Diels-Alder reactions of *N*-tosyl-2-vinylpyrrole

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Leah Leone Groess

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Professor Wayland E. Noland
University of Minnesota Chemistry Department

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Dedication

I dedicate my dissertation to my husband Brian, who has supported me in every way possible, and my wifey Kate, who knows and understands the difficulties in working towards a Ph.D.

Abstract

Many compounds containing an indole ring system have important biological and chemical significance. There are several biologically active indole-containing natural products as well as synthetic products and many indole-containing compounds have pharmaceutical applications. Research is being done to find new methods of synthesizing indole compounds with the goal of developing pathways towards natural products as well as providing access to potential anticancer drugs. The Diels-Alder reaction using vinylpyrroles is an efficient and often high-yielding way to make the indole ring system as well as setting the stereochemistry. While most Diels-Alder products from vinylpyrroles rearrange to reform the aromatic pyrrole ring, reaction of *N*-tosyl-2-vinylpyrrole with dienophiles gives an unrearranged Diels-Alder adduct. The unrearranged adduct is stable enough to be isolated and stored but is reactive enough to undergo other reactions, potentially leading to new compounds. One such case is the hydroperoxidation of the Diels-Alder adduct, when it reacts readily with oxygen from the air to form an autoxidation product. This pathway is being explored as a way to increase the functionality and variety of compounds potentially available.

Table of contents

List of Tables

Appendix

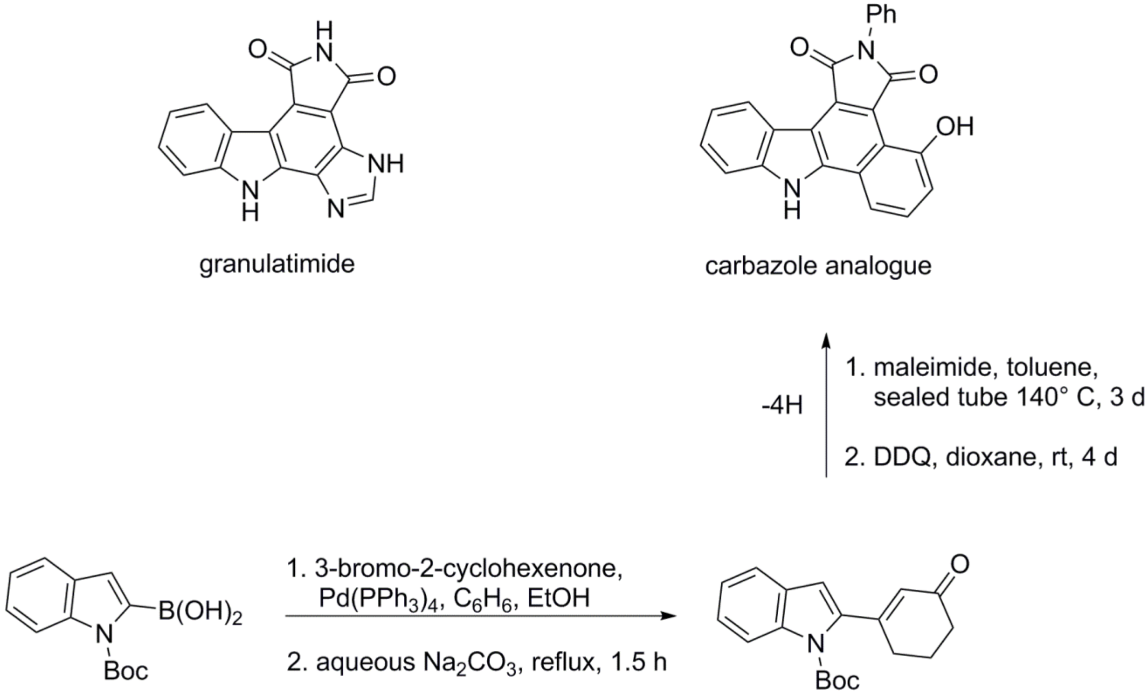
Appendix

List of Figures and Schemes

Background

An indole substructure is highly prevalent in a number of biologically active compounds, both in natural[1] and synthetic[2] molecules. The activity in these compounds ranges from antibacterial, antifungal, antitubercular, antitumor, and other properties.[3] Because of the wide variety of medical uses for indole compounds, there is interest in finding different methods of synthesizing them[4] and their analogs,[5] for research into drug design as well as natural product synthesis. Granulatimide (Scheme 1), is an indole-containing compound with a maleimide side group[6] and is one of the well-researched compounds with anticancer activity. The structure of this compound is such that a Diels-Alder[7] reaction between vinylindoles and maleimides[8] can form a reasonable analog.

Scheme 1: Granulatimide and analogue synthesis[8a]



The Noland group has a history of research into the Diels-Alder reaction of vinylindoles with dienophiles to form carbazoles. This work includes *in situ* formation of vinylindoles for use in a Diels-Alder reaction,[9] Diels-Alder reactions of vinylindoles with linear dienophiles,[10] and of nitro-containing vinylindoles to facilitate easy aromatization of the final product.[11] As analogs to the vinylindoles-Diels-Alder products, adducts from a reaction of vinylpyrroles, vinylthiophenes, or vinylfurans with dienophiles may also have significant biological activity.[12] The Diels-Alder reaction of 2-and 3-vinylpyrroles as a means of forming biologically active indoles has also been explored.[13]

Part I. Diels-Alder reaction of *N*-tosyl-2-vinylpyrroles

1.1 Introduction

The Diels-Alder reaction of vinylindoles has been studied extensively, with varying dienophiles. 2-and 3-Vinylindoles[14,15] have been used as dienes, and the dienophiles have been varied from cyclic to acyclic[16] to highly conjugated systems. In order to increase efficiency and yield, several catalysts[17] have been tried, and use of vinylindoles formed *in situ* as dienes in Diels-Alder reaction systems has been explored.[9] To parallel the work done with vinylindoles, work has been done with nitro-containing vinylpyrroles,[18] *in situ* reactions,[19] and catalyzed Diels-Alder reactions of vinyldihydropyrroles.[20]

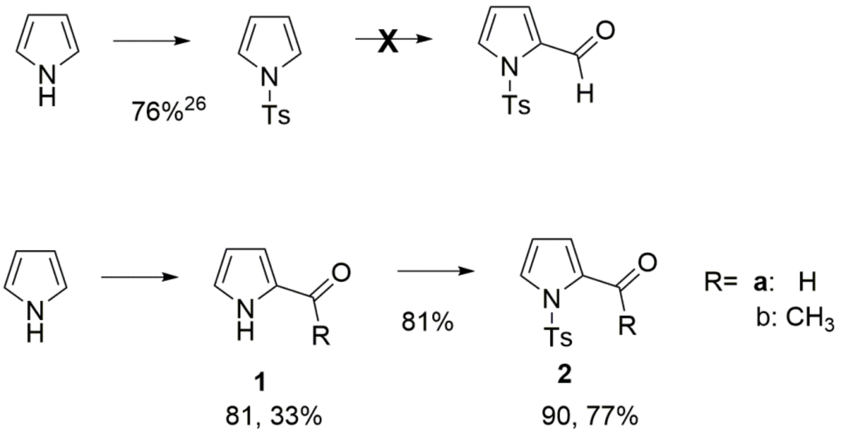
2-Vinylpyrroles undergo Diels-Alder reactions quite readily, and the adducts have a variety of biological activities.[19a , 21]The adducts of *N*-tosyl-3-vinylpyrroles, in particular, have great potential in antitumor applications.[19b] The Diels-Alder reactions of *N*-tosyl-2-vinylpyrroles may give adducts with similar biological activity. There has been only one reported case of the Diels-Alder reaction of *N*-phenylsulfonyl-2-vinylpyrroles,[22] so there is plenty of work to be done in this area.

1.2 Synthesis of starting materials

Vinylpyrroles can be synthesized in a number of ways. Because vinylpyrroles are highly reactive, it is important to use methods that don’t favor polymerization, such as avoiding exposure to acid.[23] For many vinylpyrroles, such as *N*-methylpyrrole, the *N*-substituent is attatched before the pyrrole ring is acetylated. When the *N*-substituent is particularly electron-withdrawing, such as with a phenylsulfonyl group, the overall reactivity of the pyrrole ring decreases.[22] A more stable pyrrole is easier to handle in lab but more difficult to substitute when desired.

While pyrrole typically undergoes electrophilic substitution at the 2-position, an electron-withdrawing *N*-substituent allows the substitution to occur at either the 2-or 3-positions, but the overall yield of the reaction decreases.[24] The increased reactivity of the 3 carbon has been used to selectively form the 3-substituted pyrrole when a Lewis acid is used in the acylation step.[25] Substitution at the *N*- position of the pyrrole ring is accomplished whether or not the pyrrole is acylated, so it is possible to obtain high yields when an acylpyrrole is *N*-sulfonylated rather than a sulfonylated pyrrole undergoing an acylation (Scheme 2).

Scheme 2: Order of reactions

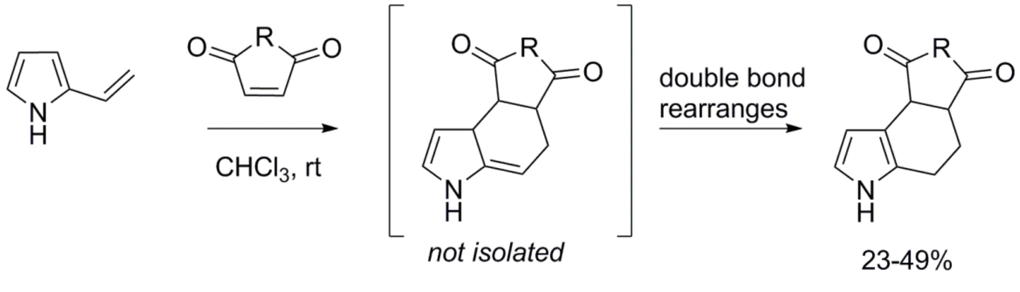


Traditionally, vinlypyrroles are synthesized by a Wittig reaction,[26, 27] which creates a significant amount of material waste due to the formation of triphenylphosphine oxide. Due to the reactivity of vinylpyrroles, especially when exposed to acid, separation by column chromatography using silica gel as the solid can cause polymerization, but basic alumina is less reactive with acid-sensitive compounds. An alternative method of forming an olefin is to alkylate the carbonyl using a Grignard reaction followed by dehydration. This method was pursued, but the low yields and difficulty of purifying the products favored the use of the Wittig reaction to form the vinylpyrrole.

1.3 Diels-Alder reaction and rearrangement

The nature of the *N*-substituent of the vinylpyrrole can greatly affect its reactivity as a diene in a Diels-Alder reaction. The stabilizing nature of the tosyl group makes the *N*-tosylated reagent easier to store and handle, because its reactivity decreases when compared with *N*-H or *N*-alkyl vinylpyrroles. The standard method[13a] for performing Diels-Alder reactions with vinylpyrroles is to reflux the reagents in chloroform, toluene, or xylene. This method produces a rearranged adduct as the sole product from 2-vinylpyrroles (Scheme 3).

<u>Scheme 3: Rearrangement of Diels-Alder adducts</u>



Xiao and Ketcha[22] have performed Diels-Alder reactions of *N*-phenylsulfonyl-2-vinylpyrroles in refluxing toluene and obtained only the rearranged adduct. Unrearranged adducts were obtained in some Diels-Alder reactions of vinylindoles[16] and from *N*-tosyl-3-vinylpyrroles,[13b] but no other unrearranged adducts have been isolated from the Diels-

Alder reaction of 2-vinylpyrroles. Unrearranged adducts have been observed in the Diels-Alder reaction of *N*-tosyl-2-vinyldihydropyrroles[20,28] and dienophiles. When *N*-tosyl-2-vinylpyrroles were refluxed in chloroform with maleimides, both rearranged and unrearranged adducts were isolated. High yields of the unrearranged adduct were obtained because the product precipitates before rearranging. Heating the unrearranged adducts to cause them to dissolve allows rearrangement in high yields.

N-Tosyl-2-vinylpyrrole **3** reacted with maleimides **5a-i** and maleic anhydride **5j** in chloroform at room temperature or reflux, and with **5a** in refluxing toluene (Scheme 4). The unrearranged adduct precipitate was separated by filtration and the remaining products were purified by column chromatography on silica gel and crystallized. When **3** and **5a** were refluxed in chloroform or toluene, the reaction produced both Diels-Alder adduct **6** and rearranged adduct **16**. In refluxing chloroform, **3** and **5b** produced only the rearranged adduct **16**. Further Diels-Alder reactions were run at room temperature to maximize the yield of unrearranged adducts **6-15**, monitored by TLC.

Scheme 4: Diels-Alder reaction of *N*-tosyl-2-vinylpyrrole

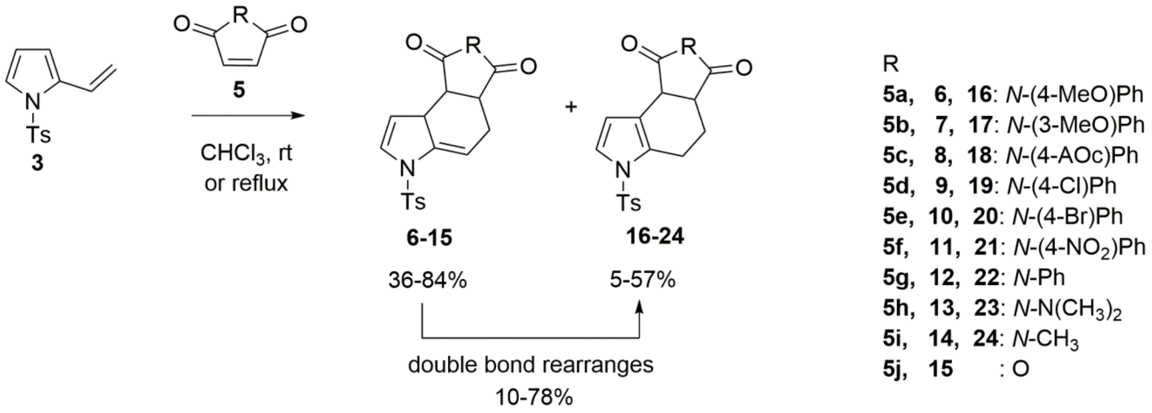


Table 1: Diels-Alder yields of 3 and 5a-j

		Diels-Alder reaction				rearrangement of adduct			
dienophile	**R**	**conditions[a]**	**time**	**product**	**yield %**	**conditions[a]**	**time**	**product**	**yield %**
5a	*N*-(4-MeO)Ph	A	5h	**6**	13	-	-	-	-
				16	54	-	-	-	-
		B	5h	**6**	54	A	2h	**16**	61
				16	13	-	-	-	-
		C	11d	**6**	69	-	-	-	-
5b	*N*-(3-MeO)Ph	B	24h	**17**	57	-	-	-	-
		C	6d	**7**	83	-	-	-	-
				17	5	-	-	-	-
5c	*N*-(4-AOc)Ph	B	4h	**8**	28	-	-	-	-
				18	18	-	-	-	-
		C	5d	**8**	36	A	2h	-	-
5d	*N*-(4-Cl)Ph	C	2d	**9**	72	B	6d	**19**	53
5e	*N*-(4-Br)Ph	C	6d	**10**	84	B	4h	**20**	13
5f	*N*-(4-NO$_2$)Ph	C	7d	**11**	76	C	13d	**21**	65
5g	*N*-Ph	B	5h	**12**	50	C	1.5h	**22**	43
		B	7h	**22**	55	-	-	-	-
5h	*N*-N(CH$_3$)$_2$	C	6d	**13**	39	-	-	-	-
				23	16	-	-	-	-
5i	*N*-CH$_3$	C	6d	**14**	37	D	4d	**24**	10
5j	O	C	24h	**15**	77	-	-		

a: A: PhCH$_3$ reflux, B: CHCl$_3$ reflux, C: CHCl$_3$ rt, D: CH$_2$Cl$_2$ reflux

*Reaction stirred at reflux for 2 h, then kept at room temperature overnight, and refluxed again for 5 h

Isolation of the unrearranged Diels-Alder adducts is desirable because they can be used in further reactions to determine the rearrangement mechanism. In related rearrangements of the adducts from Diels-Alder reactions of vinylindoles, the mechanism is always referred to as a 1,3-hydride shift. While references are made that such hydrogen shifts are not symmetry-allowed,[29] no positive explanation of the reaction is given. While an acid-catalyzed hydrogen shift is formally allowed,[30] the rearrangement has been observed in neutral solutions. Chloroform can be slightly acidic, possibly sufficiently enough to catalyze the rearrangement of the Diels-Alder adducts, but the rearrangement occurs more readily in refluxing toluene, which is neutral but warmer.

N-(*p*-toluenesulfonyl)-2 (prop-1-en-2-yl)-pyrrole **4** was refluxed with maleimides **5a** and **5g** in chloroform (Scheme 5). Due to the decreased reactivity of the 2'-substituted vinylpyrrole, the reaction required a higher temperature. The reaction between **4** and **5a** produced rearranged adduct **25** and fully aromatized compound **27**. The reaction between **4** and **5g** produced rearranged adduct **26**.

Scheme 5: Diels-Alder reactions of *N*-tosyl-2-isoprenylpyrrole

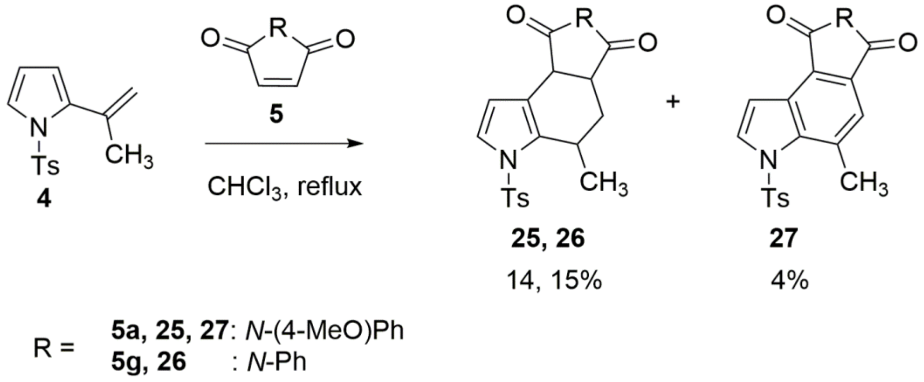


Table 2: Diels-Alder yields of 4 and 5a,g

		Diels-Alder Reaction			
dienophile	**R**	**conditions**	**time**	**product**	**yield %**
5a	*N*-(4-MeO)Ph	$CHCl_3$ reflux	6d	**25**	14
				27	4
5g	*N*-Ph	$CHCl_3$ reflux	25d	**26**	15

There are several possible ways that the tosyl group could affect the reactivity of vinylpyrroles. Pyrroles with electron-withdrawing substituents have been used as dienophiles in normal electron demand [4+2] cycloadditions.[31] An *N*-tosyl group gave moderate yields while *N*-triflylpyrroles gave increased yields, showing that an *N*-tosyl group is an effective electron-withdrawing substituent. This indicates that the subsituent on the pyrrole nitrogen can have a great effect on the energy levels of the compound.

While electronegative substituents on a diene may decrease its reactivity, the bulky nature of the tosyl group may slow the reaction by impeding free rotation of the vinyl group, keeping the diene from assuming a conformation that favors Diels-Alder reactions (Scheme 6). The decrease in reactivity only holds true for 2’-substituted vinylpyrroles, as the increase in size of the substituent would hold the alkene in an *s-anti* conformation, decreasing reactivity significantly. A methyl substituent on the vinyl group is sufficient to decrease yield and increase reaction time.

Scheme 6: Interaction of tosyl and vinyl groups

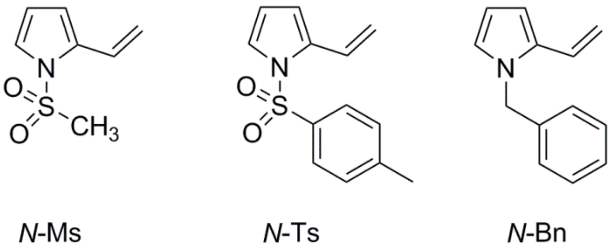
preferred *s-syn* conformation

preferred *s-anti* conformation

A way to determine whether steric or electronics effects have a greater affect would be to make *N*-methylsulfonyl (*N*-mesyl) as well as *N*-benzyl derivatives of 2-vinylpyrrole and observe any changes in their reactivity (Scheme 7). An *N*-Ms group would keep the electron-withdrawing sulfonyl but be significantly less bulky than a tosyl group. An *N*-benzyl substituent would maintain the bulky nature of a phenyl group but decrease the electronegativity. Attempts to synthesize *N*-mesyl-2-vinylpyrrole from *N*-

mesyl-2-pyrrolecarboxaldehyde gave unidentifiable black flakes as the only product. Attempts to synthesize *N*-benzyl-2-pyrrolecarboxaldehyde were not pursued.

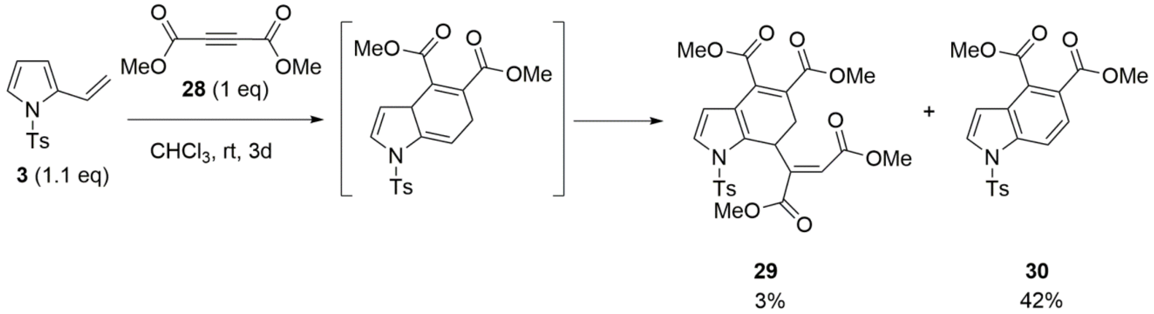
Scheme 7: Alternate *N*-substituents



1.4 Reaction with dimethyl acetylenedicarboxylate (DMAD)

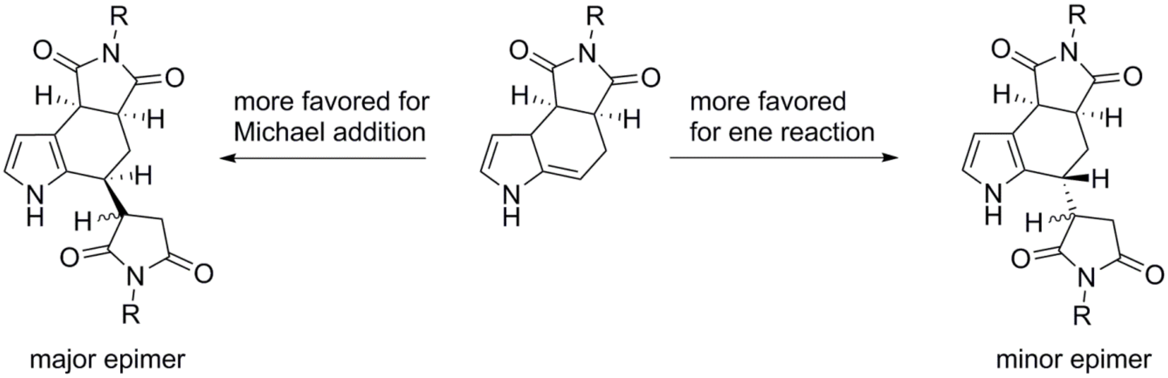
A reaction of *N*-tosyl-2-vinylpyrrole **3** with DMAD **28** gave a Michael adduct **29** and the fully aromatized Diels-Alder adduct **30** (Scheme 8). The Michael adduct was likely formed from the initial Diels-Alder adduct, which was not observed. The aromatized adduct **30** was the major product, which is readily obtained by elimination of dimethyl maleate or fumarate from the Michael adduct. Reactions between DMAD and *N*-Me-2-vinylpyrroles have been found to form Michael adducts where 2,5-disubstitued pyrroles were observed instead of the expected Diels-Alder adducts from other dienophiles.[12, 32] This demonstrates the tendency of DMAD to undergo Michael addition reactions.

Scheme 8: Diels-Alder reaction with DMAD



Michael adducts have also been isolated from Diels-Alder reactions of N-alkyl-2-vinylpyrroles with maleimides,[13a] where a mechanism for formation of these Michael adducts was determined using their isomeric ratios (Scheme 9). The ratios of the major and minor products correspond to a Michael addition and hydrogen transfer rather than a concerted ene-type reaction. These byproducts were not observed in the Diels-Alder reactions of N-tosyl-3-vinylpyrroles with maleimides,[13b] suggesting that the 3-vinylpyrrole adduct is less reactive than its indole and 2-vinylpyrrole counterparts, or that the *N*-tosyl group reduces the reactivity of the adducts.

Scheme 9: Michael addition precedent



Aside from the reaction with DMAD, Michael addition products were not observed in the *N*-tosyl-2-vinylpyrrole Diels-Alder reactions. The unrearranged adduct was refluxed in chloroform with excess maleimide to maximize potential Michael addition, but no reaction was observed. With microscale reactions, faintly visible spots on TLC suggested that the rearranged adduct may form Michael addition products when refluxed with maleimide, but a scaled up procedure showed no reaction. This demonstrates that the unrearranged adducts do not react with less reactive maleimides.

1.5 Conclusion

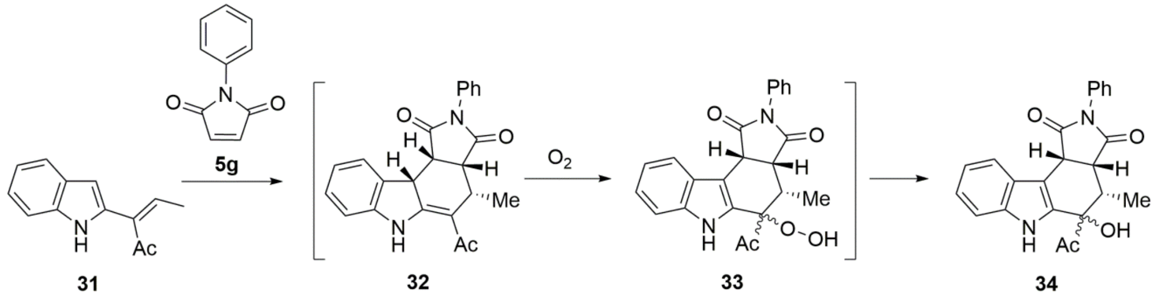
N-Tosyl-2-vinylpyrrole is a stable reagent that will readily undergo Diels-Alder reactions. The decreased reactivity enables the isolation of the unrearranged adduct, which can undergo further reactions. This can be used to investigate the rearrangement mechanism of Diels-Alder adducts of vinylpyrroles. Exploration into tuning the reactivity of vinylpyrroles based on the *N*-substituents is an intriguing future project.

Part II. Hydroperoxides and radical rearrangement

2.1 Introduction

Michael additions and ene reactions have been observed in previous Diels-Alder reactions, and alcohol product **34** was observed from the Diels-Alder reaction of vinylindole **31** and *N*-phenylmaleimide **5g**.[33b] Eitel and Pindur concluded that the Diels-Alder adduct **32** reacted with singlet oxygen to form hydroperoxide **33**, which then formed alcohol **34** (Scheme 10). The stereochemistry of the alcohol was not determined. Diels-Alder adducts from benzofurans and *N*-phenylmaleimide have been found to react with oxygen to form isolable hydroperoxides when exposed to air.[34]

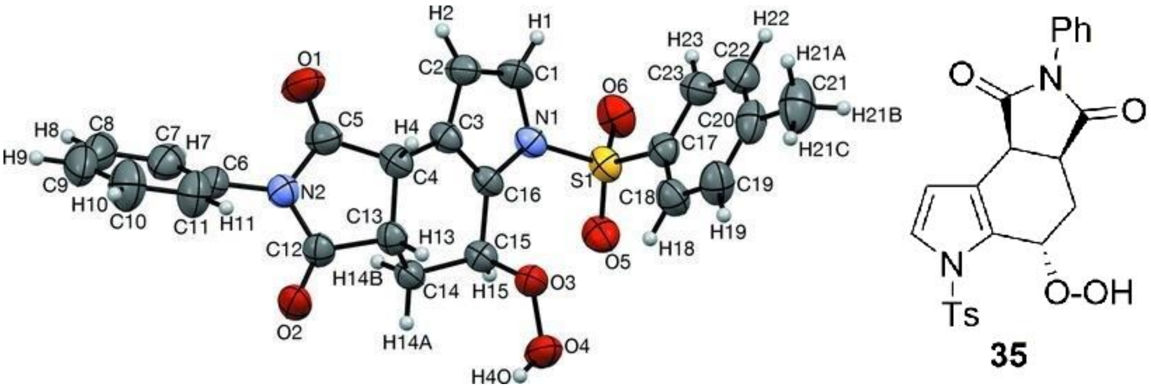
Scheme 10: Formation of an alcohol byproduct



2.2 Hydroperoxides

A hydroperoxide was first observed as a byproduct of the Diels-Alder reaction between *N*-tosyl-2-vinylpyrrole **3** and *N*-phenylmaleimide **5g** after purification by column chromatography on silica gel. The separated fractions were cooled in a freezer to promote crystallization, and the hydroperoxide **35** was the only crystalline product isolated. The structure was determined by X-ray crystallography (Fig 1).[35] ^1H NMR analysis of the mother liquor showed that the corresponding epimer remained in solution.

Figure 1: Crystal structure of hydroperoxide byproduct 35



Four other hydroperoxide byproducts were isolated in other Diels-Alder reactions of *N*-tosyl-2-vinylpyrrole (Scheme 11) and evidence of 11 others was observed in the crude NMR spectra of other reaction mixtures (Table 3).

Scheme 11: Hydroperoxide byproducts from Diels-Alder reactions

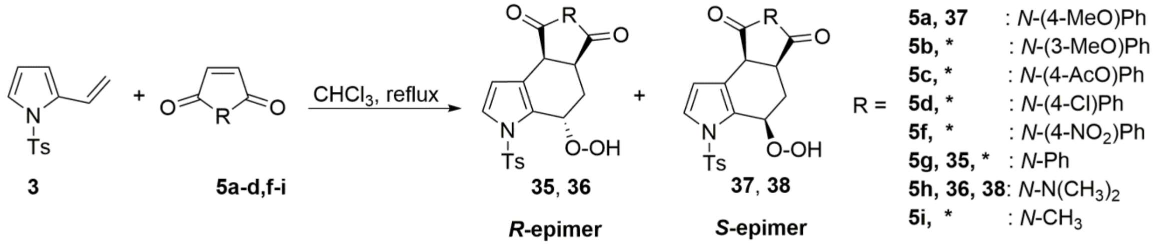


Table 3: Yields of hydroperoxides from Diels-Alder reaction

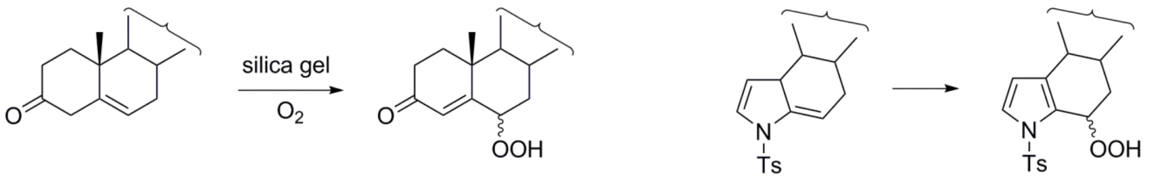
dienophile	R	*R*-epimer	yield %	*S*-epimer	yield %	molar Ratio *R*:*S*
5a	*N*-(4-MeO)Ph	*	-	**37**	17	1 : 1[a]
5b	*N*-(3-MeO)Ph	*	-	*	-	1 : 1[a]
5c	*N*-(4-AcO)Ph	*	-	*	-	1 : 1.9[a]
5d	*N*-(4-Cl)Ph	*	-	*	-	1 : 1.3[a]
5f	*N*-(4-NO_2)Ph	*	-	*	-	1.6 : 1[a]
5g	*N*-Ph	**35**	2	*	-	1 : 1[a]
5h	*N*-$N(CH_3)_2$	**36**	8	**38**	8	1 : 1
5i	*N*-CH_3	*	-	**-**	-	-

*product observed in crude NMR, not isolated

[a] ratio determined by crude NMR

Silica gel has been known to catalyze hydroperoxidation in steroidal β,γ-unsaturated ketones. Seto *et al*. established that stirring dissolved campestenone with silica gel in an oxygen atmosphere has served as a synthetic method leading to hydroperoxidation.[36] In certain steroids, hydroperoxidation transforms a β,γ-unsaturated ketone to a conjugated and more stable α,β-unsaturated ketone.[37] It is possible that the rearrangement to reform the aromatic pyrrole ring caused the Diels-Alder adduct to react similarly (Scheme 12). To test for comparible reactivity, the adduct was dissolved in chloroform with and without suspended silica gel in vessels exposed to air, and both solutions gave hydroperoxide. The silica gel is not necessary for and probably does not promote autoxidation in the Diels-Alder adduct.

Scheme 12: Stabilization comparison

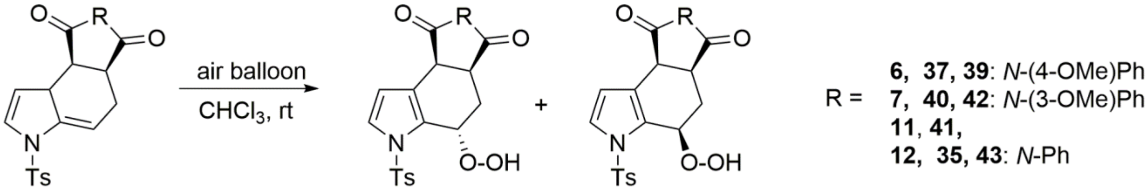


Formation of a more stable α,β saturated ketone

Re-formation of a stabilized aromatic ring

The unrearranged adduct was stirred in chloroform with air from a balloon to form the hydroperoxides. Yields up to 70% of hydroperoxide were observed from the *p*-methoxyphenyl adduct **6**, with the remainder of the product being rearranged adduct. Hydroperoxides with both *R* and *S* stereocenters were isolated. (Scheme 13). The products were isolable with column chromatography and then crystallization.

Scheme 13: Hydroperoxides from Diels-Alder adducts



6, **7**, **11**, **12**

35, 39-41

R-epimer

37, 42-43

S-epimer

Table 4: Yields of hydroperoxides from Diels-Alder adducts

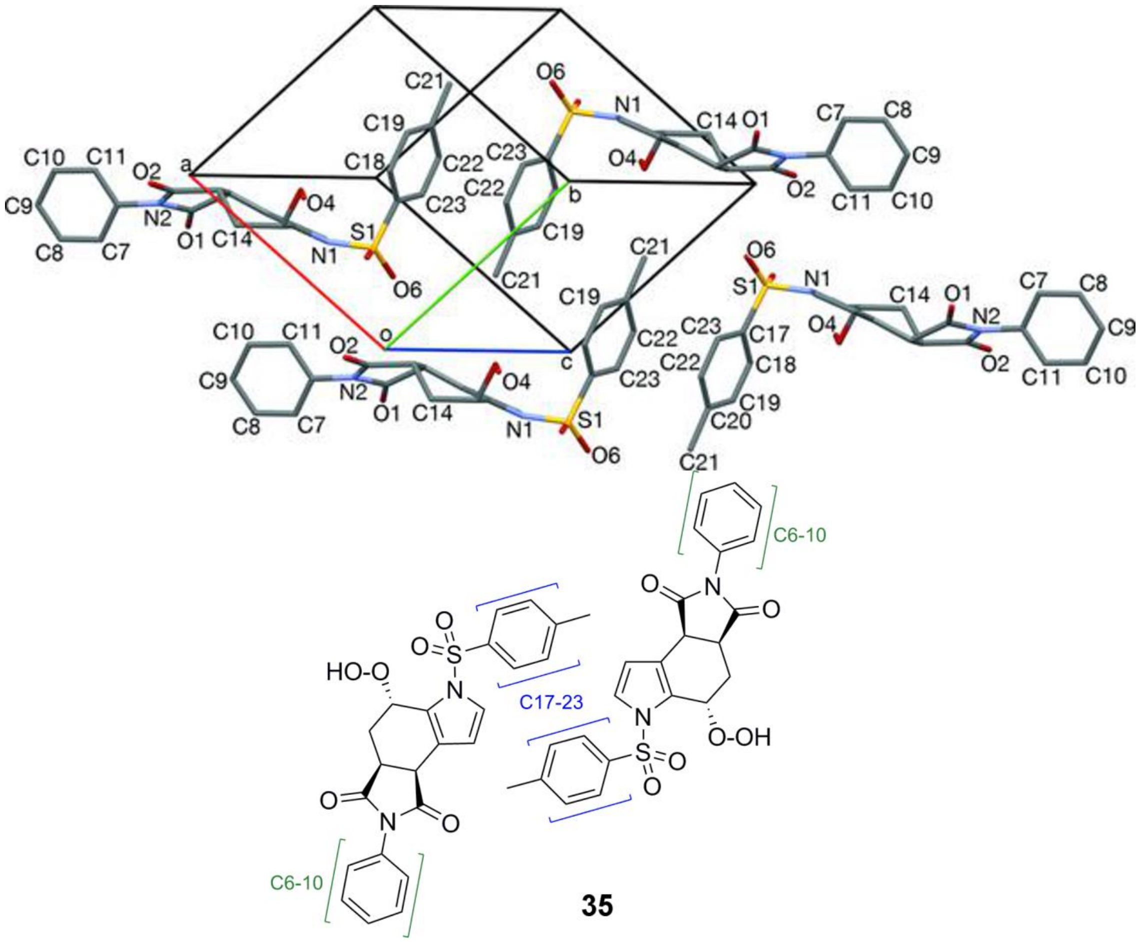
adduct	R	time	*R*-Isomer	yield %	*S*-Isomer	yield %	molar Ratio ***R*:*S***
6	*N*-(4-MeO)Ph	3d	**39**	21	**37**	39	1 : 1.4
7	*N*-(3-MeO)Ph	1d	**40**	4	**42**	25	1 : 6.3
11	*N*-(4-NO_2)Ph	13d	**41**	9	**-**	-	-
12	*N*-Ph	1d	**35**	53	**43**	17	3.1 : 1

The hydroperoxides reacted weakly in a starch-iodide test, confirming peroxide character but suggesting low reactivity. NMR spectra were taken of both epimers in deuterated chloroform with and without added deuterated water. The characteristic hydroperoxide ^{1}H peak between 9 and 10 ppm disappears when it is exposed to deuterated water, showing that the proton is readily exchangeable. NMR spectra of the crude reaction mixtures show approximately equal amounts of both epimers.

2.3 Crystal structure

Crystallographic analysis of the hydroperoxide **35** can give insight into the relative yields of hydroperoxide epimers. While crude NMR spectra indicate that approximately equal amounts of each epimer are formed initially, there is a difference in the relative amounts isolated. Hydroperoxide **35** crystallizes more readily than its epimer **43**, which was not able to be isolated in pure crystal form. The crystallographic analysis shows interlocking and stacking of tosyl groups (C17-C23) between adjacent molecules of **35**, contributing to a stable crystal structure (Figure 2).

Figure 2: Interlocked crystal structure of hydroperoxide 35

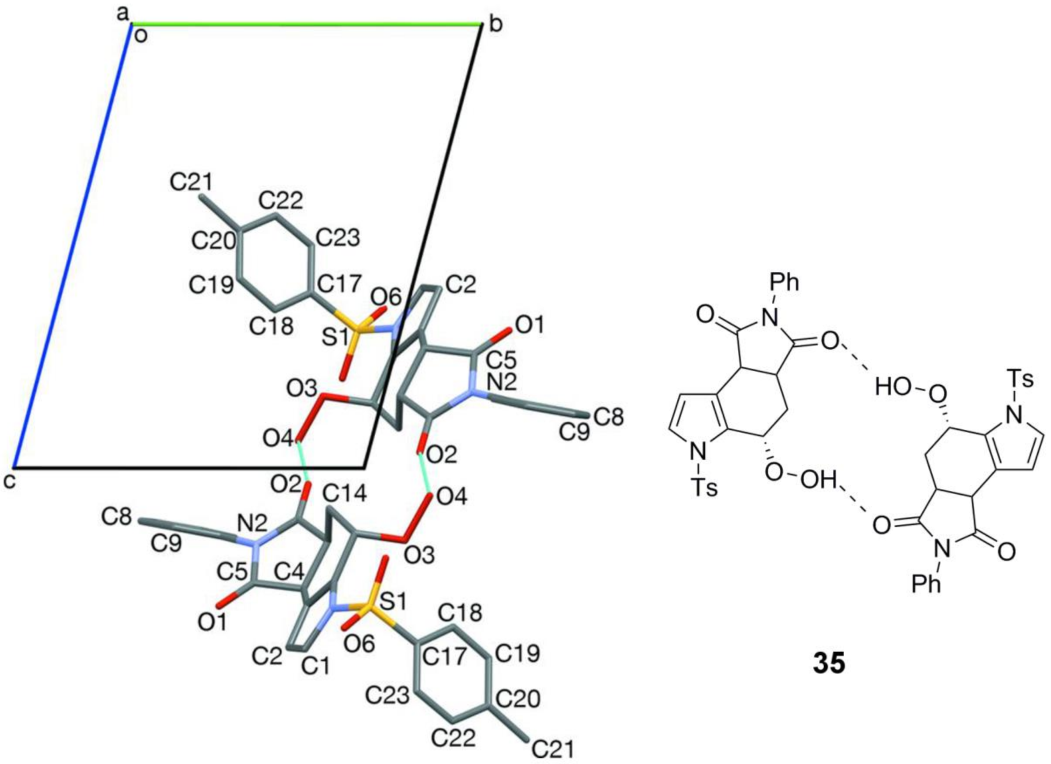


35

The increased tendency of **35** to crystallize may explain the differences in ratios of the epimers isolated. There is not much interaction between the phenyl groups in the crystal structure of **35**, but the methoxyphenyl substituted hydroperoxides **37**, **39**, **40**, and **42** may have different conformations. In **35**, the phenyl group (C6-C10) is twisted out of plane from the imido group, but introducing a substituent to the phenyl group could drive it further out of plane, or allow for better stacking. This would seem to account for the more equal ratio of the *p*-methoxyphenyl hydroperoxides **37** and **39** and the excess of the *m*-methoxyphenyl hydroperoxide *S* epimer **40** over **42**. Crystal structures for these compounds have not been studied, but would be necessary to test this theory.

Hydrogen bonding was observed between O4 of the hydroperoxide and the O2 carbonyl group in the crystal structure of **35** (Figure 3). The half chair conformation of the cyclohexene ring of **35** lines up the hydroperoxy groups with the O2 carbonyl in an adjacent molecule. The epimer **43** would not be as likely to have hydrogen bonding due to the hydroperoxide being on the opposite face of the cyclohexane ring. This is a likely explanation for the difference in solubility of the two epimers.

Figure 3: Hydrogen bonding in hydroperoxide 35

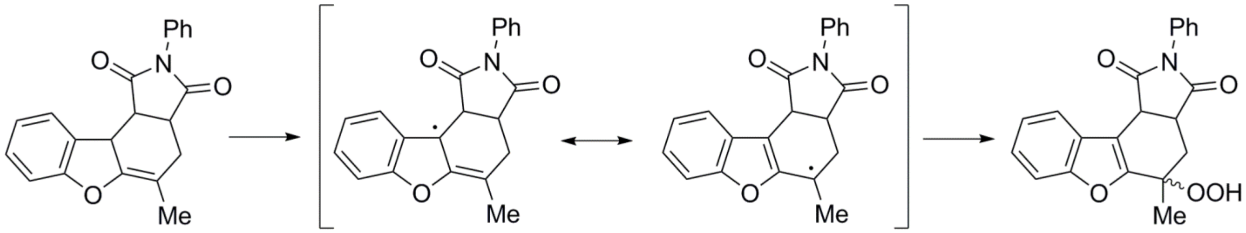


Organic peroxides are known to be highly shock-sensitive,[38] and great care must be taken when handling them or peroxide forming chemicals[39]. A hydroperoxide that is not shock-sensitive could be very useful for applications that a shock-sensitive peroxide would make dangerous. Hydroperoxide **35** did not react to a shock test.[35] It is possible that the stability of the crystal due to stacking rings (Figure 2) and hydrogen bonding (Figure 3) is sufficient to prevent the hydroperoxide from reacting to sudden shocks. As not all compounds were isolated to analytical purity, more testing would be required to see if the lack of shock-sensitivity is common to all of the hydroperoxides in this series.

2.4 Rearrangement and radical mechanism

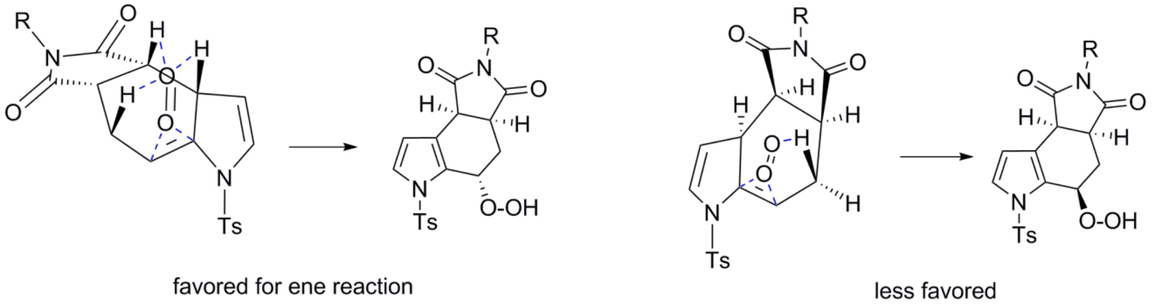
Multiple examples of hydroperoxide adducts have been isolated from the Diels-Alder reaction between 2-vinylbenzofurans and *N*-phenylmaleimide. Brewer and Elix[34] concluded that the hydroperoxides formed from a radical oxidation rather than an ene reaction with singlet oxygen. The rearrangement of the double bond greatly stabilizes the radical (Scheme 14). The proportions of hydroperoxide epimers did not vary greatly, which is consistent with a radical mechanism.

Scheme 14: Hydroperoxidation of vinylbenzofuran Diels-Alder adduct



Hydroperoxide formation is often attributed to an ene reaction between the Diels-Alder adduct and singlet oxygen.[33b,40] Ene reactions occur by singlet-oxygen forming biradical, zwitterionic, or perepoxide-like transition states.[41] In all of these cases, the β-substituted product would be preferred, due to the hydrogen bonding of the oxygen with the neighboring hydrogens in the ring system (Scheme 15). The β-face has three nearby hydrogens, while the α-face only has one. Additionally, the β-face is more accessible sterically whereas the α-face is crowded by the succinimide ring. If the reaction occurs by a singlet oxygen ene reaction, there should be an excess of the β-hydroperoxide. Because the epimers form in comparable amounts, the ene reaction does not fully explain the stereochemistry of the hydroperoxide adducts.

Scheme 15: Hydroperoxidation by ene reaction

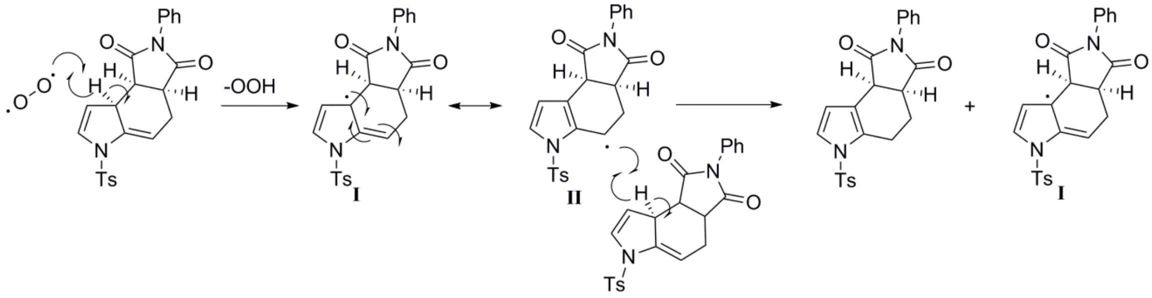


A singlet oxygen ene reaction can be disproved if the reaction is affected by radical inhibitors.[42] The unrearranged adduct was stirred in chloroform with radical inhibitor (BHT) with attached air balloon. No reaction was observed, with both TLC and NMR spectra showing only starting material after one day. With no radical inhibitor, the dissolved adduct begins to rearrange in hours. The lack of rearrangement in the presence of a radical inhibitor suggests that the rearrangement occurs by a radical mechanism, not by an ene reaction with singlet oxygen.

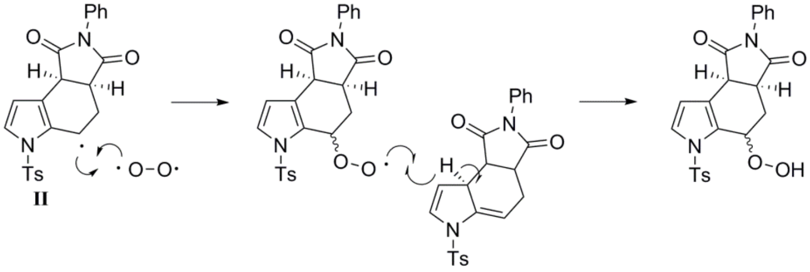
It is possible that the radical intermediate couples with triplet oxygen to form an adduct radical, which causes a chain reaction leading to either hydroperoxide or rearranged adduct (Scheme 16). When the Diels-Alder adduct was exposed to radical initiator AIBN (azobisisobutyronitrile), the product was mostly rearranged adduct with small amounts of hydroperoxides. Oxygen can act as a radical initiator, but when even a small amount of another initiator is present, rearrangement will happen more readily than oxidation.

Scheme 16: Hydroperoxide formation

Radical rearrangement:



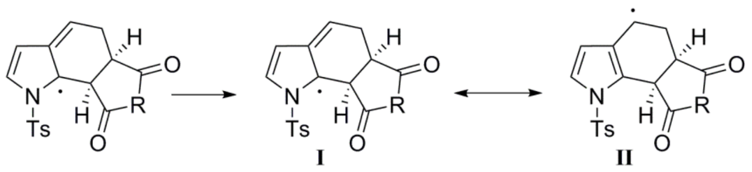
Formation of hydroperoxide



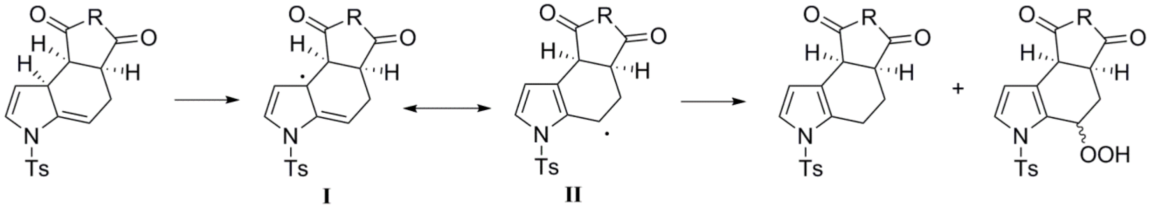
If a radical species is the intermediate between the unrearranged and rearranged adducts, hydroperoxides should be observed in other vinylpyrrole Diels-Alder reactions. When the *N*-substituent is alkyl or hydrogen, the only product isolated was rearranged adduct.[13, 14, 26, 32, 43] The rearrangement occurs too quickly to isolate the unrearranged adduct, suggesting that in some cases the unrearranged adduct is too short lived for the oxygen to attack.

The unrearranged adduct of *N*-tosyl-3-vinylpyrrole was isolable, and was tested for hydroperoxide formation. When dissolved in chloroform at room temperature and exposed to air, the 3-vinylpyrrole adduct gave no reaction. The adduct from *N*-tosyl-3-vinylpyrrole is less sensitive to radical reaction than the *N*-tosyl-2-vinylpyrrole adduct. The latter adduct would be doubly allylic and thus more stable than the singly allylic radical formed from the 3-vinyl adduct (Scheme 17).

Scheme 17: Radicals from 2-vinyl vs 3-vinylpyrrole adducts



singly allylic radical - does not form



doubly allylic radical*

*refer to scheme 16

2.5 Conclusion

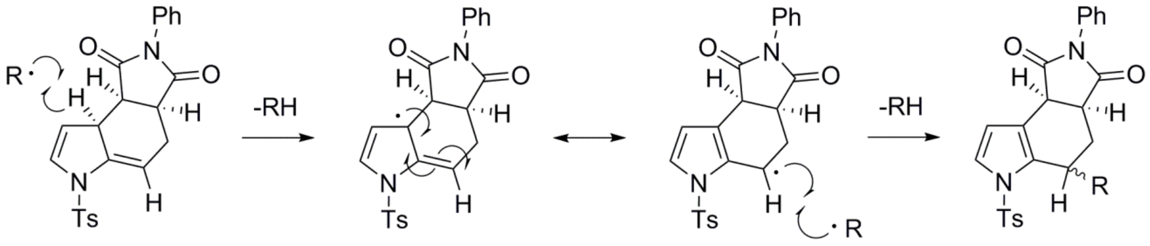
Hydroperoxides have been isolated from Diels-Alder reactions between *N*-tosyl-2-vinylpyrroles and maleimides. These hydroperoxides have been found to form from reaction of unrearranged Diels-Alder adducts and oxygen. Some hydroperoxides crystallize readily due to their stacking tosyl groups in the crystal structure. The most likely mechanism for hydroperoxide formation is a radical autoxidation reaction.

Part III. Halogenation of Diels-Alder adducts

3.1 Introduction

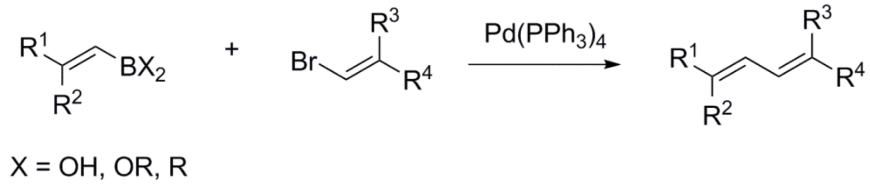
The introduction of a hydroperoxide group into the Diels-Alder adduct suggested that the substitution of different groups at the 5-position of the adduct could be possible (Scheme 18). Due to the proposed radical mechanism of hydroperoxidation and rearrangement, a reaction that has a radical mechanism would be an ideal study to further explore the theory. Using *N*-bromosuccinimide (NBS) to brominate the Diels-Alder adduct would add a useful substituent and investigate the radical reactivity of the adduct.[44]

Scheme 18: Radical substitution of unrearranged Diels-Alder adduct



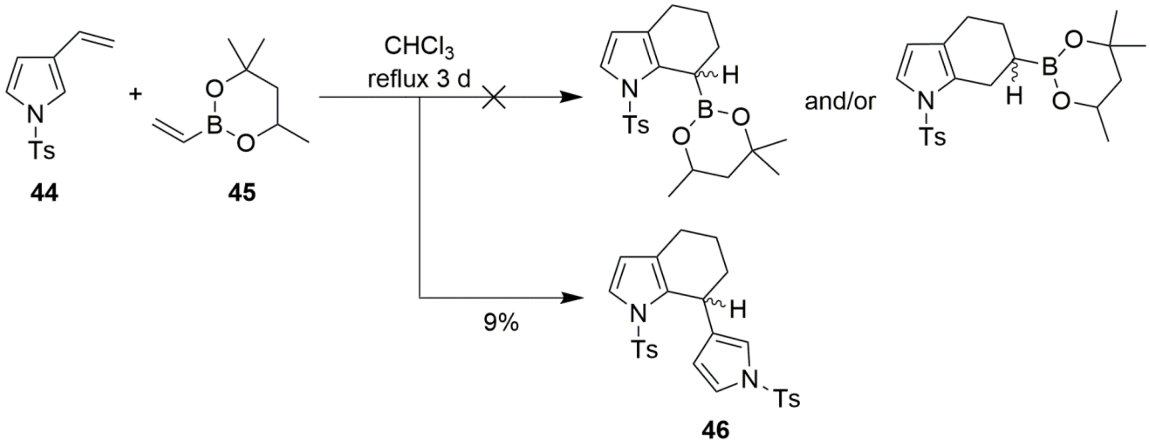
Bromine is a useful substituent due to the number of reactions that it participates in, particularly in carbon-carbon bond formations. A classic use for a brominated compound is in a Grignard reaction, where the magnesium halide reacts as a nucleophile to attack a carbonyl compound.[45] Several reactions that form carbon-carbon bonds use brominated compounds that react with palladium catalysts with examples including the Heck reaction,[46] the Stille coupling,[47] and the Suzuki coupling where a halide couples with a boronic acid (Scheme 19).[48]

Scheme 19: Suzuki coupling



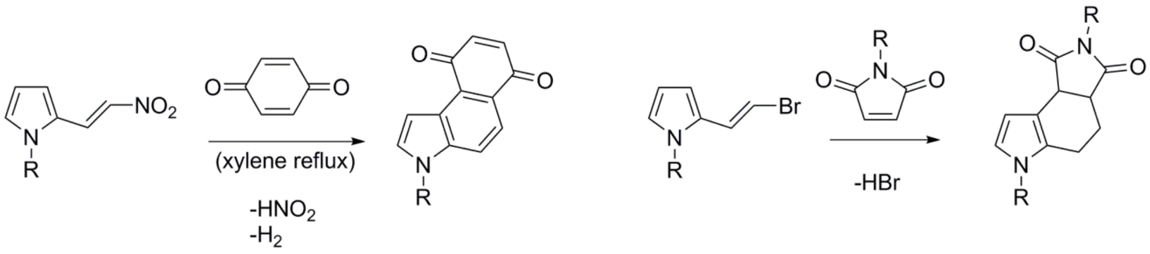
The Noland lab has explored the synthesis of Suzuki precursors in the attempted Diels-Alder reaction of tosylated vinylpyrrole **44** and vinylboronic acid **45**.[13b] Rather than vinylboronic acid **45** acting as a dienophile, two molecules of vinylpyrrole **44** undergo a Diels-Alder reaction to form dimer **46** (Scheme 20). Side reactions involving starting materials can be avoided by adding the reactive substituent after the Diels-Alder reaction. Due to the many methods of bromination,[49] attempting a synthesis of a bromide may be more successful than a boronated adduct.

Scheme 20: Attempted synthesis of Suzuki precursor[13b]



Bromine-containing compounds are useful in nucleophilic reactions. Bromide is a good leaving group, so a bromine-containing adduct could be susceptible to both substitution and elimination reactions. This could be useful for further reactions of the adducts. No reports of Diels-Alder adducts from vinylpyrroles or vinylindoles have been found to have a bromine substituent on the 4- or 5- position, and there are few reports of successful bromination of an indolocarbazole[50] It is likely that any bromine-substituted vinylpyrrole or indole undergoing a Diels-Alder reaction would eliminate HBr similar to the elimination of NO_2 in the Diels-Alder reaction of a nitro-containing vinylpyrrole (Scheme 21).[11a]

Scheme 21: Elimination of sidegroup during Diels-Alder reaction[11b]



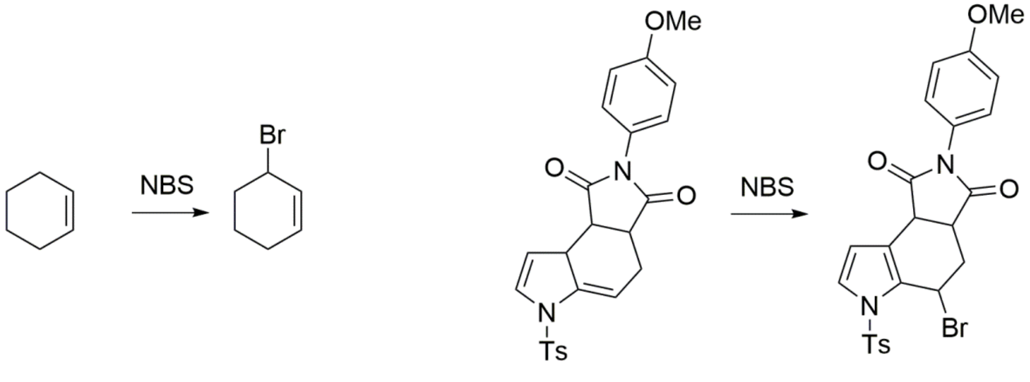
Elimination of nitro group

Elimination of bromo group

3.2 Reaction with *N*-bromosuccinimide (NBS)

NBS is an excellent brominating agent due to its low cost, solid state, stability and ease of use.[51] Bromination with Br_2 can give dibromo compounds, which are not desired in this case.[52] NBS is an excellent reagent for allylic bromination[53] of compounds such as the Diels-Alder adduct **6** (Scheme 22). The double bond would most likely rearrange to give an adduct **47** containing a rearomatized pyrrole ring, as is seen in other reactions.[11,12,22, 26, 32]

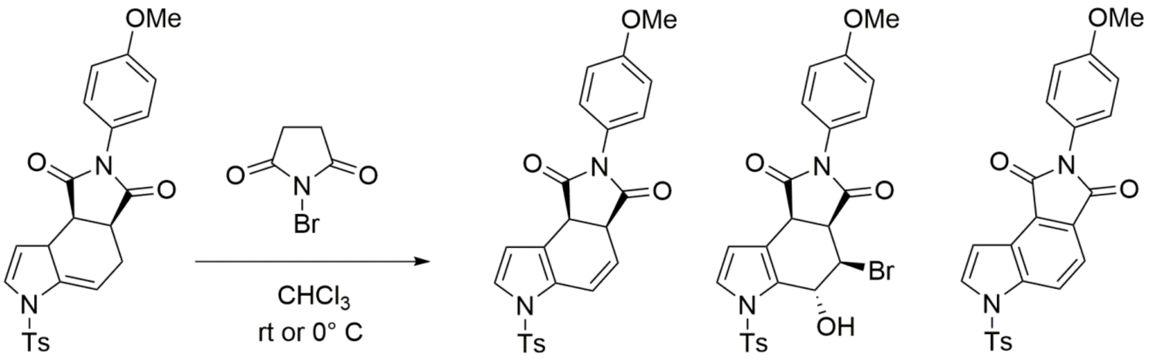
Scheme 22: Allylic bromination with NBS



6 **47**

NBS was added to a solution of Diels-Alder adduct **6** under various conditions (Scheme 23). At room temperature over three hours, the only product observed was bromohydrin **49**. The reaction, when cooled in an ice bath, gave the partially oxidized adduct **48**, bromohydrin **49**, and fully aromatized adduct **50**. The expected brominated product **47** was not observed in any of the reactions. The bromohydrin **49** and partially oxidized product **48** were difficult to purify due to co-crystallization with the succinimide formed in the reaction.

Scheme 23: Reaction of the Diels-Alder adduct 6 with NBS



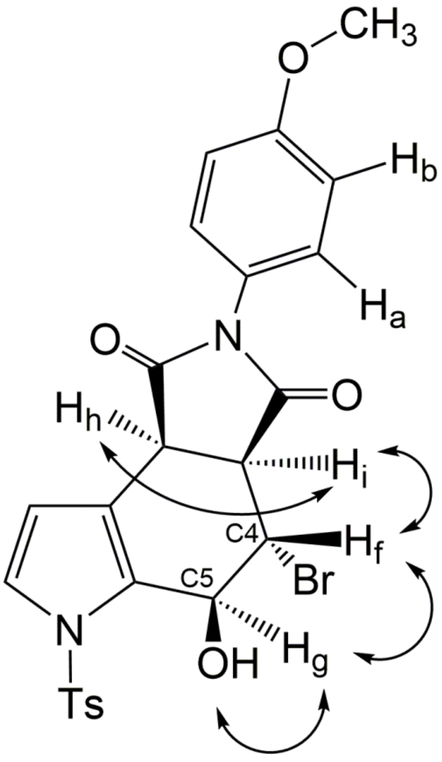
6 **48** **49** **50**

Table 5: Reaction of Diels-Alder adduct with NBS

Temperature	Time	NBS	Yield % 48	Yield % 49	Yield % 50
rt	3 h	2 eq.	0	11	0
0°	3 h	1 eq.	41	14	6
0°	1.5 h	1 eq.	21	22	6

The regiochemistry of bromohydrin **49** was confirmed by ^{1}H NMR COSY interactions (Figure 4). Based on typical ppm values, H*h* and H*i* are attatched to the same carbons as the succinimidyl group. There are correlations through adjacent carbon bonds between the protons H*h* and H*i*, H*i* and H*f*, H*f* and H*g*, as well as between H*g* and the hydroxyl proton. The lack of correlation between the hydroxyl proton and H*f* shows that the hydroxyl group is not adjacent to the succinimidyl group but rather on C5 and the bromine is on C4.

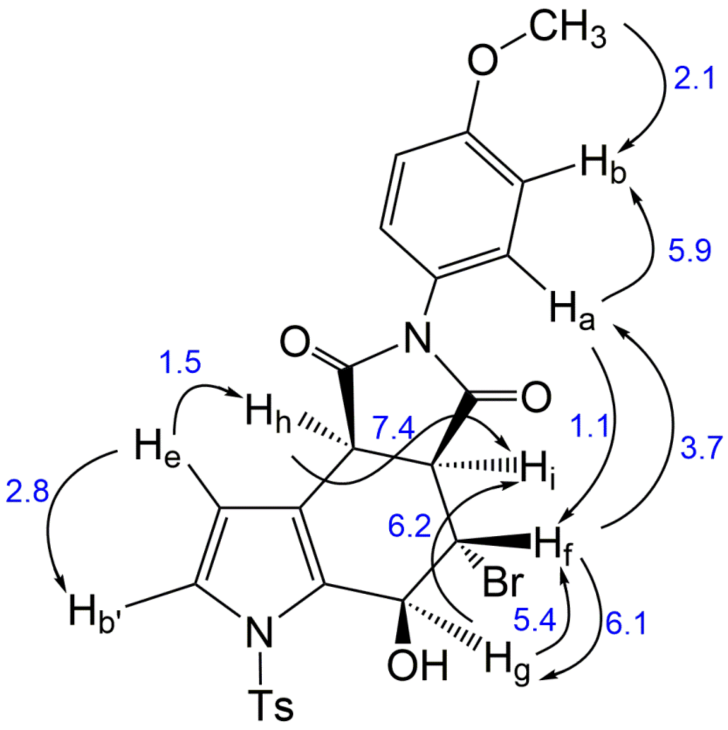
Figure 4: ^{1}H NMR COSY correlations of bromohydrin 49



49

The stereochemistry of bromohydrin **49** was confirmed by 1H NMR NOE (Nuclear Overhauser Effect) interactions (figure 5). There are through space interactions between H_h and H_i with H_g and a lack of such interactions of H_h and H_i with H_f. This indicates that Hg is *syn* to H_h and H_i and that H_f is *anti* to the other three, confirming the configurations of the hydroxyl and bromo groups. The correlation between H_f and H_a confirm that H_f is *syn* to the succinimidyl group, which is *anti* to H_h and H_i.

Figure 5: ^{1}H NMR NOE correlations of bromohydrin 49

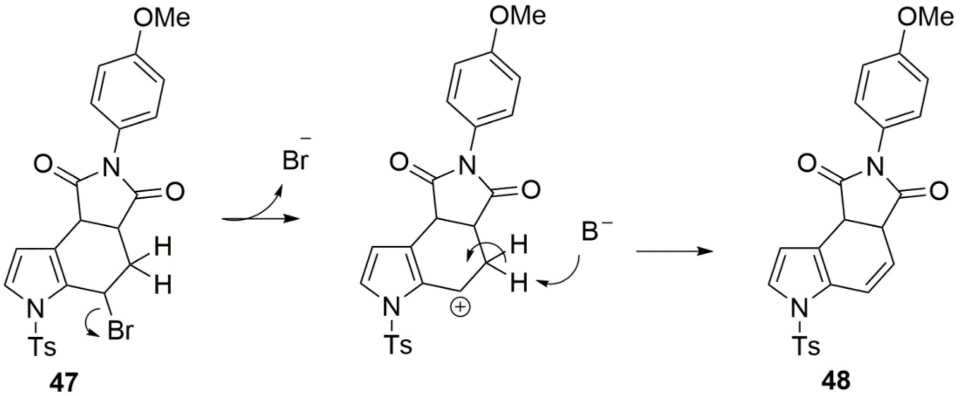


49

3.3 Products and Mechanism

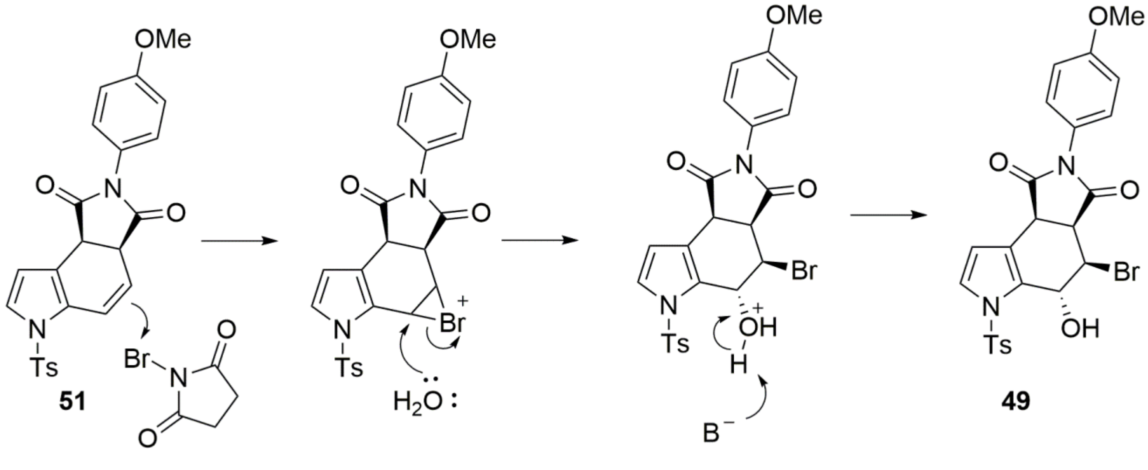
The lack of brominated product **47** observed and the presence of oxidized **48** suggests that hydrogen bromide was eliminated from the brominated adduct **49** and a double bond was formed (Scheme 24). Elimination of HBr after bromination has been used to form a conjugated double bond in a synthesis of isodicyclopentadiene,[54] and attempted bromination of an indole alkaloid resulted in dehydrogenation.[50a] The conjugation between the newly formed double bond and the pyrrole ring drives the elimination reaction so that the proposed brominated compound is never observed.

Scheme 24: Elimination of bromide



The solvent and glassware were not specifically dried, so there was likely water in the solution. NBS and water are known to react with an alkene to give a bromohydrin,[55] explaining the observation of **49**. The oxidized adduct **48** would react with NBS to give a bromonium ion, which reacts with water in the solution to give bromohydrin **49** (Scheme 25). A potential method of this mechanism would be to allow the partially oxidized adduct **48** with NBS to see if bromohydrin **49** is formed.

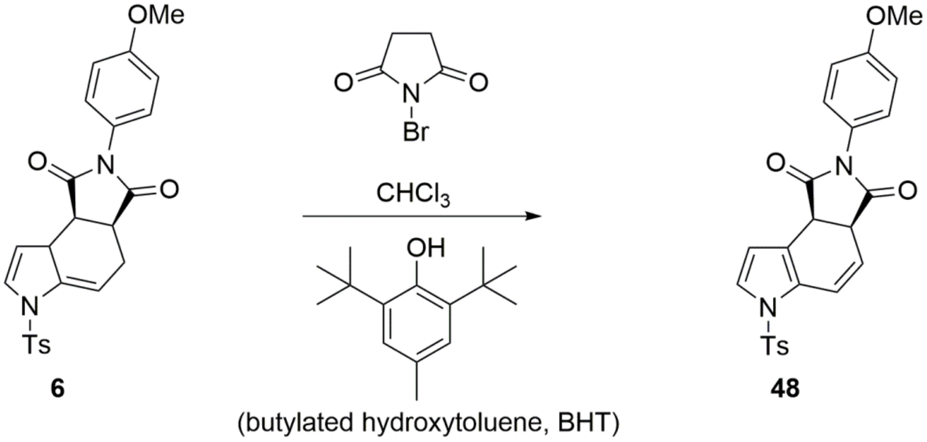
Scheme 25: Bromohydrin formation



The ionic mechanism of NBS bromination was tested by allowing the adduct to react with NBS and a radical inhibitor, butylated hydroxytoluene (BHT) (Scheme 26).

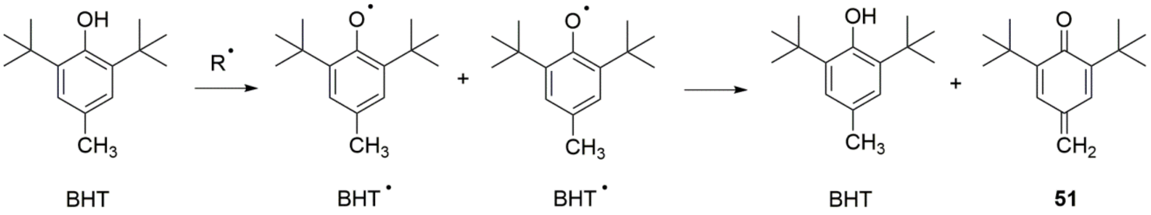
The only product observed was the oxidized adduct **48**. This supports the ionic mechanism of bromination of adduct **6** and elimination of bromine by an ionic mechanism. The formation of a bromohydrin is likely to proceed by an ionic pathway,[56] so the lack of bromohydrin formation seems odd. Most likely, BHT interferes with bromohydrin formation in a manner other than radical abstraction.

Scheme 26: Reaction of adduct with NBS and BHT



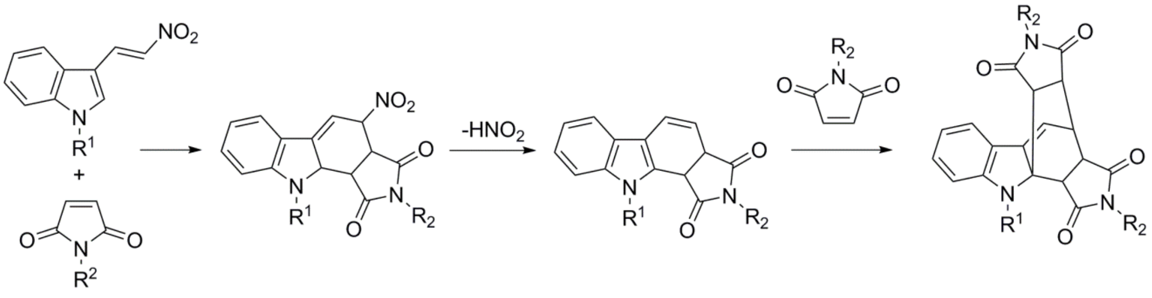
BHT stabilizes radical formation by abstracting a radical and forming a stable phenoxy radical.[57] Two phenoxy radicals react with each other to reform BHT and quinone methide **51** (Scheme 27). Quinone methide **51** can react with water,[58] which would prevent water from reacting with the bromonium compound. This can effectively prevent formation of bromohydrin **48** because there is only a trace amount of water in the system.

Scheme 27: Radical abstraction of BHT[58]



While the intended brominated product **47** was not observed, the partially oxidized product **48** could have useful applications in synthetic chemistry. The double bond adjacent to the rearomatized pyrrole ring could be used as a diene in a Diels-Alder reaction. Double Diels-Alder reactions have been observed to occur with vinylindoles (Scheme 28),[11b] vinylbenzofurans,[34] vinylthiophenes,[59] and vinylimidazoles.[60]

Scheme 28: Double Diels-Alder reaction of nitrovinylindole

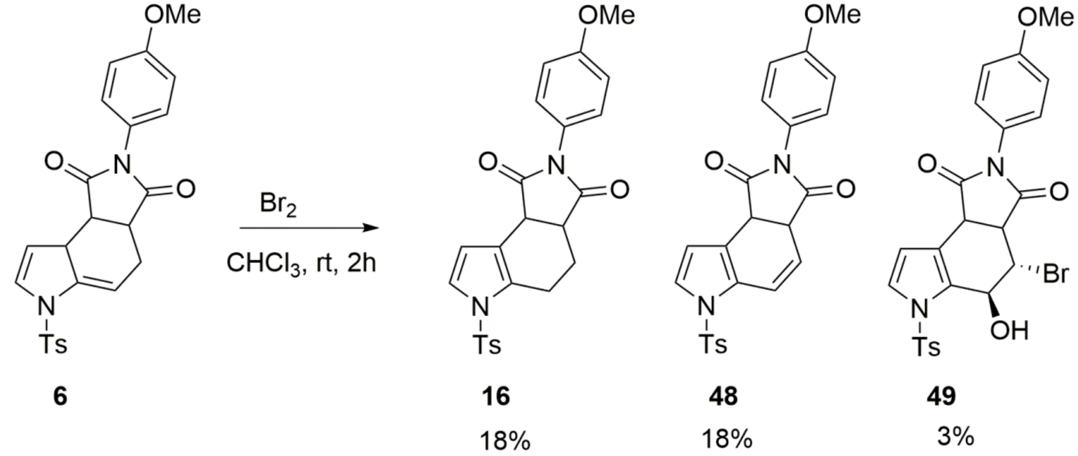


3.4 Reaction with Br_2

One problem with the reaction of Diels-Alder adduct **6** with NBS is the difficulty in separating the products from the succinimide that is formed from the reaction. The compounds **48** and **49** have a very close Rf (retention factor) with succinimide on silica gel, and they co-crystallize, making it difficult to get analytically pure samples of the products. Some suggested mechanisms state that Br_2 is formed *in situ* and acts as the brominating reagent,[44] which suggests that Br_2 would be a good alternative brominating agent. The possibility of dibromination can be controlled with a 1:1 ratio of Br atoms to Diels-Alder adduct.

The Diels-Alder **6** was stirred in chloroform with Br_2 at room temperature for two hours (Scheme 29), giving equal amounts of rearranged adduct **16** and partially oxidized adduct **48**, and a small amount of bromohydrin **49** as a minor product.

Scheme 29: Reaction of adduct 6 with Br_2



The formation of partially oxidized **48** and bromohydrin **49** suggest that HBr is too readily eliminated to enable isolation of a brominated adduct. The chloroform was not dried before use, so a small amount of water could easily cause formation of the bromohydrin. There was also no added base to counter the HBr formed *in situ*, which could explain formation of the partially oxidized adduct and rearrangement of the Diels-Alder adduct. To minimize bromohydrin formation, the reaction should be re-done with dried solvent and a pyridinium hydrobromide should be used as an alternate source of bromine to minimize HBr formation.[61]

3.5 Conclusion

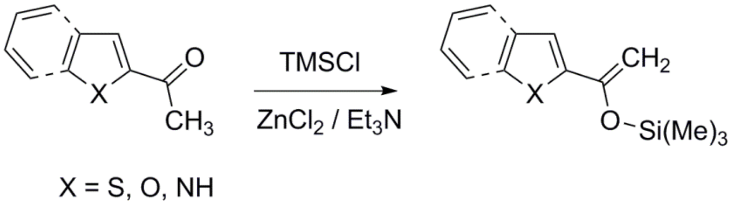
Bromination of an unrearranged Diels-Alder adduct of *N*-tosyl-2-vinylpyrrole could lead to synthetically useful compounds, but isolation of the brominated compound was unsuccessful. Isolation of partially oxidized adduct **48** and bromohydrin **49** indicate an ionic reaction mechanism. Bromination of Diels-Alder adducts using Br_2 is a further potential subject of research.

Part IV. Siloxyvinylpyrroles as dienes

4.1 Introduction

An intriguing variation of the Diels-Alder reaction of vinylheterocycles is when a silyl enol ether is incorporated into the alkene. Silyl enol ethers lend themselves to a number of cycloaddition reactions very well.[62, 63] Silylation of a ketone is a method of creating a siloxyvinyl group *in situ* and introduces an oxygen substituent into the adduct (Scheme 30). There have been some efforts to study this variation with vinylfurans,[64, 65] vinylthiophenes,[66] vinylpyrroles,[67, 68] vinylindoles,[69-71] and ring systems with multiple heteroatoms in the heterocycle.[72]

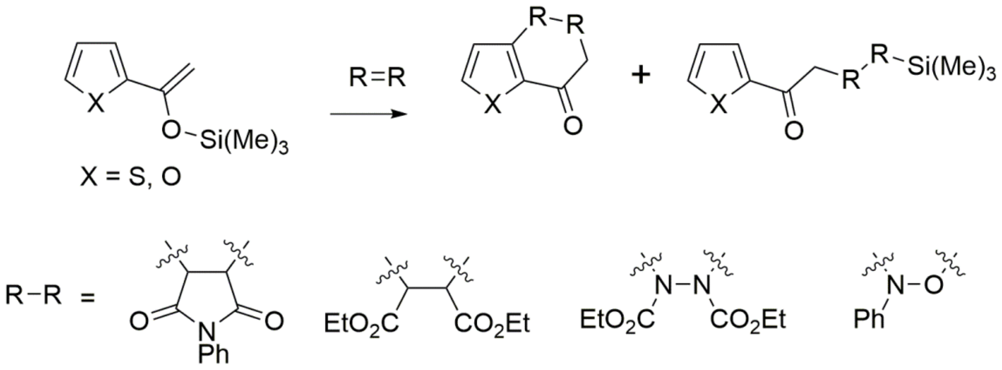
Scheme 30: Silyl enol ether formation of a diene



An allylic silyl enol ether is a good choice as a diene in a Diels-Alder reaction, because it is compatible with a multitude of dienophiles[73] and the removal of the silyl group leaves an oxygen moiety in the newly formed six-membered ring. The enol is readily formed, especially when there is conjugation with neighboring double bonds, such as in heteroaromatic systems. The electron-donating nature of the siloxy group can improve the reactivity in a system with electronegative substituents.[69, 71]

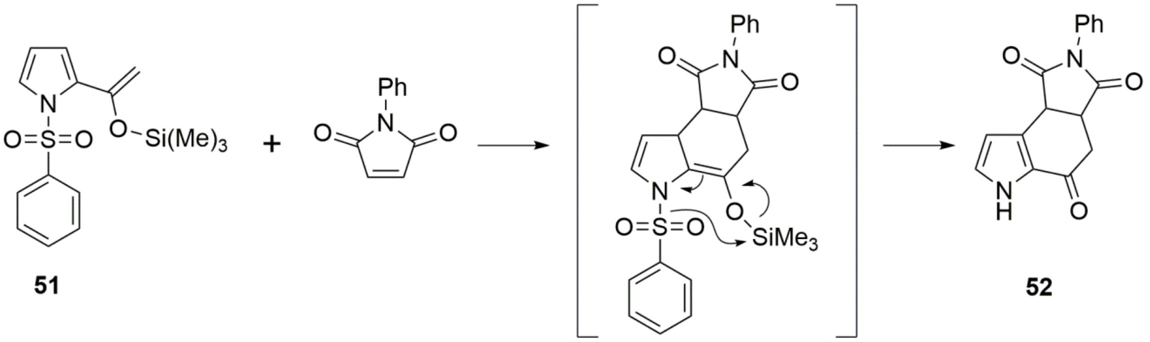
Early examples of heterocycles utilizing a silyl enol ether group for Diels-Alder reactions are with vinylthiophene and vinylfuran. Sakasi, Shimizu, and Eguchi[65] discovered that although vinylfuran is more reactive than vinylthiophene, when a silyl group is used, the reactivity reverses. When an acyclic dienophile was used, the thiophene continued to form cyclic adducts, while the furan formed an open chain product (Scheme 31). The change in reactivity is attributed to the difference in the HOMOs of the two silylated reagents. This change in reactivity could extend to pyrroles.

Scheme 31: Diels-Alder reaction with silyl enol ether as a diene[66]



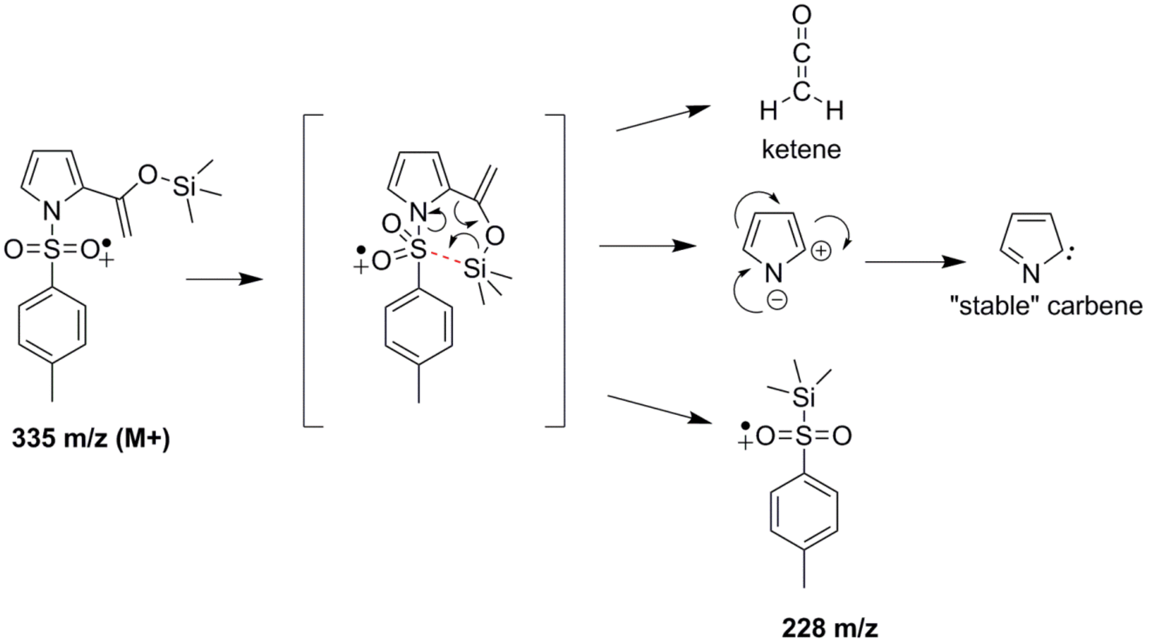
Vinylindoles with silyl groups have been studied a bit more in depth, [69-71] but silylated vinylpyrroles [67, 68] gave varying results. With alkyl and carbonyl *N*-substituents, siloxyvinylpyrroles successfully undergo Diels-Alder reactions and oxidations to form a rearomatized pyrrole. Ohno, Shimizu, and Eguchi[67a] used *N*-phenylsulfonyl-2-acetylpyrrole and trichloromethylsilane as starting materials to form diene **51**, following with addition of N-phenylmaleimide, which gave *N*-H Diels-Alder adduct **52**. It was hypothesized that the phenylsulfonyl and trimethylsilyl groups interacted to be eliminated as the rearrangement occurred (Scheme 32). They were unable to duplicate their results in a following publication, however,[67b] making this an unconfirmed claim.

Scheme 32: Diels-Alder reaction of *N*-phenylsulfonyl-2-pyrrolyl silyl enol ether 51



The suggestion of elimination of phenylsulfonyl and trimethylsilyl groups is plausible. Electron impact mass spectrometry gave peaks consistent with fragmentation at the sulfonyl and silyl groups (Scheme 33). Ionization at one of the sulfonyl oxygens shows a fragment made of the phenylsulfonyl and trimethylsilyl groups that could have been formed in a pericyclic reaction, giving neutral ketene and carbene molecules as the other stable fragments.

Scheme 33: Electron impact fragmentation of silyl enol ether 51



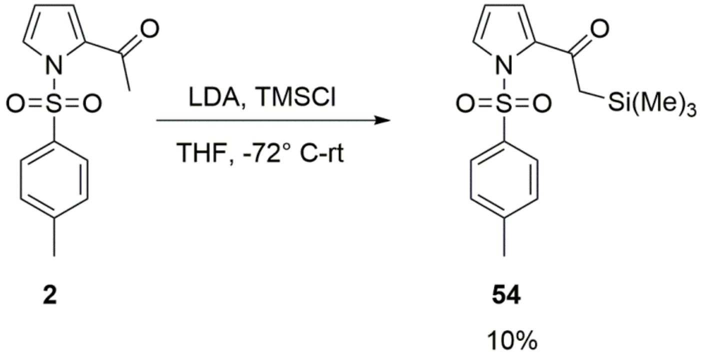
The uncertainty of the effectiveness of an *N*-phenylsulfonylated acetylpyrrole makes it an interesting subject for experimentation. If repeatable results can be obtained, the method of using multiple substituents on the pyrrole to facilitate rearrangement could have useful applications. As a *N*-phenylsulfonylpyrrole is used to make 3-acetylpyrroles,[74] the opportunities for studying a 3-substituted silyl enol ether are also apparent.

One possible difficulty with a phenylsulfonyl group is that the silyl enol ether must be used crude in the Diels-Alder reaction. Ohno *et al*. were able to purify the *N*-methyl and *N*-ethoxycarbonyl silyl enol ethers by vacuum distillation, but the boiling point of the *N*-phenylsulfonyl substituted compound was too high to distill and was used crude. This simplifies the reaction slightly by removing a purification step and forming the silyl enol ether *in situ*, but any side products that were formed in the silylation would still be present and possibly interfere with the Diels-Alder reaction.

4.2 Silylation of *N*-tosyl-2-acetylpyrrole

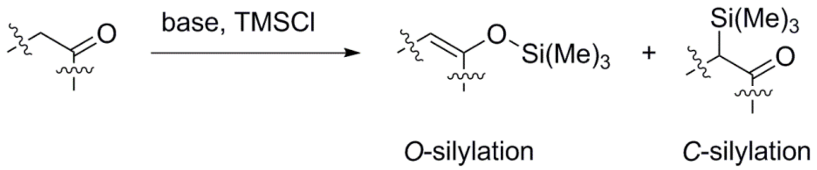
The initial method tried for deprotonating the acetylpyrrole was with *n*-buLi. This proved ineffective, as the unhindered anion acted as a nucleophile, attacking the acetyl group. A more sterically hindered base, such as lithium diisopropylamide (LDA) would prevent side reactions between the base and the pyrrole.[75] When LDA was used to deprotonate the acetyl group, formation of C-silylated silyl enol ether **53** took place (Scheme 34).

Scheme 34: Silylation of *N*-tosyl-2-acetylpyrrole



No Diels-Alder adduct was observed from the reaction of *N*-tosyl-2-siloxyvinylpyrrole with *N*-phenylmaleimide. The silylated pyrrole was not purified before addition of the maleimide, so a strong base was still in solution. A dark brown tar-like substance formed during the reaction, which may be from polymerization of the maleimide *in situ*, as maleimides can polymerize via an anionic mechanism.[76] Rather than the expected O-silylated product, the reaction gave the C-substituted isomer. Silylation of a ketone is known to give both O- and C-silylated products (Scheme 35).[77] Ketones generally give C-silylated compounds, whereas lactones and other esters tend to favor O-silylation.[78]

Scheme 35: *O*- vs *C*- silylation



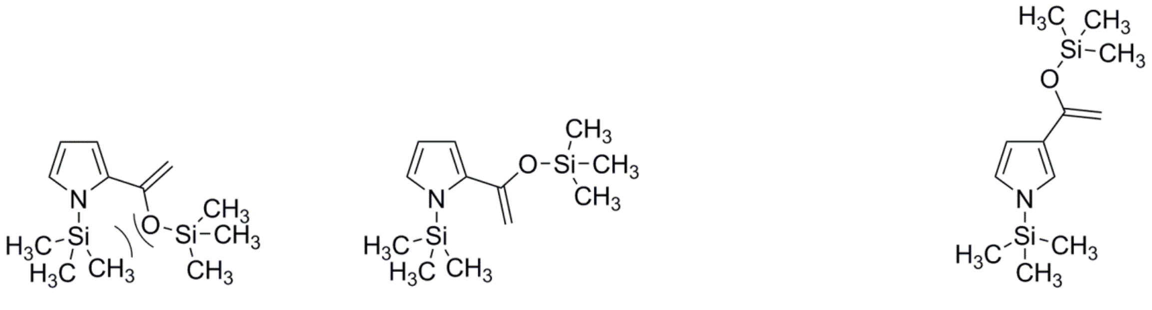
As C-silylated 2-substituted pyrroles are known,[67] the tosyl group could be affecting the reaction. An electron-withdrawing phenylsulfonyl substituent can greatly affect the reactivity of a compound. While pyrroles typically react at the 2-position,[79] *N*-

phenylsulfonylpyrroles are known to substitute at the 3-position.[68, 80] Work has been done using this reactivity to selectively substitute the 3-position on pyrrole.[81] It is likely that the electron-withdrawing from the tosyl group could cause a shift from *O*-silylation to *C*-silylation.

4.3 Silylation of *N*-tosyl-3-acetylpyrrole

3-Acylated *N*-tosylpyrroles have successfully been O-silylated in several instances,[69-71] suggesting that the 3-position of the acyl group is far enough from the electron withdrawing tosyl group. Ohno, Shimizu, and Eguchi[67a] synthesized a disilylated vinylpyrrole for use in a Diels-Alder reaction, but the steric hindrance was found to hinder further reaction. A 3-substituted acylpyrrole could provide a solution to the difficulty with steric hindrance in 2-substituted silyl enol ethers of pyrrole with a bulky substituent (Scheme 36).[67a]

Scheme 36: Steric hindrance in doubly silylated pyrroles



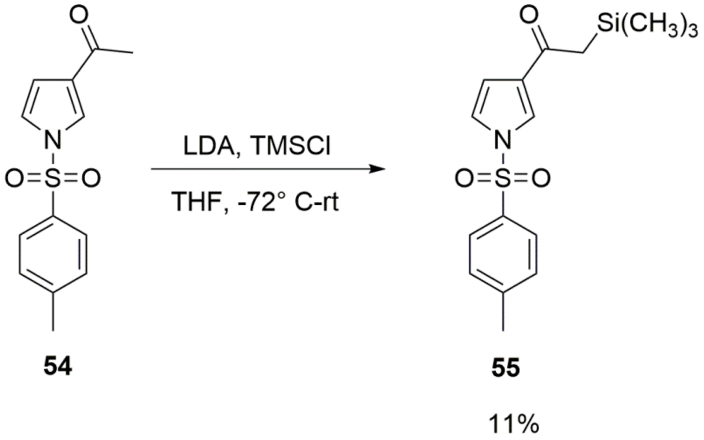
steric bulk

preferred conformation

free rotation

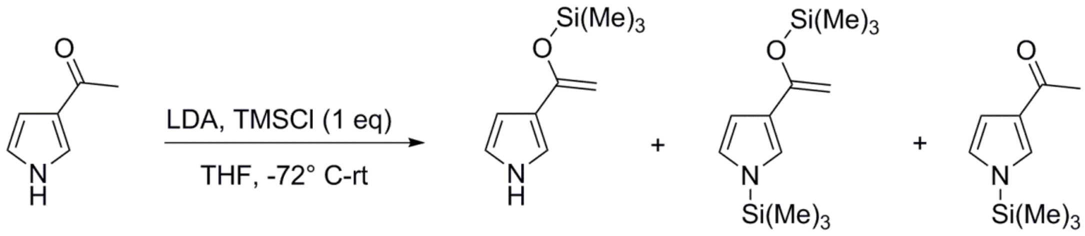
N-Tosyl-3-acetylpyrrole was deprotonated with LDA, and silylated with chlorotrimethylsilane (TMSCl). *N*-Phenylmaleimide was then added and the mixture was stirred overnight. After purification by flash column chromatography, silylated pyrrole **55** and starting material were recovered (Scheme 37).

Scheme 37: Silylation of *N*-tosyl-3-acetylpyrrole



The tosylated acetylpyrrole **54** does not lend itself to *O*-silylation, making the compounds unuseful for Diels-Alder reactions. A 3-acylpyrrole with a different *N*-substituent may yet result in a silyl enol ether to be used in a Diels-Alder reaction. A particular area of interest is in unsubstiuted 3-acetylpyrrole. If one equivalent of TMS is used to silylate the *N*-H-3-acetylpyrrole, there are several different products that could form (Scheme 38). The nitrogen or oxygen may be solely silylated, or both the nitrogen and oxygen of the acetylpyrrole could be silylated. All products would be novel and two would be suitable for Diels-Alder reactions.

Scheme 38: Silylation of 3-acetylpyrrole



4.4 Conclusion

The results of Ohno, Shizumi, and Eguchi[67a] giving an oxygenated adduct from a Diels-Alder reaction of a maleimide and a silylated pyrrole were not replicable in the Noland lab. The resulting O-silylated *N*-tosyl-acetylpyrroles **53** and **55** are likely due to the electron withdrawing effect of the tosyl substitunent. Acetylpyrroles with different *N*-substituents may still be found which form silyl enol ethers suitable for Diels-Alder reactions.

Part V. Experimental

5.1 Experimental for Part I

General method for preparation of vinylpyrroles. Potassium *tert*-butoxide (4.25 g, 0.035 mol, 1.6 eq) was added slowly to a suspension of methyltriphenylphosphonium bromide (11.48 g, 0.032 mol, 1.5 eq) in THF (50 mL) at 0 ºC, producing a bright yellow color immediately. The mixture was stirred at rt under nitrogen for 30 min. The mixture was cooled to 0 ºC, and a solution of *N*-(*p*-toluenesulfonyl)pyrrole-2-carboxaldehyde **1** (5.22 g, 21 mmol) dissolved in THF (20 mL) was added over 10 min, and the mixture was refluxed for 30 min at which time TLC analysis indicated the reaction was complete. The mixture was quenched with water (100 mL) and allowed to cool to room temperature. The mixture was extracted with dichloromethane (3 × 25 mL). The organic layers were washed with saturated $NaHCO_3$ (50 mL). saturated Na_2CO_3 (50 mL), brine (50 mL), and dried over Na_2SO_4. The solvents were removed using a rotating evaporator and the crude product was purified by flash column chromatography on basic alumina, (ethyl acetate/hexanes 1:1) to give ***N*-(*p*-toluenesulfonyl)-2-vinylpyrrole 3** as yellow oil that solidified into stacked cream needles, 70-72°C (lit.66-67 °C)[50] (3.97 g, 77%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.4 Hz, 2H, Ts-H), 7.31 (dd, *J* = 3.3, 1.8 Hz, 1H, pyrrole H), 7.28 (d, *J* = 8.1 Hz, 2H, Ts-H), 7.10 (dd, *J* = 17.4, 11.4 Hz, 1H, vinyl H), 6.45 (ddd, *J* = 3.3, 1.6, 0.6 Hz, 1H, pyrrole H), 6.25 (td, *J* = 3.3, 0.6 Hz, 1H, pyrrole H), 5.48 (dd, *J* = 17.4, 1.2 Hz, 1H, vinyl H), 5.16 (dd, *J* = 11.1, 1.2 Hz, 1H, vinyl H), 2.40 (s, 3H, CH_3) (lit.^{1}H NMR ($CDCl_3$, 300 MHz) d 7.69 (d, J = 8.4 Hz, 2H, phenyl H), 7.31-7.28 (m, 1H, pyrrole H), 7.27 (d, J = 8.1 Hz, 2H, phenyl H), 7.10 (dd, J = 17.4, 11.2 Hz, 1H, vinyl

H), 6.44 (m, 1H, pyrrole H), 6.24 (m, 1H, pyrrole H), 5.48 (dd, J = 17.4, 1.2 Hz, 1H, vinyl H), 5.15 (dd, J = 11.2, 1.5 Hz, 1H, vinyl H), 2.39 (s, 3H, CH_3)).[85]

***N*-(*p*-toluenesulfonyl)-2 (prop-1-en-2-yl)-pyrrole (4):** The general method using *N*-(*p*-toluenesulfonyl)pyrrole-2-ethan-1-one **2** (4.91 g, 19 mmol) gave an orange oil (8.50 g, 77%) that solidified and was recrystallized with hexanes giving small white crystals (1.38 g, 28%), mp = 61-62°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.4 Hz, 2H, Ts-H), 7.26 (ddd, *J* = 3.3, 1.8, 0.6 Hz, 1H, 5-H), 7.21 (dd, *J* = 8.1, 0.9, Hz, 2H, Ts-H), 6.20 (ddd,, *J* = 3.3, 3.3, 0.9 Hz, 1H, 3-H), 6.03 (ddd, *J* = 0.9, 1.8, 3.0 Hz, 1H, 4-H), 5.17 (dddd, *J* = 2.4, 1.5, 0.9, 0.9 Hz, 1H, 2'-H *trans* to pyrrole), 4.84 (ddd, *J* = 1.8, 0.9, 0.9 Hz, 1H, 2'-H *cis* to pyrrole), 2.38 (s, 3H, Ts-CH_3), 2.03 (ddd, *J* = 1.8, 0.9, 0.9 Hz, 1'-CH_3) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.4, 137.8, 136.9, 135.7, 129.3, 136.8, 123.7, 118.3, 114.1, 112.3, 24.3, 21.4; IR (KBr, cm^{-1}) 2920 (w), 1632 (w), 1596 (w), 1493 (w), 1482 (w), 1448 (w) 1365 (s), 1295 (w), 1256 (w), 1189 (m), 1177 (s), 1105 (m), 1089 (m), 1046 (m), 1017 (w), 907 (w), 870 (w), 812 (m), 704 (m), 683 (m), 617 (m) ; HRMS ES-TOF [$M+Na^+$] Calcd for $C_{14}H_{15}NO_2S$: 284.0716, Found: 284.0719 ; Anal. Calcd for $C_{14}H_{15}NO_2S$: C, 64.34; H, 5.79; N, 5.36; S, 12.27; Found: C, 64.17; H, 5.79; N, 5.37; S, 12.19. The product gave a single spot on silica gel TLC, (ethyl acetate/hexane 1:1) R_f 0.73.

General method for Diels-Alder Reactions. A mixture of vinylpyrrole (50 mmol) and maleimide (50 mmol) were stirred in chloroform (20 mL) for 24 h-11 d (method A), isolating precipitate by vacuum filtration until precipitate no longer formed and TLC showed absence of maleimide. The solution was refluxed for 4-25 d (Method B) if TLC showed no reaction at room temperature for 2 d. The product was purified by flash column chromatography on silica gel with 1:1 ethyl acetate /hexanes and crystallized with chloroform.

2-(4-Methoxyphenyl)-6-tosyl-3a,4,8a,8b-tetrahydro-2*H*,3a*H*,6*H*-pyrrolo[3,4-*e*]indole-1,3-dione (6): Method A using **3** (1.2034 g) and **5a** (0.884 g,) gave white crystals (1.32 g, 69%), mp = 124-126 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (dt, *J* = 8.4, 1.8 Hz, 2H, Ts-H), 7.17 (d, *J* = 8.1 Hz, 2H, Ts-H), 6.87 (m, 2H, Ph-H), 6.78 (m, 2H, Ph-H), 6.72 (dd, *J* = 4.5, 2.1 Hz, 1H, 8-H), 5.90 (ddd, *J* = 4.8, 3.3, 1.2 Hz, 1H, 5H), 5.71 (ddd, *J* = 4.2, 2.1, 1.2 Hz, 1H, 4-H), 3.82 (s, *J* = 8.1, 5.1Hz, 3H, Ts-CH_3), 3.58 (m, 1H, 8a-H), 3.46 (t, *J* = 8.6 Hz, 1H, 8b-H), 3.16 (ddd, *J* = 8.4, 6.3, 1.8 Hz, 1H, 3a-H), 3.06 (ddd, *J* = 15.3, 7.8, 1.8 Hz, 1H, 4-H), 2.30 (s, 3H, OCH_3), 2.10 (dddd, *J* = 9.9, 6.6, 3.3, 3.3 Hz, 1H, 4-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.0, 174.9, 159.3, 144.5, 139.2, 130.7, 129.8, 127.3, 127.2, 114.1, 111.1, 101.5, 55.5, 44.0, 4207, 38.0, 24.4, 21.7; IR (KBr, cm^{-1}) 3117 (w), 2914 (w), 2844 (w), 1710 (s), 1512 (s), 1388 (w), 1366 (w), 1347 (m), 1250 (m), 1186 (m), 1170 (s), 1128 (m), 1090 (w), 1029 (w), 839 (w), 705 (m), 699 (m), 665 (m); HRMS ES-TOF [M+Na$^+$] calcd for $C_{24}H_{22}N_2O_5S$: 473.1142. The product gave a single spot on silica gel TLC, (ethyl acetate /hexanes 1:1) R_f 0.3.

2-(3-Methoxyphenyl)-6-tosyl-3a,4,8a,8b-tetrahydro-2*H*,3a*H*,6*H*-pyrrolo[3,4-*e*]indole-1,3-dione (7): Method A using **3** (1.695 g) and **5b** (1.345 g) gave cream-colored crystals (2.48 g, 83%), mp = 148-150°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (dt, *J* = 8.4, 1.8 Hz, 2H, Ts-H), 7.24 (t, *J* = 8.1 Hz, 1H, Ts-H), 7.13 (d, *J* = 8.4 Hz, 2H, Ph-H), 6.86 (ddd, *J* = 8.4, 2.7, 0.9 Hz, 1H, Ph-H), 6.69 (dd, *J* = 4.5, 2.1 Hz, 1H, 7-H), 6.52 (t, *J* = 2.1 Hz, 1H, Ar), 6.44 (ddd, *J* = 8.1, 1.8, 0.9 Hz, 1H, Ar), 5.86 (dddd, *J* = 7.8, 4.2, 3.3, 0.9 Hz, 1H, 5-H), 5.68 (ddd, *J* = 4.5, 2.4, 1.2Hz, 1H, 8-H), 3.78 (s, 3H, OCH_3), 3.53 (m, 1H, 8a-H), 3.44 (t, J = 8.5 Hz, 1H, 8b-H), 3.14 (ddd, *J* = 8.4, 6.3, 1.8 Hz, 1H, 3a-H), 3.03 (ddd, *J* = 15.6, 8.1, 1.2 Hz, 1H, 4-H), 2.23 (s, 3H, Ts-CH_3), 2.08 (dddd, *J* = 9.6, 6.3, 3.3, 3.3 Hz, 1H, 4-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.3, 175.2, 160.4, 145.2, 139.9, 134.5, 130.5, 130.2, 127.8, 118.9, 114.5, 112.7, 111.7, 102.1, 56.1, 44.6, 43.3, 38.7, 25.1, 22.2; IR (KBr, cm^{-1}) 2954 (w), 2838 (w), 1713 (s), 1606 (m), 1493 (m), 1368 (m), 1348 (m), 1256 (m), 1191 (w), 1167 (s), 1132 (m), 1091 (w), 1042 (w), 708 (m), 688 (w), 660 (w); HRMS ES-TOF [M+Na$^+$] Calcd for $C_{24}H_{22}N_2O_5S$: 473.1093, Found: 473.1168; Anal. Calcd for $C_{24}H_{22}N_2O_5S$: C, 63.99; H, 4.92; N, 6.22; S, 7.12; Found: C, 63.54; H, 5.00; N, 6.16; S, 7.19. The product gave a single spot on silica gel TLC, (ethyl acetate /hexanes 1:1) R_f 0.25.

2-(4-Acetoxyphenyl)-6-tosyl-3a,4,8a,8b-tetrahydro-2*H*,3a*H*,6*H*-pyrrolo[3,4-*e*]indole-1,3-dione (18): Method A using **3** (1.769 g) and **5c** (1.772 g) gave cream-colored crystals (2.42 g, 72%) , mp = 125-127°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.4 Hz, 2H, Ts-H), 7.14 (d, *J* = 7.8 Hz, 2H, Ts-H), 7.10 (dt, *J* = 8.7, 2.1 Hz, 2H, Ph-H), 6.94 (dt, *J* = 9, 2.4 Hz, 2H, Ph-H), 6.73 (dd, *J* = 4.5, 2.1 Hz, 1H, 7-H), 5.89, (quintet, *J* = 3.9 Hz, 1H, 5-H), 5.70 (m, 1H, 8-H), 3.56 (m, 1H, 8a-H), 3.47 (t, *J* = 8.7 Hz, 1H, 8b-H), 3.18 (ddd, *J* = 8.4, 6.3, 1.8 Hz, 1H, 3a-H), 3.08 (ddt, *J* = 15.3, 7.2, 0.9 Hz, 1H, 4-H), 2.33 (s, 3H, $OCOCH_3$), 2.28 (s, 3H, Ts-CH_3), 2.00 (dddd, *J* = 9.0, 6.0, 3.0, 3.0 Hz, 1H, 4-H) ppm; ^{13}C NMR (100 MHz, CD_2Cl_2) 177.2, 175.7, 169.1, 150.4, 135.8, 130.1, 129.7, 129.4, 127.4, 126.7, 122.3, 121.9, 117.0, 111.6, 40.0, 39.5, 22.1, 21.4, 20.8, 19.6; IR (KBr, cm^{-1}) 1755 (m), 1710 (s), 1507 (m), 1368 (m), 1348 (m), 1198 (s), 1166 (s), 1127 (m), 706 (w), 663 (w); HRMS ES-TOF [M+Na$^+$] Calcd for for $C_{25}H_{22}N_2O_6S$: 501.1093, Found: 501.1116; Anal. Calcd for $C_{25}H_{22}N_2O_6S$: C, 62.75; H, 4.63; N, 5.85; S, 6.70; Found: C, 62.56; H, 4.83; N, 5.70; S, 6.70. The product gave a single spot on silica gel TLC, (ethyl acetate /hexanes 1:1) R_f 0.3.

2-(4-Chlorophenyl)-6-tosyl-3a,4,8a,8b-tetrahydro-2*H*,3a*H*,6*H*-pyrrolo[3,4-*e*]indole-1,3-dione (9): Method A using **3** (0.669 g) and **5d** (0.502 g) gave white crystals (0.80 g, 72%) , mp = 142-143°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (dt, *J* = 8.4, 2.1 Hz, 2H, Ts-H), 7.30 (dt, *J* = 9, 2.4 Hz, 2H, Ph-H), 7.12 (d, *J* = 8.4 Hz, 2H, Ts-H), 6.85 (dt, *J* = 8.7, 2.4 Hz, 2H, Ph-H), 6.72 (dd, *J* = 4.2, 2.1 Hz, 1H, 7-H), 5.88 (dddd, *J* = 8.1, 3.6, 3.6, 1.2 hz, 1H, 5-H), 5.68 (ddd *J* = 4.2, 2.4, 0.9 Hz, 1H, 8-H), 3.56 (m, 1H, 8a-H), 3.45 (t, *J* = 8.4 Hz, 1H, 8b-H), 3.16 (ddd, *J* = 8.4, 6.3, 1.8 Hz, 1H, 3a-H), 3.05 (ddd, *J* = 15.6, 8.1, 1.8 Hz, 1H, 4-H), 2.26 (s, 3H, Ts-CH_3), 2.10 (dddd, *J* = 15.6, 6.6, 3.3, 3.3 Hz, 1H, 4-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.1, 175.0, 145.2, 139.8, 134.6, 134.6, 131.5, 130.4, 129.6, 127.9, 127.8, 111.5, 102.1, 44.6, 43.4, 38.7, 25.1, 22.3; IR (KBr, cm^{-1}) 3147 (w), 3111 (w), 3061 (w), 2956 (w) 2927 (w)2855 (w), 1781 (w), 1716 (s), 1596 (w), 1493 (s), 1448 (w), 1373 (s), 1306 (w), 1270 (w), 1227 (m), 1175 (s), 1129 (m), 1090 (m), 1017 (w), 831 (w), 813 (m), 767 (w), 735 (m, 705 (m), 668 (m), 642 (w); HRMS ES-TOF [M+Na$^+$] Calcd for $C_{23}H_{19}ClN_2O_4S$: 477.0647, Found: 477.0652; Anal. Calcd for $C_{23}H_{19}ClN_2O_4S$: C, 60.72; H, 4.21; N, 6.16; S, 7.05; found: C, 60.46; H, 4.38; N, 5.94; S, 7.23. The product gave a single spot on silica gel TLC, (ethyl acetate /hexanes 1:1) R_f 0.33.

2-(4-Bromophenyl)-6-tosyl-3a,4,8a,8b-tetrahydro-2*H*,3a*H*,6*H*-pyrrolo[3,4-*e*]indole-1,3-dione (10): Method A using **3** (0.934 g) and **5e** (0.773 g) gave white crystals (0.94 g, 60%), mp = 205-208°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (dt, *J* = 8.1, 2.1 Hz, 2H, Ts-H), 7.45 (dt, *J* = 8.7, 2.7 Hz, 2H, Ph-H), 7.11 (d, *J* = 8.1 Hz, 2H, Ts -H), 6.78 (dt, *J* = 8.7, 2.7 Hz, 2H, Ph-H), 6.71 (dd, *J* = 4.5, 2.1 Hz, 1H, 7-H), 5.88 (dddd, *J* = 7.8, 3.3, 3.3m 1.2 Hz, 1H, 5-H), 5.68 (ddd, *J* = 4.5, 3.6, 1.2 Hz, 1H, 8-H), 3.55 (m, 1H, 8a-H), 3.45 (t, *J* = 8.4 Hz, 1H, 8b-H), 3.16 (ddd, *J* = 8.5, 6.4, 1.8 Hz, 1H, 3a-H), 3.04 (ddd, *J* = 15.3, 6.4, 1.8 Hz, 1H, 4-H), 2.25 (s, 3H, Ts-CH_3), 2.09 (dddd, *J* = 15.3, 6.6, 3.3, 3.3 Hz, 1H, 4-H) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.1, 175.0, 145.2 139.8, 134.5, 132.6, 131.5, 131.0 130.4, 128.0, 127.9, 122.7, 111.6, 102.7, 44.6, 43.4, 38.7, 25.1, 22.3; IR (KBr, cm^{-1}) 1712 (s), 1491 (m), 1376 (m), 1342 (m), 1216 (w), 1163 (s), 1134 (m), 1094 (w), 839 (w), 815 (m), 726 (w), 710 (w), 645 (w); HRMS ES-TOF [M+Na$^+$] Calcd for $C_{23}H_{19}BrN_2O_4S$: 521.0141, Found: 521.0229; Anal. Calcd for $C_{23}H_{19}BrN_2O_4S$: C, 55.32; H, 3.83; N, 5.61; S, 6.42; Found: C, 55.12; H, 3.88; N, 5.52; S, 6.61. The product gave a single spot on silica gel TLC, (ethyl acetate /hexanes 1:1) R_f 0.3.

2-(4-Nitrophenyl)-6-tosyl-3a,4,8a,8b-tetrahydro-2*H*,3a*H*,6*H*-pyrrolo[3,4-*e*]indole-1,3-dione (11): Method A using **3** (1.0463 g) and **5f** (0.8470 g) gave white solid (1.35 g, 76%) mp = 173-175°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21 (dt, *J* = 9.6, 2.4 Hz, 2H, Ph-H), 7.61 (dt, *J* = 8.4, 2.1 Hz, 2H, Ts-H), 7.18 (dt, *J* = 9.6, 2.4 Hz, 2H, Ph-H), 7.12 (dd, *J* = 8.4, 0.9 Hz, 2H,Ts-H), 6.74 (dd, *J* = 2.1, 4.5 Hz, 1H, 7-H), 5.90 (dddd, *J* = 7.8, 3.6, 3.6, 1.2 Hz, 1H, 5-H), 5.69 (ddd (*J* = 4.2, 2.4, 0.9 Hz, 1H, 8-H), 3.58 (m, 1H, 8a-H), 3.51 (t, *J* = 8.4 Hz, 1H, 8b-H), 3.23 (ddd, *J* = 8.1, 6,1.2 Hz, 1H, 3a-H), 3.08 (ddd, *J* = 15.6, 7.8, 2.1 Hz, 1H, 4-H), 2.18 (s, 3H, Ts-CH_3), 2.13 (dddd, *J* = 15.6, 4.5, 4.5, 1.2 Hz, 1H, 4-H)); ^{13}C NMR (100 MHz, DMSO) δ 178.0, 174.7, 146.8, 144.7, 139.9, 137.9, 134.1, 130.3, 130.2, 127.3, 124.3, 112.9, 101.4, 43.9, 43.2, 38.5, 24.4, 21.3; IR (KBr, cm^{-1}) 1720 (s), 1522 (m), 1495 (w), 1345 (s), 1207 (w), 1164 (s), 1119 (m), 852 (w), 662 (w); HRMS ES-TOF [M+Na^+] Calcd for $C_{23}H_{19}N_3O_6S$: 488.0887, Found:488.0917; Anal. Calcd for $C_{23}H_{19}N_3O_6S$: C, 59.35; H, 4.11; N, 9.03; S, 6.89; Found: C, 59.28; H, 4.04; N, 8.99; S, 6.74. The product gave a single spot on silica gel TLC, (ethyl acetate /hexanes 1:1) R_f 0.2.

2-Phenyl-6-tosyl-3a,4,8a,8b-tetrahydro-2*H*,3a*H*,6*H*-pyrrolo[3,4-*e*]indole-1,3-dione (12): Method B using **3** (0.247 g) and **5g** (0.202 g) gave white solid (0.193g, 50%), mp = 144-146°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.4 Hz, 2H, Ts -H),7.35 (dd, *J* = 5.1, 2.1 Hz, 2H, Ph-H), 7.34 (d, *J* = 1.8 Hz, 1H, Ph-H), 7.13 (dd, *J* = 9, 0.6 Hz, 2H, Ts -H), 6.87 (dd, *J* = 4.8, 1.8 Hz, 2H, Ph-H), 6.72 (dd, *J* = 4.5, 2.1 Hz, 1H, 8-H), 5.88 (dddd, *J* = 6.9, 2.4, 2.4, 1.2 Hz, 1H, 5-H), 5.70 (ddd, *J* = 4.5, 2.4, 1.2 Hz, 1H, 7-H), 3.57 (m, 1H, 8a-H), 3.47 (t, *J* = 8.4 Hz, 1H, 8b-H,), 3.17 (ddd, *J* = 8.4 6.6, 1.8 Hz, 1H, 3a-H), 3.06 (ddd, *j* = 15.3, 7.8, 1.8 Hz, 1H, 4-H), 2.25 (s, 3H, Ts-CH_3), 2.11 (dddd, *J* = 15.3, 6.6, 3.3, 3.3 Hz, 1H, 4-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.4, 175.3, 145.1, 139.8, 134.6, 132.1, 131.4, 130.4, 129.5, 127.8, 126.6, 111.7, 102.1, 44.6, 43.3, 38.7, 25.0, 22.3; IR (KBr, cm^{-1}) 3116 (w), 3068 (w), 2954 (w), 2847 (w), 1703 (s), 1671 (w), 1597 (w), 1498 (w), 1380 (m), 1348 (m), 1186 (w), 1166 (s), 1131 (w), 1091 (w), 938 (w), 810 (w), 756 (w), 728 (w), 707 (w), 691 (w), 660 (w); HRMS ES-TOF Calcd for [M+Na^+] $C_{23}H_{20}N_2O_4S$: 443.1036, Found: 443.1048 ; Anal. Calcd for $C_{23}H_{20}N_2O_4S$: C, 65.70; H, 4.79; N, 6.66; S, 7.63; Found: C, 65.93; H, 5.00; N, 6.61; S, 7.81. The product gave a single spot on silica gel TLC, (ethyl acetate /hexanes 1:1) R_f 0.3.

2-dimethylamino-6-tosyl-3a,4,8a,8b-tetrahydro-2*H*,3a*H*,6*H*-pyrrolo[3,4-*e*]indole-1,3-dione (13): Method A using **3** (1.0207 g) and **5h** (0.6459 g) followed by purification by silica gel chromatography with ethyl acetate/hexanes gave white powder (0.679g, 40%), mp = 200-210°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (dd, *J* = 8.4, 2.1 Hz, 2H, Ts-H), 7.07 (d, *J* = 8.4 Hz, 2H, Ts-H), 6.46 (dd, *J* = 4.5, 2.4 Hz, 1H, 7-H), 5.52 (ddd, *J* = 6.6, 2.7, 2.7 Hz, 1H, 5-H), 5.44 (ddd, *J* = 4.5, 2.4, 1.2 Hz, 1H, 8-H), 3.25 (ddd, *J* = 8.7, 6.0, 3.0, 3.0 Hz, 1H, 8a-H), 3.06 (dd, J = 8.4, 8.4 Hz, 1H, 8b-H), 2.74 (ddd, *J* = 8.7, 6.6, 1.8 Hz, 1H, 3a-H), 2.69 (ddd *J* = 15.3, 7.8, 1.8 Hz, 1H, 4-H), 2.65 (s, 6H, $NN(CH_3)_2$-H), , 2.28 (s, 3H, Ts-CH_3), 1.77 (dddd, *J* = 15.3, 6.6, 3.3, 3.3 Hz, 1H, 4-H). The product gave a single spot on silica gel TLC, (ethyl acetate /hexanes 1:1) R_f 0.16.

2-Methyl-6-tosyl-3a,4,8a,8b-tetrahydro-2*H*,3a*H*,6*H*-pyrrolo[3,4-*e*]indole-1,3-dione (14): Method A using **3** (0.2705 g) and **5i** (0.1051 g) and purification by silica gel chromatography with ethyl acetate/hexanes followed by crystallization with dichloromethane/hexanes gave cream crystals (0.12g 37%), mp = 150-151°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.7 Hz, 2H, Ts-H), 7.27 (d, *J* = 8.7 Hz, 2H, Ts-H), 6.68 (dd, *J* = 3.9, 1.8 Hz, 1H, 7-H), 5.80 (dd, *J* = 3.9, 3.9 Hz, 1H, 8-H), 5.68 (m, 1H, 5-H), 3.45 (m, 1H, 8a-H), 3.26 (dd, *J* = 8.4, 8.4 Hz, 1H, 8b-H), 2.93 (m, 2H, 3a-H, 4-H), 2.40 (s, 6H, Ts-CH_3, CH_3), 2.01 (dddd, *J* = 12.9, 6.6, 3.3, 3.3 Hz, 1H, 4-H) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.7, 175.4, 144.3, 139.1, 133.2, 130.7, 129.7, 127.7, 111.9, 101.6, 43.8, 42.7, 37.7, 24.7, 24.2, 21.7; IR (KBr, cm^{-1}) 3103 (w), 2961 (w), 1776 (w), 1700 (s), 1596 (w), 1558 (w), 1436 (m), 1382 (w), 1367 (m), 1348 (m), 1310 (w), 12/86 (m), 1166 (s), 1114 (m), 1088 (w), 1034 (w), 990 (w), 936 (w), 841 (w), 816 (w), 769 (w), 731 (w), 708 (m), 668 (m), 656 (w), 628 (w); HRMS ES-TOF [M+Na$^+$] Calcd for $C_{18}H_{18}N_2O_4S$: 381.0879, Found: 381.0860 ; Anal. Calcd for $C_{18}H_{18}N_2O_4S$: C, 60.32; H, 5.06; N, 7.82; S, 8.95; Found: C, 60.13; H, 5.16; N, 7.90; S, 9.02. The product gave a single spot on silica gel TLC, (ethyl acetate /hexanes 1:1) R_f 0.17.

6-tosyl-4,5,6,8b-tetrahydro-1H-furo[3,4-e]indole-1,3-dione (15): Method A using **3** (1.379 g) and **5j** (0.8337 g) followed by recrystallization from ethyl acetate gave pale pink needles (1.87 g, 77%), mp = 197-198°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (dd, *J* = 8.4, 2.1 Hz, 2H, Ts-H), 7.29 (dd, *J* = 8.7, 2.4 Hz, 2H, Ts-H), 6.75 (dd, *J* = 4.2, 1.8 Hz, 1H, 7-H), 5.92 (dddd, *J* = 4.5, 3.3, 3.3, 1.2 Hz, 1H, 5-H), 5.60 (ddd, *J* = 4.5, 2.4, 1.2 Hz, 1H, 8-H), 3.49 (d, *J* = 9 Hz, 1H, 8a-H), 3.42 (m, 1H, 8b-H), 3.23 (ddd, *J* = 9.6, 6.3, 2.1 Hz, 1H, 3a-H), 2.95 (ddd, *J* = 15.6, 7.8, 2.1 hz, 1H, 4-H), 2.43 (s, 3H, Ts CH_3), 2.04 (dddd, *J* = 15.6, 6.3, 3.3, 3.3 Hz, 1H, 4-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ169.8, 146.0, 140.3, 133.1, 132.1, 130.5, 128.0, 111.6, 103.3, 44.1, 44.0, 39.3, 25.2, 22.3; HRMS ES-TOF [M+Na$^+$] Calcd for $C_{17}H_{15}NO_5S$: 368.0563, Found: 368.0520; Anal. Calcd for $C_{17}H_{15}NO_5S$: C, 59.12; H, 4.38; N, 4.06; S, 9.28; Found: C, 58.86; H, 4.53; N, 4.00; S, 9.12. The product gave a single spot on silica gel TLC, (ethyl acetate /hexanes 1:1) R_f 0.3.

2-(4-Methoxyphenyl)-6-tosyl-3a,4,5,8b-tetrahydro-2*H*,3a*H*,6*H*-pyrrolo[3,4-*e*]indole-1,3-dione (16): Diels-Alder adduct **6** (0.492 g, 1mmol) was refluxed in toluene and purified by silica gel chromatography using 1:1 ethyl acetate/hexanes to give a white solid (0.30 g, 61%), mp = 106-108°C; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.67 (d, *J* = 7.8 Hz, 2H, Ts-H), 7.30 (d, *J* = 8.4 Hz, 2H, Ts-H), 7.27 (d, *J* = 3.3 Hz, 1H, 7-H), 7.04 (d, *J* = 8.7 Hz, 2H, Ph-H), 6.92 (d, *J* = 8.7 Hz, 2H, Ph-H), 6.50 (d, *J* = 3.3 Hz, 1H, 8-H), 3.97 (d, *J* = 8.1 Hz, 1H, 8b-H), 3.80 (s, 3H, OCH$_3$), 3.31 (dt, *J* = 8.1, 5.4 Hz, 1H, 3a-H), 2.93 (dt, *J* = 17.1, 5.1 Hz, 1H, 5-H), 2.64 (dq, *J* = 17.3, 5.1 Hz, 1H, 5-H), 2.42 (s, 3H, Ts-CH$_3$), 2.34 (dq *J* = 13.5, 5.4 Hz, 1H, 4-H), 1.99 (dddd, *J* = 14.4, 9.6, 5.1, 5.1 Hz, 1H, 4-H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 177.7, 176.2, 159.5, 136.0, 130.2, 129.5, 127.6, 122.1, 117.0, 114.4, 111.6, 108.9, 55.6, 40.0, 39.5, 22.1, 21.8, 19.6; IR (KBr, cm^{-1}) 3144 (w), 3059 (w), 2957 (w), 2933 (w), 2840 (w), 1780 (w), 01712 (s), 1609 (w), 1595 (w), 1513 (s), 1493 (w), 1441 (w), 1370 (m), 1300 (m), 1250 (m), 1228 (m), 1174 (s), 1128 (m), 1091 (m), 1077 (w), 1030 (m), 930 (w), 833 (w), 815 (m), 807 (w), 776 (w), 734 (m), 705 (m), 669 (m), 607 (m); HRMS ES-TOF [M+Na^{+}] Calcd for $C_{24}H_{22}N_2O_5S$:473.1142, Found: 473.1145; Anal. Calcd for $C_{24}H_{22}N_2O_5S$: C, 63.98; H, 4.92; N, 6.22; S, 7.18; Found: C, 63.76; H, 4.89; N, 5.98; S, 7.10. The product gave a single spot on silica gel TLC, (ethyl acetate /hexanes 1:1) R$_f$ 0.6.

2-(3-Methoxyphenyl)-6-tosyl-3a,4,5,8b-tetrahydro-2*H*,3a*H*,6*H*-pyrrolo[3,4-*e*]indole-1,3-dione (17): Method B using **3** (0.931 g) and **5b** (0.690 g) gave cream-colored crystals (0.88 g, 57%), mp = 136-137°C; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.67 (dt, *J* = 8.4, 2.4 Hz, 2H, Ts-H), 7.33 (d, *J* = 8.1 Hz, 1H, 7-H), 7.30 (d, *J* = 8.1 Hz, 2H, Ph-H), 7.27 (d, *J* = 3.3 Hz, 1H, Ar), 7.13 (d, *J* = 8.1 Hz, 2H, Ts-H) 6.90 (dd, *J* = 8.4, 2.4 Hz, 1H, Ph-H), 6.71 (dq, *J* = 7.8, 0.9 Hz, 1H, Ph-H), 6.68 (t, *J* = 2.4 Hz, 1H,8-H), 6.50 (d, *J* = 6.3 Hz, 1H, Ph), 3.98 (d, *J* = 8.1 Hz, 1H, 8b-H), 3.78 (s, 3H, OCH$_3$), 3.32 (ddd, *J* = 8.1, 5.4, 5.4 Hz, 1H, 3a-H), 2.94 (ddd, *J* = 17.4, 4.8, 4.8 Hz, 1H, 5-H), 2.64 (ddd, *J* = 15.6, 9.6, 5.1 Hz, 1H, 5-H), 2.41 (s, 3H, Ts CH_3), 2.34 (dddd, *J* = Hz, 1H, 4-H), 1.98 (dddd, *J* = Hz, 1H, 4-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.4, 175.9, 160.1, 145.3, 136.0, 132.8, 130.3, 129.9, 129.6, 122.2, 118.6, 117.0, 114.4, 112.4, 111.7, 55.5, 40.1, 39.7, 22.0, 21.7, 19.7; IR (KBr, cm^{-1}) 3147 (w), 2957 (w), 2939 (w), 2838 (w), 2258 (w), 1783 (w), 1715 (s), 1605 (s), 1493 (s), 1454 (m), 1440 (m), 1373 (s), 1311 (m), 1289 (m), 1256 (m), 1226 (s), 1176 (s), 1130 (s), 1091 (m), 1076 (m), 1043 (m), 911 (m), 813 (m), 771 (m), 735 (s), 707 (m), 689 (m), 669 (s), 648 (w), 635 (w); HRMS ES-TOF [$M+Na^+$] Calcd for $C_{24}H_{22}N_2O_5S$: 473.1093, Found: 473.1154; Anal. Calcd for $C_{24}H_{22}N_2O_5S$: C, 63.98; H, 4.92; N, 6.22; S, 7.12; Found: C, 63.70; H, 5.10; N, 6.17; S, 7.01. The product gave a single spot on silica gel TLC, (ethyl acetate /hexanes 1:1) R_f 0.6.

2-(4-Acetoxyphenyl)-6-tosyl-3a,4,5,8b-tetrahydro-2*H*,3a*H*,6*H*-pyrrolo[3,4-*e*]indole-1,3-dione (18): Diels-Alder adduct **8** (0.33 g) was refluxed in toluene for 5 h and purified by flash chromatography on silica gel using 1:1 ethyl acetate : hexanes to give a cream-white solid (0.26 g, 78%), mp = 170-172°C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.4 Hz, 2H, Ts-H), 7.30 (d, *J* = 7.8 Hz, 2H, Ph-H), 7.28 (d, *J* = 3.6, 1H, 7-H), 7.22-7.13 (m, 4H, Ar-H), 7.18 (d, *J* = 5.6 Hz, 2H, Ph-H), 6.50, (d, *J* = 3.6Hz 1H, 8-H), 4.00 (dt, *J* = 7.8, 1.8Hz, 1H, 8b-H), 3.34 (dt, *J* = 8.1, 5.1Hz, 1H, 3a-H), 2.96 (dt, *J* = 16.8, 4.8 Hz, 1H, 5H), 2.62 (ddd, *J* = 15.6, 9.9, 5.1 Hz, 1H, 5-H), 2.42 (s, 3H $OCOCH_3$), 2.37 (m, 1H, 5-H), 2.31 (s, 3H, Ts-CH_3), 2.00 (dddd, *J* = 15.6, 10.5, 5.7, 5.7 Hz, 1H, 5H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.3, 175.8, 169.1, 150.3, 145.3, 135.7, 130.3, 129.5, 129.2, 127.3, 126.9, 122.3, 122.1, 116.9, 111.5, 40.0, 39.5, 21.7, 21.2, 19.5, 14.3; IR (KBr, cm^{-1}) 3147 (w), 2957 (w), 2930 (w), 2856 (w), 2258 (w), 1755 (m), 1715 (s), 1559 (w), 1507 (m), 1371 (m), 1201 (s), 1176 (s), 1130 (m), 1091 (w), 1020 (w), 911 (m), 814 (w), 731 (m), 705 (m), 668(m); HRMS ES-TOF [M+Na$^+$] Calcd for $C_{25}H_{22}N_2O_6S$: 501.1093, Found: 501.1102 ; Anal. Calcd for $C_{25}H_{22}N_2O_6S$: C, 62.75; H, 4.63; N, 5.85; S, 6.70; Found: C, 62.90; H, 4.80; N, 5.66; S, 6.85. The product gave a single spot on silica gel TLC, (ethyl acetate /hexanes 1:1) R_f 0.5.

2-(4-Chlorophenyl)-6-tosyl-3a,4,5,8b-tetrahydro-2*H*,3a*H*,6*H*-pyrrolo[3,4-*e*]indole-1,3-dione (19): Diels-Alder adduct **9** (0.13 g) was refluxed in chloroform for 6 d. The product was crystallized with ethyl acetate/hexanes to give tiny white crystals (.07 g, 53%) , mp = 175-176°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.1 Hz, 2H, Ph-H), 7.38 (d, *J* = 8.4 Hz, 2H, Ts-H), 7.29 (d, *J* = 8.4 Hz, 2H, Ts-H), 7.26 (d, *J* = 2.7 Hz, 1H, 7-H), 7.11 (d, *J* = 8.4 Hz, 2H, Ph-H), 6.48 (d, *J* = 3.3 Hz, 1H, 8-H), 3.98 (d, *J* = 8.1 Hz, 1H, 8b-H), 3.32 (ddd, *J* = 7.8, 5.4, 5.4 Hz, 1H, 3a-H), 2.92 (ddd, *J* = 17.1, 4.5, 4.5 Hz, 1H, 4-H), 2.63 (ddd, *J* = 15.7, 9.3, 5.0 Hz, 1H, 4-H), 2.41 (s, 3H, CH_3), 2.34 (dddd, *J* = 9.9, 4.8, 4.8, 4.8 Hz, 1H, 5-H), 1.98 (dddd, *J* = 14.7, 10.2, 5.4, 5.4 Hz, 1H, 5-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.8, 175.3, 145.0, 135.6, 134.0, 129.9, 129.2, 129.0, 121.9, 116.4, 111.1, 39.8, 39.2, 21.6, 21.5, 19.2; IR (KBr, cm^{-1}) 2922 (w), 1717 (s), 1493 (m), 1374 (m) 1227 (w), 1175 (m), 1129 (m), 1090 (m), 1016 (w), 813 (w), 735 (s), 705 (m), 669 (m); HRMS ES-TOF [M+Na$^+$] Calcd for $C_{23}H_{19}ClN_2O_4S$: 477.0647, Found: 477.0646; Anal. Calcd for $C_{23}H_{19}ClN_2O_4S$: C, 60.72; H, 4.21; N, 6.16; S, 7.05; Found: C, 60.60; H, 4.23; N, 6.33; S, 6.93. The product gave a single spot on silica gel TLC (ethyl acetate /hexanes 1:1) R_f 0.4.

2-(4-bromophenyl)-6-tosyl-3a,4,5,8b-tetrahydro-2*H*,3a*H*,6*H*-pyrrolo[3,4-*e*]indole-1,3-dione (20): Diels-Alder adduct **10** (0.2154 g) was refluxed in chloroform for 1day . The product was purified by silica gel column chromatography with ethyl acetate/hexanes 1:3-1:1 to give fine white crystals (0.0271g, 13%), mp = 212-213°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ7.68, (d, *J* = 8Hz, 2H, Ts-H), 7.55 (d, *J* = 8Hz, 2H, Ts-H), 7.32 (d, *J* = 8 Hz, Ph-H), 7.29 (d, *J* = 1.6 Hz, 1H, 7-H), 7.08 (d, *J* = 8 Hz, 2H, Ph-H), 6.51 (d, *J* = 2.8 Hz, 1H, 8-H), 4.00 (d, *J* = 8 Hz, 1H, 8b-H), 3.33 (ddd, *J* = 8.8, 5.2, 5.2 Hz, 1H, 3a-H), 2.95 (ddd, *J* = 17.2, 4.8, 4.8 Hz, 1H, 4-H), 2.66 (ddd, *J* = 15.2, 9.2, 5.2 Hz, 1H, 5-H), 2.44n (s, 3H, CH_3-H), 2.37 (dddd, *J* = 14, 4.8, 4.8, 4.8 Hz, 4-H)), 2.00 (dddd, *J* = 14.4, 10, 5.2, 5.2 Hz, 5-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.0, 175.5, 145.2, 135.9, 132.2, 130.7, 130.1, 129.5, 127.7, 126.9, 122.3, 122.1, 116.6, 111.4, 40.1, 39.5, 21.9, 21.7, 19.5. The product gave a single spot on silica gel TLC, (ethyl acetate /hexanes 1:1) R_f 0.47.

2-(4-Nitrophenyl)-6-tosyl-3a,4,5,8b-tetrahydro-2*H*,3a*H*,6*H*-pyrrolo[3,4-*e*]indole-1,3-dione (21): Diels-Alder adduct **11** (0.4572 g) was stirred at room temperature in chloroform for 13d. The product was purified by silica gel column chromatography with ethyl acetate/hexanes 1:2 to give white solid (0.30 g, 65%), mp = 171-173°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.7 Hz, 2H, Ph-H), 7.66 (d, *J* = 8.4 Hz, 2H, Ts-H), 7.46 (dt, *J* = 9, 2.4 Hz, 2H, Ph-H), 7.29 (d, *J* = 8.4 Hz, 2H, Ts-H), 7.25 (d, *J* = 3.6 Hz, 1H, 7-H), 6.49 (d *J* = 3.3 Hz, 1H, 8-H), 4.03 (d, *J* = 8.4 Hz, 1H, 8b-H), 3.38 (ddd, *J* = 8.4, 5.4, 5.4 Hz, 1H, 3a-H), 2.90 (ddd, *J* = 9.6, 4.5, 4.5 Hz, 1H, 5-H), 2.66 (ddd, *J* = 15.6, 9, 5.1 Hz, 1H, 5-H), 2.39 (s, 3H, Ts-CH_3), 2.34 (dddd, *J* = 10.2, 5.1, 5.1, 5.1 Hz, 1H, 4-H), 1.98 (dddd, *J* = 14.7, 10.2, 5.1, 5.1 Hz, 1H, 4-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.3, 175.8, 146.0, 137.9, 136.5, 130.9, 130.1, 127.6, 127.5, 127.4, 124.9, 122.9, 116.9, 111.9, 40.8, 40.3, 22.4, 22.4, 20.1; IR (KBr, cm^{-1}) 1719 (s), 1596 (w), 1524 (m), 1497 (m), 1370 (m), 1344 (s), 1227 (w), 1189 (m), 1175 (s), 1129 (m), 852 (w), 815 (w), 737 (m), 705 (m), 668 (m); Anal. Calcd for $C_{23}H_{19}N_3O_6S$: C, 59.35; H, 4.11; N, 9.03; S, 6.89; Found: C, 59.18; H, 4.13; N, 8.94; S, 6.78. The product gave a single spot on silica gel TLC, (ethyl acetate /hexanes 1:1) R_f 0.4.

2-Phenyl-6-tosyl-3a,4,5,8b-tetrahydro-2*H*,3a*H*,6*H*-pyrrolo[3,4-*e*]indole-1,3-dione (22): Diels-Alder adduct **12** (0.042 g) was refluxed in chloroform for 1.5 h. The product was crystallized with ethyl acetate/hexanes to give tan crystals (0.018g, 43%), mp = 149-151°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.4 Hz, 2H, Ts-H), 7.40 (m, 3H, Ar), 7.29 (d, *J* = 8.1 Hz, 2H, Ts-H), 7.26 (d, *J* =3.3 Hz, 1H, 7-H), 7.12 (dd, *J* = 8.4, 1.8 Hz, 2H, Ar), 6.50 (d, *J* = 3.3 Hz, 8-H), 3.99 (dd, *J* = 8.1, 1.5 Hz, 1H, 8b-H), 3.32 (ddd, *J* = 8.1, 5.4, 5.4 Hz, 1H, 3a-H), 2.94 (ddd, *J* = 16.5, 4.8, 1.5 Hz, 1, 5-H), 2.63 (ddd, *J* = 15.9, 9.9, 5.4Hz, 1H, 5-H), 2.41 (s, 3H, Ts-CH_3), 2.34 (ddd, *J* = 8.4, 5.1, 5.1 Hz, 1H, 4-H), 1.98 (ddd, *J* = 9.6, 5.1, 0.5 Hz, 1H, 4-H) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.0, 176.5, 145.9, 136.6, 132.4, 130.8, 130.2, 129.7, 129.2, 127.5, 126.9, 122.8, 117.6, 112.2, 40.7, 40.2, 22.6, 22.4, 20.1; IR (KBr, cm^{-1}) 1716 (s), 1597 (w), 1498 (w), 1375 (m), 1226 (w), 1189 (m), 1175 (s), 1129 (m), 1091 (w), 734 (m), 705 (m), 669 (m); HRMS ES-TOF [M+Na$^+$] Calcd for $C_{23}H_{20}N_2O_4S$:443.1036, Found: 443.1059. The product gave a single spot on silica gel TLC, (ethyl acetate /hexanes 1:1) R_f 0.34.

2-dimethylamino-6-tosyl-3a,4,5,8b-tetrahydro-2*H*,3a*H*,6*H*-pyrrolo[3,4-*e*]indole-1,3-dione (23): Method A using **3** (1.0207 g) and **5h** (0.6459 g) followed by purification by silica gel chromatography with ethyl acetate/hexanes gave yellow glassy solid (0.278g, 16%), mp = 157-158°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.4 Hz, 2H, Ts-H), 7.26 (d, *J* = 8.1 Hz, 2H, Ts-H), 7.23 (d, *J* = 3.6 Hz, 1H, 7-H), 6.45 (d, *J* = 3.3 Hz, 8-H), 3.73 (dt, *J* = 7.8, 1.2 Hz, 1H, 8b-H), 3.06 (ddd, *J* = 8.1, 5.7, 5.4 Hz, 1H, 4-H), 2.85 (ddd, *J* = 17.4, 5.4, 5.4 Hz, 1H, 4-H), 2.72 (s, 6H, N-CH_3-H), 2.54 (ddd, *J* = 17.1, 9.0, 5.1 Hz, 1H, 4-H), 2.38 (s, 3H, Ts CH_3-H), 2.18 (dddd, *J* = 13.8, 5.1, 5.1, 5.1 Hz, 1H, 5-H), 1.88 (dddd, *J* = 14.4, 9.3, 5.1, 5.1 Hz, 1H, 5-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.4, 175.0, 144.9, 135.6, 129.8, 129.1, 126.5, 121.5, 116.5, 111.5, 52.1, 43.5, 38.2, 37.5, 21.7, 21.4, 19.2; IR (KBr, cm^{-1}) 2961 (w), 1784 (w), 1719 (s), 1449 (w), 1369 (m), 1229 (w), 1192 (m), 1177 (s), 1148 (m), 1129 (mm), 815 (w), 735 (w), 706 (m), 670 (m); HRMS ES-TOF Calcd for [M+Na$^+$] $C_{19}H_{21}N_3O_4S$: 410.1145, Found: 410.1157; Anal. Calcd for $C_{19}H_{21}N_3O_4S$: C, 58.90; H, 5.46; N, 10.05; S, 8.28; Found: C, 58.78; H, 5.45; N, 10.91; S, 8.13. The product gave a single spot on silica gel TLC, (ethyl acetate /hexanes 1:1) R_f 0.5.

2-methyl-6-tosyl-3a,4,5,8b-tetrahydro-2*H*,3a*H*,6*H*-pyrrolo[3,4-*e*]indole-1,3-dione (24): Diels-Alder adduct **14**(0.210 g) was refluxed in dichloromethane and crystallized with ethyl acetate/hexanes to give white solid (0.021g, 10%), mp = 172-174°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.5 Hz, 2H, Ts-H), 7.29 (d, *J* = 8.0 Hz, 2H, Ts-H), 7.23 (d, *J* = 3.5 Hz, 1H, 7-H), 6.46 (d, *J* = 3.5 Hz, 1H, 8-H), 3.82 (d, *J* = 8.0 Hz,1H, 8a-H), 3.14 (ddd, *J* = 8.0, 5.5, 5.5 Hz, 1H, 3a-H), 2.91 (s, 3H, CH_3), 2.88 (ddd, *J* = 10.2, 5.5, 5.5

Hz, 1H, 4-H), 2.53 (ddd, *J* = 15.5, 9.5, 5.0 Hz, 1H, 4-H), 2.42 (s, 3H, Ts-CH_3), 2.25 (dddd, *J* = 14.0, 5.5, 5.5, 5.5 Hz, 1H, 5-H), 1.89 (dddd, *J* = 15.0, 10.5, 5.5, 5.5 Hz, 1H, 5-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.5, 177.1, 145.2, 135.9, 130.2, 129.2, 126.9, 121.8, 116.9, 111.2, 39.7, 39.4, 24.9, 21.9, 21.7, 19.4; IR (KBr, cm^{-1}) 2950 (w), 1777 (w), 1706 (s), 1595 (w), 1434 (m), 1370 (m), 1278 (w), 1226 (w), 1192 (m), 1179 (m), 1148 (m), 1128 (m), 1089 (w), 1061 (w), 1019 (w), 997 (w), 814 w), 769 (w), 734 (w), 705 (m), 608 (w); HRMS ES-TOF [M+Na$^+$] Calcd for $C_{18}H_{18}N_2O_4S$: 381.0879, Found: 381.0860. The product gave a single spot on silica gel TLC, (hexane-ethyl acetate 1:1) R_f 0.3.

2-(3-Methoxyphenyl)-6-tosyl-5-methyl-3a,4,5,8b-tetrahydro,-2*H*,3a*H*,6*H*-pyrrolo[3,4-*e*]indole-1,3-dione (25): Method B using **4** (0.9269 g) and **5b** (0.7204 g) followed by purification by silica gel chromatography with ethyl acetate/hexanes gave cream crystals, (0.443 g, 27%) mp = 207-210°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.4 Hz, 2H, Ts-H), 7.35 (d, *J* = 8.4 Hz, 2H, Ts-H), 7.28 (dd, *J* = 8.1, 8.1 Hz, 1H, ph-H), 7.25 (d, *J* = 3.6 Hz, 1H, 7-H), 6.91 (dd, *J* = 8.4, 2.1 Hz, 1H, ph-H), 6.79 (d, *J* = 7.6 Hz, 1H, ph-H), 6.74 (dd, *J* = 2.4, 2.4 Hz, 1H, ph-H), 6.50 (d, *J* = 3.3 Hz, 8-H), 4.03 (d, *J* = 9.3 Hz, 1H, 8b-H), 3.78 (s, 3H, OCH_3-H) , 3.41 (dd, *J* = 6.0, 6.0, 1H, 3a-H), 3.30 (ddd, *J* = 9.0, 7.2, 1.8 Hz, 1H, 4-H), 2.57 (ddd, *J* = 14.1, 1.8, 1.8 Hz, 1H, 4-H), 2.41 (s, 3H, Ts CH_3-H), 1.91 (ddd, *J* = 13.7, 6.9, 6.0 Hz, 1H, 5-H), 1.15 (d, *J* = 6.9 Hz, 3H, CH_3-H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.6, 175.7, 160.1, 145.1, 136.4, 135.0, 132.9, 130.1, 129.8, 126.6, 122.7, 118.4, 116.2, 114.4, 112.2, 112.1, 55.4, 39.5, 37.6, 29.2, 26.8, 22.9, 21.6; IR (KBr, cm^{-1}) 2970 (w), 29.. (w), 1713 (s), 1606 (m), 1593 (m), 1494 (m), 1370 (m), 1257 (m), 1230 (m), 1204 (m), 1180 (s), 1158 (m), 1126 (m), 1086 (m), 815 (w), 726 (m), 708 (w), 677 (m); Anal. Calcd for $C_{25}H_{24}N_2O_5S$: C, 64.64; H, 5.21; N, 6.03; S, 6.90; Found: C, 64.35; H, 5.25; N, 5.98; S, 6.75. The product gave a single spot on TLC (ethyl acetate /hexanes 1:1) R_f 0.48.

2-phenyl-6-tosyl-5-methyl-3a,4,5,8b-tetrahydro,-2*H*,3a*H*,6*H*-pyrrolo[3,4-*e*]indole-1,3-dione (26): Method B using **4** (0.6900 g) and **5g** (0.4265 g) followed by purification by silica gel chromatography with ethyl acetate/hexanes gave a yellow solid, (0.166 g, 15%) mp = 189-196°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.4, 2H, Ts-H), 7.22-7.42 (m, 5H, ph-H), 7.25 (d, *J* = 3.6 Hz, 1H, 7-H), 7.21 (d, *J* = 8.4 Hz, 2H, Ts-H), 6.49 (d, *J* = 3.3 Hz, 1H, 8-H), 4.02 (d, *J* = 9 Hz, 1H, 8b-H), 3.40 (dd, *J* = 3, 3 Hz, 1H, 3a-H), 3.30 (ddd, *J* = 1.8, 7.2, 9 Hz, 1H, 5-H), 2.58 (ddd, *J* = 1.8, 1.8, 14.1 Hz, 1H, 4-H), 2.40 (s, 3H, Ts CH_3-H), 1.88 (ddd, *J* = 1.5, 5.7, 13.2 Hz, 1H, 4-H), 1.15 (d, *J* = 7.2 Hz, 3H, CH_3-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.5, 175.6, 144.8, 136.0, 131.6, 129.9, 128.9, 128.4, 126.4, 125.9, 122.5, 115.9, 111.8, 39.2, 37.3, 28.9, 26.5, 22.7, 21.4; IR (KBr, cm^{-1}) 1716 (s), 1597 (w), 1500 (w), 1380 (m), 1230 (w), 1206 (w), 1189 (m), 1176 (s), 1126 (m), 1087 (w), 732 (w), 692 (w), 676 (m). The product gave a single spot on TLC (ethyl acetate /hexanes 1:1) R_f 0.5.

2-(3-Methoxyphenyl)-6-(5-methyl)-tosylpyrrolo[3,4-*e*]indole-1,3-dione (27): Method B using **4** (0.9269 g) and **5b** (0.7204 g) followed by purification by silica gel chromatography with ethyl acetate/hexanes and crystallization with chloroform to give yellow needles, (0.013g, 4%) mp = 193.5-194°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (d, *J* = 3.6 Hz, 1H, 4-H), 7.58 (d, *J* =8.4 Hz, 2H, Ts-H), 7.56 (d, *J* = 2.4 Hz, 1H, 7-H), 7.40

(dd, *J* = 8.4, 8.4 Hz, 1-H, ph-H), 7.31 (d, *J* = 3.9 Hz, 1H, 8-H), 7.29 (dd, *J* = 8.7, 0.6 Hz, 2H, Ts-H), 7.02 (ddd, *J* = 7.8, 1.8, 0.9 Hz, 1H, ph-H), 6.98 (dd, *J* = 2.1, 2.1 Hz, 1H, ph-H), 6.94 (ddd, *J* = 8.1, 2.4, 0.9 Hz, 1H, ph-H), 3.84 (s, 3H, OCH_3-H), 2.71 (s, 3H, Ts CH_3-H), 2.41 (s, 3H, CH_3-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.6, 167.2, 160.2, 145.6, 138.8, 136.4, 135.1, 132.9, 131.9, 130.3, 129.7, 128.7, 127.9, 126.5, 122.3, 121.6, 118.8, 113.9. 112.3, 55.4, 22.6, 21.7; IR (KBr, cm^{-1}) 1767 (w), 1716 (s), 1604 (m), 1495 (m), 1400 (w), 1370 (s), 1274 (m), 1253 (m), 1241 (m), 1174 (s), 1126 (m), 1100 (m), 1081 (m), 732 (m), 671 (m); Anal. Calcd for $C_{25}H_{20}N_2O_5S$: C, 65.20; H, 4.38; N, 6.08; S, 6.96; Found: C, 64.48; H, 4.11; N, 6.03; S, 7.21. The product gave a single spot on TLC (ethyl acetate /hexanes 1:1) R_f 0.67.

Tetramethyl 1-tosyl-6,7-dihydro-1*H*-indole-4,5,7-ethenyl-1',2'-tetracarboxylate (29): Method A using **3** (1.1019 g) and **28** (0.5858 g) followed by purification by silica gel chromatography with ethyl acetate/hexanes and crystallization with chloroform to give pale amber crystals (0.06 g, 3%) mp = 135-140°C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.3 Hz, 2H, Ts-H), 7.32 (d, *J* = 3.4 Hz, 1H, 2-H), 7.25 (d, *J* = 8.1 Hz, 2H, Ts-H), 6.30 (d, *J* = 3.4 Hz, 1H, 3-H), 4.81 (d, *J* = 1.0 Hz, 1H,), 4.47 (d, *J* = 8.7 Hz, 1H 5-H), 3.86 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 3.56 (s, 3H, OCH_3), 3.17 (dd, *J* = 0.9, 17.6 Hz, 1H, 4-H), 2.78 (dd, *J* = 9.0, 17.7 Hz, 1H, 4-H), 2.37 (s, 3H, Ts-CH_3) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.2, 165.0, 136.5, 162.1, 144.2, 143.3, 132.9, 132.2, 127.6, 126.0, 125.1, 121.2, 119.7, 118.9, 117.8, 106.6, 50.2, 50.1, 49.9, 49.3, 32.2, 26.7, 19.2; HRMS ES-TOF [M+Na^+] Calcd for $C_{25}H_{25}NO_{10}S$:

554.1091, Found: 554.1155. The product gave a single spot on TLC (ethyl acetate /hexanes 1:1) R_f 0.4.

Dimethyl 1-tosyl-1*H*-indole-4,5 dicarboxylate (30): Method A using **3** (1.1019 g) and **31** (0.5858 g) followed by silica gel chromatography with ethyl acetate/hexanes gave yellow crystals, (0.66 g, 42 %) mp = 193-195°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.7 Hz, 1H, 7-H), 7.79 (d, *J* = 9.0 Hz, 1H, 6-H), 7.73 (d, *J* = 8.4 Hz, 2H, Ts-H), 7.68 (d, *J* = 3.6 Hz, 1H, 2-H), 7.21 (d, *J* = 8.7 Hz, 2H, Ts-H), 6.82 (d, *J* = 3.6 Hz, 1H, 3-H), 3.95 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3), 2.31 (s, 3H, Ts-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.4, 166.9, 145.5, 136.2, 134.2, 129.8, 128.9, 128.6, 126.6, 126.5, 125.2, 125.0, 114.8, 108.0, 52.5, 52.4, 21.1; HRMS ES-TOF [M+Na$^+$] Calcd for $C_{19}H_{17}NO_6S$: 410.0669, Found: 410.0695; Anal. Calcd for $C_{19}H_{17}NO_6S$: C, 58.91; H, 4.42; N, 3.62; S, 8.28; Found: C, 58.49; H, 4.47; N, 3.57; S, 8.28. The product gave a single spot on TLC (ethyl acetate /hexanes 1:1) R_f 0.63.

5.2 Experimental for Part II

General method for forming hydroperoxides. Unrearranged Diels-Alder adduct (10 mmol) was stirred in chloroform in a vessel with attached air balloon for 1-15 days at room temperature. The product was purified by silica gel chromatography with 1:1 ethyl acetate/hexanes followed by crystallization from chloroform.

3aR,5R,8bR-5-hydroperoxy-2-phenyl-6-tosyl-4,5,6,8 b-tetrahydropyrrolo [3,4-e]indole-1,3(2H,3aH)-dione (35): The general method using **12** (0.3672 g) and purification by silica gel chromatography with ethyl acetate/hexanes gave pale yellow solid, (0.698 g, 53 %), mp = 152-153°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.32 (s, 1H, OOH), 7.84 (d, *J* = 8.4 Hz, 2H, Ts-H), 7.42 (m, 3H, Ph-H), 7.33 (d, *J* = 3.6 Hz, 1H, 7-H), 7.31(d, *J* = 8.4 Hz, 2H, Ts-H), 7.26 (m, 2H, Ph-H), 6.62 (d, *J* = 3.1 Hz, 1H, 8-H), 5.64 (dd, *J* = 3, 3 Hz, 1H, 5-H), 3.98 (d, *J* = 8.4 Hz, 1H, 8b-H), 3.57 (ddd, *J* = 13.8, 8.4, 5.7 Hz, 1H, 3a-H), 3.11 (ddd, *J* = 14.4, 5.7, 3 Hz, 1H, 4-H), 2.41 (s, 3H, Ts-CH_3), 1.73 (ddd, *J* = 12.4, 12.4, 2.7 Hz, 4-H); ^{13}C NMR (125 MHz, DMSO) δ 178.1, 174.8, 145.5, 135.1, 132.4, 129.9, 128.9, 128.4, 127.6, 127.3, 125.3, 124.1, 121.6, 112.6, 70.8, 38.8, 35.3, 27.9, 21.1; IR (NaCl, cm^{-1}) 3361 (O-H), 2917 (C-H), 1713 (C=O), 1595 (C=C), 1370 (S=O), 1177 (C-O), 808, 751, 672; MS (ESI, PEG, m/z) [M+Na^+] Calcd for $C_{23}H_{20}N_2O_6S$: 475.0934, Found: 475.0921. The product gave a single spot on TLC (ethyl acetate /hexanes 1:1) R_f 0.3.

3aR,5S,8bR-5-hydroperoxy-2-dimethylamino-tosyl-4,5,6,8 b-tetrahydropyrrolo [3,4-e]indole-1,3(2H,3aH)-dione (36): A Diels-Alder reaction between **3**(1.0207 g) and **5h** (0.6459 g) and purification by silica gel chromatography with ethyl acetate/hexanes gave yellow crystals(0.1517 g, 8 %), mp = 138-140°C; ^1H NMR (300 MHz, $CDCl_3$) δ 8.67 (s, 1H, OOH), 7.78 (dd, *J* = 8.4, 2.1 Hz, 2H, Ts-H), 7.25 (d, *J* = 3.3 Hz, 1H, 7-H), 7.24 (d, *J* = 8.4 Hz, 2H, Ts-H), 6.41 (d, *J* = 3.6 Hz, 1H, 8-H), 5.01 (dd, *J* = 2.4, 2.4 Hz, 1H, 5-H), 3.91 (d, *J* = 8.7 Hz, 1H, 8b-H), 3.19 (ddd, *J* 12, 3.0, 2.1 Hz, 1H, 4-H), 3.11 (ddd, *J* = 8.4, 6.0, 2.1 Hz, 1H, 3a-H), 2.72 (s, 6H, $NN(CH_3)_2$), 2.36 (s, 3H, Ts-CH_3), 1.73 (ddd, *J* = 15, 6.0, 2.1 Hz, 1H, 4-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.5, 175.5, 146.1, 136.0, 130.5, 128.2, 125.6, 125.4, 122.2, 112.2, 72.4, 44.1, 39.2, 35.0, 25.2, 22.3; MS (ESI, PEG, m/z) [M+Na^+] Calcd for $C_{19}H_{21}N_3O_6S$: 442.1043, Found: 442.1084. The product gave a single spot on TLC (ethyl acetate /hexanes 1:1) R_f 0.23.

3aR,5S,8bR-5-hydroperoxy-2-(4-methoxyphenyl)-6-tosyl-4,5,6,8 b-tetrahydropyrrolo [3,4-e]indole-1,3(2H,3aH)-dione (37): The general method using **6** (0.537 g) and purification by silica gel chromatography with ethyl acetate/hexanes gave light yellow crystals(0.226 g, 39 %) , mp = 139-143°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.61(s, 1H, OOH), 7.86 (d, *J* = 8.4, 2H, Ts-H), 7.32 (d, *J* = 8.4 Hz, 2H, Ts-H), 7.31 (d, *J* = 3.3 Hz, 1H, 7-H), 7.04 (dt, *J* = 9.5, 2.4 Hz, 2H, Ph-H), 6.92 (dt, *J* = 9.5, 2.4 Hz, 2H, Ph-H), 6.48 (d, *J* = 3.3 Hz, 1H, 8-H), 5.83 (t, *J* = 2.5 Hz, 1H, 5-H), 4.16 (d, *J* = 8.1 Hz, 1H, 8b-H), 3.81 (s, 3H, OCH_3), 3.36 (m, 1H, 3a-H), 3.33 (m, 1H, 4-H), 2.43 (s, 3H, Ts-CH_3), 1.89 (ddd, *J* = 15.6, 6.3, 2.1 Hz, 1H, 4-H); ^{13}C NMR (75 MHz, $CDCl_3$) 180.6, 175.6, 159.4, 145.2, 135.1, 129.7, 127.4, 124.6, 124.4, 123.9, 121.4, 114.2, 114.1, 111.1, 71.6, 55.3, 39.8, 35.8, 24.5, 21.5; MS (ESI, PEG, m/z) [M+Na$^+$] Calcd for $C_{24}H_{22}N_2O_7S$: 505.1041. Found: 505.1032; The product gave a single spot on TLC (ethyl acetate /hexanes 1:1) R_f 0.4.

3aR,5R,8bR-5-hydroperoxy-2-dimethylamino-6-tosyl-4,5,6,8 b-tetrahydropyrrolo [3,4-e]indole-1,3(2H,3aH)-dione (38): A Diels-Alder reaction between **3**(1.0207 g) and **5h** (0.6459 g) and purification by silica gel chromatography with ethyl acetate/hexanes gave yellow needles(0.1500 g, 8%), mp = 145-147°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.908 (s, 1H, OOH), 7.83 (d, *J* = 8.4 Hz, 2H, Ts-H), 7.30 (d, *J* = 8.4 Hz, 2H, Ts-H), 7.29 (d, *J* = 3.6 Hz, 1H, 7-H), 6.57 (d, *J* = 3.3 Hz, 1H, 8-H), 5.60 (dd, *J* = 2.4, 2.7 Hz, 1H, 5-H), 3.73 (d, *J* = 8.4 Hz, 1H, 8b-H), 3.35 (ddd, *J* = 5.3, 8.4, 13.5 Hz, 1H, 3a-H), 3.03 (ddd, *J* = 2.7, 5.4, 14.4 Hz, 1H, 4-H), 2.88 (s, 6H, NN(CH_3)$_2$), 2.40 (s, 3H, Ts-CH_3), 1.54 (ddd, *J* = 2.7, 14.4, 15.9 Hz, 1H, 4-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.9, 173.6, 145.3, 135.5, 129.7, 124.6, 124.3, 121.0, 111.7, 71.8, 43.7, 37.3, 33.9, 28.7, 21.5. The product gave a single spot on TLC (ethyl acetate /hexanes 1:1) R_f 0.43.

3aR,5R,8bR-5-hydroperoxy-2-(4-methoxyphenyl)-6-tosyl-4,5,6,8 b-tetrahydropyrrolo [3,4-e]indole-1,3(2H,3aH)-dione (39): The general method using **3** (0.0537 g) and purification by silica gel chromatography with ethyl acetate/hexanes gave yellow solid (0.0134 g, 21 %), mp =106-108 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 8.605 (s, 1H, OOH), 7.83 (dt, *J* = 8.4, 1.8Hz, 2H, Ts), 7.33 (d, *J* = 3.3 Hz, 1H, 7-H), 7.35 (d, *J* = 8.7 Hz, 2H, Ts), 7.16 (dt, *J* = 9.0, 2.4 Hz, 2H, Ts), 6.96 (dt, *J* = 9.0, 2.1 Hz, 2H, Ts), 6.62 (d, *J* = 3.6 Hz, 1H, 8-H), 5.63 (dd, *J* = 3.0, 2.7 Hz, 1H, 5-H), 3.97 (d, *J* = 8.4 Hz, 1H, 8b-H), 3.81 (s, 3H, OCH_3), 3.54 (ddd, *J* = 13.2, 8.4, 2.7 Hz, 1H, 3a-H), 3.10 (ddd, *J* = 14.4, 5.7, 3.0 Hz, 1H, 4-H), 2.41 (s, 3H, Ts-CH_3), 1.72 (ddd, *J* = 14.4, 12.9, 2.7 Hz, 1H, 4-H) ; ^{13}C NMR (75 MHz, $CDCl_3$) 180.6, 175.6, 159.4, 145.2, 135.1, 129.7, 127.4, 121.4m 114.2, 114.1, 111.1, 71.6, 55.3, 39.8, 35.8, 24.5, 21.5; IR (KBr, cm^{-1}) 2918 (w), 1772 (w), 1714 (s), 1513 (m), 1434 (w), 1395 (m), 1374 (m), 1302 (w), 1250 (m), 1181 (m), 1141 (m), 1108 (m), 1088 (m), 1029 (w), 807 (m), 671 (m); MS (ESI, PEG, m/z) [M+Na^+] Calcd for $C_{24}H_{22}N_2O_7S$: 505.1041; Found: 505.1032. The product gave a single spot on TLC (ethyl acetate /hexanes 1:1) R_f 0.43.

3aR,5S,8bR-5-hydroperoxy-2-(3-methoxyphenyl)-6-tosyl-4,5,6,8 b-tetrahydropyrrolo [3,4-e]indole-1,3(2H,3aH)-dione (40): The general method using **7** (0.6190 g) and purification by silica gel chromatography with ethyl acetate/hexanes gave light yellow crystals (0.1680 g, 25%), mp = 130-131°C; ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.87 (s, 1H, OOH), 7.83 (dd, *J* = 2.1, 8.4 Hz, 2H, Ts-H), 7.28 (d, *J* = 3.36 Hz, 1H, 7-H), 7.27 (d, *J* = 8.4 Hz, 1H, Ph-H), 7.26 (d, *J* = 8.4 Hz, 2H, Ts-H), 6.87 (ddd, *J* = 0.9, 2.7, 8.4 Hz, 1H, Ph-H), 6.68 (ddd, *J* = 0.9, 1.8, 8.1 Hz, 1H, Ph-H), 6.62 (dd, *J* = 2.1, 2.1 Hz, 1H, Ph-H), 6.44 (d, *J* = 3.3 Hz, 1H, 8-H), 5.78 (dd, *J* = 2.1, 2.1 Hz, 1H, 5-H), 4.11 (d, *J* = 8.7 Hz, 1H, 8b-H), 3.72 (s, 3H, OCH$_3$), 3.33 (ddd, *J* = 2.7, 6.6, 9.0 Hz, 1H, 3a-H), 3.29 (ddd, *J* = 2.1, 2.7, 15.0 Hz, 1H, 4-H), 2.37 (s, 3H, Ts-CH$_3$), 1.83 (ddd, *J* = 2.7, 6.3, 15.7 Hz, 1H, 4-H); ^{13}C NMR (75 MHz, CDCl$_3$) 181.2, 176.3, 160.7, 146.19, 136.0, 133.3, 130.6, 130.5, 128.3, 125.6, 125.4, 122.4, 119.4, 115.3, 113.0, 112.2, 56.0, 40.8, 36.8, 25.4, 22.4; MS (ESI, PEG, m/z) [M+Na$^+$] Calcd for $C_{24}H_{22}N_2O_7S$: 505.1041, Found: 505.1030. The product gave a single spot on TLC (ethyl acetate /hexanes 1:1) R$_f$ 0.3.

3aR,5S,8bR-5-hydroperoxy-2-(4-Nitrophenyl)-6-tosyl-4,5,6,8 b-tetrahydropyrrolo [3,4-e]indole-1,3(2H,3aH)-dione (41): The general method using **11** (0.4572 g) and purification by silica gel chromatography with ethyl acetate/hexanes gave yellow solid, (0.0460 g), (9%); mp = 171-173 °C; ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.65 (s, 1H, OOH), 8.23 (dt, *J* = 9, 2.4 Hz, 2H, Ph-H), 7.84 (dt, *J* = 8.7, 2.1 Hz, 2H, Ts-H), 7.40 (dt, *J* = 9, 2.4 Hz, 2H, Ph-H), 7.31 (d, *J* = 3.6 Hz, 1H, 7-H), 7.29 (d, *J* = 8.7 Hz, 2H, Ts-H), 6.45 (d, *J* = 2.7 Hz, 1H, 8-H), 5.82 (dd, *J* = 2.7, 2.7 Hz, 1H, 5-H), 4.20 (d, *J* = 8.4 Hz, 1H, 8b-H), 3.42 (ddd, *J* = 8.4, 6, 2.1 Hz, 1H, 3a-H), 3.33 (ddd, *J* = 15, 3, 2.1 Hz, 1H, 4-H), 2.94 (s, 3H, Ts-CH$_3$), 1.92 (ddd, *J* = 15, 6, 2.1 Hz, 1H, 4-H) ; ^{13}C NMR (75 MHz, CDCl$_3$) δ 180.2, 175.4, 147.7, 137.8, 135.8, 131.0, 130.7, 128.4, 127.8, 125.5, 124.9, 121.7, 121.8, 111.8, 72.6, 40.8, 36.9, 25.5, 22.4. The product gave a single spot on TLC (ethyl acetate /hexanes 1:1) R_f 0.28.

3aR,5R,8bR-5-hydroperoxy-2-(3-methoxyphenyl)-6-tosyl-4,5,6,8 b-tetrahydropyrrolo [3,4-e]indole-1,3(2H,3aH)-dione(42): The general method using **7** (0.619 g) gave white crystals(0.0350 g, 4 %), mp = 151-153°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.32 (s, 1H, OOH), 7.83 (d, *J* = 8.4 Hz, 2H, Ts-H), 7.36 (d, *J* = 8.1 Hz, 1H, Ts-H), 7.34 (d, *J* = 3.6 Hz, 1H, 7-H) 7.32 (d, *J* = 8.1 Hz, 1H, Ph-H), 6.93 (dd, *J* = 2.4, 8.4 Hz, 1H, Ph-H), 6.84 (ddd, *J* = 0.9, 1.8, 8.4 Hz, 1H, Ph-H), 6.78 (dd, *J* = 2.4, 2.4 Hz, 1H, Ph-H) 6.63 (d, *J* =3.3 Hz, 1H, 8-H) 5.65 (dd, *J* = 3.0, 3.0 Hz, 1H, 5-H), 3.99 (d, *J* = 8.4 Hz, 1H, 8b-H), 3.80 (s, 3H, OCH_3), 3.55 (ddd, *J* = 5.7, 8.1, 13.2 Hz, 1H, 3a-H), 3.11 (ddd, *J* = 3.0, 6.0, 14.1 Hz, 1H, 4-H), 2.42 (s, 3H, Ts-CH_3), 1.76 (ddd, *J* = 2.7, 12.9, 15.0 Hz, 1H, 4-H); ^{13}C NMR (75 MHz, $CDCl_3$) 177.6, 174.4, 160.1, 145.6, 135.8, 132.6, 130.0, 129.9, 127.3, 124.8, 124.6, 121.6, 118.6, 114.8, 112.1, 112.0, 72.3, 55.5, 39.3, 35.8, 29.1, 21.7; MS (ESI, PEG, m/z) [$M+Na^+$] Calcd for $C_{24}H_{22}N_2O_7S$: 505.1041, Found: 505.1032 ; The product gave a single spot on TLC (ethyl acetate /hexanes 1:1) R_f 0.36.

3aR,5S,8bR-5-hydroperoxy-2-phenyl-6-tosyl-4,5,6,8 b-tetrahydropyrrolo [3,4-e]indole-1,3(2H,3aH)-dione (43): The general method using **12** (0.3672 g) gave yellow solid, (0.0208 g,17%), mp = 145-150°; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.74 (s, 1H, OOH), 7.84 (d, *J* = 8.4 Hz, 2H, Ts-H), 7.37 (m, 3H, Ph-H), 7.29 (d, *J* = 8.4 Hz, 2H, Ts-H), 7.29 (d, *J* = 3.6 Hz, 1H, 7-H), 7.11 (dd, *J* = 8.7, 1.8 Hz, 2H, Ph-H), 6.45 (d, *J* = 3.3 Hz, 1H, 8-H), 5.80 (dd, *J* = 2.4, 2.4 Hz, 1H, 5-H), 4.14 (d, *J* = 8.1 Hz, 1H, 8b-H), 3.34

(ddd, *J* = 8.4, 6, 2.4 Hz, 1H, 3a-H), 3.31 (ddd, *J* = 15.6, 2.4, 2.4 Hz, 1H, 4-H), 2.39 (s, 3H, Ts-CH_3), 1.85 (ddd, *J* = 15.3, 6, 2.1 Hz, 1H, 4-H). The product gave a single spot on TLC (ethyl acetate /hexanes 1:1) R_f 0.27.

5.3 Experimental for Part III

General method for bromination. Diels-Alder adduct **6** (10 mmol) was combined with *N*-bromosuccinimide (10 mmol) in chloroform (30 mL) at 0° C or room temperature and stirred from 1.5-3 hours. The product was purified by silica gel chromatography with 1:1 ethyl acetate/hexanes.

2-(4-methoxyphenyl)-6-tosyl-6,8b-dihydropyrrolo[3,4-*e*]indole-1,3(2*H*,3a*H*)-dione (48): (0.0939 g, 22 %); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.4 Hz, 2H, Ts-H), 7.31 (d, *J* = 8.4 Hz, 2H, Ts-H), 7.20 (d, *J* = 3.3 Hz, 1H, 7-H), 7.14 (d, *J* = 9.0 Hz, 2H, Ph-H), 6.99 (dd, *J* = 2.4, 10.2 Hz, 1H, 5-H), 6.94 (d, *J* = 9.0 Hz, 2H, Ph-H), 5.86 (dd, *J* = 4.8, 10.2 Hz, 1H, 4-H), 4.25 (d, *J* = 12.3 Hz, 1H, 8a-H), 3.99 (ddd, *J* = 2.4, 4.5, 12.3 Hz, 1H, 3a-H), 3.80 (s, O-CH_3), 2.41 (s, Ts-CH_3);. The product gave a single spot on TLC (hexane-ethyl acetate 1:1) R_f 0.46.

(4S,5S)-4-bromo-5-hydroxy-2-(4-methoxyphenyl)-6-tosyl-4,5,6,8b-tetrahydropyrrolo[3,4-*e*]indole-1,3(2*H*,3a*H*)-dione (49): (0.1127 g, 21 %), ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (dd, *J* = 8.4, 1.8 Hz, 2H, Ts-H), 7.30 (d, *J* = 8.7 Hz, 2H, Ts-H), 7.29 (d, *J* = 3.3 Hz, 1H, 7-H), 7.10 (dt, *J* = 9, 3.3 Hz, 2H, Ph-H), 7.08 (d, *J* = 3.3 Hz, 1H, 7-H), 6.91 (dt, *J* = 9, 3.3 Hz, 2H, Ph-H), 6.55 (d, *J* = 3.3 Hz, 1H, 8-H), 5.45 (d, *J* = 2.7 Hz, 1H, 5-H), 5.07 (dd, *J* = 3, 2.1 Hz, 1H, 4-H), 4.16 (d, *J* = 8.7 Hz, 1H, 8b-H), 3.78 (s, 3H, CH_3), 3.72 (dd, *J* = 8.7, 2.1 Hz, 1H, 3a-H), 2.95 (br s, 1H, OH), 2.41 (s, 3H, tosyl

CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.7, 174.4, 159.7, 145.7, 135.8, 130.3, 127.9, 127.7. 127.1, 124.3, 123.8, 118.1, 114.5, 111.9, 65.5, 55.6, 45.3, 38.6, 21.8; IR (KBr, cm^{-1}) 3470(w), 3058 (w), 2961 (w), 2924 (w), 2840 (w), 1765 (w), 1713 (s), 1609 (w), 1595 (w), 1512 (s), 1460 (m), 1442 (m), 1383 (s), 1300 (m), 1251 (s), 1176 (m), 1089 (m), 1030 (m), 988 (w), 885 (w), 810 (m), 734 (m), 703 (m), 670 (s), 633 (m); MS (ESI, PEG, m/z) [$M+Na^+$] Calcd for $C_{25}H_{22}BrNO_6S$: 567.0196, Found: 567.0194 ; The product gave a single spot on TLC (hexane-ethyl acetate 1:1) R_f 0.38.

2-(4-Methoxyphenyl)-6-tosylpyrrolo[3,4-*e*]indole-1,3-dione(50): yellow solid, (0.0250 g, 6 %), mp = 220-222°C; ^1H NMR (300 MHz, $CDCl_3$) δ 8.36 (dd, *J* = 8.4, 0.9 Hz, 1H, 5-H), 7.88 (d, *J* = 5.4 Hz, 1H, 7-H), 7.87 (d, *J* = 10.5 Hz, 1H, 4-H), 7.82 (dt, *J* = 1.8, 8.4 Hz, 2H, Ts-H), 7.34 (dt, *J* = 9, 2.4 Hz, 2H, Ph-H), 7.29 (d, *J* = 9.6 Hz, 2H, Ts-H), 7.24 (dd, *J* = 3.9, 0.9 Hz, 1H, 8-H), 7.02 (dt, *J* = 9.3, 2.4 Hz, 2H, 8-H), 3.86 (s, 3H, OCH_3), 2.39 (s, 3H, Ts-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 167.5, 159.2, 146.0, 139.1, 134.7, 131.5, 130.3, 128.0, 127.6, 127.0, 126.5, 124.5, 124.3, 119.1, 118.6, 114.5, 107.0, 55.6, 21.7; IR (KBr, cm^{-1}) 2918 (w), 1771 (w), 1714 (s), 1513 (s), 1434 (m), 1395 (s), 1374 (s), 1302 (m), 1289 (s), 1250 (m), 1181 (m), 1141 (m), 1108 (m), 1088 (m), 1029 (w), 807 (m), 671 (m) ; MS (ESI, PEG, m/z) [$M+Na^+$] Calcd for $C_{24}H_{18}N_2O_5S$: 469.0793, Found: 469.0841; Anal. Calcd for $C_{24}H_{18}N_2O_5S$: C, 64.56; H, 4.02; N, 6.27; S, 7.18; Found: C, 64.49; H, 4.51; N, 5.96; S, 6.98. The product gave a single spot on TLC (ethyl acetate /hexanes 1:1) R_f 0.8.

5.4 Experimental for Part IV

General method for silylation: Lithium diisopropylamine was formed by adding *n*-butyllithium (75 mmol) to diisopropylamine (71 mmol) at -78° C in tetrahydrofuran. *N*-tosyl-acetylpyrrole **2** or **54** (38 mmol) in tetrahydrofuran(5 mL) was added slowly and the solution was stirred for 3 hours. Trimethylchlorosilane (2 mL) was added and the solution was stirred at room temperature for 3 hours. The solution was quenched with ammonium chloride (15 mL) and diluted with water (15 mL). The organic layer was separated and the aqueous layer was extracted with dichloromethane (15 mL x 3). The organic layers were washed with brine (15 mL), dried with magnesium sulfate, and the solvent removed by rotary evaporation. The product was purified by silica gel chromatography with 1:1 ethyl acetate/hexanes.

1-(1-tosyl-1*H*-pyrro-2-yl)-2-(trimethylsilyl)ethan-1-one (53): Yellow oil, (0.1421 g, 18 %), ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.4 Hz, 2H, Ts-H), 7.82 (dd, *J* = 2, 3.2 Hz, 1H, 5-H), 7.12 (d, *J* = 8.4 Hz, 2H, Ts-H), 7.06 (dd, *J* = 2, 3.6 Hz, 1H, 3-H), 6.34 (dd, *J* = 3.6, 3.6 Hz, 1H, 4-H), 2.37 (s, 3H, Ts-CH_3), 2.19 (s, 2H, CH_2), 0.01 (s, 9H, TMS-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.7, 148.4, 134.0, 133.3, 130.4, 128.5, 127.9, 124.2, 110.1, 29.7, 28.2, 27.1, -1.95; MS (ESI, PEG, m/z) [M+Na$^+$] Calcd for $C_{16}H_{21}NO_3SSi$: 358.0904, Found: 358.0912. The product gave a single spot on TLC (ethyl acetate/hexanes 1:1) R_f 0.43.

1-(1-tosyl-1*H*-pyrro-2-yl)-3-(trimethylsilyl)ethan-1-one (55): cream crystals, (0.110 g, 11 %), mp = 96-98°C; ^{1}H NMR (500 MHz, Acetone) δ 8.01 (dd, *J* = 1.5, 2 Hz, 1H, 5-H), 7.92 (d, *J* = 8.5 Hz, 2H, Ts-H), 7.34 (d, *J* = 9 Hz, 2H, Ts-H), 7.29 (dd, *J* = 2, 3.5 Hz, 1H, 2-H), 6.67 (dd, *J* = 1.5, 3.5 Hz, 1H, 4-H), 2.40 (s, 3H, Ts-CH_3), 2.33 (s, 2H,

CH_2), 0.01 (s, 9H, TMS-CH_3); ^{13}C NMR (100 MHz, Acetone) δ 192.8, 151.0, 134.5, 130.4, 130.1, 128.4, 126.1, 122.8, 28.5, 27.4, -1.88. The product gave a single spot on TLC (ethyl acetate/hexanes 1:3) R_f 0.35.

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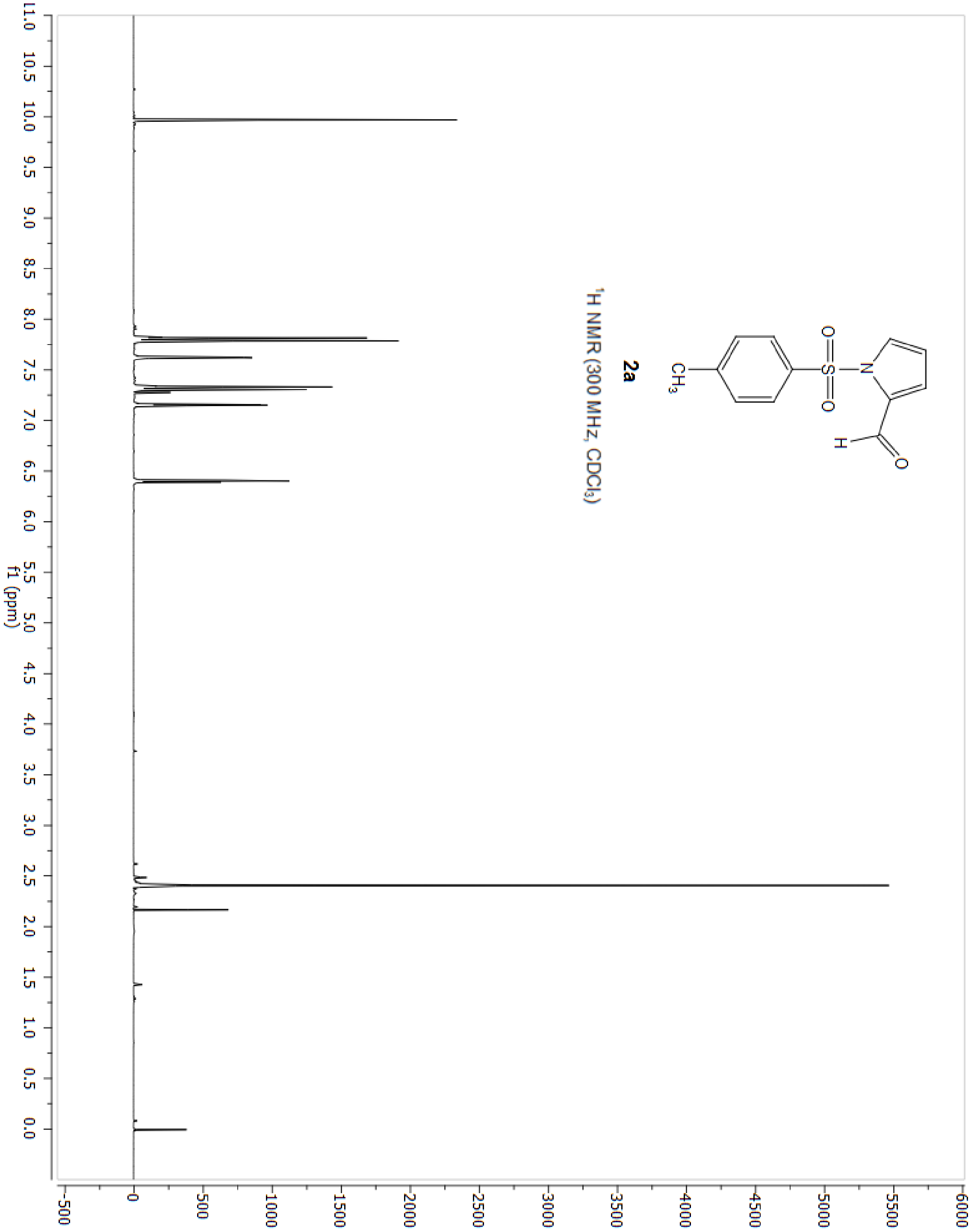
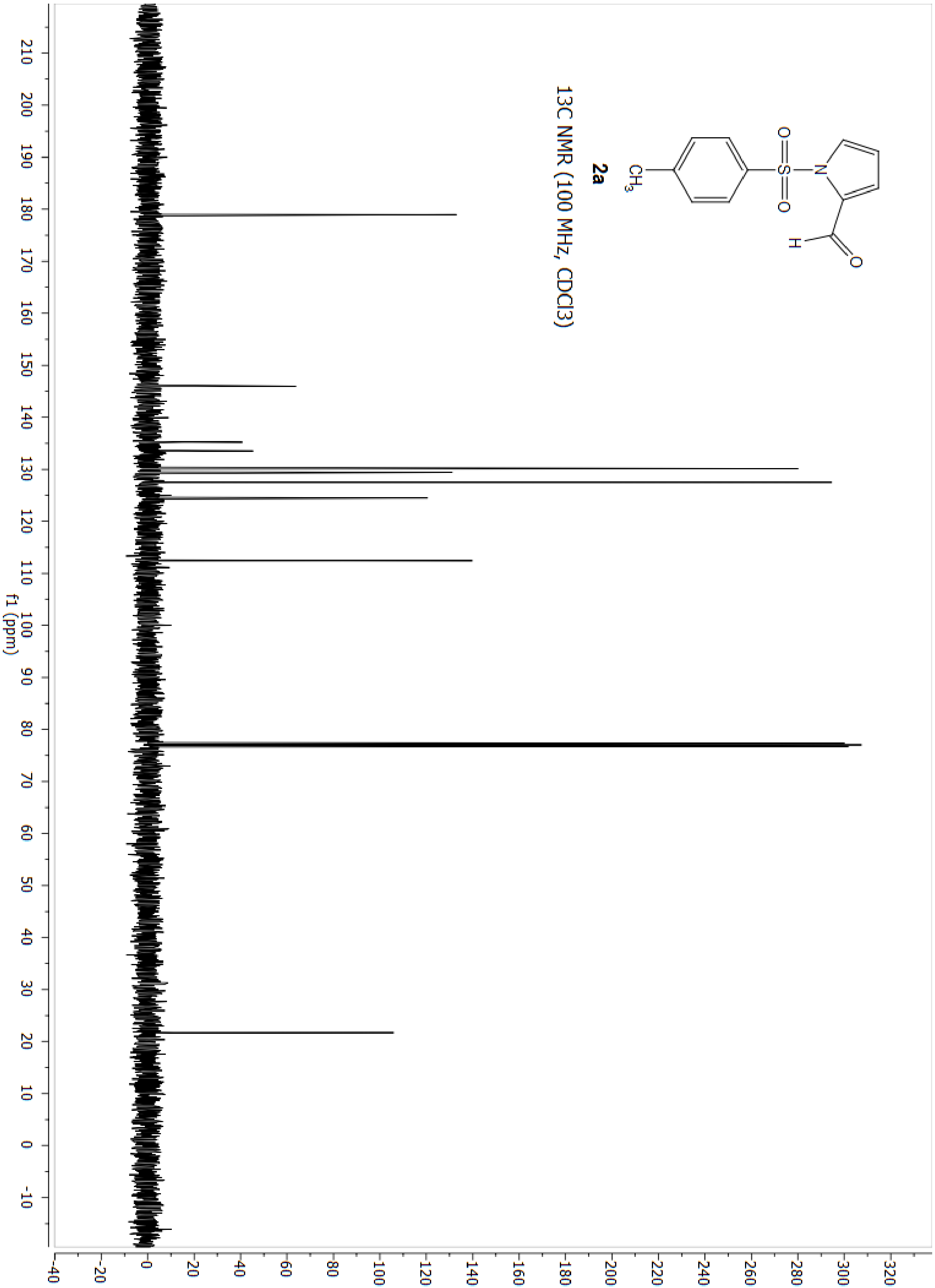
Appendix 1. 1H and 13C NMR Spectra



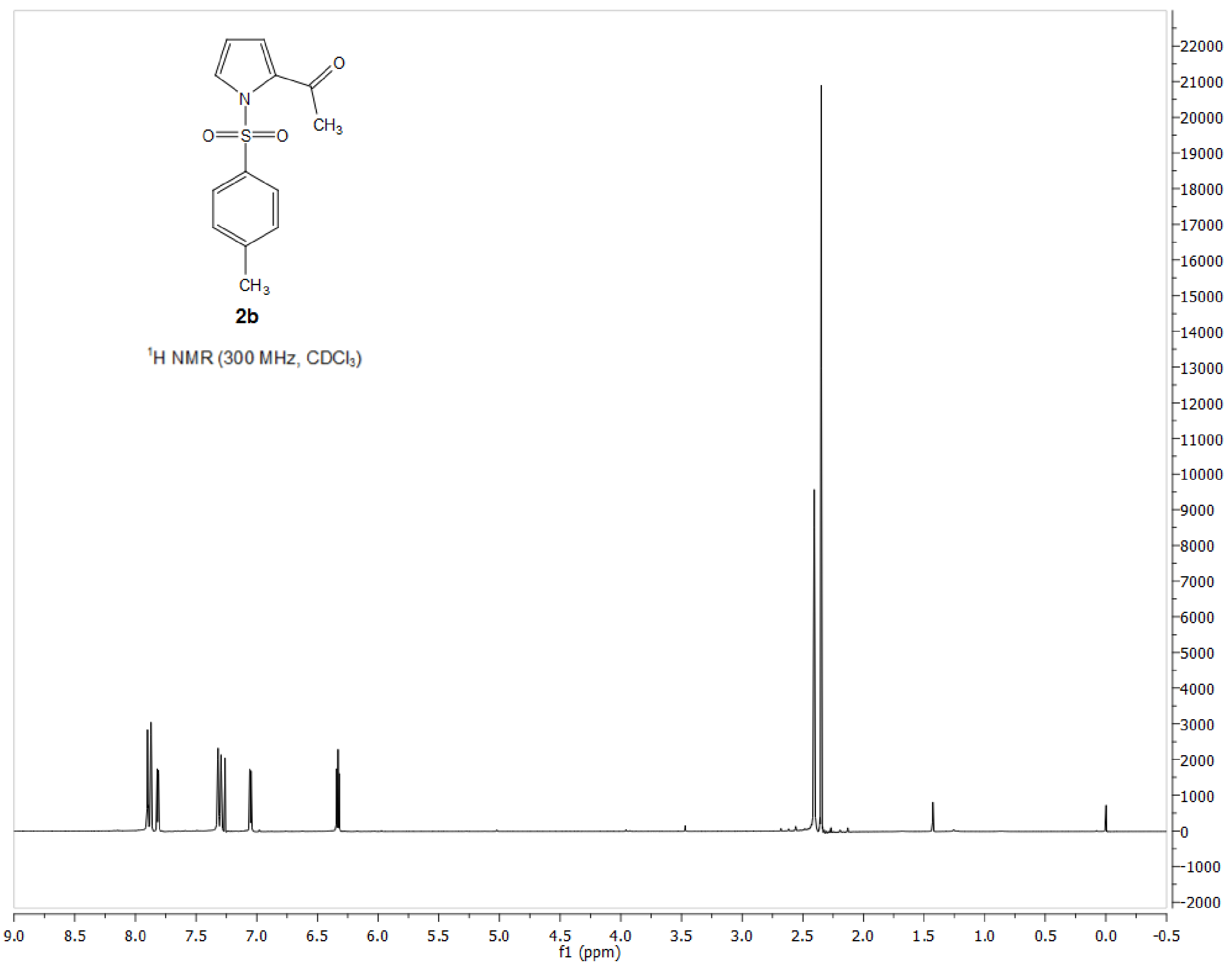
2a

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



2a

13C NMR (100 MHz, CDCl3)



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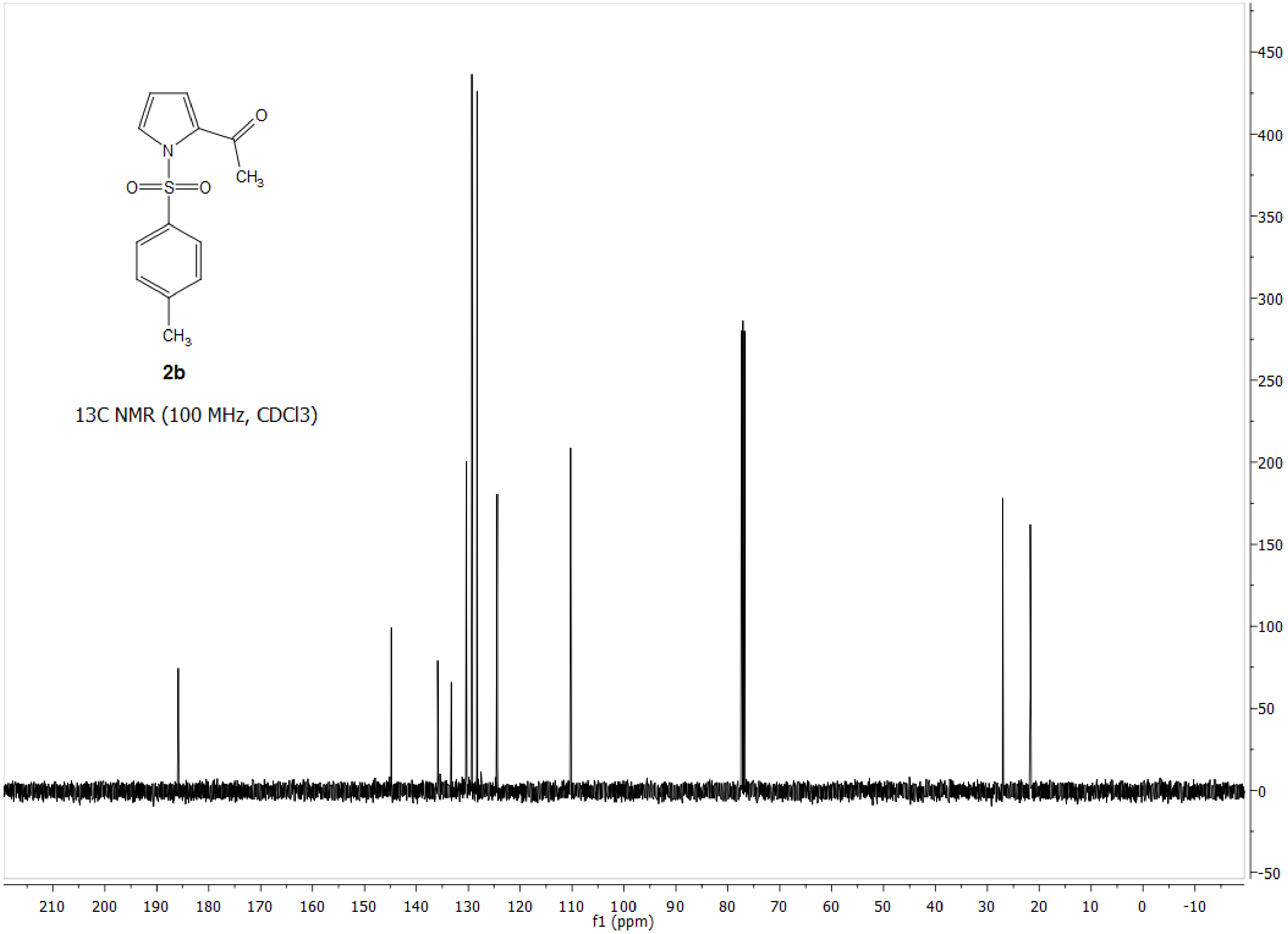

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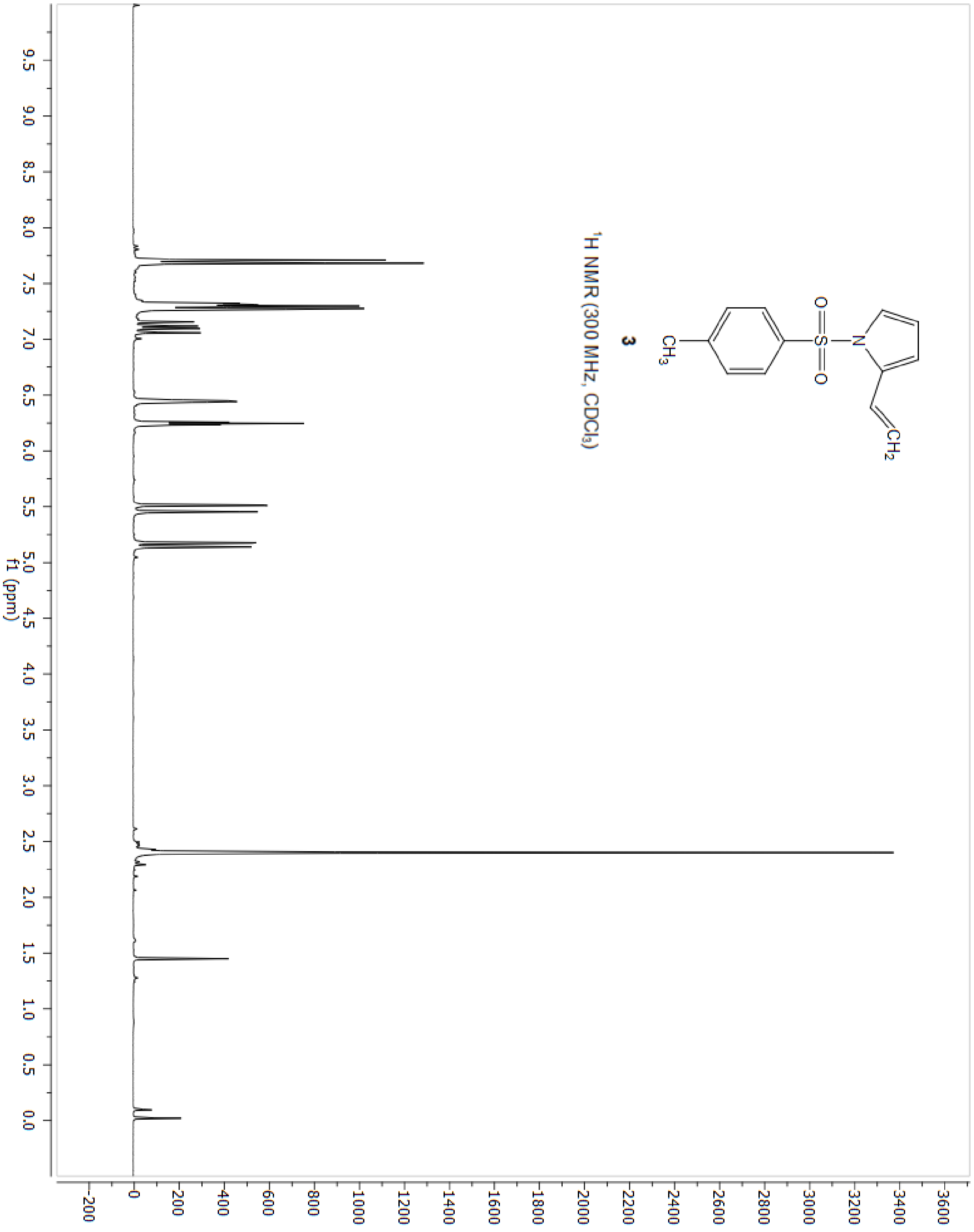

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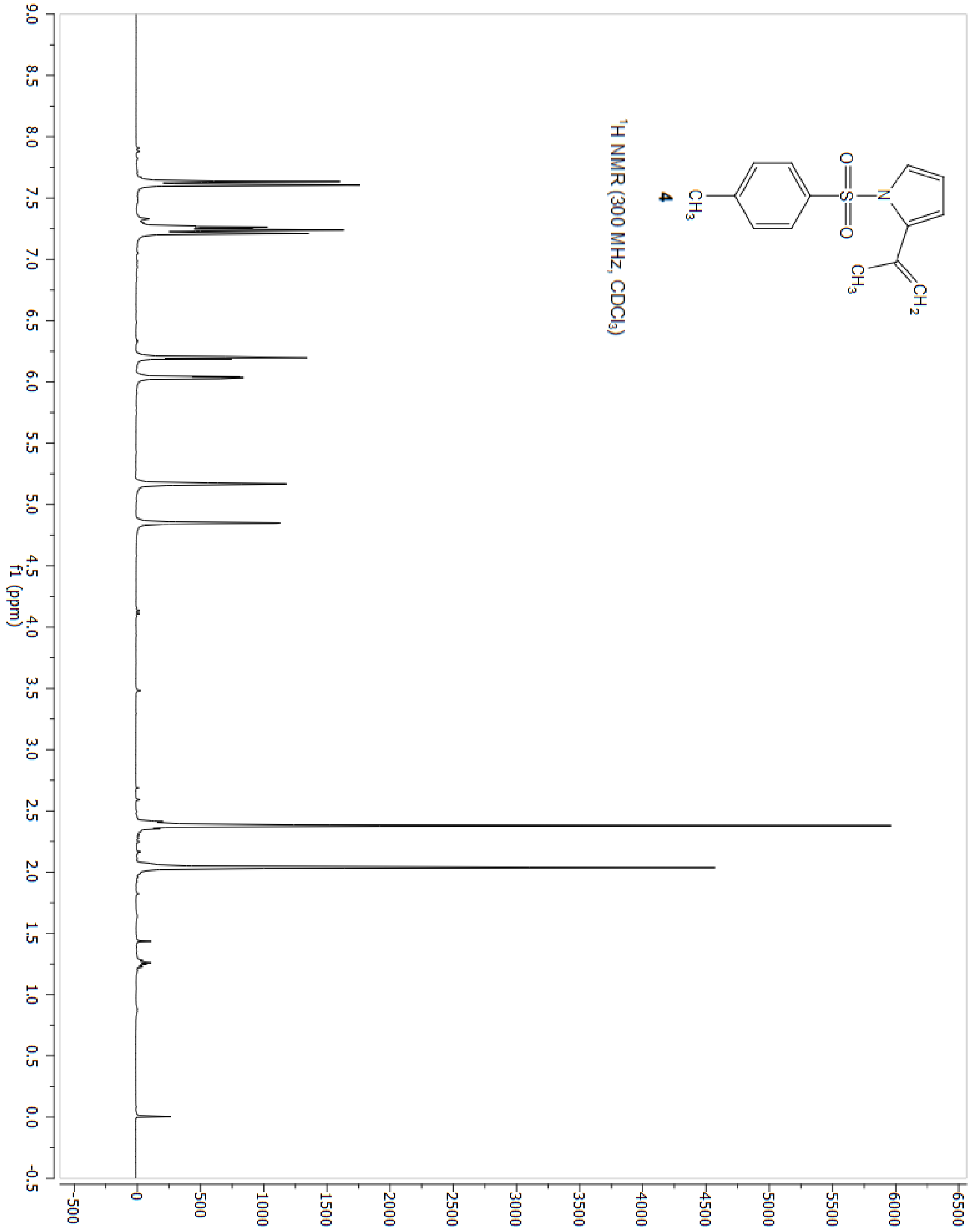
^{1}H NMR (300 MHz, CDCl$_3$)



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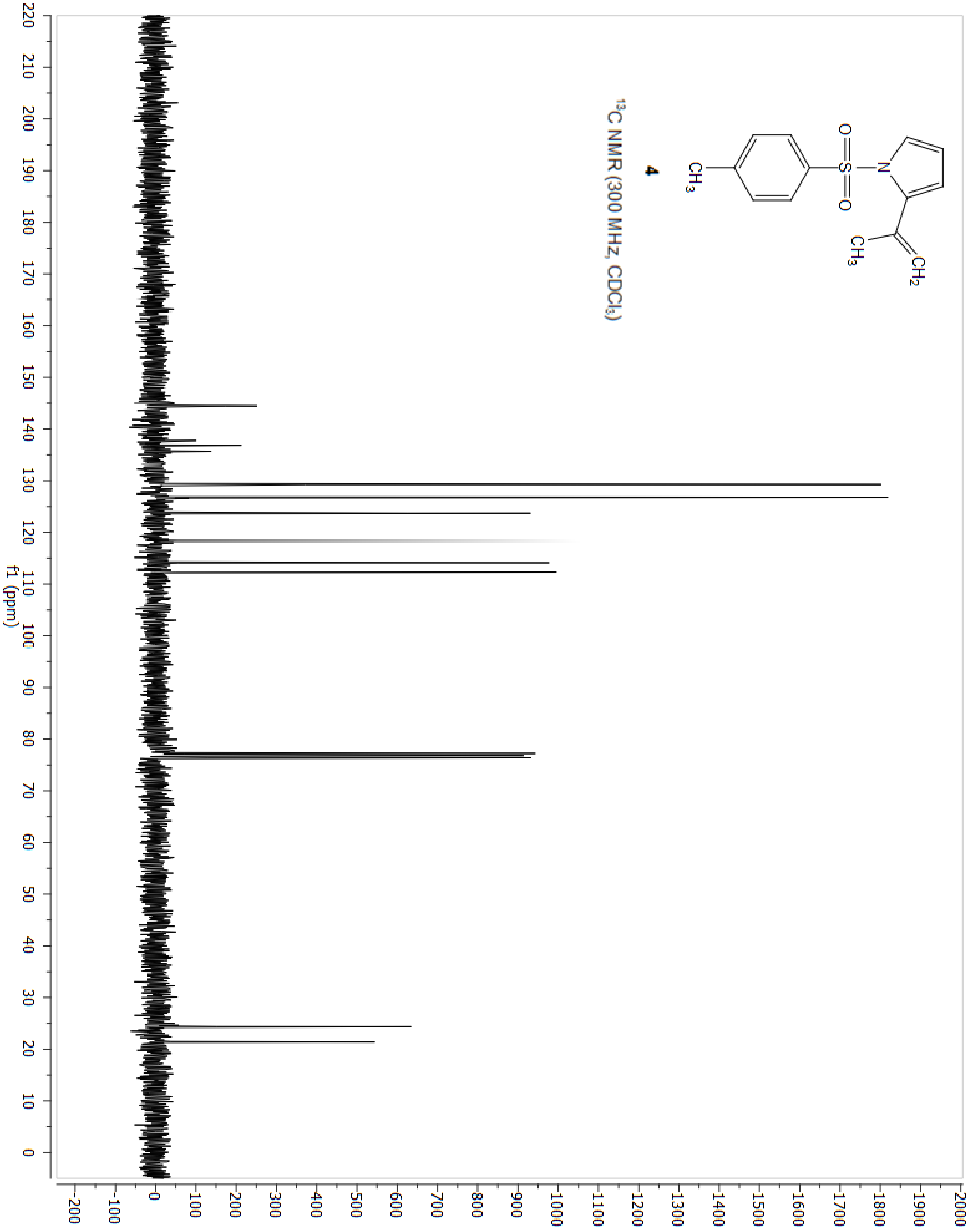

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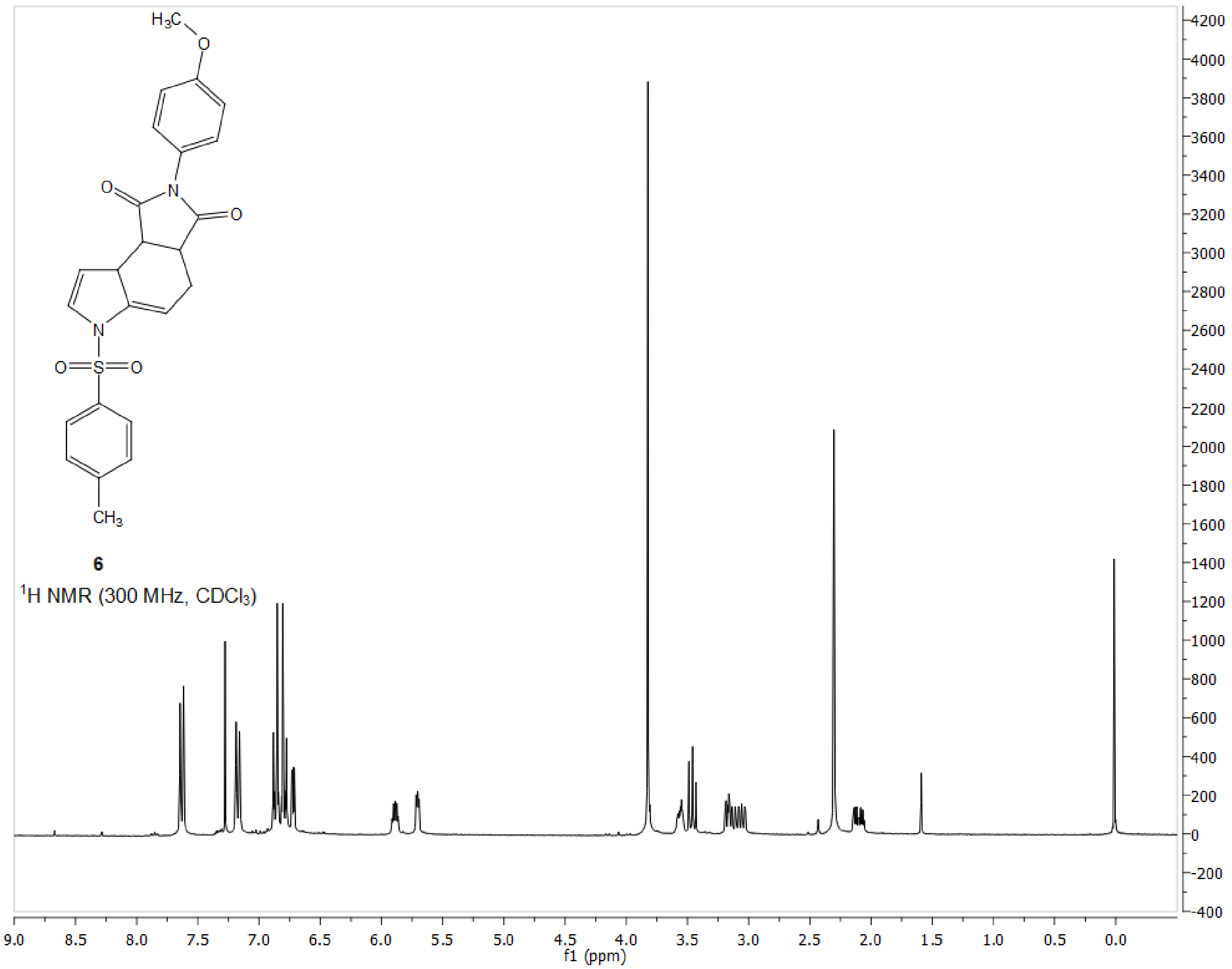

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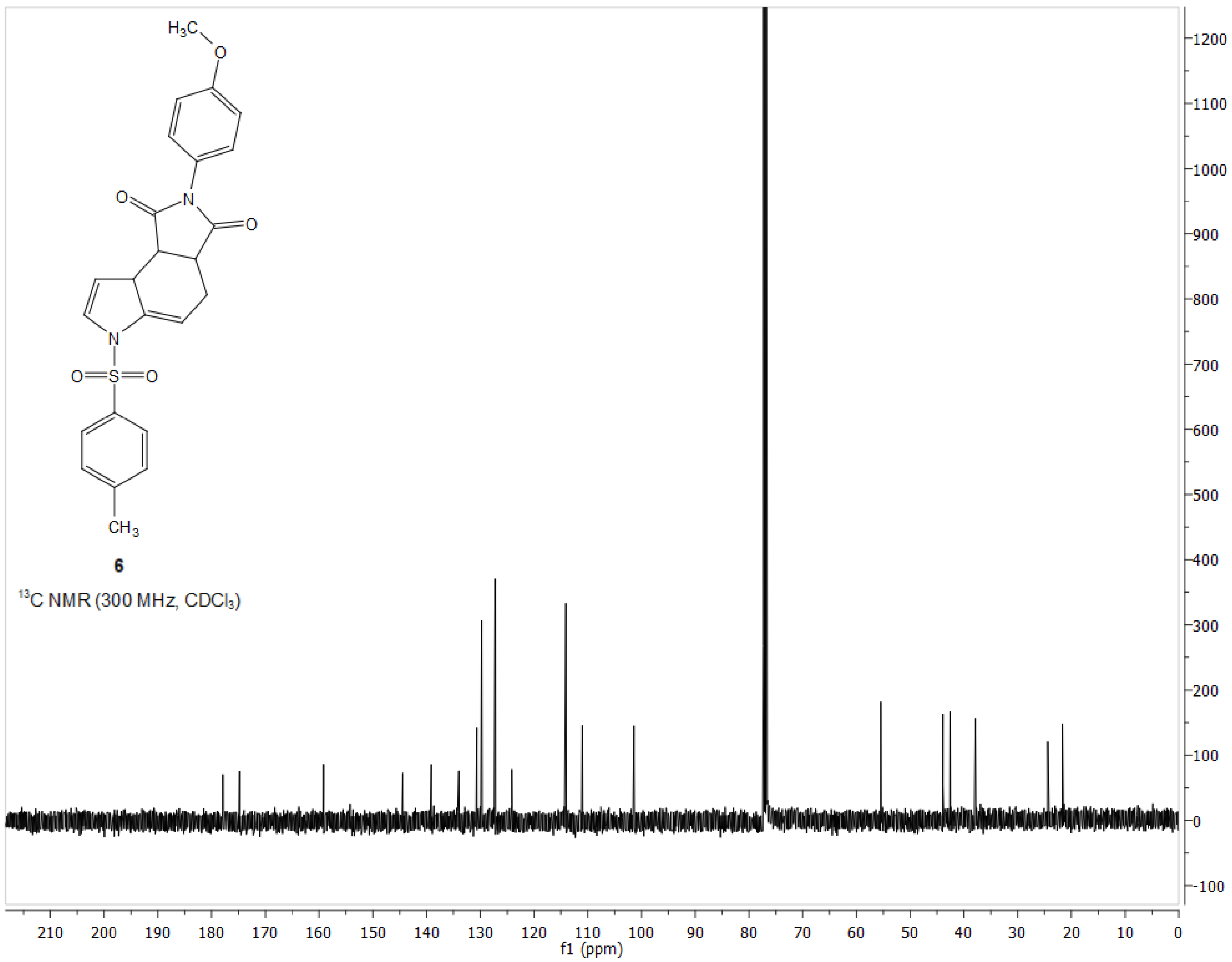

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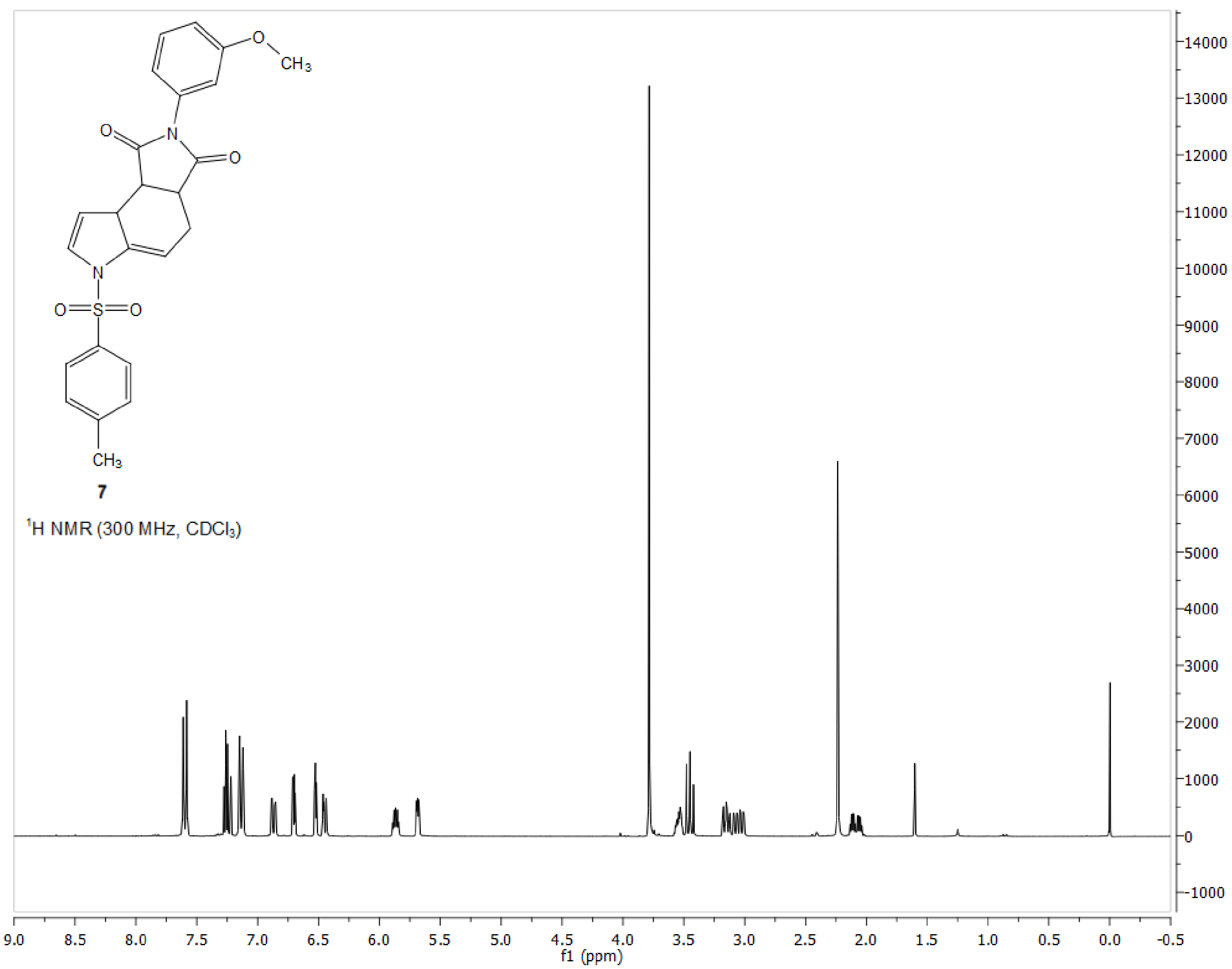

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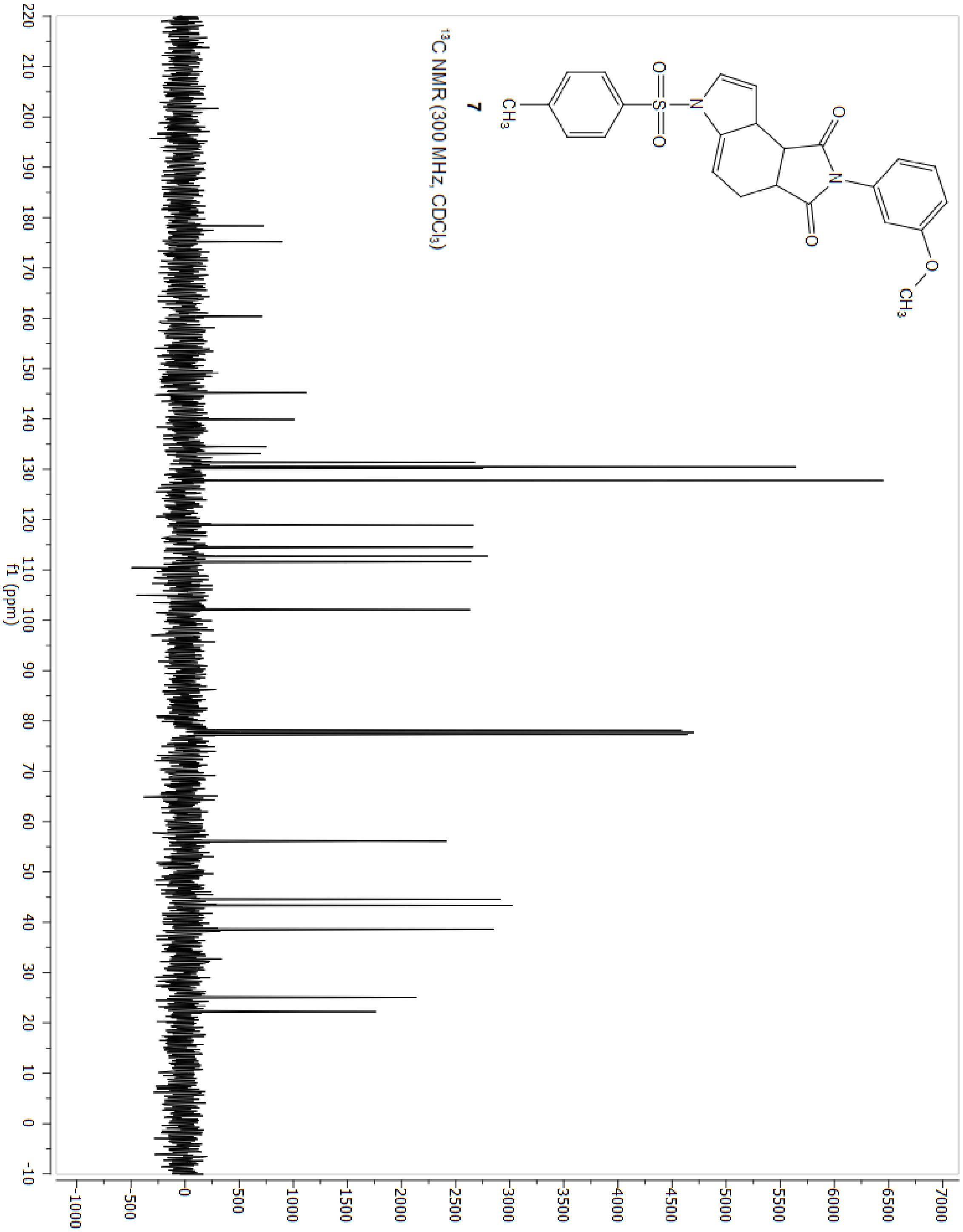

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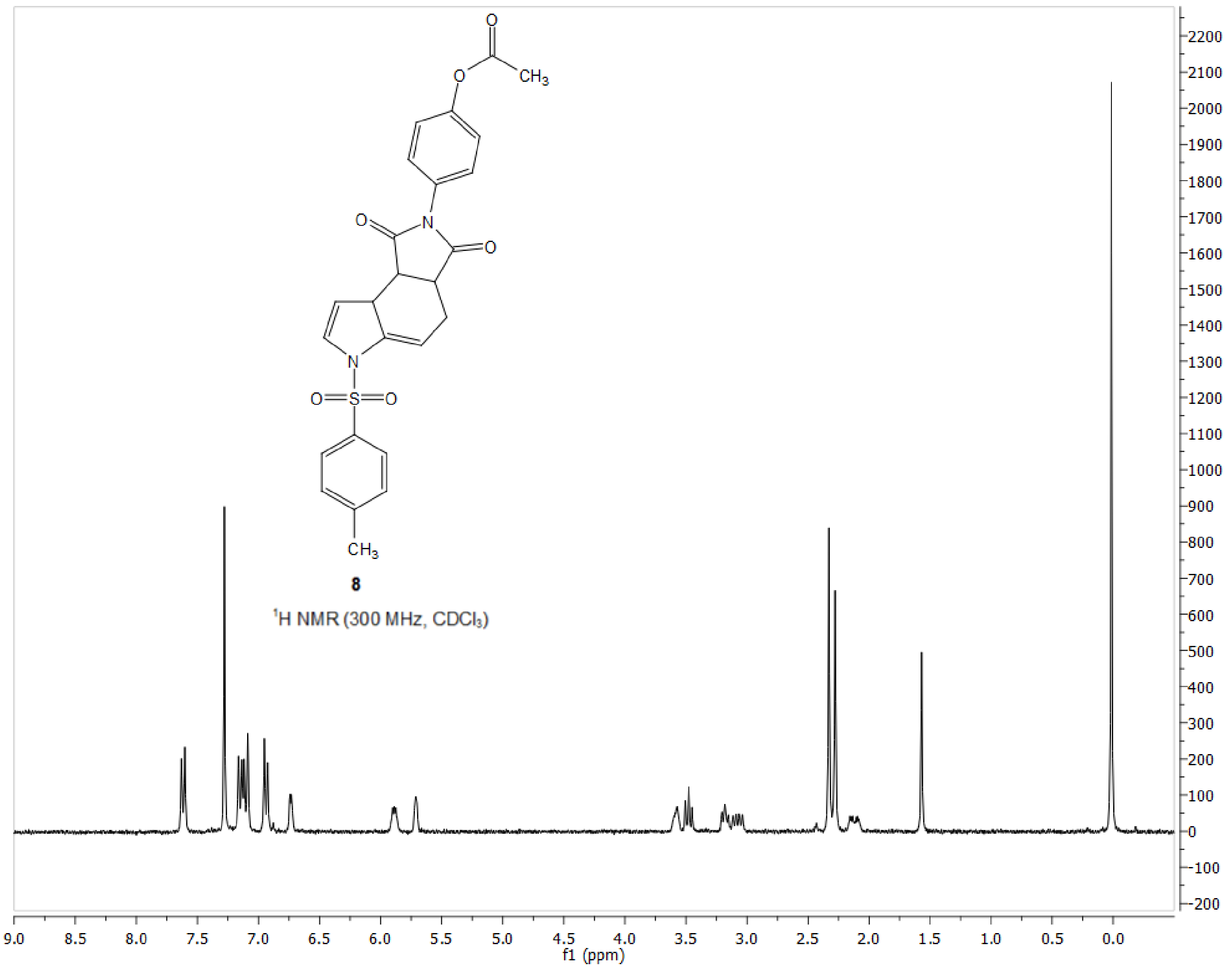

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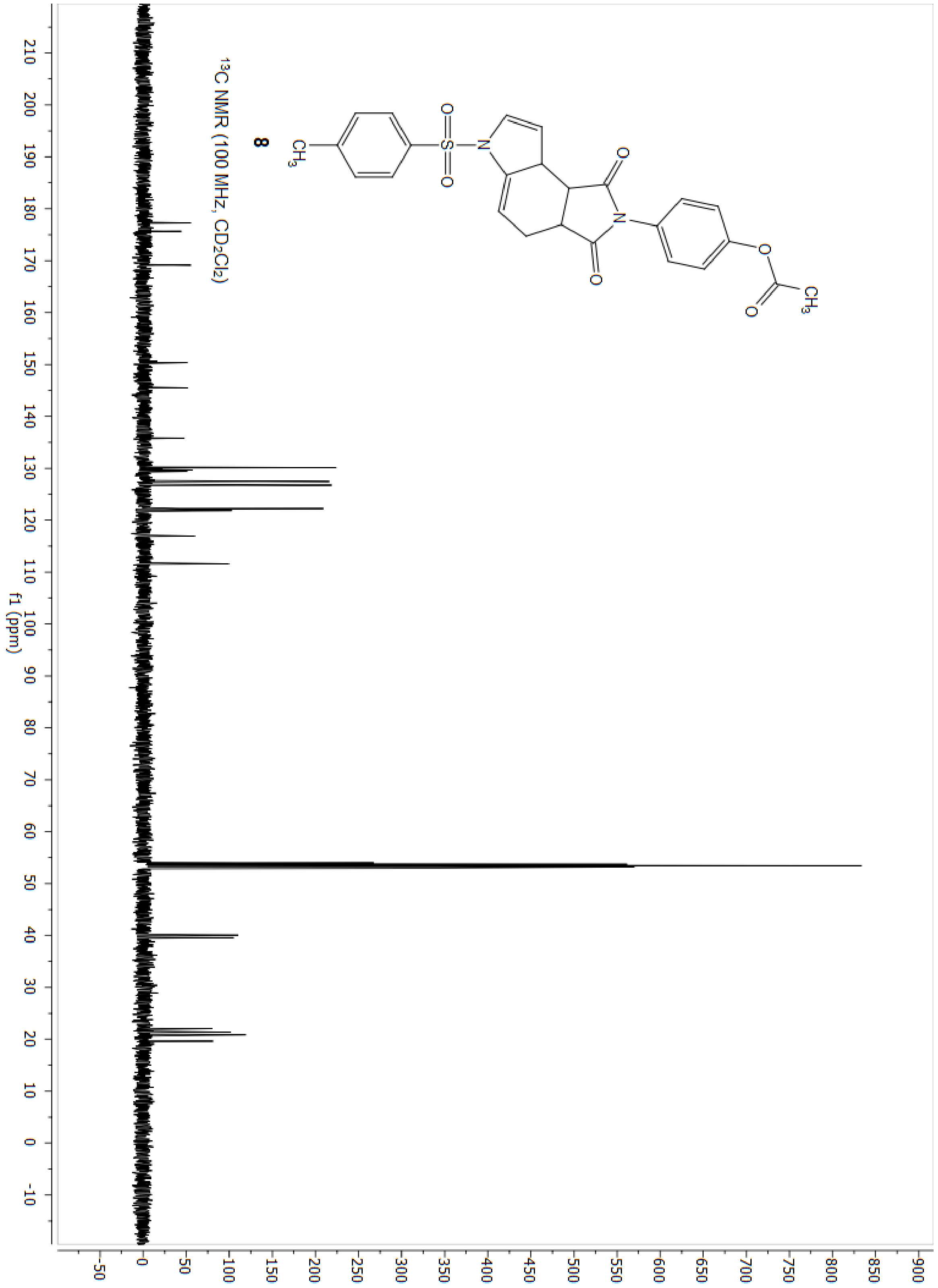
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f1 (ppm)
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200
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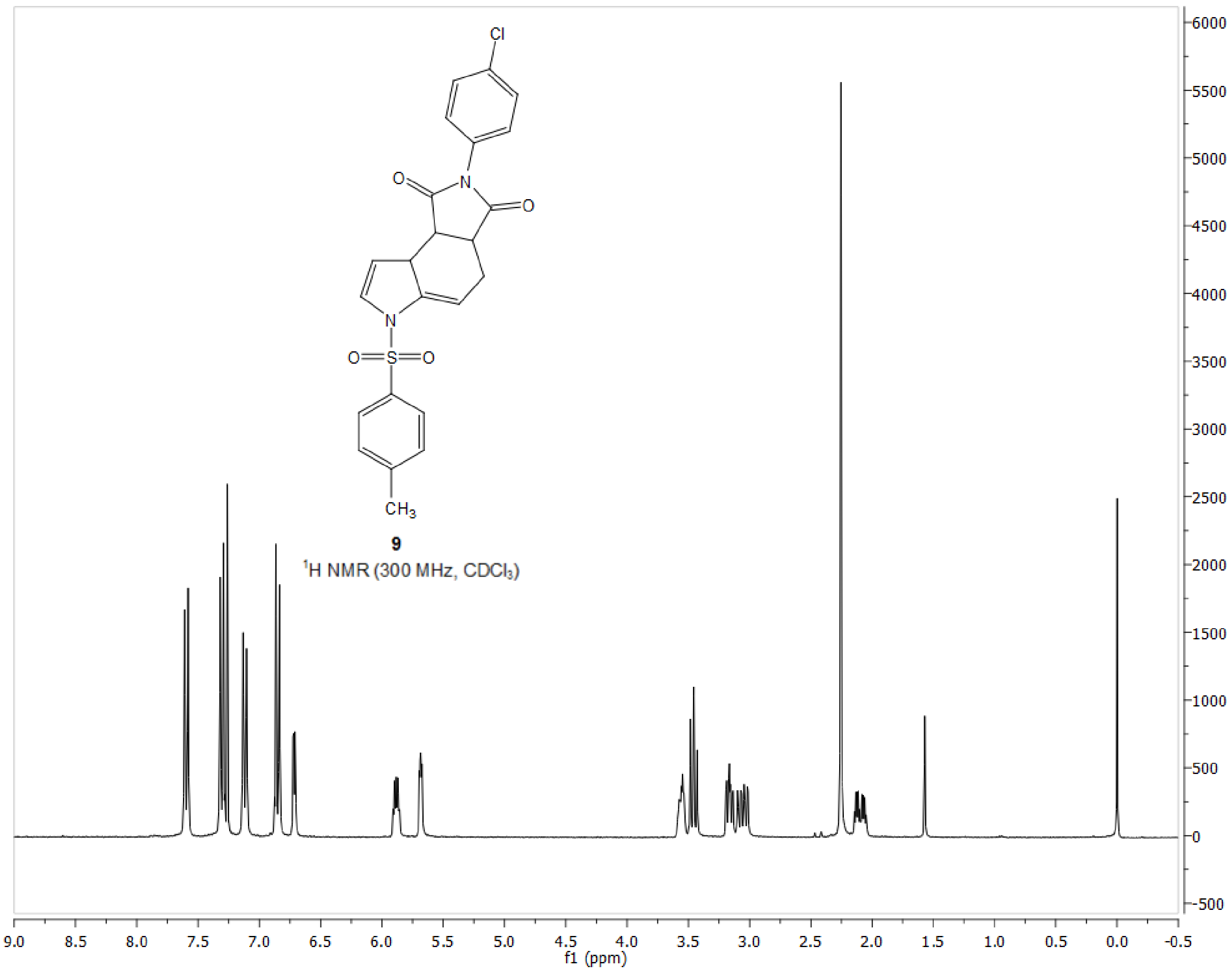
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-50
0
50
100
150
200
250
300
350
400
450
500
550
600
650
700
750
800
850
900
CH$_3$
O
S
N
O
N
O
O
CH$_3$

8



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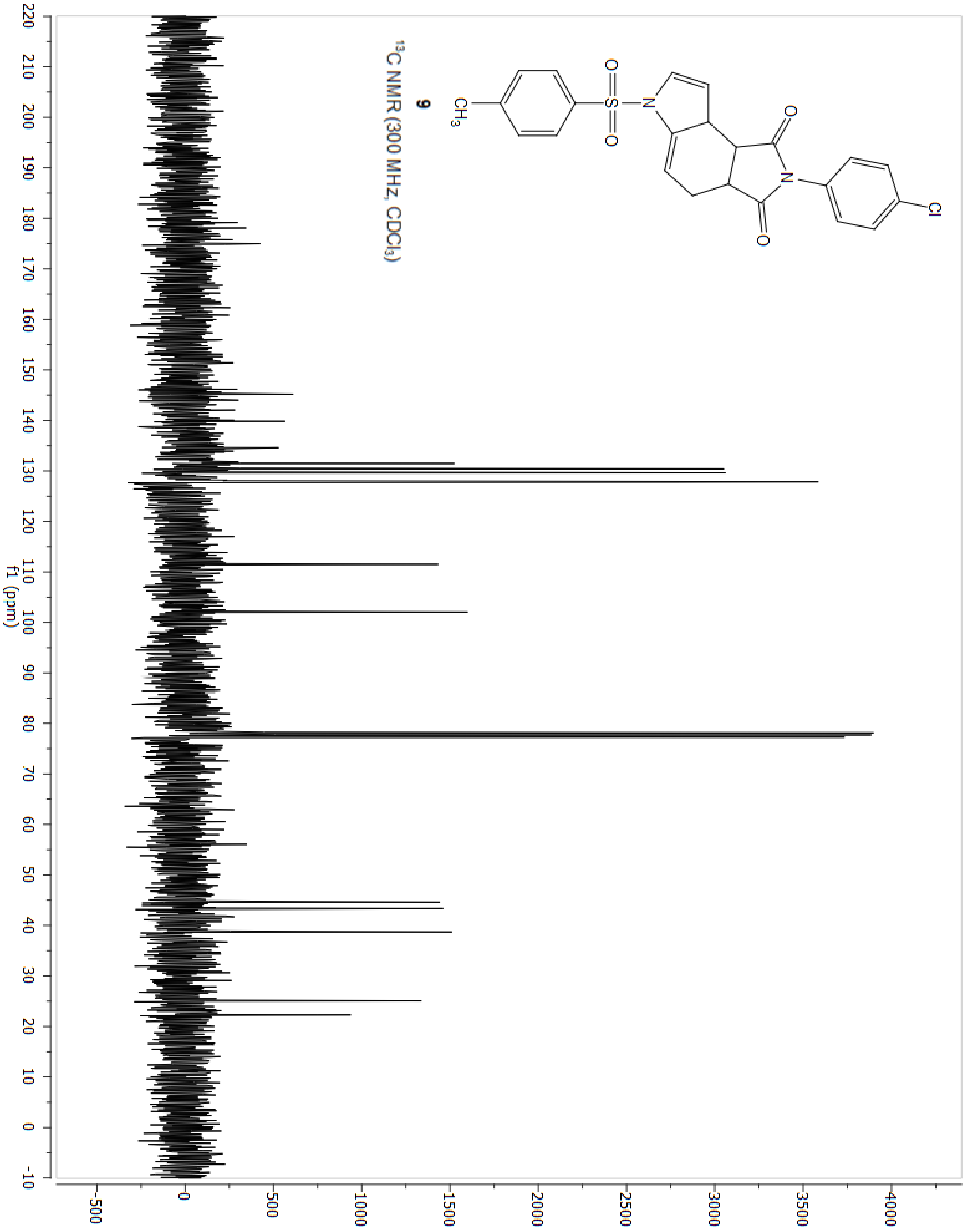

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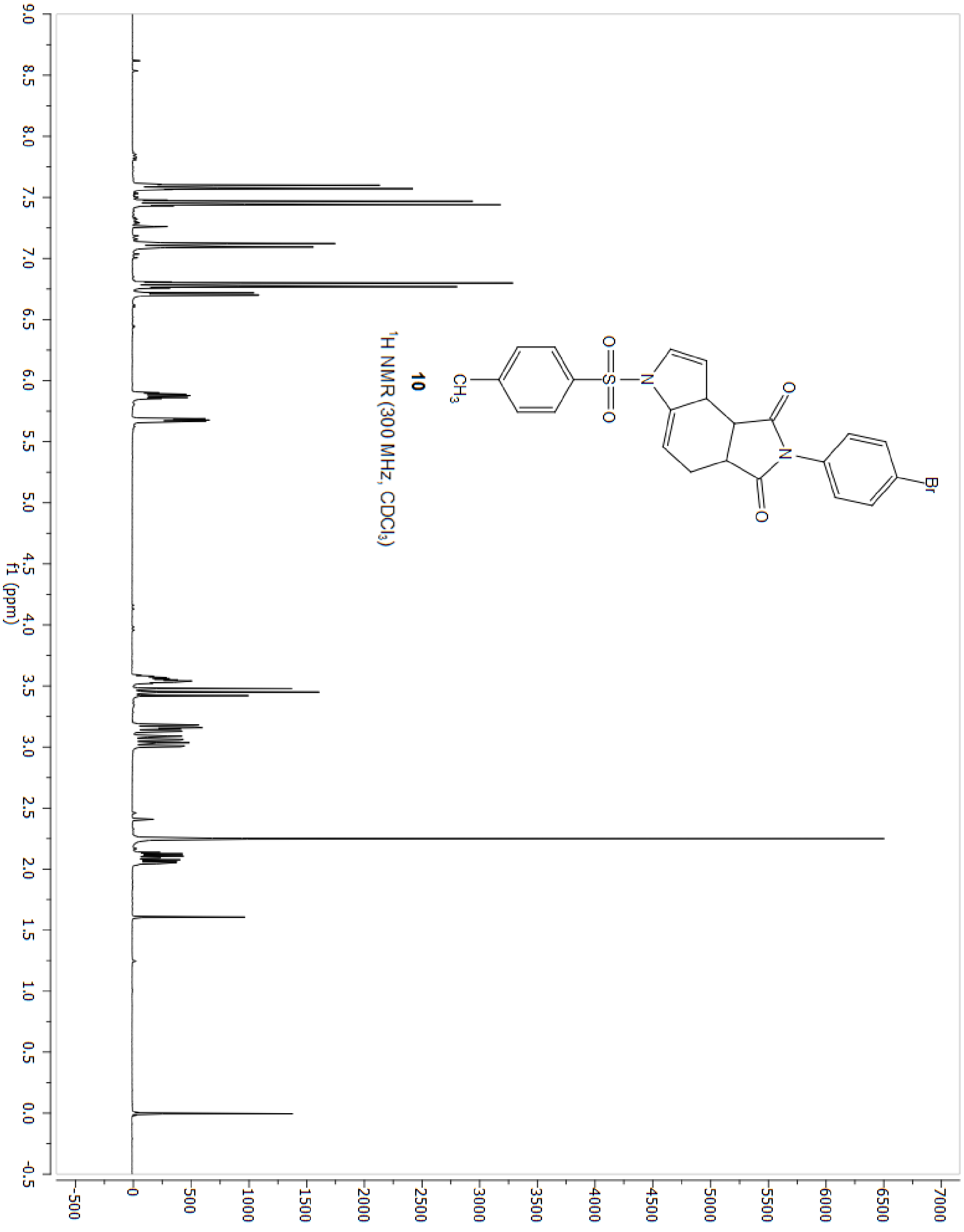

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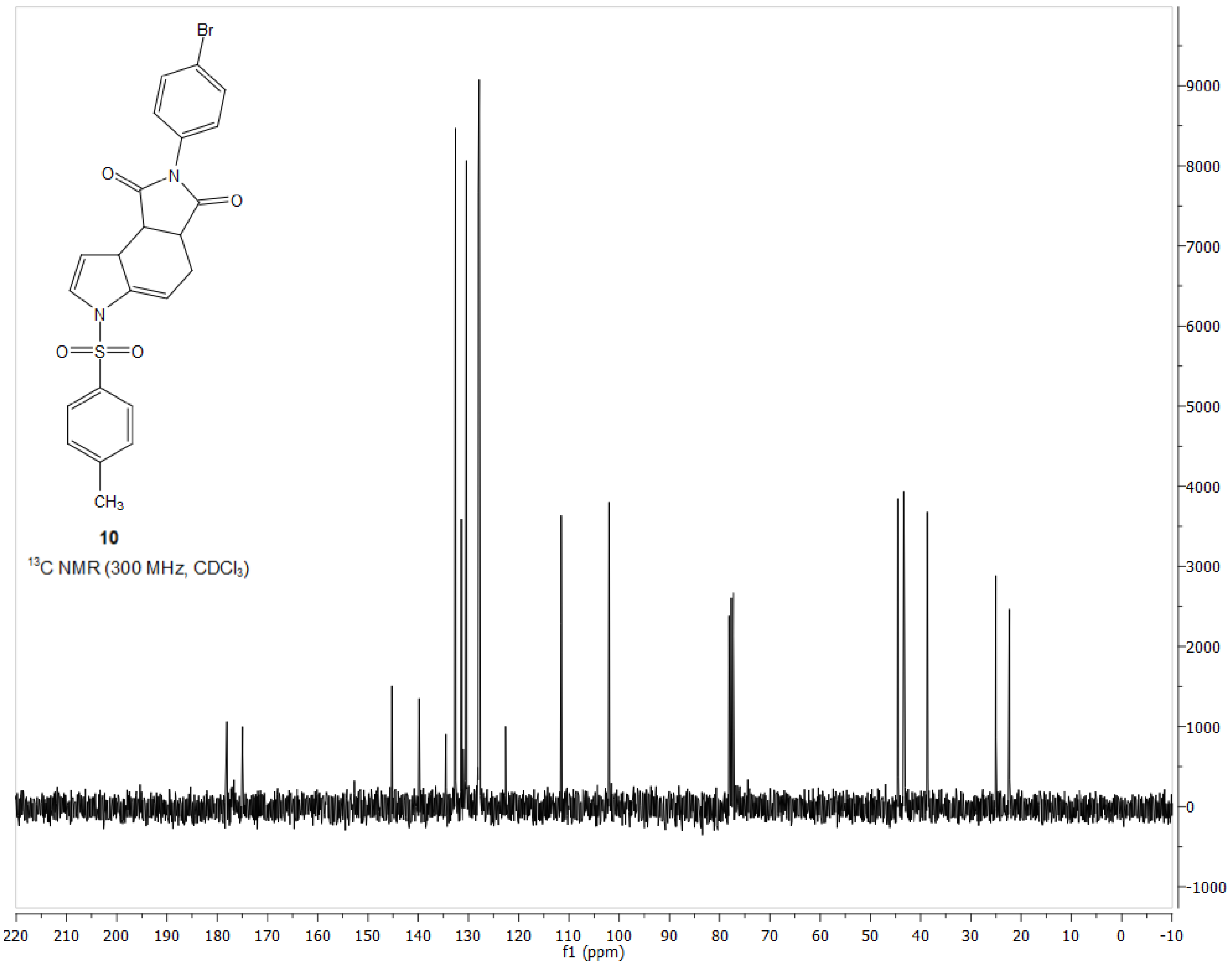

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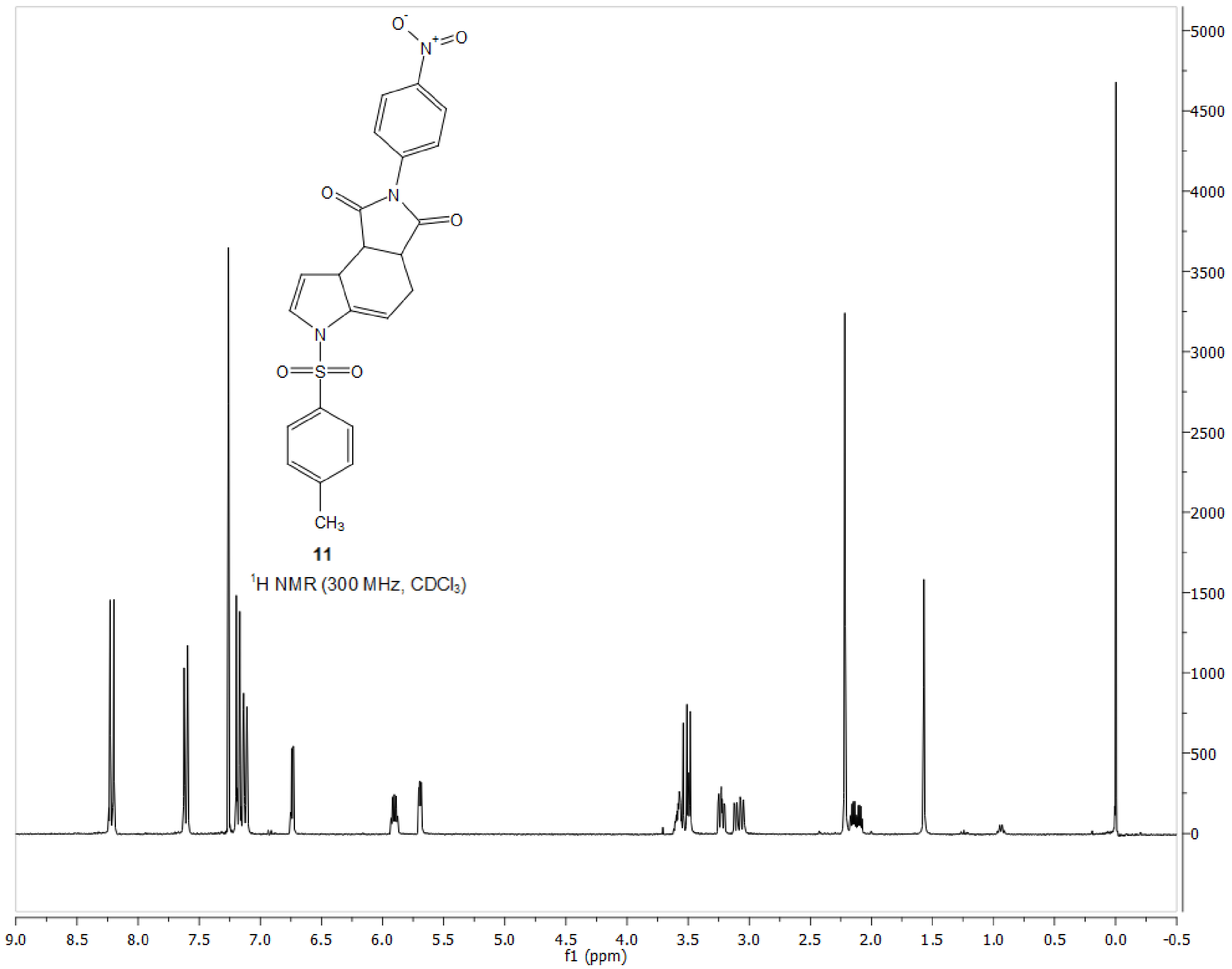
^{13}C NMR (300 MHz, $CDCl_3$)



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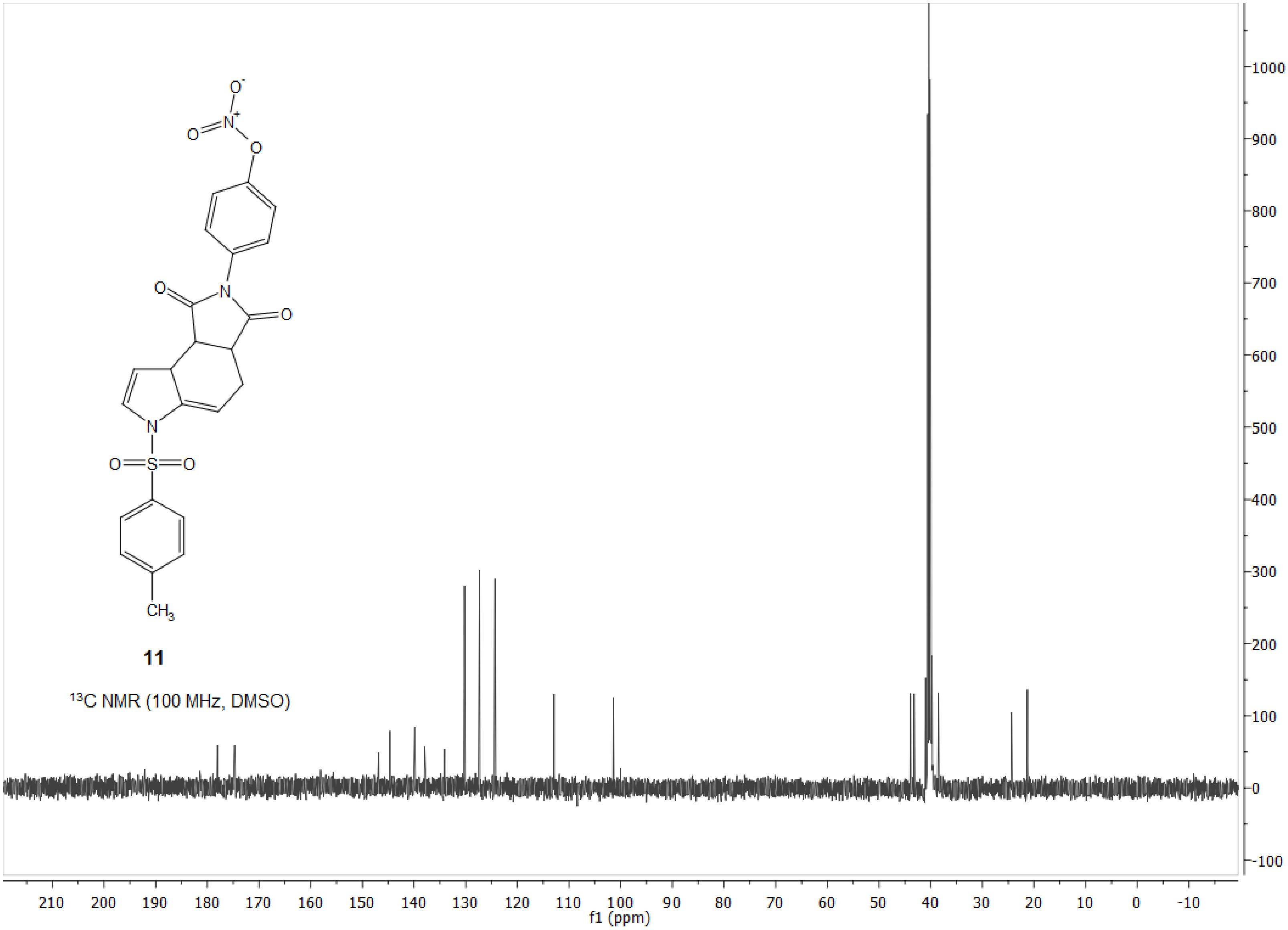
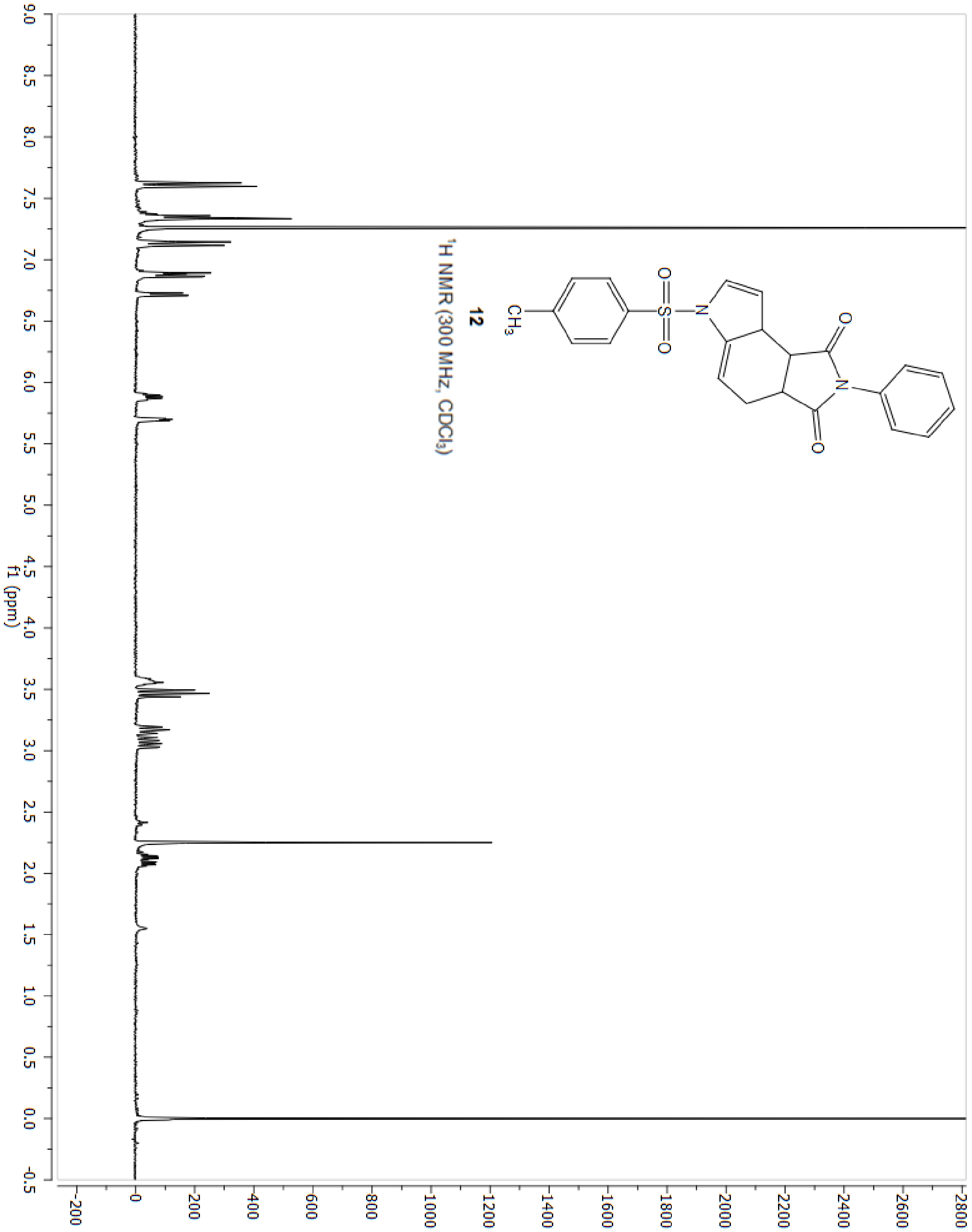
^1H NMR (300 MHz, $CDCl_3$)



11

^{13}C NMR (100 MHz, DMSO)



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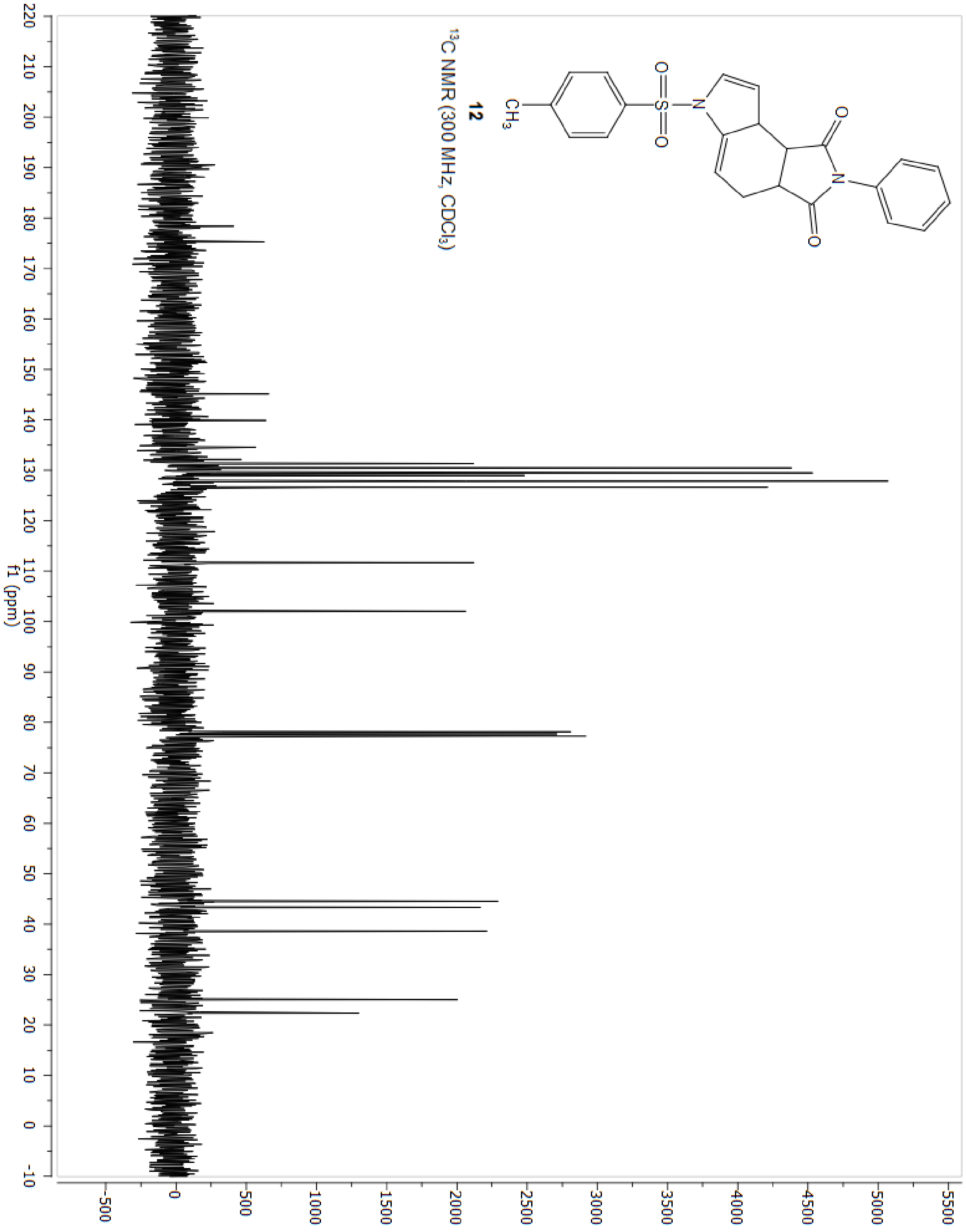
^{1}H NMR (300 MHz, $CDCl_3$)



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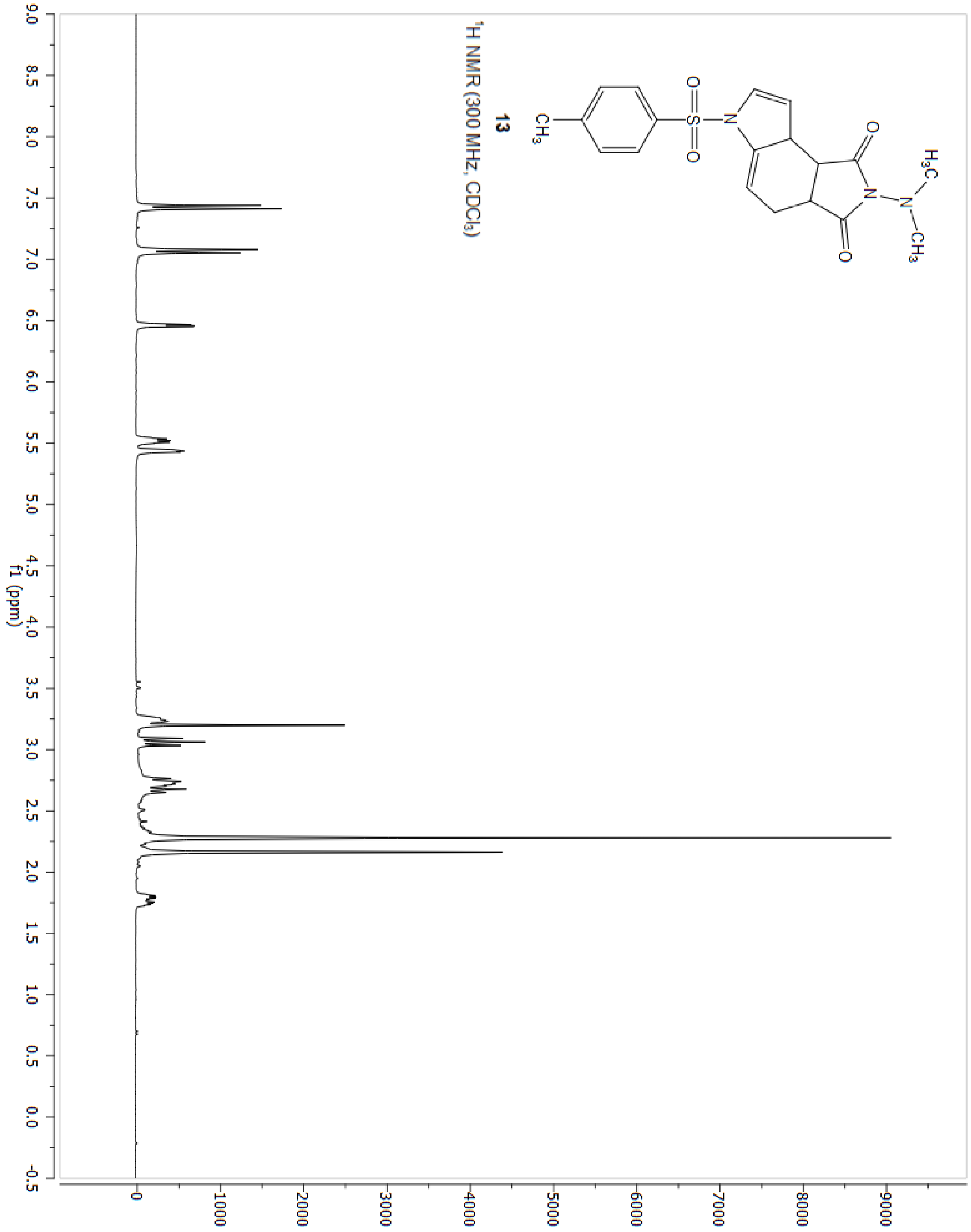

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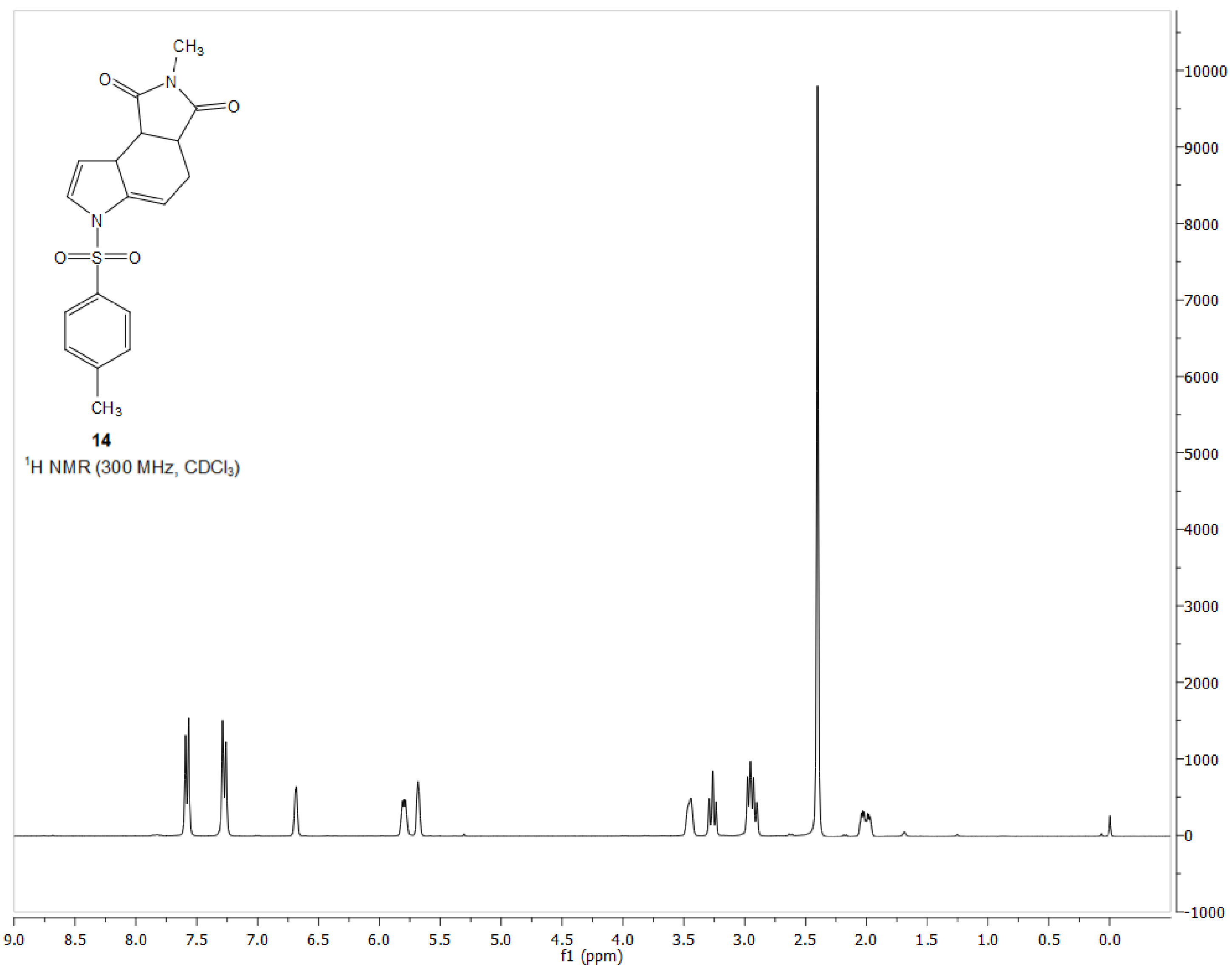

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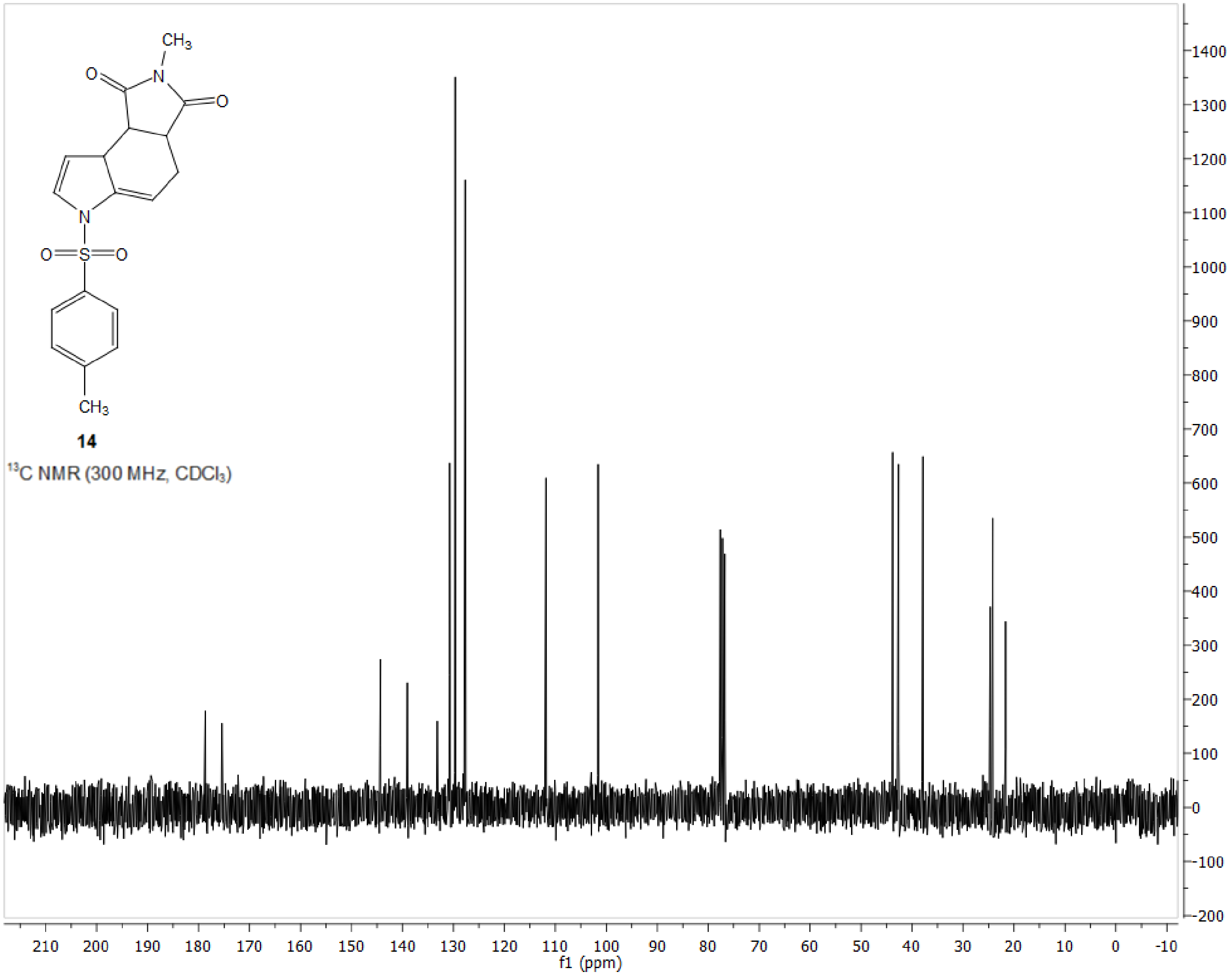

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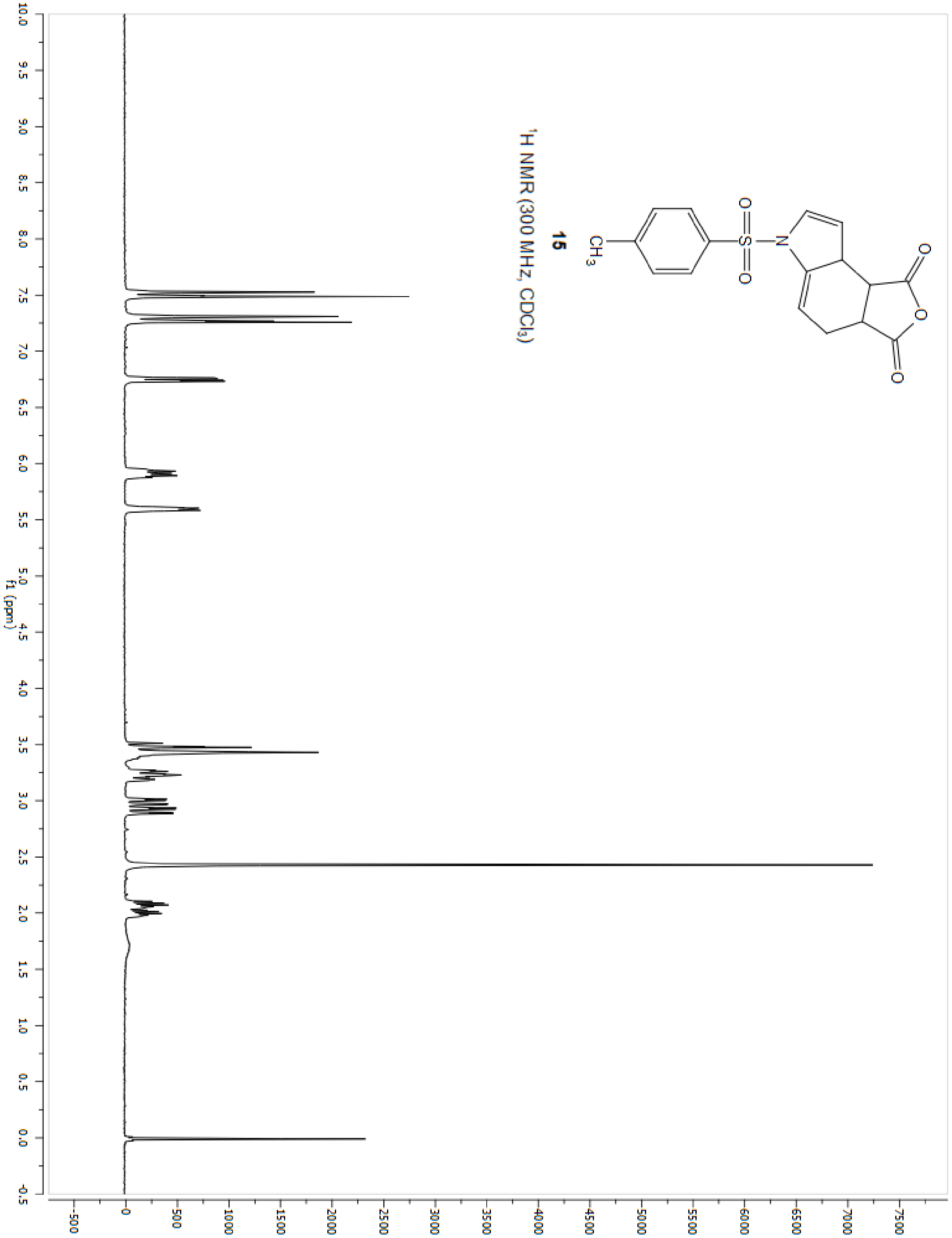

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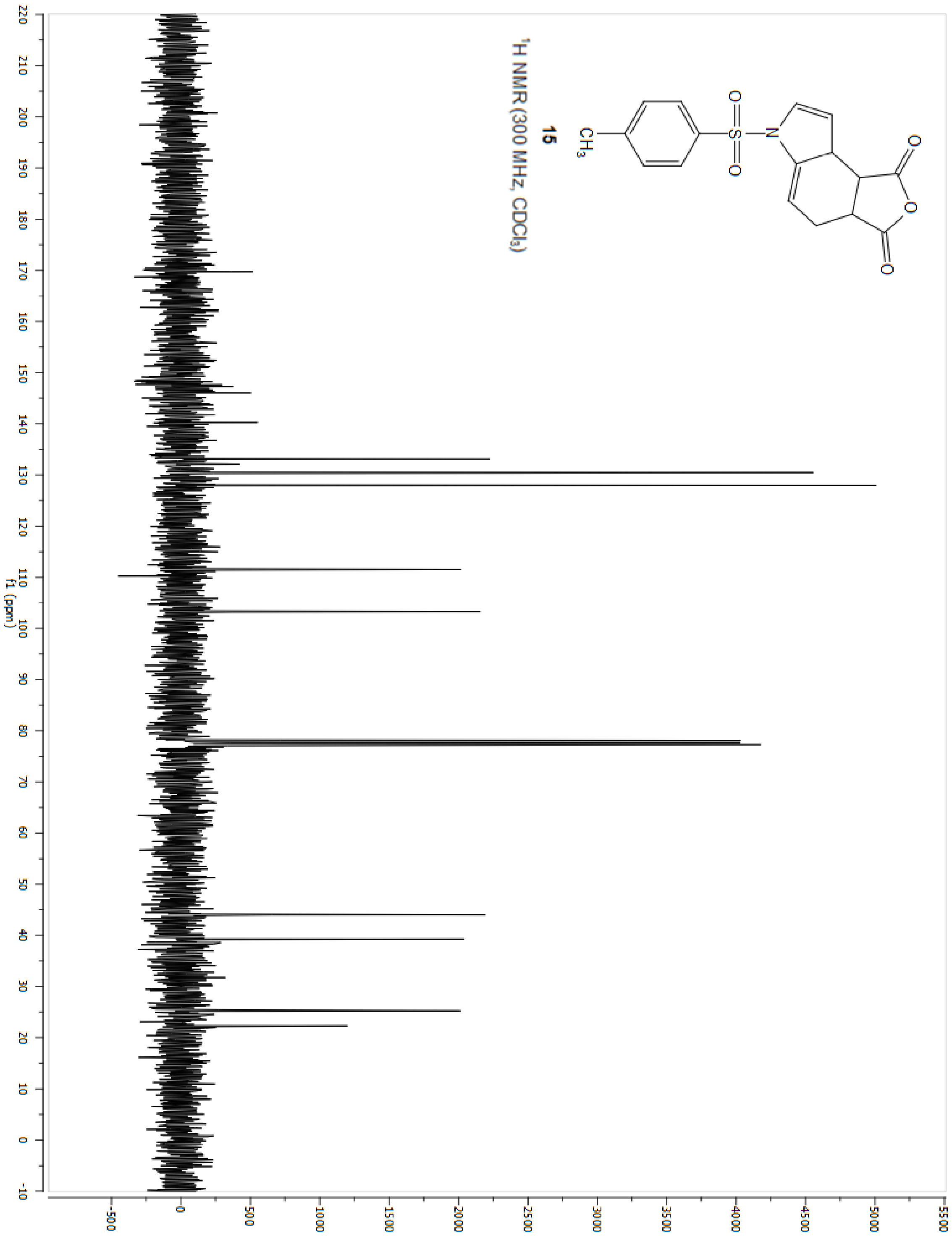

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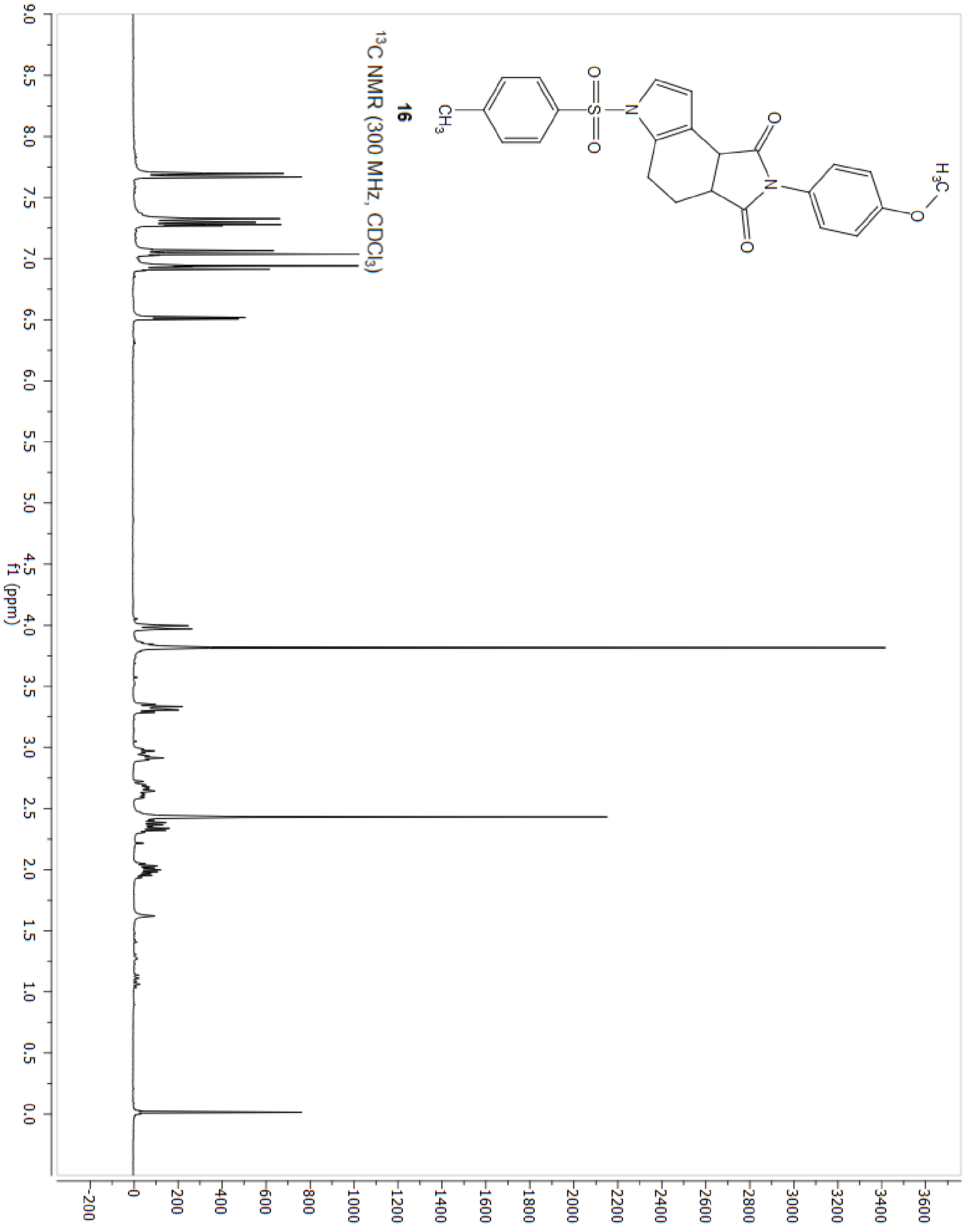

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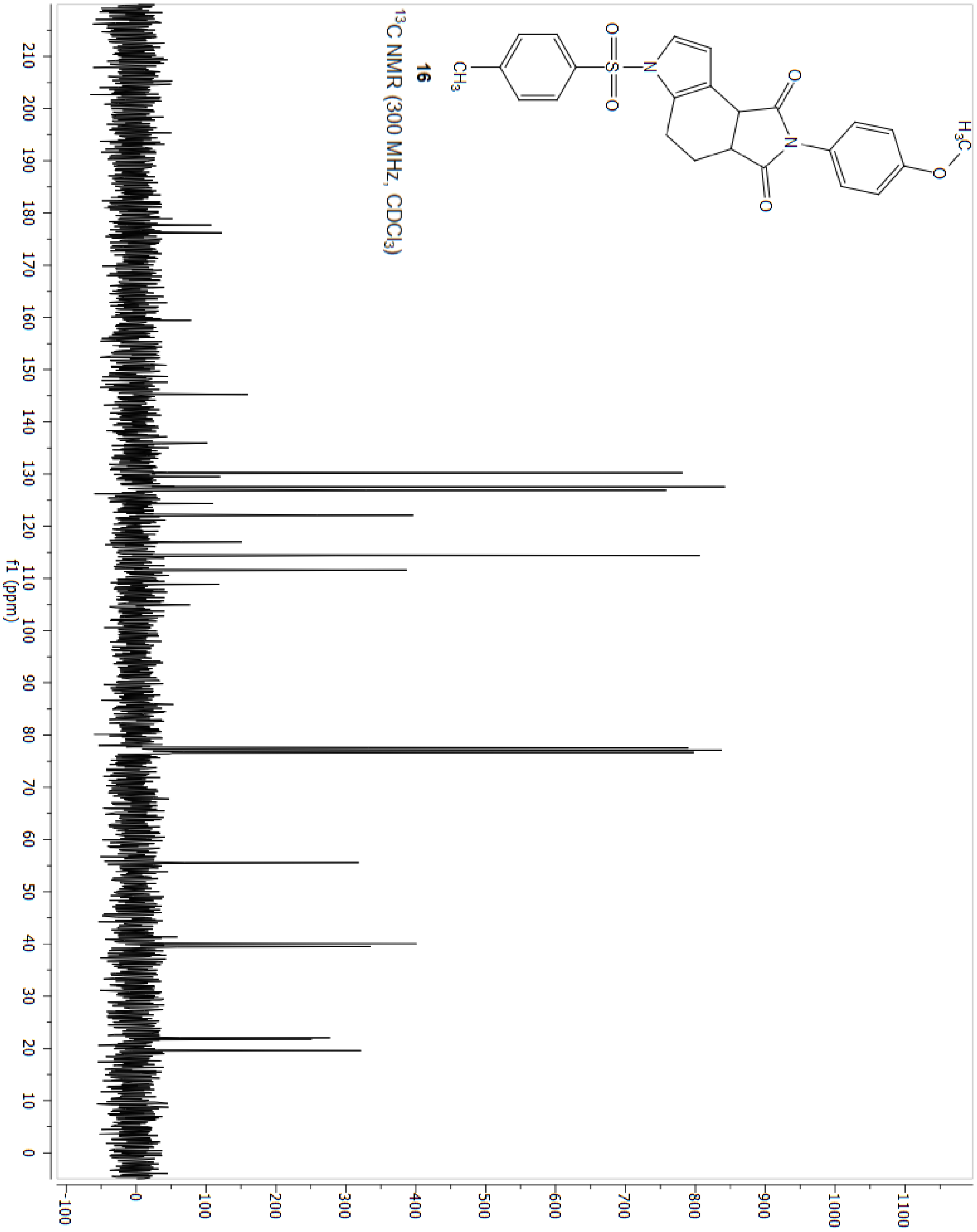
^{13}C NMR (300 MHz, CDCl$_3$)



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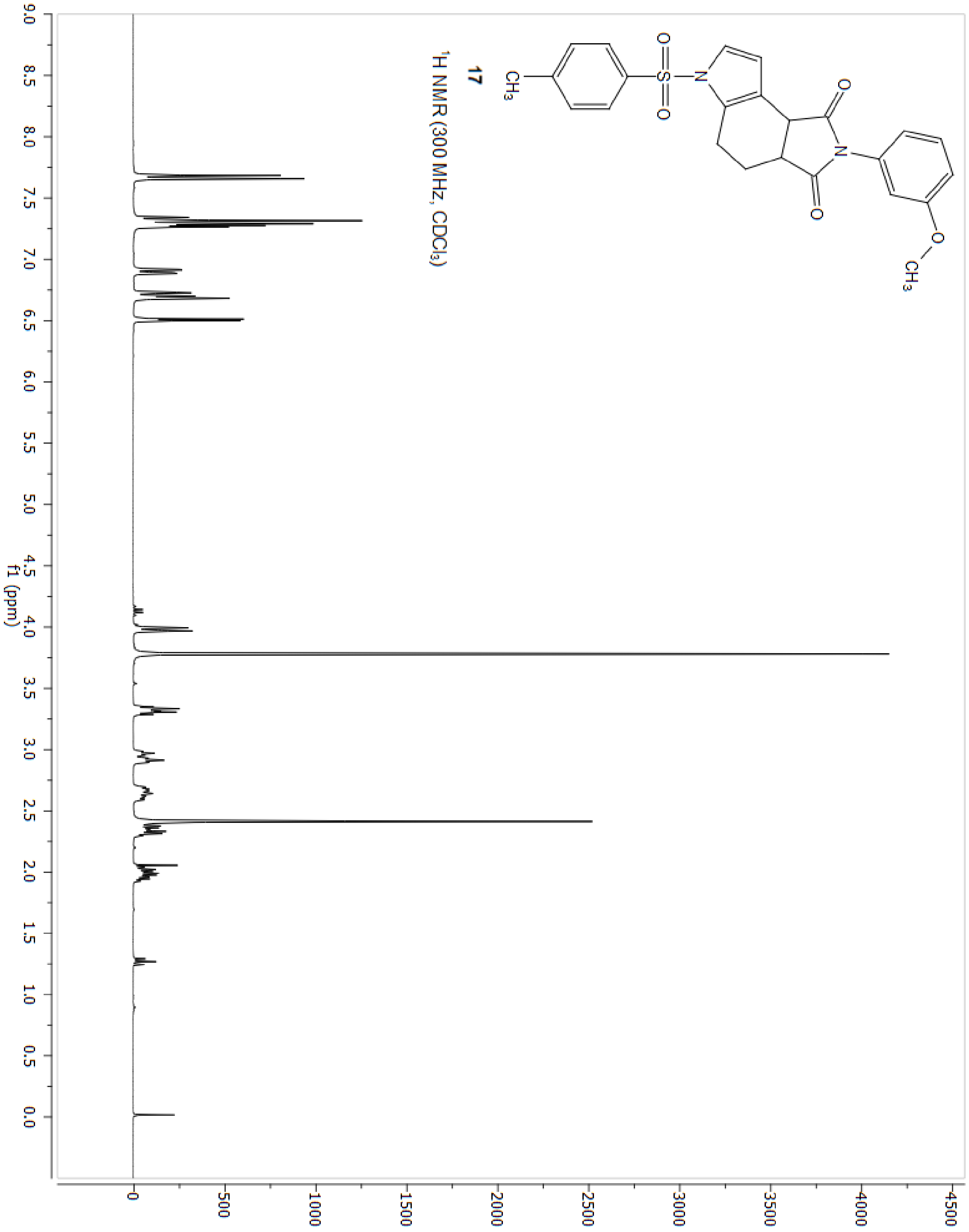

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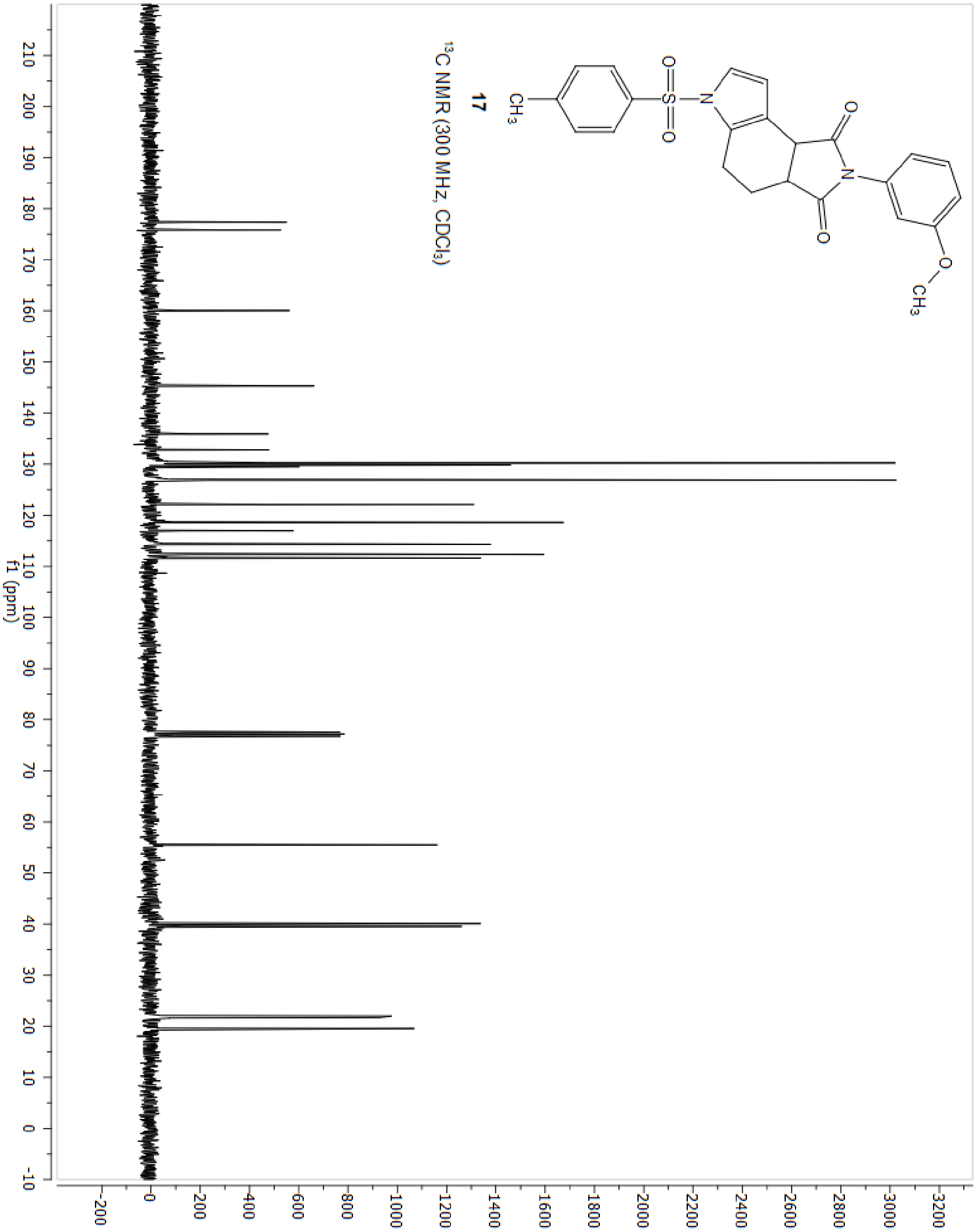

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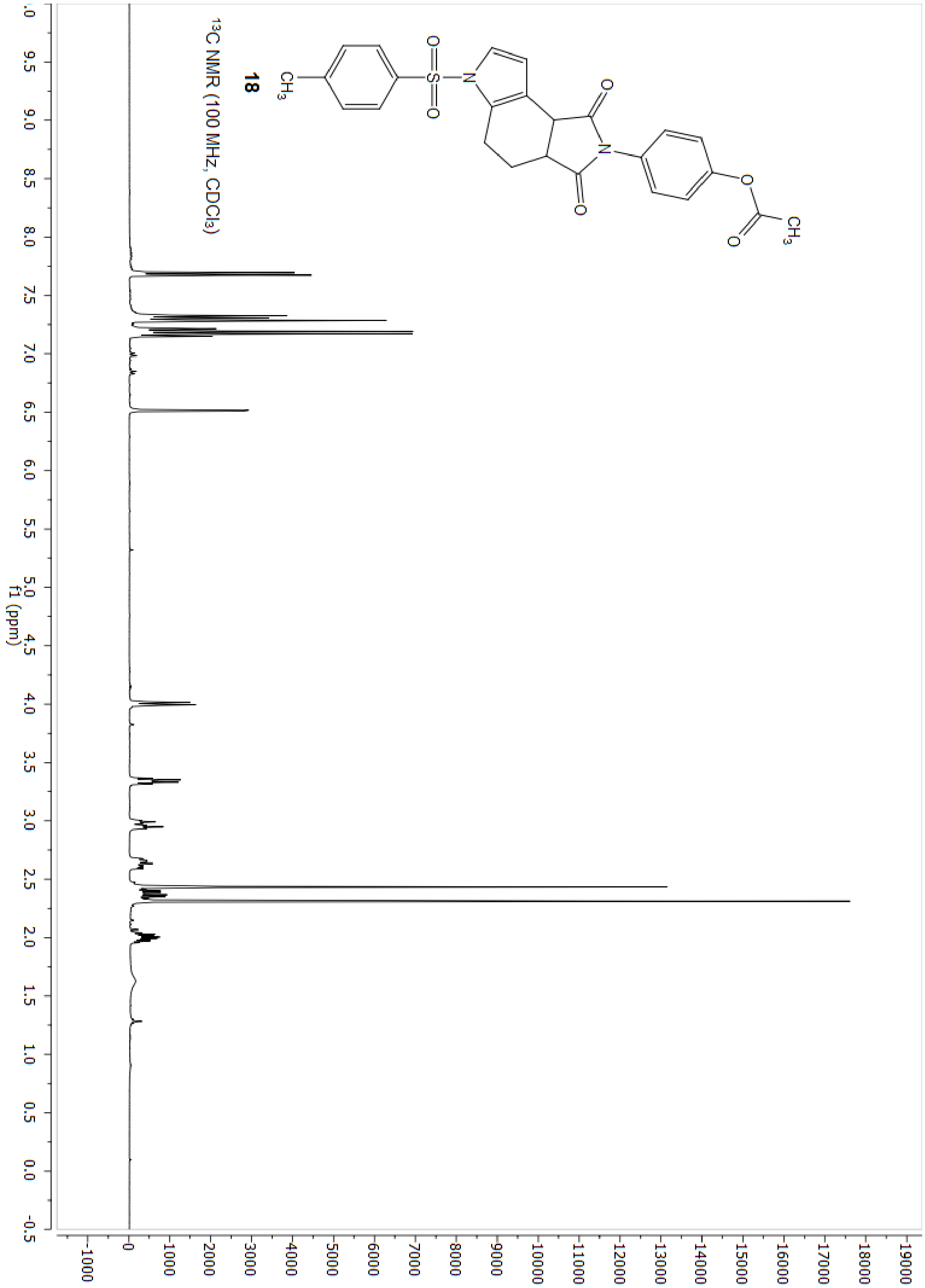

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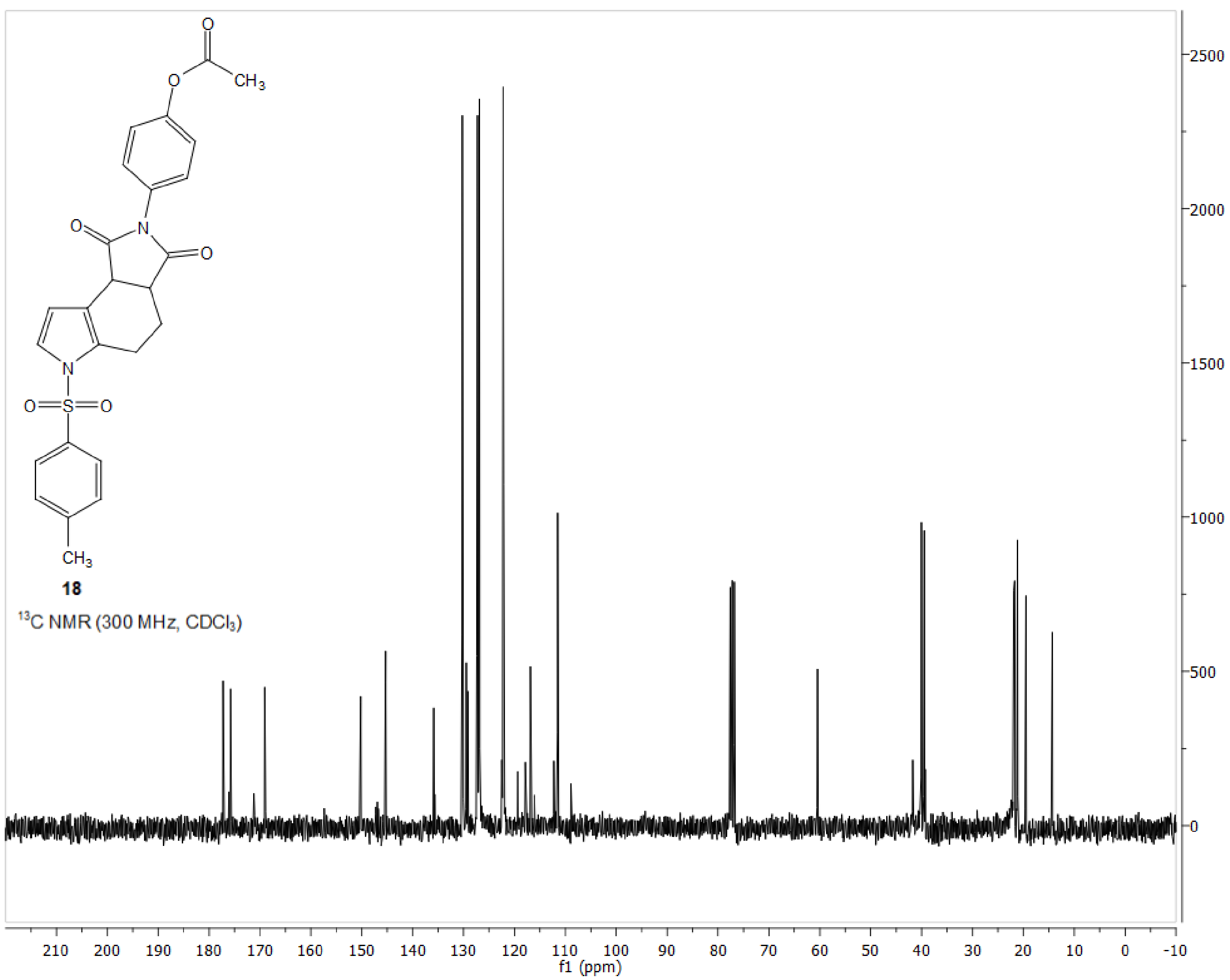

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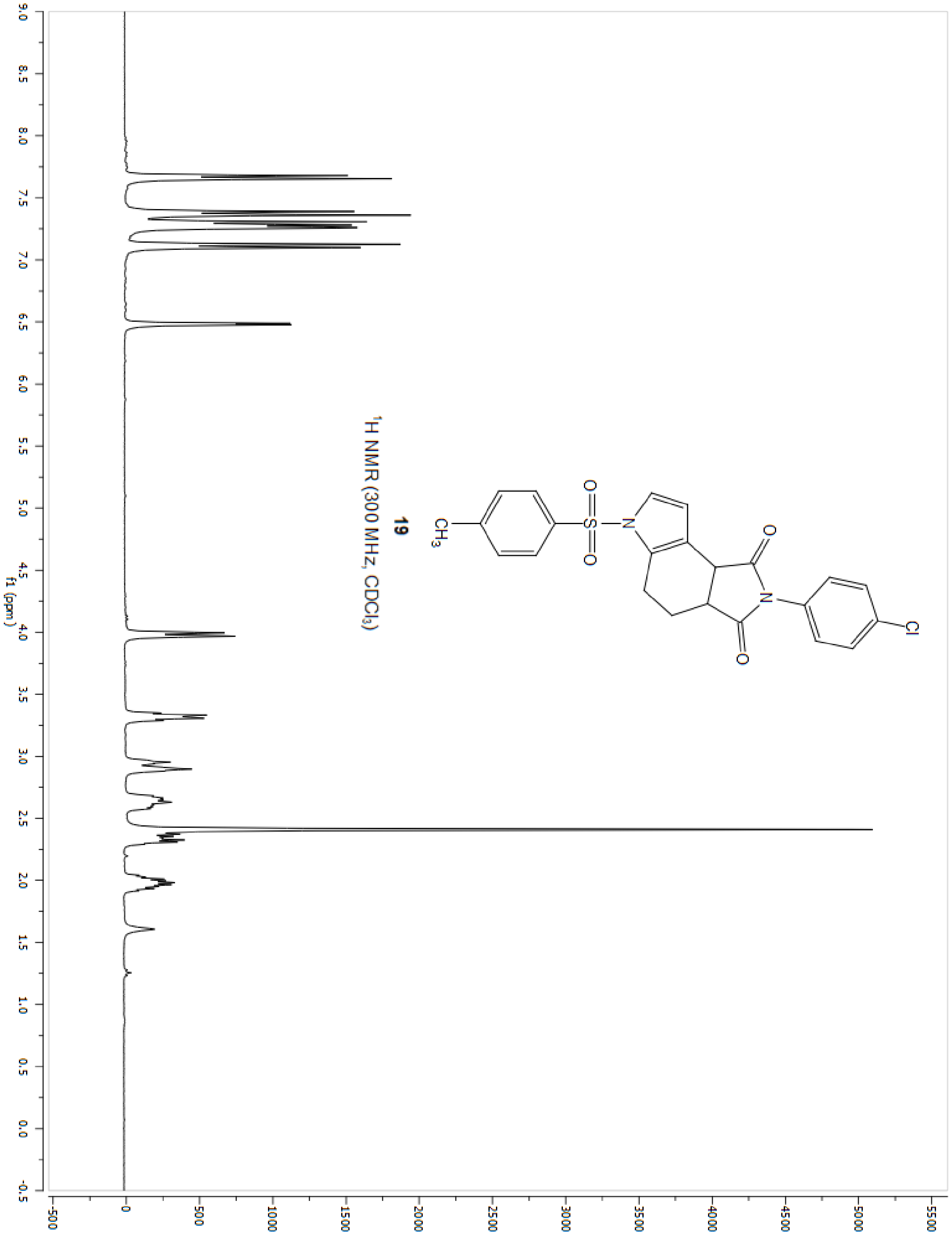

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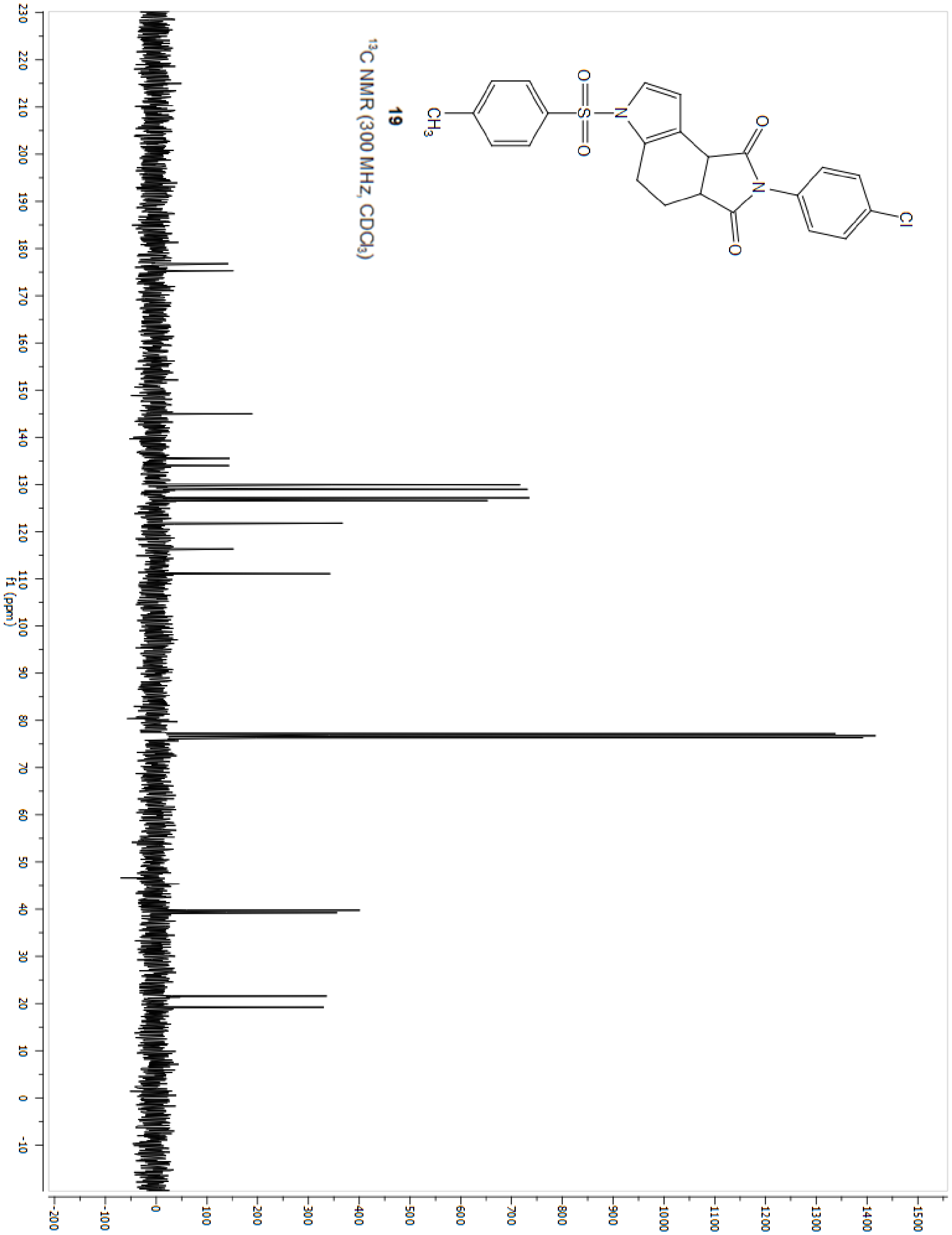

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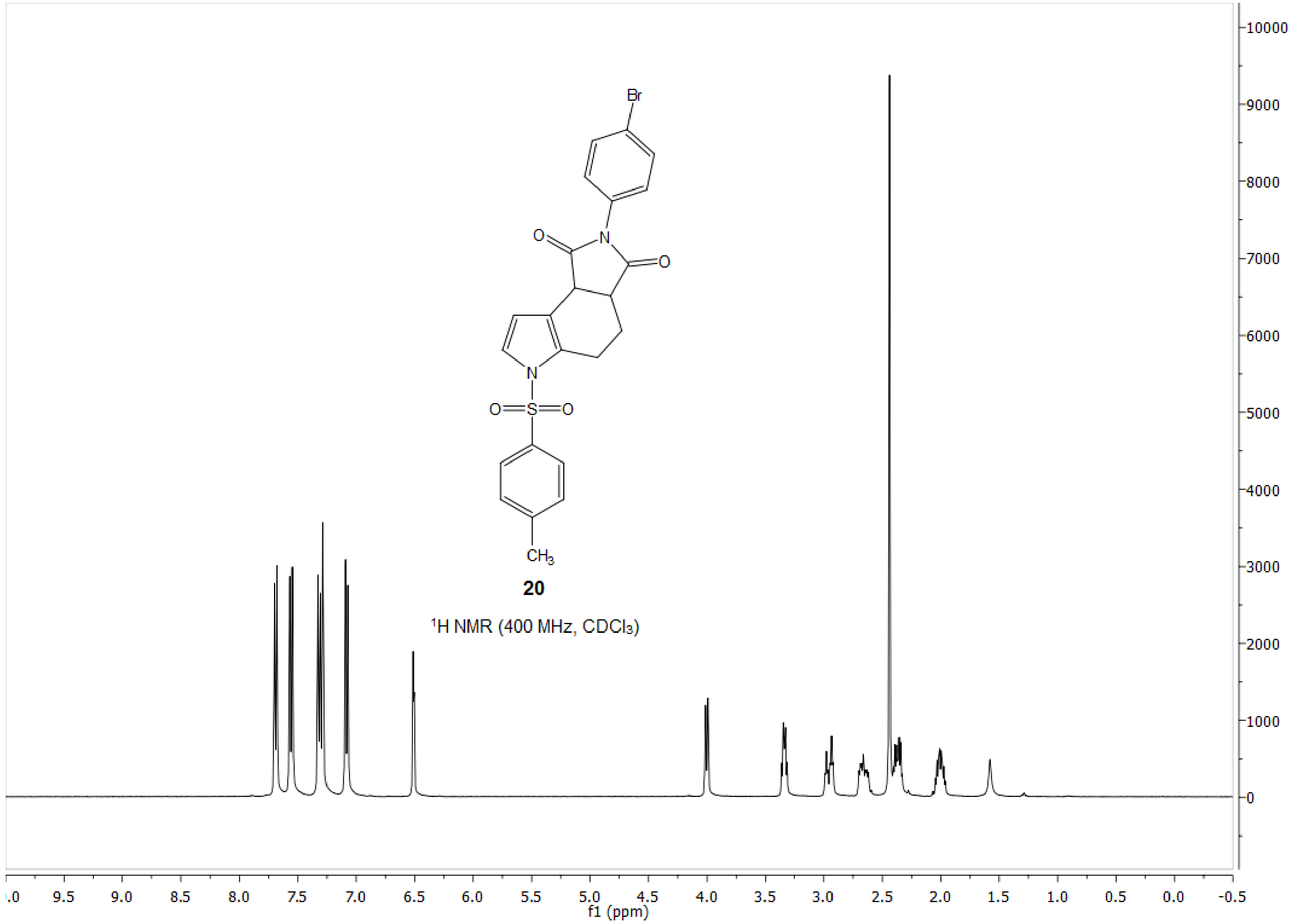

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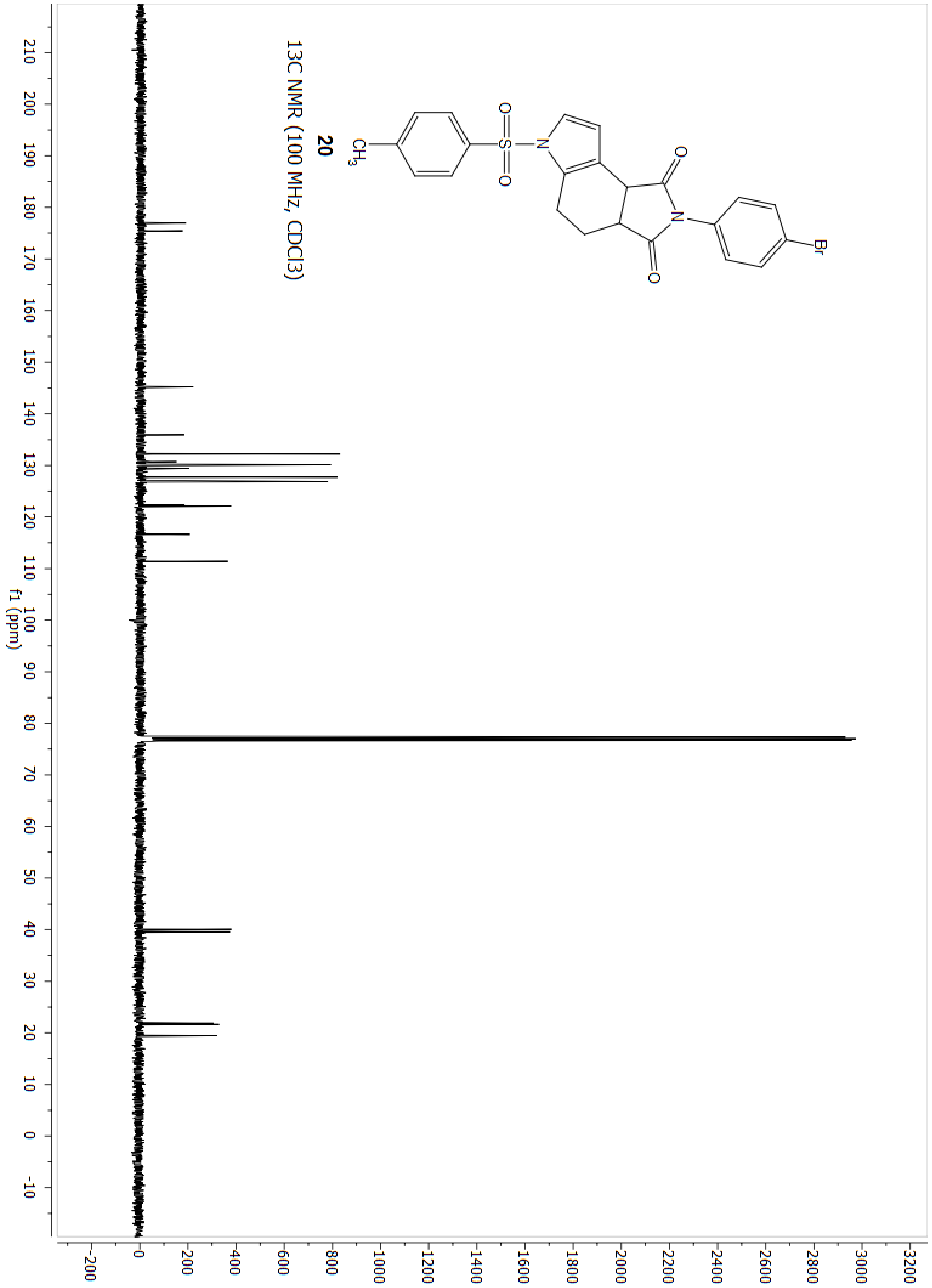

20

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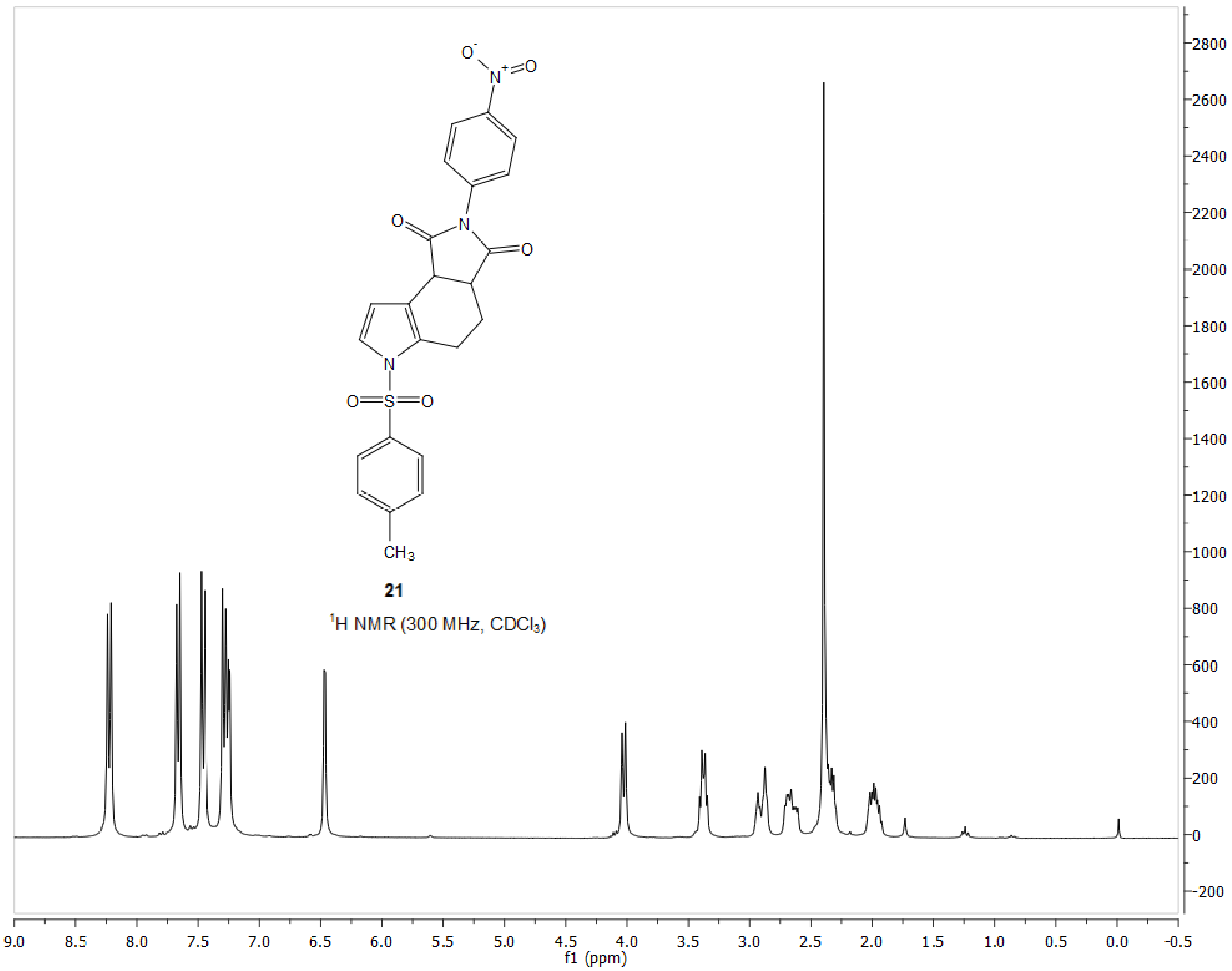

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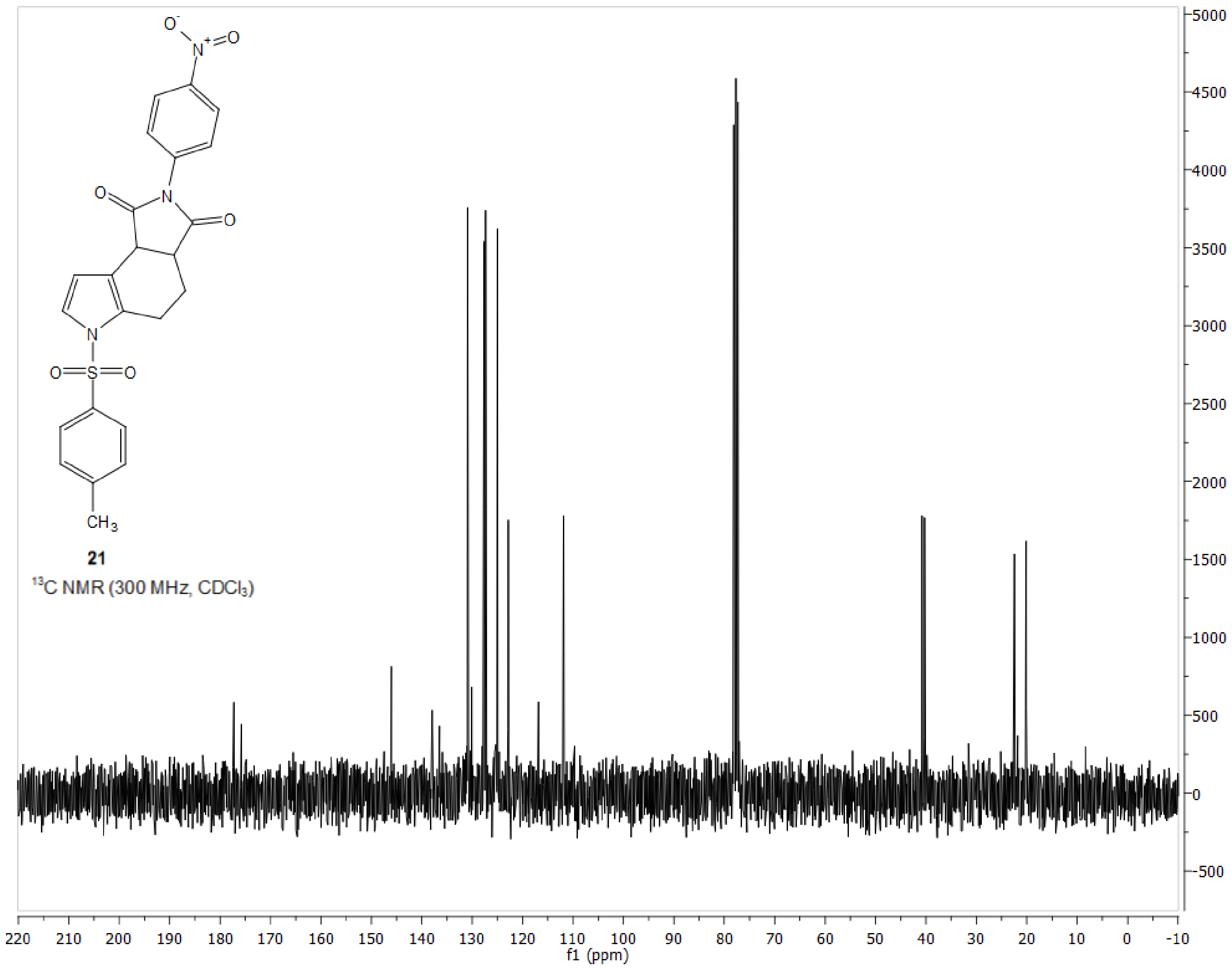
^1H NMR (300 MHz, $CDCl_3$)



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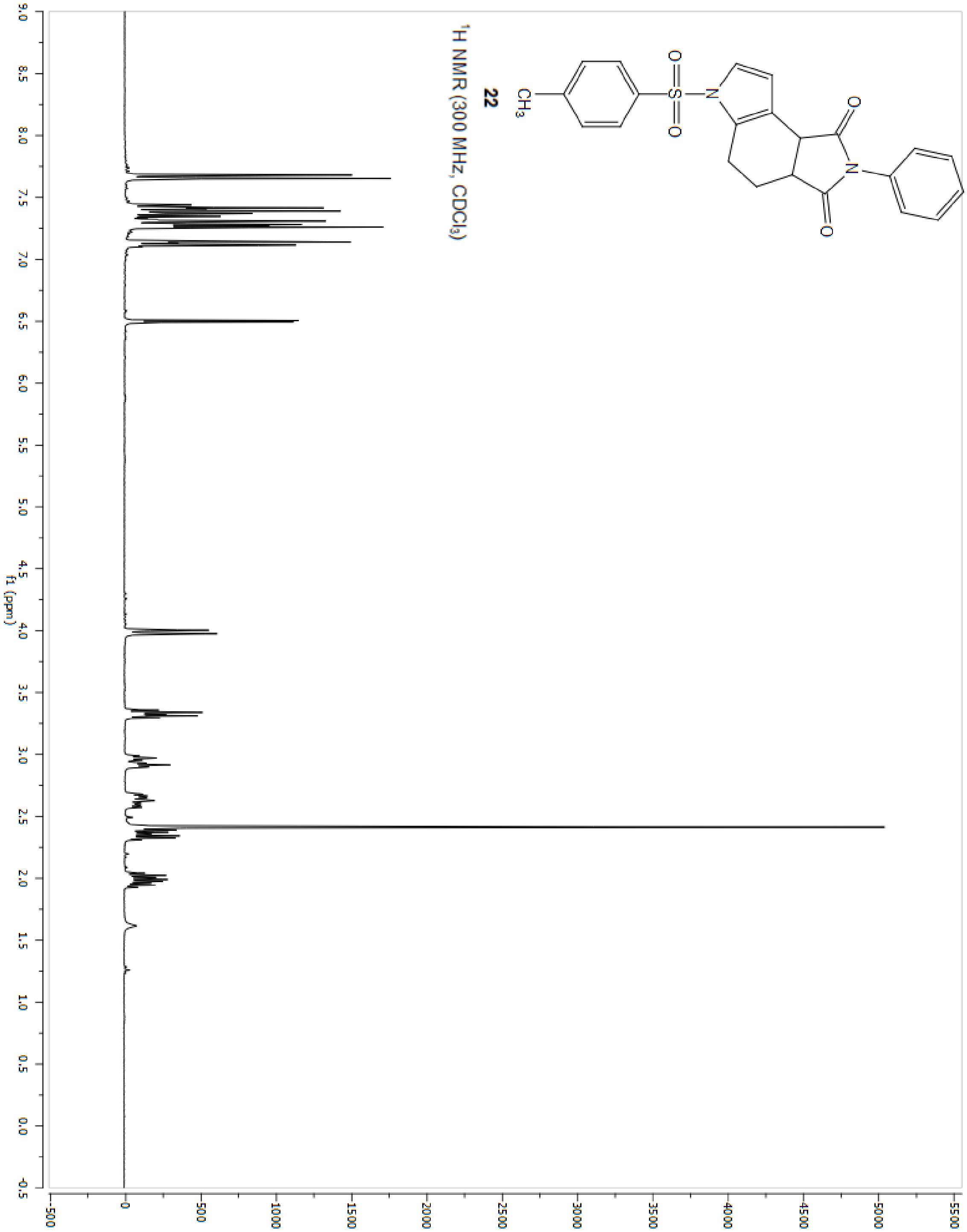

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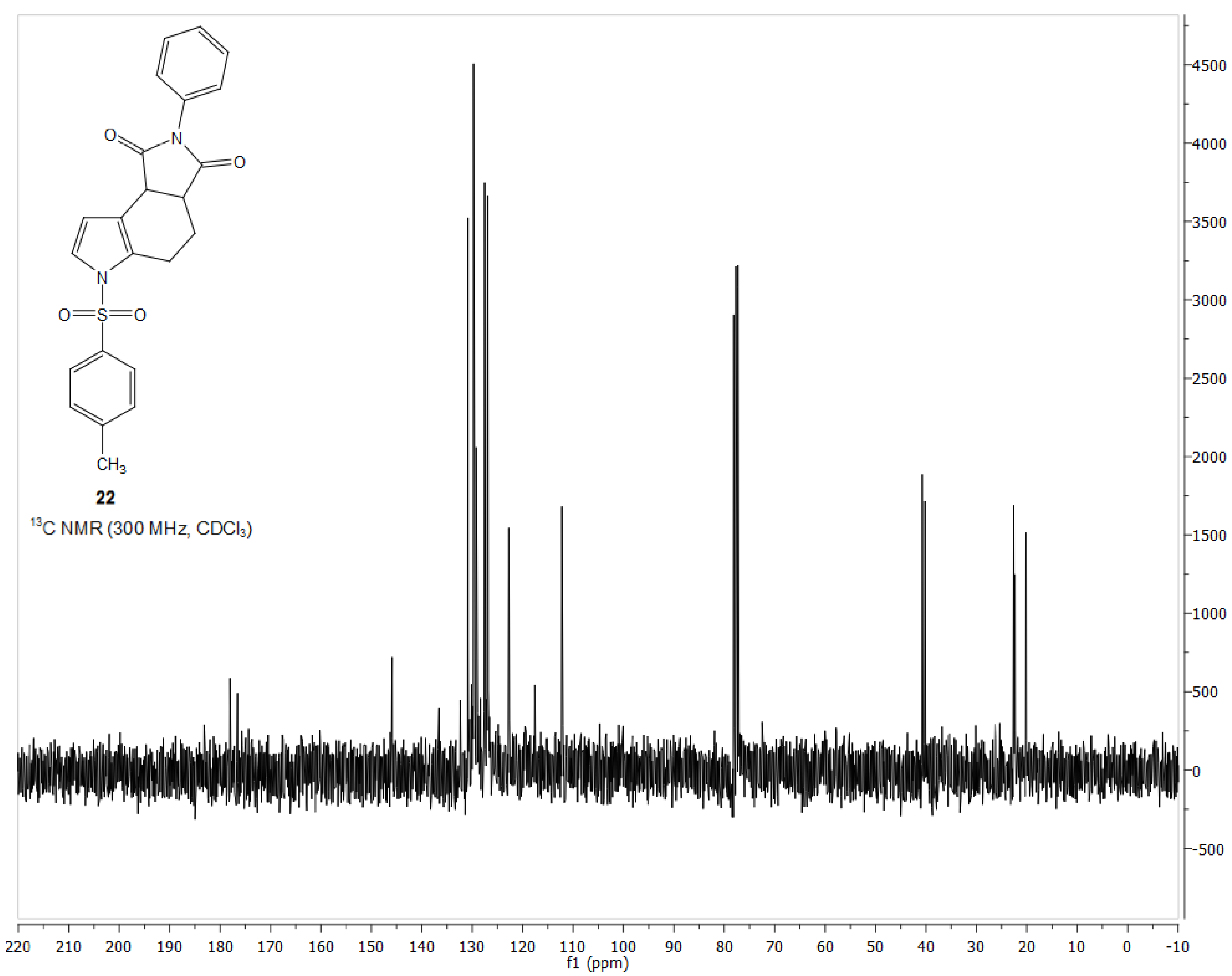

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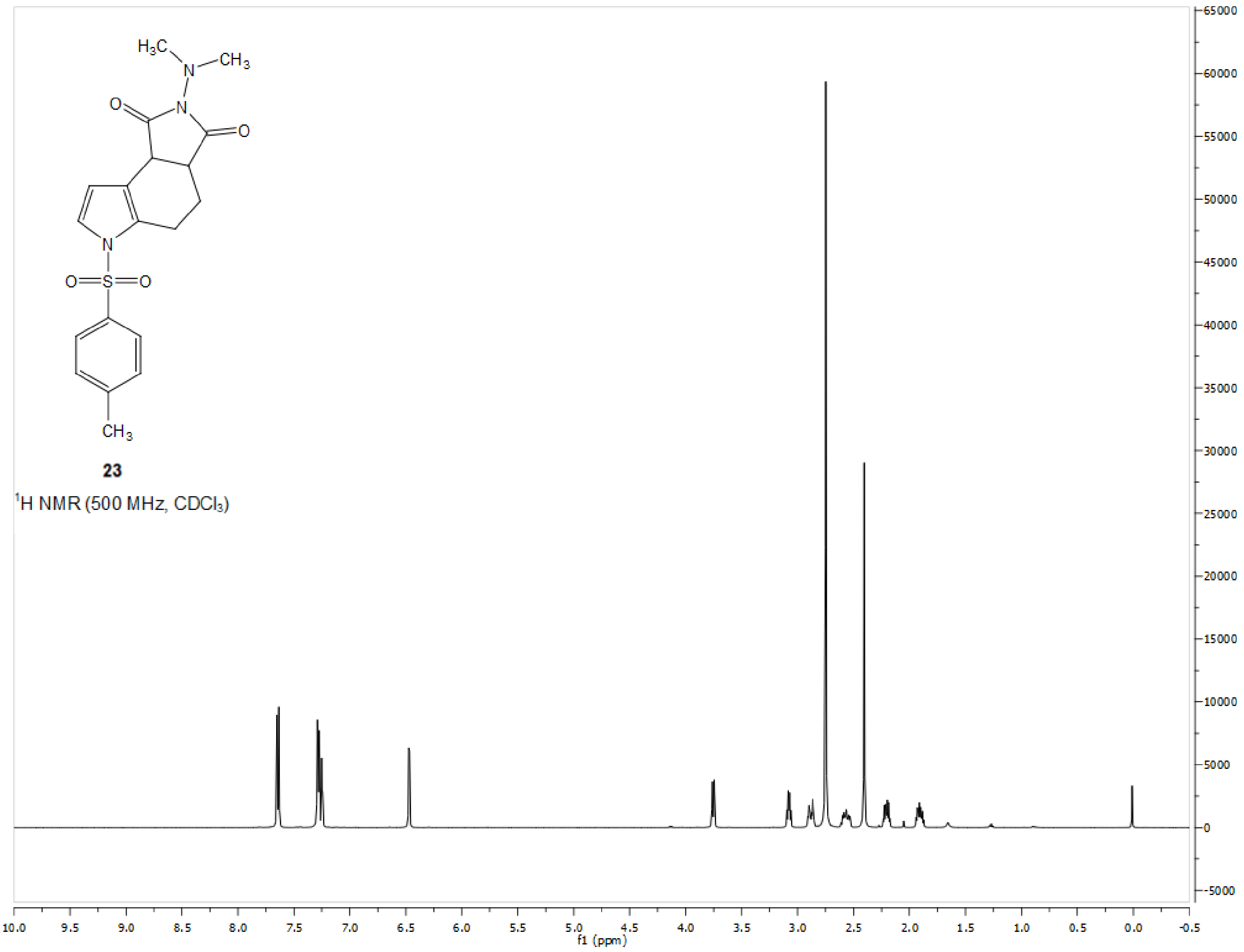

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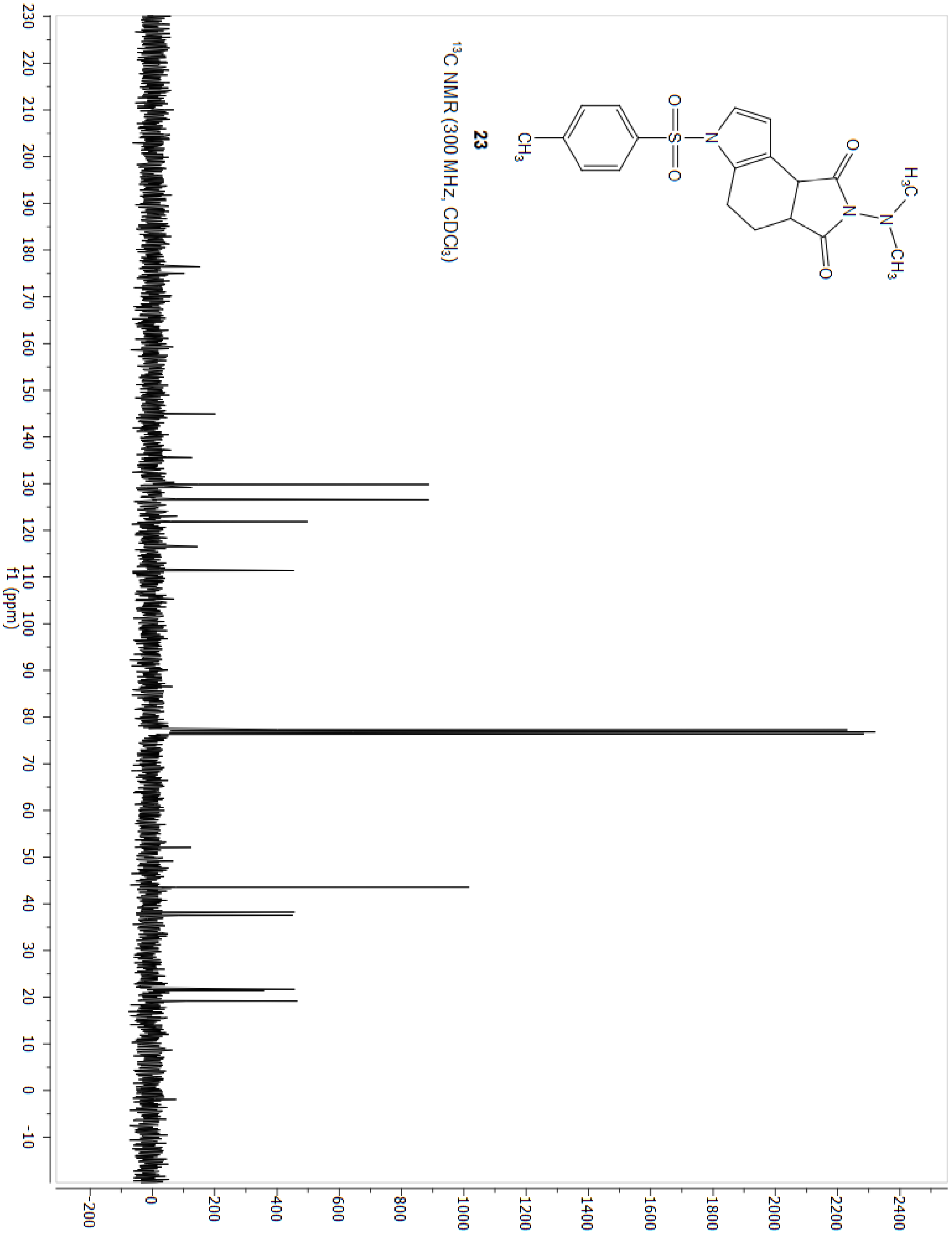

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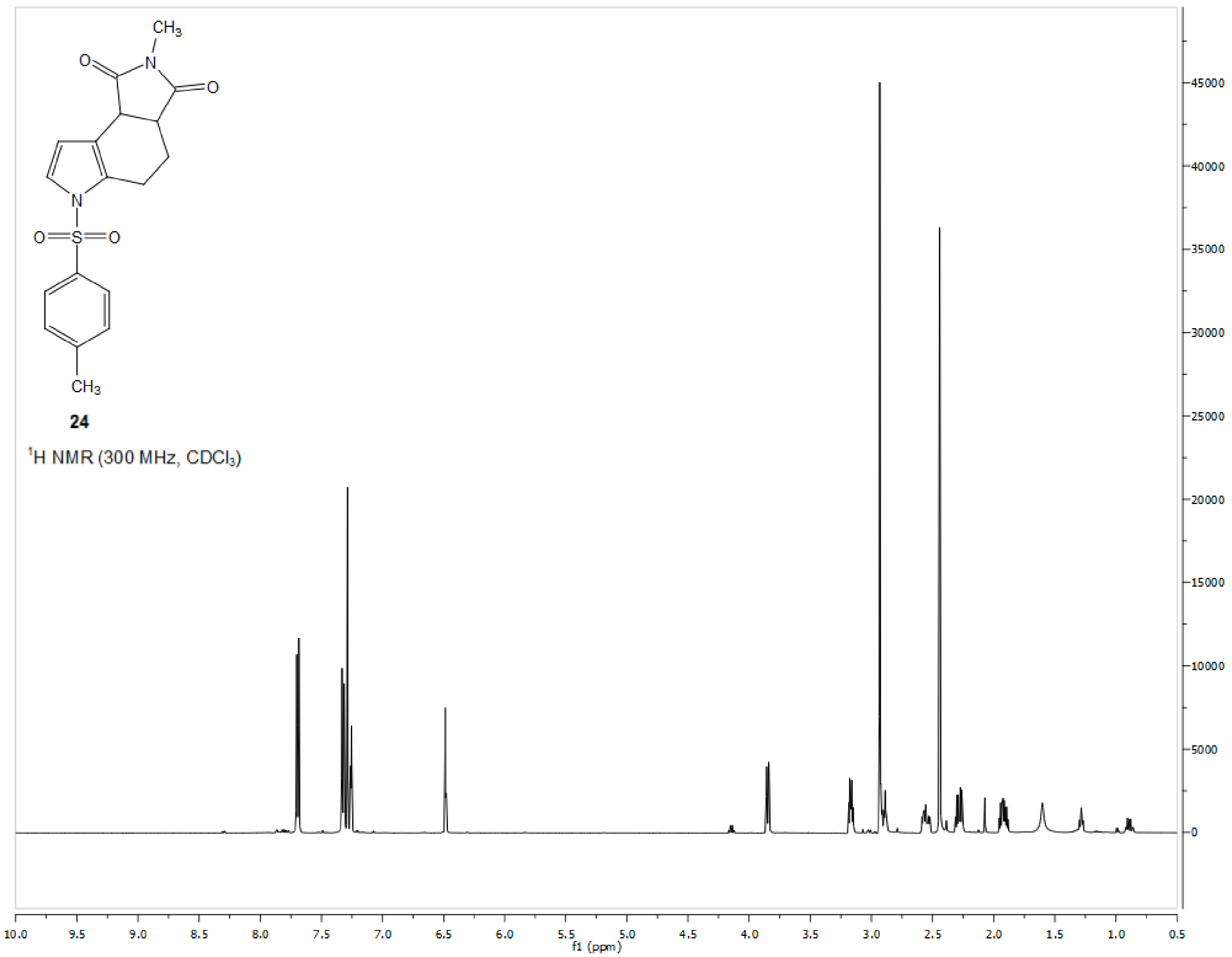

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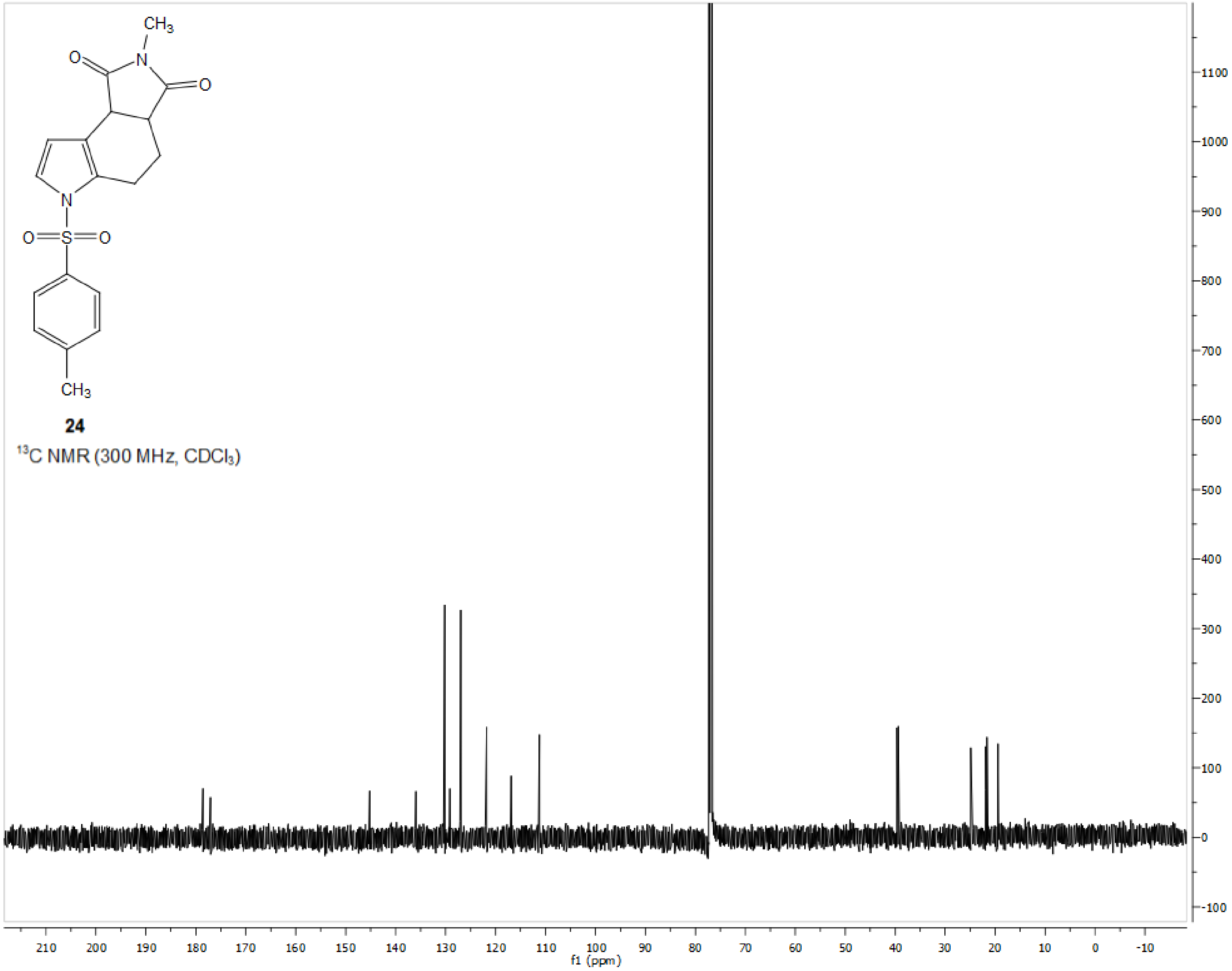

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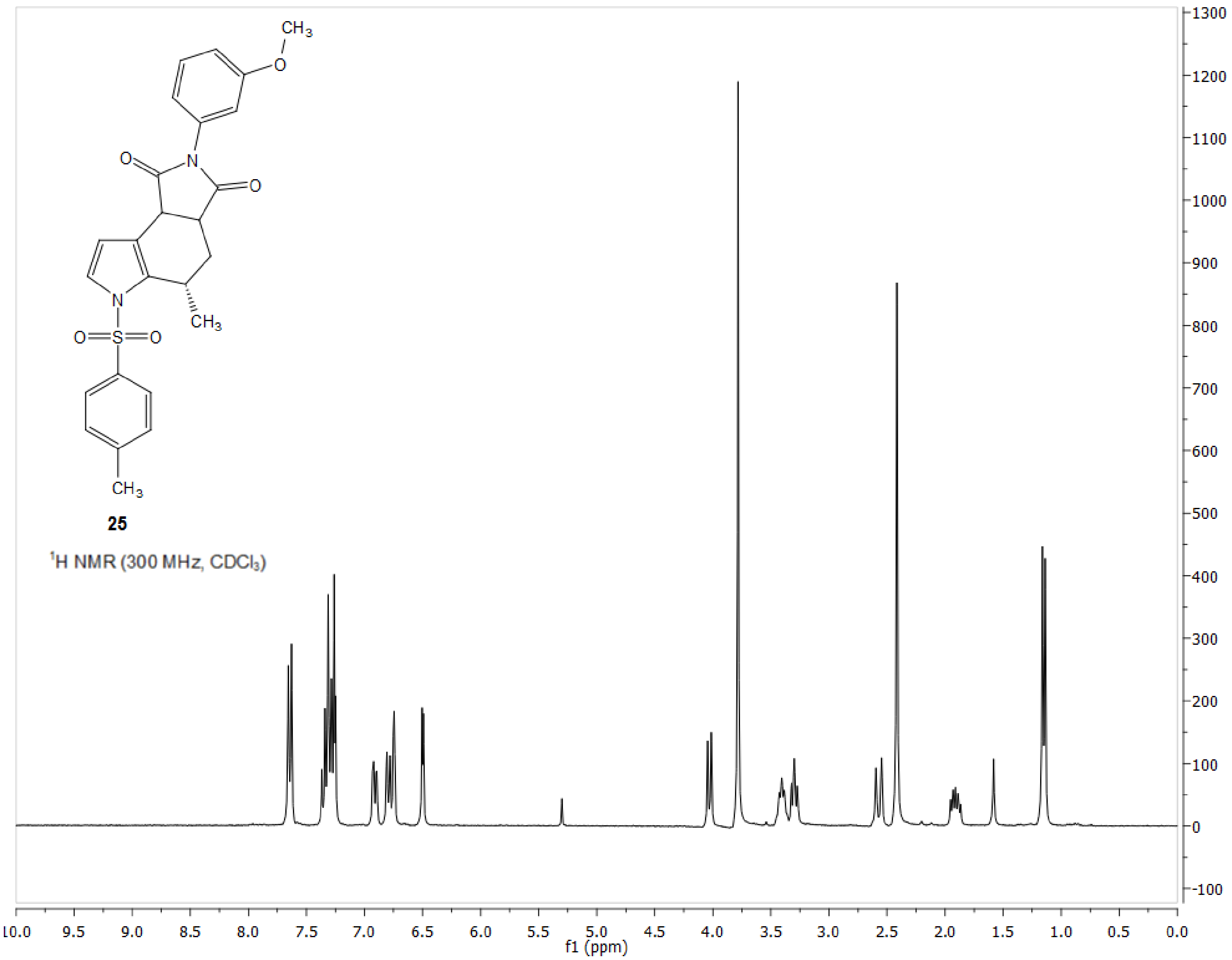

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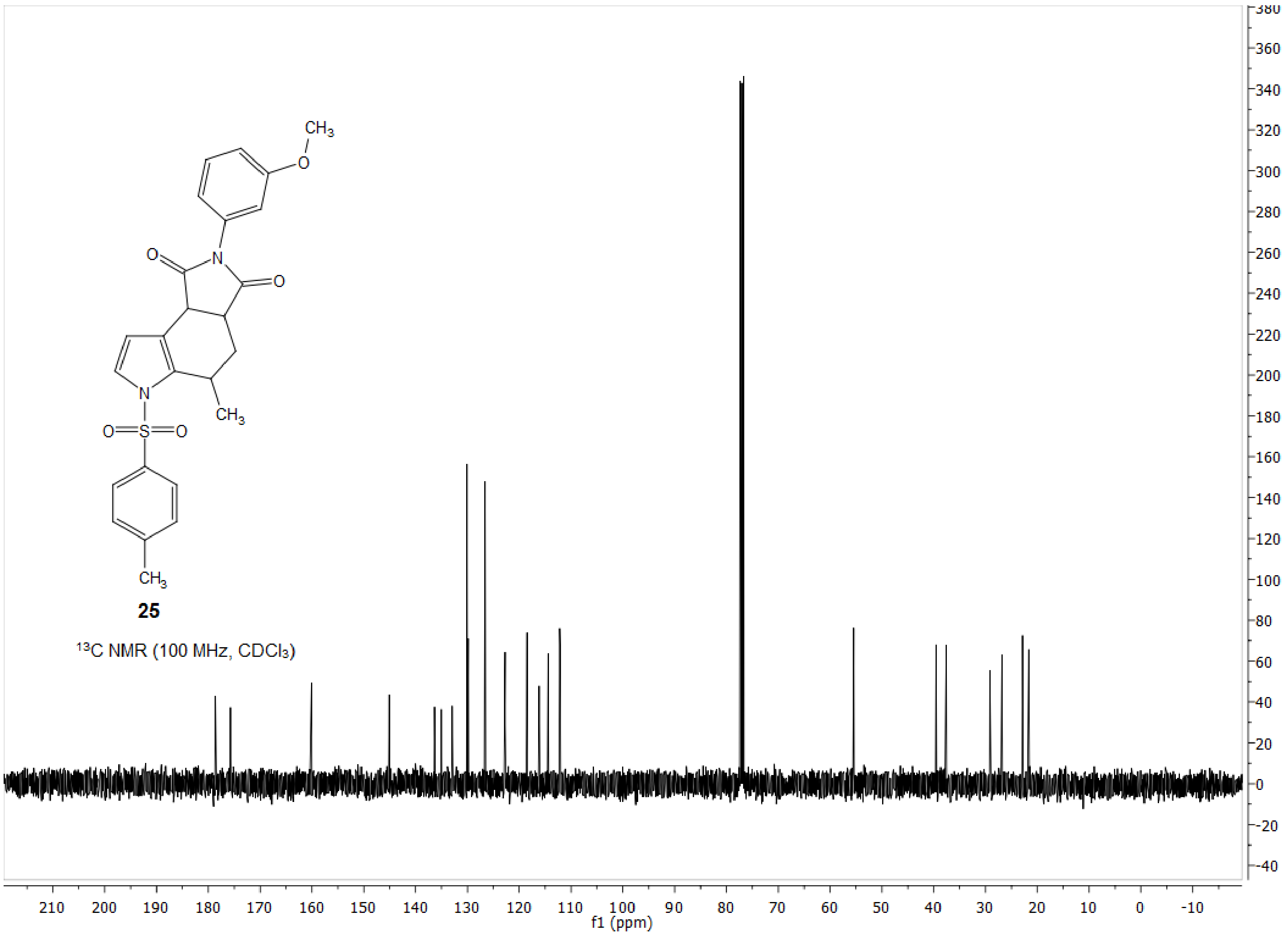

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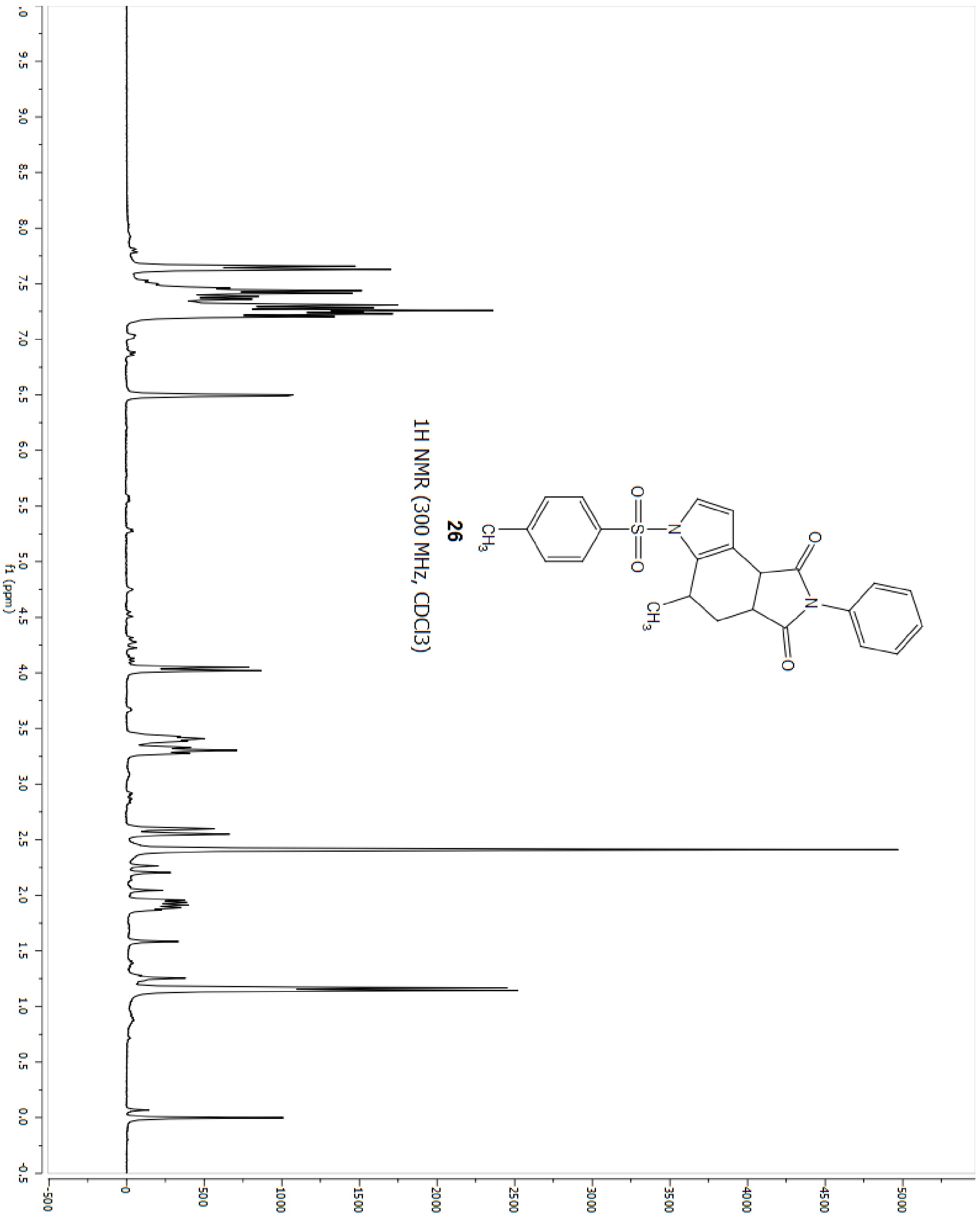

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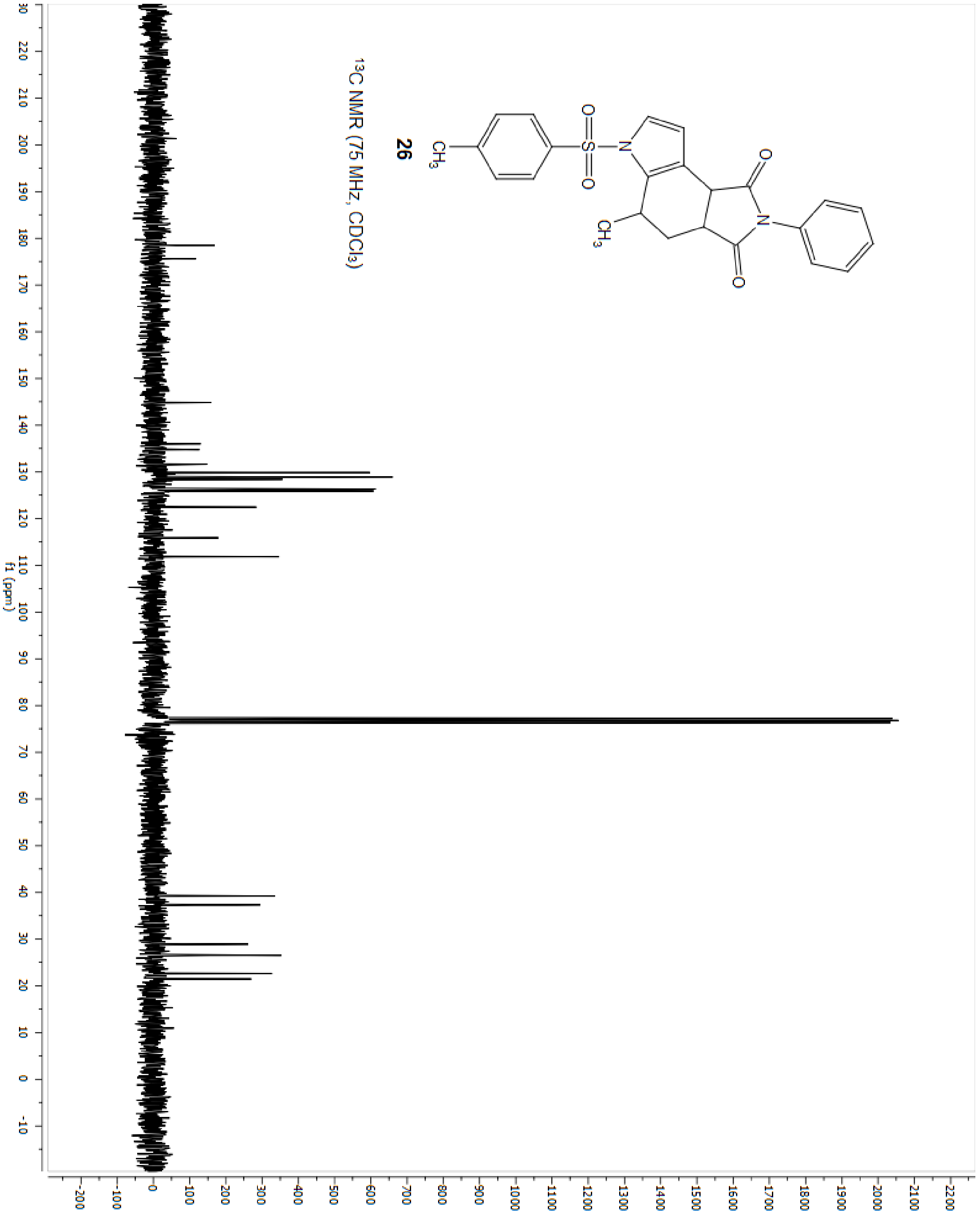
1H NMR (300 MHz, CDCl3)



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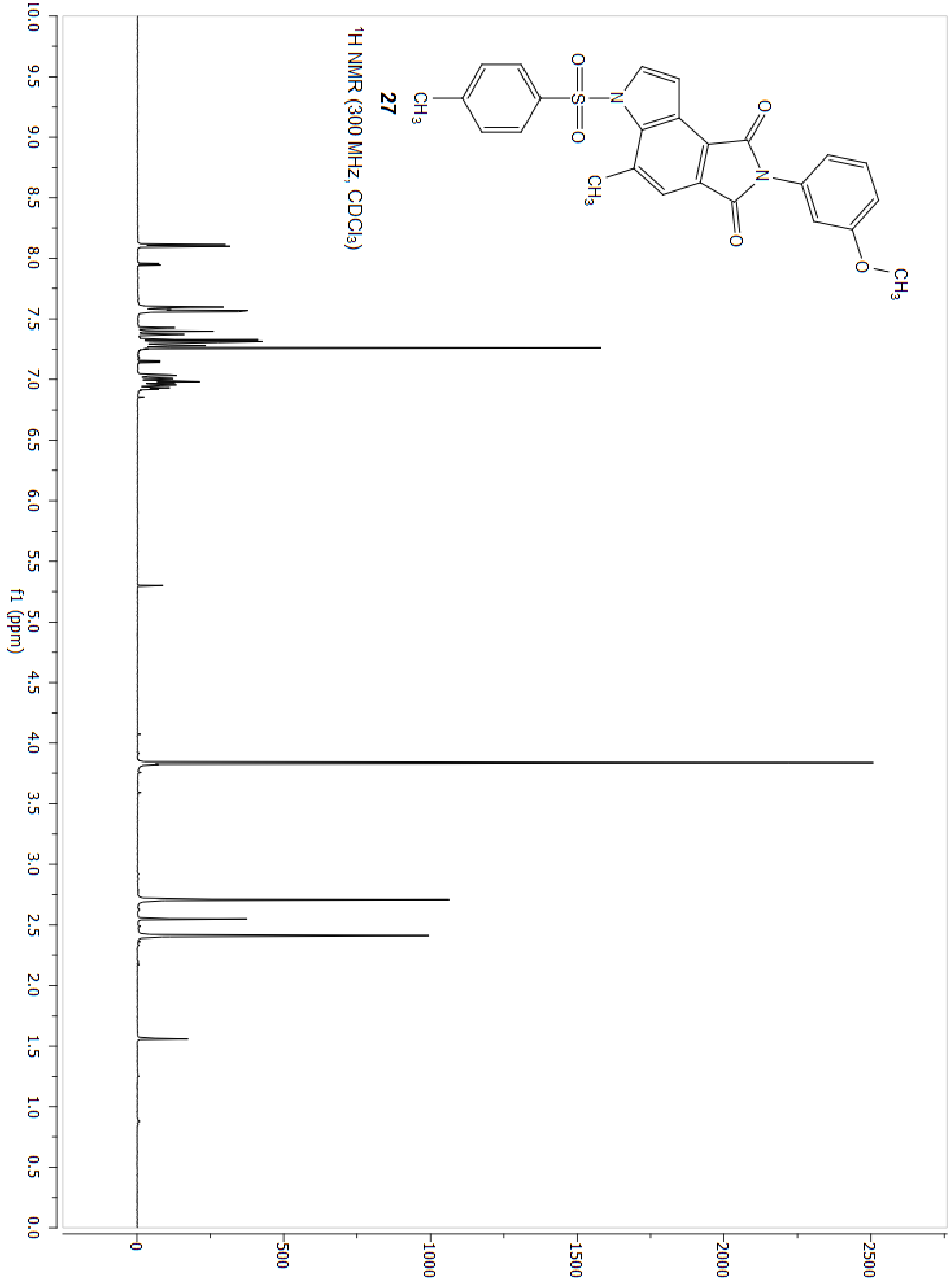

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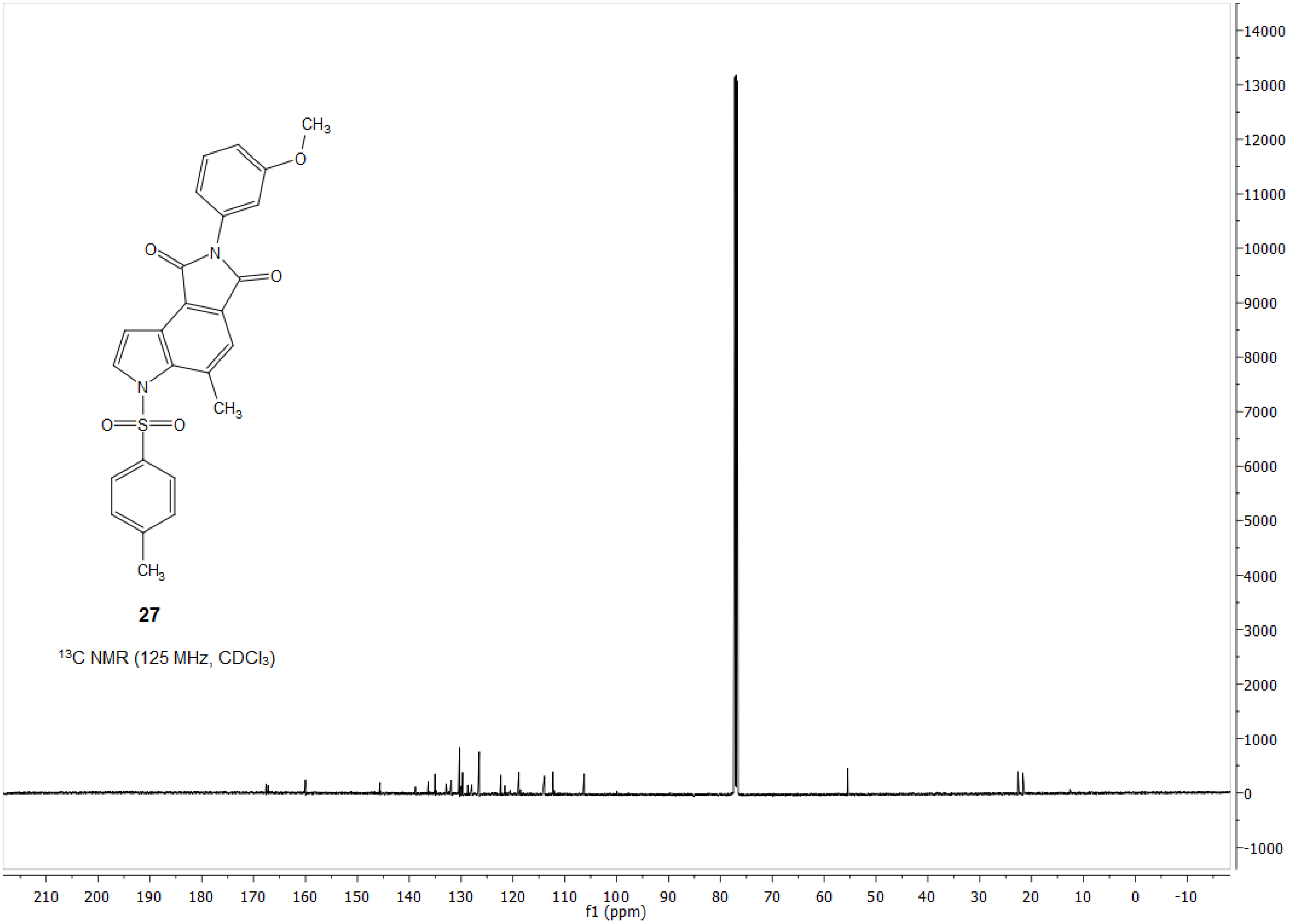

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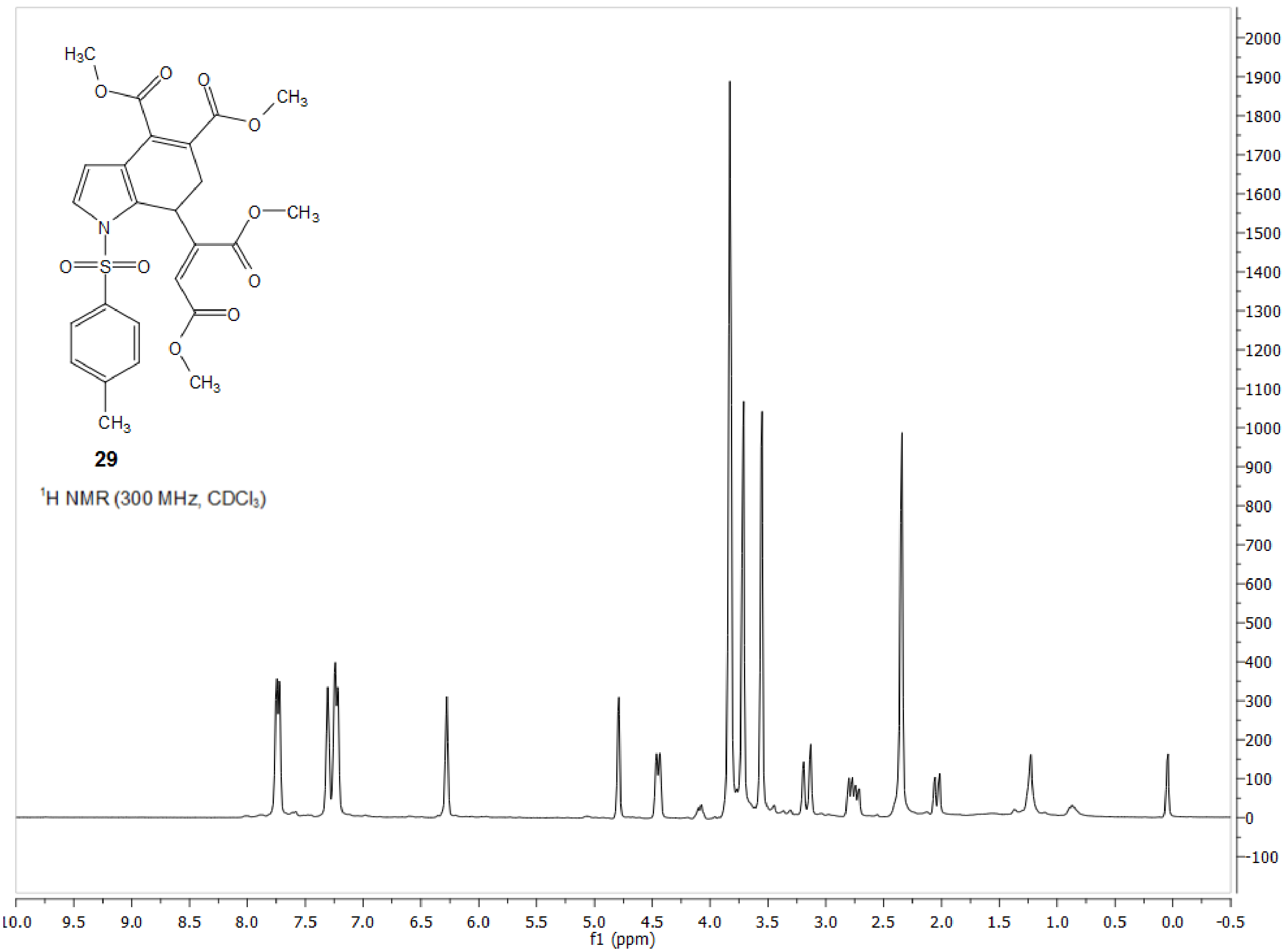

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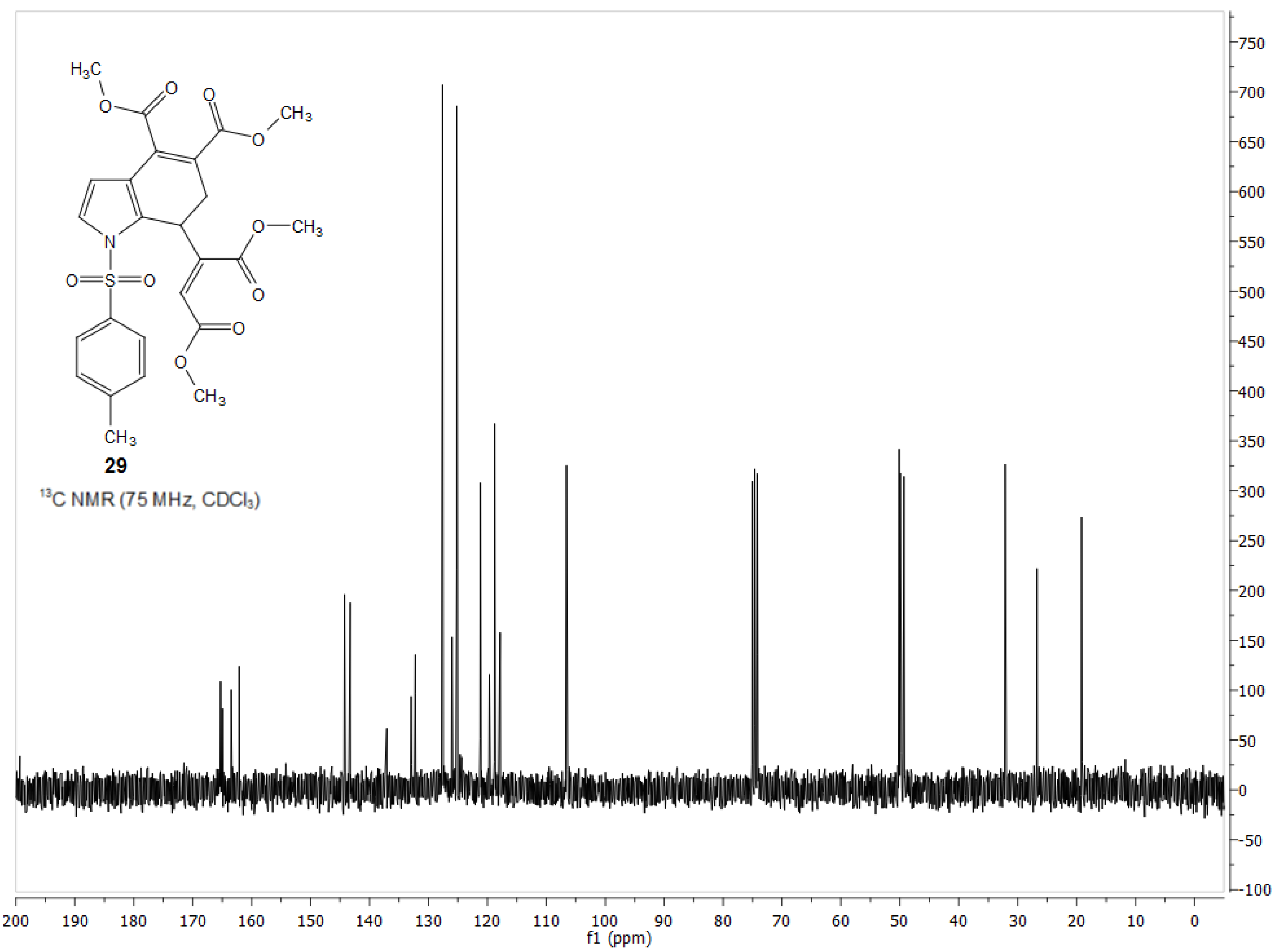

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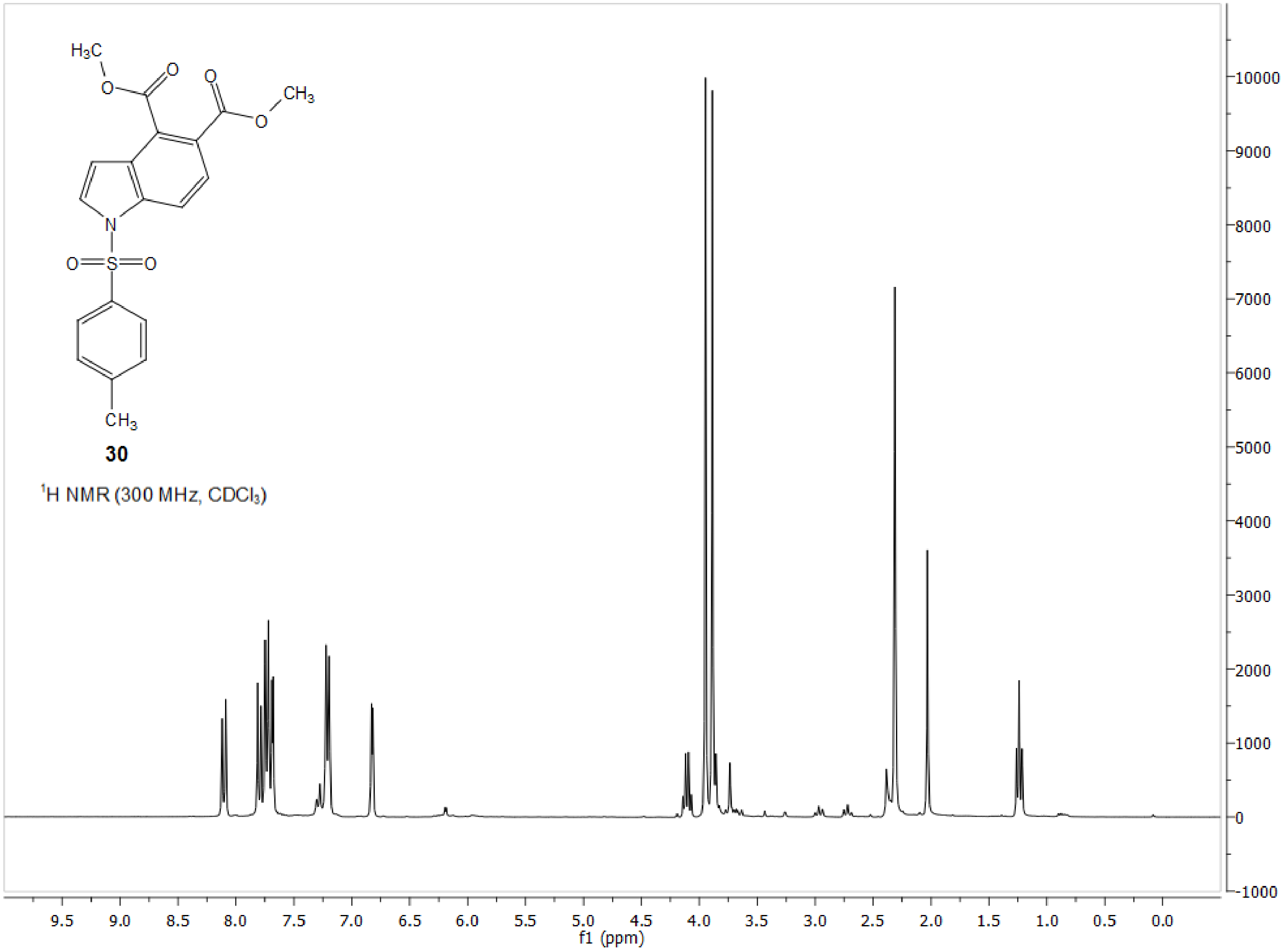

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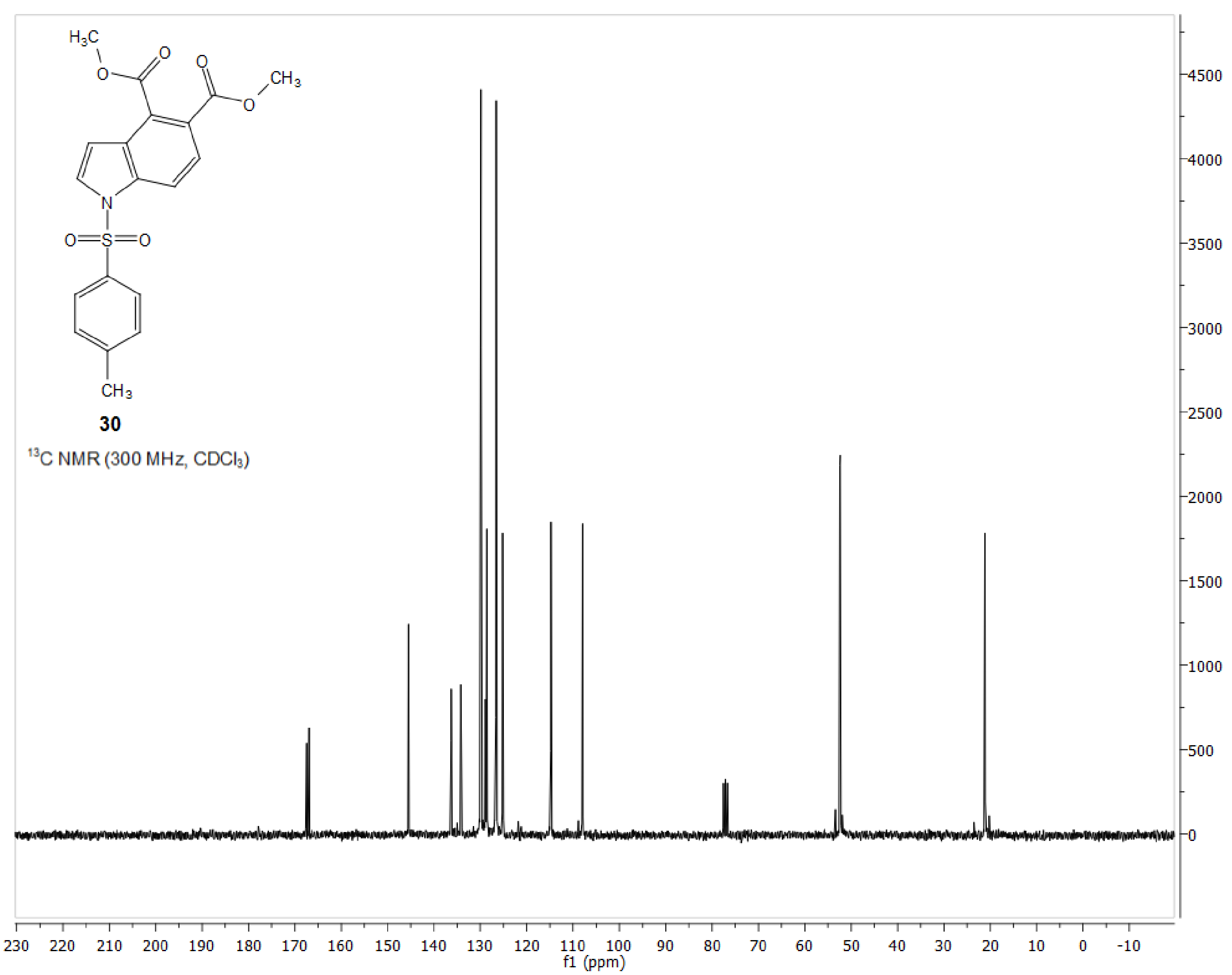
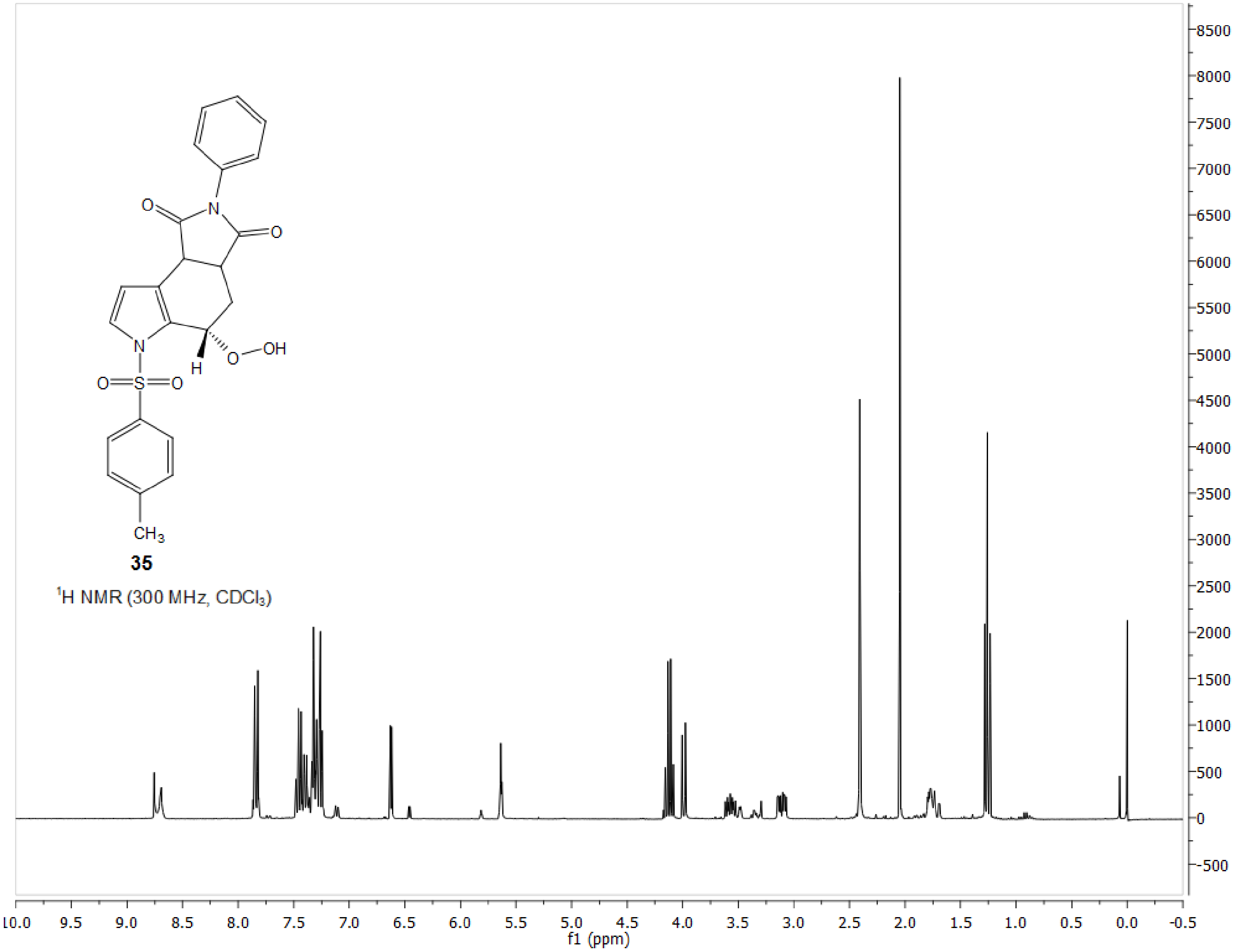


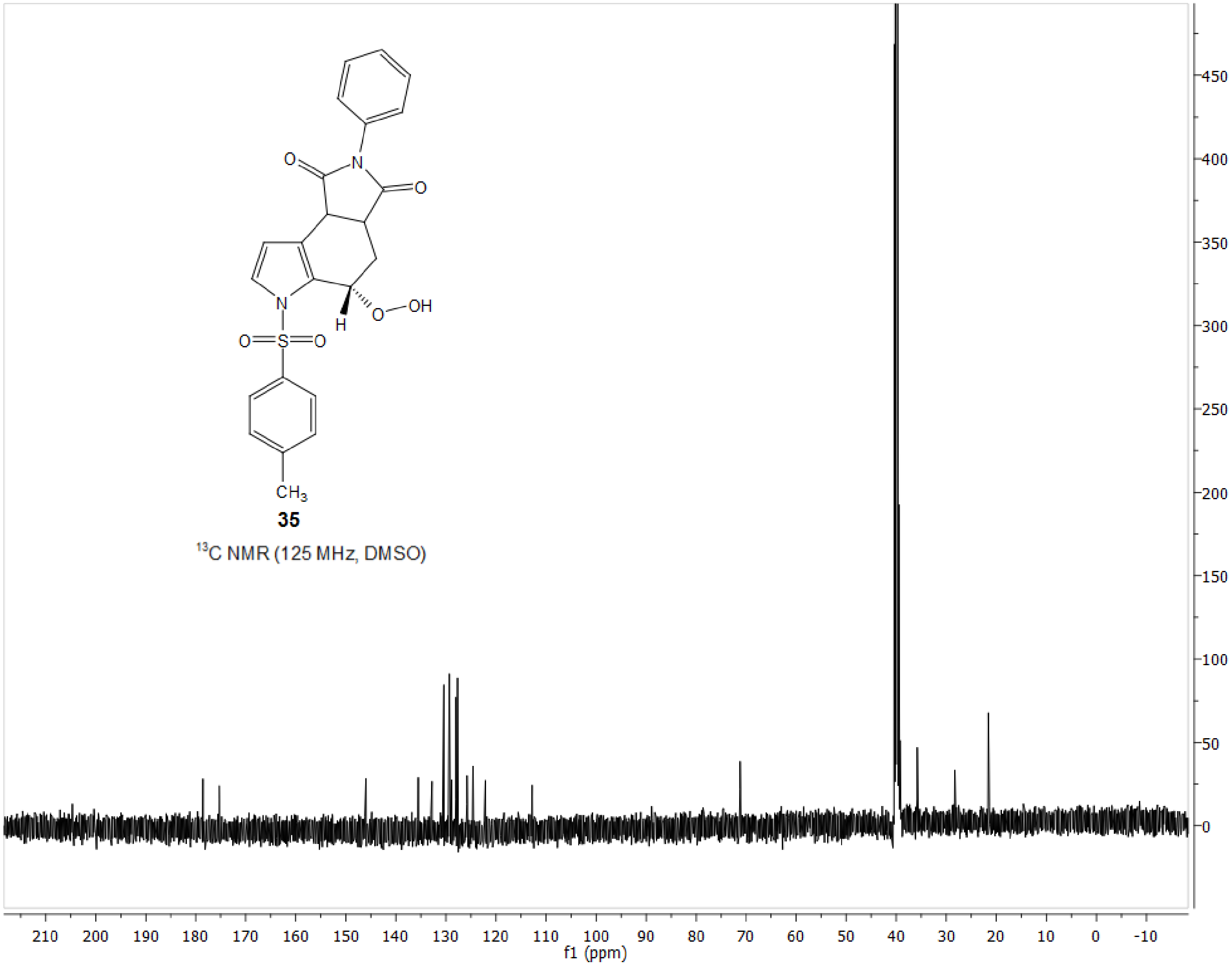
30

^{13}C NMR (300 MHz, CDCl$_3$)



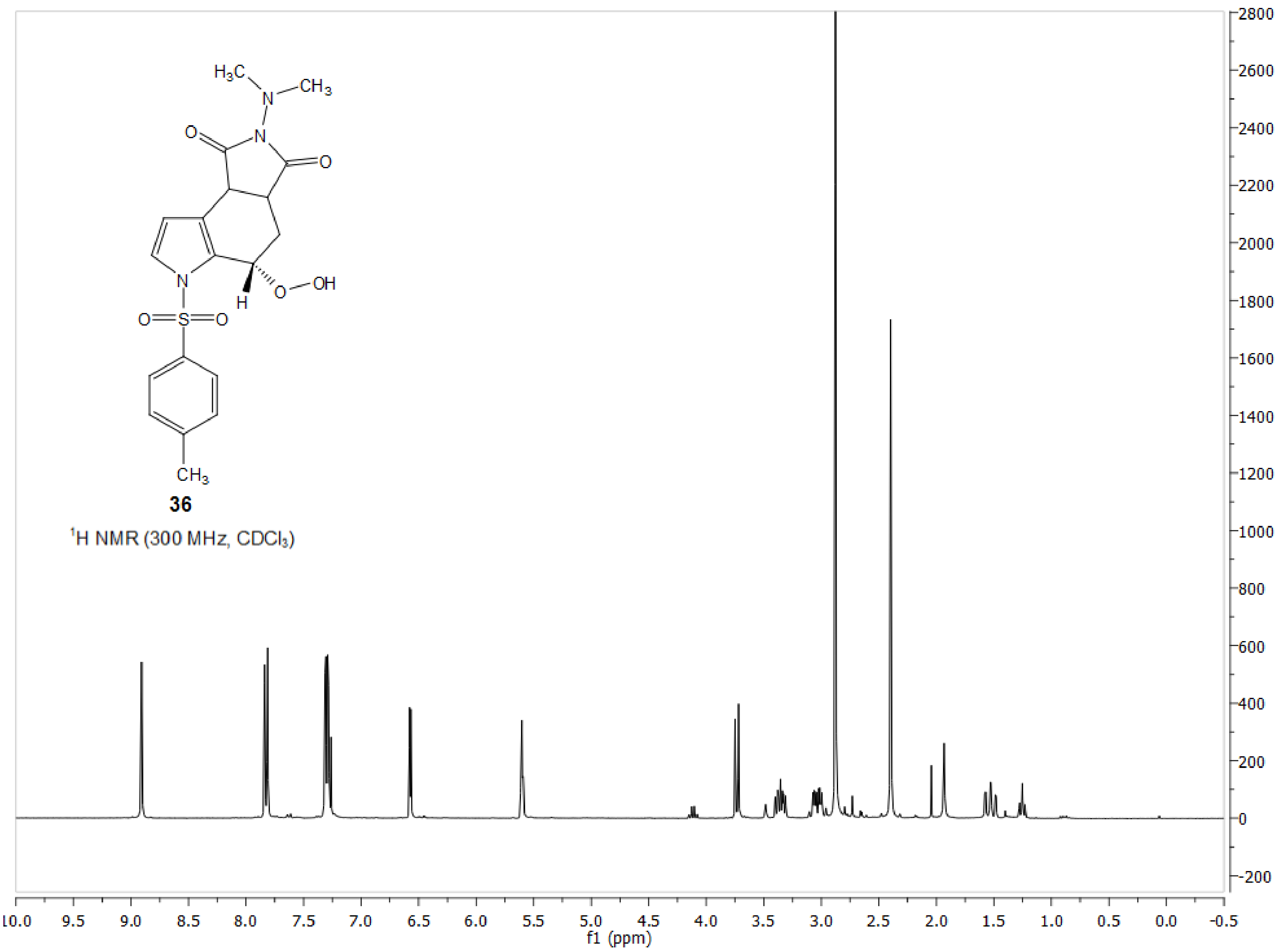
35

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



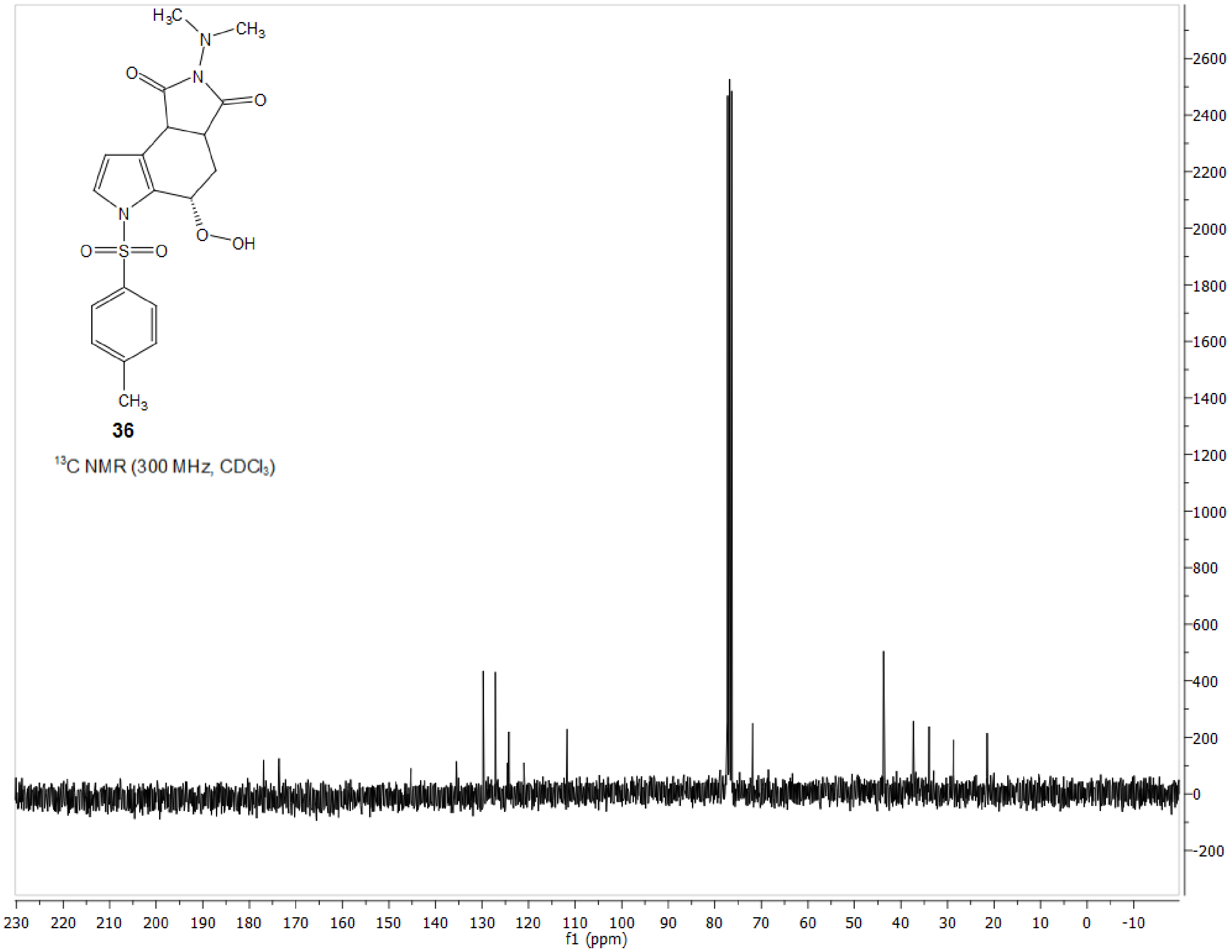
35

^{13}C NMR (125 MHz, DMSO)



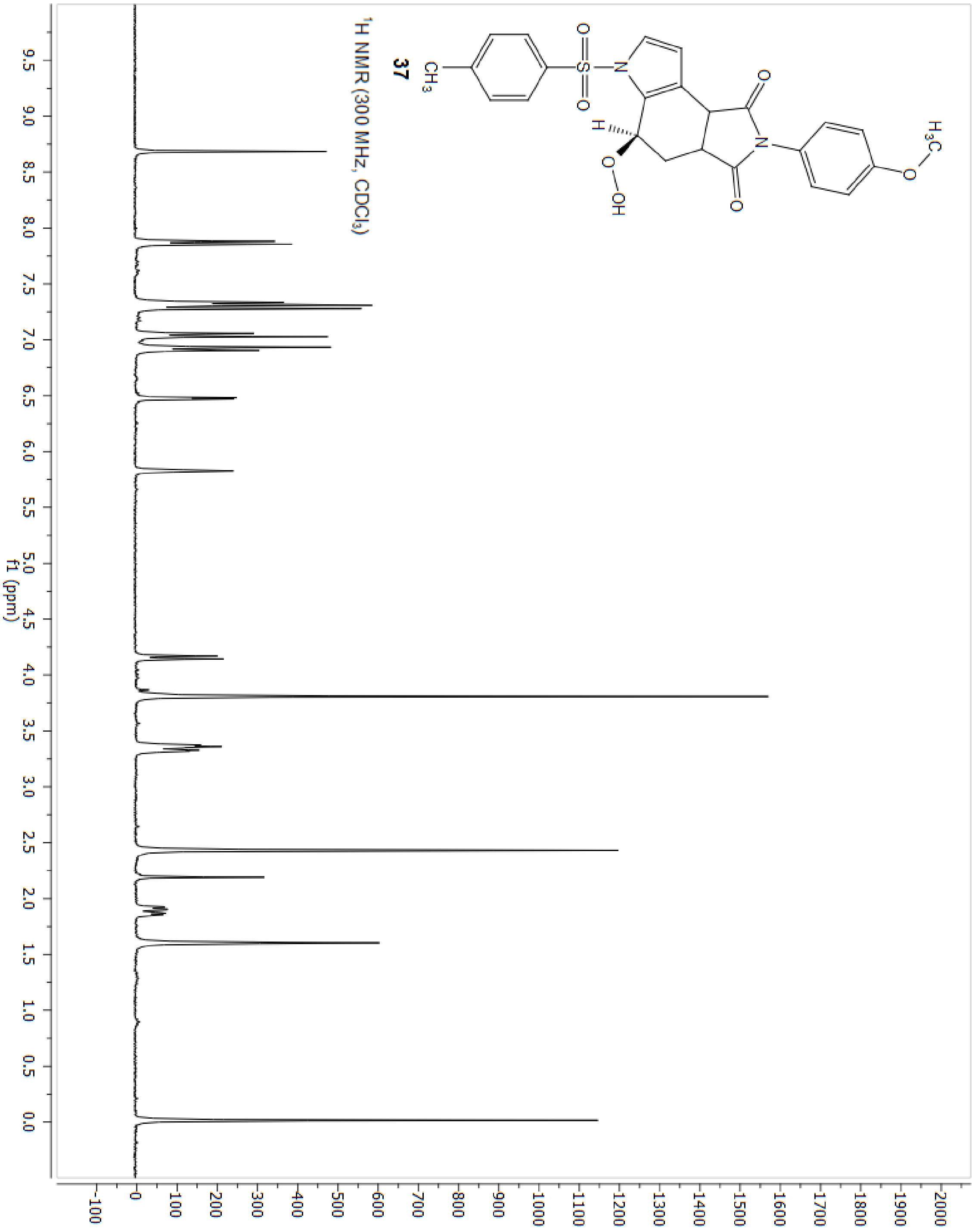
36

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



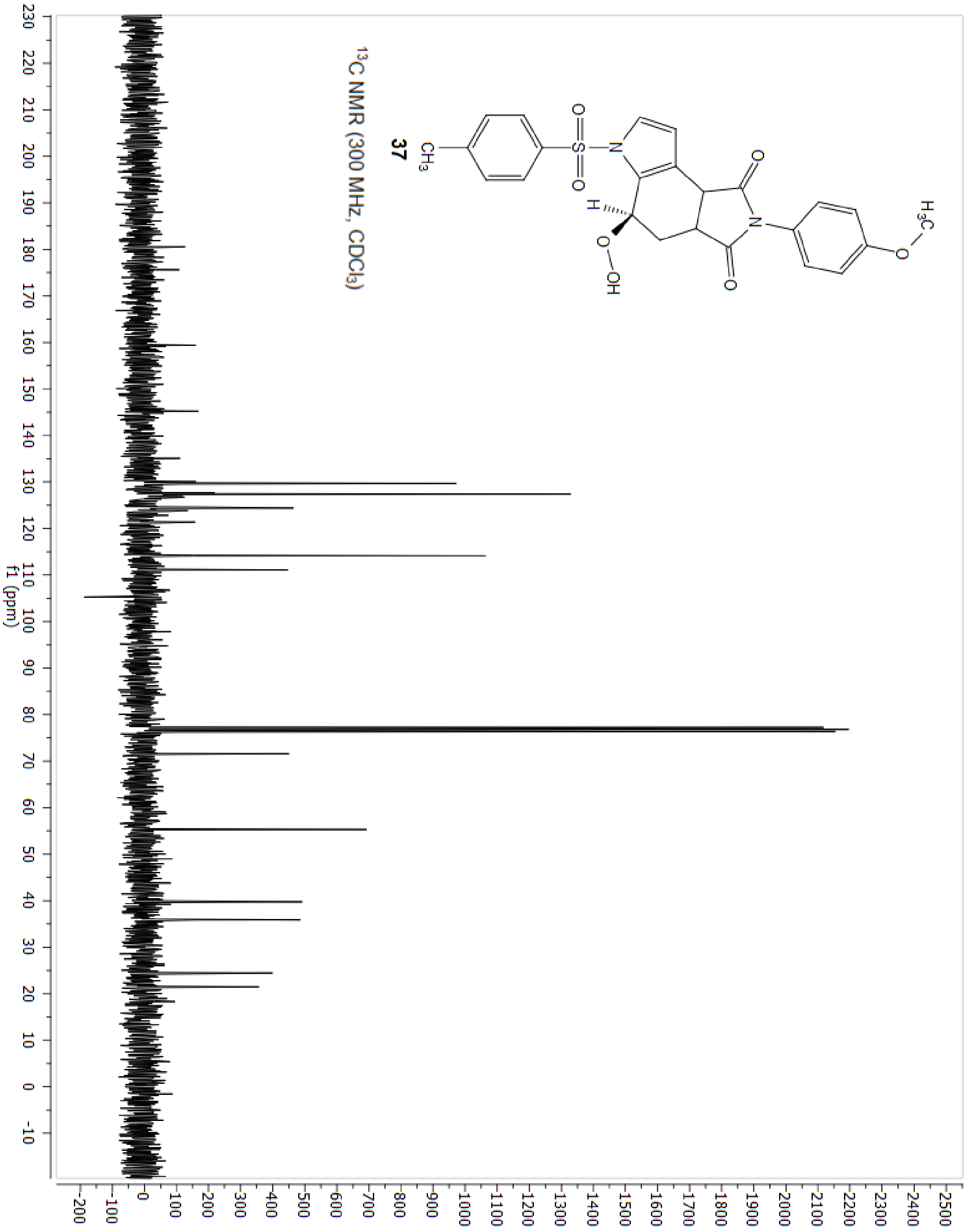
36

^{13}C NMR (300 MHz, $CDCl_3$)



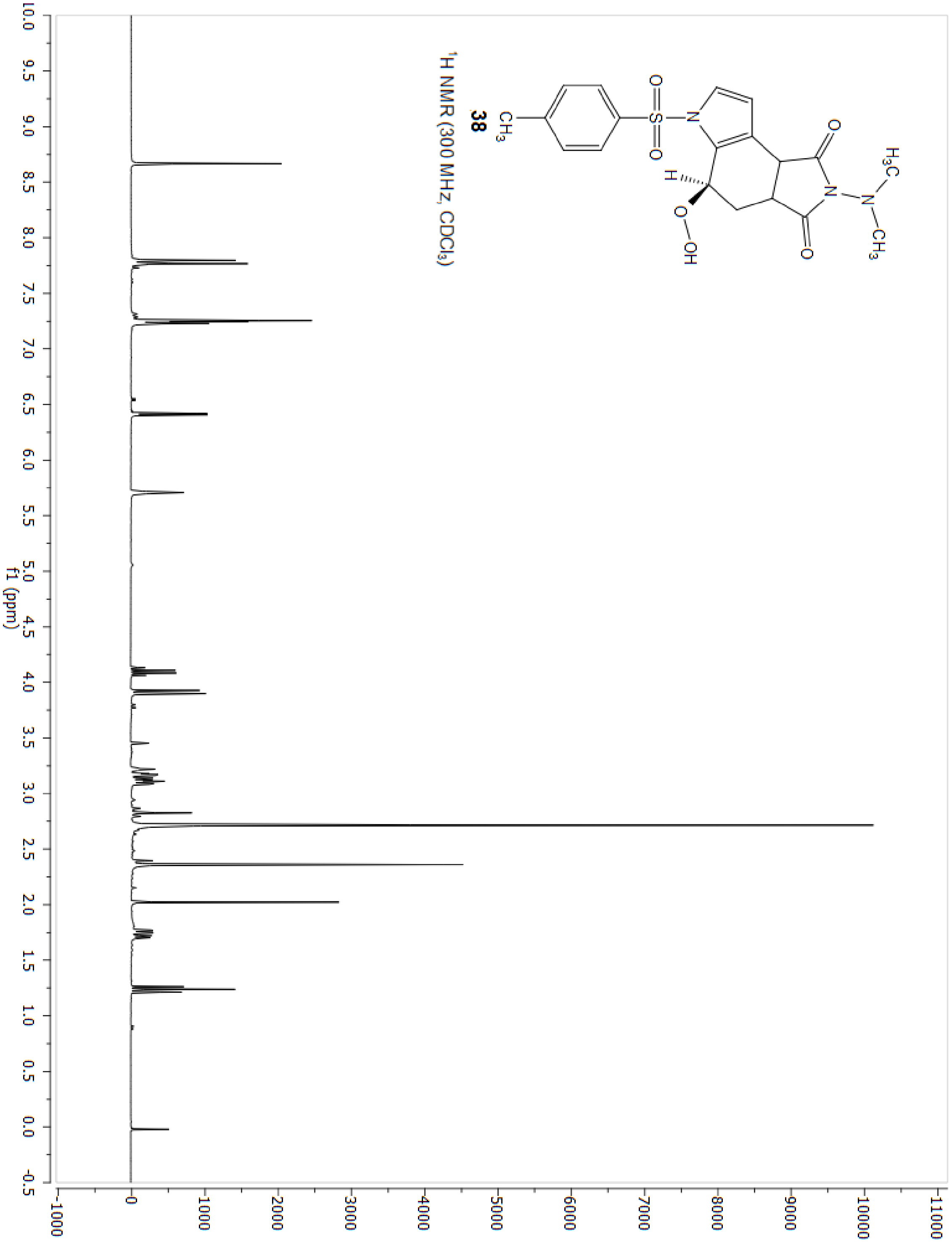
37

^{1}H NMR (300 MHz, CDCl$_3$)



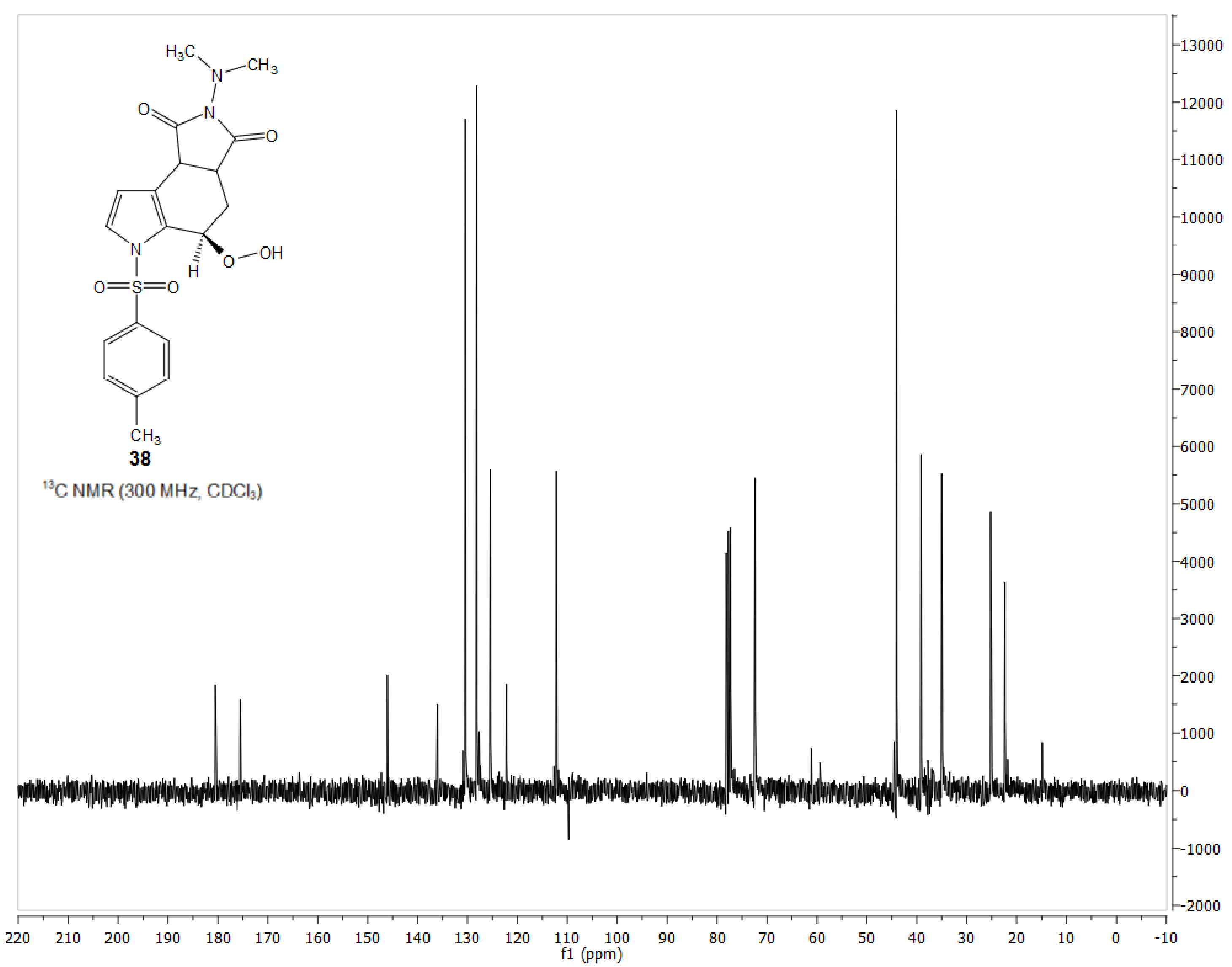
37

^{13}C NMR (300 MHz, CDCl$_3$)



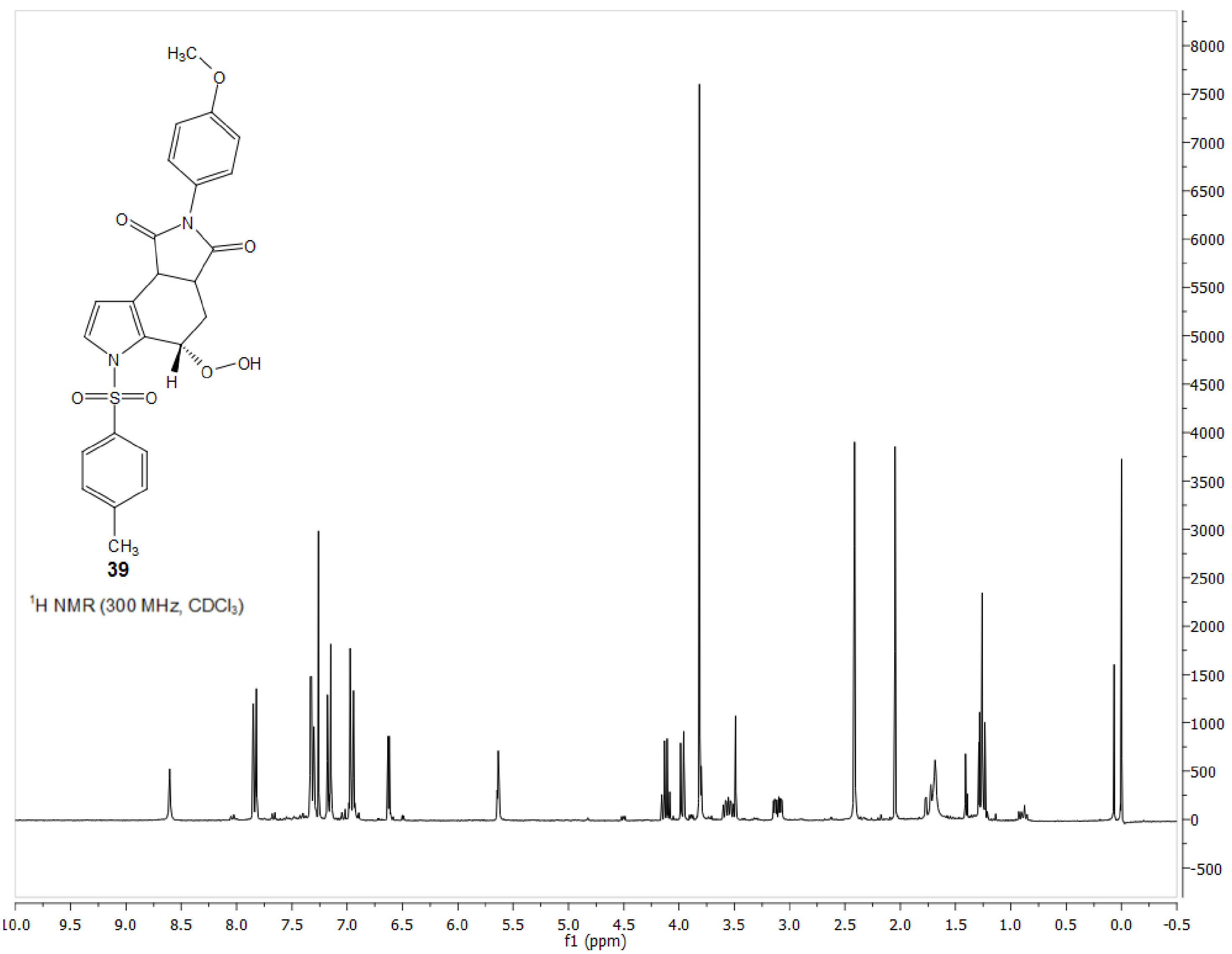
38

^{1}H NMR (300 MHz, CDCl$_3$)



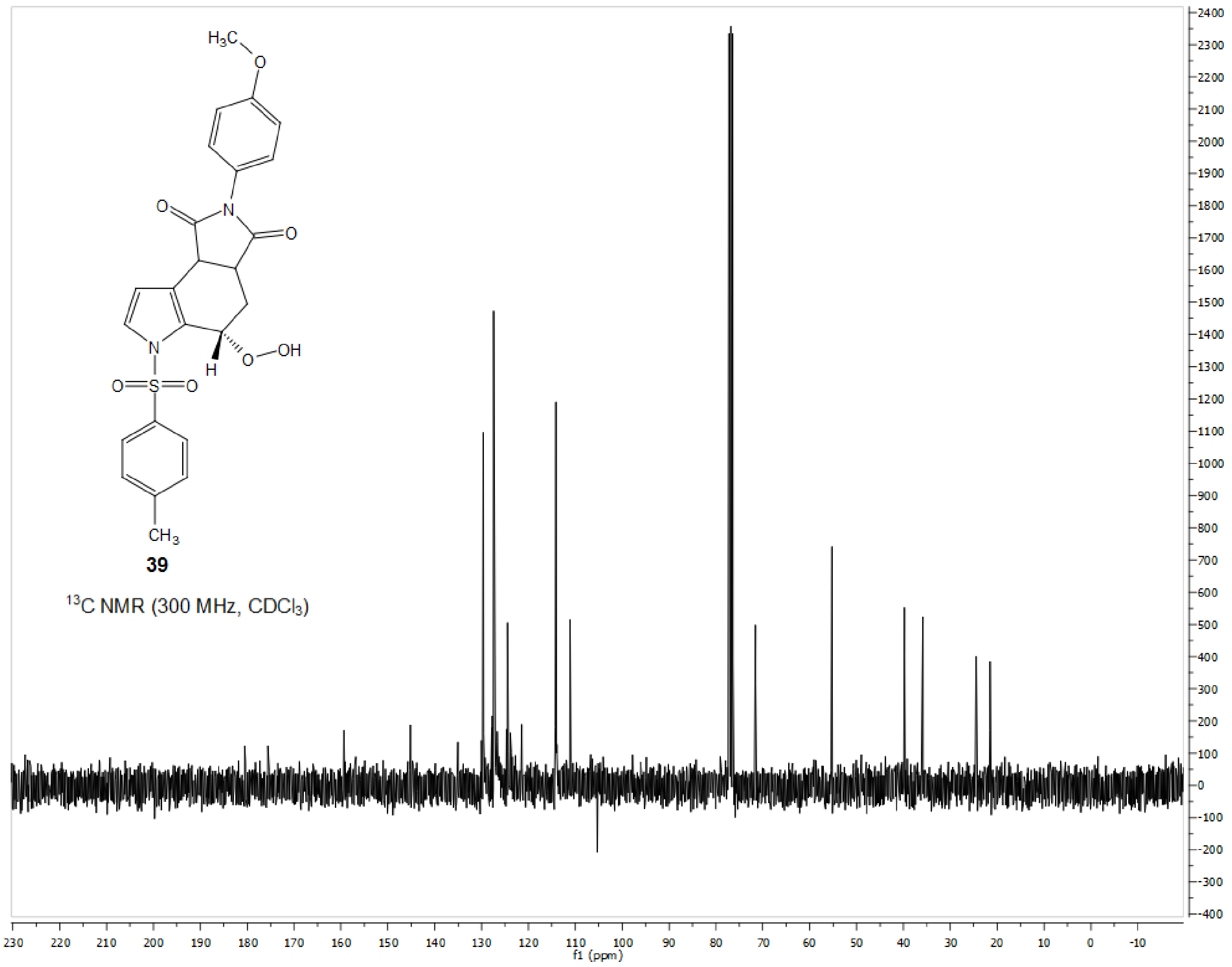
38

^{13}C NMR (300 MHz, CDCl$_3$)



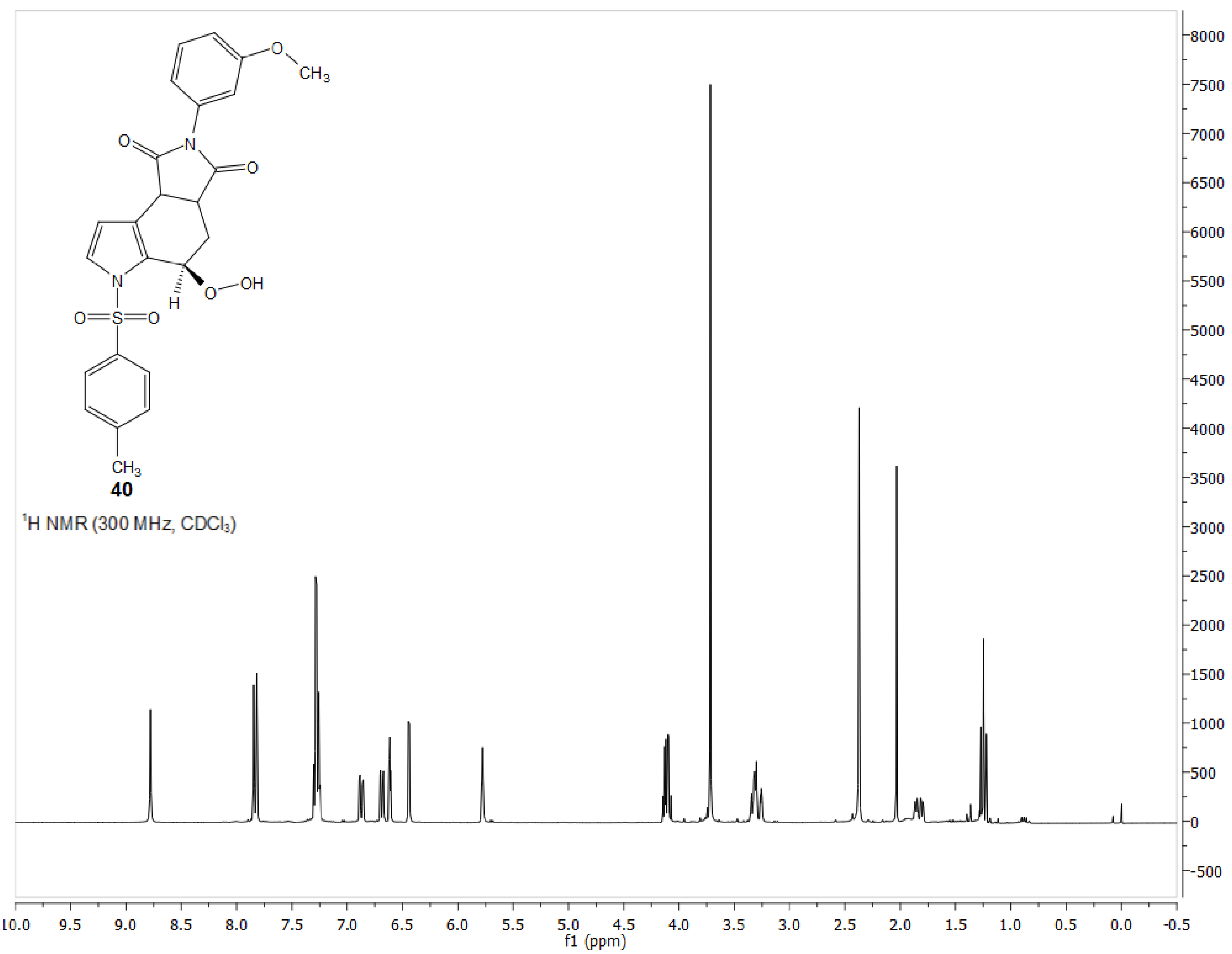
39

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



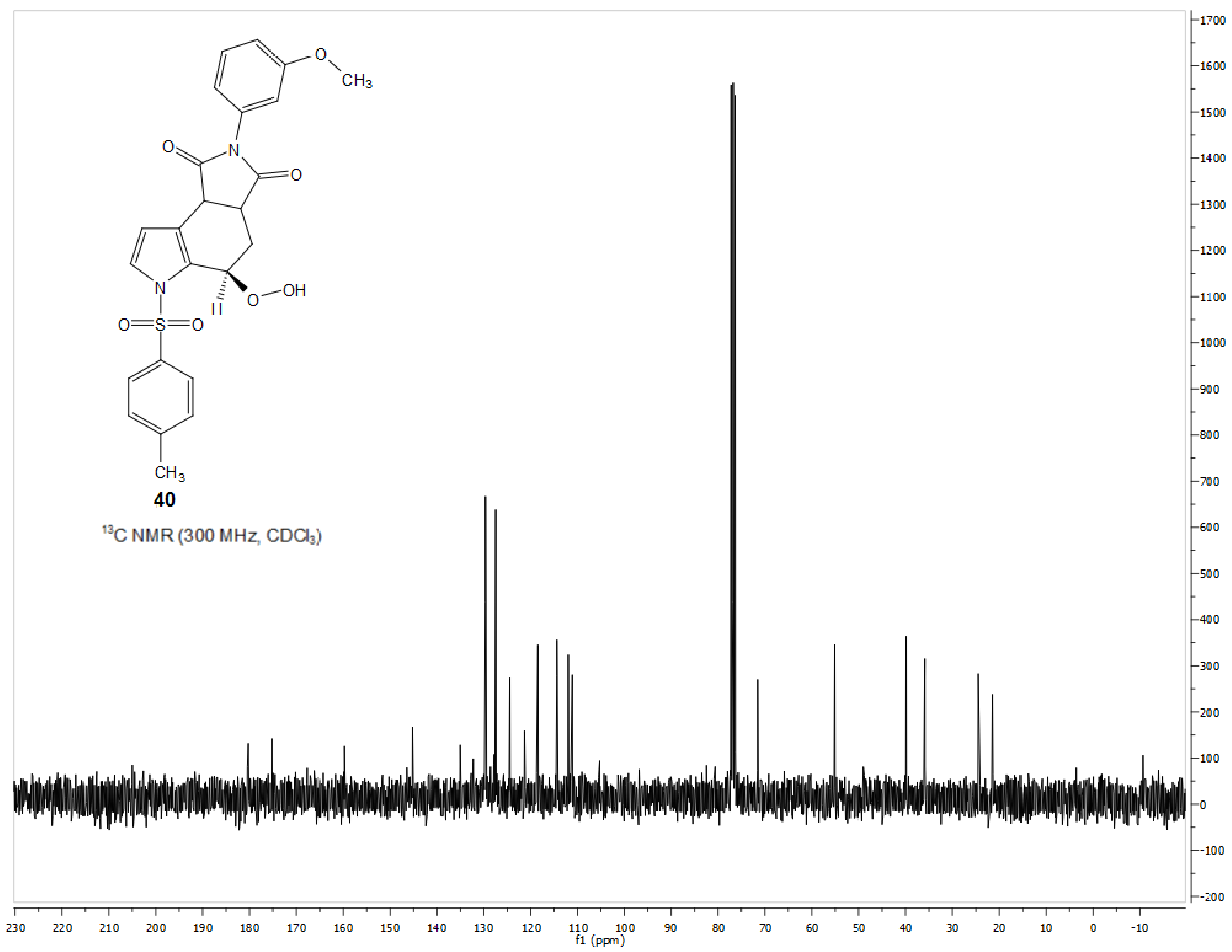
39

^{13}C NMR (300 MHz, $CDCl_3$)



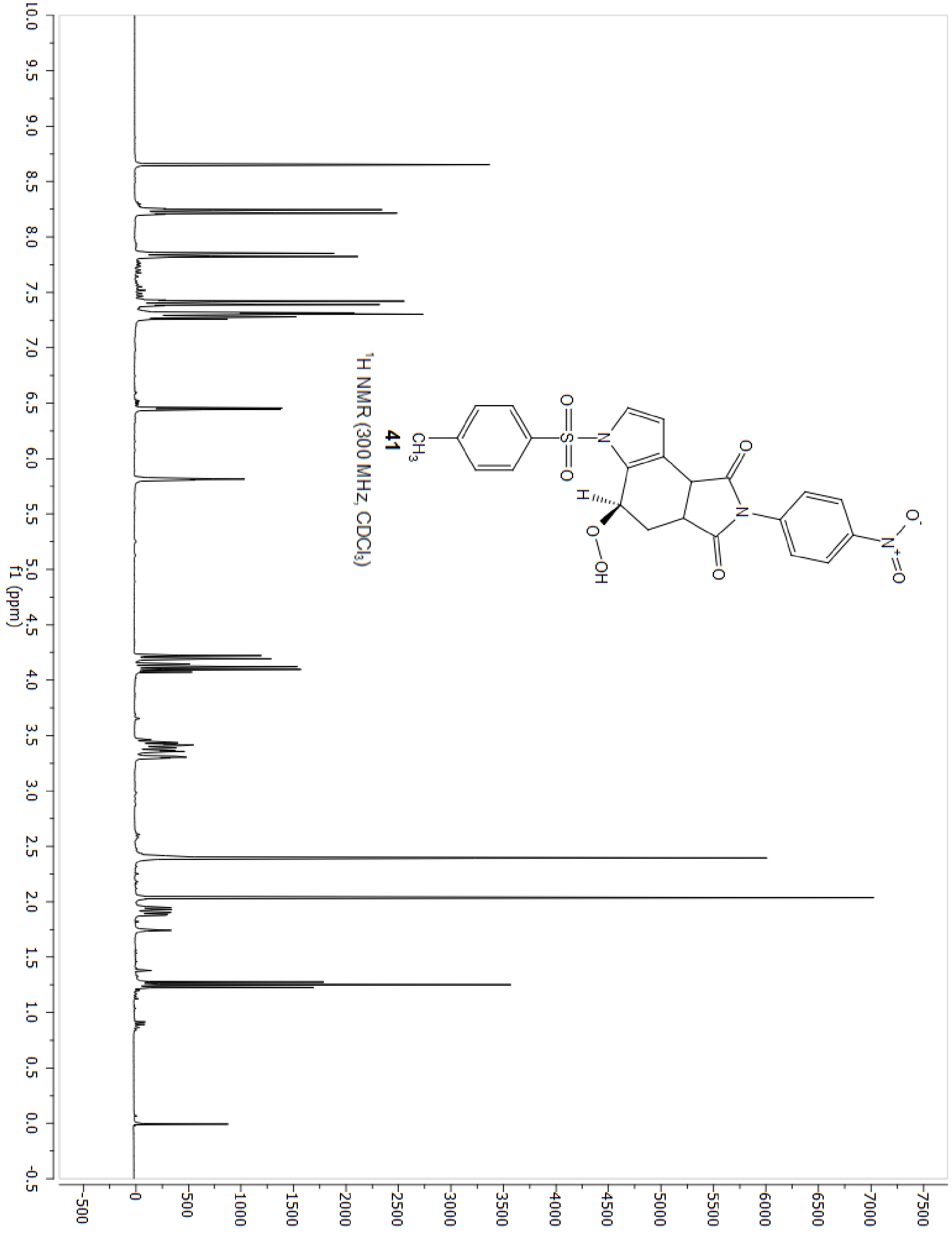
40

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



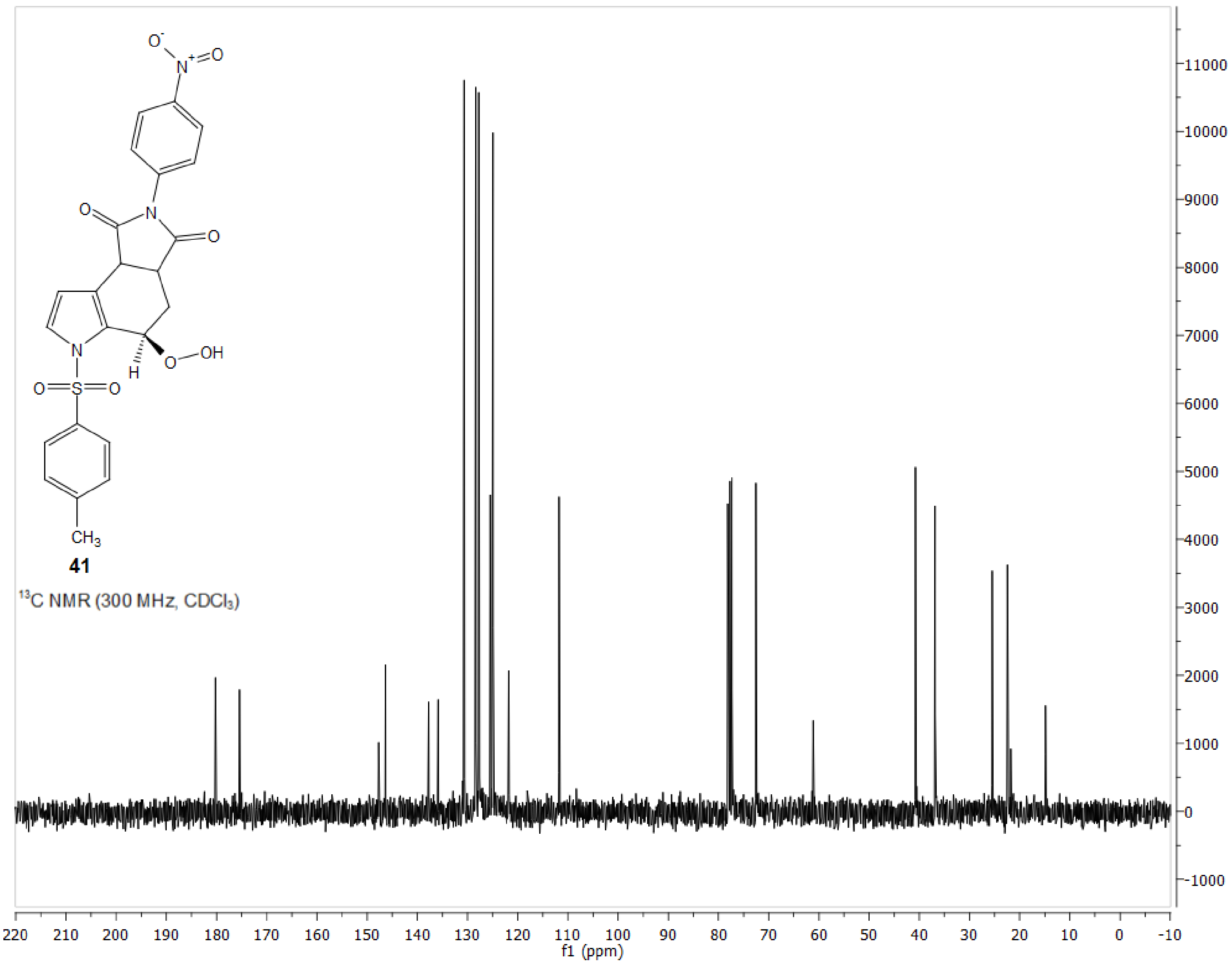
40

^{13}C NMR (300 MHz, CDCl$_3$)



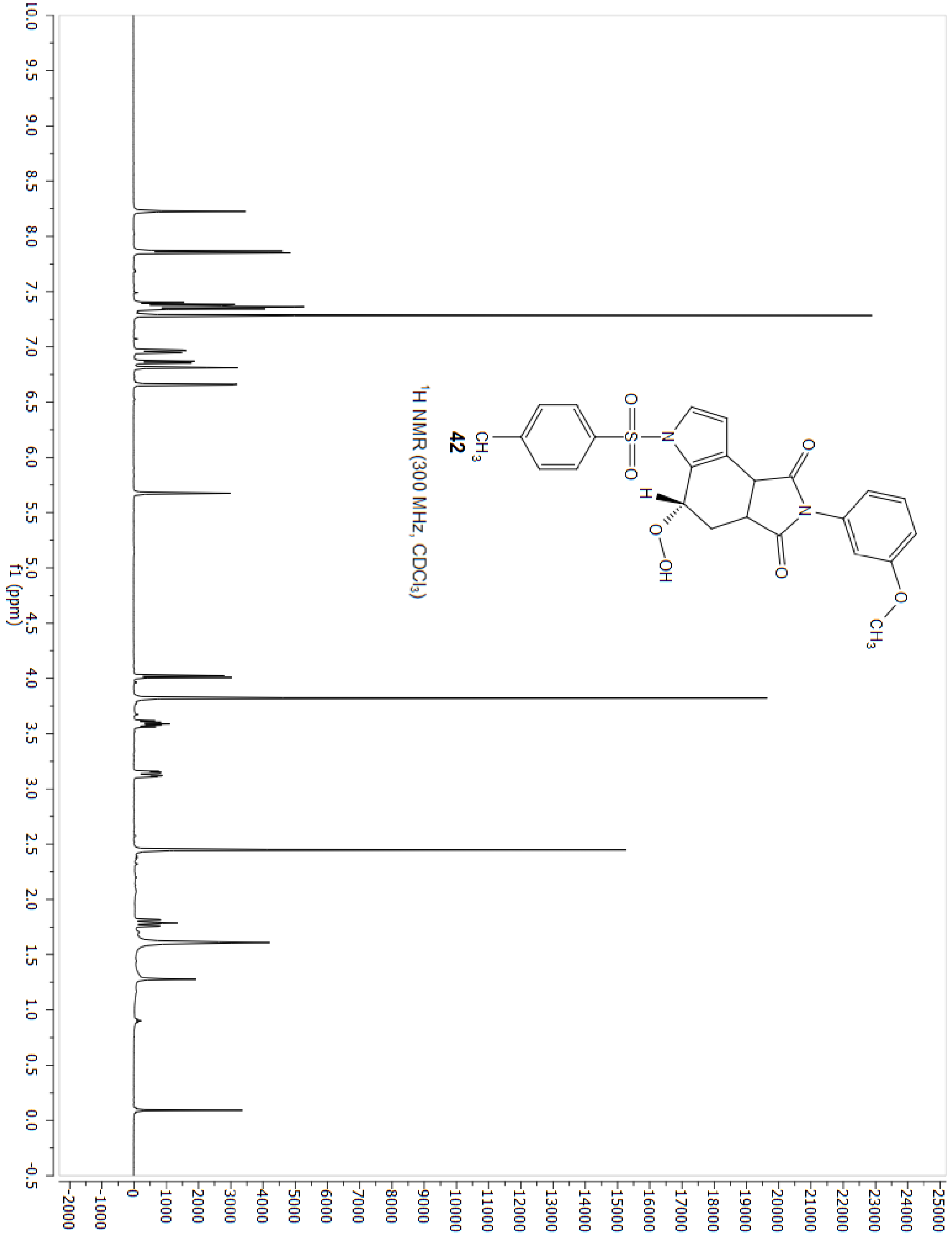
41

^{1}H NMR (300 MHz, CDCl$_3$)

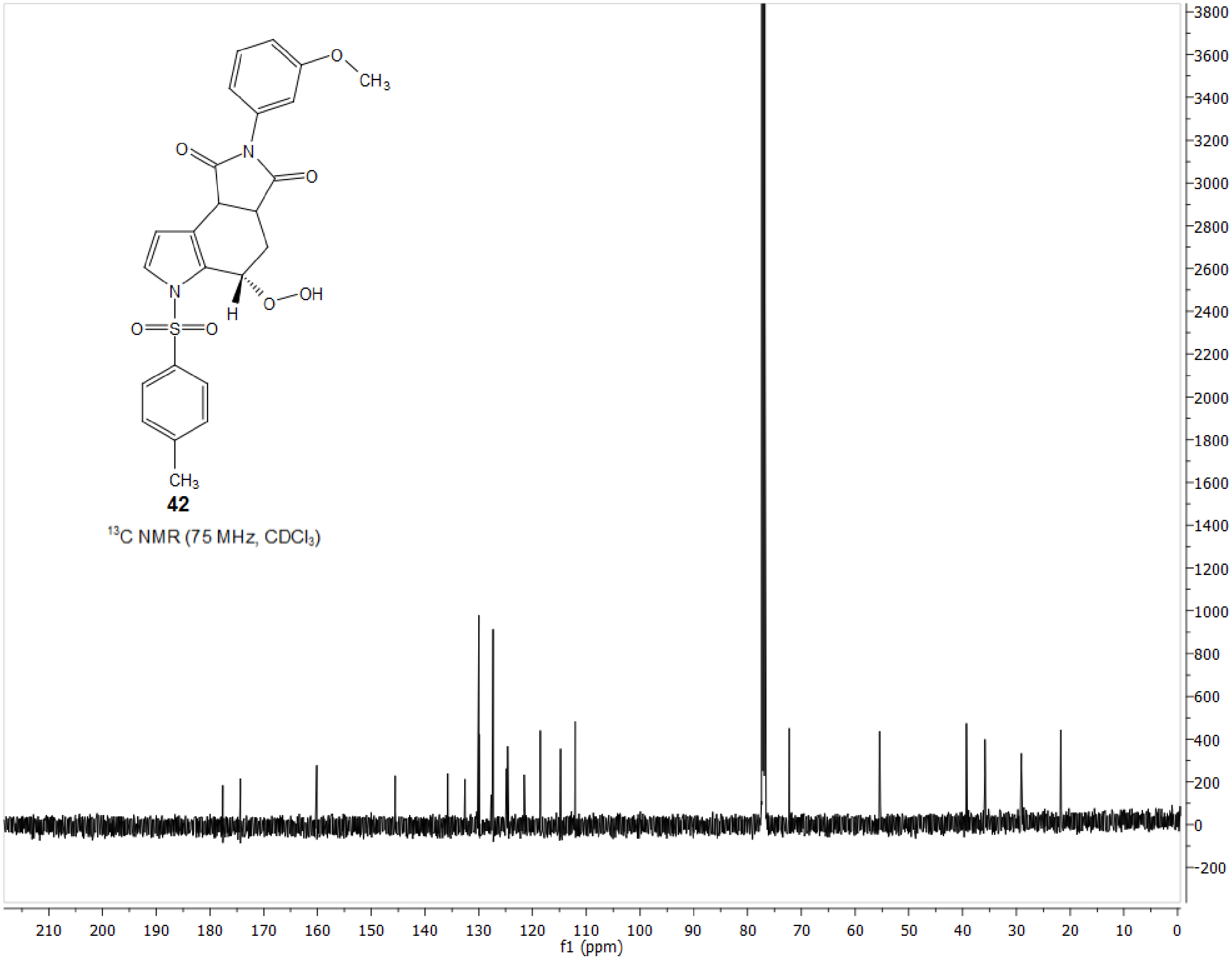


41

^{13}C NMR (300 MHz, CDCl$_3$)

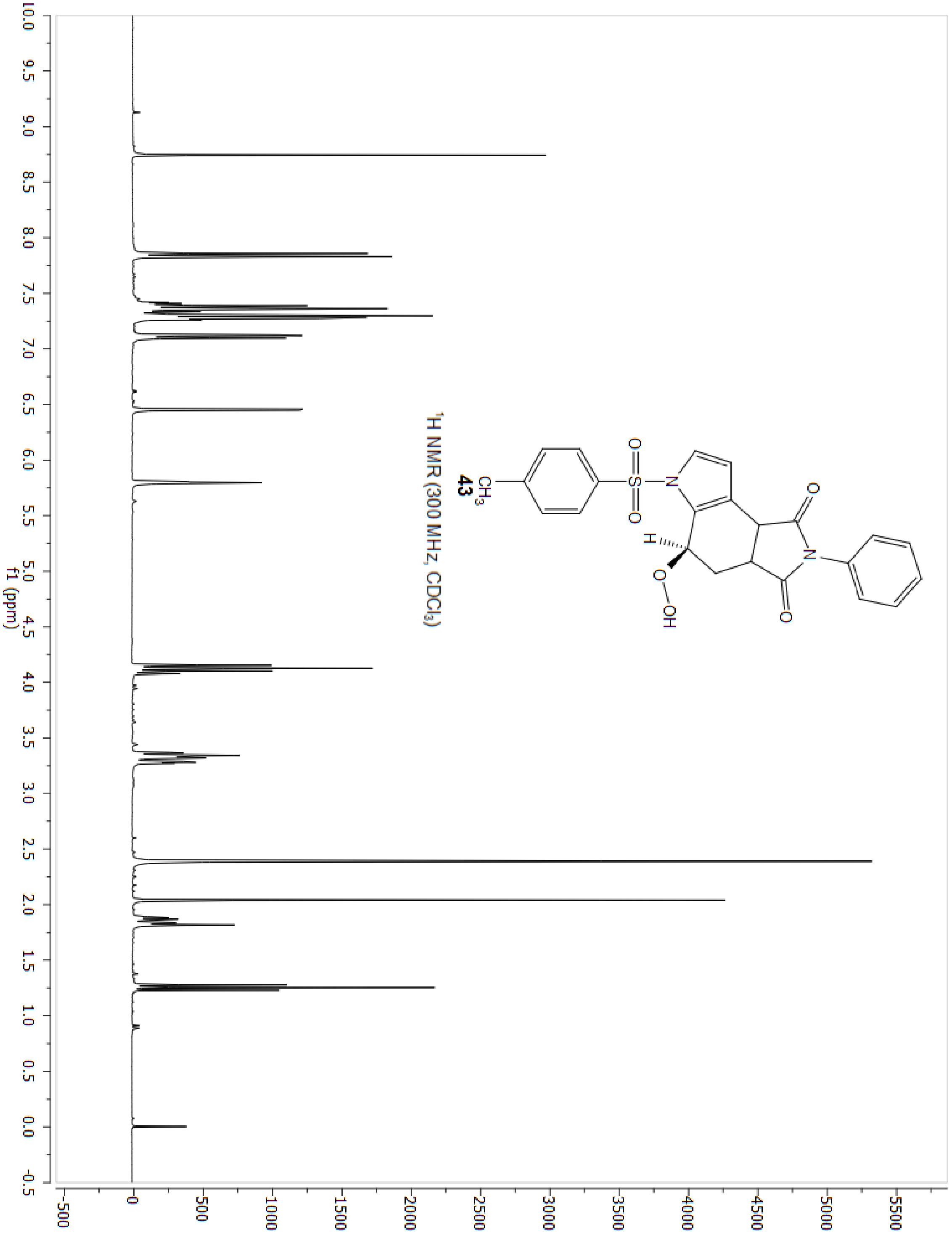

42

^{1}H NMR (300 MHz, CDCl$_3$)



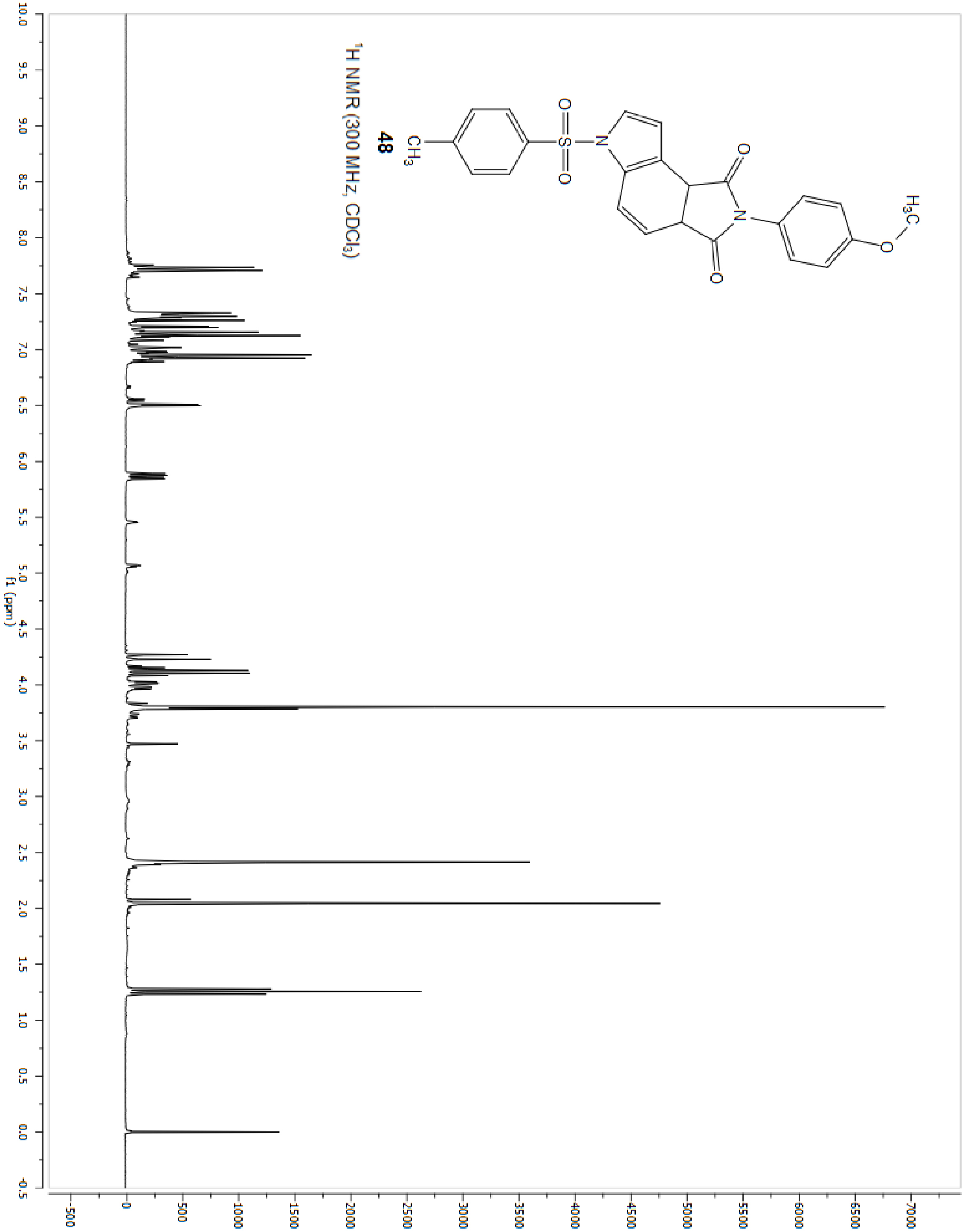
42

^{13}C NMR (75 MHz, CDCl$_3$)



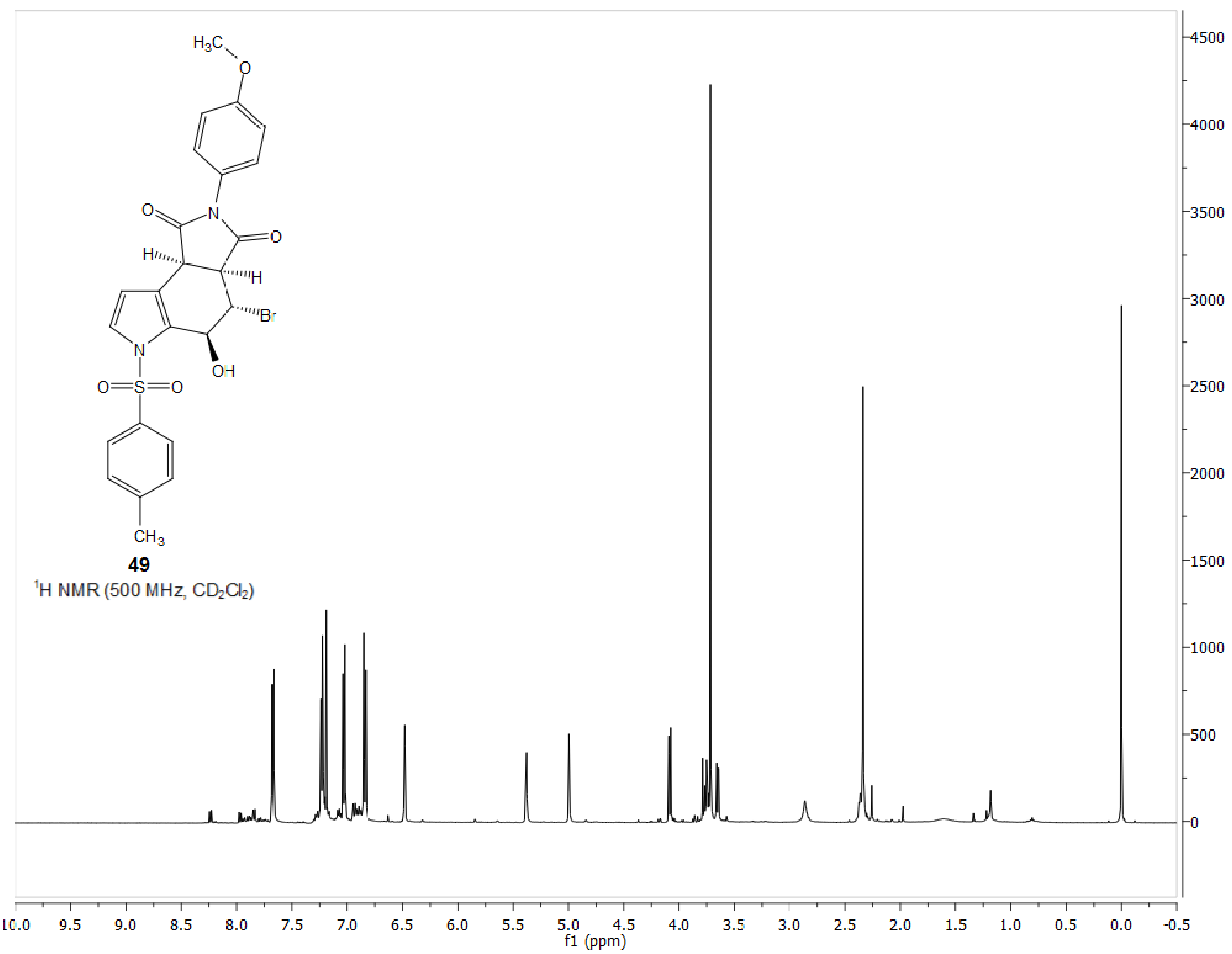
43

^{1}H NMR (300 MHz, CDCl$_3$)



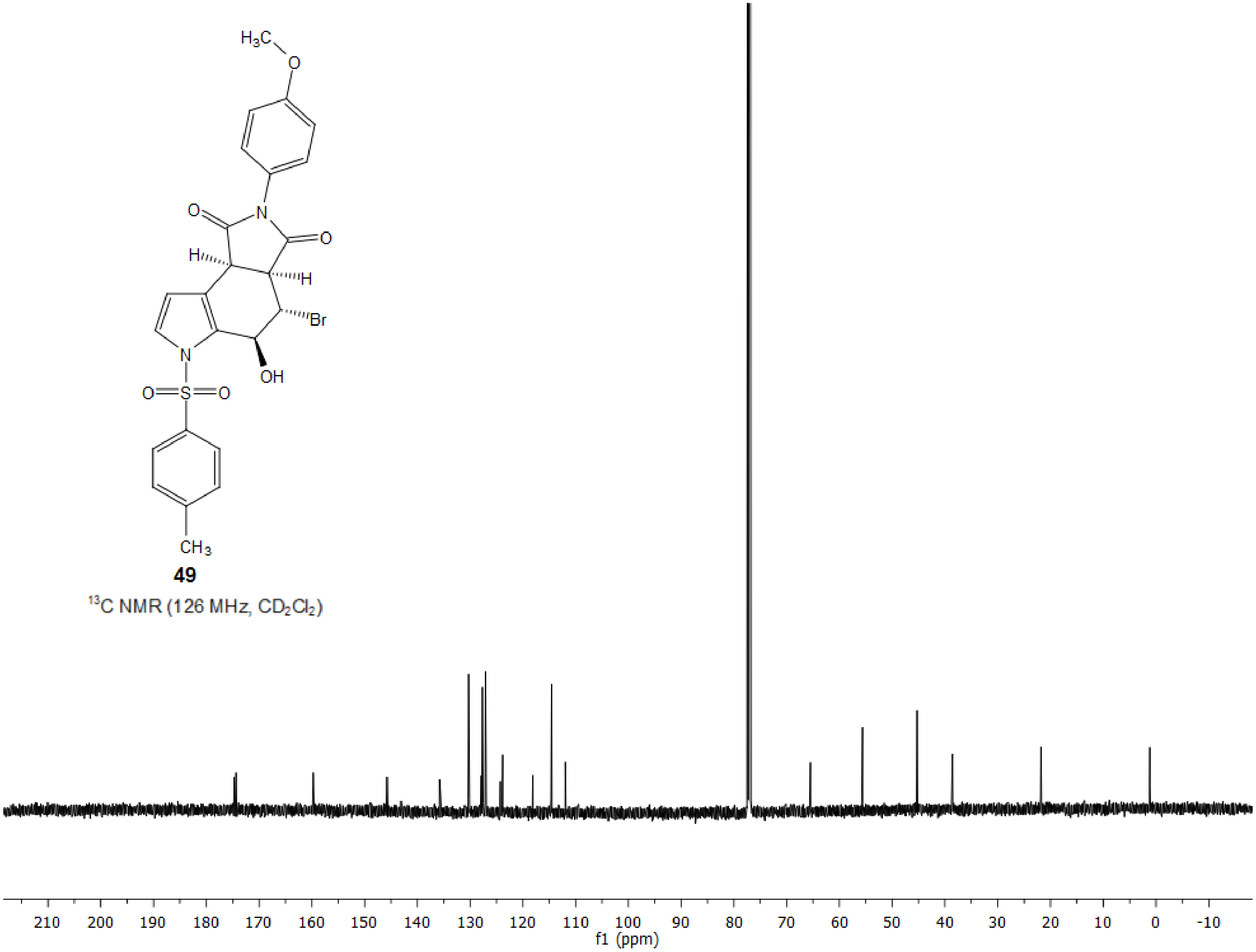
48

^{1}H NMR (300 MHz, CDCl$_3$)



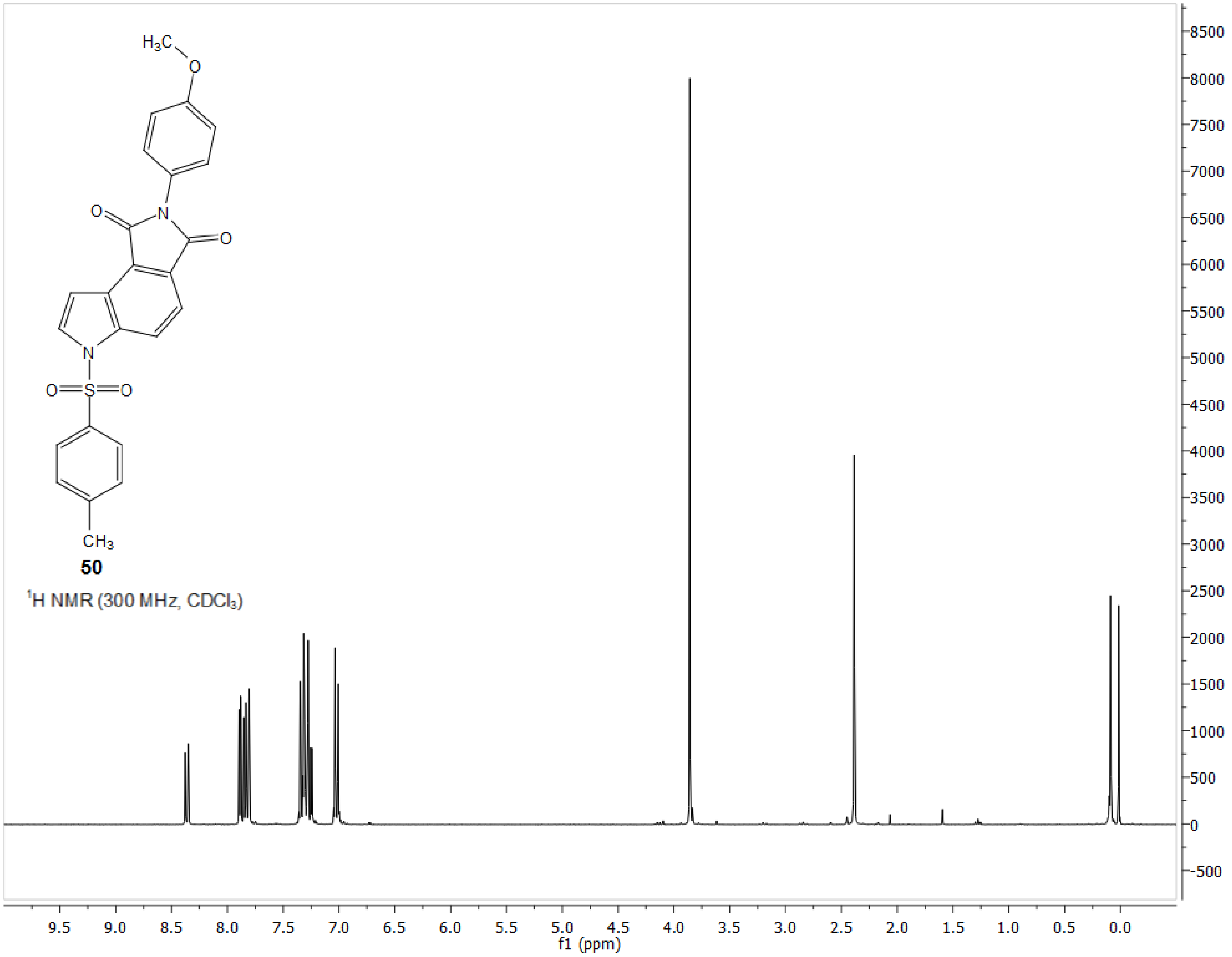
49

^{1}H NMR (500 MHz, CD_2Cl_2)



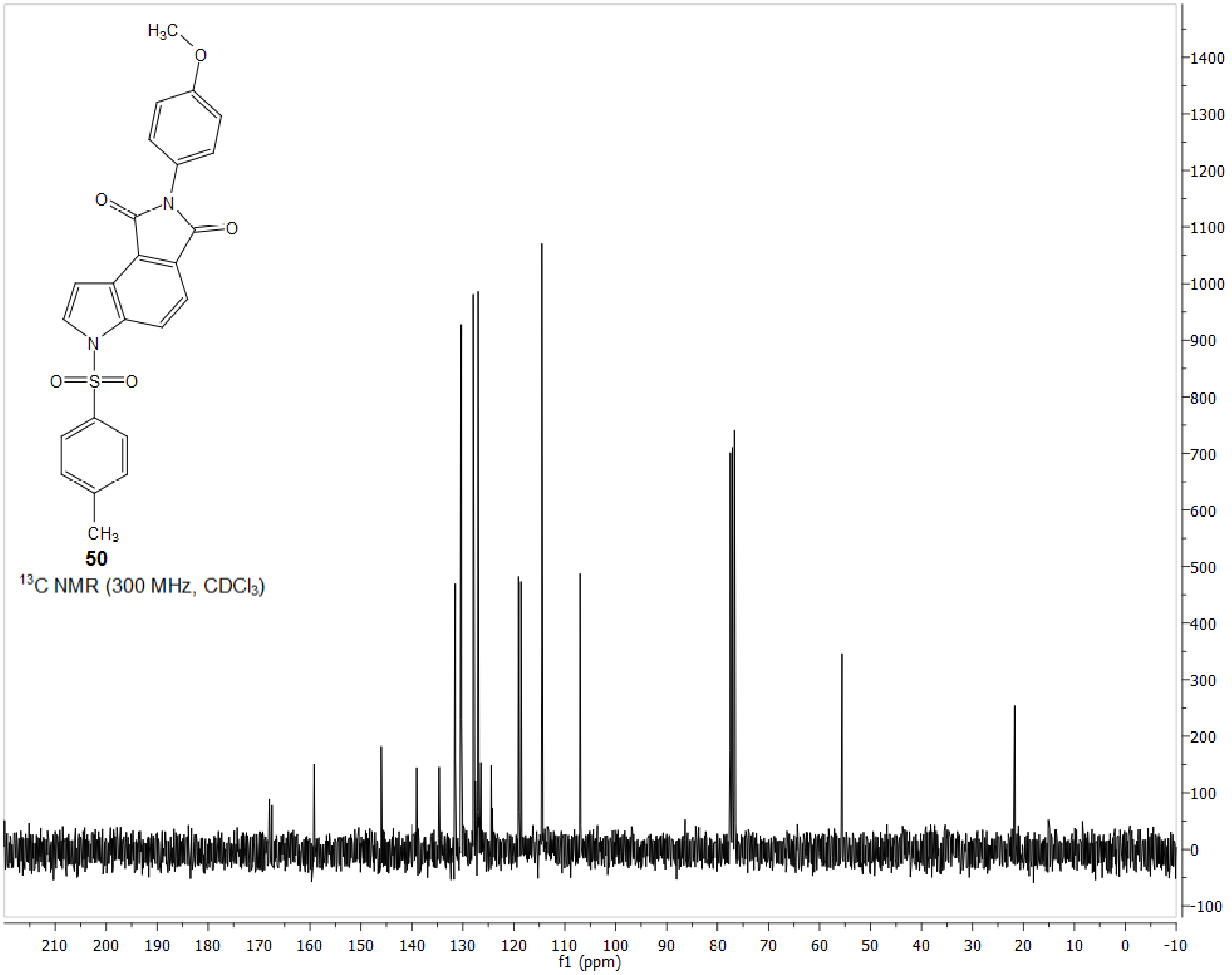
49

^{13}C NMR (126 MHz, CD_2Cl_2)



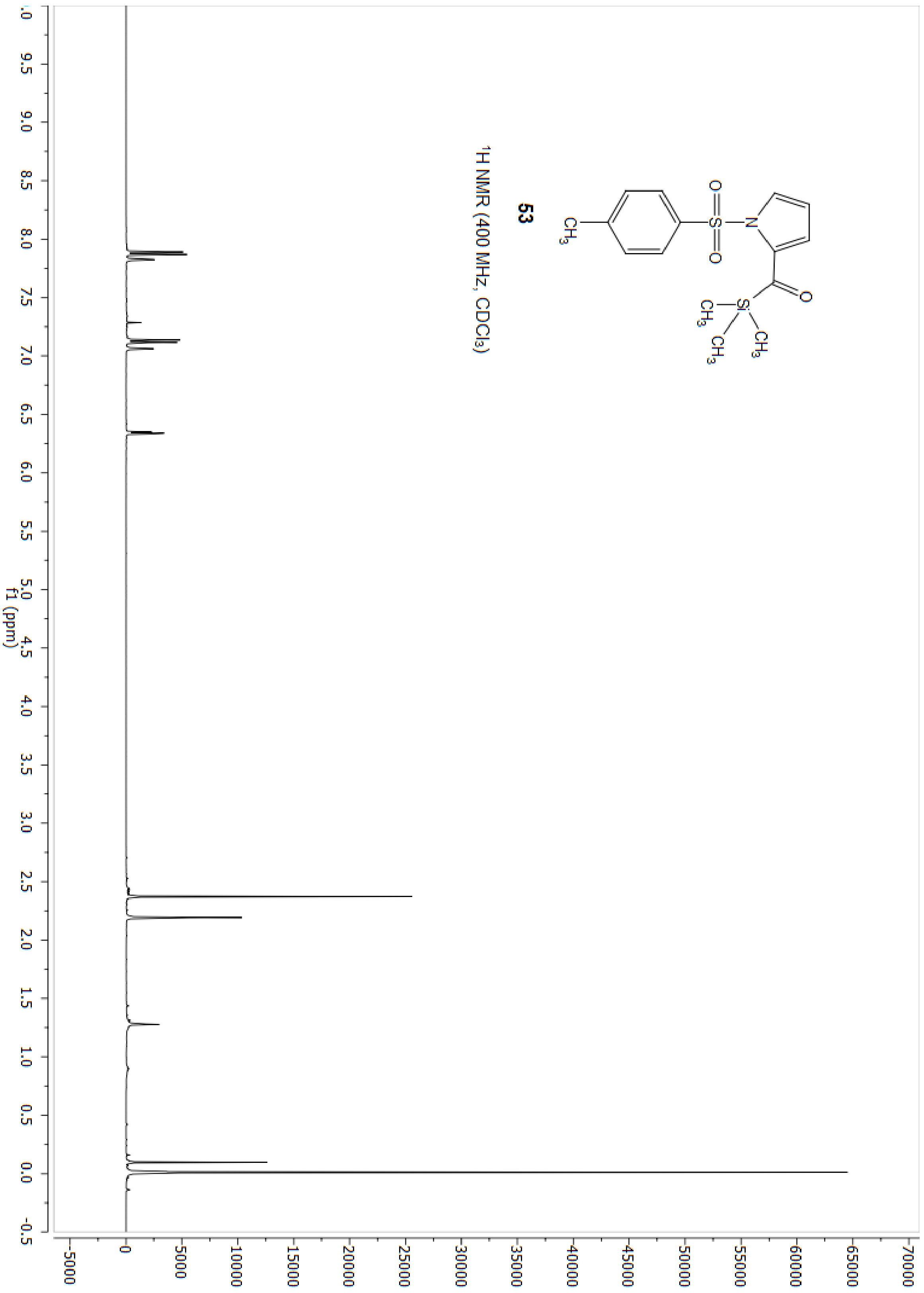
50

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



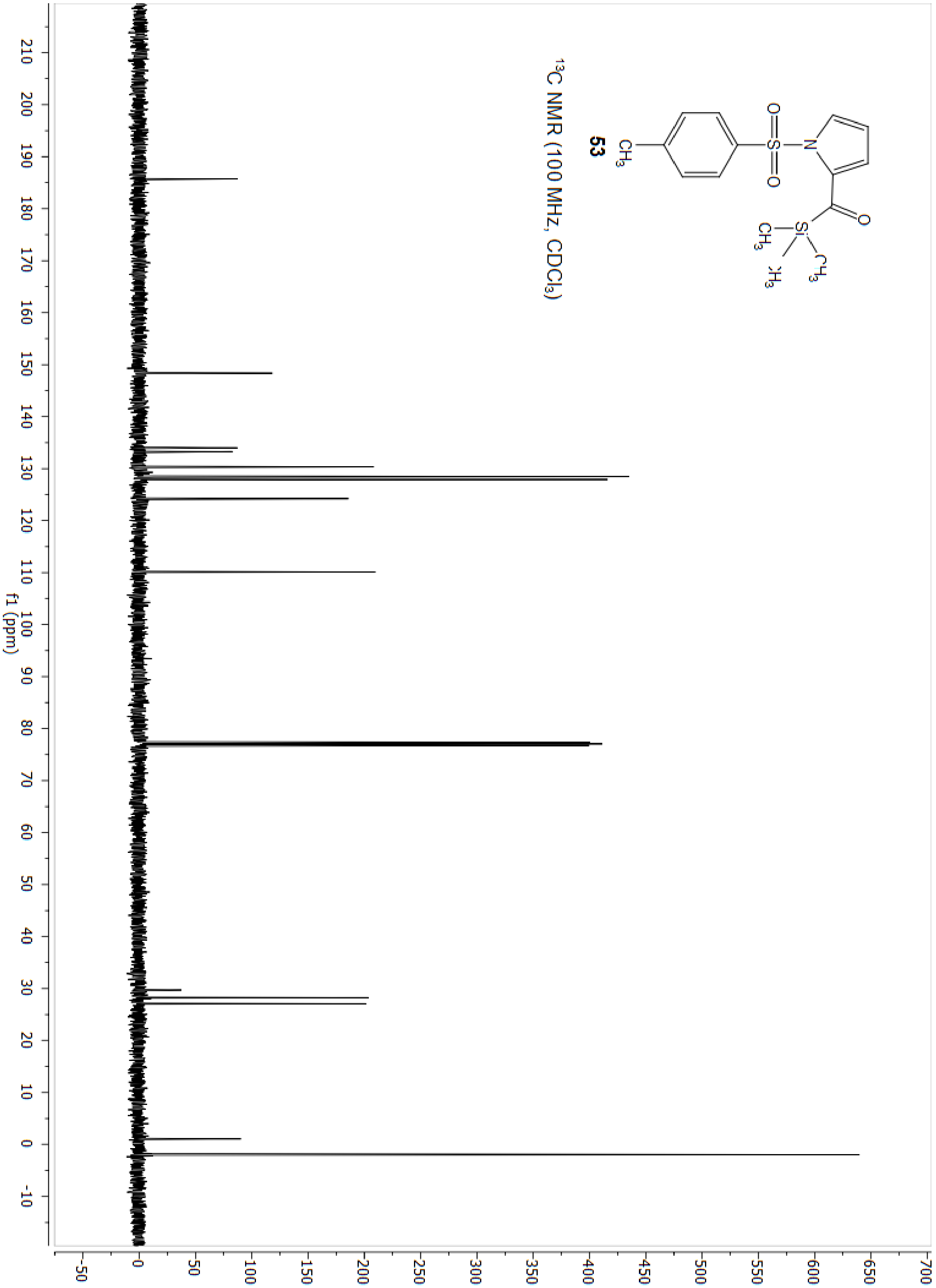
50

^{13}C NMR (300 MHz, $CDCl_3$)



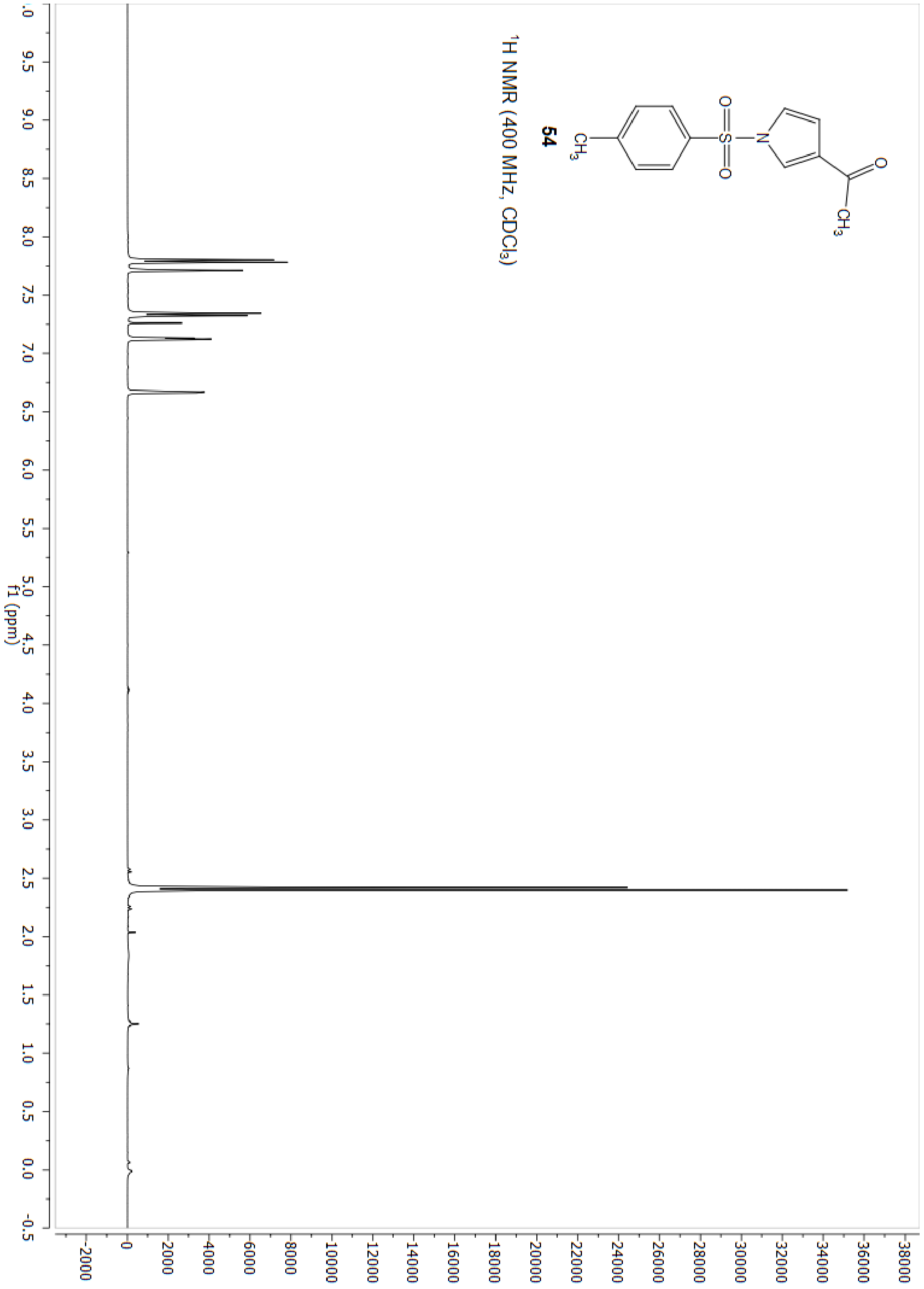
53

^1H NMR (400 MHz, CDCl$_3$)



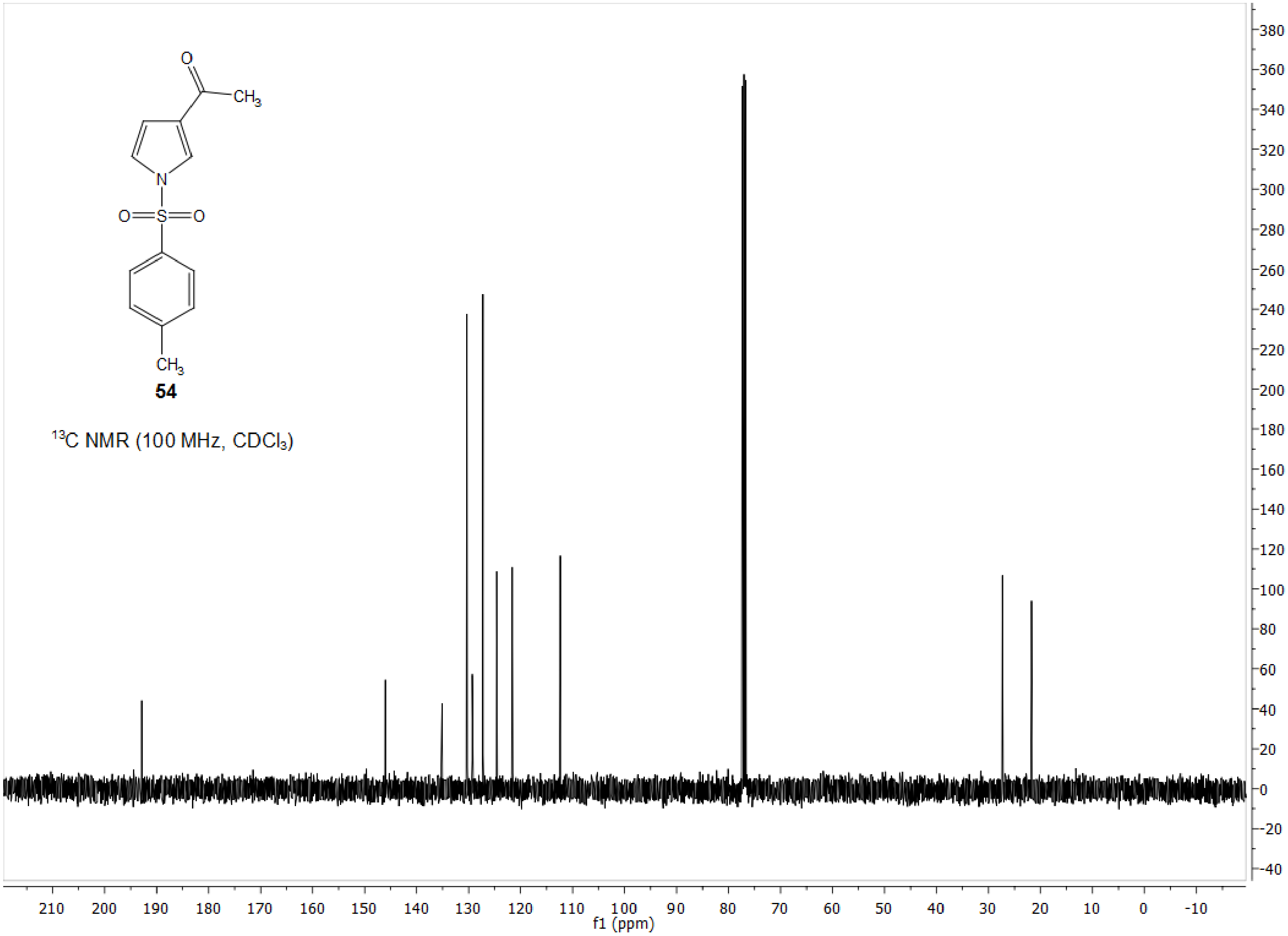
^{13}C NMR (100 MHz, CDCl$_3$)

53



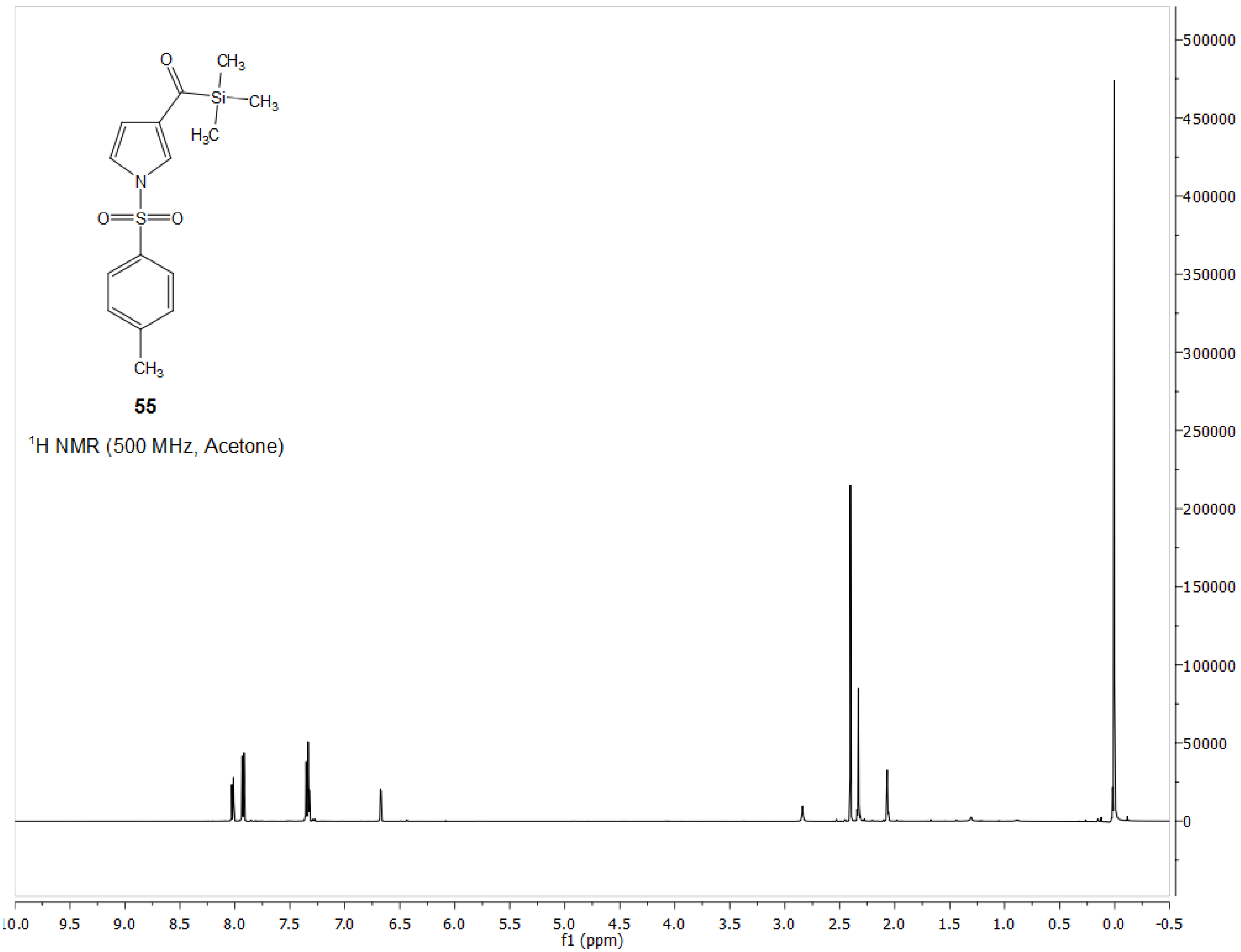
54

^{1}H NMR (400 MHz, CDCl$_3$)



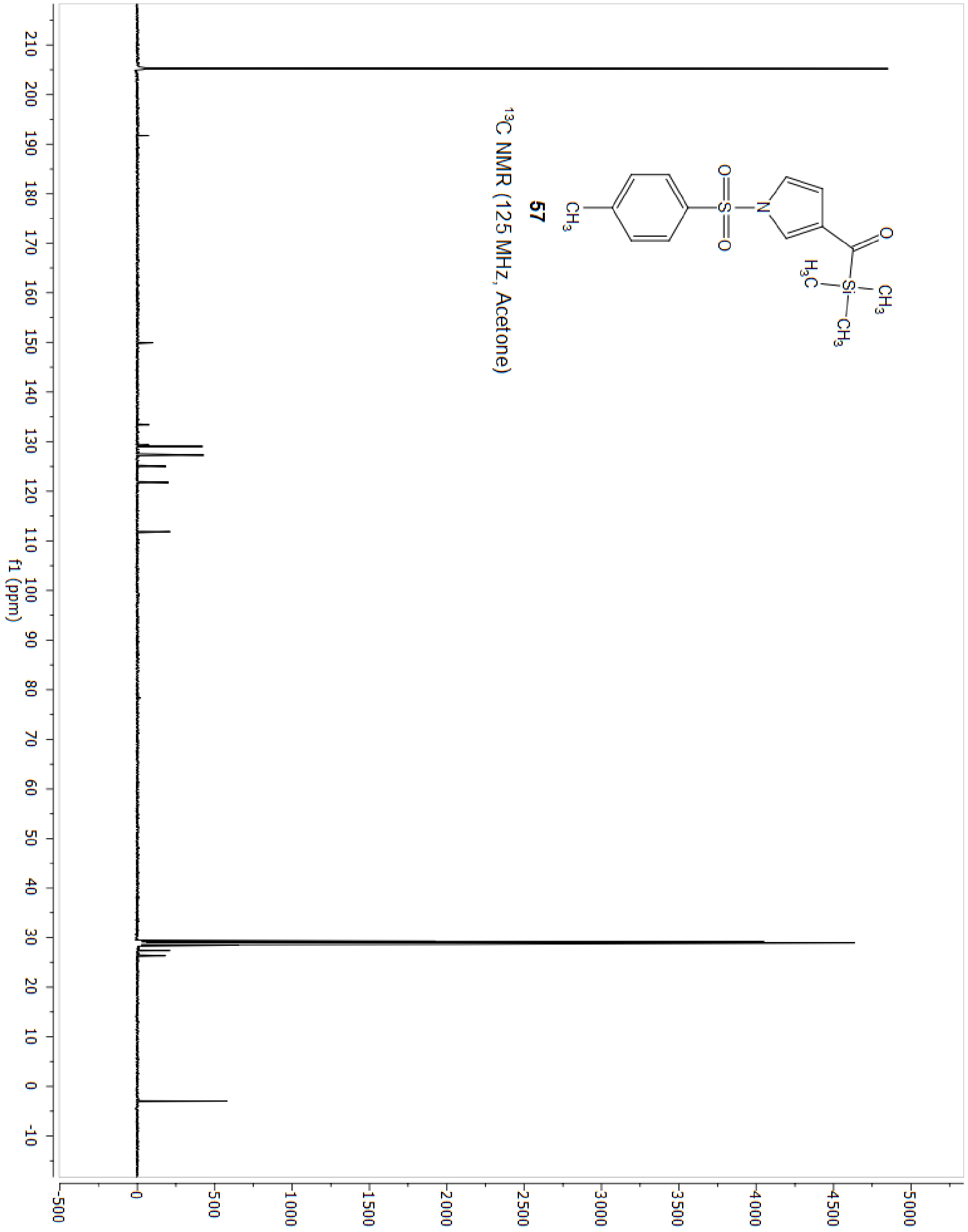
54

^{13}C NMR (100 MHz, CDCl$_3$)



55

^{1}H NMR (500 MHz, Acetone)



57

^{13}C NMR (125 MHz, Acetone)

Appendix 2. X-Ray crystollographic data for compound 35 in Part II

Table 1. Crystal data and structure refinement for 08107n.

Identification code	08107n	
Empirical formula	C23 H20 N2 O6 S	
Formula weight	452.47	
Temperature	566(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	*a* = 8.6563(13) Å	α = 102.068(3)°
b = 9.8819(15) Å	β = 107.786(2)°	
c = 13.533(2) Å	γ = 96.364(2)°	
Volume	1058.8(3) Å^3	
Z	2	
Density (calculated)	1.419 Mg/m^3	
Absorption coefficient	0.197 mm^{-1}	
F(000)	472	
Crystal color, morphology	colorless, block	
Crystal size	0.60 x 0.50 x 0.20 mm^3	
Theta range for data collection	1.64 to 25.08°	
Index ranges	$-10 \le h \le 10$, $-11 \le k \le 11$, $-16 \le l \le 16$	
Reflections collected	10544	
Independent reflections	3751 [*R*(int) = 0.0210]	
Observed reflections	3194	
Completeness to theta = 25.08°	99.5%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9617 and 0.8909	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3751 / 0 / 290	
Goodness-of-fit on F^2	1.060	
Final *R* indices [*I*>2sigma(*I*)]	*R*1 = 0.0364, *wR*2 = 0.1079	
R indices (all data)	*R*1 = 0.0439, *wR*2 = 0.1161	

Largest diff. peak and hole	0.269 and -0.282 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 08107n. U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

x	y	z	U_{eq}	
S1	4693(1)	1222(1)	3107(1)	45(1)
O1	10118(2)	-3093(2)	3105(2)	87(1)
O2	10950(2)	-1471(1)	365(1)	58(1)
O3	7479(2)	1714(1)	1624(1)	50(1)
O4	6719(2)	2086(2)	621(1)	65(1)
O5	4064(2)	1301(2)	2026(1)	57(1)
O6	3620(2)	648(2)	3595(1)	60(1)
N1	6079(2)	161(2)	3154(1)	42(1)
N2	10834(2)	-2496(2)	1721(1)	47(1)
C1	6732(2)	-313(2)	4068(2)	48(1)
C2	8110(2)	-788(2)	4035(2)	50(1)
C3	8381(2)	-580(2)	3083(1)	42(1)
C4	9808(2)	-811(2)	2712(1)	46(1)
C5	10216(2)	-2278(2)	2578(2)	54(1)
C6	11781(2)	-3573(2)	1524(2)	49(1)
C7	11125(3)	-4973(2)	1329(2)	61(1)
C8	12118(4)	-5966(2)	1190(2)	74(1)
C9	13694(4)	-5565(3)	1218(2)	80(1)
C10	14322(4)	-4178(3)	1400(2)	86(1)
C11	13370(3)	-3167(2)	1568(2)	67(1)
C12	10551(2)	-1495(2)	1143(2)	44(1)
C13	9635(2)	-475(2)	1630(1)	43(1)
C14	7826(2)	-687(2)	908(1)	43(1)
C15	6877(2)	241(2)	1462(1)	41(1)
C16	7143(2)	4(2)	2550(1)	38(1)
C17	5829(2)	2852(2)	3951(1)	44(1)
C18	6708(3)	3751(2)	3572(2)	55(1)
C19	7667(3)	5001(2)	4274(2)	62(1)
C20	7770(3)	5351(2)	5342(2)	59(1)

C21	8857(3)	6697(3)	6109(2)	85(1)
C22	6853(3)	4442(2)	5690(2)	62(1)
C23	5893(3)	3192(2)	5014(2)	56(1)

Table 3. Bond lengths [Å] and angles [°] for 08107n.

S(1)-O(5)	1.4182(14)	C(7)-H(7A)	0.9300
S(1)-O(6)	1.4278(14)	C(8)-C(9)	1.364(4)
S(1)-N(1)	1.6740(15)	C(8)-H(8A)	0.9300
S(1)-C(17)	1.7494(19)	C(9)-C(10)	1.359(4)
O(1)-C(5)	1.194(2)	C(9)-H(9A)	0.9300
O(2)-C(12)	1.208(2)	C(10)-C(11)	1.389(3)
O(3)-C(15)	1.437(2)	C(10)-H(10A)	0.9300
O(3)-O(4)	1.4590(18)	C(11)-H(11A)	0.9300
O(4)-H(4O)	0.8200	C(12)-C(13)	1.516(2)
N(1)-C(1)	1.393(2)	C(13)-C(14)	1.536(3)
N(1)-C(16)	1.407(2)	C(13)-H(13A)	0.9800
N(2)-C(12)	1.383(2)	C(14)-C(15)	1.528(2)
N(2)-C(5)	1.407(2)	C(14)-H(14A)	0.9700
N(2)-C(6)	1.443(2)	C(14)-H(14B)	0.9700
C(1)-C(2)	1.340(3)	C(15)-C(16)	1.491(2)
C(1)-H(1A)	0.9300	C(15)-H(15A)	0.9800
C(2)-C(3)	1.429(2)	C(17)-C(18)	1.382(3)
C(2)-H(2A)	0.9300	C(17)-C(23)	1.389(3)
C(3)-C(16)	1.356(2)	C(18)-C(19)	1.384(3)
C(3)-C(4)	1.492(2)	C(18)-H(18A)	0.9300
C(4)-C(5)	1.517(3)	C(19)-C(20)	1.386(3)
C(4)-C(13)	1.535(2)	C(19)-H(19A)	0.9300
C(4)-H(4A)	0.9800	C(20)-C(22)	1.381(3)
C(6)-C(11)	1.369(3)	C(20)-C(21)	1.510(3)
C(6)-C(7)	1.373(3)	C(21)-H(21A)	0.9600
C(7)-C(8)	1.396(3)	C(21)-H(21B)	0.9600

C(21)-H(21C)	0.9600	N(2)-C(5)-C(4)	106.36(16)
C(22)-C(23)	1.374(3)	C(11)-C(6)-C(7)	120.53(19)
C(22)-H(22A)	0.9300	C(11)-C(6)-N(2)	118.49(18)
C(23)-H(23A)	0.9300	C(7)-C(6)-N(2)	120.95(18)
		C(6)-C(7)-C(8)	118.6(2)
O(5)-S(1)-O(6)	120.26(9)	C(6)-C(7)-H(7A)	120.7
O(5)-S(1)-N(1)	106.58(8)	C(8)-C(7)-H(7A)	120.7
O(6)-S(1)-N(1)	104.10(8)	C(9)-C(8)-C(7)	120.9(2)
O(5)-S(1)-C(17)	110.99(9)	C(9)-C(8)-H(8A)	119.5
O(6)-S(1)-C(17)	108.79(9)	C(7)-C(8)-H(8A)	119.5
N(1)-S(1)-C(17)	104.77(8)	C(10)-C(9)-C(8)	119.9(2)
C(15)-O(3)-O(4)	107.67(12)	C(10)-C(9)-H(9A)	120.1
O(3)-O(4)-H(4O)	109.5	C(8)-C(9)-H(9A)	120.1
C(1)-N(1)-C(16)	108.04(14)	C(9)-C(10)-C(11)	120.2(3)
C(1)-N(1)-S(1)	120.64(12)	C(9)-C(10)-H(10A)	119.9
C(16)-N(1)-S(1)	127.91(12)	C(11)-C(10)-H(10A)	119.9
C(12)-N(2)-C(5)	112.50(15)	C(6)-C(11)-C(10)	119.8(2)
C(12)-N(2)-C(6)	123.69(15)	C(6)-C(11)-H(11A)	120.1
C(5)-N(2)-C(6)	123.61(15)	C(10)-C(11)-H(11A)	120.1
C(2)-C(1)-N(1)	108.87(15)	O(2)-C(12)-N(2)	124.70(16)
C(2)-C(1)-H(1A)	125.6	O(2)-C(12)-C(13)	126.41(16)
N(1)-C(1)-H(1A)	125.6	N(2)-C(12)-C(13)	108.87(15)
C(1)-C(2)-C(3)	107.45(17)	C(12)-C(13)-C(4)	103.09(14)
C(1)-C(2)-H(2A)	126.3	C(12)-C(13)-C(14)	111.55(14)
C(3)-C(2)-H(2A)	126.3	C(4)-C(13)-C(14)	112.69(14)
C(16)-C(3)-C(2)	108.74(16)	C(12)-C(13)-H(13A)	109.8
C(16)-C(3)-C(4)	121.81(16)	C(4)-C(13)-H(13A)	109.8
C(2)-C(3)-C(4)	129.26(17)	C(14)-C(13)-H(13A)	109.8
C(3)-C(4)-C(5)	117.02(16)	C(15)-C(14)-C(13)	110.81(14)
C(3)-C(4)-C(13)	113.64(15)	C(15)-C(14)-H(14A)	109.5
C(5)-C(4)-C(13)	104.65(14)	C(13)-C(14)-H(14A)	109.5
C(3)-C(4)-H(4A)	107.0	C(15)-C(14)-H(14B)	109.5
C(5)-C(4)-H(4A)	107.0	C(13)-C(14)-H(14B)	109.5
C(13)-C(4)-H(4A)	107.0	H(14A)-C(14)-H(14B)	108.1
O(1)-C(5)-N(2)	124.96(19)	O(3)-C(15)-C(16)	106.51(13)
O(1)-C(5)-C(4)	128.61(19)	O(3)-C(15)-C(14)	111.80(14)

C(16)-C(15)-C(14)	108.60(14)	C(22)-C(20)-C(19)	118.47(19)
O(3)-C(15)-H(15A)	110.0	C(22)-C(20)-C(21)	120.6(2)
C(16)-C(15)-H(15A)	110.0	C(19)-C(20)-C(21)	121.0(2)
C(14)-C(15)-H(15A)	110.0	C(20)-C(21)-H(21A)	109.5
C(3)-C(16)-N(1)	106.87(15)	C(20)-C(21)-H(21B)	109.5
C(3)-C(16)-C(15)	125.22(15)	H(21A)-C(21)-H(21B)	109.5
N(1)-C(16)-C(15)	127.44(15)	C(20)-C(21)-H(21C)	109.5
C(18)-C(17)-C(23)	120.96(18)	H(21A)-C(21)-H(21C)	109.5
C(18)-C(17)-S(1)	119.98(14)	H(21B)-C(21)-H(21C)	109.5
C(23)-C(17)-S(1)	118.99(15)	C(23)-C(22)-C(20)	121.6(2)
C(17)-C(18)-C(19)	118.74(19)	C(23)-C(22)-H(22A)	119.2
C(17)-C(18)-H(18A)	120.6	C(20)-C(22)-H(22A)	119.2
C(19)-C(18)-H(18A)	120.6	C(22)-C(23)-C(17)	118.9(2)
C(18)-C(19)-C(20)	121.3(2)	C(22)-C(23)-H(23A)	120.5
C(18)-C(19)-H(19A)	119.3	C(17)-C(23)-H(23A)	120.5
C(20)-C(19)-H(19A)	119.3		

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x 10^3$) for 08107n. 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}
S1	33(1)	52(1)	47(1)	8(1)	15(1)	6(1)
O1	110(1)	112(1)	93(1)	70(1)	67(1)	66(1)
O2	74(1)	58(1)	67(1)	25(1)	47(1)	24(1)
O3	64(1)	47(1)	46(1)	14(1)	25(1)	14(1)
O4	79(1)	80(1)	67(1)	42(1)	42(1)	40(1)
O5	45(1)	70(1)	48(1)	9(1)	8(1)	15(1)
O6	43(1)	69(1)	72(1)	11(1)	31(1)	3(1)
N1	39(1)	47(1)	43(1)	12(1)	20(1)	6(1)
N2	51(1)	48(1)	50(1)	16(1)	24(1)	15(1)
C1	55(1)	55(1)	44(1)	19(1)	27(1)	10(1)
C2	54(1)	61(1)	42(1)	20(1)	18(1)	15(1)

C3	37(1)	50(1)	38(1)	8(1)	13(1)	6(1)
C4	36(1)	58(1)	41(1)	9(1)	13(1)	9(1)
C5	50(1)	70(1)	54(1)	26(1)	24(1)	21(1)
C6	55(1)	47(1)	45(1)	12(1)	16(1)	17(1)
C7	66(1)	54(1)	55(1)	13(1)	10(1)	10(1)
C8	106(2)	46(1)	55(1)	6(1)	8(1)	23(1)
C9	93(2)	74(2)	72(2)	11(1)	20(1)	45(2)
C10	72(2)	84(2)	108(2)	20(2)	37(2)	35(1)
C11	60(1)	55(1)	87(2)	12(1)	29(1)	17(1)
C12	45(1)	42(1)	51(1)	13(1)	24(1)	7(1)
C13	43(1)	41(1)	48(1)	10(1)	23(1)	6(1)
C14	50(1)	42(1)	37(1)	9(1)	19(1)	8(1)
C15	39(1)	46(1)	38(1)	9(1)	14(1)	6(1)
C16	34(1)	42(1)	37(1)	7(1)	15(1)	2(1)
C17	37(1)	48(1)	46(1)	11(1)	14(1)	12(1)
C18	59(1)	56(1)	55(1)	10(1)	29(1)	11(1)
C19	60(1)	48(1)	82(2)	11(1)	36(1)	5(1)
C20	48(1)	49(1)	68(1)	2(1)	8(1)	17(1)
C21	71(2)	58(1)	100(2)	-8(1)	12(1)	11(1)
C22	75(2)	59(1)	45(1)	8(1)	11(1)	18(1)
C23	66(1)	56(1)	47(1)	14(1)	19(1)	11(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3) for 08107n.

x	y	z	U(eq)	
H4O	7339	2033	268	78
H1A	6284	-301	4612	58
H2A	8770	-1182	4539	60
H4A	10786	-165	3247	55
H7A	10042	-5252	1291	73

H8A	11700	-6916	1076	89
H9A	14336	-6239	1112	96
H10A	15393	-3904	1413	103
H11A	13811	-2217	1710	80
H13A	10188	496	1752	51
H14A	7783	-455	239	51
H14B	7310	-1668	739	51
H15A	5697	1	1039	50
H18A	6656	3521	2858	66
H19A	8253	5616	4024	74
H21A	9501	6498	6760	127
H21B	8180	7359	6270	127
H21C	9582	7091	5785	127
H22A	6886	4682	6399	75
H23A	5297	2585	5264	67

Table 6. Torsion angles [°] for 08107n.

O5-S1-N1-C1	-169.75(14)	C12-N2-C5-O1	169.9(2)
O6-S1-N1-C1	-41.65(15)	C6-N2-C5-O1	-15.1(3)
C17-S1-N1-C1	72.53(15)	C12-N2-C5-C4	-12.9(2)
O5-S1-N1-C16	33.70(17)	C6-N2-C5-C4	162.11(16)
O6-S1-N1-C16	161.79(14)	C3-C4-C5-O1	-35.7(3)
C17-S1-N1-C16	-84.02(16)	C13-C4-C5-O1	-162.4(2)
C16-N1-C1-C2	-1.8(2)	C3-C4-C5-N2	147.29(16)
S1-N1-C1-C2	-162.56(14)	C13-C4-C5-N2	20.51(19)
N1-C1-C2-C3	1.6(2)	C12-N2-C6-C11	56.6(3)
C1-C2-C3-C16	-0.8(2)	C5-N2-C6-C11	-117.8(2)
C1-C2-C3-C4	174.24(19)	C12-N2-C6-C7	-125.4(2)
C16-C3-C4-C5	-128.24(19)	C5-N2-C6-C7	60.2(3)
C2-C3-C4-C5	57.3(3)	C11-C6-C7-C8	0.7(3)
C16-C3-C4-C13	-6.0(2)	N2-C6-C7-C8	-177.25(18)
C2-C3-C4-C13	179.55(18)	C6-C7-C8-C9	-1.7(3)

C7-C8-C9-C10	1.1(4)
C8-C9-C10-C11	0.5(4)
C7-C6-C11-C10	0.9(4)
N2-C6-C11-C10	178.9(2)
C9-C10-C11-C6	-1.5(4)
C5-N2-C12-O2	-179.12(19)
C6-N2-C12-O2	5.9(3)
C5-N2-C12-C13	-0.4(2)
C6-N2-C12-C13	-175.46(16)
O2-C12-C13-C4	-168.10(19)
N2-C12-C13-C4	13.25(18)
O2-C12-C13-C14	70.7(2)
N2-C12-C13-C14	-107.92(17)
C3-C4-C13-C12	-148.89(15)
C5-C4-C13-C12	-20.06(18)
C3-C4-C13-C14	-28.5(2)
C5-C4-C13-C14	100.34(17)
C12-C13-C14-C15	174.11(14)
C4-C13-C14-C15	58.70(19)
O4-O3-C15-C16	-159.65(12)
O4-O3-C15-C14	81.87(16)
C13-C14-C15-O3	65.49(18)
C13-C14-C15-C16	-51.74(18)
C2-C3-C16-N1	-0.4(2)
C4-C3-C16-N1	-175.81(15)
C2-C3-C16-C15	-173.01(16)
C4-C3-C16-C15	11.5(3)
C1-N1-C16-C3	1.32(19)
S1-N1-C16-C3	160.22(13)
C1-N1-C16-C15	173.76(16)
S1-N1-C16-C15	-27.3(2)
O3-C15-C16-C3	-102.19(19)
C14-C15-C16-C3	18.4(2)
O3-C15-C16-N1	86.68(19)
C14-C15-C16-N1	-152.76(16)
O5-S1-C17-C18	-32.44(18)
O6-S1-C17-C18	-166.93(15)
N1-S1-C17-C18	82.23(16)
O5-S1-C17-C23	150.62(15)
O6-S1-C17-C23	16.13(18)
N1-S1-C17-C23	-94.71(16)
C23-C17-C18-C19	0.3(3)
S1-C17-C18-C19	-176.53(16)
C17-C18-C19-C20	0.7(3)
C18-C19-C20-C22	-1.8(3)
C18-C19-C20-C21	178.3(2)
C19-C20-C22-C23	2.0(3)
C21-C20-C22-C23	-178.1(2)
C20-C22-C23-C17	-1.0(3)
C18-C17-C23-C22	-0.2(3)
S1-C17-C23-C22	176.73(15)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for 08107n [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O4-H4O...O2#1	0.82	2.00	2.7929(19)	163.0

Symmetry transformations used to generate equivalent atoms:

#1 -x+2,-y,-z