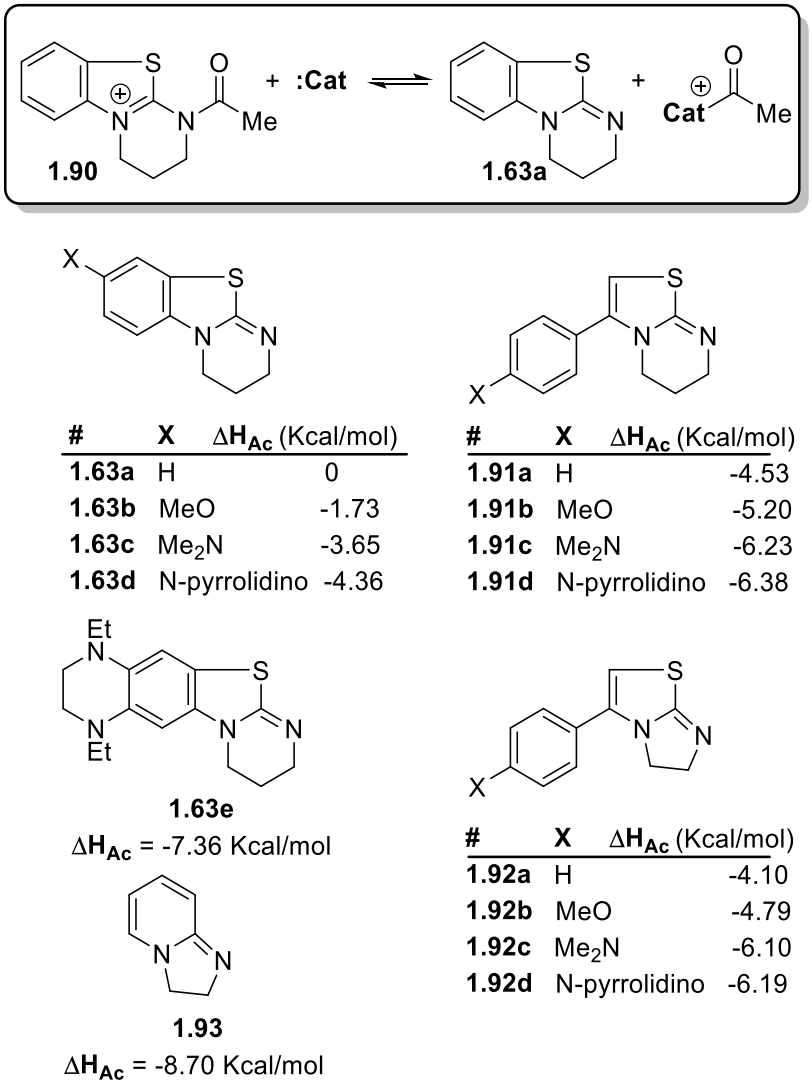


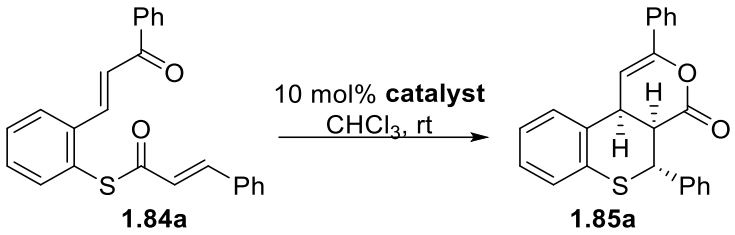
Figure 1.26: Relative acylation enthalpies of some achiral ABCs.

1.3.3 Achiral catalyst survey.

With these computations in hand, we synthesized the catalysts shown in Figure 1.26 and undertook a kinetics study of the rearrangement of thioester **1.84a**. Electron-rich derivatives of DHPB **1.63b-e** produced increased reaction rates in comparison to unsubstituted DHPB (Table 1, entries 2-5 vs. 1). Bicyclic isothioureas **1.91** and **1.92** (entries 6-13) turned out to be even more active leading to as much as a 574-fold increase in the relative reaction rate (entry 8) even though

some DHPB derivatives gave similar computed acylation enthalpies (see, e.g., **1.91b** vs. **1.63c** or **1.92c** vs. **1.63d**). Given the fact that catalysts **1.91a-c** and **1.92a** performed slower than DHPB **1.63a** in the acetylation of 1-phenylethanol with anhydrides in Okamoto's study,[28] it was somewhat surprising that these catalysts performed the best in our new tandem. This can be rationalized by the difference in mechanisms between the reactions studied. The earlier mentioned experiment with a more active enone thioester (**1.89**, Figure 1.25) demonstrated that acyl transfer (Figure1.24, Step 1) is likely our limiting step. O-acylation of enolate **1.88** (Figure 1.24) to displace the catalyst is expected to be relatively fast. In contrast, Okamoto may have observed a slower reaction rate due to slower deacylation of the catalyst with increasing Lewis basicity in their simple acetylation of 1-phenylethanol. Finally, in sharp contrast to its poor performance in the acetylation of alcohols observed in previous studies: several hundred times slower than DHPB,[13b] DHIP **1.93** displayed catalytic activity comparable to the fastest bicyclic isothioureas (entry 14). Although this dramatic reversal in the relative activity of the two catalysts can be rationalized similarly to above mentioned bicyclic catalysts in Okamoto's study, we were surprised by the magnitude of this effect nonetheless.

Table 1.3: Achiral catalyst survey.[a]



1.84a **1.85a**

entry	catalyst	$t_{1/2}$, min	relative rate	dr	Computed Relative ΔH_{Ac}, kcal
1	**1.63a**	ND[b]	1	ND	0
2	**1.63b**	7600	3.20	ND	-1.73
3	**1.63c**	998	22.6	ND	-3.65
4	**1.63d**	841	31.3	ND	-4.36
5	**1.63e**	77	221	97:3	-7.36
6	**1.91a**	92	210	95:5	-4.53
7	**1.91b**	54	308	96:4	-5.20
8	**1.91c**	27	574	96:4	-6.23
9	**1.91d**	28	537	96:4	-6.38
10	**1.92a**	184	98	93:7	-4.10
11	**1.92b**	96	180	93:7	-4.79
12	**1.92c**	40	392	92:8	-6.10
13	**1.92d**	33	509	91:9	-6.19
14	**1.93**	38	431	96:4	-8.70

[a]Conditions: 0.1 M **1.84a**, 0.01 M catalyst, $CDCl_3$, rt.

[b]The reaction stalled after 7 days at 35 % conversion

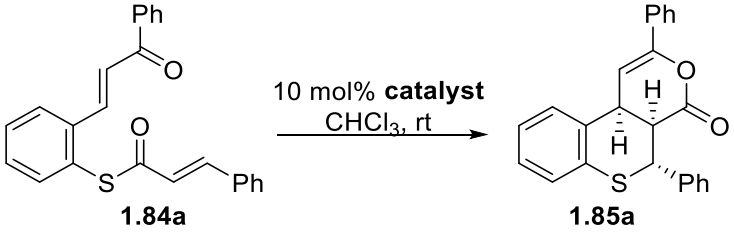
1.3.4 Chiral catalyst survey and substrate scope.

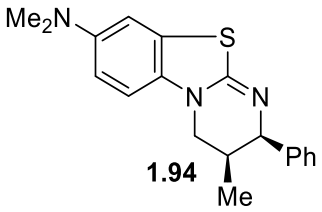
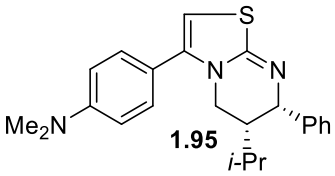
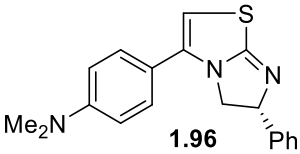
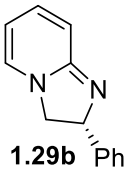
Excited by these findings, we synthesized chiral catalysts **1.94**-**1.95** and **1.29b** and evaluated their efficacy in the asymmetric version of the rearrangement (Table 1.4). Although it gave the highest enantioselectivity, catalyst **1.94**, the dimethylamino derivative of HBTM-2 (**1.32b,** Figure 1.14) required 5 days to complete the tandem reaction (entry 1). Despite having the fastest achiral analog (Table 1.3, entry 8), catalyst **1.95** displayed the worst reactivity of the chiral series of catalysts stalling at 4 days with a disappointing 32% yield. The enantioselectivity produced by **1.95** was also dreadfully poor. Delightfully, both **1.96**[28] and H-PIP **1.29b**[13a] produced excellent enantioselectivity and good activity (entries 3 and 4). Since **1.29b** was the most synthetically accessible of the four catalysts requiring only two steps, we selected it to explore the substrate scope of the enantioselective rearrangement (Figure 1.27).

First, varying the R^2 substituents on the enone while the R^1 position remained an unsubstituted phenyl, the transformation proceeded successfully with electron-deficient and electron-rich aryl groups (**1.85a-e, g, j**) as well as with a methyl group (**1.85f**). Next, the R^1 position of the enone was varied with a combination of R^2 substituents (**1.85a-f**). Substrates with an electron-deficient aryl (**1.85g** and **h**), as well as a cyclohexyl group (**1.85j** and **k**) also reacted smoothly regardless of R^2. Due its deactivating effect on the thioacyl carbonyl, a substrate with a *p*-methoxyphenyl group at R^1 displayed a loss of reactivity reaching only 20% conversion in 5 days (**1.85i**). Excellent diastereoselectivities (d.r. ca. 20:1) were observed in all thiochromanes produced in the reaction. The enantioselectivity of the reaction was also excellent providing 90% *ee* or above in all but one thiochromane (**1.85f**). Strangely, tetrakis(trifluoromethyl) substrate **1.84l** underwent a subsequent migration of the ene-lactone double bond into conjugation with the lactone ester to form **1.97**. The mechanism of this unexpected transformation has yet to be explored but

high enantioselectivity was observed nonetheless. Finally, the rearrangement was carried out with 1 g (2.7 mmol) of substrate **1.84a**, and an 86% yield and 95% *ee* were obtained demonstrating the scalability of our tandem transformation.

Table 1.4: Chiral catalyst survey.[a]



entry	catalyst	time	% yield	dr	% *ee*
1		5d	77	97:3	-99
2		4d	32	ND	-35
3		17h	83	98:2	96
4		17h	93	97:3	95

[a]Conditions: 0.2 M **1.84a**, 0.02 M catalyst, $CDCl_3$, rt.

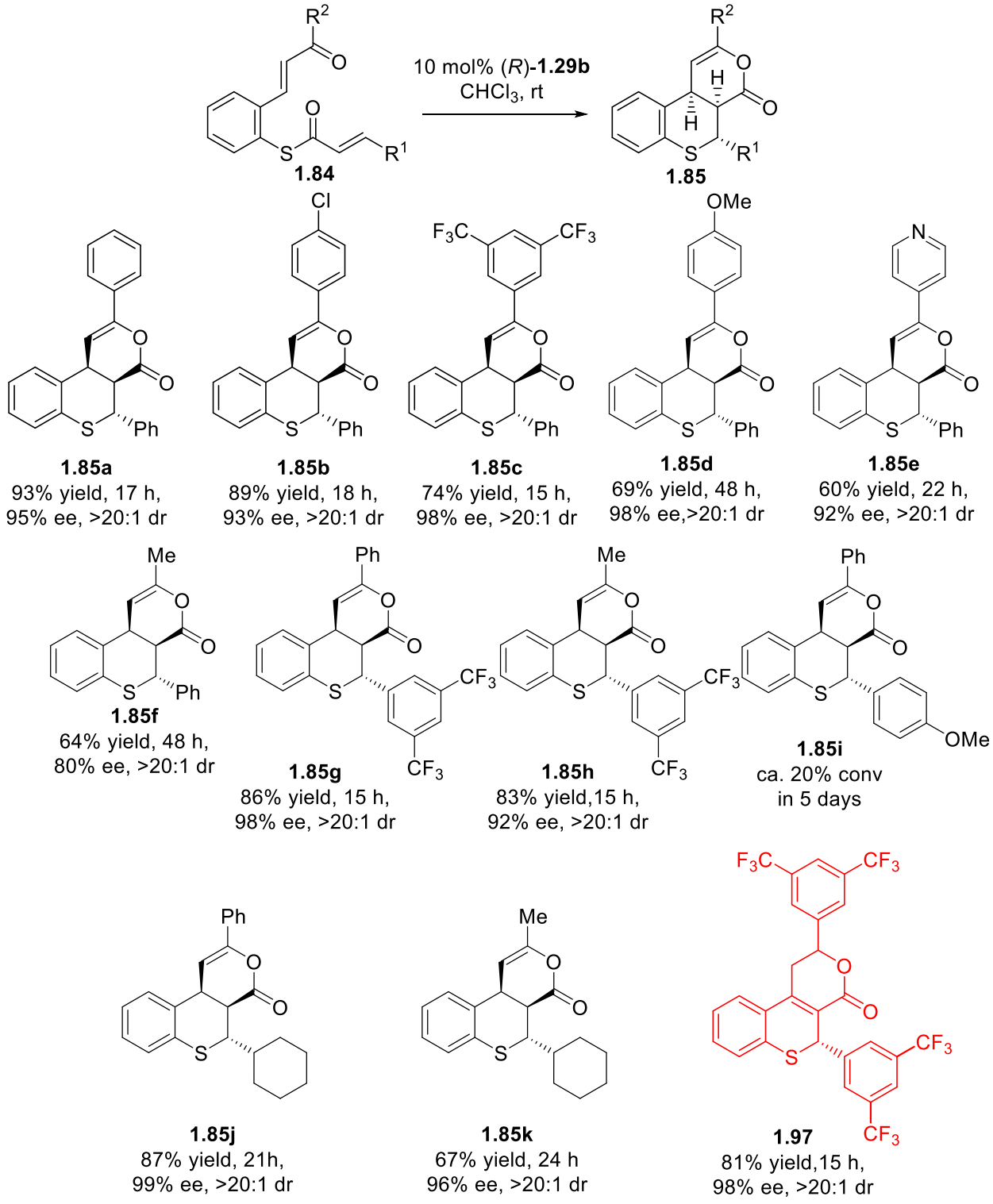


Figure 1.27: Substrate scope.

Due to its success in this study, we chose to revisit the thiochromene synthesis with H-PIP (**1.29b**). Surprisingly, it produced only modest enantioselectivity (Figure 1.27) despite the achieving great results in the synthesis of **1.85**. Demonstrated by its fast reaction time (3 hours), this diminished enantioselectivity is likely due to the increased reactivity of the *o*-formylaryl thioester (**1.44a**) compared to enone thioesters (**1.84**), which further supports the concept that acyl donors need to match the reactivity of the catalysts.

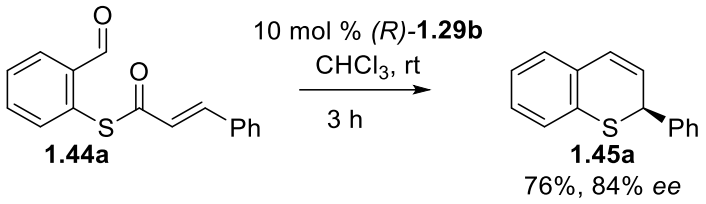


Figure 1.28: Thiochromene synthesis with **1.29b**.

While our work on this rearrangement was under consideration for publication, a paper by Xu et al.[29] describing the same transformation promoted by an NHC catalyst (**1.98**) was published (Figure 1.29). The NHC catalyzed process proceeds with good to excellent yields as well as excellent enantioselectivity and diastereoselectivity.

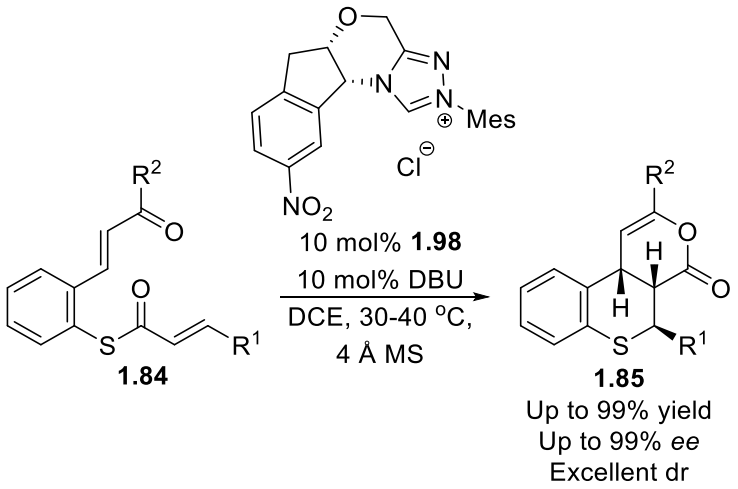


Figure 1.29: NHC catalyzed synthesis of thiochromanes.

1.4 Conclusion and future directions.

In conclusion, we have developed two highly enantioselective cascade transformations of thioesters into rearranged products. First, the synthesis of chiral, 2-substituted thiochromenes and their heterocyclic analogues exhibited a broad substrate scope without requiring additional reagents and producing only carbon dioxide as byproduct. This was the first example of acyl transfer catalysts activating thioesters, which have proven to be chromatographically stable, moderately reactive acyl donors. Additionally, we have developed a new highly enantioselective and atom-economical tandem reaction of thioesters into fused thiochromanes. This study necessitated the rational design of more electron-rich ABCs for moderately reactive acyl donors. Surprisingly, the best results were achieved with H-PIP **1.29b**, the very first chiral ABC synthesized in our lab. The original study of this catalyst in our group took place 13 years ago and focused on the acylation of benzylic alcohols with anhydrides. Since it performed poorly in the simple acylation of alcohols, H-PIP served as only a beginning to the design of more electron-deficient derivatives (e.g., CF_3-PIP **1.29a**, Figure 1.3) at the time. Its success in the present study underscores the concept of matching acyl donors to the reactivity of the catalyst as well as the potential of electron-rich ABCs to activate additional moderately reactive acyl donors including less reactive alkyl thioesters.

Our development of cascade processes of α,β-unsaturated thioesters described in this chapter paves the way for further investigation into transformations previously considered impossible by acyl transfer catalysis. For example, initial studies of problematic thiochromene substrates **1.72** and **1.74** utilizing electron-rich ABCs are underway (Figure 1.30). By simply using a dimethylamino derivative of DHPB (**1.63**), a facile synthesis of 3-fluorothiochromenes appears likely. Studies in this direction are being pursued in our group by Mr. Matthew Straub with

promising results already. He will also be pursuing the systematic electronic tuning of H-PIP based on further computational studies. Furthermore, it will be interesting to observe the reactivity of ABCs or NHCs with even more negative calculated acylation enthalpies to test the limits of acyl group activation.

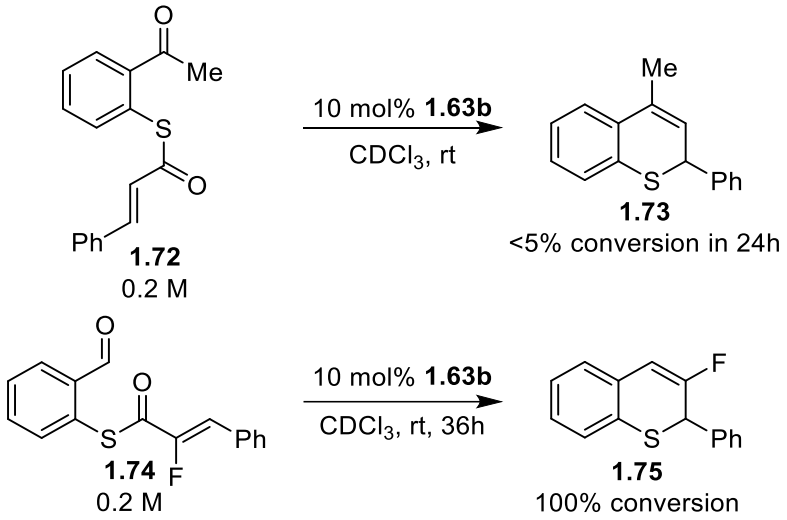
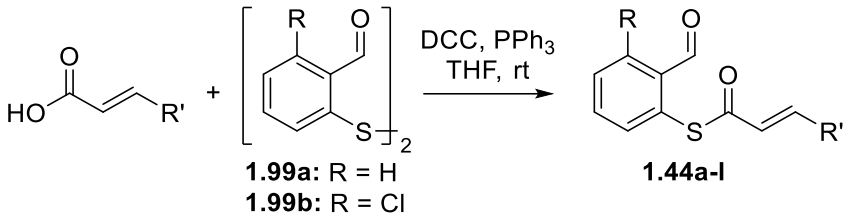


Figure 1.30: Problematic substrates revisited.

1.5 Experimental.

All reagents were obtained commercially and used as received unless specified otherwise. Catalysts **1.29a-b**,[14a] **1.30**,[14b] **1.31**,[14c] **1.32a**,[14e] **1.32b**,[14f] **1.32c**,[23] **1.63a**,[22] **1.93**[14a] were prepared as previously described. Chloroform, dichloromethane, and *N*,*N*-dimethylacetamide were freshly distilled from calcium hydride. THF was freshly distilled from sodium and benzophenone. Solvents used for chromatography were ACS or HPLC grade, as appropriate. Reactions were carried out under argon and monitored by thin layer chromatography (TLC) and by ^{1}H NMR. Uniplate HLF (250 μm) silica gel plates were used for TLC analyses. Flash column chromatography was performed over Sorbent Technologies silica gel (40-63 mm). HPLC analyses were performed on a Shimadzu LC system using Chiralcel OD-H, analytical chiral stationary phase column (4.6x250 mm, Chiral Technologies, Inc.) with a UV detector at 254 nm and a 1.0 mL/min flow rate. ^{1}H and ^{13}C NMR spectra were recorded on a Mercury 300 MHz and DD2 500 MHz Agilent spectrometer. The chemical shifts are reported as δ values (ppm) relative to TMS using residual $CHCl_3$ peak (7.26 ppm) as the reference. Melting points were measured on a Stuart SMP10 melting point apparatus. High-Resolution mass spectral analyses were performed at Washington University MS Center on a Bruker MaXis QTOF mass spectrometer using Electrospray Ionization (ESI) and Electron Impact (EI) methods.[30] Infrared spectra were recorded on a Bruker Alpha Platinum-ATR. Optical rotations were determined on a Rudolph Autopol III polarimeter.

1.5.1 Synthesis of 2-formylthioester substrates, 1.44.

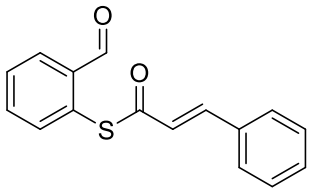


1.99a: R = H
1.99b: R = Cl

1.44a-l

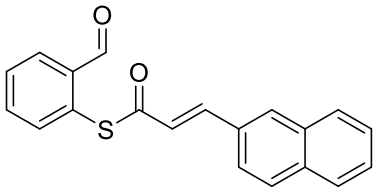
General procedure A for the synthesis of substrates 1.44a-l.[31] A round bottom flask equipped with a magnetic stir bar was charged with an α,β-unsaturated acid (1.0 equiv), N,N'-dicyclohexylcarbodiimide (0.5 equiv), and THF (0.2 M). The mixture was cooled to 0 °C, stirred for 15 min, treated with PPh_3 (0.6 equiv) and disulfide **1.99a** or **b**[32,33] (0.5 equiv) added in one portion, and allowed to slowly warm to rt. The mixture was stirred for 12 h, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography using the eluent indicated to afford the corresponding *o*-formyl thioester **12**.

S-(2-formylphenyl) (E)-3-phenylprop-2-enethioate (1.44a). Prepared from *trans*-cinnamic acid



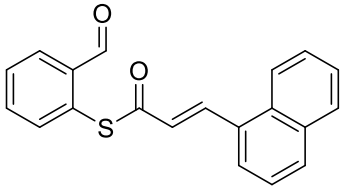
(108 mg, 0.728 mmol) and **1.99a**. White solid (103 mg, 53% yield, 1→5% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 10.27 (s, 1H), 8.08 (dd, J_1 = 7.2 Hz, J_2 = 2.0 Hz, 1H), 7.72 (d, J = 15.8 Hz, 1H), 7.68-7.55 (m, 5H), 7.45-7.30 (m, 3H), 6.83 (d, J = 15.8 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 191.03, 186.68, 143.11, 137.28, 136.75, 134.36, 133.89, 131.37, 131.10, 130.56, 129.30, 128.87, 123.64; **IR** (cm^{-1}): 3061, 3027, 3016, 2866, 1681, 1613, 1264, 1198, 985, 751, 691; **MS:** HR-ESI calculated for $[C_{16}H_{12}O_2S+Na]^+$: 291.0450, found: 291.0443; **mp**: 86-88 °C.

S-(2-formylphenyl) (E)-3-(naphthalen-2-yl)prop-2-enethioate (1.44b). Prepared from (*E*)-3-(2-



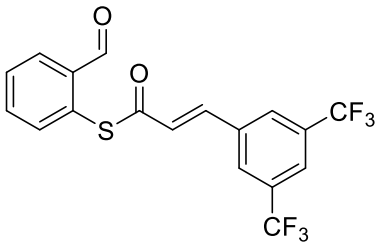
naphthyl)acrylic acid (130 mg, 0.656 mmol) and **1.99a**. White solid (153 mg, 73% yield, 2→10% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 10.30 (s, 1H), 8.09-8.06 (m, 1H), 7.95 (s, 1H), 7.88-7.81 (m, 4H), 7.67-7.48 (m, 6H), 6.91 (d, *J* = 15.7 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 190.96, 186.52, 143.06, 137.20, 136.66, 134.72, 134.29, 133.37, 131.45, 131.28, 131.11, 130.45, 129.20, 129.07, 128.86, 127.99, 127.9, 127.07, 123.61, 123.52; **IR** (cm^{-1}): 3052, 2919, 2870, 1692, 1673, 1604, 1355, 1285, 1265, 1200, 1024, 960, 831; **MS:** HR-ESI calculated for $[C_{20}H_{14}O_2S+H]^+$: 319.0787, found: 319.0789; **mp**: 135-136 °C.

S-(2-formylphenyl) (E)-3-(naphthalen-1-yl)prop-2-enethioate (1.44c). Prepared from (*E*)-3-(1-



naphthyl)acrylic acid (65 mg, 0.328 mmol) and **1.99a**. Yellow oil (72 mg, 69% yield, 2→6% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 10.32 (s, 1H), 8.55 (d, *J* = 15.5 Hz, 1H), 8.15 (d, *J* = 8.2 Hz, 1H), 8.10-8.07 (m, 1H), 7.94-7.79 (m, 3H), 7.67-7.46 (m, 6H), 6.91 (d, *J* = 15.5 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 190.96, 186.57, 139.81, 137.21, 136.64, 134.32, 133.86, 131.80, 131.65, 131.05, 131.01, 130.51, 129.24, 129.03, 127.39, 126.59, 125.80, 125.64, 125.59, 123.25; **IR** (cm^{-1}): 3059, 1673, 1599, 1570, 1345, 1264, 1198, 1042, 1021, 826, 793, 762, 706, 598, 500; **MS:** HR-ESI calculated for $[C_{20}H_{14}O_2S+Na]^+$: 341.0607, found: 341.0610.

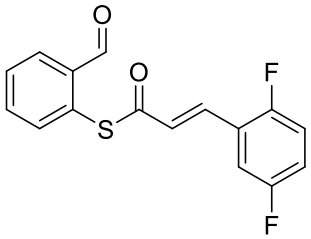
S-(2-formylphenyl) (E)-3-(3,5-bis(trifluoromethyl)phenyl)prop-2-enethioate (1.44d).



Prepared from (*E*)-3,5-bis(trifluoromethyl)cinnamic acid (186 mg, 0.656 mmol) and **1.99a**. White solid (125 mg, 47% yield, 1→3% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 10.24 (s, 1H),

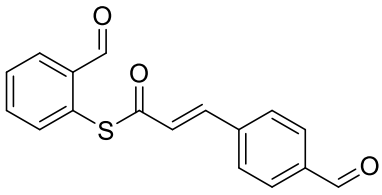
8.06 (dd, J_1 = 7.2 Hz, J_2 = 1.6 Hz, 1H), 7.98 (s, 2H), 7.91 (s, 1H), 7.70 (d, J = 15.8 Hz, 1H), 7.66-7.55 (m, 3H) 6.94 (d, J = 15.8 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 190.65, 186.20, 138.88, 137.16, 136.67, 136.10, 134.49, 133.56, 132.89 (q, J = 33.8 Hz), 130.87, 130.15, 129.74, 128.30, 127.12, 124.92, 124.22, 121.30; **IR** (cm^{-1}): 3055, 2922, 2853, 2753, 1689, 1615, 1467, 1379, 1282, 1172, 1113, 1022, 983, 947, 908, 846, 818, 754; **MS:** HR-ESI calculated for $[C_{18}H_{10}F_6O_2S+H]^+$: 405.0378, found: 405.0379; **mp**: 135-136 °C.

S-(2-formylphenyl) (E)-3-(2,5-difluorophenyl)prop-2-enethioate (1.44e). Prepared from (*E*)-



2,5-difluorocinnamic acid (81 mg, 0.438 mmol) and **1.99a**. White solid (89 mg, 67% yield, 2→4% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 10.25 (s, 1H), 8.07 (dd, J_1 = 7.1 Hz, J_2 = 1.4 Hz, 1H), 7.73 (d, J = 16.0 Hz, 1H), 7.67-7.54 (m, 3H), 7.27-7.22 (m, 1H), 7.11-7.07 (m, 2H), 6.89 (d, J = 16.0 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 190.79, 186.58, 160.03(dd, J_1 = 66.2 Hz, J_2 = 2.1 Hz), 156.76 (dd, J_1 = 73.3 Hz, J_2 = 2.1 Hz), 137.16, 136.65, 134.40, 134.24, 130.68, 130.59, 129.43, 126.96, 126.87, 123.21 (dd, J_1 = 14.1 Hz, J_2 = 8.1 Hz), 119.24 (dd, J_1 = 24.4 Hz, J_2 = 9.1 Hz), 117.78 (dd, J_1 = 25.0 Hz, J_2 = 8.5 Hz), 115.31 (dd, J_1 = 24.5 Hz, J_2 = 3.1 Hz); **IR** (cm^{-1}): 3116, 3074, 3023, 1689, 1668, 1612, 1585, 1566, 1486, 1434, 1398, 1323, 1267, 1186, 1028, 972, 856, 752, 718, 633, 579, 443; **MS:** HR-ESI calculated for $[C_{16}H_{10}F_2O_2S+Na]^+$: 327.0262, found: 327.0266; **mp**: 99-102 °C.

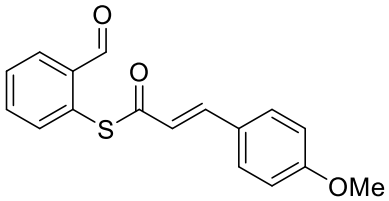
S-(2-formylphenyl) (E)-3-(4-formylphenyl)prop-2-enethioate (1.44f). Prepared from (*E*)-4-



formylcinnamic acid (116 mg, 0.656 mmol) and **1.99a**. White solid (112 mg, 57% yield, 10:10:80 EtOAc/CH_2Cl_2/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 10.24 (s, 1H), 10.03 (s, 1H), 8.06 (dd,

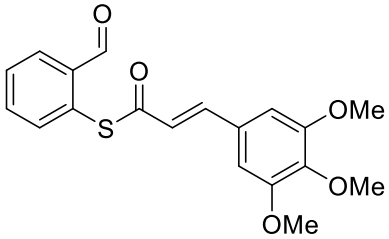
J_1 = 7.3 Hz, J_2 = 1.7 Hz, 1H), 7.91 (d, J = 8.2 Hz, 2H), 7.72-7.54 (m, 6H), 6.91 (d, J = 15.8 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 191.46, 190.76, 186.46, 140.98, 139.47, 137.84, 137.17, 136.65, 134.42, 130.73, 130.51, 130.41, 129.54, 129.23, 126.37; **IR** (cm^{-1}): 3062, 3050, 2864, 2815, 2716, 1694, 1680, 1609, 1583, 1565, 1199, 1022, 985, 884, 811, 746; **MS:** HR-ESI calculated for $[C_{17}H_{12}O_3S+Na]^+$: 319.0399, found: 319.0427; **mp**: 142-144 °C.

S-(2-formylphenyl) (E)-3-(4-methoxyphenyl)prop-2-enethioate (1.44g). Prepared from (*E*)-4-



methoxycinnamic acid (58 mg, 0.328 mmol) and **1.99a**. White solid (86 mg, 88% yield, 5→10% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 10.26 (s, 1H), 8.05 (d, J = 7.3 Hz, 1H), 7.64-7.51 (m, 6H), 6.91 (d, J = 8.5 Hz, 2H), 6.69 (d, J = 15.7 Hz, 1H), 3.84 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 191.12, 186.47, 162.36, 142.91, 137.29, 136,74, 134,28, 131.43, 130.72, 130.40, 129.13, 126.53, 121,016, 121.16, 114.77, 55.64; **IR** (cm^{-1}): 3064, 3011, 2878, 1700, 1665, 1599, 1569, 1512, 1315, 1288, 1180, 1026; **MS:** HR-ESI calculated for $[C_{17}H_{14}O_3S+Na]^+$: 321.0556, found: 321.0550; **mp**: 108-110 °C.

S-(2-formylphenyl) (E)-3-(3,4,5-trimethoxyphenyl)prop-2-enethioate (1.44h). Prepared from



(*E*)-3,4,5-trimethoxycinnamic acid (235 mg, 0.656 mmol) and **1.99a**. White solid (212 mg, 90% yield, 10→20% EtOAc). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 10.24 (s, 1H), 8.04 (dd, J_1 = 7.7 Hz, J_2 = 1.9 Hz, 1H), 7.64-7.52 (m, 4H), 6.77 (s, 2H), 6.70 (d, J = 15.6 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 190.96, 186.36, 153.68, 143.08, 141.10, 137.19, 136.68, 134.3, 131.06, 130.47, 129.26, 129.22, 122.78, 106.02, 61.16, 56.38; **IR** (cm^{-1}): 3008, 2940, 2838, 2755, 1706, 1690, 1649, 1612,

1577, 1505, 1465, 1421, 1324, 1251, 1191, 1120, 1026, 964, 828, 757; **MS:** HR-ESI calculated for $[C_{19}H_{18}O_5S+H]^+$: 359.0948, found: 359.0949; **mp**: 133-135 °C.

S-(2-formylphenyl) (E)-3-(pyridin-3-yl)prop-2-enethioate (1.44i). Prepared from (*E*)-3-(pyridin-3-yl)acrylic acid (42.7 mg, 0.286 mmol) and **1.99a**. White solid (43.8 mg, 57% yield, 10% EtOAc/CH_2Cl_2). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 10.24 (s, 1H), 8.77 (d, J = 2.1 Hz, 1H), 8.62 (dd, J_1 = 4.8 Hz, J_2 = 1.6 Hz, 1H), 8.05 (dd, J_1 = 7.3 Hz, J_2 = 2.0 Hz, 1H), 7.87 (ddd, J_1 = 8.0 Hz, J_2 = 2.0 Hz, J_3 = 2.0 Hz, 1H), 7.70 (s, 1H), 7.65-7.54 (m, 3H), 7.34 (dd, J_1 = 8.0 Hz, J_2 = 4.8 Hz, 1H), 6.87 (d, J = 15.8 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 190.82, 186.37, 151.87, 150.40, 139.16, 137.19, 136.69, 134.83, 134.43, 130.73, 130.53, 129.75, 129.53, 125.49, 124.07; **IR** (cm^{-1}): 3104, 3058, 3011, 2923, 1687, 1629, 1602, 1200, 1051, 1019, 981; **MS:** HR-ESI calculated for $[C_{15}H_{11}O_2NS+Na]^+$: 292.0403, found: 292.0421; **mp**: 139-142 °C.

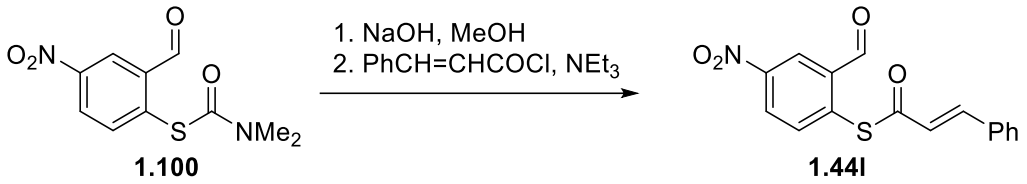
S-(2-formylphenyl) (E)-3-(furan-3-yl)prop-2-enethioate (1.44j). Prepared from (*E*)-3-(3-furyl)acrylic acid (91 mg, 0.659 mmol) and **1.99a**. White solid (60 mg, 35% yield, 2→10% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 10.24 (s, 1H), 8.05 (d, J = 5.7 Hz, 1H), 7.77-7.34 (m, 6H), 6.61 (d, J = 1.6 Hz, 1H), 6.53 (d, J = 15.6 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 171.78, 140.10, 140.05, 133.27, 133.16, 129.13, 128.72, 128.69, 128.19, 128.16, 128.21, 127.41, 127.39, 77.86, 45.44, 17.56; **IR** (cm^{-1}): 3138, 3118, 2866, 2846, 2757, 1689, 1667, 1611, 1301, 1268, 1206, 1157, 1028, 979, 846, 795, 746; **MS:** HR-ESI calculated for $[C_{14}H_{10}O_3S+H]^+$: 259.0423, found: 259.0425; **mp**: 119-120 °C.

S-(2-formylphenyl) (E)-3-cyclohexylprop-2-enethioate (1.44k). Prepared from (*E*)-3-cyclohexyl-2-propenoic acid (101 mg, 0.656 mmol) and **1.99a**. Greenish-yellow oil (62 mg, 34% yield, 1→5% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 10.21 (s, 1H), 8.03 (dd, J_1 = 7.1 Hz, J_2 = 2.1 Hz, 1H), 7.63-7.48 (m, 3H), 6.97 (dd, J_1 = 15.7 Hz, J_2 = 6.8 Hz, 1H), 6.15 (dd, J_1 = 15.7 Hz, J_2 = 1.4 Hz, 1H) 2.20-2.15 (m, 1H) 1.80-1.66 (m, 5H) 1.38-1.09 (m, 5H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 191.10, 187.06, 153.42, 137.28, 136.74, 134.27, 131.31, 130.39, 129.09, 125.16, 40.87, 31.70, 26.02, 25.82; **IR** (cm^{-1}): 3062, 2924, 2858, 2743, 1694, 1623, 1587, 1447, 1385, 1263, 1197, 1131, 1115, 1098, 1011, 963, 915, 888, 815, 758; **MS:** HR-ESI calculated for $[C_{16}H_{18}O_2S+Na]^+$: 297.0920, found: 297.0933.

S-(3-chloro-2-formylphenyl) (E)-3-phenylprop-2-enethioate (1.44l). Prepared from *trans*-cinnamic acid (56 mg, 0.380 mmol), and **1.99b**.[33] White solid (63 mg, 0.208 mmol, 55% yield, 2→5% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 10.42 (s, 1H), 7.68 (d, J = 15.8 Hz, 1H), 7.57-7.45 (m, 5H), 7.43-7.36 (m, 3H), 6.77 (d, J = 15.8 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 190.05, 186.25, 142.93, 137.04, 135.38, 135.13, 133.96, 133.13, 132.15, 131.31, 130.99, 129.28, 128.85, 123.87; **IR** (cm^{-1}): 3060, 3027, 2956, 2923, 1705, 1679, 1612, 1572, 1557, 1495, 1448, 1435, 1394, 1327, 1302, 1277, 1206, 1184, 1128, 1093, 1073, 1031, 1018, 998, 974, 883, 844; **MS:** HR-ESI calculated for $[C_{16}H_{11}ClO_2S+Na]^+$: 325.0060, found: 325.0062; **mp**: 108-110 °C.

S-(2-formylphenyl) (E)-3-phenylprop-2-enethioate (1.75). Prepared from (Z)-2-fluoro-3-phenylacrylic acid (285 mg, 1.72 mmol)[34] and **1.99a**. White solid (151 mg, 31% yield, 1→5% EtOAc/hexanes). **^{1}H NMR** (500 MHz, $CDCl_3$):

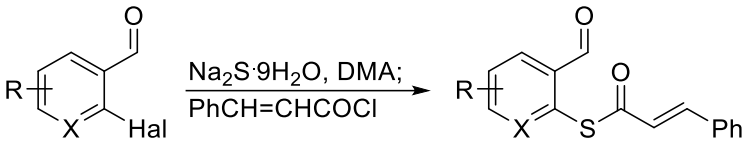
δ 10.27 (s, 1H), 8.11 (dd, J = 7.6, 1.7 Hz, 1H), 7.76 – 7.61 (m, 4H), 7.58 (dd, J = 7.5, 1.4 Hz, 1H), 7.44 (dd, J = 5.2, 2.0 Hz, 3H), 6.88 (d, J = 36.6 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 190.57, 183.82 (d, J = 38.7 Hz), 151.49 (d, J = 270.4 Hz), 137.57, 137.00, 134.48, 131.13, 131.08 (d, J = 29.1 Hz), 130.64 (d, J = 2.8 Hz), 130.55 (d, J = 4.3 Hz), 129.54, 129.34 (d, J = 5.1 Hz), 129.17, 115.20 (d, J = 4.3 Hz); **IR** (cm^{-1}): 1697, 1636, 1585, 1494, 1448, 1265, 1228, 1197, 1153, 944, 825, 750, 689, 555, 437; **MS:** HR-ESI calculated for $[C_{16}H_{11}FO_2S+Na]^+$: 287.0537, found: 287.0593; **mp**: 90-93 °C.



1.100 **1.44l**

Synthesis of S-(2-formyl-4-nitrophenyl) (E)-3-phenylprop-2-enethioate (1.44m). A mixture of S-2-formyl-4-nitrophenyl *N*,*N*-dimethylcarbamothioate **1.100**[35] (74 mg, 0.291 mmol), aqueous NaOH (3M, 1.16 mL, 3.48 mmol, 12.0 equiv), and MeOH (2.30 mL, 56.9 mmol) was refluxed for 3 h, cooled and diluted with H_2O. The aqueous layer was acidified to pH 3 with 10% HCl and extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. To the crude residue was added CH_2Cl_2 (1.45 mL) followed by NEt_3 (48 µL, 0.349 mmol). The mixture was cooled to –78 °C, treated with *trans*-cinnamoyl chloride (58 mg, 0.349 mmol) in THF (3 mL) added dropwise, allowed to slowly warm to 23 °C, and quenched with H_2O. The aqueous layer was extracted with CH_2Cl_2. The combined organic phase was washed with H_2O and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (5→10% EtOAc/hexanes) to afford **1.44l** as a white solid (57 mg, 63% yield). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 10.21 (s, 1H),

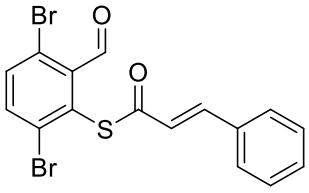
8.86 (d, J = 2.6 Hz, 1H), 8.43 (dd, J_1 = 8.5 Hz, J_2 = 2.6 Hz, 1H), 7.80 (d, J = 8.5 Hz, 1H), 7.76 (d, J = 15.6 Hz, 1H), 7.60-7.57 (m, 2H), 7.47-7.39 (m, 3H), 6.82 (d, J = 15.6 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 188.51, 184.61, 149.12, 144.67, 138.26, 138.14, 137.67, 133.51, 131.88, 129.43, 129.07, 127.72, 124.02, 122.98; **IR** (cm^{-1}): 3091, 3075, 3060, 2919, 2851, 1693, 1672, 1600, 1573, 1521, 1449, 1342, 1300, 1245, 1187, 1033, 994, 913, 882, 847, 817, 755, 741, 689, 570; **MS:** HR-ESI calculated for $[C_{16}H_{11}O_4NS+H]^+$: 314.0482, found: 314.0476; **mp**: 152-154 °C.



1.101 **1.44m-p**

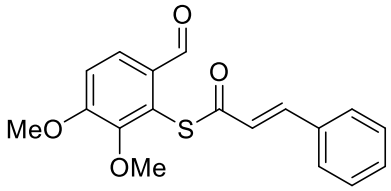
General procedure B for the synthesis of 1.44n-q. A mixture of a 2-haloaldehyde **1.101** (1.50 mmol), sodium sulfide nonahydrate (432 mg, 1.80 mmol, 1.2 equiv), and N,N-dimethylacetamide (0.3 M, 5 mL) was stirred at the temperature indicated until completion by TLC, then cooled to 0 °C, and treated with cinnamoyl chloride (375 mg, 2.25 mmol, 1.5 equiv) in THF (0.45 M, 5 mL). The mixture was stirred for 15 min and quenched with H_2O. The aqueous layer was extracted with Et_2O. The combined organic phase was washed with H_2O and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography using the eluent indicated to afford the corresponding *o*-formyl thioester **1.44**.

S-(3,6-dibromo-2-formylphenyl) (E)-3-phenylprop-2-enethioate (1.44n). Prepared from 3,6-dibromo-2-fluorobenzaldehyde (423 mg, 1.50 mmol, 1 h at 23 °C). White, crystalline solid (207 mg, 32% yield, 2% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 10.14 (s, 1H), 7.70 (d, J = 15.8 Hz, 1H), 7.69 (d, J = 8.6 Hz, 1H), 7.59-7.54 (m, 3H), 7.43-7.36 (m, 3H), 6.77 (d, J = 15.8 Hz, 1H); **^{13}C**



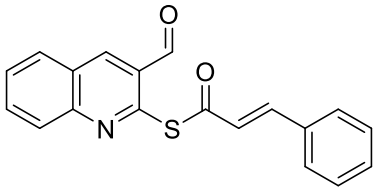
NMR (75 MHz, $CDCl_3$): δ 190.47, 184.40, 143.69, 140.34, 137.01, 136.34, 133.71, 131.46, 131.28, 131.07, 129.26, 128.90, 123.37, 122.05; **IR** (cm^{-1}): 3070, 3056, 3004, 1697, 1671, 1610, 1573, 1545, 1449, 1418, 1400, 1326, 1305, 1278, 1199, 1158, 1115, 1068, 1021, 976, 884, 812, 756, 690, 573, 482; **MS:** HR-ESI calculated for $[C_{16}H_{10}Br_2O_2S+Na]^+$: 446.8660, found: 446.8667; **mp**: 120-123 °C.

S-(6-formyl-2,3-dimethoxyphenyl) (E)-3-phenylprop-2-enethioate (1.44o). Prepared from 2-



chloro-3,4-dimethoxy-benzaldehyde (301 mg, 1.5 mmol, 30 min at 80 °C). White solid (60 mg, 12% yield, 2→20% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 10.16 (s, 1H), 7.86 (d, *J* = 8.7 Hz, 1H), 7.70 (d, *J* = 15.8 Hz, 1H), 7.58-7.55 (m, 2H), 7.41-7.38 (m, 3H), 7.11 (d, *J* = 8.7 Hz, 1H), 6.85 (d, *J* = 15.8 Hz, 1H), 3.96 (s, 3H), 3.83 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 190.19, 186.50, 158.07, 150.00, 142.81, 133.97, 131.24, 130.66, 129.26, 128.82, 126.18, 125.65, 123.79, 113.76, 61.41, 56.35; **IR** (cm^{-1}): 3082, 3016, 2989, 2942, 1673, 1610, 1573, 1482, 1464, 1327, 1302, 1279, 1254, 1214, 1171, 1015, 974, 932, 883, 826, 751, 687, 566, 497, 480; **MS:** HR-ESI calculated for $[C_{18}H_{16}O_4S+H]^+$: 329.0842, found: 329.0838; **mp**: 164-166°C.

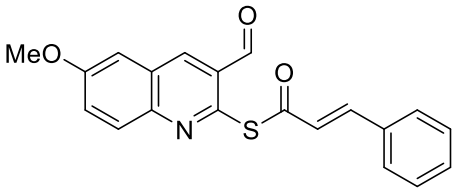
S-(3-formylquinolin-2-yl) (E)-3-phenylprop-2-enethioate (1.44p). Prepared from 2-chloro-3-



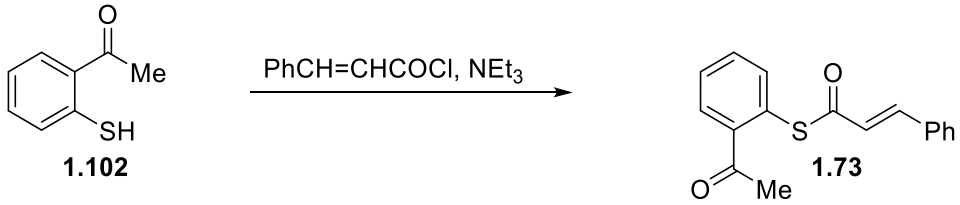
quinolinecarboxaldehyde (287 mg, 1.50 mmol, 30 min at 80 °C). White solid (162 mg, 34% yield, 10:6:84 EtOAc/CH_2Cl_2/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 10.27 (s, 1H), 8.85 (s, 1H), 8.17 (d, *J* = 8.5 Hz, 1H), 8.01 (dd, J_1 = 8.2 Hz, J_2 = 1.0 Hz, 1H), 7.86 (ddd, J_1 = 8.6 Hz, J_2 = 6.9 Hz, J_3 = 1.4 Hz, 1H), 7.75 (d, *J* = 15.8 Hz, 1H), 7.66 (ddd, J_1 = 8.6 Hz, J_2 = 6.9 Hz, J_3 = 1.4 Hz, 1H), 7.58-7.55 (m, 2H), 7.44-7.37 (m, 3H), 6.85 (d, *J* = 15.8 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$):

δ 190.09, 186.90, 151.50, 150.32, 143.95, 138.69, 133.73, 133.00, 131.51, 130.82, 129.80, 129.71, 129.30, 128.95, 128.88, 127.44, 123.70; **IR** (cm^{-1}): 3048, 3032, 1689, 1666, 1607, 1575, 1486, 1447, 1368, 1302, 1165, 1022, 975, 913, 888, 807, 771, 749, 690, 574, 467; **MS:** HR-ESI calculated for $[C_{19}H_{13}O_2NS+Na]^+$: 342.0559, found: 342.0572; **mp**: 154-156 °C dec.

S-(3-formyl-6-methoxyquinolin-2-yl) (E)-3-phenylprop-2-enethioate (1.44q). Prepared from



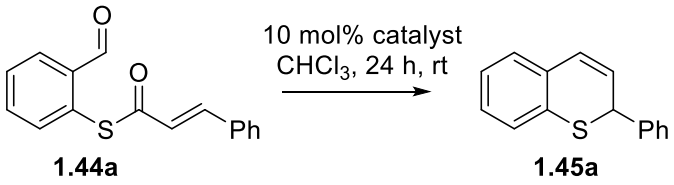
2-chloro-6-methoxyquinoline-3-carboxaldehyde (332 mg, 1.50 mmol, 30 min at 80 °C). Yellow solid (140 mg, 27% yield, 5:20:75 EtOAc/CH_2Cl_2/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 10.25 (s, 1H), 8.70 (s, 1H), 8.04 (d, J = 9.2 Hz, 1H), 7.73 (d, J = 15.8 Hz, 1H), 7.57-7.53 (m, 2H), 7.48 (dd, J_1 = 9.2 Hz, J_2 = 2.7 Hz, 1H), 7.40-7.38 (m, 3H), 7.19 (d, J = 2.7 Hz, 1H), 6.84 (d, J = 15.8 Hz, 1H), 3.93 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 190.38, 187.20, 159.46, 148.37, 146.73, 143.70, 136.99, 133.77, 131.42, 131.07, 131.00, 129.26, 128.90, 126.17, 123.73, 110.16, 106.33, 55.97; **IR** (cm^{-1}): 3055, 3042, 3025, 3002, 1687, 1647, 1617, 1596, 1574, 1493, 1449, 1421, 1395, 1371, 1331, 1233, 1130, 1057, 1023, 969, 926, 842, 810, 748; **MS:** HR-ESI calculated for $[C_{20}H_{15}O_3NS+H]^+$: 350.0845, found: 350.0848; **mp**: 159-162 °C dec.



Synthesis of S-(2-acetylphenyl) (E)-3-phenylprop-2-enethioate (1.73). A mixture of 1-(2-mercaptophenyl)ethan-1-one **1.102**[36] (457 mg, 3.0 mmol) and NEt_3 (0.63 mL, 4.5 mmol) in CH_2Cl_2 (5 mL) was cooled to 0 °C, treated with *trans*-cinnamoyl chloride (750 mg, 4.5 mmol) in CH_2Cl_2 (5 mL) added dropwise, allowed to slowly warm to 23 °C, and quenched with H_2O. The aqueous

layer was extracted with CH_2Cl_2. The combined organic phase was washed with H_2O and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (5→10% EtOAc/hexanes) to afford **1.73** as a white solid (381 mg, 45% yield). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.71 – 7.68 (m, 1H), 7.66 (d, J = 15.8 Hz, 1H), 7.64 – 7.60 (m, 1H), 7.57 – 7.46 (m, 4H), 7.44 – 7.33 (m, 3H), 6.79 (d, J = 15.8 Hz, 1H), 2.61 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 200.92, 187.26, 143.20, 141.96, 136.71, 134.00, 131.27, 130.96, 129.45, 129.11, 128.64, 128.59, 125.88, 124.16, 29.44; **IR** (cm^{-1}): 1675, 1611, 1448, 1247, 1122, 1016, 997, 883, 753, 690, 594, 573; **MS:** HR-ESI calculated for $[C_{17}H_{14}O_2S+H]^+$: 283.0787, found: 283.0843; **mp**: 125-128 °C.

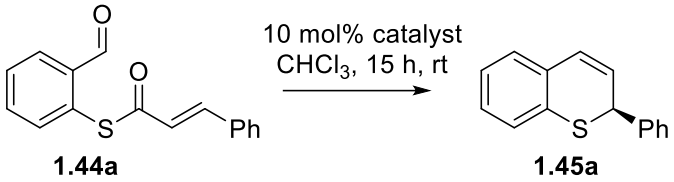
1.5.2 Achiral catalyst survey, synthesis of 1.45a.



1.44a **1.45a**

A mixture of **1.44a** (32 mg, 0.119 mmol), achiral catalyst (10 mol%), and chloroform (0.6 mL, 0.2 M) was stirred at room temperature for 24 h and concentrated under reduced pressure. The residue was purified by flash chromatography (0.5% EtOAc/hexanes) to afford thiochromene **1.45a**. The results are summarized in Table 1.1.

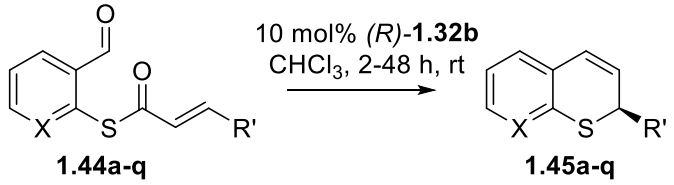
1.5.3 Chiral catalyst survey, synthesis of 1.45a.



1.44a **1.45a**

A mixture of **1.44a** (32 mg, 0.119 mmol), chiral catalyst (10 mol%), and chloroform (0.6 mL, 0.2 M) was stirred at room temperature for 15 h and concentrated under reduced pressure. The residue was purified by flash chromatography (0.5% EtOAc/hexanes) to afford thiochromene **1.45a**, which was analyzed by chiral stationary phase HPLC (see Appendix). The results are summarized in Table 1.2.

1.5.4 Enantioselective synthesis of thiochromenes, general procedure.

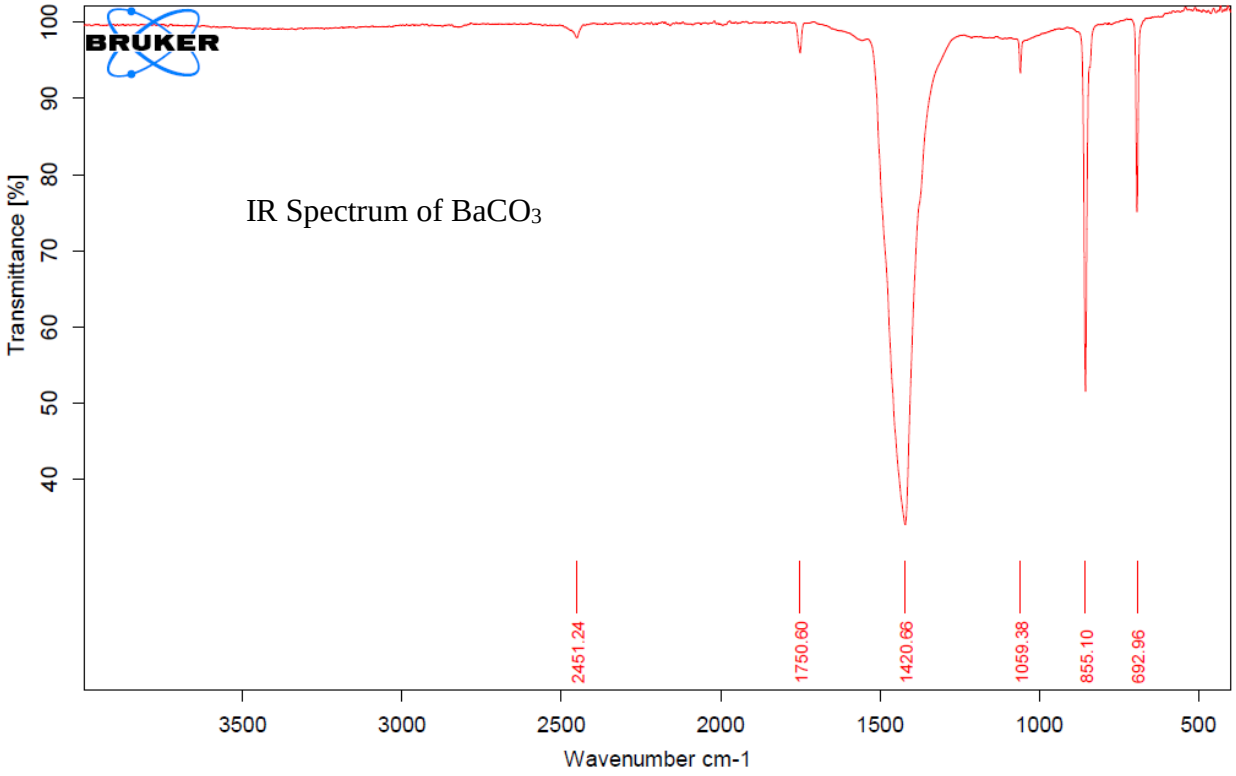


1.44a-q **1.45a-q**

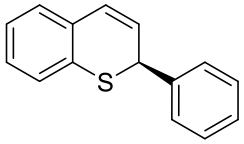
The reaction was carried out as described above using (*R*)-HBTM-2 (**1.32b**) as a catalyst and monitoring the progress by TLC. The mixture was stirred at room temperature for 2-48 h and then concentrated under reduced pressure. The residue was purified by flash chromatography using the eluent indicated. The absolute stereochemistry of **1.45q** was determined by X-ray structure (see below). In all other cases, it was assigned by analogy.

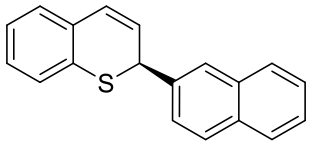
1.5.5 Detection of carbon dioxide.

Thioester **1.44f** (48 mg, 0.16 mmol) was subjected to the usual reaction conditions in the presence of 10 mol % of (*R*)-HBTM-2 **(1.32b)**. During the reaction, a slow stream of argon was passed over the mixture and, via cannula, through an aqueous solution of barium hydroxide in a separate flask. Formation of a heavy white precipitate was observed. After 5 h, the precipitate was collected, rinsed with deionized water, and dried in an oven for 4 h. Barium carbonate thus obtained was weighed (21 mg, 65% yield). Its identity was confirmed by IR.

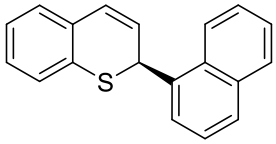


1.5.6 Characterization data for the thiochromene products.

(S)-**2-phenyl-2H-thiochromene (1.45a).** Prepared from **1.44a** (32 mg, 0.119 mmol). Colorless oil  (26.4 mg, 99% yield, 15 h, 0.5% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.35-7.21 (m, 5H), 7.13-7.06 (m, 4H), 6.65 (dd, J_1 = 10.2 Hz, J_2 = 1.5 Hz, 1H), 6.00 (dd, J_1 = 10.2 Hz, J_2 = 5.2 Hz, 1H), 4.87 (dd, J_1 = 5.2 Hz, J_2 = 1.5 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 142.08, 131.26, 130.83, 128.98, 128.94, 128.59, 128.38, 127.96, 127.81, 127.02, 125.80, 125.76, 43.20; **IR** (cm^{-1}): 3061, 3030, 2977, 2930, 1733, 1152, 743, 698; **MS:** HR-ESI calculated for $[C_{15}H_{12}S+Na]^+$: 247.0552, found: 247.0562; **HPLC:** (0.25% isopropanol/hexanes): *(R)*-enantiomer: 17.8 min; *(S)*-enantiomer: 19.5 min; >99% *ee*; $[\alpha]_D^{23}$=+158° (c=1.28, CH_2Cl_2).

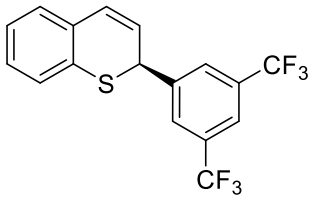
(S)-**2-(naphthalen-2-yl)-2H-thiochromene (1.45b).** Prepared from **1.44b** (70 mg, 0.22 mmol).  White solid (57.1 mg, 95% yield, 24 h, 0.5% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.80-7.73 (m, 4H), 7.52-7.42 (m, 3H), 7.17-7.08 (m, 4H), 6.71 (dd, J_1 = 10.2 Hz, J_2 = 1.2 Hz, 1H), 6.08 (dd, J_1 = 10.2 Hz, J_2 = 5.3 Hz, 1H), 5.04 (dd, J_1 = 5.3 Hz, J_2 = 1.2 Hz, 1H); **^{13}C NMR** (75 MHz $CDCl_3$): δ 139.15, 133.42, 133.08, 131.20, 130.72, 129.20, 128.89, 128.65, 128.43, 128.17, 127.83, 127.04, 126.42, 126.40, 126.24, 126.04, 125.78, 125.48, 43.33; **IR** (cm^{-1}): 2254, 1265, 905, 726, 650; **MS:** HR-ESI calculated for $[C_{19}H_{14}S+Na]^+$: 297.0708, found: 297.0726; **mp**: 90-92 °C; **HPLC:** (0.25% isopropanol/hexanes): *(R)*-enantiomer: 30.0 min; *(S)*-enantiomer: 38.4 min; >99% *ee*; $[\alpha]_D^{24}$=+93.3° (c=1.76, CH_2Cl_2).

(S)-**2-(naphthalen-1-yl)-2H-thiochromene (1.45c).** Prepared from **1.44c** (14 mg, 0.044 mmol).



Colorless oil (11.1 mg, 92% yield, 24 h, 0.5% EtOAc/hexanes).**^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.20 (d, J = 8.5 Hz, 1H), 7.87 (dd, J_1 = 7.9 Hz, J_2 = 1.5 Hz, 1H), 7.76 (d, J =8.3, 1H), 7.59-7.47 (m, 3H), 7.37 (dd, J_1 = 8.1 Hz, J_2 = 7.3 Hz, 1H), 7.18-7.13 (m, 1H), 7.10-7.07 (m, 3H), 6.77 (dd, J_1 = 10.2 Hz, J_2 = 1.7 Hz, 1H), 6.10 (dd, J_1 = 10.2 Hz, J_2 = 5.1 Hz, 1H), 5.72 (dd, J_1 = 5.1 Hz, J_2 = 1.7 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 136.43, 134.42, 131.36, 131.24, 130.62, 129.78, 129.29, 128.62, 128.58, 128.53, 127.24, 126.69, 126.59, 125.99, 125.85, 125.69, 123.52, 39.05; **IR** (cm^{-1}): 3057, 2920, 2851, 1686, 1623, 1509, 1469, 1439, 1324, 1264, 1233, 1072, 777, 757, 736; **MS:** HR-ESI calculated for $[C_{19}H_{14}S+Na]^+$: 297.0708, found: 297.0720; **HPLC:** (0.25% isopropanol/hexanes): *(S)*-enantiomer: 56.1 min; *(R)*-enantiomer: 62.5 min; 99% *ee*; $[\alpha]_D^{24}$=+24° (c=7.7, CH_2Cl_2).

(S)-**2-(3,5-bis(trifluoromethyl)phenyl)-2H-thiochromene (1.45d).** Prepared from **1.44d** (24.5

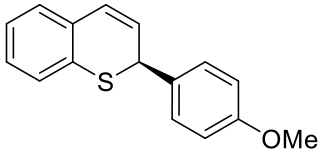


mg, 0.0606 mmol). Colorless oil (21.5 mg, 99% yield, 2 h, 0.5% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.78 (s, 2H), 7.74 (s, 1H), 7.18-7.10 (m, 4H), 6.77 (dd, J_1 = 10.2 Hz, J_2 = 1.3 Hz, 1H), 6.02 (dd, J_1 = 10.2 Hz, J_2 = 5.7 Hz, 1H), 4.90 (dd, J_1 = 5.7 Hz, J_2 = 1.3 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 144.57, 132.12 (q, J = 33.3 Hz), 130.85, 130.50, 129.26, 129.17, 128.67, 127.99 (m), 127.28, 126.42, 125.18, 123.45, 121.86 (sep, J = 3.8 Hz), 121.56, 41.88; **IR** (cm^{-1}): 3063, 1623, 1469, 1439, 1370, 1274, 1165, 1124, 1072, 897, 841, 783, 703, 681; **MS:** HR-ESI calculated for $[C_{17}H_{10}F_6S+H]^+$: 361.0480, found: 361.0481; **HPLC:** (0.25% isopropanol/hexanes): *(R)*-enantiomer: 16.5 min; *(S)*-enantiomer: 18.9 min; 97% *ee*; $[\alpha]_D^{23}$=+150° (c=3.12, CH_2Cl_2).

(S)-**2-(2,5-difluorophenyl)-2H-thiochromene (1.45e).** Prepared from **1.44e** (38 mg, 0.125 mmol). Colorless oil (28.6 mg, 88% yield, 15 h, 2% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.15-7.08 (m, 4H), 7.02-6.95 (m, 2H), 6.90-6.82 (m, 1H), 6.74 (dd, J_1 = 10.2 Hz, J_2 = 1.2 Hz, 1H), 5.95 (dd, J_1 = 10.2 Hz, J_2 = 6.2 Hz, 1H), 5.06 (d, J = 6.2 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 158.89 (dd, J_1 = 242.6, Hz, J_2 = 2.4 Hz), 155.14 (dd, J_1 = 243.2 Hz, J_2 = 2.5 Hz), 138.80, 130.69 (dd, J_1 = 16.2 Hz, J_2 = 7.3 Hz), 130.14, 129.72, 128.96, 128.64, 127.41, 126.11, 123.08, 116.68 (dd, J_1 = 24.9 Hz, J_2 = 8.6 Hz), 116.13 (dd, J_1 = 25.3 Hz, J_2 = 3.6 Hz), 115.72 (dd, J_1 = 24.3 Hz, J_2 = 8.6 Hz), 34.61; **IR** (cm^{-1}): 3064, 2921, 2850, 1623, 1589, 1488, 1438, 1423, 1272, 1241, 1176, 872, 816, 765, 752, 734; **MS:** HR-ESI calculated for $[C_{15}H_{10}F_2S+Na]^+$: 283.0363, found: 283.0370; **HPLC:** (0.25% isopropanol/hexanes): *(R)*-enantiomer: 12.4 min; *(S)*-enantiomer: 13.8 min; >99% *ee*; $[\alpha]_D^{23}$=+222° (c=0.89, CH_2Cl_2).

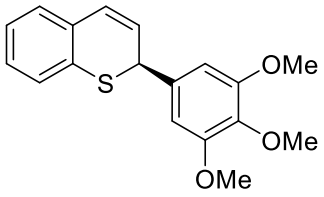
(S)-**4-(2H-thiochromen-2-yl)benzaldehyde (1.45f).** Prepared from **1.44f** (41 mg, 0.138 mmol). Colorless oil (26.3 mg, 99% yield, 5 h, 6% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 9.94 (s, 1H), 7.78 (d, J = 2.2 Hz, 2H), 7.48 (d, J = 2.2 Hz, 2H), 7.15-7.08 (m, 4H), 6.71 (dd, J_1 = 10.2 Hz, J_2 = 1.2 Hz, 1H), 6.01 (dd, J_1 = 10.2 Hz, J_2 = 5.6 Hz, 1H), 4.86 (dd, J_1 = 5.6 Hz, J_2 = 1.2 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 191.84, 148.69, 135.92, 131.01, 130.38, 129.90, 129.65, 128.88, 128.53, 128.31, 127.15, 126.07, 124.34, 42.62; **IR** (cm^{-1}): 3057, 3031, 2920, 2827, 2734, 1698, 1604, 1576, 1469, 1305, 1209, 1167, 1072, 809; **MS:** HR-ESI calculated for $[C_{16}H_{12}OS+Na]^+$: 275.0501, found: 275.0519; **HPLC:** (1% isopropanol/hexanes): *(R)*-enantiomer: 35.0 min; *(S)*-enantiomer: 42.4 min; 99% *ee*; $[\alpha]_D^{22}$=+270° (c=2.63, CH_2Cl_2).

(S)-**2-(4-methoxyphenyl)-2H-thiochromene (1.45g).** Prepared from **1.44g** (23 mg, 0.077 mmol).



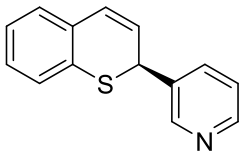
Colorless oil (19.3 mg, 99% yield, 48 h, 0.5% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.24-7.21 (m, 2H), 7.10-7.04 (m, 4H), 6.79 (d, J = 8.4 Hz, 2H), 6.61 (d, J = 10.2 Hz, 1H), 5.96 (dd, J_1 = 10.2 Hz, J_2 = 5.2 Hz, 1H), 4.82 (d, J = 5.2 Hz, 1H), 3.74 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 159.39, 134.18, 131.27, 130.91, 128.93, 128.79, 128.54, 128.32, 127.05, 126.12, 125.68, 114.31, 55.49, 42.62; **IR** (cm^{-1}): 3057, 3029, 3004, 2954, 2928, 2834, 1606, 1581, 1507, 1466, 1438, 1302, 1245, 1173, 1109, 1071, 1031, 880, 832, 787, 763, 737; **MS:** HR-ESI calculated for $[C_{16}H_{14}OS+H]^+$: 255.0838, found: 255.0840; **HPLC:** (0.5% isopropanol/hexanes): *(R)*-enantiomer: 16.9 min; *(S)*-enantiomer: 19.6 min; >99% *ee*; $[\alpha]_D^{24}$=+171° (c=1.48, CH_2Cl_2).

(S)-**2-(3,4,5-trimethoxyphenyl)-2H-thiochromene (1.45h).** Prepared from **1.44h** (61 mg, 0.17 mmol). Colorless oil (50.6 mg, 95% yield, 48 h, 0.5% EtOAc/hexanes).



^{1}H NMR (300 MHz, $CDCl_3$): δ 7.15-7.06(m, 4H), 6.64(dd, J_1 = 10.2 Hz, J_2 = 1.4 Hz, 1H), 6.56(s, 2H), 5.99(dd, J_1 = 10.2 Hz, J_2 = 5.1 Hz, 1H), 4.97(dd, J_1 = 5.1 Hz, J_2 = 1.4 Hz, 1H), 3.80(s, 3H), 3.77(s,6H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 153.46, 137.74, 137.46, 131.23, 130.85, 129.01, 128.65, 128.26, 127.07, 125.98, 125.86, 104.81, 61.01, 56.23, 43.64; **IR** (cm^{-1}): 1265, 904, 726, 650; **MS:** HR-ESI calculated for $[C_{18}H_{18}O_3S+Na]^+$: 337.0869, found: 337.0897; **HPLC:** (5% isopropanol/hexanes): *(R)*-enantiomer: 14.9 min; *(S)*-enantiomer: 18.5 min; >99% *ee*; $[\alpha]_D^{24}$=+45.4° (c=2.60, CH_2Cl_2).

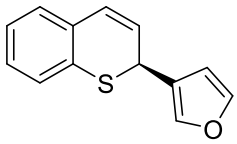
(S)-**3-(2H-thiochromen-2-yl)pyridine (1.45i).** Prepared from **1.44i** (21 mg, 0.0932 mmol).



Colorless oil (16.9 mg, 80% yield, 24 h, 0.5% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.55 (d, J = 2.3 Hz, 1H), 8.47 (dd, J_1 = 4.8 Hz, J_2 = 1.6

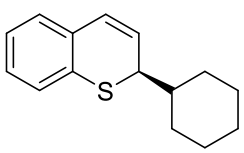
Hz, 1H), 7.63 (ddd, J_1 = 7.9 Hz, J_2 = 2.3, J_3 = 1.6 Hz, 1H), 7.20-7.07 (m, 5H), 6.71 (dd, J_1 = 10.2 Hz, J_2 = 1.3 Hz, 1H), 6.00 (dd, J_1 = 10.2 Hz, J_2 = 5.7 Hz, 1H), 4.80 (dd, J_1 = 5.7 Hz, J_2 = 1.3 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 149.09, 148.87, 137.76, 135.34, 131.10, 129.76, 128.91, 128.54, 127.27, 126.13, 124.24, 123.83, 40.24; **IR** (cm^{-1}): 3051, 3030, 1574, 1469, 1422, 1071, 1025, 777, 710; **MS:** HR-ESI calculated for $[C_{14}H_{11}NS+H]^+$: 226.0685, found: 226.0689; **HPLC:** (20% isopropanol/hexanes): *(S)*-enantiomer: 12.1 min; *(R)*-enantiomer: 15.4 min; 99% *ee*; $[\alpha]_D^{22}$=+195° (c=1.39, CH_2Cl_2).

(S)-**3-(2H-thiochromen-2-yl)furan (1.45j).** Prepared from **1.44j** (23.9 mg, 0.0925 mmol).



Colorless oil (15.2 mg, 77% yield, 24 h, 0.5% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.30 (dd, J_1 = 1.7 Hz, J_2 = 1.7 Hz, 1H), 7.25 (dd, J_1 = 1.7 Hz, J_2 = 0.8 Hz, 1H), 7.18-7.05 (m, 4H), 6.60 (d, J = 10.1 Hz, 1H), 6.33 (dd, J_1 = 1.7 Hz, J_2 = 0.8 Hz, 1H), 6.03 (dd, J_1 = 10.1 Hz, J_2 = 5.7 Hz, 1H), 4.68 (d, J = 5.7 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 143.69, 140.21, 131.53, 130.54, 128.82, 128.48, 128.32, 127.53, 125.99, 125.87, 125.08, 109.89, 34.01; **IR** (cm^{-1}): 3058, 2919, 2850, 1585, 1501, 1469, 1438, 1371, 1278, 1156, 1135, 1071, 1021, 872, 800, 784, 735; **MS:** HR-ESI calculated for $[C_{13}H_{10}OS+H]^+$: 215.0525, found: 215.0526; **HPLC:** (0.25% isopropanol/hexanes): *(R)*-enantiomer: 19.3 min; *(S)*-enantiomer: 23.7 min; >99% *ee*; $[\alpha]_D^{23}$=+23.8° (c=1.60, CH_2Cl_2).

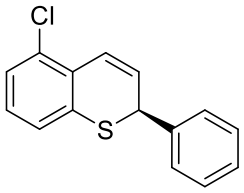
(R)-**2-cyclohexyl-2H-thiochromene (1.45k).** Prepared from **1.44k** (10 mg, 0.0365 mmol).



Colorless oil (8.3 mg, 99% yield, 24 h, 0.5% EtOAc/hexanes). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.17 (s, J = 7.7 Hz, 1H), 7.08-6.99 (m, 3H), 6.48 (d, J = 10.3 Hz, 1H), 5.88 (dd, J_1 = 10.3 Hz, J_2 = 6.0 Hz, 1H), 3.41 (ddd, J_1 = 7.1 Hz, J_2 = 6.0 Hz, J_3 = 1.1 Hz, 1H), 1.88-1.85 (m, 1H), 1.74-1.49 (m, 5H), 1.19-1.00 (m, 5H); **^{13}C NMR** (125 MHz, $CDCl_3$):

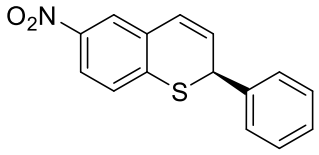
δ 131.94, 131.93, 128.32, 128.10, 128.01, 127.03, 125.54, 125.23, 45.18, 44.21, 29.70, 29.39, 26.59, 26.39, 26.34; **IR** (cm^{-1}): 3054, 3026, 3011, 2923, 2851, 1470, 1440, 1073, 778; **MS:** HR-ESI calculated for $[C_{15}H_{18}S+H]^+$: 231.1202, found: 231.1201; **HPLC:** (0.05% isopropanol/hexanes): *(R)*-enantiomer: 18.2 min; *(S)*-enantiomer: 20.8 min; 95% *ee*; $[\alpha]_D^{23}$=-67° (c=0.97, CH_2Cl_2).

(S)-**5-chloro-2-phenyl-2H-thiochromene (1.45l).** Prepared from **1.44l** (26 mg, 0.086 mmol).



Colorless oil (12 mg, 54% yield, 24 h, 0.5% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.34-7.25 (m, 5H), 7.15-6.98 (m, 4H), 6.14 (dd, J_1 = 10.4 Hz, J_2 = 5.3 Hz, 1H), 4.86 (dd, J_1 = 5.3 Hz, J_2 = 1.6 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 141.09, 133.55, 133.45, 129.01, 128.93, 128.69, 128.16, 127.90, 127.41, 126.88, 125.65, 125.37, 42.81; **IR** (cm^{-1}): 3082, 3059, 3029, 2955, 2922, 2851, 1599, 1574, 1547, 1491, 1431, 1380, 1262, 1190, 1098, 1076, 1030, 881, 844, 773, 759, 699; **MS:** HR-ESI calculated for $[C_{15}H_{11}ClS+Na]^+$: 281.0162, found: 281.0171; **HPLC:** (hexanes): *(R)*-enantiomer: 34.5 min; *(S)*-enantiomer: 37.3 min; 98% *ee*; $[\alpha]_D^{23}$=+230° (c=0.68, CH_2Cl_2).

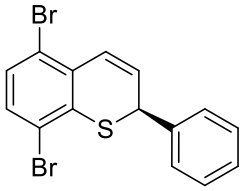
(S)-**6-nitro-2-phenyl-2H-thiochromene (1.45m).** Prepared from **1.44m** (27 mg, 0.0862 mmol).



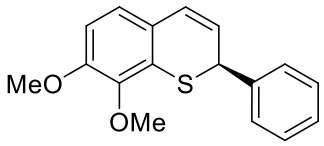
Colorless oil (12.3 mg, 53% yield, 24 h, 0.5% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.98 (d, J = 2.4 Hz, 1H), 7.94 (dd, J_1 = 8.5 Hz, J_2 = 2.4 Hz, 1H), 7.30-7.21 (m, 6H), 6.72 (dd, J_1 = 10.3 Hz, J_2 = 1.6 Hz, 1H), 6.11 (dd, J_1 = 10.3 Hz, J_2 = 5.3 Hz, 1H), 4.97 (dd, J_1 = 5.3 Hz, J_2 = 1.6 Hz, 1H), 3.89 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 141.13, 140.57, 131.27, 129.22, 128.52, 127.77, 127.70, 127.28, 127.15, 123.20, 122.88, 43.48; **IR** (cm^{-1}): 2921, 2852, 1597, 1565, 1514, 1337, 1066, 759; **MS:** HR-ESI calculated

for $[C_{15}H_{11}NO_2S+H]^+$: 270.0583, found: 270.0584; **HPLC:** (0.5% isopropanol/hexanes): *(R)*-enantiomer: 40.4 min; *(S)*-enantiomer: 49.0 min; 97% *ee*; $[\alpha]_D^{23}$=+217° (c=0.45, CH_2Cl_2).

(S)-**5,8-dibromo-2-phenyl-2H-thiochromene (1.45n).** Prepared from **1.44n** (60.1 mg, 0.141 mmol). Colorless oil (43.6 mg, 81% yield, 24 h, 2% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.38-7.18 (m, 7H), 7.03 (dd, J_1 = 10.3 Hz, J_2 = 1.9 Hz, 1H), 6.07 (dd, J_1 = 10.3 Hz, J_2 = 4.9 Hz, 1H), 4.97 (dd, J_1 = 4.9 Hz, J_2 = 1.9 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 140.41, 136.18, 132.87, 132.07, 130.26, 129.08, 128.60, 128.39, 128.24, 128.00, 122.90, 120.17, 44.24; **IR** (cm^{-1}): 3082, 3058, 3028, 2919, 2868, 2850, 1598, 1490, 1452, 1425, 1382, 1361, 1082, 897, 798, 759, 695; **MS:** HR-EI calculated for $[C_{15}H_{10}Br_2S\bullet]^+$: 381.8844, found: 381.8904; **HPLC:** (hexanes): *(R)*-enantiomer: 41.3 min; *(S)*-enantiomer: 45.3 min; 96% *ee*; $[\alpha]_D^{22}$=+62.0° (c=3.35, CH_2Cl_2).



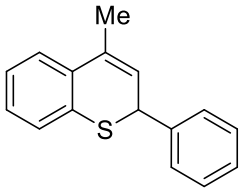
(S)-**7,8-dimethoxy-2-phenyl-2H-thiochromene (1.45o).** Prepared from **1.44o** (27 mg, 0.0822 mmol). Colorless oil (21 mg, 90% yield, 24 h, 5% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.37-7.23 (m, 5H), 6.86 (d, J = 8.4 Hz, 1H), 6.63 (d, J = 8.4 Hz, 1H), 6.57 (dd, J_1 = 10.2 Hz, J_2 = 1.6 Hz, 1H), 5.84 (dd, J_1 = 10.2 Hz, J_2 = 4.9 Hz, 1H), 4.89 (dd, J_1 = 4.9 Hz, J_2 = 1.6 Hz, 1H), 3.83 (s, 3H), 3.76 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 153.01, 144.51, 142.47, 128.84, 128.45, 128.00, 127.83, 126.54, 125.03, 124.36, 123.30, 108.76, 60.24, 56.02, 42.76; **IR** (cm^{-1}): 2997, 2934, 2835, 1592, 1483, 1444, 1406, 1274, 1046, 1015, 754; **MS:** HR-ESI calculated for $[C_{17}H_{16}O_2S+Na]$: 307.0763, found: 307.0767; **HPLC:** (5% isopropanol/hexanes): *(R)*-enantiomer: 12.0 min; *(S)*-enantiomer: 13.1 min; 99% *ee*; $[\alpha]_D^{22}$=-6.8° (c=0.76, CH_2Cl_2).



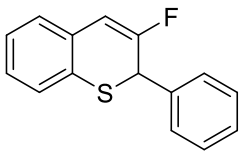
(S)-**2-phenyl-2H-thiopyrano[2,3-b]quinoline (1.45p).** Prepared from **1.44p** (46 mg, 0.144 mmol). White solid (26 mg, 66% yield, 24 h, 5:5:90 EtOAc/CH_2Cl_2/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.89 (d, J = 8.4 Hz, 1H), 7.72 (s, 1H), 7.70 (d, J = 9.4 Hz, 1H), 7.60 (ddd, J_1 = 8.4 Hz, J_2 = 6.9 Hz, J_3 = 1.4 Hz, 1H), 7.44-7.24 (m, 6H), 6.73 (dd, J_1 = 10.3 Hz, J_2 = 1.6 Hz, 1H), 6.14 (dd, J_1 = 10.3 Hz, J_2 = 4.9 Hz, 1H), 5.26 (dd, J_1 = 4.9 Hz, J_2 = 1.6 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 156.86, 148.05, 141.83, 133.37, 130.10, 129.12, 128.22, 128.20, 128.16, 127.92, 127.90, 127.27, 126.99, 126.12, 125.11, 46.08; **IR** (cm^{-1}): 3058, 3027, 2923, 2858, 1614, 1584, 1556, 1487, 1394, 1137, 1063, 750, 698; **MS:** HR-ESI calculated for $[C_{18}H_{13}NS+Na]^+$: 298.0661, found: 298.0668; **HPLC:** (20% isopropanol/hexanes): *(R)*-enantiomer: 14.1 min; *(S)*-enantiomer: 25.9 min; >99% *ee*; $[\alpha]_D^{22}$=-47° (c=0.81, CH_2Cl_2).

(S)-**7-methoxy-2-phenyl-2H-thiopyrano[2,3-b]quinoline (1.45q).** Prepared from **1.44q** (89.1 mg, 0.255 mmol). Yellow crystalline solid (59.6 mg, 77% yield, 24 h, 5:5:90 EtOAc/CH_2Cl_2/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.79(d, J = 9.2 Hz, 1H), 7.61(s, 1H), 7.38-7.23(m, 6H), 6.98(d, J = 2.8 Hz, 1H) 6.70(dd, J_1 = 10.3 Hz, J_2 = 1.7 Hz, 1H), 6.13(dd, J_1 = 10.3 Hz, J_2 = 5.0 Hz, 1H), 5.22(dd, J_1 = 5.0 Hz, J_2 = 1.7 Hz, 1H), 3.89(s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 157.57, 153.62, 144.12, 141.83, 132.43, 129.63, 129.06, 128.41, 128.09, 127.89, 127.87, 127.40, 125.43, 122.23, 105.87, 55.73, 45.92; **IR** (cm^{-1}): 3059, 3027, 3003, 2959, 2931, 1619, 1584, 1492, 1452, 1370, 1346, 1288, 1252, 1229, 1167, 1070, 1028, 956, 912, 830, 755, 698; **MS:** HR-ESI calculated for $[C_{19}H_{15}NOS+H]^+$: 306.0947, found: 306.0953; **mp**: 152-154 °C; **HPLC:** (20% isopropanol/hexanes): *(R)*-enantiomer: 10.2 min; *(S)*-enantiomer: 31.9 min; 99% *ee*; $[\alpha]_D^{22}$=+6.57° (c=2.04, CH_2Cl_2).

4-methyl-2-phenyl-2H-thiochromene (1.74). Prepared from **1.73** (32 mg, 0.11 mmol) with DHPB **1.63a**. Colorless oil (trace yield, 72 h, 2% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.44-7.14 (m, 9H), 6.00 (dd, J_1 = 5.3 Hz, J_2 = 1.4 Hz, 1H), 4.85 (dd, J_1 = 5.3 Hz, J_2 = 1.4 Hz, 1H), 2.25 (s, 3H).



3-fluoro-2-phenyl-2H-thiochromene (1.76). Prepared from **1.75** using catalyst **1.63a** (40 mg, 0.14 mmol). Colorless oil (9 mg, 28% yield, 72 h, 0.5% EtOAc/hexanes). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.31-7.25 (m, 5H), 7.19-7.17 (m, 1H), 7.15-7.09 (m, 3H), 6..42 (d, J = 14.6 Hz, 1H), 4.77 (d, J = 12.6 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 157.71 (d, J = 272.8 Hz), 139.77, 130.62 (d, J = 8.1 Hz), 129.03, 128.38, 127.89, 127.88 (d, J = 8.7 Hz), 126.95, 126.46, 126.12, 107.55 (d, J = 22.8 Hz), 43.11 (d, J = 28.7 Hz); **IR** (cm^{-1}): 2997, 2934, 2835, 1592, 1483, 1444, 1406, 1274, 1046, 1015, 754; **MS:** HR-ESI calculated for $[C_{15}H_{11}FS+H]^+$:: 241.1335, found: 241.1341.



1.5.7 X-Ray structure of 1.45q.

Table 1.5: Crystal data and structure refinement for **1.45q**.

Identification code	v23315/lt/x8/Birman-NAA-III-23	
Empirical formula	C19 H15 N O S	
Formula weight	305.38	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 5.5711(2) Å	α= 90°.
	b = 6.5999(2) Å	β= 90°.
	c = 40.0657(12) Å	γ = 90°.
Volume	1473.16(8) $Å^3$	
Z	4	
Density (calculated)	1.377 Mg/m^3	
Absorption coefficient	0.220 mm^{-1}	
F(000)	640	
Crystal size	0.459 x 0.372 x 0.283 mm^3	
Theta range for data collection	2.033 to 40.295°.	
Index ranges	$-10\leq h\leq 10$, $-11\leq k\leq 12$, $-72\leq l\leq 72$	
Reflections collected	74764	
Independent reflections	9271 [R(int) = 0.033]	
Completeness to theta = 25.242°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8628 and 0.8254	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	9271 / 0 / 259	
Goodness-of-fit on F^2	1.085	
Final R indices [I>2sigma(I)]	R1 = 0.0317, wR2 = 0.0832	
R indices (all data)	R1 = 0.0335, wR2 = 0.0841	
Absolute structure parameter	-0.020(9)	
Largest diff. peak and hole	0.525 and -0.193 $e.Å^{-3}$	

Table 1.6: Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for **1.45q**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(15)	-583(1)	9299(1)	6255(1)	15(1)
O(22)	10260(1)	4125(1)	5273(1)	17(1)
N(1)	2817(1)	8362(1)	5854(1)	14(1)
C(2)	1477(2)	7558(1)	6088(1)	13(1)
C(3)	1760(2)	5551(1)	6214(1)	14(1)
C(4)	3554(2)	4388(1)	6073(1)	14(1)
C(5)	5045(2)	5182(1)	5819(1)	13(1)
C(6)	6952(2)	4069(1)	5671(1)	15(1)
C(7)	8357(2)	4986(1)	5431(1)	14(1)
C(8)	7884(2)	6999(1)	5327(1)	15(1)
C(9)	6047(2)	8082(1)	5466(1)	15(1)
C(10)	4590(2)	7206(1)	5717(1)	13(1)
C(11)	10808(2)	2073(2)	5354(1)	22(1)
C(12)	267(2)	4790(1)	6485(1)	16(1)
C(13)	-1558(2)	5786(2)	6628(1)	17(1)
C(14)	-2524(2)	7828(1)	6534(1)	15(1)
C(16)	-2984(2)	9190(1)	6832(1)	14(1)
C(17)	-1295(2)	9322(2)	7088(1)	16(1)
C(18)	-1666(2)	10610(2)	7357(1)	19(1)
C(19)	-3726(2)	11811(2)	7371(1)	21(1)
C(20)	-5405(2)	11695(2)	7116(1)	20(1)
C(21)	-5044(2)	10382(2)	6848(1)	17(1)

Table 1.7: Bond lengths (Å) and angles (°) for **1.45q**.

S(15)-C(2)	1.7561(9)	C(4)-H(4)	0.98(2)	C(11)-H(11A)	0.954(19)	C(16)-C(17)	1.3945(12)
S(15)-C(14)	1.8325(10)	C(5)-C(10)	1.4199(12)	C(11)-H(11B)	0.89(2)	C(17)-C(18)	1.3876(14)
O(22)-C(7)	1.3603(11)	C(5)-C(6)	1.4201(12)	C(11)-H(11C)	0.966(17)	C(17)-H(17)	0.88(2)
O(22)-C(11)	1.4256(13)	C(6)-C(7)	1.3802(13)	C(12)-C(13)	1.3390(14)	C(18)-C(19)	1.3960(16)
N(1)-C(2)	1.3126(12)	C(6)-H(6)	0.961(19)	C(12)-H(12)	0.96(2)	C(18)-H(18)	0.95(2)
N(1)-C(10)	1.3633(12)	C(7)-C(8)	1.4168(13)	C(13)-C(14)	1.4994(14)	C(19)-C(20)	1.3897(16)
C(2)-C(3)	1.4258(12)	C(8)-C(9)	1.3665(13)	C(13)-H(13)	0.974(18)	C(19)-H(19)	0.94(2)
C(3)-C(4)	1.3806(12)	C(8)-H(8)	1.006(18)	C(14)-C(16)	1.5176(13)	C(20)-C(21)	1.3943(14)
C(3)-C(12)	1.4576(12)	C(9)-C(10)	1.4141(12)	C(14)-H(14)	0.955(19)	C(20)-H(20)	0.92(2)
C(4)-C(5)	1.4155(12)	C(9)-H(9)	0.968(17)	C(16)-C(21)	1.3926(13)	C(21)-H(21)	0.95(2)

C(2)-S(15)-C(14)	105.73(4)	O(22)-C(11)-H(11C)	110.3(12)
C(7)-O(22)-C(11)	117.23(8)	H(11A)-C(11)-H(11C)	109.8(15)
C(2)-N(1)-C(10)	118.30(8)	H(11B)-C(11)-H(11C)	111.1(16)
N(1)-C(2)-C(3)	124.43(8)	C(13)-C(12)-C(3)	125.64(9)
N(1)-C(2)-S(15)	112.32(6)	C(13)-C(12)-H(12)	115.8(12)
C(3)-C(2)-S(15)	123.09(7)	C(3)-C(12)-H(12)	118.5(12)
C(4)-C(3)-C(2)	116.91(8)	C(12)-C(13)-C(14)	127.34(9)
C(4)-C(3)-C(12)	121.75(8)	C(12)-C(13)-H(13)	116.8(11)
C(2)-C(3)-C(12)	121.32(8)	C(14)-C(13)-H(13)	115.9(11)
C(3)-C(4)-C(5)	120.87(8)	C(13)-C(14)-C(16)	113.25(8)
C(3)-C(4)-H(4)	120.9(11)	C(13)-C(14)-S(15)	114.66(7)
C(5)-C(4)-H(4)	118.0(11)	C(16)-C(14)-S(15)	105.43(6)
C(4)-C(5)-C(10)	116.79(8)	C(13)-C(14)-H(14)	109.6(11)
C(4)-C(5)-C(6)	123.16(8)	C(16)-C(14)-H(14)	108.4(11)
C(10)-C(5)-C(6)	120.03(8)	S(15)-C(14)-H(14)	105.0(11)
C(7)-C(6)-C(5)	119.16(8)	C(21)-C(16)-C(17)	119.20(8)
C(7)-C(6)-H(6)	122.5(11)	C(21)-C(16)-C(14)	120.56(8)
C(5)-C(6)-H(6)	118.2(11)	C(17)-C(16)-C(14)	120.19(8)
O(22)-C(7)-C(6)	125.72(8)	C(18)-C(17)-C(16)	120.58(9)
O(22)-C(7)-C(8)	113.59(8)	C(18)-C(17)-H(17)	119.8(12)
C(6)-C(7)-C(8)	120.70(8)	C(16)-C(17)-H(17)	119.6(12)
C(9)-C(8)-C(7)	120.66(8)	C(17)-C(18)-C(19)	120.16(9)
C(9)-C(8)-H(8)	120.5(10)	C(17)-C(18)-H(18)	118.2(12)
C(7)-C(8)-H(8)	118.8(10)	C(19)-C(18)-H(18)	121.6(12)
C(8)-C(9)-C(10)	120.35(8)	C(20)-C(19)-C(18)	119.45(9)
C(8)-C(9)-H(9)	121.7(10)	C(20)-C(19)-H(19)	120.9(13)
C(10)-C(9)-H(9)	118.0(10)	C(18)-C(19)-H(19)	119.6(13)
N(1)-C(10)-C(9)	118.21(8)	C(19)-C(20)-C(21)	120.31(9)
N(1)-C(10)-C(5)	122.69(8)	C(19)-C(20)-H(20)	118.7(13)
C(9)-C(10)-C(5)	119.09(8)	C(21)-C(20)-H(20)	121.0(13)
O(22)-C(11)-H(11A)	106.4(12)	C(16)-C(21)-C(20)	120.30(9)
O(22)-C(11)-H(11B)	111.2(13)	C(16)-C(21)-H(21)	118.2(13)
H(11A)-C(11)-H(11B)	108.0(16)	C(20)-C(21)-H(21)	121.4(13)

Table 1.8: Anisotropic displacement parameters ($Å^2$ x 10^3) for **1.45q**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(15)	17(1)	13(1)	16(1)	1(1)	3(1)	2(1)
O(22)	18(1)	14(1)	19(1)	2(1)	4(1)	3(1)
N(1)	15(1)	13(1)	14(1)	1(1)	1(1)	1(1)
C(2)	14(1)	12(1)	13(1)	0(1)	-1(1)	0(1)
C(3)	15(1)	11(1)	14(1)	1(1)	0(1)	-1(1)
C(4)	16(1)	11(1)	15(1)	1(1)	2(1)	0(1)
C(5)	15(1)	11(1)	14(1)	1(1)	0(1)	0(1)
C(6)	16(1)	12(1)	15(1)	1(1)	1(1)	1(1)
C(7)	14(1)	13(1)	14(1)	0(1)	0(1)	1(1)
C(8)	17(1)	14(1)	15(1)	2(1)	2(1)	1(1)
C(9)	17(1)	13(1)	15(1)	3(1)	1(1)	1(1)
C(10)	14(1)	11(1)	13(1)	1(1)	-1(1)	1(1)
C(11)	22(1)	15(1)	27(1)	1(1)	6(1)	4(1)
C(12)	20(1)	12(1)	16(1)	1(1)	3(1)	-1(1)
C(13)	20(1)	14(1)	18(1)	0(1)	4(1)	-3(1)
C(14)	14(1)	15(1)	15(1)	-2(1)	1(1)	-2(1)
C(16)	13(1)	14(1)	13(1)	0(1)	1(1)	-1(1)
C(17)	15(1)	18(1)	15(1)	-2(1)	-2(1)	0(1)
C(18)	21(1)	21(1)	16(1)	-3(1)	-2(1)	-1(1)
C(19)	24(1)	20(1)	18(1)	-4(1)	3(1)	0(1)
C(20)	19(1)	19(1)	21(1)	-2(1)	2(1)	2(1)
C(21)	15(1)	18(1)	17(1)	-1(1)	0(1)	2(1)

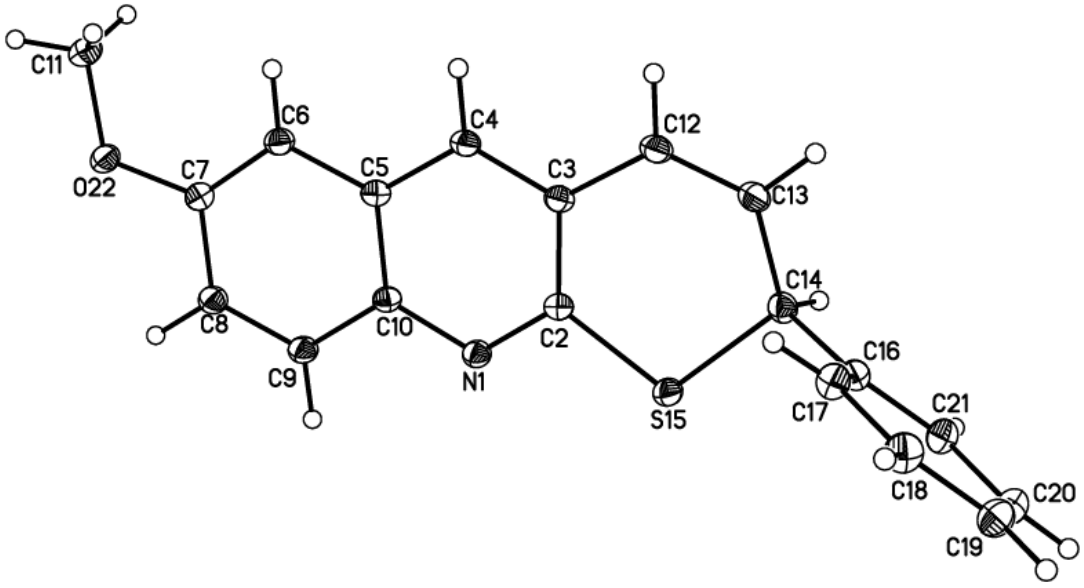
Table 1.9: Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for **1.45q**.

	x	y	z	U(eq)
H(4)	3920(30)	3030(30)	6159(5)	25(4)
H(6)	7260(30)	2720(30)	5752(5)	23(4)
H(8)	8930(30)	7620(30)	5150(4)	21(4)
H(9)	5710(30)	9460(30)	5400(4)	16(4)
H(11A)	12220(30)	1740(30)	5232(5)	22(4)
H(11B)	9640(40)	1240(30)	5288(5)	26(4)
H(11C)	11100(30)	1940(30)	5591(4)	20(4)
H(12)	540(40)	3440(30)	6564(5)	28(5)
H(13)	-2380(30)	5100(30)	6810(4)	21(4)
H(14)	-3990(30)	7670(30)	6414(4)	20(4)
H(17)	30(40)	8600(30)	7077(4)	27(5)
H(18)	-450(30)	10680(30)	7525(5)	26(4)
H(19)	-3960(40)	12690(30)	7553(5)	31(5)
H(20)	-6750(40)	12510(30)	7126(5)	30(5)
H(21)	-6210(40)	10240(30)	6676(5)	34(5)

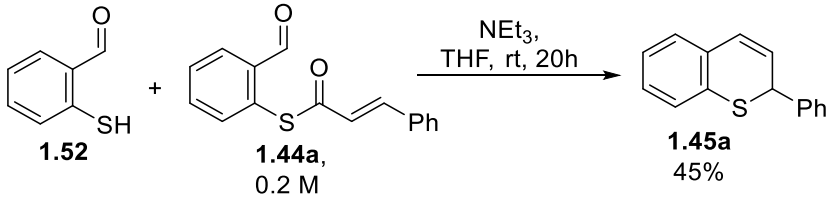
Table 1.10: Torsion angles (°) for **1.45q**.

C(10)-N(1)-C(2)-C(3)	0.69(13)	C(8)-C(9)-C(10)-C(5)	-0.77(14)
C(10)-N(1)-C(2)-S(15)	176.17(6)	C(4)-C(5)-C(10)-N(1)	0.07(13)
C(14)-S(15)-C(2)-N(1)	172.73(7)	C(6)-C(5)-C(10)-N(1)	-178.67(8)
C(14)-S(15)-C(2)-C(3)	-11.73(9)	C(4)-C(5)-C(10)-C(9)	179.21(8)
N(1)-C(2)-C(3)-C(4)	-0.92(13)	C(6)-C(5)-C(10)-C(9)	0.47(13)
S(15)-C(2)-C(3)-C(4)	-175.93(7)	C(4)-C(3)-C(12)-C(13)	-177.58(10)
N(1)-C(2)-C(3)-C(12)	177.36(9)	C(2)-C(3)-C(12)-C(13)	4.22(15)
S(15)-C(2)-C(3)-C(12)	2.35(12)	C(3)-C(12)-C(13)-C(14)	2.72(17)
C(2)-C(3)-C(4)-C(5)	0.70(13)	C(12)-C(13)-C(14)-C(16)	-134.92(11)
C(12)-C(3)-C(4)-C(5)	-177.58(8)	C(12)-C(13)-C(14)-S(15)	-13.86(14)
C(3)-C(4)-C(5)-C(10)	-0.32(13)	C(2)-S(15)-C(14)-C(13)	16.16(8)
C(3)-C(4)-C(5)-C(6)	178.38(8)	C(2)-S(15)-C(14)-C(16)	141.43(6)
C(4)-C(5)-C(6)-C(7)	-178.20(8)	C(13)-C(14)-C(16)-C(21)	-138.40(9)
C(10)-C(5)-C(6)-C(7)	0.46(13)	S(15)-C(14)-C(16)-C(21)	95.46(9)
C(11)-O(22)-C(7)-C(6)	2.20(14)	C(13)-C(14)-C(16)-C(17)	44.18(12)
C(11)-O(22)-C(7)-C(8)	-177.83(9)	S(15)-C(14)-C(16)-C(17)	-81.96(10)
C(5)-C(6)-C(7)-O(22)	178.87(8)	C(21)-C(16)-C(17)-C(18)	0.57(15)
C(5)-C(6)-C(7)-C(8)	-1.10(13)	C(14)-C(16)-C(17)-C(18)	178.02(9)
O(22)-C(7)-C(8)-C(9)	-179.16(9)	C(16)-C(17)-C(18)-C(19)	-0.90(16)
C(6)-C(7)-C(8)-C(9)	0.82(14)	C(17)-C(18)-C(19)-C(20)	0.42(17)
C(7)-C(8)-C(9)-C(10)	0.14(14)	C(18)-C(19)-C(20)-C(21)	0.37(17)
C(2)-N(1)-C(10)-C(9)	-179.40(8)	C(17)-C(16)-C(21)-C(20)	0.23(14)
C(2)-N(1)-C(10)-C(5)	-0.25(13)	C(14)-C(16)-C(21)-C(20)	-177.22(9)
C(8)-C(9)-C(10)-N(1)	178.41(9)	C(19)-C(20)-C(21)-C(16)	-0.70(16)

Projection view of **1.45q** with 50% probability ellipsoids:

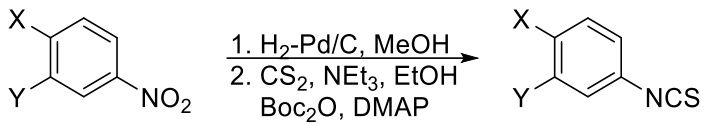


1.5.8 Thiolate promoted synthesis of 1.45a.



A mixture of **1.44a** (32 mg, 0.119 mmol), triethylamine (0.119 mmol), 2-mercaptobenzaldehyde (0.119 mmol), and THF (0.6 mL, 0.2 M) was stirred at room temperature for 20 h and concentrated under reduced pressure. The residue was purified by flash chromatography (0.5% EtOAc/hexanes) to afford thiochromene **1.45a** (12 mg, 45%).

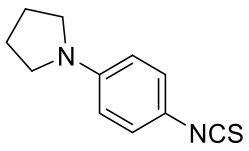
1.5.9 Preparation of isothiocyanates 1.104d and 1.104e.[37]



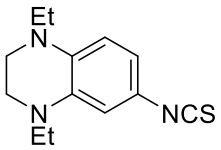
1.103d, X = N-pyrrolidino, Y = H
1.103e, X+Y = $EtNCH_2CH_2NEt$

1.104d, X = N-pyrrolidino, Y = H
1.104e, X+Y = $N(Et)CH_2CH_2N(Et)$

The starting nitroarene **1.103d**[38] or **e**[39] was hydrogenated in methanol over 5% Pd/C (ca. 50 mg per 1 mmol of substrate) at 20-40 psi in a Parr shaker apparatus. The resulting solution was filtered through Celite to remove the catalyst and rotary evaporated to give the crude aniline as thick brown oil, which was protected from air and dissolved in 95% ethanol (ca. 0.15 M). The solution was treated with triethylamine (1 equiv) and carbon disulfide (10 equiv) at room temperature. After 1.5 h, the reaction mixture was cooled to 0 °C and treated with a solution of Boc_2O (1 equiv) and DMAP (3 mol %) in ethanol (1 mL per 1 mmol) added dropwise. The resulting mixture was stirred for a 0.5 h at 0 °C, then at room temperature for 3.5 h, and rotary evaporated. The evaporation residue was loaded directly onto a silica gel column and eluted with ethyl acetate in hexanes.

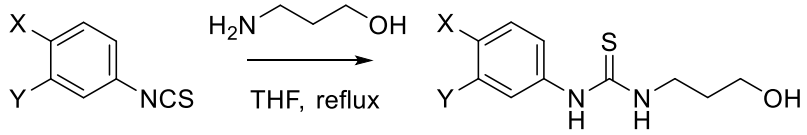


1.104d: Isolated as a pale-yellow powder (672 mg; 89% yield,) after chromatography (5% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δδ 7.08 (d, J = 9.0 Hz, 2H), 6.43 (d, J = 9.0 Hz, 2H), 3.34 – 3.22 (m, 4H), 2.06 – 1.96 (m, 4H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 146.87, 131.77, 126.84, 117.59, 111.80, 47.69, 25.55; **IR** (cm^{-1}): 2969, 2090, 1776, 1739, 1598, 1512, 1482, 1369, 1137, 1081, 916, 827, 804, 676, 505, 458; **MS:** HR-ESI calculated for $[C_{11}H_{12}N_2S+H]^+$: 205.0794, found: 205.0815; **mp** 76-79 °C.



1.104e: Isolated as a pale yellow viscous liquid (1.85 g; 71% yield) after chromatography (5→15% EtOAc/hexanes). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.52 (dd, *J* = 8.4, 2.3 Hz, 1H), 6.38 (d, *J* = 8.5 Hz, 1H), 6.35 (d, *J* = 2.3 Hz, 1H), 3.35 – 3.26 (m, 8H), 1.18 – 1.13 (m, 6H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 135.32, 134.70, 130.81, 119.45, 115.19, 109.96, 107.50, 46.30, 46.06, 45.41, 45.32, 10.34, 10.22; **IR** (cm^{-1}): 2968, 2117, 1592, 1513, 1358, 1310, 1250, 1174, 1092, 993, 827, 770, 593; **MS:** HR-ESI calculated for $[C_{13}H_{17}N_3S]^+$: 247.1138, found: 247.1162.

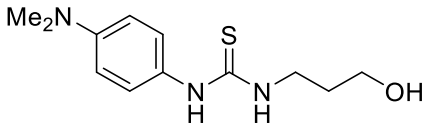
1.5.10 Preparation of thioureas 1.105c-e.



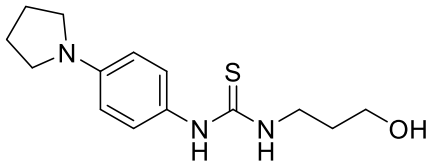
1.104c, X = Me_2N, Y = H
1.104d, X = N-pyrrolidino, Y = H
1.104e, X+Y =N(Et)CH_2CH_2N(Et)

1.105c-e

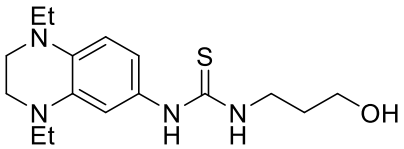
A solution of a 3-amino-1-propanol (1 equiv) was treated with the corresponding isothiocyanate **1.104c-e**(1 equiv) in refluxing THF (0.4 M) overnight and rotary evaporated. The residue was purified by column chromatography on silica gel under conditions outlined below.



1.105c: Isolated as a light-brown solid (1.67 g; 99% yield) after chromatography (15% i-PrOH/Dichloromethane). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.82 (s, 1H), 7.00 (d, J = 8.7 Hz, 2H), 6.65 (d, J = 8.7 Hz, 2H), 6.25 (s, 1H), 3.71 (q, J = 6.0 Hz, 2H), 3.57 (t, J = 5.5 Hz, 2H), 2.91 (s, 6H), 1.63 (t, J = 6.0 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$): δδ 181.31, 149.86, 127.51, 113.04, 59.08, 42.22, 40.46, 32.05, 25.27; **IR** (cm^{-1}): 1519, 1165, 905, 725, 646; **MS:** HR-ESI calculated for $[C_{12}H_{19}N_3OS+H]^+$: 254.1322, found: 254.1347; **mp**: 96-99 °C.

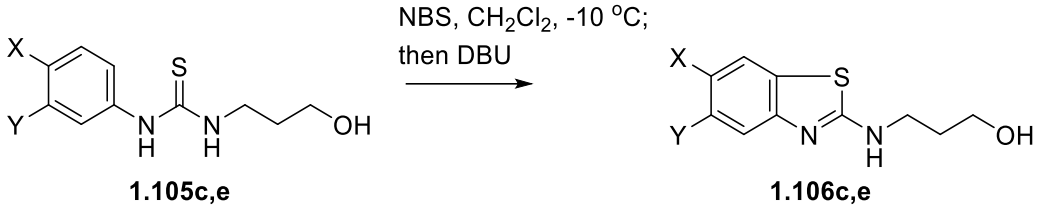


1.105d: Isolated as an orange solid (58 mg, 70% yield) after chromatography (5→25% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.45 (s, 1H), 7.03 (d, J = 8.8 Hz, 2H), 6.53 (d, J = 8.8 Hz, 2H), 6.08 (s, 1H), 3.85-3.74 (m, 2H), 3.69-3.59 (m, 2H), 3.34 – 3.22 (m, 4H), 3.01-2.92 (m, 1H), 2.09 – 1.94 (m, 4H), 1.72-1.61 (m, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ182.06, 147.72, 128.18, 122.68, 112.43, 59.07, 47.81, 42.19, 32.48, 25.65. **IR** (cm^{-1}): 3375, 3294, 2812, 1605, 1553, 1519, 1366, 1165, 1112, 1061, 994, 947, 853, 819, 739, 660, 607, 496; **MS:** HR-ESI calculated for $[C_{14}H_{21}N_3OS+H]^+$: 280.1478, found: 280.1519. **mp** 124-125 °C.

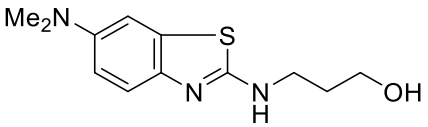


1.105e: Isolated as a light-brown semisolid (2.10 g; 88% yield) after chromatography (1→5% EtOAc in MeOH). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.47 (s, 1H), 6.47 (d, *J* = 8.4 Hz, 1H), 6.41 (d, *J* = 8.5 Hz, 1H), 6.29 (s, 1H), 6.21 (d, *J* = 6.3 Hz, 1H), 3.80 (q, *J* = 6.2 Hz, 2H), 3.63 (q, *J* = 5.7 Hz, 2H), 3.35 – 3.24 (m, 8H), 3.17 (t, *J* = 6.6 Hz, 1H), 1.67 (p, *J* = 5.7 Hz, 2H), 1.21 – 1.04 (m, 6H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 181.65, 136.09, 134.89, 124.90, 115.26, 110.59, 108.49, 58.63, 46.28, 46.23, 45.44, 45.38, 41.79, 32.68, 10.37, 10.20; **IR** (cm^{-1}): 3351, 2931, 1509, 1245, 1168, 1076, 936, 790, 720, 612, 427; **MS:** HR-ESI calculated for $[C_{16}H_{26}N_4OS]^+$: 322.1822, found: 322.1839.

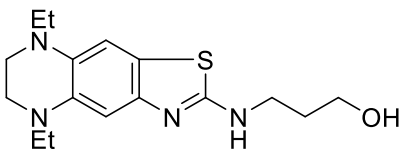
1.5.11 Preparation of aminobenzothiazoles 1.106c and 1.106e.[40]



A solution of thiourea **1.105c** or **1.105e** (1 equiv) in CH_2Cl_2 (ca. 0.125 M) was cooled to –10 °C and treated with solid NBS (1 equiv) added in one portion. The reaction mixture was stirred at for 1 h and then treated with DBU (2 equiv) added dropwise. After stirring at the same temperature for 1.5 h, the reaction was quenched with 5% aqueous $Na_2S_2O_3$. The organic layer was separated, dried over Na_2SO_4, and rotary evaporated. The residue was loaded directly onto a silica gel column and eluted as outlined below.



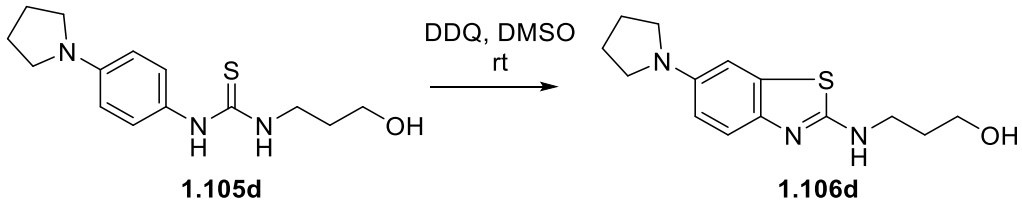
1.106c: Isolated as a light-brown solid (573 mg; 71% yield) after chromatography (15% i-PrOH/Dichloromethane). **^{1}H NMR** (300 MHz, $CDCl_3$): 7.40 (d, J = 8.8 Hz, 1H), 6.94 (d, J = 2.6 Hz, 1H), 6.79 (dd, J = 8.8, 2.6 Hz, 1H), 5.11 (broad s, 1H), 4.18 (broad s, 1H), 3.81 – 3.57 (m, 4H), 2.93 (s, 6H), 1.81 (tt, J = 6.7, 5.1 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 165.40, 147.19, 143.76, 131.74, 119.04, 113.15, 105.08, 59.20, 41.88, 41.80, 33.06; **IR** (cm^{-1}): 3234, 3044, 2942, 2885, 2825, 2785, 1590, 1544, 1470, 1329, 1225, 1073, 1049, 942, 835, 797, 587; **MS:** HR-ESI calculated for $[C_{12}H_{17}N_3OS+H]^+$: 252.1165, found: 252.1163; **mp**: 126-129 °C.



1.106e: Isolated as a light-brown semisolid (1.55 g; 76% yield) after chromatography (20% i-PrOH+5% NEt_3/CH_2Cl_2). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.77 (s, 1H), 6.68 (s, 1H), 5.63 (s,

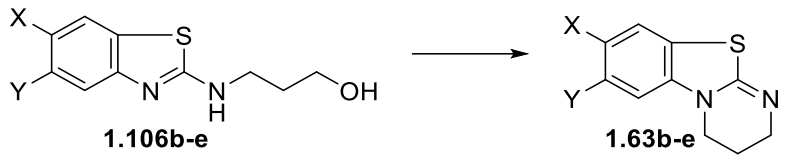
1H), 4.80 (s, 1H), 3.68 (t, *J* = 5.5 Hz, 2H), 3.55 (t, *J* = 6.0 Hz, 2H), 3.47 – 3.08 (m, 8H), 1.75 (p, *J* = 5.3, 4.6 Hz, 2H), 1.38 – 0.94 (m, 6H), 6H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 165.98, 144.38, 135.23, 132.09, 118.01, 102.73, 101.60, 59.06, 46.64, 46.51, 45.90, 45.59, 41.77, 32.99, 10.34, 10.16; **IR** (cm^{-1}): 3244, 2816, 1581, 1538, 1477, 1338, 1211, 1173, 1111, 1052, 938, 910, 868, 839, 792, 733, 702, 580. **MS:** HR-ESI calculated for $[C_{16}H_{24}N_4OS]^+$: 320.1665, found: 320.1690.

1.5.12 Preparation of aminobenzothiazole 1.106d.[41]

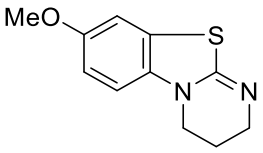


To a solution of thiourea **1.105d** (140 mg, 0.500 mmol) in 2.5 mL of DMSO stirring at rt was added a solution of DDQ (136 mg, 0.6 mmol) in 1.5 mL of DMSO. After stirring for 3d, the mixture was quenched with 5% aqueous $Na_2S_2O_3$ and extracted with EtOAc (×3). The organic extract was washed with 5% aqueous $Na_2S_2O_3$ **(**×3), NaCl, and 10% Na_2CO_3 and dried over $MgSO_4$. Chromatography (25% *i*-PrOH/hexanes) afforded the product as an off-white solid (60 mg, 43% yield). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.38 (d, J = 8.7 Hz, 1H), 6.74 (d, J = 2.4 Hz, 1H), 6.58 (dd, J = 8.8, 2.4 Hz, 1H), 5.12 (s, 1H), 3.71 (t, J = 5.6 Hz, 2H), 3.65 (t, J = 5.9 Hz, 2H), 3.37 – 3.10 (m, 4H), 2.06-1.95 (m, 4H), 1.87 – 1.76 (m, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 164.40, 144.62, 142.52, 132.04, 119.40, 111.33, 102.98, 59.07, 48.34, 41.64, 33.40, 25.59; **IR** (cm^{-1}): 3202, 2834, 1607, 1570, 1540, 1477, 1367, 1246, 1217, 1094, 1064, 1041, 981, 934, 906, 888, 813, 796, 730, 633, 585, 570, 510; **MS:** HR-ESI calculated for $[C_{14}H_{19}N_3OS+H]^+$: 278.1322, found: 278.1354. **mp** 167-170°C dec.

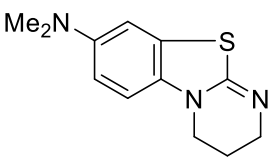
1.5.13 Preparation of DHPB derivatives, general procedure.[14d]



The starting material was partially dissolved in CH_2Cl_2 at 0 °C (10 mL per 1 mmol of the aminobenzothiazole) and treated with NEt_3 (3 equiv) and then MsCl (1.5 equiv) added dropwise. After stirring for 45 minutes at 0 °C, the reaction mixture was brought to rt and treated with methanol (9 equiv) and additional NEt_3 (3 equiv). After refluxing overnight, the mixture was cooled to rt, rinsed with water, dried with Na_2SO_4, and rotary evaporated. The crude product was purified by column chromatography using the eluent shown below.

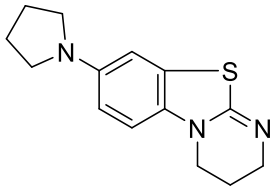


1.63b: Previously reported without characterization.[28] Isolated as a pale-yellow solid (124 mg; 62% yield) after chromatography (1:4:15 NEt_3/*i*-PrOH/ CH_2Cl_2). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.88 (d, *J* = 2.5 Hz, 1H), 6.73 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.63 (d, *J* = 8.7 Hz, 1H), 3.77 (s, 3H), 3.73 (t, *J* = 6.0 Hz, 2H), 3.54 (t, *J* = 5.6 Hz, 2H), 2.00 (p, *J* = 5.9 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 158.25, 155.27, 135.17, 123.63, 111.63, 108.20, 107.67, 56.06, 45.32, 42.13, 19.72. **IR** (cm^{-1}): 2936, 2836, 1612, 1579, 1487, 1438, 1328, 1265, 1225, 1185, 1104, 1071, 1030, 961, 826, 708, 657, 558; **MS:** HR-ESI calculated for $[C_{11}H_{12}N_2OS+H]^+$: 221.0743, found: 221.0775; **mp** 89-93°C.

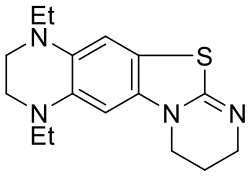


1.63c: Isolated as a light-brown solid (218 mg; 41% yield) after chromatography (5% *i*-PrOH+1% NEt_3/Hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 6.75 (dd, J = 1.9, 1.0 Hz, 1H), 6.64 – 6.51 (m, 2H), 3.70 (t, J = 6.2 Hz, 2H), 3.53 (t, J = 6.6, Hz, 2H), 2.87 (s, 6H), 1.97 (dt, J = 11.9, 5.8 Hz, 2H); **^{13}C NMR** (75

MHz, $CDCl_3$): δ 158.18, 146.96, 132.98, 123.65, 111.17, 107.64, 107.47, 45.57, 41.97, 41.71, 19.83; **IR** (cm^{-1}): 2931, 2874, 2845, 2805, 1617, 1565, 1503, 1447, 1336, 1227, 1199, 1101, 1067, 986, 955, 824, 788, 704, 640, 559, 474; **MS:** HR-ESI calculated for $[C_{12}H_{15}N_3S+H]^+$: 234.1059, found: 234.1093; **mp**: 142-145 °C dec.

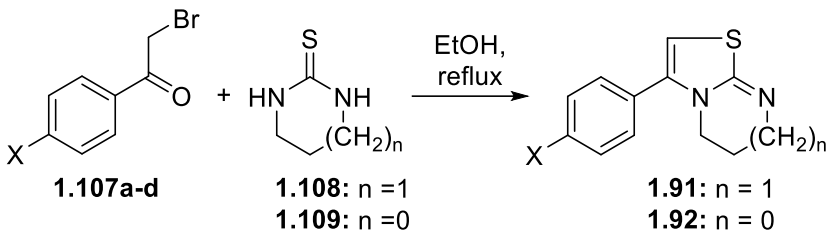


1.63d: Isolated as a white powder (43 mg, 83% yield) after chromatography (25% *i*-PrOH+2% NEt_3/hexane). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 6.63 (d, J = 8.6 Hz, 1H), 6.56 (d, J = 2.3 Hz, 1H), 6.40 (dd, J = 8.6, 2.4 Hz, 1H), 3.72 (t, J = 6.1 Hz, 2H), 3.54 (t, J = 5.6 Hz, 2H), 3.30 – 3.14 (m, 4H), 2.06-1.95 (m, J = 6.8, 3.8 Hz, 6H); **^{13}C NMR** (500 MHz, $CDCl_3$): δ 158.52, 144.43, 131.63, 123.89, 109.30, 108.06, 105.49, 48.31, 45.34, 42.02, 25.52, 19.86; **IR** (cm^{-1}): 3445, 2844, 1604, 1565, 1497, 1369, 1340, 1238, 1184, 1103, 1068, 992, 958, 871, 824, 792, 701, 628, 589, 556, 480, 427; **MS:** HR-ESI calculated for $[C_{14}H_{17}N_3S+H]^+$: 260.1216, found: 260.1242; **mp** 165-168°C (dec).



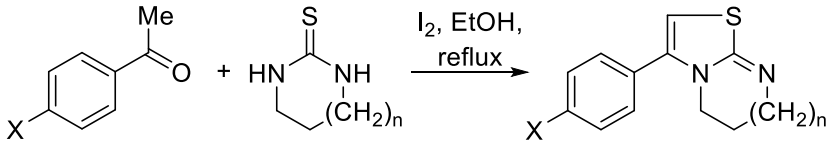
1.63e: Isolated as a light-brown amorphous solid (1.2 g; 82% yield) after chromatography (20% *i*-PrOH+1% NEt_3/CH_2Cl_2). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.51 (s, 1H), 6.03 (s, 1H), 3.69 (t, *J* = 6.1 Hz, 2H), 3.52 (t, *J* = 5.5 Hz, 2H), 3.35 – 3.28 (m, 4H), 3.27 – 3.18 (m, 4H), 1.96 (p, *J* = 4.9 Hz, 2H), 1.24 – 1.06 (m, 6H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 159.46, 134.70, 133.43, 130.99, 108.60, 105.62, 92.24, 46.78, 46.28, 46.15, 45.80, 45.53, 42.04, 19.92, 10.54, 10.40; **IR** (cm^{-1}): 2836, 1603, 1567, 1503, 1305, 1233, 1180, 1107, 928, 795, 709, 556, 467; **MS:** HR-ESI calculated for $[C_{16}H_{22}N_4S]^+$: 302.1560, found: 302.1583.

1.5.14 Preparation of bicyclic isothioureas 1.91a-d and 1.92a-d.[42]



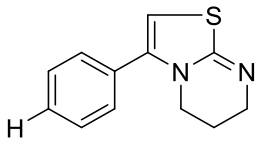
1.107a-d **1.108:** n =1, **1.109:** n =0 **1.91:** n = 1, **1.92:** n = 0

Method A. A mixture of a 2-bromoketone[43] (1 equiv) and a cyclic thiourea (n = 0, 1; 1.2 equiv) in EtOH (0.1 M in bromoketone) was refluxed for a minimum of 20 hours. The reaction mixture was allowed to cool to room temperature, concentrated down, and the residue taken up in CH_2Cl_2. The mixture was washed with saturated aqueous Na_2SO_3 and basified with 1M NaOH. The organic layer was then dried over Na_2SO_4 salt and evaporated, yielding a colorless to light-tan oil, which crystallized on standing. The crude product was pure enough by ^{1}H NMR to be used without further purification.



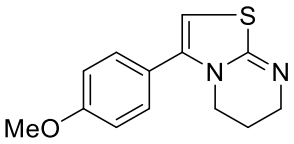
1.110c,d **1.108:** n =1, **1.109:** n = 0 **1.91c, d:** n = 1, **1.92c:** n = 0

Method B. A mixture of a substituted acetophenone[44] (1.0 equiv), iodine (2.15 equiv), and a cyclic thiourea (n = 0, 1; 2 equiv) in EtOH (0.1 M in ketone) was refluxed for a minimum of 20 hours. The reaction mixture was worked up as described above.

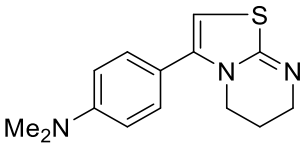


1.91a: Prepared by Method A in 72% yield. Previously reported without full characterization.[45] **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.42 – 7.29 (m, 5H), 5.60 (s, 1H), 3.57 (t, J = 6.0 Hz, 2H), 3.46 (t, J = 5.5 Hz, 2H), 1.79 (tt, J = 5.8 Hz,

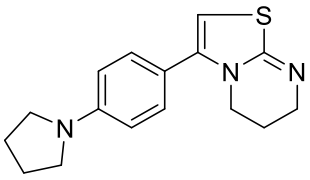
5.7 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 160.89, 139.97, 130.97, 128.93, 128.69, 128.26, 95.05, 45.42, 44.76, 20.09; **IR** (cm^{-1}): 2940, 1606, 1491, 1442, 1363, 1269, 1180, 1092, 1048, 974, 766, 702, 555, 449; **MS:** HR-ESI calculated for $[C_{12}H_{12}N_2S+H]^+$: 217.0794, found: 217.0808. **mp** 107-110 °C.



1.91b: Prepared by Method A in 96% yield. Previously reported without full characterization.[46] **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.23 (d, J = 8.3 Hz, 2H), 6.90 (d, J = 8.4 Hz, 2H), 5.52 (s, 1H), 3.80 (s, 3H), 3.54 (t, J = 6.0 Hz, 2H), 3.44 (t, J = 5.5 Hz, 2H), 1.77 (tt, J = 5.7H, 5.8 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 161.00, 160.13, 139.72, 129.70, 123.32, 114.11, 94.15, 55.40, 45.36, 44.66, 20.11; **IR** (cm^{-1}): 2937, 2837, 1599, 1507, 1455, 1360, 1272, 1247, 1177, 1092, 1028, 975, 841, 817, 732, 698, 632, 586, 555, 477; **MS:** HR-ESI calculated for $[C_{13}H_{14}N_2OS+H]^+$: 247.0900, found: 247.0915. **mp** 97-98 °C.

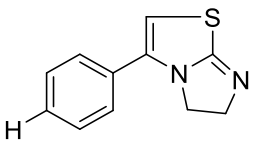


1.91c: Prepared via Method B in 25% yield. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.19 (d, J = 8.8 Hz, 2H), 6.70 (d, J = 8.8 Hz, 2H), 5.49 (s, 1H), 3.59 (t, J = 6.0 Hz, 2H), 3.47 (t, J = 5.5 Hz, 2H), 2.99 (s, 4H), 1.79 (p, J = 5.8, 5.7 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 161.39, 150.75, 140.58, 129.39, 118.48, 111.97, 93.14, 45.46, 44.77, 40.40, 20.25; **IR** (cm^{-1}): 2933, 2844, 1600, 1517, 1445, 1354, 1270, 1230, 1183, 1092, 1069, 975, 944, 815, 731, 660, 634, 602, 554, 483; **MS:** HR-ESI calculated for $[C_{14}H_{17}N_3S+H]^+$: 260.1216, found: 260.1237. **mp** 145-148 °C (dec).

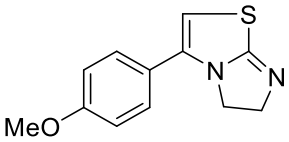


1.91d: Prepared via Method B in 36% yield. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.16 (d, J = 8.7 Hz, 2H), 6.54 (d, J = 8.7 Hz, 2H), 5.47 (s, 1H), 3.59 (t, J = 5.9 Hz, 2H), 3.46 (t, J = 5.6 Hz, 2H), 3.30 (t, J = 6.6

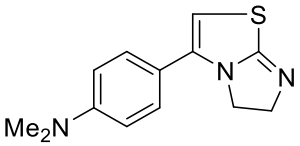
Hz, 4H), 2.07 – 1.97 (m, 4H), 1.79 (tt, J = 5.7, 5.7 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$): 161.43, 148.17, 140.83, 129.47, 117.51, 111.39, 92.76, 47.65, 45.47, 44.74, 25.58, 20.26; **IR** (cm^{-1}): 2840, 1600, 1517, 1485, 1376, 1270, 1187, 975, 810, 730, 555; **MS:** HR-ESI calculated for $[C_{16}H_{19}N_3S+H]^+$: 286.1372, found: 286.1403. **mp** 142-146 °C (dec).



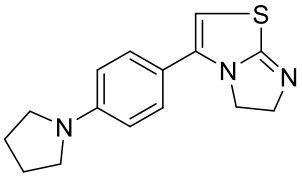
1.92a: Prepared via method A in quantitative yield. The NMR spectra matched those reported in the literature.[42a]



1.92b: Prepared via Method A in 96% yield. Previously reported without full characterization.[28] **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.35 (d, J = 8.7 Hz, 2H), 6.92 (d, J = 8.8 Hz, 2H), 5.58 (s, 1H), 4.24 (t, J = 9.2 Hz, 2H), 3.89-3.75 (m, 5H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 170.46, 160.18, 137.14, 127.87, 123.59, 114.36, 96.44, 60.60, 55.45, 48.37; **IR** (cm^{-1}): 2932, 1590, 1505, 1455, 1419, 1371, 1293, 1248, 1178, 1112, 1030, 971, 835, 807, 729, 684, 632, 584, 519; **MS:** HR-ESI calculated for $[C_{12}H_{12}N_2OS+H]^+$: 233.0743, found: 233.0758. **mp** 89-90 °C.

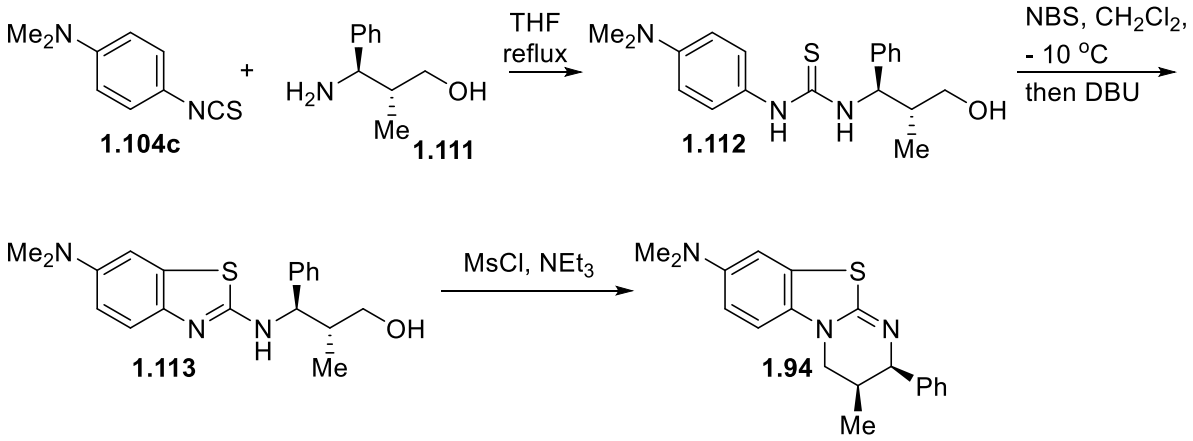


1.92c: Prepared via Method B in 25% yield. Previously reported without full characterization[28] **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.29 (d, J = 8.7 Hz, 2H), 6.70 (d, J = 8.7 Hz, 2H), 5.50 (s, 1H), 4.24 (t, J = 9.2 Hz, 2H), 3.85 (t, J = 9.2 Hz, 2H), 2.99 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 170.83, 150.79, 137.84, 127.55, 118.76, 112.18, 94.90, 60.50, 48.46, 40.40. **IR** (cm^{-1}): 2888, 1592, 1515, 1444, 1364, 1293, 1231, 1200, 1066, 946, 823, 666, 633, 520. **MS:** HR-ESI calculated for $[C_{13}H_{15}N_3S+H]^+$: 246.1059, found: 246.1080. **mp** 149-152 °C (dec).



1.92d: Prepared via Method A in 52% yield. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.27 (d, J = 8.9 Hz, 2H), 6.54 (d, J = 8.8 Hz, 2H), 5.47 (s, 1H), 4.23 (t, J = 9.3 Hz, 2H), 3.84 (t, J = 9.2 Hz, 2H), 3.36 – 3.25 (m, 4H), 2.05 – 1.95 (m, 4H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 170.87, 148.23, 138.09, 127.66, 117.93, 111.64, 94.30, 60.66, 48.49, 47.69, 25.63; **IR** (cm^{-1}): 2836, 1585, 1513, 1374, 1182, 962, 814, 726, 663, 631, 513; **MS:** HR-ESI calculated for $[C_{15}H_{17}N_3S+H]^+$: 272.1216, found: 272.1261; **mp** 143-144 °C.

1.5.15 Preparation of chiral catalyst 1.94.



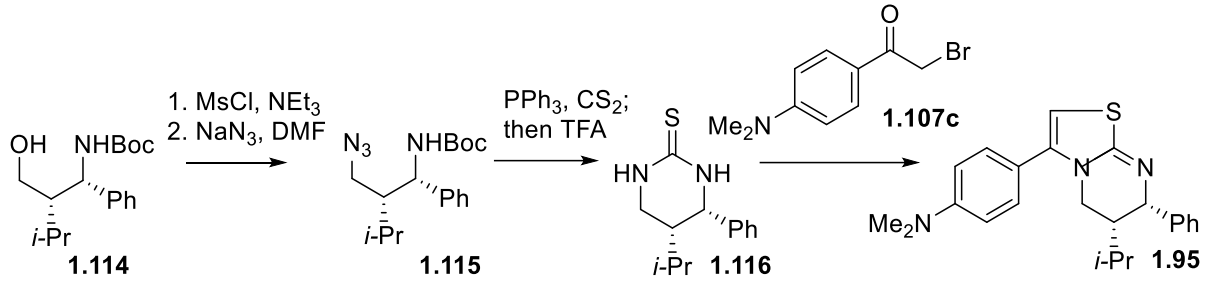
Thiourea 1.112. Prepared analogously to thioureas **1.105c-e** starting with chiral aminoalcohol **1.111**[47]. Isolated as a light-brown solid (602 mg; 99% yield) after chromatography (15% *i*-PrOH+1% NEt_3/Hexanes). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.48 (s, 1H), 7.39 – 7.17 (m, 2H), 7.16 – 6.97 (m, 5H), 6.74 (d, J = 8.9 Hz, 2H), 6.60 (d, J = 9.9 Hz, 1H), 5.96 (d, J = 9.8 Hz, 1H), 3.60 – 3.28 (m, 3H), 3.00 (s, 6H), 2.47 – 2.11 (m, 1H), 0.56 (d, J = 7.0 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 181.75, 150.41, 139.78, 128.58, 128.12, 127.17, 126.63, 113.14, 64.53, 58.69, 40.87, 40.53, 10.97; **IR** (cm^{-1}): 3195, 2958, 2877, 2803, 1609, 1515, 1166, 1029, 946, 813, 700, 551;

MS: HR-ESI calculated for $[C_{19}H_{25}N_3OS+H]^+$: 344.1791, found: 344.1811; **mp**: 123-125 °C; $[\alpha]_D^{23}$= -0.98° (c= 0.58, CH_2Cl_2).

1.113. Prepared analogously to benzothiazoles **1.106c** and **e**. Isolated as a light-brown solid (122 mg; 22% yield) after chromatography (40% EtOAc/Hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.55 – 7.26 (m, 6H), 6.97 (d, J = 2.5 Hz, 1H), 6.83 (dd, J = 8.8, 2.5 Hz, 1H), 6.25 (broad s, 1H), 5.29 (d, J = 3.3 Hz, 1H), 4.90 (broad s, 1H), 3.83 – 3.43 (m, 2H), 2.96 (s, 6H), 2.43 (m, 1H), 0.85 (d, J = 7.0 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 165.19, 147.24, 143.38, 140.22, 131.79, 128.60, 127.38, 127.07, 119.14, 113.23, 105.01, 64.69, 59.95, 41.80, 41.32, 11.33; **IR** (cm^{-1}): 3259, 2933, 2917, 2873, 2861, 2788, 1603, 1522, 1487, 1337, 1212, 1090, 1046, 909, 806, 734, 696, 531, 489; **MS:** HR-ESI calculated for $[C_{19}H_{23}N_3OS+H]^+$: 342.1635, found: 342.1660; **mp**: 185-190 °C dec.; $[\alpha]_D^{23}$= +0.66° (c= 0.7, CH_2Cl_2).

Dimethylamino-HBTM-2 (1.94). Prepared analogously to catalysts **1.63b-e** Isolated as a light-brown solid (56 mg; 57% yield) after chromatography (20→40% EtOAc/Hexanes). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.32 – 7.09 (m, 5H), 6.74 (d, J = 2.2 Hz, 1H), 6.65 – 6.47 (m, 2H), 4.64 (d, J = 4.2 Hz, 1H), 3.73 (dd, J = 11.4, 4.9 Hz, 1H), 3.24 (dd, J = 11.4, 7.5 Hz, 1H), 2.83 (s, 6H), 2.42 – 2.21 (m, 1H), 0.73 (d, J = 7.0 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 158.11, 147.19, 141.32, 132.68, 128.12, 127.92, 126.89, 124.20, 111.27, 107.96, 107.55, 62.92, 46.38, 41.75, 29.37, 14.07; **IR** (cm^{-1}): 2964, 2876, 2786, 1600, 1572, 1496, 1335, 1240, 1197, 978, 957, 860, 796, 752, 700, 583, 528; **MS:** HR-ESI calculated for $[C_{19}H_{21}N_3S+H]^+$: 324.1529, found: 324.1555; **mp**: 122-123 °C; $[\alpha]_D^{23}$= -0.61° (c= 0.35, CH_2Cl_2).

1.5.16 Preparation of chiral catalyst 1.95.



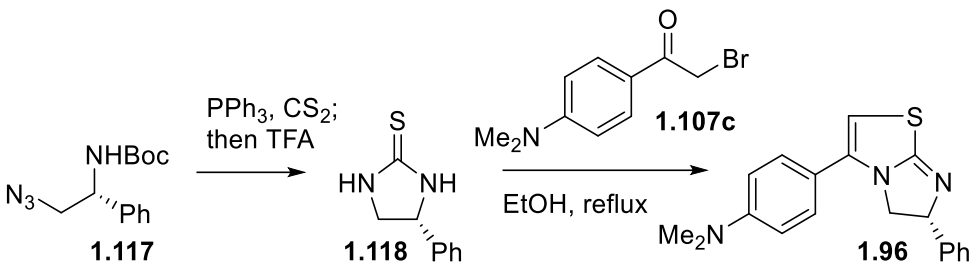
(a) A solution of carbamate **1.114**[23a] (3.00 g, 10.3 mmol) in 60 mL of CH_2Cl_2 at 0 °C, was treated with NEt_3 (2.20 mL, 15.5 mmol) followed by methanesulfonyl chloride (0.88 mL, 11 mmol). The reaction mixture was stirred for 1 h at 0 °C and 1 hat rt and quenched by adding saturated aqueous NH_4Cl. The organic phase was separated, dried over Na_2SO_4 and evaporated. The crude mesylate was dissolved in DMF (30 mL) and treated with NaN_3 (3.10 g, 47.2 mmol). stirring at 80 °C for 16 h, the reaction mixture was cooled to rt, quenched by adding saturated NH_4Cl and the extracted with Et_2O. The organic layer was washed with saturated NH_4Cl, brine and dried over Na_2SO_4. The solvent was evaporated to give the azide **1.115** (2.86 g, 96% yield) in sufficiently pure form for the next step. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.34 – 7.23 (m, 2H), 7.23 – 7.15 (m, 3H), 5.08 (s, 1H), 4.76 (d, *J* = 5.3 Hz, 1H), 3.26 – 2.99 (m, 2H), 1.96 – 1.66 (m, 2H), 1.33 (s, 9H), 0.98 (d, *J* = 6.9 Hz, 3H), 0.87 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 155.12, 141.11, 128.71, 127.47, 127.11, 79.59, 55.47, 50.24, 48.84, 28.46, 27.29, 21.95, 18.67; **IR** (cm^{-1}): 3390, 2963, 2096, 1682, 1517, 1363, 1251, 1167, 1081, 751.

(b) A solution of azide **1.115** (954 mg, 3.00 mmol) and CS_2 (0.90 mL, 15 mmol) in 10 mL of CH_2Cl_2 was treated with solid PPh_3 (865 mg, 3.3 mmol) and stirred at 50 °C for 16 h. The solvent was evaporated and 10 mL of a 1:1 Et_2O/hexanes mixture was added. The resulting

white precipitate ($Ph_3P=S$) was filtered off and the filtrate evaporated to give the crude isothiocyanate, which was dissolved in 20 mL of CH_2Cl_2 and treated with TFA (1 mL) at rt. The reaction mixture was stirred overnight and then neutralized with 1M NaOH. The organic layer was separated, dried over Na_2SO_4 and evaporated. The evaporation residue was purified by chromatography (20→60% EtOAc/hexanes to afford the product **1.116** as a white solid (397 mg; 56% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.37 (s, 1H), 7.35 – 7.25 (m, 3H), 7.20 (s, 1H), 7.19 – 7.15 (m, 2H), 4.60 (t, *J* = 4.1 Hz, 1H), 3.40 – 3.29 (m, 1H), 3.03 (t, *J* = 12.4 Hz, 1H), 1.93 – 1.83 (m, 1H), 1.16 – 1.09 (m, 1H), 1.07 (d, *J* = 6.0 Hz, 3H), 0.73 (d, *J* = 6.4 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 176.27, 139.21, 128.68, 128.13, 127.75, 56.94, 41.44, 40.65, 26.39, 21.79, 19.89; **IR** (cm^{-1}): 3161, 2954, 1569, 1525, 1453, 1370, 1268, 1225, 774, 702; **MS:** HR-ESI calculated for $[C_{13}H_{18}N_2S+H]^+$: 235.1263, found: 235.1290.

(c) Catalyst **1.95** was prepared analogously to achiral isothioureas **1.91** and **1.92**, except 10% excess of bromoketone **1.107c** was used. Isolated as a light yellow solid (324 mg, 57% yield) after chromatography (1→20% MeOH/EtOAc). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.34 (t, *J* = 7.6 Hz, 2H), 7.30 – 7.25 (m, 3H), 7.23 (d, *J* = 8.5 Hz, 2H), 6.71 (d, *J* = 8.4 Hz, 2H), 5.66 (s, 1H), 4.88 (d, *J* = 4.1 Hz, 1H), 3.65 (dd, *J* = 12.4, 4.8 Hz, 1H), 3.31 (t, *J* = 11.6 Hz, 1H), 3.00 (s, 6H), 1.79 – 1.71 (m, 1H), 1.29 – 1.20 (m, 1H), 1.06 (d, *J* = 6.5 Hz, 3H), 0.66 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 161.88, 150.43, 141.18, 140.42, 128.86, 127.97, 127.75, 126.73, 117.67, 111.67, 93.80, 60.21, 44.22, 40.89, 39.99, 26.34, 21.98, 19.76. **IR** (cm^{-1}): 2961, 1599, 1518, 1354, 1264, 1196, 945, 814, 730; **MS:** HR-ESI calculated for $[C_{23}H_{27}N_3S+H]^+$: 378.1998, found: 378.2028; **mp**: 88-91 °C; $[\alpha]_D^{23} = +2.51°$ (c= 0.65, CH_2Cl_2).

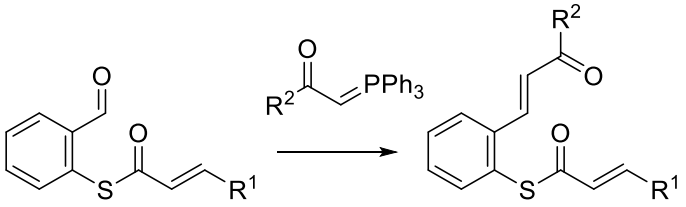
1.5.17 Preparation of chiral catalyst 1.96.



(a) Thiourea **1.118** was prepared analogously to **1.116** via the known *(R)*-N-Boc-2-azido-1-phenylethylamine **1.117**[48] Isolated as a pale pink powder (411 mg, 52% yield) after chromatography (1:1 hexane/CH_2Cl_2 → 1:9 EtOAc/ CH_2Cl_2). Previously reported without characterization.[28] **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.45-7.29 (m, 5H), 6.45 (s, 1H), 6.38 (s, 1H), 5.08 (dd, J = 9.9, 7.6 Hz, 1H), 4.12 (t, J = 9.8 Hz, 1H), 3.59 (dd, J = 9.7, 7.6 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 184.37, 140.02, 129.28, 128.85, 126.30, 61.14, 53.64; **IR** (cm^{-1}): 3212, 1746, 1521, 1478, 1463, 1446, 1372, 1301, 1257, 1182, 1032, 917, 756, 724, 694, 589, 531, 505; **MS:** HR-ESI calculated for $[C_{13}H_{17}N_3S+H]^+$: 179.0637, found: 179.0649. **mp** 148-150 °C; $[\alpha]_D^{23} = +0.071°$ (c= 0.31, CH_2Cl_2).

(b) Catalyst **1.96** was prepared analogously to achiral isothioureas **1.91** and **1.92**. Isolated as a pale orange powder (225 mg; 73% yield). Previously reported without full characterization.[28] **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.43 – 7.33 (m, 4H), 7.32 – 7.25 (m, 3H), 6.69 (d, J = 8.8 Hz, 2H), 5.63 – 5.56 (m, 2H), 4.32 (t, J = 9.6 Hz, 1H), 3.71 (t, J = 9.0 Hz, 1H), 2.99 (s, 6H); **^{13}C NMR** (500 MHz, $CDCl_3$): δ 170.62, 150.82, 143.67, 137.80, 128.70, 127.55, 127.43, 126.68, 118.62, 112.18, 95.11, 75.62, 56.14, 40.40; **IR** (cm^{-1}): 1592, 1515, 1445, 1356, 1227, 826, 743, 698, 665, 643, 581, 528; **MS:** HR-ESI calculated for $[C_{19}H_{19}N_3S+H]^+$: 322.1372, found: 322.1401; **mp** 140-143 °C; $[\alpha]_D^{23} = +2.51°$ (c= 0.31, CH_2Cl_2).

1.5.18 Synthesis of the enone substrates.

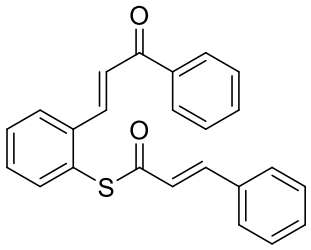


1.44a: R^1 = Ph
1.44d: R^1 = 3,5-$(CF_3)_2C_6H_3$
1.44k: R^1 = cyclohexyl
1.44g: R^1 = 4-$(MeO)C_6H_4$

1.84a-l

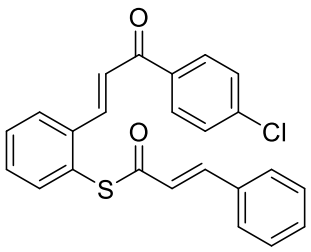
Method A. A round bottom flask equipped with a magnetic stir bar was charged with an o-(acylthio)benzaldehyde (1.0 equiv), a Wittig Reagent (1.3 equiv), and dichloromethane (0.33 M in the aldehyde). The mixture was stirred for 24 to 48 h at rt and concentrated under reduced pressure. The residue was purified by flash chromatography using the eluent indicated to afford the corresponding enone **1.84**.

Method B. The reaction was carried out as described above, but with a larger excess of the Wittig reagent (2.0 equiv), and heating in toluene (0.33 M) at 80 °C for 24 h.

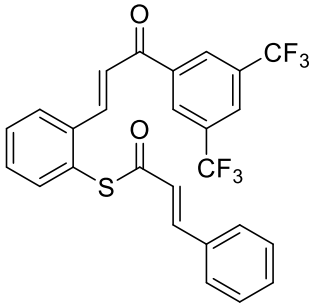


1.84a: Prepared using Method A. Isolated as a white solid (103 mg, 53% yield) after chromatography (5% EtOAc/15%CH_2Cl_2/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.16 (d, *J* = 15.8 Hz, 1H), 8.04 – 7.96 (m, 2H), 7.90 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.69 (d, *J* = 15.8 Hz, 1H), 7.62 – 7.38 (m, 12H), 6.82 (d, *J* = 15.3 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 190.69, 186.75, 142.26, 142.16, 138.84, 138.02, 137.07, 133.93, 132.85, 130.98, 130.61, 130.42, 129.12, 129.09, 128.71, 128.65, 128.64, 127.36, 124.88, 123.99; **IR** (cm^{-1}): 3055, 3020, 2919, 2851, 1682, 1659, 1599,

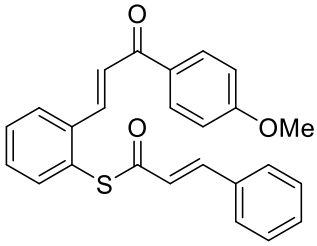
1446, 1304, 1270, 1213,1013, 977, 880, 752, 724, 683, 568, 497; **MS:** HR-ESI calculated for $[C_{24}H_{18}O_2S+Na]^+$: 393.0920, found: 393.0952; **mp**: 132-135 °C.



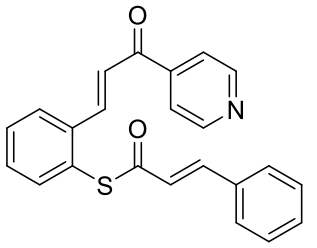
1.84b: Prepared using Method B. Isolated as a white solid (141 mg, 93% yield) after chromatography (5→10% EtOAc/hexanes). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.15 (d, *J* = 15.7 Hz, 1H), 7.92 (d, *J* = 8.6 Hz, 2H), 7.88 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.68 (d, *J* = 15.8 Hz, 1H), 7.62 – 7.36 (m, 11H), 6.81 (d, *J* = 15.8 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 189.58, 186.84, 142.77, 142.47, 139.36, 138.75, 137.18, 136.42, 133.97, 131.10, 130.85, 130.52, 130.20, 129.29, 129.18, 129.05, 128.73, 127.43, 124.47, 124.01; **IR** (cm^{-1}): 3060, 3025, 2953, 2923, 2855, 1687, 1662, 1598, 1461, 1329, 1265, 1207, 1089, 1010, 881, 832, 750, 686, 568, 534, 497; **MS:** HR-ESI calculated for $[C_{24}H_{17}ClO_2S+Na]^+$: 427.0530, found: 427.0567; **mp**: 114-116 °C.



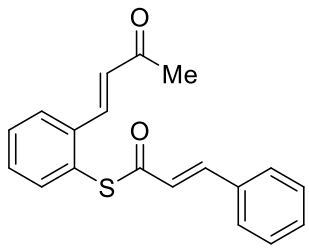
1.84c: Prepared using Method B. Isolated as a white solid (275 mg, 61% yield) after chromatography 5% EtOAc/15%CH_2Cl_2/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ **^{1}H NMR** (300 MHz, $CDCl_3$): 8.42 (s, 2H), 8.24 (d, J = 15.7 Hz, 1H), 8.06 (s, 1H), 7.92 (dd, J = 7.6, 1.7 Hz, 1H), 7.68 (d, J = 15.8 Hz, 1H), 7.63 – 7.37 (m, 9H), 6.81 (d, J = 15.8 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 187.90, 186.63, 144.84, 142.69, 139.69, 138.29, 137.32, 133.94, 132.46 (q, *J* = 33.9 Hz), 131.42, 131.17, 130.64, 129.70, 129.19, 128.75, 128.74 (q, *J* = 2.8 Hz), 127.66, 126.06 (sept, *J* = 3.7 Hz), 123.85, 123.32, 123.08 (q, *J* = 273.2 Hz); **IR** (cm^{-1}): 2957, 2922, 2852, 1681, 1613, 1586, 1445, 1313, 1281, 1167, 1130, 1019, 984, 904, 878, 848, 758, 694, 681, 570, 484, 442; **MS:** HR-ESI calculated for $[C_{26}H_{16}F_6O_2S+Na]^+$: 529.0667, found: 529.0658; **mp**: 148-151 °C.



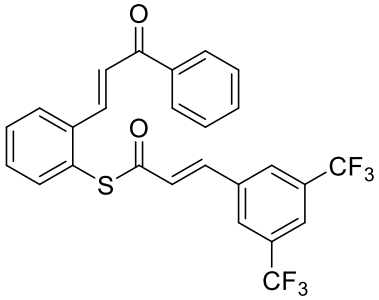
1.84d: Prepared using Method A. Isolated as a white solid (143 mg, 89% yield) after chromatography (10→20→30% EtOAc/hexanes). **^{1}H NMR** δ 8.15 (d, *J* = 15.6 Hz, 1H), 8.00 (ddd, *J* = 8.7, 2.8, 0.2 Hz, 2H), 7.87 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.68 (d, *J* = 15.8 Hz, 1H), 7.59 – 7.33 (m, 9H), 6.92 (ddd, *J* = 8.7, 2.8, 0.2 Hz, 2H), 6.81 (d, *J* = 15.8 Hz, 1H), 3.78 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 188.77, 186.74, 163.41, 142.08, 141.10, 138.93, 136.96, 133.83, 130.97, 130.90, 130.80, 130.36, 130.33, 129.01, 128.87, 128.57, 127.26, 124.68, 123.93, 113.83, 55.39; **IR** (cm^{-1}): 3055, 2961, 2924, 2838, 1687, 1653, 1604, 1509, 1461, 1335, 1306, 1257, 1215, 1163, 1020, 973, 880, 827, 751, 685, 632, 569, 502; **MS:** HR-ESI calculated for $[C_{25}H_{20}O_3S+Na]^+$: 423.1025, found: 423.1063; **mp**: 107-109 °C.



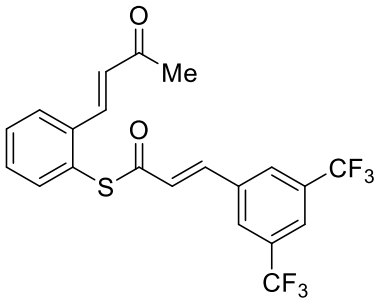
1.84e: Prepared using Method B. Isolated as a light-yellow solid (108 mg, 78% yield) after chromatography (10→40% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.76 (dd, J = 4.5, 1.6 Hz, 2H), 8.14 (d, J = 15.8 Hz, 1H), 7.89 (dd, J = 7.4, 1.8 Hz, 1H), 7.79 – 7.62 (m, 3H), 7.61 – 7.38 (m, 8H), 7.35 (d, J = 15.8 Hz, 1H), 6.80 (d, J = 15.8 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 190.45, 186.68, 150.83, 144.36, 144.33, 142.62, 138.30, 137.17, 133.86, 131.26, 131.20, 130.59, 129.55, 129.21, 128.74, 127.48, 124.13, 123.84, 121.83; **IR** (cm^{-1}): 1669, 1613, 1465, 1327, 1211, 1031 975, 884, 764, 713, 619, 572; **MS:** HR-ESI calculated for $[C_{23}H_{17}NO_2S+H]^+$: 372.1053, found: 372.1073; **mp**:124 -127 °C



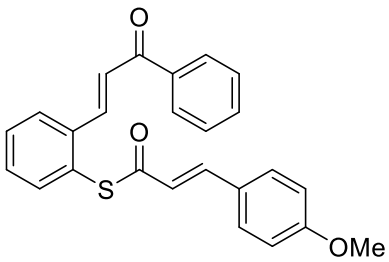
1.84f: Prepared using Method A. Isolated as a white solid (115 mg, 99% yield) after chromatography (5→10→20% EtOAc/hexanes). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.90 (d, *J* = 16.2 Hz, 1H), 7.76 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.69 (d, *J* = 15.8 Hz, 1H), 7.56 (dt, *J* = 7.8, 2.0 Hz, 2H), 7.50 – 7.36 (m, 5H), 6.82 (d, *J* = 15.8 Hz, 1H), 6.68 (d, *J* = 16.3 Hz, 1H), 2.34 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 198.23, 186.51, 142.31, 140.62, 138.23, 136.93, 133.78, 131.03, 130.60, 130.45, 129.43, 129.07, 128.71, 128.62, 127.25, 123.73, 27.48; **IR** (cm^{-1}): 3063, 3023, 2919, 1681, 1664, 1613, 1446, 1253, 1202, 1018, 968, 878, 752, 689, 567, 482, 438; **MS:** HR-ESI calculated for $[C_{19}H_{16}O_2S+H]^+$: 309.0944, found: 309.0943; **mp**: 95-97 °C.



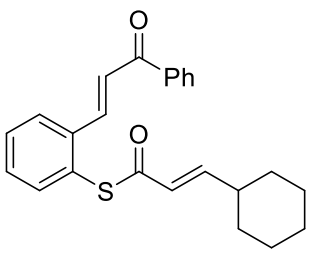
1.84g: Prepared using Method A. Isolated as a white solid (389 mg, 78% yield) after chromatography (5→10% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.14 (d, *J* = 15.7 Hz, 1H), 8.01 (dd, *J* = 1.4, 1.4 Hz, 1H), 8.00 – 7.97 (m, 3H), 7.94 – 7.87 (m, 2H), 7.68 (d, *J* = 15.8 Hz, 1H), 7.62 – 7.43 (m, 7H), 6.93 (d, *J* = 15.7 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ190.37, 186.32, 141.80, 138.97, 138.25, 138.06, 137.04, 136.25, 133.08, 132.77 (q, *J* = 33.8 Hz), 130.84, 130.81, 128.79, 128.76, 128.41, 128.21, 128.18, 127.57, 125.01, 124.06 – 123.64 (m), 123.08 (q, *J* = 273.0 Hz); **IR** (cm^{-1}): 3070, 3050, 1685, 1657, 1578, 1377, 1274, 1223, 1172, 1123, 1015, 977, 944, 898, 845, 820, 756, 726, 681, 658, 581; **MS:** HR-ESI calculated for $[C_{26}H_{16}F_6O_2S+Na]^+$: 529.0667, found: 529.0711; **mp**: 186-190 °C.



1.84h: Prepared using Method A. Isolated as a white solid (50 mg, 49% yield) after chromatography (5→10% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.00 (s, 2H), 7.92 (s, 1H), 7.87 (d, *J* = 16.2 Hz, 1H), 7.81 – 7.75 (m, 1H), 7.70 (d, *J* = 15.8 Hz, 1H), 7.62 – 7.38 (m, 3H), 6.95 (d, *J* = 15.8 Hz, 1H), 6.71 (d, *J* = 16.2 Hz, 1H), 2.35 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 198.13, 186.12, 140.26, 138.38, 138.32, 136.94, 136.15, 132.79 (q, *J* = 33.7 Hz), 130.90, 130.83, 129.65, 128.20 (q, *J* = 3.9 Hz), 128.03, 127.52, 127.33, 124.03 (sept, *J* = 7.6 Hz), 123.06 (q, *J* = 273.0 Hz), 27.88; **IR** (cm^{-1}): 1672, 1610, 1467, 1378, 1276, 1173, 1129, 1020, 973, 900, 821, 755, 699, 683, 583; **MS:** HR-ESI calculated for $[C_{21}H_{14}F_6O_2S+Na]^+$: 467.0511, found: 467.0539; **mp**: 109-112 °C.

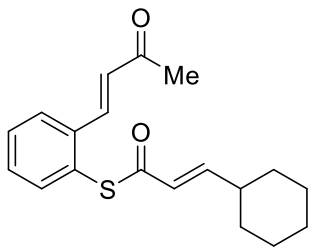


1.84i: Prepared using Method A. Isolated as a white amorphous solid (282 mg, 52% yield) after chromatography (5→10→15% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.17 (d, *J* = 15.7 Hz, 1H), 8.06 – 7.94 (m, 2H), 7.88 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.64 (d, *J* = 15.7 Hz, 1H), 7.60 – 7.38 (m, 9H), 6.92 (d, *J* = 8.8 Hz, 2H), 6.69 (d, *J* = 15.7 Hz, 1H), 3.83 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 190.76, 186.60, 162.02, 142.32, 142.06, 138.83, 138.04, 137.11, 132.81, 130.56, 130.45, 130.30, 129.41, 128.71, 128.64, 127.31, 126.58, 124.80, 121.58, 114.57, 55.47; **IR** (cm^{-1}): 3059, 2933, 2838, 1663, 1597, 1511, 1464, 1312, 1256, 1215, 1174, 1024, 805, 755; **MS:** HR-ESI calculated for $[C_{25}H_{20}O_3S+NH]^+$: 401.1206, found: 401.1199.

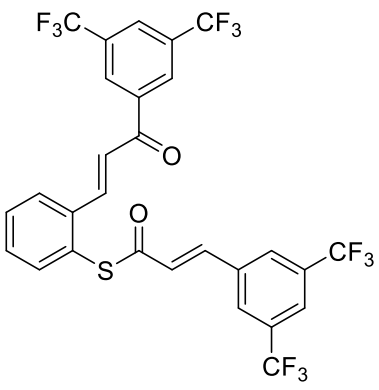


1.84j: Prepared using Method A. Isolated as a greenish-yellow oil (94 mg, 68% yield) after chromatography (1→5% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.13 (d, *J* = 15.7 Hz, 1H), 8.04 – 7.93 (m, 2H), 7.87 (dd, *J* = 7.7, 1.5 Hz, 2H), 7.66 – 7.35 (m, 10H), 6.95 (dd, *J* =

15.6, 6.7 Hz, 1H), 6.15 (dd, *J* = 15.7, 1.4 Hz, 1H), 2.22 – 2.09 (m, 1H), 1.87 – 1.56 (m, 5H), 1.43 – 1.07 (m, 5H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 190.78, 187.28, 152.49, 142.36, 138.93, 138.13, 137.18, 132.88, 130.59, 130.31, 129.37, 128.77, 128.70, 127.33, 125.49, 124.81, 40.73, 31.66, 26.00, 25.80; **IR** (cm^{-1}): 2926, 2851, 1665, 1604, 1448, 1314, 1271, 1214, 1015, 975, 817, 754, 692; **MS:** HR-ESI calculated for $[C_{24}H_{24}O_2S+H]^+$: 377.1570, found: 377.1569.



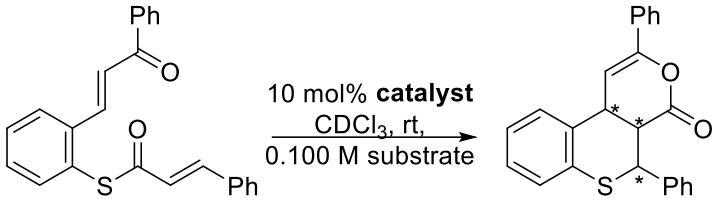
1.84k: Prepared using Method A. Isolated as a greenish-yellow oil (144 mg, 48% yield) after chromatography (1→5% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.85 (d, *J* = 16.2 Hz, 1H), 7.73 (dd, *J* = 7.4, 1.9 Hz, 1H), 7.54 – 7.34 (m, 3H), 6.95 (dd, *J* = 15.6, 6.7 Hz, 1H), 6.65 (d, *J* = 16.2 Hz, 1H), 6.15 (dd, *J* = 15.6, 1.4 Hz, 1H), 2.33 (s, 3H), 2.27 – 2.10 (m, 1H), 1.87 – 1.62 (m, 5H), 1.38 – 1.07 (m, 5H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 190.78, 187.28, 152.49, 142.36, 138.93, 138.13, 137.18, 132.88, 130.59, 130.31, 129.37, 128.77, 128.70, 127.33, 125.49, 124.81, 40.73, 31.66, 26.00, 25.80; **IR** (cm^{-1}): 2925, 2851, 1672, 1624, 1448, 1358, 1256, 1178, 1012, 973, 816, 754; **MS:** HR-ESI calculated for $[C_{19}H_{22}O_2S+H]^+$: 315.1413, found: 315.1410.



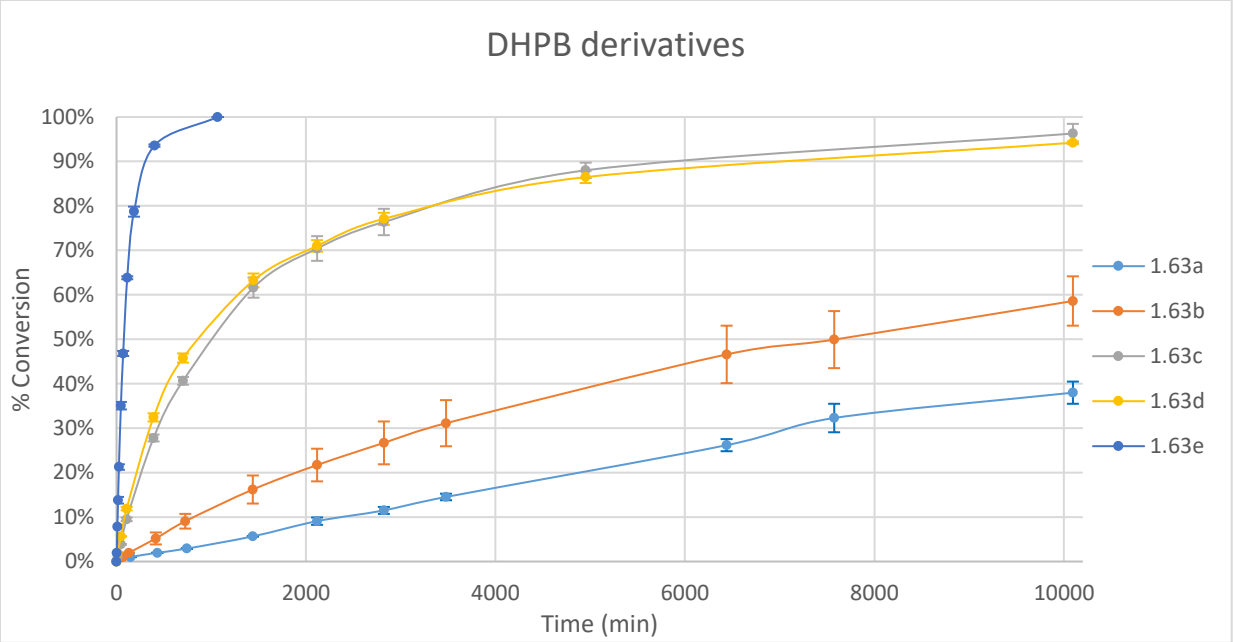
1.84l: Prepared using Method B. Isolated as a White solid (140 mg, 47% yield, 5→10% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.41 (s, 2H), 8.20 (d, *J* = 15.6 Hz, 1H), 8.07 (s, 1H), 7.99 (s, 2H), 7.94 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.92 (s, 1H), 7.69 (d, *J* = 15.8 Hz, 1H), 7.62 – 7.50 (m, 3H), 7.45 (d, *J* = 15.6 Hz, 1H), 6.94 (d, *J* = 15.8 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 187.70, 186.10, 144.36, 139.60, 138.51, 138.23, 137.15, 136.12, 132.80 (q, *J* = 33.9 Hz), 132.49 (q, *J* = 33.9 Hz), 131.52, 130.96, 128.84, 128.70 (q, *J* = 3.9 Hz), 128.21 (q, *J* = 4.0 Hz), 127.80, 127.30, 126.15 (sept, *J* = 3.7 Hz), 124.07 (sept, *J* = 3.8 Hz), 123.48, 123.07 (q, *J* = 272.9 Hz); **IR** (cm^{-1}):

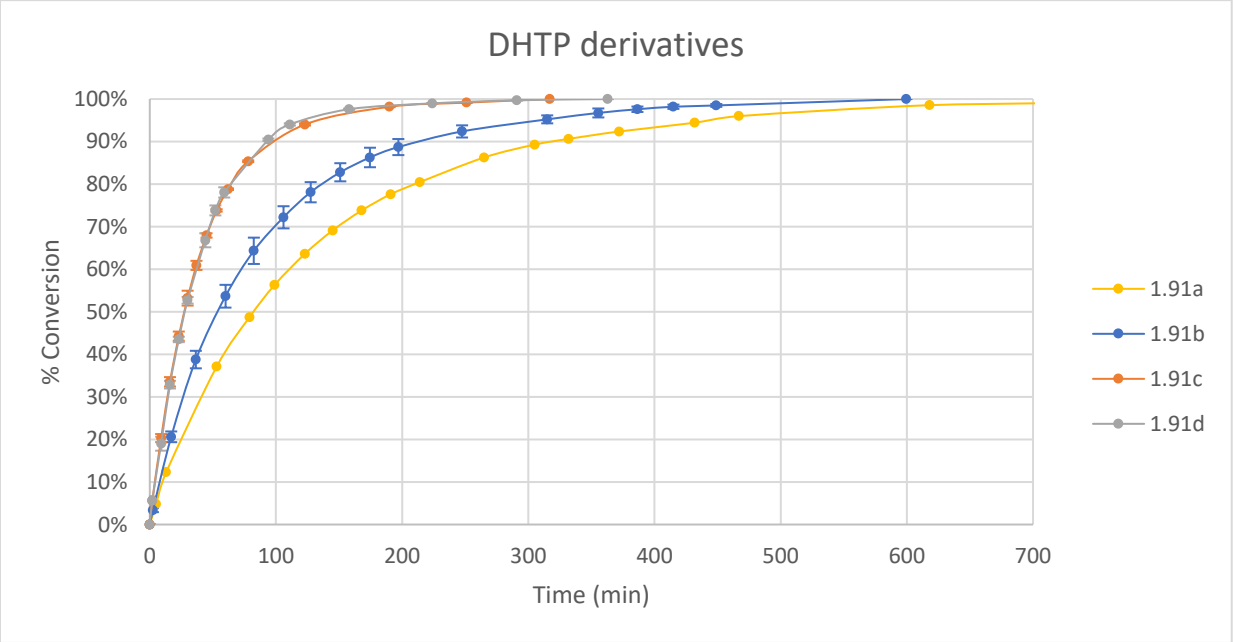
1672, 1617, 1378, 1275, 1126, 1020, 902, 843, 734, 698, 681, 583; **MS:** HR-ESI calculated for $[C_{28}H_{14}F_{12}O_2S+H]^+$: 643.0596, found: 643.0.550; **mp**: 1159-162 °C dec.

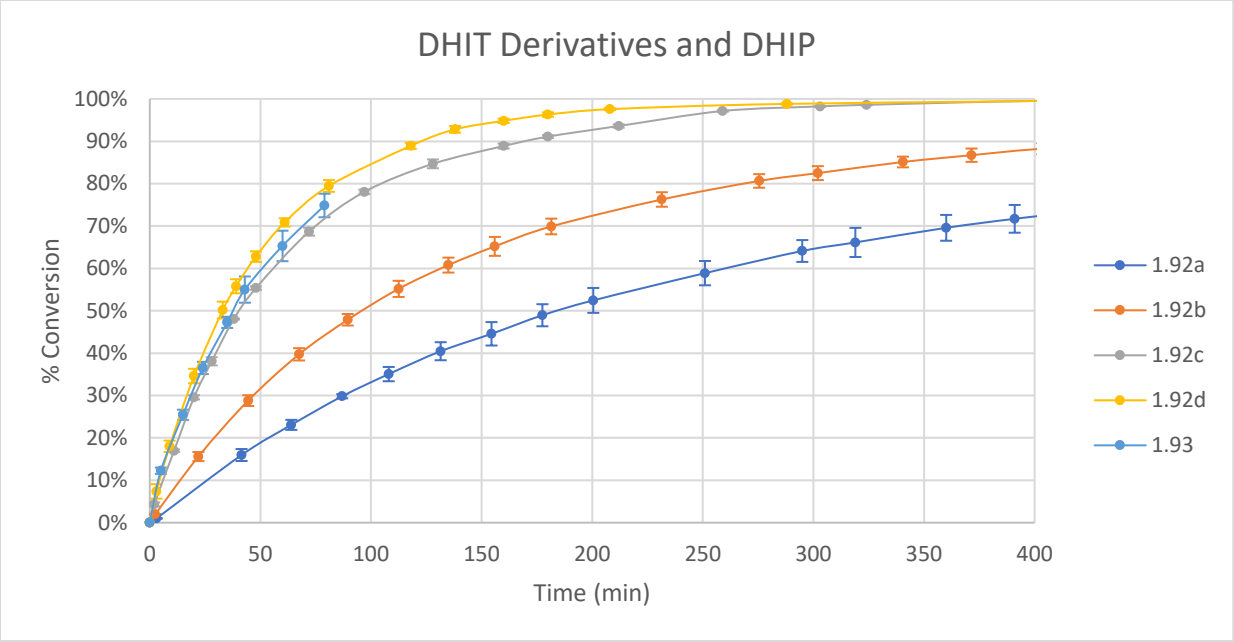
1.5.19 Achiral catalyst survey.



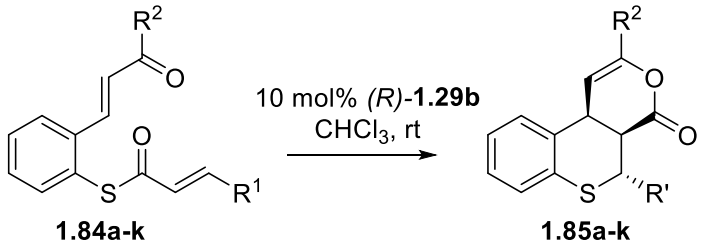
Each experiment was performed in duplicate. A stock solution containing 0.00675 mmol of a catalyst in freshly distilled $CDCl_3$ was added into an NMR tube containing 0.0675 mmol of substrate **1.84a** in enough $CDCl_3$ to produce 0.675 mL total volume (final concentration: 0.100 M in the substrate, 0.010 M in the catalyst). The reaction was monitored by ^1H NMR. The conversion was measured by comparing the peaks of the product and the catalyst. The results are summarized in plots shown below. The reaction rates relative to that of DHPB (**1.63a**) shown in Table 1.3 were estimated from the slope of each graph at low conversions.


DHPB derivatives
% Conversion
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
2000
4000
6000
8000
10000
Time (min)
1.63a
1.63b
1.63c
1.63d
1.63e


DHTP derivatives
% Conversion
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
100
200
300
400
500
600
700
Time (min)
1.91a
1.91b
1.91c
1.91d



1.5.20 Enantioselective synthesis of thiochromanes, general procedure.

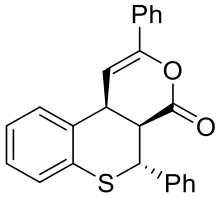


A solution of substrate **1.84** and catalyst *(R)*-**1.85b** (10 mol%) in freshly distilled chloroform (0.2 M in the substrate) was stirred at room temperature under argon until the reaction was complete by TLC. The reaction mixture was concentrated under reduced pressure and purified by flash chromatography using the eluent indicated below. The resulting thiochromane **1.85** was analyzed by chiral stationary phase HPLC.

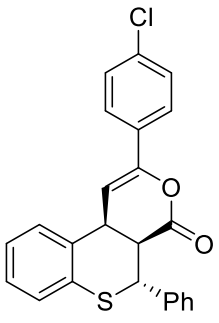
1.5.21 Preparative Scale Synthesis of 1.85a.

A solution of substrate **1.84a** (1.000 g, 2.70 mmol) and catalyst *(R)*-**1.29b** (10 mol%, 53 mg) in freshly distilled chloroform (13.5 mL) was stirred at room temperature under argon for 48 h. The reaction mixture was concentrated under reduced pressure and purified by flash chromatography (2% EtOAc in hexane) to give **1.85a** (861 mg, 86% yield, 97:3 dr, 95% *ee*).

1.5.22 Characterization data for the thiochromane products.

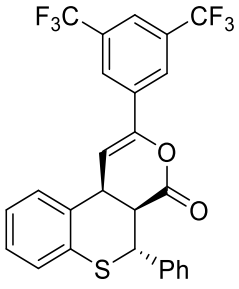


1.85a: Isolated as a white solid (49 mg; 93% yield) after chromatography (2% EtOAc in hexane). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.75 – 7.60 (m, 2H), 7.59 – 7.03 (m, 12H), 6.10 (d, *J* = 5.3 Hz, 1H), 4.79 (d, *J* = 8.2 Hz, 1H), 4.21 (dd, *J* = 7.0, 5.3 Hz, 1H), 3.68 (dd, *J* = 8.2, 7.1 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 167.88, 150.22, 139.36, 135.35, 134.59, 131.87, 129.63, 129.09, 128.77, 128.49, 128.39, 128.22, 128.09, 127.90, 126.40, 124.89, 102.98, 49.48, 45.45, 37.00. **IR** (cm^{-1}): 2927, 1754, 1459, 1276, 1231, 1142, 1075, 1001, 949, 819, 759, 738, 687, 605, 549; **MS:** ESI calculated for $[C_{24}H_{18}O_2S+H]^+$: 371.1100, found: 371.1124; **mp**: 157-161 °C; **HPLC:** (3% isopropanol/hexanes): Minor enantiomer: 22.192 min; Major enantiomer: 26.039 min; 95% *ee*; $[\alpha]_D^{23}$= -1.5° (c= 0.44, CH_2Cl_2).

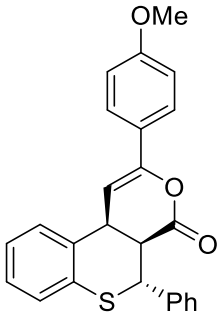


1.85b: Isolated as a white solid (36 mg; 89% yield) after chromatography (5→15% EtOAc/hexanes). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.7 Hz, 2H), 7.49 (d, *J* = 6.9 Hz, 2H), 7.41 – 7.27 (m, 7H), 7.26 – 7.18 (m, 2H), 6.08 (d, *J* = 5.3 Hz, 1H), 4.76 (d, *J* = 8.1 Hz, 1H), 4.21 (t, *J* = 6.2 Hz, 1H), 3.67 (dd, *J* = 8.1, 7.0 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.59, 149.30, 139.24, 135.63, 135.35, 134.36, 130.34, 129.12, 129.04, 128.56, 128.37, 128.29, 128.04, 127.99, 126.45,

126.18, 103.44, 49.41, 45.44, 37.00. **IR** (cm^{-1}): 1762, 1544, 1492, 1264, 732, 700; **MS:** HR-ESI calculated for $[C_{24}H_{17}ClO_2S+H]^+$: 405.0711, found: 405.0719; **mp**: 166-169 °C; **HPLC:** (3% isopropanol/hexanes): Minor enantiomer: 19.78 min; Major enantiomer: 35.94 min; 93% *ee*; $[\alpha]_D^{23}$= -1.5° (c= 0.61, CH_2Cl_2).

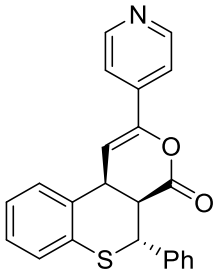


1.85c: Isolated as a white solid (39 mg, 74% yield) after chromatography (5% EtOAc/hexanes). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.02 (s, 2H), 7.82 (s, 1H), 7.50 – 6.99 (m, 9H), 6.22 (d, J = 5.3 Hz, 1H), 4.68 (d, J = 8.1 Hz, 1H), 4.20 (dd, J = 6.2 Hz, 1H), 3.63 (dd, J = 7.6 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 166.86, 147.70, 138.95, 135.32, 133.99, 133.63, 132.49 (q, J = 33.7 Hz), 129.20, 128.69, 128.43, 128.31, 128.26, 127.96, 126.59, 124.91 (q, J = 3.8 Hz), 123.24 – 122.82 (m), 123.17 (q, J = 273.0 Hz), 106.40, 49.26, 45.36, 37.00; **IR** (cm^{-1}): 1773, 1384, 1278, 1132, 899, 752, 698; **MS:** HR-ESI calculated for $[C_{26}H_{16}F_6O_2S+Na]^+$: 529.0667, found: 529.0709; **mp**: 187-190 °C; **HPLC:** (1% isopropanol/hexanes): Minor enantiomer: 9.761 min; Major enantiomer: 41.15 min; 96% *ee*; $[\alpha]_D^{23}$= +0.39° (c= 0.14, CH_2Cl_2).

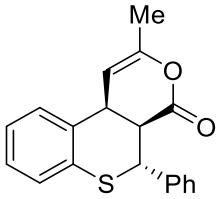


1.85d: Isolated as a white solid (41 mg, 69% yield) after chromatography (5% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.61 (d, J = 8.9 Hz, 2H), 7.50 (dd, J = 8.1, 1.6 Hz, 2H), 7.43 – 7.28 (m, 5H), 7.21 (td, J = 6.8, 1.9 Hz, 2H), 6.92 (d, J = 8.9 Hz, 2H), 5.95 (d, J = 5.3 Hz, 1H), 4.78 (d, J = 8.1 Hz, 1H), 4.18 (dd, J = 7.0, 5.3 Hz, 1H), 3.84 (s, 3H), 3.66 (dd, J = 8.1, 7.0 Hz, 1H; **^{13}C NMR** (125 MHz, $CDCl_3$): δ 168.08, 160.76, 150.05, 139.44, 135.35, 134.85, 131.89, 129.07, 128.46, 128.41, 128.19, 128.13, 127.83, 126.37, 114.15, 113.97, 100.97, 55.53, 49.58, 45.48, 37.00; **IR** (cm^{-1}): 1760, 1607, 1511, 1455, 1250, 1168, 1030, , 907, 835, 728, 698; **MS:** HR-ESI calculated

for $[C_{25}H_{20}O_3S+Na]^+$: 423.1025, found: 423.1063; **mp**: 122-125 °C; **HPLC:** (3% isopropanol/hexanes): Minor enantiomer: 34.388 min; Major enantiomer: 38.702 min; 98% *ee*; $[\alpha]_D^{23}$= -0.98° (c= 1.03, CH_2Cl_2).

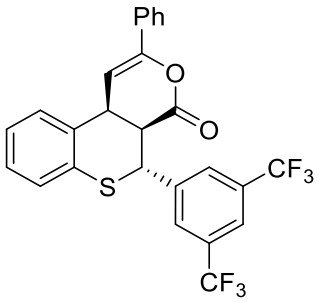


1.85e: Isolated as a light yellow solid (34 mg; 92% yield) after chromatography (50→80% EtOAc/hexanes). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.67 (d, *J* = 6.3 Hz, 2H), 7.54 (d, *J* = 6.3 Hz, 2H), 7.49 (d, *J* = 6.9 Hz, 2H), 7.40 – 7.31 (m, 4H), 7.29 – 7.26 (m, 2H), 7.21 (td, *J* = 7.4, 1.4 Hz, 1H), 6.34 (d, *J* = 5.3 Hz, 1H), 4.74 (d, *J* = 8.2 Hz, 1H), 4.26 (dd, *J* = 7.0, 5.3 Hz, 1H), 3.69 (dd, *J* = 8.2, 7.1 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.06, 150.54, 148.09, 139.09, 139.03, 135.35, 133.77, 129.16, 128.64, 128.39, 128.33, 128.17, 127.94, 126.54, 118.75, 106.83, 49.28, 45.41, 36.99; **IR** (cm^{-1}): 1764, 1596, 1410, 1265, 1242, 1166, 1072, 1041, 809, 732, 696. **MS:** HR-ESI calculated for $[C_{23}H_{17}NO_2S+H]^+$: 372.1053, found: 372.1058; **mp**: 124-127 °C; **HPLC:** (30% isopropanol/hexanes): Major enantiomer: 24.98 min; Minor enantiomer: 32.19 min; 96% *ee*; $[\alpha]_D^{23}$= -0.97° (c= 0.24, CH_2Cl_2).

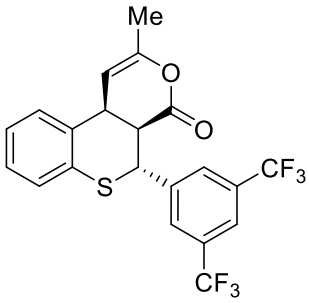


1.85f: Isolated as a yellow oil (40 mg, 64% yield) after chromatography (5% EtOAc/hexanes). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.49 (dd, J = 7.5, 1.7 Hz, 2H), 7.42 – 7.30 (m, 5H), 7.20 (td, J = 7.0, 1.7 Hz, 2H), 5.34 (d, J = 4.6 Hz, 1H), 4.71 (d, J = 7.7 Hz, 1H), 3.95 (t, J = 6.3 Hz, 1H), 3.57 (t, J = 7.7 Hz, 1H), 2.00 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 168.43, 149.94, 139.79, 135.49, 135.28, 129.05, 128.36, 128.35, 128.31, 127.81, 127.77, 127.69, 126.38, 126.36, 102.78, 49.76, 45.83, 36.46, 18.80; IR (cm^{-1}): 2923, 2853, 1766, 1462, 1278, 1152, 1073, 749, 698; **IR** (cm^{-1}): 2923, 2853, 1766, 1462, 1278, 1152, 1073, 749, 698; **MS:** HR-ESI calculated for $[C_{19}H_{16}O_2S+Na]^+$: 331.0763, found: 331.0776; **HPLC:**

(0.25% isopropanol/hexanes): Minor enantiomer: 48.147 min; Major enantiomer: 69.56 min; 80% *ee*; $[\alpha]_D^{23}$=-0.11° (c= 0.46, CH_2Cl_2).

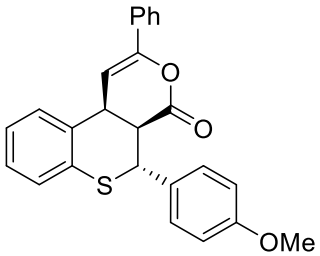


1.85g: Isolated as a white solid (86 mg, 86% yield) after chromatography (5% EtOAc/hexanes). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.92 (s, 2H), 7.77 (s, 1H), 7.65 – 7.53 (m, 2H), 7.53 – 7.32 (m, 4H), 7.30 – 7.25 (m, 1H), 7.25 – 7.07 (m, 2H), 6.09 (d, J = 5.9 Hz, 1H), 4.76 (d, J = 8.1 Hz, 1H), 4.15 (dd, J = 7.7, 5.9 Hz, 1H), 3.62 (dd, J = 8.0 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 167.76, 151.00, 142.57, 135.46, 134.89, 132.47 (q, J = 33.7 Hz), 131.57, 129.90, 129.06, 128.88, 128.79 – 128.60 (m), 128.22, 127.69, 127.42, 124.92, 123.20 (q, J = 272.8 Hz), 122.70 – 122.26 (m), 101.49, 50.21, 46.34, 37.19; **IR** (cm^{-1}): 2254, 1764,1378, 1279, 1177, 1142, 904, 726; **MS:** HR-ESI calculated for $[C_{26}H_{16}F_6O_2S+H]^+$: 507.0848, found: 507.0804; **mp**: 87-91 °C; **HPLC:** (3% isopropanol/hexanes): Minor enantiomer: 9.829 min; Major enantiomer: 12.077 min; 98% *ee*; $[\alpha]_D^{23}$= -0.79° (c= 7.15, CH_2Cl_2).

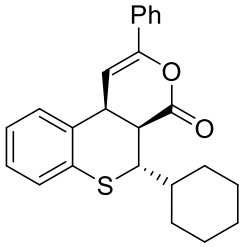


1.85h: Isolated as a clear oil (16 mg, 83% yield) after chromatography (5% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): 7.97 (s, 2H), 7.84 (s, 1H), 7.46 – 7.35 (m, 1H), 7.34 – 7.11 (m, 3H), 5.41 (dq, J = 5.7, 1.0 Hz, 1H), 4.74 (d, J = 8.1 Hz, 1H), 3.96 (t, J = 7.0 Hz, 1H), 3.58 (td, J = 8.1, 0.8 Hz, 1H), 2.04 (d, J = 1.0 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): 168.21, 150.72, 142.86, 136.01, 135.04, 132.42 (q, J = 33.6 Hz), 130.12, 129.11, 128.72 (q, J = 3.8 Hz), 128.02, 127.41, 127.37, 122.85 (q, J = 272.7 Hz), 122.36 (sept, J = 3.8 Hz), 50.37, 46.65, 36.74, 18.85; **IR** (cm^{-1}): 1759, 1378, 1278, 1134; **MS:** HR-ESI calculated for $[C_{21}H_{14}F_6O_2S+Na]^+$:

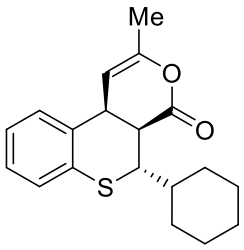
467.0511, found: 467.0537. **HPLC:** (0.25% isopropanol/hexanes): Minor enantiomer: 13.251 min; Major enantiomer: 26.708 min; 92% *ee*; $[\alpha]_D^{23}$= -0.42° (c= 0.1, CH_2Cl_2).



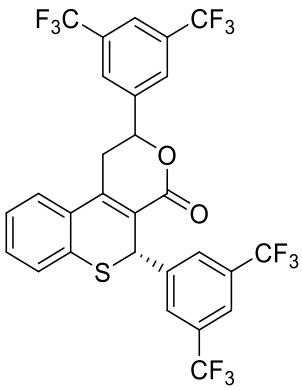
1.85i: Isolated as a racemic, white solid from catalyst **18c** (14 mg, 79% yield) after chromatography (5% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.85 – 7.56 (m, 2H), 7.50 – 7.37 (m, 5H), 7.34 – 7.14 (m, 4H), 6.90 (d, J = 8.8 Hz, 2H), 6.05 (dd, J = 5.0, 0.6 Hz, 1H), 4.74 (d, J = 8.6 Hz, 1H), 4.23 (dd, J = 6.8, 5.0 Hz, 1H), 3.81 (s, 3H), 3.64 (dd, J = 8.4, 6.7 Hz, 1H; **^{13}C NMR** (125 MHz, $CDCl_3$): δ 167.86, 159.71, 149.96, 135.42, 134.24, 131.90, 130.94, 129.62, 129.56, 128.78, 128.31, 127.99, 127.88, 126.26, 124.88, 114.47, 103.36, 55.46, 49.32, 44.53, 37.25; **IR** (cm^{-1}): 1760, 1510, 1438, 1239, 1179, 1025, 826, 809, 753, 720, 685, 631, 537; **MS:** HR-ESI calculated for $[C_{25}H_{20}O_3S+Na]^+$: 423.1025, found: 423.1060; **mp:** 157-160 °C dec.



1.85j: Isolated as a white solid (33 mg; 87% yield), after chromatography (5→15% EtOAc/hexanes). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 7.9, 1.8 Hz, 2H), 7.45 – 7.39 (m, 3H), 7.35 (d, *J* = 7.8 Hz, 1H), 7.24 (d, *J* = 7.5 Hz, 1H), 7.19 (t, *J* = 7.3 Hz, 1H), 7.14 (t, *J* = 7.4 Hz, 1H), 6.13 (d, *J* = 5.8 Hz, 1H), 3.91 (t, *J* = 6.5 Hz, 1H), 3.68 (dd, *J* = 7.2, 5.1 Hz, 1H), 3.41 (t, *J* = 7.2 Hz, 1H), 2.06 – 1.96 (m, 1H), 1.86 – 1.77 (m, 3H), 1.76 – 1.67 (m, 2H), 1.36 – 1.18 (m, 5H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.13, 150.63, 136.00, 135.13, 131.98, 129.56, 129.23, 128.76, 127.74, 127.25, 126.23, 124.89, 102.74, 47.84, 45.43, 42.09, 36.91, 31.26, 29.51, 26.54, 26.41, 26.37; **IR** (cm^{-1}): 1759, 1445, 1278, 1136, 1063, 759, 689, 597. **MS:** HR-ESI calculated for $[C_{24}H_{24}O_2S+H]^+$: 377.1570, found: 377.1573; **mp**: 116-119 °C; **HPLC:** (0.20% isopropanol/hexanes): Major enantiomer: 36.78 min; Minor enantiomer: 47.47 min; 99% *ee*; $[\alpha]_D^{23}$= -1.7° (c= 0.87, CH_2Cl_2).

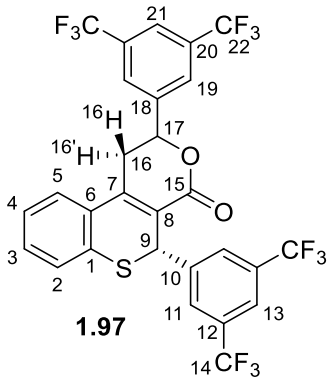


1.85k: Isolated as a clear oil (79 mg, 67% yield), after chromatography (5% EtOAc/hexanes). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.36 – 7.29 (m, 1H), 7.23 – 7.08 (m, 3H), 5.35 (d, J = 5.7 Hz, 1H), 3.71 – 3.59 (m, 1H), 3.59 (dd, J = 5.5 Hz, 1H), 3.29 (t, J = 7.4 Hz, 1H), 2.02 (s, 3H), 1.98 – 1.63 (m, 7H), 1.40 – 0.71 (m, 7H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 169.62, 150.18, 136.46, 135.12, 129.22, 127.52, 127.05, 126.13, 102.67, 48.08, 45.42, 42.03, 36.32, 31.31, 29.63, 26.56, 26.44, 26.40, 18.79; **IR** (cm^{-1}): 2925, 1763, 1702, 1445, 1148, 472, 451, 432; **MS:** HR-ESI calculated for $[C_{19}H_{22}O_2S+Na]^+$: 337.1233, found: 337.1236; **HPLC:** (0.25% isopropanol/hexanes): Minor enantiomer: 16.581 min; Major enantiomer: 21.232 min; 96% *ee*; $[\alpha]_D^{23}$= -0.97° (c= 1.93, CH_2Cl_2).



1.96: Isolated as a white amorphous solid (50 mg, 81% yield) after chromatography (5% EtOAc/hexanes). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.00 (s, 2H), 7.94 (s, 1H), 7.72 (s, 1H), 7.70 (s, 2H), 7.60 (dd, J = 8.0, 1.1 Hz, 1H), 7.45 (dd, J = 7.8, 1.3 Hz, 1H), 7.39 (td, J = 7.3, 1.3 Hz, 1H), 7.30 (td, J = 8.0, 1.4 Hz, 1H), 5.69 (dd, J = 12.3, 3.6 Hz, 1H), 5.69 (s, 1H), 3.54 (dd, J = 18.0, 3.6 Hz, 1H), 2.92 (ddd, J = 18.0, 12.3, 0.7 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 164.03, 145.18, 143.41, 140.71, 133.03, 132.37 (q, J = 33.7 Hz), 132.17, 132.10 (q, J = 33.4 Hz), 129.49, 128.89, 127.32, 127.07 – 127.04 (m), 126.81, 126.59 – 126.56 (m), 123.15 (q, J = 272.9 Hz), 123.12 (sept, J = 3.7 Hz), 122.02 (sept, J = 3.8 Hz), 119.82, 76.55, 37.06, 32.95; **IR** (cm^{-1}): 1715, 1372, 1278, 1134; **MS:** HR-ESI calculated for $[C_{28}H_{14}F_{12}O_2S+H]^+$: 643.0596, found: 643.0547; **HPLC:** (1% isopropanol/hexanes): Major enantiomer: 7.934 min; Minor enantiomer: 39.076 min; 98% *ee*.

Table 1.11: 2D NMR characterization data for **1.97**.

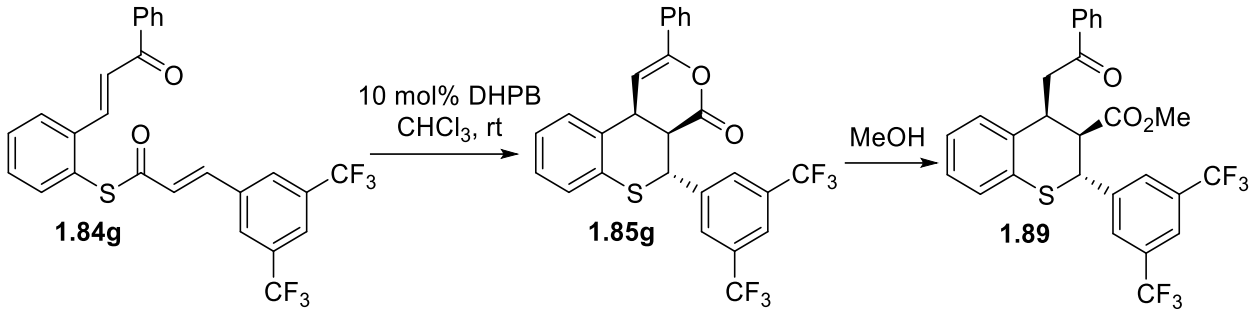


1.97

Atom	^{13}C (ppm), multiplets in Hz	^{1}H (ppm), multiplets in Hz	gCOSY ^{1}H-^{1}H 3 bond	TOCSY ^{1}H-^{1}H 3-5 bond	HSQC ^{1}H-^{13}C 1 bond	HMBC ^{1}H-^{13}C 2-3 bond	NOESY ^{1}H-^{1}H through space
1	133.03					3, 5, 9	
2	128.89	7.45 (dd, J = 7.8, 1.3 Hz, 1H)	3, 4	3, 4, 5	2	3	
3	126.81	7.30 (td, J = 8.0, 1.4 Hz, 1H)	2, 4	2, 4, 5	3	2, 4	
4	132.17	7.39 (td, J = 7.3, 1.3 Hz, 1H)	3, 5	2, 3, 5	4	5	
5	127.32	7.60 (dd, J = 8.0, 1.1 Hz, 1H)	3, 4	2, 3, 4	5	4	16’
6	129.49					2, 4	
7	145.18					5, 9, 16, 16’, 17	
8	119.82					9, 16, 16’	
9	37.06	5.69 (s, 1H)			9	11	
10	143.41					9	
11	127.07 – 127.04 (m)	7.70 (s, 2H)			11		
12	132.37 (q, J = 33.7 Hz)						
13	122.02 (sept, J = 3.8 Hz)	7.72 (s, 1H)			13	11	

Atom	^{13}C (ppm), multiplets in Hz	^{1}H (ppm), multiplets in Hz	gCOSY ^{1}H-^{1}H 3 bond	TOCSY ^{1}H-^{1}H 3-5 bond	HSQC ^{1}H-^{13}C 1 bond	HMBC ^{1}H-^{13}C 2-3 bond	NOESY ^{1}H-^{1}H through space
14	123.15 (q, J = 272.9 Hz)					11, 13	
15	164.03						
16	32.95	2.92 (ddd, J = 18.0, 12.3, 0.7 Hz, 1H)	16', 17	16', 17	16		16
16'	32.95	3.54 (dd, J = 18.0, 3.6 Hz, 1H)	16, 17	16, 17	16		5, 16
17	76.55	5.69 (dd, J = 12.3, 3.6 Hz, 1H)		19	17	16, 19	
18	140.71					16	
19	126.59 – 126.56 (m)	8.00 (s, 2H)		17	19	17	
20	132.10 (q, J = 33.4 Hz)						
21	123.12 (sept, J = 3.7 Hz)	7.94 (s, 1H)			21	19	
22	123.15 (q, J = 272.9 Hz)					19, 21	

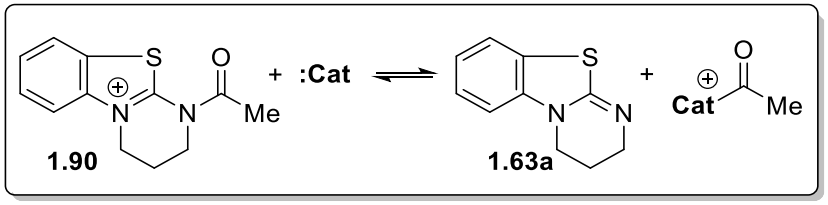
1.5.23 Methanolysis of thiochromane product 1.85g.



A solution of substrate **1.84g** (122 mg, 0.24 mmol) and DHPB (10 mol%) in freshly distilled chloroform (0.2 M in the substrate) was stirred at room temperature under argon for 48h. Methanol (2 mL) was added and the mixture was stirred for an additional 48h. The reaction mixture was concentrated under reduced pressure and chromatographed (5% EtOAc/hexanes) to give **1.89** as a yellow oil (84 mg, 77%). **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.92-7.91 (m, 2H), 7.89 (s, 2H), 7.79 (s, 1H), 7.55 (dd, J = 7.4, 1.3 Hz, 1H), 7.46 – 7.43 (m, 2H), 7.38 (dd, J = 7.7, 1.4 Hz, 1H), 7.22 – 7.17 (m, 2H), 7.09 (td, J = 7.3, 1.5 Hz, 1H), 4.98 (d, J = 11.8 Hz, 1H), 4.27 – 4.24 (m, 1H), 3.59 (dd, J = 17.4, 4.5 Hz, 1H), 3.56 (s, 3H), 3.54 (dd, J = 17.4, 4.5 Hz, 1H), 3.22 (dd, J = 11.8, 2.9 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 197.43, 172.2, 143.97, 136.91, 136.90, 133.46, 132.06 (q, J = 33.5 Hz), 131.27, 130.13, 128.86 – 128.84 (m), 128.77, 128.18, 128.11, 126.39, 125.46, 123.23 (q, J = 272.8 Hz), 122.17 – 122.12 (m), 52.62, 50.50, 43.29, 38.05, 37.80; **IR** (cm^{-1}): 1731, 1686, 1374, 1277, 1170, 1131, 906, 730, 682; **MS:** HR-ESI calculated for $[C_{27}H_{20}F_6O_3S+H]^+$: 539.1110, found: 539.1095.

1.5.24 Computational studies.

Geometry optimization of the structures of all the catalysts shown in Figure 1 and the corresponding N-acetyl cations was performed at the B3LYP/6-31G* level of theory[49] using a nonpolar solvent model. Single point energies calculations were then conducted on the lowest energy conformer identified in each case at B3LYP/6-311+G(2d,p) level of theory. The results are shown in the table below.



Catalyst	$\Delta H_{[Cat]}$ (a.u.)	$\Delta H_{[Cat\text{-}Ac+]}$ (a.u.)	$\Delta H_{Ac\ (Cat)} = \Delta H_{[Cat\text{-}Ac+]} - \Delta H_{[Cat]}$ (a.u.)	$\Delta H_{Ac(rel)} = \Delta H_{Ac\ (Cat)} - \Delta H_{Ac\ (9a)}$	
				a.u.	Kcal/mol
1.63a	-894.961284	-1048.11526	-153.153976	0	0
1.63b	-1009.52043	-1162.67717	-153.15674	-0.002764	-1.73441
1.63c	-1028.96613	-1182.12592	-153.15979	-0.005814	-3.648285
1.63d	-1106.41125	-1259.57217	-153.16092	-0.006944	-4.35736
1.63e	-1240.42151	-1393.58722	-153.16571	-0.011734	-7.363085
1.90a	-972.381199	-1125.54239	-153.161191	-0.007215	-4.5274125
1.90b	-1086.94349	-1240.10576	-153.16227	-0.008294	-5.204485
1.90c	-1106.39051	-1259.55441	-153.1639	-0.009924	-6.22731
1.90d	-1183.83625	-1337.0004	-153.16415	-0.010174	-6.384185
1.91a	-933.047734	-1086.20824	-153.160506	-0.00653	-4.097575
1.91b	-1047.61014	-1200.77175	-153.16161	-0.007634	-4.790335
1.91c	-1067.05721	-1220.2209	-153.16369	-0.009714	-6.095535
1.91d	-1144.50315	-1297.66699	-153.16384	-0.009864	-6.18966
1.92	-381.16045	-534.328297	-153.167847	-0.013871	-8.7040525

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1552, 1432, 1411, 1388, 1281, 1194, 1078, 835, 787, 769; **MS:** HR-ESI calculated for $[C_{14}H_8O_2S_2Cl_2+Na]^+$: 364.9235, found: 364.9232; **mp**: 226-228 °C dec.

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Chapter 2: Fused Imidazoline Ligands

2.1 Introduction.

Asymmetric catalysis using chiral metal complexes is a fundamentally important area of organic synthesis. Synthetic chiral catalysts can exhibit good levels of enantioselectivities for a broad range of substrates, and both enantiomers can be accessed depending on the chirality of the catalyst. Dubbed "privileged," certain classes of synthetic catalysts even retain their enantioselectivities across a broad range of reactions. Privileged chiral ligands (Figure 2.1) offer effective asymmetric environments for mechanistically different metal-catalyzed reactions.[1] Despite the wide range of known catalysts, there are still many important synthetic transformations that have no asymmetric alternative.

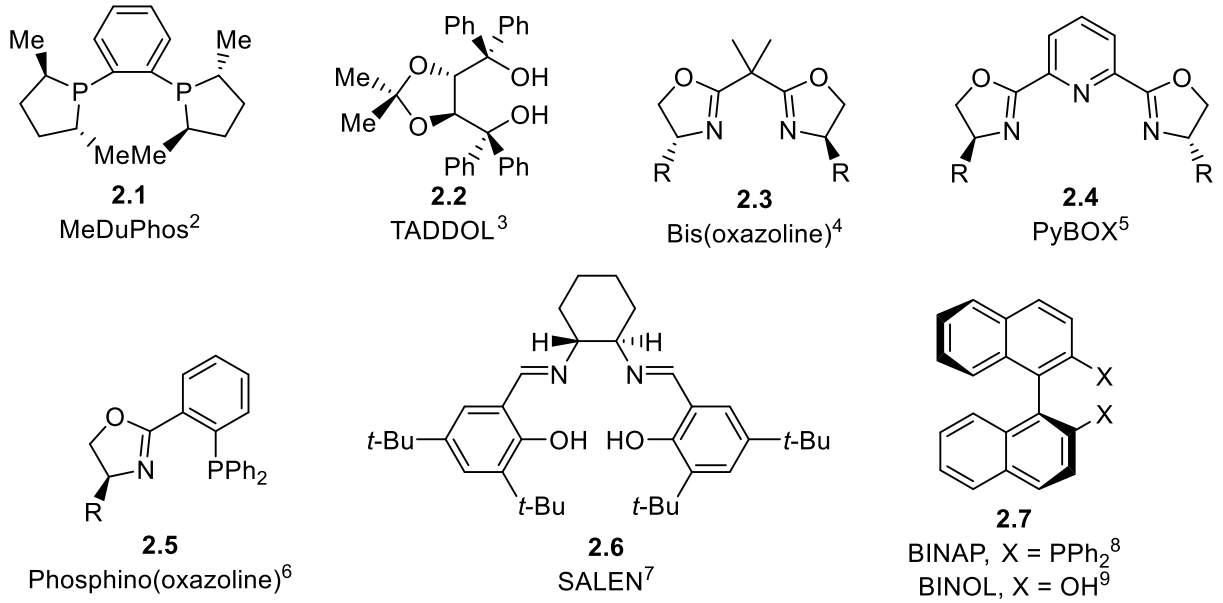


Figure 2.1: Examples of privileged chiral ligands.

2.2 New ligand design.

Over the last decade, our group has developed amidine-based catalysts (ABCs) in the field of organocatalysis (Figure 2.2).[10] These catalysts have proven to be highly effective for enantioselective acyl transfer reactions.[11] Seeking to diversify our asymmetric catalysis portfolio, we envisioned a new chiral ligand for metal catalysis using a fused-imidazoline moiety.

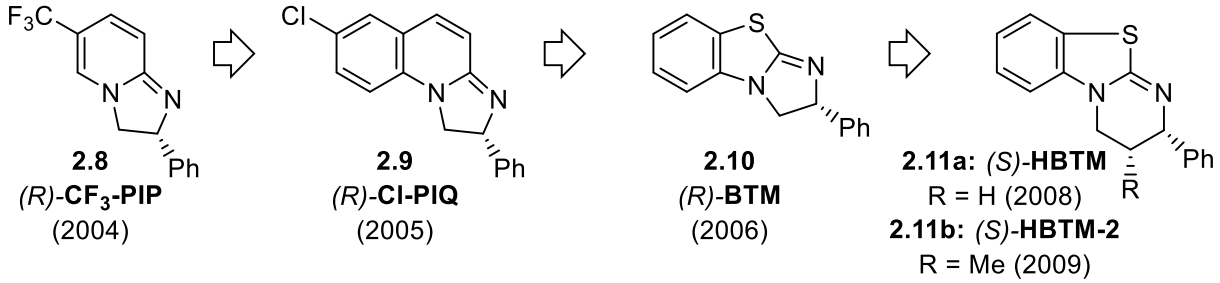


Figure 2.2: Evolution of amidine-based catalyst design in our group.

Of the above mentioned privileged ligands, Bis(oxazoline) ligands (BOX) (**2.3**) served as our primary inspiration for our design due to their ability to coordinate with a wide range of metals and their C_2-axis, a feature that has shown to be valuable in designing asymmetric processes due to the equivalency of structures upon rotation by 180^o reducing the number of possible transition states. Furthermore, the reliable mechanistic understanding of BOX-metal complexes in many asymmetric processes corroborated by X-ray structure analysis provides insight into how these and similar ligands operate.[12]

One design feature that we sought to improve upon from BOX ligand was the electronic tunability of the donor nitrogen atoms of the ligand. Despite a report by Nishiyama[13] demonstrating that electronic control of PyBOX **2.4a-e** (Figure 2.3) affects the catalytic activity and enantioselectivity in PyBOX-Rhodium catalyzed cyclopropanation, relatively little exploration into the electronic effects on BOX ligands have been explored possibly due to the synthetic

difficulty of introducing in conjugation with the donor nitrogen atoms. Evans et al.[14] disclosed that para electron-donating or -withdrawing groups had only a slight effect on hetero-Diels-Alder reactions catalyzed by BOX-metal complexes (**2.3a-c**). This was unsurprising since the remote electronic changes in the phenyl groups were not in conjugation with the donor nitrogen atoms. Pagenkopf et al.[15] disclosed an *m*-(tert-butyl)-*o*-methoxyphenyl BOX ligand (**2.3e**) that showed improved performance in an asymmetric aldol reaction. This improvement in enantioselectivity can most likely be attributed to steric factors rather than electronic factors since removing the *m*-(*tert*-butyl) group severely diminishes the *ee*. Beginning in 2005, Burke et al. explored a series of BOX ligands with conjugation to the donor nitrogens. First, they reported isobutylene bis(oxazoline) (IsBut-BOX **2.12**)[16] with an isopropylidene in place of the *gem*-dimethyl groups resulting in poor *ee* in cyclopropanation. Further modification led them to synthesize bis(oxazolines) with an arylidene bridging unit (Arylid-BOX **2.13a-e**)[17] that contained either *ortho* or *para* electron-donating and -withdrawing groups. This new design produced up to 89% *ee* with modest yields and only slight effects observed by electronic changes in the ligand most likely due to the narrow range of electronic tuning groups tested.

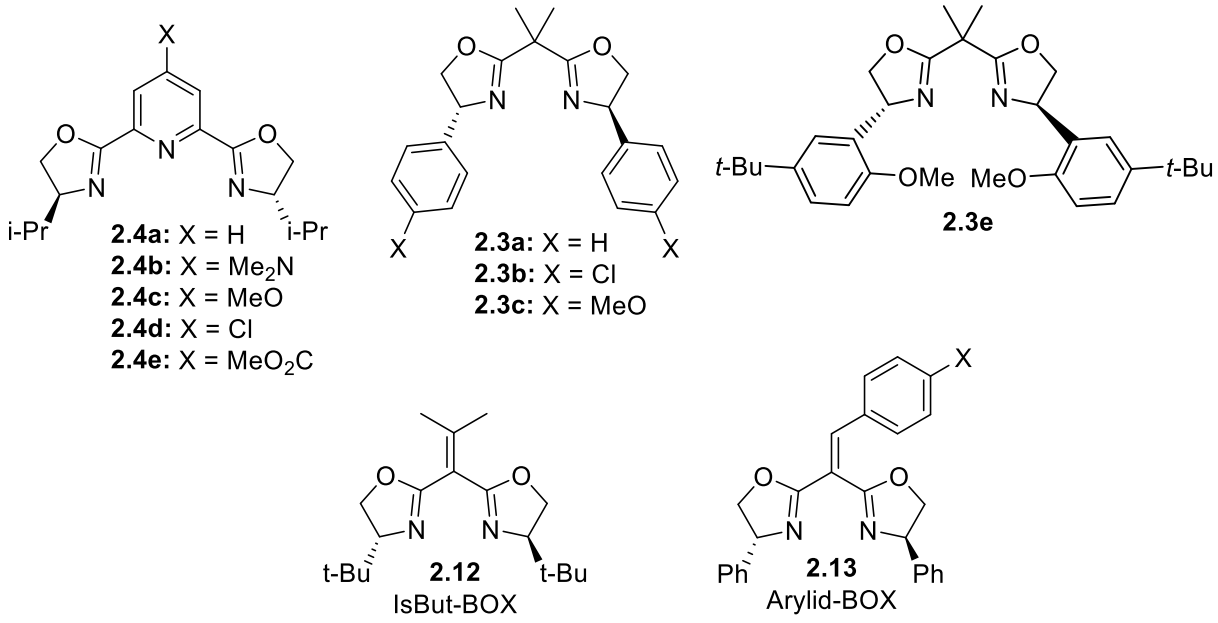


Figure 2.3: Electronic tuning of PyBOX and BOX ligands.

With the added factor of electronic tunability in mind, we looked to Cl-PIQ (**2.9**)[10b] as a building block for designing new chiral ligands due to its efficacy and synthetic accessibility. We envisioned that aldehyde **2.14** could serve as a key intermediate to a variety of chiral ligands for metal catalysis with electronic tuning groups (R^1 and R^2) shown in Figure 2.4. In our proposed design, the aldehyde gives the added synthetic flexibility of varying the denticity as well as the types of donor atoms and groups in potential ligands (Figure 2.5).

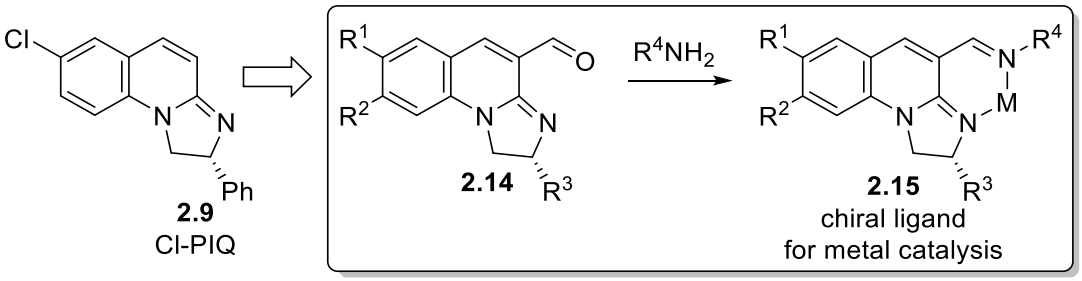


Figure 2.4: Proposed new ligand design.

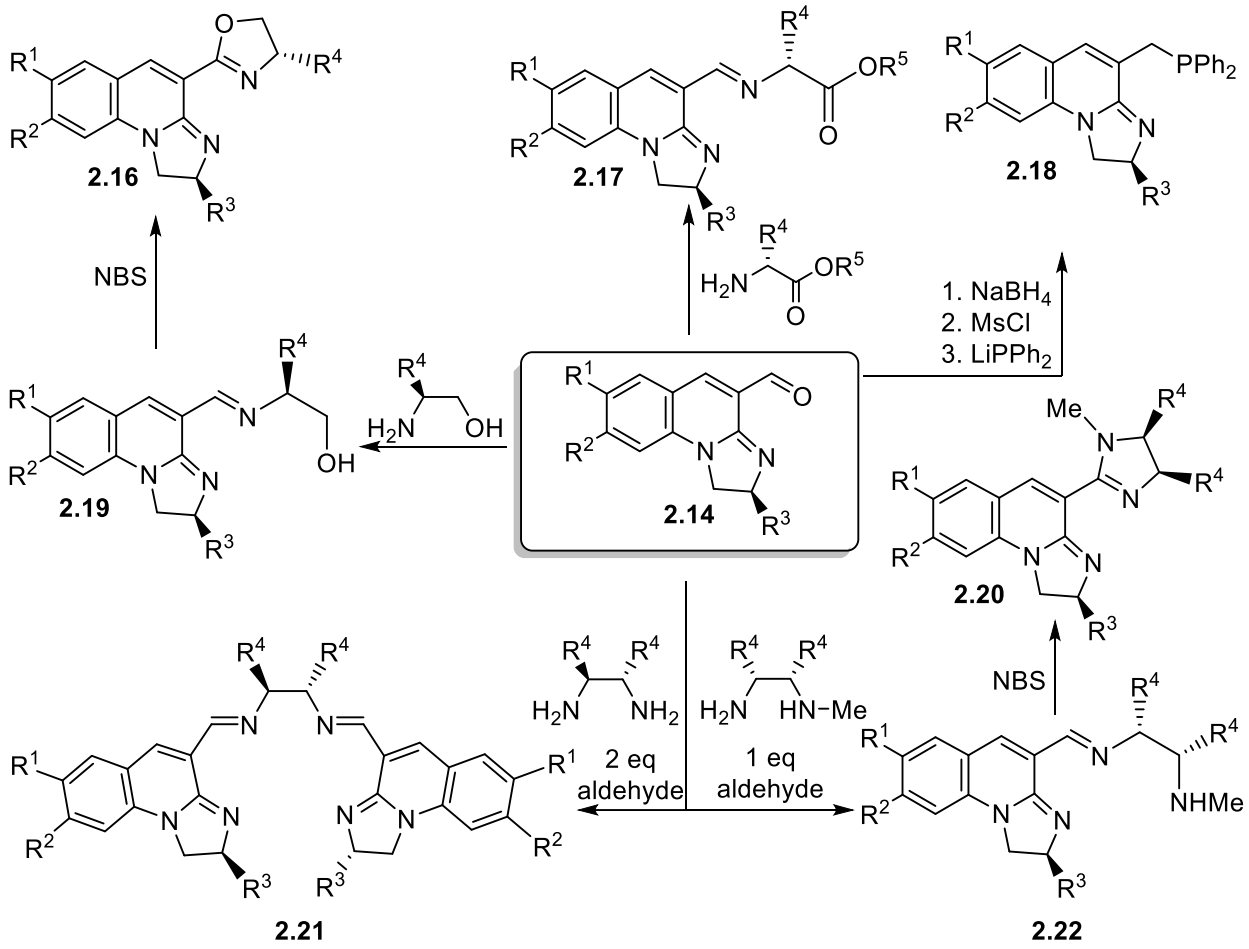


Figure 2.5: Proposed synthetic transformations of key aldehyde **2.14**.

Prior to our work, few examples of asymmetric reactions using ligands containing a fused-imidazoline moiety were reported in the literature. In 2011, Deng et al.[18] reported a planar chiral Ferrocene ligand **2.24** combining the structures of Fu's planar chiral DMAP catalyst (**2.23**)[19] and our CF_3-PIP catalyst (**2.8**)[10a] shown in Figure 2.6. The complex, new N,O-ligand (**2.24**) relies on both planar chirality and a chiral carbon next to the nitrogen donor atom to achieve up to 95% *ee* in a copper catalyzed asymmetric Michael addition.

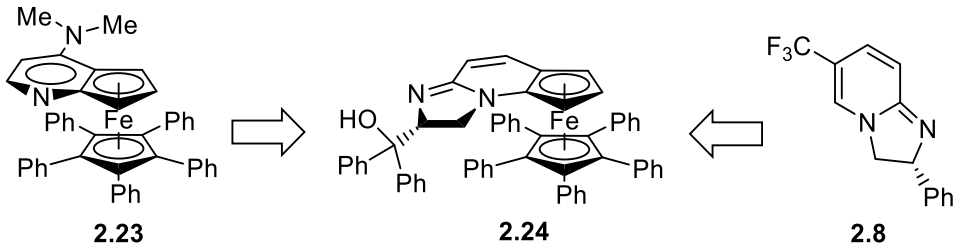


Figure 2.6: Deng's planar chiral N,O-ligand.

2.2.1 Synthesis of key aldehyde intermediate.

Our first objective was to develop a flexible synthetic scheme to produce aldehyde **2.14** with various substituents. Basing our synthesis on Cl-PIQ and other ABCs from our lab,[10] we began by testing a series of amino alcohols (**2.25**) in a nucleophilic aromatic substitution on chloroaldehyde **2.26** followed by mesylation and spontaneous cyclization shown in Figure 2.7. Summarized in Table 2.1, the initial nucleophilic aromatic substitution proceeded with poor to moderate yields to give yellow, crystalline amino aldehyde **2.27** for all amino alcohols tested except *trans*-1-amino-2-indanol. Shown in Table 2.2, the subsequent cyclization with mesyl chloride occurred spontaneously with near quantitative yields to give the cyclized aldehyde (**2.14**) as a deep red product.

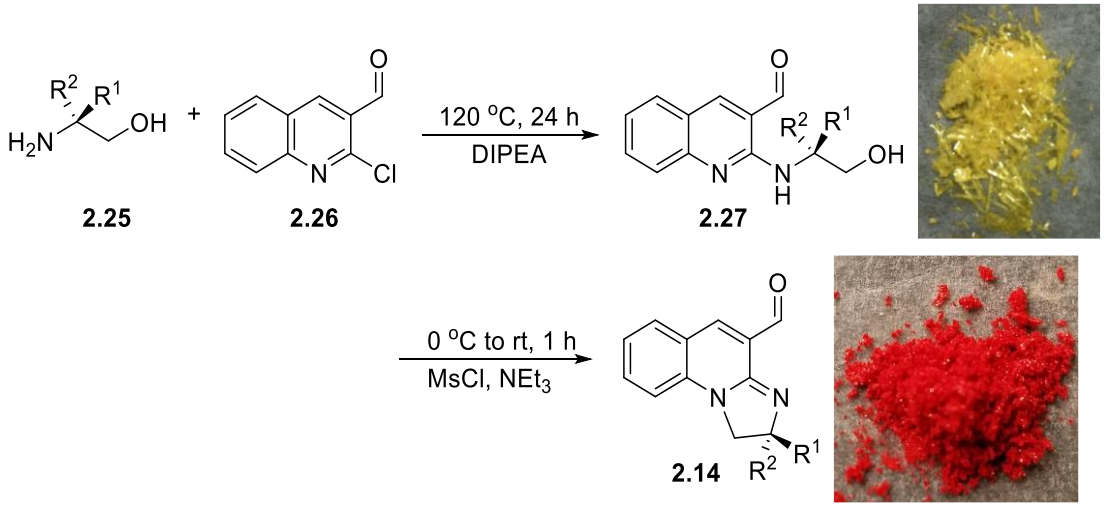
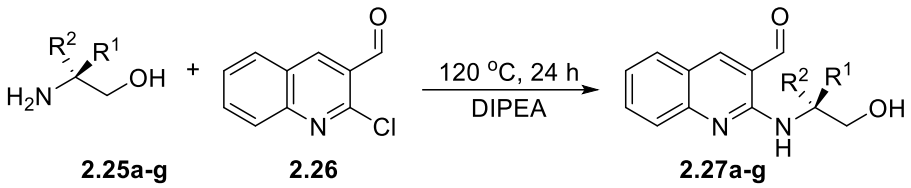


Figure 2.7: Synthesis of key aldehyde intermediate.

Table 2.1: Nucleophilic aromatic substitution of **2.26**.[a]

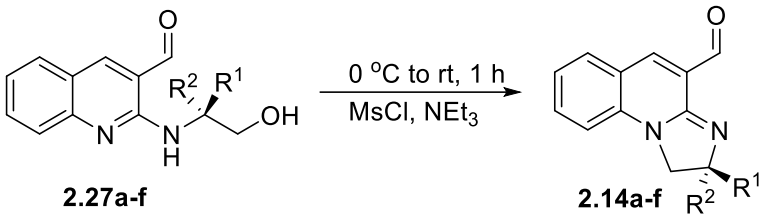


2.25a-g **2.26** **2.27a-g**

entry	product	R^1	R^2	yield, %
1	**2.27a**	H	H	63
2	**2.27b**	Me	Me	20
3	**2.27c**	*i*-Pr	H	75
4	**2.27d**	Ph	H	9
5	**2.27e**	H	$CHPh_2$	32
6	**2.27f**	*t*-Bu	H	46
7	**2.27g**	*trans*-1-amino-2-indanol	*trans*-1-amino-2-indanol	0

[a]Conditions: 2.1 equivalent **2.25**, 1.0 equivalent **2.26**, 1.0 equivalent DIPEA, 120 °C, 24 h.

Table 2.2: Cyclization of **2.27**.[a]



2.27a-f **2.14a-f**

entry	product	R^1	R^2	yield, %
1	**2.14a**	H	H	89
2	**2.14b**	Me	Me	84
3	**2.14c**	*i*-Pr	H	99
4	**2.14d**	Ph	H	71
5	**2.14e**	H	$CHPh_2$	95
6	**2.14f**	*t*-Bu	H	93

[a]Conditions: 1.0 equivalent **2.27**, 1.5 equivalent MsCl, 3.0 equivalent NEt_3, $CDCl_3$ (0.1 M), 0 °C to rt, 1 h

2.2.2 Fused imidazoline imine ligand design.

With aldehyde **2.14** in hand, we turned our attention to converting the aldehyde moiety to a group that would transform **2.14** into a ligand for metal catalysis. Rather than attempting to create a ligand with pseudo-C_2-symmetry, our initial design was a fused imidazoline imine ligand (**2.29**) derived from anilines with *ortho* substituents orthogonal to the plane of the fused imidazoline moiety. These *ortho* groups function to block an entire face of the ligand-metal complex limiting the desired transition states to one rather than two due to a lack of equivalency of structures as observed in BOX ligands with a C_2-axis (Figure 2.8).[12] The new ligands (**2.29**) were easily prepared from **2.14** by heating with the requisite anilines (**2.28**) followed by drying.

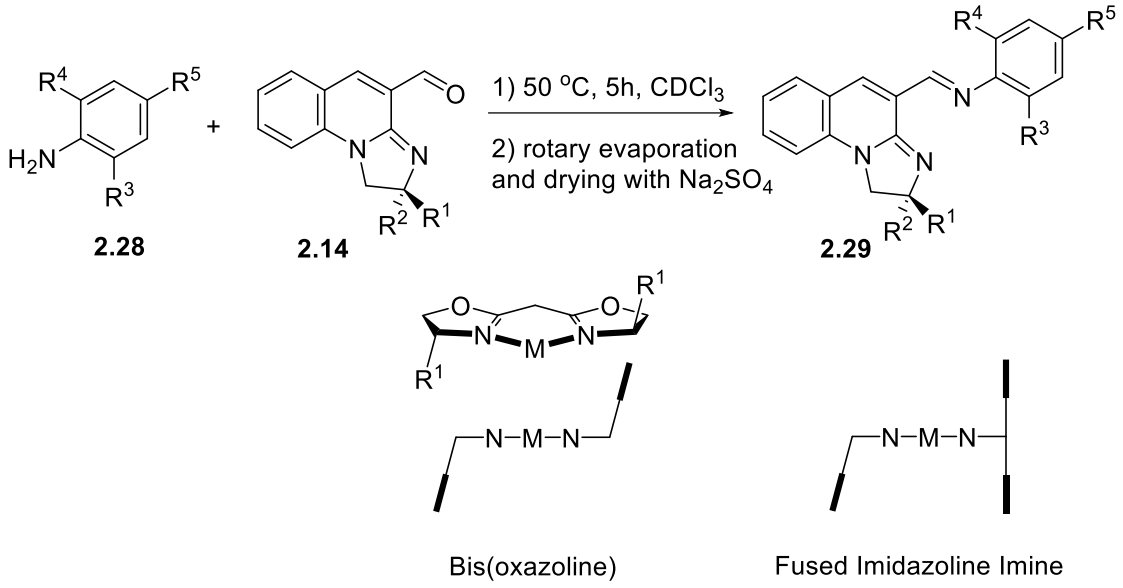


Figure 2.8: Synthesis of fused imidazoline imine ligand and comparison to BOX ligand.

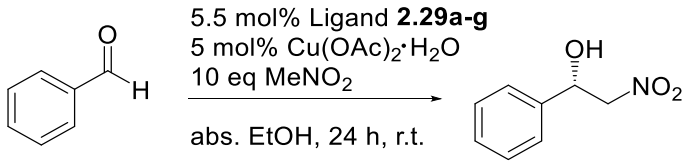
2.3 Evaluation of ligand in the Henry reaction.

2.3.1 Optimization of chiral ligand.

To evaluate the efficacy of the new ligands (**2.29**), we selected the asymmetric Henry reaction between nitromethane and an aldehyde (**2.30**) catalyzed by Cu(II) salts which had been previously shown by Evans to proceed with excellent enantioselectivity in the presence of BOX ligands.[20] A series of fused imidazoline imine ligands (**2.29**) were tested in the Henry reaction of benzaldehyde (**2.30a**) to produce nitroalkanol **2.31a** summarized in Table 2.3. Varying the imine group only (entries 1-4), *o*-isopropyl groups (**2.29b**) produced the best combination of yield and enantioselectivity. Bulkier (diphenyl)methyl groups (**2.29c-d**) shut down the reactivity of the resulting copper complexes giving poor yields without an improvement in enantioselectivity. Keeping the *o*-isopropyl groups constant and varying the chiral group only (entries 2, 5-7), isopropyl and (diphenyl)methyl groups (**2.29b** and **2.29f**) produced comparable but modest yields

and enantioselectivities. Poor yield and enantioselectivity were observed when a phenyl group (**2.29e**) was used. Finally, a ligand with a *tert*-butyl group (**2.29g**) produced the best enantioselectivity (82% *ee*) while maintaining a similar yield (55%).

Table 2.3: Chiral ligand survey.[a]



2.30a **2.31a**

entry	ligand	R^1	R^2	R^3	R^4	R^5	yield, %	*ee*, %
1	**2.29a**	*i*-Pr	H	Me	Me	Me	42	65
2	**2.29b**	*i*-Pr	H	*i*-Pr	*i*-Pr	H	58	75
3	**2.29c**	*i*-Pr	H	Me	$CHPh_2$	Me	23	71
4	**2.29d**	*i*-Pr	H	$CHPh_2$	$CHPh_2$	Me	6	74
5	**2.29e**	Ph	H	*i*-Pr	*i*-Pr	H	36	44
6	**2.29f**	H	$CHPh_2$	*i*-Pr	*i*-Pr	H	60	-73
7	**2.29g**	*t*-Bu	H	*i*-Pr	*i*-Pr	H	55	82

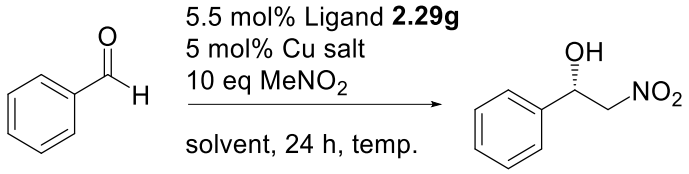
[a]Conditions: 1 mmol **2.30a**, 10 mmol $MeNO_2$, 0.055 mmol **2.31a-g**, 0.05 mmol $Cu(OAc)_2 \cdot H_2O$, 1.5 mL absolute ethanol, 24 h.

2.3.2 Optimization of reaction conditions.

With improving the enantioselectivity of the reaction in mind, we proceeded to vary the reaction conditions with our best ligand (**2.29g**) as shown in Table 2.4. Using isopropanol as the solvent produced a poor yield with only a slight improvement in enantioselectivity (entry 1). Surprisingly, reducing the temperature produced an even worse *ee* to go with the expected drop in yield over the same reaction time (entry 2). Varying the counter ion of the copper salt produced a

slight improvement in enantioselectivity (entries 3-4), but only the pivalate also maintained the previously achieved yields. Ultimately, we decided to proceed with the original reaction conditions (Table 2.3) for the remaining studies due to the only modest improvements in enantioselectivity and the commercial availability of copper acetate salts.

Table 2.4: Optimization of reaction conditions.[a]



2.30a **2.31a**

entry	Cu salt	solvent	temperature, °C	yield, %	*ee*, %
1	$Cu(OAc)_2 \cdot H_2O$	*i*-PrOH	23	32	86
2	$Cu(OAc)_2 \cdot H_2O$	*i*-PrOH	0	18	76
3	$Cu(OPiv)_2$	EtOH	23	61	86
4	$Cu(O(4\text{-}Cl\text{-}Bz))_2$	EtOH	23	15	86

[a]Conditions: 1 mmol **2.30a**, 10 mmol $MeNO_2$, 0.055 mmol **2.29g**, 0.05 mmol Cu salt, 1.5 mL solvent, 24 h.

2.3.3 Exploration of substrate scope.

Shown in Figure 2.9, a limited series of aromatic aldehydes were subjected to nitromethane in the presence of copper-ligand **2.29g** complex. *Ortho* substituents (**2.31b-c**) drastically diminished the yields of the reaction while only the *o*-methoxy substrate reduced the *ee* (**2.31c**). An electron-withdrawing group (**2.31d**) increased the reactivity and yield at a cost of slightly reduced enantioselectivity.

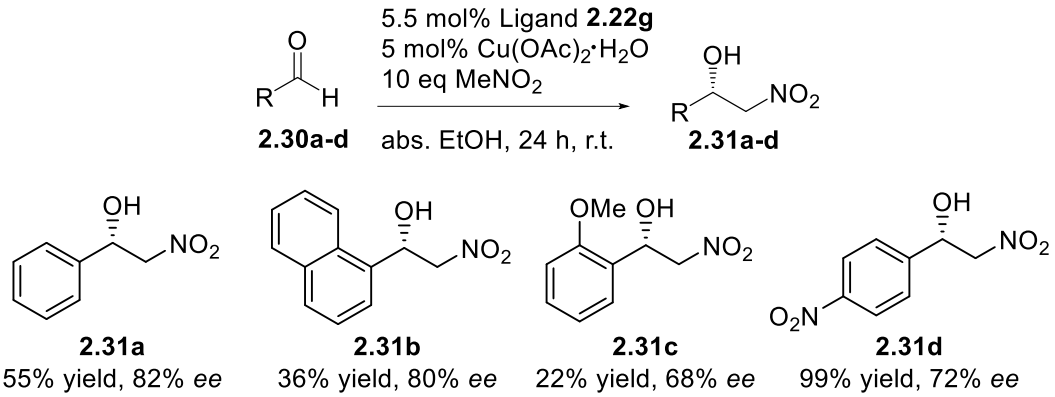


Figure 2.9: Substrate scope.

2.4 Conclusions and future directions.

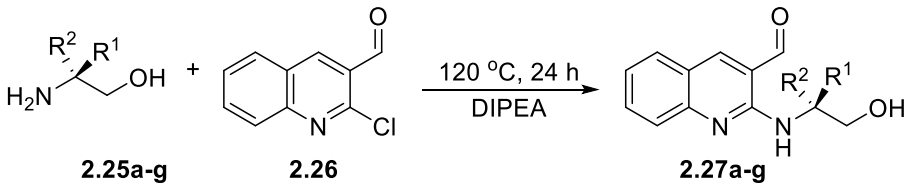
Our results thus far with the asymmetric Henry reaction indicate that our fused imidazoline ligand design could serve as a promising ligand in asymmetric reactions catalyzed by metal-complexes. Intriguingly, our imine ligands (**2.29**) with a simple blocking group on the aniline compared favorably in enantioselectivity to BOX ligands with the same chiral groups. Evans achieved the highest enantioselectivities (up to 94%) with indanyl BOX ligand.[20] Unfortunately, efforts to synthesize indanyl substituted ligands were unsuccessful with our current methods. Additionally, electronically tuned derivatives of our ligand design have yet to be fully explored. Ms. Masha Elkin investigated the synthesis of some methoxy substituted ligands but found the nucleophilic aromatic substitution to form complex mixtures. Perhaps, a more rigorous exploration of conditions to form **2.27** including metal catalyzed couplings is needed to fully develop our ideas.

In the future development of these ligands, electronic tuning and variation of the donor group derived from the aldehyde moiety of **2.14** as outlined in Figure 2.5 would be interesting to explore in new, untested asymmetric reactions.

2.5 Experimental.

All reagents were obtained commercially and used as received unless specified otherwise. $Cu(OPiv)_2$ and $Cu(O(4\text{-}Cl\text{-}Bz))_2$ were prepared following a literature procedure.[21] Chloroform and dichloromethane were freshly distilled from calcium hydride. Solvents used for chromatography were ACS or HPLC grade, as appropriate. Reactions were carried out under argon and monitored by thin layer chromatography (TLC) and by ^1H NMR. Uniplate HLF (250 μm) silica gel plates were used for TLC analyses. Flash column chromatography was performed over Sorbent Technologies silica gel (40-63 mm). HPLC analyses were performed on a Shimadzu LC system using Chiralcel OD-H, analytical chiral stationary phase column (4.6x250 mm, Chiral Technologies, Inc.) with UV detectors at 254 nm and 204 nm and a 1.0 mL/min flow rate. ^1H and ^{13}C NMR spectra were recorded on a Mercury 300 MHz and DD2 500 MHz Agilent spectrometer. The chemical shifts are reported as δ values (ppm) relative to TMS using residual $CHCl_3$ peak (7.26 ppm) as the reference. Melting points were measured on a Stuart SMP10 melting point apparatus. High-Resolution mass spectral analyses were performed at Washington University MS Center on a Bruker MaXis QTOF mass spectrometer using Electrospray Ionization (ESI) and Electron Impact (EI) methods.[22] Infrared spectra were recorded on a Bruker Alpha Platinum-ATR. Optical rotations were determined on a Rudolph Autopol III polarimeter.

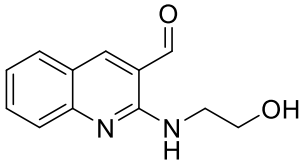
2.5.1 Preparation of amino aldehydes 2.27.



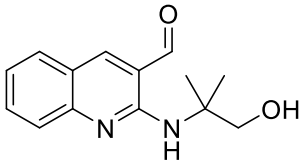
2.25a-g **2.26** **2.27a-g**

To a pressure tube with stir bar, was added 2-chloro-3-quinolinecarboxaldehyde[23] (1.0 equiv) followed by DIPEA (1 equiv) and the requisite amino alcohol (2.1 equiv). The resulting heterogeneous mixture was flushed with Argon and stirred for a 24 h at 120 °C. The crude mixture was washed with 1 M HCl, basified with 2 M NaOH, then extracted with dichloromethane and dried with sodium sulfate. The evaporation residue was chromatographed with dichloromethane to afford the 2-amino-3-quinolinecarboxaldehyde **2.20**.

2-((2-hydroxyethyl)amino)quinoline-3-carbaldehyde (2.27a): Isolated as a yellow solid (355 mg; 63% yield,) after chromatography (dichloromethane). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 10.00 (s, 1H), 8.48 (broad s, 1H), 8.30 (s, 1H), 7.76 – 7.64 (m, 3H), 7.35 – 7.25 (m, 1H), 5.59 (broad s, 1H), 4.00 – 3.91 (m, 2H), 3.90 – 3.80 (m, 2H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 192.83, 155.65, 149.76, 148.99, 134.06, 129.30, 125.81, 123.14, 122.06, 117.70, 64.46, 45.16; **IR** (cm^{-1}): 3341, 2952, 1663, 1618, 1575, 1537, 1467, 1393, 1345, 1169, 1077, 1051, 760, 729, 602, 552, 480, 423; **MS:** HR-ESI calculated for $[C_{12}H_{12}N_2O_2+H]^+$: 217.0972, found: 217.0977; **mp** 93-95 °C.



2-((1-hydroxy-2-methylpropan-2-yl)amino)quinoline-3-carbaldehyde (2.27b): Isolated as a yellow solid (127 mg; 20% yield) after chromatography (dichloromethane). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 9.96 (s, 1H), 8.38 (broad s, 1H), 8.29 (s, 1H), 7.92 (broad s, 1H), 7.73 – 7.60 (m, 3H), 7.33 – 7.22 (m, 1H), 3.75 (s,



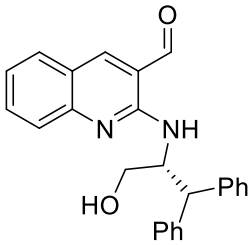
2H), 1.51 (s, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 192.89, 153.85, 149.73, 148.93, 134.20, 129.27, 125.34, 123.18, 121.63, 118.08, 71.63, 57.00, 25.35; **IR** (cm^{-1}): 3333, 3309, 2962, 2919, 2850, 1670, 1619, 1536, 1395, 1271, 1157, 1120, 1056, 923, 864, 779, 758, 727, 603, 553, 484, 424; **MS:** HR-ESI calculated for $[C_{14}H_{16}N_2O_2+H]^+$: 245.1285, found: 245.1289; **mp** 129-132 °C.

(*S*)-2-((1-hydroxy-3-methylbutan-2-yl)amino)quinoline-3-carbaldehyde (2.27c): Isolated as a yellow solid (1.01 g; 75% yield) after chromatography (dichloromethane). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 10.00 (s, 1H), 8.40 (broad d, J = 5.9 Hz, 1H), 8.29 (s, 1H), 7.73 – 7.57 (m, 3H), 7.29 – 7.21 (m, 1H), 5.90 (broad s, 1H), 4.13 – 4.02 (m, 1H), 3.94 (dd, J = 10.9, 2.1 Hz, 1H), 3.78 (dd, J = 10.9, 7.9 Hz, 1H), 2.13 (octet, J = 6.9 Hz, 1H), 1.08 (dd, J = 6.9, 2.1 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 193.05, 155.86, 149.82, 149.21, 134.11, 129.33, 125.79, 123.07, 122.04, 117.77, 67.28, 60.56, 30.15, 19.85, 18.53; **IR** (cm^{-1}): 3343, 3289, 2965, 2875, 1671, 1617, 1576, 1535, 1402, 1275, 1167, 1120, 1054, 869, 777, 756, 728, 604, 579, 479, 452; **MS:** HR-ESI calculated for $[C_{15}H_{18}N_2O_2+H]^+$: 259.1441, found: 259.1457; **mp** 156-158 °C; $[\alpha]_D^{23}$= -0.64° (c= 0.38, CH_2Cl_2).

(*S*)-2-((2-hydroxy-1-phenylethyl)amino)quinoline-3-carbaldehyde (2.27d): Isolated as a yellow solid (67 mg; 9% yield) after chromatography (dichloromethane). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 9.98 (s, 1H), 8.70 (broad d, J = 5.7 Hz, 1H), 8.29 (s, 1H), 7.84 – 7.59 (m, 3H), 7.56 – 7.19 (m, 6H), 5.49 (ddd, J = 7.3, 5.7, 3.6 Hz, 1H), 4.06 (dd, J = 11.5, 7.3 Hz, 1H), 4.01 (dd, J = 11.5, 3.6 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 192.91, 155.07, 149.84, 149.03, 139.86, 134.08, 129.32, 129.16, 128.04, 126.88, 126.10, 123.31, 122.26, 117.74, 69.57, 59.23; **IR** (cm^{-1}): 3332, 3266, 2916, 2866, 1668, 1620, 1572, 1524, 1398, 1168, 1058, 752, 739, 694, 583, 448; **MS:** HR-

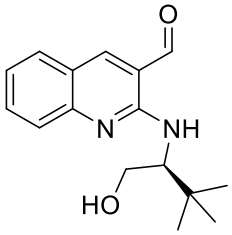
ESI calculated for $[C_{18}H_{16}N_2O_2+H]^+$: 293.1285, found: 293.1295; **mp** 123-125°C; $[\alpha]_D^{23}$= +1.04° (c= 0.35, CH_2Cl_2).

(*R*)-2-((3-hydroxy-1,1-diphenylpropan-2-yl)amino)quinoline-3-carbaldehyde (2.27e):



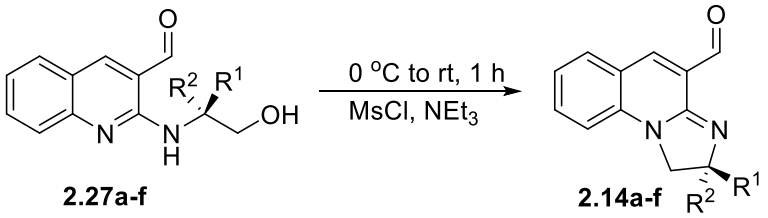
Prepared from **2.18e**.[24] Isolated as a yellow solid (195 mg; 32% yield) after chromatography (dichloromethane). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.23 (broad s, 1H), 8.20 (s, 1H), 7.86 – 7.57 (m, 3H), 7.59 – 7.01 (m, 11H), 5.46 (broad s, 1H), 5.20 – 5.07 (m, 1H), 4.39 (d, J = 10.6 Hz, 1H), 3.97 (dd, J = 11.1, 2.2 Hz, 1H), 3.72 (dd, J = 11.1, 6.6 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 192.40, 148.99, 141.51, 134.08, 129.33, 129.01, 128.76, 128.57, 128.29, 127.00, 126.90, 126.02, 123.28, 117.72, 66.63, 58.01, 53.30, 19.85, 18.53; **IR** (cm^{-1}): 3309, 3060, 3029, 2958, 1660, 1619, 1577, 1538, 1489, 1400, 1163, 1041, 752, 701, 603, 565, 472; **MS:** HR-ESI calculated for $[C_{25}H_{22}N_2O_2+H]^+$: 383.1754, found: 383.1768; **mp** 162-165 °C; $[\alpha]_D^{23}$= -1.04° (c= 0.74, CH_2Cl_2).

(*S*)-2-((1-hydroxy-3,3-dimethylbutan-2-yl)amino)quinoline-3-carbaldehyde (2.27e):



Isolated as a yellow solid (650 mg; 46% yield) after chromatography (dichloromethane). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 10.02 (s, 1H), 8.53 (broad d, J = 6.4 Hz, 1H), 8.29 (d, J = 0.7 Hz, 1H), 7.76 – 7.56 (m, 3H), 7.30 – 7.21 (m, 1H), 4.19 – 4.11 (m, 2H), 3.71 (dd, J = 11.2, 8.8 Hz, 1H), 1.13 (s, 9H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 193.12, 156.22, 149.92, 149.20, 134.11, 129.33, 125.82, 123.02, 122.07, 117.72, 66.22, 63.71, 33.62, 27.22; **IR** (cm^{-1}): 3338, 2964, 2886, 2870, 2852, 1668, 1620, 1579, 1538, 1398, 1368, 1165, 1122, 1043, 861, 757, 728, 582, 450; **MS:** HR-ESI calculated for $[C_{16}H_{20}N_2O_2+H]^+$: 273.1598, found: 273.1602; **mp** 85-87 °C; $[\alpha]_D^{23}$= -1.10° (c= 0.31, CH_2Cl_2).

2.5.2 Preparation of cyclized aldehydes 2.14.



2.27a-f **2.14a-f**

A solution of **2.27** (1.0 equiv) in chloroform (0.1 M) was cooled to 0 °C and treated with triethylamine (3.0 equiv) followed by mesyl chloride (1.5 equiv) and stirred for 1h. The resulting deep red solution was quenched with water was washed with saturated Na_2CO_3 then extracted with dichloromethane and dried with sodium sulfate. The evaporation residue was dissolved in a minimal amount of dichloromethane, precipitated with hexane, and vacuum filtered to give **2.14**. **2.14** can also purified by column chromatography on silica gel (5% *i*-PrOH, 1% NEt_3/hexanes).

1,2-dihydroimidazo[1,2-a]quinoline-4-carbaldehyde (2.14a): Isolated as a red amorphous solid (491 mg; 89% yield,). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 10.11 (s, 1H), 7.77 (s, 1H), 7.45 – 7.35 (m, 2H), 6.93 (t, J = 7.5 Hz, 1H), 6.67 (d, J = 8.2 Hz, 1H), 4.13 (t, J = 10.2 Hz, 2H), 3.89 (t, J = 10.2 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 188.83, 154.88, 141.67, 141.25, 134.02, 131.25, 123.42, 120.82, 119.46, 112.04, 53.79, 45.47; **IR** (cm^{-1}): 2945, 2927, 2873, 1688, 1629, 1572, 1554, 1455, 1273, 1210, 749, 514; **MS:** HR-ESI calculated for $[C_{12}H_{10}N_2O+H]^+$: 199.0866, found: 199.0863.

2,2-dimethyl-1,2-dihydroimidazo[1,2-a]quinoline-4-carbaldehyde (2.14b): Isolated as a red amorphous solid (135 mg; 84% yield). **^{1}H NMR** (300 MHz, $CDCl_3$) 10.16 (s, 1H), 7.88 (s, 1H), 7.57 – 7.27 (m, 2H), 6.94 (t, J = 7.6 Hz, 1H), 6.72 (d, J = 8.5 Hz, 1H), 3.65 (s, 2H), 1.39 (s, 6H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 189.06,

152.04, 141.21, 141.01, 134.00, 131.37, 122.84, 121.09, 119.57, 112.26, 66.03, 57.91, 29.86; **IR** (cm^{-1}): 2966, 2925, 2867, 1689, 1625, 1554, 1456, 1277, 1197, 751, 727, 536; **MS:** HR-ESI calculated for $[C_{14}H_{14}N_2O+H]^+$: 227.1179, found: 227.1187.

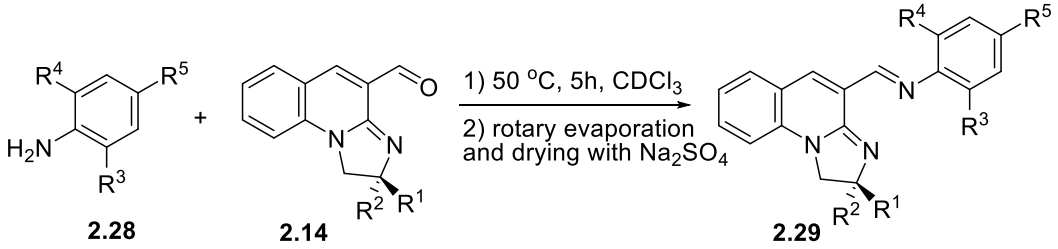
(*S*)-2-isopropyl-1,2-dihydroimidazo[1,2-a]quinoline-4-carbaldehyde (2.14c): Isolated as a red amorphous solid (479 mg; 99% yield). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 10.25 (s, 1H), 7.85 (s, 1H), 7.47 – 7.41 (m, 2H), 6.96 (dd, J = 7.5 Hz, 1H), 6.73 (d, J = 8.5 Hz, 1H), 4.23 – 4.15 (m, 1H), 3.91 (dd, J = 10.7 Hz, 1H), 3.61 (dd, J = 10.7, 8.4 Hz, 1H), 1.94 (octet, J = 6.7 Hz, 1H), 1.06 (d, J = 6.7 Hz, 3H), 0.96 (d, J = 6.7 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 189.30, 154.09, 141.21, 140.73, 133.98, 131.49, 123.12, 121.01, 119.77, 112.14, 71.12, 48.01, 33.61, 18.92, 17.86; **IR** (cm^{-1}): 2956, 2929, 2870, 1689, 1627, 1609, 1570, 1554, 1526, 1455, 1421, 1375, 1314, 1269, 1209, 1153, 1023, 951, 920, 750, 534; **MS:** HR-ESI calculated for $[C_{15}H_{16}N_2O+H]^+$: 241.1335, found: 241.1341; $[\alpha]_D^{23}$= -3.01° (c= 0.34, CH_2Cl_2).

(*S*)-2-phenyl-1,2-dihydroimidazo[1,2-a]quinoline-4-carbaldehyde (2.14d): Isolated as a red amorphous solid (311 mg; 71% yield). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 10.32 (s, 1H), 7.93 (s, 1H), 7.48 – 7.26 (m, 7H), 6.99 (dd, J = 7.6, 0.9 Hz, 1H), 6.70 (d, J = 8.2 Hz, 1H), 5.46 (dd, J = 11.5, 8.4 Hz, 1H), 4.36 (dd, J = 11.5, 10.4 Hz, 1H), 3.84 (dd, J = 11.5, 8.4 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 189.08, 155.05, 143.97, 141.01, 140.50, 133.93, 131.47, 128.87, 127.59, 126.77, 123.12, 121.10, 119.78, 112.11, 68.59, 53.57; **IR** (cm^{-1}): 1690, 1627, 1554, 1494, 1455, 1268, 1209, 1174, 908, 727, 552; **MS:** HR-ESI calculated for $[C_{18}H_{14}N_2O+H]^+$: 275.1179, found: 275.1186; $[\alpha]_D^{23}$= -3.72° (c= 1.42, CH_2Cl_2).

(*R*)-2-benzhydryl-1,2-dihydroimidazo[1,2-a]quinoline-4-carbaldehyde (2.14e): Isolated as a red solid (202 mg; 95% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.20 (s, 1H), 7.83 (s, 1H), 7.45 – 7.07 (m, 15H), 6.93 (td, J = 7.5, 1.0 Hz, 1H), 6.59 (d, J = 8.2, 1H), 5.20 (ddd, J = 10.6, 8.9, 7.9 Hz, 1H), 4.12 (d, J = 8.9 Hz, 1H), 3.97 (dd, J = 10.6 Hz, 1H), 3.63 (dd, J = 10.6, 7.9 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 189.52, 154.88, 142.35, 142.23, 141.16, 139.54, 133.70, 131.47, 128.96, 128.86, 128.78, 128.43, 126.86, 126.58, 123.22, 120.86, 119.63, 112.02, 69.06, 58.05, 50.04; **IR** (cm^{-1}): 2953, 2925, 2858, 1689, 1627, 1555, 1494, 1453, 1209, 908, 729, 699, 522; **MS:** HR-ESI calculated for $[C_{25}H_{20}N_2O+H]^+$: 365.1648, found: 365.1676; **mp** 195-200 °C dec.; $[\alpha]_D^{23}$=+4.68° (c= 0.25, CH_2Cl_2).

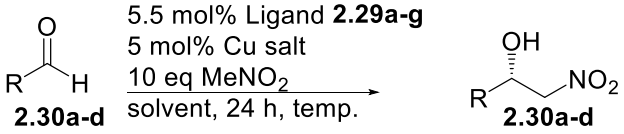
(*S*)-2-(tert-butyl)-1,2-dihydroimidazo[1,2-a]quinoline-4-carbaldehyde (2.14f): Isolated as a red amorphous solid (201 m g; 93% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.28 (s, 1H), 7.83 (s, 1H), 7.50 – 7.33 (m, 2H), 6.95 (td, J = 7.6, 1.0 Hz, 1H), 6.73 (dd, J = 8.2, 0.9 Hz, 1H), 4.10 (dd, J = 11.2, 8.4 Hz, 1H), 3.84 (dd, J = 11.2, 10.5 Hz, 1H), 3.67 (dd, J = 10.5, 8.4 Hz, 1H), 0.99 (s, 9H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 189.55, 154.26, 141.43, 139.65, 133.76, 131.49, 123.34, 120.72, 119.71, 111.93, 75.18, 46.73, 34.80, 25.90; **IR** (cm^{-1}): 2952, 2928, 2866, 1692, 1633, 1556, 1457, 1362, 1273, 1208, 750; **MS:** HR-ESI calculated for $[C_{16}H_{18}N_2O+H]^+$: 255.1492, found: 255.1501; $[\alpha]_D^{23}$= -2.55° (c= 0.29, CH_2Cl_2).

2.5.3 Preparation of imine ligands 2.29.



A solution of **2.14** (1.0 equiv) in chloroform (0.18 M) was treated with the requisite aniline **2.28**[25] (1.0 equiv) and stirred at 50 °C for 5h. The mixture was dried with sodium sulfate and concentrated under reduced pressure to give **2.29** which was used as a crude ligand in the subsequent Henry reaction. Crude ^{1}H NMR of **2.29g** showing an imine peak at 8.53 ppm is provided as a representative example.

2.5.4 Asymmetric Henry reaction, general procedure.



Ligand **2.29a-g** (0.055 mmol) and Cu salt (0.05 mmol) were added to a vial containing a stir bar. The solvent (1.5 mL) was added and the mixture was stirred for 1 h to form the ligand-metal complex in situ. To resulting dark colored solution, nitromethane (0.54 mL, 10 mmol) and aldehyde (1 mmol) were added and stirred for 24 h. The crude mixture was then evaporated under reduced pressure, purified by column chromatography, and analyzed by chiral HPLC using the conditions described by Evans.[20] The absolute configurations were assigned by comparison of HPLC elution order with Evans.[20] The results are summarized in Table 2.3, Table 2.4, and Figure 2.9.

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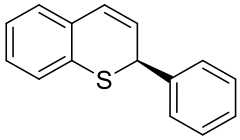
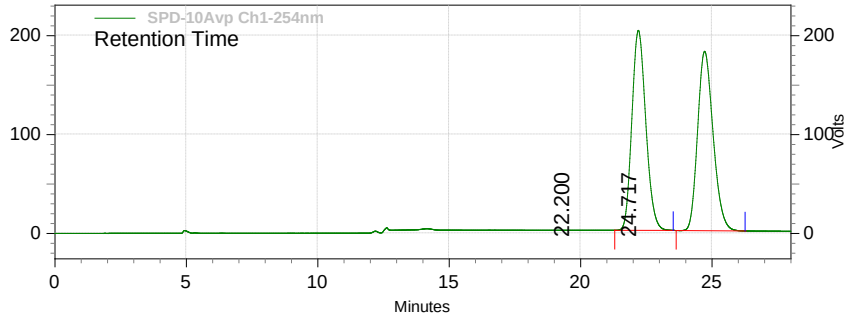
APPENDIX

A.1 HPLC chromatograms.

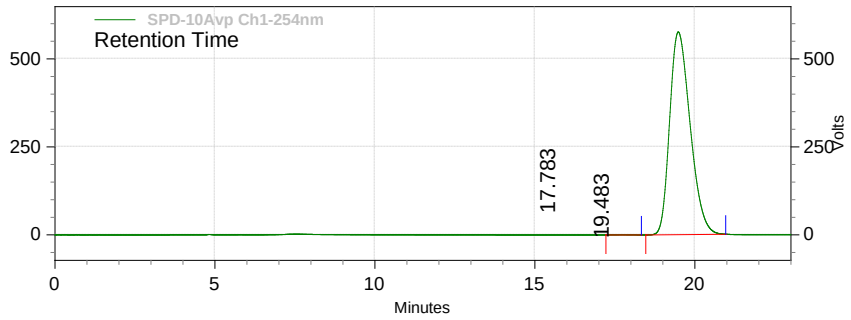


1.45a



Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
22.200	7455601	50.04	202251	52.72
24.717	7443890	49.96	181394	47.28
Totals	14899491	100.00	383645	100.00



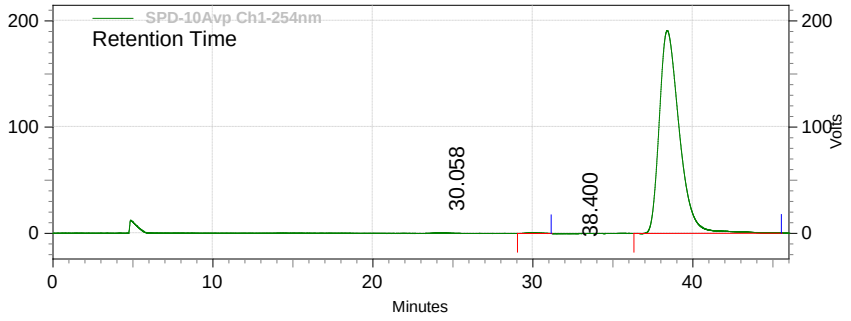
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
17.783	11026	0.04	304	0.05
19.483	25611100	99.96	575834	99.95
Totals	25622126	100.00	576138	100.00

1.45b

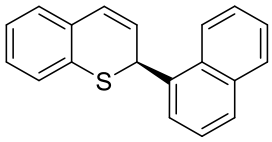
SPD-10Avp Ch1-254nm Results

Retention Time	Area	Area %	Height	Height %
26.917	8395567	49.90	136662	55.99
34.525	8429322	50.10	107428	44.01
Totals	16824889	100.00	244090	100.00



SPD-10Avp Ch1-254nm Results

Retention Time	Area	Area %	Height	Height %
30.058	26292	0.16	433	0.23
38.400	16585675	99.84	190972	99.77
Totals	16611967	100.00	191405	100.00



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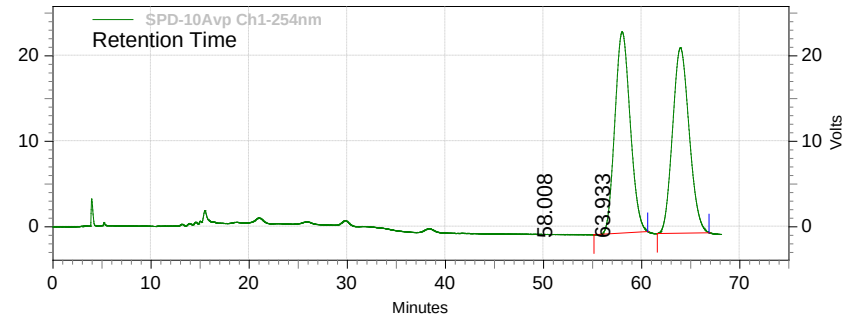
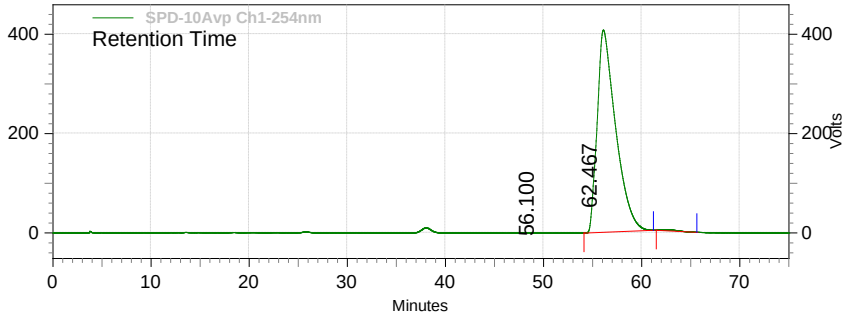


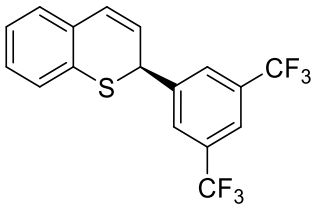
SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
58.008	2557287	50.02	23555	52.06
63.933	2555451	49.98	21687	47.94
Totals	5112738	100.00	45242	100.00

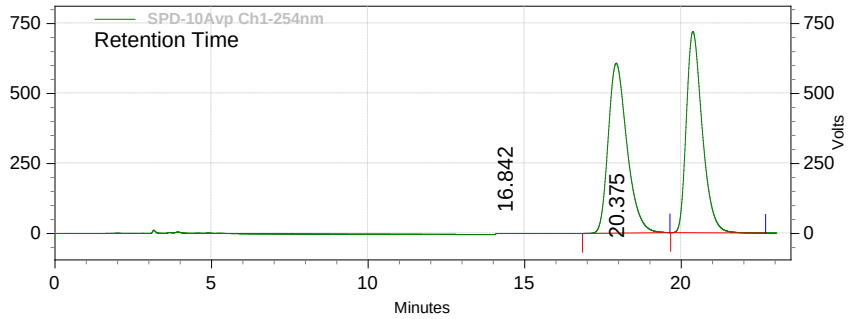


SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
56.100	53259258	99.59	407123	99.54
62.467	218982	0.41	1888	0.46
Totals	53478240	100.00	409011	100.00

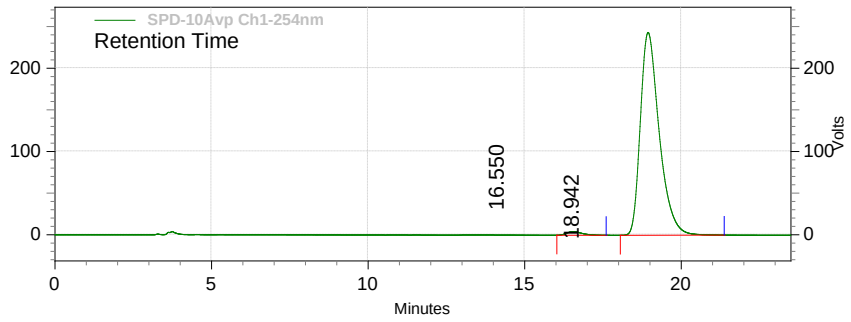


1.45d



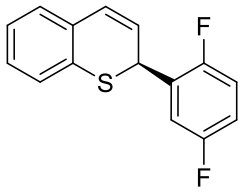
SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
16.842	25296210	49.98	0	0.00
20.375	25313197	50.02	718795	100.00
Totals	50609407	100.00	718795	100.00

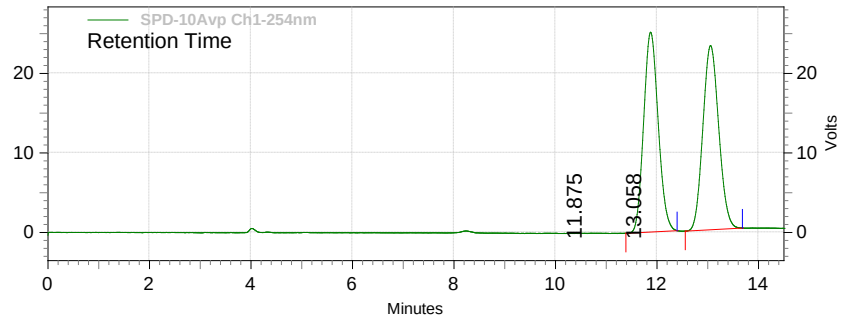


SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
16.550	152465	1.47	4470	1.80
18.942	10190414	98.53	243498	98.20
Totals	10342879	100.00	247968	100.00

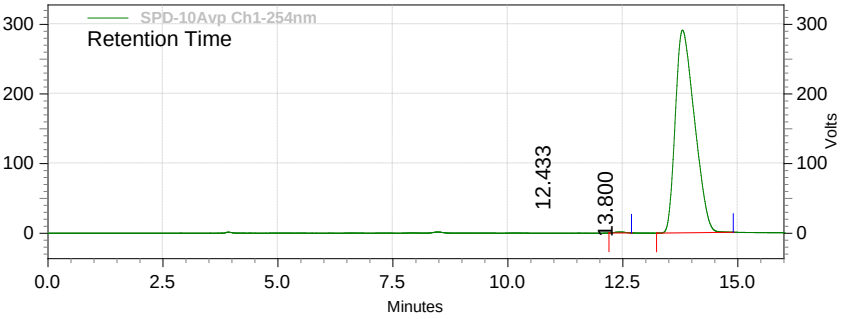


1.45e



SPD-10Avp
Ch1-254nm
Results

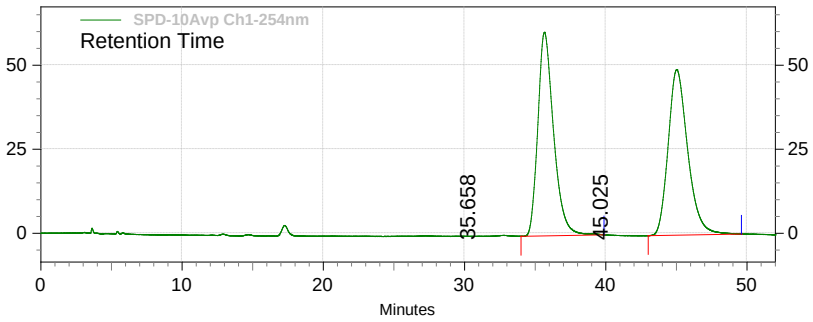
Retention Time	Area	Area %	Height	Height %
11.875	499776	49.79	25128	52.04
13.058	503905	50.21	23154	47.96
Totals	1003681	100.00	48282	100.00



SPD-10Avp
Ch1-254nm
Results

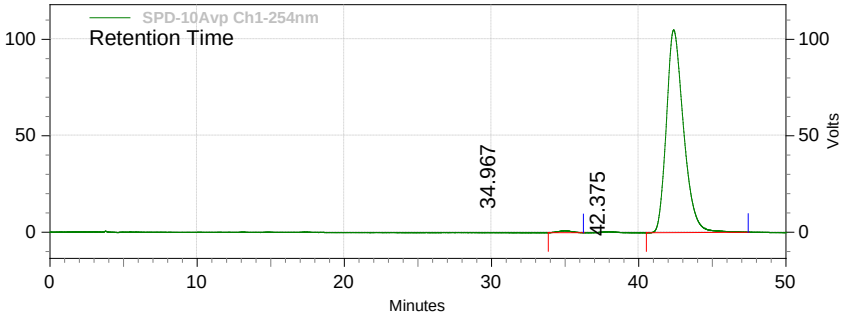
Retention Time	Area	Area %	Height	Height %
12.433	20876	0.25	1254	0.43
13.800	8426895	99.75	291060	99.57
Totals	8447771	100.00	292314	100.00

1.45f



SPD-10Avp
Ch1-254nm
Results

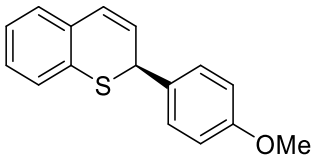
Retention Time	Area	Area %	Height	Height %
35.658	4708733	49.85	60575	55.15
45.025	4737319	50.15	49261	44.85
Totals	9446052	100.00	109836	100.00

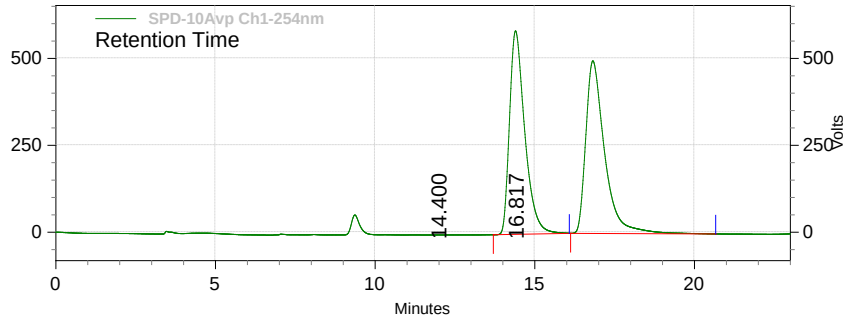


SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
34.967	58336	0.68	959	0.90
42.375	8516655	99.32	105080	99.10
Totals	8574991	100.00	106039	100.00

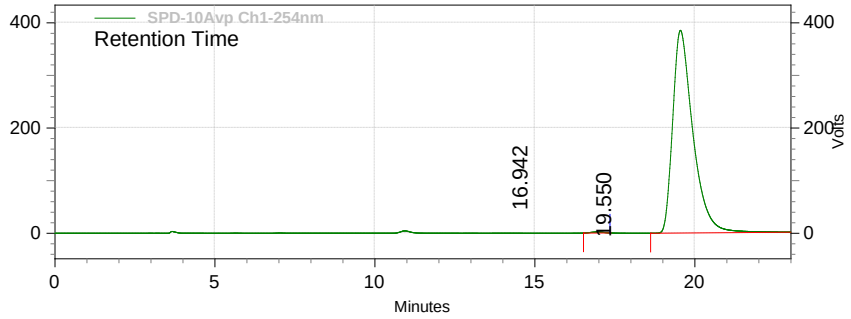
1.45g





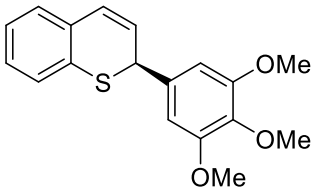
SPD-10Avp Ch1-254nm Results

Retention Time	Area	Area %	Height	Height %
14.400	19407837	48.88	585030	54.10
16.817	20297396	51.12	496311	45.90
Totals	39705233	100.00	1081341	100.00

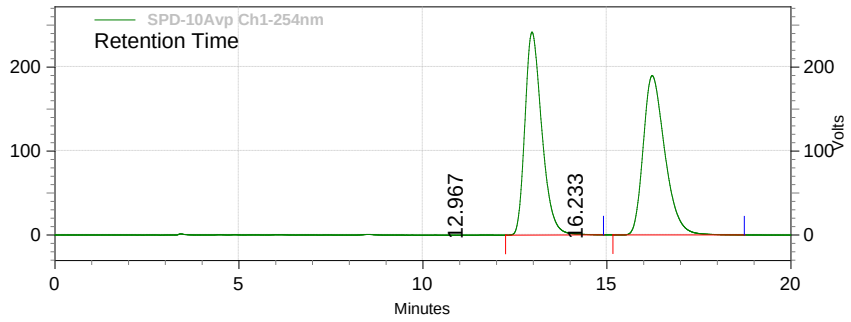


SPD-10Avp Ch1-254nm Results

Retention Time	Area	Area %	Height	Height %
16.942	52325	0.31	1964	0.51
19.550	16891196	99.69	385081	99.49
Totals	16943521	100.00	387045	100.00

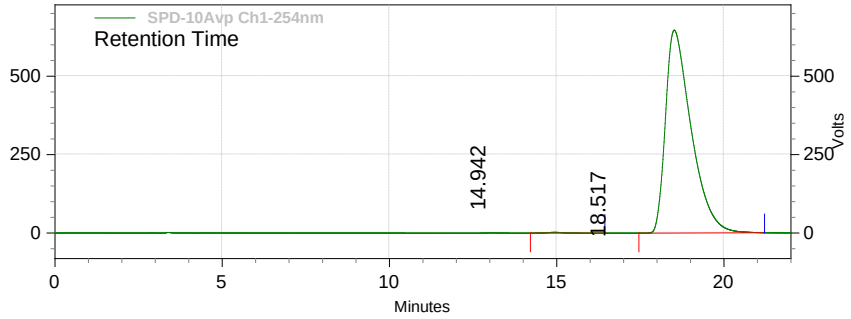


1.45h



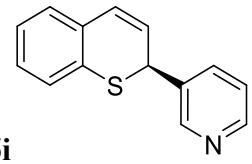
SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
12.967	7720906	49.92	241667	56.02
16.233	7745431	50.08	189742	43.98
Totals	15466337	100.00	431409	100.00

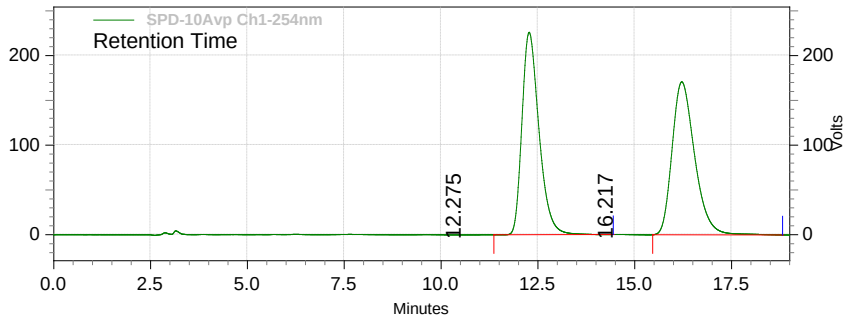


SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
14.942	89879	0.26	2527	0.39
18.517	34537379	99.74	646789	99.61
Totals	34627258	100.00	649316	100.00

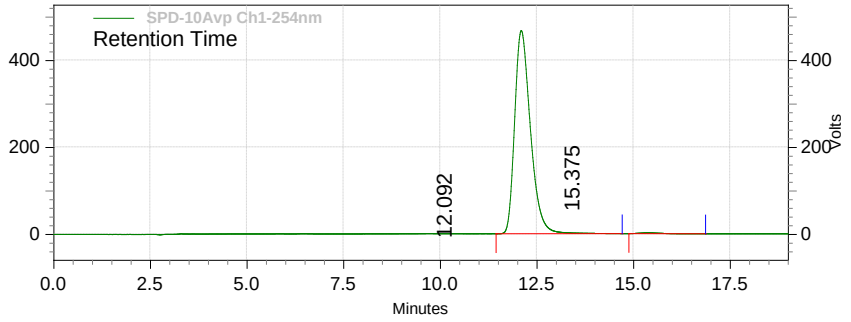


1.45i



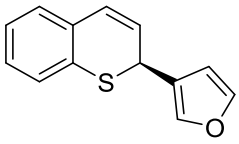
SPD-10Avp Ch1-254nm Results

Retention Time	Area	Area %	Height	Height %
12.275	6903854	49.98	225947	56.95
16.217	6909196	50.02	170803	43.05
Totals	13813050	100.00	396750	100.00



SPD-10Avp Ch1-254nm Results

Retention Time	Area	Area %	Height	Height %
12.092	13252676	99.57	467180	99.63
15.375	57386	0.43	1724	0.37
Totals	13310062	100.00	468904	100.00



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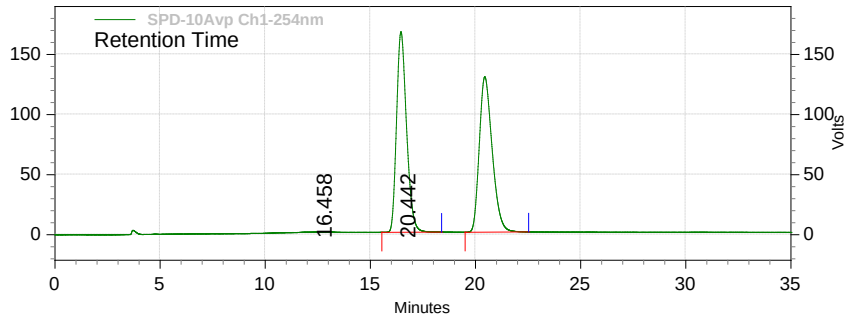
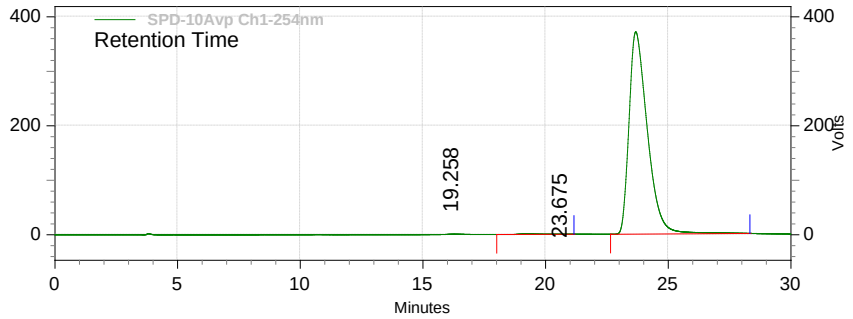


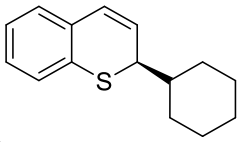
SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
16.458	5508264	49.98	166779	56.34
20.442	5512219	50.02	129265	43.66
Totals	11020483	100.00	296044	100.00



SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
19.258	50767	0.26	1153	0.31
23.675	19328870	99.74	371356	99.69
Totals	19379637	100.00	372509	100.00



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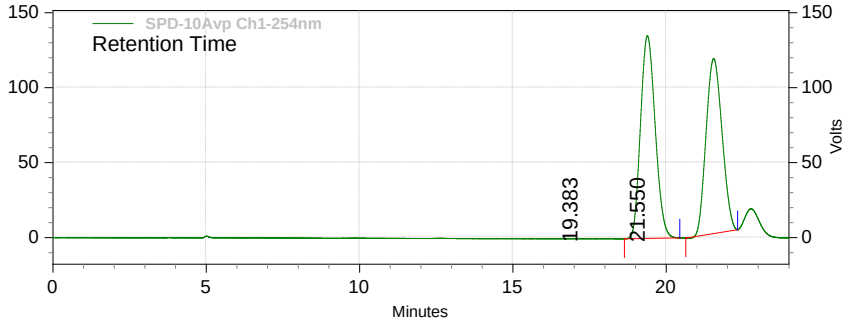
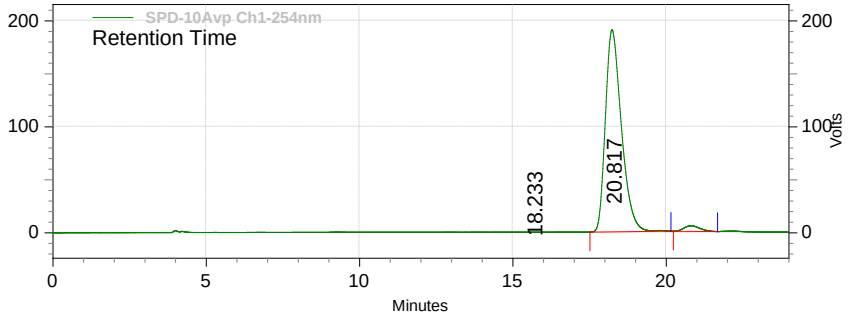


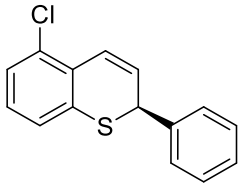
SPD-10Avp Ch1-254nm Results

Retention Time	Area	Area %	Height	Height %
19.383	4492601	51.52	135160	53.66
21.550	4226962	48.48	116707	46.34
Totals	8719563	100.00	251867	100.00



SPD-10Avp Ch1-254nm Results

Retention Time	Area	Area %	Height	Height %
18.233	6914822	97.34	190639	97.28
20.817	189131	2.66	5321	2.72
Totals	7103953	100.00	195960	100.00



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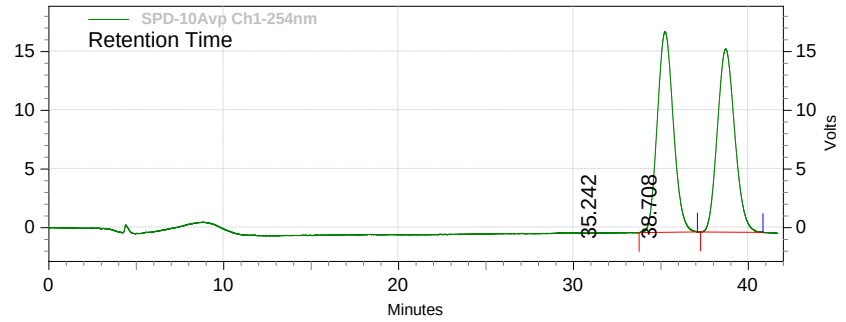
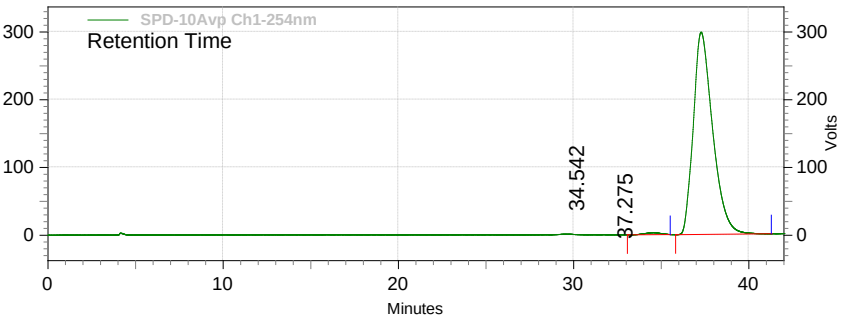


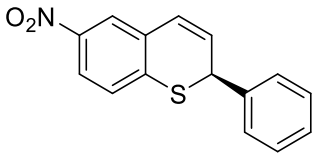
SPD-10Avp Ch1-254nm Results

Retention Time	Area	Area %	Height	Height %
35.242	1088460	50.22	17080	52.27
38.708	1078990	49.78	15596	47.73
Totals	2167450	100.00	32676	100.00

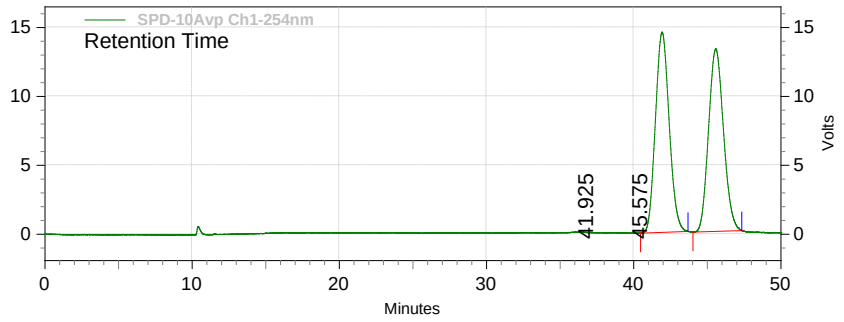


SPD-10Avp Ch1-254nm Results

Retention Time	Area	Area %	Height	Height %
34.542	174604	0.76	2876	0.95
37.275	22902082	99.24	298502	99.05
Totals	23076686	100.00	301378	100.00

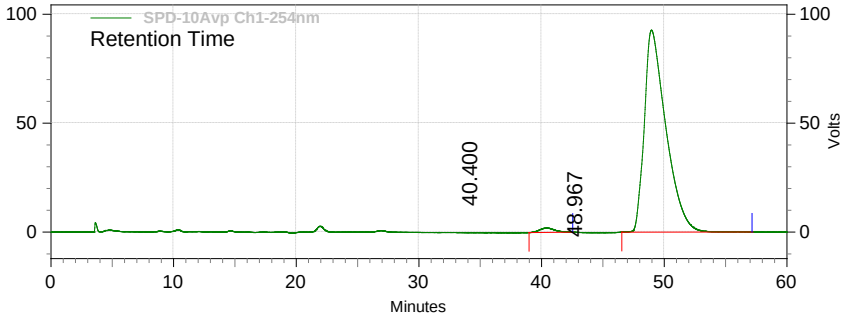


1.45m



SPD-10Avp Ch1-254nm Results

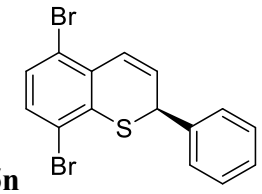
Retention Time	Area	Area %	Height	Height %
41.925	944502	50.26	14523	52.32
45.575	934615	49.74	13235	47.68
Totals	1879117	100.00	27758	100.00

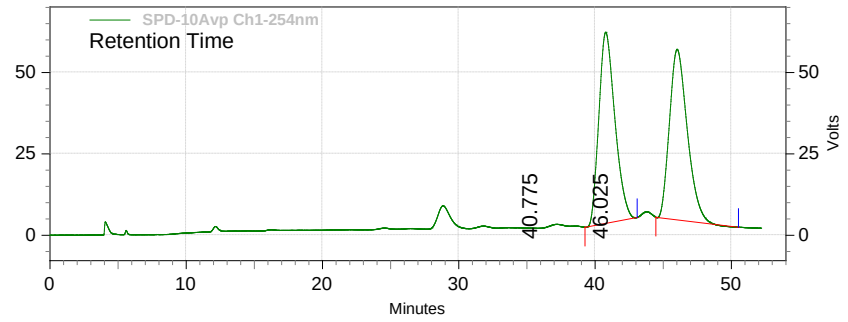


SPD-10Avp Ch1-254nm Results

Retention Time	Area	Area %	Height	Height %
40.400	173640	1.51	2021	2.13
48.967	11343697	98.49	92689	97.87
Totals	11517337	100.00	94710	100.00

1.45n

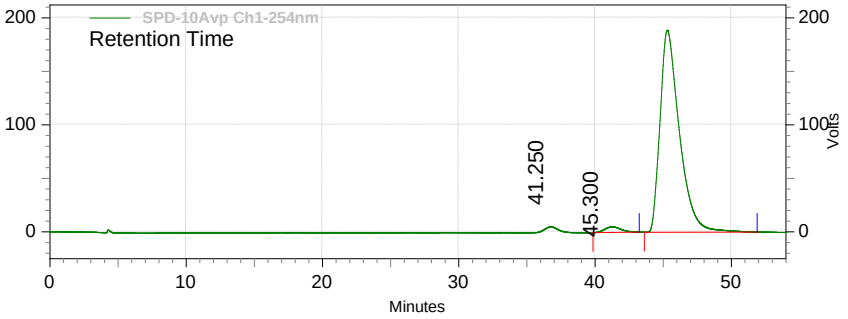




SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
40.775	4809959	50.23	58716	52.85
46.025	4766452	49.77	52384	47.15

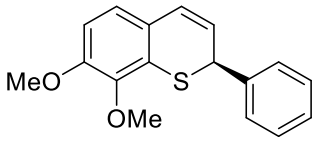
Totals	9576411	100.00	111100	100.00



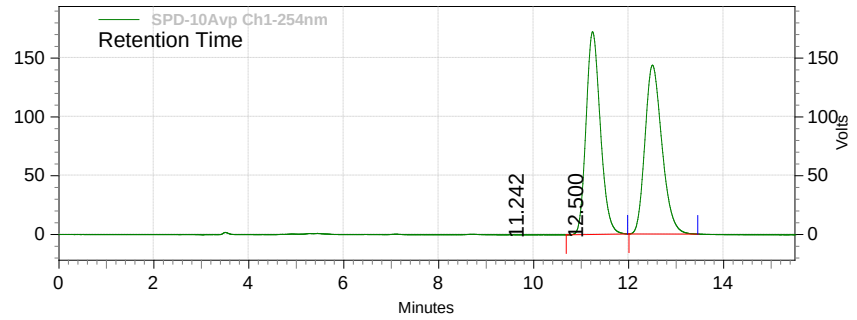
SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
41.250	439681	2.31	5324	2.74
45.300	18595726	97.69	188794	97.26

Totals	19035407	100.00	194118	100.00

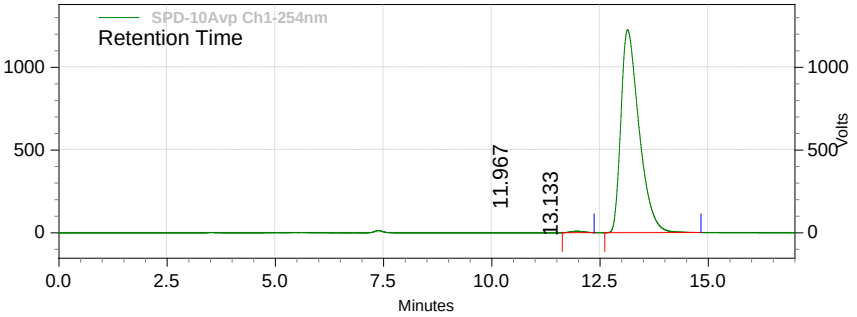


1.45o



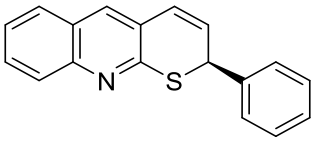
SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
11.242	3595329	50.12	172312	54.55
12.500	3577587	49.88	143589	45.45
Totals	7172916	100.00	315901	100.00

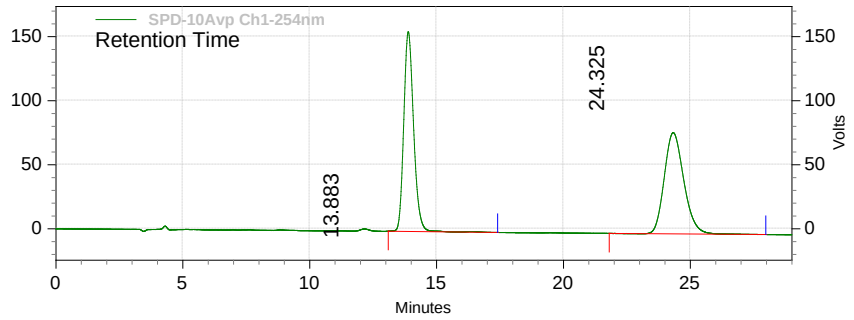


SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
11.967	179886	0.50	8690	0.70
13.133	35741844	99.50	1225960	99.30
Totals	35921730	100.00	1234650	100.00

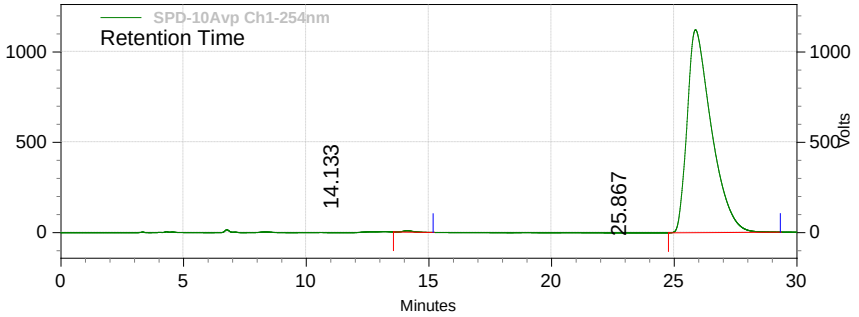


1.45p



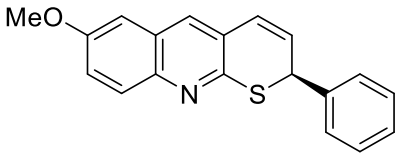
SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
13.883	4212876	49.91	155882	66.35
24.325	4227885	50.09	79066	33.65
Totals	8440761	100.0	234948	100.00

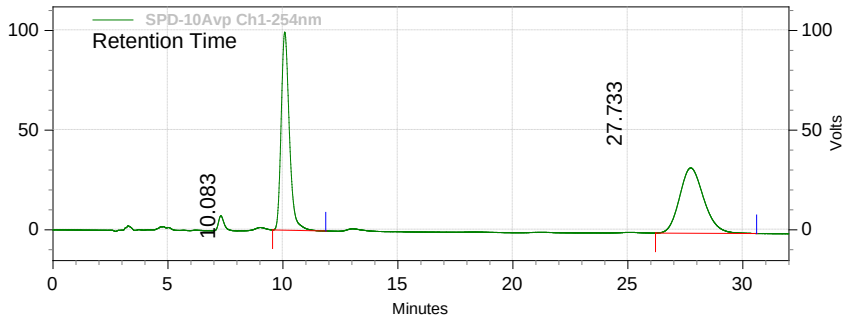


SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
14.133	201230	0.26	7550	0.67
25.867	77253063	99.74	1122574	99.33
Totals	77454293	100.00	1130124	100.00

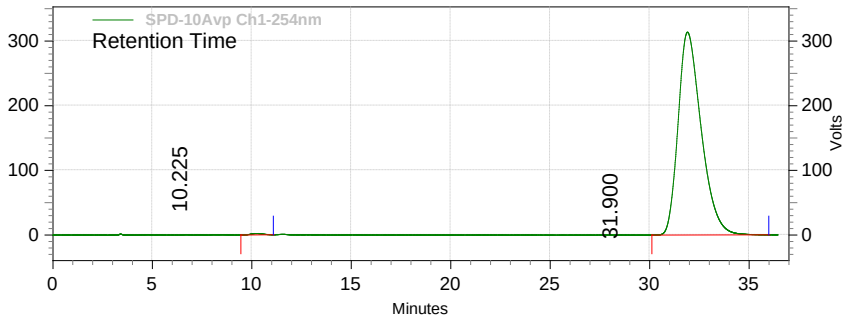


1.45q



SPD-10Avp Ch1-254nm Results

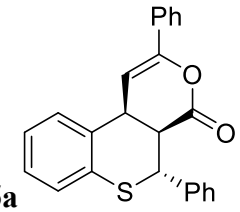
Retention Time	Area	Area %	Height	Height %
10.083	2459804	50.70	99332	75.21
27.733	2391741	49.30	32749	24.79
Totals	4851545	100.00	132081	100.00

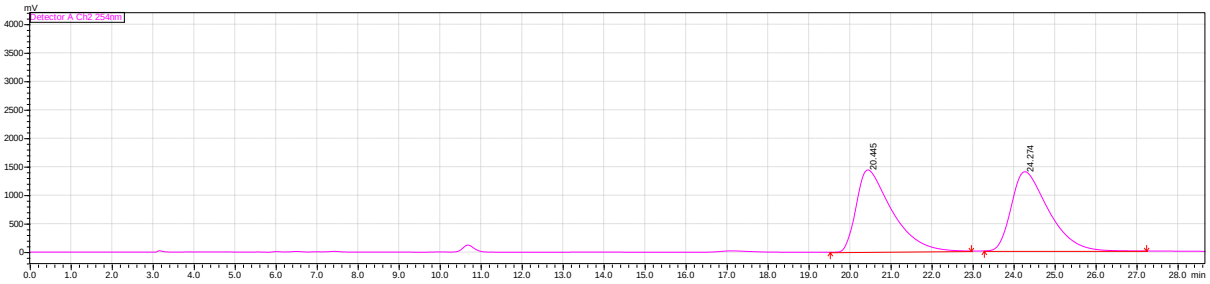


SPD-10Avp Ch1-254nm Results

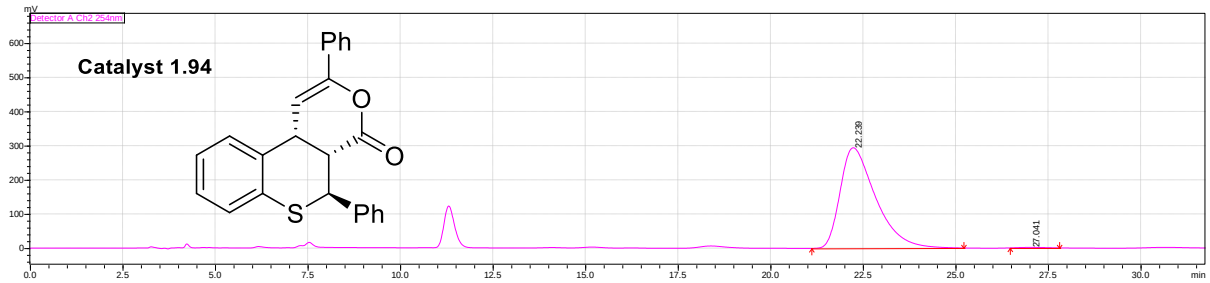
Retention Time	Area	Area %	Height	Height %
10.225	84265	0.33	2114	0.67
31.900	25332360	99.67	313650	99.33
Totals	25416625	100.00	315764	100.00

1.85a

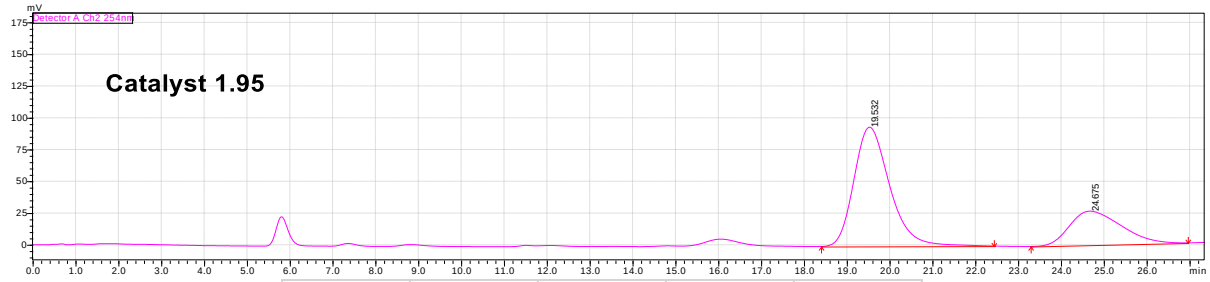




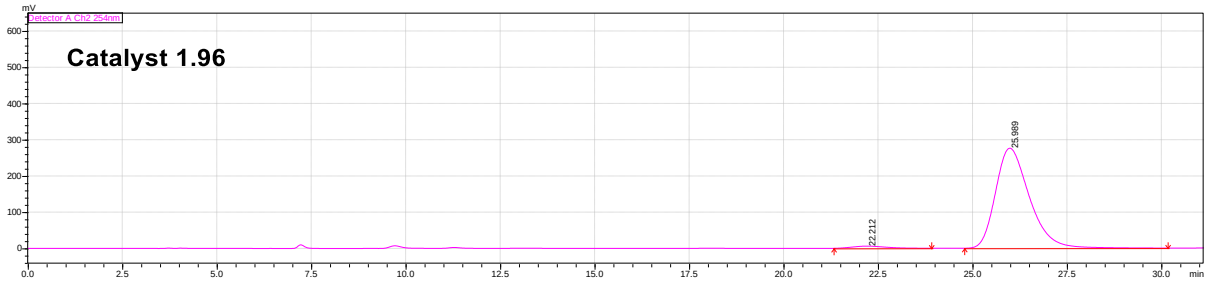
Peak#	Ret. Time	Area	Height
1	20.445	86677541	1438103
2	24.274	87312132	1390691
Total		173989672	2828794



Peak#	Ret. Time	Area	Height	Area%
1	22.239	19633363	294299	99.644
2	27.041	70217	1471	0.356
Total		19703580	295770	100

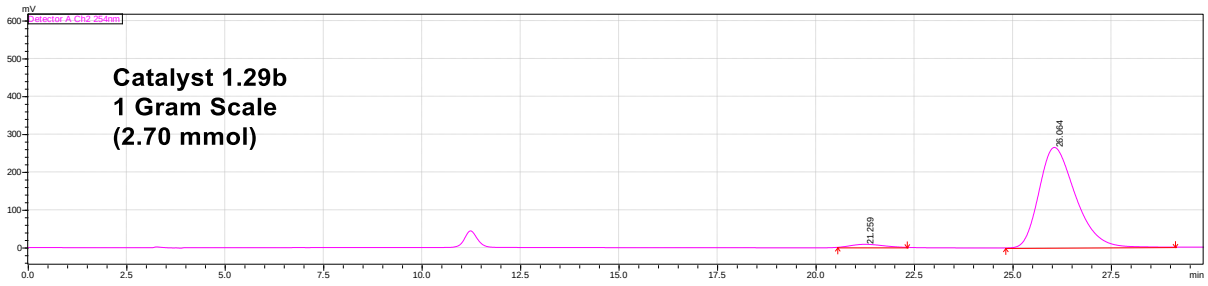


Peak#	Ret. Time	Area	Height	Area%
1	19.532	5438050	93790	70.931
2	24.675	2228585	26713	29.069
Total		7666634	120503	100



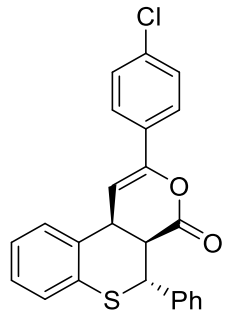
Peak#	Ret. Time	Area	Height	Area%
1	22.212	357955	5952	2.04
2	25.989	17189449	276083	97.96
Total		17547404	282035	100

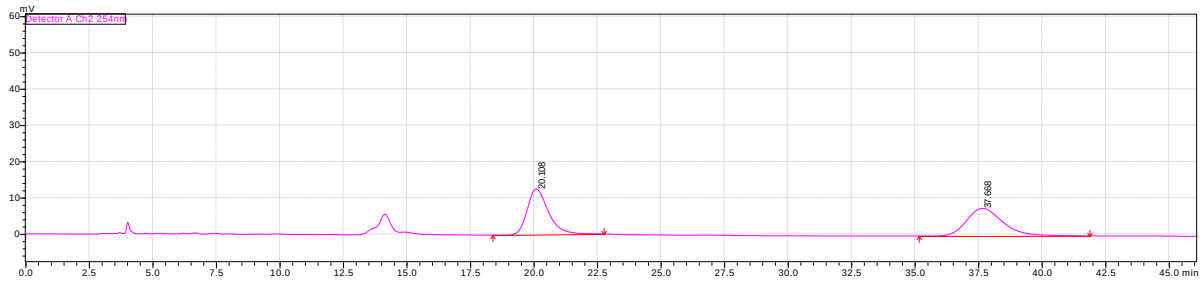
Peak#	Ret. Time	Area	Height	Area%
1	22.192	144628	2675	2.311
2	26.039	6114031	98882	97.689
Total		6258659	101557	100



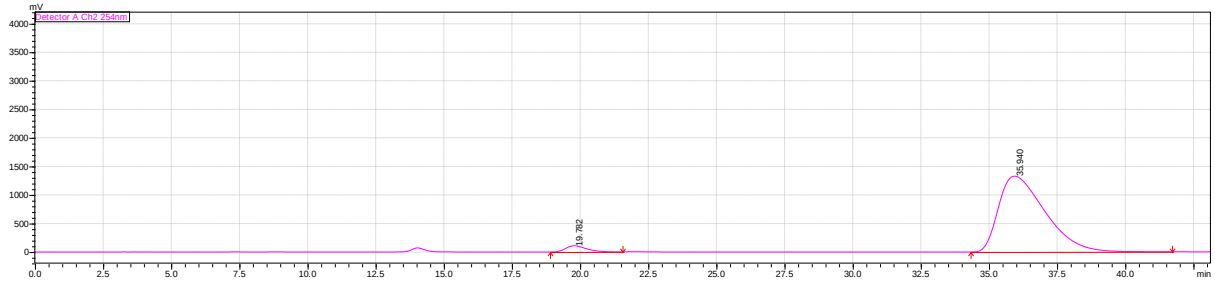
Peak#	Ret. Time	Area	Height	Area%
1	21.259	439909	8113	2.521
2	26.064	17012001	265052	97.479
Total		17451910	273165	100

1.85b



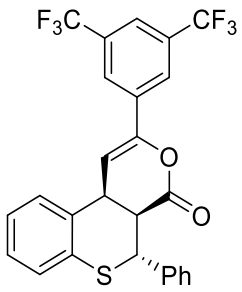


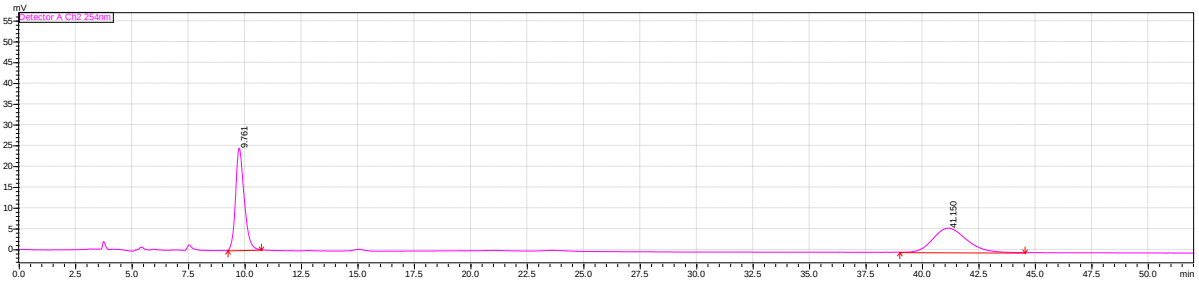
Peak#	Ret. Time	Area	Height	Area%
1	20.108	726815	12585	49.213
2	37.668	750054	7606	50.787
Total		1476869	20191	100



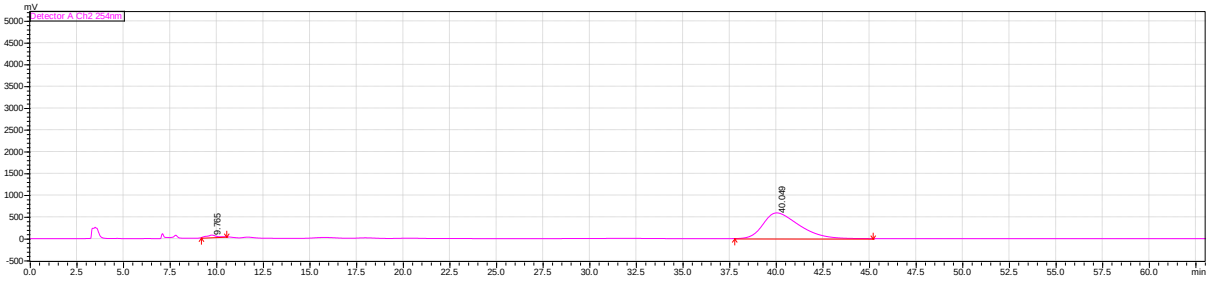
Peak#	Ret. Time	Area	Height	Area%
1	19.782	5748020	107705	3.526
2	35.94	157270787	1328376	96.474
Total		163018808	1436081	100

1.85c



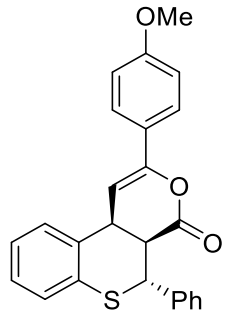


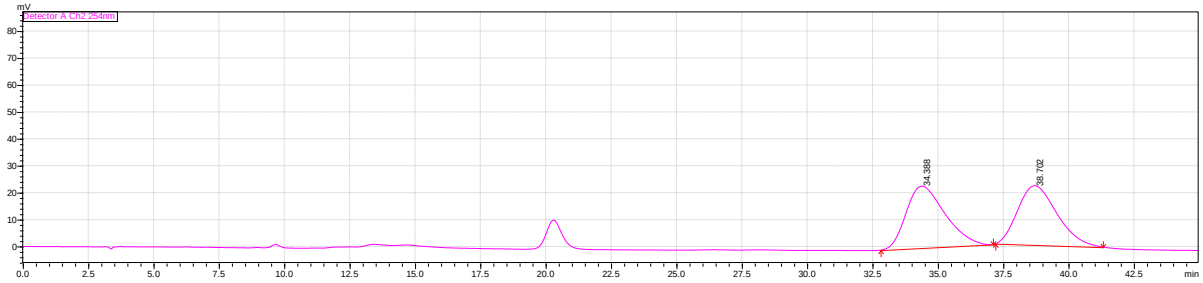
Peak#	Ret. Time	Area	Height	Area%
1	9.761	648293	24550	51.994
2	41.15	598572	5828	48.006
Total		1246866	30378	100



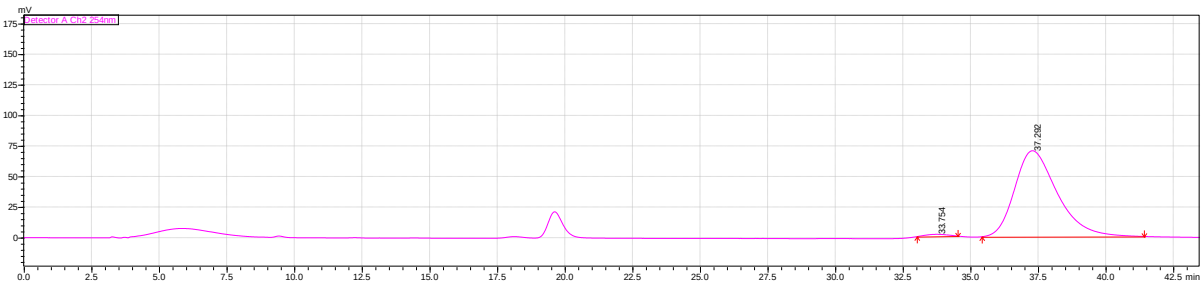
Peak#	Ret. Time	Area	Height	Area%
1	9.765	1693606	50465	2.108
2	40.049	78663177	588948	97.892
Total		80356784	639414	100

1.85d



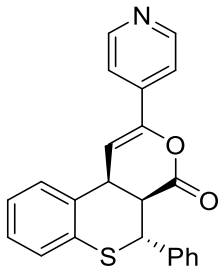


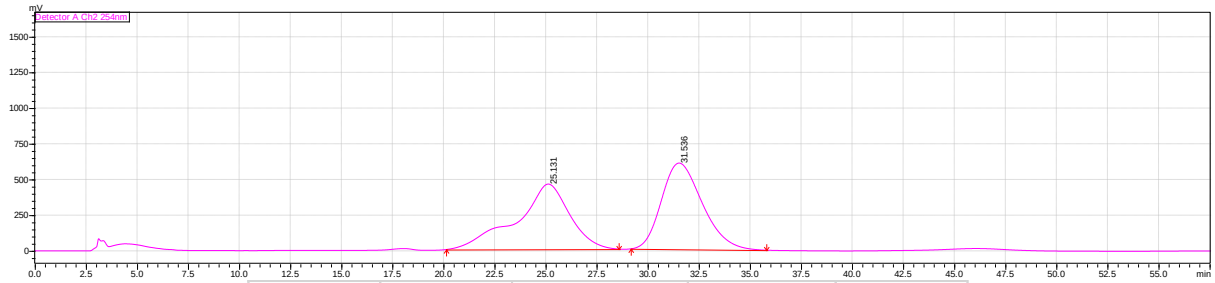
Peak#	Ret. Time	Area	Height	Area%
1	34.388	2366281	22972	50.809
2	38.702	2290952	21987	49.191
Total		4657233	44959	100



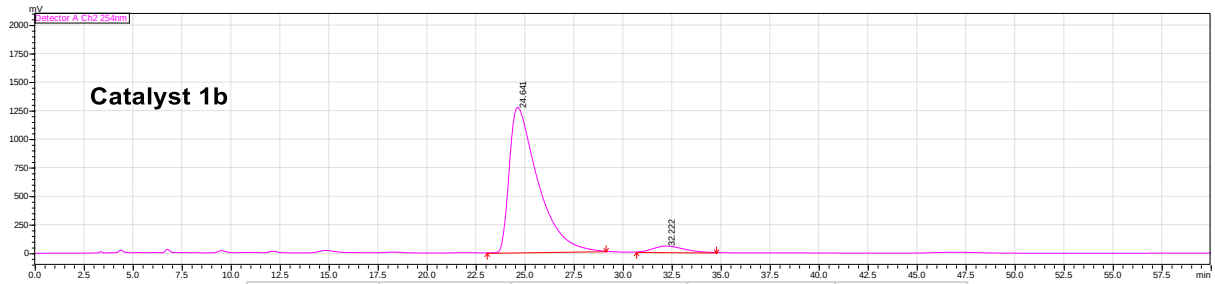
Peak#	Ret. Time	Area	Height	Area%
1	33.754	92587	1656	1.19
2	37.292	7686697	70245	98.81
Total		7779284	71900	100

1.85e

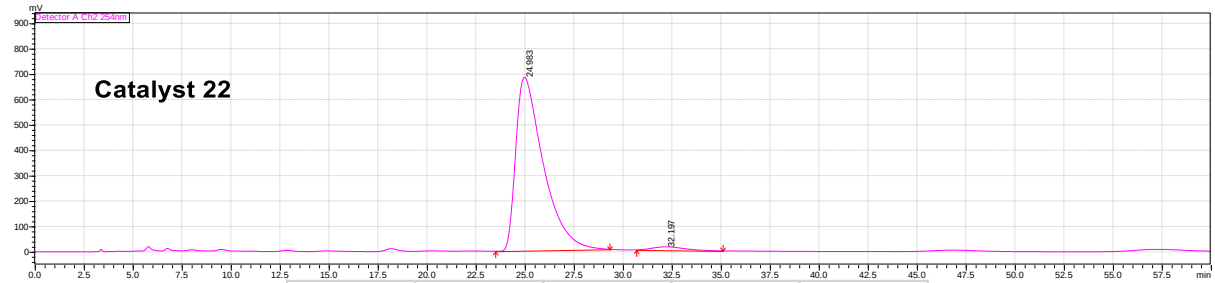




Peak#	Ret. Time	Area	Height	Area%
1	25.131	82767729	456584	49.576
2	31.536	84182574	604137	50.424
Total		166950303	1060721	100

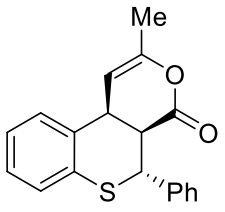


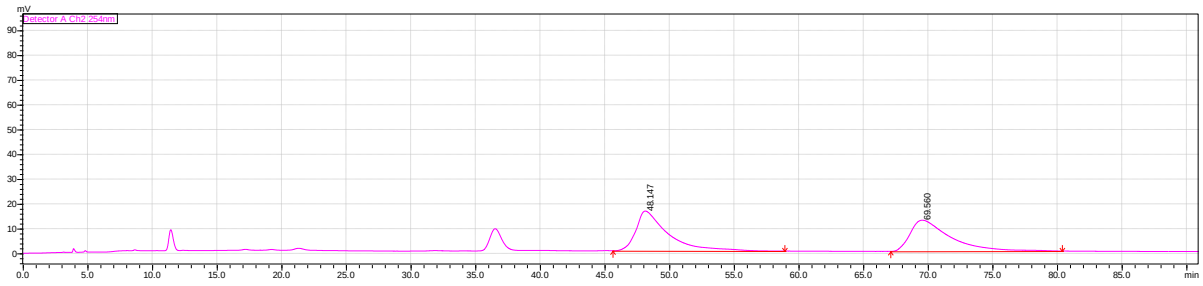
Peak#	Ret. Time	Area	Height	Area%
1	24.641	128523485	1270111	95.74
2	32.222	5718496	53606	4.26
Total		134241981	1323717	100



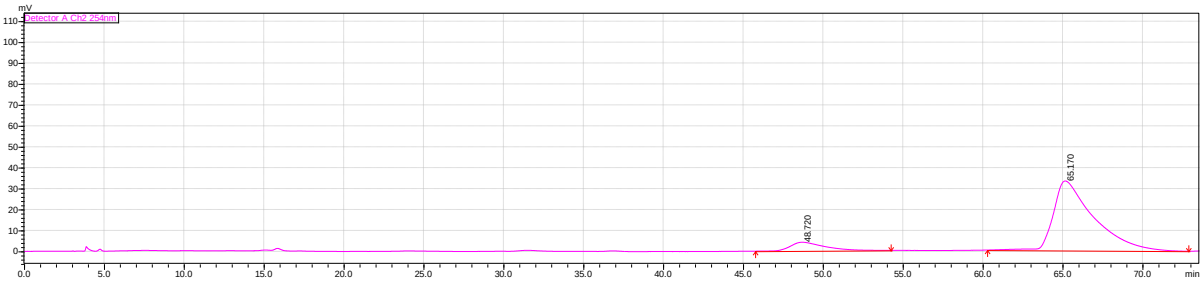
Peak#	Ret. Time	Area	Height	Area%
1	24.983	66706184	682738	97.83
2	32.197	1479657	13466	2.17
Total		68185841	696205	100

1.85f

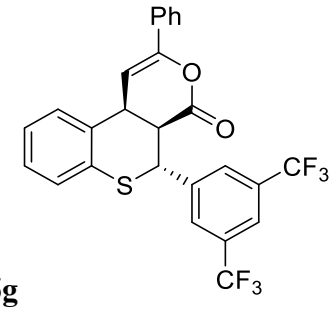




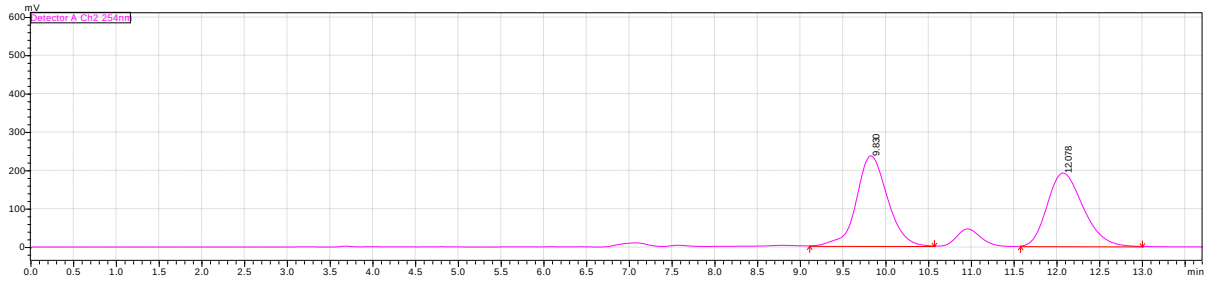
Peak#	Ret. Time	Area	Height	Area%
1	48.147	2750760	16052	50.479
2	69.56	2698599	12559	49.521
Total		5449359	28611	100



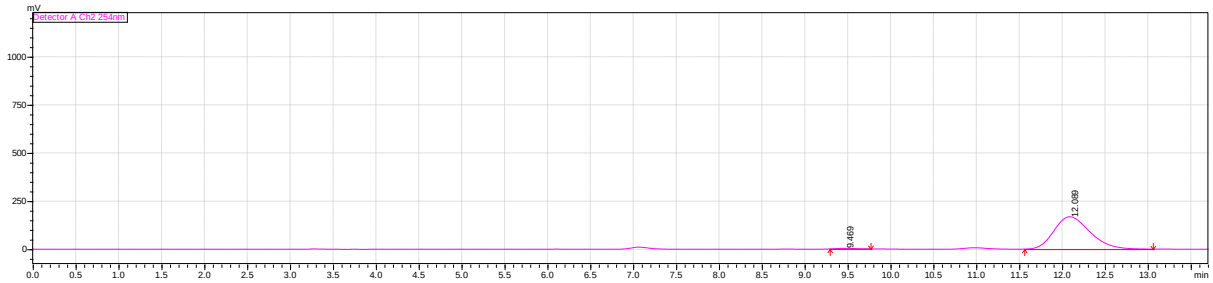
Peak#	Ret. Time	Area	Height	Area%
1	48.72	608807	4136	9.466
2	65.17	5822573	33239	90.534
Total		6431380	37375	100



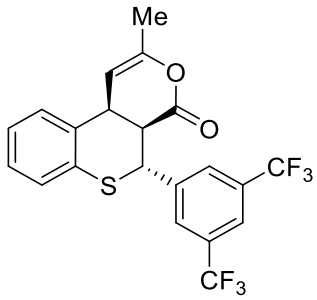
1.85g



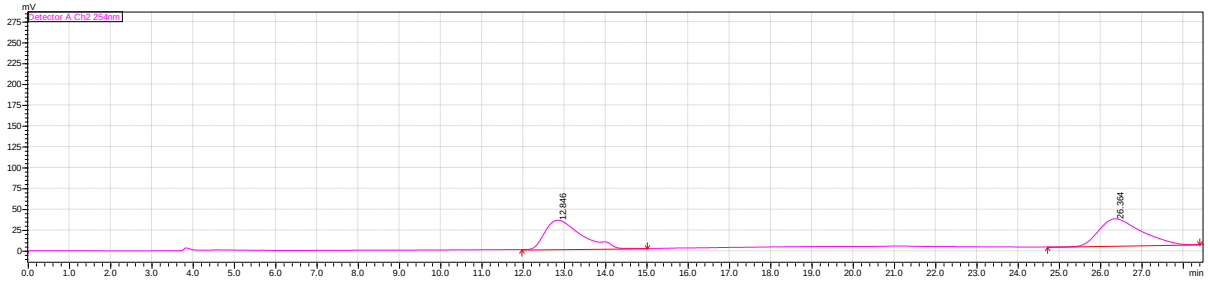
Peak#	Ret. Time	Area	Height	Area%
1	9.829	14261380	575941	50.642
2	12.077	13899697	471783	49.358
Total		28161077	1047725	100



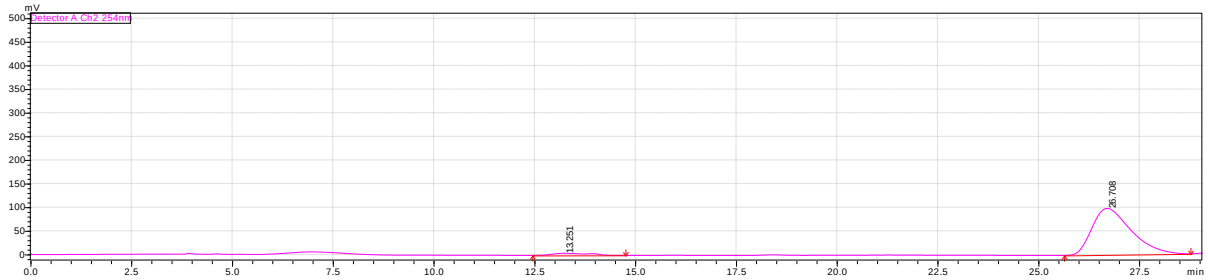
Peak#	Ret. Time	Area	Height	Area%
1	9.469	44077	2959	0.891
2	12.089	4904268	168239	99.109
Total		4948345	171198	100



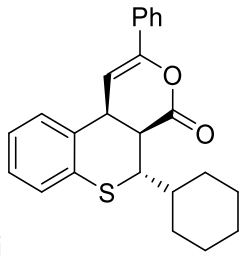
1.85h



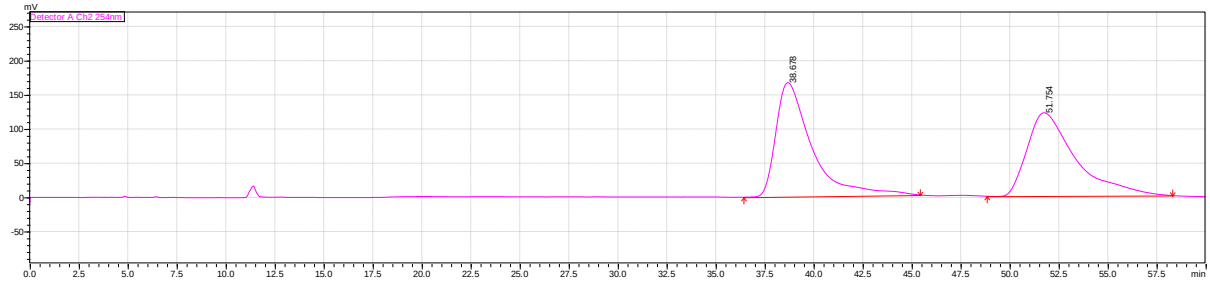
Peak#	Ret. Time	Area	Height	Area%
1	12.846	2132123	34785	48.219
2	26.364	2289606	32411	51.781
Total		4421730	67196	100



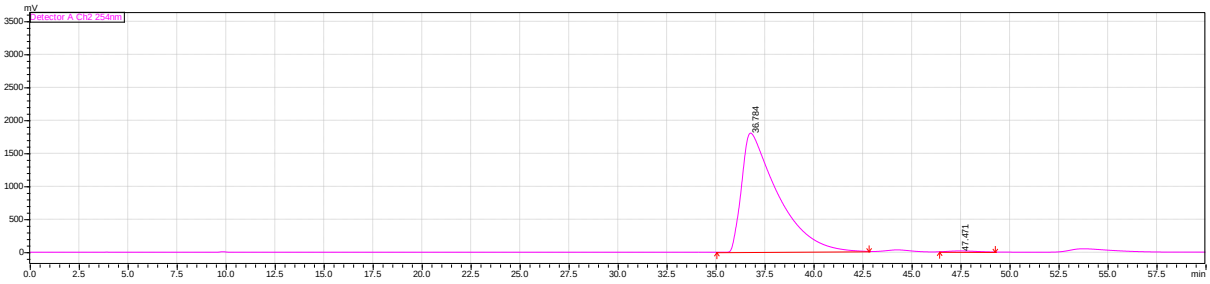
Peak#	Ret. Time	Area	Height	Area%
1	13.251	289009	4488	4.185
2	26.708	6616788	98310	95.815
Total		6905797	102798	100



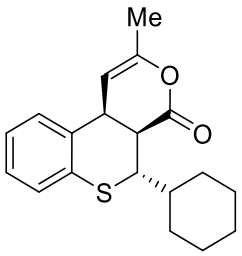
1.85j



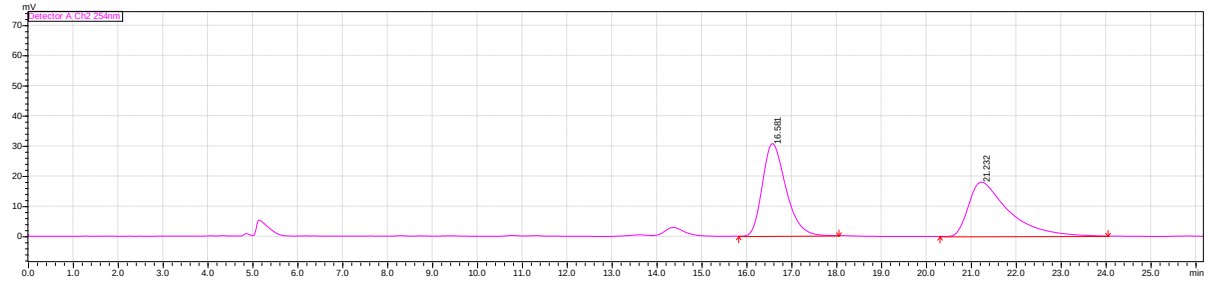
Peak#	Ret. Time	Area	Height	Area%
1	38.678	21175489	166722	50.412
2	51.754	20829768	121794	49.588
Total		42005257	288515	100



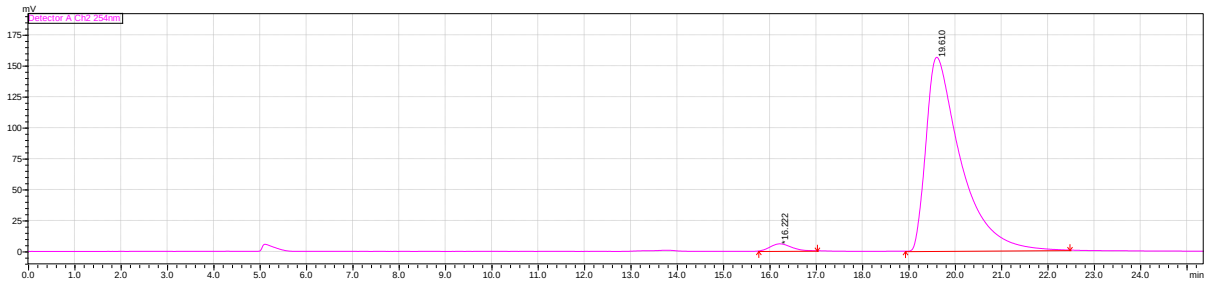
Peak#	Ret. Time	Area	Height	Area%
1.00	36.78	230618535.00	1802746.00	99.44
2.00	47.47	1288615.00	14169.00	0.56
Total		231907150.00	1816915.00	100.00



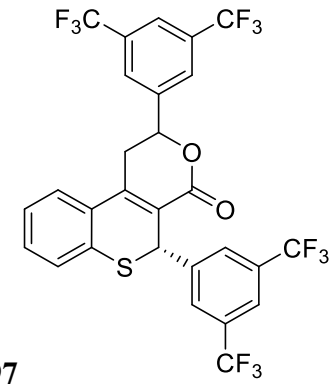
1.85k



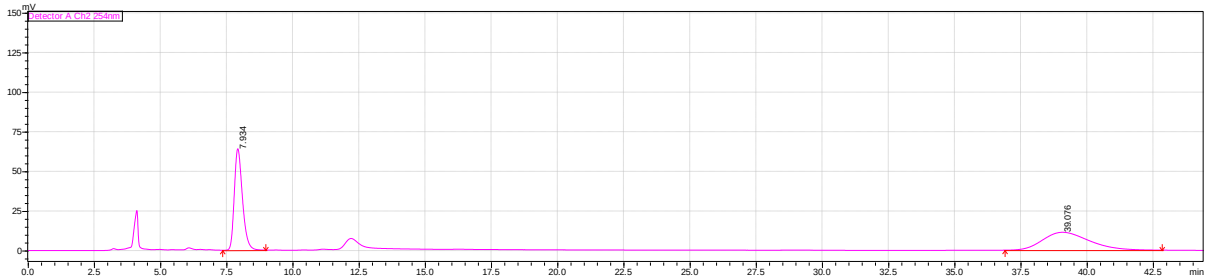
Peak#	Ret. Time	Area	Height	Area%
1	16.581	1111531	30595	49.983
2	21.232	1112288	17985	50.017
Total		2223819	48579	100



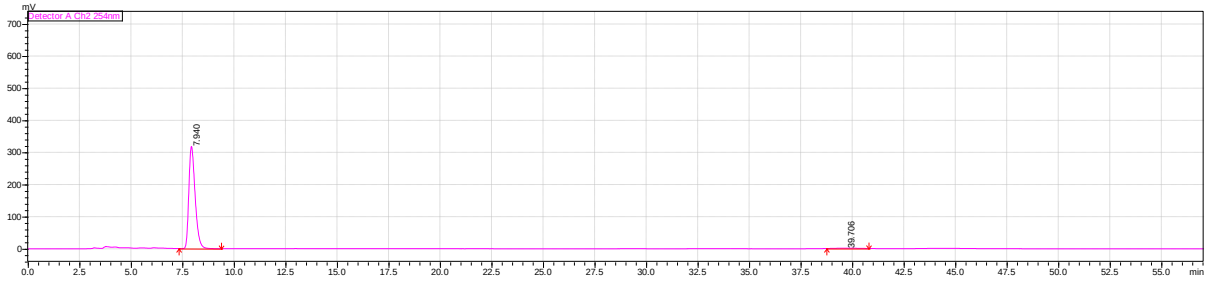
Peak#	Ret. Time	Area	Height	Area%
1	16.222	175885	5690	2.124
2	19.61	8104633	156422	97.876
Total		8280518	162113	100



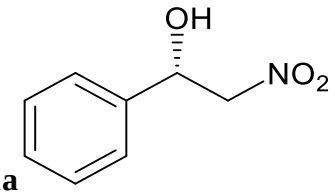
1.97



Peak#	Ret. Time	Area	Height	Area%
1	7.934	1371015	64003	49.946
2	39.076	1374004	11269	50.054
Total		2745019	75272	100

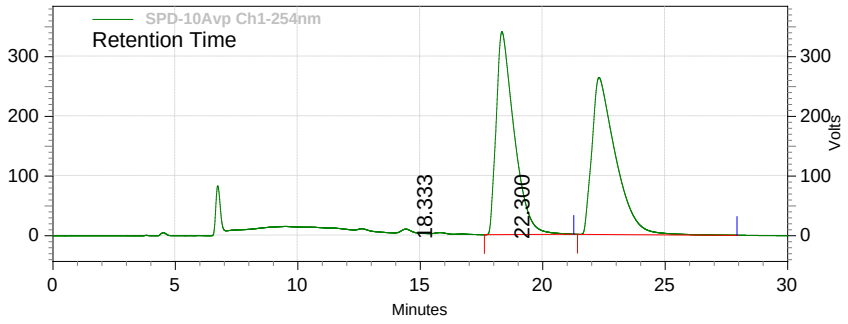


Peak#	Ret. Time	Area	Height	Area%
1	7.94	6750320	318039	98.971
2	39.706	70174	943	1.029
Total		6820494	318981	100



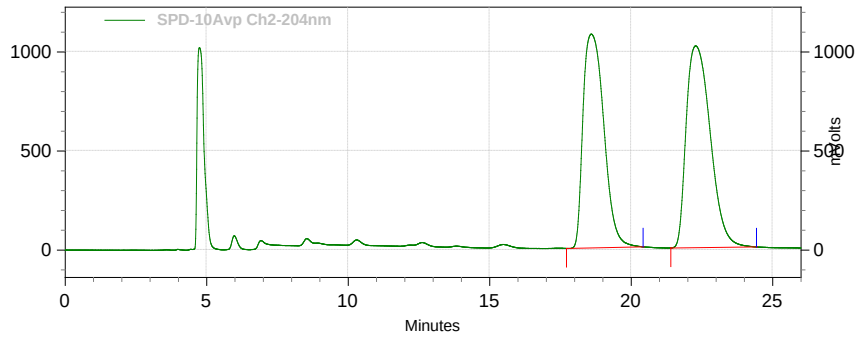
2.31a racemate

HPLC conditions: 10% isopropanol/hexanes



SPD-10Avp
Ch1-254nm
Results

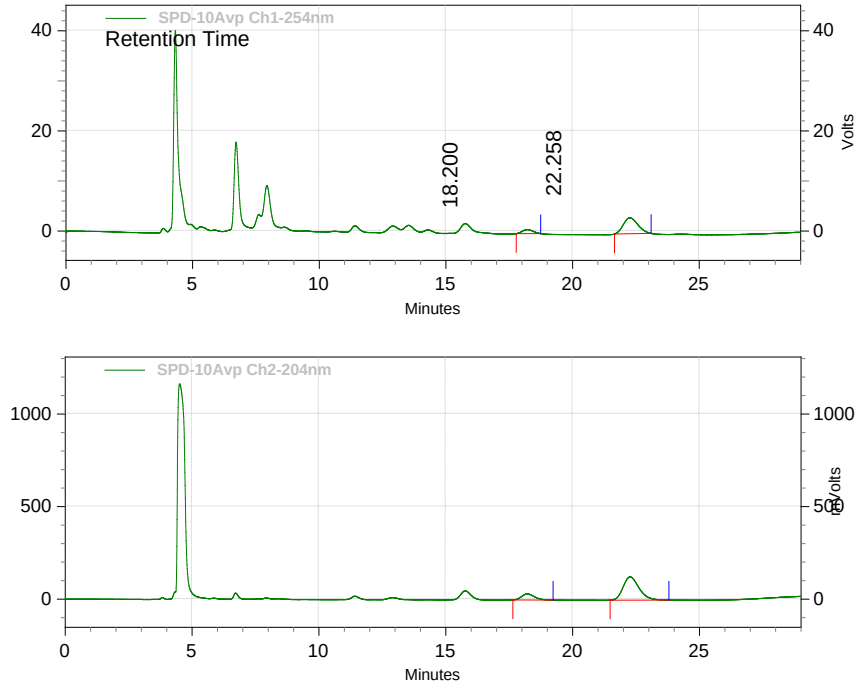
Retention Time	Area	Area %	Height	Height %
18.333	17299132	49.63	339903	56.36
22.300	17555916	50.37	263154	43.64
Totals	34855048	100.00	603057	100.00



SPD-10Avp
Ch2-204nm
Results

Retention Time	Area	Area %	Height	Height %
18.592	55215825	47.80	1078958	51.44
22.275	60287082	52.20	1018634	48.56
Totals	115502907	100.00	2097592	100.00

2.31a from ligand **2.29a**



SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
18.200	23658	15.75	794	19.99
22.258	126519	84.25	3177	80.01

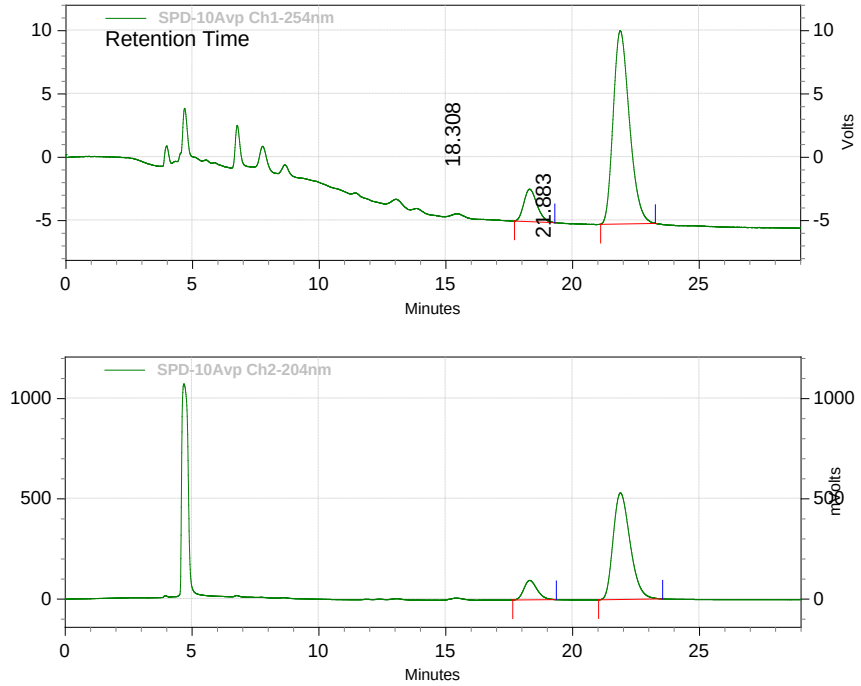
Totals	150177	100.00	3971	100.00

SPD-10Avp
Ch2-204nm
Results

Retention Time	Area	Area %	Height	Height %
18.217	1147949	17.31	32955	20.75
22.267	5484377	82.69	125891	79.25

Totals	6632326	100.00	158846	100.00

2.31a from ligand **2.29b**



SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
18.308	92588	11.98	2558	14.35
21.883	680586	88.02	15263	85.65

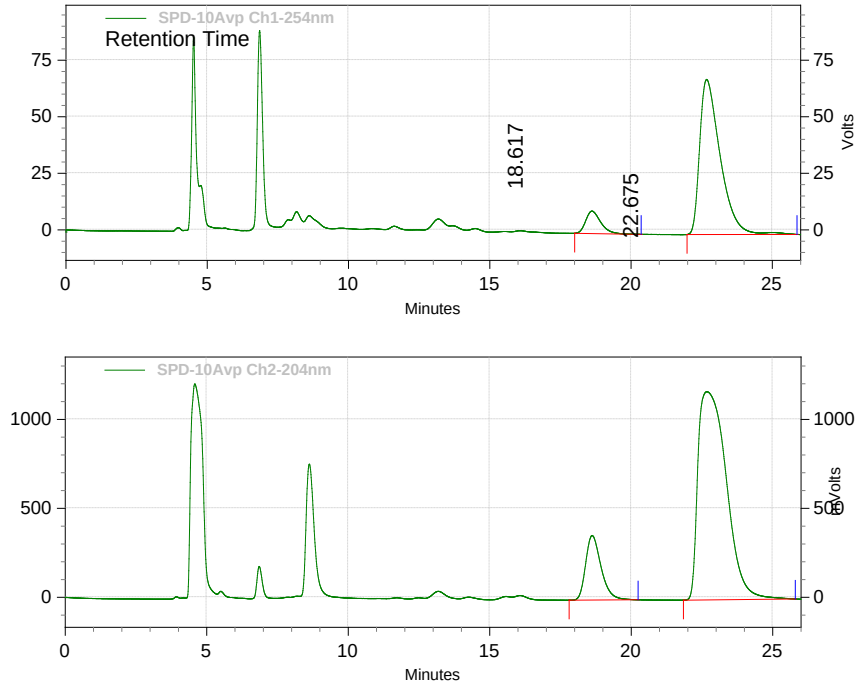
Totals	773174	100.00	17821	100.00

SPD-10Avp
Ch2-204nm
Results

Retention Time	Area	Area %	Height	Height %
18.308	3522717	12.45	96874	15.41
21.883	24767764	87.55	531769	84.59

Totals	28290481	100.00	628643	100.00

2.31a from ligand **2.29c**



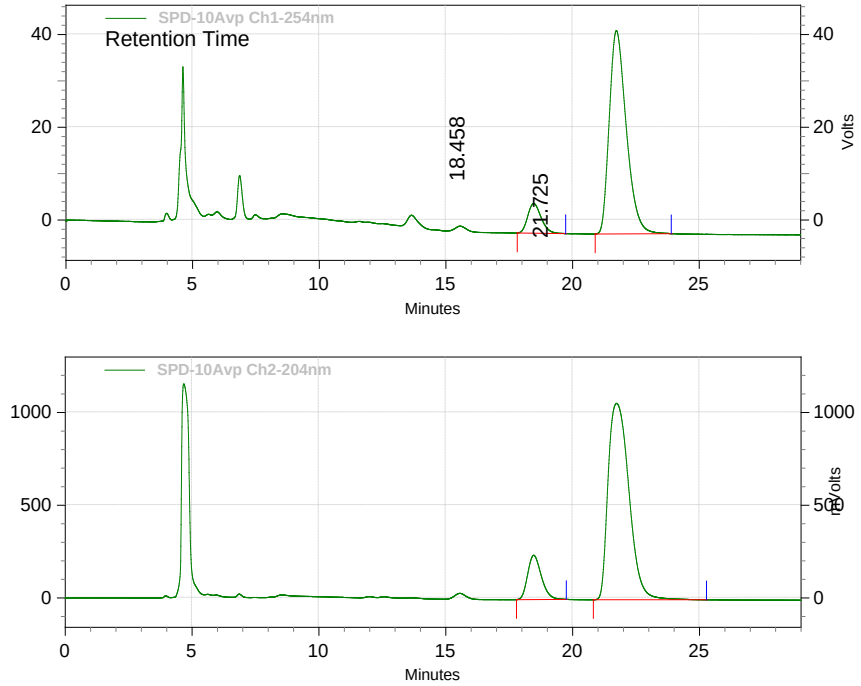
SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
18.617	368661	9.63	9937	12.67
22.675	3458046	90.37	68477	87.33
Totals	3826707	100.00	78414	100.00

SPD-10Avp
Ch2-204nm
Results

Retention Time	Area	Area %	Height	Height %
18.617	13755576	14.44	362383	23.66
22.675	81504225	85.56	1169566	76.34
Totals	95259801	100.00	1531949	100.00

2.31a from ligand **2.29d**



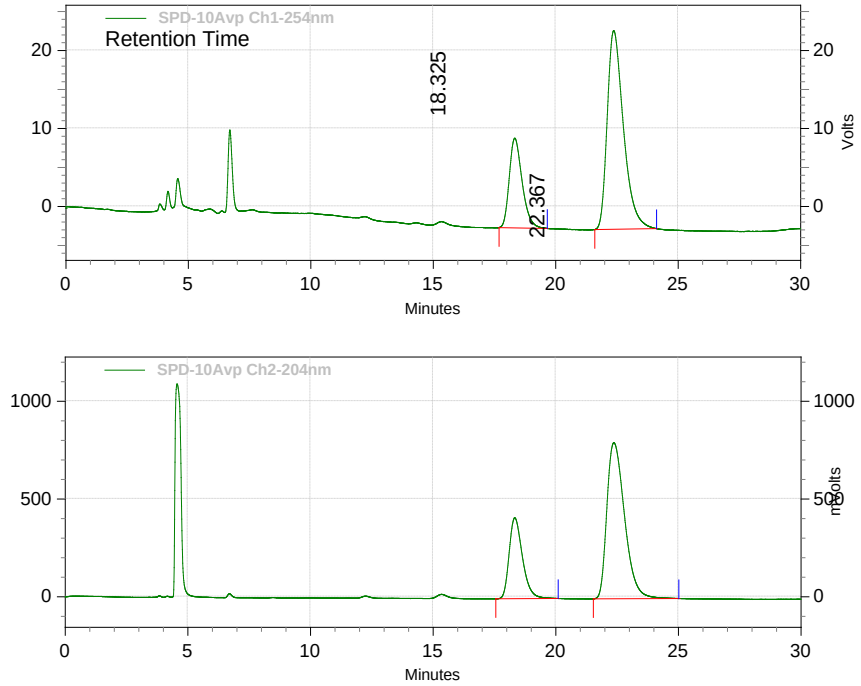
SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
18.458	236431	10.36	6408	12.75
21.725	2045883	89.64	43833	87.25
Totals	2282314	100.00	50241	100.00

SPD-10Avp
Ch2-204nm
Results

Retention Time	Area	Area %	Height	Height %
18.467	8958442	12.91	238603	18.39
21.733	60416112	87.09	1058678	81.61
Totals	69374554	100.00	1297281	100.00

2.31a from ligand **2.29e**



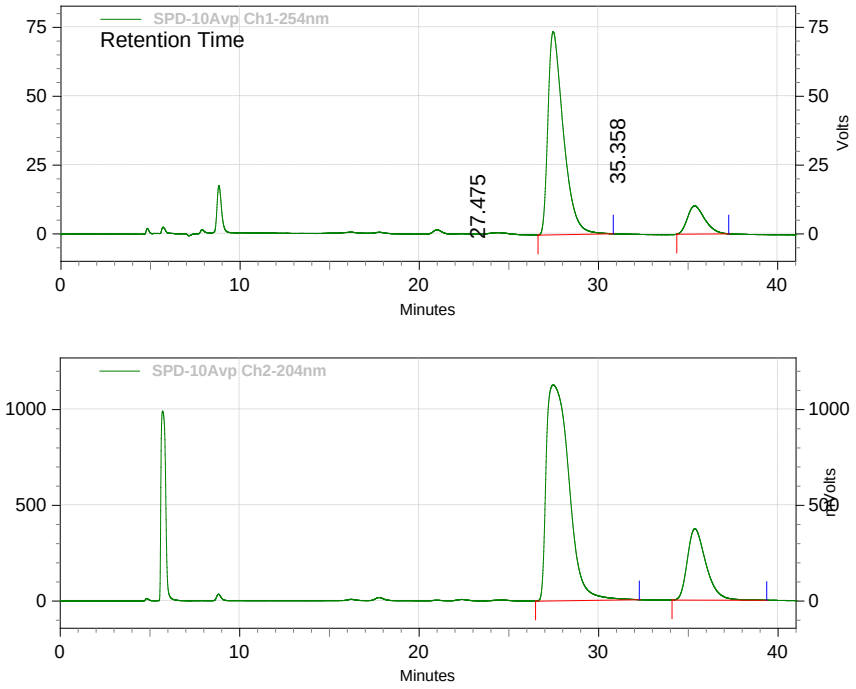
SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
18.325	419705	26.32	11495	31.10
22.367	1174861	73.68	25467	68.90
Totals	1594566	100.00	36962	100.00

SPD-10Avp
Ch2-204nm
Results

Retention Time	Area	Area %	Height	Height %
18.325	15624653	28.08	413887	34.14
22.367	40017268	71.92	798493	65.86
Totals	55641921	100.00	1212380	100.00

2.31a from ligand **2.29f**



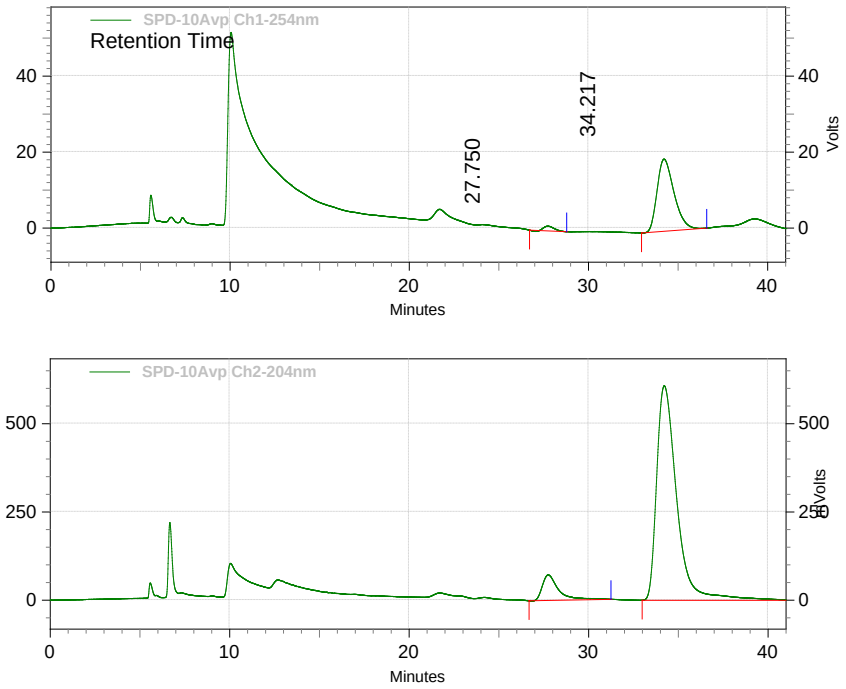
SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
27.475	4413447	86.49	73788	87.82
35.358	689442	13.51	10233	12.18
Totals	5102889	100.00	84021	100.00

SPD-10Avp
Ch2-204nm
Results

Retention Time	Area	Area %	Height	Height %
27.483	98216368	78.50	1127592	75.13
35.358	26894472	21.50	373187	24.87
Totals	125110840	100.00	1500779	100.00

2.31a from ligand **2.29g**



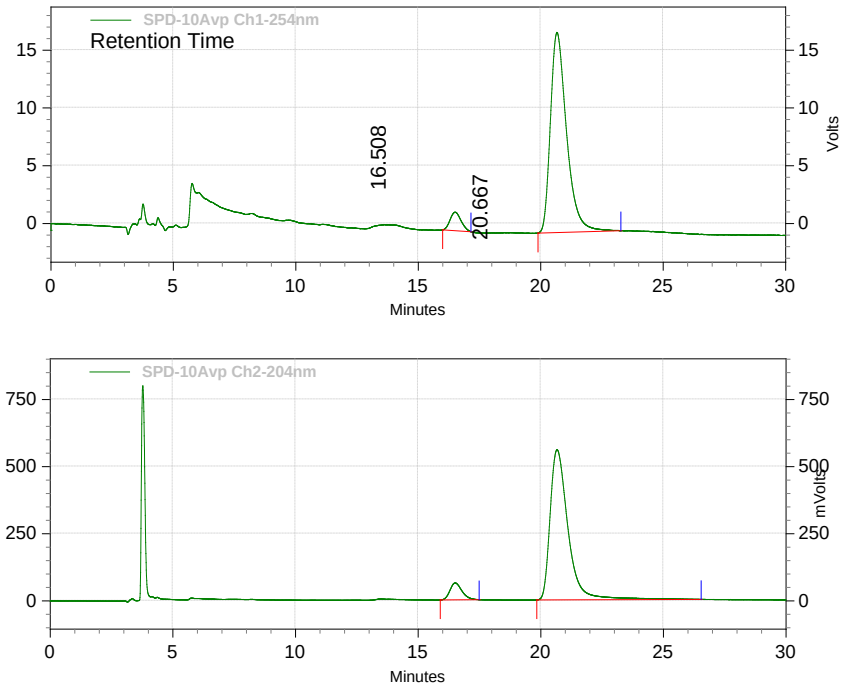
SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
27.750	46982	3.64	1270	6.27
34.217	1245435	96.36	18986	93.73
Totals	1292417	100.00	20256	100.00

SPD-10Avp
Ch2-204nm
Results

Retention Time	Area	Area %	Height	Height %
27.750	4578187	8.80	72547	10.67
34.217	47454774	91.20	607634	89.33
Totals	52032961	100.00	680181	100.00

2.31a from ligand **2.29g** in *i*-PrOH



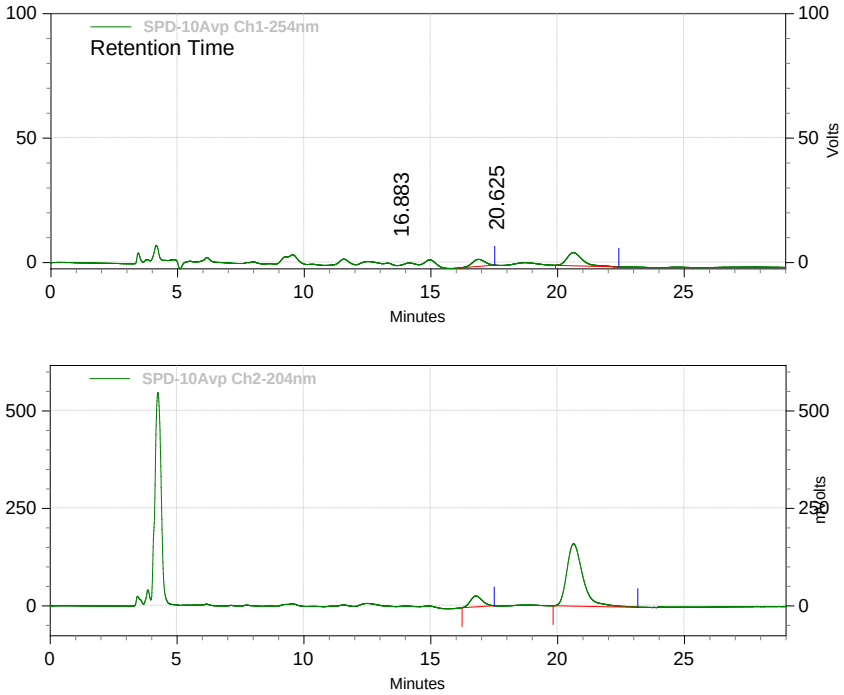
SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
16.508	50126	5.95	1597	8.45
20.667	792892	94.05	17312	91.55
Totals	843018	100.00	18909	100.00

SPD-10Avp
Ch2-204nm
Results

Retention Time	Area	Area %	Height	Height %
16.517	2142803	6.99	63040	10.13
20.667	28509830	93.01	559179	89.87
Totals	30652633	100.00	622219	100.00

2.31a from ligand **2.29g** in *i*-PrOH at 0 ºC



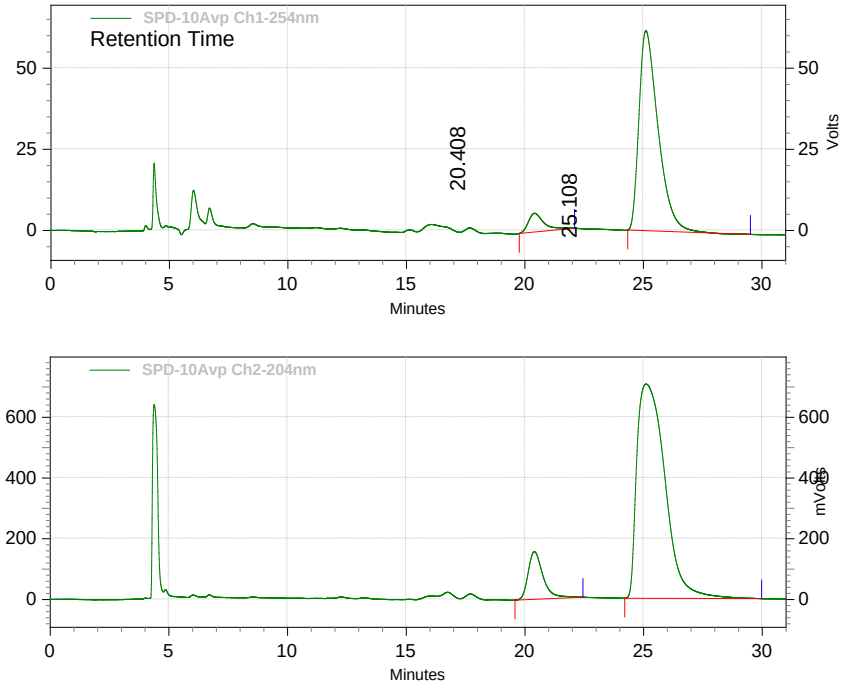
SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
16.883	99425	30.65	2821	34.81
20.625	224987	69.35	5282	65.19
Totals	324412	100.00	8103	100.00

SPD-10Avp
Ch2-204nm
Results

Retention Time	Area	Area %	Height	Height %
16.775	912585	11.49	27922	14.86
20.625	7032282	88.51	159994	85.14
Totals	7944867	100.00	187916	100.00

2.31a from $Cu(O(4\text{-}Cl\text{-}Bz))_2$ with ligand **2.29g**



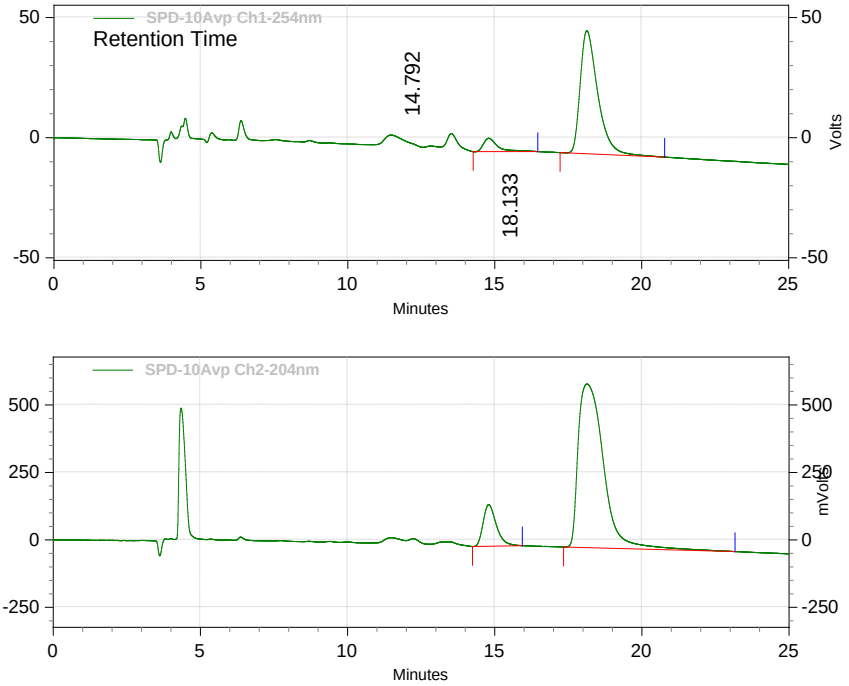
SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
20.408	266643	7.17	5761	8.55
25.108	3453946	92.83	61590	91.45
Totals	3720589	100.00	67351	100.00

SPD-10Avp
Ch2-204nm
Results

Retention Time	Area	Area %	Height	Height %
20.392	6865369	10.58	157101	18.21
25.100	58026457	89.42	705613	81.79
Totals	64891826	100.00	862714	100.00

2.31a from $Cu(OPiv)_2$ with ligand **2.29g**

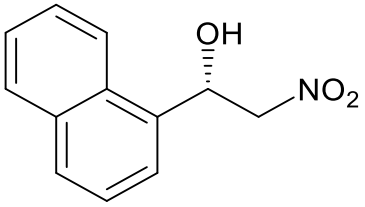


SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
14.792	188344	8.13	5558	9.79
18.133	2129651	91.87	51222	90.21
Totals	2317995	100.00	56780	100.00

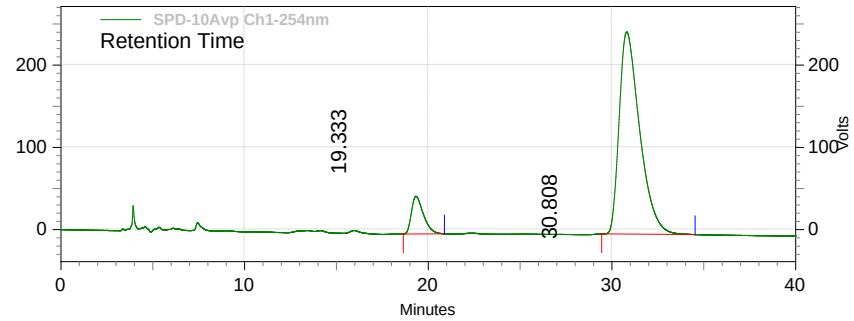
SPD-10Avp
Ch2-204nm
Results

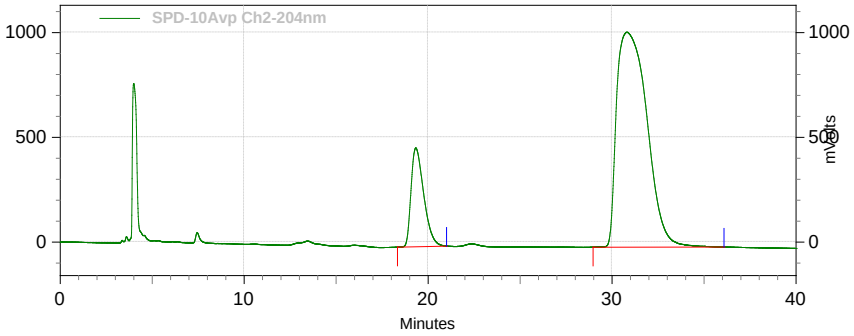
Retention Time	Area	Area %	Height	Height %
14.792	4809449	11.73	154044	20.26
18.133	36183907	88.27	606115	79.74
Totals	40993356	100.00	760159	100.00



2.31b

HPLC conditions: 10% isopropanol/hexanes



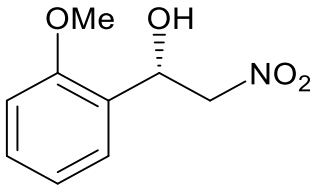


SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
19.333	2078149	9.84	45753	15.70
30.808	19047137	90.16	245723	84.30
Totals	21125286	100.00	291476	100.00

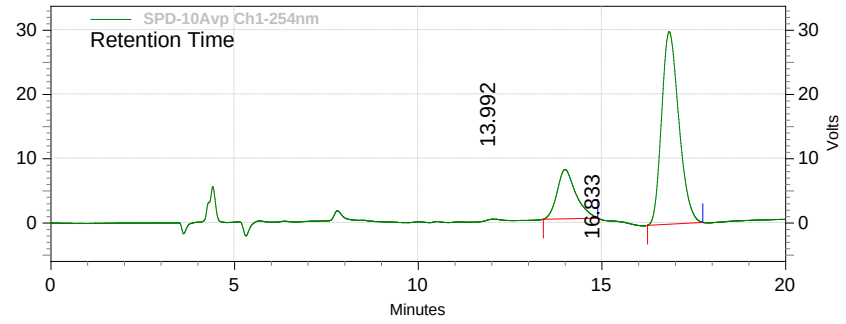
SPD-10Avp
Ch2-204nm
Results

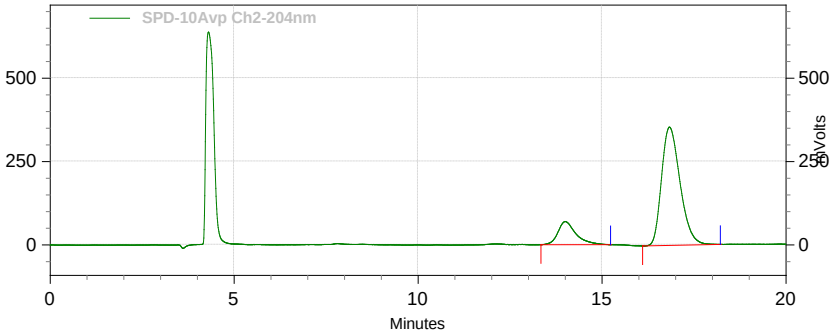
Retention Time	Area	Area %	Height	Height %
19.333	22608605	16.12	471788	31.51
30.825	117685070	83.88	1025578	68.49
Totals	140293675	100.00	1497366	100.00



2.31c

HPLC conditions: 10% isopropanol/hexanes



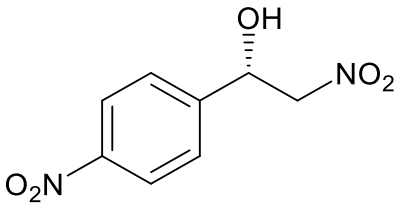


SPD-10Avp
Ch1-254nm
Results

Retention Time	Area	Area %	Height	Height %
13.992	271881	21.76	7674	20.40
16.833	977694	78.24	29950	79.60
Totals	1249575	100.00	37624	100.00

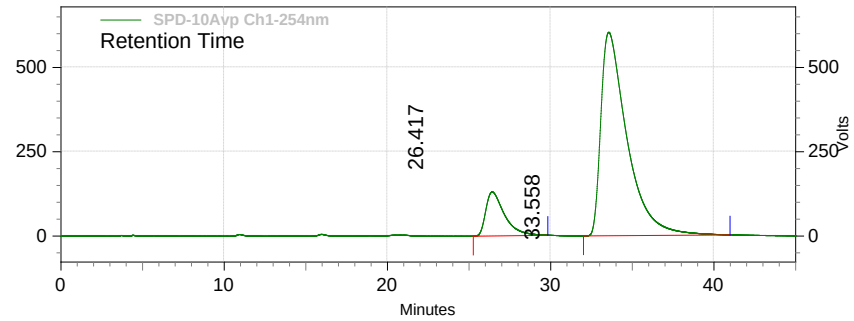
SPD-10Avp
Ch2-204nm
Results

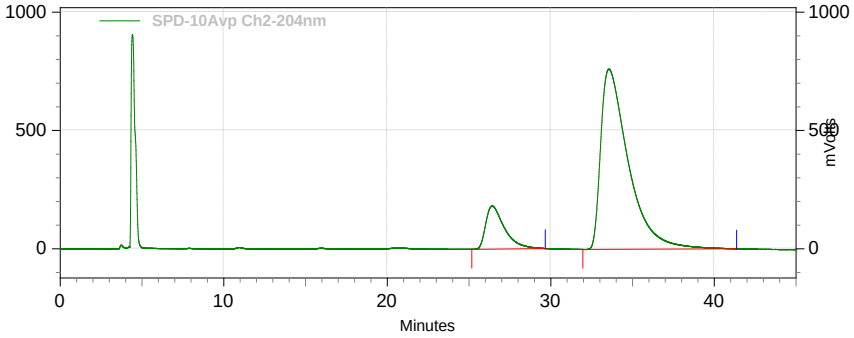
Retention Time	Area	Area %	Height	Height %
14.000	2365462	16.03	69327	16.35
16.833	12394170	83.97	354628	83.65
Totals	14759632	100.00	423955	100.00



2.31d

HPLC conditions: 10% isopropanol/hexanes





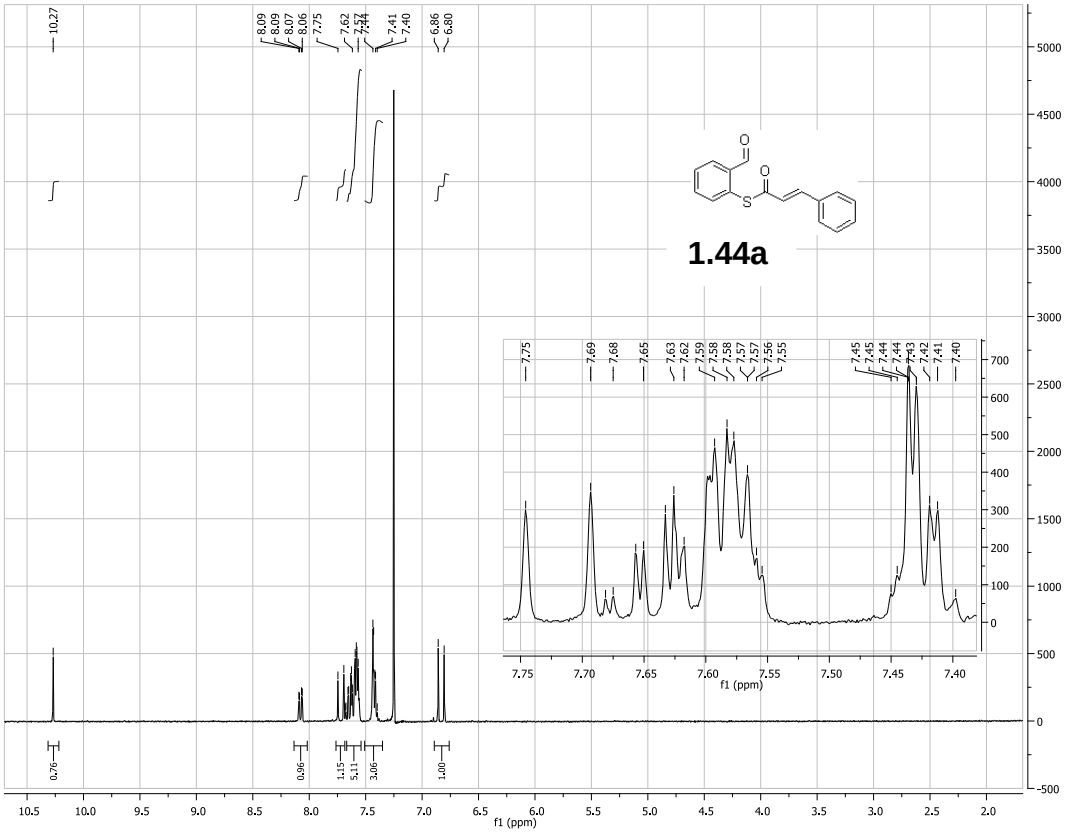
SPD-10Avp
Ch1-254nm
Results

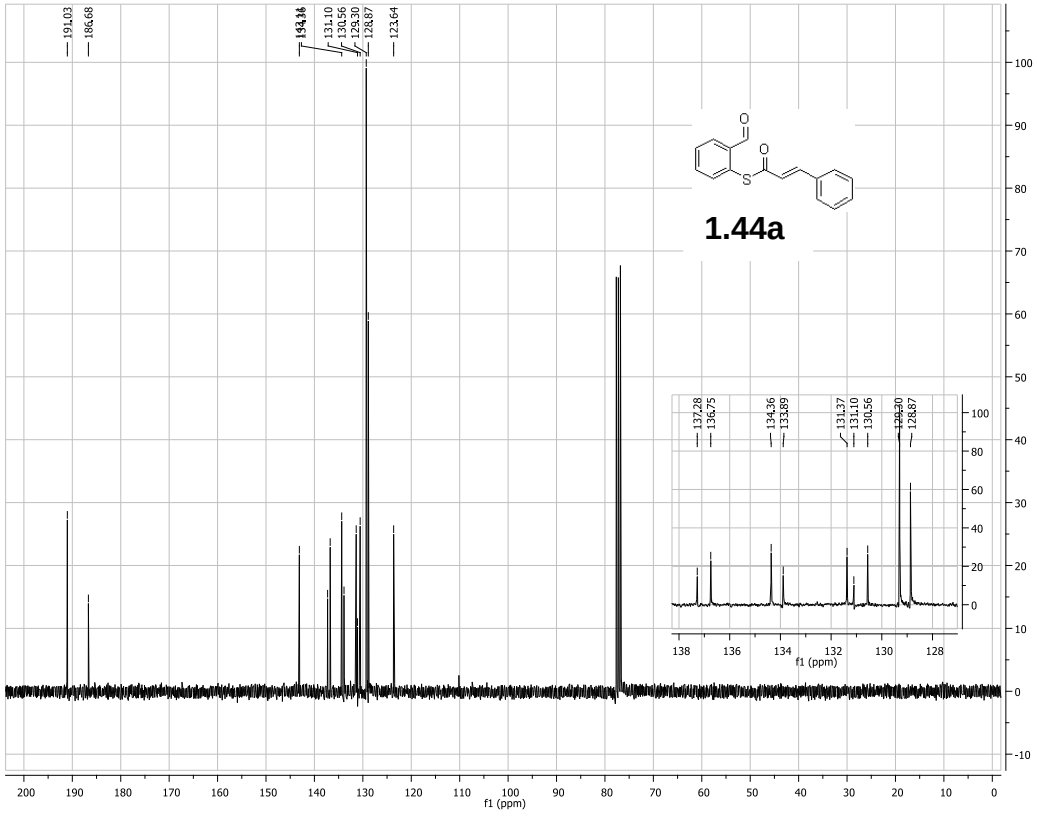
Retention Time	Area	Area %	Height	Height %
26.417	10379466	13.39	130741	17.81
33.558	67164575	86.61	603487	82.19
Totals	77544041	100.00	734228	100.00

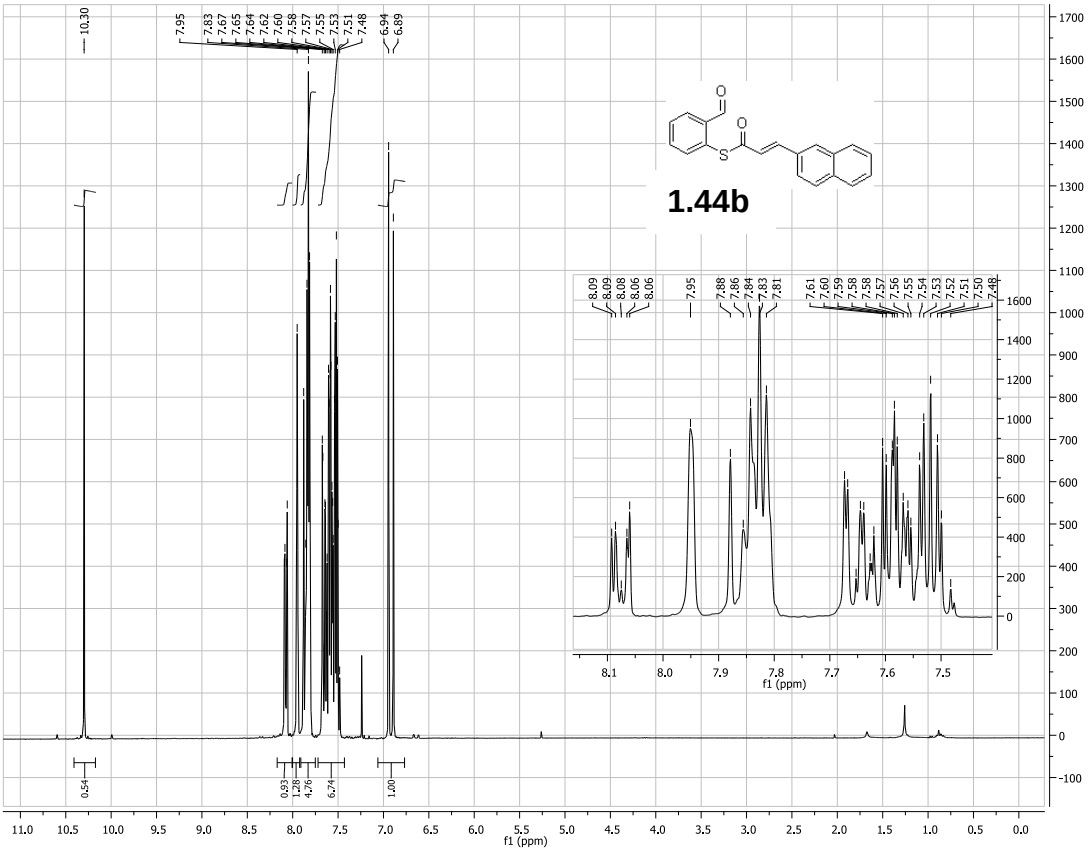
SPD-10Avp
Ch2-204nm
Results

Retention Time	Area	Area %	Height	Height %
26.417	14528627	14.00	182117	19.30
33.558	89281954	86.00	761456	80.70
Totals	103810581	100.00	943573	100.00

A.2 NMR spectra.






10.30
7.95
7.83
7.67
7.65
7.64
7.62
7.60
7.58
7.57
7.55
7.53
7.51
7.48
6.94
6.89
1.44b
8.09
8.08
8.06
7.88
7.86
7.84
7.83
7.81
7.61
7.60
7.59
7.58
7.58
7.57
7.56
7.55
7.54
7.53
7.52
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7.48
f1 (ppm)
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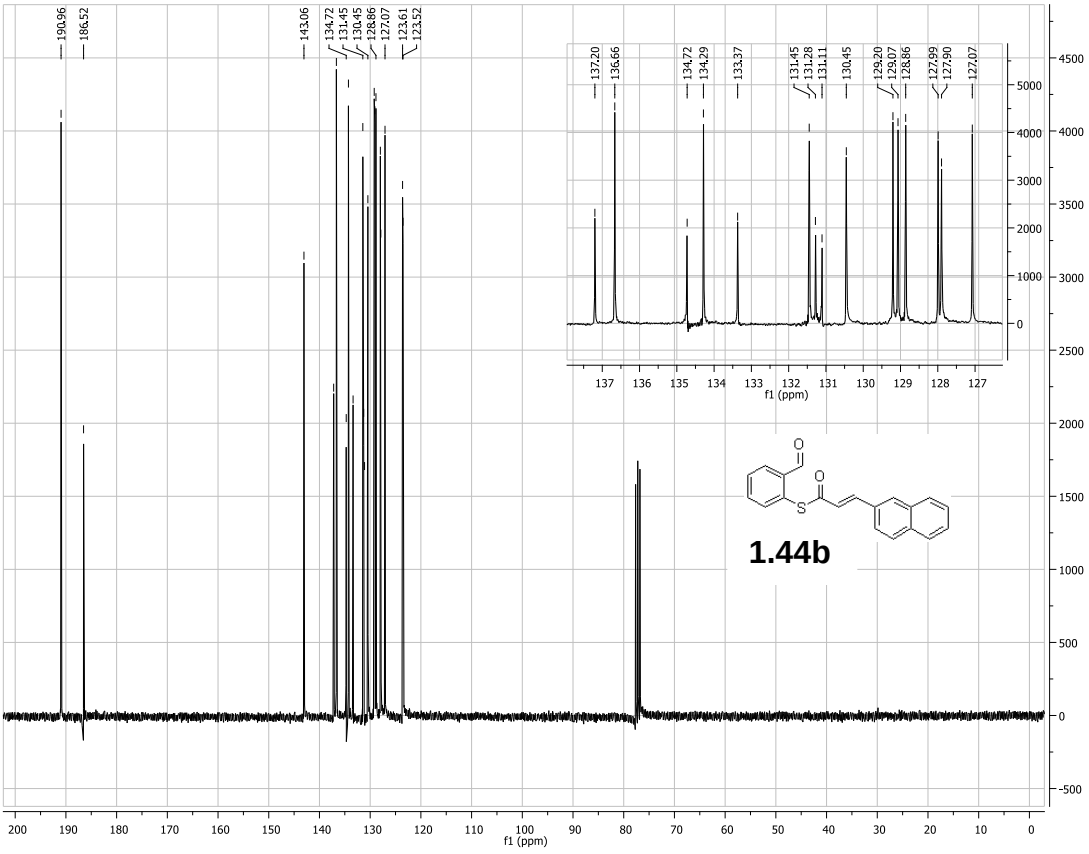
1.28
4.76
6.74
1.00
f1 (ppm)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130.45
128.86
127.07
123.61
123.52
137.20
136.66
134.72
134.29
133.37
131.45
131.28
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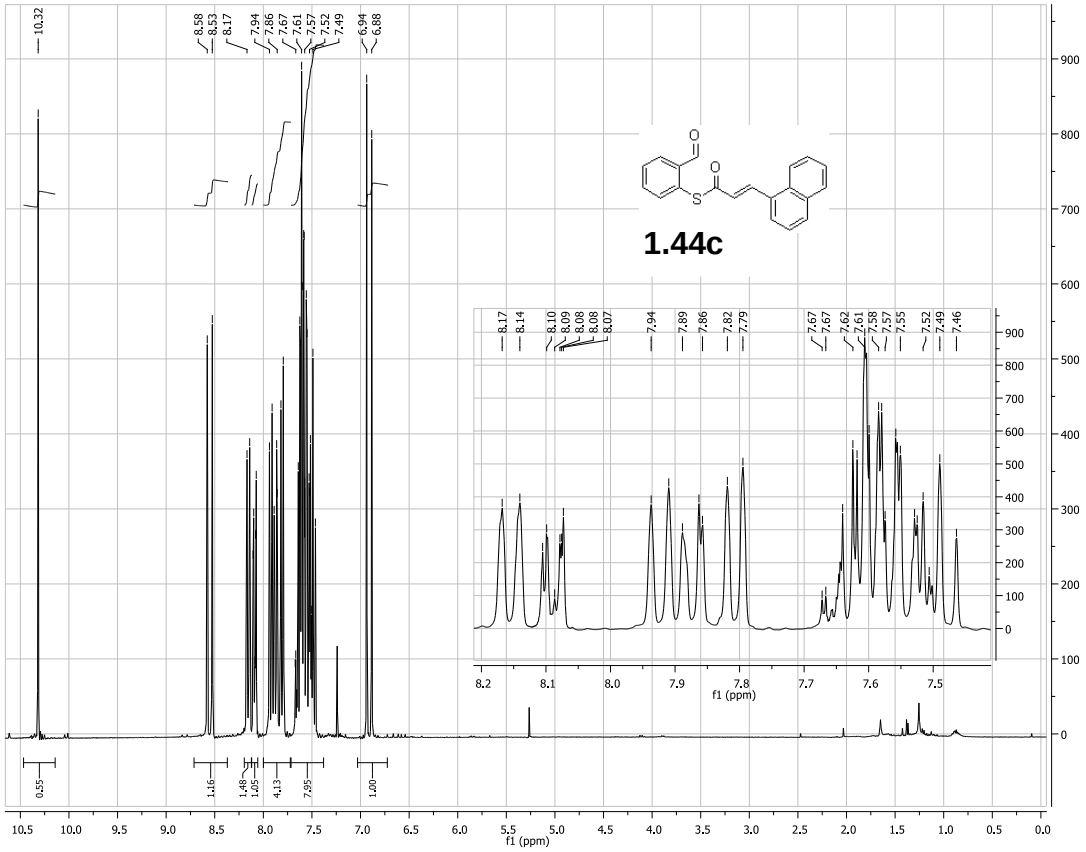
129.07
128.86
127.99
127.90
127.07
f1 (ppm)
1.44b
f1 (ppm)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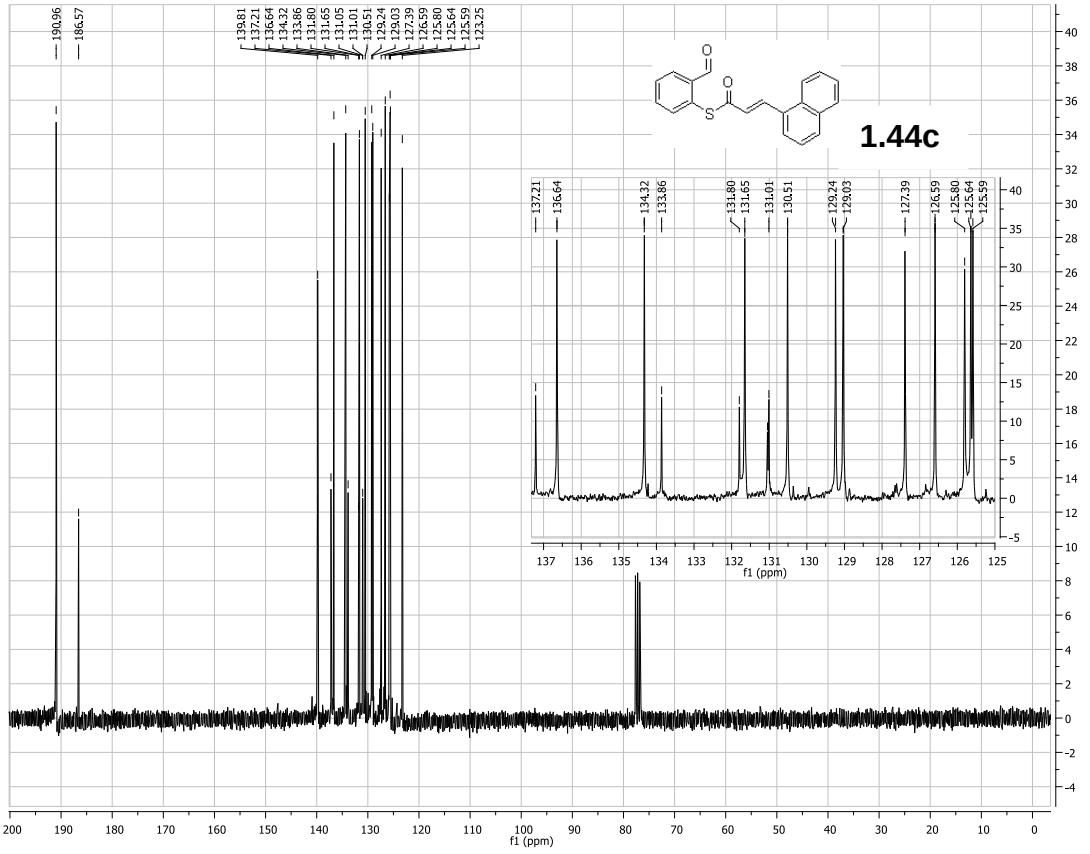
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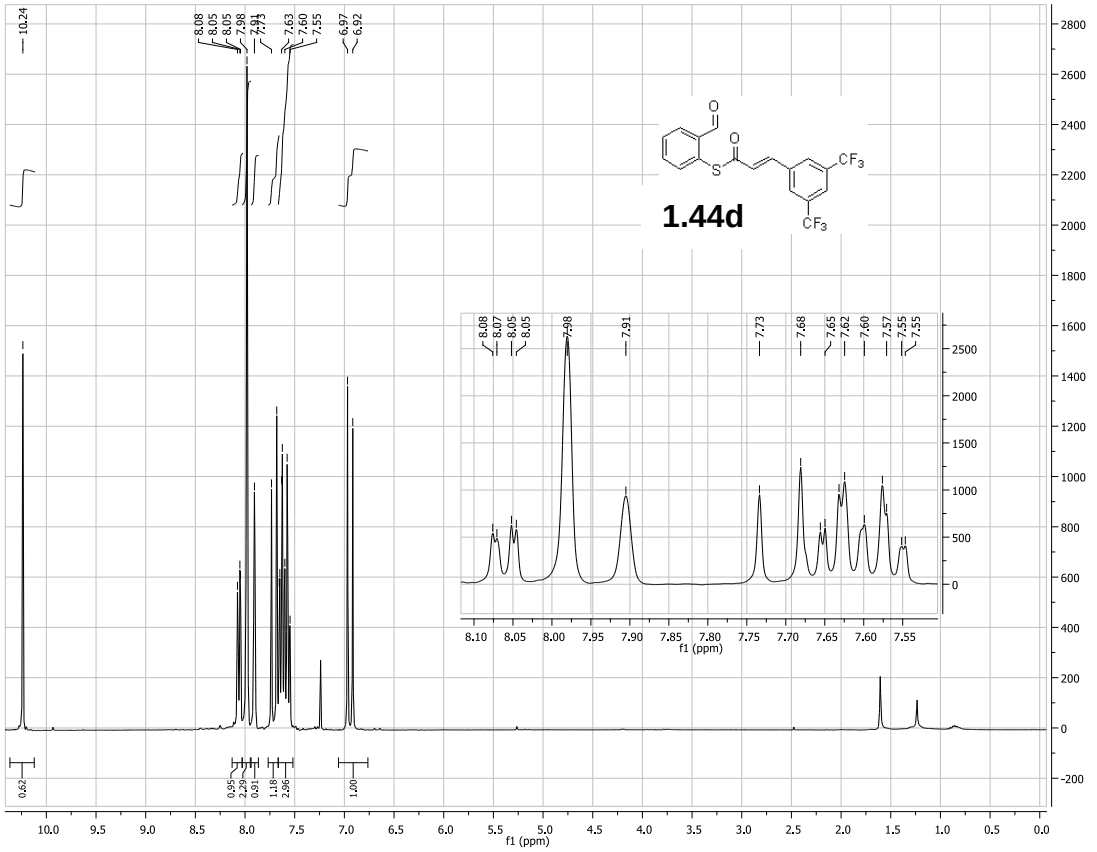
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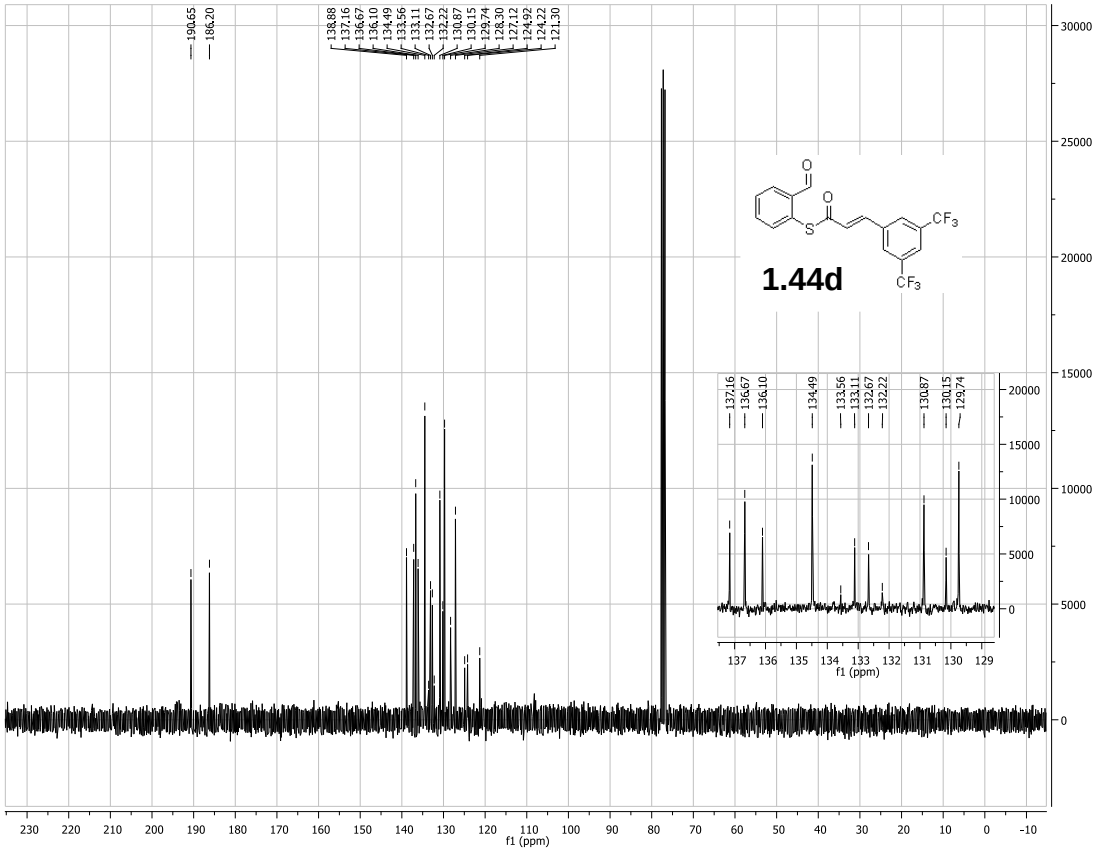
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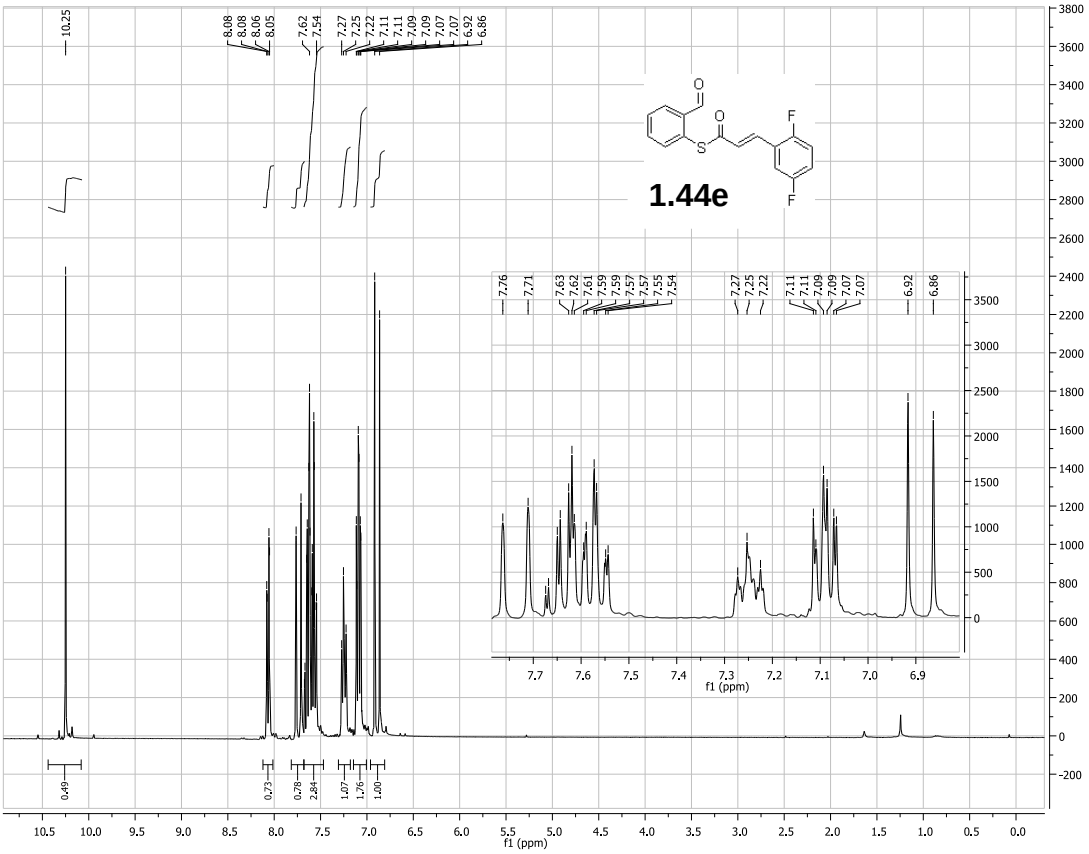
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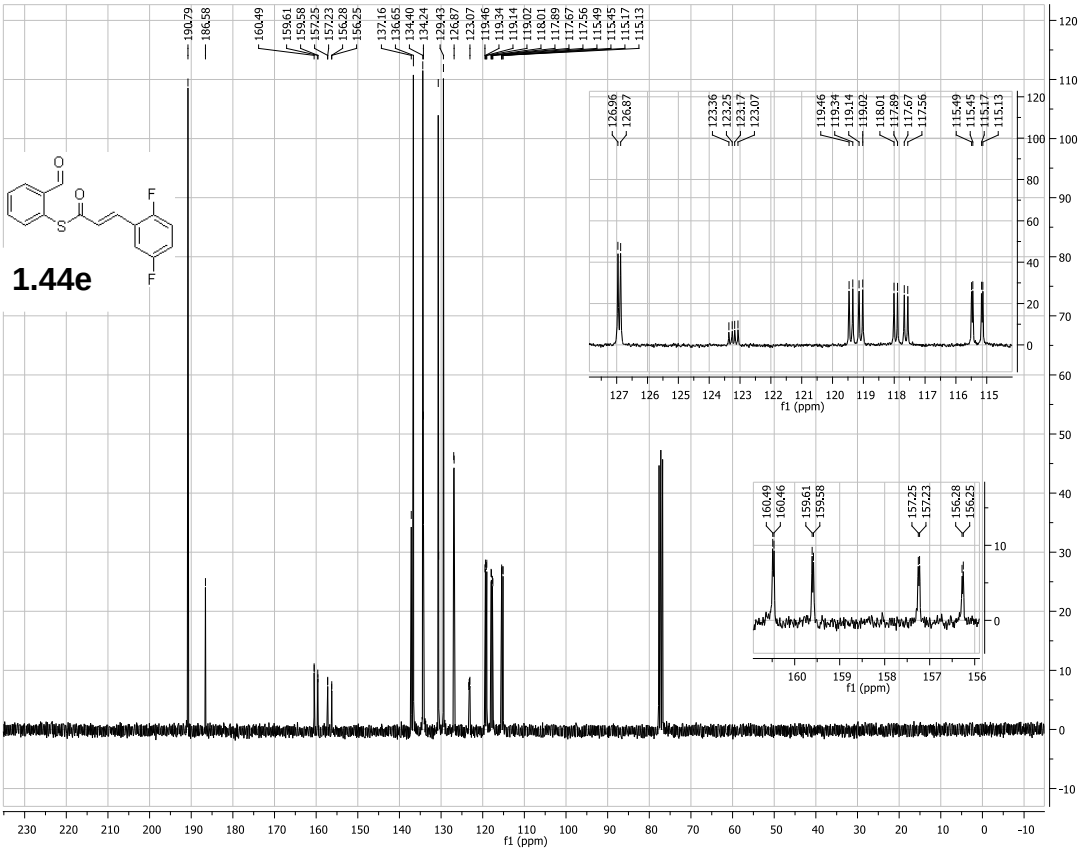
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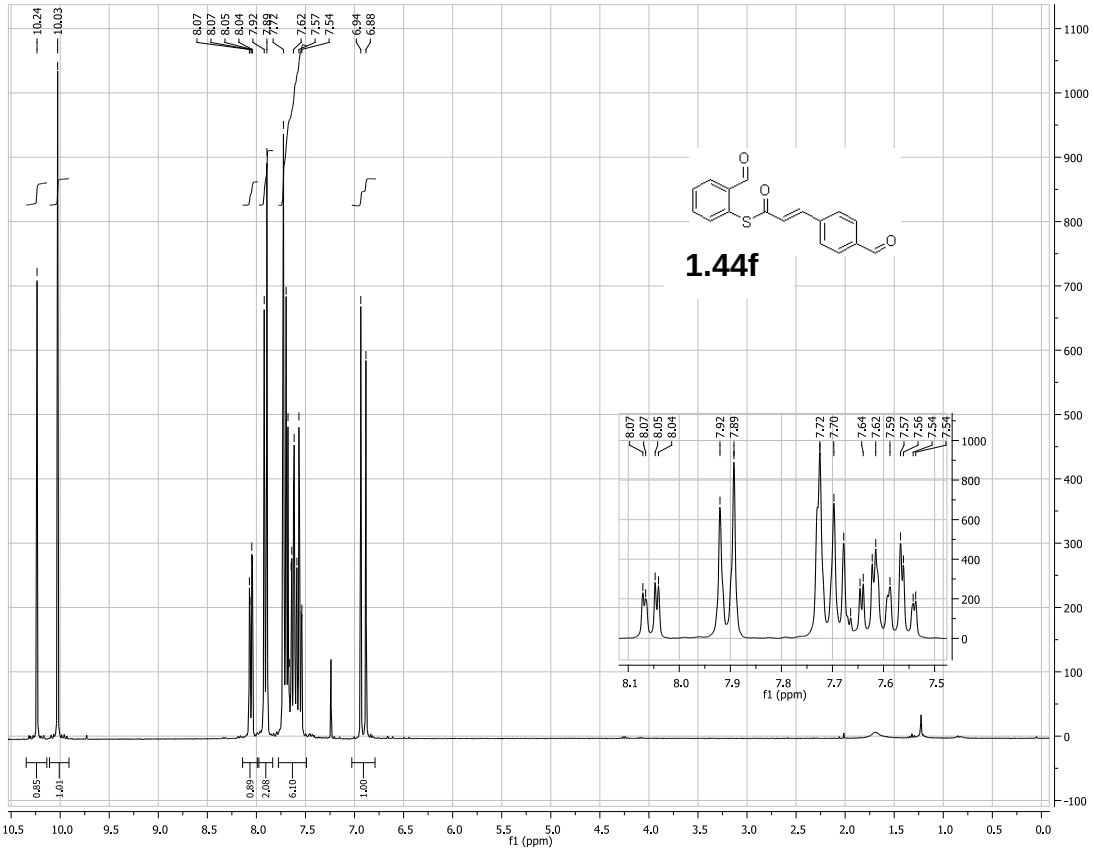
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8.07
8.05
8.04
7.92
7.89
7.72
7.70
7.62
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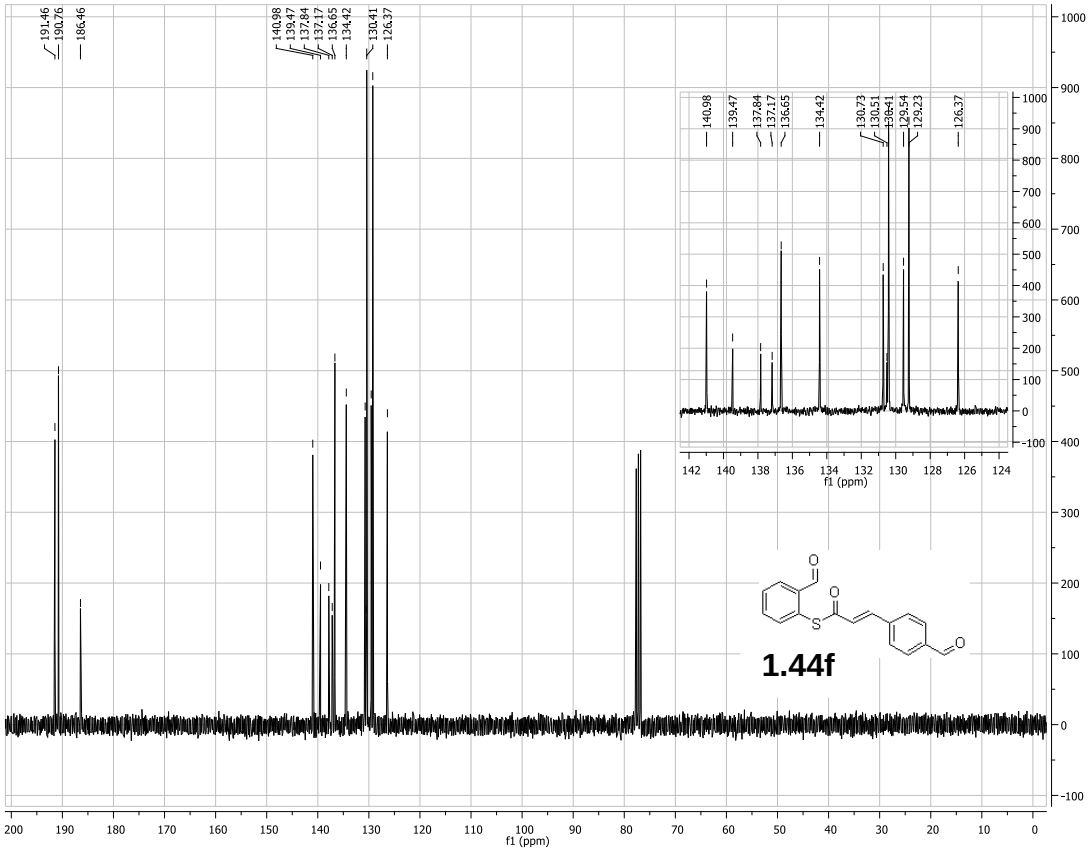
7.54
6.94
6.88
0.85
1.01
0.89
2.08
6.10
1.00
f1 (ppm)
1.44f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190.76
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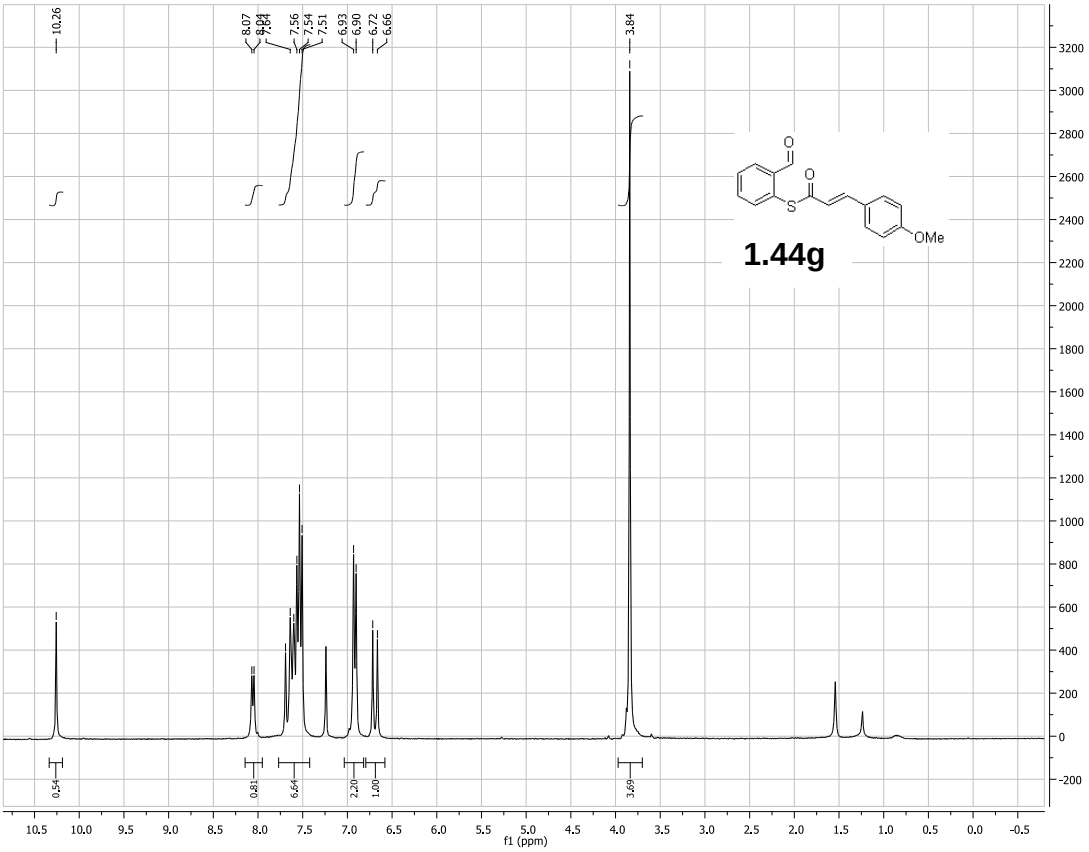
137.84
137.17
136.65
134.42
130.41
126.37
f1 (ppm)
1.44f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8.07
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7.54
7.51
6.93
6.90
6.72
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0.54
0.81
6.64
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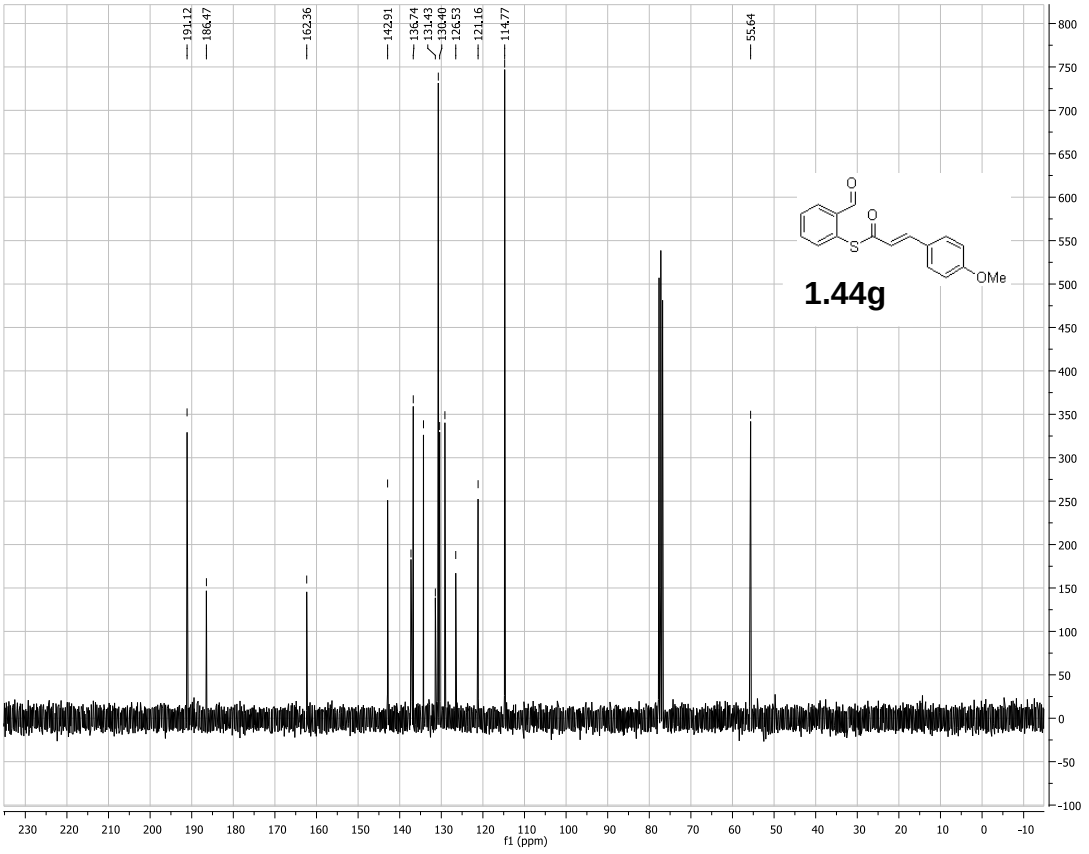
1.00
3.69
f1 (ppm)
1.44g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130.40
126.53
121.16
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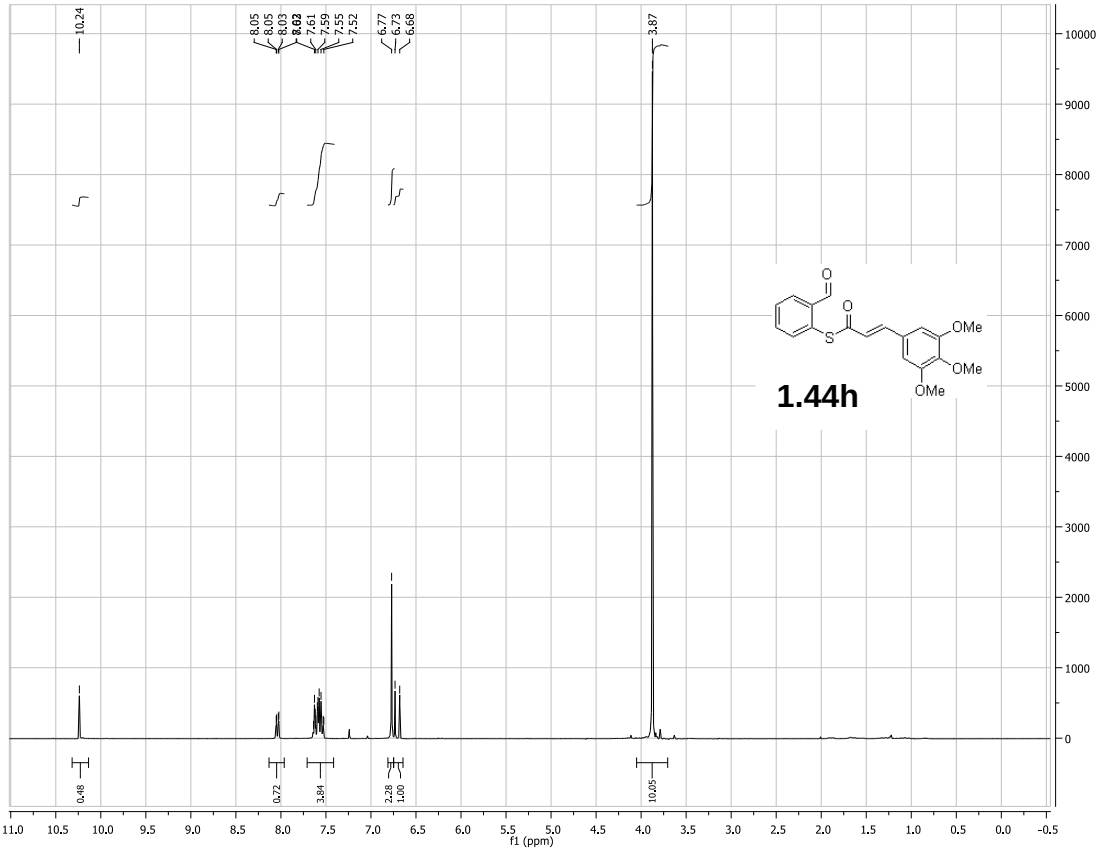
55.64
f1 (ppm)
1.44g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8.05
8.05
8.03
8.02
7.61
7.59
7.55
7.52
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6.73
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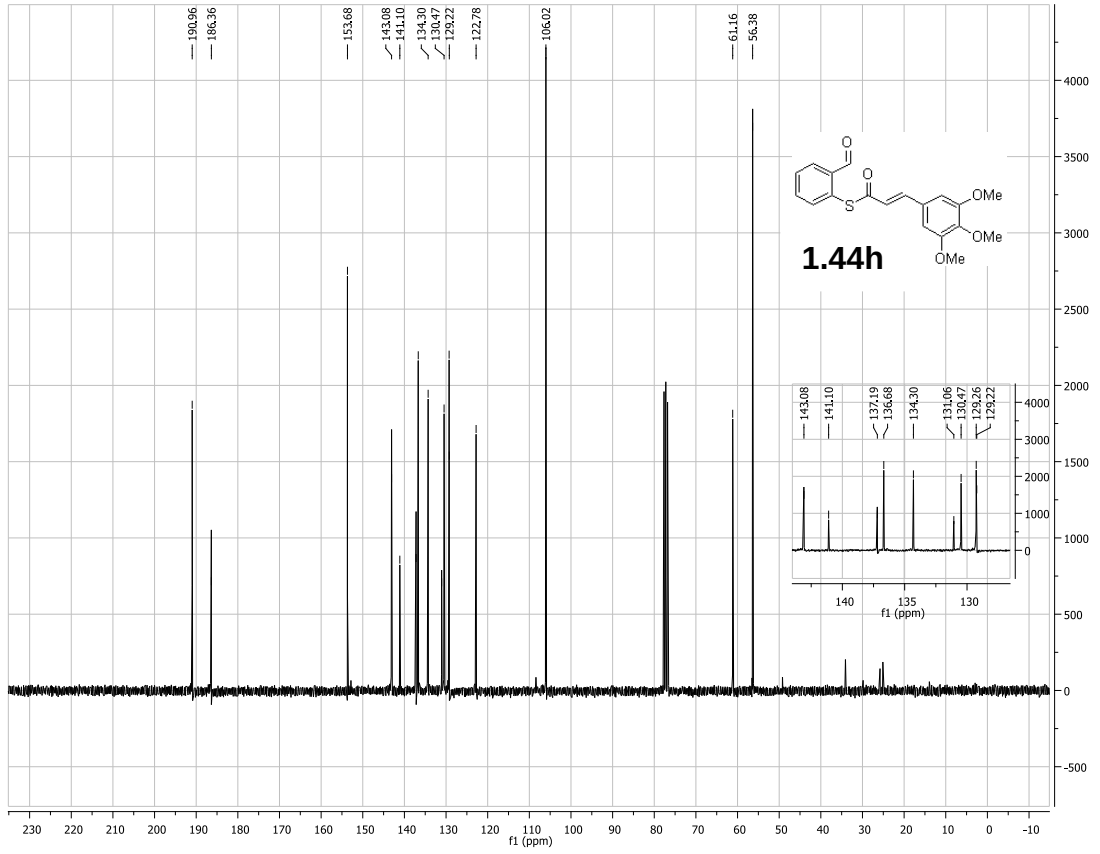
3.87
0.48
0.72
3.84
2.28
1.00
10.05
f1 (ppm)
1.44h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143.08
141.10
134.30
130.47
129.22
122.78
106.02
61.16
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137.19
136.68
134.30
131.06
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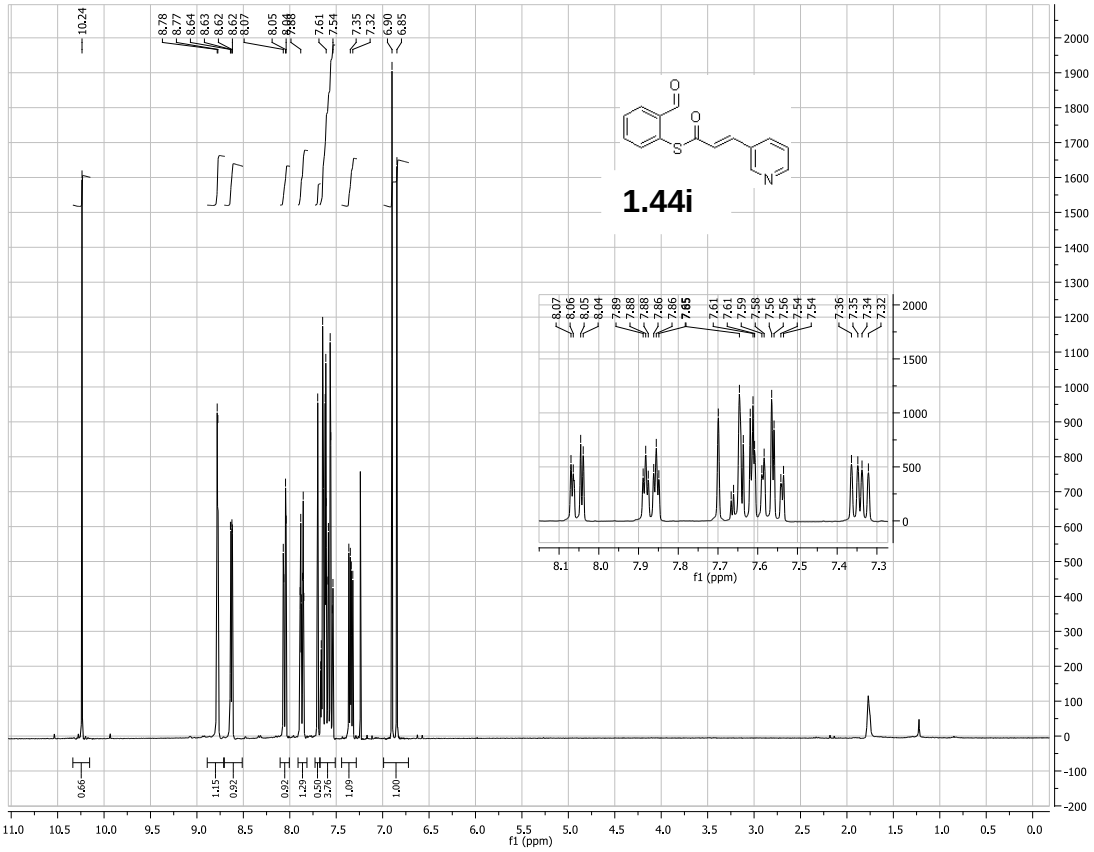
123.26
123.22
f1 (ppm)
1.44h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8.78
8.77
8.64
8.63
8.62
8.62
8.07
8.05
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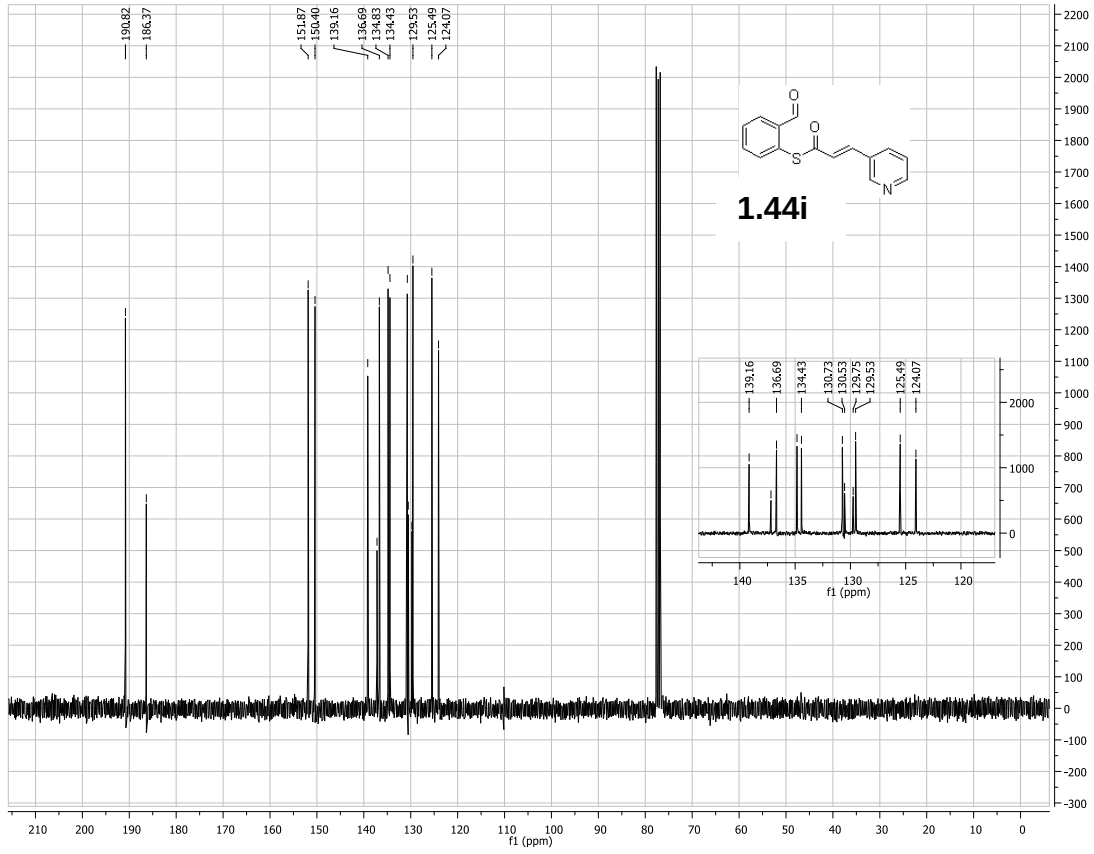
7.88
7.61
7.54
7.35
7.32
6.90
6.85
1.44i
f1 (ppm)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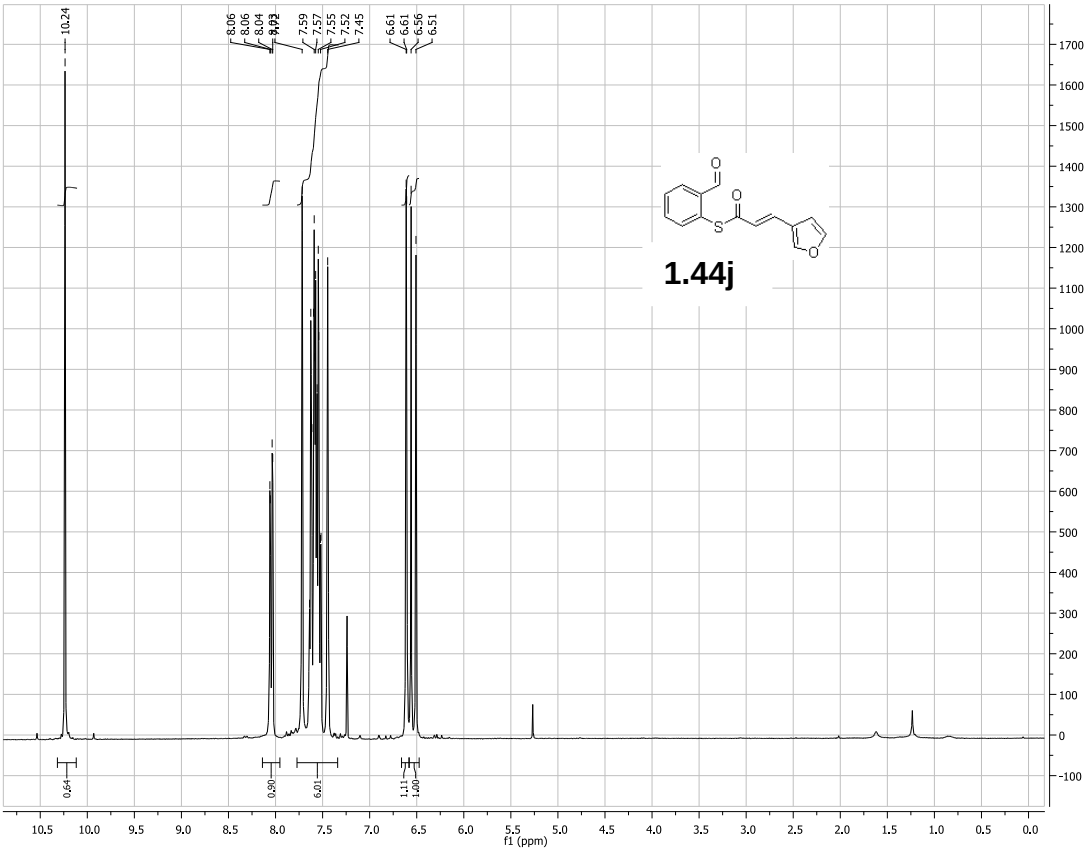
139.16
136.69
134.83
134.43
129.53
125.49
124.07
1.44i
f1 (ppm)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8.06
8.06
8.04
7.59
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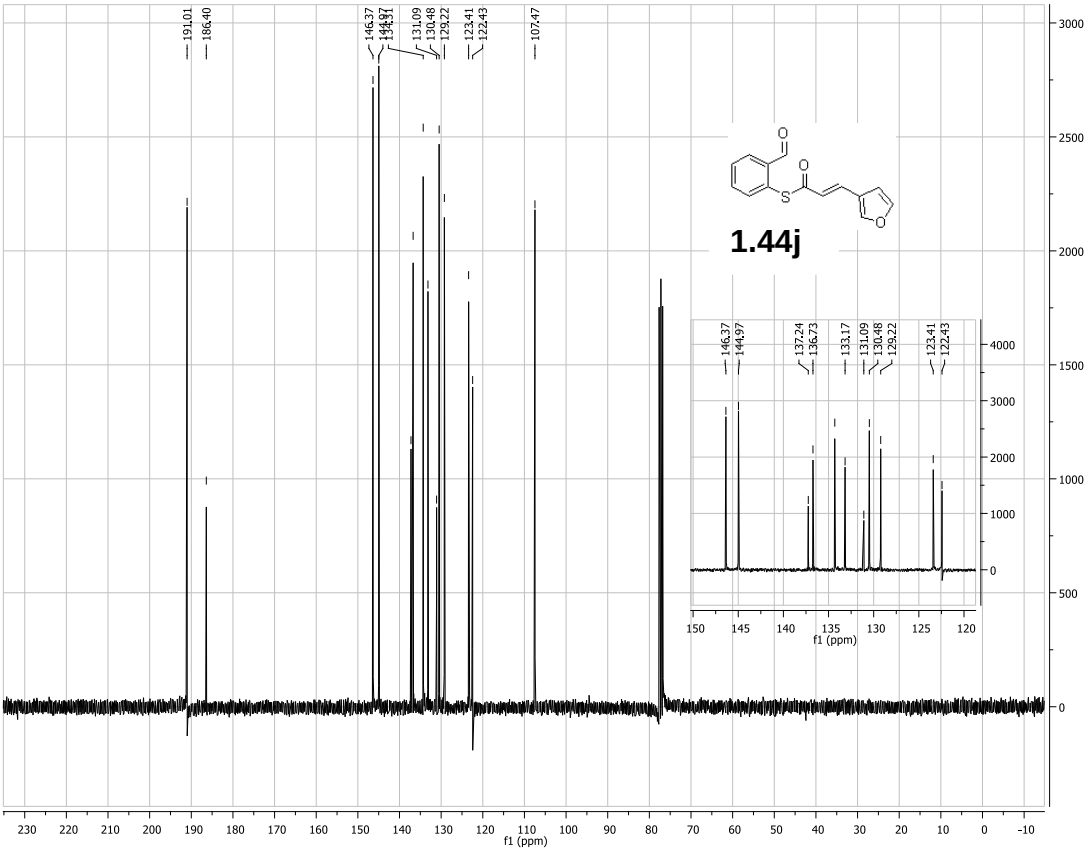
7.55
7.52
7.45
6.61
6.61
6.56
6.51
0.64
0.90
6.01
1.11
1.00
f1 (ppm)
1.44j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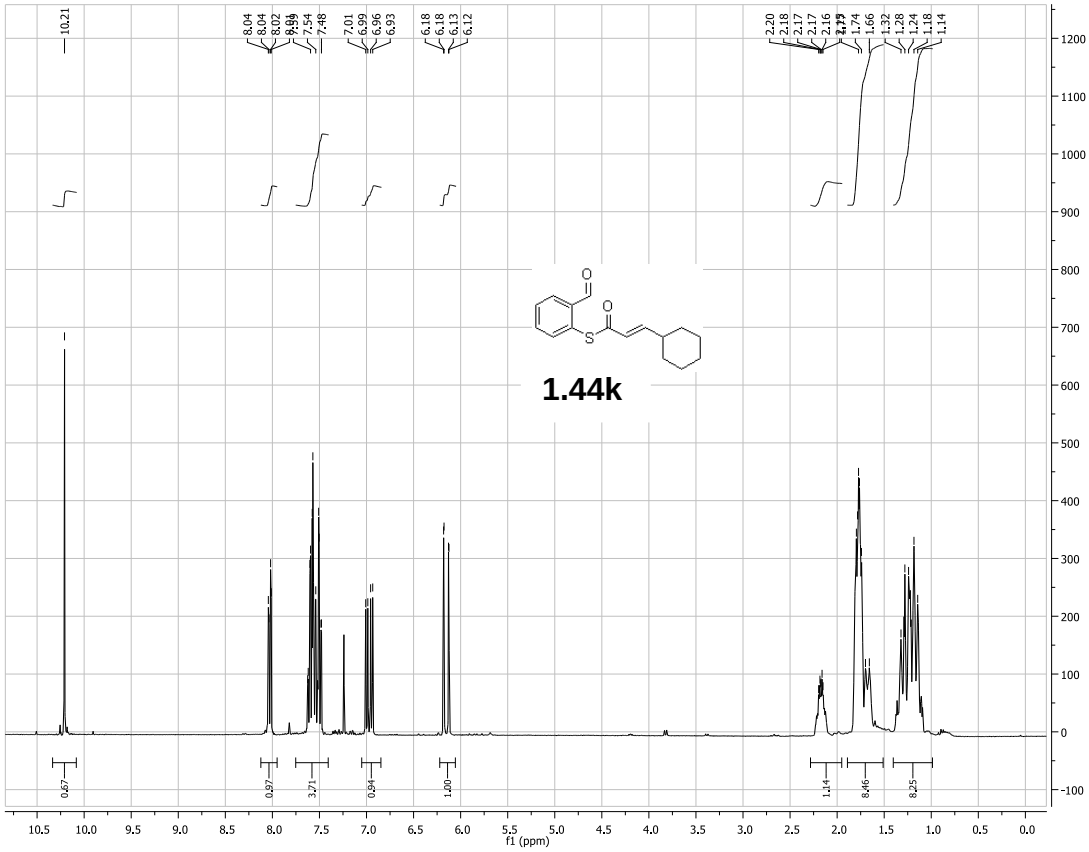
130.48
129.22
123.41
122.43
107.47
f1 (ppm)
1.44j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8.02
8.02
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7.01
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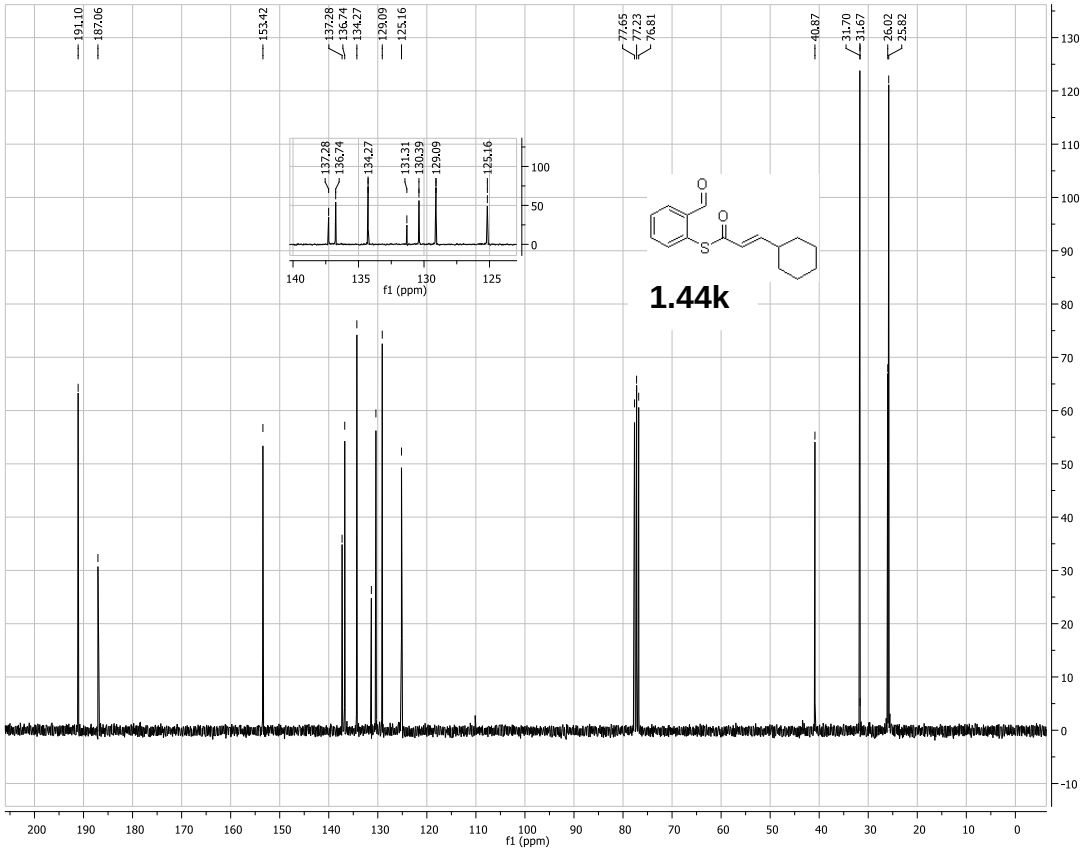
6.96
6.93
6.18
6.18
6.13
6.12
2.20
2.18
2.17
2.17
2.16
1.74
1.66
1.32
1.28
1.24
1.18
1.14
1.44k
0.87
0.97
3.71
0.84
1.00
1.44
8.46
8.25
f1 (ppm)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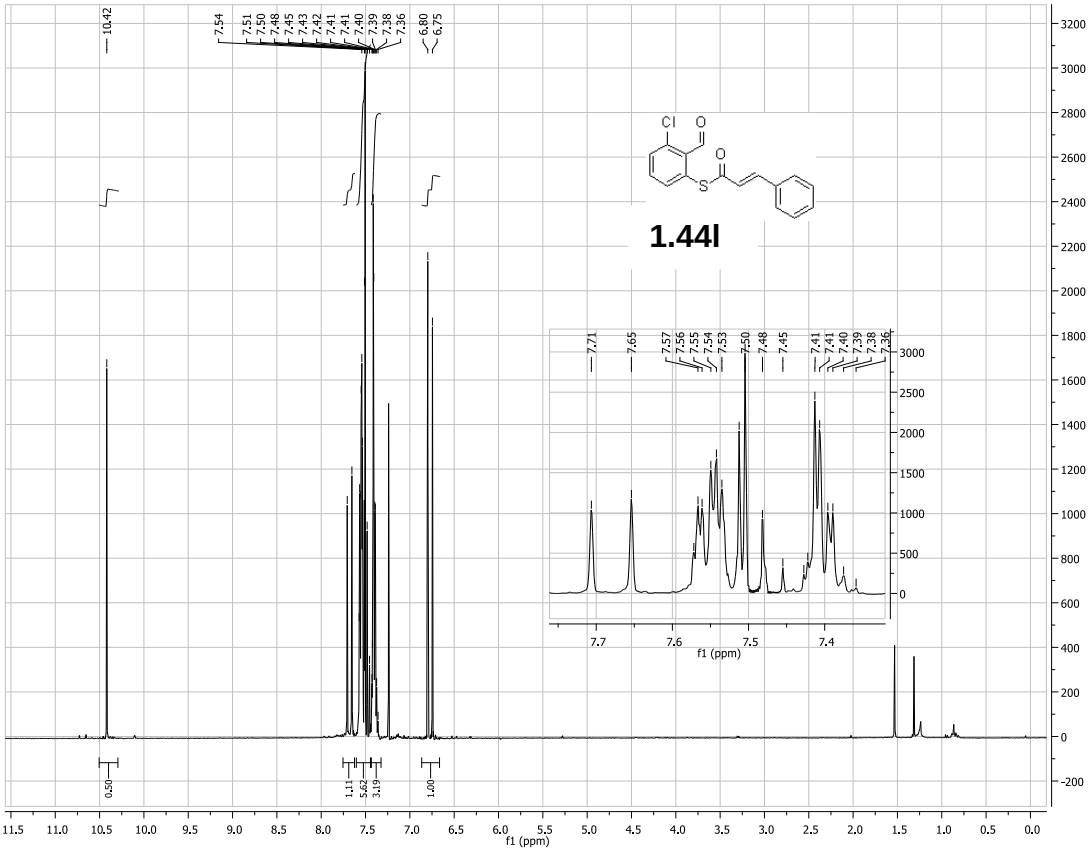
26.02
25.82
1.44k
f1 (ppm)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7.41
7.40
7.39
7.38
7.36
6.80
6.75
Cl
O
O
S
1.44l
7.71
7.65
7.57
7.56
7.55
7.54
7.53
7.50
7.48
7.45
7.41
7.41
7.40
7.39
7.38
7.36
f1 (ppm)
0.50
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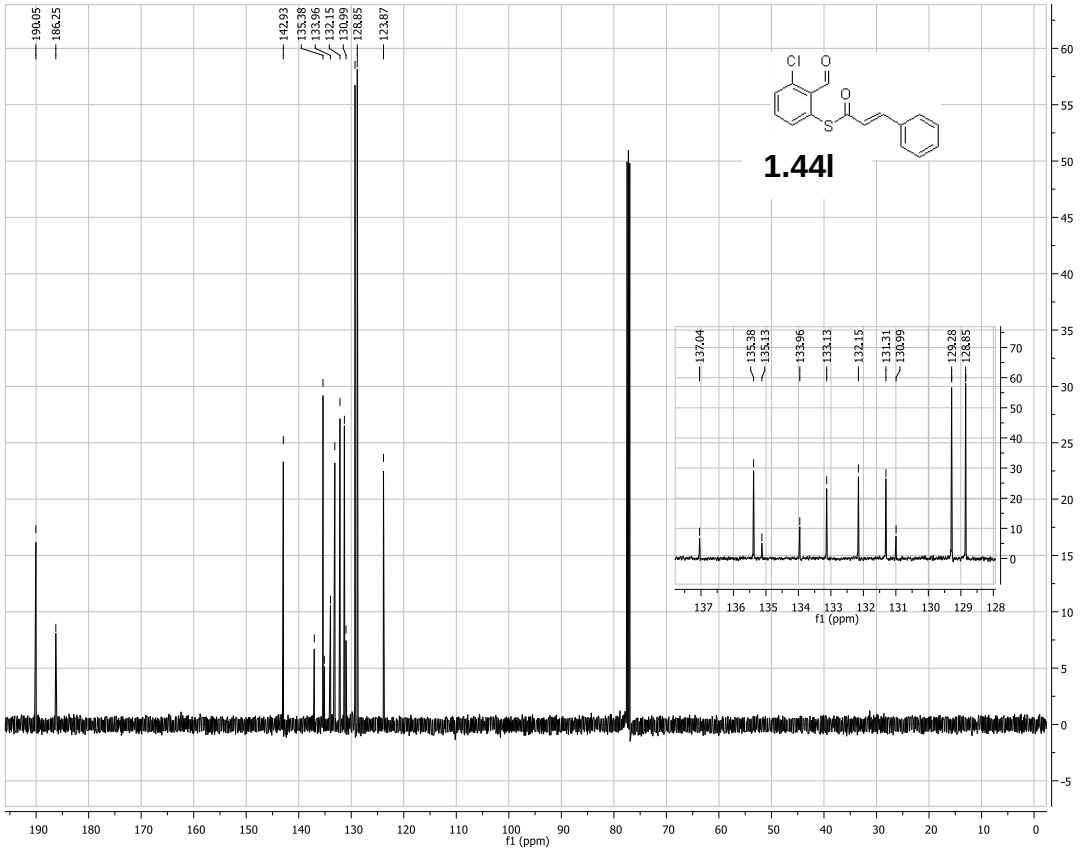
5.62
3.19
1.00
f1 (ppm)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Cl
O
O
S
1.44l
137.04
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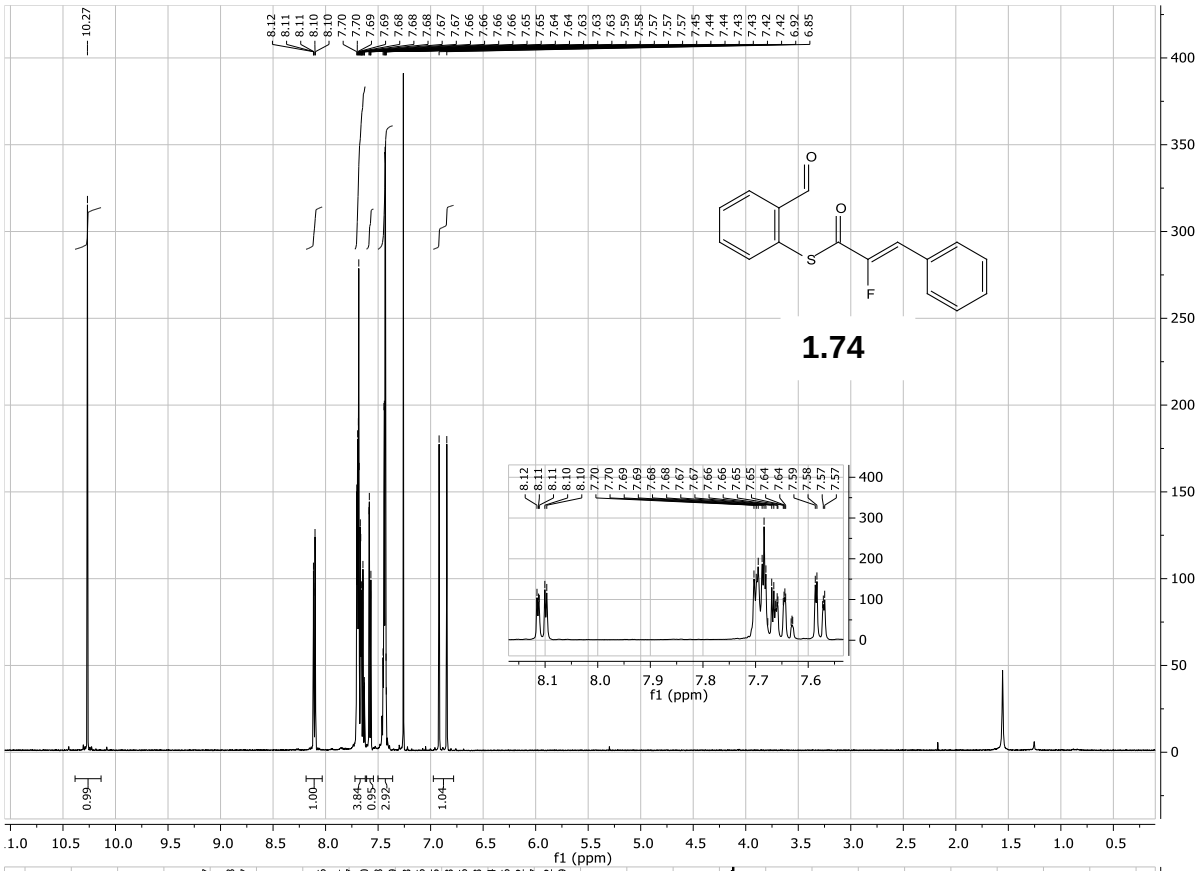
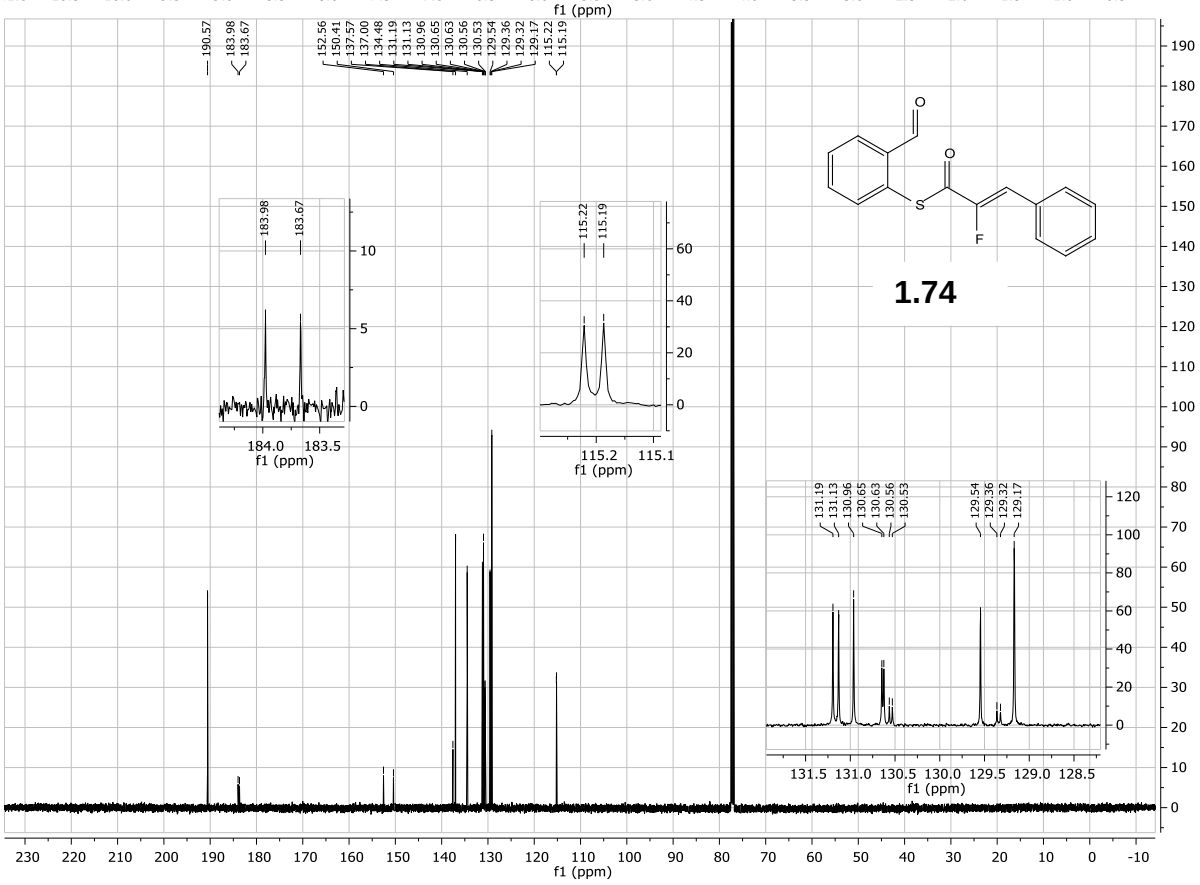
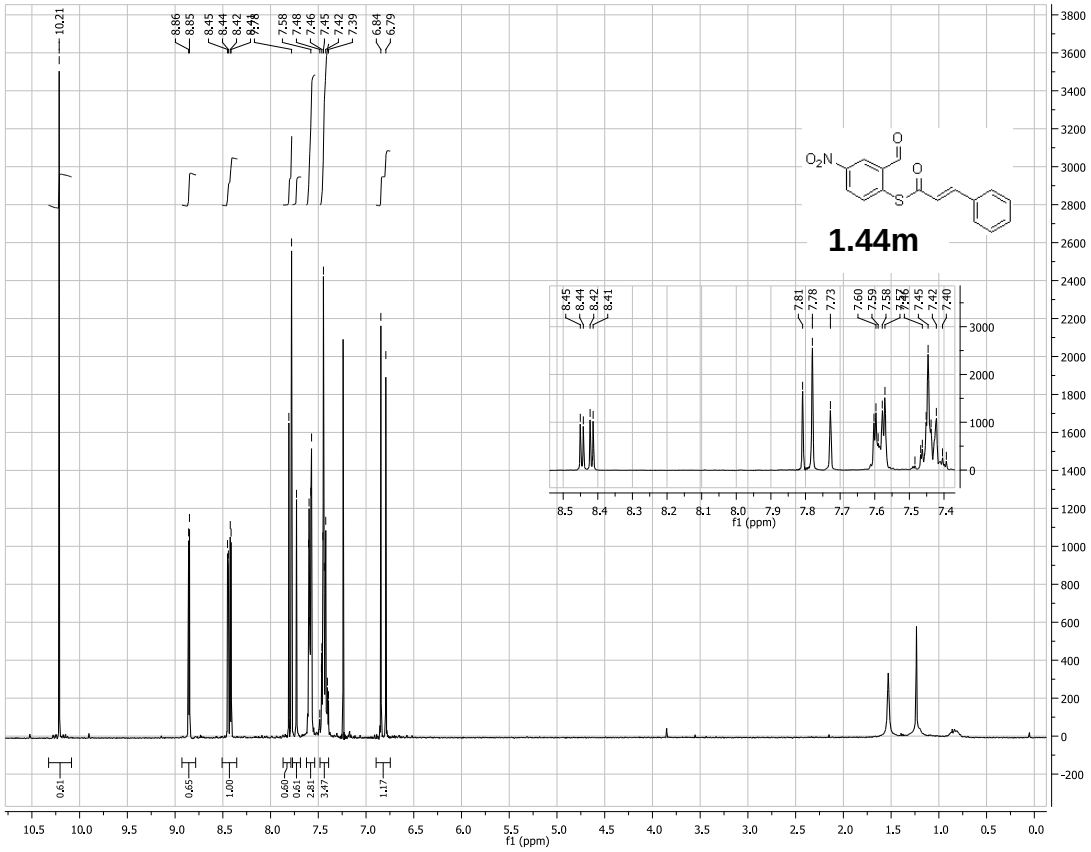
133.96
133.13
132.15
131.31
130.99
129.28
128.85
f1 (ppm)
f1 (ppm)


10.27
8.12 8.11 8.11 8.10 8.10 7.70 7.70 7.69 7.69 7.68 7.68 7.68 7.67 7.67 7.66 7.66 7.66 7.65 7.65 7.64 7.64 7.63 7.63 7.63 7.59 7.58 7.57 7.57 7.57 7.45 7.44 7.44 7.43 7.43 7.42 7.42 6.92 6.85
O
O
S
F
1.74
0.99
1.00
3.84
0.95
2.92
1.04
f1 (ppm)


190.57
183.98
183.67
152.56 150.41 137.57 137.00 134.48 131.19 131.13 130.96 130.65 130.63 130.56 130.53 129.54 129.36 129.32 129.17 115.22 115.19
O
O
S
F
1.74
f1 (ppm)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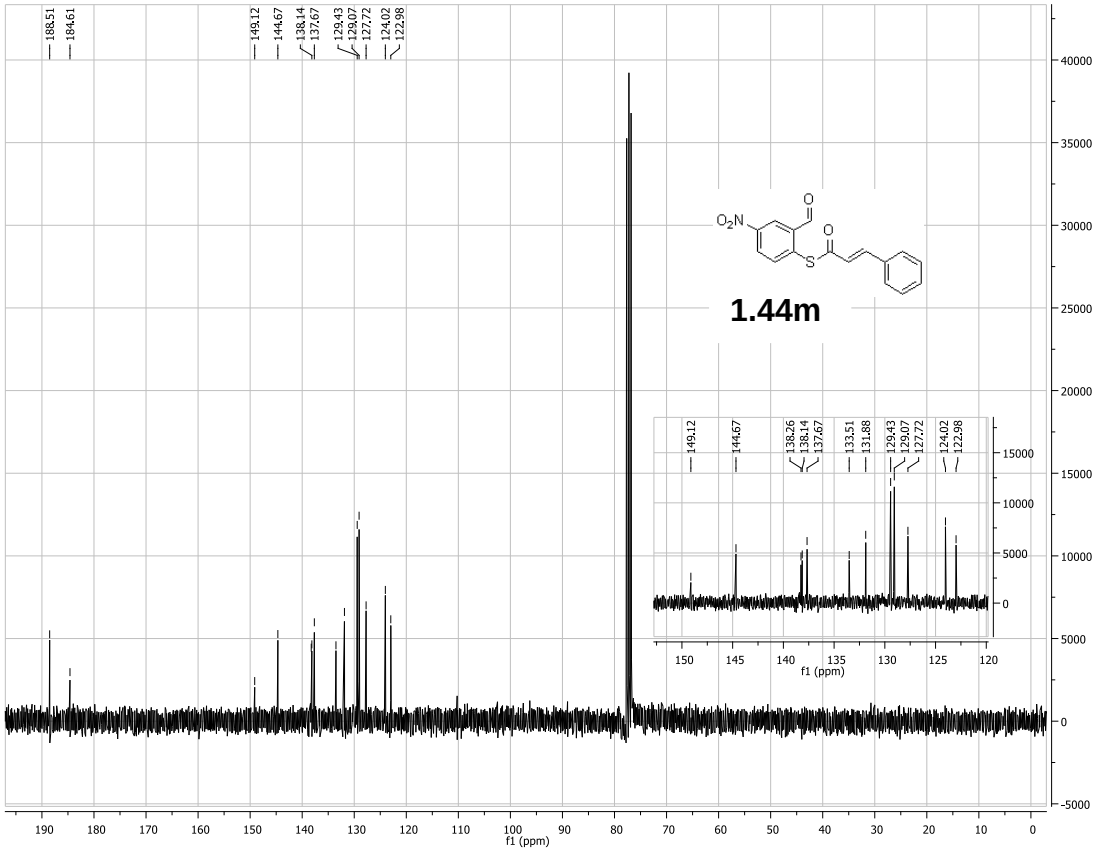
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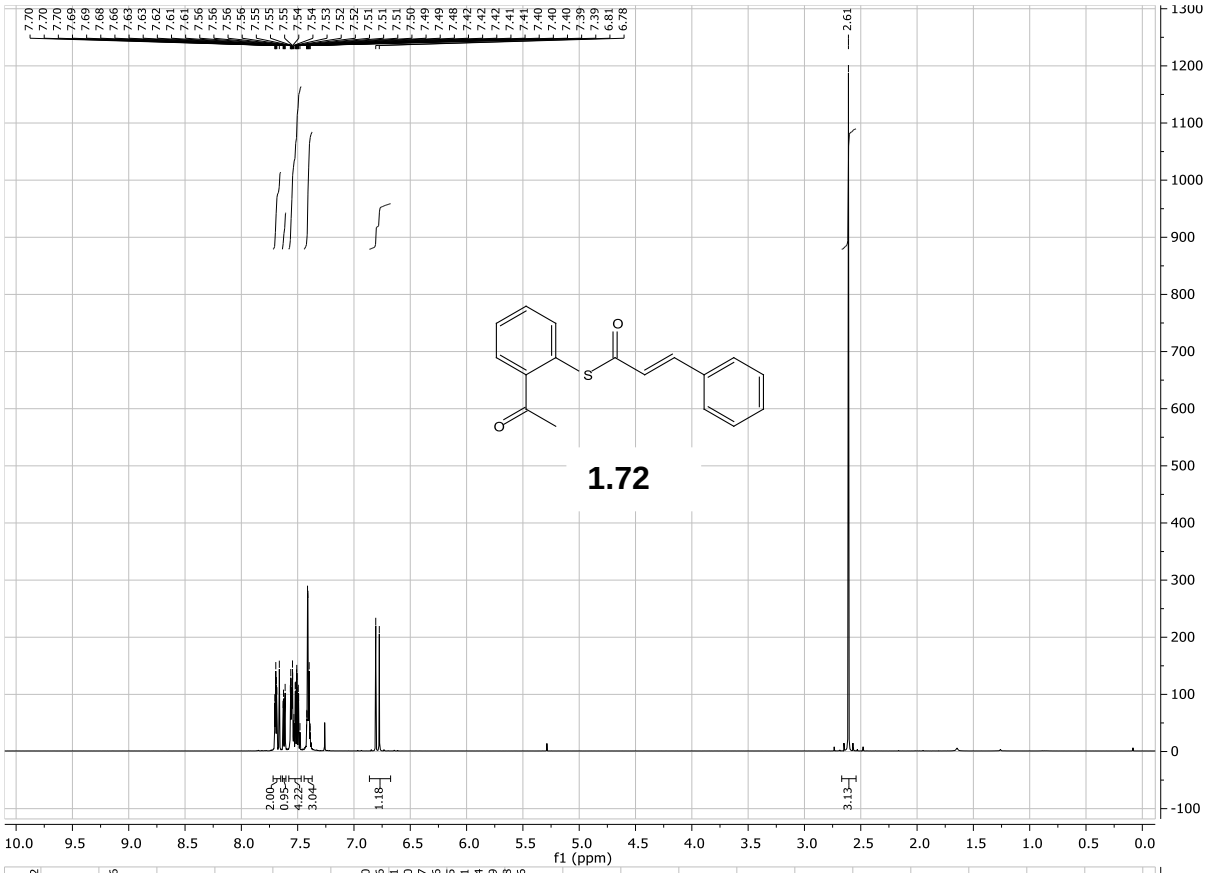
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7.42
7.42
7.41
7.41
7.40
7.40
7.40
7.39
6.81
6.78
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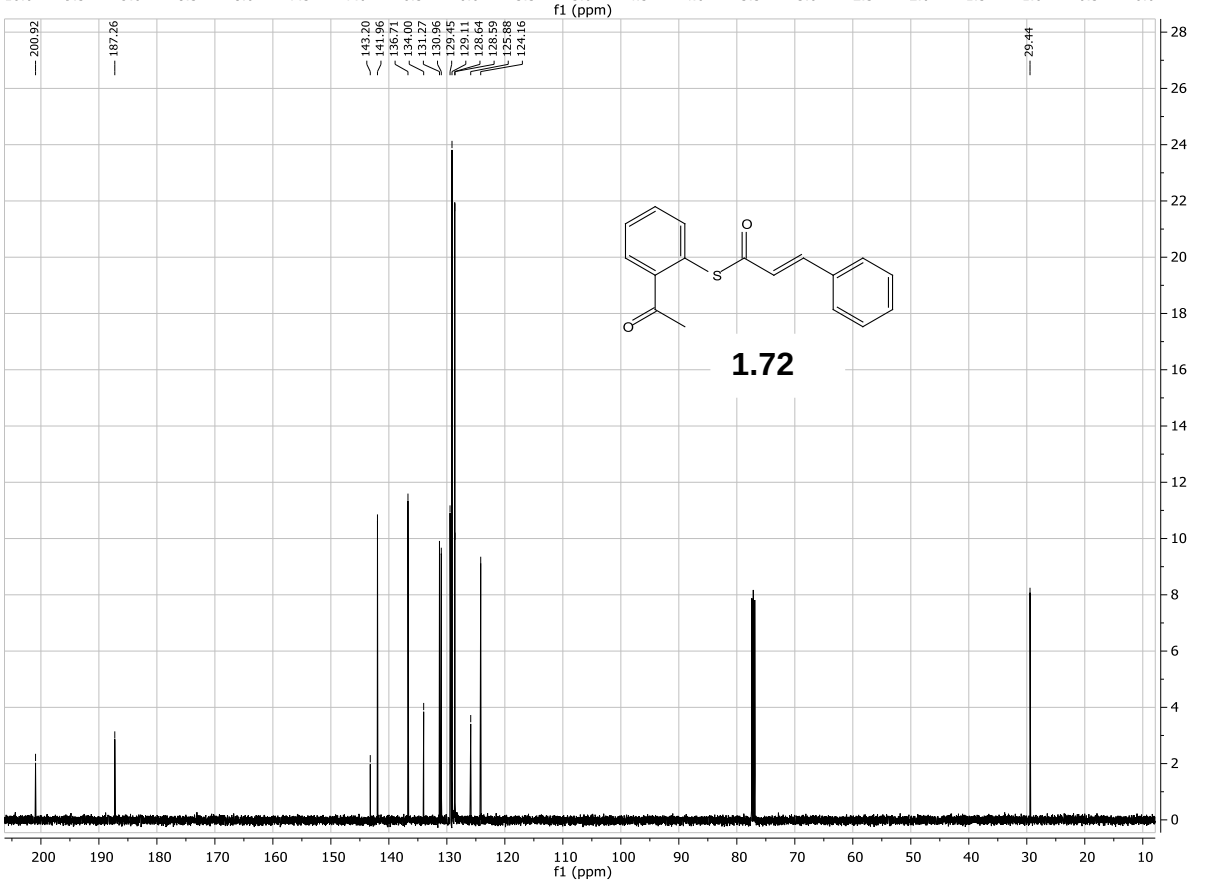
0.95
4.22
3.04
1.18
3.13
O
S
O
1.72
f1 (ppm)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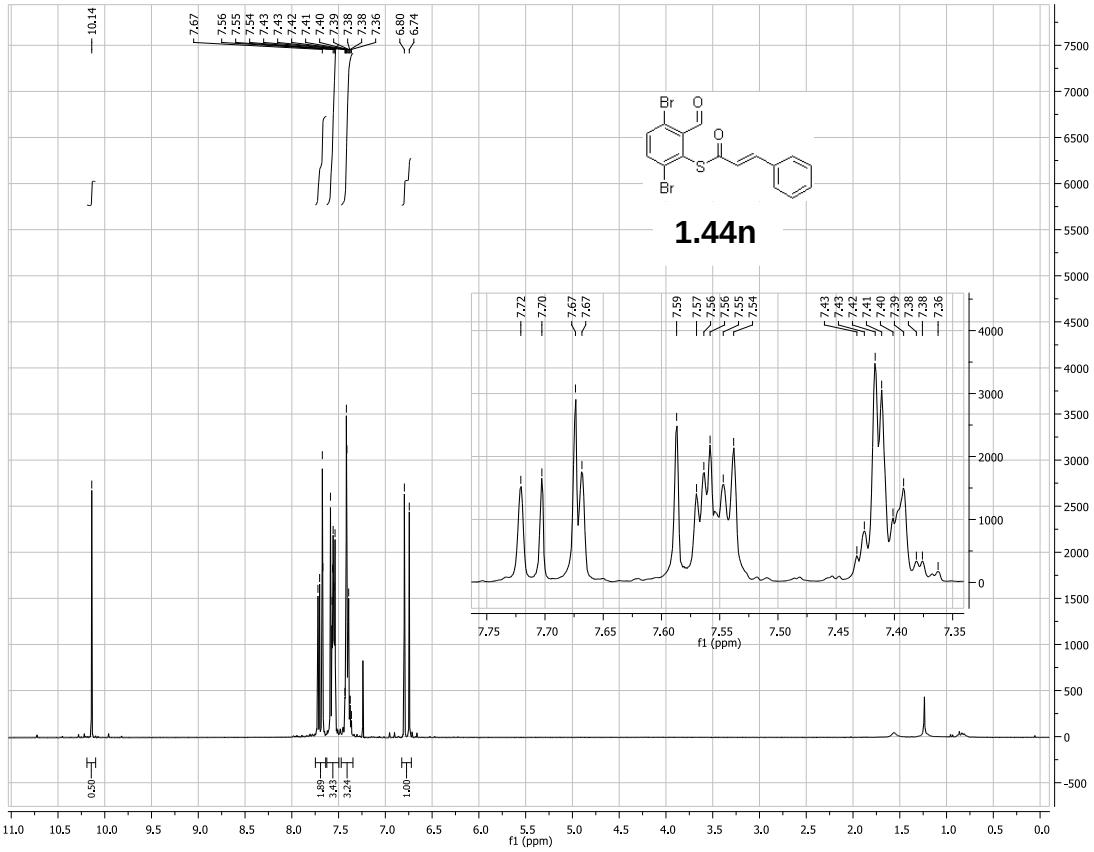
128.64
128.59
125.88
124.16
29.44
O
S
O
1.72
f1 (ppm)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7.39
7.38
7.38
7.36
6.80
6.74
Br
O
O
S
Br
1.44n
7.72
7.70
7.67
7.67
7.59
7.57
7.56
7.56
7.55
7.54
7.43
7.43
7.42
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7.40
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7.38
7.38
7.36
0.50
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3.43
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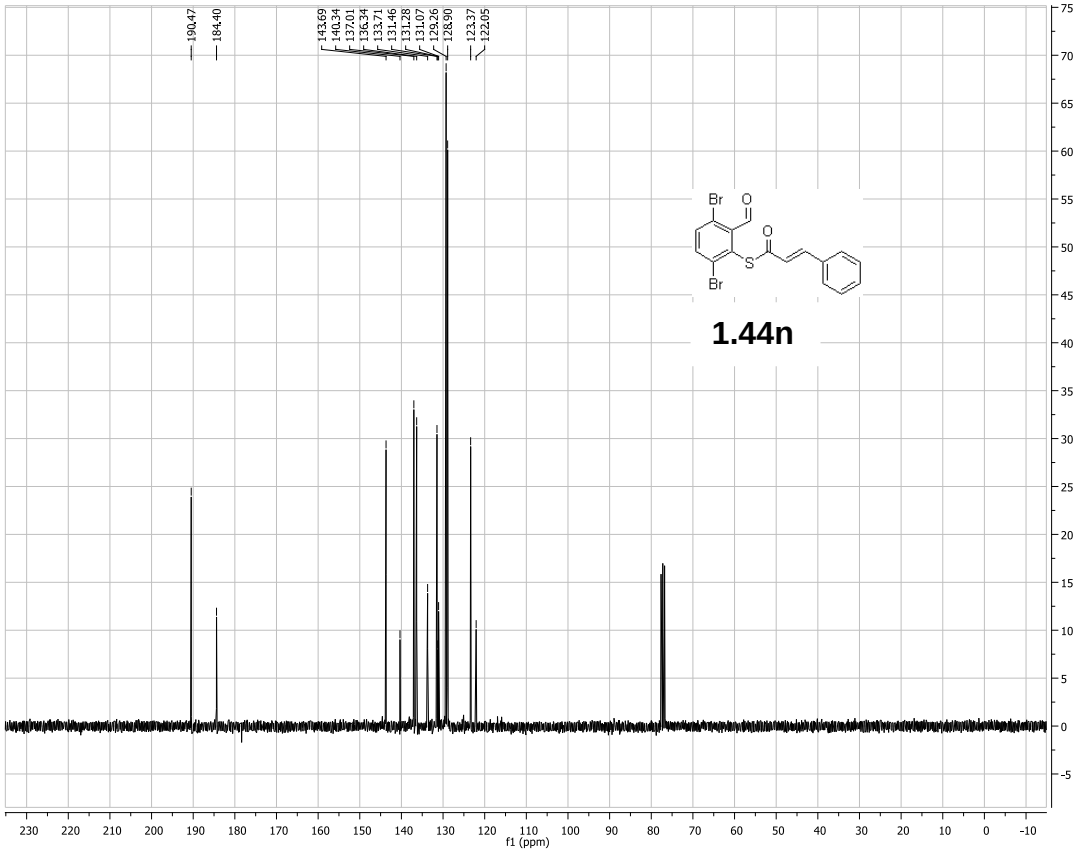
1.00
f1 (ppm)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136.34
133.71
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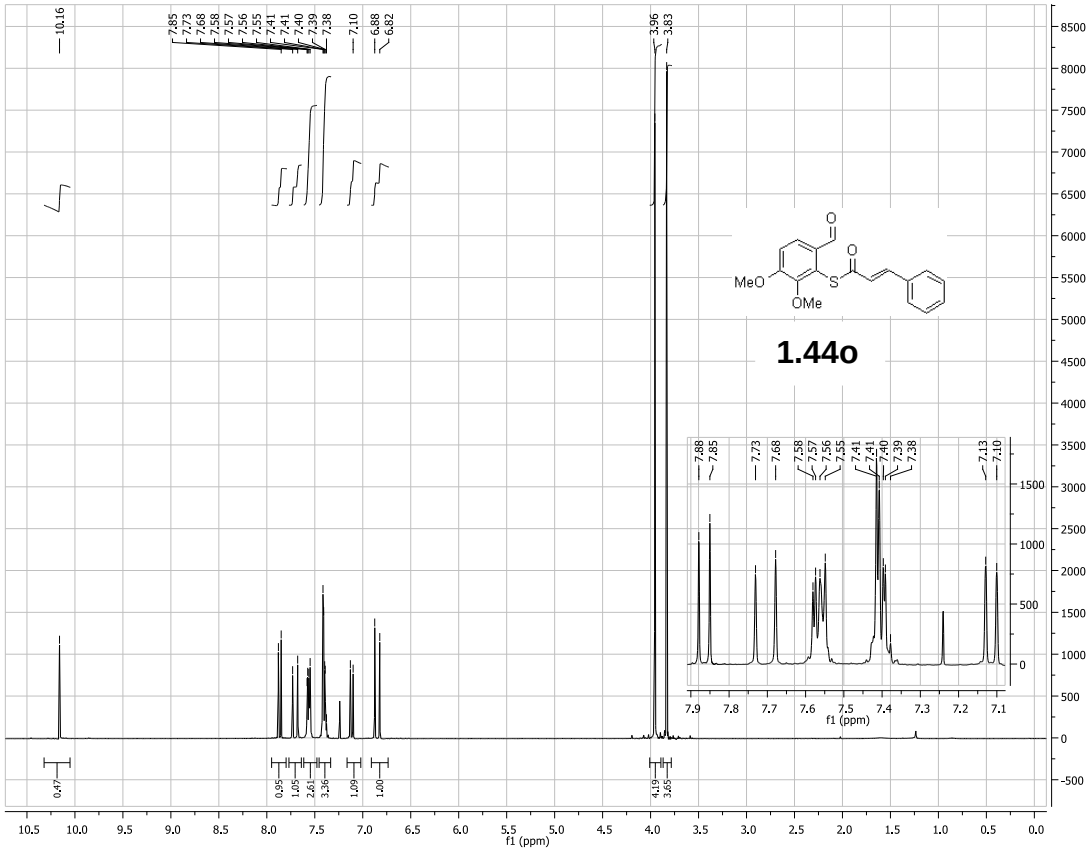
128.90
123.37
122.05
Br
O
O
S
Br
1.44n
f1 (ppm)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7.55
7.41
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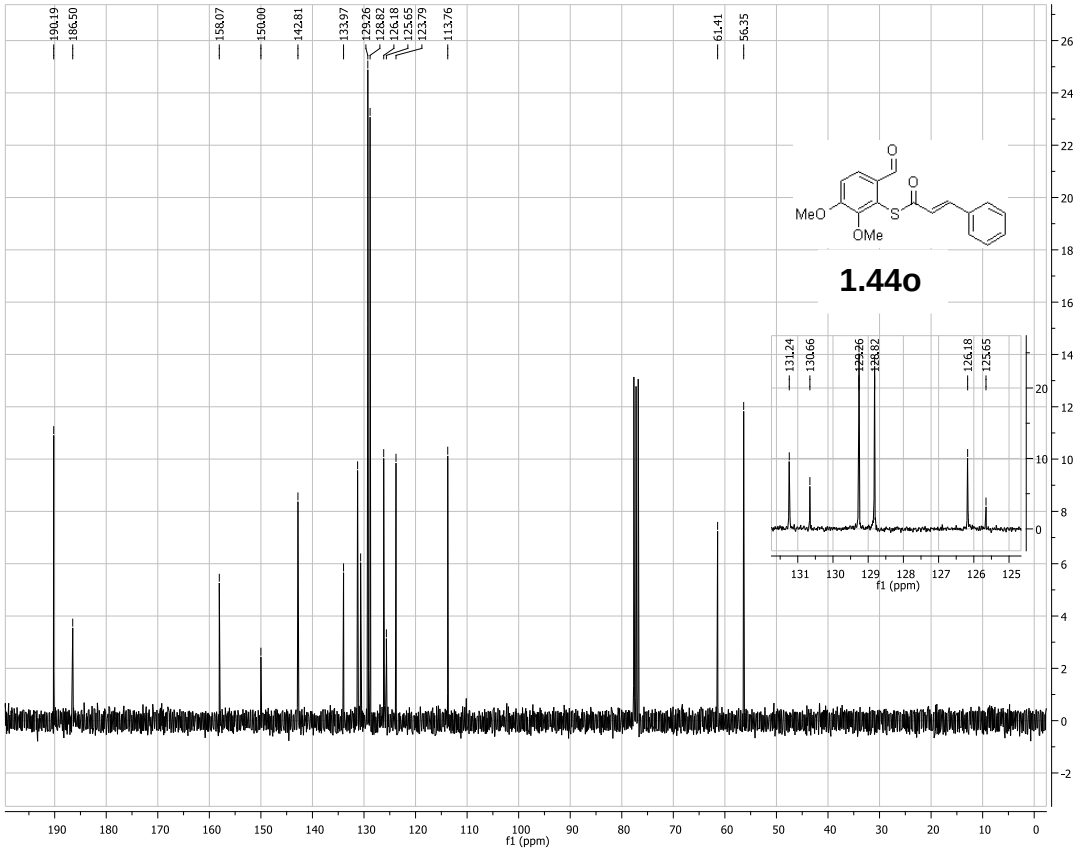
7.10
6.88
6.82
3.96
3.83
MeO
OMe
1.44o
f1 (ppm)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125.65
123.79
113.76
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OMe
1.44o
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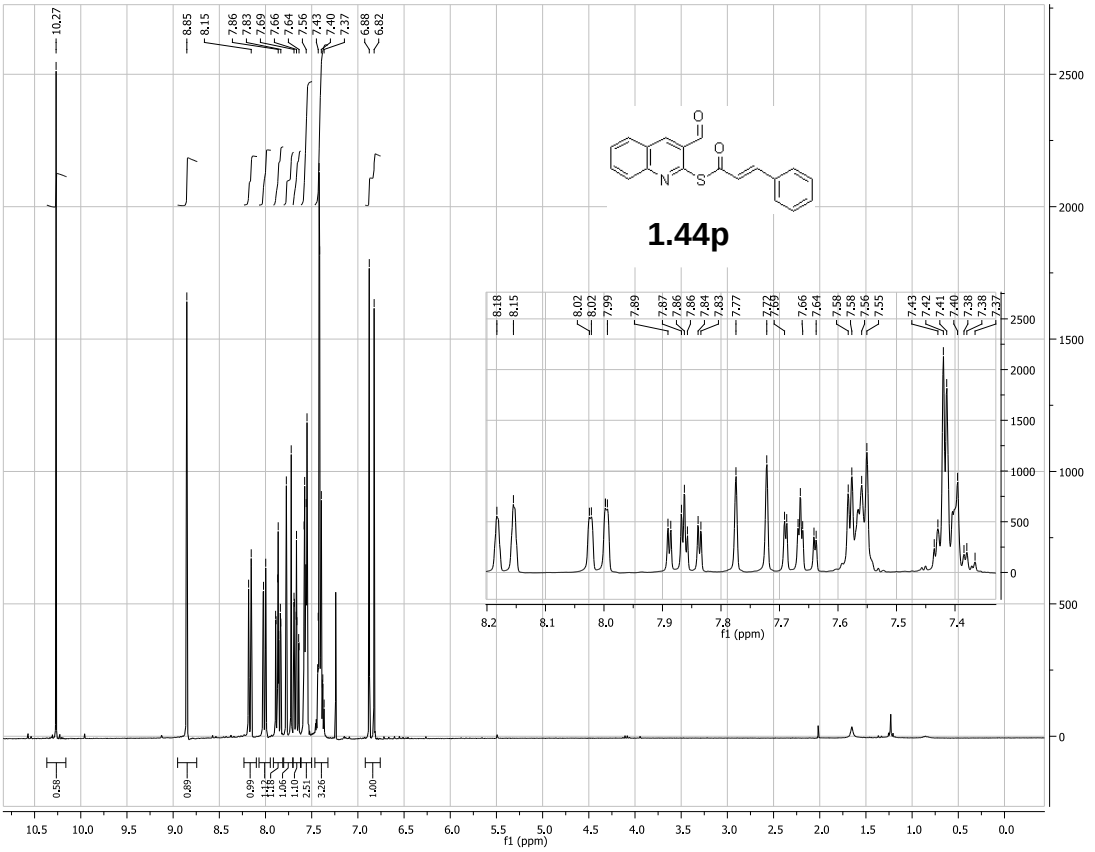
130.66
129.36
128.82
126.18
125.65
f1 (ppm)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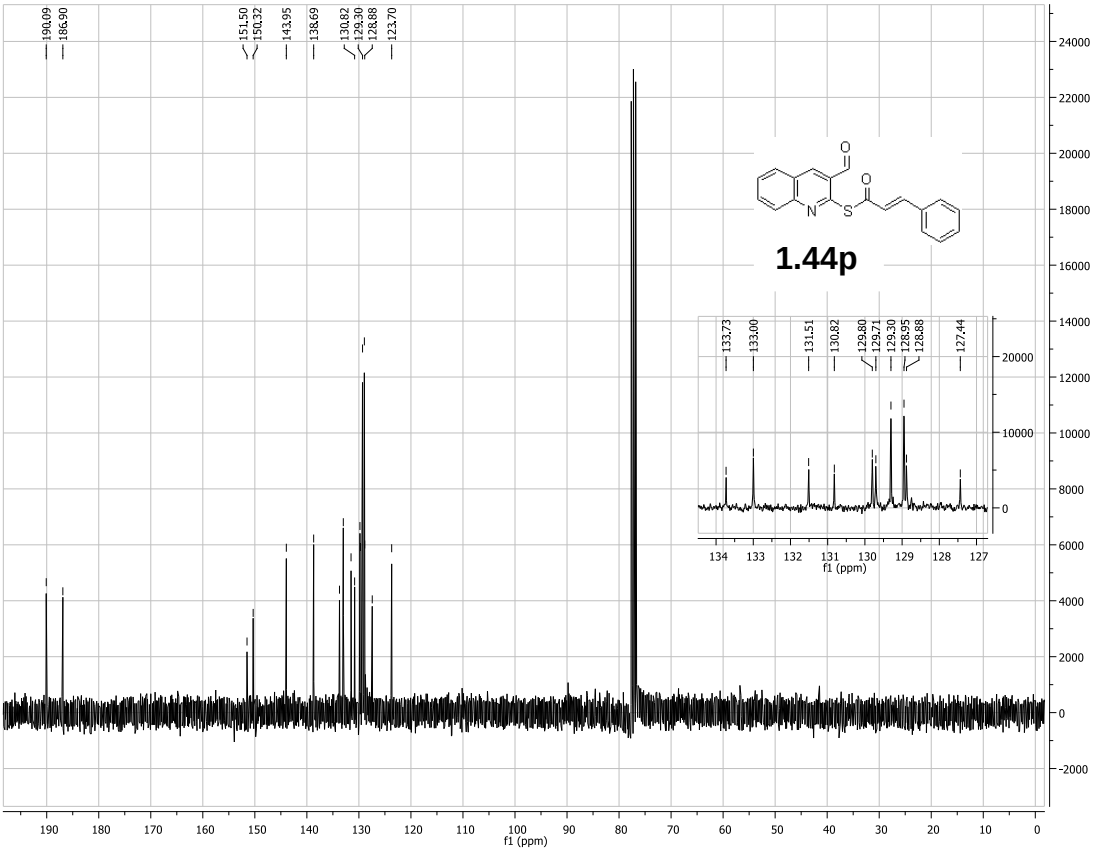
7.56
7.43
7.40
7.37
6.88
6.82
1.44p
f1 (ppm)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143.95
138.69
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128.88
123.70
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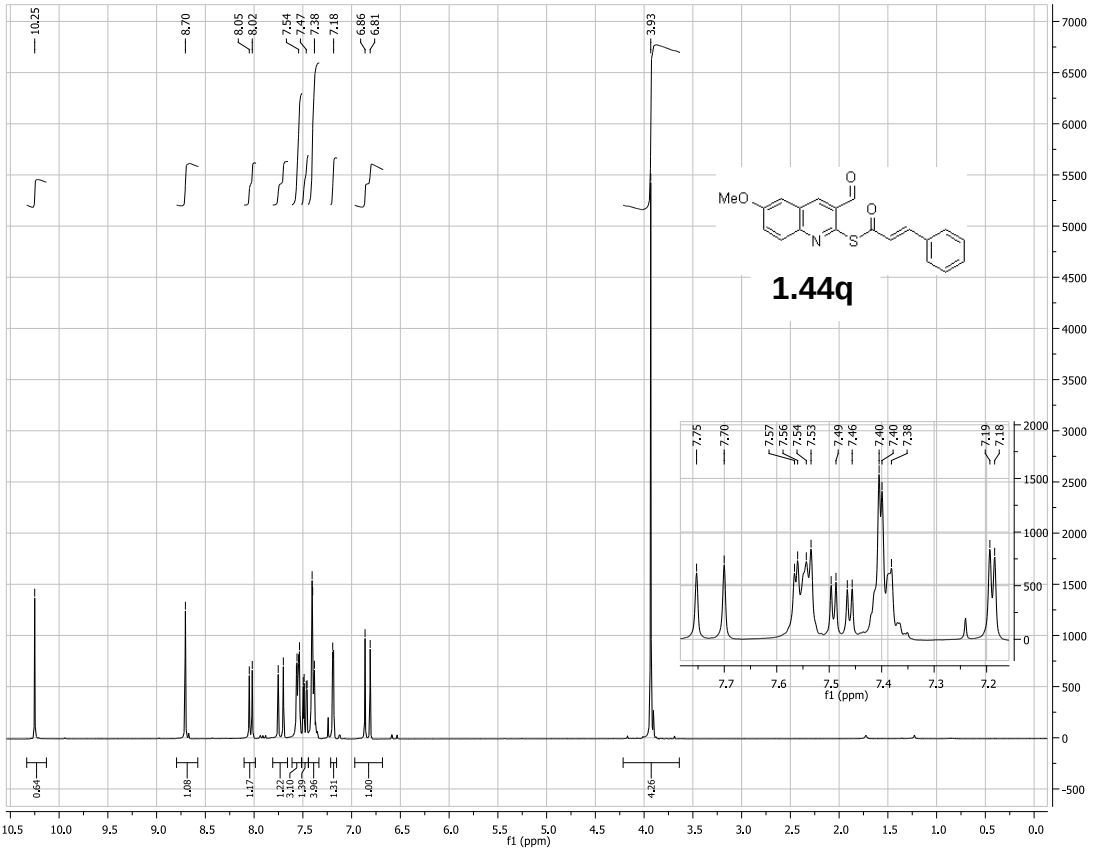
131.51
130.82
129.80
129.71
129.30
128.95
128.88
127.44
f1 (ppm)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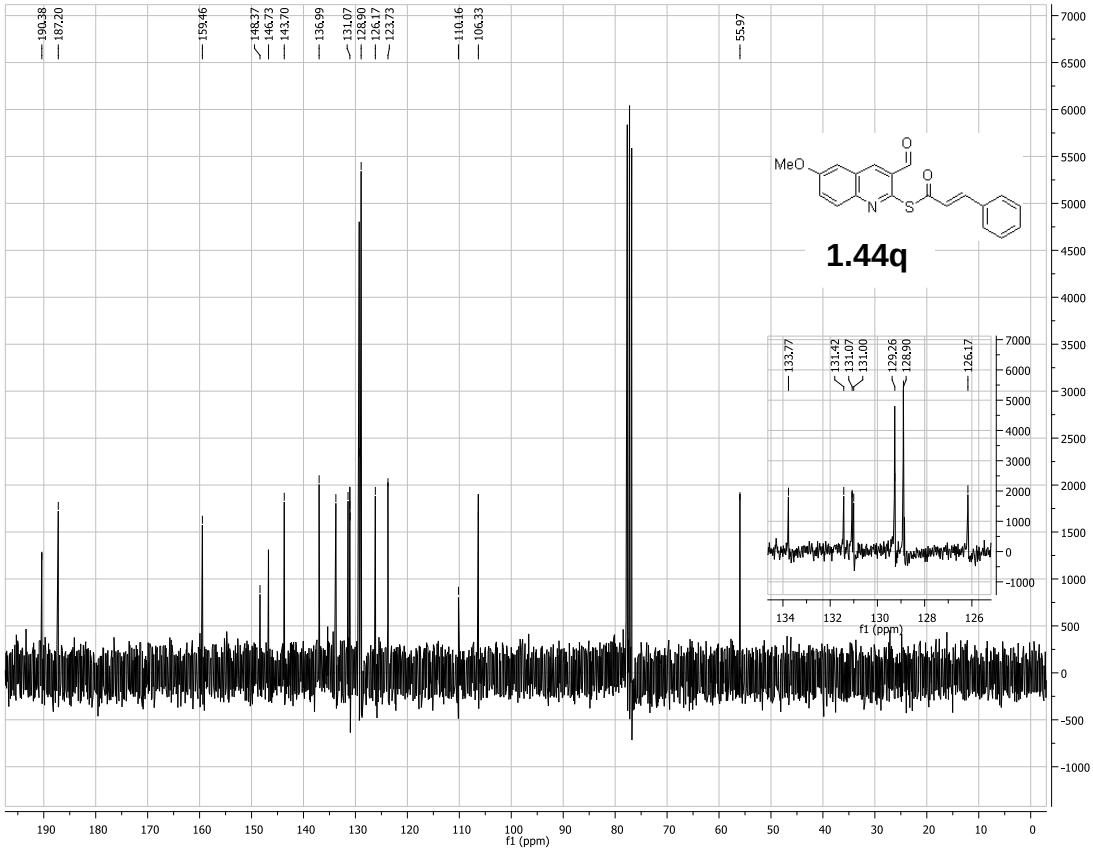
8.02
7.54
7.47
7.38
7.18
6.86
6.81
3.93
MeO
O
N
S
O
1.44q
7.75
7.70
7.57
7.56
7.54
7.53
7.49
7.46
7.40
7.40
7.38
7.19
7.18
f1 (ppm)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110.16
106.33
55.97
MeO
O
N
S
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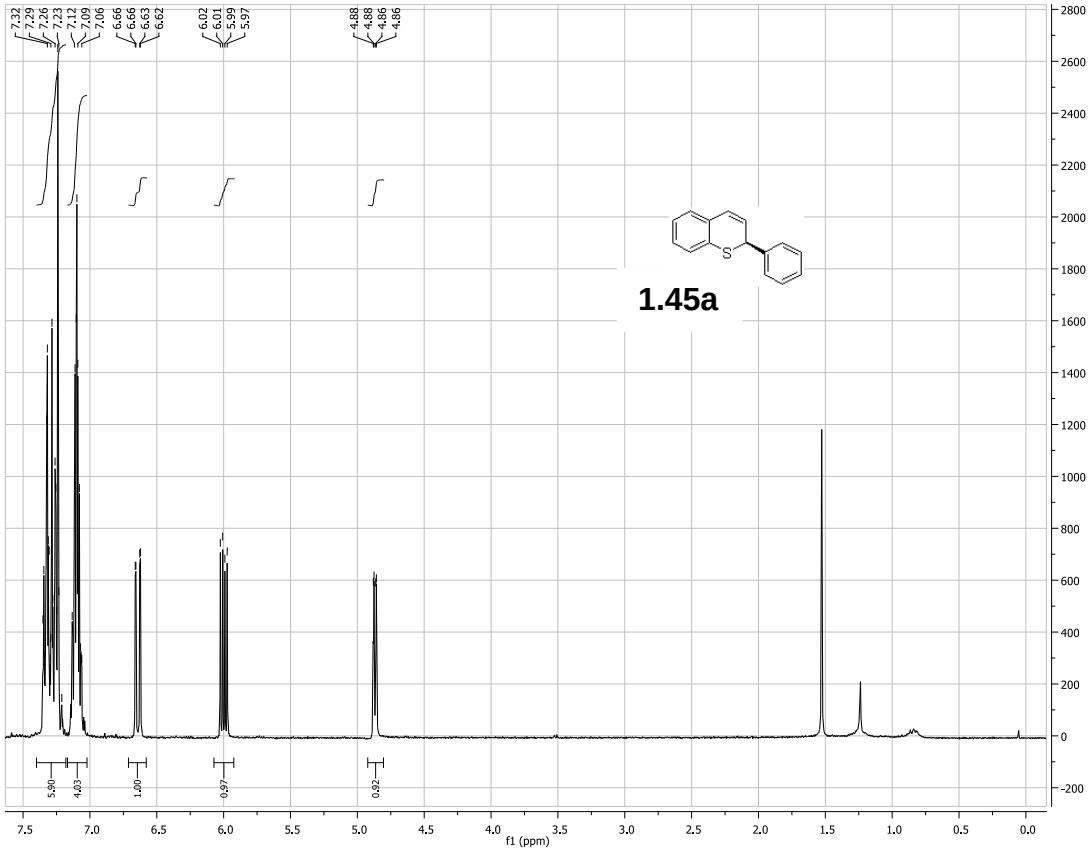
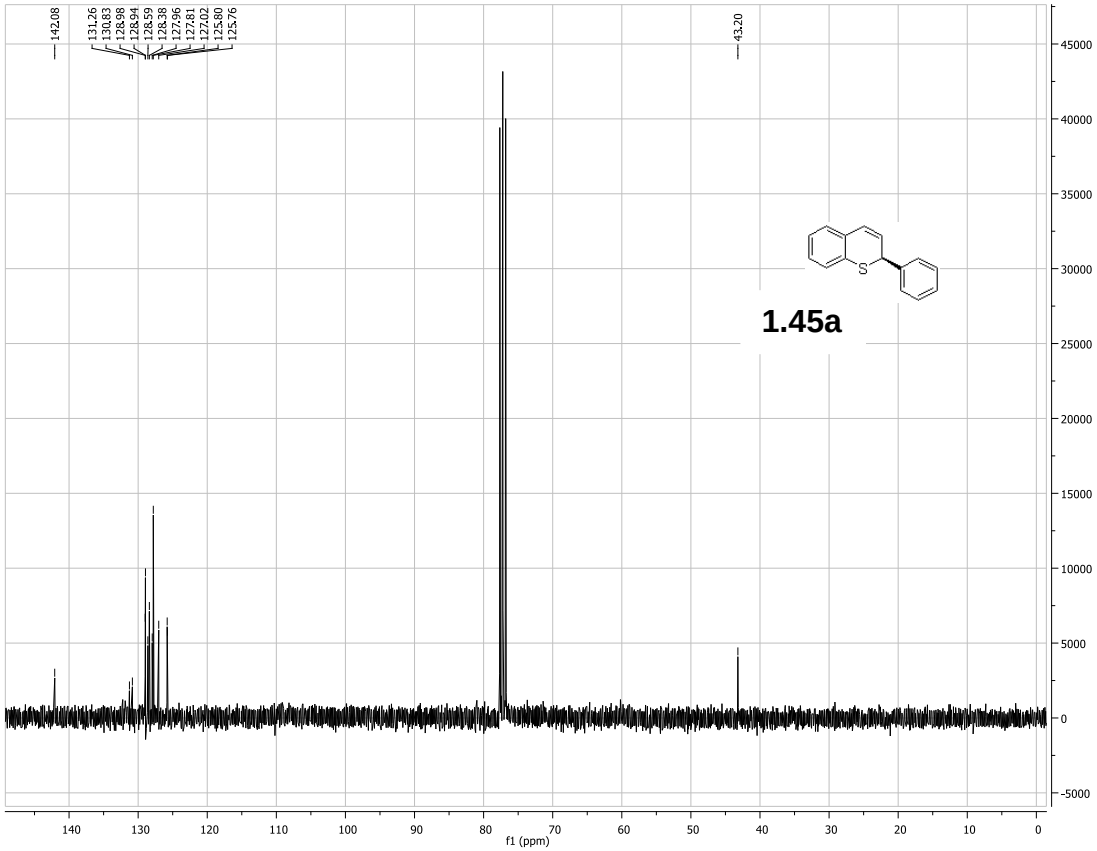
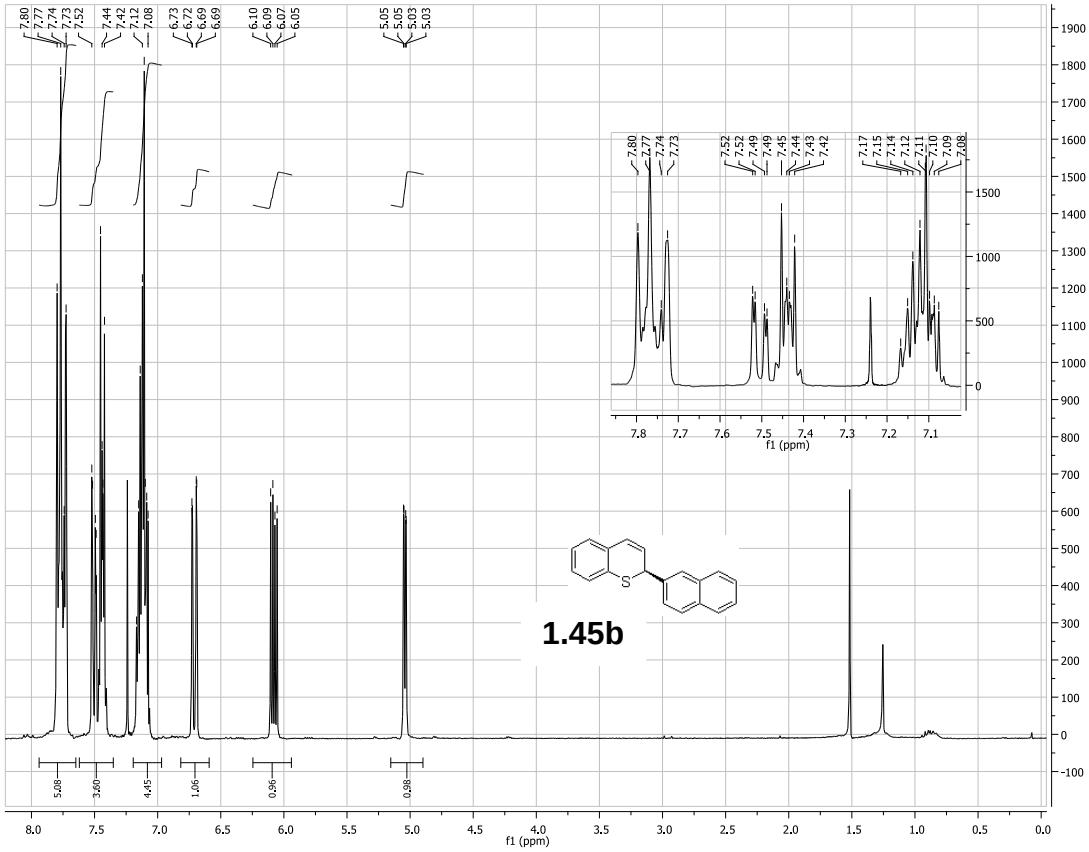
1.44q
133.77
131.42
131.07
131.00
129.26
128.90
126.17
f1 (ppm)


7.32
7.29
7.26
7.23
7.12
7.09
7.06
6.66
6.66
6.63
6.62
6.02
6.01
5.99
5.97
4.88
4.88
4.86
4.86
5.90
4.03
1.00
0.97
0.92
1.45a
f1 (ppm)


142.08
131.26
130.83
128.98
128.94
128.59
128.38
127.96
127.81
127.02
125.80
125.76
43.20
1.45a
f1 (ppm)


7.80
7.77
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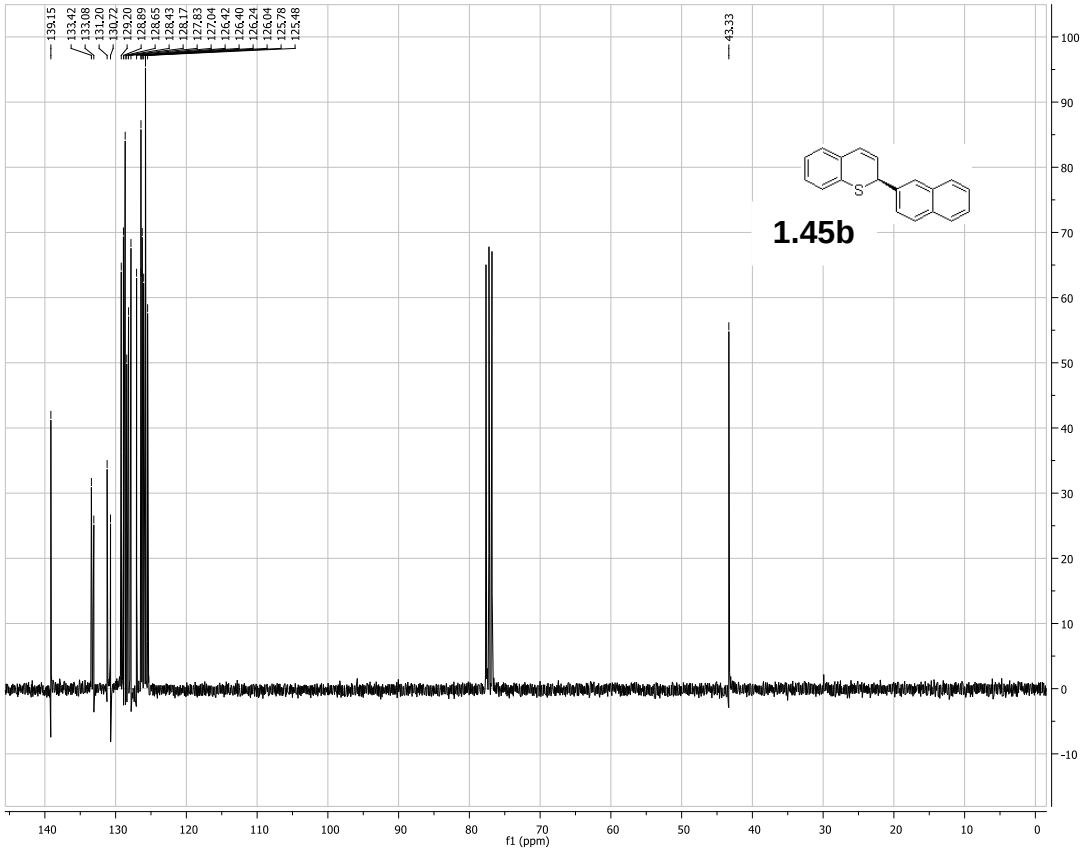
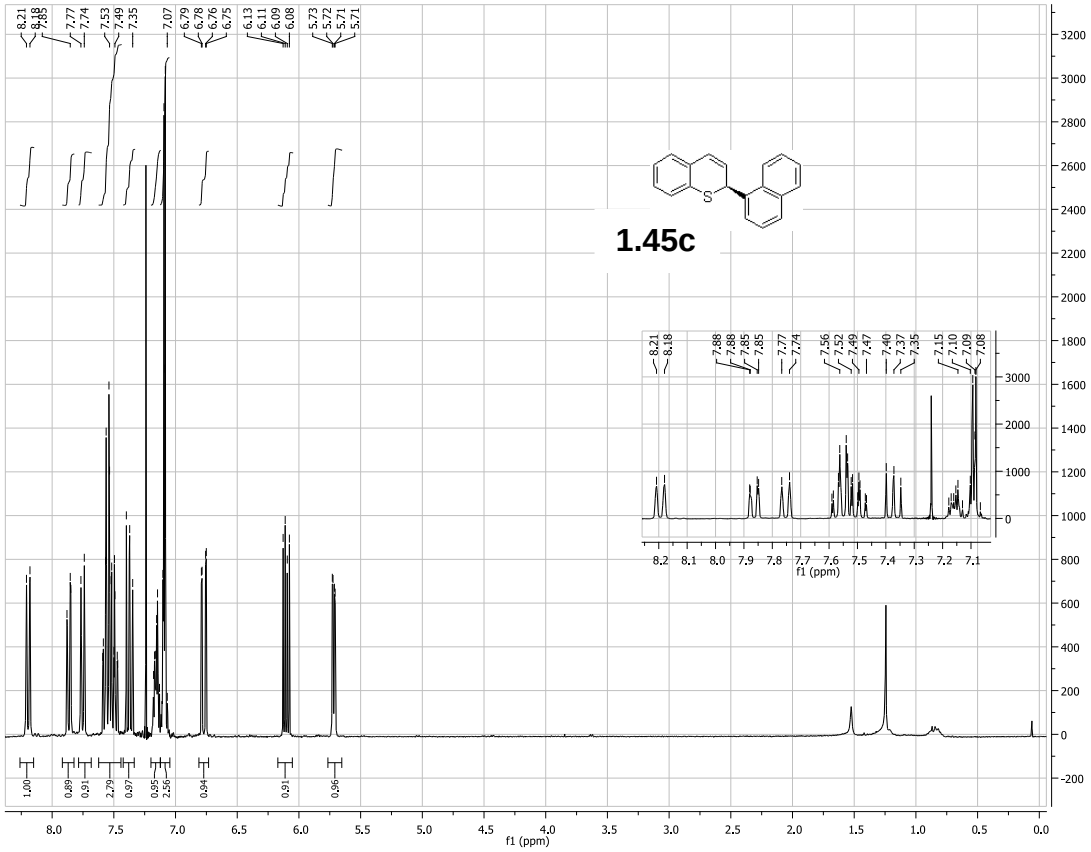
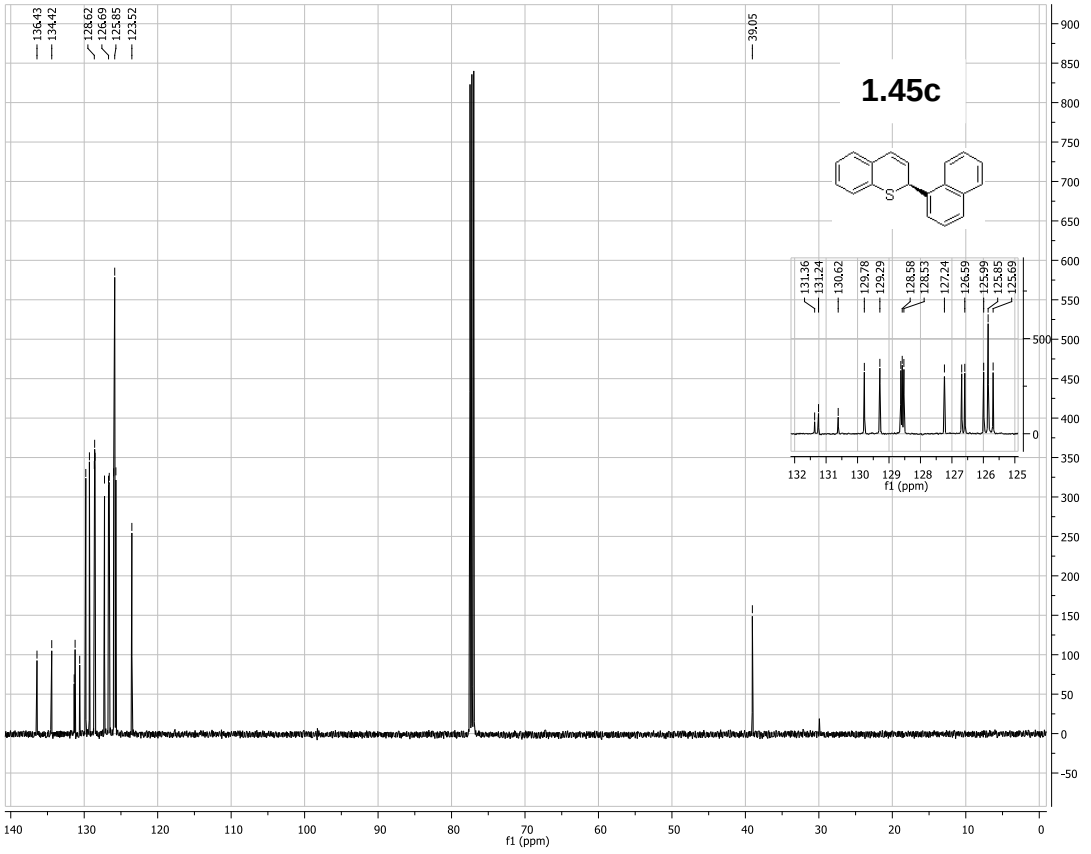
7.73
7.52
7.44
7.42
7.12
7.08
6.73
6.72
6.69
6.69
6.10
6.09
6.07
6.05
5.05
5.05
5.03
5.03
5.08
3.60
4.45
1.06
0.96
0.98
f1 (ppm)
1.45b


139.15
133.42
133.08
131.20
130.72
129.20
128.89
128.65
128.43
128.17
127.83
127.04
126.42
126.40
126.24
126.04
125.78
125.48
43.33
f1 (ppm)
1.45b


1.45c
f1 (ppm)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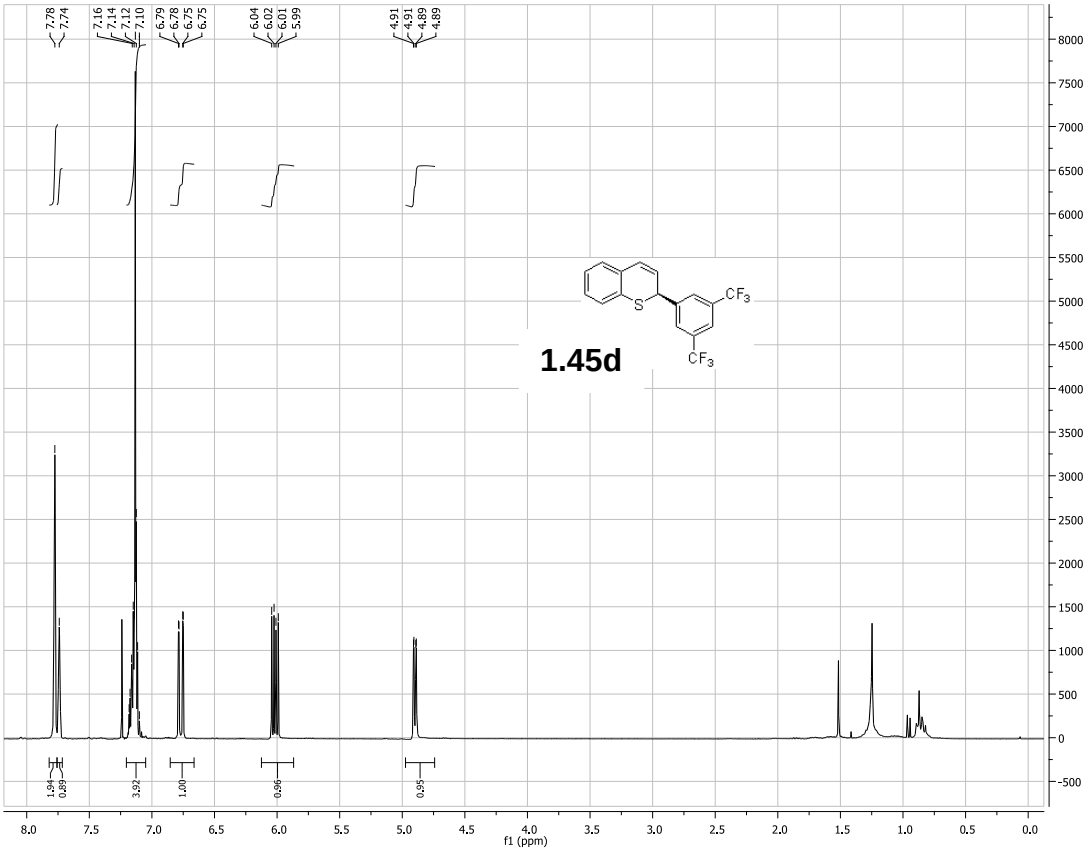
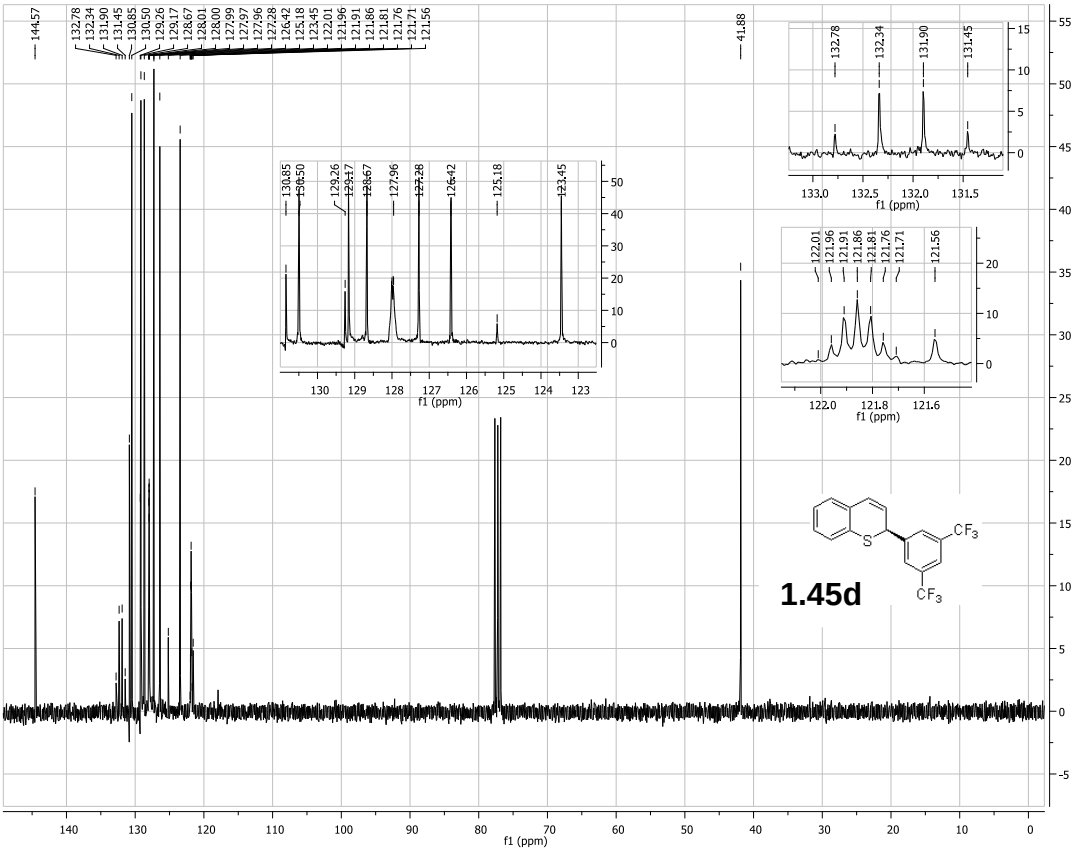
f1 (ppm)


7.78
7.74
7.16
7.14
7.12
7.10
6.79
6.78
6.75
6.75
6.04
6.02
6.01
5.99
4.91
4.91
4.89
4.89
1.94
0.89
3.92
1.00
0.96
0.95
f1 (ppm)
CF3
CF3
1.45d


144.57
132.78
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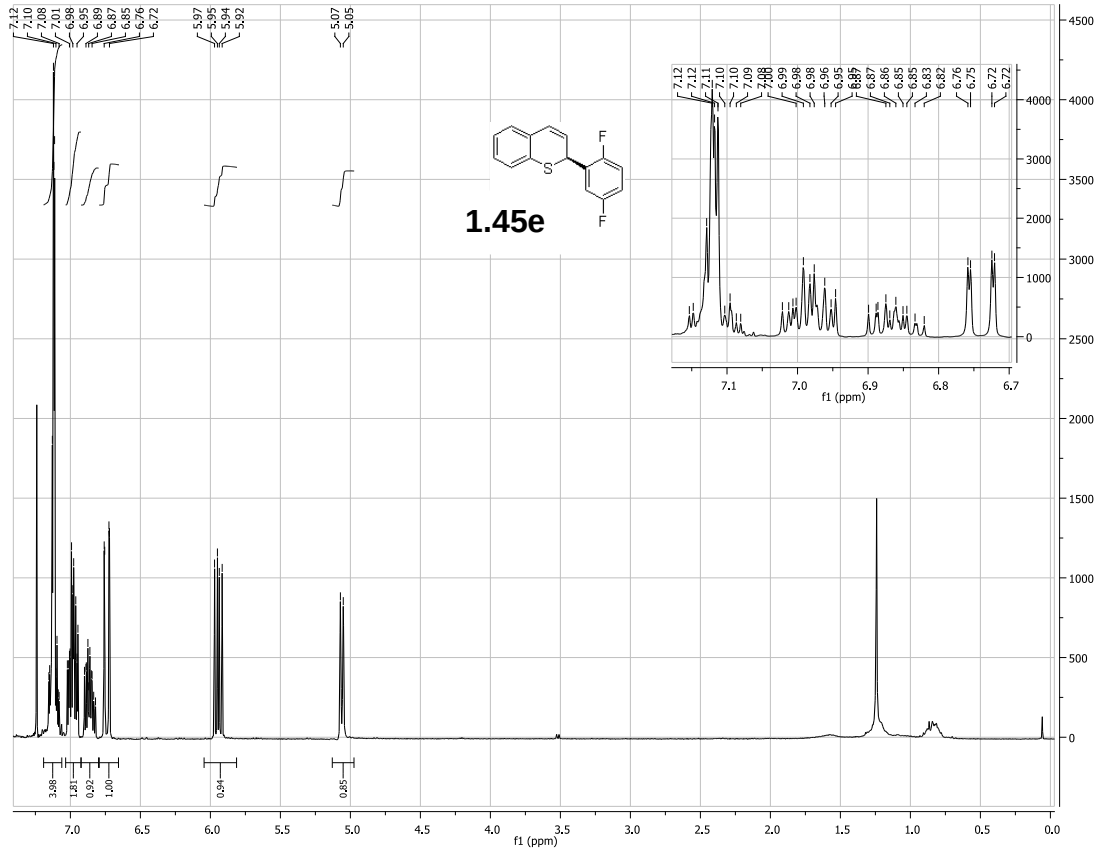
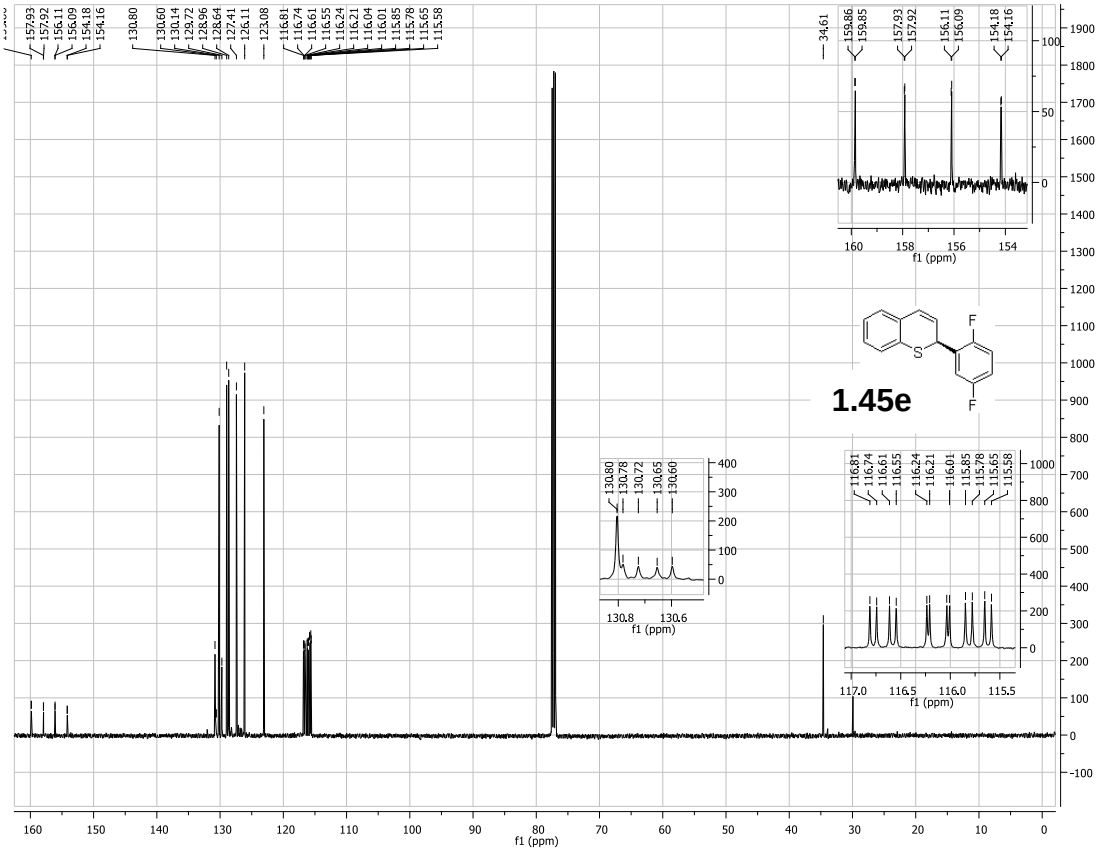
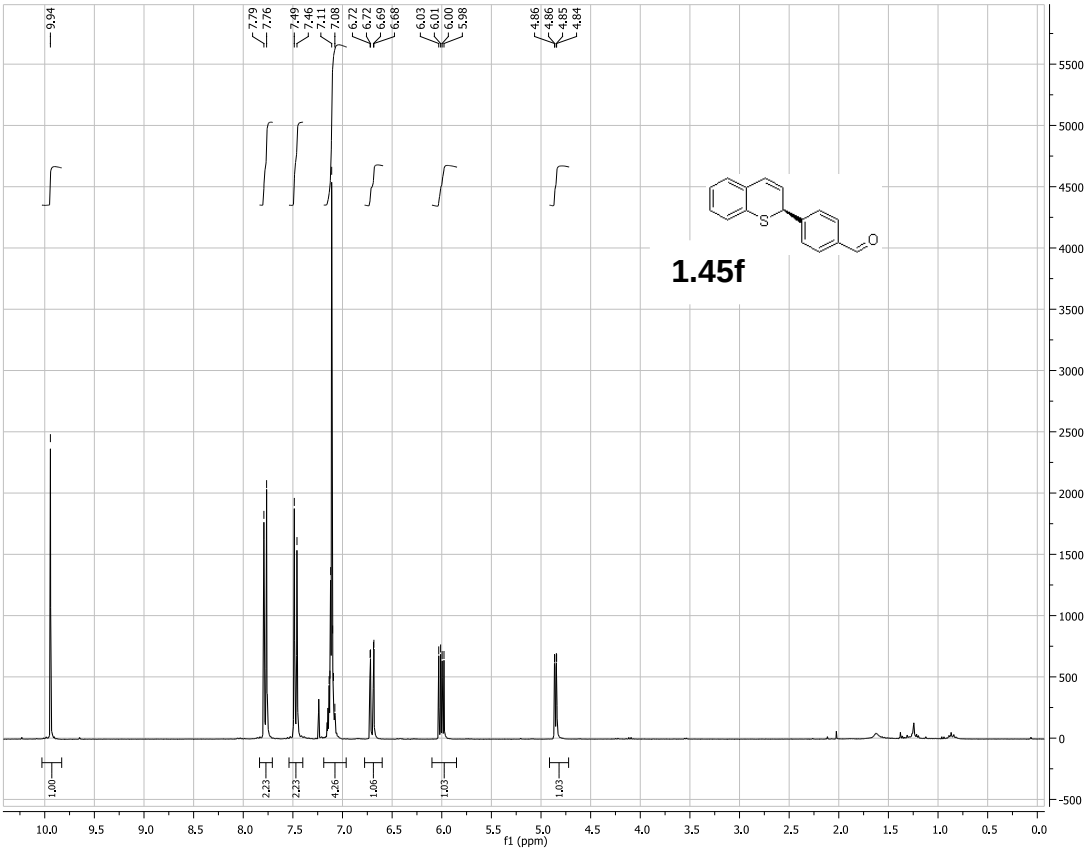
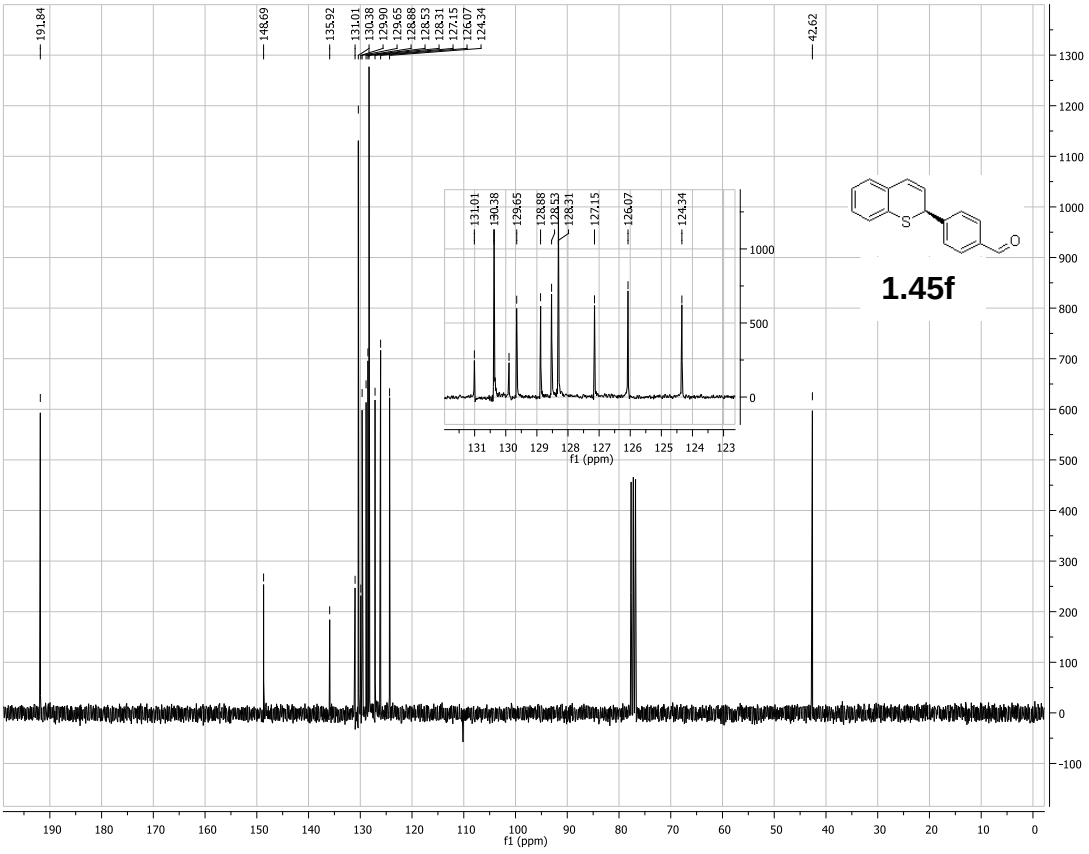
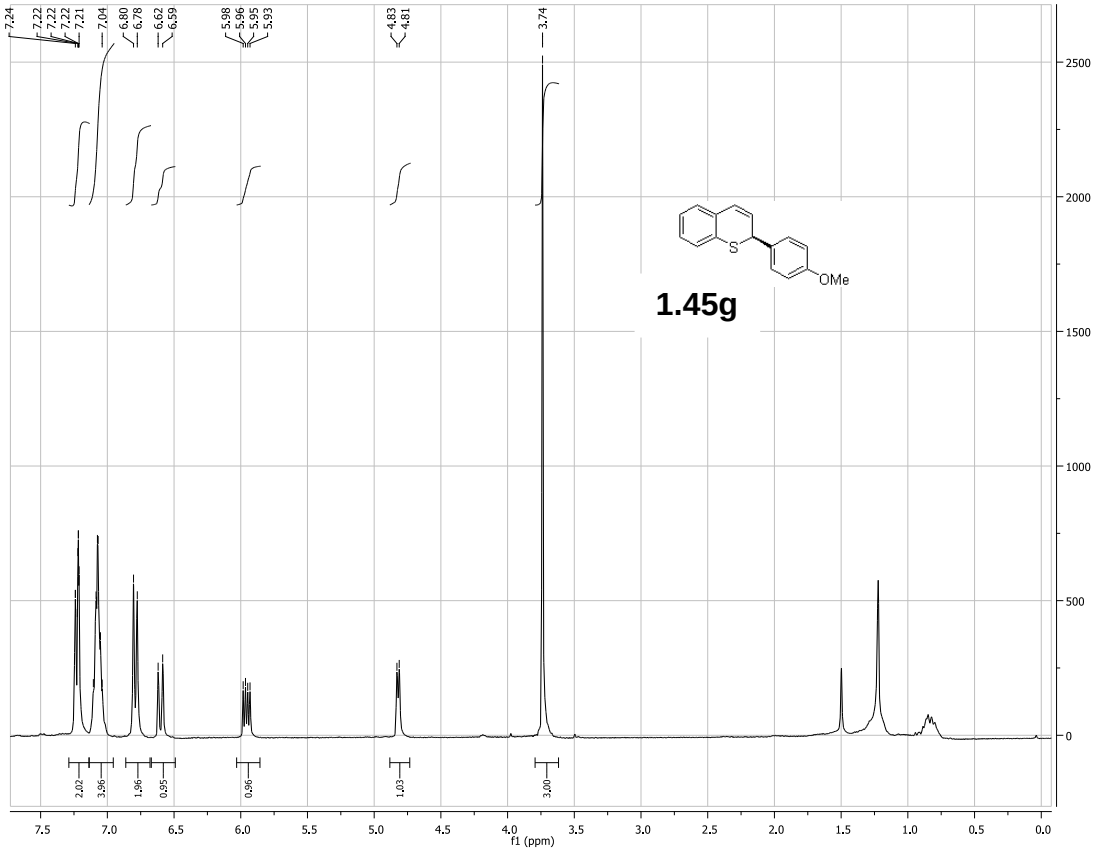
131.90
131.45
130.85
130.50
129.26
129.17
128.67
128.01
128.00
127.99
127.97
127.96
127.28
126.42
125.18
123.45
122.01
121.96
121.91
121.86
121.81
121.76
121.71
121.56
41.88
f1 (ppm)
CF3
CF3
1.45d

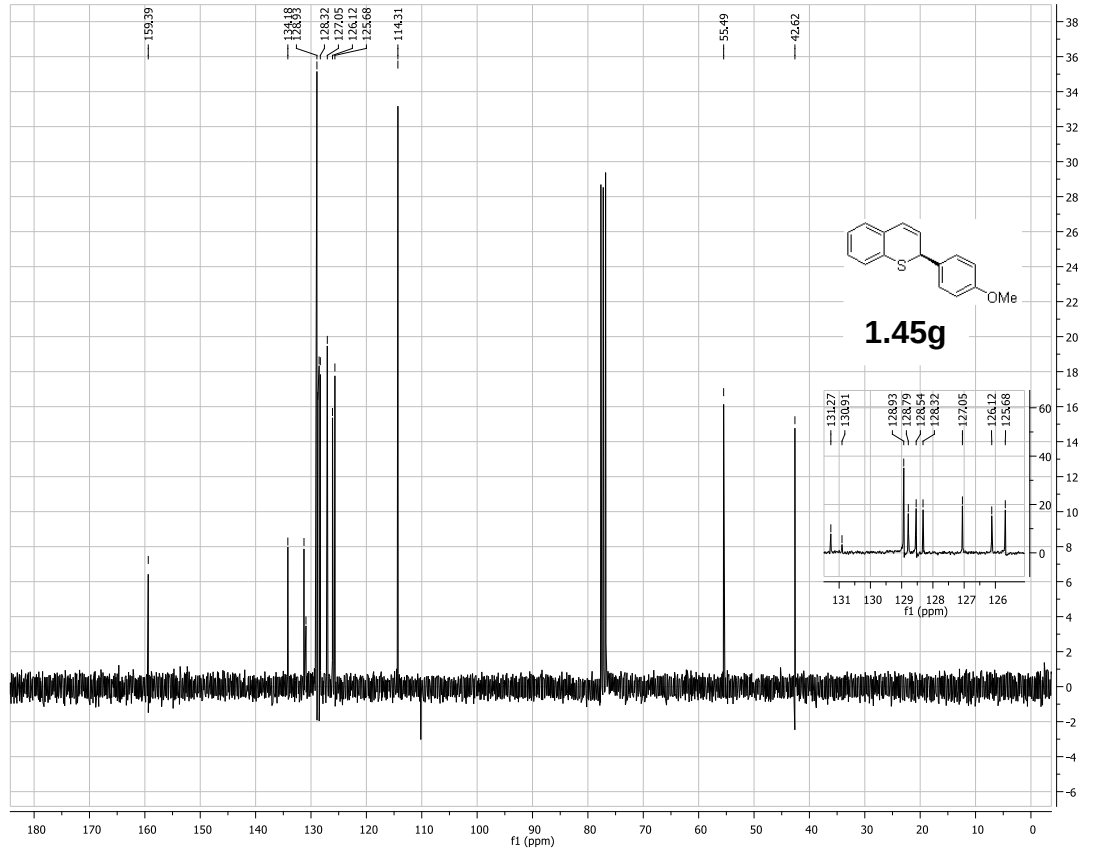

1.45e
f1 (ppm)

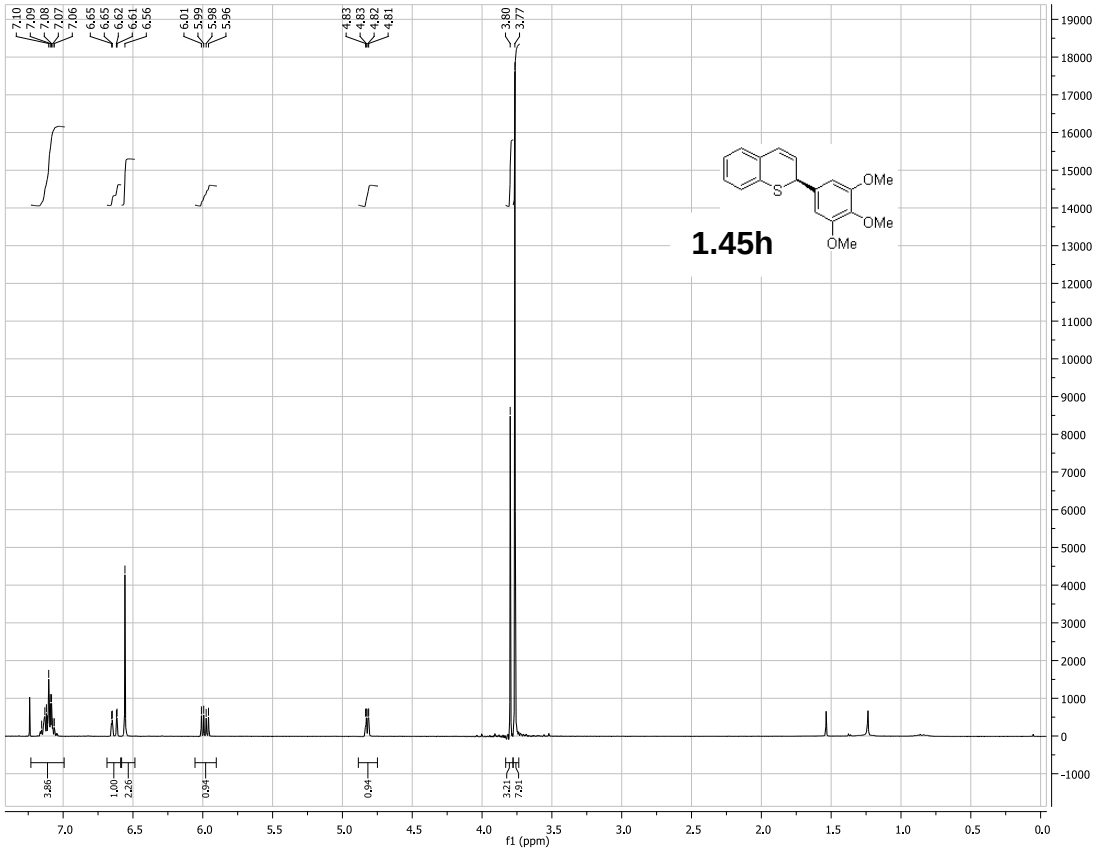

1.45e
f1 (ppm)

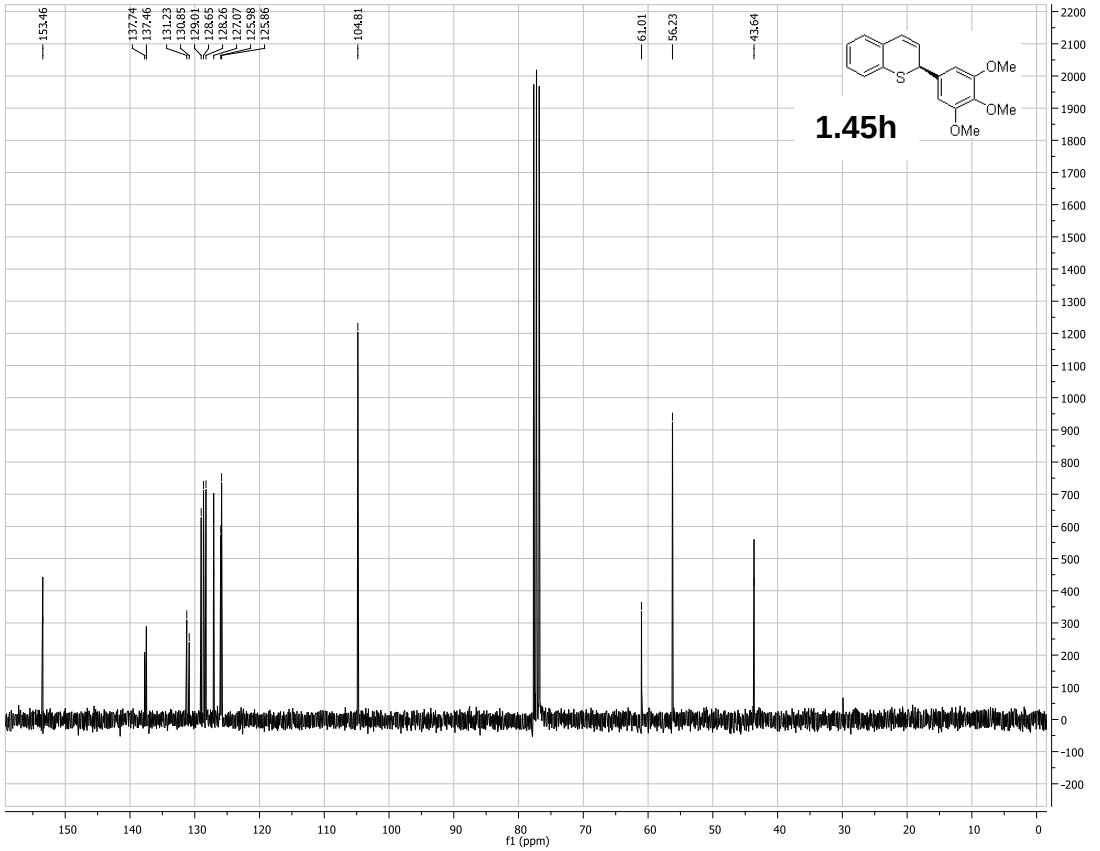

9.94
7.79
7.76
7.49
7.46
7.11
7.08
6.72
6.72
6.69
6.68
6.03
6.01
6.00
5.98
4.86
4.86
4.85
4.84
1.00
2.23
2.23
4.26
1.06
1.03
1.03
f1 (ppm)
1.45f

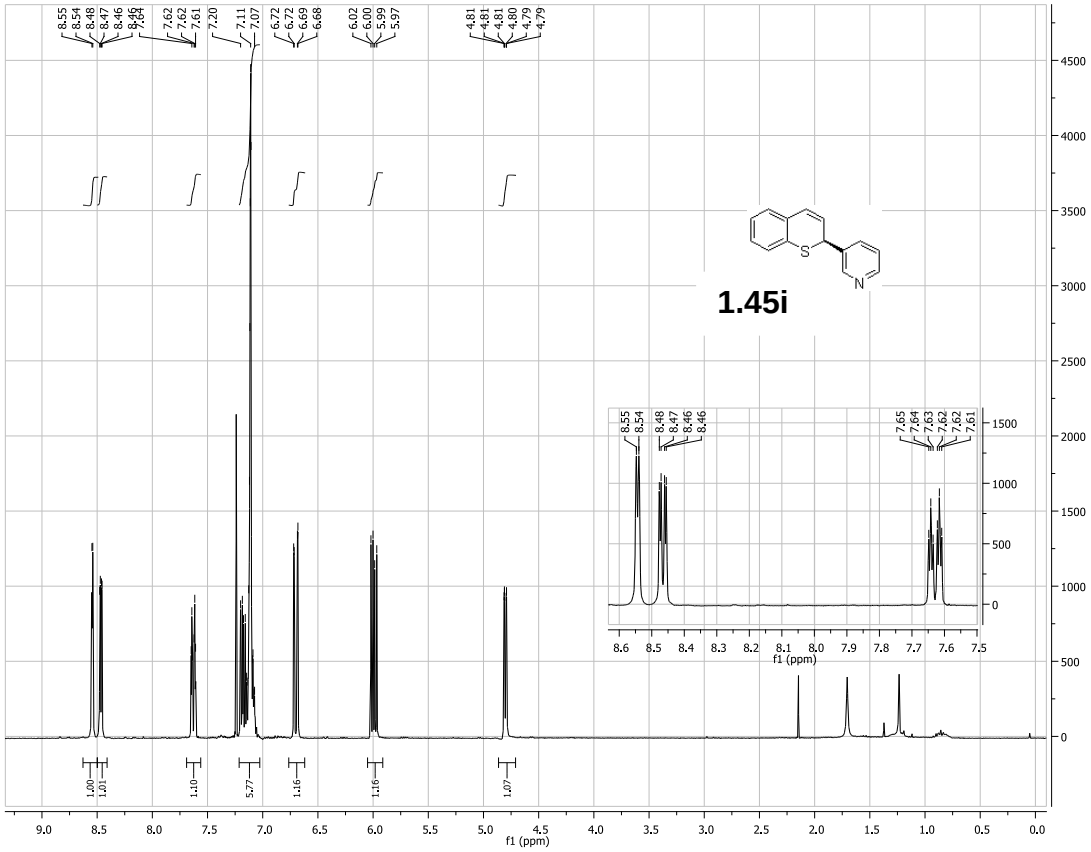

191.84
148.69
135.92
131.01
130.38
129.90
129.65
128.88
128.53
128.31
127.15
126.07
124.34
42.62
f1 (ppm)
1.45f


7.24
7.22
7.22
7.22
7.21
7.04
6.80
6.78
6.62
6.59
5.98
5.96
5.95
5.93
4.83
4.81
3.74
OMe
1.45g
2.02
3.96
1.96
0.95
0.96
1.03
3.00
f1 (ppm)


159.39
134.18
128.93
128.32
127.05
126.12
125.68
114.31
55.49
42.62
OMe
1.45g
131.27
130.91
128.93
128.79
128.54
128.32
127.05
126.12
125.68
f1 (ppm)


7.10
7.09
7.08
7.07
7.06
6.65
6.65
6.62
6.61
6.56
6.01
5.99
5.98
5.96
4.83
4.83
4.82
4.81
3.80
3.77
OMe
OMe
OMe
1.45h
3.86
1.00
2.26
0.94
0.94
3.21
7.91
f1 (ppm)


153.46
137.74
137.46
131.23
130.85
129.01
128.65
128.26
127.07
125.98
125.86
104.81
61.01
56.23
43.64
OMe
OMe
OMe
1.45h
f1 (ppm)


8.55
8.54
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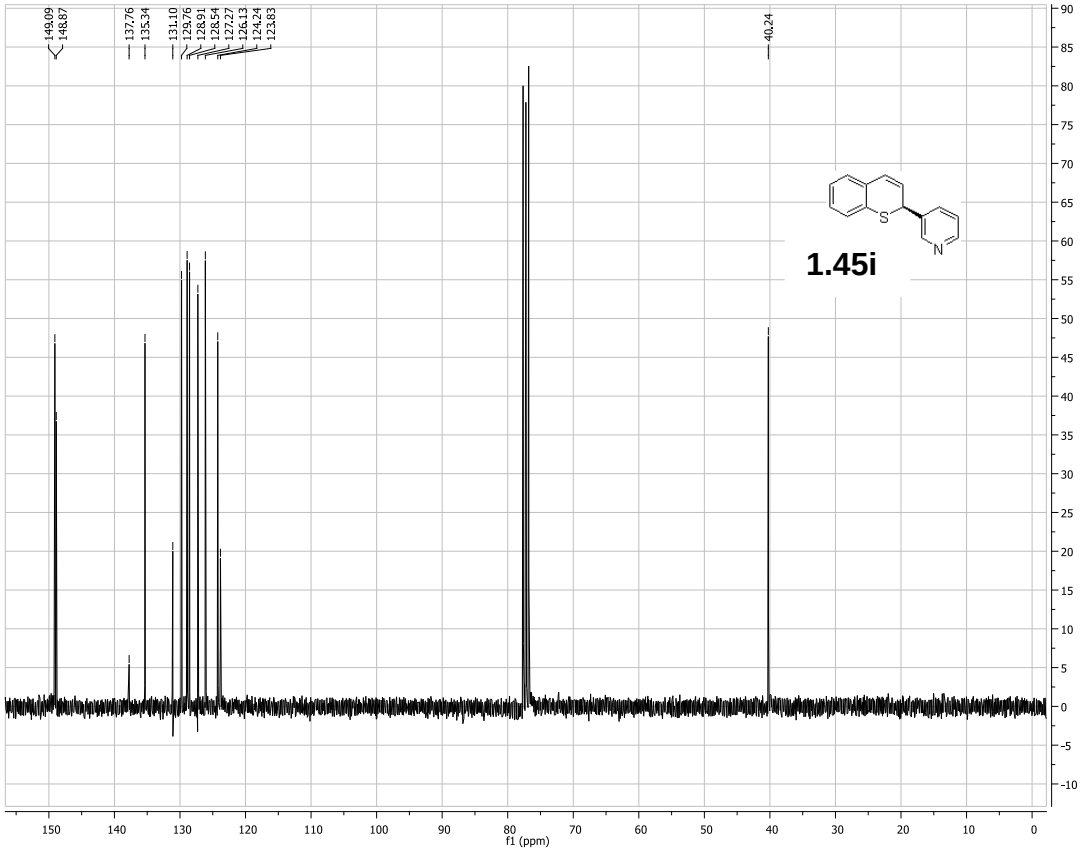
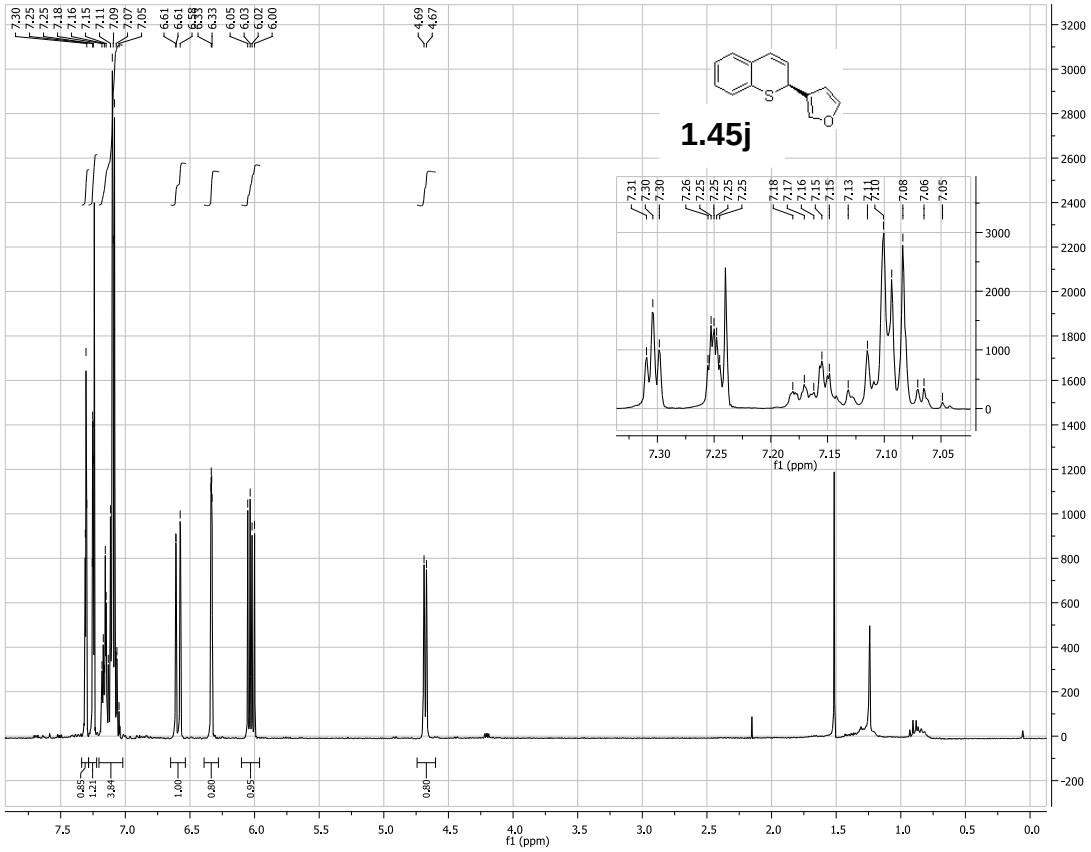
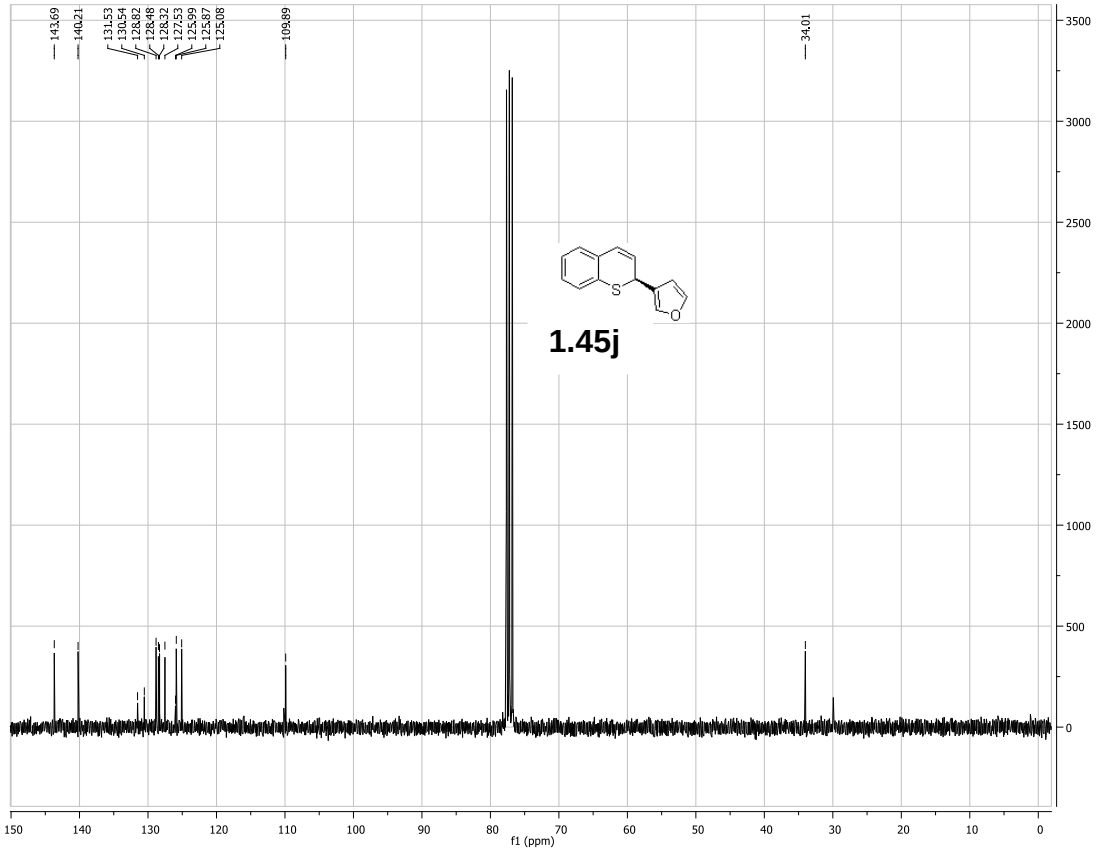
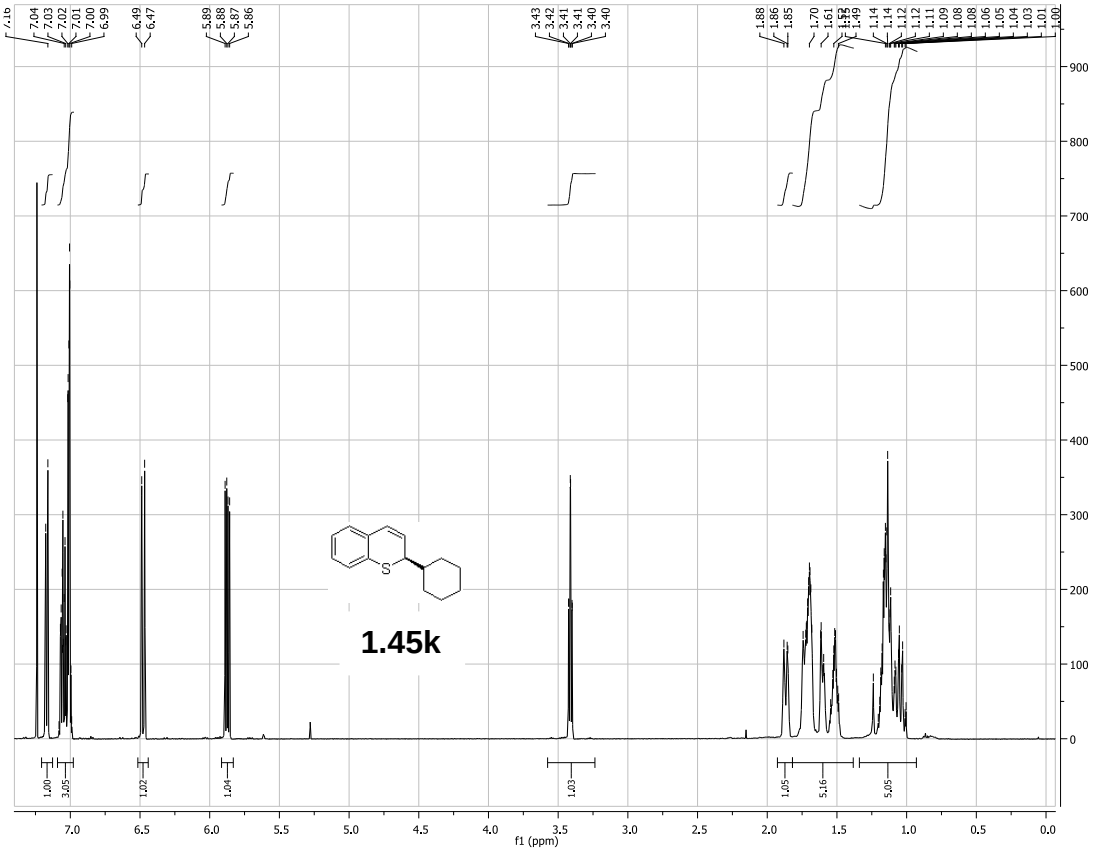
8.47
8.46
8.46
7.64
7.62
7.62
7.61
7.20
7.11
7.07
6.72
6.72
6.69
6.68
6.02
6.00
5.99
5.97
4.81
4.81
4.81
4.80
4.79
4.79
1.45i
1.00
1.01
1.10
5.77
1.16
1.16
1.07
f1 (ppm)


149.09
148.87
137.76
135.34
131.10
129.76
128.91
128.54
127.27
126.13
124.24
123.83
40.24
1.45i
f1 (ppm)


1.45j
f1 (ppm)


1.45j
f1 (ppm)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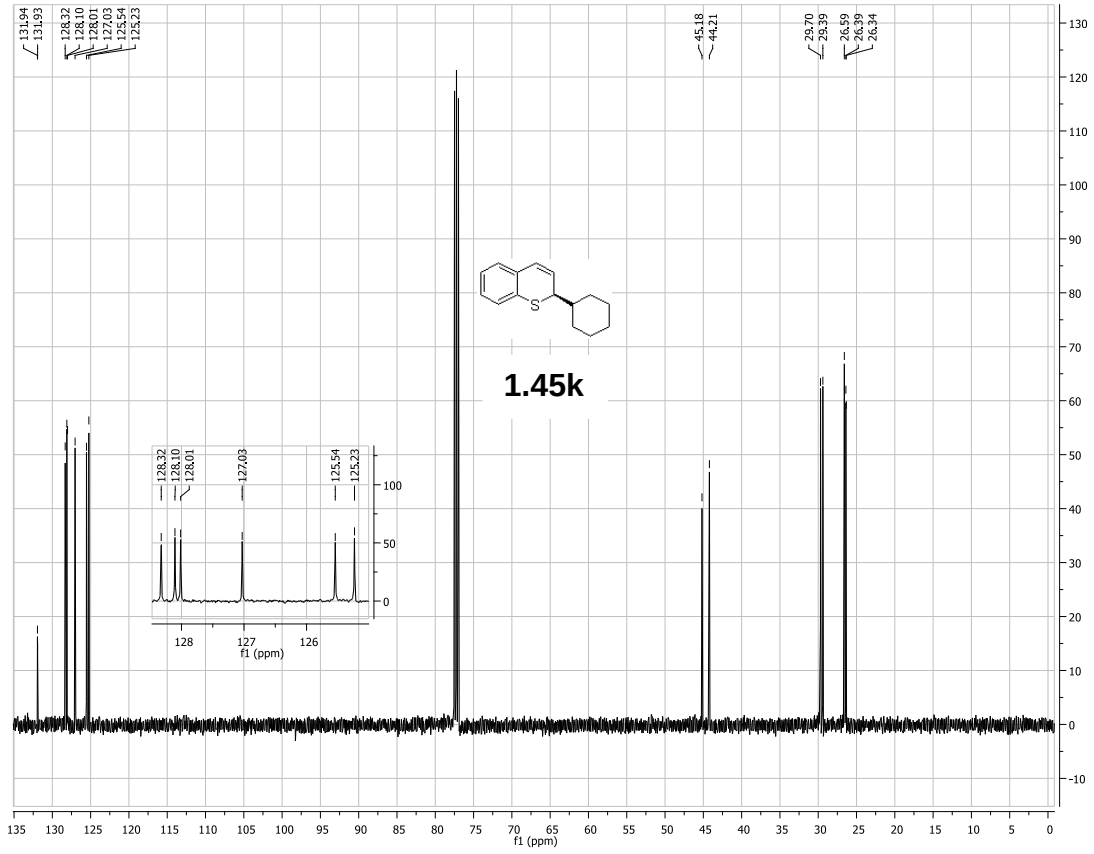
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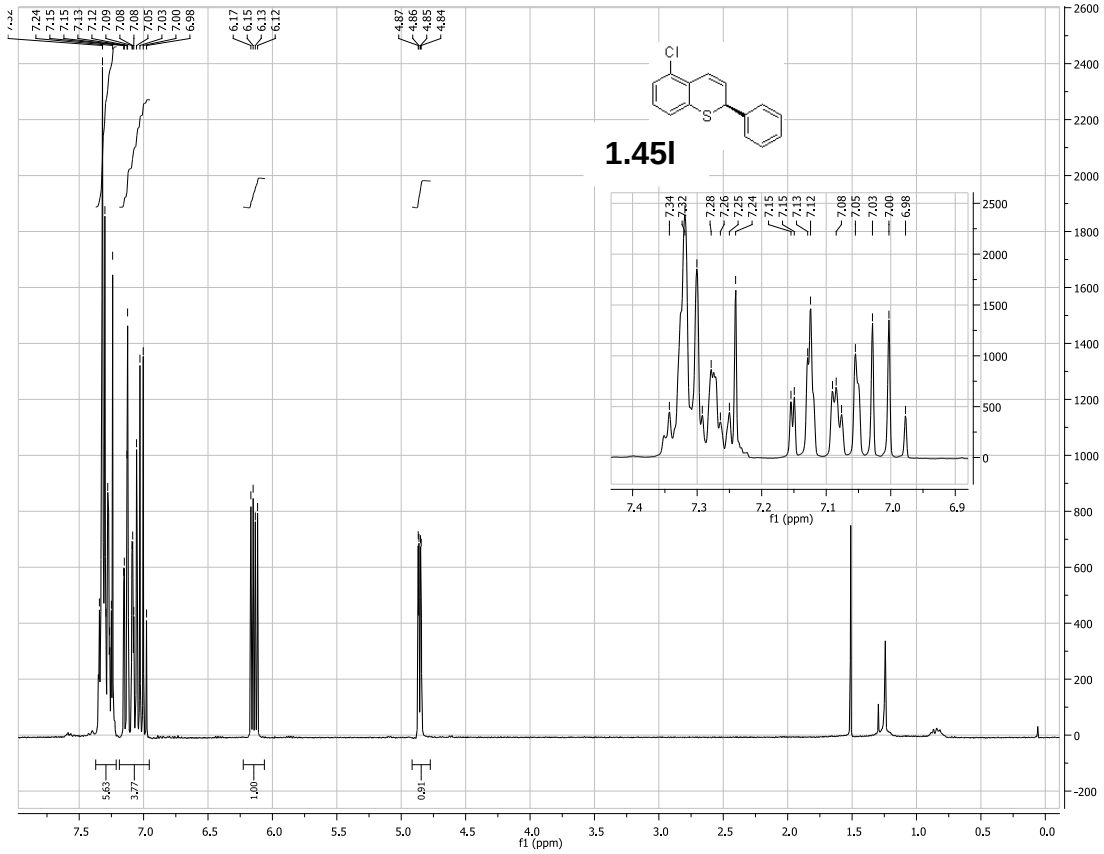
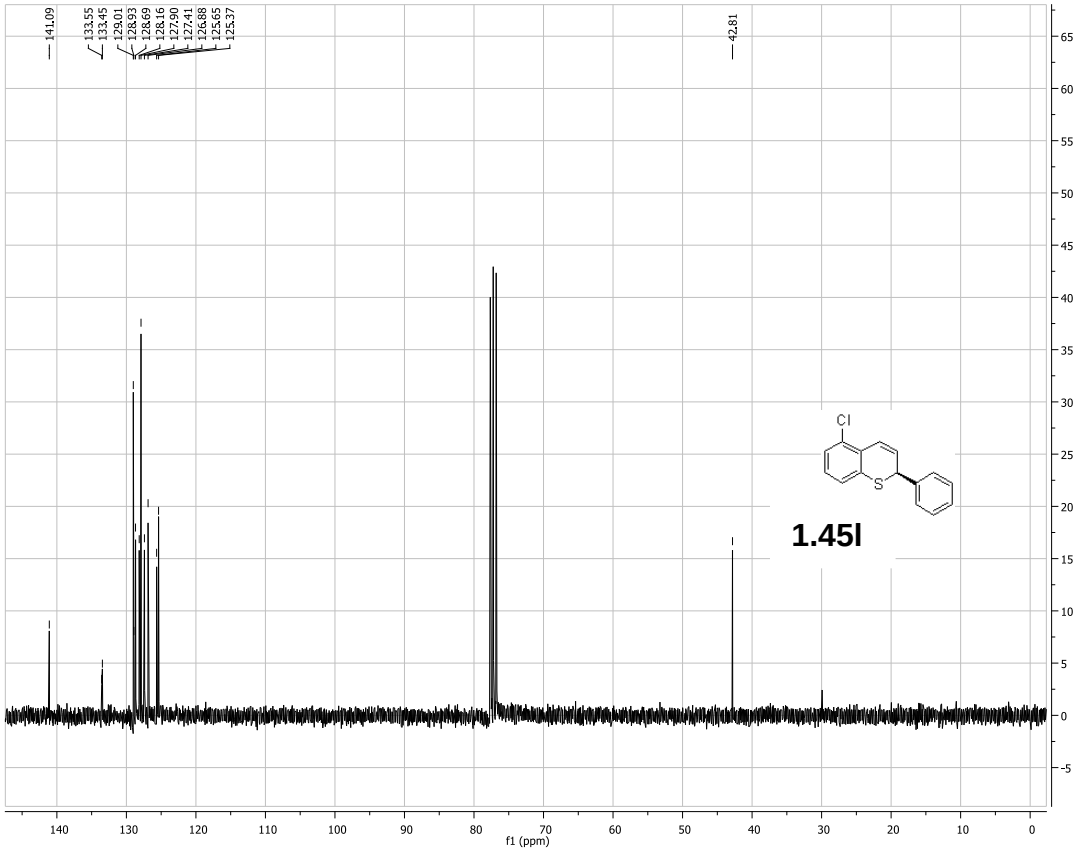

7.24
7.15
7.15
7.13
7.12
7.09
7.08
7.08
7.05
7.03
7.00
6.98
6.17
6.15
6.13
6.12
4.87
4.86
4.85
4.84
Cl
S
1.45l
7.34
7.32
7.28
7.26
7.25
7.24
7.15
7.15
7.13
7.12
7.08
7.05
7.03
7.00
6.98
f1 (ppm)
5.63
3.77
1.00
0.91
f1 (ppm)


141.09
133.55
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129.01
128.93
128.69
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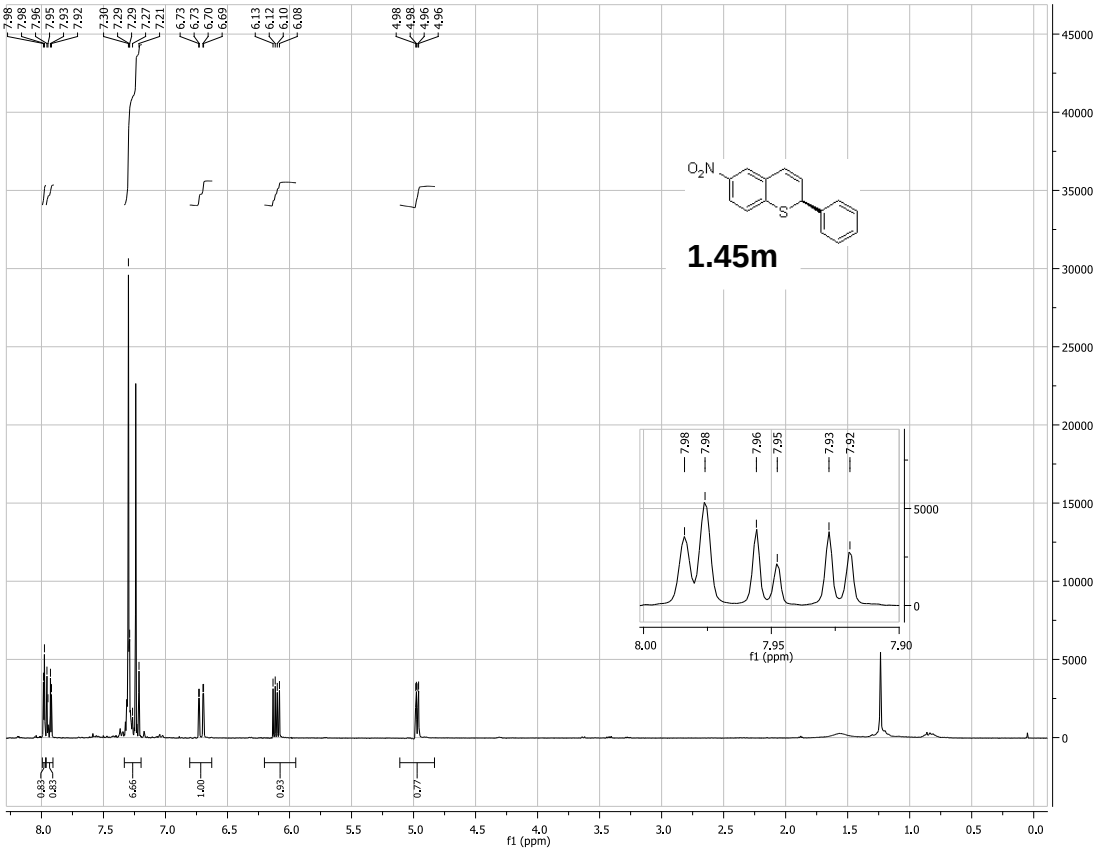
127.90
127.41
126.88
125.65
125.37
42.81
Cl
S
1.45l
f1 (ppm)


7.98
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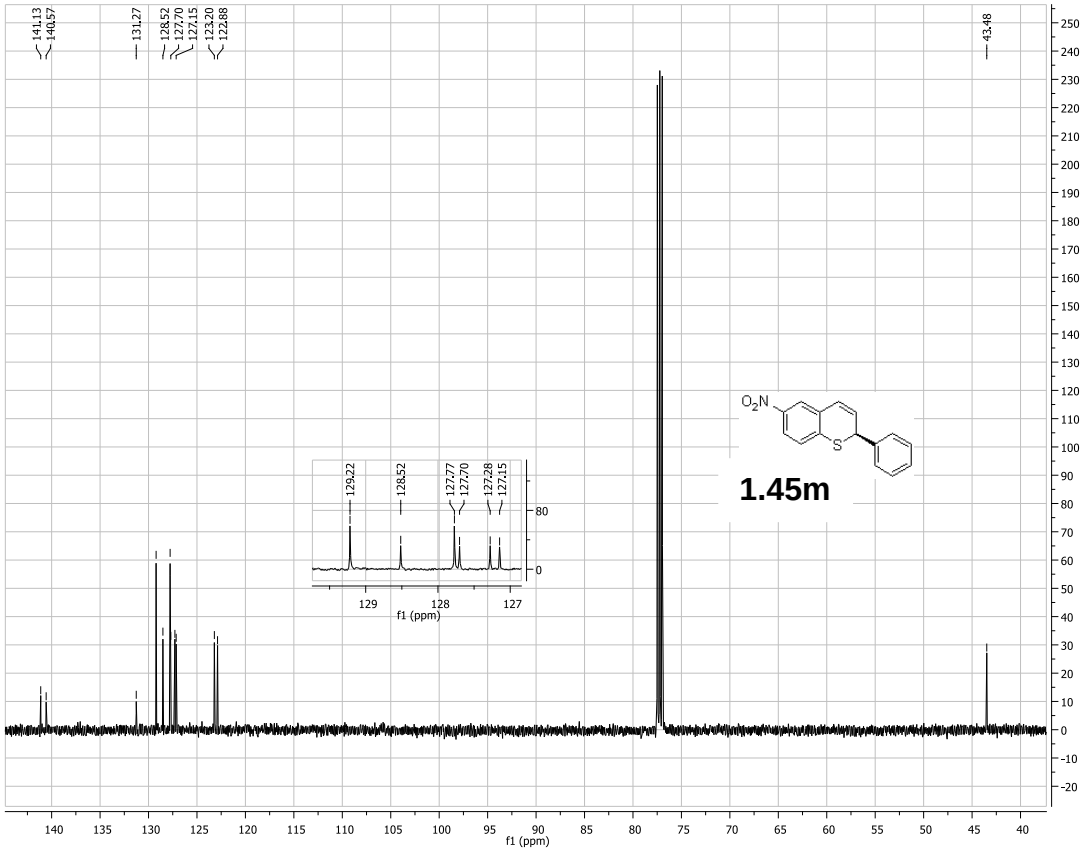
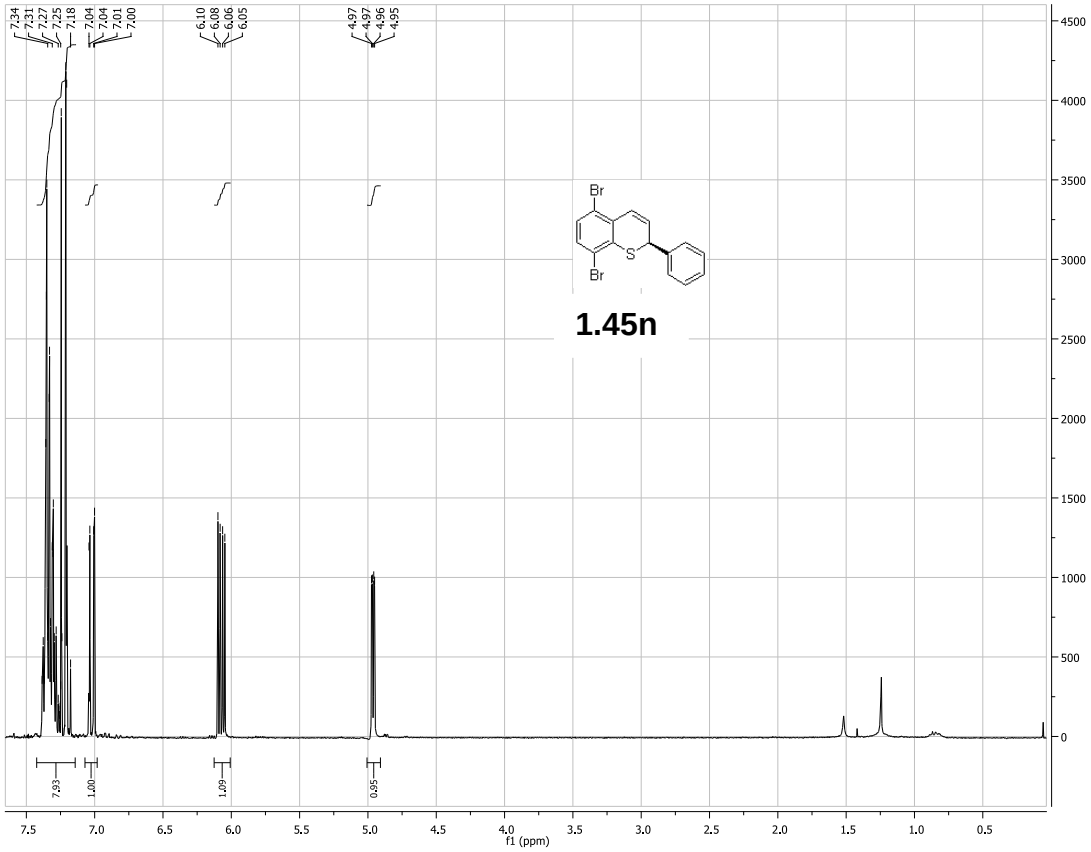
7.93
7.92
7.30
7.29
7.29
7.27
7.21
6.73
6.73
6.70
6.69
6.13
6.12
6.10
6.08
4.98
4.98
4.96
4.96
O2N
S
1.45m
7.98
7.98
7.96
7.95
7.93
7.92
5000
0
8.00
7.95
7.90
f1 (ppm)
0.83
0.83
6.66
1.00
0.93
0.77
f1 (ppm)


141.13
140.57
131.27
128.52
127.70
127.15
123.20
122.88
43.48
O2N
S
1.45m
129.22
128.52
127.77
127.70
127.28
127.15
80
0
129
128
127
f1 (ppm)
f1 (ppm)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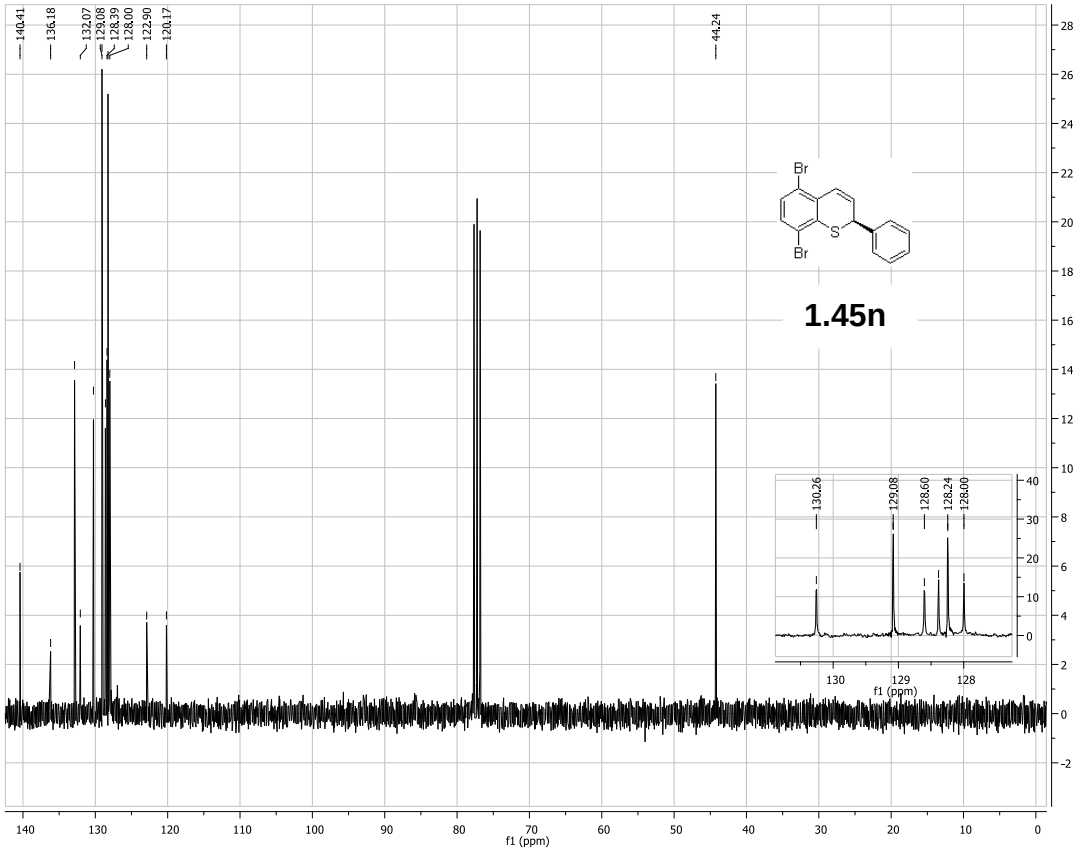
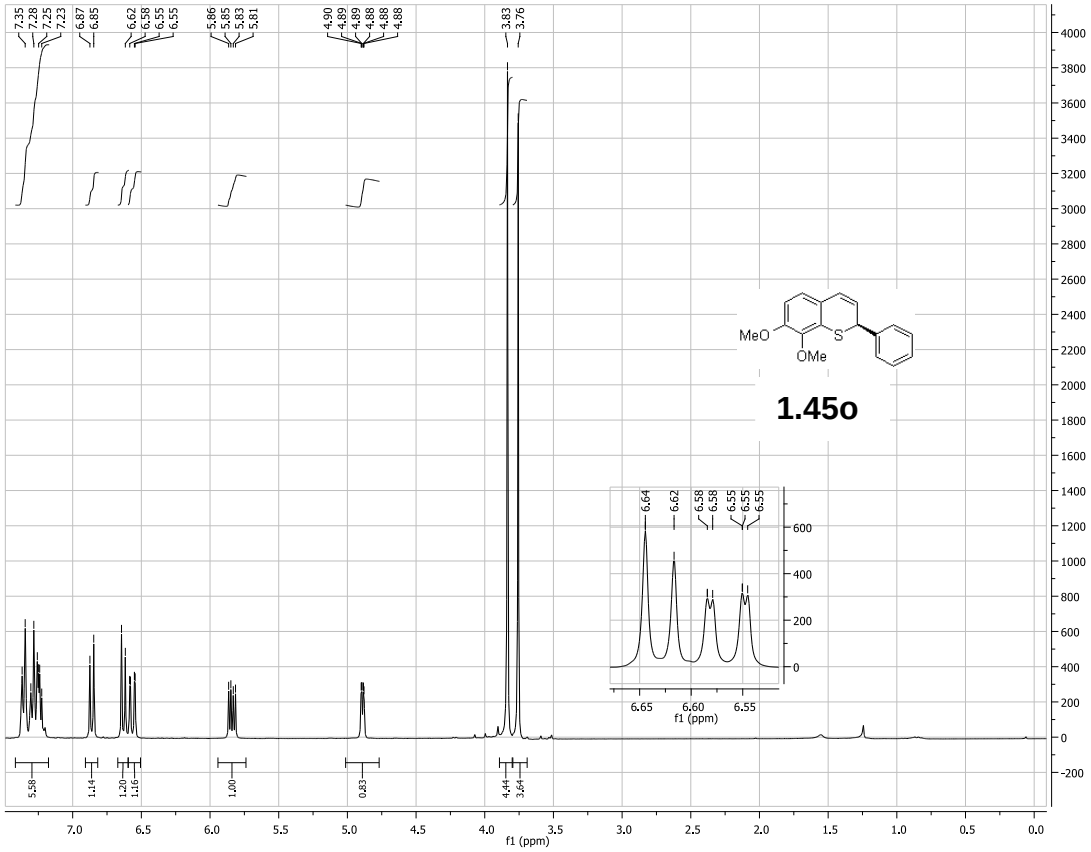
7.31
7.27
7.25
7.18
7.04
7.04
7.01
7.00
6.10
6.08
6.06
6.05
4.97
4.97
4.96
4.95
Br
S
Br
1.45n
7.93
1.00
1.09
0.95
f1 (ppm)


140.41
136.18
132.07
129.08
128.39
128.00
122.90
120.17
44.24
Br
S
Br
1.45n
130.26
129.08
128.60
128.24
128.00
f1 (ppm)
f1 (ppm)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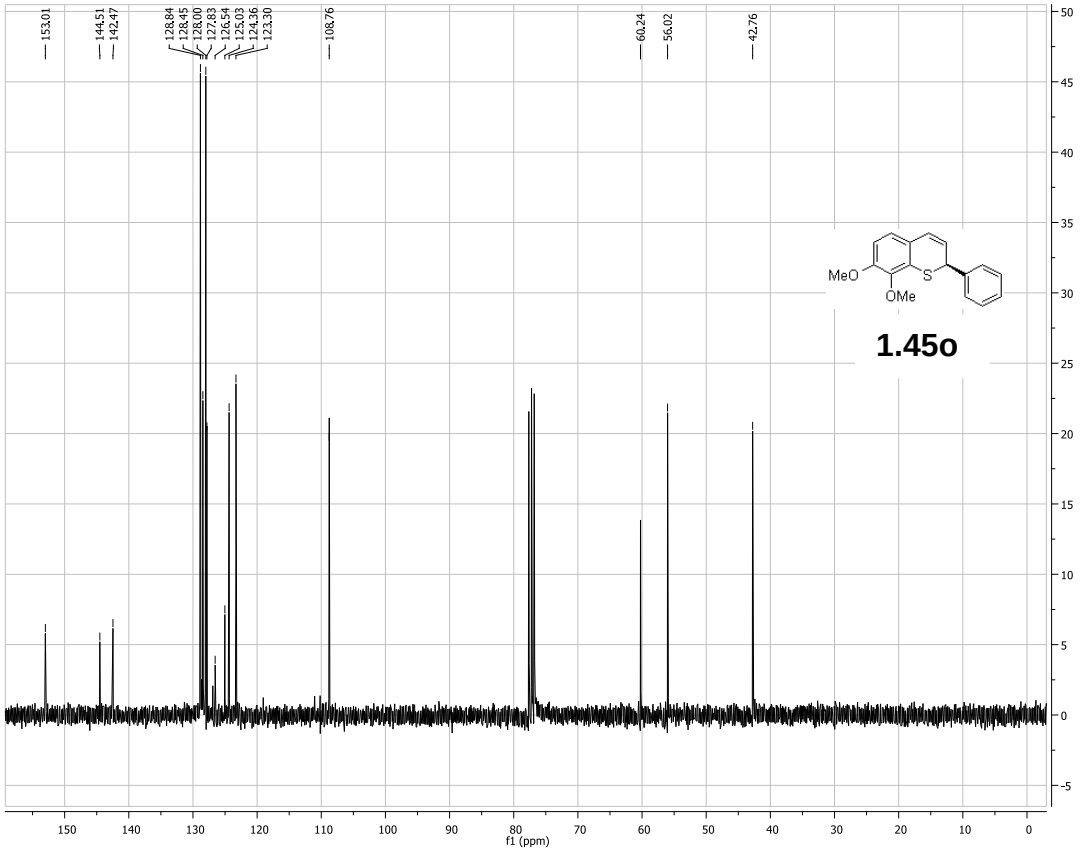
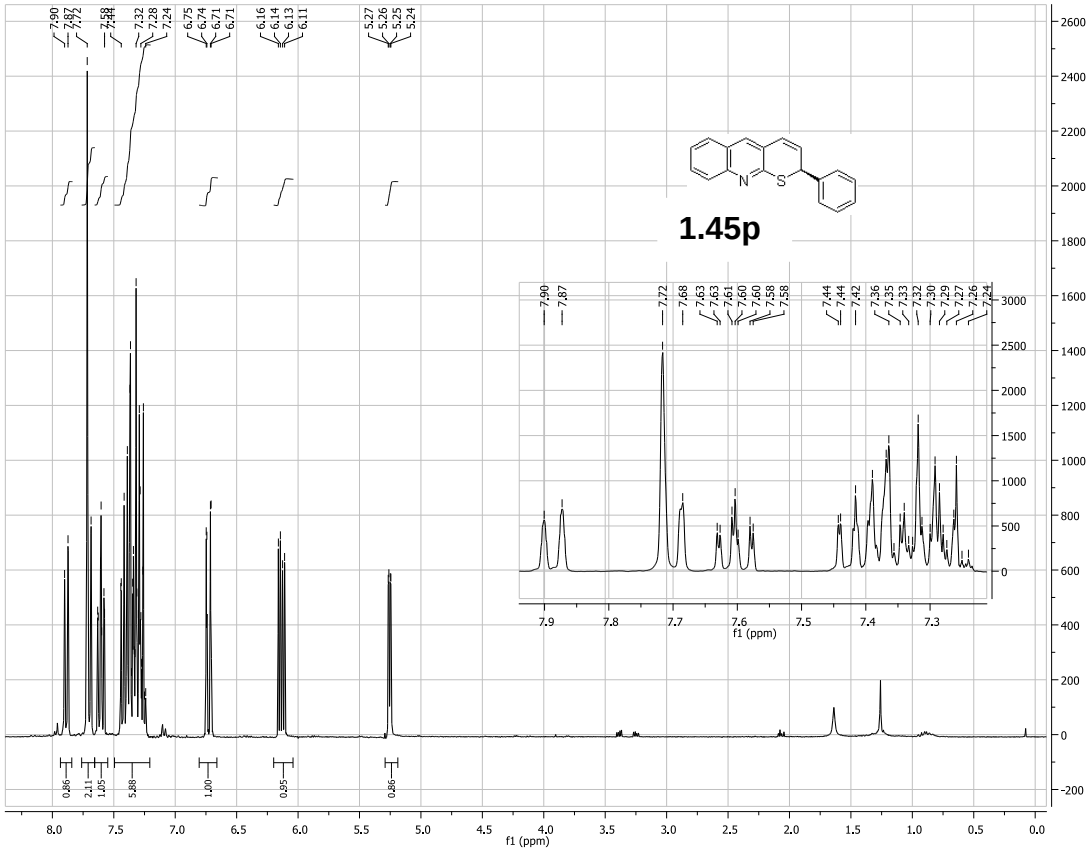
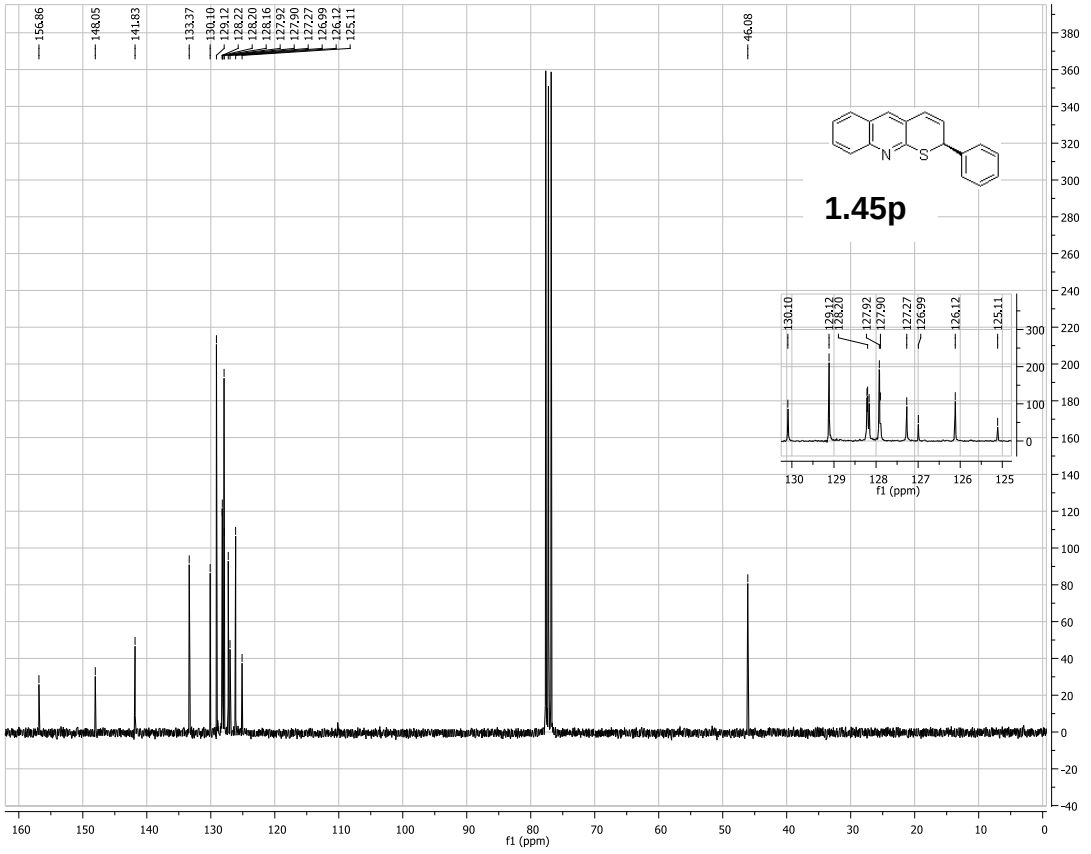
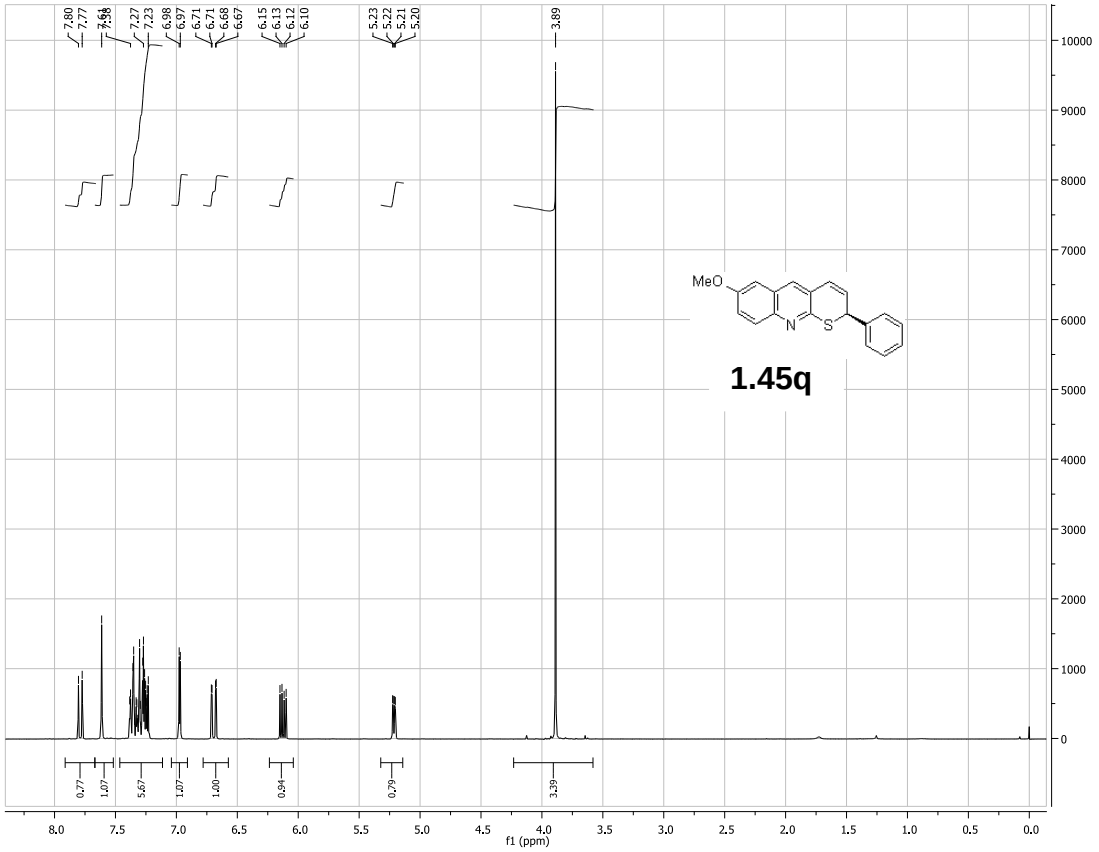
7.25
7.23
6.87
6.85
6.62
6.58
6.55
6.55
5.86
5.85
5.83
5.81
4.90
4.89
4.89
4.88
4.88
4.88
3.83
3.76
MeO
OMe
S
1.45o
6.64
6.62
6.58
6.58
6.55
6.55
6.55
f1 (ppm)
5.58
1.14
1.20
1.16
1.00
0.83
4.44
3.64
f1 (ppm)


153.01
144.51
142.47
128.84
128.45
128.00
127.83
126.54
125.03
124.36
123.30
108.76
60.24
56.02
42.76
MeO
OMe
S
1.45o
f1 (ppm)


1.45p
f1 (ppm)


1.45p
f1 (ppm)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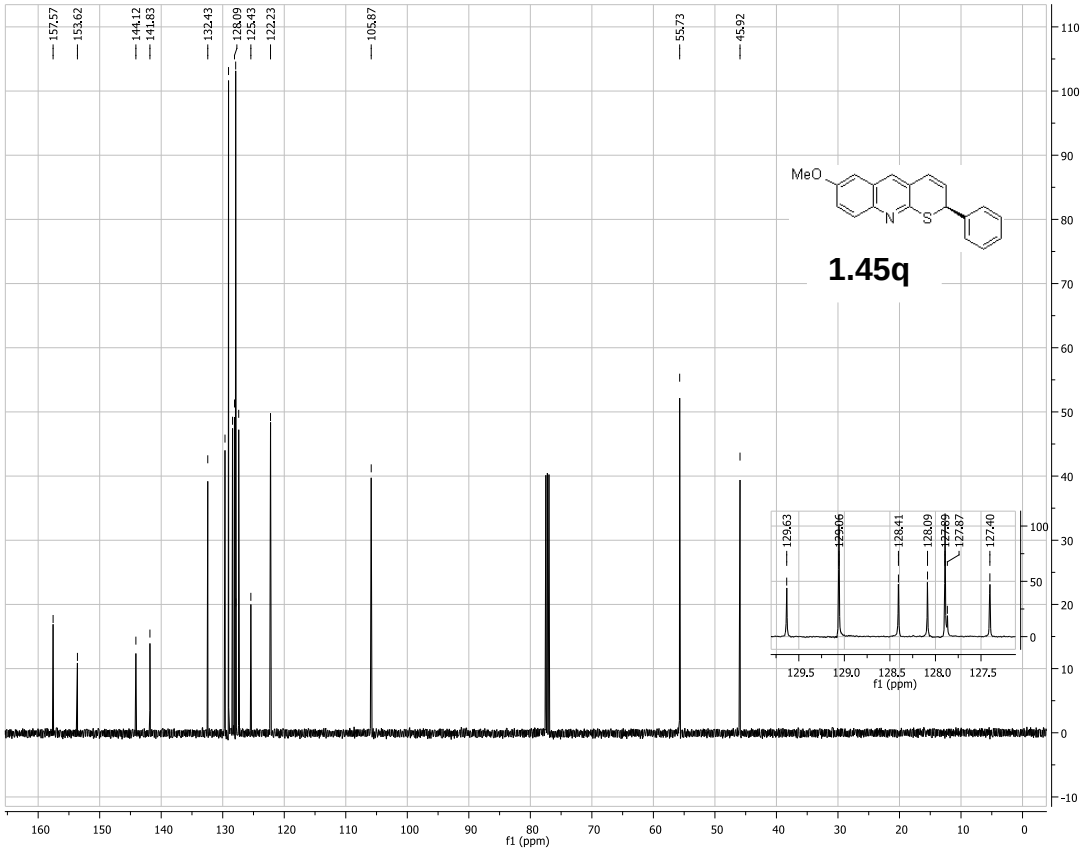
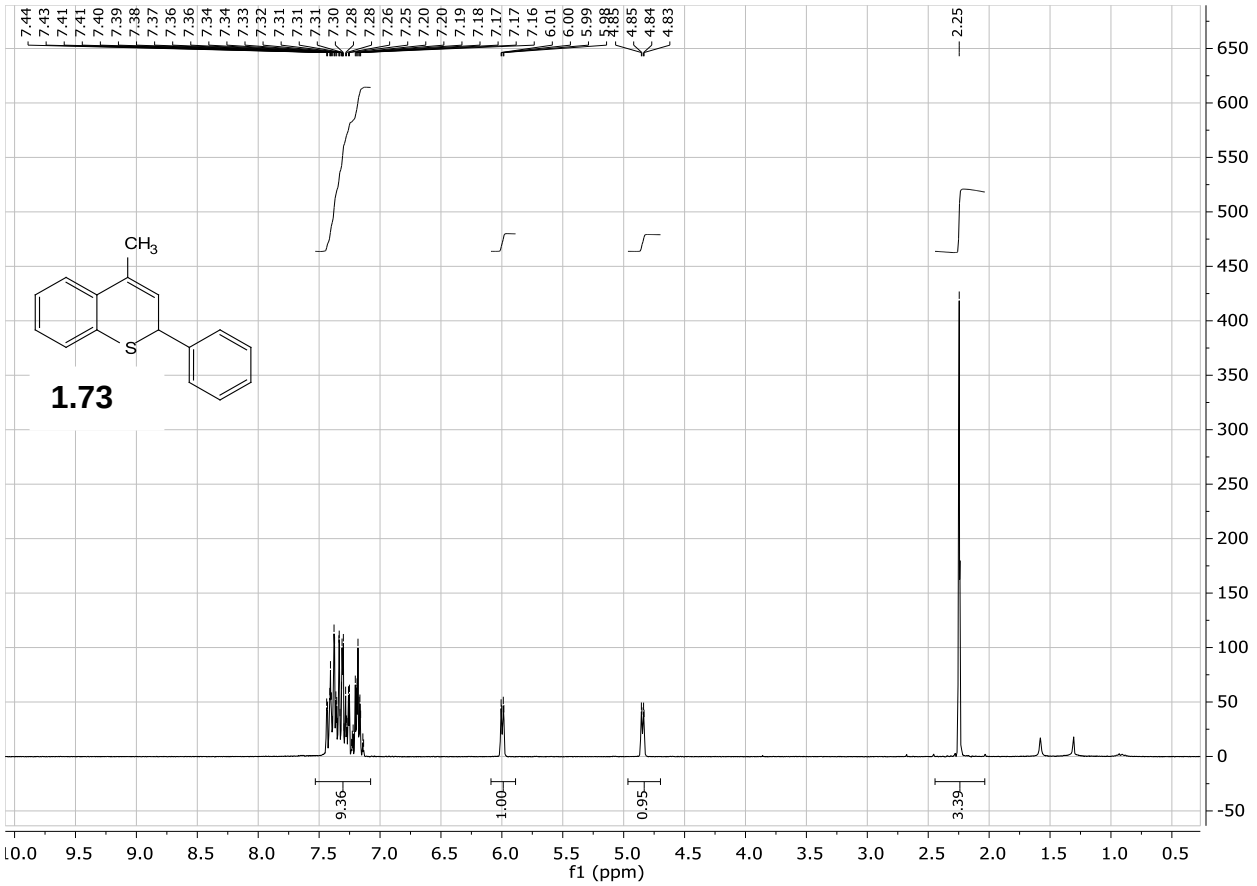
7.58
7.27
7.23
6.98
6.97
6.71
6.71
6.68
6.67
6.15
6.13
6.12
6.10
5.23
5.22
5.21
5.20
3.89
MeO
N
S
1.45q
0.77
1.07
5.67
1.07
1.00
0.94
0.79
3.39
f1 (ppm)


157.57
153.62
144.12
141.83
132.43
128.09
125.43
122.23
105.87
55.73
45.92
MeO
N
S
1.45q
129.63
129.06
128.41
128.09
127.89
127.87
127.40
f1 (ppm)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7.43
7.41
7.41
7.40
7.39
7.38
7.37
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7.34
7.34
7.33
7.32
7.31
7.31
7.31
7.30
7.28
7.28
7.26
7.25
7.20
7.20
7.19
7.18
7.17
7.17
7.16
6.01
6.00
5.99
4.85
4.85
4.84
4.83
2.25
CH3
S
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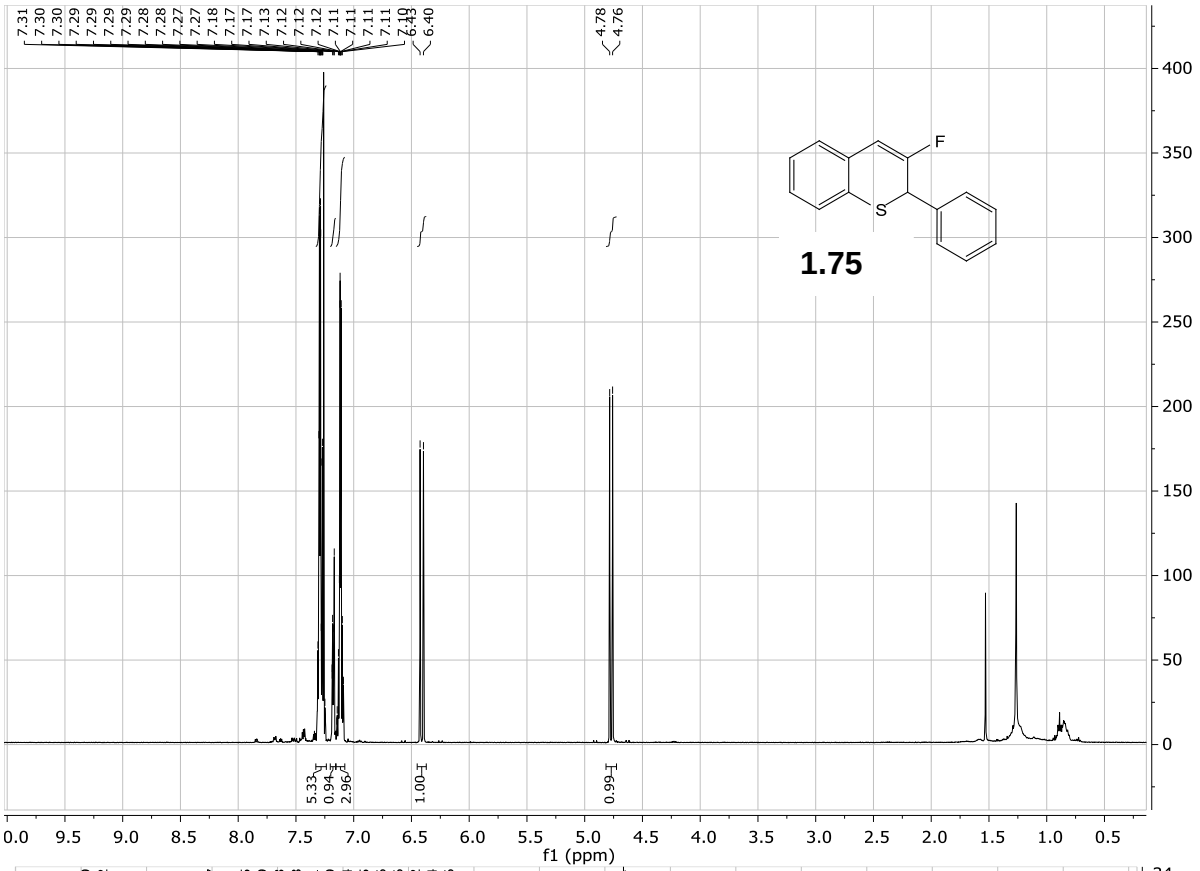
9.36
1.00
0.95
3.39
f1 (ppm)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7.28
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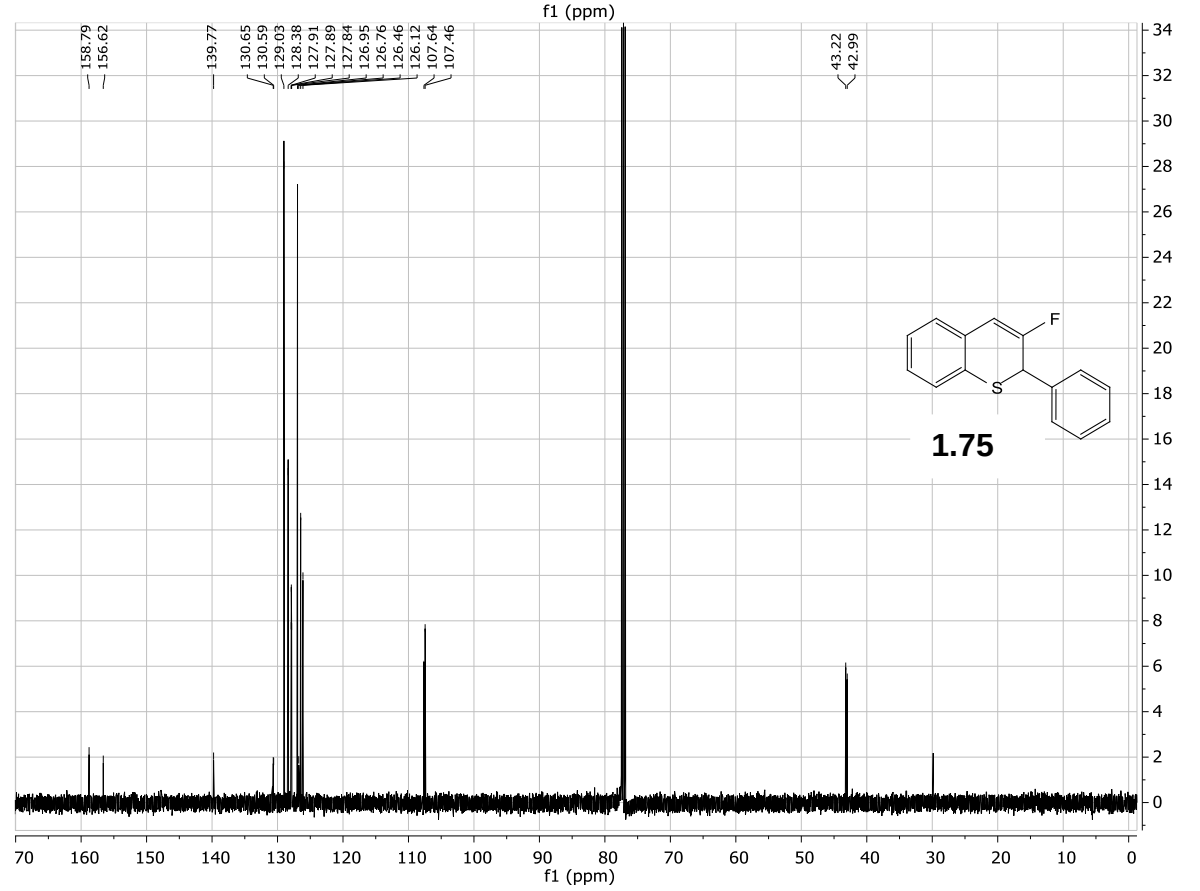
7.27
7.27
7.18
7.17
7.17
7.13
7.12
7.12
7.12
7.11
7.11
7.11
7.11
7.10
6.43
6.40
4.78
4.76
F
S
1.75
5.33
0.94
2.96
1.00
0.99
f1 (ppm)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156.62
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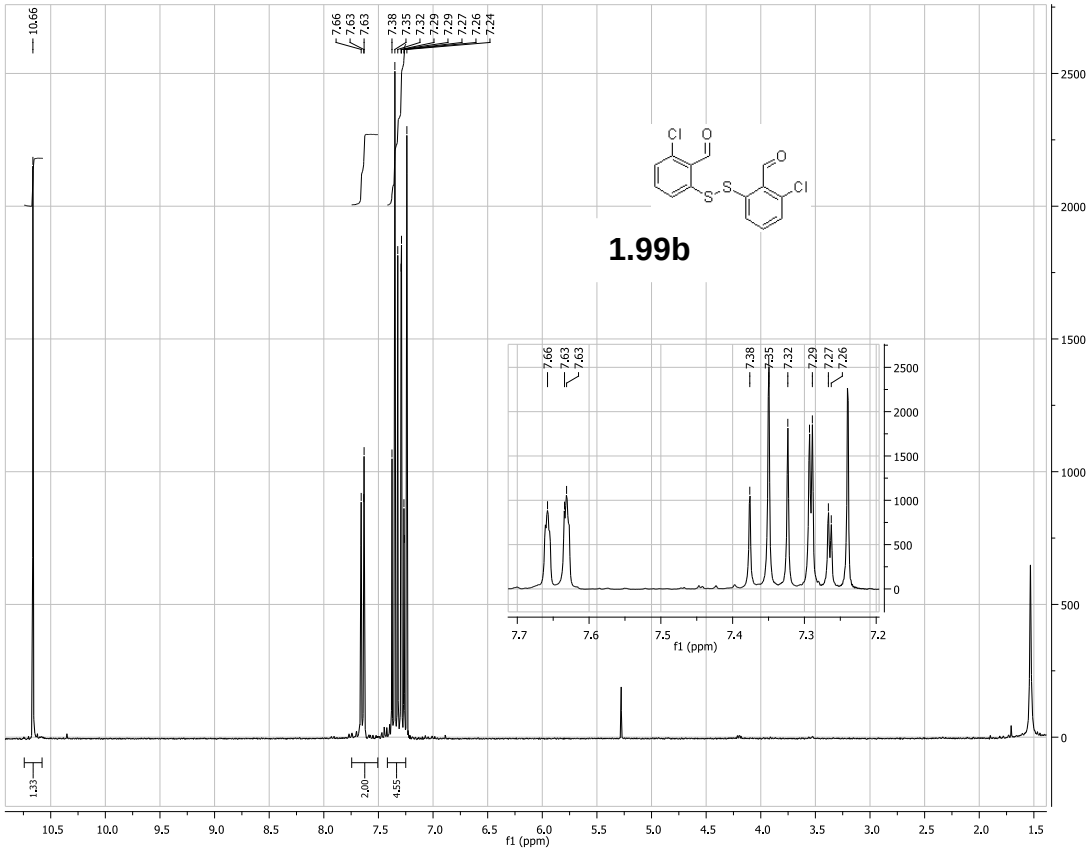
130.59
129.03
128.38
127.91
127.89
127.84
126.95
126.76
126.46
126.12
107.64
107.46
43.22
42.99
F
S
1.75
f1 (ppm)


10.66
7.66
7.63
7.63
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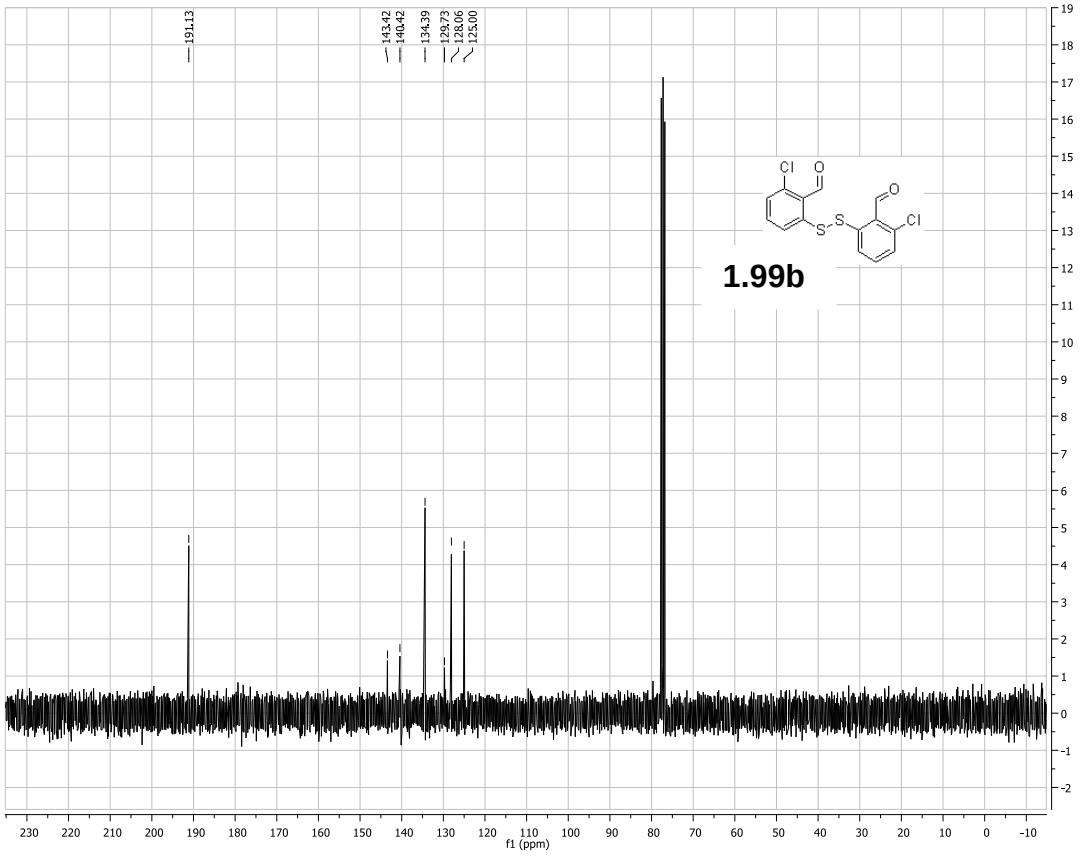
7.32
7.29
7.29
7.27
7.26
7.24
1.33
2.00
4.55
f1 (ppm)
1.99b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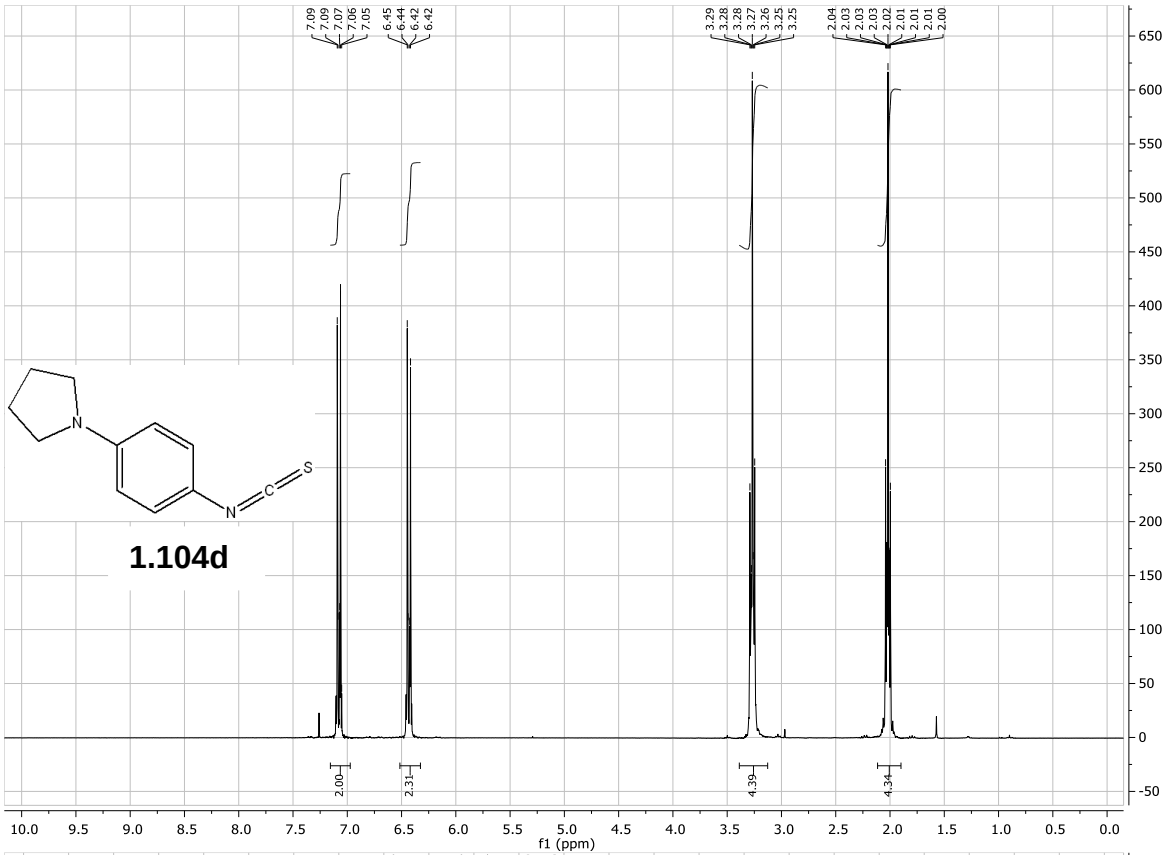
143.42
140.42
134.39
129.73
128.06
125.00
f1 (ppm)
1.99b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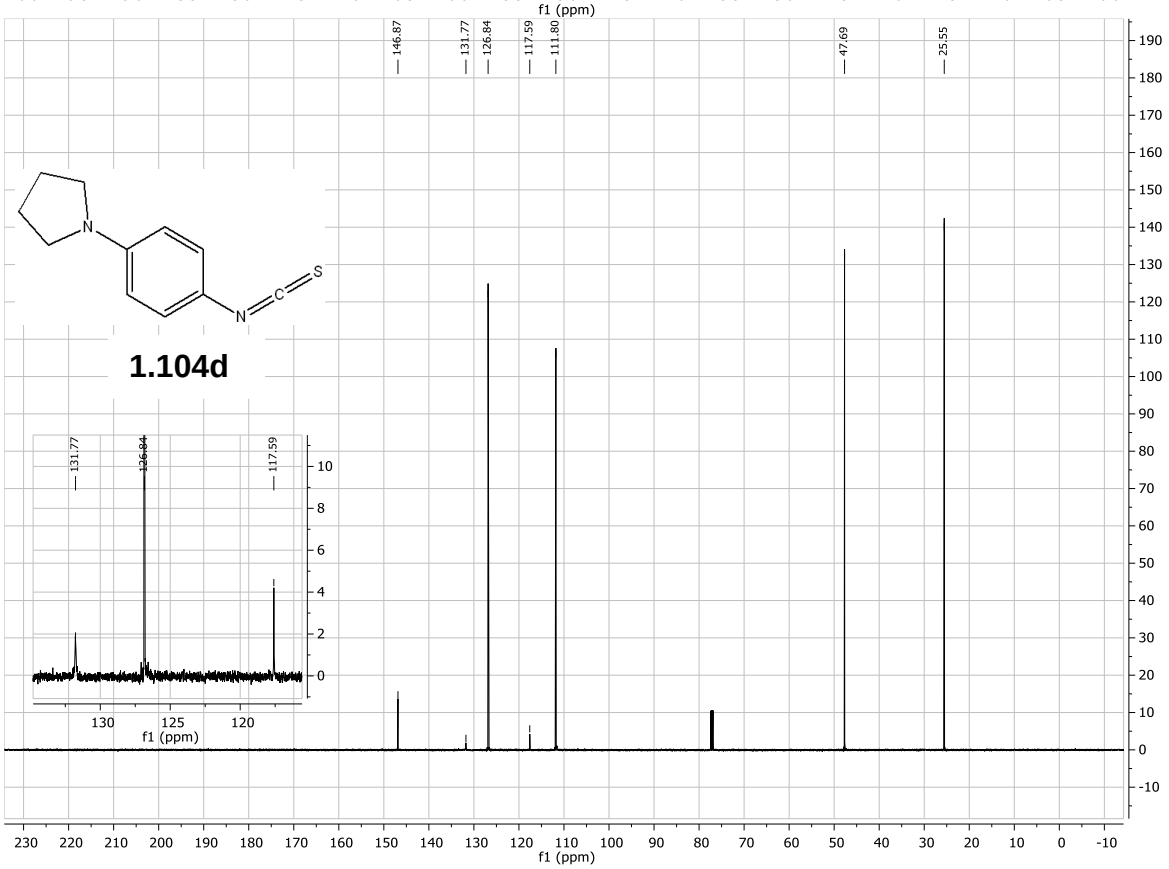
7.07
7.06
7.05
6.45
6.44
6.42
6.42
3.29
3.28
3.28
3.27
3.26
3.25
3.25
2.04
2.03
2.03
2.03
2.02
2.01
2.01
2.01
2.00
2.00
2.31
4.39
4.34
f1 (ppm)
1.104d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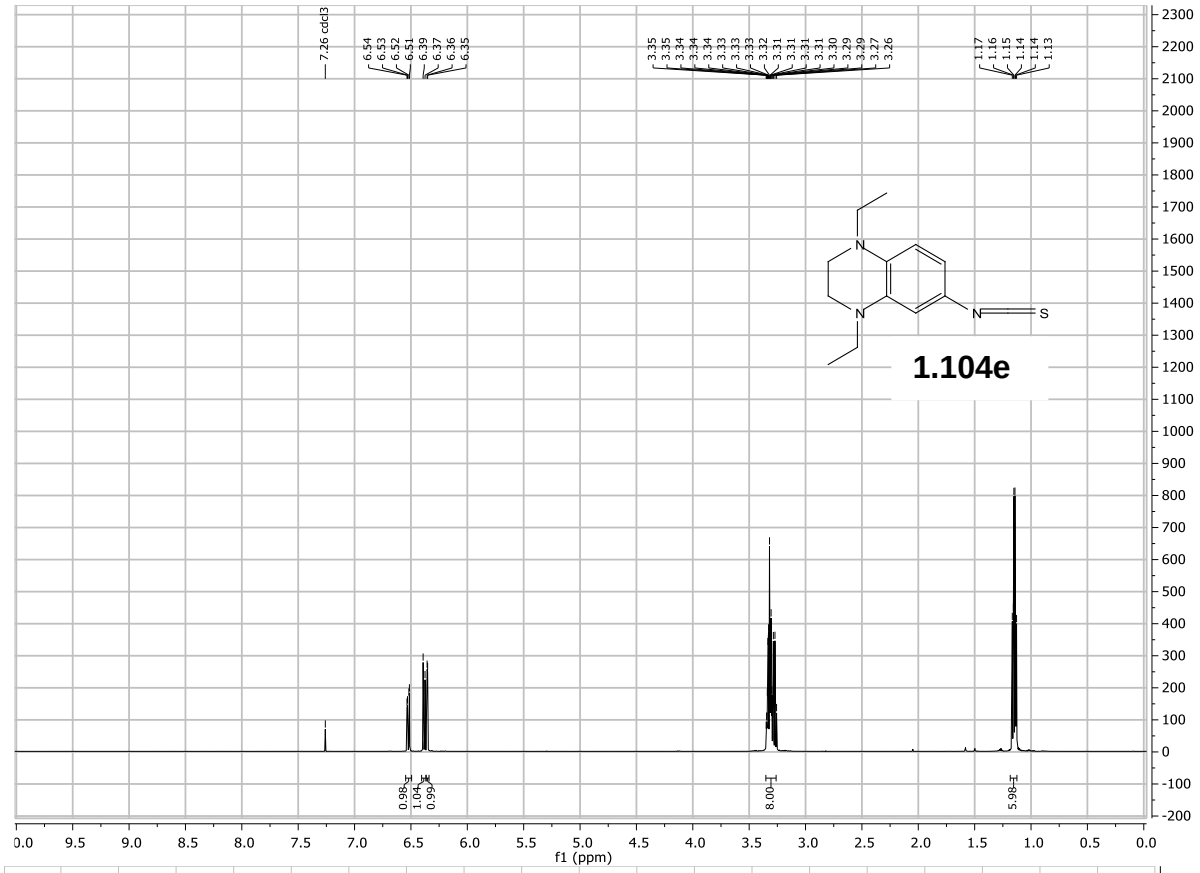
117.59
111.80
47.69
25.55
131.77
126.84
117.59
f1 (ppm)
1.104d


7.26 cdcl3
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6.53
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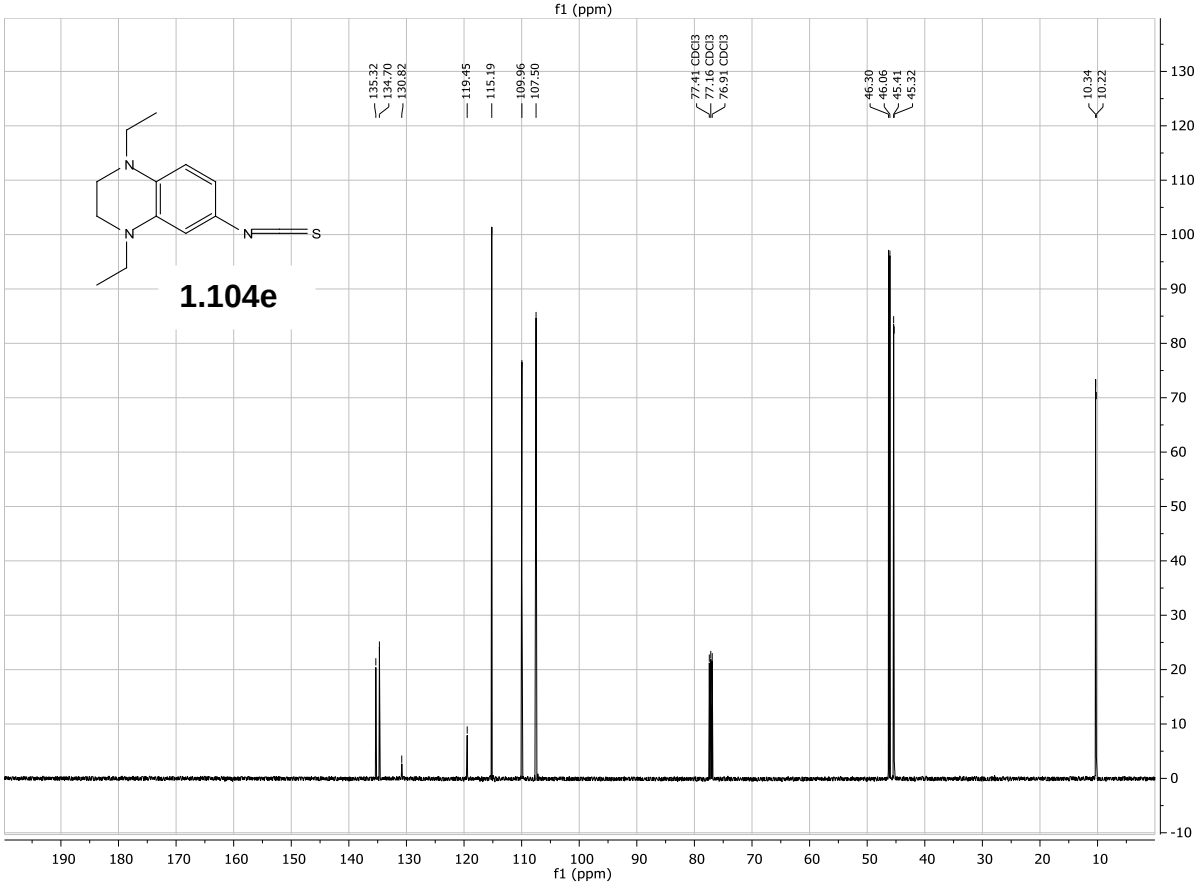
6.39
6.37
6.36
6.35
3.35
3.34
3.33
3.32
3.31
3.30
3.29
3.27
3.26
1.17
1.16
1.15
1.14
1.13
0.98
1.04
0.99
8.00
5.98
f1 (ppm)
1.104e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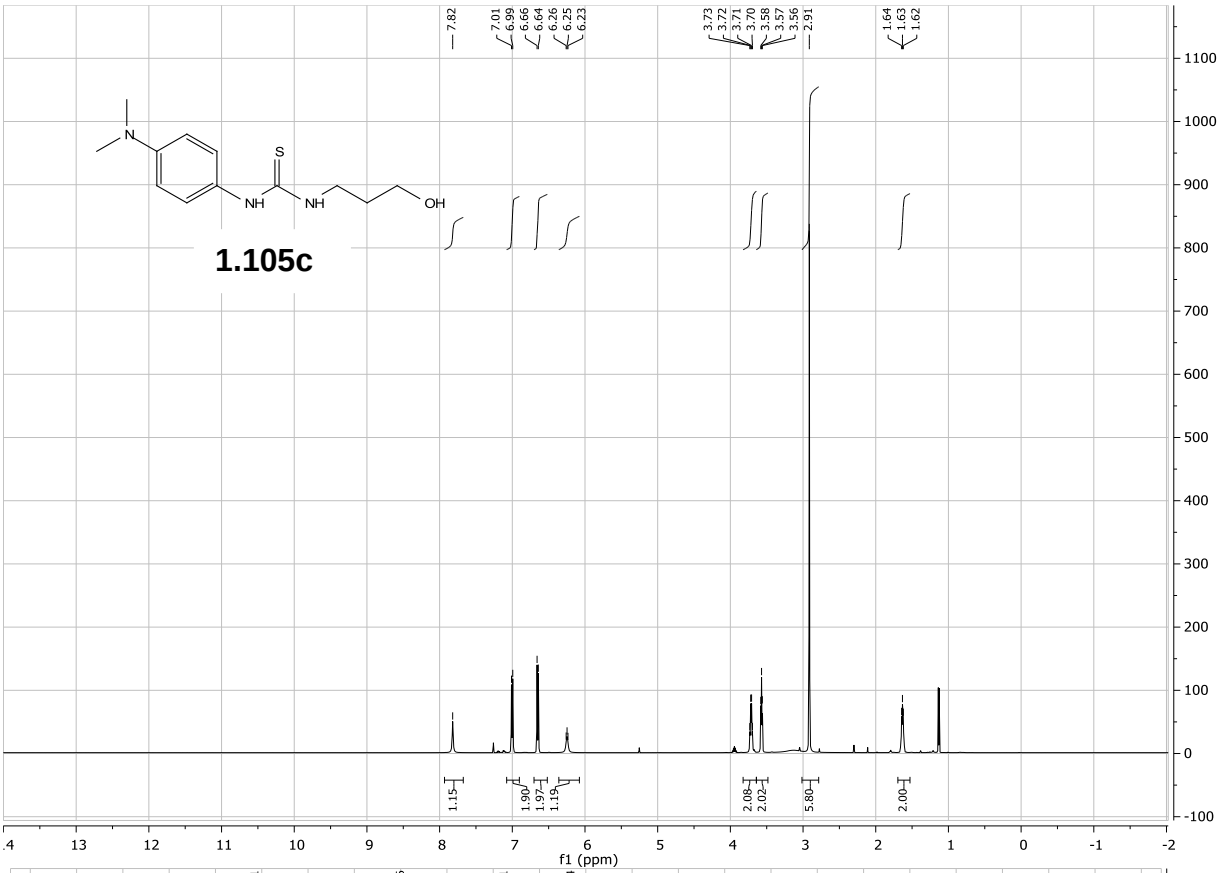
134.70
130.82
119.45
115.19
109.96
107.50
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
46.30
46.06
45.41
45.32
10.34
10.22
f1 (ppm)
1.104e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7.01
6.99
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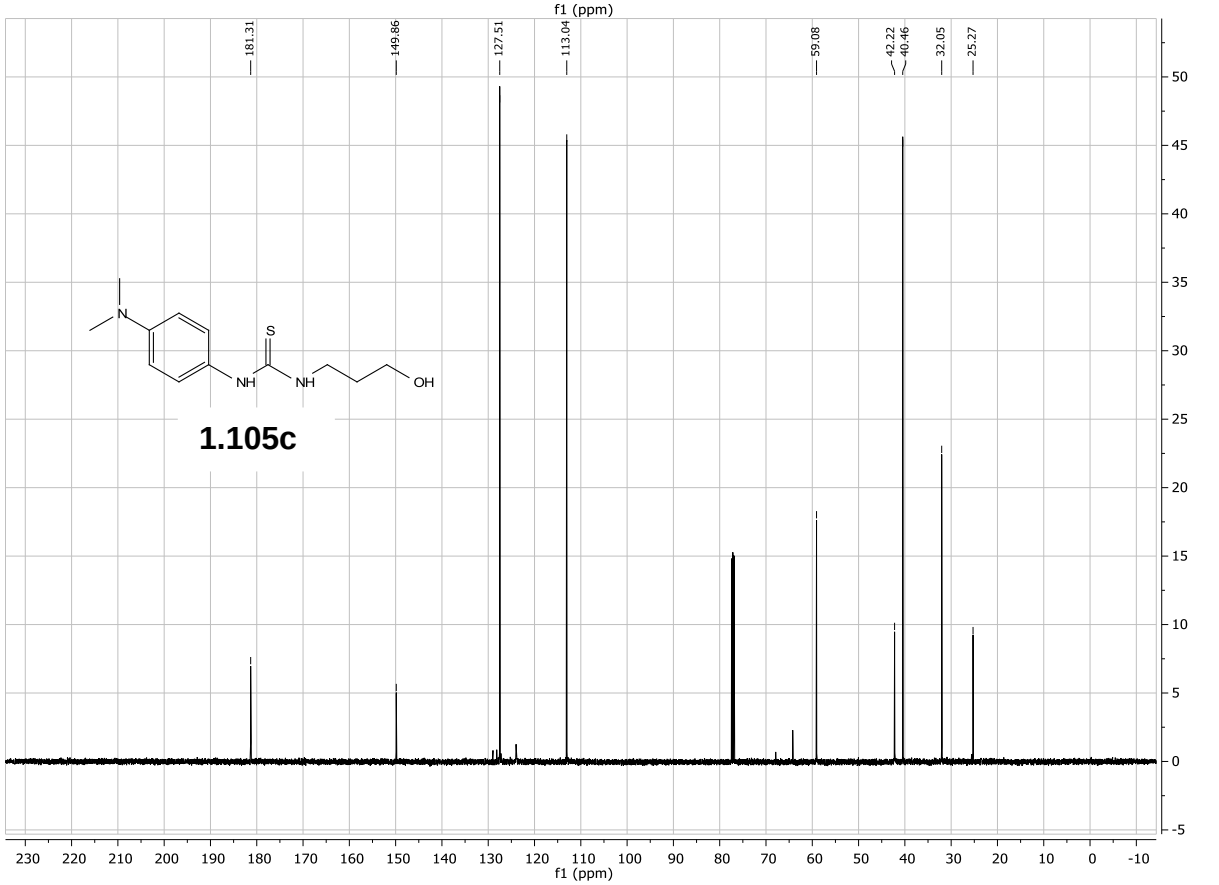
6.64
6.26
6.25
6.23
3.73
3.72
3.71
3.70
3.58
3.57
3.56
2.91
1.64
1.63
1.62
1.15
1.90
1.97
1.19
2.08
2.02
5.80
2.00
f1 (ppm)
1.105c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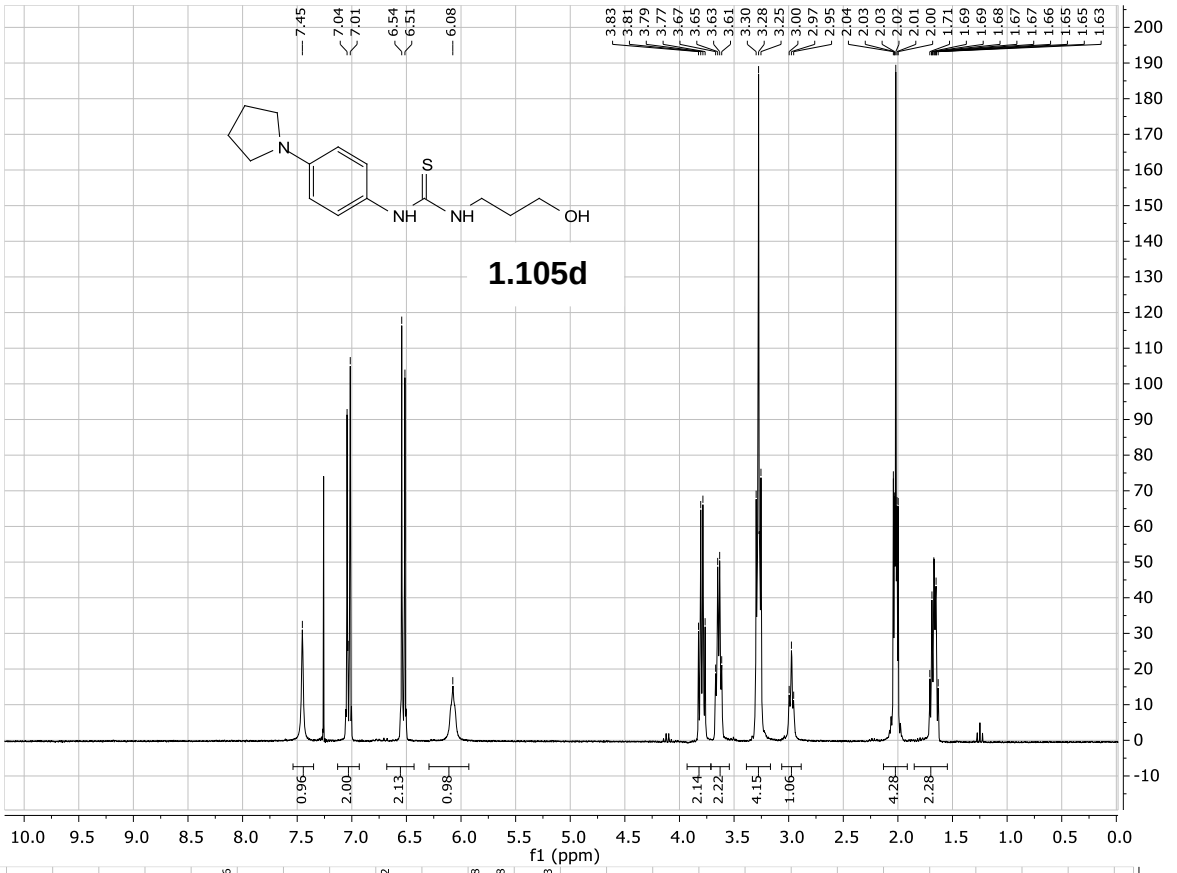
127.51
113.04
59.08
42.22
40.46
32.05
25.27
f1 (ppm)
1.105c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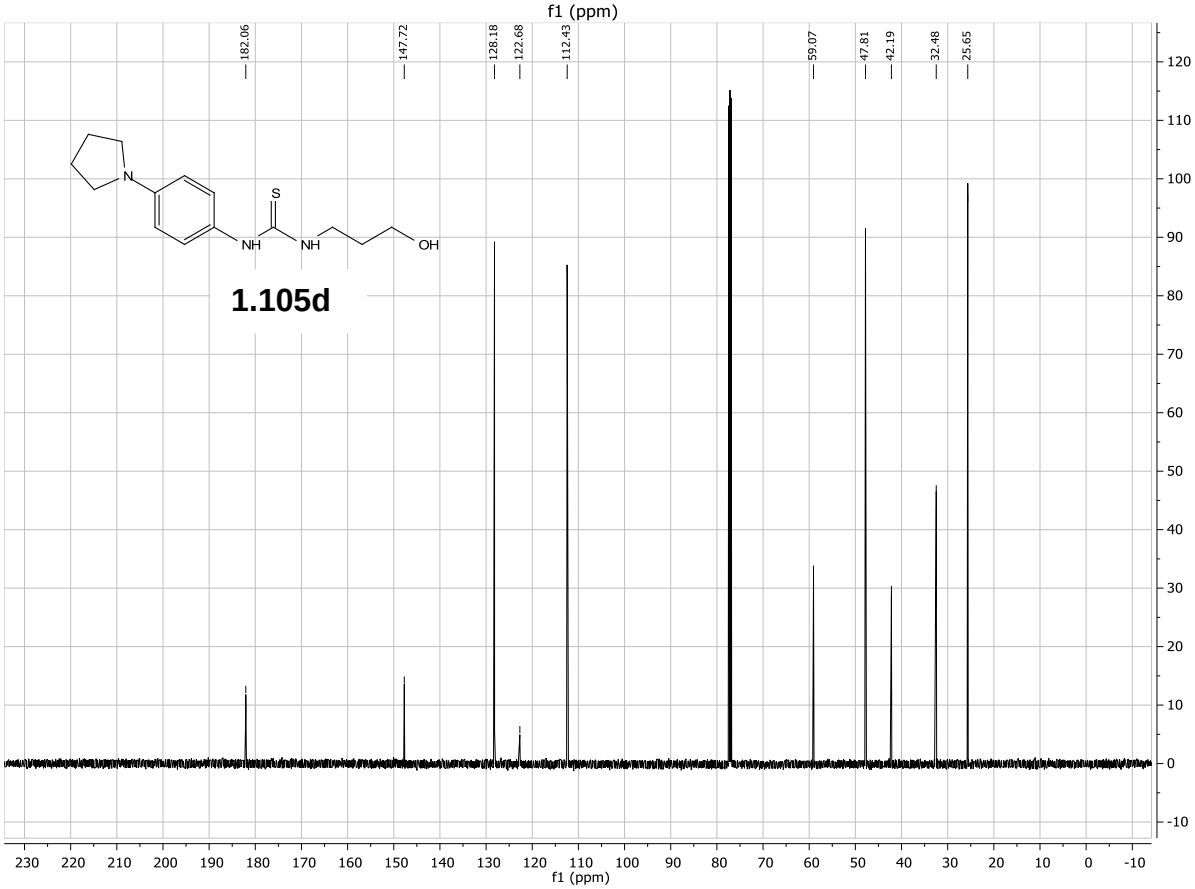
7.04
7.01
6.54
6.51
6.08
3.83
3.81
3.79
3.77
3.67
3.65
3.63
3.61
3.30
3.28
3.25
3.00
2.97
2.95
2.04
2.03
2.03
2.02
2.01
2.00
1.71
1.69
1.69
1.68
1.67
1.67
1.66
1.65
1.65
1.63
N
S
NH
NH
OH
1.105d
0.96
2.00
2.13
0.98
2.14
2.22
4.15
1.06
4.28
2.28
f1 (ppm)


182.06
147.72
128.18
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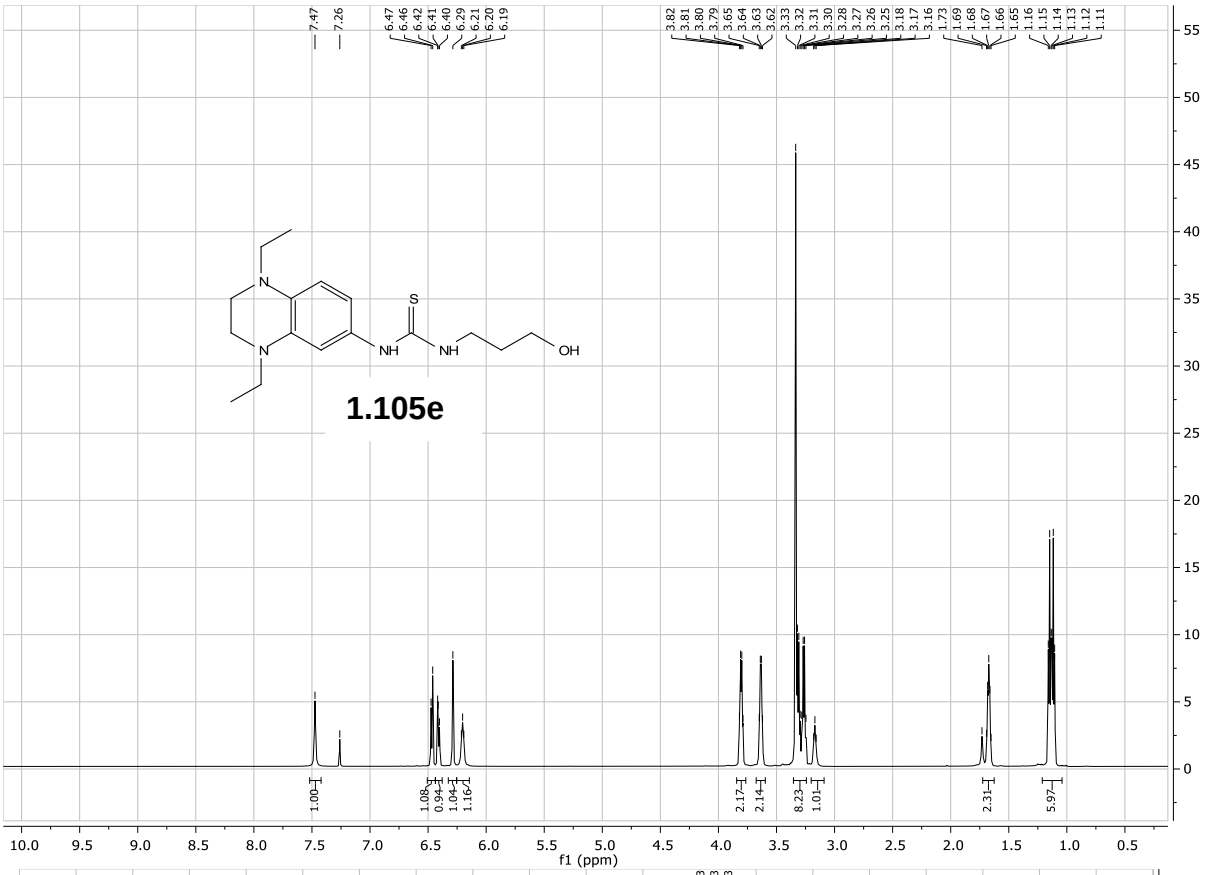
47.81
42.19
32.48
25.65
N
S
NH
NH
OH
1.105d
f1 (ppm)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6.41
6.40
6.29
6.21
6.20
6.19
3.82
3.81
3.80
3.79
3.65
3.64
3.63
3.62
3.33
3.32
3.31
3.30
3.28
3.27
3.26
3.25
3.18
3.17
3.16
1.73
1.69
1.68
1.67
1.66
1.65
1.16
1.15
1.14
1.13
1.12
1.11
1.00
1.08
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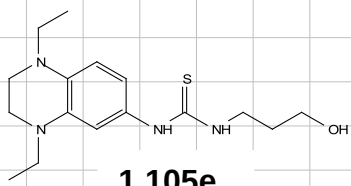
1.04
1.16
2.17
2.14
8.23
1.01
2.31
5.97
f1 (ppm)

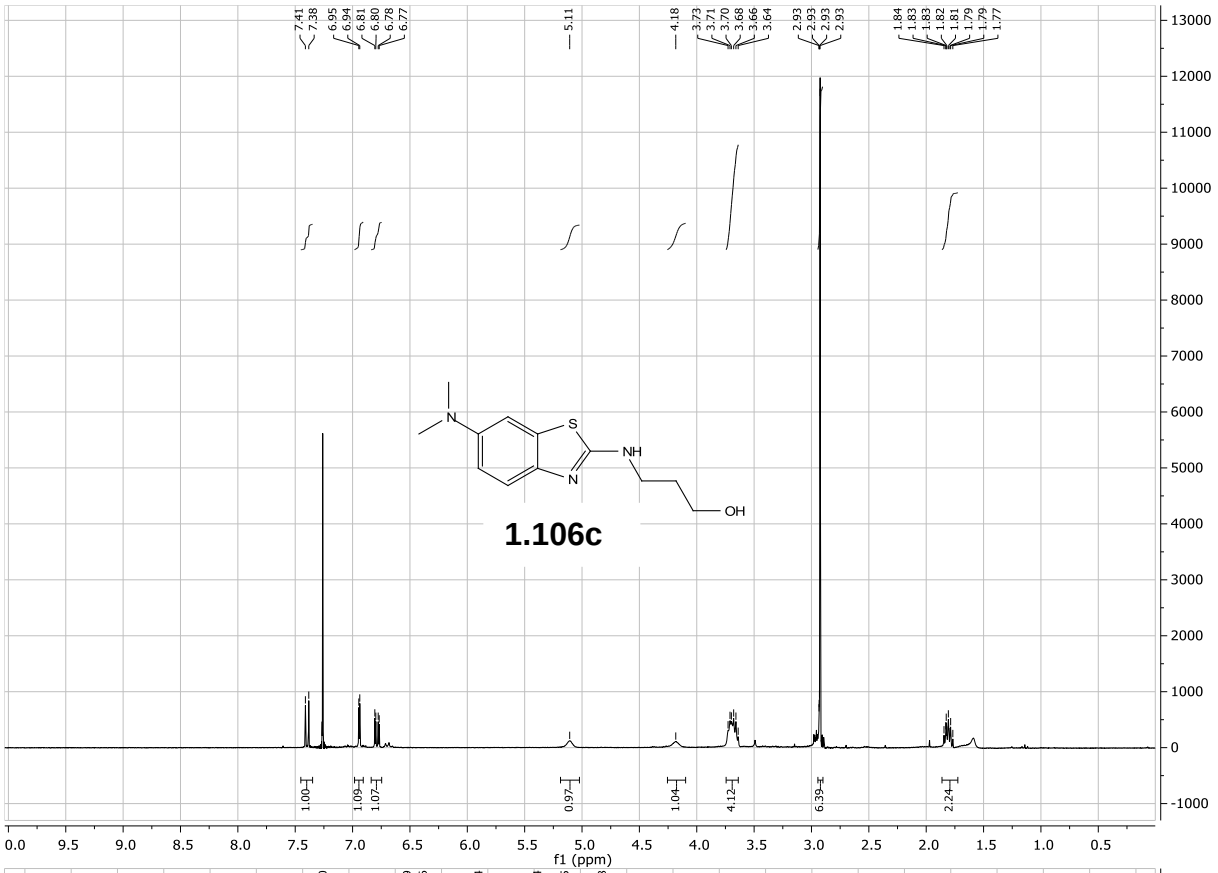

S
NH
NH
OH

1.105e

181.65
136.09
134.89
124.90
115.26
110.59
108.49
77.37 cdcl3
77.16 cdcl3
76.95 cdcl3
58.63
46.28
46.23
45.44
45.38
41.79
32.68
10.37
10.20
f1 (ppm)

S
NH
NH
OH

1.105e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6.78
6.77
5.11
4.18
3.73
3.71
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3.68
3.66
3.64
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2.93
2.93
2.93
1.84
1.83
1.83
1.82
1.81
1.79
1.79
1.77
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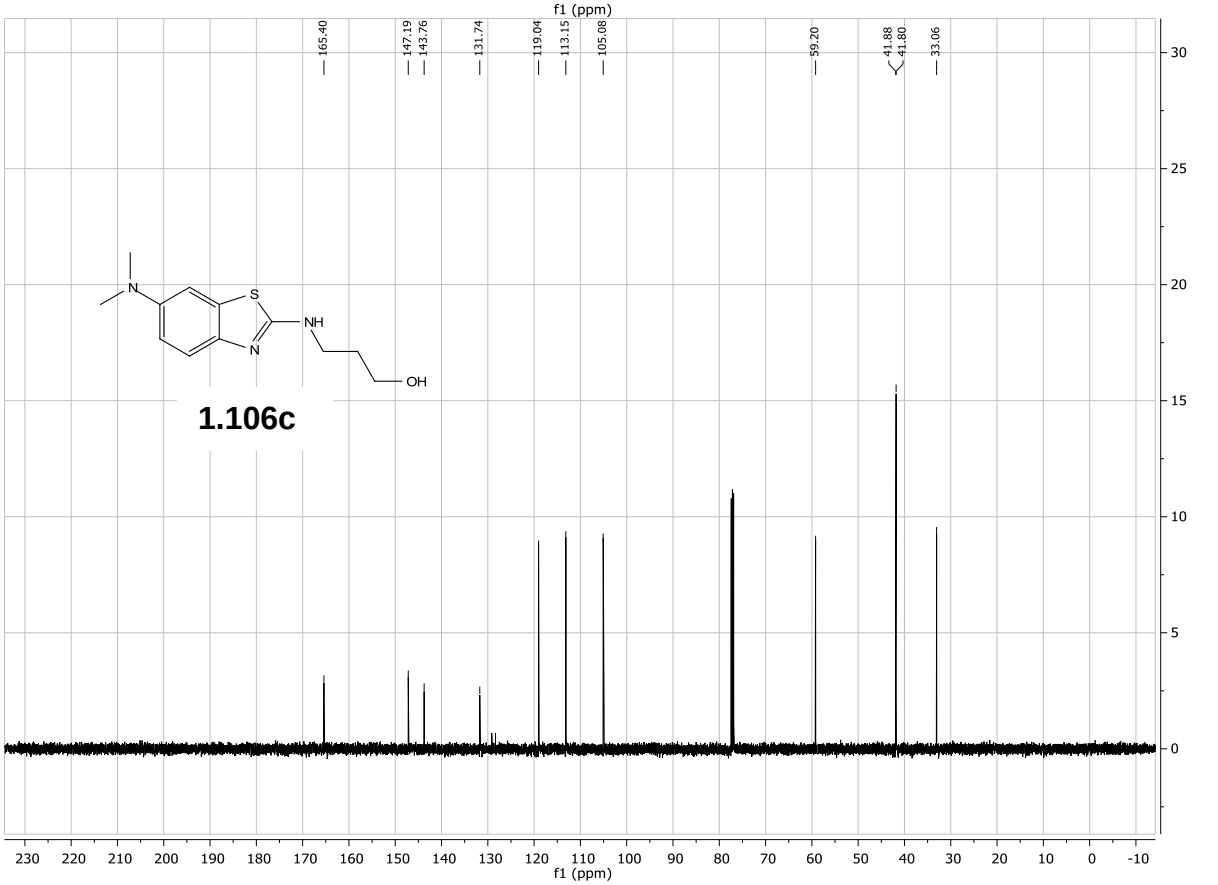
1.09
1.07
0.97
1.04
4.12
6.39
2.24
f1 (ppm)
1.106c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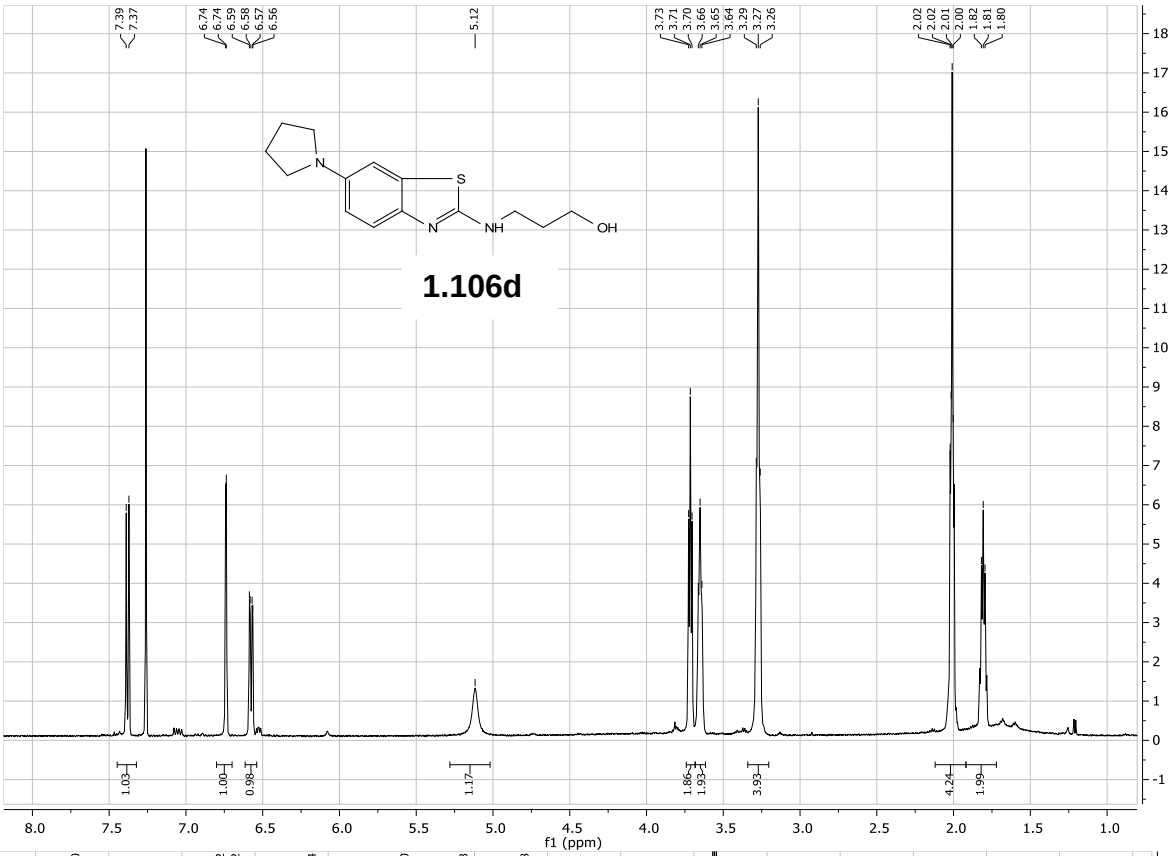
113.15
105.08
59.20
41.88
41.80
33.06
f1 (ppm)
1.106c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6.57
6.56
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3.71
3.70
3.66
3.65
3.64
3.29
3.27
3.26
2.02
2.02
2.01
2.00
1.82
1.81
1.80
N
S
N
NH
OH
1.106d
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1.00
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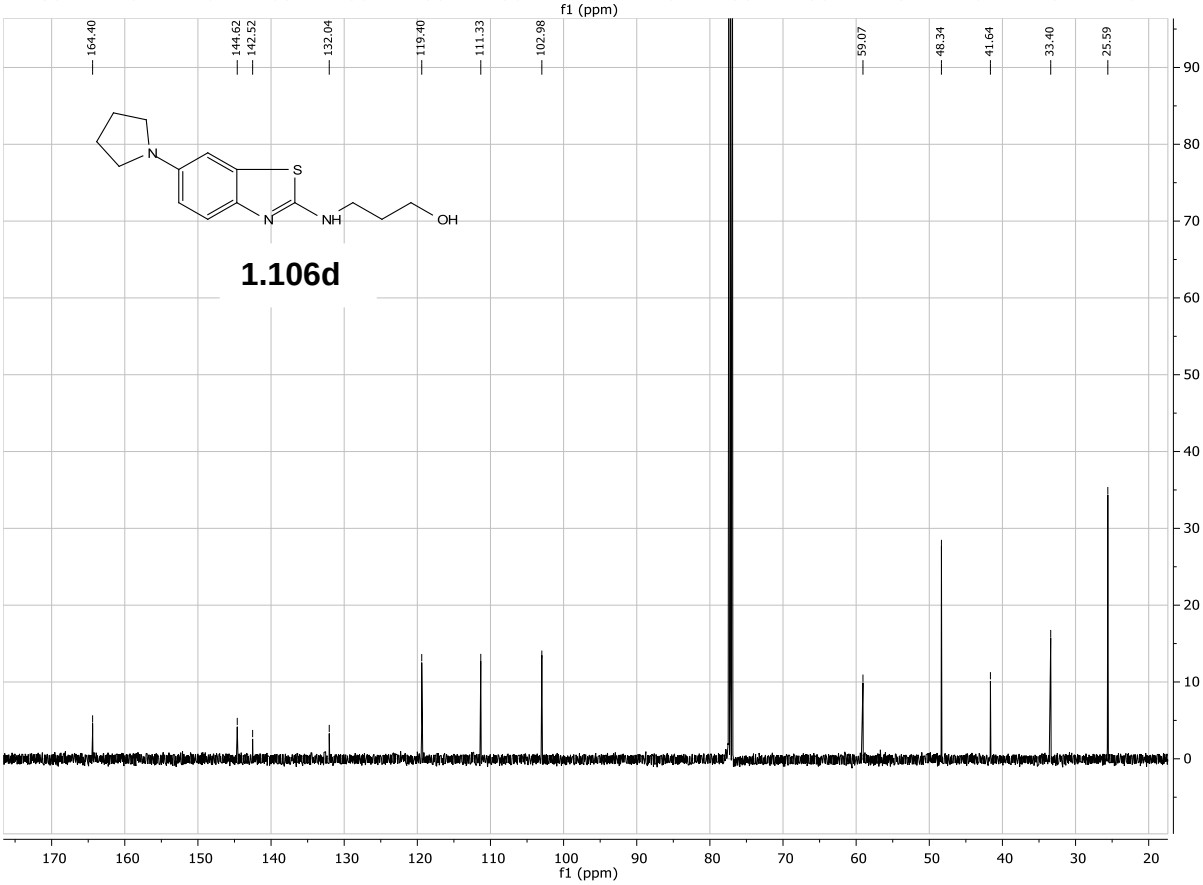
1.17
1.86
1.93
3.93
4.24
1.99
f1 (ppm)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119.40
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41.64
33.40
25.59
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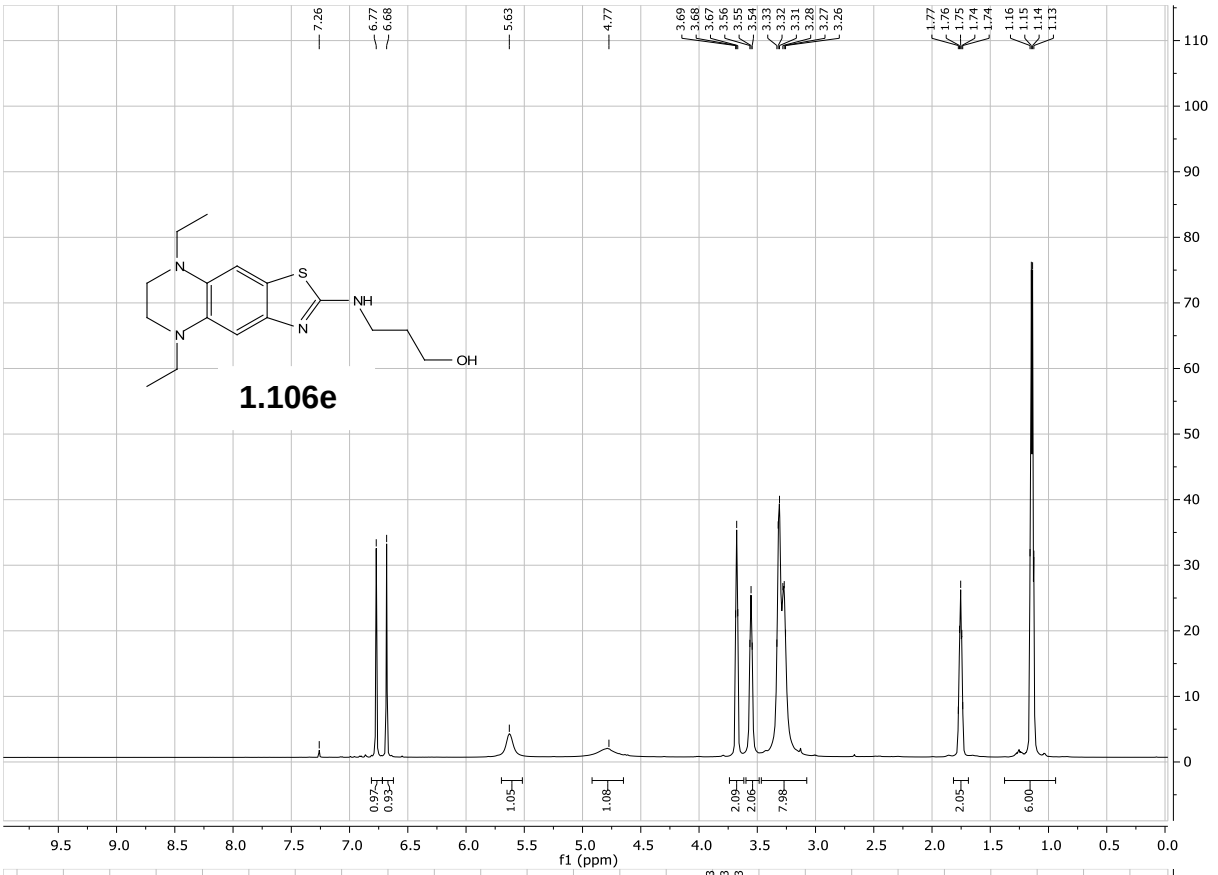
S
N
NH
OH
1.106d
f1 (ppm)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3.54
3.33
3.32
3.31
3.28
3.27
3.26
1.77
1.76
1.75
1.74
1.74
1.16
1.15
1.14
1.13
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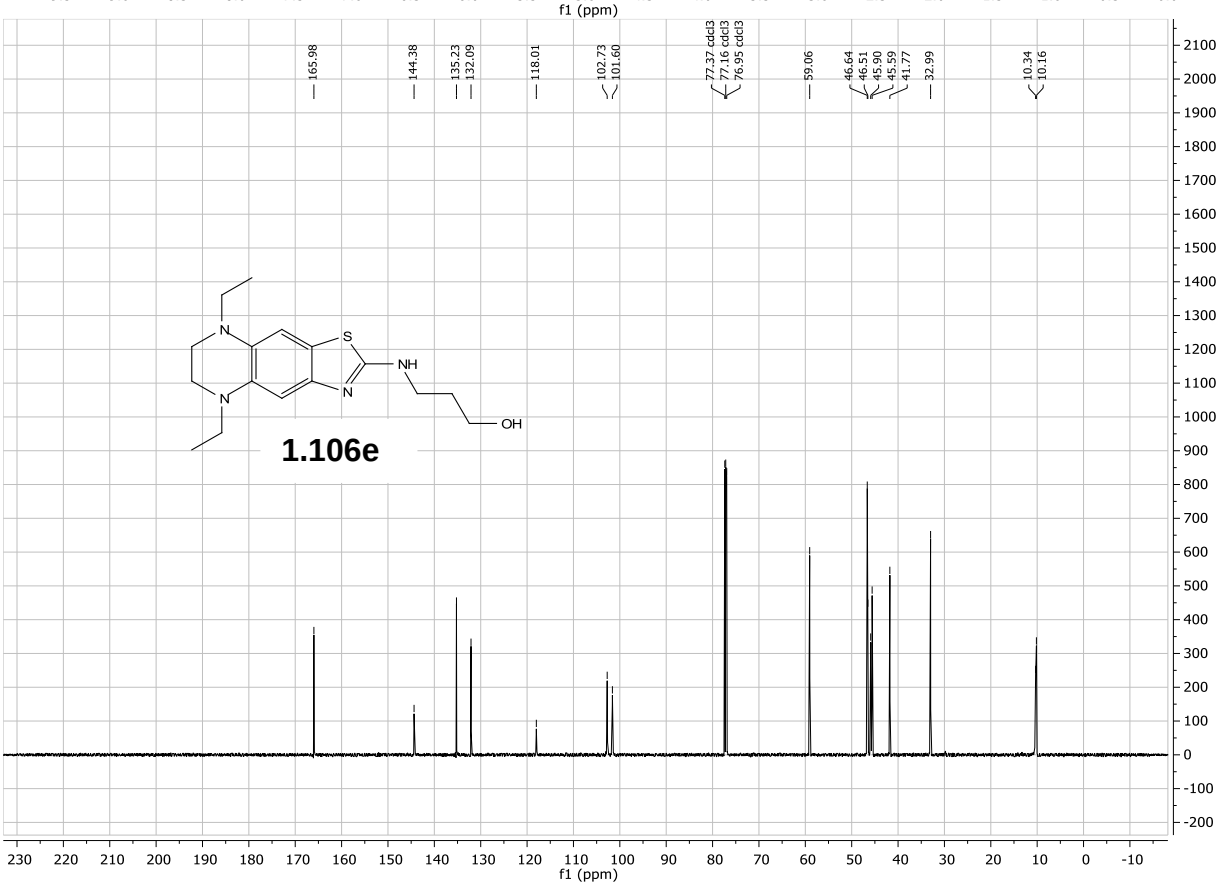
0.93
1.05
1.08
2.09
2.06
7.98
2.05
6.00
f1 (ppm)

1.106e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132.09
118.01
102.73
101.60
77.37 cdcl3
77.16 cdcl3
76.95 cdcl3
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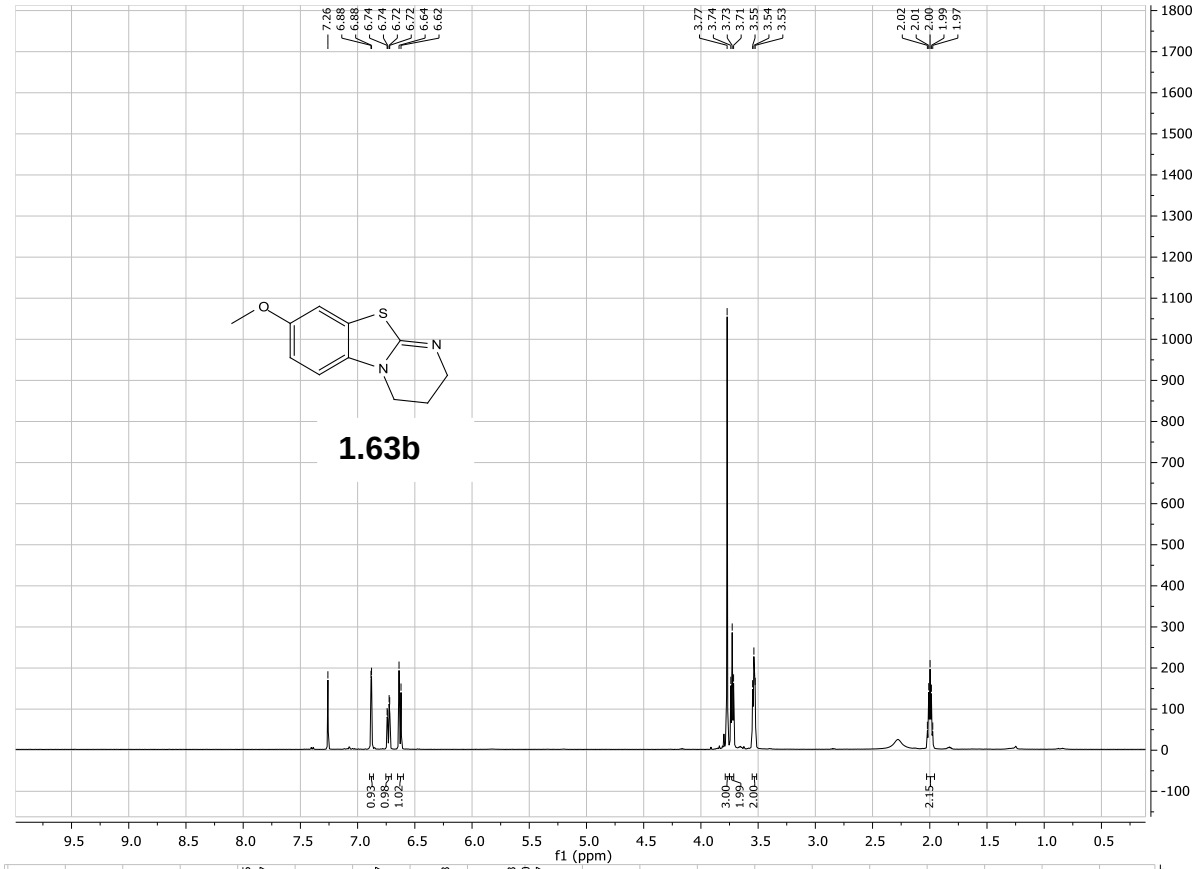
46.51
45.90
45.59
41.77
32.99
10.34
10.16
f1 (ppm)

1.106e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6.64
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3.74
3.73
3.71
3.55
3.54
3.53
2.02
2.01
2.00
1.99
1.97
O
S
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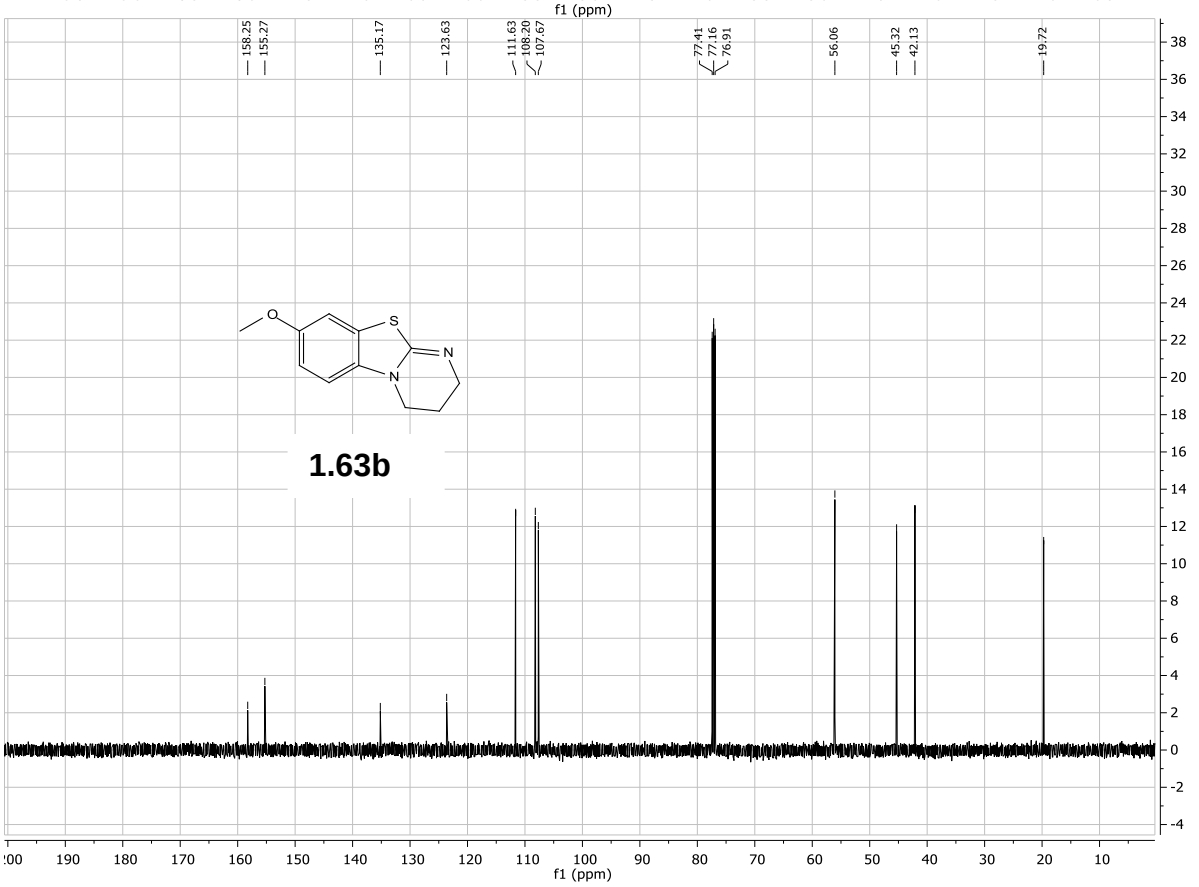
N
1.63b
0.93
0.98
1.02
3.00
1.99
2.00
2.15
f1 (ppm)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107.67
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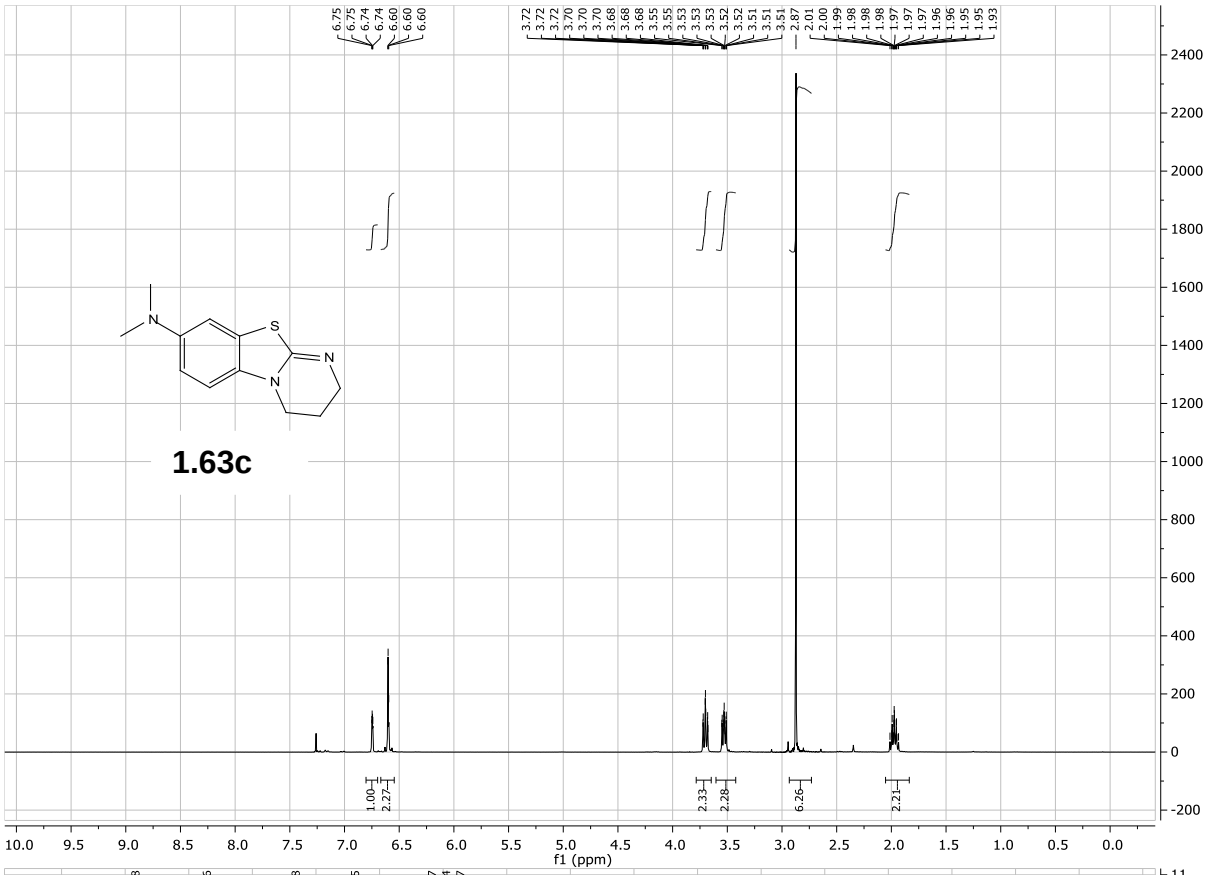
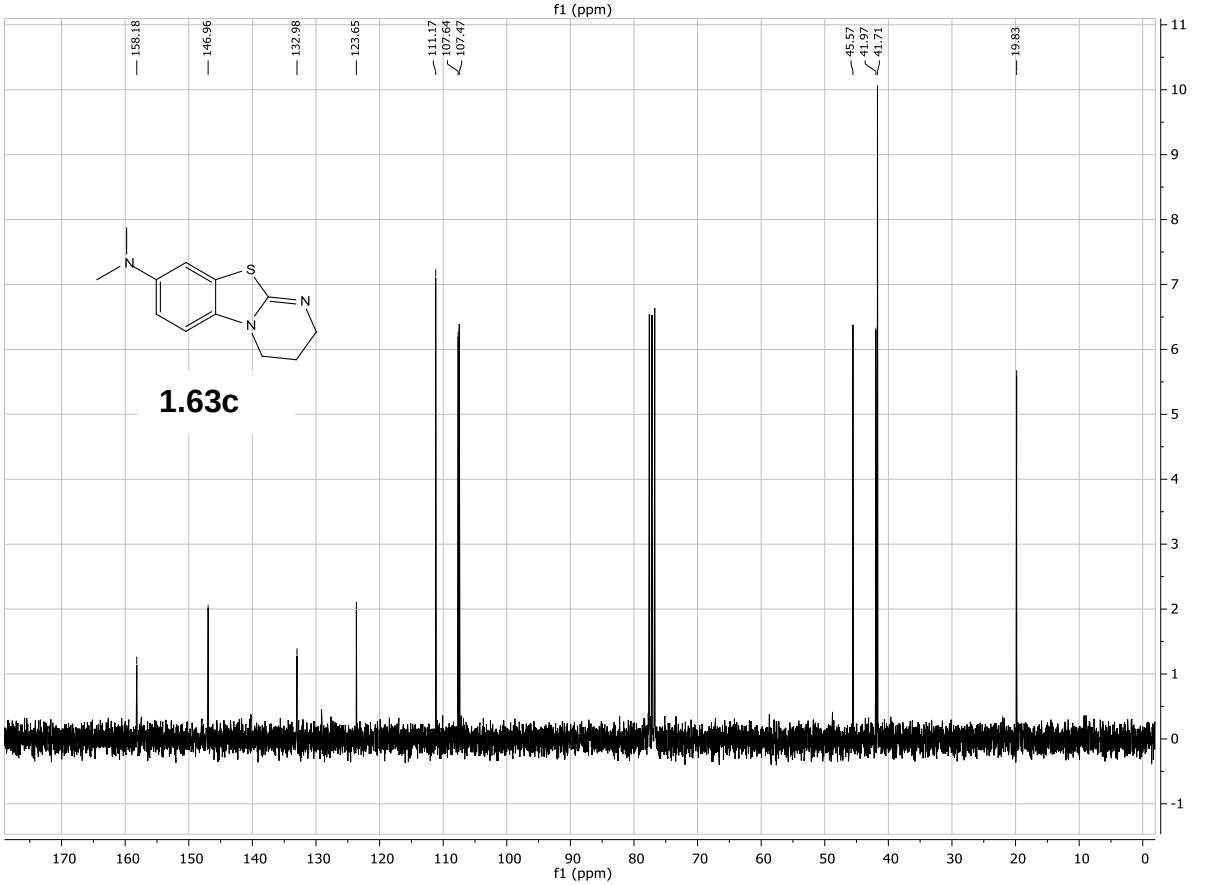
77.16
76.91
56.06
45.32
42.13
19.72
O
S
N
N
1.63b
f1 (ppm)


1.63c
f1 (ppm)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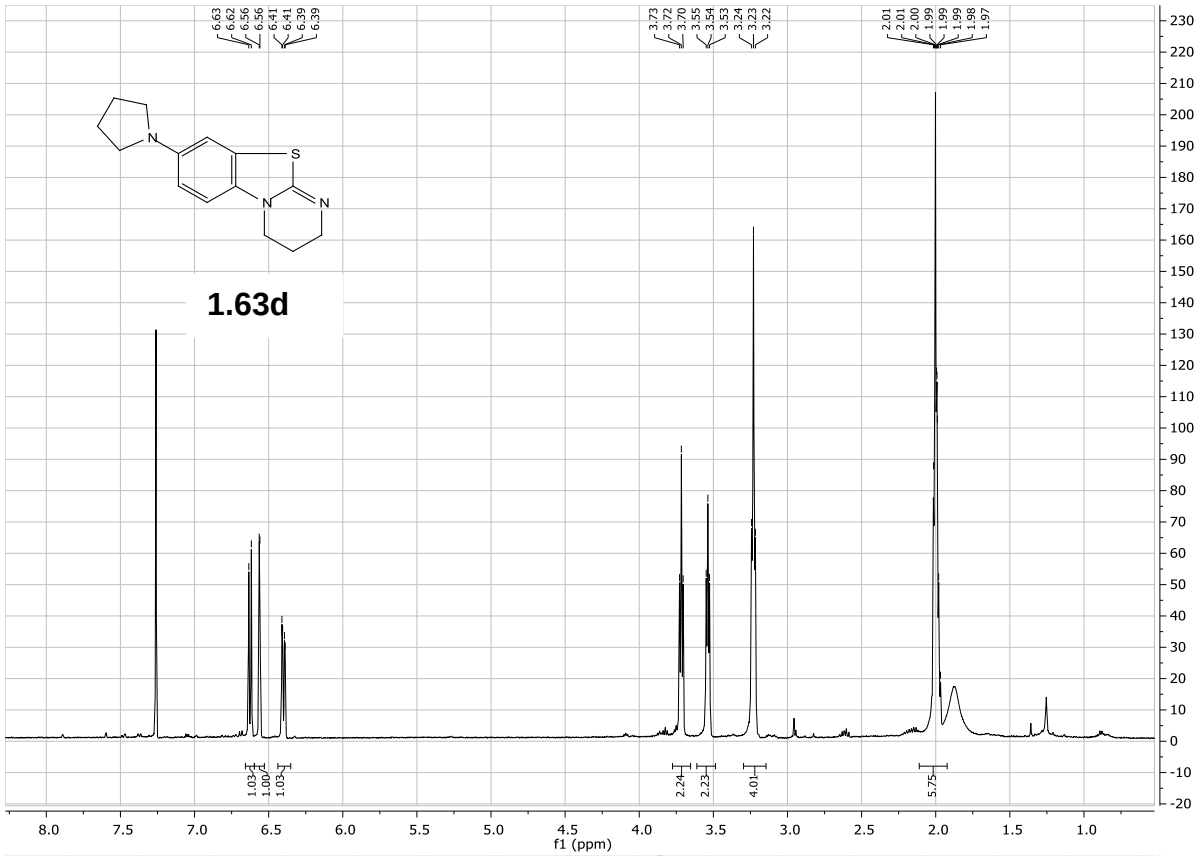
f1 (ppm)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3.70
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3.54
3.53
3.24
3.23
3.22
2.01
2.01
2.00
1.99
1.99
1.99
1.98
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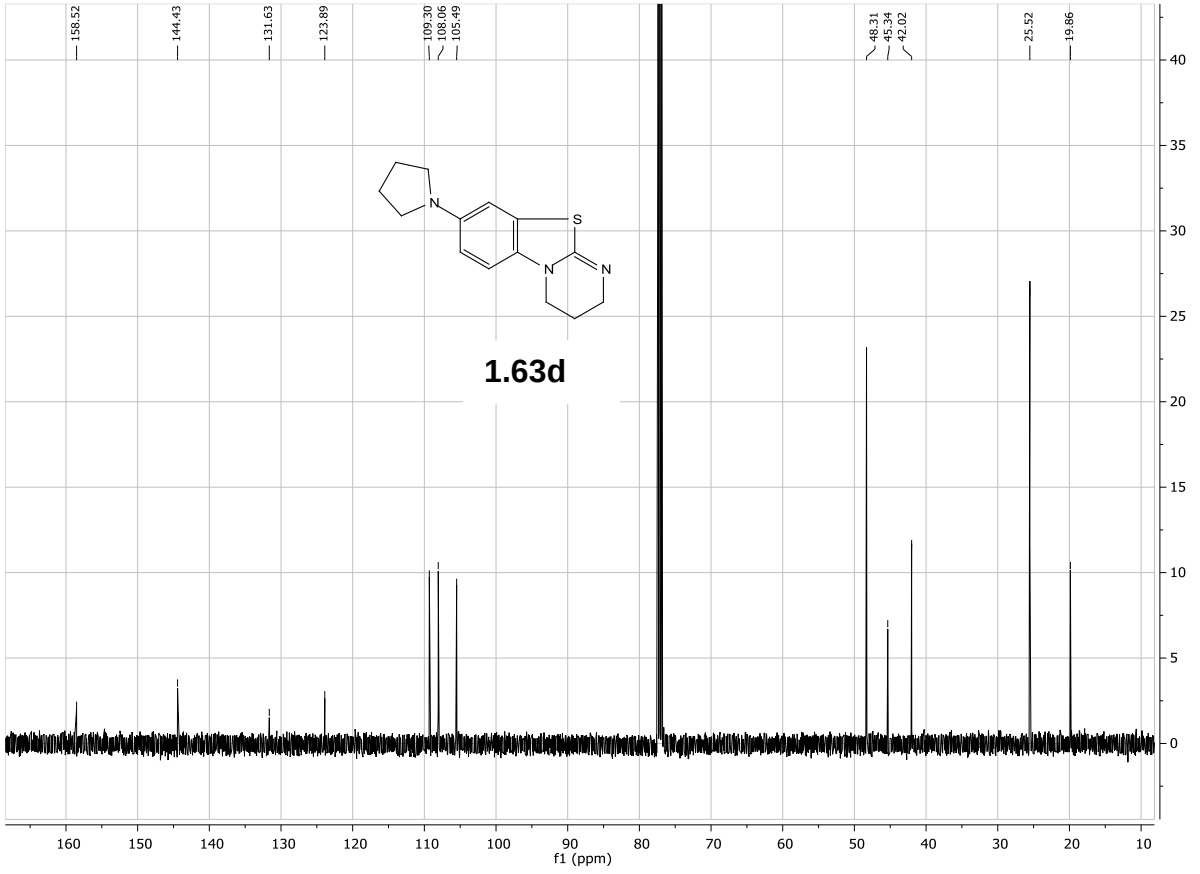
1.03
1.00
1.03
2.24
2.23
4.01
5.75
f1 (ppm)

1.63d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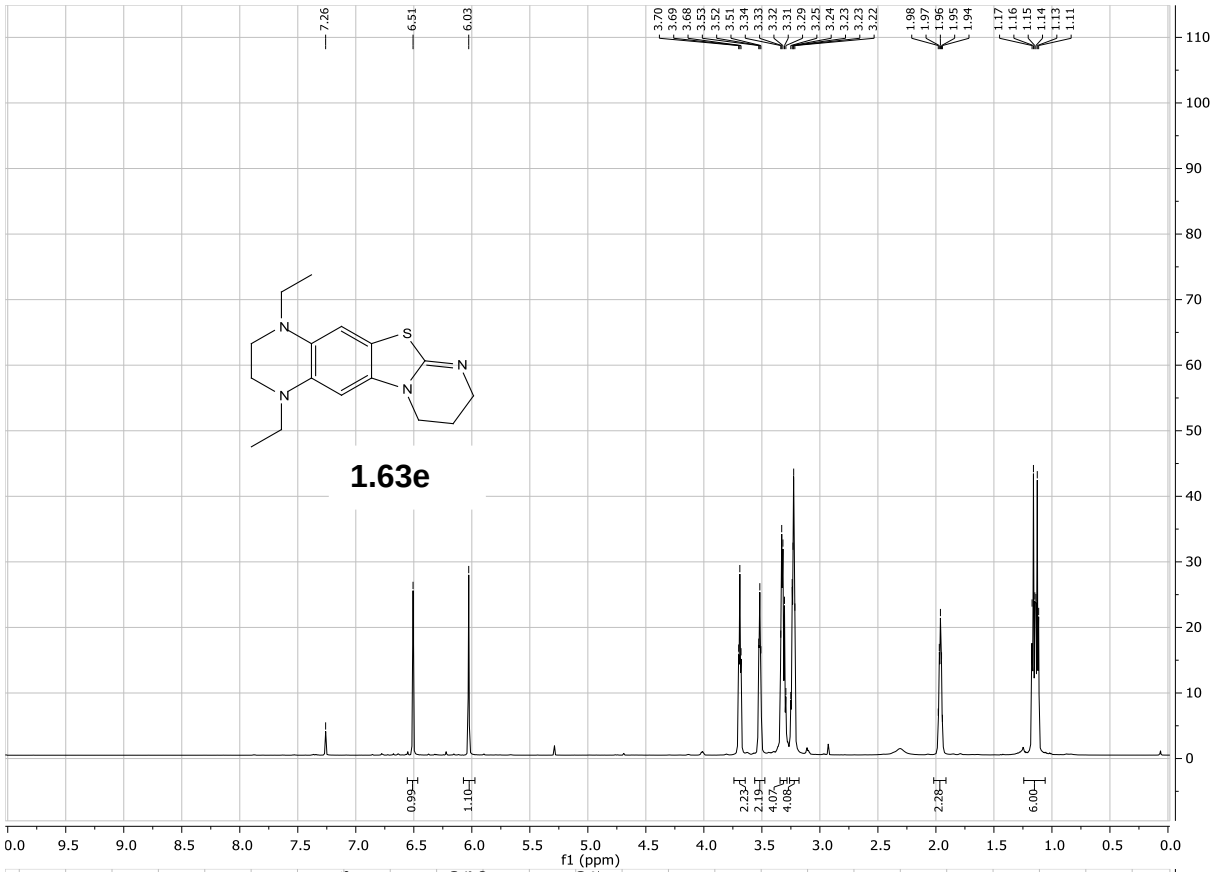
25.52
19.86
f1 (ppm)

1.63d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3.31
3.29
3.25
3.24
3.23
3.23
3.22
1.98
1.97
1.96
1.95
1.94
1.17
1.16
1.15
1.14
1.13
1.11
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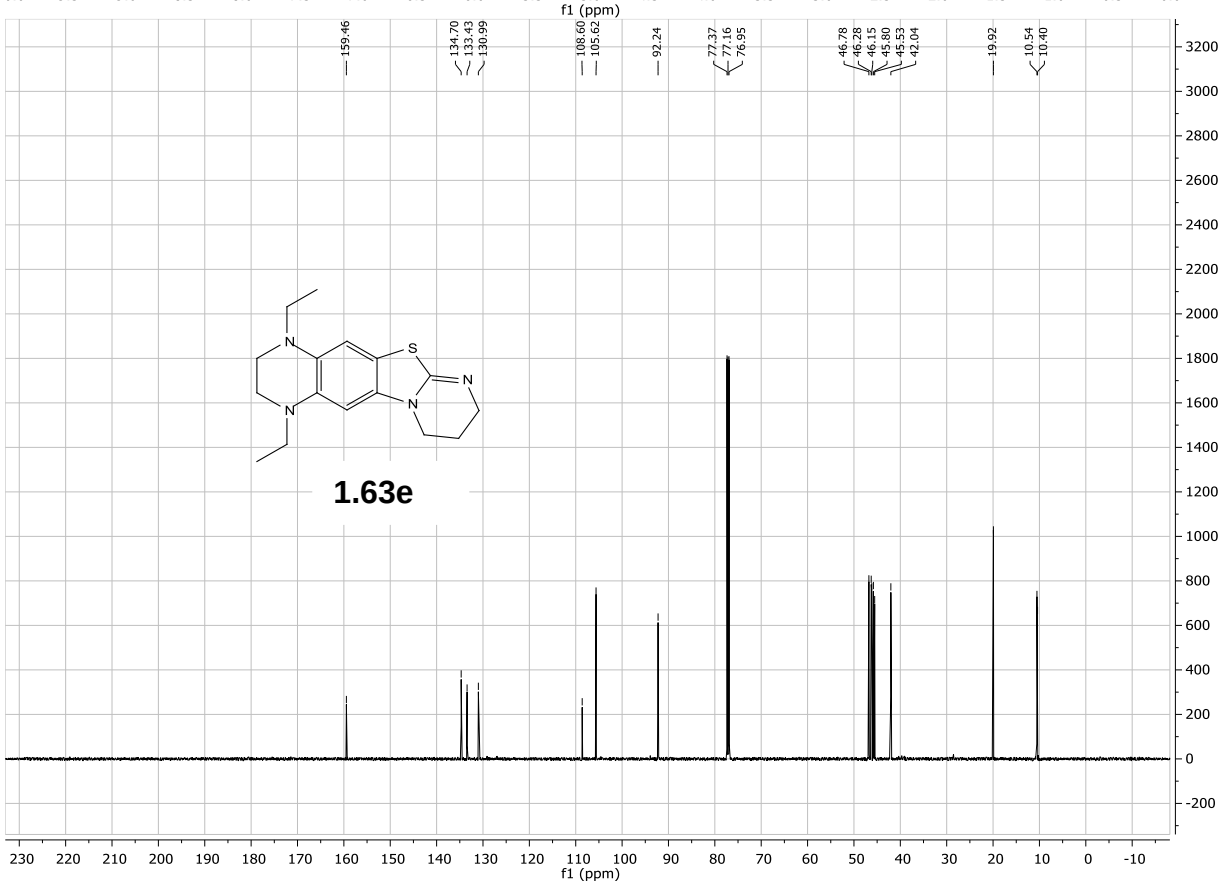
0.99
1.10
2.23
2.19
4.07
4.08
2.28
6.00
f1 (ppm)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105.62
92.24
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77.16
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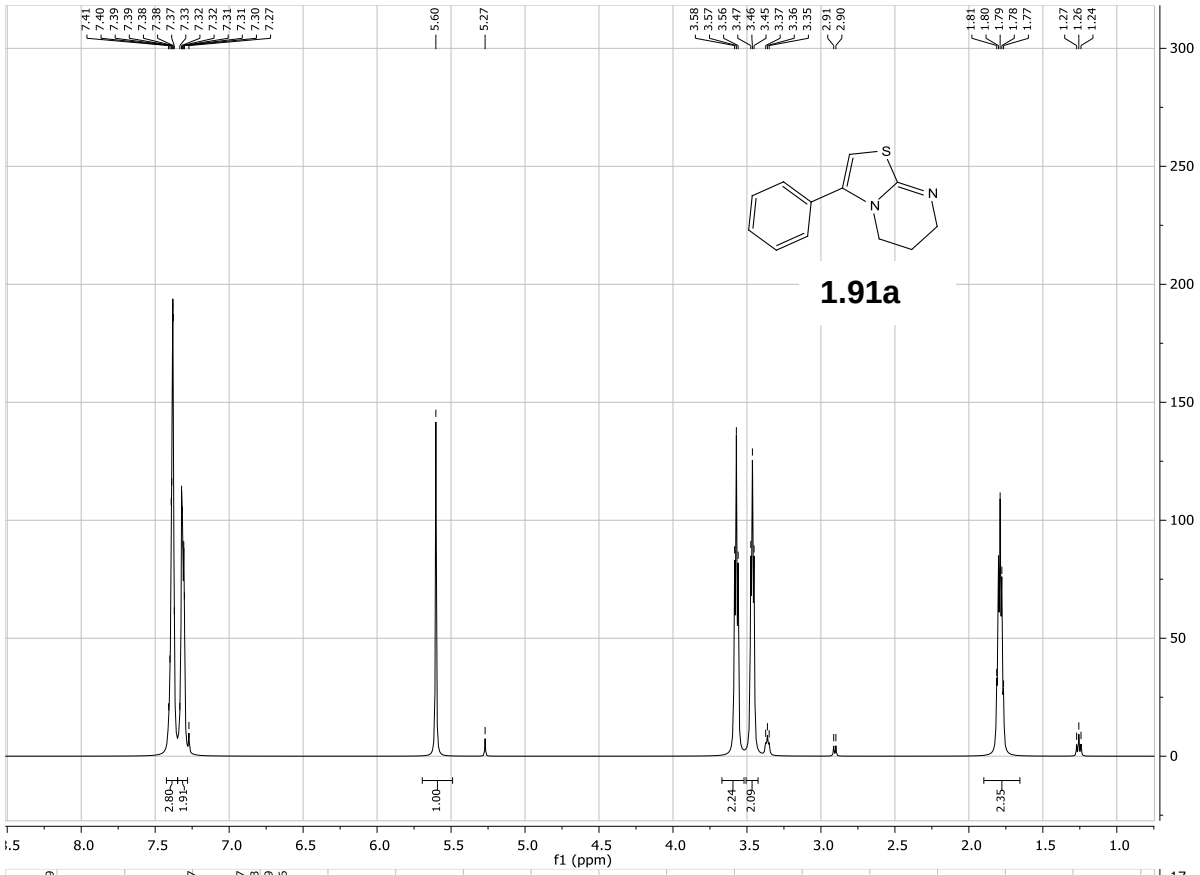
45.80
45.53
42.04
19.92
10.54
10.40
1.63e
f1 (ppm)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7.31
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3.46
3.45
3.37
3.36
3.35
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1.81
1.80
1.79
1.78
1.77
1.27
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1.24
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N
N
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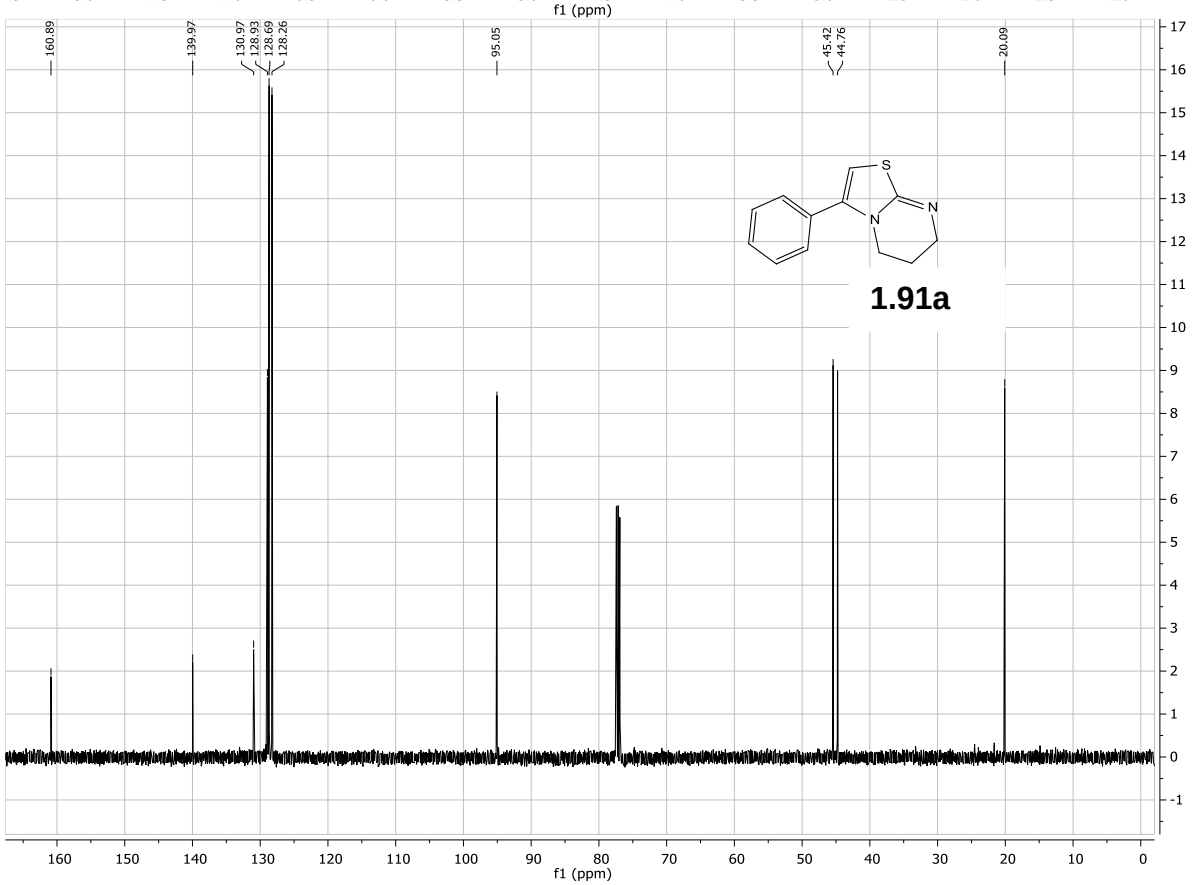
1.91
1.00
2.24
2.09
2.35
f1 (ppm)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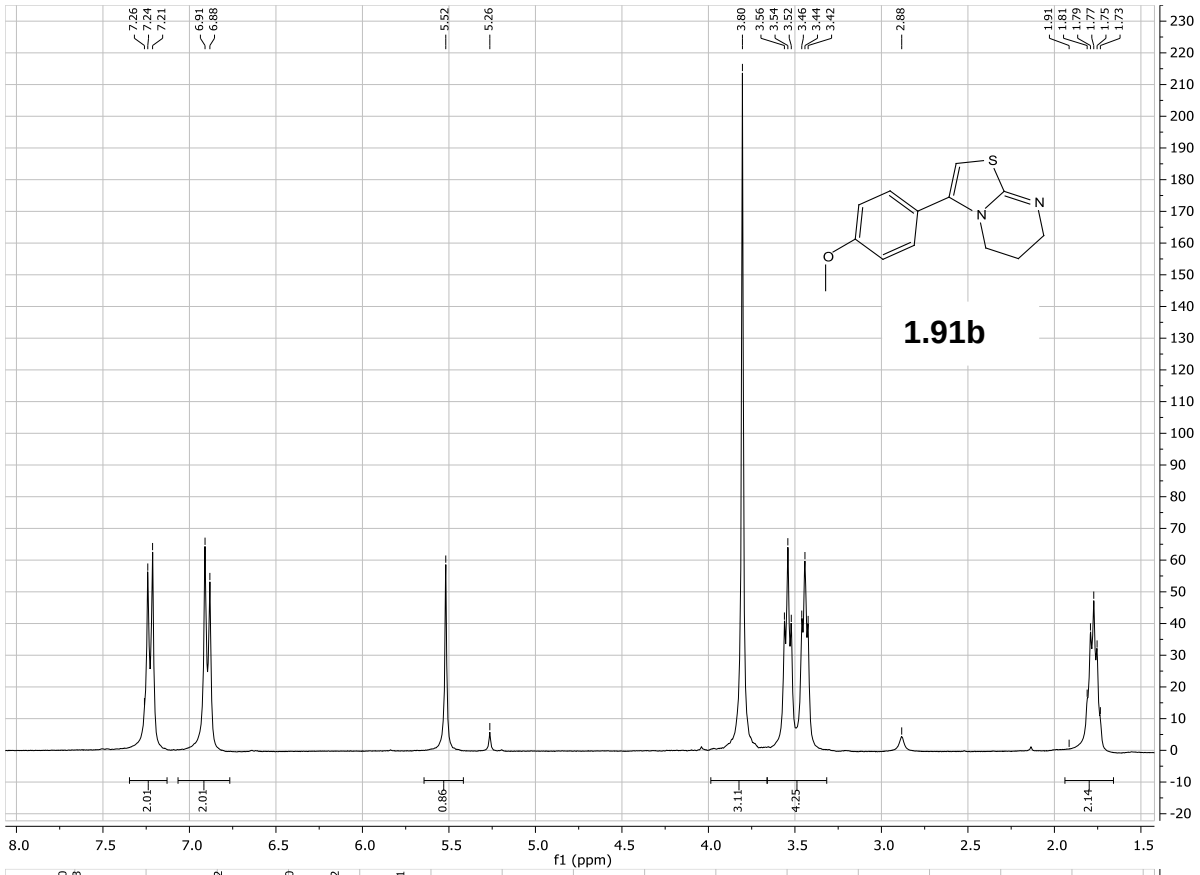
45.42
44.76
20.09
S
N
N
1.91a
f1 (ppm)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5.26
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3.54
3.52
3.46
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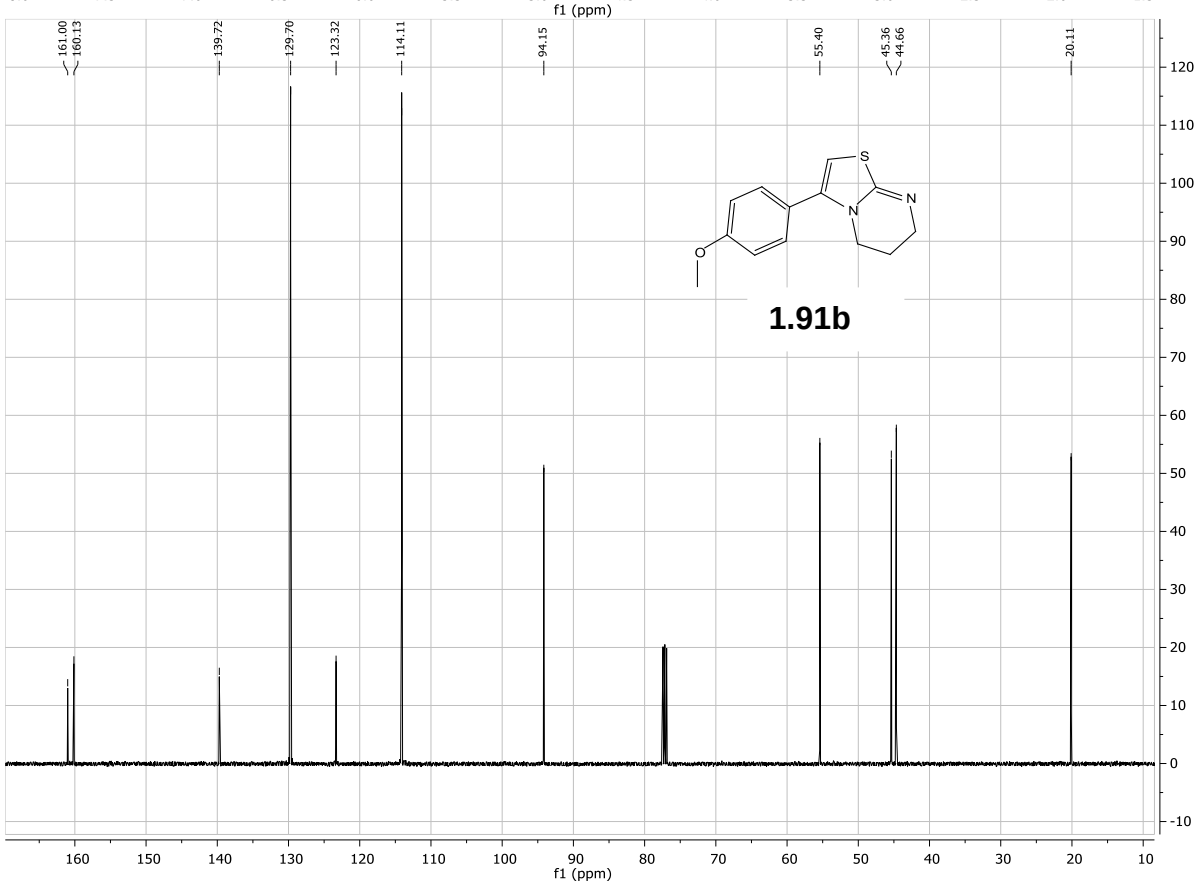
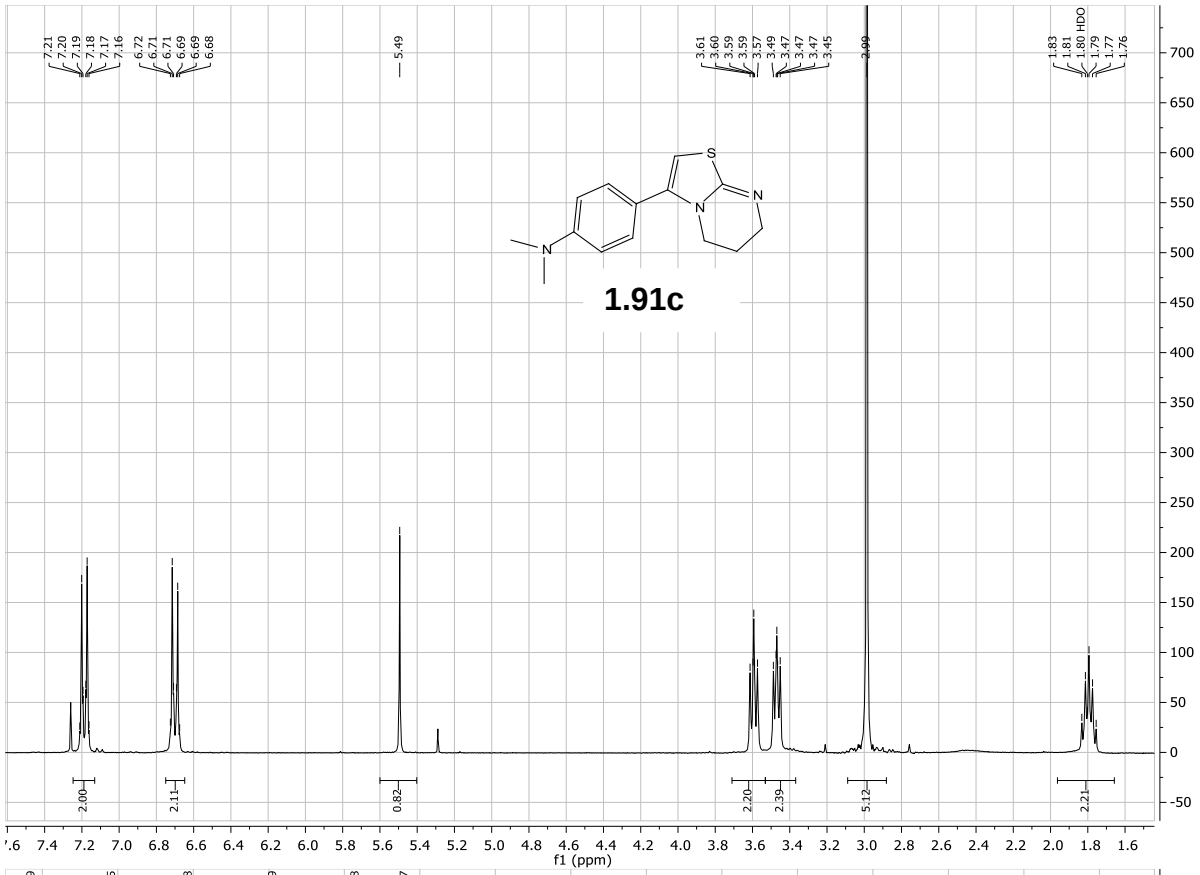
1.91
1.81
1.79
1.77
1.75
1.73
S
N
N
O
1.91b
2.01
2.01
0.86
3.11
4.25
2.14
f1 (ppm)


161.00
160.13
139.72
129.70
123.32
114.11
94.15
55.40
45.36
44.66
20.11
S
N
N
O
1.91b
f1 (ppm)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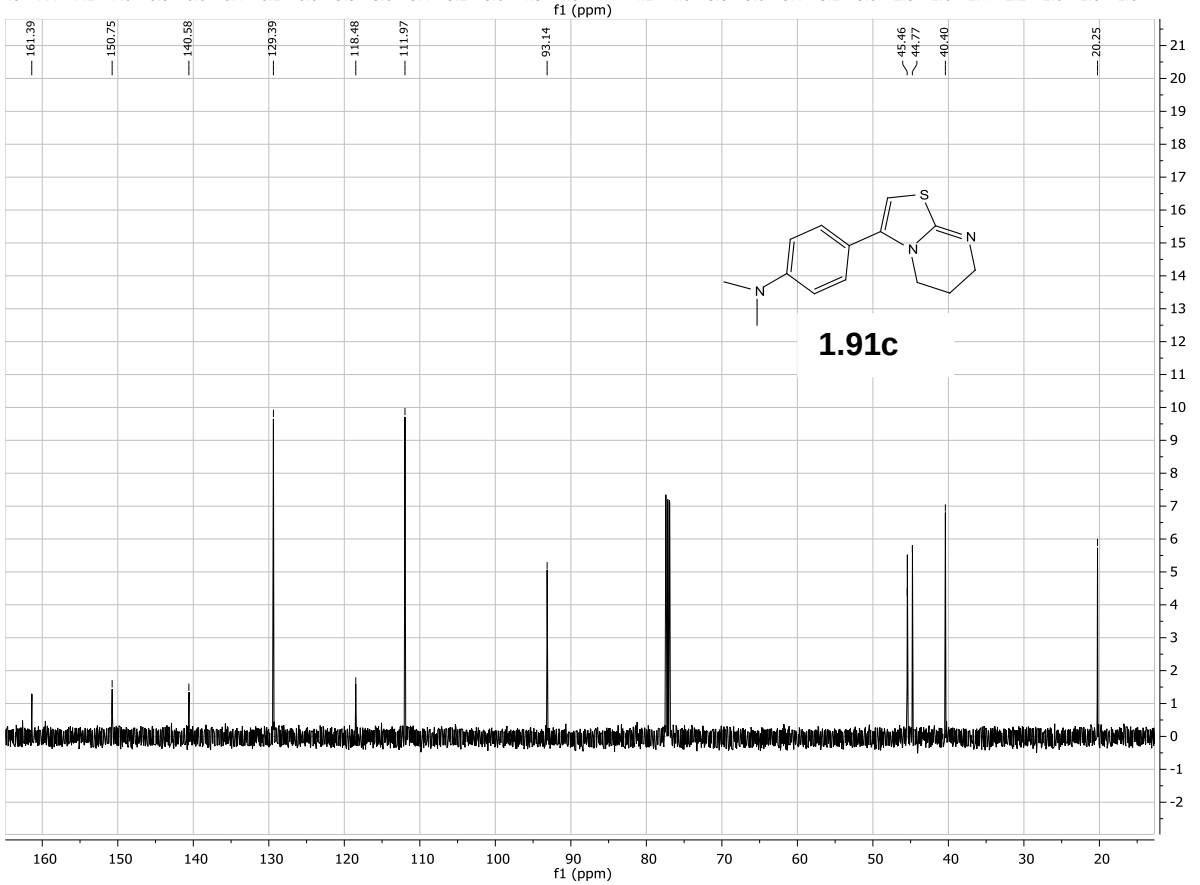
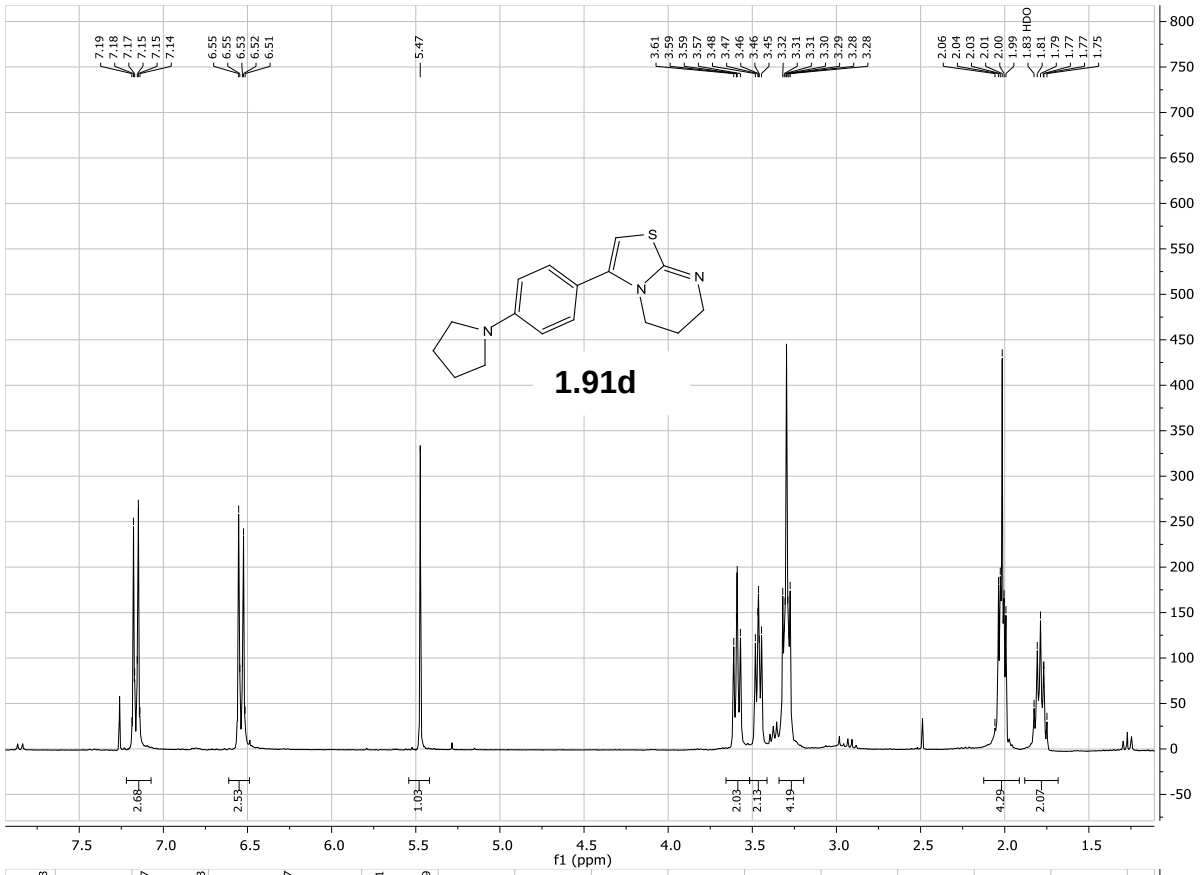
7.20
7.19
7.18
7.17
7.16
6.72
6.71
6.71
6.69
6.69
6.68
5.49
3.61
3.60
3.59
3.59
3.57
3.49
3.47
3.47
3.47
3.45
2.99
1.83
1.81
1.80 HDO
1.79
1.77
1.76
2.00
2.11
0.82
2.20
2.39
5.12
2.21
f1 (ppm)

1.91c


161.39
150.75
140.58
129.39
118.48
111.97
93.14
45.46
44.77
40.40
20.25
f1 (ppm)

1.91c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7.17
7.15
7.15
7.14
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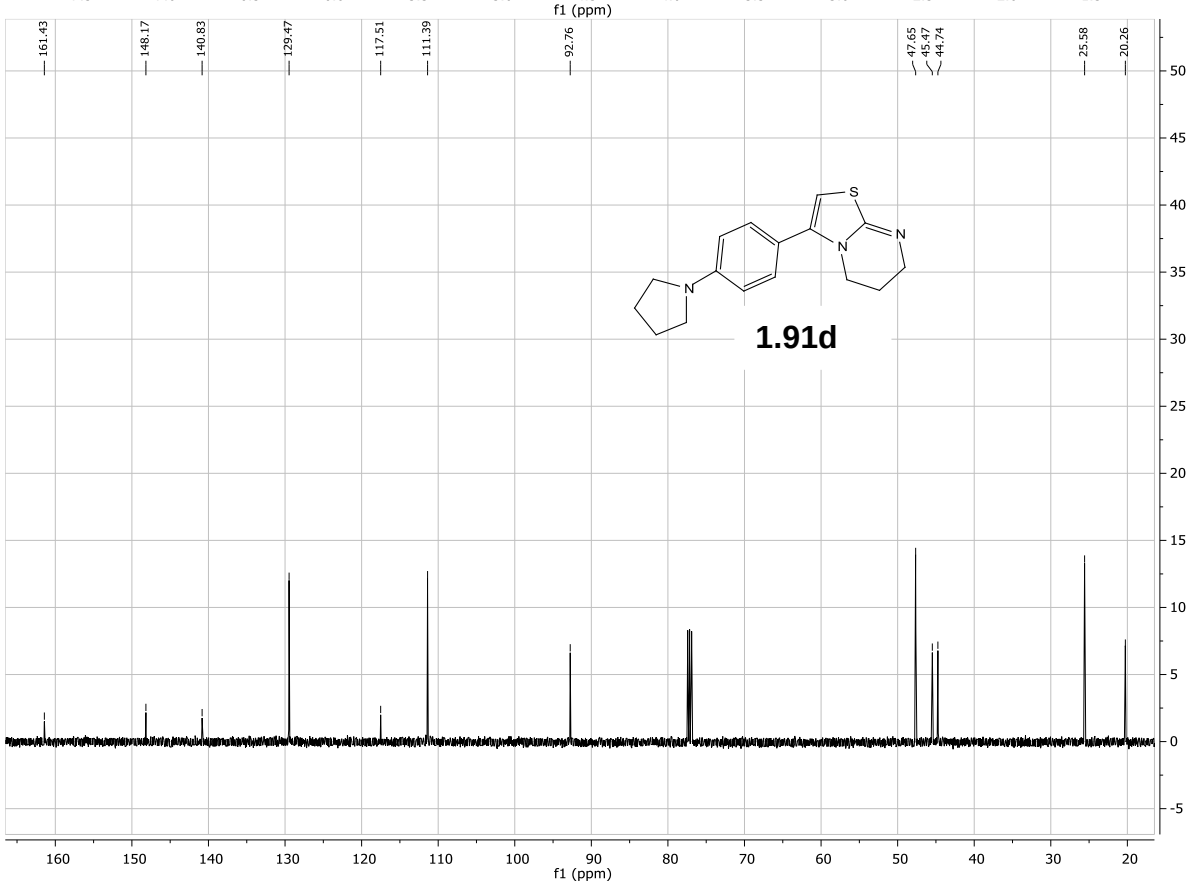
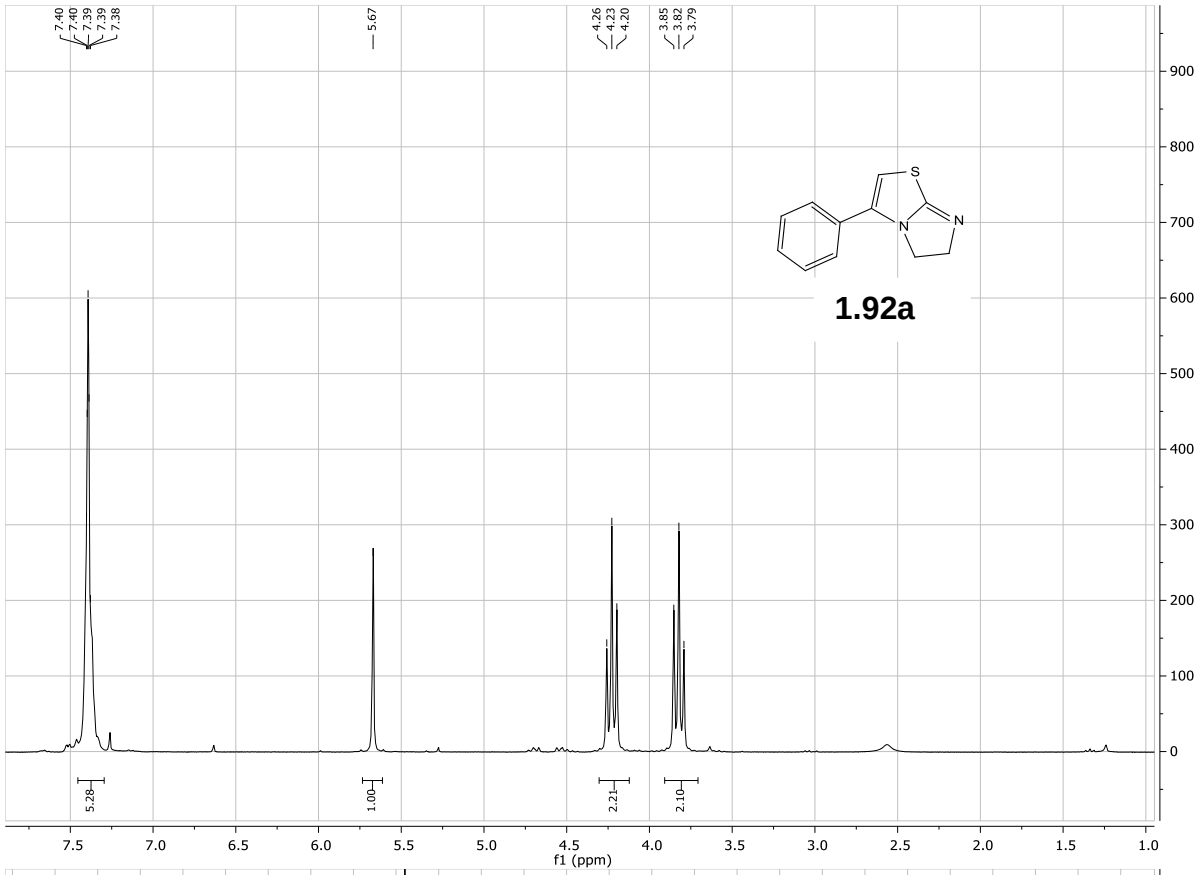
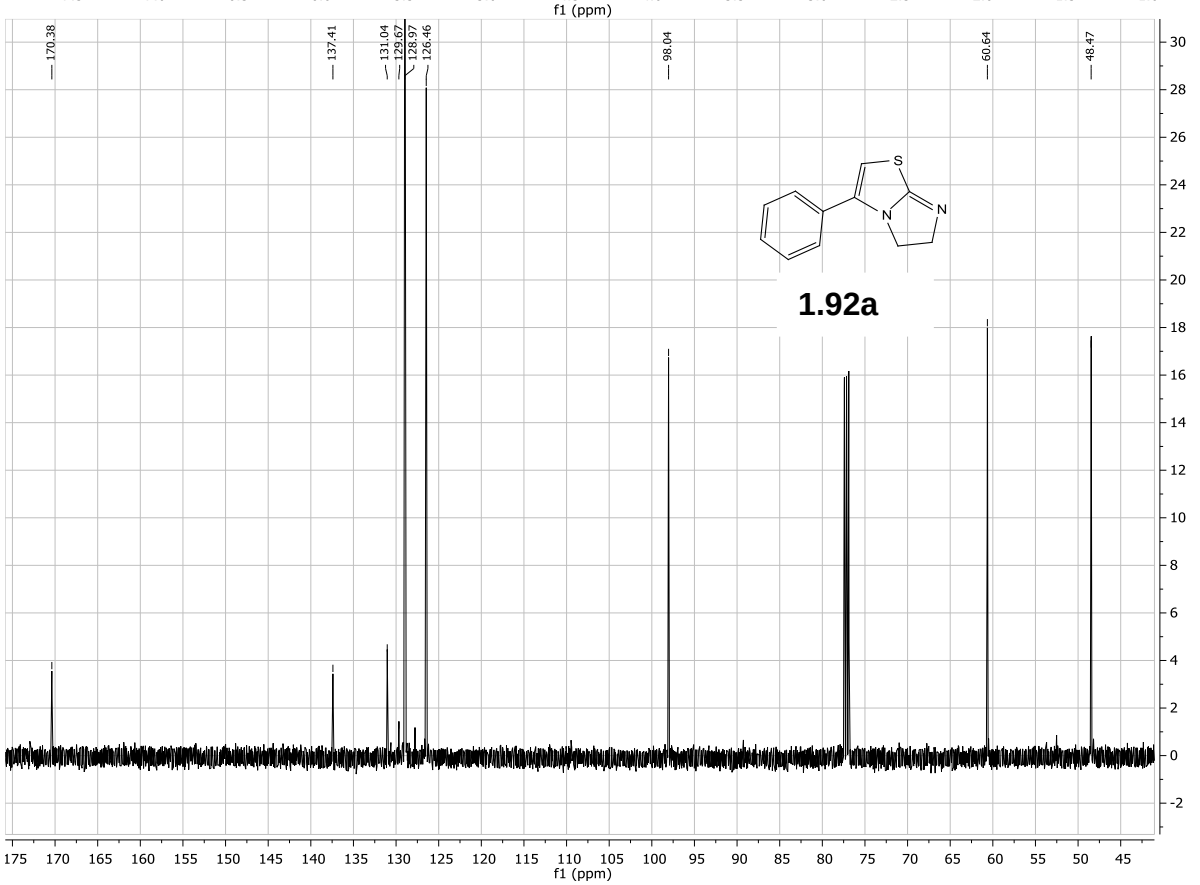
6.55
6.53
6.52
6.51
5.47
3.61
3.59
3.59
3.57
3.48
3.47
3.46
3.46
3.45
3.32
3.31
3.31
3.30
3.29
3.28
3.28
2.06
2.04
2.03
2.01
2.00
1.99
1.83 HDO
1.81
1.79
1.77
1.77
1.75
S
N
N
N
1.91d
2.68
2.53
1.03
2.03
2.13
4.19
4.29
2.07
f1 (ppm)


161.43
148.17
140.83
129.47
117.51
111.39
92.76
47.65
45.47
44.74
25.58
20.26
S
N
N
N
1.91d
f1 (ppm)


7.40
7.40
7.39
7.39
7.38
5.67
4.26
4.23
4.20
3.85
3.82
3.79
S
N
N
1.92a
5.28
1.00
2.21
2.10
f1 (ppm)


170.38
137.41
131.04
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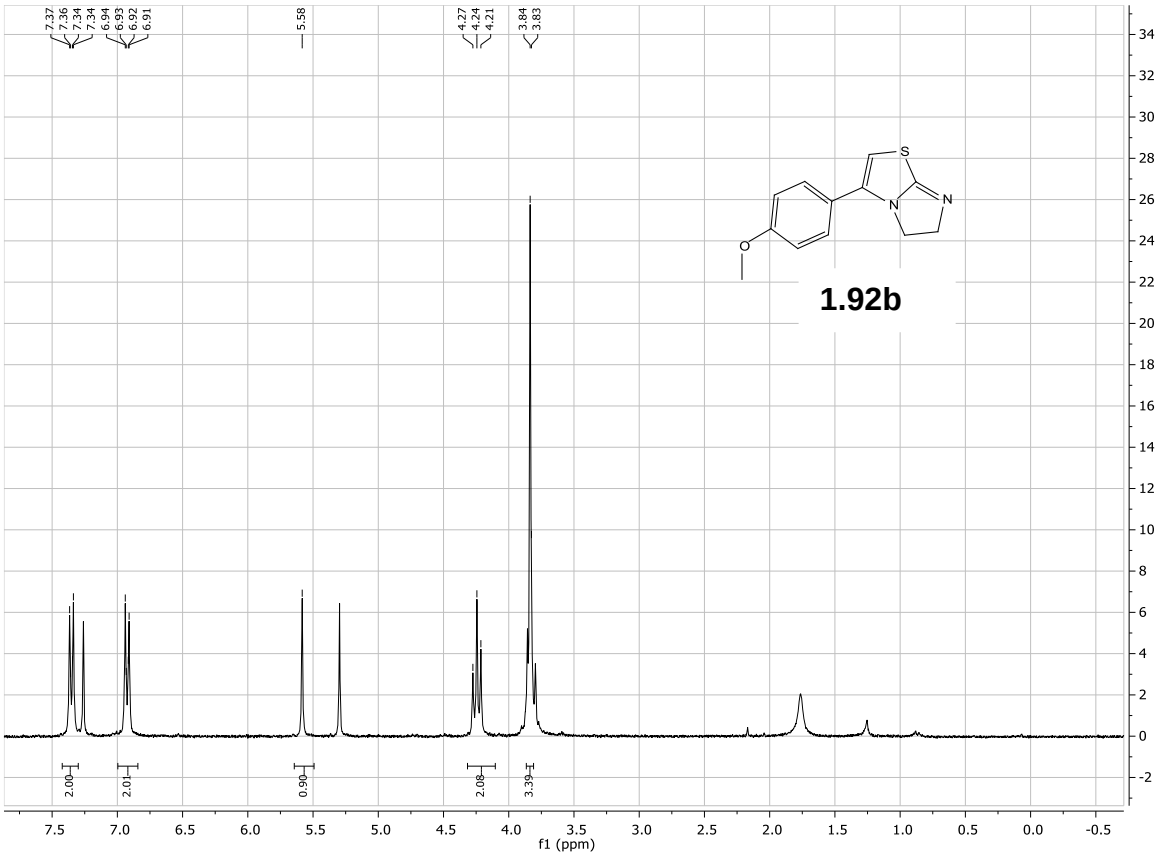
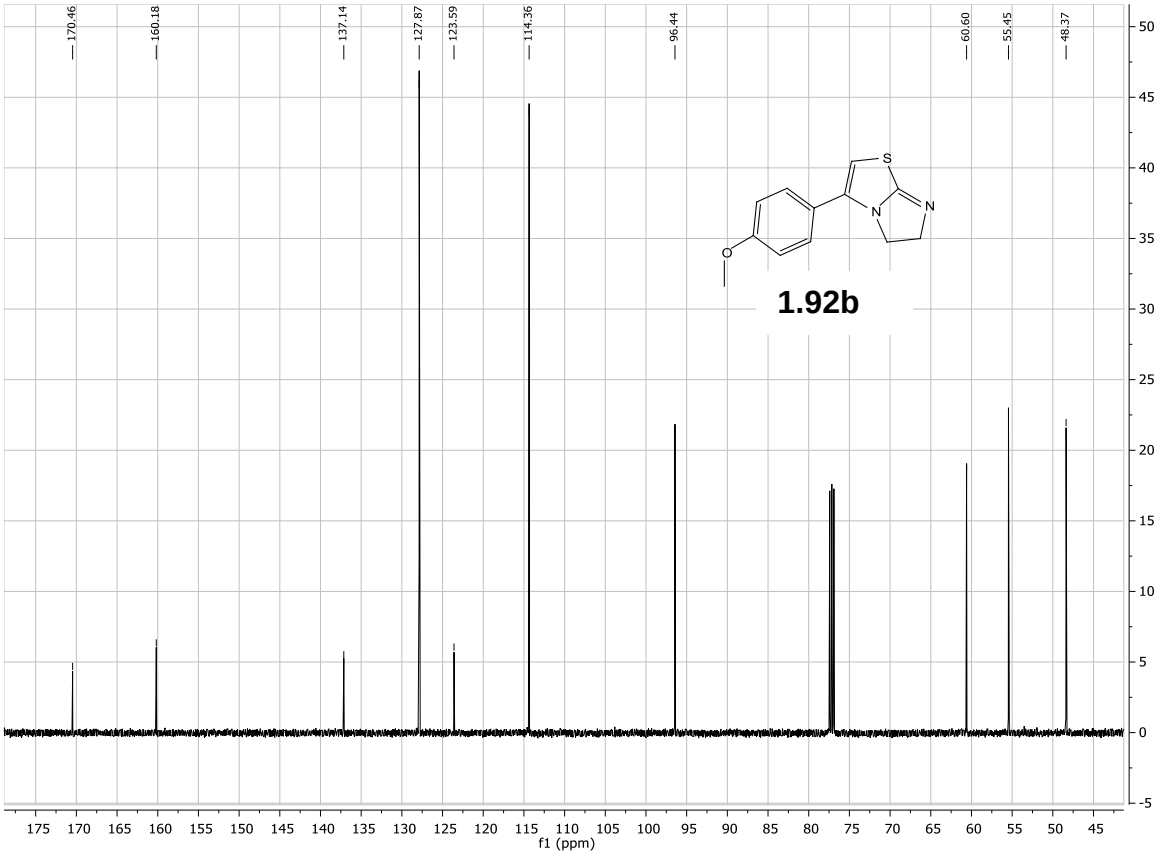
128.97
126.46
98.04
60.64
48.47
S
N
N
1.92a
f1 (ppm)


7.37
7.36
7.34
7.34
6.94
6.93
6.92
6.91
5.58
4.27
4.24
4.21
3.84
3.83
2.00
2.01
0.90
2.08
3.39
f1 (ppm)

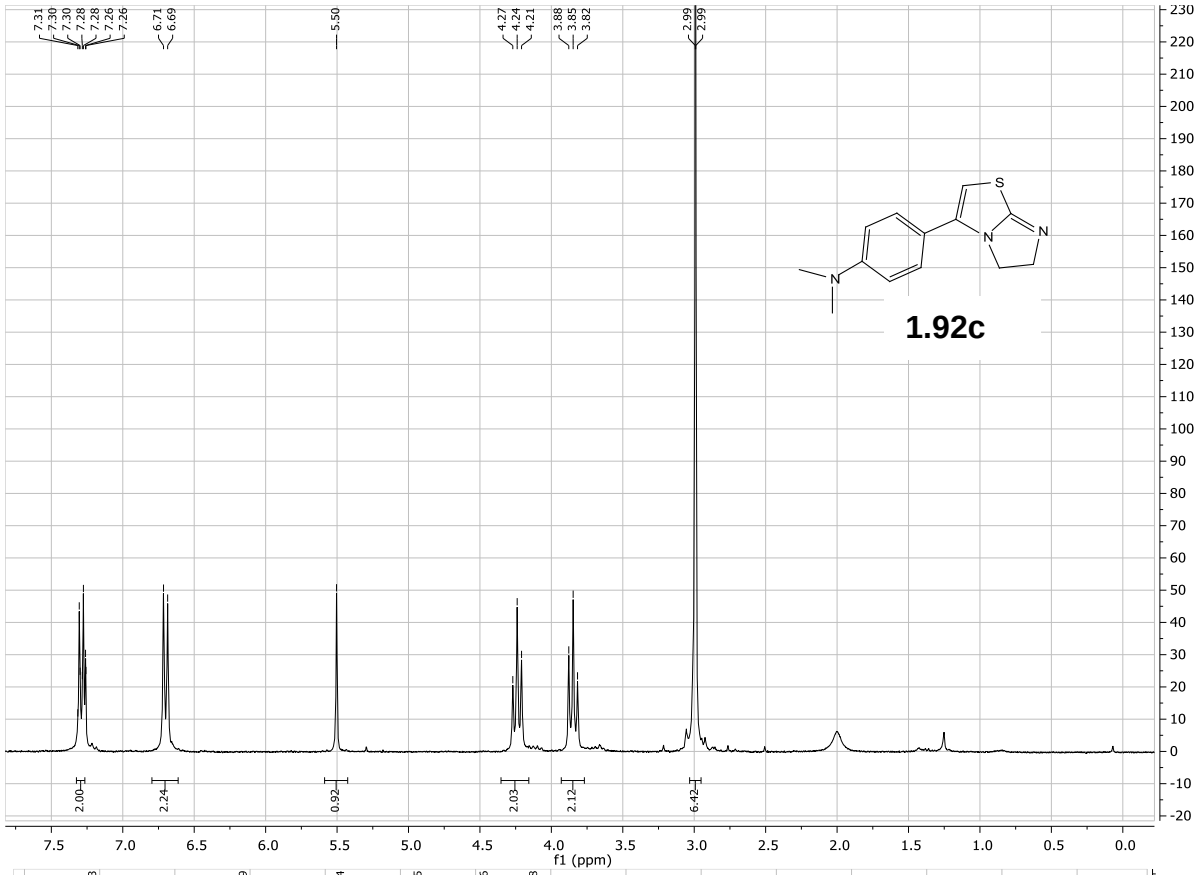
S
N
N
O

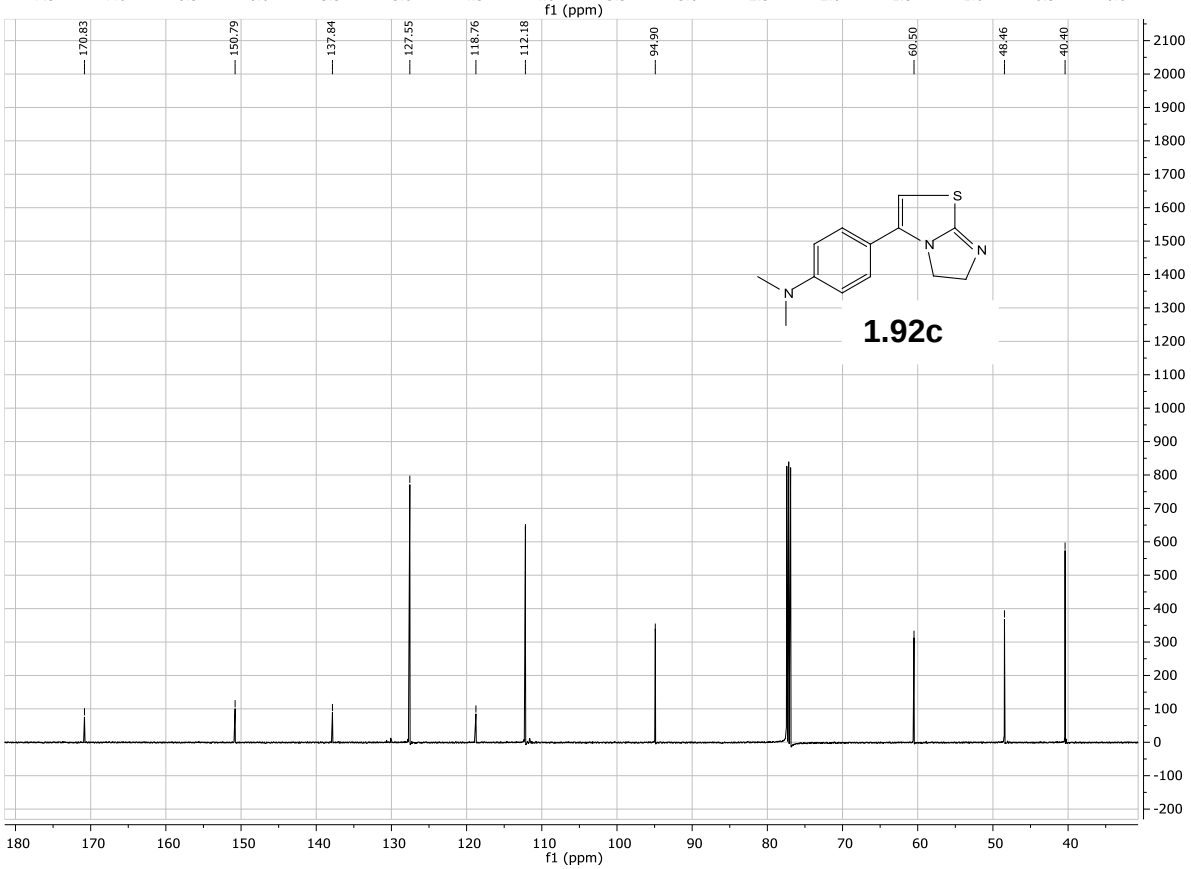
1.92b


170.46
160.18
137.14
127.87
123.59
114.36
96.44
60.60
55.45
48.37
f1 (ppm)

S
N
N
O

1.92b


7.31
7.30
7.30
7.28
7.28
7.26
7.26
7.26
6.71
6.69
5.50
4.27
4.24
4.21
3.88
3.85
3.82
2.99
2.99
S
N
N
N
1.92c
2.00
2.24
0.92
2.03
2.12
6.42
f1 (ppm)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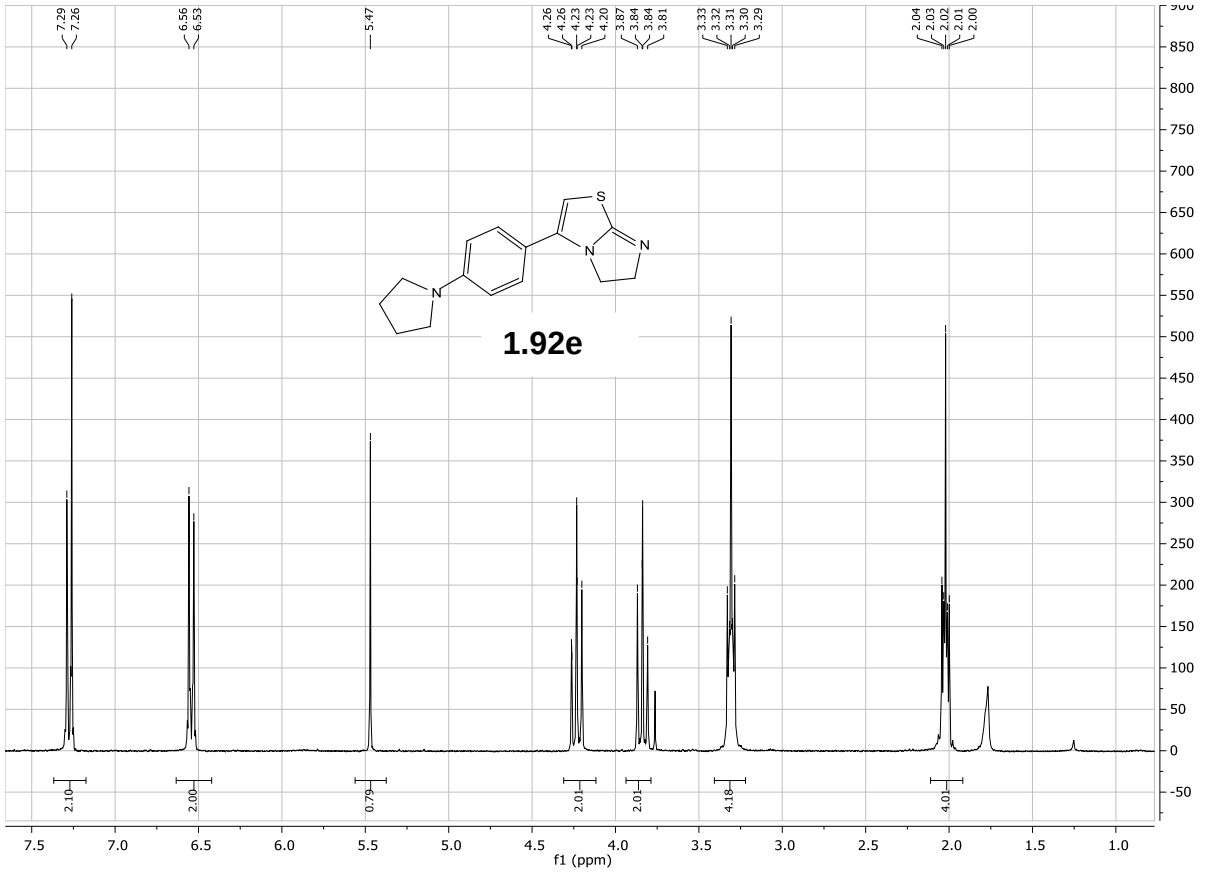
150.79
137.84
127.55
118.76
112.18
94.90
60.50
48.46
40.40
S
N
N
N
1.92c
f1 (ppm)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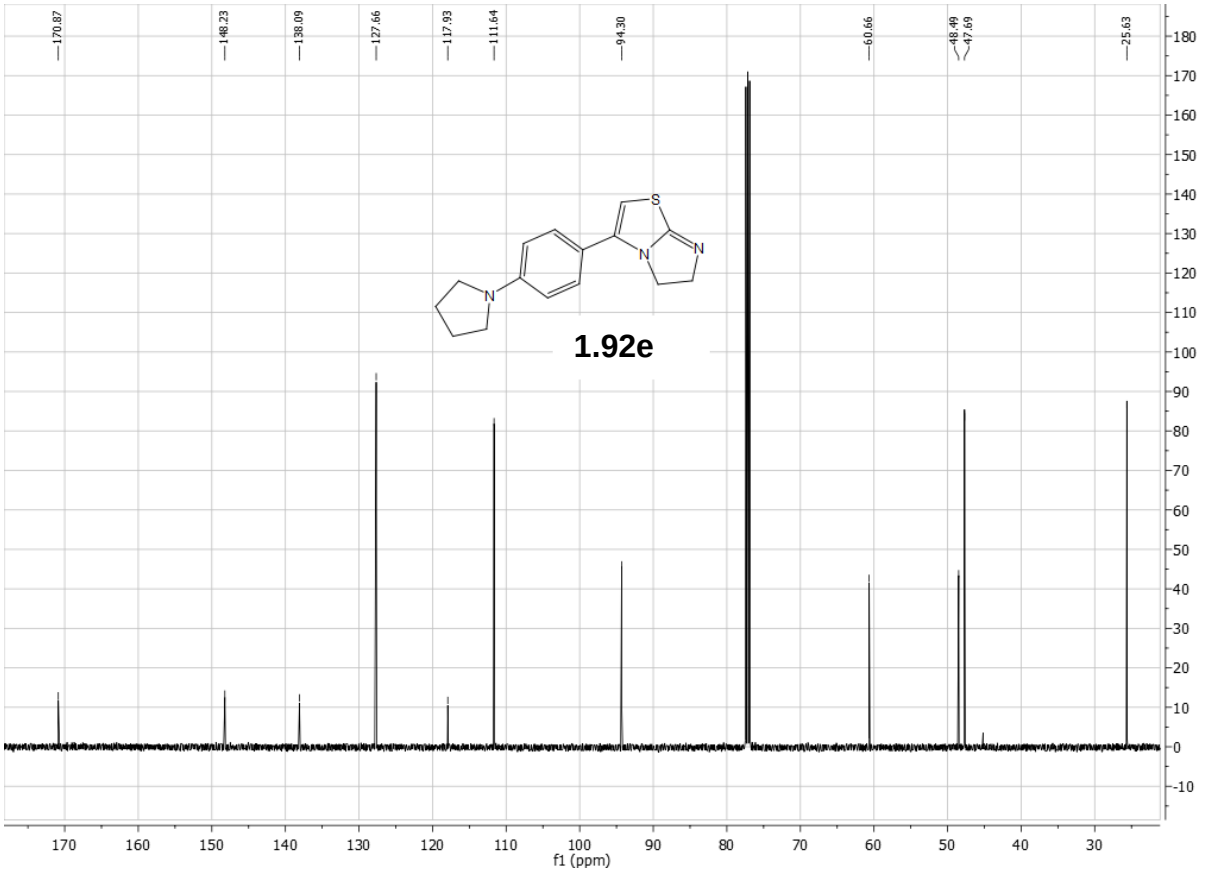
7.26
6.56
6.53
5.47
4.26
4.26
4.23
4.23
4.20
3.87
3.84
3.84
3.81
3.33
3.32
3.31
3.30
3.29
2.04
2.03
2.02
2.01
2.00
S
N
N
N
1.92e
2.10
2.00
0.79
2.01
2.01
4.18
4.01
f1 (ppm)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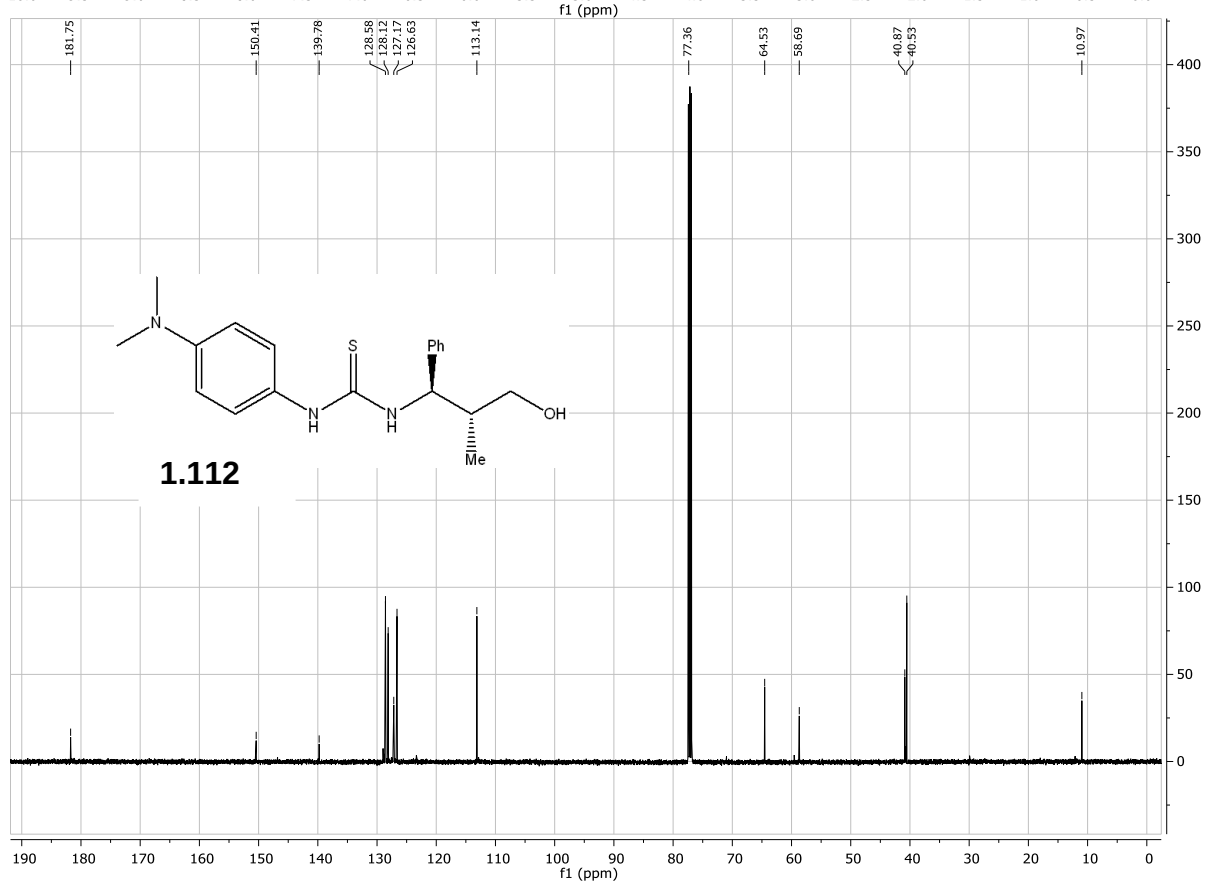
148.23
138.09
127.66
117.93
111.64
94.30
60.66
48.49
47.69
25.63
S
N
N
N
1.92e
f1 (ppm)


7.48
7.32
7.31
7.30
7.29
7.23
7.21
7.21
7.20
7.18
7.15
7.14
7.14
7.13
7.12
7.11
7.09
6.74
6.73
6.61
6.59
5.97
5.95
3.50
3.49
3.48
3.43
3.41
3.39
3.00
2.32
2.31
2.30
2.30
2.29
2.28
2.28
0.56
0.55
N
S
Ph
N
H
N
H
OH
Me
1.112
1.18
1.91
1.35
3.82
1.92
1.03
1.07
3.06
5.98
1.44
3.14
f1 (ppm)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128.58
128.12
127.17
126.63
113.14
77.36
64.53
58.69
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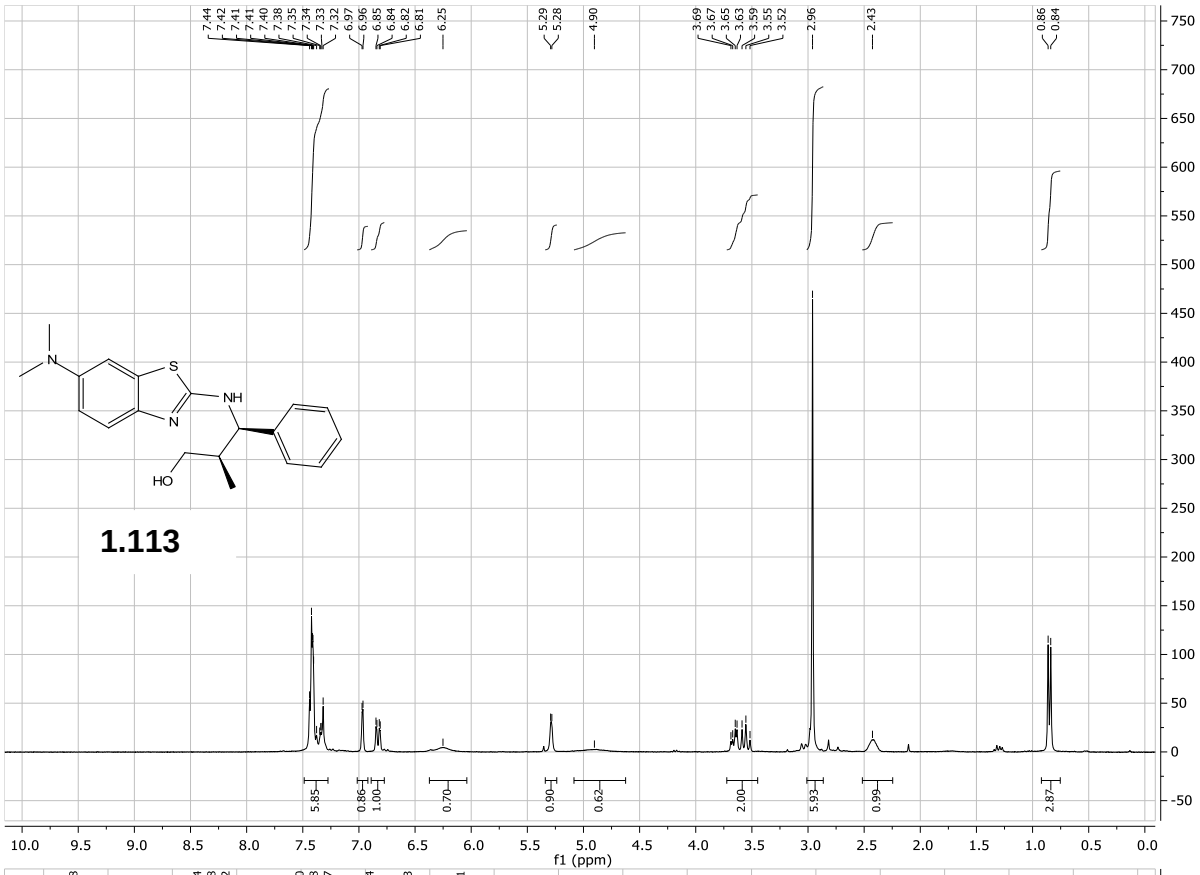
40.53
10.97
N
S
Ph
N
H
N
H
OH
Me
1.112
f1 (ppm)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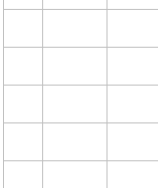
7.41
7.41
7.40
7.38
7.35
7.34
7.33
7.32
6.97
6.96
6.85
6.84
6.82
6.81
6.25
5.29
5.28
4.90
3.69
3.67
3.65
3.63
3.59
3.55
3.52
2.96
2.43
0.86
0.84
5.85
0.86
1.00
0.70
0.90
0.62
2.00
5.93
0.99
2.87
f1 (ppm)

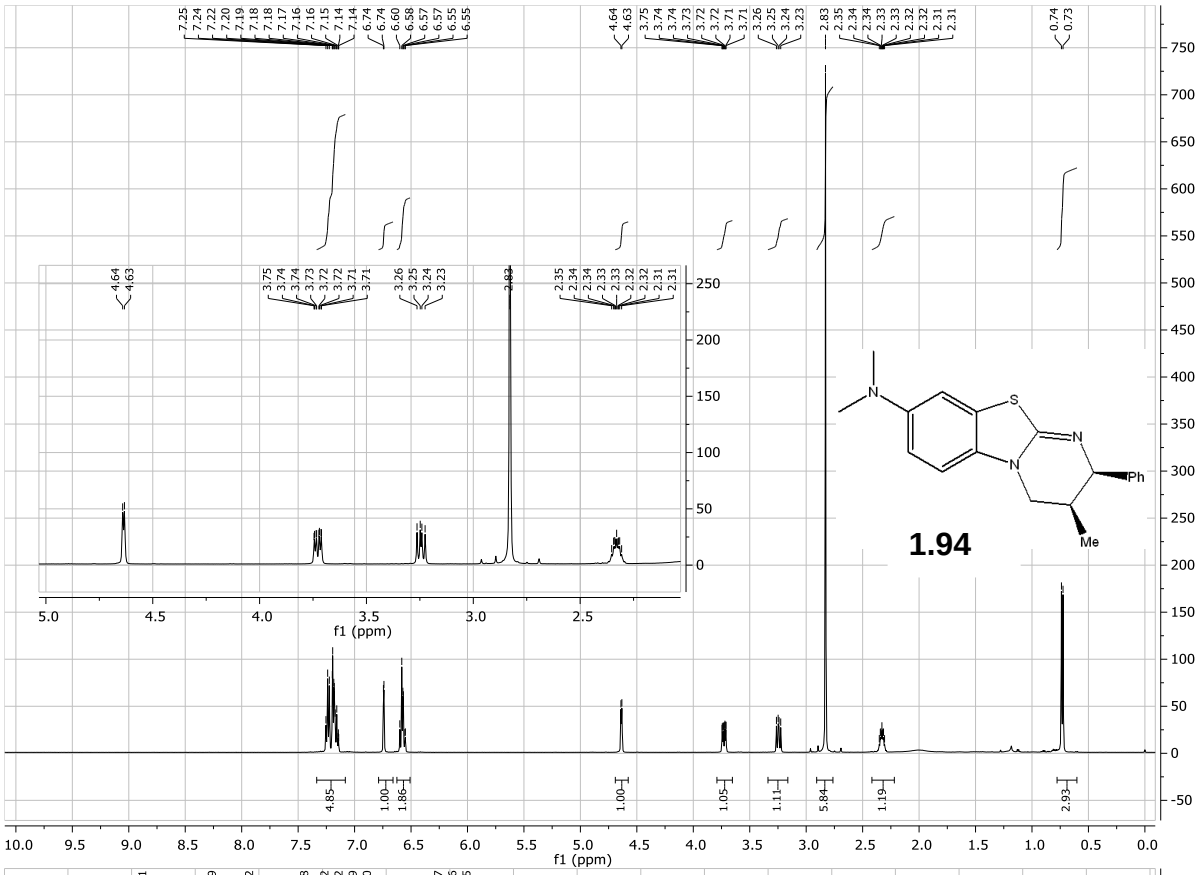

N
S
NH
N
HO

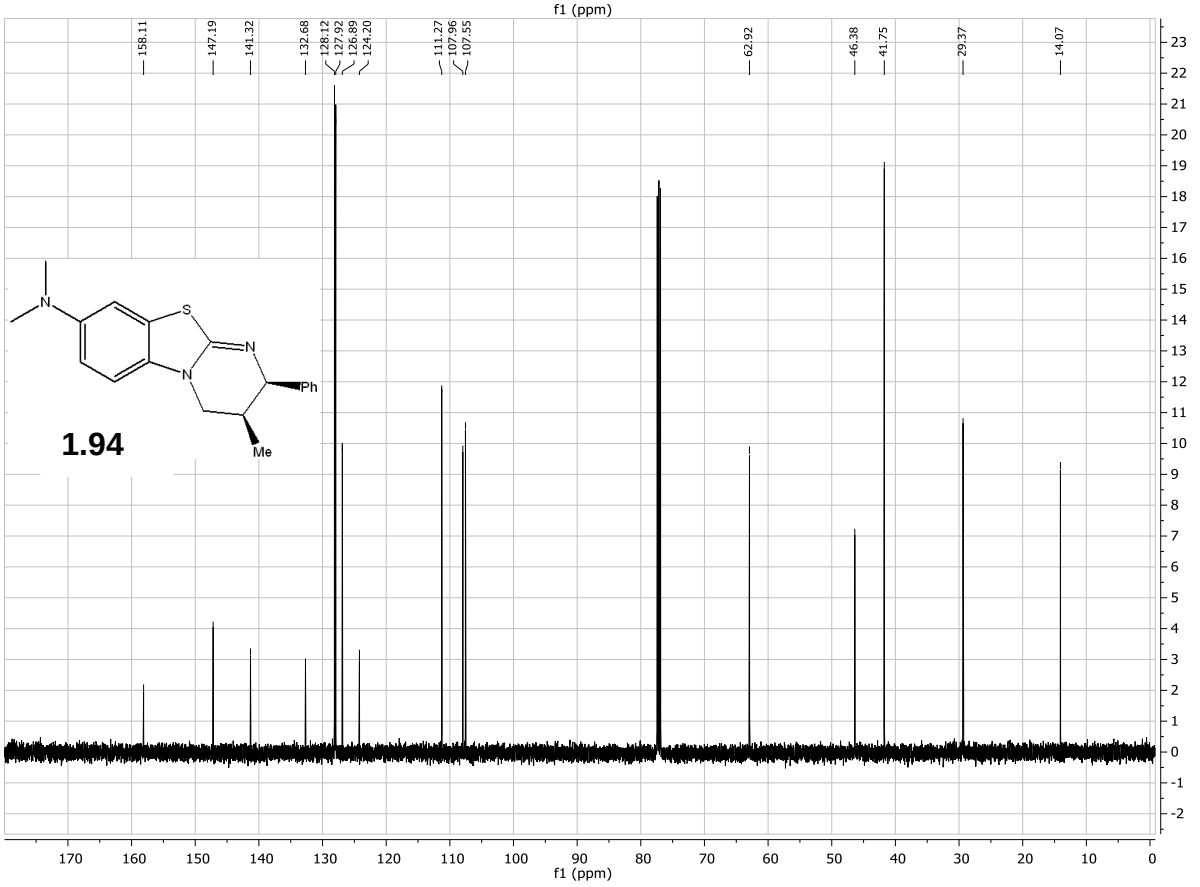
1.113

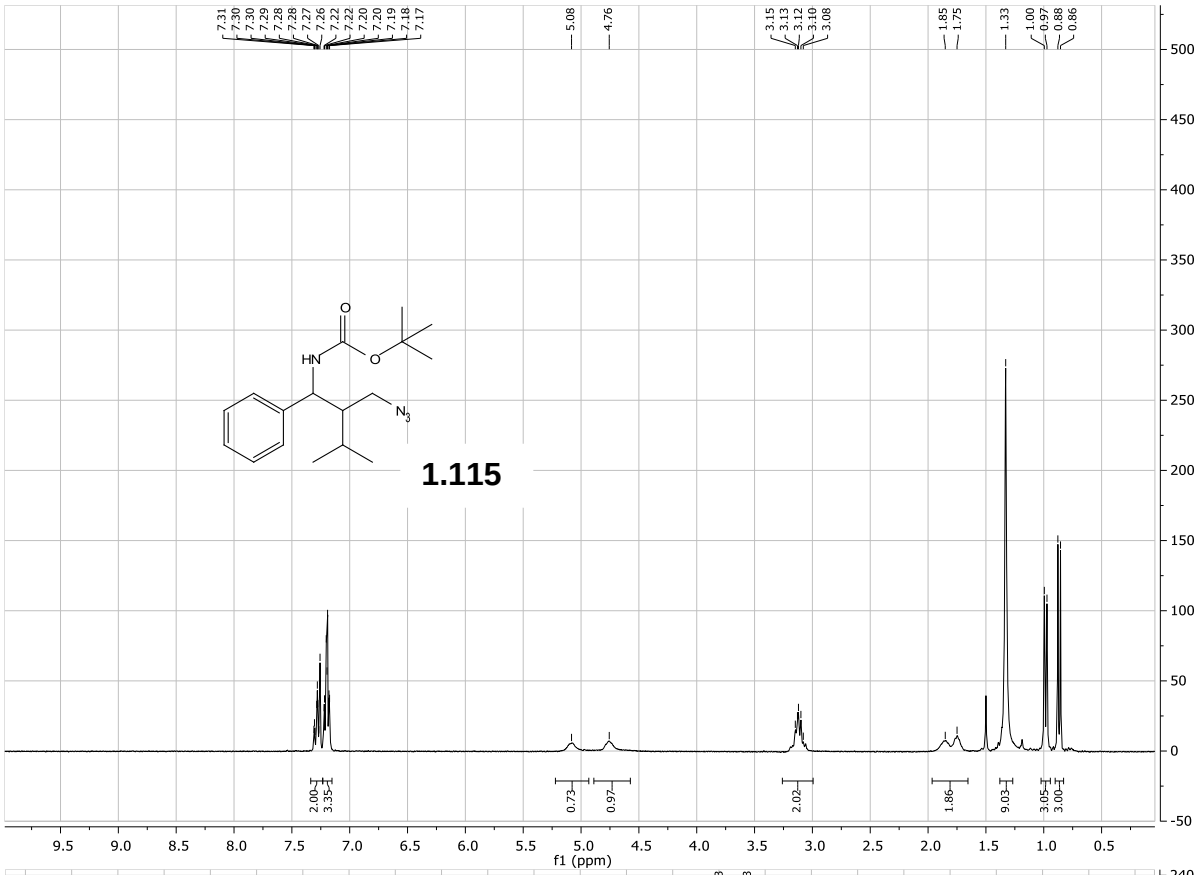
165.18
147.24
143.38
140.22
128.60
127.38
127.07
119.14
113.23
105.01
64.69
59.95
41.80
41.32
11.33
f1 (ppm)

N
S
NH
N
HO

1.113


1.94
f1 (ppm)


1.94
f1 (ppm)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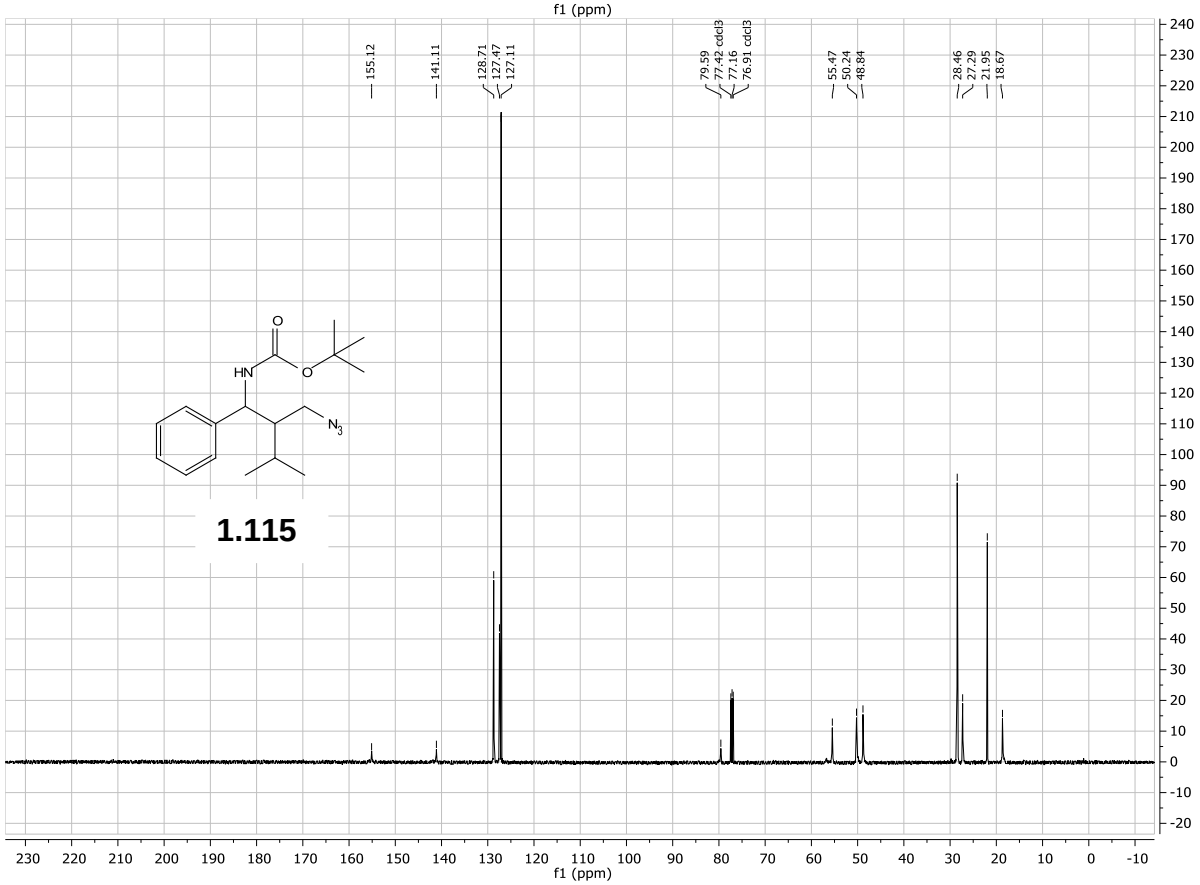
7.22
7.20
7.20
7.19
7.18
7.17
5.08
4.76
3.15
3.13
3.12
3.10
3.08
1.85
1.75
1.33
1.00
0.97
0.88
0.86
HN
O
O
N3
1.115
2.00
3.35
0.73
0.97
2.02
1.86
9.03
3.05
3.00
f1 (ppm)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141.11
128.71
127.47
127.11
79.59
77.42 cdcl3
77.16
76.91 cdcl3
55.47
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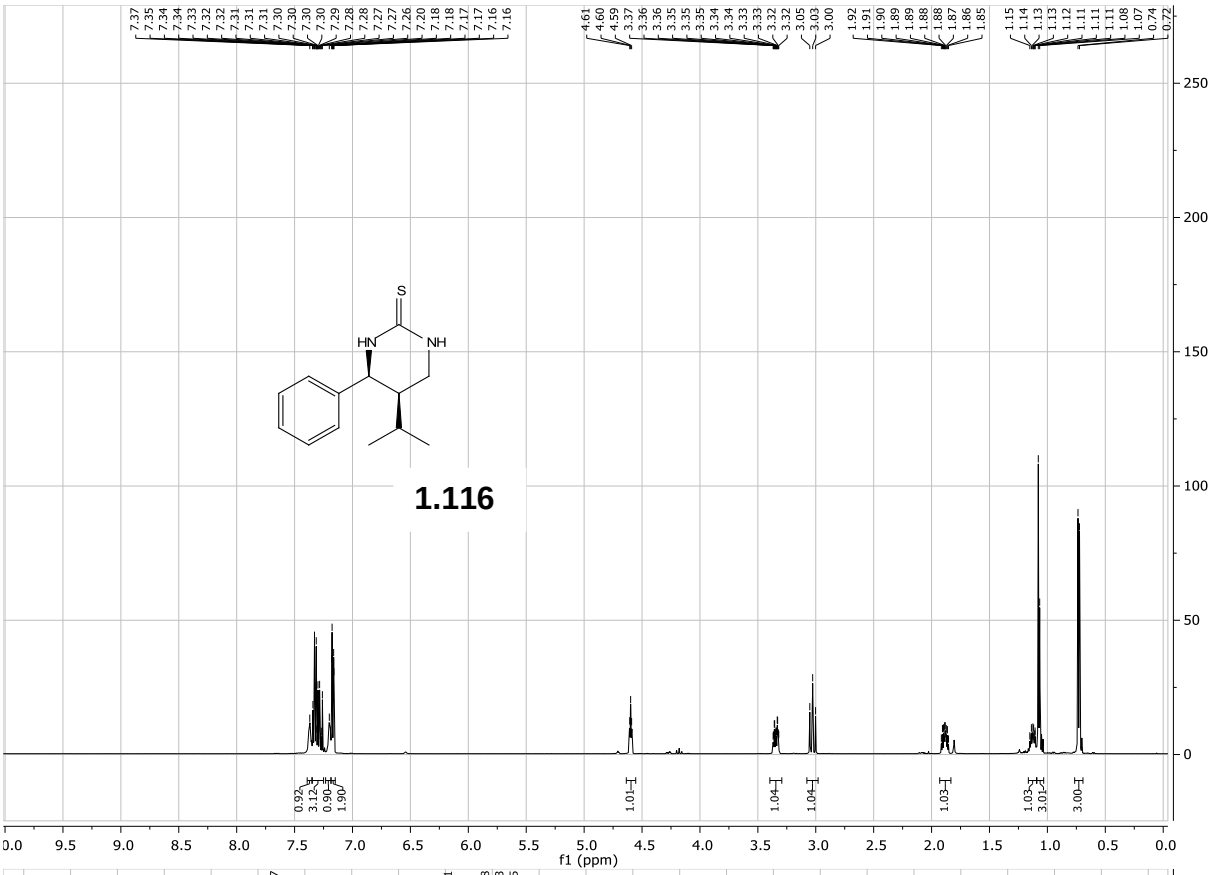
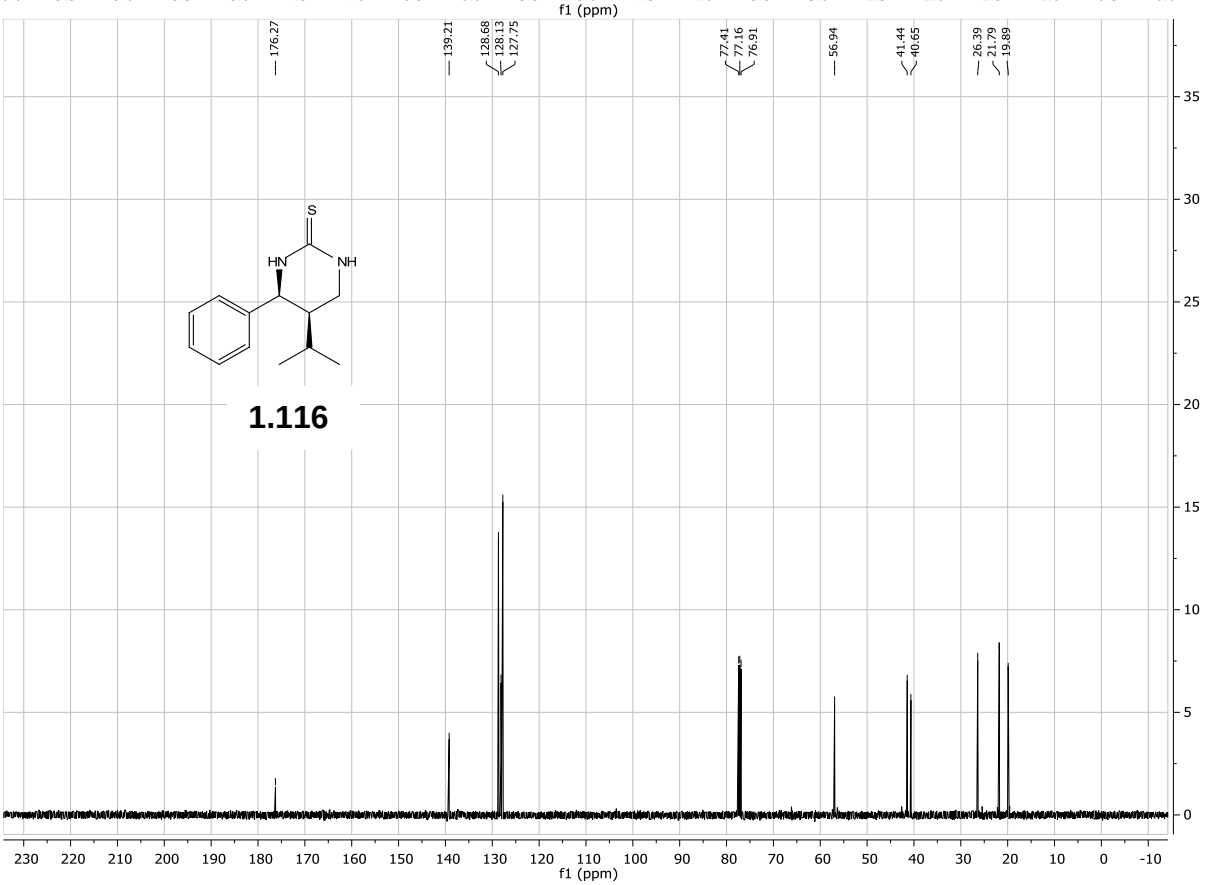
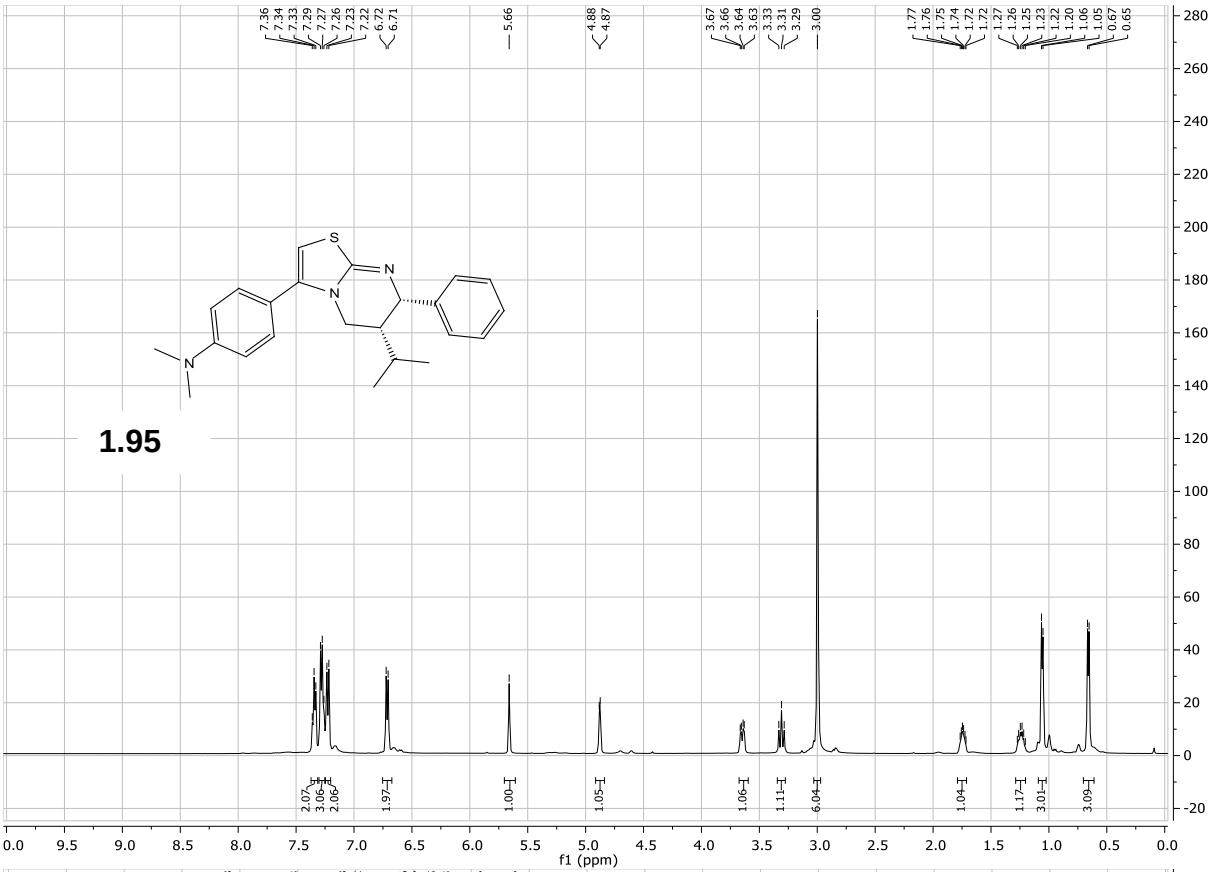
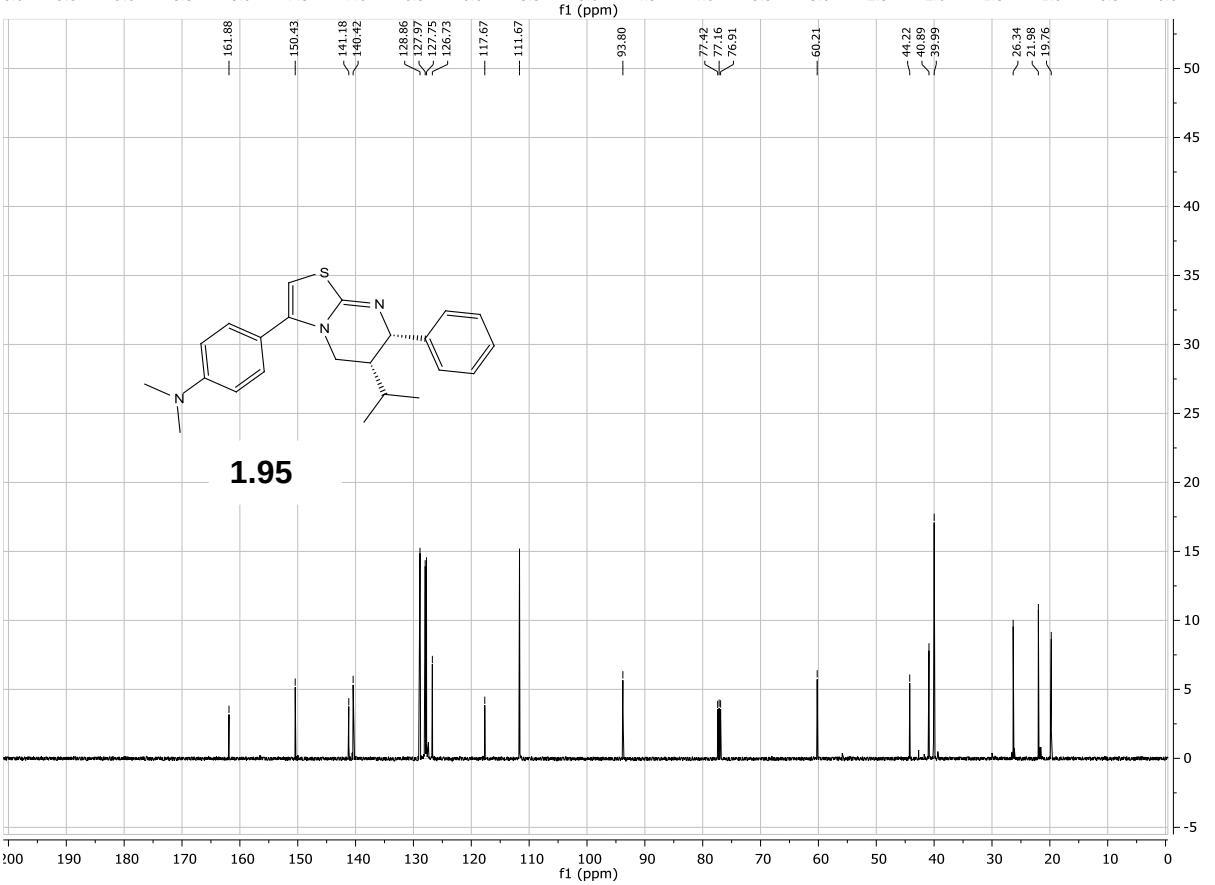
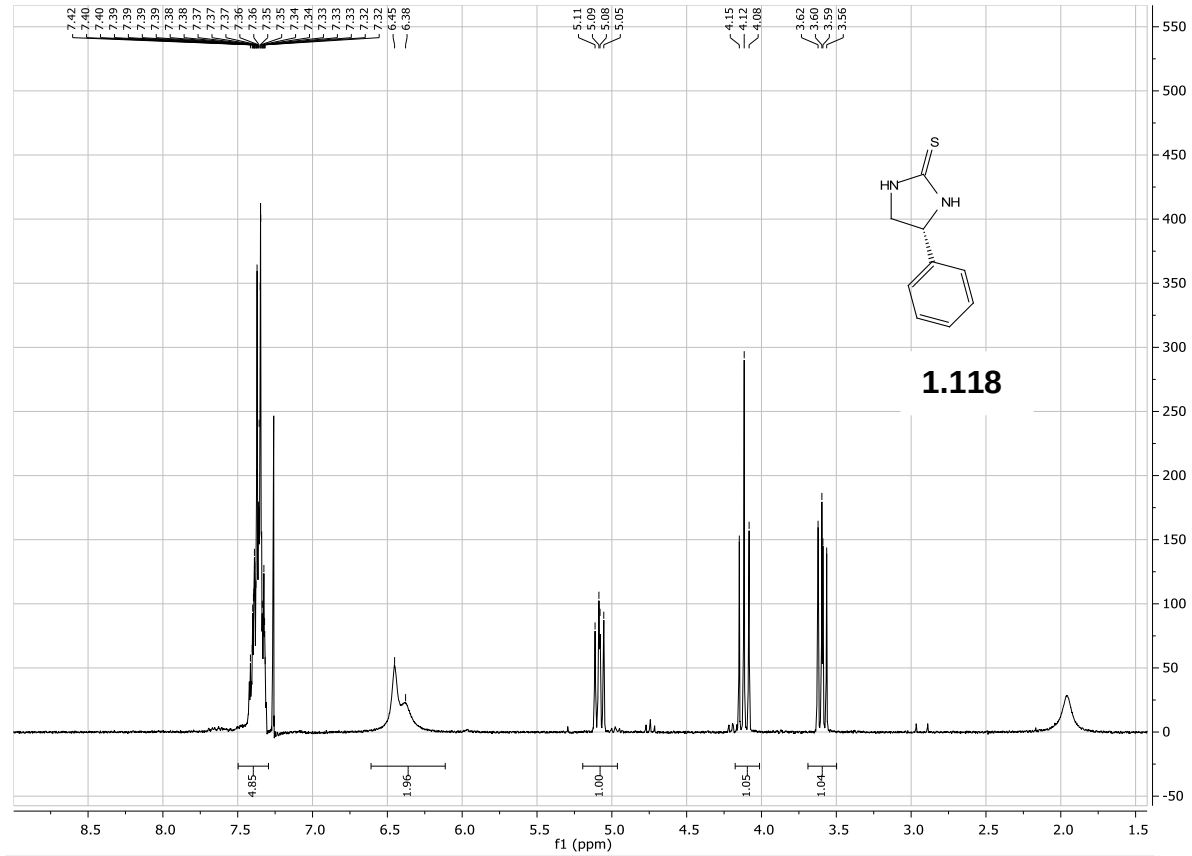
48.84
28.46
27.29
21.95
18.67
HN
O
O
N3
1.115
f1 (ppm)


S
HN
NH
1.116
f1 (ppm)


S
HN
NH
1.116
f1 (ppm)


1.95
f1 (ppm)


1.95
f1 (ppm)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7.39
7.39
7.38
7.38
7.37
7.37
7.37
7.36
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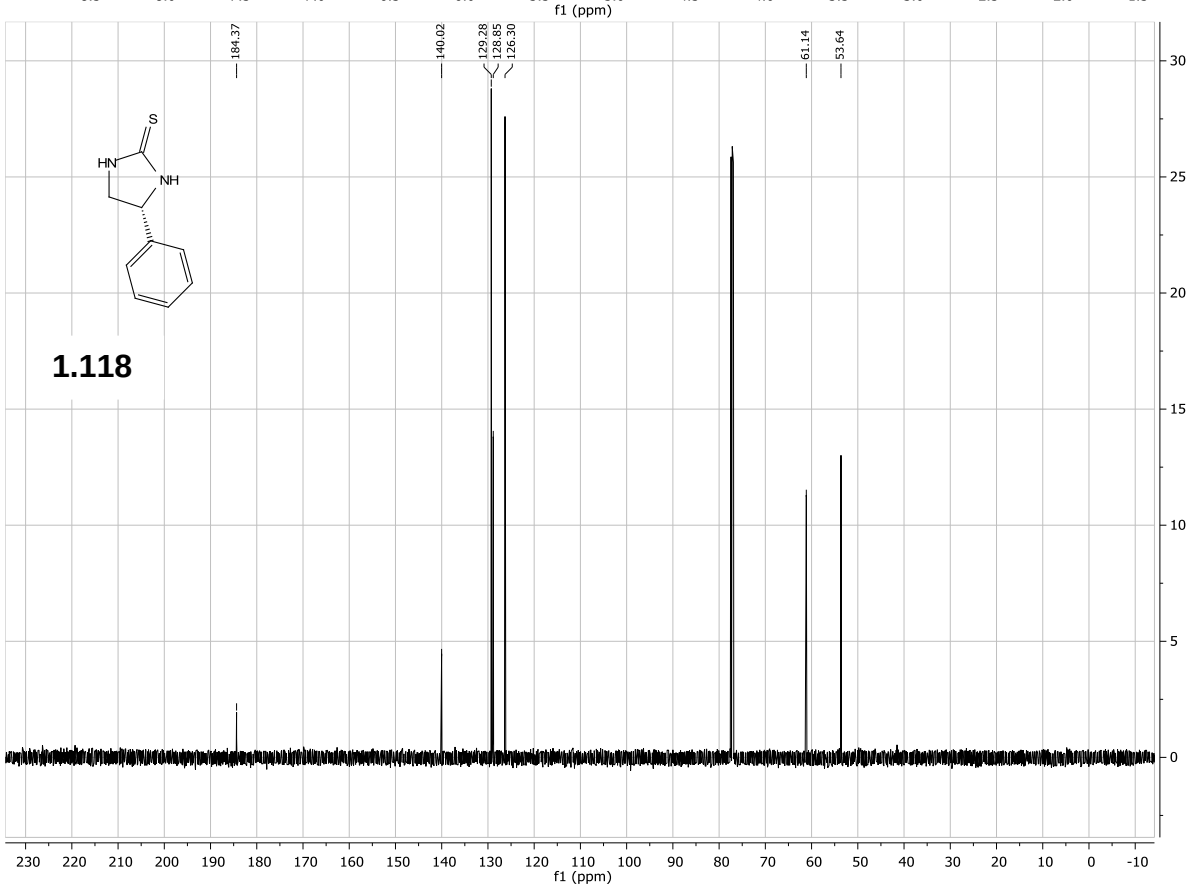
7.35
7.35
7.34
7.34
7.33
7.33
7.32
7.32
6.45
6.38
5.11
5.09
5.08
5.05
4.15
4.12
4.08
3.62
3.60
3.59
3.56
S
HN
NH
1.118
4.85
1.96
1.00
1.05
1.04
f1 (ppm)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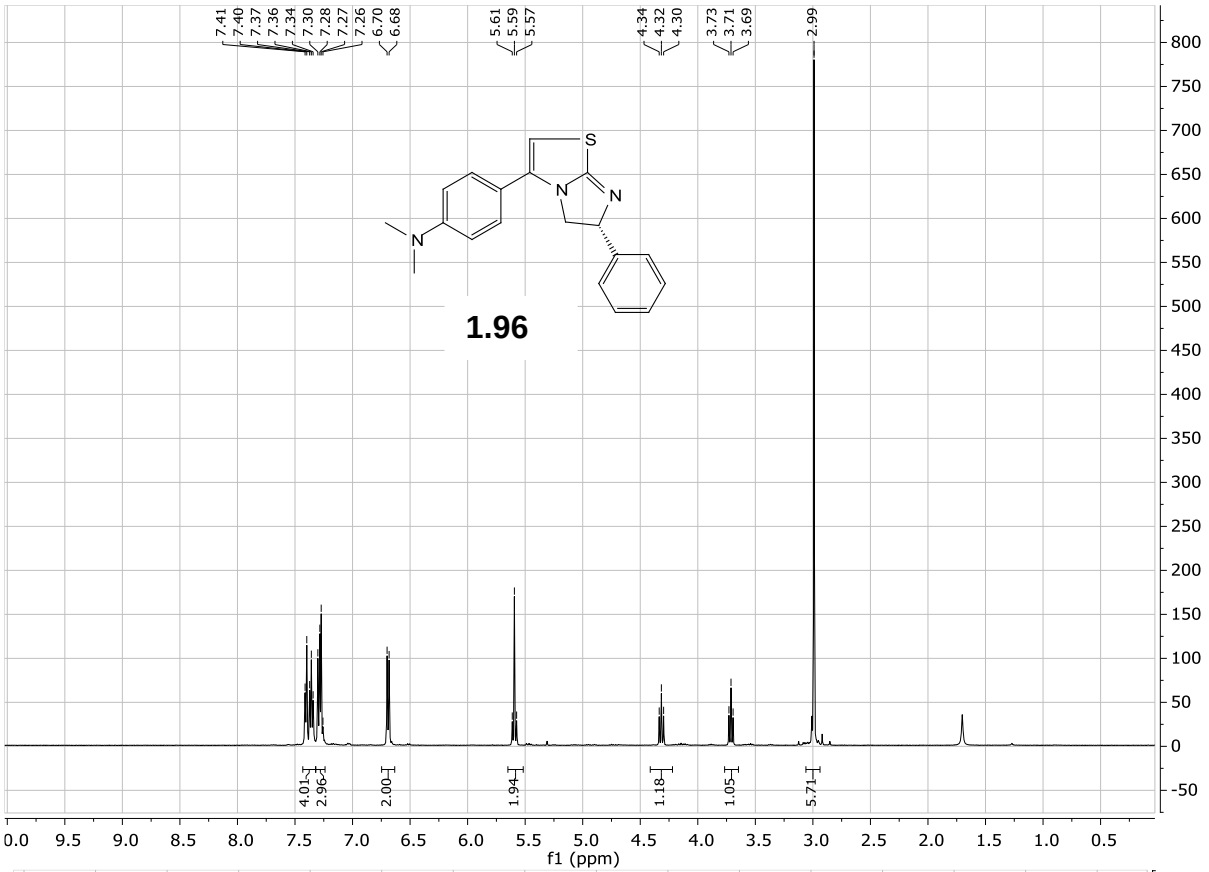
126.30
61.14
53.64
S
HN
NH
1.118
f1 (ppm)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7.40
7.37
7.36
7.34
7.30
7.28
7.27
7.26
6.70
6.68
5.61
5.59
5.57
4.34
4.32
4.30
3.73
3.71
3.69
2.99
S
N
N
N
1.96
4.01
2.96
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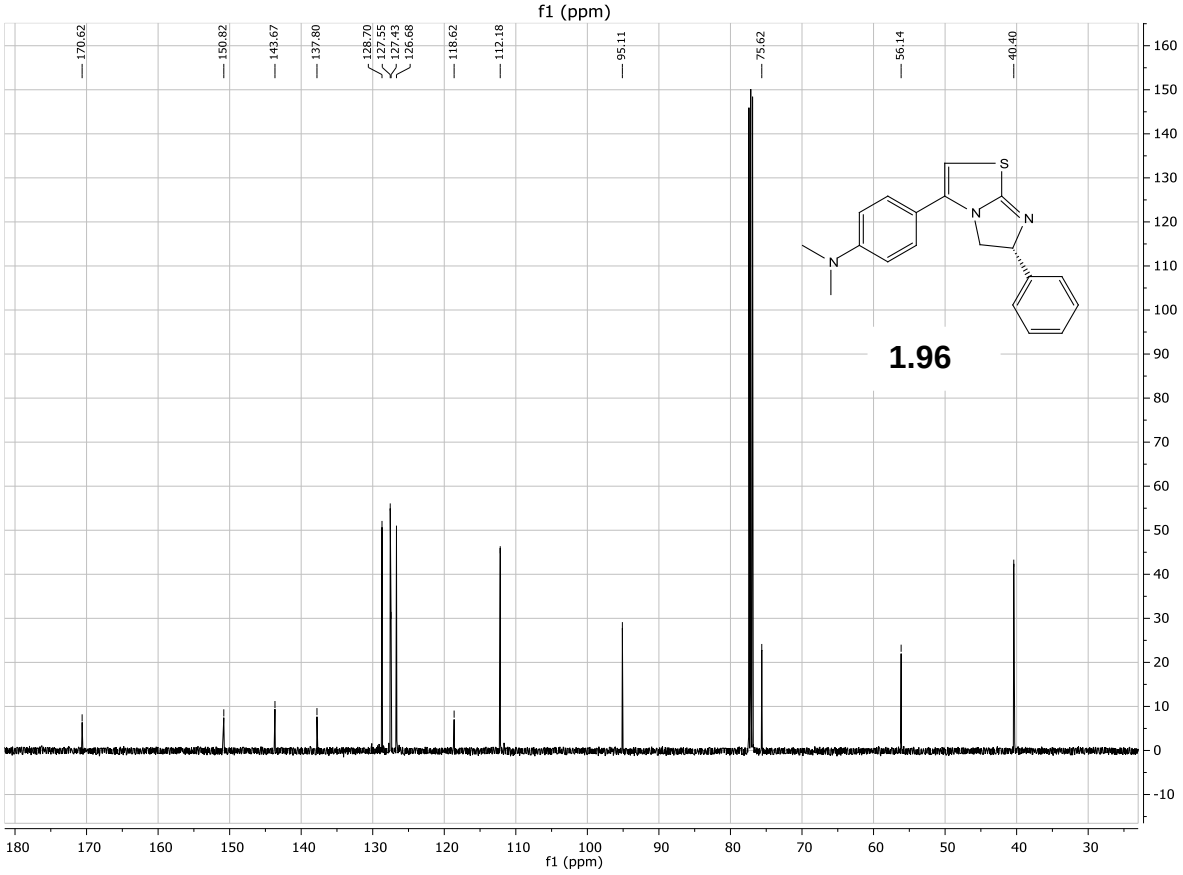
1.94
1.18
1.05
5.71
f1 (ppm)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143.67
137.80
128.70
127.55
127.43
126.68
118.62
112.18
95.11
75.62
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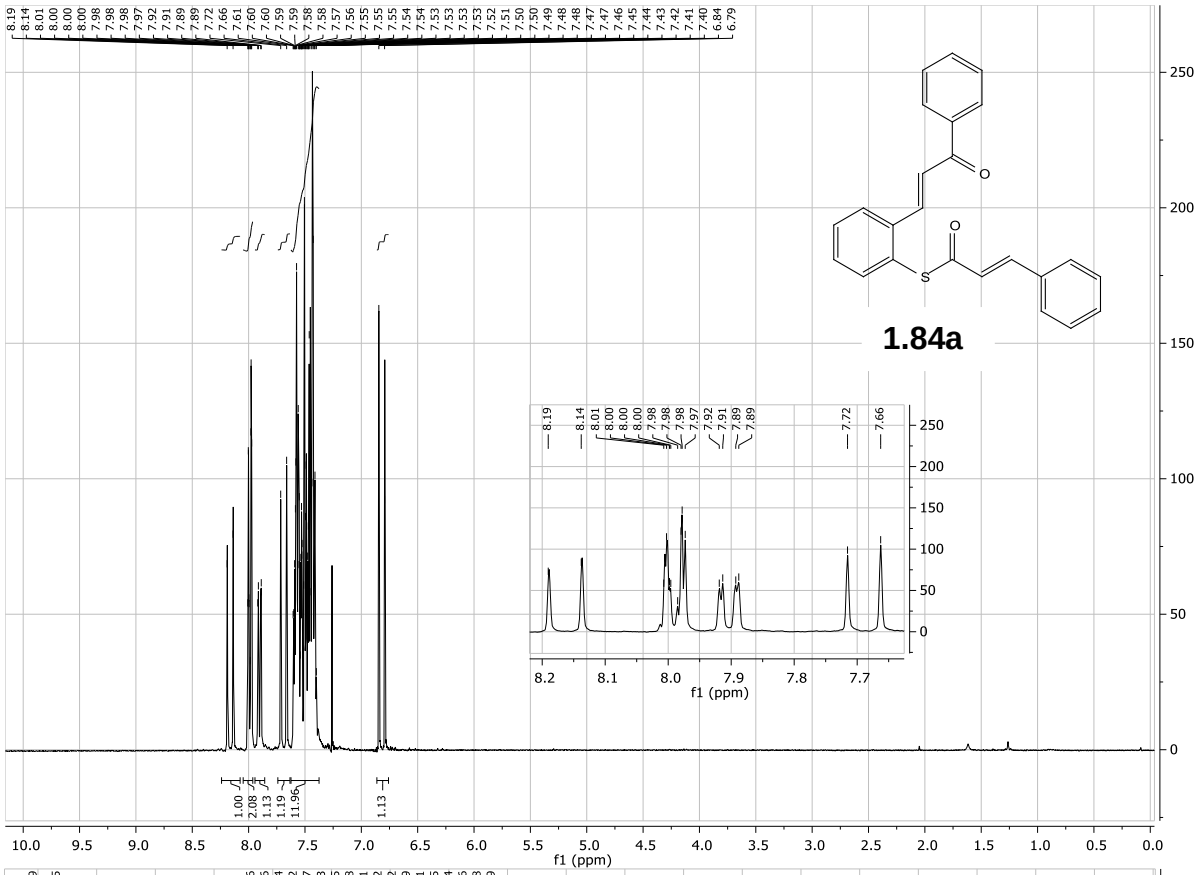
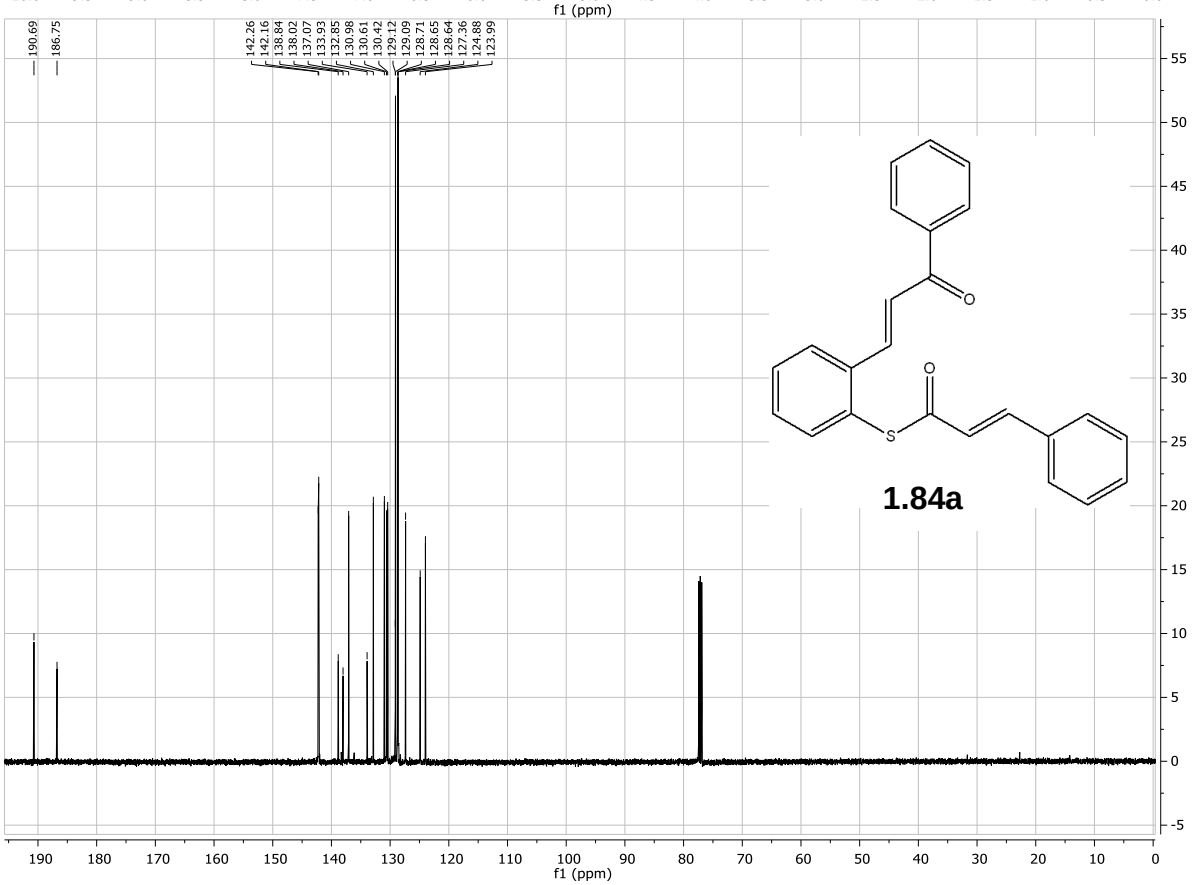
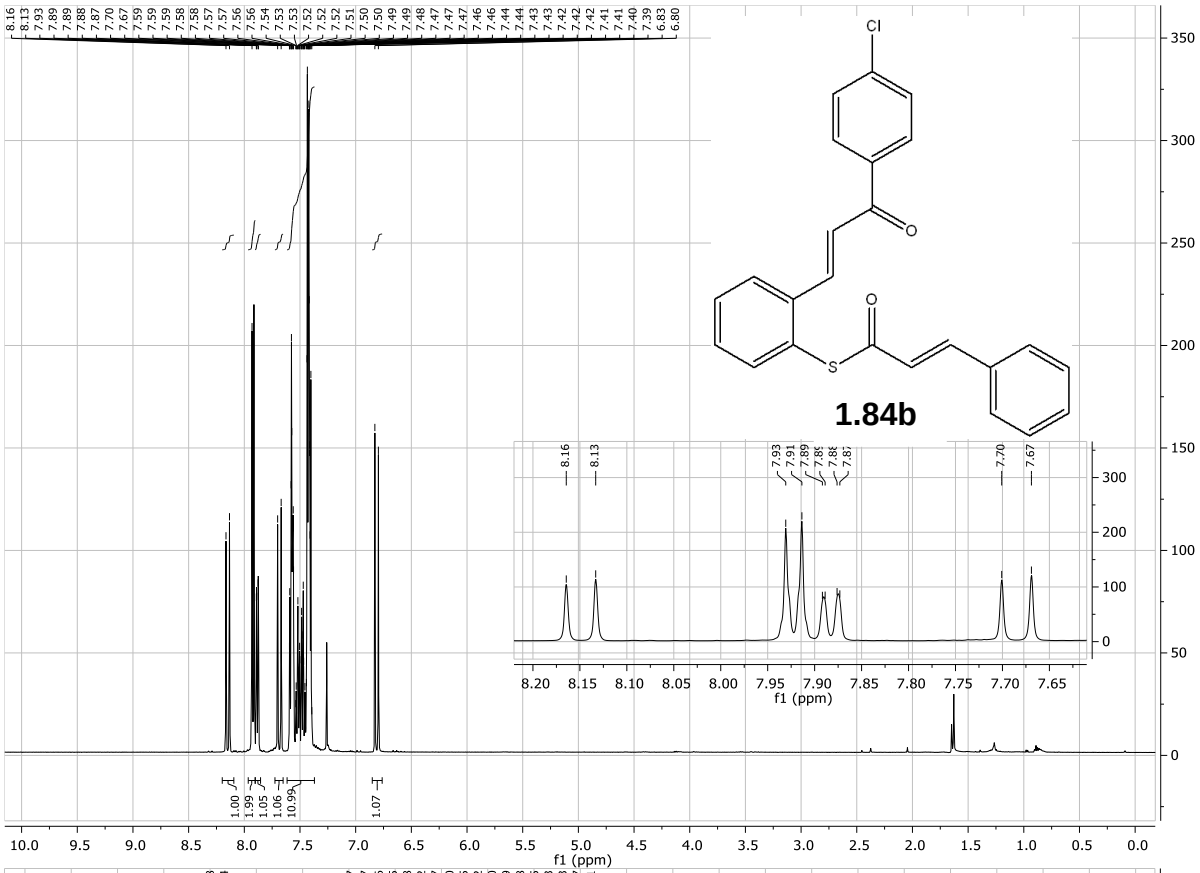
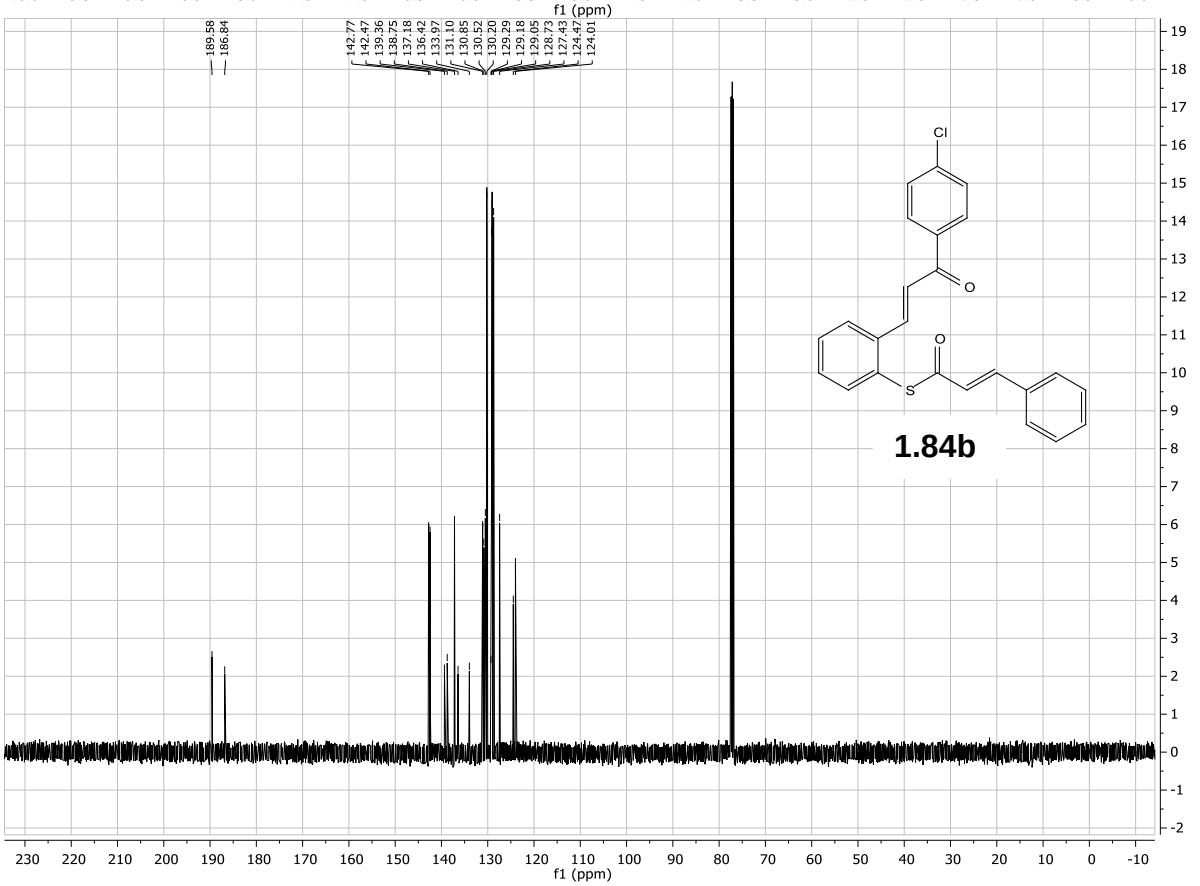
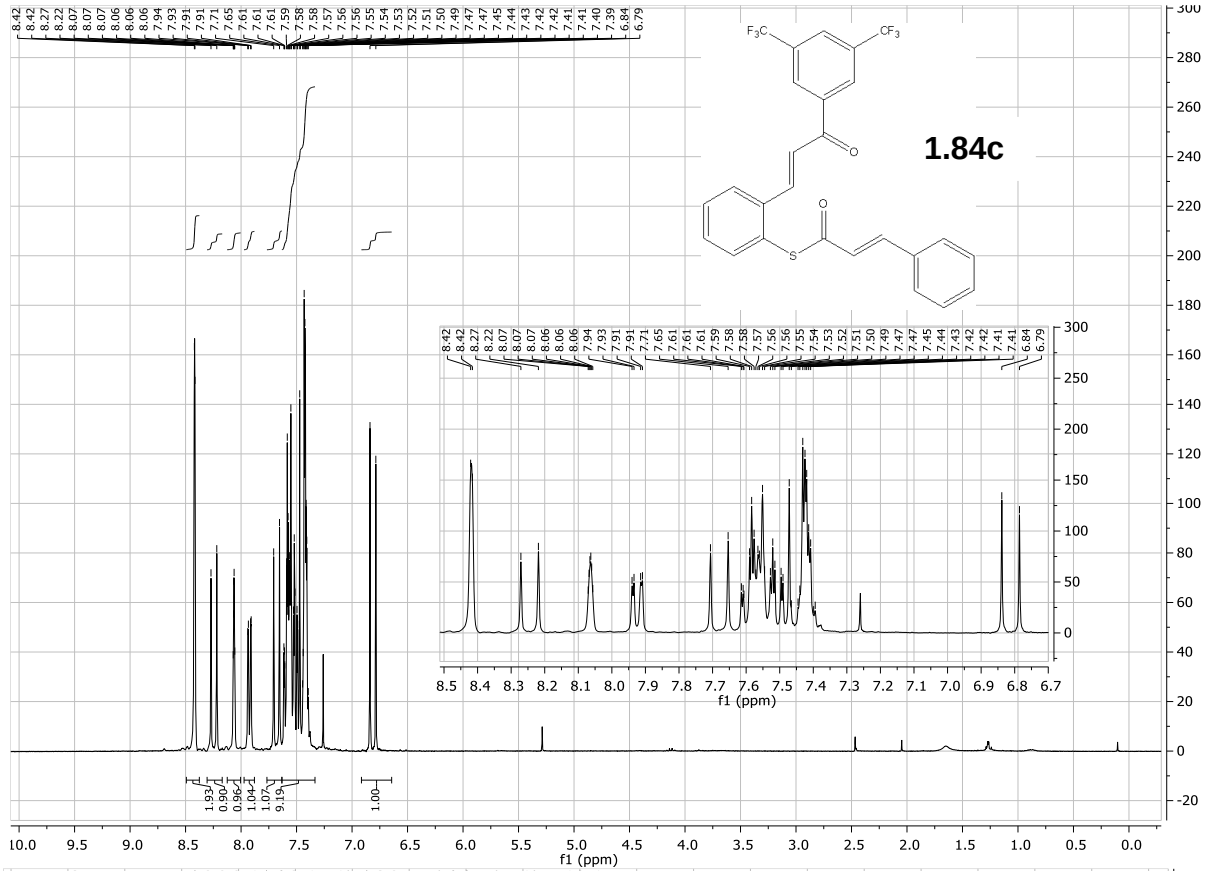
40.40
S
N
N
N
1.96
f1 (ppm)

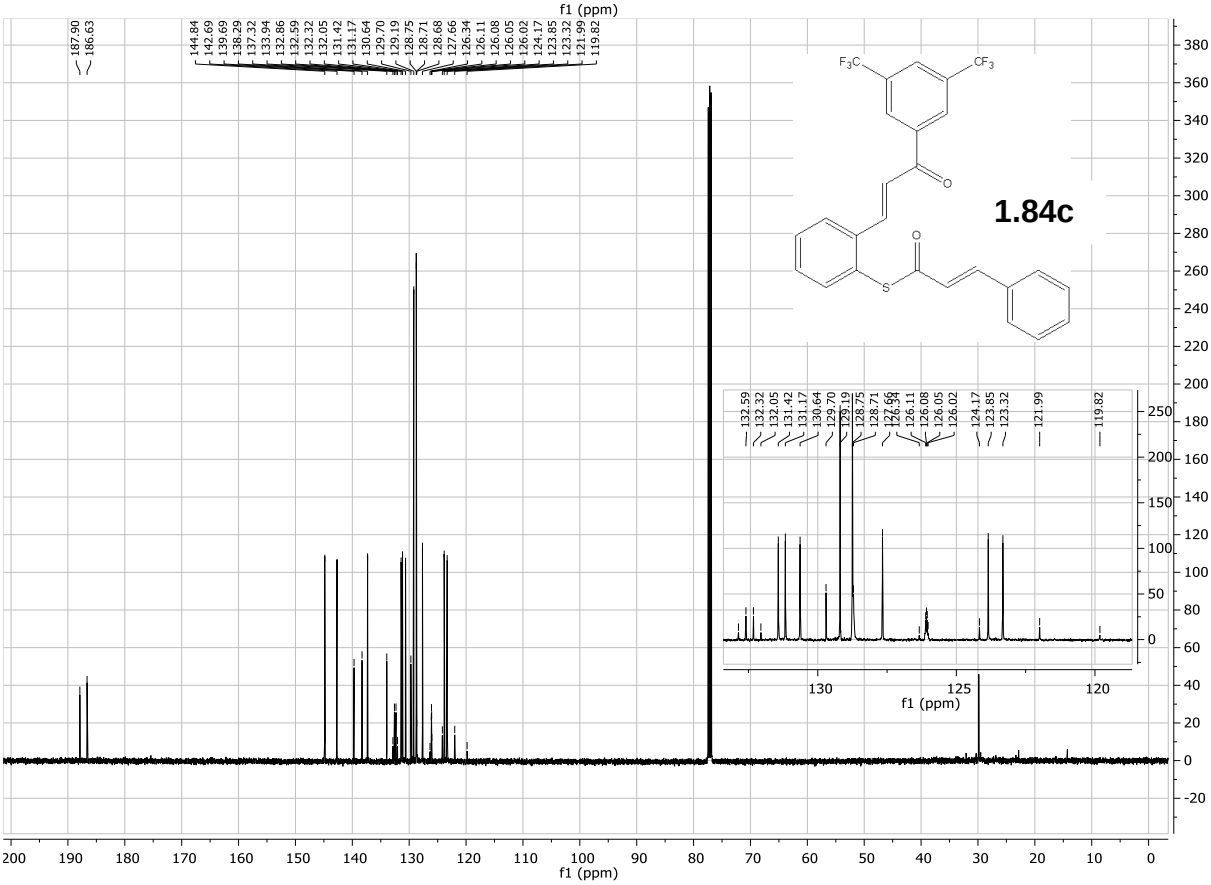

1.84a
f1 (ppm)

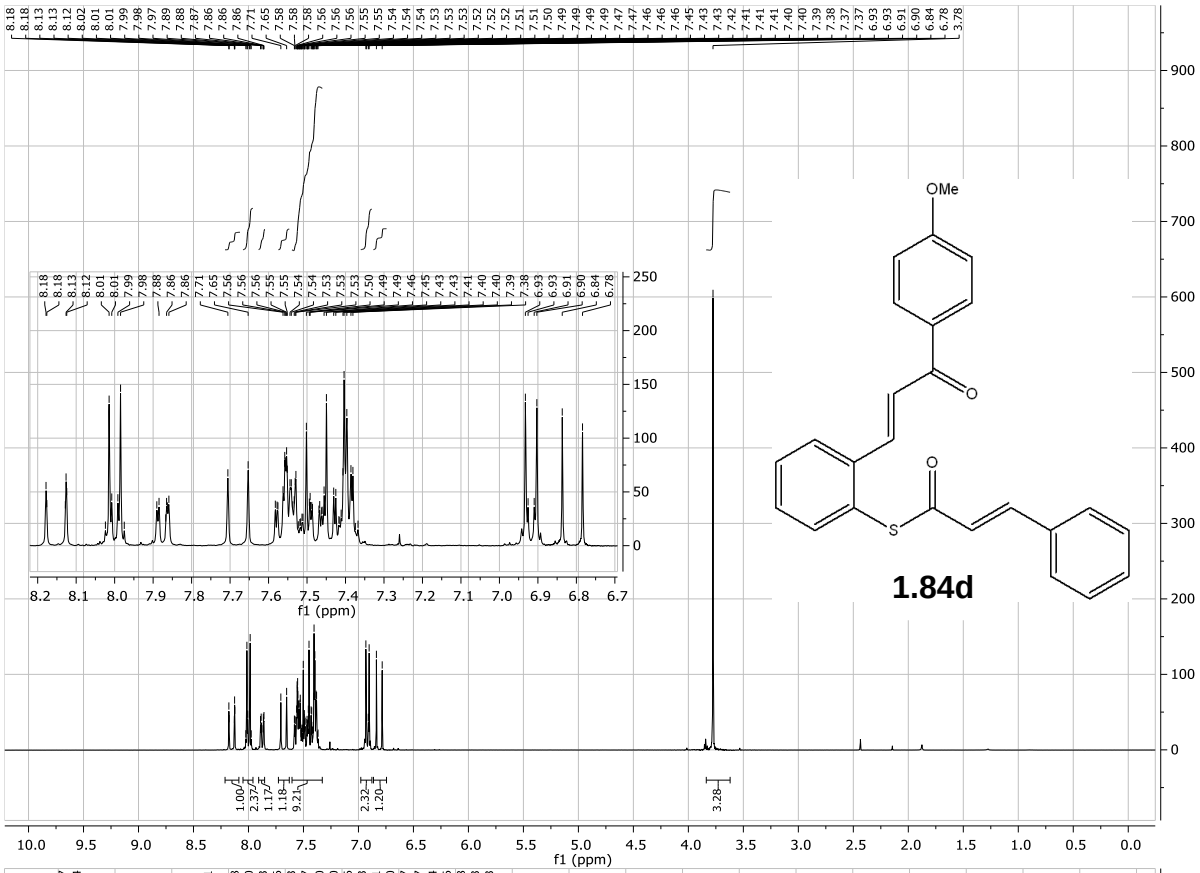

1.84a
f1 (ppm)

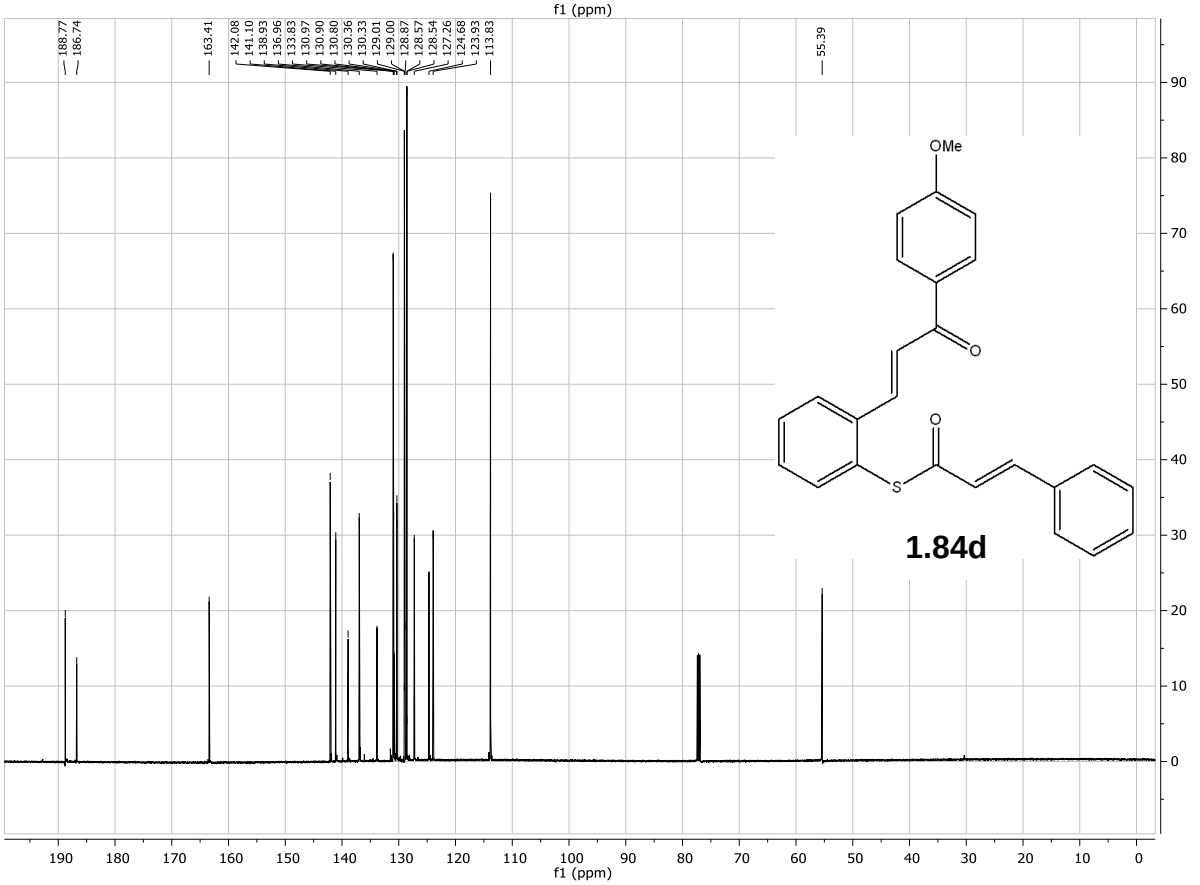

Cl
O
O
S
1.84b
f1 (ppm)

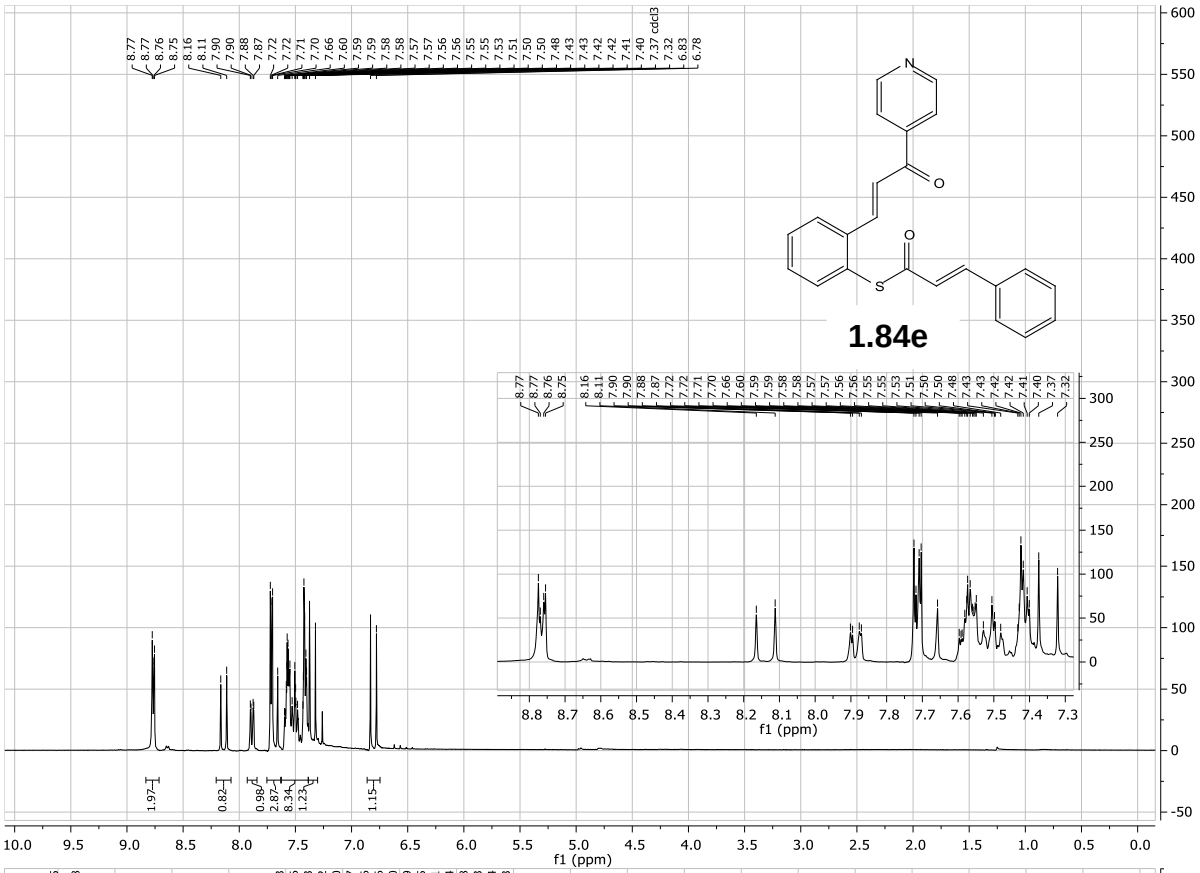

Cl
O
O
S
1.84b
f1 (ppm)

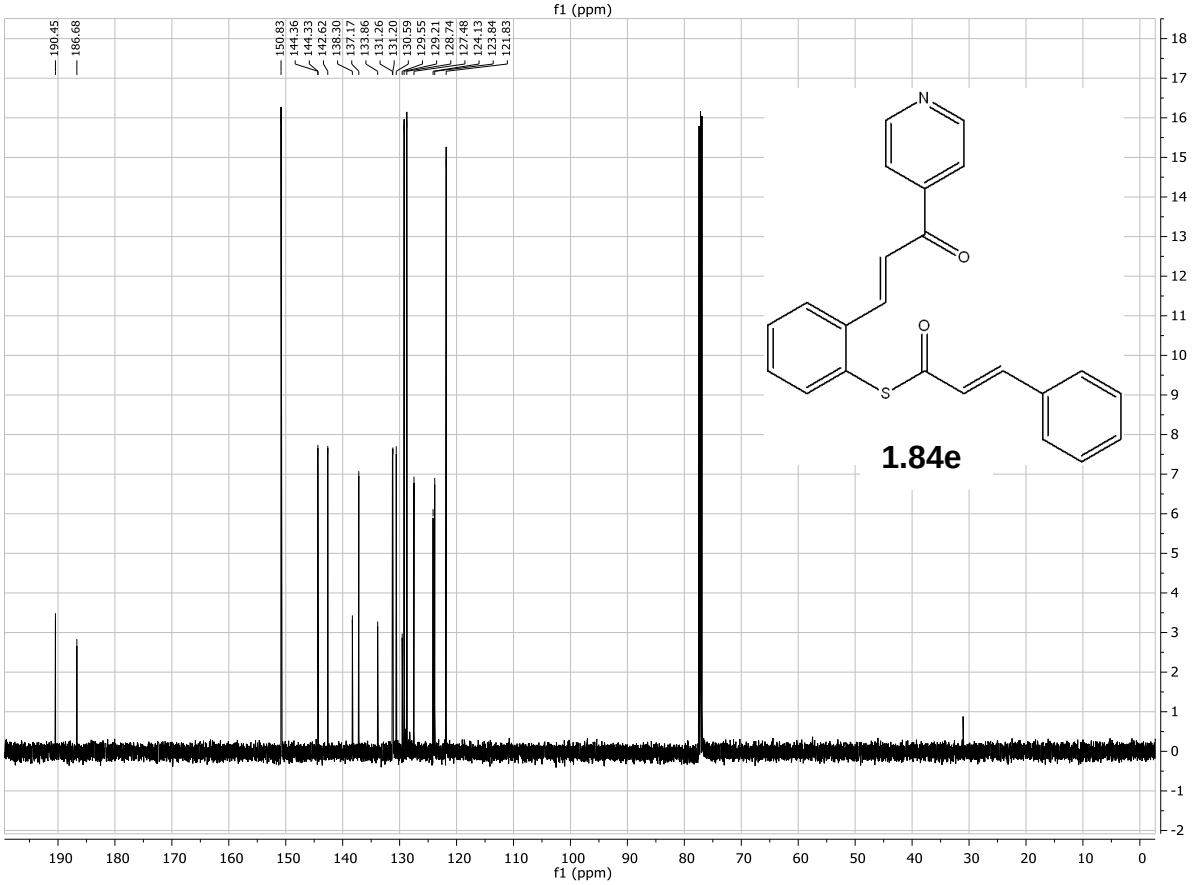

1.84c
f1 (ppm)

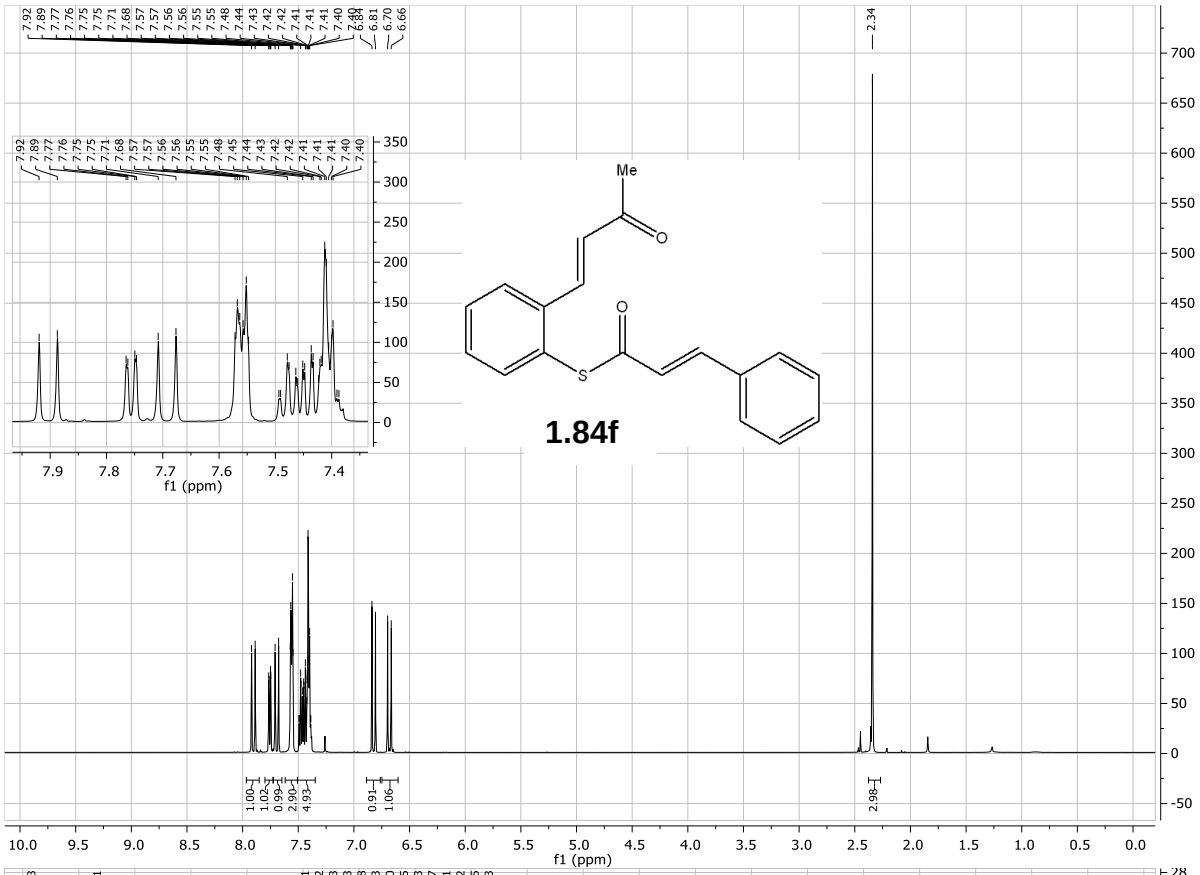

1.84c
f1 (ppm)

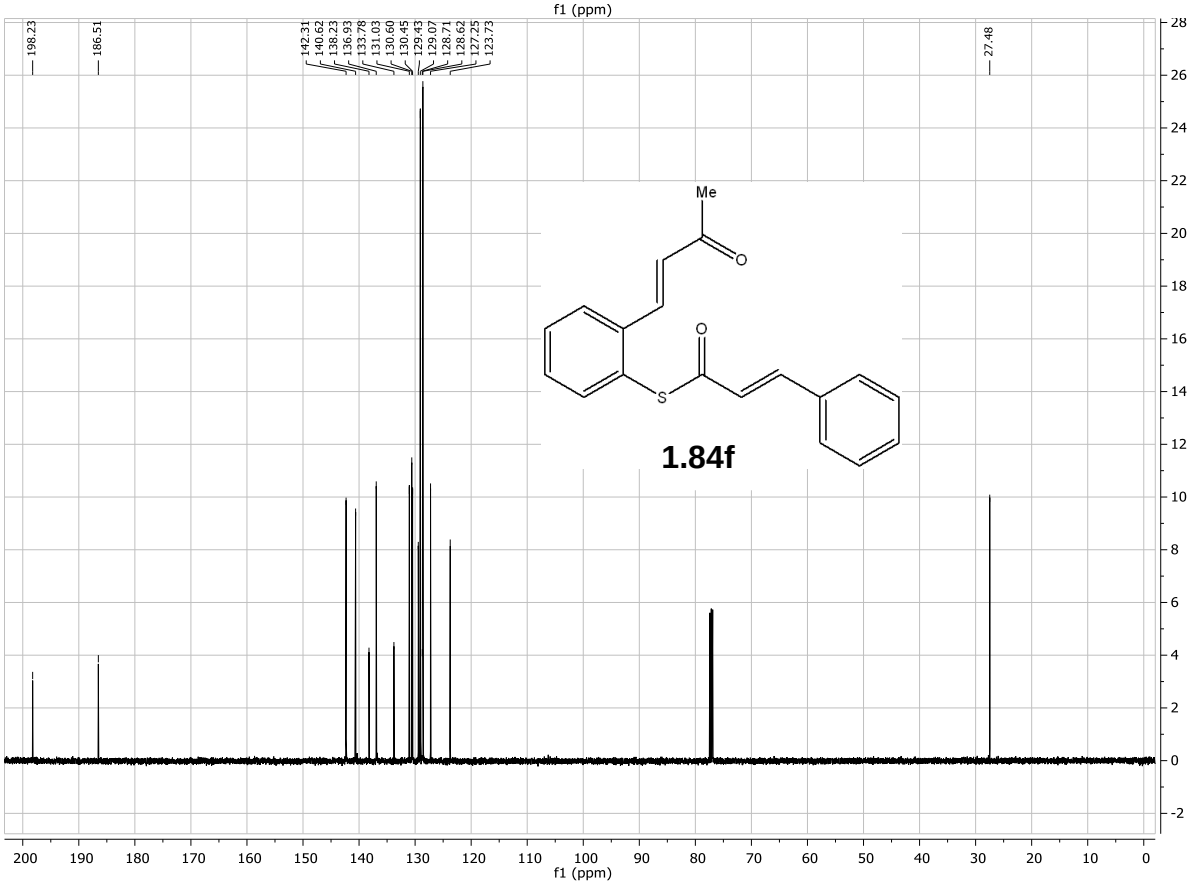

OMe
O
O
S
1.84d
f1 (ppm)

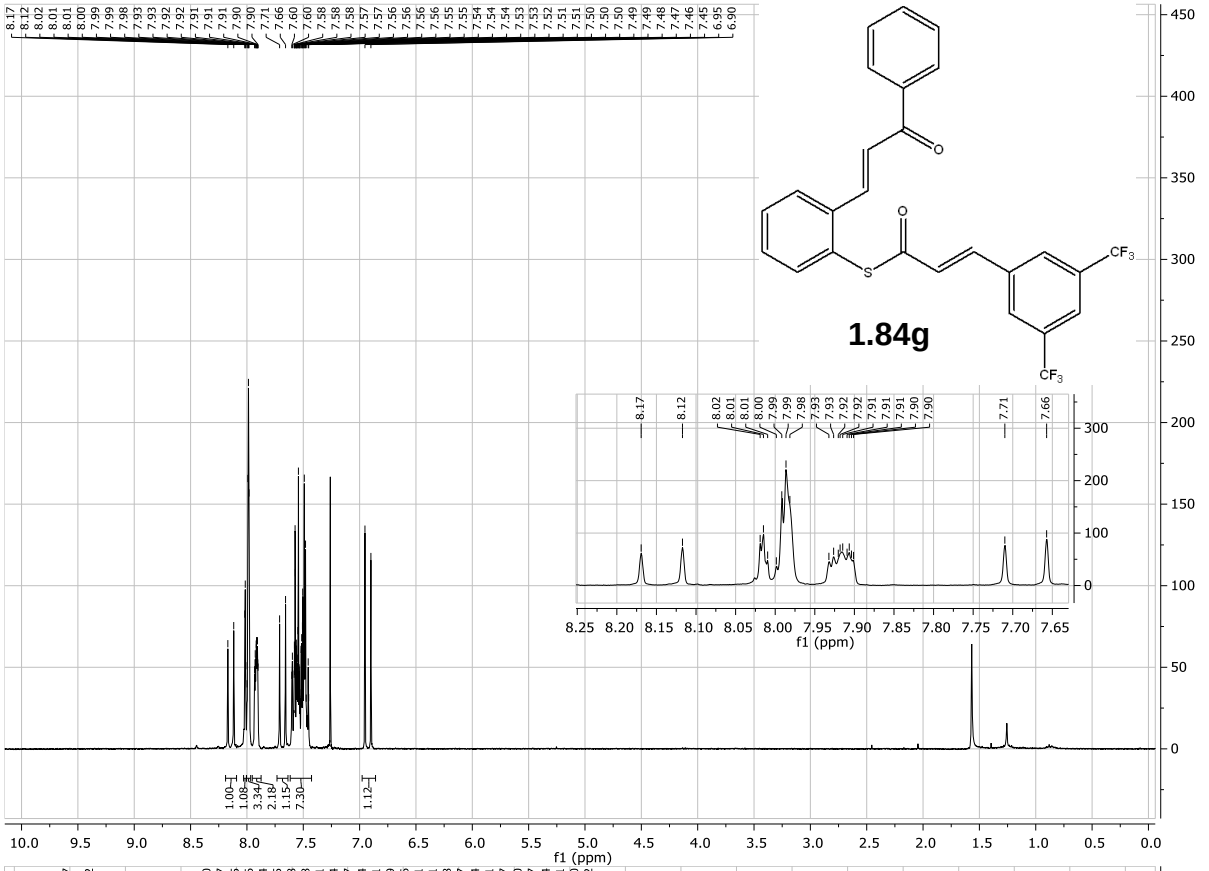

OMe
O
O
S
1.84d
f1 (ppm)

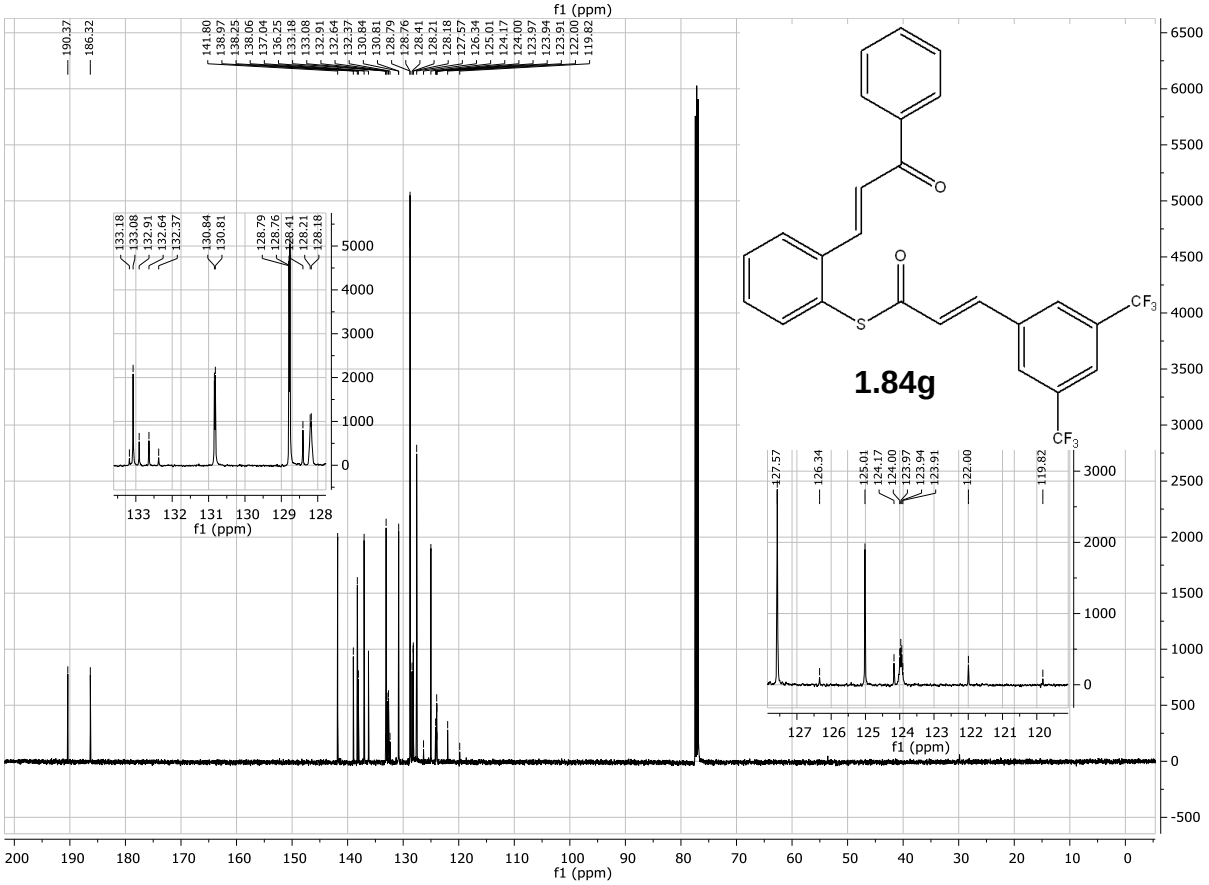

1.84e
f1 (ppm)

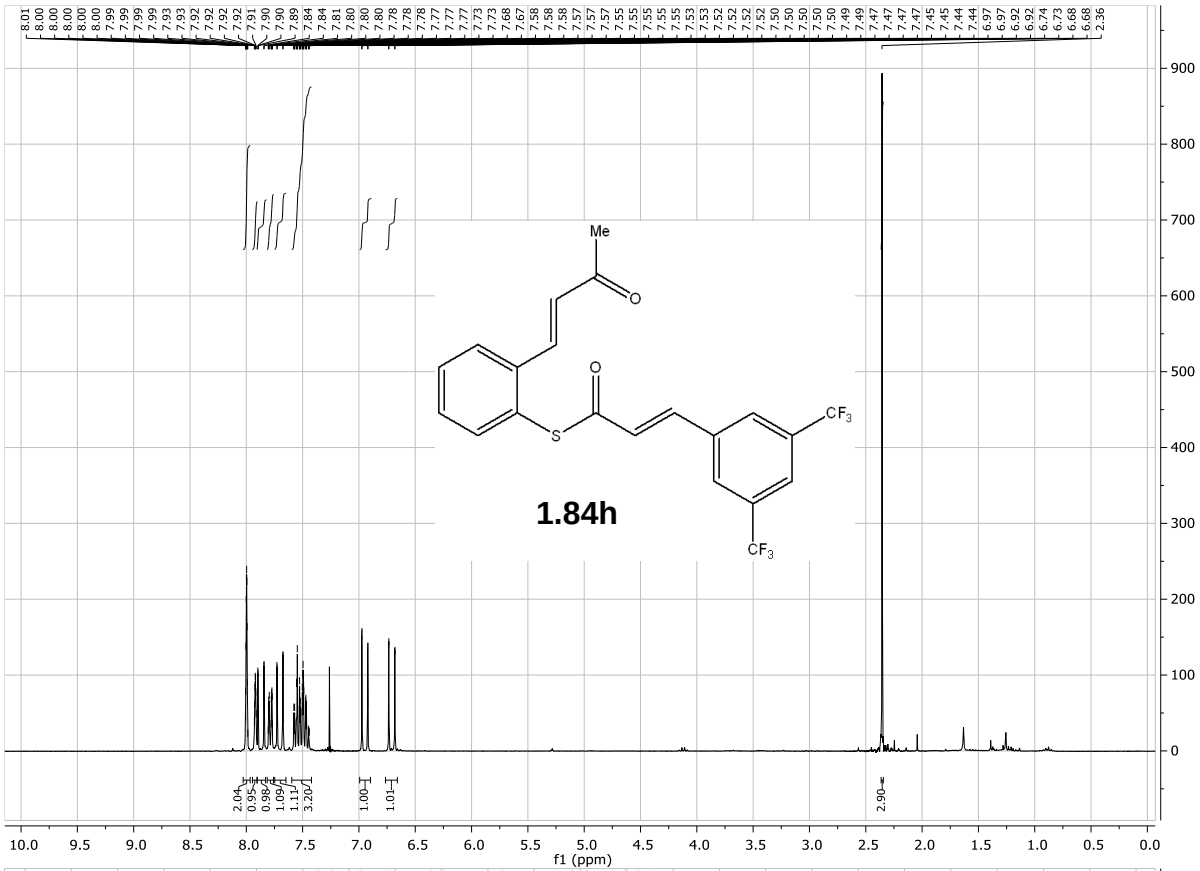

1.84e
f1 (ppm)

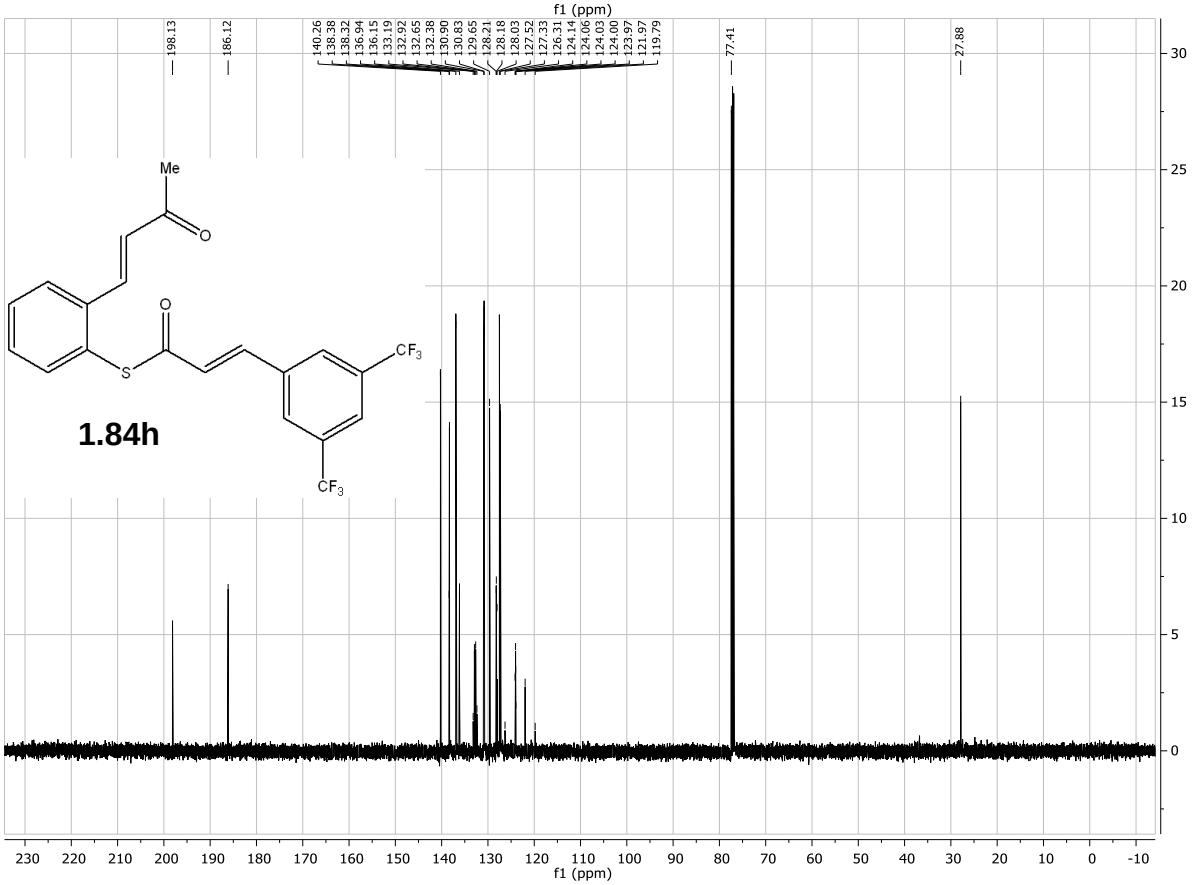

Me
O
O
S
1.84f
f1 (ppm)

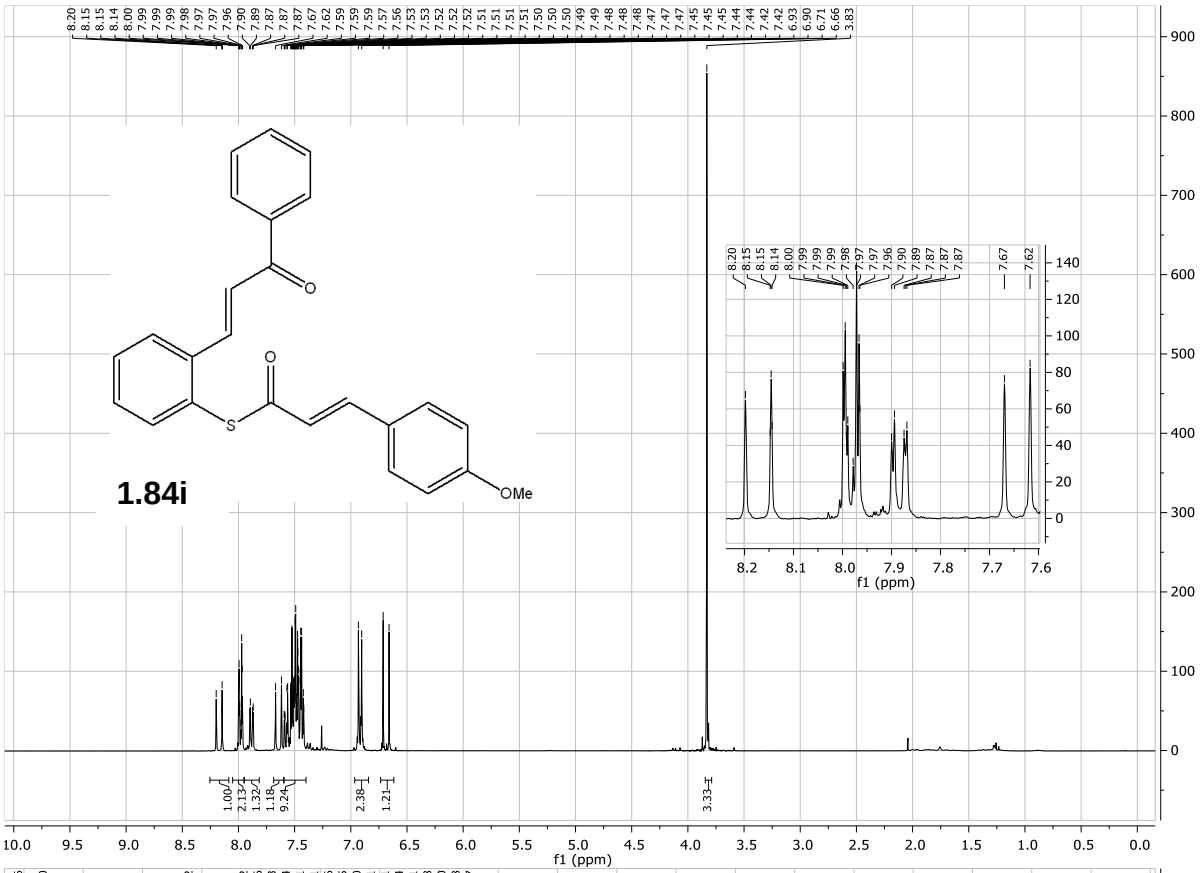

Me
O
O
S
1.84f
f1 (ppm)

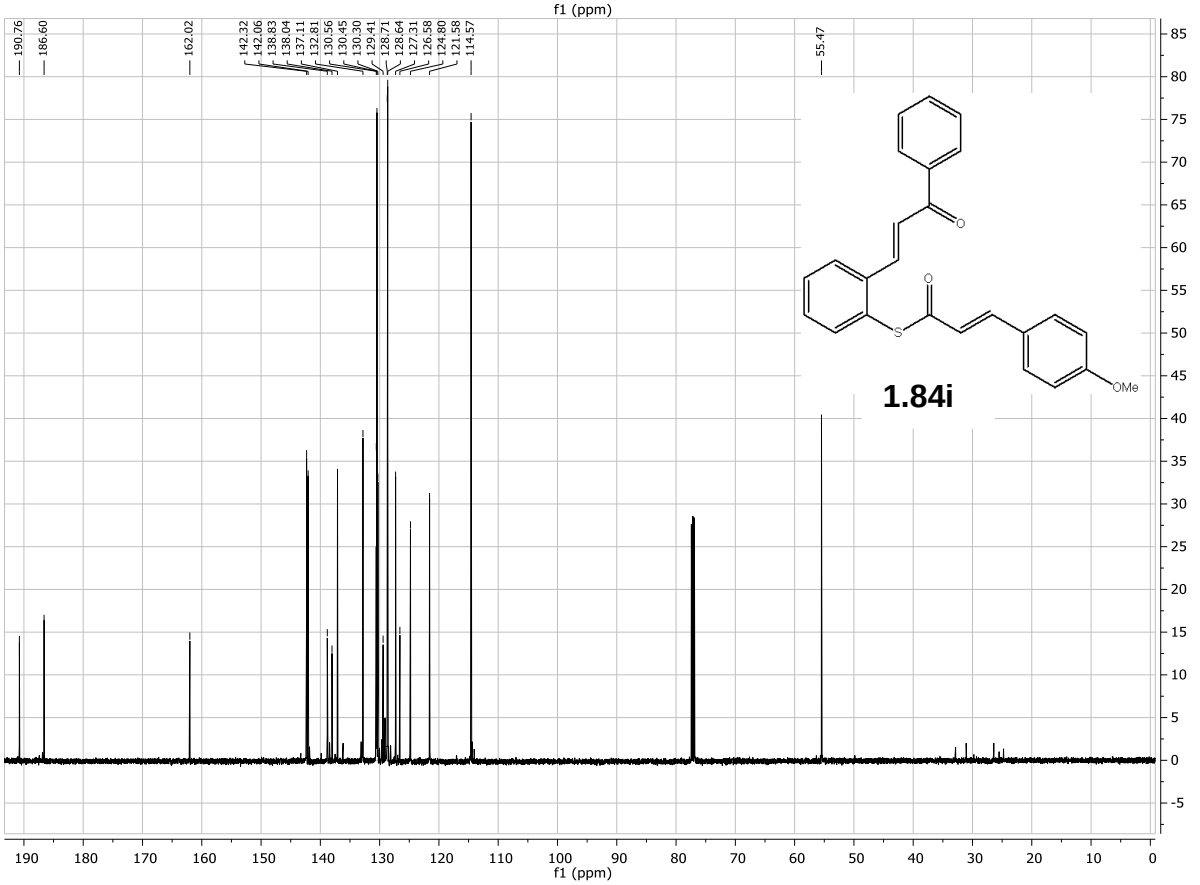

1.84g
f1 (ppm)

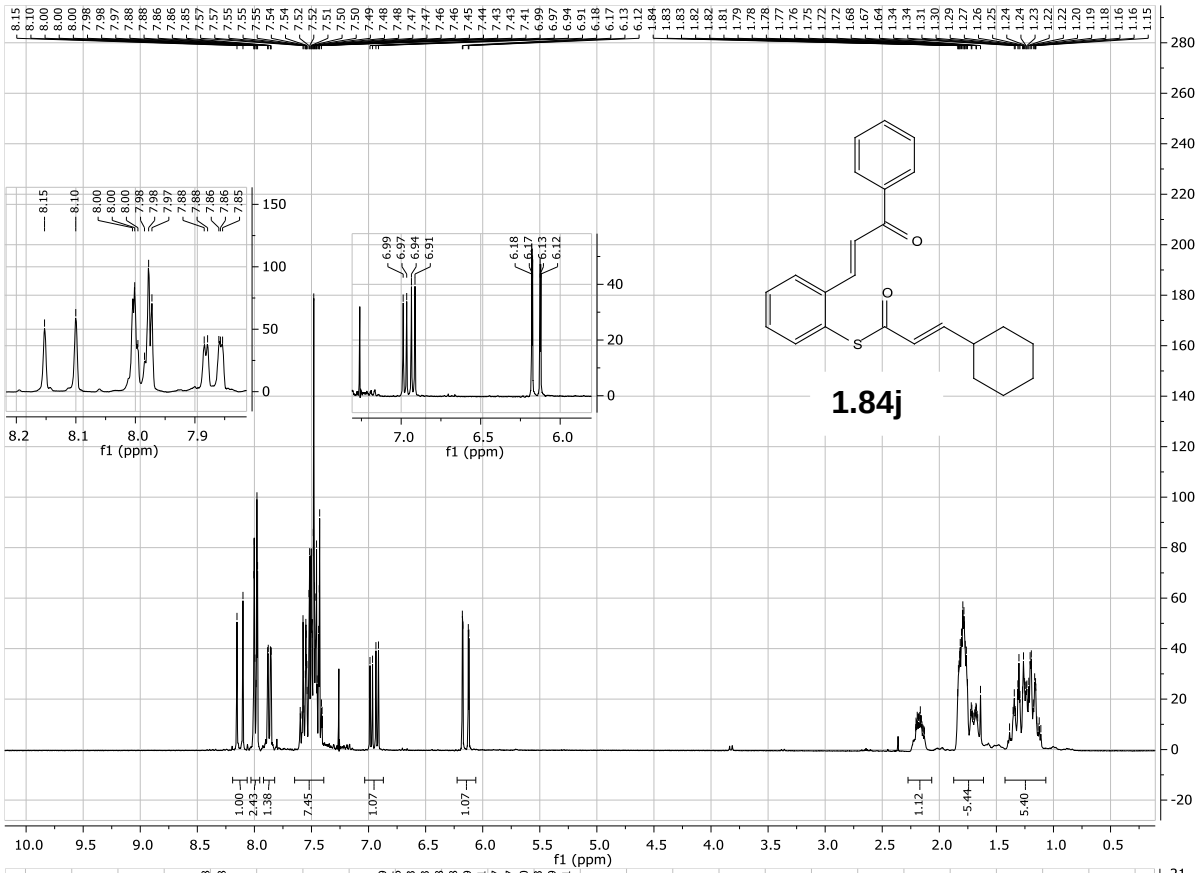

1.84g
f1 (ppm)

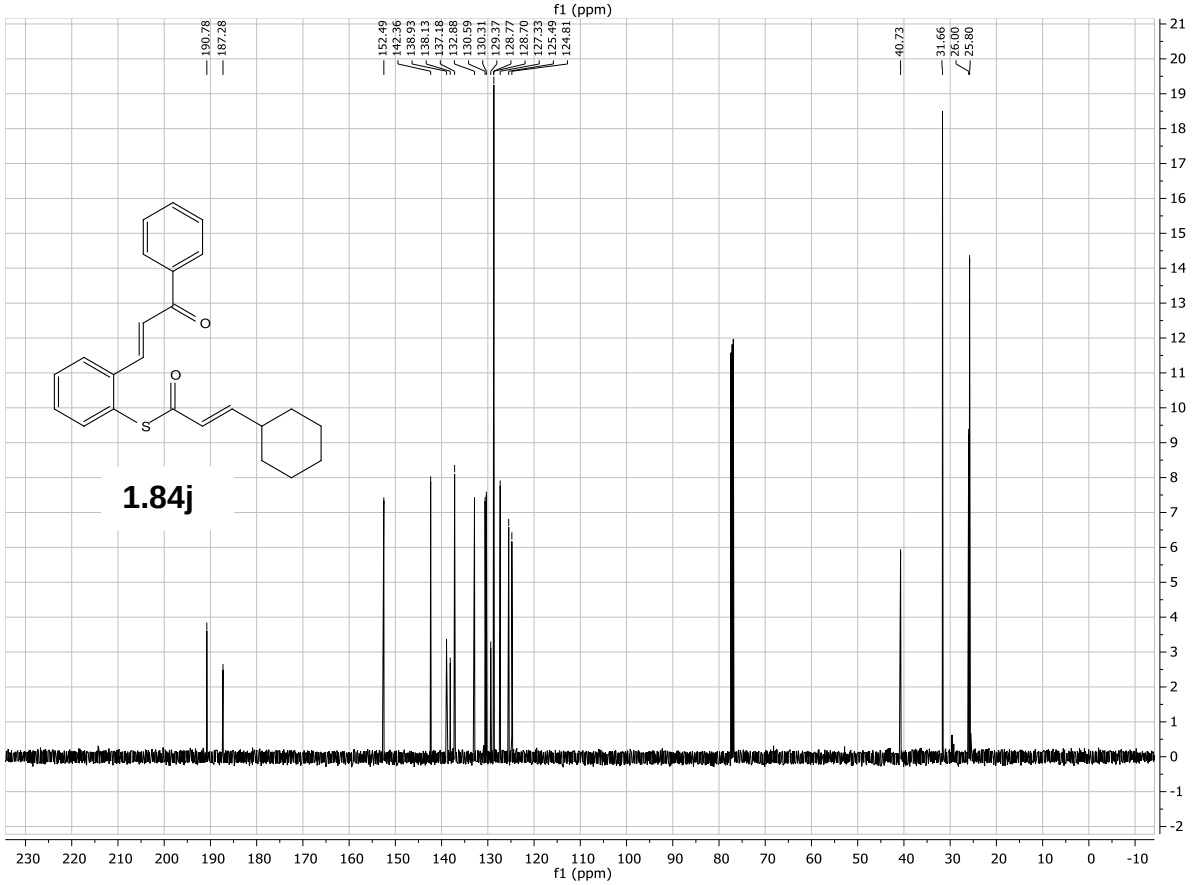

Me
O
O
S
CF3
CF3
1.84h
f1 (ppm)

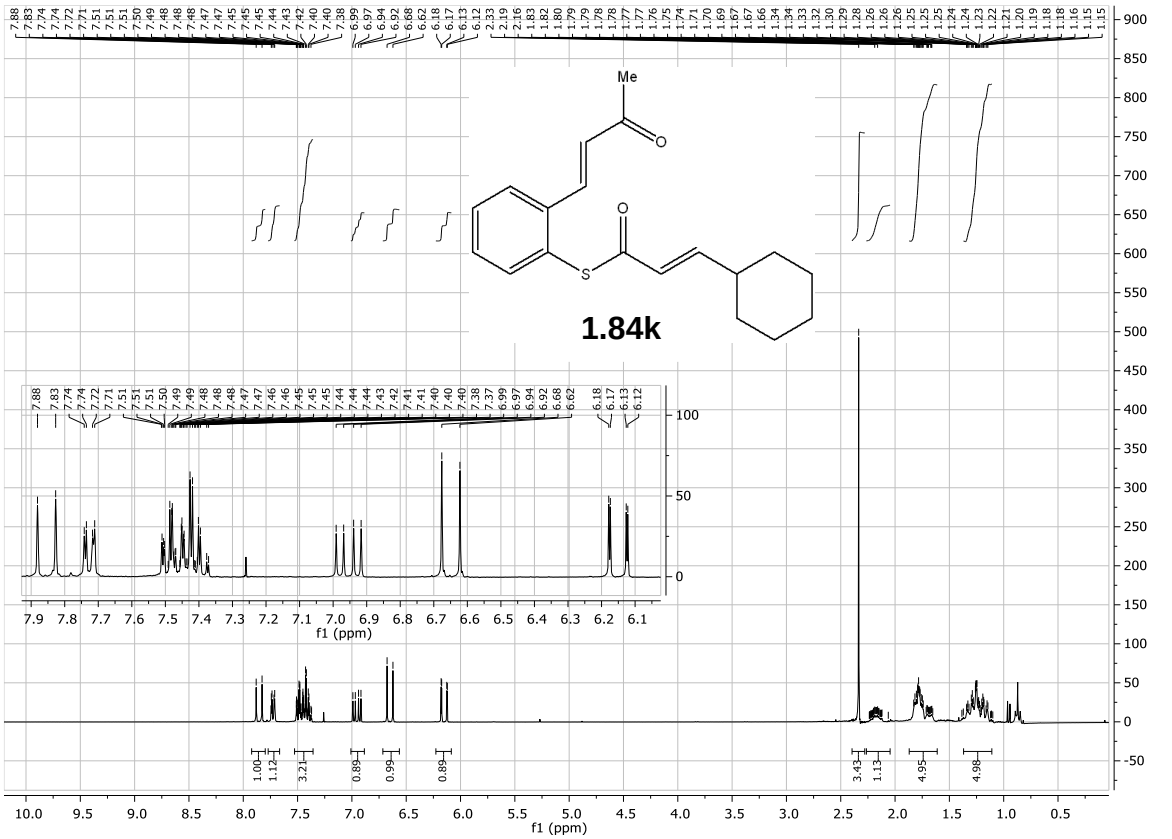

Me
O
O
S
CF3
CF3
1.84h
198.13
186.12
77.41
27.88
f1 (ppm)

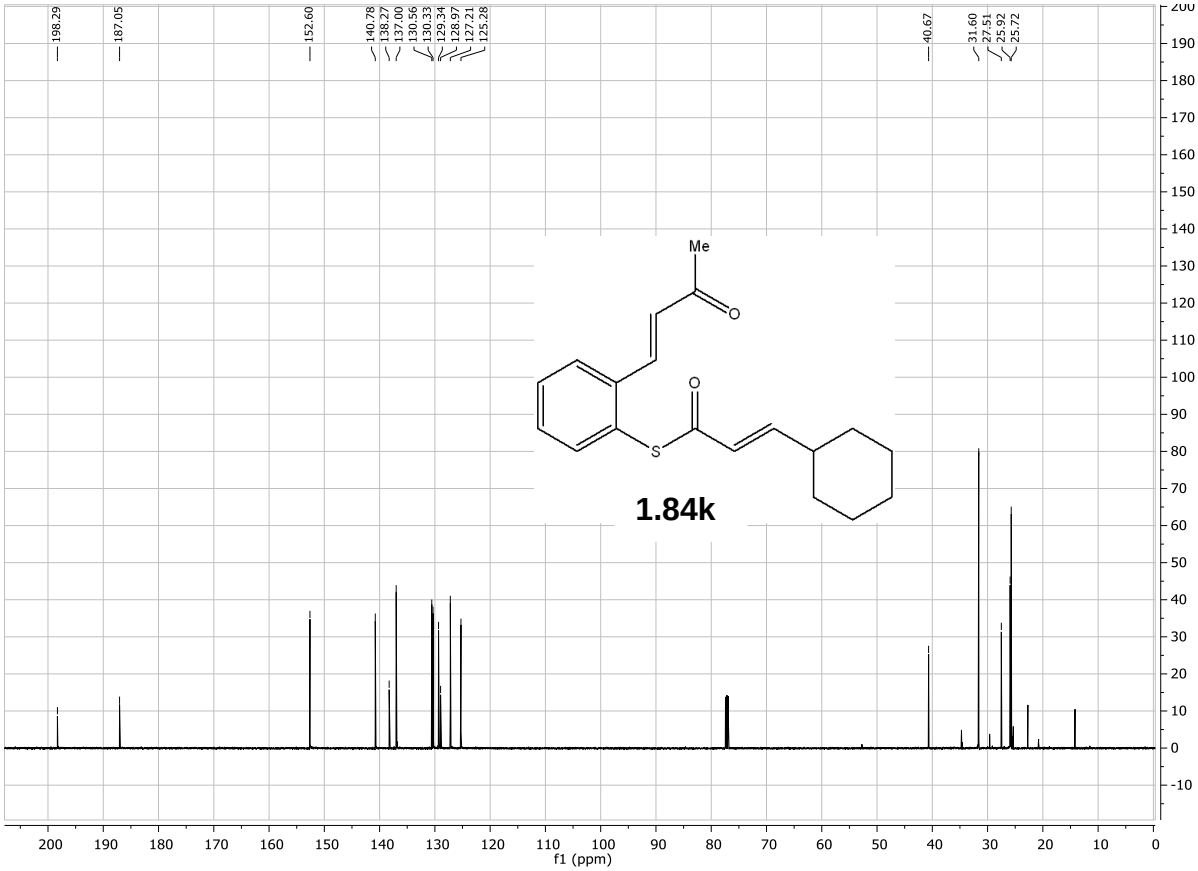

1.84i
OMe
f1 (ppm)

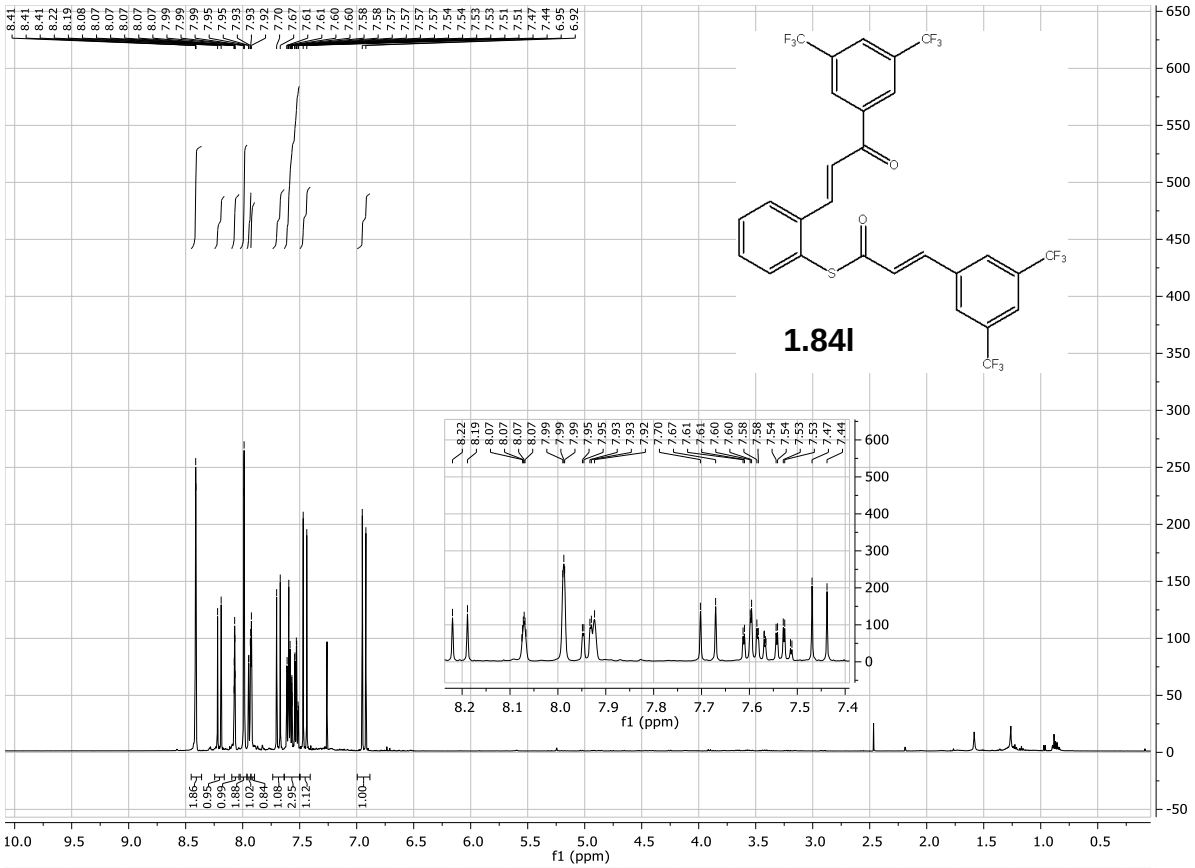

1.84i
OMe
f1 (ppm)

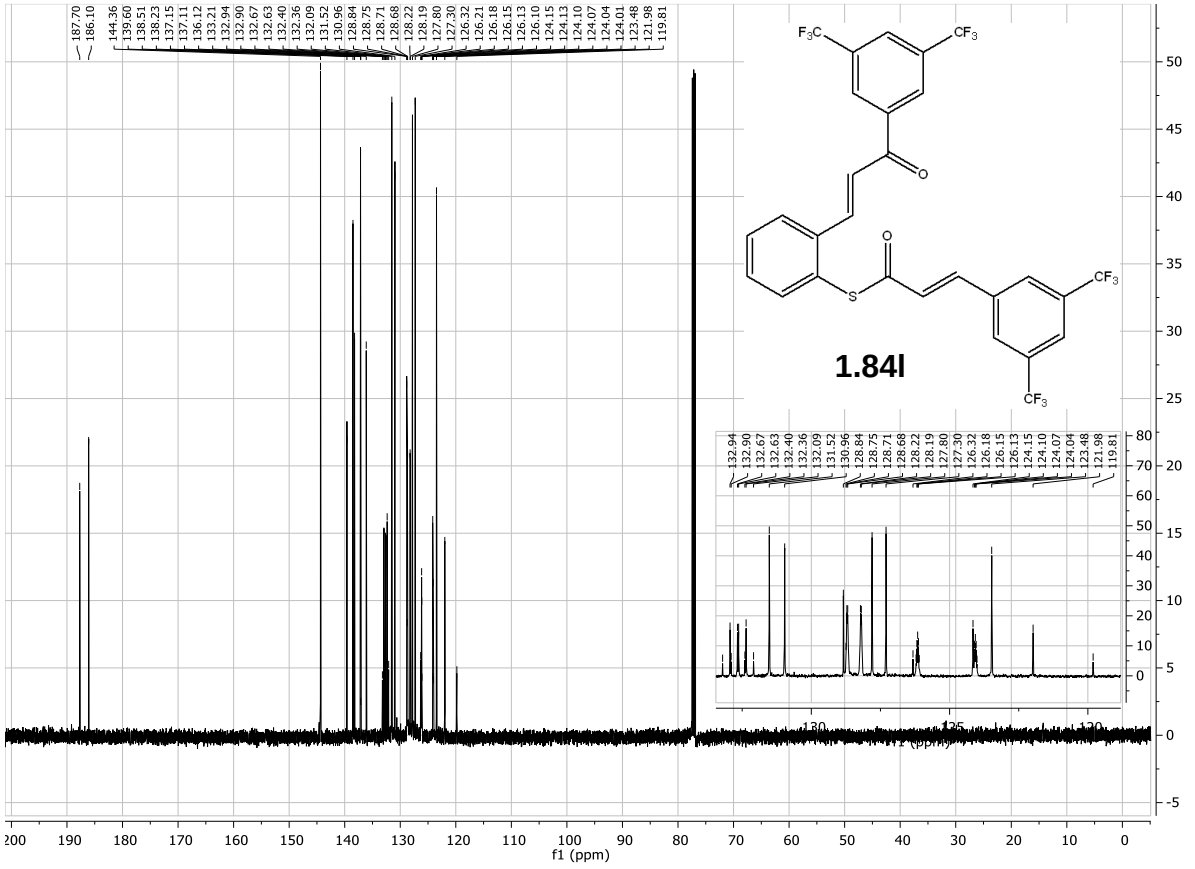

1.84j
f1 (ppm)

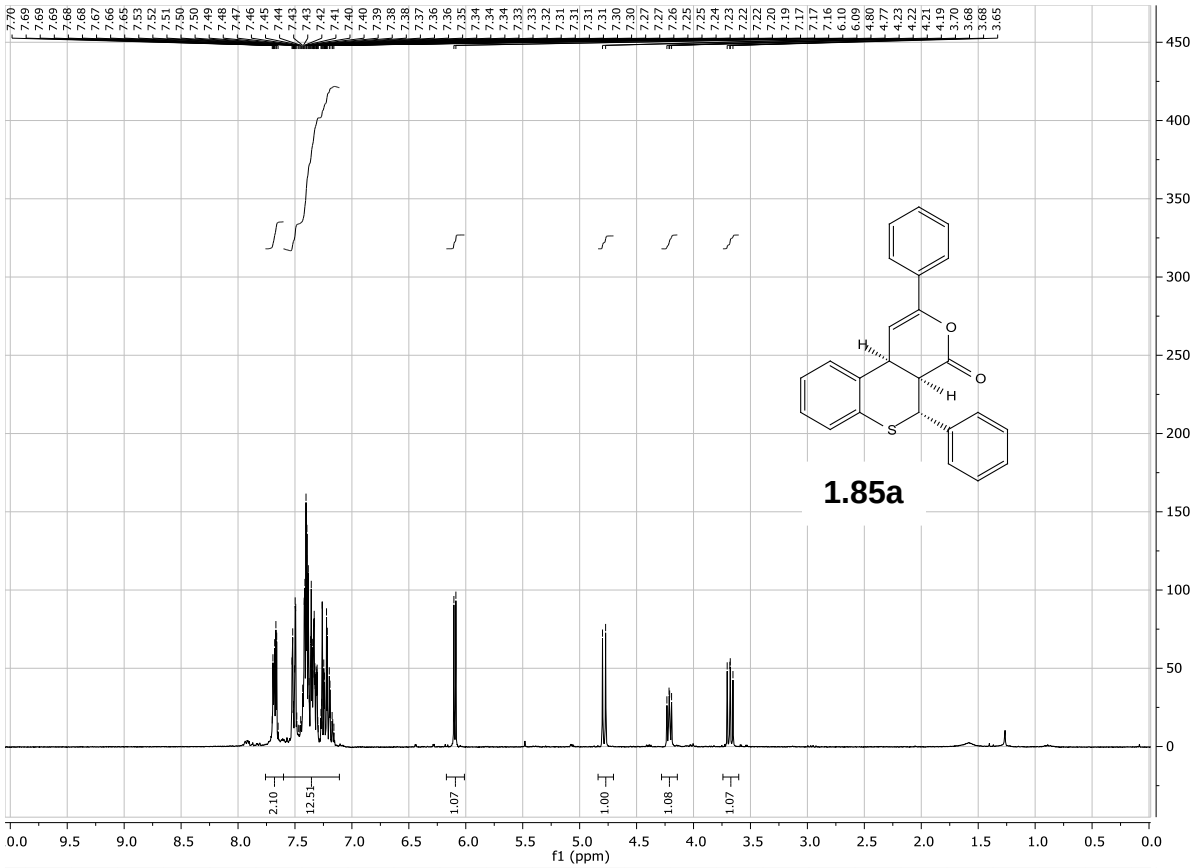

1.84j
f1 (ppm)

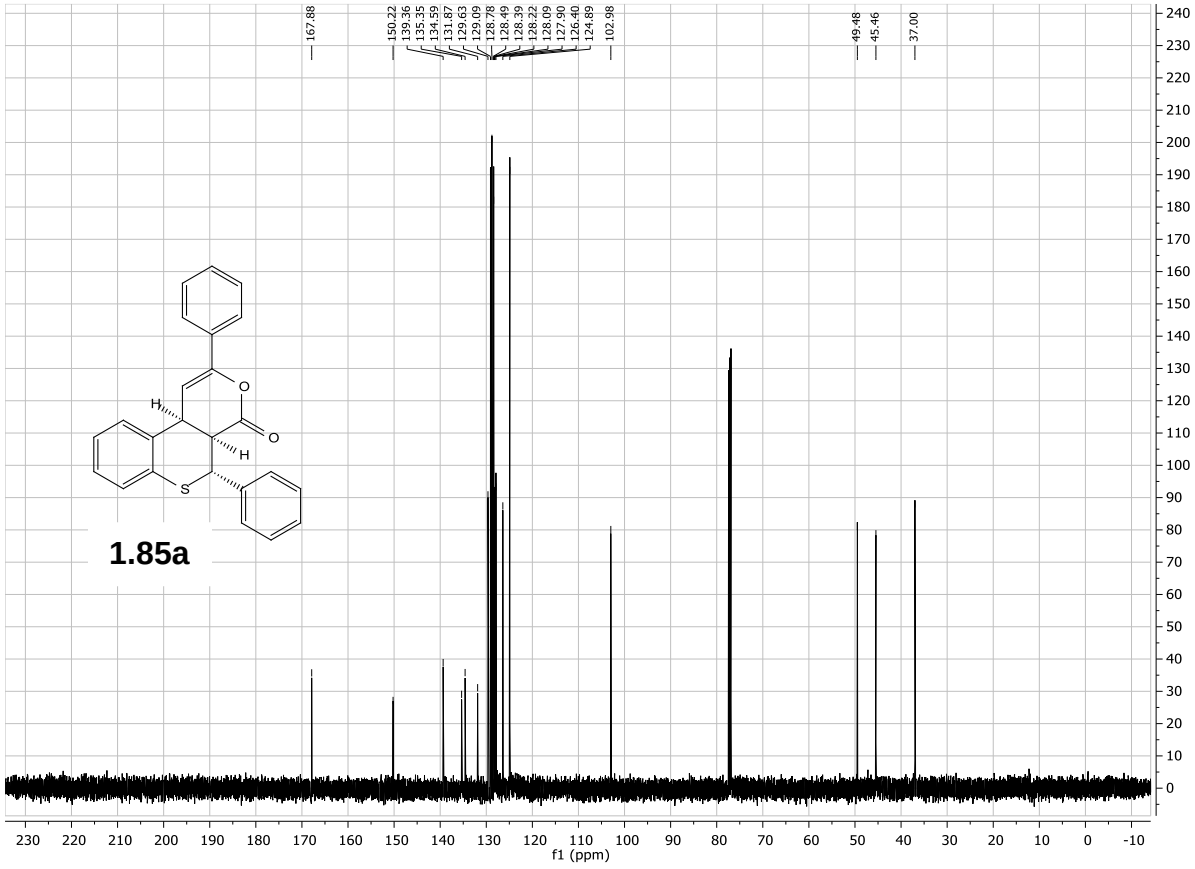

Me
O
O
S
1.84k
f1 (ppm)

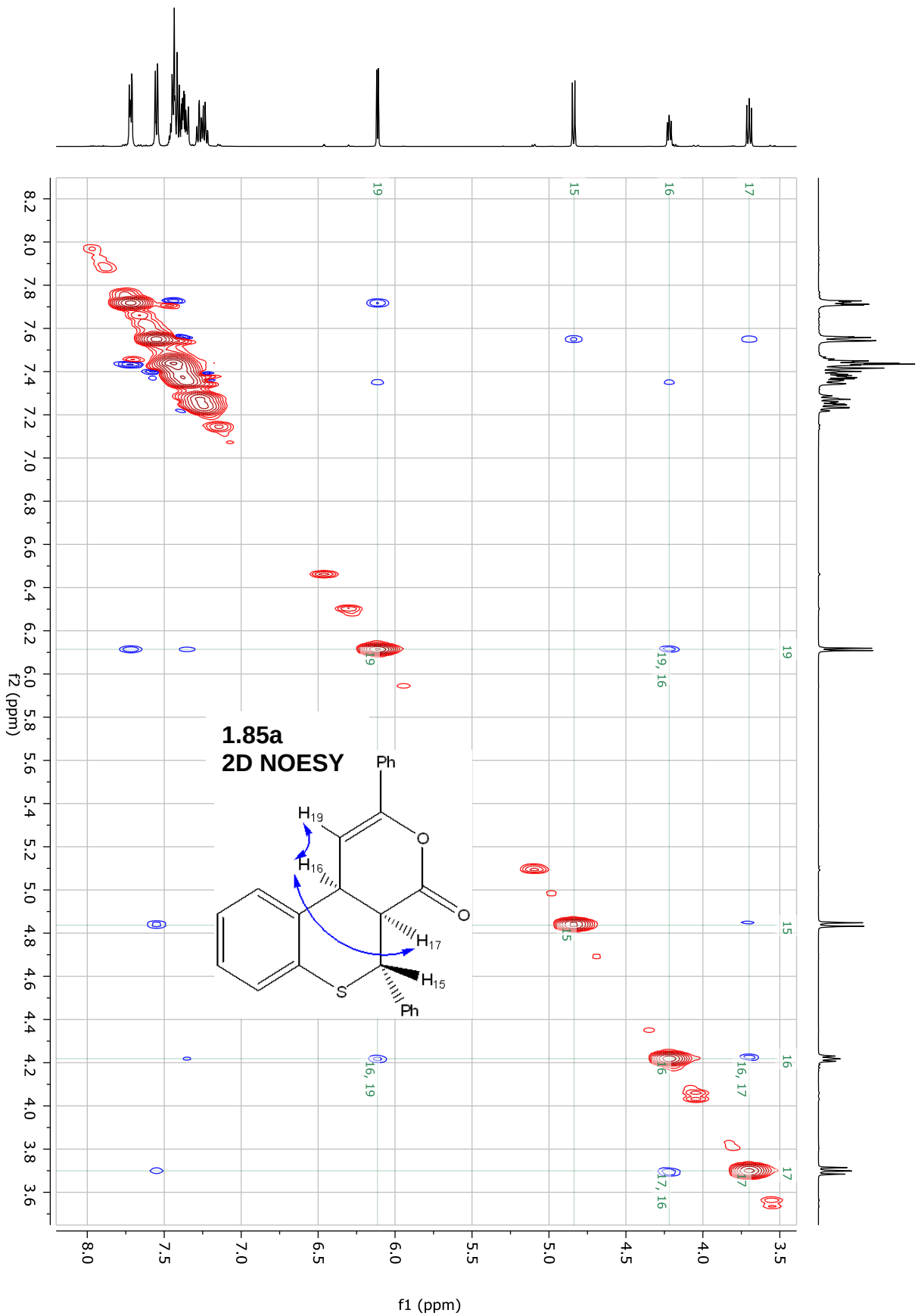

198.29
187.05
152.60
140.78
138.27
137.00
130.56
130.33
129.34
128.97
127.21
125.28
40.67
31.60
27.51
25.92
25.72
Me
O
O
S
1.84k
f1 (ppm)

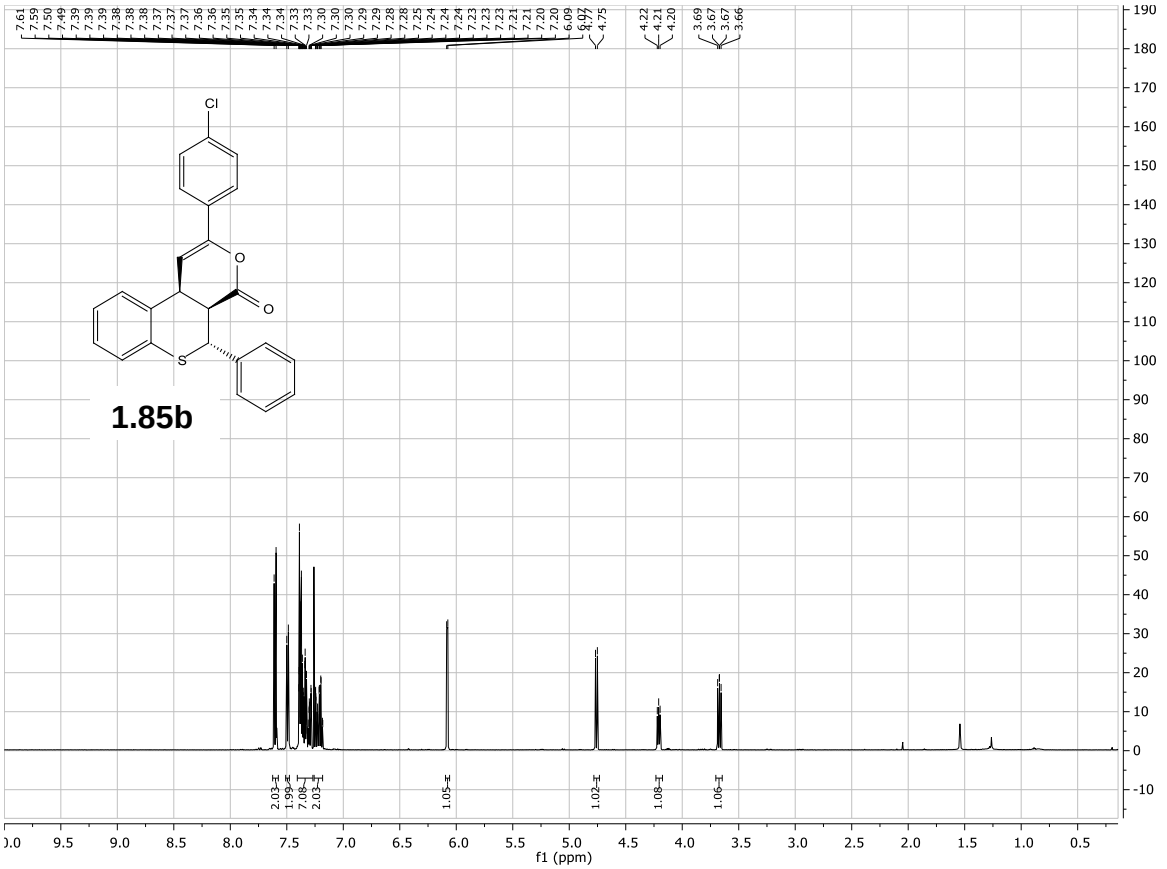

1.84l
f1 (ppm)

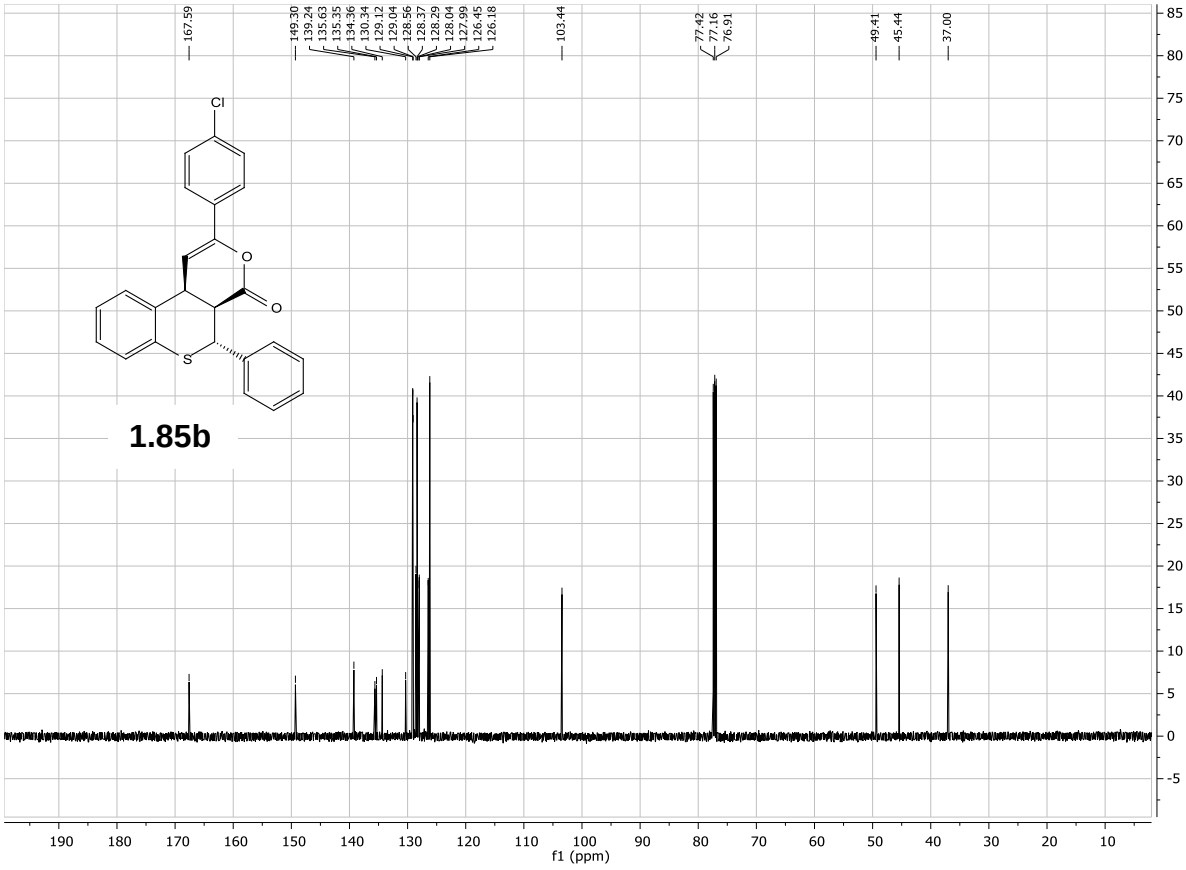

1.84l
f1 (ppm)

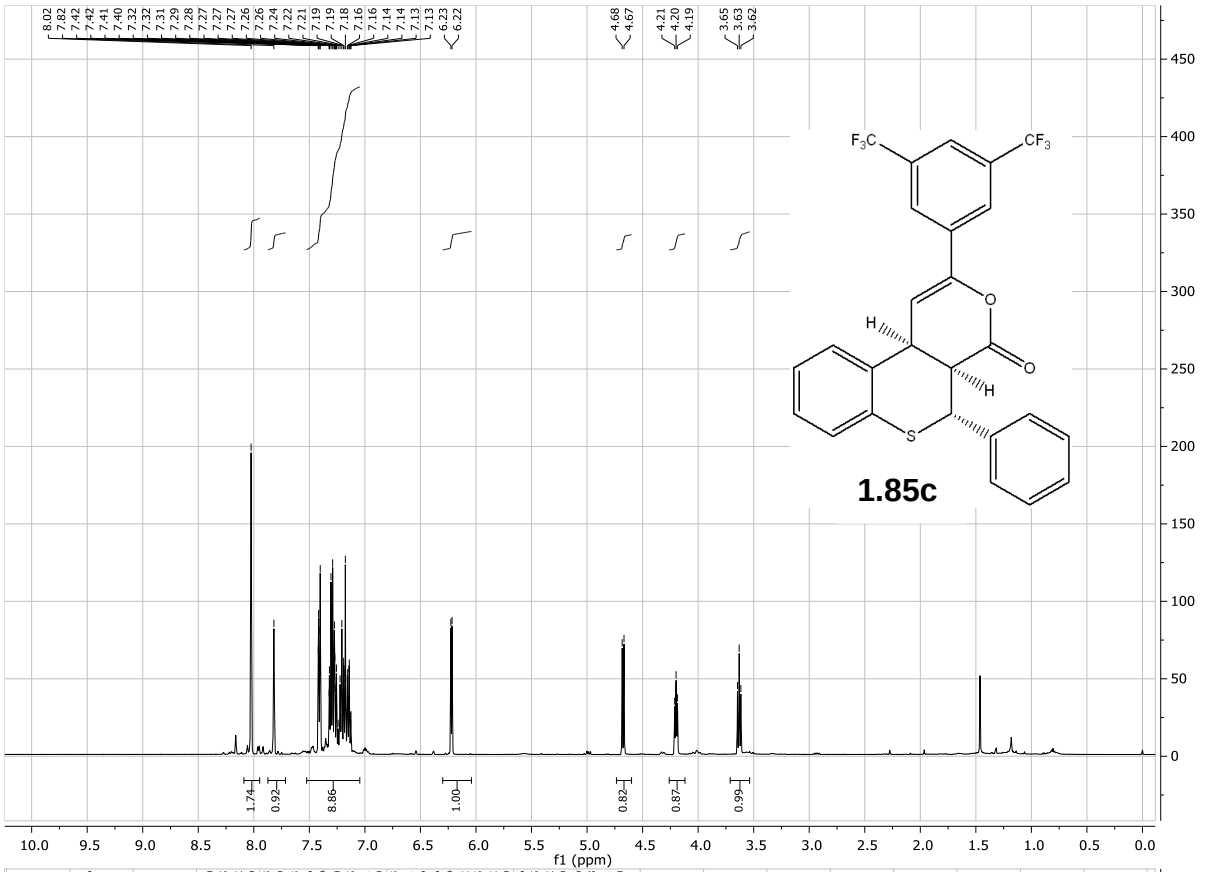

1.85a
f1 (ppm)

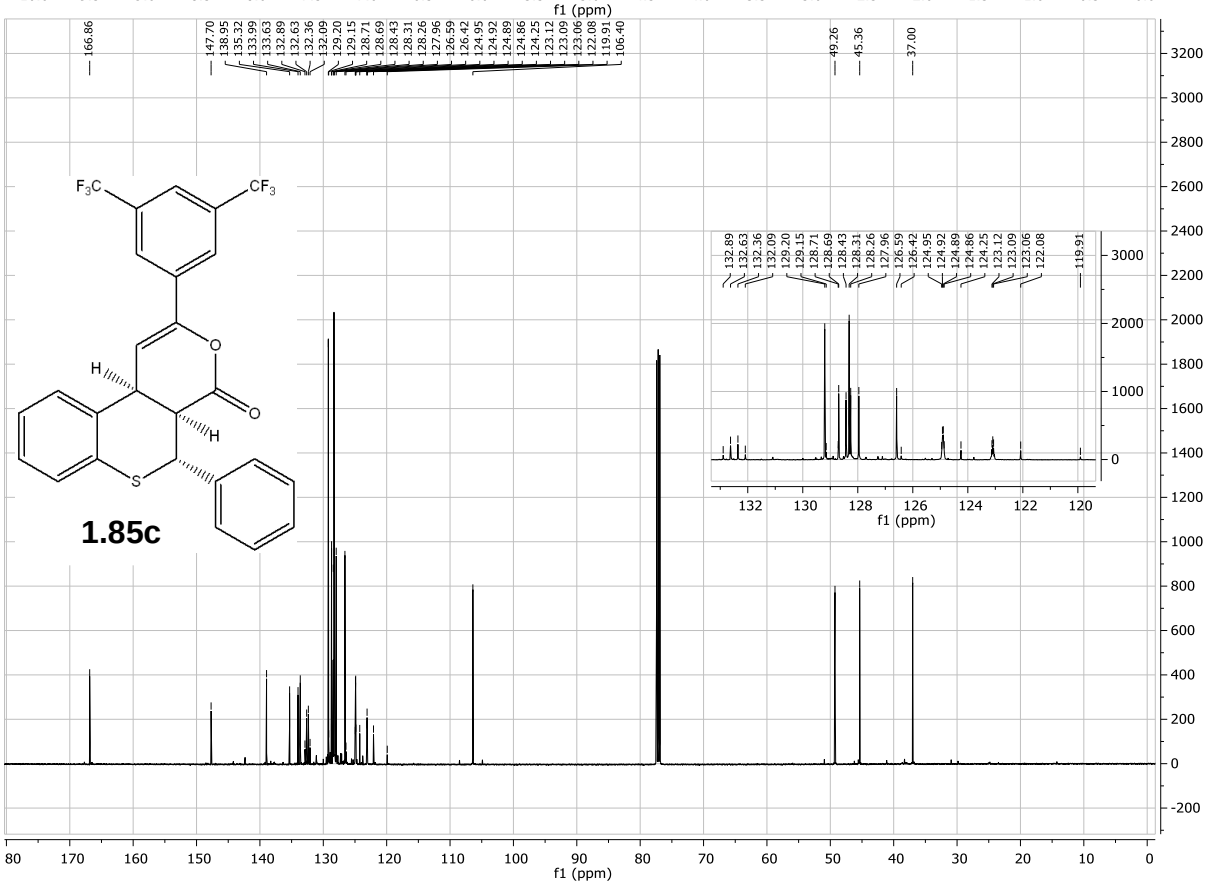

1.85a
f1 (ppm)

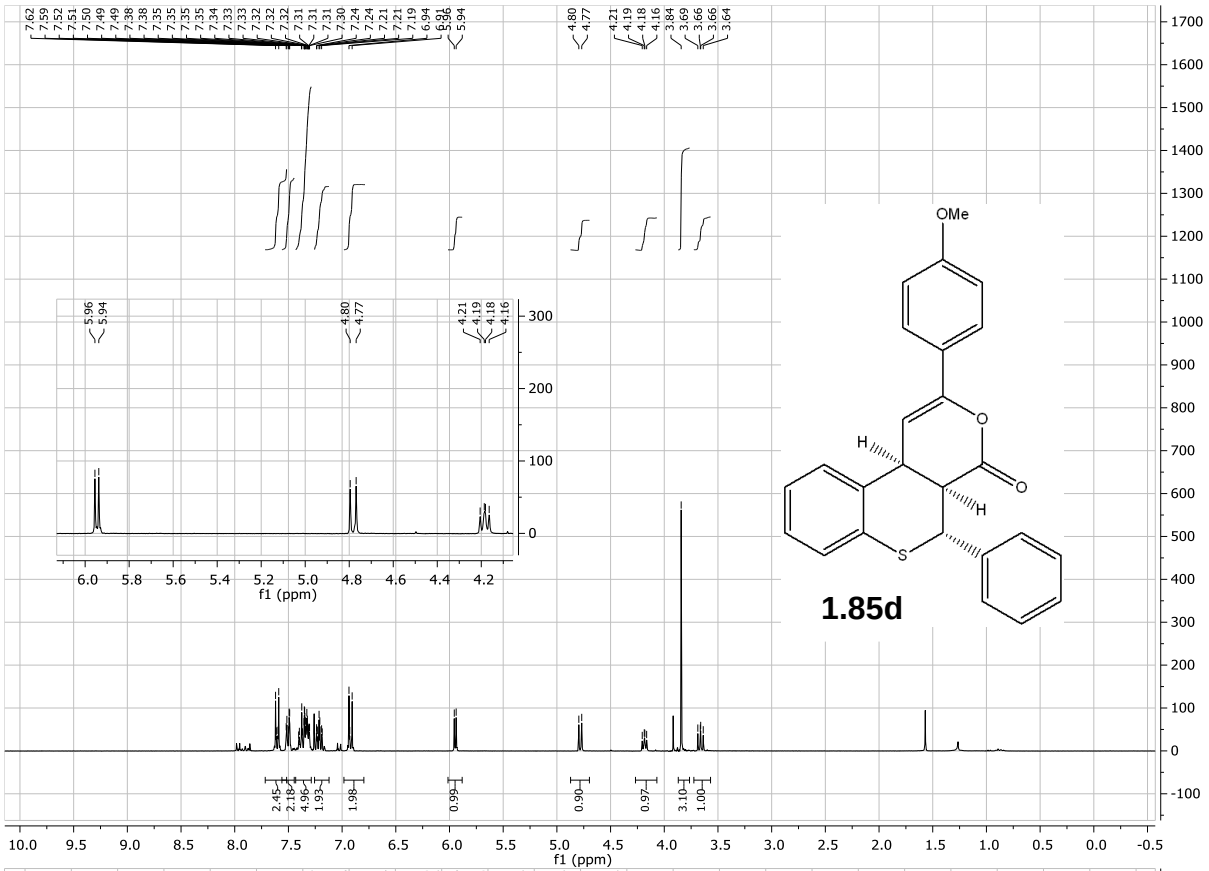

1.85a
2D NOESY
Ph
H19
O
H16
O
H17
H15
S
Ph
f2 (ppm)
f1 (ppm)

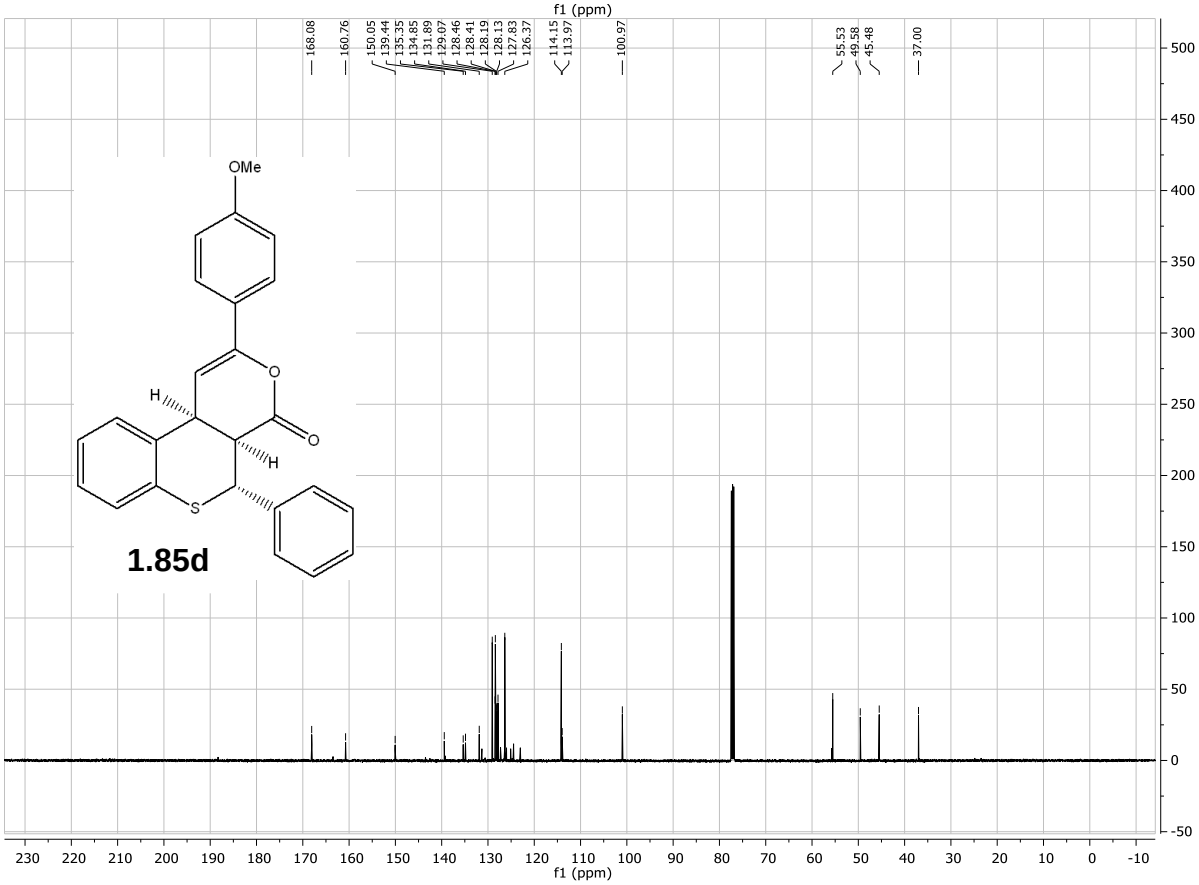

Cl
O
O
S
1.85b
f1 (ppm)

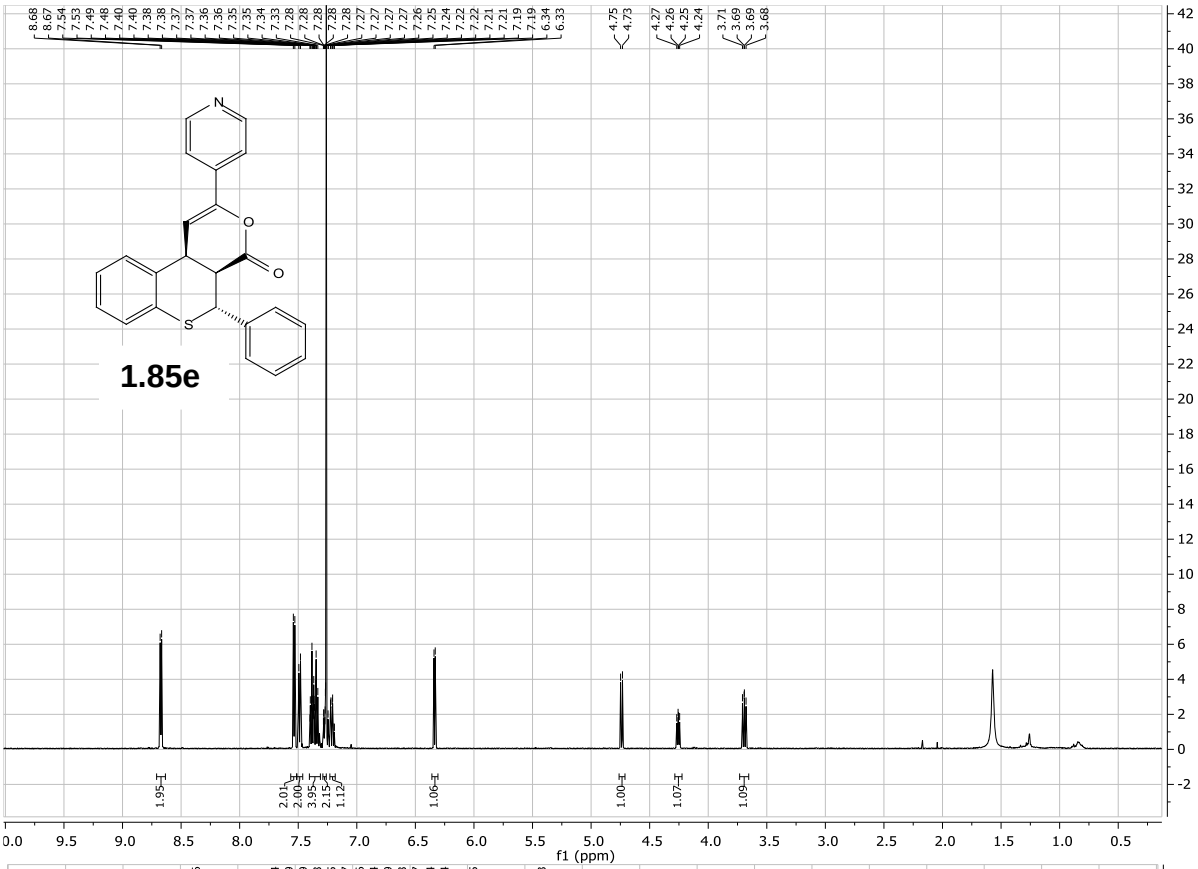

Cl
O
O
S
1.85b
f1 (ppm)

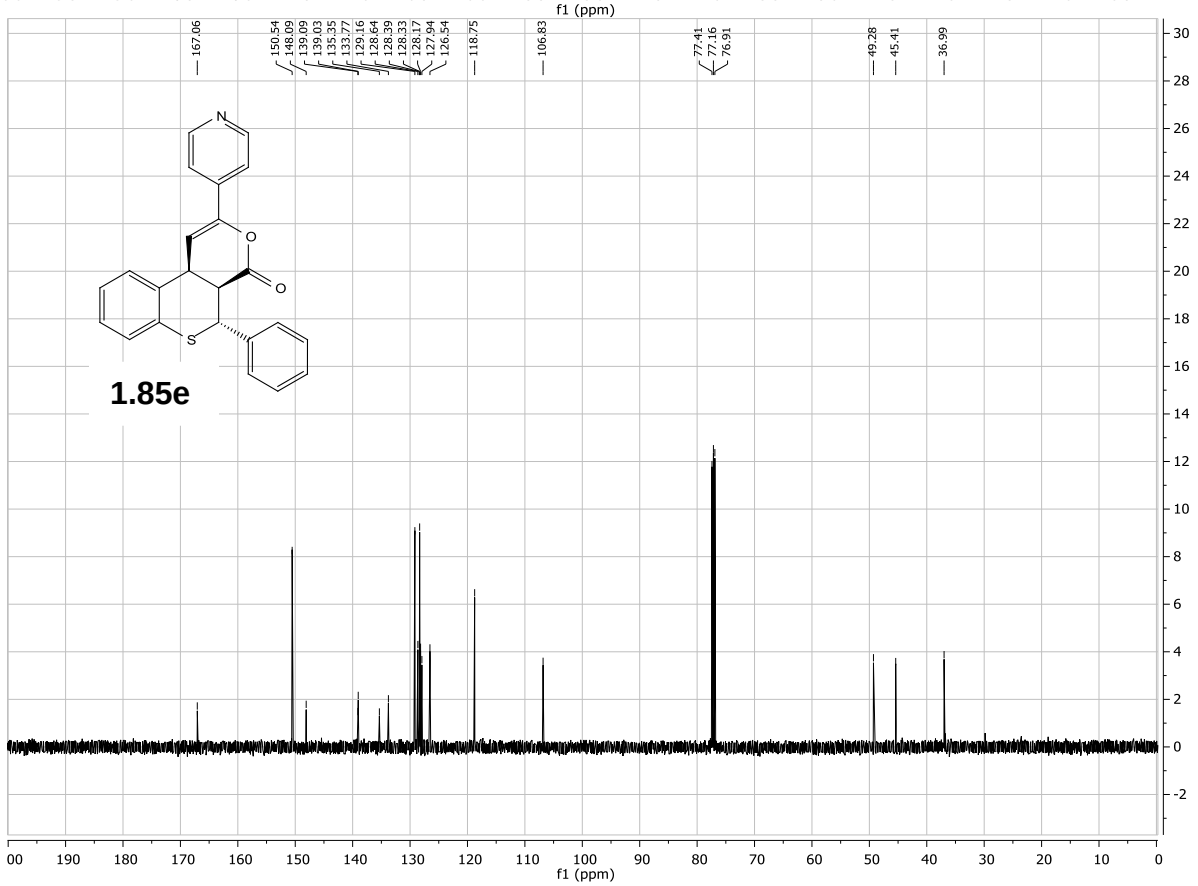

8.02
7.82
7.42
7.42
7.41
7.40
7.32
7.32
7.31
7.29
7.28
7.27
7.27
7.27
7.26
7.26
7.24
7.22
7.21
7.19
7.19
7.18
7.16
7.16
7.14
7.14
7.13
7.13
6.23
6.22
4.68
4.67
4.21
4.20
4.19
3.65
3.63
3.62
F3C
CF3
O
H
O
H
S
1.85c
1.74
0.92
8.86
1.00
0.82
0.87
0.99
f1 (ppm)

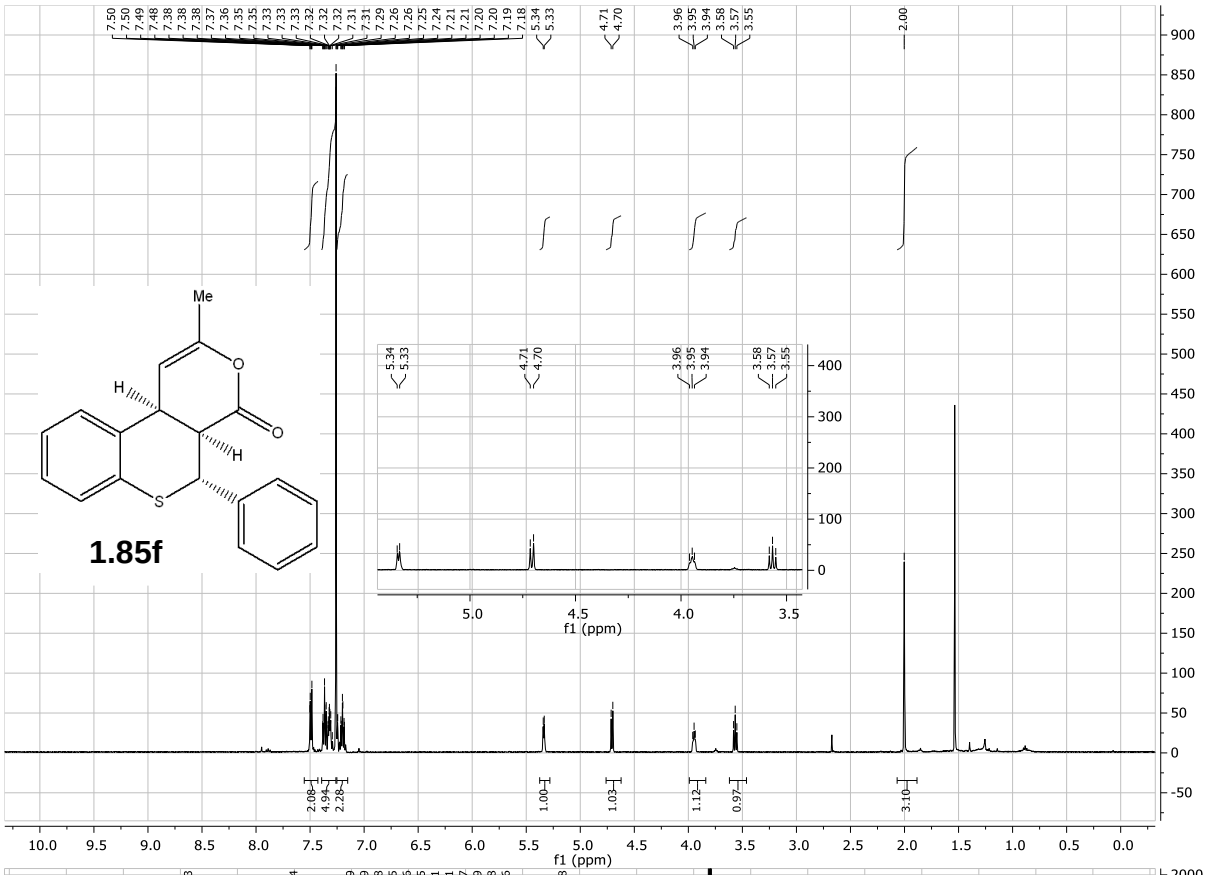

166.86
147.70
138.95
135.32
133.99
133.63
132.89
132.63
132.36
132.09
129.20
129.15
128.71
128.69
128.43
128.31
128.26
127.96
126.59
126.42
124.95
124.92
124.89
124.86
124.25
123.12
123.09
123.06
122.08
119.91
106.40
49.26
45.36
37.00
F3C
CF3
O
H
O
H
S
1.85c
f1 (ppm)
f1 (ppm)

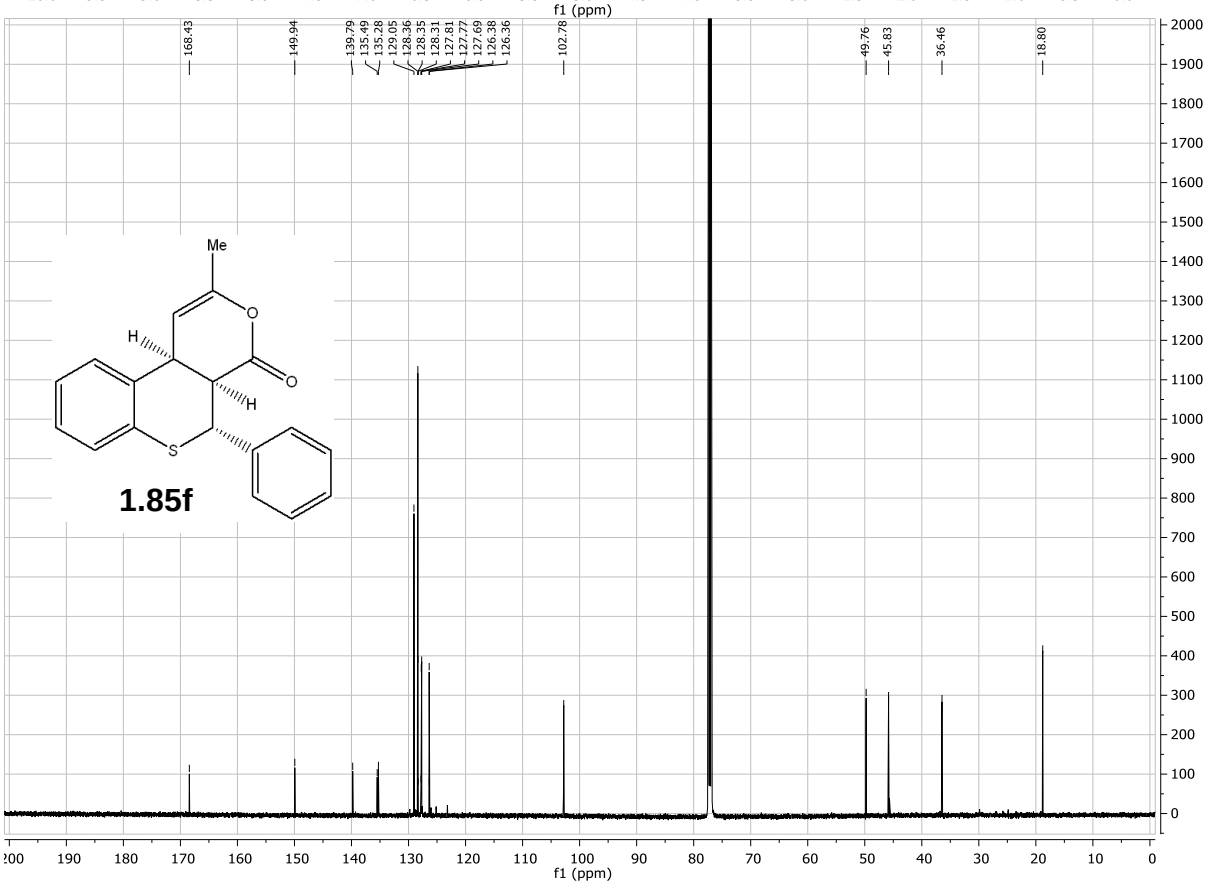

OMe
O
H
O
H
S
1.85d
f1 (ppm)

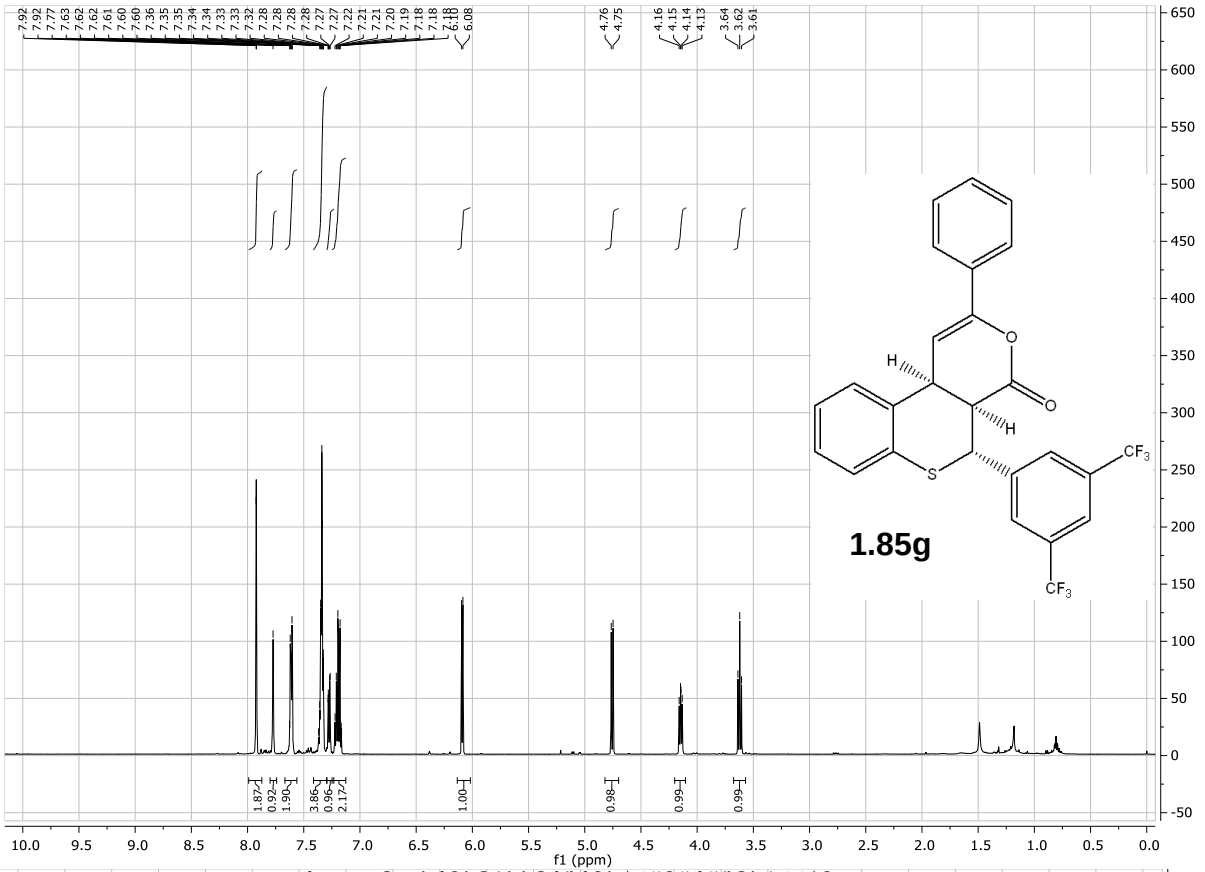

OMe
O
H
O
H
S
1.85d
f1 (ppm)

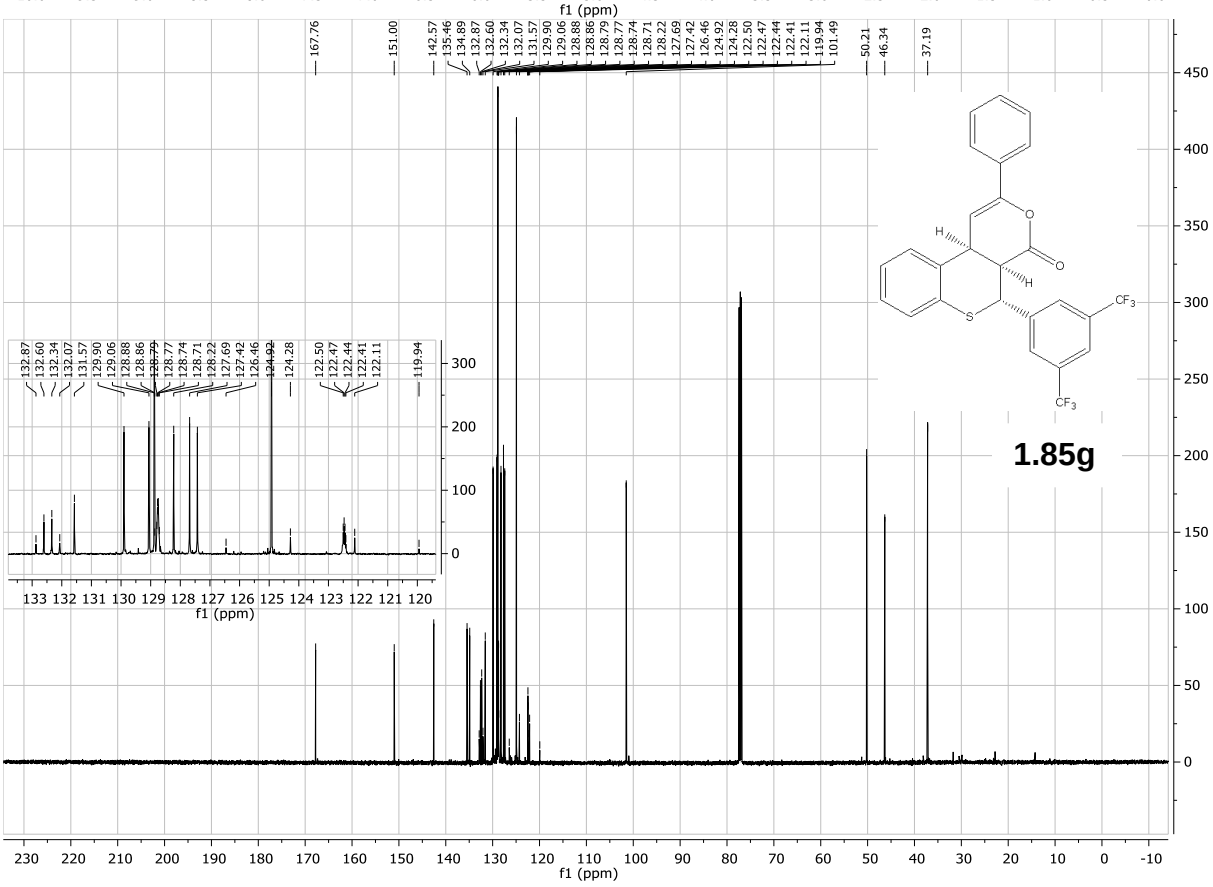

1.85e
f1 (ppm)

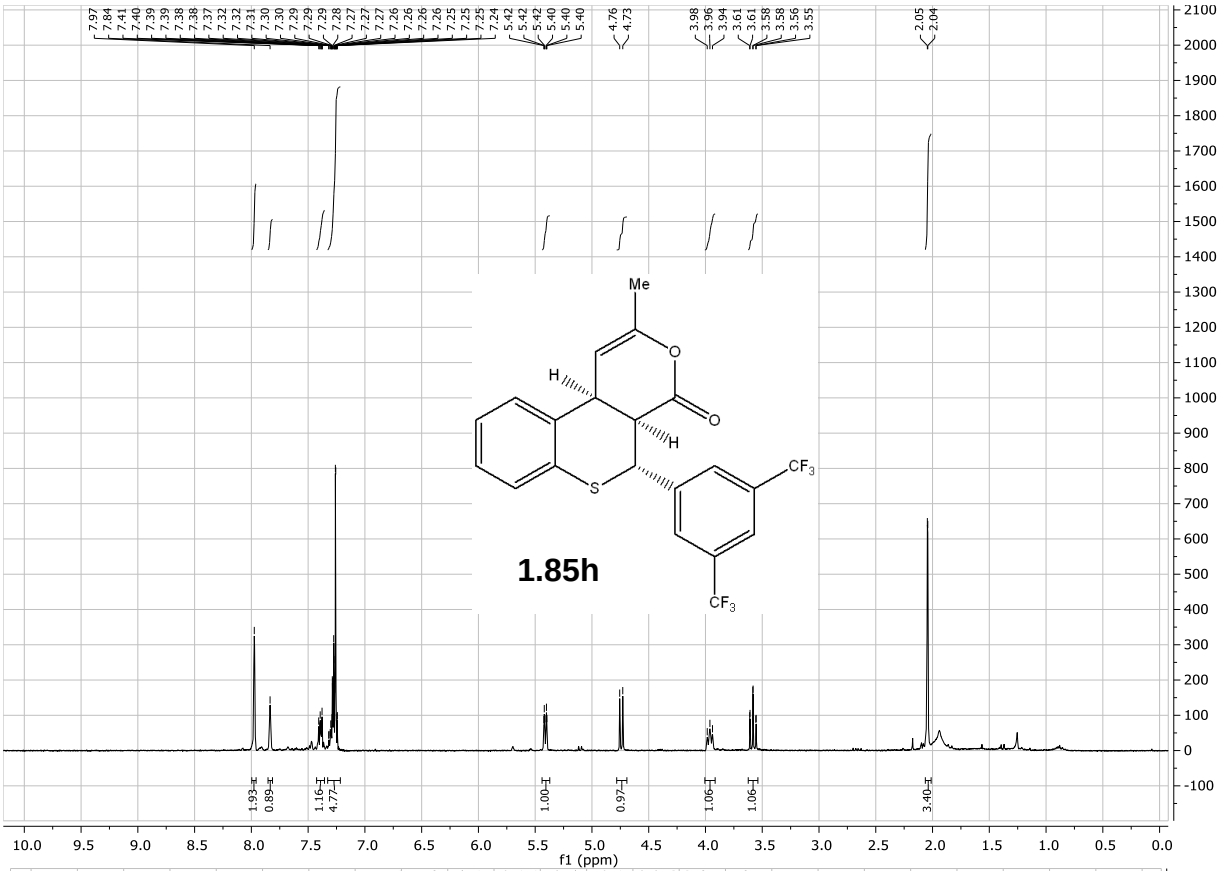

1.85e
f1 (ppm)

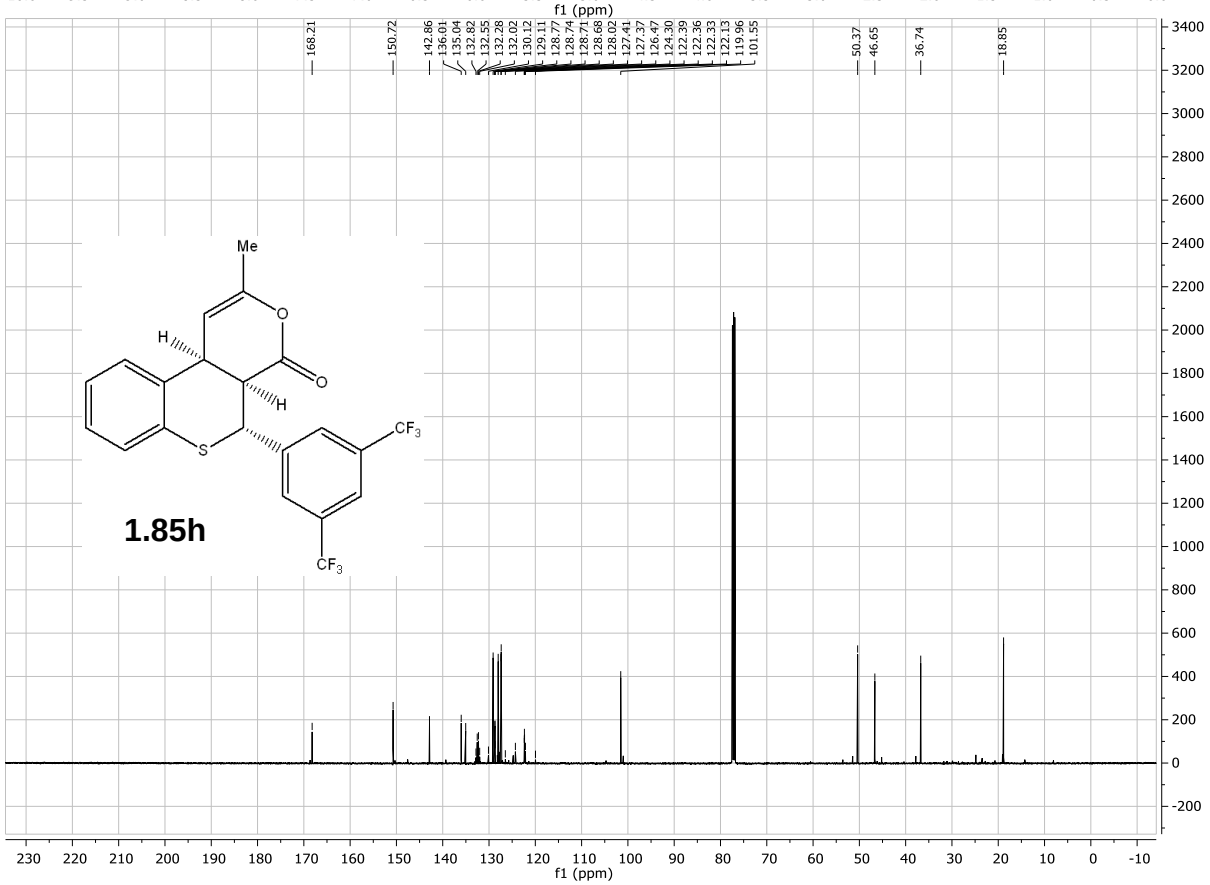

Me
O
H
O
H
S
1.85f
f1 (ppm)

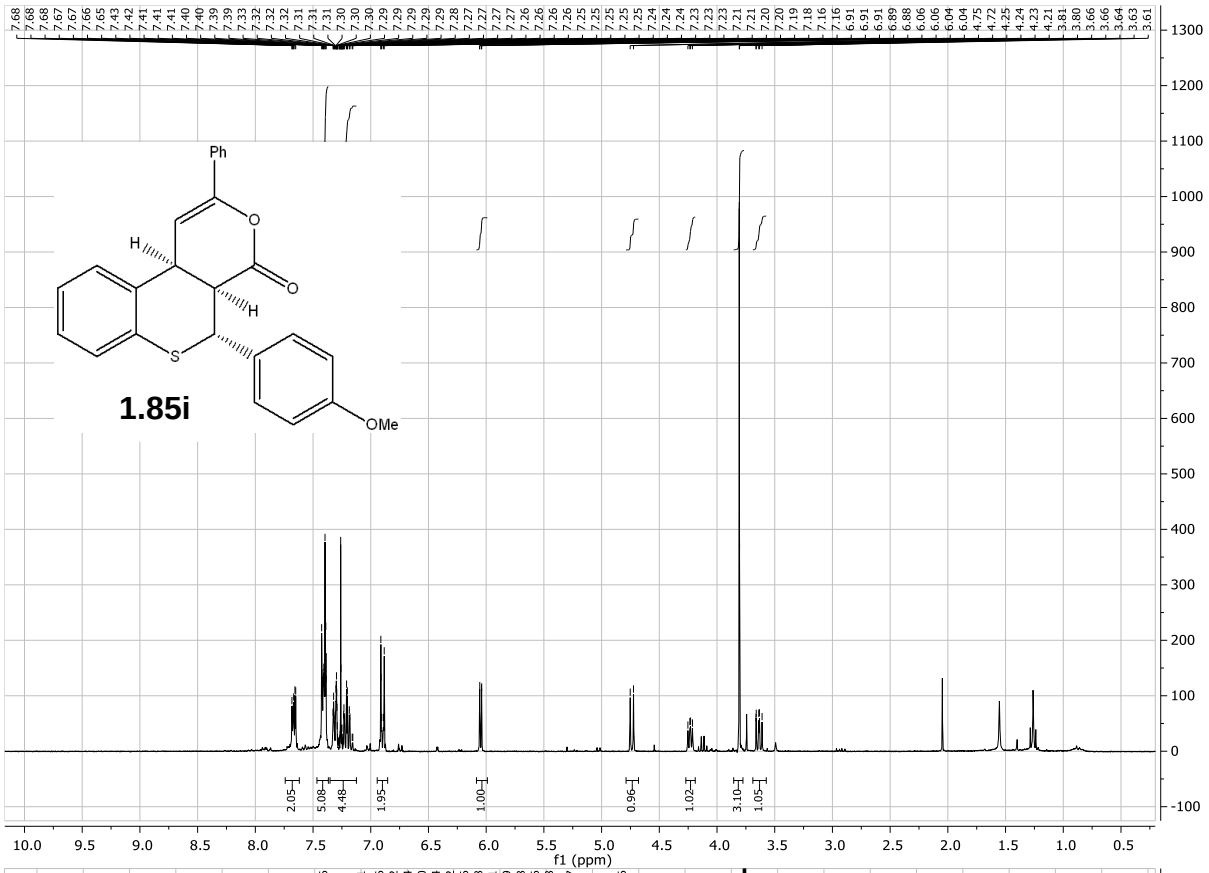

Me
O
H
O
H
S
1.85f
f1 (ppm)

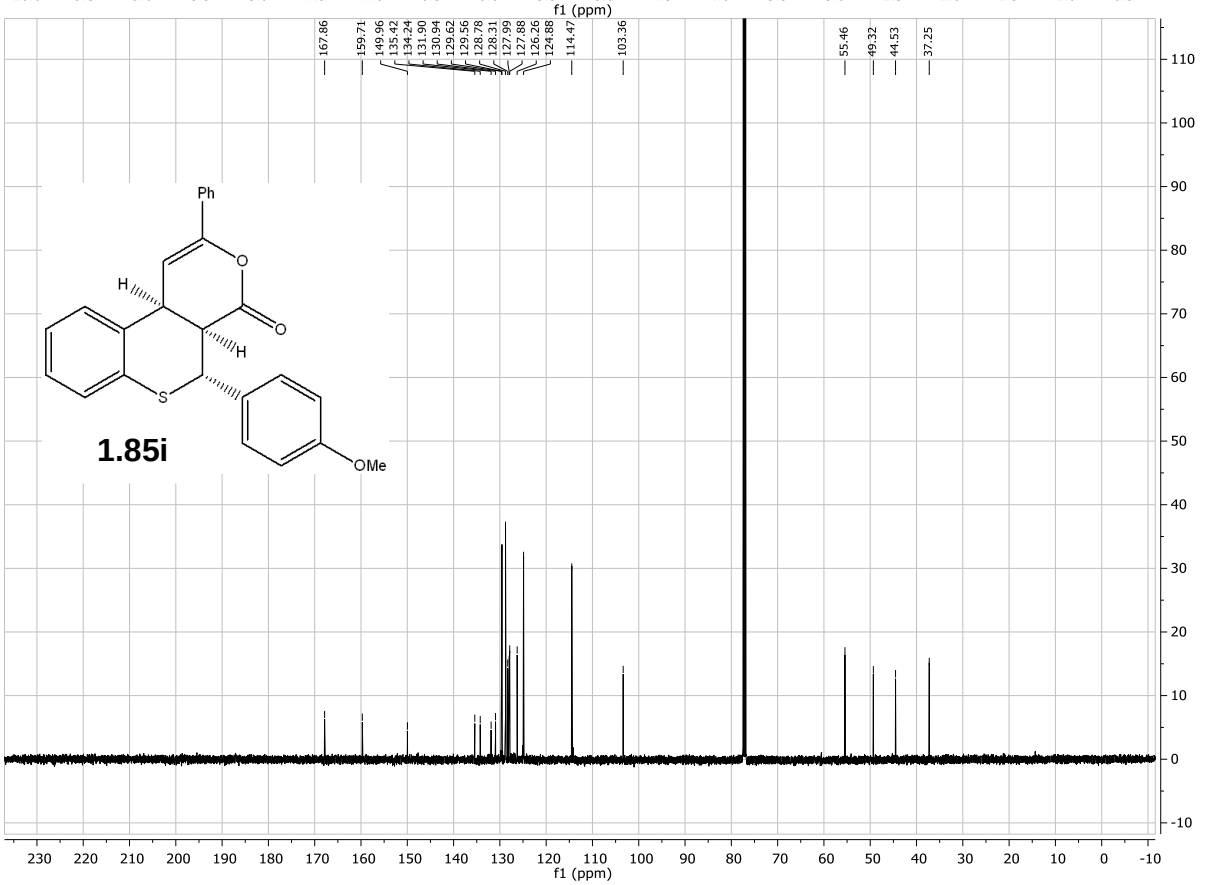

1.85g

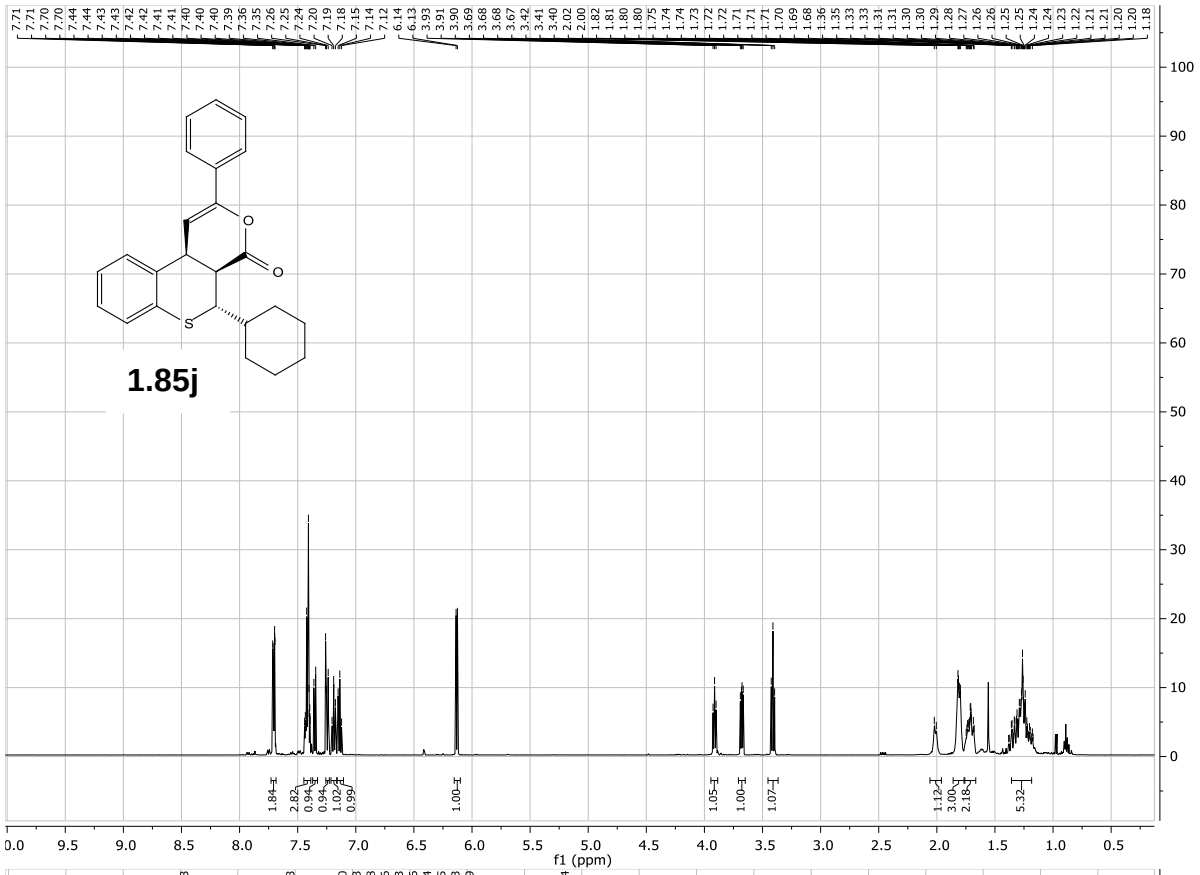

1.85g
f1 (ppm)

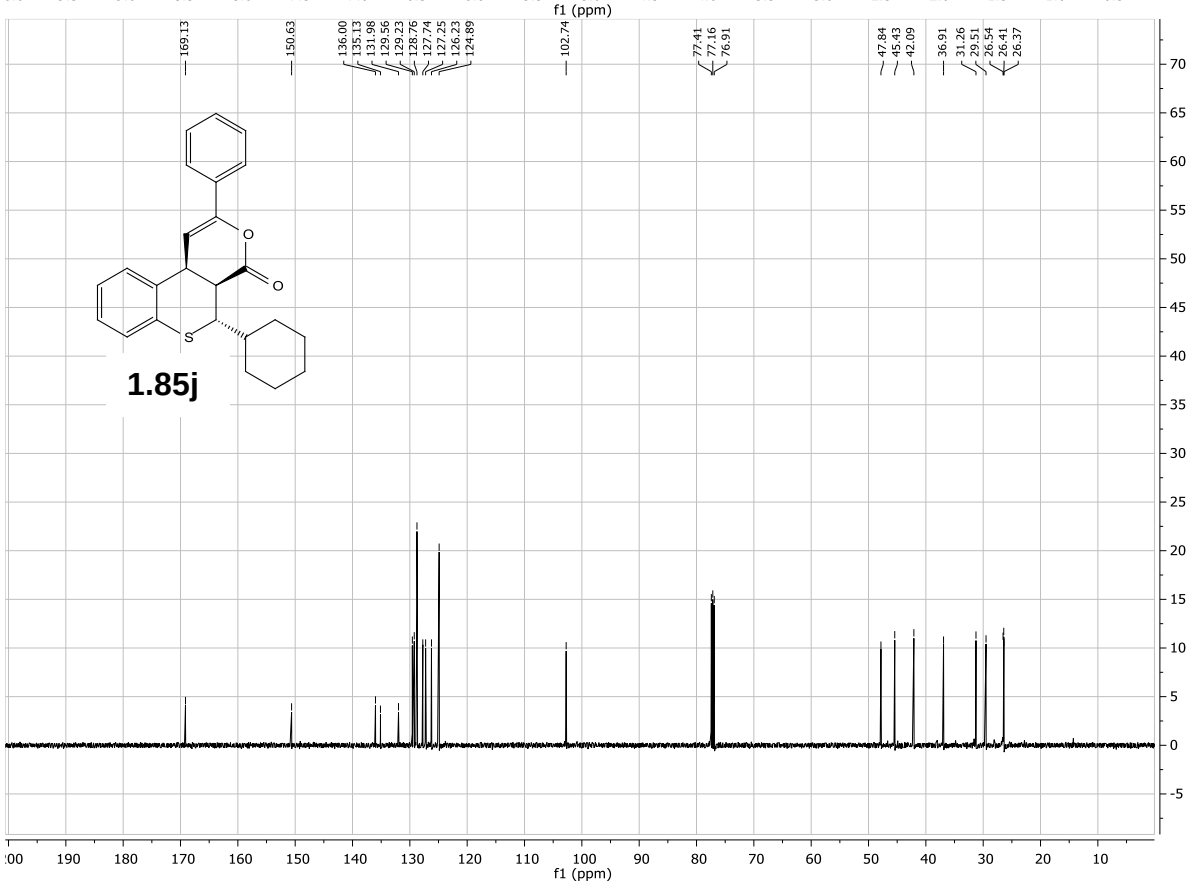

Me
O
H
O
H
S
CF3
CF3
1.85h
f1 (ppm)

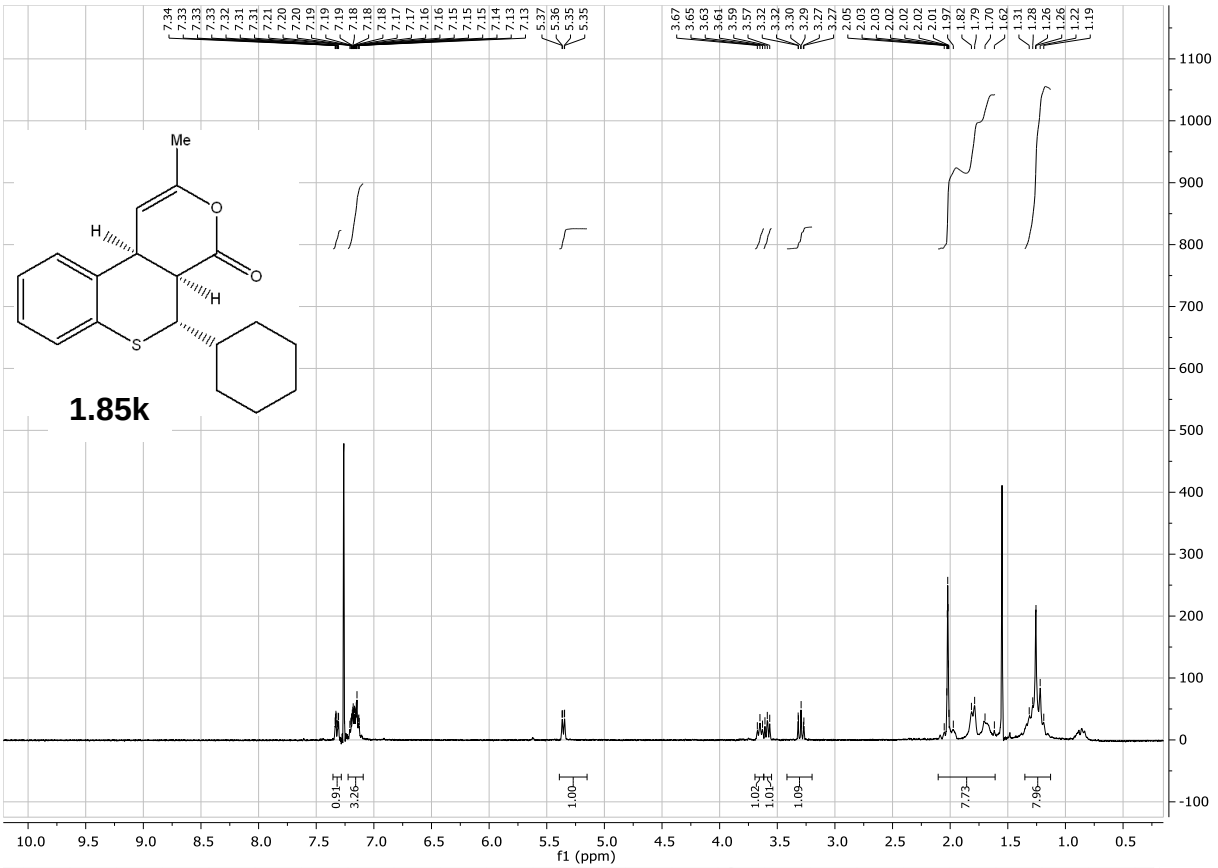

Me
O
H
O
H
S
CF3
CF3
1.85h
f1 (ppm)

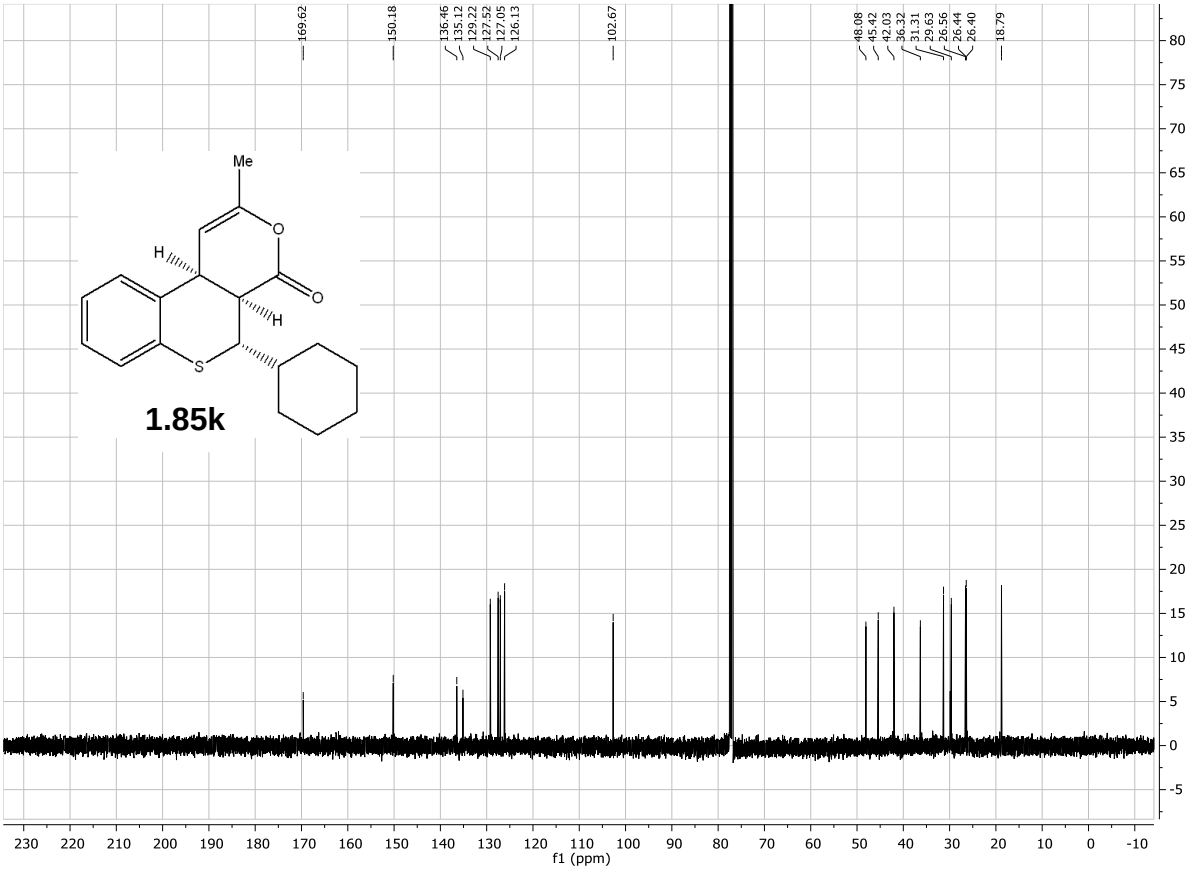

Ph
O
H
O
H
S
OMe
1.85i
f1 (ppm)

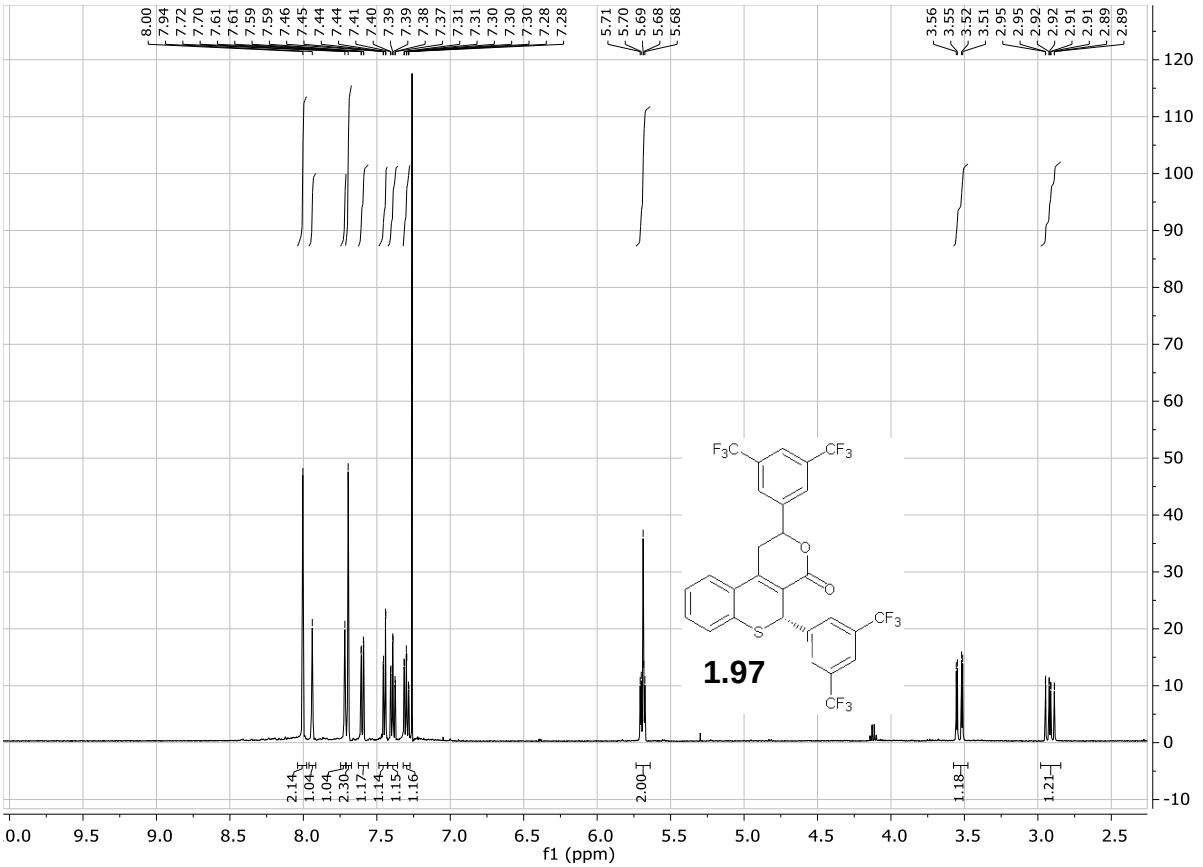

Ph
O
H
O
H
S
OMe
1.85i
f1 (ppm)

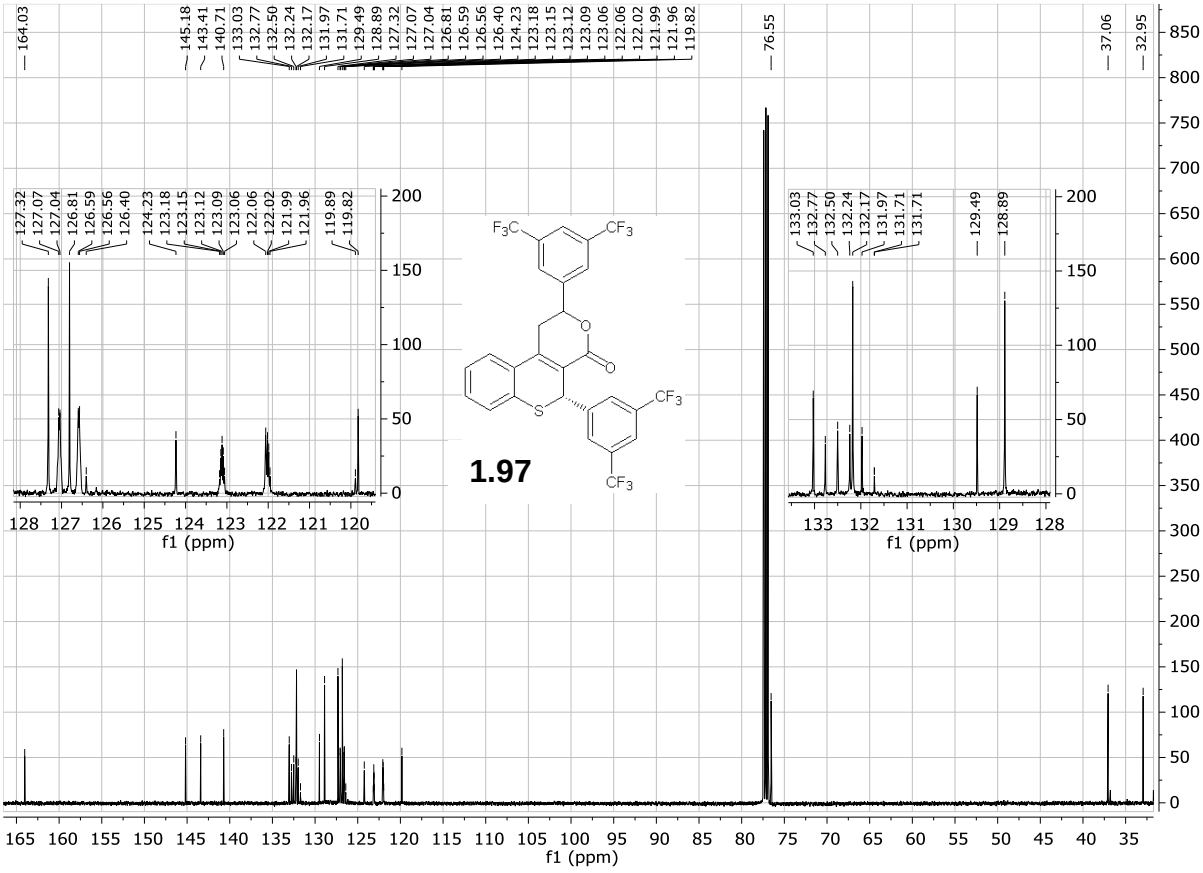

1.85j
f1 (ppm)


1.85j
f1 (ppm)

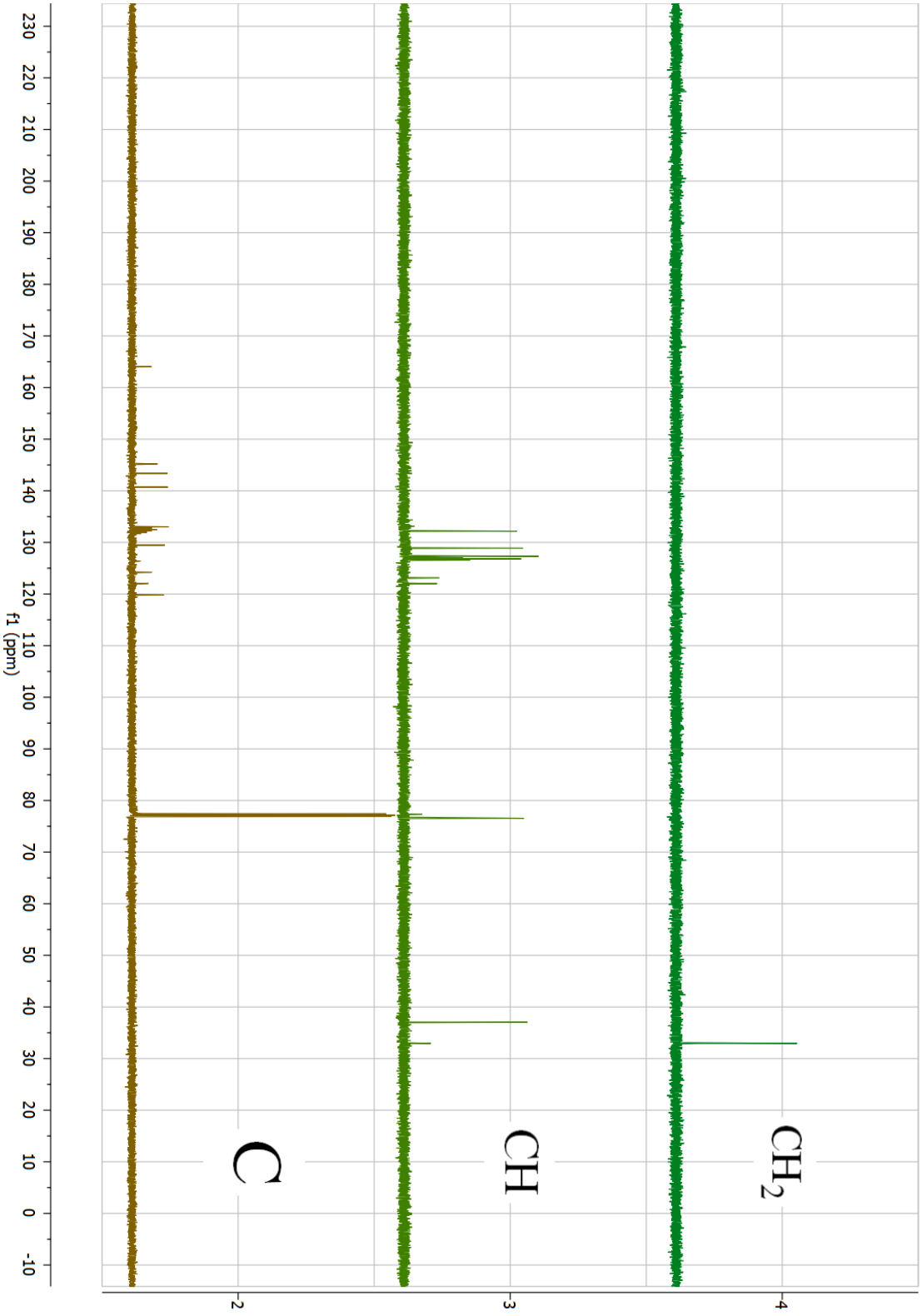

Me
O
H
O
H
S
1.85k
f1 (ppm)


Me
O
H
O
H
S
1.85k
f1 (ppm)

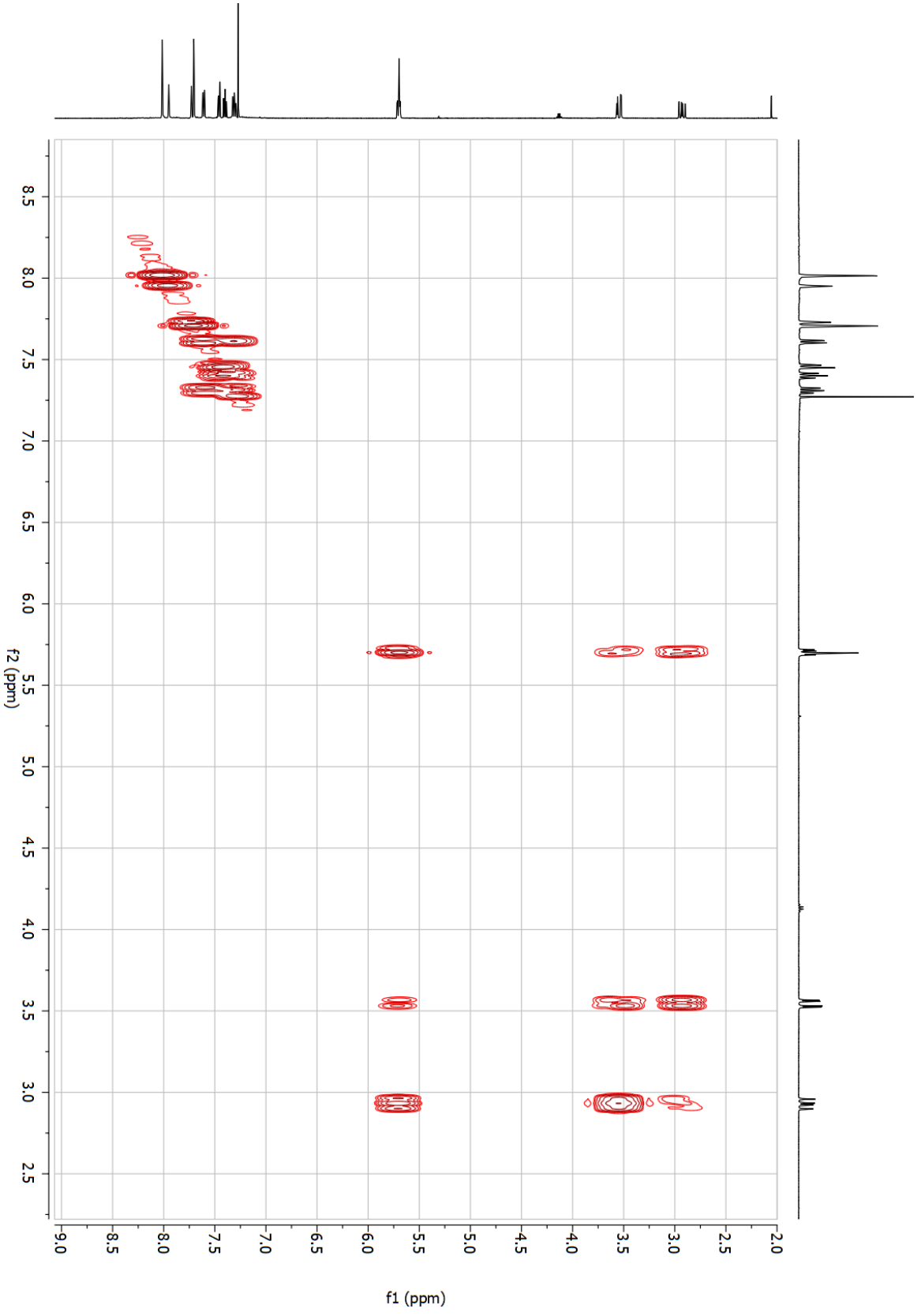

1.97
f1 (ppm)


1.97
f1 (ppm)
f1 (ppm)
f1 (ppm)

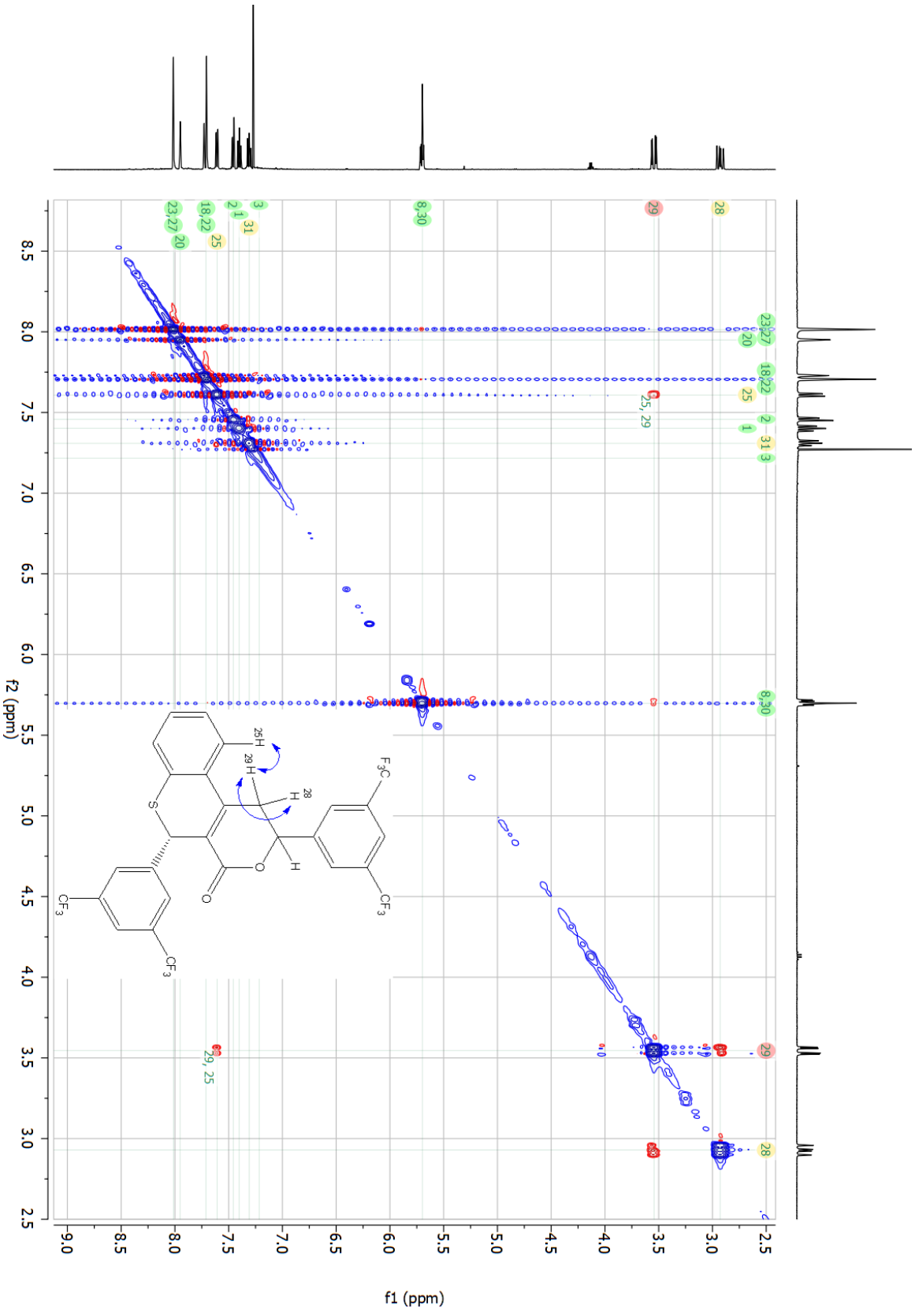
DEPT of **1.97**


230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
C
CH
CH2
2
3
4

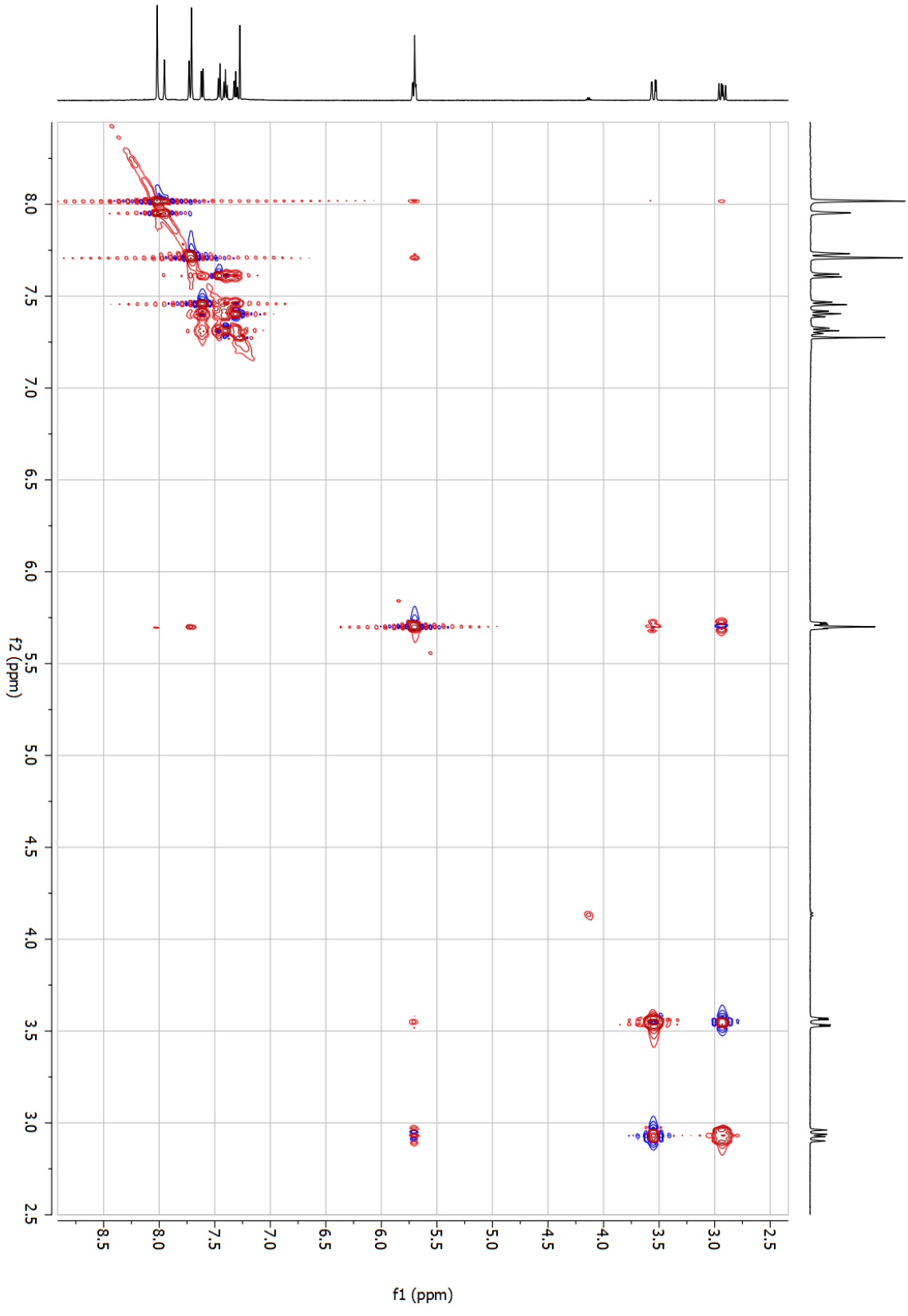
gCOSY of **1.97**


f2 (ppm)
f1 (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0

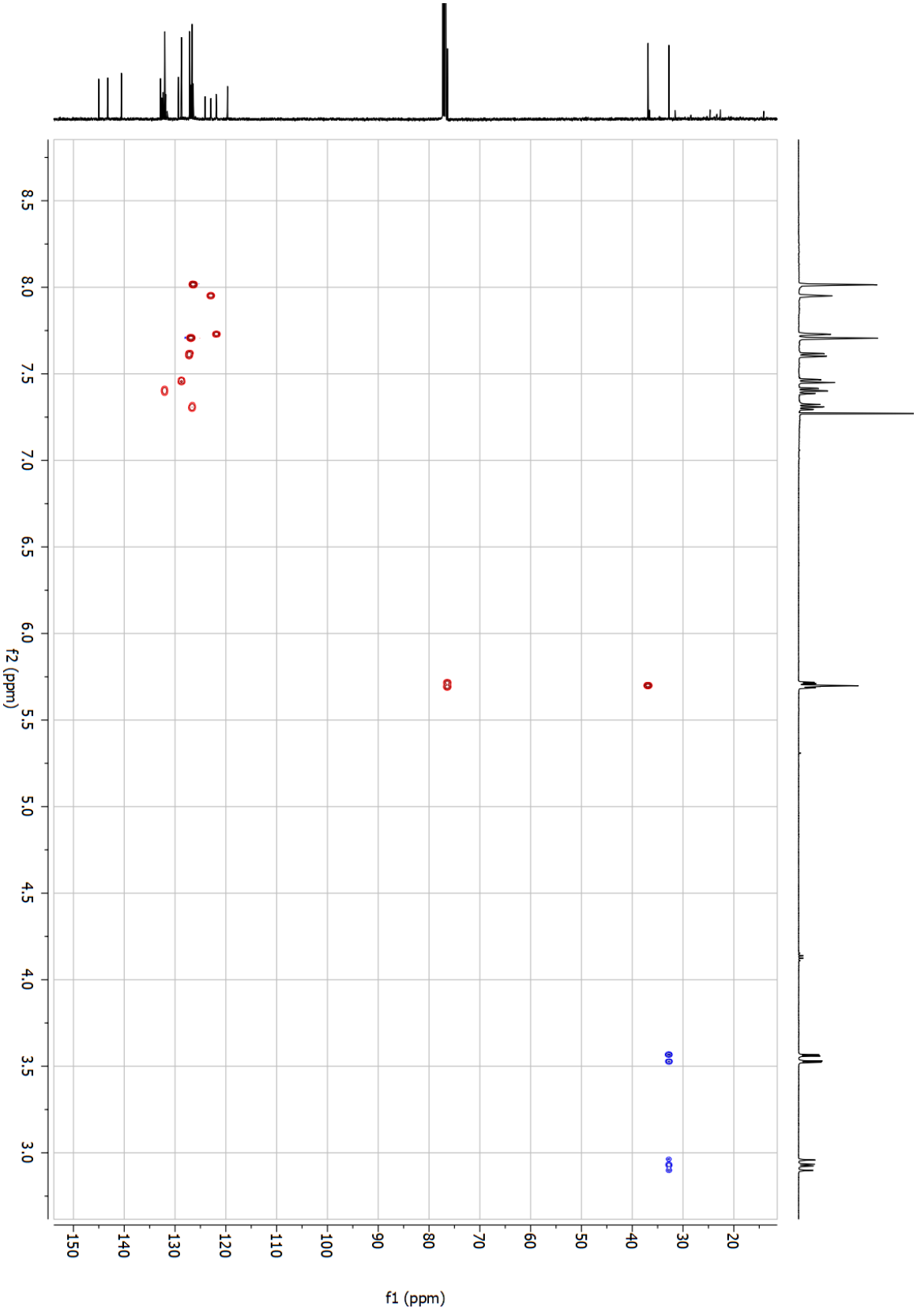
2D NOESY of **1.97**



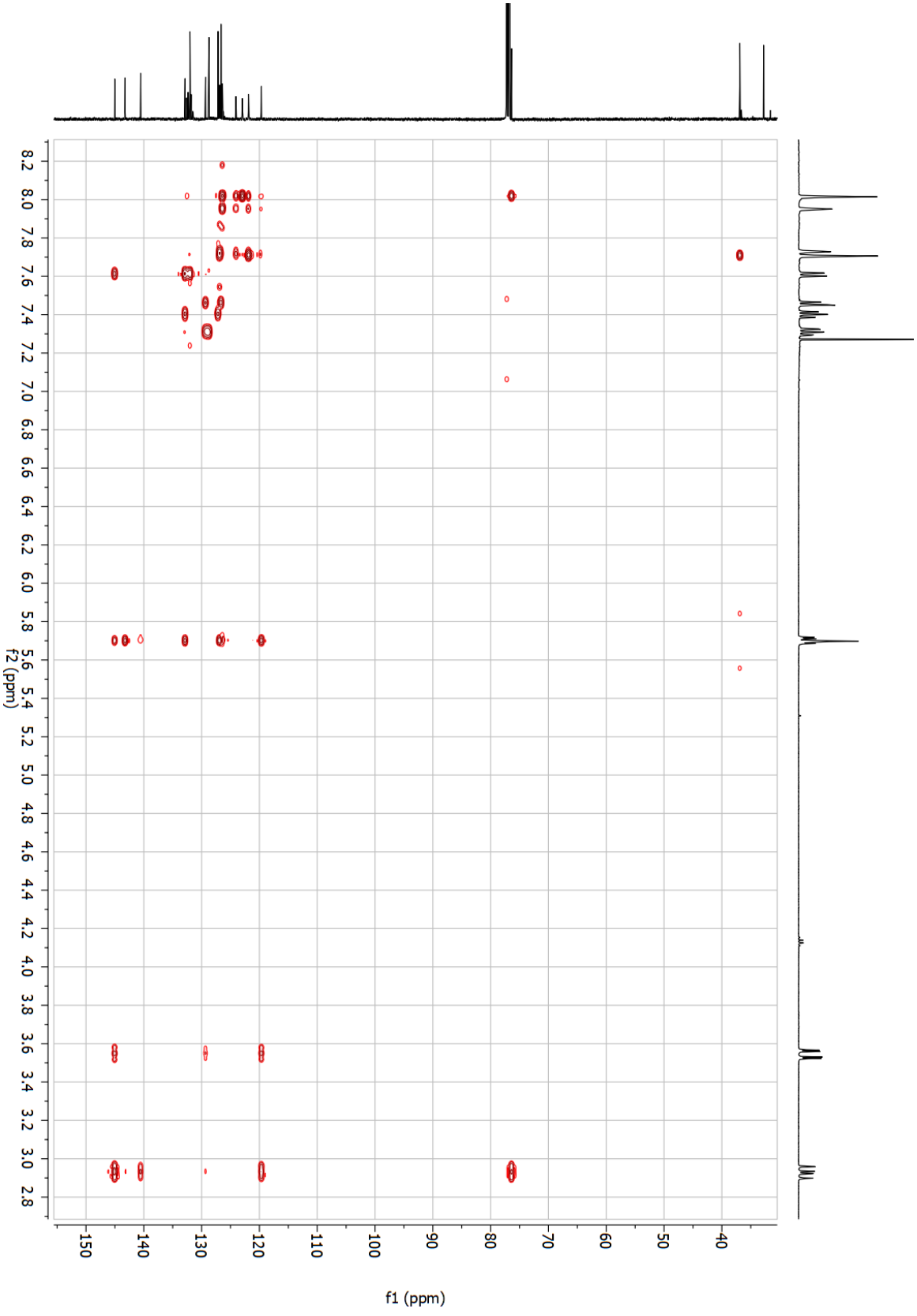
TOCSY of **1.97**

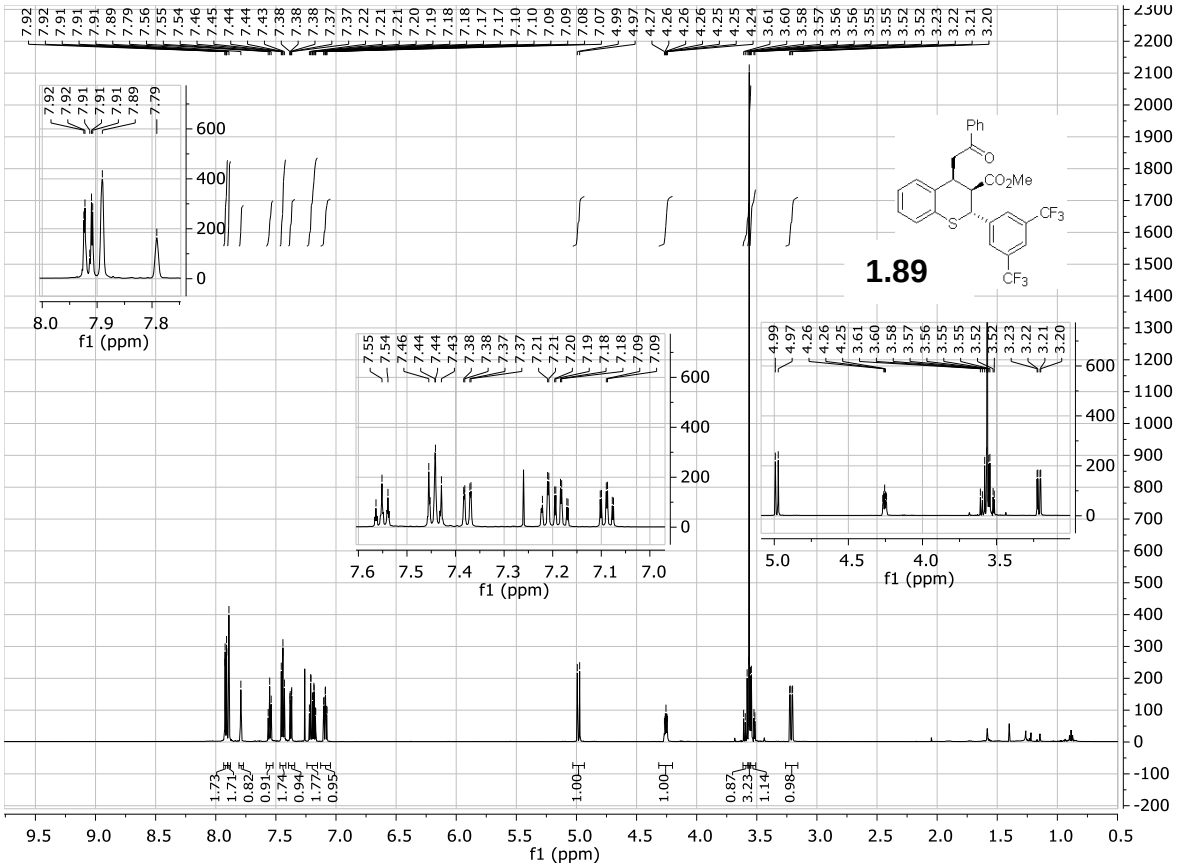


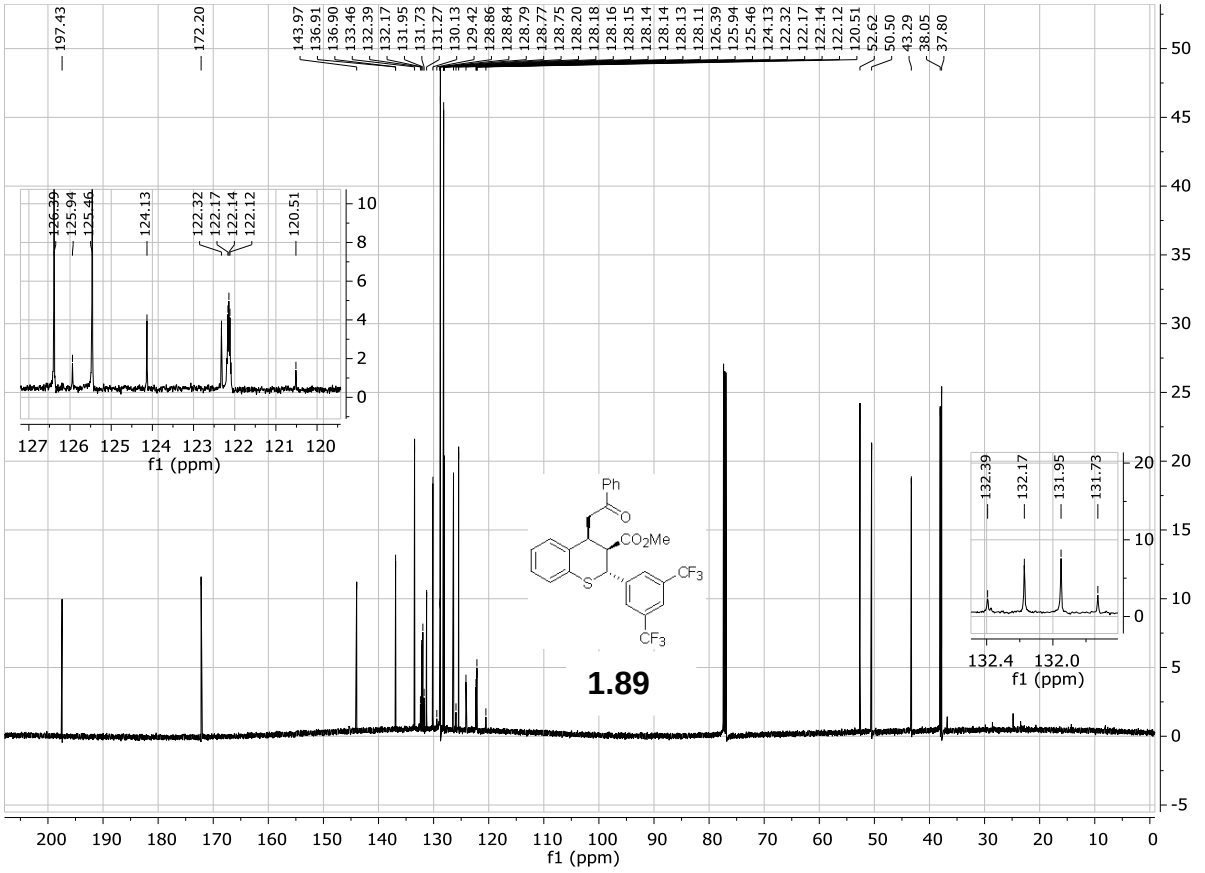
HSQC of **1.97**

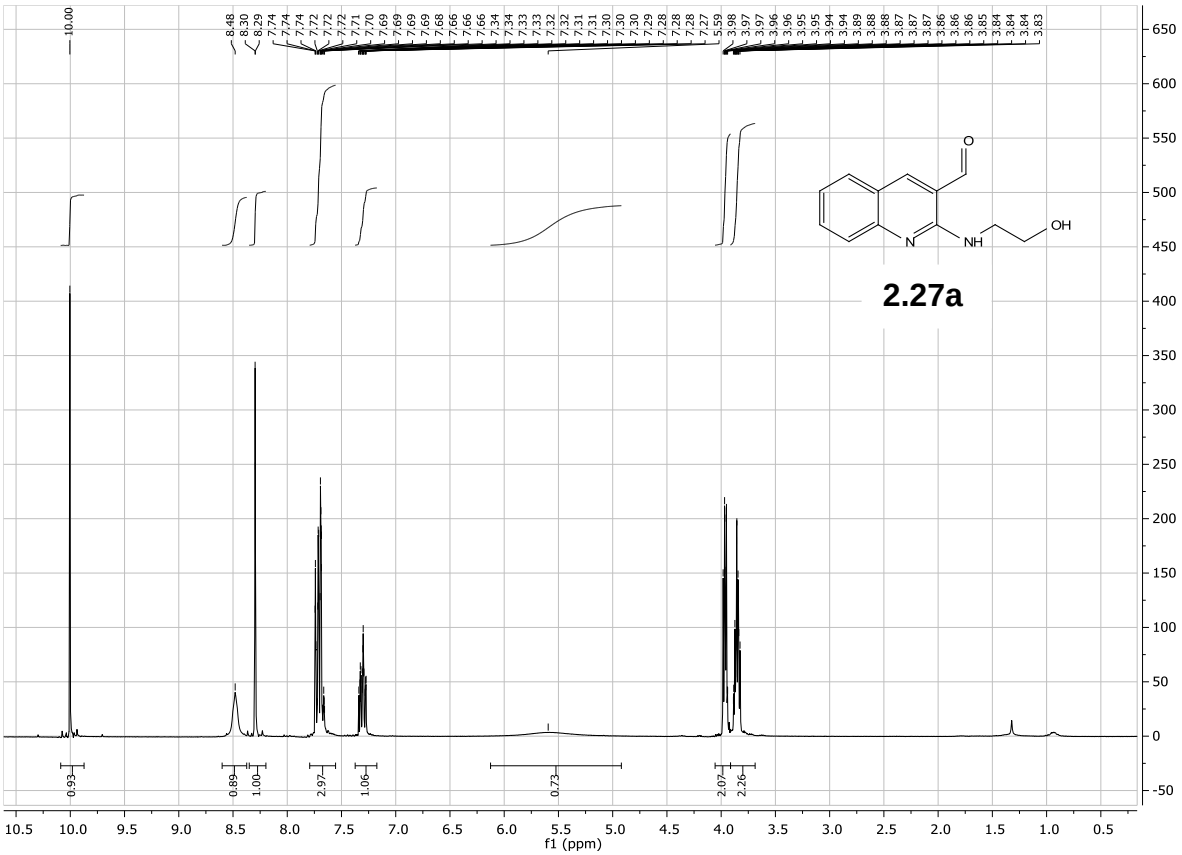

f2 (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
f1 (ppm)
150
140
130
120
110
100
90
80
70
60
50
40
30
20

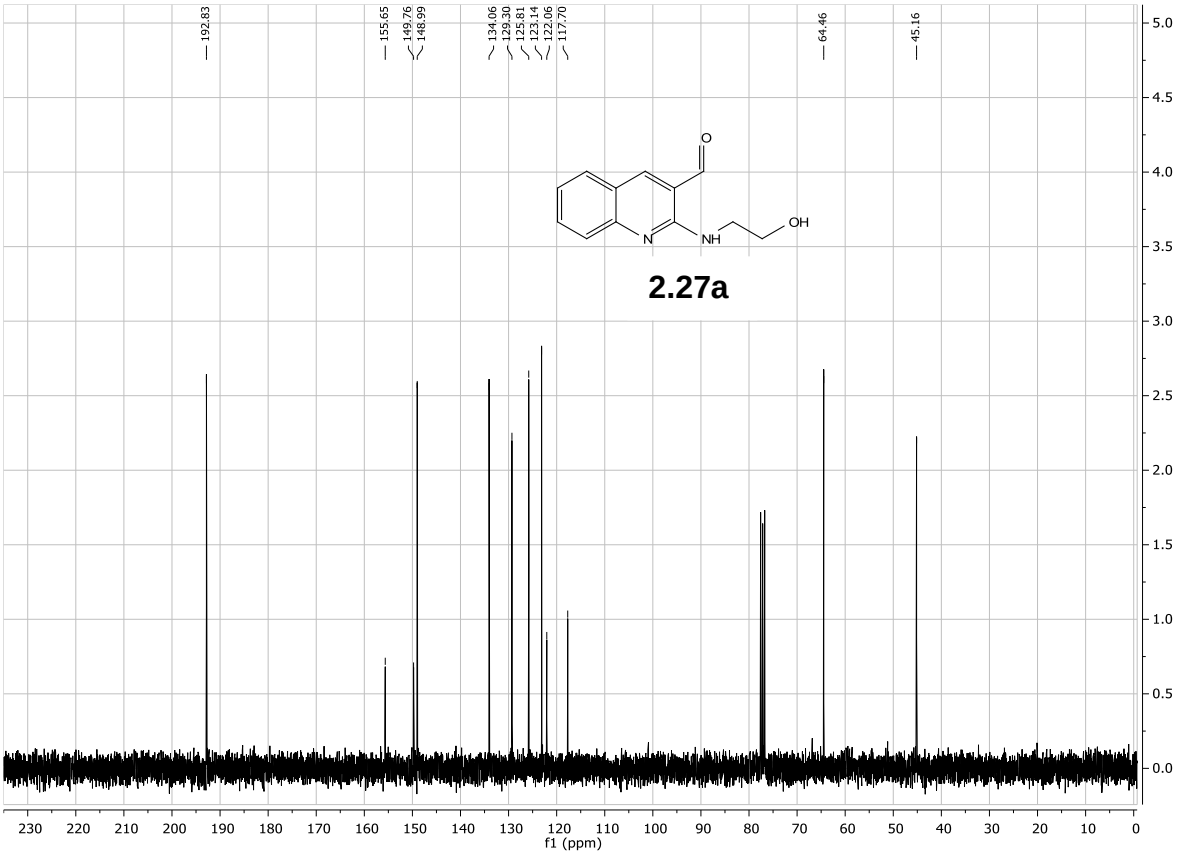
HMBC of **1.97**

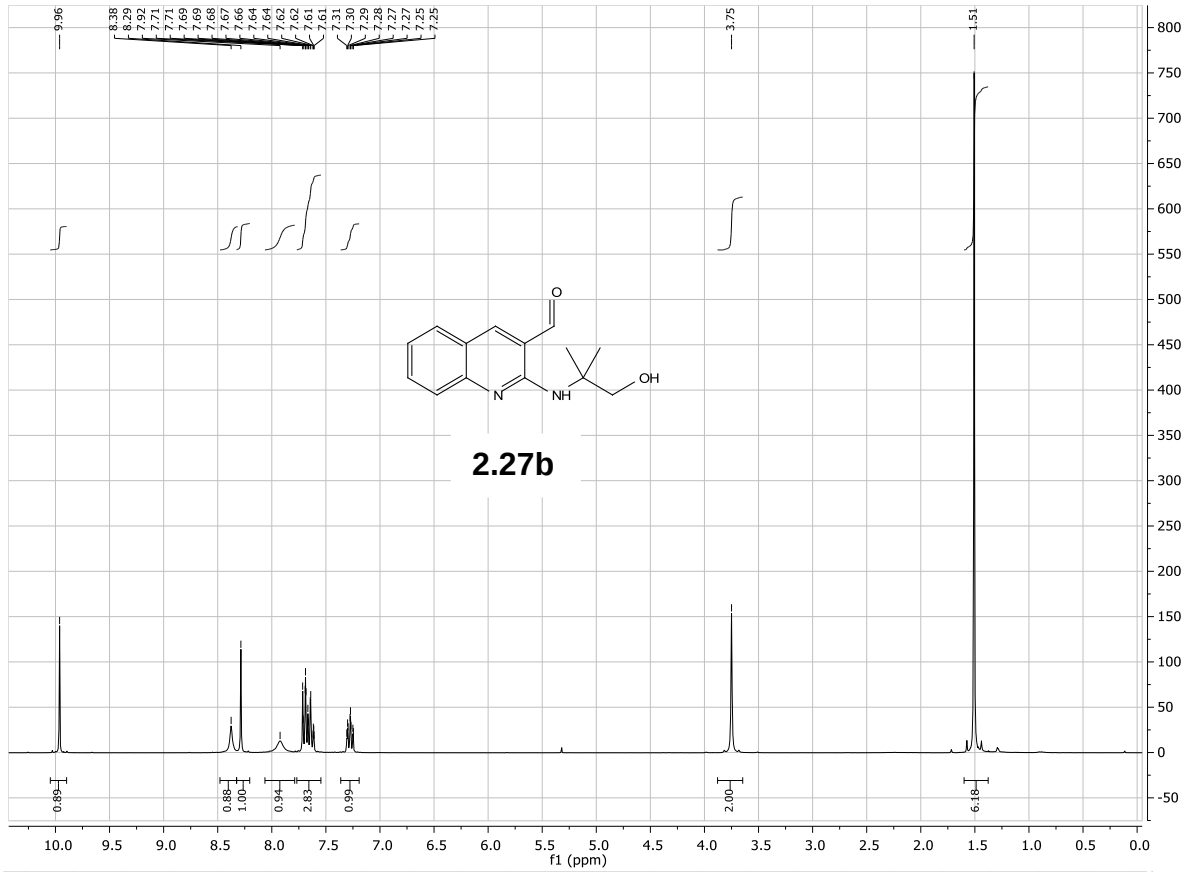


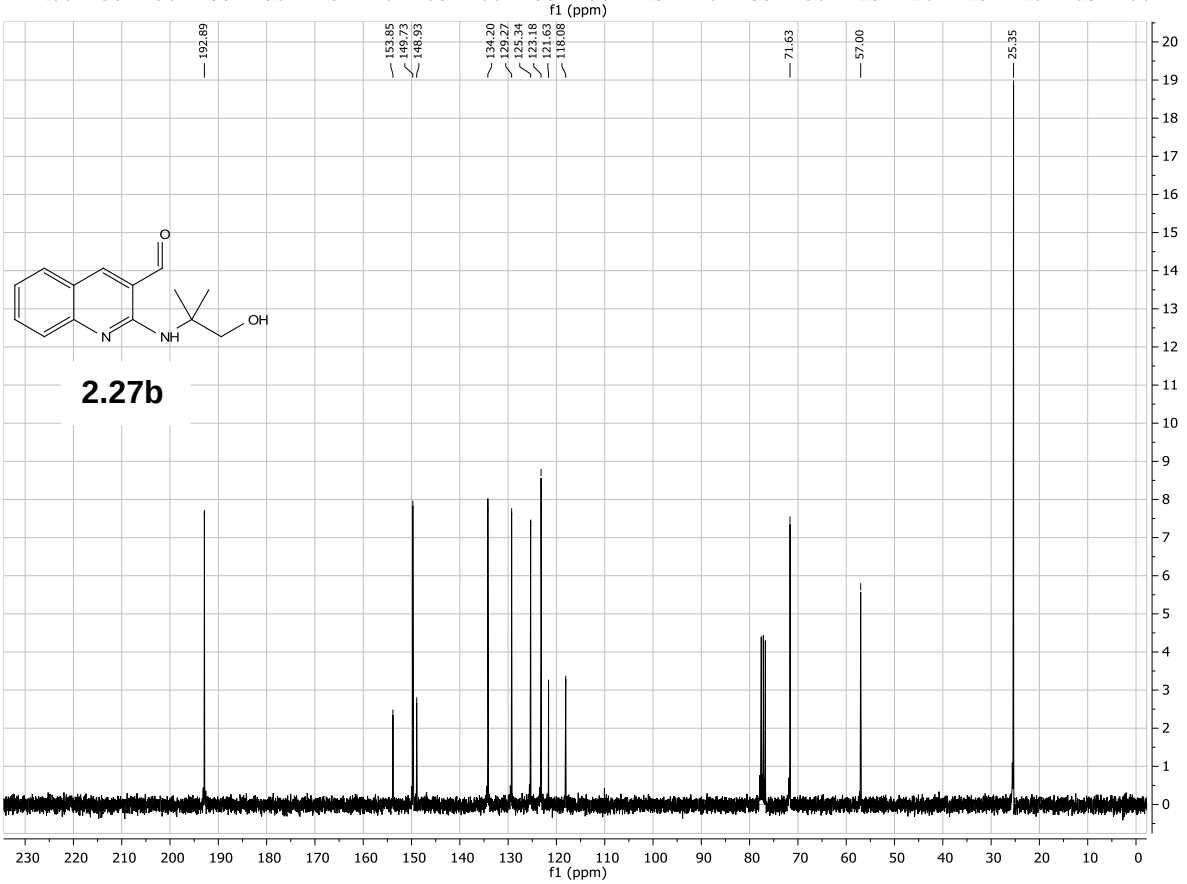

1.89
f1 (ppm)

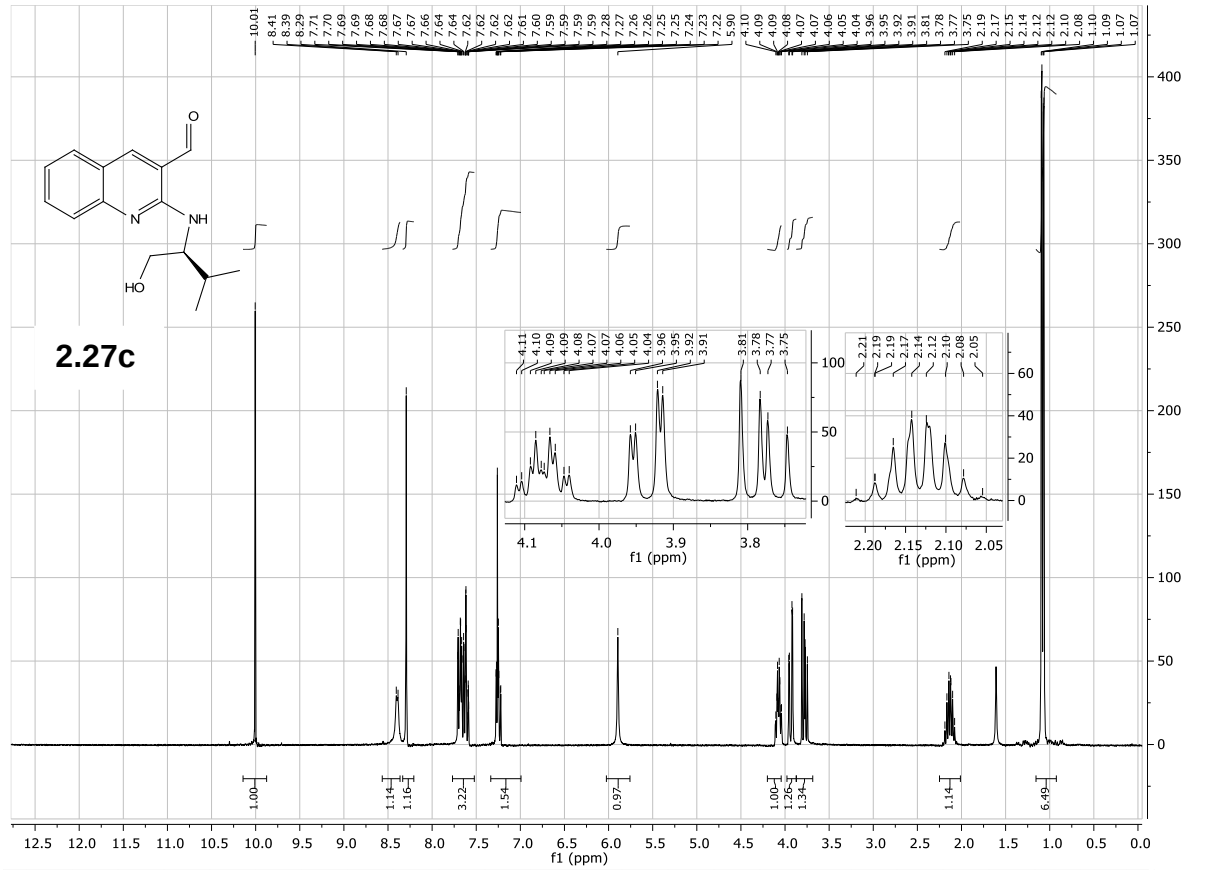

1.89
f1 (ppm)

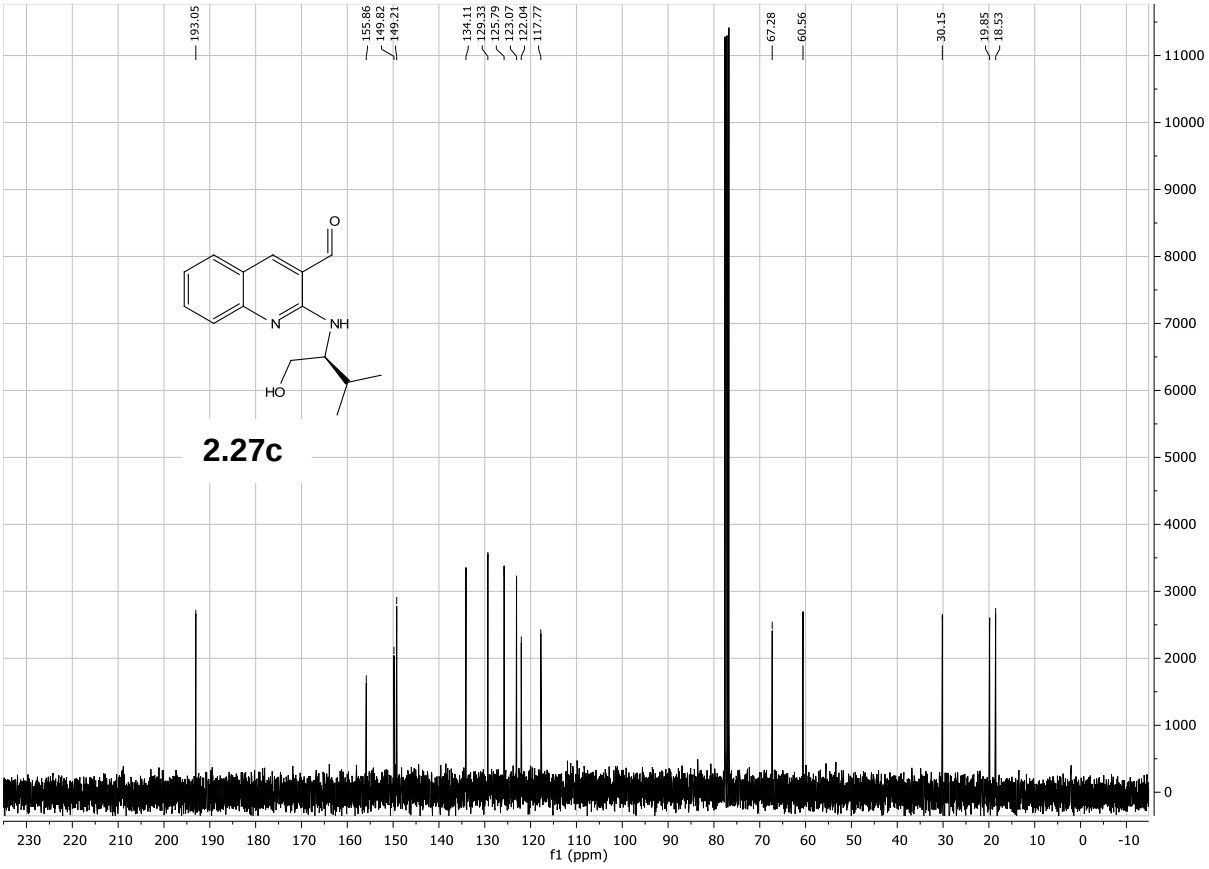

10.00
8.48
8.30
8.29
7.74
7.72
7.71
7.70
7.69
7.68
7.66
7.34
7.33
7.32
7.31
7.30
7.29
7.28
7.27
5.59
3.98
3.97
3.96
3.95
3.94
3.89
3.88
3.87
3.86
3.85
3.84
3.83
0.93
0.89
1.00
2.97
1.06
0.73
2.07
2.26
O
OH
N
NH
2.27a
f1 (ppm)

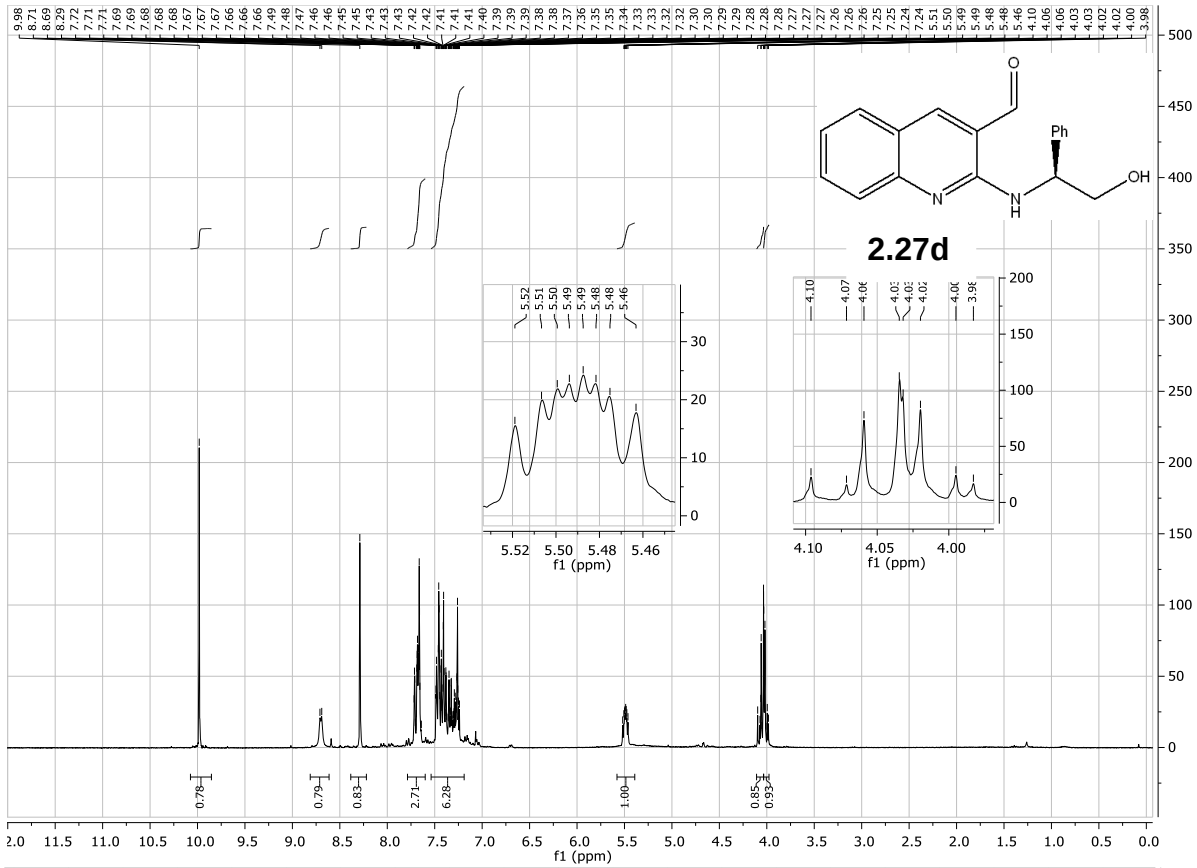

192.83
155.65
149.76
148.99
134.06
129.30
125.81
123.14
122.06
117.70
64.46
45.16
O
OH
N
NH
2.27a
f1 (ppm)


9.96
8.38
8.29
7.92
7.71
7.71
7.69
7.69
7.68
7.67
7.66
7.64
7.64
7.62
7.62
7.61
7.61
7.31
7.30
7.29
7.28
7.27
7.27
7.25
7.25
3.75
1.51
O
N
NH
OH
2.27b
0.89
0.88
1.00
0.94
2.83
0.99
2.00
6.18
f1 (ppm)


192.89
153.85
149.73
148.93
134.20
129.27
125.34
123.18
121.63
118.08
71.63
57.00
25.35
O
N
NH
OH
2.27b
f1 (ppm)


2.27c
f1 (ppm)


2.27c
f1 (ppm)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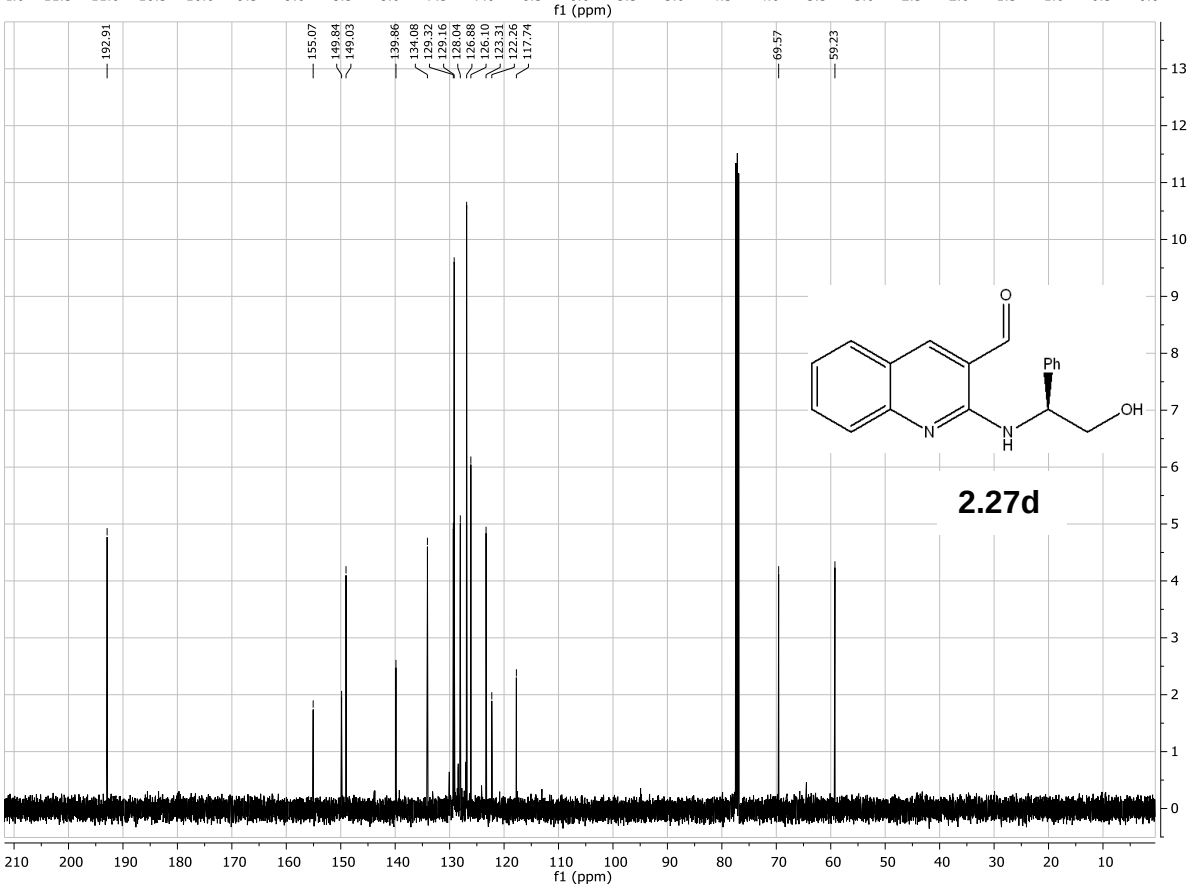
f1 (ppm)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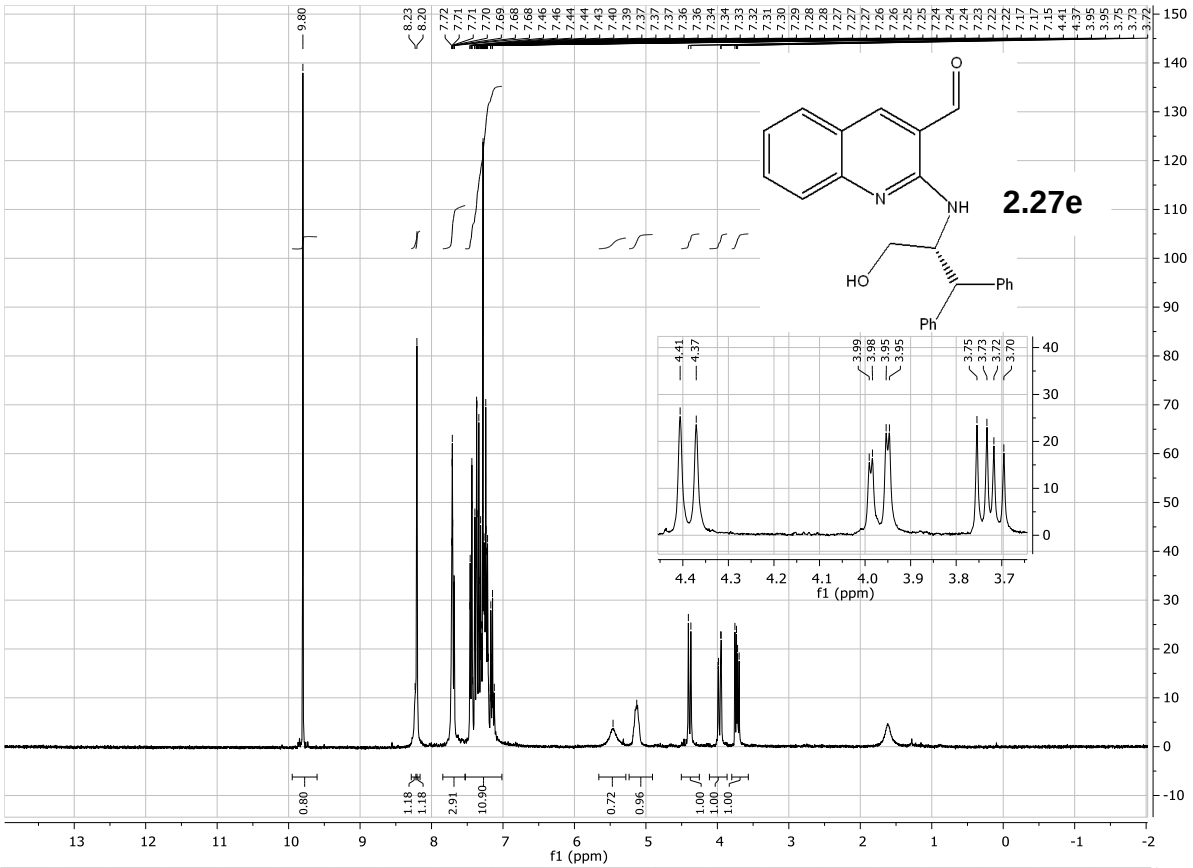
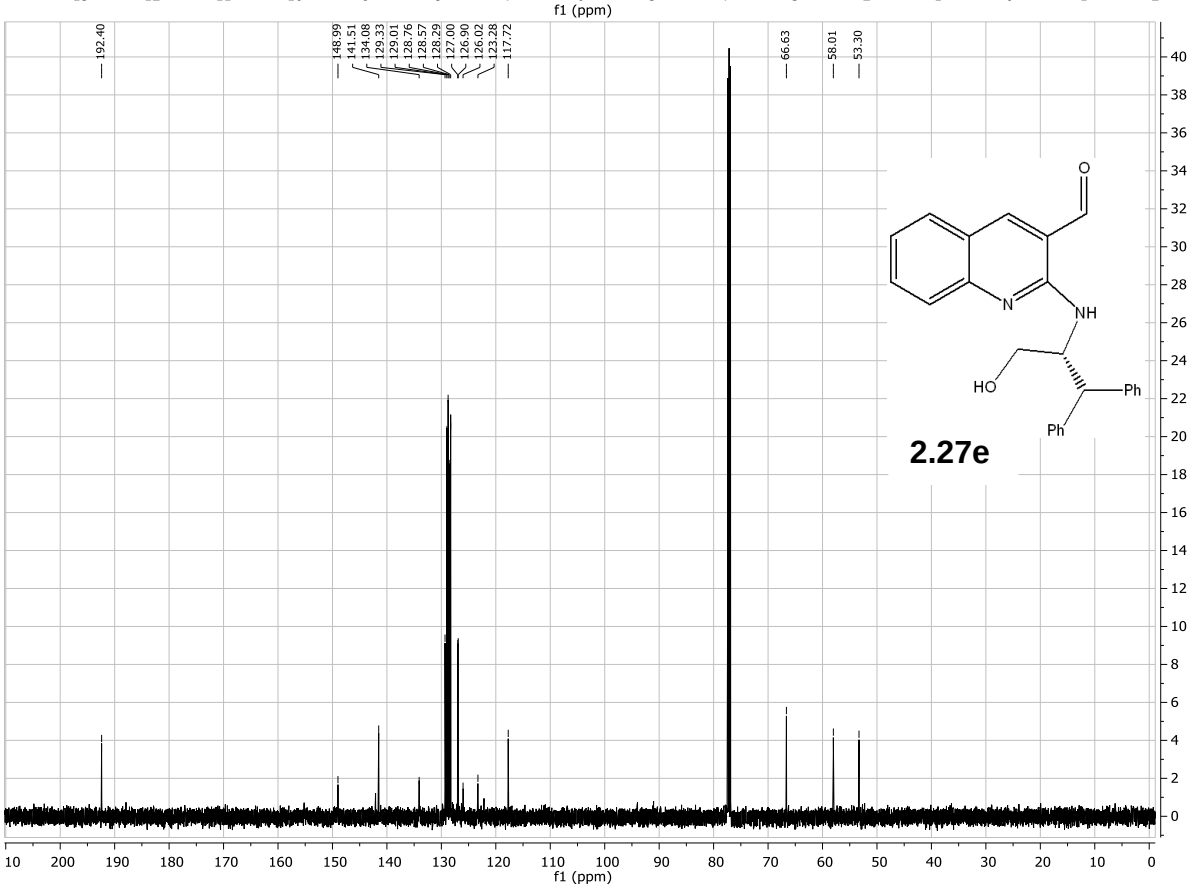
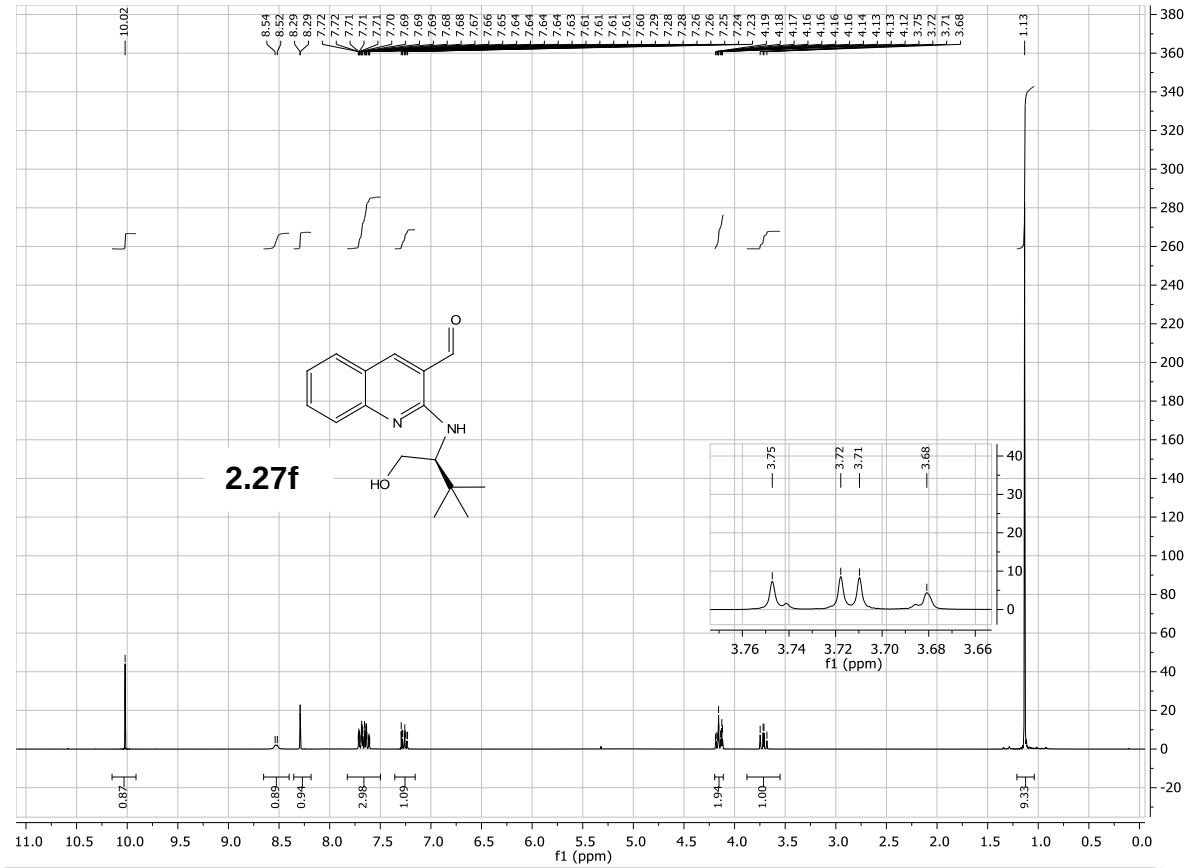
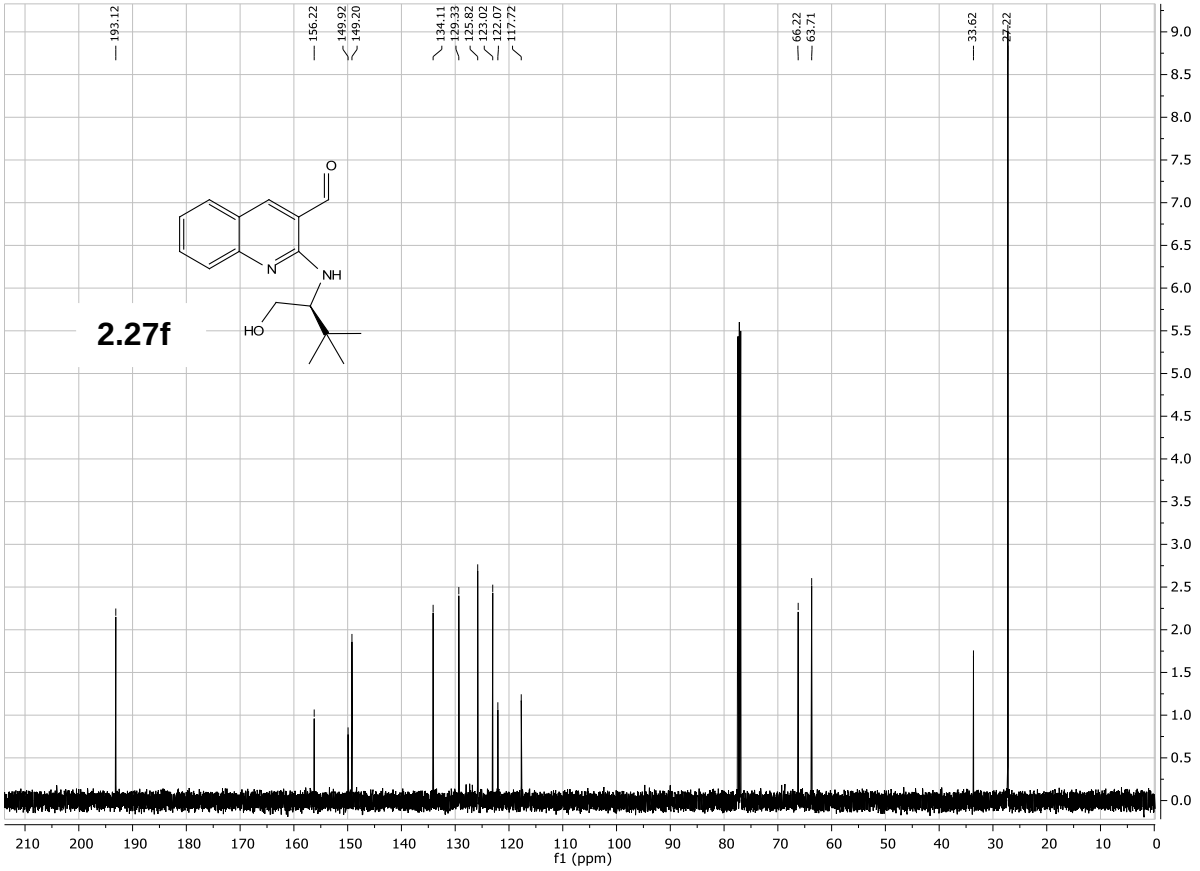
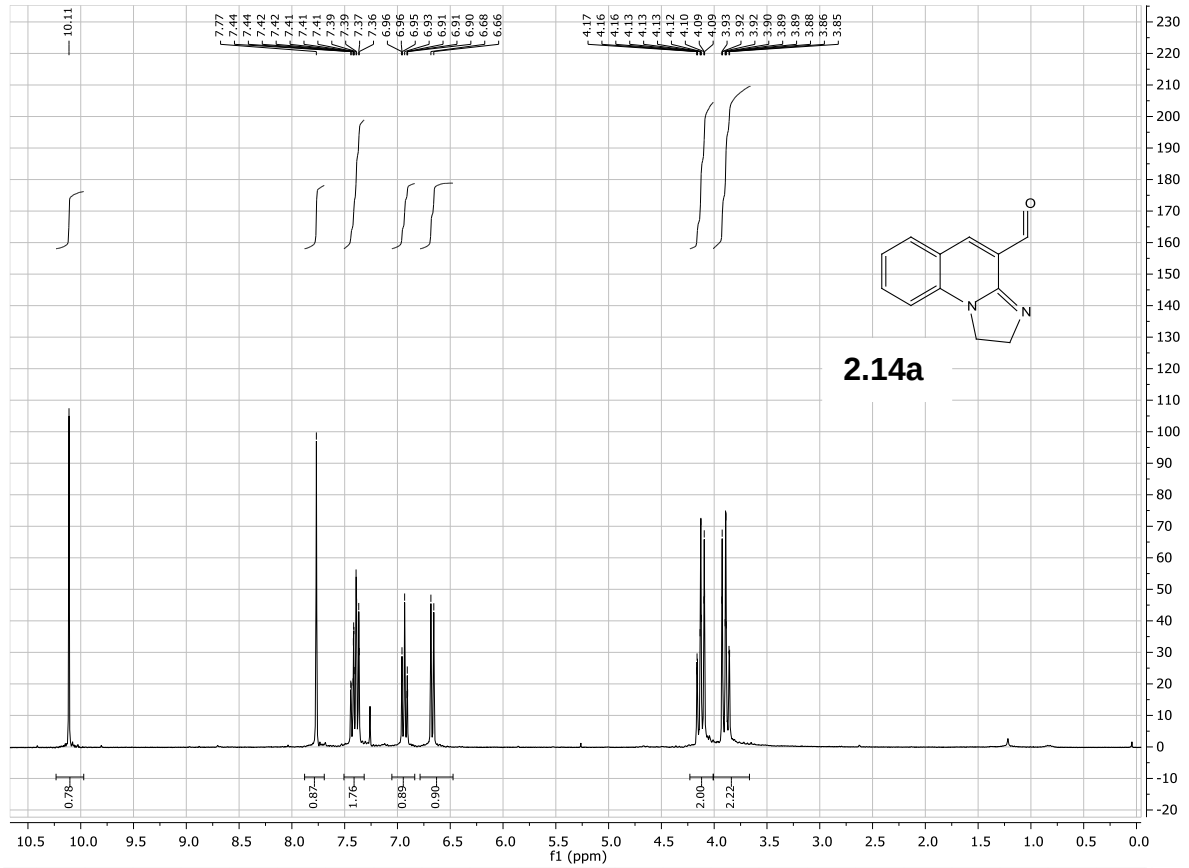
f1 (ppm)

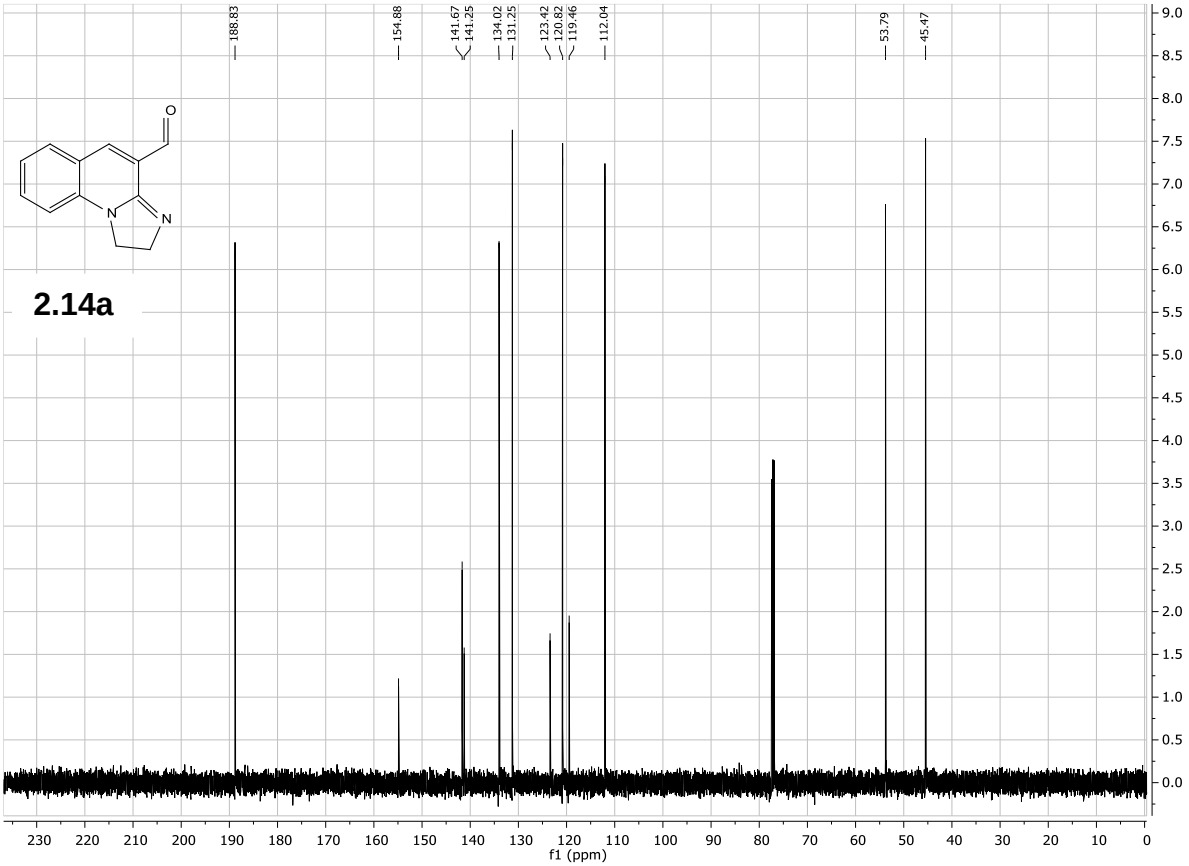

2.27e
f1 (ppm)

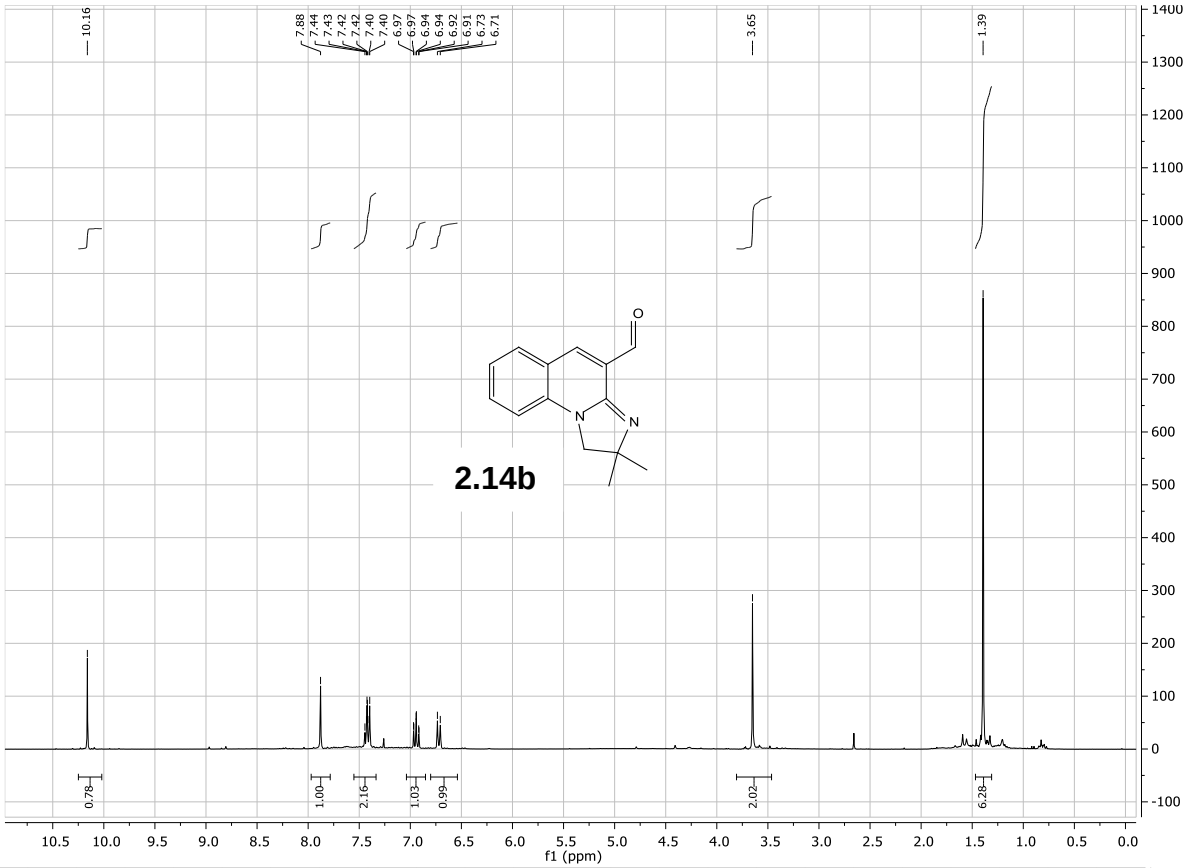

2.27e
f1 (ppm)


2.27f
f1 (ppm)


2.27f
f1 (ppm)


10.11
7.77
7.44
7.44
7.42
7.42
7.41
7.41
7.41
7.39
7.39
7.37
7.36
6.96
6.96
6.95
6.93
6.91
6.90
6.68
6.66
4.17
4.16
4.16
4.13
4.13
4.13
4.12
4.10
4.09
4.09
3.93
3.92
3.92
3.90
3.89
3.89
3.88
3.86
3.85
O
N
N
2.14a
0.78
0.87
1.76
0.89
0.90
2.00
2.22
f1 (ppm)


188.83
154.88
141.67
141.25
134.02
131.25
123.42
120.82
119.46
112.04
53.79
45.47
O
N
N
2.14a
f1 (ppm)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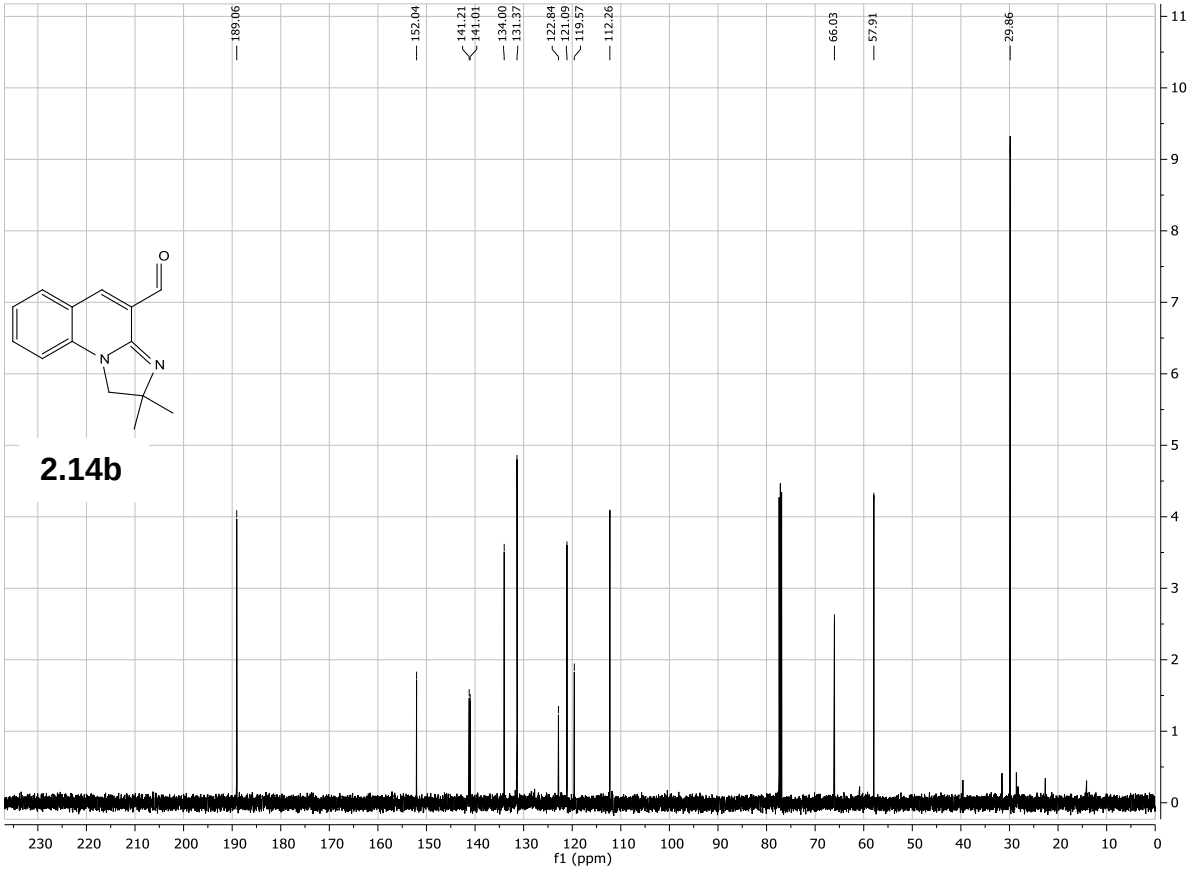
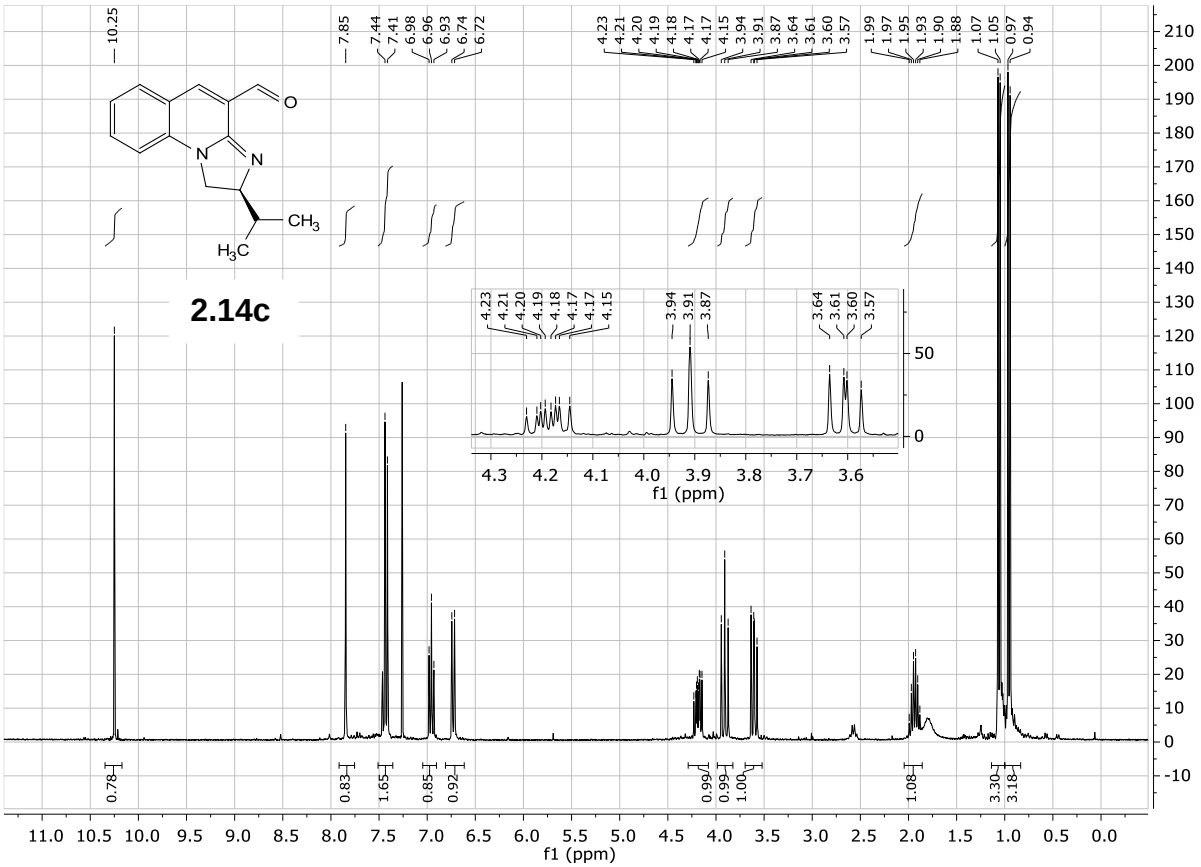
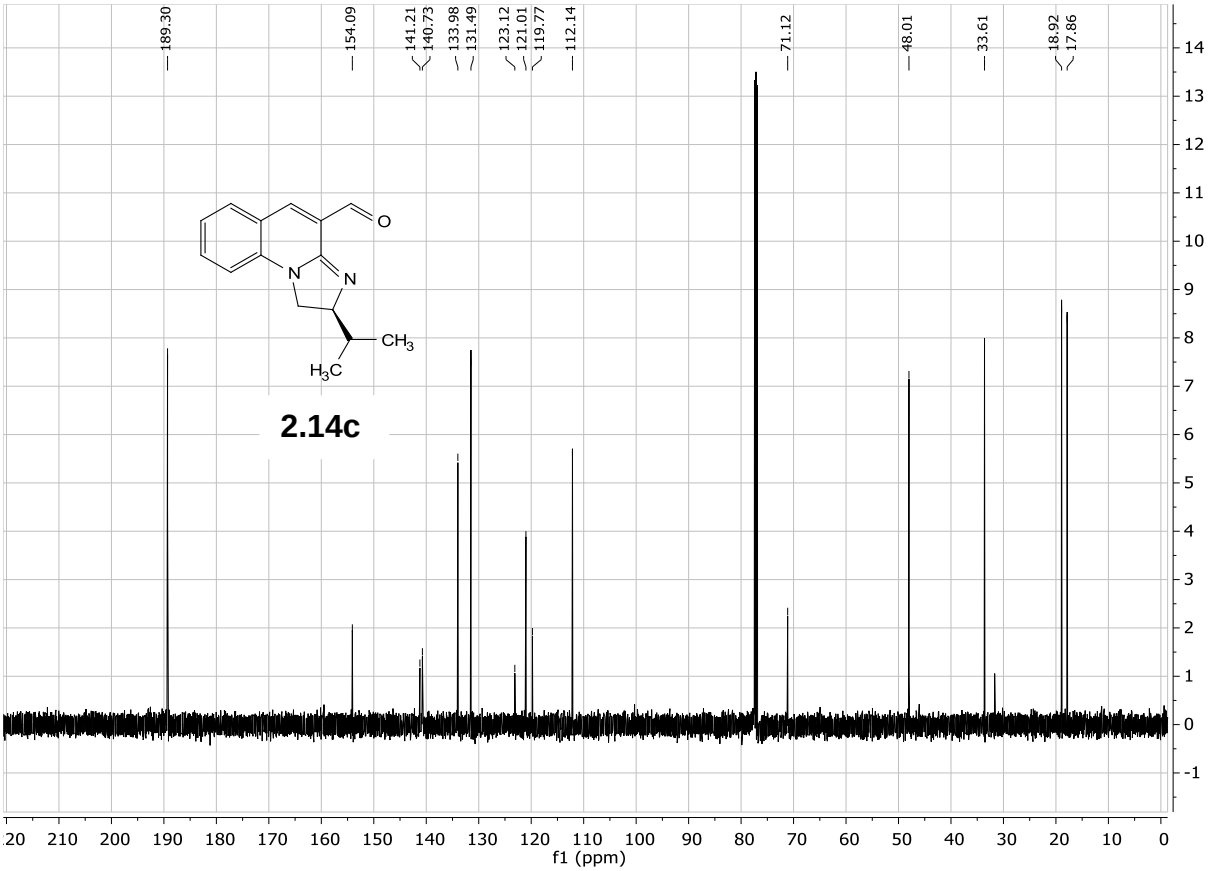
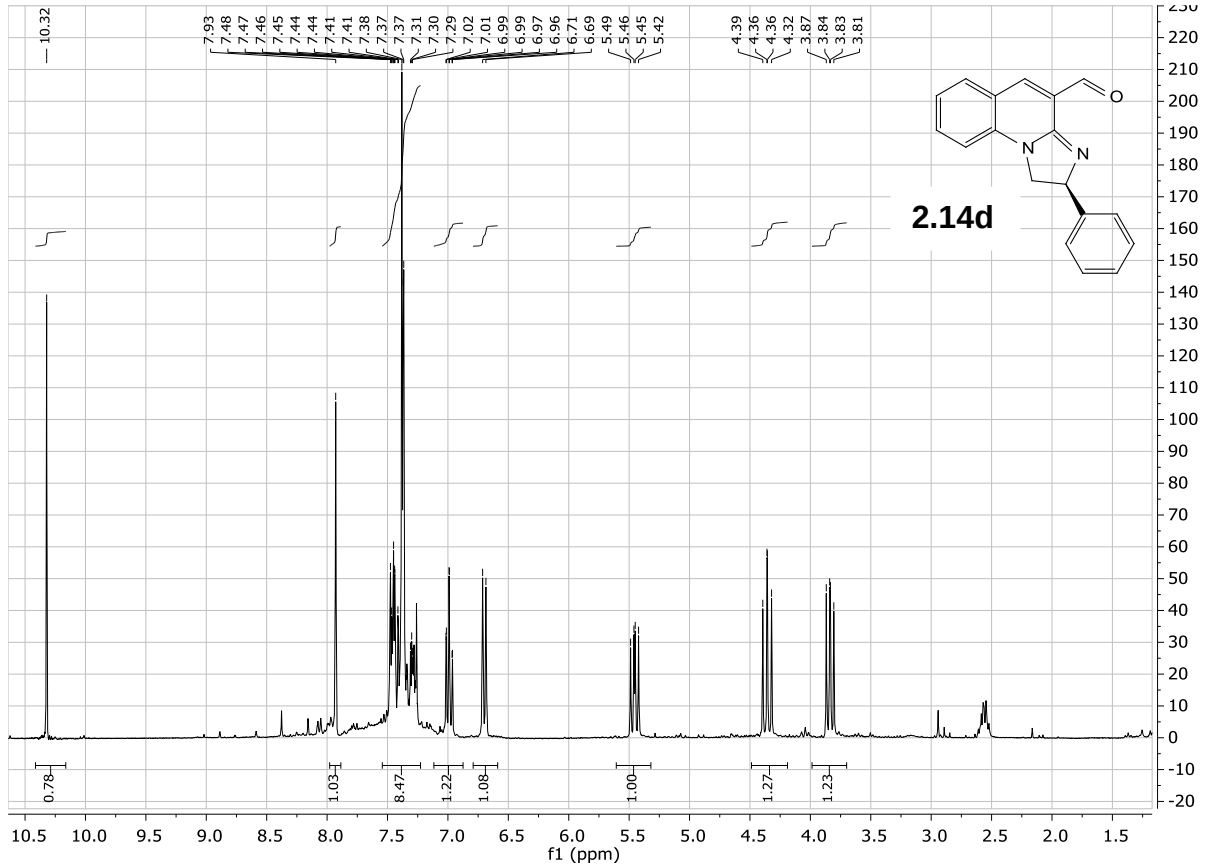
7.88
7.44
7.43
7.42
7.42
7.40
7.40
6.97
6.97
6.94
6.94
6.92
6.91
6.73
6.71
3.65
1.39
2.14b
0.78
1.00
2.16
1.03
0.99
2.02
6.28
f1 (ppm)


189.06
152.04
141.21
141.01
134.00
131.37
122.84
121.09
119.57
112.26
66.03
57.91
29.86
2.14b
f1 (ppm)


10.25
7.85
7.44
7.41
6.98
6.96
6.93
6.74
6.72
4.23
4.21
4.20
4.19
4.18
4.17
4.17
4.15
3.94
3.91
3.87
3.64
3.61
3.60
3.57
1.99
1.97
1.95
1.93
1.90
1.88
1.07
1.05
0.97
0.94
O
N
N
CH3
H3C
2.14c
f1 (ppm)
0.78
0.83
1.65
0.85
0.92
0.99
0.99
1.00
1.08
3.30
3.18


189.30
154.09
141.21
140.73
133.98
131.49
123.12
121.01
119.77
112.14
71.12
48.01
33.61
18.92
17.86
O
N
N
CH3
H3C
2.14c
f1 (ppm)


10.32
7.93
7.48
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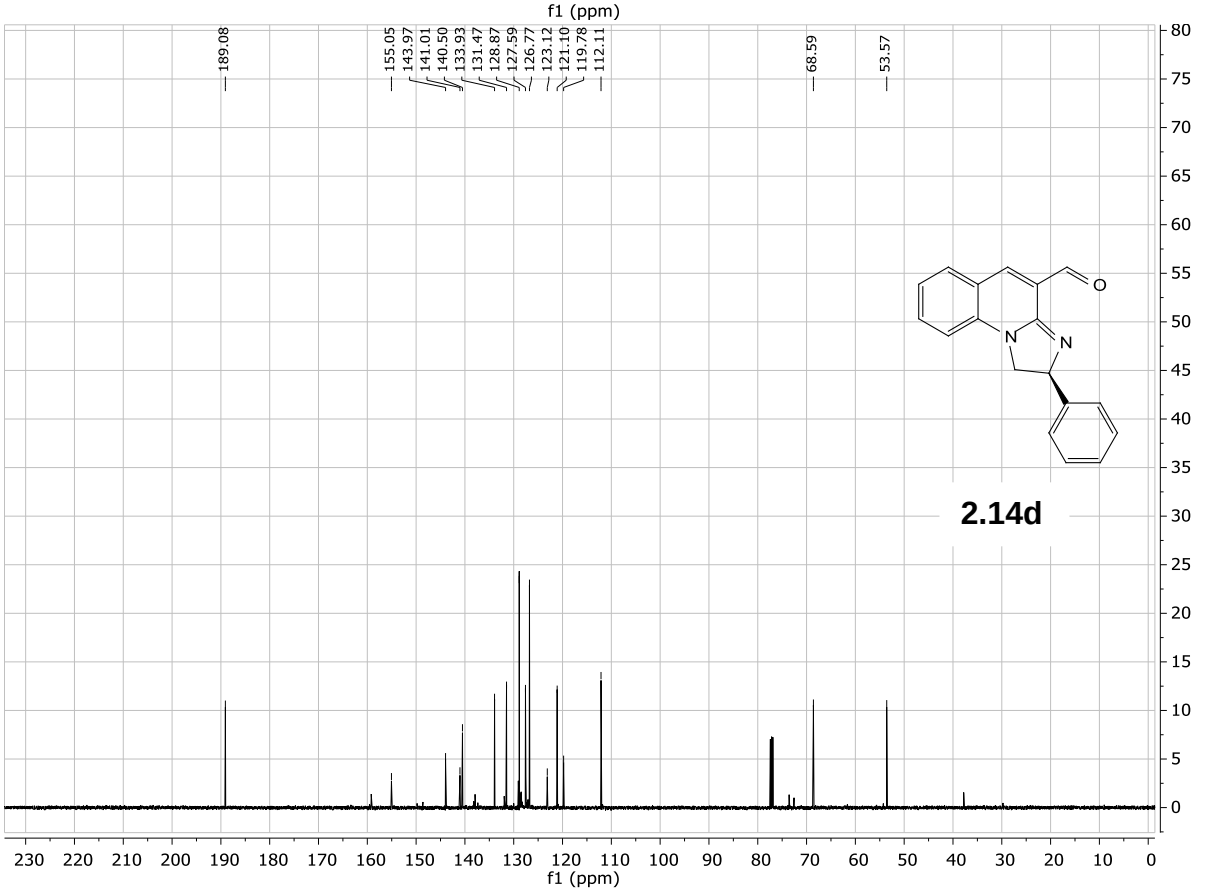
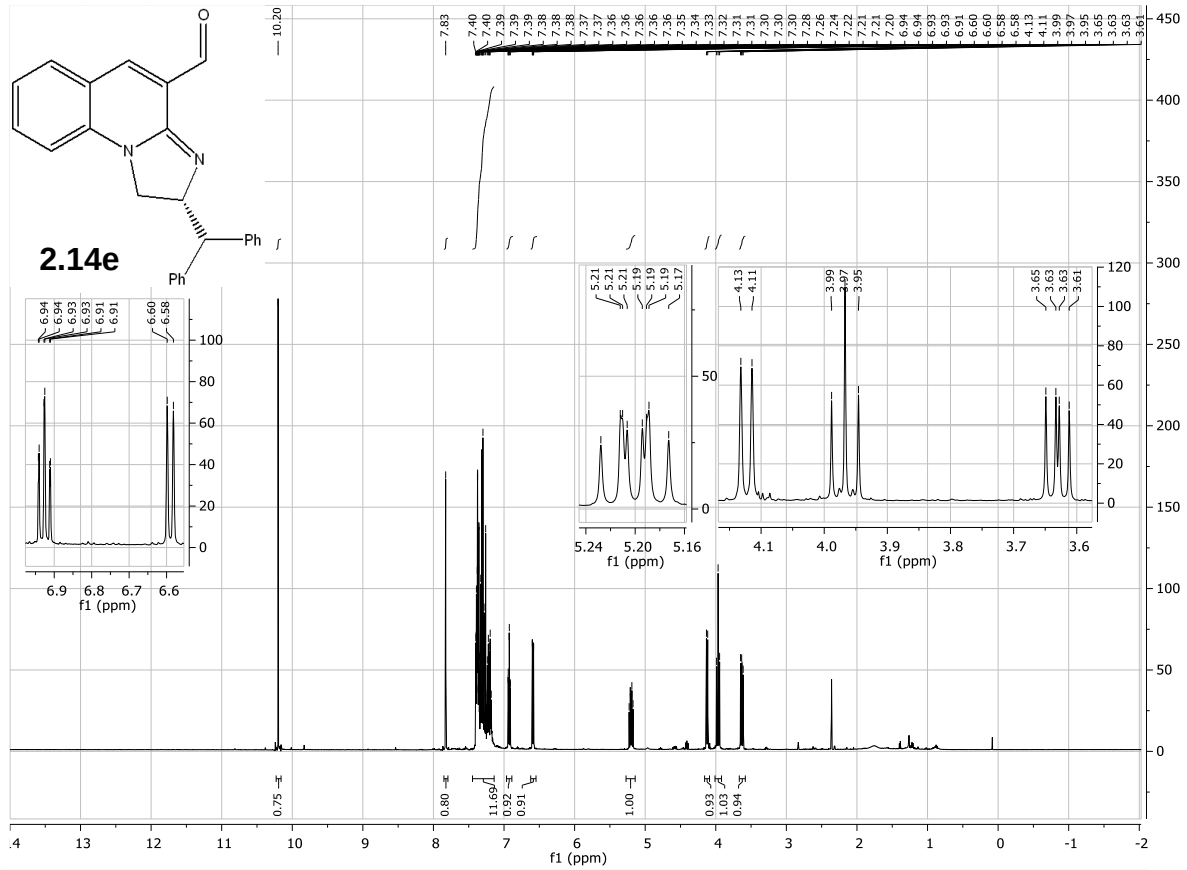
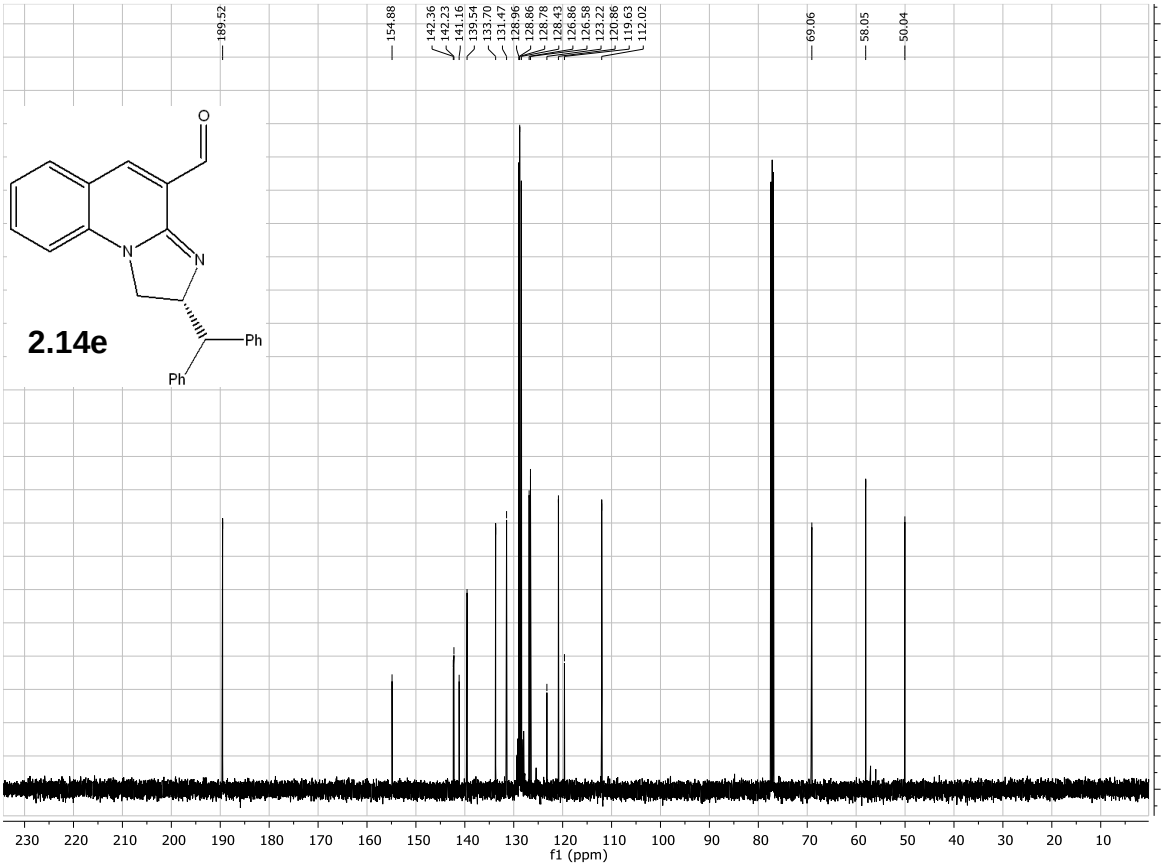
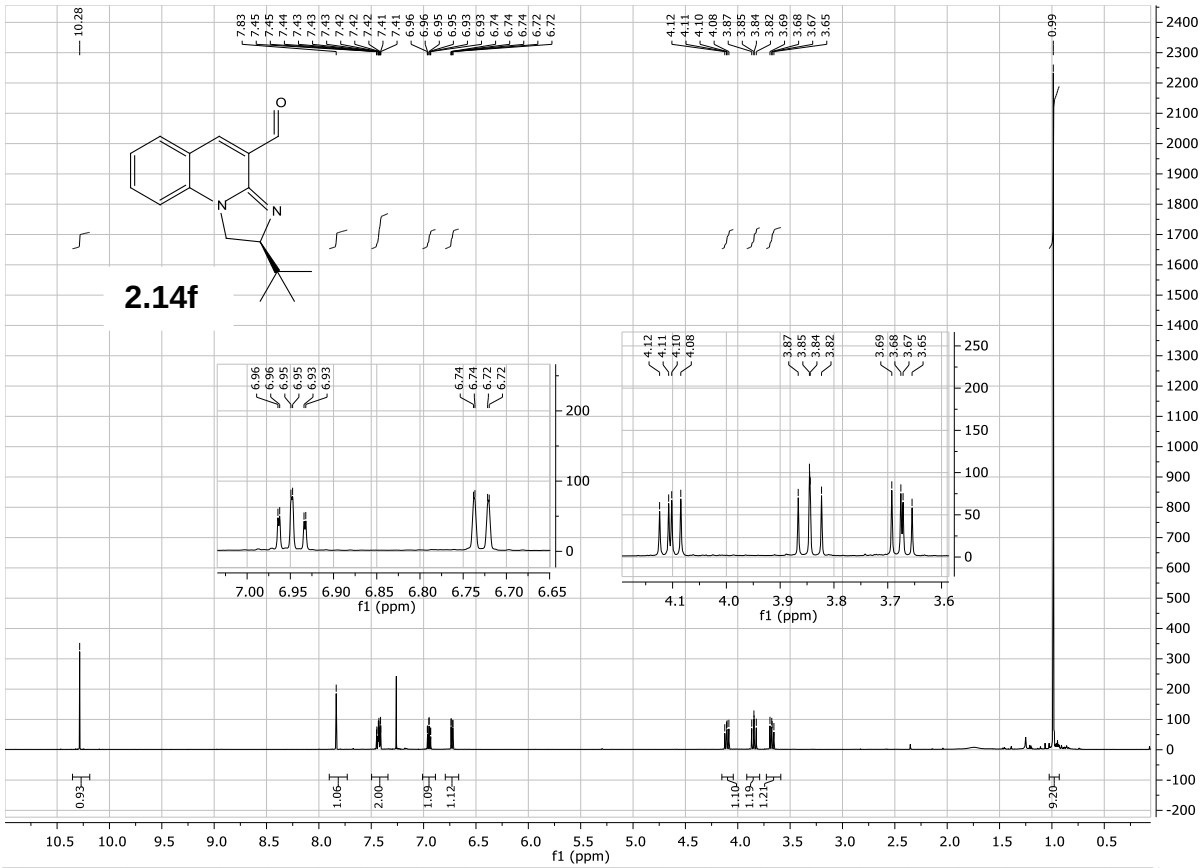
7.45
7.44
7.44
7.41
7.41
7.38
7.37
7.37
7.31
7.30
7.29
7.02
7.01
6.99
6.99
6.97
6.96
6.71
6.69
5.49
5.46
5.45
5.42
4.39
4.36
4.36
4.32
3.87
3.84
3.83
3.81
0.78
1.03
8.47
1.22
1.08
1.00
1.27
1.23
f1 (ppm)
2.14d


189.08
155.05
143.97
141.01
140.50
133.93
131.47
128.87
127.59
126.77
123.12
121.10
119.78
112.11
68.59
53.57
f1 (ppm)
2.14d


2.14e
Ph
Ph
f1 (ppm)


2.14e
Ph
Ph
f1 (ppm)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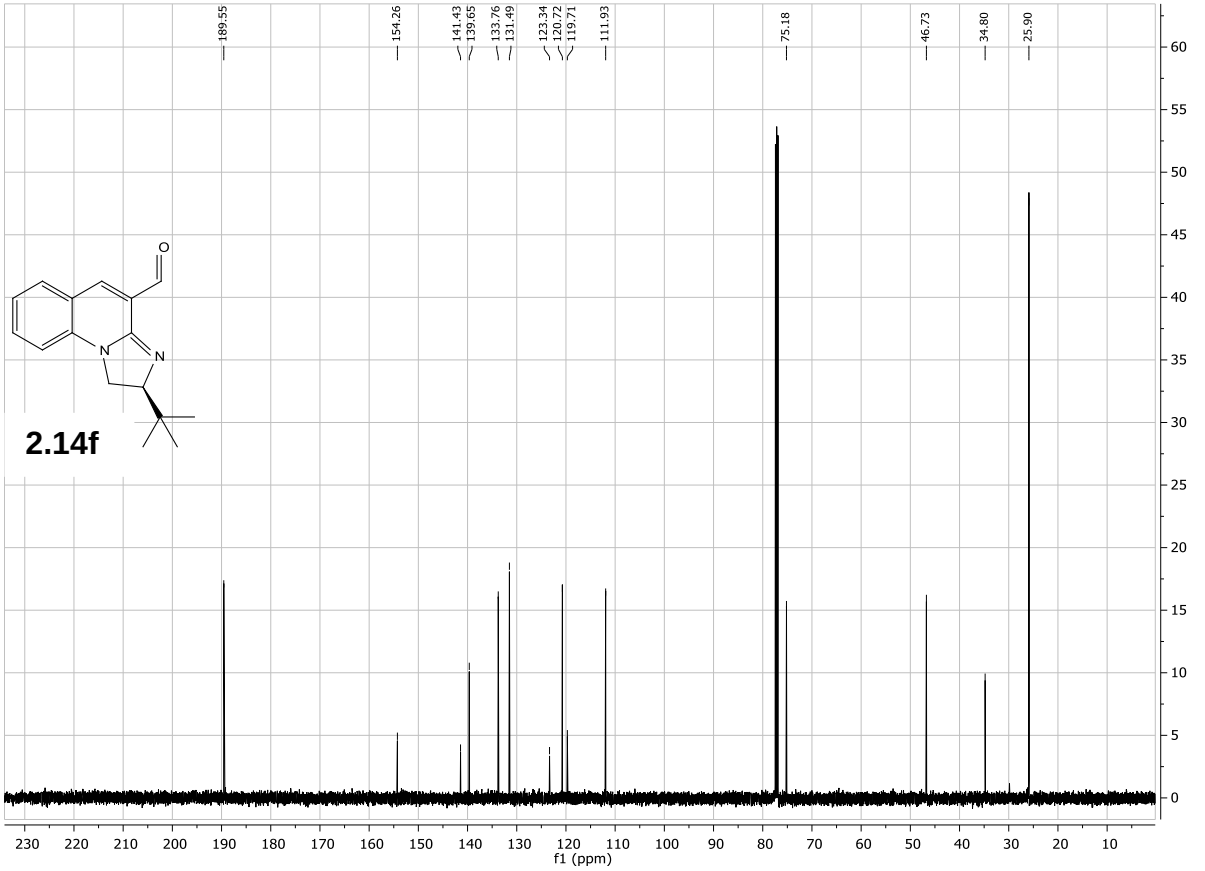
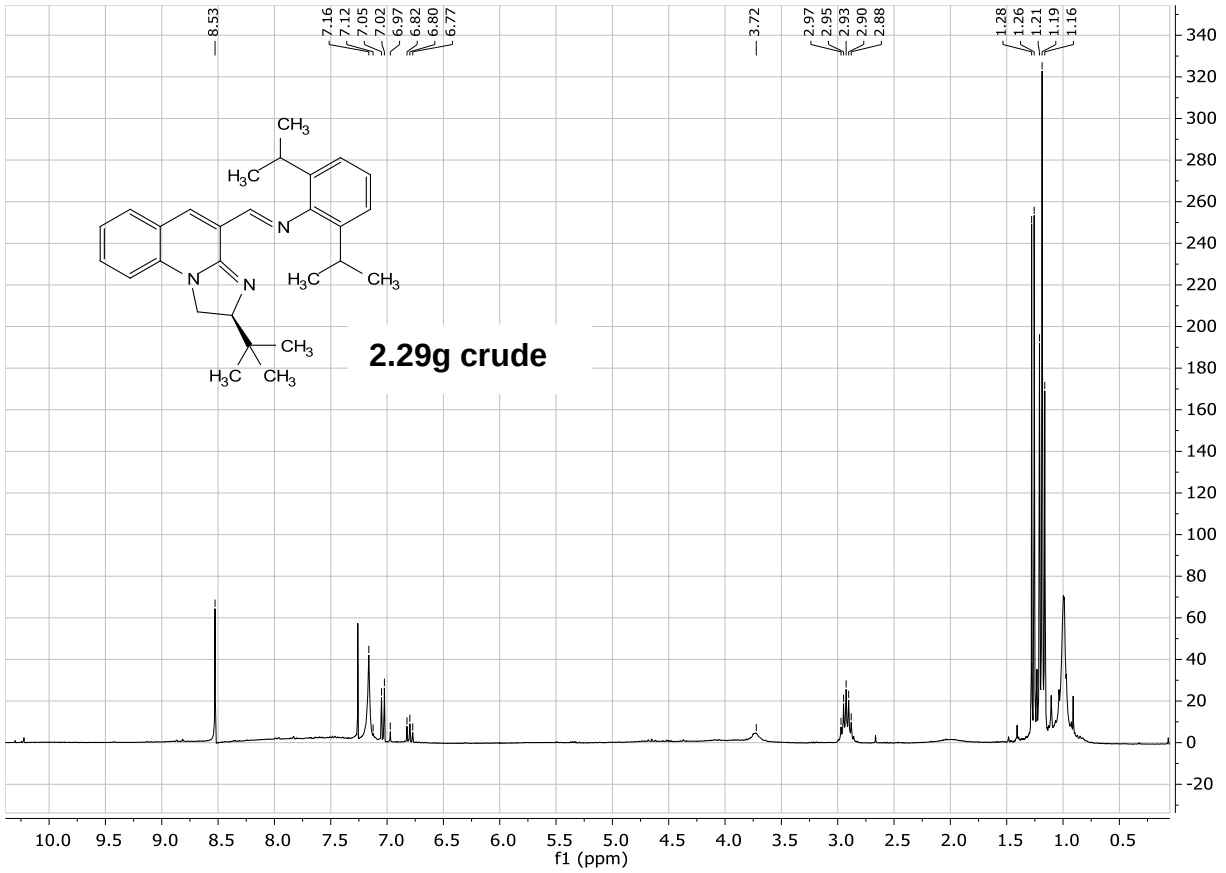
f1 (ppm)


2.14f
f1 (ppm)


8.53
7.16
7.12
7.05
7.02
6.97
6.82
6.80
6.77
3.72
2.97
2.95
2.93
2.90
2.88
1.28
1.26
1.21
1.19
1.16
2.29g crude
f1 (ppm)