NOVEL METHODOLOGY TOWARDS THE INDOLE CORE AND IRON-CATALYZED ELECTROPHILIC HYDROAMINATION OF ALKENES

A Dissertation

by

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ABSTRACT

Indole-containing structures and their generation still draw much attention because of their ubiquity in natural products, medicinal compounds, and organic materials. Given this prevalence, synthetic methods toward these structural motifs are numerous, each with a distinct set of advantages and disadvantages. One significant challenge is the generation of 3,3-disubstituted indolines that are frequently encountered in indole cores. The discovery, optimization, and scope of a C3-quaternary indolenine synthesis, as well as, efforts to expand the methodology for the generation of higher order indole-containing polycycles, will be discussed. This novel reactivity also lead to a generalized synthesis of α,β-unsaturated *N*-aryl ketonitrones which has few literature examples. A modest start to realizing the success of 3-substituted non-*N*-protected indoles as a Michael donor will also be explored.

Green chemistry continues to play an important role in creating a sustainable world. At the core of green chemistry is the reduction or elimination of the use or generation of hazardous substances. Catalysis by definition is green by reduction; however, many of the catalytic systems utilize toxic metals that can hamper or cause further concerns with allowable limits on industrial scales. Iron catalyzed reactions seek to replace these toxic metals with a benign one that is also relatively cheap. Nitrogen containing compounds are an important feed stock for the pharmaceutical and other industries. The iron catalyzed intermolecular hydroamination of alkenes with electrophilic amines will be discussed.

DEDICATION

To my wife

and my son

Clifford

ACKNOWLEDGEMENTS

I would like to thank my committee chair, Dr. Jiong Yang, for support and providing the opportunity and lab to conduct this research. I would also like to thank my committee members, Dr. Romo, Dr. Wooley, Dr. Zhu, for their guidance and support throughout the course of this research. Thanks also goes to all my colleagues and the department faculty and staff for this educational experience.

I would also like to thank all my friends for helping to keep me sane. Sometimes the best thing to do is to walk away from your research and allow other distractions in. Thank you for all the conversations and mind clearing opportunities.

Finally, I am thankful for my family and their continued understanding in the value of education. But most importantly, I am grateful for my wife, Candace, and her patience with my education. The time will soon be yours.

NOMENCLATURE

Ac	Acetyl
ACS	American Chemical Society
BBN	9-Borabicyclo(3.3.1)nonane
Boc	*tert*-Butoxycarbonyl
BOX	Bisoxazoline
Bz	Benzoyl
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DCM	Dichloromethane, methylene chloride
DMF	*N*,*N*'-Dimethylformamide
EDTA	Ethylenediaminetetraacetic acid
Et	Ethyl
i-Pr	*iso*-Propyl
LG	Leaving group
M	Metal atom
*m*CPBA	*meta*-chloroperbenzoic acid
Me	Methyl
MVK	Methyl vinyl ketone
NMR	Nuclear Magnetic Resonance
OAc	Acetate
PDI	Bis(imino)pyridine

PG	Protecting group
Ph	Phenyl
R	Any alkyl, aryl, vinyl, or alkynyl group
t-Bu	*tert*-Butyl
Tf	Trifluoromethanesulfonyl
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
TLC	Thin layer chromatography
Ts	Tosyl
X	Any halide

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CHAPTER I

INTRODUCTION AND LITERATURE REVIEW

1.1 Indoles

Over 10,000 natural and unnatural indole derivatives have been discovered to date.[1] Many of these indole derivatives were isolated from natural sources in the animal, fungal, microbial, and plant kingdoms.[2] The indole core is present in indolenine, indoline, oxindole, spiroindoline, pyrroloindoline, furoindoline, carbazole, α-carboline, β-carboline, etc. (Figure 1.1). Due to their biological activity and other properties, it is of little surprise that many indole derivatives have found application within the pharmaceutical, agricultural, dye, essential oil, and perfume industries. More than 200 natural and unnatural indole derivatives are currently in clinical use or under clinical development.[1] For example, these indole cores may be found within

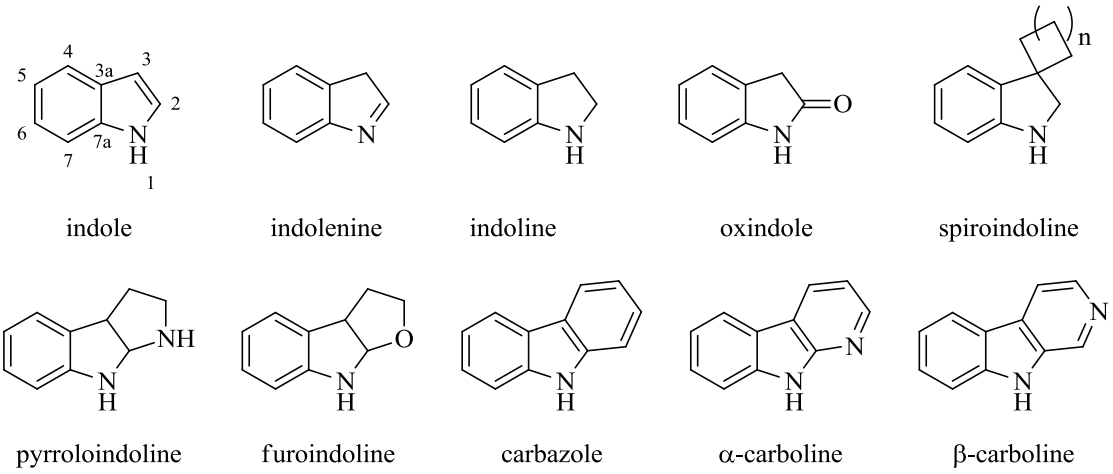
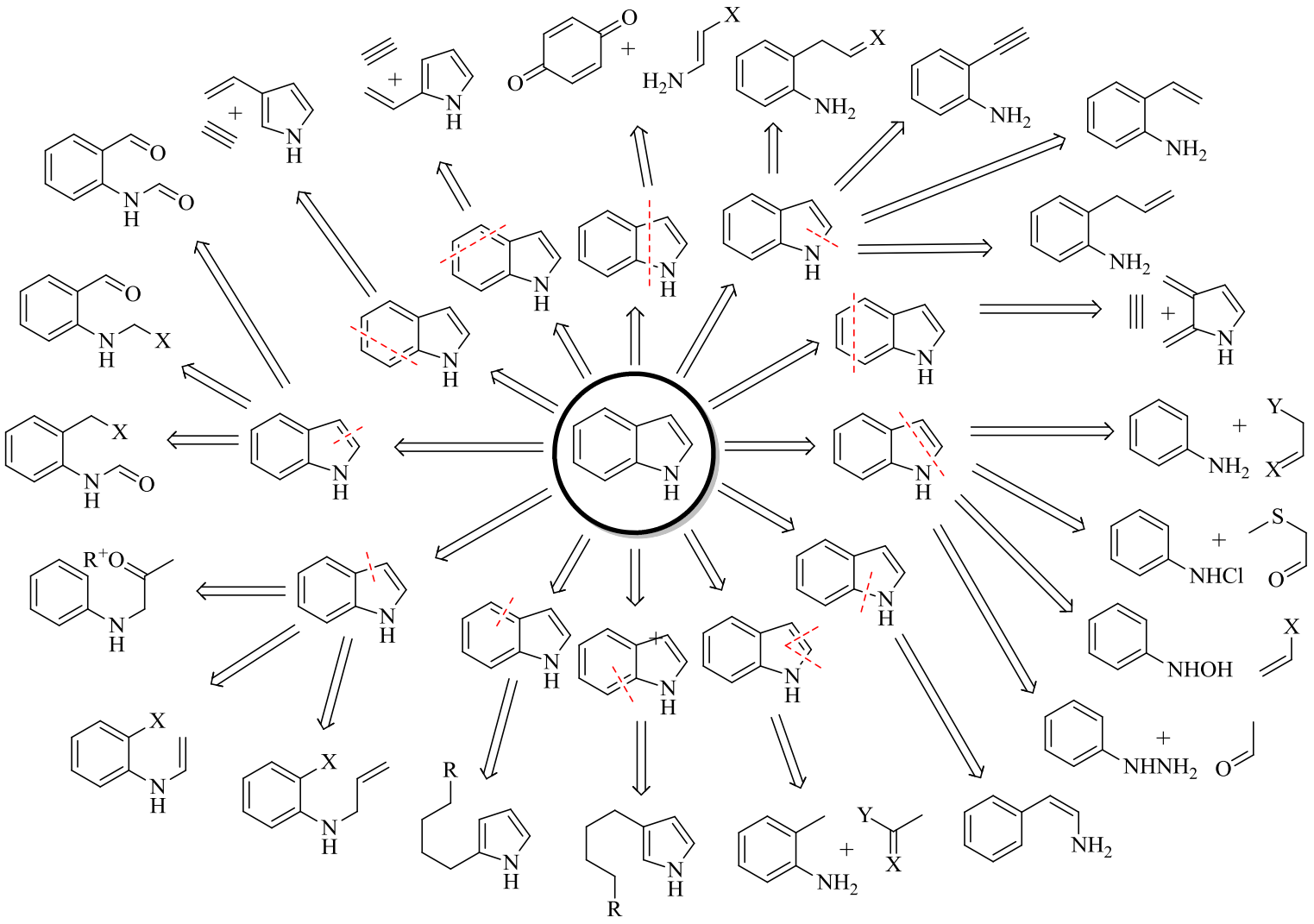


Figure 1.1 Generalized indole cores

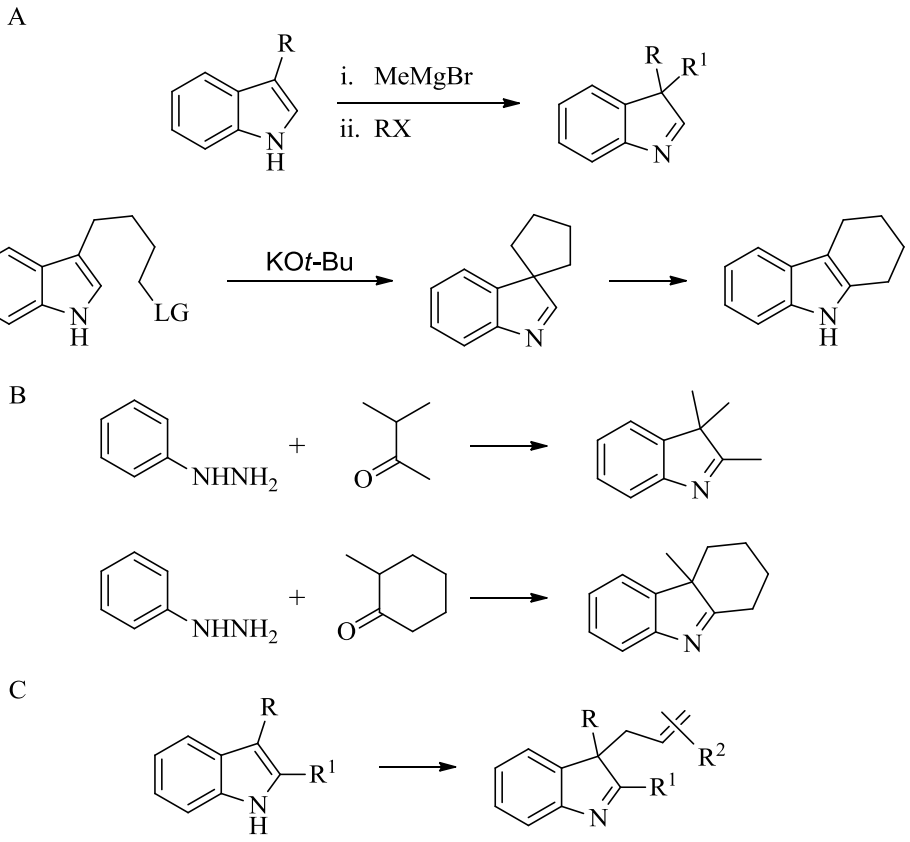
prescription and over-the-counter drugs and dietary supplements.[3] Entire classes of drugs exist, such as triptans for migraine sufferers, based on tryptamine, an indole core. They are also found in common dietary supplements such as tryptophan, serotonin, and melatonin. Many agricultural pesticides, herbicides, and fungicides, as well as auxins used by horticulturalists, contain this moiety. It is also found in the most common dye for blue jeans, indigo; the core may be found in dyes that cover the visible region. Many indole compounds are highly odiferous and found within essential oils and perfumes. This prevalence in commercial applications demonstrates the rich functional diversity offered by these compounds.

With the high prevalence of the indole cores and their unique biological activity, synthesis and derivatization is of the utmost importance. The vast quantity and variation in synthetic approaches validate the importance of these molecules and also demonstrates the synthetic challenges involved.[4] Each synthesis has its own set of advantages and disadvantages. For example, common advantages may include high yield, selectivity, ease of purification, etc. while common disadvantages may relate to substrate scope and synthetic difficulty of making the starting material. See Scheme 1.1 for a generalized approach for indole synthesis. This schematic is based on Sundberg's 1996 book[5] and as such does not show approximately the last twenty years of innovation. It does succeed in demonstrating the vast number of synthetic routes.

Existing methods to synthesize C3-quaternary indole cores typically rely on C3 substituted indoles or oxindoles as the starting material,[6] thus are typically limited by the commercial availability and ease of preparation of precursors. Preparation of benzenoid



Scheme 1.1 Generalized synthetic approach to indoles

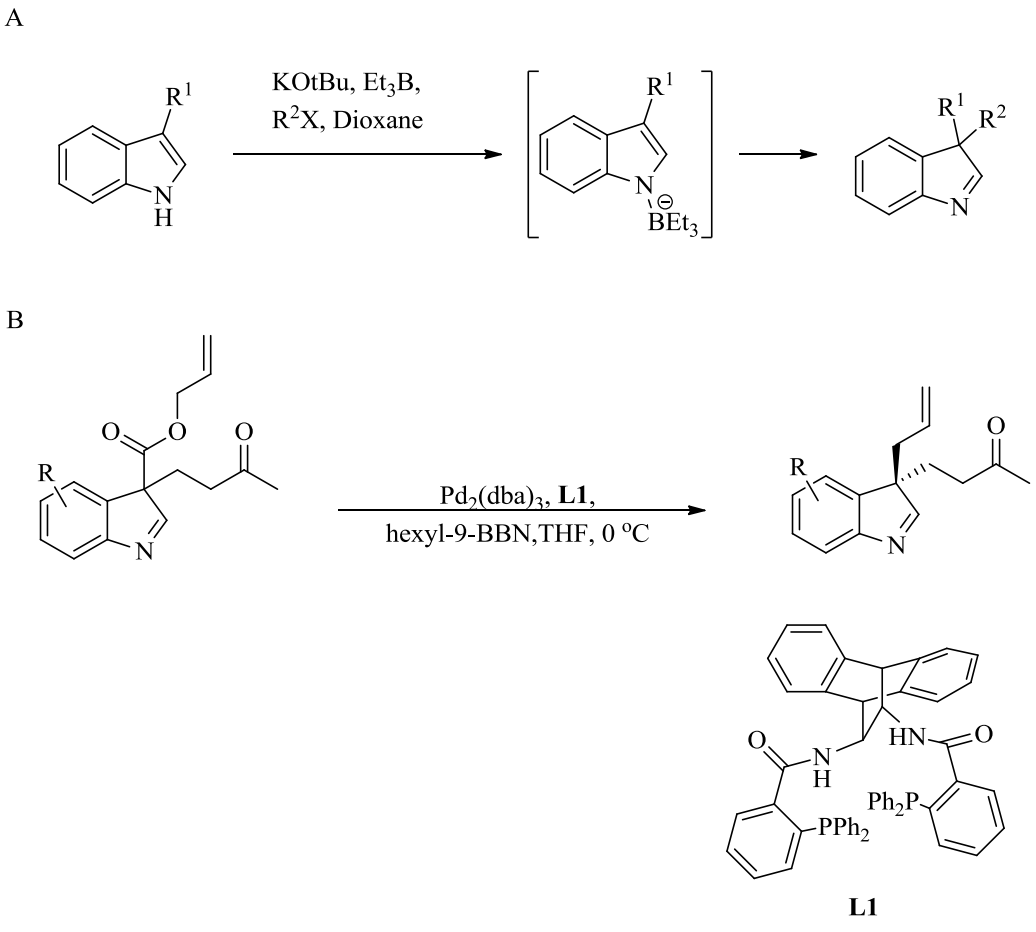


Scheme 1.2 Example indolenine synthesis

substituted indoles remain a significant challenge.[7] A further challenge exists in the generation of indolenines due to their high propensity for rearrangement.

Current methods for synthesis of indolenines mainly fall into three categories, basic conditions, Fischer's indole synthesis, and palladium catalysis (Scheme 1.2). Under basic conditions, low yields and rearrangement products typically result.[8] Upon using a Grignard reagent to form the magnesium amide with a 3-substituted indole followed by alkylation with an alkyl halide, low yields of the indolenine prevail. Treatment with potassium *tert*-butoxide of 3-substituted indole with a tethered leaving group attached forms the spiro-indolenine; however, these indolenines are typically

unstable and readily migrate to form the rearrangement product. Under certain circumstances, the Fischer's indole synthesis will produce indolenines (Scheme 1.2, B).[9] Typically, the Fischer's indole synthesis forces rearrangement products due to the high temperatures and strong acid conditions. If the substrates are chosen that have a low propensity for migration such as those in Scheme 1.2 B, the indolenine may survive. More recently, palladium catalyzed allylic alkylation of 3-substituted indoles has been developed (Scheme 1.2, C). In 2005, Tamaru succeeded in utilizing allyl alcohols in this



Scheme 1.3 Recent advances by Yang group in indolenine chemistry

palladium catalyzed transformation[10] and in 2006 Trost succeeded in an enantioselective variant by changing the ligand.[11] Allyl methyl carbonate was used by Rawal in his catalytic transformation in 2008.[12]

Recently our group has tackled a few of these challenges. Similar to the magnesium amide in Scheme 1.2, Yang changed the Grignard reagent to an inorganic base and triethyl borane to form the *N*-indolyltriethylborate and achieved typical yields in a range between 80% and 95% (Scheme 1.3, A).[13] With a few methods developed to form indolenines, Yang also sought to generate the C3-stereocenter asymmetrically through a catalytic enantioconvergent decarboxylative allylic alkylation of allyl indolenine-3-carboxylates (Scheme 1.3, B).[14]

1.2 Green chemistry and iron catalysis

Green chemistry in the most simplified definition is pollution prevention. Pollution can be anything from toxins to wasted energy and/or materials. The ACS Green Chemistry Institute® lists and describes the "12 Principles of Green Chemistry" as follows:

1. **Prevention**: It is better to prevent waste than to treat or clean up waste after it has been created.
2. **Atom Economy**: Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product.

3. **Less Hazardous Chemical Syntheses**: Wherever practicable, synthetic methods should be designed to use and generate substances that possess little or no toxicity to human health and the environment.
4. **Designing Safer Chemicals**: Chemical products should be designed to affect their desired function while minimizing their toxicity.
5. **Safer Solvents and Auxiliaries**: The use of auxiliary substances (e.g., solvents, separation agents, etc.) should be made unnecessary wherever possible and innocuous when used.
6. **Design for Energy Efficiency**: Energy requirements of chemical processes should be recognized for their environmental and economic impacts and should be minimized. If possible, synthetic methods should be conducted at ambient temperature and pressure.
7. **Use of Renewable Feedstocks**: A raw material of feedstock should be renewable rather than depleting whenever technically and economically practicable.
8. **Reduce Derivatives**: Unnecessary derivatization (use of blocking groups, protection/deprotection, temporary modification of physical/chemical processes) should be minimized or avoided if possible, because such steps required addional reagents and can generate waste.
9. **Catalysis**: Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.

10. **Design for Degradation**: Chemical products should be designed so that at the end of their function they break down into innocuous degradation products and do not persist in the environment.
11. **Real-time analysis for Pollution Prevention**: Analytical methodologies need to be further developed to allow for real-time, in-process monitoring and control prior to the formation of hazardous substances.
12. **Inherently Safer Chemistry for Accident Prevention**: Substances and the form of a substance used in a chemical process should be chosen to minimize the potential for chemical accidents, including releases, explosion, and fires. [15]

Though these principles are listed by ACS as a way to prevent pollution in more of an altruistic manner without regard to politics but an emphasis on bettering the environment, the reality is that money speaks louder than words, and green chemistry is cheap chemistry. Any business model would see that using less is going to save money, and virtually every principle saves money for the company. Where exceptions exist, laws make the costs comparable. For example, Europe has, or at least has begun to, pass laws requiring manufacturers to be responsible for the end of life of products. Though the United States does not currently have any laws regarding this Extended Producer Responsibility (EPR), states can and are passing laws.[16] This means that if disposal is expensive they are being taxed more, thus making it more profitable to design the products with end of life in mind.

Iron catalysis fits into this model for more reasons than just being a catalyst and as such has experienced significant growth in recent decades.[17] Compared with other

heavy or rare metals, iron and many of its salts have low toxicity. Iron is also one of the most abundant metals on earth. This makes it one of the most inexpensive and environmentally friendly choices. Many of the iron salts and complexes are commercially available or easily prepared. An additional feature of many of the iron-catalyzed reactions is complementary reactivities and selectivities to other transition metal catalysis.

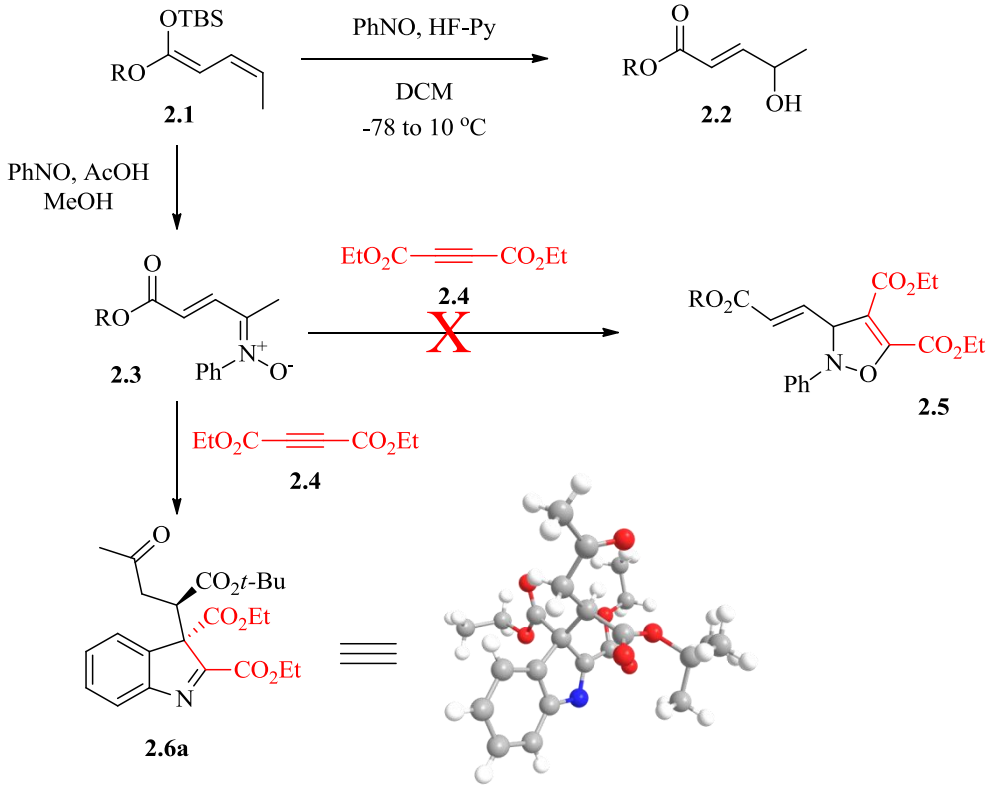
Though the pioneering work of iron catalysis began in the 1940's,[18] in the 1970's iron catalysis did not gain the popularity that palladium and nickel found that has virtually led their dominance in catalytic systems ever since.[19] In the early 1990's, pollution laws were being passed in the United States and by the end of the decade green chemistry was being promoted. Coinciding with this green chemistry push, alternative catalysts were investigated and groups such as Fürstner, Cahiez, and Nakamura helped to bring iron catalysis to the forefront in the late 1990's and early 2000's.[20]

CHAPTER II

INDOLENINE SYNTHESIS*

2.1 Indolenine synthesis

While optimizing γ-oxidation of esters, Yang group discovered the formation of the α,β-unsaturated *N*-phenyl ketonitrone **2.3** from PhNO by changing the solvent (Scheme 2.1).[21] Efforts to optimize and expand the scope of this nitrone synthesis met significant challenges and low yields resulting in efforts to trap **2.3** *in situ* with alkyne

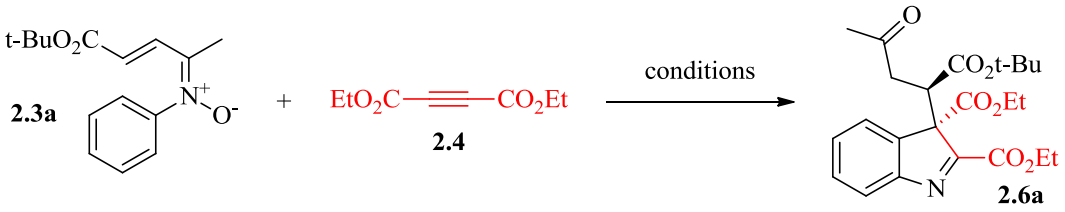


Scheme 2.1 Discovery and crystal structure of **2.6a**

* Adapted with permission from Huehls, C. B.; Hood, T. S.; Yang, *J. Angew. Chem. Int. Ed.* **2012**, *51*, 5110; Copyright 2012 John Wiley & Sons, Inc. and Hood, T. S.; Huehls, C. B.; Yang, J. *Tetrahedron Lett.* **2012**, *53*, 4679; Copyright 2012 Elsevier.

2.4 and form **2.5**, a method to quantify unstable nitrone formation. Interestingly, formation of **2.6a** resulted.[22] The formation of the indolenine prompted the investigation into the possible synthetic utility of this transformation as a means to C3 quaternary indolenines through the use of α,β-unsaturated *N*-arylnitrones and activated alkynes.

2.2 Optimization



Entry	Solvent	Additive[a]	T[°C]	**2.6a**[b]
1	CH_2Cl_2	-	RT	64
2	THF	-	RT	48
3	ether	-	RT	21
4	DMF	-	RT	trace
5	*i*-PrOH	-	RT	trace
6	toluene	-	RT	68
7[c]	toluene	HOAc	RT	7
8[c,d]	toluene	HOAc/H_2O	RT	45
9	toluene	TFA	RT	trace
10	toluene	TfOH	RT	15
11	toluene	$ZnCl_2$	RT	trace
12	toluene	$SnCl_4$	RT	trace
13	toluene	$FeCl_3$	RT	trace
14	toluene	$TiCl_4$	RT	trace
15	toluene	-	40	73
16	toluene	-	80	79

All reactions were carried out using 1 equiv of **2.3a** and 3 equiv of **2.4**. [a] Unless noted otherwise, 1.2 equiv of the additive was used. [b] Yield of the isolated product. [c] 0.2 equiv of HOAc was used. [d] The reaction was carried out in a mixture of toluene/H_2O (10:1).

Table 2.1 Optimization of conditions for formation of **2.6a**

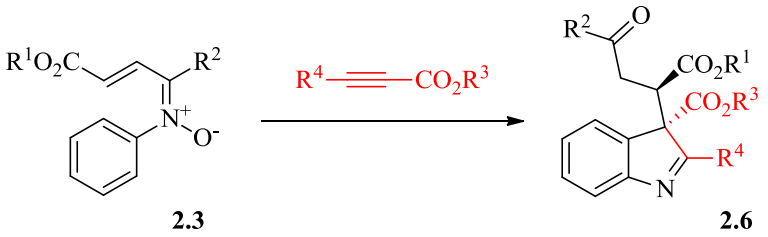
Various reaction parameters were examined in an attempt to improve reaction efficiency (Table 2.1). The reaction was found to give better yields in non-polar solvents (CH_2Cl_2 or toluene; Table 2.1, entries 1-6). The addition of both Brønsted and Lewis acids decreased the reaction efficiency or shut down the reaction completely (Table 2.1, entries 7-14). Elevated temperature (40 to 80 ^oC) not only accelerated the reaction, but led to improved yields as well (Table 2.1, entries15 and 16). Thus, all subsequent reactions were carried out in toluene at 80 ^oC unless noted otherwise.

2.3 Scope

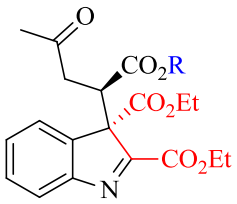
The scope of the reaction was investigated under the optimized reaction conditions using a range of α,β-unsaturated *N*-phenyl ketonitrones **2.3** and activated alkynes (Scheme 2.2). The yields of **2.6** were affected by the size of the alkyl ester groups of both the ketonitrones and the activated alkynes, but in opposite ways. Higher yields were achieved when the ketonitrone with a bulky *tert*-butyl carboxylate substituent was used (**2.6a** versus **2.6b** and **2.6c**), however, a lower yield was observed when an alkyne with an ester of increased steric bulk was used (**2.6e** versus **2.6c** and **2.6d**). The α'-alkyl (R^2) substituent of the α,β-unsaturated ketonitrones only exerted a slight influence over the reaction efficiency (**2.6f** and **2.6g**).

Excellent regioselectivity was observed when alkyl propiolates (R^4 = H) were used. Only the C3-quaternary indolenines (**2.6h**, **2.6i**, and **2.6j**) were formed upon reaction of **2.3a** with unsymmetrical monoactivated alkynes. The steric characteristics of the ester groups of these monoactivated alkynes had a more pronounced effect over

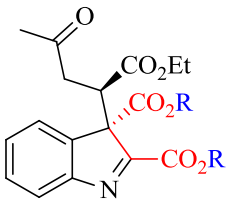
the reaction yields than that of the ester groups of symmetrical activated alkynes. For example, **2.3a** with methyl propiolate led to formation of **2.6h** in 61% yield whereas **2.6j** was obtained in only 32% yield from the reaction of **2.3a** and *tert*-butyl propiolate. A C3-quaternary indolenine **2.6k** was also formed when the monoactivated alkyne ethyl 3-



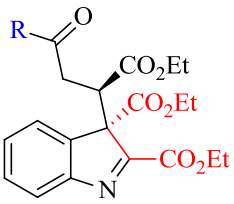
2.3 **2.6**



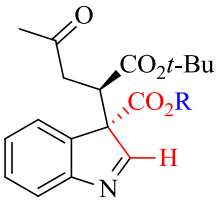
2.6b (R = Me, 58%)
2.6c (R = Et, 61%)



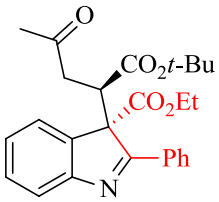
2.6d (R = Me, 57%)
2.6e (R = t-Bu, 42%)



2.6f (R = n-C_7H_{15}, 70%)
2.6g (R = CH_2CH_2Ph, 61%)



2.6h (R = Me, 61%)
2.6i (R = Et, 45%)
2.6j (R = t-Bu, 32%)

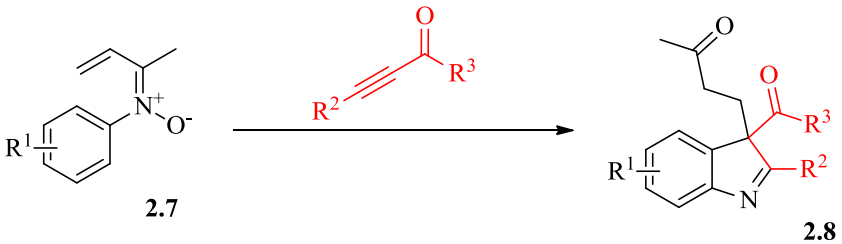


2.6k (37%)

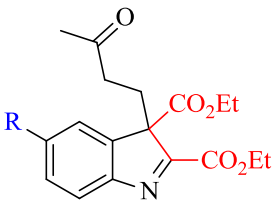
All reactions were carried out using 1 equivalent of **2.7** and 3 equivalents of activated alkynes at 80 ^{o}C in toluene until the reaction was complete by TLC analysis (8 – 12 h). The yields are of the isolated products.

Scheme 2.2 Reaction of **2.3** and activated alkynes to form **2.6**

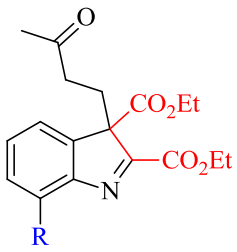
phenylpropiolate was used. Alkynes without activating groups (such as 6-dodecyne, phenylacetylene, and diphenylacetylene; not shown) did not participate in the reaction.



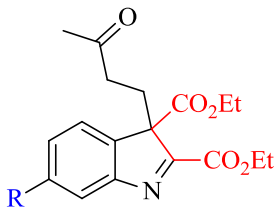
2.7 **2.8**



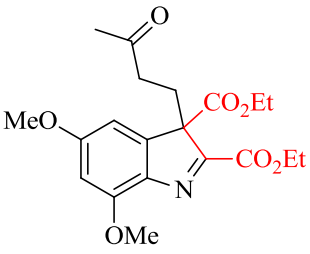
2.8a (R = H, 70%)
2.8b (R = Me, 52%)
2.8c (R = Cl, 57%)
2.8d (R = OMe, 52%)
2.8e (R = NMe_2, 53%)
2.8f (R = CN, 22%)



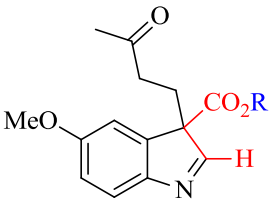
2.8g (R = Me, 78%)
2.8h (R = Br, 74%)



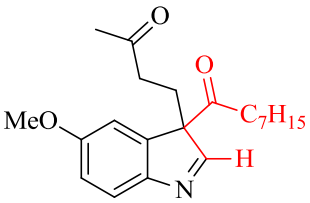
2.8i (R = Me, 61%)
2.8j (R = Cl, 33%)



2.8k (52%)



2.8l (R = Me, 66%)[a]
2.8m (R = Et, 52%)
2.8n (R = allyl, 61%)[a]
2.8o (R = Bn, 69%)[a]



2.8p (70%)[a]

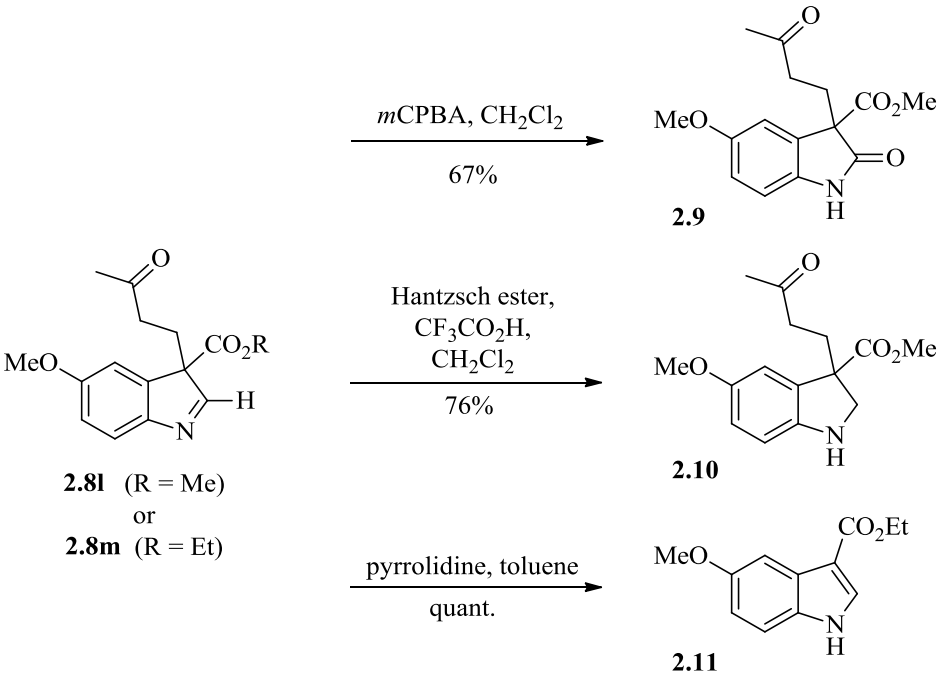
All reactions were carried out using 1 equivalent of **2.7** and 3 equivalents of activated alkynes at 80 °C in toluene until the reaction was complete by TLC analysis (8 – 12 h). The yields are of the isolated products. [a] These reactions were conducted at RT.

Scheme 2.3 Reaction of **2.7** and activated alkynes to form **2.8**

To further explore the generality of this method a series of *N*-aryl ketonitrones without β substituents (**2.7**) were also investigated (Scheme 2.3).[23] Good to moderate yields were obtained for reactions of α,β-unsaturated *N*-tolyl ketonitrones with diethyl acetylenedicarboxylate **2.4**: the 6-methyl indolenine **2.8i** was regioselectively generated from the *N*-*meta*-tolyl ketonitrone and 5- and 7-methyl indolenines **2.8b** and **2.8g** were formed from the *N*-*para*-tolyl and *N*-*ortho*-tolyl ketonitrones, respectively. α,β-Unsaturated ketonitrones with 2'-bromo, 3'-chloro, and 4'-chloro-*N*-phenyl groups reacted to give indolenines **2.8h**, **2.8j**, and **2.8c** regioselectively. Substitution of the *N*-phenyl group with electron-donating methoxy, dimethylamino, and dimethoxy groups was found to be compatible with this reaction (**2.8d**, **2.8e**, and **2.8k**). A significantly reduced yield was observed when the *N*-phenyl ring was substituted with the electron-withdrawing cyano group **2.8f**. Monoactivated terminal alkynes in the form of methyl, ethyl, allyl, and benzyl esters of propiolic acid readily reacted with the α,β-unsaturated *N*-4'-anisyl ketonitrone to give C3-quaternary indolenines **2.8l** – **2.8o**. A preliminary study showed that the alkyne with a keto activating group rather than an ester was also compatible with the reaction (**2.8p**).

To further demonstrate the usefulness and potential synthetic application of these C3-quaternary indolenines, simple manipulations were performed. For example, the indolenine moiety of **2.8l** could be oxidized with *m*CPBA to form oxindole **2.9** (Scheme 2.4).[24] Also, reduction of **2.8l** with the Hantzsch ester gave **2.10** in 76% yield.[25] Complex mixtures were formed when other reducing agents such as $NaBH_4$, $NaBH_3CN$, and $NaBH(OAc)_3$/HOAc were used. The 3-substitued indole **2.11** was quantitatively

formed by the retro-Michael cleavage of one of the C3-substituents when **2.8m** was treated with pyrrolidine. This method provides a unique entry to substituted indoles by reaction of α,β-unsaturated *N*-aryl ketonitrones and activated alkynes.

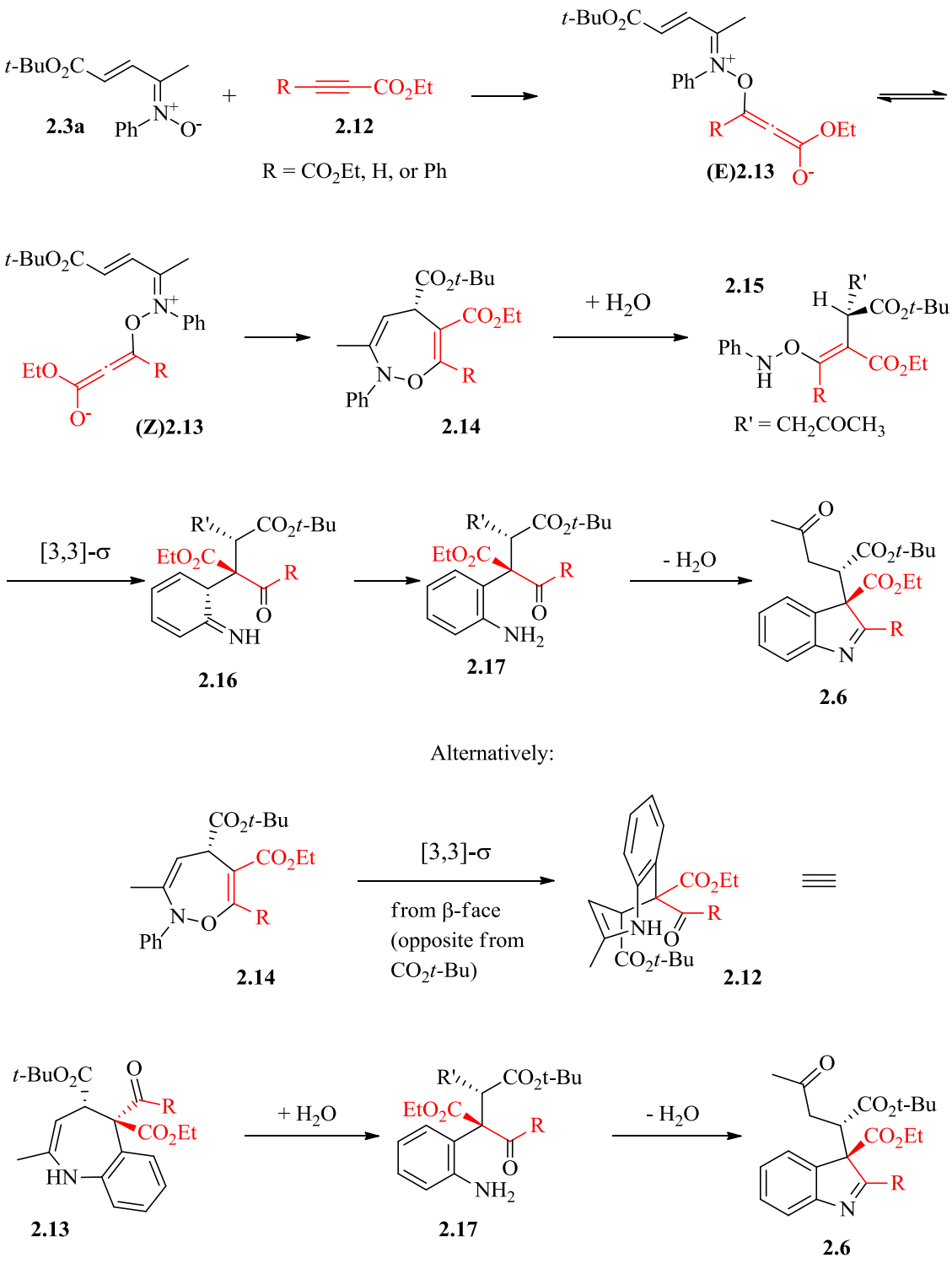


Hantzsch ester = diethyl 2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate.

Scheme 2.4 Some transformations of **2.8l** and **2.8m**

2.4 Proposed mechanism

The formation of **2.6** may initiate with the [5+2] cyclization of **2.3a** and **2.12** to generate the seven-membered heterocycle **2.14** (Scheme 2.5).[26] This may proceed through a stepwise process initiated by a nucleophilic Michael attack of the oxygen atom of the nitrone to the activated alkyne.[27] Formation of the zwitterion (E)-**2.13** is



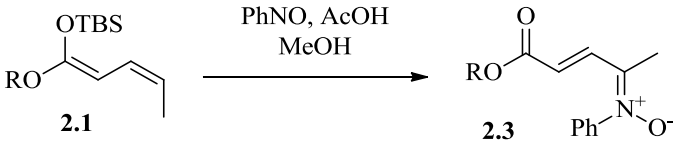
Scheme 2.5 Proposed mechanism for formation of **2.6**

accompanied by significant reduction of the energy barrier for C=N double bond isomerization to give (Z)-**2.13**, which cyclizes to form **2.14**. Hydrolysis of **2.14** forms **2.15**. Further transformations of **2.15** via the [3,3]-sigmatropic rearrangement, tautomerization, and intramolecular condensation lead to formation of the C3-quaternary indolenine **2.6**.[28] Only catalytic amount of water is necessary for the entire process since it is regenerated upon formation of **2.6**. Alternatively, the [3,3]-sigmatropic rearrangement may precede the hydrolysis as shown in Scheme 2.5.

Such a mechanism is consistent with the stereoselective formation of the diastereomer illustrated for **2.6**. Specifically, minimization of the 1,3-allylic strain requires **2.15** to adopt the conformation shown.[29] When **2.3** contained an ester group, complete stereoselectivity for the *anti* diastereomer was observed. This strain directs the [3,3]-sigmatropic rearrangement to occur from the sterically less hindered β face to give **2.6** stereoselectively. Since the nucleophilic attack of the oxygen atom of the nitrone will occur at the β position of the activated alkyne, this mechanism also rationalizes the regioselectivity in formation of C3-quaternary indolenines when mono-activated alkynes are used.

2.5 Nitrone synthesis

With the seemingly broad scope and reactivity of the discovered indolenine synthesis, *N*-aryl ketonitrone synthesis needed to be addressed. Efforts to expand upon

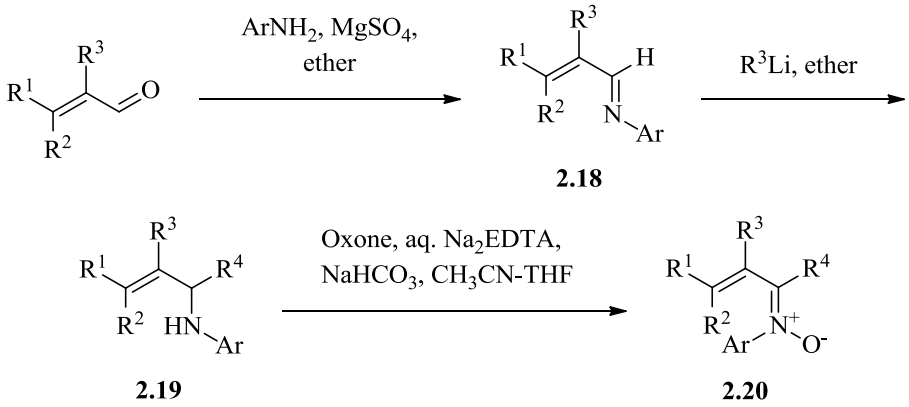


Entry	R	Yield
1	*t*-Bu	**2.3a** (64%)
2	Me	**2.3b** (8%)
3	Et	**2.3c** (11%)

Table 2.2 Nitrone synthesis with PhNO

the scope of nitrone **2.3** formation under these conditions failed (Table 2.2). Though the *tert*-butyl ester **2.3a** was synthesized in good yield, **2.3b** and **2.3c** (the methyl and ethyl ester) presented challenges. Formation of **2.3b** resulted in an 8% yield with similar disappointing results for **2.3c** (Table 2.2, entries 1 and 2). Condensation of ethyl 4-oxopent-2-enoate with phenylhydroxylamine to form **2.3c** failed to occur. Nitrones **2.7** without β substituents were readily prepared, this approach contains limitations in part due to the use of Grignard reagents.[23] A fairly robust, general approach was needed to synthesize this virtually unused class of α,β-unsaturated nitrones.[30]

A number of nitrone preparations exist,[31] but the most convenient and commonly used consists of condensing *N*-monosubstituted hydroxylamines and carbonyl compounds or oxidation of the corresponding hydroxylamine, imine, or amine.[32] The reaction of *N*-substituted hydroxylamines and aldehydes typically proceeds to give aldonitrones in high yield. Excluding intramolecular variations, the condensation of *N*-substituted hydroxylamines and ketones typically requires harsh conditions and is of limited scope. Though a few efforts of condensing *N*-alkyl hydroxylamines and α,β-



Scheme 2.6 Modular approach to α,β-unsaturated nitrones

unsaturated ketones have been reported,[33] our efforts to condense *N*-aryl hydroxylamines and α,β-unsaturated ketones have been unsuccessful. Thus subsequent efforts focused on developing an approach based on oxidation of *N*-allyl anilines that could be formed by condensation of anilines with α,β-unsaturated aldehydes to form *N*-allylideneanilines that could further be alkylated utilizing organometallic reagents (Scheme 2.6).

The condensation of anilines and α,β-unsaturated aldehydes was carried out at room temperature in ether with $MgSO_4$ as a dehydrating agent.[34] Although all the anilines tested condensed with one equivalent of cinnamaldehyde efficiently, a slight excess of cinnamaldehyde (1.2 equiv.) produced optimal yields and purity. Due to the instability of the *N*-allylideneanilines, only filtration and concentration of the reaction *in vacuo* were performed prior to subsequent reactions. Relatively high yields were obtained for alkylation of these non-enolizable imines with alkyl and phenyl lithium reagents to give *N*-allyl anilines **2.19** that were relatively pure based on crude ^{1}H NMR spectra (Table 2.3).[35] Oxidation with Oxone® under conditions adapted by Busqué and

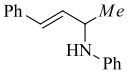
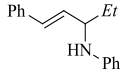
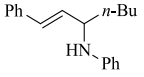
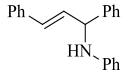
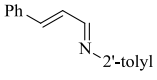
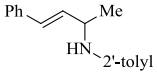
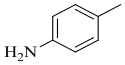
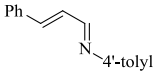
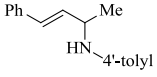
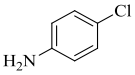
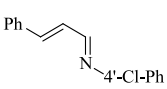
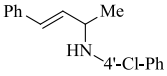
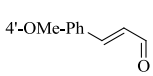
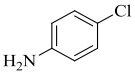
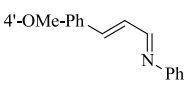
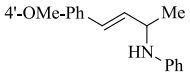
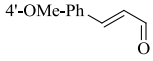
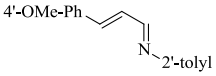
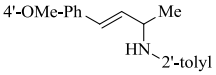
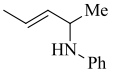
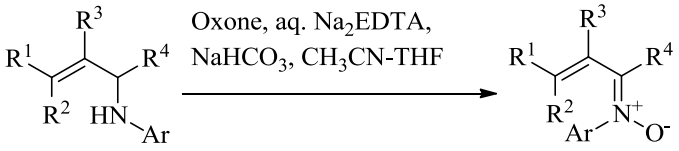
Entry	Aldehyde	Aniline Derivative	Imine	Alkylating Agent	*N*-Allylideneaniline	yield
1				MeLi		**2.19a** (79%)
2				EtLi		**2.19b** (78%)
3				BuLi		**2.19c** (71%)
4				PhLi		**2.19d** (88%)
5				MeLi		**2.19e** (91%)
6				MeLi		**2.19f** (44%)
7				MeLi		**2.19g** (64%)
8				MeLi		**2.19h** (74%)
9				MeLi		**2.19i** (73%)
10				MeLi		**2.19j** (83%)
11				MeLi		**2.19k** (89%)
12				MeLi		**2.19l** (75%)

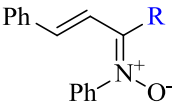
Table 2.3 Results for imine formation and following alkylation

Figueredo formed the α,β-unsaturated nitrones **2.20**.[36] This modular approach allowed synthesis of α,β-unsaturated *N*-aryl ketonitrones with diverse substitution patterns (Scheme 2.7).

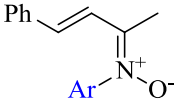
This modular approach allowed for preparations of the ketonitrone substituted by more than just a methyl (**2.20a**) at R^4, but ethyl (**2.20b**), butyl (**2.20c**), and phenyl



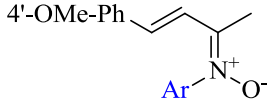
2.19 **2.20**



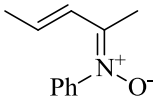
2.20a (R = Me, 80%, 3.6:1)
2.20b (R = Et, 22%, 3.3:1)
2.20c (R = *n*-Bu, 82%, 2:1)
2.20d (R = Ph, 52%, <1:5)



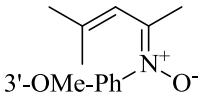
2.20e (Ar = 2'-tolyl, 67%, 2.7:1)
2.20f (Ar = 4'-tolyl, 62%, 3.7:1)
2.20g (Ar = 4'-Cl-Ph, 34%, 2:1)



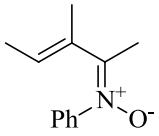
2.20h (Ar = Ph, 74%, 4:1)
2.20i (Ar = 2'-tolyl, 49%, 2:1)



2.20j (70%, 2:1)[a]



2.20k (70%, >10:1)[a]



2.20l (20%, 3:1)

Yields of isolated product and ratios given as E:Z. [a] Yields and ratios estimated from crude ^{1}H NMR spectra.

Scheme 2.7 Oxidation of **2.19** to form **2.20**

(**2.20d**) were all easily installed. The *N*-aryl group was also easily modified with such substituents as 2'-methyl (**2.20e**), 4'-methyl (**2.20f**), 4'-chloro (**2.20g**). The α- and β-positions of the α,β- unsaturated *N*-aryl ketonitrones accepted substitution as well (**2.20j**, **2.20k**, and **2.20l**). The ketonitrones formed demonstrated a degree of stability. Most could be purified by column chromatography with minimal decomposition over silica gel. However, ketonitrones **2.20j**, **2.20k**, and **2.20l** showed extensive decomposition over silica gel.

While the C=C double bonds of **2.20** appeared to be generated in the *E*- geometry when relevant, the C=N double bonds formed as *E*,*Z*- mixtures in a range of ratios.

Determination of the C=N double bond geometry was straightforward when the α'-substituent was a methyl since Bartoli had established that the geometry is correlated with the ^{1}H NMR chemical shift of the methyl group.[23] A chemical shift of 2.25-2.31 ppm associates with a C=N double bond in the *E*- configuration while a chemical shift of 1.76-1.91 ppm associates with the *Z*- double bond geometry. This also allowed the geometries of ketonitrones with α'-ethyl- and butyl-groups to be similarly assigned. Ketonitrone **2.20d** with a phenyl group at the α'-position formed mainly one diastereomer. When R^4 = alkyl, the two vinyl protons of the α,β-unsaturation showed a large chemical difference in the *Z*-isomer ($\Delta\delta$ = 1.0-1.5 ppm) while a smaller chemical shift difference ($\Delta\delta$ < 0.5 ppm) was observed for the *E*-isomer. A chemical shift difference of $\Delta\delta$ = 1.5 ppm was observed for **2.20d** and thus tentatively assigned as the *Z*-isomer.

CHAPTER III

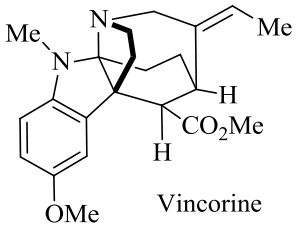
EFFORTS TOWARD HIGHER ORDER INDOLE CONTAINING POLYCYCLES

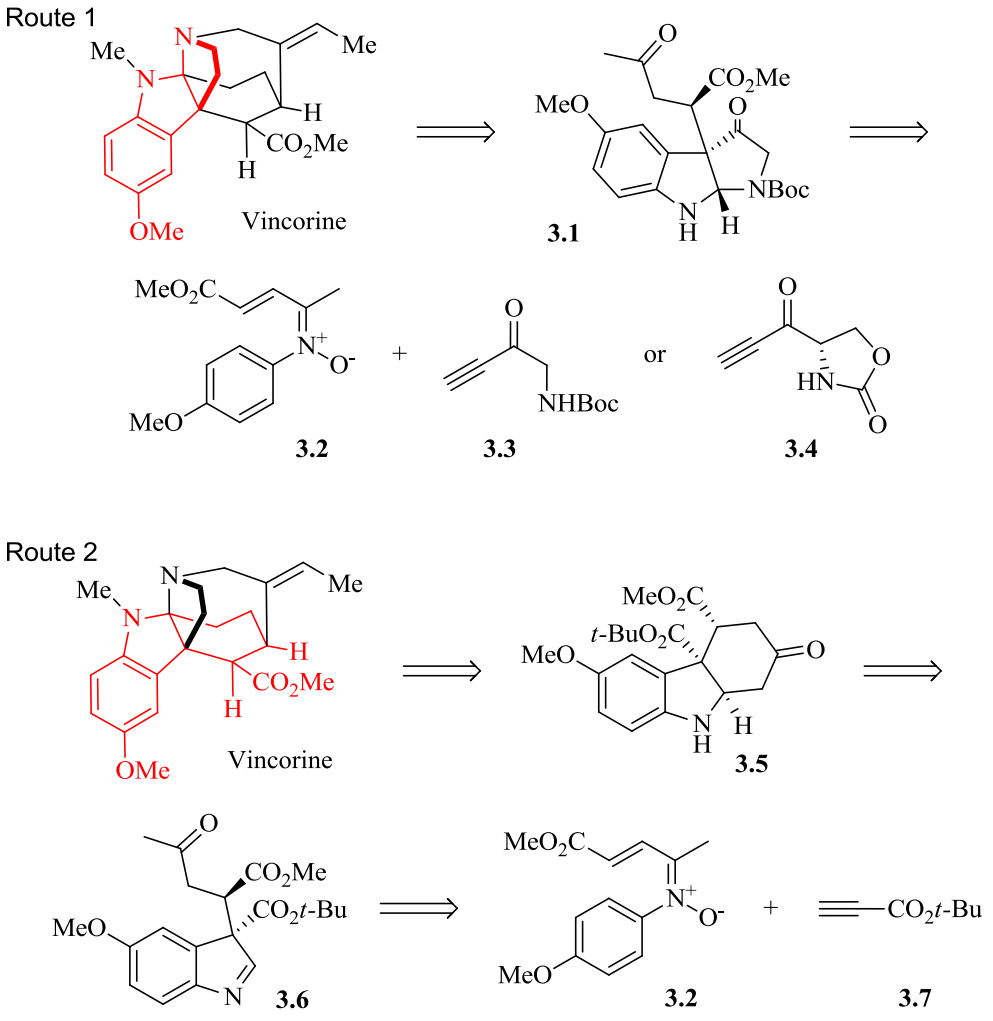
3.1 Introduction

Many natural products contain the indole core within larger polycyclic structures. Significant challenges exist in the generation of these natural products. Due to the high number of bioactive compounds that contain the indole core, the desire to perform bioassays and test for bioactivity of indole natural products exists. However, when new natural products are discovered the minute quantities obtained typically prevent much of the desired testing.

Pyrroloindolines and hydrocarbazoles are a few of the typical polycycles observed. Efforts to expand upon the former indolenine synthesis to generate these polycycles were investigated by either modifying the starting alkyne or utilizing the formed indolenine. As is often the case with methodology, structure is the basis for innovation, and vincorine was targeted. By slight variations in the synthetic route, vincorine could possibly be formed through either the initial formation of the pyrroloindoline or the hydrocarbazole (Scheme 3.1).

Vincorine is the parent compound of an akuammiline alkaloid subclass. This subclass is characterized by a synthetically challenging cage-like system. Related alkaloids showed anti-cancer activity in preliminary assays and has spurred efforts to





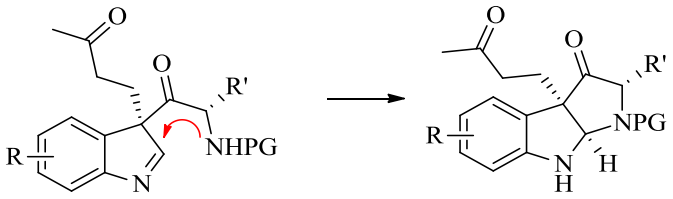
Scheme 3.1 Possible routes to vincorine from either the pyrroloindoline or hydrocarbazole

synthesize this subclass. Qin group synthesized racemic vincorine in 35 steps.[37] Ma group improved upon the synthesis with an 18 step synthesis in 64% ee.[38] As we set out on this investigation, only Qin and Ma had completed total syntheses. Recently, MacMillan has completed a highly enantioselective total synthesis in 9 steps.[39]

We envisioned that either route (Scheme 3.1) could be used to enantioselectively synthesize vincorine in approximately 9-11 steps. In route 1, the chirality would be imparted by the use of the amino acid derived acetylenes. In route 2, we sought to develop an enantioselective indolenine formation and a general cyclization procedure.

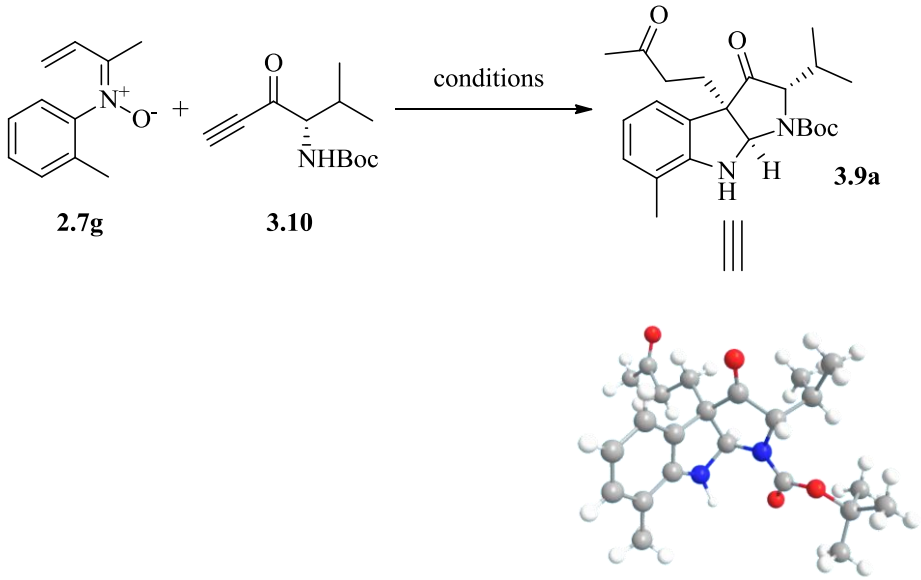
3.2 Pyrroloindolines

In an effort to form the pyrroloindoline, the indolenine synthesis was performed with an alkyne of greater complexity. We envisioned that an appending nitrogen atom would attack the indolenine intramolecularly at the imine moiety (Scheme 3.2). Efforts to utilize a keto activated alkyne had been shown to be successful (**2.8p**) and effort began based on the conditions used to obtain **2.8** with amino acid derived alkynes. These alkynes **3.3**, **3.4**, and similar alkynes are known compounds and easily



3.8 **3.9**

Scheme 3.2 Rationale for pyrroloindoline formation



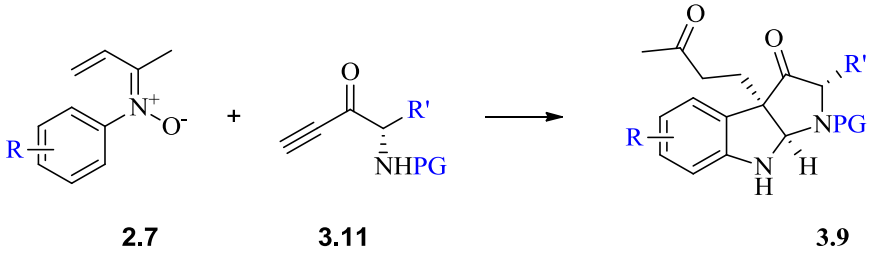
Scheme 3.3 Reaction used for optimization and crystal structure of **3.9a**

synthesized from amino acids.[40]

Notable differences from the indolenine synthesis of chapter II exist. The former synthesis utilized 3 equivalencies of acetylene to 1 equivalent of nitrone. When utilizing propiolates and/or keto activating groups, the former synthesis also provided better results at room temperature. Under these conditions, the pyrroloindoline synthesis produced low quantities of the desired product **3.9a** with nitrone **2.7g** and acetylene **3.10** (11-15%). However, utilizing 1 equivalent of acetylene and 3 equivalencies of nitrone improved the yield and heating to 60 ^{o}C consistently increased the yield to 30 – 35%.

Efforts to further optimize the reaction included screening of solvents such as toluene, dichloromethane, tetrahydrofuran, ether, ethanol, and ethyl acetate. A range of acid and base additives were tested which include acetic acid, pyridinium p-toluenesulfonate, silica gel, triethyl amine, 1,8-diazabicyclo[5.4.0]undec-7-ene, and

cesium carbonate. Other additives included copper (I) iodide and triethyl borane. These additives typically lowered the yield to approximately 20% but rarely completely shut down the reaction. A range of workup conditions was also applied in effort to optimize and increase cyclization to no avail. It has yet to be determined the underlying challenges preventing us from reaching a synthetically useful reaction. See Appendix D for a more complete discussion of the effects of the alkyne on the reaction in this study (Scheme 3.4).

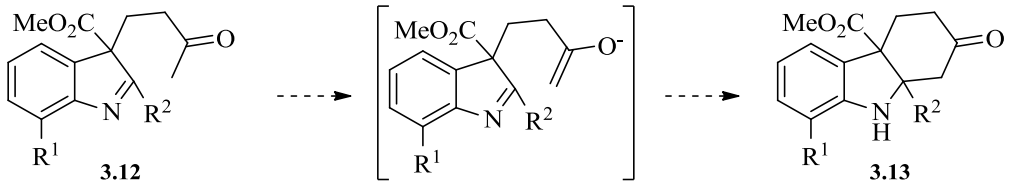


2.7 **3.11** **3.9**

Scheme 3.4 Investigation into pyrroloindoline formation

3.3 Hydrocarbazoles

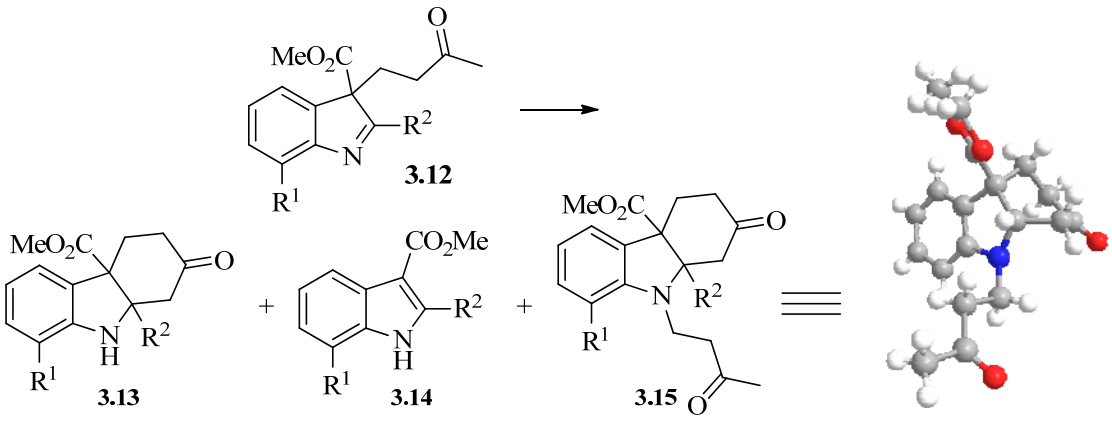
Our group efforts to reach vincorine through Scheme 3.1 route 2 were initiated by focusing on the two parts needed to form the chiral hydrocarbazole, an asymmetric indolenine synthesis and a protocol for cyclization. The group investigated an asymmetric indolenine synthesis through the use of chiral auxiliaries and asymmetric catalysis utilizing iminium and H-bond catalysis (not shown); their efforts failed to produce any enantioenriched indolenine product. However, initial efforts in reaching a cyclization protocol were achieved.



Scheme 3.5 Efforts toward the hydrocarbazole

Initial efforts focused on forming the enolate or the silyl enol ether of **3.12** from the appended 2-butanone fragment (Scheme 3.5); however intramolecular cyclization to C2 failed to occur. Efforts then switched to organocatalysts. Our previous studies showed that pyrrolidine would initiate the retro-Michael reaction and eliminate the 2-butanone fragment to form the 1H-indole (Scheme 2.4). This prompted investigation into a buffered solution of pyrrolidine and acetic acid in an effort to prevent this side reaction pathway from occurring (Table 3.1) resulting in a mixture of the desired hydrocarbazole (**3.13**), the 1H-indole (**3.14**), and the hydrocarbazole with the aza-Michael reaction (**3.15**). Excess pyrrolidine was necessary to prevent the aza-Michael reaction from occurring on the synthesized hydrocarbazole with the retro-Michael fragment forming **3.15**. Cyclization was also possible when R^2 was not H (Table 3.1, entry 2). Reducing the temperature to 0 ^oC lowered the ratio of **3.14**; however, further reduction in temperature caused the ratio to start to increase (Table 3.1, entries 4-7).

Proline was also tested in the organocatalyzed cyclization reaction by screening solvents (Table 3.2). All of the reactions resulted in high conversion with approximately 5% of unreacted recoverable starting material. The optimized pyrrolidine catalyzed cyclization (Table 3.1, entry 5) and the initial screening of solvents with proline (Table



Entry	AcOH	Pyrrolidine	T (^{o}C)	**3.13** : **3.14** : **3.15**
1	2 equiv[a]	0.2 equiv	RT	0 : 1 : 1.1
2	2 equiv[b]	0.2 equiv	RT	1 : 12.3 : 0
3	0.4 equiv	0.2 equiv	RT	**3.13** << **3.14** >> **3.15**
4	8 equiv	4 equiv	RT	1 : 3.2 : 0
5	8 equiv	4 equiv	0	1 : 1.6 : 0
6	8 equiv	4 equiv	-20	1 : 1.7 : 0
7	8 equiv	4 equiv	-75	1: 1.9 : 0

R^1 = Me and R^2 = H unless noted. [a] R^1 = H. [b] R^1 = H and R^2 = CO_2Me.

Table 3.1 Efforts towards the hydrocarbazole core and crystal structure of **3.15**

3.2, entry 1) were comparable in yield and selectivity. With several chiral proline derived organocatalysts available, these results suggest that the enantioenriched hydrocarbazole may be obtained by resolution of the racemic indolenine. However, this line of research was not explored further due to the relatively low overall efficiency of the process.

Entry	Solvent	AcOH	Proline	T (^{o}C)	**3.14** : **3.15** : **3.15**
1	MeOH	-	1 equiv	RT	1 : 1.6 : 0
2	DCM	1 equiv	1 equiv	RT	1 : 2.0 : 0.6
3	Tolune	1 equiv	1 equiv	RT	1 : 2.7 : 1.1

Table 3.2 Proline as an organocatalyst for hydrocarbazole formation

CHAPTER IV

EFFORTS TOWARD 3-SUBSTITUTED INDOLE MICHAEL REACTIONS

4.1 Background

Conjugate additions of indole to Michael acceptors are relatively well studied under various reaction conditions.[41] These transformations typically lead to C3-alkylations to generate C3-mono-alkylated indoles. Enantioselective variants exist when a chiral center is generated in these reactions. Challenges remain for the alkylation of C3-substituted indoles to form the 3,3-disubstituted indoline or indolenine. Part of the challenge is the reversibility of the reaction. Efforts to perform this transformation usually include the trapping of the initially formed indolenine. This may be done by formation of the pyrroloindoline or the furoindoline by an appending *N*- or *O*-nucleophilic group. A few groups, including those of MacMillan, You, and Reisman, have demonstrated some success.

MacMillan utilized organocatalysis to enantioselectively add α,β-unsaturated aldehydes to tryptamine or tryptophol derivatives (Figure 4.1, a).[42] You activated 3-acryloyloxazolidin-2-one with the Lewis acid scandium triflate (Figure 4.1, b)[43] or used a chiral primary amine to catalyze the enantioselective reaction with methyl vinyl ketone (MVK) (Figure 4.1, c).[44] Reisman utilized a Lewis acid catalyzed reaction with amidoacrylates to form pyrroloindolines (Figure 4.1, d).[45] Interestingly, only You (Figure 4.1, c) attempted to perform the reaction without an *N*-alkyl group attached. In his efforts, he was unable to prevent the aza-Michael reaction with MVK.

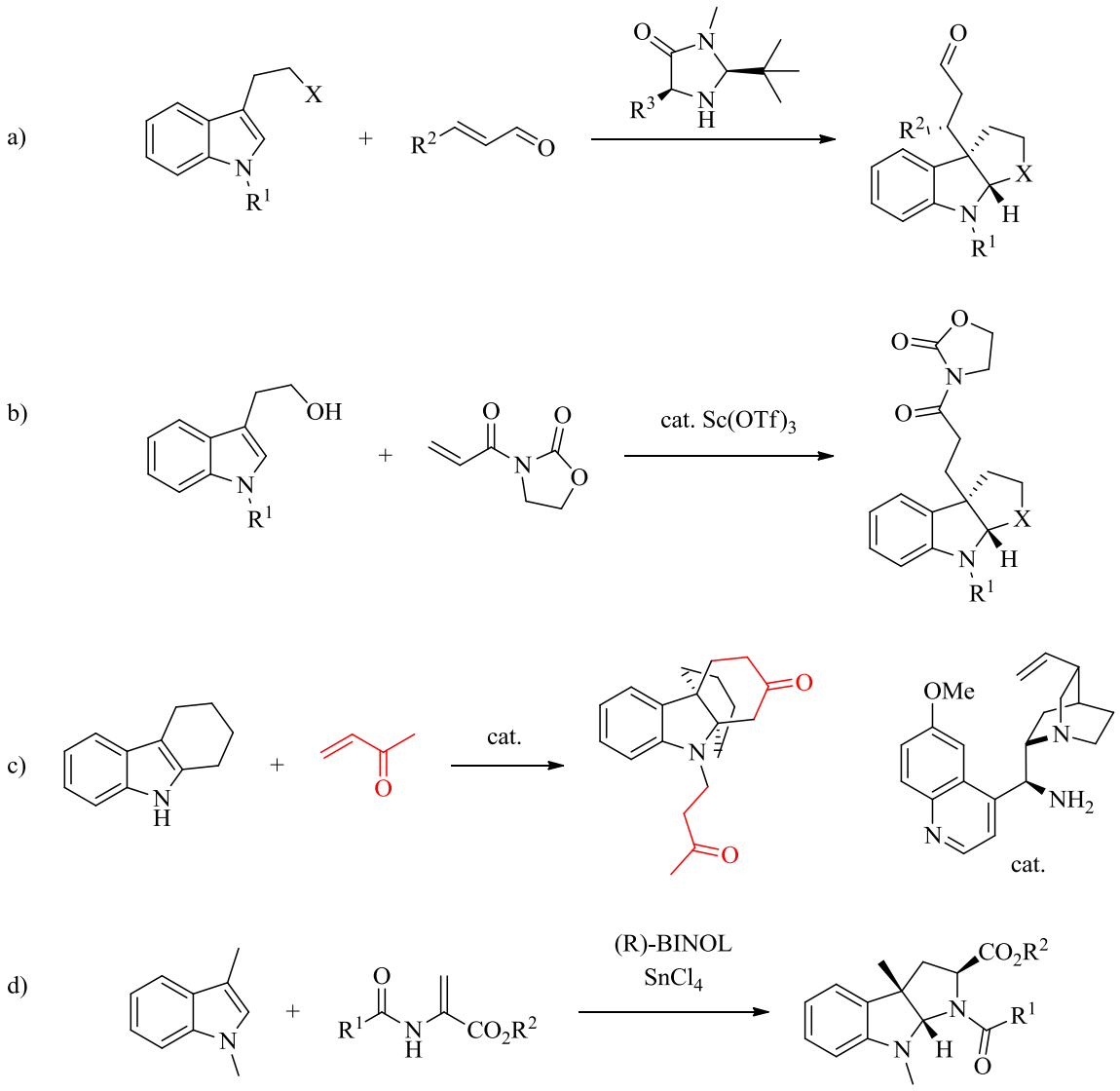
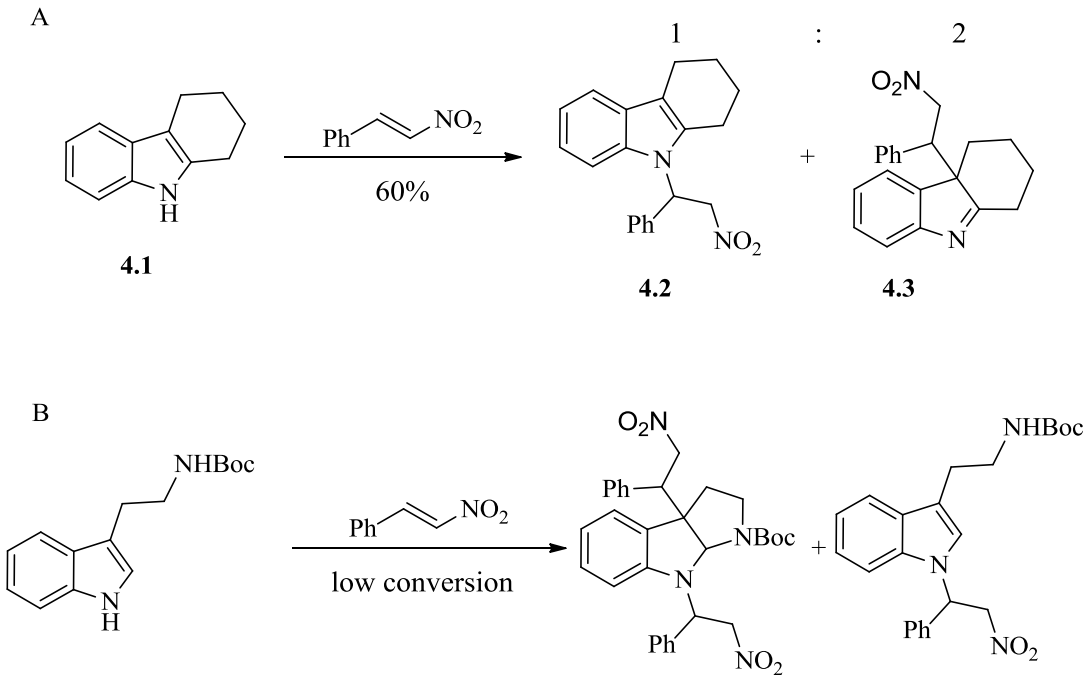


Figure 4.1 Reported Michael reactions with 3-substituted indoles

Interestingly, early efforts to alkylate non-C3 substituted indoles with Michael acceptors started by using N1 alkylated indoles similar to the examples in Figure 4.2. Efforts in this research sought to initially perform the Michael reaction without cyclizing to the pyrroloindoline and without alkylated N1, but the need to cyclize to affect the reaction did prove necessary.

4.2 3-Substituted indole Michael reaction

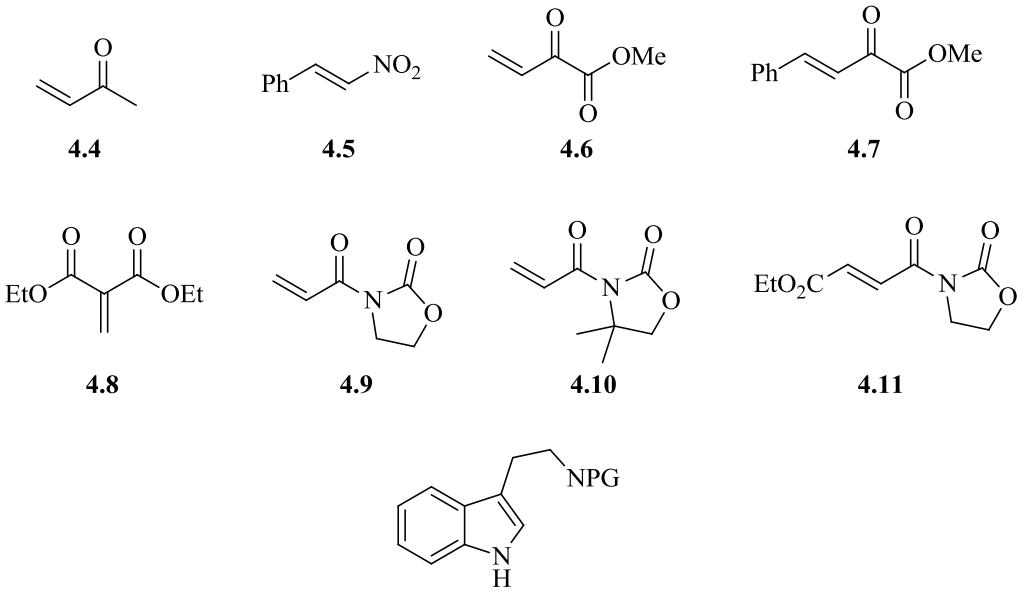
Building upon our group's recent advancement of C3-substituted indole alkylation with alkyl halides using *N*-indolyltriethylborates (Scheme 1.3, A),[13] efforts to alkylate skatole with the Michael acceptor MVK were initiated. Unfortunately, under similar conditions the *N*-indolyltriethylborate and the MVK failed to react. After replacing the Michael acceptor with β-nitrostyrene, the reaction still failed to occur (trace aza-Michael product was observed). This Michael acceptor allowed for activation of the nitro group with copper (II) triflate and a bisoxazoline (BOX) ligand, which led to C2 alkylation in trace quantity with low conversion of the starting indole. In an effort to prevent C2 alkylation, skatole was replaced with 2,3,4,9-tetrahydro-1H-carbazole **4.1**,



Scheme 4.1 Initial efforts to form the Michael adduct

and resulted in 60% yield of the desired C3 alkylated product to the aza-Michael product in a 2:1 ratio (Scheme 4.1, A). This result was not reproducible; subsequent reactions typically resulted in trace aza-Michael and recovered **4.1**. This suggested that the product's stability may be an issue. To overcome this challenge, tryptamine was utilized to cyclize the initial indolenine into the pyrroloindoline (Scheme 4.1, B). Again, low conversion resulted.

Efforts to investigate Michael acceptors amenable to Lewis acid activation were further investigated along with different tryptamine derivatives (Figure 4.2). With Michael acceptors **4.4**–**4.8**, the starting tryptamine derivative **4.12** was recovered. Approximately 50% conversion occurred when **4.9**, **4.10**, or **4.11** reacted with the tosyl protected tryptamine derivative **4.12** producing the desired pyrroloindolines in 40-50%

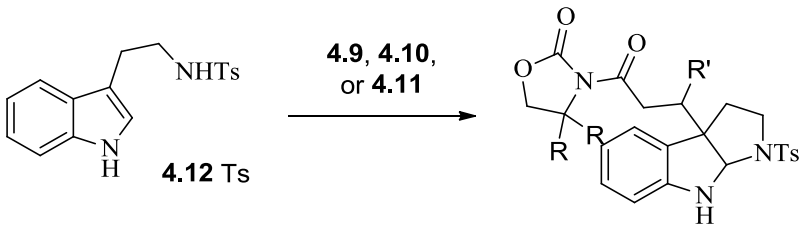


4.4 **4.5** **4.6** **4.7**

4.8 **4.9** **4.10** **4.11**

4.12 PG = Boc, CO_2Me, Ac, Ts

Figure 4.2 Michael acceptors and tryptamine derivatives investigated



Acceptor		Yield
4.9	R = H, R' = H	43%
4.10	R = Me, R' = H	50%
4.11	R = H, R = CO_2Et	50%
		60-70%[a]

Activated with KO*t*-Bu/Et_3B and $Cu(OTf)_2$ unless noted. [a] activated with $SnCl_4$/BINOL

Scheme 4.2 Michael reactions

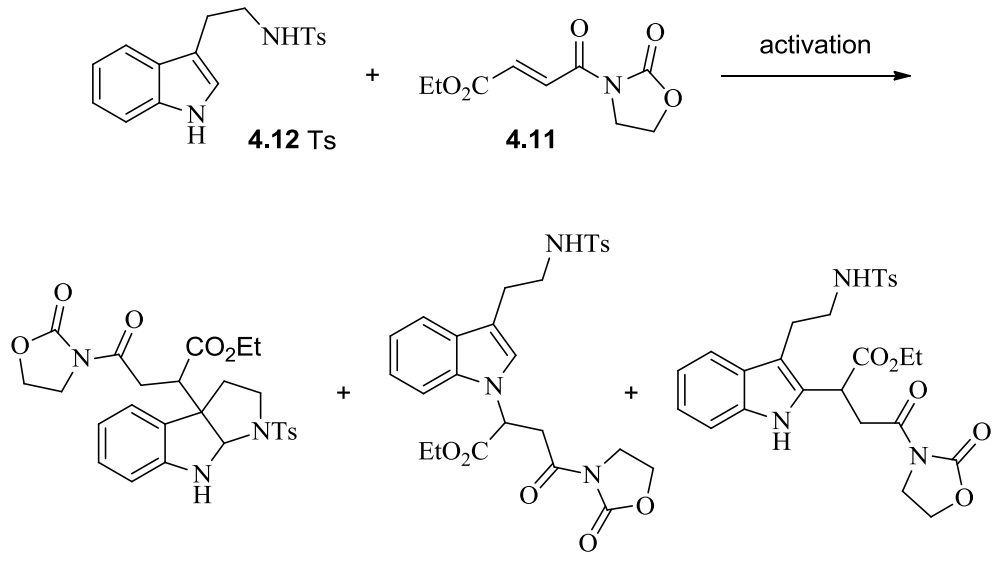
yields (Scheme 4.2). When Boc, CO_2Me, or Ac was utilized as the protecting group, the reaction failed to occur and the starting tryptamine derivative **4.12** was recovered. Unfortunately, no enantiomeric excess (ee) was observed with **4.9**. Michael acceptor **4.10** was then tested to limit the conformations and hopefully induce ee. Again, no ee was observed. In a further effort to induce asymmetry, Michael acceptor **4.11** was utilized. A dr of 2.4:1 was observed without any ee for the pyrrololoindoline.

In an effort to increase the conversion and induce asymmetry, Reisman's conditions (Figure 4.1, d) were adapted for use with tosyl protected tryptamine and **4.11**. Gratifyingly, the reaction proceeded to completion (Scheme 4.2). However, a considerable amount of C2 alkylated product formed that was inseparable from the desired product. Furthermore, on the chiral column of the HPLC, there was overlap with the product. The dr and ee was determined as best as possible for comparison with the

previously described method. For these conditions an approximate dr of 1.9:1 was observed with 76% ee for the more abundant isomer.

4.3 Conclusions

Consistent reproducible results were not obtainable until the Michael donor was switched to the *N*-tosyl tryptamine derivative **4.12**. Furthermore, both methods, [KO*t*-Bu/Et_3B and $Cu(OTf)_2$/BOX] and [$SnCl_4$/BINOL], allowed the reaction to proceed with



KO*t*-Bu/Et_3B and $Cu(OTf)_2$/BOX	$SnCl_4$/BINOL
• Approximately 50% conversion • Trace aza-Michael reaction • Isolatable 40-50% yields • dr = 2.4:1 • No ee	• Complete conversion • No aza-Michael reaction • Inseparable 60-70% product • dr 1.9:1 • One diastereomer 76% ee • Approximately 30% C2-alkylation

Figure 4.3 Side by side comparison of reaction results

varying degrees of success (Figure 4.3). Activation with KO*t*-Bu/Et_3B and $Cu(OTf)_2$/BOX allowed for isolatable product in 40-50% yield to be obtained with a 2.4:1 dr and no ee; approximately 50% conversion occurred with trace aza-Michael alkylation. While complete conversion and no aza-Michael reaction occurred with $SnCl_4$/BINOL, the product was inseparable from the C2 alkylation product. A higher yield of product (60-70%) was obtained with a 1.9:1 dr and 76% ee for the greater isomer.

CHAPTER V

IRON CATALYZED HYDROAMINATION

5.1 Background

Amines constitute an important class of organic compounds because of their ubiquity as bulk chemicals, specialty chemicals, materials, and pharmaceuticals.[46] Most classical approaches to their generation require refined starting material and generate byproducts (Figure 5.1, A). Furthermore, selectivity is an issue (Figure 5.1, B). For

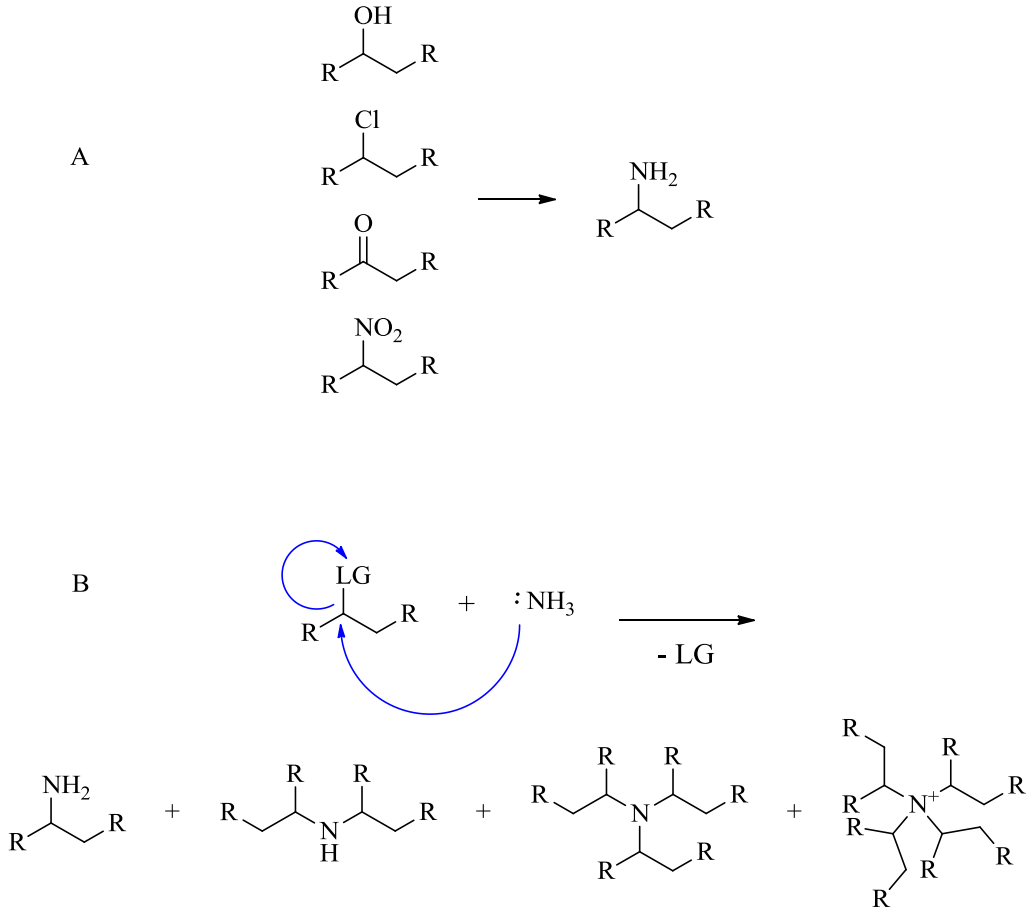
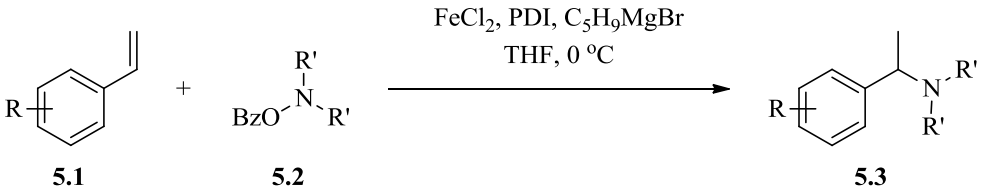


Figure 5.1 Classical approaches to amines

example, substituted amines may be formed by the nucleophilic displacement of alkyl halides with amines. Each newly formed primary, secondary, and tertiary amine is still nucleophilic and may perform the same attack on the starting material giving a mixture of amine products.

Transition metal-catalyzed hydroamination of unactivated alkenes represents an effective approach to amines that allows substituted amines to be prepared from readily available alkenes.[47] Eliminating the need to functionalize the alkene prior to the amine formation saves time, material, and money all while reducing the generated waste. Typical transition metal-catalyzed hydroamination involves the addition of H-NR_2 across the double bond. Development of alternative routes to aminate alkenes is desirable due to the potential of complementary reactivities, selectivities, and efficiencies of these new methods.

In the past few years, electrophilic amination reagents such as *N*-chloroamines and hydroxylamine-*O*-esters have emerged as versatile tools for synthesis of substituted amines.[48] In connection with our group's interests in low-valent iron-catalyzed functionalization of unactivated alkenes,[49] the umpolung reactivity of electrophilic



5.1 **5.2** **5.3**

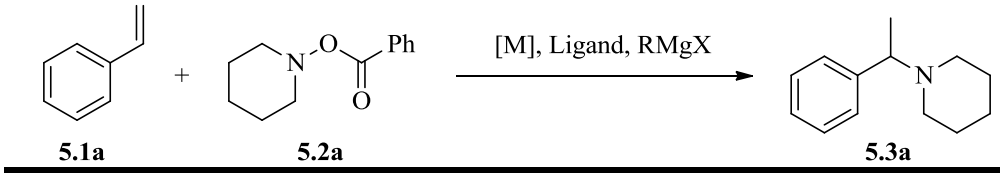
Scheme 5.1 Generalized amination to form **5.3**

nitrogen reagents was investigated in this iron-catalyzed formal electrophilic amination of alkenes (Scheme 5.1).

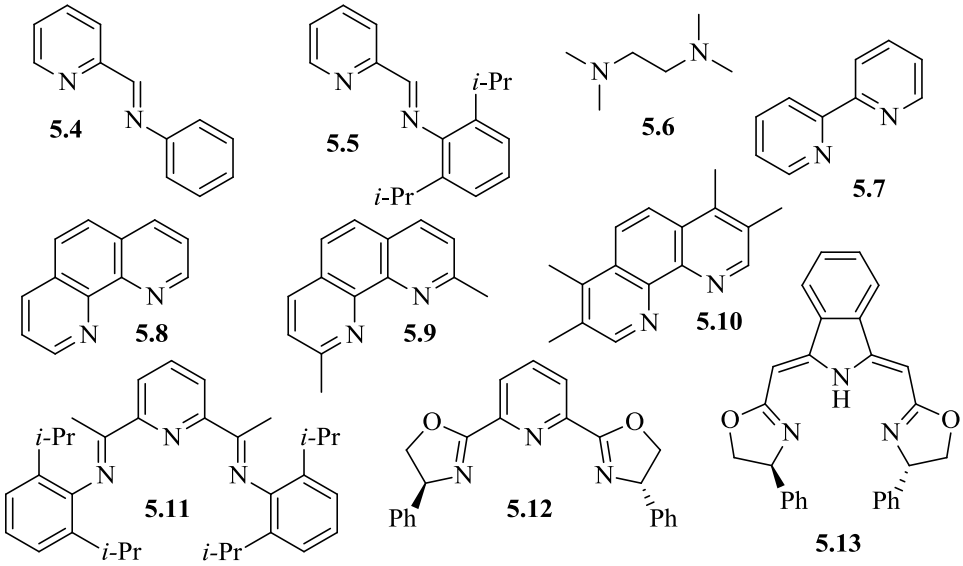
5.2 Reaction development

Investigation commenced with the screening of iron-ligand systems for electrophilic hydroamination of styrene **5.1a** with *O*-benzoyl-*N*-hydroxypiperidine **5.2a** to form **5.3a**. Initial results were disappointing as only a small amount of product **5.3a** formed when a solution of **5.1a** and **5.2a** in THF was treated with $FeCl_2$, iminopyridine ligands **5.4** or **5.5**, and cyclopentylmagnesium bromide. Speculating that the reducing conditions of the reaction could be detrimental to **5.2a**, efforts to increase the yield included slow addition of **5.2a**. Gratifyingly, the desired product was obtained in 34% and 55% yields with iminopyridine ligands **5.4** and **5.5**, respectively, when **5.2a** was added slowly via a syringe pump (Table 5.1, entries 1 and 2). The regioselectivity of the reaction was excellent as none of the isomeric anti-Markovnikov hydroamination product was observed.

A number of common bidentate and tridentate ligands were screened under similar conditions (Table 5.1, entries 3-10) and bis(imino)pyridine (PDI) **5.11** was found to be superior giving amine **5.3a** in 71% yield. The desired amine **5.3a** was also formed when chiral tridentate **5.12** and **5.13** were employed, however with minimal enantiomeric excess (Table 5.1, entries 9 and 10). Testing of different Grignard reagents each gave **5.3a** but with different efficiencies. The lowest yield of 11% (Table 5.1, entry 13) was observed with *tert*-butylmagnesium chloride. It was followed by



5.1a **5.2a** **5.3a**



5.4 **5.5** **5.6** **5.7** **5.8** **5.9** **5.10** **5.11** **5.12** **5.13**

Entry	[M]	Ligand	RMgX	Yield **5.3a** (%)
1	$FeCl_2$	**5.4**	C_5H_9MgBr	34
2	$FeCl_2$	**5.5**	C_5H_9MgBr	55
3	$FeCl_2$	**5.6**	C_5H_9MgBr	60
4	$FeCl_2$	**5.7**	C_5H_9MgBr	49
5	$FeCl_2$	**5.8**	C_5H_9MgBr	48
6	$FeCl_2$	**5.9**	C_5H_9MgBr	55
7	$FeCl_2$	**5.10**	C_5H_9MgBr	<55
8	$FeCl_2$	**5.11**	C_5H_9MgBr	71
9	$FeCl_2$	**5.12**	C_5H_9MgBr	27
10	$FeCl_2$	**5.13**	C_5H_9MgBr	47
11	$FeCl_2$	**5.11**	EtMgBr	51
12	$FeCl_2$	**5.11**	i-PrMgBr	64
13	$FeCl_2$	**5.11**	*t*-BuMgCl	11
14	$FeCl_3$	**5.11**	C_5H_9MgBr	40
15	$Fe(OAc)_2$	**5.11**	C_5H_9MgBr	26
16	$Fe(acac)_3$	**5.11**	C_5H_9MgBr	42
17	$CoCl_2$	**5.8**	C_5H_9MgBr	25
18	$NiCl_2$	**5.8**	C_5H_9MgBr	53

[a] Reactions were carried out with 10 mol % of [M], 10 mol % of ligand, 2.0 equiv. of styrene, 4 equiv. of RMgX, and 1.0 equiv. of *O*-benzoyl-*N*-hydroxypiperidine.

Table 5.1 Screening of reaction conditions[a]

ethylmagnesium bromide (Table 5.1, entry 11) and isopropylmagnesium bromide (Table 5.1, entry 12), in 51% and 64% respectively. Cyclopentylmagnesium bromide remained the reagent of choice.

The desired amine **5.3a** was also formed with the use of other ferrous and ferric salts under the reaction conditions even though they were not as effective (Table 5.1, entries 14-16). The use of $NiCl_2$ was also found to yield amine **5.3a** in comparable yield to that of $FeCl_2$, but $CoCl_2$ was less effective for the reaction (Table 5.1, entries 17 and 18).

5.3 Scope

The scope of the reaction was evaluated using the optimized reaction condition. The reaction appeared to be general for amination with the *N*-benzoyloxy derivative of cyclic secondary amines to give the tertiary amine in good yields with exclusive Markovnikov selectivity. For example, reaction of styrene with *N*-benzoylpyrrolidine gave **5.3b** in 70% yield while the corresponding azepane and morpholine derivatives gave **5.3c** and **5.3d** in 61% and 52% yields, respectively. The reaction was not limited to cyclic amines as **5.3e** was obtained in 80% yield with *N*-benzoyloxydiethylamine. However, when *N*-benzoyloxydibenzylamine was used, efforts to isolate **5.3f** failed, possibly due to decomposition of the substrate under the reducing reaction conditions.

The reaction was also found to be compatible with styrene derivatives substituted with electron-neutral or electron-donating groups. For example, *ortho*-, *meta*-, and *para*-methyl styrene all gave the expected hydroamination product (**5.3g-i**). Though the yield

for the *ortho*- substituted substrate **5.3i** (49%) was lower than the other two isomers **5.3g** (66%) and **5.3h** (62%) possibly due to steric reasons. A similar trend was observed with methoxy-substituted styrene derivatives. Good yields were observed for the

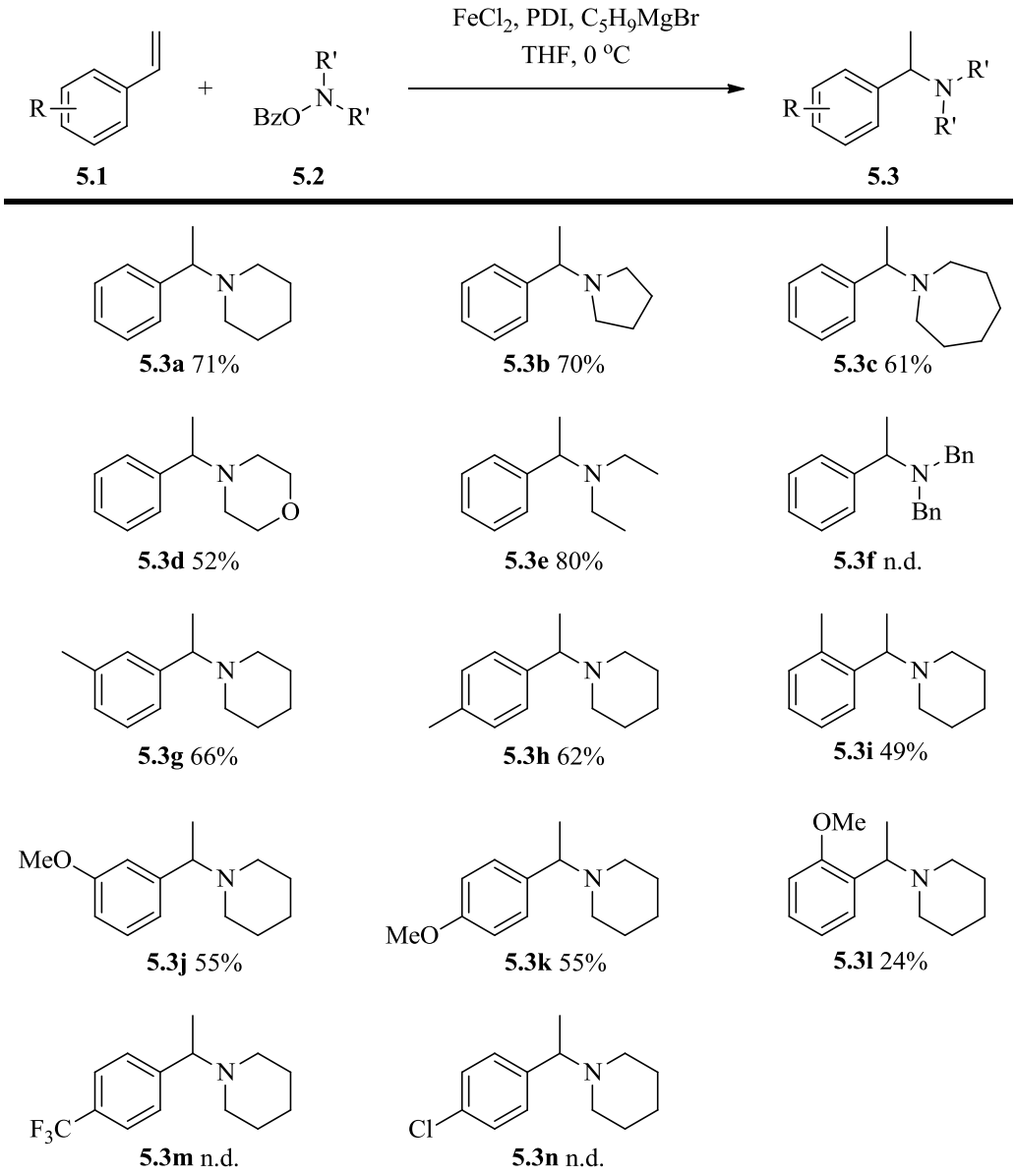
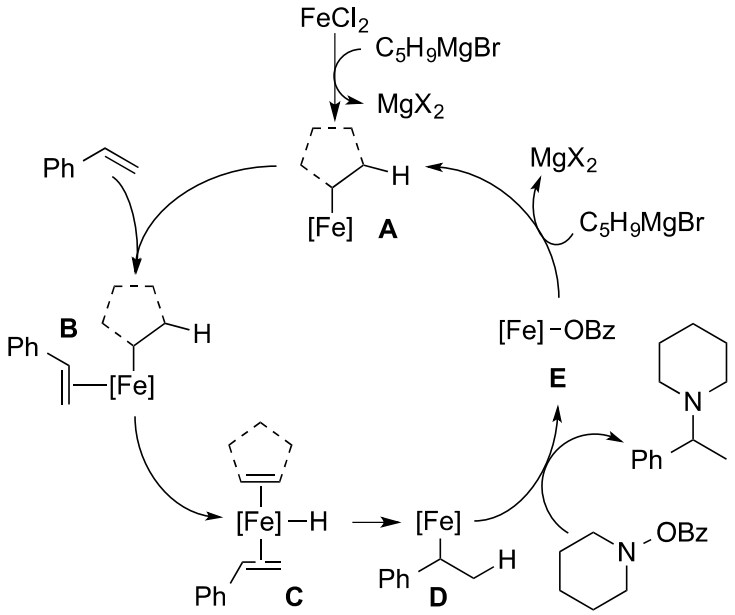


Figure 5.2 Substrate scope of hydroamination

electrophilic hydroamination of *meta*- and *para*-methoxy substituted styrene derivatives **5.3j** (55%) and **5.3k** (55%); again, a significantly reduced yield (24%) was observed when the methoxy group was at the *ortho*- position, possibly due to the ability of the methoxy group to also interfere with the reaction through coordination to the metal center of the reaction intermediates. Halogen substituents appear to be incompatible with the reaction. When 4-chlorostyrene was treated under the reaction conditions, not only was the hydroamination observed, but dehalogenation also occurred resulting in **5.3a** instead of **5.3n**. The reaction with aliphatic terminal alkenes was also unsuccessful with no observable desired product detected (not shown).

5.4 Proposed mechanism for hydroamination

The proposed mechanism of the reaction is shown in Scheme 5.2. The reaction may initiate with the alkylation of $FeCl_2$ with the Grignard reagent to form organoferrate **A**. Coordination of this intermediate with styrene followed by β-hydride elimination of the alkyl group would give iron hydride complex **C**. This can then undergo hydrometalation with styrene to form **D**.[50] The tertiary amine product may then be formed by the reaction of **D** with the benzoyloxyamine leaving the iron benzoate intermediate **E**. Reaction of **E** with the Grignard reagent can then regenerate **A** and complete the catalytic cycle.



Scheme 5.2 Proposed reaction mechanism for hydroamination

5.5 Conclusion

In summary, an operationally simple iron-catalyzed formal hydroamination reaction has been developed. The reaction employs electrophilic benzoyloxyamines as the source of nitrogen and cyclopentylmagnesium bromide as the reducing agent. A range of styrene derivatives were employed to give the products with good yields and excellent Markovnikov regioselectivity. To the best of our knowledge, this reaction represents the first example of an iron-catalyzed amination reaction with electrophilic nitrogen sources.

CHAPTER VI

CONCLUSIONS

6.1 Indole core generation

A novel indolenine synthesis was reported from simple starting materials, activated alkynes and α,β-unsaturated *N*-aryl ketonitrones. The reaction was optimized, the scope investigated, and a possible mechanism proposed. The use of these indolenines was then demonstrated by manipulation into other indole cores.

This indolenine synthesis led to a generalized approach to generate α,β-unsaturated *N*-aryl ketonitrones as only a couple of literature examples previously existed to generate such species. α,β-Unsaturated aldehydes were condensed with aniline derivatives in the presence of magnesium sulfate as a drying agent. Without purification, the imine could be alkylated utilizing alkyl lithium reagents to give *N*-allyl anilines. Oxidation of the *N*-allyl anilines provided the desired α,β-unsaturated *N*-aryl ketonitrones.

Further efforts to utilize the novel reaction pathway and simple starting materials of the indolenine synthesis to generate higher order polycycles was investigated, though met with limited success. Pyrroloindolines were synthesized utilizing α,β-unsaturated *N*-aryl ketonitrones and alkynes derived from amino acids with a tethered nucleophilic nitrogen for intramolecular cyclization with the formed indolenine. Approximate yields of 35% were observed for a range of substrates which, considering the complexity and number of steps occurring, was rather gratifying. Efforts to utilize the formed

indolenines and cyclize the appending C3 butanone fragment also met with modest success. Though an asymmetric indolenine synthesis has failed to come to fruition, the general organocatalyzed cyclization with proline suggests that an asymmetric cyclization may be possible.

A modest start to realizing the success of 3-substituted non-*N*-protected indoles as a Michael donor was achieved. Efforts to block C2 alkylation with Et_3B to form the *N*-indolyltriethylborate were successful and up to 50% of the desired product was obtained. However, conversion of the reaction was also relatively low with approximately 50% of the starting indole being recovered. Switching of the catalytic system proved to fully activate the reaction; however, C2 alkylation occurred and was inseparable from the desired product, though the approximate yield of the product was 60-70% and the approximate ee was determined to be 76%.

6.2 Iron catalysis

In efforts to expand upon group efforts into iron-catalyzed chemistry an operationally simple iron-catalyzed formal hydroamination reaction has been developed and described. The reaction employs electrophilic benzoyloxyamines as the source of nitrogen and cyclopentylmagnesium bromide as the reducing agent. A range of styrene derivatives were employed to give the products with good yields and excellent Markovnikov regioselectivity. To the best of our knowledge, this reaction represents the first example of an iron-catalyzed amination reaction with electrophilic nitrogen sources.

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APPENDIX A

Experimental procedures

A.1 General Information

All moisture sensitive reactions were carried out in flame-dried flasks under nitrogen atmosphere. Solvents were purified by passage through an activated alumina based solvent purification system. All commercial reagents were used as received. Reactions, in general, were magnetically stirred and monitored by TLC performed on pre-coated glass-backed TLC plates (Silica Gel 60 F254 250μm thickness). Spots were visualized by UV or by staining with ethanolic phosphomolybdic acid solution. Flash column chromatography was performed using 60 Å Silica Gel (Silicycle, 230-400 mesh) as the stationary phase. ^{1}H NMR chemical shifts are reported as δ values in ppm relative to $CDCl_3$ (7.26), coupling constants (*J*) are reported in Hertz (Hz), and multiplicity follows normal convention. $CDCl_3$ (77.16) served as an internal standard for ^{13}C NMR spectra. Chiral HPLC analyses were performed on a Shimadzu Prominence SiL-20A UFLC using Daicel Chemical Industries CHIRALPAK® columns (IA, IB, IC, and AD) eluting with hexane / *iso*-propanol mixtures as indicated. Mass spectra were obtained at the Center for Chemical Characterization and Analysis (Texas A&M University).

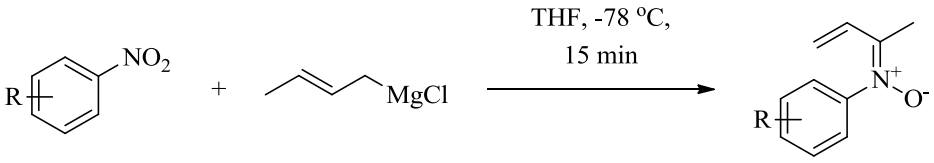
A.2 Experimental procedure for Chapter 2 section 3

A.2.1 Synthesis of α,β-unsaturated N-aryl ketonitrones

A.2.1.1 Synthesis of α,β-unsaturated N-phenyl ketonitrones 2.3

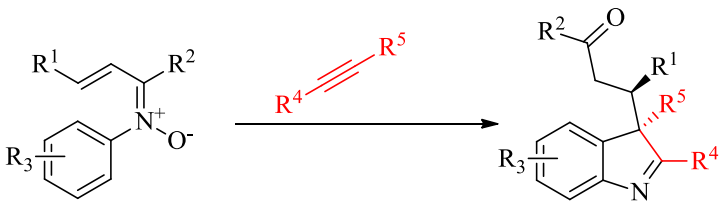
α,β-Unsaturated *N*-phenyl ketonitrones **2.3** were synthesized according to the procedure we previously described.[21]

A.2.1.2 General procedure for synthesis of α,β-unsaturated *N*-aryl ketonitrones **2.7**[23]



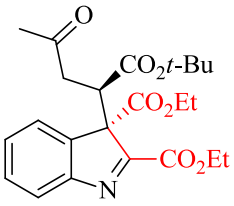
A solution of the nitroarene (0.16 M, 1 equiv.) in anhydrous THF was cooled to -78 °C and treated with a solution of crotylmagnesium chloride (1.6 M in THF, 1.1 equiv.) dropwise. The mixture was stirred at the same temperature for 15 min before the reaction was quenched with aq. NH_4Cl and extracted with diethyl ether (3x). The organic phase was dried over anhydrous $MgSO_4$, filtered, and the solvent was removed under reduced pressure. The crude was purified by silica gel column chromatography (eluted with 100% ethyl acetate or 5% methanol in CH_2Cl_2) to give **2.7**.

A.2.2 Representative procedure for the synthesis of the C3-quaternary indolenines



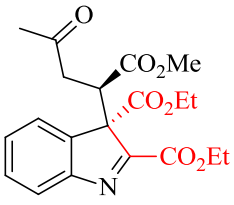
A solution of the α,β-unsaturated *N*-aryl ketonitrone (0.2 M, 1 equiv.) and the activated alkyne (3 equiv.) in toluene was stirred at 80 °C until TLC indicated the reaction was complete. The homogenous solution was concentrated in vacuo and the residue was purified by silica gel column chromatography, eluted with hexanes–ethyl acetate, to give the C3-quaternary indolenines.

A.2.3 Spectra data for compounds



2.6a

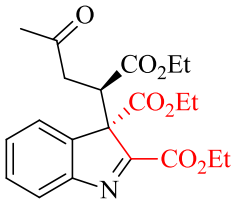
Diethyl 3-(1-(tert-butoxy)-1,4-dioxopentan-2-yl)-*3H*-indole-2,3-dicarboxylate (2.6a). Prepared according to the general procedure in 79% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.7 Hz, 1H), 7.54 – 7.35 (m, 3H), 4.58 – 4.36 (m, 2H), 4.23 (dd, *J* = 11.0, 2.6 Hz, 1H), 4.12 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.95 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.36 (dd, *J* = 17.5, 2.5 Hz, 1H), 3.13 (dd, *J* = 17.5, 11.0 Hz, 1H), 2.18 (s, 3H), 1.45 (t, *J* = 7.1 Hz, 3H), 1.21 (s, 9H), 1.06 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.0, 169.6, 169.5, 167.9, 161.4, 154.5, 137.0, 130.0, 128.7, 123.9, 123.9, 82.3, 66.8, 62.4, 62.2, 44.0, 41.8, 30.1, 27.6, 14.4, 13.9. HRMS (ESI, m/z): $[M]^+$ calc.: 432.1083; found: 432.1090.



2.6b

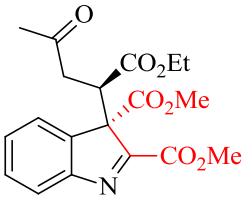
Diethyl 3-(1-methoxy-1,4-dioxopentan-2-yl)-*3H*-indole-2,3-dicarboxylate (2.6b). Prepared according to the general procedure in 58% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.7 Hz, 1H), 7.55 – 7.35 (m, 3H), 4.46 (qd, *J* = 7.1, 1.7 Hz, 2H), 4.32 (dd, *J* = 10.9, 2.5 Hz, 1H), 4.21 – 3.91 (m, 4H), 3.54 (s, 3H), 3.01 (dd, *J* = 17.4, 11.0 Hz,

1H), 2.73 (dd, J = 17.5, 2.5 Hz, 1H), 2.10 (s, 3H), 1.43 (t, J = 7.1 Hz, 3H), 1.10 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.8, 171.1, 169.2, 167.7, 161.6, 153.9, 136.8, 130.2, 129.0, 123.9, 123.8, 67.0, 62.5, 62.4, 52.4, 43.6, 40.8, 30.1, 14.3, 13.8. HRMS (ESI, m/z): $[M]^+$ calc.: 390.1553; found: 390.1562.



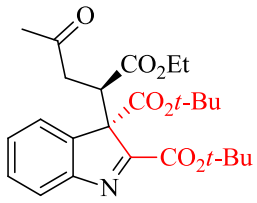
2.6c

Diethyl 3-(1-ethoxy-1,4-dioxopentan-2-yl)-*3H*-indole-2,3-dicarboxylate (2.6c). Prepared according to the general procedure in 61% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, J = 7.6 Hz, 1H), 7.57 – 7.38 (m, 3H), 4.53 – 4.40 (m, 2H), 4.33 (dd, J = 10.8, 2.6 Hz, 1H), 4.23 – 4.07 (m, 2H), 4.07 – 3.89 (m, 2H), 3.05 (dd, J = 17.4, 10.8 Hz, 1H), 2.83 (dd, J = 17.5, 2.6 Hz, 1H), 2.12 (s, 3H), 1.45 (t, J = 7.1 Hz, 3H), 1.12 (dt, J = 8.4, 7.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.9, 170.6, 169.3, 167.8, 161.6, 154.1, 136.9, 130.2, 129.0, 124.0, 123.9, 67.1, 62.5, 62.3, 61.6, 43.64, 40.9, 30.1, 14.4, 13.9. HRMS (ESI, m/z): $[M]^+$ calc.: 404.1709; found: 404.1719.



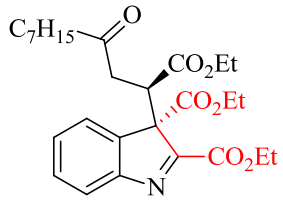
2.6d

Dimethyl 3-(1-ethoxy-1,4-dioxopentan-2-yl)-*3H*-indole-2,3-dicarboxylate (2.6d). Prepared according to the general procedure in 57% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.0 Hz, 1H), 7.56 – 7.37 (m, 3H), 4.32 (dd, *J* = 10.9, 2.6 Hz, 1H), 4.00 (s, 3H), 3.62 (s, 3H), 3.03 (dd, *J* = 17.4, 11.0 Hz, 1H), 2.73 (dd, *J* = 17.4, 2.5 Hz, 1H), 2.12 (s, 3H), 1.14 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.7, 170.5, 168.7, 168.2, 161.9, 153.8, 136.7, 130.3, 129.2, 124.0, 123.9, 67.0, 61.6, 53.2, 53.2, 43.6, 40.6, 30.1, 13.8. HRMS (ESI, m/z): $[M]^+$ calc.: 376.1396; found: 376.1407.



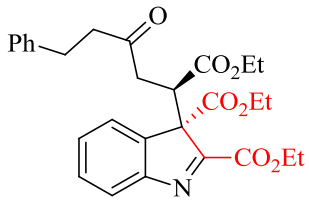
2.6e

Di-tert-butyl 3-(1-ethoxy-1,4-dioxopentan-2-yl)-*3H*-indole-2,3-dicarboxylate (2.6e). Prepared according to the general procedure in 42% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (dd, *J* = 7.2, 1.8 Hz, 1H), 7.47 – 7.31 (m, 3H), 4.27 (dd, *J* = 11.0, 2.5 Hz, 1H), 4.00 – 3.78 (m, 2H), 3.33 (dd, *J* = 17.6, 2.5 Hz, 1H), 3.12 (dd, *J* = 17.6, 11.0 Hz, 1H), 2.15 (s, 3H), 1.63 (s, 9H), 1.23 (s, 9H), 1.09 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.1, 170.9, 170.7, 166.7, 160.1, 154.7, 137.2, 129.7, 128.3, 123.8, 123.4, 83.7, 82.8, 67.3, 61.4, 30.0, 28.1, 27.7, 13.9. HRMS (ESI, m/z): $[M]^+$ calc.: 460.2335; found: 460.2328.



2.6f

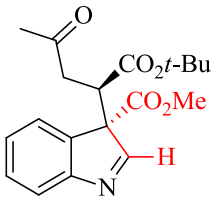
Diethyl 3-(1-ethoxy-1,4-dioxoundecan-2-yl)-3*H*-indole-2,3-dicarboxylate (2.6f). Prepared according to the general procedure in 70% yield. ^{1}H NMR (300MHz, $CDCl_3$) δ 7.77 (m, 1H), 7.55-7.35 (m, 3H), 4.55-3.90 (m, 7H), 3.00 (dd, J = 17.1, 10.5 Hz, 1H), 2.75 (dd, J = 17.4, 2.7 Hz, 1H), 2.35 (m, 2H), 1.44 (t, J = 7.2 Hz, 3H), 1.35-1.17 (m, 10H), 1.13 (t, J = 6.9 Hz, 3H), 1.10 (t, J = 7.2 Hz, 3H), 0.85 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75MHz, $CDCl_3$) δ 208.5, 170.9, 169.6, 168.0, 161.8, 154.2, 137.1, 130.3, 129.2, 124.1, 102.8 67.4, 62.7, 62.5, 61.8, 43.7, 43.1, 40.2, 32.0, 29.4, 29.3, 23.9, 22.9, 14.5, 14.4, 14.3, 14.0. HRMS (ESI, m/z): $[M+H]^+$ calc.: 460.2335; found: 460.2328.



2.6g

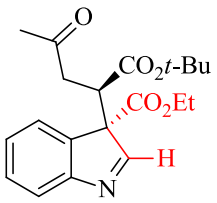
Diethyl 3-(1-ethoxy-1,4-dioxo-6-phenylhexan-2-yl)-*3H*-indole-2,3-dicarboxylate (2.6g). Prepared according to the general procedure in 61% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 – 7.75 (m, 1H), 7.52 – 7.34 (m, 3H), 7.29 – 7.10 (m, 5H), 4.53 – 4.40 (m, 2H), 4.36 (dd, J = 10.8, 2.7 Hz, 1H), 4.19 – 4.06 (m, 2H), 4.06 – 3.90 (m, 2H), 3.02 (dd, J = 17.3, 10.8 Hz, 1H), 2.88 – 2.76 (m, 2H), 2.76 – 2.64 (m, 2H), 1.45 (t, J = 7.1 Hz, 3H), 1.12 (dt, J = 7.7, 7.2 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.1, 170.6, 169.3,

167.7, 161.6, 154.0, 141.0, 136.9, 130.2, 129.0, 128.6, 128.6, 128.4, 126.2, 123.9, 123.9, 67.2, 62.5, 62.3, 61.6, 44.5, 43.6, 40.1, 29.6, 14.4, 13.9. HRMS (ESI, m/z): $[M]^+$ calc.: 494.2179; found: 494.2169.



2.6h

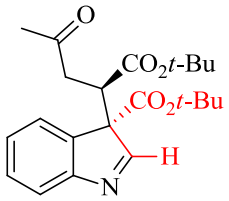
Methyl 3-(1-(tert-butoxy)-1,4-dioxopentan-2-yl)-*3H*-indole-3-carboxylate (2.6h). Prepared according to the general procedure in 61% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.30 (s, 1H), 7.64 (d, *J* = 7.7 Hz, 1H), 7.42 (t, *J* = 7.7 Hz, 2H), 7.28 (t, *J* = 7.5 Hz, 1H), 4.11 (dd, *J* = 8.3, 4.4 Hz, 1H), 3.68 (s, 3H), 2.35 (dd, *J* = 17.6, 8.3 Hz, 1H), 1.83 (s, 3H), 1.67 (dd, *J* = 17.6, 4.4 Hz, 1H), 1.47 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.3, 171.2, 171.1, 169.6, 155.4, 134.5, 129.9, 127.3, 123.7, 121.6, 82.7, 67.9, 53.1, 44.8, 39.5, 30.0, 28.0. HRMS (ESI, m/z): $[M]^+$ calc.: 346.1654; found: 346.1641.



2.6i

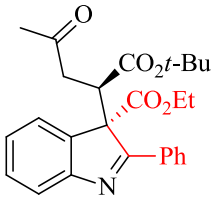
Ethyl 3-(1-(tert-butoxy)-1,4-dioxopentan-2-yl)-*3H*-indole-3-carboxylate (2.6i). Prepared according to the general procedure in 45% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.47 – 7.36 (m, 2H), 7.31 – 7.22 (m, 1H), 4.21 –

4.02 (m, 3H), 2.34 (dd, J = 17.5, 8.4 Hz, 1H), 1.83 (s, 3H), 1.67 (dd, J = 17.6, 4.4 Hz, 1H), 1.46 (s, 9H), 1.18 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.3, 171.4, 171.1, 168.9, 155.4, 134.6, 129.8, 127.2, 123.6, 121.6, 82.6, 68.0, 62.2, 44.7, 39.6, 30.0, 28.0, 14.0. HRMS (ESI, m/z): $[M]^+$ calc.: 360.1811; found: 360.1802.



2.6j

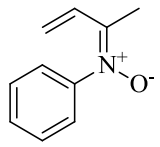
tert-Butyl 3-(1-(tert-butoxy)-1,4-dioxopentan-2-yl)-*3H*-indole-3-carboxylate (2.6j). Prepared according to the general procedure in 32% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.34 (s, 1H), 7.61 (d, J = 7.2 Hz, 1H), 7.44 – 7.35 (m, 2H), 7.30 – 7.21 (m, 1H), 4.02 (dd, J = 8.3, 4.5 Hz, 1H), 2.32 (dd, J = 17.3, 8.3 Hz, 1H), 1.83 (s, 3H), 1.72 (dd, J = 17.4, 4.5 Hz, 1H), 1.45 (s, 9H), 1.35 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.2, 172.0, 171.4, 167.7, 155.6, 135.0, 129.6, 127.0, 123.4, 121.5, 83.1, 82.5, 69.1, 44.8, 40.1, 30.0, 28.1, 27.9. HRMS (ESI, m/z): $[M]^+$ calc.: 388.2124; found: 388.2132.



2.6k

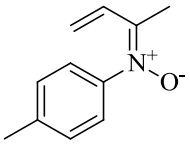
Ethyl 3-(1-(tert-butoxy)-1,4-dioxopentan-2-yl)-2-phenyl-*3H*-indole-3-carboxylate (2.6k). Prepared according to the general procedure in 37% yield. ^{1}H NMR (300 MHz,

$CDCl_3$) δ 8.14 – 8.06 (m, 2H), 7.68 (d, *J* = 7.6 Hz, 1H), 7.51 – 7.40 (m, 5H), 7.31 – 7.23 (m, 1H), 4.17 – 3.89 (m, 3H), 3.34 (dd, *J* = 17.5, 3.1 Hz, 1H), 3.16 (dd, *J* = 17.5, 10.3 Hz, 1H), 2.19 (s, 3H), 1.01 – 0.92 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.3, 170.2, 169.2, 155.9, 137.6, 133.2, 131.0, 130.3, 129.7, 128.7, 128.6, 126.1, 123.3, 121.5, 81.6, 67.1, 62.2, 44.8, 42.3, 30.1, 27.3, 13.8. HRMS (MALDI, m/z): $[M]^+$ calc.: 436.2118; found: 436.2112.



2.7a

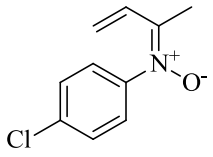
(*E*)-*N*-(But-3-en-2-ylidene)aniline oxide (2.7a). Prepared according to the general procedure in 86% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 – 7.40 (m, 3H), 7.36 – 7.28 (m, 2H), 6.33 (dd, *J* = 17.1, 11.1 Hz, 1H), 5.51 (d, *J* = 17.1 Hz, 1H), 5.23 (d, *J* = 11.1 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 129.9, 129.6, 129.5, 124.4, 123.6, 118.5, 12.8. HRMS (ESI, m/z): $[M]^+$ calc.: 162.0919; found: 162.0914.



2.7b

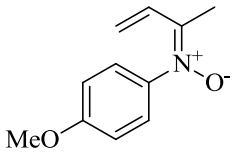
(*E*)-*N*-(But-3-en-2-ylidene)-4-methylaniline oxide (2.7b). Prepared according to the general procedure in 45% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 – 7.17 (m, 4H), 6.36 (dd, *J* = 17.1, 11.1 Hz, 1H), 5.49 (d, *J* = 17.2 Hz, 1H), 5.21 (d, *J* = 11.2 Hz, 1H),

2.39 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.6, 130.0, 130.0, 124.2, 123.4, 118.1, 21.3, 12.8. HRMS (ESI, m/z): $[M]^+$ calc.: 176.1075; found: 176.1071.



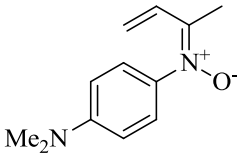
2.7c

(*E*)-*N*-(But-3-en-2-ylidene)-4-chloroaniline oxide (2.7c). Prepared according to the general procedure in 78% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 6.33 (dd, *J* = 17.1, 11.1 Hz, 1H), 5.54 (d, *J* = 17.1 Hz, 1H), 5.27 (d, *J* = 11.1 Hz, 1H), 2.39 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.4, 129.7, 129.5, 125.8, 125.1, 119.1, 12.8. HRMS (ESI, m/z): $[M]^+$ calc.: 196.0529; found: 196.0537.



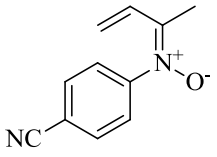
2.7d

(*E*)-*N*-(But-3-en-2-ylidene)-4-methoxyaniline oxide (2.7d). Prepared according to the general procedure in 65% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.9 Hz, 2H), 6.93 (d, *J* = 9.0 Hz, 2H), 6.38 (dd, *J* = 17.2, 11.1 Hz, 1H), 5.49 (d, *J* = 17.1 Hz, 1H), 5.22 (d, *J* = 11.1 Hz, 1H), 3.83 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 130.1, 125.7, 118.1, 114.5, 55.7, 12.9. HRMS (ESI, m/z): $[M]^+$ calc.: 192.1025; found: 192.1028.



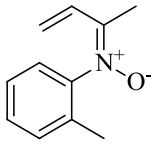
2.7e

(*E*)-*N*-(But-3-en-2-ylidene)-4-(dimethylamino)aniline oxide (2.7e). Prepared according to the general procedure in 56% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (d, *J* = 9.1 Hz, 2H), 6.67 (d, *J* = 9.1 Hz, 2H), 6.46 (dd, *J* = 17.2, 11.1 Hz, 1H), 5.45 (d, *J* = 17.2 Hz, 1H), 5.18 (d, *J* = 11.1 Hz, 1H), 2.99 (s, 6H), 2.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 130.6, 125.3, 117.3, 111.8, 40.6, 13.1. HRMS (ESI, m/z): $[M]^+$ calc.: 205.1341; found: 205.1333.



2.7f

(*E*)-*N*-(But-3-en-2-ylidene)-4-cyanoaniline oxide (2.7f). Prepared according to the general procedure in 20% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.6 Hz, 2H), 7.41 (d, *J* = 8.5 Hz, 2H), 6.20 (dd, *J* = 17.0, 11.1 Hz, 1H), 5.56 (d, *J* = 17.0 Hz, 1H), 5.29 (d, *J* = 11.1 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 133.53, 128.68, 125.36, 120.23, 117.49, 113.46, 12.68. HRMS (ESI, m/z): $[M]^+$ calc.: 187.0871; found: 187.0876.

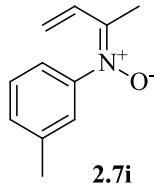


2.7g

(*E*)-*N*-(But-3-en-2-ylidene)-2-methylaniline oxide (2.7g). Prepared according to the general procedure in 70% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 – 7.15 (m, 4H), 6.15 (dd, *J* = 17.1, 11.1 Hz, 1H), 5.52 (d, *J* = 17.1 Hz, 1H), 5.22 (d, *J* = 11.1 Hz, 1H), 2.41 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.9, 131.5, 129.4, 129.2, 127.2, 124.2, 118.8, 16.7, 12.1. HRMS (ESI, m/z): $[M]^+$ calc.: 176.1075; found: 176.1071.

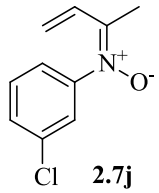
2.7h

(*E*)-2-Bromo-*N*-(but-3-en-2-ylidene)aniline oxide (2.7h). Prepared according to the general procedure in 67% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.46 – 7.27 (m, 3H), 6.11 (dd, *J* = 17.0, 11.1 Hz, 1H), 5.57 (d, *J* = 17.0 Hz, 1H), 5.28 (d, *J* = 11.1 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 133.9, 130.6, 128.9, 128.8, 126.1, 119.6, 117.5, 12.1. HRMS (ESI, m/z): $[M]^+$ calc.: 240.0024; found: 240.0021.



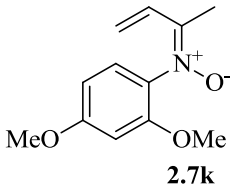
2.7i

(*E*)-*N*-(But-3-en-2-ylidene)-3-methylaniline oxide (2.7i). Prepared according to the general procedure in 70% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 – 7.07 (m, 3H), 6.35 (dd, *J* = 17.0, 11.2 Hz, 1H), 5.50 (d, *J* = 17.1 Hz, 1H), 5.23 (d, *J* = 11.1 Hz, 1H), 2.39 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 130.2, 130.0, 129.3, 124.9, 121.4, 118.3, 21.4, 12.7. HRMS (ESI, m/z): $[M]^+$ calc.: 176.1075; found: 176.1068.



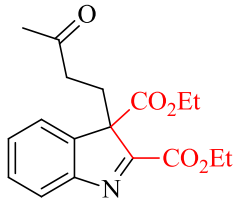
2.7j

(*E*)-*N*-(But-3-en-2-ylidene)-3-chloroaniline oxide (2.7j). Prepared according to the general procedure in 48% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 – 7.34 (m, 3H), 7.24 – 7.19 (m, 1H), 6.31 (dd, *J* = 17.1, 11.1 Hz, 1H), 5.54 (d, *J* = 17.1 Hz, 1H), 5.28 (d, *J* = 11.1 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 130.6, 129.8, 129.4, 124.9, 122.6, 119.3, 12.8. HRMS (ESI, m/z): $[M]^+$ calc.: 196.0529; found: 196.0532.



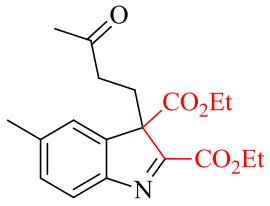
2.7k

(*E*)-*N*-(But-3-en-2-ylidene)-2,4-dimethoxyaniline oxide (2.7k). Prepared according to the general procedure in 71% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.18 (d, *J* = 9.5 Hz, 1H), 6.56 – 6.48 (m, 2H), 6.23 (dd, *J* = 17.2, 11.1 Hz, 1H), 5.48 (d, *J* = 17.1 Hz, 1H), 5.20 (d, *J* = 11.2 Hz, 1H), 3.83 (s, 3H), 3.80 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.4, 153.0, 129.9, 126.4, 118.2, 104.8, 99.7, 56.1, 55.8, 12.4. HRMS (SI, m/z): $[M]^+$ calc.: 222.1130; found: 222.1132.



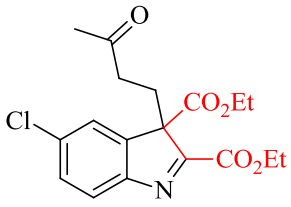
2.8a

Diethyl 3-(3-oxobutyl)-*3H*-indole-2,3-dicarboxylate (2.8a). Prepared according to the general procedure in 70% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.6 Hz, 1H), 7.50 – 7.36 (m, 3H), 4.44 (qd, *J* = 14.2, 7.1, 1.8 Hz, 2H), 4.14 (ddd, *J* = 17.9, 9.0, 5.3 Hz, 1H), 3.95 (dq, *J* = 14.2, 10.8, 7.1 Hz, 1H), 2.90 – 2.67 (m, 2H), 1.86 (s, 3H), 1.97 – 1.64 (m, 2H), 1.42 (t, *J* = 7.1 Hz, 3H), 1.07 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.7, 170.0, 168.7, 161.4, 154.0, 138.5, 129.8, 129.2, 123.7, 122.7, 66.6, 62.4, 62.0, 37.1, 29.9, 27.0, 14.3, 13.9. HRMS (ESI, m/z): $[M]^+$ calc.: 332.1498; found: 332.1504.



2.8b

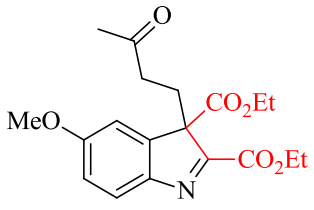
Diethyl 5-methyl-3-(3-oxobutyl)-*3H*-indole-2,3-dicarboxylate (2.8b). Prepared according to the general procedure in 52% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.9 Hz, 1H), 7.30 – 7.16 (m, 2H), 4.44 (qd, *J* = 7.1, 2.2 Hz, 2H), 4.17 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.95 (dq, *J* = 10.7, 7.1 Hz, 1H), 2.90 – 2.65 (m, 2H), 2.42 (s, 3H), 1.97 – 1.83 (m, 1H), 1.89 (s, 3H), 1.78 – 1.67 (m, 1H), 1.42 (t, *J* = 7.1 Hz, 3H), 1.09 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.9, 169.0, 169.0, 161.6, 151.9, 139.9, 138.7, 130.6, 123.4, 123.3, 66.3, 62.3, 62.0, 37.2, 30.0, 27.1, 21.9, 14.4, 14.0. HRMS (ESI, m/z): $[M]^+$ calc.: 346.1655; found: 346.1653.



2.8c

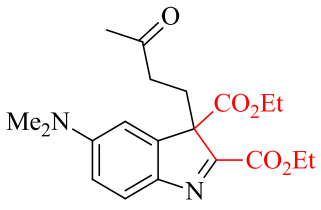
Diethyl 5-chloro-3-(3-oxobutyl)-*3H*-indole-2,3-dicarboxylate (2.8c). Prepared according to the general procedure in 57% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.3 Hz, 1H), 7.49 – 7.37 (m, 2H), 4.45 (dq, *J* = 14.2, 7.1, 1.6 Hz, 2H), 4.18 (dq, *J* = 14.2, 10.8, 7.1 Hz, 1H), 3.98 (dq, *J* = 14.1, 10.6, 7.0 Hz, 1H), 2.92 – 2.63 (m, 2H), 1.92 (s, 3H), 1.98 – 1.77 (m, 2H), 1.42 (t, *J* = 7.1 Hz, 3H), 1.11 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR

(75 MHz, $CDCl_3$) δ 206.4, 168.1, 161.2, 152.5, 140.2, 135.4, 130.2, 124.6, 123.3, 66.9, 62.6, 62.4, 37.1, 29.9, 27.1, 14.3, 13.9. HRMS (ESI, m/z): $[M]^+$ calc.: 366.1108; found: 366.1097.



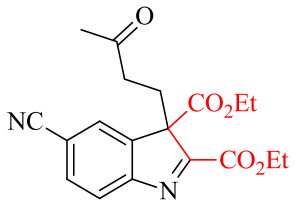
2.8d

Diethyl 5-methoxy-3-(3-oxobutyl)-3H-indole-2,3-dicarboxylate dicarboxylate (2.8d). Prepared according to the general procedure in 52% yield. ^1H NMR (300 MHz, $CDCl_3$) δ 7.72 (d, J = 8.5 Hz, 1H), 7.00 – 6.89 (m, 2H), 4.43 (dq, J = 7.1, 2.3 Hz, 2H), 4.17 (dq, J = 10.8, 7.1 Hz, 1H), 3.96 (dq, J = 10.7, 7.1 Hz, 1H), 3.84 (s, 3H), 2.84 (ddd, J = 14.2, 9.7, 6.1 Hz, 1H), 2.75 – 2.63 (m, 1H), 1.97 – 1.84 (m, 1H), 1.89 (s, 3H), 1.72 (ddd, J = 17.8, 9.7, 5.3 Hz, 1H), 1.42 (t, J = 7.1 Hz, 3H), 1.09 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.8, 168.9, 167.6, 161.5, 161.1, 147.5, 140.6, 124.6, 115.4, 108.3, 66.5, 62.2, 62.1, 56.0, 37.1, 30.0, 27.3, 14.4, 14.0. HRMS (ESI, m/z): $[M]^+$ calc.: 362.1604; found: 362.1607.



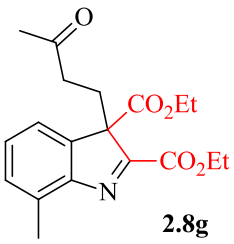
2.8e

Diethyl 5-(dimethylamino)-3-(3-oxobutyl)-*3H*-indole-2,3-dicarboxylate (2.8e). Prepared according to the general procedure in 53% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.7 Hz, 1H), 6.71 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.65 (d, *J* = 2.5 Hz, 1H), 4.42 (qd, *J* = 7.1, 2.7 Hz, 2H), 4.19 (dq, *J* = 14.2, 10.8, 7.1 Hz, 1H), 3.94 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.04 (s, 6H), 2.83 (ddd, *J* = 14.1, 10.3, 5.8 Hz, 1H), 2.75 – 2.61 (m, 1H), 2.02 – 1.85 (m, 1H), 1.90 (s, 3H), 1.77 – 1.62 (m, 1H), 1.41 (t, *J* = 7.1 Hz, 3H), 1.10 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.2, 169.6, 164.0, 161.7, 151.4, 143.8, 141.1, 124.4, 112.4, 105.5, 65.9, 61.8, 61.8, 40.7, 37.1, 30.0, 27.6, 14.4, 14.0. HRMS (ESI, m/z): $[M]^+$ calc.: 375.1920; found: 375.1911.



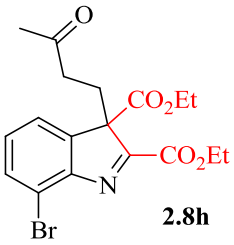
2.8f

Diethyl 5-cyano-3-(3-oxobutyl)-*3H*-indole-2,3-dicarboxylate (2.8f). Prepared according to the general procedure in 22% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.0 Hz, 1H), 7.80 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.71 (d, *J* = 0.9 Hz, 1H), 4.49 (qd, *J* = 7.1, 0.9 Hz, 2H), 4.19 (dq, *J* = 14.2, 10.8, 7.1 Hz, 1H), 4.01 (dq, *J* = 14.2, 10.8, 7.1 Hz, 1H), 2.96 – 2.83 (m, 1H), 2.80 – 2.67 (m, 1H), 1.94 (s, 3H), 1.95 – 1.84 (m, 2H), 1.45 (t, *J* = 7.1 Hz, 3H), 1.12 (t, *J* = 7.1 Hz, 3H); HRMS (ESI, m/z): $[M]^+$ calc.: 357.1450; found: 357.1442.



2.8g

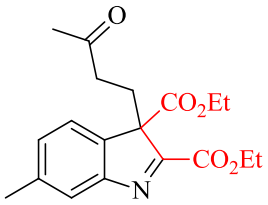
Diethyl 7-methyl-3-(3-oxobutyl)-*3H*-indole-2,3-dicarboxylate (2.8g). Prepared according to the general procedure in 78% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 – 7.17 (m, 3H), 4.46 (qd, *J* = 7.1, 0.9 Hz, 2H), 4.15 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.95 (dq, *J* = 10.8, 7.1 Hz, 1H), 2.89 – 2.68 (m, 2H), 2.67 (s, 1H), 1.89 (s, 1H), 1.96 – 1.82 (m, 1H), 1.79 – 1.65 (m, 1H), 1.43 (t, *J* = 7.1 Hz, 3H), 1.09 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.9, 169.0, 168.8, 161.6, 152.9, 138.5, 134.0, 131.2, 129.2, 120.0, 66.7, 62.4, 62.0, 37.2, 30.0, 27.1, 17.2, 14.3, 14.0. HRMS (ESI, m/z): $[M]^+$ calc.: 346.1655; found: 346.1646.



2.8h

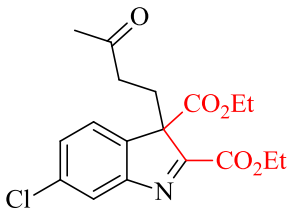
Diethyl 7-bromo-3-(3-oxobutyl)-*3H*-indole-2,3-dicarboxylate (2.8h). Prepared according to the general procedure in 74% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.38 – 7.21 (m, 2H), 4.45 (qd, *J* = 7.1, 1.7 Hz, 2H), 4.15 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.96 (dq, *J* = 10.8, 7.1 Hz, 1H), 2.92 – 2.64 (m, 2H), 2.02 – 1.85 (m, 1H), 1.90 (s, 3H), 1.71 (ddd, *J* = 17.9, 9.7, 5.3 Hz, 1H), 1.42 (t, *J* = 7.1 Hz, 3H), 1.09 (t,

J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.5, 170.9, 168.2, 161.3, 152.6, 140.0, 133.5, 130.4, 121.7, 117.7, 68.3, 62.6, 62.4, 37.0, 30.0, 27.2, 14.3, 13.9. HRMS (ESI, m/z): $[M]^+$ calc.: 410.0603; found: 410.0609.



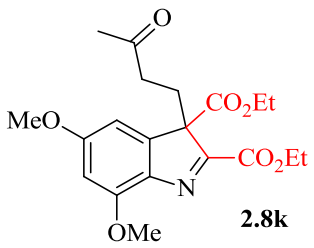
2.8i

Diethyl 6-methyl-3-(3-oxobutyl)-*3H*-indole-2,3-dicarboxylate (2.8i). Prepared according to the general procedure in 61% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62 (s, 1H), 7.32 – 7.17 (m, 2H), 4.46 (dq, J = 7.1, 1.8 Hz, 2H), 4.15 (dq, J = 14.2, 10.8, 7.1 Hz, 1H), 3.95 (dq, 1H), 2.88 – 2.66 (m, 2H), 2.44 (s, 3H), 1.89 (s, 3H), 1.97 – 1.82 (m, 1H), 1.82 – 1.66 (m, 1H), 1.43 (t, J = 7.1 Hz, 3H), 1.09 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.8, 170.1, 168.9, 161.4, 154.3, 140.1, 135.5, 130.0, 124.3, 122.2, 66.2, 62.3, 61.9, 37.11, 29.9, 26.9, 21.7, 14.3, 13.9. HRMS (ESI, m/z): $[M]^+$ calc.: 352.1736; found: 352.1745.



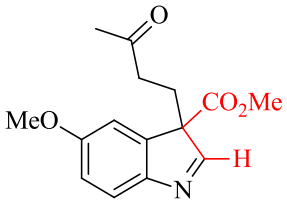
2.8j

Diethyl 6-chloro-3-(3-oxobutyl)-*3H*-indole-2,3-dicarboxylate (2.8j). Prepared according to the general procedure in 33% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 1.8, 0.5 Hz, 1H), 7.42 – 7.31 (m, 2H), 4.47 (qd, 2H), 4.16 (dq, *J* = 14.2, 10.7, 7.1 Hz, 1H), 3.98 (dq, *J* = 10.8, 7.1 Hz, 1H), 2.92 – 2.67 (m, 2H), 1.91 (s, 3H), 1.98 – 1.75 (m, 2H), 1.44 (t, *J* = 7.1, 2.5 Hz, 3H), 1.11 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.31, 168.09, 161.05, 160.31, 154.98, 136.62, 135.45, 129.10, 123.90, 123.38, 66.47, 62.50, 62.18, 36.94, 29.80, 26.73, 14.15, 13.77. HRMS (ESI, m/z): $[M]^+$ calc.: 366.1108; found: 366.1104.



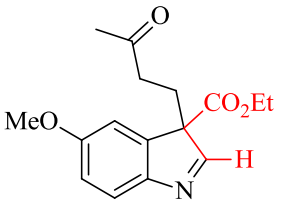
2.8k

Diethyl 5,7-dimethoxy-3-(3-oxobutyl)-*3H*-indole-2,3-dicarboxylate (2.8k). Prepared according to the general procedure in 52% yield. ^{1}H NMR (300 MHz, $cdcl_3$) δ 6.49 (s, 6H), 4.45 – 4.32 (dq, 2H), 4.22 – 4.08 (dq, 1H), 3.96 (s, 3H), 4.01 – 3.88 (dq, 1H), 3.83 (s, 3H), 2.82 (ddd, *J* = 14.3, 10.4, 5.7 Hz, 1H), 2.71 – 2.57 (m, 1H), 1.99 – 1.83 (m, 1H), 1.90 (s, 3H), 1.75 – 1.60 (m, 1H), 1.37 (td, *J* = 7.1Hz, 3H), 1.07 (t, *J* = 7.1Hz, 3H). HRMS (ESI, m/z): $[M]^+$ calc.: 392.1709; found: 392.1717.



2.8l

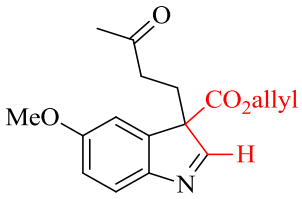
Methyl 5-methoxy-3-(3-oxobutyl)-*3H*-indole-3-carboxylate (2.8l). Prepared according to the general procedure in 66% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.54 (d, *J* = 8.5 Hz, 1H), 7.04 (d, *J* = 2.5 Hz, 1H), 6.92 (dd, *J* = 8.5, 2.6 Hz, 1H), 3.84 (s, 3H), 3.69 (s, 3H), 2.56 (ddd, *J* = 14.0, 9.3, 6.1 Hz, 1H), 2.46 – 2.32 (m, 1H), 2.21 – 2.01 (m, 2H), 1.99 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.8, 170.1, 169.4, 159.3, 148.9, 137.8, 122.0, 114.3, 109.8, 66.9, 56.0, 53.1, 37.8, 30.1, 27.7. HRMS (ESI, m/z): $[M]^+$ calc.: 276.1236; found: 276.1241.



2.8m

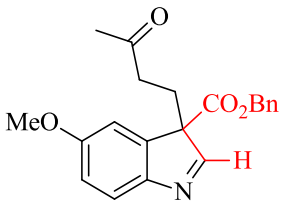
Ethyl 5-methoxy-3-(3-oxobutyl)-*3H*-indole-3-carboxylate (2.8m). Prepared according to the general procedure in 52% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.51 (d, *J* = 8.5 Hz, 1H), 7.03 (d, *J* = 2.5 Hz, 1H), 6.90 (dd, *J* = 8.5, 2.6 Hz, 1H), 4.25 – 4.02 (m, 2H), 3.82 (s, 3H), 2.54 (ddd, *J* = 14.1, 9.3, 6.1 Hz, 1H), 2.46 – 2.29 (m, 1H), 2.14 – 2.00 (m, 2H), 1.97 (s, 3H), 1.20 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ

206.7, 169.5, 169.4, 159.1, 148.7, 137.7, 121.7, 114.1, 109.7, 66.8, 62.0, 55.8, 37.6, 29.9, 27.6, 14.0. HRMS (ESI, m/z): $[M]^+$ calc.: 290.1393; found: 290.1397.



2.8n

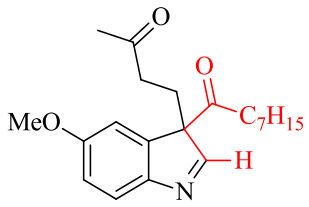
Allyl 5-methoxy-3-(3-oxobutyl)-3H-indole-3-carboxylate (2.8n). Prepared according to the general procedure in 61% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.54 (d, *J* = 8.5 Hz, 1H), 7.04 (d, *J* = 2.5 Hz, 1H), 6.92 (dd, *J* = 8.5, 2.6 Hz, 1H), 5.83 (ddt, *J* = 17.2, 10.4, 5.7 Hz, 1H), 5.30 – 5.16 (m, 2H), 4.67 – 4.49 (m, 2H), 3.84 (s, 3H), 2.58 (ddd, *J* = 14.1, 9.4, 6.1 Hz, 1H), 2.49 – 2.32 (m, 1H), 2.15 – 2.01 (m, 2H), 1.98 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.8, 169.3, 169.2, 159.3, 148.9, 137.7, 131.3, 122.0, 119.0, 114.4, 109.8, 66.9, 66.5, 55.9, 37.7, 30.1, 27.7. HRMS (ESI, m/z): $[M]^+$ calc.: 302.1392; found: 302.1386.



2.8o

Benzyl 5-methoxy-3-(3-oxobutyl)-*3H*-indole-3-carboxylate (2.8o). Prepared according to the general procedure in 69% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.54 (d, *J* = 8.5 Hz, 1H), 7.38 – 7.29 (m, 3H), 7.27 – 7.20 (m, 2H), 7.01 (d, *J* = 2.5

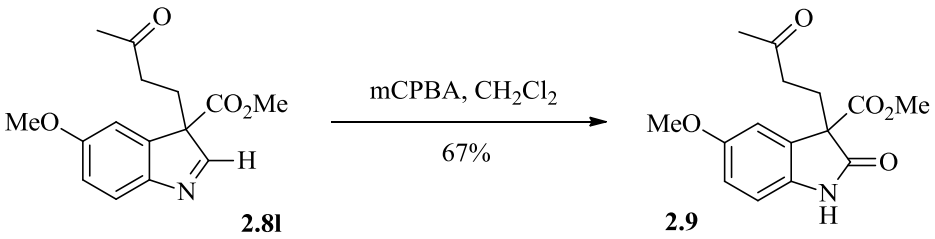
Hz, 1H), 6.92 (dd, J = 8.5, 2.6 Hz, 1H), 5.12 (q, J = 12.3 Hz, 2H), 3.81 (s, 3H), 2.56 (ddd, J = 14.0, 9.4, 6.0 Hz, 1H), 2.47 – 2.31 (m, 1H), 2.12 – 1.99 (m, 2H), 1.95 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.8, 169.3, 159.3, 135.2, 128.7, 128.6, 128.2, 122.0, 114.6, 109.6, 67.6, 55.9, 37.7, 30.1, 27.7. HRMS (ESI, m/z): $[M]^+$ calc.: 352.1549; found: 352.1556.



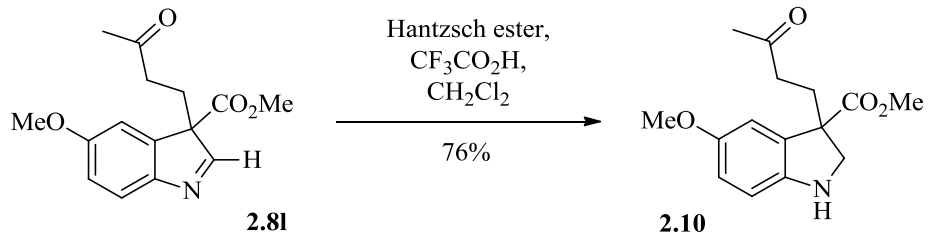
2.8p

1-(5-methoxy-3-(3-oxobutyl)-3H-indol-3-yl)octan-1-one (2.8p). Prepared according to the general procedure in 69% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.63 (d, J = 8.5 Hz, 1H), 6.97 (dd, J = 8.5, 2.5 Hz, 1H), 6.83 (d, J = 2.5 Hz, 1H), 3.83 (s, 3H), 2.64 – 2.50 (m, 1H), 2.44 – 2.30 (m, 1H), 2.06 – 1.88 (m, 7H), 1.38 (dt, J = 14.3, 7.2 Hz, 2H), 1.30 – 0.94 (m, 8H), 0.82 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.3, 203.8, 169.5, 159.5, 150.3, 138.4, 122.4, 114.7, 109.0, 75.2, 55.9, 39.4, 37.8, 31.7, 30.1, 29.0, 28.9, 24.8, 23.7, 22.7, 14.2. HRMS (ESI, m/z): $[M]^+$ calc.: 344.2226; found: 344.2234.

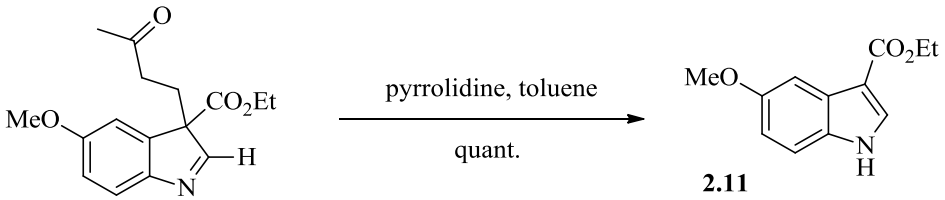
*7.2.4 Procedures for synthesis of **2.9**, **2.10**, and **2.11***



Methyl 5-methoxy-2-oxo-3-(3-oxobutyl)indoline-3-carboxylate (2.9). A mixture of **2.8l** (210 mg, 0.76 mmol) and $NaHCO_3$ (64 mg, 0.76 mmol) in methylene chloride (10 mL) was treated with mCPBA (70%, 376 mg, 1.53 mmol) and stirred at room temperature until the reaction was complete as shown by TLC. The mixture was taken into ethyl acetate and washed with aq. $NaHSO_3$, Na_2CO_3, and brine. The organic phase was separated, dried over anhydrous $MgSO_4$, filtered, and concentrated. The residue was purified by silica gel column chromatography, eluted with hexanes-ethyl acetate (1:3), to give **2.9** (148 mg, 67%) as colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.11 (s, 1H), 6.97 – 6.67 (m, 3H), 3.76 (s, 3H), 3.69 (s, 3H), 2.59 – 2.23 (m, 4H), 2.04 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.3, 176.5, 169.5, 156.3, 134.5, 129.5, 114.3, 111.0, 110.6, 59.1, 55.9, 53.3, 37.81, 30.0, 28.1. HRMS (ESI, m/z): $[M]^+$ calc.: 298.1267; found: 298.1263.



Methyl 5-methoxy-3-(3-oxobutyl)indoline-3-carboxylate (2.10). A solution of **2.8l** (38 mg, 0.14 mmol) and trifluoroacetic acid (27.6 μL, 41 mg, 0.36 mmol) in dichloromethane (1.5 mL) was treated with the Hantzsch ester (35 mg, 0.14 mmol) and stirred in the dark at room temperature overnight. After dilution with diethyl ether, the mixture was washed with aq. Na_2CO_3 and dried over anhydrous $MgSO_4$ before it was filtered and concentrated. The residue was purified by silica gel column chromatography eluting with hexanes-ethyl acetate (1:3) to give **2.10** (29 mg, 76%) as yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.91 (d, *J* = 2.5 Hz, 1H), 6.68 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.60 (d, *J* = 8.5 Hz, 1H), 4.08 (d, *J* = 9.9 Hz, 1H), 3.75 (s, 3H), 3.72 (s, 3H), 3.37 (d, *J* = 9.9 Hz, 1H), 2.53 – 2.18 (m, 4H), 2.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.8, 174.1, 153.8, 144.7, 131.1, 114.5, 111.5, 111.2, 56.2, 56.1, 55.2, 52.6, 39.1, 31.6, 30.1. HRMS (ESI, m/z): $[M]^+$ calc.: 278.1392; found: 278.1384.



2.8m **2.11**

Ethyl 5-methoxy-1*H*-indole-3-carboxylate (2.11). A solution of **2.8m** (50 mg, 0.17 mmol) in toluene (1 mL) was treated with pyrrolidine (28.9 μL, 24.4 mg, 0.34 mmol) and stirred at room temperature until the reaction was complete as shown by TLC. The residue was purified by silica gel column chromatography eluting with hexanes-ethyl acetate (1:3) to give **2.11** (38.3 mg, quantitative). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.81

(bs, 1H), 7.86 (d, J = 3.1 Hz, 1H), 7.68 (d, J = 2.5 Hz, 1H), 7.29 (dd, J = 8.8, 0.5 Hz, 1H), 6.94 – 6.88 (m, 1H), 4.39 (q, J = 7.1 Hz, 2H), 3.88 (s, 3H), 1.42 (t, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.6, 155.9, 131.4, 131.1, 126.9, 113.7, 112.5, 108.7, 102.9, 59.9, 55.8, 14.7.

A.2.5 Crystal and molecular structure determination of ***2.6a***

X-ray Diffraction Laboratory

Department of Chemistry

Texas A&M University

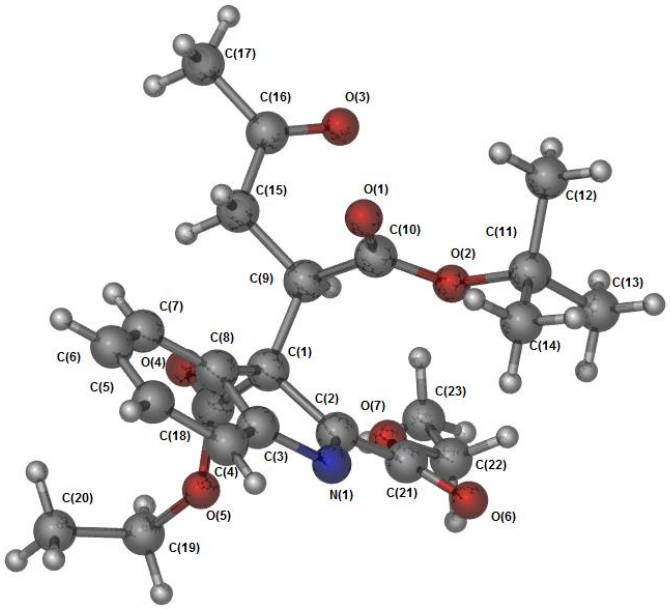


Table A.1. Crystal data and structure refinement for **2.6a**.

Empirical formula	C23 H29 N O7	
Formula weight	431.47	
Temperature	110(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P2(1)/n	
Unit cell dimensions	a = 14.1598(11) Å	α= 90°.
	b = 9.3637(7) Å	β= 110.345(4)°.
	c = 18.1995(18) Å	γ = 90°.
Volume	2262.5(3) $Å^3$	
Z	4	
Density (calculated)	1.267 Mg/m^3	
Absorption coefficient	0.776 mm^{-1}	
F(000)	920	
Crystal size	0.10 x 0.05 x 0.05 mm^3	
Theta range for data collection	3.43 to 59.99°.	
Index ranges	-15<=h<=15, -10<=k<=10, -20<=l<=18	
Reflections collected	17097	
Independent reflections	3293 [R(int) = 0.0635]	
Completeness to theta = 59.99°	98.1 %	
Absorption correction	None	
Max. and min. transmission	0.9622 and 0.9265	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3293 / 0 / 281	
Goodness-of-fit on F^2	1.012	
Final R indices [I>2sigma(I)]	R1 = 0.0439, wR2 = 0.1072	
R indices (all data)	R1 = 0.0647, wR2 = 0.1224	
Extinction coefficient	0.0035(4)	
Largest diff. peak and hole	0.231 and -0.224 $e.Å^{-3}$	

Table A.2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **2.6a**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	5586(1)	4984(2)	1197(1)	41(1)
O(2)	5928(1)	3554(2)	2264(1)	36(1)
O(3)	6108(1)	1488(2)	726(1)	46(1)
O(4)	2877(1)	1050(2)	638(1)	45(1)
O(5)	2099(1)	2371(2)	1289(1)	41(1)
O(6)	4473(1)	3422(2)	3426(1)	51(1)
O(7)	4211(1)	1593(2)	2568(1)	43(1)
N(1)	3456(1)	5140(2)	2089(1)	41(1)
C(1)	3599(2)	3325(2)	1217(1)	34(1)
C(2)	3753(2)	3854(2)	2044(1)	36(1)
C(3)	3043(2)	5657(2)	1307(1)	38(1)
C(4)	2616(2)	6991(3)	1084(2)	46(1)
C(5)	2252(2)	7304(3)	289(2)	48(1)
C(6)	2298(2)	6299(3)	-254(2)	46(1)
C(7)	2718(2)	4962(3)	-28(1)	40(1)
C(8)	3105(2)	4652(2)	763(1)	35(1)
C(9)	4609(2)	2842(2)	1114(1)	34(1)
C(10)	5430(2)	3923(2)	1516(1)	35(1)
C(11)	6715(2)	4506(2)	2792(1)	38(1)
C(12)	7573(2)	4711(3)	2476(1)	46(1)
C(13)	7074(2)	3672(3)	3552(1)	47(1)
C(14)	6241(2)	5904(3)	2899(2)	48(1)
C(15)	4517(2)	2666(2)	260(1)	34(1)
C(16)	5386(2)	1864(2)	159(1)	37(1)
C(17)	5312(2)	1577(3)	-663(1)	42(1)
C(18)	2831(2)	2093(3)	1008(1)	36(1)
C(19)	1252(2)	1376(3)	1076(1)	46(1)
C(20)	454(2)	1874(4)	339(2)	70(1)
C(21)	4190(2)	2976(3)	2765(2)	40(1)
C(22)	4657(2)	595(3)	3213(2)	54(1)

C(23)	4721(2)	-804(3)	2870(2)	67(1)

Table A.3. Bond lengths [Å] and angles [°] for **2.6a**.

O(1)-C(10)	1.209(3)
O(2)-C(10)	1.343(3)
O(2)-C(11)	1.489(3)
O(3)-C(16)	1.225(3)
O(4)-C(18)	1.201(3)
O(5)-C(18)	1.332(3)
O(5)-C(19)	1.460(3)
O(6)-C(21)	1.202(3)
O(7)-C(21)	1.347(3)
O(7)-C(22)	1.460(3)
N(1)-C(2)	1.288(3)
N(1)-C(3)	1.423(3)
C(1)-C(8)	1.522(3)
C(1)-C(2)	1.526(3)
C(1)-C(18)	1.539(3)
C(1)-C(9)	1.572(3)
C(2)-C(21)	1.489(3)
C(3)-C(4)	1.386(3)
C(3)-C(8)	1.390(3)
C(4)-C(5)	1.387(4)
C(4)-H(4A)	0.9500
C(5)-C(6)	1.383(4)
C(5)-H(5A)	0.9500
C(6)-C(7)	1.386(3)
C(6)-H(6A)	0.9500
C(7)-C(8)	1.380(3)
C(7)-H(7A)	0.9500
C(9)-C(10)	1.523(3)
C(9)-C(15)	1.524(3)

C(9)-H(9A)	1.0000
C(11)-C(13)	1.515(3)
C(11)-C(14)	1.515(3)
C(11)-C(12)	1.526(3)
C(12)-H(12A)	0.9800
C(12)-H(12B)	0.9800
C(12)-H(12C)	0.9800
C(13)-H(13A)	0.9800
C(13)-H(13B)	0.9800
C(13)-H(13C)	0.9800
C(14)-H(14A)	0.9800
C(14)-H(14B)	0.9800
C(14)-H(14C)	0.9800
C(15)-C(16)	1.505(3)
C(15)-H(15A)	0.9900
C(15)-H(15B)	0.9900
C(16)-C(17)	1.488(3)
C(17)-H(17A)	0.9800
C(17)-H(17B)	0.9800
C(17)-H(17C)	0.9800
C(19)-C(20)	1.496(4)
C(19)-H(19A)	0.9900
C(19)-H(19B)	0.9900
C(20)-H(20A)	0.9800
C(20)-H(20B)	0.9800
C(20)-H(20C)	0.9800
C(22)-C(23)	1.467(4)
C(22)-H(22B)	0.9900
C(22)-H(22C)	0.9900
C(23)-H(23A)	0.9800
C(23)-H(23B)	0.9800
C(23)-H(23C)	0.9800

C(10)-O(2)-C(11)	120.76(17)
C(18)-O(5)-C(19)	116.79(18)
C(21)-O(7)-C(22)	116.43(18)
C(2)-N(1)-C(3)	106.47(18)
C(8)-C(1)-C(2)	98.71(17)
C(8)-C(1)-C(18)	109.02(17)
C(2)-C(1)-C(18)	109.50(18)
C(8)-C(1)-C(9)	115.82(18)
C(2)-C(1)-C(9)	112.78(17)
C(18)-C(1)-C(9)	110.38(17)
N(1)-C(2)-C(21)	120.3(2)
N(1)-C(2)-C(1)	115.41(19)
C(21)-C(2)-C(1)	124.3(2)
C(4)-C(3)-C(8)	122.0(2)
C(4)-C(3)-N(1)	125.8(2)
C(8)-C(3)-N(1)	112.1(2)
C(3)-C(4)-C(5)	117.5(2)
C(3)-C(4)-H(4A)	121.2
C(5)-C(4)-H(4A)	121.2
C(6)-C(5)-C(4)	120.6(2)
C(6)-C(5)-H(5A)	119.7
C(4)-C(5)-H(5A)	119.7
C(5)-C(6)-C(7)	121.6(2)
C(5)-C(6)-H(6A)	119.2
C(7)-C(6)-H(6A)	119.2
C(8)-C(7)-C(6)	118.3(2)
C(8)-C(7)-H(7A)	120.9
C(6)-C(7)-H(7A)	120.9
C(7)-C(8)-C(3)	120.0(2)
C(7)-C(8)-C(1)	132.7(2)
C(3)-C(8)-C(1)	107.25(19)
C(10)-C(9)-C(15)	109.98(18)
C(10)-C(9)-C(1)	109.02(17)

C(15)-C(9)-C(1)	113.22(17)
C(10)-C(9)-H(9A)	108.2
C(15)-C(9)-H(9A)	108.2
C(1)-C(9)-H(9A)	108.2
O(1)-C(10)-O(2)	125.4(2)
O(1)-C(10)-C(9)	123.6(2)
O(2)-C(10)-C(9)	111.05(19)
O(2)-C(11)-C(13)	102.66(17)
O(2)-C(11)-C(14)	109.55(18)
C(13)-C(11)-C(14)	110.55(19)
O(2)-C(11)-C(12)	110.34(18)
C(13)-C(11)-C(12)	110.56(19)
C(14)-C(11)-C(12)	112.7(2)
C(11)-C(12)-H(12A)	109.5
C(11)-C(12)-H(12B)	109.5
H(12A)-C(12)-H(12B)	109.5
C(11)-C(12)-H(12C)	109.5
H(12A)-C(12)-H(12C)	109.5
H(12B)-C(12)-H(12C)	109.5
C(11)-C(13)-H(13A)	109.5
C(11)-C(13)-H(13B)	109.5
H(13A)-C(13)-H(13B)	109.5
C(11)-C(13)-H(13C)	109.5
H(13A)-C(13)-H(13C)	109.5
H(13B)-C(13)-H(13C)	109.5
C(11)-C(14)-H(14A)	109.5
C(11)-C(14)-H(14B)	109.5
H(14A)-C(14)-H(14B)	109.5
C(11)-C(14)-H(14C)	109.5
H(14A)-C(14)-H(14C)	109.5
H(14B)-C(14)-H(14C)	109.5
C(16)-C(15)-C(9)	113.21(18)
C(16)-C(15)-H(15A)	108.9

C(9)-C(15)-H(15A)	108.9
C(16)-C(15)-H(15B)	108.9
C(9)-C(15)-H(15B)	108.9
H(15A)-C(15)-H(15B)	107.7
O(3)-C(16)-C(17)	122.8(2)
O(3)-C(16)-C(15)	121.3(2)
C(17)-C(16)-C(15)	115.94(19)
C(16)-C(17)-H(17A)	109.5
C(16)-C(17)-H(17B)	109.5
H(17A)-C(17)-H(17B)	109.5
C(16)-C(17)-H(17C)	109.5
H(17A)-C(17)-H(17C)	109.5
H(17B)-C(17)-H(17C)	109.5
O(4)-C(18)-O(5)	125.1(2)
O(4)-C(18)-C(1)	125.3(2)
O(5)-C(18)-C(1)	109.61(19)
O(5)-C(19)-C(20)	109.5(2)
O(5)-C(19)-H(19A)	109.8
C(20)-C(19)-H(19A)	109.8
O(5)-C(19)-H(19B)	109.8
C(20)-C(19)-H(19B)	109.8
H(19A)-C(19)-H(19B)	108.2
C(19)-C(20)-H(20A)	109.5
C(19)-C(20)-H(20B)	109.5
H(20A)-C(20)-H(20B)	109.5
C(19)-C(20)-H(20C)	109.5
H(20A)-C(20)-H(20C)	109.5
H(20B)-C(20)-H(20C)	109.5
O(6)-C(21)-O(7)	124.7(2)
O(6)-C(21)-C(2)	125.6(2)
O(7)-C(21)-C(2)	109.7(2)
O(7)-C(22)-C(23)	107.6(2)
O(7)-C(22)-H(22B)	110.2

C(23)-C(22)-H(22B)	110.2
O(7)-C(22)-H(22C)	110.2
C(23)-C(22)-H(22C)	110.2
H(22B)-C(22)-H(22C)	108.5
C(22)-C(23)-H(23A)	109.5
C(22)-C(23)-H(23B)	109.5
H(23A)-C(23)-H(23B)	109.5
C(22)-C(23)-H(23C)	109.5
H(23A)-C(23)-H(23C)	109.5
H(23B)-C(23)-H(23C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table A.4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **2.6a**. 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}
O(1)	37(1)	41(1)	42(1)	5(1)	9(1)	-5(1)
O(2)	29(1)	38(1)	36(1)	0(1)	6(1)	-1(1)
O(3)	36(1)	57(1)	45(1)	8(1)	14(1)	11(1)
O(4)	40(1)	42(1)	53(1)	-8(1)	17(1)	-4(1)
O(5)	32(1)	44(1)	49(1)	-3(1)	16(1)	-3(1)
O(6)	53(1)	59(1)	39(1)	-5(1)	14(1)	8(1)
O(7)	47(1)	40(1)	41(1)	3(1)	15(1)	4(1)
N(1)	31(1)	44(1)	47(1)	-3(1)	13(1)	2(1)
C(1)	27(1)	37(1)	38(1)	0(1)	10(1)	2(1)
C(2)	26(1)	42(1)	41(1)	-2(1)	12(1)	0(1)
C(3)	26(1)	41(1)	47(2)	1(1)	11(1)	0(1)
C(4)	32(1)	40(2)	65(2)	-3(1)	16(1)	2(1)
C(5)	29(1)	44(2)	66(2)	10(1)	10(1)	4(1)
C(6)	32(1)	48(2)	53(2)	12(1)	10(1)	6(1)
C(7)	28(1)	47(2)	43(2)	2(1)	10(1)	1(1)
C(8)	23(1)	38(1)	44(1)	1(1)	11(1)	-1(1)
C(9)	28(1)	35(1)	40(1)	-1(1)	11(1)	2(1)
C(10)	28(1)	42(1)	35(1)	0(1)	10(1)	5(1)
C(11)	30(1)	41(1)	37(1)	-6(1)	6(1)	-5(1)
C(12)	32(1)	55(2)	48(2)	-4(1)	10(1)	-4(1)
C(13)	42(2)	50(2)	39(2)	1(1)	3(1)	-4(1)
C(14)	41(2)	44(2)	54(2)	-10(1)	10(1)	0(1)
C(15)	28(1)	40(1)	32(1)	-1(1)	8(1)	0(1)
C(16)	29(1)	38(1)	44(2)	1(1)	13(1)	-4(1)
C(17)	37(1)	46(1)	44(2)	-1(1)	17(1)	1(1)
C(18)	27(1)	40(1)	38(1)	2(1)	10(1)	3(1)
C(19)	33(1)	52(2)	55(2)	-1(1)	18(1)	-9(1)
C(20)	42(2)	102(3)	56(2)	-10(2)	5(1)	-5(2)

C(21)	32(1)	45(2)	45(2)	-2(1)	15(1)	1(1)
C(22)	61(2)	53(2)	49(2)	13(1)	20(1)	12(1)
C(23)	73(2)	53(2)	70(2)	10(2)	17(2)	9(2)

Table A.5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^{-3}) for **2.6a**.

	x	y	z	U(eq)
H(4A)	2574	7666	1461	56
H(5A)	1968	8216	117	58
H(6A)	2036	6531	-796	55
H(7A)	2738	4276	-406	47
H(9A)	4810	1900	1382	41
H(12A)	7849	3778	2414	69
H(12B)	8103	5294	2843	69
H(12C)	7316	5193	1966	69
H(13A)	6515	3548	3746	70
H(13B)	7621	4196	3942	70
H(13C)	7320	2734	3461	70
H(14A)	5694	5714	3099	72
H(14B)	5971	6398	2394	72
H(14C)	6751	6506	3273	72
H(15A)	3884	2151	-24	41
H(15B)	4474	3622	19	41
H(17A)	5913	1058	-663	62
H(17B)	5264	2484	-942	62
H(17C)	4711	1001	-924	62
H(19A)	974	1322	1505	55
H(19B)	1484	410	996	55
H(20A)	-115	1207	198	105

H(20B)	730	1914	-85	105
H(20C)	223	2826	423	105
H(22B)	4234	531	3545	65
H(22C)	5337	925	3543	65
H(23A)	5016	-1498	3290	101
H(23B)	5144	-728	2545	101
H(23C)	4044	-1119	2546	101

A.3 Experimental procedure for Chapter 2 section 5

A.3.1 General experimental procedure

A.3.1.1 Synthesis of imines 2.18

A solution of aniline (12.5 mmol) in diethyl ether (30 mL) was treated with anhydrous $MgSO_4$ (5.0 g) followed by dropwise addition of the α,β-unsaturated aldehyde (12 mmol for cinnamaldehydes and 15 mmol for others). The suspension was stirred at room temperature for 15 h under a nitrogen atmosphere before the solid was removed by filtration. The filtrate was then concentrated under reduced pressure to give crude *N*-allylideneanilines **2.18** that were essentially pure by ^{1}H NMR. *N*-Allylideneanilines **2.18** were used in the next step without purification.

A.3.1.2 Synthesis of *N*-allyl anilines 2.19

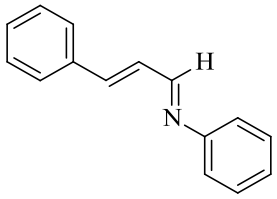
N-allylideneaniline **2.18** (6.50 mmol) was taken into THF and cooled to -78 ^oC before dropwise treatment with an ethereal solution of alkyl or phenyl lithium reagent (9.75 mmol). The mixture was stirred for 20-30 minutes before being quenched with aq. NH_4Cl. The aqueous phase was extracted with ethyl acetate (2x). The combined

organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The crude was used without further purification

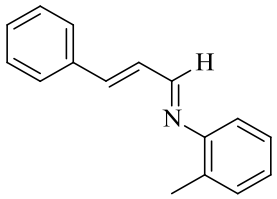
A.3.1.2 Synthesis of *N*-aryl ketonitrones 2.20

The *N*-aryl aniline **2.19** (0.26 mmol) was taken into a mixed solvent of THF (0.75 mL) and CH_3CN (2.9 mL), and 0.01 M aq. Na_2EDTA (2.9 mL). The mixture was cooled to 4 ^oC and treated with $NaHCO_3$ (0.108g, 1.29 mmol). The mixture was warmed to RT and Oxone® (0.437g, 0.71 mmol) was added in portions. After 20 min, EtOAc was added. The organic layer was separated and the aqueous layer was extracted with EtOAc (3x). The combined organic layers were washed with brine, dried over anhydrous Ns_2SO_4, and concentrated to give the crude nitrone, which was purified by silica gel chromatography eluting with dichloromethane-methanol or ethyl acetate-acetone.

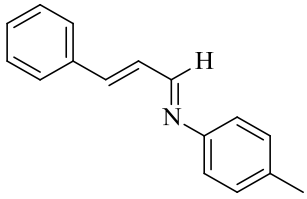
A.3.2 Spectra data for compounds



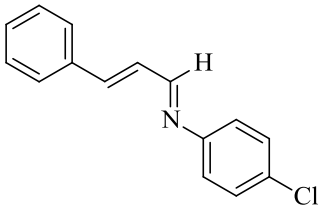
(E)-N-((E)-3-phenylallylidene)aniline (**2.18a**) Yield: 77%. Spectral data for this compound were consistent with those found in the literature.[51]



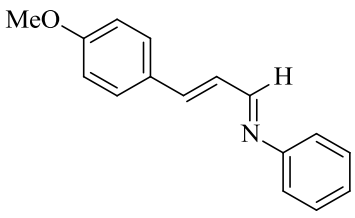
(E)-2-methyl-N-((E)-3-phenylallylidene)aniline (**2.18e**) Yield: 95%. Spectral data for this compound were consistent with those found in the literature.[52]



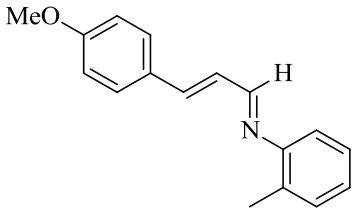
(E)-4-methyl-N-((E)-3-phenylallylidene)aniline (**2.18f**) Yield: 45%. Spectral data for this compound were consistent with those found in the literature.[52]



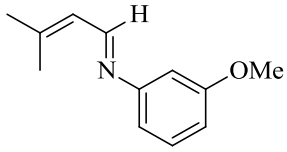
(E)-4-chloro-N-((E)-3-phenylallylidene)aniline (**2.18g**) Yield: 65%. Spectral data for this compound were consistent with those found in the literature.[53]



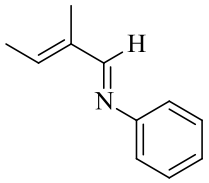
(E)-N-((E)-3-(4-methoxyphenyl)allylidene)aniline (**2.18h**) Yield: 75%. Spectral data for this compound were consistent with those found in the literature.[54]



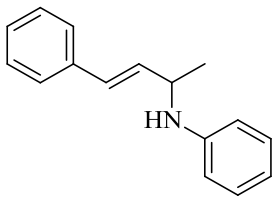
(E)-N-((E)-3-(4-methoxyphenyl)allylidene)-2-methylaniline (**2.18i**). Yield 74%; ^{1}H NMR (300MHz, $CDCl_3$) δ 8.12 (dd, *J* = 7.8, 0.6 Hz, 1H), 7.53-7.47 (m, 2H), 7.24-7.16 (m, 2H), 7.14-7.09 (m, 1H), 7.09-7.05 (m, 1H), 7.04 (d, *J* = 7.8 Hz, 1H), 6.96-6.90 (m, 2H), 6.89-6.84 (m, 1H), 3.85 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (75MHz, $CDCl_3$) *δ* 161.7, 160.7, 151.5, 143.4, 131.6, 130.2, 129.0, 128.4, 126.7, 126.6, 125.4, 117.8, 114.3, 55.4, 17.9. HRMS (ESI, m/z): $[M]^+$ calc.: 251.1388; found: 252.1396.



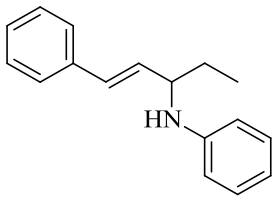
(E)-3-methoxy-N-(3-methylbut-2-en-1-ylidene)aniline (**2.18k**). Yield 93%; ^{1}H NMR (300MHz, $CDCl_3$) δ 8.37 (d, *J* = 9.6 Hz, 1H), 7.28-7.21 (m, 1H), 6.78-6.65 (m, 3H), 6.25-6.18 (m, 1H), 3.82, (s, 3H), 2.02 (m, 3H), 1.97 (d, *J* = 1.2 Hz, 3H); ^{13}C NMR (75MHz, $CDCl_3$) *δ* 160.6, 159.3, 154.4, 150.9, 130.1, 126.5, 113.2, 111.6, 107.1, 55.6, 27.2, 19.3. HRMS (ESI, m/z): $[M]^+$ calc.: 190.1232; found: 190.1228.



(E)-N-((E)-2-methylbut-2-en-1-ylidene)aniline (**2.18l**). Yield 91%. ^{1}H NMR (300MHz, $CDCl_3$) δ 8.37 (d, *J* = 9.6 Hz, 1H), 7.40-7.30 (m, 2H), 7.22-7.15 (m, 1H), 7.14-7.08 (m, 2H), 6.26-6.20 (m, 1H), 2.04-2.00 (m, 3H), 1.99-1.95 (m, 3H); ^{13}C NMR (75MHz, $CDCl_3$) *δ* 159.2, 153.0, 150.6, 129.4, 126.6, 125.8, 121.2, 27.2, 19.3. HRMS (ESI, m/z): $[M]^+$ calc.: 160.1126; found: 160.1121.

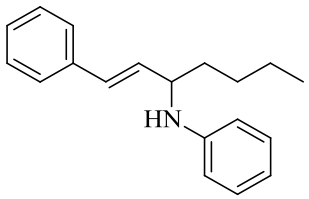


(E)-N-(4-phenylbut-3-en-2-yl)aniline (**2.19a**). Yield: Quantitative. Spectral data for this compound were consistent with those found in the literature.[55]

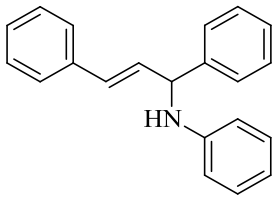


(E)-N-(1-phenylpent-1-en-3-yl)aniline (**2.19b**). Yield 98%; ^{1}H NMR (300MHz, $CDCl_3$) δ 7.40-7.13 (m, 7H), 6.72-6.63 (m, 3H), 6.59 (d, *J* = 15.9 Hz, 1H), 6.14 (dd, *J* = 15.9, 6.3 Hz, 1H), 3.94-3.86 (m, 1H), 3.75 (br. s, 1H), 1.80-1.67 (m, 2H), 1.04 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75MHz, $CDCl_3$) δ 148.0, 137.4, 132.3, 130.7, 128.8, 127.6, 126.7,

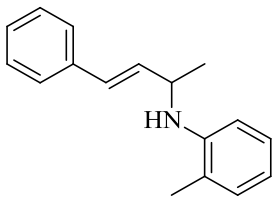
117.5, 113.7, 57.5, 29.4, 10.8 ppm. HRMS (ESI, m/z): $[M]^+$ calc.: 238.1596; found: 238.1607.



(E)-N-(1-phenylhept-1-en-3-yl)aniline (**2.19c**) Yield: 91%. Spectral data for this compound were consistent with those found in the literature.[56]

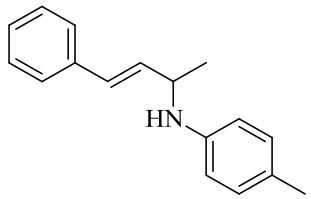


(E)-N-(1,3-diphenylallyl)aniline (**2.19d**) Yield: Quantitative. Spectral data for this compound were consistent with those found in the literature.[57]

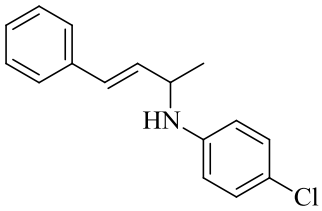


(E)-2-methyl-N-(4-phenylbut-3-en-2-yl)aniline (**2.19e**). Yield 96%; ^{1}H NMR (300MHz, $CDCl_3$) δ 7.40-7.12 (m, 5H), 7.13-7.05 (m, 2H), 6.71-6.62 (m, 2H), 6.59 (dd, *J* = 15.9, 1.2 Hz, 1H), 4.25-4.15 (m, 1H), 3.56 (br. s, 1H), 2.19 (s, 3H), 1.46 (d, *J* = 6.6

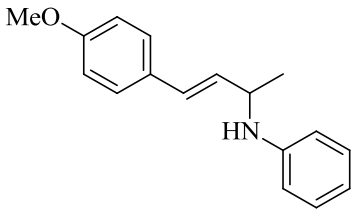
Hz, 3H); ^{13}C NMR (75MHz, $CDCl_3$) δ 145.7, 137.3, 133.7, 130.4, 129.6, 128.8, 127.7, 127.4, 126.7, 122.0, 117.2, 111.2, 51.0, 22.6, 18.0. HRMS (ESI, m/z): $[M]^+$ calc.: 238.1596; found: 238.1589.



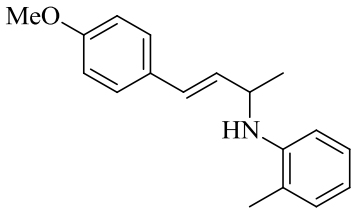
(E)-4-methyl-N-(4-phenylbut-3-en-2-yl)aniline (**2.19f**). Yield 97%; ^{1}H NMR (300MHz, $CDCl_3$) δ 7.40-7.16 (m, 5H), 7.01-6.95 (m, 2H), 6.63-6.54 (m, 3H), 6.23 (dd, *J* = 16.2, 6 Hz, 1H), 4.18-4.07 (m, 1H), 3.58 (br. s, 1H), 2.24 (s, 3H), 1.40 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (75MHz, $CDCl_3$) δ 145.4, 137.4, 133.8, 130.0, 129.5, 128.8, 127.6, 126.9, 126.6, 114.0, 51.5, 22.4, 20.7. HRMS (ESI, m/z): $[M]^+$ calc.: 238.1596; found: 238.1601.



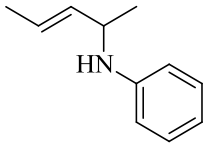
(E)-4-chloro-N-(4-phenylbut-3-en-2-yl)aniline (**2.19g**). Yield 99%; ^{1}H NMR (300MHz, $CDCl_3$) δ 7.38-7.18 (m, 5H), 7.13-7.07 (m, 2H), 6.60-6.51 (m, 3H), 6.18 (dd, *J* = 15.9, 5.7 Hz, 1H), 4.17-4.04 (m, 1H), 3.73 (br. s, 1H), 1.41 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (75MHz, $CDCl_3$) δ 146.3, 137.1, 132.9, 129.9, 129.3, 128.9, 127.8, 126.7, 122.2, 114.8, 51.4, 22.4.



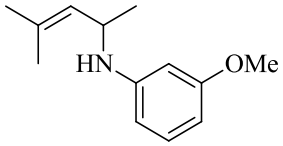
(E)-N-(4-(4-methoxyphenyl)but-3-en-2-yl)aniline (**2.19h**). Yield 98%; ^{1}H NMR (300MHz, $CDCl_3$) δ 7.32-7.27 (m, 2H), 7.21-7.13 (m, 2H), 6.88-6.81 (m, 2H), 6.73-6.63 (m, 3H), 6.52 (d, *J* = 15.9 Hz, 1H), 6.08 (dd, *J* = 15.9, 6 Hz, 1H), 4.18-4.08 (m, 1H), 3.80 (s, 3H), 3.70 (br. s, 1H), 1.40 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (75MHz, $CDCl_3$) δ 159.4, 147.8, 131.3, 130.1, 129.5, 129.0, 127.8, 114.6, 114.3, 113.7, 55.6, 51.2, 22.5. HRMS (ESI, m/z): $[M]^+$ calc.: 254.1545; found: 254.1548.



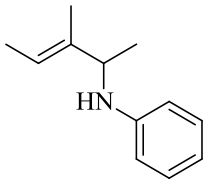
(E)-N-(4-(4-methoxyphenyl)but-3-en-2-yl)-2-methylaniline (**2.19i**). Yield 99%; ^{1}H NMR (300MHz, $CDCl_3$) δ 7.33-7.27 (m, 2H), 7.12-7.04(m, 2H), 6.87-6.81 (m, 2H), 6.71-6.61 (m, 2H), 6.53 (d, *J* = 15.9 Hz, 1H), 6.11 (dd, *J* = 15.9, 5.7 Hz, 1H), 4.23-4.13 (m, 1H), 3.80 (s, 3H), 3.55 (br. s, 1H), 2.18 (s, 3H), 1.44 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (75MHz, $CDCl_3$) δ 159.4, 145.72, 131.5, 130.1, 129.0, 127.8, 127.4, 122.0, 117.1, 114.2, 111.2, 55.6, 51.1, 227, 18.0.



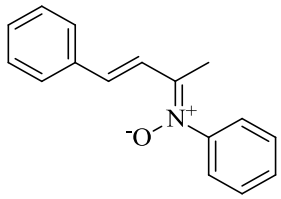
(E)-N-(pent-3-en-2-yl)aniline (**2.19j**) Yield: 91%. Spectral data for this compound were consistent with those found in the literature.[58]



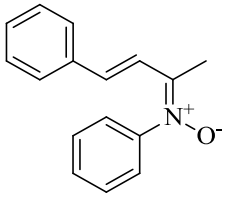
3-methoxy-N-(4-methylpent-3-en-2-yl)aniline (**2.19k**). Yield 95%; ^{1}H NMR (300MHz, $CDCl_3$) δ 7.05 (t, *J* = 8.1 Hz, 1H), 6.27-6.13 (m, 3H), 5.09-5.03 (m, 1H), 4.18-4.07 (m, 1H), 3.80-3.77 (m, 1H), 3.76 (s, 3H) 3.62 (br. s, 1H) 1.74 (d, *J* = 1.5 Hz, 3H), 1.70 (d, *J* = 2.4 Hz, 3H), 1.24 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (75MHz, $CDCl_3$) δ 161.0, 149.4, 133.0, 130.1, 129.7, 106.8, 102.6, 99.3, 55.3, 47.6, 26.0, 22.4, 18.5. HRMS (ESI, m/z): $[M]^+$ calc.: 206.1545; found: 206.1554.



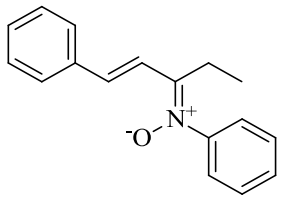
(E)-N-(3-methylpent-3-en-2-yl)aniline (**2.19l**) Yield: 82%. Spectral data for this compound were consistent with those found in the literature.[59]



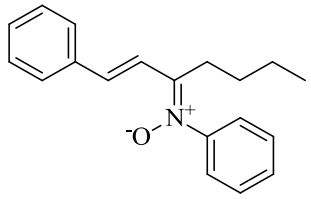
(Z)-N-((E)-4-phenylbut-3-en-2-ylidene)aniline oxide (**Z-2.20a**). Yield 80% combined isomers; ^{1}H NMR (300MHz, $CDCl_3$) δ 8.05 (d, 1H, *J* = 16.5 Hz), 7.64-7.59 (m, 2H), 7.52-7.29 (m, 8H), 7.12 (d, *J* = 16.8 Hz, 2H), 2.14 (s, 3H); ^{13}C NMR (75MHz, $CDCl_3$) δ 138.1, 136.5, 129.9, 129.8, 129.7, 129.6, 129.2, 128.0, 128.0, 124.0, 120.8, 16.7. HRMS (ESI, m/z): $[M]^+$ calc.: 238.1232; found: 238.1221.



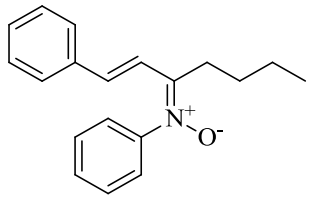
(E)-N-((E)-4-phenylbut-3-en-2-ylidene)aniline oxide (**E-2.20a**). ^{1}H NMR (300MHz, $CDCl_3$) δ 7.54-7.46 (m, 3H), 7.43-7.38 (m, 2H), 7.31-7.19 (m, 5H), 6.8 (d, *J* = 18 Hz, 1H), 6.71 (d, *J* = 15.9 Hz, 1H), 2.54 (s, 3H); ^{13}C NMR (75MHz, $CDCl_3$) δ 148.4, 145.7, 136.3, 133.3, 129.8, 129.8, 129.2, 129.1, 127.2, 124.8, 121.3, 13.7. HRMS (ESI, m/z): $[M]^+$ calc.: 238.1232; found: 238.1224.



(E)-N-((E)-1-phenylpent-1-en-3-ylidene)aniline oxide (**2.20b**). Yield 22%; 3.3:1 E:Z. ^{1}H NMR (300MHz, $CDCl_3$) δ 7.52-7.45 (m, 3H), 7.42-7.36 (m, 3H), 7.29-7.20 (m, 4H), 6.80 (d, *J* = 15.9, Hz, 1H), 6.64 (d, *J* = 16.2 Hz, 1H), 3.03 (q, *J* = 7.5 Hz, 2H), 1.33 (t, *J* = 7.5); ^{13}C NMR (75MHz, $CDCl_3$) δ 152.6, 145.9, 138.0, 132.4, 129.7, 129.7, 129.1, 127.2, 124.8, 120.4, 20.4, 10.4. HRMS (ESI, m/z): $[M]^+$ calc.: 252.1371; found: 252.1371.

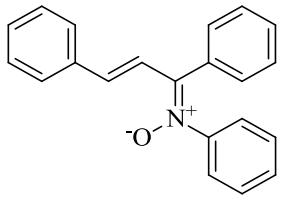


(Z)-N-((E)-1-phenylhept-1-en-3-ylidene)aniline oxide (**Z-2.20c**). Yield 82% combined isomers; ^{1}H NMR (300MHz, $CDCl_3$) δ 7.92 (d, *J* = 16.8 Hz, 1H), 7.64-7.59 (m, 2H), 7.52-7.44 (m, 3H), 7.42-7.32 (m, 3H), 7.19 (d, *J* = 68 Hz, 1H), 2.49-2.42 (m, 2H), 1.60-1.45 (m, 2H), 1.30-1.17 (m, 2H), 0.79 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75MHz, $CDCl_3$) δ 149.8, 146.3, 138.1, 136.6, 129.8, 129.6, 129.5, 129.2, 127.9, 123.8, 119.6, 30.9, 29.6, 22.9, 13.8.

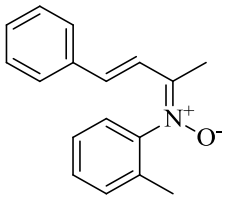


(E)-N-((E)-1-phenylhept-1-en-3-ylidene)aniline oxide (**E-2.20c**). ^{1}H NMR (300MHz, $CDCl_3$) δ 7.48 (m, 3H), 7.39 (m, 2H), 7.25 (m, 5H), 6.79 (d, *J* = 15.9 Hz, 1H), 6.65 (d, *J*

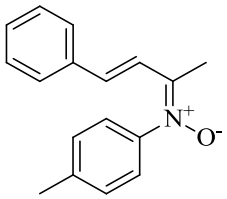
= 15.9 Hz, 1H), 3.00 (m, 2H), 1.74 (m, 2H), 1.57 (m, 2H), 1.02 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75MHz, $CDCl_3$) δ 151.7, 145.7, 136.3, 132.5, 129.6, 129.6, 129.0, 129.0, 127.1, 124.7, 120.8, 28.0, 16.7, 23.3, 14.2. HRMS (ESI, m/z): $[M]^+$ calc.: 280.1701; found: 280.1704.



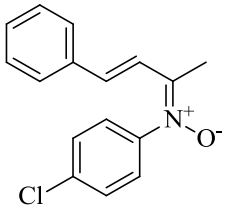
(Z)-N-((E)-1,3-diphenylallylidene)aniline oxide (**2.20d**). Yield 52%; ^{1}H NMR (300MHz, $CDCl_3$) δ 8.18 (d, *J* = 16.5 Hz, 1H), 7.53 (m, 3H), 7.38-7.14 (m, 12H), 6.71 (d, *J* = 16.2 Hz, 1H); ^{13}C NMR (75MHz, $CDCl_3$) δ 150.2, 147.4, 141.2, 136.6, 133.1, 131.2, 129.7, 129.3, 129.1, 129.0, 128.9, 128.8, 128.0, 125.2, 122.3. HRMS (ESI, m/z): $[M]^+$ calc.: 300.1388; found: 300.1396.



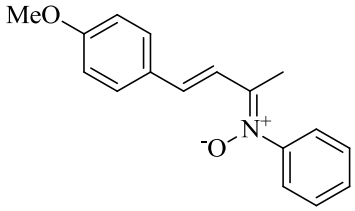
(E)-2-methyl-N-((E)-4-phenylbut-3-en-2-ylidene)aniline oxide (**2.20e**). Yield 51%; 2.7:1 E:Z. ^{1}H NMR (300MHz, $CDCl_3$) δ 7.40-7.15 (m, 9H), 6.82 (d, *J* = 15.9 Hz, 1H), 6.52 (d, *J* = 15.9 Hz, 1H), 2.54 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (75MHz, $CDCl_3$) δ 148.3, 144.6, 136.2, 133.4, 131.7, 129.6, 129.1, 129.1, 127.4, 127.2, 124.6, 120.6,17.0, 12.9. HRMS (ESI, m/z): $[M]^+$ calc.: 252.1388; found: 252.1379.



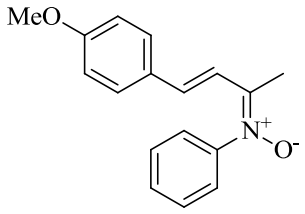
(E)-4-methyl-N-((E)-4-phenylbut-3-en-2-ylidene)aniline oxide (**2.20f**). Yield 67%; 3.7:1 E:Z. ^{1}H NMR (300MHz, $CDCl_3$) δ 7.40-7.20 (m, 9H), 6.84-6.70 (m, 2H), 2.51 (d, *J* = 2.1 Hz, 3H), 2.42 (d, *J* = 2.4 Hz, 3H); ^{13}C NMR (75MHz, $CDCl_3$) δ 147.9, 143.4, 139.9, 136.4, 132.8, 130.2, 129.1, 129.0, 127.1, 124.5, 121.5. HRMS (ESI, m/z): $[M]^+$ calc.: 252.1388; found: 252.1382.



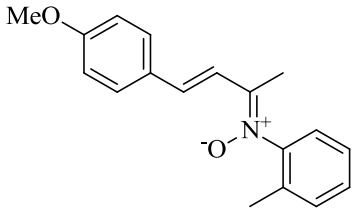
(E)-4-chloro-N-((E)-4-phenylbut-3-en-2-ylidene)aniline oxide (**2.20g**). Yield 34%; 2:1 E:Z. ^{1}H NMR (300MHz, $CDCl_3$) δ 7.50-7.44 (m, 2H), 7.39-7.33 (m, 2H), 7.31-7.23 (m, 4H), 6.84 (d, *J* =15.9 Hz, 1H), 6.69 (d, *J* = 15.9 Hz, 1H), 2.52 (s, 3H); ^{13}C NMR (75MHz, $CDCl_3$) δ 148.5, 144.2, 136.1, 135.6, 133.6, 130.0, 129.4, 129.2, 127.3, 126.2, 120.9, 13.8. HRMS (ESI, m/z): $[M]^+$ calc.: 272.0842; found: 272.0831.



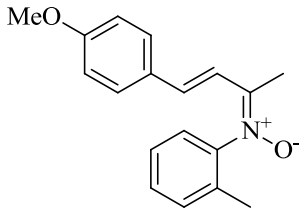
(Z)-N-((E)-4-(4-methoxyphenyl)but-3-en-2-ylidene)aniline oxide (**Z-2.20h**). Yield 74% combined isomers; ^{1}H NMR (300MHz, $CDCl_3$) δ 7.93 (d, *J* = 16.5 Hz, 1H), 7.57 (d, *J* = 8.7 Hz, 2H), 7.44 (m, 5H), 7.08 (d, *J* = 16.5 Hz, 1H), 6.91 (d, *J* = 8.7 Hz, 2H), 3.84 (s, 3H), 2.11 (s, 3H); ^{13}C NMR (75MHz, $CDCl_3$) δ 161.0, 146.6, 145.2, 137.9, 129.8, 129.5, 129.4, 129.3, 124.1, 118.6, 114.7, 55.7, 16.6. HRMS (ESI, m/z): $[M]^+$ calc.: 268.1338; found: 268.1332.



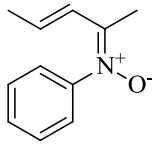
(E)-N-((E)-4-(4-methoxyphenyl)but-3-en-2-ylidene)aniline oxide (**E-2.20h**). ^{1}H NMR (300MHz, $CDCl_3$) δ 7.45 (m, 5H), 7.17 (d, *J* = 8.7 Hz, 2H), 6.79 (m, 3H), 6.57 (d, *J* = 15.9 Hz), 3.78 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (75MHz, $CDCl_3$) δ 160.5, 148.4, 145.8, 132.9, 129.7, 129.7, 129.1, 128.7, 124.8, 119.3, 114.6, 55.6, 13.6. HRMS (ESI, m/z): $[M]^+$ calc.: 268.1338; found: 268.1350.



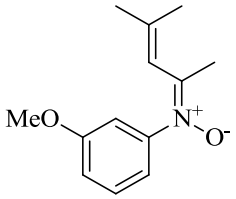
(Z)-N-((E)-4-(4-methoxyphenyl)but-3-en-2-ylidene)-2-methylaniline oxide (**Z-2.20i**). Yield 49% combined isomers; ^{1}H NMR (300MHz, $CDCl_3$) δ 7.94 (d, *J* = 16.5 Hz, 1H), 7.57 (m, 2H), 7.30 (m, 3H), 7.22 (m, 1H), 7.08 (d, *J* = 16.5 Hz, 1H), 6.91 (m, 2H), 3.84 (s, 3H), 2.30 (s, 3H), 2.02 (s, 3H); ^{13}C NMR (75MHz, $CDCl_3$) δ 161.0, 145.6, 145.5, 137.9, 131.8, 129.5, 129.3, 129.2, 127.5, 123.9, 118.1, 114.7, 55.7, 16.9, 15.7. HRMS (ESI, m/z): $[M]^+$ calc.: 282.1494; found: 282.1502.



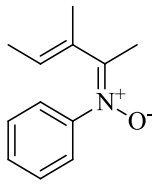
(E)-N-((E)-4-(4-methoxyphenyl)but-3-en-2-ylidene)-2-methylaniline oxide (**E-2.20i**). ^{1}H NMR (300MHz, $CDCl_3$) δ 7.32 (m, 4H), 7.15 (m, 2H), 6.78 (m, 3H), 6.37 (d, *J* = 14.7 Hz), 3.78 (s, 3H), 2.53 (s, 3H), 2.25 (s, 3H).



(E)-N-((E)-pent-3-en-2-ylidene)aniline oxide (**2.20j**). Yield 70% estimated; ^{1}H NMR (300MHz, $CDCl_3$) δ 7.44 (m, 3H), 7.33 (m, 2H), 6.05 (m, 2H), 2.40 (s, 3H), 1.75 (d, *J* = 5.4 Hz, 3H); ^{13}C NMR (75MHz, $CDCl_3$) δ 132.5, 129.8, 129.7, 129.5, 125.1, 124.6, 123.9, 19.3, 13.7. HRMS (ESI, m/z): $[M]^+$ calc.: 176.1075; found: 176.1079.



(E)-3-methoxy-N-(4-methylpent-3-en-2-ylidene)aniline oxide (**2.20k**). Yield 70% estimated; ^{1}H NMR (300MHz, $CDCl_3$) δ 7.28 (m, 1H), 6.91 (m, 3H), 5.66 (m, 1H), 3.80 (s, 1H), 2.47 (s, 3H), 1.83 (d, *J* = 0.9 Hz, 3H), 1.70 (d, *J* = 1.2 Hz, 3H). HRMS (ESI, m/z): $[M]^+$ calc.: 206.1545; found: 206.1554.



(E)-N-((E)-3-methylpent-3-en-2-ylidene)aniline oxide (**2.20l**). Yield: 20%. ^{1}H NMR (300MHz, $CDCl_3$) δ 7.32 (m, 6H), 2.38 (t, *J* = 1.2 Hz, 3H), 1.52 (s, 3H), 1.46 (d, *J* = 6.6 Hz); ^{13}C NMR (75MHz, $CDCl_3$) δ 131.3, 129.7, 129.1, 129.0, 124.1, 123.6, 123.3. HRMS (ESI, m/z): $[M]^+$ calc.: 190.1232; found: 190.1239.

A.4 Experimental procedure for Chapter 3 section 2

A.4.1 Experimental procedure for pyrroloindoline synthesis

The general procedure for indolenine synthesis found in section A.2.2 was adapted until the best results occurred. A solution of the α,β-unsaturated *N*-aryl ketonitrone (3 equiv.) and the activated alkyne **3.11** (0.2 M, 1 equiv.) in toluene was

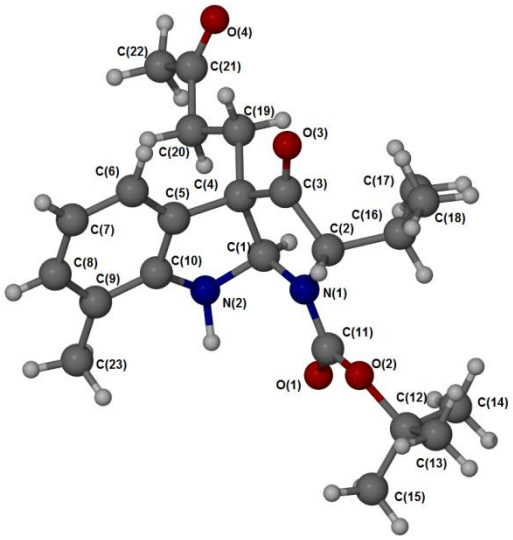
stirred at 60 ^{o}C until TLC indicated the reaction was complete. The homogenous solution was concentrated in vacuo and the residue was purified by silica gel column chromatography, eluted with hexanes–ethyl acetate, to give the pyrroloindolines.

*A.4.2 Crystal and molecular structure determination of **3.9a***

X-ray Diffraction Laboratory

Department of Chemistry

Texas A&M University



TableA.6. Crystal data and structure refinement for **3.9a**.

Empirical formula	C23 H32 N2 O4
Formula weight	400.51
Temperature	110(2) K
Wavelength	1.54178 Å
Crystal system	Orthorhombic
Space group	P2(1)2(1)2(1)

Unit cell dimensions	a = 6.2646(6) Å	α= 90°.
	b = 18.5214(17) Å	β= 90°.
	c = 18.8373(16) Å	γ = 90°.
Volume	2185.7(3) $Å^3$	
Z	4	
Density (calculated)	1.217 Mg/m^3	
Absorption coefficient	0.668 mm^{-1}	
F(000)	864	
Crystal size	0.12 x 0.02 x 0.02 mm^3	
Theta range for data collection	4.78 to 60.00°.	
Index ranges	-7<=h<=7, -20<=k<=20, -21<=l<=21	
Reflections collected	38180	
Independent reflections	3101 [R(int) = 0.1666]	
Completeness to theta = 60.00°	96.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9868 and 0.9241	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3101 / 0 / 272	
Goodness-of-fit on F^2	1.010	
Final R indices [I>2sigma(I)]	R1 = 0.0496, wR2 = 0.0532	
R indices (all data)	R1 = 0.0856, wR2 = 0.0566	
Absolute structure parameter	0.01(19)	
Extinction coefficient	0.0218(5)	
Largest diff. peak and hole	0.157 and -0.167 e.$Å^{-3}$	

Table A.7. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **3.9a**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	-5(4)	3061(1)	-2016(1)	51(1)

O(2)	3310(3)	2863(1)	-2456(1)	49(1)
O(3)	6641(3)	5037(1)	-1236(1)	55(1)
O(4)	1187(4)	6782(1)	-212(1)	66(1)
N(1)	2783(4)	3768(1)	-1699(1)	45(1)
N(2)	576(4)	3746(1)	-628(1)	47(1)
C(1)	1485(5)	4182(2)	-1193(2)	47(1)
C(2)	4878(5)	4088(2)	-1876(2)	48(1)
C(3)	5106(6)	4642(2)	-1305(2)	47(1)
C(4)	3162(5)	4667(2)	-826(2)	48(1)
C(5)	3610(6)	4243(2)	-152(2)	50(1)
C(6)	5197(6)	4334(2)	349(2)	53(1)
C(7)	5180(6)	3889(2)	941(2)	58(1)
C(8)	3556(6)	3377(2)	1023(2)	55(1)
C(9)	1962(6)	3277(2)	534(2)	48(1)
C(10)	2032(6)	3725(2)	-67(2)	49(1)
C(11)	1850(7)	3223(2)	-2064(2)	49(1)
C(12)	2675(6)	2410(2)	-3064(2)	55(1)
C(13)	4816(6)	2225(2)	-3391(2)	69(1)
C(14)	1357(5)	2864(2)	-3558(2)	66(1)
C(15)	1536(6)	1754(2)	-2809(2)	72(1)
C(16)	5006(6)	4408(2)	-2621(2)	54(1)
C(17)	3493(6)	5053(2)	-2716(2)	64(1)
C(18)	7283(5)	4628(2)	-2808(2)	57(1)
C(19)	2511(5)	5460(2)	-683(2)	55(1)
C(20)	626(5)	5525(2)	-179(2)	49(1)
C(21)	-6(6)	6293(2)	-52(2)	51(1)
C(22)	-2138(5)	6424(2)	286(2)	66(1)
C(23)	279(5)	2722(2)	624(2)	59(1)

Table A.8. Bond lengths [Å] and angles [°] for **3.9a**.

O(1)-C(11)	1.204(4)

O(2)-C(11)	1.351(4)
O(2)-C(12)	1.475(3)
O(3)-C(3)	1.215(3)
O(4)-C(21)	1.212(3)
N(1)-C(11)	1.354(4)
N(1)-C(2)	1.478(4)
N(1)-C(1)	1.469(3)
N(2)-C(10)	1.397(4)
N(2)-C(1)	1.452(3)
N(2)-H(2N)	1.0926
C(1)-C(4)	1.546(4)
C(1)-H(1)	1.0000
C(2)-C(3)	1.494(4)
C(2)-C(16)	1.524(4)
C(2)-H(2)	1.0000
C(3)-C(4)	1.516(4)
C(4)-C(5)	1.520(4)
C(4)-C(19)	1.548(4)
C(5)-C(6)	1.381(4)
C(5)-C(10)	1.387(4)
C(6)-C(7)	1.387(4)
C(6)-H(6)	0.9500
C(7)-C(8)	1.398(4)
C(7)-H(7)	0.9500
C(8)-C(9)	1.371(4)
C(8)-H(8)	0.9500
C(9)-C(10)	1.403(4)
C(9)-C(23)	1.482(4)
C(12)-C(15)	1.490(4)
C(12)-C(14)	1.501(4)
C(12)-C(13)	1.515(4)
C(13)-H(13A)	0.9800
C(13)-H(13B)	0.9800

C(13)-H(13C)	0.9800
C(14)-H(14A)	0.9800
C(14)-H(14B)	0.9800
C(14)-H(14C)	0.9800
C(15)-H(15A)	0.9800
C(15)-H(15B)	0.9800
C(15)-H(15C)	0.9800
C(16)-C(18)	1.525(4)
C(16)-C(17)	1.535(4)
C(16)-H(16)	1.0000
C(17)-H(17A)	0.9800
C(17)-H(17B)	0.9800
C(17)-H(17C)	0.9800
C(18)-H(18A)	0.9800
C(18)-H(18B)	0.9800
C(18)-H(18C)	0.9800
C(19)-C(20)	1.521(4)
C(19)-H(19A)	0.9900
C(19)-H(19B)	0.9900
C(20)-C(21)	1.496(4)
C(20)-H(20A)	0.9900
C(20)-H(20B)	0.9900
C(21)-C(22)	1.500(4)
C(22)-H(22A)	0.9800
C(22)-H(22B)	0.9800
C(22)-H(22C)	0.9800
C(23)-H(23A)	0.9800
C(23)-H(23B)	0.9800
C(23)-H(23C)	0.9800
C(11)-O(2)-C(12)	121.5(3)
C(11)-N(1)-C(2)	124.5(3)
C(11)-N(1)-C(1)	118.7(3)
C(2)-N(1)-C(1)	115.5(3)

C(10)-N(2)-C(1)	108.3(2)
C(10)-N(2)-H(2N)	116.2
C(1)-N(2)-H(2N)	115.3
N(2)-C(1)-N(1)	113.7(2)
N(2)-C(1)-C(4)	105.3(3)
N(1)-C(1)-C(4)	102.5(3)
N(2)-C(1)-H(1)	111.6
N(1)-C(1)-H(1)	111.6
C(4)-C(1)-H(1)	111.6
N(1)-C(2)-C(3)	101.4(3)
N(1)-C(2)-C(16)	114.3(3)
C(3)-C(2)-C(16)	113.0(3)
N(1)-C(2)-H(2)	109.3
C(3)-C(2)-H(2)	109.3
C(16)-C(2)-H(2)	109.3
O(3)-C(3)-C(2)	124.5(3)
O(3)-C(3)-C(4)	123.6(3)
C(2)-C(3)-C(4)	111.9(3)
C(5)-C(4)-C(3)	109.5(3)
C(5)-C(4)-C(1)	101.5(3)
C(3)-C(4)-C(1)	105.2(3)
C(5)-C(4)-C(19)	113.2(3)
C(3)-C(4)-C(19)	110.2(3)
C(1)-C(4)-C(19)	116.7(3)
C(6)-C(5)-C(10)	121.3(3)
C(6)-C(5)-C(4)	129.9(3)
C(10)-C(5)-C(4)	108.8(3)
C(7)-C(6)-C(5)	118.1(3)
C(7)-C(6)-H(6)	121.0
C(5)-C(6)-H(6)	121.0
C(6)-C(7)-C(8)	119.8(3)
C(6)-C(7)-H(7)	120.1
C(8)-C(7)-H(7)	120.1

C(9)-C(8)-C(7)	123.2(3)
C(9)-C(8)-H(8)	118.4
C(7)-C(8)-H(8)	118.4
C(8)-C(9)-C(10)	116.0(3)
C(8)-C(9)-C(23)	122.3(3)
C(10)-C(9)-C(23)	121.7(3)
C(5)-C(10)-N(2)	111.0(3)
C(5)-C(10)-C(9)	121.6(4)
N(2)-C(10)-C(9)	127.3(3)
O(1)-C(11)-O(2)	124.9(3)
O(1)-C(11)-N(1)	124.3(4)
O(2)-C(11)-N(1)	110.7(3)
O(2)-C(12)-C(15)	110.0(3)
O(2)-C(12)-C(14)	108.1(3)
C(15)-C(12)-C(14)	113.2(3)
O(2)-C(12)-C(13)	101.9(3)
C(15)-C(12)-C(13)	111.8(3)
C(14)-C(12)-C(13)	111.2(3)
C(12)-C(13)-H(13A)	109.5
C(12)-C(13)-H(13B)	109.5
H(13A)-C(13)-H(13B)	109.5
C(12)-C(13)-H(13C)	109.5
H(13A)-C(13)-H(13C)	109.5
H(13B)-C(13)-H(13C)	109.5
C(12)-C(14)-H(14A)	109.5
C(12)-C(14)-H(14B)	109.5
H(14A)-C(14)-H(14B)	109.5
C(12)-C(14)-H(14C)	109.5
H(14A)-C(14)-H(14C)	109.5
H(14B)-C(14)-H(14C)	109.5
C(12)-C(15)-H(15A)	109.5
C(12)-C(15)-H(15B)	109.5
H(15A)-C(15)-H(15B)	109.5

C(12)-C(15)-H(15C)	109.5
H(15A)-C(15)-H(15C)	109.5
H(15B)-C(15)-H(15C)	109.5
C(18)-C(16)-C(2)	111.5(3)
C(18)-C(16)-C(17)	110.0(3)
C(2)-C(16)-C(17)	112.2(3)
C(18)-C(16)-H(16)	107.6
C(2)-C(16)-H(16)	107.6
C(17)-C(16)-H(16)	107.6
C(16)-C(17)-H(17A)	109.5
C(16)-C(17)-H(17B)	109.5
H(17A)-C(17)-H(17B)	109.5
C(16)-C(17)-H(17C)	109.5
H(17A)-C(17)-H(17C)	109.5
H(17B)-C(17)-H(17C)	109.5
C(16)-C(18)-H(18A)	109.5
C(16)-C(18)-H(18B)	109.5
H(18A)-C(18)-H(18B)	109.5
C(16)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5
C(20)-C(19)-C(4)	112.8(3)
C(20)-C(19)-H(19A)	109.0
C(4)-C(19)-H(19A)	109.0
C(20)-C(19)-H(19B)	109.0
C(4)-C(19)-H(19B)	109.0
H(19A)-C(19)-H(19B)	107.8
C(21)-C(20)-C(19)	112.4(3)
C(21)-C(20)-H(20A)	109.1
C(19)-C(20)-H(20A)	109.1
C(21)-C(20)-H(20B)	109.1
C(19)-C(20)-H(20B)	109.1
H(20A)-C(20)-H(20B)	107.9

O(4)-C(21)-C(22)	122.2(3)
O(4)-C(21)-C(20)	120.5(3)
C(22)-C(21)-C(20)	117.3(3)
C(21)-C(22)-H(22A)	109.5
C(21)-C(22)-H(22B)	109.5
H(22A)-C(22)-H(22B)	109.5
C(21)-C(22)-H(22C)	109.5
H(22A)-C(22)-H(22C)	109.5
H(22B)-C(22)-H(22C)	109.5
C(9)-C(23)-H(23A)	109.5
C(9)-C(23)-H(23B)	109.5
H(23A)-C(23)-H(23B)	109.5
C(9)-C(23)-H(23C)	109.5
H(23A)-C(23)-H(23C)	109.5
H(23B)-C(23)-H(23C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table A.9. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **3.9a**. 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}
O(1)	41(2)	47(2)	66(2)	1(1)	1(1)	-6(1)
O(2)	46(2)	35(1)	68(2)	-2(1)	0(1)	-1(1)
O(3)	43(1)	43(1)	78(2)	-2(1)	-5(1)	-6(1)
O(4)	64(2)	46(2)	89(2)	-6(1)	1(2)	-6(2)
N(1)	41(2)	33(2)	60(2)	-4(2)	0(2)	-3(2)
N(2)	40(2)	40(2)	60(2)	1(2)	0(2)	-8(2)
C(1)	43(2)	35(2)	64(2)	-2(2)	-12(2)	3(2)
C(2)	43(2)	30(2)	72(2)	9(2)	-3(2)	-3(2)
C(3)	43(2)	30(2)	69(3)	6(2)	-11(2)	10(2)
C(4)	43(2)	33(2)	70(3)	-1(2)	-2(2)	-2(2)

C(5)	43(2)	38(2)	67(3)	6(2)	2(2)	-7(2)
C(6)	48(2)	42(2)	70(3)	-8(2)	-4(2)	-13(2)
C(7)	54(2)	49(2)	70(3)	9(2)	-12(2)	3(2)
C(8)	57(2)	47(2)	60(3)	4(2)	-1(2)	-2(2)
C(9)	41(2)	37(2)	67(3)	3(2)	9(2)	4(2)
C(10)	34(2)	46(2)	69(3)	0(2)	4(2)	-3(2)
C(11)	45(2)	40(2)	62(3)	8(2)	-1(2)	-2(2)
C(12)	54(3)	39(2)	72(3)	-8(2)	3(2)	-3(2)
C(13)	61(3)	69(3)	77(3)	-14(2)	9(2)	9(3)
C(14)	69(3)	60(2)	69(3)	-1(2)	-9(2)	8(2)
C(15)	87(3)	50(2)	78(3)	-5(2)	12(2)	-17(3)
C(16)	56(2)	37(2)	70(3)	6(2)	-1(2)	-7(2)
C(17)	61(2)	57(2)	75(3)	16(2)	-7(2)	3(2)
C(18)	48(2)	50(2)	74(3)	9(2)	5(2)	-1(2)
C(19)	51(2)	44(2)	70(3)	-7(2)	2(2)	-3(2)
C(20)	44(2)	43(2)	61(2)	0(2)	-1(2)	4(2)
C(21)	50(2)	47(2)	56(2)	-7(2)	-3(2)	0(2)
C(22)	59(3)	57(3)	81(3)	-18(2)	1(2)	7(2)
C(23)	63(2)	44(2)	70(2)	9(2)	2(2)	-2(2)

Table A.10. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^{3}) for **3.9a**.

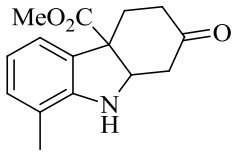
	x	y	z	U(eq)
H(2N)	-84	3227	-795	70(10)
H(1)	368	4475	-1440	57
H(2)	6015	3714	-1820	58
H(6)	6270	4692	290	64
H(7)	6268	3930	1290	69
H(8)	3557	3085	1437	66

H(13A)	4594	1927	-3815	104
H(13B)	5679	1957	-3046	104
H(13C)	5559	2671	-3524	104
H(14A)	2173	3293	-3697	99
H(14B)	43	3014	-3317	99
H(14C)	994	2583	-3981	99
H(15A)	1553	1384	-3181	108
H(15B)	56	1878	-2693	108
H(15C)	2250	1567	-2384	108
H(16)	4557	4025	-2964	65
H(17A)	3519	5211	-3213	97
H(17B)	3956	5451	-2409	97
H(17C)	2039	4909	-2587	97
H(18A)	8241	4216	-2737	86
H(18B)	7730	5028	-2503	86
H(18C)	7341	4780	-3306	86
H(19A)	3746	5722	-480	66
H(19B)	2140	5694	-1140	66
H(20A)	-605	5259	-379	59
H(20B)	1003	5298	280	59
H(22A)	-2392	6945	322	98
H(22B)	-2158	6210	762	98
H(22C)	-3259	6204	-4	98
H(23A)	-1127	2944	558	88
H(23B)	371	2517	1103	88
H(23C)	479	2339	272	88

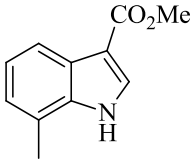
A.5 Experimental procedure for Chapter 3 section 3

A.5.1 Product distribution determination

A.5.1.1 Spectra data for compounds



methyl 8-methyl-2-oxo-2,3,4,4a,9,9a-hexahydro-1H-carbazole-4a-carboxylate (**3.13**) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.18 (d, *J* = 7.1 Hz, 1H), 6.95 (d, *J* = 7.4 Hz, 1H), 6.72 (t, *J* = 7.5 Hz, 1H), 4.89 (t, *J* = 3.5 Hz, 1H), 3.81 (s, 3H), 2.78 (dd, *J* = 16.5, 3.6 Hz, 1H), 2.65 (dd, *J* = 16.5, 3.5 Hz, 1H), 2.48 – 2.34 (m, 1H), 2.34 – 2.19 (m, 2H), 2.08 (s, 3H), 2.15 – 1.99 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.7, 174.4, 148.9, 130.3, 128.3, 122.3, 119.6, 119.2, 59.1, 54.9, 52.9, 42.9, 35.7, 31.7, 16.9. HRMS (ESI, m/z): $[M]^+$ calc.: 260.1287; found: 260.1283.



(E)-N-((E)-3-methylpent-3-en-2-ylidene)aniline oxide (**3.14**). Yield: 20%. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.74 (bs, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.92 (d, *J* = 3.0 Hz, 1H), 7.20 (t, *J* = 7.6 Hz, 1H), 7.08 (d, *J* = 7.2 Hz, 1H), 3.93 (s, 3H), 2.51 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0, 135.8, 130.9, 125.5, 123.9, 122.4, 120.8, 119.3, 109.3, 51.3, 16.7. HRMS (ESI, m/z): $[M]^-$ calc.: 188.0712; found: 188.0702.

A.5.1.2 Ratio determination

Indolenine was taken up in solvent and temperature adjusted. Acid was added followed by dropwise addition of the base. The reaction was then followed by TLC for disappearance of starting material. If toluene was solvent, the reaction was loaded onto a column and eluted. Otherwise, the solvent was removed under vacuum and then loaded onto column. A quick column separated **3.15** (more polar) from **3.13** and **3.14**.

^{1}H NMR was then used to determine the ratio and yield of each compound by utilizing the integration of the methyl ester. The peak for **3.13** appeared at 3.83 ppm and for **3.14** at 3.92 ppm (FigureA.1). By setting the peak at 3.8 ppm to 1 and plugging the integration of the peak at 3.9 into Scheme A.1, the mass of **3.13** and **3.14** could be determined and yields calculated. This was need to calculate the true ratio while **3.15** was being formed. Once **3.15** was eliminated, the ratio was simply read from the spectra.

$$mass\ \mathbf{3.13} = \left(\frac{mass\ ratio\ \mathbf{3.13}}{mass\ ratio\ of\ \mathbf{3.13 + 3.14}}\right) * y\ (total\ mass\ from\ column)$$

or

$$mass\ \mathbf{3.13} = \frac{259.3004y}{259.3004 + 189.2105x}\ where\ x = integral\ value\ at\ 3.9\ ppm$$

Scheme A.1 Ratio determination

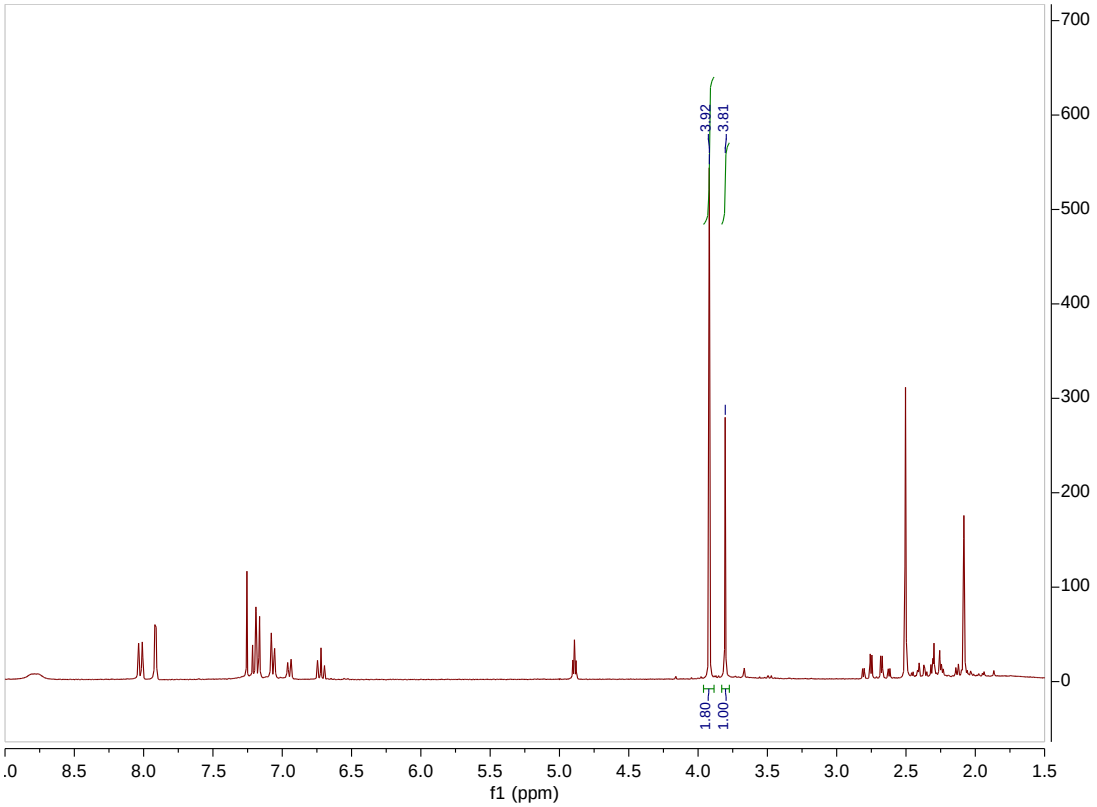


Figure A.1 Example spectrum in ratio determination

*A.5.2 Crystal and molecular structure determination of **3.15***

X-ray Diffraction Laboratory

Department of Chemistry

Texas A&M University

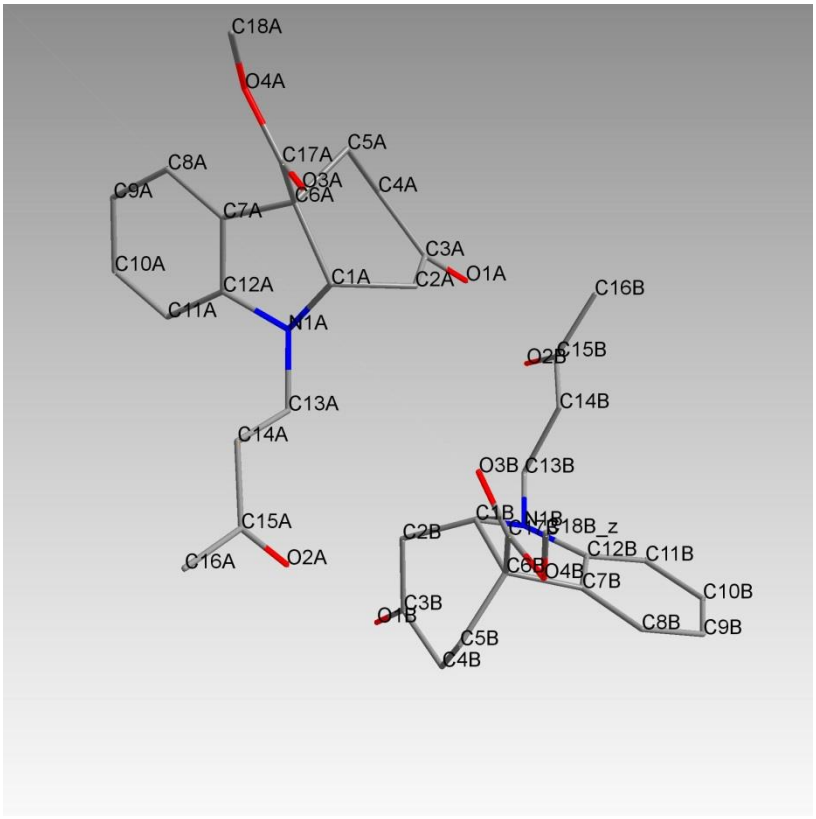


Table A.11. Crystal data and structure refinement for **3.15**.

Empirical formula	C36 H42 N2 O8	
Formula weight	630.72	
Temperature	110(2) K	
Wavelength	1.54178 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 8.5078(7) Å	α= 90.062(6)°.
	b = 9.5433(7) Å	β= 98.589(6)°.
	c = 20.0777(15) Å	γ = 90.427(6)°.
Volume	1611.8(2) $Å^3$	
Z	2	
Density (calculated)	1.300 Mg/m^3	
Absorption coefficient	0.750 mm^{-1}	

F(000)	672
Crystal size	0.10 x 0.05 x 0.01 mm^3
Theta range for data collection	4.45 to 59.99°.
Index ranges	-9<=h<=8, -10<=k<=10, -22<=l<=22
Reflections collected	28556
Independent reflections	4259 [R(int) = 0.1315]
Completeness to theta = 59.99°	88.6 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9925 and 0.9288
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4259 / 0 / 426
Goodness-of-fit on F^2	1.008
Final R indices [I>2sigma(I)]	R1 = 0.0643, wR2 = 0.0923
R indices (all data)	R1 = 0.1113, wR2 = 0.0973
Extinction coefficient	0.0041(2)
Largest diff. peak and hole	0.300 and -0.291 e.$Å^{-3}$

Table A.12. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **3.15**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1A)	3709(4)	3550(3)	3949(1)	43(1)
N(1A)	1800(4)	6405(3)	2809(1)	21(1)
C(1A)	544(5)	5512(4)	3027(2)	19(1)
O(2A)	2413(4)	5555(3)	794(1)	35(1)
C(2A)	1248(5)	4099(4)	3275(2)	25(1)
O(3A)	-2744(3)	5631(3)	3078(1)	34(1)
C(3A)	2532(5)	4255(4)	3869(2)	26(1)
O(4A)	-2480(3)	7110(3)	3943(1)	41(1)
C(4A)	2257(5)	5397(4)	4370(2)	30(1)
C(5A)	502(5)	5785(4)	4302(2)	25(1)
C(6A)	-98(5)	6383(4)	3584(2)	21(1)

C(7A)	591(5)	7840(4)	3506(2)	21(1)
C(8A)	371(5)	9067(4)	3836(2)	22(1)
C(9A)	1167(5)	10262(4)	3680(2)	28(1)
C(10A)	2164(5)	10201(4)	3189(2)	29(1)
C(11A)	2405(5)	8977(4)	2870(2)	26(1)
C(12A)	1615(5)	7788(4)	3033(2)	19(1)
C(13A)	2238(5)	6151(4)	2141(2)	22(1)
C(14A)	991(5)	6652(4)	1575(2)	28(1)
C(15A)	1297(5)	6279(4)	880(2)	25(1)
C(16A)	107(5)	6800(4)	304(2)	35(1)
C(17A)	-1897(5)	6307(4)	3486(2)	25(1)
C(18A)	-4193(5)	7034(5)	3919(2)	59(2)
C(1B)	5093(5)	2577(4)	1895(2)	21(1)
N(1B)	6527(4)	1724(3)	2141(1)	21(1)
O(1B)	7843(4)	4521(3)	1107(1)	40(1)
C(2B)	5634(5)	4020(4)	1672(2)	26(1)
O(2B)	8458(4)	2496(3)	4184(1)	37(1)
C(3B)	6630(5)	3846(4)	1127(2)	25(1)
O(3B)	1836(4)	2326(3)	1804(2)	44(1)
C(4B)	6028(5)	2770(4)	587(2)	27(1)
O(4B)	1561(4)	805(3)	954(1)	45(1)
C(5B)	4332(5)	2327(4)	614(2)	27(1)
C(6B)	4156(5)	1705(4)	1316(2)	22(1)
C(7B)	4940(5)	266(4)	1409(2)	20(1)
C(8B)	4558(5)	-986(4)	1082(2)	28(1)
C(9B)	5472(5)	-2147(4)	1259(2)	31(1)
C(10B)	6751(5)	-2068(4)	1773(2)	30(1)
C(11B)	7164(5)	-810(4)	2103(2)	26(1)
C(12B)	6273(5)	344(4)	1914(2)	20(1)
C(13B)	7387(5)	2001(4)	2818(2)	23(1)
C(14B)	6465(5)	1448(4)	3374(2)	29(1)
C(15B)	7278(5)	1773(4)	4070(2)	26(1)
C(16B)	6513(5)	1148(4)	4632(2)	33(1)

C(17B)	2391(6)	1635(5)	1391(2)	39(1)
C(18B)	-132(7)	797(7)	1071(3)	41(2)
C(1B')	136(18)	1953(16)	1664(7)	33(5)

Table A.13. Bond lengths [Å] and angles [°] for **3.15**.

O(1A)-C(3A)	1.202(5)
N(1A)-C(12A)	1.412(4)
N(1A)-C(13A)	1.465(4)
N(1A)-C(1A)	1.478(4)
C(1A)-C(2A)	1.533(5)
C(1A)-C(6A)	1.559(5)
C(1A)-H(1A)	1.0000
O(2A)-C(15A)	1.212(5)
C(2A)-C(3A)	1.499(5)
C(2A)-H(2AA)	0.9900
C(2A)-H(2AB)	0.9900
O(3A)-C(17A)	1.192(4)
C(3A)-C(4A)	1.525(5)
O(4A)-C(17A)	1.347(4)
O(4A)-C(18A)	1.453(5)
C(4A)-C(5A)	1.528(5)
C(4A)-H(4AA)	0.9900
C(4A)-H(4AB)	0.9900
C(5A)-C(6A)	1.565(5)
C(5A)-H(5AA)	0.9900
C(5A)-H(5AB)	0.9900
C(6A)-C(17A)	1.514(5)
C(6A)-C(7A)	1.522(5)
C(7A)-C(8A)	1.373(5)
C(7A)-C(12A)	1.382(5)
C(8A)-C(9A)	1.383(5)

C(8A)-H(8A)	0.9500
C(9A)-C(10A)	1.395(5)
C(9A)-H(9A)	0.9500
C(10A)-C(11A)	1.362(5)
C(10A)-H(10A)	0.9500
C(11A)-C(12A)	1.379(5)
C(11A)-H(11A)	0.9500
C(13A)-C(14A)	1.514(5)
C(13A)-H(13A)	0.9900
C(13A)-H(13B)	0.9900
C(14A)-C(15A)	1.500(5)
C(14A)-H(14A)	0.9900
C(14A)-H(14B)	0.9900
C(15A)-C(16A)	1.507(5)
C(16A)-H(16A)	0.9800
C(16A)-H(16B)	0.9800
C(16A)-H(16C)	0.9800
C(18A)-H(18A)	0.9800
C(18A)-H(18B)	0.9800
C(18A)-H(18C)	0.9800
C(1B)-N(1B)	1.494(5)
C(1B)-C(2B)	1.537(5)
C(1B)-C(6B)	1.545(5)
C(1B)-H(1B)	1.0000
N(1B)-C(12B)	1.398(5)
N(1B)-C(13B)	1.467(4)
O(1B)-C(3B)	1.219(5)
C(2B)-C(3B)	1.492(5)
C(2B)-H(2BA)	0.9900
C(2B)-H(2BB)	0.9900
O(2B)-C(15B)	1.207(5)
C(3B)-C(4B)	1.521(5)
O(3B)-C(17B)	1.210(5)

O(3B)-C(1B')	1.473(15)
C(4B)-C(5B)	1.509(5)
C(4B)-H(4BA)	0.9900
C(4B)-H(4BB)	0.9900
O(4B)-C(17B)	1.303(5)
O(4B)-C(18B)	1.493(6)
C(5B)-C(6B)	1.558(5)
C(5B)-H(5BA)	0.9900
C(5B)-H(5BB)	0.9900
C(6B)-C(7B)	1.531(5)
C(6B)-C(17B)	1.533(6)
C(7B)-C(8B)	1.376(5)
C(7B)-C(12B)	1.405(5)
C(8B)-C(9B)	1.375(5)
C(8B)-H(8B)	0.9500
C(9B)-C(10B)	1.384(5)
C(9B)-H(9B)	0.9500
C(10B)-C(11B)	1.388(5)
C(10B)-H(10B)	0.9500
C(11B)-C(12B)	1.363(5)
C(11B)-H(11B)	0.9500
C(13B)-C(14B)	1.547(5)
C(13B)-H(13C)	0.9900
C(13B)-H(13D)	0.9900
C(14B)-C(15B)	1.495(5)
C(14B)-H(14C)	0.9900
C(14B)-H(14D)	0.9900
C(15B)-C(16B)	1.506(5)
C(16B)-H(16D)	0.9800
C(16B)-H(16E)	0.9800
C(16B)-H(16F)	0.9800
C(18B)-H(18D)	0.9800
C(18B)-H(18E)	0.9800

C(18B)-H(18F)	0.9800
C(1B')-H(1BA)	0.9800
C(1B')-H(1BB)	0.9800
C(1B')-H(1BC)	0.9800

C(12A)-N(1A)-C(13A)	120.2(3)
C(12A)-N(1A)-C(1A)	108.7(3)
C(13A)-N(1A)-C(1A)	118.0(3)
N(1A)-C(1A)-C(2A)	109.6(3)
N(1A)-C(1A)-C(6A)	104.7(3)
C(2A)-C(1A)-C(6A)	113.6(3)
N(1A)-C(1A)-H(1A)	109.6
C(2A)-C(1A)-H(1A)	109.6
C(6A)-C(1A)-H(1A)	109.6
C(3A)-C(2A)-C(1A)	112.3(3)
C(3A)-C(2A)-H(2AA)	109.1
C(1A)-C(2A)-H(2AA)	109.1
C(3A)-C(2A)-H(2AB)	109.1
C(1A)-C(2A)-H(2AB)	109.1
H(2AA)-C(2A)-H(2AB)	107.9
O(1A)-C(3A)-C(2A)	123.2(4)
O(1A)-C(3A)-C(4A)	121.6(4)
C(2A)-C(3A)-C(4A)	115.2(4)
C(17A)-O(4A)-C(18A)	115.0(3)
C(3A)-C(4A)-C(5A)	111.3(3)
C(3A)-C(4A)-H(4AA)	109.4
C(5A)-C(4A)-H(4AA)	109.4
C(3A)-C(4A)-H(4AB)	109.4
C(5A)-C(4A)-H(4AB)	109.4
H(4AA)-C(4A)-H(4AB)	108.0
C(4A)-C(5A)-C(6A)	110.7(3)
C(4A)-C(5A)-H(5AA)	109.5
C(6A)-C(5A)-H(5AA)	109.5

C(4A)-C(5A)-H(5AB)	109.5
C(6A)-C(5A)-H(5AB)	109.5
H(5AA)-C(5A)-H(5AB)	108.1
C(17A)-C(6A)-C(7A)	114.9(3)
C(17A)-C(6A)-C(1A)	110.0(3)
C(7A)-C(6A)-C(1A)	103.4(3)
C(17A)-C(6A)-C(5A)	106.8(3)
C(7A)-C(6A)-C(5A)	110.6(3)
C(1A)-C(6A)-C(5A)	111.3(3)
C(8A)-C(7A)-C(12A)	120.8(4)
C(8A)-C(7A)-C(6A)	130.1(4)
C(12A)-C(7A)-C(6A)	109.1(3)
C(7A)-C(8A)-C(9A)	119.0(4)
C(7A)-C(8A)-H(8A)	120.5
C(9A)-C(8A)-H(8A)	120.5
C(8A)-C(9A)-C(10A)	119.6(4)
C(8A)-C(9A)-H(9A)	120.2
C(10A)-C(9A)-H(9A)	120.2
C(11A)-C(10A)-C(9A)	121.4(4)
C(11A)-C(10A)-H(10A)	119.3
C(9A)-C(10A)-H(10A)	119.3
C(10A)-C(11A)-C(12A)	118.7(4)
C(10A)-C(11A)-H(11A)	120.7
C(12A)-C(11A)-H(11A)	120.7
C(11A)-C(12A)-C(7A)	120.6(4)
C(11A)-C(12A)-N(1A)	127.6(4)
C(7A)-C(12A)-N(1A)	111.6(3)
N(1A)-C(13A)-C(14A)	112.8(3)
N(1A)-C(13A)-H(13A)	109.0
C(14A)-C(13A)-H(13A)	109.0
N(1A)-C(13A)-H(13B)	109.0
C(14A)-C(13A)-H(13B)	109.0
H(13A)-C(13A)-H(13B)	107.8

C(15A)-C(14A)-C(13A)	115.0(4)
C(15A)-C(14A)-H(14A)	108.5
C(13A)-C(14A)-H(14A)	108.5
C(15A)-C(14A)-H(14B)	108.5
C(13A)-C(14A)-H(14B)	108.5
H(14A)-C(14A)-H(14B)	107.5
O(2A)-C(15A)-C(14A)	121.1(4)
O(2A)-C(15A)-C(16A)	122.4(4)
C(14A)-C(15A)-C(16A)	116.4(4)
C(15A)-C(16A)-H(16A)	109.5
C(15A)-C(16A)-H(16B)	109.5
H(16A)-C(16A)-H(16B)	109.5
C(15A)-C(16A)-H(16C)	109.5
H(16A)-C(16A)-H(16C)	109.5
H(16B)-C(16A)-H(16C)	109.5
O(3A)-C(17A)-O(4A)	121.8(4)
O(3A)-C(17A)-C(6A)	127.3(4)
O(4A)-C(17A)-C(6A)	110.9(3)
O(4A)-C(18A)-H(18A)	109.5
O(4A)-C(18A)-H(18B)	109.5
H(18A)-C(18A)-H(18B)	109.5
O(4A)-C(18A)-H(18C)	109.5
H(18A)-C(18A)-H(18C)	109.5
H(18B)-C(18A)-H(18C)	109.5
N(1B)-C(1B)-C(2B)	108.9(3)
N(1B)-C(1B)-C(6B)	105.0(3)
C(2B)-C(1B)-C(6B)	113.7(3)
N(1B)-C(1B)-H(1B)	109.7
C(2B)-C(1B)-H(1B)	109.7
C(6B)-C(1B)-H(1B)	109.7
C(12B)-N(1B)-C(13B)	119.9(3)
C(12B)-N(1B)-C(1B)	109.4(3)
C(13B)-N(1B)-C(1B)	118.7(3)

C(3B)-C(2B)-C(1B)	109.8(3)
C(3B)-C(2B)-H(2BA)	109.7
C(1B)-C(2B)-H(2BA)	109.7
C(3B)-C(2B)-H(2BB)	109.7
C(1B)-C(2B)-H(2BB)	109.7
H(2BA)-C(2B)-H(2BB)	108.2
O(1B)-C(3B)-C(2B)	122.7(4)
O(1B)-C(3B)-C(4B)	121.7(4)
C(2B)-C(3B)-C(4B)	115.6(4)
C(17B)-O(3B)-C(1B')	102.3(7)
C(5B)-C(4B)-C(3B)	112.4(3)
C(5B)-C(4B)-H(4BA)	109.1
C(3B)-C(4B)-H(4BA)	109.1
C(5B)-C(4B)-H(4BB)	109.1
C(3B)-C(4B)-H(4BB)	109.1
H(4BA)-C(4B)-H(4BB)	107.9
C(17B)-O(4B)-C(18B)	109.4(4)
C(4B)-C(5B)-C(6B)	110.9(3)
C(4B)-C(5B)-H(5BA)	109.5
C(6B)-C(5B)-H(5BA)	109.5
C(4B)-C(5B)-H(5BB)	109.5
C(6B)-C(5B)-H(5BB)	109.5
H(5BA)-C(5B)-H(5BB)	108.0
C(7B)-C(6B)-C(17B)	111.7(3)
C(7B)-C(6B)-C(1B)	102.9(3)
C(17B)-C(6B)-C(1B)	110.4(3)
C(7B)-C(6B)-C(5B)	110.8(3)
C(17B)-C(6B)-C(5B)	109.3(3)
C(1B)-C(6B)-C(5B)	111.6(3)
C(8B)-C(7B)-C(12B)	119.5(4)
C(8B)-C(7B)-C(6B)	130.9(4)
C(12B)-C(7B)-C(6B)	109.7(3)
C(9B)-C(8B)-C(7B)	119.6(4)

C(9B)-C(8B)-H(8B)	120.2
C(7B)-C(8B)-H(8B)	120.2
C(8B)-C(9B)-C(10B)	120.4(4)
C(8B)-C(9B)-H(9B)	119.8
C(10B)-C(9B)-H(9B)	119.8
C(9B)-C(10B)-C(11B)	120.8(4)
C(9B)-C(10B)-H(10B)	119.6
C(11B)-C(10B)-H(10B)	119.6
C(12B)-C(11B)-C(10B)	118.5(4)
C(12B)-C(11B)-H(11B)	120.8
C(10B)-C(11B)-H(11B)	120.8
C(11B)-C(12B)-N(1B)	128.4(4)
C(11B)-C(12B)-C(7B)	121.3(4)
N(1B)-C(12B)-C(7B)	110.3(4)
N(1B)-C(13B)-C(14B)	111.9(3)
N(1B)-C(13B)-H(13C)	109.2
C(14B)-C(13B)-H(13C)	109.2
N(1B)-C(13B)-H(13D)	109.2
C(14B)-C(13B)-H(13D)	109.2
H(13C)-C(13B)-H(13D)	107.9
C(15B)-C(14B)-C(13B)	113.1(3)
C(15B)-C(14B)-H(14C)	109.0
C(13B)-C(14B)-H(14C)	109.0
C(15B)-C(14B)-H(14D)	109.0
C(13B)-C(14B)-H(14D)	109.0
H(14C)-C(14B)-H(14D)	107.8
O(2B)-C(15B)-C(14B)	123.3(4)
O(2B)-C(15B)-C(16B)	121.3(4)
C(14B)-C(15B)-C(16B)	115.4(4)
C(15B)-C(16B)-H(16D)	109.5
C(15B)-C(16B)-H(16E)	109.5
H(16D)-C(16B)-H(16E)	109.5
C(15B)-C(16B)-H(16F)	109.5

H(16D)-C(16B)-H(16F)	109.5
H(16E)-C(16B)-H(16F)	109.5
O(3B)-C(17B)-O(4B)	124.2(5)
O(3B)-C(17B)-C(6B)	122.3(4)
O(4B)-C(17B)-C(6B)	113.4(4)
O(4B)-C(18B)-H(18D)	109.5
O(4B)-C(18B)-H(18E)	109.5
O(4B)-C(18B)-H(18F)	109.5
O(3B)-C(1B')-H(1BA)	109.5
O(3B)-C(1B')-H(1BB)	109.5
H(1BA)-C(1B')-H(1BB)	109.5
O(3B)-C(1B')-H(1BC)	109.5
H(1BA)-C(1B')-H(1BC)	109.5
H(1BB)-C(1B')-H(1BC)	109.5

Symmetry transformations used to generate equivalent atoms:

Table A.14. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **3.15**. 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}
O(1A)	39(2)	35(2)	55(2)	3(2)	4(2)	9(2)
N(1A)	22(2)	27(2)	16(2)	-2(2)	6(2)	-2(2)
C(1A)	22(3)	14(2)	21(2)	-2(2)	4(2)	-5(2)
O(2A)	37(2)	44(2)	26(2)	1(2)	8(1)	7(2)
C(2A)	32(3)	24(3)	19(2)	0(2)	4(2)	-4(2)
O(3A)	29(2)	41(2)	28(2)	-11(2)	-4(1)	-10(2)
C(3A)	29(3)	23(3)	30(3)	8(2)	12(2)	-5(2)
O(4A)	25(2)	47(2)	52(2)	-26(2)	13(2)	-12(2)
C(4A)	33(3)	35(3)	23(2)	3(2)	4(2)	-8(2)
C(5A)	30(3)	23(3)	20(2)	7(2)	2(2)	-4(2)

C(6A)	20(3)	29(3)	15(2)	-5(2)	4(2)	-6(2)
C(7A)	20(3)	23(3)	20(2)	6(2)	2(2)	-4(2)
C(8A)	27(3)	16(3)	23(2)	-6(2)	3(2)	-3(2)
C(9A)	38(3)	17(3)	29(3)	0(2)	3(2)	-7(2)
C(10A)	29(3)	22(3)	34(3)	9(2)	0(2)	-9(2)
C(11A)	23(3)	26(3)	28(3)	2(2)	3(2)	-2(2)
C(12A)	22(3)	21(3)	14(2)	-2(2)	-2(2)	-2(2)
C(13A)	29(3)	21(3)	17(2)	-2(2)	6(2)	-6(2)
C(14A)	31(3)	32(3)	21(2)	2(2)	6(2)	-1(2)
C(15A)	29(3)	27(3)	22(2)	3(2)	9(2)	-2(2)
C(16A)	31(3)	48(3)	25(3)	11(2)	-1(2)	0(2)
C(17A)	32(3)	21(3)	24(3)	3(2)	11(2)	1(2)
C(18A)	21(4)	67(4)	93(4)	-40(3)	21(3)	-12(3)
C(1B)	23(3)	18(3)	22(2)	-2(2)	3(2)	-1(2)
N(1B)	22(2)	23(2)	15(2)	1(2)	-5(1)	-3(2)
O(1B)	35(2)	44(2)	40(2)	-2(2)	6(2)	-20(2)
C(2B)	31(3)	21(3)	25(2)	0(2)	1(2)	-2(2)
O(2B)	41(2)	43(2)	25(2)	-1(2)	1(2)	-12(2)
C(3B)	27(3)	26(3)	20(2)	6(2)	-2(2)	-1(2)
O(3B)	23(2)	58(2)	55(2)	5(2)	15(2)	-2(2)
C(4B)	29(3)	35(3)	15(2)	1(2)	3(2)	0(2)
O(4B)	21(2)	53(2)	58(2)	-4(2)	-4(2)	-9(2)
C(5B)	34(3)	28(3)	18(2)	2(2)	2(2)	-7(2)
C(6B)	18(3)	27(3)	24(2)	4(2)	6(2)	-4(2)
C(7B)	24(3)	20(3)	17(2)	1(2)	4(2)	-7(2)
C(8B)	29(3)	30(3)	22(2)	1(2)	-4(2)	-4(2)
C(9B)	49(4)	20(3)	22(2)	-1(2)	4(2)	-7(2)
C(10B)	42(3)	24(3)	23(3)	4(2)	7(2)	-5(2)
C(11B)	28(3)	27(3)	23(2)	3(2)	4(2)	-2(2)
C(12B)	26(3)	20(3)	15(2)	-1(2)	2(2)	-5(2)
C(13B)	27(3)	25(3)	16(2)	2(2)	-1(2)	-6(2)
C(14B)	38(3)	31(3)	14(2)	4(2)	-4(2)	-12(2)
C(15B)	24(3)	25(3)	28(3)	1(2)	-2(2)	-2(2)

C(16B)	35(3)	40(3)	24(3)	5(2)	5(2)	2(2)
C(17B)	24(3)	45(4)	44(3)	28(3)	-6(3)	-4(3)
C(18B)	24(5)	45(5)	53(5)	-8(4)	2(3)	-11(3)

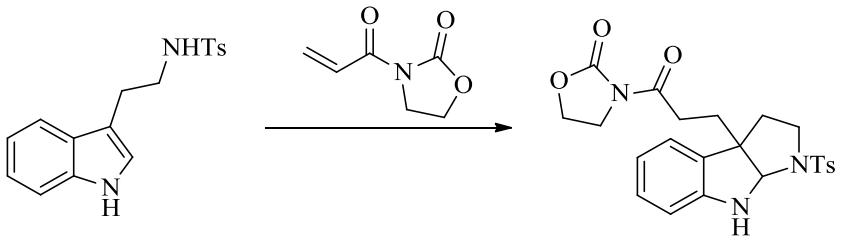
Table A.15. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^{3}) for **3.15**.

	x	y	z	U(eq)
H(1A)	-326	5357	2640	23
H(2AA)	391	3492	3400	30
H(2AB)	1690	3633	2904	30
H(4AA)	2890	6239	4291	36
H(4AB)	2625	5066	4834	36
H(5AA)	353	6495	4647	30
H(5AB)	-133	4945	4381	30
H(8A)	-318	9094	4167	27
H(9A)	1036	11120	3905	34
H(10A)	2687	11030	3074	35
H(11A)	3102	8944	2542	31
H(13A)	2403	5134	2085	26
H(13B)	3257	6637	2110	26
H(14A)	-51	6250	1642	34
H(14B)	914	7684	1607	34
H(16A)	458	6551	-124	52
H(16B)	21	7821	334	52
H(16C)	-932	6367	325	52
H(18A)	-4715	7375	3482	89
H(18B)	-4506	7616	4279	89
H(18C)	-4515	6060	3980	89
H(1B)	4437	2694	2265	26

H(2BA)	4693	4595	1506	31
H(2BB)	6255	4511	2061	31
H(4BA)	6100	3171	138	32
H(4BB)	6718	1935	647	32
H(5BA)	4001	1615	260	32
H(5BB)	3626	3146	522	32
H(8B)	3668	-1048	735	33
H(9B)	5226	-3008	1028	37
H(10B)	7352	-2885	1901	35
H(11B)	8048	-754	2452	31
H(13C)	7563	3023	2877	28
H(13D)	8440	1546	2865	28
H(14C)	5393	1868	3310	35
H(14D)	6331	420	3324	35
H(16D)	5412	1468	4595	50
H(16E)	7104	1446	5066	50
H(16F)	6527	124	4600	50
H(18D)	-553	1750	1023	61
H(18E)	-195	452	1526	61
H(18F)	-759	182	739	61
H(1BA)	-393	2551	1303	49
H(1BB)	-350	2090	2072	49
H(1BC)	19	969	1523	49

A.6 Experimental procedure for Chapter 4

A.6.1 General experimental procedure



A.6.1.1 Using Et_3B

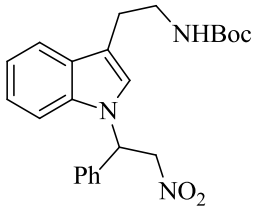
BOX ligand (0.12 mmol) and $Cu(OTf)_2$ (0.10 mmol) were stirred in dioxane (2 mL) for 1 hour. The Michael acceptor (0.75 mmol) was added and stirred for 10 min prior to the dropwise addition of the activated tryptamine derivative. The flask was rinsed with 1mL of dioxane and also added. The tryptamine derivative (0.50 mmol) was activated by stirring in dioxane (2 mL) with KO*t*-Bu (0.55 mmol) for 30 min prior to addition of Et_3B (0.55 mmol) and subsequent stirring for 1 hour. The reaction was diluted with EtOAc and quenched with H_2O. The aqueous layer was extracted with EtOAc (3x). The combined organic layers were dried, filtered, and concentrated prior to column chromatography.

A.6.1.2 Using $SnCl_4$

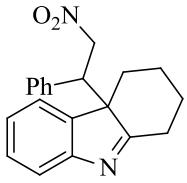
Tryptamine derivative (0.20 mmol), Michael acceptor (0.20 mmol), and (*S*)-BINOL (0.04 mmol) were added to a flask. CH_2Cl_2 (1.5 mL) was added followed by a 1 M solution of $SnCl_4$ (0.24 mmol) in CH_2Cl_2 and stirred for 1 hour. The reaction was

quenched by diluting with 1 mL of MeCN and 1 mL of 1 M HCl followed by 5 mL H_2O. The aqueous layer was then extracted with EtOAc (3x) and then the combined organic layers was washed with saturated aqueous $NaHCO_3$. The organic layer was dried, filtered, and concentrated prior to column chromatography.

A.6.2 Spectra data for compounds

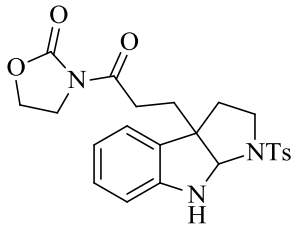


***tert*-butyl (2-(1-(2-nitro-1-phenylethyl)-1H-indol-3-yl)ethyl)carbamate** (**A.1**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 – 7.54 (m, 1H), 7.43 – 7.06 (m, 9H), 7.03 (s, 1H), 6.37 (dt, *J* = 18.9, 9.4 Hz, 1H), 5.17 (qd, *J* = 13.3, 7.6 Hz, 2H), 3.43 (dd, *J* = 13.0, 6.6 Hz, 2H), 2.93 (t, *J* = 7.0 Hz, 2H), 1.45 (s, 9H).



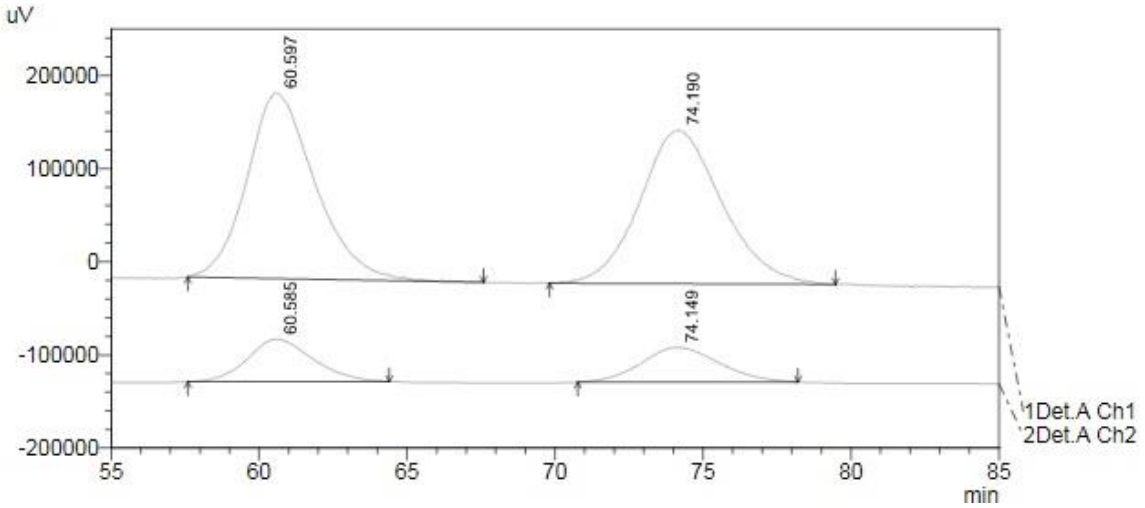
4a-(2-nitro-1-phenylethyl)-2,3,4,4a-tetrahydro-1H-carbazole (**4.3**). Two diastereomers. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (d, *J* = 13.7 Hz, 1H), 7.65 – 6.96 (m, 17H), 5.06 (ddd, *J* = 10.1, 6.5, 3.4 Hz, 1H), 4.67 – 4.47 (m, 4H), 4.38 (ddd, *J* = 12.7, 3.4,

1.3 Hz, 1H), 3.53 – 3.25 (m, 4H), 1.82 – 1.60 (m, 3H), 1.56 – 1.43 (m, 1H), 1.39 – 1.21 (m, 2H), 1.16 (t, *J* = 7.0 Hz, 1H), 0.92 – 0.79 (m, 5H).



3-(3-(1-tosyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indol-3a-yl)propanoyl)oxazolidin-2-one (**A.2**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.07 (td, *J* = 7.7, 1.2 Hz, 1H), 6.99 (d, *J* = 6.8 Hz, 1H), 6.73 (td, *J* = 7.4, 0.9 Hz, 1H), 6.60 (d, *J* = 7.8 Hz, 1H), 5.14 (s, 1H), 4.86 (s, 1H), 4.37 – 4.28 (m, 2H), 4.03 – 3.94 (m, 1H), 3.92 – 3.83 (m, 1H), 3.46 – 3.37 (m, 1H), 3.09 (td, *J* = 10.7, 5.9 Hz, 1H), 2.93 – 2.80 (m, 1H), 2.78 – 2.65 (m, 1H), 2.42 (s, 3H), 2.19 – 2.09 (m, 1H), 2.07 – 1.99 (m, 1H), 1.95 – 1.85 (m, 1H), 1.81 – 1.69 (m, 1H). Chiral HPLC (Chiralpak IC, 50:50 hexane:*i*PrOH, 0.5 mL/min)

Chiral Chromatogram for **A.2**

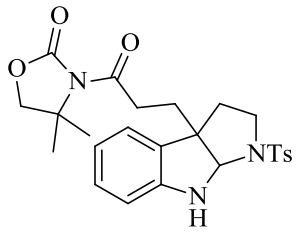


Peak Table Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	60.597	31993540	199331	50.096	54.686
2	74.190	31871387	165170	49.904	45.314
Total		63864927	364501	100.000	100.000

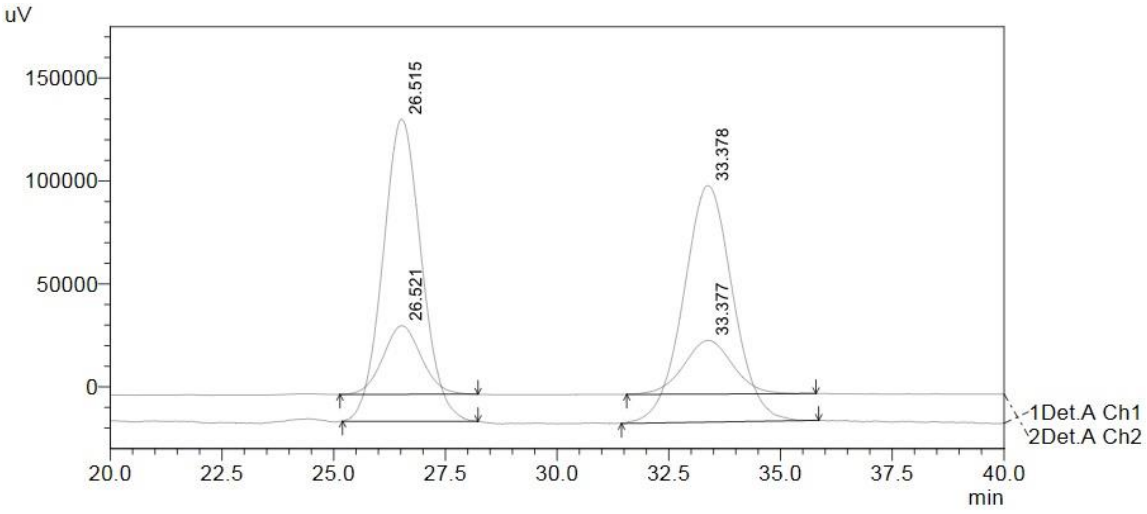
Peak Table Detector A Ch2 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	60.585	7064223	45646	50.848	55.091
2	74.149	6828508	37209	49.152	44.909
Total		13892731	82855	100.000	100.000



4,4-dimethyl-3-(3-(1-tosyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indol-3a-yl)propanoyl)oxazolidin-2-one (**A.3**). Spectra contains 1:1 product to starting tryptamine derivative. Chiral HPLC (Chiralpak IC, 50:50 hexane:*i*PrOH, 1.0 mL/min)

Chiral Chromatogram for **A.3**

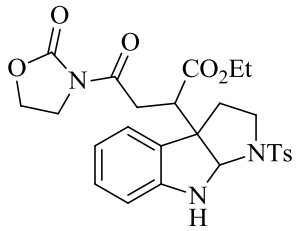


Peak Table Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.515	8837756	146871	49.956	56.101
2	33.378	8853428	114924	50.044	43.899
Total		17691183	261795	100.000	100.000

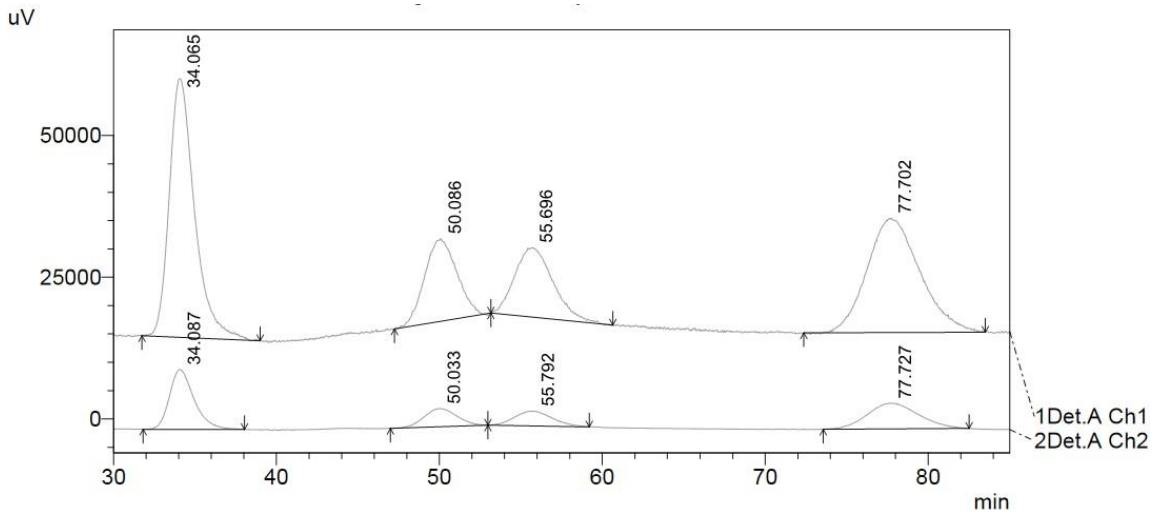
Peak Table Detector A Ch2 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.521	1992809	33361	50.063	56.164
2	33.377	1987777	26039	49.937	43.836
Total		3980586	59400	100.000	100.000



ethyl 4-oxo-4-(2-oxooxazolidin-3-yl)-2-(1-tosyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indol-3a-yl)butanoate (**A.4**). Two conformers. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 – 7.63 (m, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.16 – 6.95 (m, 2H), 6.79 – 6.69 (m, 1H), 6.63 (dd, *J* = 10.9, 7.8 Hz, 1H), 5.53 (s, 0.7H), 5.28 (s, 0.3H), 4.93 (s, 0.3H), 4.89 (s, 0.7H), 4.32 (t, *J* = 8.2 Hz, 2H), 4.02 – 3.93 (m, 2H), 3.92 – 3.78 (m, 2H), 3.48 – 3.00 (m, 4H), 2.81 (dd, *J* = 18.3, 3.1 Hz, 1H), 2.42 (s, 0.3H), 2.42 (s, 0.7H), 2.21 – 2.09 (m, 1H), 1.98 – 1.89 (m, 1H), 1.19 (t, *J* = 7.1 Hz, 0.3H), 1.12 (t, *J* = 7.1 Hz, 0.7H). The dr for the BOX ligand was determined to be 2.4:1 and the dr for (*R*)-BINOL was calculated to be 1.9:1 with the greater isomer having 76% ee by chiral HPLC (Chiralpak IC, 50:50 hexane:*i*PrOH, 0.75 mL/min)

Chiral Chromatogram for **A.4** from BOX ligand



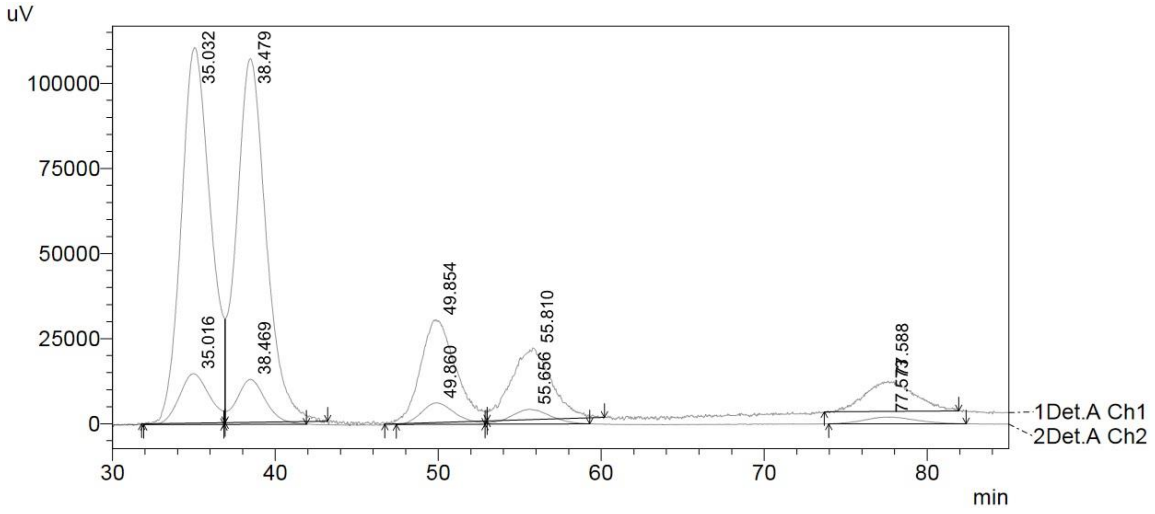
Peak Table Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	34.065	4930038	45632	36.637	49.267
2	50.086	1996126	14554	14.834	15.713
3	55.696	1998018	12273	14.848	13.251
4	77.702	4532330	20162	33.681	21.768
Total		13456512	92621	100.000	100.000

Peak Table Detector A Ch2 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	34.087	1117025	10557	37.428	50.428
2	50.033	450421	3212	15.092	15.342
3	55.792	417976	2620	14.005	12.514
4	77.727	999026	4547	33.474	21.717
Total		2984449	20935	100.000	100.000

Chiral Chromatogram for **A.4** from (*S*)-BINOL ligand



Peak Table Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	35.032	13809116	110355	36.906	39.772
2	38.479	13559417	106829	36.239	38.501
3	49.854	4549530	30285	12.159	10.915
4	55.810	3633192	21080	9.710	7.597
5	77.588	1865822	8922	4.987	3.215
Total		37417078	277471	100.000	100.000

Peak Table Detector A Ch2 254nm

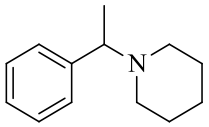
Peak#	Ret. Time	Area	Height	Area %	Height %
1	35.016	1911042	14865	33.821	36.527
2	38.469	1649519	13165	29.193	32.349
3	49.860	910659	6296	16.117	15.470
4	55.656	731799	4319	12.951	10.612
5	77.573	447417	2052	7.918	5.041
Total		5650436	40695	100.000	100.000

A.7 Experimental procedure for Chapter 5

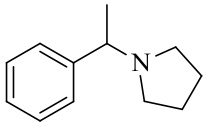
A.7.1 General experimental procedure

Styrene derivative (1.4 mmol) was added to a solution of iron (II) chloride (9.3 mg, 0.07 mmol) in THF (3 mL) at room temperature. Cyclopentylmagnesium bromide (1.4 mL, 2M in Et_2O, 2.8 mmol) was added dropwise and the reaction stirred for 2 hours. The reaction was cooled to 0 ^oC and a solution of hydroxylamine (0.7 mmol) in THF (1 mL) was added over 1 hour. After 30 min, the reaction was quenched with sat. aq. $NaHCO_3$ and Et_2O was added. The aqueous layer was extracted with Et_2O (3x). The combined organic layer was then extracted with 1M HCl (3x). NaOH pellets were added until the solution was strongly basic. The aqueous layer was then extracted with Et_2O (3x), dried, and concentrated *in vacuo* to give the product as a clear to yellow oil that was pure by ^1H NMR.

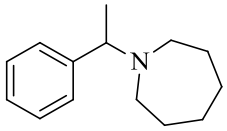
A.7.2 Spectra data for compounds



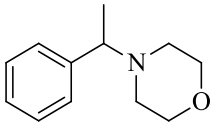
1-(1-phenylethyl)piperidine (5.3a). Prepared according to the general procedure in 71% yield as light yellow oil. Spectral data for this compound were consistent with those found in the literature.[60]



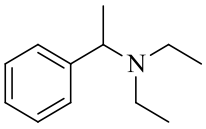
1-(1-phenylethyl)pyrrolidine (**5.3b**). Prepared according to the general procedure in 70% yield as light yellow oil. Spectral data for this compound were consistent with those found in the literature.[60]



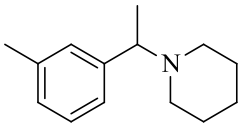
1-(1-phenylethyl)azepane (**5.3c**). Prepared according to the general procedure in 61% yield as light yellow oil. Spectral data for this compound were consistent with those found in the literature.[60]



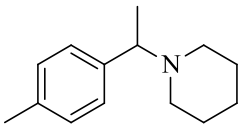
4-(1-phenylethyl)morpholine (**5.3d**). Prepared according to the general procedure in 52% yield as light yellow oil. Spectral data for this compound were consistent with those found in the literature.[60]



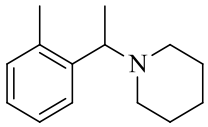
N,N-diethyl-1-phenylethanamine (**5.3e**). Prepared according to the general procedure in 80% yield as light yellow oil. Spectral data for this compound were consistent with those found in the literature.[61]



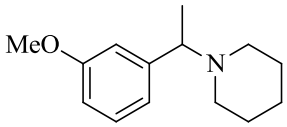
1-(1-(m-tolyl)ethyl)piperidine (**5.3g**). Prepared according to the general procedure in 66% yield as light yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (t, *J* = 7.3 Hz, 1H), 7.16 – 7.00 (m, 3H), 3.34 (q, *J* = 6.8 Hz, 1H), 2.48 – 2.25 (m, 4H), 2.35 (s, 3H), 1.62 – 1.50 (m, 4H), 1.45 – 1.31 (m, 2H), 1.36 (d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.0, 137.7, 128.6, 128.0, 127.6, 125.0, 65.5, 51.8, 26.4, 24.7, 21.6, 19.7. HRMS (ESI, m/z): $[M]^+$ calc.: 204.1752; found: 204.1753.



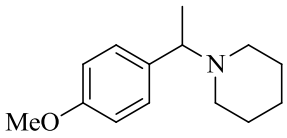
1-(1-(p-tolyl)ethyl)piperidine (**5.3h**). Prepared according to the general procedure in 62% yield as light yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21 – 7.15 (m, 2H), 7.15 – 7.09 (m, 2H), 3.38 (q, J = 6.8 Hz, 1H), 2.47 – 2.26 (m, 4H), 2.33 (s, 3H), 1.61 – 1.50 (m, 4H), 1.43 – 1.32 (m, 2H), 1.36 (d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.7, 136.4, 128.8, 127.9, 65.0, 51.6, 26.4, 24.7, 21.2, 19.6. HRMS (ESI, m/z): $[M]^+$ calc.: 204.1752; found: 204.1750.



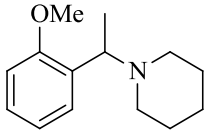
1-(1-(o-tolyl)ethyl)piperidine (**5.3i**). Prepared according to the general procedure in 49% yield as light yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 (d, J = 7.4 Hz, 1H), 7.23 – 7.09 (m, 3H), 3.56 (q, J = 6.6 Hz, 1H), 2.55 – 2.41 (m, 2H), 2.37 (s, 3H), 2.39 – 2.28 (m, 2H), 1.59 – 1.49 (m, 4H), 1.48 – 1.36 (m, 2H), 1.29 (d, J = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.7, 136.0, 130.4, 126.8, 126.2, 125.9, 60.9, 51.8, 26.5, 24.9, 19.7, 18.6. HRMS (ESI, m/z): $[M]^+$ calc.: 204.1752; found: 204.1759.



1-(1-(4-methoxyphenyl)ethyl)piperidine (**5.3j**). Prepared according to the general procedure in 55% yield as light yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 – 7.18 (m, 1H), 6.92 – 6.86 (m, 2H), 6.80 – 6.74 (m, 1H), 3.80 (s, 3H), 3.36 (q, J = 6.8 Hz, 1H), 2.46 – 2.29 (m, 4H), 1.62 – 1.48 (m, 4H), 1.44 – 1.36 (m, 2H), 1.36 (d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.5, 145.9, 129.0, 120.2, 113.5, 111.9, 65.3, 55.2, 51.6, 26.4, 24.7, 19.6. HRMS (ESI, m/z): $[M]^+$ calc.: 220.1701; found: 220.1692.

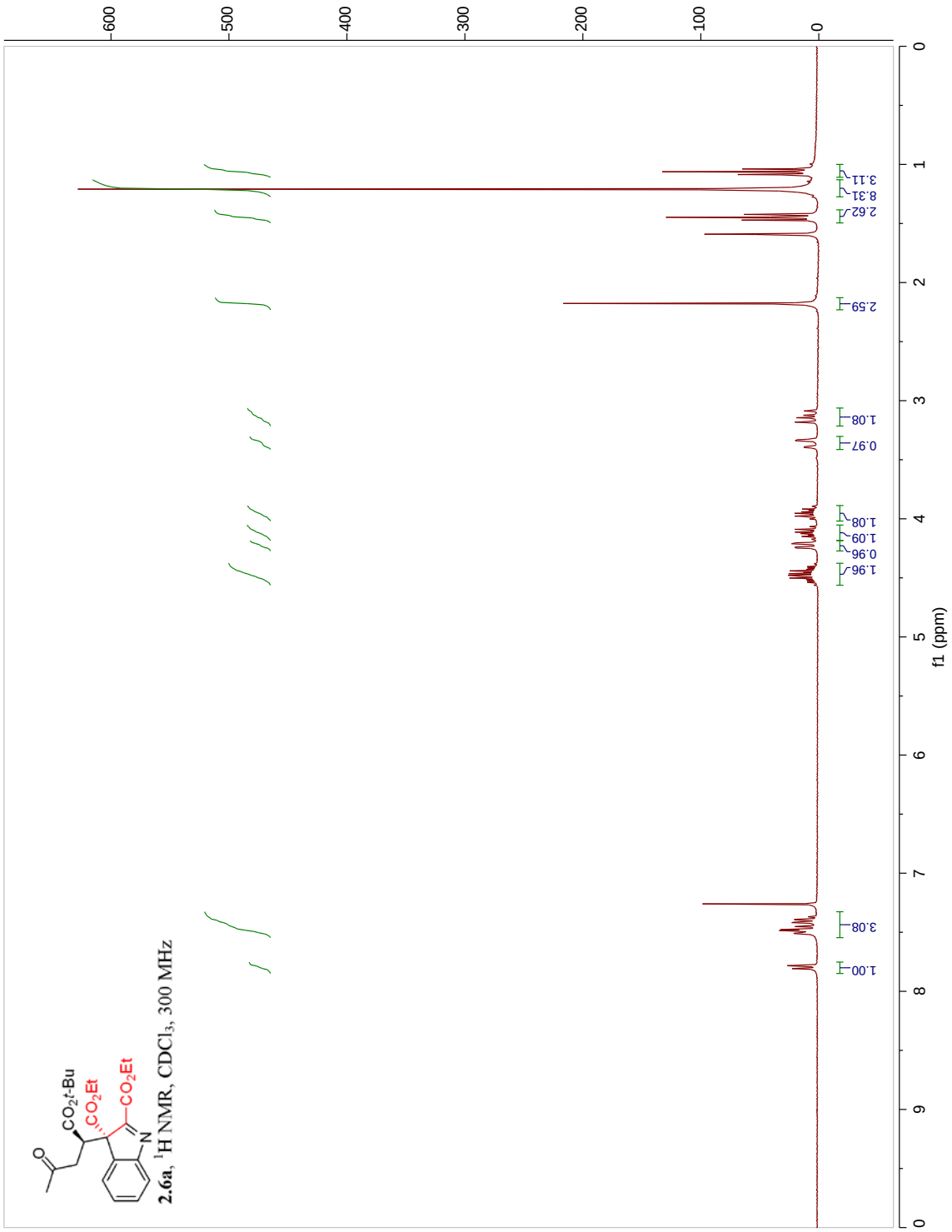


1-(1-(3-methoxyphenyl)ethyl)piperidine (**5.3k**). Prepared according to the general procedure in 55% yield as light yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 – 7.17 (m, 2H), 6.89 – 6.80 (m, 2H), 3.80 (s, 3H), 3.38 (q, J = 6.8 Hz, 1H), 2.43 – 2.28 (m, 4H), 1.61 – 1.48 (m, 4H), 1.43 – 1.32 (m, 2H), 1.36 (d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.5, 135.7, 128.9, 113.4, 64.6, 55.3, 51.5, 26.3, 24.7, 19.4. HRMS (ESI, m/z): $[M]^+$ calc.: 220.1701; found: 220.1711.



1-(1-(2-methoxyphenyl)ethyl)piperidine (**5.3l**). Prepared according to the general procedure in 24% yield as light yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 (dd, J = 7.6, 1.8 Hz, 1H), 7.19 (ddt, J = 9.0, 7.1, 3.5 Hz, 1H), 6.94 (td, J = 7.5, 1.2 Hz, 1H), 6.86 (d, J = 8.1 Hz, 1H), 3.97 (q, J = 6.8 Hz, 1H), 3.81 (s, 3H), 2.52 – 2.28 (m, 4H), 1.61 – 1.50 (m, 4H), 1.43 – 1.34 (m, 2H), 1.31 (d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.2, 132.3, 128.1, 127.4, 120.6, 110.7, 56.4, 55.6, 51.7, 26.4, 24.8, 19.8. HRMS (ESI, m/z): $[M]^+$ calc.: 204.1752; found: 204.1759.

APPENDIX B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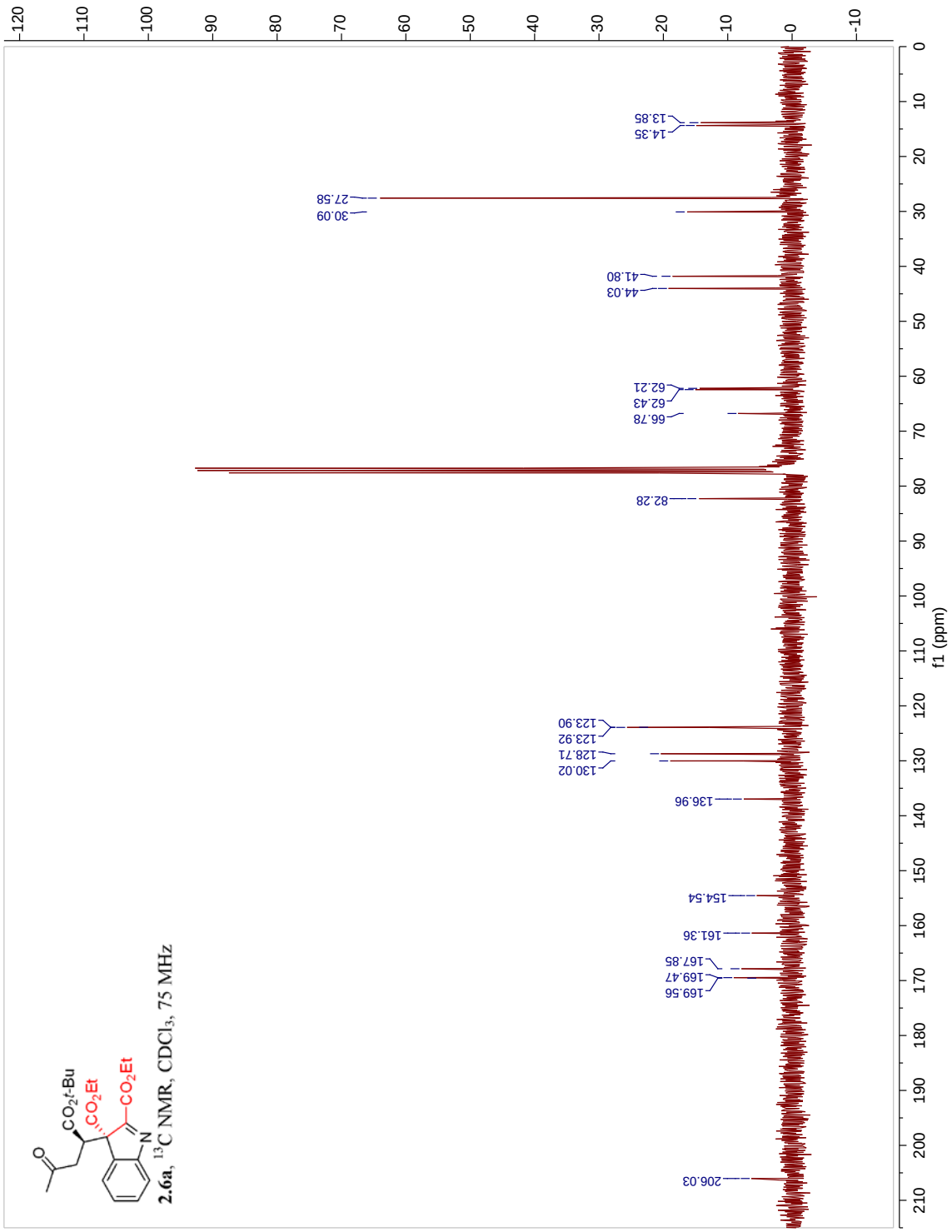
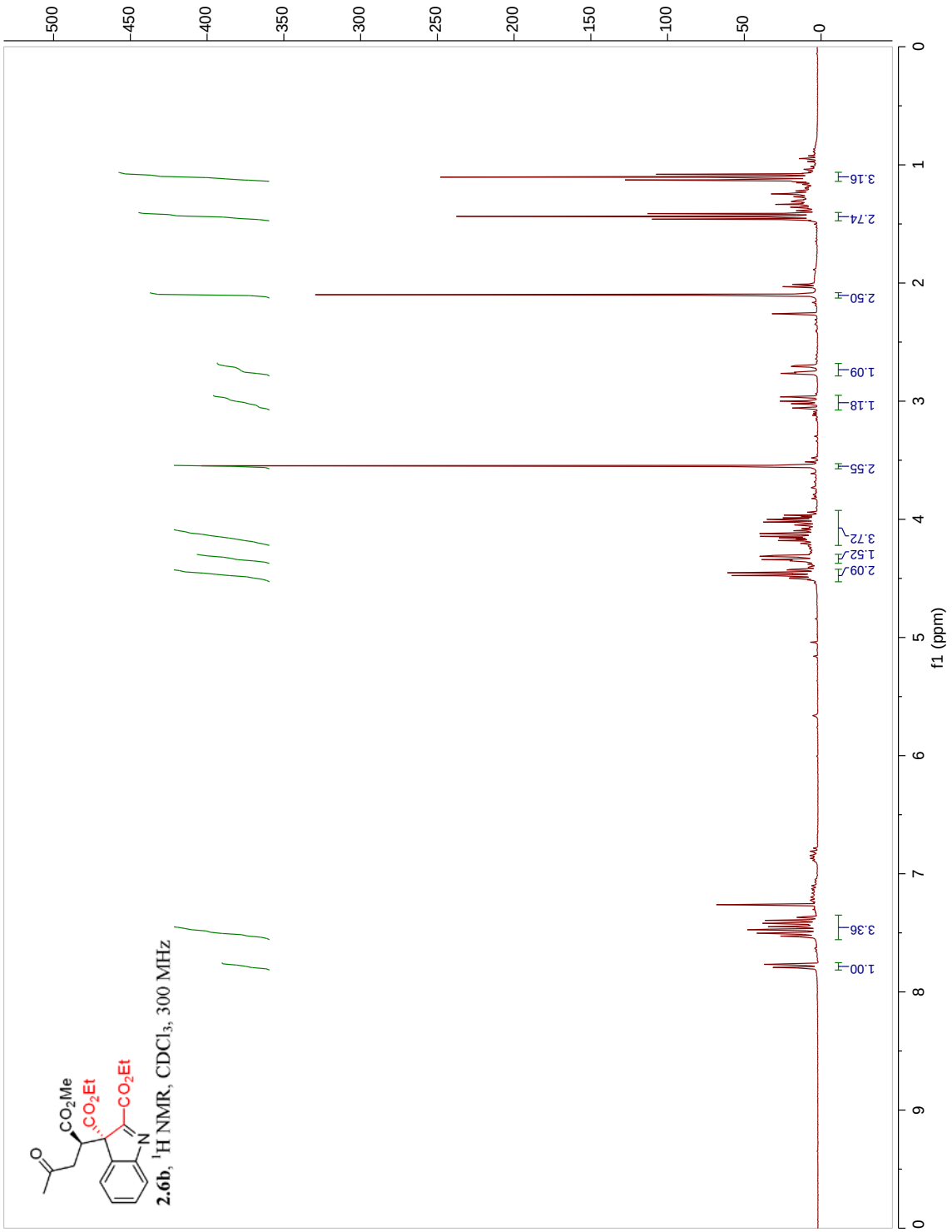
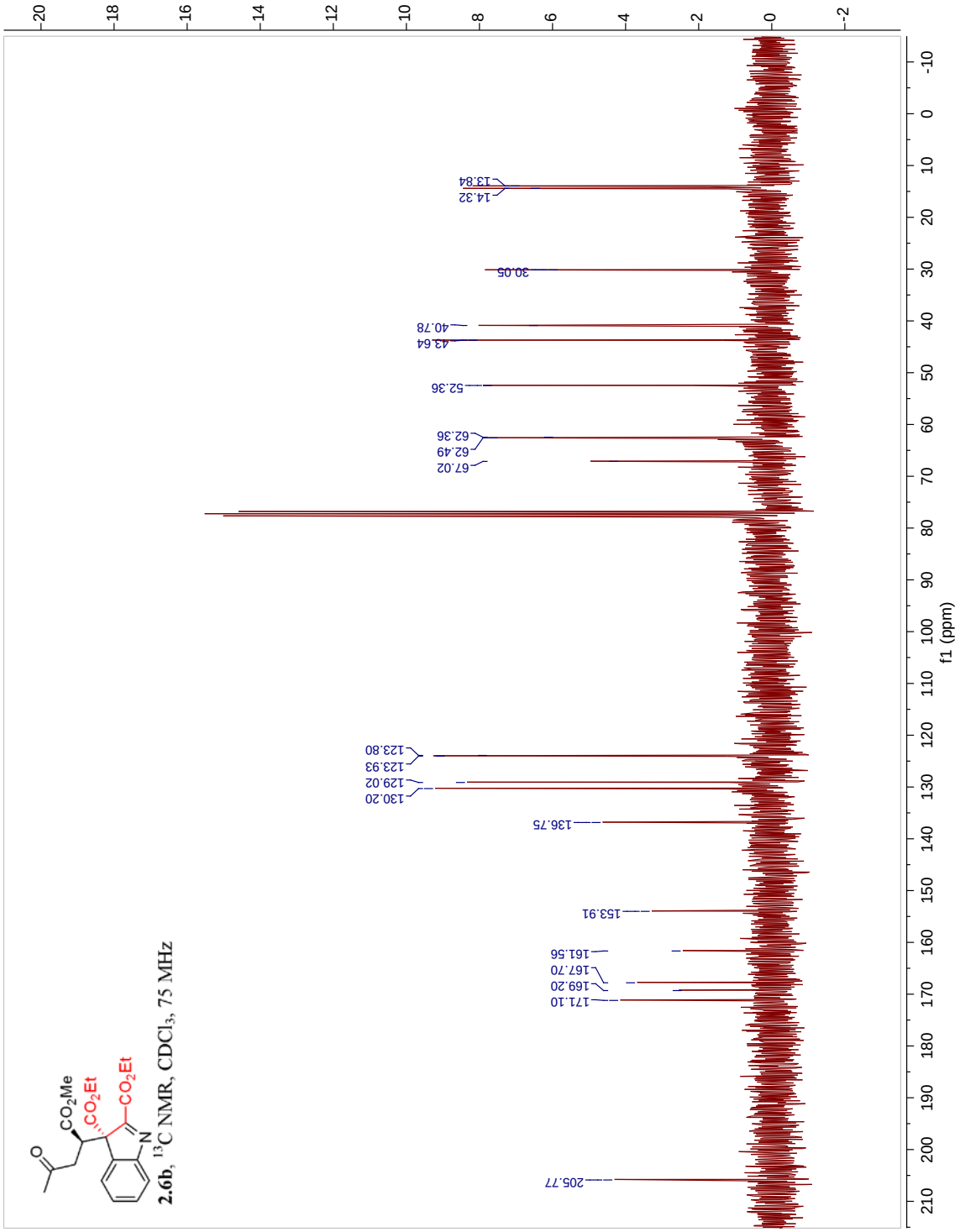
500
400
300
200
100
0
f1 (ppm)
0
1
2
3
4
5
6
7
8
9
0
3.11
8.31
2.62
2.59
1.08
0.97
1.08
1.09
0.96
1.96
3.08
1.00
CO2t-Bu
CO2Et
CO2Et
N
O
2.6a, 1H NMR, CDCl3, 300 MHz



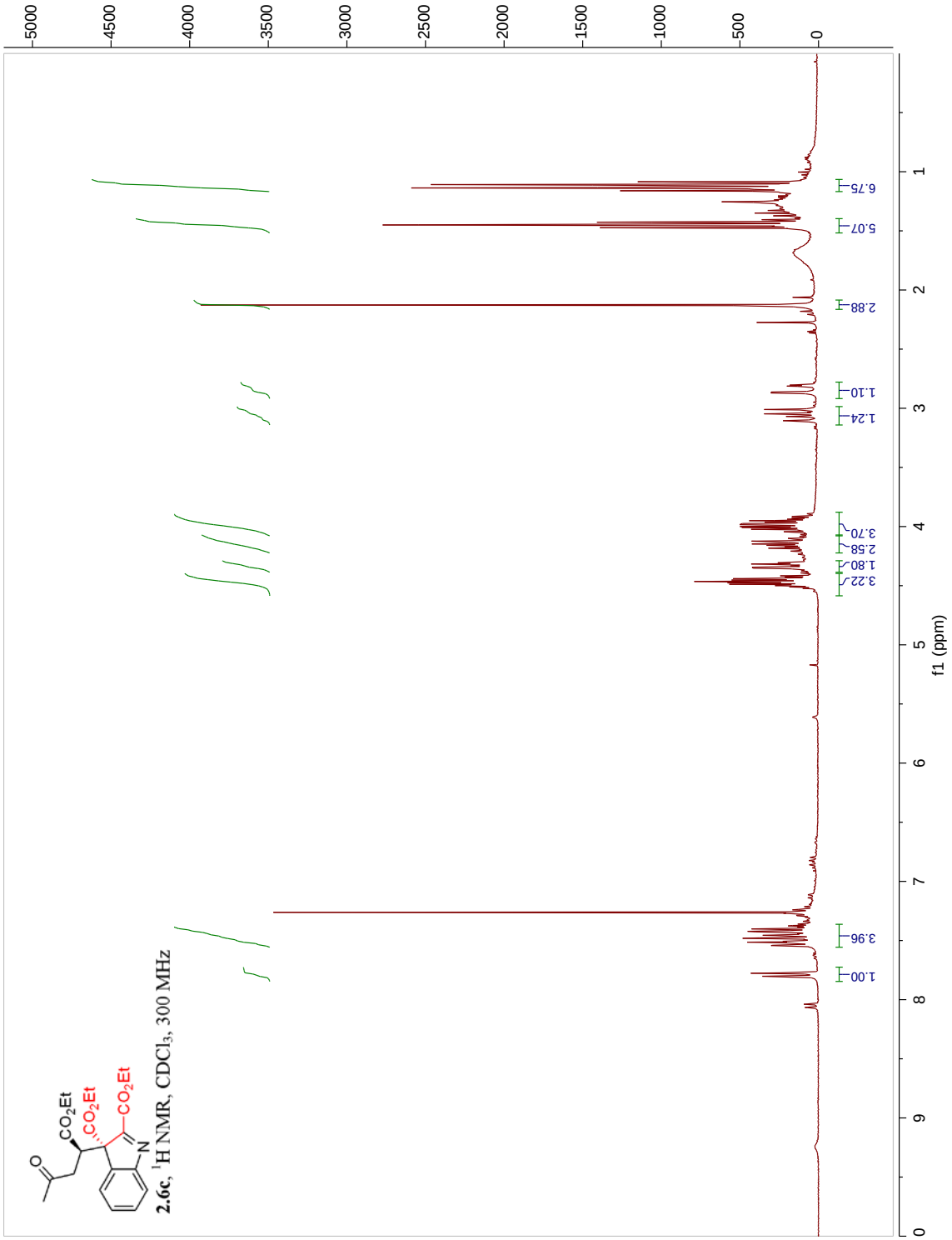
2.6a, ^{13}C NMR, $CDCl_3$, 75 MHz

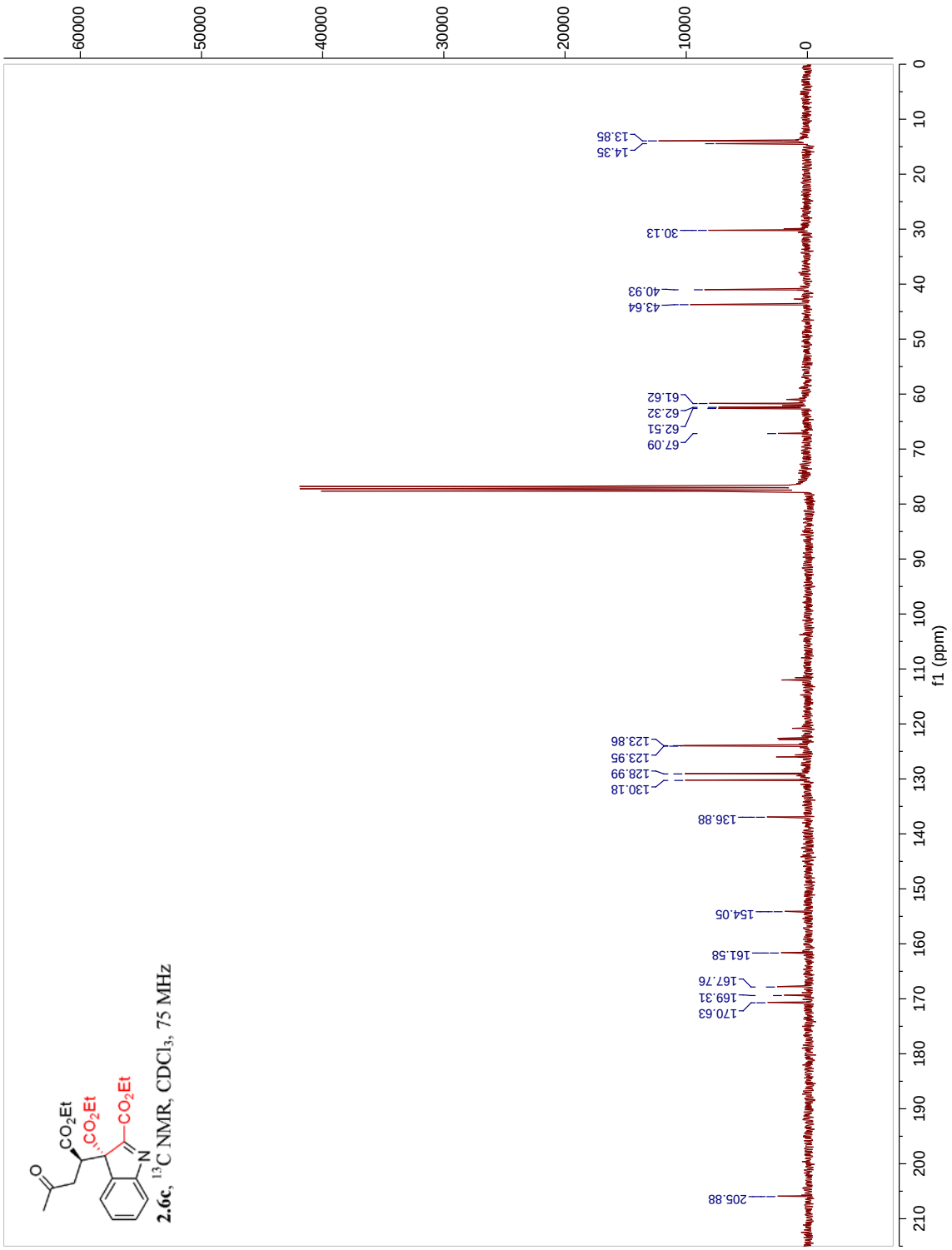


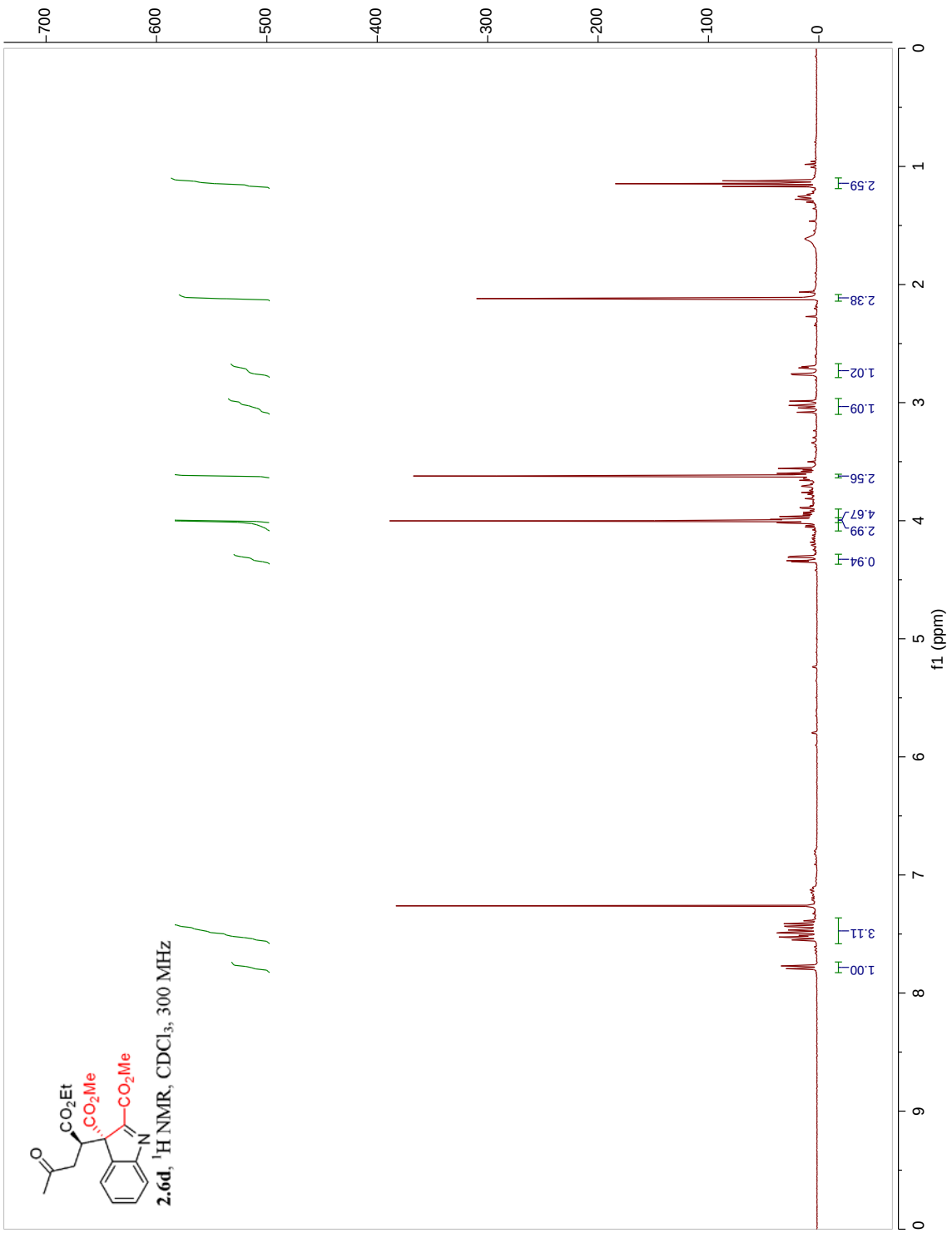
2.6b, ^{1}H NMR, $CDCl_3$, 300 MHz



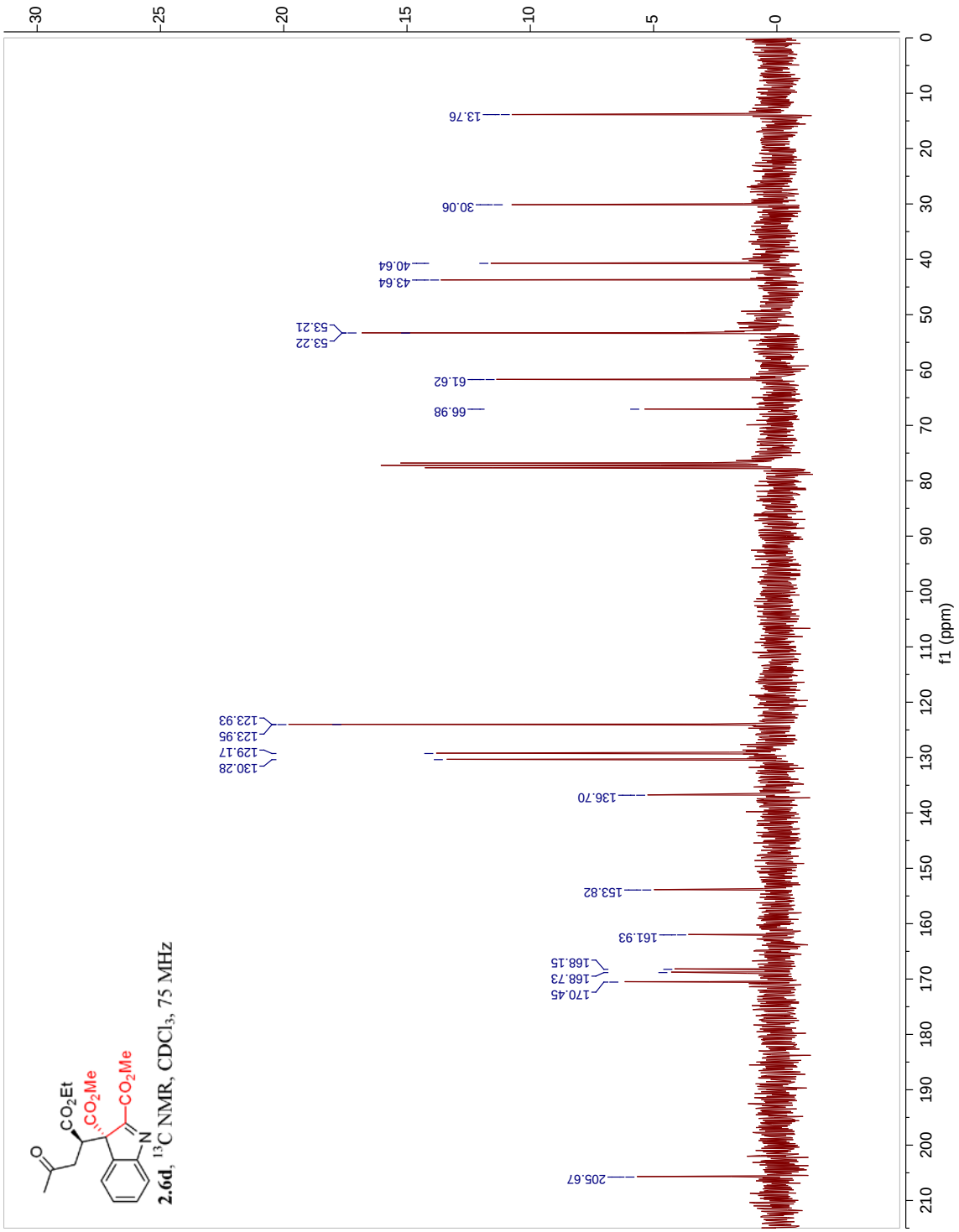
2.6b, ^{13}C NMR, $CDCl_3$, 75 MHz


5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
6.75
5.07
2.88
1.10
1.24
3.70
2.58
1.80
3.22
3.96
1.00
0
1
2
3
4
5
6
7
8
9
f1 (ppm)
CO2Et
CO2Et
CO2Et
O
N
2.6c, 1H NMR, CDCl3, 300 MHz

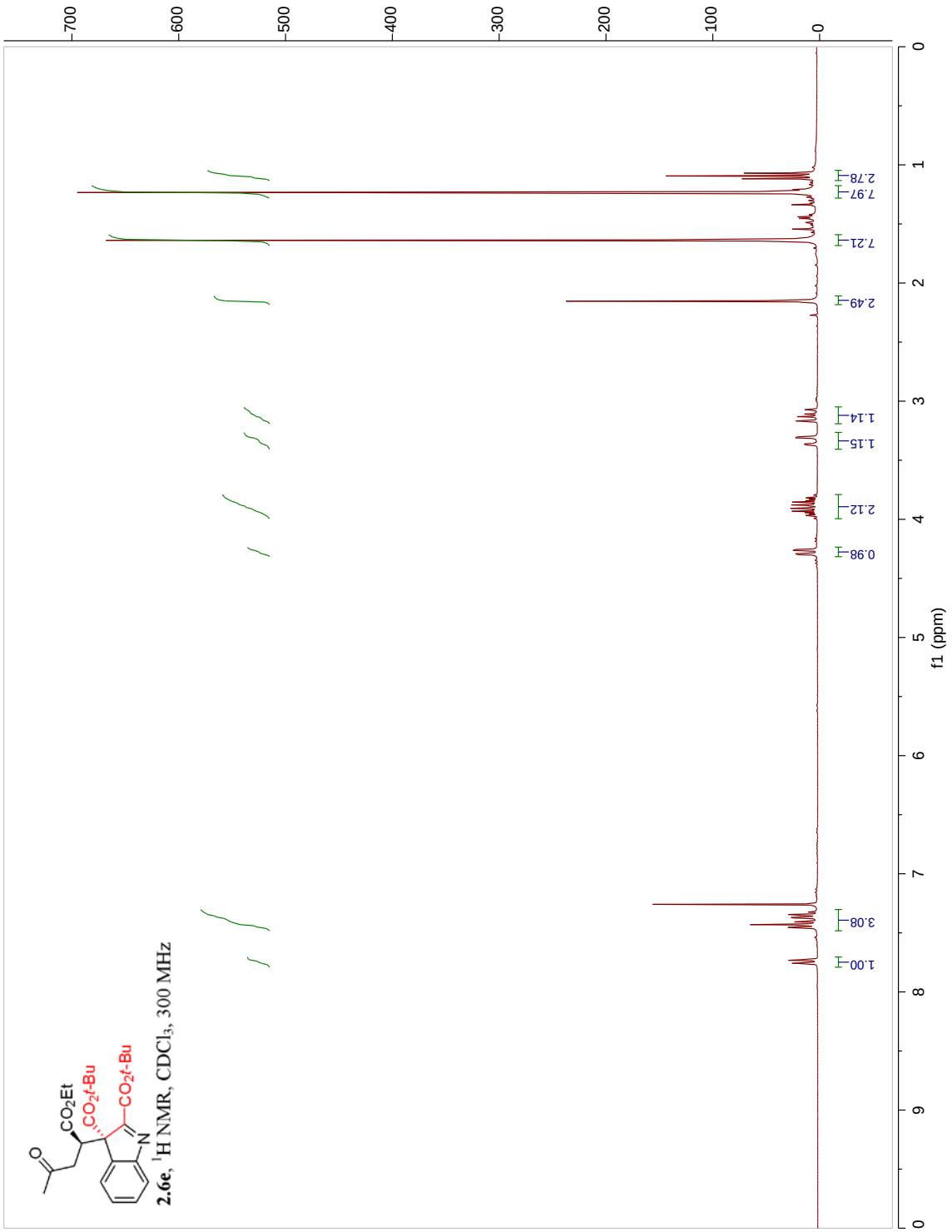

60000
50000
40000
30000
20000
10000
0
13.85
14.35
30.13
40.93
43.64
61.62
62.32
62.51
67.09
123.86
123.95
128.99
130.18
136.88
154.05
161.58
167.76
169.31
170.63
205.88
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
f1 (ppm)
CO2Et
CO2Et
CO2Et
O
N
2.6c, 13C NMR, CDCl3, 75 MHz



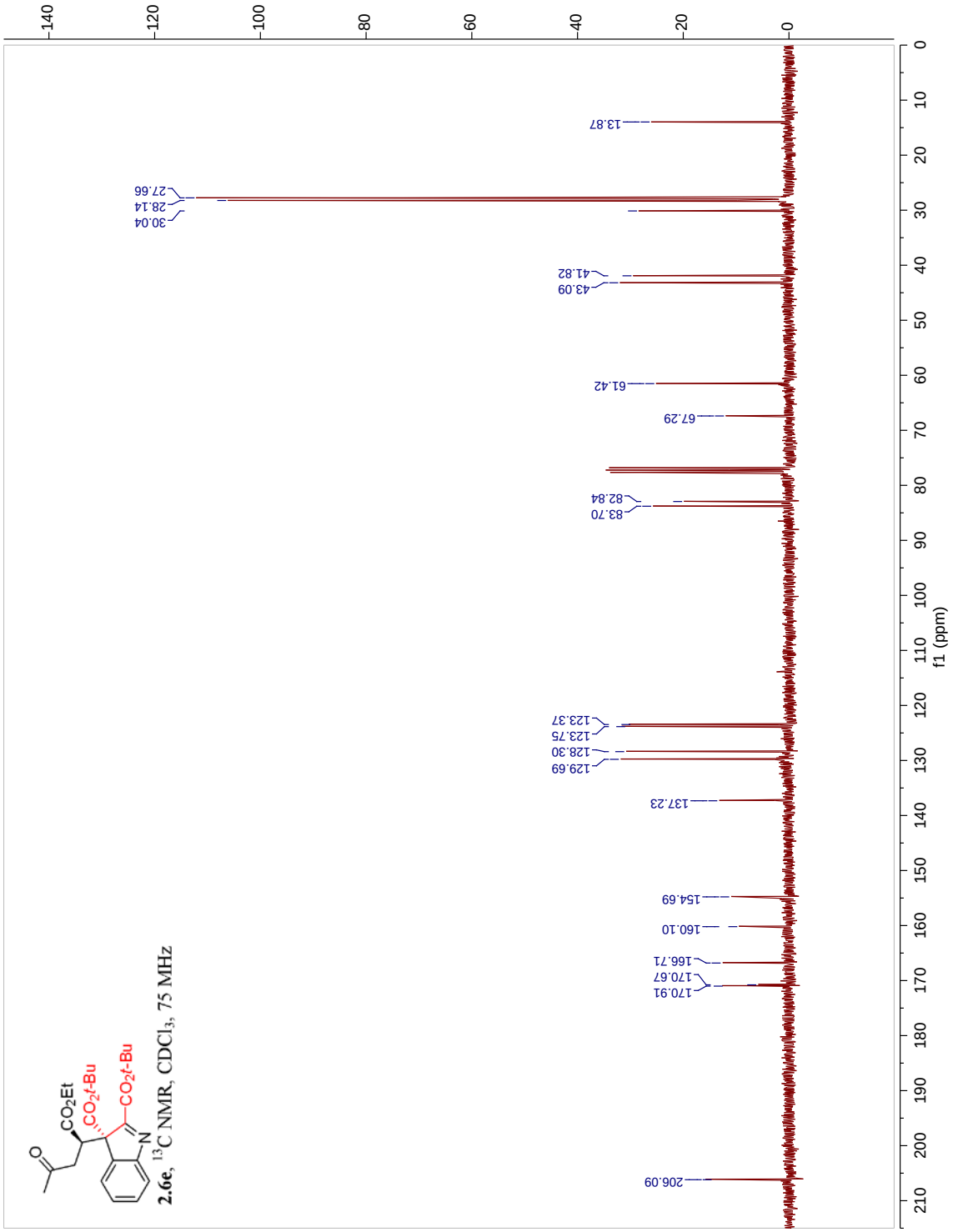
2.6d, ^{1}H NMR, $CDCl_3$, 300 MHz



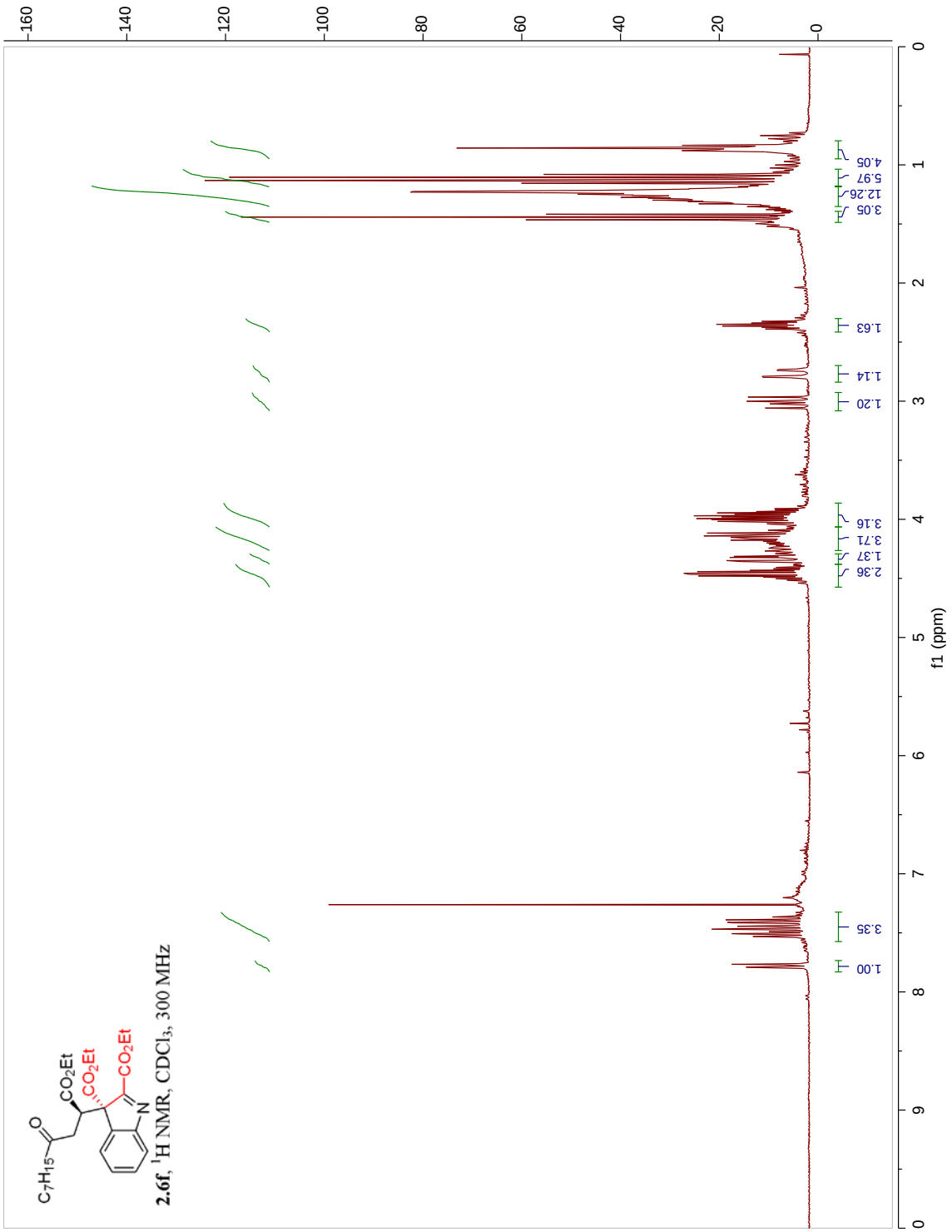
2.6d, ^{13}C NMR, $CDCl_3$, 75 MHz



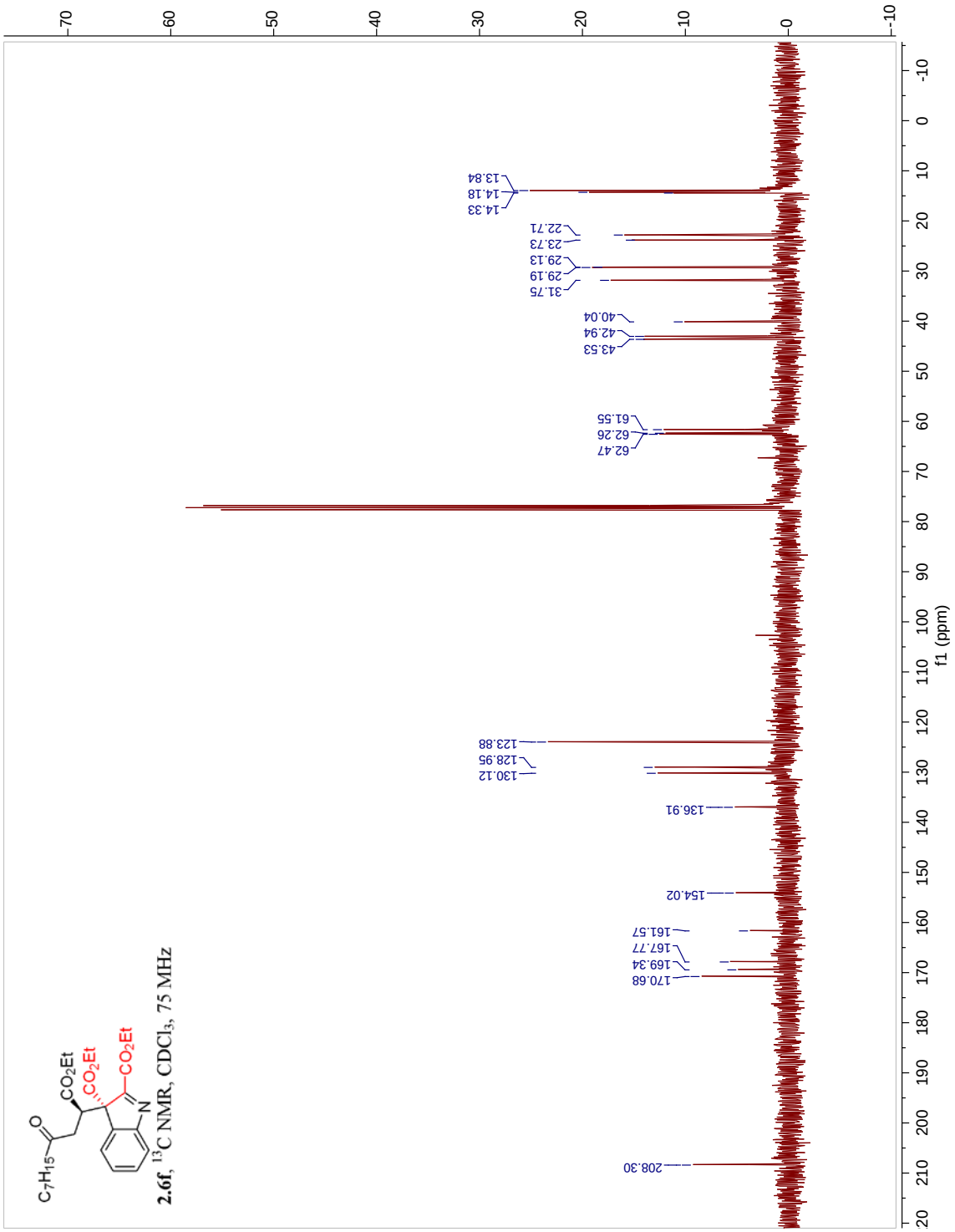
2.6e, ^{1}H NMR, $CDCl_3$, 300 MHz

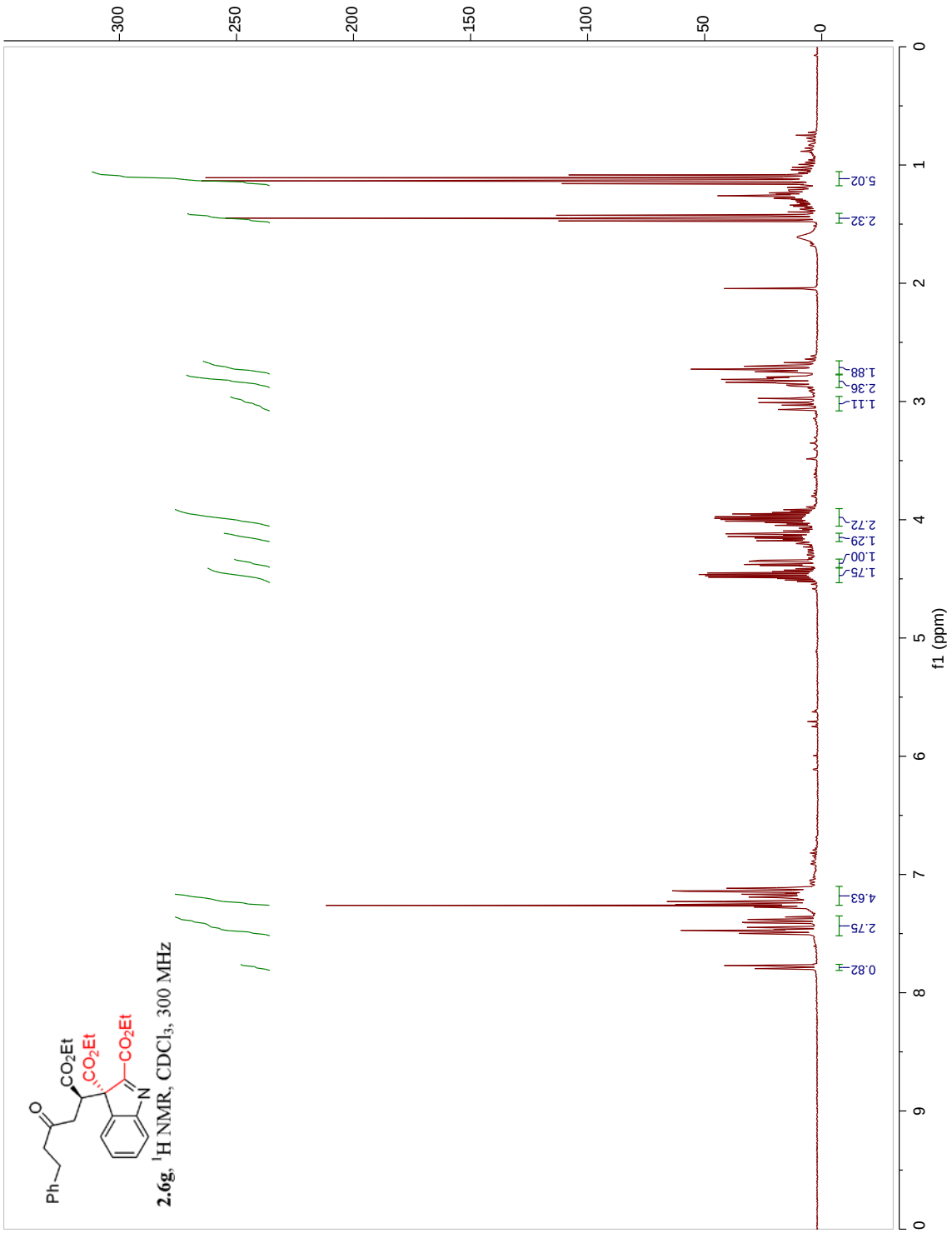


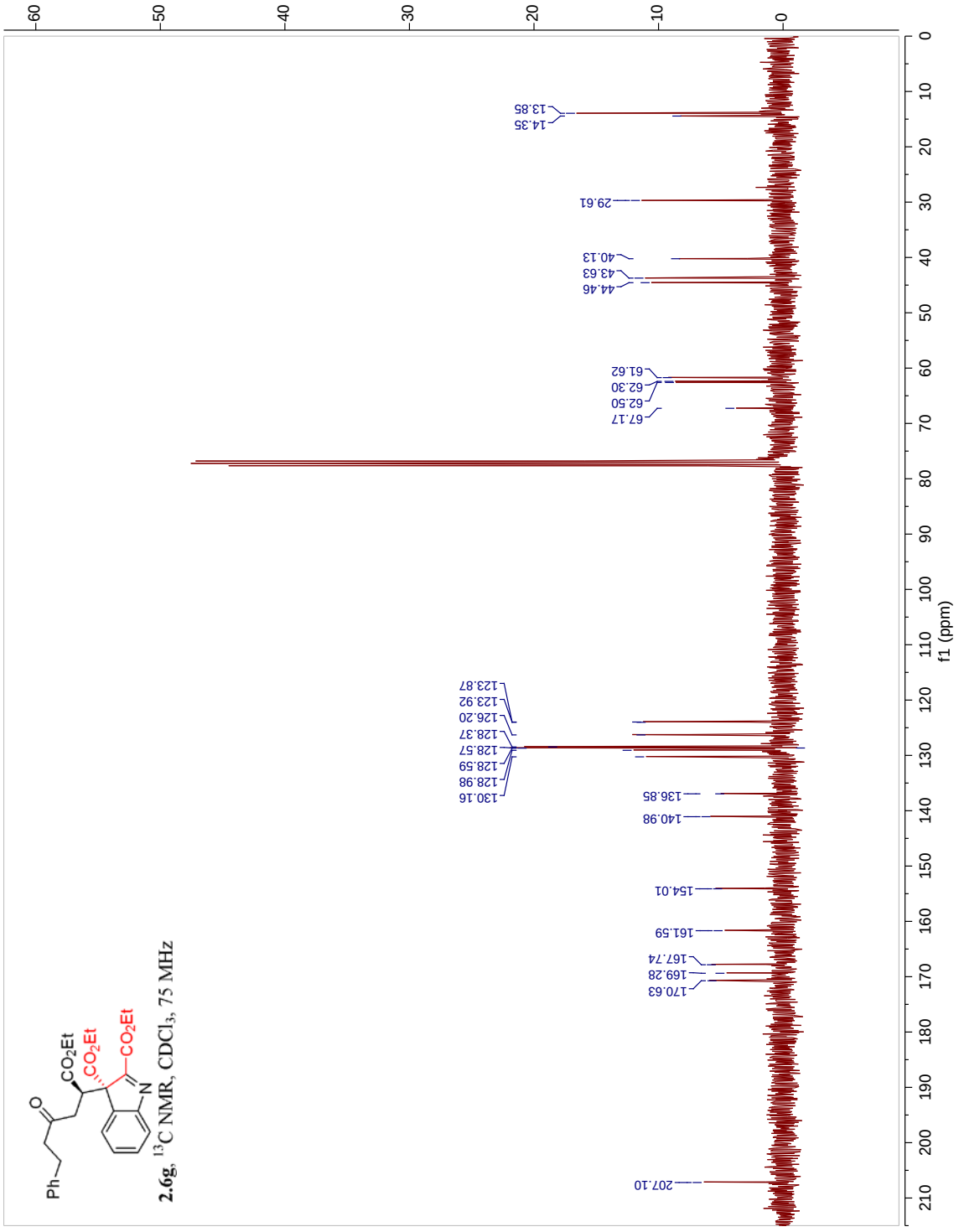
2.6e, ^{13}C NMR, $CDCl_3$, 75 MHz



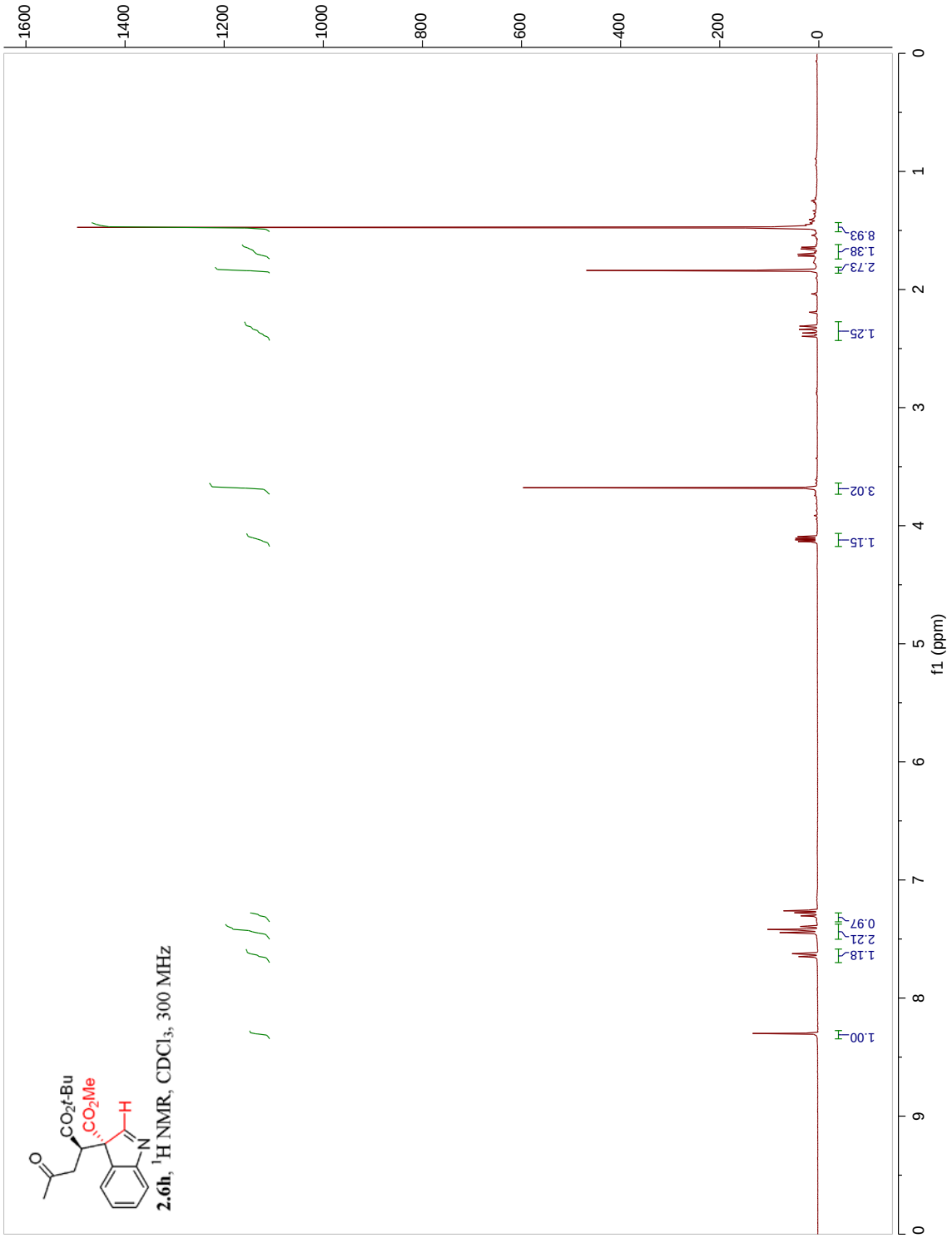
2.6f, ^{1}H NMR, $CDCl_3$, 300 MHz

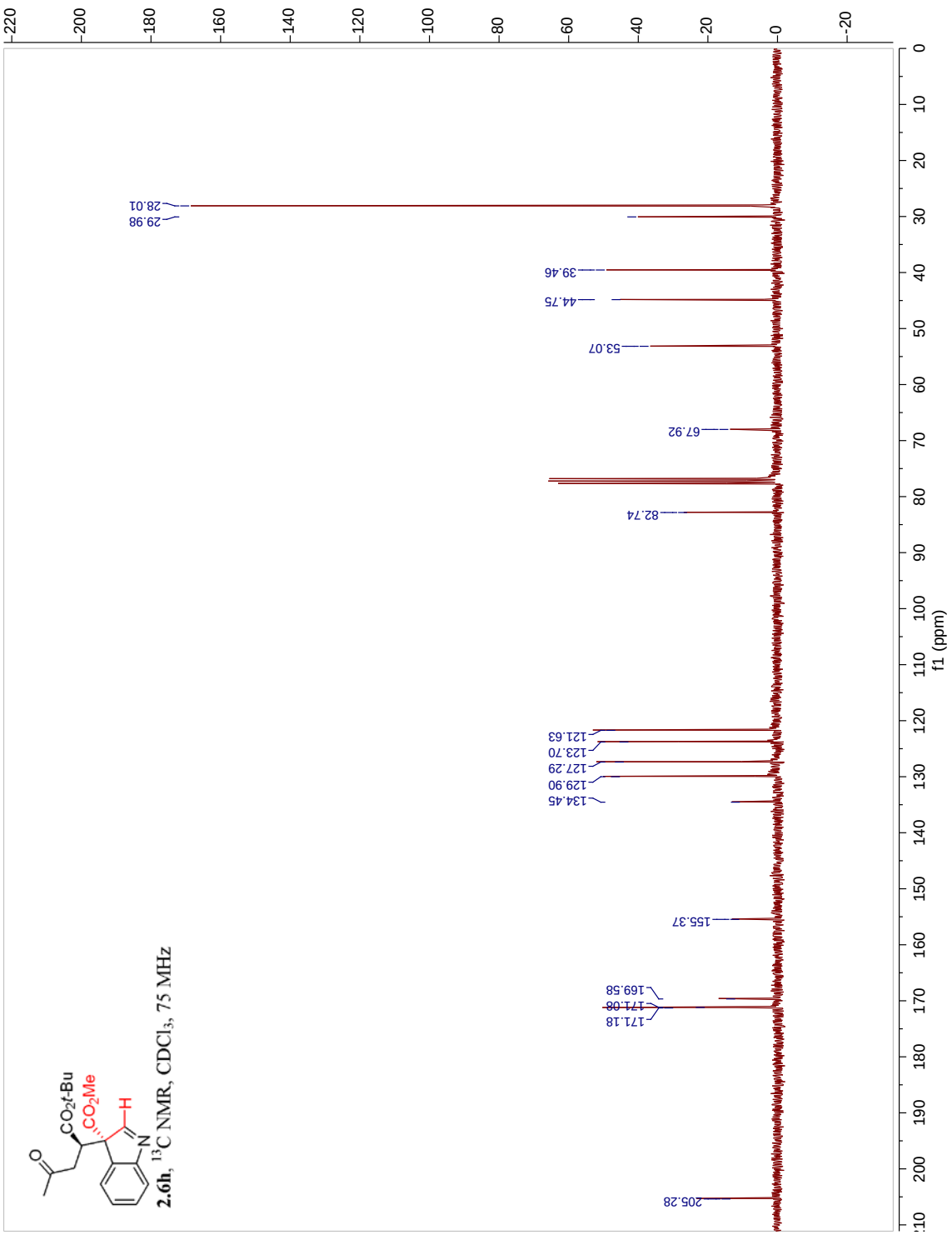

2.6f, ^{13}C NMR, $CDCl_3$, 75 MHz
C_7H_{15}
CO_2Et
CO_2Et
CO_2Et
N
O
13.84
14.18
14.33
22.71
23.73
29.13
29.19
31.75
40.04
42.94
43.53
61.55
62.26
62.47
123.88
128.95
130.12
136.91
154.02
161.57
167.77
169.34
170.68
208.30
f1 (ppm)


CO2Et
CO2Et
CO2Et
N
O
Ph
2.6g, ^{1}H NMR, $CDCl_3$, 300 MHz
5.02
2.32
1.88
2.36
1.11
2.72
1.29
1.00
1.75
4.63
2.75
0.82
f1 (ppm)

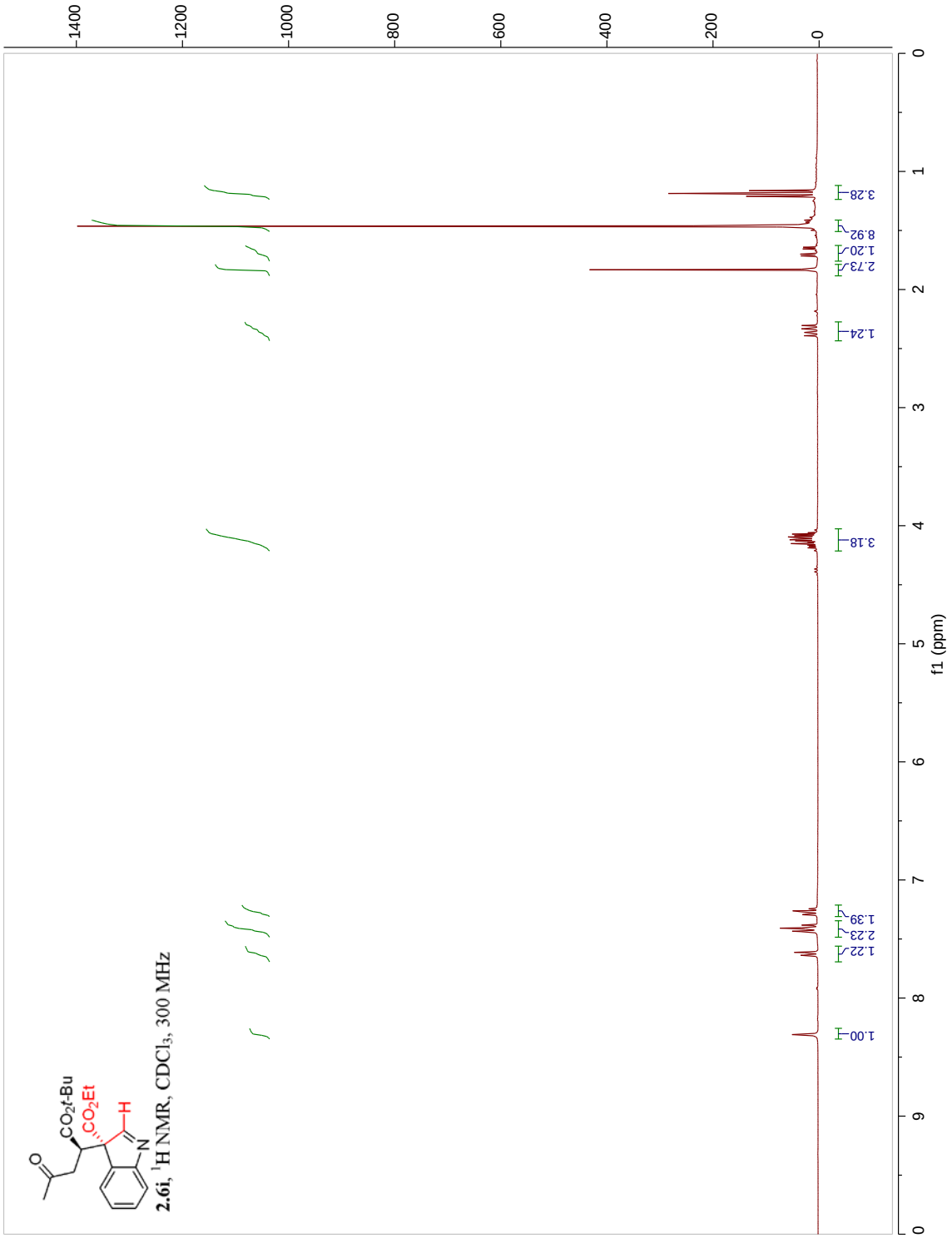


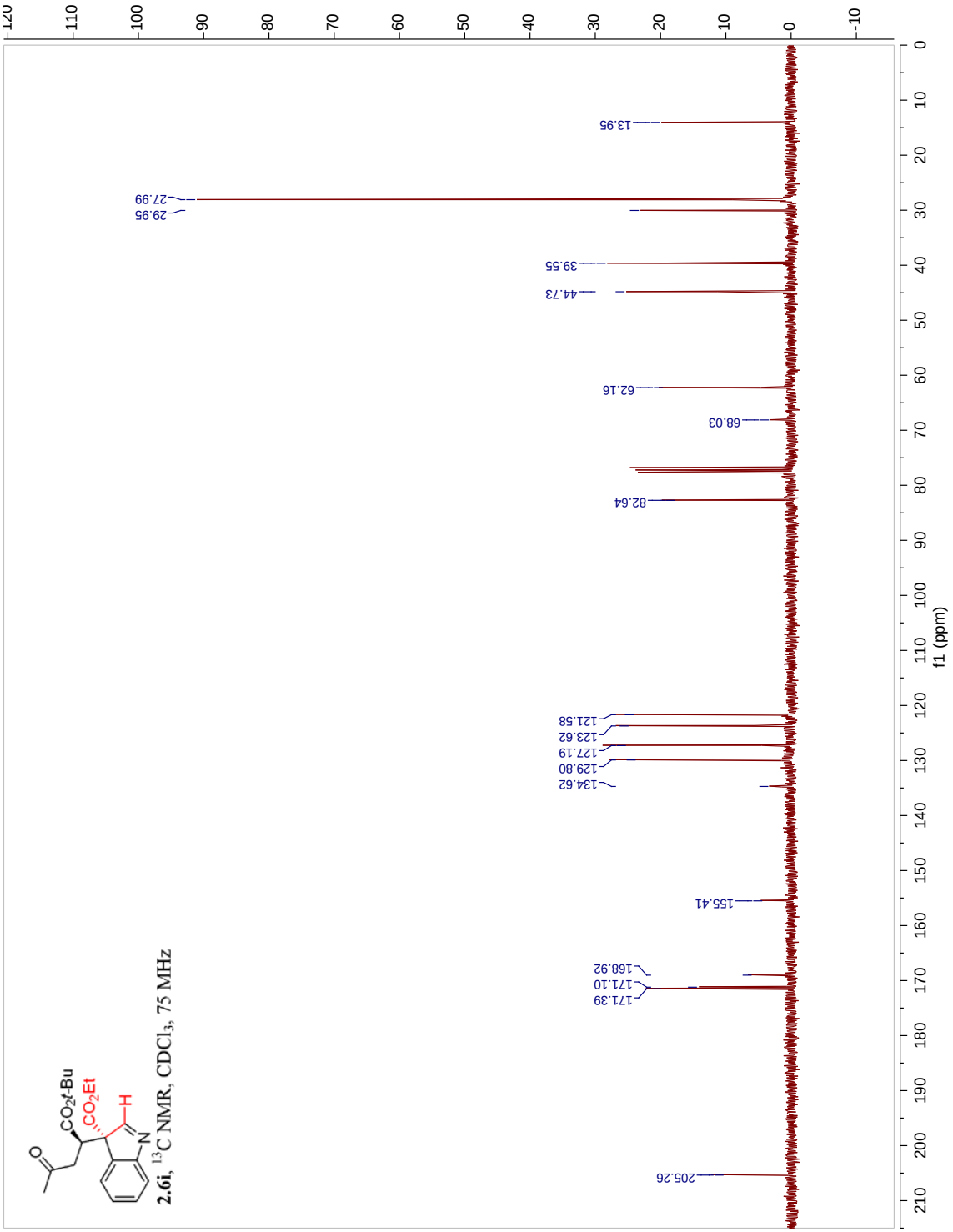
2.6g, ^{13}C NMR, $CDCl_3$, 75 MHz


1600
1400
1200
1000
800
600
400
200
0
8.93
1.38
2.73
1.25
3.02
1.15
0.97
2.21
1.18
1.00
0
1
2
3
4
5
6
7
8
9
0
f1 (ppm)
CO2t-Bu
CO2Me
H
N
O
2.6h, 1H NMR, CDCl3, 300 MHz

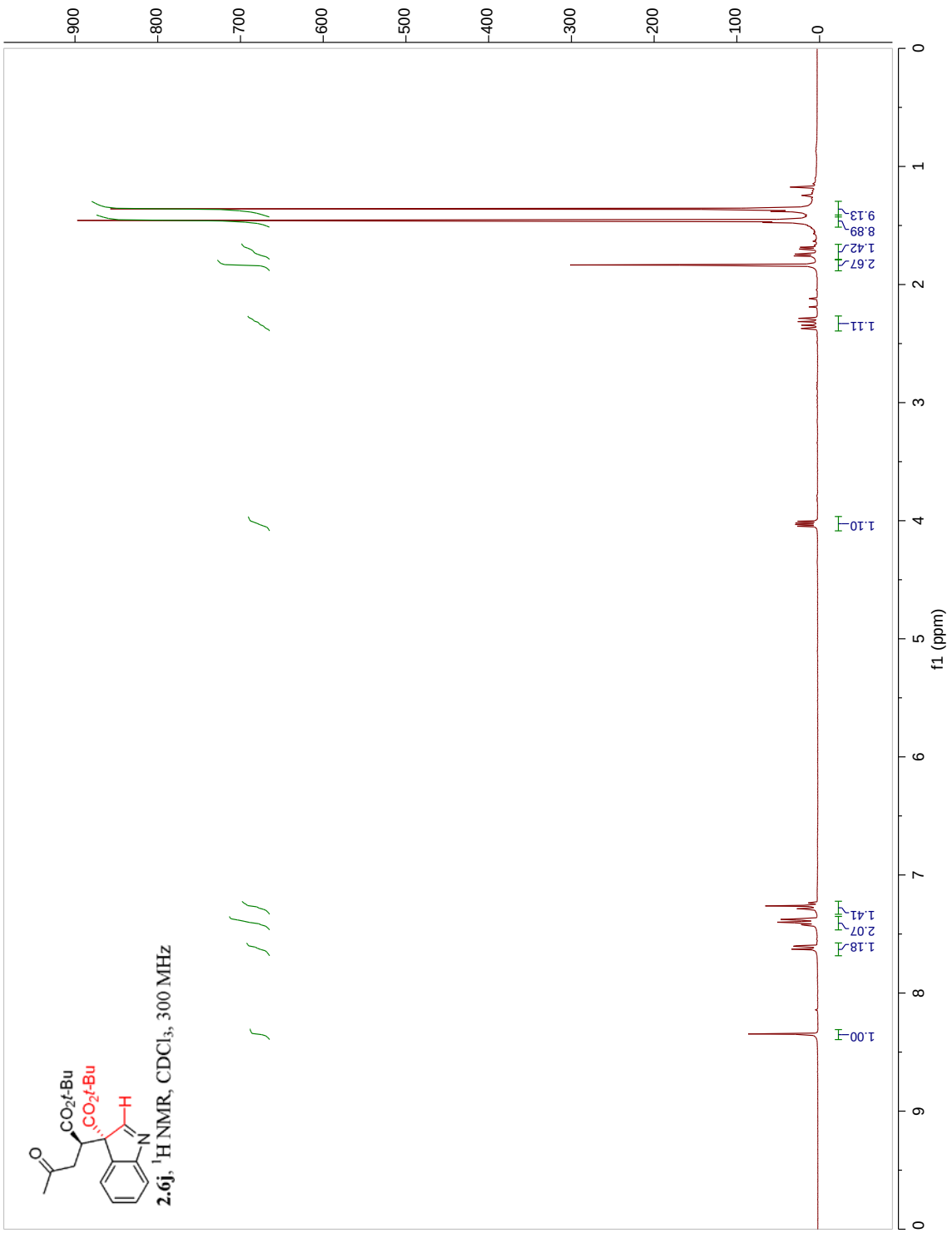


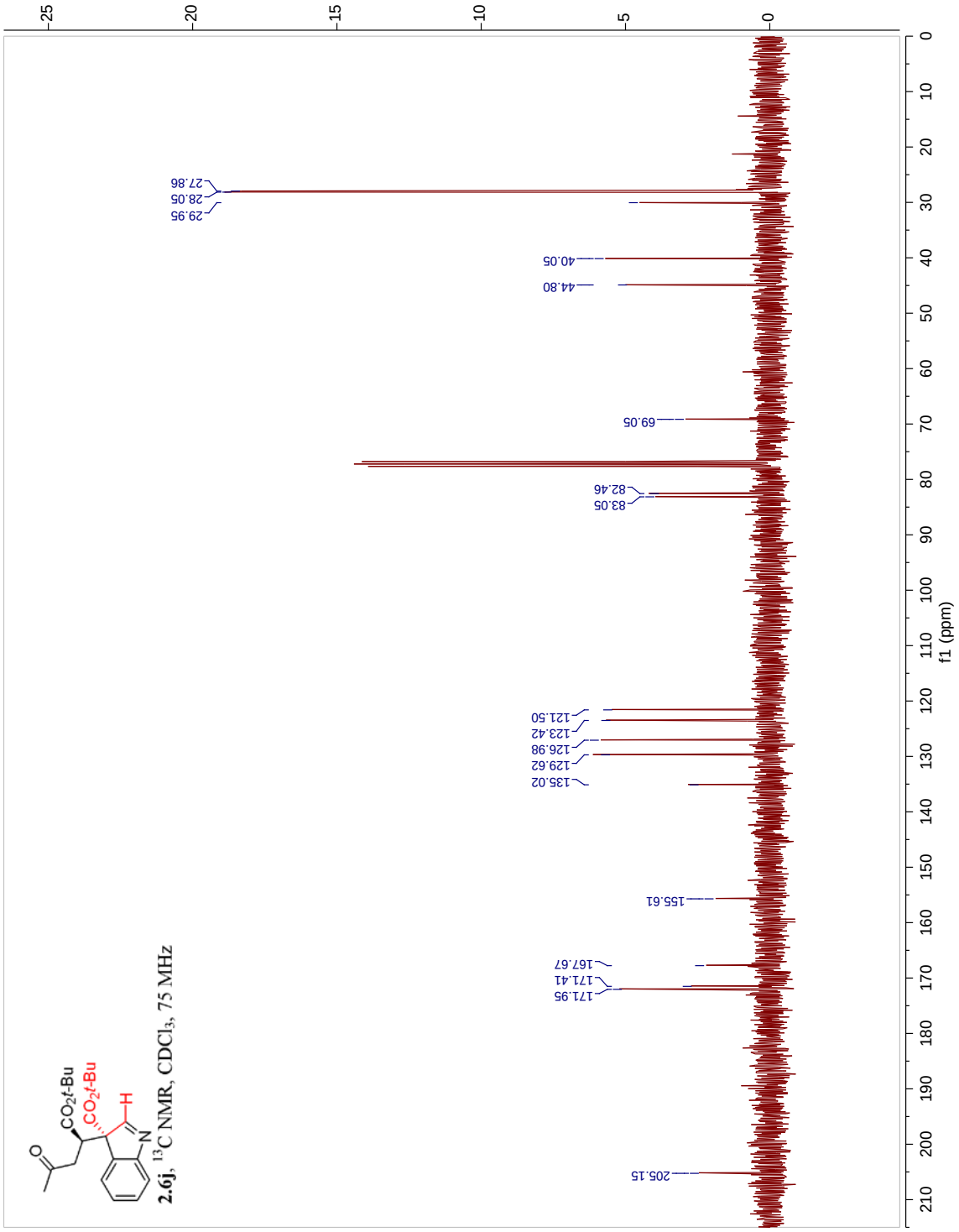
2.6h, ^{13}C NMR, $CDCl_3$, 75 MHz


1400
1200
1000
800
600
400
200
0
3.28
8.92
1.20
2.73
1.24
3.18
1.39
2.23
1.22
1.00
0
1
2
3
4
5
6
7
8
9
0
f1 (ppm)
CO2t-Bu
CO2Et
H
N
O
2.6i, 1H NMR, CDCl3, 300 MHz

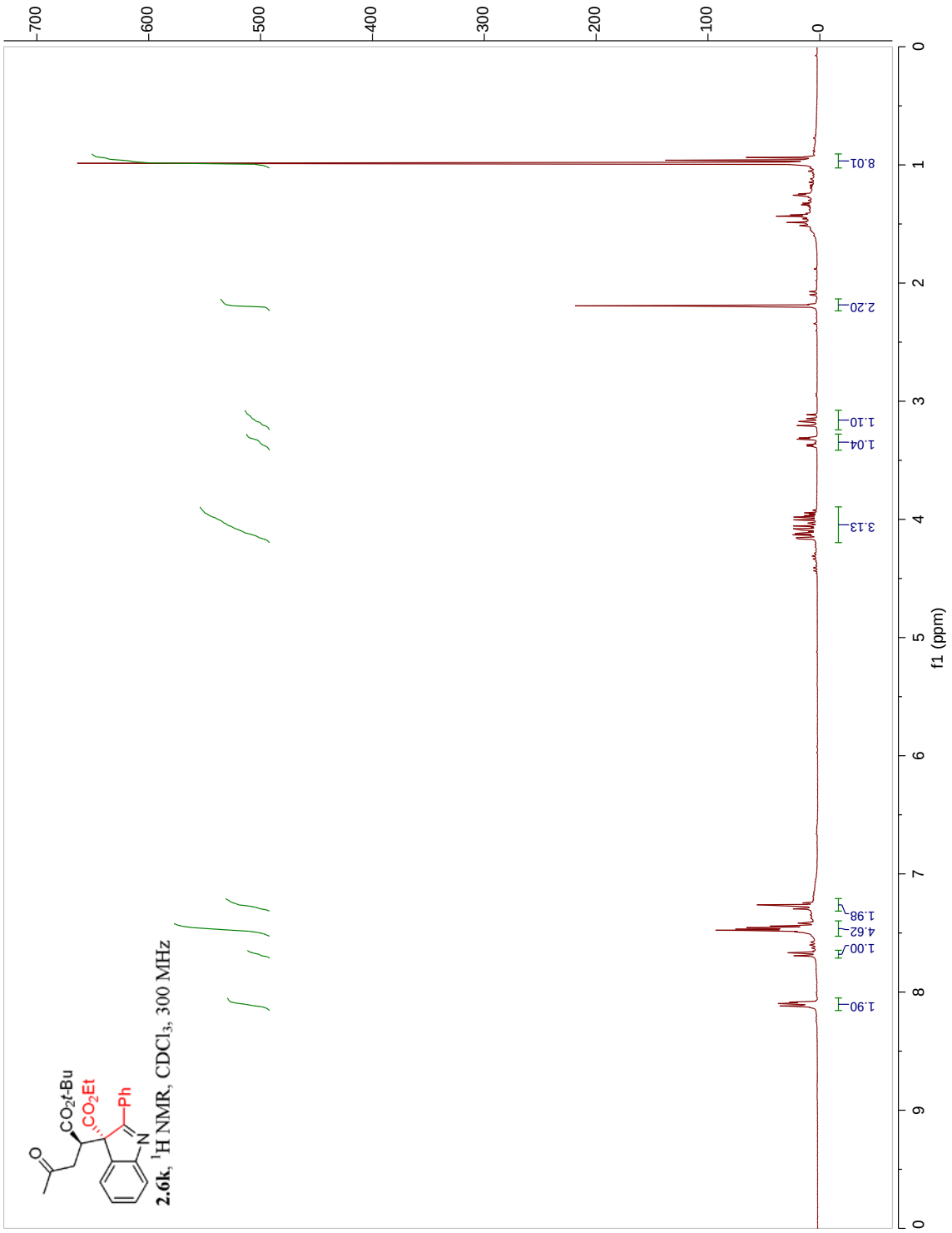


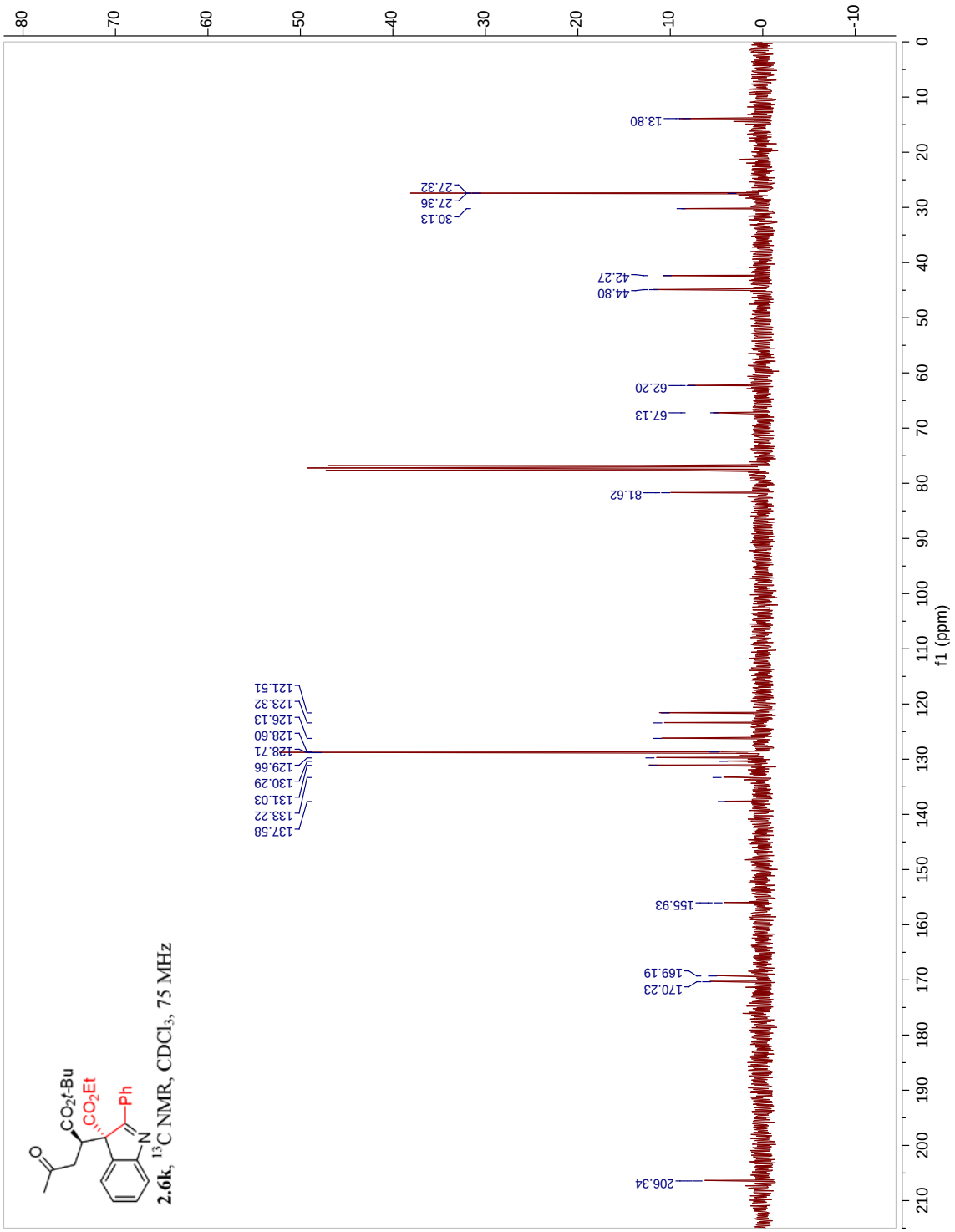
2.6i, ^{13}C NMR, $CDCl_3$, 75 MHz

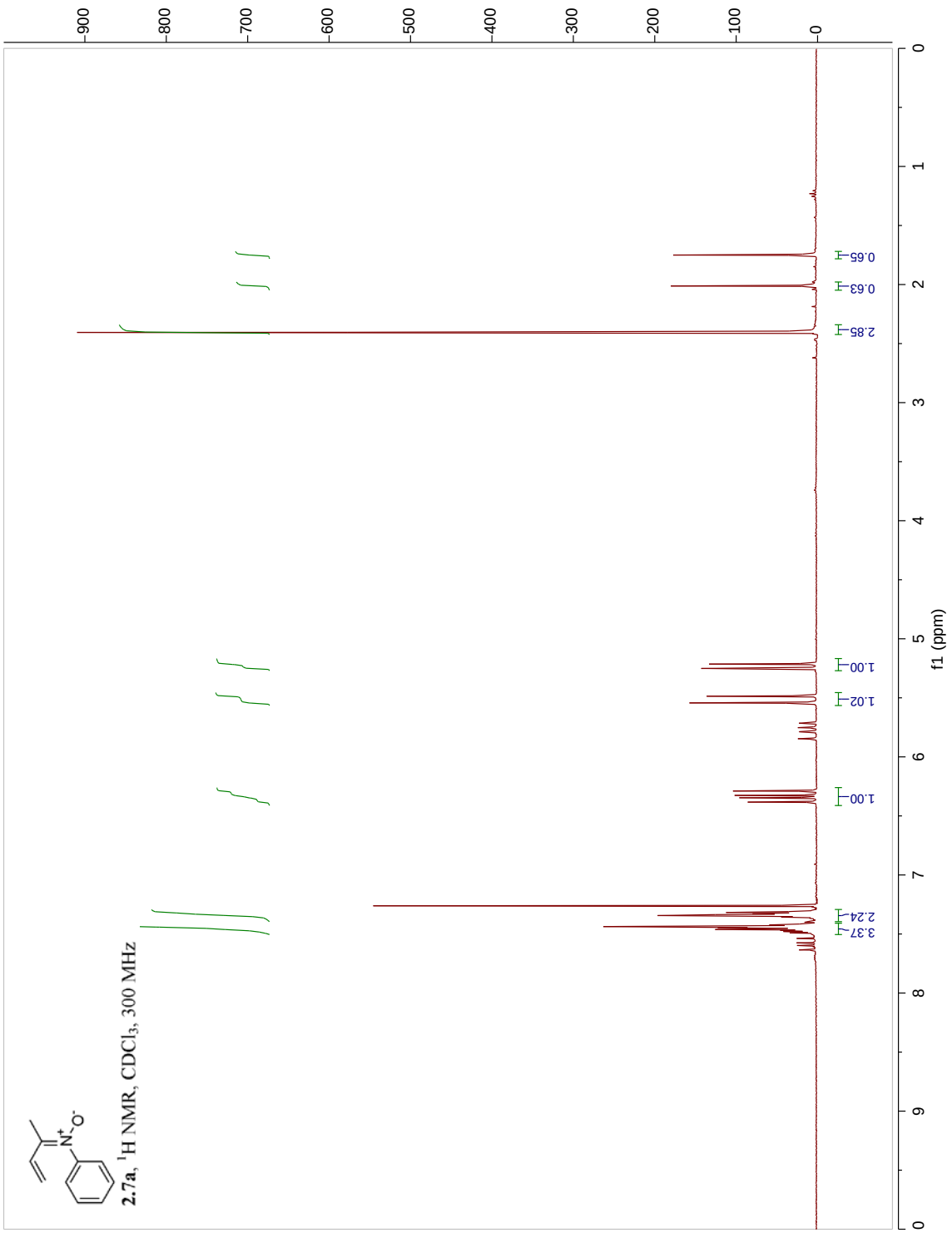

CO2t-Bu
CO2t-Bu
H
N
O
2.6j, 1H NMR, CDCl3, 300 MHz
900
800
700
600
500
400
300
200
100
0
9.13
8.89
1.42
2.67
1.11
1.10
1.41
2.07
1.18
1.00
0
1
2
3
4
5
6
7
8
9
0
f1 (ppm)

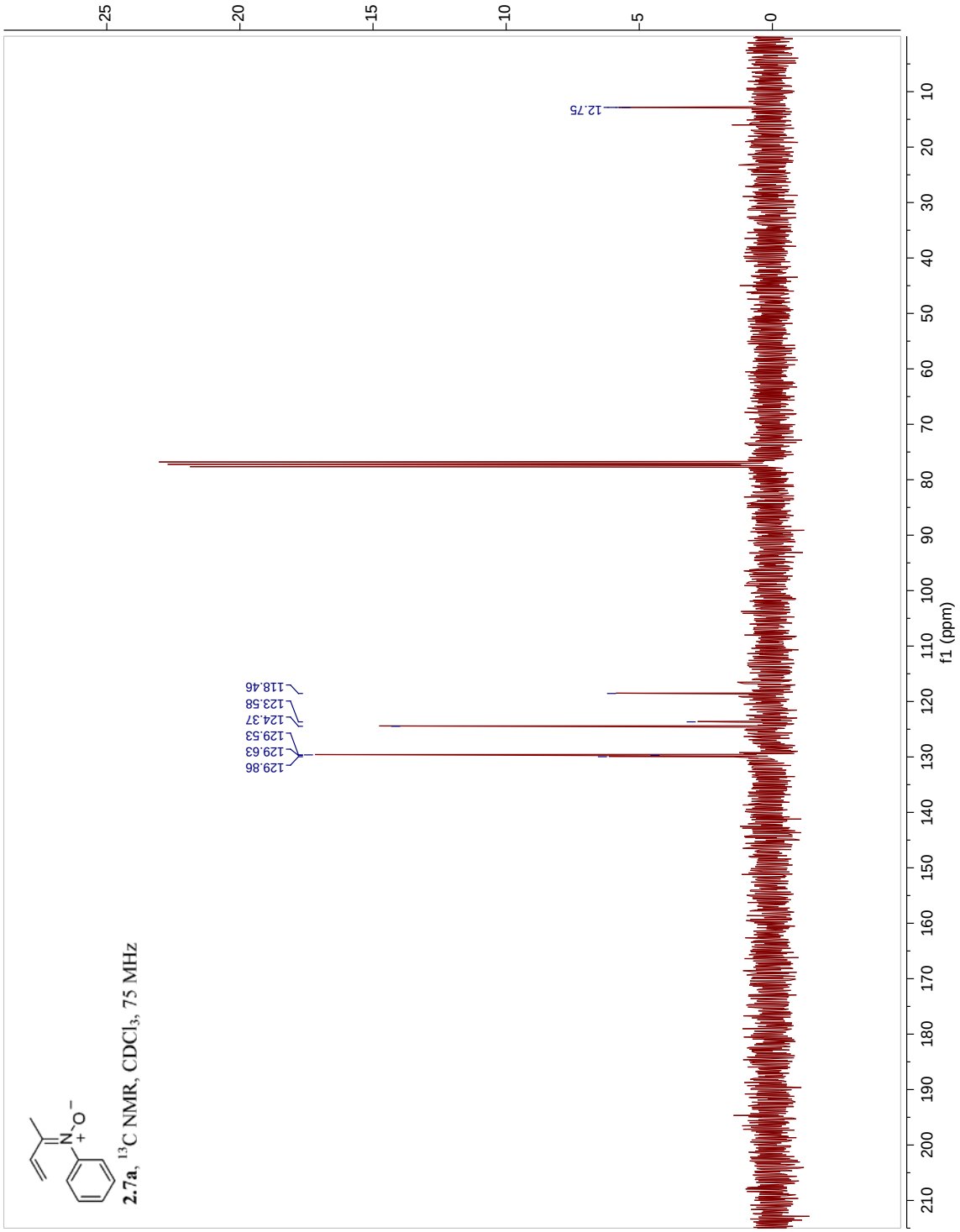


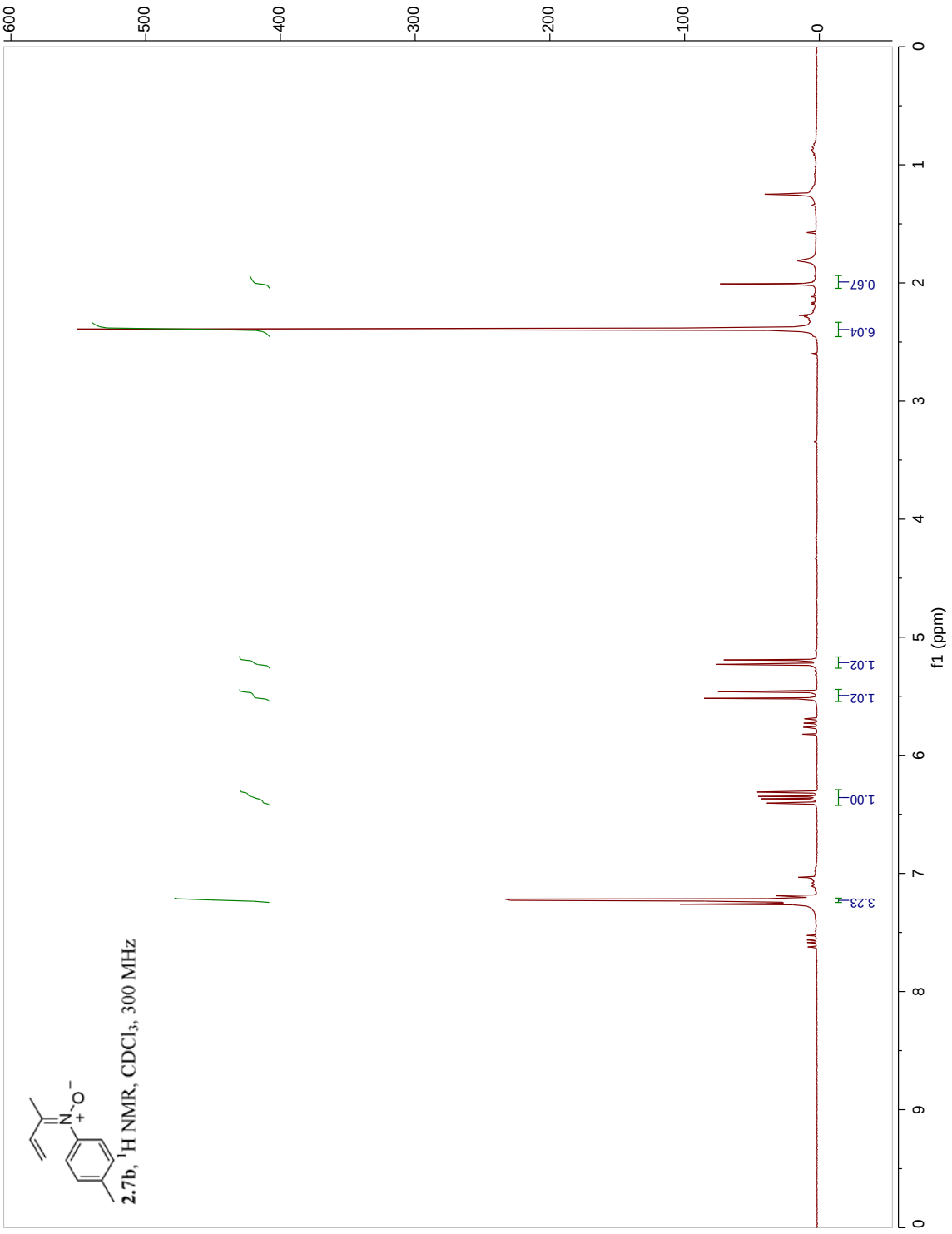
2.6j, ^{13}C NMR, $CDCl_3$, 75 MHz


700
600
500
400
300
200
100
0
8.01
2.20
1.10
1.04
3.13
1.98
4.62
1.00
1.90
0
1
2
3
4
5
6
7
8
9
0
f1 (ppm)
CO2t-Bu
CO2Et
Ph
N
O
2.6k, 1H NMR, CDCl3, 300 MHz

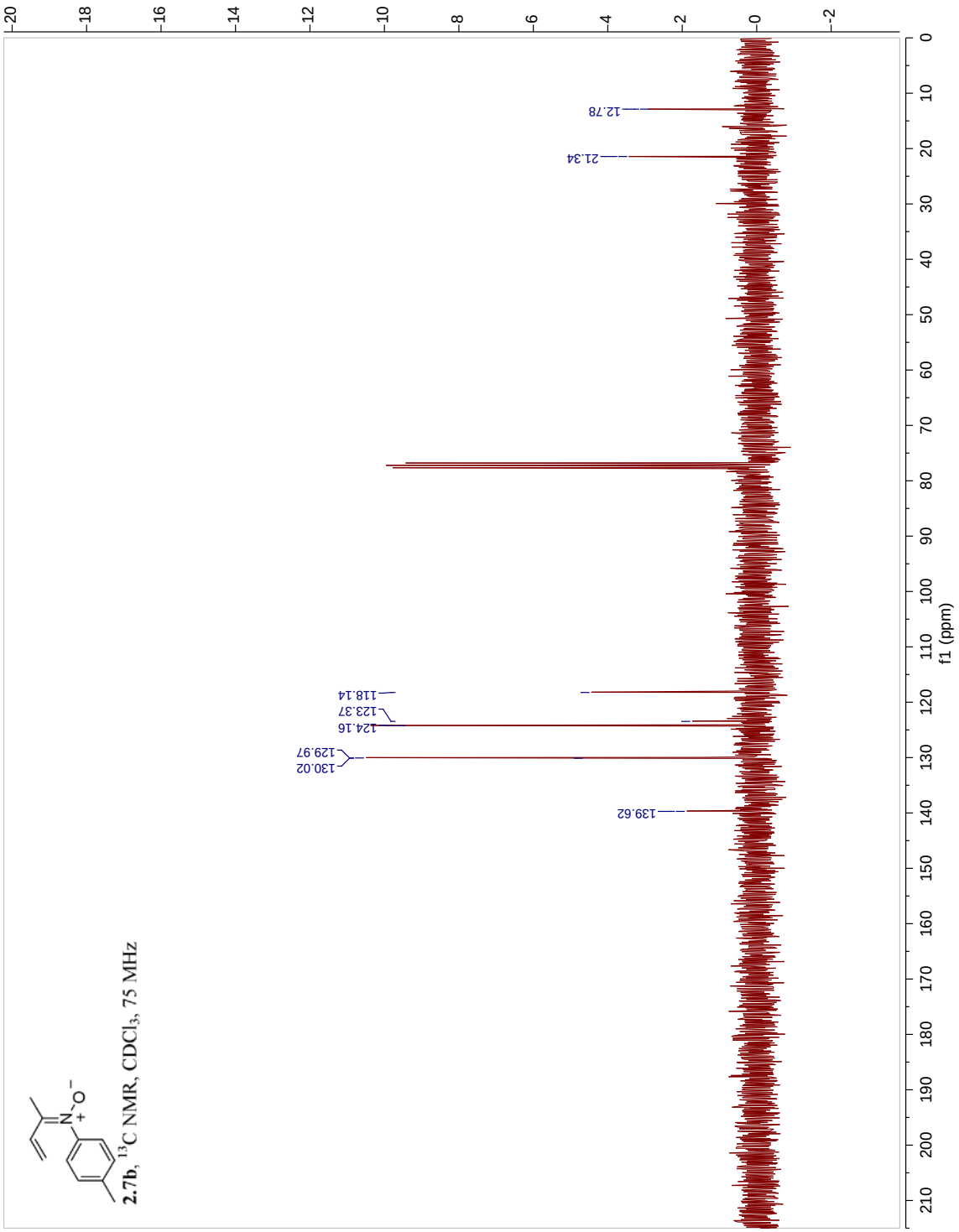

206.34
169.19
170.23
155.93
137.58
133.22
131.03
130.29
129.66
128.71
128.60
126.13
123.32
121.51
81.62
67.13
62.20
44.80
42.27
30.13
27.36
27.32
13.80
f1 (ppm)
2.6k, ^{13}C NMR, $CDCl_3$, 75 MHz
CO2t-Bu
CO2Et
Ph
N
O

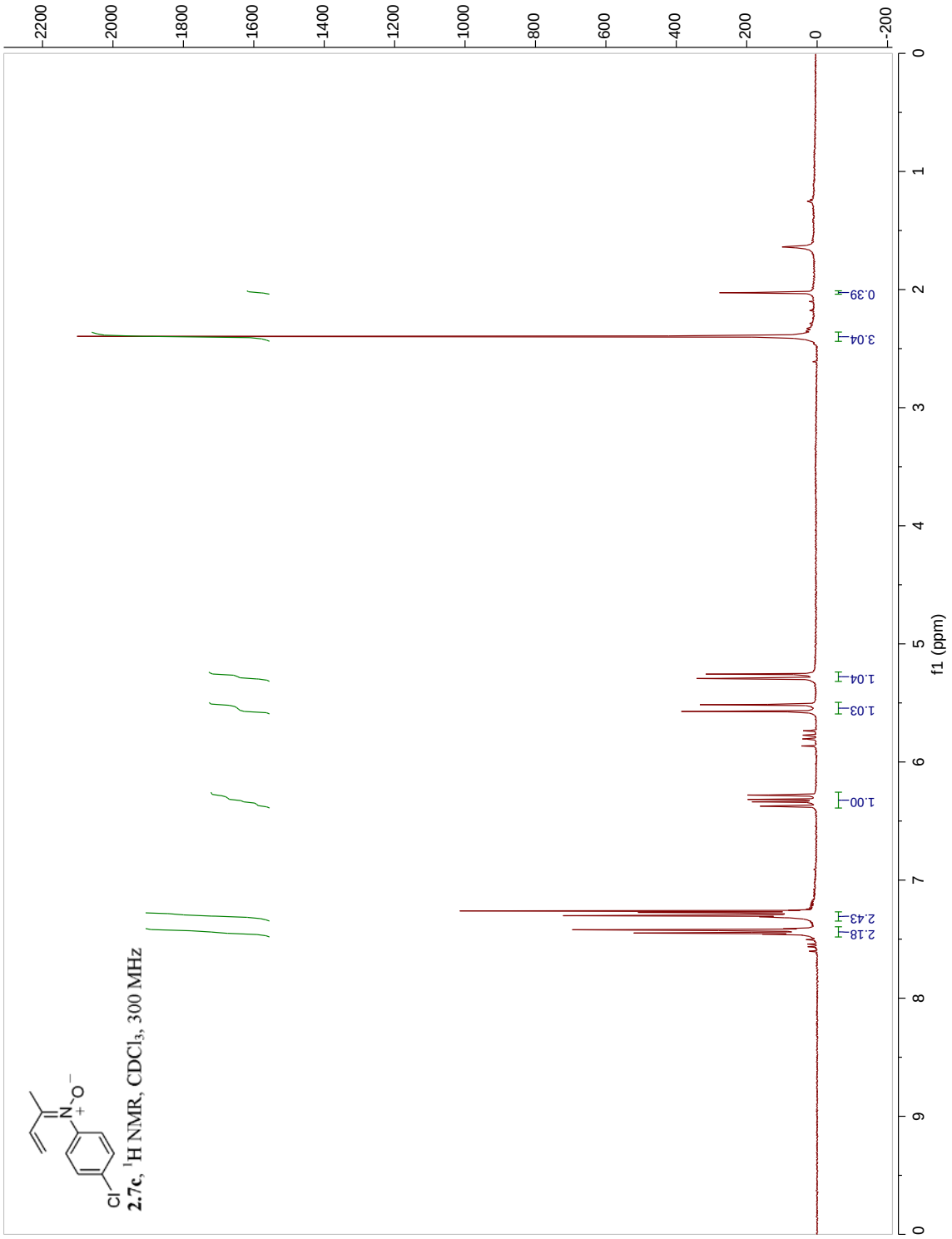

2.7a, ^{1}H NMR, $CDCl_3$, 300 MHz
f1 (ppm)
0.65
0.63
2.85
1.00
1.02
1.00
2.24
3.37

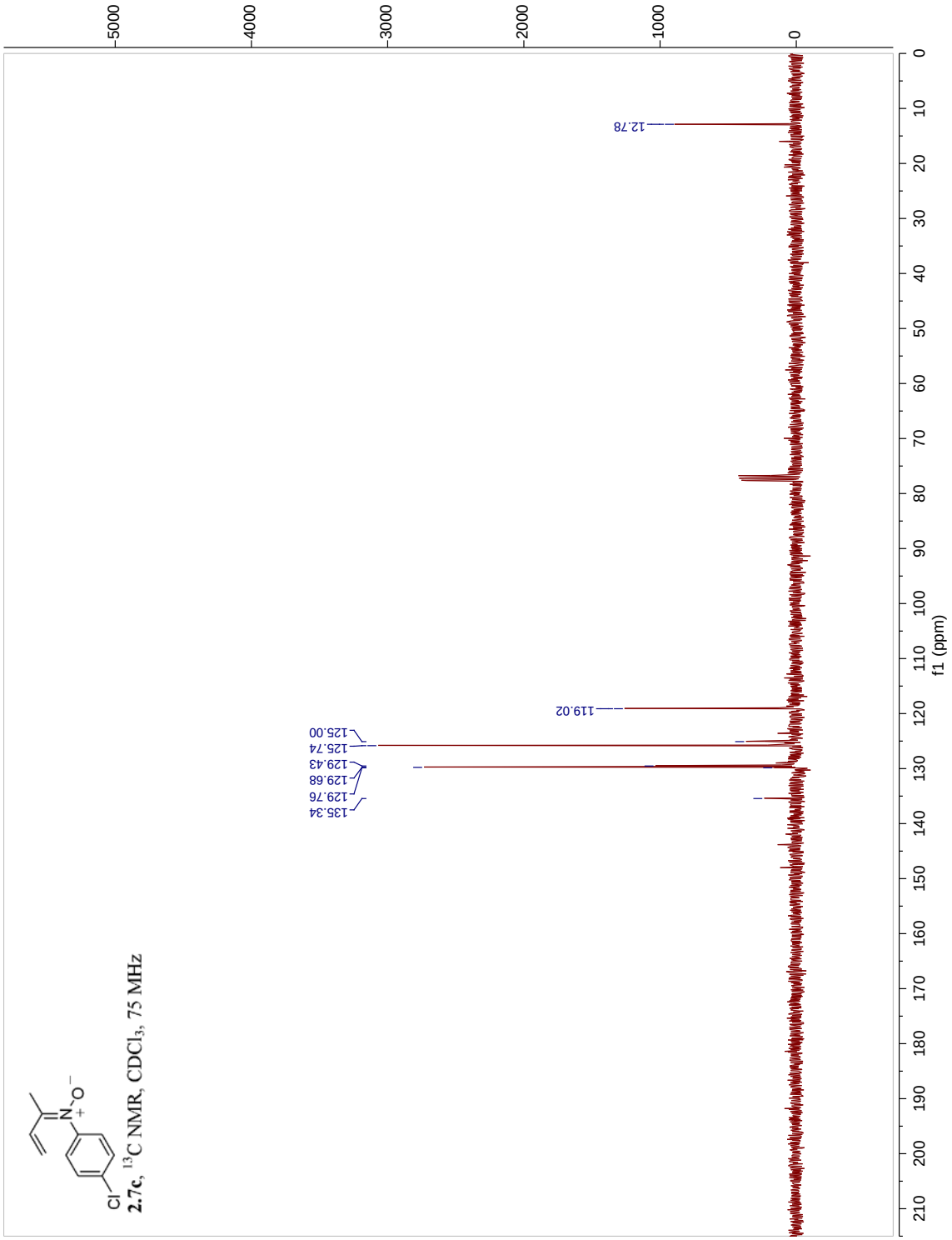

2.7a, ^{13}C NMR, $CDCl_3$, 75 MHz
12.75
118.46
123.58
124.37
129.53
129.63
129.86
f1 (ppm)

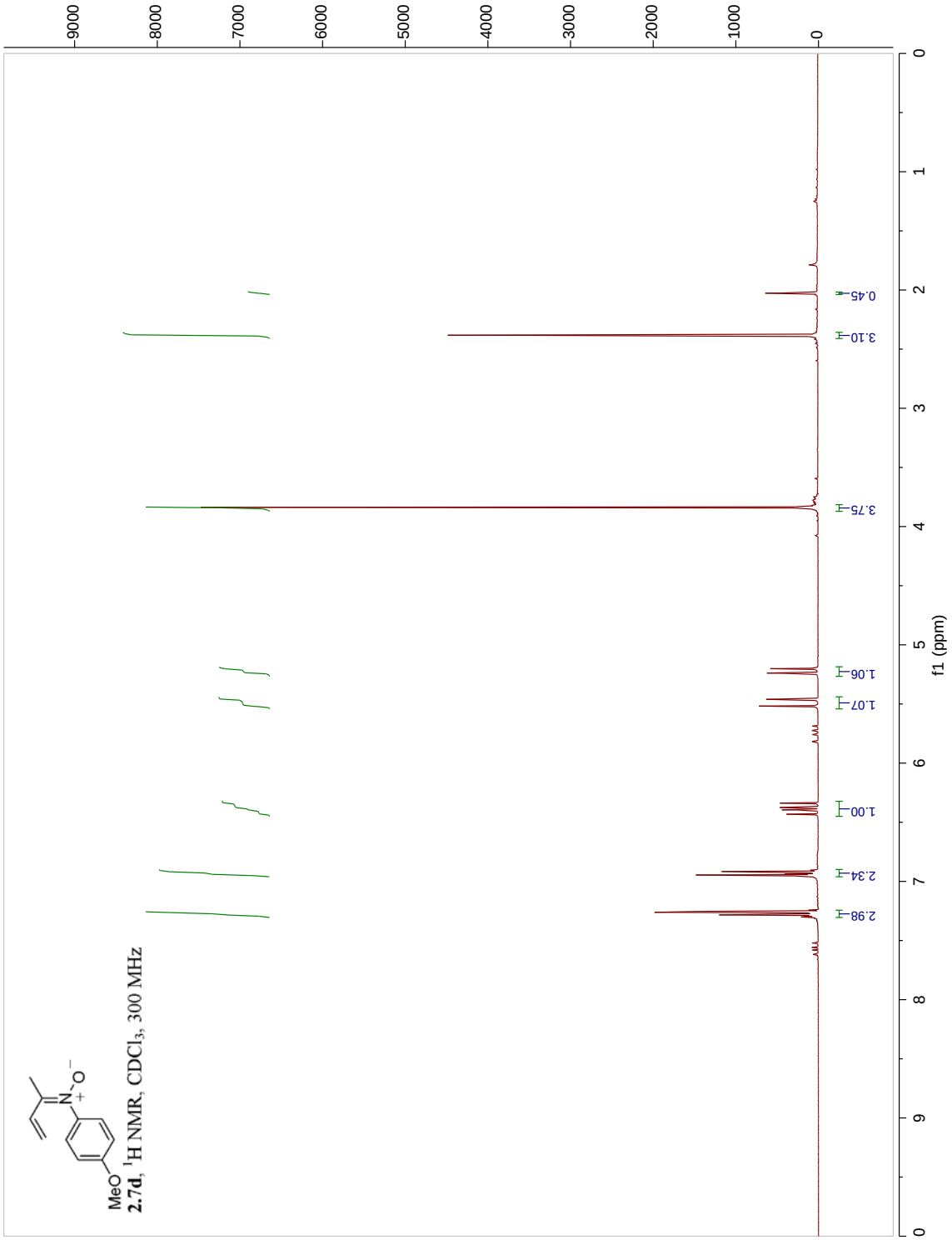


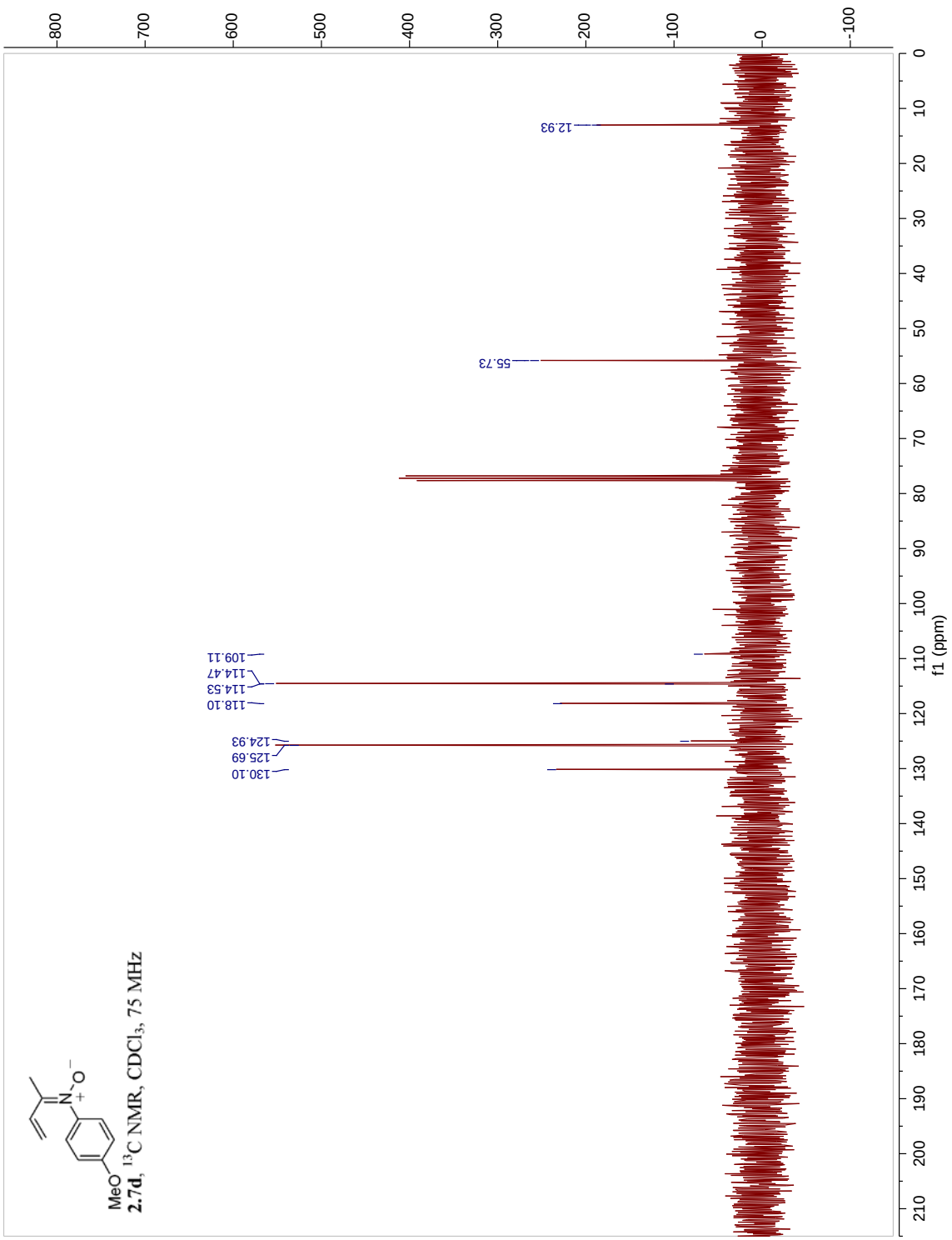
2.7b, ^{1}H NMR, $CDCl_3$, 300 MHz

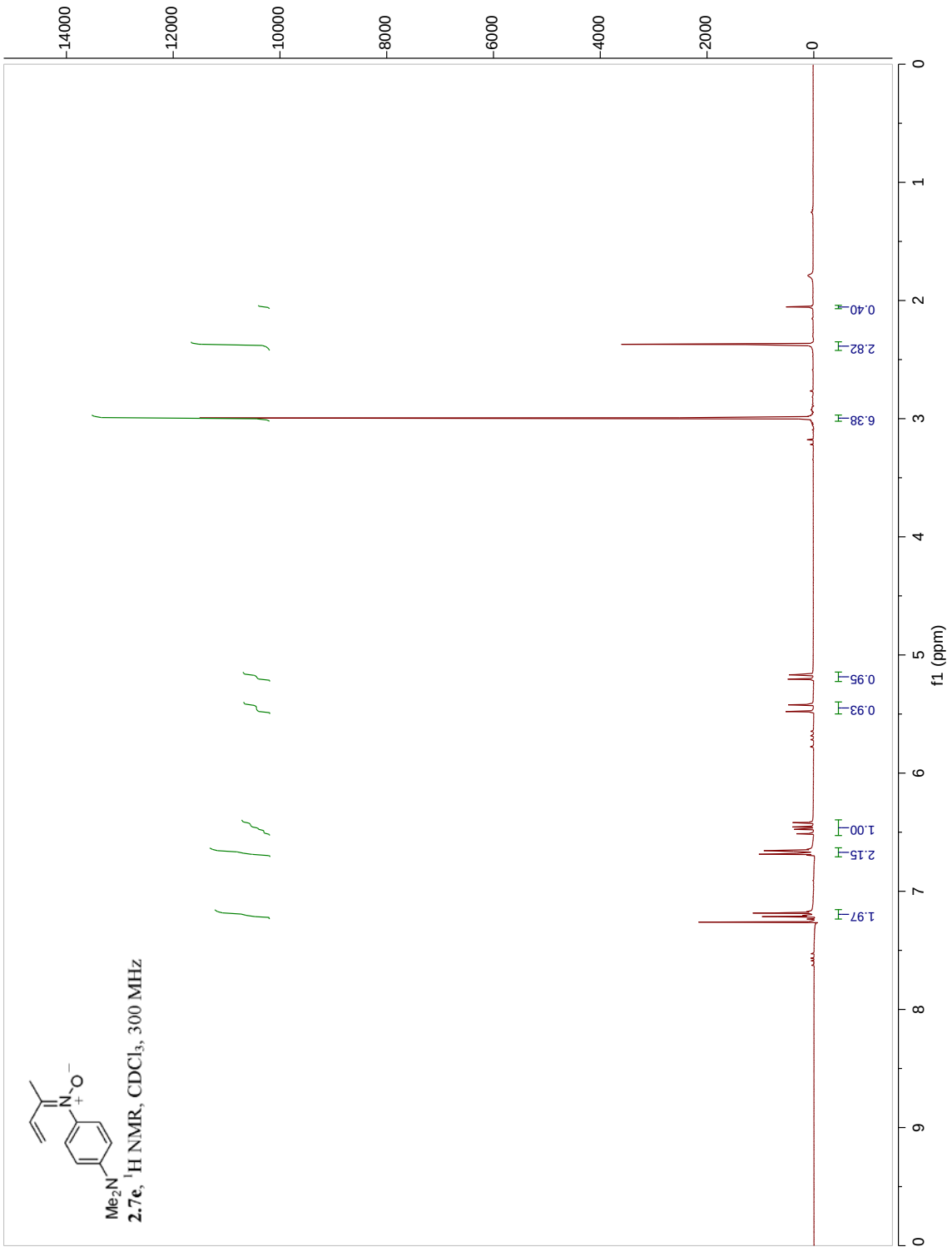

2.7b, ^{13}C NMR, $CDCl_3$, 75 MHz
12.78
21.34
118.14
123.37
124.16
129.97
130.02
139.62
f1 (ppm)

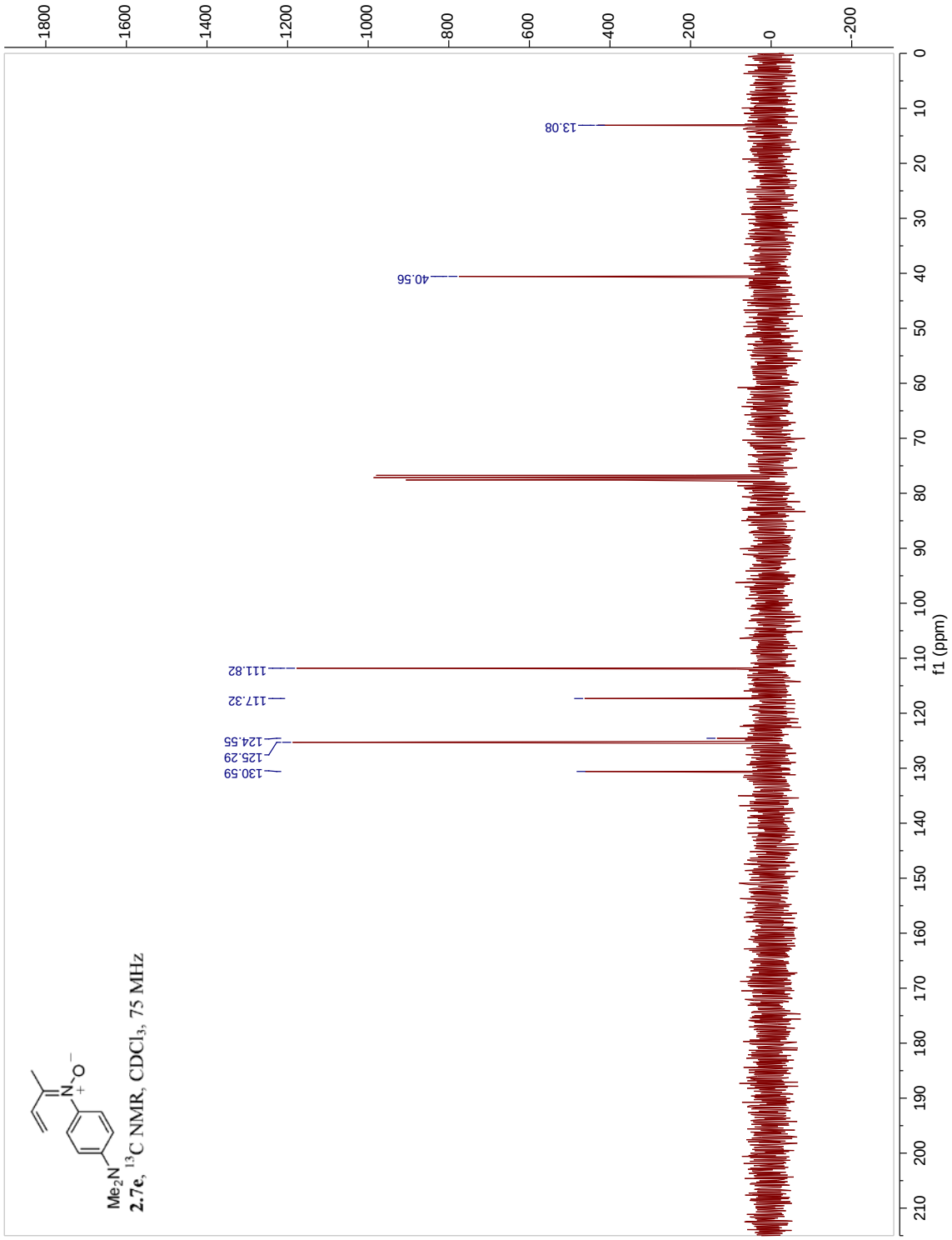

2.7c, ^{1}H NMR, $CDCl_3$, 300 MHz
f1 (ppm)
0.39
3.04
1.04
1.03
1.00
2.43
2.18

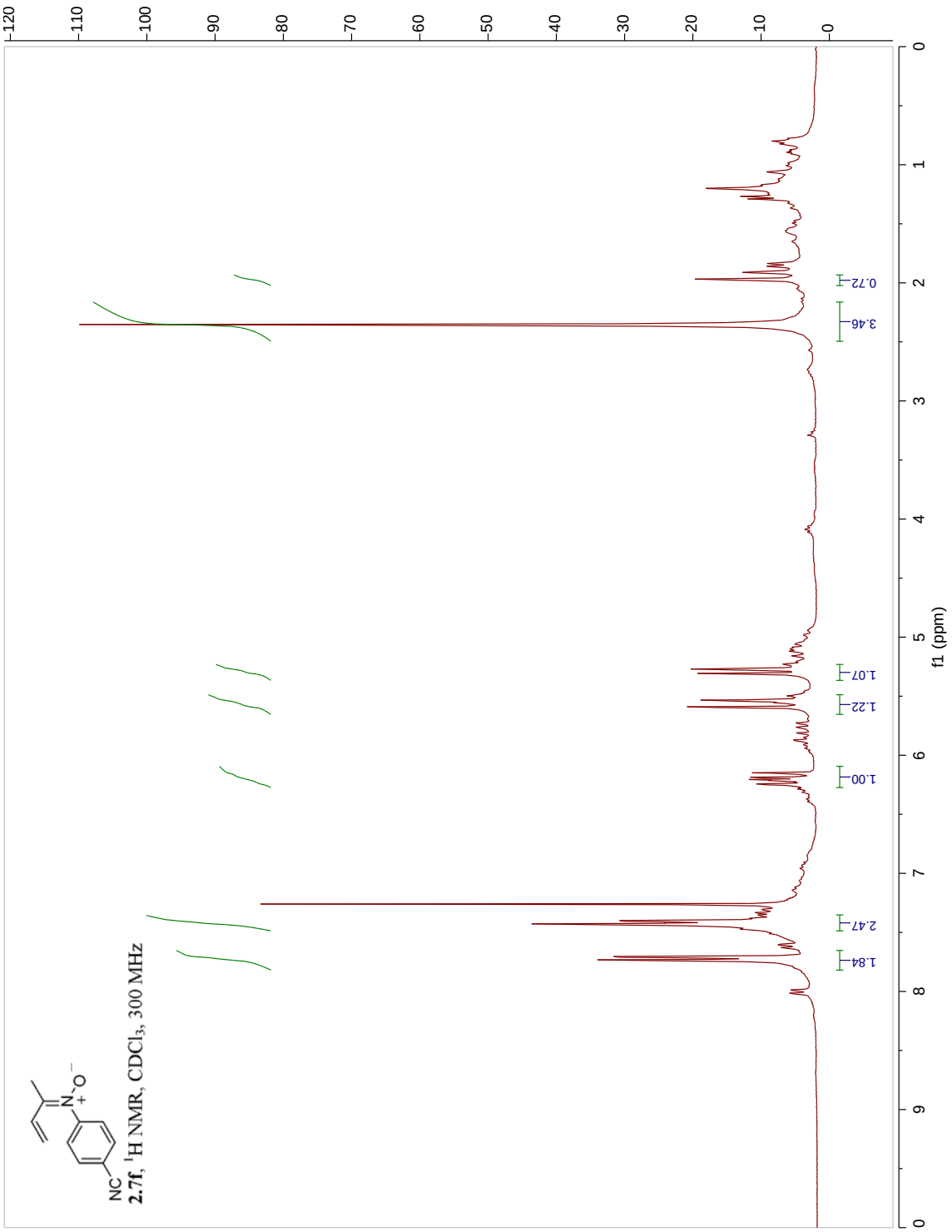

2.7c, ^{13}C NMR, $CDCl_3$, 75 MHz
Cl
N
O
12.78
119.02
125.00
125.74
129.43
129.68
129.76
135.34
f1 (ppm)

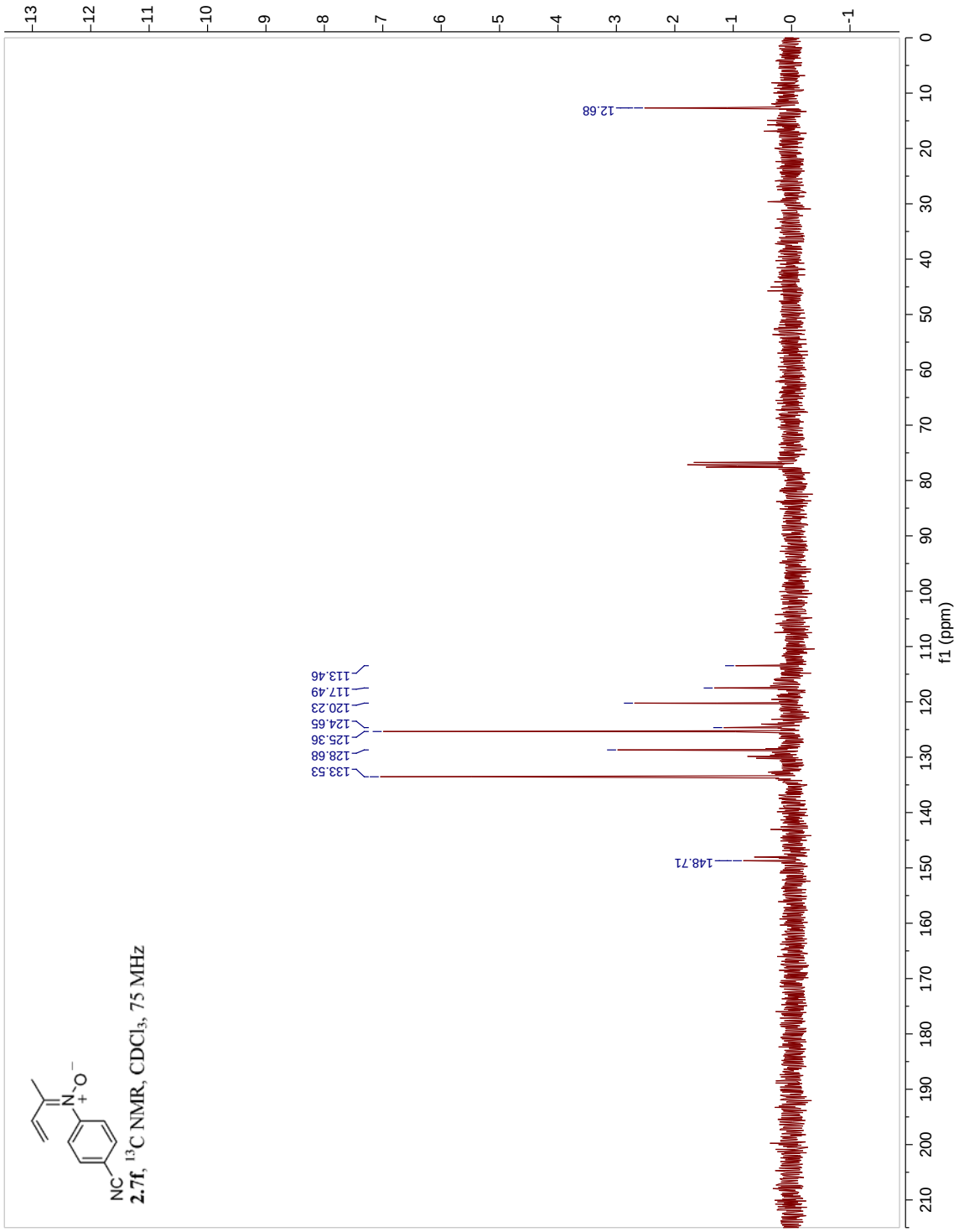

MeO
2.7d, ^{1}H NMR, $CDCl_3$, 300 MHz
0.45
3.10
3.75
1.06
1.07
1.00
2.34
2.98
f1 (ppm)


MeO
2.7d, ^{13}C NMR, $CDCl_3$, 75 MHz
12.93
55.73
109.11
114.47
114.53
118.10
124.93
125.69
130.10
f1 (ppm)

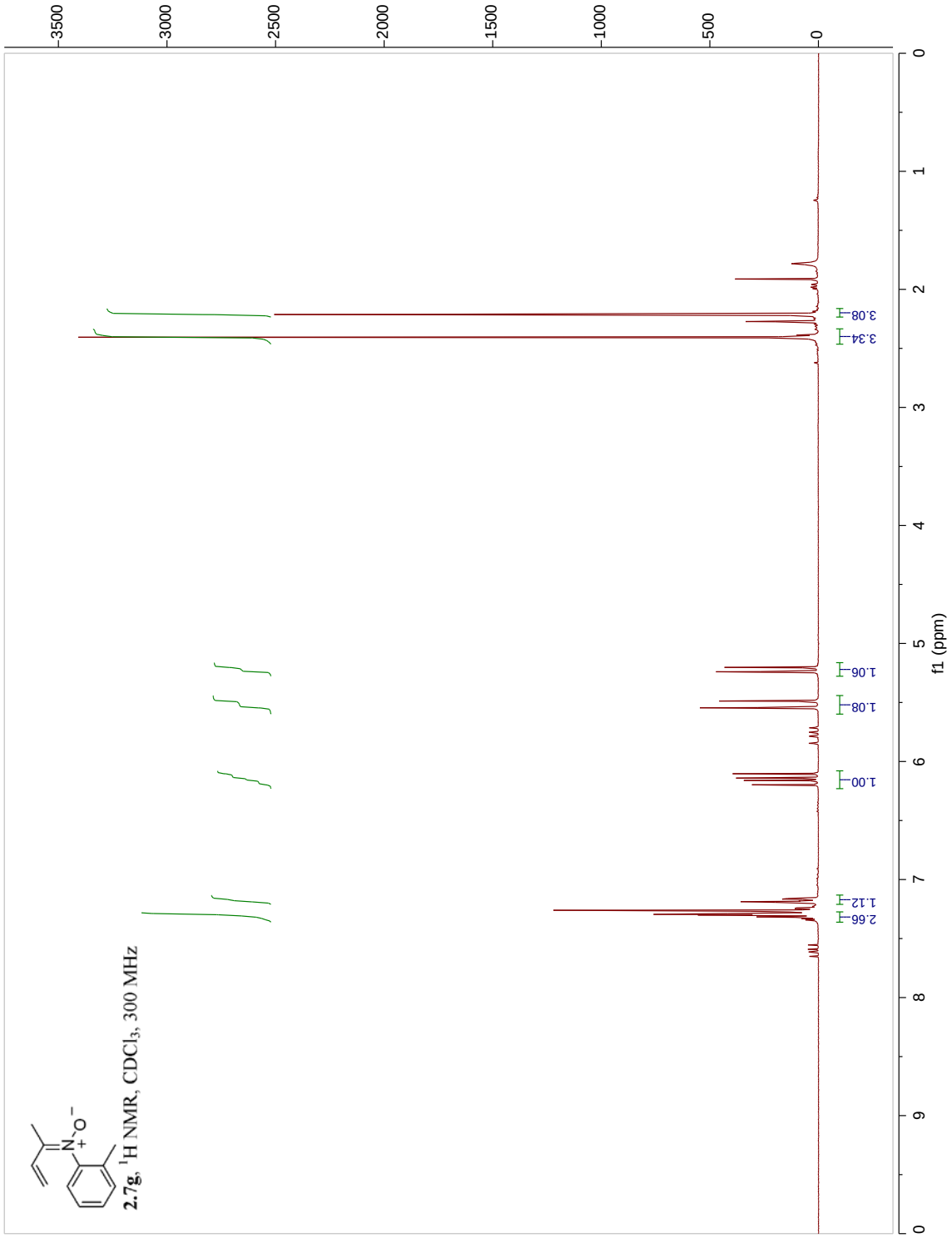

14000
12000
10000
8000
6000
4000
2000
0
0.40
2.82
6.38
0.95
0.93
1.00
2.15
1.97
0
1
2
3
4
5
6
7
8
9
0
f1 (ppm)
Me2N
2.7e, 1H NMR, CDCl3, 300 MHz

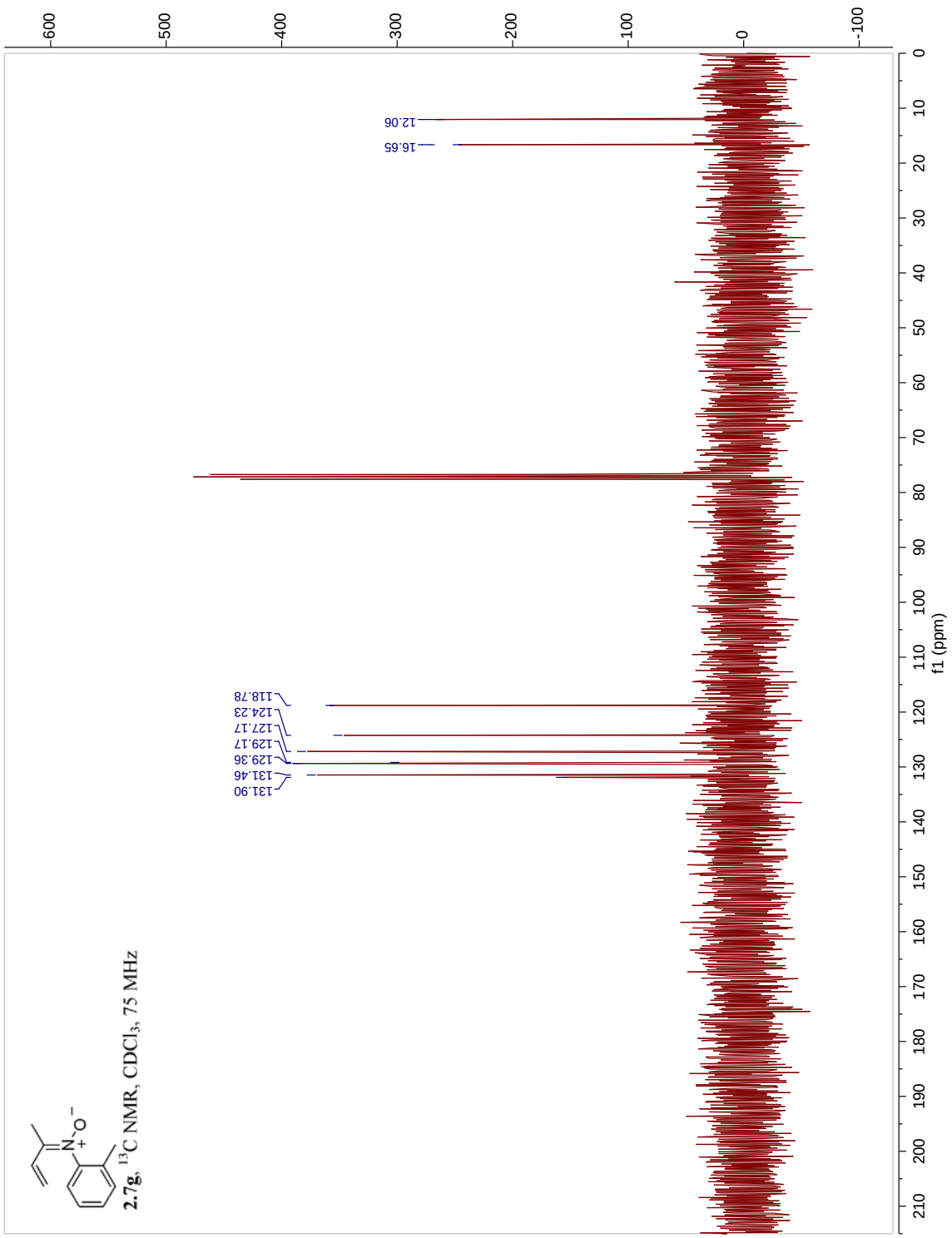

13.08
40.56
111.82
117.32
124.55
125.29
130.59
f1 (ppm)
Me2N
2.7e, 13C NMR, CDCl3, 75 MHz

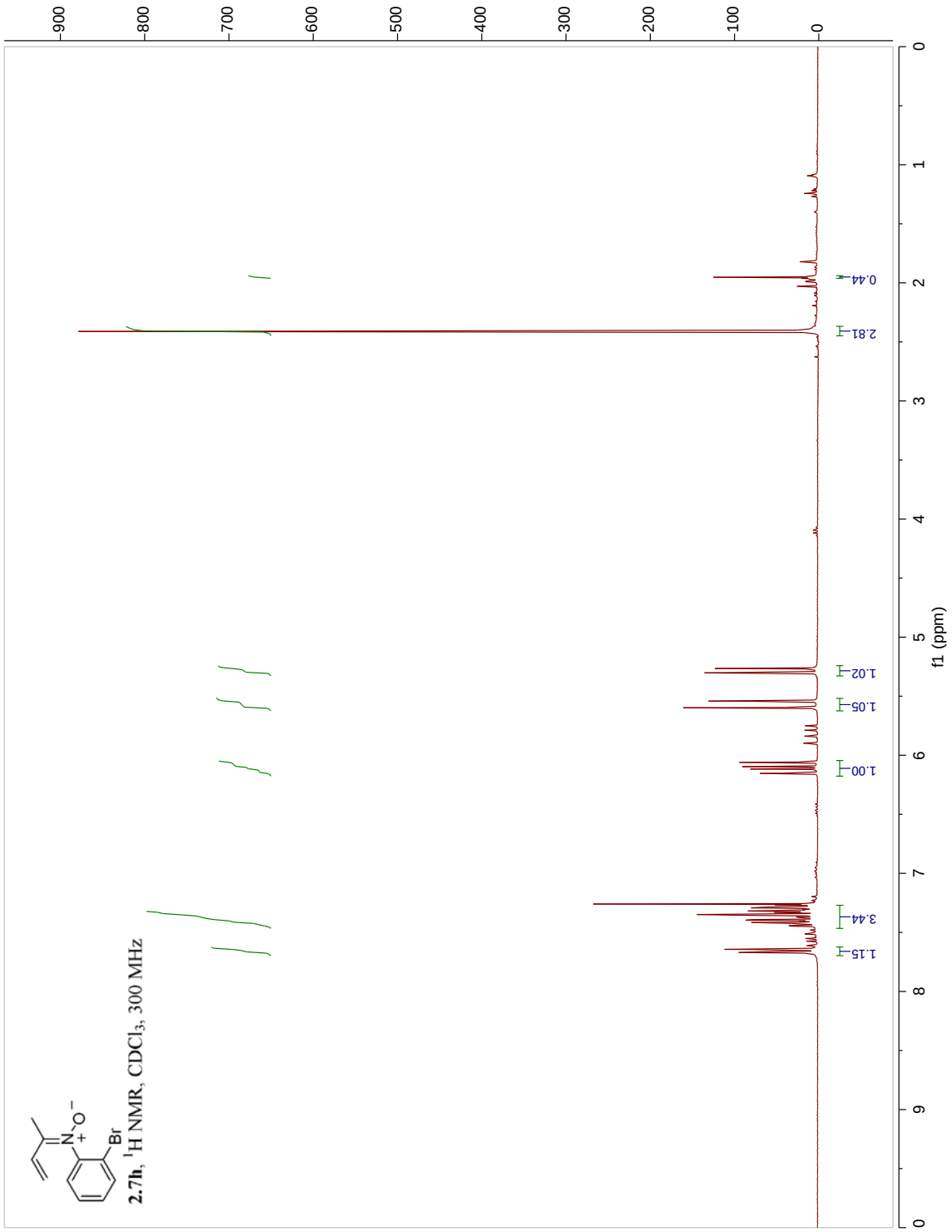

2.7f, ^{1}H NMR, $CDCl_3$, 300 MHz
NC
N
O
f1 (ppm)
0.72
3.46
1.07
1.22
1.00
2.47
1.84

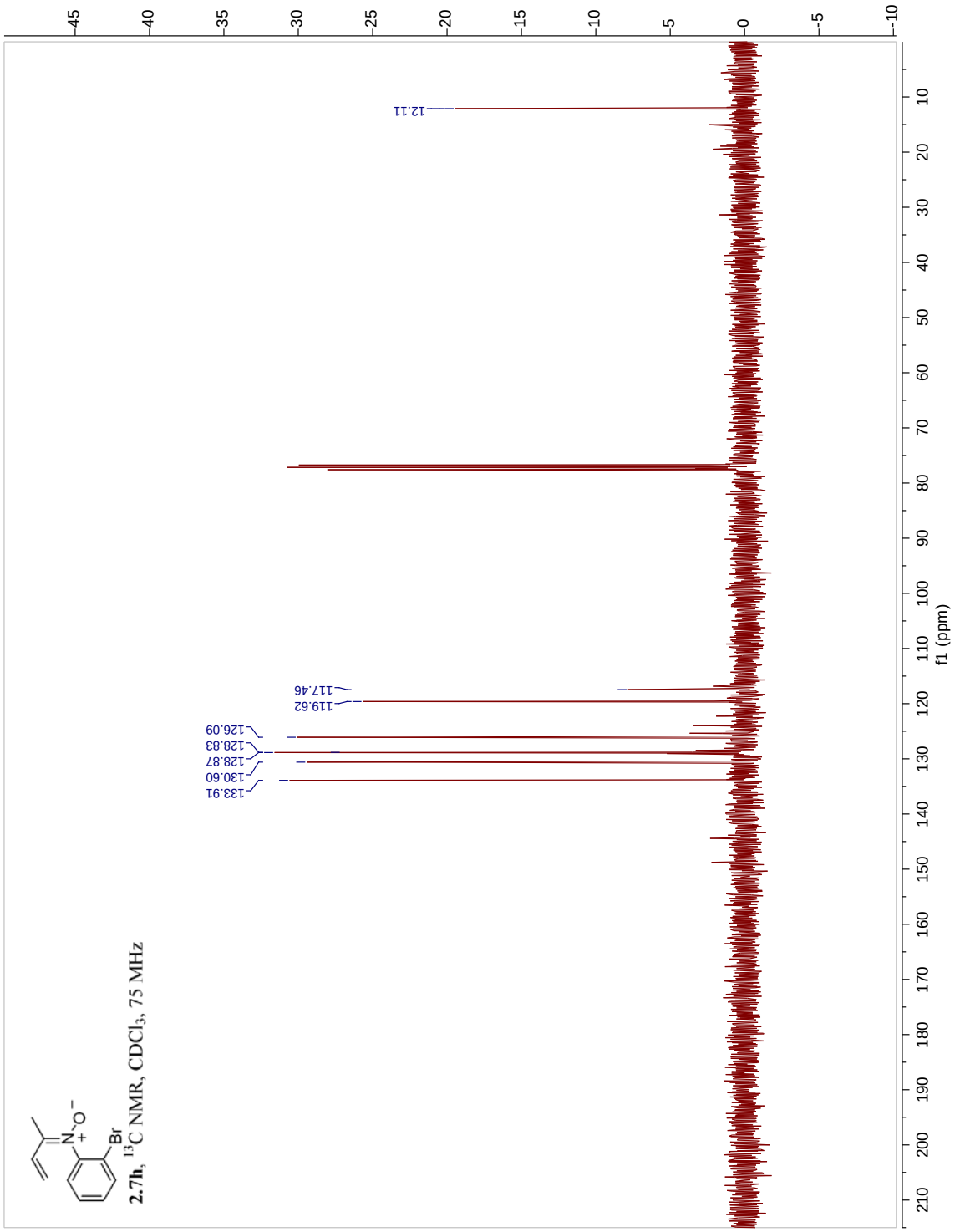


2.7f, ^{13}C NMR, $CDCl_3$, 75 MHz

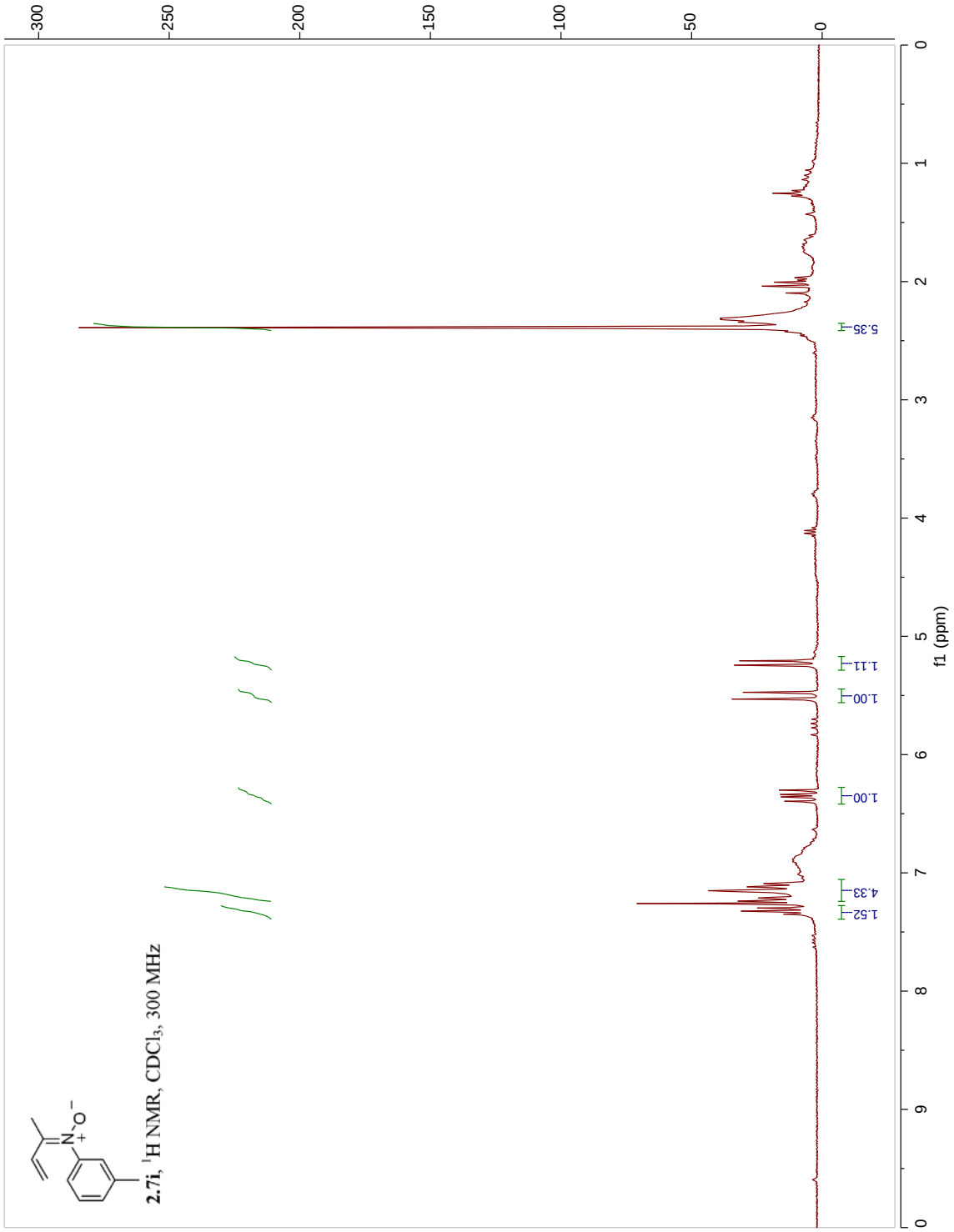

2.7g, ^{1}H NMR, $CDCl_3$, 300 MHz
3.08
3.34
1.06
1.08
1.00
2.66
1.12
f1 (ppm)

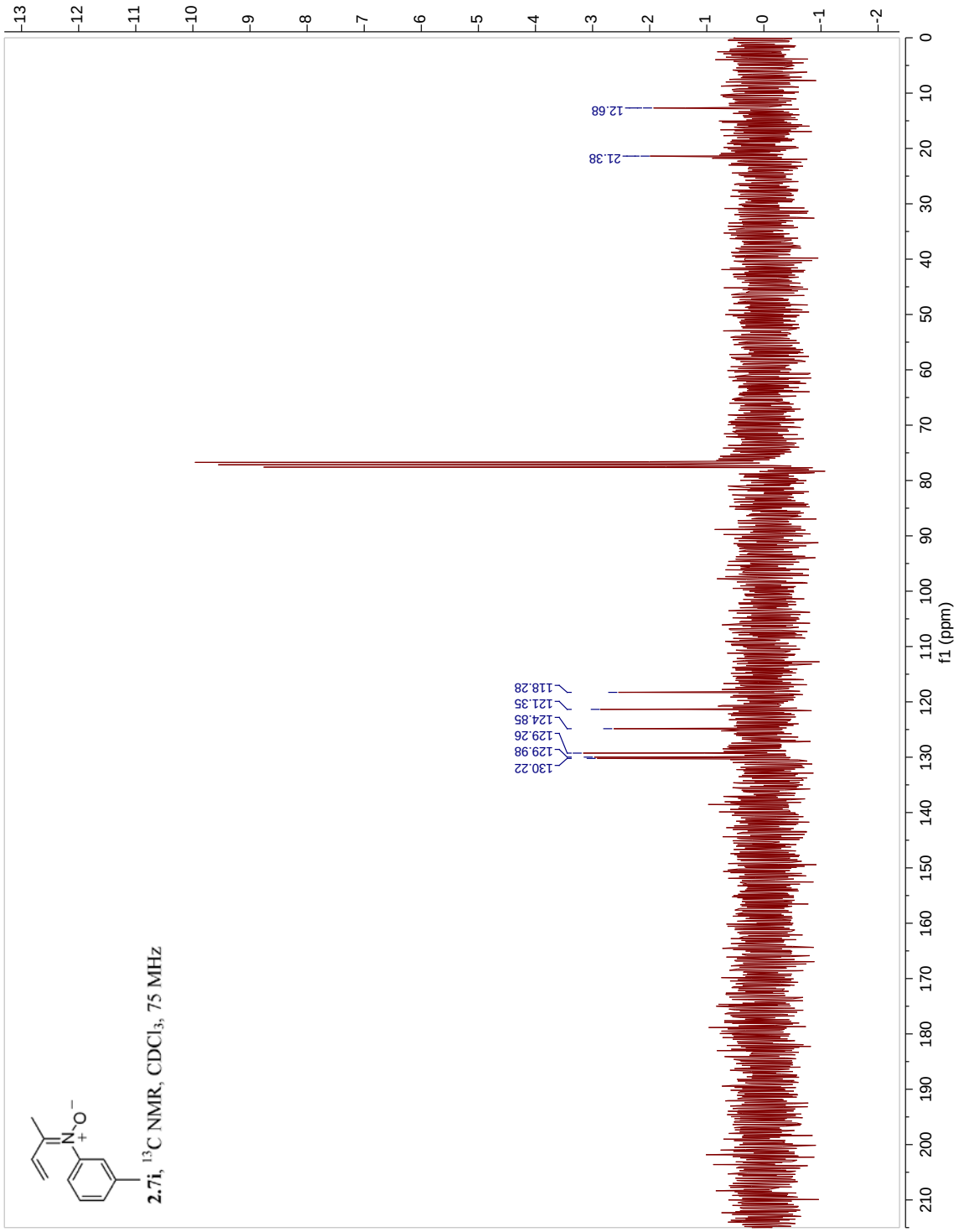

2.7g, ^{13}C NMR, $CDCl_3$, 75 MHz
12.06
16.65
118.78
124.23
127.17
129.17
129.36
131.46
131.90
f1 (ppm)


2.7h, ^{1}H NMR, $CDCl_3$, 300 MHz
Br
N
O
f1 (ppm)
0.44
2.81
1.02
1.05
1.00
3.44
1.15

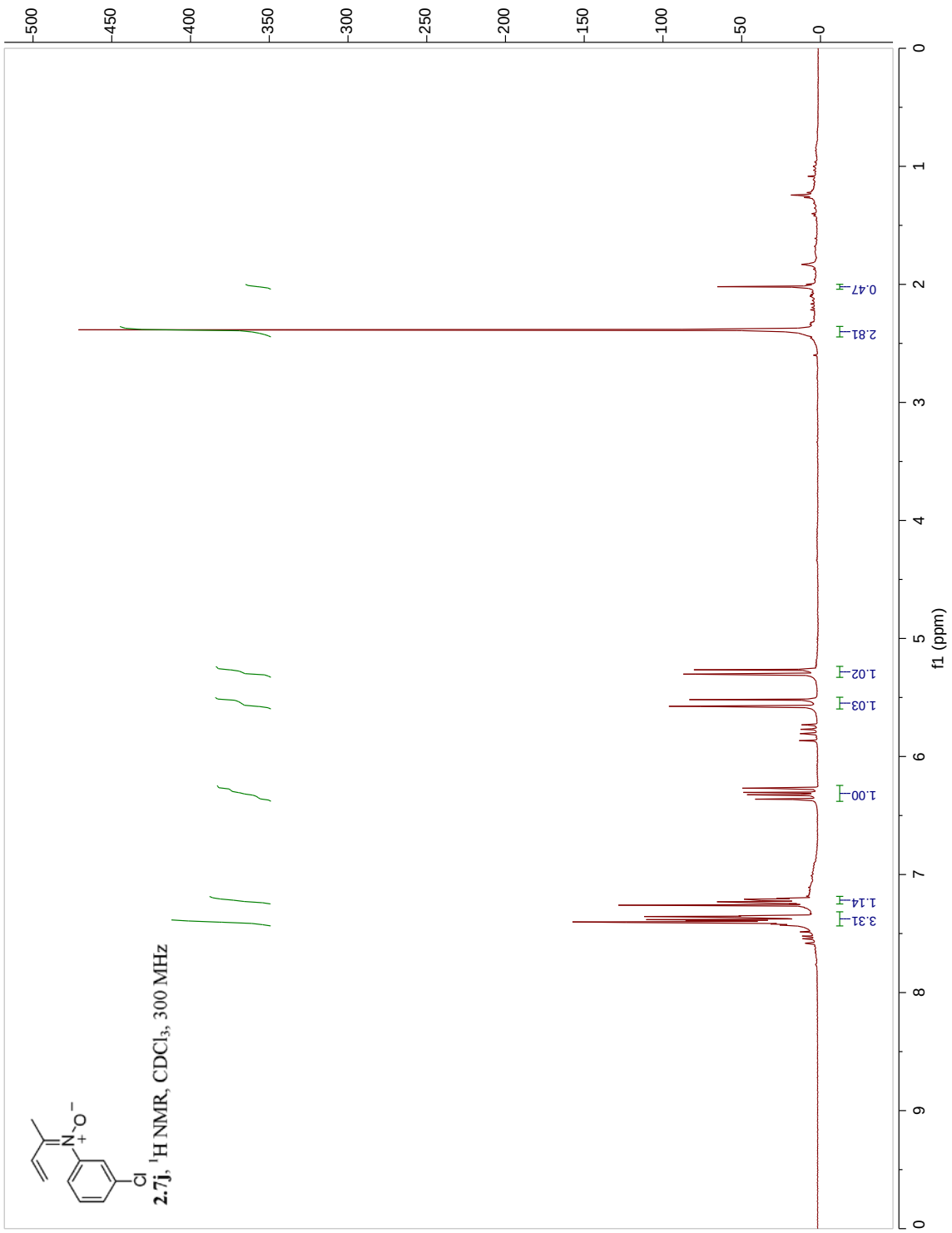


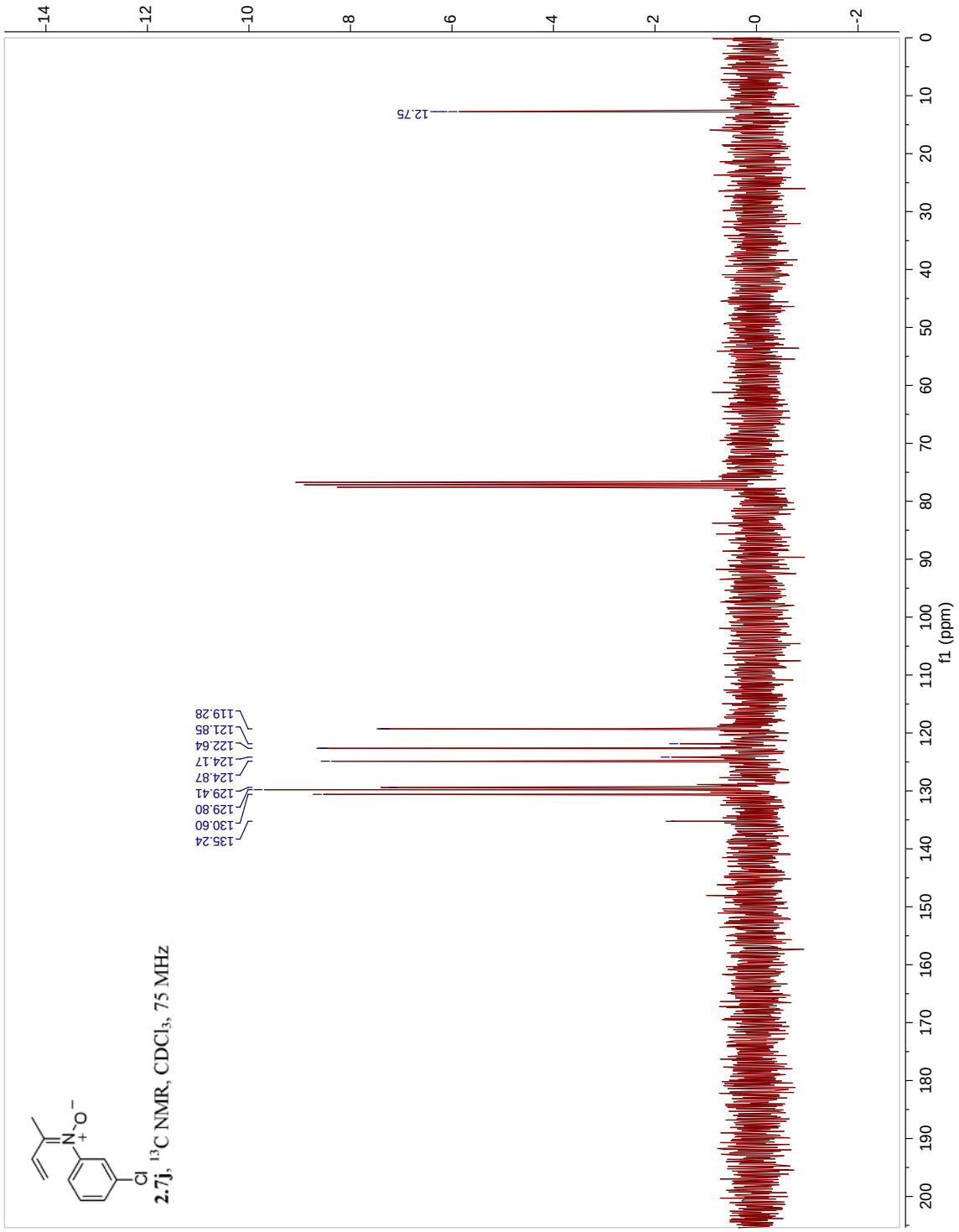
2.7h, ^{13}C NMR, $CDCl_3$, 75 MHz


2.7i, ^{1}H NMR, $CDCl_3$, 300 MHz
5.35
1.11
1.00
1.00
4.33
1.52
f1 (ppm)

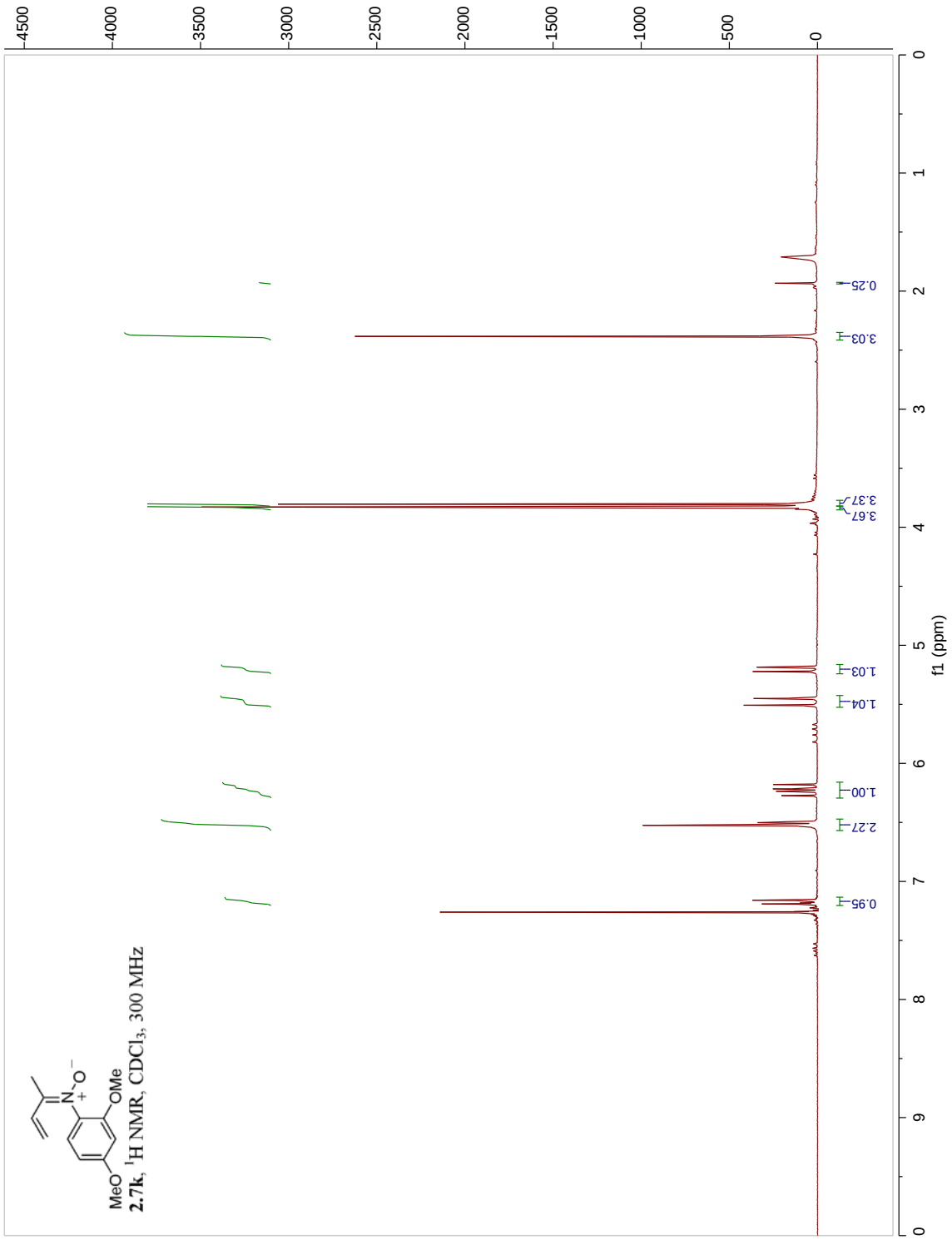


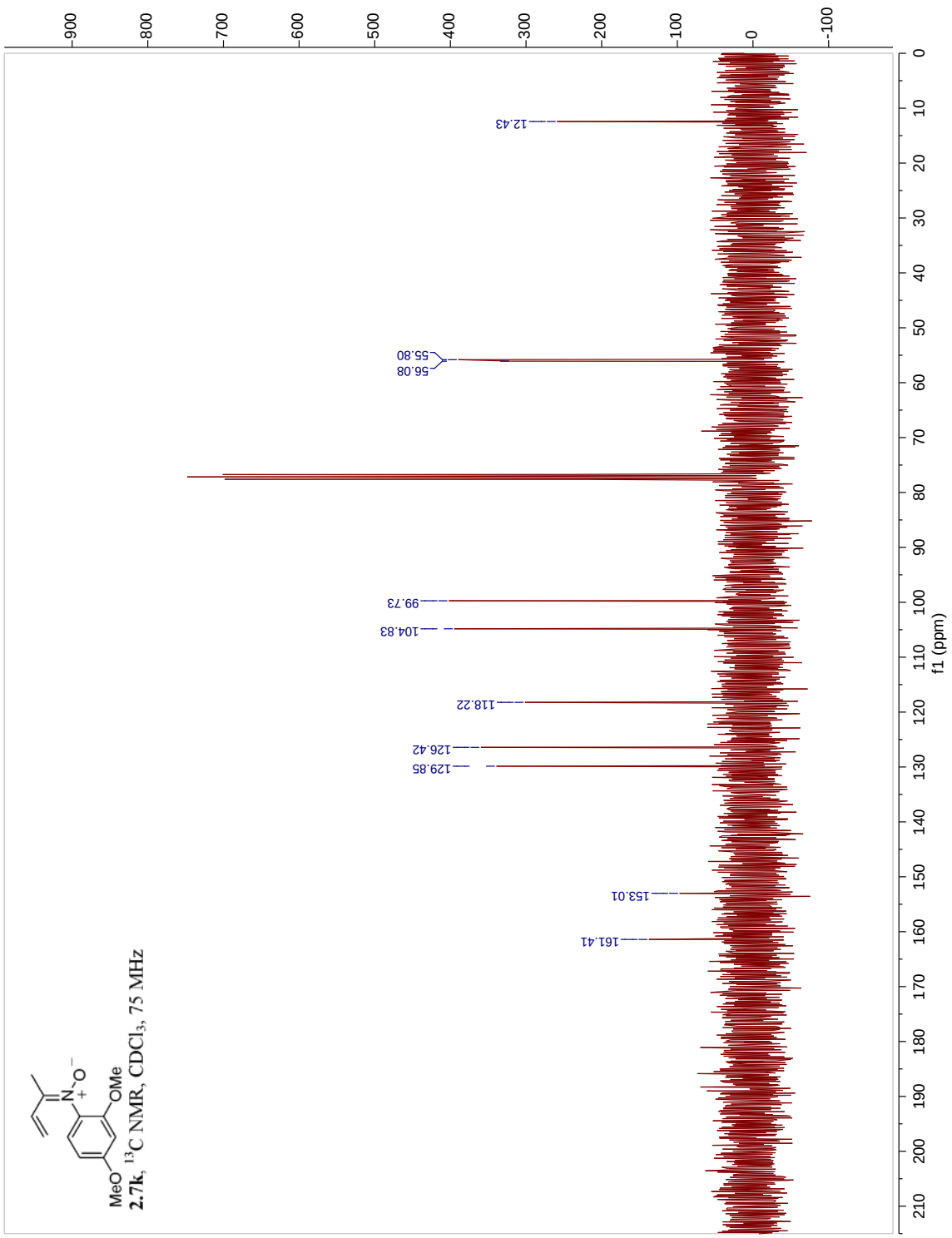
2.7i, ^{13}C NMR, $CDCl_3$, 75 MHz


2.7j, ^{1}H NMR, $CDCl_3$, 300 MHz
f1 (ppm)
0.47
2.81
1.02
1.03
1.00
1.14
3.31

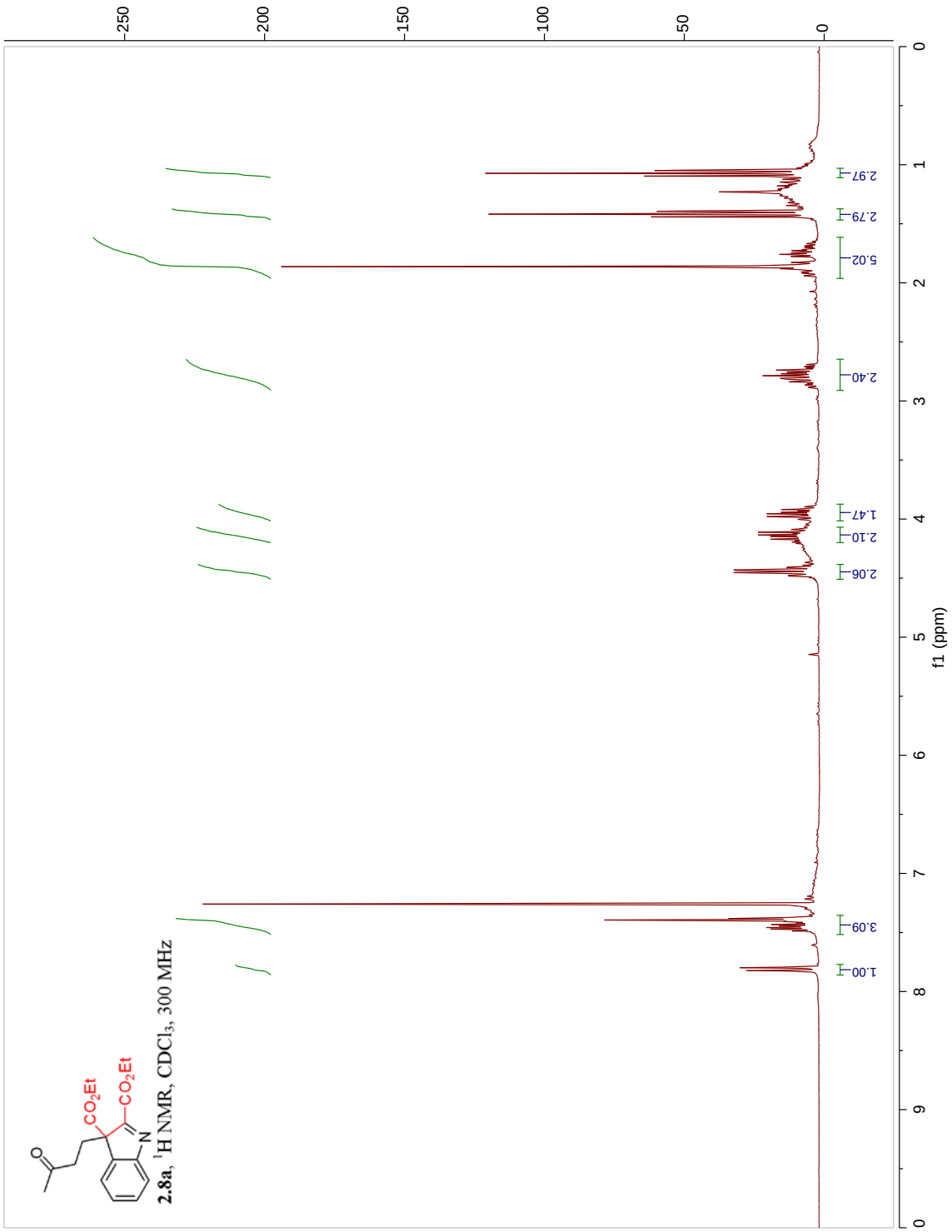


2.7j, ^{13}C NMR, $CDCl_3$, 75 MHz

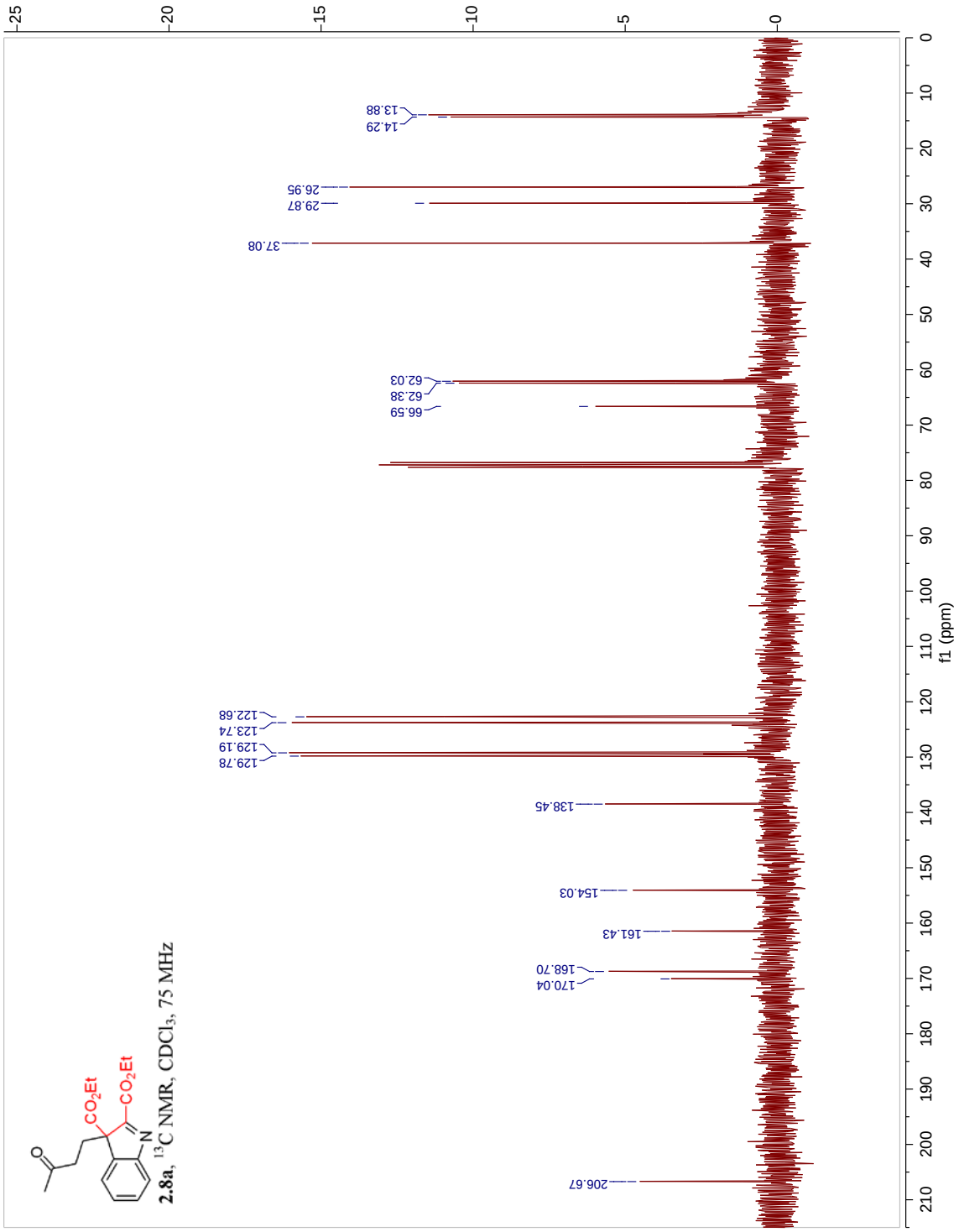

4500
4000
3500
3000
2500
2000
1500
1000
500
0
0.25
3.03
3.67
3.37
1.03
1.04
1.00
2.27
0.95
0
1
2
3
4
5
6
7
8
9
0
f1 (ppm)
MeO
OMe
2.7k, ^{1}H NMR, $CDCl_3$, 300 MHz

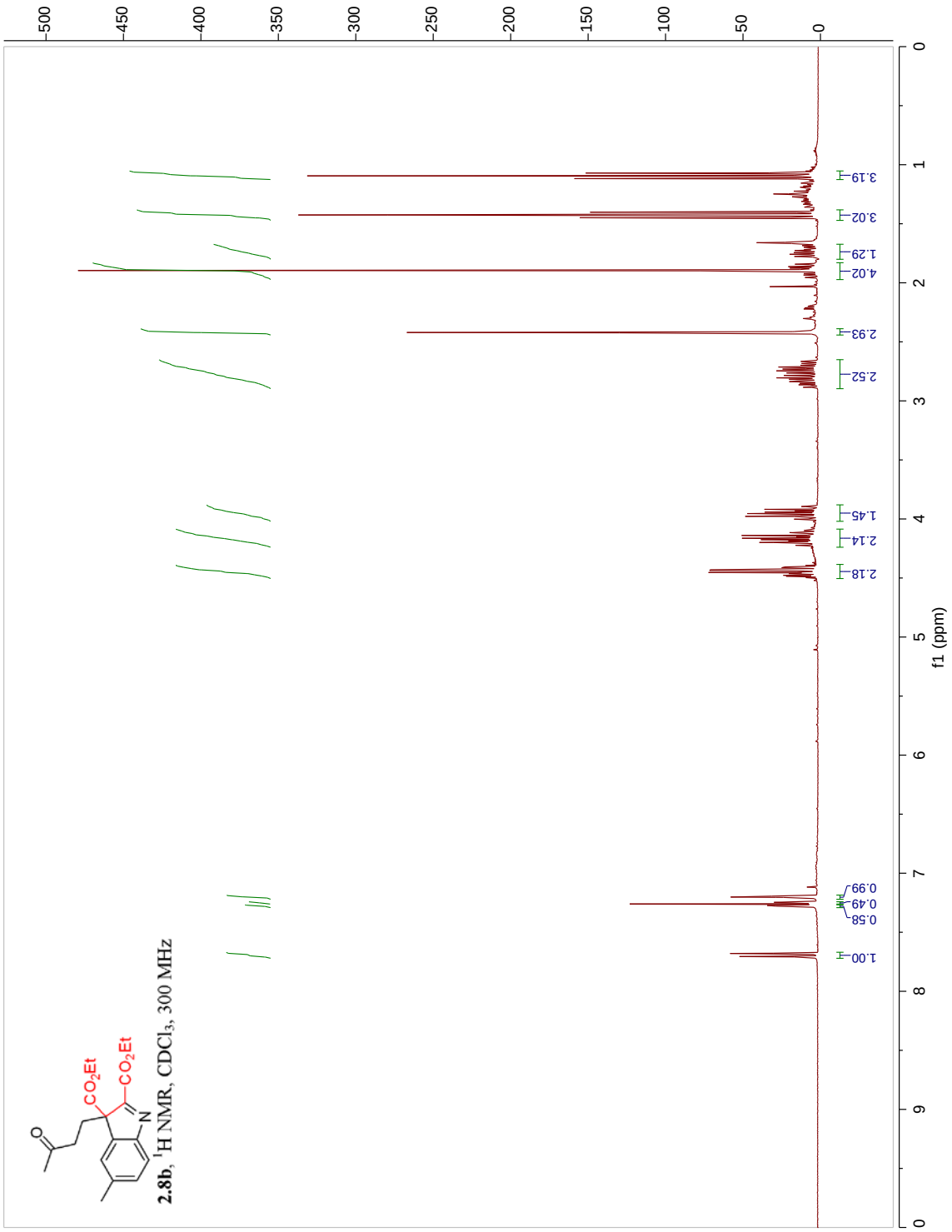


2.7k, ^{13}C NMR, $CDCl_3$, 75 MHz

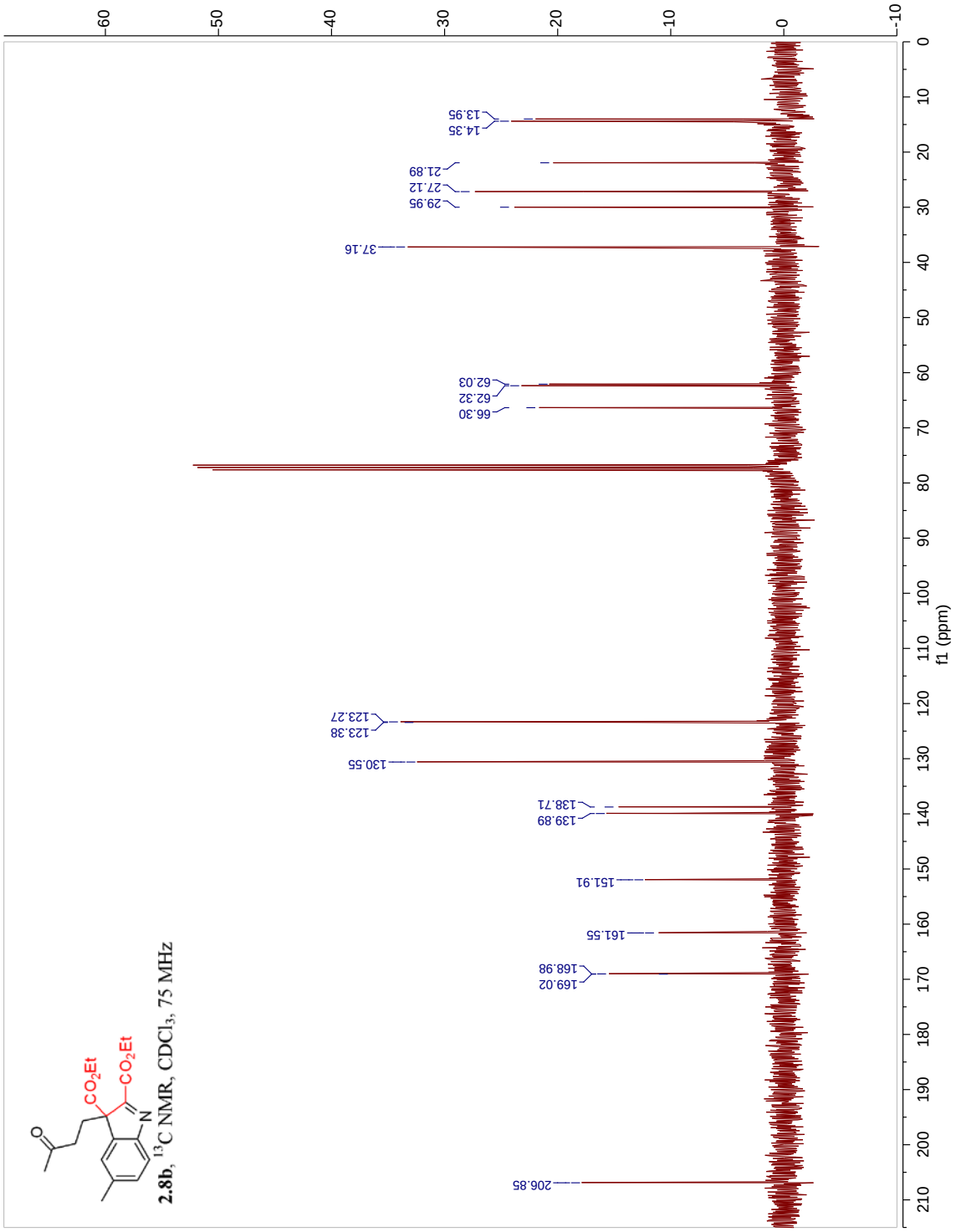


2.8a, ^{1}H NMR, $CDCl_3$, 300 MHz

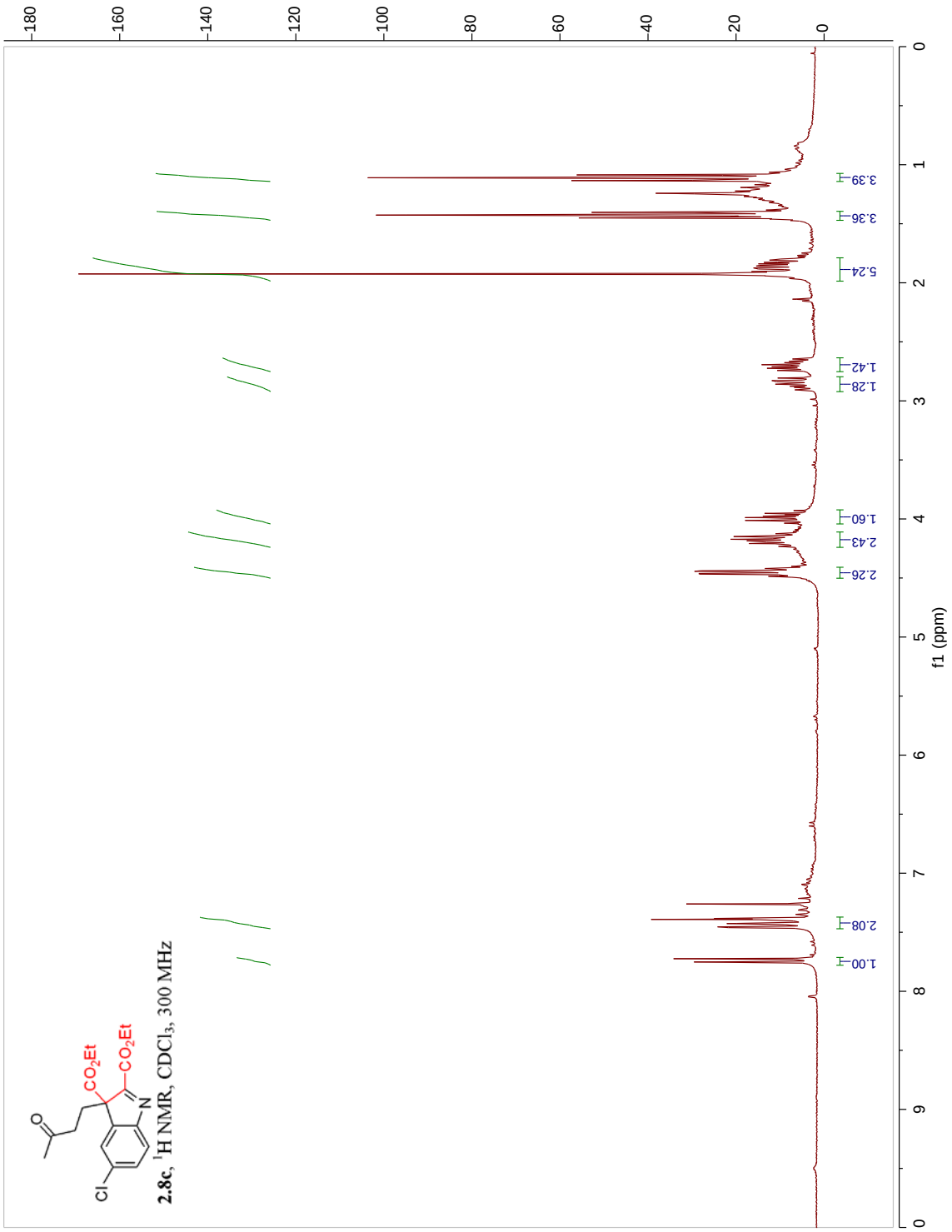

2.8a, ^{13}C NMR, $CDCl_3$, 75 MHz
CO2Et
CO2Et
N
O
206.67
170.04
168.70
161.43
154.03
138.45
129.78
129.19
123.74
122.68
66.59
62.38
62.03
37.08
29.87
26.95
14.29
13.88
f1 (ppm)

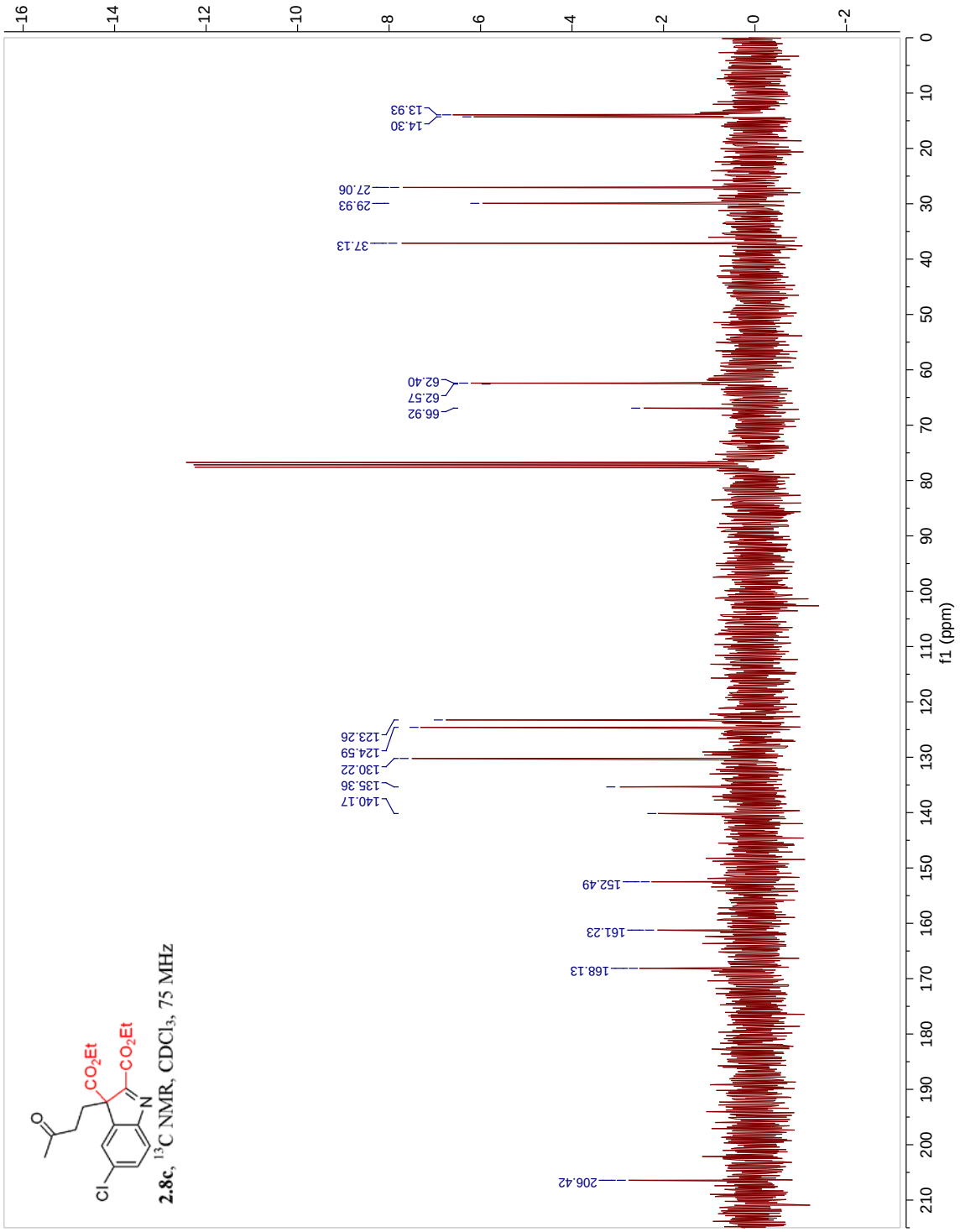


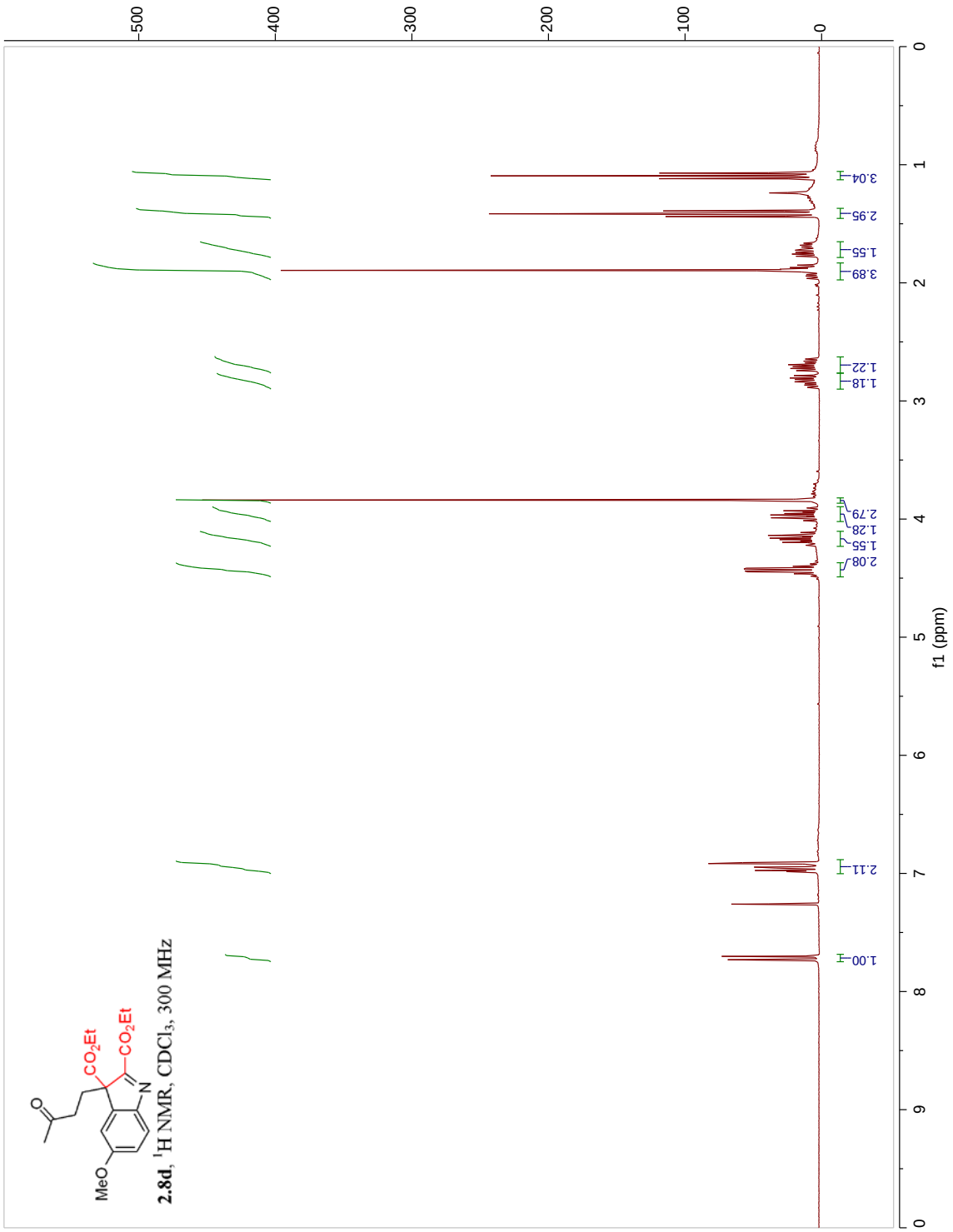
2.8b, ^{1}H NMR, $CDCl_3$, 300 MHz

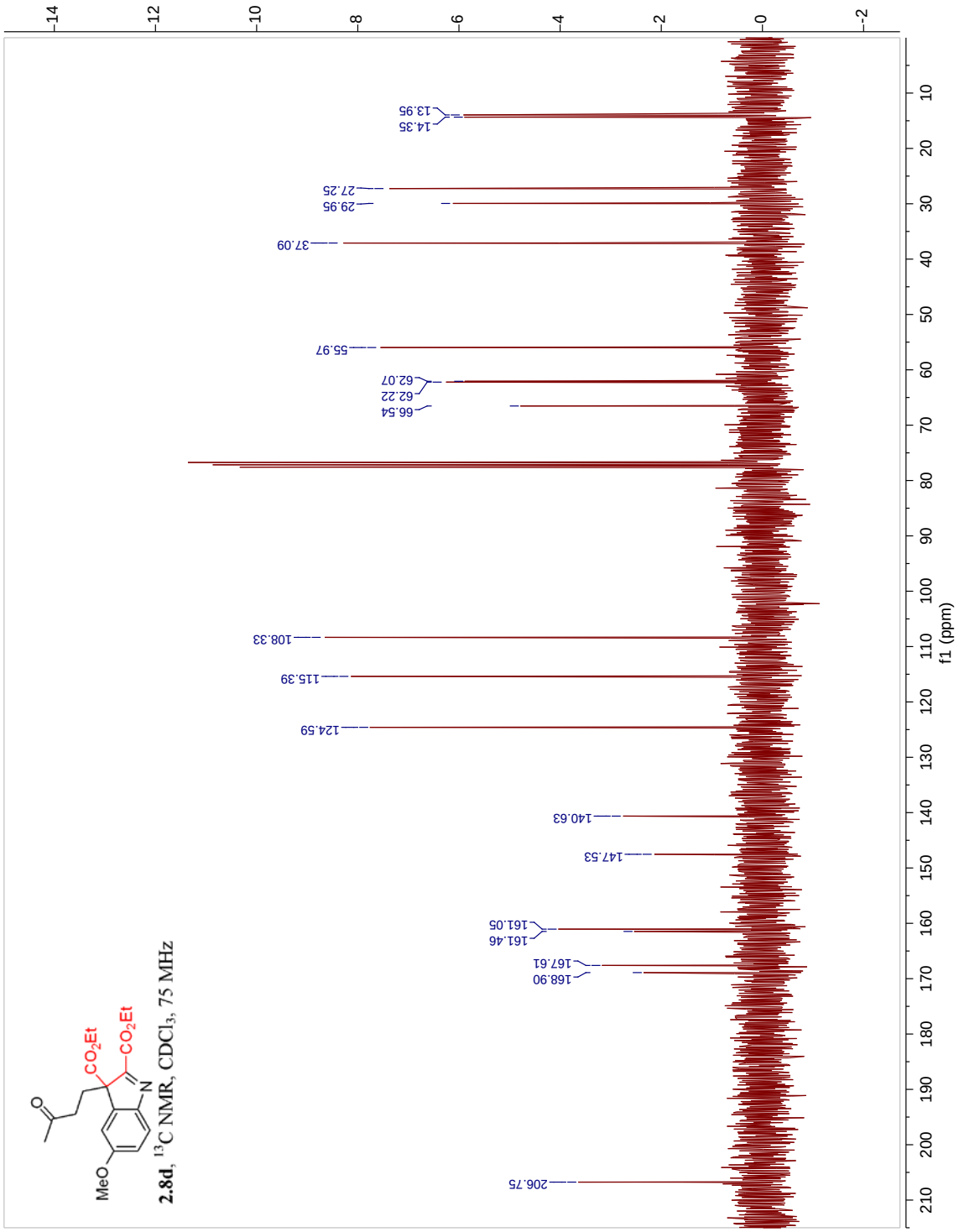


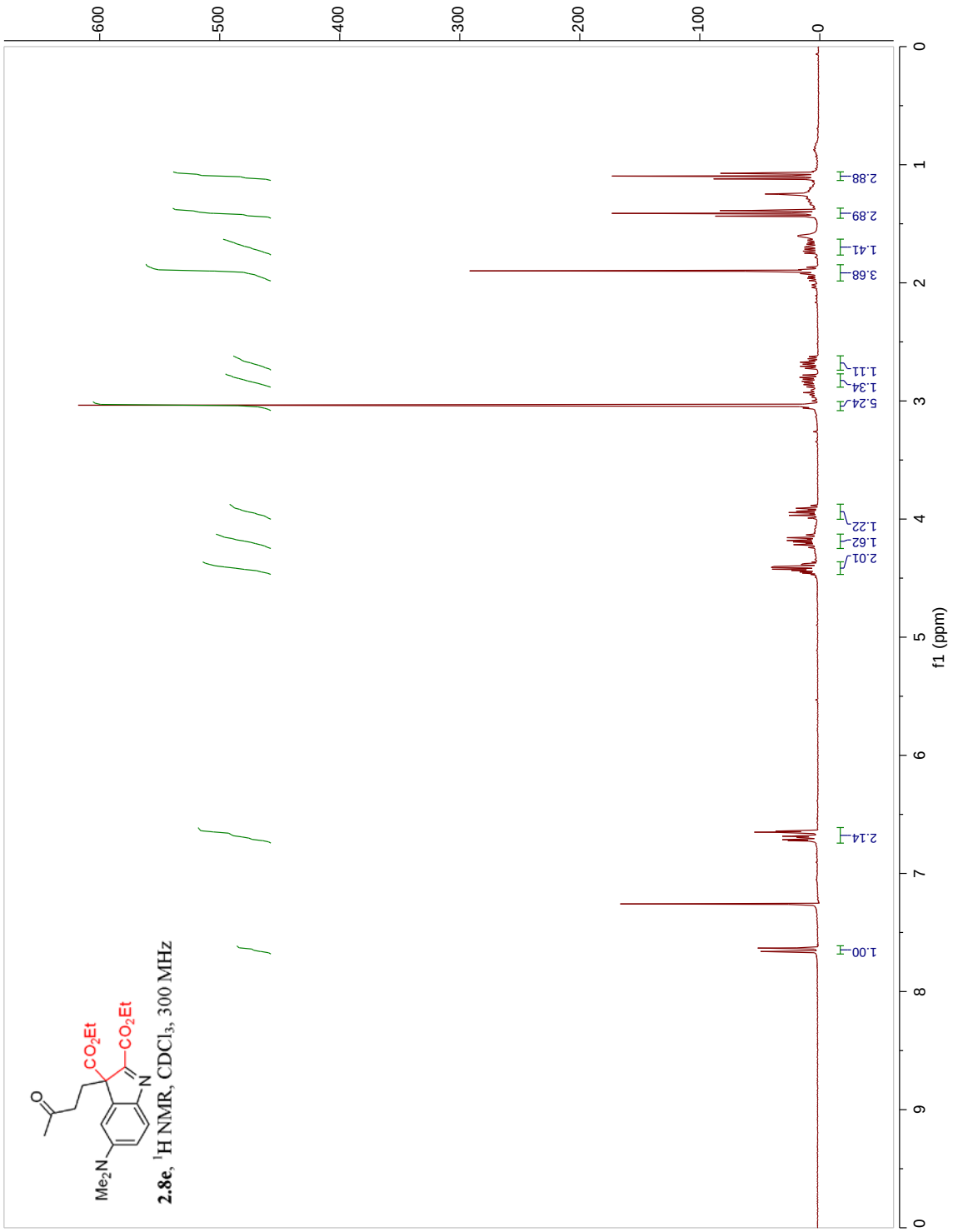
2.8b, ^{13}C NMR, $CDCl_3$, 75 MHz


2.8c, ^{1}H NMR, $CDCl_3$, 300 MHz
CO_2Et
CO_2Et
N
O
Cl
3.39
3.36
5.24
1.42
1.28
1.60
2.43
2.26
2.08
1.00
f1 (ppm)

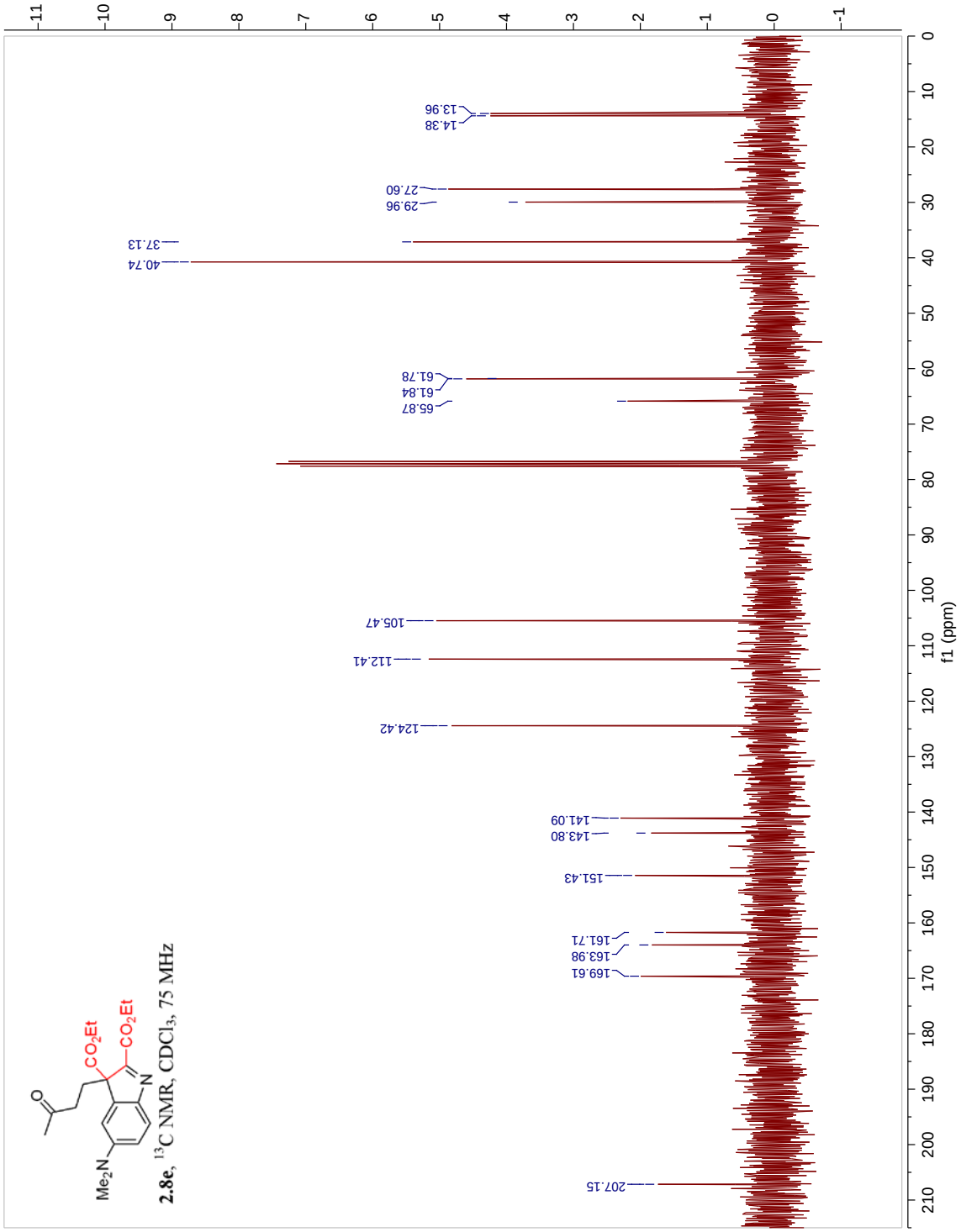

206.42
168.13
161.23
152.49
140.17
135.36
130.22
124.59
123.26
66.92
62.57
62.40
37.13
29.93
27.06
14.30
13.93
f1 (ppm)
2.8c, ^{13}C NMR, $CDCl_3$, 75 MHz
CO_2Et
CO_2Et
N
O
Cl

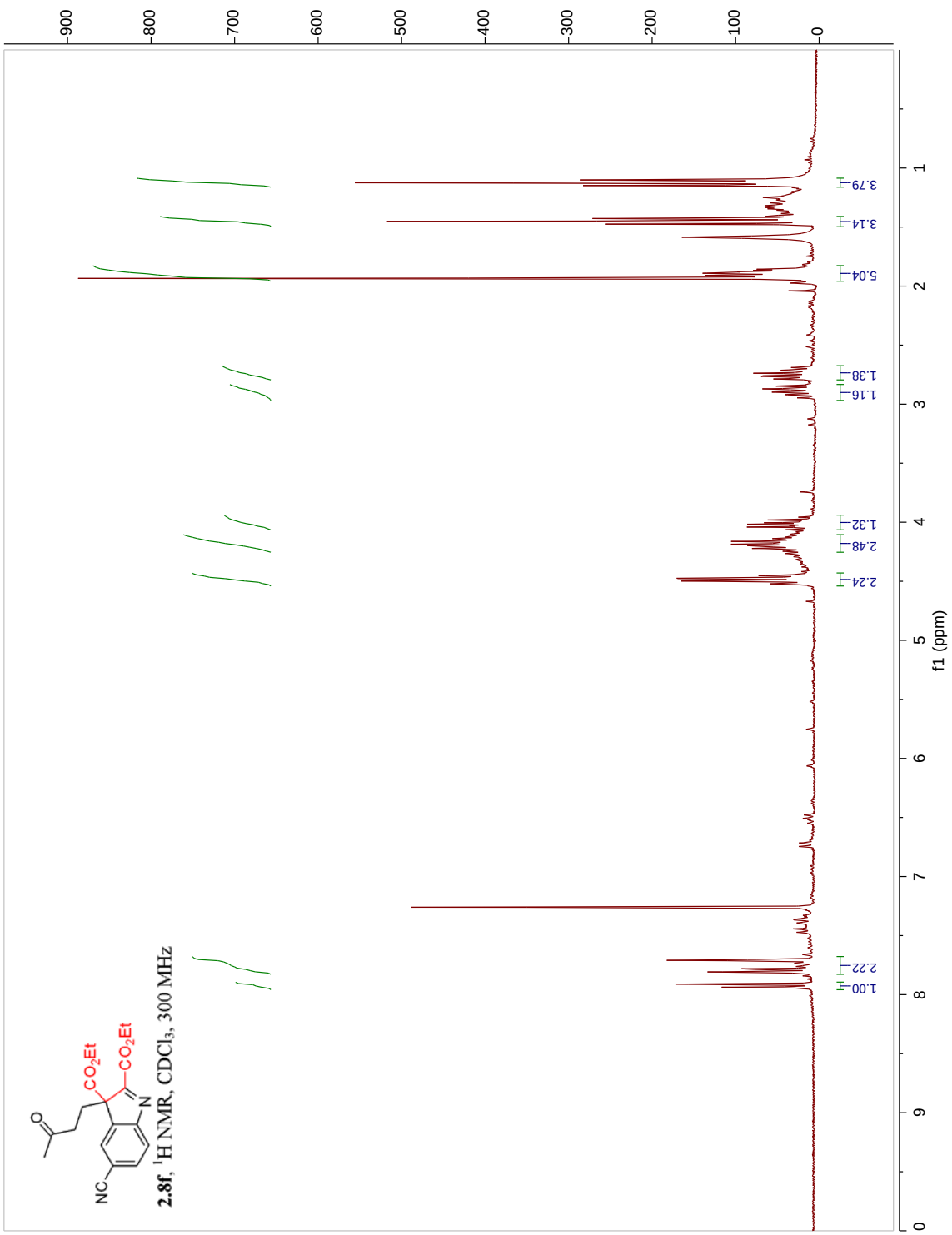

2.8d, ^{1}H NMR, $CDCl_3$, 300 MHz
MeO
CO_2Et
CO_2Et
N
O
3.04
2.95
1.55
3.89
1.22
1.18
2.79
1.28
1.55
2.08
2.11
1.00
f1 (ppm)

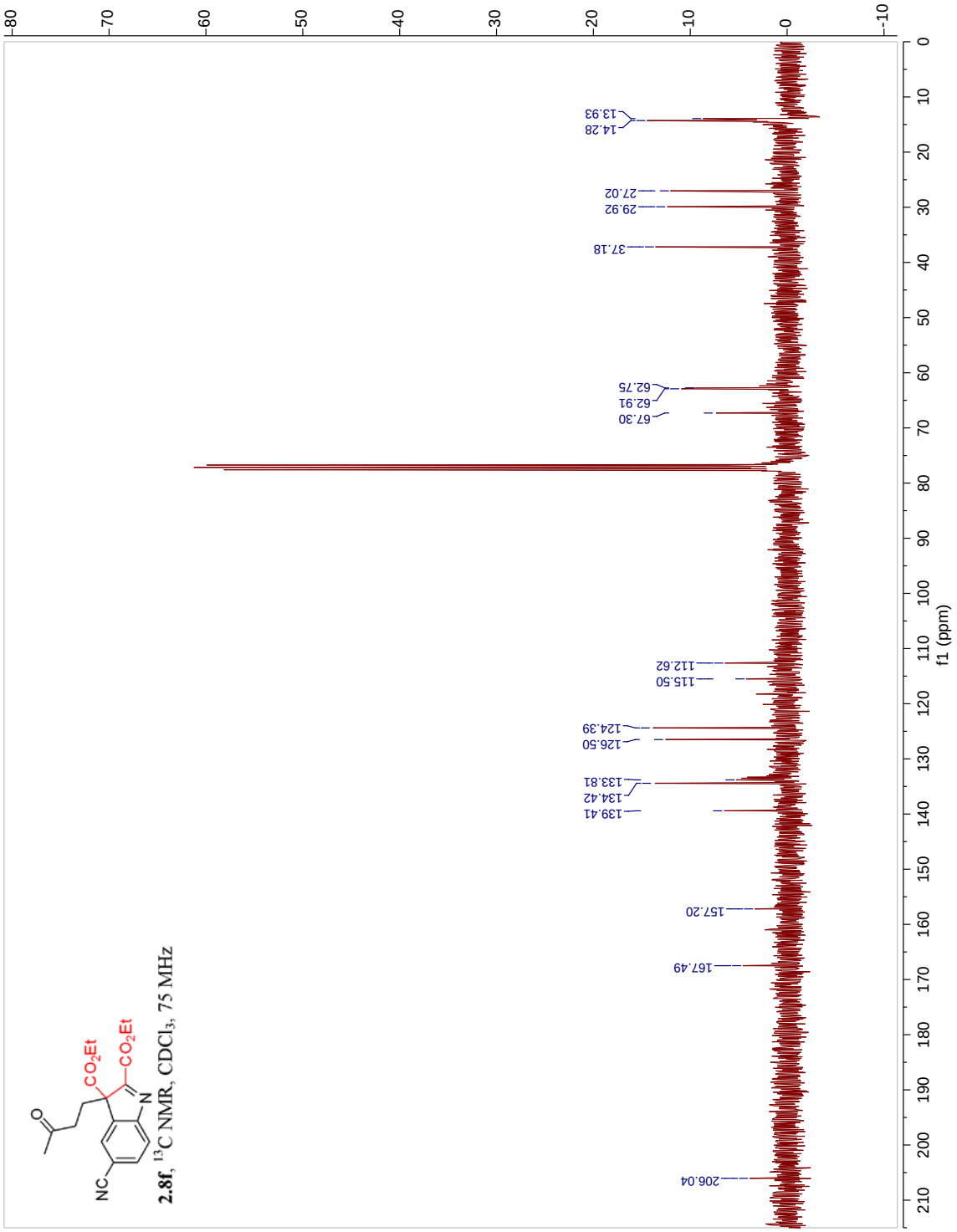

2.8d, ^{13}C NMR, $CDCl_3$, 75 MHz
MeO
CO2Et
CO2Et
N
O
206.75
168.90
167.61
161.46
161.05
147.53
140.63
124.59
115.39
108.33
66.54
62.22
62.07
55.97
37.09
29.95
27.25
14.35
13.95
f1 (ppm)



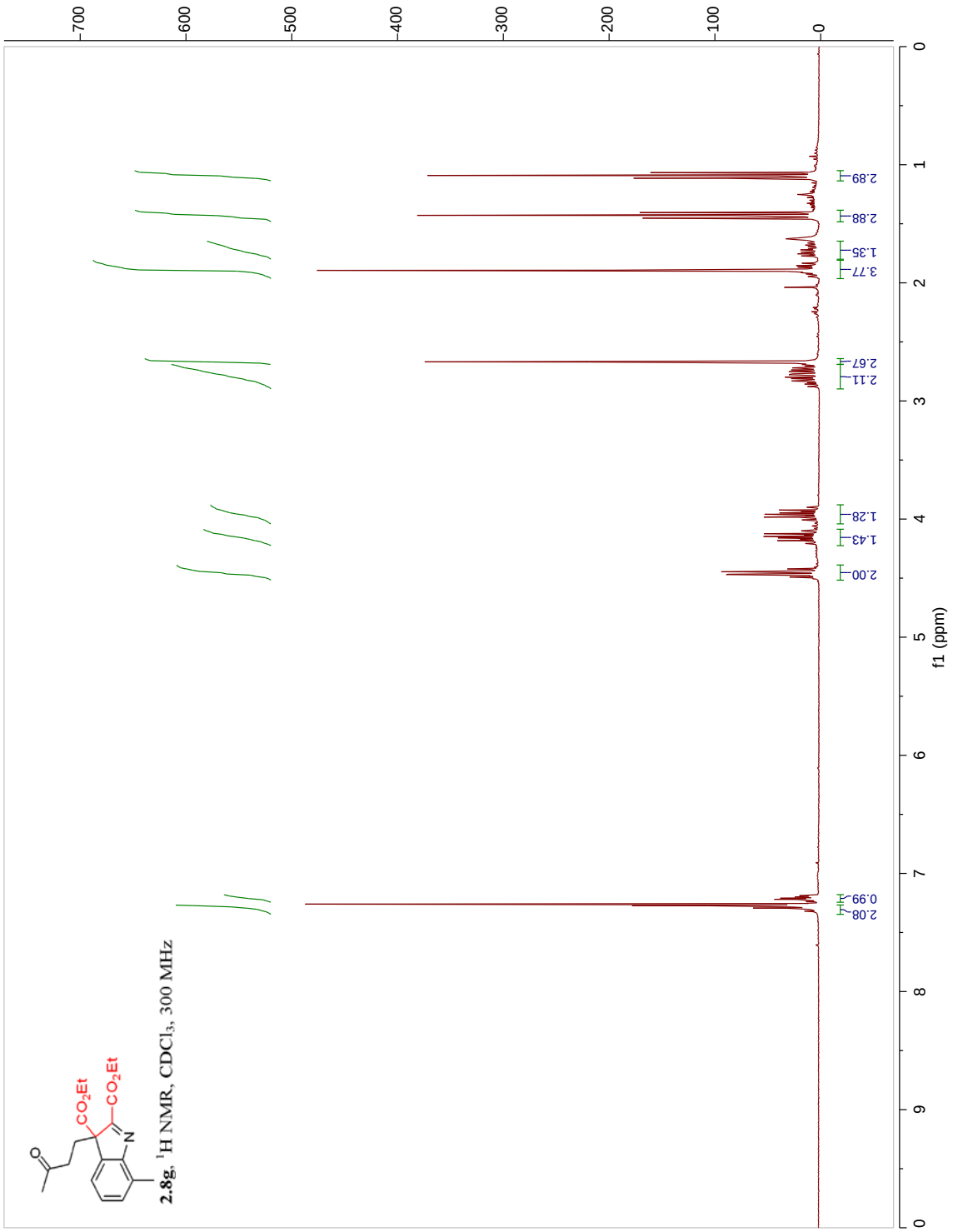
2.8e, ^{1}H NMR, $CDCl_3$, 300 MHz


13.96
14.38
27.60
29.96
37.13
40.74
61.78
61.84
65.87
105.47
112.41
124.42
141.09
143.80
151.43
161.71
163.98
169.61
207.15
f1 (ppm)
2.8e, ^{13}C NMR, $CDCl_3$, 75 MHz
CO_2Et
CO_2Et
Me_2N
O
N

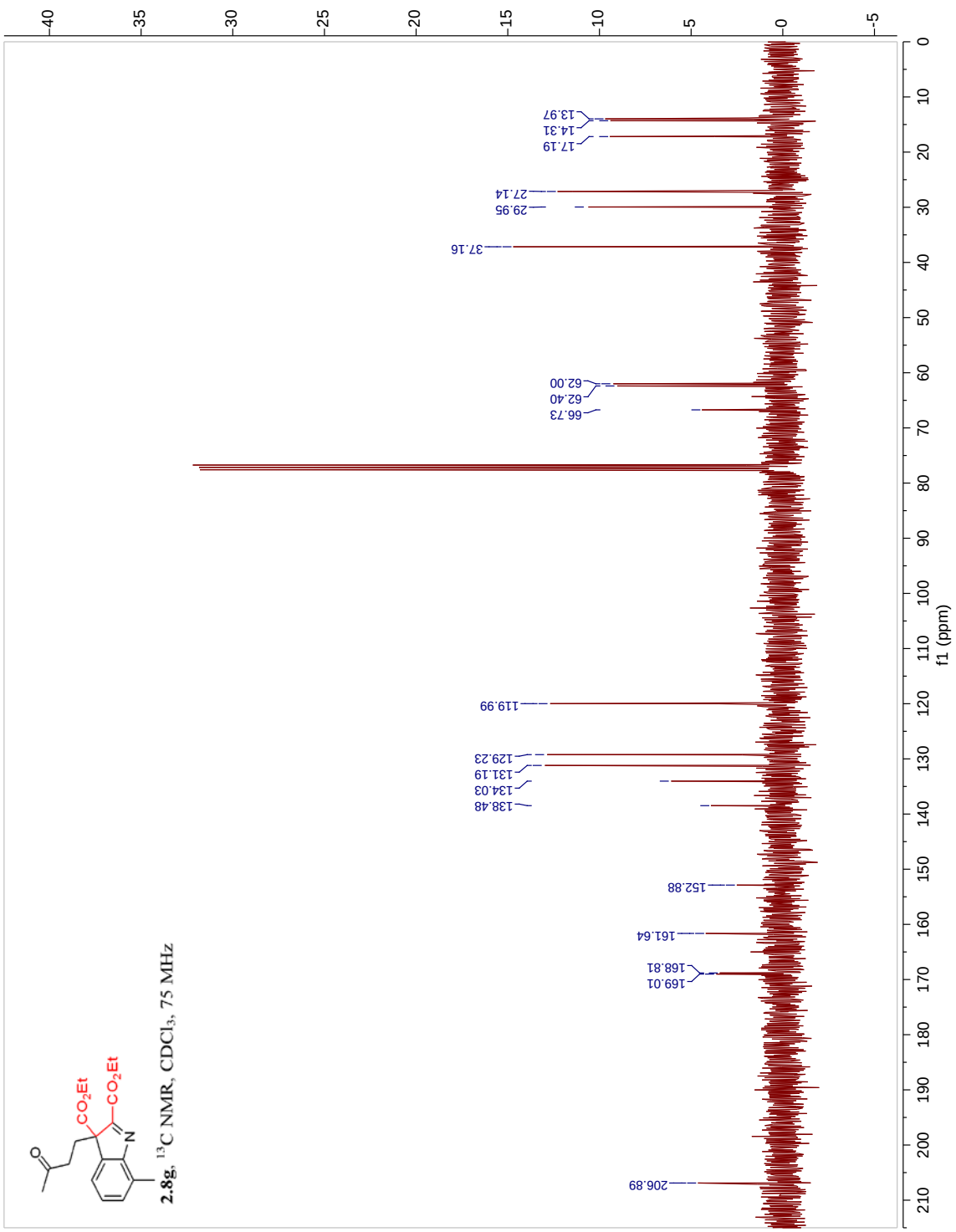

2.8f, ^{1}H NMR, $CDCl_3$, 300 MHz
CO_2Et
CO_2Et
N
O
NC
3.79
3.14
5.04
1.38
1.16
1.32
2.48
2.24
2.22
1.00
f1 (ppm)



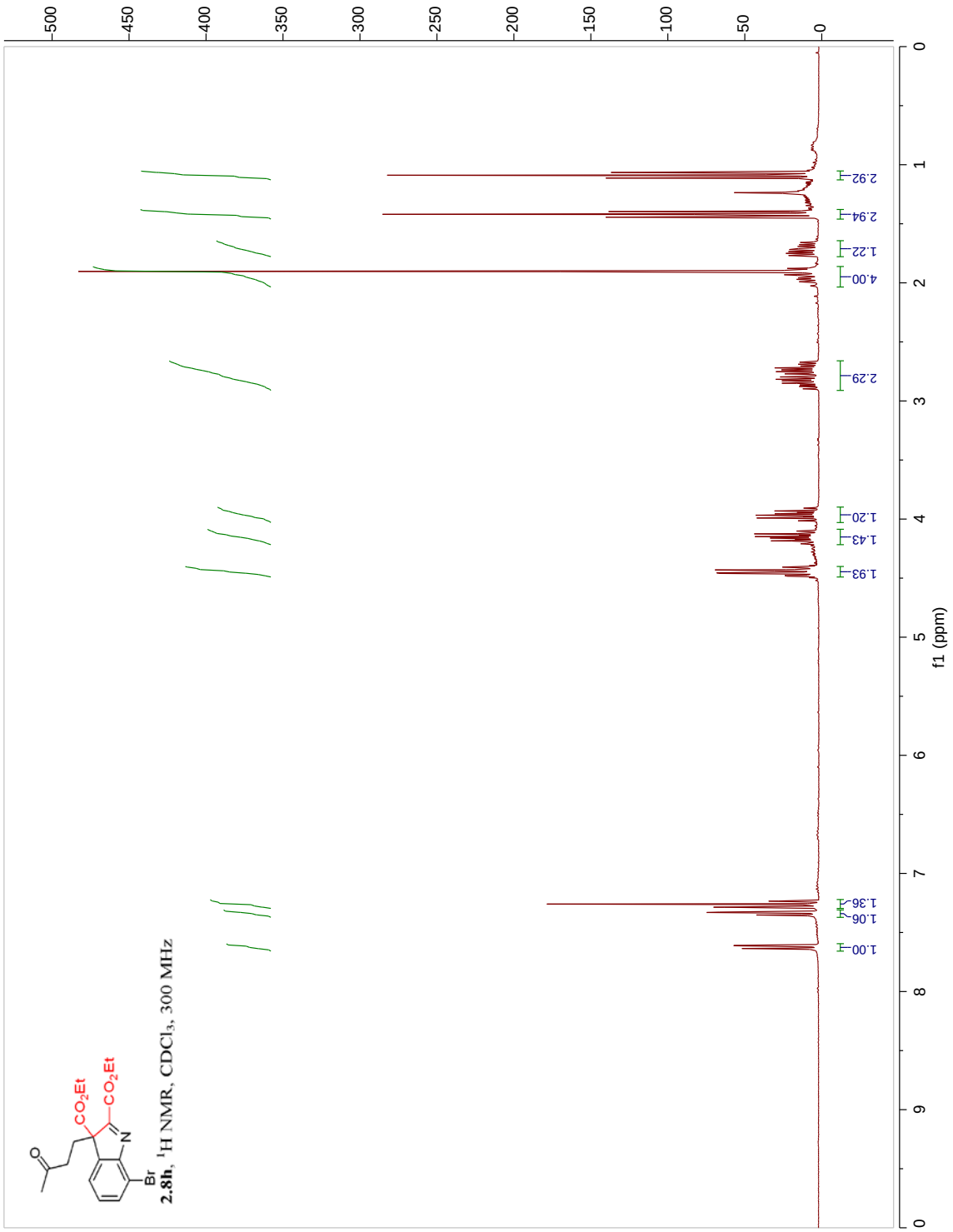
2.8f, ^{13}C NMR, $CDCl_3$, 75 MHz

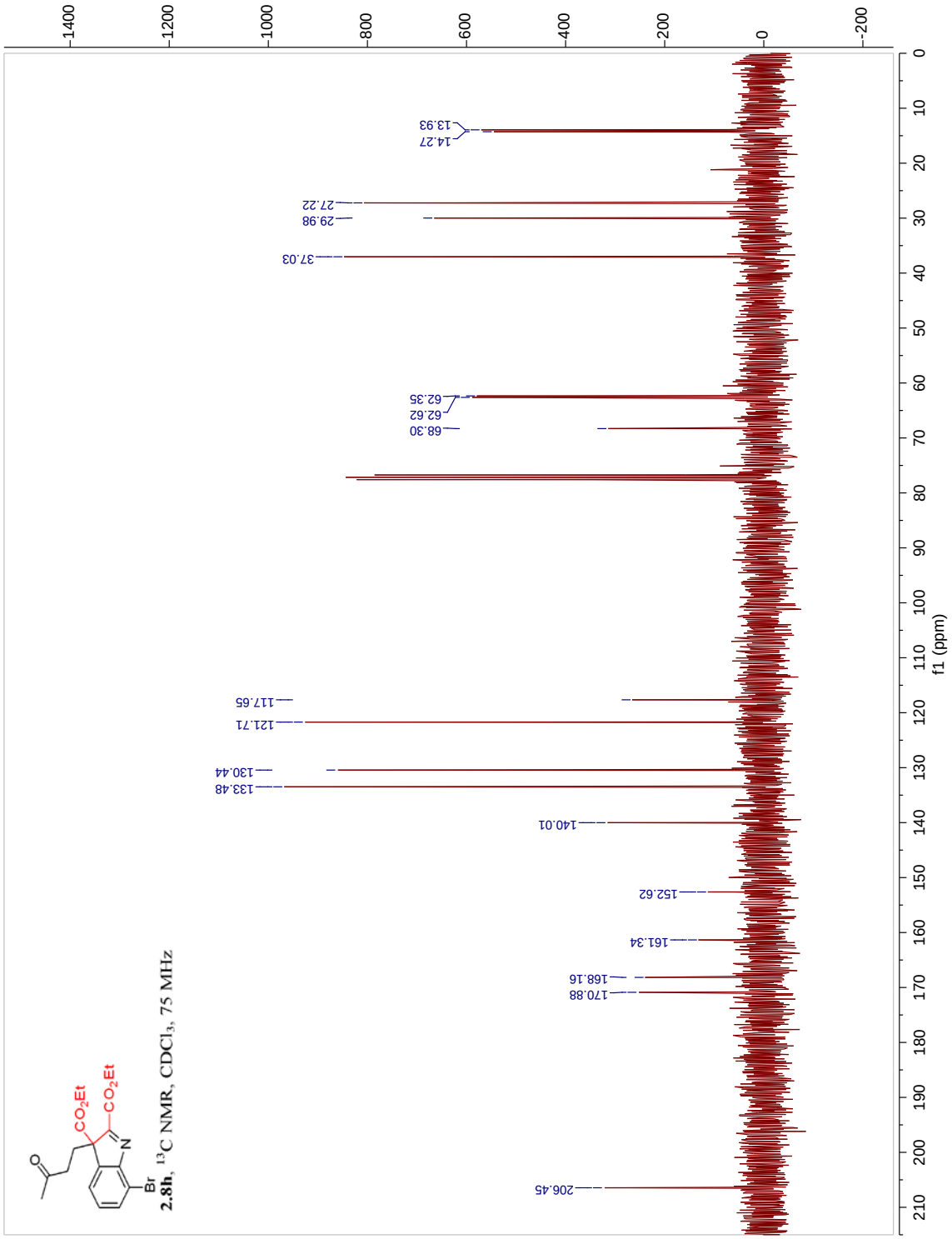


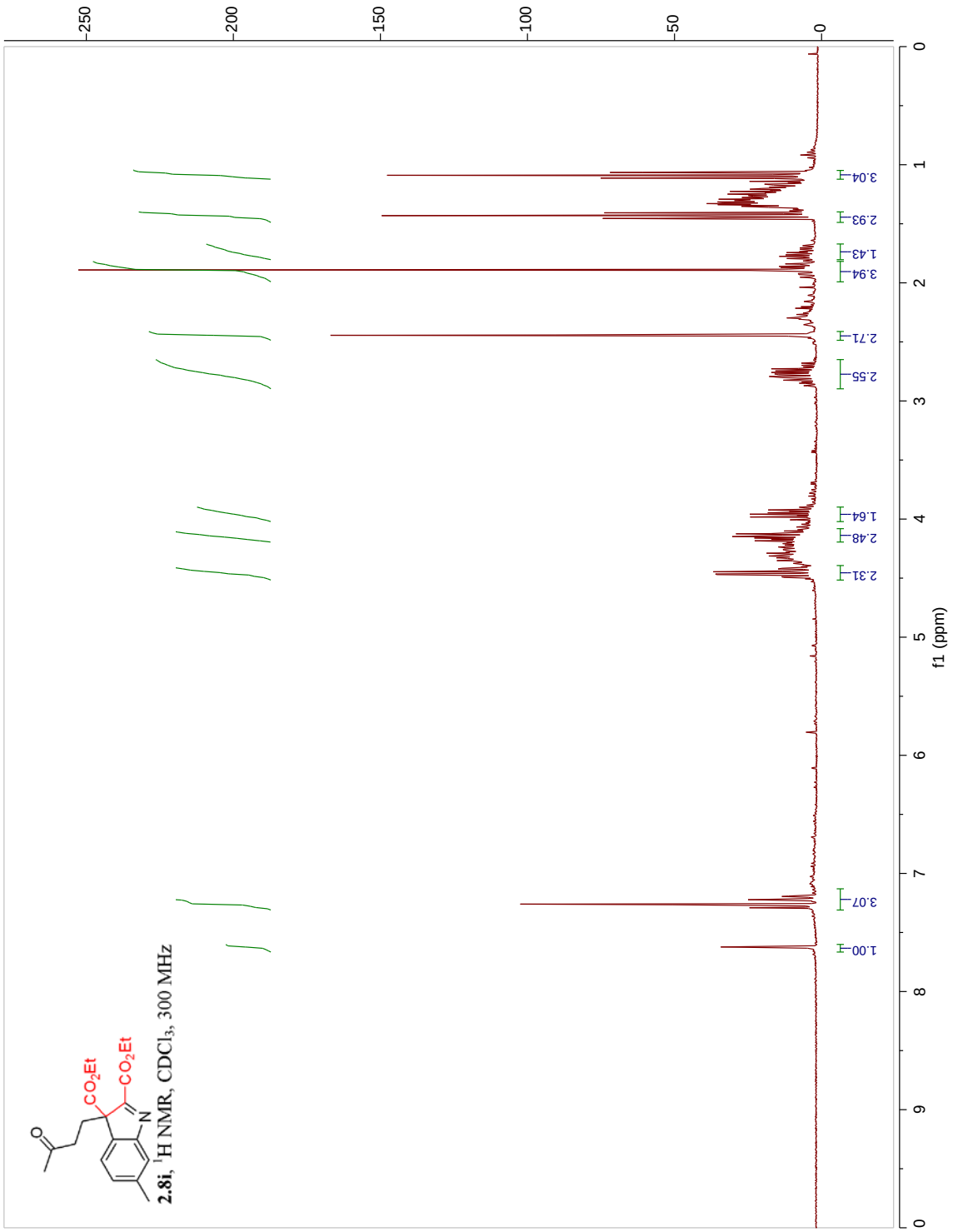
2.8g, ^{1}H NMR, $CDCl_3$, 300 MHz



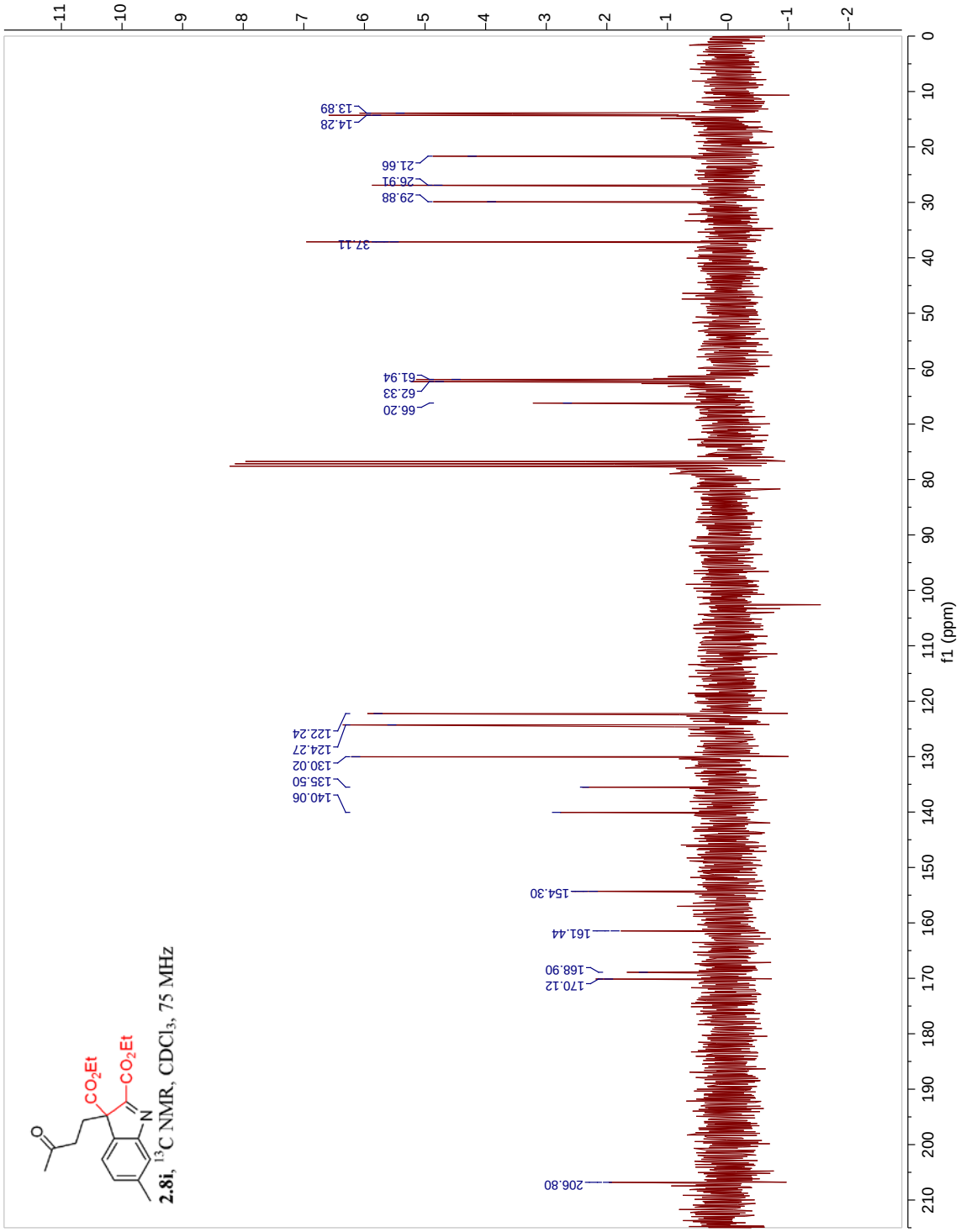
2.8g, ^{13}C NMR, $CDCl_3$, 75 MHz


2.92
2.94
1.22
4.00
2.29
1.20
1.43
1.93
1.36
1.06
1.00
f1 (ppm)
2.8h, ^{1}H NMR, $CDCl_3$, 300 MHz

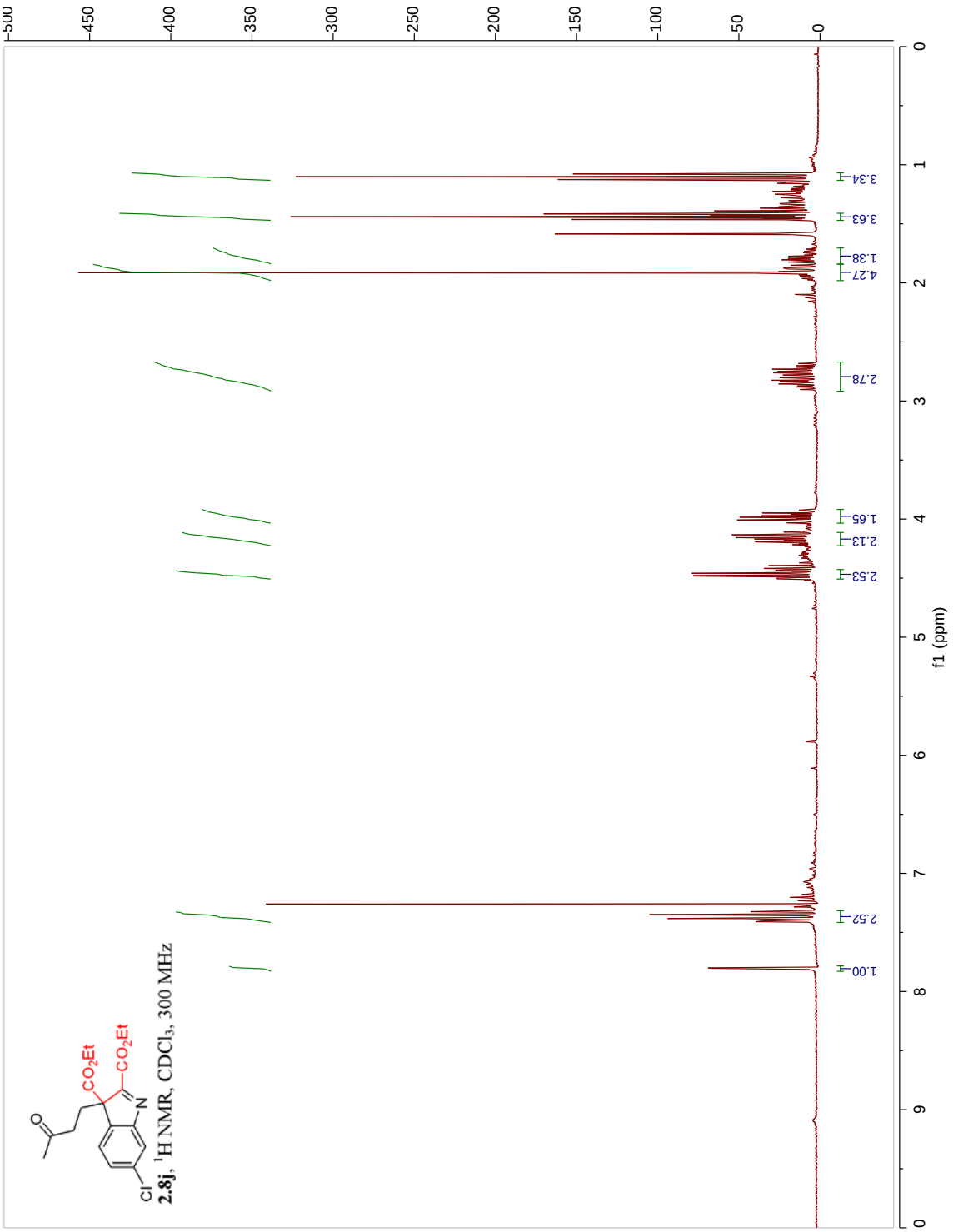

206.45
170.88
168.16
161.34
152.62
140.01
133.48
130.44
121.71
117.65
68.30
62.62
62.35
37.03
29.98
27.22
14.27
13.93
f1 (ppm)
2.8h, ^{13}C NMR, $CDCl_3$, 75 MHz
CO_2Et
CO_2Et
Br
N
O

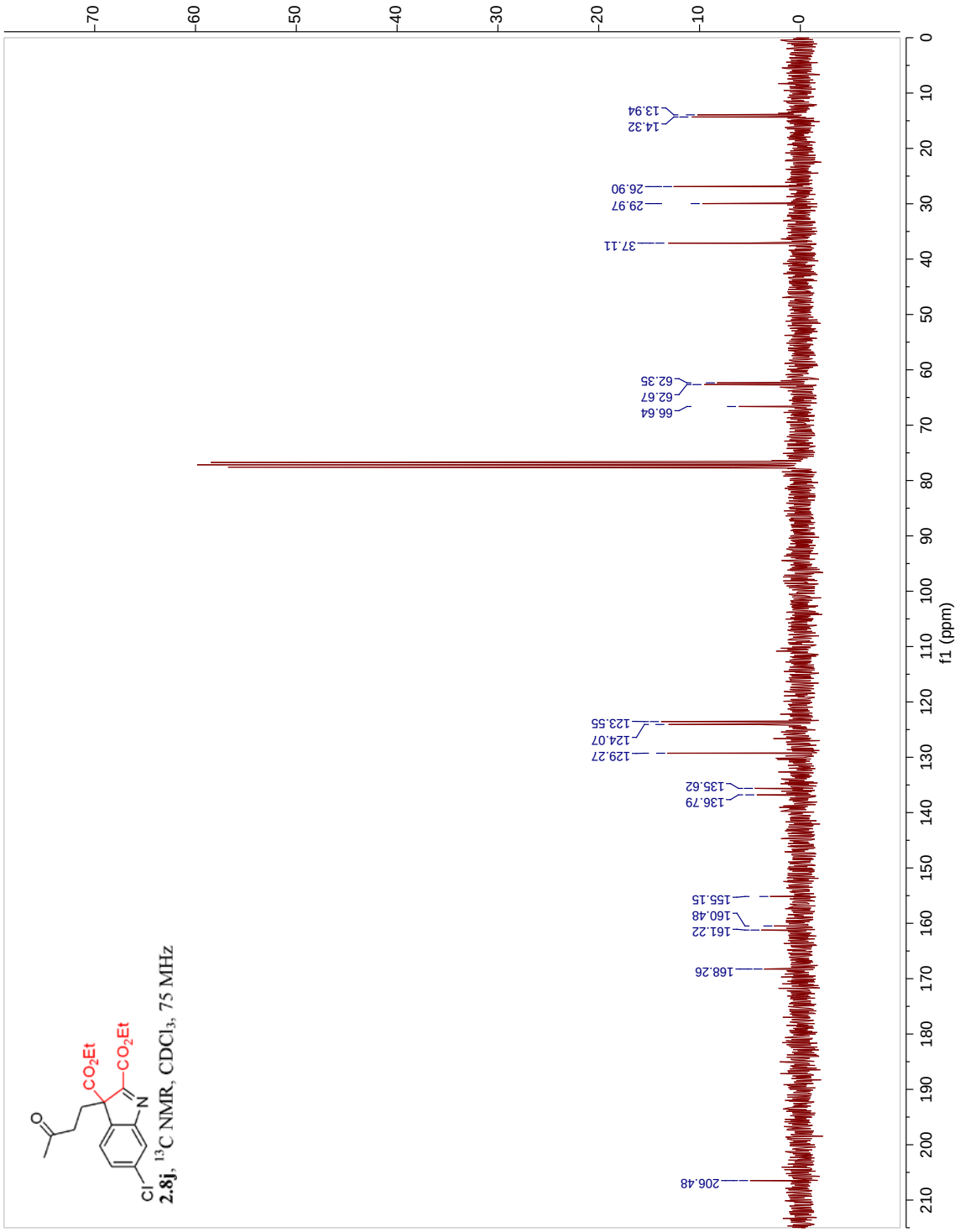


2.8i, ^{1}H NMR, $CDCl_3$, 300 MHz

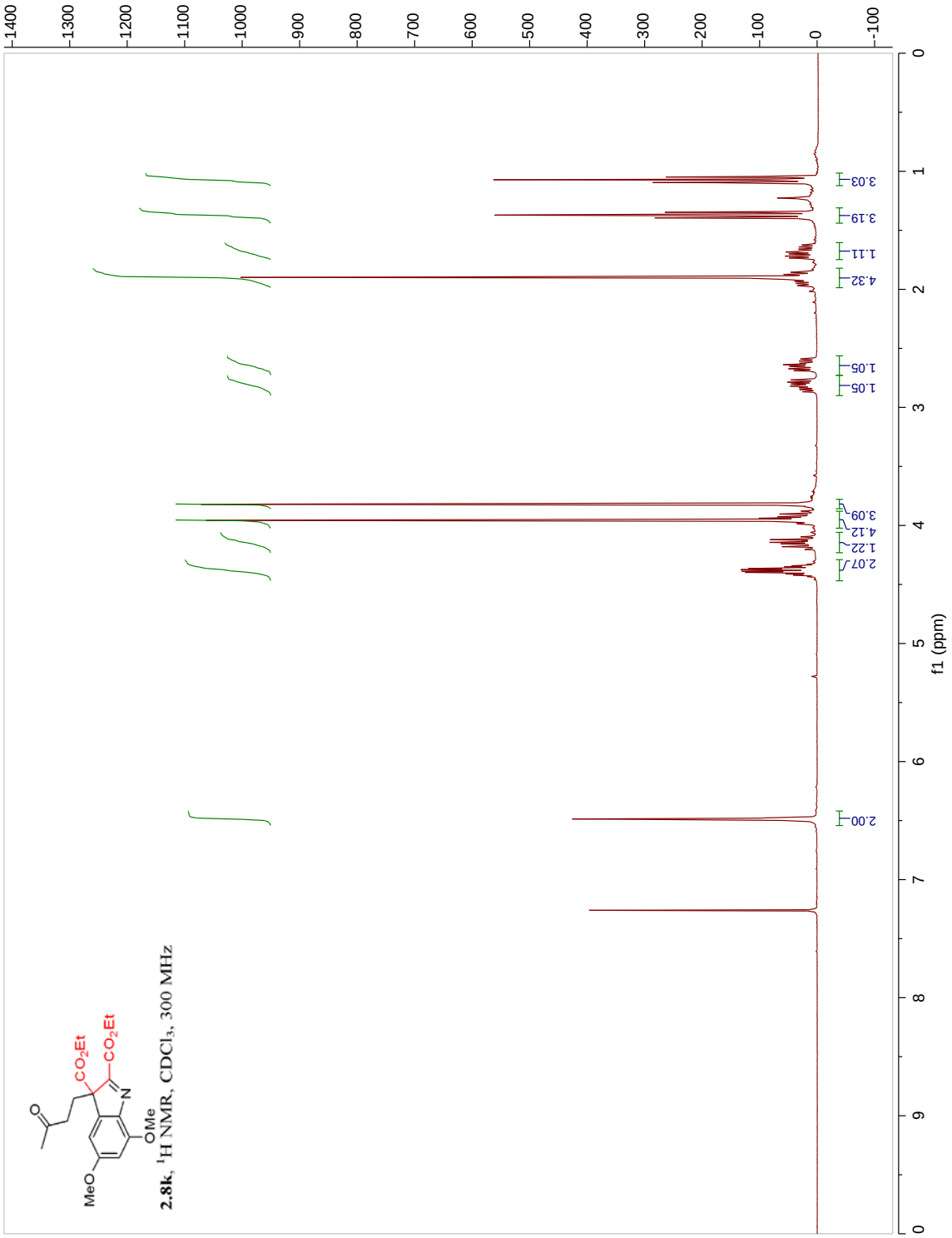


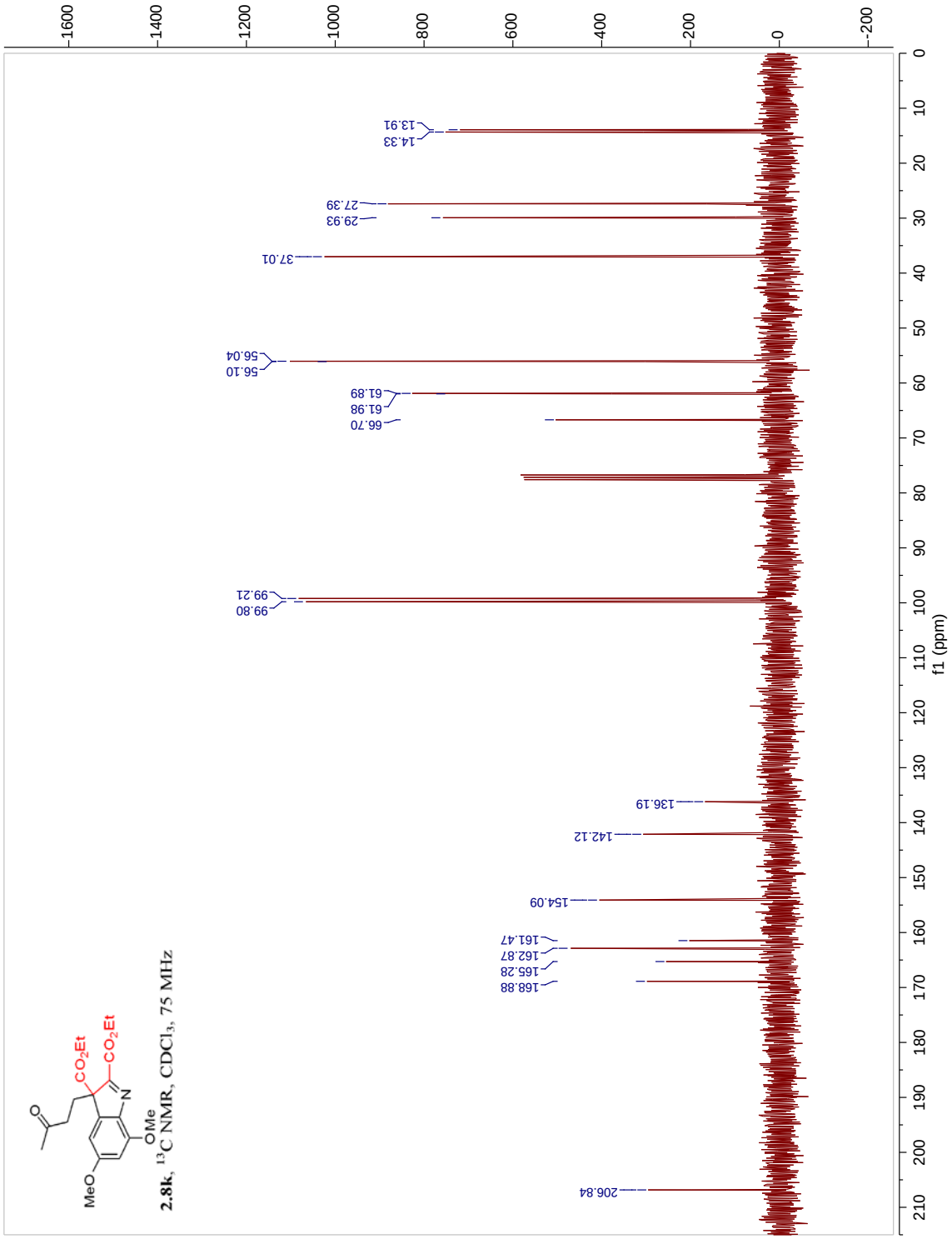
2.8i, ^{13}C NMR, $CDCl_3$, 75 MHz

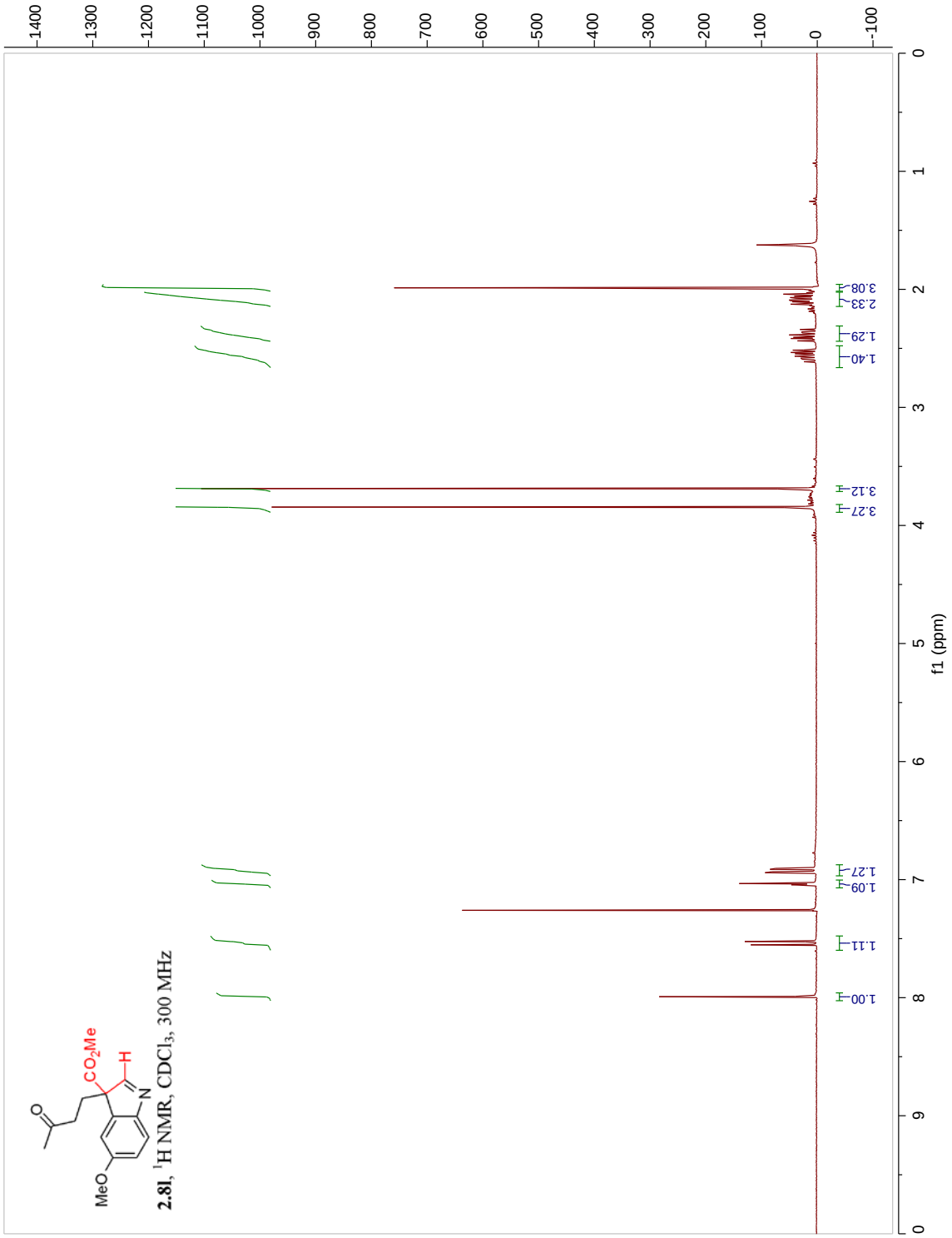

2.8j, ^{1}H NMR, $CDCl_3$, 300 MHz
CO_2Et
CO_2Et
N
O
Cl
3.34
3.63
1.38
4.27
2.78
1.65
2.13
2.53
2.52
1.00
f1 (ppm)

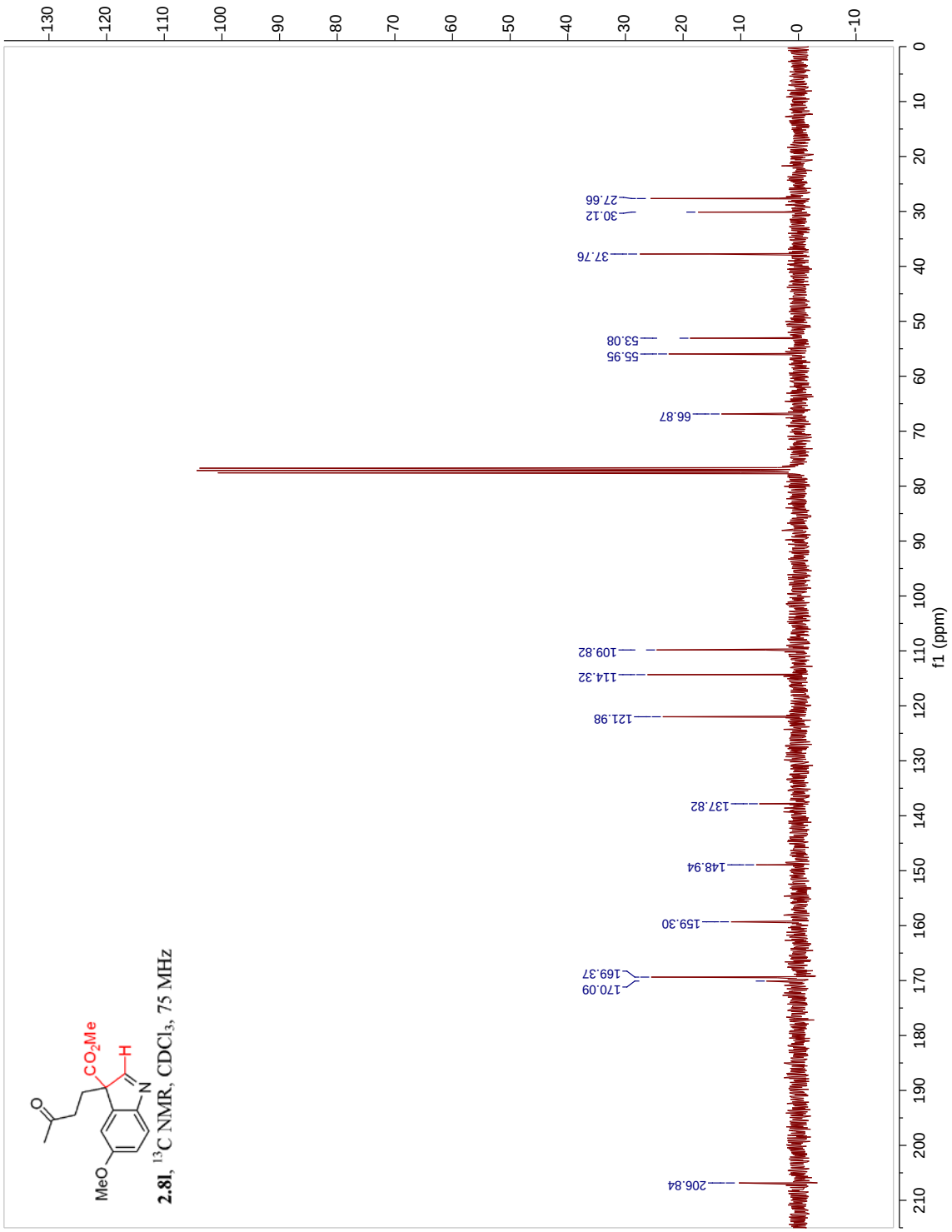


2.8j, ^{13}C NMR, $CDCl_3$, 75 MHz

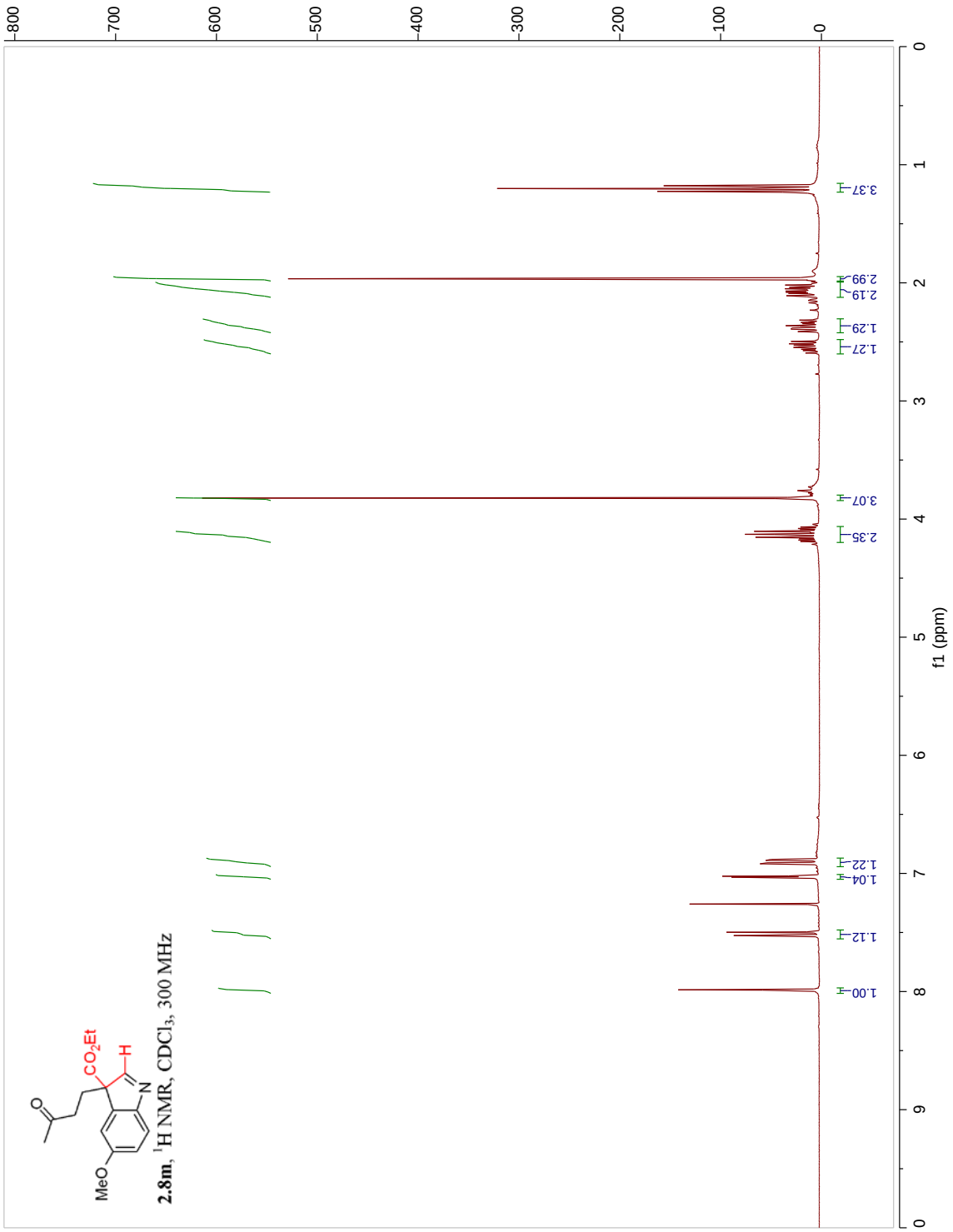

2.8k, ^{1}H NMR, $CDCl_3$, 300 MHz
MeO
OMe
N
CO_2Et
CO_2Et
O
f1 (ppm)
2.00
2.07
1.22
4.12
3.09
1.05
1.05
4.32
1.11
3.19
3.03


13.91
14.33
27.39
29.93
37.01
56.04
56.10
61.89
61.98
66.70
99.21
99.80
136.19
142.12
154.09
161.47
162.87
165.28
168.88
206.84
f1 (ppm)
2.8k, ^{13}C NMR, $CDCl_3$, 75 MHz
MeO
OMe
N
CO_2Et
CO_2Et
O

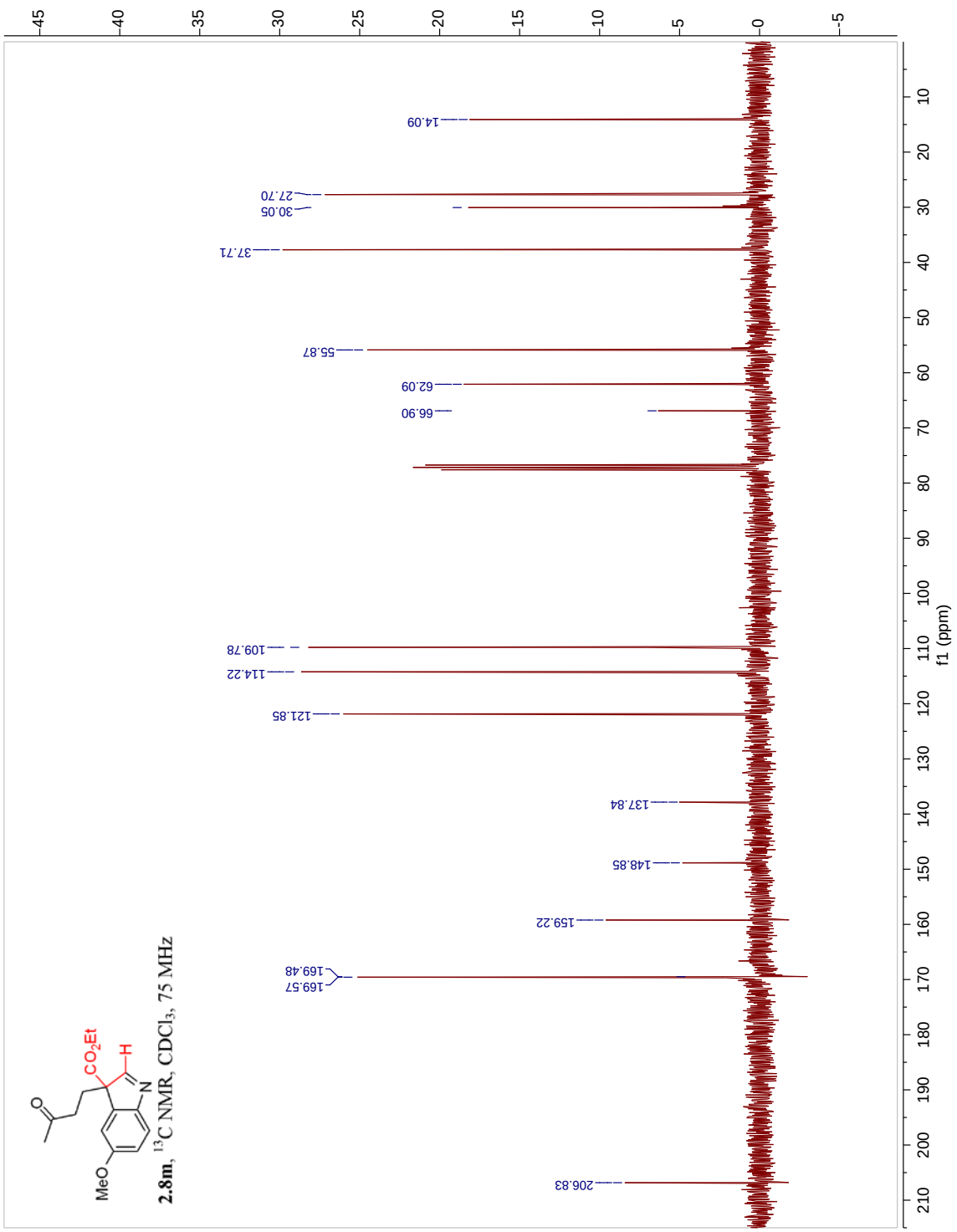

2.81, ^{1}H NMR, $CDCl_3$, 300 MHz
MeO
CO_2Me
H
N
O
3.08
2.33
1.29
1.40
3.12
3.27
1.27
1.09
1.11
1.00
f1 (ppm)

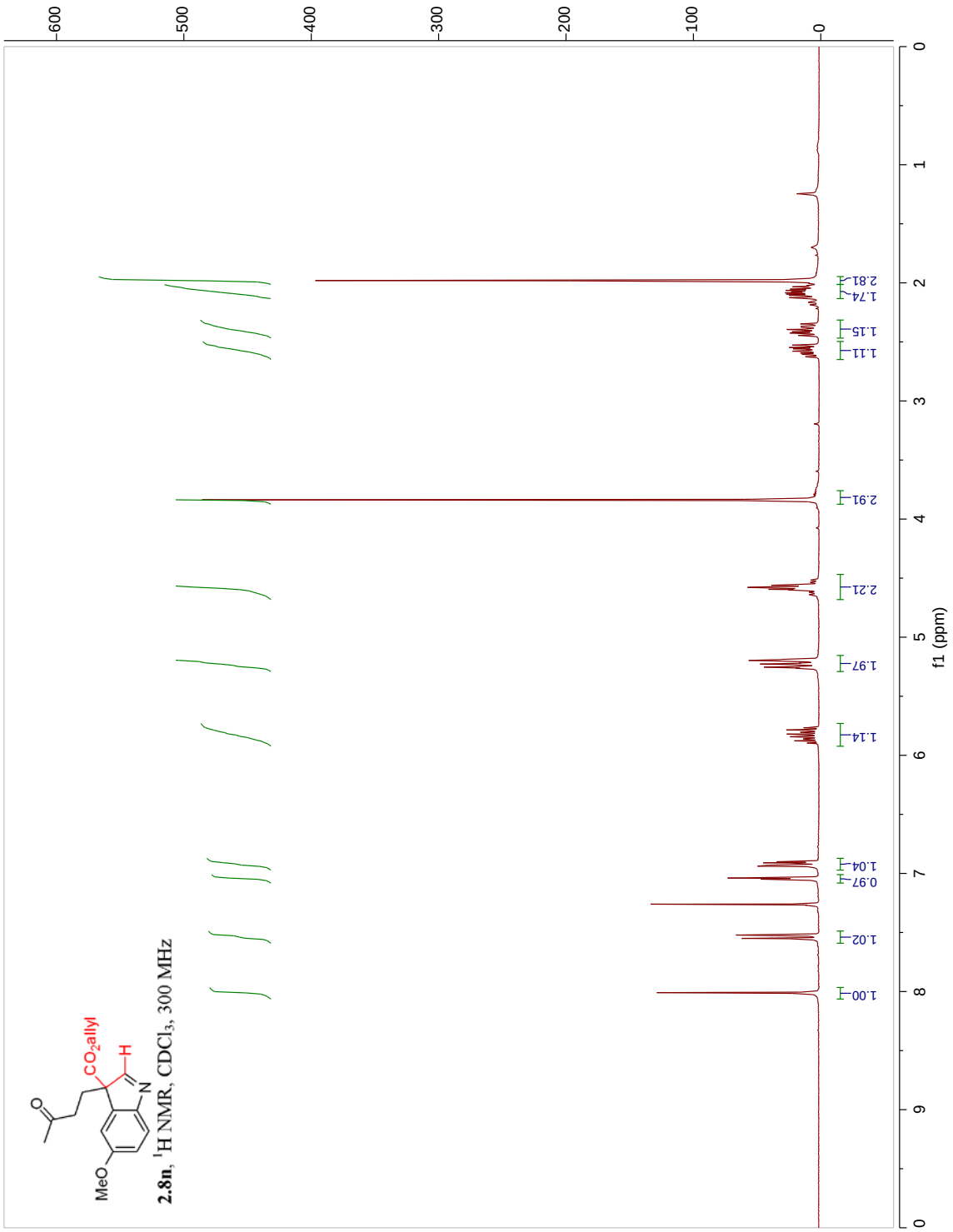


2.81, ^{13}C NMR, $CDCl_3$, 75 MHz

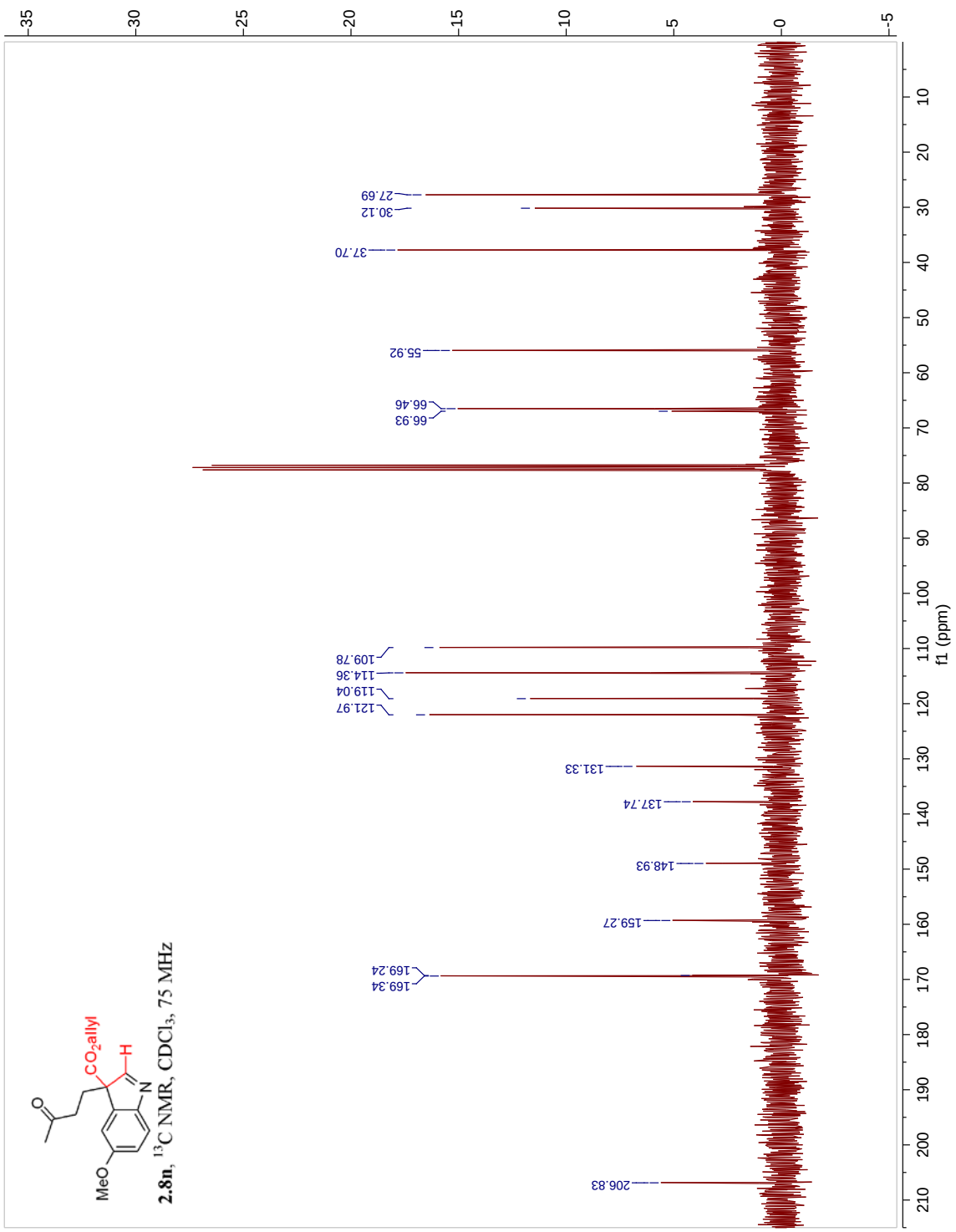


2.8m, ^{1}H NMR, $CDCl_3$, 300 MHz

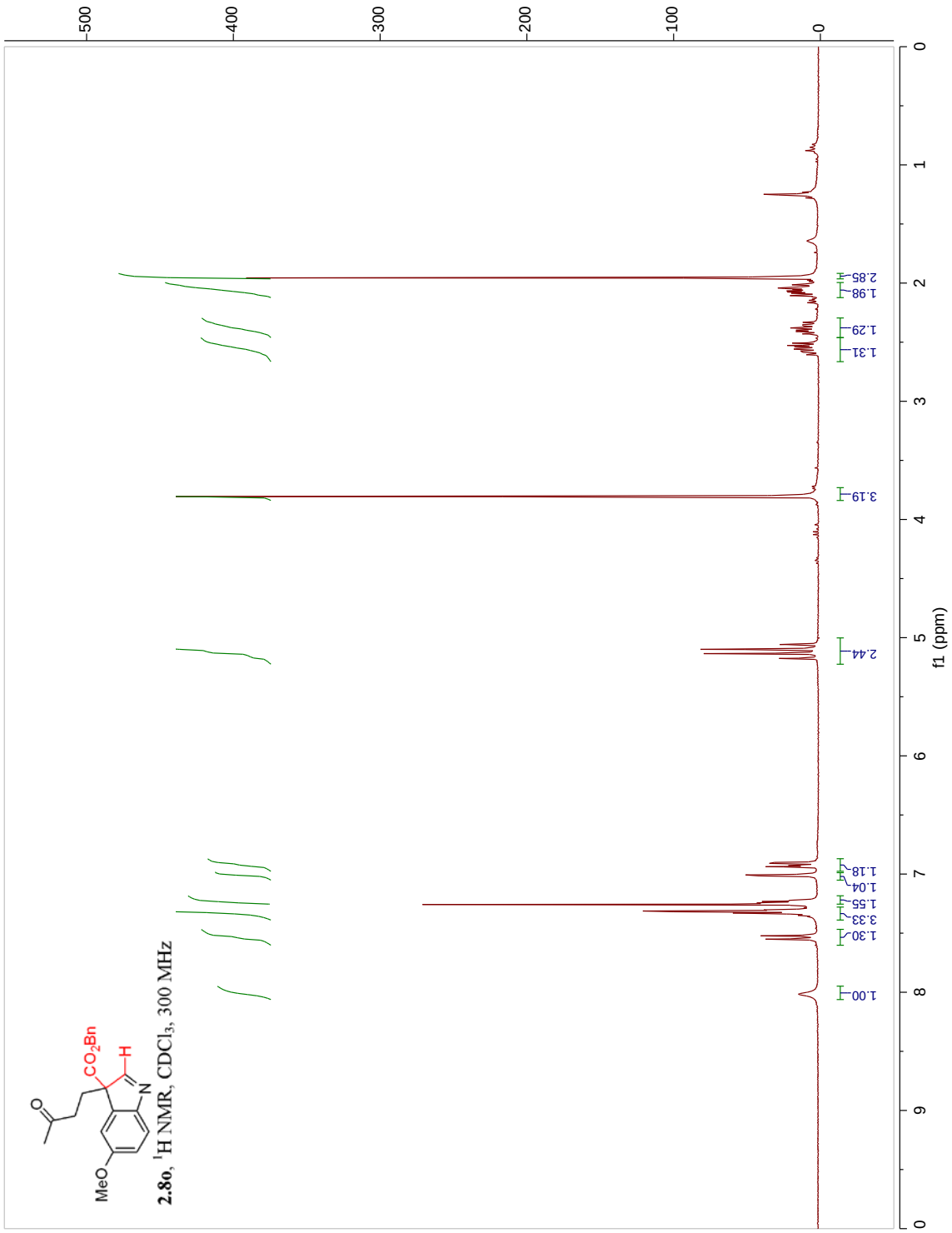

206.83
169.57
169.48
159.22
148.85
137.84
121.85
114.22
109.78
66.90
62.09
55.87
37.71
30.05
27.70
14.09
f1 (ppm)
MeO
CO2Et
H
N
O
2.8m, 13C NMR, CDCl3, 75 MHz



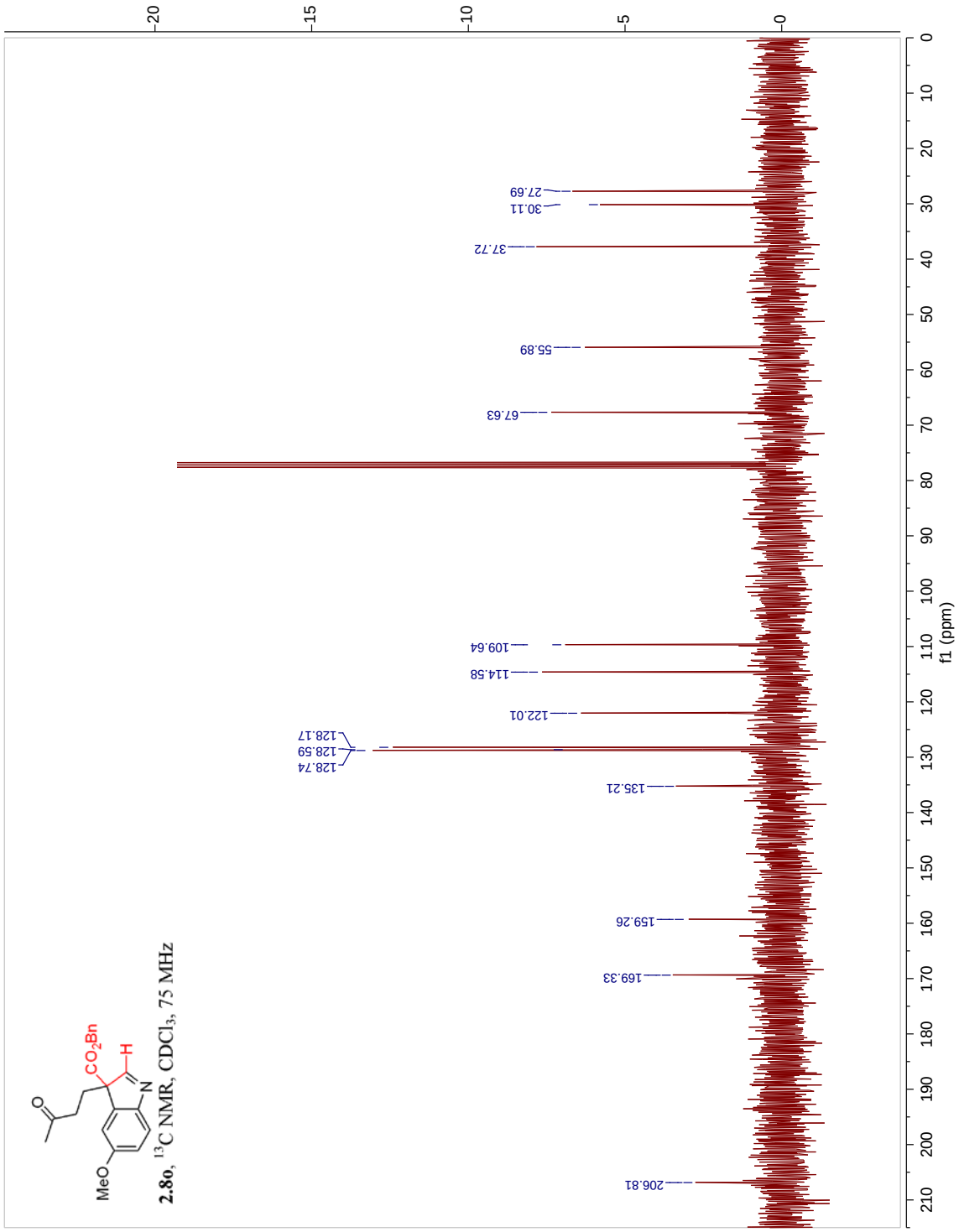
2.8n, ^{1}H NMR, $CDCl_3$, 300 MHz



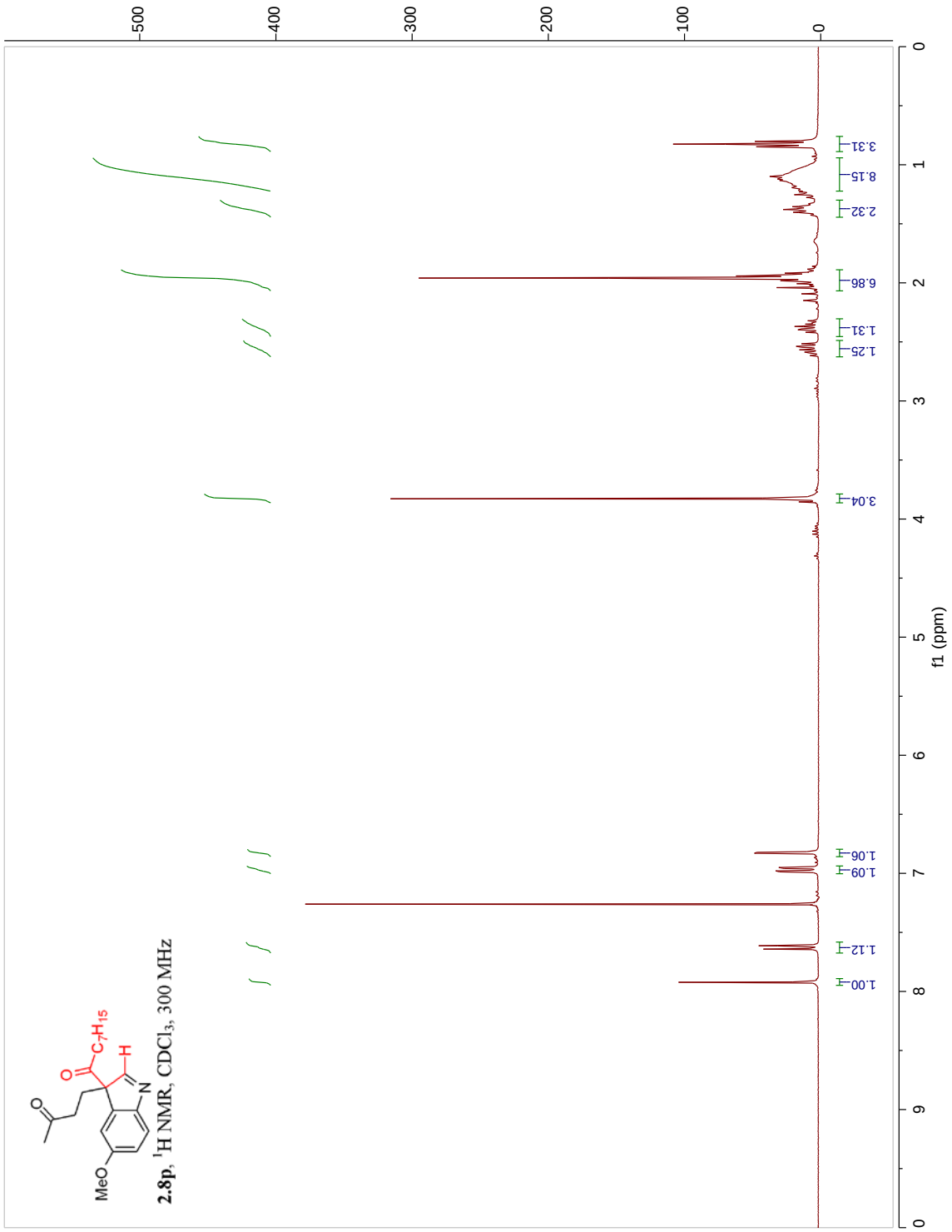
2.8n, ^{13}C NMR, $CDCl_3$, 75 MHz

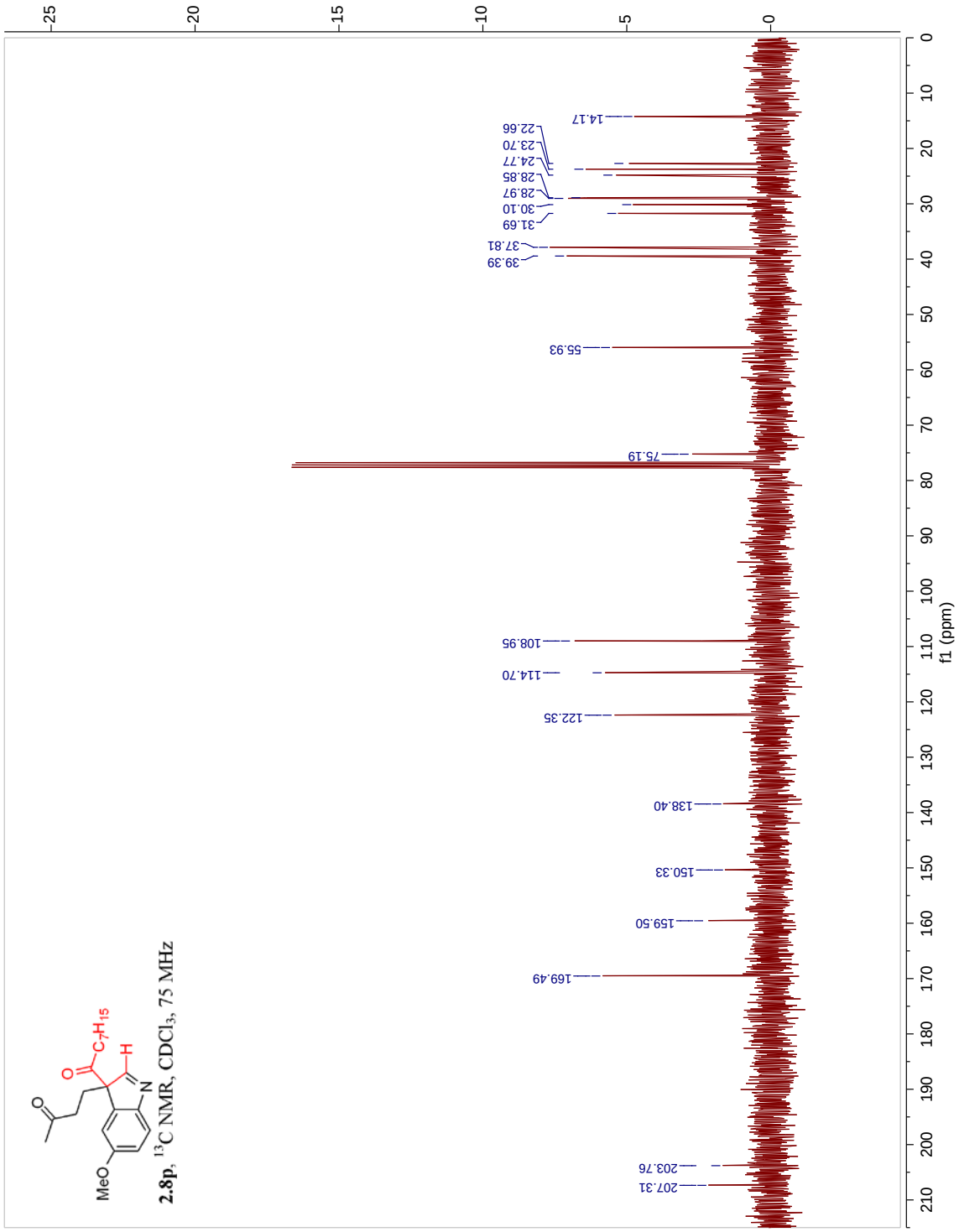


2.8o, ^{1}H NMR, $CDCl_3$, 300 MHz

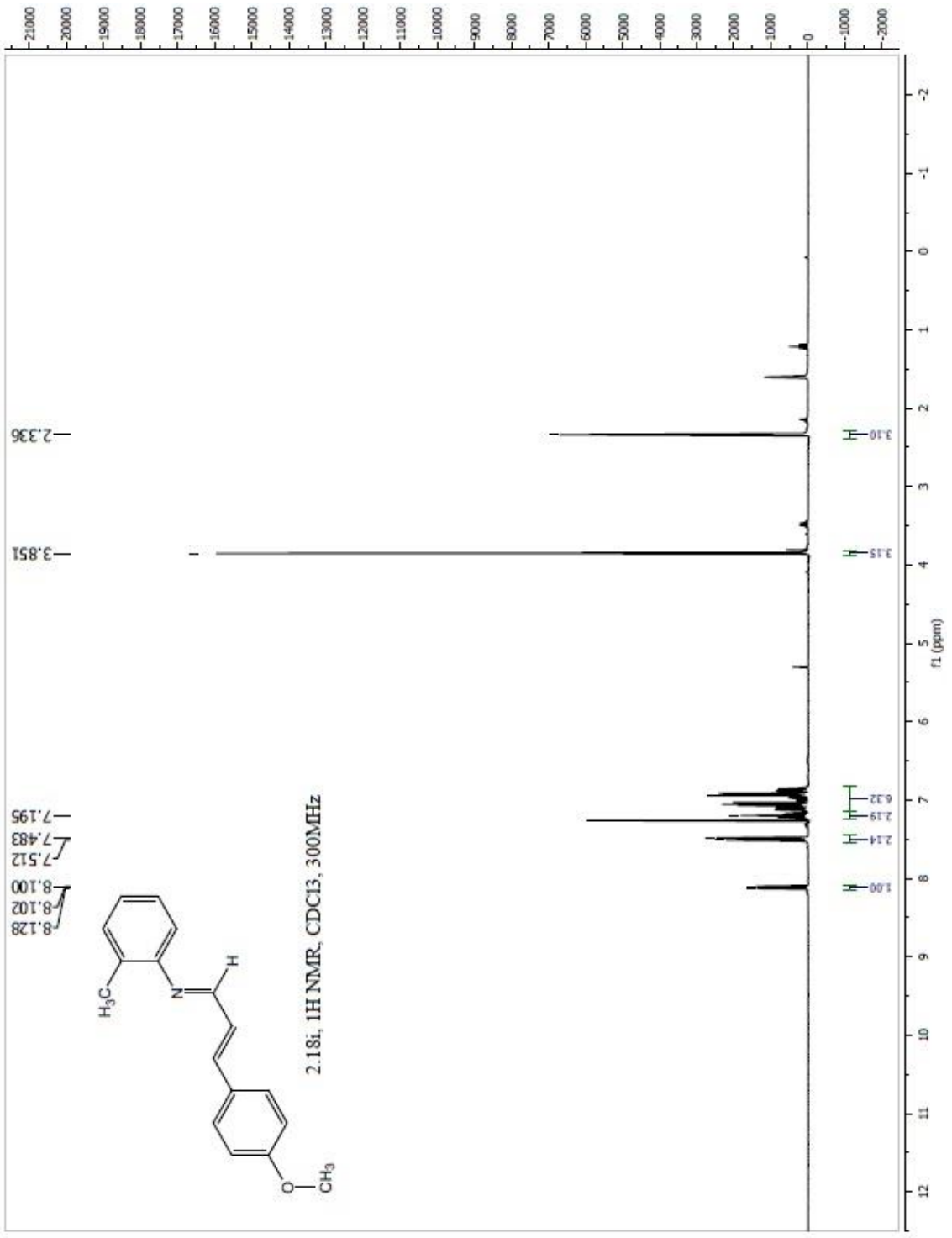


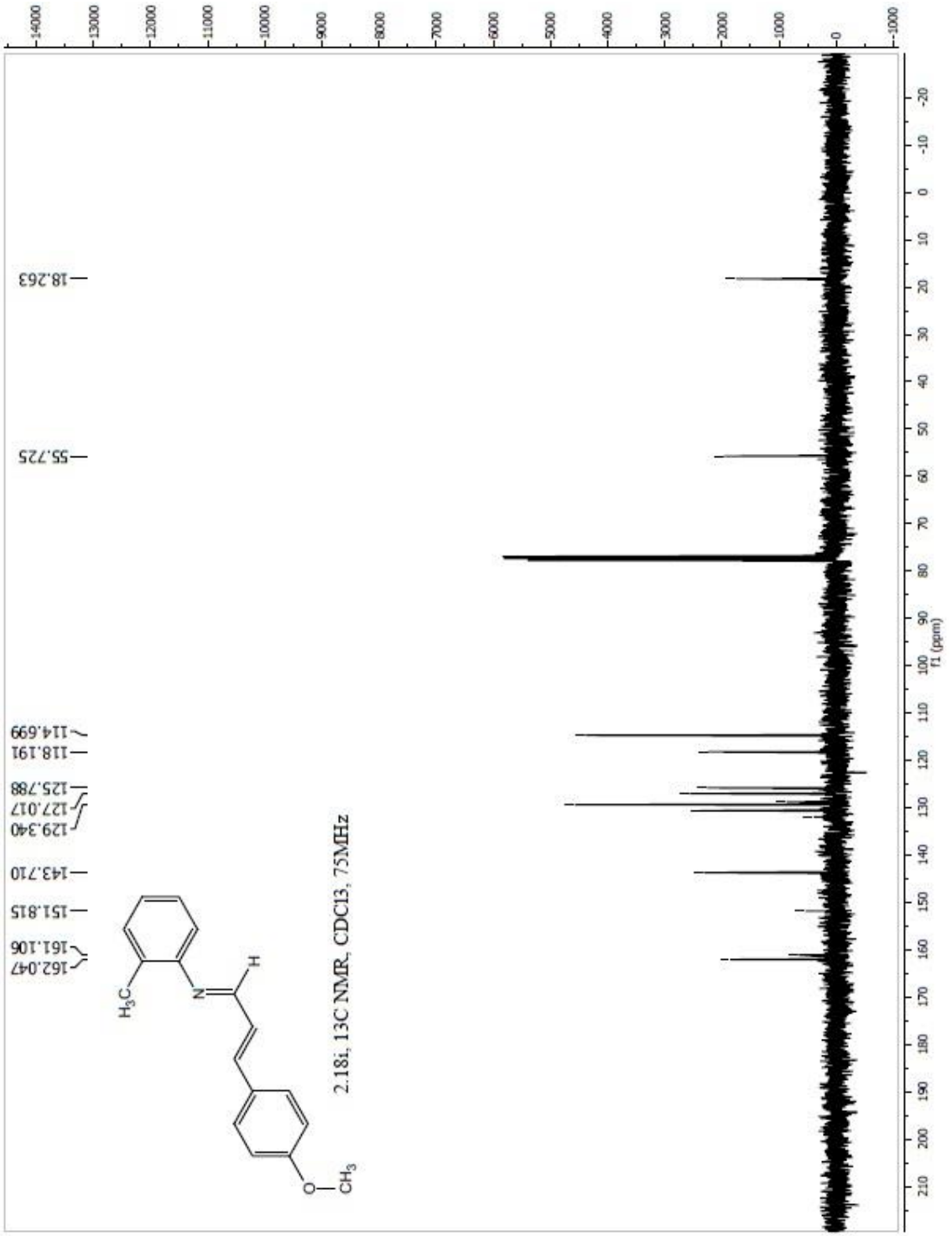
2.8o, ^{13}C NMR, $CDCl_3$, 75 MHz

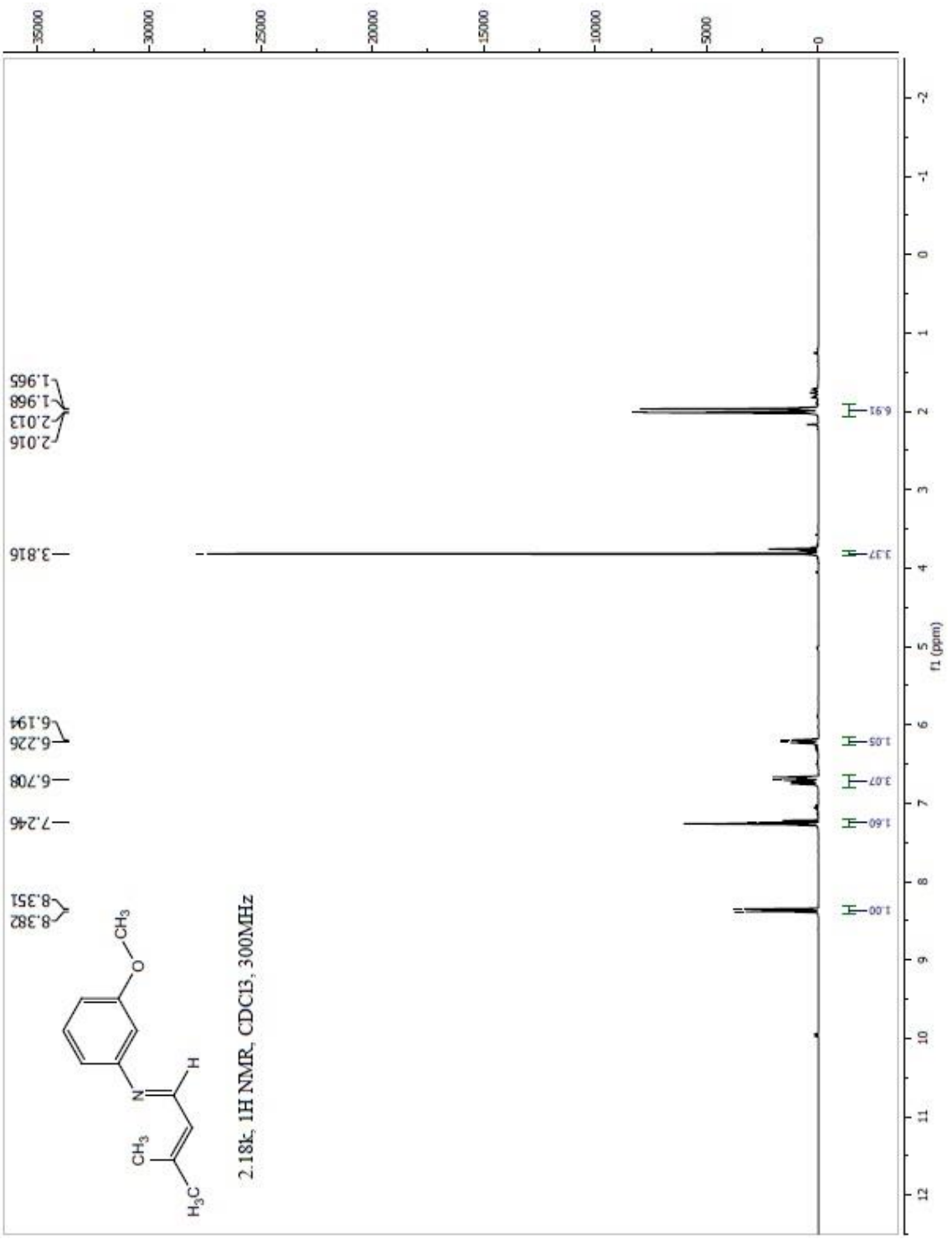

2.8p, ^{1}H NMR, $CDCl_3$, 300 MHz
MeO
O
C_7H_{15}
H
N
f1 (ppm)
3.31
8.15
2.32
6.86
1.31
1.25
3.04
1.06
1.09
1.12
1.00

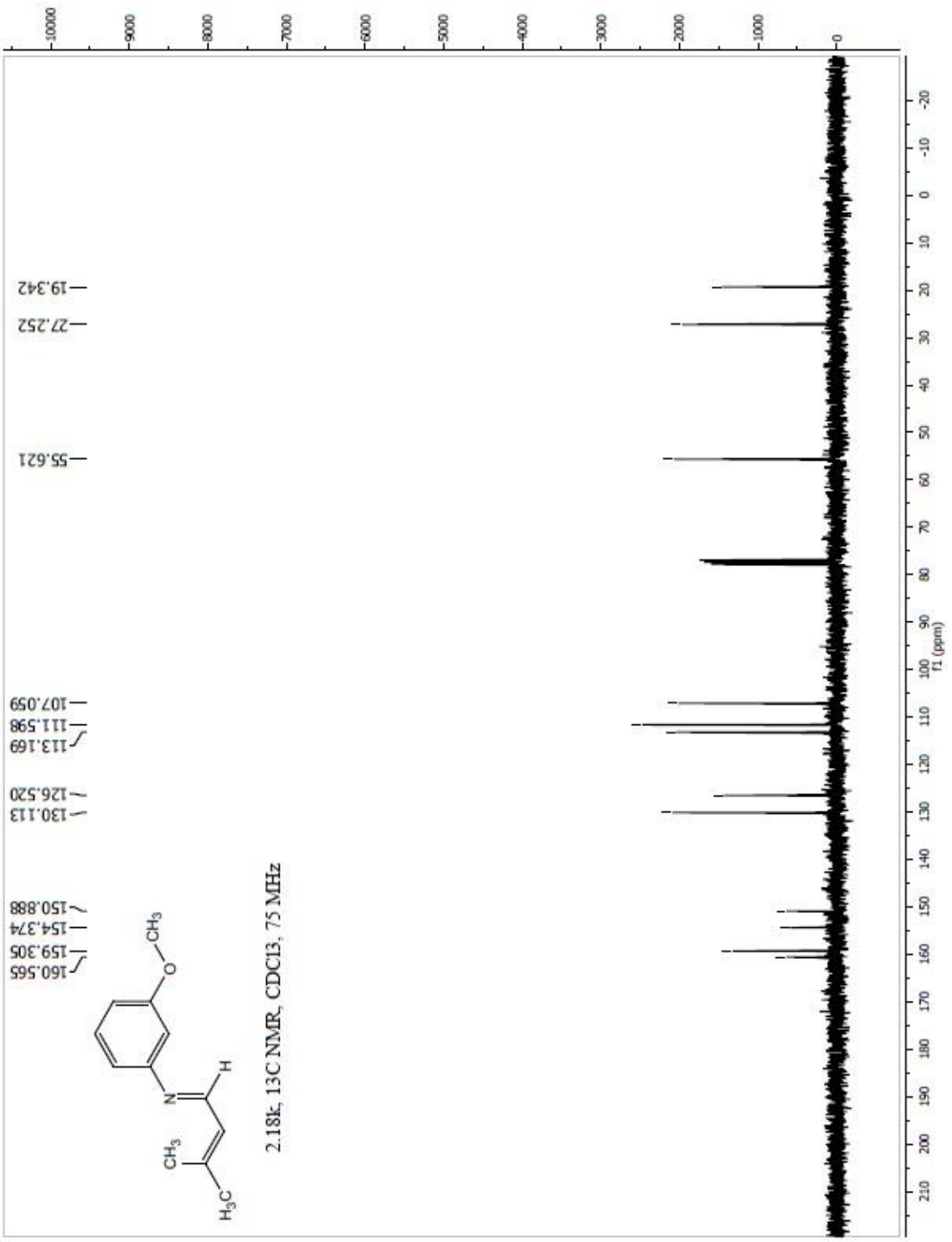

2.8p, ^{13}C NMR, $CDCl_3$, 75 MHz
MeO
C_7H_{15}
H
N
O
O
207.31
203.76
169.49
159.50
150.33
138.40
122.35
114.70
108.95
75.19
55.93
39.39
37.81
31.69
30.10
28.97
28.85
24.77
23.70
22.66
14.17
f1 (ppm)

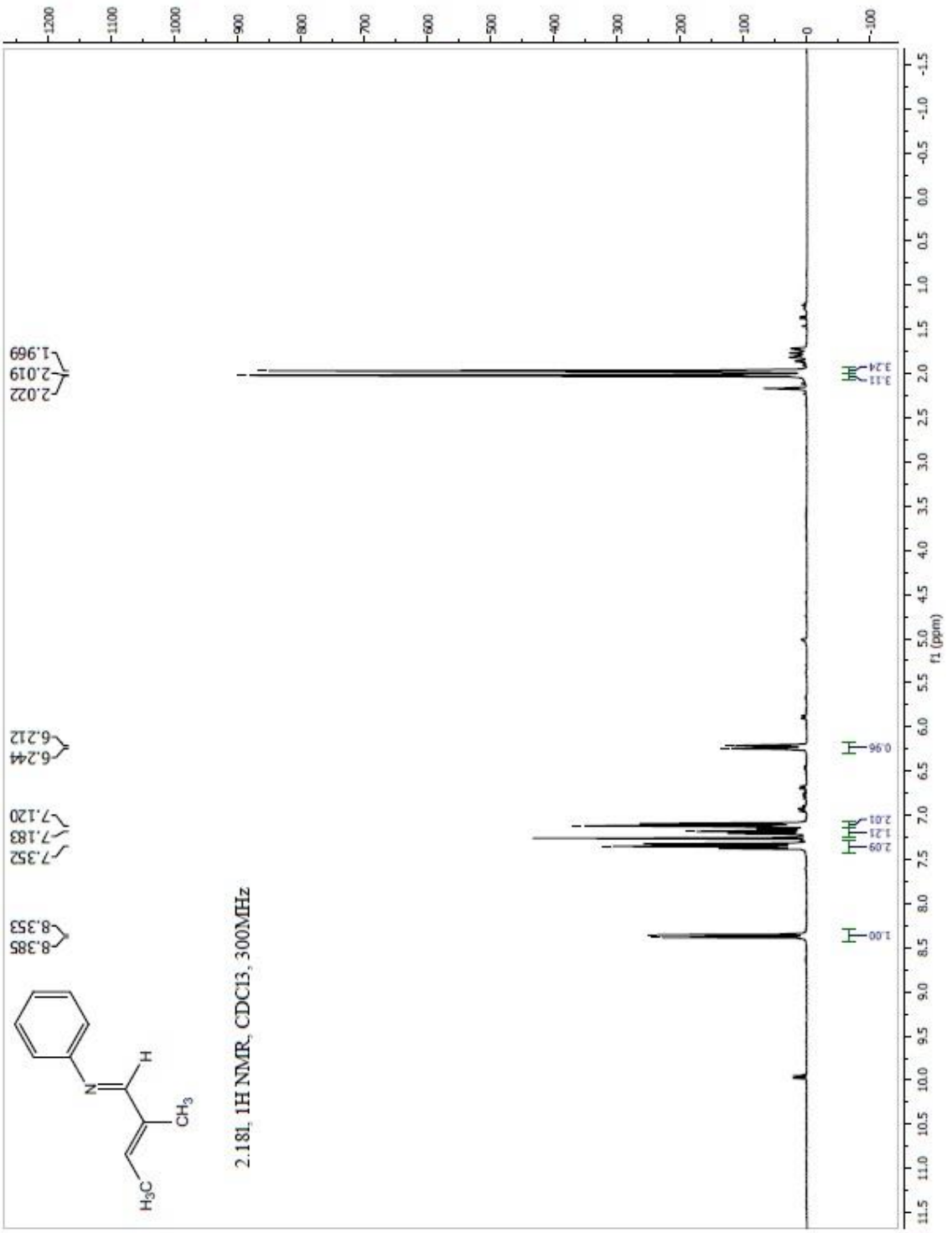
APPENDIX C

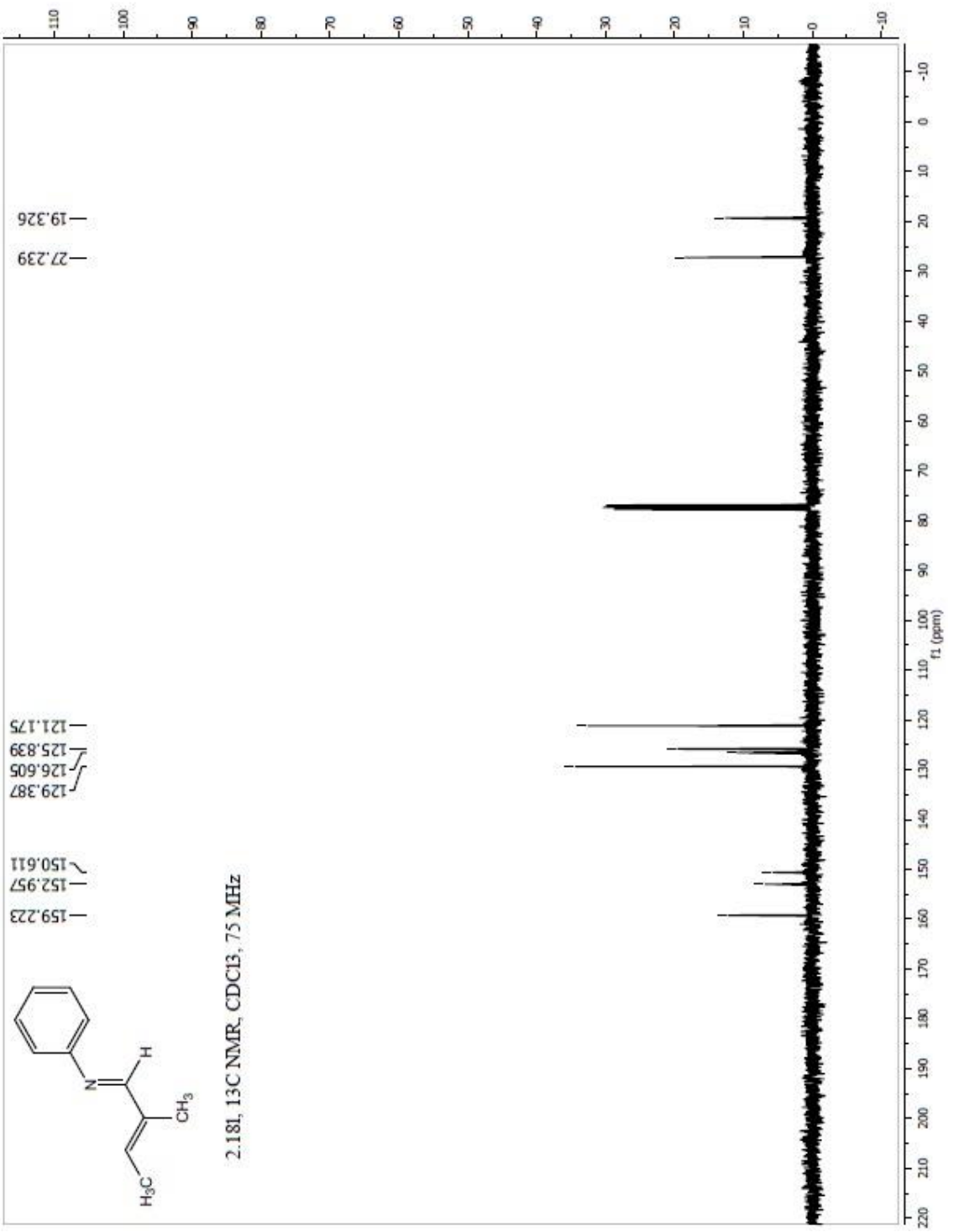

2.18i, 1H NMR, CDC13, 300MHz
2.336
3.851
7.195
7.483
7.512
8.100
8.102
8.128
3.10
3.15
6.32
2.19
2.14
1.00
f1 (ppm)

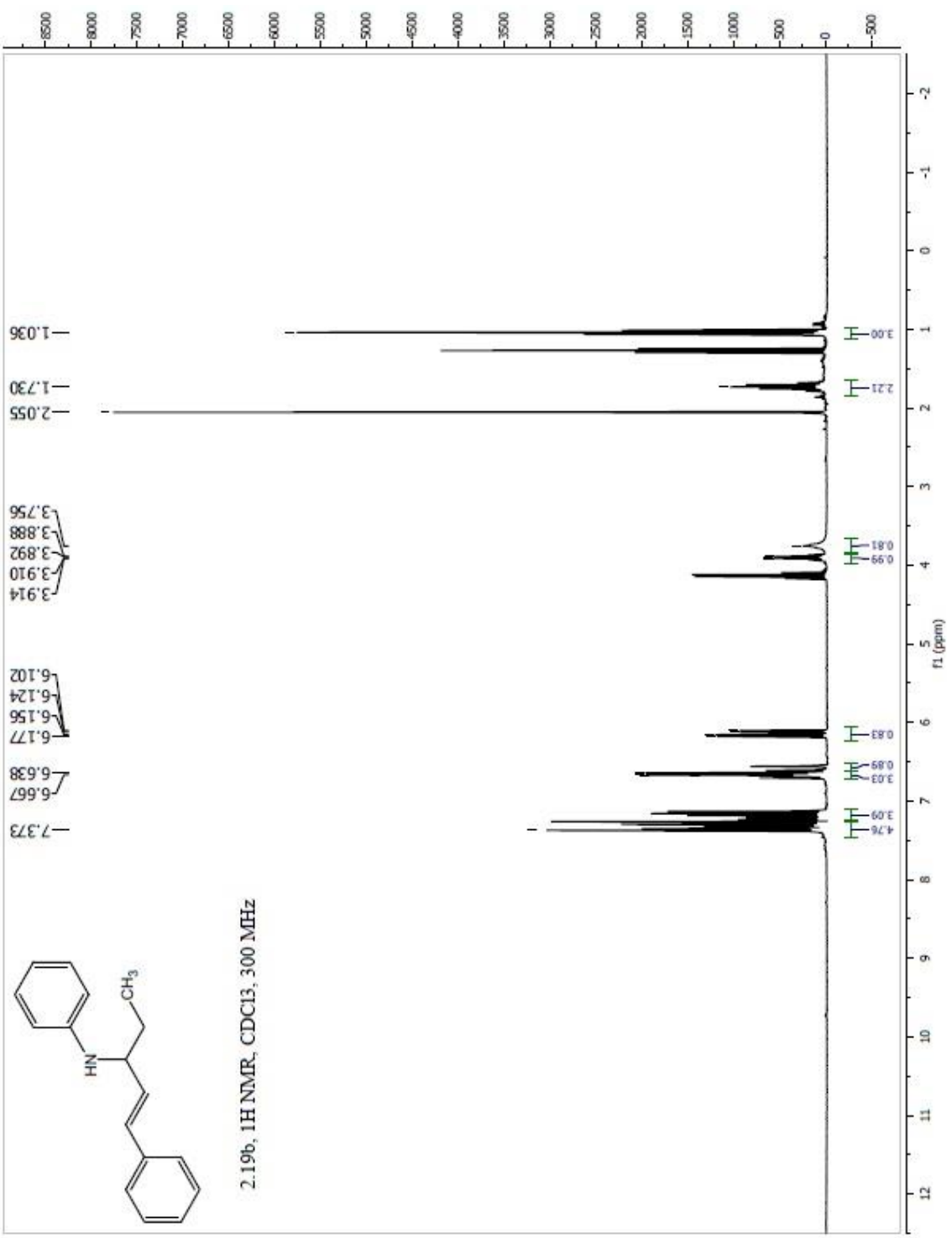

18.263
55.725
114.699
118.191
125.788
127.017
129.340
143.710
151.815
161.106
162.047
2.18i, 13C NMR, CDC13, 75MHz
f1 (ppm)

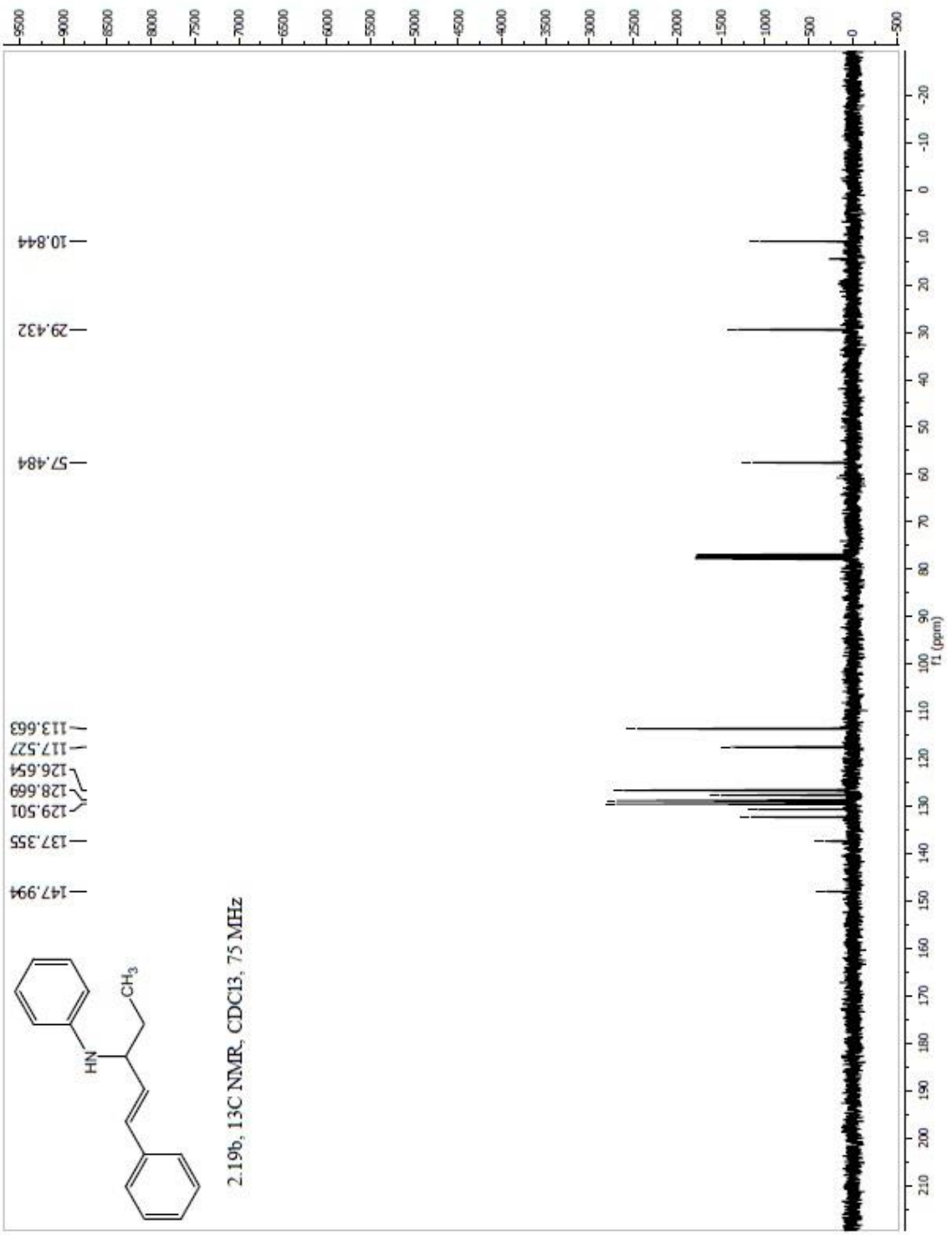

2.18k, 1H NMR, CDCl3, 300MHz
8.382
8.351
7.246
6.708
6.226
6.194
3.816
2.016
2.013
1.968
1.965
1.00
1.60
3.07
1.05
3.37
6.91
f1 (ppm)

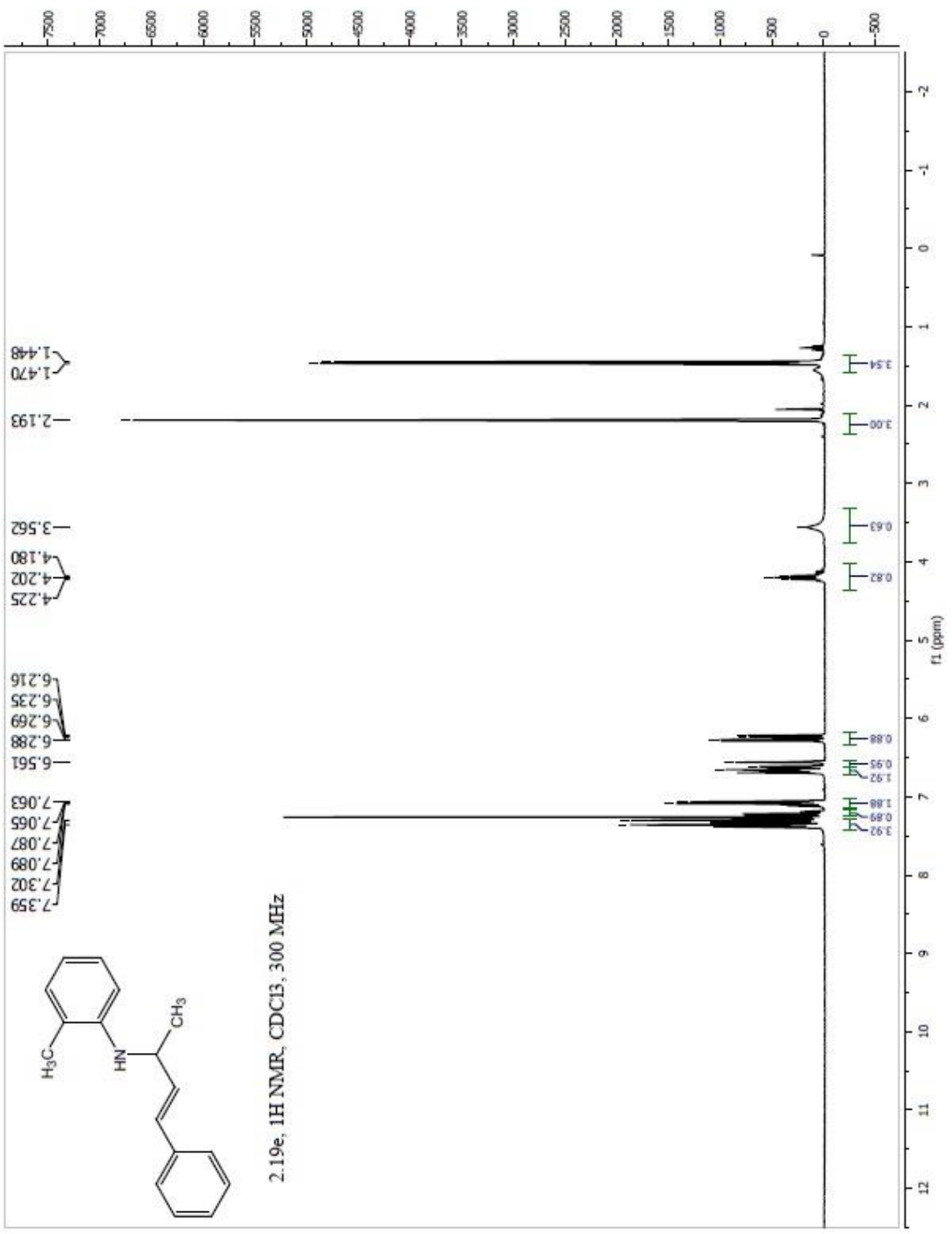

19.342
27.252
55.621
107.059
111.598
113.169
126.520
130.113
150.888
154.374
159.305
160.565
2.18k, 13C NMR, CDCl3, 75 MHz
f1 (ppm)

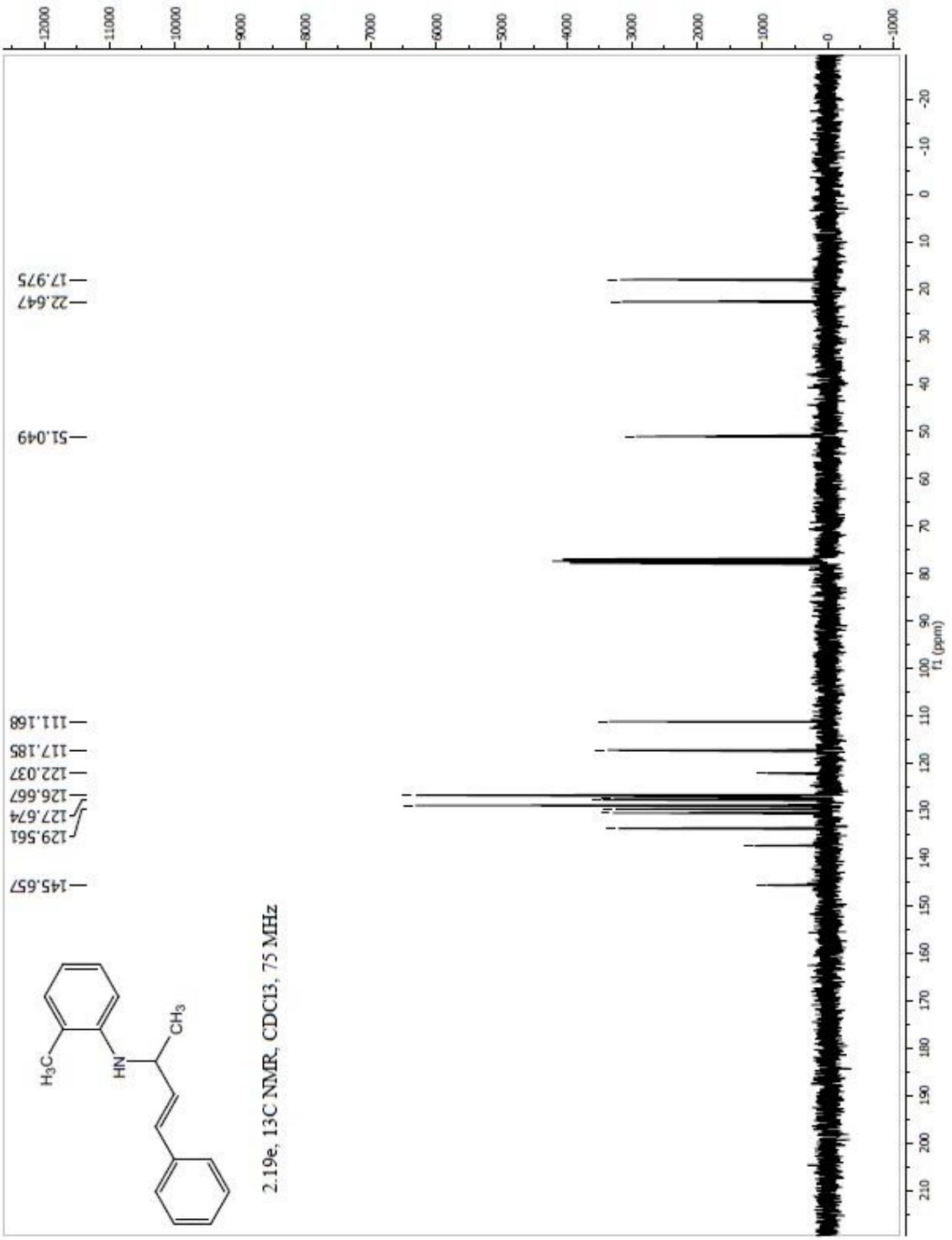

2.181, 1H NMR, CDCl3, 300MHz
8.385
8.353
7.352
7.183
7.120
6.244
6.212
2.022
2.019
1.969
1.00
2.09
1.21
2.01
0.96
3.11
3.24
f1 (ppm)

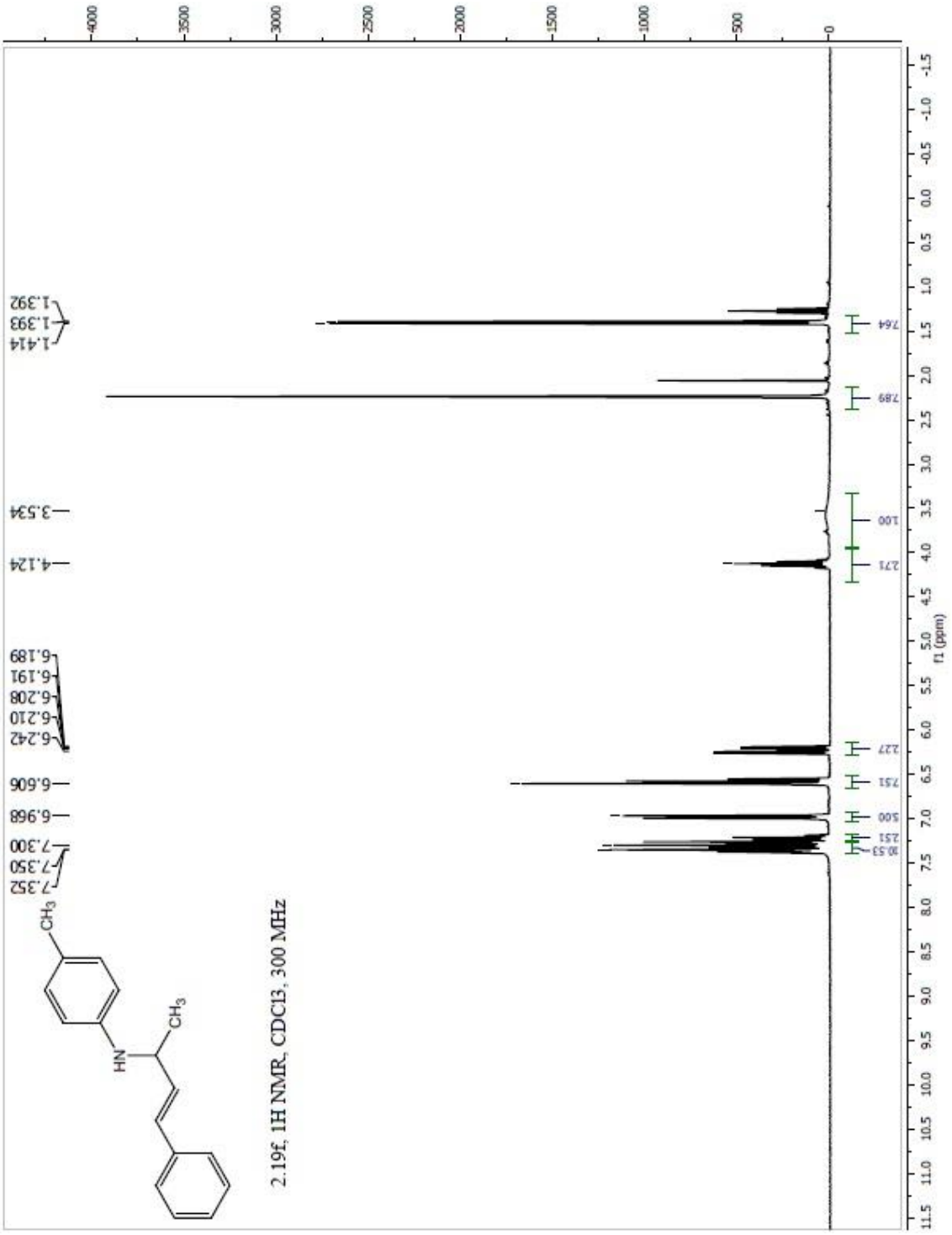

19.326
27.239
121.175
125.839
126.605
129.387
150.611
152.957
159.223
2.181, 13C NMR, CDCl3, 75 MHz
f1 (ppm)

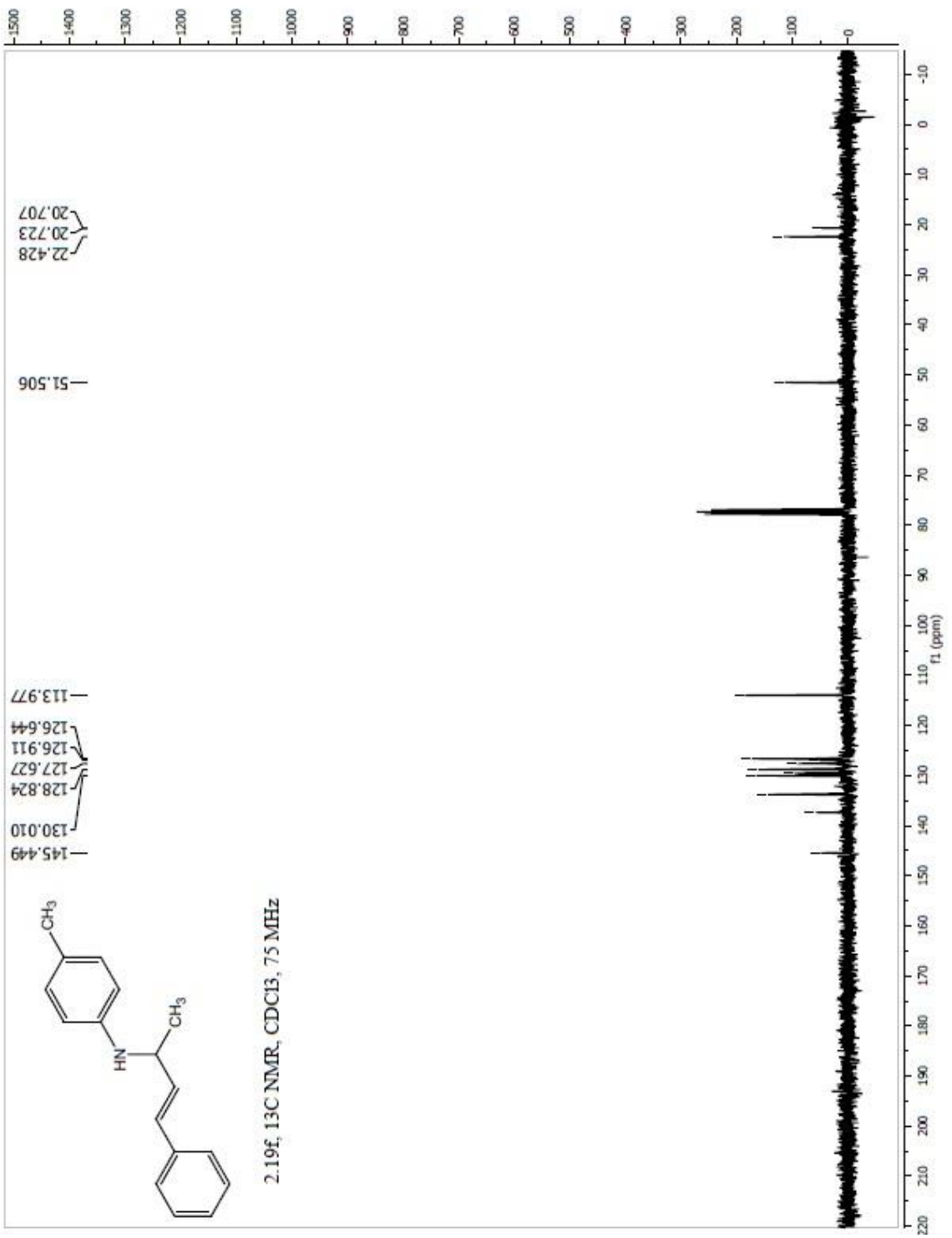

2.19b, 1H NMR, CDCl3, 300 MHz
HN
CH3
7.373
6.667
6.638
6.177
6.156
6.124
6.102
3.914
3.910
3.892
3.888
3.756
2.055
1.730
1.036
4.76
3.09
3.03
0.89
0.83
0.99
0.81
2.21
3.00
f1 (ppm)

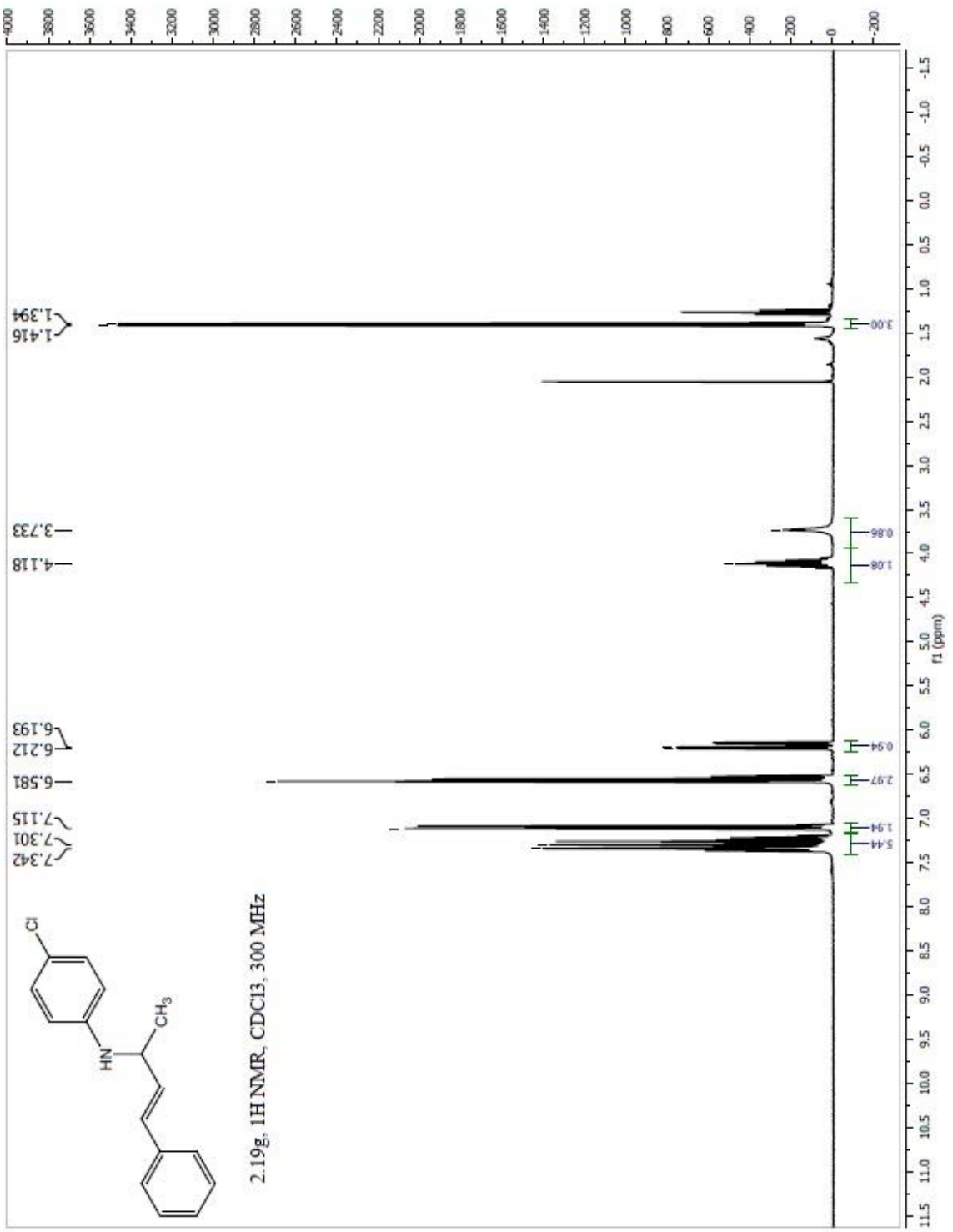

2.19b, 13C NMR, CDCl3, 75 MHz
147.994
137.355
129.501
128.669
126.654
117.527
113.663
57.484
29.432
10.844
HN
CH3
f1 (ppm)

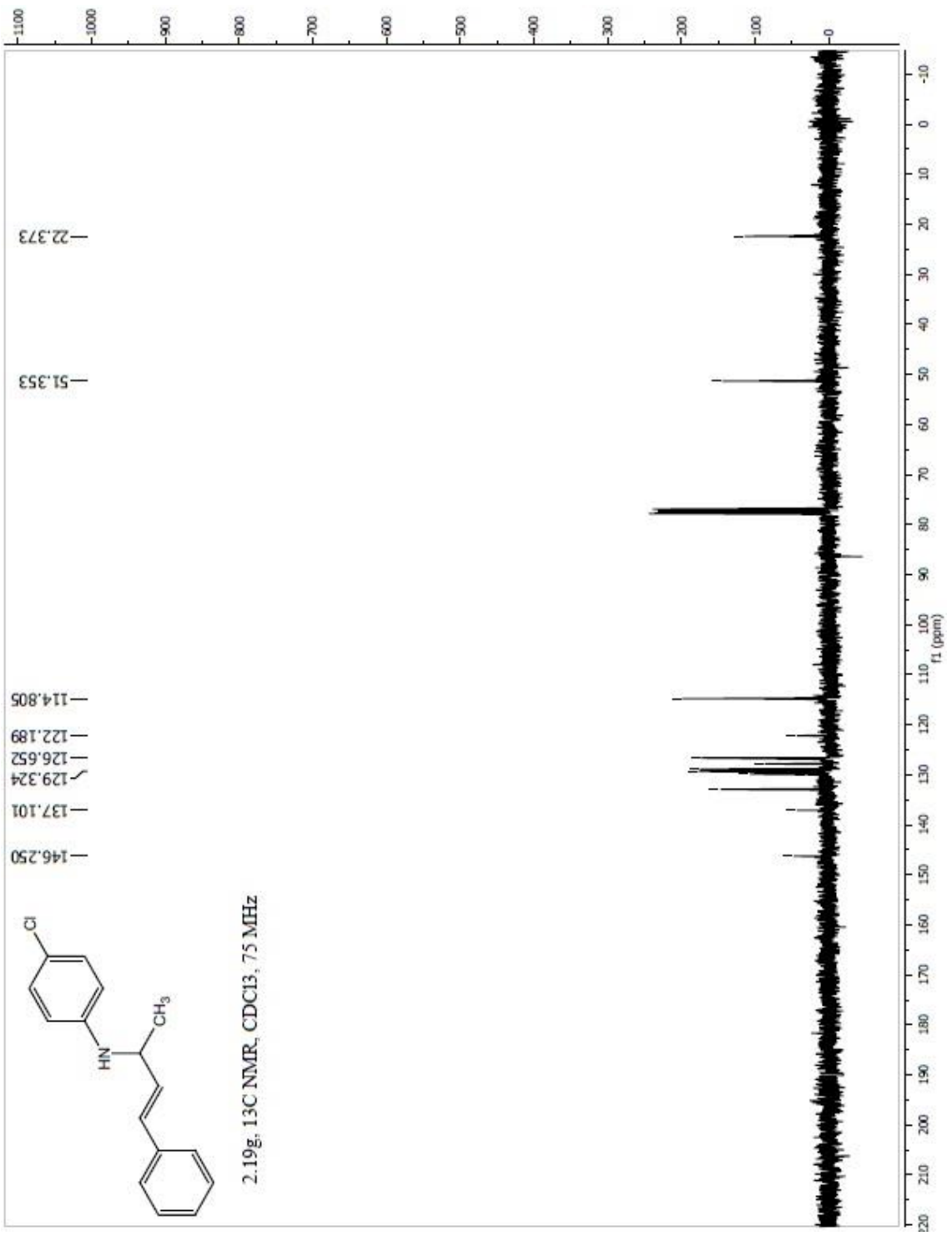

2.19e, 1H NMR, CDCl3, 300 MHz
H3C
HN
CH3
7.359
7.302
7.089
7.087
7.065
7.063
6.561
6.288
6.269
6.235
6.216
4.225
4.202
4.180
3.562
2.193
1.470
1.448
3.54
3.00
0.63
0.82
0.88
1.92
0.95
1.88
0.89
3.92
f1 (ppm)

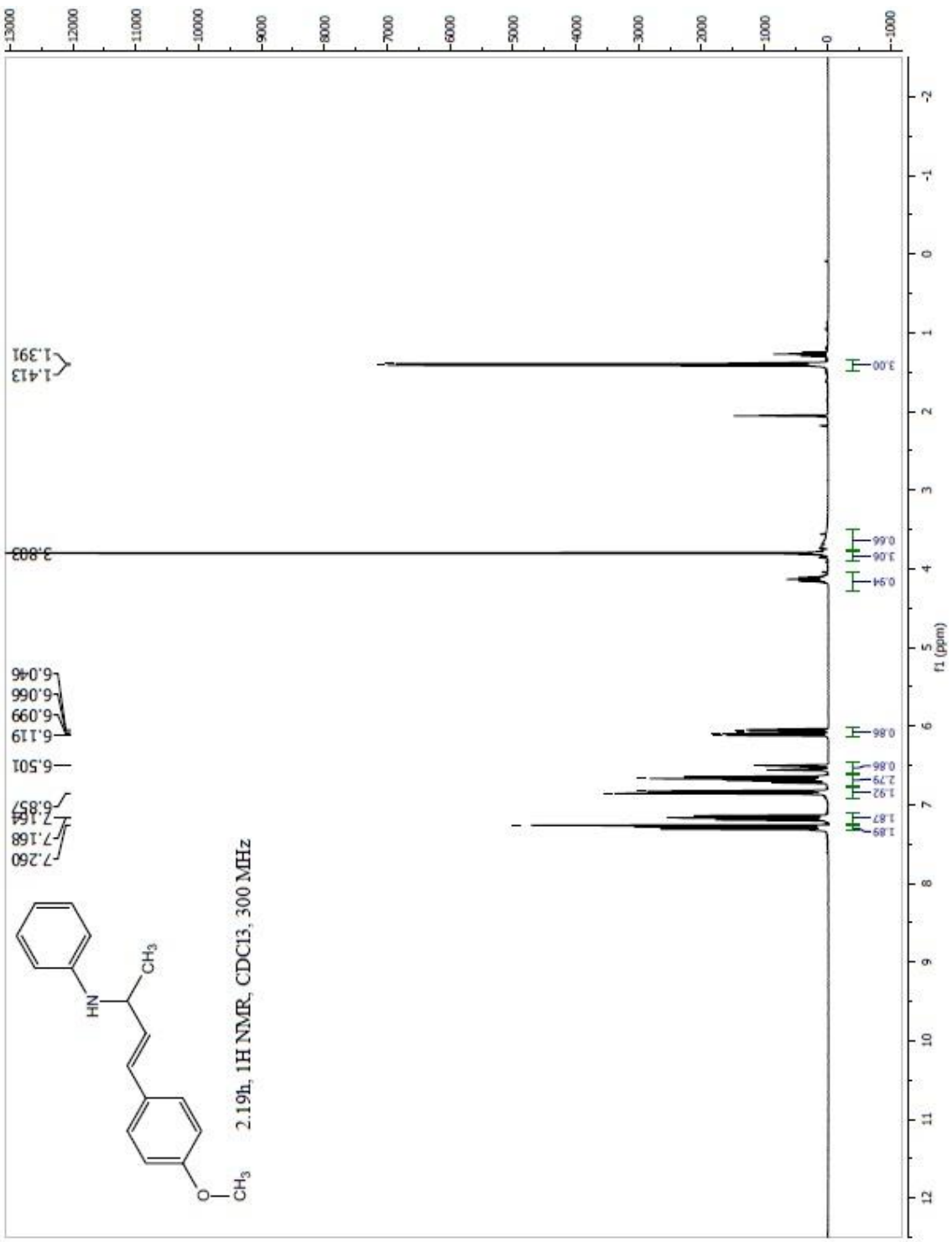

145.657
129.561
127.674
126.667
122.037
117.185
111.168
51.049
22.647
17.975
f1 (ppm)
2.19e, 13C NMR, CDCl3, 75 MHz
H3C
HN
CH3

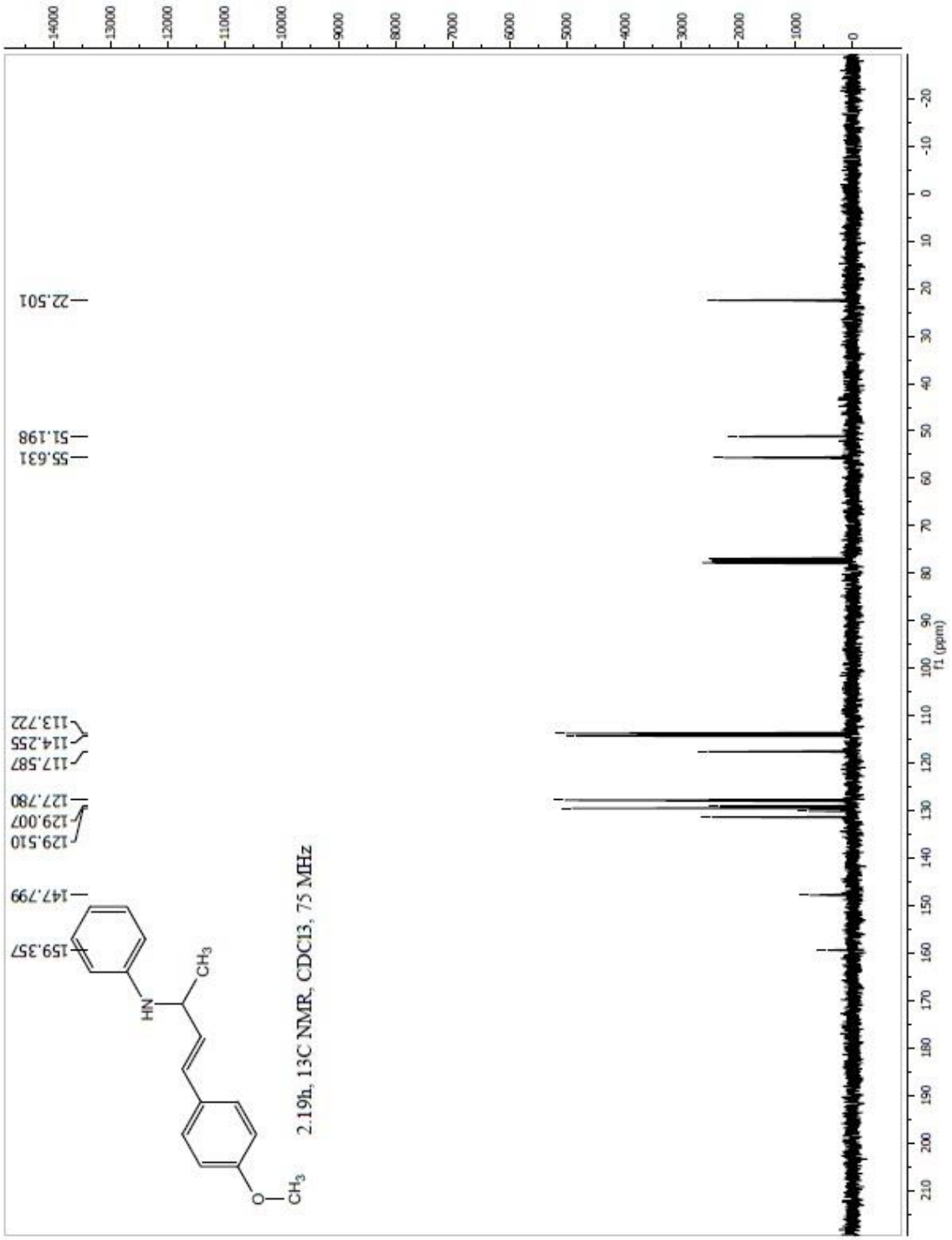

2.19f, 1H NMR, CDCl3, 300 MHz
1.392
1.393
1.414
3.534
4.124
6.189
6.191
6.208
6.210
6.242
6.606
6.968
7.300
7.350
7.352
f1 (ppm)

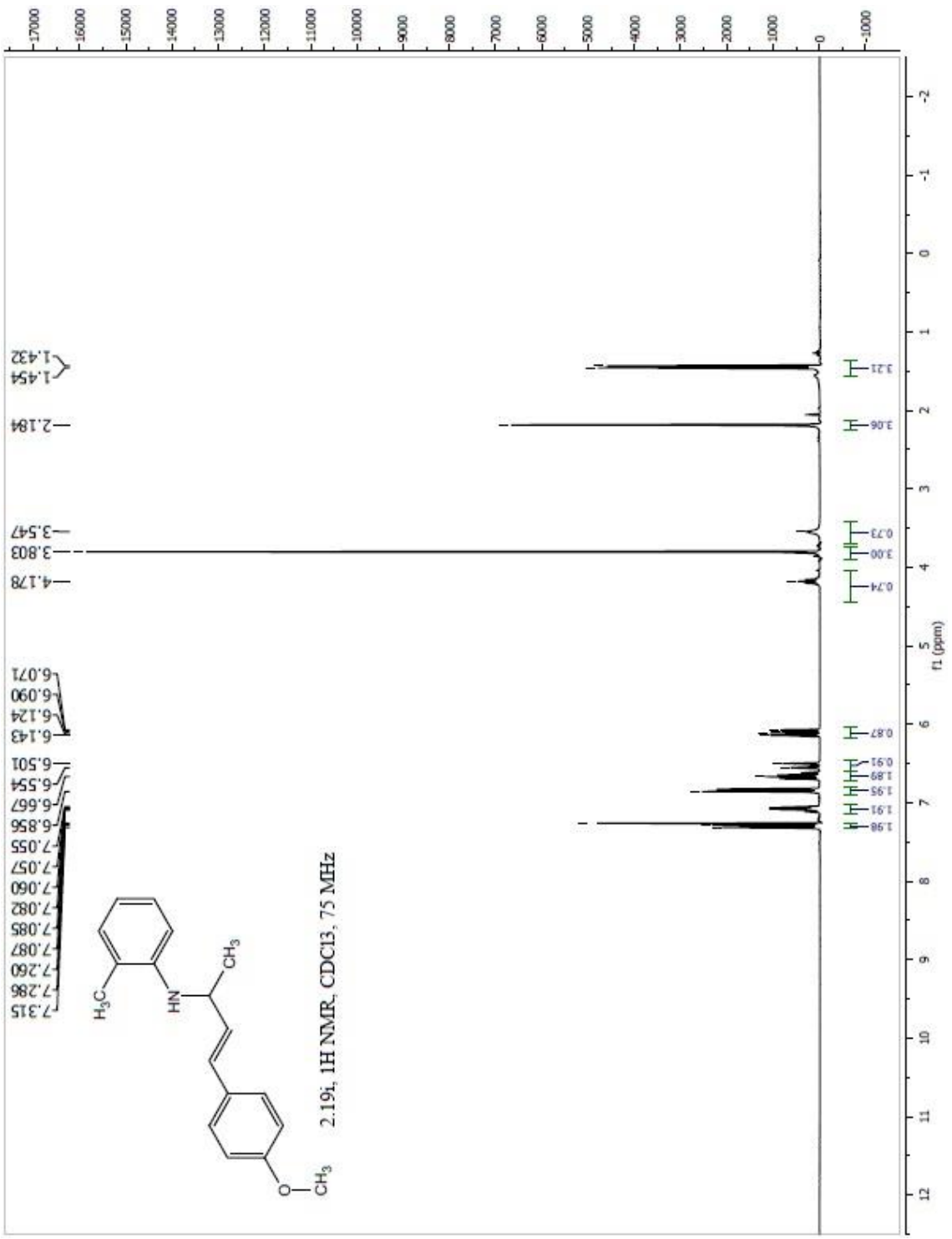

2.19f, 13C NMR, CDCl3, 75 MHz
145.449
130.010
128.824
127.627
126.911
126.644
113.977
51.506
22.428
20.723
20.707
HN
CH3
CH3
f1 (ppm)

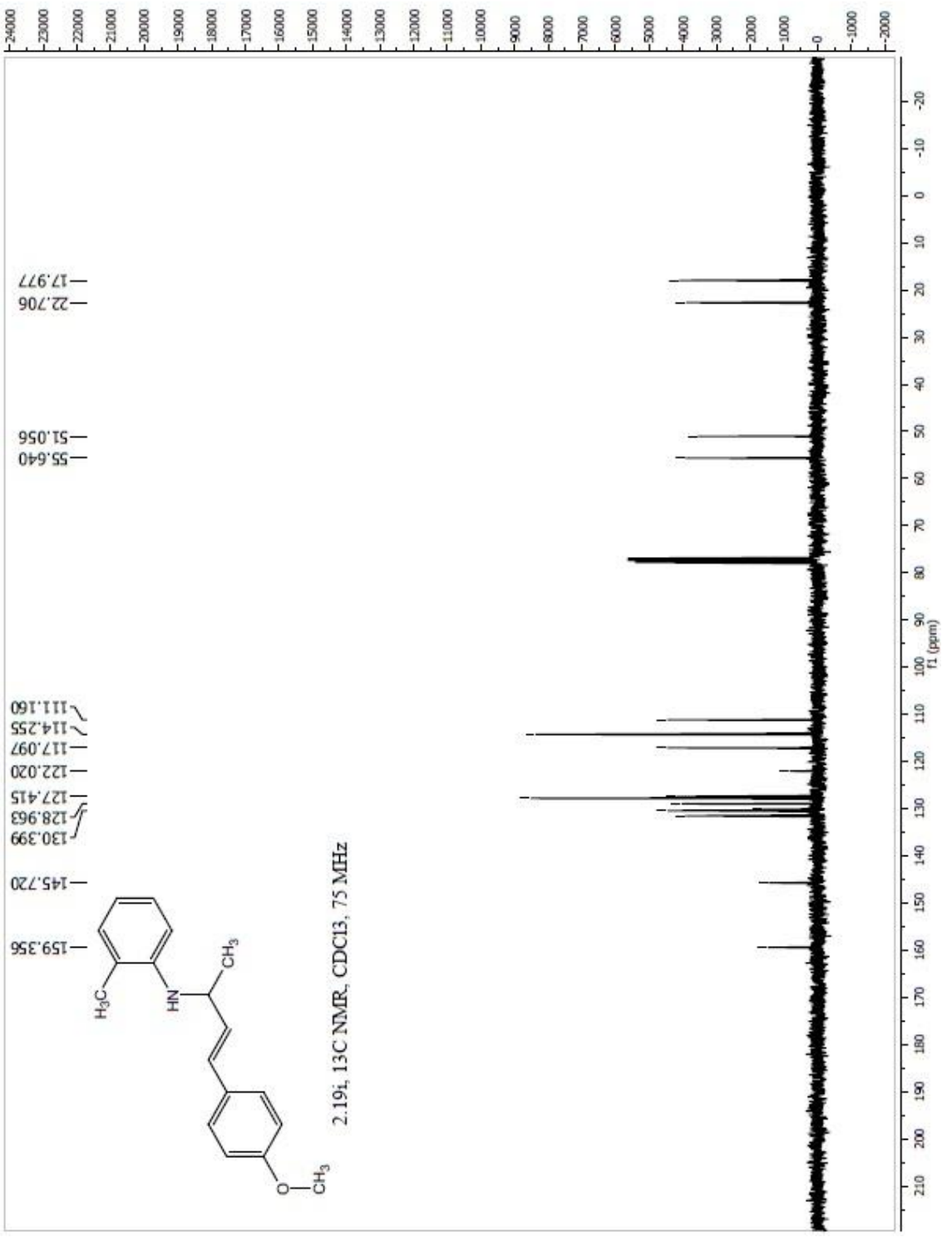

2.19g, 1H NMR, CDCl3, 300 MHz
Cl
HN
CH3
7.342
7.301
7.115
6.581
6.212
6.193
4.118
3.733
1.416
1.394
5.44
1.94
2.97
0.94
1.08
0.86
3.00
f1 (ppm)


22.373
51.353
114.805
122.189
126.652
129.324
137.101
146.250
Cl
HN
CH3
2.19g, 13C NMR, CDCl3, 75 MHz
f1 (ppm)

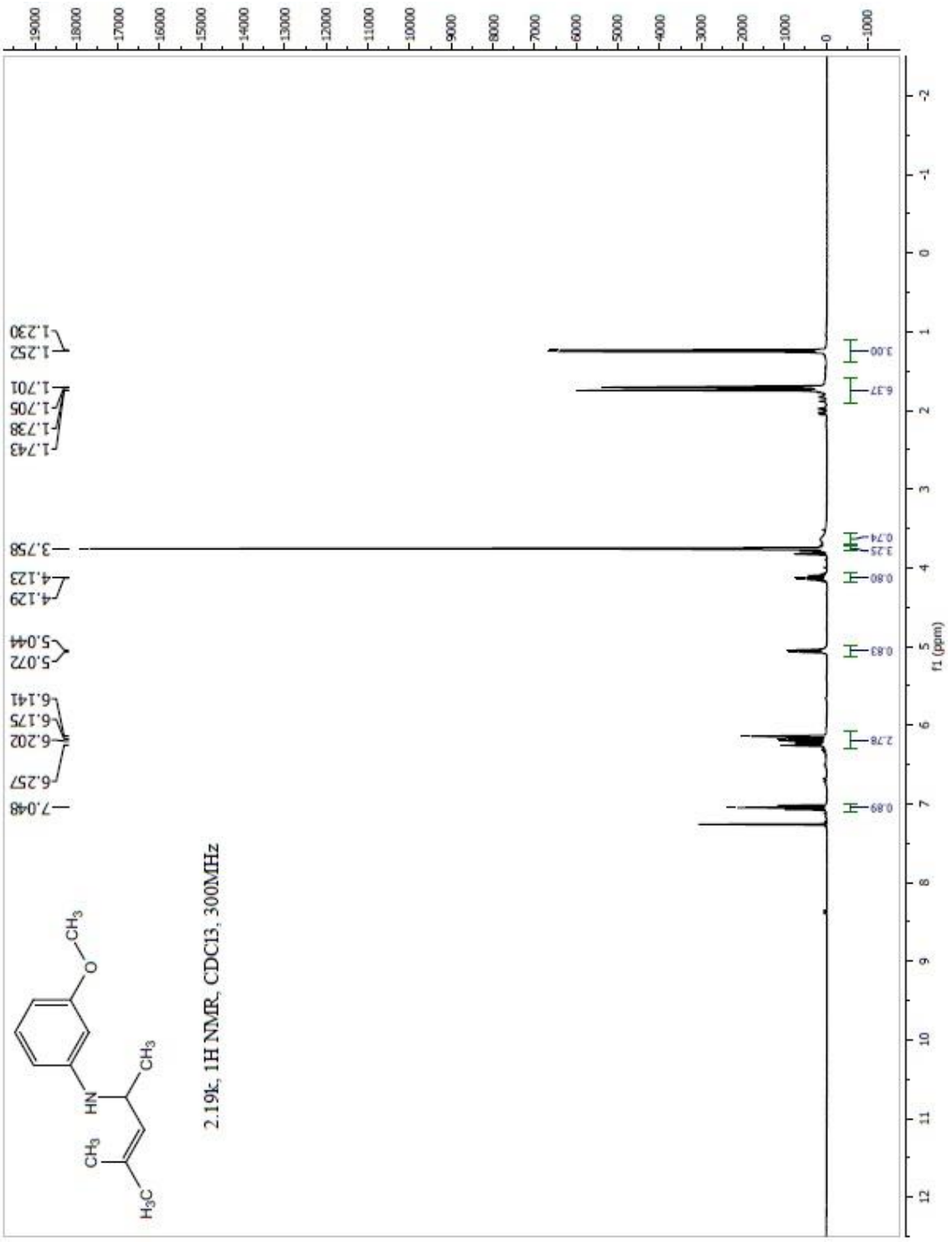

2.19h, 1H NMR, CDCl3, 300 MHz
HN
CH3
O
CH3
7.260
7.168
7.164
6.857
6.501
6.119
6.099
6.066
6.046
3.803
1.413
1.391
3.00
0.66
3.06
0.94
0.86
0.86
2.79
1.92
1.87
1.89
f1 (ppm)

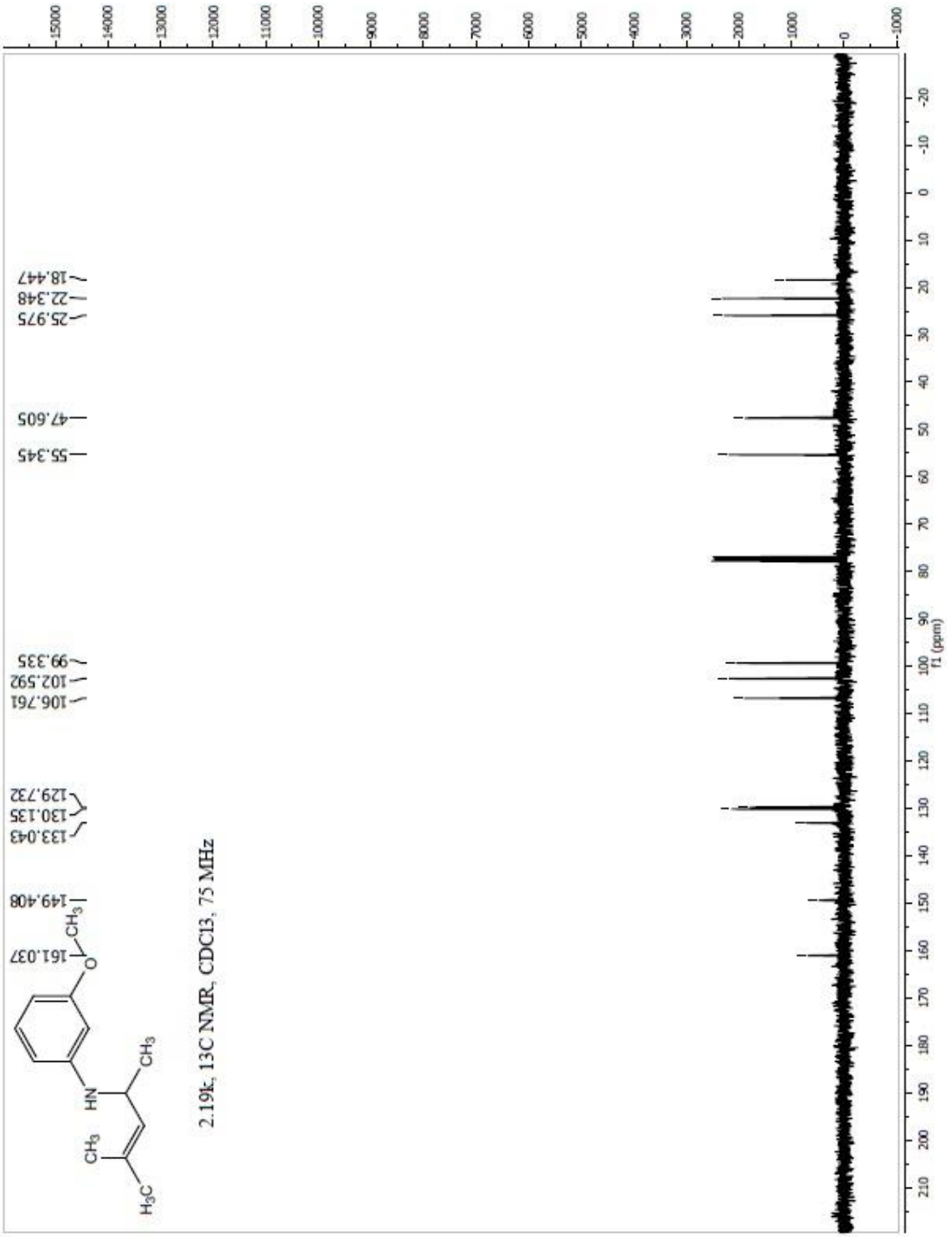

2.19h, 13C NMR, CDCl3, 75 MHz
159.357
147.799
129.510
129.007
127.780
117.587
114.255
113.722
55.631
51.198
22.501
HN
CH3
O
CH3
f1 (ppm)


2.19i, 1H NMR, CDCl3, 75 MHz
f1 (ppm)

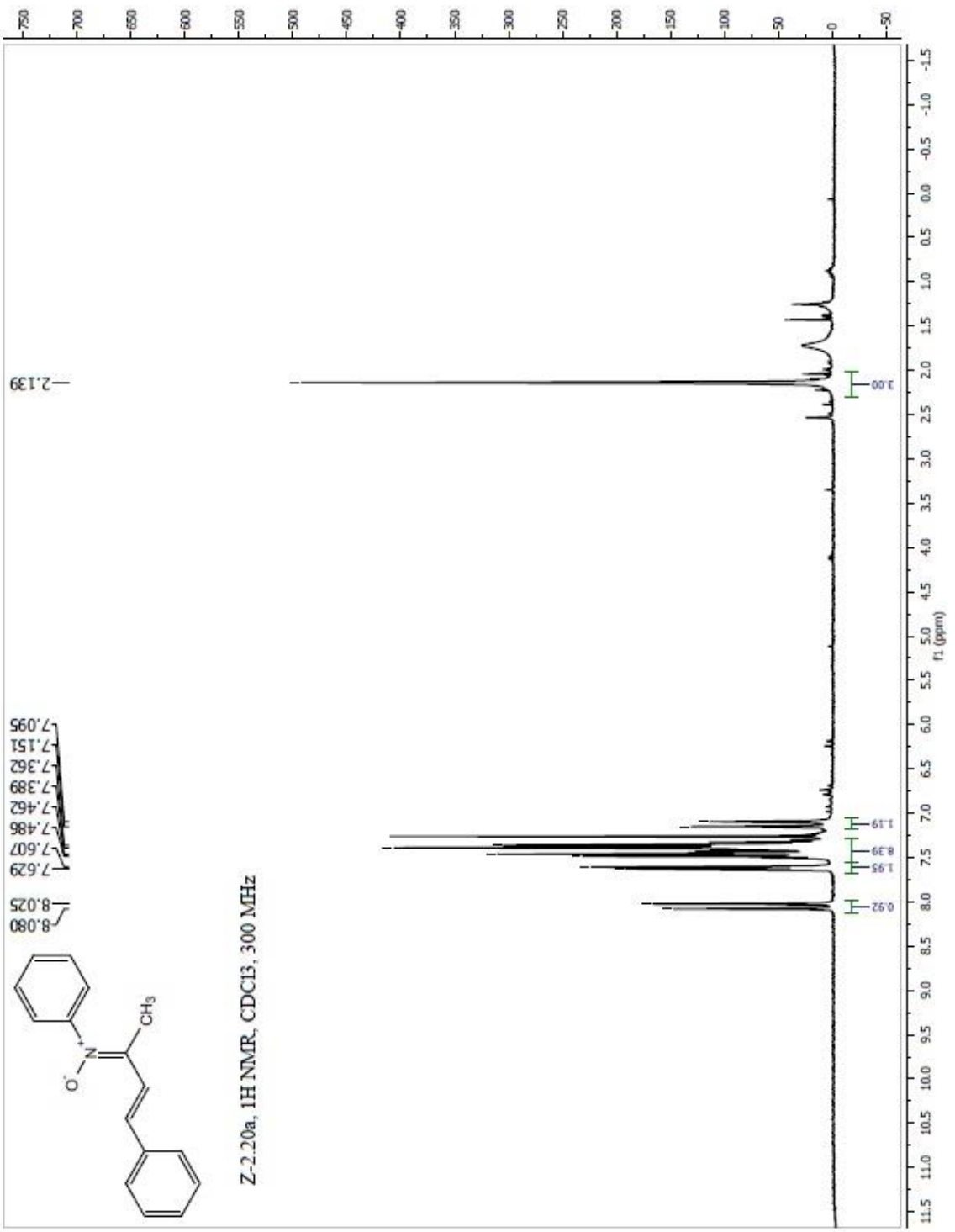


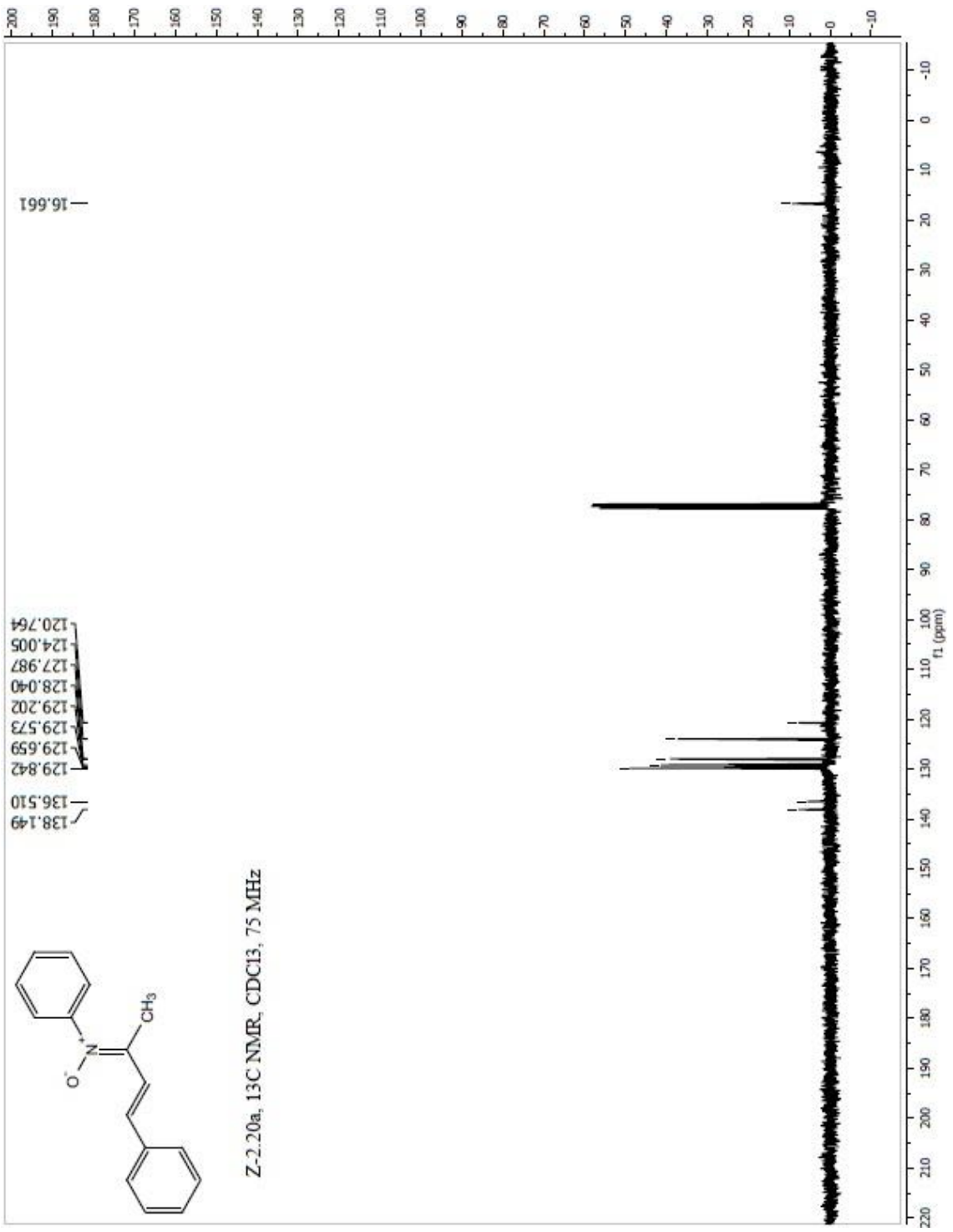
2.19i, 13C NMR, CDCl3, 75 MHz

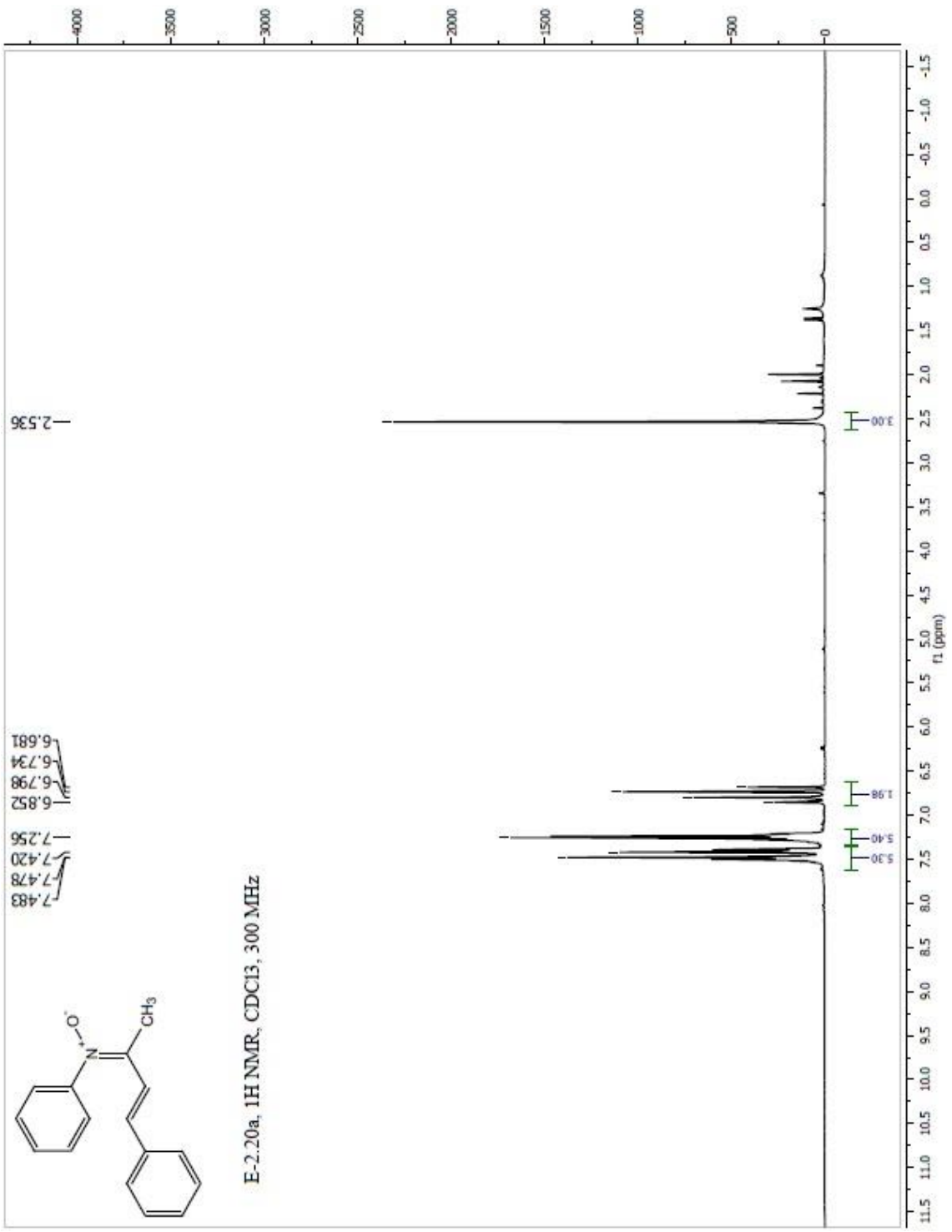

1.230
1.252
1.701
1.705
1.738
1.743
3.758
4.123
4.129
5.044
5.072
6.141
6.175
6.202
6.257
7.048
3.00
6.37
0.74
3.25
0.80
0.83
2.78
0.89
f1 (ppm)
2.19k, 1H NMR, CDCl3, 300MHz
CH3
O
HN
CH3
CH3
H3C

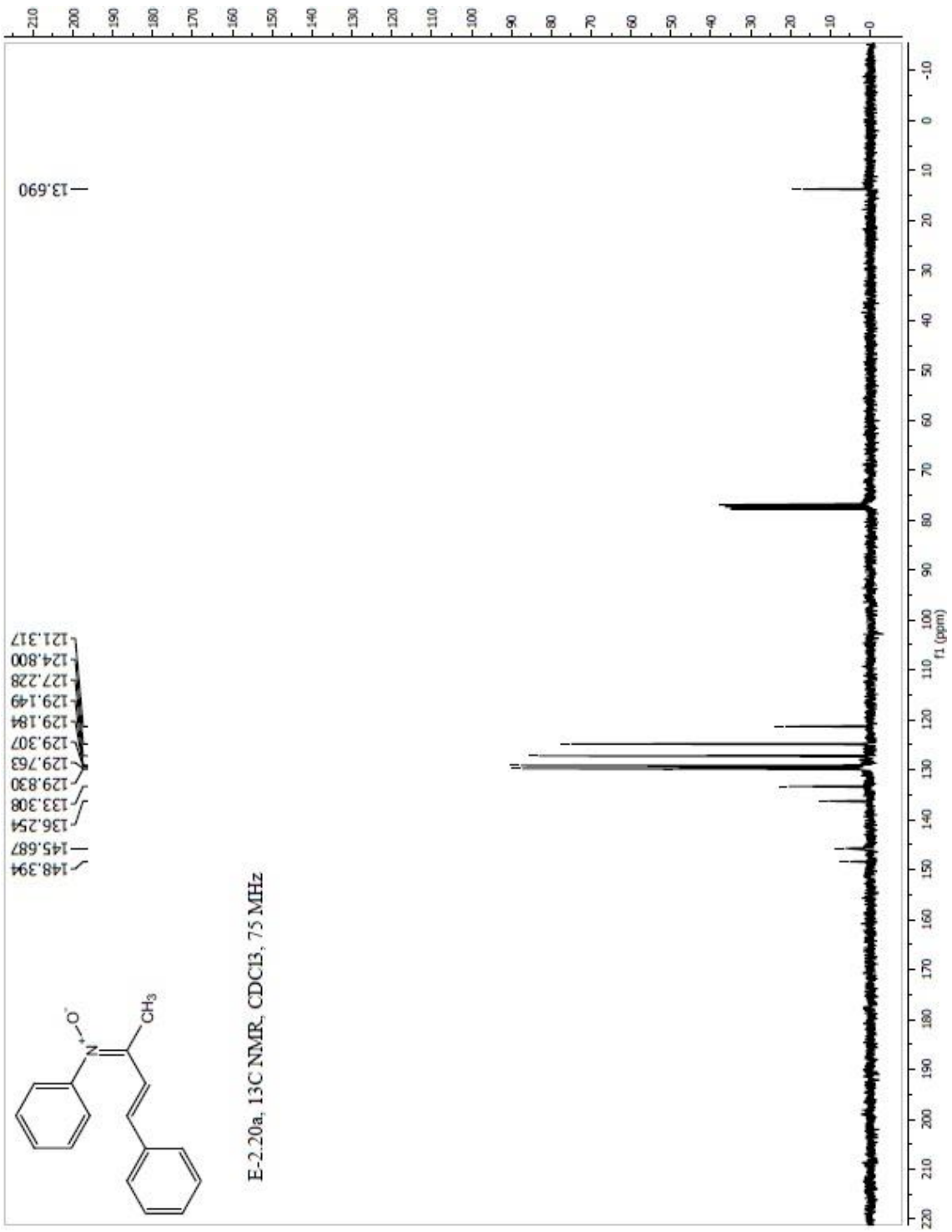


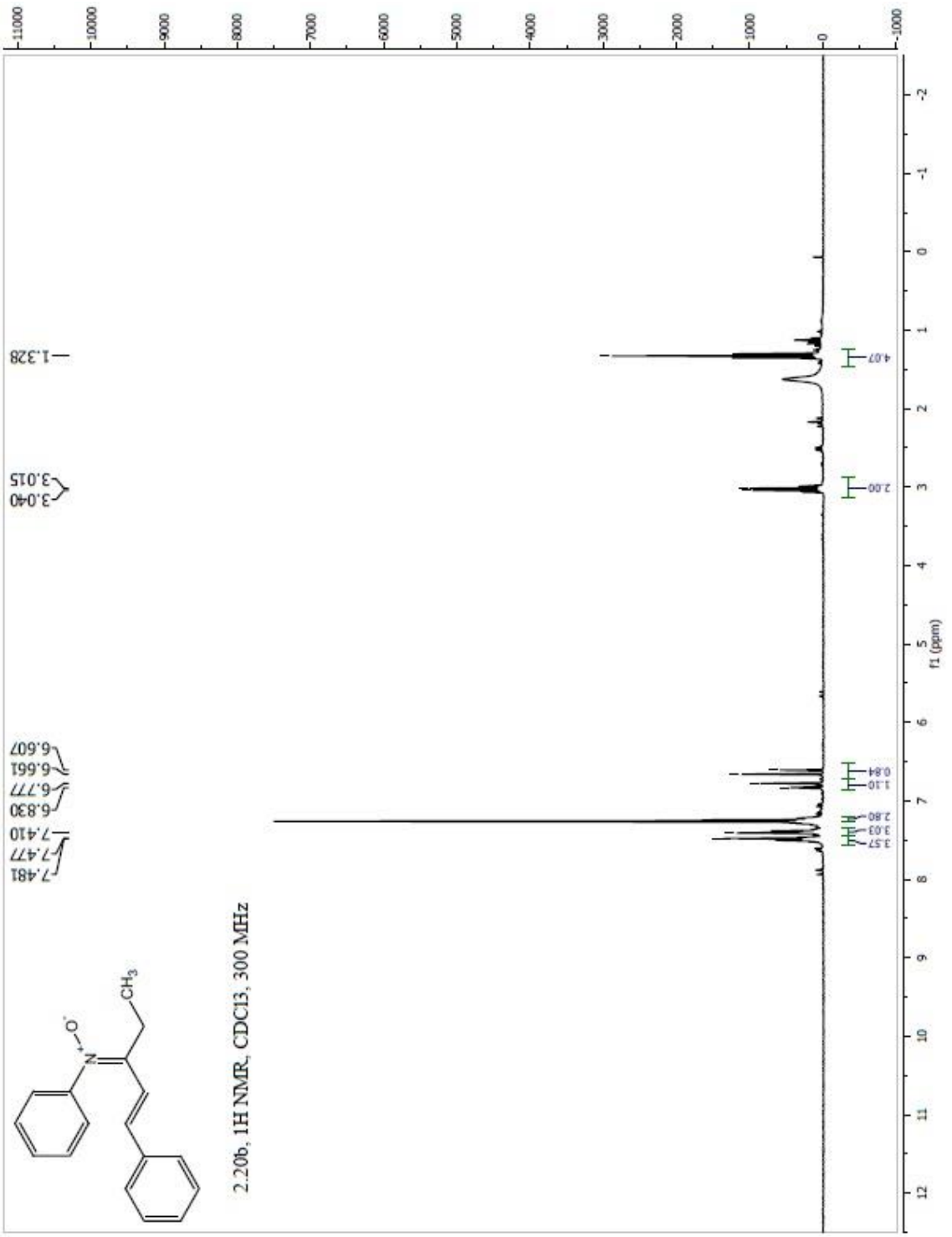
2.19k, 13C NMR, CDCl3, 75 MHz

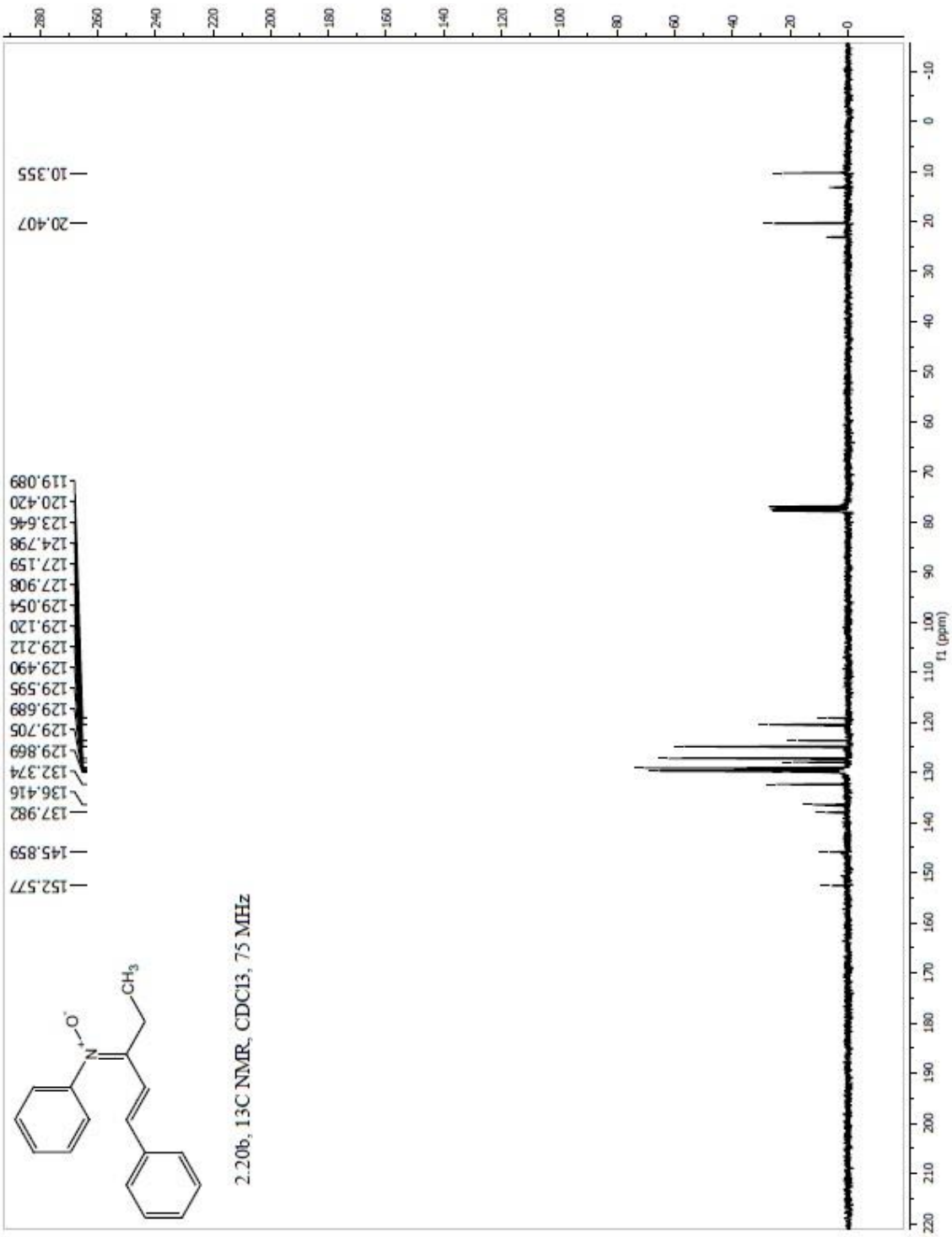

Z-2.20a, 1H NMR, CDCl3, 300 MHz
8.080
8.025
7.629
7.607
7.486
7.462
7.389
7.362
7.151
7.095
2.139
3.00
1.19
8.39
1.95
0.92
f1 (ppm)


16.661
138.149
136.510
129.842
129.659
129.573
129.202
128.040
127.987
124.005
120.764
Z-2.20a, 13C NMR, CDCl3, 75 MHz
f1 (ppm)

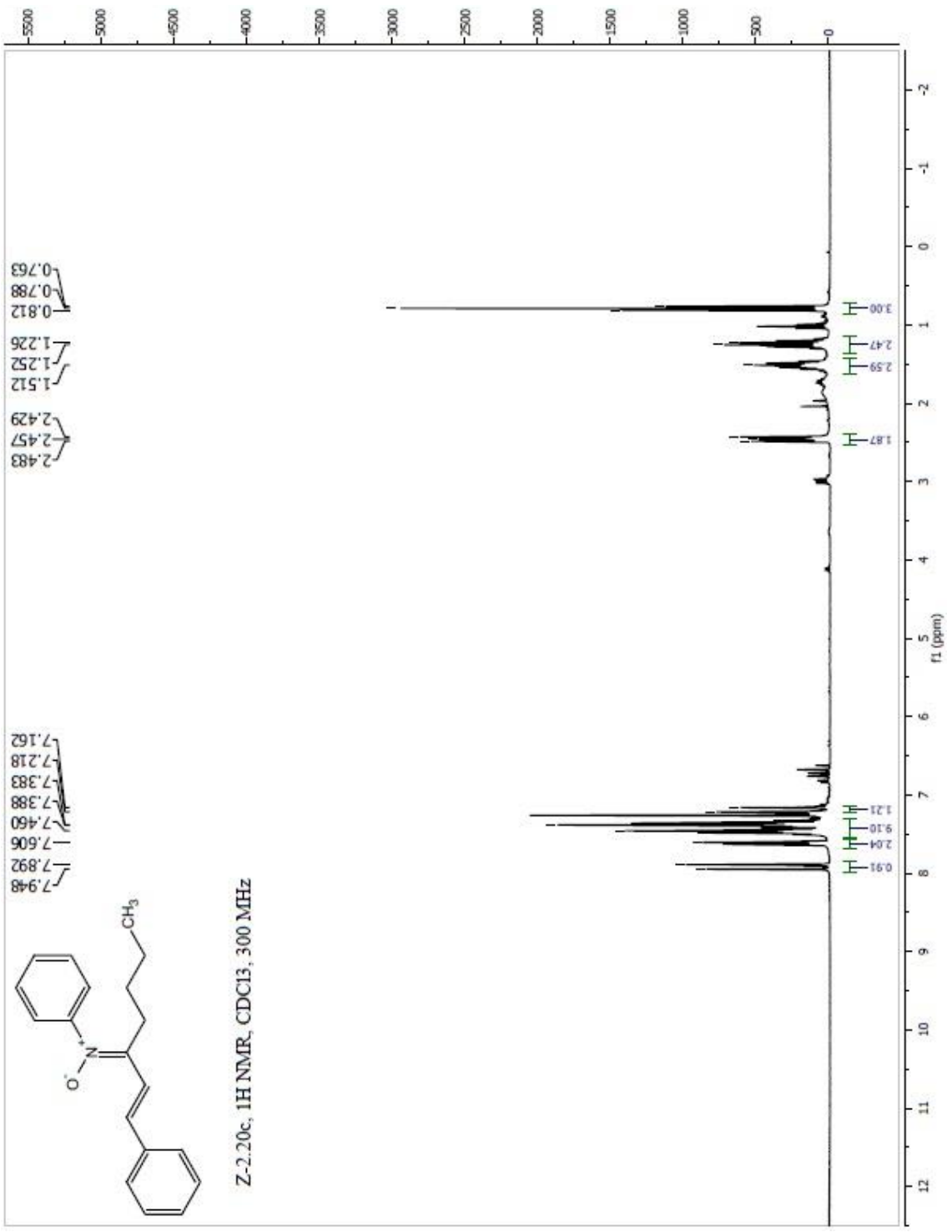

E-2.20a, 1H NMR, CDCl3, 300 MHz
2.536
6.681
6.734
6.798
6.852
7.256
7.420
7.478
7.483
3.00
1.98
5.40
5.30
f1 (ppm)

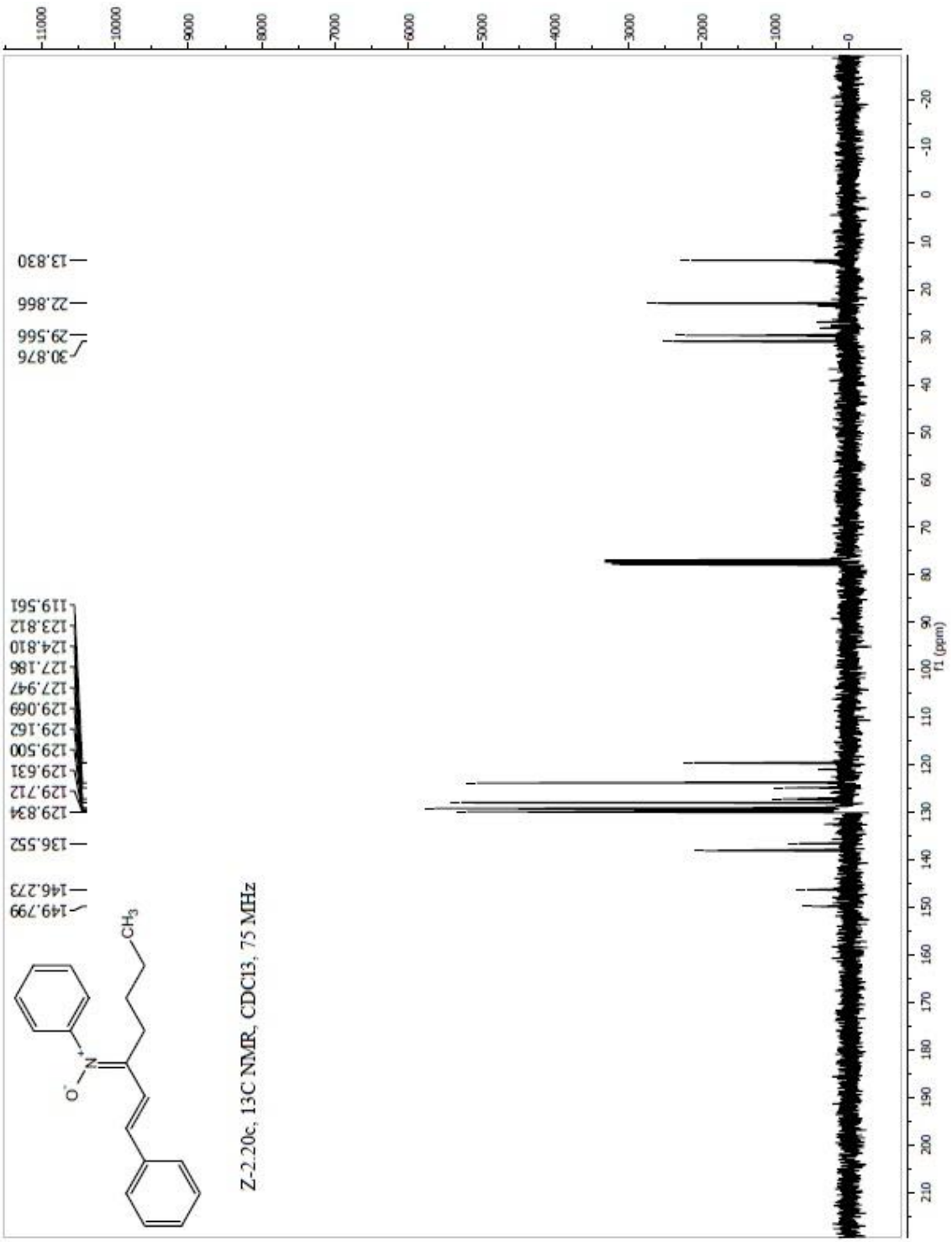

E-2.20a, 13C NMR, CDCl3, 75 MHz
13.690
148.394
145.687
136.254
133.308
129.830
129.763
129.307
129.184
129.149
127.228
124.800
121.317
f1 (ppm)

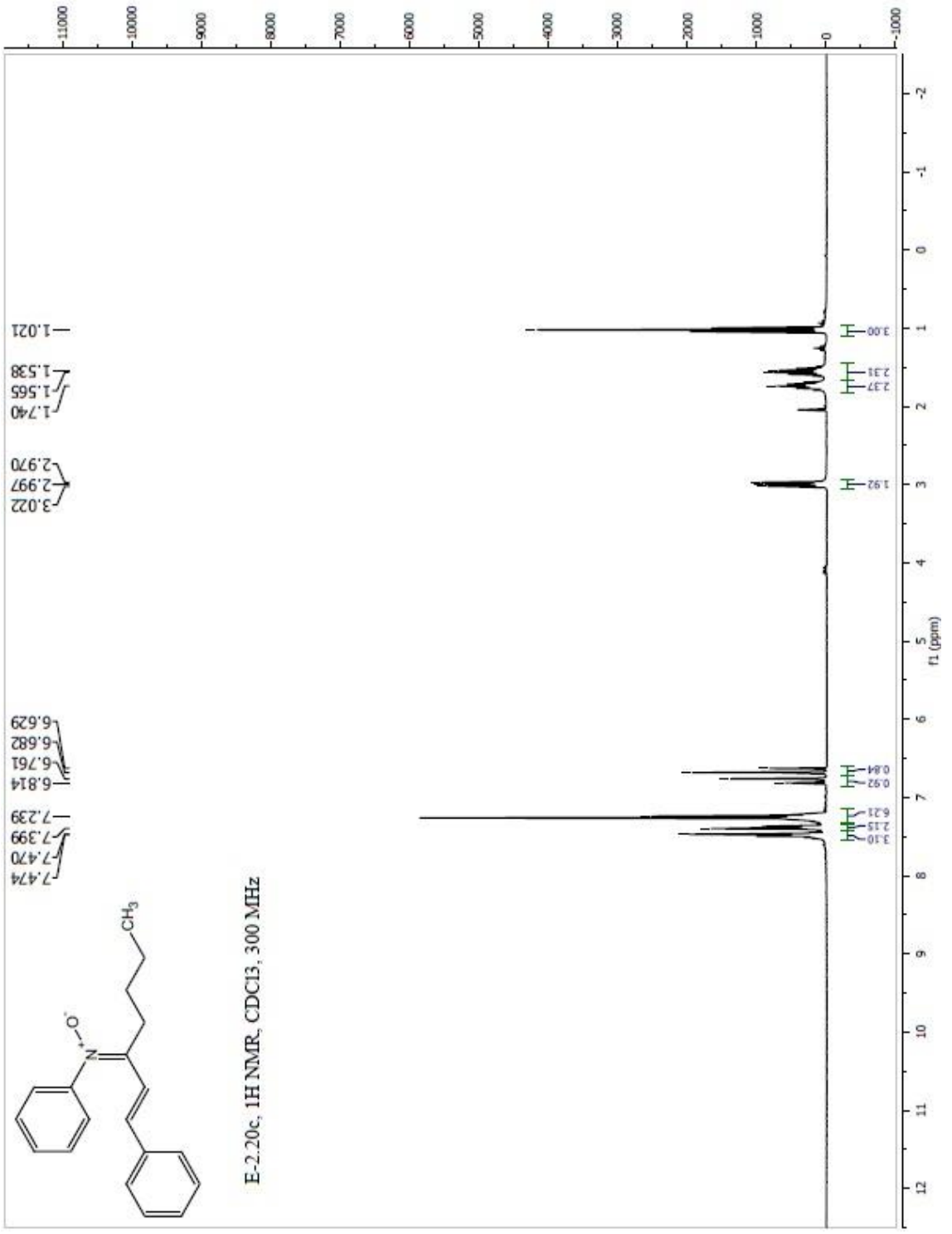

2.20b, 1H NMR, CDCl3, 300 MHz
7.481
7.477
7.410
6.830
6.777
6.661
6.607
3.040
3.015
1.328
4.07
2.00
0.84
1.10
2.80
3.03
3.57
f1 (ppm)

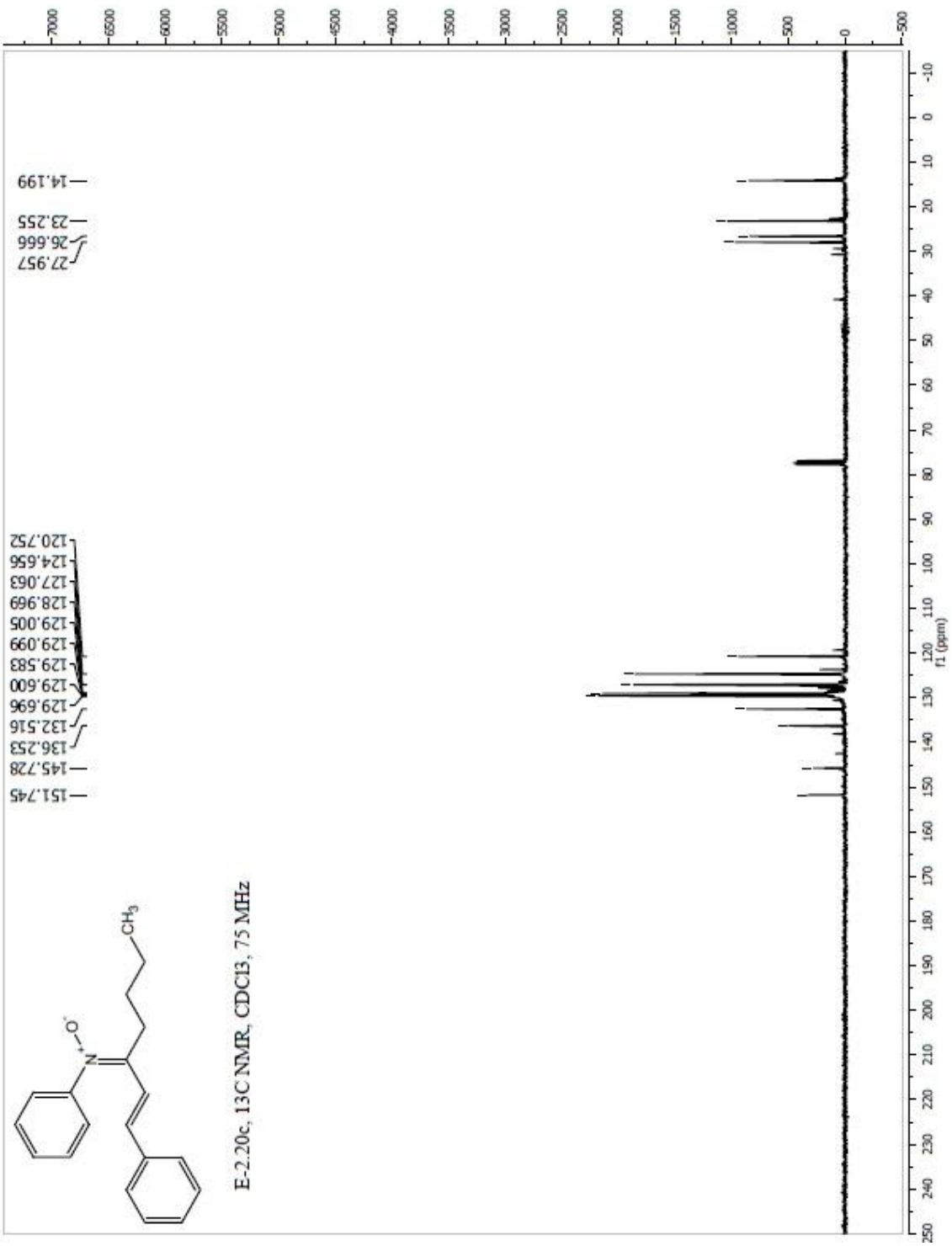


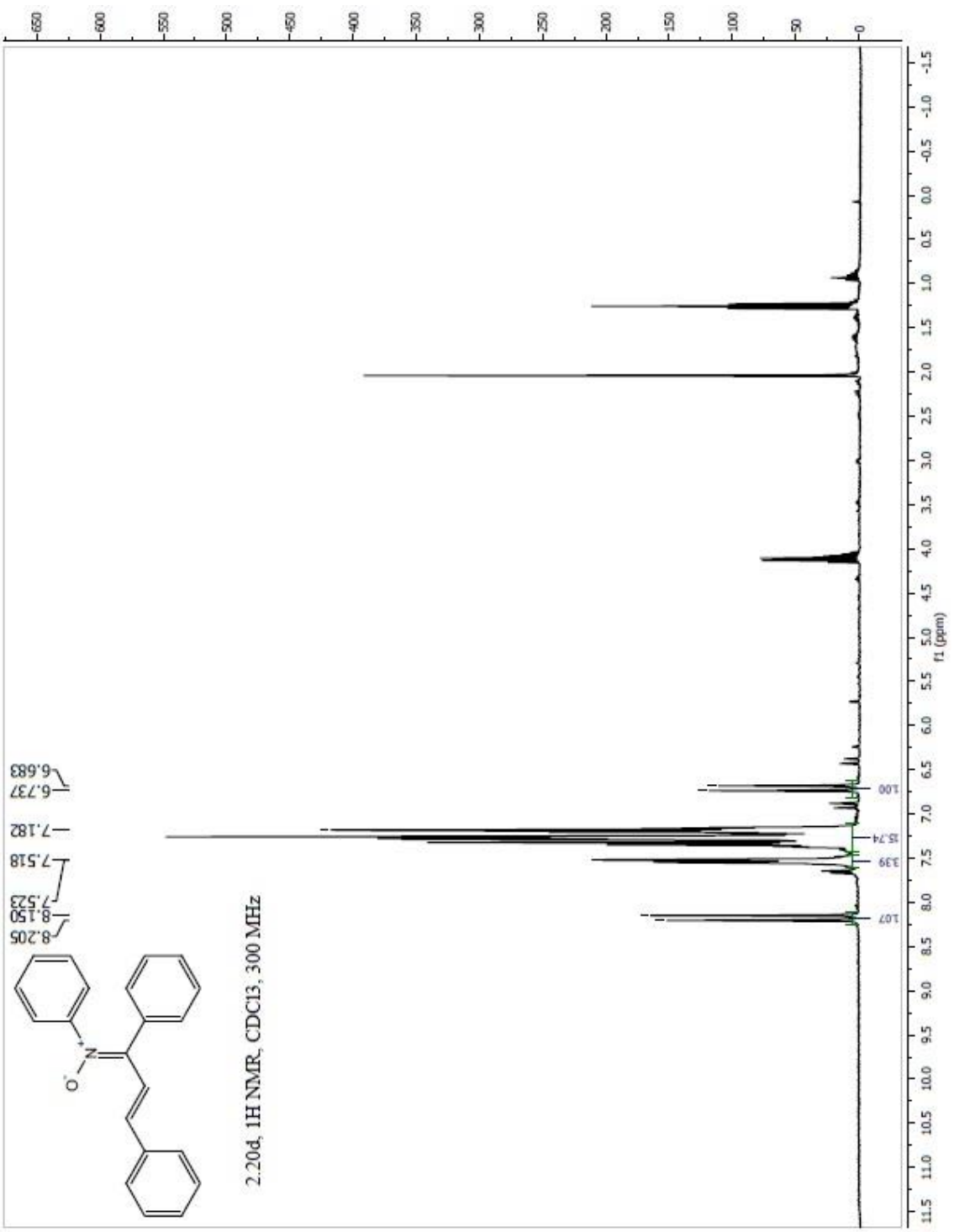
2.20b, 13C NMR, CDCl3, 75 MHz

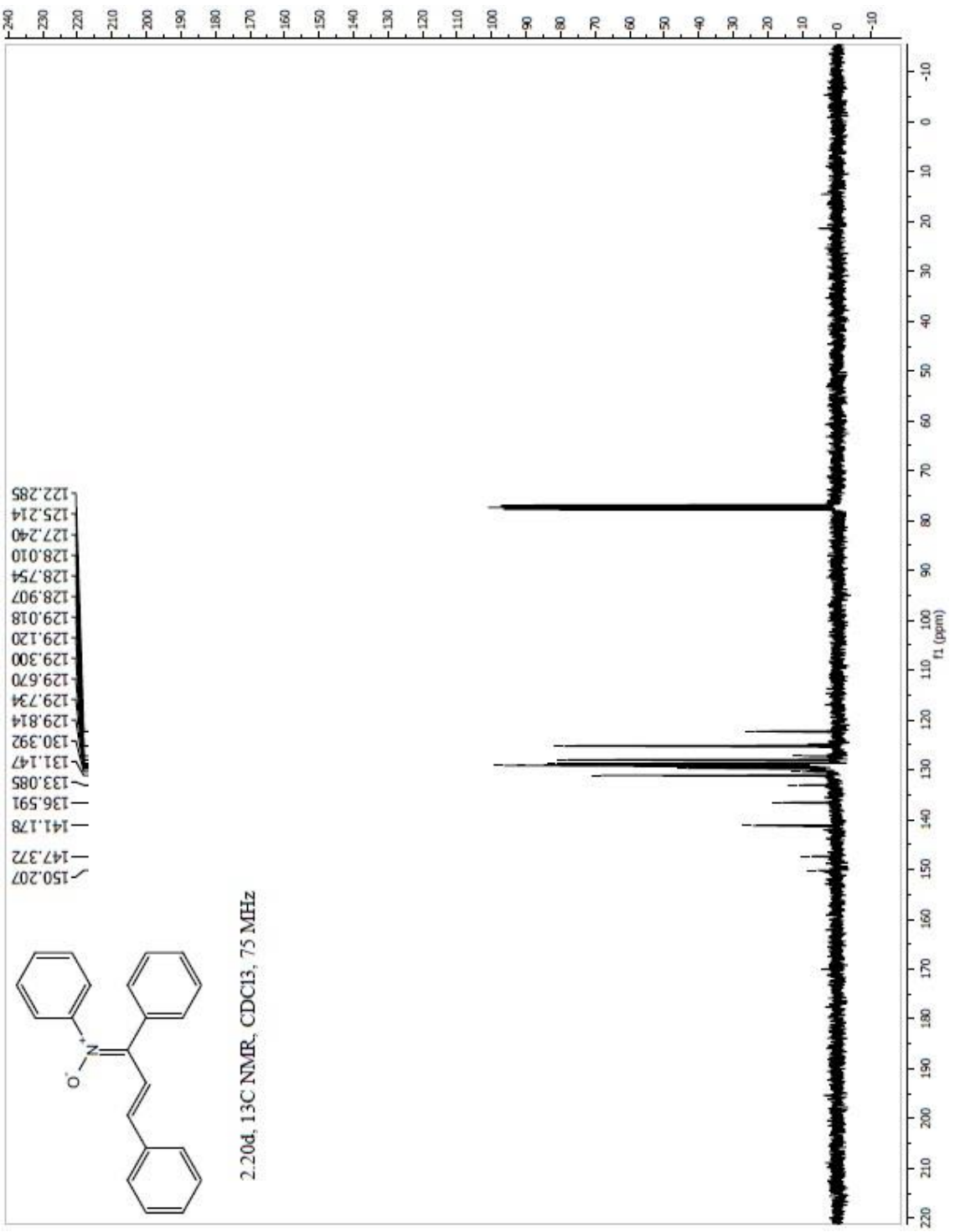

Z-2.20c, 1H NMR, CDCl3, 300 MHz
CH3
N
O
7.948
7.892
7.606
7.460
7.388
7.383
7.218
7.162
2.483
2.457
2.429
1.512
1.252
1.226
0.812
0.788
0.763
0.91
2.04
9.10
1.21
1.87
2.59
2.47
3.00
f1 (ppm)

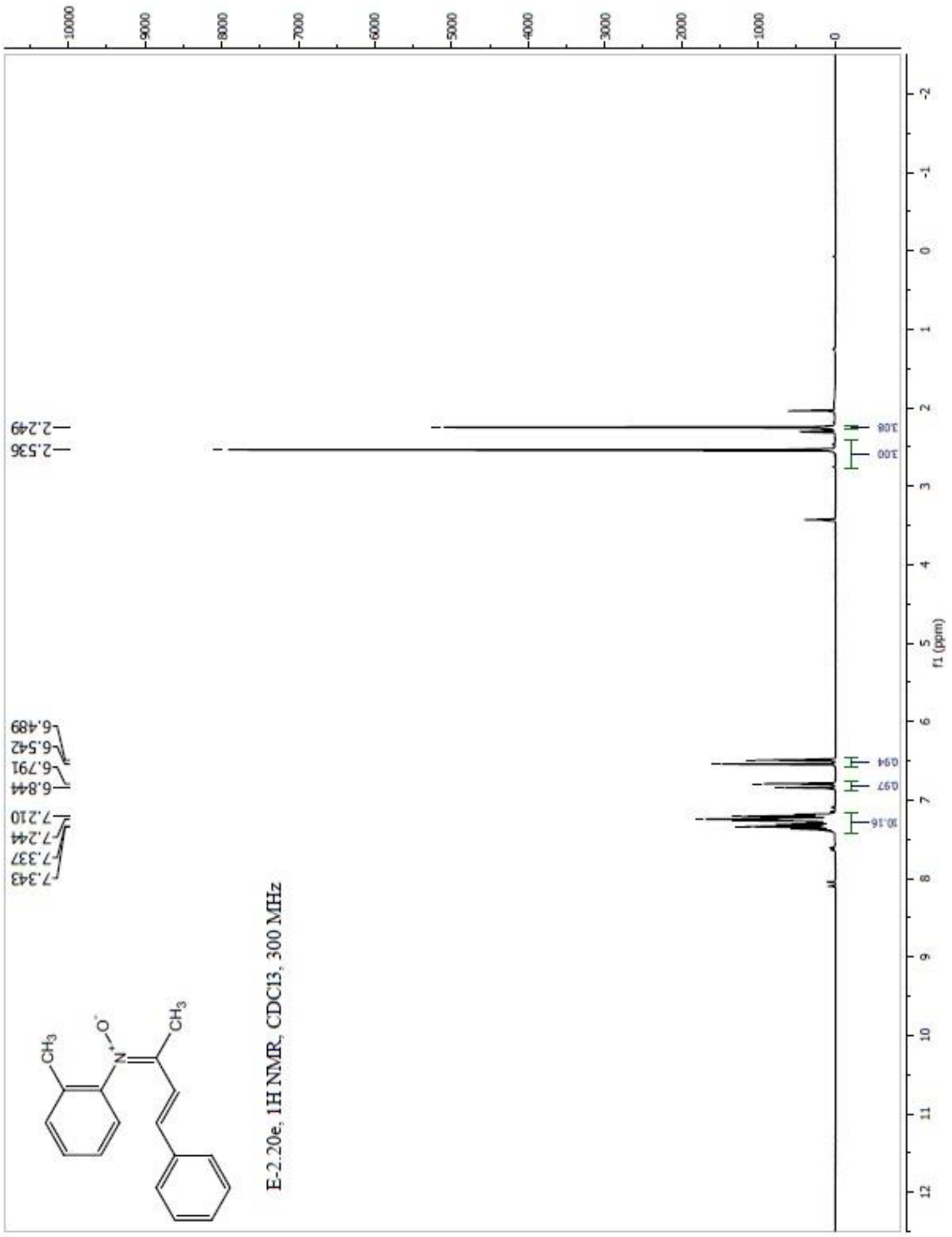

Z-2.20c, 13C NMR, CDCl3, 75 MHz
149.799
146.273
136.552
129.834
129.712
129.631
129.500
129.162
129.069
127.947
127.186
124.810
123.812
119.561
30.876
29.566
22.866
13.830
f1 (ppm)

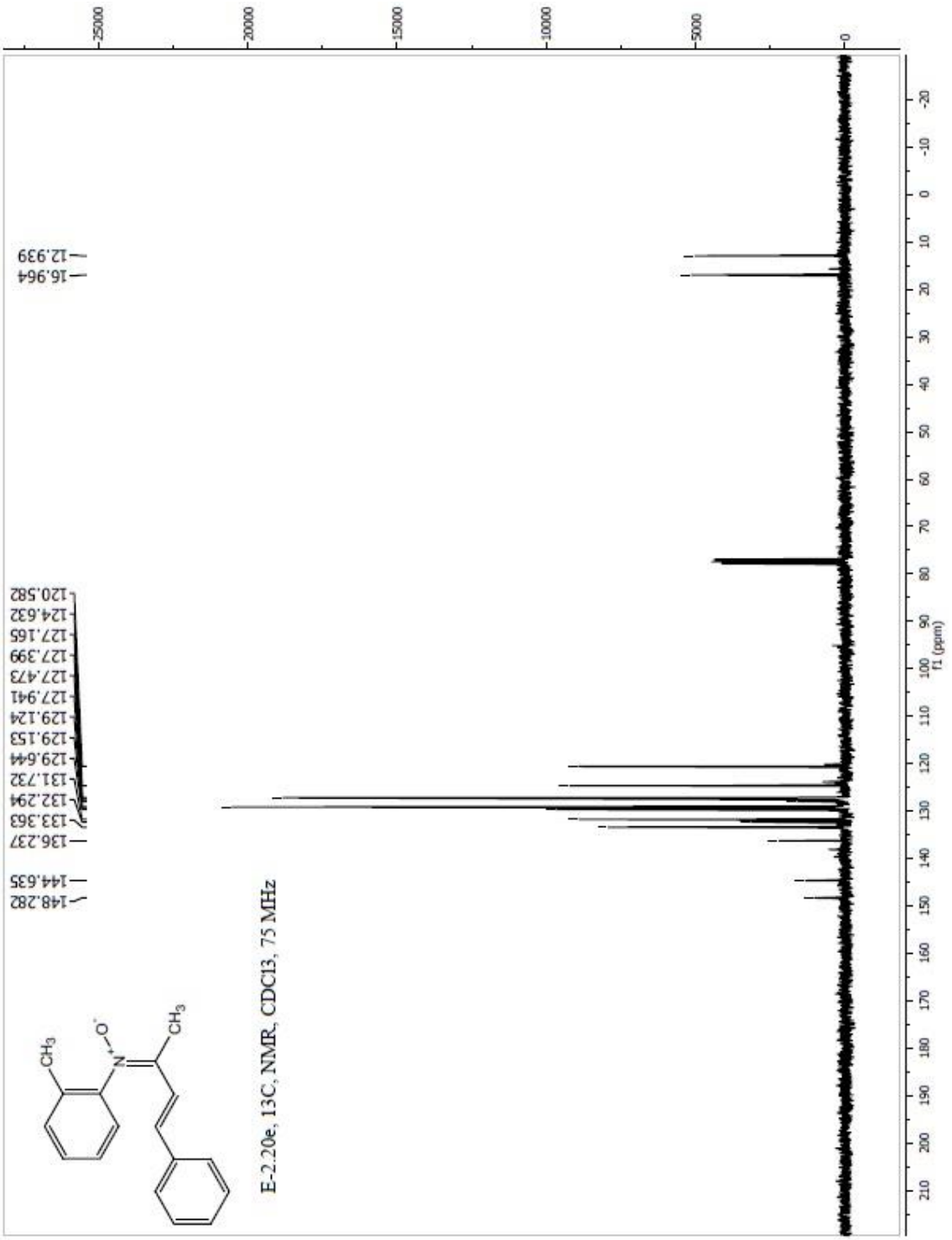

E-2.20c, 1H NMR, CDCl3, 300 MHz
f1 (ppm)

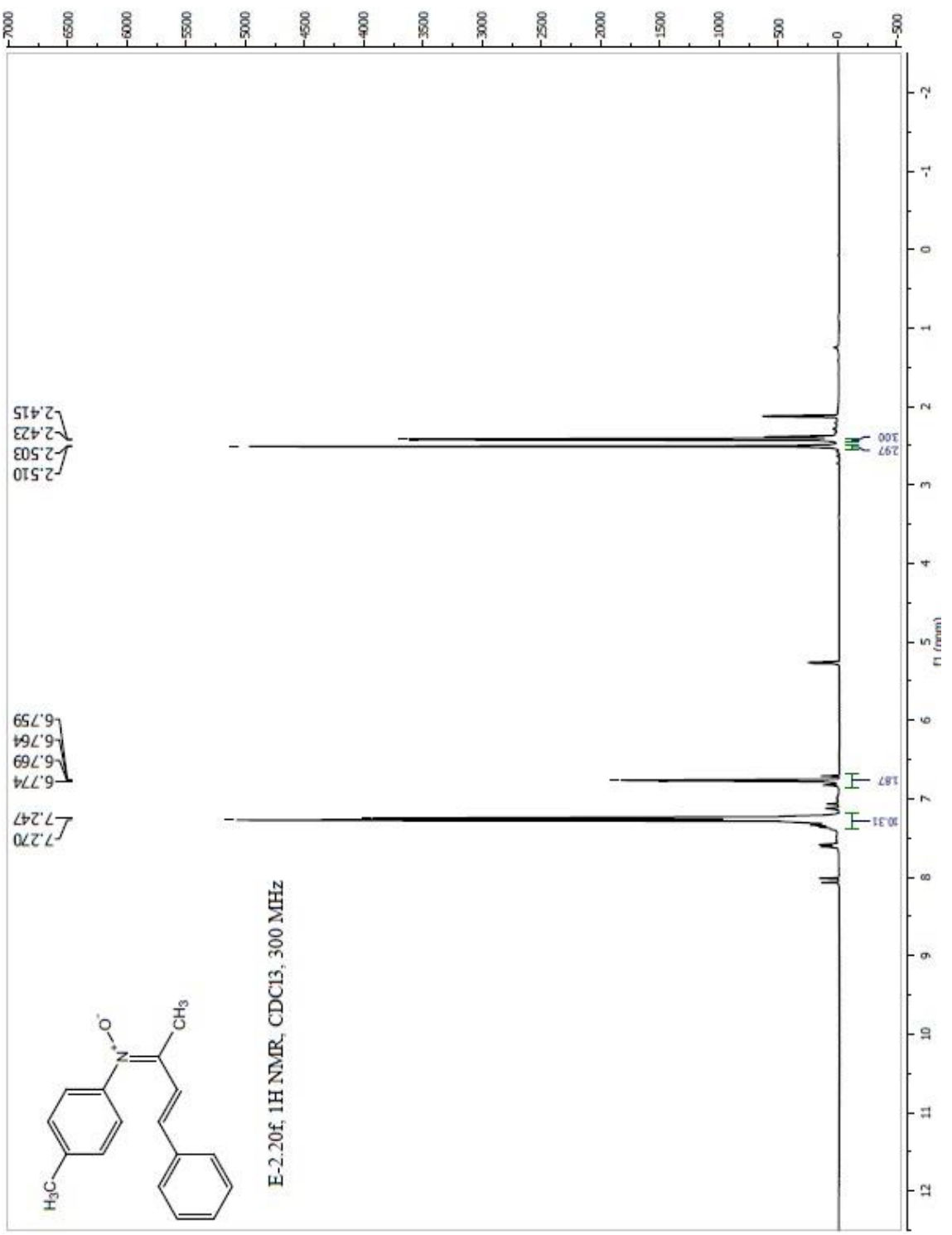

E-2.20c, 13C NMR, CDCl3, 75 MHz
151.745
145.728
136.253
132.516
129.696
129.600
129.583
129.099
129.005
128.969
127.063
124.656
120.752
27.957
26.666
23.255
14.199
f1 (ppm)

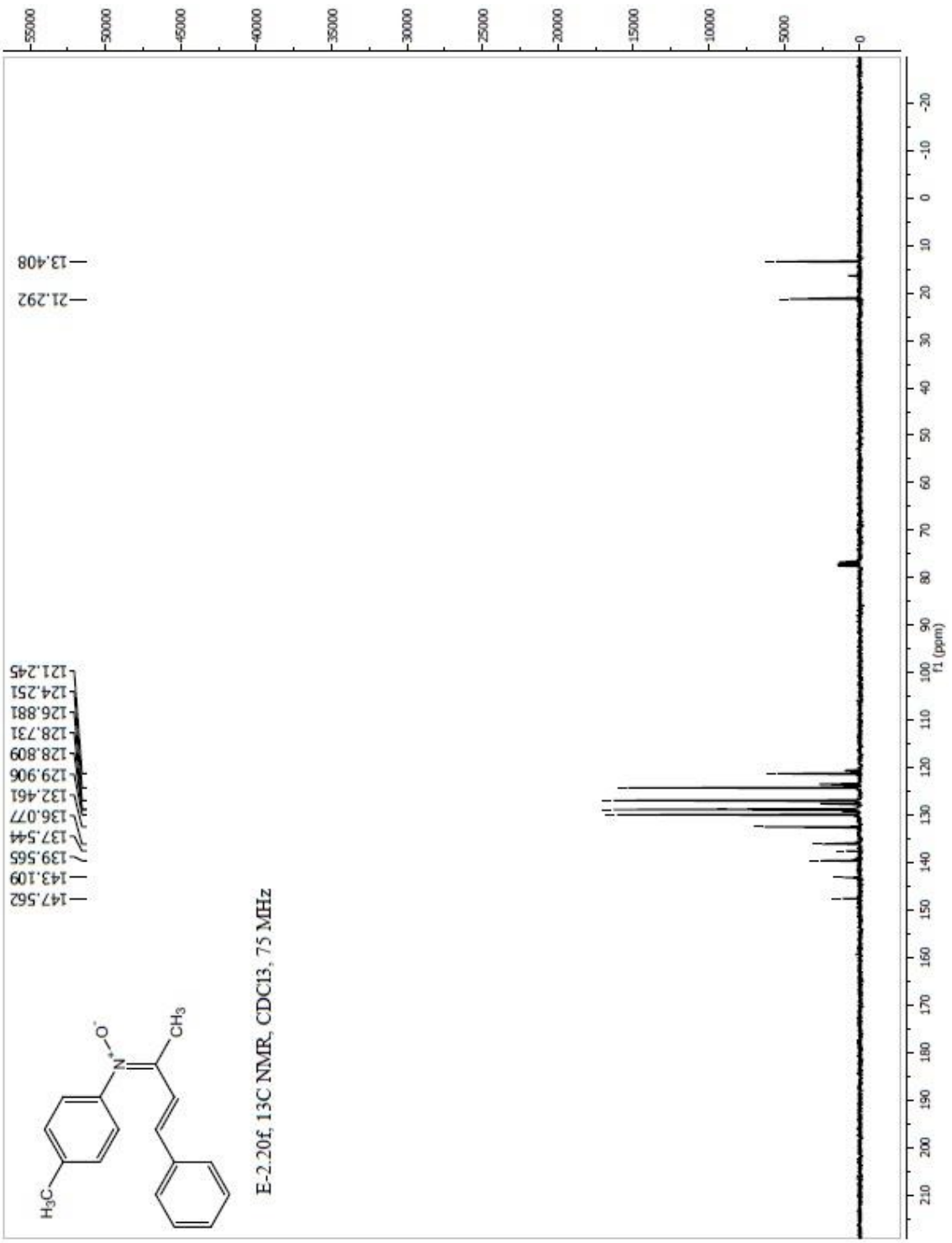

2.20d, 1H NMR, CDCl3, 300 MHz
8.205
8.150
7.523
7.518
7.182
6.737
6.683
1.00
15.74
3.39
1.07
f1 (ppm)

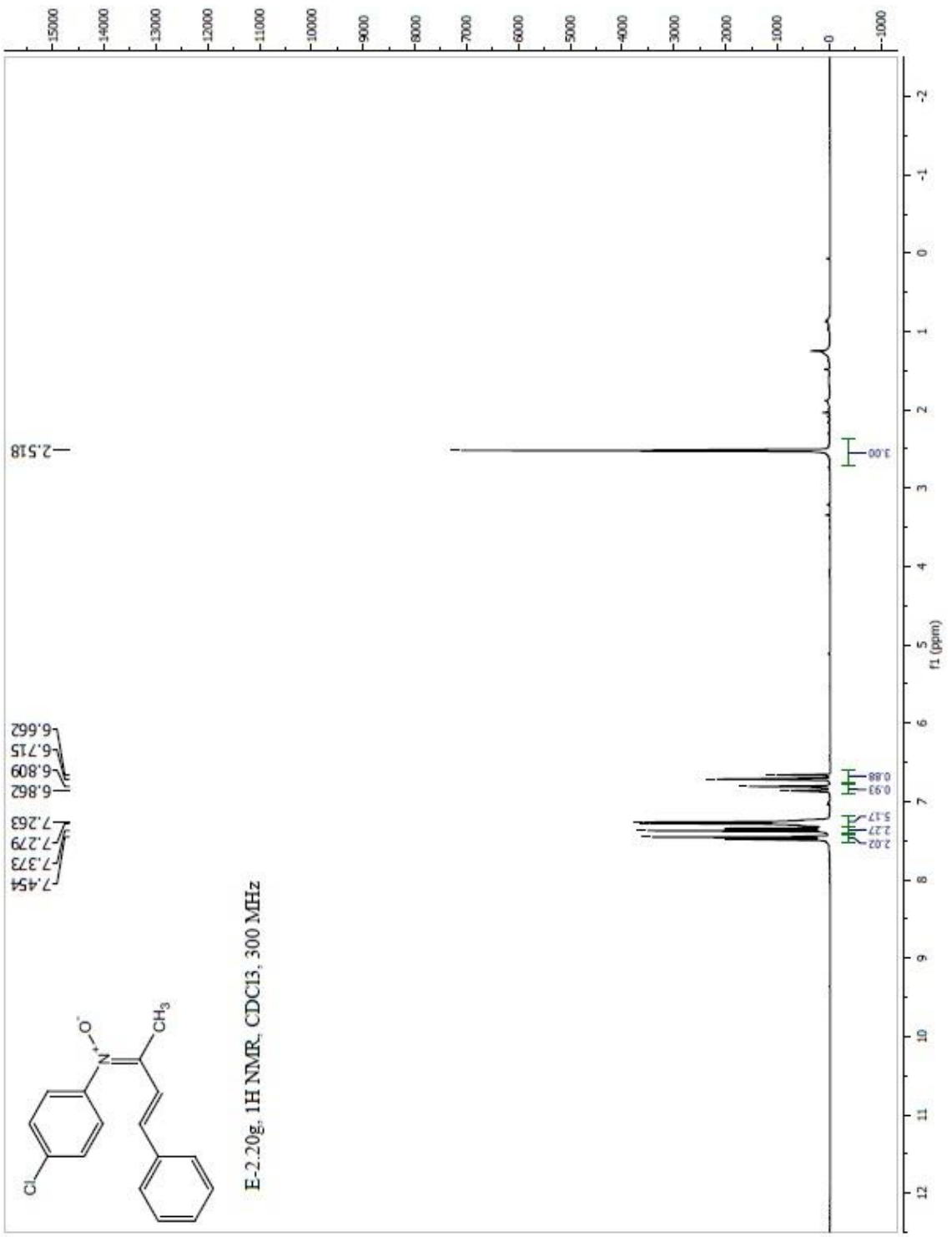

2.20d, 13C NMR, CDCl3, 75 MHz
150.207
147.372
141.178
136.591
133.085
131.147
130.392
129.814
129.734
129.670
129.300
129.120
129.018
128.907
128.754
128.010
127.240
125.214
122.285
f1 (ppm)

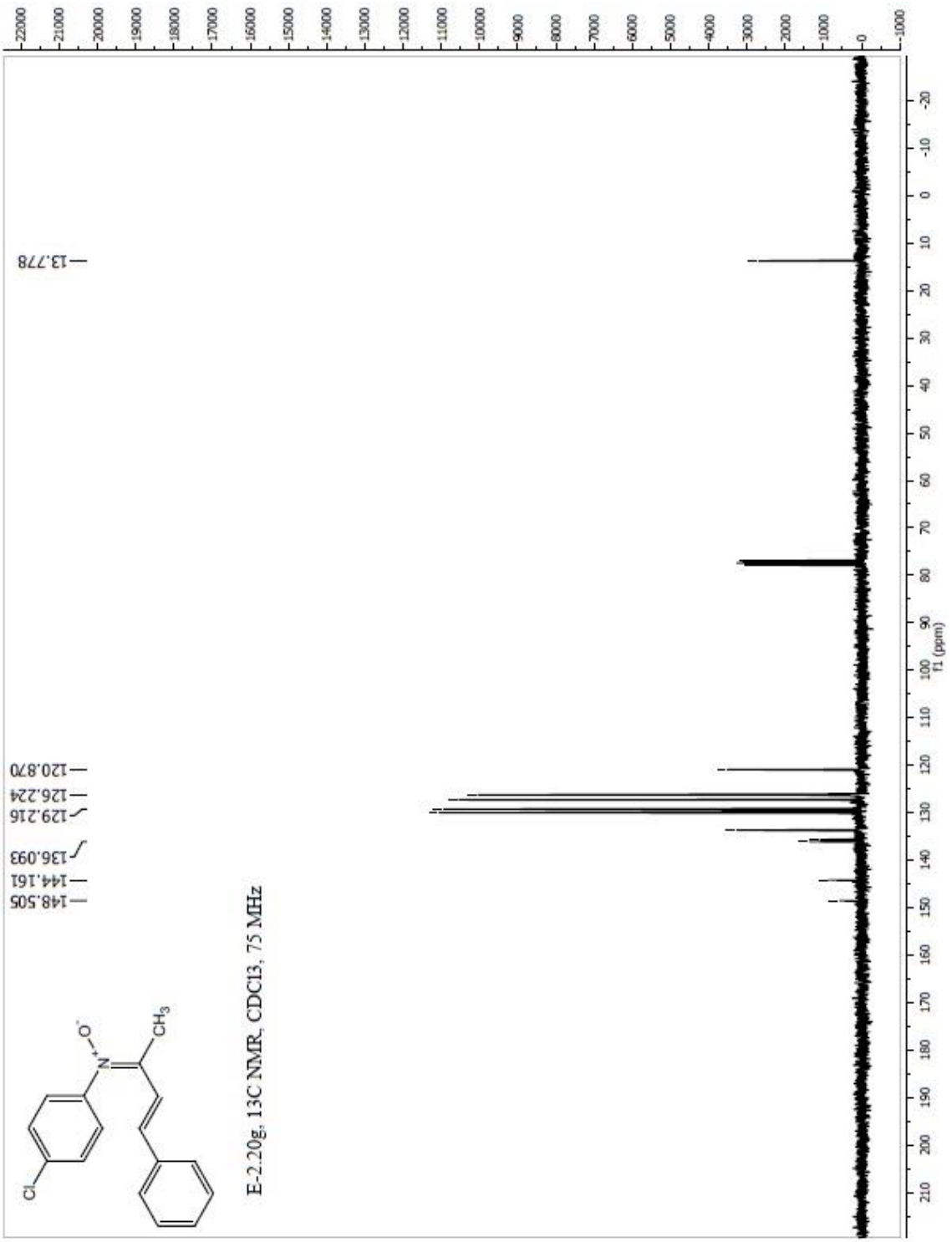

E-2.20e, 1H NMR, CDCl3, 300 MHz
2.536
2.249
7.343
7.337
7.244
7.210
6.844
6.791
6.542
6.489
3.08
3.00
0.94
0.97
10.16
f1 (ppm)

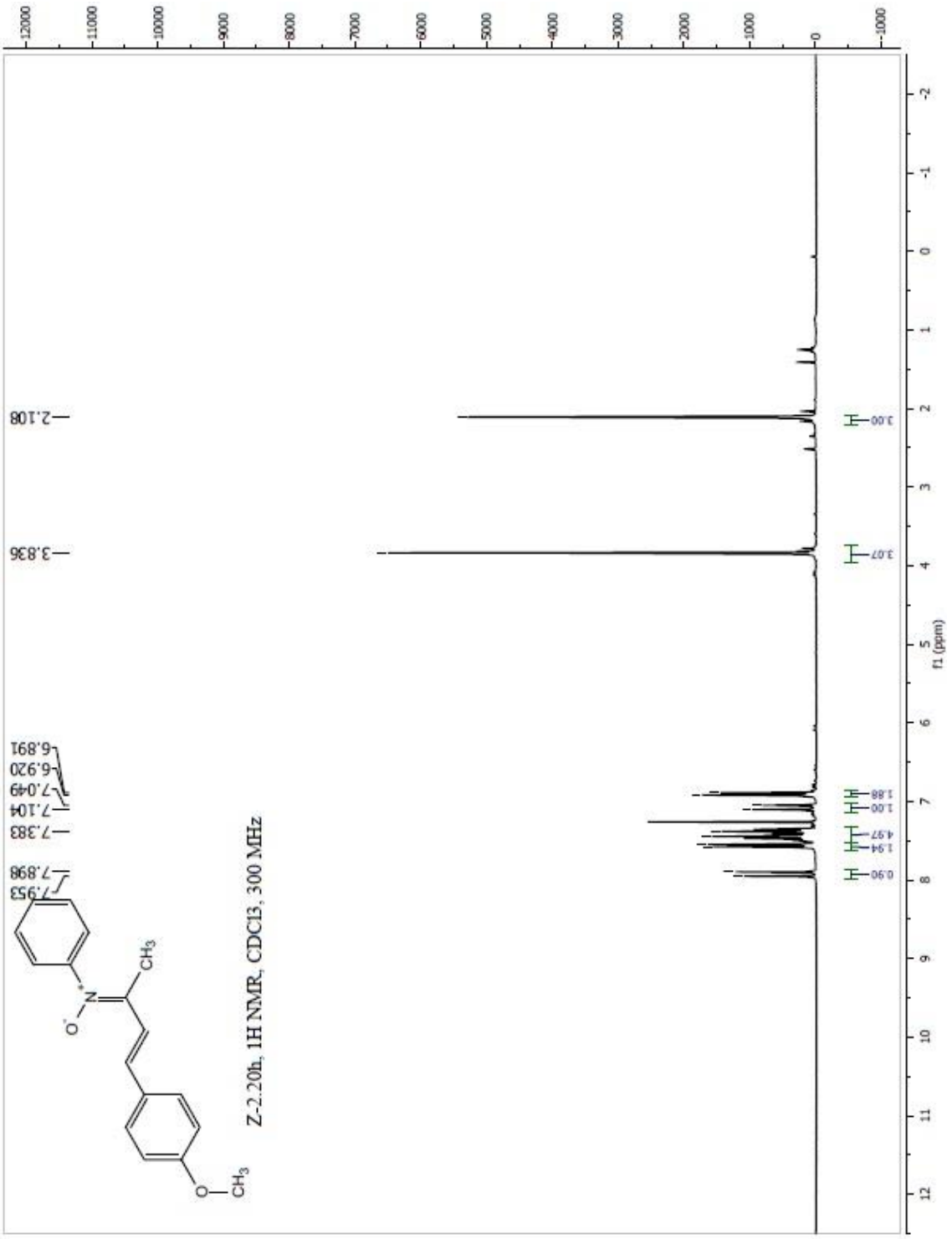

E-2.20e, 13C, NMR, CDCl3, 75 MHz
CH3
CH3
N
O
148.282
144.635
136.237
133.363
132.294
131.732
129.644
129.153
129.124
127.941
127.473
127.399
127.165
124.632
120.582
16.964
12.939
f1 (ppm)

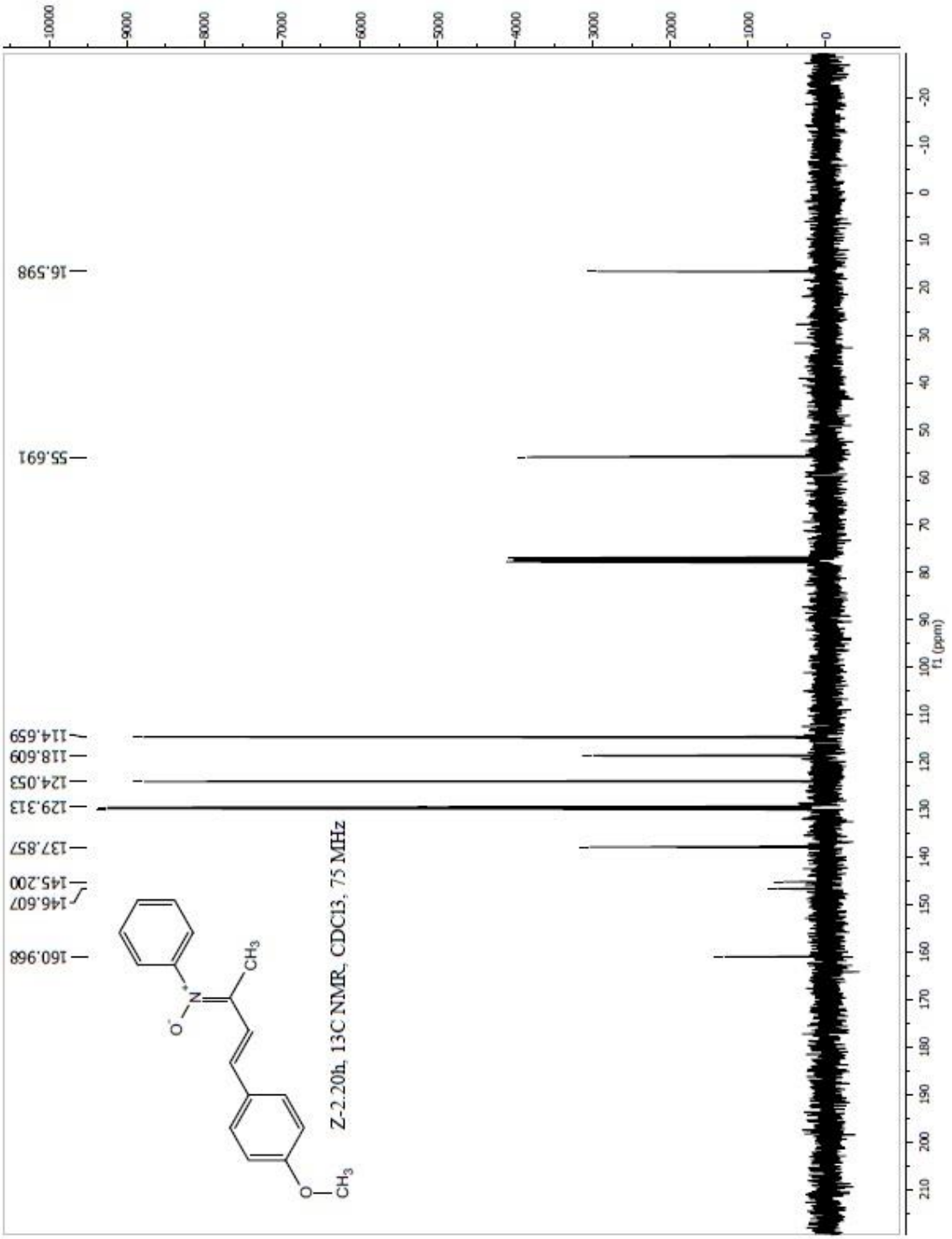

E-2.20f, 1H NMR, CDCl3, 300 MHz
7.270
7.247
6.774
6.769
6.764
6.759
2.510
2.503
2.423
2.415
30.31
1.87
3.00
2.97
f1 (ppm)

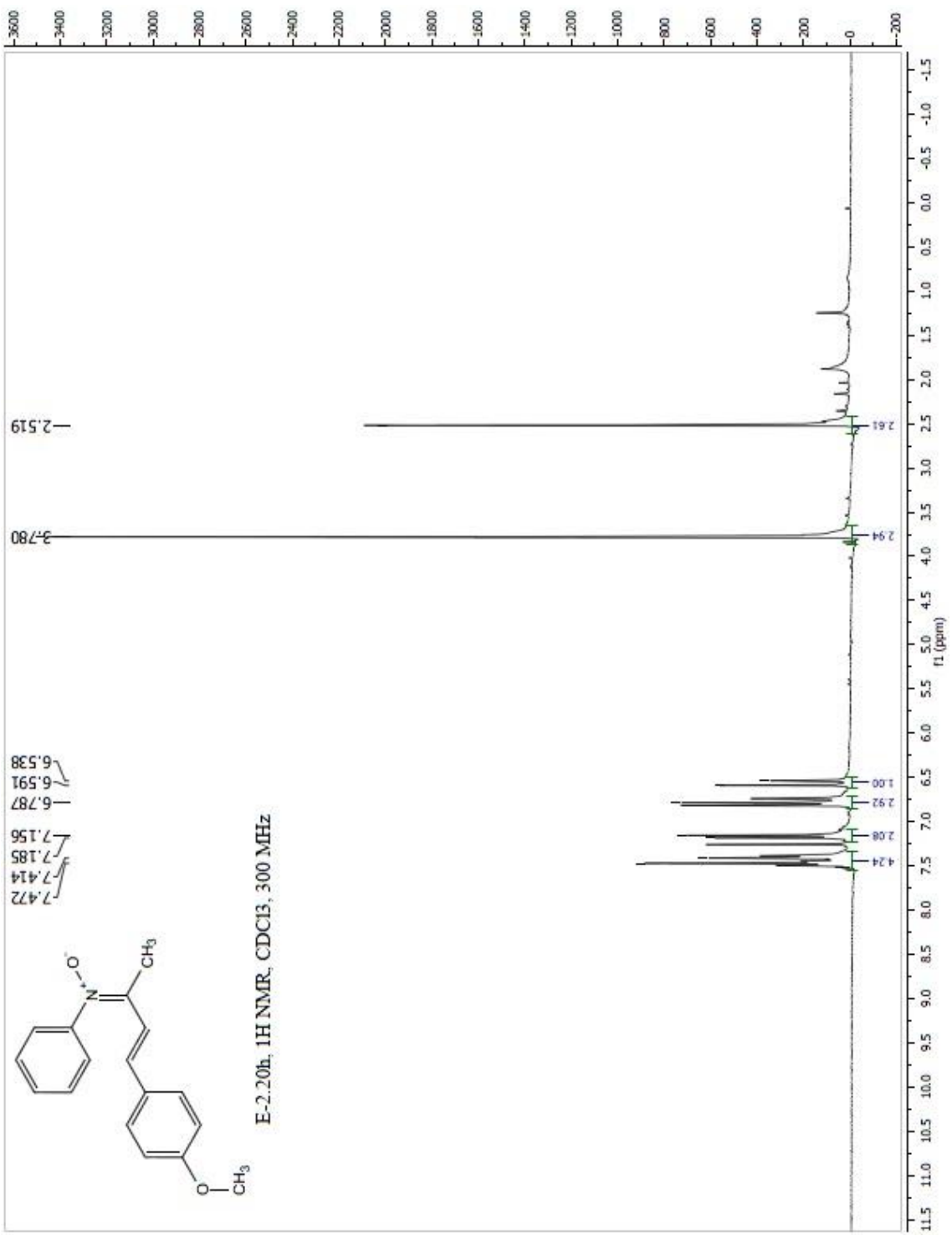

147.562
143.109
139.565
137.544
136.077
132.461
129.906
128.809
128.731
126.881
124.251
121.245
21.292
13.408
f1 (ppm)
E-2.20f, 13C NMR, CDCl3, 75 MHz

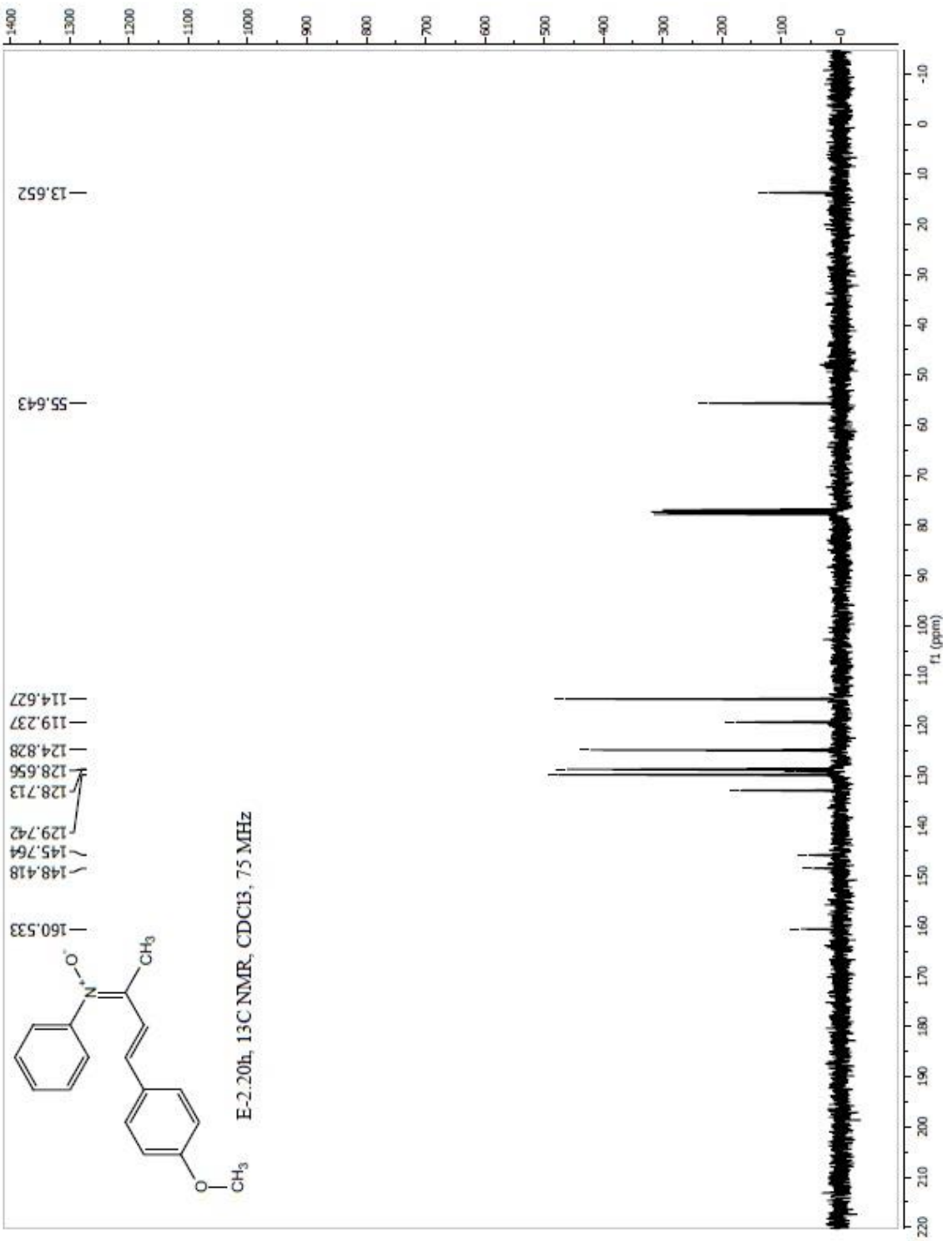

E-2.20g, 1H NMR, CDCl3, 300 MHz
2.518
7.454
7.373
7.279
7.263
6.862
6.809
6.715
6.662
3.00
0.88
0.93
5.17
2.27
2.02
f1 (ppm)

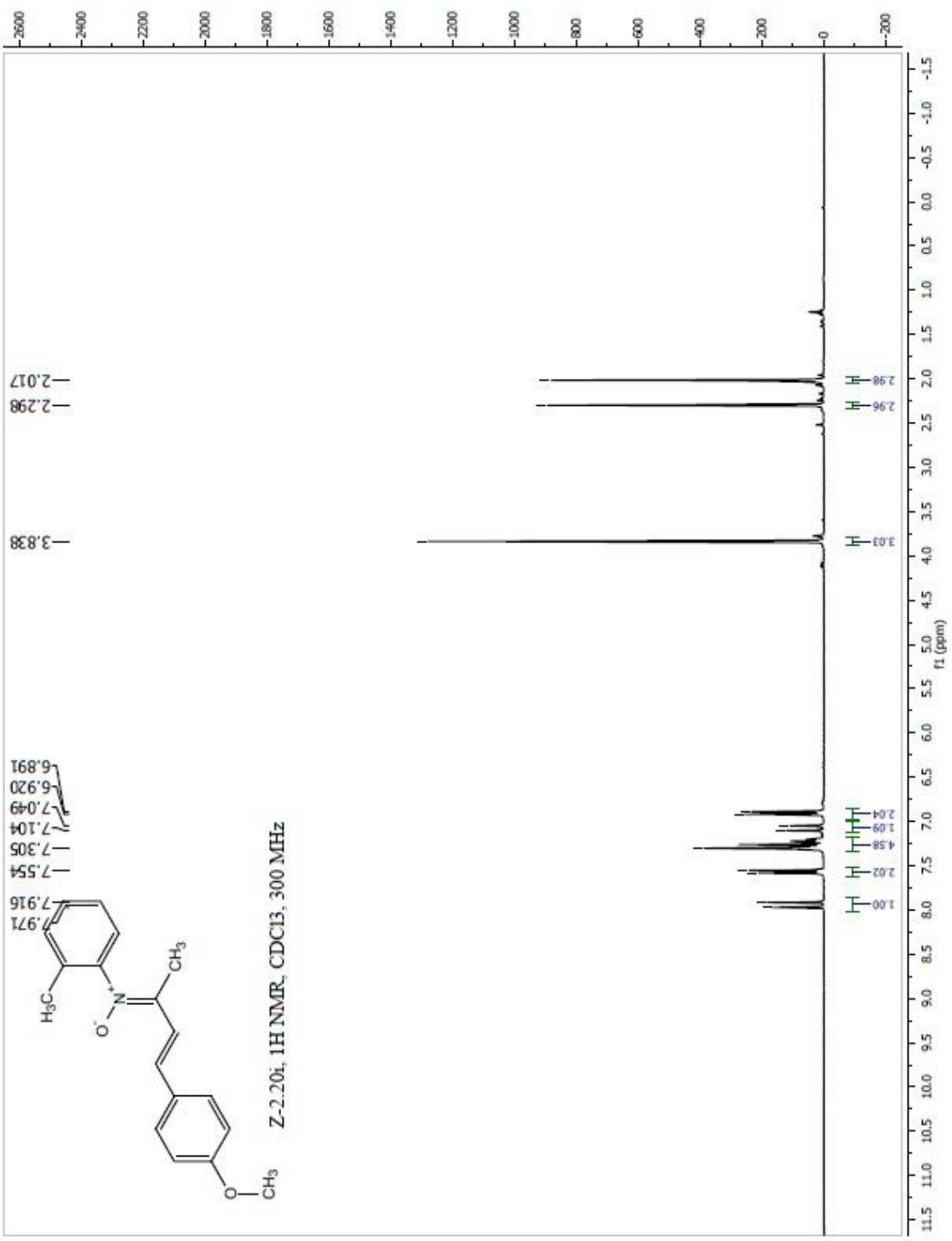

E-2.20g, 13C NMR, CDCl3, 75 MHz
148.505
144.161
136.093
129.216
126.224
120.870
13.778
f1 (ppm)

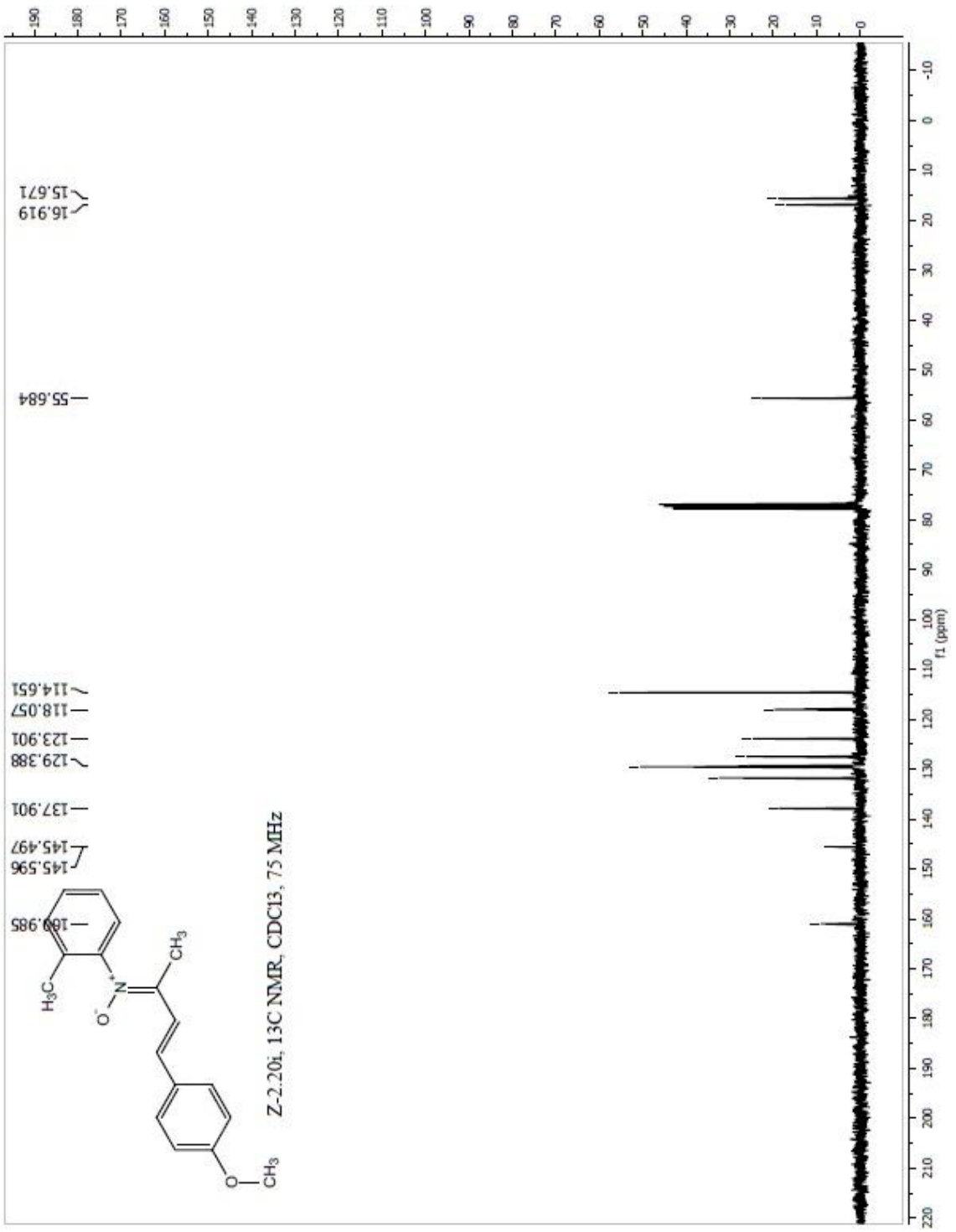

Z-2.20b, 1H NMR, CDCl3, 300 MHz
2.108
3.836
6.891
6.920
7.049
7.104
7.383
7.898
7.953
3.00
3.07
1.88
1.00
1.94
4.97
0.90
f1 (ppm)

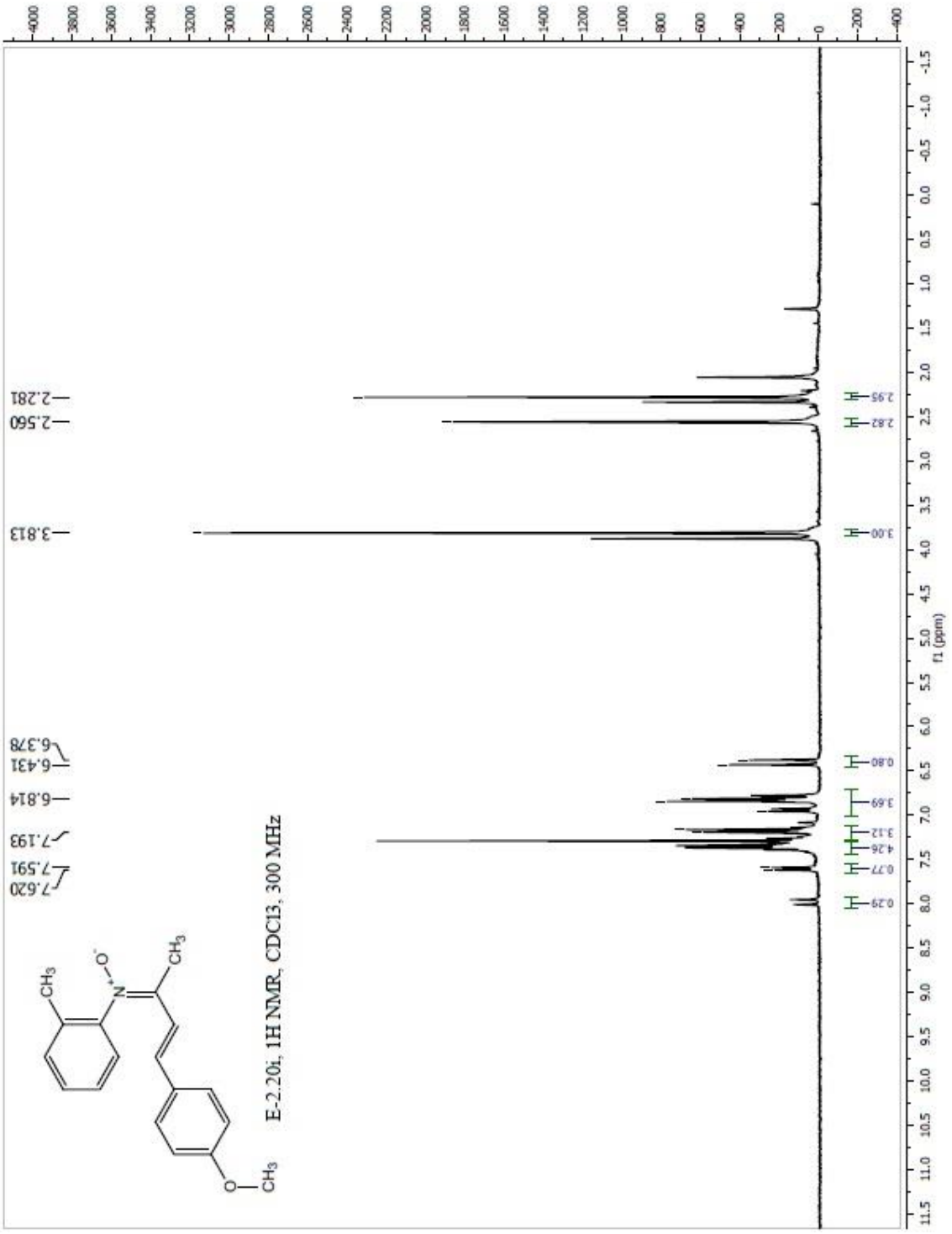

Z-2.20h, 13C NMR, CDCl3, 75 MHz
16.598
55.691
114.659
118.609
124.053
129.313
137.857
145.200
146.607
160.968
f1 (ppm)

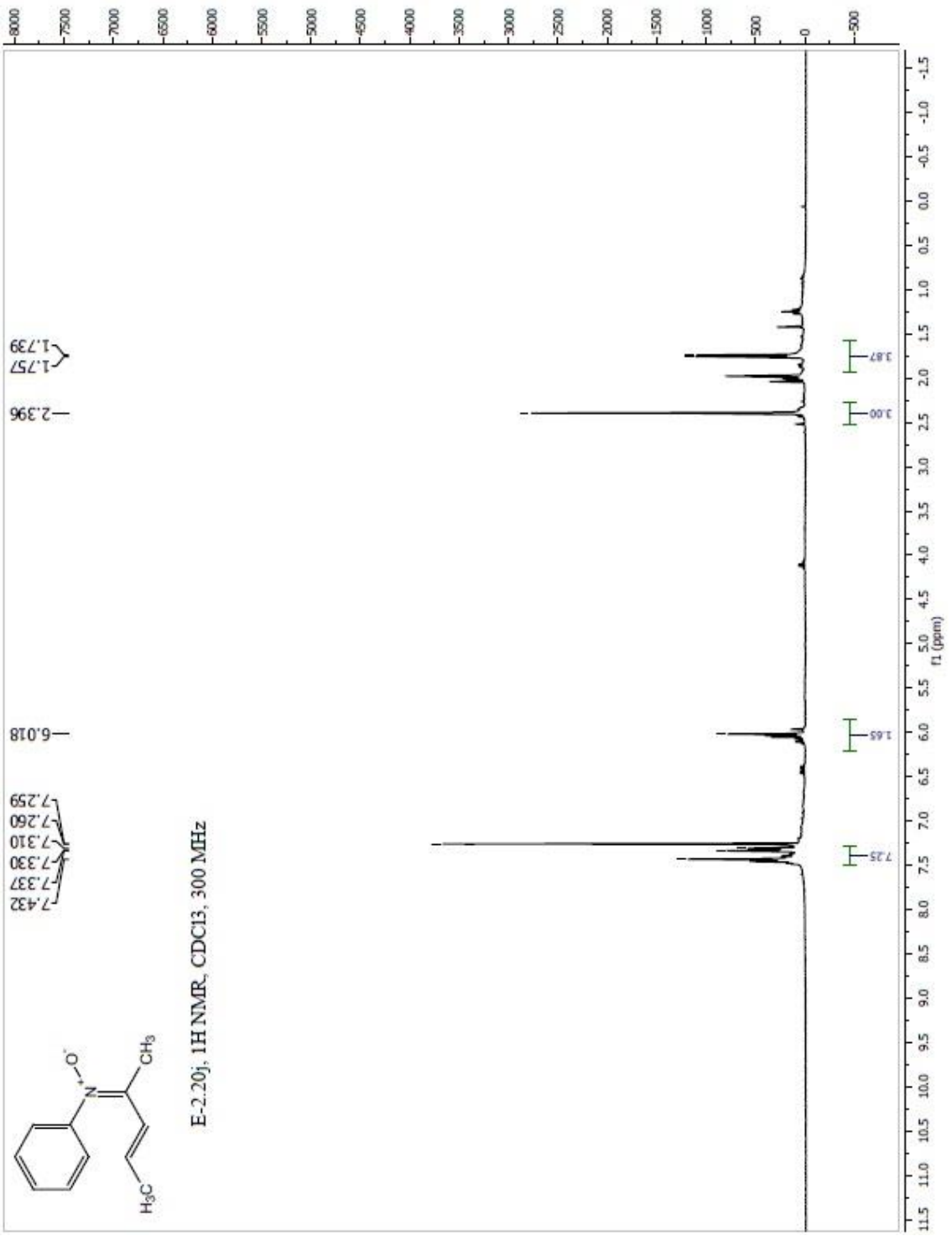

E-2.20h, 1H NMR, CDCl3, 300 MHz
2.519
3.780
6.538
6.591
6.787
7.156
7.185
7.414
7.472
2.61
2.94
1.00
2.92
2.08
4.24
f1 (ppm)

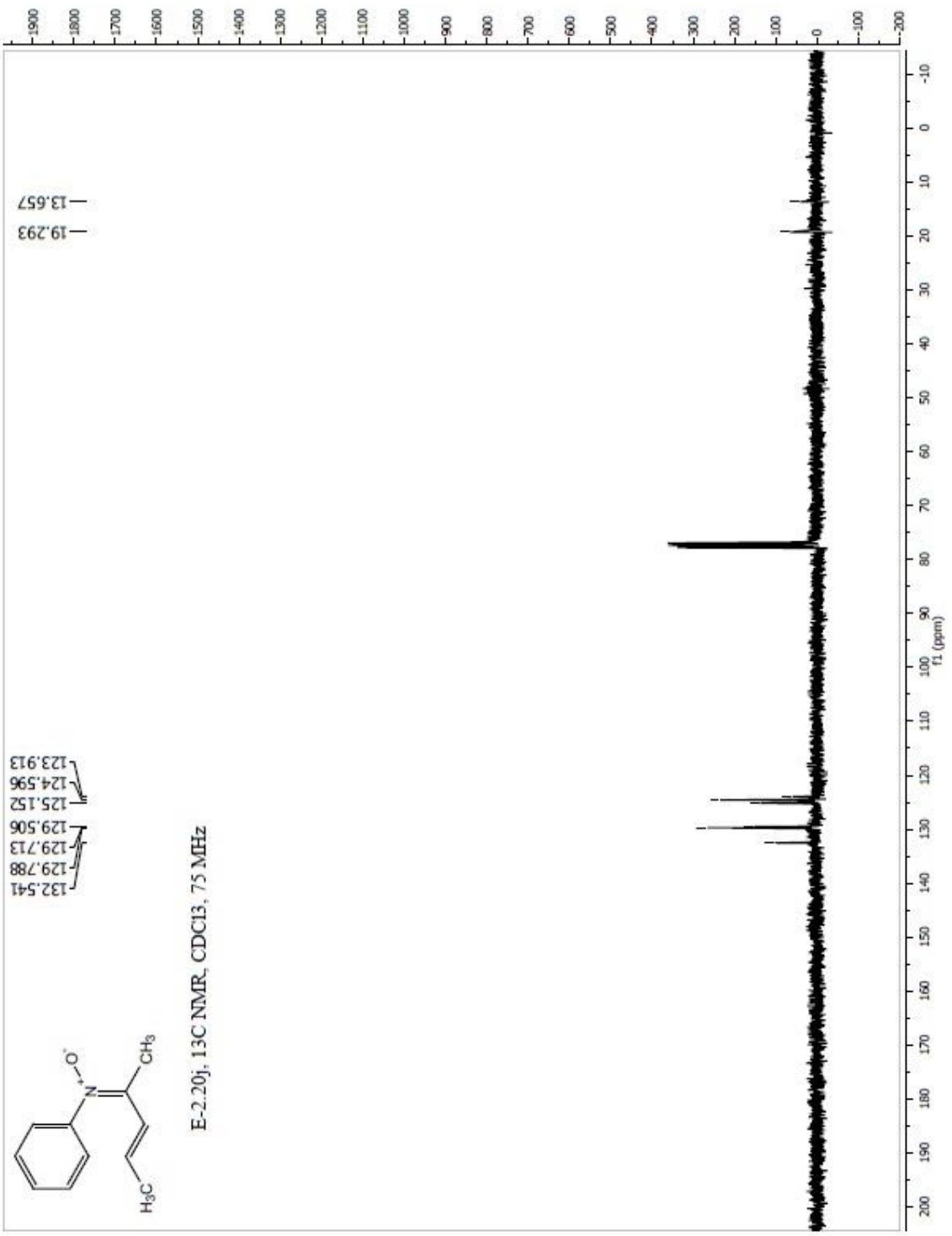

E-2.20h, 13C NMR, CDCl3, 75 MHz
160.533
148.418
145.764
129.742
128.713
128.656
124.828
119.237
114.627
55.643
13.652
f1 (ppm)

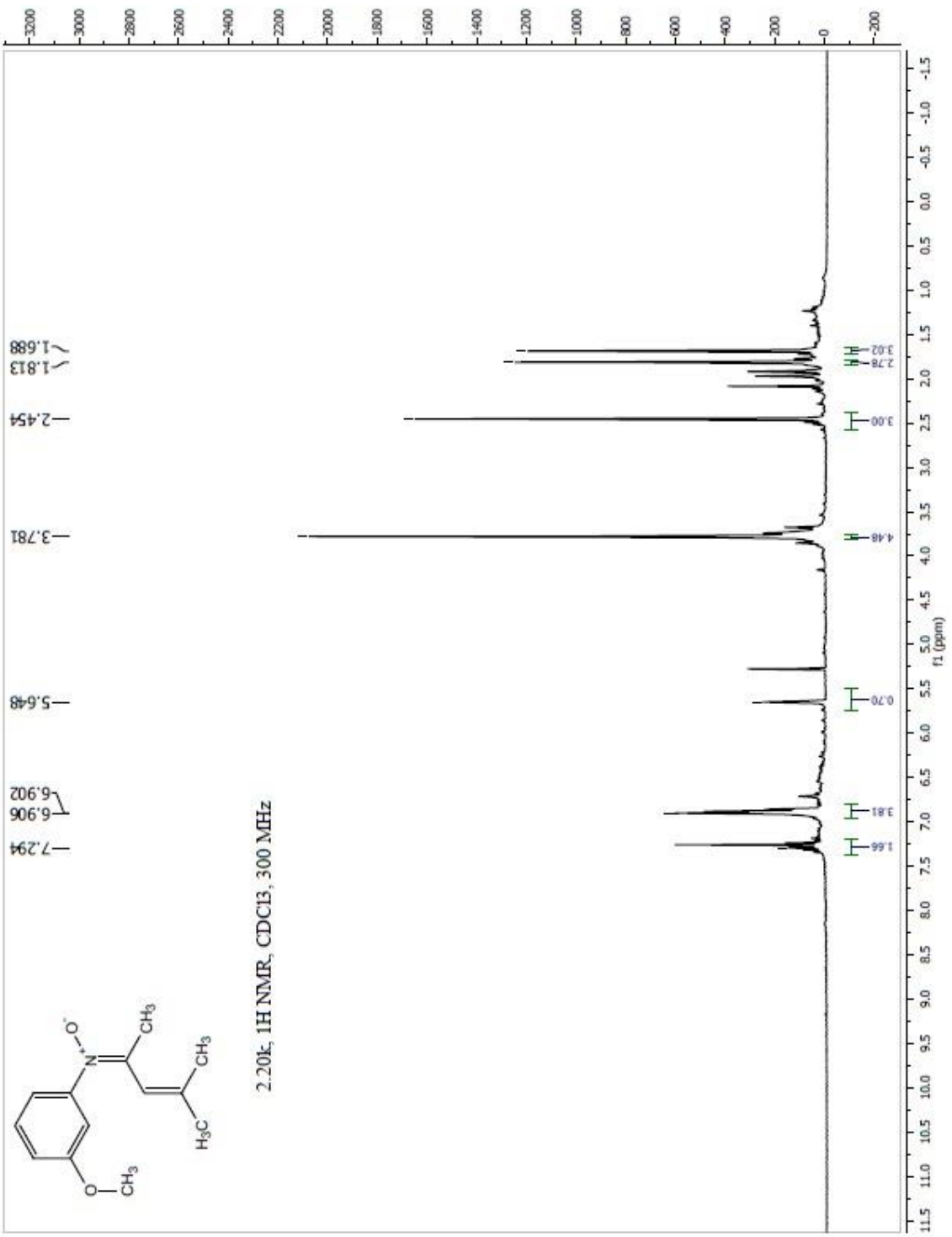

Z-2.20i, 1H NMR, CDCl3, 300 MHz
7.971
7.916
7.554
7.305
7.104
7.049
6.920
6.891
3.838
2.298
2.017
f1 (ppm)

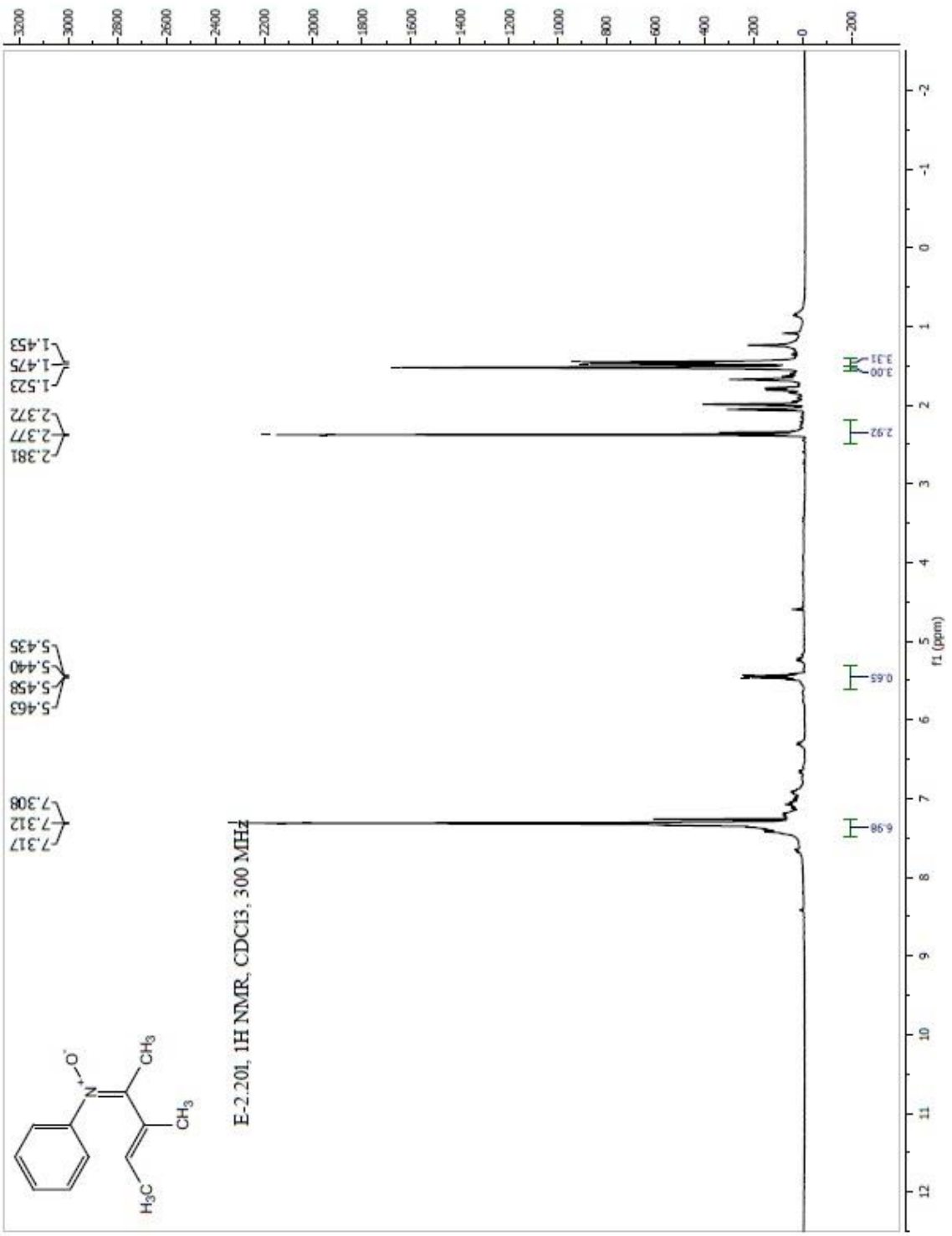

15.671
16.919
55.684
114.651
118.057
123.901
129.388
137.901
145.497
145.596
159.985
Z-2.20i, 13C NMR, CDCl3, 75 MHz
f1 (ppm)


E-2.20i, 1H NMR, CDCl3, 300 MHz
7.620
7.591
7.193
6.814
6.431
6.378
3.813
2.560
2.281
0.29
0.77
4.26
3.12
3.69
0.80
3.00
2.82
2.95
f1 (ppm)


E-2.20j, 1H NMR, CDCl3, 300 MHz
1.739
1.757
2.396
6.018
7.259
7.260
7.310
7.330
7.337
7.432
1.87
3.00
1.65
7.25
f1 (ppm)


E-2.20j, 13C NMR, CDCl3, 75 MHz
13.657
19.293
123.913
124.596
125.152
129.506
129.713
129.788
132.541
f1 (ppm)

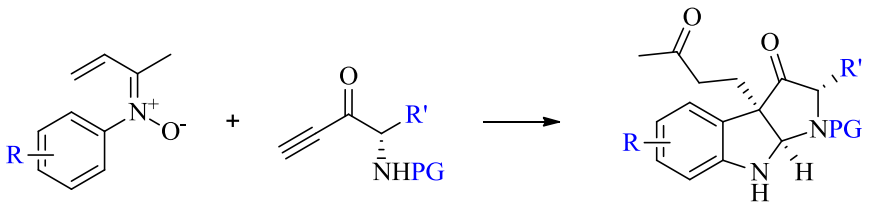

2.20k, 1H NMR, CDCl3, 300 MHz
7.294
6.906
6.902
5.648
3.781
2.454
1.813
1.688
3.02
2.78
3.00
4.48
0.70
3.81
1.66
f1 (ppm)


E-2.201, 1H NMR, CDCl3, 300 MHz
7.317
7.312
7.308
5.463
5.458
5.440
5.435
2.381
2.377
2.372
1.523
1.475
1.453
6.98
0.65
2.92
3.00
3.31
f1 (ppm)

APPENDIX D

Note: Due to the lack of reaching synthetically useful yields, characterization was determined off of ^{1}H NMR comparing to the spectra obtained from the crystal structure.

In an effort to determine if the low yields during optimization were substrate specific, a range of nitrones and acetylenes were tested with 3 equivalencies of nitrone to 1 equivalent of acetylene at 60 ^{o}C (Table C-1). Nitrone **2.7g** was typically used due to its stability as compared to the other nitrones in optimization efforts. When **2.7g** or **2.7a** were reacted with **3.11a**, yields of 35% and 34% (Table C-1, entries 1 and 2) were obtained. Similarly, when **2.7i** or **2.7a** were reacted with **3.11e**, yields of 28% and 29% (Table C-1, entries 7 and 6) were obtained. These preliminary results suggest that



2.7 **3.11** **3.9**

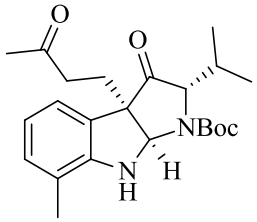
Entry	R		R'		PG	% Yield
1	2'-Me	**2.7g**	*i*-Pr	**3.11a**	Boc	**3.9a** 35%
2	H	**2.7a**	*i*-Pr	**3.11a**	Boc	**3.9b** 34%
3	2'-Me	**2.7g**	*i*-Pr	**3.11b**	Ac	**3.9c** 29%
4	2'-Me	**2.7g**	*i*-Pr	**3.11c**	Ts	**3.9d** 27%
5	2'-Me	**2.7g**	*i*-Pr	**3.11d**	$COCF_3$	**3.9e** 23%
6	H	**2.7a**	Me	**3.11e**	Boc	**3.9f** 29%
7	3'-Me	**2.7i**	Me	**3.11e**	Boc	**3.9g** 28%
8	H	**2.7a**	Isobutyl	**3.11f**	Boc	**3.9h** 43%
9	H	**2.7a**	H	**3.11g**	Boc	**3.9i** 25%

Table C-1 Scope of pyrroloindoline **3.9**

substitution on the phenyl ring of the nitrone plays an insignificant role in the reaction. The acetylene seems to play an important role. The protecting group also seems to have an impact. Acetylenes **3.11a** and **3.11b** yielded similar results with a slight decrease with the use of **3.11b** (35% and 29% yield, Table C-1, entries 1 and 3). The tosyl and trifluoroacetyl protecting groups resulted in more complex reactions with approximate yields of 27% and 23% (Table C-1, entries 4 and 5). The larger the R group in **3.11**, the higher the yield. As R increased from hydrogen (**3.11g**) to a methyl (**3.11e**) to *iso*-propyl (**3.11a**) to isobutyl (**3.11f**), the respective yields increased from 25% to 29% to 34% and to 43% (Table C-1, entries 9, 6, 2, and 8).

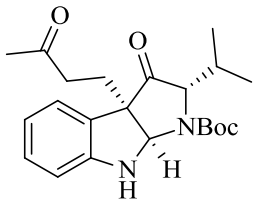
Spectral data for compounds

Note: spectra typically contain degradation products believed to originate from the indolenine formation. As such, full characterization was not always performed since we were not able to complete a synthetically useful transformation (low yields).

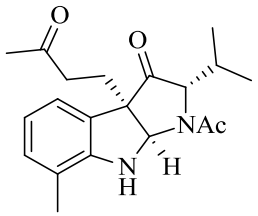


(2S,3aR,8aR)-tert-butyl 2-isopropyl-7-methyl-3-oxo-3a-(3-oxobutyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (**3.9a**). Yield = 35%. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.98 (dd, *J* = 7.5, 2.2 Hz, 2H), 6.71 (t, *J* = 7.5 Hz, 1H), 5.83 (s, 1H), 5.41 (s, 1H), 3.80 (d, *J* = 3.3 Hz, 1H), 2.47 – 2.17 (m, 4H), 2.14 (s, 3H), 2.02 (s,

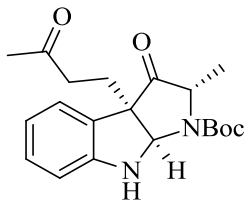
3H), 2.00 - 1.91 (m, 1H), 1.60 (s, 3H), 1.44 (s, 6H), 1.09 (d, *J* = 7.0 Hz, 3H), 0.91 (d, *J* = 7.1 Hz, 3H).



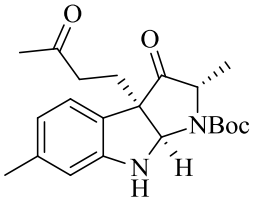
(2S,3aR,8aR)-tert-butyl 2-isopropyl-3-oxo-3a-(3-oxobutyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (**3.9b**). Yield = 34%. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.13 (d, *J* = 7.4 Hz, 2H), 6.77 (t, *J* = 7.5 Hz, 1H), 6.66 (d, *J* = 7.8 Hz, 1H), 5.90 (s, 1H), 5.39 (s, 1H), 3.82 (d, *J* = 3.4 Hz, 1H), 2.43 – 2.20 (m, 4H), 2.02 (s, 3H), 1.99 – 1.90 (m, 1H), 1.44 (s, 9H), 1.10 (d, *J* = 7.1 Hz, 3H), 0.90 (d, *J* = 7.0 Hz, 3H). HRMS (ESI, m/z): $[M]^+$ calc.: 387.2284; found: 387.2280.



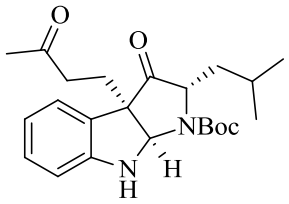
(2S,3aR,8aR)-1-acetyl-2-isopropyl-7-methyl-3a-(3-oxobutyl)-1,2,8,8a-tetrahydropyrrolo[2,3-b]indol-3(3aH)-one (**3.9c**). Yield = 29%. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.01 – 6.94 (m, 2H), 6.70 (t, *J* = 7.5 Hz, 1H), 5.94 (s, 1H), 5.56 (s, 1H), 3.86 (d, *J* = 3.7 Hz, 1H), 2.37 – 2.23 (m, 4H), 2.12 (s, 3H), 2.03 (s, 3H), 2.01 (s, 3H), 1.17 (d, *J* = 7.0 Hz, 3H), 0.94 (d, *J* = 6.9 Hz, 3H).



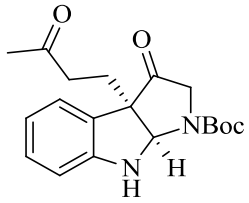
(2S,3aR,8aR)-tert-butyl 2-methyl-3-oxo-3a-(3-oxobutyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (**3.9f**). Yield = 29%. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.18 – 7.09 (m, 2H), 6.76 (t, *J* = 7.5 Hz, 1H), 6.65 (d, *J* = 7.7 Hz, 1H), 5.64 (s, 1H), 5.46 (s, 1H), 3.90 (q, *J* = 6.8Hz, 1H), 2.43 – 2.20 (m, 4H), 2.06 (s, 3H), 1.48 (s, 9H), 1.39 (d, *J* = 6.8 Hz, 3H). HRMS (ESI, m/z): $[M]^+$ calc.: 359.1971; found: 359.1967.



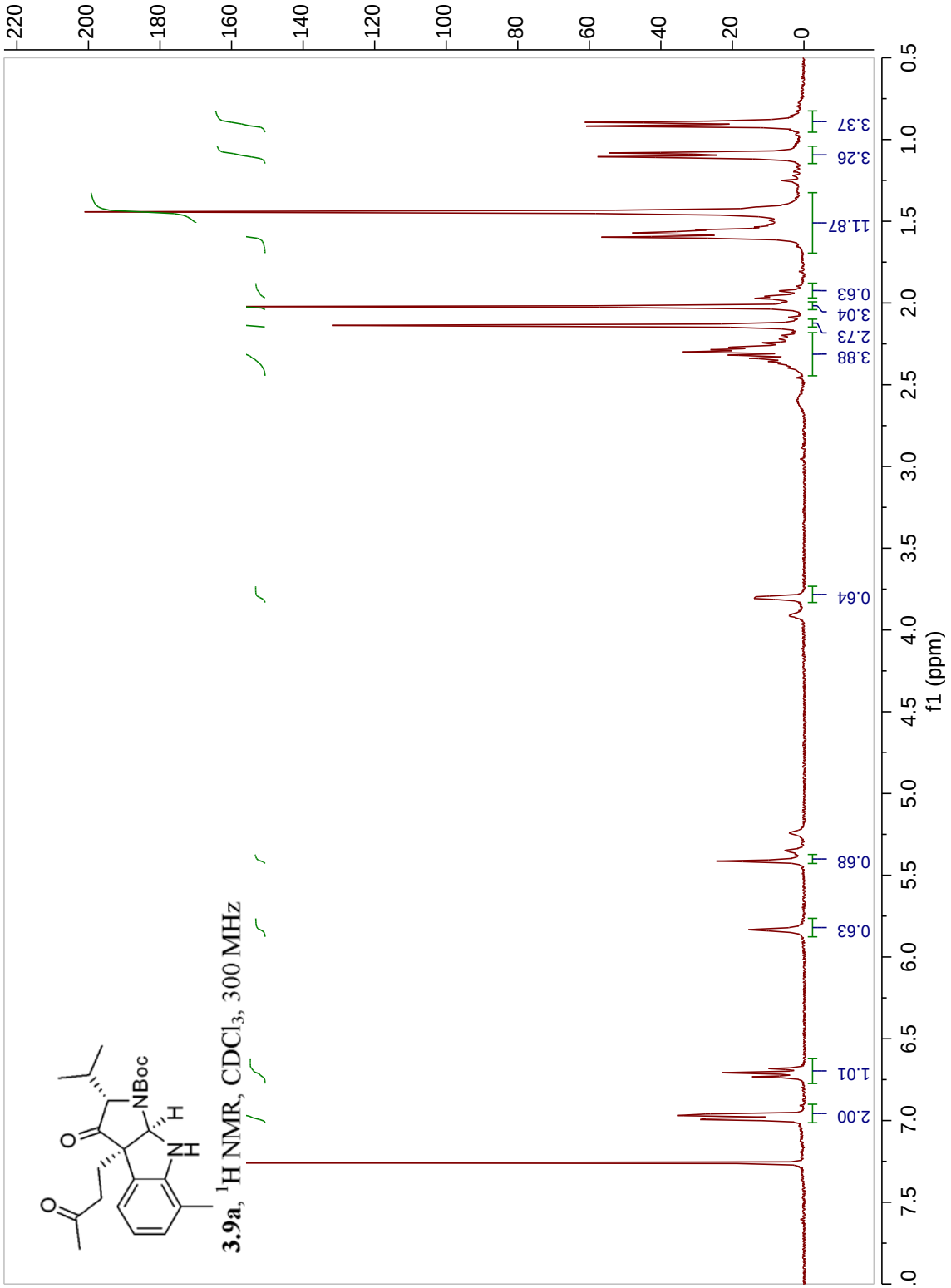
(2S,3aR,8aR)-tert-butyl 2,6-dimethyl-3-oxo-3a-(3-oxobutyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (**3.9g**). Yield = 28%. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.00 (d, *J* = 7.7 Hz, 1H), 6.59 (d, *J* = 7.7 Hz, 1H), 6.49 (s, 1H), 5.58 (s, 1H), 5.44 (s, 1H), 3.91 (q, *J* = 7.2 Hz, 1H), 2.43 – 2.16 (m, 4H), 2.27 (s, 3H), 2.06 (s, 3H), 1.47 (s, 9H), 1.38 (d, *J* = 7.0 Hz, 3H).

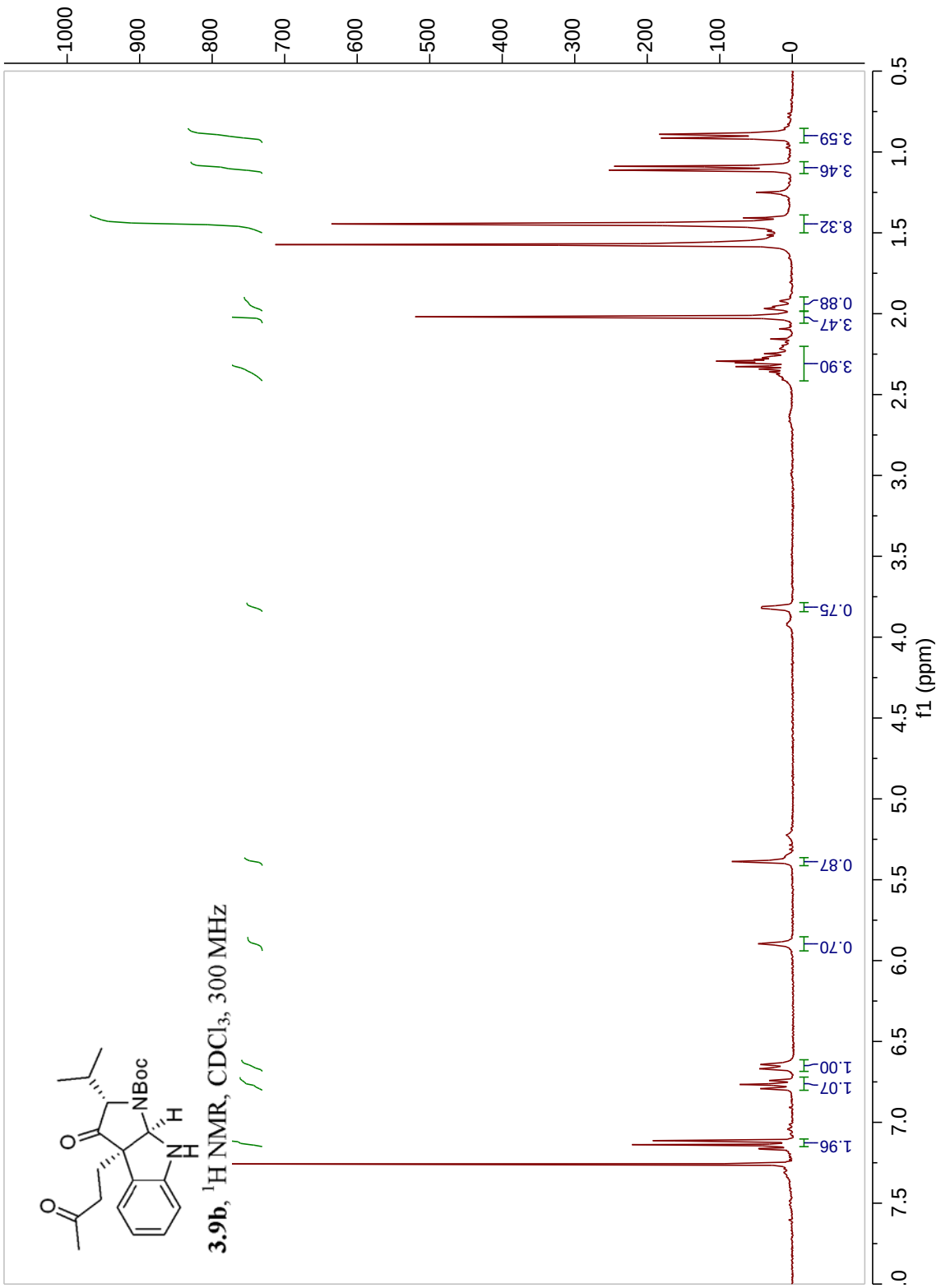


(2S,3aR,8aR)-tert-butyl 2-isobutyl-3-oxo-3a-(3-oxobutyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (**3.9h**). Yield = 43%. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.17 – 7.10 (m, 2H), 6.77 (t, *J* = 7.5 Hz, 1H), 6.66 (d, *J* = 7.9 Hz, 1H), 5.77 (s, 1H), 5.40 (s, 1H), 3.95 – 3.84 (m, 1H), 2.44 – 2.20 (m, 4H), 2.04 (s, 3H), 1.47 (s, 6H), 1.41 (s, 3H), 0.93 (d, *J* = 6.4 Hz, 3H), 0.88 (d, *J* = 6.4 Hz, 3H).

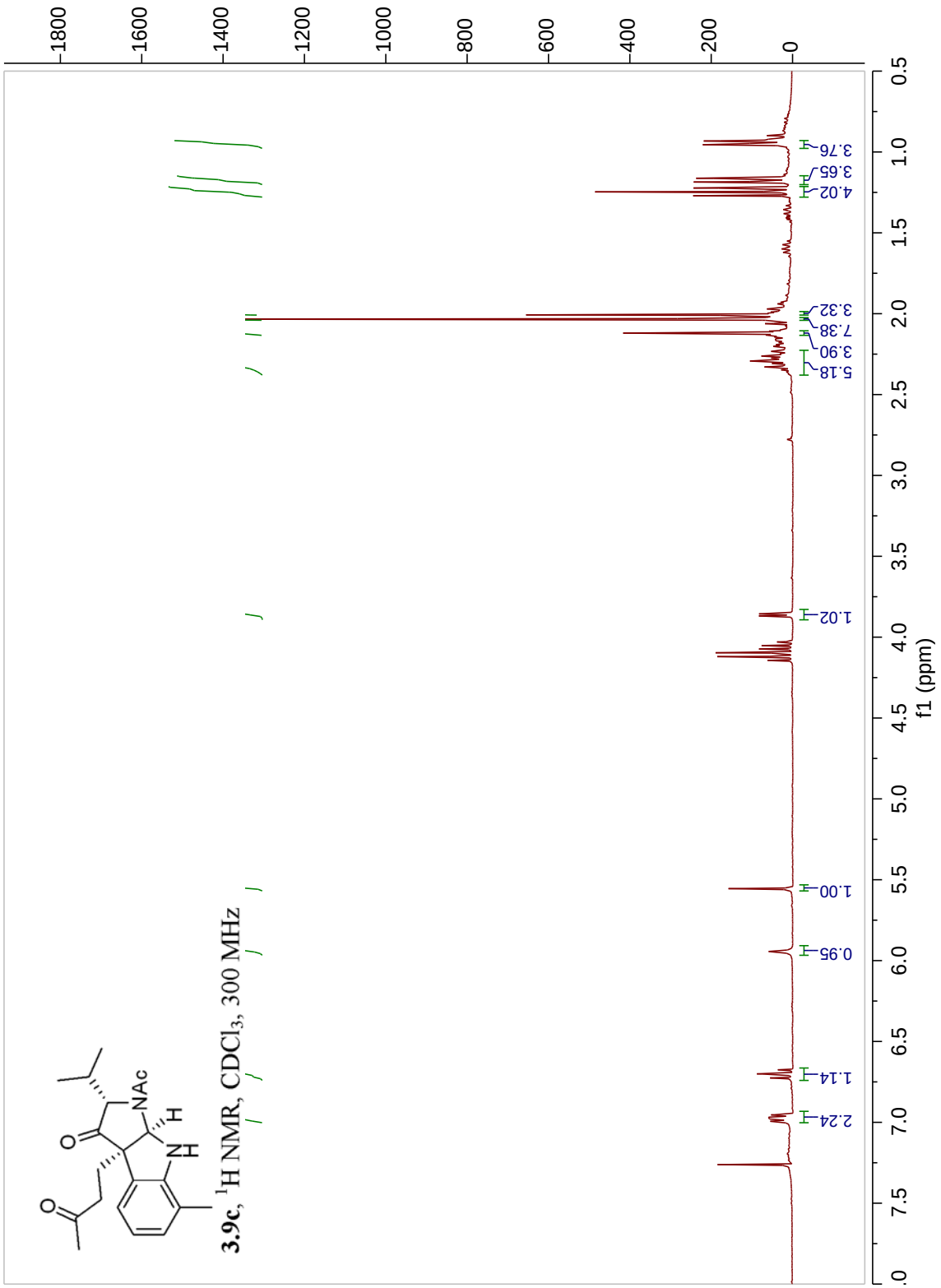


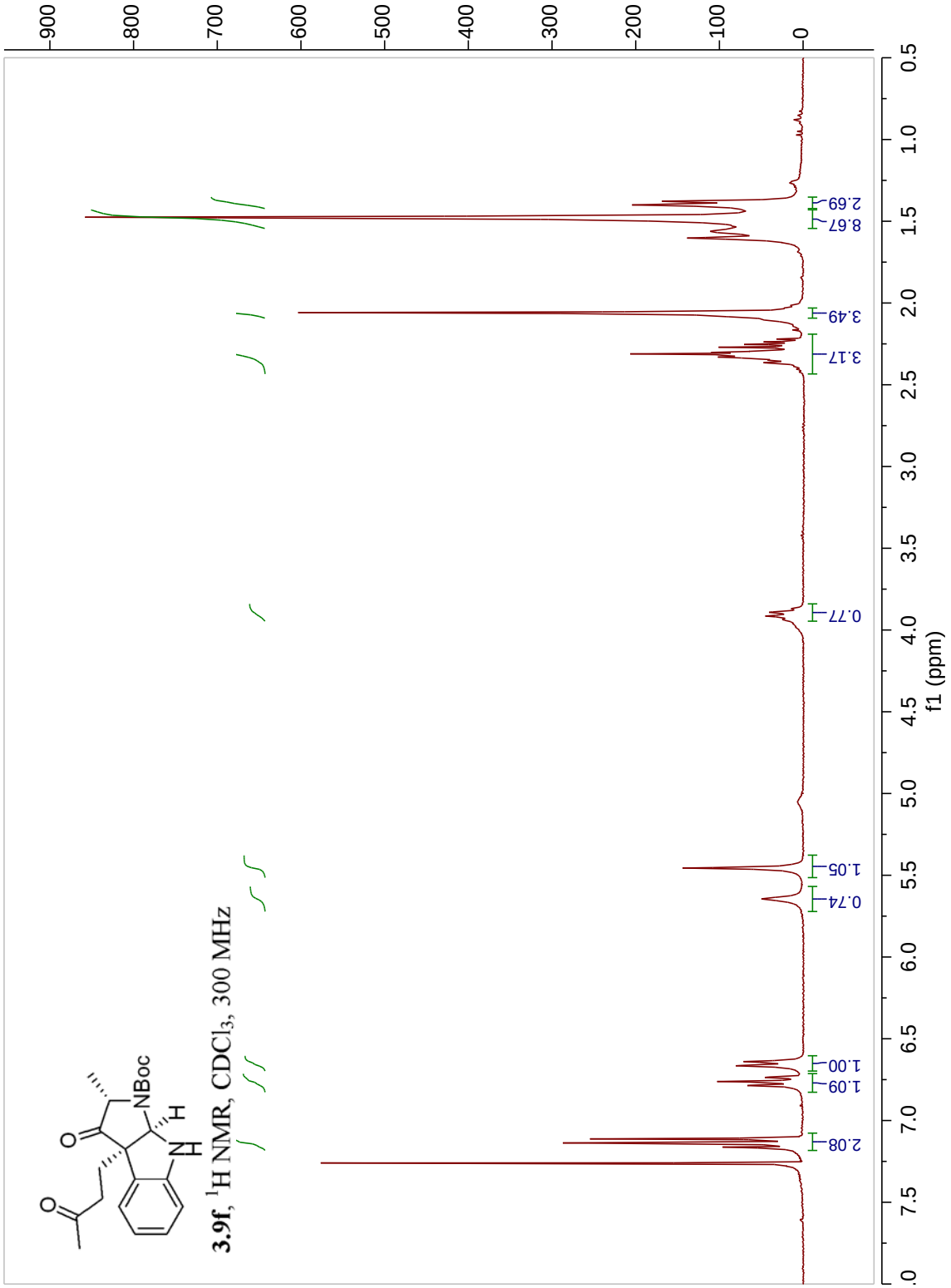
(3aR,8aR)-tert-butyl 3-oxo-3a-(3-oxobutyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (**3.9i**). Yield = 25%. ^{1}H NMR (300 MHz,$CDCl_3$) δ 7.19 – 7.03 (m, 2H), 6.76 (t, *J* = 7.1 Hz, 1H), 6.66 (d, *J* = 7.8 Hz, 1H), 5.50 (s, 1H), 3.87 – 3.73 (m, 2H), 2.40 – 2.20 (m, 3H), 2.17 – 2.09 (m, 1H), 2.05 (s, 3H), 1.47 (s, 9H).

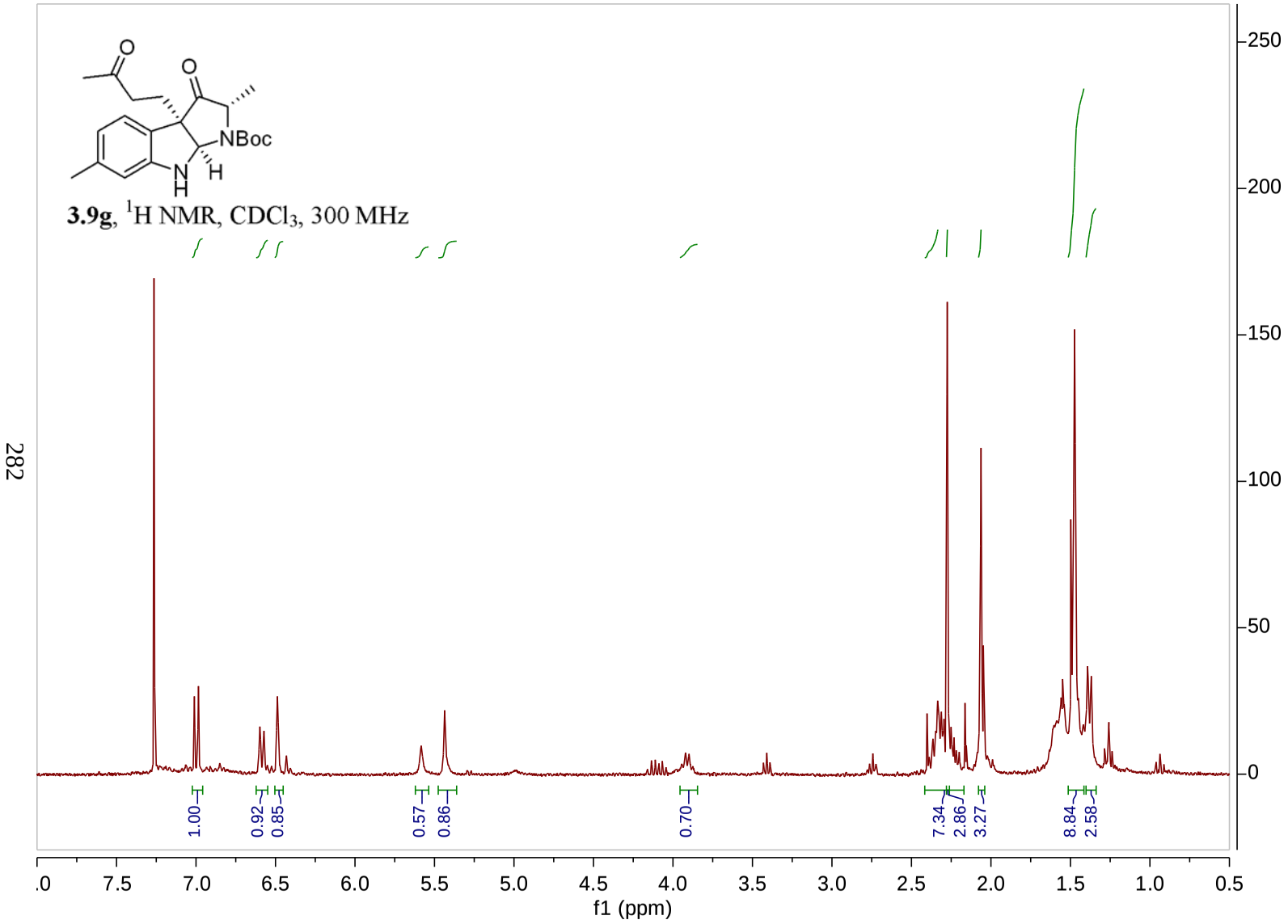

3.9a, ^{1}H NMR, $CDCl_3$, 300 MHz
NBoc
H
N
O
O
2.00
1.01
0.63
0.68
0.64
3.88
2.73
3.04
0.63
11.87
3.26
3.37
f1 (ppm)

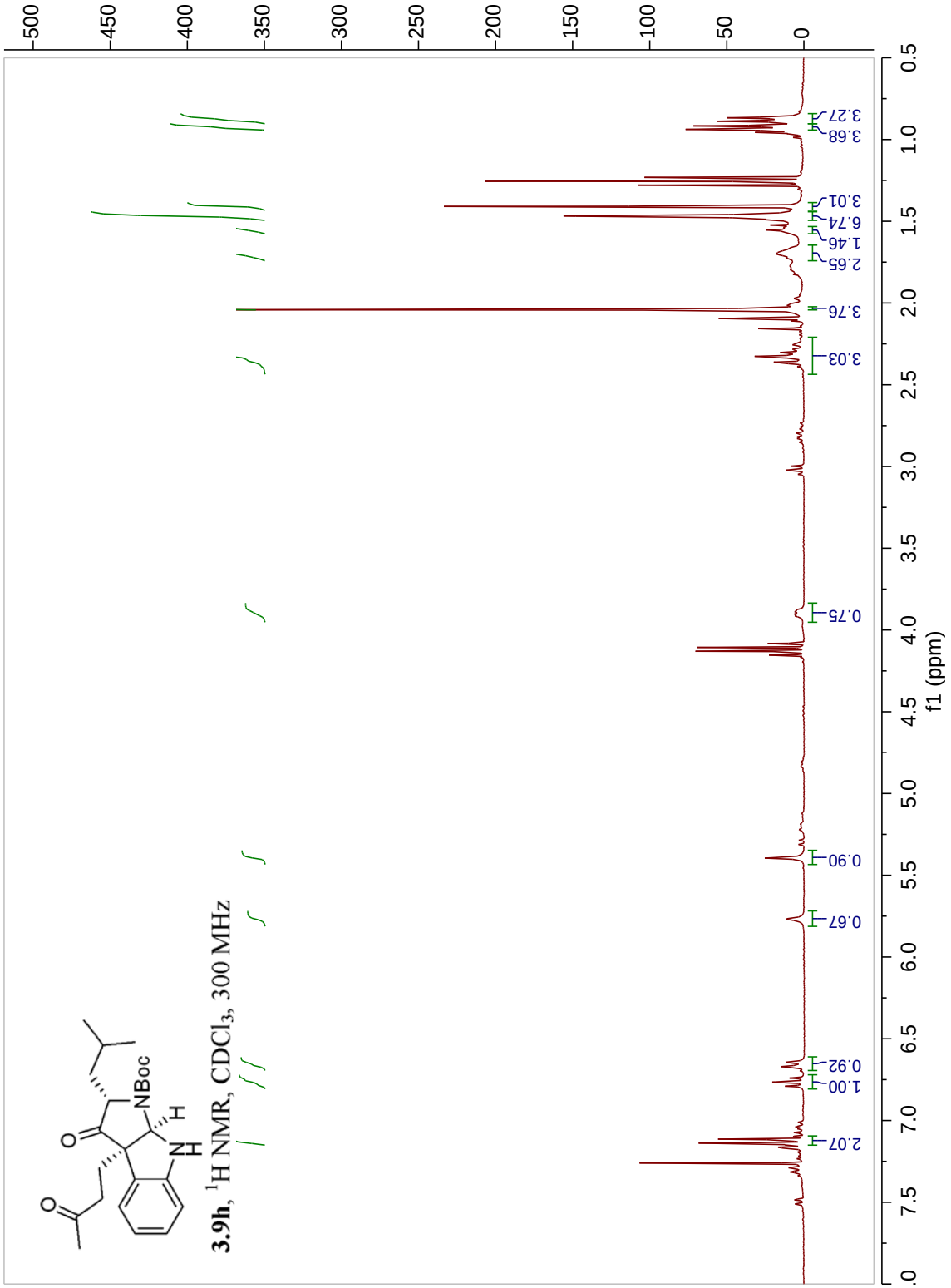


3.9b, ^{1}H NMR, $CDCl_3$, 300 MHz

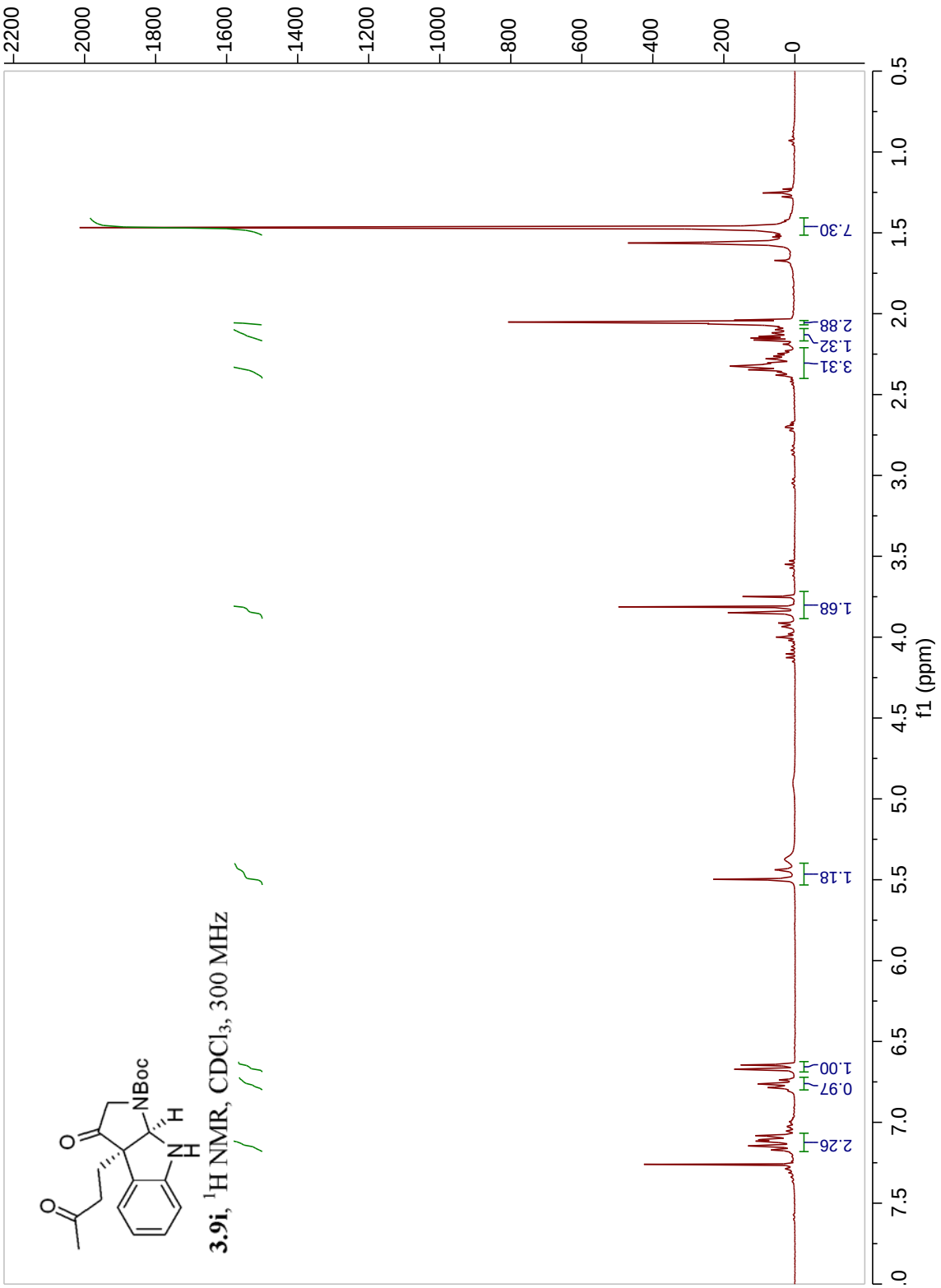

3.9c, ^{1}H NMR, $CDCl_3$, 300 MHz
NAc
O
O
H
N
1800
1600
1400
1200
1000
800
600
400
200
0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
.0
f1 (ppm)
3.76
3.65
4.02
3.32
7.38
3.90
5.18
1.02
1.00
0.95
1.14
2.24


NBoc
O
O
H
N
3.9f, ^{1}H NMR, $CDCl_3$, 300 MHz
2.69
8.67
3.49
3.17
0.77
1.05
0.74
1.00
1.09
2.08
f1 (ppm)


O
O
NBoc
N
H
H
3.9g, 1H NMR, CDCl3, 300 MHz
282
250
200
150
100
50
0
1.00
0.92
0.85
0.57
0.86
0.70
7.34
2.86
3.27
8.84
2.58
.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

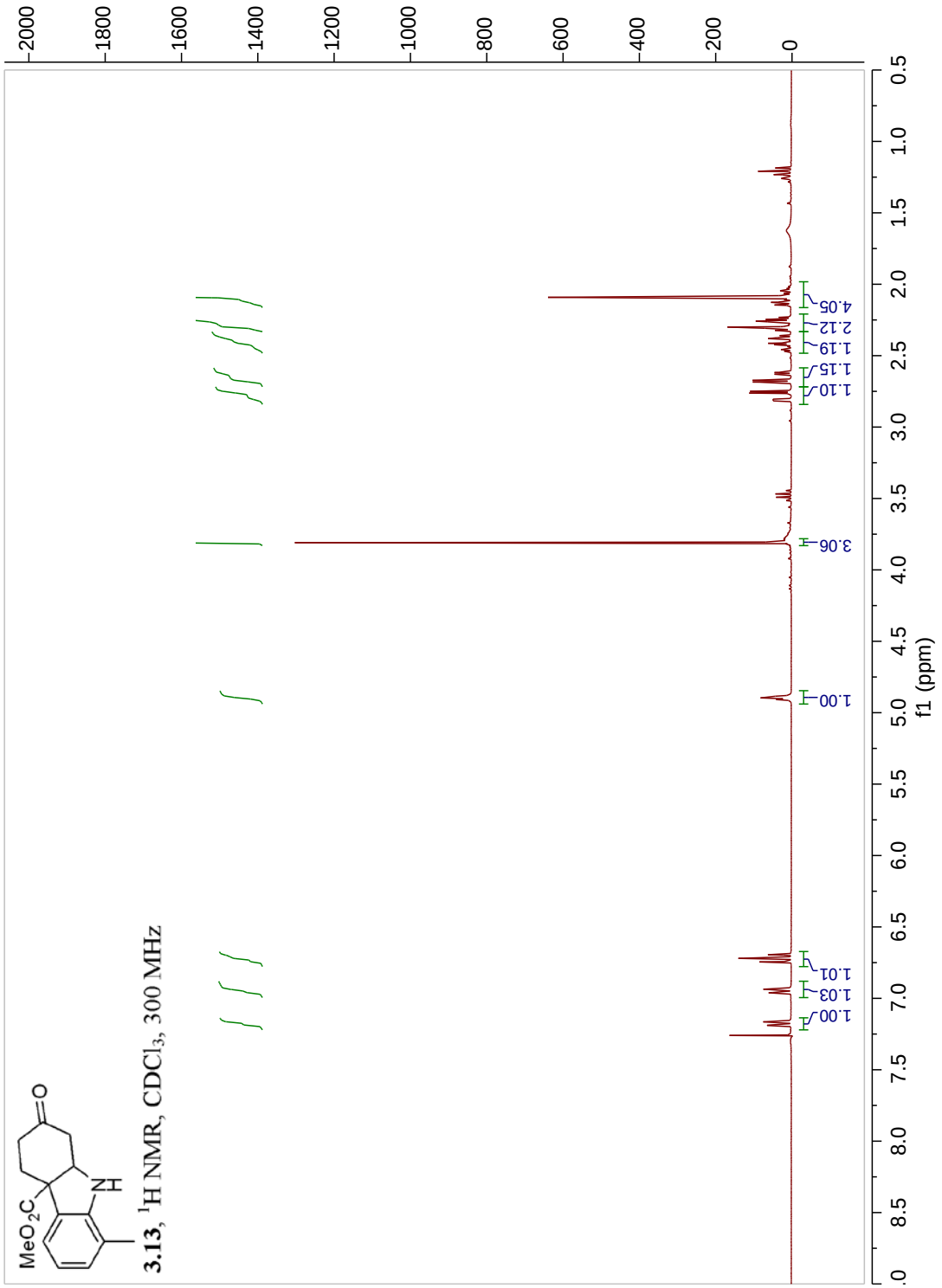


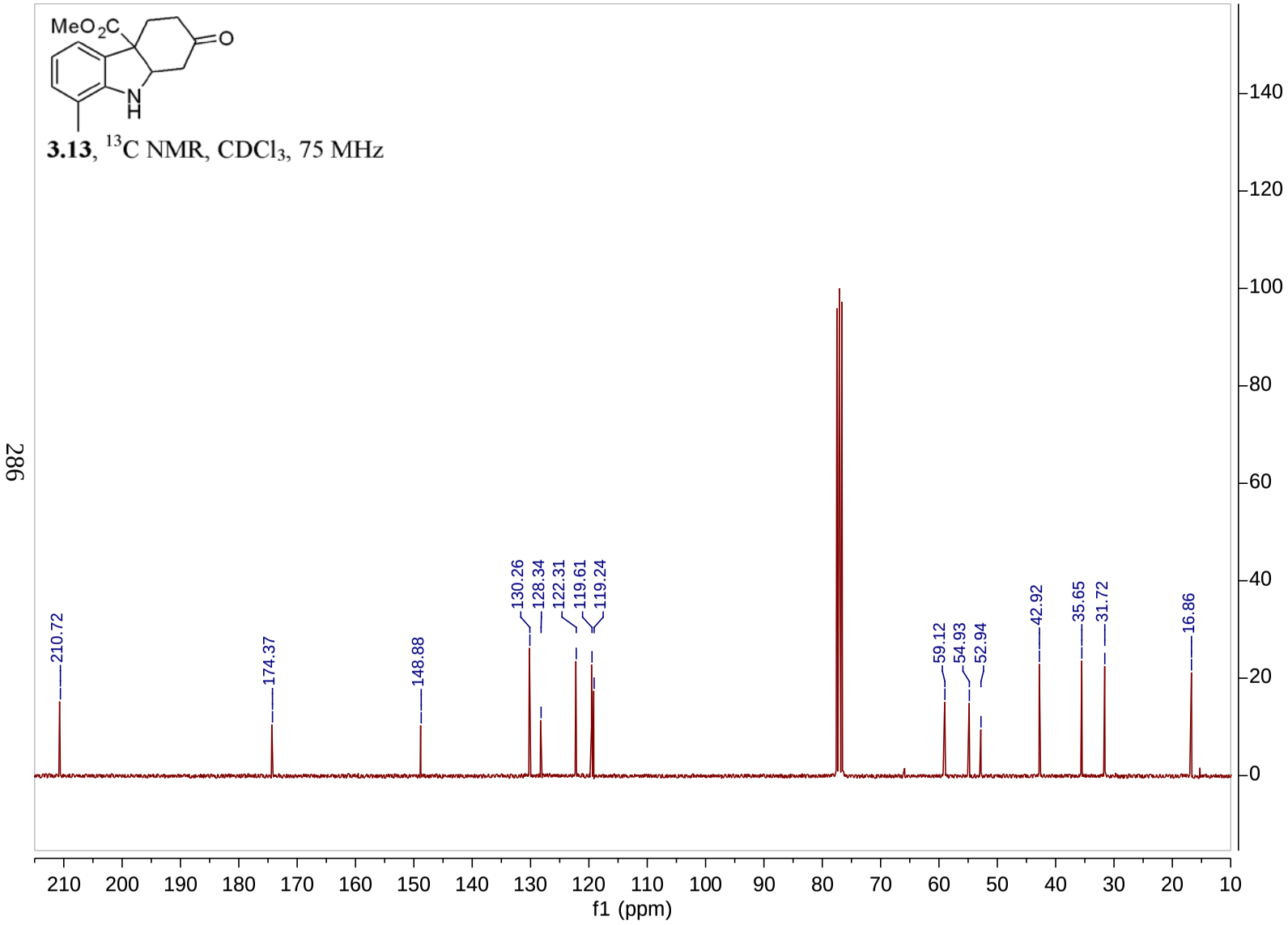
3.9h, ^{1}H NMR, $CDCl_3$, 300 MHz

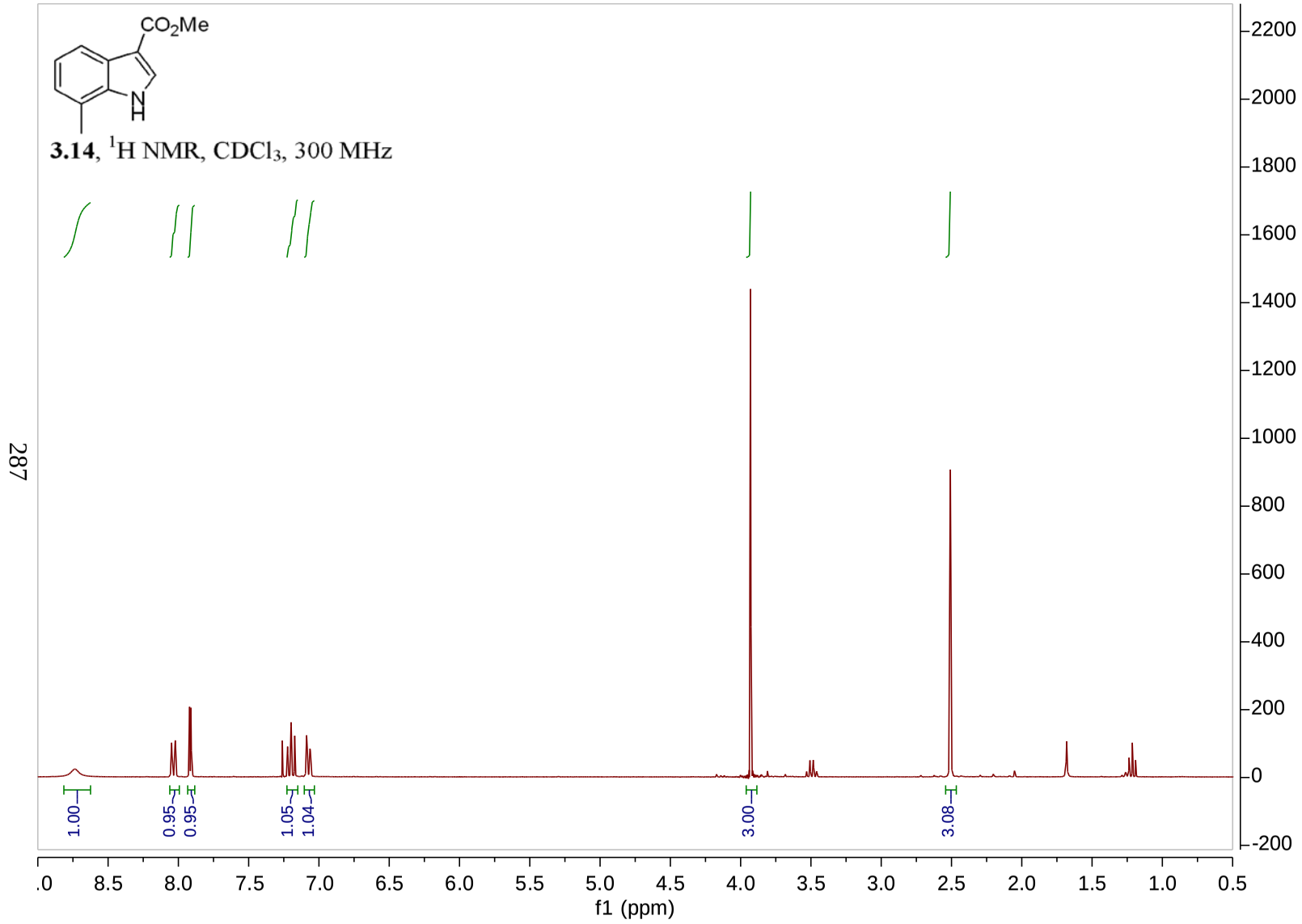


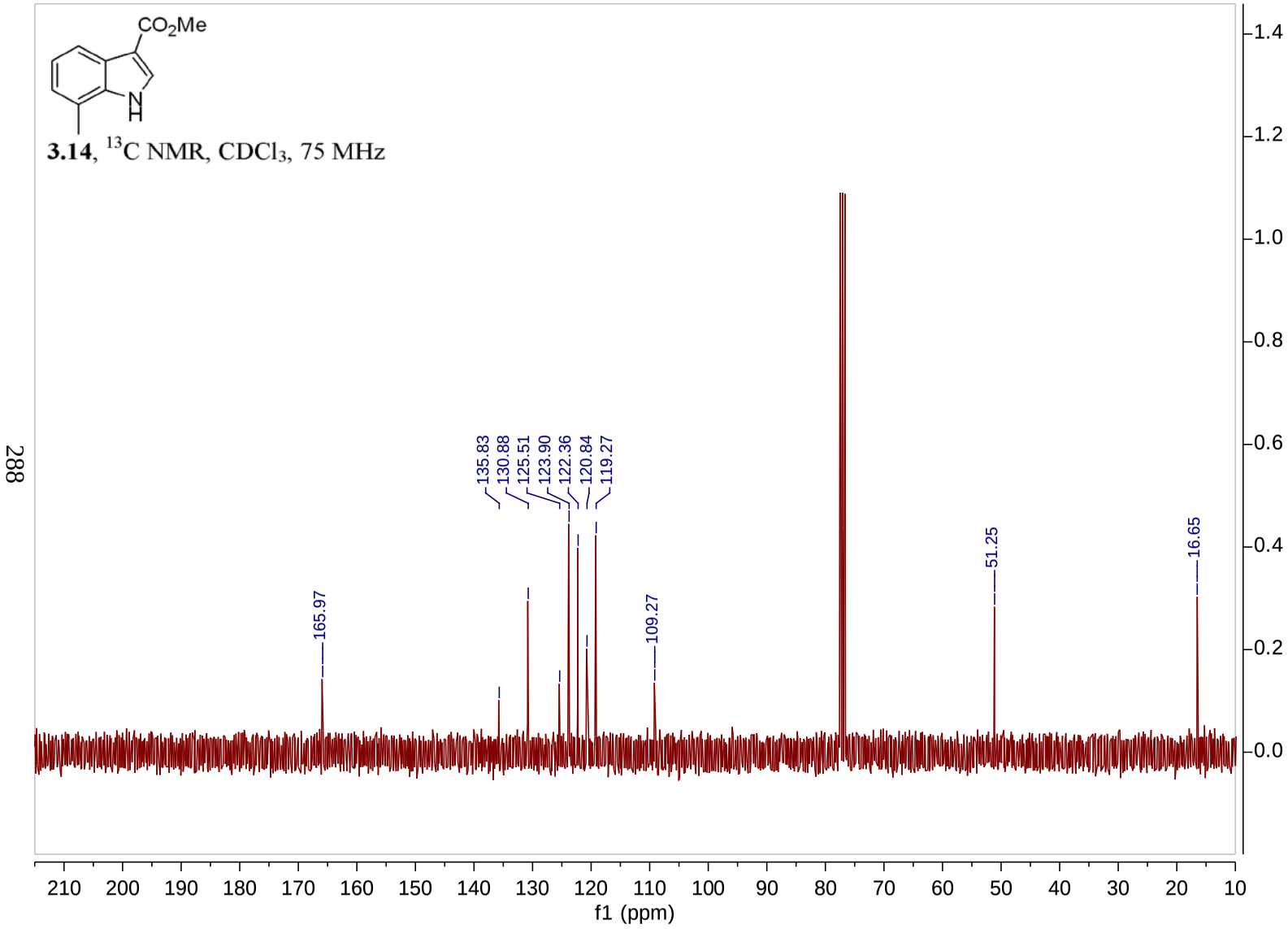
3.9i, ^{1}H NMR, $CDCl_3$, 300 MHz

APPENDIX E

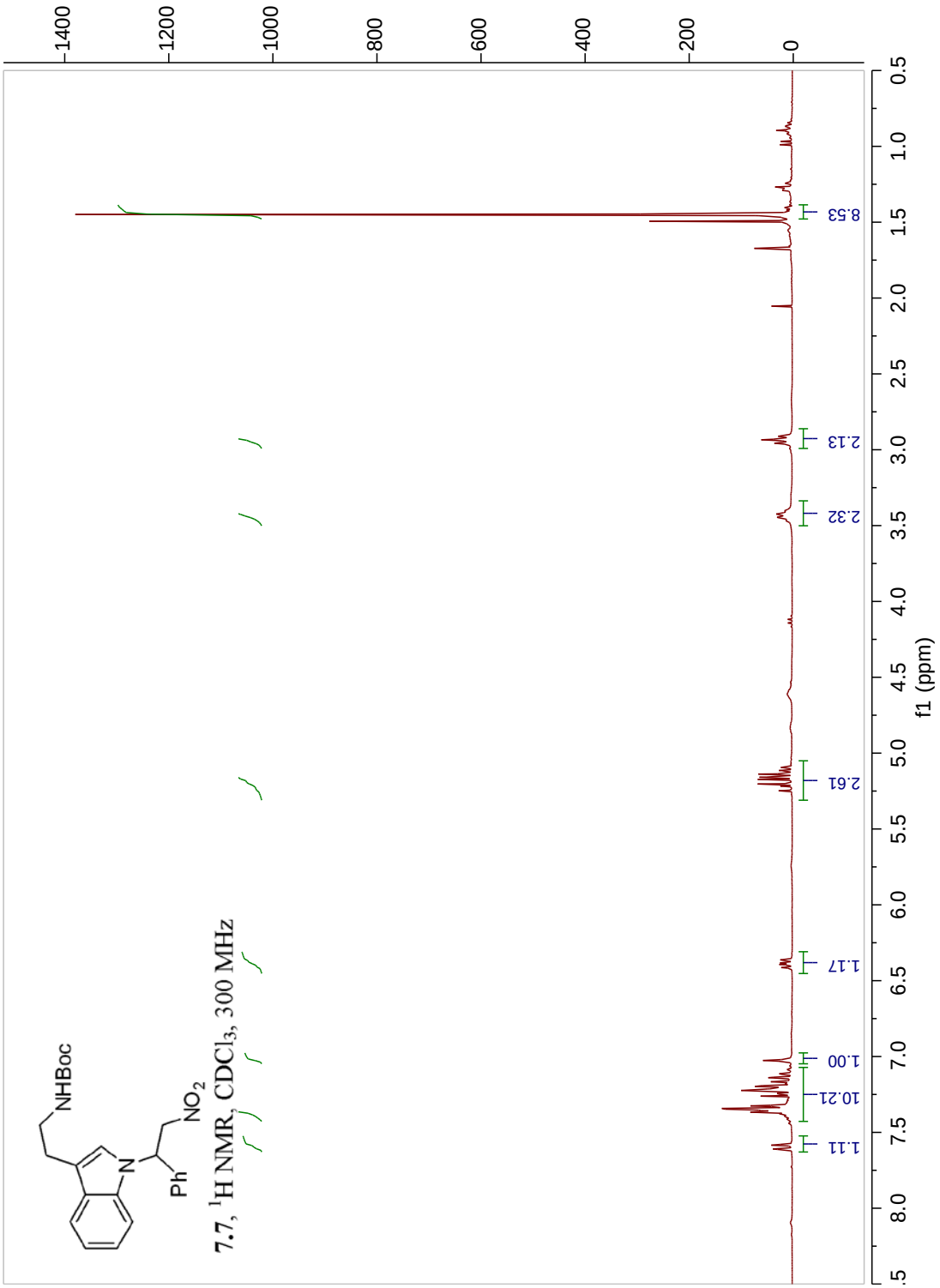

3.13, ^{1}H NMR, $CDCl_3$, 300 MHz
MeO_2C
O
N
H
f1 (ppm)
1.00
1.01
1.03
1.00
3.06
1.00
1.10
1.15
1.19
2.12
4.05

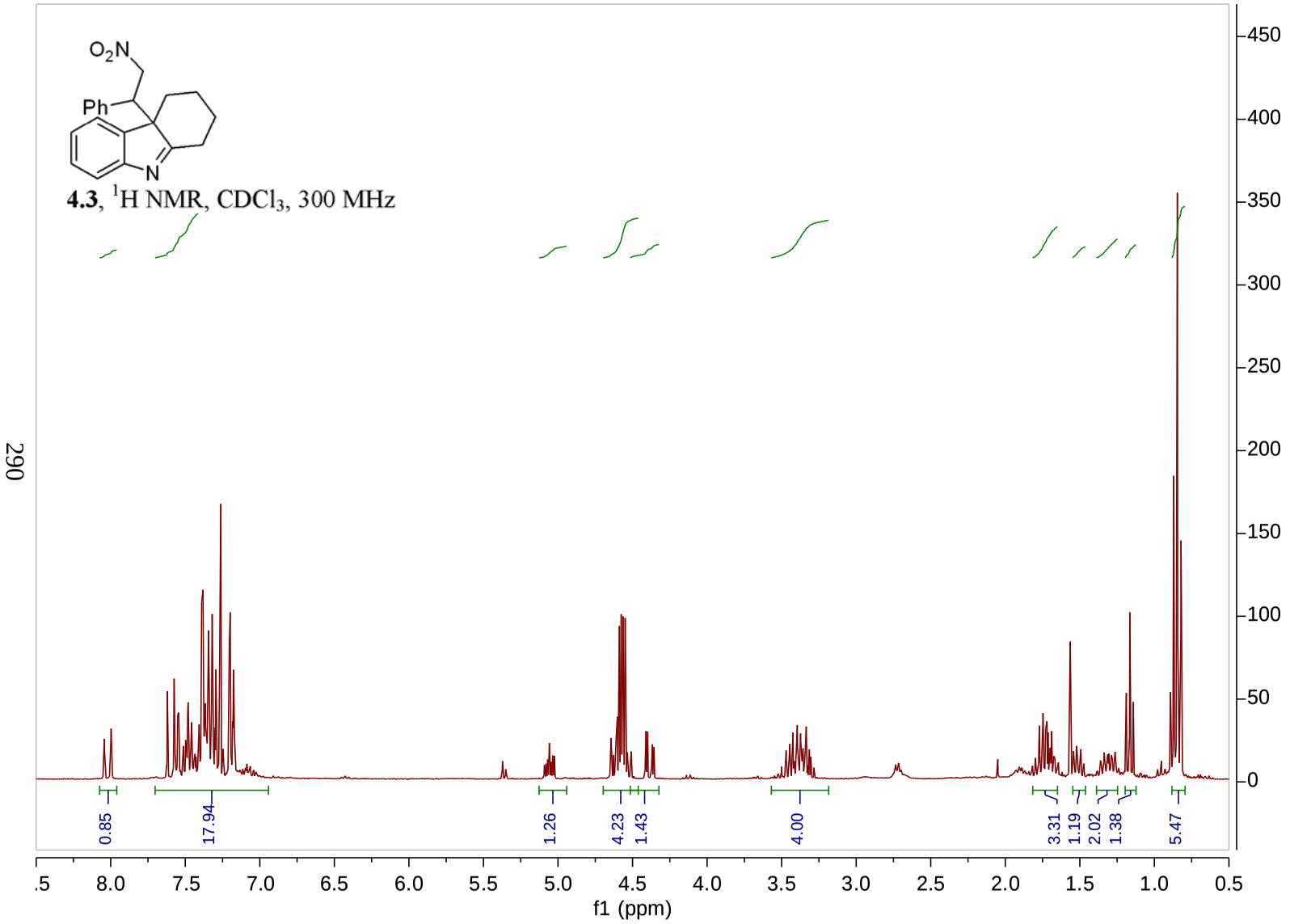

MeO2C
O
N
H
3.13, 13C NMR, CDCl3, 75 MHz
286
210.72
174.37
148.88
130.26
128.34
122.31
119.61
119.24
59.12
54.93
52.94
42.92
35.65
31.72
16.86
f1 (ppm)

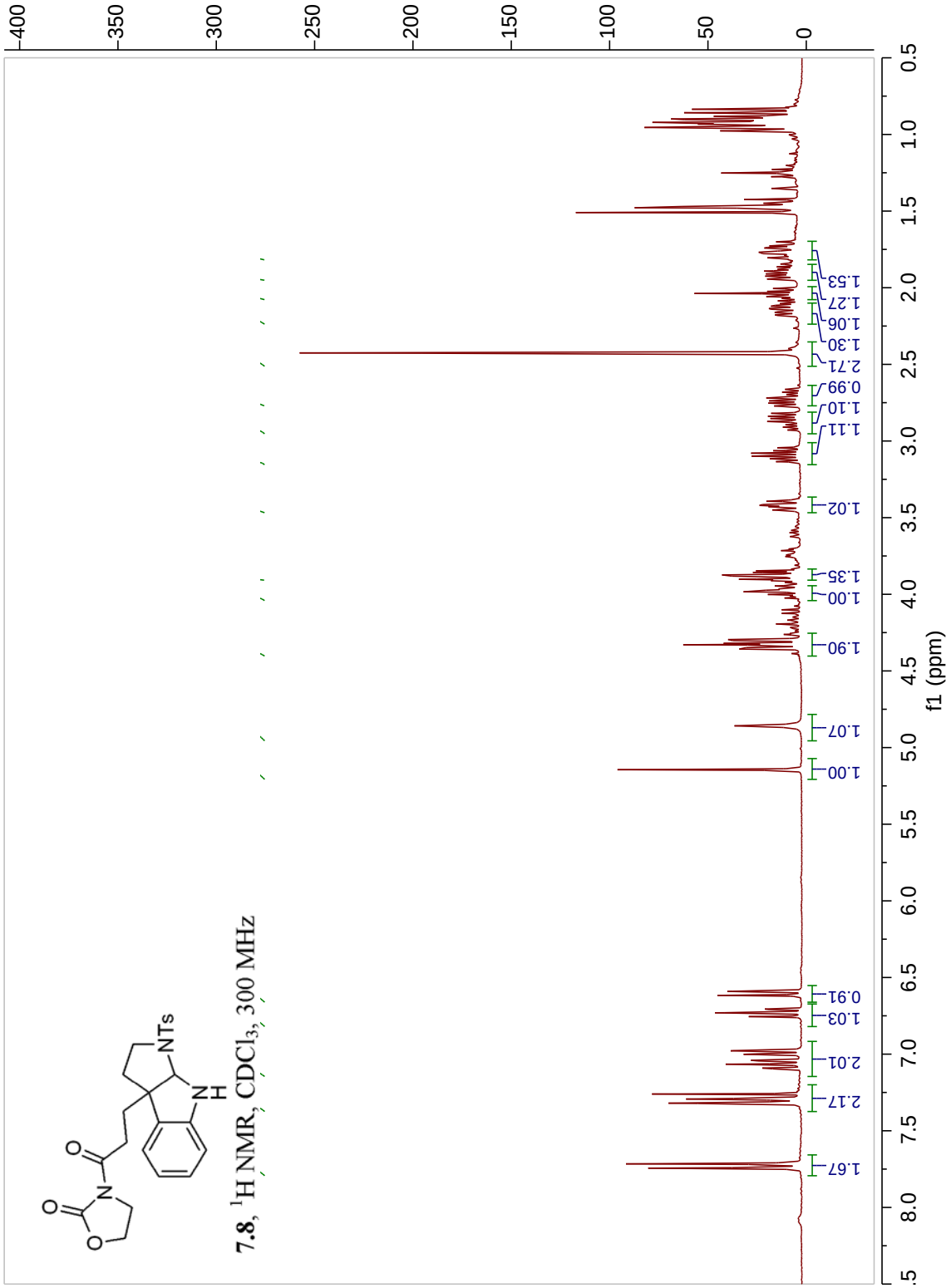

CO2Me
N
H
3.14, 1H NMR, CDCl3, 300 MHz
287
1.00
0.95
0.95
1.05
1.04
3.00
3.08
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

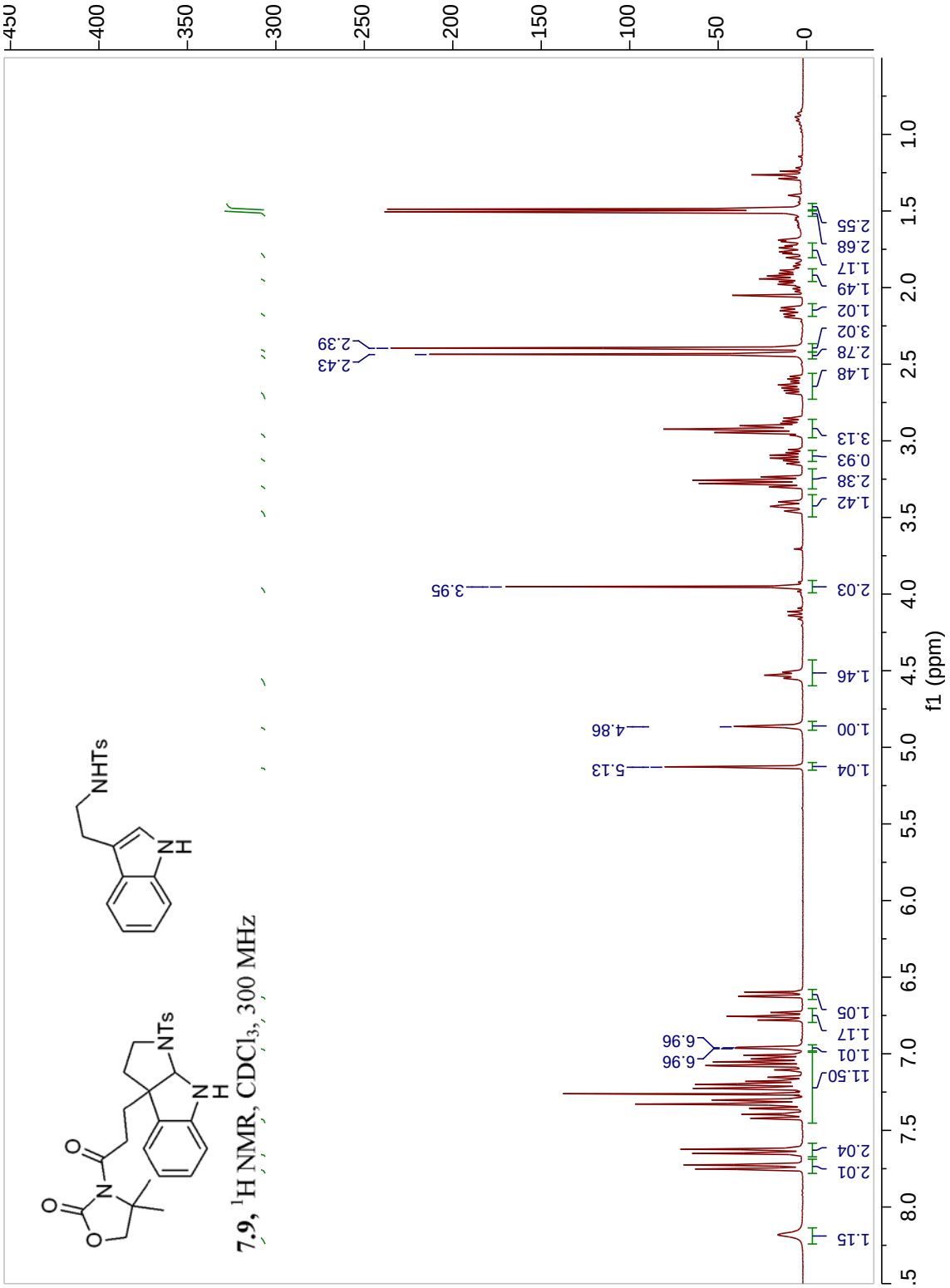

CO2Me
N
H
3.14, 13C NMR, CDCl3, 75 MHz
288
135.83
130.88
125.51
123.90
122.36
120.84
119.27
165.97
109.27
51.25
16.65
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

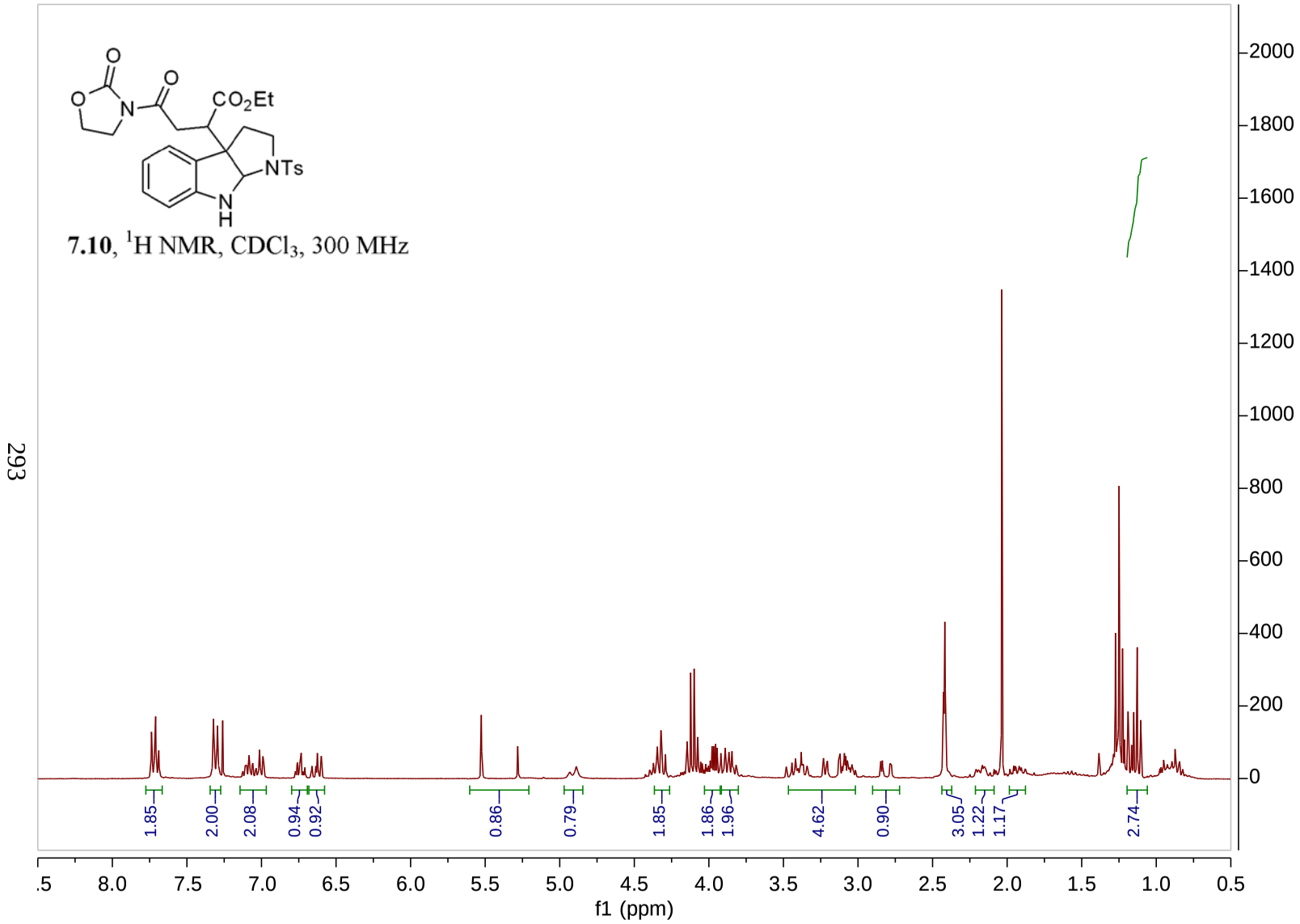
APPENDIX F

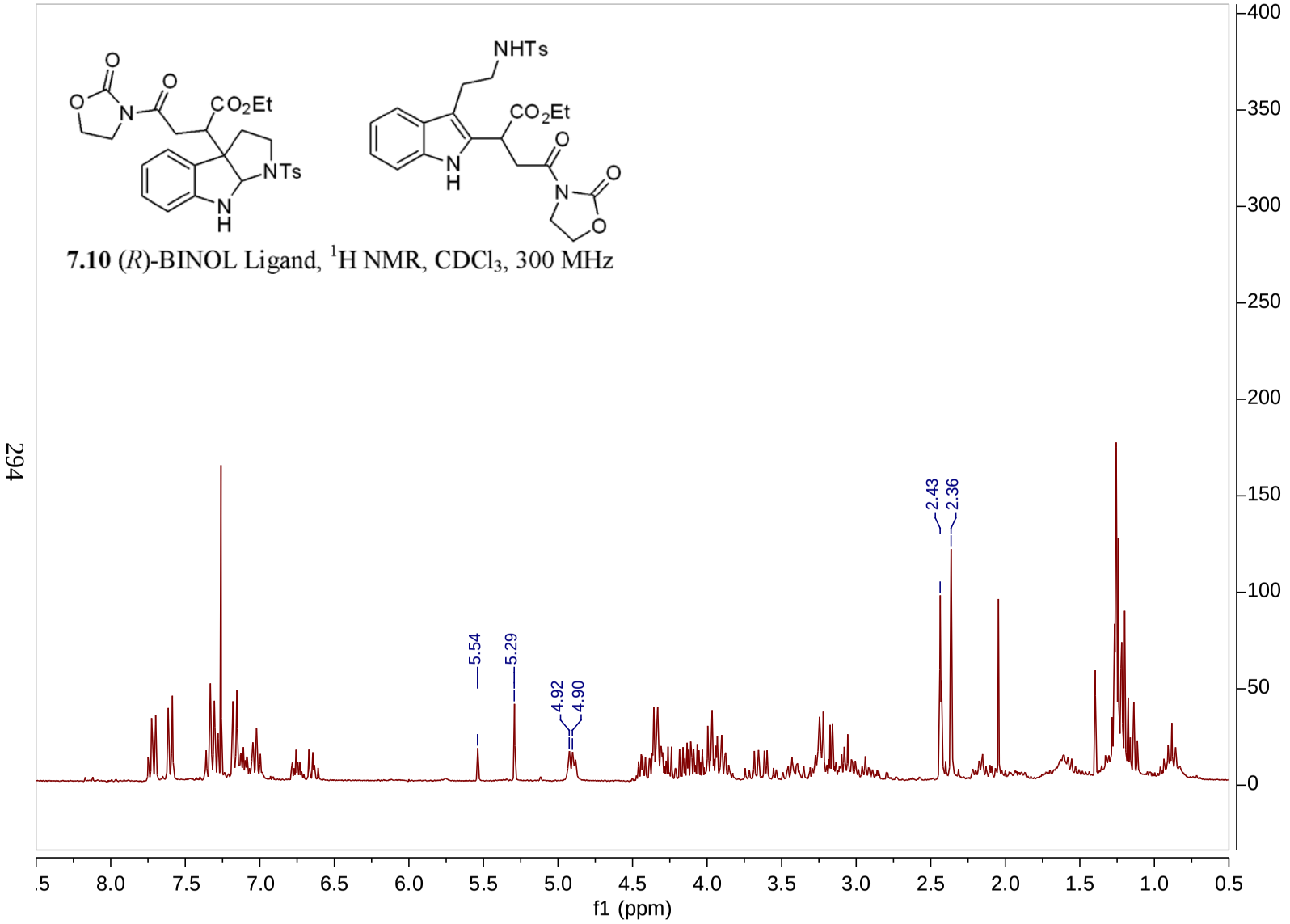

7.7, ^{1}H NMR, $CDCl_3$, 300 MHz
NHBoc
N
Ph
NO_2
8.53
2.13
2.32
2.61
1.17
1.00
10.21
1.11
f1 (ppm)


O2N
Ph
N
4.3, 1H NMR, CDCl3, 300 MHz
290
0.85
17.94
1.26
4.23
1.43
4.00
3.31
1.19
2.02
1.38
5.47
f1 (ppm)

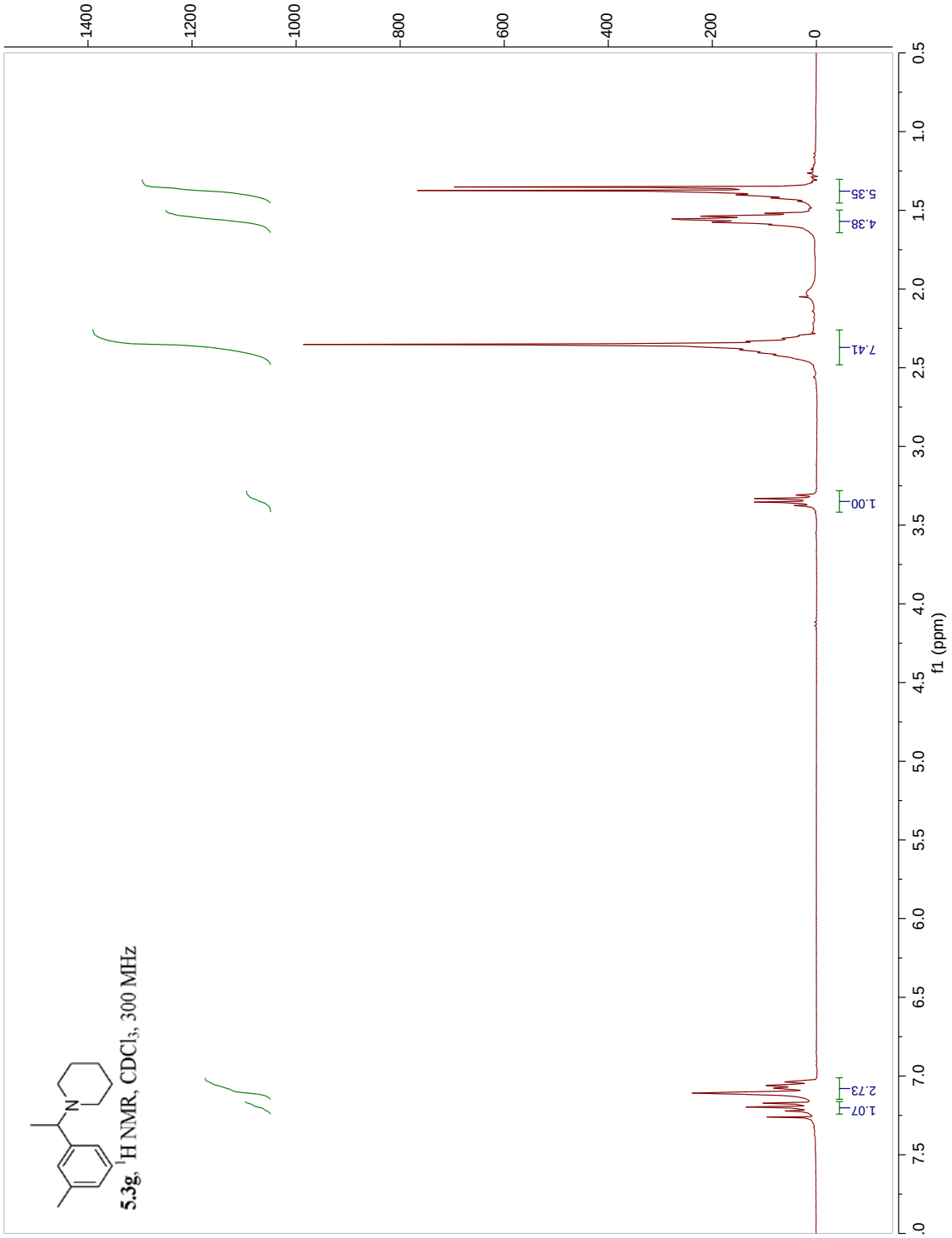

7.8, ^{1}H NMR, $CDCl_3$, 300 MHz
NTs
N
H
O
O
N
O
O
f1 (ppm)
1.67
2.17
2.01
1.03
0.91
1.00
1.07
1.90
1.00
1.35
1.02
1.11
1.10
0.99
2.71
1.30
1.06
1.27
1.53

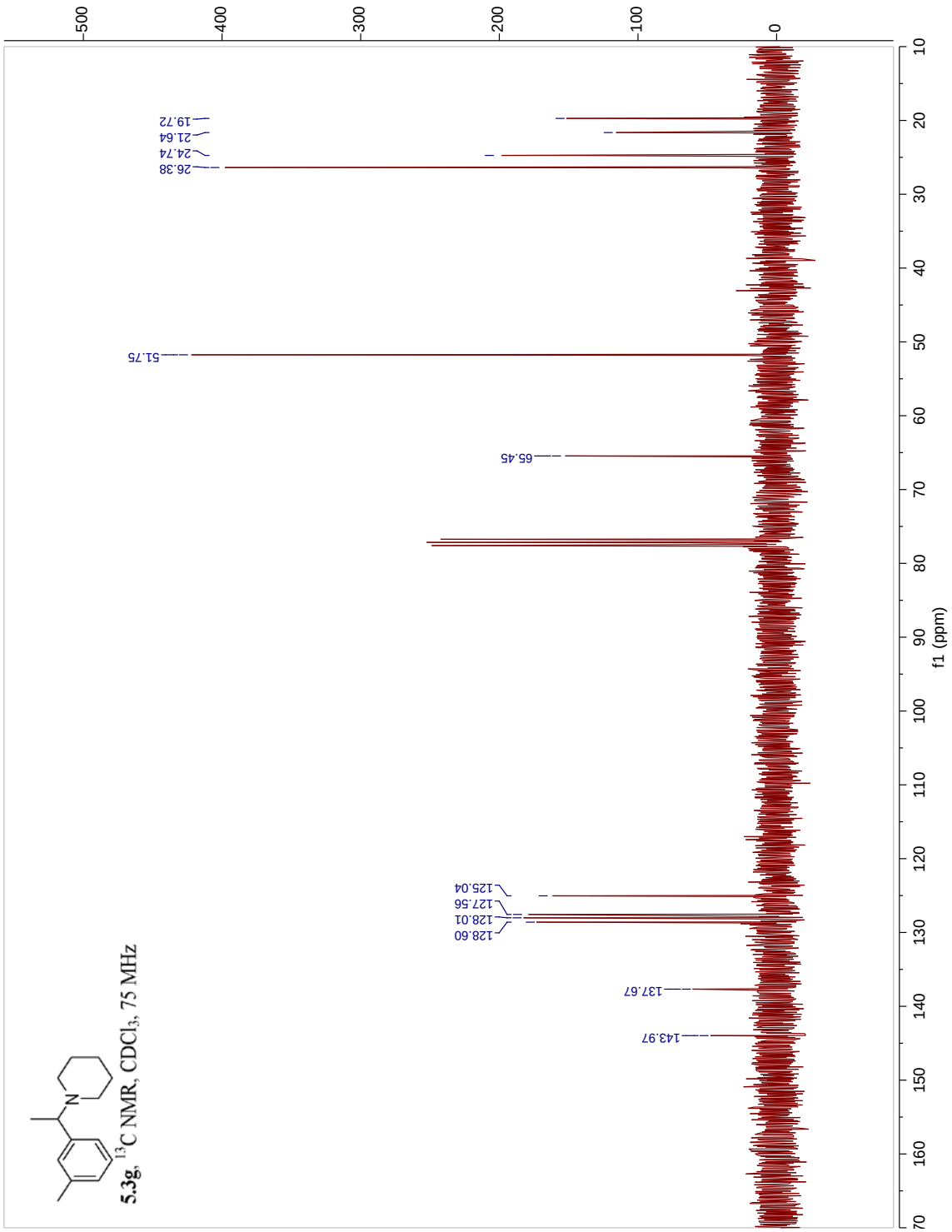

7.9, ^{1}H NMR, $CDCl_3$, 300 MHz
NHTs
NTs
H
N
O
O
O
N
f1 (ppm)
1.15
2.01
2.04
11.50
6.96
6.96
1.01
1.17
1.05
5.13
4.86
1.04
1.00
1.46
3.95
2.03
1.42
2.38
0.93
3.13
1.48
2.78
3.02
1.02
1.49
1.17
2.68
2.55
2.43
2.39

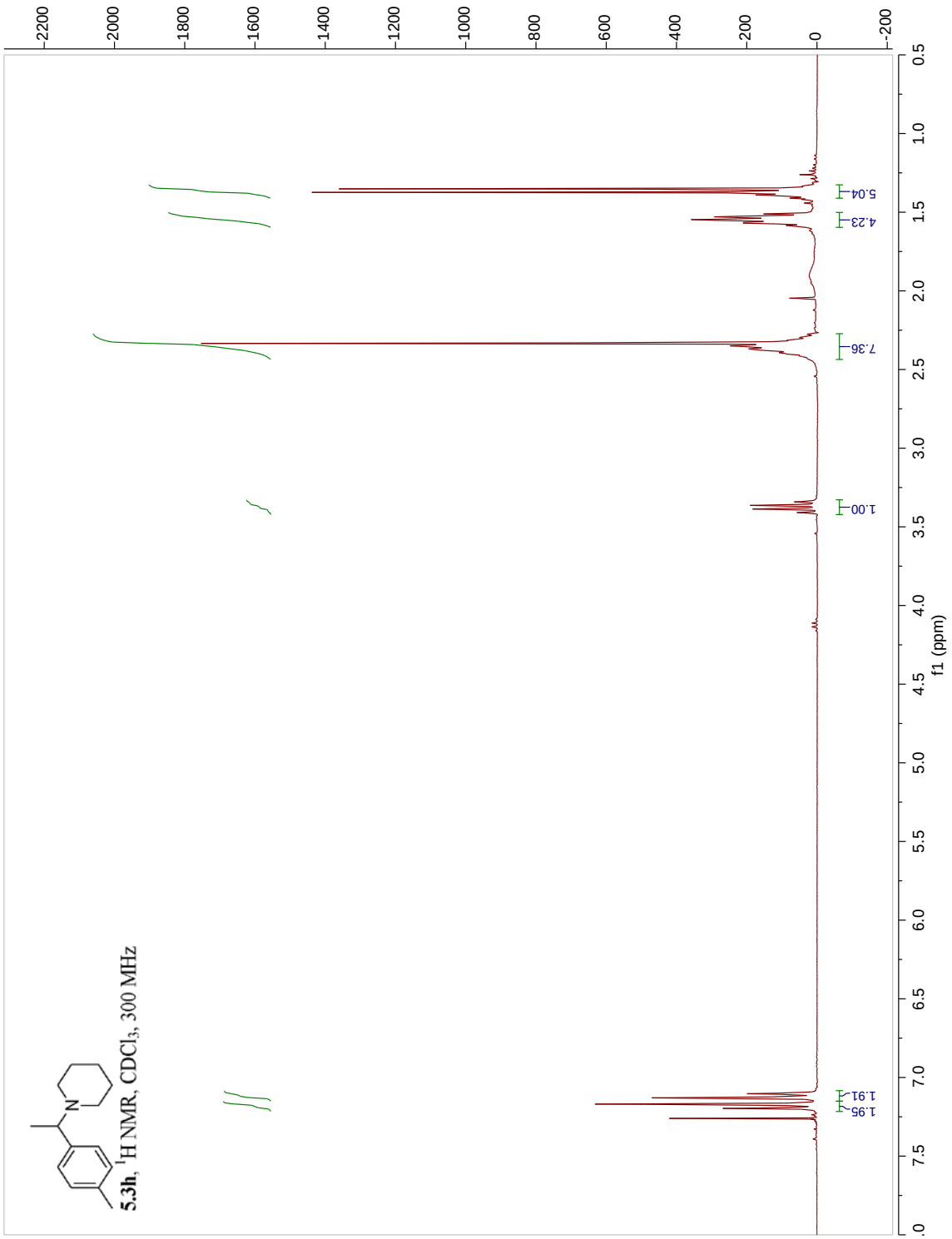

O
O
N
O
CO2Et
NTs
N
H
7.10, 1H NMR, CDCl3, 300 MHz
293
2000
1800
1600
1400
1200
1000
800
600
400
200
0
1.85
2.00
2.08
0.94
0.92
0.86
0.79
1.85
1.86
1.96
4.62
0.90
3.05
1.22
1.17
2.74
.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

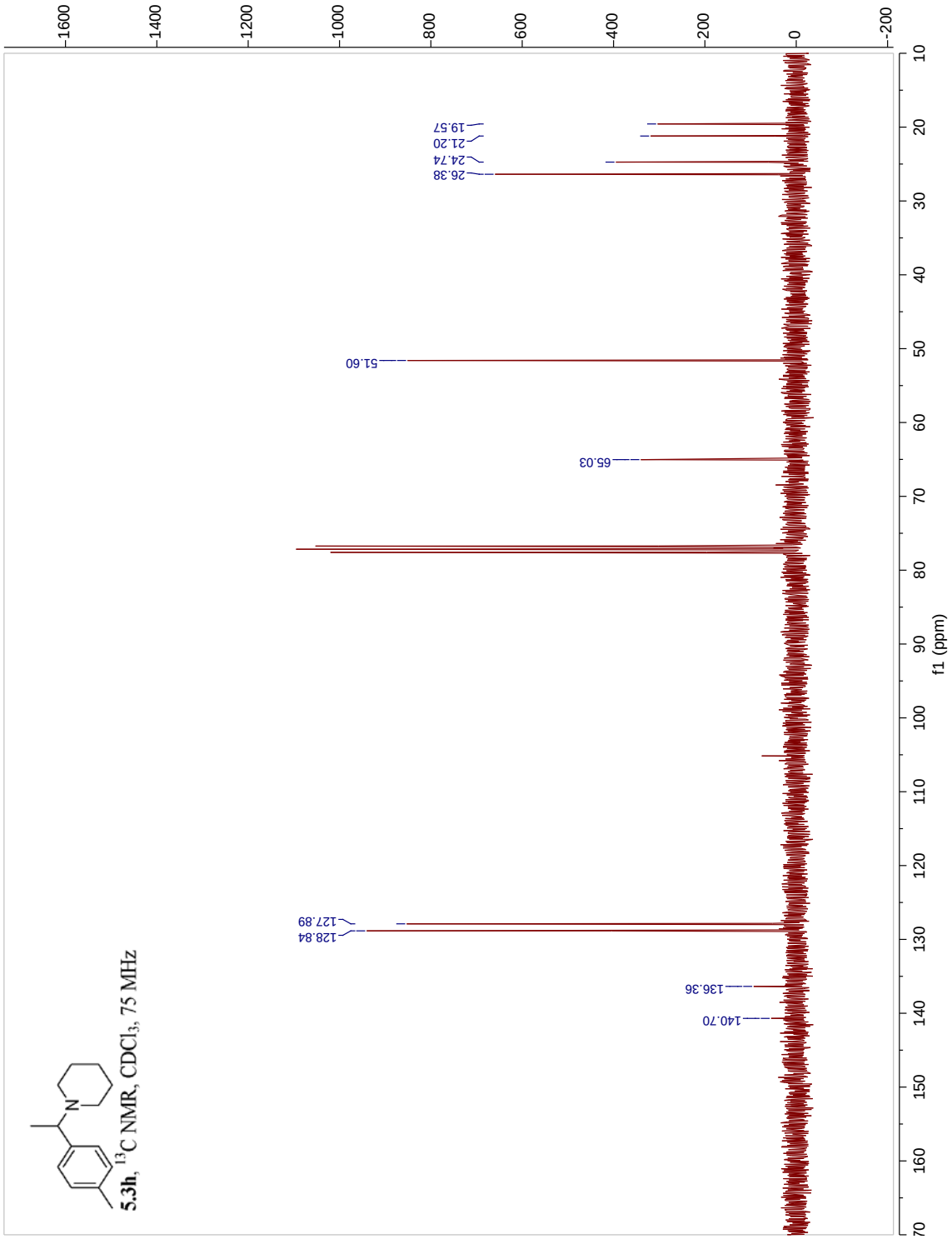

NHTs
CO2Et
O
N
NTs
H
7.10 (R)-BINOL Ligand, 1H NMR, CDCl3, 300 MHz
294
5.54
5.29
4.92
4.90
2.43
2.36
400
350
300
250
200
150
100
50
0
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

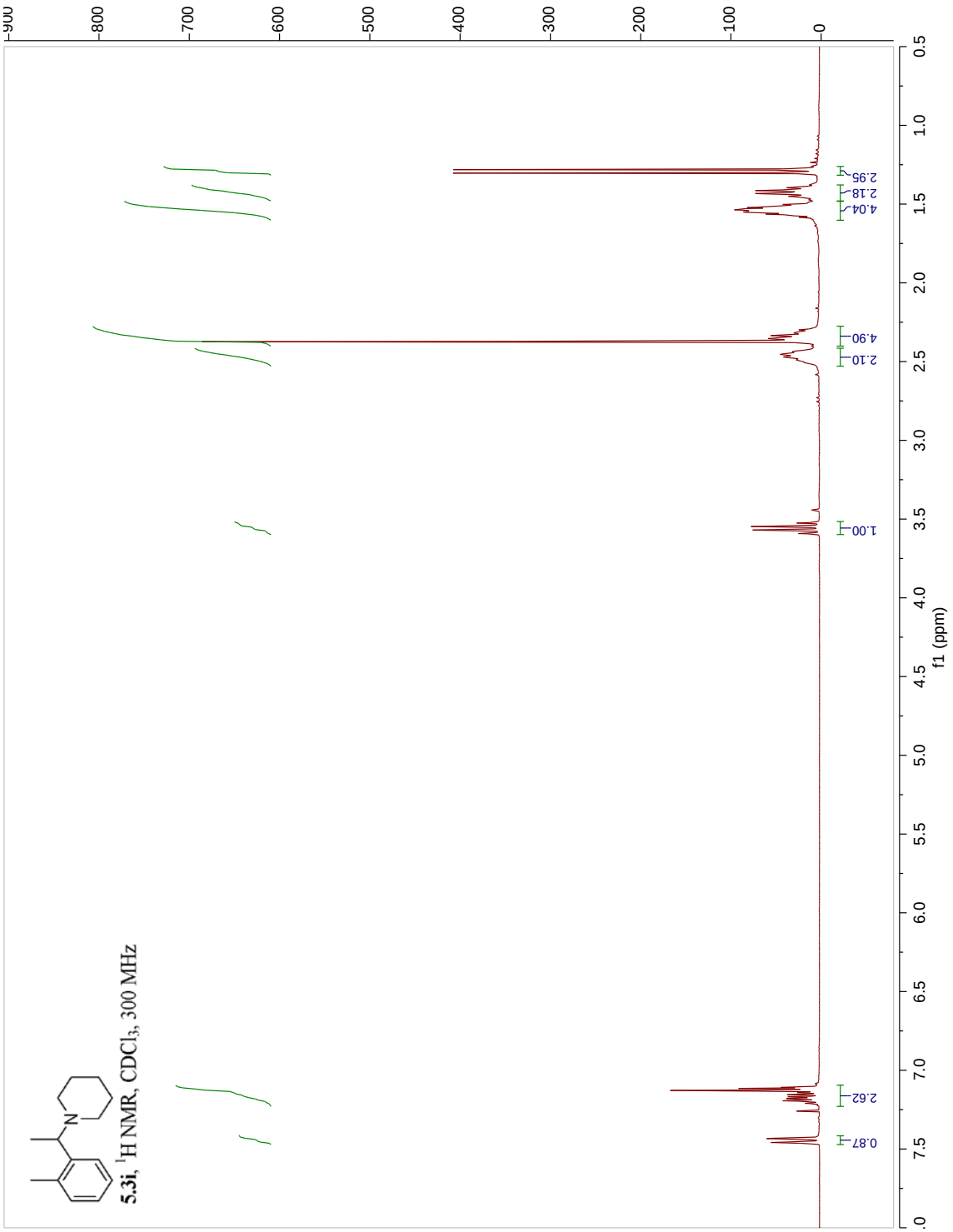
APPENDIX G

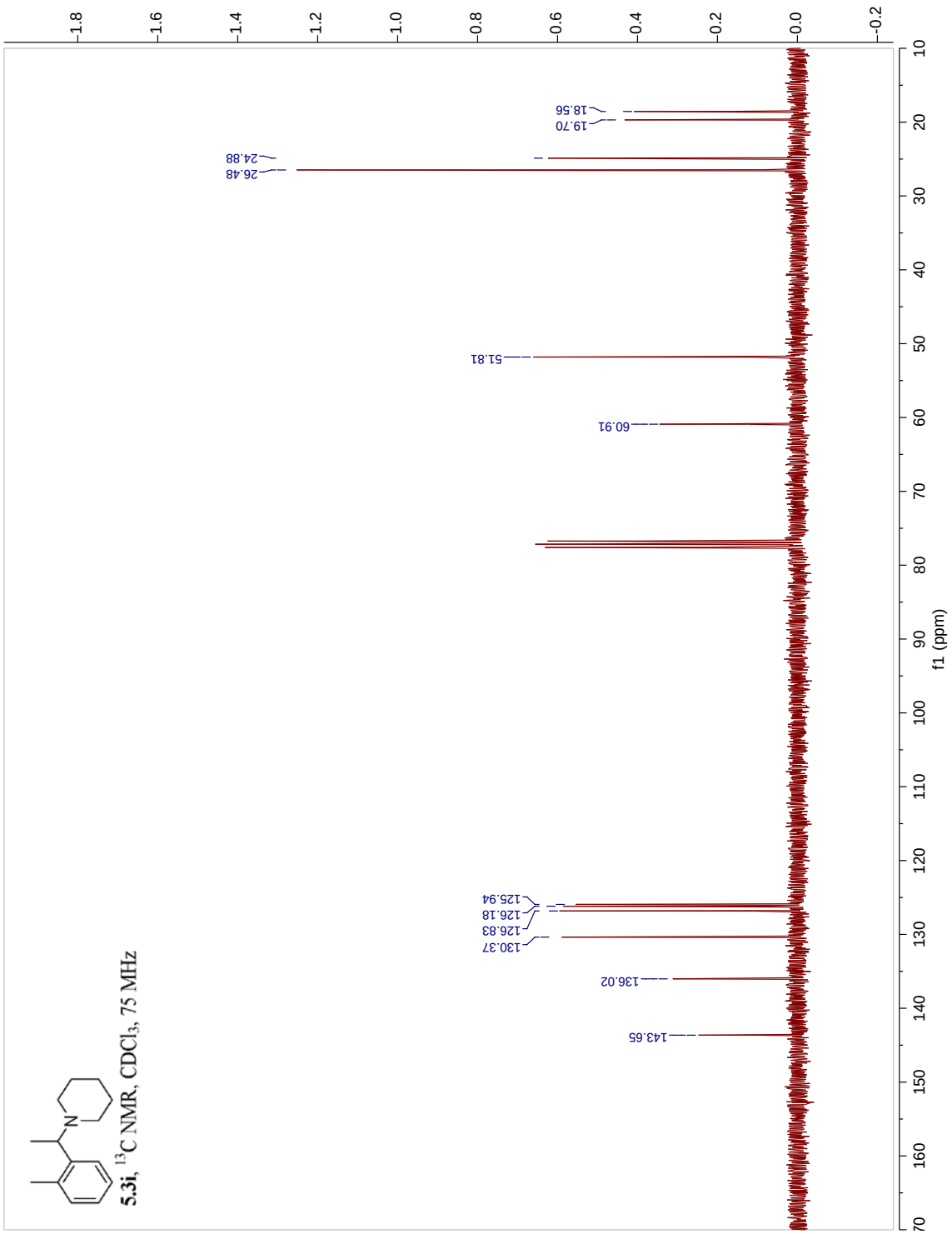

5.3g, ^{1}H NMR, $CDCl_3$, 300 MHz
1400
1200
1000
800
600
400
200
0
5.35
4.38
7.41
1.00
2.73
1.07
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
.0
f1 (ppm)

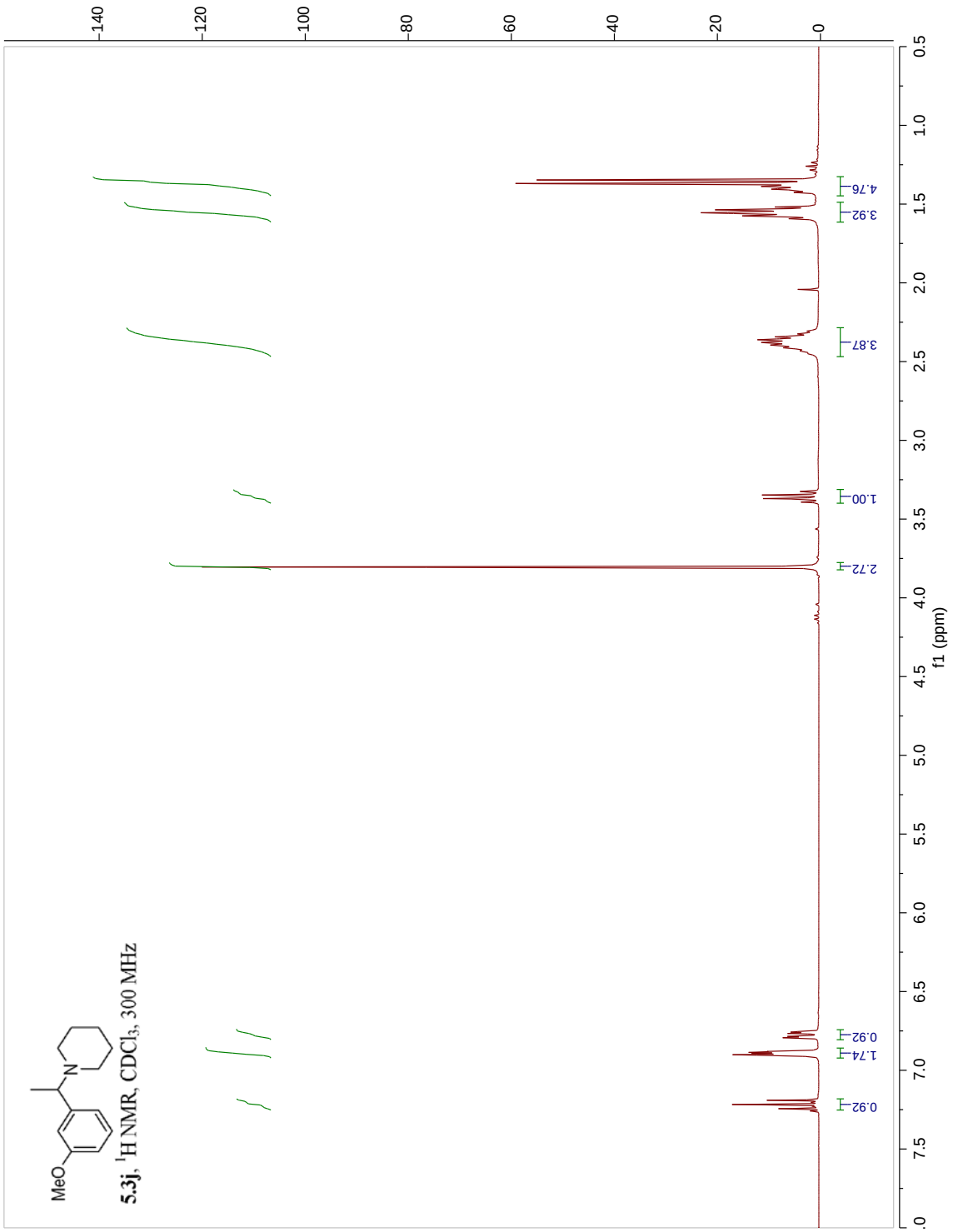

5.3g, ^{13}C NMR, $CDCl_3$, 75 MHz
N
143.97
137.67
128.60
128.01
127.56
125.04
65.45
51.75
26.38
24.74
21.64
19.72
f1 (ppm)

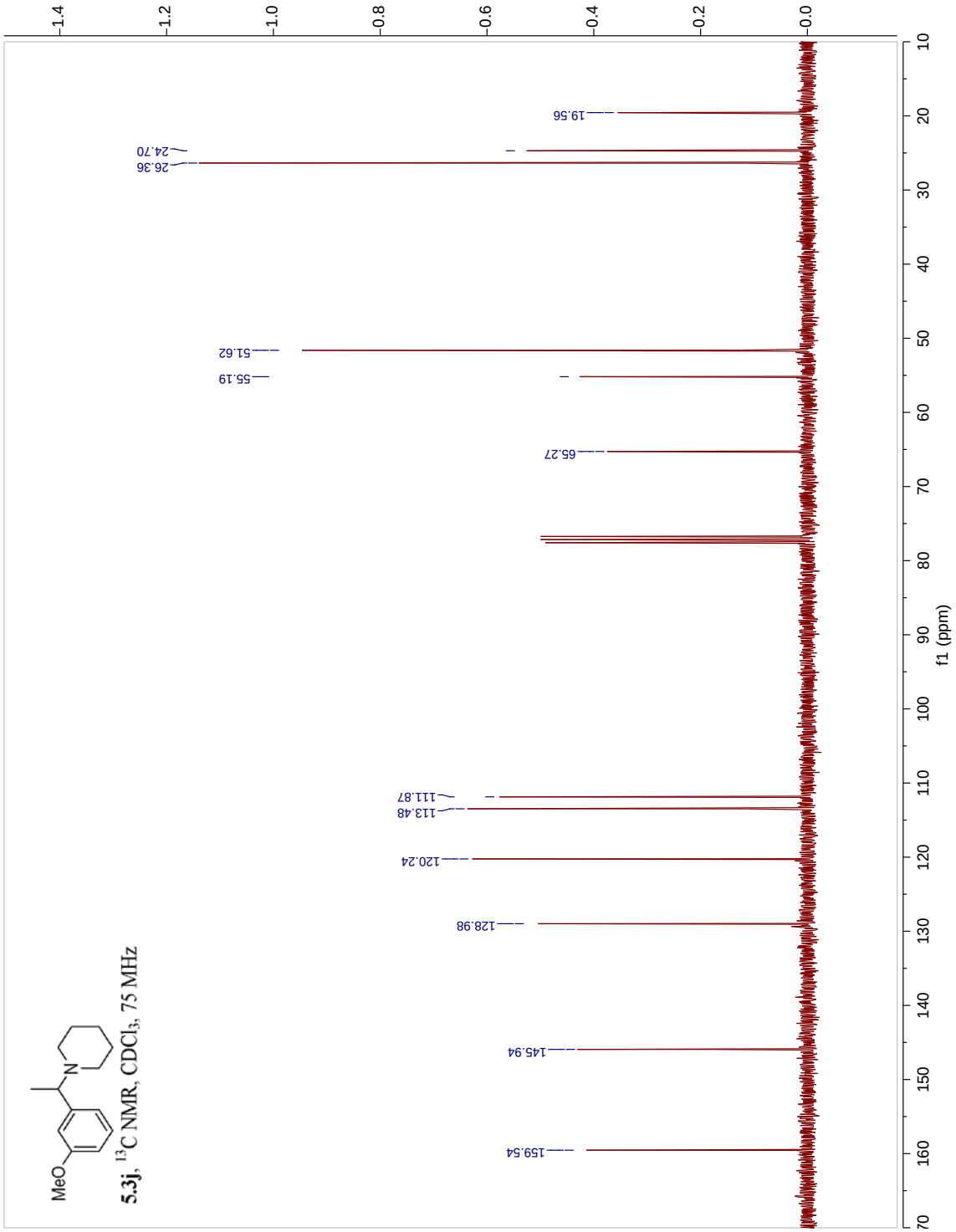

5.3h, ^{1}H NMR, $CDCl_3$, 300 MHz
5.04
4.23
7.36
1.00
1.95
1.91
f1 (ppm)

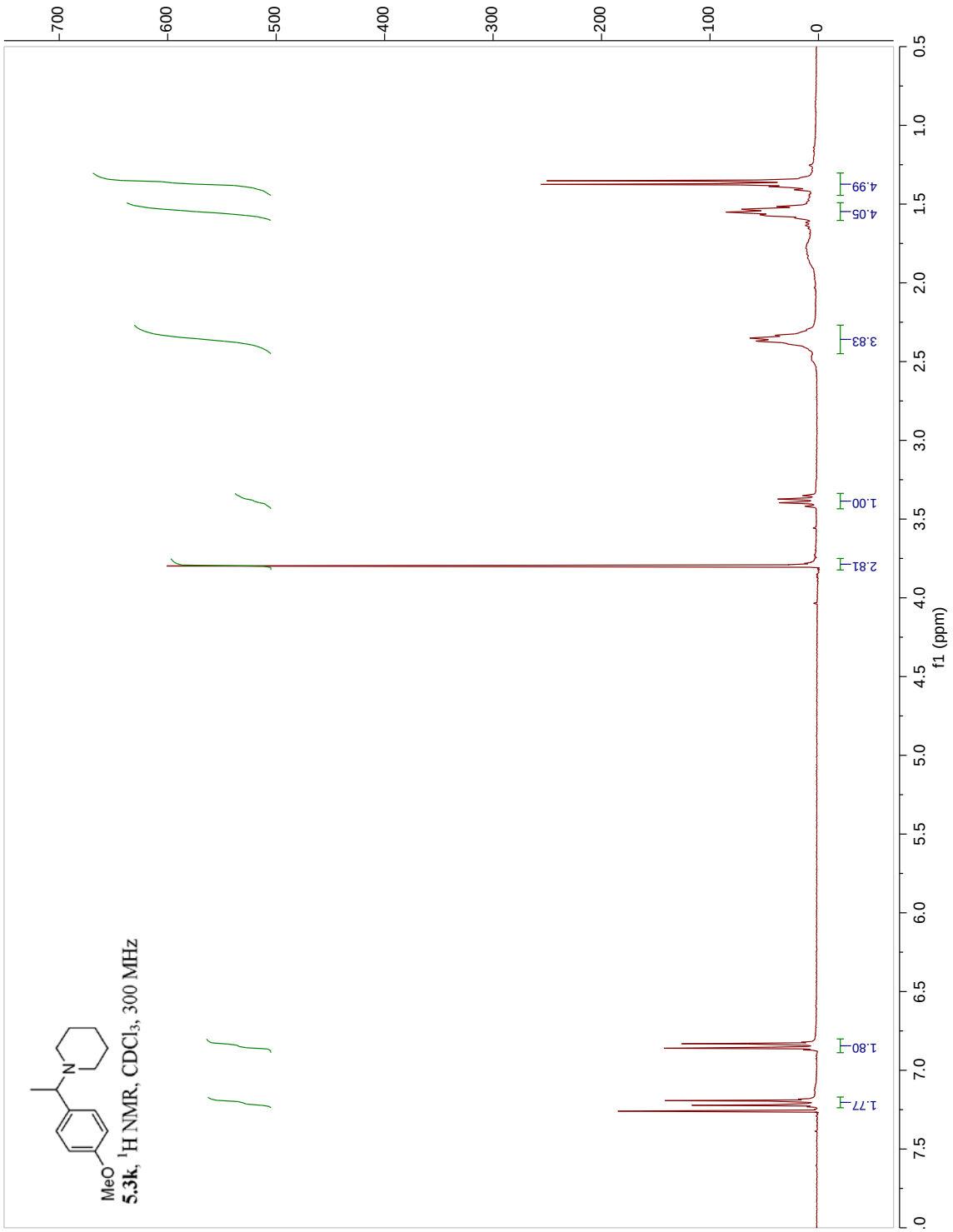

5.3h, ^{13}C NMR, $CDCl_3$, 75 MHz
N
140.70
136.36
128.84
127.89
65.03
51.60
26.38
24.74
21.20
19.57
f1 (ppm)

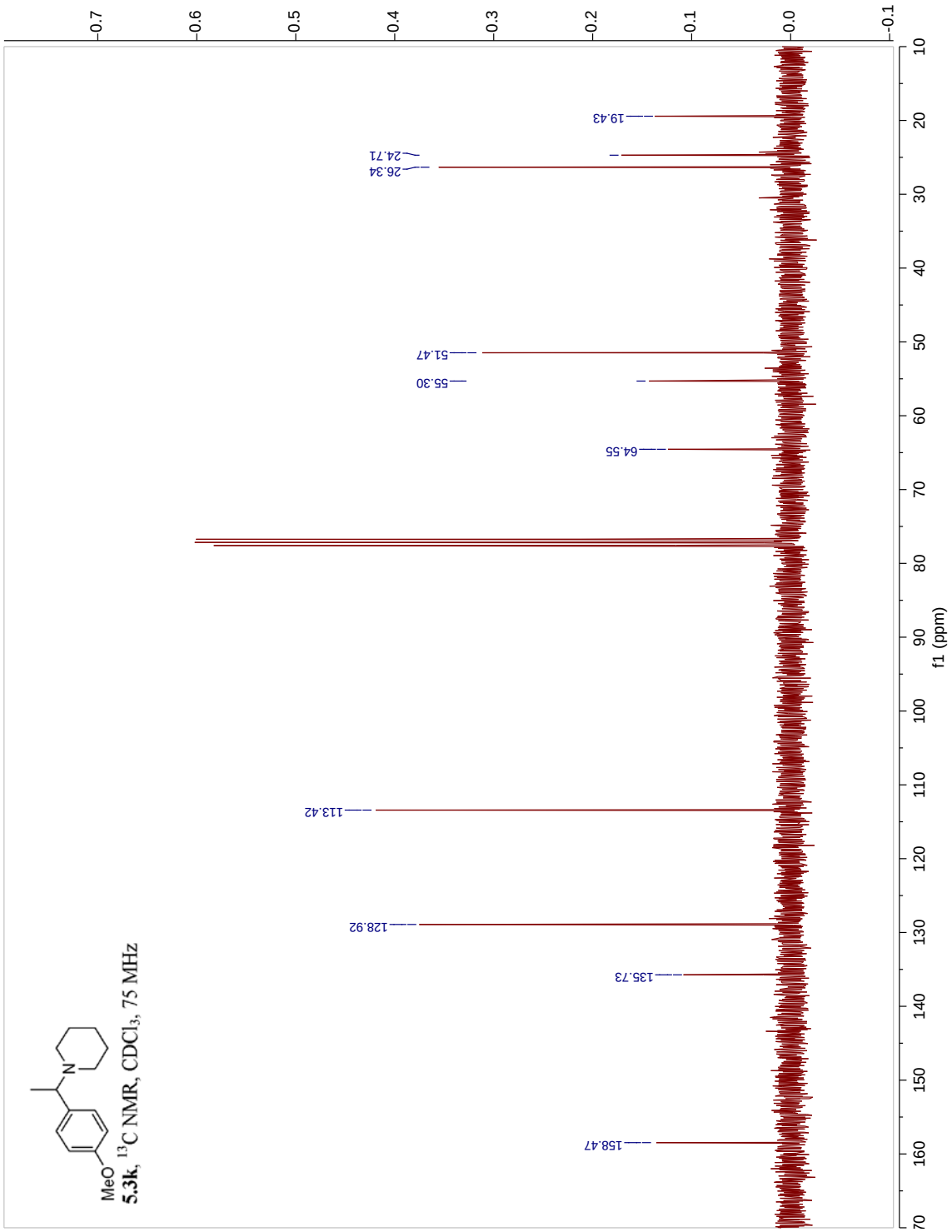

5.3i, ^{1}H NMR, $CDCl_3$, 300 MHz
f1 (ppm)
2.95
2.18
4.04
4.90
2.10
1.00
2.62
0.87

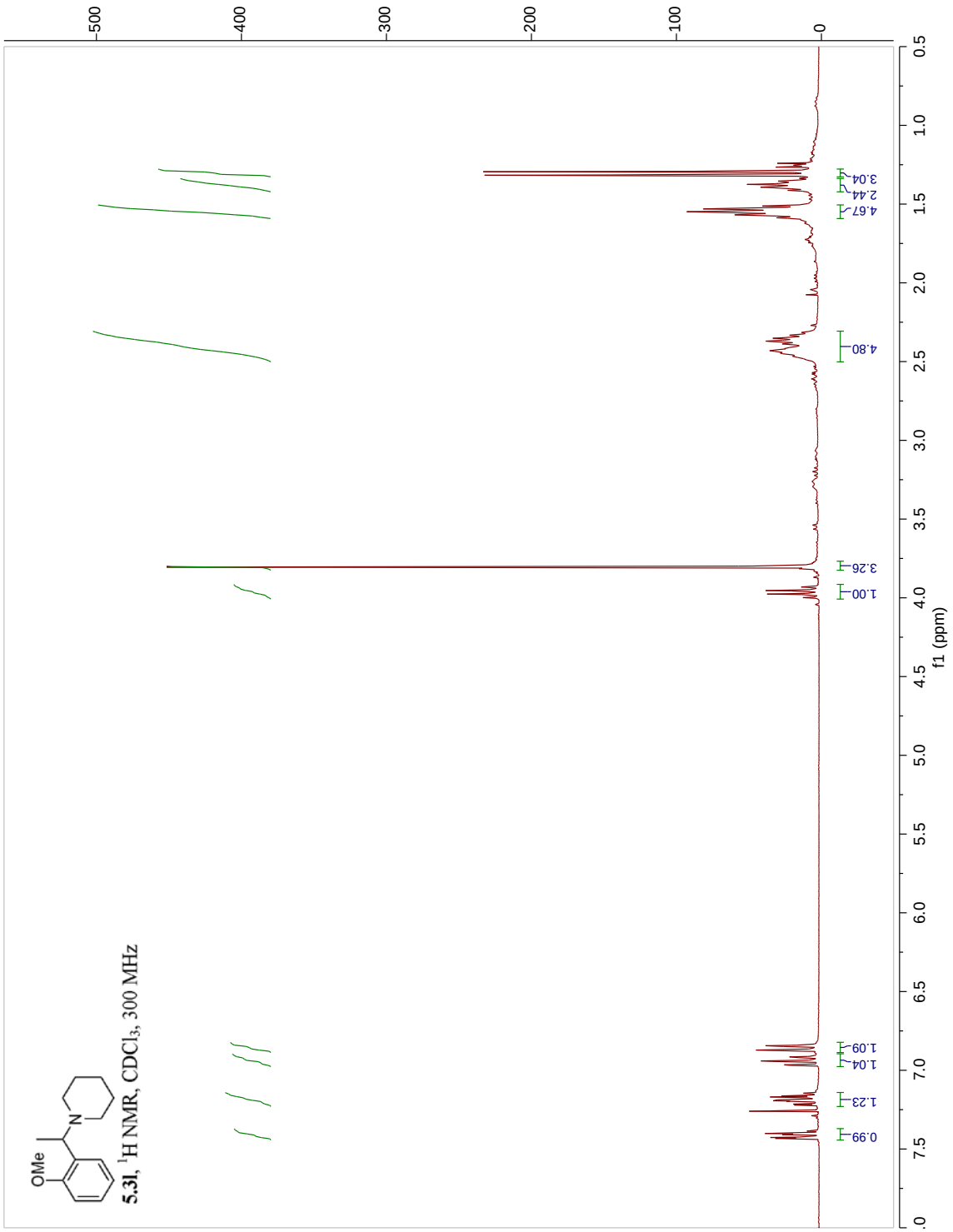

5.3i, ^{13}C NMR, $CDCl_3$, 75 MHz
N
143.65
136.02
130.37
126.83
126.18
125.94
60.91
51.81
26.48
24.88
19.70
18.56
f1 (ppm)

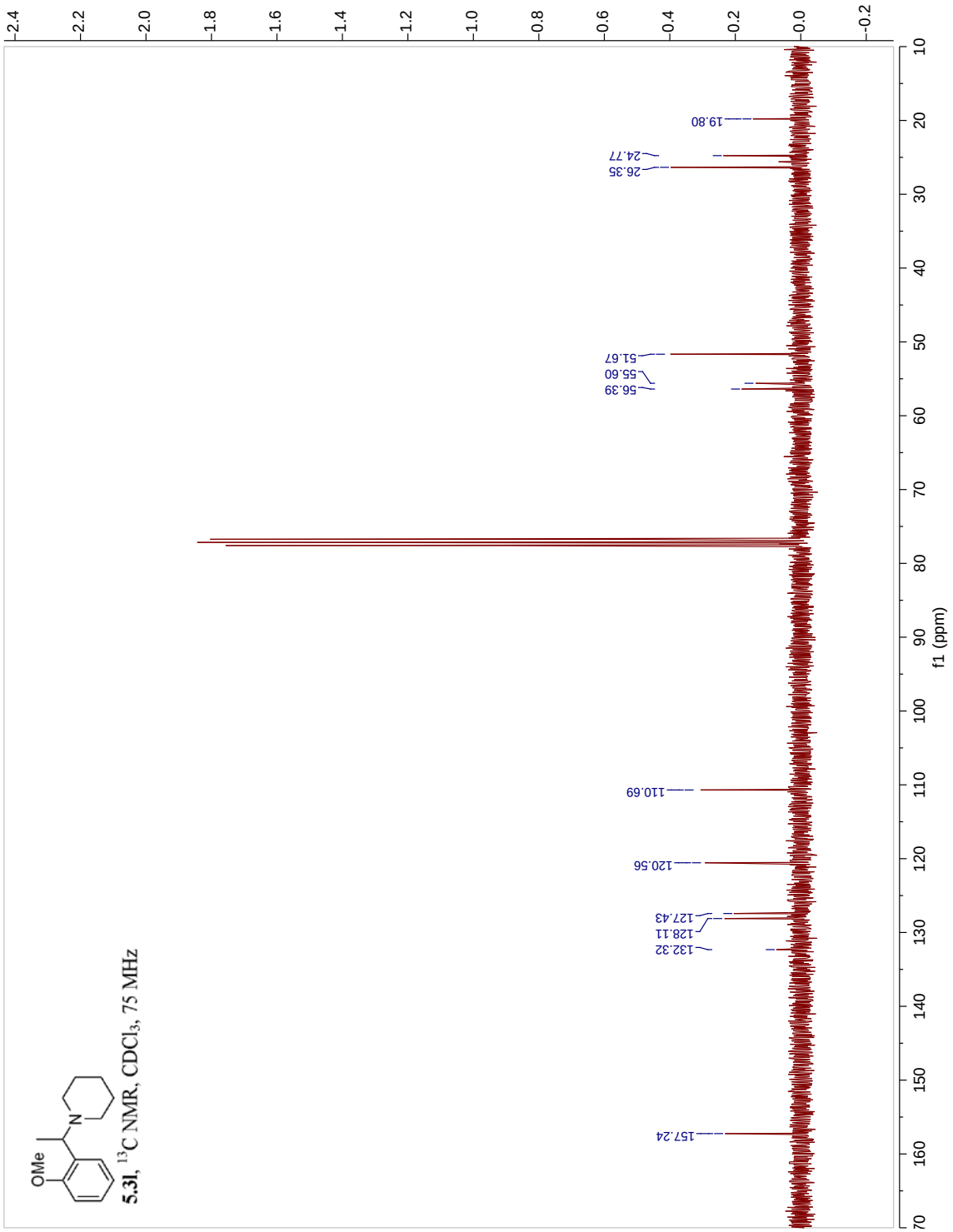

MeO
N
5.3j, ^{1}H NMR, $CDCl_3$, 300 MHz
4.76
3.92
3.87
1.00
2.72
0.92
1.74
0.92
f1 (ppm)


5.3j, ^{13}C NMR, $CDCl_3$, 75 MHz
MeO
N
159.54
145.94
128.98
120.24
113.48
111.87
65.27
55.19
51.62
26.36
24.70
19.56
f1 (ppm)


MeO
5.3k, ^{1}H NMR, $CDCl_3$, 300 MHz
4.99
4.05
3.83
1.00
2.81
1.80
1.77
f1 (ppm)


MeO
N
5.3k, ^{13}C NMR, $CDCl_3$, 75 MHz
158.47
135.73
128.92
113.42
64.55
55.30
51.47
26.34
24.71
19.43
f1 (ppm)


OMe
N
5.31, ^{1}H NMR, $CDCl_3$, 300 MHz
f1 (ppm)
0.99
1.23
1.04
1.09
1.00
3.26
4.80
4.67
2.44
3.04


OMe
N
5.31, ^{13}C NMR, $CDCl_3$, 75 MHz
157.24
132.32
128.11
127.43
120.56
110.69
56.39
55.60
51.67
26.35
24.77
19.80
f1 (ppm)

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