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Synthesis of polycyclic aromatics having unusual molecular architectures via cascade cyclization reactions of enyne -allenes

Yu-Hsuan Wang
West Virginia University

Synthesis of Polycyclic Aromatics Having Unusual Molecular Architectures via Cascade Cyclization Reactions of Enyne-Allenes

YU-HSUAN WANG

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Kung K. Wang, Ph.D., Chair
Peter M. Gannett, Ph.D.
George A. O'Doherty, Ph.D.
Jeffrey L. Petersen, Ph.D.
John H. Penn, Ph.D.

C. Eugene Bennett Department of Chemistry

Morgantown, West Virginia

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ABSTRACT

Synthesis of Polycyclic Aromatics Having Unusual Molecular Architectures via Cascade Cyclization Reactions of Enyne-Allenes

YU-HSUAN WANG

The C^2–C^6 Schmittel cyclization reaction of the benzannulated enyne−allenes provides an efficient synthetic pathway for the construction of a variety of polycyclic aromatics. By starting from truxenone, the cascade cyclization reactions furnished several unusual and congested polycyclic compounds. The in situ generated enyne−allenes are key intermediates in these cyclization reactions.

A new synthetic approach to 2,2′-disubstituted 1,1′-binaphthyls and related compounds was also successfully developed by using the benzannulated enediynes as precursors. These 1,1′-binaphthyls derivatives can serve as potential BINOL type ligands. The assembly of the enediynyl precursors from three separate aromatic fragments allows the possibility of placing a variety of functional groups at various positions of the 1,1′-binaphthyl system.

A 12-step non-pyrolytic synthetic pathway employing the Schmittel cyclization reactions has been developed, leading to a bowl-shaped polycyclic aromatic hydrocarbon (PAH) having a 54-carbon framework of the surface of C_{60}. Incorporating of sp^3-carbons on the 54-carbon framework facilitates the connection of carbon atoms intramolecularly.

Dedicated to

My parents, brother, Leo, and sisters

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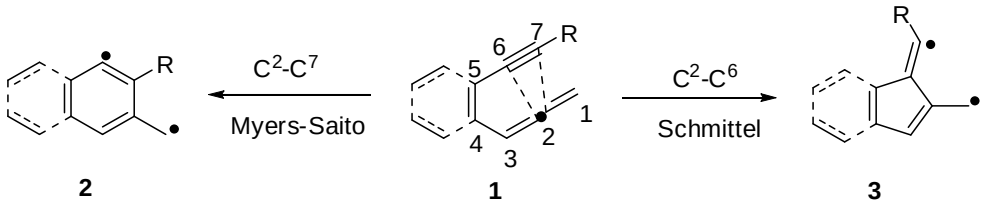
CHAPTER I

Construction of Unusual and Congested Polycyclic Structures via Benzannulated Enediynyl Alcohols Derived from Truxenone

1. Introduction

The cyclization reactions of enyne−allenes via biradical intermediates have been extensively investigated for the past decades. Under thermal conditions, (*Z*)-1,2,4-heptatrien-6-yne (enyne−allenes) **1** could undergo two different cyclization pathways (Scheme 1): one is to involve the bond formation between the C2 and the C7 carbon atoms leading to α,3-didehydrotoluene biradicals **2**[1] (Myers−Saito cyclization); the other is to proceed through C^2–C^6 pathway affording the five-membered fulvene biradicals **3** (Schmittel cyclization).[2] In general, the regioselectivity of enyne−allenes is determined by the alkynyl terminus R group. The Myers−Saito cyclization reaction is preferred when R is hydrogen or a sterically non-demanding alkyl group. On the other hand, when R group is an aryl group or sterically demanding substituent, such as *t*-butyl or TMS, the Schmittel cyclization pathway is favored.

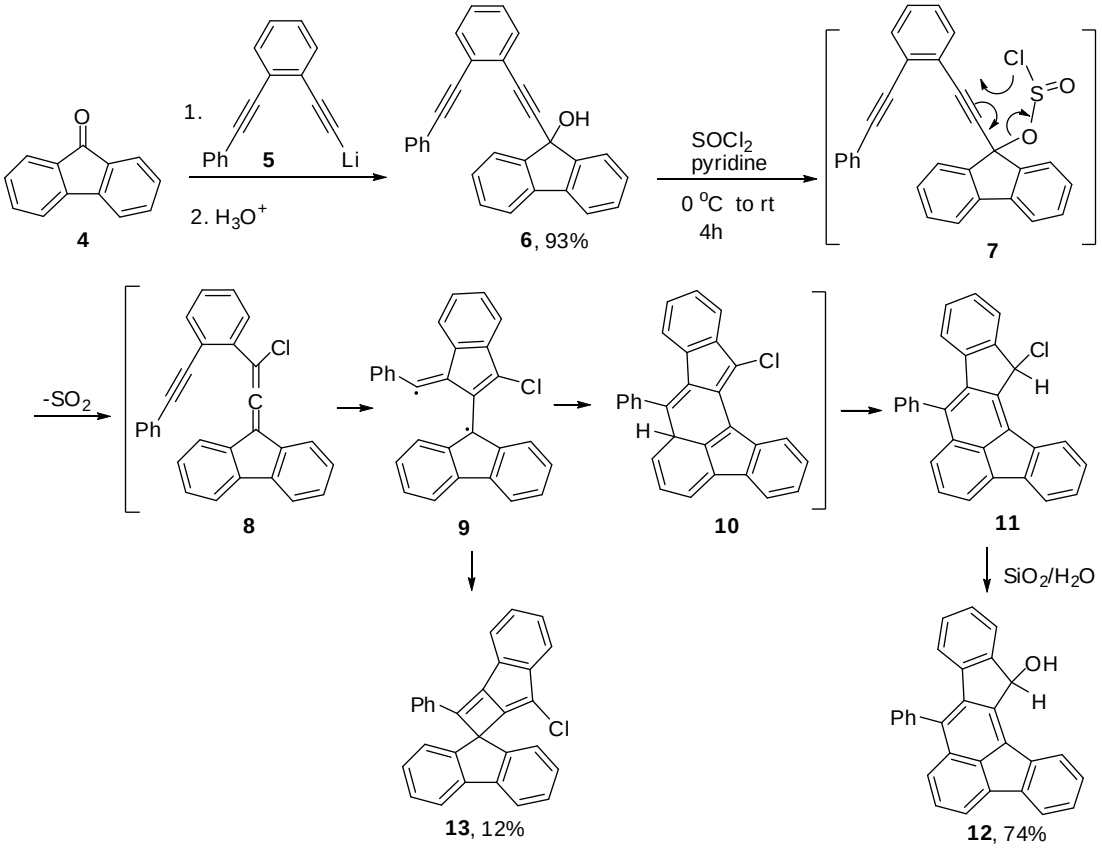


Scheme 1. Cyclization reactions of enyne−allenes.

The current research on the thermal biradical cyclization of enyne−allenes is not only focused on the synthesis of simple model compounds with potential antitumor and antibiotic activities mimicing the naturally occurring enediyne antitumor antibiotics, but also on using

them for the construction of polycyclic ring systems.[3] In particular, the Schmittel cyclization reaction has played an important role in the synthesis of carbocyclic[4] and heterocyclic[5,6] ring systems, beacuse the biradical intermediate may undergo a rapid radical−radical coupling reaction leading to the formal Diels–Alder adducts that provide easy access to polycyclic aromatic systems.

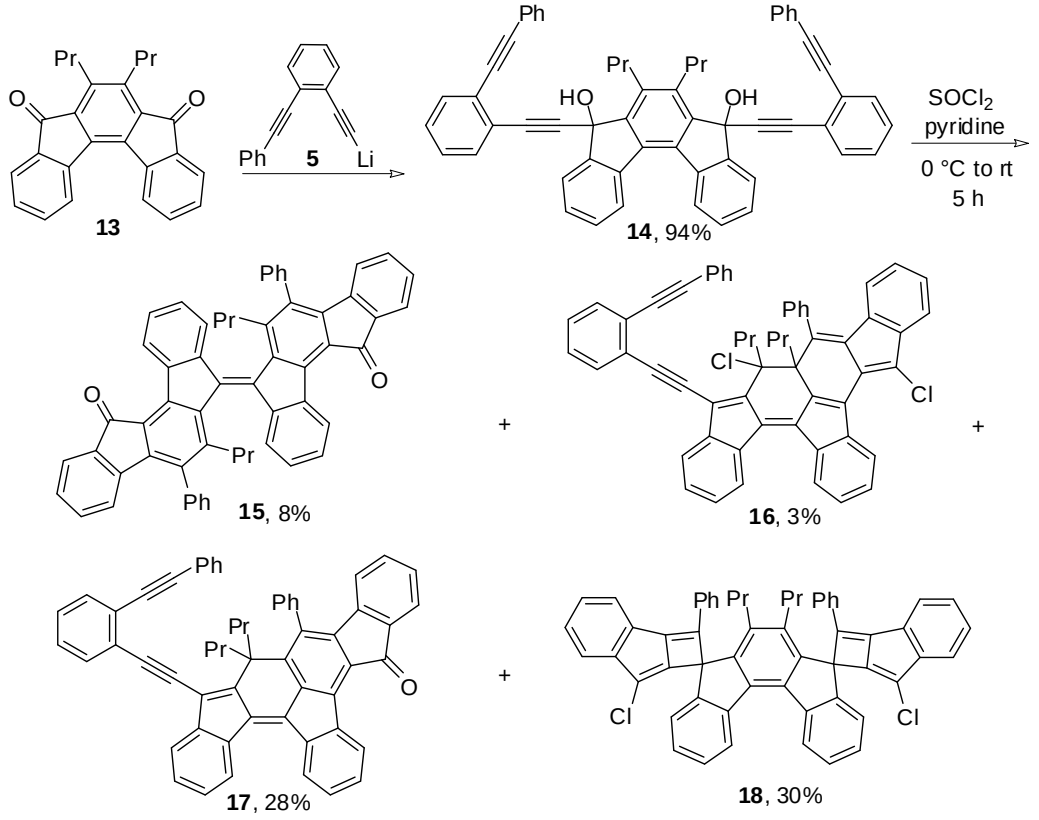
Benzannulated enediynyl alcohols, readily prepared from condensation between ketones and benzannulated enediynes and other related procedures, are excellent precursors of the reactive benzannulated enyne−allenes.[2a,b,d,7] Dr. Hongbin Li of our research group recently reported an efficient pathway to produce chlorinated benzoenyne−allene **8** in situ via a S_Ni' reaction promoted by thionyl chloride with benzannulated enediynyl propargylic alcohol **6** (Scheme 2).[7a]



Scheme 2. Schmittel cyclization of chlorinated benzoenyne−allene.

Benzannulated enediynyl alcohol **6** can be readily prepared from condensation between 9-fluorenone (**4**) and lithium acetylide **5**. A subsequent Schmittel C^2–C^6 cyclization then generated the biradical **9**, which underwent an intramolecular radical−radical coupling to give the formal Diels−Alder adduct **10**. Tautomerization followed by hydrolysis then afforded **12** and a minor [2 + 2] adduct **13**. The cascade cyclization reactions of the benzannulated enyne−allenes provide new pathways to a variety of highly unusual and congested polycyclic compounds.[8]

In particular, Dr. Yonghong Yang of our research group previously reported an unusual synthesis of involving condensation between diketone **13** and the lithium acetylide **5**, prepared from treatment of 1-ethynyl-2-(phenylethynyl)benzene as a benzannulated enediyne with *n*-butyllithium to produce diol **14**, which on exposure to thionyl chloride furnished polycyclic products **15** to **18** (Scheme 3).[8a]

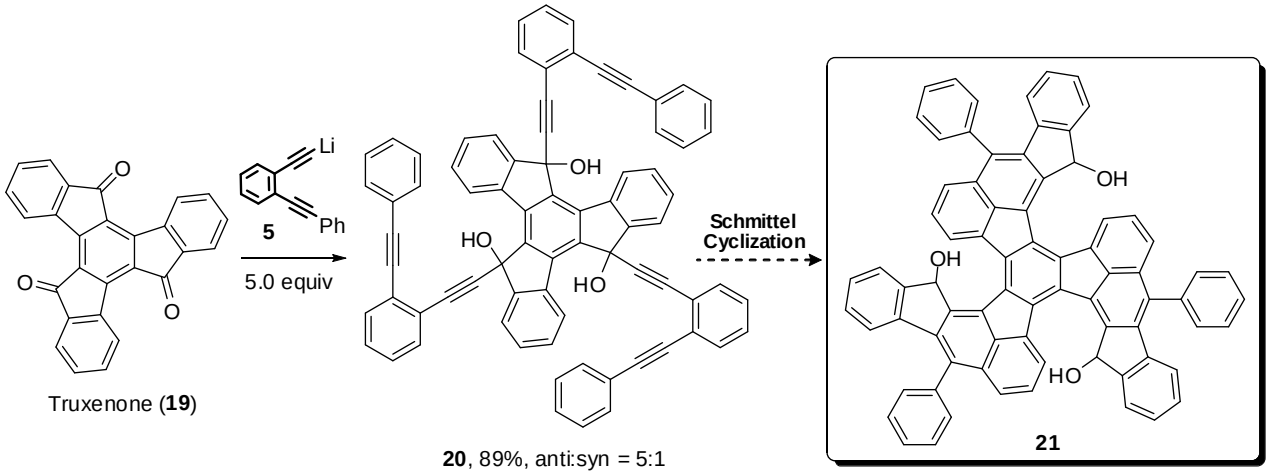


Scheme 3. Unusual cascade C^2–C^6 cyclization of chlorinated benzoenyne−allenes.

It is worth noting that in producing the twisted 1,1′-dipropyl-9,9′-bifluorenylidene **15**, a rare and unusual process involving the cleavage of the central benzene ring of **14** occurred. However, the loss of the resonance energy is more than compensated for with the eventual formation of two new benzene rings in **15**.

2. Research Objective

Based on our previous discovery of the formation of chlorinated benzannulated enyne-allenes via a S_Ni' reaction promoted by thionyl chloride and subsequent C^2–C^6 cyclization, we were interested in further exploring the use of molecules having three benzannulated enyne-allene units for the synthesis of polycyclic aromatic compounds. The readily available truxenone (**19**)[9] bearing three keto groups provides excellent opportunities for further expanding the use of benzannulated enediynyl alcohols for the synthesis of polycyclic compounds possessing interesting and unusual architectures. We envisioned the use of benzannulated enediynyl alcohol **20** as a potential precursor of the C_3 molecular propeller **21**, if the reaction would proceed through the normal Schmittel cyclization pathway. However, this reaction unexpectedly led to the formation of highly congested polycyclic structures.



Scheme 4. Triol **20** as potential precursor of C_3 molecular propeller **21.**

3. Literature Survey of the Synthesis of C_3 Symmetric Polycyclic Aromatics

In 2004, Echavarren *et al.* reported a synthesis of a C_3 symmetrical "crushed fullerene derivatives" by intramolecular palladium-catalyzed arylation reactions.[10] A versatile method from truxene derivatives can lead to the synthesis of large C_{48} polyaromatics **22**, as well as of C_{60} polycyclic aromatics **23a, b,** and **c**. The synthesis of $C_{60}H_{30}$ (**23a**) by Echavarren *et al.* is the most efficient reported to date and proceeds in just three steps from truxene in 33% overall yield. In 2001, Scott *et al.* also reported a synthesis of **23a** by employing $TiCl_4$-catalyzed trimerization of 5*H*-benzo[*f*] acephenanthrylen-4-one.[11a] His approach was later applied for the preparation of chlorinated derivatives of **23** in 11 steps from 1-bromo-4-chlorobenzene, which furnished C_{60} in 0.1-1.0% yield upon flash vacuum pyrolysis at 1100 ^{o}C.[11b]

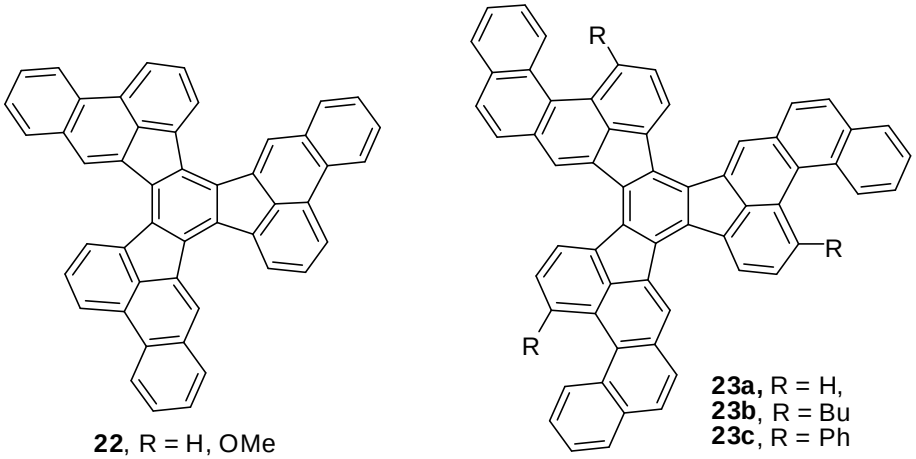


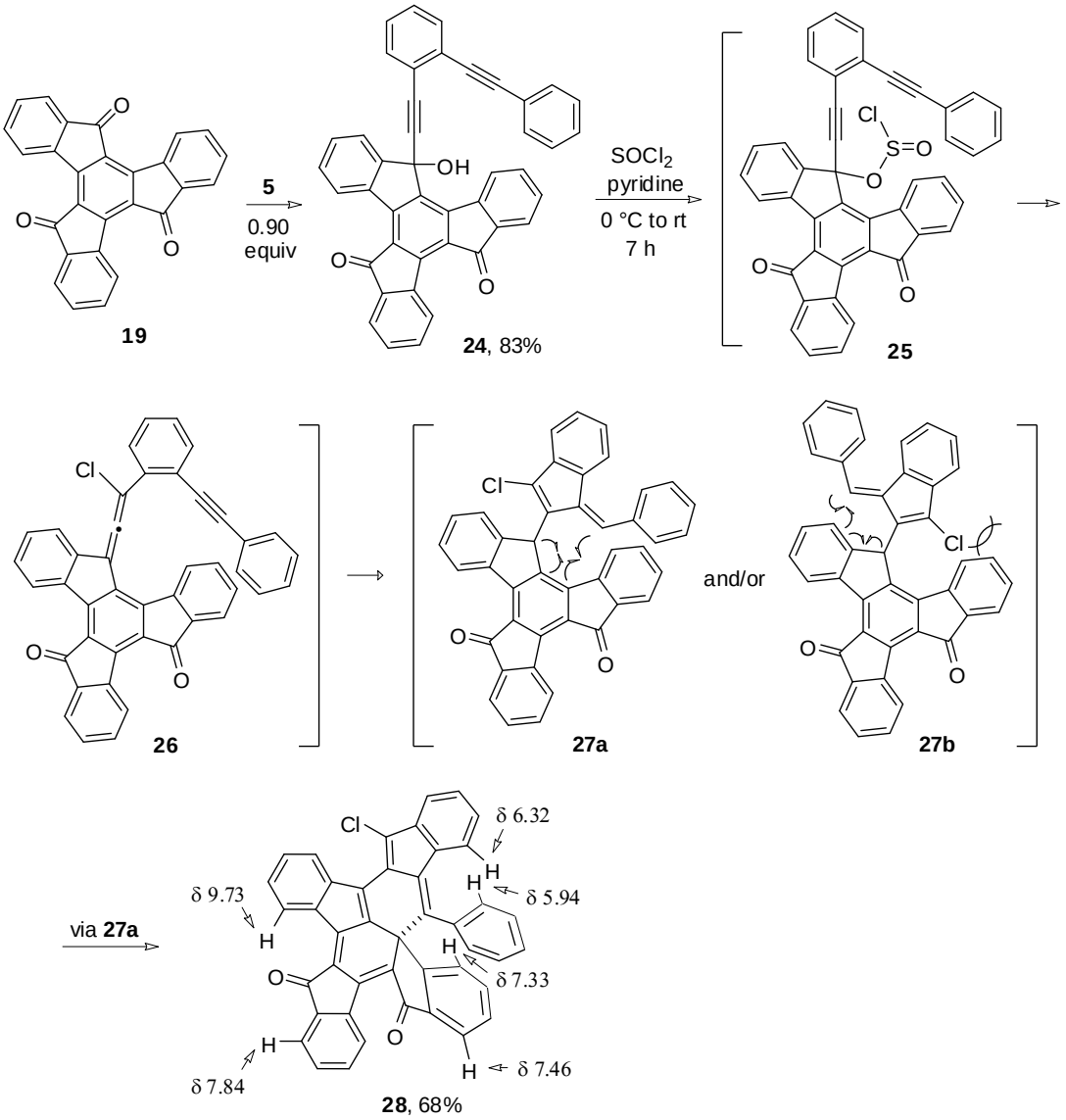
Figure 1. Some examples of C_3 symmetric polycyclic aromatics.

4. Results and Discussion

4.1 Unusual Cascade Cyclization of Mono-propargylic Alcohol 24

Condensation between truxenone (**19**) and 0.90 equiv. of lithium acetylide **5** furnished the benzannulated enediynyl propargylic alcohol **24**, which on exposure to thionyl chloride was smoothly converted to the polycyclic product **28** (Scheme 5). The structure of **28** was established by X-ray structure analysis (Figure 2). The formation of the product **28** was unexpected.

Presumably, the initially formed chlorosulfite **25** underwent an S_Ni' reaction[12] to give the benzannulated enyne−allene **26**.[7a,8j] A subsequent Schmittel cyclization reaction[2c,5] to generate biradical **27** followed by an intramolecular radical−radical coupling reaction via **27a** then produced **28** in a single cascade sequence. It is worth noting that the radical−radical coupling step involved the more congested central benzene ring to form the new quaternary carbon center in **28** instead of involving the neighboring less hindered benzene ring on the periphery as depicted in **27b**.



Scheme 5. Preparation of polycyclic diketone **28**.

Molecular modeling suggests that the pathway involving the attack of the peripheral benzene ring via **27b** suffers from the emergence of nonbonded steric interactions between the chloro substituent and one of the other two peripheral benzene rings.[7a,8a] This observation is reminiscent of what was observed previously for **14** in which the preferential attack of the central benzene ring led to **15**, **16**, and **17**. The aromaticity of the central benzene ring in **26** is disrupted in producing **28**. However, trading two π bonds in **26** for two σ bonds in **28** is more than sufficient to compensate for the loss of aromaticity.

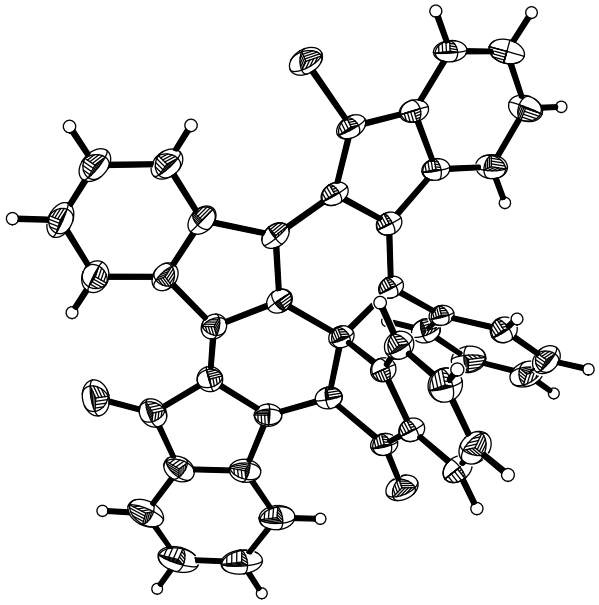


Figure 2. ORTEP drawing of the crystal structure of **28**.

It is worth noting that with the loss of the aromaticity of the central benzene ring in **19** the resultant structure of **28** contains a twisted enone system having four conjugated carbon−carbon double bonds and one keto group at its longest linear extension along with one cross-conjugated carbon−carbon double bond and one cross-conjugated keto group. In addition, the structure could also be regarded as bearing two connected benzofulvene moieties. Furthermore, the original

central benzene ring in **19** is transformed to a reactive 5-methylene-1,3-cyclohexadiene moiety.[14] The newly formed chlorofluorenyl group also contains an acid-sensitive 3-methylene-1,4-cyclohexadiene substructure.[15]

4.2 NMR Studies and Complete Signal Assignment of Compound 28

The X-ray structure of **28** indicates that the phenyl substituent is in a sterically congested environment, which could cause a relatively slow rate of rotation. In addition, the phenyl substituent is oriented roughly perpendicular to the newly formed chlorofluorenyl moiety, placing one of the *ortho* hydrogens in the magnetic shielding region of the neighboring indanone group. Indeed, the ^{1}H NMR spectrum of **28** in C_6D_6 using the 1D/2D TOCSY and COSY techniques revealed five distinct signals at δ 5.94 (*ortho*), 6.89 (*meta*), 7.15 (*ortho*), 7.17 (*para*), and 7.24 (*meta*) for the five hydrogens on the phenyl substituent, indicating a slow rate of rotation on the NMR time scale (Figure 3).

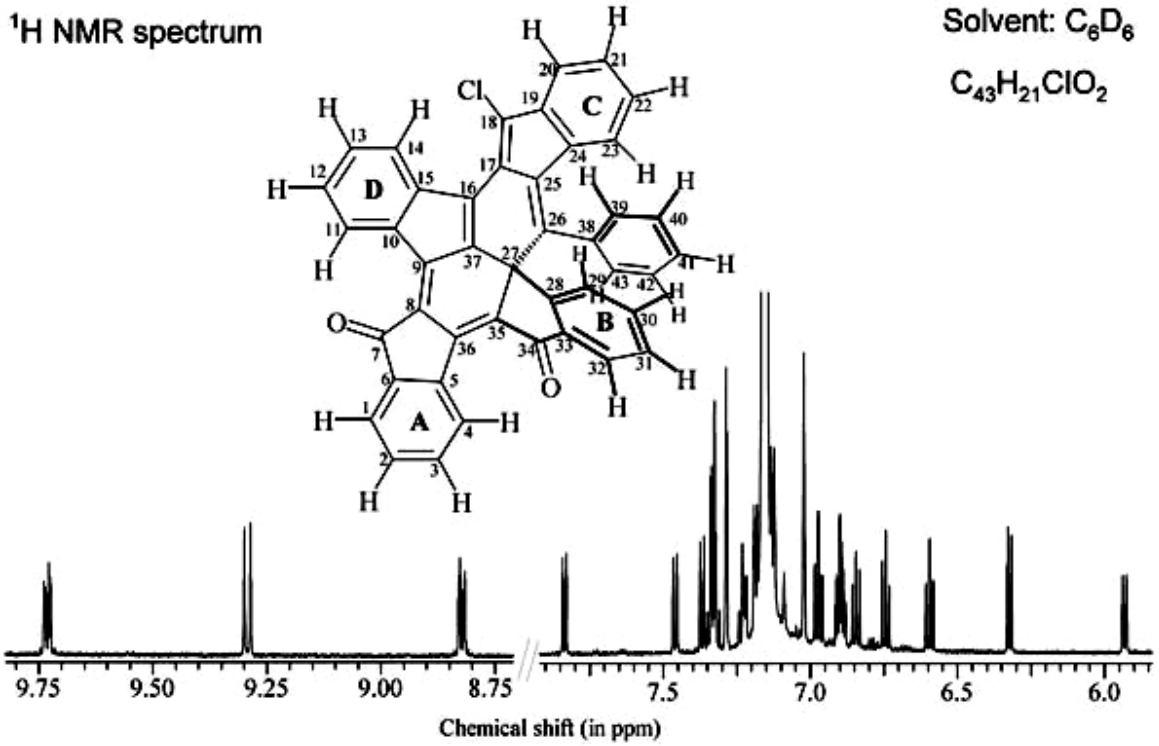


Figure 3. ^{1}H NMR spectrum of **28** in C_6D_6.

In addition, the DEPT spectrum exhibited 21 signals for the 21 proton-bearing carbons, including five signals from the phenyl substituent and 16 signals from the rest of the molecule. The magnetic shielding was observed for one of the *ortho* hydrogens, which gave a significantly upfield shift signal at δ 5.94 indicated in Scheme 5. Even at 80 °C, this signal remained virtually unchanged and without significant line broadening. The perpendicular orientation of the phenyl substituent relative to the newly formed chlorofluorenyl moiety is also responsible for upfield shifting the proton signal of the neighboring hydrogen atom on the chlorofluorenyl moiety to δ 6.32 (H23).[7a,8j] In the contour plot of the COSY spectrum (Figure 4), this signal was also used to locate the remaining three hydrogens on the same benzene ring at δ 6.60 (*ortho*), 6.90 (*meta*), and 7.37 (*para*).

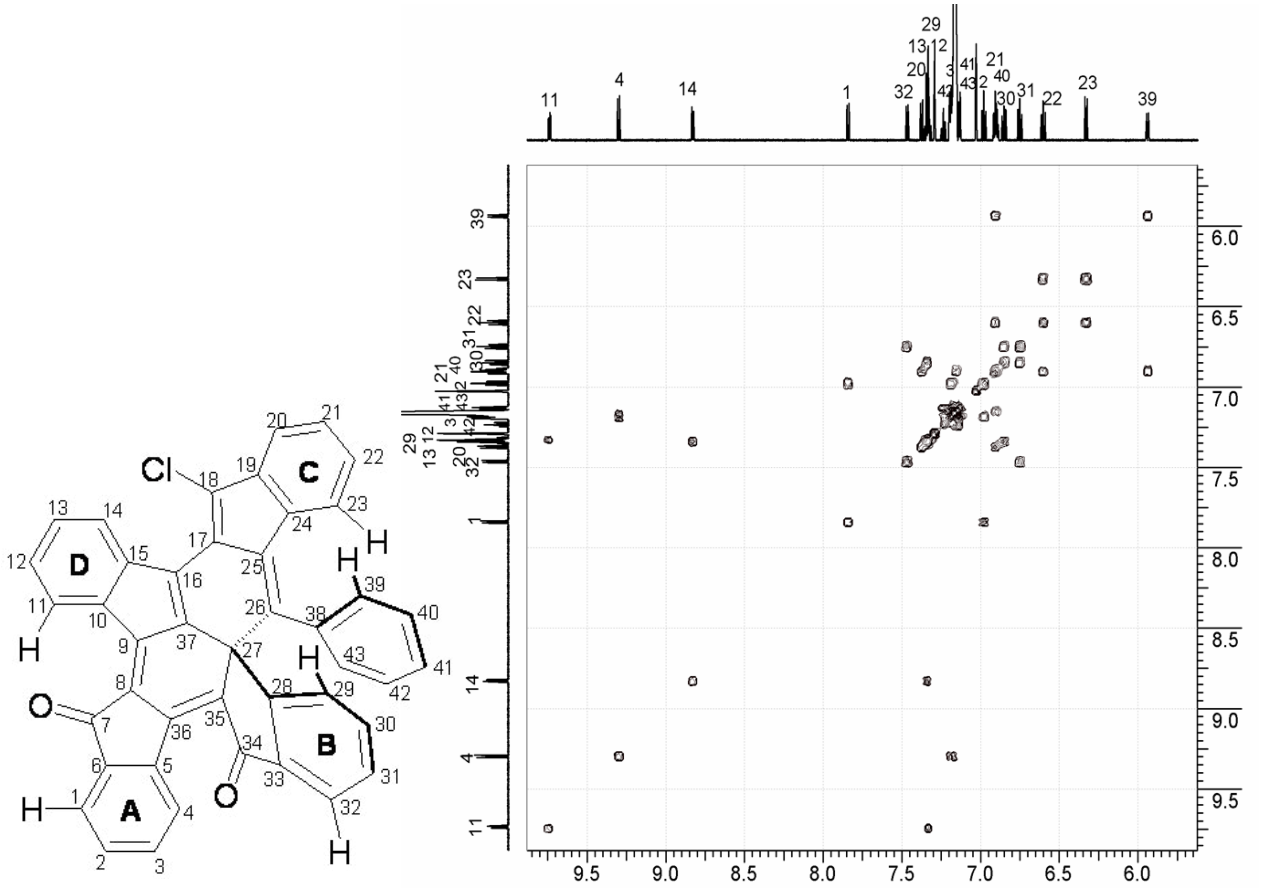


Figure 4. COSY spectrum of **28** in C_6D_6.

A complete assignment of the ^{1}H NMR chemical shifts to the remaining hydrogens of **28** and the ^{13}C NMR chemical shifts to the 43 carbons were made by an analysis strategy based on the application of several gradient selected two-dimensional experiments, such as gHSQC, gHMBC, and gHSQC-TOCSY. Again, the proton connectivities were identified from the COSY and 1D/2D TOCSY spectra. The gHSQC correlations were used to confirm the proton bearing carbons, and the gHMBC cross peaks were used to define the locations of the quaternary carbons. The gHMBC correlation with the quaternary sp^3 carbon resonance at δ 57.6 allowed the assignment of the proton signal at δ 7.33 to the hydrogen three bonds away, which in turn allowed the assignment of the remaining three hydrogens on the same benzene ring at δ 6.84 (*ortho*), 6.75 (*meta*), and 7.46 (*para*) based on 2D TOCSY and COSY correlations.

Using the gHMBC technique, the proton signal at δ 7.46 was used to locate the ^{13}C chemical shift of the neighboring carbonyl carbon at δ 187.7. Similarly, the chemical shift of the hydrogen three bonds away from the other carbonyl carbon at δ 190.3 was identified at δ 7.84, which in turn allowed the assignment of the remaining three hydrogens on the same benzene ring at δ 6.97 (*ortho*), 7.19 (*meta*), and 9.29 (*para*). The most downfield proton signal at δ 9.73 was assigned to the hydrogen on the remaining benzene ring closest to the carbonyl carbon with a chemical shift at δ 190.3. The last three proton signals at δ 7.32 (*ortho*), 7.34 (*meta*), and 8.82 (*para*) were then assigned by COSY. The 1D TOCSY spectra (Figure 5) show all the spin-spin coupling network of hydrogens shown individually on the phenyl group, ring A, B, C and D.

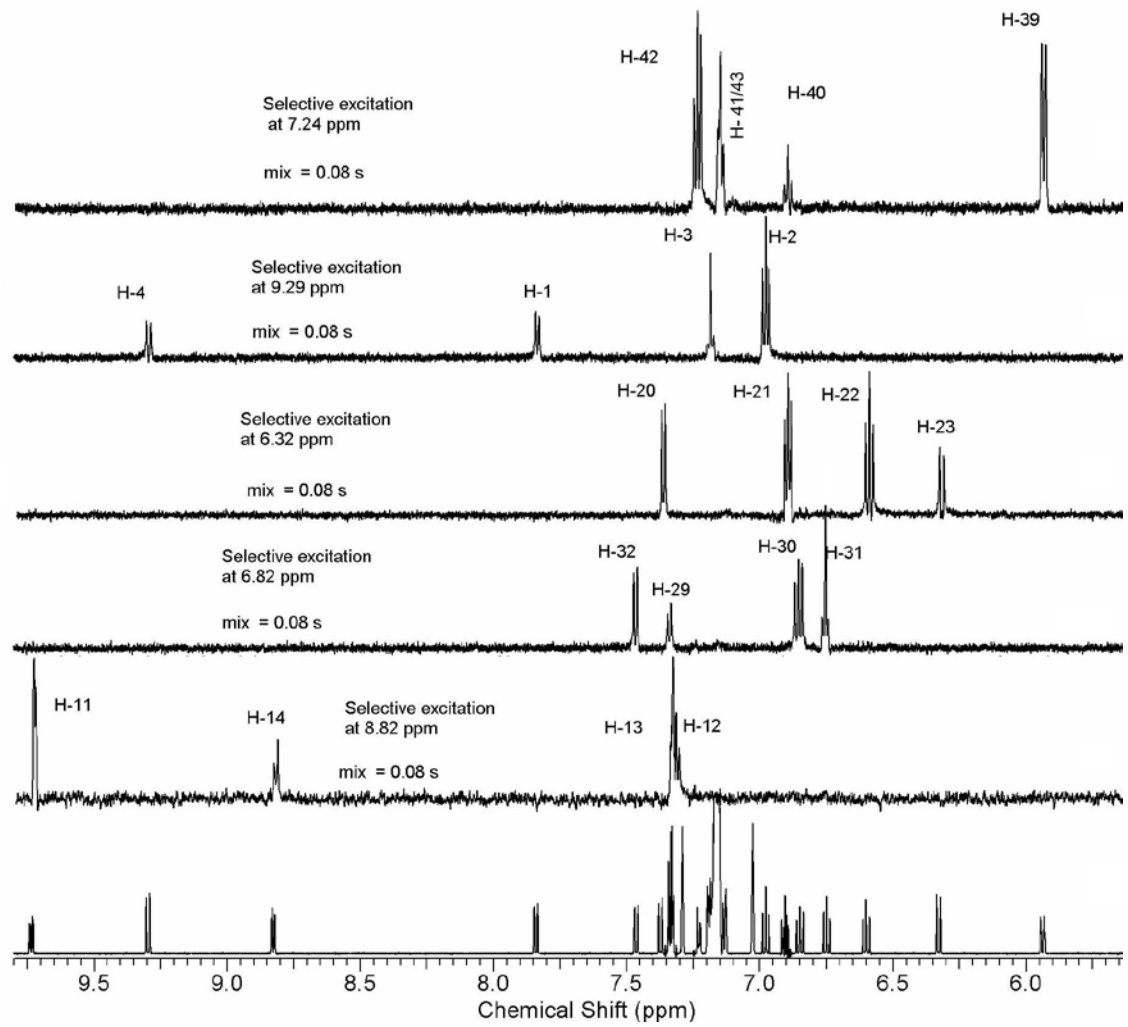


Figure 5. 1D TOCSY spectra of **28** in C_6D_6.

4.3 Unusual Transformation of 28 in $CDCl_3$ to Other Unknown Compounds

It was observed that the polycyclic compound **28** gradually and cleanly transformed to an unknown compound II in $CDCl_3$, which on further studying in air led to another unknown compound III. Compounds II and III exhibit a very different proton NMR spectrum with the two most upfield shift signals appearing at δ 5.28 (1 H, d, J = 7.8 Hz) for compound II and 5.33 (1 H, d, J = 7.8 Hz) for compound III (Figure 6). The structures of these two new compounds have not been elucidated. However, NMR studies of unknown II showed that there are still 21 hydrogens,

two keto groups and four ring substructures. One possible structure of compound III is depicted as **29** (Scheme 6). Further investigation is needed to determine its structures.

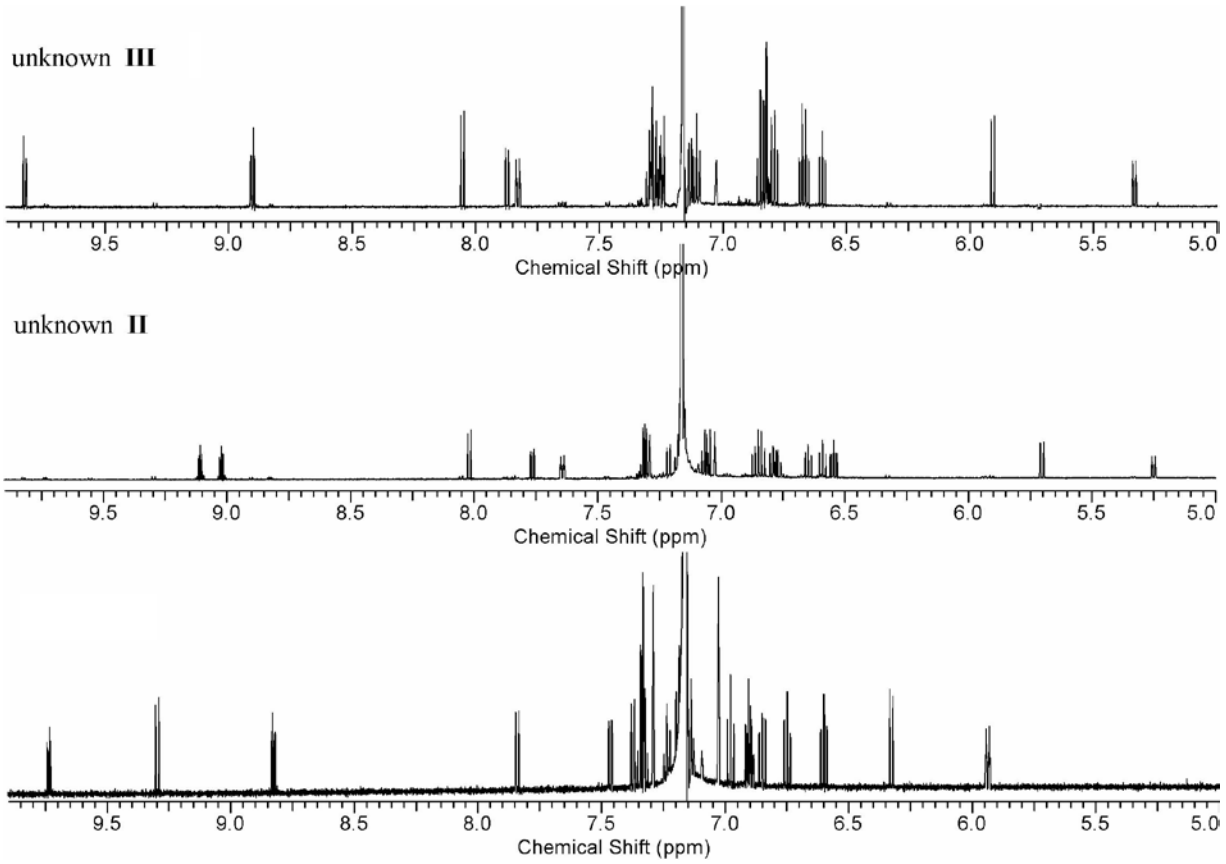
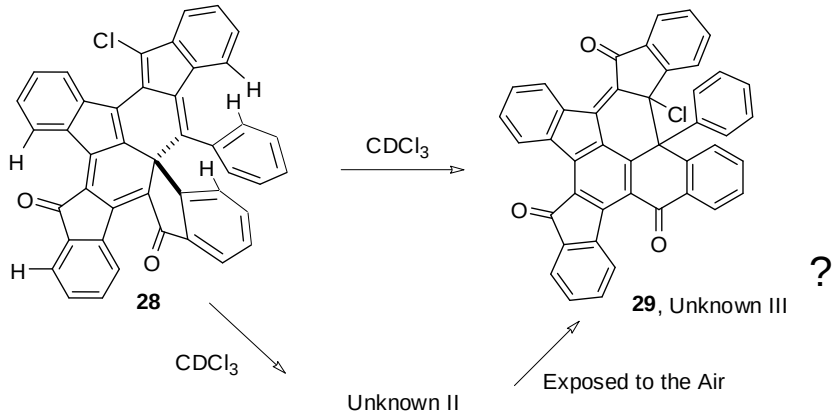


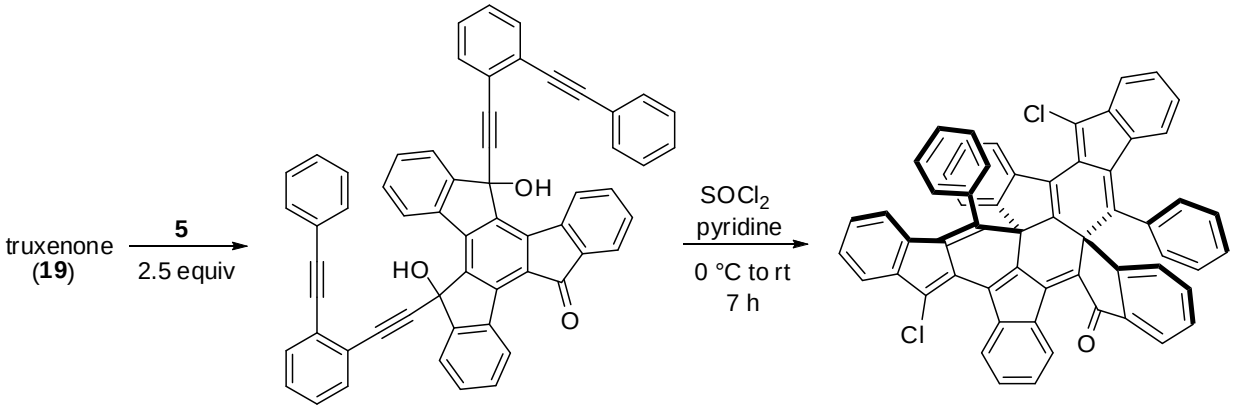
Figure 6. ^{1}H NMR spectra comparison of compound **28** and two unknowns in C_6D_6.



Scheme 6. Proposed transformation of polycyclic diketone **28.**

4.4 Unusual Cascade Cyclization of Di-propargylic Alcohol 30

Treatment of truxenone with 2.5 equiv of **5** allowed the isolation of the *cis* diol **30** in 76% yield along with the corresponding *trans* diol in 13% yield (Scheme 7). The structure of the *cis* diol was established by X-ray structure analysis. On exposure of a mixture of the *cis* and *trans* isomers of diol **30** to thionyl chloride, the product **31** bearing two quaternary carbon centers was produced. In addition, the two chlorinated fluorenyl moieties are *trans* to each other with respect to the central six-membered ring. The structure of **31** was established by X-ray structure analysis (Figure 7). Apparently, the second cascade cyclization reaction also involved a carbon−carbon double bond of the central six-membered ring. In addition, the second radical−radical coupling reaction occurred from the direction *trans* to the first chlorinated fluorenyl unit. As observed in **28**, several ^{1}H NMR signals of **31** in C_6D_6 showed significant upfield shifts with the most upfield signal appearing at δ 5.62.



Scheme 7. Preparation of congested polycyclic ketone **31**.

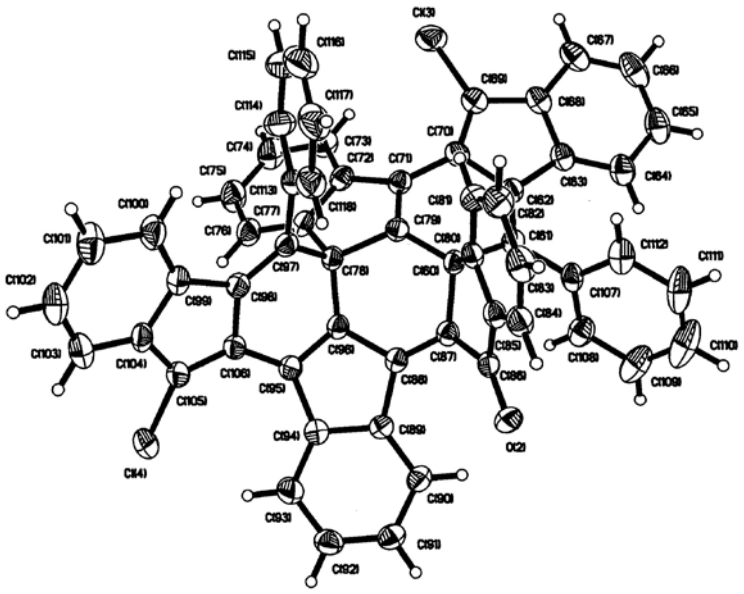
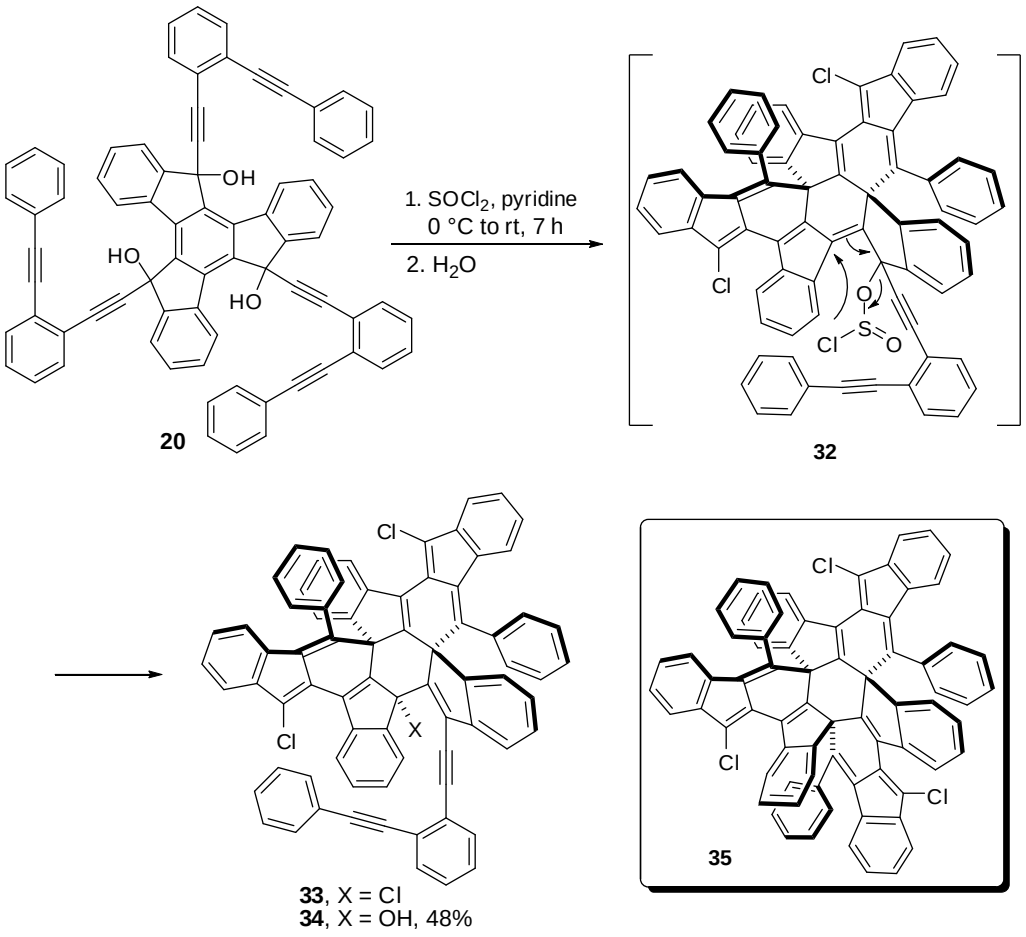


Figure 7. ORTEP drawing of the crystal structure of **31** with atom labeling.

4.5 Unusual Cascade Cyclization of Propargylic Triol 20

When truxenone was treated with 5.0 equiv of **5**, triol **20** was obtained as a mixture of the *anti* and *syn* isomers (5:1) in 89% combined yield (Scheme 4). On exposure of a mixture of the *anti* and *syn* isomers of **20** to thionyl chloride, the product **34** was produced in 48% yield (Scheme 8). The structure of **34** was established by X-ray structure analysis (Figure 8). Clearly, the third benzannulated enediynyl alcohol unit did not undergo the anticipated cascade cyclization reaction. Instead, the third chlorosulfite **32** underwent an S_Ni' reaction involving the remaining carbon−carbon double bond of the central six-membered ring might have occurred to give **33**, which on hydrolytic workup then furnished **34**. The attempt to synthesize highly congested compound **35** by heating the reaction to higher temperature at 80 ^oC was unsuccessful. The ^1H NMR spectrum of the crude reaction mixture showed very complicated broad peaks in the aromatic region, indicating that the starting material decomposed or polymerized. Apparently, the severe steric congestion of central six-membered ring prevented the cascade cyclization reaction from attacking the third carbon−carbon double bond of the central benzene ring.



Scheme 8. Preparation of polycyclic compound **34.**

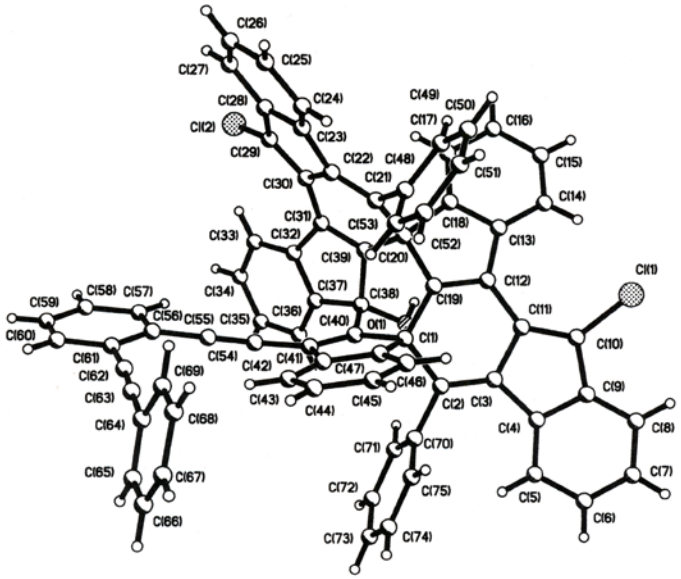
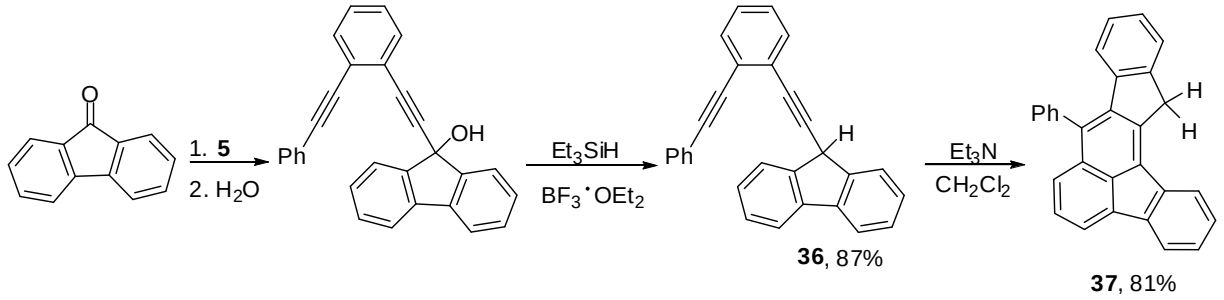


Figure 8. ORTEP drawing of the crystal structure of **34** with atom labeling.

4.6 Other Attempts to Synthesize Polycyclic Aromatic Compounds

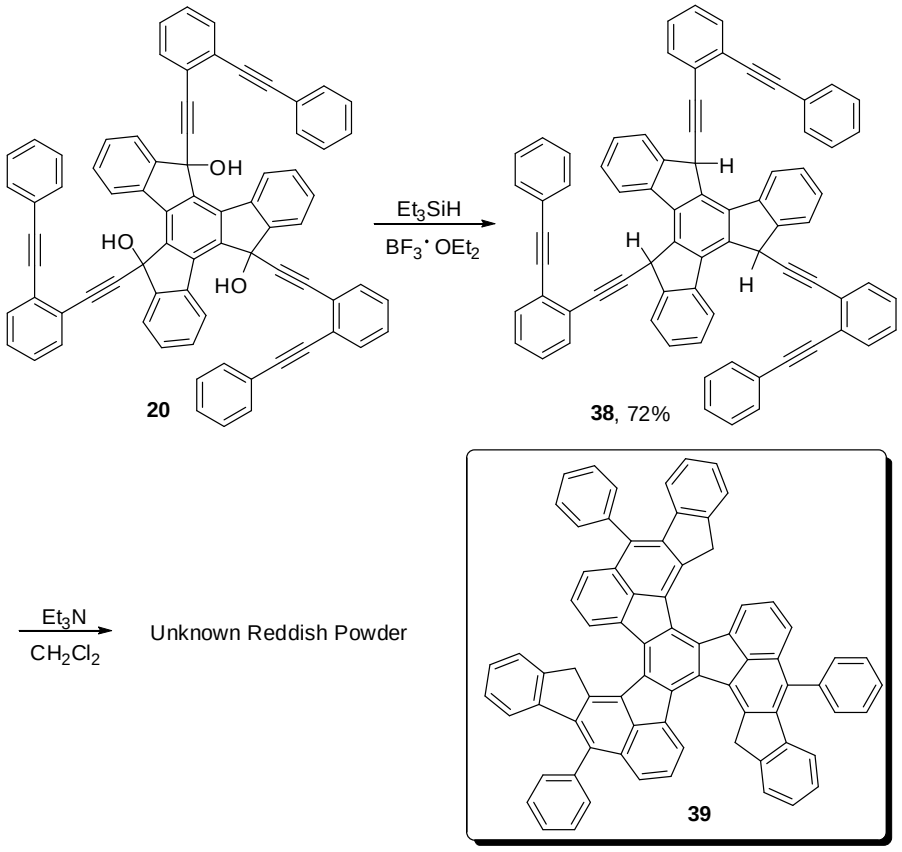
Dr. Yonghong Yang developed a new synthetic pathway to generate the benzannulated enyne-allenes in situ from crude propargylic acetate promoted by $Pd(PPh_3)_4$, 2-propanol and SmI_2·THF, and then followed by cascade radical cyclization leading to the polycyclic hydrocarbon **37** in a single operation with 34% yield in two steps.[16] Scheme 9 outlines a study to generate the benzannulated enyne-allenes in situ without a chloro-substituent. Reduction of the hydroxyl group was carried out by treatment with triethylsilane in the presence of BF_3·OEt_2 to afford hydrocarbon **36**.[9a] A prototropic rearrangement of **36** promoted by triethylamine to form benzannulated enyne-allene in situ followed by a cascade Schmittel cyclization and tautomerization led to the corresponding polycyclic aromatic hydrocarbons **37** in a single operation.[17] However, the reduction by using trifluoroacetic acid in the presence of triethylsilane developed by Dr. Hongbin Li of our group failed in this case. Also, an attempt to promote cascade cyclization reactions of **36** with potassium *tert*-butoxide under refluxing toluene at 110 ^oC also was unsuccessful.



Scheme 9. A new synthetic pathway to polycyclic hydrocarbon **37**.

Scheme 10 outlines the attempts to synthesize polycyclic aromatic hydrocarbon **39** via cascade radical cyclization of the molecule having three units of benzannulated enyne-allenes without a chloro substituent. Treatment of triol **20** with triethylsilane in the presence of BF_3·OEt_2 afforded the hexacetylenic hydrocarbon **38**. On exposure to triethylamine, the reaction mixture

immediately became reddish in color. The ^{1}H NMR spectra of the crude and also the product after silica gel column chromatography showed very broad and complicated peaks in the aromatic region, indicating that the starting material decomposed or polymerized.



Scheme 10. Attempt to synthesize **39** via a new synthetic pathway.

5. Conclusions

Benzannulated enediynyl alcohols **24**, **30**, and **20**, derived from condensations of truxenone and the lithium acetylide **5**, were readily converted to the polycyclic compounds **28**, **31**, and **34** by thionyl chloride-promoted cascade cyclization reactions. The aromaticity of the central benzene ring of truxenone is disrupted in all three of the resultant products. Transformation of two π bonds to two σ bonds in each of the cascade cyclization sequence provides the necessary driving force for the construction of these unusual and congested

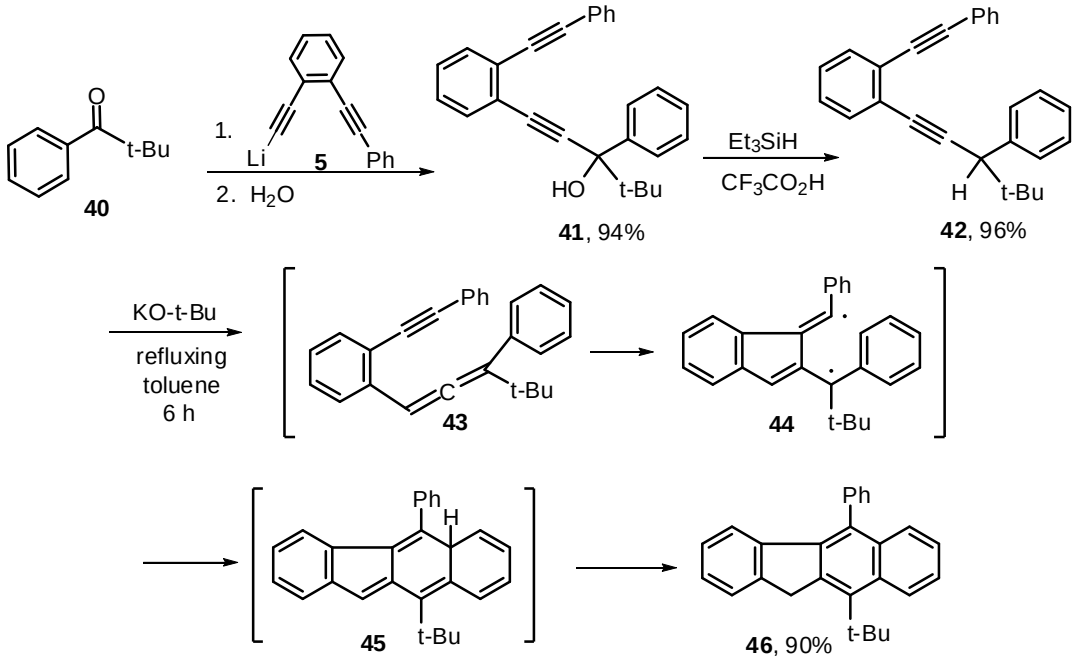
polycyclic structures. Other attempts to prepare polycyclic aromatic compounds **21**, **35**, and **39** via different synthetic pathways were unsuccessful.

CHAPTER II

Synthesis of 5-(2-Methoxy-1-naphthyl)- and 5-[2-(Methoxymethyl)-1-naphthyl]-11*H*-benzo[*b*]fluorene as 2,2′-Disubstituted 1,1′-Binaphthyls

1. Introduction

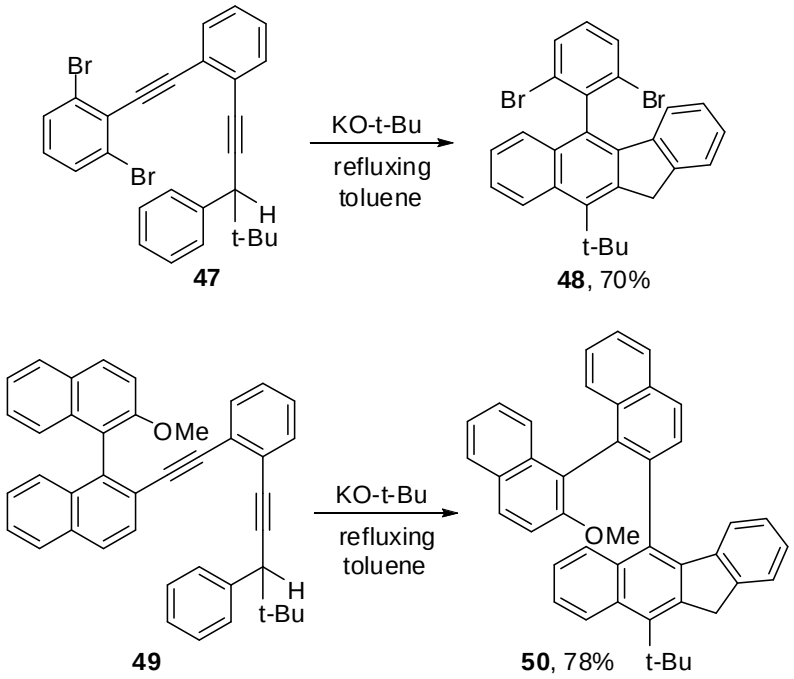
We recently reported an efficient synthesis of 5-phenyl-11*H*-benzo[*b*]fluorene **46** in a single cascade sequence by treatment of the benzannulated enediyne **42** having a phenyl substituent attached directly at one of the alkynyl termini with potassium *t*-butoxide in refluxing toluene for six hours (Scheme 11).[7a] The benzannulated enediyne **42** was prepared from the condensation between lithium acetylide **5** and 2,2-dimethylpropiophenone (**40**) to furnish the corresponding propargylic alcohol **41**, followed by reduction with triethylsilane in the presence of trifluoroacetic acid.



Scheme 11. Synthesis of 11*H*-benzo[*b*]fluorene **46** via Schmittel cyclization.

Presumably, an initial 1,3-prototropic rearrangement of **42** afforded the benzannulated enyne−allene **43** in situ, followed by a Schmittel cyclization reaction to generate benzofulvene biradical **44**. A subsequent intramolecular radical−radical coupling then gave the formal Diels−Alder adduct **45**, which in turn undergoes a second prototropic rearrangement to regain aromaticity leading to 11*H*-benzo[*b*]fluorene **46** in 90% yield.

The reaction is not sensitive to the steric requirement of the substituent at the alkynyl terminus. We also reported that the benzannulated enediyne **47** having a sterically demanding 2,6-dibromophenyl substituent was also smoothly converted to **48**.[8c] With the benzannulated enediyne **49** having a 1,1′-binaphthyl substituent, a 1:1 mixture of the *syn* and the *anti* atropisomers of **50** was likewise obtained.[8f]



Scheme 12. Syntheses of 11*H*-benzo[*b*]fluorene derivatives.

It is interesting to note that the newly formed benzo[*b*]fluorenyl moiety in **46** and **48** could also be regarded as a 1-arylnaphthyl derivative with three additional substituents at the 2, 3, and 4 positions. We now have successfully extended the cascade sequence to the synthesis of

other sterically congested analogues with an *ortho*-methoxyl or an *ortho*-methoxymethyl group on the phenyl substituent. In addition, by placing a 2-methoxy-1-naphthyl or a 2-(methoxymethyl)-1-naphthyl group at one of the alkynyl termini, the resulting naphthyl-substituted benzo[*b*]fluorenes could be regarded as 2,2′-disubstituted 1,1′-binaphthyls with two additional substituents at the 3 and 4 positions.

2. Research Objective

The versatility of 1,1′-binaphthyl-2,2′-diol (BINOL, **51**) and BINOL derivatives as chiral reagents in asymmetric synthesis has stimulated the development of new synthetic methods for 2,2′-disubstituted 1,1′-binaphthyls.[18] In 1979, the potential of BINOL as a ligand for metal-mediated catalysis was first recognized by Noyori *et al.*[19b] in the reduction of aromatic ketones and aldehydes. However, BINOL has its limitation and does not always give satisfactory results in asymmetric catalysis. As a result, there has been an intensive interest in designing and synthesizing novel modified BINOL ligands. The optimization of a given asymmetric transformation process depends on both steric and electronic properties of the chiral ligand therefore a strategic placement of substituents onto the framework of a BINOL derivative may lead to improvement of catalysis. The great majority of the reported methods involved coupling of two properly substituted 1-naphthyl derivatives. Construction of a new 1-naphthyl ring as an essential step toward 1,1′-binaphthyls is rare.[19] Herein, we employed the Schmittel cyclization to construct the core structure of 1,1′-binaphthyls in a single operation as shown in Scheme 12.

3. Literature Survey of BINOL derivatives and Synthesis of Bidentate Fluorenyl Complex

3.1 Literature Survey of the BINOL derivatives

BINOL derivatives can be generally categorized into two main types: one is C_2-symmetrical homo bi-dentate ligand such as BINAP (**52**),[20] BINAM (**53**),[21] and 2,2′-bis(2-indenyl)binaphthyl (**54**);[22] The other is non-C_2-symmetrical hetero bi-dentate ligand

including NOBIN (**55**),[23] MOP (**56**),[24] and MAP (**57**).[25] Both of these BINOL derivatives have been widely investigated and used in the development of asymmetric catalysis (Figure 9).[18h]

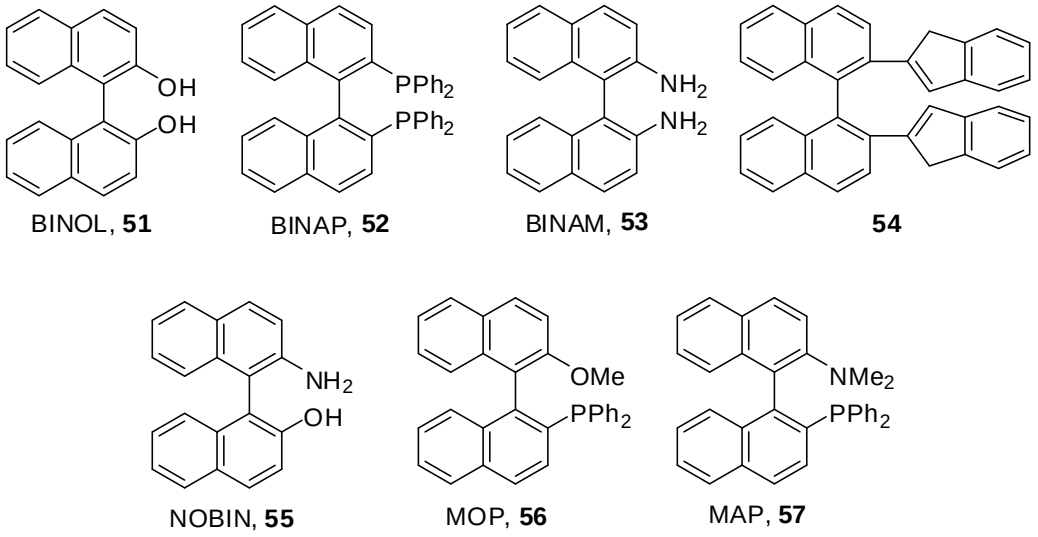


Figure 9. Examples of BINOL derivatives.

Considering the rotational barrier around the carbon−carbon single bond connecting the two C1 carbons of these 2,2′-disubstituted binaphthyls, the type of non-symmetrical 1,1'-binaphthyls can provide higher rotation barrier since the lack of C_2 symmetry.[26] This feature further gives stability to the chiral configuration even at high temperature which allows these molecules to be more attractive for synthetic applications and asymmetric catalysis.

3.2 Literature Survey of Synthesis of Bidentate Fluorenyl Complexes

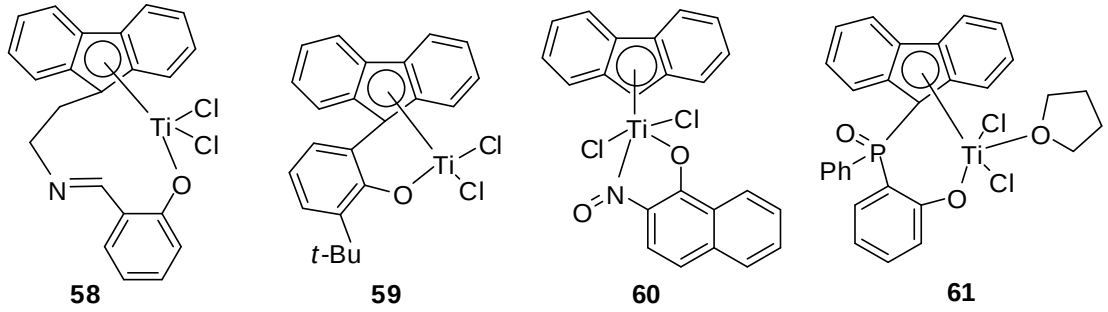
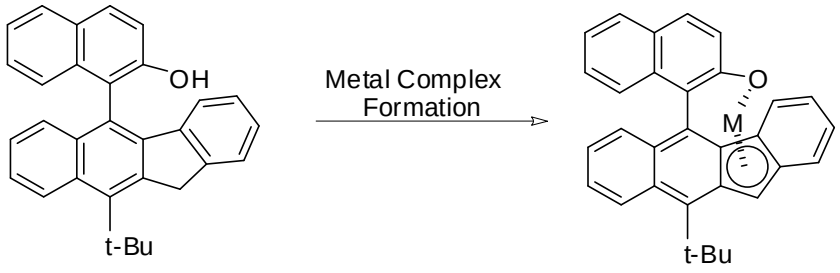


Figure 10. Examples of novel bidetate metallocene titanium complexes.

In 1996, Kashiwamura *et al.* reported the synthesis of novel bidentate fluorene complex **58** and employed this kind of complex to catalyze the polymerization of propylene.[27] Several other novel phenoxy side chain-containing metallocene titanium complexes (**59**-**61**) have also been synthesized and used for various olefin polymerizations (Figure 10).[28] We envisioned the possibility of producing metallocene complexes **63** from **62**, which could be readily prepared by employing the Schmittel cyclization reaction (Scheme 13).



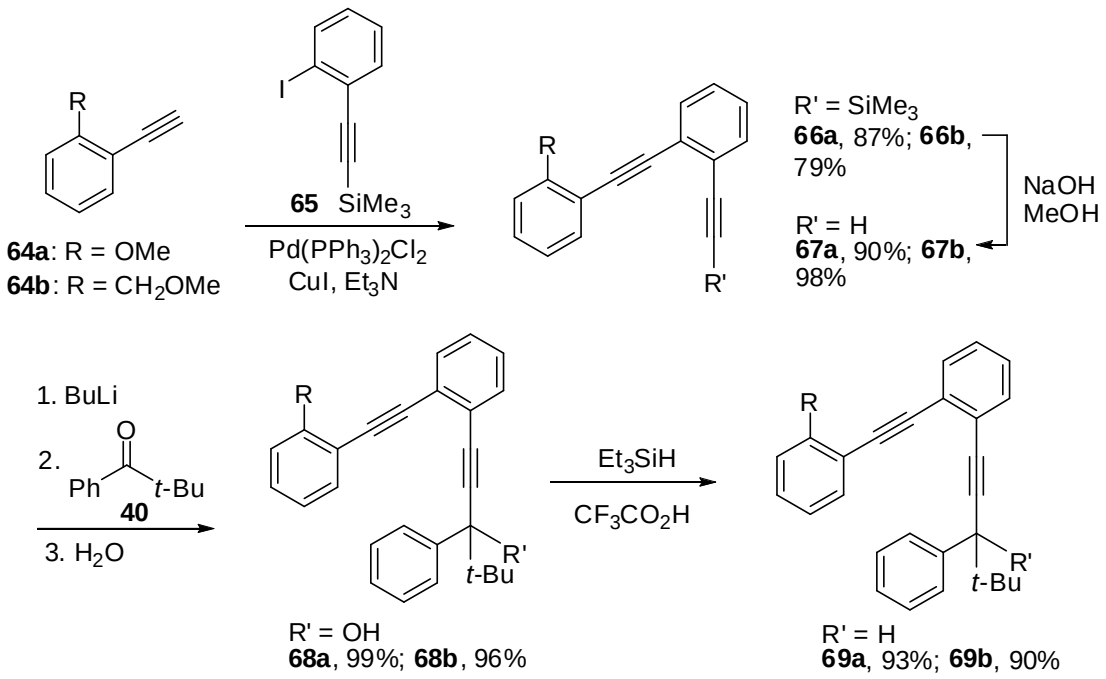
62 **63**

Scheme 13. Anticipated formation of metallocene complex.

4. Results and Discussion

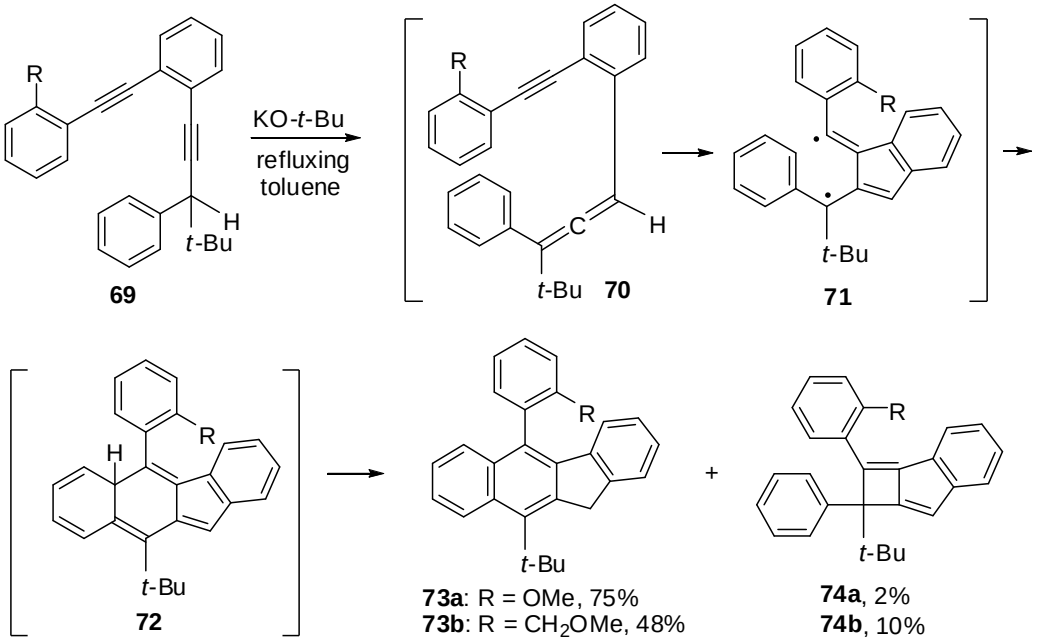
4.1 Synthesis of 1-Arylnaphthyl Derivatives

The Sonogashira reaction between 1-ethynyl-2-methoxybenzene (**64a**) and aryl iodide **65** produced **66a**, which was desilylated to give **67a** (Scheme 14). Condensation between **67a** and pivalophenone (**40**) then furnished the benzannulated enediynyl alcohol **68a**. Subsequent reduction with triethylsilane in the presence of trifluoroacetic acid afforded the benzannulated enediyne **69a**. Similarly, the benzannulated enediyne **69b** was synthesized from 1-ethynyl-2-(methoxymethyl)benzene (**64b**). Upon exposure to potassium *t*-butoxide in refluxing toluene for five hours, **69a** was transformed to 5-(2-methoxyphenyl)-11*H*-benzo[*b*]fluorene **73a** along with a small amount (ca. 2%) of **74a** in a single operation (Scheme 15).



Scheme 14. Prepararion of benzannulated enediyne **69**.

Presumably, the cascade sequence involved an initial 1,3-prototropic rearrangement to form the corresponding benzannulated enyne−allene **70a**. A Schmittel cyclization reaction[2,13b] to generate biradical **71a** for an intramolecular radical−radical coupling to afford **72a** followed by a second prototropic rearrangement to regain aromaticity then furnished **73a** as proposed previously. An intramolecular [2 + 2] cycloaddition reaction of **70a** or a direct radical−radical coupling of **71a** could account for the formation of **74a**.[7a] By starting from **69b**, 5-[2-(methoxymethyl)phenyl]-11*H*-benzo[*b*]fluorene **73b** and the [2 + 2] cycloaddition adduct **74b** in a 5:1 ratio were produced. The presence of the carbon−carbon double bonds in **74b** allows easy removal of **74b** by treatment of the resulting mixture with BH_3·THF followed by silica gel column chromatography. The presence of a benzofluorenyl moiety and a methoxyl or a methoxymethyl group in **73a** and **73b** could allow them to serve as hetero-bidentate ligands for complex formation with transition metals.[29]

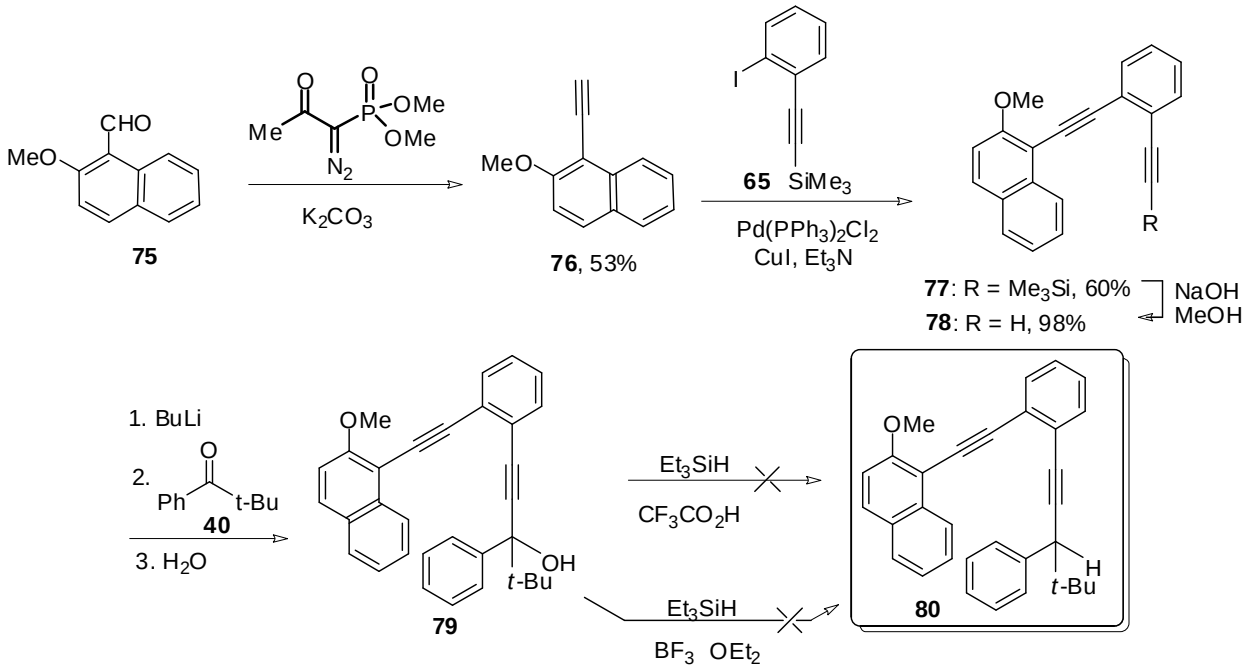


Scheme 15. Synthesis of 1-arylnaphthyl derivative **73**.

4.2 Synthesis of 2,2′-Disubstituted 1,1′-Binaphthyls

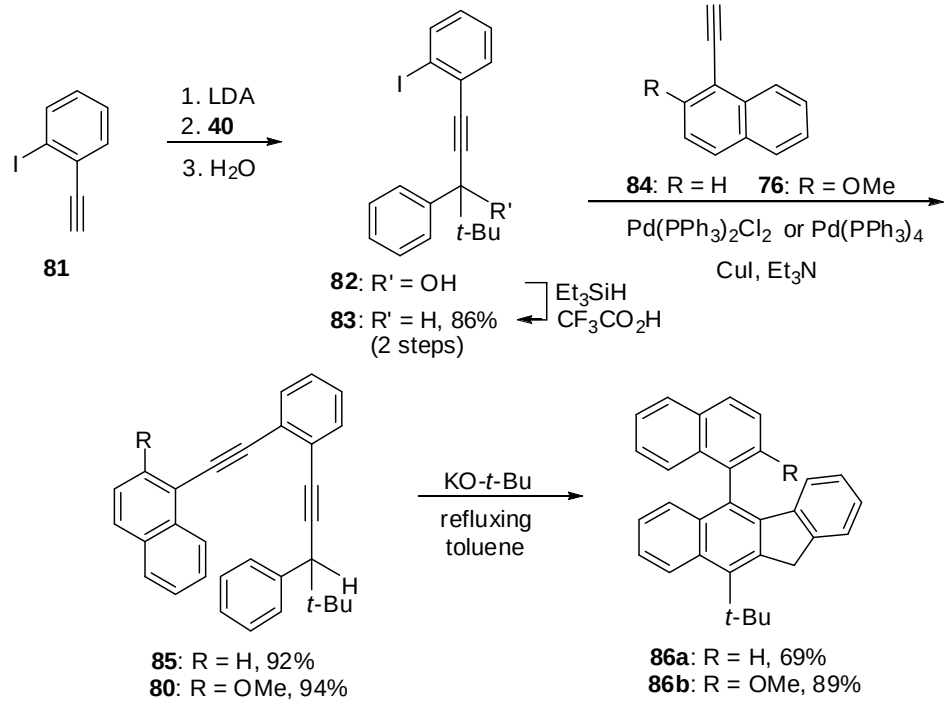
4.2.1 Preparation of Benzannulated Enediyne 80

We also investigated the possibility of using the benzannulated enediynes bearing a 1-naphthyl, a 2-methoxy-1-naphthyl, or a 2-(methoxymethyl)-1-naphthyl substituent at one of the alkynyl termini for the cascade cyclization reaction. Treatment of 2-methoxy-1-naphthaldehyde (**75**) with dimethyl(1-diazo-2-oxopropyl)phosphonate and K_2CO_3 gave acetylene **76** (Scheme 16). The Sonogashira reaction between **76** and aryl iodide **65** furnished **77**. Subsequent desilylation and condensation gave the benzannulated enediynyl alcohol **79**. However, reduction by using triethylsilane in either trifluoroacetic acid or $BF_3{\cdot}OEt_2$ were unsuccessful to afford the desired benzannulated enediyne **80**. Therefore, the synthetic pathway was slightly modified by first preparing the fragment of reduced aryl iodide **83** followed by coupling with acetylene **76** (Scheme 17). The benzannulated enediyne **80** was successfully obtained.



Scheme 16. Attempted synthetic pathway to benzannulated enediyne **80**.

4.2.2 Synthesis of 1,1′-Binaphthyls 86a and 86b



Scheme 17. Revised synthetic route toward 1,1′-binaphthyls **86a** and **86b**.

The benzannulated enediynes bearing a 1-naphthyl group **85** was also synthesized by using the same synthetic sequence as shown in Scheme 17. It was gratifying to observe that on treatment with potassium *t*-butoxide, benzannulated enediynes **85** and **80** were smoothly converted to 1,1′-binaphthyls **86a** and **86b**, respectively. The structure of **86b** was established by X-ray structure analysis (Figure 11).

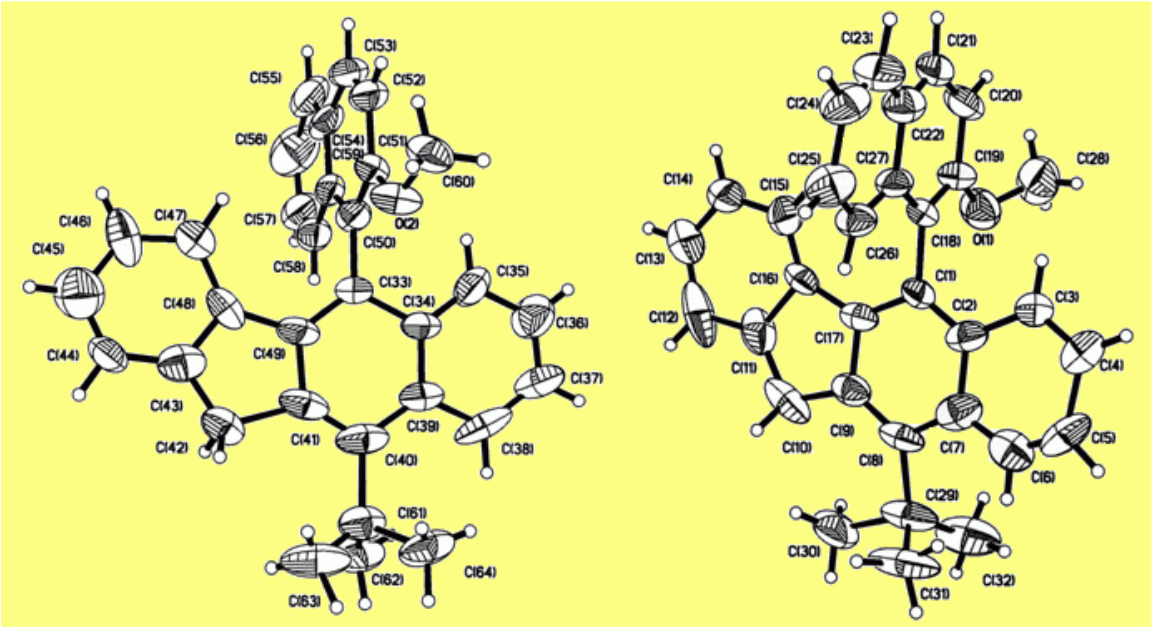
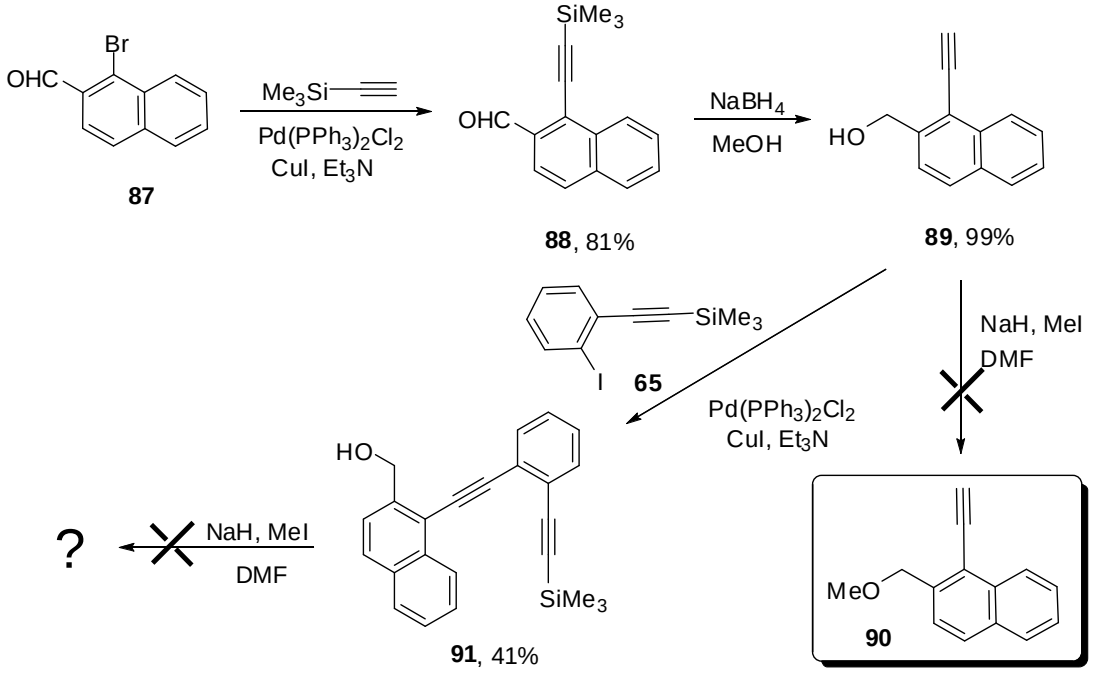


Figure 11. ORTEP Drawings for two molecules in the asymmetric unit of **86b.**

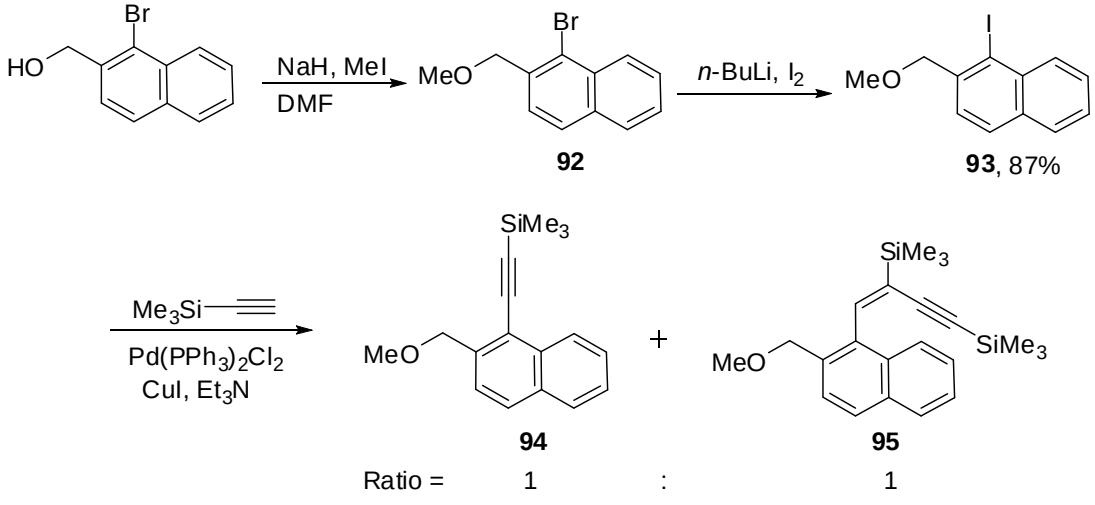
4.2.3 Preparation of Precursor Acetylene 90

Scheme 18 outlines the synthetic pathway toward the precursor acetylene **90** bearing a 2-methoxymethyl substituent. The Sonogashira reaction between 1-bromo-naphthalidehyde (**87**) and trimethylsilylyacetylene furnished **88**, which was reduced with $NaBH_4$ to generate the corresponding primary alcohol **89**. However, methylation of alcohol **89** to give the desired acetylene precursor **90** was unsuccessful. Alternatively, the Sonogashira reaction between **89** and aryl iodide **65** furnished **91**. Nevertheless, attempts to methylate **91** were unsuccessful. A revised synthetic pathway was made by starting with the methylation of (1-bromonaphthalen-2-yl)

methanol to give bromide **92**, which was converted to the corresponding iodide **93** (Scheme 19). A subsequent Sonogashira reaction with TMS-acetylene led to a 1:1 ratio mixture of the desired product **94** and unexpected byproduct **95**, which are inseparable by silica gel chromatography.

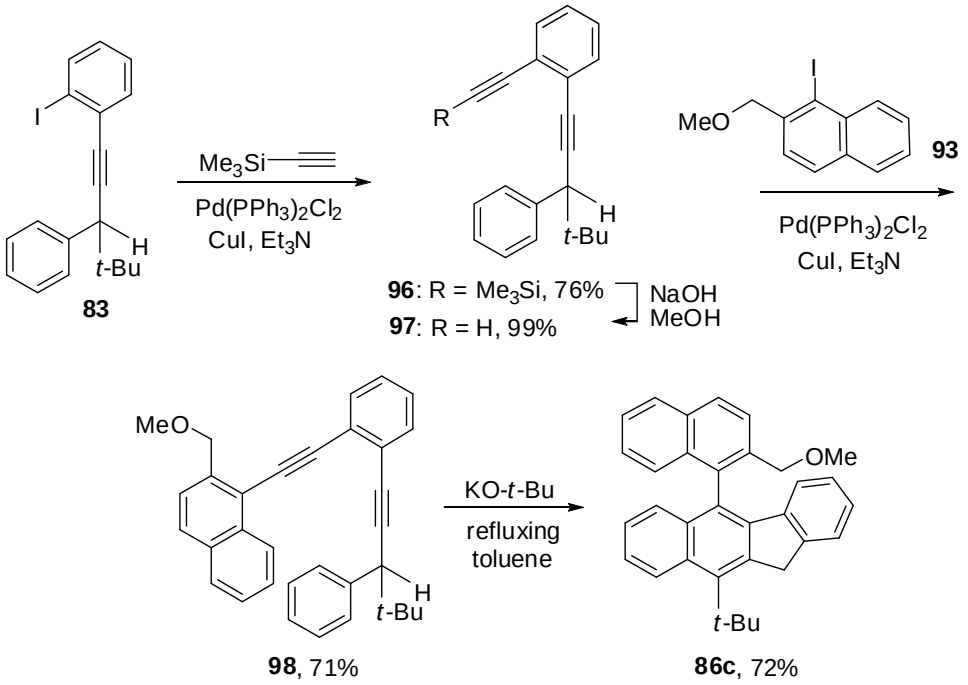


Scheme 18. Attempted synthetic pathway to acetylene **90**.



Scheme 19. Attempted synthetic pathway to TMS-acetylene **94**.

4.2.4 Synthesis of 1,1′-Binaphthyl 86c



Scheme 20. Revised synthetic route toward 1,1′-binaphthyl **86c**.

Again, with previously prepared iodide **83** in hand, the synthetic route was revised to conduct the Sonogashira reaction first with TMS-acetylene, followed by desilylation to give **97** (Scheme 20). The Sonogashira reaction between **97** and iodide **93** then afforded benzannulated enediyne **98**, which on exposure to the potassium *t*-butoxide in refluxing toluene was successfully converted to 1,1′-binaphthyl **86c**. It is worth noting that the synthetic sequences outlined in Schemes 17 and 20 represent new routes to 2,2′-disubstituted 1,1′-binaphthyls with the benzofluorenyl moiety newly constructed along the reaction pathways serving as one of the naphthyl groups.

4.3 NMR Studies of 1-Arylnaphthyl Derivatives and 1,1′-Binaphthyls

The ^{1}H NMR spectrum of **73a** in C_6D_6 recorded on a 600 MHz NMR spectrometer exhibited a set of AB quartet signals at δ 4.21 (J = 21.0 Hz) and 4.13 (J = 21.0 Hz), attributable to the methylene hydrogens on the five-membered ring (Figure 12). The AB quartet signals from

the methylene hydrogens were also observed in other similar 11*H*-benzo[*b*]fluorenyl structures.[7a, 8d,e,g] The AB pattern remained unchanged at 70 °C, suggesting a relatively slow rotation, on the NMR time scale, around the carbon−carbon single bond connecting the 2-methoxyphenyl substituent to the C5 of the benzofluorenyl moiety.

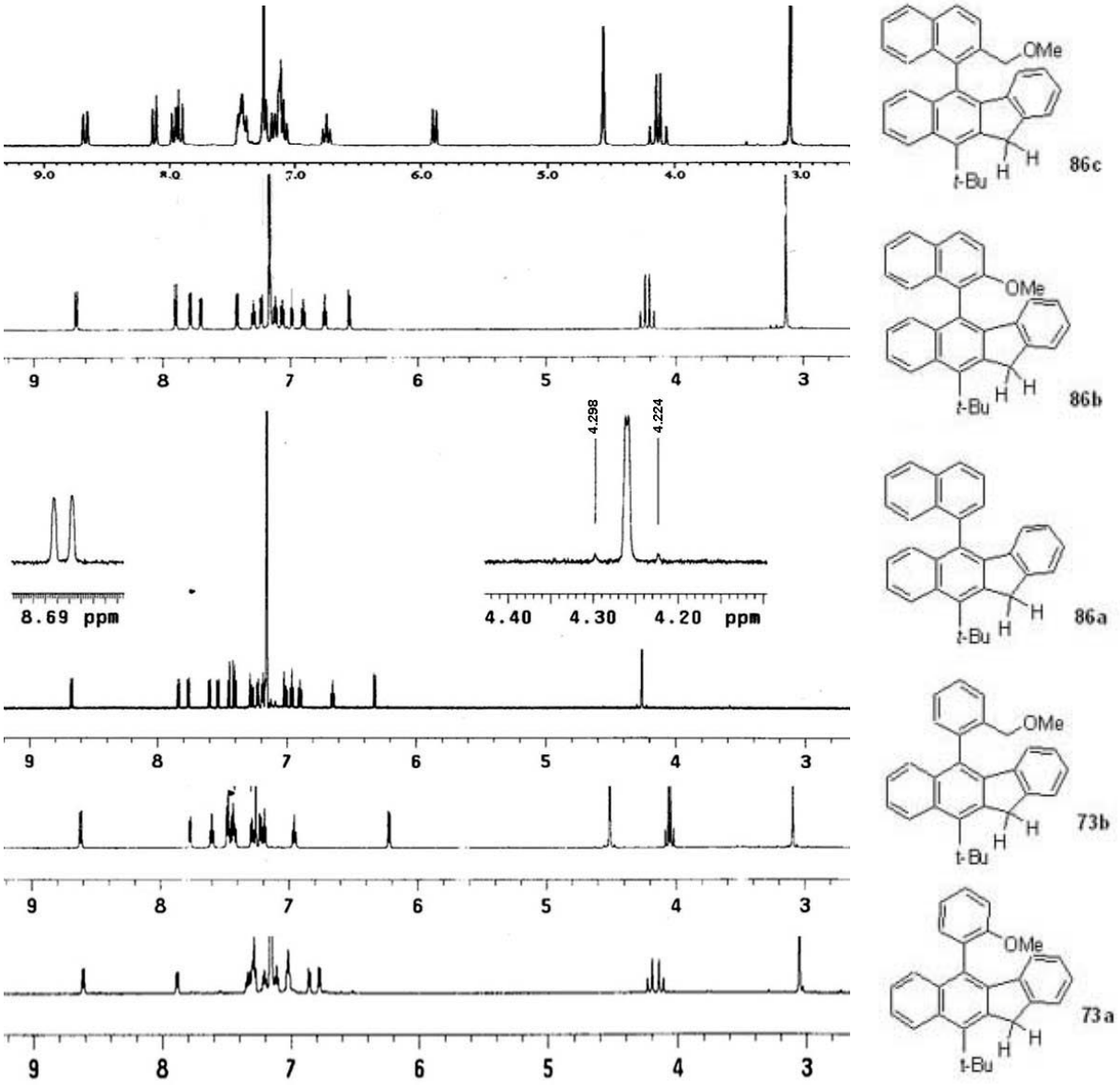


Figure 12. AB patterns of **73a**,**b**, and **86a**,**b**,**c** shown on the ^{1}H NMR spectra.

The rotational barrier is calculated to be at least 16.7 kcal/mol at 70 °C on the basis of the lack of coalescence of signals at this temperature. This lowest possible rotational barrier is

significantly higher than that of 1-phenylnaphthalene, which was calculated by MM2′ to be 12.4 kcal/mol.[30] Similarly, the ^{1}H NMR spectrum of **73b** taken in $CDCl_3$ showed a clear set of AB quartet signals at δ 4.07 (J = 13.8 Hz) and 4.04 (J = 13.8 Hz), attributable to the methylene hydrogens on the carbon attached with the methoxyl group. The signals of the methylene hydrogens on the five-membered ring could barely be discerned as AB quartets with the two inner signals overlapped at δ 4.51 and two small outer signals appeared at δ 4.55 and 4.47.

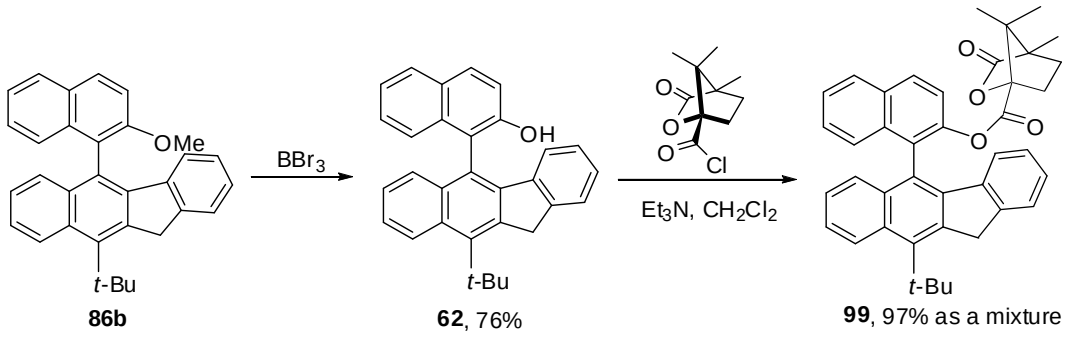
The rotational barrier of the parent 1,1′-binaphthyl in dimethylformamide was determined to be 23.5 kcal/mol at 50 °C, corresponding to a half-life of 14.5 minutes for racemization.[31] Because of the structure of **86a** could be regarded as a 2,3,4-trisubstituted 1,1′-binaphthyl, the rate of rotation can be expected to be even slower. Again, in C_6D_6 recorded on a 600 MHz NMR spectrometer, the signals of the methylene hydrogens on the five-membered ring could be discerned as AB quartets at δ 4.27 (J = 21 Hz) and 4.25 (J = 21 Hz).

The rotational barrier of BINOL as a member of the 2,2′-disubstituted 1,1′-binaphthyls was determined to be 37.2 kcal/mol at 195 °C in naphthalene, corresponding to a half-life of 4.5 hours for racemization.[31b] The high stability of the configuration even at such an elevated temperature allows BINOL to be used in a variety of synthetic applications. The configurational stability of **86b** and **86c**, which could be regarded as 2,2′-disubstituted 1,1′-binaphthyls with two additional substituents at the 3 and 4 positions, could also be expected to be high. The AB quartet signals were observed for the methylene hydrogens on the five-membered ring of **86b** and on the carbon bearing the methoxyl group of **86c**.

4.4 Resolution of 1,1′-Binaphthyl 86b

Treatment of **86b** with boron tribromide converted the methoxyl group to the hydroxyl group, providing a handle for resolution of **62** with (1*S*)-(−)-camphanoyl chloride (Scheme 21).[32] It was possible to achieve partial separation of a small fraction of the two diastereomeric

(1*S*)-camphanates with a 5:1 ratio by silica gel column chromatography shown on the ^{1}H NMR spectrum (Figure 13). From ^{1}H NMR spectrum, there are clear sets of AB quartets indicating the two methylene hydrogens on the five-membered ring with the ratio of 5:1. Attempts to separate the resulting diastereomers by using (1*S*)-(+)-10-camphorsulfonyl chloride or Mosher's reagent were unsuccessful.



86b **62**, 76% **99**, 97% as a mixture

Scheme 21. Resolution of 1,1′-binaphthyl **86b**.

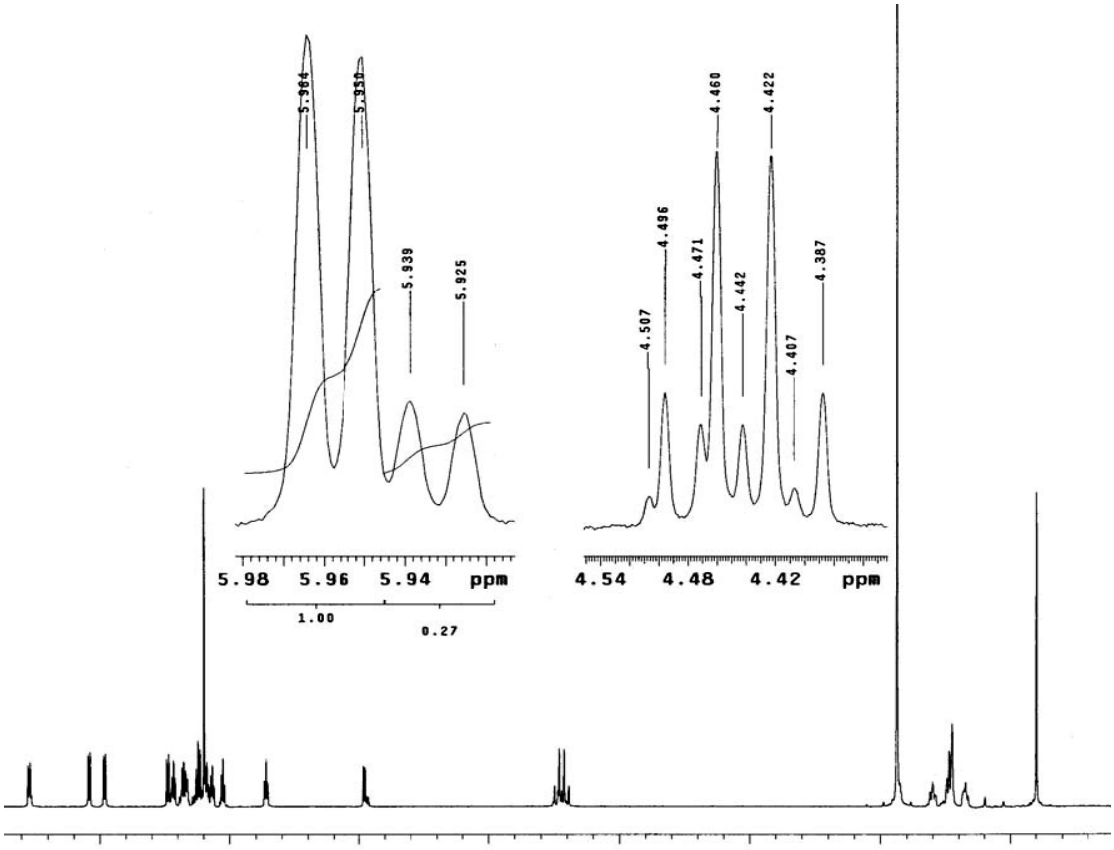
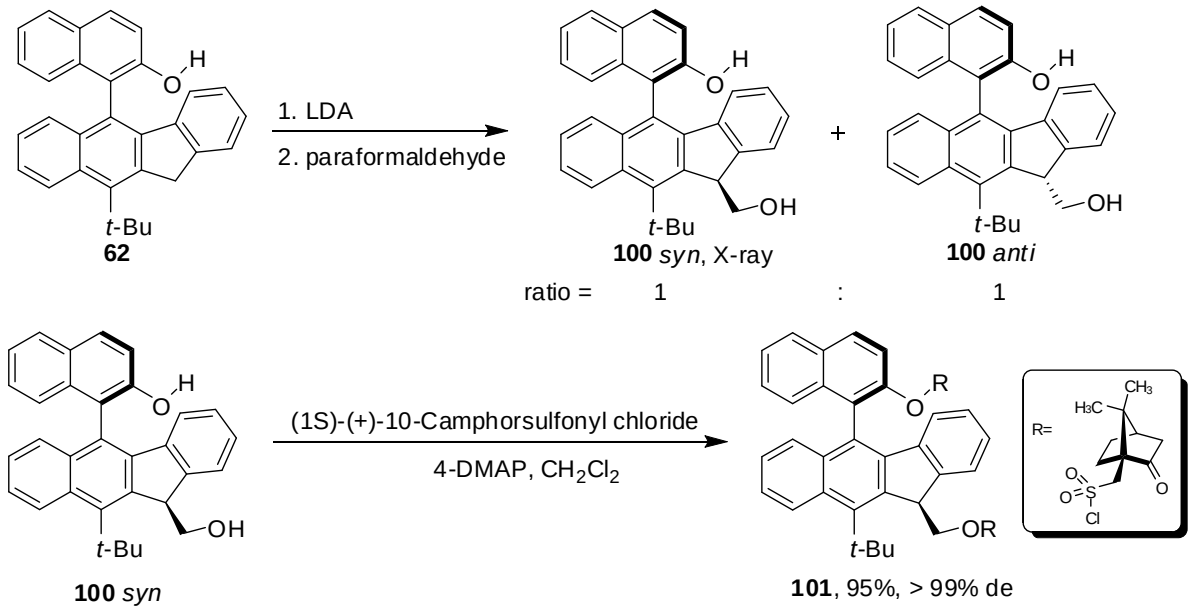


Figure 13. ^{1}H-NMR spectrum of partially separated (1*S*)-camphanates **99**.

The resolution was optimized by Cui Hu of our group by converting the methylene hydrogens to the corresponding primary alcohol to afford a 1:1 ratio mixture of the *syn* and *anti* isomers **100** (Scheme 22). Treatment of *syn*-diol **100** with (1*S*)-(+)-10-camphorsulfonyl chloride gave *syn* **100**-camphorsulfonate **101**, which can be separated by silica gel chromatography and found to be of high diastereomeric purity (> 99% de) in its ^{1}H NMR spectrum.



Scheme 22. Optimized synthetic route for the resolution of **62**.

5. Conclusions

In conclusion, the use of benzannulated enediynes as precursors of 2,2′-disubstituted 1,1′-binaphthyls represents a new synthetic approach to these sterically hindered molecules. The assembly of the enediynyl precursors from three separate aromatic fragments allows the possibility of placing a variety of functional groups at various positions of the 1,1′-binaphthyl system. Transformation of the methoxyl group in **86b** to a hydroxyl group provides a handle for resolution with optically active reagents.

CHAPTER III

Synthesis of a Novel Bowl-Shaped Polycyclic Aromatic Hydrocarbon Having a 54-Carbon Framework Represented on the Surface of C_{60}

1. Introduction

The discovery and continuous investigation of buckminsterfullerene (C_{60}),[33] also called "buckyball", has aroused considerable interest in bowl-shaped polycyclic aromatic hydrocarbons (PAHs) and stimulated the development of new synthetic designs for their preparation over the last two decades. In 1996, Kroto, Curl, and Smalley, were awarded the Nobel Prize in chemistry by discovering the first closed geodesic polyarene C_{60}.[34] Open geodesic bowl-shaped PAHs, referred to as "buckybowls" or "fullerene fragments", comprise five- and six-membered rings, which can be mapped onto the surface of C_{60}. Several examples of these curved hydrocarbons, such as corannulene **102** ($C_{20}H_{10}$),[35] sumanene **103** ($C_{21}H_{12}$),[36] hemibuckminsterfullerene **104** ($C_{30}H_{12}$),[37] circumtrindene **105** ($C_{36}H_{12}$)[38] and indeno[*bc*]-circumtrindene ($C_{42}H_{14}$)[39] have been accessed and characterized by either conventional organic techniques[40] or using efficient flash vacuum pyrolysis (FVP)[41] (Figure 14). PAHs **105** and **106** which represent 60 and 70% of the C_{60} are the largest fullerene fragments synthesized up until 2006.

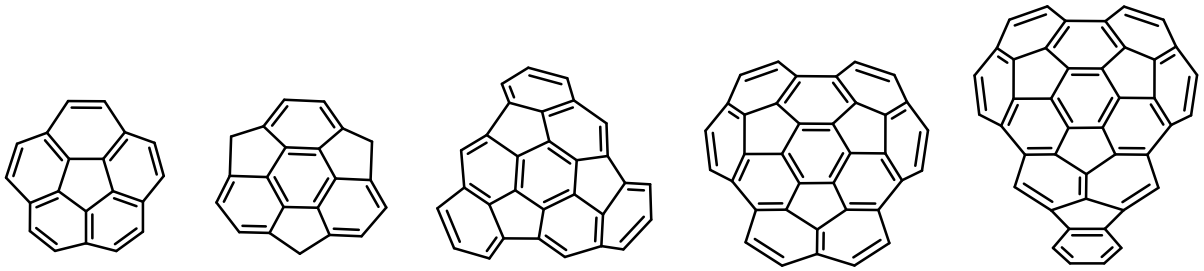


Figure 14. Representative examples of buckybowls.

In 2007, Scott *et al.* reported the syntheses of indenocorannulenes **107** and **108**, the largest curved subunits of C_{60} with curvatures surpassing that of C_{60} (Figure 15). This achievement demonstrates unequivocally that rational synthetic method toward bowl-shaped PAHs by exclusively solution chemical methods is accessible and high-temperature vacuum pyrolysis method is no longer necessary.[42]

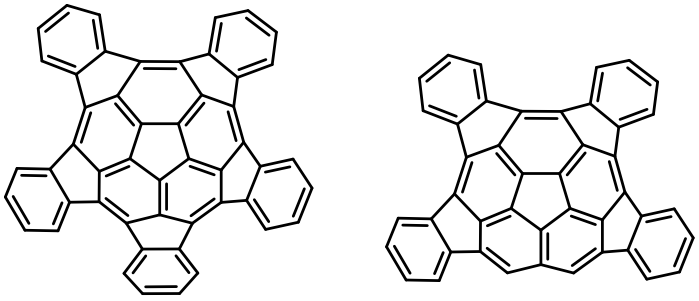


Figure 15. The largest buckybowls.

These bowl-shaped PAHs can serve as potential precursors of buckyball and related carbon cages. The most intriguing property of buckybowls is its electron-holding capability, which could further facilitate the invention of plastic batteries.[43] For example, corannulene has the ability to accommodate up to four electrons to form a tetraanions. In addition, the outside (convex or *exo*) and the inside (concave or *endo*) unsaturated carbon surfaces could exhibit different physical and chemical properties. The more readily accessible concave surface of buckybowls provide opportunity for metal binding to mimic the endohedral chemistry of the spherical cluster.[44] Also, they have rim or edge carbon atoms capped by hydrogen atoms for coordination, allowing buckybowls to possess multi-site coordination possibilities and preferences for metal binding. These appealing features of buckybowls could open new routes toward synthesis of fullerenes or nanotube inclusion complexes,[45] which are of great interest for future applications such as drug delivery,[46] molecular container, medical imaging,[47] sieving

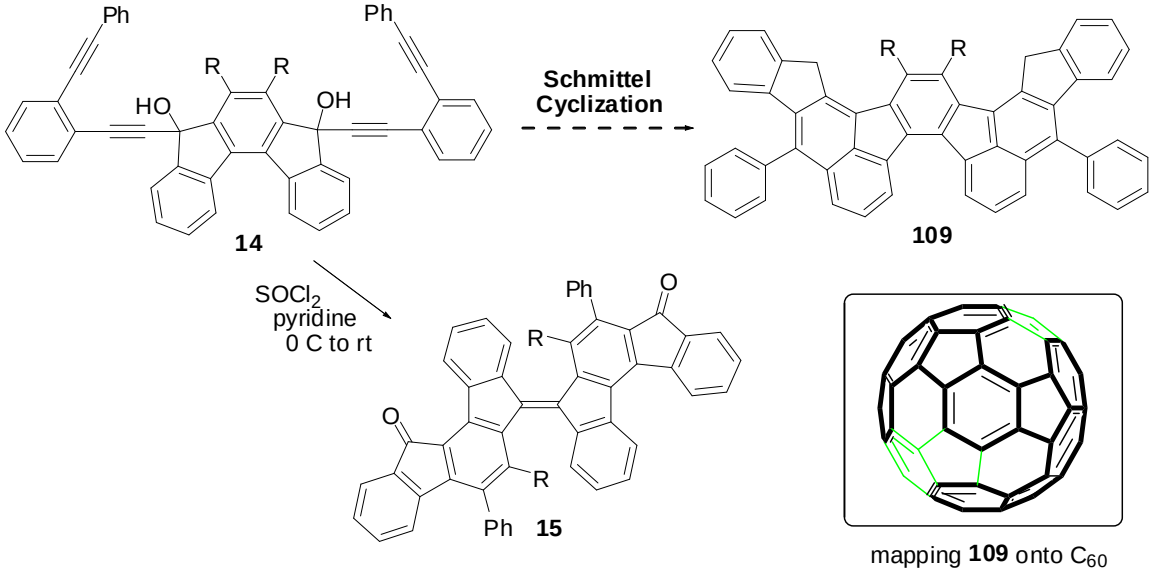
systems and catalysis.[48]

Because buckybowls hold many promising potentials for applications in a variety of areas, it has attracted the attention of many researchers in trying to develop new synthetic pathways toward these bowl-shaped polycyclic hydrocarbons. The first synthesis of corannulene, the smallest subunit of buckybowl on the surface of C_{60}, was reported by Barth and Lawton in 1966.[35a] Their 16-step synthesis was a remarkable achievement which demonstrated the feasibility of synthesizing such bowl-shaped PAHs by non-pyrolytic pathways.[35b] Twenty five years later in 1991, the flash vacuum pyrolysis (FVP) [35g] as a new strategy for the synthesis of corannulene was reported. The process required only three steps for the synthesis of corannulene and provided a more direct access toward many other bowl-shaped PAH targets that were previously considered difficult to prepare by other methods. However, under the high-temperature (1000 ^{o}C or higher) conditions, the buckybowl precursors with more delicate structures may not survive. As a consequence, recent efforts have turned toward the development of practical, non-pyrolytic and milder synthetic methods for the construction of buckybowls in order to realize the full potential of this emerging new field.

2. Research Objective

As a part of our continuing efforts toward the synthesis of polycyclic hydrocarbons via Schmittel cyclization reaction of enyne−allenes, we envisioned that this biradical cascade reaction pathway could lead to a variety of polycyclic aromatics as potential buckybowl precursors. Dr. Yonghong Yang of our research group reported the use of thionyl chloride to promote Schmittel cyclization of diol **14** having two benzannulated enyne−allene units.[8a] It was assumed that the Schmittel cyclization reaction of **14** would give the desired polycyclic hydrocarbon **109**, which has a 52-carbon framework represented on the surface of C_{60} (Scheme 23) and may eventually lead to the formation of a bowl-shaped polycyclic aromatic hydrocarbon.

Unexpectedly, the cleavage of the central benzene ring occurred during the cyclization sequence to give the highly twisted 1,1′-dialkyl-9,9′-bifluorenylidene **15**.



Scheme 23. Schmittel cyclization of diol **14**.

We envisioned an alternative approach to buckybowls by incorporating sp^3-hybridized carbons in the precursors (Figure 16). There are several potential advantages of such an approach. The presence of sp^3-hybridized carbons could greatly relieve the strain of buckybowl structures. They would also allow the intramolecular carbon−carbon formation more feasible. These sp^3-hybridized carbons could permit attaching additional functional groups onto the carbon frameworks of buckybowls.

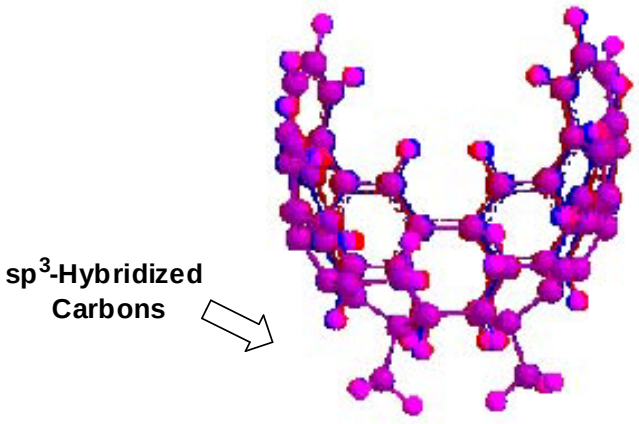


Figure 16. A buckybowl containing sp^3-carbons.

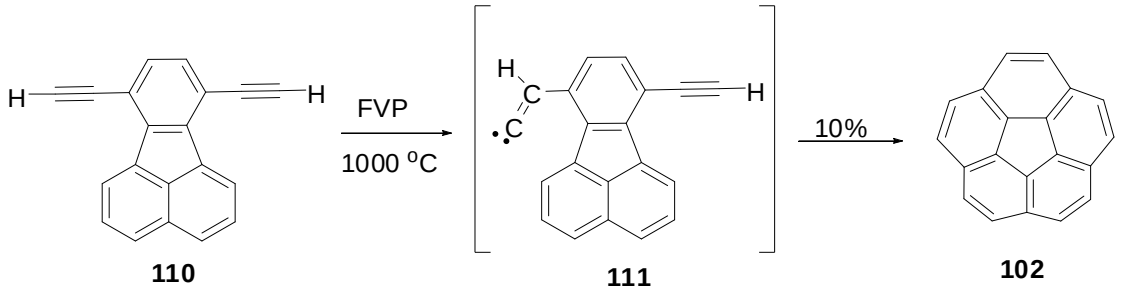
3. Literature Survey of Synthesis of Buckybowls, Coordination Chemistry of Buckybowls and Fluorenyl Ligands and Molecular Tweezers

3.1 Synthesis of Buckybowls

The synthesis of fullerene C_{60} by rational or controlled means has been a challenge for organic chemists since 1985. The considerable attention given to C_{60} has led to renewed interest in the bowl-shaped polycyclic aromatic hydrocarbons. The first synthesis of the smallest buckybowl, corannulene, was achieved by Barth and Lawton in 1966 by using classic functional group transformations and catalytic dehydration.[35a,b] Twenty five years later, a new synthesis of corannulene by flash vacuum pyrolysis (FVP) was reported by Scott *et al.*[35g] in 1991. To date, over two dozen buckybowls have been prepared and developed by either FVP or non-pyrolytic pathway.

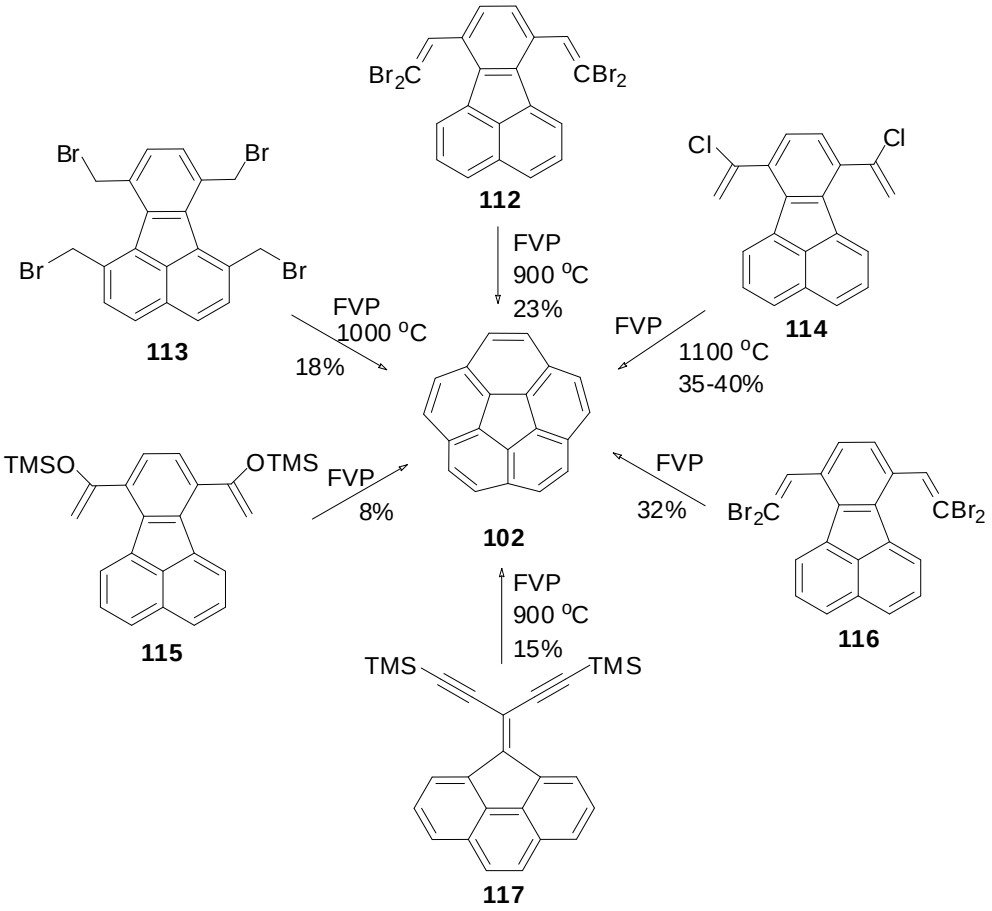
3.1.1 Flash Vacuum Pyrolysis (FVP)

In 1991, Scott *et al.* first reported the strategy of employing flat PAHs under thermal condition for C−C bond formation at the rim to form curved buckybowls (Scheme 24). Presumably, by proceeding via carbene **111**, the starting **110** was converted to corannulene **102** in 10% yield. The low yield was due to polymerization of diyne **110** under the harsh thermal reaction condition.[35g]



Scheme 24. The first FVP synthesis of corannulene.

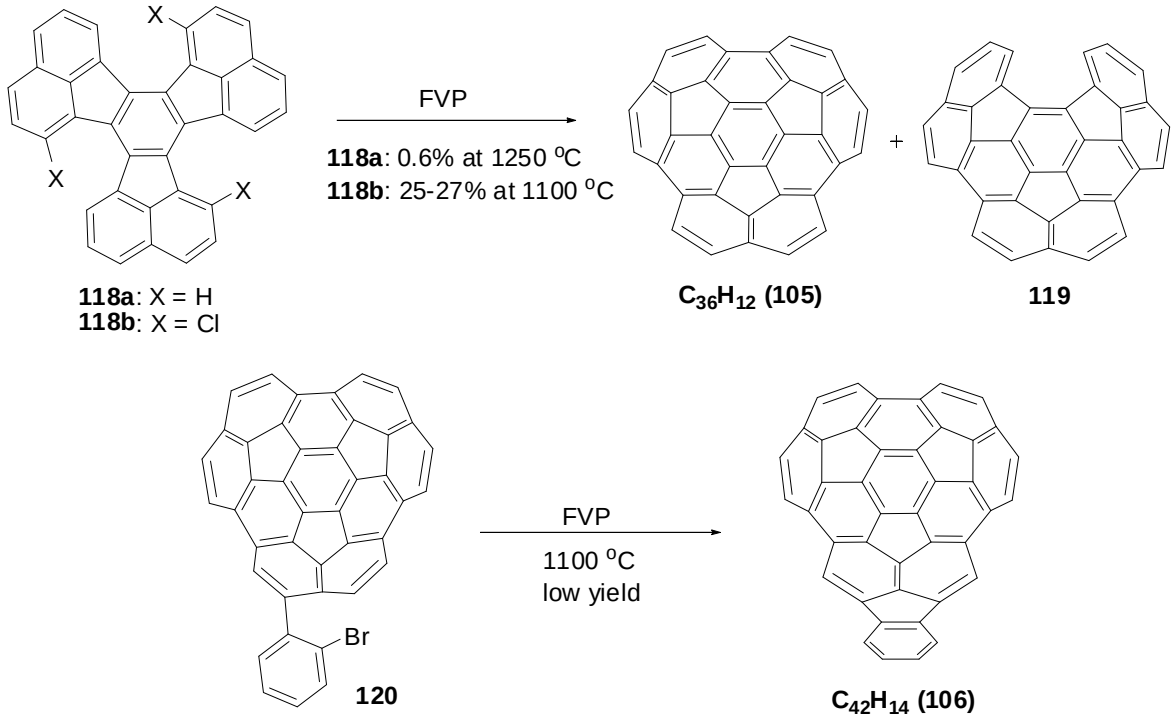
By using FVP, various precursors **112**−**117** were converted to corannulene (Scheme 25). The precursors **112**[35c]**, 114**[35j]**,** and **115**[35e] could be regarded as "masked acetylene (**110**)", which were less prone to polymerization and provide better yields. The key to the success of these strategies is to start with a precursor containing a properly fused central five-membered ring for FVP.



Scheme 25. Various syntheses toward corannulene via FVP.

Some larger fullerene fragments, such as **105** and **106,** were obtained by using the FVP method (Scheme 26). The commercially available decacyclene **118a** underwent a triple cyclodehydrogenation under FVP at 1200–1300 °C to give circumtrindene **105** in low yield along with a comparable quantity of byproduct **119**.[38a,40] The synthesis of circumtrindene was dramatically improved by starting with precursor trichlrodecacyclene **118b** under lower temperature for FVP.[39c] In addition, the open geodesic PAHs can be expanded to contain 70% of

C_{60} by FVP of a 2-bromophenyl-substituted bowl **120**, which can be prepared from monobromination of **105** followed by Suzuki–Miyaura coupling to yield an unseparable small amount of **106** together with a large amount of **105**.[40]

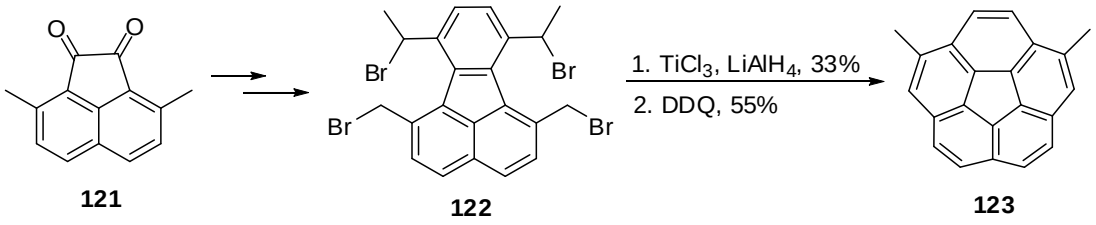


Scheme 26. Syntheses of larger buckybowls **105** and **106**.

The experimental results have shown that the FVP method is a useful and efficient synthetic tool for the construction of buckybowls in moderate to low yields. However, the limitations of the method include low yield, many byproducts, difficulty to scale up, lack of functional group tolerance, and not applicable to nonvolatile systems.[49]

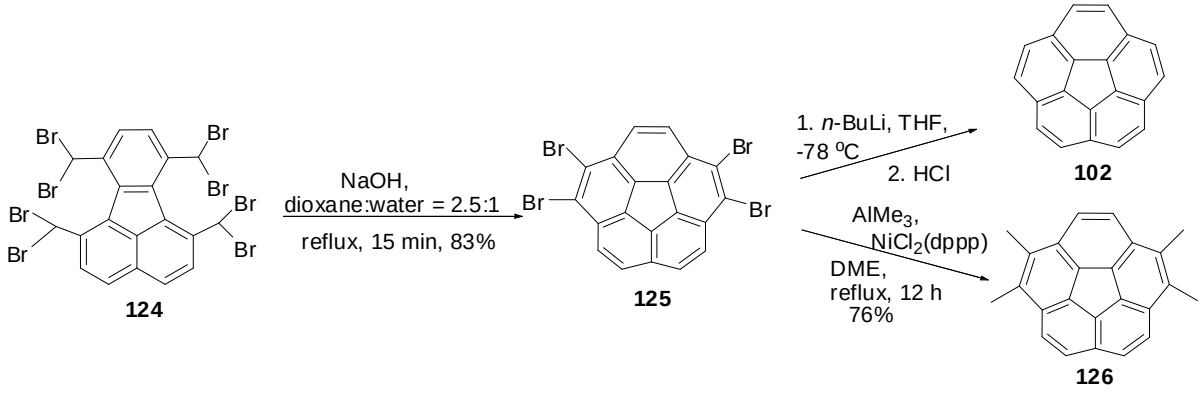
3.1.2 Non-pyrolytic Pathways

In 1996, Siegel *et al.* reported the first non-pyrolytic synthesis of corannulene derivatives by employing the McMurry-type reductive coupling of **122** with $TiCl_3/LiAlH_4$ or $VCl_3/LiAlH_4$ followed by DDQ dehydrogenation to give dimethylcorannulene **123**. (Scheme 27).[40a] Later on, this methodology was utilized for preparation of several more complex corannulene derivatives by the Siegel and Rabideau's groups.[40b-d]



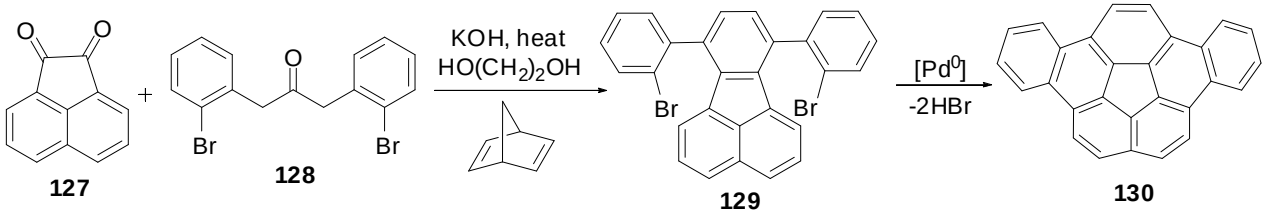
Scheme 27. Siegel's non-pyrolytic approach to dimethylcorannulene **123**.

In 2000, Rabideau *et al.* reported a new non-pyrolytic synthesis of corannulene and its derivatives in a convenient and inexpensive way by simply refluxing **124** under a mild condition in the presence of a small amount of NaOH in aqueous dioxane (Scheme 28).[40g,50]



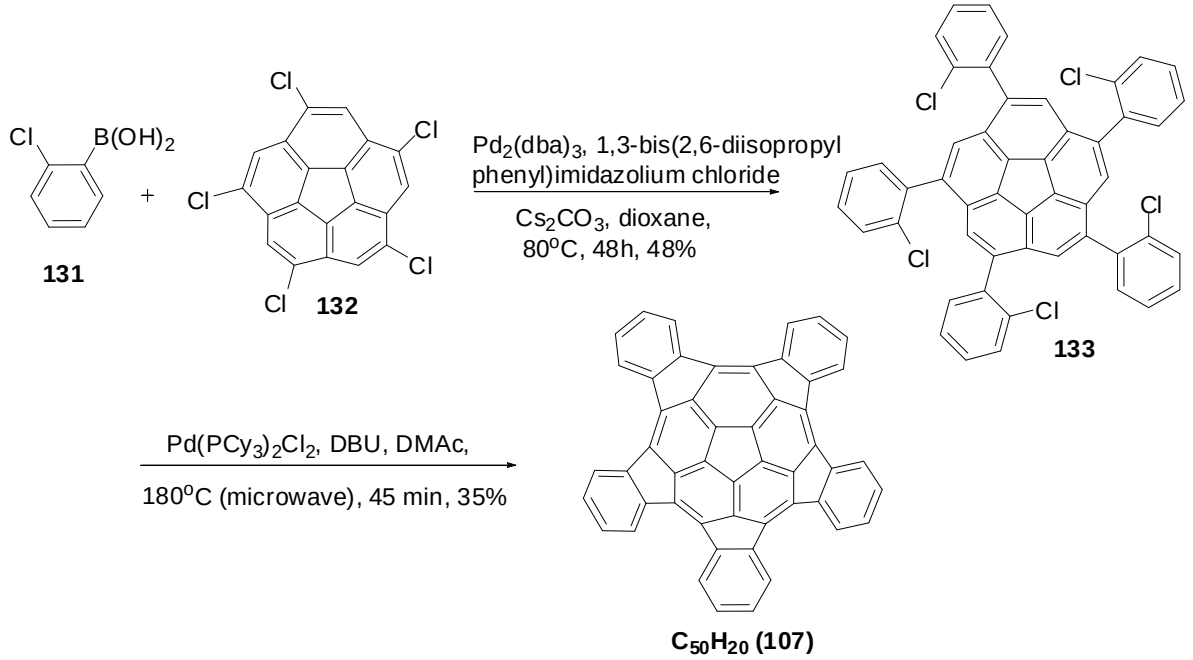
Scheme 28. Rabideau's approach toward corannulene derivatives **125** and **126**.

Scott *et al.* also reported a three-step synthesis of dibenzo[*a*,*g*]corannulene by employing palladium-catalyzed intramolecular arylation reaction (Scheme 29).[40e] At 150 °C dibromide **129** was converted to the bowl-shaped PAH **130** in 60% yield using a suitable palladium catalyst and DBU in DMF for 3 days.



Scheme 29. Scott's non-pyrolytic approach to dibenzocorannulene **130**.

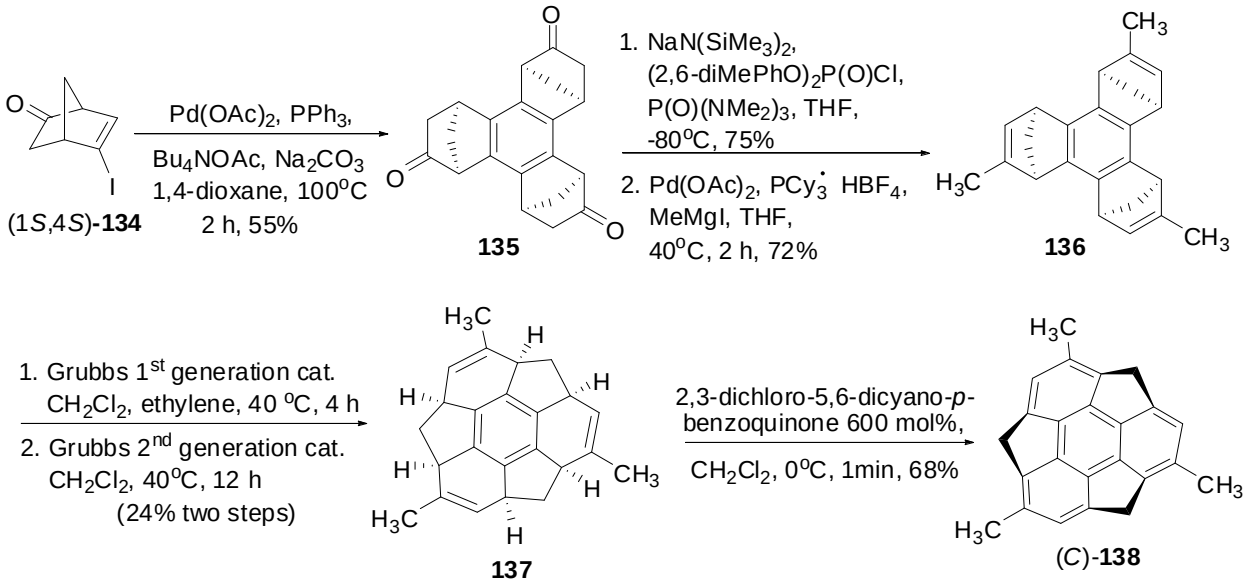
In 2007, Scott *et al.* reported the synthesis of the largest fullerene fragment (**107**, $C_{50}H_{20}$) of C_{60} via a non-pyrolytic pathway involving a five-fold Suzuki−Miyaura coupling of chlorinated corannulene **132** with 2-chlorophenylboronic acid **131** under the condition reported by Nolan *et al.*[51] to give **133** (Scheme 30).[42] By microwave heating, the subsequent palladium-catalyzed intramolecular arylation reactions of **133** furnished pentaindenocorannulene **107**.



Scheme 30. Scott's non-pyrolytic route to the largest bowckybowl **107**.

Most recently, Sakurai *et al.* reported the first asymmetric synthesis of a chiral buckybowl, (*C*)-(*M*)-8,13,18-trimethylsumanene (**138**), by a non-pyrolytic synthetic pathway (Scheme 31).[52] The synthetic strategy involved the use of sp^3 chiral halonorborene **134**, which underwent cyclotrimerization to give *syn*-benzocyclotrimer **135**. A subsequent conversion of carbonyl groups to the methyl olefins was accomplished by cross−coupling with MeMgI of the corresponding alkenyl phosphates to afford **136**. Then tandem ring-opening/closing olefin metathesis with a Grubbs catalyst successfully afforded the bowled-shaped structure **137**, which

is chiral. The final key aromatization step was carried out at a low temperature to give chiral buckybowl (*C*)-**138**.



Scheme 31. Sakurai's asymmetric synthesis of chiral buckybowl **138**.

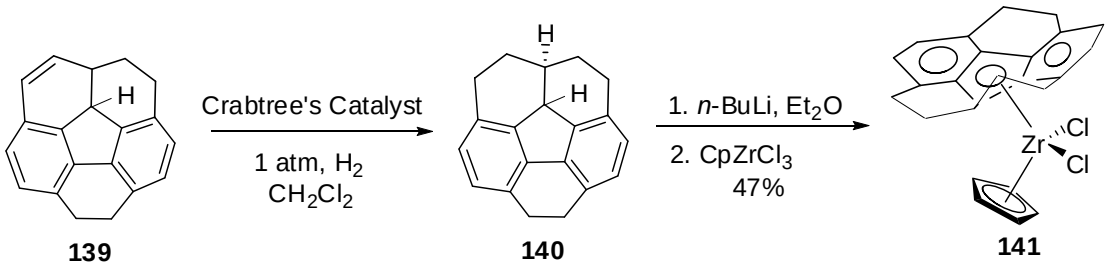
3.2 Coordination Chemistry of Buckybowls and Fluorenyl Ligands

Buckybowls with two distinct concave and convex surfaces have attracted substantial attention for the investigation of transition-metal complexes of bowl-shaped polycyclic aromatic hydrocarbons in recent years.[53,54] Unlike the characterized transition-metal fullerene complexes where C_{60} serves as an electron-deficient polyalkene and the metal atom is attached in an η^2-fashion to the fused carbon–carbon bond of two six-membered rings, buckybowls having a readily accessible internal surface can give rise to π systems with different coordination fashions ($\eta^2 \rightarrow \eta^6$) for transition-metal complexes.

In the studies of transition-metal coordination with the smallest buckybowl, corannulene, there are three major types of corannulene complexes observed: one is η^2-coordinated; the other is η^6-coordinated metal; [54] another is where the metal σ-bonded to the rim carbon atom. The first η^6-coordinated transition metal complex of corannulene, [Cp*Ru(η^6-$C_{20}H_{10}$)](O_3SCF_3) was

reported by Seiders *et al.* in 1997.[55] Since then, many research groups have reported the synthesis of various η^6-coordinated transition metal complexes, such as $[(Cp^*Ru)_2(\mu_2\text{-}\eta^6\text{:}\eta^6\text{-}C_{20}H_{10})][X]_2$ (X = BF_4^-, PF_6^-, or SbF_6^-)[56] and $[Cp^*Ir(\eta^6\text{-}C_{20}H_{10})][BF_4]_2$.[57] The η^2-coordinated corannulene complexes, such as $[Rh_2(O_2CCF_3)_4]\bullet(C_{20}H_{10})$ and $Ru_2(O_2CCF_3)_2(CO)_4\bullet(\eta^2\text{-}C_{20}H_{10})_2$, were prepared and characterized by X-ray structural analyses.[58] In addition, there are several examples of complexes where a hydrogen of corannulene was replaced by a metal, such as $(\eta^1\text{-}C_{20}H_9)Ni(PEt_3)_2Br$.[59]

In addition to the π-system coordinated corannulene complexes, an interesting was reported by Chin *et al.* showed that a partially hydrogenated corannulene **139**[43d] can function as a curved fluorenyl anion analogue with unique curvature as a ligand (Scheme 32).[60a] By employing Crabtree's catalyst under 1 atm of hydrogen, **139** was hydrogenated to octahydrocorannulene **140**, which was deprotonated with *n*-BuLi followed by treatment with $CpZrCl_3$ to afford complex **141**. It is worth noting that the Zr–C bond length ranges from 2.46 to 2.60 Å, which is about the same as other zirconium fluorenyl complexes.[60b-d] Also, the bond angle of $C_{20}H_{17}$(C)–Zr–Cp(C) is 128.8º, which is also similar to other reported fluorenyl Cp complexes (129.8–131.2 º).

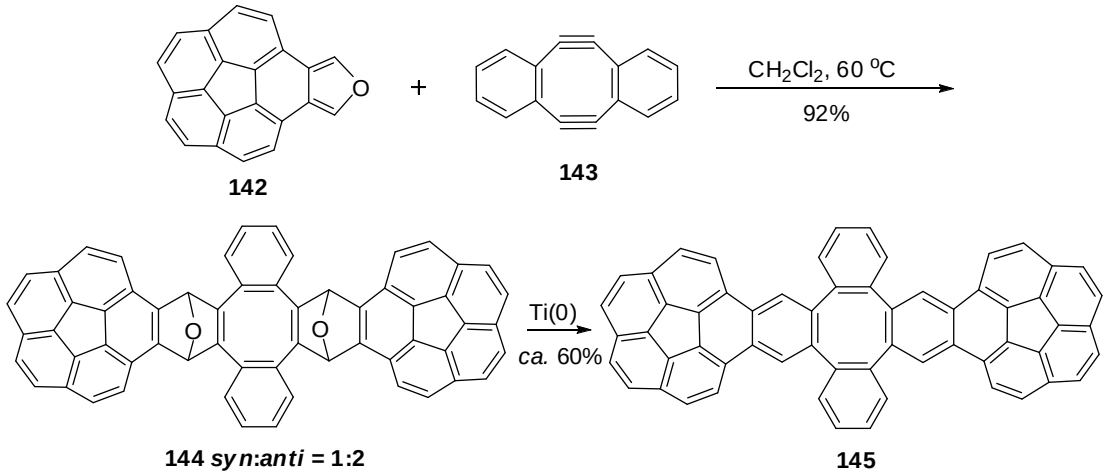


Scheme 32. Chin's zirconium complex **141** containing a fluorenyl ligand.

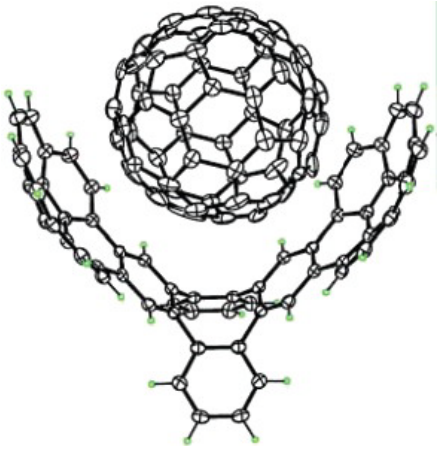
3.3 Molecular Tweezers

Buckybowls having an open curved π interior cavity can be ideal candidates to serve for molecular receptors such as molecular tweezers,[61] also referred to as "molecular clips" to bind

the guest molecules by non-covalent bonding including hydrogen bonding, metal coordination, and π–π interactions.[62] In 2007, Sygula *et al.* reported the synthesis of a $C_{60}H_{24}$ molecular tweezer **145** possessing double concave corannulene subunits, which can catch a C_{60} to form a concave−convex π–π interaction complex in a 1:1 inclusion (Scheme 33).[63] The complexation was also confirmed by X-ray structural analysis. The study is an excellent example of rich supramolecular chemistry[64] of buckybowls and related materials (Figure 17).



Scheme 33. The synthesis of double concave hydrocarbon buckycatcher **145**.



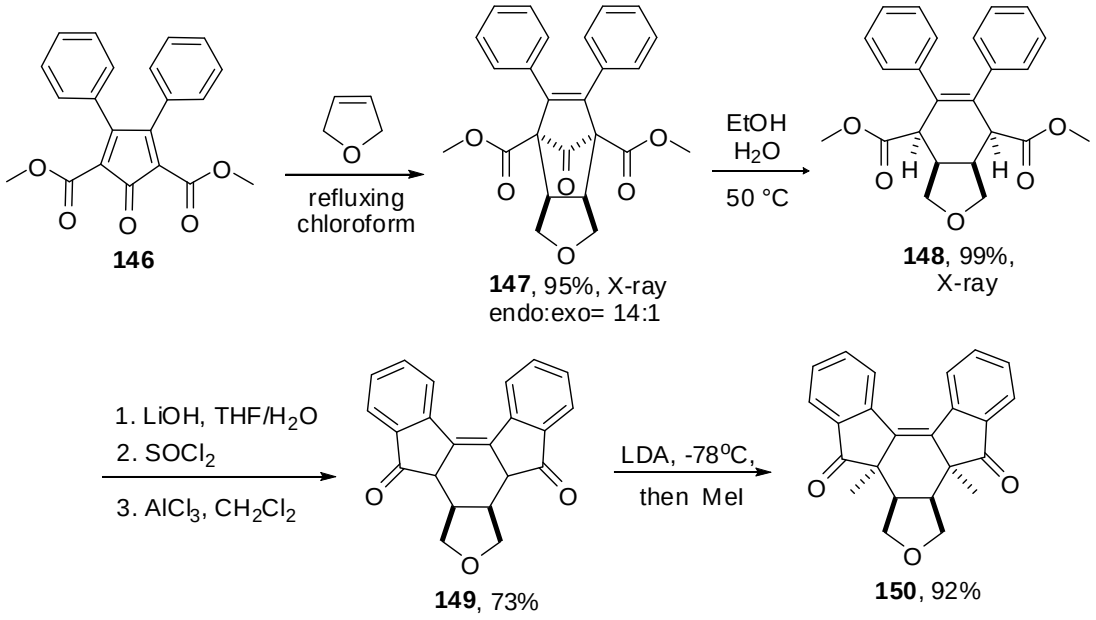
(Sygula *et al. J. Am. Chem. Soc.* **2007**, *129*, 3842−3843)

Figure 17. ORTEP X-ray structure of 1:1 inclusion complex of C_{60} and **145**.

4 Results and Discussion

4.1 Preparation of Precursor Diketone 150

Dr. Hua Yang of our group initiated a research project involving the development of new synthetic pathways toward bowl-shaped polycyclic aromatic hydrocarbon with a 54-carbon framework represented on the surface of C_{60}.[65] Herein, a continuing investigation with optimized yields and alternative pathways is reported leading to a buckybowl having a 54-carbon framework of C_{60}. The synthetic sequence starts with 2,5-dicarbomethoxy-3,4-diphenylcyclopentadienone (**146),**[66] which underwent a Diels-Alder reaction with 2,5-dihydrofuran to furnish the *endo*-cycloadduct **147** as the major product in 95% yield (Scheme 34). The structure of **147** was elucidated by X-ray structure analysis. A subsequent decarbonylation of **147** was achieved with excellent yield to give **148** by stirring in a mixture of methylene chloride/ethanol/water at 50 ^{o}C for 1 day.

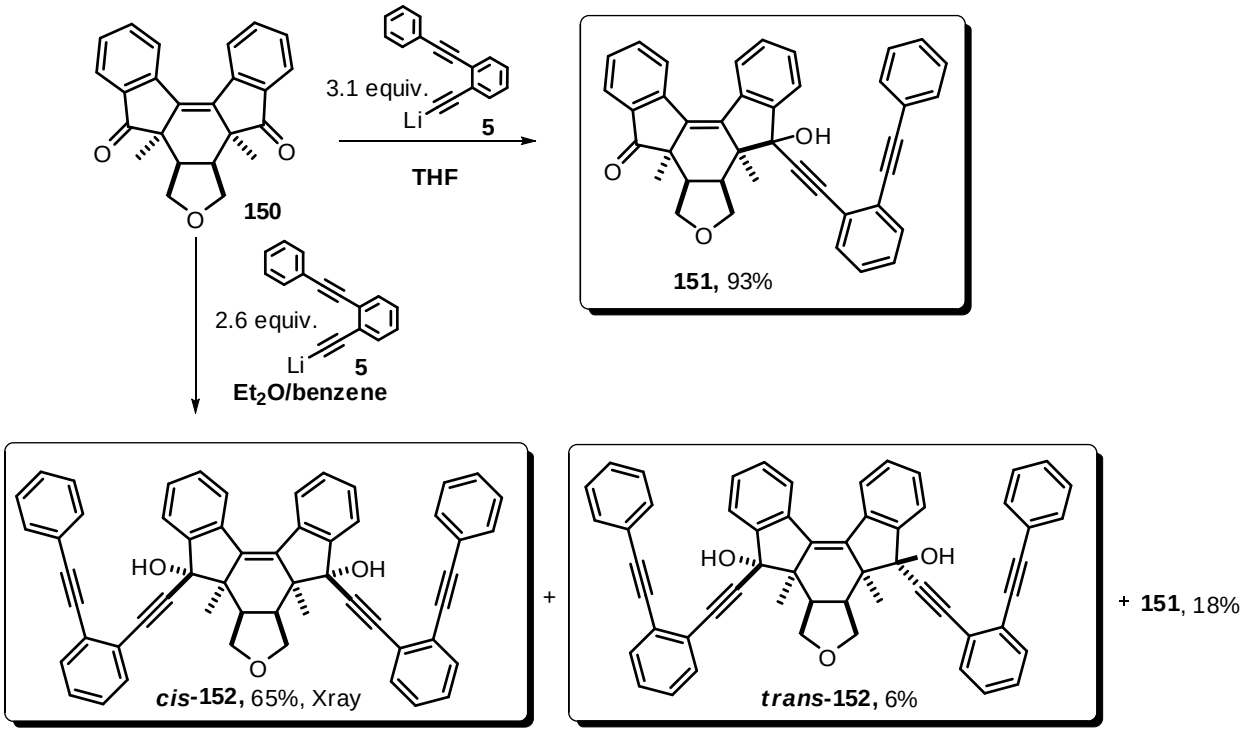


Scheme 34. Preparation of precursor diketone **150**.

As far as we know, this type of water-catalyzed decarbonylation has never been reported before. The structure of **148** was also established by X-ray structure analysis.[65] The X-ray structure shows that the four hydrogens on the cyclohexenyl ring are *cis* to one another.

Hydrolysis of diester **148** by treatment with an excess of aqueous LiOH solution in refluxing THF for 18 h followed by acidification with 1 M HCl afforded the corresponding diacid. The crude diacid was treated with thionyl chloride under reflux to yield the corresponding diacid chloride, which underwent two Friedel-Crafts reactions to give **149** in 73% overall yield in three steps. The following double methylation of **149** by LDA and iodomethane led to the desired precursor diketone **150** in 92% yield.

4.2 Condensation of Diketone 150



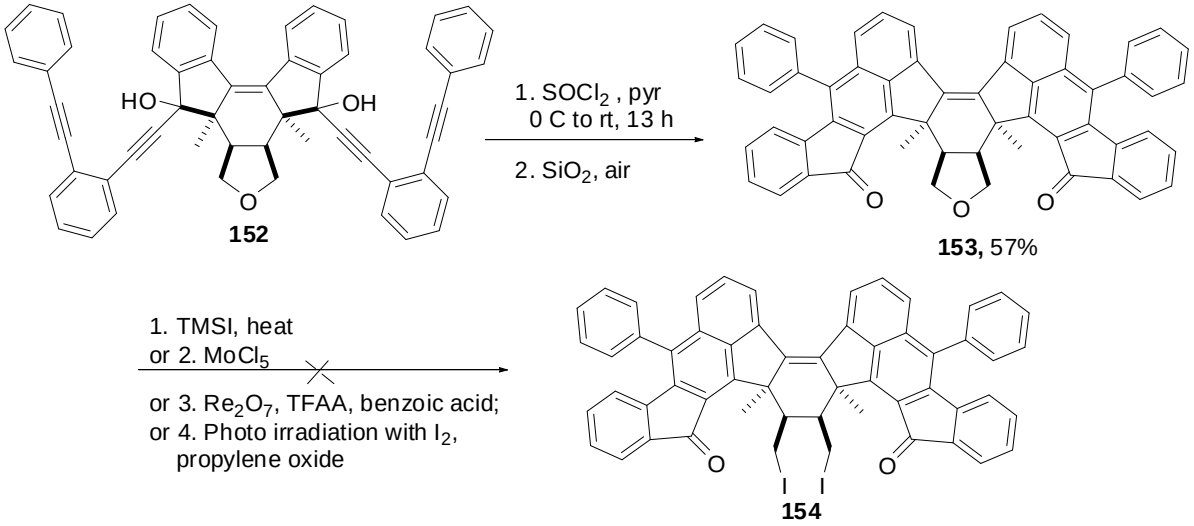
Scheme 35. Condensation of diketone **150** and acetylide **5**.

Condensation between diketone **150** and 3.1 equiv of lithium acetylide **5** in THF produced the benzannulated enediynyl propargylic alcohol **151** in 91% yield (Scheme 35).

Interestingly, when solvent was changed to a combination of diethyl ether and benzene, both carbonyl groups can be converted to propargylic alcohol to give a mixture of *cis*/*trans* isomers **152** in 10:1 ratio as well as a **151**.

4.3 Schmittel Cyclization of 152 and Furan-ring Opening

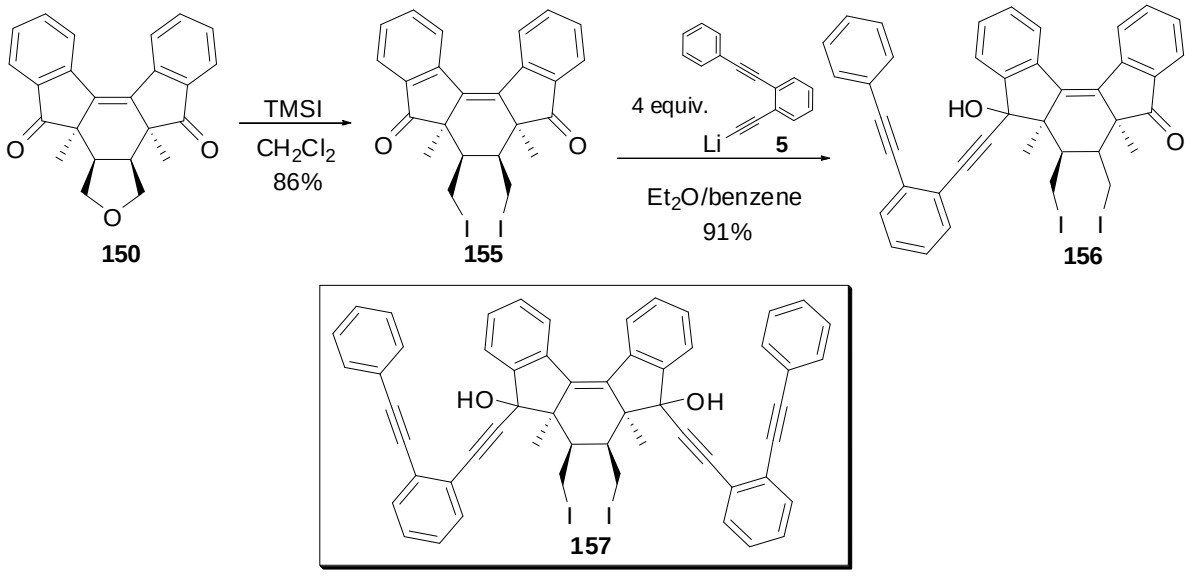
Dr. Yang reported that a C^2–C^6 Schmittel cyclization of diol **152** promoted by thionyl chloride followed by silica gel chromatography led to diketone **153** in 57% yield.[65] The structure of **153** was established by X-ray structure analysis (Scheme 36). Unfortunately, all the attempts toward the opening of furan ring[67] under a variety of reaction conditions, such as heating in TMSI, diiodosilane (DIS), cleavage with transition metals, and photo irradiation were all unsuccessful. Interestingly, treatment of **153** with DIS, the two carbonyl groups in **153** were completely reduced to the methylene groups which were confirmed by ^{1}H NMR spectrum from previous synthetic work.[65] From the X-ray structure of **153**, it was clear that the central cyclohexenyl group with four sp^3-hybridized carbons causes the furan ring to fold inside, preventing ring opening by trimethylsilyl iodide.



Scheme 36. Attempts toward the furan ring opening of **153**.

4.4 Alternative Route Toward Diol 157

Since all the attempts toward furan ring opening failed, we revised the synthetic route by opening the furan ring at an early synthetic stage. Conversion of **150** to diiodide **155** was achieved in 86% yield (Scheme 37). Unfortunately, the following condensation between **155** and lithium acetylide **5** only led to the mono-propargylic alcohol **156** even in the solvent combination of ether and benzene or other condition such as cerium acetylide. The expected diol **157** was not observed. Examining the 3D structural modeling of **156** showed that the steric interactions between two iodide substitutes causes one iodide to sit in the axial position while the other in the equatorial position. The one in the axial position completely blocked the neighboring carbonyl group from being attacked by the acetylide **5**.

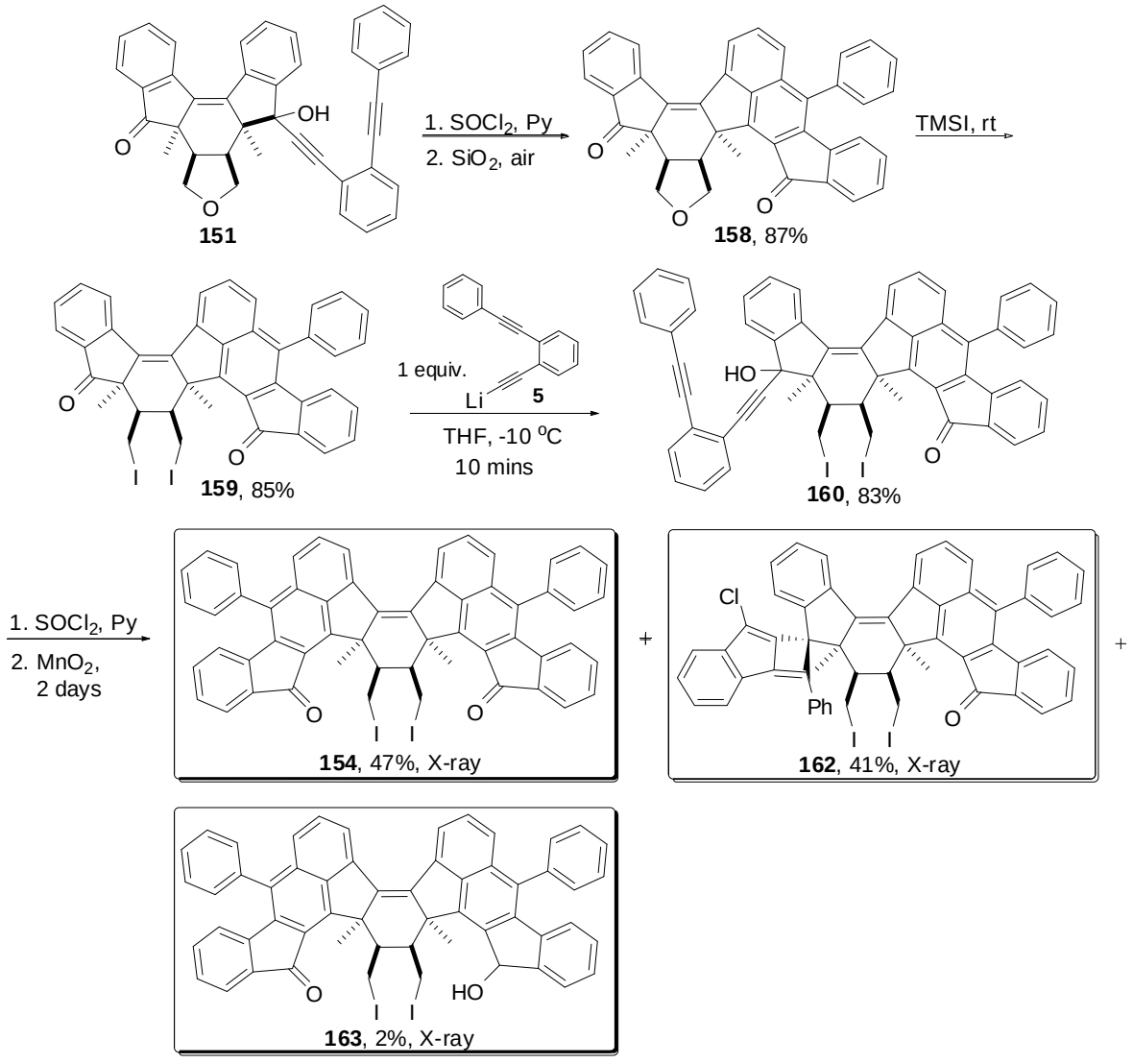


Scheme 37. Attempted synthetic route toward diol **157**.

4.5. Revised Synthetic Pathway Toward I_2-Diketone 154

As an alternative synthetic pathway, we envisioned that by employing a stepwise cyclization of one side of propargylic alcohol followed by a second condensation and cyclization could lead to **154**. A Schmittel cyclization of mono-propargylic alcohol **151** promoted by thionyl chloride followed by silica gel chromatography produced diketone **158** (Scheme 38). The furan

ring of **158** was successfully opened by stirring with TMSI at room temperature to afford diiodide **159** in 85% yield.



Scheme 38. Revised synthetic pathway toward I_2-diketone **154**.

We envisioned that the two carbonyl groups in **159** have different steric environments, which could allow selective condensation with lithium acetylide **5**. Fortunately, a regio-selective condensation was successfully achieved by a treatment with 1 equiv of lithium acetylide stirring at –10 ^{o}C for 10 minutes to give the desired propargylic alcohol **160** in 83% yield. The structure of **160** was confirmed by ^{13}C NMR spectrum with the carbonyl carbon signal at δ 203 belonging

to the fluorenyl keto group disappears while the carbonyl carbon signal at δ 193 of the benzofluorenyl group still remains.

On exposure to thionyl chloride followed by oxidation with MnO_2 for two days, propargylic alcohol **160** was converted to three products, including the desired I_2-diketone **154**, spiro [2 + 2] adduct **162**, and a trace amount of mono-alcohol **163**. Alcohol **163** can be further oxidized to the desired diketone **154** by MnO_2. The structures of these three products were established by X-ray structure analyses. The X-ray crystal structure of **154** reveals that the one of the iodomethyl substitutes is in the axial position while the other is in the equatorial position (Figure 18).

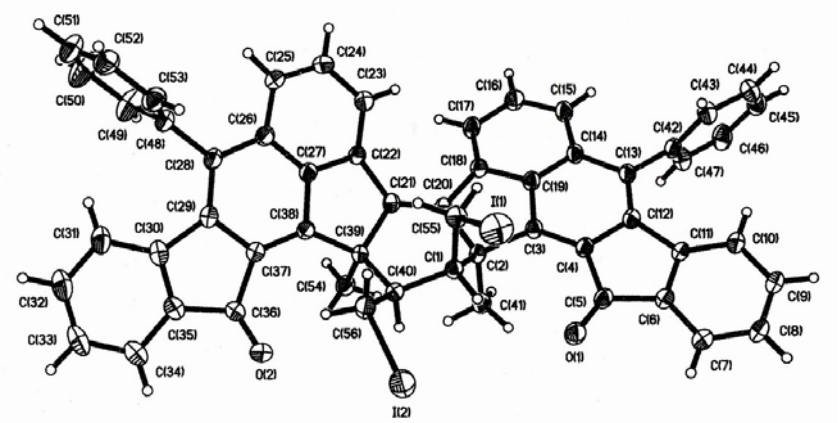


Figure 18. ORTEP drawing of the crystal structure of $C_{56}H_{36}I_2O_2$ (**154**).

The formation of [2 + 2] cycloadduct **162** was unexpected with the steric hindered phenyl group on the same side of the sterically hindered $–CH_2I$ group as shown by the X-ray structure analysis (Figure 19). However, the preference of the [2 + 2] cycloadduct might be minimized by introducing a highly steric hindered substituent, such as 2,6-dibromophenyl group, on the terminus alkynes in **160** to further optimize this cyclization step. Also, by introducing bromo-substituents on the phenyl rings, it would be possible to further form carbon−carbon bonds by intramolecular Heck reactions to connect the peripheral two phenyl groups to form curved

buckybasket with a deeper pocket. This type of intramolecular Heck reaction has been investigated and reported by Daehwan Kim of our group.[8c]

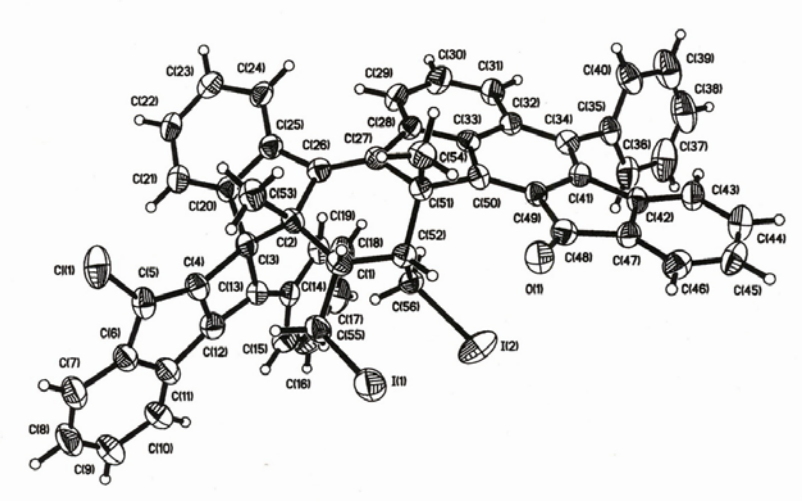


Figure 19. ORTEP drawing of the crystal structure of [2+2] cycloadduct **162**.

4.6. NMR Studies of I_2-Diketone 154

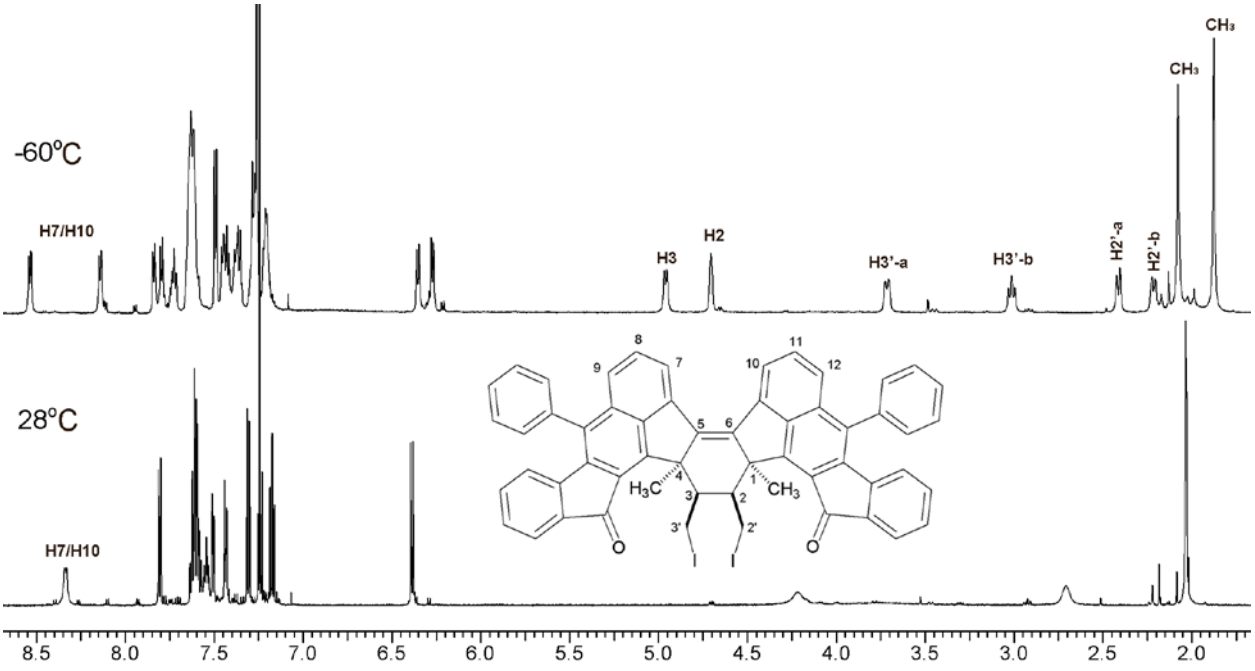


Figure 20. Temperature-dependent ^{1}H spectra of **154** in $CDCl_3$.

The X-ray structure of **154** indicates that the two iodomethyl substituents are in sterically hindered environments. Indeed, the ^{1}H NMR spectrum of **154** recorded on a 600 MHz

spectrometer at room temperature exhibits several sets of broadened signals at δ 8.36, 4.23, 3.89, 2.72 attributable to a rapid conformational exchange on the NMR time scale. The temperature-dependent ^{1}H NMR spectra show that at –60 ^{o}C, all the broad peaks turn to sharp distinct peaks with well defined splitting patterns (Figure 20). A complete assignment of the aliphatic ^{1}H NMR chemical shifts was made by using selective decoupling and 1D TOCSY techniques. The line sharpening was observed for all the aliphatic protons as the temperature is lowered from 28 ^{o}C to –60 ^{o}C, which is explained by the slow conformational exchange on the NMR time scale. Six different aliphatic signals at δ 4.96 (H3), 4.71 (H2), 3.72 (H3′-a), 3.02 (H3′-b), 2.42 (H2′-a), 2.22 (H2′-b) were observed due to unsymmetrical nature of the structure with one iodomethyl substituent in the equatorial while the other sits in the axial position.

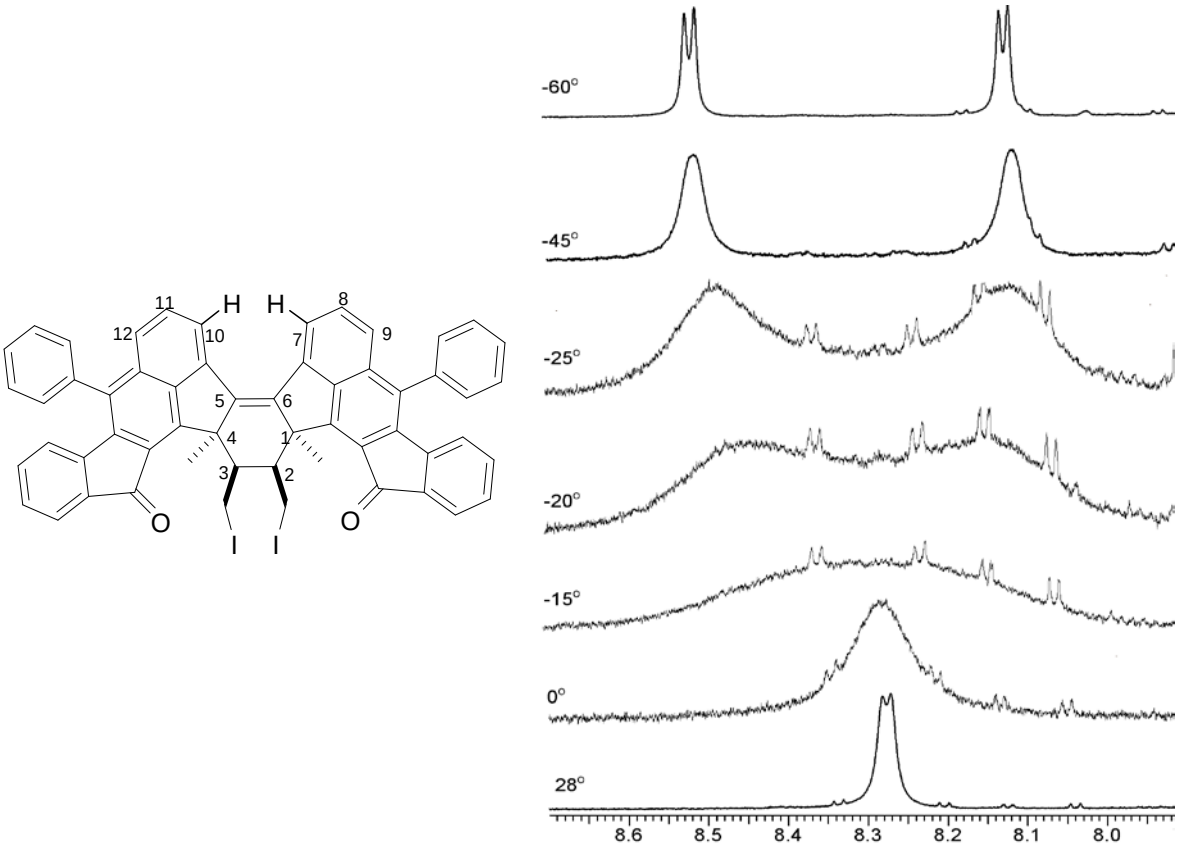
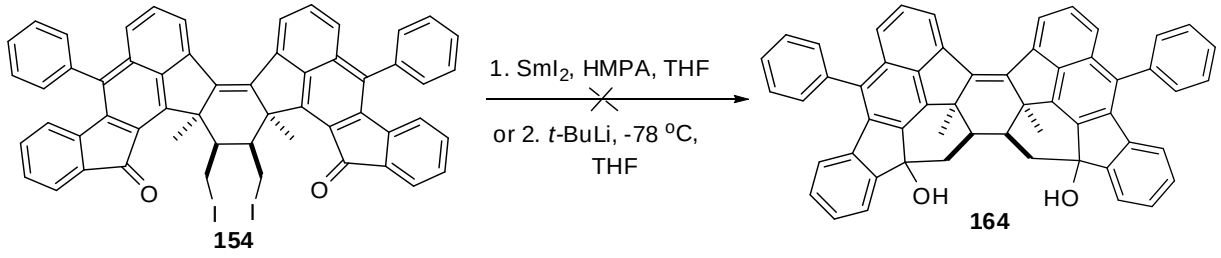


Figure 20. Temperature-dependent ^{1}H spectra of H7 and H10.

In addition, the most downfield aliphatic signal at δ 4.96 was assigned to be the axial hydrogen of the central cyclohexenyl ring with an equatorial iodomethyl substituent. Figure 21 also shows the coalescence of two aromatic peaks (H7/H10) in temperature-dependent ^{1}H NMR studies. The energy barrier of conformational exchange $\Delta G^{\ddagger}$ was calculated at the coalescence temperature of –15 ^{o}C to be 11.8 kcal/mol.

4.7 Intramolecular Cyclization of I_2-Diketone (154)

Scheme 39 outlines the attempts to synthesize the bowl-shaped diol **164** by employing intramolecular Barbier-type cyclizations[68] of the I_2-diketone **154**. However, the ^{1}H NMR spectrum of the isolated compound showed only broad and complicated peaks in the aromatic region, which indicate that the starting material decomposed or polymerized. Also, attempts to treat **154** with *t*-BuLi[69] under a nitrogen atmosphere at –78 ^{o}C were unsuccessful in giving the desired product. Instead, simple reduction of the two carbonyl groups to hydroxyl groups was observed.



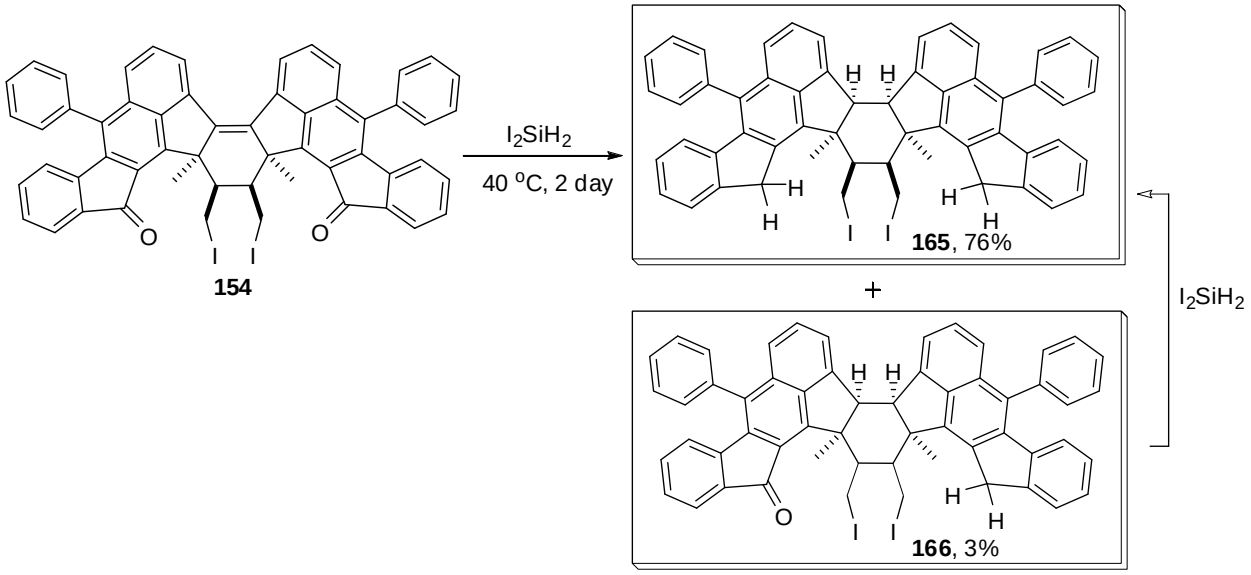
154 **164**

Scheme 39. Attempts toward the synthesis of buckybowl **164**.

4.8 Reduction of I_2-Diketone 154

Surprisingly, reduction of diketone **154** by treatment with freshly prepared diiodosilane (DIS)[70] at 40 ^{o}C for two days produced **165** in 76% yield and a trace amount of mono-reduced byproduct **166** (Scheme 40). It is interesting to note that the central carbon–carbon double bond in **154** was also reduced, giving rise to two additional sp^3-hybridized carbons in **165**. The

presence of these two additional sp^3-hybridized carbons appears to shorten the distance between the carbon on the five-membered ring and the neighboring iodomethyl substituent.



Scheme 40. Preparation of I_2-hydrocarbon **165**.

Monoketone **166** can be converted to **165** by stirring with DIS for a longer time. The stereochemistry of **165** and **166** were characterized and confirmed by NMR studies. Presumably, the double bond on the central six-membered ring was initially protonated by a trace amount of HI present in the freshly prepared DIS, followed by hydride attack to afford the *cis*-hydrogenated compound.

4.9 NMR Studies of 166 and 165

The ^{1}H NMR spectrum of **166** exhibits a set of AB quartet at δ 4.52/4.12 with a large geminal coupling constant of 22 Hz, indicating the formation of methylene groups of the fluorenyl groups. The selective decoupled ^{1}H NMR spectra of **166** allowed the assignment of the entire coupling network between the geminal or vicinal hydrogens on the two $-CH_2I$ substituents. A complete assignment of the entire aliphatic hydrogen chemical shifts was made by using 1D/2D TOCSY, 1D/2D NOESY and COSY. The very upfield shift aromatic signal at δ 4.97 was

assigned to H7 on the basis of the observation that when it was irradiated, the aromatic signal at δ6.73 as a triplet becomes a doublet. It is worth noting that there is a dramatic chemical upfield shift of H7 from δ8.36 of diketone **154** to δ4.97 of the reduced compound **166**. Such an upfield aromatic shift was attributed to a flexible central boat-conformation of the central six-membered ring of **166**, causing the two benzofluorenyl groups to orient roughly perpendicular to each other, thus placing H7 in the magnetic shielding region of the other benzofluorenyl group. Again, in the contour plot of the COSY spectrum, the H7 signal at δ4.97 was also used to locate the remaining two hydrogens on the same aromatic ring (ring A) at δ6.85 and 6.73.

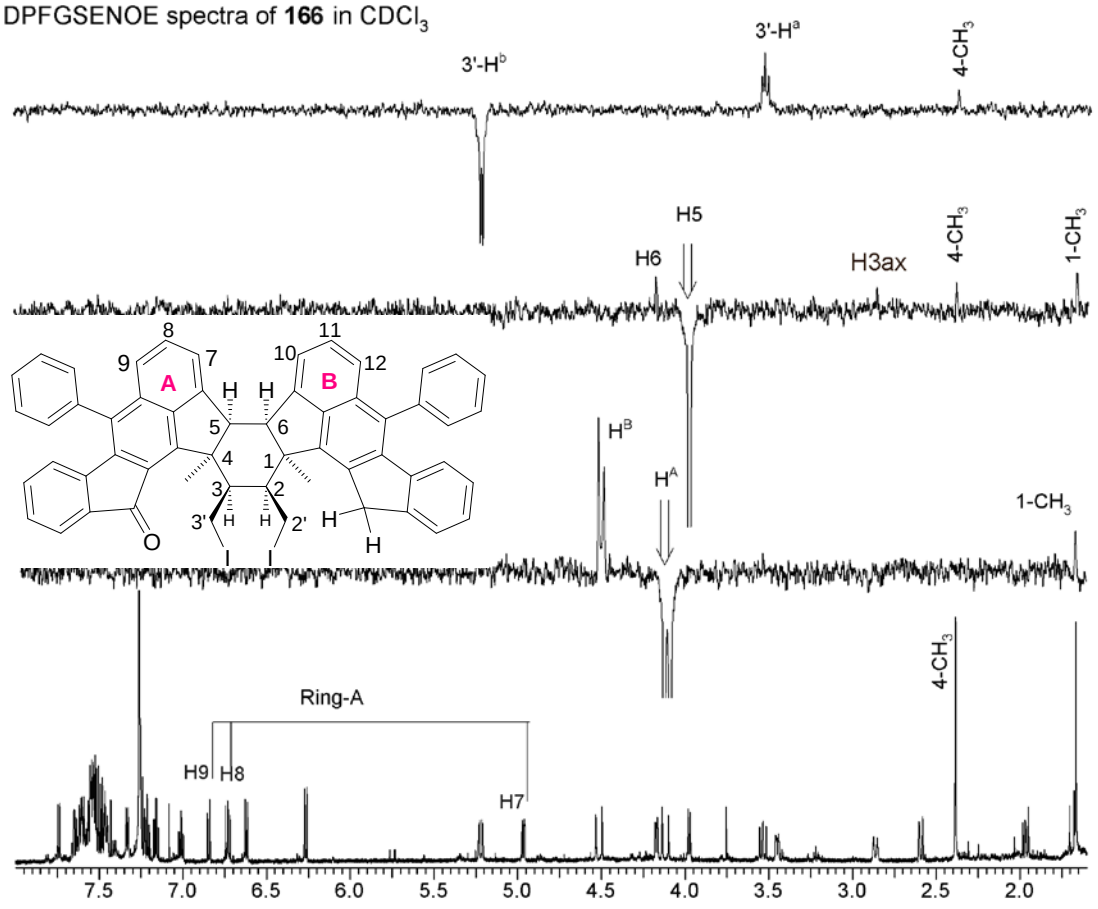


Figure 22. NOE spectra of **166.**

In addition, the NOE spectra (Figure 22) allowed the assignment of the methyl group signal at δ1.67 to be on the same side of the methylene hydrogens on the five-membered ring by

irradiating one of the AB pattern methylene hydrogen signals at δ 4.12. The stereochemistry of H5 and H6 is also identified to be *cis* to each other from NOE spectra. The irradiation of H5 at δ 3.98 gave a *cis* NOE enhancement on the signal at δ 4.17 which was assigned to H6. The H5 signal at δ 3.98 is also used to locate the two methyl groups and confirm that H3 (δ 2.87) is situated in the axial position. In other words, the $-CH_2I$ group neighboring the keto group is in the equatorial position where as the other $-CH_2I$ group is in the axial position. Moreover, the 1D TOCSY spectra allowed the connection of the spin-spin coupling network of hydrogens on ring A and the connection to H5 and H6 by longer mixing time that the signals at δ 4.97 (doublet), δ 6.73 (triplet), δ 6.85 (doublet) constitute one spin system (Ring A protons: H7, H8 and H9).

It is worth noting that the 3D structural modeling of **165** (Figure 23) reveals unsymmetrical structure with the central six-membered ring having a boat conformation. The ^{1}H NMR spectrum of **165** showed two sets of AB quartet at δ 4.48/4.12 and δ 4.43/4.34 with a large geminal coupling constant of 22 Hz, indicating that both keto groups in **154** were successfully converted to methylene hydrogens on the five-membered rings.

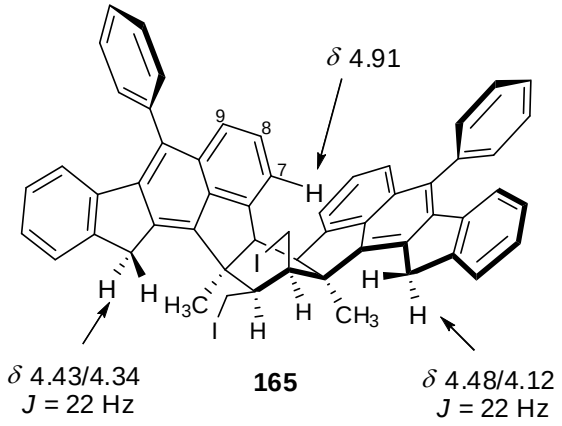


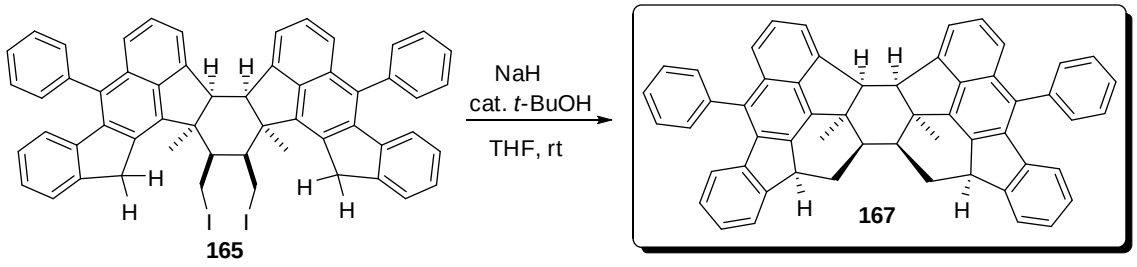
Figure 23. 3D structure of **165**.

The remaining aliphatic peaks are completely assigned by 1D/2D TOCSY, COSY and 1D NOESY techniques. Similar to the mono-reduced compound **166**, there is also an extremely

upfield shift of aromatic signal at δ 4.91, indicating that H7 is situated inside the magnetic shielding region of the other benzofluorenyl group.

4.10 Intramolecular S_N2 Cyclization of Diiodide 165

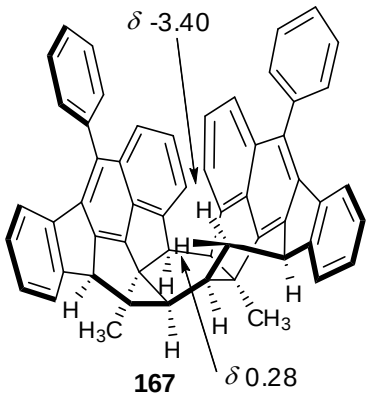
The final step employing a classical intramolecular S_N2 reationn of diiodide **165** under a very mild condition of sodium hydride in the presence of a catalytic amount of *t*-butyl alcohol at room temperature was successful in producing buckybowl **167** (Scheme 41). The presence of the two additional sp^3-hybridized carbons on the six-membered ring of **167** is key to the success of the intramolecular S_N2 reactions. The methylene hydrogens of the fluorenyl system now are relatively close to the iodomethyl substituents to facilitate the intramolecular S_N2 reaction. The stereochemistry of **167** was characterized and confirmed by NMR studies.

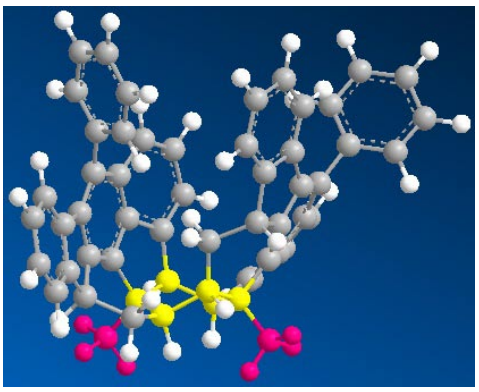


Scheme 41. Synthesis of chiral buckybowl **167**.

4.11 NMR Studies of Buckybowl 167

The 3D molecular modeling of buckybowl **167** calculated by MM2 was shown in Figure 24. Interestingly, the structure of **167** is unsymmetrical due to the presence of a very flexible central six-membered ring with a boat-conformation, which twists the two benzofluorene groups to orient roughly perpendicular to each other. As a result, the ^{1}H NMR spectrum of **167** in $CDCl_3$ revealed two extremely upfield shift aliphatic signals at δ –3.40 and 0.28. A complete assignment of entire aliphatic hydrogen was made by using 1D/2D TOCSY, COSY and 1D NOESY techniques.





(Red atoms: CH_3 groups; yellow bond: the central cyclohexanyl group)

Figure 24. 3D structure of chiral buckybowl **167**.

In addition, the 1D TOCSY spectra (Figure 25) reveals the spin-spin coupling network of hydrogens shown on one of the benzofluorenyl groups, H11, H12 and H13 as well as further connection to H8 and H9 on the central cyclohexyl ring. In addition, a very upfield shift of aromatic hydrogen H11 was found at δ 3.89, indicating that the two benzofluorenyl groups are oriented perpendicular to each other.

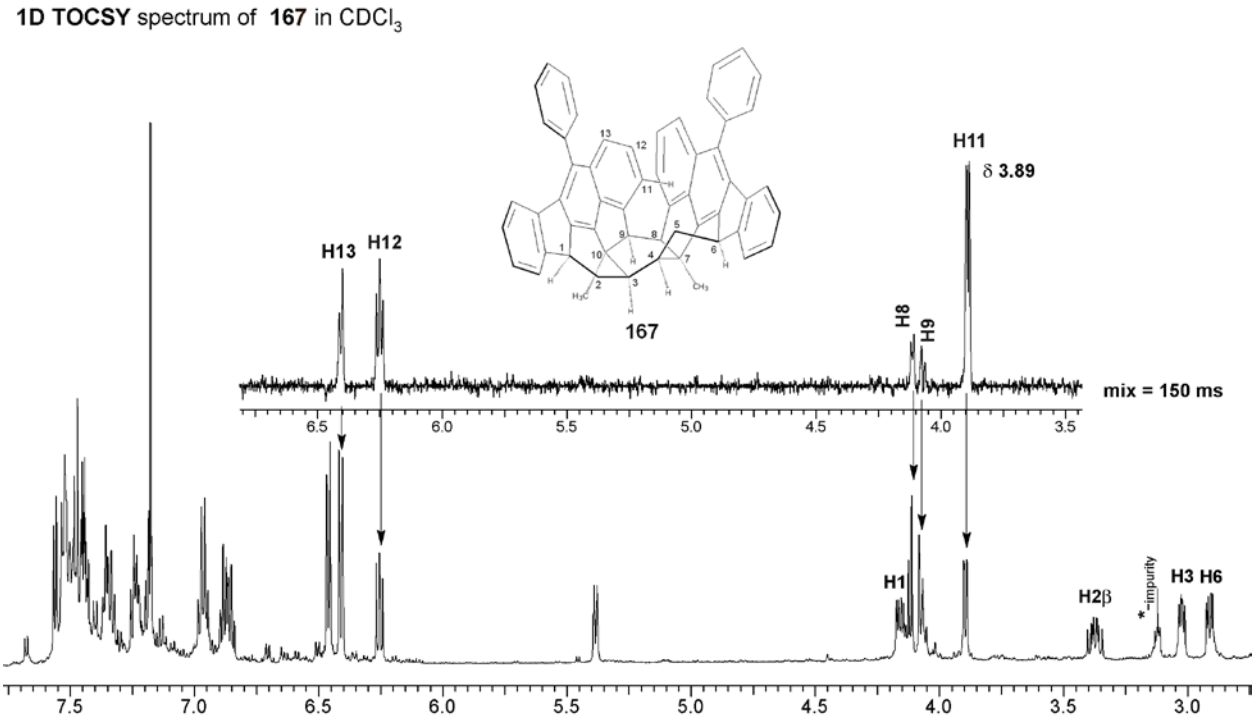
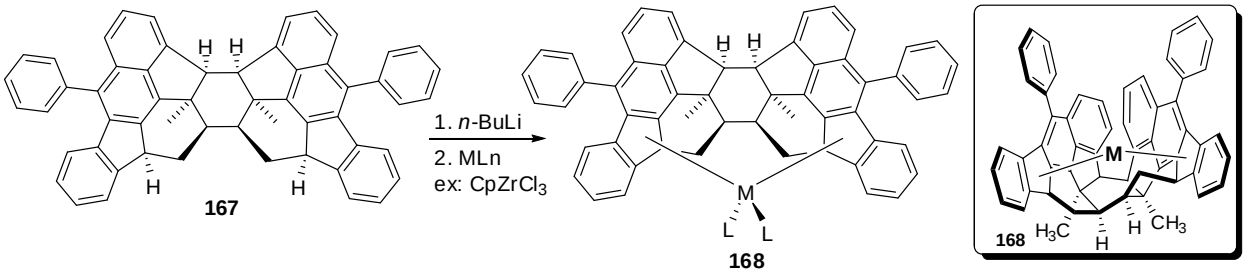


Figure 25. 1D TOCSY spectrum of **167** in $CDCl_3$.

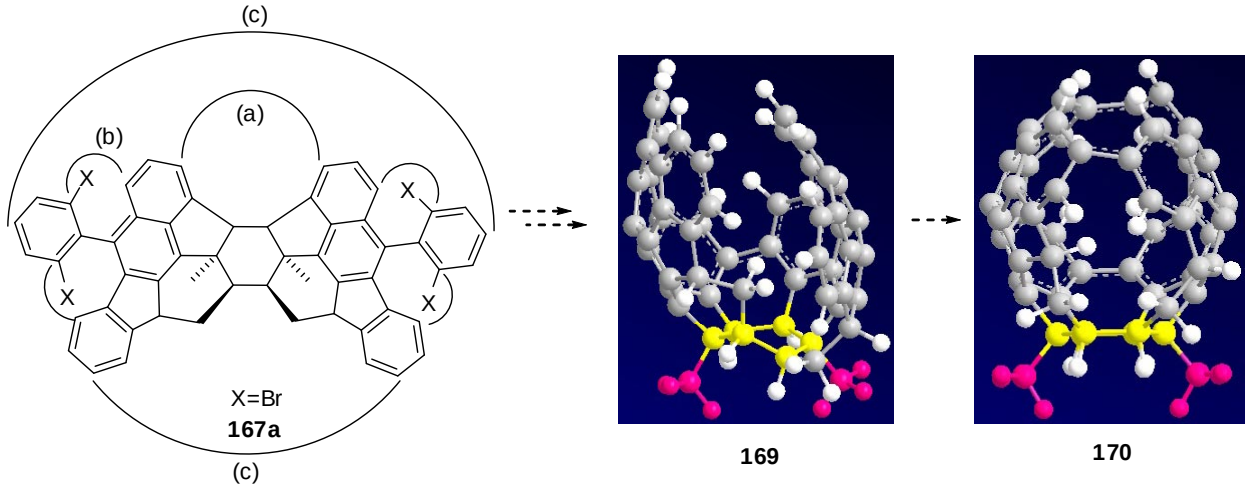
4.12 Future Prospects

This buckybowl **167** can serve as a potential bidentate chiral ligand having two fluorenyl moieties. The acidic hydrogens on the benzofluorenyl groups can be deprotonated and the resulting dianion could form metal-complexes with transition-metals (Scheme 42).



Scheme 42. Proposed further application of **167** in coordination chemistry.

It is worth noting that hydrocarbon **167** possesses a 54-carbon framework represented on the surface of C_{60}. Moreover, it could undergo further transformations for the construction of buckybaskets **169** and **170** (Scheme 43).



Scheme 43. Proposed further application of **167a**.

Presumably, a brominated **167,** such as **167a**, could be converted to bowl-shaped hydrocarbon **169** by initially using Müllen's method[71] to connect the two benzene ring indicated as a connection followed by intramolecular Heck coupling reactions to connect the two

dibromophenyl substituents with the benzofluorenyl groups indicated as b connection. Buckybasket **169** may ultimately lead to a novel buckybasket **170** having a hole via c connection.[72] These promising PAHs, **169** and **170**, unlike other buckybowls, are less strained surface and more accessible for further applications in nanotechnology. In addition, the sp^3-hybridized carbons on the surface could be functionalized to undergo further chemical transformations.

5. Conclusions

A unique, non-pyrolytic synthetic pathway employing Schmittel cyclization reactions has been developed to synthesize chiral bowl-shaped polycyclic aromatic hydrocarbon (PAH). Introduction of sp^3-hybridized carbons facilitates the cyclization step. Buckybowl **167** having a 54-carbon framework mapped onto the surface of C_{60} can serve as a potential precursor for a novel buckybasket. In addition, the structure of **167** could find applications in supramolecular chemistry and allow the study of endohedral chemistry.

CHAPTER IV

Experimental Section

General Experimental Methods

All reactions were conducted in oven-dried (120 °C) glassware under a nitrogen atmosphere. Diethyl ether and tetrahydrofuran (THF) were distilled from benzophenone ketyl prior to use. Methylene chloride, benzene and toluene were distilled over calcium hydride (CaH_2) prior to use. Silica gel for flash column chromatography was purchased from chemical supplies. Melting points were uncorrected. ^1H (270 MHz, 600 MHz) and ^{13}C (67.9 MHz, 150 MHz) NMR spectra were recorded in $CDCl_3$ using $CHCl_3$ (^1H δ 7.26) and $CDCl_3$ (^{13}C δ 77.0) as internal standards unless otherwise indicated. IR spectra were taken on Perkin-Elmer LX10-8704 Spectrum One FT-IR spectrometer. Mass spectra and high resolution mass spectra were obtained on Hewlett Packard 5970B GC/MSD instrument at 70 eV, VG 7070 by DEI, VG-ZAB by FAB and DE-STR by MALDI. 3D structural modeling was obtained on computations using the MM2 force field provided by CambridgeSoft Corporation.

Experimental Section of Chapter I

1-Ethynyl-2-(phenylethynyl)benzene was prepared according to the reported procedure.[8i] Truxenone (**19**), 1.6 M solution of *n*-butyllithium in hexanes, and thionyl chloride were purchased from chemical suppliers and were used as received.

Benzannulated Enediynyl Alcohol 24. To 0.049 g (0.243 mmol) of 1-ethynyl-2-(phenylethynyl) benzene in 5 mL of THF under a nitrogen atmosphere at 0 °C was added 0.15 mL of a 1.6 M solution of *n*-butyllithium (0.24 mmol) in hexanes. After 30 min of stirring, a solution of 0.102 g of truxenone (**19**, 0.266 mmol) in 10 mL of THF was introduced via cannula, and the reaction mixture was allowed to warm to room temperature. After an

additional 18 h, 15 mL of water was introduced, and the reaction mixture was extracted with methylene chloride. The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. The residue was purified by flash chromatography (silica gel/methylene chloride) to afford 0.129 g (0.220 mmol, 83%) of **24** as a pale yellow solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 9.18−9.17 (1 H, m), 9.03 (1 H, d, J = 7.2 Hz), 8.82 (1 H, d , J = 7.8 Hz), 7.93−7.92 (1 H, m), 7.64 (2 H, d, J = 6.6 Hz), 7.56−7.52 (2 H, m), 7.44−7.41 (3 H, m), 7.37−7.32 (3 H, m), 7.24−7.15 (7 H, m), 3.35 (I H, br); MS *m/z* 569 (M^+ − OH); HRMS calcd for $C_{43}H_{21}O_2$ (M^+ − OH) 569.1542, found 569.1543.

Diketone 28. To a solution of 0.102 g (0.174 mmol) of **24** in 10 mL of THF under a nitrogen atmosphere at 0 °C was added slowly via cannula a solution of 0.1 mL (1.4 mmol) of thionyl chloride and 0.16 mL (2.0 mmol) of pyridine in 5 mL of THF. The reaction mixture then was allowed to warm to room temperature. After 7 h, 10 mL of water was introduced, and the organic layer was separated. The aqueous layer was back extracted with diethyl ether. The combined organic layers were washed with brine and water, dried over sodium sulfate, and concentrated. The residue was purified by flash chromatography (silica gel/50% methylene chloride in hexanes) to afford 0.071 g (0.118 mmol, 68%) of **28** as a green solid: IR 1701, 1434 cm^{-1}; ^{1}H (C_6D_6, 600 MHz) δ 9.73 (1 H, ddd, J = 7.4, 1.2, 0.7 Hz), 9.29 (1 H, dt, J = 7.9, 0.9 Hz), 8.82 (1 H, ddd, J = 7.6, 1.1, 0.7 Hz), 7.84 (1 H, ddd, J = 7.5, 1.2, 0.7 Hz), 7.46 (1 H, ddd, J = 7.5, 1.2, 0.7 Hz), 7.37 (1 H, ddd, J = 7.5, 1.1, 1.0 Hz), 7.34 (1 H, td, J = 7.6, 1.2 Hz), 7.33 (1 H, ddd, J = 7.9, 1.1, 0.7 Hz), 7.32 (1 H, ddd, J = 7.6, 7.4, 1.1 Hz), 7.24 (1 H, td, J = 7.5, 1.2 Hz), 7.19 (1 H, ddd, J = 7.9, 7.3, 1.2 Hz), 7.17 (1 H, m), 7.15 (1 H, m), 6.97 (1 H, td, J = 7.4, 1.0 Hz), 6.90 (1 H, td, J = 7.5, 0.9 Hz), 6.89 (1 H, m), 6.84 (1 H, ddd, J = 7.9, 7.3, 1.2 Hz), 6.75 (1 H, td, J = 7.7, 1.1 Hz), 6.60 (1 H, td, J = 7.5, 1.1 Hz), 6.32 (1 H, dt, J =7.6, 0.9 Hz), 5.94 (1 H, dt, J = 7.2, 1.2 Hz); ^{1}H ($CDCl_3$, 600 MHz) δ 9.22 (1 H, d, J = 7.2 Hz), 8.99 (1 H, d, J = 7.8 Hz), 8.69 (1 H, d, J = 7.8

Hz), 7.93 (1 H, d, J = 7.8 Hz), 7.72 (1 H, t, J = 7.8 Hz), 7.59 (1 H, t, J = 7.2 Hz), 7.53−7.47 (7 H, m), 7.44 (1 H, t, J = 7.2 Hz), 7.30 (1 H, t, J = 7.8 Hz), 7.25−7.22 (2 H, m), 7.18−7.16 (1 H, m), 6.88 (1 H, t, J = 7.8 Hz), 6.16 (1 H, d, J = 7.8 Hz), 5.88 (1 H, d, J = 6.6 Hz); ^{13}C (C_6D_6, 150 MHz) δ 190.3, 187.7, 150.0, 147.5, 145.1, 142.6, 142.2, 142.0, 141.6, 140.1, 139.7, 137.9, 135.7, 135.4, 134.88, 134.79, 134.36, 134.28, 133.9, 133.3, 131.33, 131.24, 131.20, 130.22, 130.11, 129.63, 129.59, 129.3, 129.15, 129.11, 128.8, 128.56, 128.37, 128.15, 127.91, 127.83, 124.5, 123.5, 123.02, 122.96, 122.8, 120.0, 57.6; ^{13}C ($CDCl_3$, 150 MHz) δ 190.6, 188.1, 149.7, 146.9, 145.3, 142.0, 141.8, 141.6, 140.8, 139.5, 139.1, 138.1, 135.2, 135.0, 134.9, 134.4, 133.9, 133.1, 132.9, 131.6, 131.4, 131.1, 129.9, 129.7, 129.10, 129.07, 128.97, 128.8, 128.54, 128.52, 128.47, 128.3, 128.1, 127.83, 127.77, 124.3, 123.5, 122.93, 122.87, 122.5, 119.8, 57.3; HRMS calcd for $C_{43}H_{21}ClO_2$ (M^+) 604.1230, found 604.1231. Recrystallization of **28** from a mixture of methylene chloride and 2-propanol produced a single crystal suitable for X-ray structure analysis.

In $CDCl_3$, **28** gradually and cleanly transformed to a new compound exhibiting a very different proton NMR spectrum with the two most upfield shift signals appearing at δ 5.28 (1 H, d, J = 7.8 Hz) and 5.60 (1 H, d, J = 8.4 Hz). The structure of the new compound has not been elucidated.

Diol 30. To 0.155 g (0.767 mmol) of 1-ethynyl-2-(phenylethynyl)benzene in 10 mL of THF under a nitrogen atmosphere at 0 °C was added 0.461 mL of a 2.0 M solution of LDA (0.921 mmol) in THF. After 30 min of stirring, a solution of 0.118 g of truxenone (**19**, 0.307 mmol) in 20 mL of THF was introduced via cannula, and the reaction mixture was allowed to warm to room temperature. After an additional 18 h, 30 mL of a saturated aqueous ammonium chloride solution was introduced, and the reaction mixture was extracted with diethyl ether. The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. The residue was purified by flash chromatography (silica gel/5 to 20% ethyl

acetate in methylene chloride) to afford 0.184 g of the *cis*-diol **30** (0.234 mmol, 76%) as a bright yellow solid and 0.031 g of the *trans*-diol **30** (0.040 mmol, 13%) as a pale yellow solid. *cis*-**30**: IR 3400, 1689, 1605 cm^{-1}; ^{1}H ($CDCl_3$, 600 MHz) δ 8.93−8.90 (2 H, m), 8.65 (1 H, d, J = 7.8 Hz), 7.89 (1 H, d, J = 7.2 Hz), 7.81 (1 H, d, J = 7.8 Hz), 7.43−7.34 (5 H, m), 7.33−7.24 (7 H, m), 7.22−7.13 (8 H, m), 7.11−7.06 (4 H, m), 7.02 (1 H, t, J = 7.5 Hz), 3.36 (1 H, s), 2.64 (1 H, s); ^{13}C ($CDCl_3$, 150 MHz) δ 193.9, 149.1, 148.7, 142.5, 142.1, 141.8, 141.4, 141.0, 140.2, 136.5, 135.5, 134.9, 134.3, 132.2, 132.1, 131.7, 131.4, 130.6, 130.3, 130.1, 129.7, 129.2, 128.3, 128.24, 128.21, 128.20, 128.1, 127.7, 127.3, 127.0, 126.2, 126.1, 124.62, 124.58, 124.0, 123.9, 123.8, 122.9, 122.7, 93.5, 93.4, 91.2, 91.0, 87.8, 87.6, 83.0, 82.9, 74,8, 74.6; MS *m/z* 771 (M^+ − OH), 754; HRMS calcd for $C_{59}H_{32}O_3Na$ (MNa^+) 811.2249, found 811.2245. Recrystallization of *cis*-**30** from a mixture of methylene chloride and 2-propanol produced a single crystal suitable for X-ray structure analysis. *trans*-**30**: IR 3529, 3398, 1686, 1603 cm^{-1}; ^{1}H ($CDCl_3$, 600 MHz) δ 8.88 (1 H, d, J = 7.8 Hz), 8.68 (1 H, d, J = 7.8 Hz), 8.58 (1 H, d, J = 7.8 Hz), 7.87 (1 H, d, J = 7.2 Hz), 7.77 (1 H, d, J = 7.2 Hz), 7.40 (1 H, td, J = 7.2, 1.2 Hz), 7.38 (1 H, d, J = 7.8 Hz), 7.34 (1 H, d, J = 7.8 Hz), 7.31 (1 H, td, J = 7.8, 1.2 Hz), 7.28−7.24 (4 H, m), 7.22 (2 H, d, J = 7.8 Hz), 7.20−7.13 (8 H, m), 7.12−7.04 (6 H, m), 6.86 (1 H, d, J = 7.2 Hz), 3.73 (1 H, s), 2.66 (1 H, s); ^{13}C ($CDCl_3$, 150 MHz) δ 194.4, 149.1, 148.7, 142.6, 141.8, 141.2, 141.0, 140.2, 136.3, 135.4, 134.6, 134.3, 132.2, 132.1, 131.7, 131.6, 131.4, 130.5, 130.3, 130.0, 129.5, 129.1, 128.23, 128.19, 128.15, 128.12, 128.10, 127.9, 127.6, 127.1, 126.7, 126.1, 126.0, 124.7, 124.6, 124.0, 123.9, 123.8, 122.9, 122.6, 93.4, 93.3, 91.3, 91.0, 87.7, 87.5, 82.8, 82.5, 74,8, 74.5; MS *m/z* 771 (M^+ − OH), 754; HRMS calcd for $C_{59}H_{32}O_3Na$ (MNa^+) 811.2249, found 811.2251.

Ketone 31. To a solution of 0.097 g (0.123 mmol) of a mixture of the *cis* and *trans* isomers of diol **30** in 8 mL of diethyl ether under a nitrogen atmosphere at 0 °C was added slowly via cannula a solution of 0.09 mL (1.2 mmol) of thionyl chloride and 0.14 mL (1.7 mmol) of

pyridine in 7 mL of diethyl ether. The reaction mixture was then allowed to warm to room temperature. After 7 h, 15 mL of water was introduced, and the organic layer was separated. The aqueous layer was back extracted with methylene chloride. The combined organic layers were washed with brine and water, dried over sodium sulfate, and concentrated. The residue was purified by flash chromatography (silica gel/50% methylene chloride in hexanes) to afford 0.056 g (0.068 mmol, 55%) of **31** as a red solid and ca. 0.004 g of an unidentified green solid. **31**: ^{1}H (C_6D_6, 600 MHz) δ 8.73−8.71 (1 H, m), 8.68−8.66 (1 H, m), 8.62 (1 H, d, J = 7.8 Hz), 7.83 (1 H, d, J = 7.8 Hz), 7.45 (1 H, d, J = 7.8 Hz), 7.43 (1 H, d, J = 7.8 Hz), 7.31 (1 H, d, J = 7.8 Hz), 7.27 (1 H, d, J = 7.2 Hz), 7.25−7.23 (2 H, m), 7.19−7.13 (2 H, m), 7.10 (1 H, d, J = 6.6 Hz), 7.06 (1 H, t, J = 7.2 Hz), 7.03−7.01 (1 H, m), 6.98 (1 H, t, J = 7.8 Hz), 6.91 (1 H, t, J = 7.5 Hz), 6.85 (1 H, t, J = 7.8 Hz), 6.81 (1 H, t, J = 7.5 Hz), 6.76 (1 H, t, J = 7.2 Hz), 6.74 (1 H, t, J = 7.2 Hz), 6.68 (1 H, t, J = 7.8 Hz), 6.66 (1 H, t, J = 7.8 Hz), 6.59 (1 H, t, J = 7.8 Hz), 6.49 (1 H, t, J = 7.8 Hz), 6.25 (1 H, d, J = 7.8 Hz), 6.23 (1 H, d, J = 7.8 Hz), 6.15 (1 H, d, J = 7.8 Hz), 6.07 (1 H, d, J = 7.8 Hz), 5.62 (1 H, d, J = 7.8 Hz); ^{13}C (C_6D_6, 150 MHz) δ 185.1, 151.4, 149.5, 147.1, 146.74, 146.57, 145.1, 143.7, 142.84, 142.65, 142.52, 142.1, 141.6, 139.9, 138.6, 137.2, 136.4, 135.6, 134.7, 134.5, 134.2, 133.3, 131.9, 131.7, 131.3, 130.4, 130.2, 129.6, 128.90, 128.77, 128.6, 127.5, 126.9, 125.8, 125.4, 125.1, 124.4, 124.1, 123.2, 122.7, 122.4, 119.9, 119.5, 64.8, 58.2; HRMS calcd for $C_{59}H_{31}Cl_2O$ (MH^+) 825.1752, found 825.1755. Recrystallization of **31** from a mixture of methylene chloride and hexanes produced a single crystal suitable for X-ray structure analysis.

In $CDCl_3$, **31** gradually and cleanly transformed to the unidentified green solid, which exhibited the two most upfield shift signals at δ 5.56 (1 H, d, J = 7.8 Hz) and 6.00 (1 H, d, J = 7.8 Hz).

Triol 20. To 0.158 g (0.782 mmol) of 1-ethynyl-2-(phenylethynyl)benzene in 5 mL of THF under a nitrogen atmosphere at 0 °C was added 0.49 mL of a 1.6 M solution of *n*-butyllithium (0.78 mmol) in hexanes. After 30 min of stirring, a solution of 0.060 g of truxenone (**19**, 0.156 mmol) in 10 mL of THF was introduced via cannula, and the reaction mixture was allowed to warm to room temperature. After an additional 18 h, 15 mL of water was introduced, and the reaction mixture was extracted with diethyl ether. The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. The residue was purified by flash chromatography (methylene chloride followed by 20% diethyl ether in methylene chloride) to afford 0.114 g of the *anti* isomer of **20** (0.115 mmol, 74%) as a pale yellow solid and 0.024 g of the *syn* isomer of **20** (0.023 mmol, 15%) as a brown solid. *anti*-**20**: IR 3538, 1606, 1494 cm^{-1}; ^{1}H ($CDCl_3$, 600 MHz) δ 8.95 (1 H, d, J = 7.8 Hz), 8.94 (1 H, d, J = 7.8 Hz), 8.88 (1 H, d, J = 7.8 Hz), 7.88 (2 H, t, J = 7.8 Hz), 7.84 (1 H, d, J = 7.2 Hz), 7.45−7.36 (8 H, m), 7.32−7.27 (6 H, m), 7.23−7.16 (15 H, m), 7.12−7.08 (3 H, m), 7.01 (1 H, t, J = 7.2 Hz), 2.59 (1 H, s), 2.44 (1 H, s), 2.00 (1 H, s); ^{13}C ($CDCl_3$, 150 MHz) δ 148.50, 148.46, 148.37, 140.15, 140.11, 140.08, 138.74, 138.66, 138.61, 136.3, 136.1, 136.0, 132.2, 131.74, 131.72, 131.68, 131.65, 131.5, 129.7, 129.56, 129.53, 129.4, 128.27, 128.22, 128.18, 127.76, 127.75, 127.73, 127.2, 127.1, 127.0, 126.1, 126.00, 125.96, 124.8, 124.72, 124.70, 124.2, 124.02, 124.00, 123.10, 123.06, 122.9, 93.29, 93.23, 93.15, 91.55, 91.52, 91.48, 87.90, 87.88, 87.79, 82.9, 82.7, 82.4, 75.24, 75.20, 75.19; MS *m/z* 973 (M^+ − OH), 771; HRMS calcd for $C_{75}H_{42}O_3Na$ (MNa^+) 1013.3032, found 1013.3031. *syn*-**20**: IR 3529, 1600, 1494 cm^{-1}; ^{1}H ($CDCl_3$, 600 MHz) δ 8.88 (3 H, d, J = 7.2 Hz), 7.81 (3 H, d, J = 7.8 Hz), 7.39−7.35 (6 H, m), 7.29−7.27 (6 H, m), 7.20 (3 H, td, J = 7.2, 1.2 Hz), 7.17−7.14 (6 H, m), 7.13−7.10 (6 H, m), 7.09−7.06 (3 H, m), 7.03 (3 H, td, J = 7.8, 1.2 Hz), 2.74 (3 H, s); ^{13}C ($CDCl_3$, 150 MHz) δ 148.4, 140.1, 138.5, 136.1, 132.3, 131.64, 131.61, 129.6, 129.3, 128.19,

128.13, 128.08, 127.6, 126.9, 126.0, 124.6, 124.0, 122.9, 93.5, 91.3, 87.9, 82.9, 75.0; MS *m/z* 973 ($M^+ - OH$); HRMS calcd for $C_{75}H_{42}O_3Na$ (MNa^+) 1013.3032, found 1013.3036.

Alcohol 34. To a solution of 0.089 g (0.090 mmol) of the *anti* and *syn* isomers of **20** in 10 mL of diethyl ether under a nitrogen atmosphere at 0 °C was added slowly via cannula a solution of 0.07 mL (0.9 mmol) of thionyl chloride and 0.11 mL (1.4 mmol) of pyridine in 5 mL of diethyl ether. The reaction mixture then was allowed to warm to room temperature. After 7 h, 15 mL of water was introduced, and the organic layer was separated. The aqueous layer was back extracted with methylene chloride. The combined organic layers were washed with brine and water, dried over sodium sulfate, and concentrated. The residue was purified by flash chromatography (silica gel/40% methylene chloride in hexanes) to afford 0.044 g (0.043 mmol, 48%) of **34** as a bright yellow solid: IR 1643, 1600 cm^{-1}; ^1H (C_6D_6, 600 MHz) δ 8.88 (1 H, d, J = 7.8 Hz), 8.85 (1 H, d, J = 7.8 Hz), 7.99 (1 H, d, J = 7.2 Hz), 7.77 (1 H, d, J = 7.2 Hz), 7.57 (1 H, d, J = 7.2 Hz), 7.48−7.46 (2 H, t, J = 6.3 Hz), 7.42 (1 H, t, J = 7.5 Hz), 7.34 (1 H, d, J = 7.8 Hz), 7.31 (1 H, t, J = 7.2 Hz), 7.27−7.21 (6 H, m), 7.03−6.84 (10 H, m), 6.76−6.69 (3 H, m), 6.66−6.61 (3 H, m), 6.53 (1 H, t, J = 7.5 Hz), 6.45 (1 H, d, J = 7.8 Hz), 6.34 (1 H, d, J = 7.8 Hz), 6.27 (1 H, d, J = 7.8 Hz), 6.14 (1 H, d, J = 7.8 Hz), 6.01 (1 H, d, J = 7.8 Hz), 5.83 (1 H, d, J = 7.8 Hz), 1.07 (1 H, s); ^{13}C (C_6D_6, 150 MHz) δ 152.2, 151.6, 148.7, 148.3, 147.9, 147.0, 146.25, 146.18, 144.3, 142.4, 142.2, 141.7, 141.4, 139.0, 136.7, 136.42, 136.36, 134.2, 133.9, 133.8, 133.3, 132.2, 132.1, 131.1, 130.82, 130.79, 129.8, 129.4, 127.4, 127.2, 127.1, 126.9, 126.7, 126.5, 126.1, 126.0, 125.8, 125.7, 125.4, 125.0, 124.6, 124.48, 124.43, 123.6, 122.9, 122.6, 122.0, 121.6, 119.7, 119.4, 100.2, 93.7, 89.1, 86.1, 85.4. (The ^{13}C NMR signals of the two sp^3-hybridized quaternary carbons without a hydroxyl substituent are too weak to be discerned.); MS *m/z* 1009 ($M^+ - OH$); HRMS calcd for $C_{75}H_{40}Cl_2ONa$ (MNa^+) 1049.2354, found 1049.2361. Recrystallization of **34**

from a mixture of methylene chloride and 2-propanol produced a single crystal suitable for X-ray structure analysis.

Experimental Section of Chapter II

1-Ethynyl-2-methoxybenzene (**64a**), pivalophenone (**40**), *n*-butyllithium (1.6 M) in hexanes, 1-bromo-2-[(trimethylsilyl)ethynyl]benzene, triethylsilane, trifluoroacetic acid, potassium *t*-butoxide (1.0 M) in 2-methyl-2-propanol, lithium diisopropylamide (LDA, 2.0 M) in heptane/THF/ethylbenzene, $Pd(PPh_3)_2Cl_2$, $Pd(PPh_3)_4$, copper(I) iodide, triethylamine, 1.0 M BH_3•THF solution in THF, 1-ethynylnaphthalene (**84**), 2-methoxy-1-naphthaldehyde, 1-bromo-2-(methoxymethyl)naphthalene, (trimethylsilyl)acetylene, boron tribromide, and (1*S*)-(−)-camphanoyl chloride were purchased from chemical suppliers and were used as received. 1-Iodo-2-[(trimethylsilyl)ethynyl]benzene (**65**) was prepared by treatment of 1-bromo-2-[(trimethylsilyl)ethynyl]benzene in THF with *n*-butyllithium at −78 °C followed by iodine.[8f] 1-Ethynyl-2-iodo-benzene (**81**) was prepared in quantitative yield by desilylation of **65** with sodium hydroxide in methanol. 1-Ethynyl-2-(methoxymethyl)benzene (**64b**)[12] and dimethyl (1-diazo-2-oxopropyl)phosphonate[13] were prepared according to the reported procedures.

Trimethyl[[2-[(2-methoxyphenyl)ethynyl]phenyl]ethynyl]silane (66a). To a mixture of 0.318 g of **65** (1.059 mmol), $Pd(PPh_3)_2Cl_2$ (0.027 g, 0.039 mmol), and copper(I) iodide (0.008 g, 0.04 mmol) in 15 mL of triethylamine was added via cannula a solution of 0.103 g of **64a** (0.780 mmol) in 5 mL of triethylamine. After 5 h of stirring at 70 °C, 20 mL of a saturated ammonium chloride solution and 20 mL of diethyl ether were added. The organic layer was separated, and the aqueous layer was back extracted with diethyl ether. The combined organic layers were washed with brine and water, dried over sodium sulfate, and concentrated. Purification of the residue by flash column chromatography (silica gel/30% methylene chloride in hexanes)

afforded 0.206 g of **66a** (0.677 mmol, 87%) as a colorless liquid: ^{1}H ($CDCl_3$, 270 MHz) δ 7.59−7.47 (3 H, m), 7.35−7.20 (3 H, m), 6.94 (1 H, t, J = 7.7 Hz), 6.91 (1 H, d, J = 7.7 Hz), 3.91 (3 H, s), 0.26 (9 H, s) ; ^{13}C ($CDCl_3$, 67.9 MHz) δ 159.9, 133.9, 132.2, 131.9, 129.9, 128.1, 127.6, 126.4, 125.4, 120.4, 112.5, 110.7, 103.6, 98.4, 92.0, 89.9, 55.8, −0.1.

Benzannulated Enediyne 67a. To 0.201 g (0.660 mmol) of **66a** in 10 mL of diethyl ether were added 4 mL of a 10% sodium hydroxide solution and 10 mL of methanol. After 30 min of stirring at room temperature, 20 mL of water and 20 mL of diethyl ether were added. The organic layer was separated, and the aqueous layer was back extracted with diethyl ether. The combined organic layers were washed with brine and water, dried over sodium sulfate, and concentrated. Purification of the residue by flash column chromatography (silica gel/30% methylene chloride in hexanes) afforded 0.137 g of **67a** (0.591 mmol, 90%) as a yellow liquid: IR 3286, 2114, 1496, 1247 cm^{-1}; ^{1}H ($CDCl_3$, 270 MHz) δ 7.60−7.51 (3 H, m), 7.36−7.23 (3 H, m), 6.95 (1 H, t, J = 7.6 Hz), 6.90 (1 H, d, J = 8.2 Hz), 3.91 (3 H, s), 3.37 (1 H, s); ^{13}C ($CDCl_3$, 67.9 MHz) δ 160.0, 133.8, 132.5, 131.8, 130.0, 128.4, 127.7, 126.6, 124.4, 120.4, 112.3, 110.7, 91.8, 90.0, 82.3, 81.0, 55.8. MS *m/z* 232 (M^+); HRMS calcd for $C_{17}H_{12}O$ (M^+) 232.0888, found 232.0883.

α-[[2-[(2-Methoxyphenyl)ethynyl]phenyl]ethynyl]-α-(1,1-dimethylethyl)benzenemethanol (68a). To 0.065 g (0.28 mmol) of **67a** in 5 mL of anhydrous diethyl ether under a nitrogen atmosphere at 0 °C was added 0.18 mL of a 1.6 M solution of *n*-butyllithium (0.28 mmol) in hexanes. After 30 min of stirring, a solution of 0.064 g of **40** (0.39 mmol) in 10 mL of THF was introduced via cannula, and the reaction mixture was allowed to warm to room temperature. After an additional 3 h, 15 mL of water was introduced, and the reaction mixture was extracted with diethyl ether. The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. The residue was purified by flash column chromatography

(silica gel/15% diethyl ether in hexanes) to provide 0.109 g (0.276 mmol, 99%) of **68a** as a light yellow liquid: ^{1}H ($CDCl_3$, 270 MHz) δ 7.78−7.71 (2 H, m), 7.61−7.57 (1 H, m), 7.53−7.49 (1 H, m), 7.41 (1 H, dd, J = 7.9, 1.7 Hz), 7.35−7.20 (6 H, m), 6.94−6.87 (2 H, m), 3.84 (3 H, s), 2.67 (1 H, s), 1.07 (9 H, s); ^{13}C ($CDCl_3$, 67.9 MHz) δ 159.9, 142.1, 133.7, 132.2, 131.9, 129.9, 127.9, 127.8, 127.2, 126.9, 126.1, 125.1, 120.5, 112.4, 110.9, 96.2, 92.1, 89.5, 84.6, 79.4, 55.9, 39.7, 25.5.

Benzannulated Enediyne 69a. To a mixture of **68a** (0.109 g, 0.276 mmol) and triethylsilane (0.048 g, 0.41 mmol) in 10 mL of methylene chloride was added trifluoroacetic acid (0.126 g, 1.11 mmol). After 1 h of stirring at room temperature, 0.11 g of sodium carbonate (4.6 mmol) was added followed by 10 mL of water and 10 mL of diethyl ether. The organic layer was separated, dried over sodium sulfate, and concentrated. Purification of the residue by flash column chromatography (silica gel/25% methylene chloride in hexanes) provided 0.097 g (0.256 mmol, 93%) of **69a** as a light yellow liquid: ^{1}H ($CDCl_3$, 270 MHz) δ 7.61−7.55 (1 H, m), 7.48−7.16 (10 H, m), 6.92−6.85 (2 H, m), 3.87 (3 H, s), 3.69 (1 H, s), 1.04 (9 H, s); ^{13}C ($CDCl_3$, 67.9 MHz) δ 160.0, 139.2, 133.7, 132.2, 132.0, 129.8, 129.7, 127.7, 127.5, 127.2, 126.5, 126.3, 125.9, 120.3, 112.5, 110.5, 95.5, 92.4, 89.1, 82.6, 55.7, 50.6, 35.5, 27.7.

5-(2-Methoxyphenyl)-10-(1,1-dimethylethyl)-11*H*-benzo[*b*]fluorene (73a) To 0.097 g of **69a** (0.256 mmol) in 10 mL of anhydrous toluene under a nitrogen atmosphere was added 0.33 mL of a 1.0 M solution of potassium *t*-butoxide (0.33 mmol) in 2-methyl-2-propanol. The reaction mixture was then heated to reflux for 5 h. After the reaction mixture was allowed to cool to room temperature, 10 mL of water and 20 mL of methylene chloride were introduced, and the organic layer was separated, dried over sodium sulfate, and concentrated. The residue was purified by flash column chromatography (silica gel/20 % methylene chloride in hexanes) to provide 0.073 g of **73a** (0.192 mmol, 75%) as a light yellow liquid and 0.002g of **74a** (0.005 mmol, 2%). **73a**: IR

1330, 811, 739 cm^{-1}; ^1H (C_6D_6, 600 MHz) δ 8.62 (1 H, d, J = 9.0 Hz), 7.89 (1 H, d, J = 8.4 Hz), 7.35−7.27 (4 H, m), 7.22 (1 H, t, J = 7.2 Hz), 7.11 (1 H, t, J = 7.2 Hz), 7.04−7.02 (2 H, m), 6.86 (1 H, d, J = 7.8 Hz), 6.78 (1 H, d, J = 8.4 Hz), 4.21 (1 H, d, J = 21.0 Hz), 4.13 (1 H, d, J = 21.0 Hz), 3.06 (3 H, s), 1.71 (9 H, s); ^{13}C ($CDCl_3$, 67.9 MHz) δ 157.7, 144.2, 140.7, 140.5, 138.4, 137.7, 134.4, 131.8, 131.5, 129.6, 129.3, 128.3, 128.0, 127.2, 126.7, 126.3, 124.0, 123.8, 123.2, 123.1, 121.5, 111.6, 55.8, 40.2, 38.8, 34.4; MS *m/z* 378 (M^+), 363, 349, 321; HRMS calcd for $C_{28}H_{26}O$ 378.1984, found 378.1971. The ^1H NMR signals attributable to **74a** (ca. 2%) were observed at δ ($CDCl_3$) 6.25 (1 H, s), 3.86 (3 H, s), and 1.23 (9 H, s).

Trimethyl[[2-[[2-(methoxymethyl)phenyl]ethynyl]phenyl]ethynyl]silane (66b). The same procedure was repeated as described for **66a** except that 0.445 g of **65** (1.482 mmol), $Pd(PPh_3)_2Cl_2$ (0.040 g, 0.056 mmol), and copper(I) iodide (0.015 g, 0.080 mmol) in 10 mL of triethylamine were treated with a solution of 0.167 g of **64b** (1.140 mmol) in 5 mL of triethylamine to afford 0.287 g of **66b** (0.900 mmol, 79%) as a colorless liquid: IR 2959, 2156, 1490, 1473, 1250 cm^{-1}; ^1H ($CDCl_3$, 600 MHz) δ 7.31 (1 H, d, J = 7.2 Hz), 7.28−7.23 (2 H, m), 7.11 (1 H, t, J = 7.2 Hz), 7.06−7.00 (4 H, m), 4.52 (2 H, s), 3.22 (3 H, s), 0.01 (9 H, s); ^{13}C ($CDCl_3$, 150 MHz) δ 140.0, 132.6, 132.3, 131.9, 128.7, 128.2, 127.9, 127.4, 127.2, 125.9, 125.4, 121.8, 103.6, 98.6, 92.5, 90.9, 72.6, 58.5, −0.04.

Benzannulated Enediyne 67b. The same procedure was repeated as described for **67a** except that a solution of 0.255 g (0.800 mmol) **66b** in 15 mL of diethyl ether was treated with 6 mL of a 10% sodium hydroxide solution and 15 mL of methanol to afford 0.193 g of **67b** (0.785 mmol, 98%) as a yellow liquid: ^1H ($CDCl_3$, 600 MHz) δ 7.56 (1 H, dd, J = 7.8, 1.2 Hz), 7.55−7.53 (2 H, m), 7.50 (1 H, d, J = 8.4 Hz), 7.36 (1 H, td, J = 7.7, 1.2 Hz), 7.33 (1 H, td, J = 7.8, 1.2 Hz), 7.30−7.26 (2 H, m), 4.80 (2 H, s), 3.47 (3 H, s), 3.37 (1 H, s); 13C (CDCl3, 150 MHz) δ 140.3, 132.7, 132.2, 131.9, 128.8, 128.6, 128.0, 127.21, 127.18, 126.3, 124.3, 121.5, 92.2, 91.0, 82.5,

81.1, 72.6, 58.5. MS *m/z* 341 (MNa^+), 267; HRMS calcd for $C_{21}H_{22}OSi$ (MNa^+) 341.1332, found 341.1334.

α-[[2-[[2-(Methoxymethyl)phenyl]ethynyl]phenyl]ethynyl]-α-(1,1-dimethylethyl)benzenemethanol (68b). The same procedure was repeated as described for **68a** except that 0.165 g (1.015 mmol) of **40** was treated with the lithium acetylide derived from 0.178 g (0.725 mmol) of **67b** and 0.45 mL of a 1.6 M solution of *n*-butyllithium (0.72 mmol) in hexanes to afford 0.284 g (0.696 mmol, 96%) of **68b** as a light yellow liquid: IR 3410, 2961, 1490, 758 cm^{-1}; ^1H (CDCl3, 270 MHz) δ 7.74−7.69 (2 H, m), 7.57−7.53 (2 H, m), 7.46−7.21 (7 H, m), 4.67 (1 H, d, J =12.6 Hz), 4.40 (1 H, d, J =12.4 Hz), 3.31 (3 H, s), 1.68 (1 H, s, broad), 1.07 (9 H, s); ^{13}C ($CDCl_3$, 67.9 MHz) δ 142.4, 139.4, 132.4, 132.2, 128.5, 128.2, 128.07, 128.02, 127.8, 127.5, 127.2, 127.0, 125.6, 125.3, 122.3, 96.8, 92.6, 90.8, 84.4, 79.3, 72.5, 57.7, 39.7, 25.6. MS *m/z* 431 (MNa^+), 359; HRMS calcd for $C_{29}H_{28}O_2$ (MNa^+) 431.1982, found 431.1983.

Benzannulated Enediyne 69b. The same procedure was repeated as described for **69a** except that 0.163 g of **68b** (0.400 mmol) and 0.070 g of triethylsilane (0.601 mmol) was treated with 0.182 g of trifluoroacetic acid (1.602 mmol) to afford 0.141 g (0.360 mmol, 90%) of **69b** as a light yellow liquid: ^1H ($CDCl_3$, 600 MHz) δ 7.54−7.52 (1 H, m), 7.50−7.48 (1 H, m), 7.47 (1 H, d, J = 7.2 Hz), 7.41−7.38 (3 H, m), 7.34 (1 H, t, J =7.8 Hz), 7.29−7.27 (2 H, m), 7.21 (1 H, t, J =7.8 Hz), 7.19−7.17 (3 H, m), 4.70 (1 H, d, J =12.6 Hz), 4.63 (1 H, d, J =13.2 Hz), 3.69 (1 H, s), 3.41 (3 H, s), 1.03 (9 H, s); ^{13}C ($CDCl_3$, 150 MHz) δ 140.2, 139.1, 132.3, 132.11, 132.05, 129.7, 128.5, 128.0, 127.6, 127.4, 127.2, 127.1, 126.7, 126.3, 125.5, 121.7, 95.7, 93.0, 90.3, 82.5, 72.5, 58.5, 50.6, 35.5, 27.7.

5-[2-(Methoxymethyl)phenyl]-10-(1,1-dimethylethyl)-11*H*-benzo[*b*]fluorene (73b). The same procedure was repeated as described for **73a** except that 0.119 g of **69b** (0.303 mmol) was treated with 0.39 mL of a 1.0 M solution of potassium *t*-butoxide (0.39 mmol) in

2-methyl-2-propanol to afford 0.075 g of a mixture of **73b** and **74b** in a 5:1 ratio as a light yellow liquid. The mixture was then dissolved in 8 mL of THF and treated with 1 mL of a 1.0 M BH_3•THF solution under a nitrogen atmosphere. After 5 h of stirring at room temperature, 10 mL of water and 10 mL of diethyl ether were added. The organic layer was separated, and the aqueous layer was back extracted with diethyl ether. The combined organic layers were washed with brine and water, dried over sodium sulfate, and concentrated. Purification of the residue by flash column chromatography (silica gel/30% methylene chloride in hexanes) afforded 0.057 g of **73b** (0.145 mmol, 48%) as a colorless liquid: IR 2923, 1088, 764, 732 cm^{-1}; ^1H ($CDCl_3$, 600 MHz) δ 8.62 (1 H, d, J = 9.6 Hz), 7.77 (1 H, d, J = 7.8 Hz), 7.60 (1 H, t, J = 7.8 Hz), 7.49−7.41 (4 H, m), 7.29 (1 H, t, J = 7.2 Hz), 7.22 (1 H, d, J = 7.8 Hz), 7.19 (1 H, t, J = 7.2 Hz), 6.96 (1 H, t, J = 7.8 Hz), 6.22 (1 H, d, J = 7.8 Hz), 4.522 (1 H, d, J = 21 Hz), 4.504 (1 H, d, J = 21 Hz), 4.07 (1 H, d, J = 13.8 Hz), 4.04 (1 H, d, J = 13.8 Hz), 3.10 (3 H, s), 1.93 (9 H, s); ^{13}C ($CDCl_3$, 67.9 MHz) δ 144.1, 141.2, 140.1, 138.3, 137.9, 137.5, 137.4, 134.1, 131.4, 130.7, 130.3, 128.2, 128.0, 127.0, 126.5, 124.3, 123.9, 123.4, 123.1, 71.7, 58.3, 40.2, 38.9, 34.4; MS *m/z* 392 (M^+), 377, 343; HRMS calcd for $C_{29}H_{28}O$ 392.2140, found 392.2135. The ^1H NMR signals attributable to **74b** (ca. 10%) before treatment with BH_3•THF were observed at δ ($CDCl_3$) 6.36 (1 H, s), 4.31 (1 H, d, J = 13.2 Hz), 3.83 (1 H, d, J = 13.2 Hz), 2.9 (3 H, s), and 1.21 (9 H, s).

1-Iodo-2-(4,4-dimethyl-3-phenyl-1-pentynyl)benzene (83). To 1.032 g (4.528 mmol) of **81** in 10 mL THF under a nitrogen atmosphere at 0 °C was added 3.77 mL of a 2.0 M solution of LDA (7.55 mmol) in THF. After 30 min of stirring, a solution of 0.616 g of **40** (3.774 mmol) in 10 mL of THF was introduced via cannula, and the reaction mixture was allowed to warm to room temperature. After an additional 3 h, 20 mL of water was introduced, and the reaction mixture was extracted with diethyl ether. The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. The residue was purified by flash

chromatography (silica gel/10% diethyl ether in hexanes) to afford 1.476 g of crude **82** as a light yellow liquid. The crude product of **82** without further purification was treated with 0.810 g of triethylsilane (6.983 mmol) and 2.1 g of trifluoroacetic acid (18.4 mmol) to afford 1.382 g (3.699 mmol, 86% for 2 steps) of **83** as a colorless liquid: IR 2966, 1463 cm^{-1}; ^{1}H ($CDCl_3$, 270 MHz) δ 7.83 (1 H, dd, J =7.9, 1.2 Hz), 7.47−7.41 (3 H, m), 7.36−7.23 (4 H, m), 6.96 (1 H, td, J =7.7, 1.7 Hz), 3.69 (1 H, s), 1.09 (9 H, s); ^{13}C ($CDCl_3$, 67.9 MHz) δ 138.9, 138.6, 132.9, 130.5, 129.9, 128.8, 127.6, 126.7, 100.5, 95.5, 85.5, 50.6, 35.7, 27.9. HRMS calcd for $C_{19}H_{19}I$ (MH^+) 374.0604, found 375.0610.

Benzannulated Enediyne 85. To a mixture of 0.193 g of **83** (0.516 mmol), $Pd(PPh_3)_2Cl_2$ (0.018 g, 0.026 mmol), and copper(I) iodide (0.010 g, 0.053 mmol) in 10 mL of triethylamine was added via cannula a solution of 0.102 g of **84** (0.670 mmol) in 3 mL of triethylamine. After 12 h of stirring at 60 °C, 15 mL of a saturated ammonium chloride solution and 15 mL of diethyl ether were added. The organic layer was separated, and the aqueous layer was back extracted with diethyl ether. The combined organic layers were washed with brine and water, dried over sodium sulfate, and concentrated. Purification of the residue by flash column chromatography (silica gel/5% methylene chloride in hexanes) afforded 0.189 g of **85** (0.475 mmol, 92%) as a light yellow liquid: IR 2227, 1481, 758 cm^{-1}; ^{1}H ($CDCl_3$, 270 MHz) δ 8.53−8.46 (1 H, m), 7.90−7.82 (2 H, m), 7.68−7.62 (2 H, m), 7.56−7.48 (3 H, m), 7.44−7.38 (3 H, m), 7.34−7.30 (2 H, m), 7.16−7.12 (3 H, m) 3.71 (1 H, s), 1.01 (9 H, s); ^{13}C ($CDCl_3$, 67.9 MHz) δ 138.9, 133.2, 133.1, 132.3, 132.1, 130.4, 129.7, 128.7, 128.1, 128.0, 127.5, 127.4, 126.7, 126.6, 126.4, 126.3, 125.6, 125.2, 120.9, 95.8, 93.4, 90.9, 82.6, 50.6, 35.5, 27.7. MS *m/z* 399 (MH^+), 359, 279; HRMS calcd for $C_{31}H_{26}$ (MH^+) 399.2107, found 399.2109.

10-(1,1-Dimethylethyl)-5-(1-naphthyl)-11*H*-benzo[*b*]fluorene (86a). To 0.189 g of **85** (0.475 mmol) in 10 mL of anhydrous toluene under a nitrogen atmosphere was added 0.50 mL of a 1.0

M solution of potassium *t*-butoxide (0.50 mmol) in 2-methyl-2-propanol. The reaction mixture was then heated to reflux for 6 h. After the reaction mixture was allowed to cool to room temperature, 10 mL of water and 40 mL of methylene chloride were introduced, and the organic layer was separated, dried over sodium sulfate, and concentrated. The residue was purified by flash column chromatography (silica gel/5 % methylene chloride in hexanes) to provide 0.131 g of **86a** (0.328 mmol, 69%) as a bright yellow liquid: IR 1191, 1015 cm^{-1}; ^1H (C_6D_6, 600 MHz) δ 8.68 (1 H, d, *J* = 9.0 Hz), 7.84 (1 H, d, *J* =7.8 Hz), 7.76 (1 H, d, *J* = 8.4 Hz), 7.60 (1 H, dd, *J* = 8.4, 1.2 Hz), 7.54 (1 H, d, *J* = 8.4 Hz), 7.45 (1 H, dd, *J* = 6.6, 1.2 Hz), 7.41 (1 H, dd, *J* = 8.1, 6.9 Hz), 7.27 (1 H, ddd, *J* = 9.0, 6.6, 1.2 Hz), 7.23 (1 H, d, *J* = 7.2 Hz), 7.19 (1 H, ddd, *J* = 8.4, 6.6, 1.2 Hz), 7.01 (1 H, ddd, *J* = 8.4, 6.6, 1.2 Hz), 6.96 (1 H, td, *J* = 7.2, 1.2 Hz), 6.90 (1 H, ddd, *J* = 8.4, 6.6, 1.2 Hz), 6.65 (1 H, t, *J* = 7.2 Hz), 6.32 (1 H, d, *J* = 7.8 Hz), 4.27 (1 H, d, *J* = 21 Hz), 4.25 (1 H, d, *J* = 21 Hz), 1.81 (9 H, s); ^1H ($CDCl_3$, 270 MHz) δ 8.66 (1 H, d, *J* = 8.7 Hz), 8.07 (1 H, d, *J* = 8.4 Hz), 8.00 (1 H, d, *J* = 8.4 Hz), 7.68 (1 H, t, *J* = 7.7 Hz), 7.52−7.15 (10 H, m), 7.11 (1 H, td, *J* = 7.4, 1.0 Hz), 6.75 (1 H, t, *J* = 7.4 Hz), 5.89 (1 H, d, *J* = 8.2 Hz), 4.56 (2 H, s), 1.96 (9 H, s); ^{13}C ($CDCl_3$, 67.9 MHz) δ 144.2, 141.2, 139.9, 139.1, 137.6, 137.4, 134.9, 133.8, 132.8, 131.4, 130.8, 128.16, 128.03, 127.97, 127.88, 127.7, 126.7, 126.3, 126.2, 124.2, 123.8, 123.5, 123.4, 40.2, 38.9, 34.4; MS *m/z* 398 (M^+), 383, 341; HRMS calcd for $C_{31}H_{26}$ 398.2035, found 398.2028.

1-Ethynyl-2-methoxynaphthalene (76). To a solution of 1.05 g (5.64 mmol) of 2-methoxy-1-naphthaldehyde and 2.80 g of potassium carbonate in 20 mL of anhydrous methanol was added 1.37 g (7.15 mmol) of dimethyl (1-diazo-2-oxopropyl)phosphonate, and the reaction mixture was stirred at room temperature for 6 days. The reaction mixture was then diluted with diethyl ether, washed with a 5% aqueous sodium bicarbonate solution, dried over sodium sulfate, and concentrated. Purification of the residue by flash column chromatography (silica gel/25%

methylene chloride in hexanes) afforded 0.545 g of **76** (3.00 mmol, 53%) as a white solid: IR 3260, 1274, 1083, 809 cm^{-1}; ^{1}H ($CDCl_3$, 270 MHz) δ 8.27 (1 H, d, J = 8.4 Hz), 7.86 (1 H, d, J = 8.9 Hz), 7.79 (1 H, d, J = 8.2 Hz), 7.56 (1 H, ddd, J = 8.2, 6.9, 1.2 Hz), 7.39 (1 H, ddd, J = 8.2, 6.9, 1.2 Hz), 7.27 (1 H, d, J = 9.2 Hz), 4.05 (3 H, s), 3.76 (1 H, s); ^{13}C ($CDCl_3$, 150 MHz) δ 159.8, 134.8, 130.7, 128.4, 128.1, 127.6, 125.1, 124.3, 112.5, 105.0, 86.5, 78.2, 56.6; HRMS calcd for $C_{13}H_{11}O$ (MH^+) 183.0810, found 183.0804.

Benzannulated Enediyne 80. To a mixture of 0.307 g of **83** (0.822 mmol), $Pd(PPh_3)_4$ (0.040 g, 0.035 mmol), and copper(I) iodide (0.015 g, 0.080 mmol) in 10 mL of toluene was added via cannula a solution of 0.150 g of **76** (0.824 mmol) in 5 mL of triethylamine. After 12 h of stirring at 120 °C, 15 mL of a saturated ammonium chloride solution and 15 mL of diethyl ether were added. The organic layer was separated, and the aqueous layer was back extracted with diethyl ether. The combined organic layers were washed with brine and water, dried over sodium sulfate, and concentrated. Purification of the residue by flash column chromatography (silica gel/30% methylene chloride in hexanes) afforded 0.331 g of **80** (0.773 mmol, 94%) as a colorless liquid: IR: 2207, 1271, 1078 cm^{-1}; ^{1}H ($CDCl_3$, 270 MHz) δ 8.43−8.39 (1 H, m), 7.85 (1 H, d, J = 9.2 Hz), 7.82−7.77 (1 H, m), 7.70−7.65 (1 H, m), 7.56−7.52 (1 H, m), 7.43−7.25 (7 H, m), 7.10−7.00 (3 H, m), 4.00 (3 H, s), 3.66 (1 H, s), 0.95 (9 H, s); ^{13}C ($CDCl_3$, 67.9 MHz) δ 158.9, 139.0, 134.5, 132.3, 130.2, 129.7, 128.4, 127.9, 127.8, 127.3, 127.2, 126.4, 126.3, 126.0, 125.7, 124.1, 112.6, 106.5, 97.8, 95.5, 87.3, 82.6, 56.6, 50.5, 35.5, 27.7; HRMS calcd for $C_{32}H_{29}O$ (MH^+) 429.2218, found 429.2217.

5-(2-Methoxy-1-naphthyl)-10-(1,1-dimethylethyl)-11*H*-benzo[*b*]fluorene (86b). The same procedure was repeated as described for **86a** except that 0.295 g of **80** (0.689 mmol) was treated with 0.77 mL of a 1.0 M solution of potassium *t*-butoxide (0.77 mmol) in 2-methyl-2-propanol to afford 0.263 g of **86b** (0.614 mmol, 89%) as a light yellow liquid: IR 1267, 1250, 766 cm^{-1}; ^{1}H

($CDCl_3$, 600 MHz) δ 8.66 (1 H, d, J = 9.0 Hz), 8.11 (1 H, d, J = 9.6 Hz), 7.92 (1 H, d, J = 8.4 Hz), 7.53 (1 H, d, J = 9.0 Hz), 7.44 (1 H, d, J = 7.2 Hz), 7.40 (1 H, ddd, J = 8.4, 6.6, 1.8 Hz), 7.35 (1 H, d, J = 9.0 Hz), 7.31 (1 H, td, J = 6.6, 1.2 Hz), 7.18 (1 H, t, J = 7.8 Hz), 7.13−7.05 (3 H, m), 6.77 (1 H, t, J = 7.8 Hz), 6.08 (1 H, d, J = 7.8 Hz), 4.55 (2 H, s), 3.68 (3 H, s), 1.97 (9 H, s); ^{1}H (C_6D_6, 600 MHz) δ 8.67 (1 H, d, J = 9.0 Hz), 7.90 (1 H, d, J = 9.6 Hz), 7.79 (1 H, d, J = 8.4 Hz), 7.70 (1 H, d, J = 8.4 Hz), 7.42 (1 H, d, J = 8.4 Hz), 7.29 (1 H, t, J = 7.8 Hz), 7.23 (1 H, d, J = 7.2 Hz), 7.17 (1 H, d, J = 6.6 Hz), 7.12 (1 H, t, J = 7.5 Hz), 7.06 (1 H, t, J = 7.5 Hz), 6.98 (1 H, t, J = 7.2 Hz), 6.89 (1 H, t, J = 7.8 Hz), 6.72 (1 H, t, J = 7.5 Hz), 6.53 (1 H, d, J = 7.8 Hz), 4.25 (1 H, d, J = 21.6 Hz), 4.19 (1 H, d, J = 21.6 Hz), 3.13 (3 H, s), 1.77 (9 H, s); ^{13}C ($CDCl_3$, 150 MHz) δ 154.8, 144.2, 141.0, 140.3, 139.3, 137.9, 134.7, 133.9, 131.8, 129.8, 129.5, 128.1, 127.8, 127.2, 127.0, 126.7, 126.6, 126.4, 125.2, 124.1, 123.9, 123.7, 123.3, 122.8, 122.2, 114.4, 56.9, 40.3, 38.9, 34.5; MS *m/z* 428 (M^+), 413, 400, 371; HRMS calcd for $C_{32}H_{28}O$ 428.2140, found 428.2126. Recrystallization from a mixture of isopropyl alcohol and methylene chloride produced a crystal for X-ray structure analysis. Although the week diffracting crystal limited the amount of observed data, the analysis of these data supports the structural assignment of **86b**.

Benzannulated Enediyne 96. The same procedure was repeated as described for **66a** except that 0.200 g of **83** (0.535 mmol), $Pd(PPh_3)_2Cl_2$ (0.016 g, 0.023 mmol), and copper(I) iodide (0.015 g, 0.080 mmol) in 10 mL of triethylamine was treated with a solution of 0.263 g of (trimethylsilyl)acetylene (2.675 mmol) in 5 mL of triethylamine to afford 0.140 g of **96** (0.407 mmol, 76%) as a colorless liquid: ^{1}H ($CDCl_3$, 270 MHz) δ 7.50−7.39 (4 H, m), 7.35−7.20 (5 H, m), 3.69 (1 H, s), 1.09 (9 H, s), 0.24 (9 H, s); ^{13}C ($CDCl_3$, 67.9 MHz) δ 139.1, 132.8, 132.2, 129.8, 128.0, 127.6, 127.2, 126.6, 126.4, 125.3, 104.0, 98.0, 95.5, 82.3, 50.6, 35.5, 27.9, −0.1.

Benzannulated Enediyne 97. The same procedure was repeated as described for **67a** except that a solution of 0.140 g (0.407 mmol) of **96** in 20 mL of diethyl ether was treated with 8 mL of a

10% sodium hydroxide solution and 20 mL of methanol to afford 0.110 g of **97** (0.403 mmol, 99%) as a light yellow liquid: ^{1}H ($CDCl_3$, 270 MHz) δ 7.55−7.44 (4 H, m), 7.38−7.22 (5 H, m), 3.72 (1 H, s), 3.31 (1 H, s), 1.11 (9 H, s); ^{13}C ($CDCl_3$, 67.9 MHz) δ 139.1, 132.5, 132.0, 129.8, 128.4, 127.5, 127.3, 127.1, 126.7, 124.4, 95.7, 82.8, 82.0, 80.7, 50.5, 35.5, 27.8.

1-Iodo-2-(methoxymethyl)naphthalene (93). To a solution of 0.500 g of 1-bromo-2-(methoxymethyl)naphthalene (1.99 mmol) in 10 mL of THF at −78 °C was added dropwise 1.8 mL of a 1.6 M solution of *n*-butyllithium (3.06 mmol) in hexanes. After 1 h of stirring at −78 °C, a solution of 1.02 g of iodine (4.02 mmol) in 10 mL of THF was added dropwise via cannula. The reaction mixture then was allowed to warm to room temperature before 20 mL of a 5% sodium thiosulfate solution was introduced. The organic layer was separated, and the aqueous layer was back extracted with diethyl ether. The combined organic layers were washed with brine and water, dried over sodium sulfate, and concentrated. Purification of the residue by flash column chromatography (silica gel/30% methylene chloride in hexanes) afforded 0.516 g of **93** (1.73 mmol, 87%) as a pale yellow liquid: IR 2922, 1500, 1113, 814 cm^{-1}; ^{1}H ($CDCl_3$, 270 MHz) δ 8.26 (1 H, d, J = 7.7 Hz), 7.83 (1 H, d, J = 8.4 Hz), 7.78 (1 H, dd, J = 7.9, 1.5 Hz), 7.61−7.48 (3 H, m), 4.74 (2 H, s), 3.53 (3 H, s); ^{13}C ($CDCl_3$, 67.9 MHz) δ 139.8, 134.6, 133.6, 132.2, 128.7, 128.3, 127.7, 126.4, 125.8, 103.1, 79.8, 58.6. MS *m/z* 267 (M^+ − OMe); HRMS calcd for $C_{12}H_{11}IO$ (MH^+) 298.9927, found 298.9930.

Benzannulated Enediyne 98. The same procedure was repeated as described for **85** except that a solution of 0.242 g of **93** (0.812 mmol), $Pd(PPh_3)_2Cl_2$ (0.030 g, 0.043 mmol), and copper(I) iodide (0.015 g, 0.080 mmol) in 6 mL of triethylamine was treated with a solution of 0.265 g of **97** (0.974 mmol) in 2 mL of triethylamine to afford 0.255 g of **98** (0.577 mmol, 71%) as a colorless liquid: ^{1}H ($CDCl_3$, 270 MHz) δ 8.51 (1 H, d, J = 7.7 Hz), 7.88−7.83 (2 H, m), 7.67−7.57 (3 H, m), 7.53−7.42 (2 H, m), 7.38−7.32 (4 H, m), 7.12−7.05 (3 H, m), 4.92 (1 H, d, J

= 13.1 Hz), 4.83 (1 H, d, *J* = 12.9 Hz), 3.69 (2 H, s), 3.41 (3 H, s), 0.97 (9 H, s); ^{13}C ($CDCl_3$, 67.9 MHz) δ 139.1, 138.9, 133.2, 132.5, 132.1, 129.6, 128.7, 128.1, 128.0, 127.4, 126.8, 126.6, 126.3, 126.2, 125.5, 125.0, 119.0, 98.3, 96.0, 88.4, 82.7, 72.8, 58.3, 50.5, 35.5, 27.7.

5-[2-(Methoxymethyl)-1-naphthyl]-10-(1,1-dimethylethyl)-11*H*-benzo[*b*]fluorene (86c). The same procedure was repeated as described for **86a** except that 0.142 g of **98** (0.321 mmol) was treated with 0.48 mL of a 1.0 M solution of potassium *t*-butoxide (0.48 mmol) in 2-methyl-2-propanol to afford 0.102 g of **86c** (0.231 mmol, 72%) as a light yellow liquid: IR 2943, 1273, 1248, 774 cm^{-1}; ^{1}H ($CDCl_3$, 270 MHz) δ 8.67 (1 H, d, *J* = 8.9 Hz), 8.12 (1 H, d, *J* = 8.7 Hz), 7.97 (1 H, d, *J* = 8.2 Hz), 7.91 (1 H, d, *J* = 8.6 Hz), 7.47−7.39 (3 H, m), 7.28−7.08 (5 H, m), 6.75 (1 H, t, *J* = 7.7 Hz), 5.89 (1 H, d, *J* = 7.9 Hz), 4.56 (2 H, s), 4.16 (1 H, d, *J* = 13.4 Hz), 4.10 (1 H, d, *J* = 13.3 Hz), 3.09 (3 H, s), 1.98 (9 H, s); ^{13}C ($CDCl_3$, 67.9 MHz) δ 144.1, 141.5, 139.7, 139.2, 137.7, 135.3, 134.3, 134.0, 133.2, 132.7, 131.6, 128.4, 128.1, 127.9, 126.95, 126.91, 126.6, 126.4, 126.0, 125.9, 124.9, 124.5, 123.8, 123.6, 122.9, 71.9, 58.4, 40.3, 39.0, 34.5; MS *m/z* 442 (M^+), 427, 395; HRMS calcd for $C_{33}H_{30}O$ 442.2297, found 442.2283.

1,1′-Binaphthyl 62. To a solution of **86b** (0.234 g, 0.546 mmol) in 10 mL of methylene chloride was added dropwise 0.5 mL of boron tribromide at 0 °C. The reaction mixture was stirred at 0 °C for 2 h before 10 mL of water and 20 mL of methylene chloride were introduced. The organic layer was separated, dried over sodium sulfate, and concentrated. The residue was purified by flash column chromatography (silica gel/50% methylene chloride in hexanes) to provide 0.172 g (0.42 mmol, 76%) of **62** as a pale yellow solid: ^{1}H ($CDCl_3$, 270 MHz) δ 8.69 (1 H, d, *J* = 8.9 Hz), 8.03 (1 H, d, *J* = 8.9 Hz), 7.92 (1 H, d, *J* = 7.9 Hz), 7.47 (1 H, d, *J* = 7.4 Hz), 7.48−7.12 (8 H, m), 7.05 (1 H, d, *J* = 8.4 Hz), 6.83 (1 H, t, *J* = 7.4 Hz), 6.21 (1 H, d, *J* = 7.9 Hz), 4.89 (1 H, br s), 4.59 (1 H, d, *J* = 21 Hz), 4.54 (1 H, d, *J* = 21 Hz), 1.97 (9 H, s); ^{13}C ($CDCl_3$, 67.9 MHz) δ 151.1, 144.2, 142.8, 141.1, 139.3, 138.2, 134.6, 133.5, 132.0, 130.1, 129.3, 128.3, 128.1, 127.5, 126.8,

126.6, 125.1, 124.8, 124.1, 123.9, 123.6, 123.0, 117.6, 117.5, 40.3, 39.1, 34.4; HRMS calcd for $C_{31}H_{26}ONa$ (MNa^+) 437.1881, found 437.1877.

(1*S*)-Camphanates of 62 (99). To a solution of 0.039 g of **62** (0.095 mmol) and 0.2 mL of triethylamine (0.4 mmol) in 3 mL of anhydrous methylene chloride at room temperature under a nitrogen atmosphere was added 0.062 g of (1*S*)-(−)-camphanoyl chloride (0.29 mmol). The mixture was stirred for 12 h and then quenched with a saturated sodium bicarbonate solution. After 5 mL of methylene chloride was added, the organic layer was separated, and the aqueous layer was back extracted with methylene chloride. The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. The residue was purified by flash column chromatography (silica gel/20% ethyl acetate in hexanes). A small fraction of the eluent contained partially separated (1*S*)-camphanates in a 5:1 ratio. The solvent of this fraction was evaporated to afford a white solid: ^{1}H ($CDCl_3$, 600 MHz) δ 8.54 (1 H, d, J = 9.0 Hz), 8.08 (1 H, d, J = 9.0 Hz), 7.96 (1 H, d, J = 8.4 Hz), 7.48 (1 H, dd, J = 9.0, 1.8 Hz), 7.43 (1 H, t, J = 7.2 Hz), 7.39−7.32 (2 H, m), 7.29−7.16 (4 H, m), 7.13 (1 H, t, J = 7.2 Hz), 7.05 (1 H, t, J = 7.8 Hz), 5.96 (1 H, d, J = 8.4 Hz), 4.47 (1 H, d, J = 21.6 Hz), 4.41 (1 H, d, J = 21.0 Hz), 1.87 (9 H, s), 1.63−1.57 (1 H, m), 1.50−1.45 (2 H, m), 1.38−1.32 (1 H, m), 0.80 (3 H, s), 0.07 (3 H, s), 0.00 (3 H, s). A minor set of the ^{1}H NMR signals at δ 5.93 (1 H, d, J = 8.4 Hz), 4.48 (1 H, d, J = 21.6 Hz), 4.43 (1 H, d, J = 21.0 Hz), 0.02 (3 H, s), and 0.01 (3 H, s) attributable to the other camphanate diastereomer were also observed. MS *m/z* 594 (MH^+), 381; HRMS calcd for $C_{41}H_{38}O_4$ (MH^+) 595.2843, found 595.2848.

Experimental Section of Chapter III

1-Ethynyl-2-(phenylethynyl)benzene was prepared according to the reported procedure.[8i] 2,5-Dihydrofuran, anhydrous aluminum trichloride, lithium diisopropylamide (LDA, 2.0 M) in

heptane/THF/ethylbenzene, iodomethane, tri-*n*-butyltinhydride, AIBN, iodotrimethylsilane, phenylsilane, sodium hydride (60% dispersion in mineral oil), 1.6 M solution of *n*-butyllithium in hexanes, and thionyl chloride were purchased from chemical suppliers and were used as received. 2,5-Dicarbomethoxy-3,4-diphenylcyclopentadienone was prepared according to the reported procedures.[66] Diiodosilane was also prepared from the iodine and phenylsilane according to the reported procedure.[70]

Diels-Alder Adduct 147. A mixture of 0.682 g (1.96 mmol) of 2,5-dicarbomethoxy-3,4-diphenylcyclopentadienone and 0.4 mL (5.30 mmol) of 2, 5-dihydrofuran in 20 mL of chloroform was heated under reflux for 15 h. The solvent was removed in vacuo. The residue was purified by recrystallization from methylene chloride and hexanes to afford 0.729 g of **147** (1.74 mmol, 95%) as white solid: *endo*-**147**: IR (neat) 2953, 1780, 1732, 1248, 700 cm^{-1}; ^{1}H ($CDCl_3$, 600 MHz) δ 7.22−7.16 (6 H, m), 7.20−7.09 (4 H, m), 4.12 (2 H, dd, J = 9.7, 1.7 Hz), 3.94−3.88 (2 H, m), 3.68 (6 H, s), 3.52-3.50 (2 H, m); ^{13}C ($CDCl_3$, 150 MHz) δ 188.4, 167.7, 136.5, 133.9, 128.8, 128.4, 128.0, 70.1, 67.5, 52.4, 43.5. Recrystallization of *endo*-**147** from methylene chloride/hexanes produced a crystal suitable for X-ray structure analysis. *exo*-**147**: ^{1}H ($CDCl_3$, 600 MHz) δ 7.23−7.17 (6 H, m), 7.08−7.04 (4 H, m), 4.16−4.09 (2 H, m), 3.87−3.80 (2 H, m), 3.60 (6 H, s), 3.28−3.24 (2 H, m).[65]

Diester 148. To 2.30 g (5.50 mmol) of **147** in 5 mL methylene chloride, 20 mL ethanol was added 10 mL water. The reaction mixture was heated at 50 ^{o}C for 24 hr. The solvent was removed in vacuo. The residue was purified by flash column chromatography (silica gel/20% ethyl acetate in hexanes) to provide 2.14 g (5.45 mmol, 99%) of **148** as a white solid. mp 205−207^{o}C; ^{1}H ($CDCl_3$, 600 MHz) δ 7.11−7.00 (6 H, m), 6.93−6.89 (4 H, m), 4.33−4.26 (2 H, m), 3.93−3.87 (2 H, m), 3.74−3.72 (2 H, m), 3.33 (6 H, s), 3.13−2.99 (2 H, m). Recrystallization of **148** from methylene chloride/ethanol produced a crystal suitable for X-ray structure analysis.

Diketone 149. To a solution of 1.24 g of **148** (3.16 mmol) in 51 mL of THF was added aqueous lithium hydroxide (38 mL, 1.0 M). The resulting solution was refluxed at 65 °C for 18 h and then concentrated under pressure. The residue was diluted with water (50 mL) and extracted with diethyl ether (3 × 10 mL). The diethyl ether extracts were discarded. The aqueous solution was acidified with 1 M hydrochloric acid to pH around 4. The white precipitate was filtered and dried. The crude product was used for next step without any further purification and characterization. A mixture of 1.13 g (3.10 mmol) of solid acid and 8.5 mL of thionyl chloride were refluxed at 70 ^{o}C for 18 h. Then thionyl chloride was removed in vacuo and pumped to extremely dry for two days. To a residue dissolved in 100 mL of anhydrous methylene chloride at 0 °C under a nitrogen atmosphere was added 1.42 g of anhydrous aluminum chloride (10.6 mmol) slowly over a period of 15 minutes. After 2 h at 0 °C, the reaction mixture was allowed to warm to room temperature. After additional 7 h at room temperature, the reaction mixture was cooled to 0 °C and 15 mL of saturated ammonium chloride solution was introduced slowly and the organic layer was separated. The aqueous layer was back extracted with ether. The combined organic layers were washed with brine, water, dried over sodium sulfate, and concentrated. The residue was purified by flash column chromatography (silica gel/ethyl acetate:methylene chloride:hexanes = 1:5:5) to provide 0.757 g (2.31 mmol, 73 %) of **149** as a pale yellow liquid: IR (neat) 2875, 1716, 1265, 732 cm^{-1}; ^{1}H ($CDCl_3$, 600 MHz) δ 8.37 (2 H, d, J = 7.8 Hz), 7.92 (2 H, d, J = 7.2 Hz), 7.79 (2 H, t, J = 7.2 Hz), 7.55 (2 H, t, J = 7.8 Hz), 4.32−4.30 (2 H, m), 4.06−4.04 (2 H, m), 3.21−3.19 (2 H, m), 2.56−2.53 (2 H, m); ^{13}C ($CDCl_3$, 150 MHz) δ 203.2, 145.5, 138.0, 135.3, 132.5, 129.7, 124.8, 124.6, 73.1, 53.4, 42.0. MS *m/z* 329 (MH^+), 307; HRMS calcd for $C_{22}H_{16}O_3$ (MH^+) 329.1178, found 329.1173.

Diketone 150. To 0.206 g (0.627 mmol) of **149** in 15 mL of anhydrous THF under a nitrogen atmosphere at −78 °C was added 0.7 mL of a 2 M solution of lithium diisopropylamide (1.40

mmol) in THF/*n*-heptane. After 30 min of stirring, 0.2 mL of iodomethane was added. After an additional 18 h, 20 mL of saturated ammonium chloride solution was introduced, and the reaction mixture was extracted with diethyl ether. The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. The residue was purified by flash column chromatography (silica gel/ethyl acetate:methylene chloride:hexanes = 1:5:5) to provide 0.212 g (0.596 mmol, 95 %) of **150** as a pale yellow solid : mp 152−154 ^{o}C; ^{1}H ($CDCl_3$, 600 MHz) δ 8.43 (2 H, d, J = 7.8 Hz), 7.88 (2 H, d, J = 7.8 Hz), 7.74 (2 H, td, J = 8.4, 1.2 Hz), 7.54 (2 H, t, J = 7.8 Hz), 4.10−4.07 (2 H, m), 3.11−3.06 (2 H, m), 2.77−2.71 (2 H, m), 1.63 (6 H, s); ^{13}C δ 206.0, 146.9, 136.9, 135.6, 134.9, 129.9, 125.3, 124.8, 72.3, 54.0, 45.4, 27.8. MS *m/z* 356 (M^+), 288; HRMS calcd for $C_{24}H_{20}O_3$ 356.1412, found 356.1413.

Alcohol 151. To 0.452 g (2.24 mmol) of **5** in 15 mL of anhydrous THF under a nitrogen atmosphere at 0 °C was added 1.4 mL of a 1.6 M solution of *n*-butyllithium (2.2 mmol) in hexanes. After 30 min of stirring, a solution of 0.319 g of **150** (0.896 mmol) in 20 mL of THF was introduced via cannula. The reaction mixture was then allowed to warm up to room temperature. After an additional 18 h, 30 mL of water was introduced, and the reaction mixture was extracted with diethyl ether. The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. The residue was purified by flash column chromatography (silica gel/ethyl acetate:methylene chloride:hexanes = 1:10:10) to provide 0.465 g (0.833 mmol, 93%) of **151** as a yellow liquid: ^{1}H ($CDCl_3$, 600 MHz) δ 8.53 (1 H, d, J = 8.4 Hz), 8.00 (1 H, d, J = 7.8 Hz), 7.82 (2 H, d, J = 7.2 Hz), 7.61 (1 H, t, J = 7.2 Hz), 7.60−7.57 (2 H, m), 7.44 (2 H, t, J = 7.8 Hz), 7.44 (2 H, d, J = 6.6 Hz), 7.36−7.27 (6 H, m), 6.28 (1 H, s), 5.24 (1 H, d, J = 9.6 Hz), 3.88 (1 H, t, J = 7.2 Hz), 3.82 (1 H, q, J = 7.2 Hz), 3.13−3.10 (1 H, m), 3.05−3.00 (1 H, m), 2.08 (1 H, t, J = 5.4 Hz), 1.46 (3 H, s), 1.44 (3 H, s); ^{13}C ($CDCl_3$, 150 MHz) δ 206.7, 148.3, 146.8, 141.0, 138.1, 135.4, 134.2, 132.6, 132.2, 132.1, 131.7, 129.2, 129.1, 128.5,

128.4, 128.3, 128.0, 127.9, 126.6, 125.9, 124.9, 124.4, 124.2, 124.0, 122.9, 93.1, 88.2, 86.9, 80.7, 77.5, 77.2, 77.0, 76.5, 70.9, 68.6, 60.0, 49.8, 47.0, 45.3, 31.9, 26.1. MS *m/z* 581 (MNa^+), 541; HRMS calcd for $C_{40}H_{30}O_3$ (MNa^+) 581.2087, found 556.2086.

***cis*-152, *trans*-152.** To 0.152 g (0.752 mmol) of **5** in 10 mL of anhydrous diethyl ether under a nitrogen atmosphere at 0 °C was added 0.48 mL of a 1.6 M solution of *n*-butyllithium (0.77 mmol) in hexanes. After 30 min of stirring, a solution of 0.102 g of **150** (0.286 mmol) in 5 mL of diethyl ether was introduced via cannula, and 20 mL of anhydrous benzene was added to the mixture. After an additional 10 h, 30 mL of water was introduced, and the reaction mixture was extracted with diethyl ether. The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. The residue was purified by flash column chromatography (silica gel/ethyl acetate:methylene chloride:hexanes = 1:4:4) to provide 0.142 g (0.187 mmol, 65%) of ***cis*-152** as a pale yellow solid, 0.013 g of ***trans*-152** (0.0171 mmol, 6%) as a yellow solid and 0.029 g of **151** (0.0520 mmol, 18%) as yellow liquid. ***cis*-152**: ^1H ($CDCl_3$, 600 MHz) δ 8.05 (2 H, d, J = 7.2 Hz), 7.52 (2 H, dd, J = 7.2, 1.2 Hz), 7.40−7.37 (6 H, m), 7.33−7.26 (6 H, m), 7.20 (2 H, td, J = 7.2, 1.2 Hz), 7.16 (2 H, td, J = 7.2, 1.2 Hz), 7.11(2 H, td, J = 7.2, 1.2 Hz), 7.00 (2 H, td, J = 7.8, 1.2 Hz), 4.45 (4 H, d, J = 6.0 Hz), 2.96−2.92 (2 H, m), 2.89 (2 H, s), 1.41 (6 H, s); ^{13}C ($CDCl_3$, 150 MHz) δ 148.1, 137.2, 136.6, 132.0, 131.72, 131.65, 128.8, 128.3, 128.2, 127.99, 127.95, 127.8, 125.7, 124.8, 124.5, 123.3, 123.1, 94.8, 92.9, 87.9, 87.5, 79.6, 68.8, 57.6, 48.2, 27.9. MS *m/z* 783 (MNa^+); HRMS calcd for $C_{56}H_{40}O_3$ 760.2977, found 783.2832 (MNa^+). Recrystallization of ***cis*-152** from methylene chloride/ethanol produced a crystal suitable for X-ray structure analysis. ***trans*-152**: ^1H ($CDCl_3$, 600 MHz) δ 8.22 (1 H, d, J = 7.0 Hz), 8.05 (1 H, d, J = 7.7 Hz), 7.81 (1 H, d, J = 6.7 Hz), 7.64−7.54 (3 H, m), 7.51−7.41 (6 H, m), 7.39−7.17 (14 H, m), 6.73 (1 H, s), 5.15 (1 H, d, J = 9.7 Hz), 4.65 (1 H, t, J = 8.7 Hz), 3.88−3.81 (1 H, m), 3.72−3.67 (1 H, m), 3.05−2.94 (1 H, m), 2.78−2.74 (2 H, m), 1.47 (3 H, s), 1.46 (3 H, s); ^{13}C

($CDCl_3$, 150 MHz) δ 148.0, 146.9, 138.3, 138.0, 137.3, 136.7, 132.3, 132.1, 131.9, 131.73, 131.70, 131.6, 129.3, 128.9, 128.47, 128.42, 128.36, 128.31, 126.25, 128.2, 128.0, 127.8, 125.9, 125.2, 124.6, 124.3, 124.1, 123.7, 123.0, 122.8, 95.3, 94.1, 93.2, 93.1, 88.2, 87.8, 87.4, 86.2, 80.5, 79.2, 69.5, 69.4, 58.0, 56.4, 49.8, 47.1, 32.6, 26.1.

Diketone 153. To **152** (0.142 g, 0.187 mmol) in 10 mL of THF at 0 °C was added via cannula a solution of thionyl chloride (0.1 mL, 1.4 mmol) and anhydrous pyridine (0.16 mL) in 5 mL of THF. The reaction mixture then was allowed to warm to room temperature. After an additional 12 h, 10 mL of water was introduced, and the reaction mixture was extracted with 30 mL of diethyl ether. The combined organic extracts were washed with water, dried over magnesium sulfate, and concentrated. Flash column chromatography (silica gel/ethyl acetate:methylene chloride:hexanes = 1:5:5) provided 0.080 g of **153** (0.106 mmol, 57%) as a yellow solid: IR (neat) 2947, 1719, 1366, 1216, 900 cm^{-1}; ^1H ($CDCl_3$, 600 MHz) δ 8.45 (2 H, d, J = 7.2 Hz), 7.75 (2 H, d, J = 7.8 Hz), 7.63−7.58 (8 H, m), 7.48−7.46 (4 H, m), 7.32 (2 H, d, J = 8.4 Hz), 7.24 (2 H, d, J = 7.8 Hz), 7.18 (2 H, t, J = 7.8 Hz), 6.42 (2 H, d, J = 7.2 Hz), 4.37−4.32 (2 H, m), 3.90 (2 H, t, J = 8.4 Hz), 2.87−2.84 (2 H, m), 2.06 (6 H, s); ^{13}C ($CDCl_3$, 150 MHz) δ 192.6, 151.2, 145.1, 142.8, 141.5, 137.94, 137.88, 136.9, 136.3, 135.0, 134.4, 131.9, 131.0, 129.8, 129.7, 129.3, 128.7, 128.3, 125.1, 124.6, 123.9, 123.8, 121.9, 73.6, 52.3, 46.4, 29.5; MS *m/z* 756 (M^+); HRMS calcd for $C_{56}H_{36}O_3$ 756.2664, found 756.2655. Recrystallization of **153** from methylene chloride/hexanes produced a crystal suitable for X-ray structure analysis.

Diiodide 155. To 0.420 g (1.18 mmol) of **150** in 10 mL of anhydrous methylene chloride under a nitrogen atmosphere at rt was added 0.8 mL of trimethylsilyl iodide. After 18 h of stirring, the reaction mixture was concentrated to remove TMSI and methylene chloride. The residue was purified by flash column chromatography (silica gel/ethyl acetate:methylene chloride:hexanes = 1:50:50) to provide 0.599 g (1.01 mmol, 86%) of **155** as a pale yellow solid, ^1H ($CDCl_3$, 270

MHz) δ 8.30 (2 H, d, J = 7.9 Hz), 7.89 (2 H, d, J = 7.6 Hz), 7.75 (2 H, t, J = 7.6 Hz), 7.54 (2 H, t, J = 7.4 Hz), 3.08 (6 H, br), 1.55 (3 H, s), 1.49 (3 H, s); ^{13}C ($CDCl_3$, 67.9 MHz)δ 204.0, 146.1, 135.7, 134.8, 129.8, 125.6, 124.9, 56.7, 47.3 (br), 28.0 (br). MS *m/z* 594 (MH^+), 467; HRMS calcd for $C_{24}H_{20}I_2O_2$ (MH^+) 594.9631, found 594.9623.

Alcohol 156. To 0.464 g (2.30 mmol) of **5** in 10 mL of anhydrous diethyl ether under a nitrogen atmosphere at 0 °C was added 1.4 mL of a 1.6 M solution of *n*-butyllithium (2.3 mmol) in hexanes. After 30 min of stirring, a solution of 0.440 g of **155** (0.741 mmol) in 20 mL of diethyl ether was introduced via cannula, and 30 mL of anhydrous benzene was added to the mixture. After an additional 18 h, 30 mL of water was introduced, and the reaction mixture was extracted with diethyl ether. The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. The residue was purified by flash column chromatography (silica gel/ethyl acetate:methylene chloride:hexanes = 2:50:50) to provide 0.537 g (0.674 mmol, 65%) of **156** as a pale yellow solid: ^{1}H ($CDCl_3$, 600 MHz) δ 8.27 (1 H, d, J = 7.8 Hz), 7.87 (1 H, d, J = 7.2 Hz), 7.82 (1 H, dd, J = 7.8, 0.6 Hz), 7.47−7.45 (2 H, m), 7.43−7.41 (2 H, m), 7.40−7.39 (1 H, m), 7.36−7.31 (3 H, m), 7.28−7.22 (2 H, m) 7.20−7.12 (4 H, m), 7.06 (1 H, t, J = 7.8 Hz), 4.33 (1 H, dd, J = 10.2, 3.6 Hz), 4.21 (1 H, t, J = 4.8 Hz), 3.76 (1 H, dd, J = 11.4, 4.8 Hz), 3.27 (1 H, q, J = 4.8 Hz), 2.70 (1 H, dt, J = 12, 4.2 Hz), 2.33 (1 H, dd, J = 11.4, 4.8 Hz), 2.03 (1 H, s, br), 1.28 (3 H, s), 1.22 (3 H, s).

Ketone 158. To **151** (0.382 g, 0.685 mmol) in 10 mL of THF at 0 °C was added via cannula a solution of thionyl chloride (0.30 mL, 4.1 mmol) and anhydrous pyridine (0.55 mL) in 10 mL of THF. The reaction mixture then was allowed to warm to room temperature. After an additional 10 h, 10 mL of water was introduced, and the reaction mixture was extracted with 20 mL of diethyl ether. The combined organic extracts were washed with water, dried over magnesium sulfate, and concentrated. The residue was then purified by flash column chromatography (silica

gel/ethyl acetate:methylene chloride:Hexanes = 1:5:5) provided 0.331 g of **158** (0.596 mmol, 87%) as a yellow solid: mp 268 ^{o}C turned black without melting; ^{1}H ($CDCl_3$, 600 MHz) δ 8.42 (1 H, d, J = 7.2 Hz), 7.90 (1 H, d, J = 7.2 Hz), 7.81 (1 H, t, J = 7.8 Hz), 7.73 (1 H, d, J = 7.2 Hz), 7.64−7.58 (3 H, m), 7.53 (1 H, t, J = 7.8 Hz), 7.52 (1 H, td, J = 7.2, 1.8 Hz), 7.45 (2 H, t, J = 7.8 Hz), 7.32 (1 H, dd, J = 7.8, 1.2 Hz), 7.25 (1 H, t, J = 6.6 Hz), 7.19 (1 H, t, J = 7.8 Hz), 6.41 (1 H, d, J = 7.8 Hz), 4.18 (1 H, t, J = 8.4 Hz), 4.15 (1 H, t, J = 8.4 Hz), 3.86 (1 H, t, J = 8.4 Hz), 3.17 (1 H, q, J = 9.6 Hz), 2.77 (1 H, t, J = 9.6 Hz), 2.73 (1 H, t, J = 7.8 Hz), 1.96 (3 H, s), 1.75 (3 H, s); ^{13}C ($CDCl_3$, 150 MHz) δ 206.5, 192.9, 150.0, 148.5, 145.1, 143.1, 140.4, 138.1, 137.8, 136.7, 136.6, 136.3, 135.5, 135.1, 134.48, 134.44, 132.0, 131.2, 129.8, 129.7, 129.4, 129.31, 129.25, 128.7, 128.4, 126.6, 125.6, 124.8, 124.7, 123.94, 123.87, 120.2, 73.3, 72.7, 55.6, 52.0, 46.9, 44.9, 29.5, 28.0. MS *m/z* 556 (M^+), 487; HRMS calcd for $C_{40}H_{28}O_3$ 556.2038, found 556.2051. Recrystallization of **158** from methylene chloride/ethanol produced a crystal suitable for X-ray structure analysis.

Diiodide 159. To 0.331 g (0.595 mmol) of **158** in 10 mL of anhydrous methylene chloride under a nitrogen atmosphere at room temperature was added 1.0 mL of trimethylsilyl iodide. After 18 h of stirring, the reaction mixture was concentrated to remove TMSI and methylene chloride. The residue was purified by flash column chromatography (silica gel/ethyl acetate:methylene chloride:hexanes = 1:50:50) to provide 0.402 g (0.506 mmol, 85%) of **159** as a bright yellow solid, mp 215 ^{o}C turned black without melting; IR 2927, 1719, 1701, 1612 cm^{-1}; ^{1}H ($CDCl_3$, 600 MHz) δ 8.28 (1 H, d, J = 7.8 Hz), 8.26 (1 H, d, J = 7.8 Hz), 7.83 (1 H, d, J = 7.2 Hz), 7.81 (1 H, d, J = 7.2 Hz), 7.77 (1 H, t, J = 7.2 Hz), 7.64−7.59 (3 H, m), 7.54 (1 H, t, J = 7.8 Hz), 7.50 (1 H, t, J = 7.8 Hz), 7.48−7.45 (3 H, m), 7.34 (1 H, d, J = 8.4 Hz), 7.24 (1 H, t, J = 7.2 Hz), 7.18 (1 H, t, J = 7.2 Hz), 6.41 (1 H, d, J = 7.8 Hz), 4.76 (1 H, dd, J = 10.8, 3.6 Hz), 4.53−4.51 (1 H, m), 3.84 (1 H, t, J = 11.4 Hz), 3.23 (1 H, dt, J = 12.0, 3.6 Hz), 2.55 (2 H, d, J = 3.6 Hz), 1.76 (3 H,

s), 1.67 (3 H, s); ^{13}C ($CDCl_3$, 150 MHz) δ 203.5, 192.8, 148.2, 146.5, 145.0, 140.7, 140.4, 138.7, 138.4, 138.0, 136.8, 136.4, 135.7, 135.0, 134.4, 134.0, 132.3, 131.2, 129.9, 129.7, 129.32, 129.29, 129.2, 128.8, 128.4, 126.5, 126.2, 125.7, 124.6, 124.3, 123.9, 121.0, 56.0, 55.3, 49.4, 43.4, 30.9, 25.0, 8.4, −0.9. MS *m/z* 795 (MH^+), 638; HRMS calcd for $C_{40}H_{28}I_2O_2$ (MH^+) 795.0257, found 795.0264. Recrystallization of **159** from methylene chloride/hexanes produced a crystal suitable for X-ray structure analysis.

Alcohol 160. To a solution of 0.477 g of **5** (0.601 mmol) in 20 mL of anhydrous THF under a nitrogen atmosphere at −10 ^{o}C was added 0.1 M lthium acetylide/THF solution 6.1mL via a syringe. The 0.1 M lithium acetylide solution was prepared from 0.329 g (1.63 mmol) of **159** in 15 mL THF under a nitrogen atmosphere at 0 °C and 1.0 mL of a 1.6 M solution of *n*-butyllithium (1.6 mmol) in hexanes. After 10 min of stirring, 20 mL of water was introduced, and the reaction mixture was extracted with diethyl ether. The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. The residue was purified by flash column chromatography (silica gel/ethyl acetate:methylene chloride:hexanes = 1:50:50) to provide 0.503 g (0.505 mmol, 84%) of **160** as a yellow solid: mp 175 ^{o}C turned dask without meling; IR 2340, 1702, 1613 cm^{-1}; ^{1}H ($CDCl_3$, 600 MHz) δ 8.24 (1 H, d, *J* = 7.2 Hz), 8.04 (1 H, d, *J* = 7.8 Hz), 7.81 (2 H, d, *J* = 6.6 Hz), 7.63−7.56 (3 H, m), 7.53 (1 H, d, *J* = 7.8 Hz), 7.49−7.39 (6 H, m), 7.36 (1 H, t, *J* = 7.8 Hz), 7.29−7.20 (4 H, m) 7.16 (1 H, td, *J* = 7.8, 1.2 Hz), 7.13 (1 H, td, *J* = 7.2, 1.2 Hz), 6.40 (1 H, d, *J* = 7.8 Hz), 4.53−4.49 (2 H, m), 4.33 (1 H, t, *J* = 11.4 Hz), 3.96 (1 H, td, *J* = 11.4, 4.2 Hz), 3.11 (1 H, td, *J* = 11.4, 4.2 Hz), 2.40(1 H, dd, *J* = 11.4, 4.8 Hz), 2.92 (1 H, br), 1.80 (3 H, s), 1.43 (3 H, s); ^{13}C ($CDCl_3$, 150 MHz) δ 193.1, 148.8, 148.5, 145.1, 141.0, 140.0, 139.2, 138.3, 137.7, 137.1, 136.6, 135.0, 134.1, 132.1, 132.0, 131.9, 131.8, 131.1, 130.0, 129.2, 129.18, 128.7, 128.6, 128.56, 128.4, 128.3, 127.9, 127.8, 127.1, 126.0, 125.9, 125.0, 124.3, 123.8, 123.6, 123.0, 122.8, 119.3, 96.0, 93.3, 89.2, 87.7, 78.7, 62.7, 54.9,

50.5, 44.3, 27.4, 24.8, 5.1, 0.7. MS *m/z* 996 (M^+), 868; HRMS calcd for $C_{56}H_{38}I_2O_2$ (M^+) 996.0961, found 996.0935.

Diketone 154, Spiro-162, Alcohol 163. To **160** (0.303 g, 0.304 mmol) in 10 mL of THF at 0 °C was added via cannula a solution of thionyl chloride (0.25 mL, 3.4 mmol) and anhydrous pyridine (0.45 mL) in 10 mL of THF. The reaction mixture then was allowed to warm to room temperature. After an additional 18 h, 20 mL of water was introduced, and the reaction mixture was extracted with 20 mL of diethyl ether. The combined organic extracts were washed with water, dried over magnesium sulfate, and concentrated. The crude product was directly for next oxidation step without any further purification. To a solution of crude solid product in 20 mL toluene was added 0.060 g of MnO_2 at room temperature. After 2 days of stirring, MnO_2 was filtered out followed by evaporation to remove toluene. The residue was then purified by flash column chromatography (silica gel/50% methylene chloride in hexanes) to afford 0.143 g of **154** (0.144 mmol, 47 %) as a orange-yellow solid, (silica gel/30% methylene chloride in hexanes) 0.126 g of **162** (0.125 mmol, 41 %) as a bright yellow solid and (silica gel/ethyl acetate:methylene chloride:hexanes = 1:50:50) 0.006 g of **163** (0.006 mmol, 2 %) as a yellow solid: **154**: mp 247^{o}C turned black without melting; IR 3058, 2121, 1698, 1602 cm^{-1}; ^1H ($CDCl_3$, 600 MHz, room temperature) δ 8.36 (2 H, br), 7.83 (2 H, d, *J* = 7.2 Hz), 7.64−7.59 (6 H, m), 7.56 (2 H, t, *J* = 7.8 Hz), 7.52 (2 H, d, *J* = 7.2 Hz), 7.45 (2 H, t, *J* = 6.6 Hz), 7.33 (2 H, d, *J* =8.4 Hz), 7.26 (2 H, td, *J* = 7.2, 0.6 Hz), 7.19 (2 H, td, *J* = 7.8, 1.2 Hz), 6.41 (2 H, d, *J* = 7.8 Hz), 4.23 (2 H, br), 3.80 (2 H, br), 2.72 (2 H, br), 2.05 (6 H, s); ^1H ($CDCl_3$, 600 MHz, at −60 ^{o}C) δ 8.53 (1 H, d, *J* = 7.2 Hz), 8.14 (1 H, d, *J* = 7.2 Hz), 7.83 (2 H, d, *J* = 7.2 Hz), 7.80 (2 H, d, *J* = 7.2 Hz), 7.73 (1 H, t, *J* = 6.6 Hz), 7.63−7.62 (4 H, m), 7.49 (2 H, d, *J* = 7.8 Hz), 7.46−7.42 (2 H, m), 7.39−7.35 (2 H, m), 7.28−7.27 (2 H, m), 7.22−7.19 (2 H, m), 6.25 (1 H, d, *J* = 7.8 Hz), 6.27(1 H, d, *J* = 7.8 Hz), 4.96 (1 H, d, *J* = 7.2 Hz), 4.71 (1 H, s, br), 3.72 (1 H, d, *J* = 12 Hz), 3.02 (1 H, t, *J* = 11.4

Hz), 2.42 (1 H, d, *J* = 11.4 Hz), 2.22 (1 H, s, br), 2.08 (3 H, s), 1.88 (3 H,s); ^{13}C ($CDCl_3$, 150 MHz, room temperature) δ 193.3, 149.2, 144.9, 140.9, 138.3, 138.2, 136.8, 136.4, 135.1, 134.5, 132.4, 131.0, 129.9, 129.7, 129.34, 129.30, 128.8, 128.4, 126.8, 125.3, 124.4, 123.9, 121.1 (br), 56.4 (br), 49.1 (br), 4.6 (br). MS *m/z* 1017 (MNa^+), 995; HRMS calcd for $C_{56}H_{36}I_2O_2$ (MNa^+) 1017.0703, found 1017.0698. Recrystallization of **154** from methylene chloride/hexanes/ethyl acetate produced a crystal suitable for X-ray structure analysis.**162**: mp 225 ^{o}C turned dark without melting; IR 3058, 2967, 2325, 1703, 1614 cm^{-1}; ^{1}H ($CDCl_3$, 600 MHz) δ 8.48 (1 H, d, *J* = 7.8 Hz), 8.20 (1 H, d, *J* = 7.2 Hz), 7.76 (1 H, d, *J* = 6.6 Hz), 7.73 (1 H, d, *J* = 7.8 Hz), 7.65−7.58 (3 H, m), 7.57−7.53 (3 H, m), 7.51−7.48 (3 H, m), 7.35 (1 H, d, *J* = 7.8 Hz), 7.52 (2 H, d, *J* = 7.2 Hz), 7.45 (2 H, t, *J* = 6.6 Hz), 7.33 (2 H, d, *J* =8.4 Hz), 7.32−7.29 (2 H, m), 7.20 (1 H, td, *J* = 7.2, 0.6 Hz), 7.15 (1 H, td, *J* = 7.8, 1.2 Hz), 7.12 (1 H, d, *J* = 7.8 Hz), 7.04 (1 H, t, *J* = 7.2 Hz), 6.93 (1 H, br), 6.40 (1 H, d, *J* = 7.8 Hz), 4.36−4.34 (1 H, m), 4.05 (1 H, dd, *J* = 10.2, 3 Hz), 3.62 (1 H, t, *J* = 11.4 Hz), 3.19 (1 H, dt, *J* = 13.2, 3.6 Hz), 2.40 (1 H, dd, *J* = 11.4, 3 Hz), 1.83 (3 H, s), 1.78 (3 H, s), 1.65 (1 H, dd, *J* = 11.4, 5.4 Hz); ^{13}C ($CDCl_3$, 150 MHz) δ 193.0, 152.7, 148.8, 148.3, 148.1, 147.0, 145.1, 142.5, 141.2, 140.5, 140.1, 138.6, 137.8, 137.3, 137.1, 136.6, 135.2, 134.1, 133.2, 132.1, 131.2, 130.2, 130.1, 129.8, 129.7, 129.4, 129.24, 129.22, 128.8, 128.79, 128.6, 128.3, 127.8, 127.3, 126.4, 125,5, 125.1, 125.0, 124.2, 123.9, 123.8, 120.6, 118.1, 112.7, 74.9, 57.3, 54.5, 51.9, 43.7, 32.0, 25.1, 6.7, 0.2. MS *m/z* 1014 (M^+), 637; HRMS calcd for $C_{56}H_{37}ClI_2O$ (MH^+) 1015.0695, found 1015.0686. Recrystallization of **162** from methylene chloride/hexanes produced a crystal suitable for X-ray structure analysis. **163:** ^{1}H ($CDCl_3$, 600 MHz) δ 8.54 (1 H, d, *J* = 7.8 Hz), 8.18 (1 H, d, *J* = 7.2 Hz), 7.81 (1 H, d, *J* = 7.2 Hz), 7.75 (1 H, d, *J* = 7.2 Hz), 7.65−7.58 (6 H, m), 7.52 (1 H, d, *J* = 7.8 Hz), 7.49 (1 H, d, *J* = 7.2 Hz), 7.46 (1 H, d, *J* = 7.2 Hz), 7.44−7.41 (3 H, m), 7.30 (1 H, t, *J* = 7.2 Hz), 7.27−7.25 (2 H, m) 7.19 (1 H, t, *J* = 7.8 Hz), 7.08 (1 H, d, *J* = 7.8 Hz), 6.53 (1 H, s, br), 6.50 (1 H, d, *J* = 7.8 Hz),

6.37 (1 H, d, *J* = 7.2 Hz), 4.96 (2 H, s, br), 4.14−4.11 (1 H, m), 3.85 (1 H, s, br), 3.17−3.13 (1 H, m) 2.95, (1 H, s, br), 2.33 (1 H, m, br), 2.14 (3 H, s), 2.01 (1 H, m, br), 2.03 (3 H, s); ^{13}C ($CDCl_3$, 150 MHz) δ 193.9, 148.8, 146.6, 145.8, 144.8, 140.0, 139.8, 138.5, 138.2, 138.1, 137.9, 137.6, 136.9, 136.2, 135.6, 135.4, 134.6, 132.7, 132.3, 131.7, 131.3, 130.2, 129.9, 129.8, 129.7, 129.4, 129.3, 129.2, 129.17, 128.9, 128.7, 128.4, 128.2, 128.0, 127.8, 127.3, 125.2, 125.0, 124.5, 124.4, 123.9, 123.8, 122.6 (br), 118.3 (br), 74.3, 58.5, 55.1, 52.8 (br), 47.9 (br), 8.0 (br), 3.5 (br). MS *m/z* 1019 (MNa^+), 979; HRMS calcd for $C_{56}H_{36}I_2O_2$ (MNa^+) 1019.0859, found 1019.0889. Recrystallization of **163** from methylene chloride/hexanes/ethyl acetate produced a crystal suitable for X-ray structure analysis.

I_2-Hydrocarbon 165, Ketone 166. To **154** (0.038 g, 0.038 mmol) in 8 mL of chloroform was added 0.5 mL freshly prepared 1.0 M diiodosilane[70] at 40 ^{o}C under a nitrogen gas atmosphere. After 2 days of stirring, the reaction mixture was quenched with 2 mL 20 % aqueous $NaHCO_3$. The aqueous layer was separated and back extracted twice with methylene chloride, and the combined organic layers were dried over sodium sulfate and concentrated. The residue was then purified by flash column chromatography (silica gel/30% methylene chloride in hexanes) to afford 0.028 g of **165** (0.028 mmol, 76 %) as a white solid and (silica gel/50% methylene chloride in hexanes) 0.001 g **166** (0.001 mmol, 3 %) as a pale yellow solid. **165**: ^{1}H ($CDCl_3$, 600 MHz) δ 7.66 (1 H, dt, *J* = 7.2, 1.2 Hz), 7.63−7.41 (12 H, m), 7.36 (1 H, d, *J* = 7.2 Hz), 7.28−7.24 (2 H, m), 7.21 (1 H, dt, *J* = 7.2, 0.6 Hz), 7.03 (1 H, t, *J* = 7.8 Hz), 7.01 (1 H, t, *J* = 7.8 Hz), 6.95 (1 H, d, *J* = 8.4 Hz), 7.65−6.62 (2 H, m), 6.52 (1 H, d, *J* = 7.8 Hz), 4.91 (1 H, d, *J* = 7.8 Hz), 4.67 (1 H, dd, *J* = 9.6, 3.0 Hz), 4.48 (1 H, d, *J* = 22.2 Hz), 4.43 (1 H, d, *J* = 21.0 Hz), 4.34 (1 H, d, *J* = 21.6 Hz), 4.23 (1 H, d, *J* = 6.6 Hz), 4.12 (1 H, d, *J* = 22.2 Hz), 3.97 (1 H, d, *J* = 6.6 Hz), 3.70 (1 H, dd, *J* = 12.0, 3.6 Hz), 3.44 (1 H, d, *J* = 9.0 Hz), 2.81 (1 H, d, *J* = 12.0 Hz), 2.61 (1 H, d, *J* = 11.4 Hz), 2.16 (3 H, s), 2.12 (1 H, dd, *J* = 11.7, 9.0 Hz), 1.67 (3 H, s); ^{13}C ($CDCl_3$, 150 MHz) δ

144.0, 143.9, 143.5, 142.8, 141.1, 141.0, 140.9, 140.1, 139.7, 138.6, 138.3, 138.1, 137.5, 135.9, 135.0, 132.3, 131.4, 131.3, 130.6, 130.3, 130.2, 129.7, 129.1, 129.08, 129.06, 128.9, 127.8, 127.7, 127.5, 127.2, 126.7, 126.5, 125.0, 124.6, 123.8, 123.7, 123.0, 122.1, 120.2, 120.2, 58.3, 53.9, 53.0, 52.0, 51.9, 46.1, 26.8, 35.3, 30.3, 26.8, 11.6, 0.8. MS *m/z* 968 (M^+), 876; HRMS calcd for $C_{56}H_{42}I_2$ (MH^+) 969.1449, found 969.1499. **166:** ^{1}H ($CDCl_3$, 600 MHz) δ 7.74 (1 H, d, J = 7.2 Hz), 7.66−7.45 (13 H, m), 7.34 (1 H, d, J = 6.6 Hz), 7.24−7.20 (2 H, m) 7.16 (1 H, t, J = 7.8 Hz), 7.01 (1 H, t, J = 8.4 Hz), 6.85 (1 H, d, J = 7.8 Hz), 6.73 (1 H, t, J = 7.8 Hz), 6.62 (1 H, d, J = 8.4 Hz), 6.27 (1 H, d, J = 7.8 Hz), 5.22 (1 H, dd, J = 10.2, 3 Hz), 4.97 (1 H, d, J = 7.2 Hz), 4.52 (1 H, d, J = 21.6 Hz), 4.17 (1 H, d, J = 7.2 Hz), 4.12 (1 H, d, J = 21.6 Hz), 3.98 (1 H, d, J = 6.0 Hz), 3.54 (1 H, dd, J = 18, 10.2 Hz), 3.45 (1 H, d, J = 9 Hz), 2.87 (1 H, d, J = 12 Hz), 2.59 (1 H, d, J = 12 Hz), 2.39 (3 H, s), 1.97 (1 H, dd, J = 11.1, 8.4 Hz), 1.67 (3 H, s); ^{13}C ($CDCl_3$, 150 MHz) δ 193.5, 149.6, 147.2, 144.4, 144.1, 143.6, 141.1, 139.5, 138.5, 138.1, 137.4, 136.8, 136.2, 135.1, 134.7, 134.3, 133.3, 131.4, 131.3, 131.0, 130.2, 129.8, 129.4, 129.3, 129.2, 129.1, 129.0, 128.7, 128.3, 127.8, 127.5, 127.2, 126.5, 125.0, 124.2, 123.9, 123.7, 123.1, 123.0, 121.8, 120.2, 58.5, 53.7, 53.3, 53.1, 51.6, 45.8, 35.3, 30.1, 26.7, 10.3, 0.5. MS *m/z* 982 (M^+), 855; HRMS calcd for $C_{56}H_{40}I_2O$ (MH^+) 983.1241, found 983.1223.

Hydrocarbon 167. To a solution of NaH (0.002 g, 0.063 mmol) and catalytic amount of *t*-BuOH in 8 mL of anhydrous THF was added **165** (0.010 g, mmol) via cannula at −78 ^{o}C under a nitrogen gas atmosphere. Degas the reaction mixture for three times followed by warming up to the room temperature. After 18 h of stirring, the reaction mixture was quenched with aqueous NH_4Cl solution under nitrogen gas. The aqueous layer was separated and back extracted twice with methylene chloride, and the combined organic layers were dried over sodium sulfate and concentrated. The residue was then purified by flash column chromatography (silica gel/20% methylene chloride in hexanes) to afford **167.** ^{1}H ($CDCl_3$, 600 MHz) δ 7.64 (1 H, d, J = 6.6 Hz),

7.63−7.51 (10 H, m), 7.45−7.40 (3 H, m), 7.34−7.29 (3 H, m), 7.27−7.25 (2 H, m), 7.07−7.03 (2 H, m), 6.97 (1 H, dt, *J* = 7.2, 1.2 Hz), 6.94 (1 H, dt, *J* = 7.82, 1.8 Hz), 6.54 (2 H, d, *J* = 7.2 Hz), 6.48 (1 H, d, *J* = 8.4 Hz), 6.34 (1 H, t, *J* = 7.8 Hz), 5.47 (1 H, d, *J* = 7.2 Hz), 4.24 (1 H, dd, *J* = 12.0, 5.4 Hz), 4.20 (1 H, d, *J* = 7.8 Hz), 4.16 (1 H, d, *J* = 7.8 Hz), 3.98 (1 H, dd, *J* = 7.2, 1.2 Hz), 3.46 (1 H, dt, *J* = 14.7, 8.4 Hz), 3.11 (1 H, dd, *J* = 7.8, 5.4 Hz), 2.99 (1 H, dd, *J* = 10.8, 4.2 Hz), 1.90 (1 H, dt, *J* = 13.2, 4.5 Hz), 1.76 (1 H, dd, *J* = 14.7, 0.01 Hz), 1.79 (3 H, s), 1.57 (3 H, s), 0.29 (1 H, dt, *J* = 12.0, 4.2 Hz), −3.32 (1 H, ddd, *J* = 13.2, 12.7, 11.2, Hz); MS *m/z* 712 (M^+), 711; HRMS calcd for $C_{56}H_{40}$ (M^+) 712.31300, found 712.30795.

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Appendix

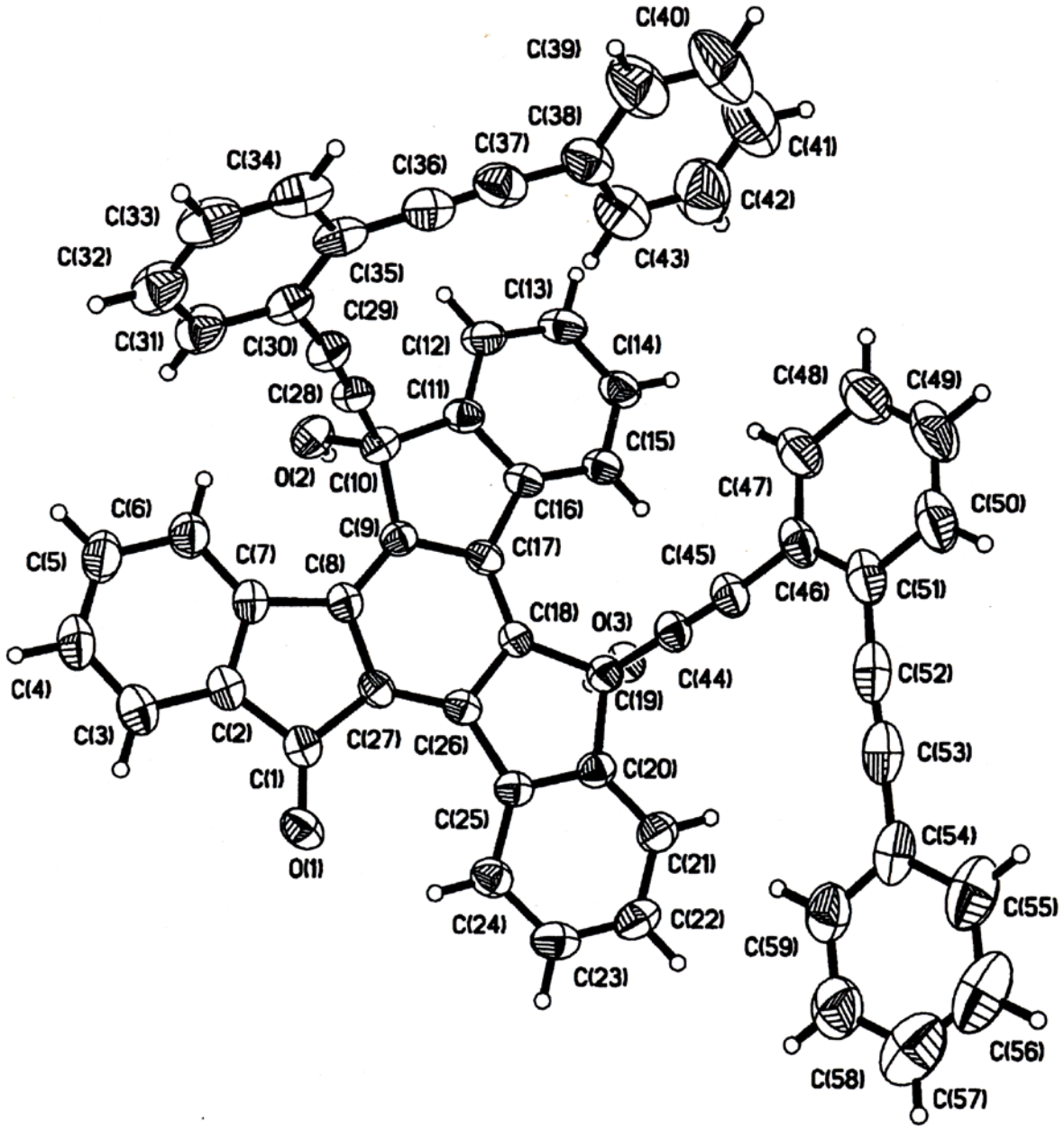


Figure 26. ORTEP drawing of the crystal structure of benzannulated enediynyl *cis*-diol **30**.

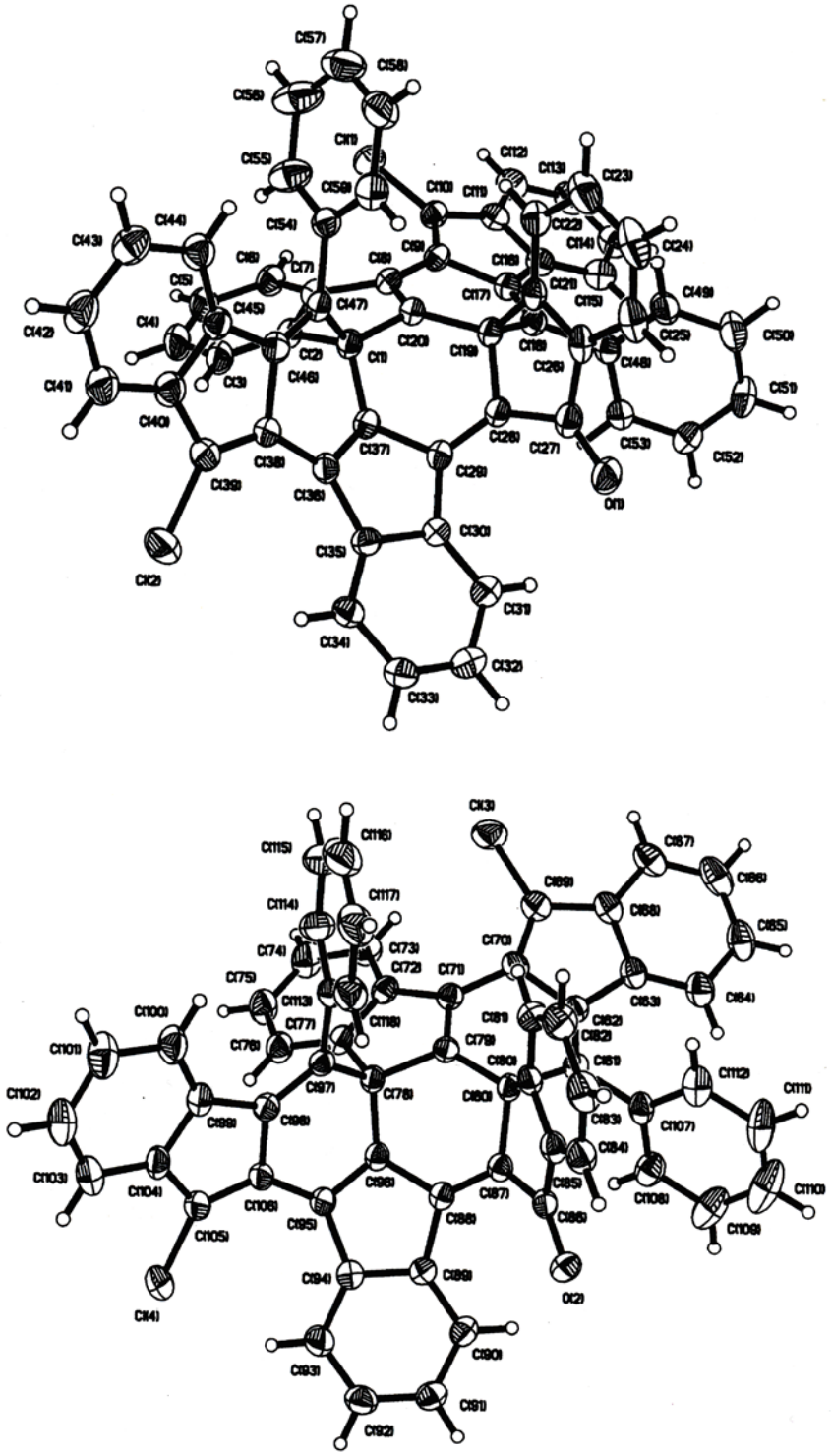


Figure 27. ORTEP drawing of the crystal structure of ketone **31** with two independent molecules per unit cell.

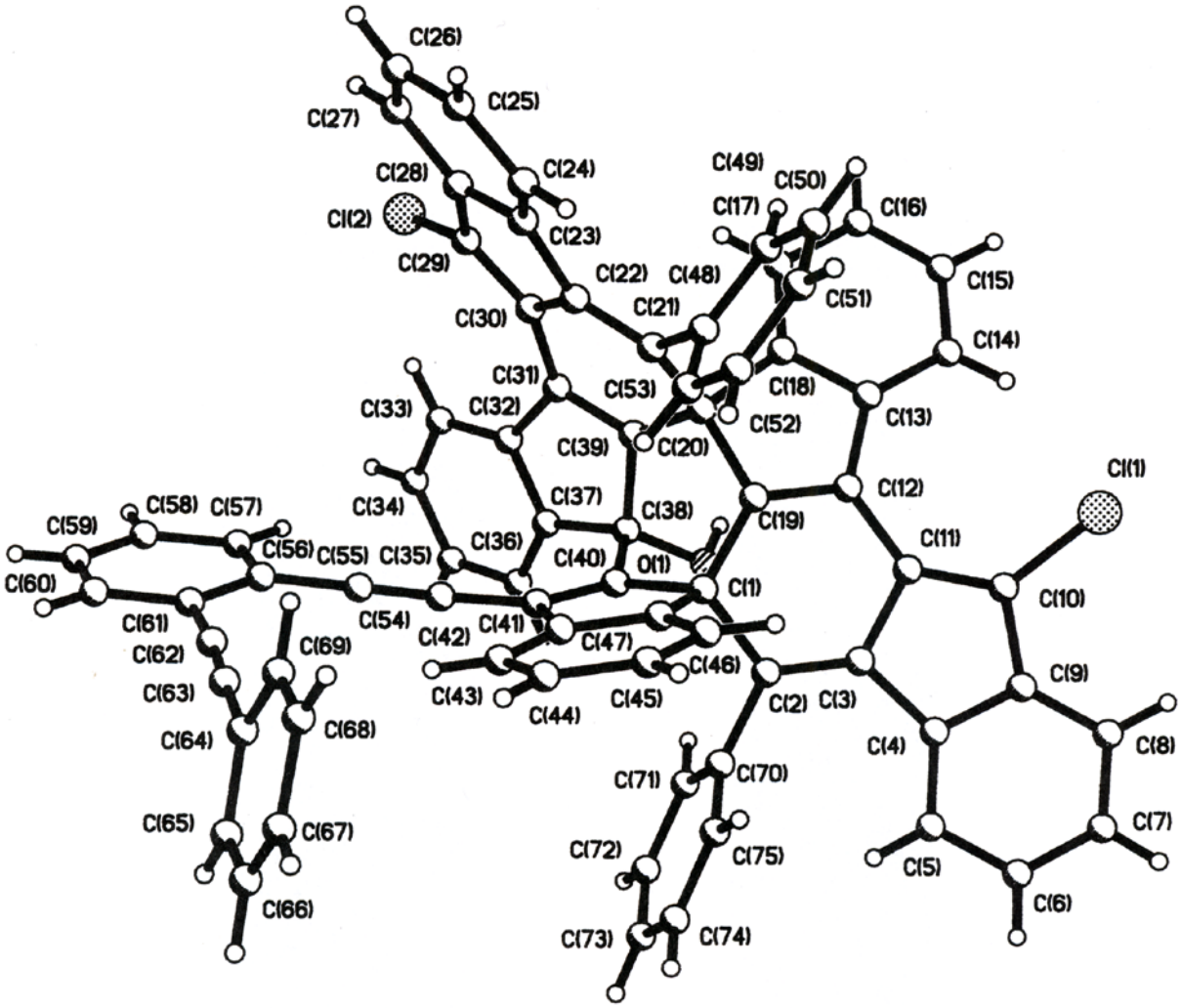


Figure 28. Perspective view of molecular structure of alcohol **34** with the atom labeling scheme.

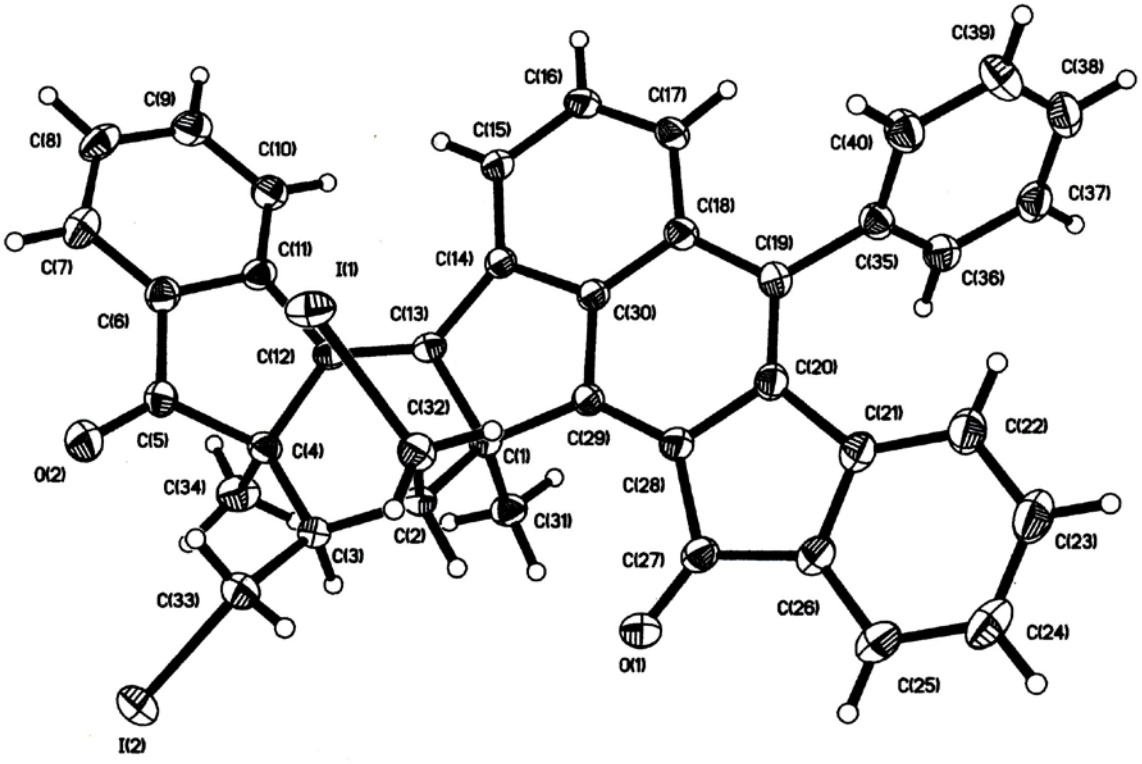


Figure 29. Perspective view of molecular structure of $C_{40}H_{28}O_2I_2$ (**159**). The thermal ellipsoids are scaled to enclose 30% probability.

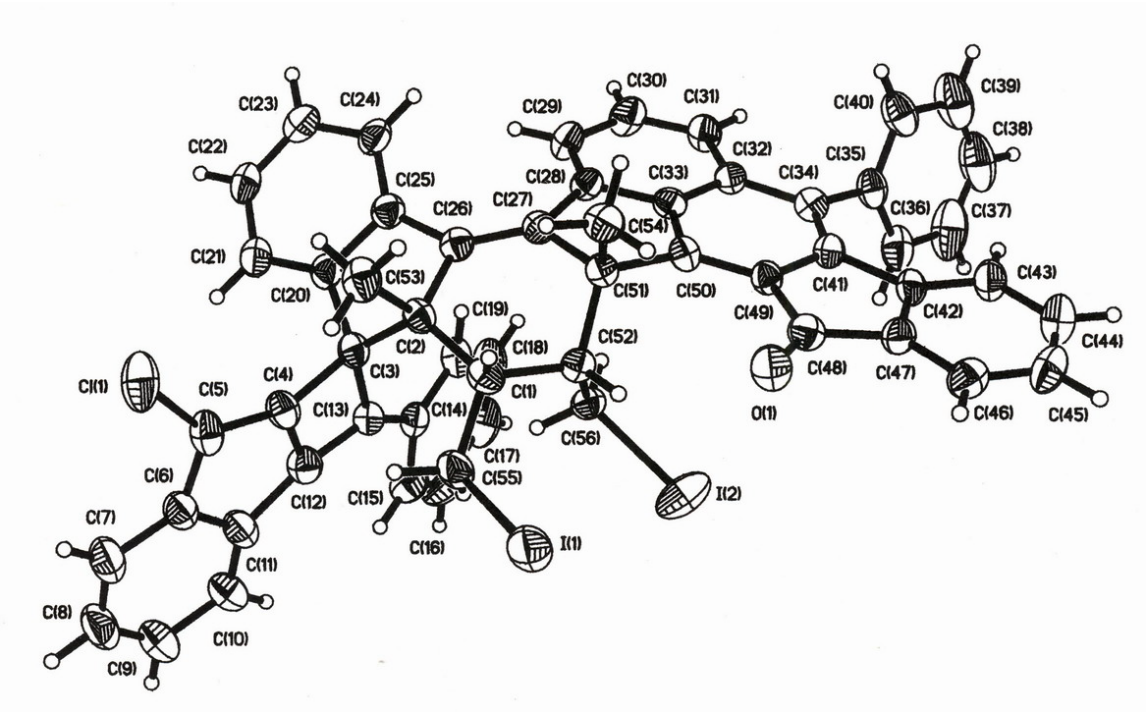


Figure 30. Perspective view of molecular structure of molecule 1 of **162** with the atom labeling scheme. The thermal ellipsoids are scaled to enclose 30% probability.

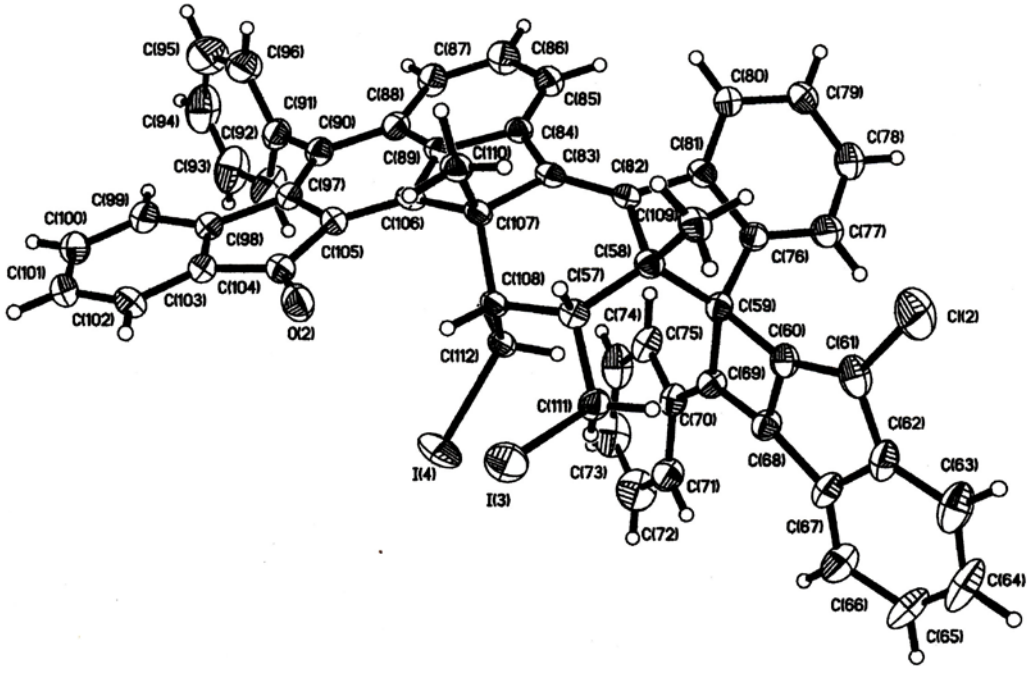


Figure 31. Perspective view of molecular structure of molecule 2 of **162** with the atom labeling scheme. The thermal ellipsoids are scaled to enclose 30% probability.

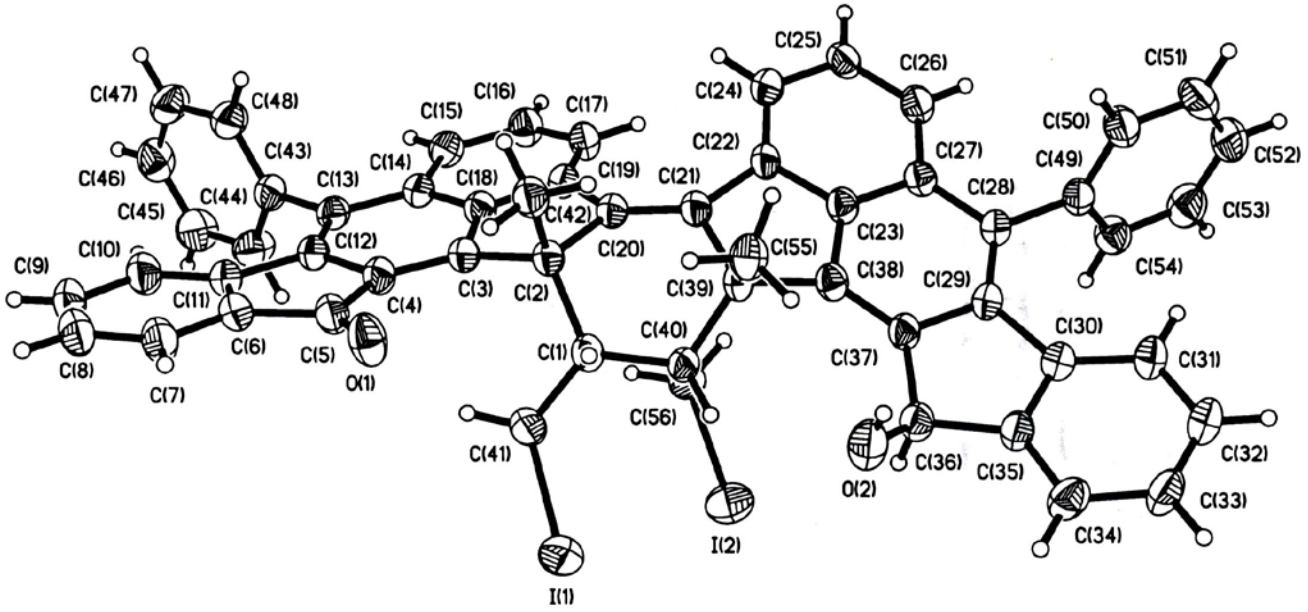
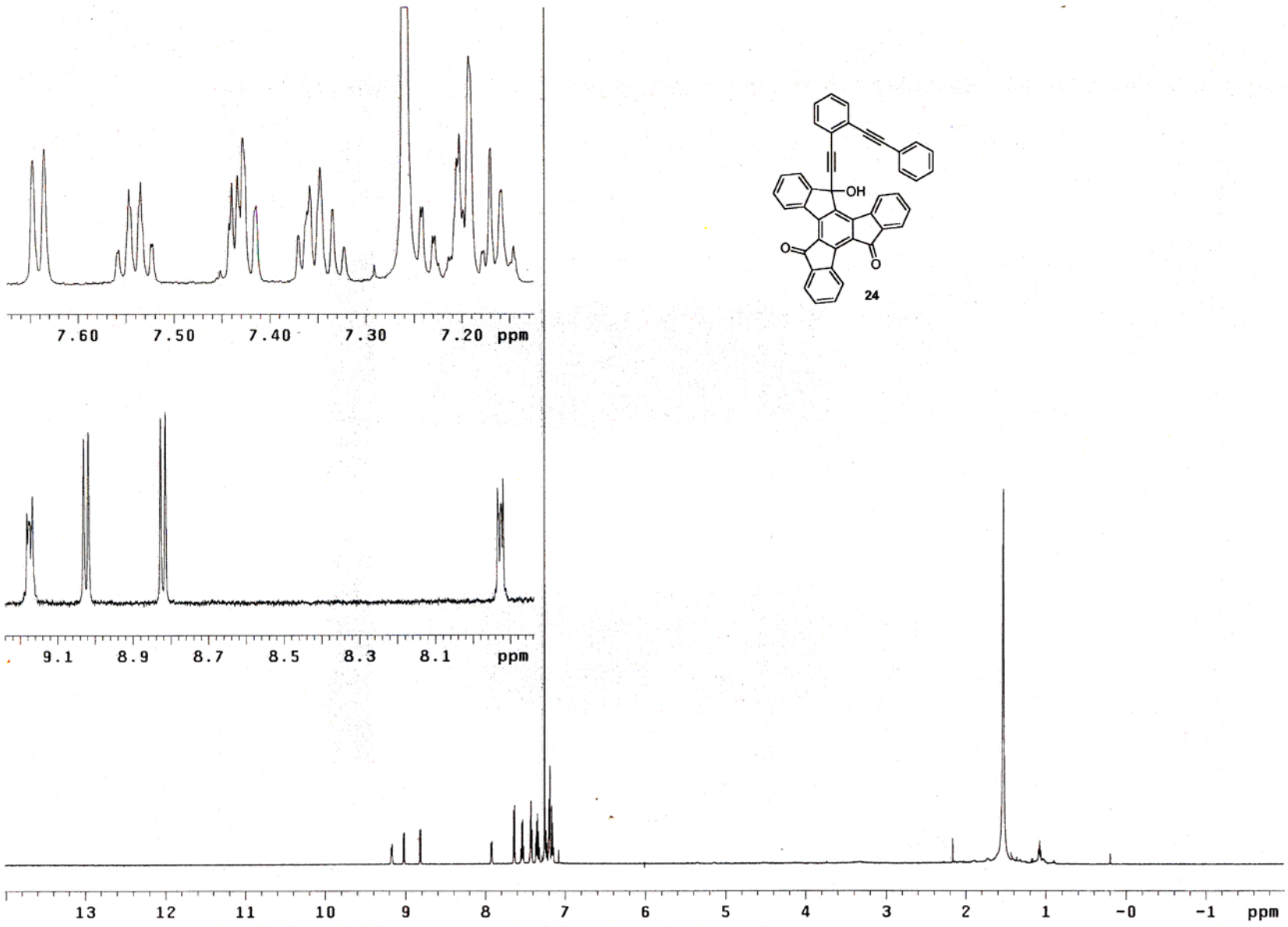
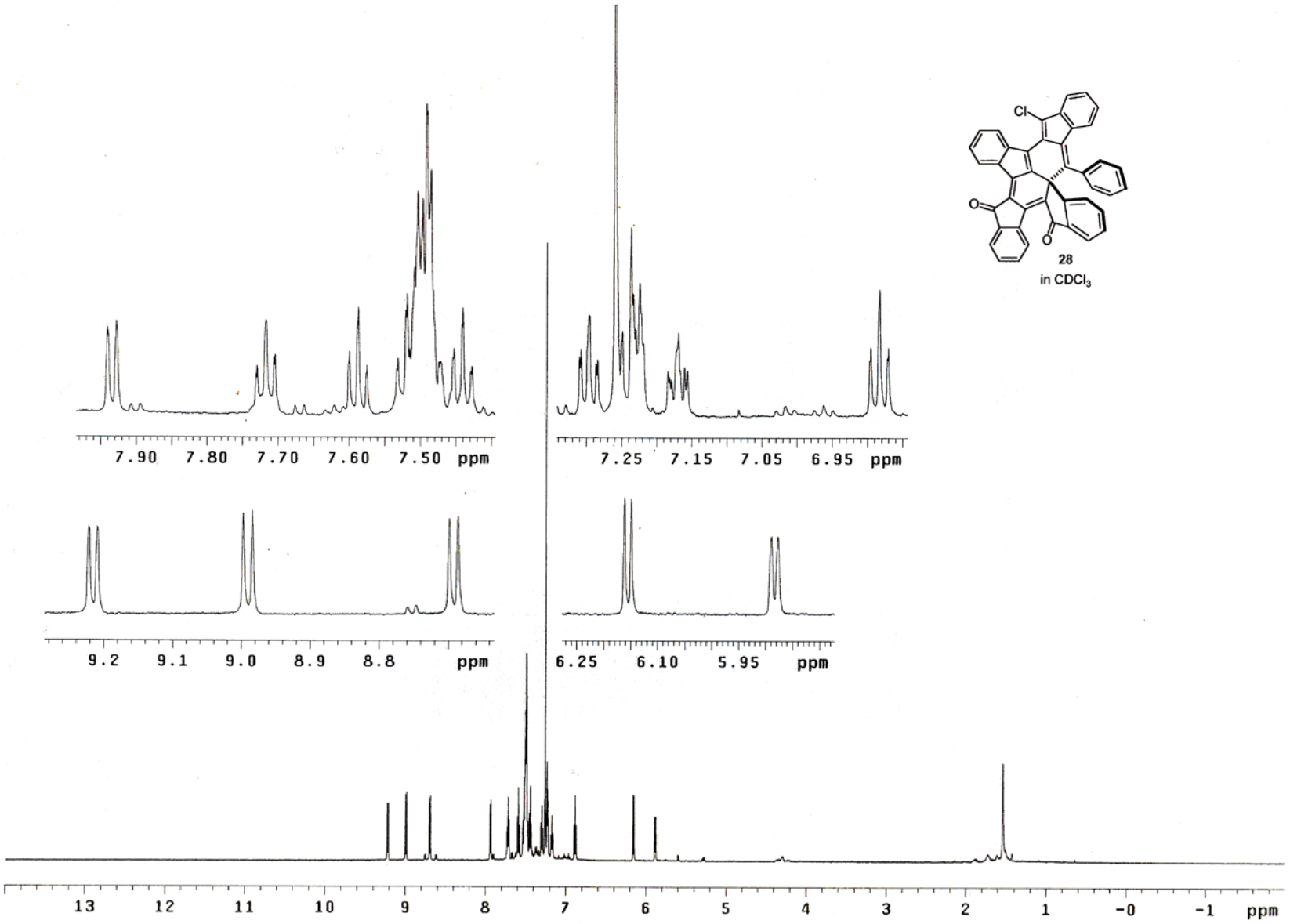
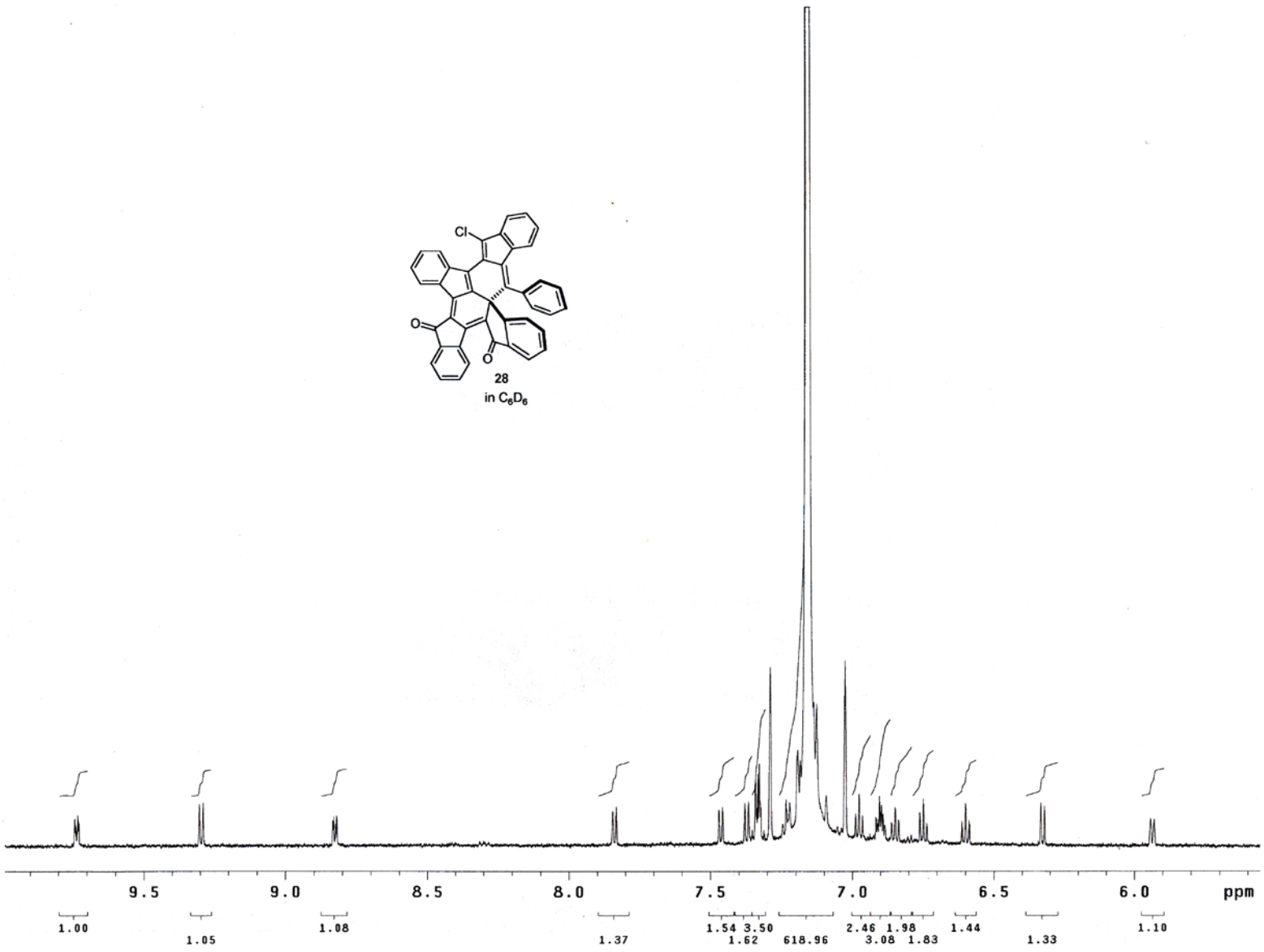
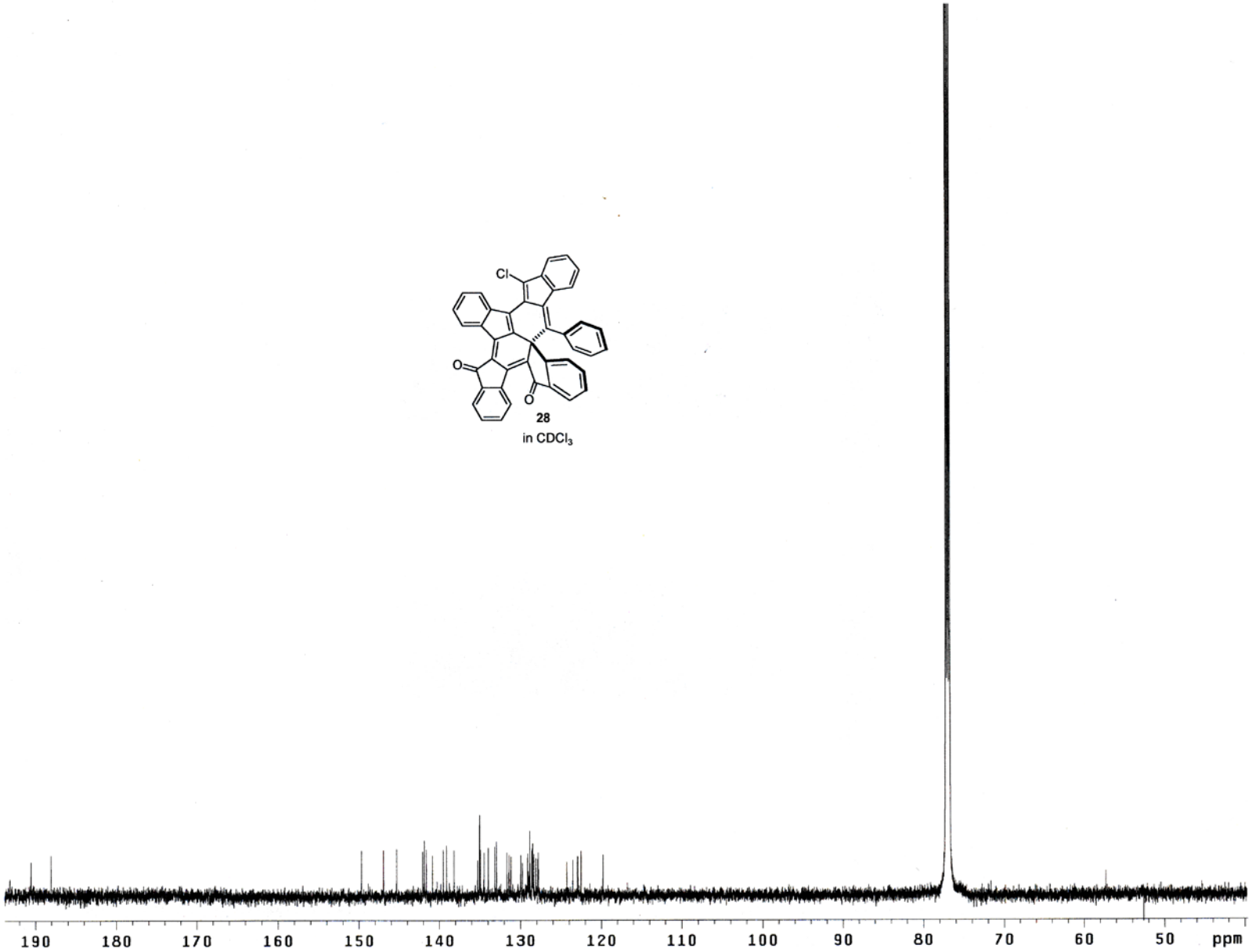


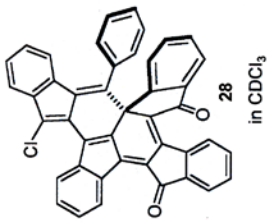
Figure 32. Perspective view of molecular structure of alcohol **163** with the atom labeling scheme.


OH
O
O
24
7.60
7.50
7.40
7.30
7.20
ppm
9.1
8.9
8.7
8.5
8.3
8.1
ppm
13
12
11
10
9
8
7
6
5
4
3
2
1
-0
-1
ppm


Cl
O
O
28
in CDCl3
7.90 7.80 7.70 7.60 7.50 ppm
7.25 7.15 7.05 6.95 ppm
9.2 9.1 9.0 8.9 8.8 ppm
6.25 6.10 5.95 ppm
13 12 11 10 9 8 7 6 5 4 3 2 1 -0 -1 ppm

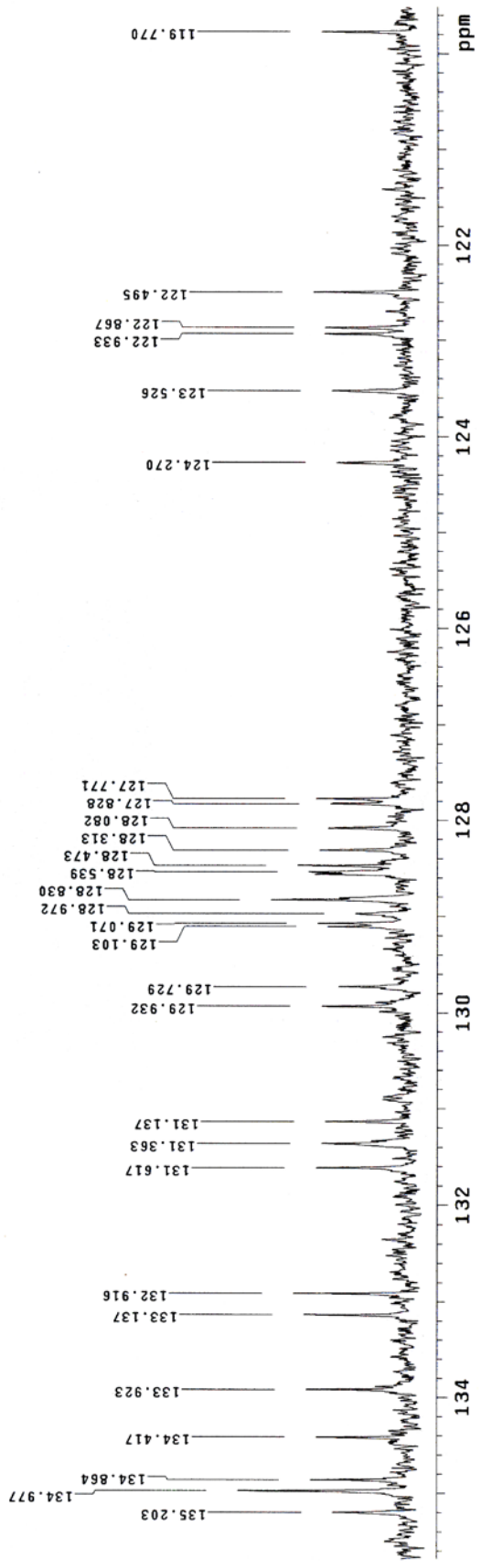

Cl
O
O
28
in C_6D_6
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
ppm
1.00
1.05
1.08
1.37
1.54 3.50
1.62
618.96
2.46 1.98
3.08 1.83
1.44
1.33
1.10

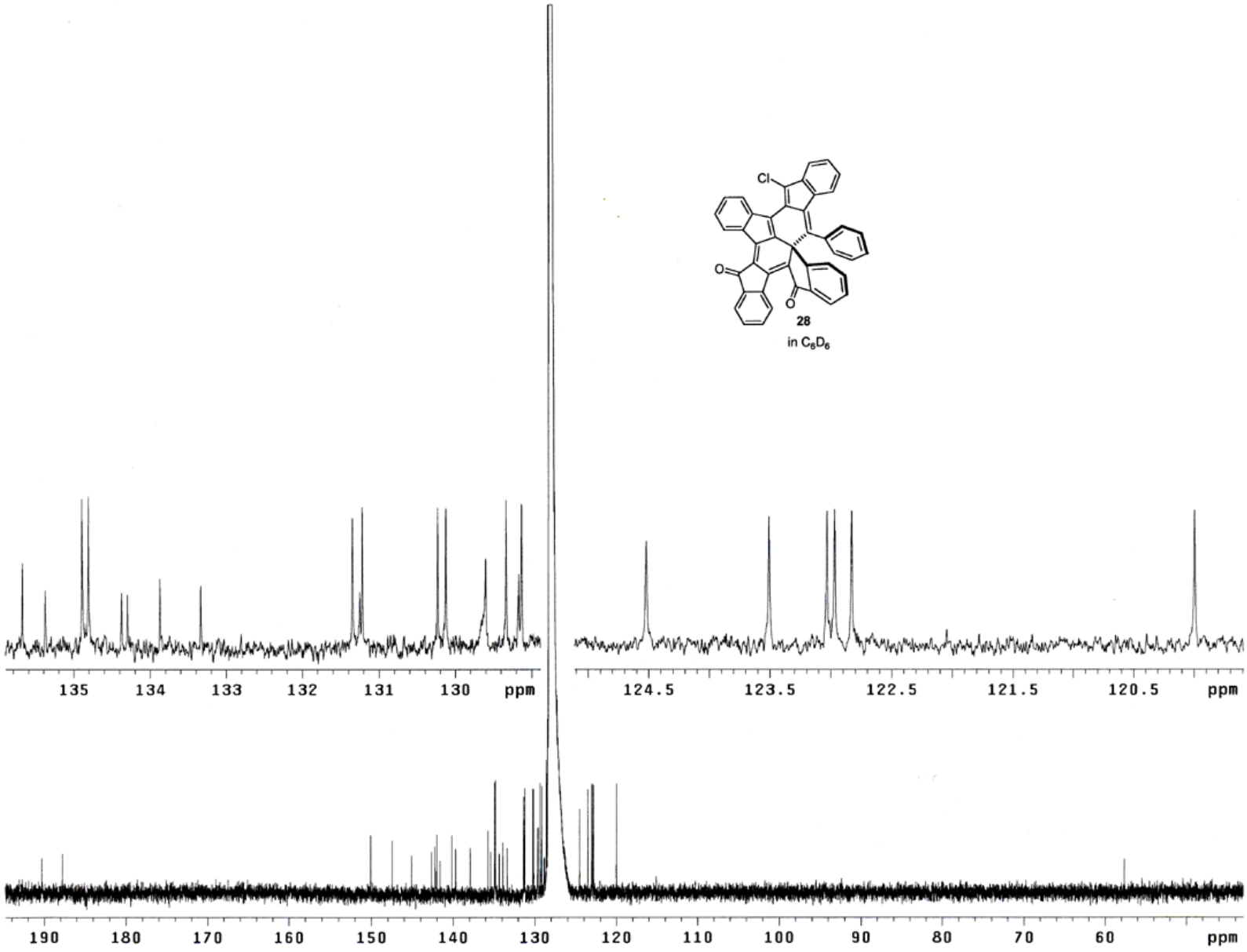

Cl
O
O
28
in CDCl3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
ppm

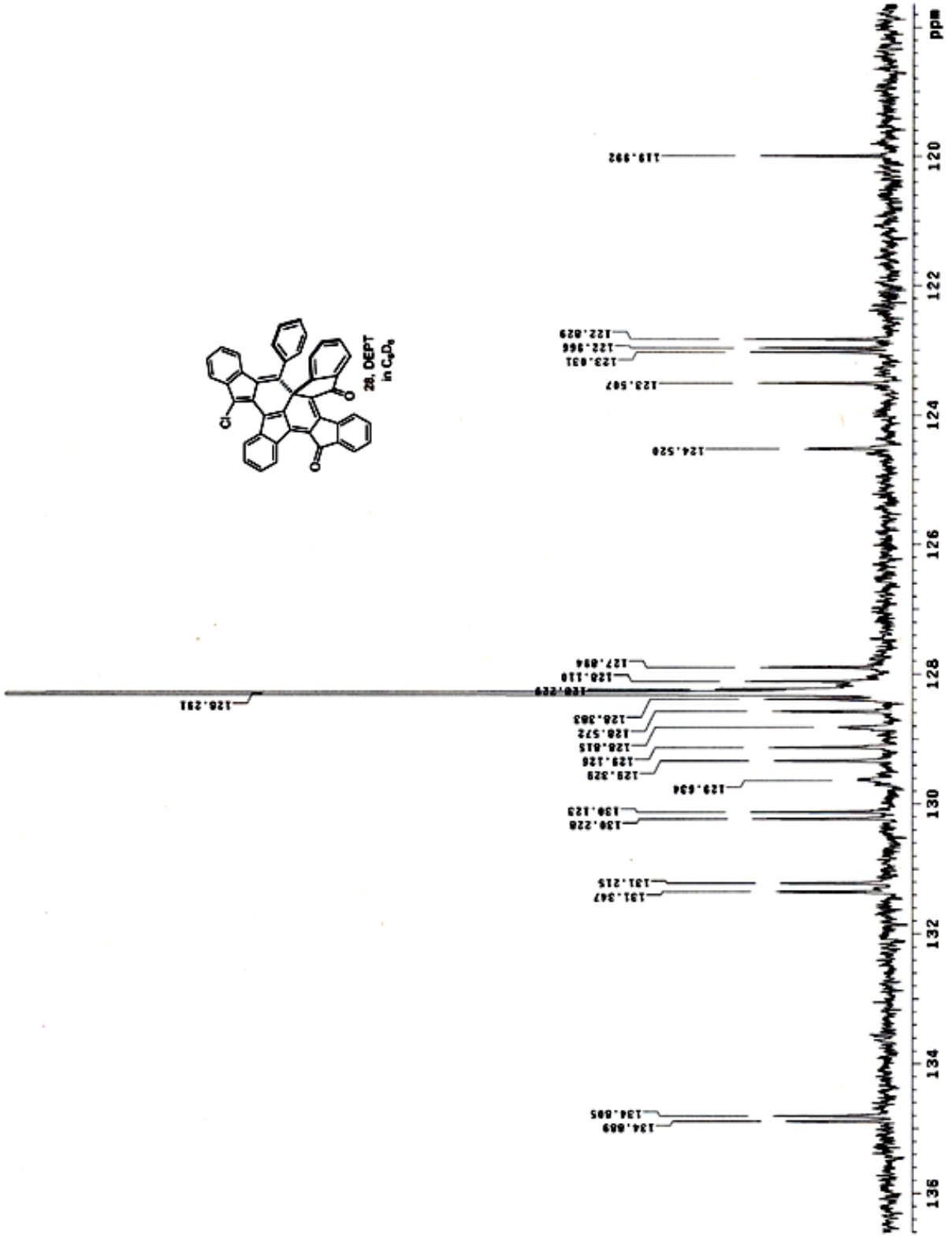

Cl
O
O

28

in $CDCl_3$


119.770
122.495
122.867
122.933
123.526
124.270
127.771
127.828
128.082
128.313
128.473
128.539
128.830
128.972
129.071
129.103
129.729
129.932
131.137
131.363
131.617
132.916
133.137
133.923
134.417
134.864
134.977
135.203
ppm
122
124
126
128
130
132
134

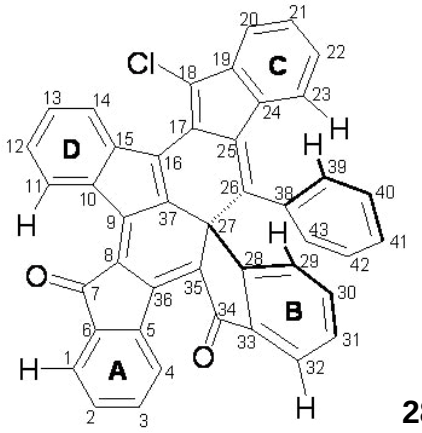

Cl
O
O
28
in C_6D_6
135
134
133
132
131
130
ppm
124.5
123.5
122.5
121.5
120.5
ppm
190
180
170
160
150
140
130
120
110
100
90
80
70
60
ppm


28, DEPT
in C_6D_6
Cl
O
O
119.992
122.829
122.966
123.031
123.587
124.520
126.291
127.894
128.110
128.229
126.383
126.572
126.815
129.126
129.329
129.634
130.123
130.226
131.215
131.347
134.809
134.885
ppm
120
122
124
126
128
130
132
134
136

Chemical Shifts (δ/ppm) and Coupling Constants (J/Hz)[a] in **28**.

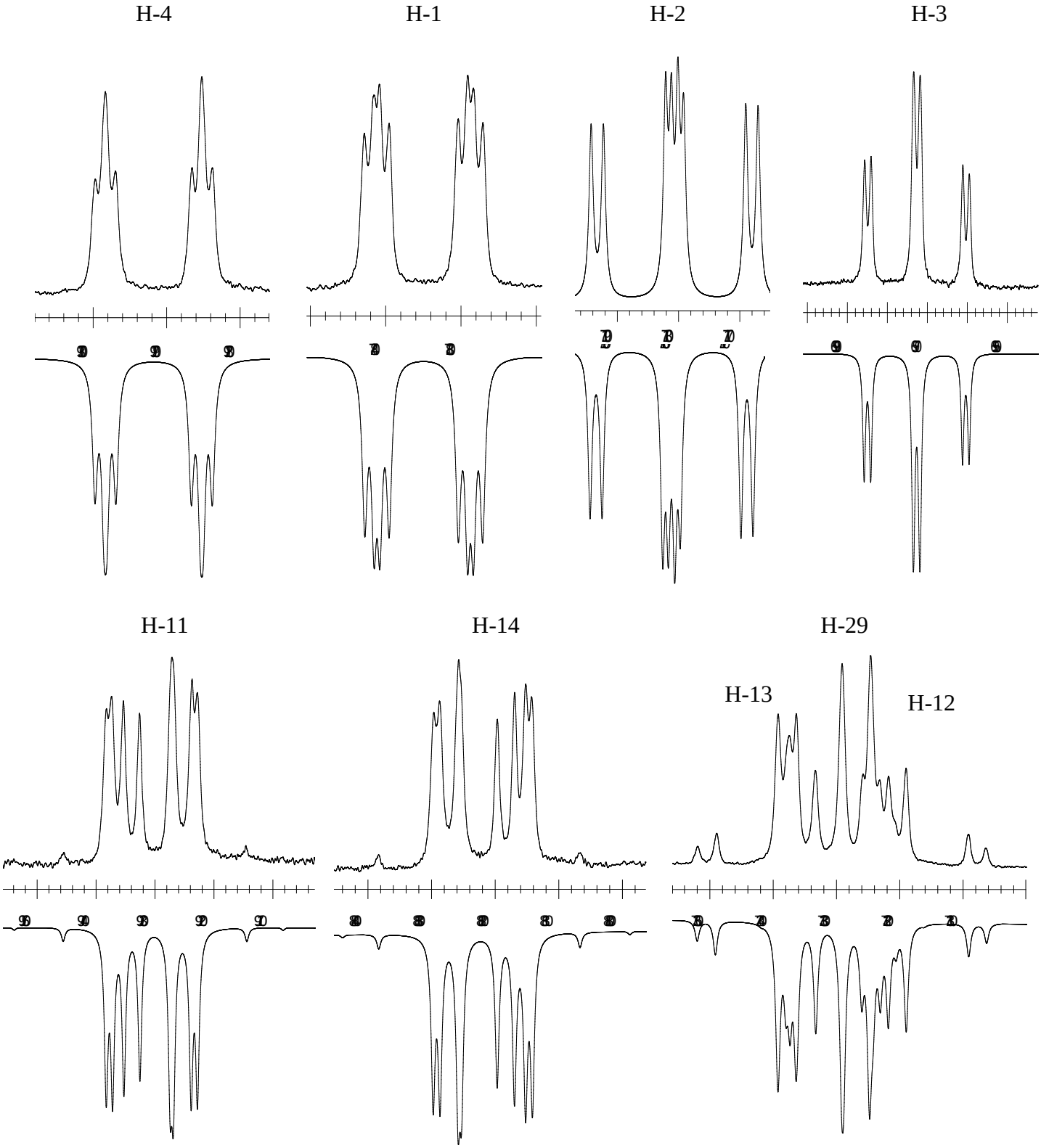
Ring	Protons	$CDCl_3$	C_6D_6	$\Delta(\delta) = \delta_{H}^{CDCl_3} - \delta_{H}^{C_6D_6}$	Coupling constants (J/Hz)					
A	H-1	7.938	7.835	0.103	$^3J_{1,2}$	$^4J_{1,3}$	$^5J_{1,4}$	$^3J_{2,3}$	$^4J_{2,4}$	$^3J_{3,4}$
	H-2	7.590	6.973	0.617	7.46	1.20	0.74	7.30	0.98	7.87
	H-3	7.720	7.187	0.533						
	H-4	8.992	9.292	-0.300						
B	H-29	7.503	7.331	0.172	$^3J_{29,30}$	$^4J_{29,31}$	$^5J_{29,32}$	$^3J_{30,31}$	$^4J_{30,32}$	$^3J_{31,32}$
	H-30	7.490	6.844	0.646						
	H-31	7.297	6.745	0.552	7.89	1.06	0.68	7.28	1.23	7.53
	H-32	7.495	7.459	0.036						
C	H-20	7.501	7.368	0.133	$^3J_{20,21}$	$^4J_{20,22}$	$^5J_{20,23}$	$^3J_{21,22}$	$^4J_{21,23}$	$^3J_{22,23}$
	H-21	7.240	6.900	0.340						
	H-22	6.890	6.596	0.294	7.54	1.05	0.96	7.54	0.90	7.64
	H-23	6.155	6.324	-0.169						
D	H-11	9.215	9.731	-0.526	$^3J_{11,12}$	$^4J_{11,13}$	$^5J_{11,14}$	$^3J_{12,13}$	$^4J_{12,14}$	$^3J_{13,14}$
	H-12	7.444	7.322	0.122						
	H-13	7.522	7.336	0.186	7.43	1.17	0.65	7.62	1.12	7.60
	H-14	8.695	8.822	-0.127						

[a] The precise values of the long-range coupling constants in C_6D_6 solution were deduced from the simulated spectra using gNMR software.



28

gNMR-Simulated ^{1}H NMR Spectra of **28** in C_6D_6 (top – experimental, bottom – calculated)

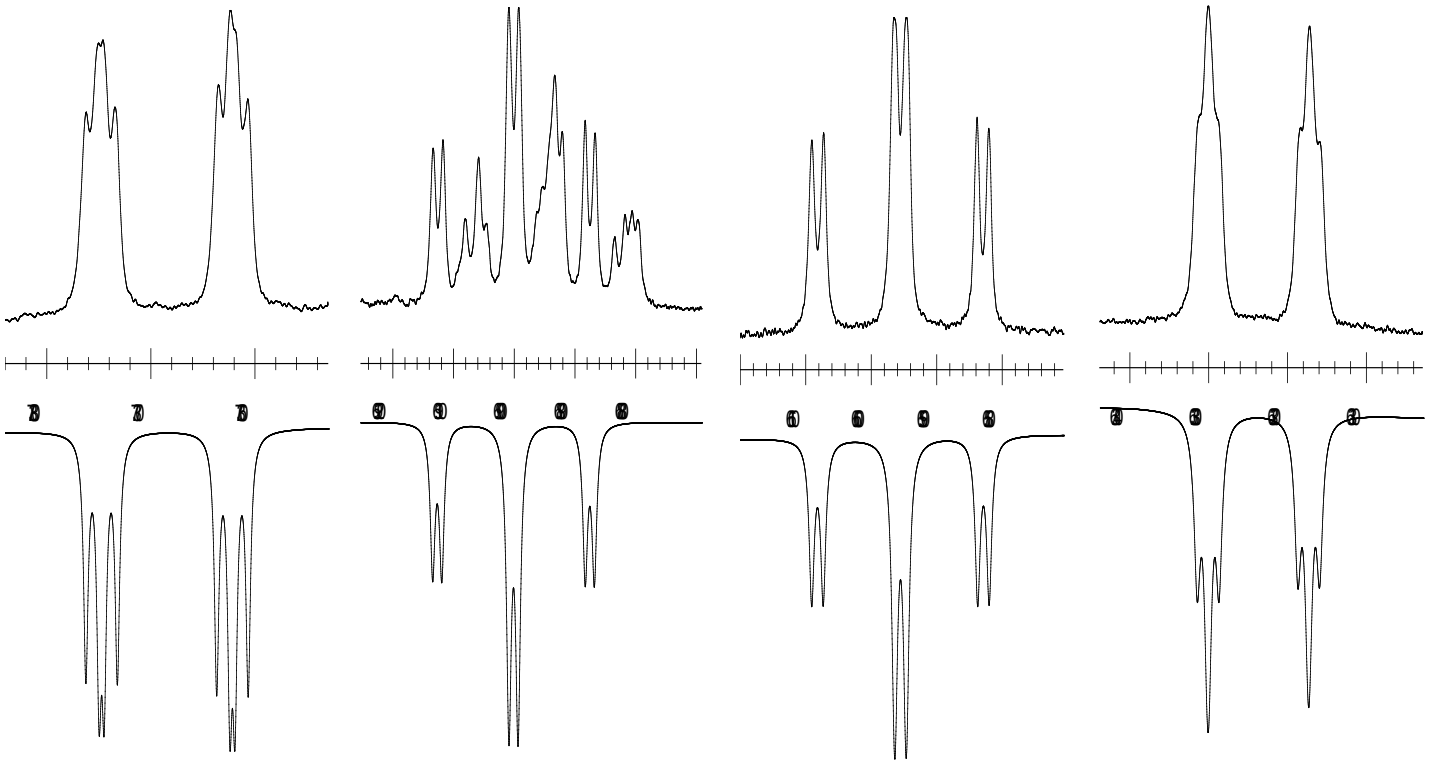


H-20

H-21

H-22

H-23

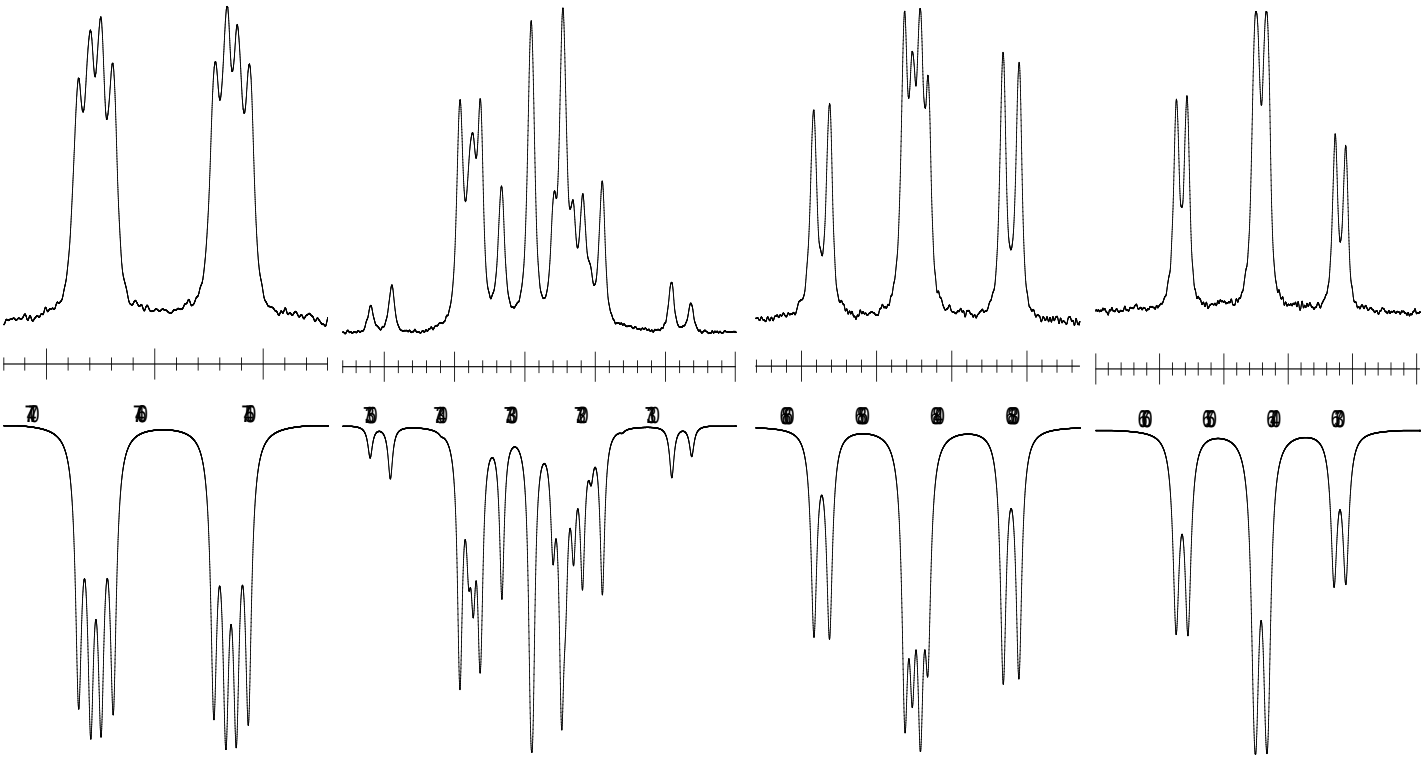


H-32

H-29

H-30

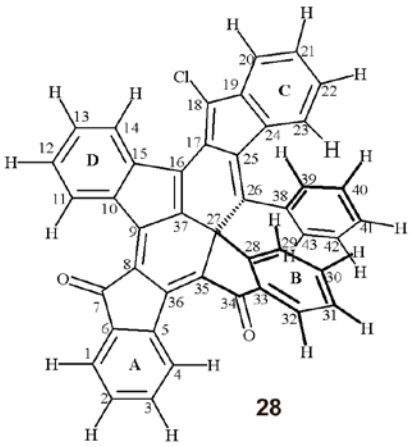
H-31



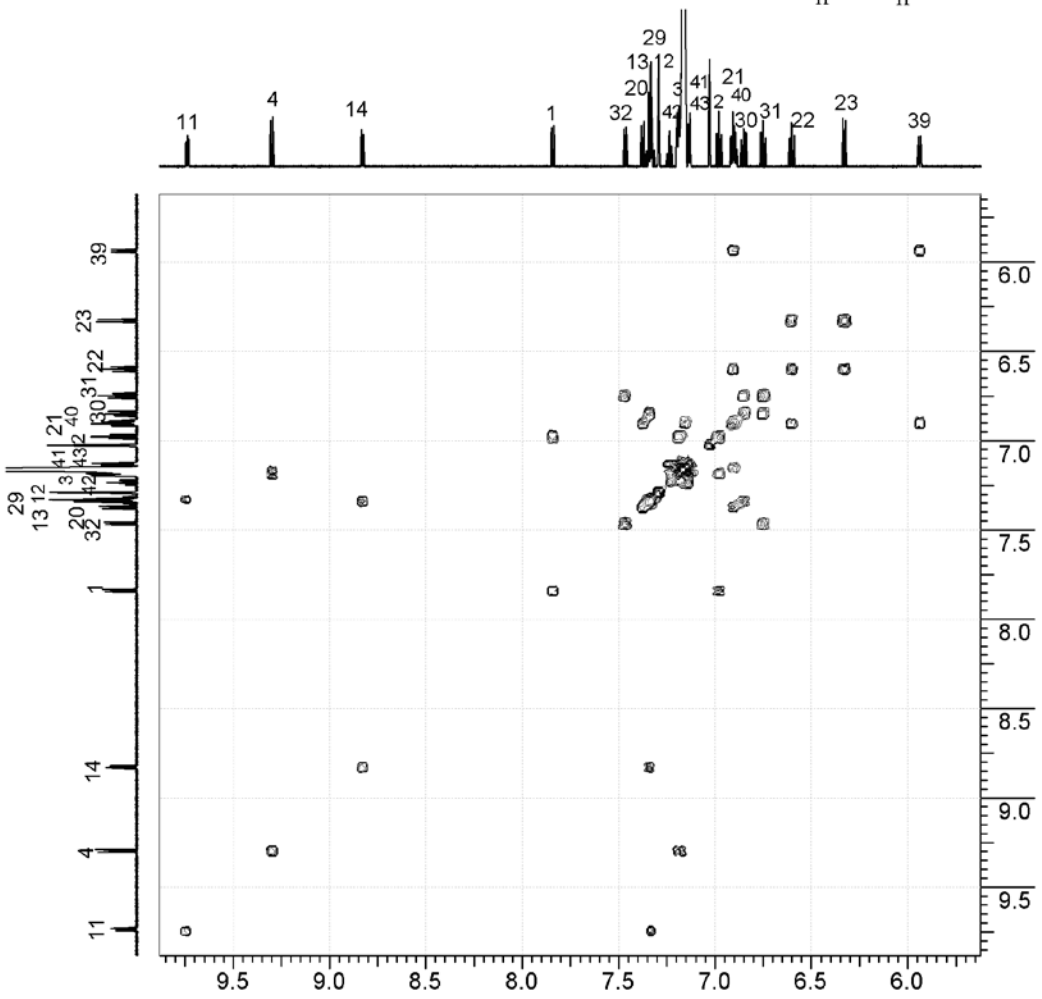
^{1}H and ^{13}C NMR Chemical Shifts of **28** in C_6D_6

Carbon and Proton	^{13}C NMR chemical shift (ppm)	^{1}H NMR chemical shift (ppm)	
C1–H1	123.49	7.84	
C2–H2	131.33	6.97	
C3–H3	134.88	7.19	
C4–H4	128.79	9.29	
C5	142.22		
C6	139.66		
C7	190.30		
C8	129.15		
C9	145.06		
C10	133.86		
C11–H11	129.63	9.73	
C12–H12	127.91	7.32	
C13–H13	131.20	7.34	
C14–H14	124.51	8.82	
C15	142.61		
C16	137.87		
C17	134.36		
C18	131.24		
C19	142.00		
C20–H20	119.98	7.37	
C21–H21	128.56	6.90	
C22–H22	127.83	6.60	
C23–H23	122.82	6.32	
C24	133.32		
C25	134.28		
C26	147.45		
C27	57.63		
C28	150.04		
C9–H29	123.02	7.33	
C-30-H30	134.79	6.84	
C31–H31	128.37	6.75	
C32–H32	122.96	7.46	
C33	140.12		
C34	187.73		
C35	129.59		
C36	135.37		
C37	141.62		
C38	135.67		
C39–H39^{ortho}	130.11	5.94	
C40–H-40^{meta}	128.15	6.89	
C41–H41^{para}	129.11	7.17	
C42–H42^{meta}	129.32	7.24	
C43–H43^{ortho}	130.22	7.15	

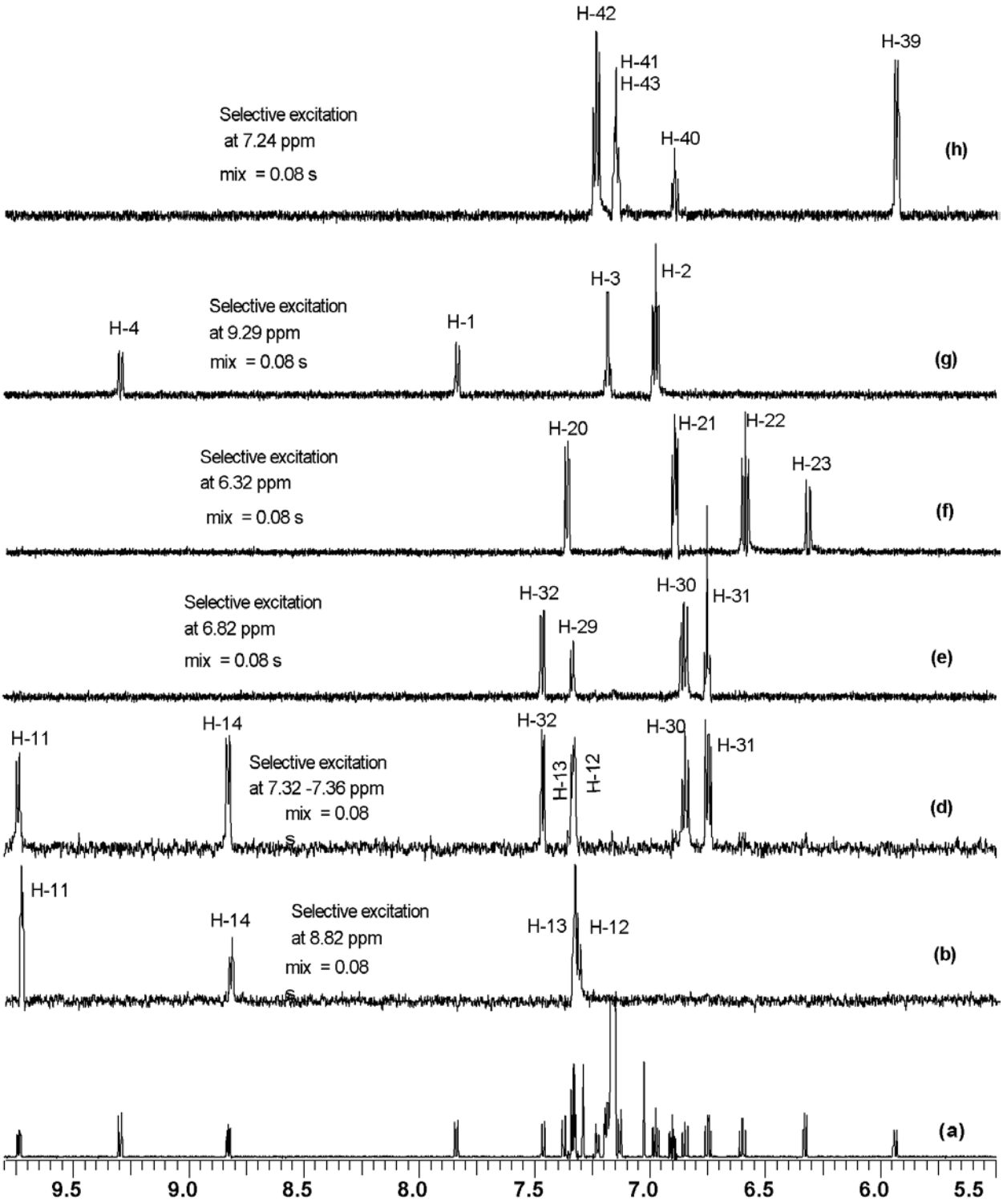
gCOSY spectrum of **28** in C_6D_6



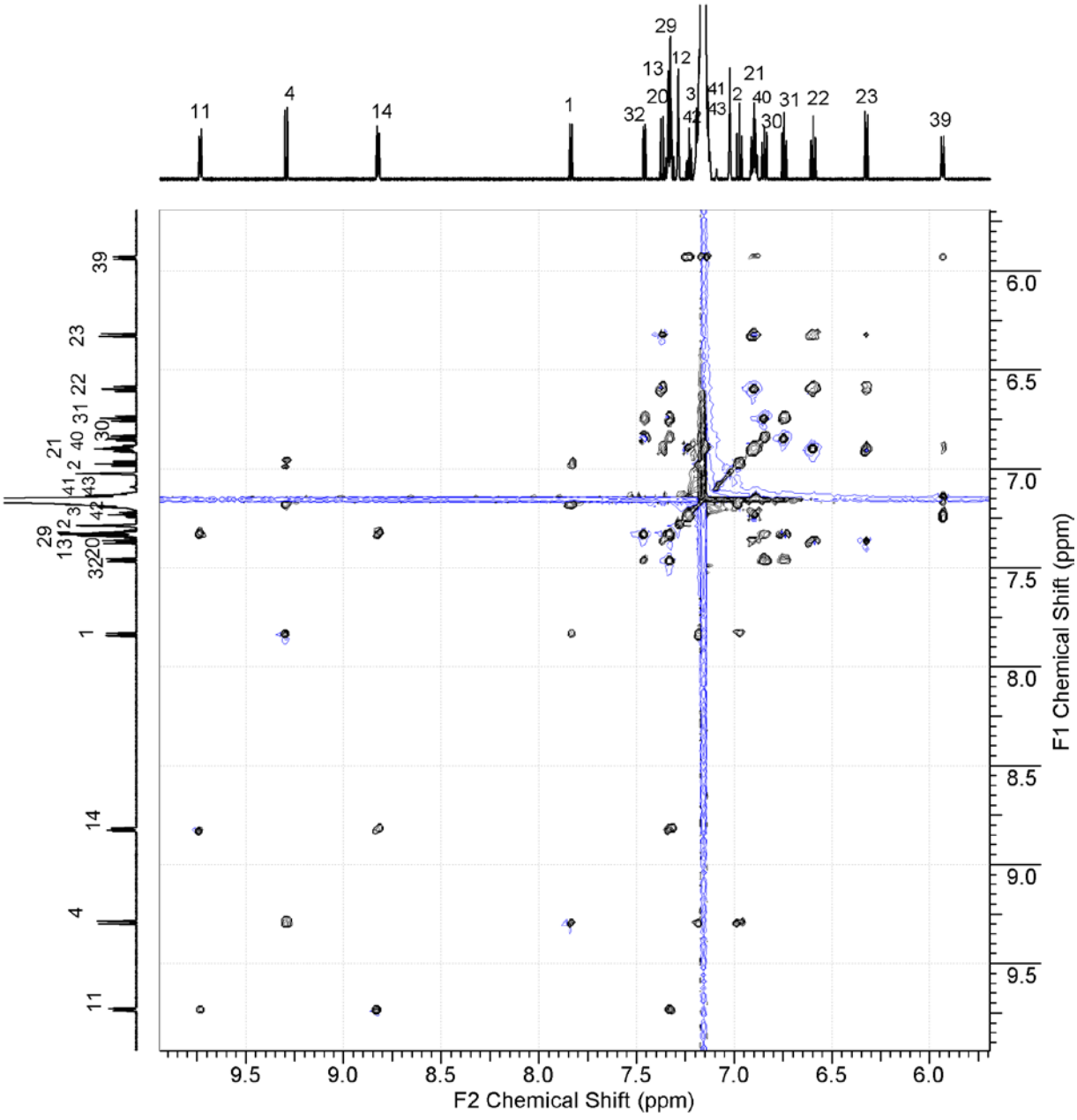
28



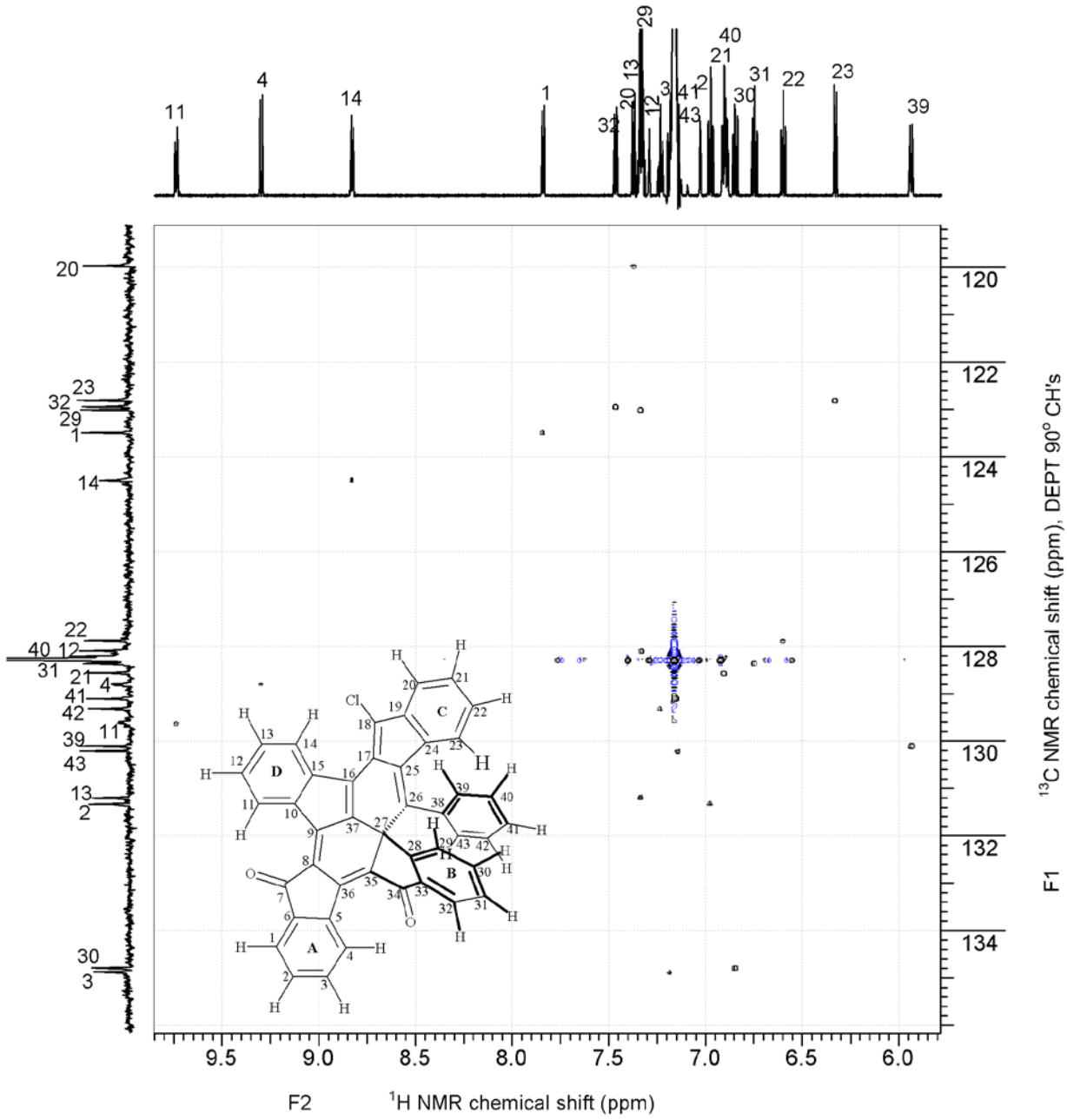
1D TOCSY spectra of **28** in C_6D_6



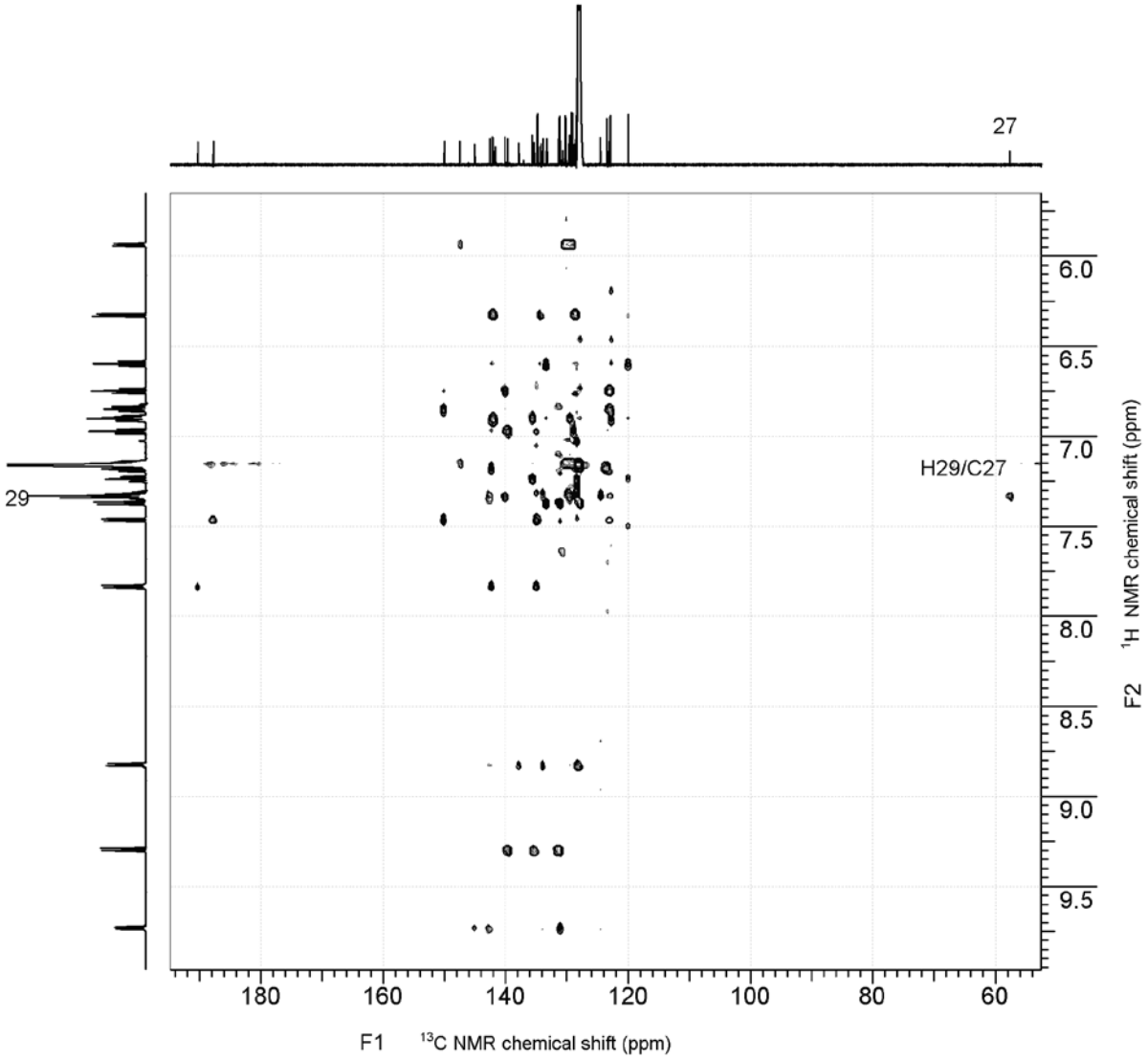
2D TOCSY spectrum of **28** in C_6D_6



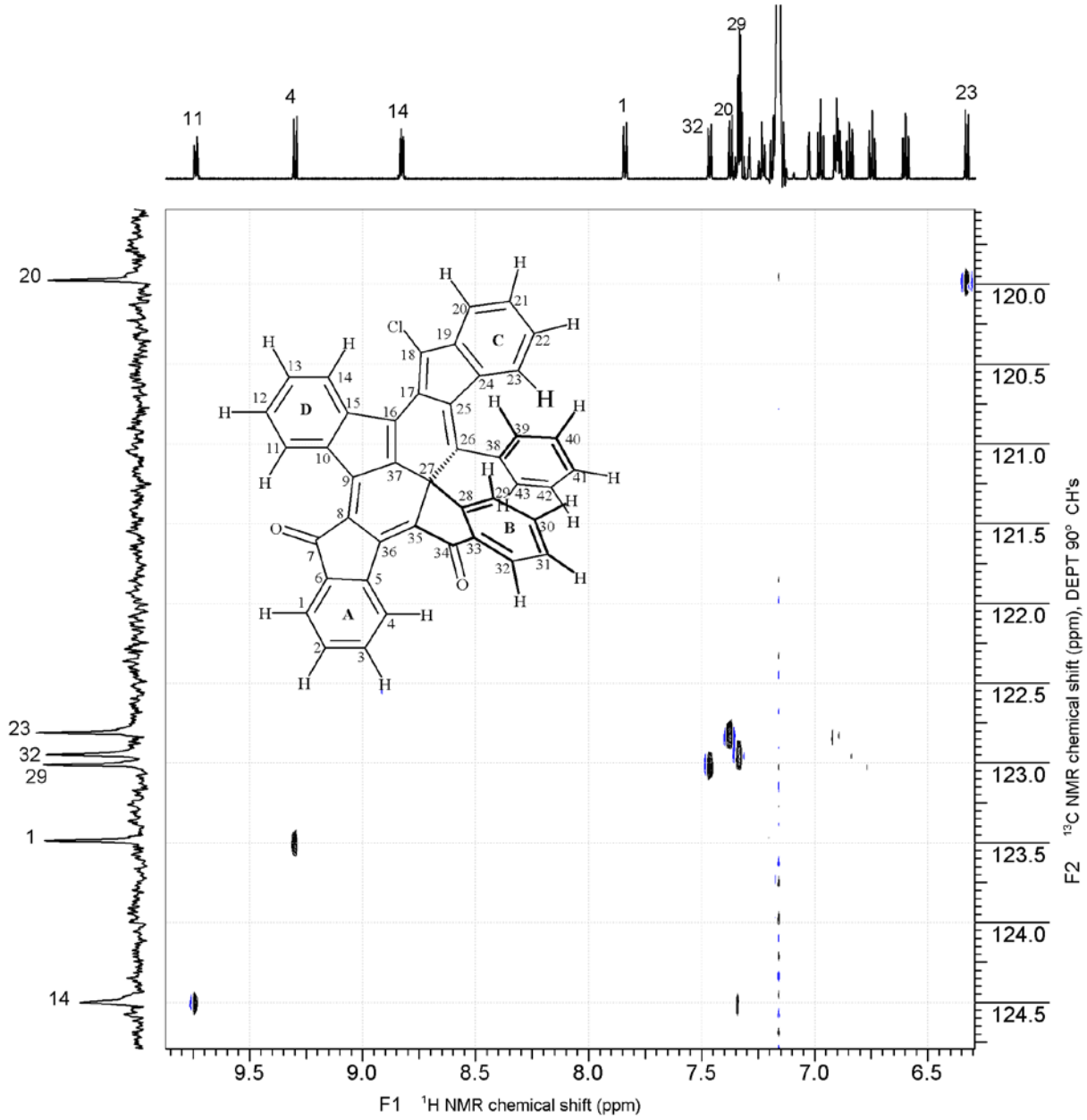
gHSQC spectrum of **28** in C_6D_6

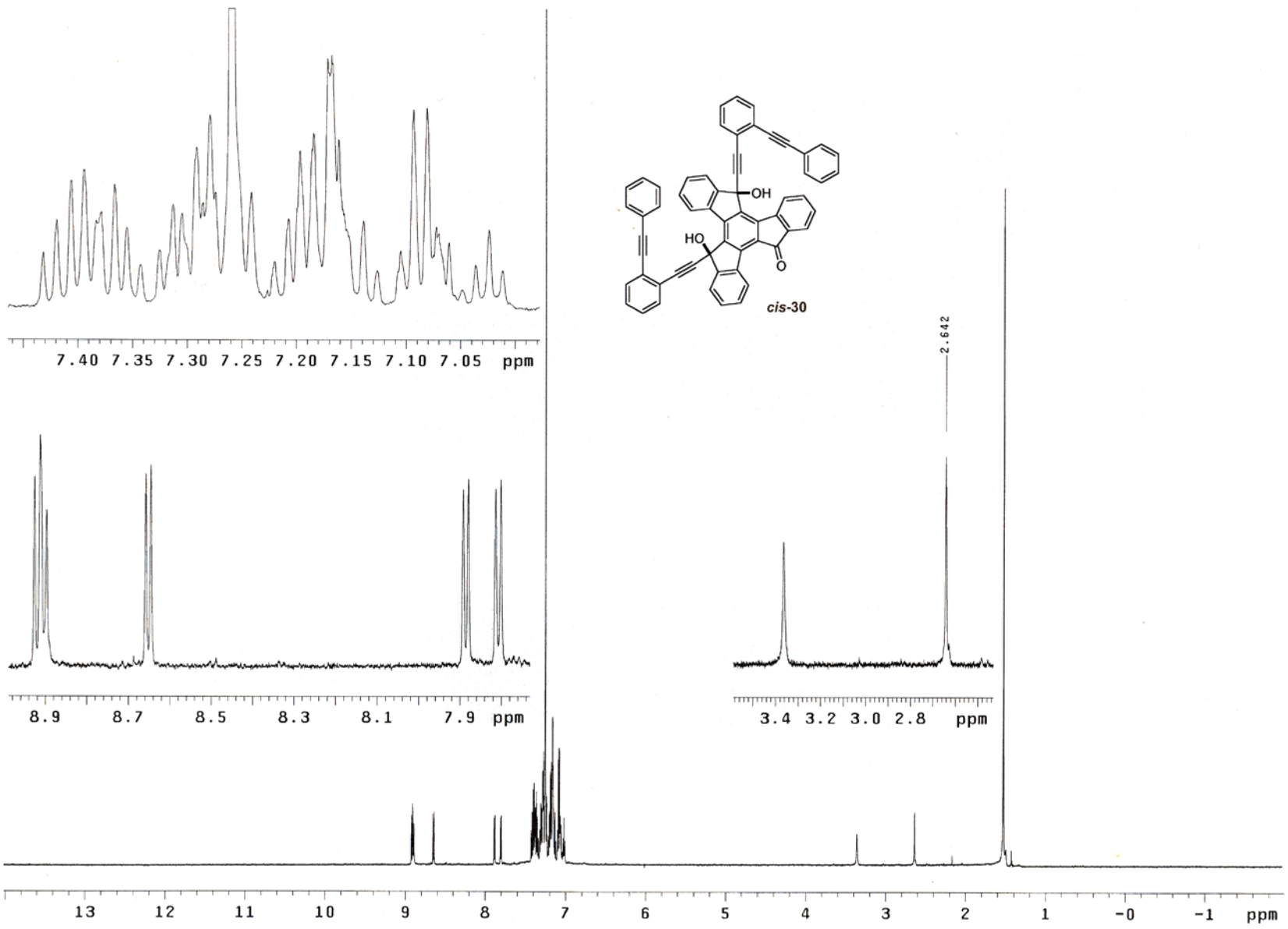


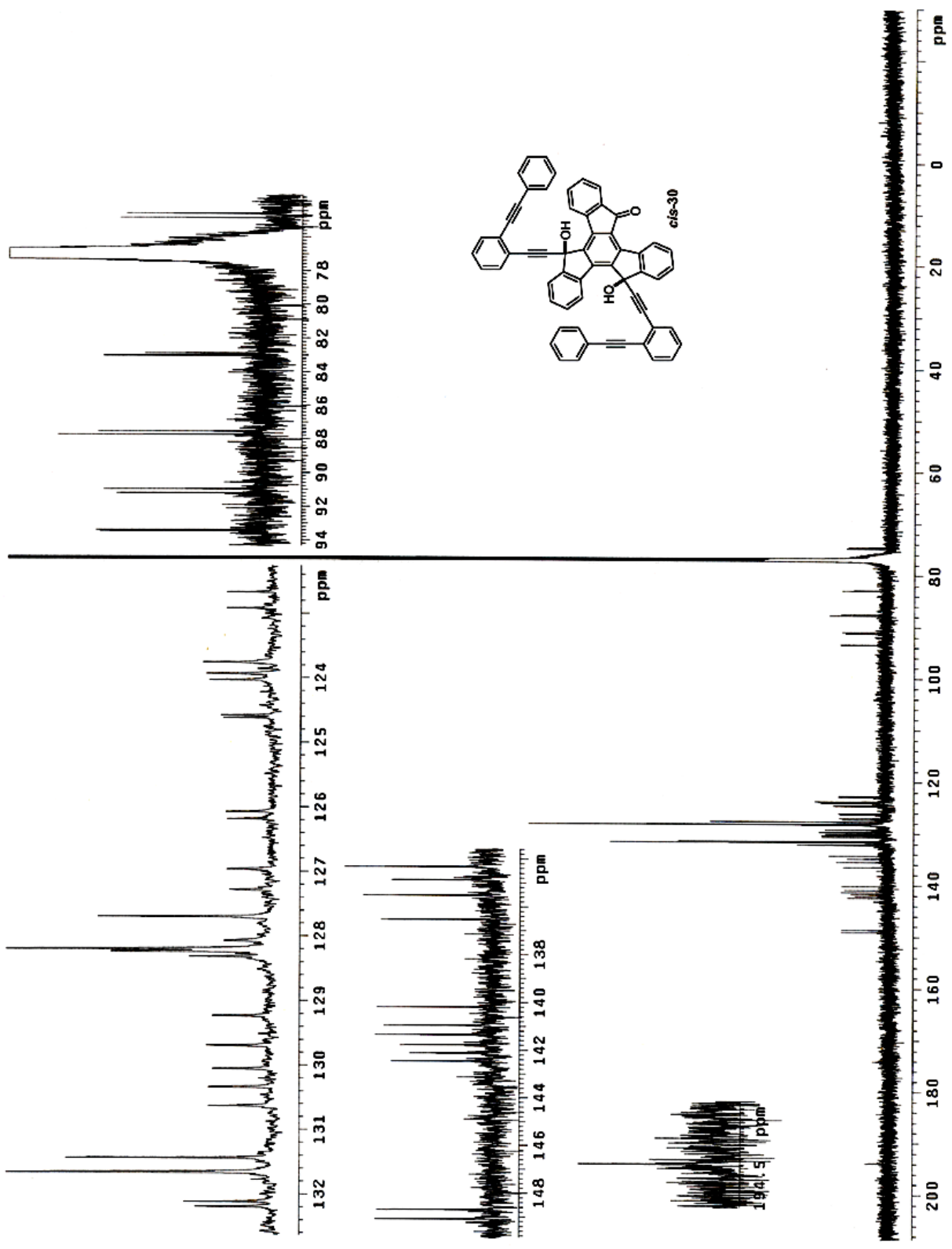
gHMBC spectrum of **28** in C_6D_6

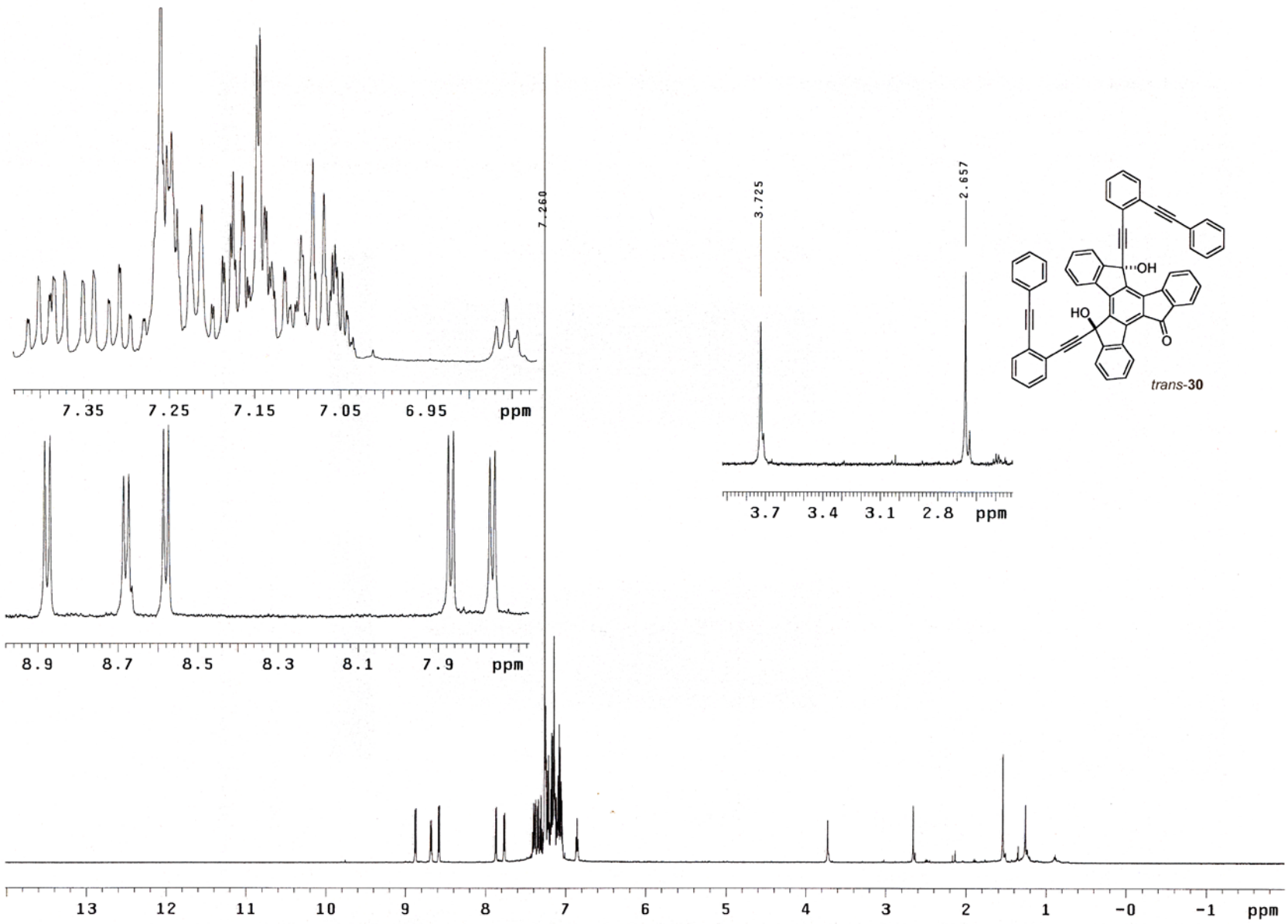


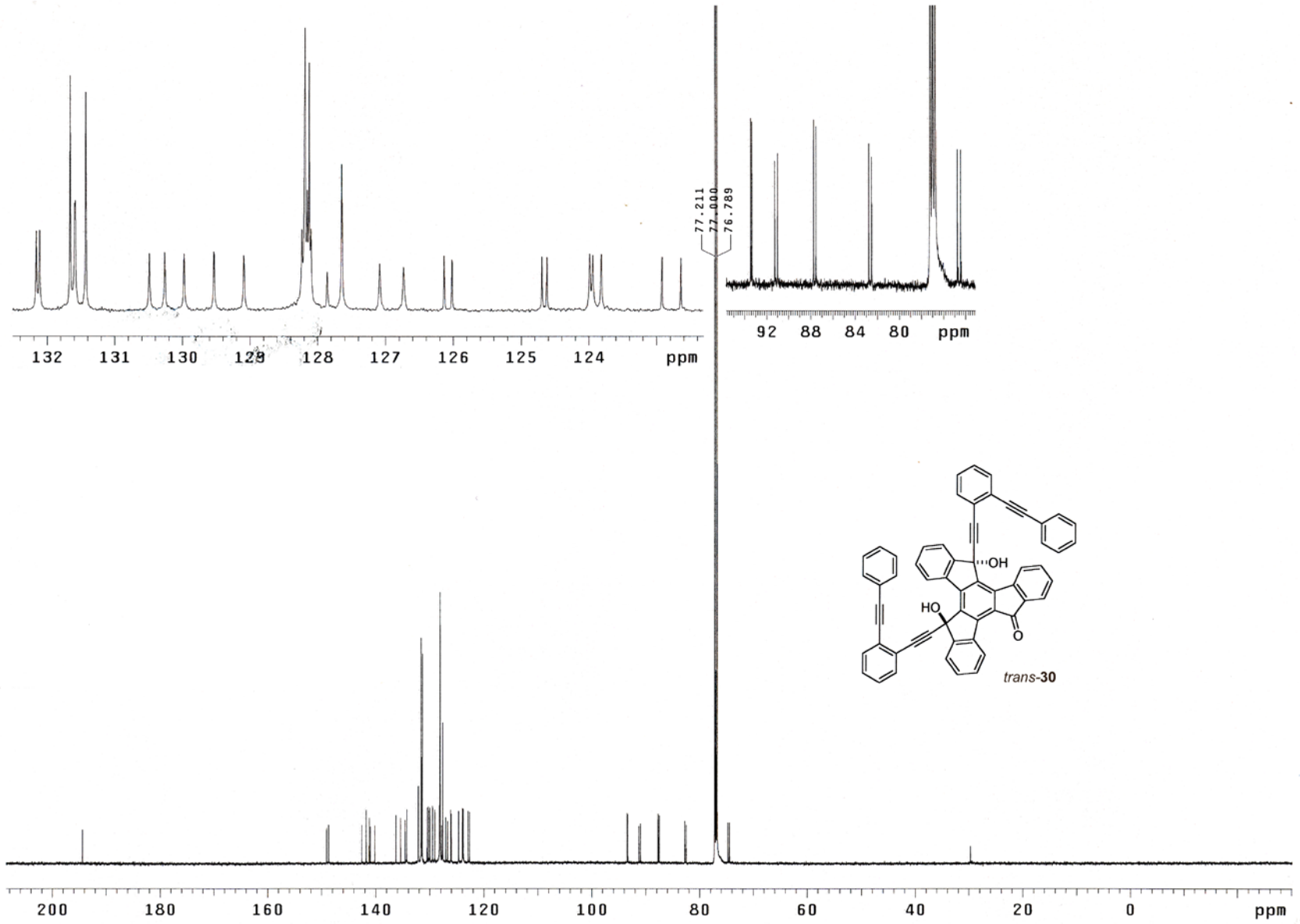
gHSQC-TOCSY spectrum of **28** in C_6D_6
(mix = 80 ms)

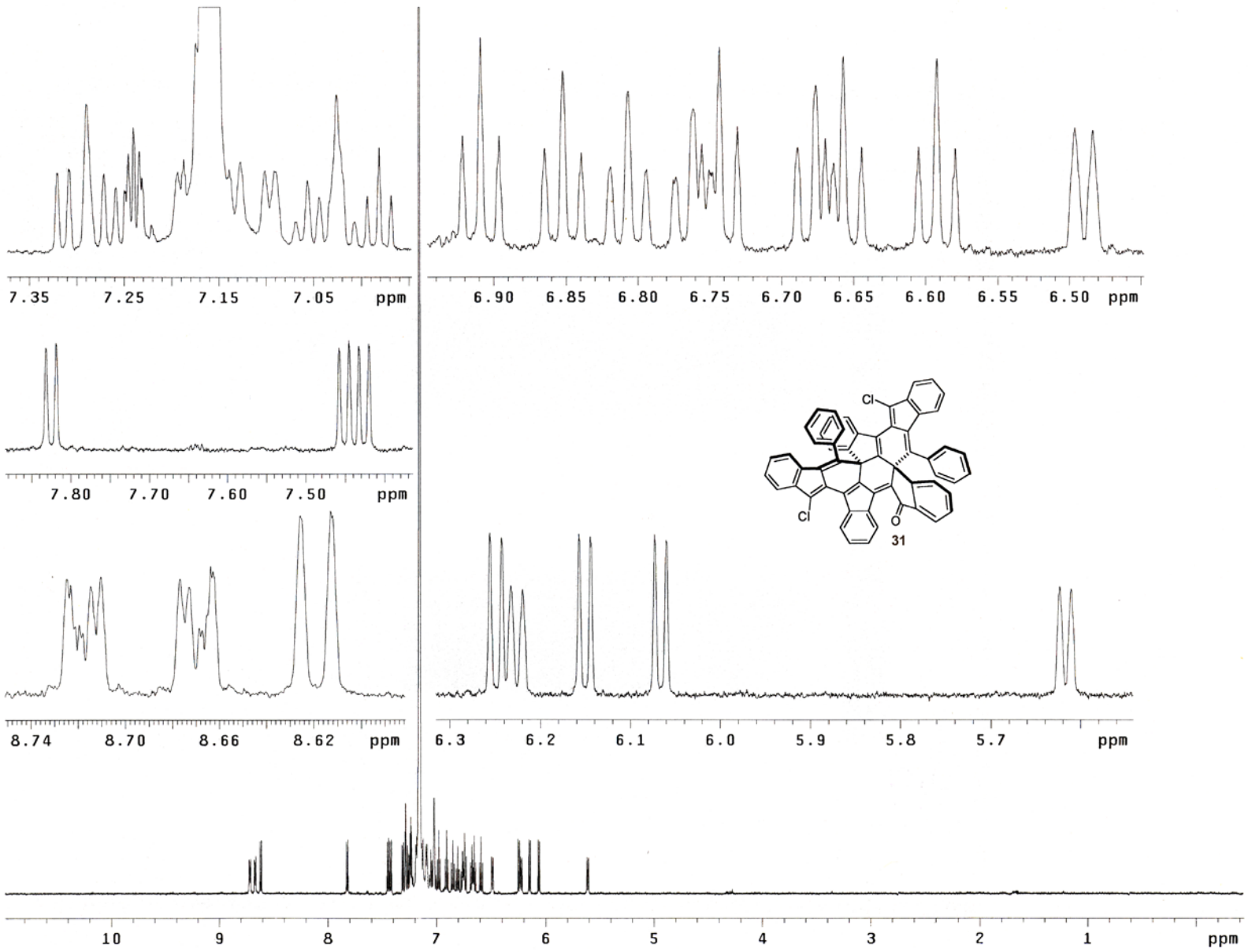


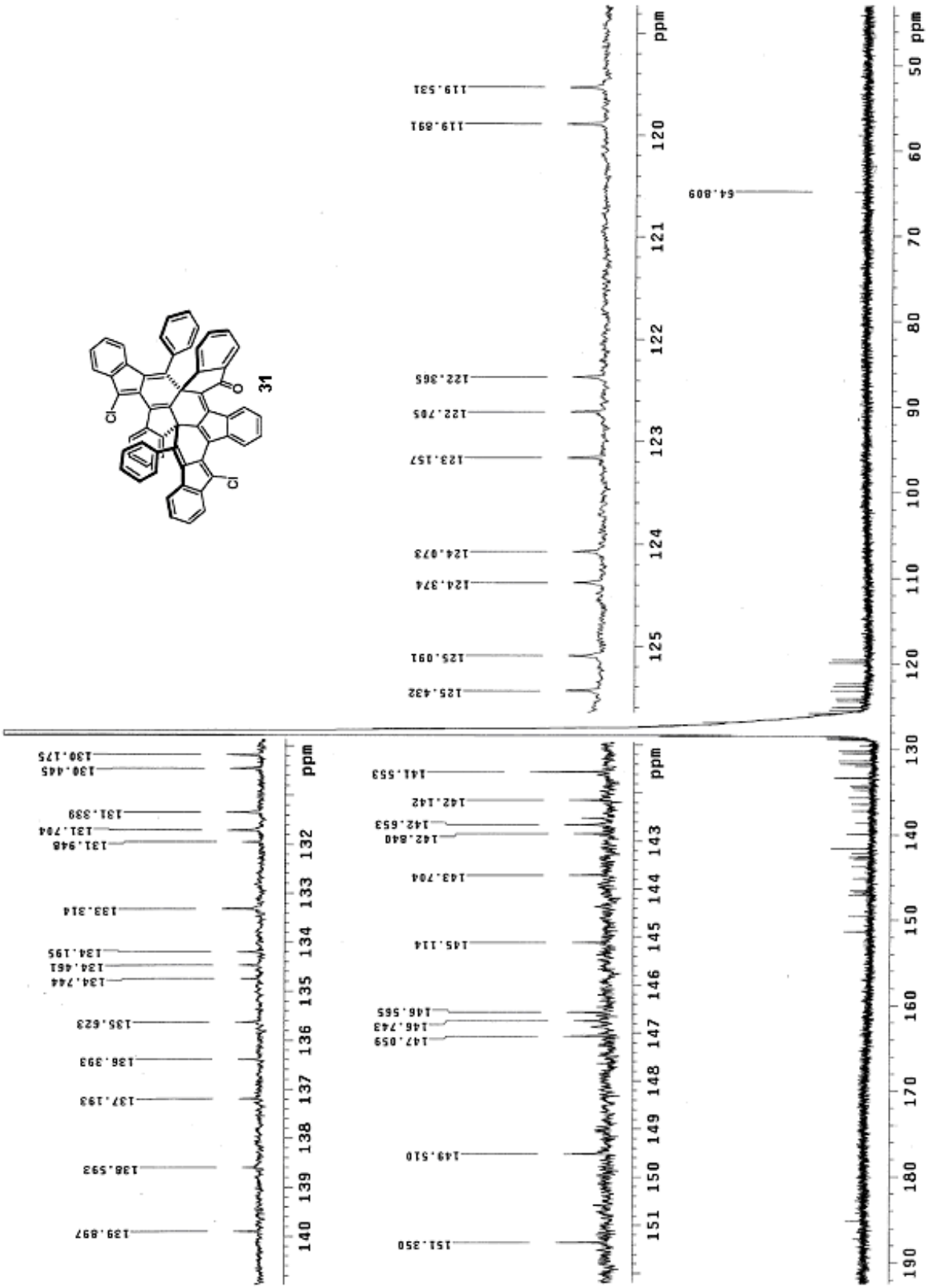

OH
HO
O
cis-30
2.642
7.40 7.35 7.30 7.25 7.20 7.15 7.10 7.05 ppm
8.9 8.7 8.5 8.3 8.1 7.9 ppm
3.4 3.2 3.0 2.8 ppm
13 12 11 10 9 8 7 6 5 4 3 2 1 -0 -1 ppm


OH
HO
O
cis-30
94 92 90 88 86 84 82 80 78 ppm
132 131 130 129 128 127 126 125 124 ppm
148 146 144 142 140 138 ppm
194.5 ppm
200 180 160 140 120 100 80 60 40 20 0 ppm

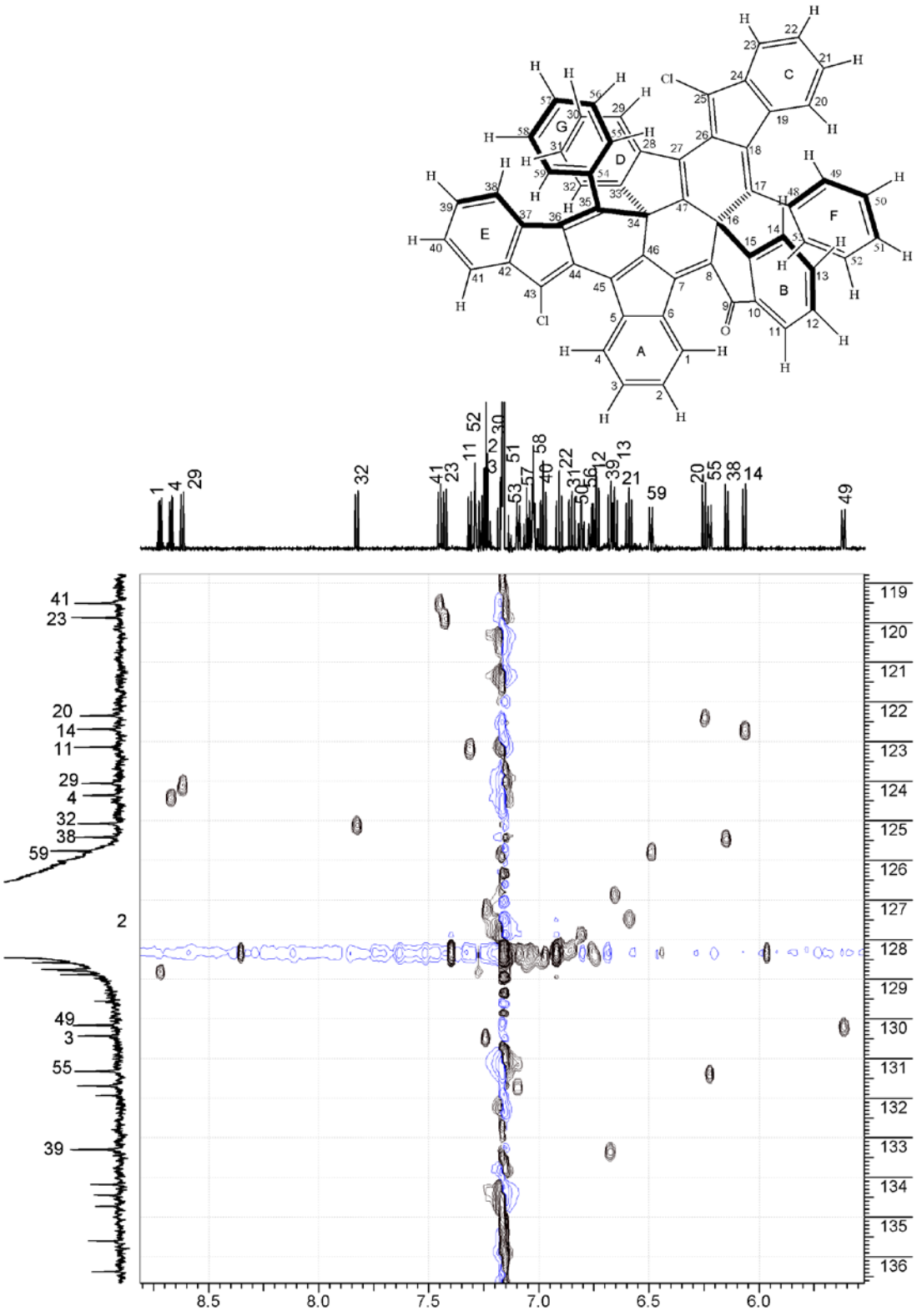

7.260
7.35
7.25
7.15
7.05
6.95
ppm
8.9
8.7
8.5
8.3
8.1
7.9
ppm
3.725
2.657
3.7
3.4
3.1
2.8
ppm
OH
HO
O
trans-30
13
12
11
10
9
8
7
6
5
4
3
2
1
-0
-1
ppm


77.211
77.000
76.789
132
131
130
129
128
127
126
125
124
ppm
92
88
84
80
ppm
OH
HO
O
trans-30
200
180
160
140
120
100
80
60
40
20
0
ppm

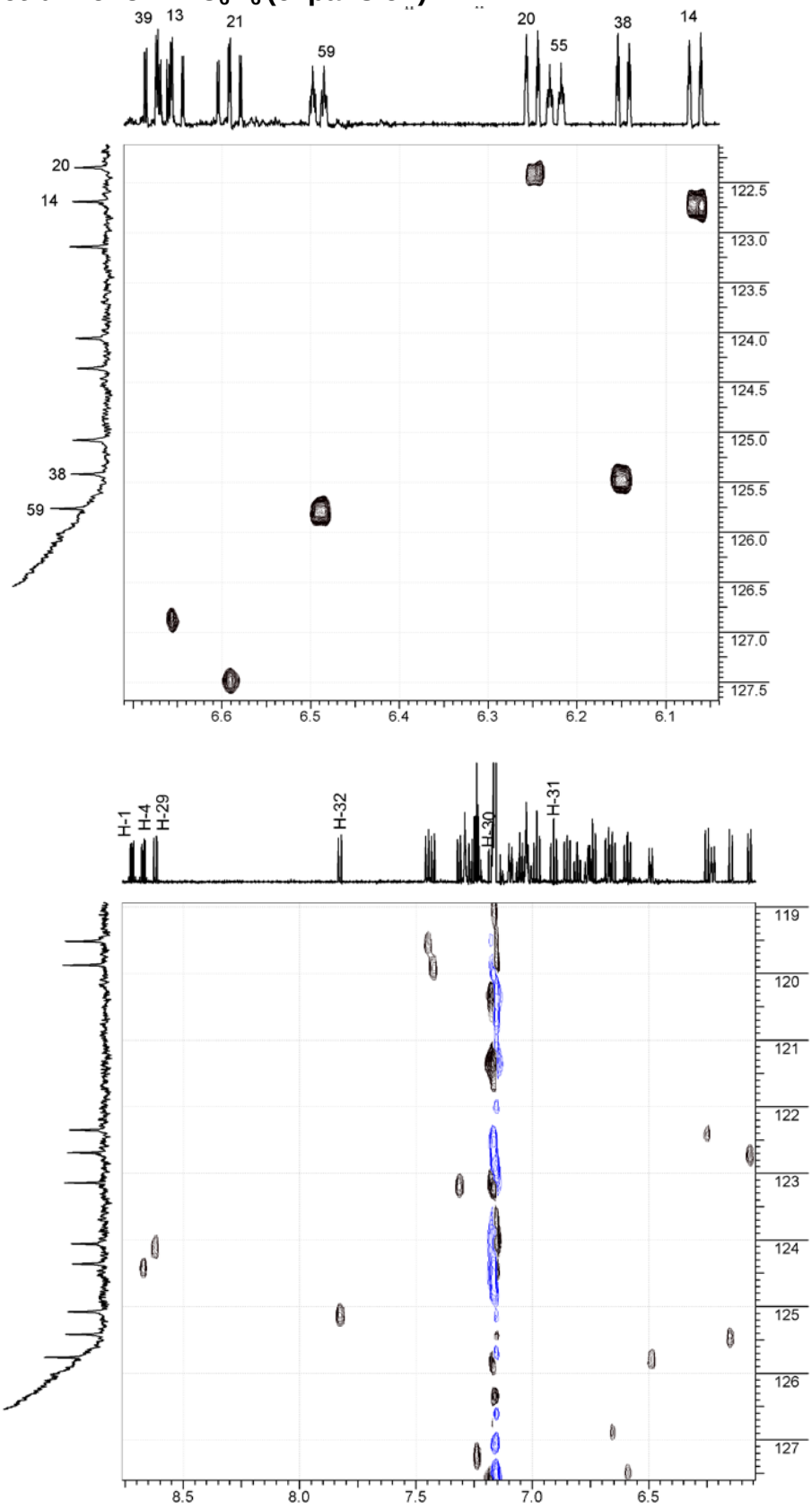

7.35
7.25
7.15
7.05
ppm
6.90
6.85
6.80
6.75
6.70
6.65
6.60
6.55
6.50
ppm
7.80
7.70
7.60
7.50
ppm
Cl
Cl
O
31
8.74
8.70
8.66
8.62
ppm
6.3
6.2
6.1
6.0
5.9
5.8
5.7
ppm
10
9
8
7
6
5
4
3
2
1
ppm


31
O
Cl
Cl
119.531
119.091
122.365
122.705
123.157
124.073
124.374
125.091
125.432
64.809
141.553
142.142
142.653
142.840
143.704
145.114
146.565
146.743
147.059
149.510
151.350
130.175
130.445
131.389
131.704
131.948
133.314
134.195
134.461
134.744
135.623
136.393
137.193
138.593
139.897
ppm

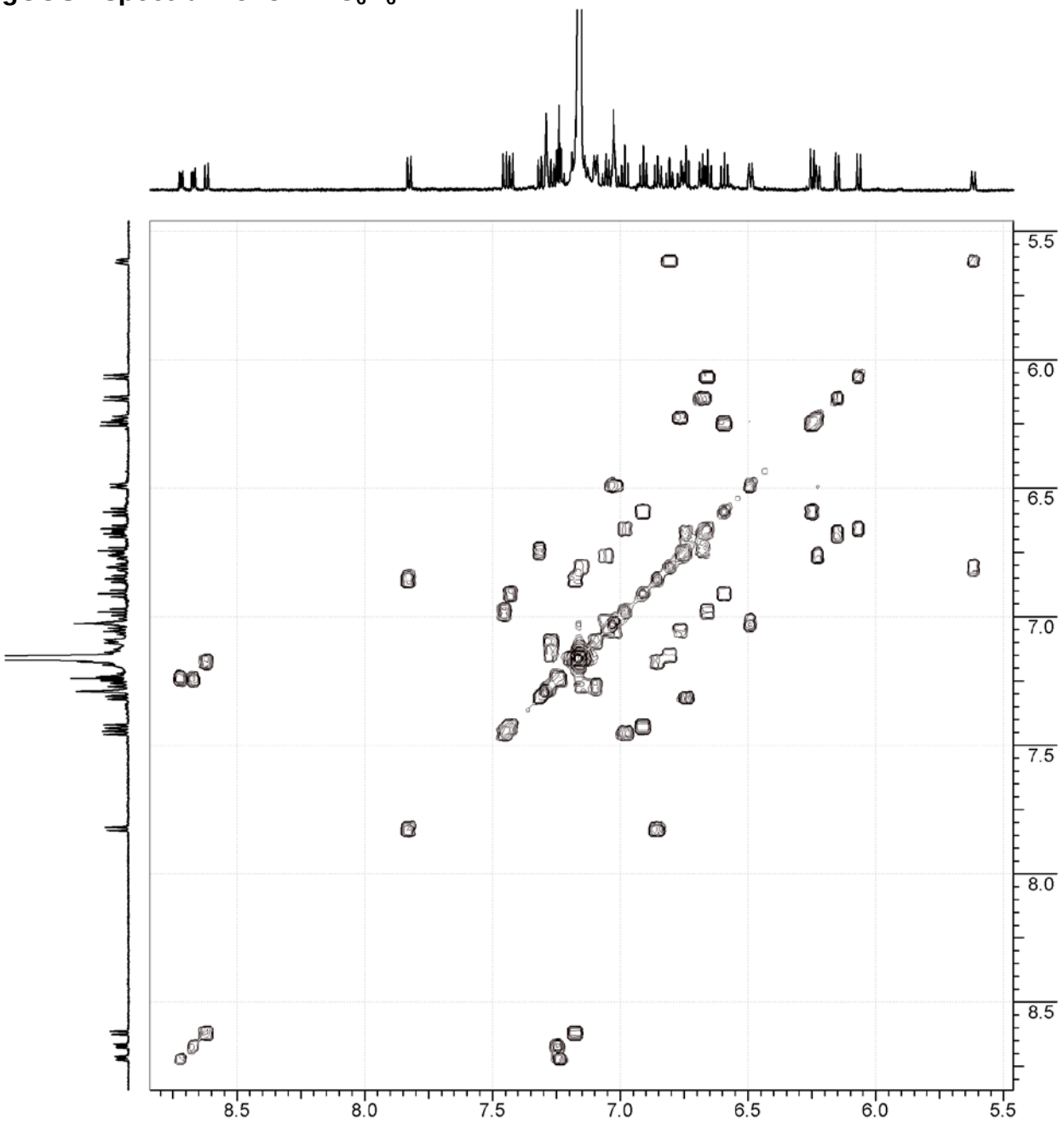
gHSQC spectrum of 31 in C_6D_6



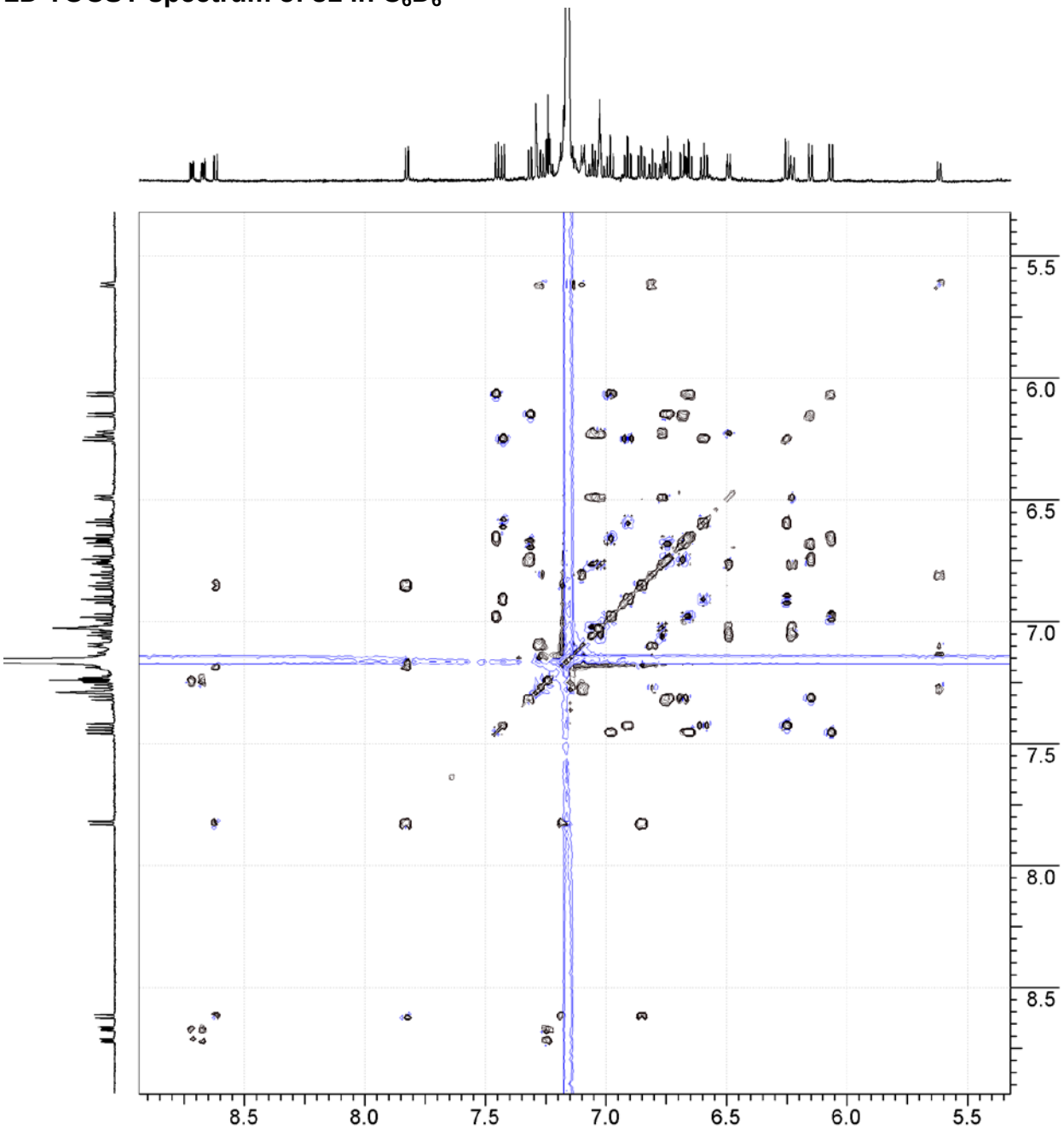
gHSQC spectrum of 31 in C_6D_6 (expansion)



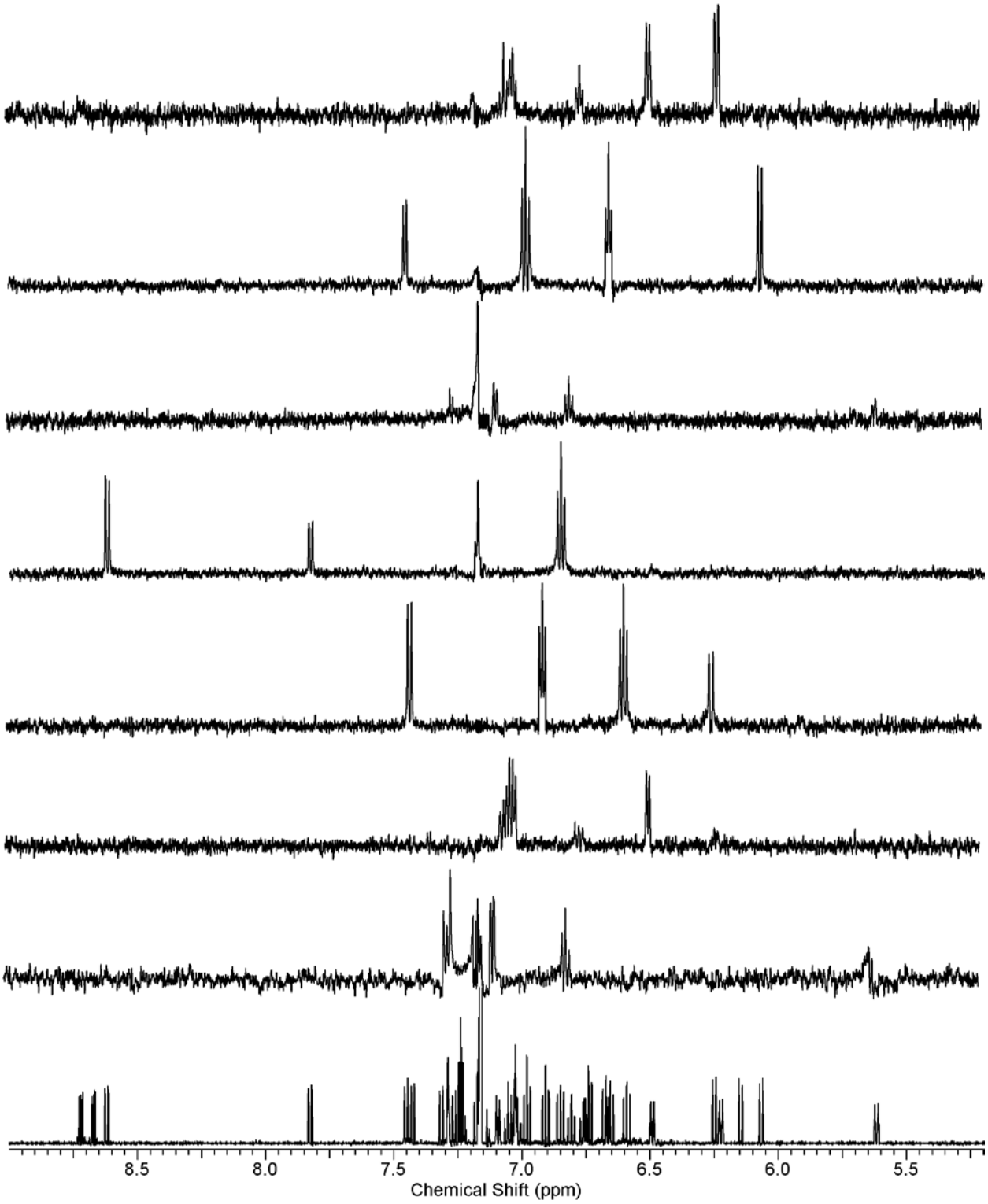
gCOSY spectrum of 31 in C_6D_6



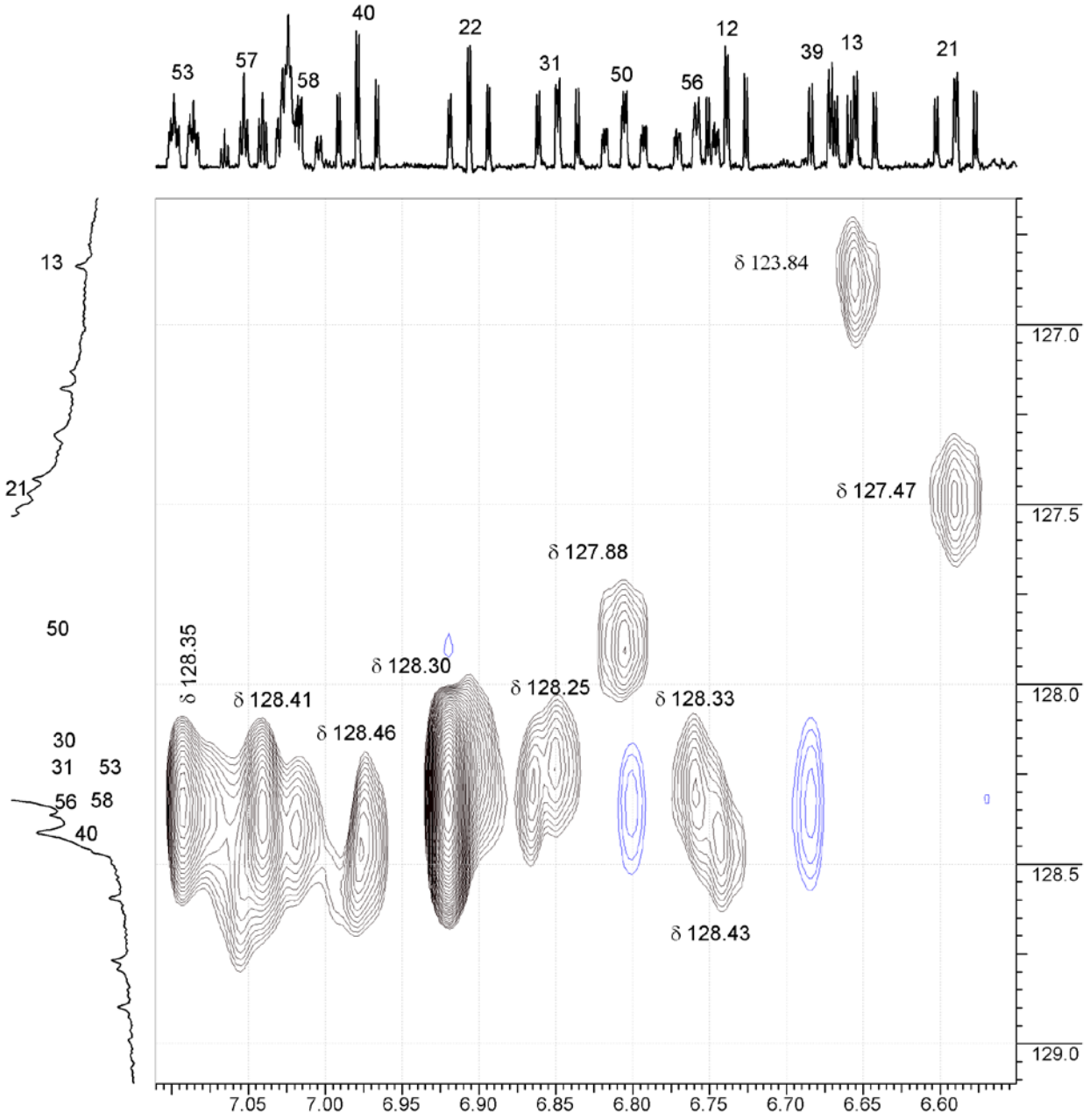
2D TOCSY spectrum of 31 in C_6D_6

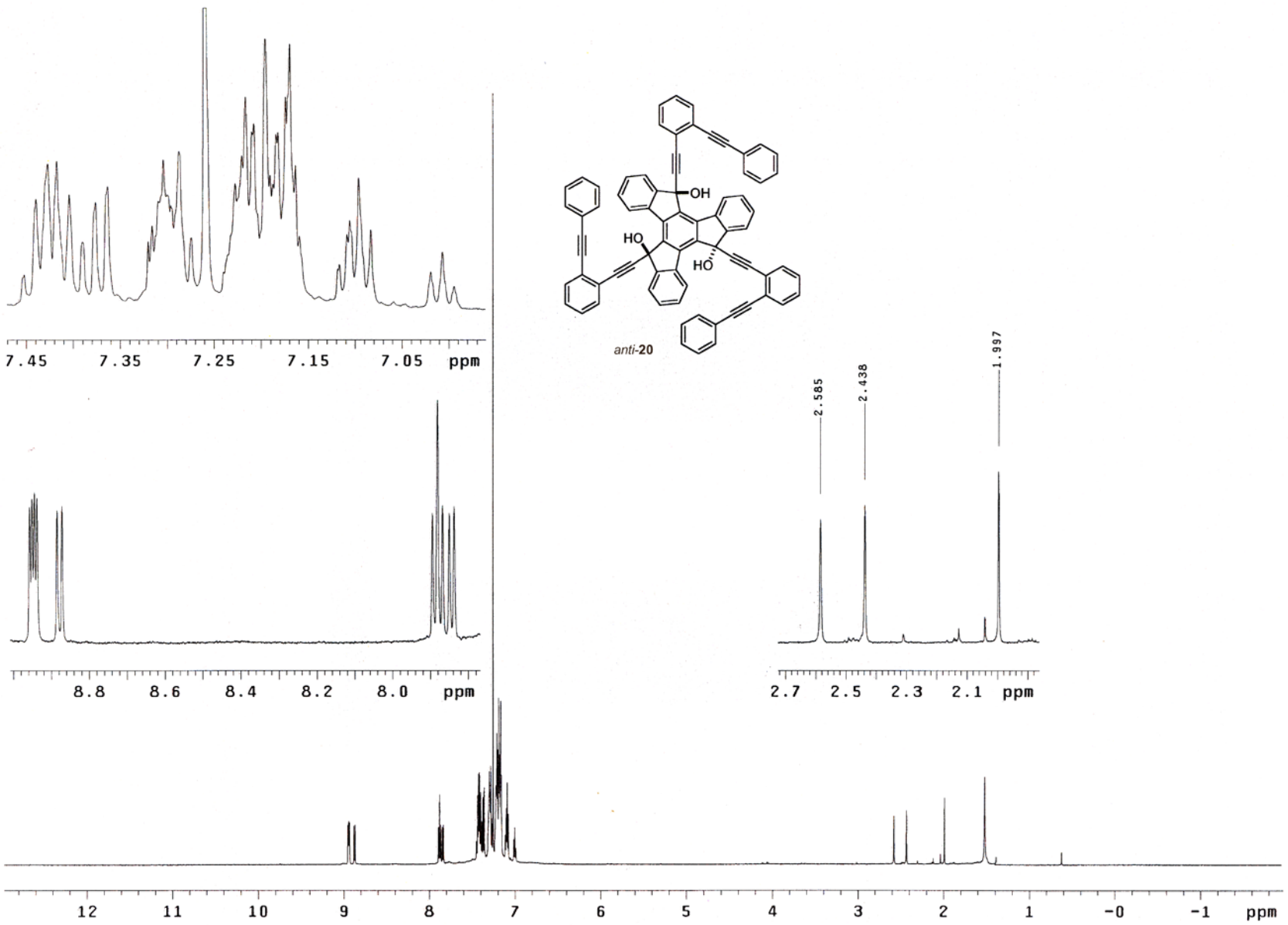


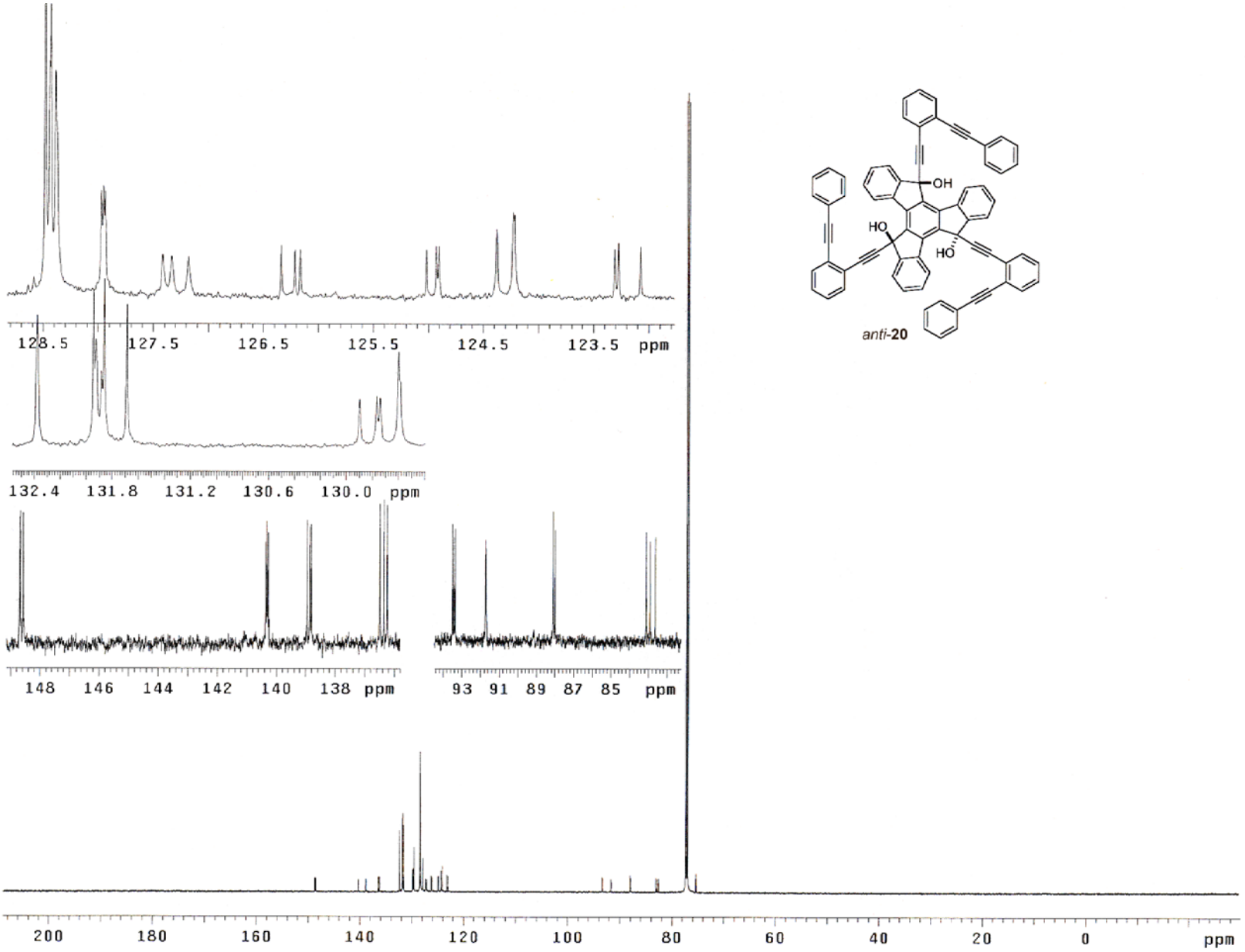
1D TOCSY spectra of 31 in C_6D_6 (mix = 80ms)

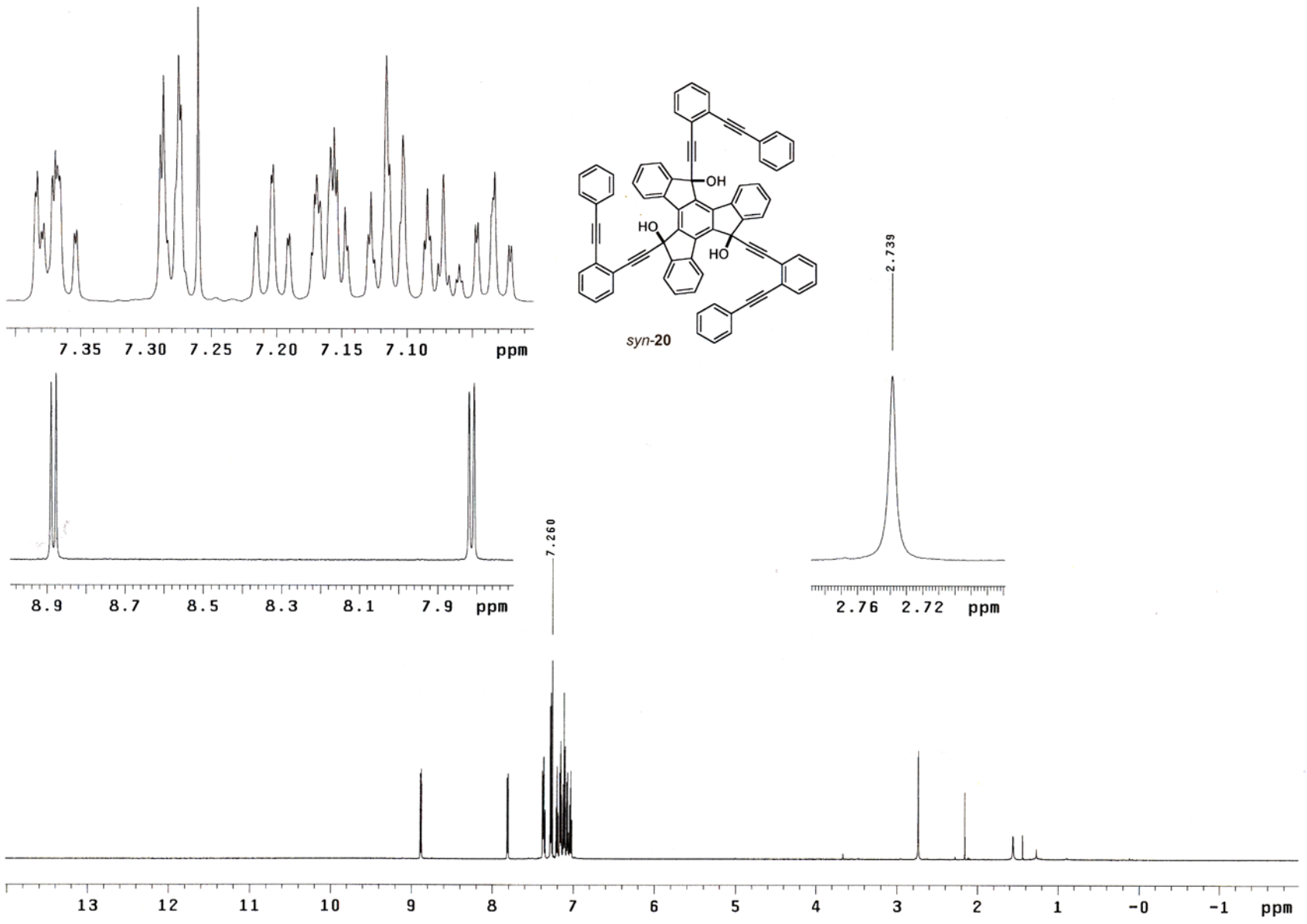


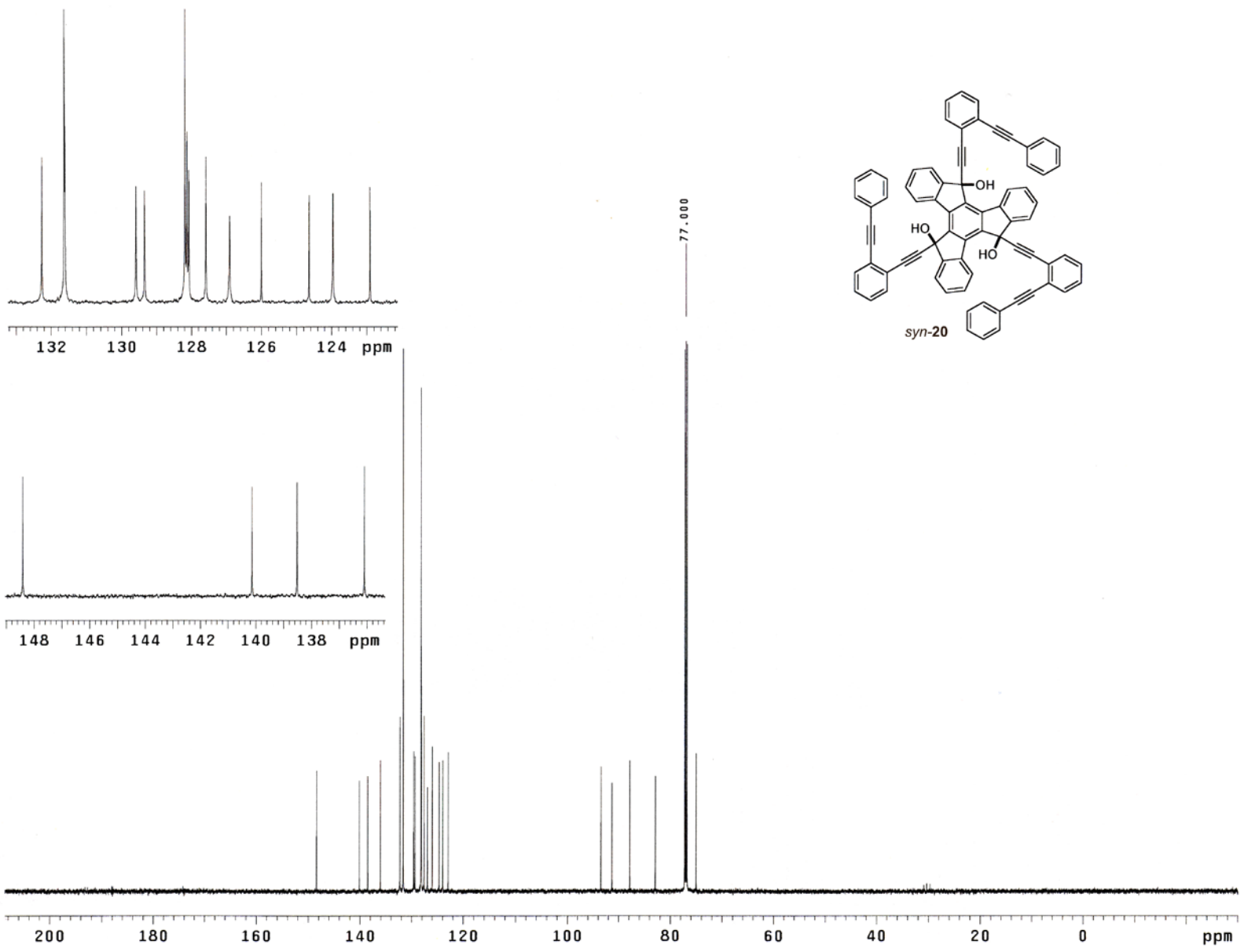
gHMBC spectrum of 31 in C_6D_6 (expansion)



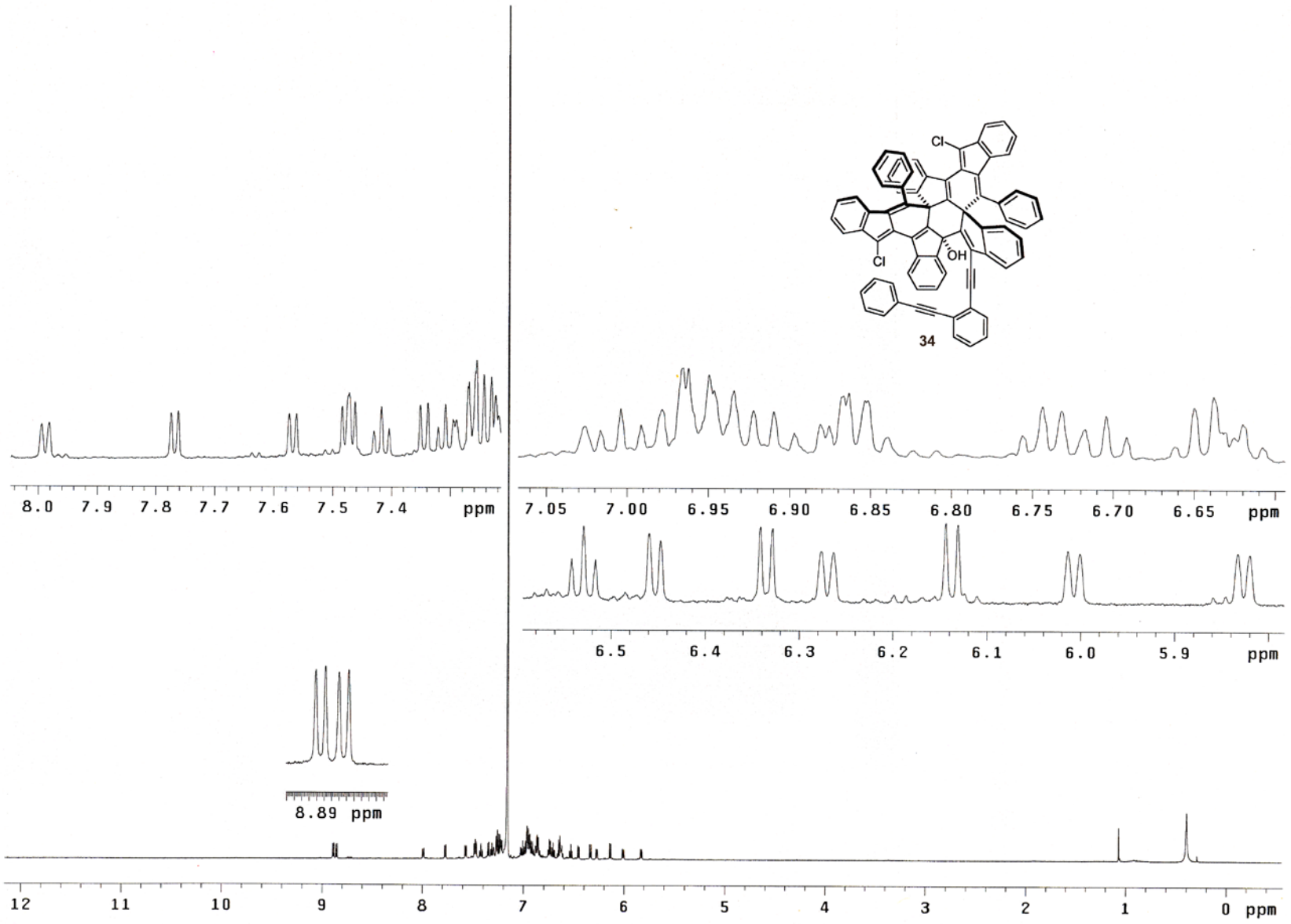

OH
HO
HO
anti-20
2.585
2.438
1.997
7.45
7.35
7.25
7.15
7.05
ppm
8.8
8.6
8.4
8.2
8.0
ppm
2.7
2.5
2.3
2.1
ppm
12
11
10
9
8
7
6
5
4
3
2
1
-0
-1
ppm

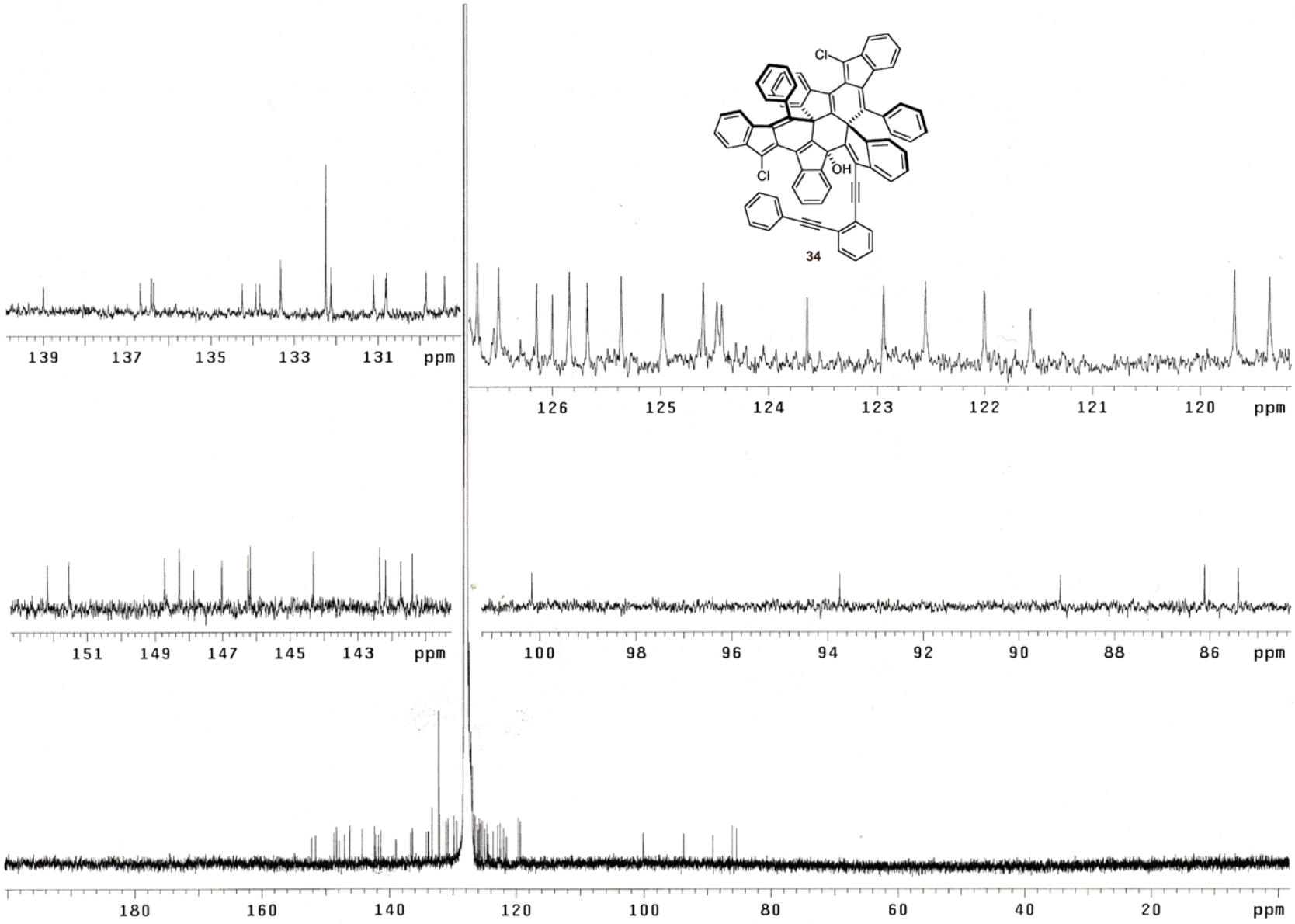

128.5
127.5
126.5
125.5
124.5
123.5
ppm
132.4
131.8
131.2
130.6
130.0
ppm
148
146
144
142
140
138
ppm
93
91
89
87
85
ppm
200
180
160
140
120
100
80
60
40
20
0
ppm
OH
HO
HO
anti-20


OH
HO
HO
syn-20
7.35 7.30 7.25 7.20 7.15 7.10 ppm
8.9 8.7 8.5 8.3 8.1 7.9 ppm
2.76 2.72 ppm
7.260
2.739
13 12 11 10 9 8 7 6 5 4 3 2 1 -0 -1 ppm

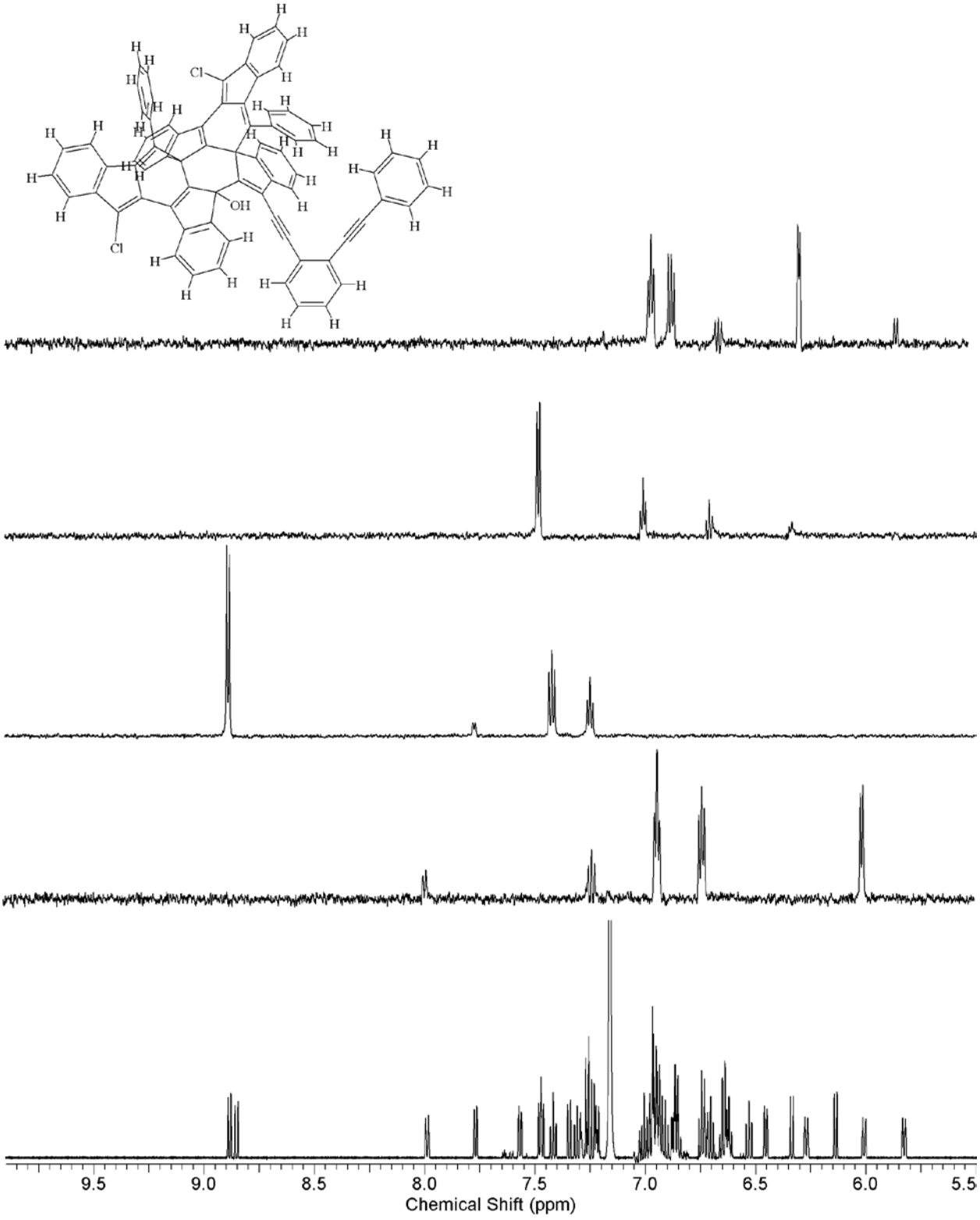

77.000
OH
HO
HO
132 130 128 126 124 ppm
148 146 144 142 140 138 ppm
200 180 160 140 120 100 80 60 40 20 0 ppm

syn-**20**

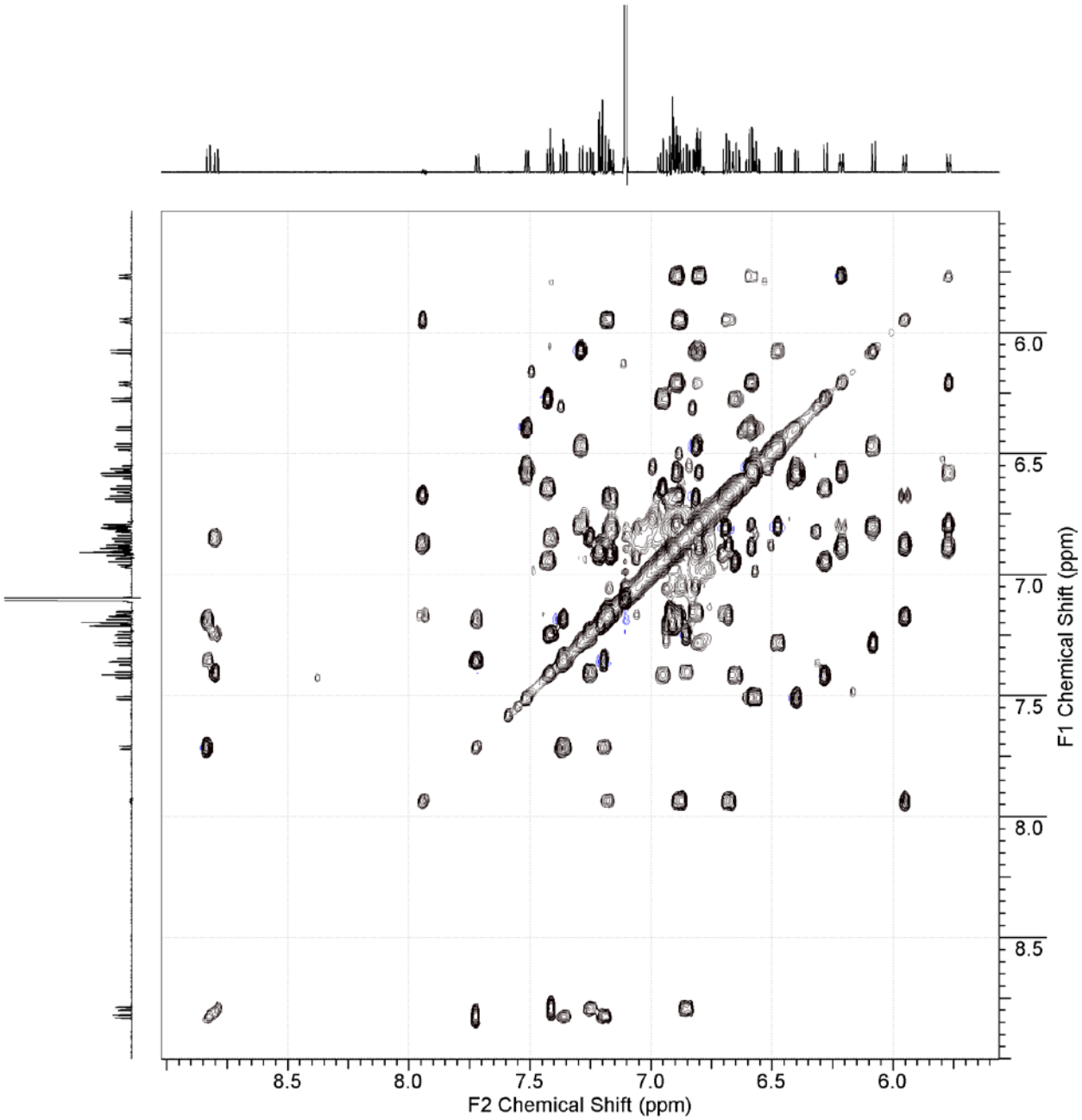

Cl
Cl
OH
34
8.0 7.9 7.8 7.7 7.6 7.5 7.4 ppm
7.05 7.00 6.95 6.90 6.85 6.80 6.75 6.70 6.65 ppm
6.5 6.4 6.3 6.2 6.1 6.0 5.9 ppm
8.89 ppm
12 11 10 9 8 7 6 5 4 3 2 1 0 ppm


Cl
Cl
OH
34
139
137
135
133
131
ppm
126
125
124
123
122
121
120
ppm
151
149
147
145
143
ppm
100
98
96
94
92
90
88
86
ppm
180
160
140
120
100
80
60
40
20
ppm

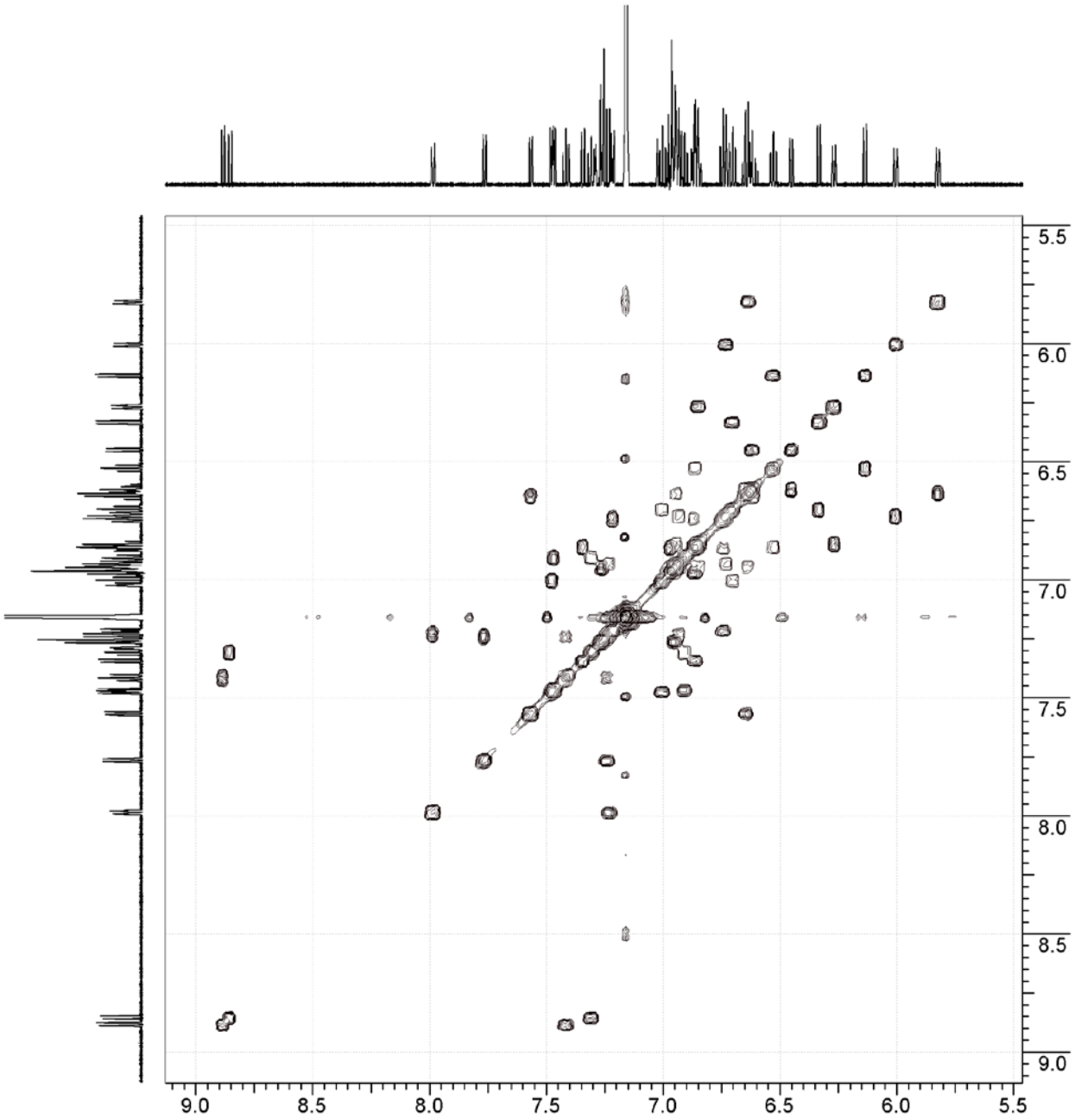
1D TOCSY Spectrum of 34 in C_6D_6



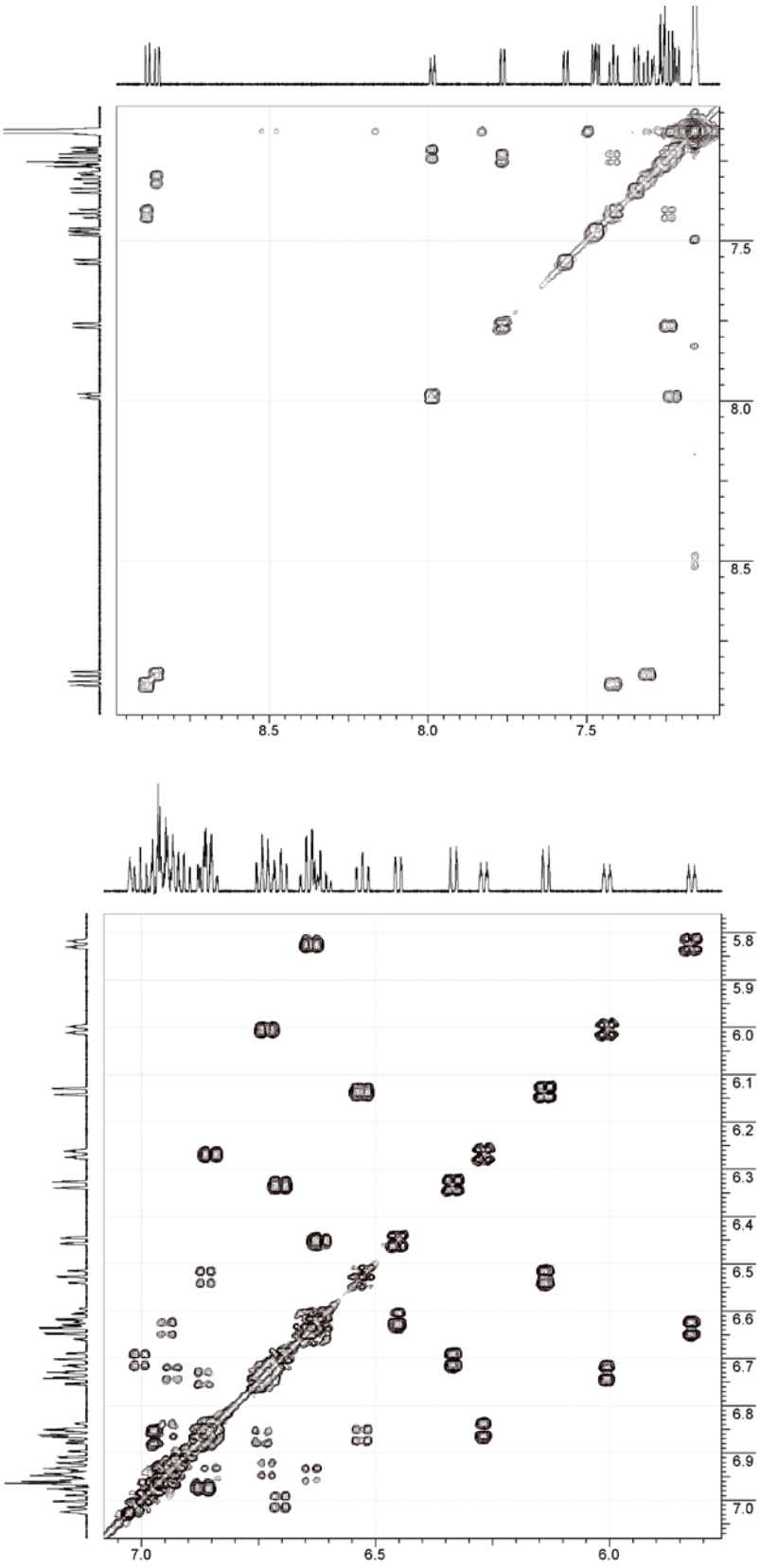
2D TOCSY Spectrum of 34 in C_6D_6

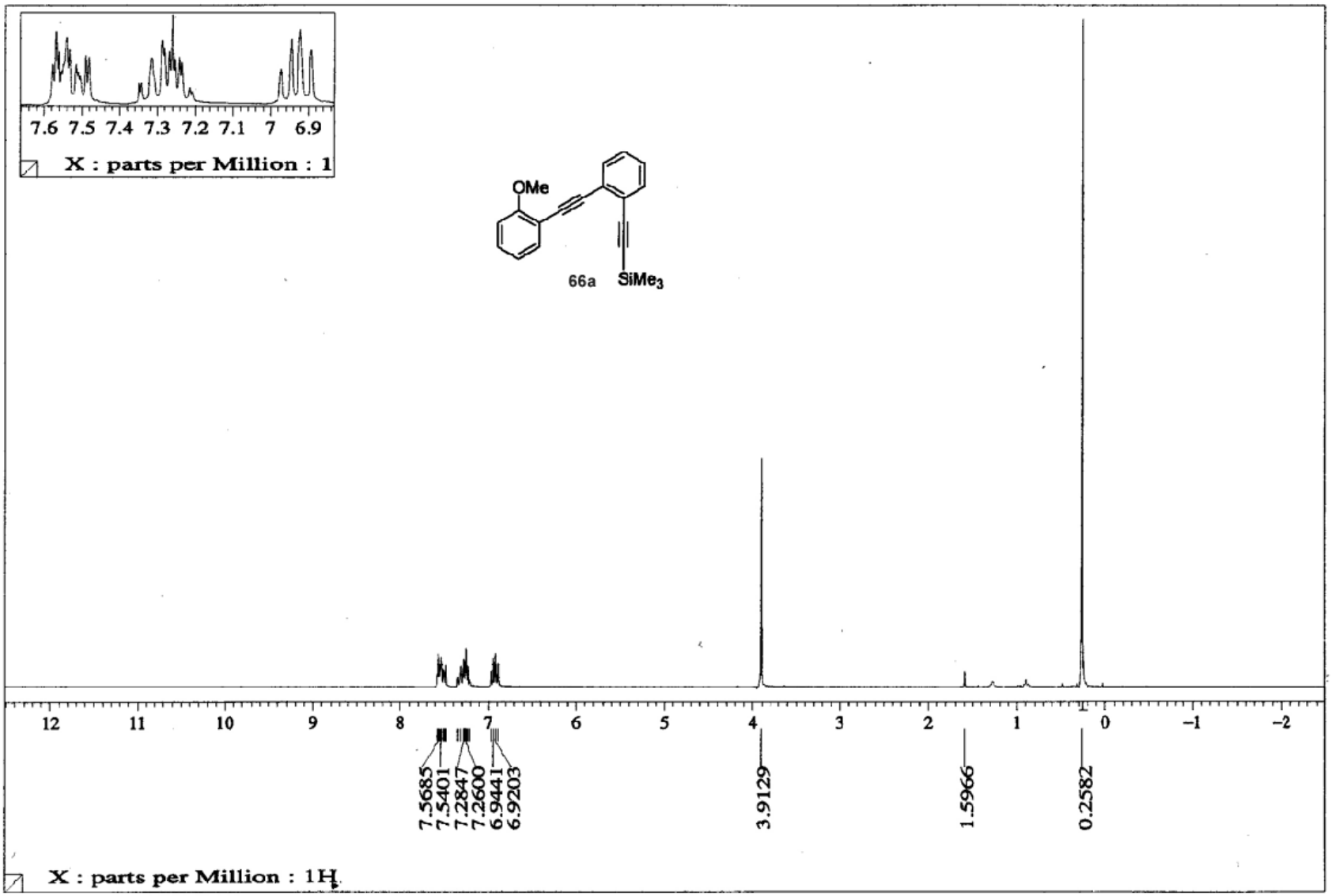


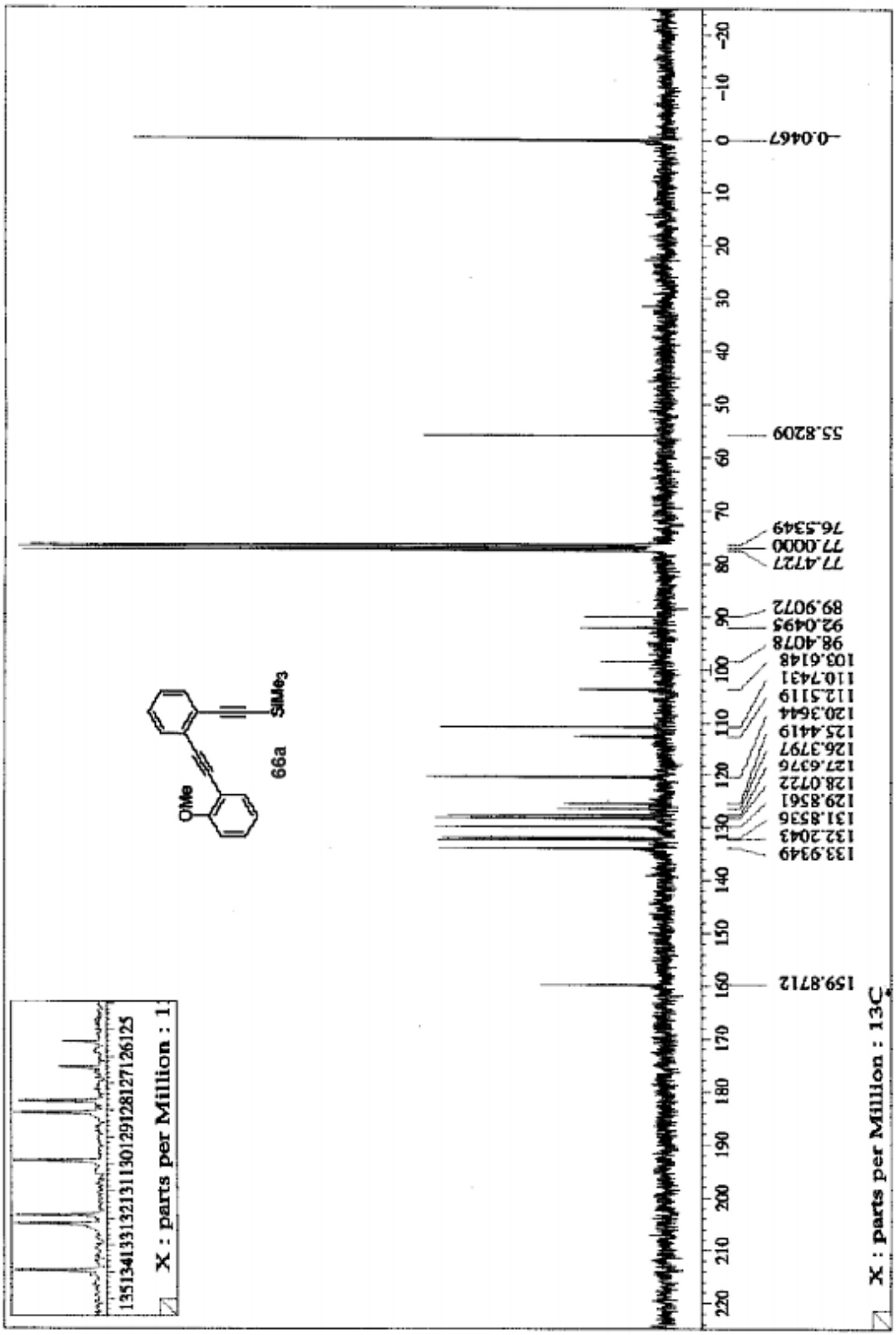
gCOSY Spectrum of 34 in C_6D_6

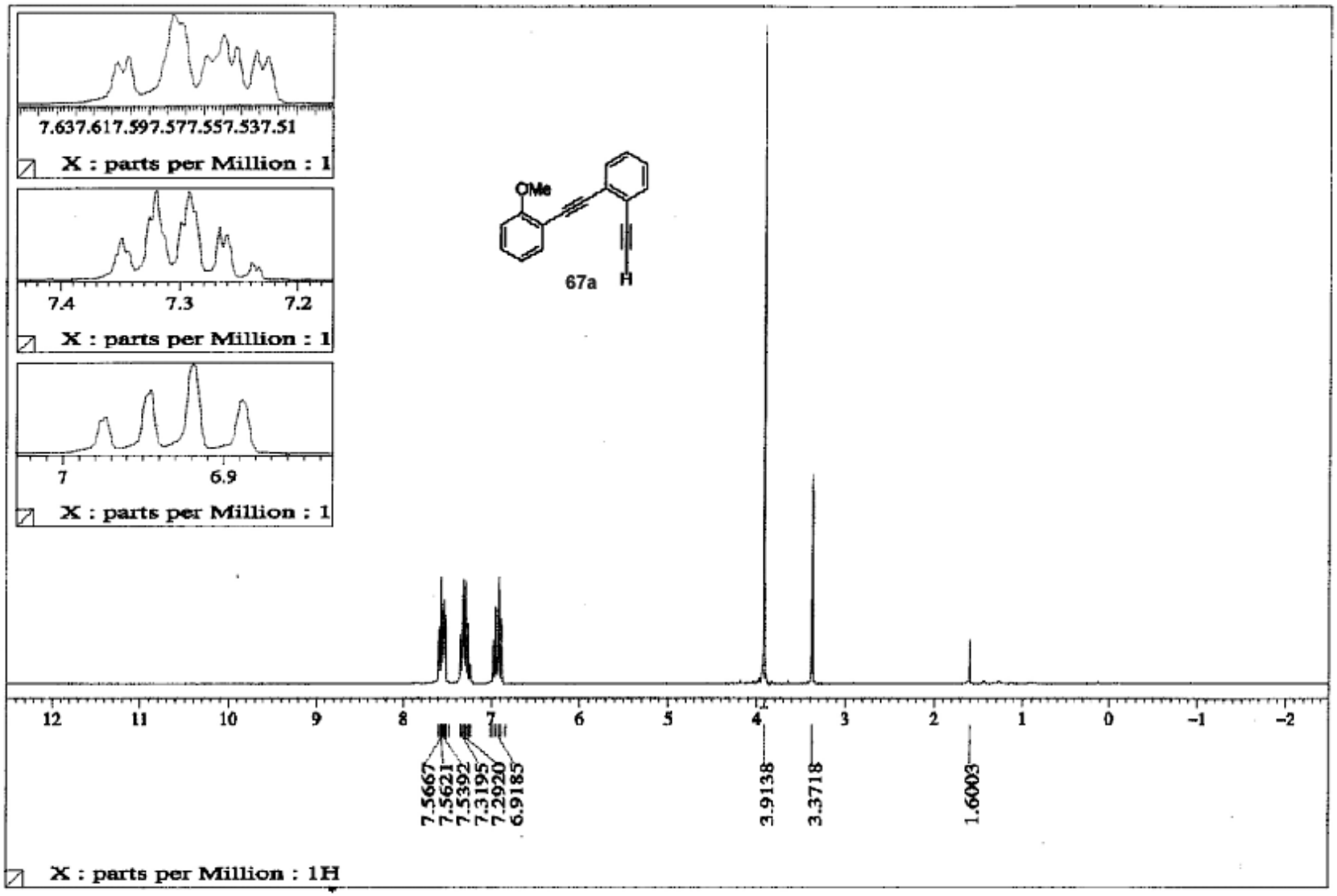


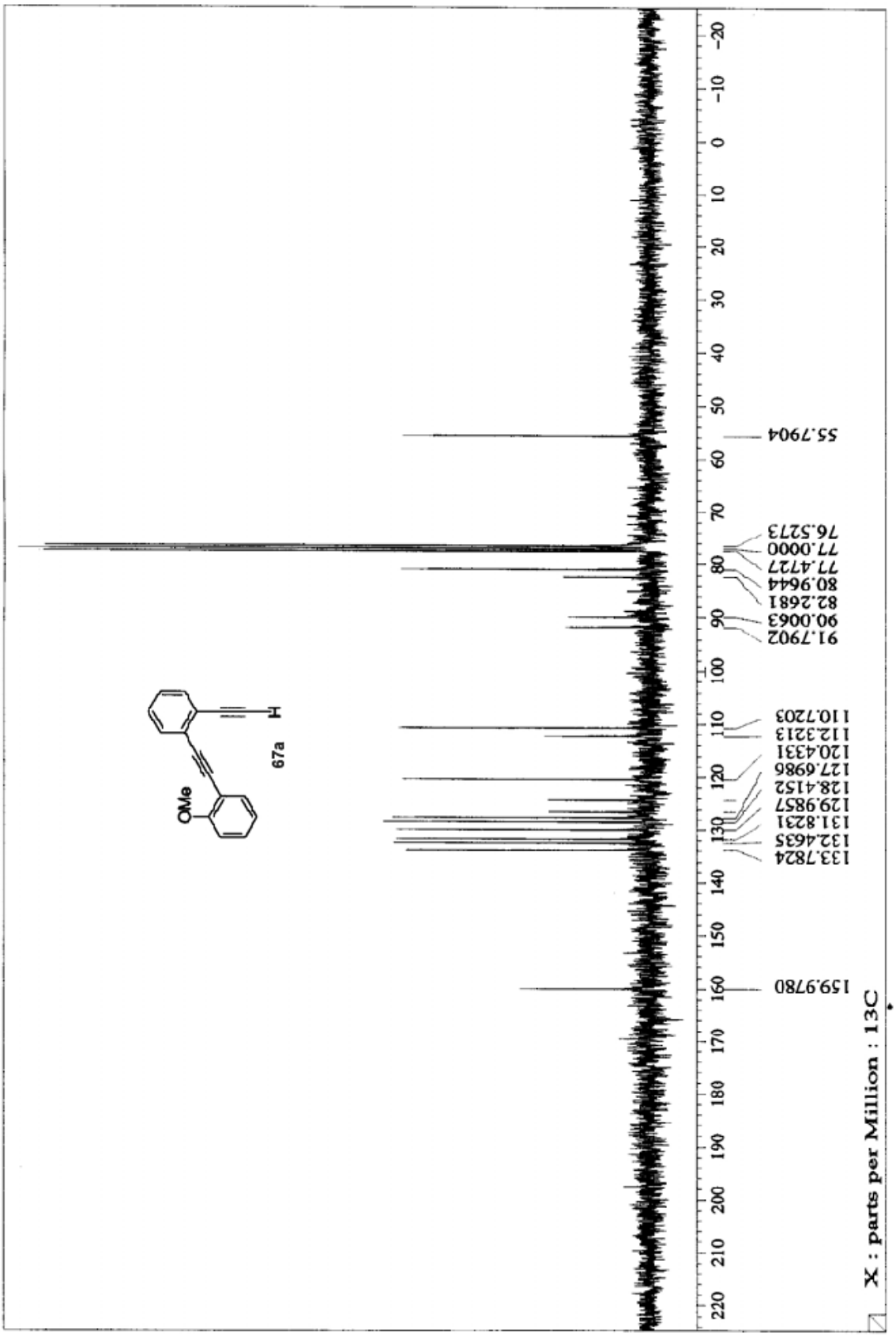
gCOSY Spectrum of 34 in C_6D_6 (expansion)

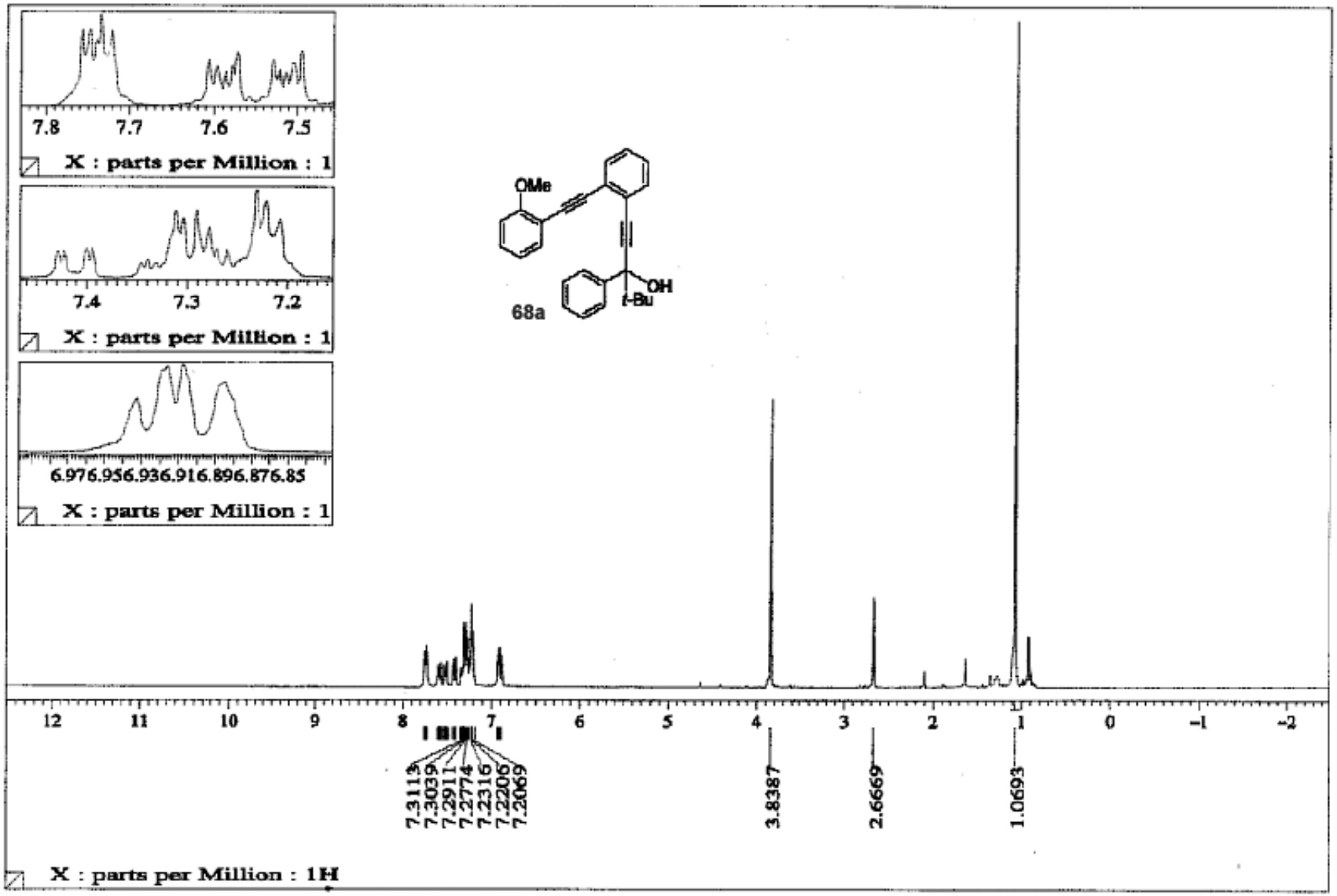



7.6 7.5 7.4 7.3 7.2 7.1 7 6.9
X : parts per Million : 1
OMe
66a
SiMe3
12 11 10 9 8 7 6 5 4 3 2 1 0 −1 −2
7.5685
7.5401
7.2847
7.2600
6.9441
6.9203
3.9129
1.5966
0.2582
X : parts per Million : 1H

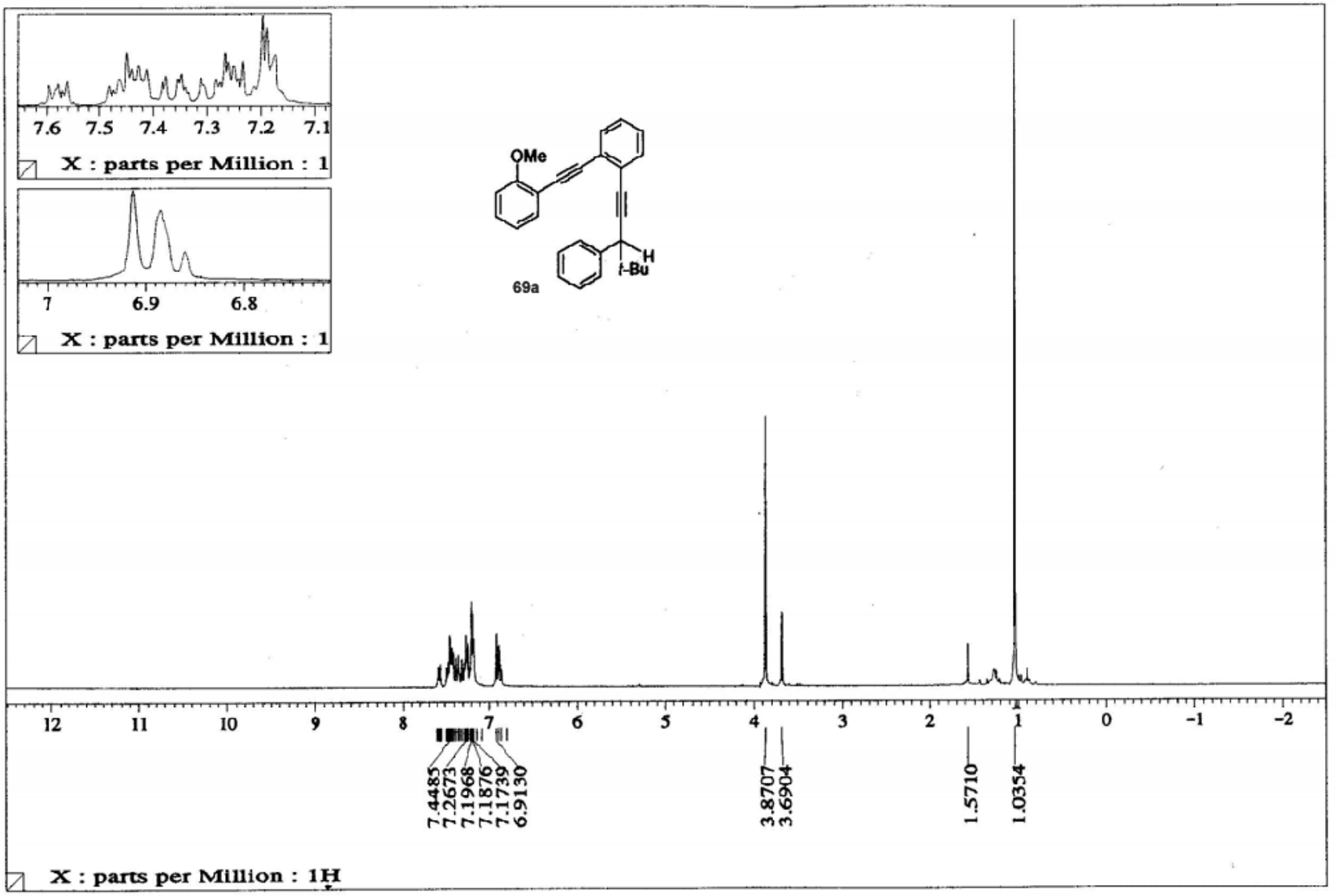

66a
OMe
SiMe3
X : parts per Million : 13C
X : parts per Million : 1
0.0467
55.8209
76.5349
77.0000
77.4727
89.9072
92.0495
98.4078
103.6148
110.7431
112.5119
120.3644
125.4419
126.3797
127.6376
128.0722
129.8561
131.8536
132.2043
133.9349
159.8712


7.637.617.597.577.557.537.51
X : parts per Million : 1
7.4
7.3
7.2
X : parts per Million : 1
7
6.9
X : parts per Million : 1
OMe
67a
H
12
11
10
9
8
7
6
5
4
3
2
1
0
−1
−2
7.5667
7.5621
7.5392
7.3195
7.2920
6.9185
3.9138
3.3718
1.6003
X : parts per Million : 1H

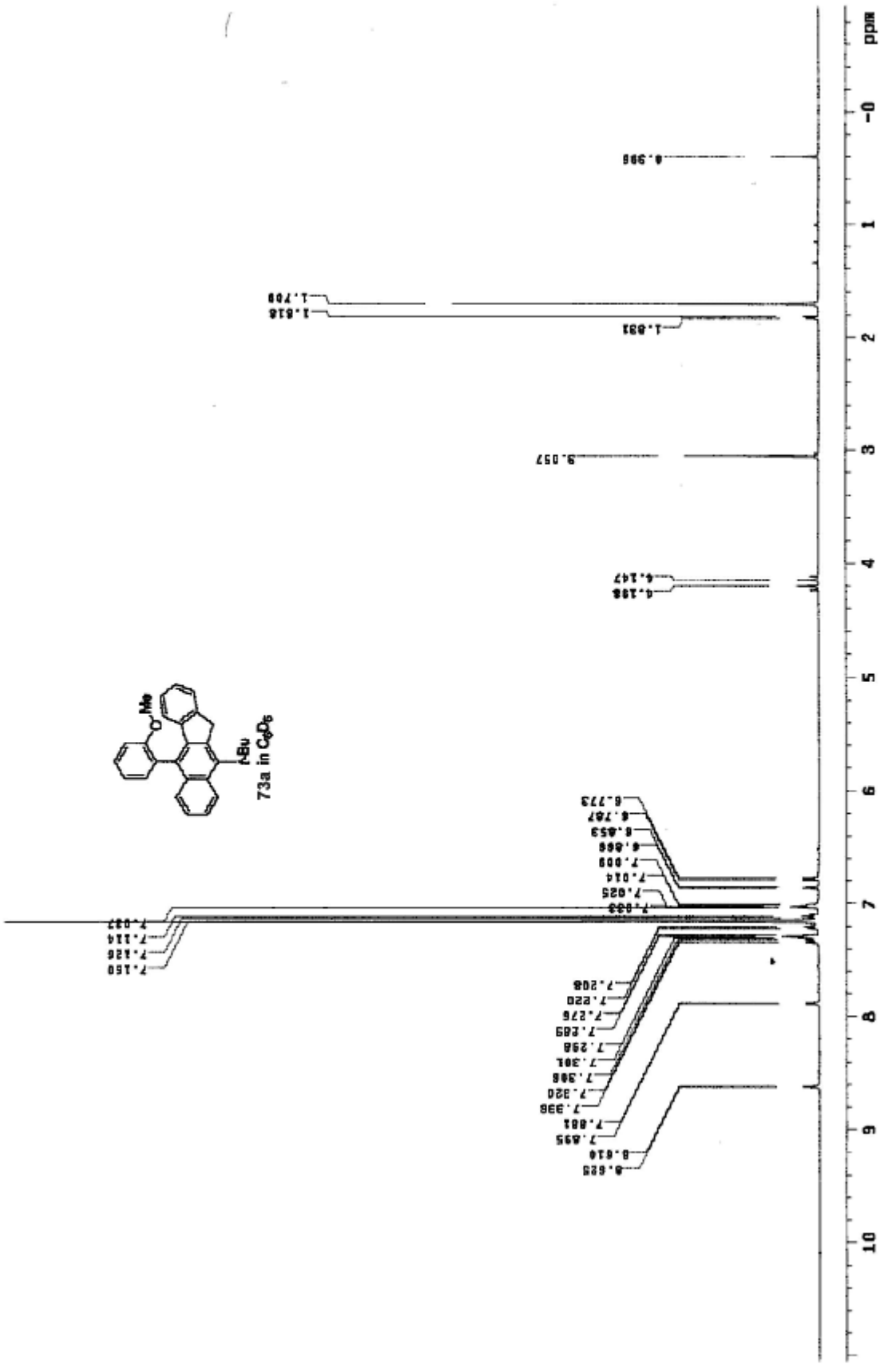

OMe
H
67a
X : parts per Million : 13C
159.9780
133.7824
132.4635
131.8231
129.9857
128.4152
127.6986
120.4331
112.3213
110.7203
91.7902
90.0063
82.2681
80.9644
77.4727
77.0000
76.5273
55.7904


7.8
7.7
7.6
7.5
X : parts per Million : 1
7.4
7.3
7.2
X : parts per Million : 1
6.976.956.936.916.896.876.85
X : parts per Million : 1
OMe
OH
t-Bu
68a
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
7.3113
7.3039
7.2911
7.2774
7.2316
7.2206
7.2069
3.8387
2.6669
1.0693
X : parts per Million : 1H

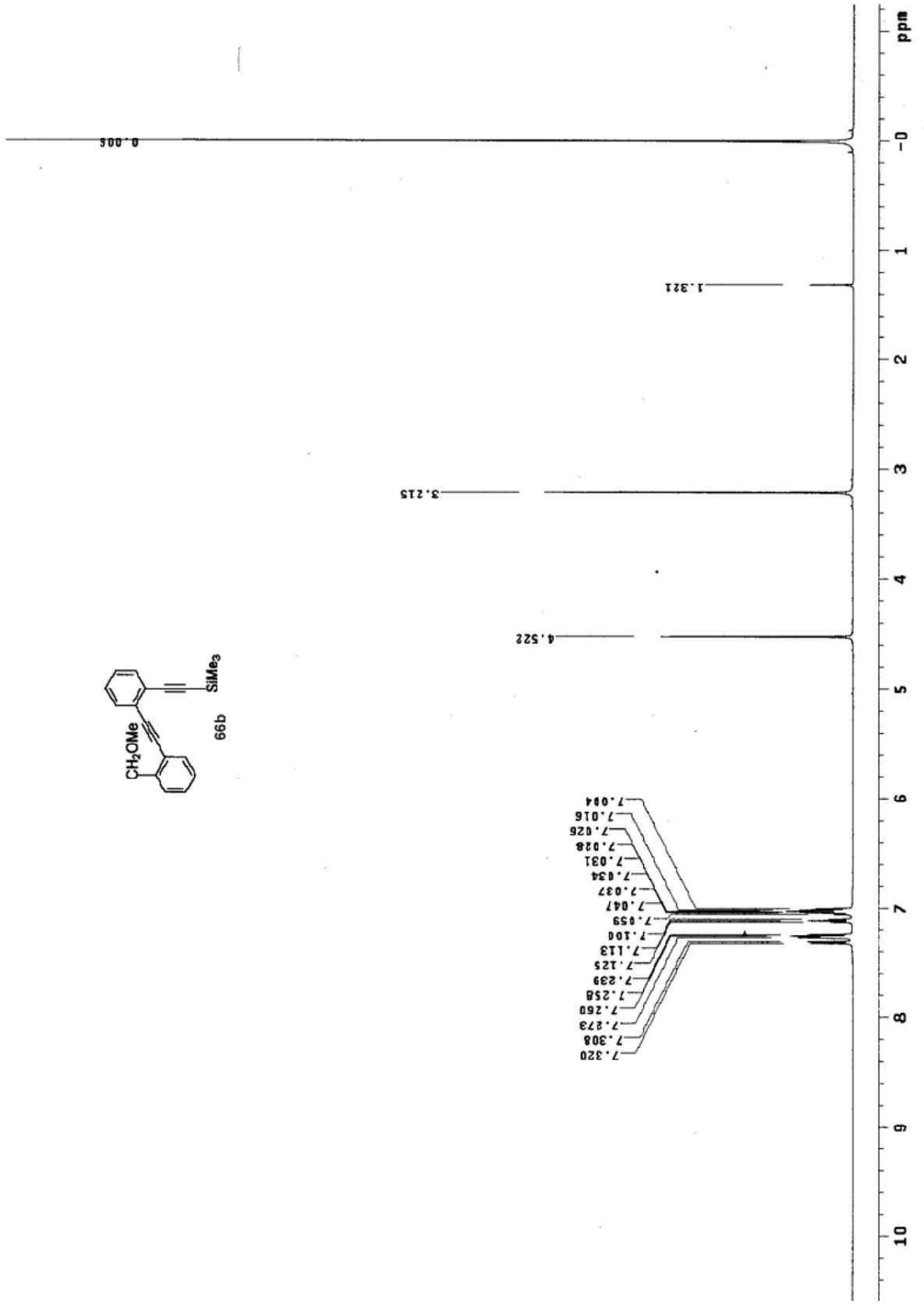
OMe
OH
t-Bu
68a
159.8941
142.0619
133.6909
132.1509
131.8688
129.8942
127.9196
127.8129
127.1649
126.9133
126.0899
120.5245
110.8727
96.2120
89.5412
84.6162
79.3709
77.4726
76.9999
76.5273
55.9276
39.6659
25.5008
X : parts per Million : 13C
X : parts per Million : 1

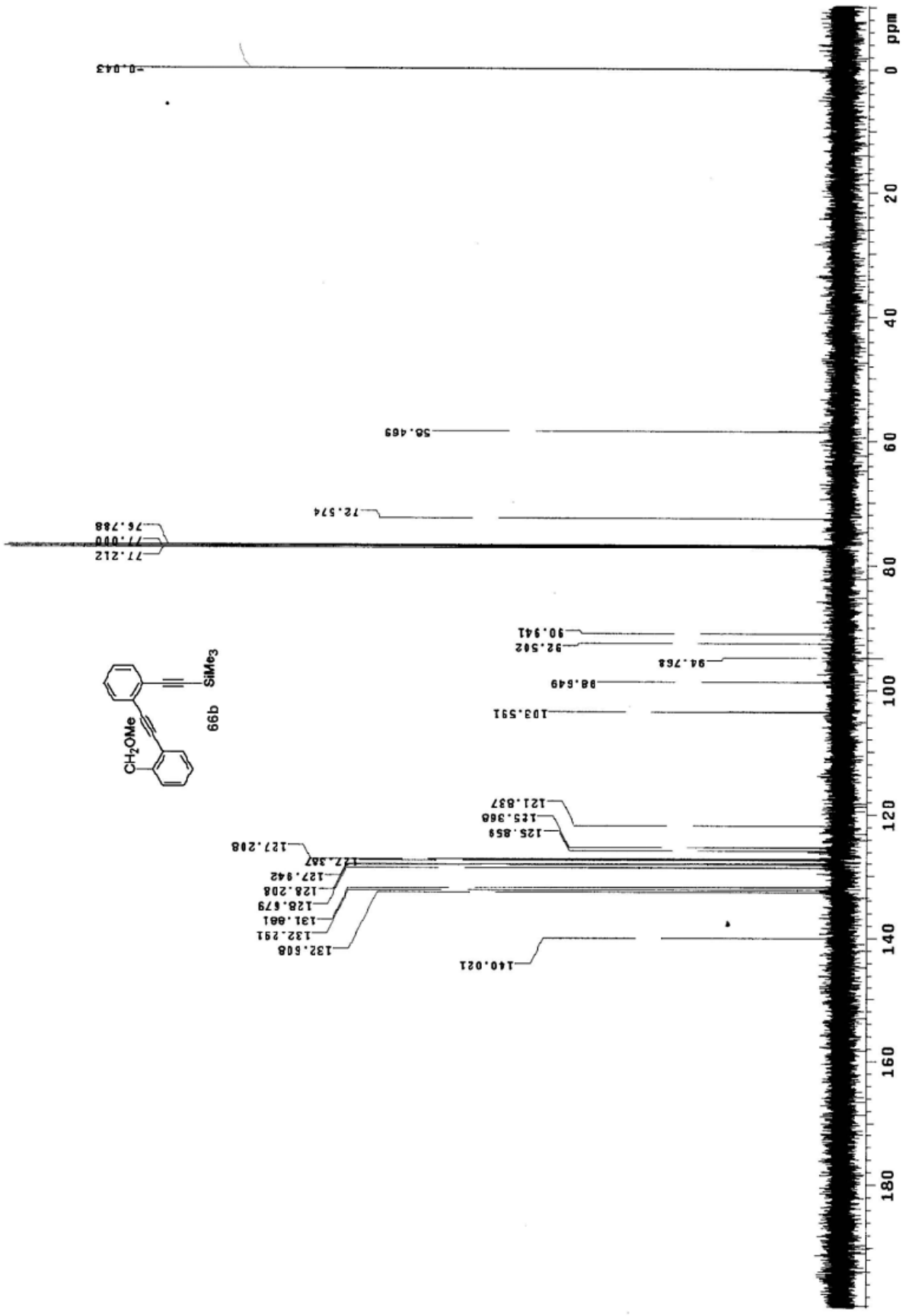

7.6 7.5 7.4 7.3 7.2 7.1
X : parts per Million : 1
7 6.9 6.8
X : parts per Million : 1
OMe
H
t-Bu
69a
12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2
7.4485
7.2673
7.1968
7.1876
7.1739
6.9130
3.8707
3.6904
1.5710
1.0354
X : parts per Million : 1H

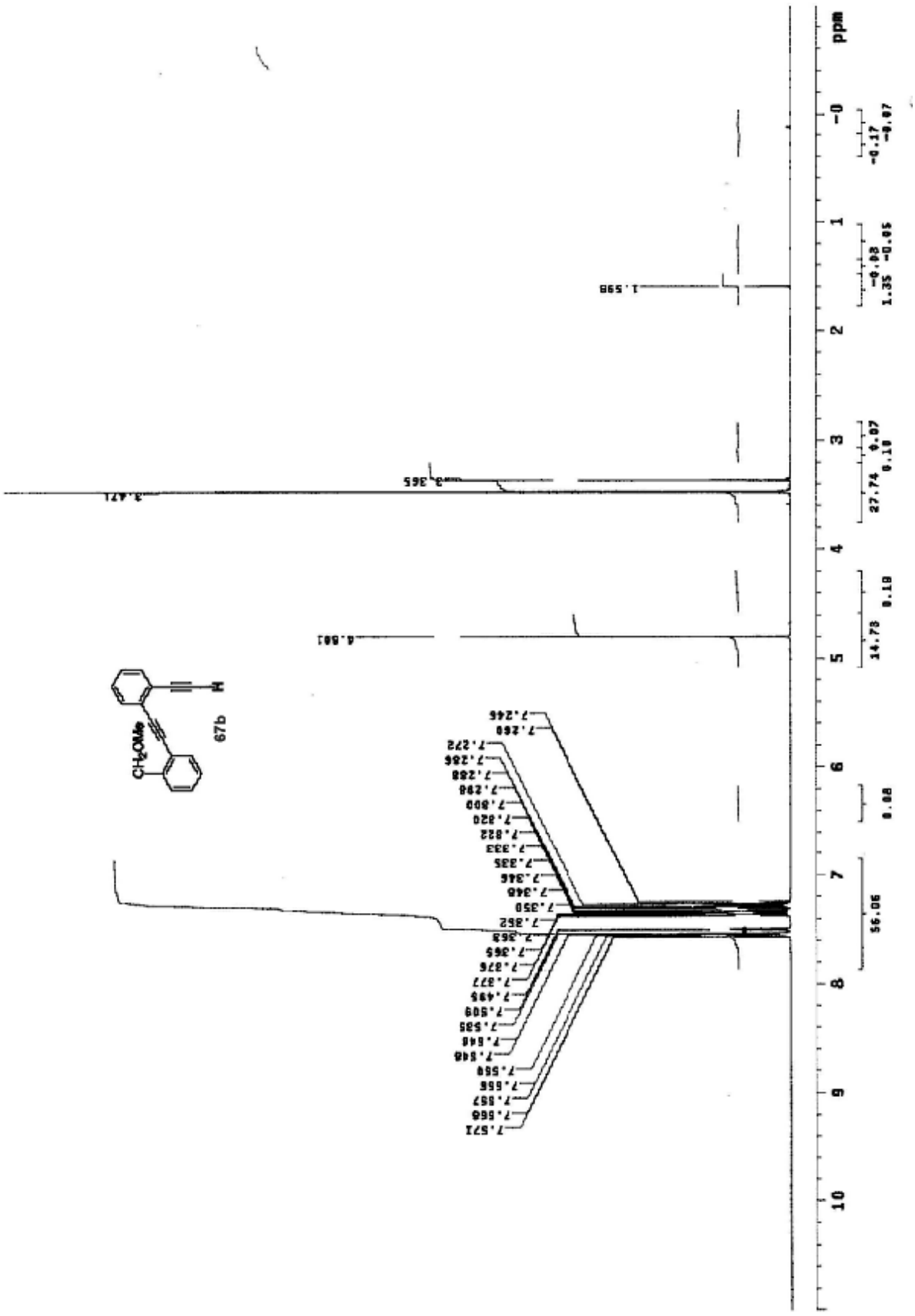
OMe
t-Bu
H
69a
X : parts per Million : 1
X : parts per Million : 13C
159.9627
133.6986
132.1891
132.0442
129.8104
129.6961
127.7062
127.4775
127.2259
126.5322
120.2959
110.5145
95.4802
92.3770
89.1140
82.5803
77.4651
77.0000
76.5273
55.7218
50.5986
35.4653
27.7194

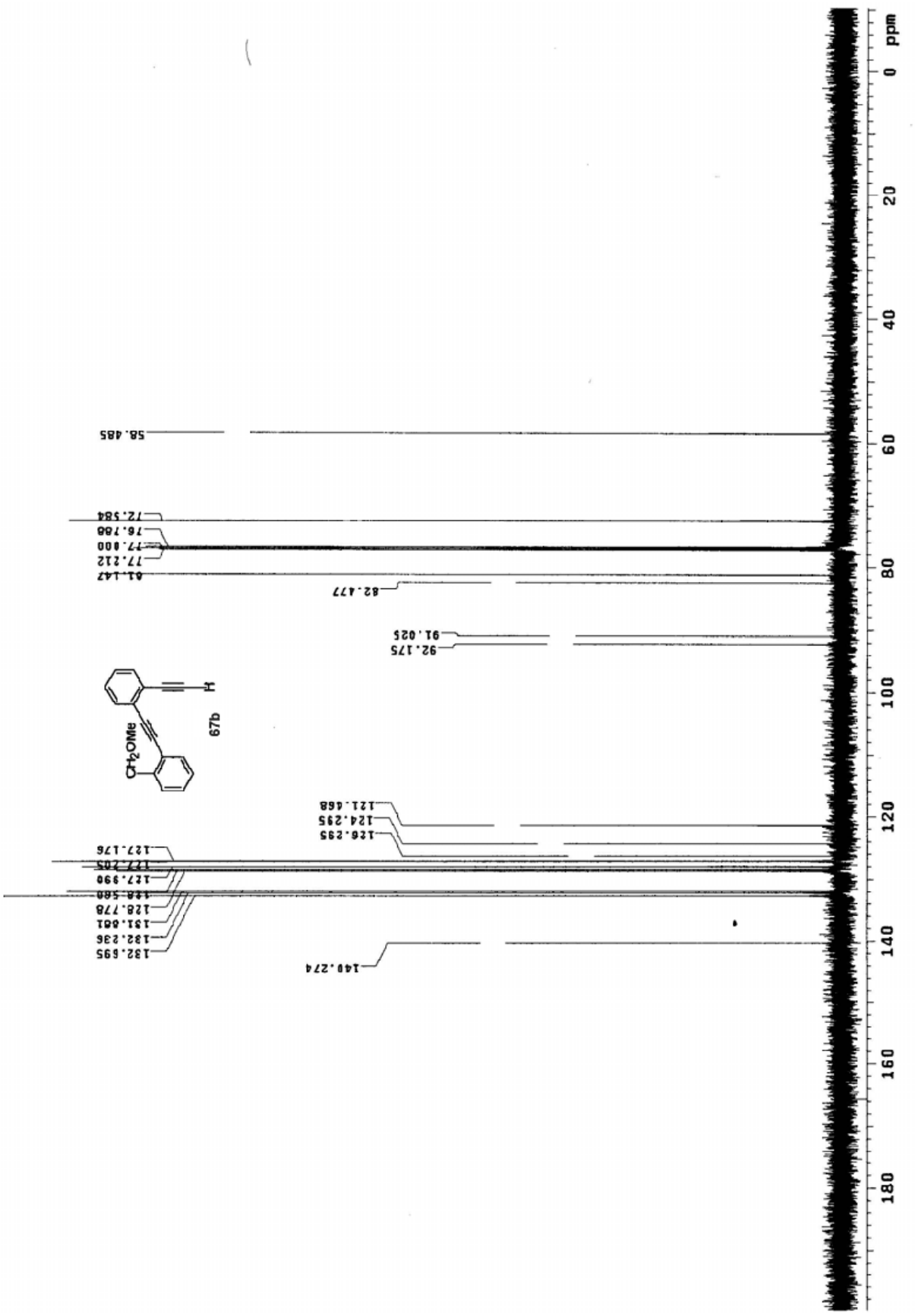

Me
O
t-Bu
73a in C6D6
8.988
1.709
1.616
1.083
9.057
4.247
4.198
6.773
6.787
6.859
6.866
7.009
7.014
7.025
7.033
7.037
7.114
7.126
7.150
7.208
7.220
7.276
7.289
7.298
7.301
7.308
7.320
7.338
7.801
7.895
8.516
8.525
ppm

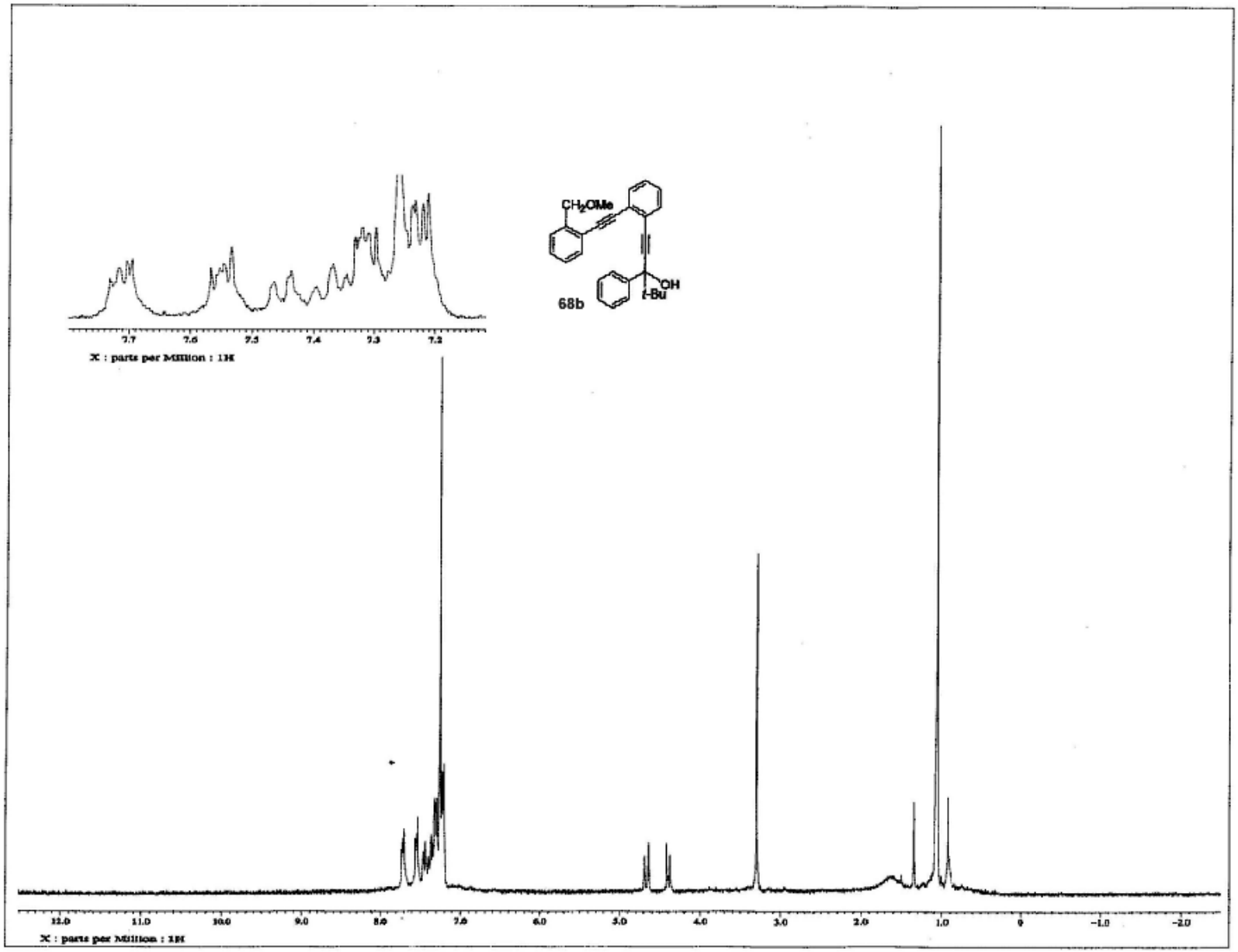
Me
t-Bu
73a in CDCl3
X : parts per Million : 13C
157.7368
131.8309
129.3379
127.2032
126.2884
123.9707
123.8335
123.2236
123.0711
121.5006
111.5744
77.4652
77.0002
76.5275
55.7830
40.2075
38.8123
34.3752

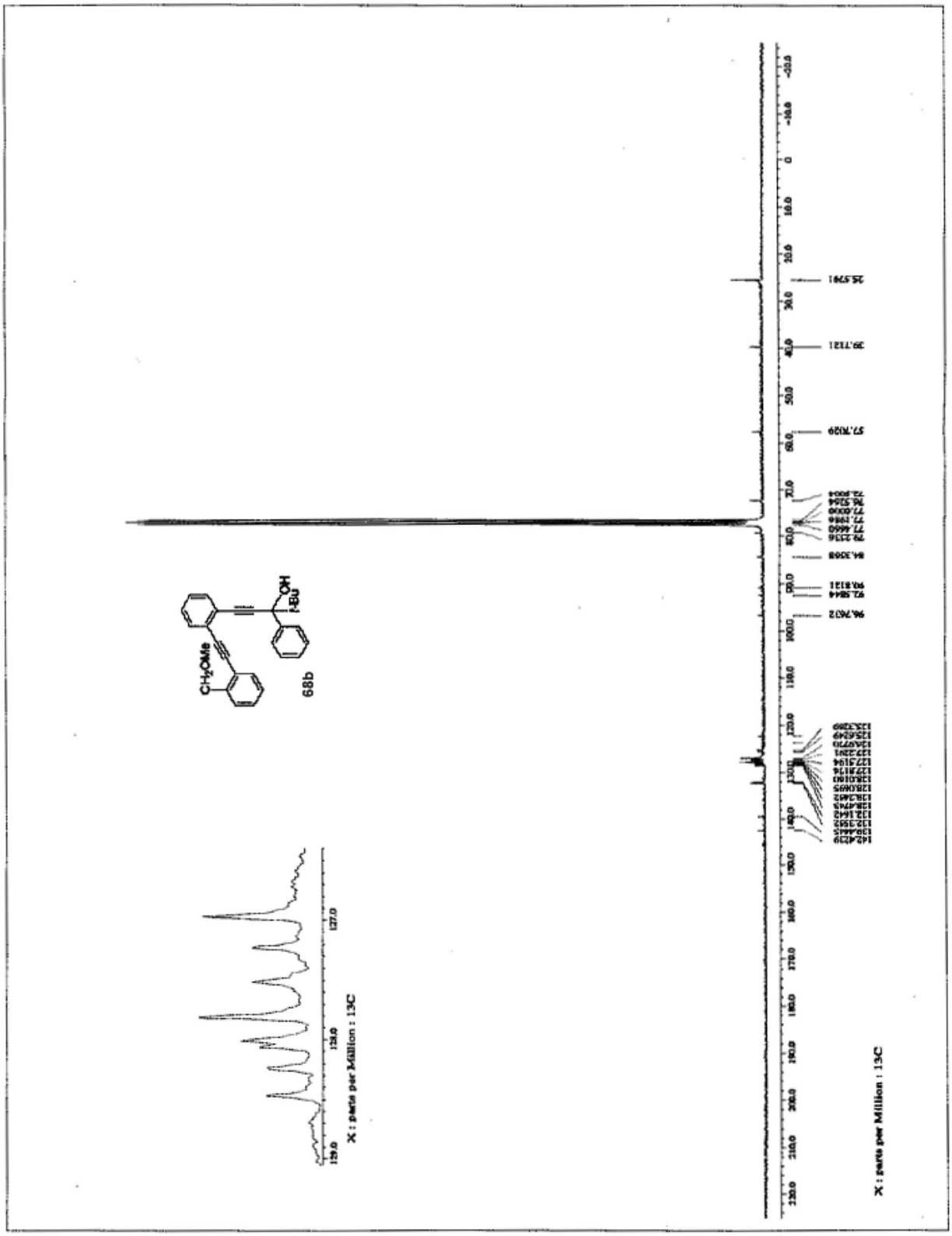

0.005
1.321
3.215
4.522
7.320
7.308
7.273
7.260
7.258
7.239
7.125
7.113
7.100
7.059
7.047
7.037
7.034
7.031
7.028
7.026
7.016
7.004
ppm
SiMe3
CH2OMe
66b

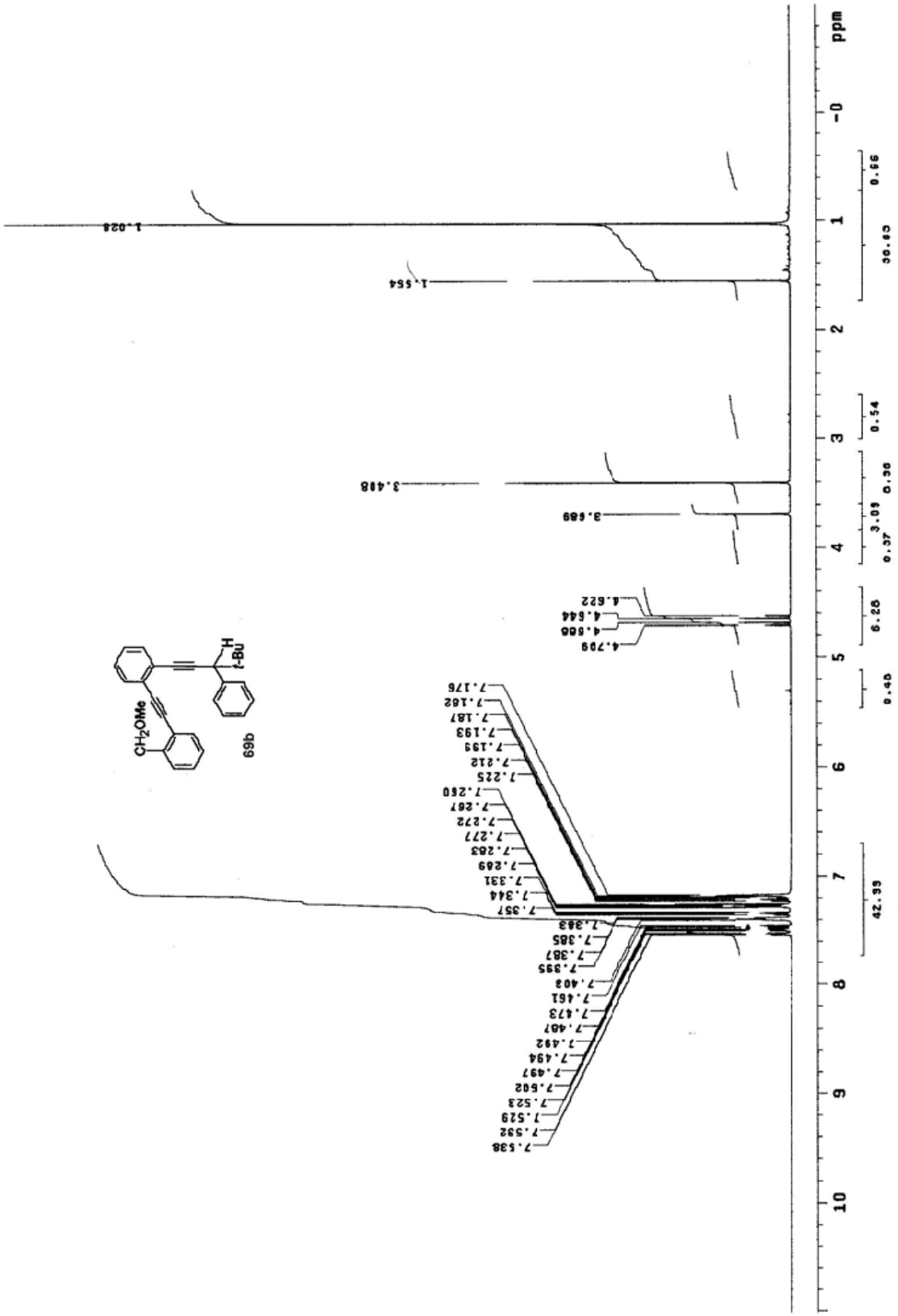

-0.043
56.469
72.574
76.768
77.000
77.212
90.941
92.502
94.768
98.549
103.591
121.837
125.368
125.859
127.208
127.367
127.842
128.208
128.679
131.061
132.291
132.508
140.021
0
20
40
60
80
100
120
140
160
180
ppm
SiMe3
CH2OMe
66b

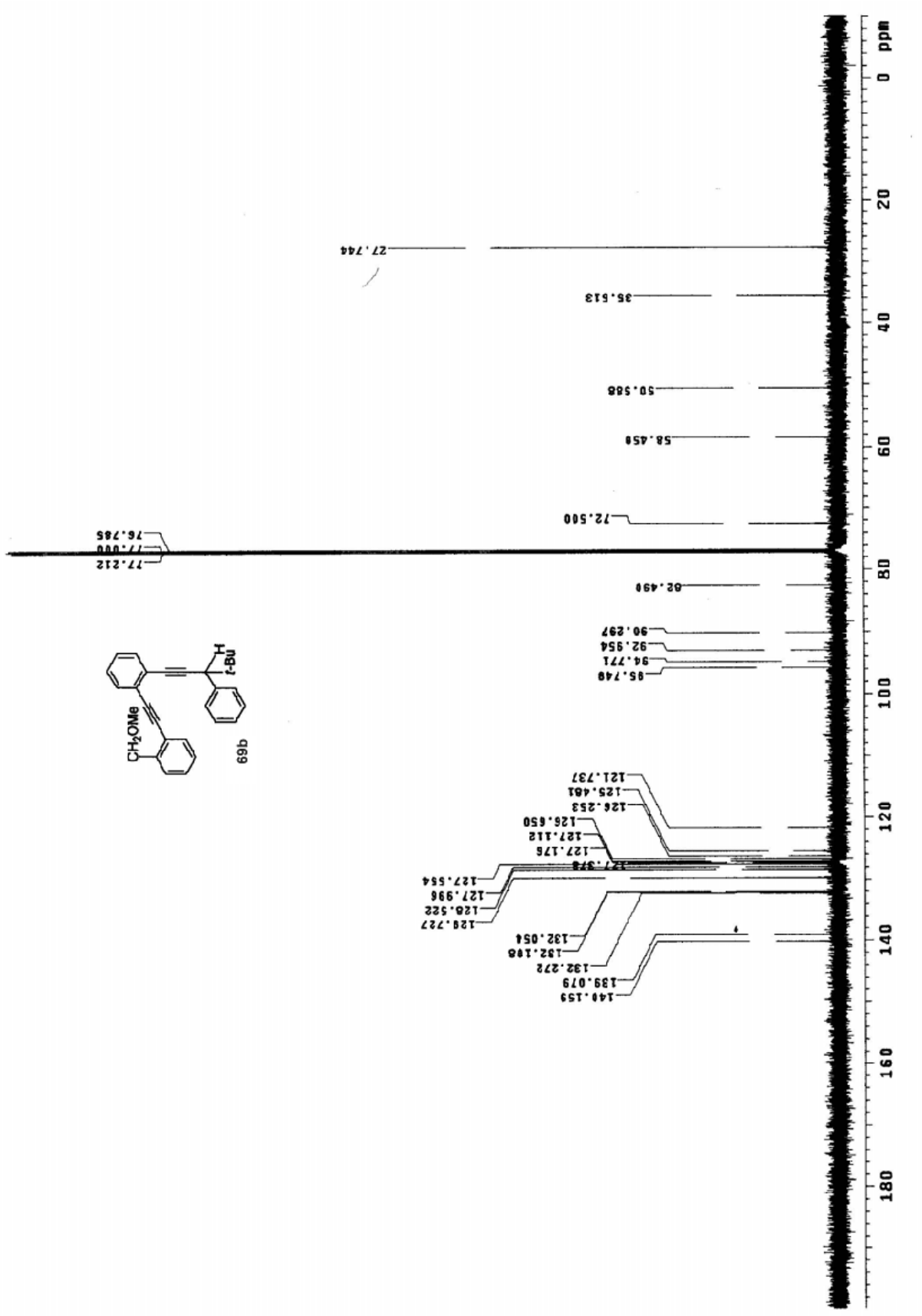

67b
CH2OMe
H
1.598
3.365
3.471
4.881
7.246
7.269
7.272
7.286
7.288
7.298
7.800
7.820
7.822
7.333
7.335
7.346
7.348
7.350
7.352
7.363
7.365
7.376
7.377
7.495
7.509
7.525
7.646
7.648
7.660
7.656
7.657
7.666
7.571
ppm
-0.17
-0.07
-0.08
1.35
-0.05
27.74
0.07
0.10
14.78
0.10
0.08
55.06

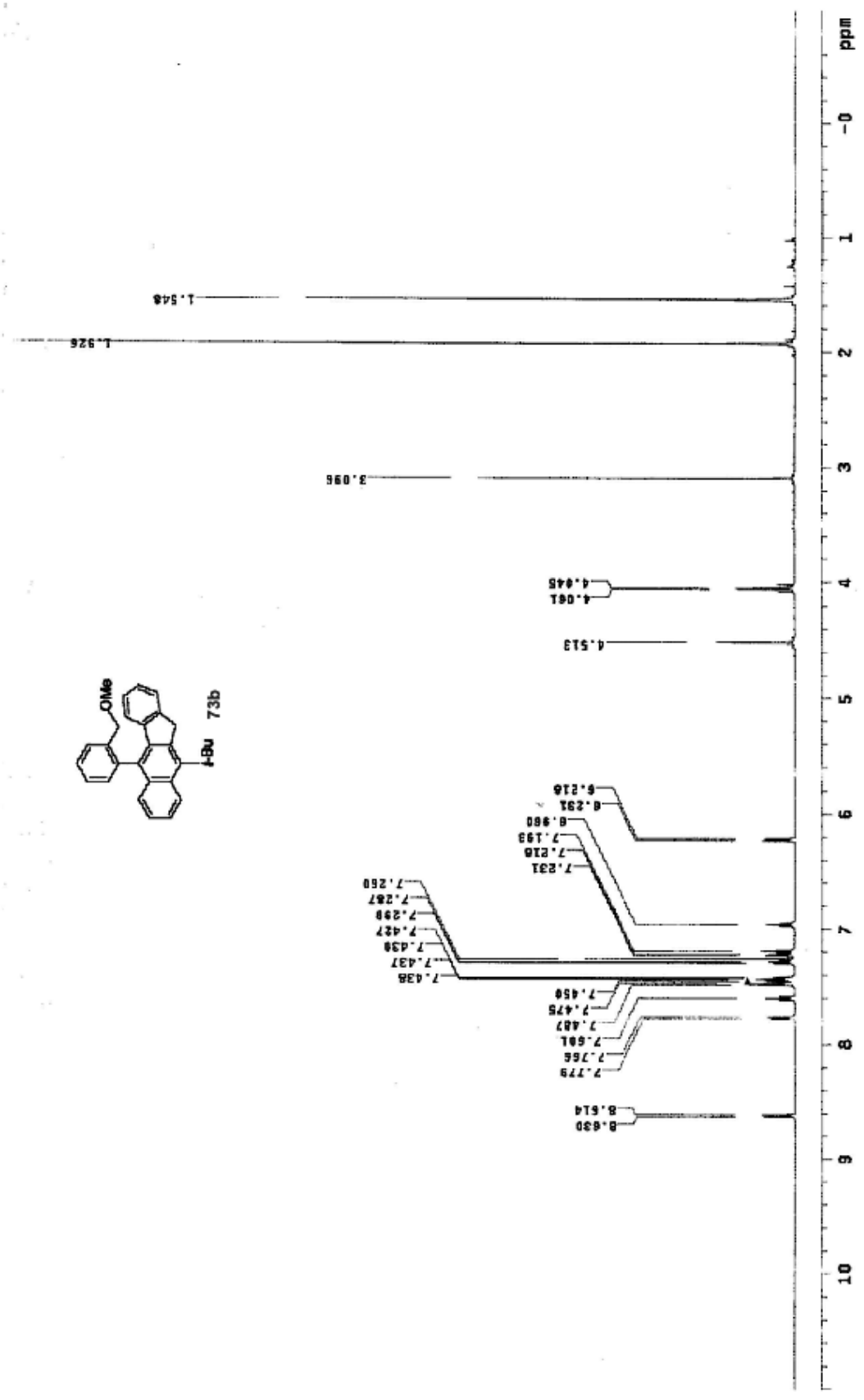

58.485
72.584
76.766
77.000
77.212
81.147
82.477
91.025
92.175
121.668
124.295
126.295
127.176
127.705
127.990
128.580
128.778
131.661
132.236
132.695
140.274
67b
CH2OMe
H
0
20
40
60
80
100
120
140
160
180
ppm

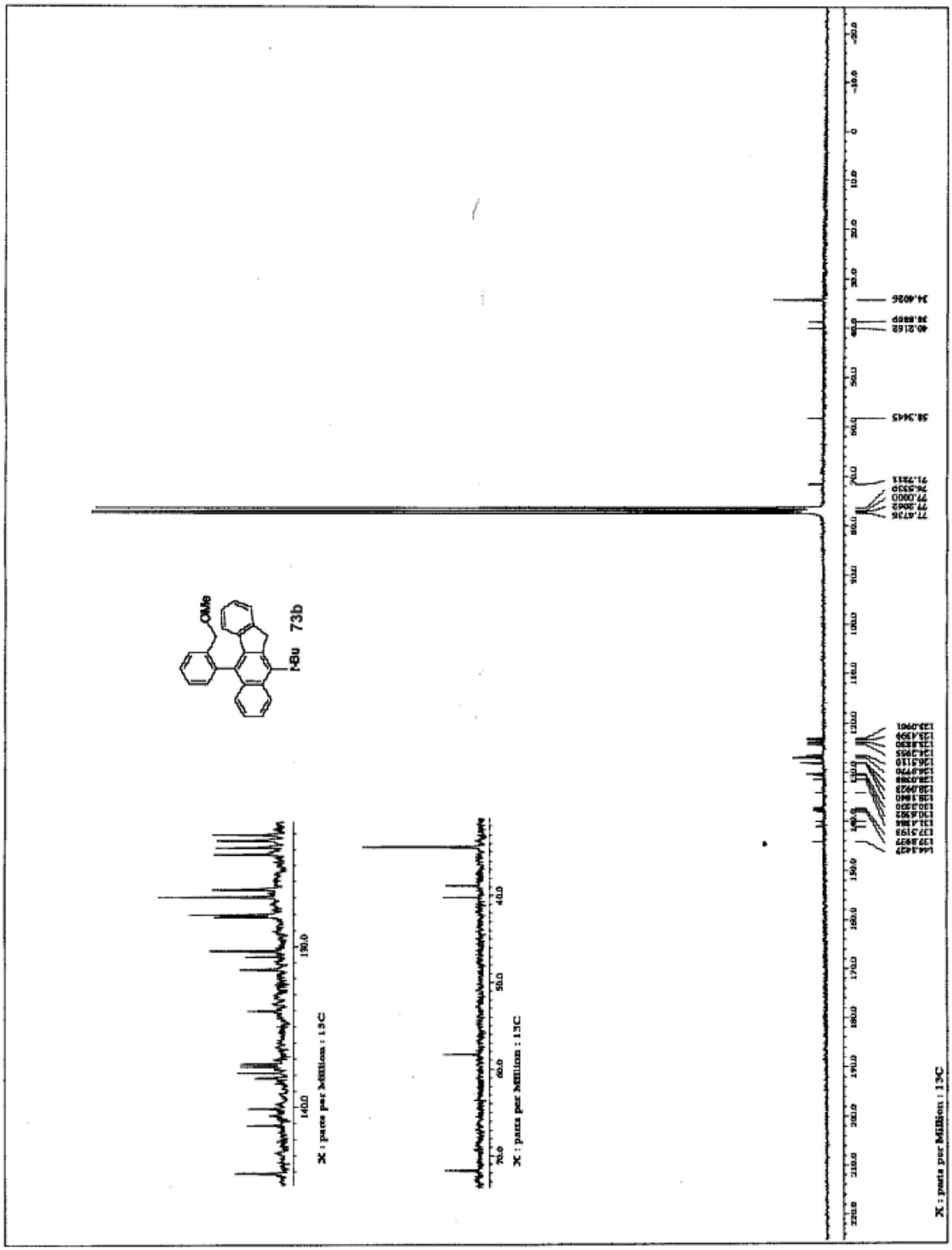

CH2OMe
OH
t-Bu
68b
7.7
7.6
7.5
7.4
7.3
7.2
X : parts per Million : 1H
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
-1.0
-2.0
X : parts per Million : 1H

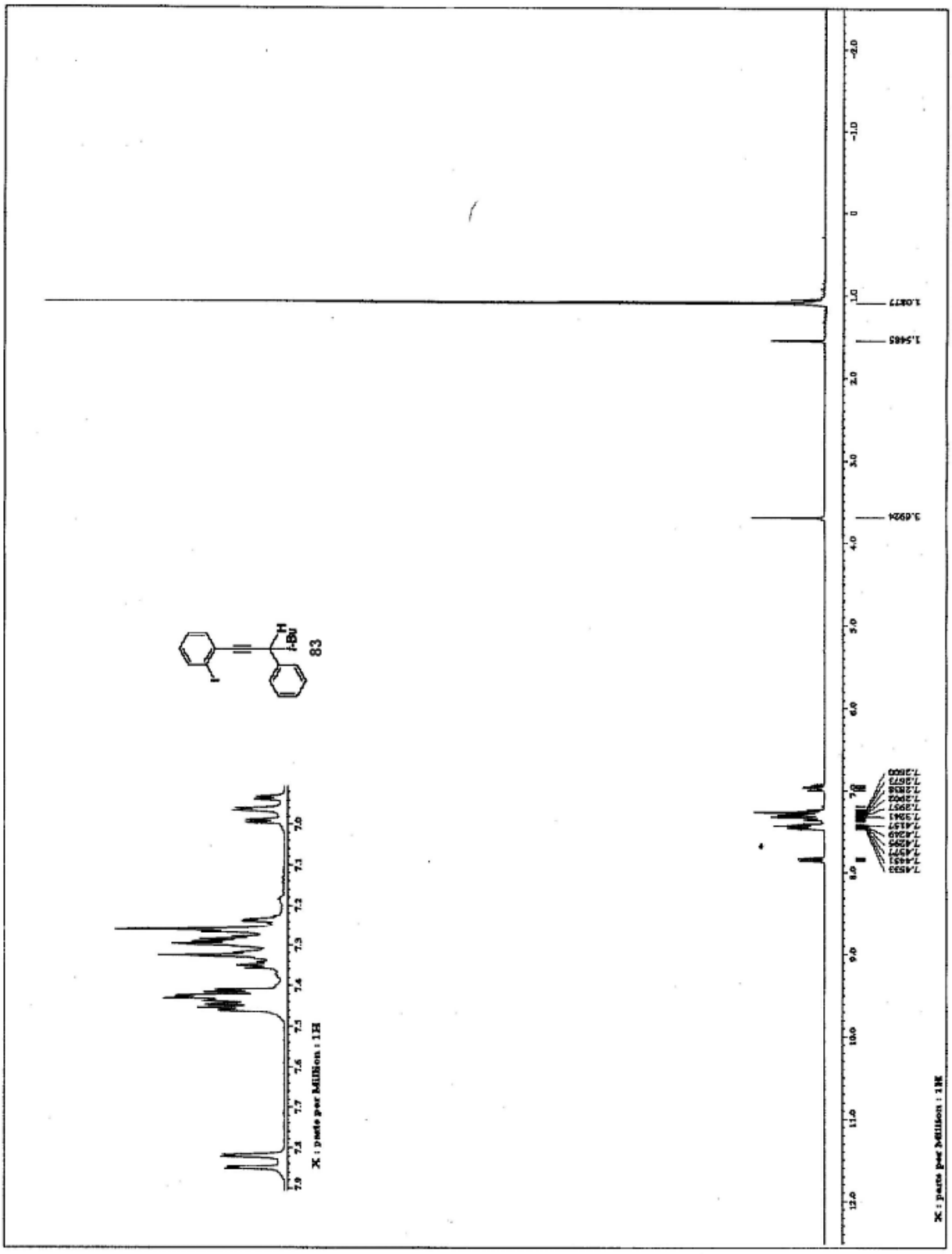

OH
t-Bu
CH2OMe
68b
X : parts per Million : 13C

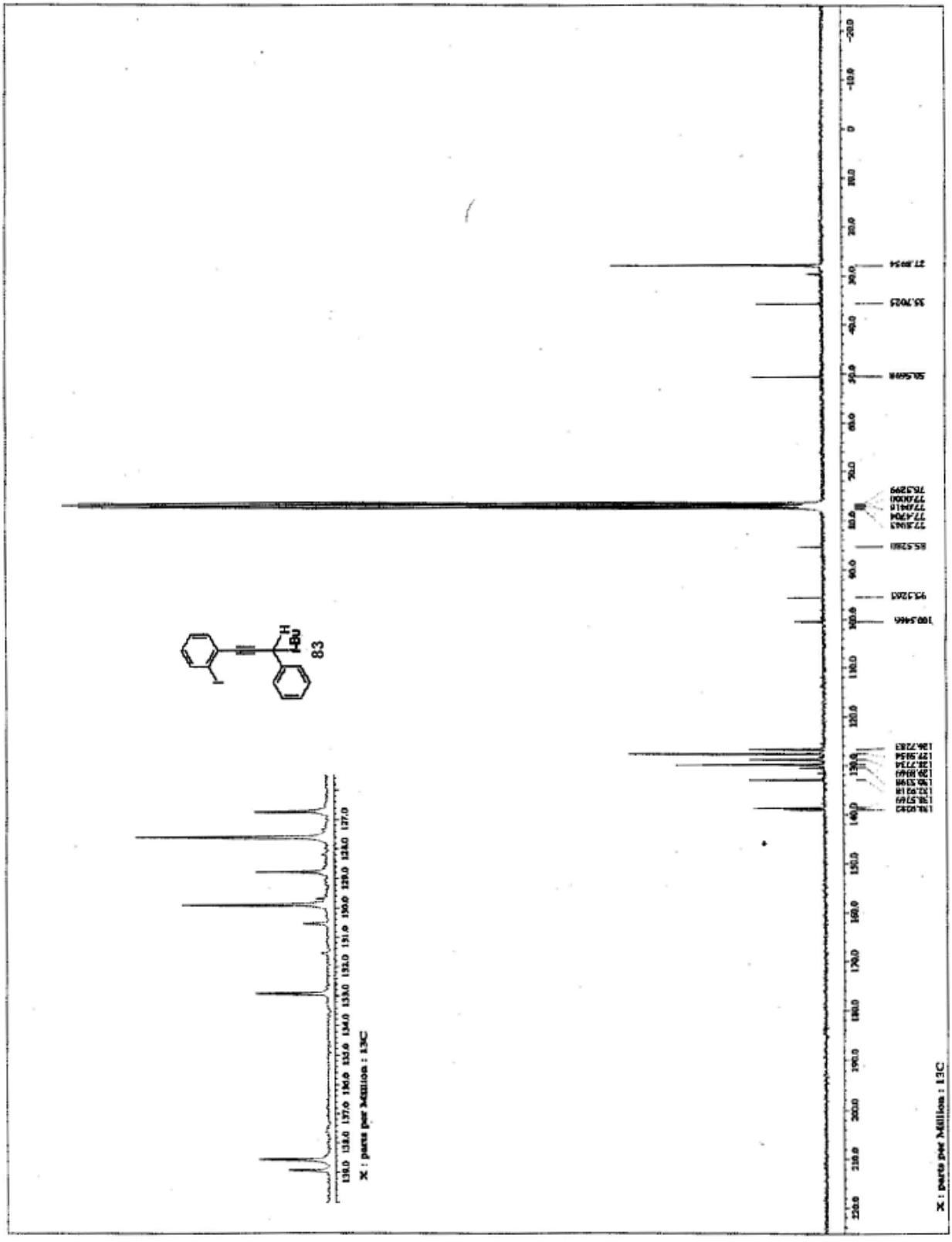

1.028
1.554
3.488
3.689
4.622
4.644
4.666
4.709
7.176
7.182
7.187
7.193
7.199
7.212
7.225
7.260
7.267
7.272
7.277
7.283
7.289
7.331
7.344
7.357
7.383
7.385
7.387
7.395
7.403
7.461
7.473
7.487
7.492
7.494
7.497
7.502
7.523
7.529
7.582
7.586
t-Bu
H
CH2OMe
69b
ppm

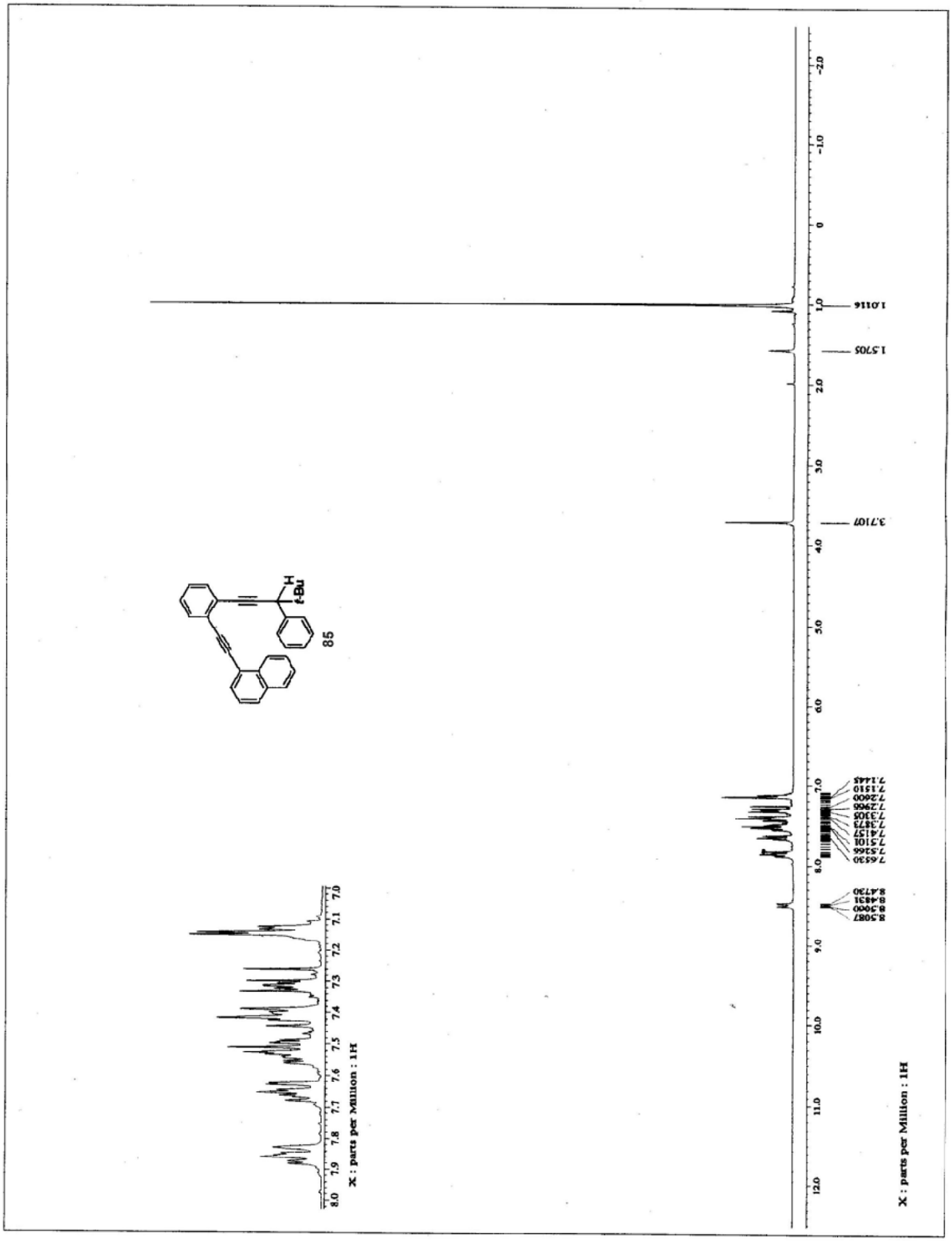

27.744
35.513
50.588
58.458
72.500
76.785
77.000
77.212
82.490
85.748
94.771
92.954
90.297
121.737
125.461
126.253
126.650
127.112
127.176
127.378
127.554
127.998
128.522
128.727
132.054
132.186
132.272
139.079
140.159
t-Bu
CH2OMe
69b
0 ppm
20
40
60
80
100
120
140
160
180

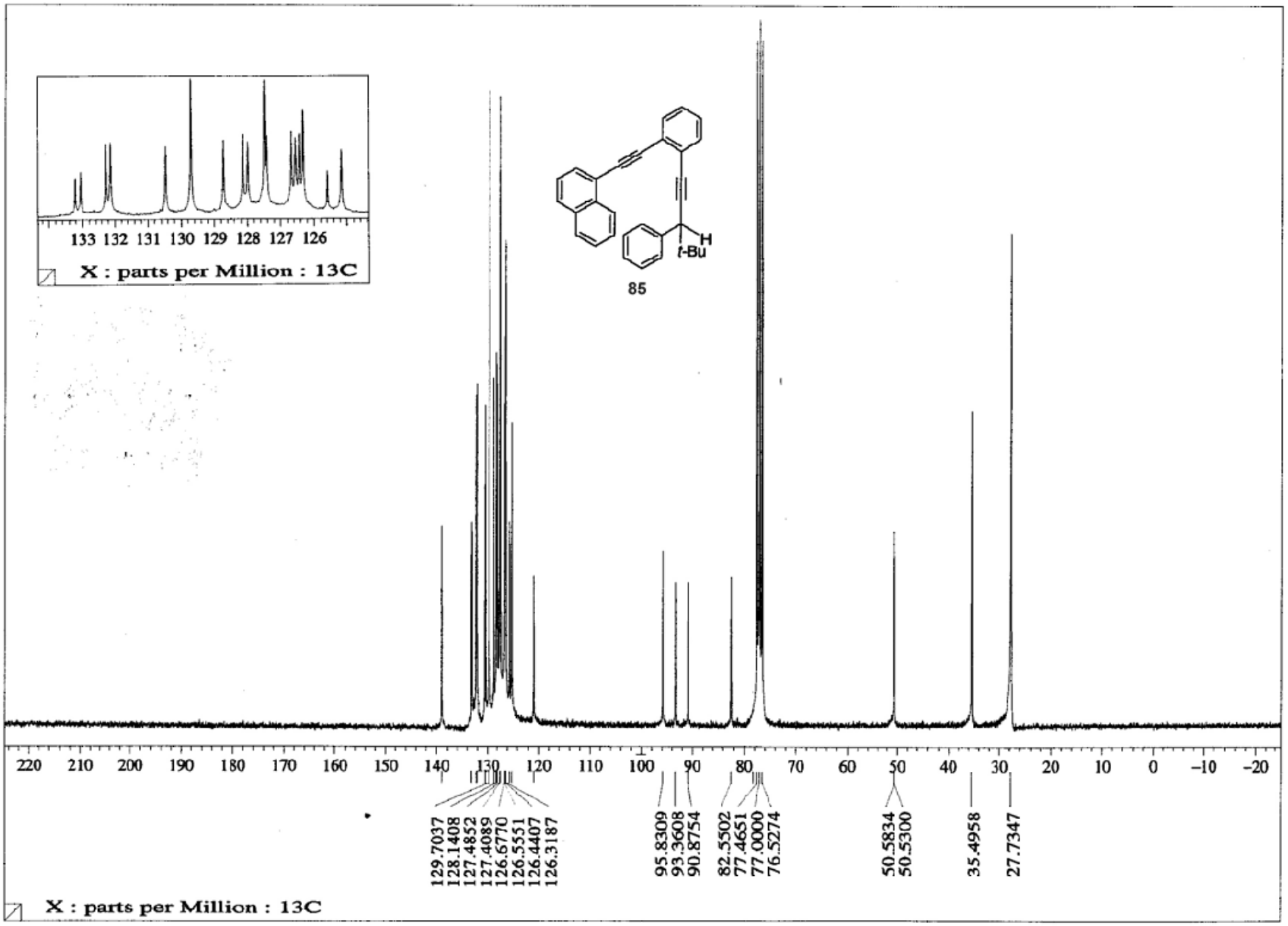

ppm
1.548
1.926
3.096
4.045
4.061
4.513
6.216
6.231
6.980
7.193
7.218
7.231
7.260
7.287
7.298
7.427
7.439
7.437
7.436
7.458
7.475
7.487
7.681
7.756
7.779
8.630
8.614
OMe
nBu
73b

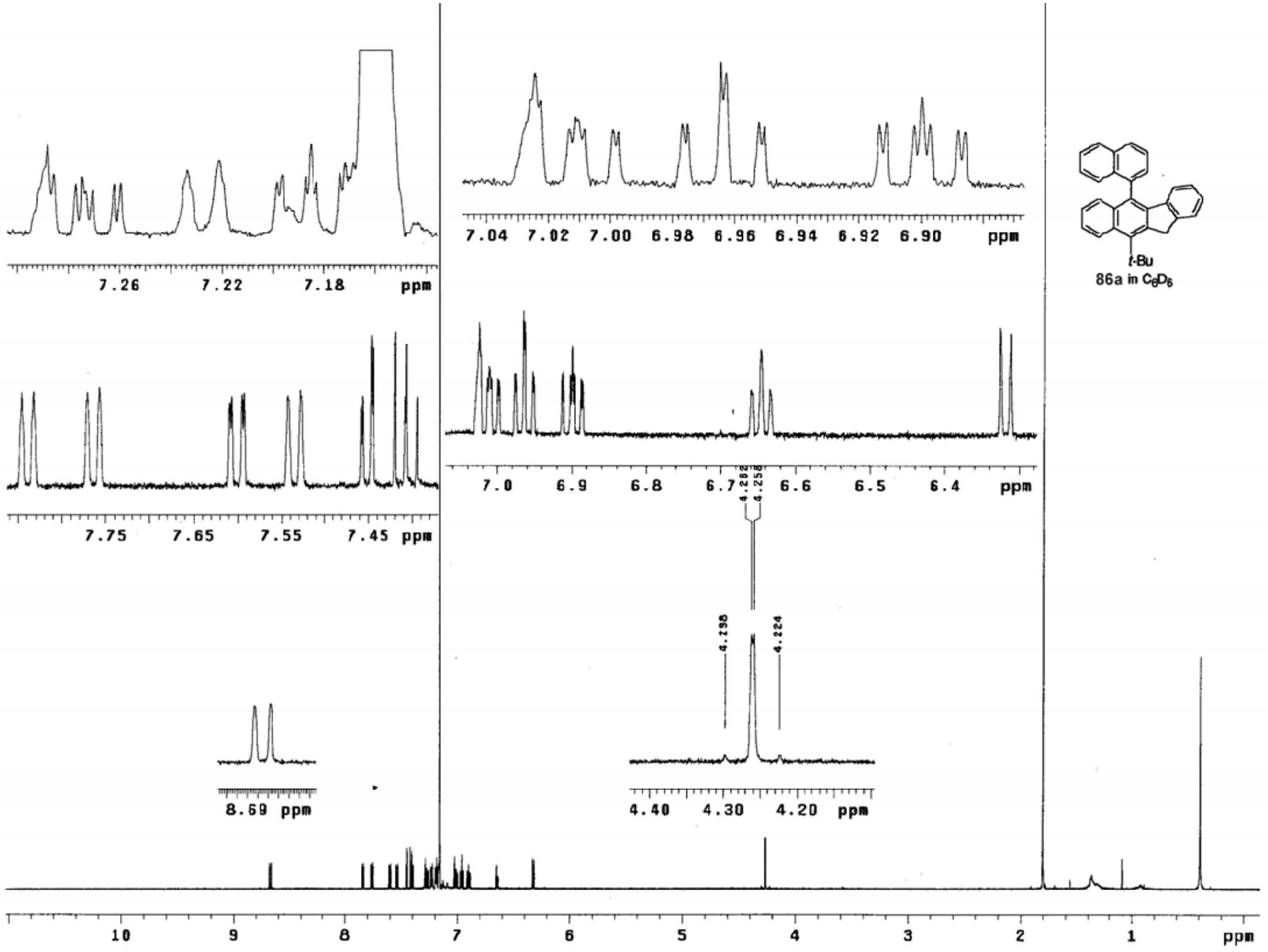

OMe
nBu
73b

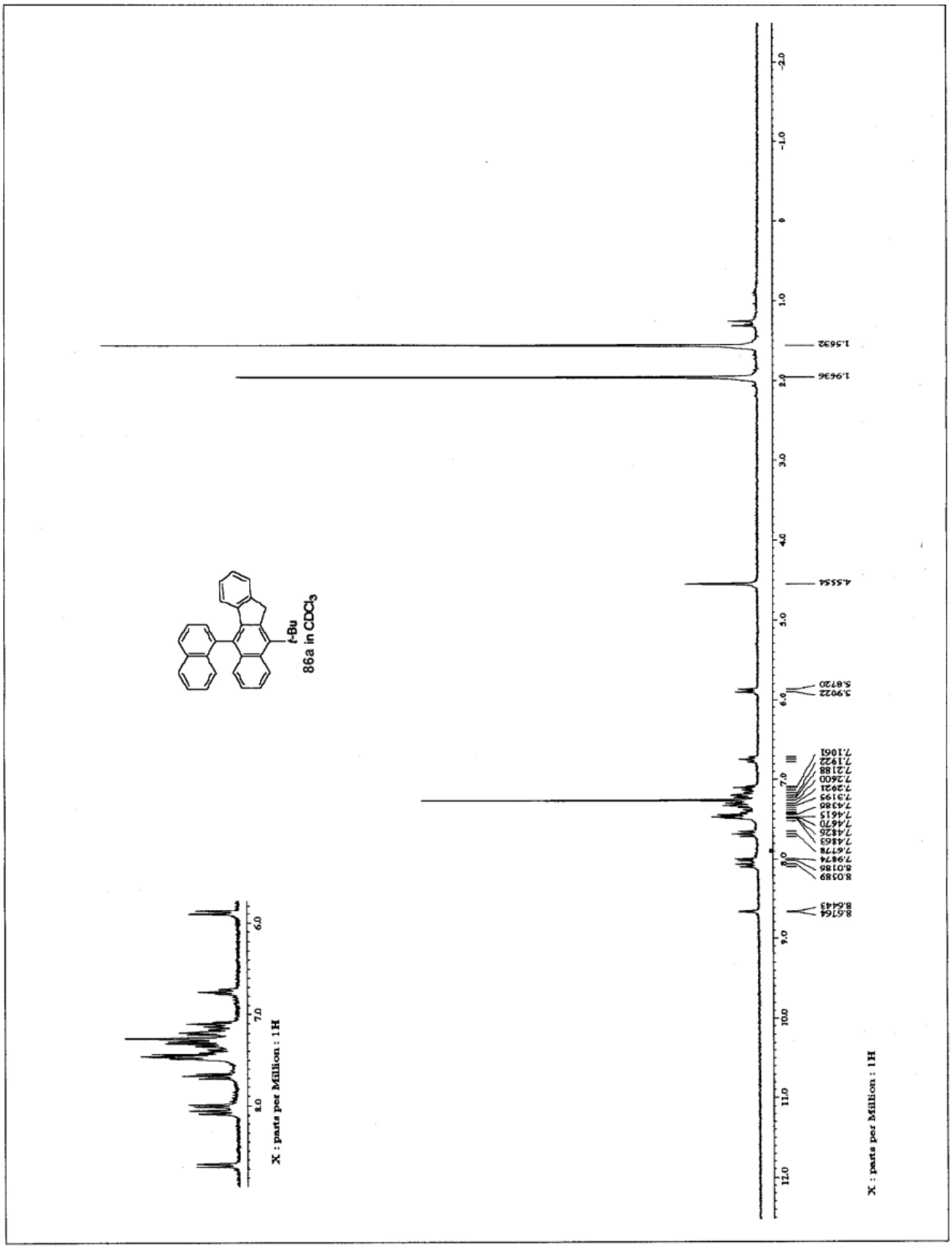

i-Bu
83
X : parts per Million : 1H

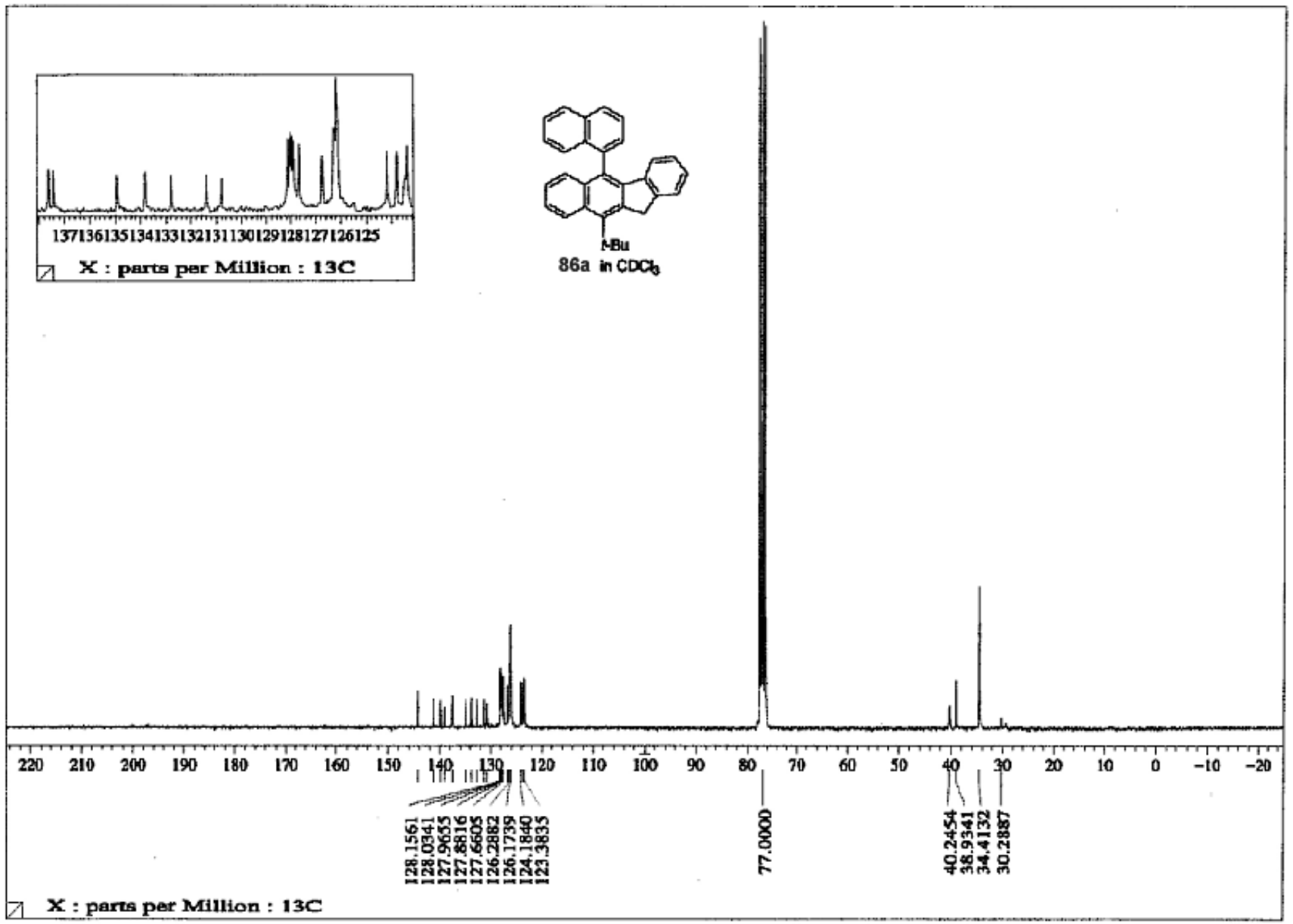

83
13C : parts per Million : 13C

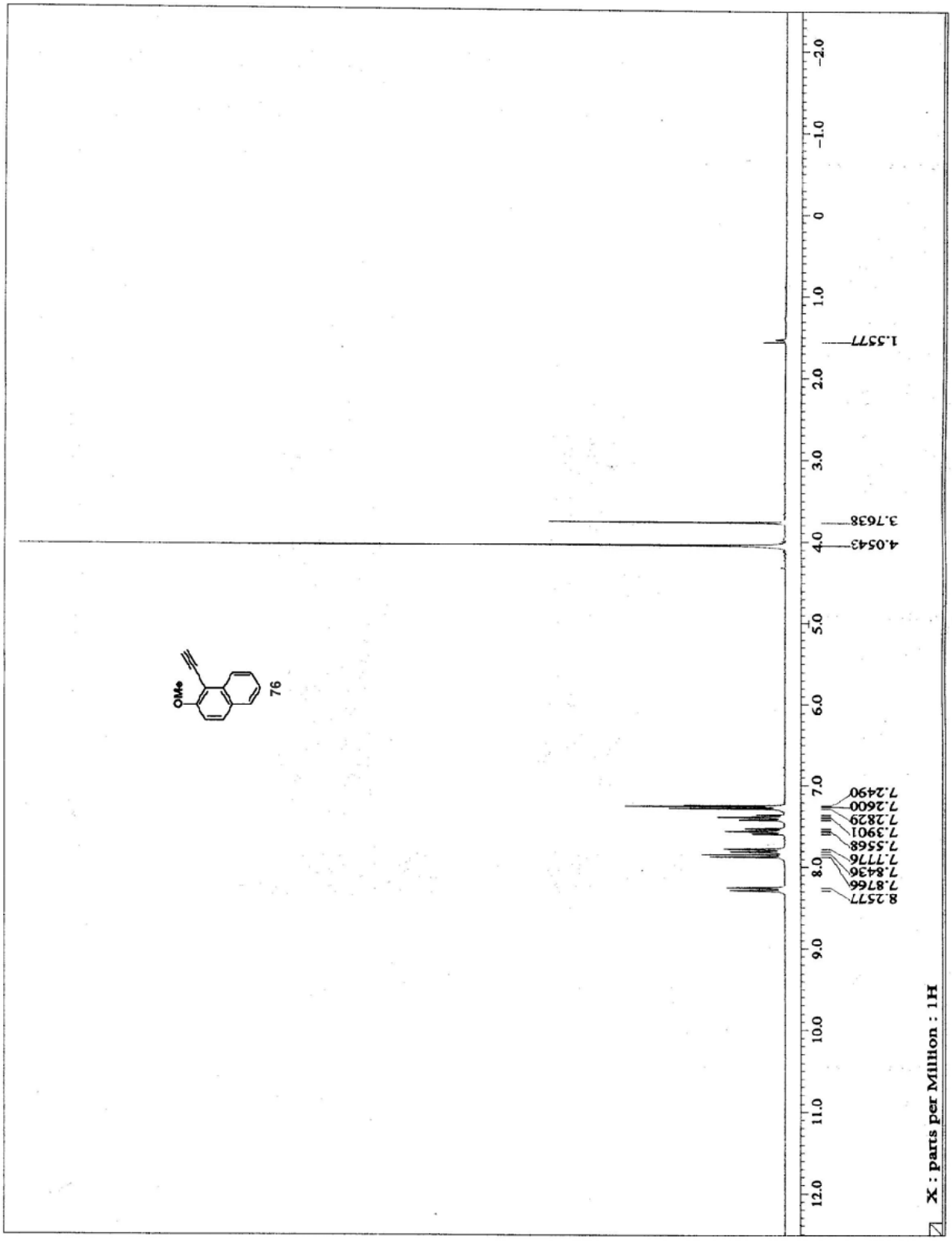

85
X : parts per Million : 1H
X : parts per Million : 1H

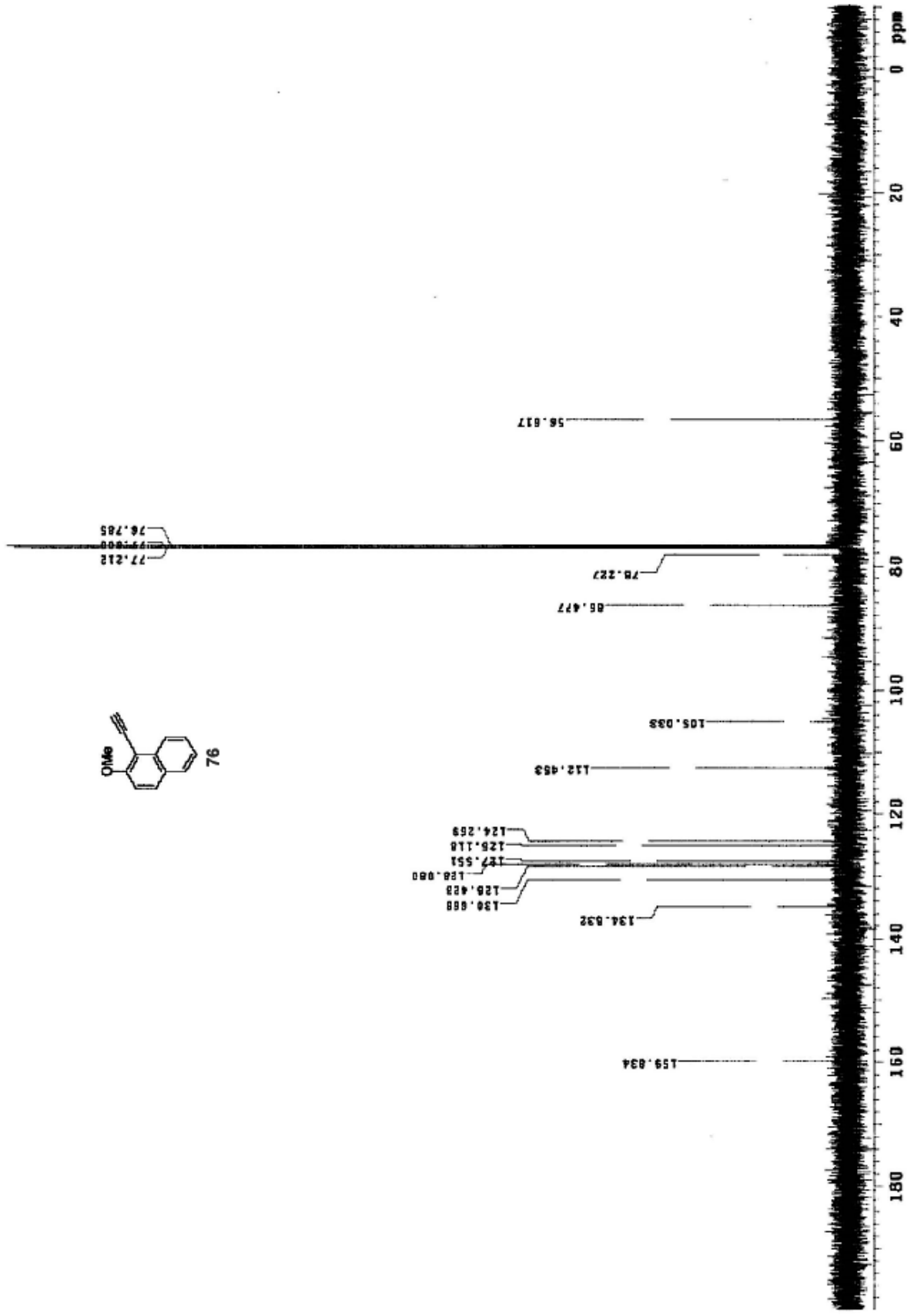

133 132 131 130 129 128 127 126
X : parts per Million : 13C
t-Bu
H
85
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
129.7037
128.1408
127.4852
127.4089
126.6770
126.5551
126.4407
126.3187
95.8309
93.3608
90.8754
82.5502
77.4651
77.0000
76.5274
50.5834
50.5300
35.4958
27.7347
X : parts per Million : 13C

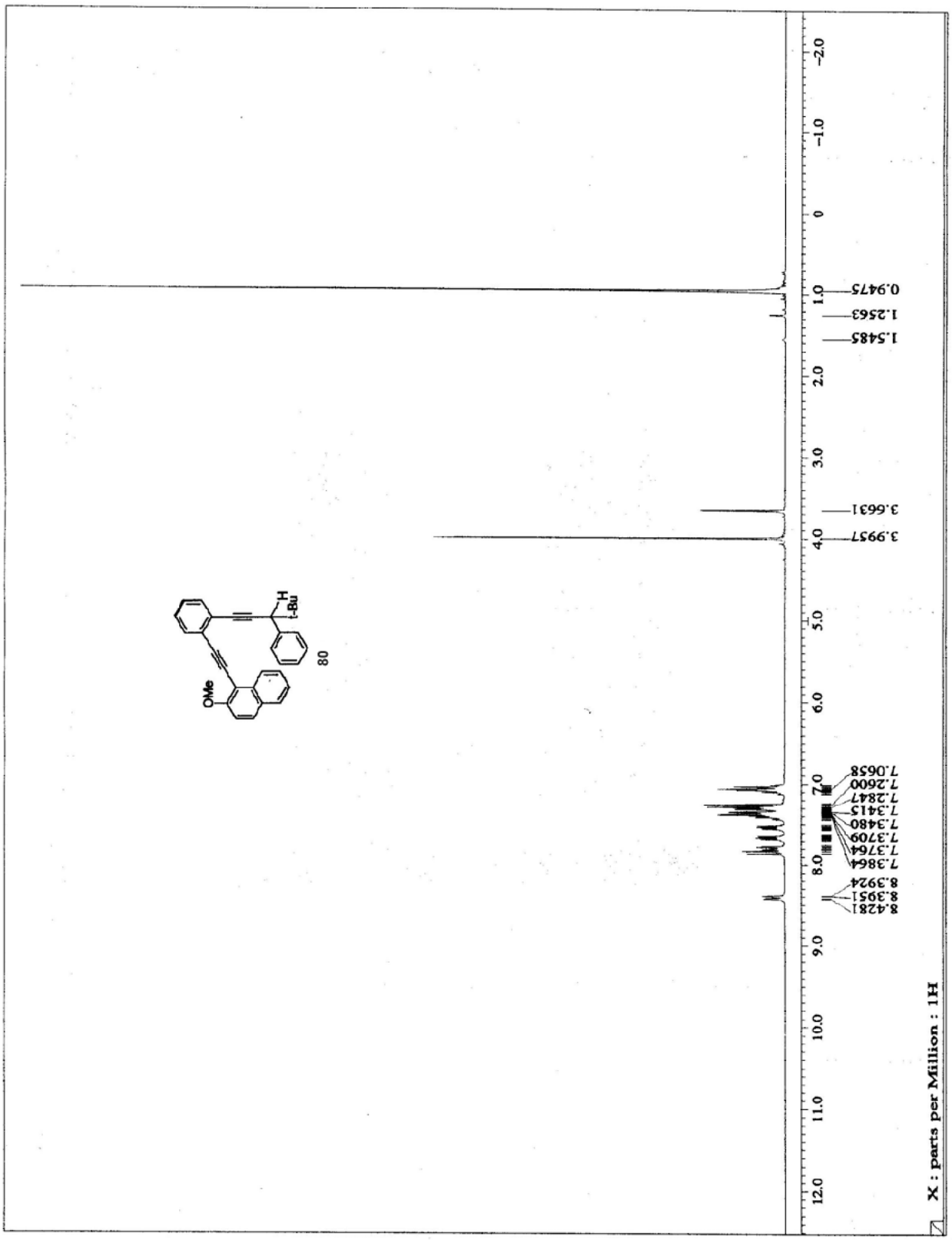

7.26 7.22 7.18 ppm
7.04 7.02 7.00 6.98 6.96 6.94 6.92 6.90 ppm
t-Bu
86a in C6D6
7.75 7.65 7.55 7.45 ppm
7.0 6.9 6.8 6.7 6.6 6.5 6.4 ppm
4.282
4.258
4.195
4.224
8.69 ppm
4.40 4.30 4.20 ppm
10 9 8 7 6 5 4 3 2 1 ppm

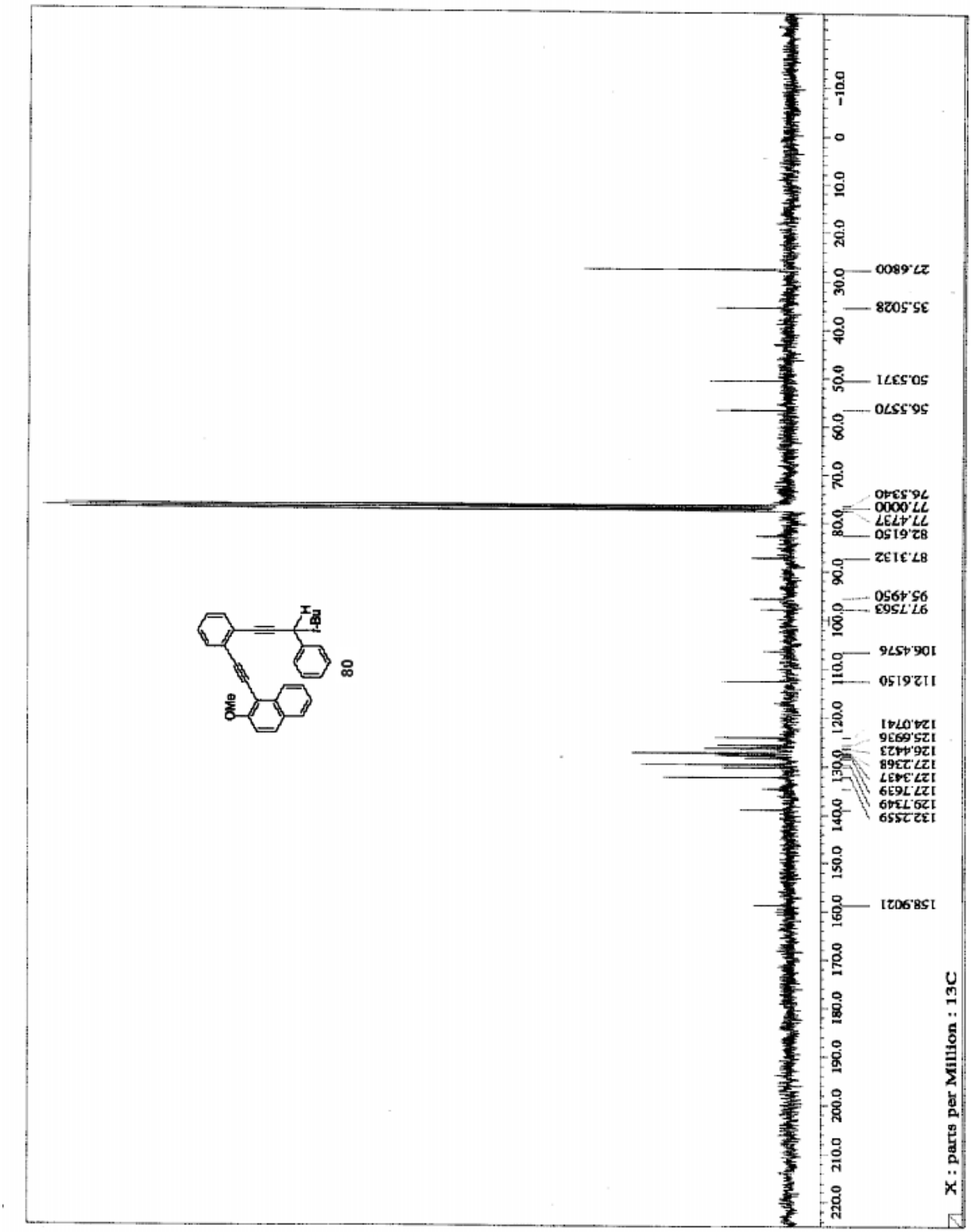

t-Bu
86a in CDCl3
X : parts per Million : 1H
X : parts per Million : 1H

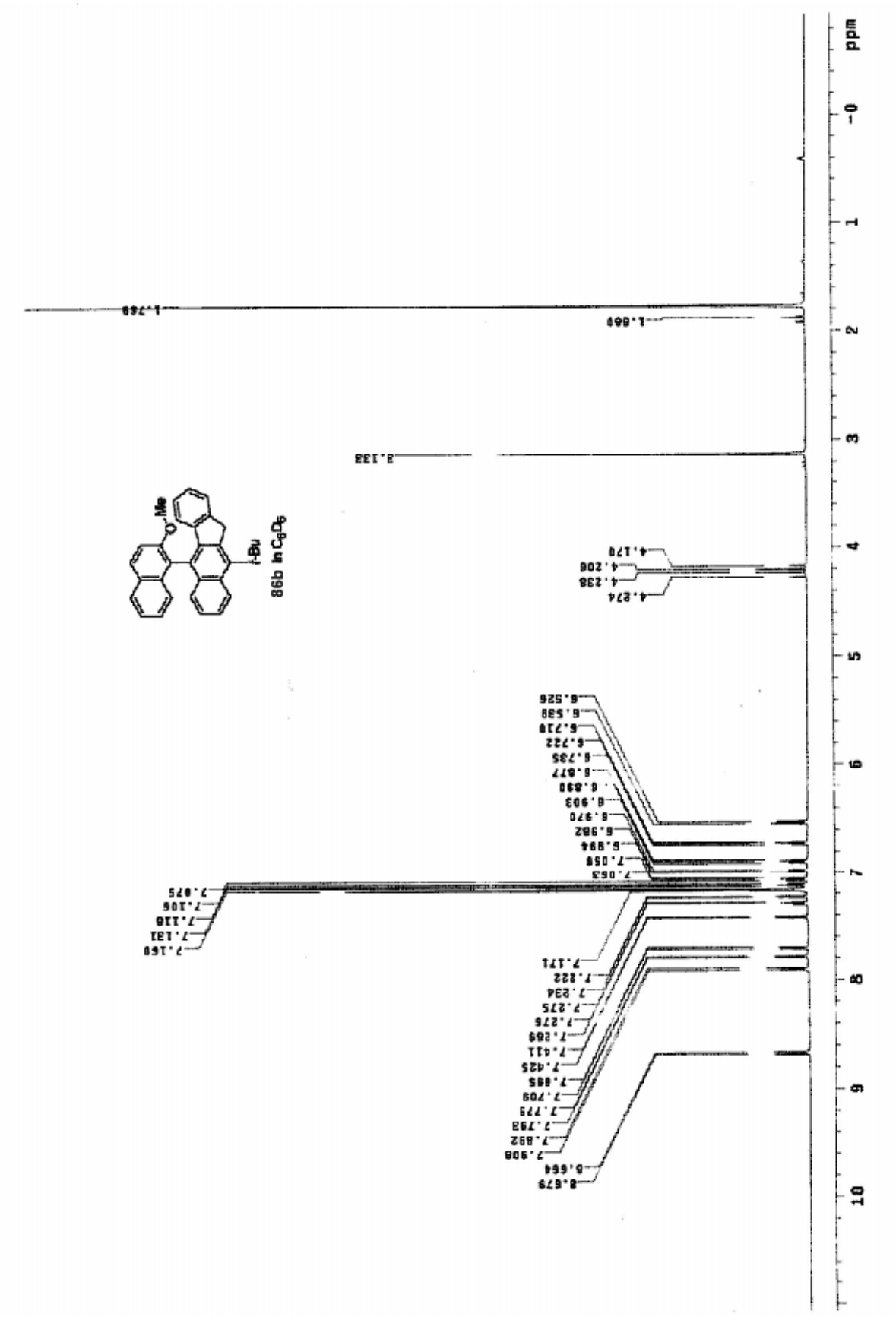

137136135134133132131130129128127126125
X : parts per Million : 13C
N-Bu
86a in CDCl3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
128.1561
128.0341
127.9655
127.8816
127.6605
126.2882
126.1739
124.1840
123.3835
77.0000
40.2454
38.9341
34.4132
30.2887
X : parts per Million : 13C

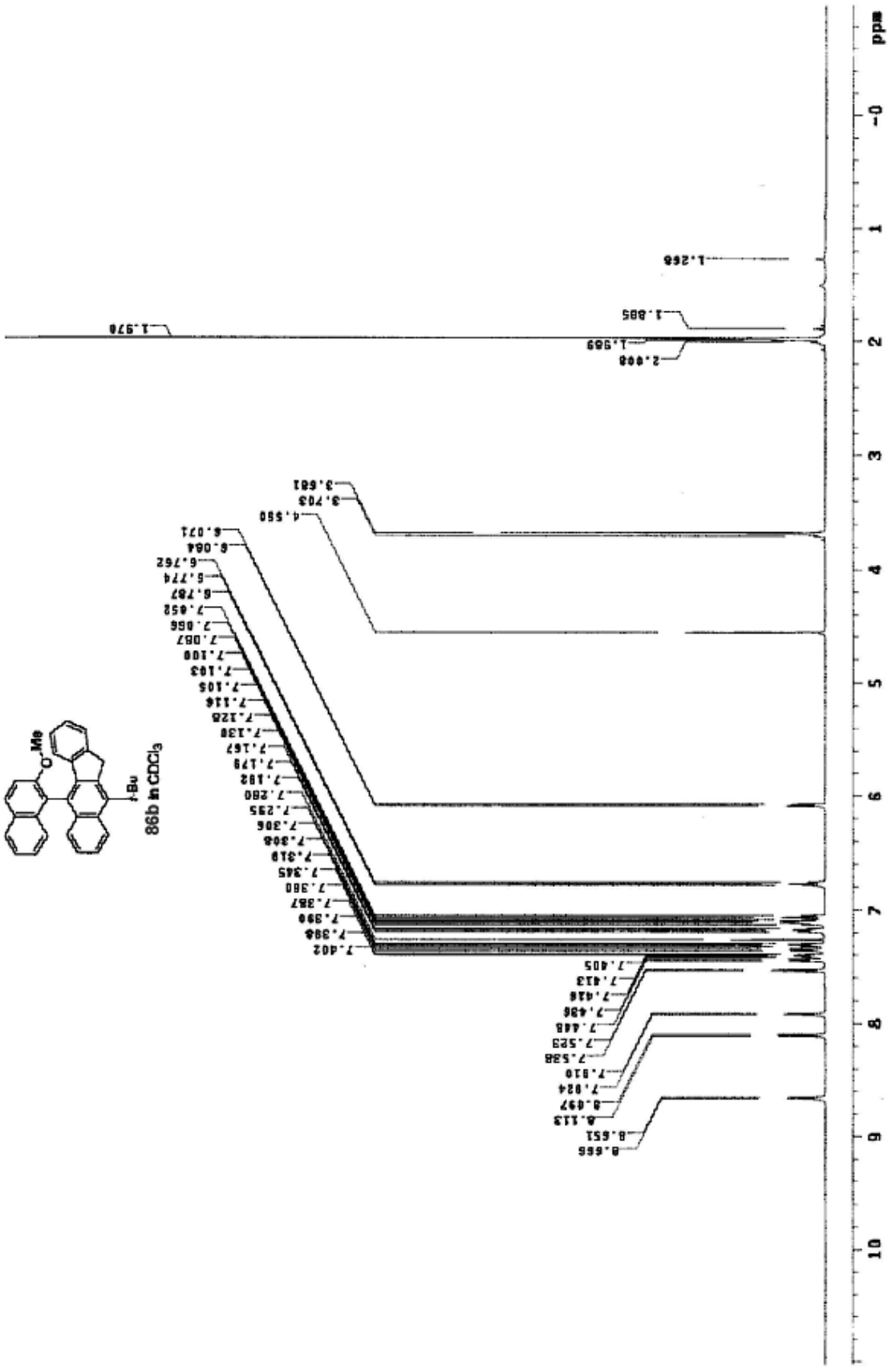

OMe
76
1.3577
3.7638
4.0543
7.2490
7.2600
7.2829
7.3901
7.5568
7.7776
7.8436
7.8766
8.2577
X : parts per Million : 1H

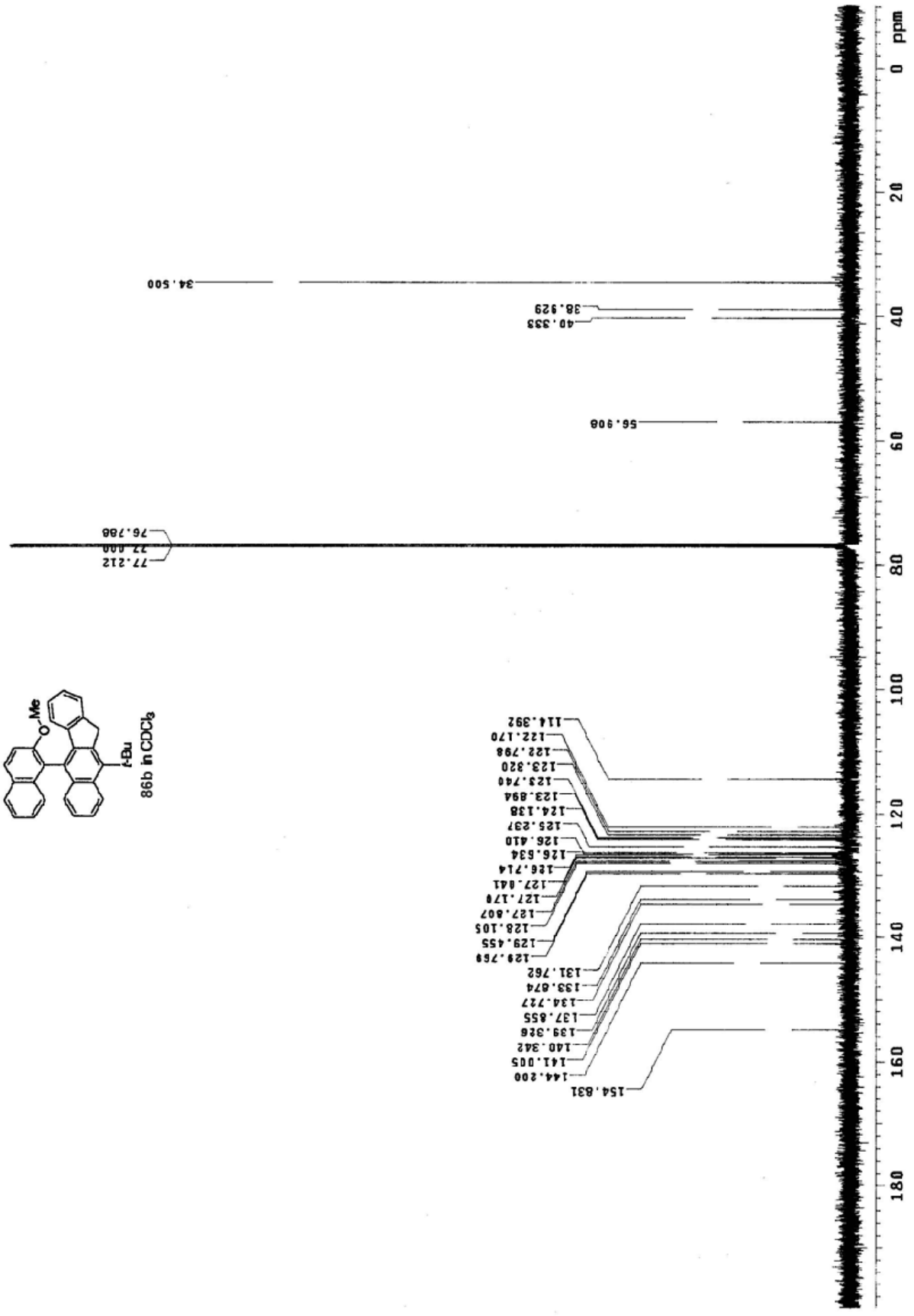

OMe
76
ppm

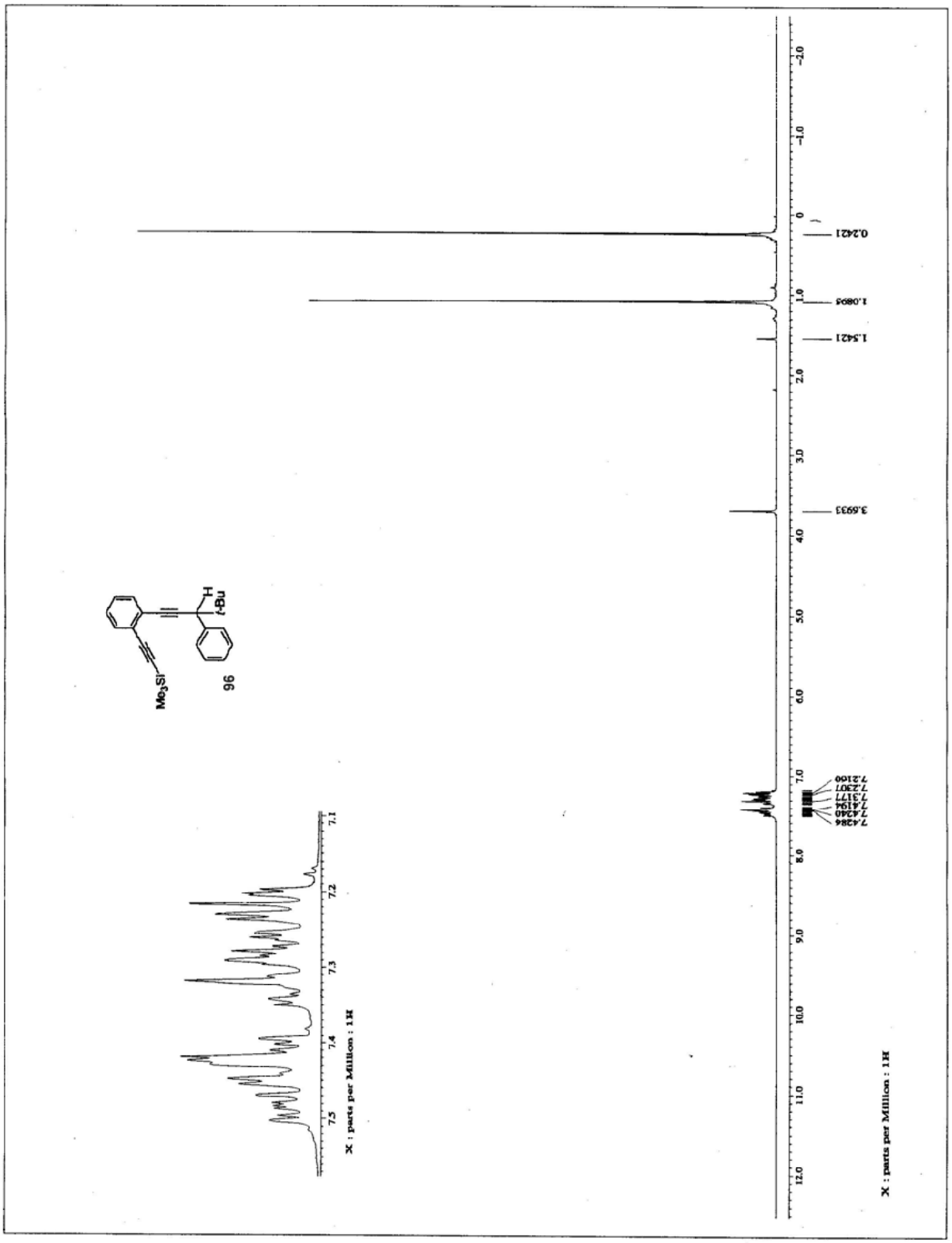

0.9475
1.2563
1.5485
3.6631
3.9957
7.0658
7.2600
7.2847
7.3415
7.3480
7.3709
7.3764
7.3864
8.3924
8.3951
8.4281
X : parts per Million : 1H
80
OMe
t-Bu
H

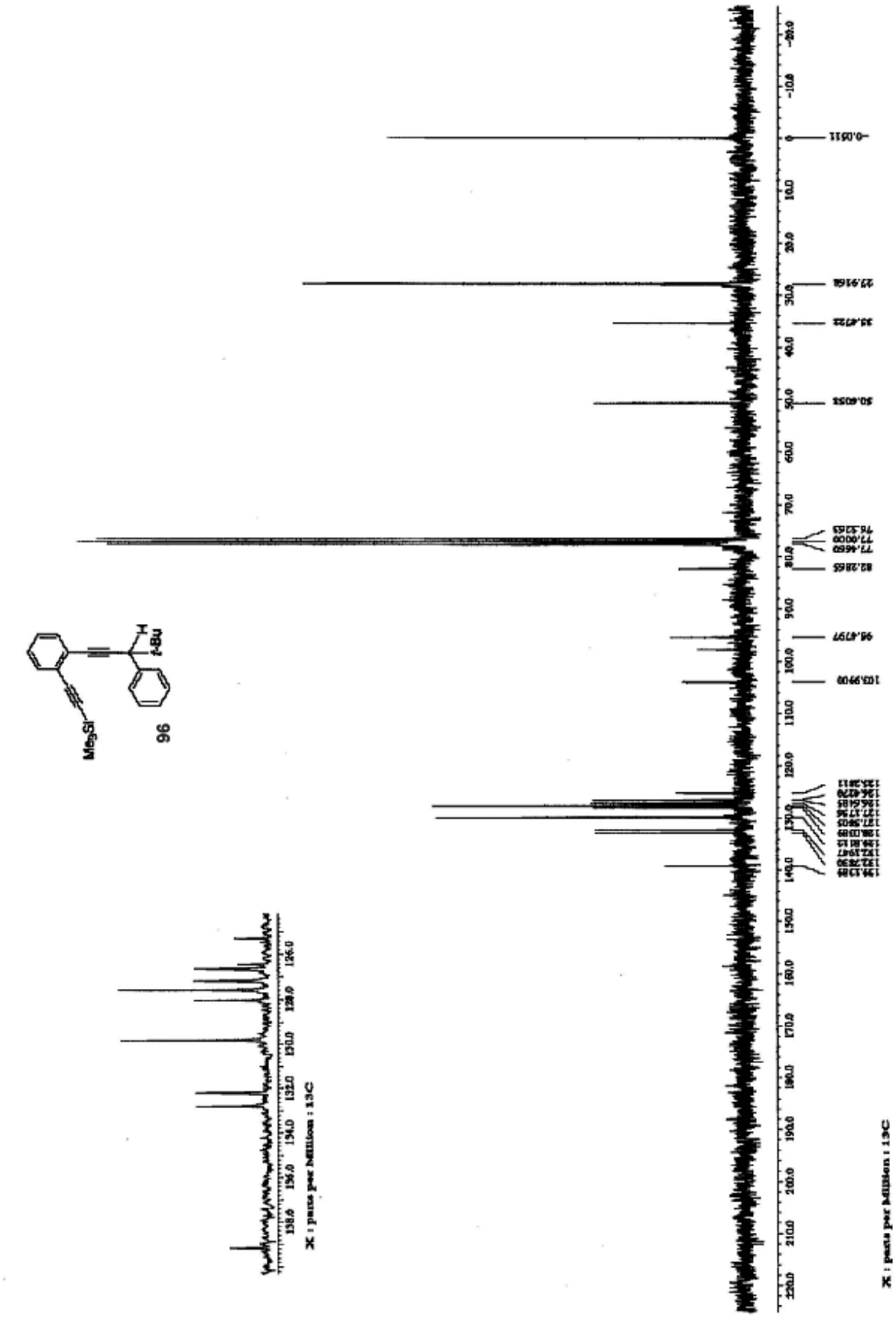

OMe
i-Bu
80
X : parts per Million : 13C
158.9021
132.2559
129.7349
127.7639
127.3437
127.2368
126.4423
125.6936
124.0741
112.6150
106.4576
97.7563
95.4950
87.3132
82.6150
77.4737
77.0000
76.5340
56.5570
50.5371
35.5028
27.6800

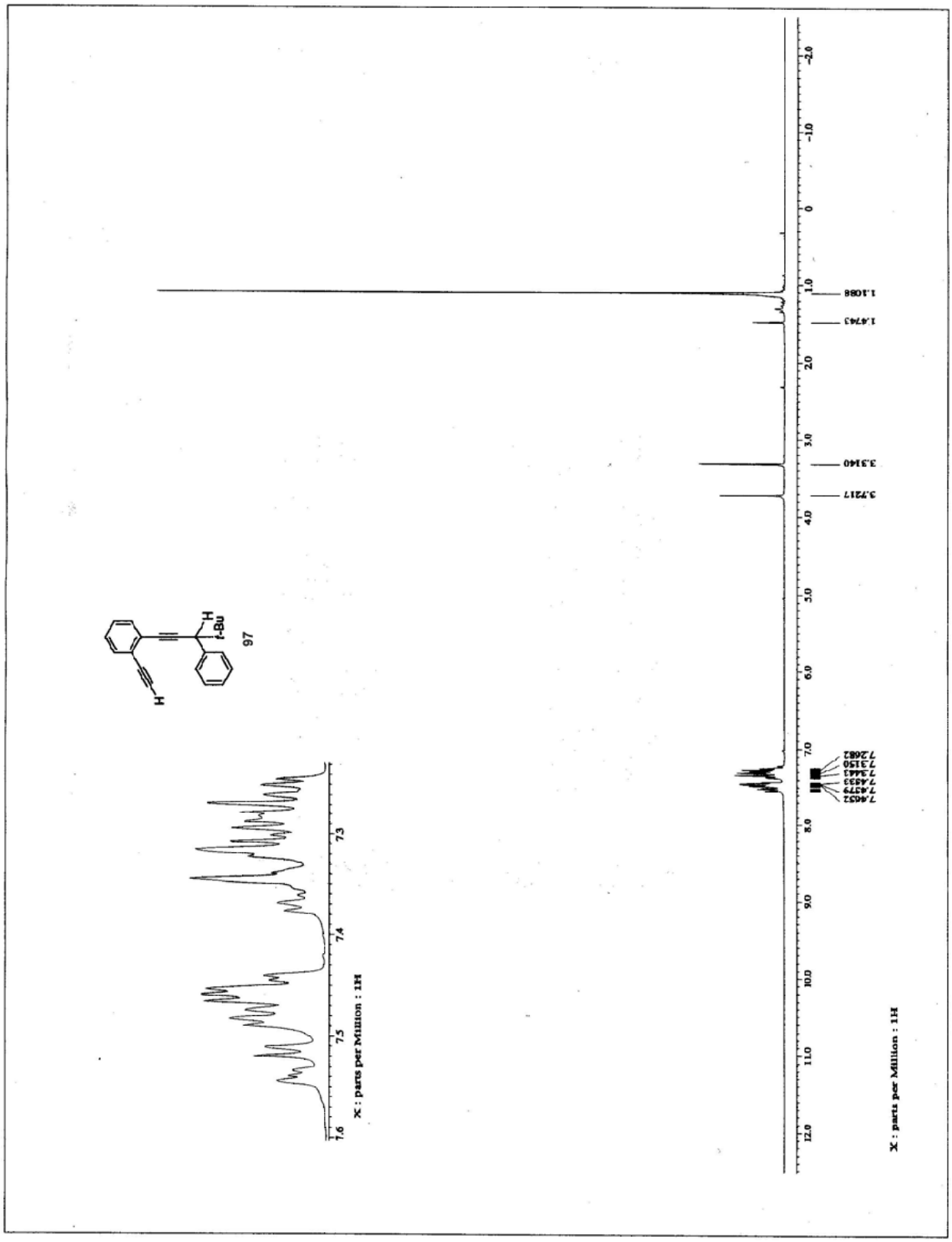

Me
t-Bu
86b in C_6D_6
1.768
1.869
3.133
4.179
4.208
4.238
4.274
6.526
6.588
6.719
6.722
6.735
6.877
6.890
6.903
6.970
6.982
6.994
7.058
7.063
7.075
7.106
7.118
7.131
7.169
7.171
7.222
7.234
7.275
7.276
7.289
7.411
7.425
7.885
7.908
7.892
7.932
7.975
7.989
8.679
ppm

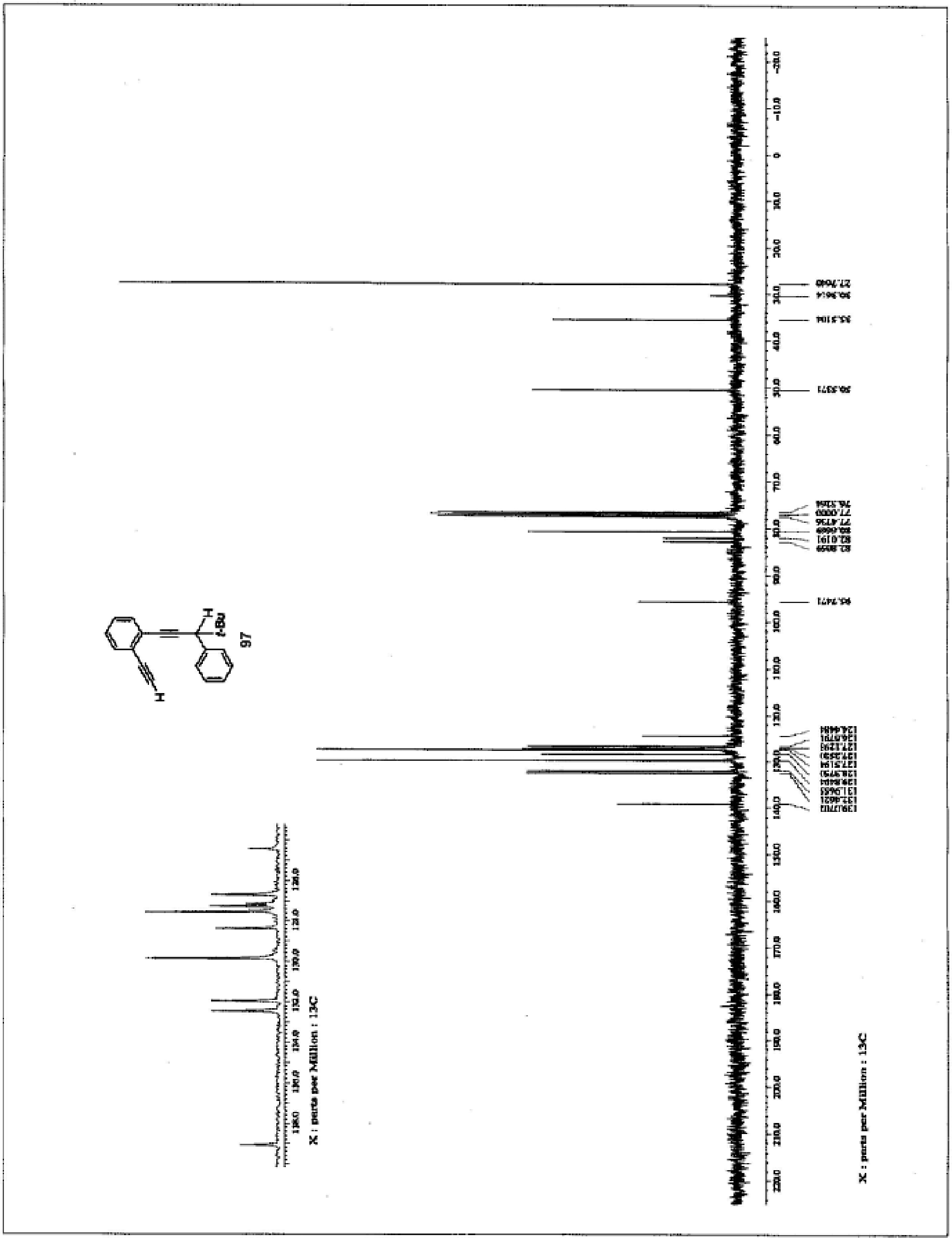

86b in CDCl3
Me
t-Bu
O
1.970
1.266
1.885
1.569
2.008
3.681
3.703
4.560
6.071
6.084
6.762
6.774
6.787
7.052
7.056
7.087
7.100
7.103
7.105
7.114
7.126
7.138
7.167
7.179
7.182
7.280
7.295
7.306
7.308
7.319
7.345
7.380
7.387
7.399
7.388
7.402
7.405
7.413
7.438
7.456
7.468
7.523
7.538
7.810
7.824
8.097
8.113
8.651
8.666
ppm

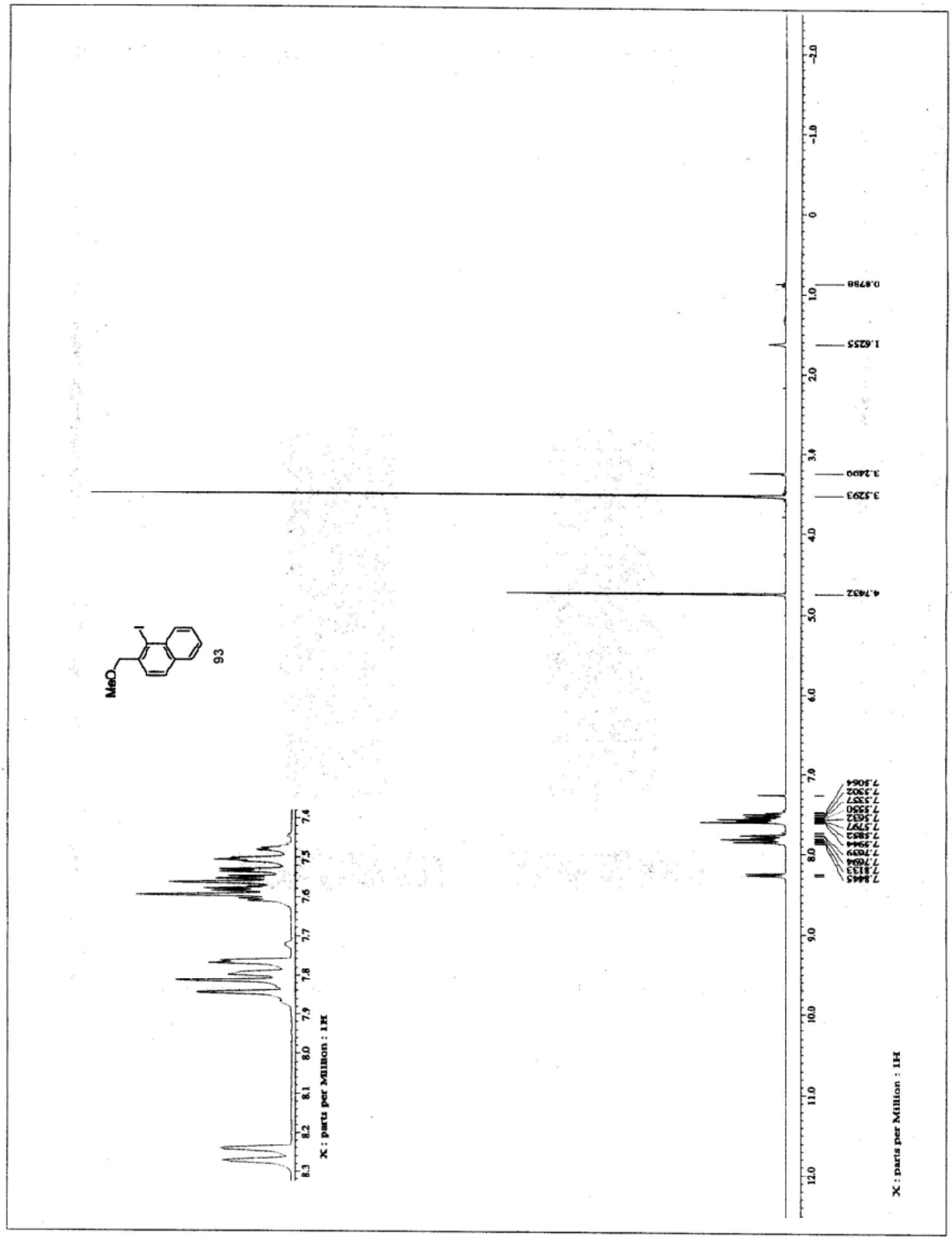

86b in CDCl3
Me
t-Bu
154.831
144.200
141.005
140.342
139.326
137.855
134.727
133.874
131.762
129.759
129.455
128.105
127.607
127.179
127.041
126.714
126.534
126.410
125.237
124.138
123.894
123.740
123.320
122.798
122.170
114.392
77.212
77.000
76.788
56.908
40.333
38.929
34.500
0 ppm
20
40
60
80
100
120
140
160
180

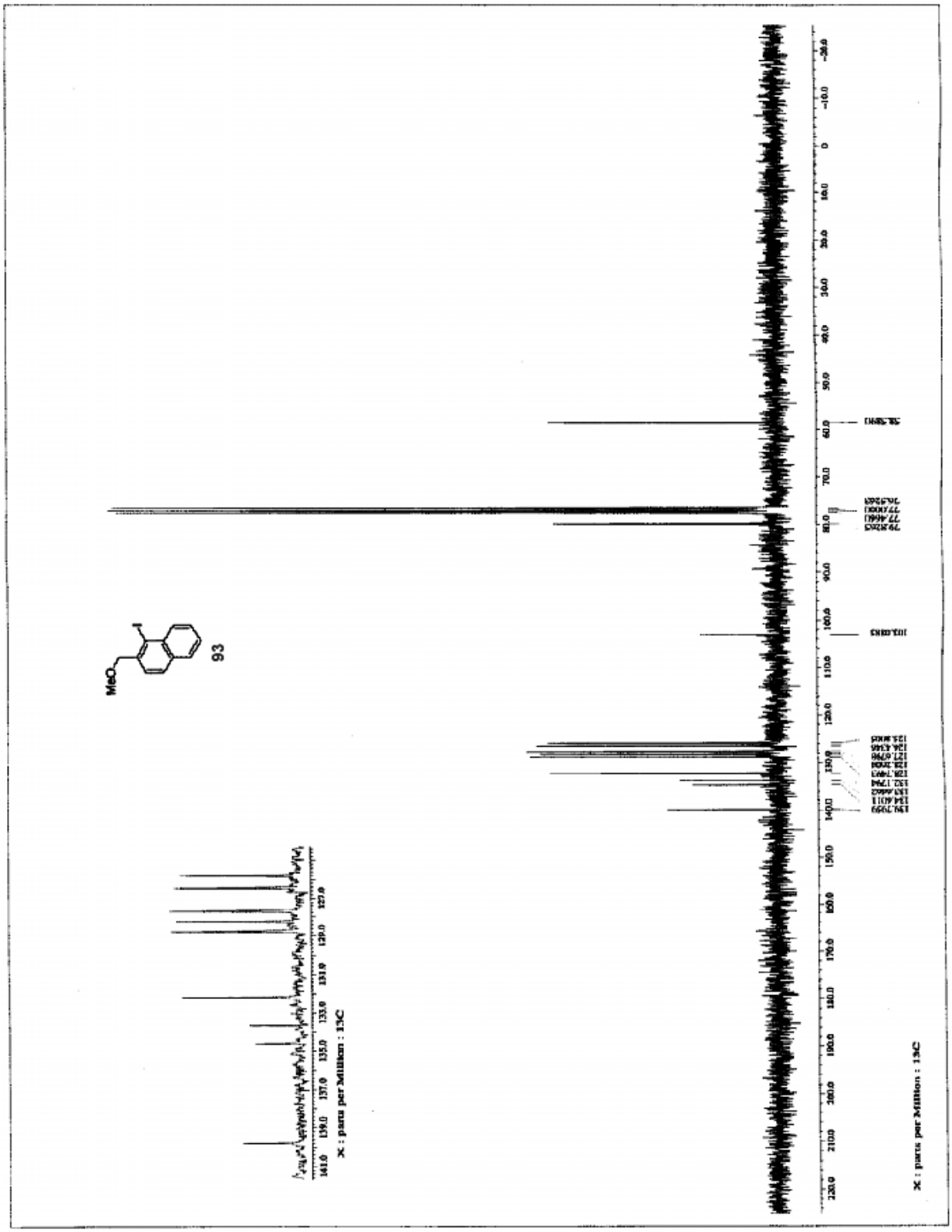

Me3Si
t-Bu
H
96
0.2421
1.0805
1.5421
3.6933
7.4284
7.4240
7.4194
7.3177
7.2307
7.2106
X : parts per Million : 1H
X : parts per Million : 1H

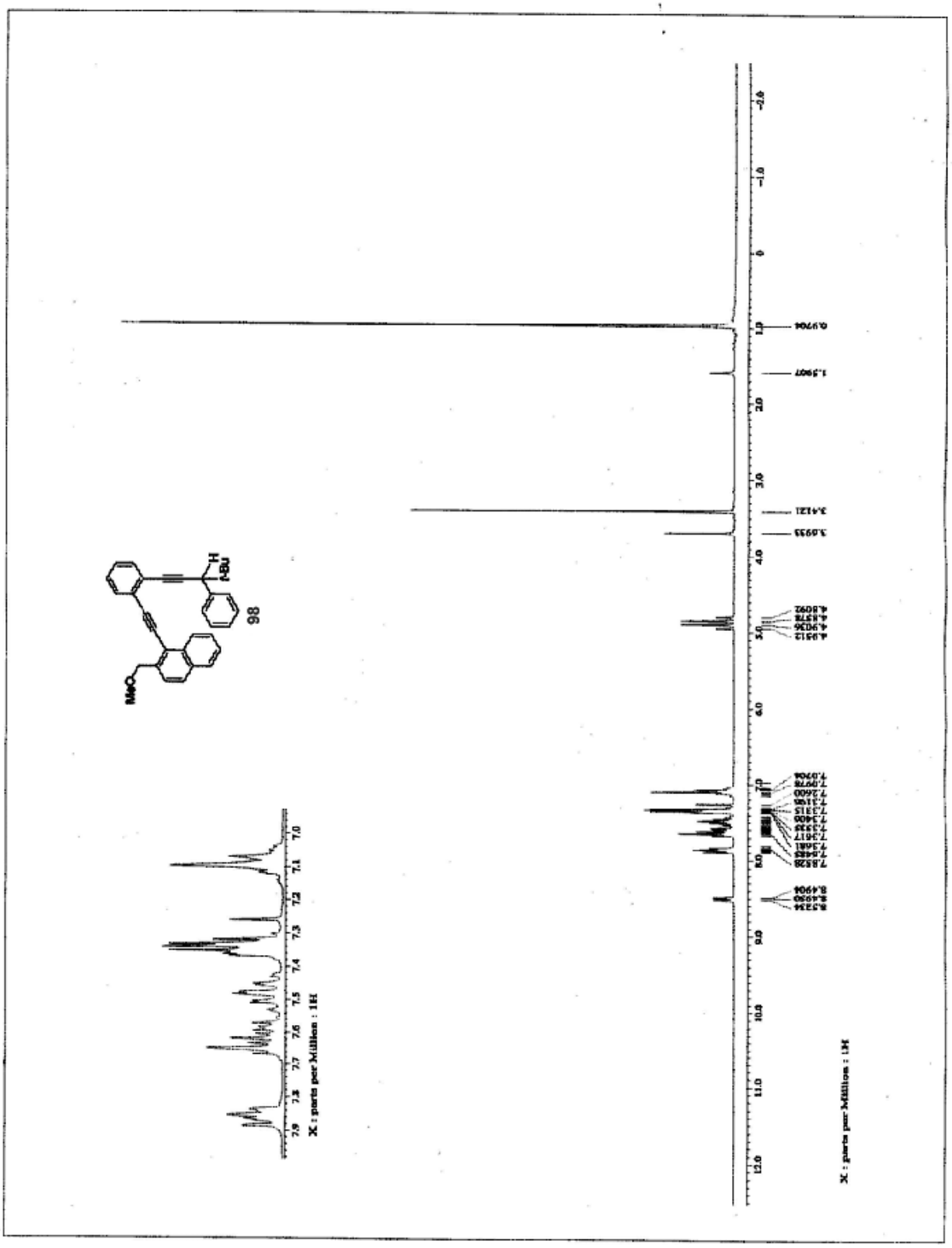

Me3Si
t-Bu
96

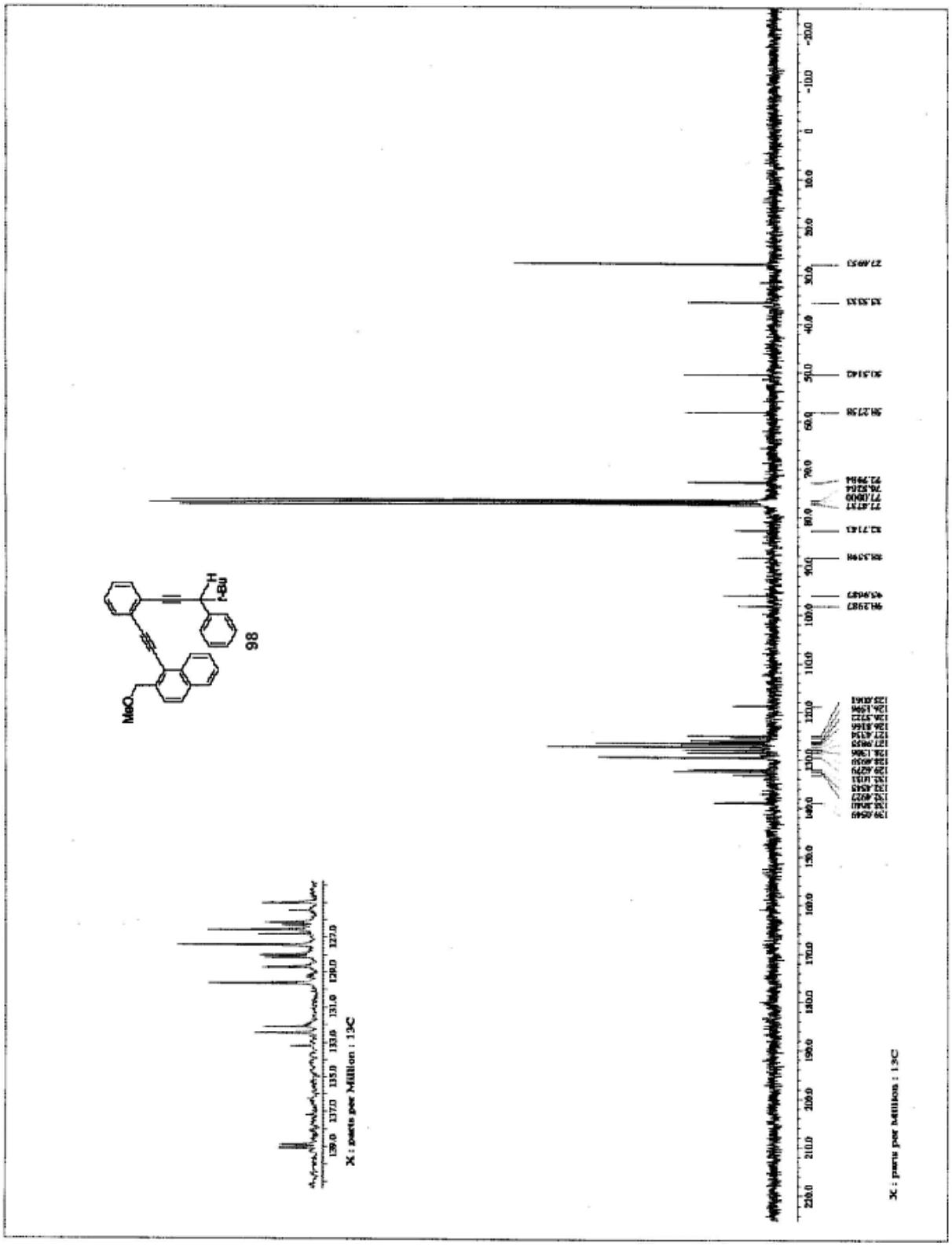

97
t-Bu
H
H
1.1088
1.6743
3.3140
3.7217
7.4052
7.4379
7.4533
7.5443
7.5150
7.2082
X : parts per Million : 1H
X : parts per Million : 1H

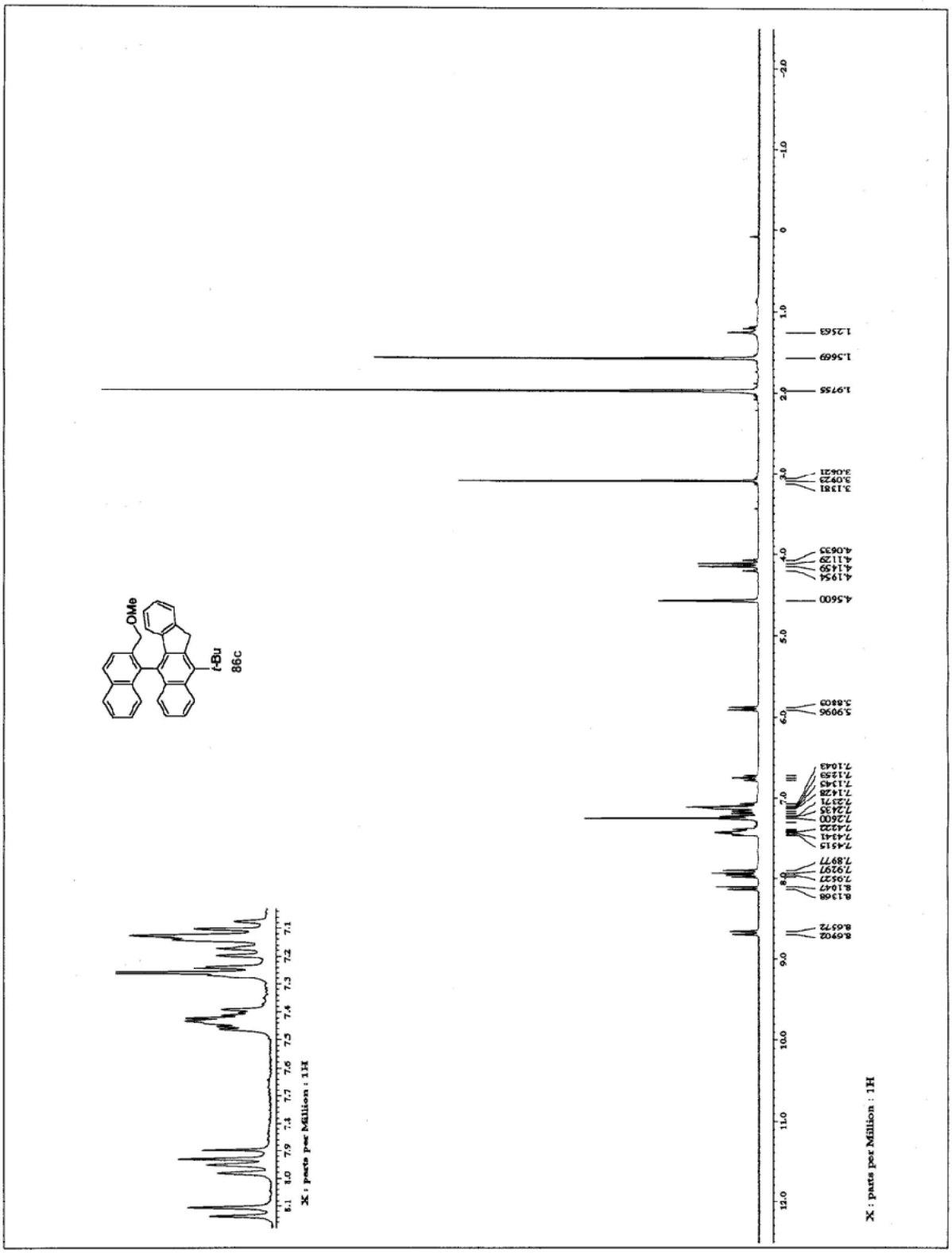


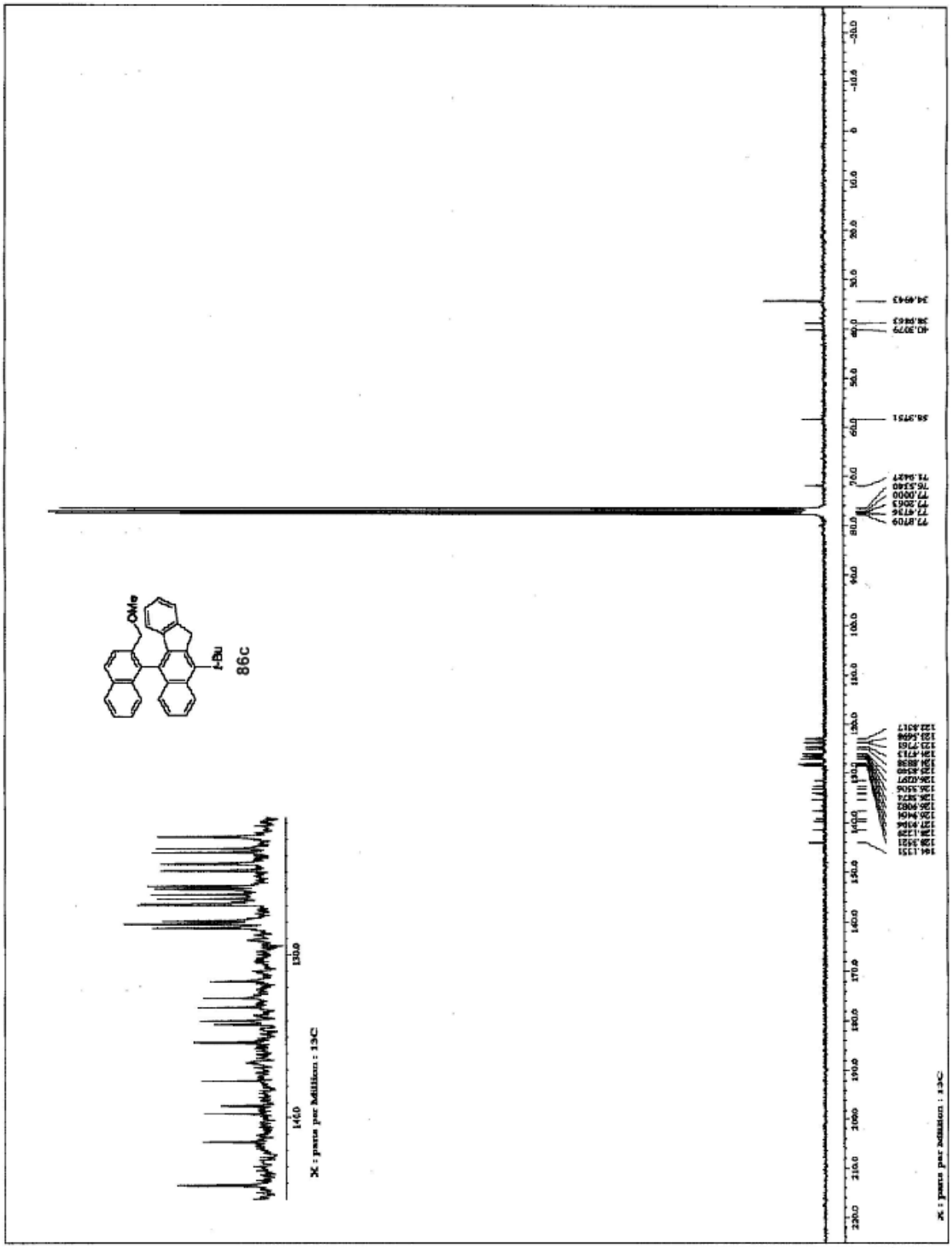

MeO
I
93
0.8788
1.6255
3.2400
3.5293
4.7452
7.3064
7.3302
7.3357
7.3590
7.3652
7.3797
7.3983
7.3984
7.7609
7.7664
7.8135
7.8145
X : parts per Million : 1H
X : parts per Million : 1H

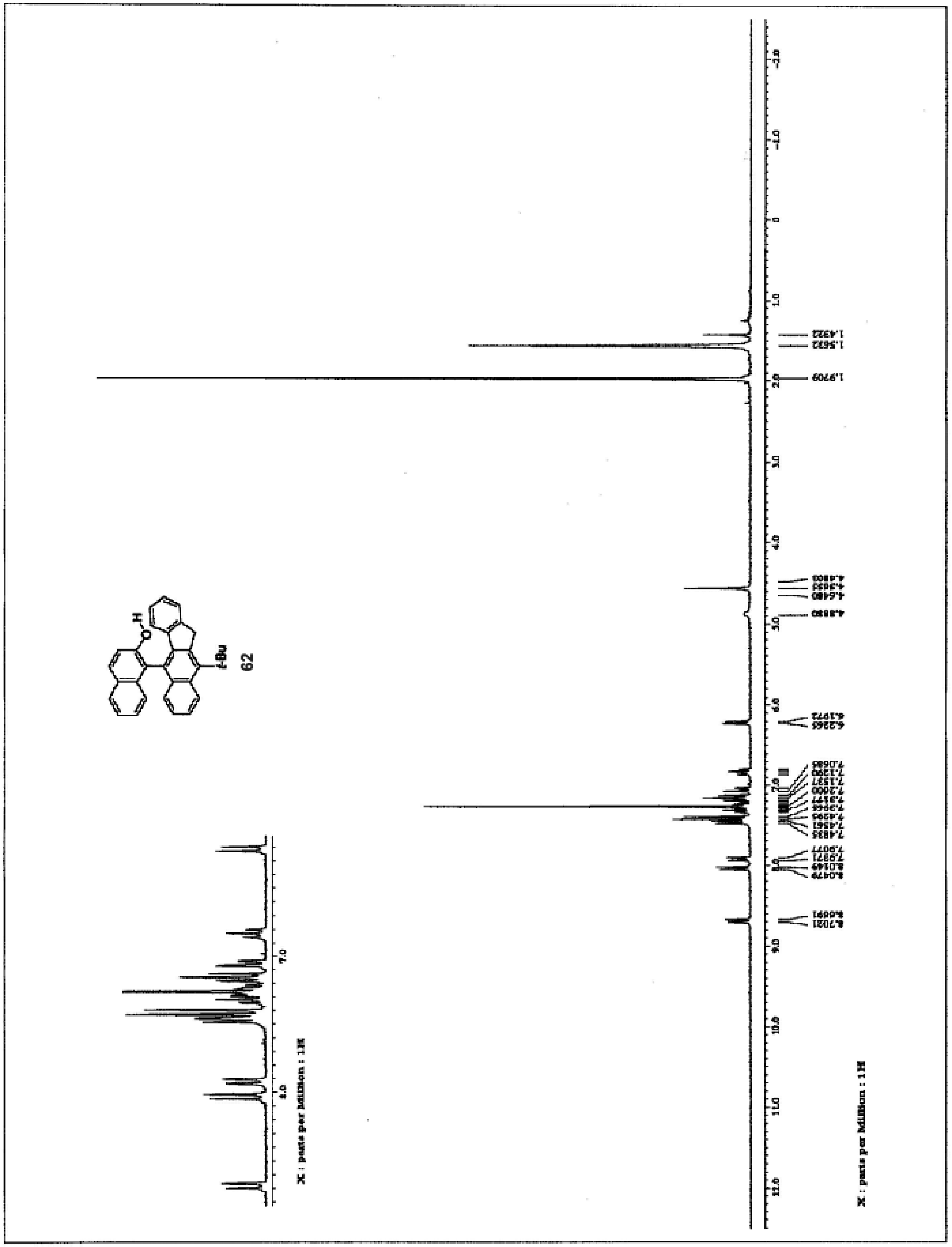

MeO
I
93
X : parts per Million : 13C


MeO
NBu
H
98
X : parts per Million : 1H

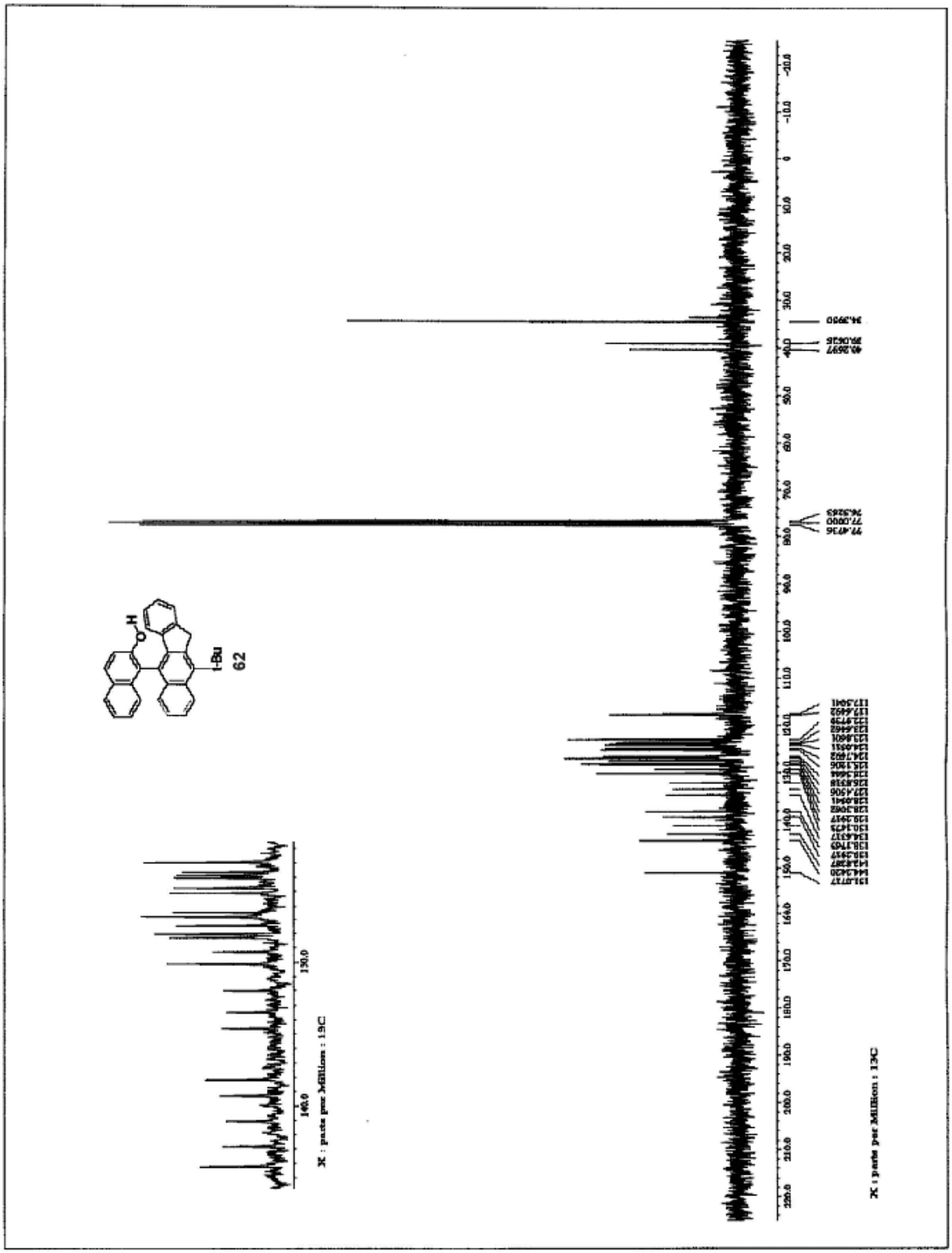

MeO
t-Bu
98
13C : parts per Million : 13C

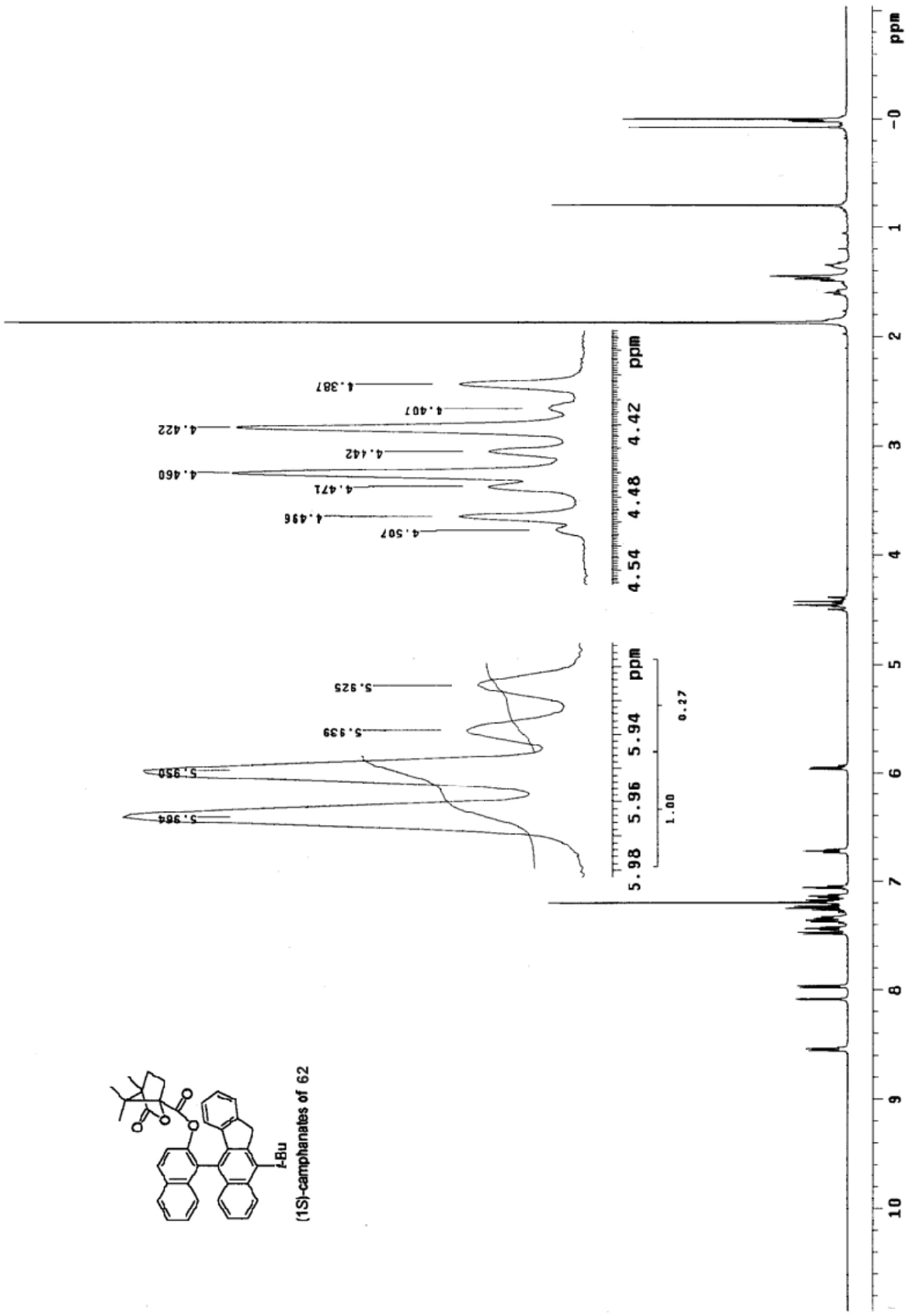

OMe
t-Bu
86c
X : parts per Million : 1H

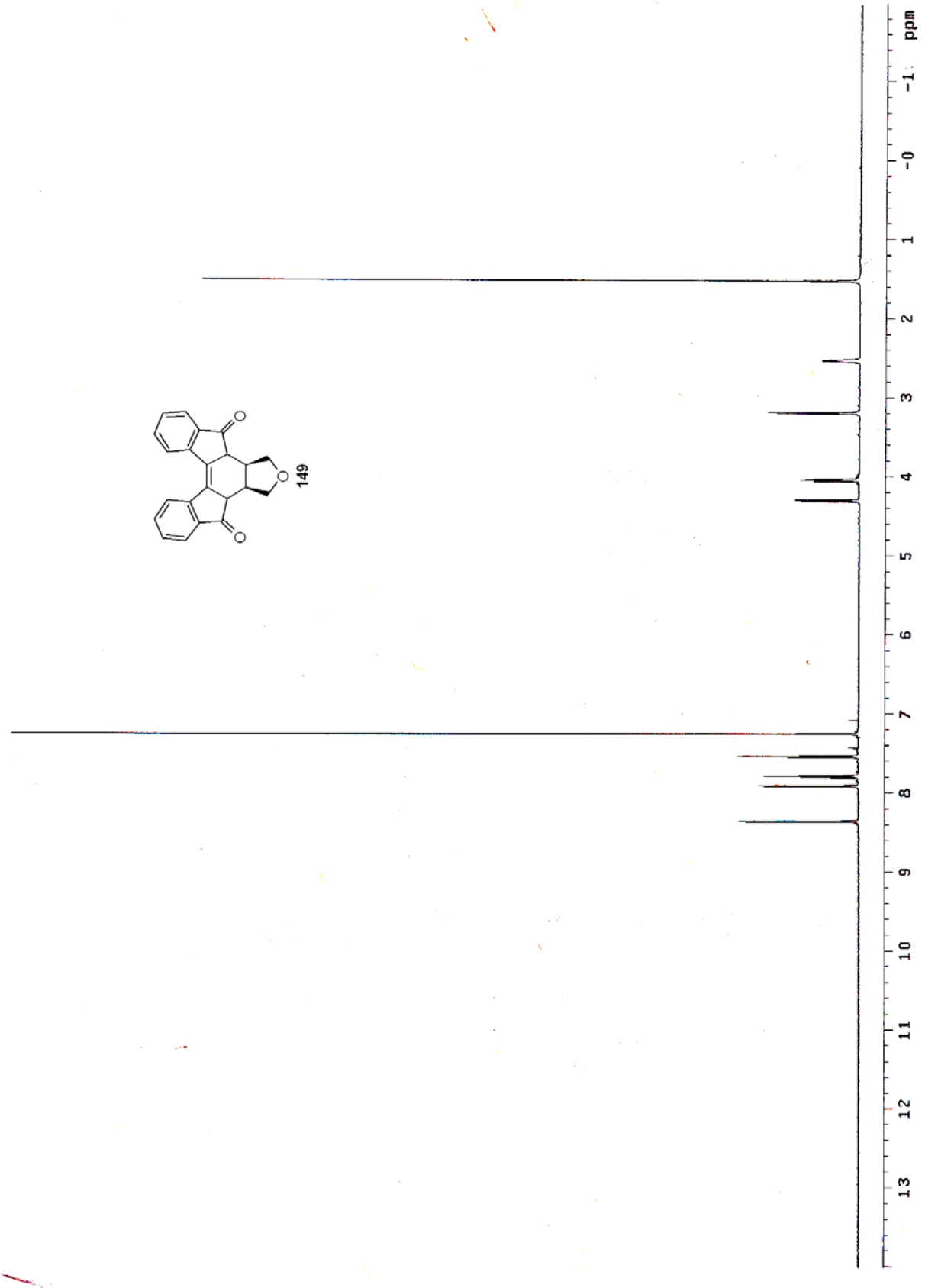

OMe
t-Bu
86c

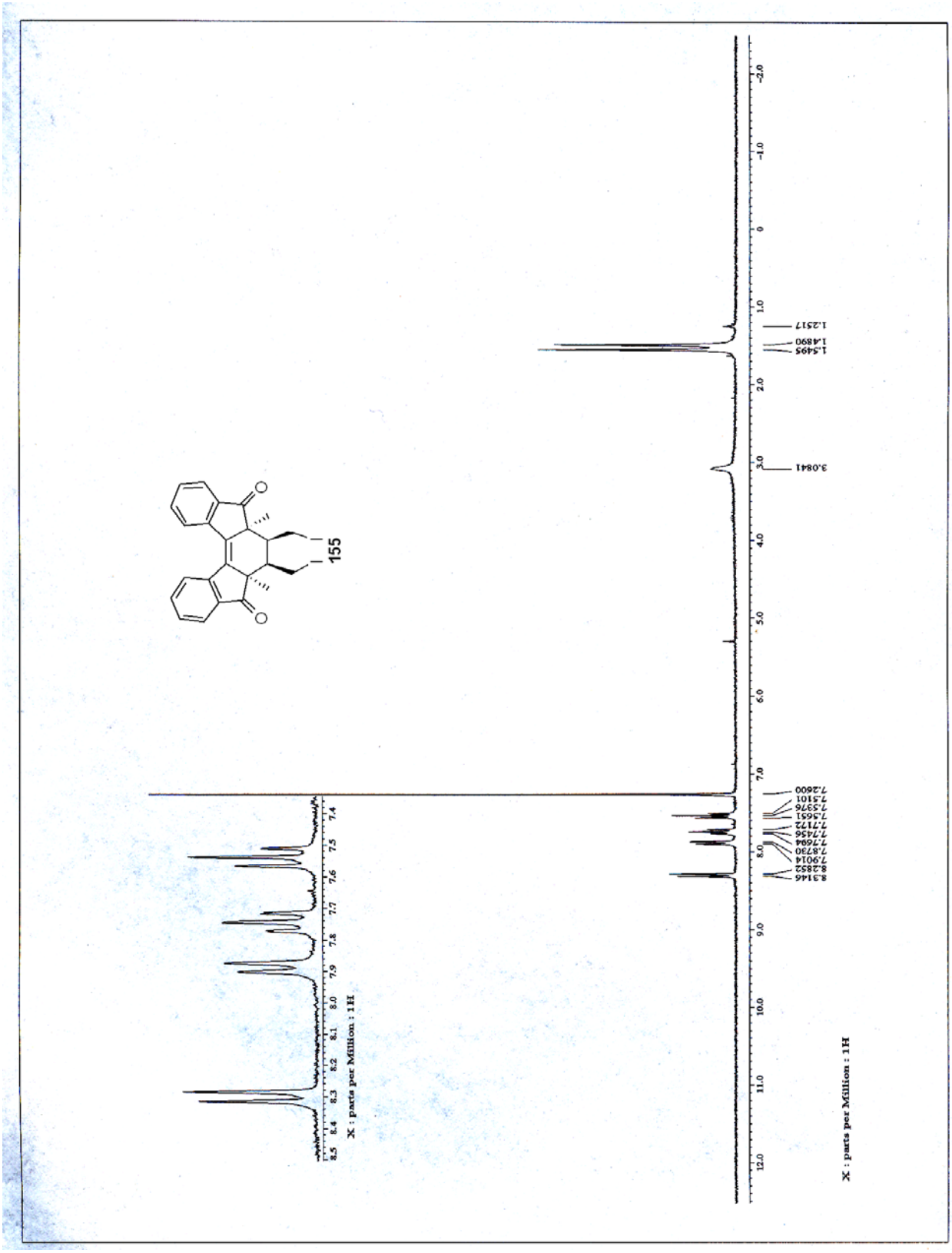


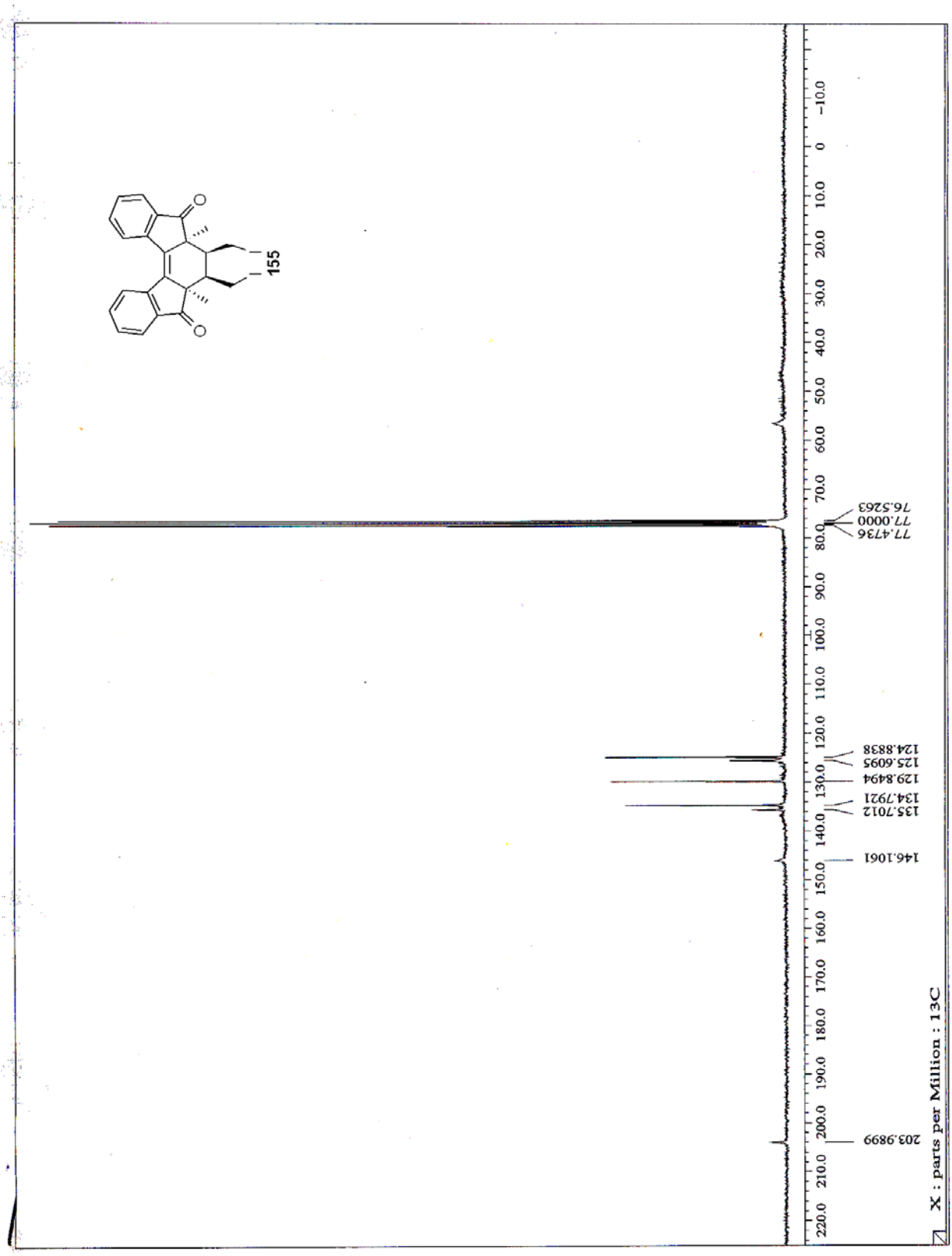
t-Bu
62
X : parts per Million : 1H
1.4322
1.5632
1.9709

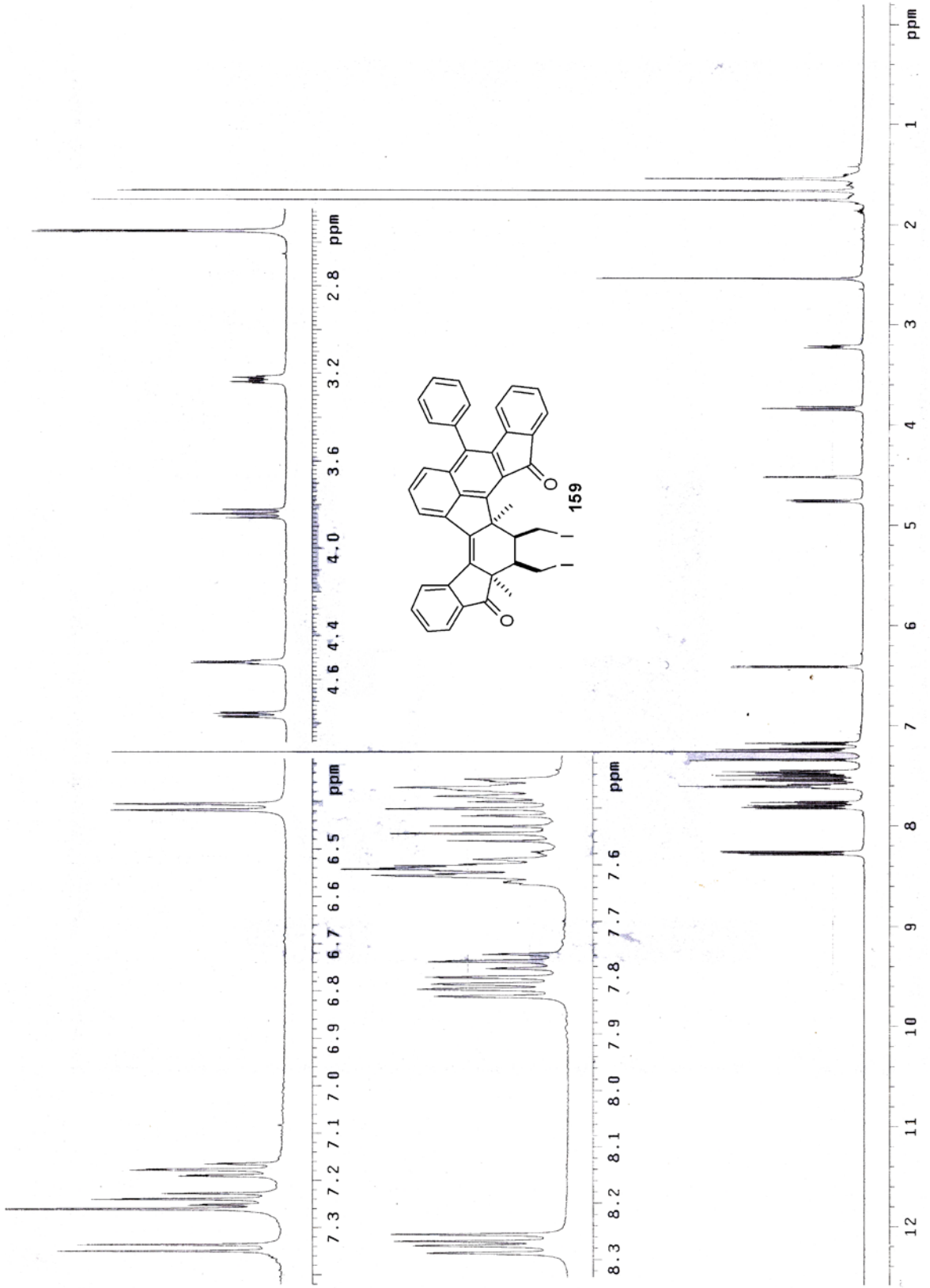

t-Bu
62

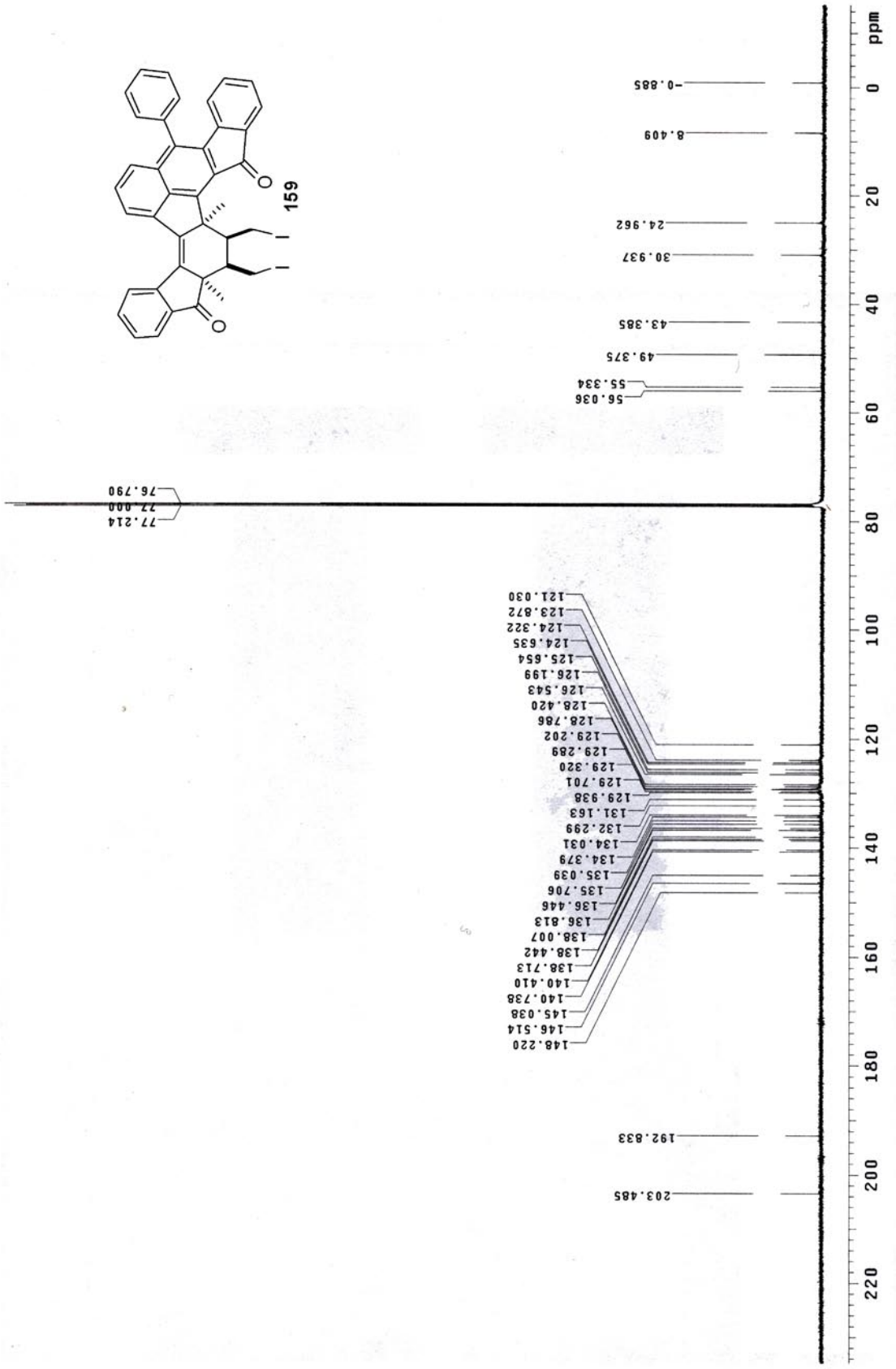

t-Bu
(1S)-camphanates of 62
5.964
5.950
5.939
5.925
4.507
4.496
4.471
4.460
4.442
4.422
4.407
4.387
5.98 5.96 5.94 ppm
1.00
0.27
4.54 4.48 4.42 ppm
ppm

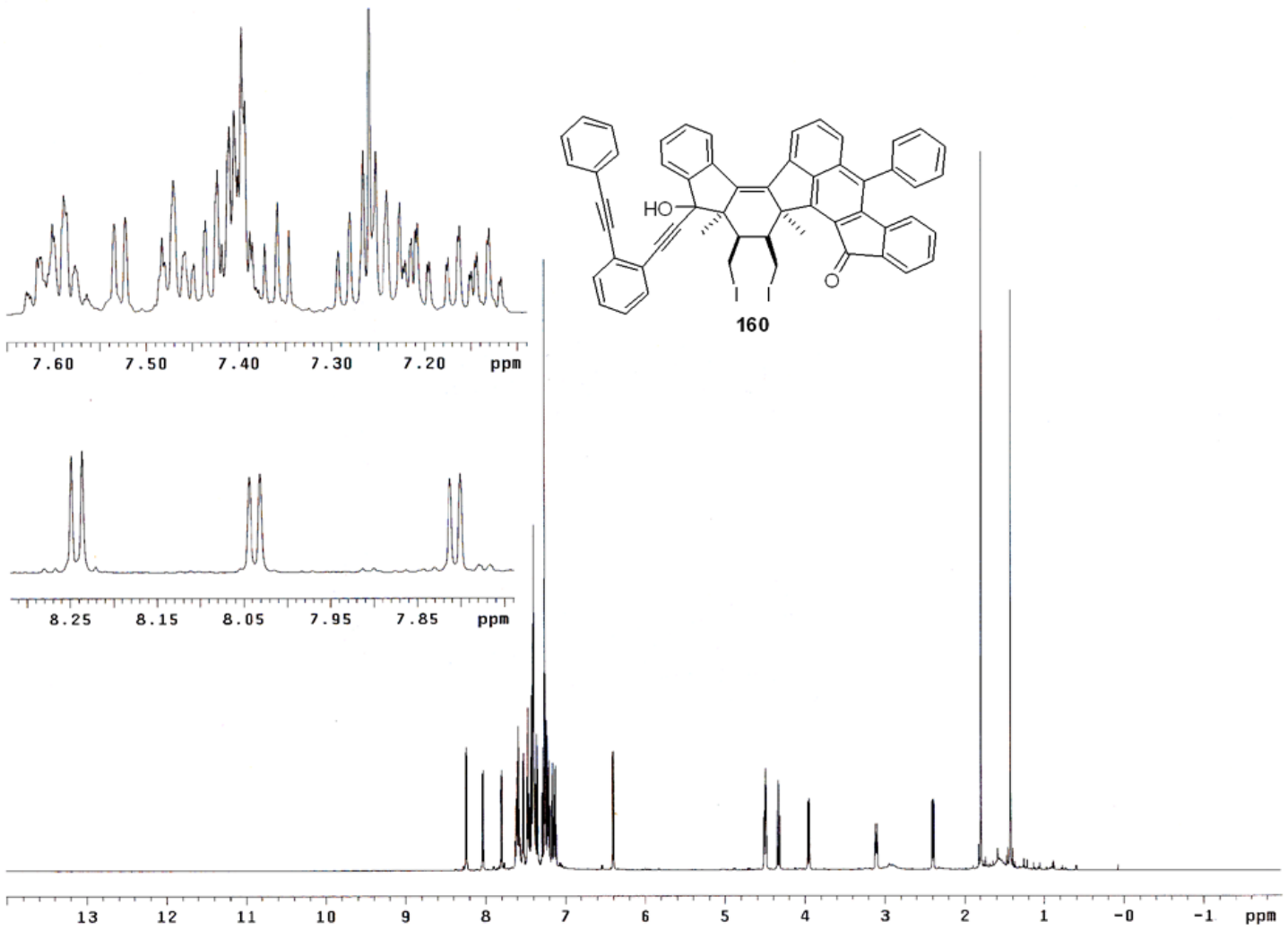

149
13
12
11
10
9
8
7
6
5
4
3
2
1
-0
-1
ppm

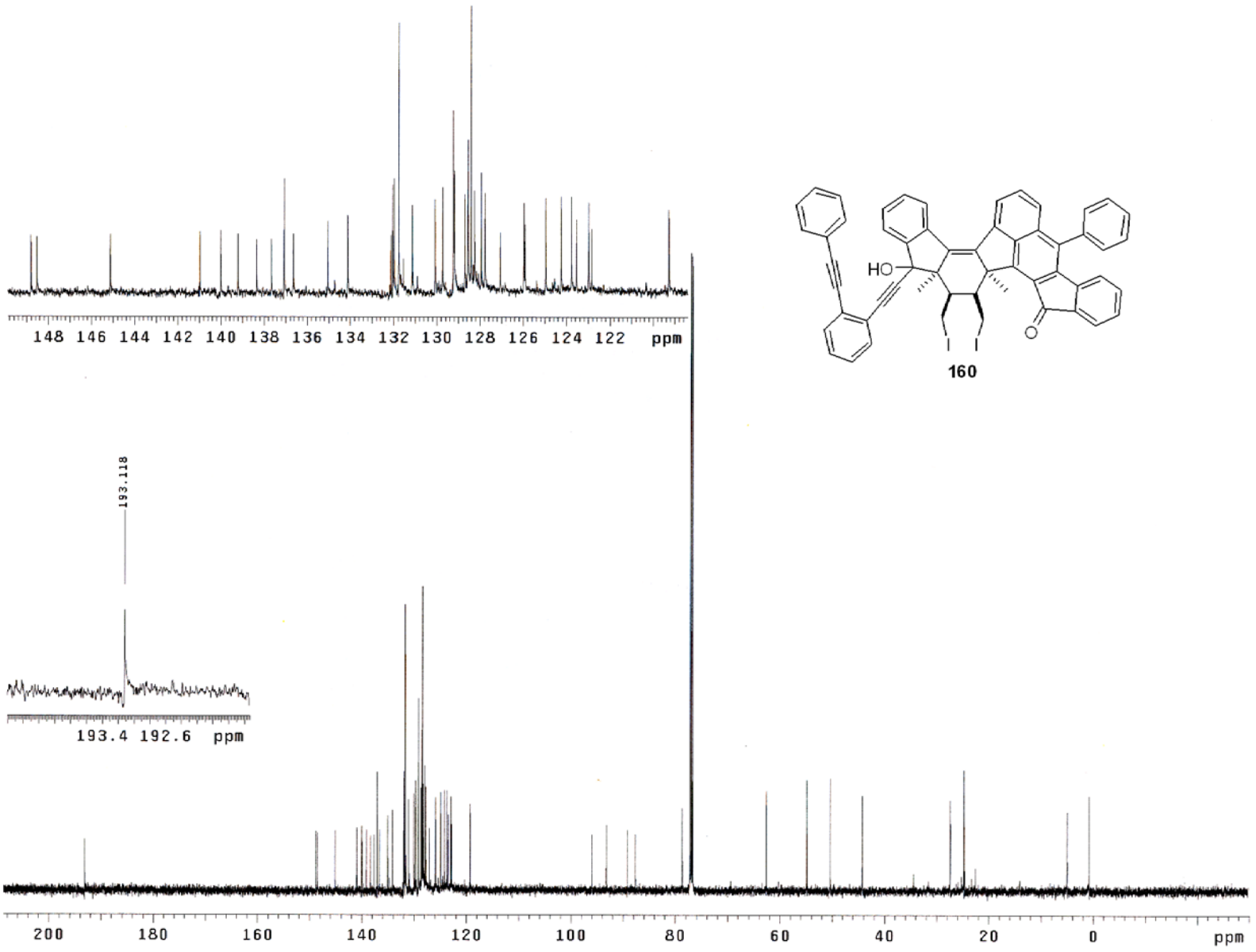

155
X : parts per Million : 1H
X : parts per Million : 1H
8.3146
8.2852
7.9014
7.8730
7.7694
7.7456
7.7172
7.5691
7.5376
7.5101
7.2600
3.0841
1.5495
1.4890
1.2517


155
X : parts per Million : 13C
203.9899
146.1061
135.7012
134.7921
129.8494
125.6095
124.8838
77.4736
77.0000
76.5263

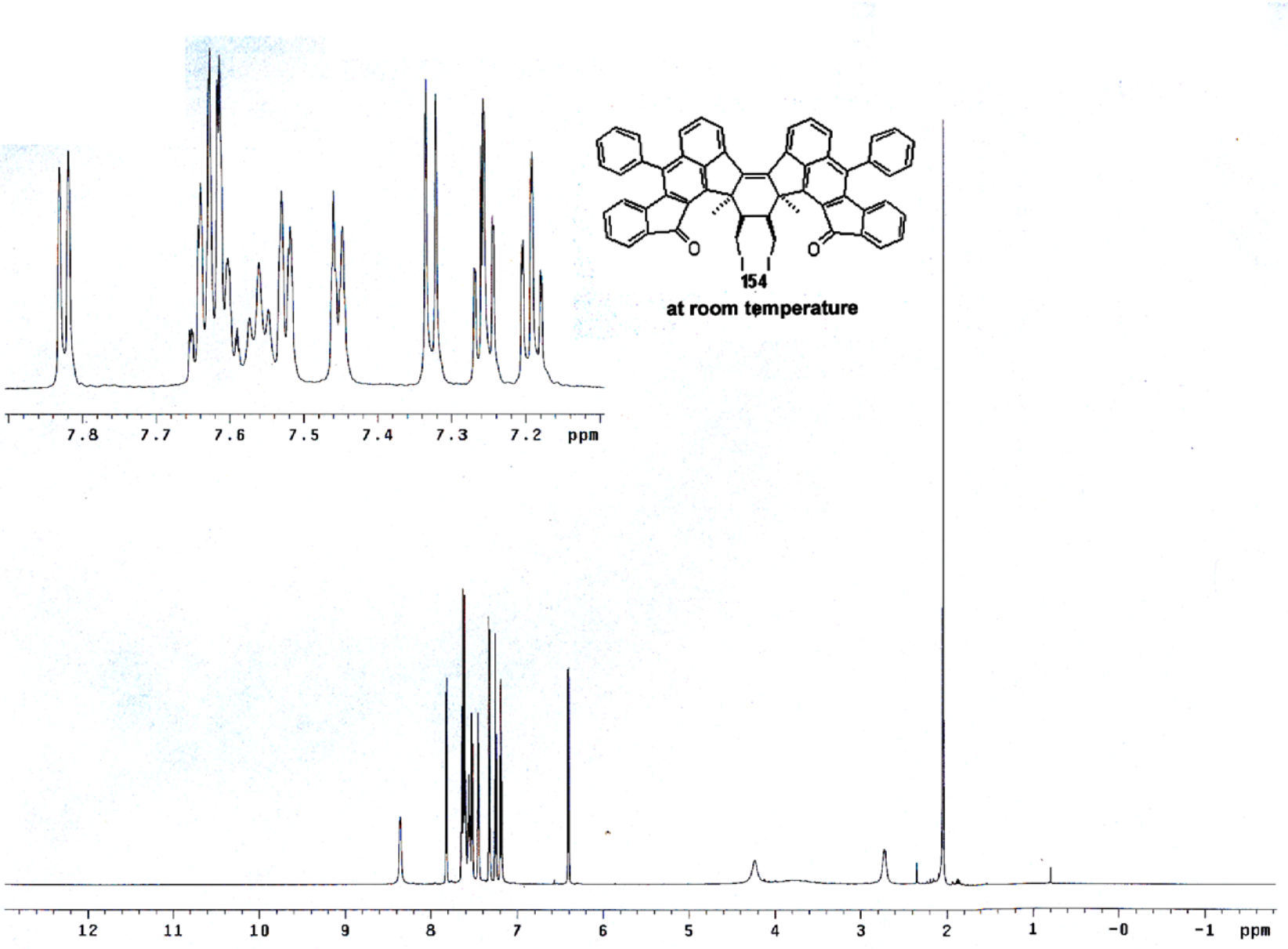

159
ppm

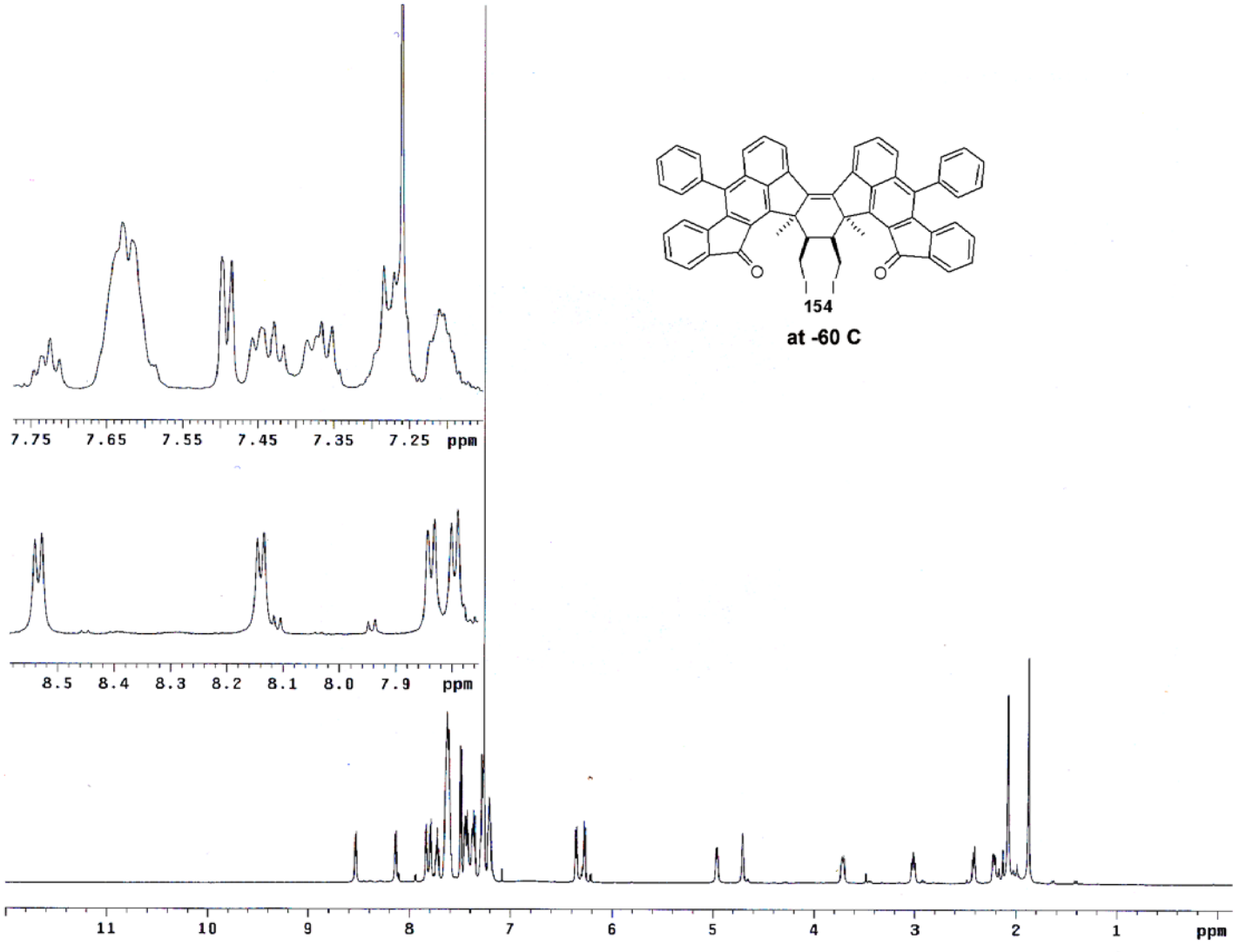

159
-0.885
8.409
24.962
30.937
43.385
49.375
55.334
56.036
76.790
77.214
77.000
121.030
123.872
124.322
124.635
125.654
126.199
126.543
128.420
128.786
129.202
129.289
129.320
129.701
129.938
131.163
132.299
134.031
134.379
135.039
135.706
136.446
136.813
138.007
138.442
138.713
140.410
140.738
145.038
146.514
148.220
192.833
203.485
ppm
0
20
40
60
80
100
120
140
160
180
200
220

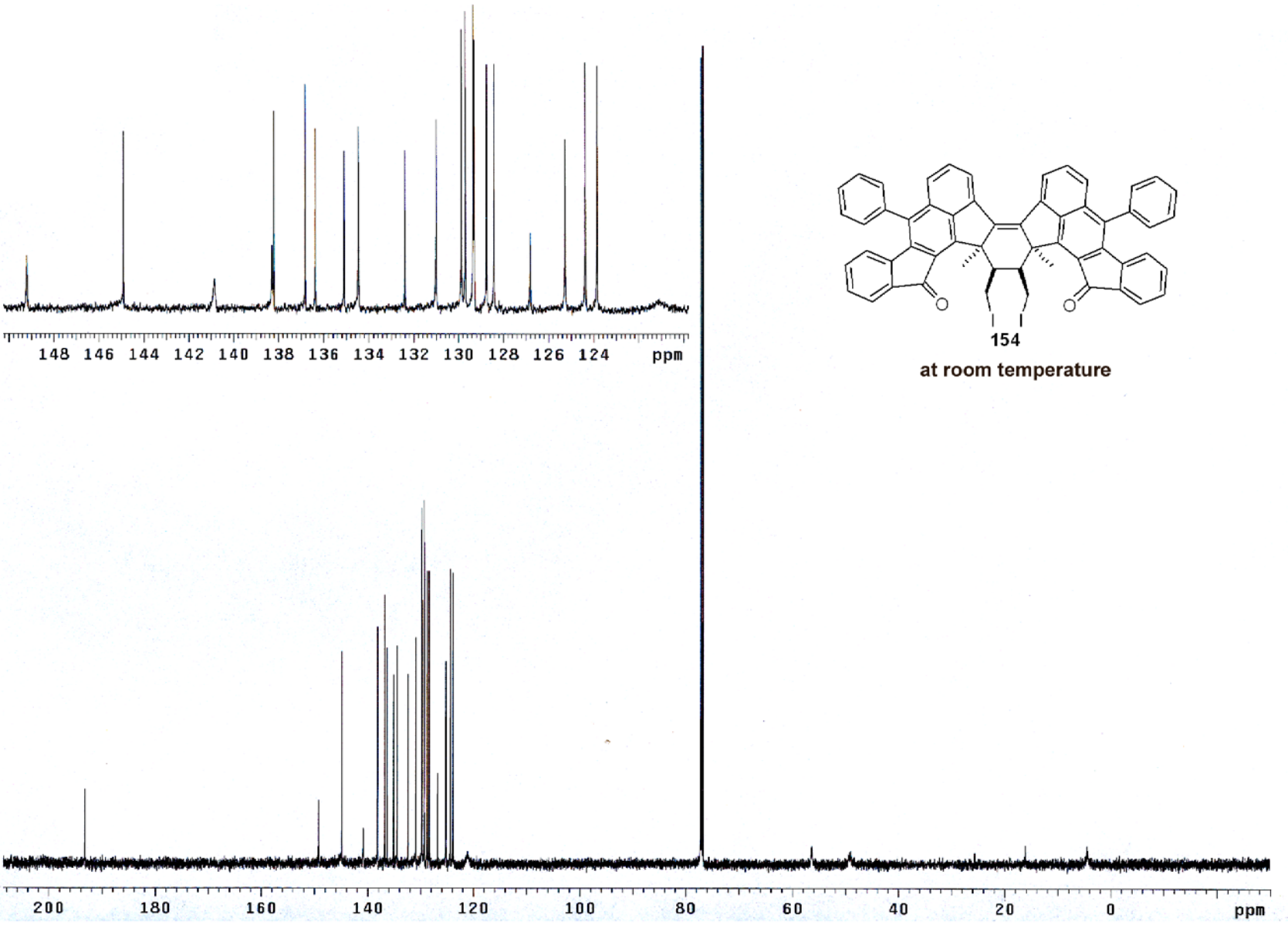

HO
O
160
7.60
7.50
7.40
7.30
7.20
ppm
8.25
8.15
8.05
7.95
7.85
ppm
13
12
11
10
9
8
7
6
5
4
3
2
1
-0
-1
ppm


148 146 144 142 140 138 136 134 132 130 128 126 124 122 ppm
193.118
193.4 192.6 ppm
200 180 160 140 120 100 80 60 40 20 0 ppm
HO
O

160

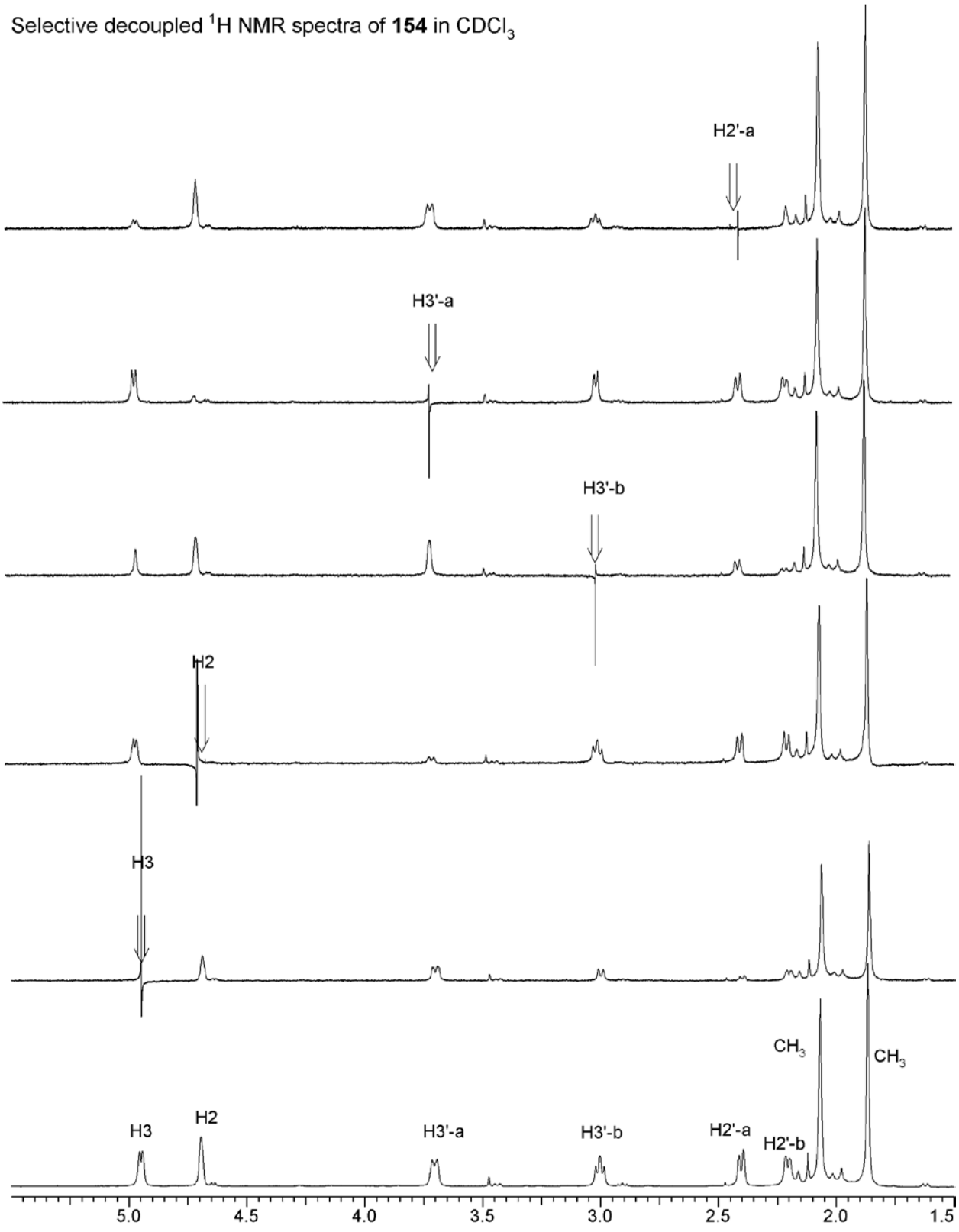

154
at room temperature
7.8
7.7
7.6
7.5
7.4
7.3
7.2
ppm
12
11
10
9
8
7
6
5
4
3
2
1
-0
-1
ppm


154
at -60 C
7.75 7.65 7.55 7.45 7.35 7.25 ppm
8.5 8.4 8.3 8.2 8.1 8.0 7.9 ppm
11 10 9 8 7 6 5 4 3 2 1 ppm



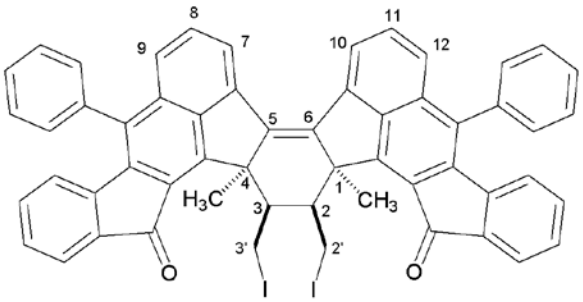
154

at room temperature

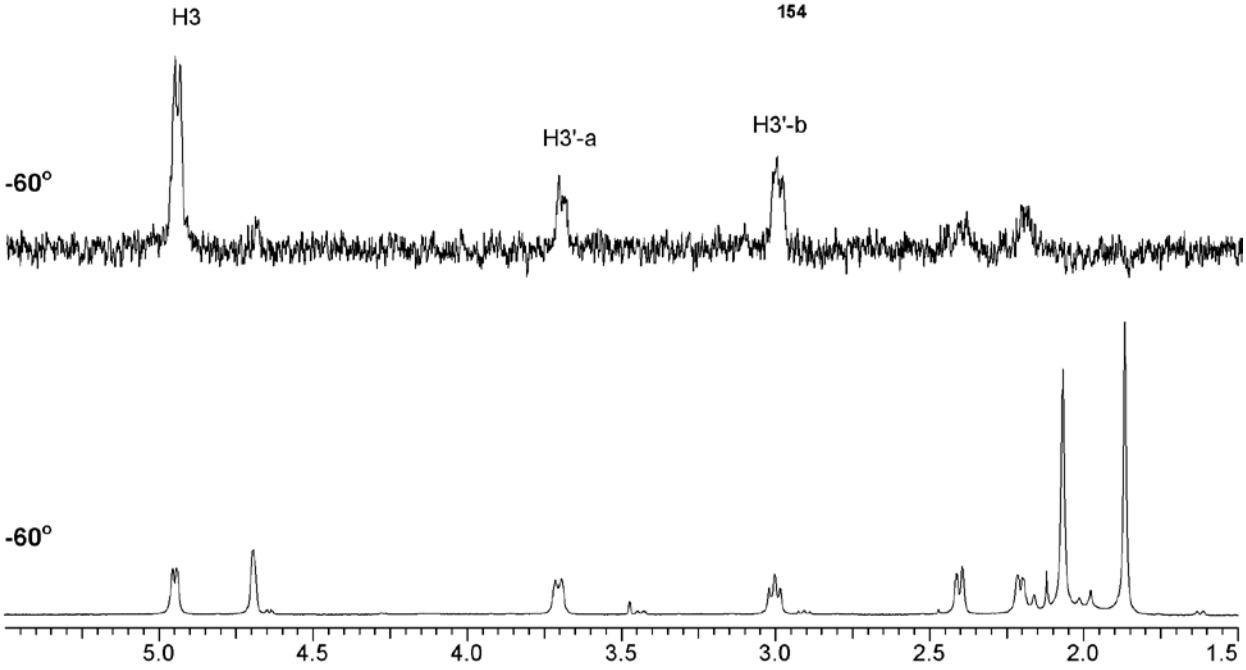

Selective decoupled ^{1}H NMR spectra of **154** in $CDCl_3$
H2'-a
H3'-a
H3'-b
H2
H3
CH_3
CH_3
H3
H2
H3'-a
H3'-b
H2'-a
H2'-b
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5

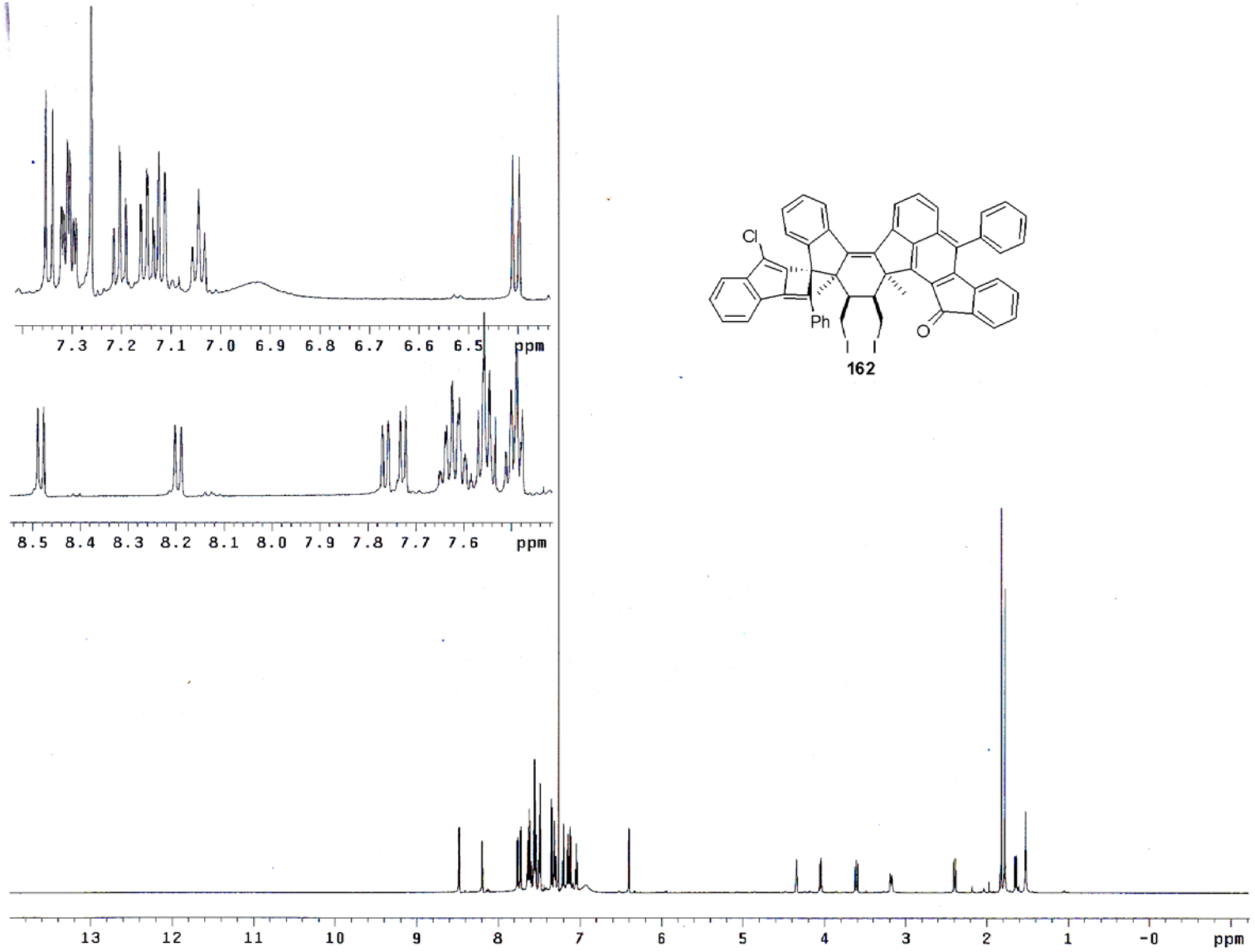
1D TOCSY spectrum of **154** in $CDCl_3$

mix = 30 ms

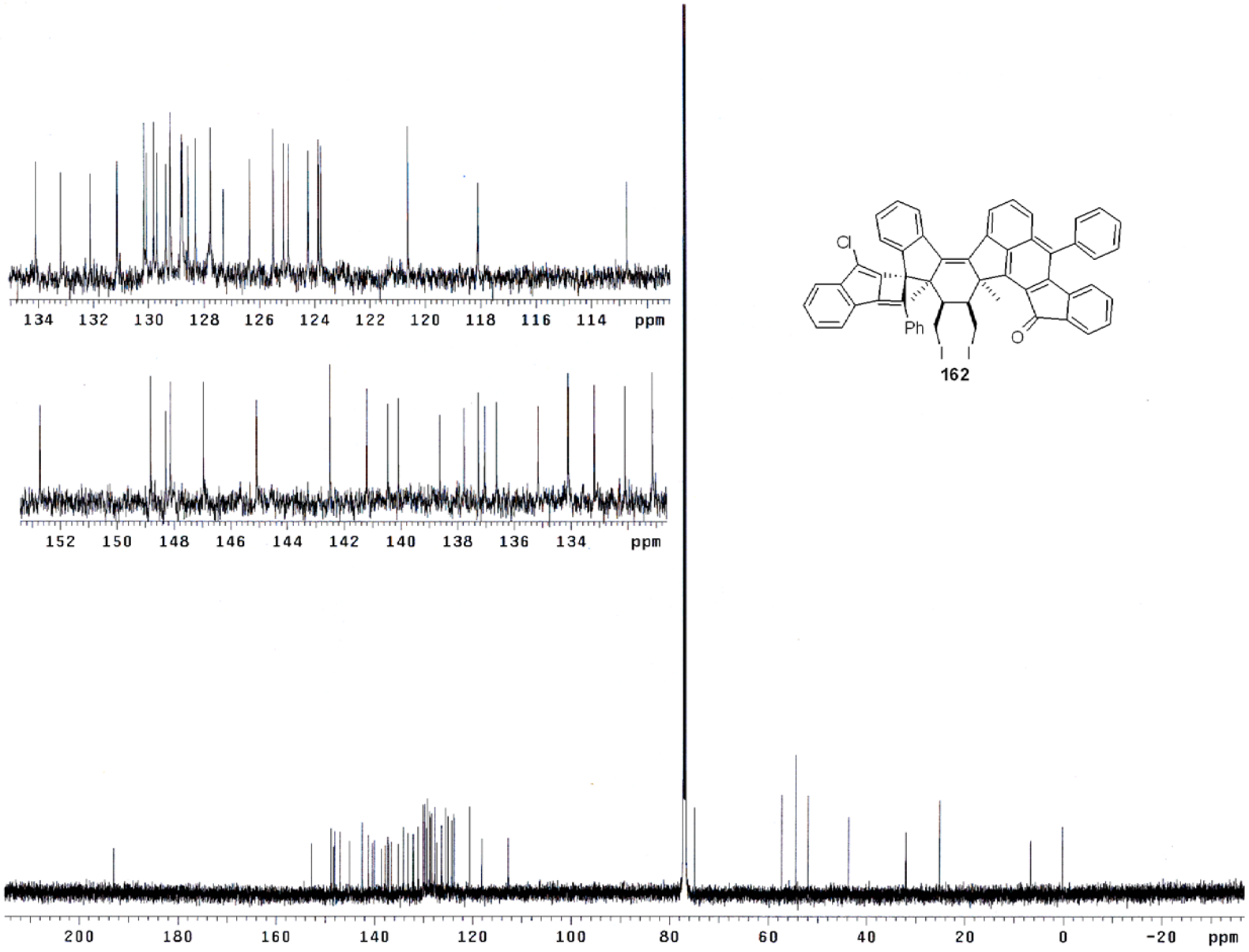


154




Cl
Ph
O
I
I
7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6 6.5 ppm
8.5 8.4 8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 ppm
13 12 11 10 9 8 7 6 5 4 3 2 1 -0 ppm

162

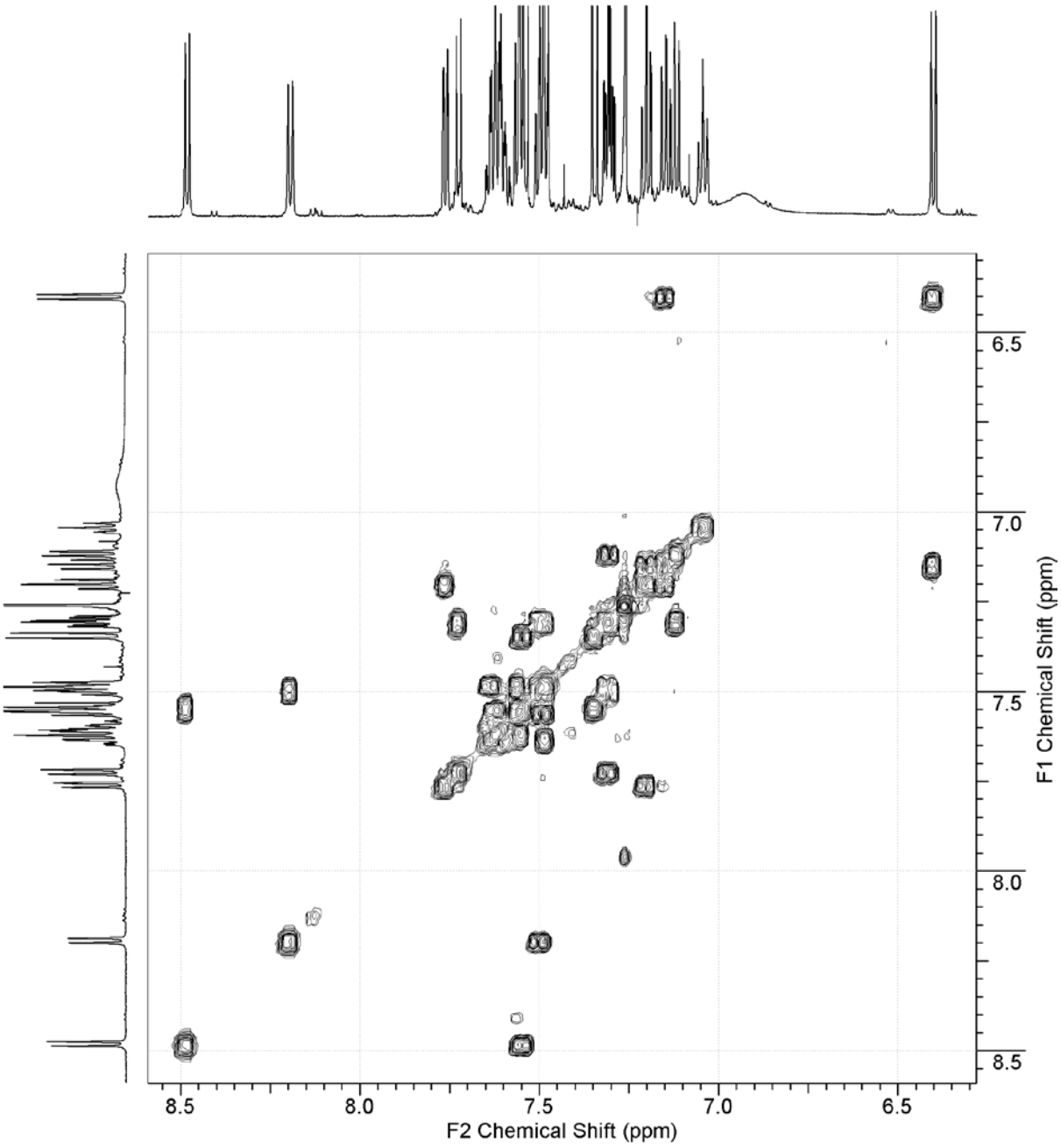

134 132 130 128 126 124 122 120 118 116 114 ppm
152 150 148 146 144 142 140 138 136 134 ppm
200 180 160 140 120 100 80 60 40 20 0 -20 ppm

Cl
Ph
O

162

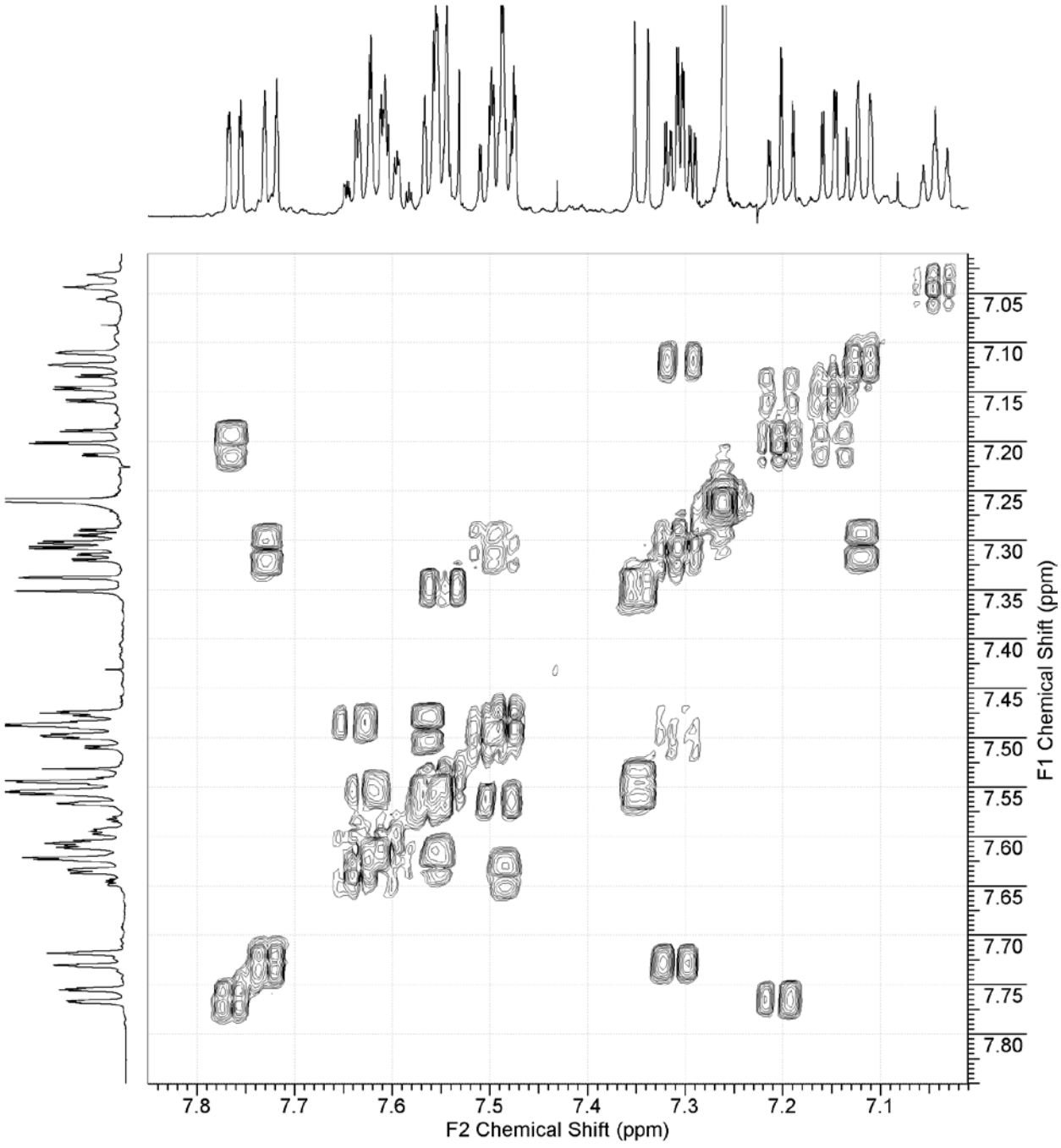
COSY spectrum of **162** in $CDCl_3$

(aromatic region)



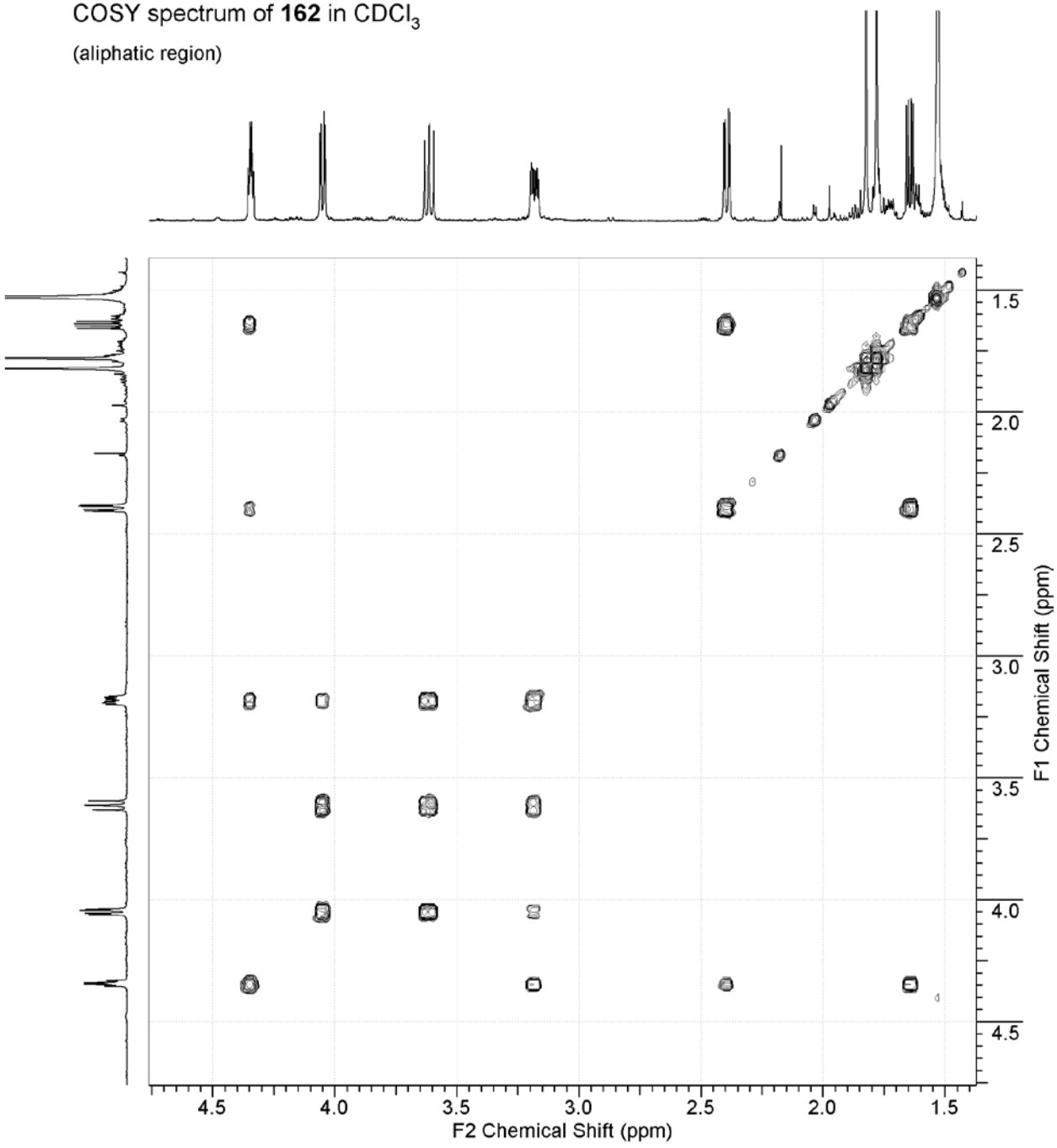
COSY spectrum of **162** in $CDCl_3$

(aromatic region)

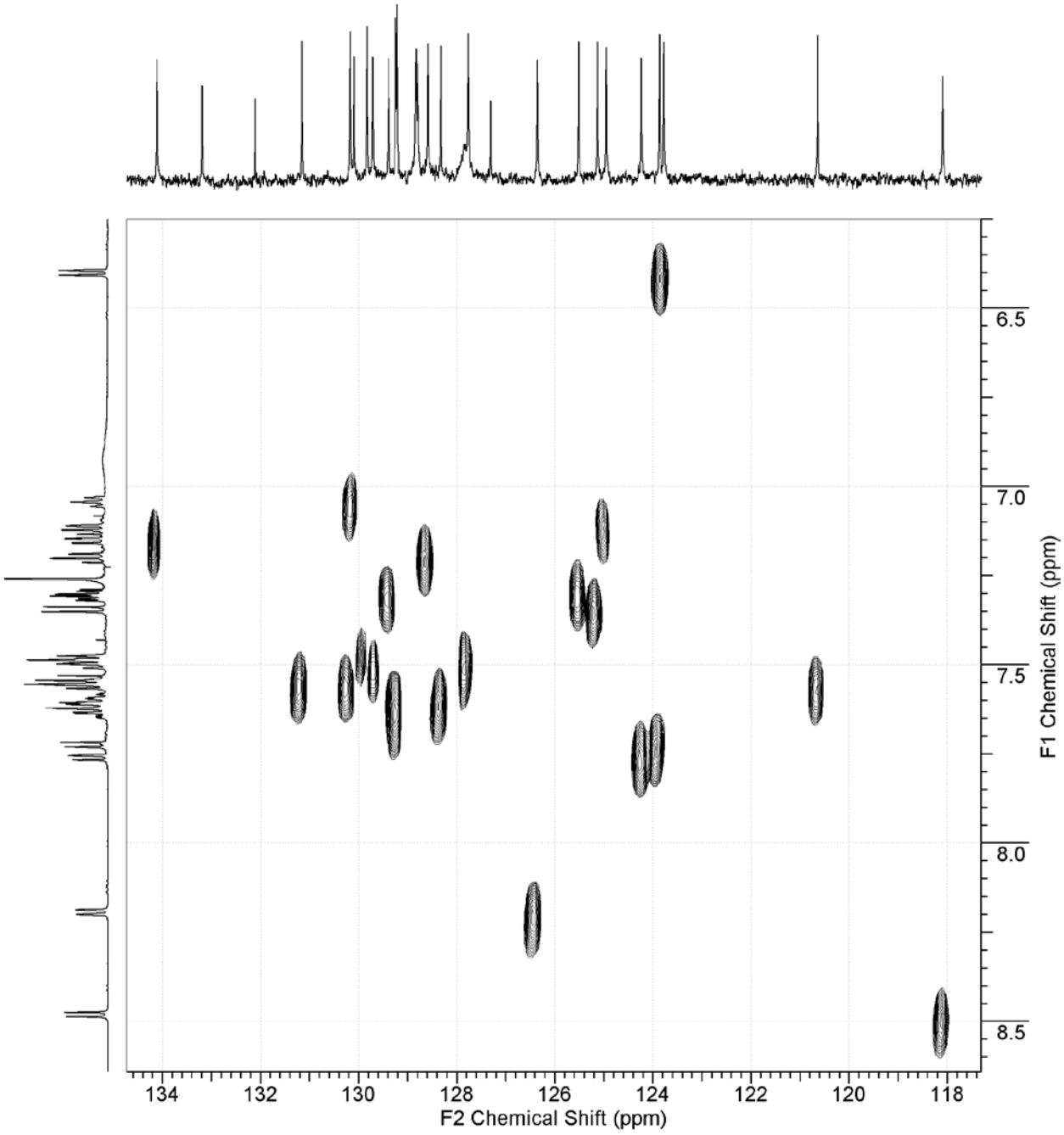


COSY spectrum of **162** in $CDCl_3$

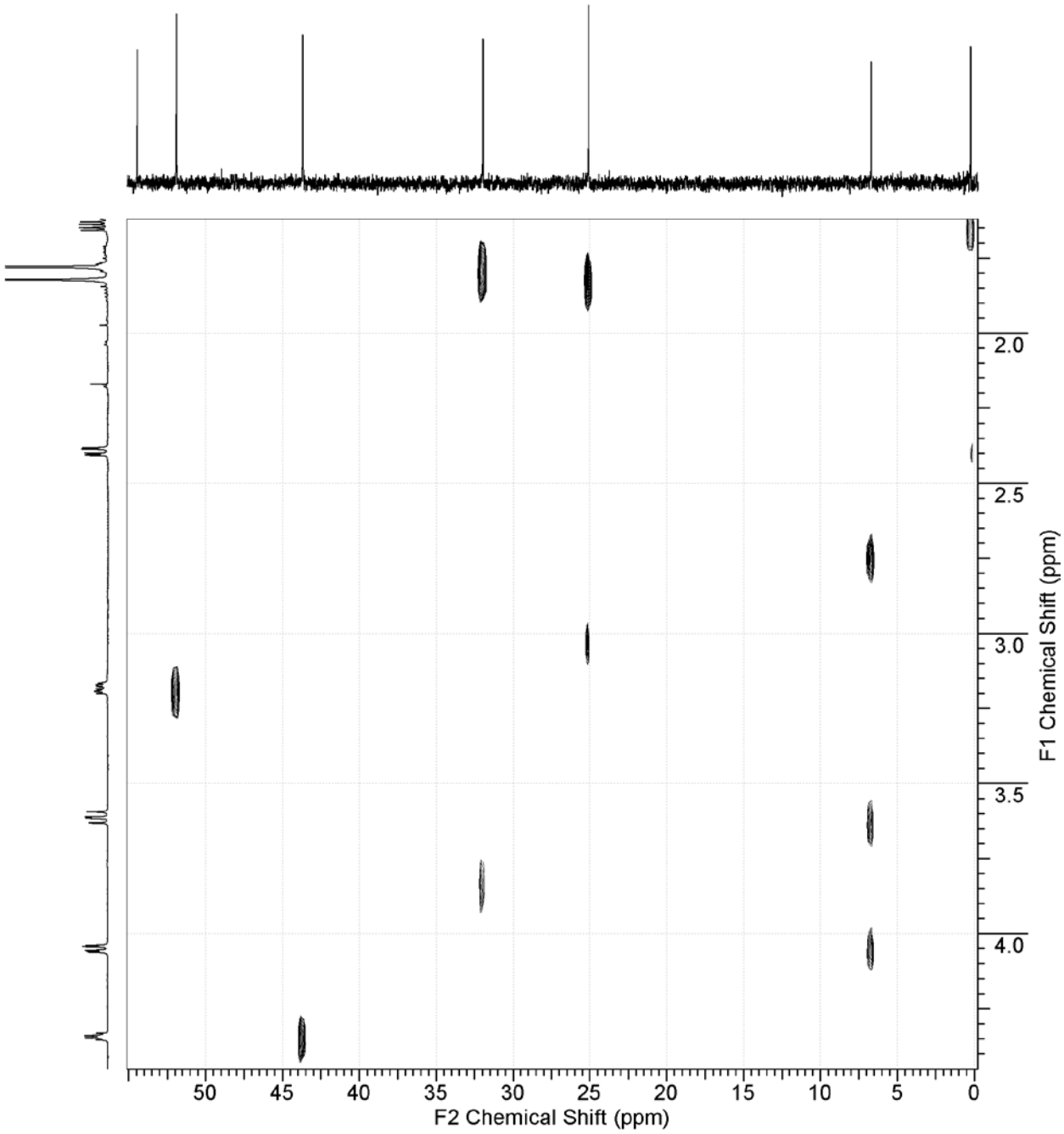
(aliphatic region)

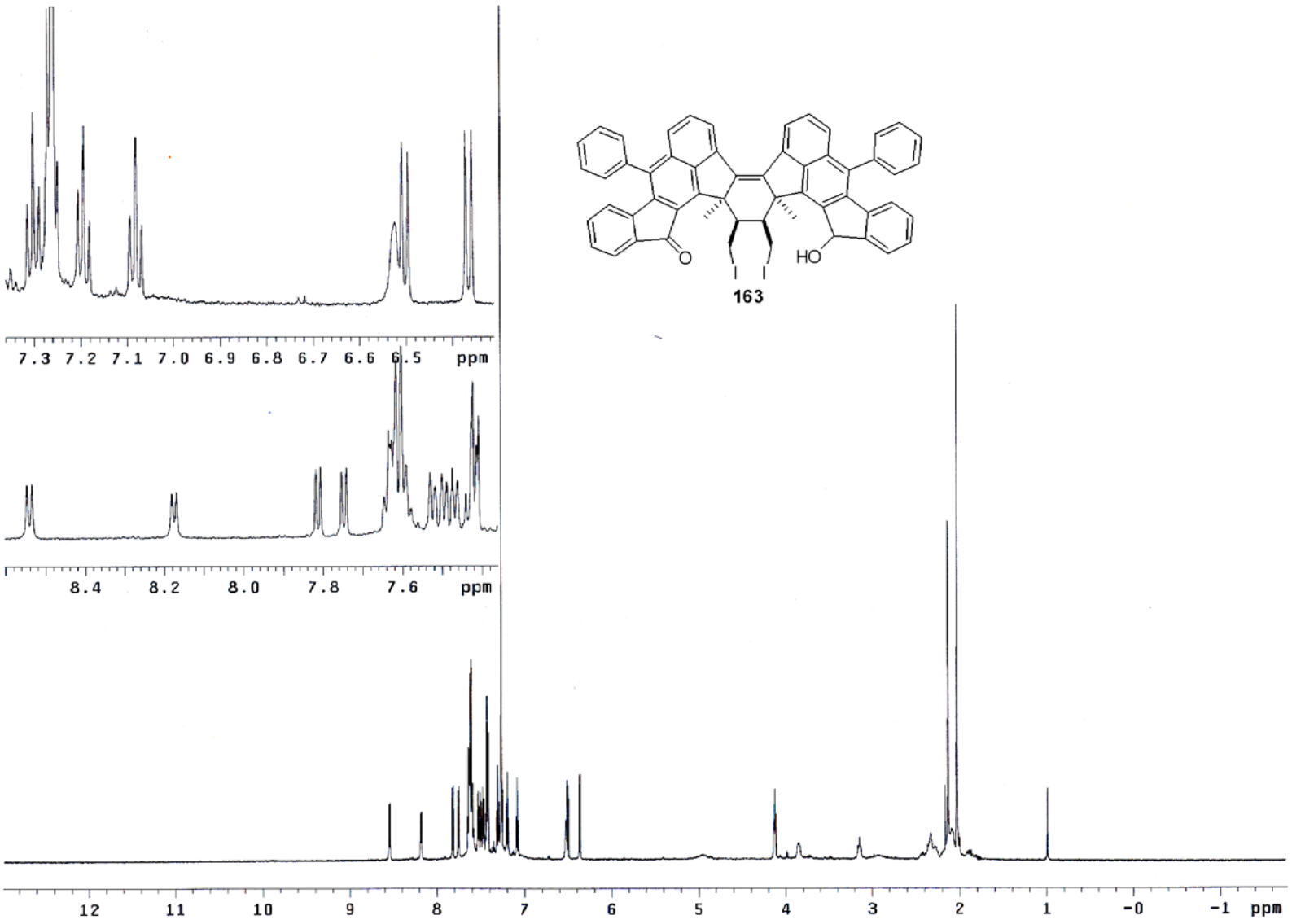


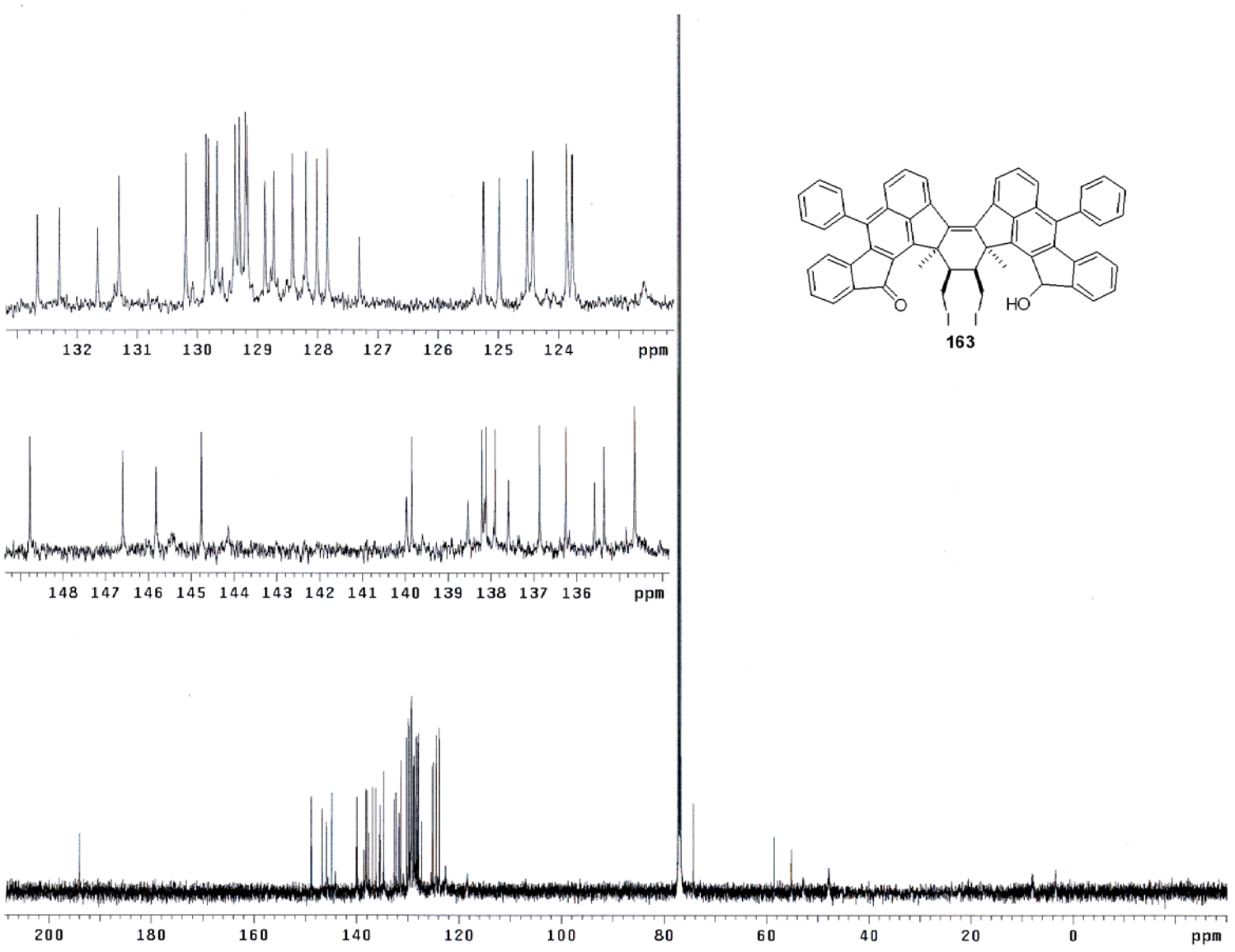
HETCOR spectrum of **162** in $CDCl_3$ (aromatic region)



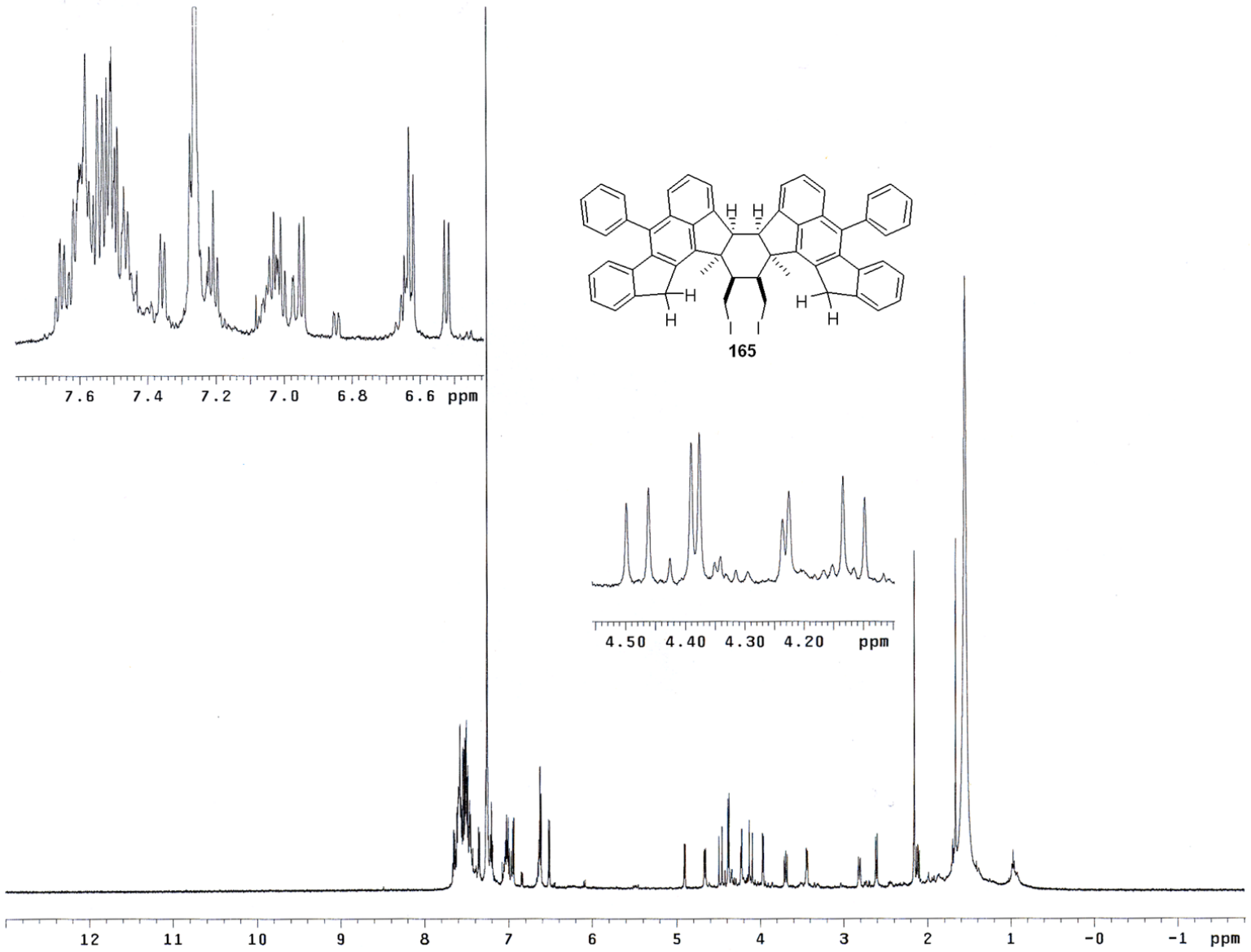
HETCOR spectrum of **162** in $CDCl_3$ (aliphatic region)




7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6 6.5 ppm
8.4 8.2 8.0 7.8 7.6 ppm
O
HO
I
I
163
12 11 10 9 8 7 6 5 4 3 2 1 -0 -1 ppm

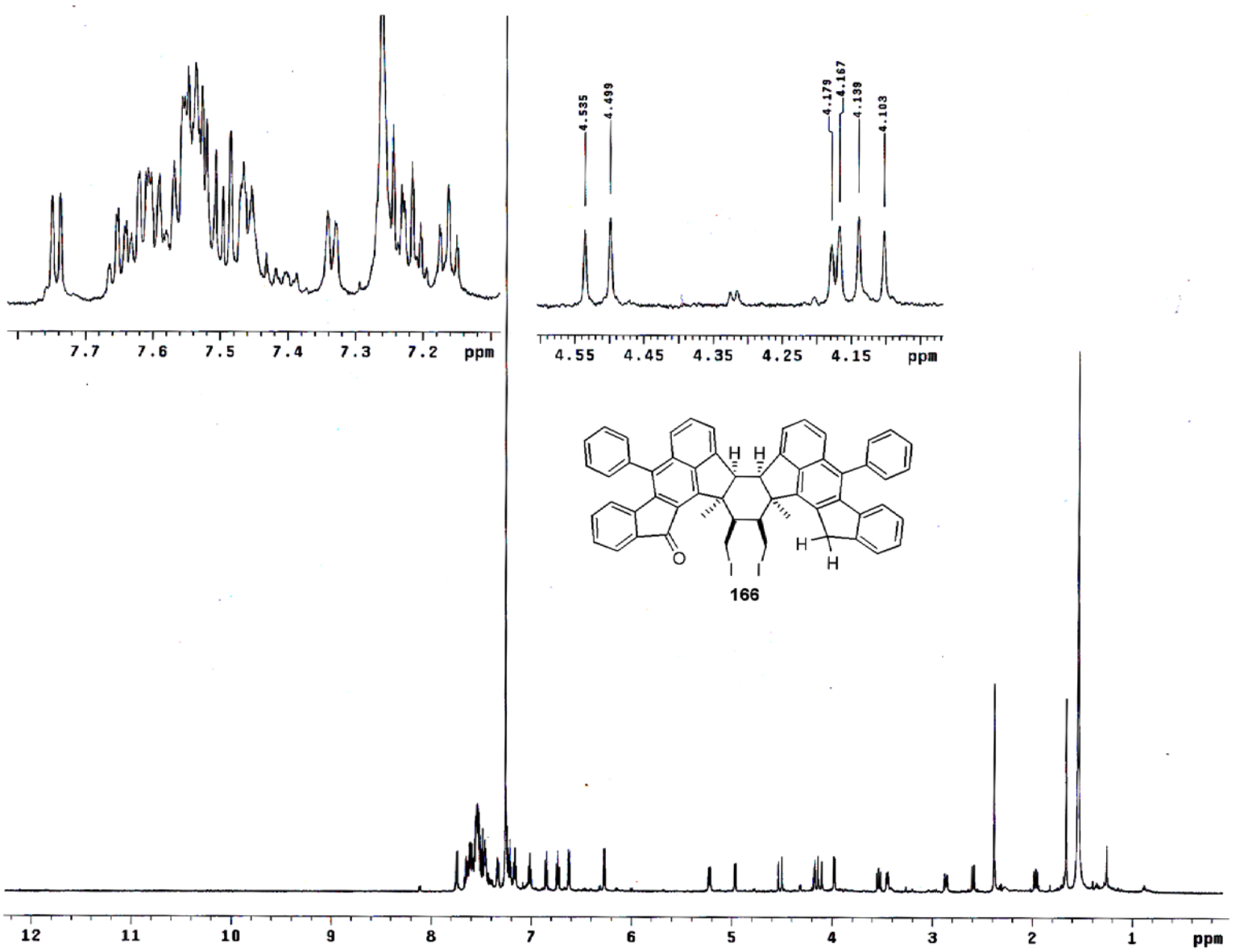

132 131 130 129 128 127 126 125 124 ppm
148 147 146 145 144 143 142 141 140 139 138 137 136 ppm
200 180 160 140 120 100 80 60 40 20 0 ppm
O
HO

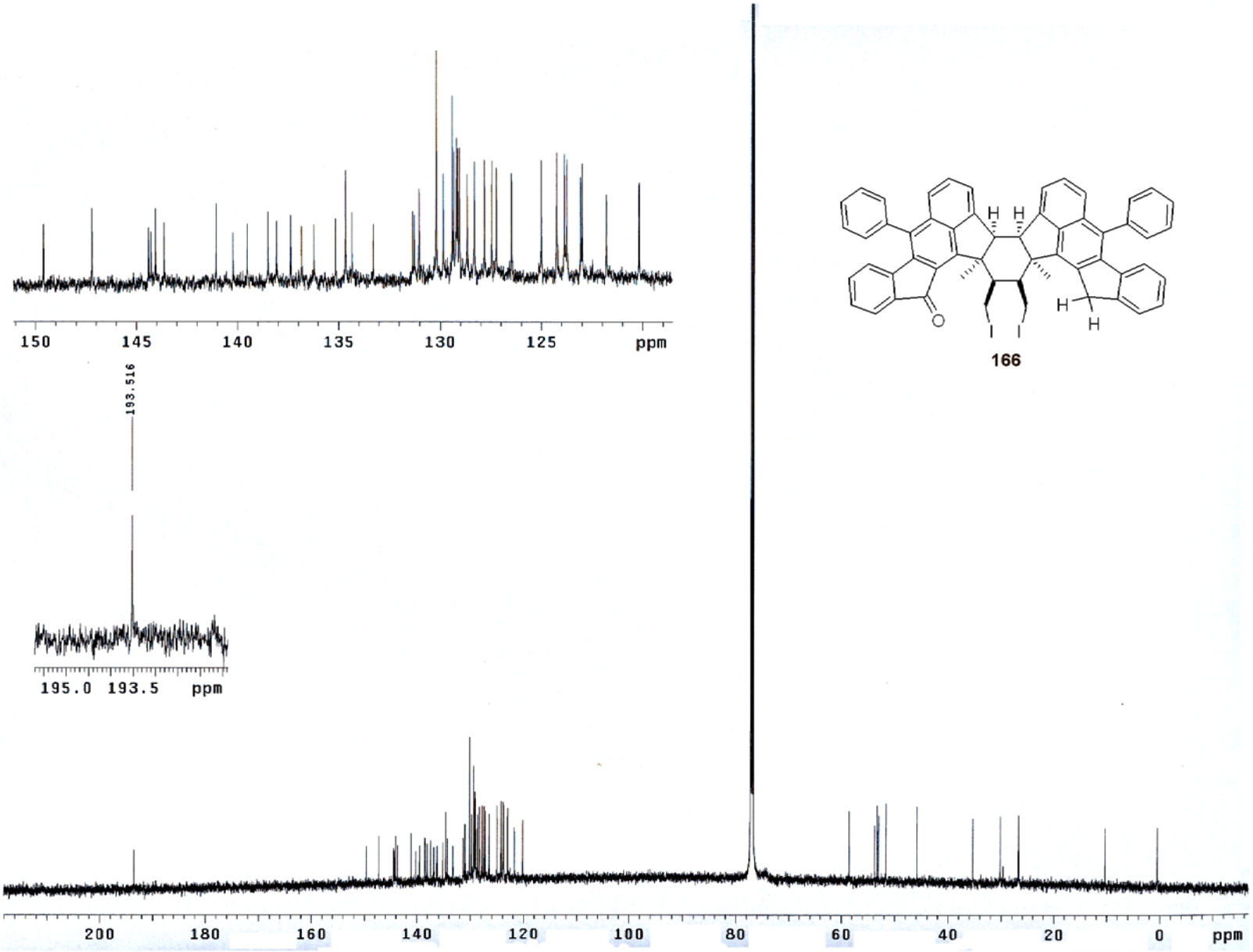
163


7.6 7.4 7.2 7.0 6.8 6.6 ppm
4.50 4.40 4.30 4.20 ppm
12 11 10 9 8 7 6 5 4 3 2 1 -0 -1 ppm

165

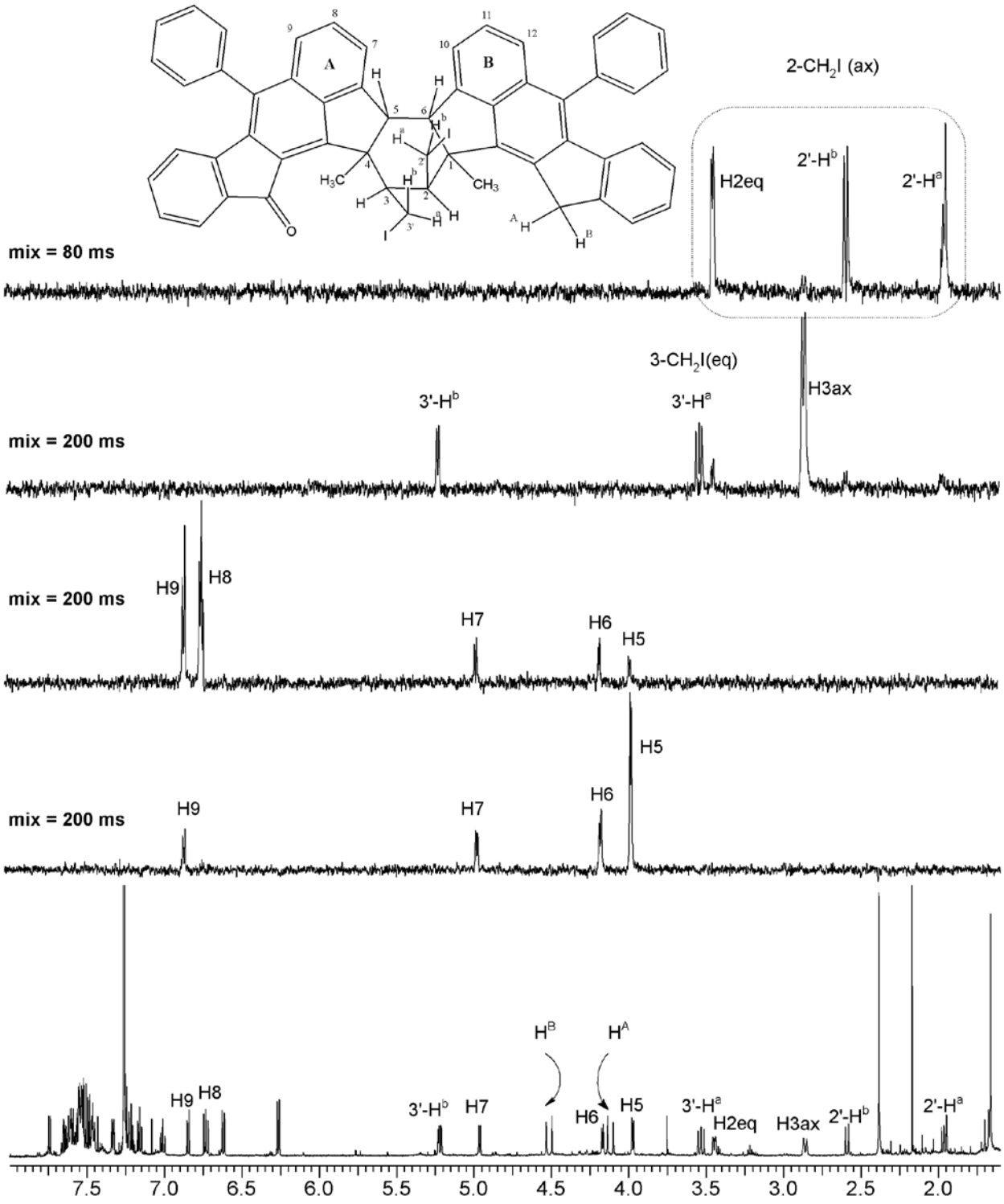
165
ppm
142 140 138 136 134 132 130 128 126 124
200 180 160 140 120 100 80 60 40 20 0
ppm


4.535
4.499
4.179
4.167
4.139
4.103
7.7
7.6
7.5
7.4
7.3
7.2
ppm
4.55
4.45
4.35
4.25
4.15
ppm
H
H
H
H
O
I
I
166
12
11
10
9
8
7
6
5
4
3
2
1
ppm

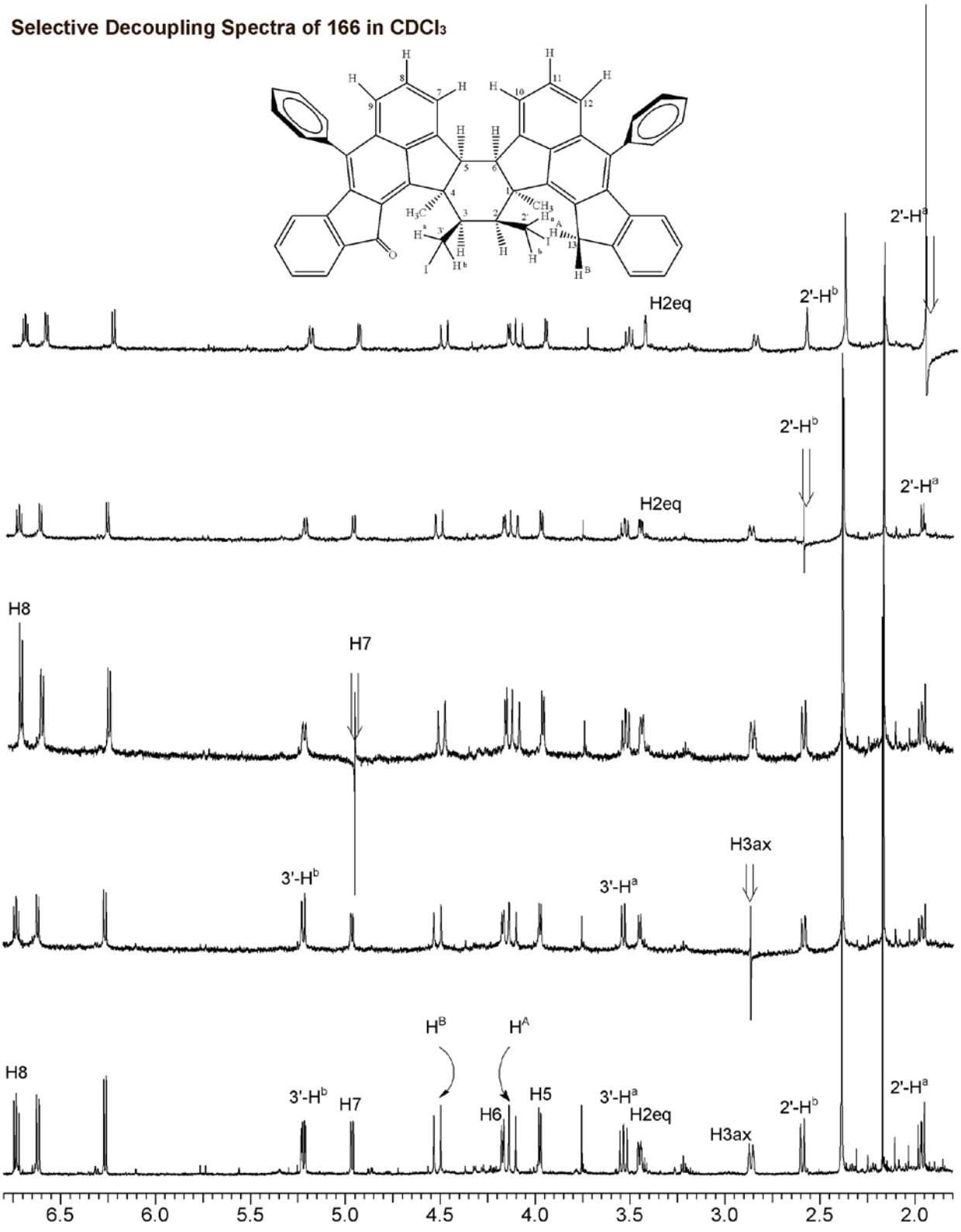

150
145
140
135
130
125
ppm
193.516
195.0
193.5
ppm
200
180
160
140
120
100
80
60
40
20
0
ppm
H
H
H
H
O
I
I

166

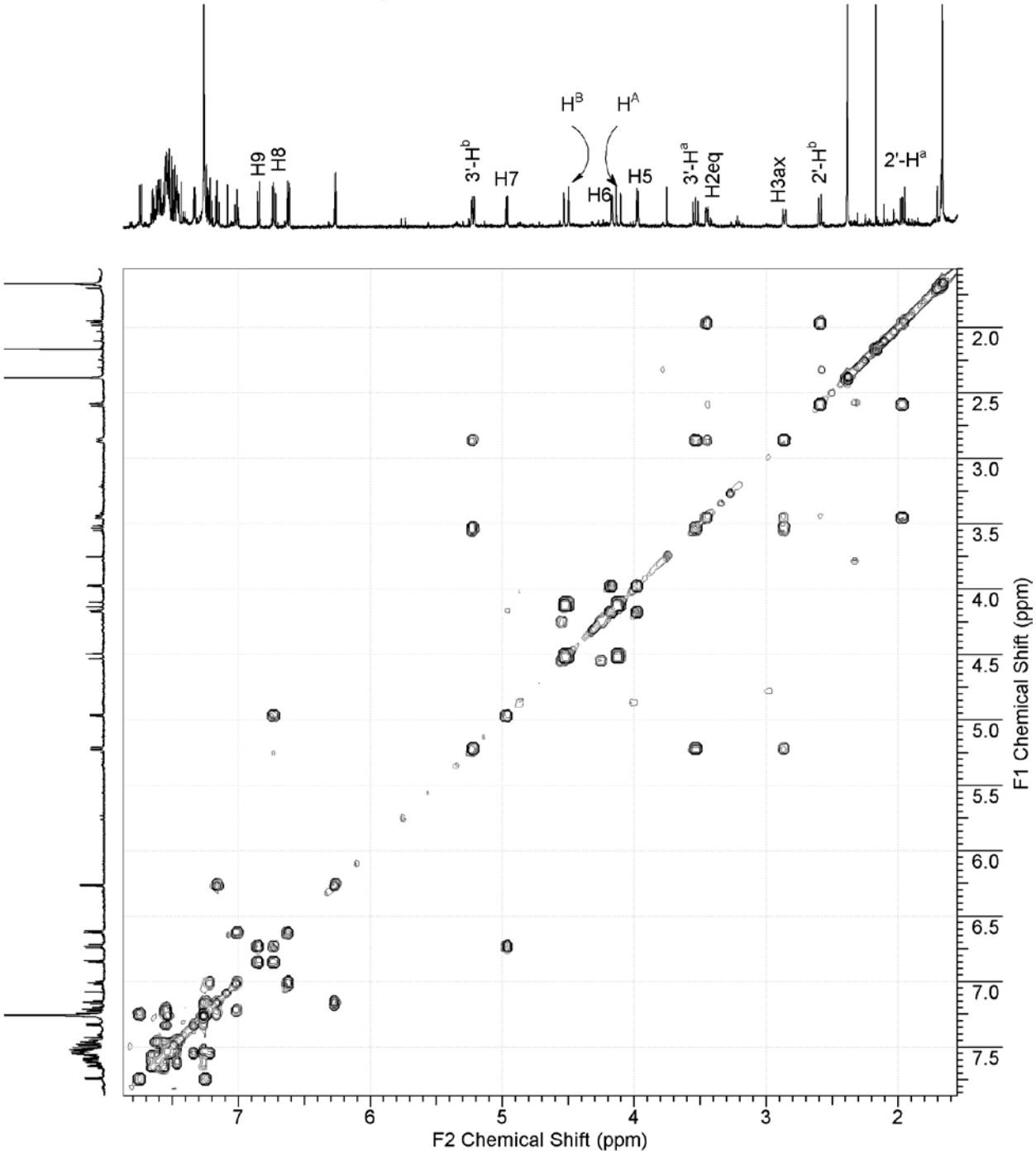
1D TOCSY spectra of **166** in $CDCl_3$



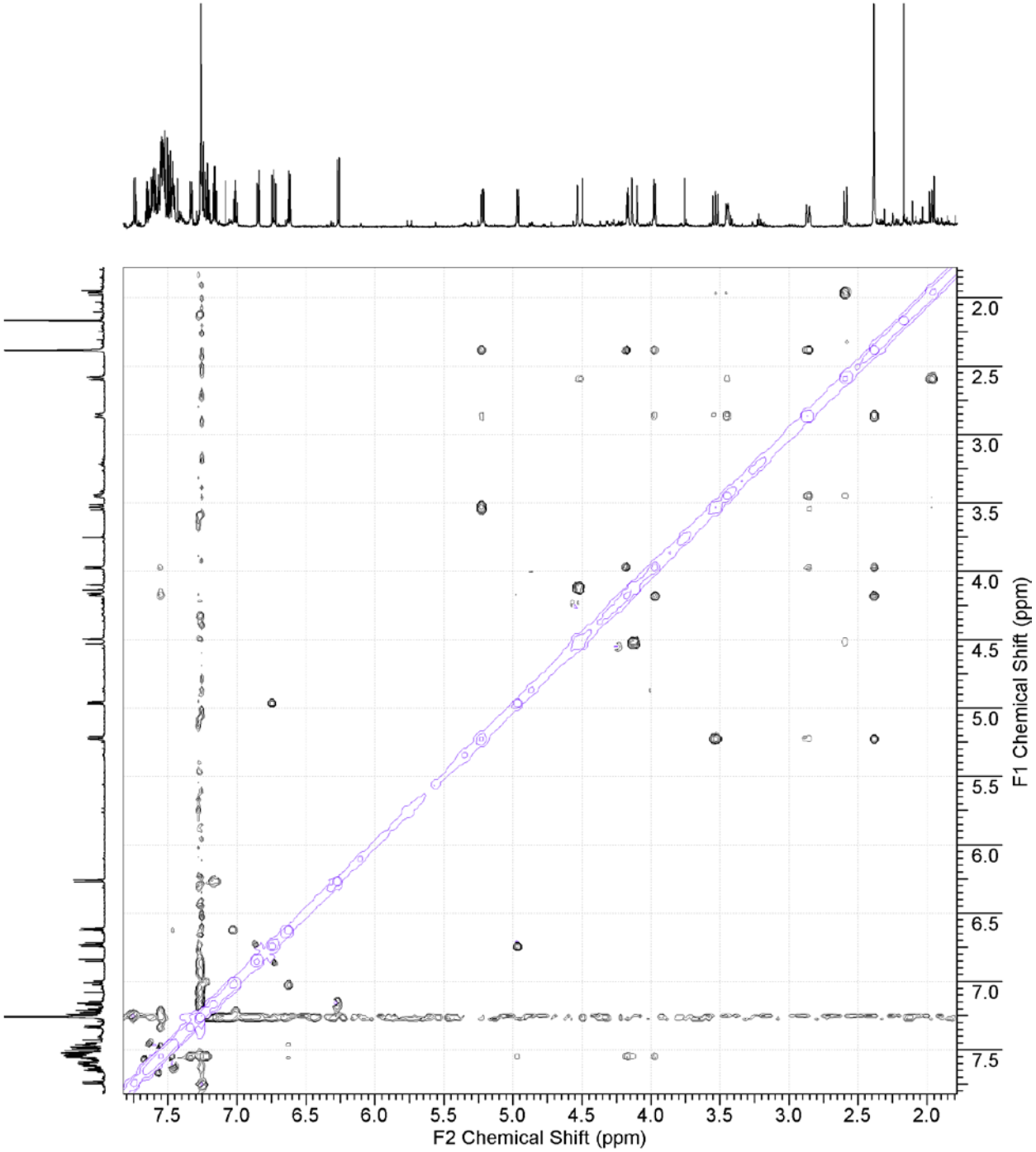
Selective Decoupling Spectra of 166 in $CDCl_3$



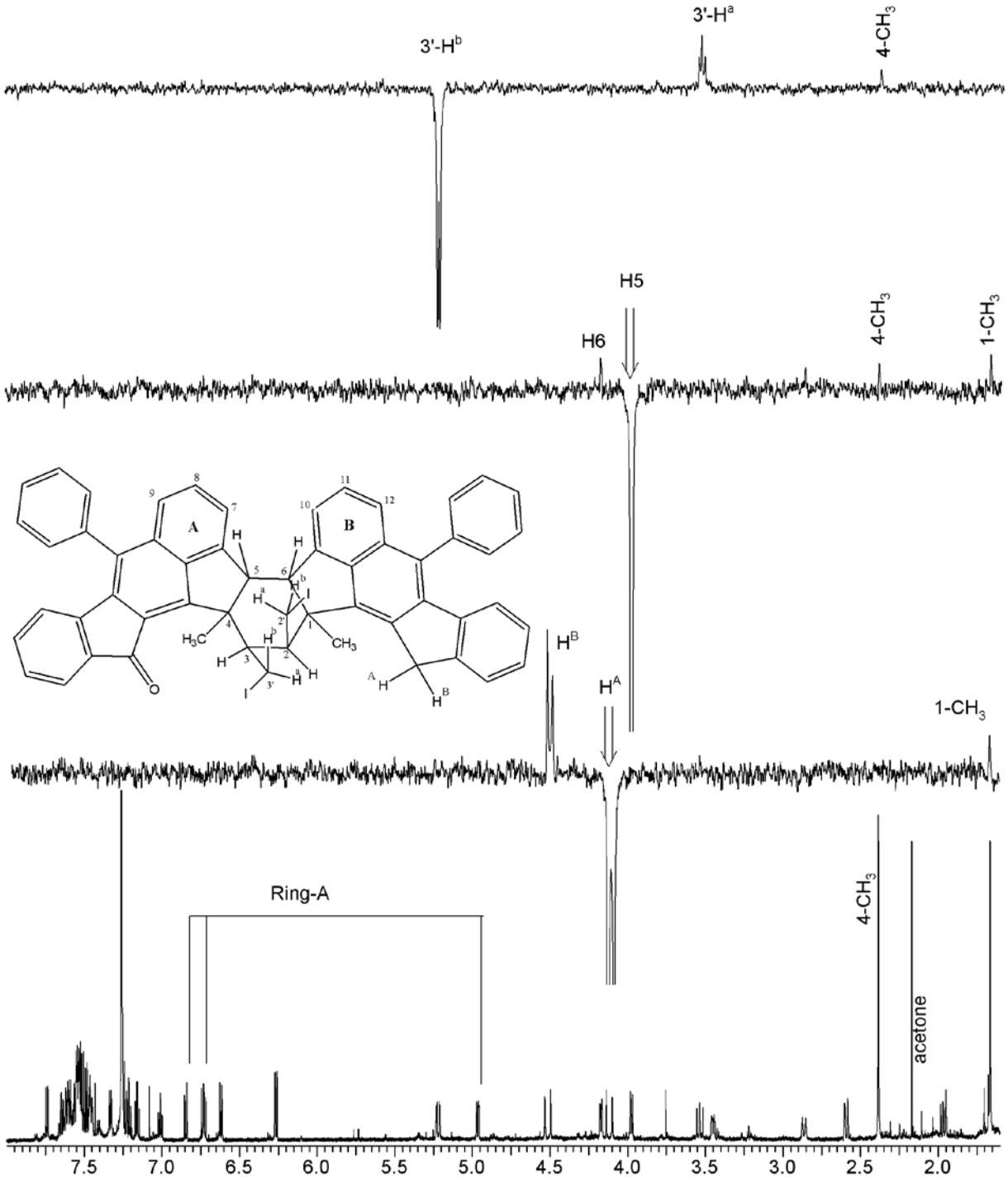
COSY spectrum of **166** in $CDCl_3$



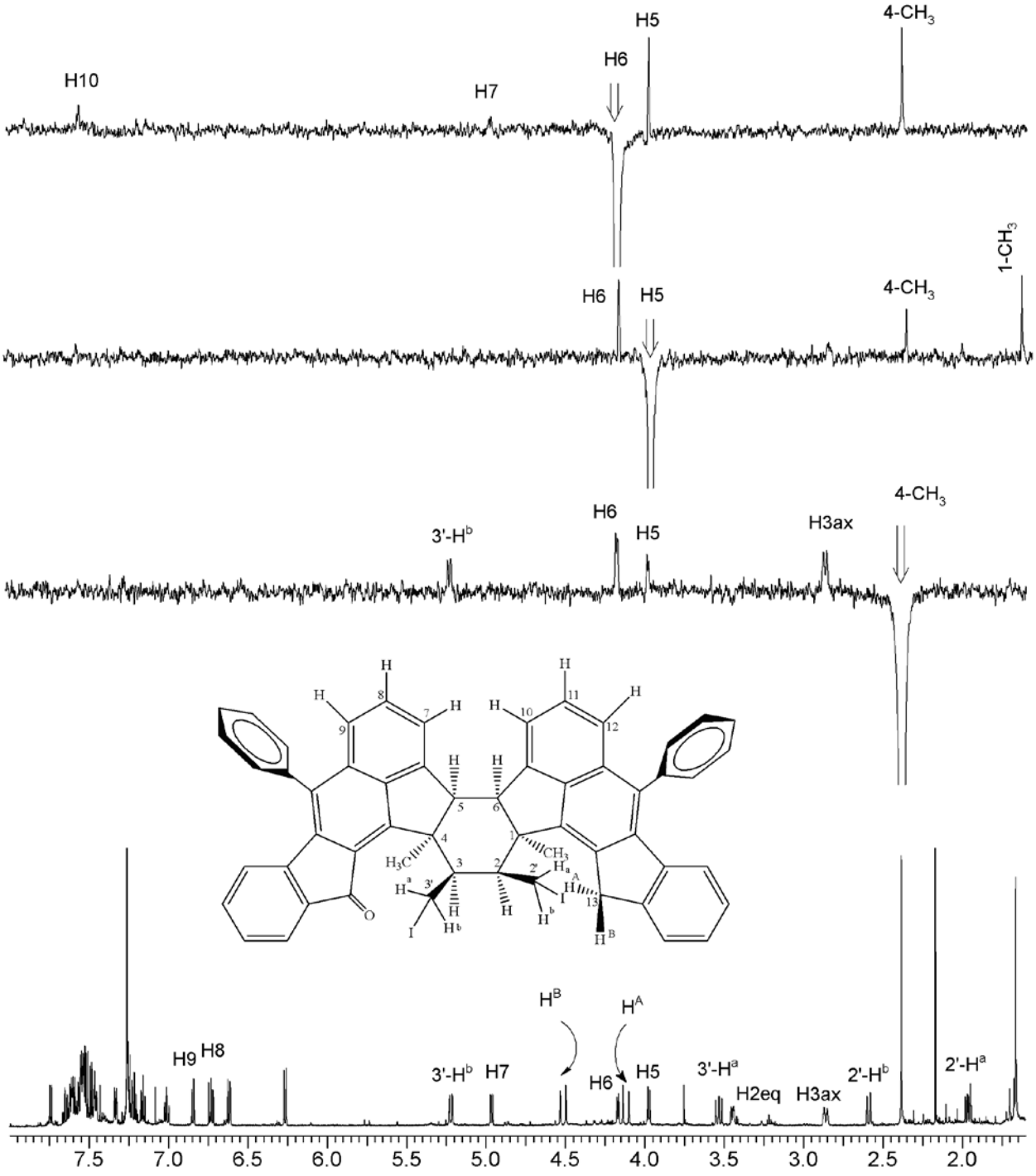
NOESY spectrum of **166** in $CDCl_3$



DPFGSENOE spectra of **166** in $CDCl_3$

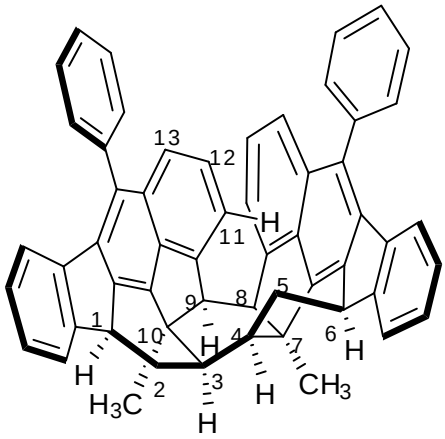


DPFGSENOE spectra of **166** in $CDCl_3$



Chemical Shifts (δ/ppm) and Coupling Constants (J/Hz) in **167**.

Protons	$CDCl_3$[b]	C_6D_6	Coupling constant (in Hz)[a]
H1	4.16	4.17	$J_{1,2\alpha} = 5.4$ $J_{1,2\beta} = 12.14$
H2α	1.68	1.56	$J_{2\alpha,2\beta} = 14.68$ $J_{2\alpha,3} = 0.01$
H2β	3.37	3.04	$J_{2\beta,3} = 8.41$
H3	3.02	2.78	$J_{3,4} = 5.42$
H4	1.82	1.63	$J_{4,5\alpha} = 13.23$ $J_{4,5\beta} = 4.53$
H5α	-3.4	-3.15	$J_{5\alpha,5\beta} = 12.68$ $J_{5\alpha,6} = 11.17$
H5β	0.28	0.20	$J_{5\beta,6} = 4.36$
H6	2.91	2.80	-
H8	4.11	4.02	$J_{8,9} = 8.00$
H9	4.07	3.94	-
7-CH_3	1.50	1.42	-
10-CH_3	1.70	1.55	-
H11	3.89	-	-
H12	6.25	-	-
H13	6.40	-	-

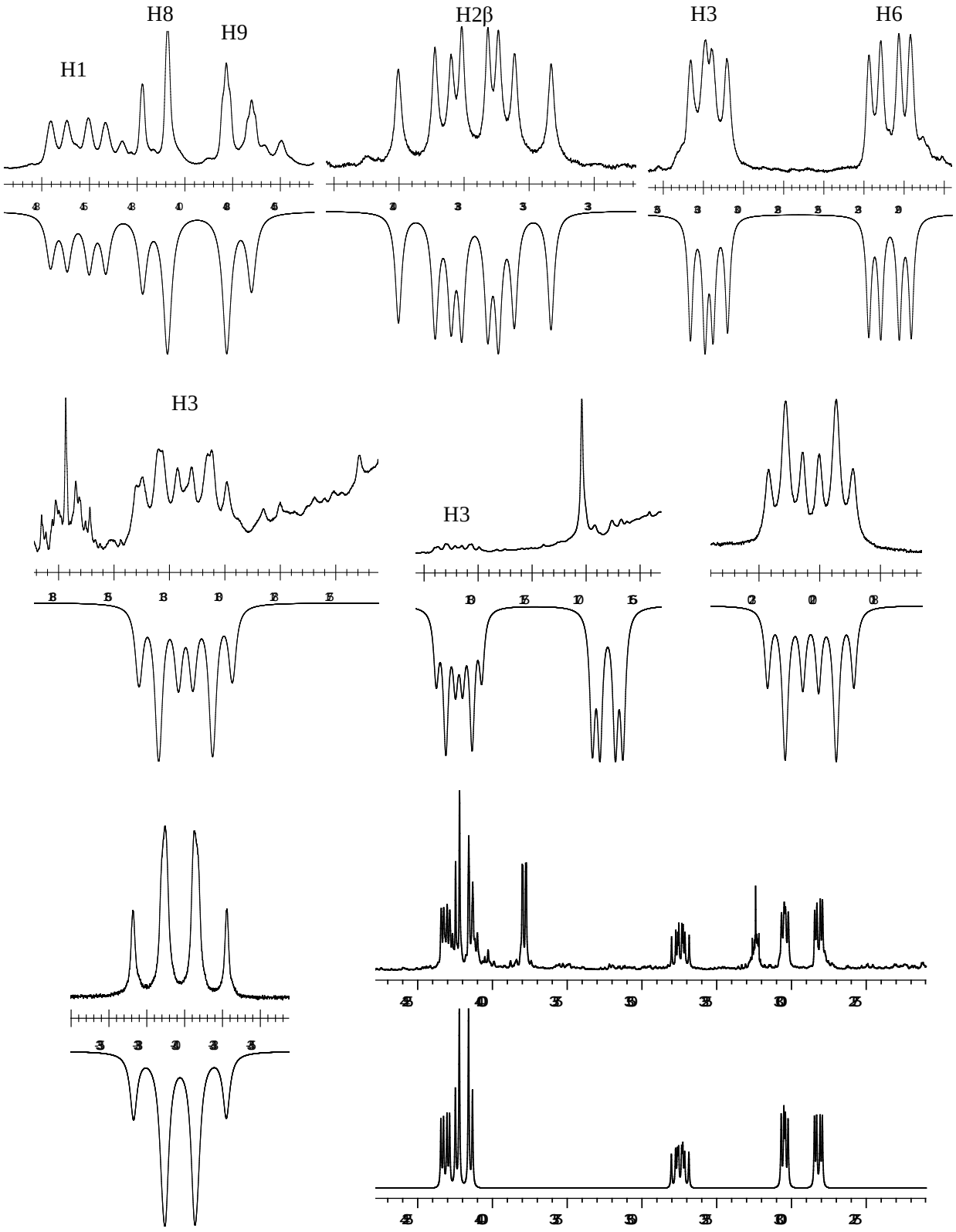


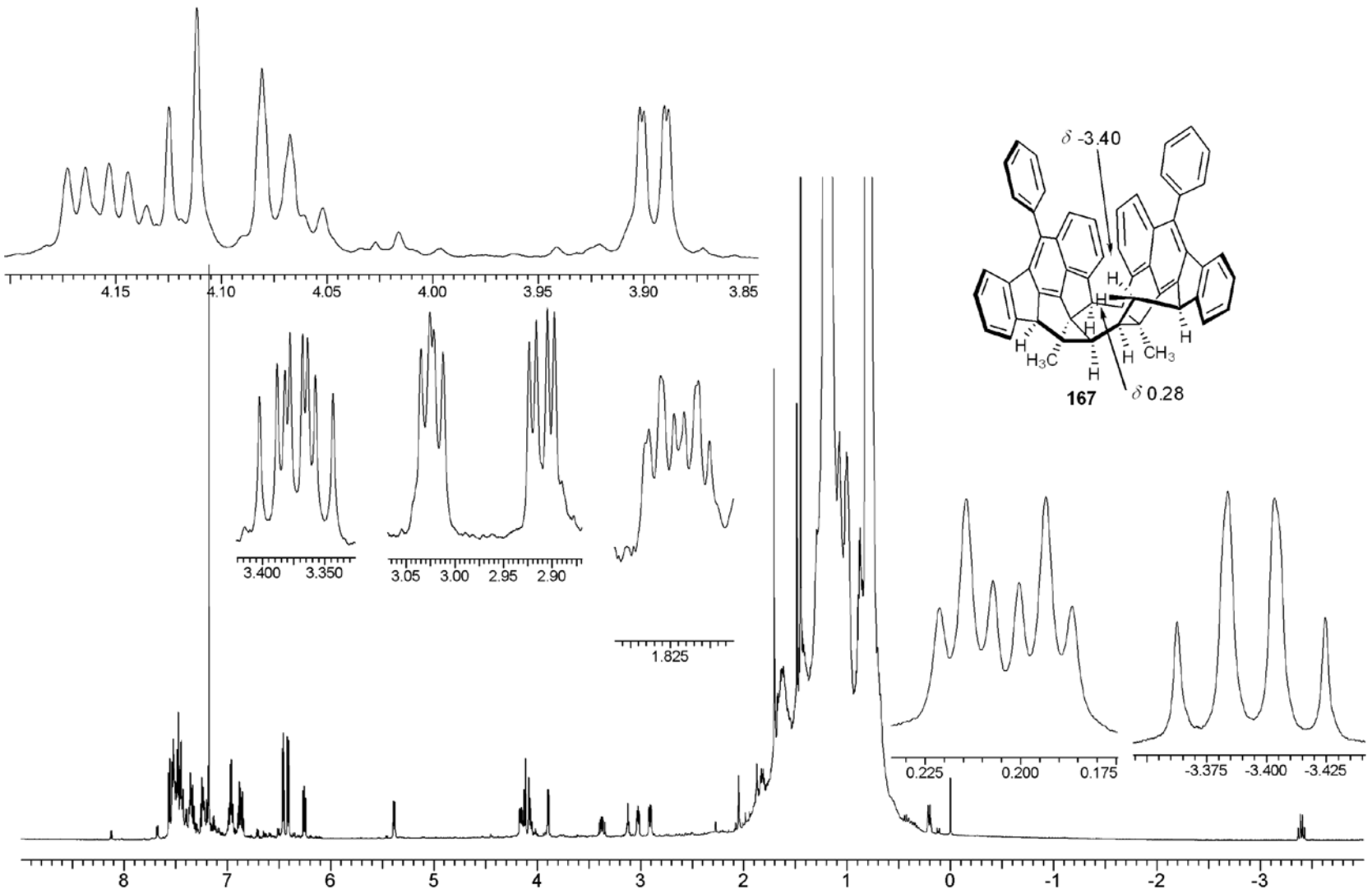
167

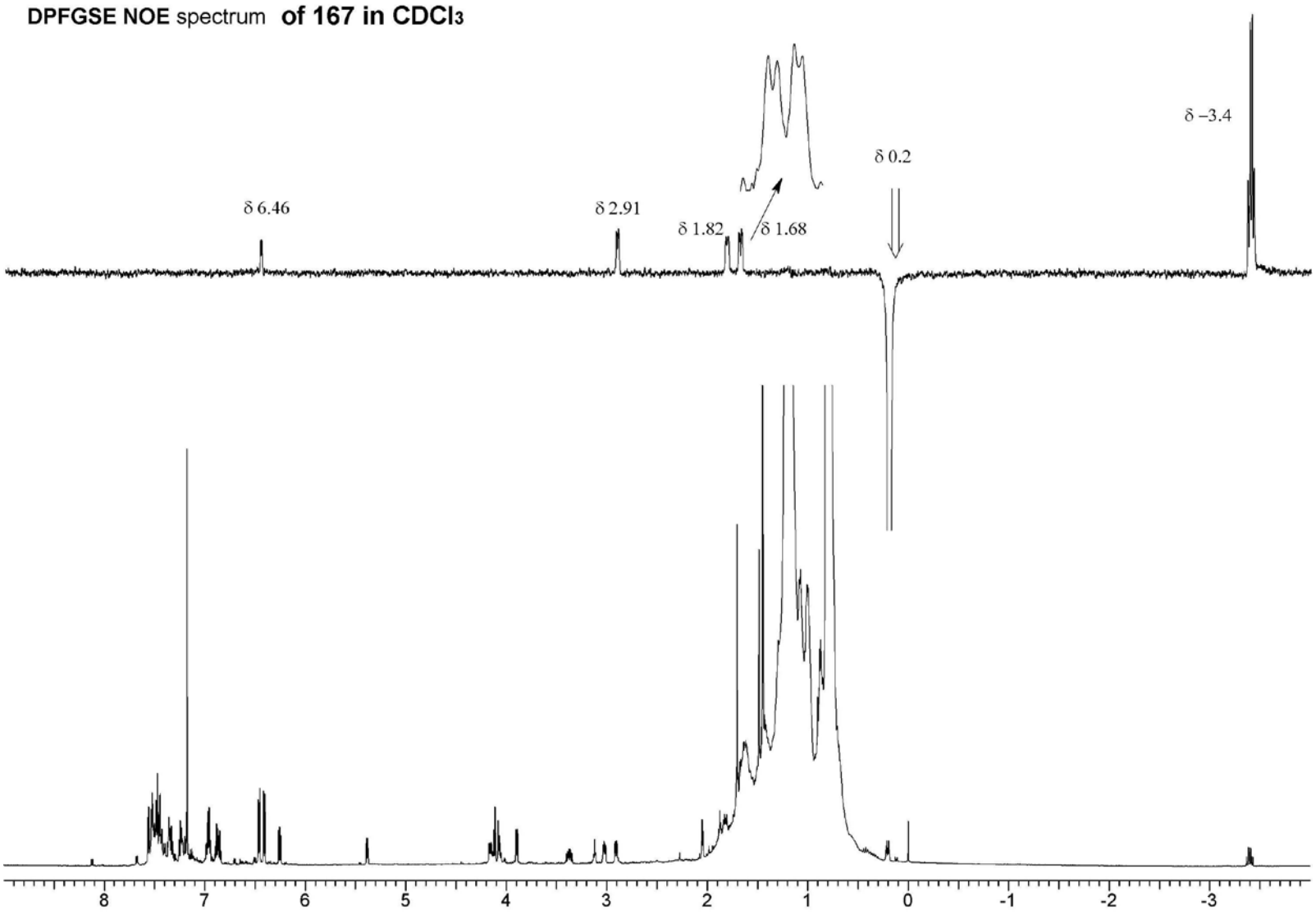
[a] in $CDCl_3$

[b] data were recorded as the reference set to TMS (^1H δ 0.00)

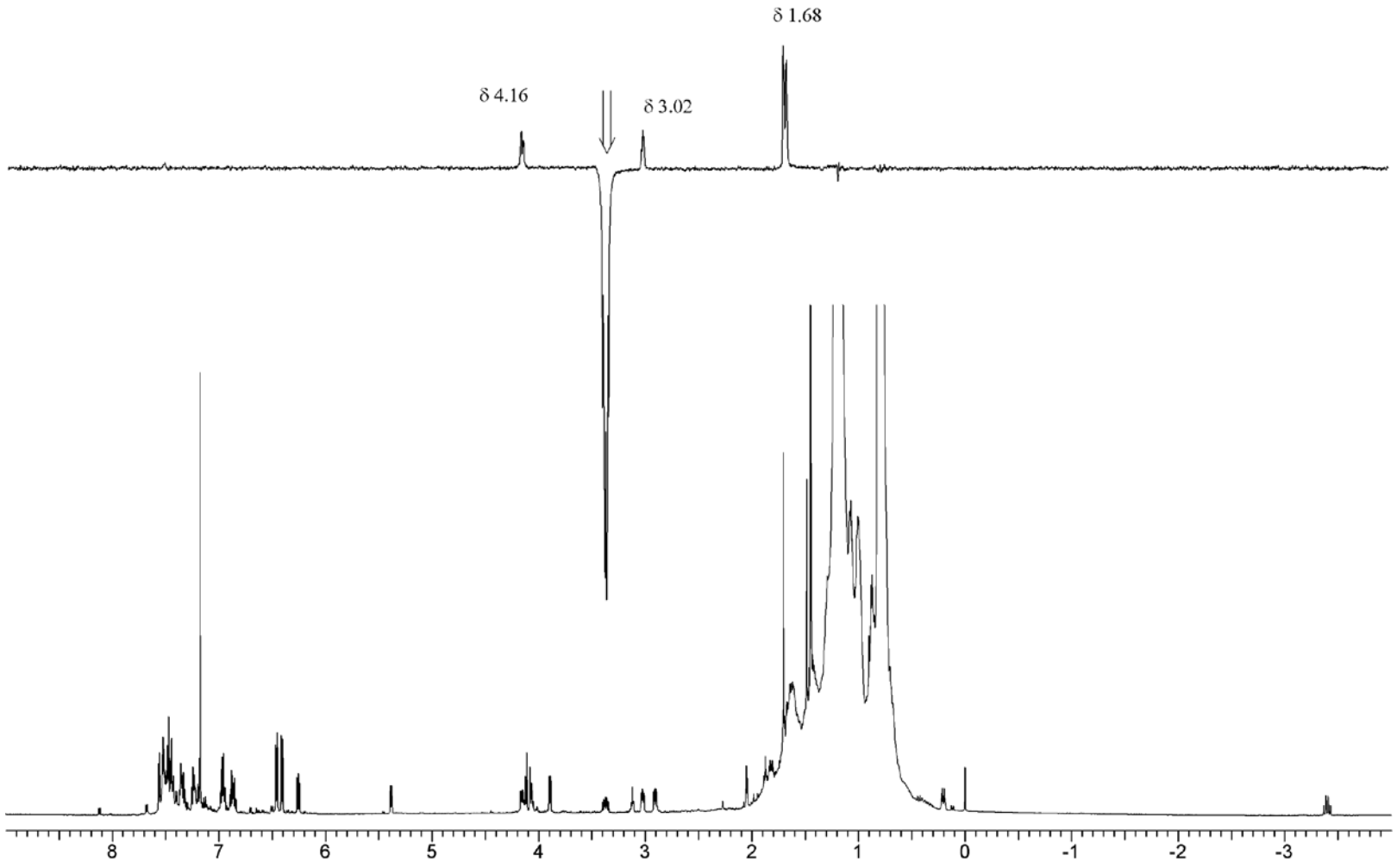
gNMR-Simulated ^{1}H NMR Spectra of **167** in $CDCl_3$ (top – experimental, bottom – calculated)



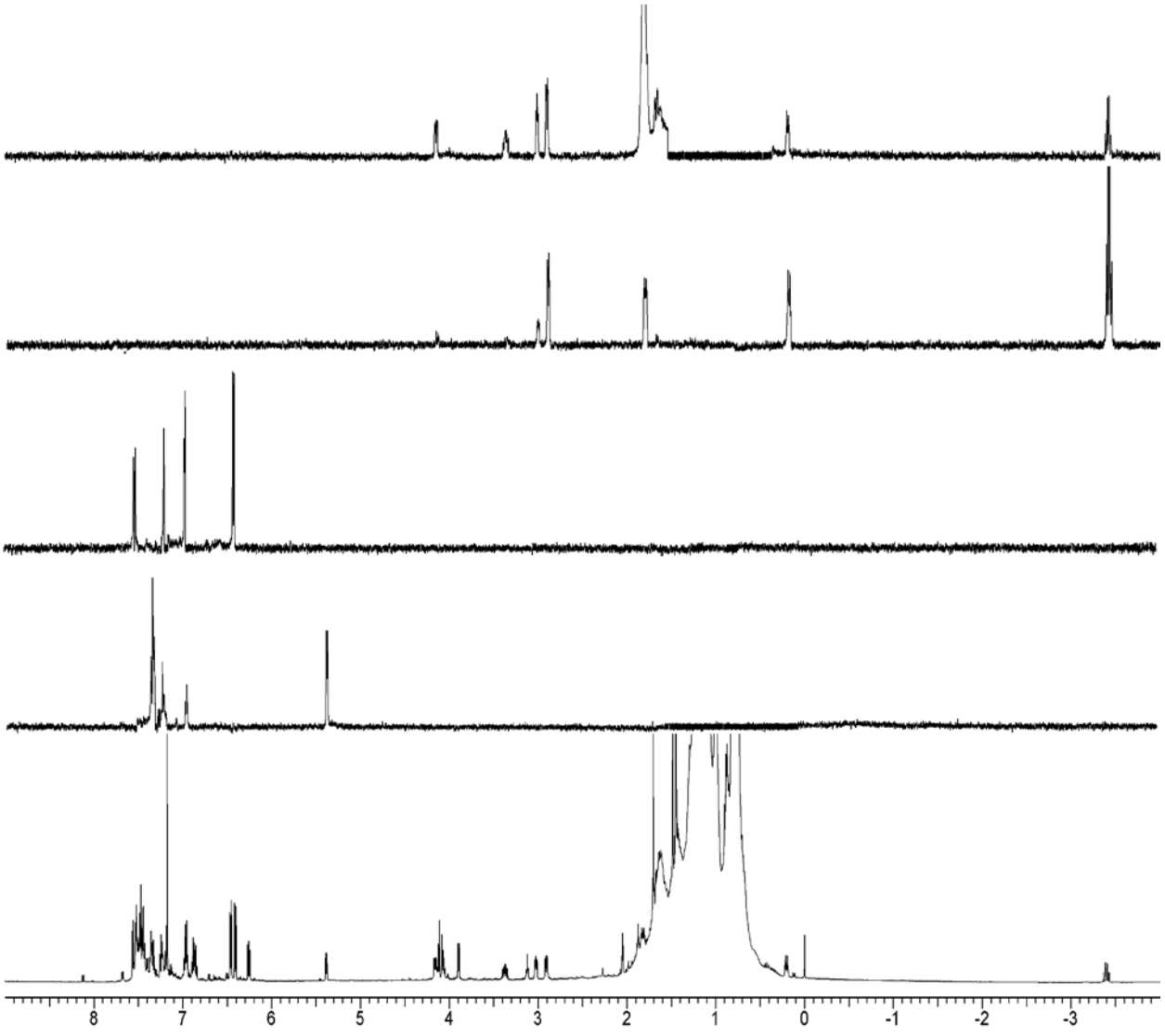

δ -3.40
δ 0.28
167
H
H
H
H
H
H
H3C
CH3
4.15
4.10
4.05
4.00
3.95
3.90
3.85
3.400
3.350
3.05
3.00
2.95
2.90
1.825
0.225
0.200
0.175
-3.375
-3.400
-3.425
8
7
6
5
4
3
2
1
0
-1
-2
-3


DPFGSE NOE spectrum of 167 in CDCl3
δ 6.46
δ 2.91
δ 1.82
δ 1.68
δ 0.2
δ −3.4
8
7
6
5
4
3
2
1
0
-1
-2
-3

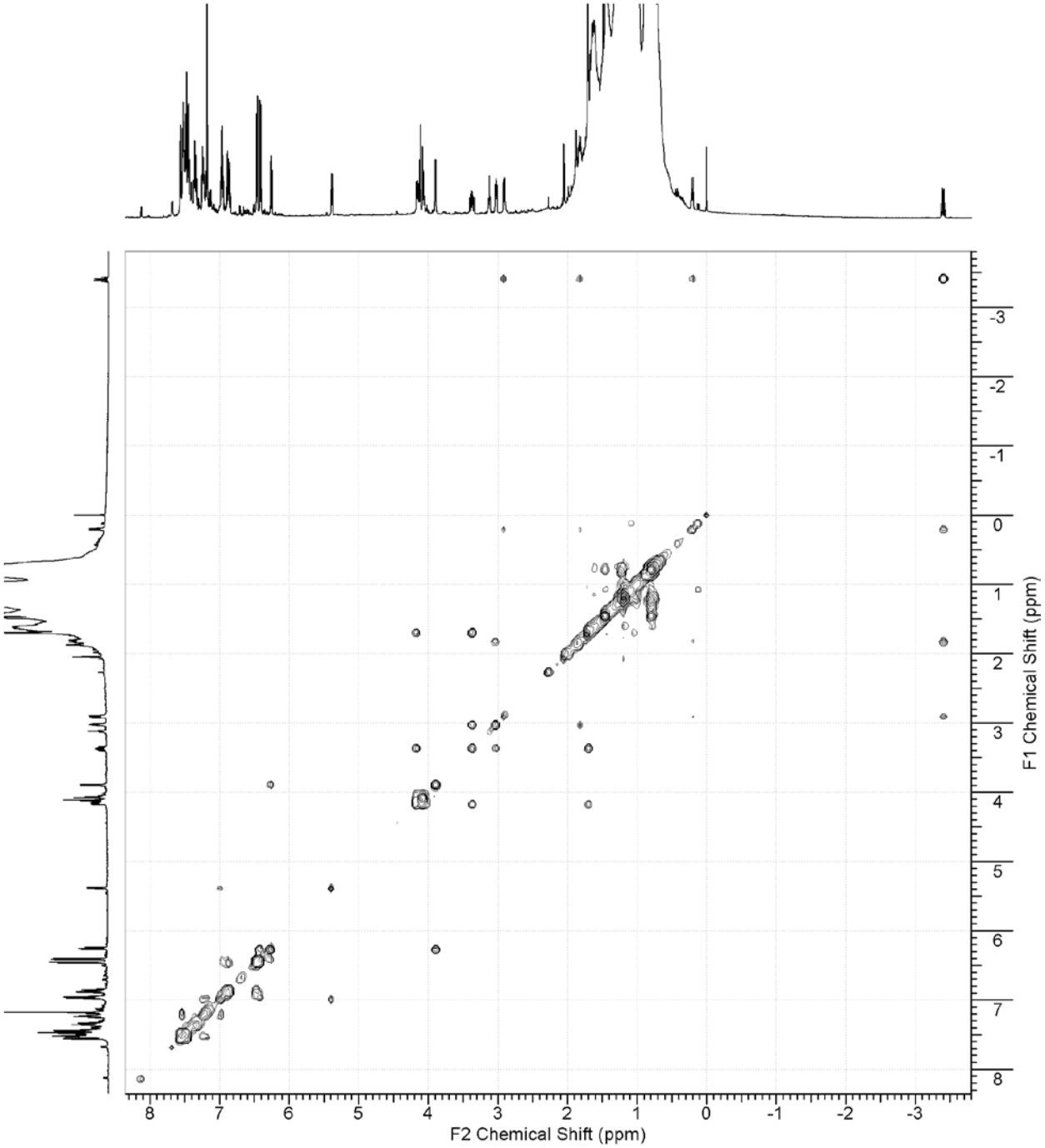
DPFGSE NOE spectrum **of 167 in $CDCl_3$**



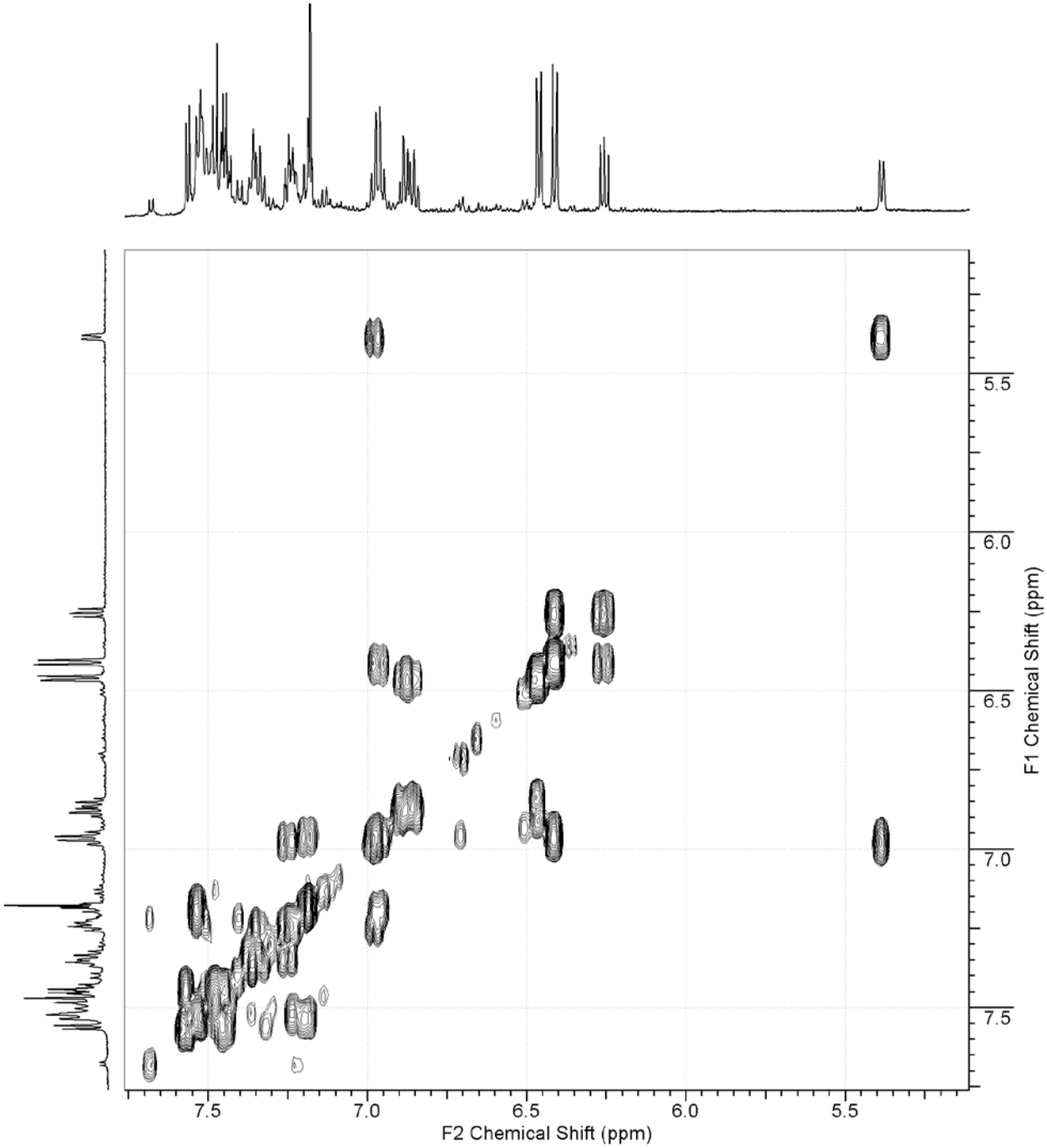
1D TOCSY Spectra of 167 in $CDCl_3$



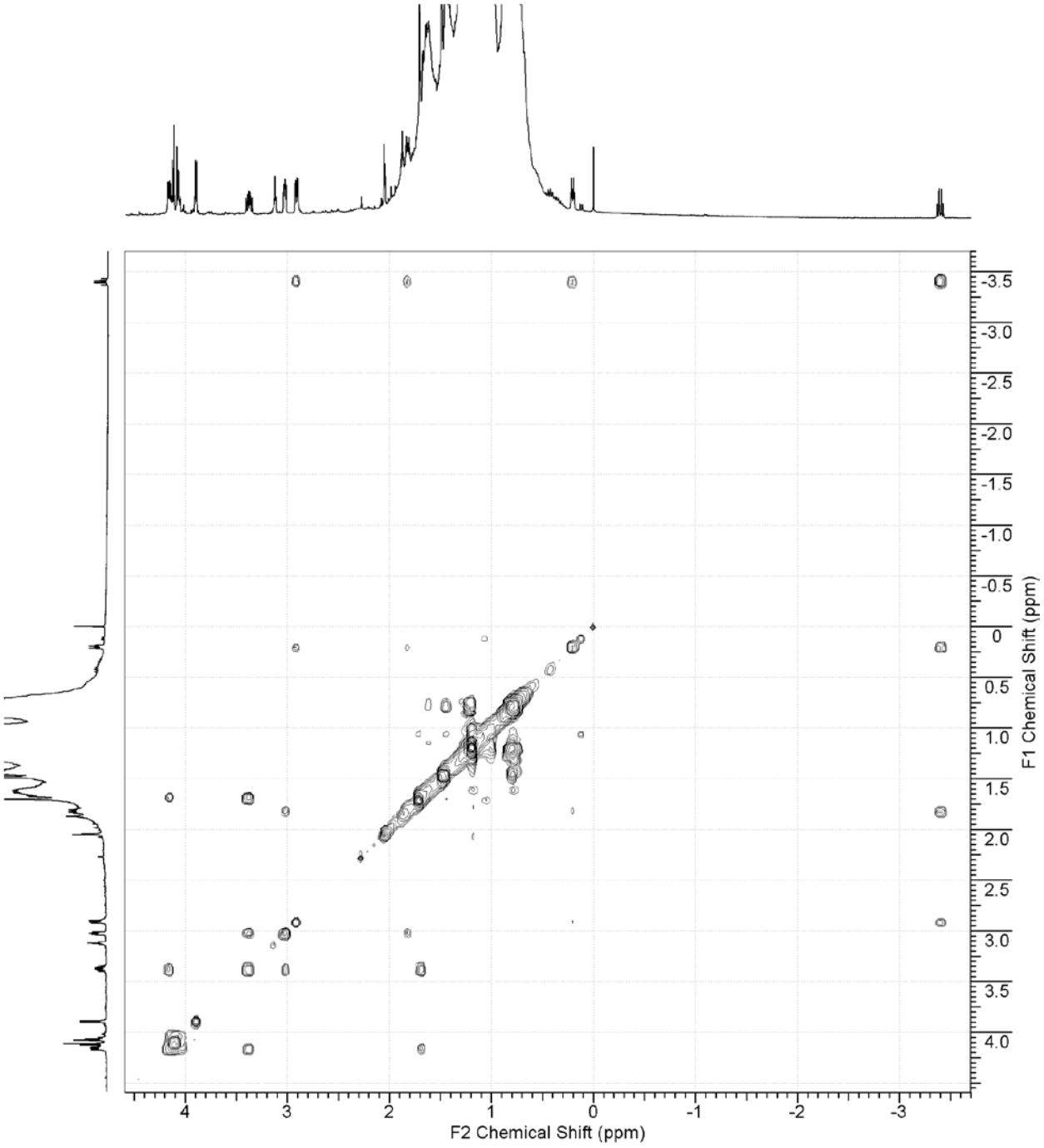
COSY Spectrum of 167 in $CDCl_3$



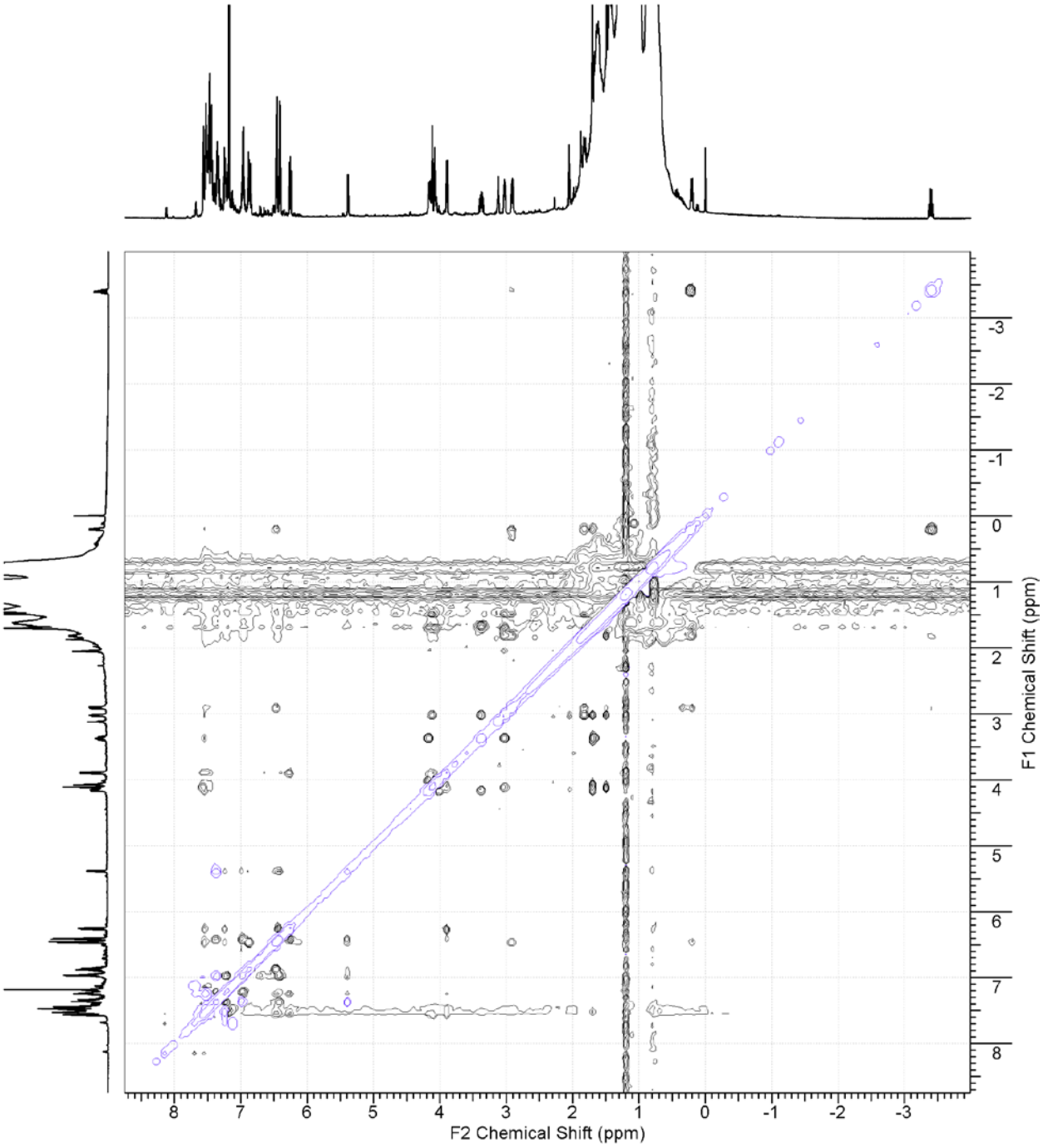
COSY Spectrum of 167 in $CDCl_3$ (Aromatic Region)



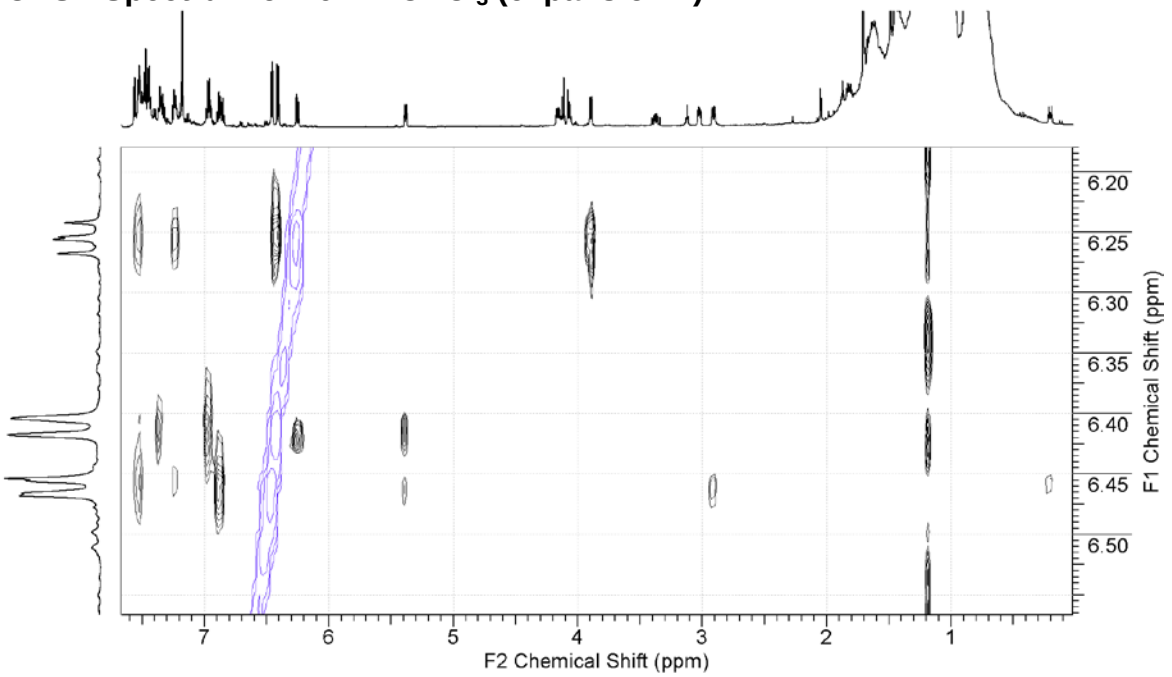
COSY Spectrum of 167 in $CDCl_3$ (Aliphatic Region)

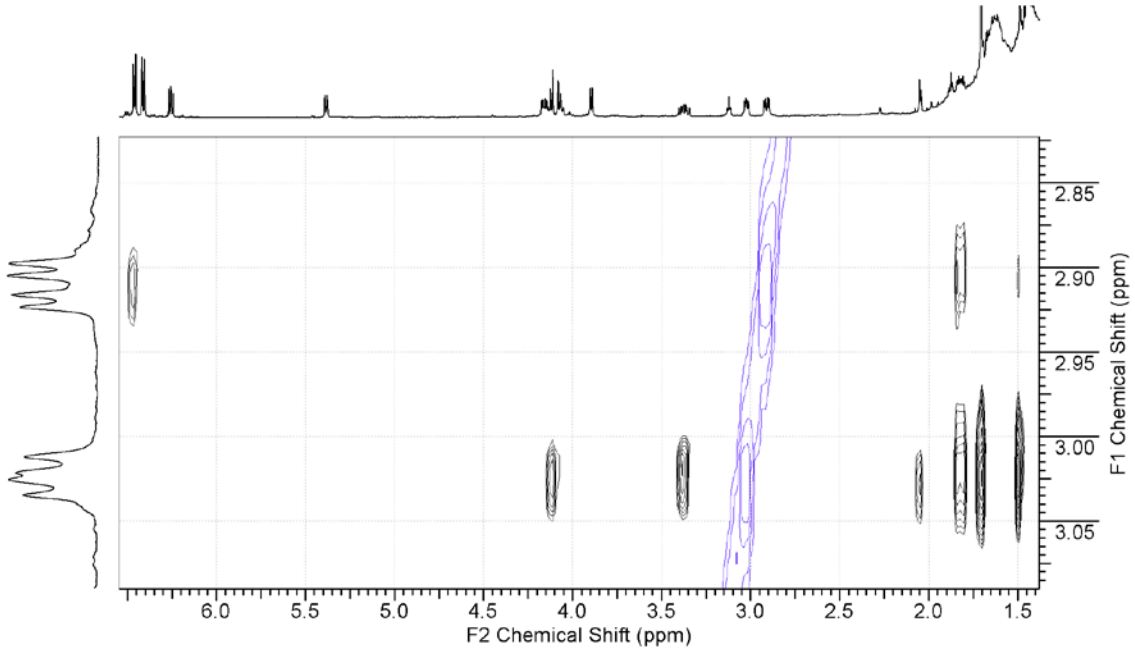


NOESY Spectrum of 167 in $CDCl_3$



NOESY Spectrum of 167 in $CDCl_3$ (expansion 1)





NOESY Spectrum of 167 in $CDCl_3$ (expansion 2)