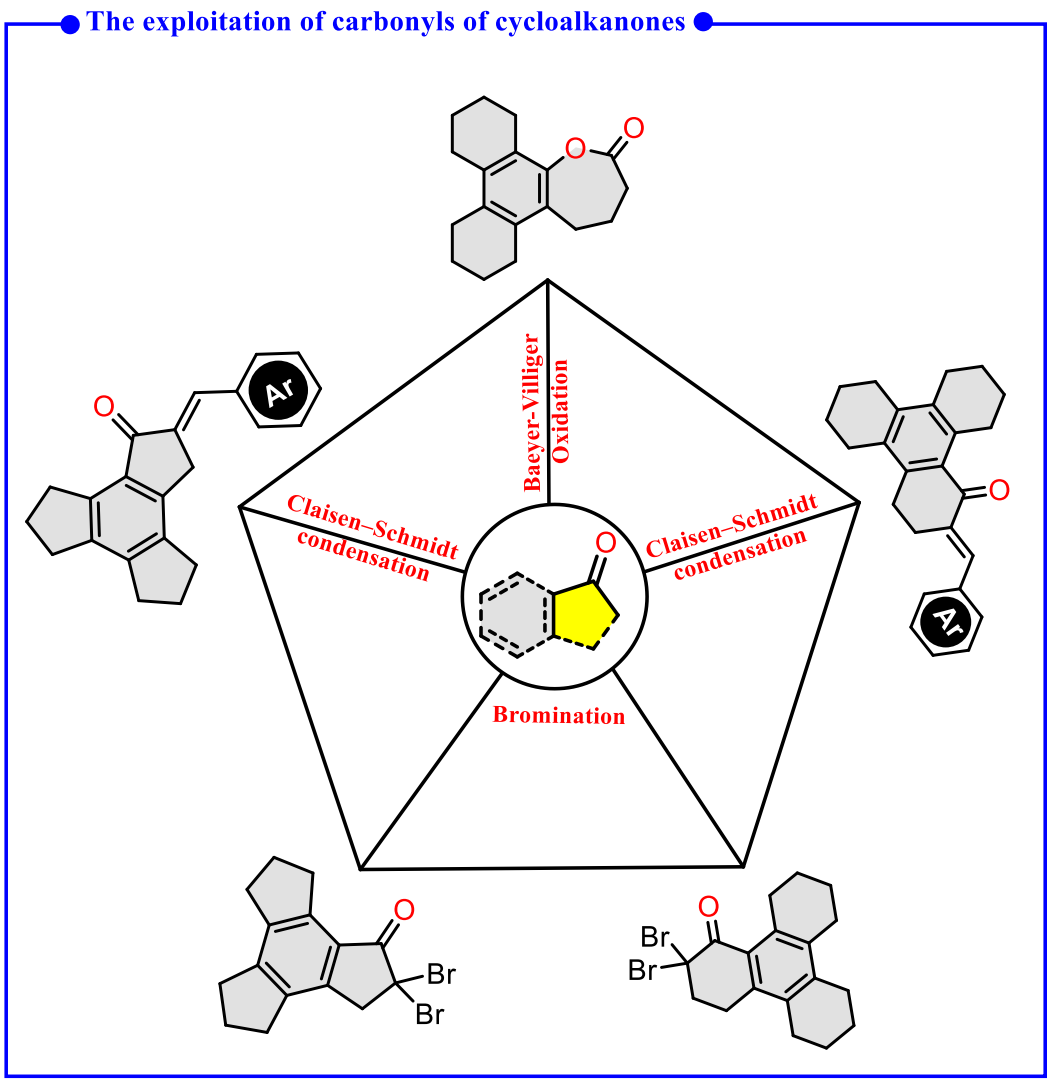
CHAPTER 4

Expanding the Library of Carbocycles by Exploiting its Carbonyls



4.1 Abstract

Our engagement with BCTs like trindane and dodecahydrotriphenylene prompted us to explore and expand the library of its derivatives. Herein, we report synthesis of a new group of carbocycles by exploiting their carbonyl chemistry using classical Claisen-Schmidt condensation, Baeyer-Villiger oxidation and simple α,α-dibromination reactions.

4.2 Introduction

In organic chemistry, the utilization of carbonyl group has very long synthetic potential with great success.[1] Significant biological activity[2] like multi-inhibition properties against Alzheimer's disease, have been shown by chalcones of the type **151** and 2-benzylidenecycloalkanones **152** having α,β–unsaturated carbonyl group.[3] (**Fig. 4.1**)

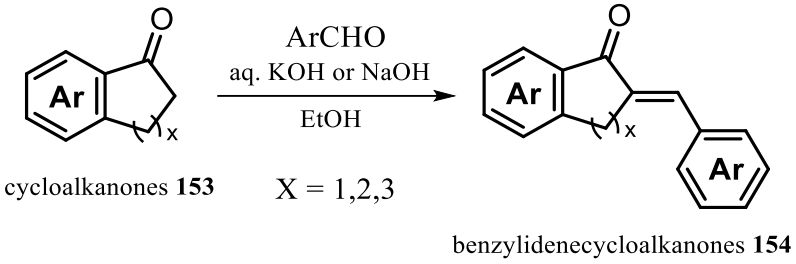
Chalcones **151** 2-benzylidenecycloalkanones **152**

Figure 4.1 α,β-unsaturated carbonyl derivatives

In context with the advancement of more efficient synthetic techniques, the synthesis of α,β-unsaturated carbonyl compounds continues to be a fascinating task for organic chemists. Conventionally, they are prepared by Aldol/Claisen-Schmidt[4], Knoevenagel condensations,[5] Horner-Wadsworth-Emmons reactions,[6] or particular oxidations such as Saegusa-oxidation.[7] A number of well-known methodologies make use of α,β-unsaturated carbonyl compounds to develop diverse molecules. By using such transformations, this class of molecules is still often employed to create bio-active compounds,[8, 9] materials,[10] flavours and perfumes,[11, 12] as well as optically active molecules.[13, 14] Besides, exocyclic α,β -unsaturated ketones are excellent precursors in the synthesis of heterocyclic compounds with polycyclic frameworks. Moreover, α,β-enones of these molecules are favorable functionalities for dipolar cycloaddition and nucleophilic 1,4-

addition.[15-18] Alternatively, benzylidenecycloalkanone compounds were utilized into almost all major polymer scaffolds, ranging from polyester to polyimide.[19]

The most commonly used synthetic approaches for generating, exocyclic α,β-enones are based on the conventional Claisen-Schmidt condensation conditions, which involves the use of suitable aldehydes and ketones with NaOH/KOH in water and EtOH mixture.[20] High yields of a plethora of substituted chalcones and benzylidenecycloalkanones **154** with arylaldehydes from substituted cycloalkanones **153** have been reported.[21, 22] (**Scheme 4.1**)



Scheme 4.1 Claisen-Schmidt condensation of cycloalkanones

To extend the scope of some additional transformations,[23] dibenzylidene cycloalkanone moieties, called cross-conjugated dienones **155** and **156**, are also synthesized utilizing a similar strategy under the appropriate molar equivalent amount of aldehyde against substituted cyclopentanones and cyclohexanones.[24, 25] (**Fig. 4.2**)

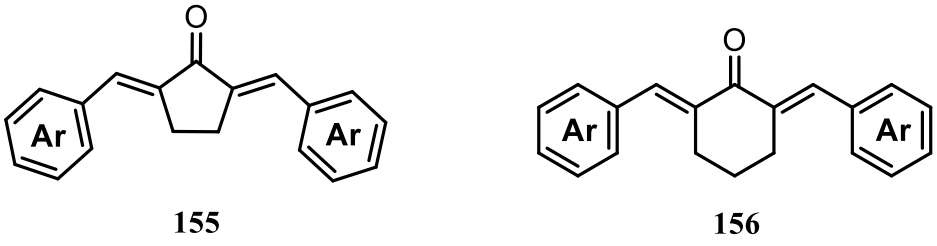
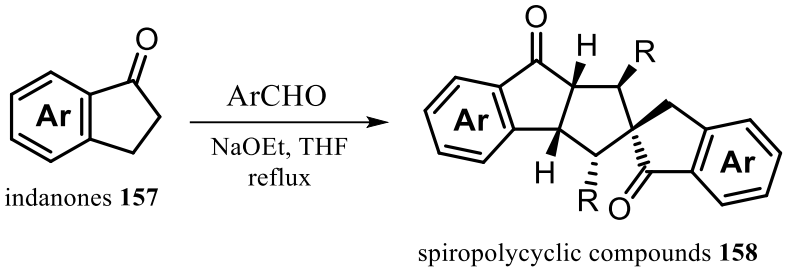


Figure 4.2 Structures of Dibenzylidenecycloalkanones **155**, **156**

In order to improve the yield of 2-arylideneindanones, Camps *et al.* modified the reaction conditions by employing sodium ethoxide in THF in reflux. Interestingly, this resulted in complex spiropolycyclic compounds **158** *via* a four-component reaction. The synthesis of compound Z in one-pot reaction of two molecules of indanone **157** and two molecules of arylaldehydes.[26] (**Scheme 4.2**)



Scheme 4.2 Multicomponent reaction of indanones **157**

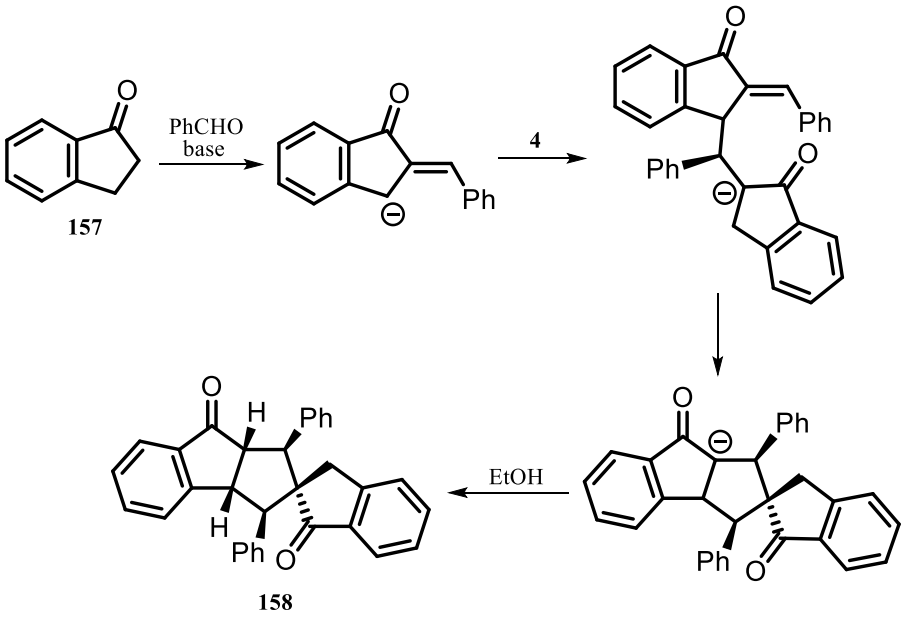
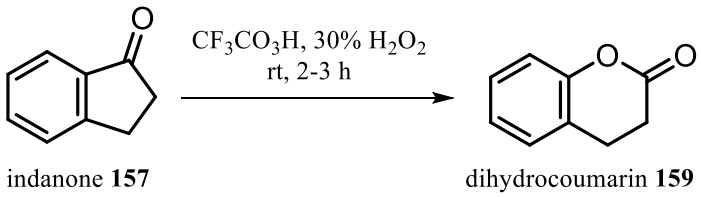


Figure 4.3 Plausible mechanism of formation of spiroenones **158**

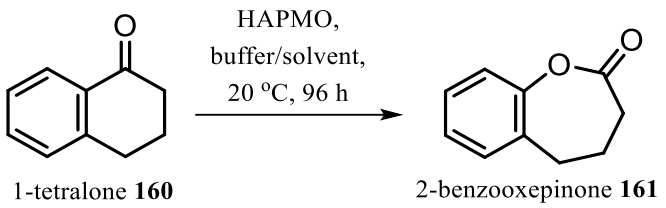
They state that the enones **158** produced as a result of the reaction seem to experience cross-aldol condensation, dehydration, and dimerization. The dimerization form *via* deprotonation of **157** at the benzylic position, followed by a Michael addition of a second molecule of **157** to a generated carbanion, consequently an intramolecular Michael addition takes place in the corresponding intermediate. The generation of the *cis*–fused pentacyclic framework is the outcome of the protonation of subsequent anion in last step. (**Fig. 4.3**)

Cyclic carbonyls have been utilized to synthesize lactones using peracids *via* Baeyer-Villiger (B–V) oxidations. The end products of this reaction provide a desirable easy access to various types of biologically active chemicals. In classical B–V oxidation, trifluoroperacetic acid, pentafluoroperbenzoic acid, 3-chloroperbenzoic acid and peroxy benzoic acid were used as an oxidants.[27, 28] Elie Stephan has produced dihydrocoumarin **159** using 1-indanone **157** in presence of peroxytrifluoroacetic acid and 30% hydrogen peroxide at room temperature.[29] (**Scheme 4.3**)



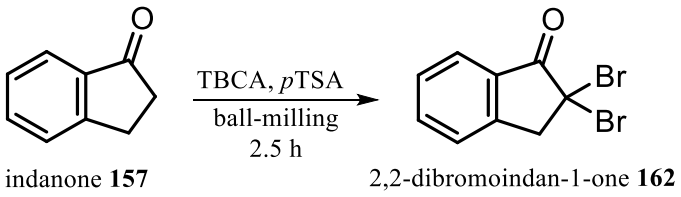
Scheme 4.3 B–V oxidation of indanone **157**

Also, 4-hydroxyacetophenone monooxygenase (HAPMO) was used as a catalyst for the enzymatic bio-oxidation of 1-tetralone **160** into 2-benzoxepinone **161** after 96 h.[30] (**Scheme 4.4**)



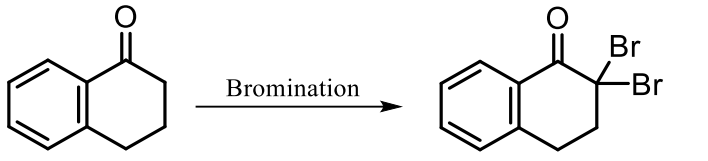
Scheme 4.4 Enzymatic B–V oxidation of 1-tetralone **160**

gem–Dihalides are significant building blocks for organic synthesis and are often utilized as precursors to carbenes to integrate small molecules.[31] On the other hand, organohalogenated compounds particularly α,α–dibromoketones and various other *gem*–dibromides are key intermediates for the synthesis of pharmaceuticals, agrochemicals and natural products.[32, 33] Moorthy *et al.* have reported α,α-dihalogenation of carbonyl compounds with tribromoisocyanuric acid (TBCA) directly under ball-milling and α,α-dihalocarbonyl compounds **162** have been isolated in quantitative yield.[34] (**Scheme 4.5**)



Scheme 4.5 α,α-dhalogenation of indanone **157**

Various reaction conditions, such as liquid bromine in acetic acid,[35] bromine with KOH,[36] *N*-bromosuccinimide with *p*TSA,[37] bromine in chloroform,[38] have been used to synthesize 2,2-dibromoindan-1-one **162**. Similarly, 1-tetralone **160** have also been explored on several occasions to form its α,α-dibromocarbonyl **163**.[39-42] (**Scheme 4.6**)



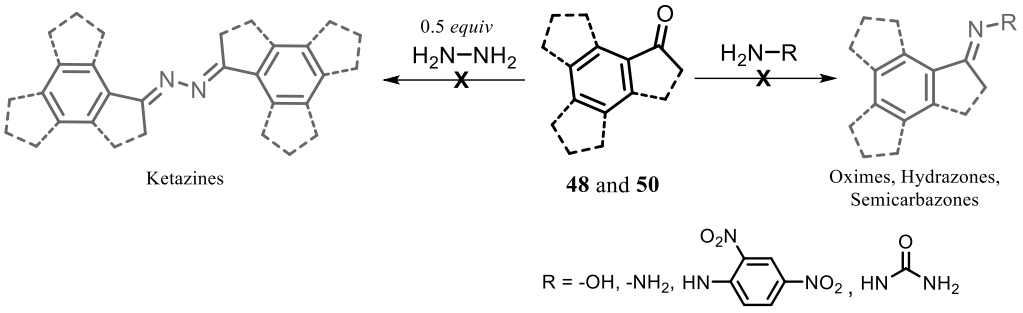
160 2,2-dibromotetralon-1-one **163**

Scheme 4.6 Synthesis of *gem*-dibromocarbonyl of **160**

The limited reports on decahydrotriphenylene-1-one **48** and trindanone **50** piqued our interest in the challenge of obtaining its carbonyl derivatives. To the best of our knowledge, there are no examples of exploitation of the carbonyls of systems **35** and **36**, with the exceptions of two reports wherein α-position of trindanone **50** has been functionalized.[43, 44] Encouraged by our own recent findings in functionalizing compounds **35** and **36**, we decided to explore such variants that makes a rapid access to construct new potential small molecules without using any fancy reagents or catalysts.

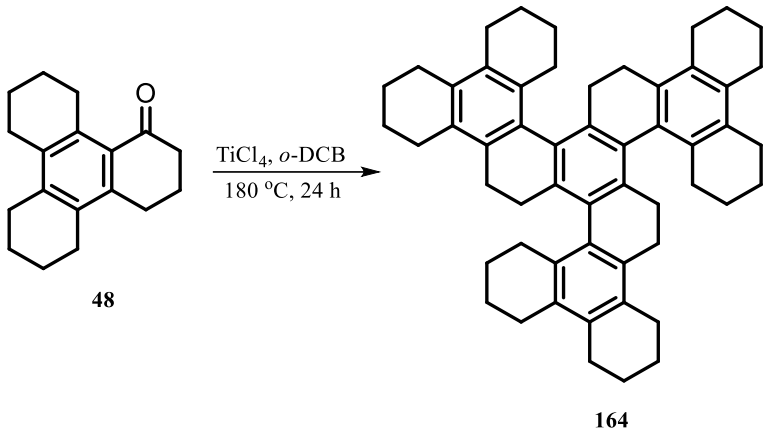
4.3 Results and Discussions

The carbonyl functionality interested us to develop a novel family of carbo- and heterocycles. For the development of heterocycles, numerous reactions were planned considering the substrates **48** and **50** in our hand. (**Scheme 4.7**) Several conventional approaches have been attempted to transform carbonyls into oximes, hydrazones semicarbazones and ketazines. However, all the attempts towards the synthesis of heterocycles were in vain.



Scheme 4.7 Attempts to prepare heterocycles of **48** and **50**

We then tempted to synthesize the larger polycyclic aromatic of **48** *via* aldol trimerization reaction. To access the 54-carbon target molecule **164**, we attempted the aldol trimerization of ketone **48** using number of methods. However, the synthesis of trimer **164** did not occurred as anticipated even after multiple attempts of this aldol trimerization reaction by varying the different Lewis acid catalysts, reaction times, solvents, and temperatures. According to various studies, $TiCl_4$ driven cyclizations in hot *o*-dichlorobenzene (*o*-DCB) were used in the synthesis of such large trimmers however some of them were completely insoluble in nature, making it impossible to separated and purified by chromatographic techniques. Then, we intended to use titanium tetrachloride as the Lewis acid in *o*-DCB to trigger the aldol trimerization of ketone **48**. (**Scheme 4.8**)



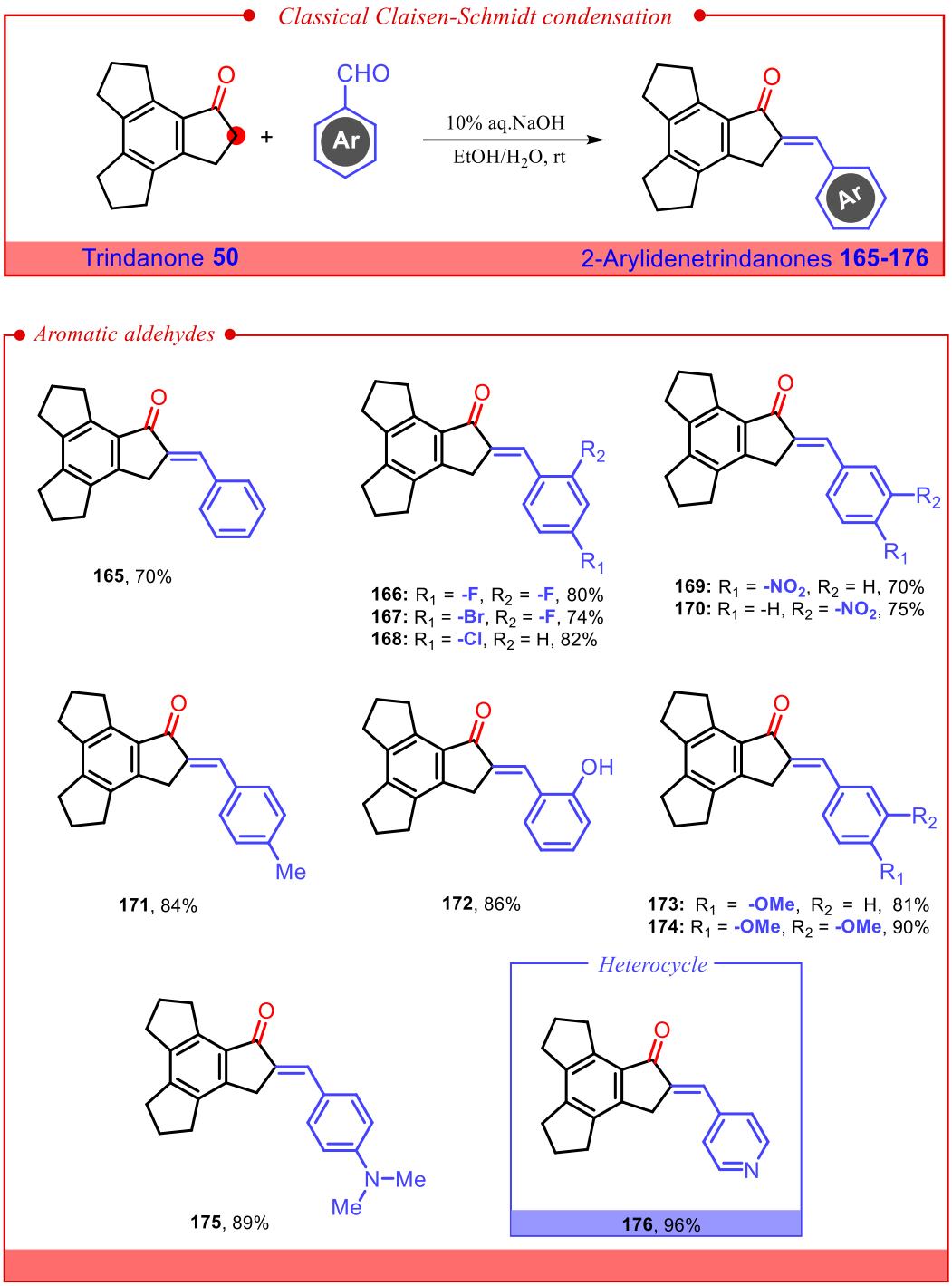
Scheme 4.8 Synthesis of **164** *via* aldol trimerization

The isolated product after workup was too insoluble for NMR analysis in number of solvents, even at elevated temperatures as anticipated. This problem clearly poses a hurdle for synthetic organic chemists. Nevertheless we were able to acquire the MALDI-TOF spectrum of compound **164**. (Section 4.7.1) After encountering difficulties towards the functionalization of keto group, the work was concentrated on manipulation of its α–position *via* condensation reaction.

According to various reports, the temperature and electronic nature of arylaldehydes in aq. NaOH / EtOH influence the behavior of cycloalkanones during the reaction.[26, 45] Moreover, the conventional Claisen-Schmidt condensation requires harsh reaction conditions such as vortex stirring and heating, which slow down the reactions and lower the yield of products and led to product decomposition.[46, 47] There have been studies of a number of chalcones with various substituents at various positions exhibiting an array of biological activities.[48-55] We were spurred by these findings for the synthesis of 2-arylidenecycloalkanones *via* Claisen-Schmidt condensation in order to explore the scope and generality of trindane and DDHTP scaffolds.

Before approaching towards the synthesis of trindanone derivatives, trindanone **50** was freshly prepared by reported method[44] as described in the Chapter **3**. Carbonyl functionality served as a handle to exploit its α–position. Ketone **50** was treated with various arylaldehydes bearing EWG/EDG at ambient temperature under Claisen-Schmidt condensation. Under this condition, high yield of various aldol products (**165-176**) were obtained by employing various aromatic aldehydes. The structures of all the synthesized compounds were fully discernible from FTIR, NMR and HRMS. Initially, benzaldehyde reacted with trindan-1-one **50** using aqueous NaOH in dry EtOH for 4 h to furnish corresponding benzylidene derivative **165** in 70% yield. (**Scheme 4.9**)

The structure of 2-benzylidenetrindanone **165** was confirmed by its spectral data. Its IR spectrum showed band at 1681 cm^{-1} indicates the α,β-unsaturated carbonyl group.



Scheme 4.9 Preparation of 2-arylidenetrindanones **(14-25)**

The ^{1}H NMR spectrum of **165** displayed a singlet at δ 7.56 for one olefinic proton, five aromatic protons at δ 7.65, 7.45 and 7.37, singlet at δ 3.80 for benzylic

two protons adjacent to α,β-enone. The other remaining twelve benzylic and homobenzylic protons gave signals at δ 3.30, 2.90, 2.79 and 2.18. The ^{13}C NMR spectrum of **165** exhibited signal at δ 194.80 for carbonyl carbon, signals at δ 147.38, 143.76, 142.06, 140.34, 138.62, 136.07, 135.82, 132.38, 132.33, 130.54, 129.21, 128.83 for twelve aromatic and two olefinic carbons and signals at 32.06, 31.16, 30.48, 30.16, 25.54, 25.18, and 24.59 for seven remaining methylene carbons. Its HRMS gave a molecular ion peak $[M+H]^+$ at 301.1573 for $C_{22}H_{21}O$ confirms the structure.

The reaction using halogenated aromatic aldehydes such as 2,4-difluorobenzaldehyde, 4-bromo-2-fluorobenzaldehyde and 4-chlorobenzaldehyde afforded desired products (**166-168**) in 4 h with fairly good yield as anticipated (74-82%). The structures of **166-168** were confirmed by FTIR, NMR and HRMS.

The FTIR of **166** showed a characteristic strong band at 1689 cm^{-1} for the carbonyl group. The ^{1}H NMR spectrum of **166** displayed a singlet at δ 7.70 for one olefinic proton, signals at δ 7.35, 7.14 – 6.98 for three aromatic protons, singlet at δ 3.74 for benzylic two protons of same peripheral cyclopentene ring. The twelve remaining methylene protons gave signals at δ 3.27, 2.90, 2.79 and 2.18. Its ^{13}C NMR spectrum displayed signal at δ 193.91 for carbonyl carbon, signals at δ 159.46–115.82 for olefinic and aromatic carbons and signals at δ 32.08, 31.14, 30.77, 30.46, 30.15, 25.47 and 25.15 for seven methylene carbons. The structure of **166** was further confirmed by its HRMS which gave a molecular ion peak $[M+H]^+$ at 337.1399 for $C_{22}H_{19}OF_2$.

When, the reaction was carried out with different electron-withdrawing substituents like nitro-substituted aromatic aldehydes, 2-nitroarylidenetrindanones (**169, 170**) were isolated in 70-75% yield in 4h at ambient temperature. The ^{1}H NMR of 2-(4-nitrobenzylidene)trindanone **169** exhibited a singlet at δ 7.59 for one olefinic proton, signals at δ 8.32 – 8.27 and 7.82 – 7.77 for four aromatic protons and signals at δ 3.89, 3.30, 2.94, 2.83 and 2.21 for methylene protons. Its ^{13}C NMR showed signal at δ 194.00 for carbonyl carbon, signals at δ 148.22, 147.48, 143.37, 142.56, 142.17, 140.82, 139.96, 138.74, 131.96, 130.80, 129.47, 124.02 for two

olefinic and twelve aromatic carbons, signals at δ 32.14, 31.21, 31.13, 30.50, 30.18, 25.53 and 25.21 for remaining methylene protons. Its HRMS gave a molecular ion peak $[M+H]^+$ at 346.1447 for $C_{22}H_{20}NO_3$ confirms the structure. The structure of 2-(3-nitrobenzylidene)trindanone **170** was easily discernible from its spectral data. It is important to note that the ^{13}C NMR of **170** revealed twelve aromatic carbons signals at δ 148.65, 148.11, 143.37, 142.44, 140.74, 138.83, 138.81, 137.49, 136.15, 131.96, 129.81, 129.43, whereas **169** showed only ten signals for twelve aromatic carbons, allowing us to differentiate between these two nitroarylidenetrindanones (**169, 170**) isomers.

The most obvious finding to emerge from the reaction time that it has been slightly increased to 6 to 8 h when electron-donating groups were used as the substituents. This could be a result of EWGs turning the aldehydes more reactive as an electrophile. However, the reactions with EDG substituents like methyl, hydroxyl, methoxy were well-tolerated at *ortho*-, *meta*- or *para*-positions of the aromatic ring of the aldehydes and the corresponding expected products were obtained in good yield (81-90%).

The ^1H NMR of **171** showed a characteristic signal at δ 2.31 (s, 3H) for the methyl group. Further the ^{13}C NMR of **171** displayed signals at δ 194.88 for carbonyl carbon, twelve signals at δ 147.20 – 129.59 for aromatic and olefinic carbons and signals δ 32.04 – 21.48 for eight methyl and methylene carbons. The structure of **171** was further confirmed by its HRMS which gave a molecular ion peak $[M+H]^+$ at 315.1752 for $C_{23}H_{23}O$.

Reaction of **50** with salicylaldehyde gave corresponding aldol product, 2-(2-hydroxybenzylidene)trindan-1-one **172** in 8 h. Compound **172** was barely soluble in DMSO and not soluble in any polar organic solvents. It was not melted at 320 °C (observed in polarizing microscope). Despite its poor solubility in DMSO, we were able to record its NMR and HRMS. Its FTIR showed bands at 3163 cm^{-1} for –OH group and 1663 cm^{-1} for carbonyl group. The ^1H NMR of **172** exhibited signals at δ 10.08 of one –OH proton, at δ 7.78 – 6.87 for olefinic and aromatic protons and at δ 3.82 – 2.00 for methylene protons. Its ^{13}C NMR gave signals at δ

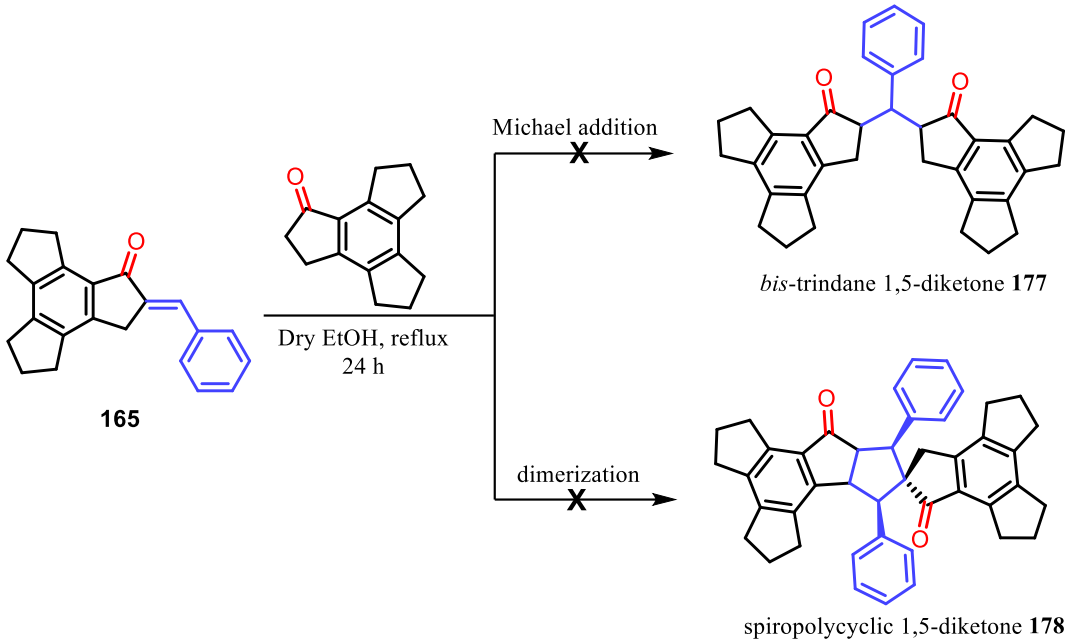
193.71 for –CO along with aromatic and olefinic carbons at δ 146.64 – 115.80 and seven methylene carbons at δ 36.28 – 24.57. Its HRMS gave a molecular ion peak $[M+H]^+$ at 317.1538 for $C_{22}H_{21}O_2$ confirms the structure.

Derivatives of 2-methoxybenzylidene (**173, 174**) have also been accomplished in 6 h and thoroughly characterized in a similar manner. The ^{1}H NMR of **173** displayed a characteristic signal at δ 3.86 (s, 3H) for $–OCH_3$ group. The ^{1}H NMR of **174** also revealed signals at δ 3.94 (d, *J* = 9.7 Hz, 6H), indicating the presence of two $–OCH_3$ groups.

The ^{1}H NMR of 2-(4-(dimethylamino)benzylidene)trindan-1-one **175** clearly exhibited singlet at δ 3.03 for six equivalent methyl protons. It also gave one signal at δ 40.14 in ^{13}C NMR for the methyl carbons situated on tertiary amine.

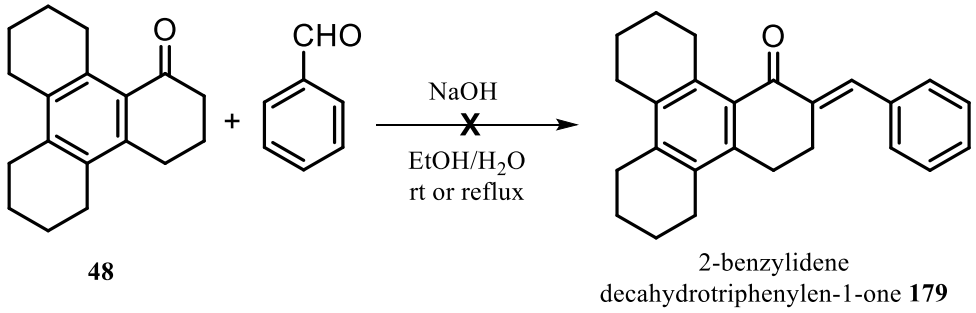
Heteroaromatic aldehyde like 4-pyridinecarboxaldehyde has been used to obtain corresponding product **176** with the highest 96% yield in 6 h. Its ^{1}H NMR exhibited two doublets at δ 8.68 and 7.46 for four aromatic protons, singlet at δ 7.42 for one olefinic proton and signals at δ 3.83 – 2.18 for all the methylene protons present in the structure. The ^{13}C NMR of **176** showed signal at δ 193.99 for carbonyl carbon, signals at δ 150.34 – 124.05 for eleven aromatic carbons and two olefinic carbons and signals at δ 32.12 – 25.18 for seven methylene carbons. The structure of **176** was further confirmed by its HRMS which gave a molecular ion peak $[M+H]^+$ at 302.1542 for $C_{21}H_{20}NO$.

Based on these observations, we were attempted to direct the course of reaction towards Michael addition and dimerization to achieve *bis*-trindane 1,5-diketone **177** and spiropolycyclic 1,5-diketone **178**. (**Scheme 4.10**) According to previous report, these reactions depend upon the influence of temperature.[45] In an attempt to assess the reactivity, **165** was treated with **50** to obtain the *bis*-trindane 1,5-diketone **177** *via* Michael addition under reflux condition, but the expected product was not formed. Similarly, spiropolycyclic 1,5-diketone **178** was not formed at reflux temperature *via* dimerization. This may be due to substantial steric accommodation offered by trindane moieties during the course of reaction.



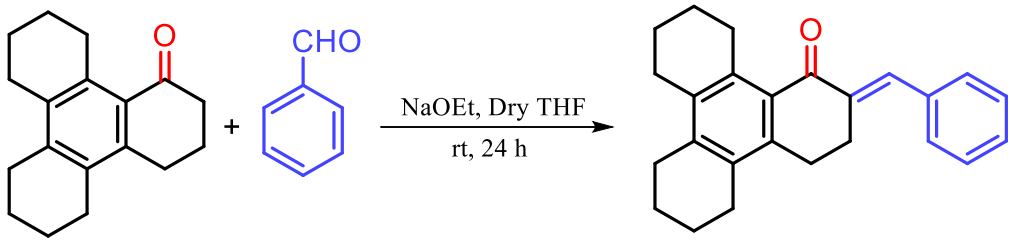
Scheme 4.10 Attempts towards the reactions of **165**

After manipulating the α–position of **50**, we extended our exploration towards the synthesis of 2-benzylidenedecahydrotriphenylen-1-one **179**. Having prepared the decahydrotriphenylen-1-one **48**, we proceeded towards the synthesis of target molecule **179** under similar reaction conditions and under reflux condition. (**Scheme 4.11**) However, the coupling reaction did not proceed (TLC observations) and mainly the starting materials were recovered using column chromatography.



Scheme 4.11 Attempts towards the synthesis of 2-benzylidene derivative **179**

In connection with the synthesis of novel enone **179**, we carried out the reaction of **48** with benzaldehyde in the presence of freshly prepared NaOEt in THF and it was obtained in 59% yield. (**Scheme 4.12**) Compound **179** was thoroughly confirmed by FTIR, NMR and HRMS data to confirm its structure.



48

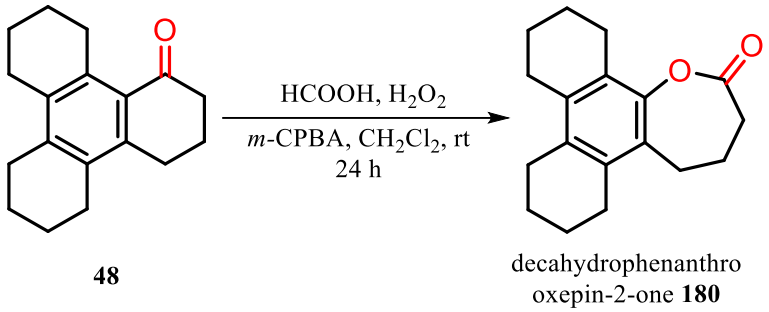
2-benzylidene decahydrotriphenylen-1-one **179**

Scheme 4.12 Preparation of enone **179** using NaOEt/Dry THF

The ^{1}H NMR of **179** displayed a one singlet at δ 7.78 for one olefinic proton, signals at δ 7.44, 7.39, 7.31 for aromatic protons, a triplet at δ 3.16 for homobenzylic protons adjacent to enone moiety, and signals at δ 2.99, 2.74, 2.71 – 2.56, 1.87 – 1.77, 1.71 for remaining eighteen methylene protons. The ^{13}C NMR of **179** showed one signal at δ 189.60 for carbonyl carbon, signals at δ 141.01 – 128.26 for two olefinic and twelve aromatic carbons carbons and signals at δ 29.58 – 22.73 for ten remaining methylene carbons. The structure of **179** was further confirmed by its HRMS which gave a molecular ion peak $[M+H]^+$ at 343.2045 for $C_{25}H_{26}O$.

Benzo-fused lactones are essential synthesis intermediates and the fundamental building blocks of a wide range of biologically active substances. Benzo-fused lactones have been widely synthesized by executing Baeyer-Villiger (B–V) oxidation reactions.[56] We were interested in obtaining lactones of carbocyclic ketones **48** and **50**. In the beginning, decahydrotriphenylen-1-one **48** was subjected to Baeyer–Villiger oxidation. The reaction was carried out in dry methylene chloride. We utilized meta-chloroperoxybenzoic acid (*m*-CPBA) for this

oxidation reaction and adjusted the medium by adding a small the amount of formic acid and H_2O_2. (**Scheme 4.13**)

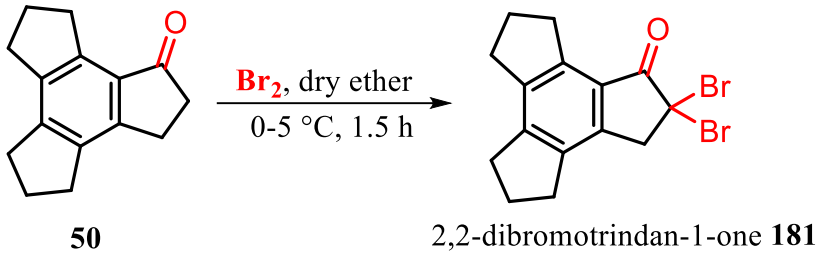


Scheme 4.13 B–V oxidation of ketone **48**

The novel Benzo-fused lactone **180** has been fully characterized by NMR, HRMS and IR analysis. The FTIR analysis of **180** showed a carbonyl absorption band at 1759 cm^{-1} indicating a significant shift (ca. 87 cm^{-1}) from carbonyl of ketone **28** at 1672 cm^{-1}. The increasing value of CO absorption band indicated the formation of lactone ring. The ^1H NMR (500 MHz, $CDCl_3$) of **180** displayed a triplet at δ 2.77 for methylene protons adjacent to carbonyl group, signals at δ 2.69, 2.55 for eight benzylic protons of peripheral cyclohexene rings, signals at δ 2.42 and 2.08 for benzylic and homobenzylic protons present in lactone ring and signals at δ 1.84 – 1.75, 1.73 for eight homobenzylic protons of cyclohexene rings. Its ^{13}C NMR spectrum exhibited signal at δ 172.50 for carbonyl carbon, signals at δ 147.85 – 124.71 for six aromatic carbons and signals at δ 31.41 – 22.05 for remaining eleven methylene carbons. The structure of **180** was further confirmed by its HRMS which gave a molecular ion peak $[M+H]^+$ at 271.1706 for $C_{18}H_{23}O_2$. Unfortunately, trindan-1-one **50** under this oxidation reaction condition did not show the formation of corresponding lactone.

These results encouraged us to manipulate the α–position of carbonyls to extend our exploration towards the synthesis of α,α–dibromoketones. With the requisite partners **48** and **50** in hand, bromination was performed in liquid bromine

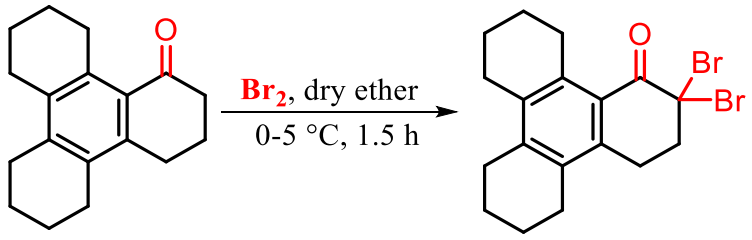
in dry solvent ether and without acid/base in the medium. Bromination of trindan-1-one **50** at room temperature furnished 2,2-dibromotrindan-1-one **181** in 67% yield. (**Scheme 12**)



50 2,2-dibromotrindan-1-one **181**

Scheme 4.14 α,α–dibromination of trindan-1-one **50**

The ^{1}H NMR of **181** exhibited singlet at δ 4.16 for two methylene protons adjacent to *gem*-dibromo functionality, triplets at δ 3.26, 2.90, 2.83 for benyzlic methylene protons and at δ 2.19 for four homobenzylic methylene protons. Its ^{13}C NMR gave signals at δ 192.90 for carbonyl carbon, at δ 150.30 – 122.89 for aromatic carbons, at 58.83 for C–Br_2 and 51.49 – 25.10 for seven remaining methylene carbons. Moreover, *gem*-dibromo substitution in **181** was further confirmed by its HRMS which gave a characteristic three molecular ion peaks $[M+H]^+$ at 368.9484(M-2):370.9479(M):372.9449(M+2) in approximately ratio of 1:2:1 for $C_{15}H_{15}OBr_2$.



48 2,2-dibromodecahydro triphenylen-1-one **182**

Scheme 4.15 Synthesis of 2,2-dibromodecahydrotriphenylen-1-one **182**

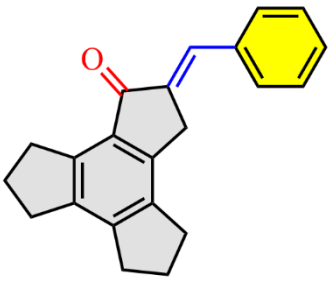
Fortuitously, 2,2-dibromodecahydrotriphenylen-1-one **182,** a higher homologue of **181** was obtained under similar reaction conditions. (**Scheme 4.15**) Likewise, The HRMS of **182** also showed characteristic three molecular ion peaks $[M+H]^+$ at 410.9943(M-2): 412.9928(M): 414.9912(M+2) in approximately ratio of 1:2:1 for $C_{18}H_{21}OBr_2$ indicating the presence of two bromine atoms in the molecule.

4.4 Experimental section

4.4.1 *General procedure for 2-arylidenetrindan-1-ones* **165-176**

Trindan-1-one **50** (2.35 mmol) was mixed with dry ethanol (5 mL) and 10% aqueous solution of sodium hydroxide (5 mL) in a round-bottom flask at 0 °C. Arylaldehydes (3.055 mmol) was then added and mixture was stirred after at room temperature for 4–8 h. After completion of reaction (TLC), precipitates were collected on a filter, thoroughly washed with water and dried. The powder was purified by recrystallization with $CHCl_3$/EtOH for further characterization.

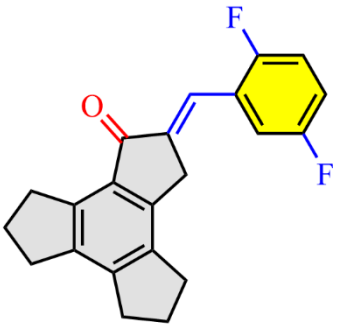
(*E*)-2-benzylidene-2,3,4,5,6,7,8,9-octahydro-1*H*-cyclopenta[*e*]-*as*-indacen-1-one **165**



Fine yellow powder, 70% yield, mp 286 °C, R*f*: 0.60 (4.5:0.5, Pet. Ether:EtOAc); **IR (KBr, cm^{-1})** 2963, 2887, 1681; **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.65 (d, *J* = 7.3 Hz, 2H), 7.56 (s, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.37 (t, *J* = 7.4 Hz, 1H), 3.80 (s, 2H), 3.30 (t, *J* = 7.5 Hz, 2H), 2.90 (dt, *J* = 24.1, 7.5 Hz, 4H), 2.79 (t, *J* = 7.5 Hz, 2H),

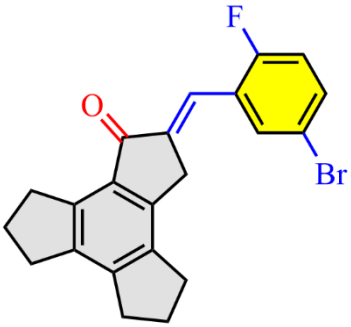
2.18 (dp, *J* = 18.0, 7.5 Hz, 4H); **^{13}C NMR (126 MHz, CDCl$_3$)** δ 194.80, 147.38, 143.76, 142.06, 140.34, 138.62, 136.07, 135.82, 132.38, 132.33, 130.54, 129.21, 128.83, 32.06, 31.16, 30.48, 30.16, 25.54, 25.18, 24.59; **HRMS (ESI)** *m/z* calculated for $C_{22}H_{21}O$ $[M+H]^+$: 301.1592, found 301.1573.

(*E*)-2-(2,4-difluorobenzylidene)-2,3,4,5,6,7,8,9-octahydro-1H-cyclopenta[*e*]-*as*-indacen-1-one **166**



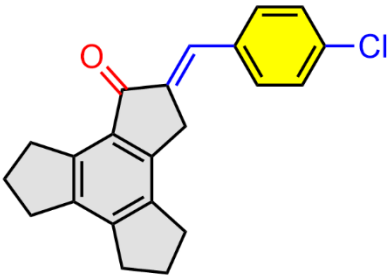
Yellow powder, 80% yield, mp 246 °C, R*f*: 0.65 (4.5:0.5, Pet. Ether:EtOAc); **IR (KBr, cm^{-1})** 2963, 1689, 1275, 1141; **^{1}H NMR (500 MHz, CDCl$_3$)** δ 7.70 (s, 1H), 7.35 (ddd, *J* = 9.0, 5.8, 3.1 Hz, 1H), 7.14 – 6.98 (m, 2H), 3.74 (s, 2H), 3.27 (t, *J* = 7.5 Hz, 2H), 2.90 (dt, *J* = 21.2, 7.5 Hz, 5H), 2.79 (t, *J* = 7.5 Hz, 2H), 2.18 (dp, *J* = 20.2, 7.6 Hz, 4H); **^{13}C NMR (126 MHz, CDCl$_3$)** δ 193.91, 159.46, 158.81, 157.54, 156.83, 147.86, 143.39, 142.28, 140.55, 138.83, 138.70, 132.03, 125.16, 125.09, 125.04, 124.98, 122.73, 122.71, 122.69, 122.67, 117.23, 117.16, 117.11, 117.04, 116.97, 116.91, 116.84, 115.84, 115.82, 115.65, 115.62, 32.08, 31.14, 30.77, 30.46, 30.15, 25.47, 25.15; **HRMS (ESI)** *m/z* calculated for $C_{22}H_{19}OF_2$ $[M+H]^+$: 337.1404, found 337.1399.

(*E*)-2-(4-bromo-2-fluorobenzylidene)-2,3,4,5,6,7,8,9-octahydro-1H-cyclopenta[*e*]-*as*-indacen-1-one **167**



Yellow powder, 74% yield, mp 268 °C, R*f*: 0.65 (4.5:0.5, Pet. Ether:EtOAc); **IR (KBr, cm^{-1})** 2959, 2891, 1689, 1141; **^{1}H NMR (500 MHz, CDCl$_3$)** δ 7.74 (dd, *J* = 6.5, 2.5 Hz, 1H), 7.66 (s, 1H), 7.43 (dq, *J* = 6.9, 2.2 Hz, 1H), 7.05 – 6.98 (m, 1H), 3.74 (s, 2H), 3.27 (t, *J* = 7.5 Hz, 2H), 2.91 (dt, *J* = 25.9, 7.5 Hz, 5H), 2.79 (t, *J* = 7.5 Hz, 2H), 2.18 (dp, *J* = 19.2, 7.6 Hz, 5H); **^{13}C NMR (126 MHz, CDCl$_3$)** δ 193.87, 161.64, 159.62, 147.90, 143.44, 142.33, 140.57, 139.06, 138.73, 133.38, 133.31, 132.30, 132.28, 132.03, 126.01, 125.90, 122.47, 122.43, 117.84, 117.65, 116.80, 116.77, 32.10, 31.17, 30.67, 30.48, 30.22, 25.50, 25.17; **HRMS (ESI)** *m/z* calculated for $C_{22}H_{19}OFBr$ $[M+H]^+$: 397.0603, found 397.0601.

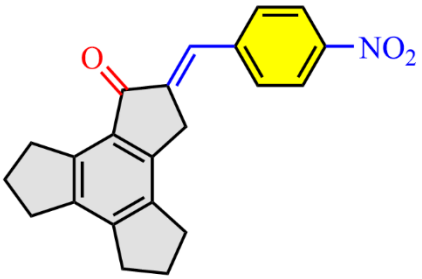
(*E*)-2-(4-chlorobenzylidene)-2,3,4,5,6,7,8,9-octahydro-1H-cyclopenta[*e*]-*as*-indacen-1-one **168**



Fine yellow crystals, 82% yield, mp 297 °C, R*f*: 0.60 (4.5:0.5, Pet. Ether:EtOAc); **IR (KBr, cm^{-1})** 2952, 2834, 1689; **^{1}H NMR (500 MHz, CDCl$_3$)** δ 7.51 (d, *J* = 5.7 Hz, 2H), 7.42 (s, 1H), 7.35 (d, *J* = 5.5 Hz, 2H), 3.75 (s, 2H), 3.23 – 3.17 (m, 2H), 2.89 – 2.79 (m, 4H), 2.74 (d, *J* = 7.6 Hz, 2H), 2.12 (ddd, *J* = 14.9, 7.5, 4.0 Hz, 4H); **^{13}C NMR (126 MHz, CDCl$_3$)** δ 194.47, 147.59, 143.47, 141.98, 140.40, 138.63,

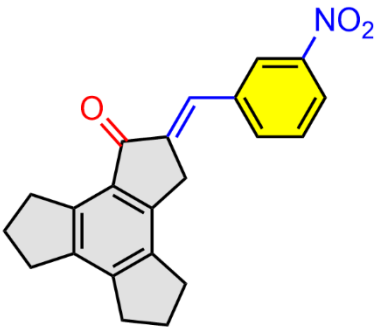
136.53, 135.03, 134.17, 132.08, 131.57, 130.85, 129.03, 32.00, 31.08, 31.00, 30.39, 30.09, 25.45, 25.11; **HRMS (ESI)** *m/z* calculated for $C_{22}H_{20}OCl$ $[M+H]^+$: 335.1203, found 335.1199.

(*E*)-2-(4-nitrobenzylidene)-2,3,4,5,6,7,8,9-octahydro-1H-cyclopenta[*e*]-*as*-indacen-1-one **169**



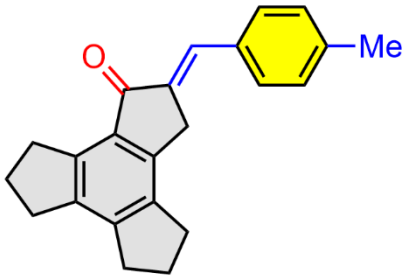
Mud brown powder, 70% yield, mp 308 °C, R*f*: 0.55 (4.5:0.5, Pet. Ether:EtOAc); **IR (KBr cm^{-1})** 2952, 2838, 1689, 1514; **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.32 – 8.27 (m, 2H), 7.82 – 7.77 (m, 2H), 7.59 (s, 1H), 3.89 (s, 2H), 3.30 (t, *J* = 7.5 Hz, 2H), 2.94 (dt, *J* = 18.2, 7.5 Hz, 5H), 2.83 (t, *J* = 7.5 Hz, 2H), 2.21 (dp, *J* = 16.9, 7.5 Hz, 4H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ 194.00, 148.22, 147.48, 143.37, 142.56, 142.17, 140.82, 139.96, 138.74, 131.96, 130.80, 129.47, 124.02, 32.14, 31.21, 31.13, 30.50, 30.18, 25.53, 25.21; **HRMS (ESI)** *m/z* calculated for $C_{22}H_{20}NO_3$ $[M+H]^+$: 346.1443, found 346.1447.

(*E*)-2-(3-nitrobenzylidene)-2,3,4,5,6,7,8,9-octahydro-1H-cyclopenta[*e*]-*as*-indacen-1-one **170**



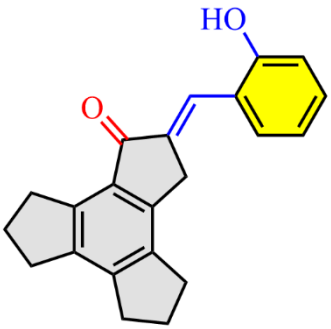
Slightly grey powder, 75% yield, mp 298 °C, R*f*: 0.55 (4.5:0.5, Pet. Ether:EtOAc); **IR (KBr, cm^{-1})** 2957, 2838, 1689, 1529; **^{1}H NMR (500 MHz, CDCl$_3$)** δ 8.49 (s, 1H), 8.21 (d, *J* = 6.0 Hz, 1H), 7.93 (d, *J* = 7.7 Hz, 1H), 7.63 (t, *J* = 8.0 Hz, 1H), 7.58 (s, 1H), 3.90 (s, 2H), 3.29 (t, *J* = 7.5 Hz, 2H), 2.94 (dt, *J* = 27.5, 7.5 Hz, 4H), 2.82 (t, *J* = 7.5 Hz, 2H), 2.24 – 2.16 (m, 4H); **^{13}C NMR (126 MHz, CDCl$_3$)** δ 194.05, 148.65, 148.11, 143.37, 142.44, 140.74, 138.83, 138.81, 137.49, 136.15, 131.96, 129.81, 129.43, 124.25, 123.46, 32.12, 31.20, 30.89, 30.50, 30.22, 25.52, 25.21; **HRMS (ESI)** *m/z* calculated for $C_{22}H_{20}NO_3$ $[M+H]^+$: 346.1443, found 346.1440.

(*E*)-2-(3-methylbenzylidene)-2,3,4,5,6,7,8,9-octahydro-1H-cyclopenta[*e*]-*as*-indacen-1-one **171**



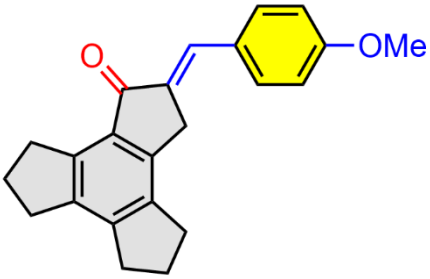
Light yellow crystals, 84% yield, mp 298 °C, R*f*: 0.6 (4.5:0.5, Pet. Ether:EtOAc); **IR (KBr, cm^{-1})** 2952, 2838, 1689; **^{1}H NMR (500 MHz, CDCl$_3$)** δ 7.49 – 7.43 (m, 3H), 7.16 (d, *J* = 7.6 Hz, 2H), 3.70 (s, 2H), 3.21 (t, *J* = 7.5 Hz, 2H), 2.82 (dt, *J* = 24.0, 7.5 Hz, 4H), 2.70 (t, *J* = 7.5 Hz, 2H), 2.31 (s, 3H), 2.09 (dp, *J* = 18.4, 7.5 Hz, 4H); **^{13}C NMR (126 MHz, CDCl$_3$)** δ 194.88, 147.20, 143.72, 141.95, 140.26, 139.58, 138.58, 135.14, 133.05, 133.02, 132.43, 130.58, 129.59, 32.04, 31.19, 31.15, 30.47, 30.17, 25.54, 25.18, 21.48; **HRMS (ESI)** *m/z* calculated for $C_{23}H_{23}O$ $[M+H]^+$: 315.1749, found 315.1752.

(*E*)-2-(2-hydroxybenzylidene)-2,3,4,5,6,7,8,9-octahydro-1H-cyclopenta[*e*]-*as*-indacen-1-one **172**



Dusty yellow powder, 86% yield, mp >320 °C, R*f*: 0.3 (4.5:0.5, Pet. Ether:EtOAc); **IR (KBr, cm^{-1})** 3163, 2956, 1663; **^{1}H NMR (500 MHz, DMSO)** δ 10.08 (s, 1H), 7.78 (t, *J* = 2.1 Hz, 1H), 7.65 (d, *J* = 6.2 Hz, 1H), 7.19 (t, *J* = 6.9 Hz, 1H), 6.87 (dd, *J* = 7.8, 2.8 Hz, 2H), 3.82 (s, 2H), 3.09 (t, *J* = 7.5 Hz, 2H), 2.79 (dt, *J* = 15.0, 7.5 Hz, 4H), 2.10 – 1.99 (m, 7H); **^{13}C NMR (126 MHz, DMSO)** δ 193.71, 146.64, 143.82, 140.45, 139.46, 138.59, 134.45, 131.68, 130.91, 129.33, 126.22, 122.00, 115.80, 36.28, 31.44, 30.59, 29.80, 29.49, 24.98, 24.57; **HRMS (ESI)** *m/z* calculated for $C_{22}H_{21}O_2$ $[M+H]^+$: 317.1542, found 317.1538.

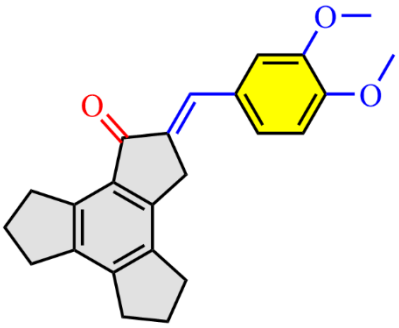
(*E*)-2-(3-methoxybenzylidene)-2,3,4,5,6,7,8,9-octahydro-1H-cyclopenta[*e*]-*as*-indacen-1-one **173**



Fine yellow crystals, 81% yield, mp 272 °C, R*f*: 0.6 (4.5:0.5, Pet. Ether:EtOAc); **IR (KBr, cm^{-1})** 2941, 2838, 1681, 1251; **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.61 (d, *J* = 8.8 Hz, 2H), 7.53 (s, 1H), 6.97 (d, *J* = 8.8 Hz, 2H), 3.86 (s, 3H), 3.78 (s, 2H), 3.30 (t, *J* = 7.5 Hz, 2H), 2.91 (dt, *J* = 22.8, 7.4 Hz, 4H), 2.79 (t, *J* = 7.5 Hz, 2H), 2.22 – 2.12 (m, 4H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ 194.89, 160.50, 147.03, 143.62, 141.87, 140.23, 138.55, 133.80, 132.52, 132.28, 132.20, 128.58, 114.35, 55.37,

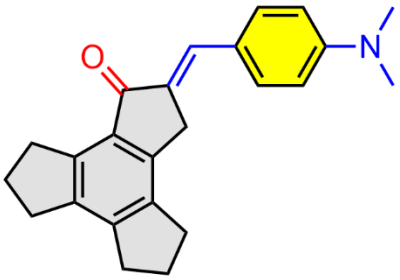
32.03, 31.18, 31.14, 30.47, 30.16, 25.56, 25.18; **HRMS (ESI)** *m/z* calculated for $C_{23}H_{23}O_2$ $[M+H]^+$: 331.1698, found 331.1696.

(*E*)-2-(3,4-dimethoxybenzylidene)-2,3,4,5,6,7,8,9-octahydro-1H-cyclopenta[*e*]-*as*-indacen-1-one **174**



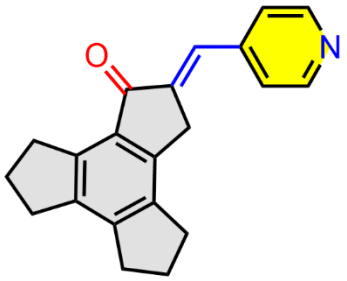
Light yellow crystals, 90% yield, mp 245 °C, R*f*: 0.5 (4.5:0.5, Pet. Ether:EtOAc); **IR (KBr, cm^{-1})** 2956, 2834, 1685, 1271; **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.50 (s, 1H), 7.29 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.15 (d, *J* = 2.0 Hz, 1H), 6.94 (d, *J* = 8.4 Hz, 1H), 3.94 (d, *J* = 9.7 Hz, 6H), 3.78 (s, 2H), 3.29 (t, *J* = 7.5 Hz, 2H), 2.90 (dt, *J* = 20.3, 7.4 Hz, 4H), 2.79 (t, *J* = 7.5 Hz, 2H), 2.18 (dp, *J* = 17.7, 7.5 Hz, 4H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ 194.75, 150.24, 149.02, 147.08, 143.52, 141.90, 140.27, 138.52, 134.09, 132.47, 132.44, 128.86, 124.00, 113.75, 111.28, 56.01, 55.97, 32.03, 31.15, 31.05, 30.47, 30.12, 25.54, 25.17; **HRMS (ESI)** *m/z* calculated for $C_{24}H_{25}O_3$ $[M+H]^+$: 361.1804, found 361.1806.

(*E*)-2-(4-(dimethylamino)benzylidene)-2,3,4,5,6,7,8,9-octahydro-1H-cyclopenta[*e*]-*as*-indacen-1-one **175**



Curcumin yellow crystals, 89% yield, mp 317 °C, R*f*: 0.4 (4.5:0.5, Pet. Ether:EtOAc); **IR (KBr, cm^{-1})** 2952, 2838, 1678, 1370; **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.58 (d, *J* = 8.9 Hz, 2H), 7.54 (s, 1H), 6.74 (d, *J* = 8.9 Hz, 2H), 3.78 (s, 2H), 3.32 (t, *J* = 7.5 Hz, 2H), 3.03 (s, 6H), 2.91 (dt, *J* = 22.5, 7.4 Hz, 4H), 2.80 (t, *J* = 7.5 Hz, 2H), 2.23 – 2.13 (m, 4H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ 195.00, 150.86, 146.49, 143.56, 141.60, 140.02, 138.44, 133.28, 132.93, 132.42, 131.43, 123.77, 112.00, 40.14, 32.00, 31.40, 31.12, 30.49, 30.17, 25.62, 25.21; **HRMS (ESI)** *m/z* calculated for $C_{24}H_{26}NO$ $[M+H]^+$: 344.2014, found 344.2003.

(*E*)-2-(pyridin-4-ylmethylene)-2,3,4,5,6,7,8,9-octahydro-1H-cyclopenta[*e*]-*as*-indacen-1-one **176**



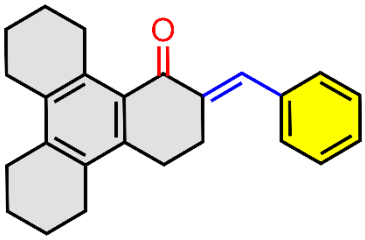
White crystals, 96% yield, mp 306 °C, R*f*: 0.6 (4.5:0.5, Pet. Ether:EtOAc); **IR (KBr, cm^{-1})** 2956, 2898, 1685, 1282; **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.68 (d, *J* = 6.1 Hz, 2H), 7.46 (d, *J* = 6.2 Hz, 2H), 7.42 (s, 1H), 3.83 (s, 2H), 3.26 (t, *J* = 7.5 Hz, 2H), 2.90 (dt, *J* = 19.3, 7.5 Hz, 4H), 2.79 (t, *J* = 7.5 Hz, 2H), 2.18 (dp, *J* = 19.2, 7.5 Hz, 4H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ 193.99, 150.34, 148.19, 143.42, 143.02, 142.48, 140.74, 140.58, 138.74, 131.94, 129.14, 124.05, 32.12, 31.19, 31.01, 30.48, 30.15, 25.50, 25.18; **HRMS (ESI)** *m/z* calculated for $C_{21}H_{20}NO$ $[M+H]^+$: 302.1545, found 302.1542.

4.4.2 *Synthetic procedure of 2-benzylidenedecahydrotriphenylen-1-one* **179**

To a sodium ethoxide solution which was freshly prepared by dissolving sodium metal (1 g, 43.37 mmol) in absolute ethanol (5 mL), decahydrotriphenlylen-

1-one **48** (0.5 g, 1.97 mmol) in THF (5 mL) was added. After 10 mins of stirring, benzaldehyde (0.30 mL, 2.56 mmol) was added in the reaction mixture and was thoroughly stirred under reflux temperature for 24 h. The resulting suspension was cooled to room temperature and concentrated under reduced pressure. The residue was then purify by column chromatography on a silica gel column using light petroleum and ethyl acetate to get 0.39 g light yellow solid.

(*E*)-2-benzylidene-3,4,5,6,7,8,9,10,11,12-decahydrotriphenylen-1(*2H*)-one **179**



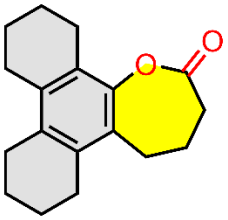
Yellow powder, 59% yield, mp 160 °C, R*f*: 0.75 (4.5:0.5, Pet. Ether:EtOAc) **IR (KBr, cm^{-1})** 3055, 1662, 1599; **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.78 (s, 1H), 7.44 (d, *J* = 7.2 Hz, 2H), 7.39 (t, *J* = 7.6 Hz, 2H), 7.31 (t, *J* = 7.3 Hz, 1H), 3.16 (t, *J* = 6.3 Hz, 2H), 2.99 (td, *J* = 6.4, 2.0 Hz, 2H), 2.77 – 2.72 (m, 2H), 2.71 – 2.56 (m, 6H), 1.81 (ddd, *J* = 14.8, 7.9, 4.3 Hz, 6H), 1.73 – 1.66 (m, 2H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ 189.60, 141.01, 140.13, 137.37, 137.18, 136.31, 134.91, 134.62, 131.33, 130.80, 129.84, 128.41, 128.26, 29.58, 27.76, 27.29, 27.19, 26.72, 24.76, 23.09, 22.94, 22.78, 22.73; **HRMS (ESI)** *m/z* calculated for $C_{25}H_{27}O$ $[M+H]^+$: 343.2062, found 343.2045.

4.4.3 *Synthetic procedure of decahydrophenanthrooxepinone* **180**

To a solution of 30% H_2O_2 with 10 mL dichloromethane, decahydrotriphenlylen-1-one **48** (0.5 g, 1.97 mmol) in CH_2Cl_2 (10 mL) was added in an ice water bath. After 10 mins of stirring, *m*-CPBA (0.67 g, 3.94 mmol) and 3 mL of formic acid was added to the mixture. After completion (monitored by TLC), the reaction was quenched by 25 ml of water and extracted with 2 x 20 mL EtOAc.

The combined organic layers were washed with 10% sodium bisulfite to remove excess of peroxides. Organic phase was dried by sodium sulfate and purify by column chromatography on a silica gel column using light petroleum and ethyl acetate afforded 0.28 g off-white solid.

4,5,6,7,8,9,10,11,12,13-decahydrophenanthro[9,10-*b*]oxepin-2(*3H*)-one **180**

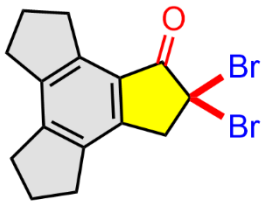


White solid, 52% yield, mp 197 °C, R*f*: 0.4 (4.5:0.5, Pet. Ether:EtOAc); **IR (KBr, cm^{-1})** 2860,1760; **^{1}H NMR (500 MHz, $CDCl_3$)** δ 2.77 (t, *J* = 7.1 Hz, 2H), 2.74 – 2.63 (m, 4H), 2.55 (t, *J* = 6.3 Hz, 4H), 2.42 (t, *J* = 7.1 Hz, 2H), 2.08 (quint, *J* = 7.2 Hz, 2H), 1.84 – 1.75 (m, 6H), 1.73 (ddt, *J* = 8.5, 6.2, 2.8 Hz, 2H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ 172.50, 147.85, 135.27, 133.02, 131.86, 125.05, 124.71, 31.41, 26.92, 26.76, 26.51, 25.68, 24.02, 22.94, 22.89, 22.83, 22.42, 22.05; **HRMS (ESI)** *m/z* calculated for $C_{18}H_{23}O_2$ $[M+H]^+$: 271.1698, found 271.1706.

4.4.4 *Synthetic procedure of gem-dibromocarbonyls* **182** and **182**

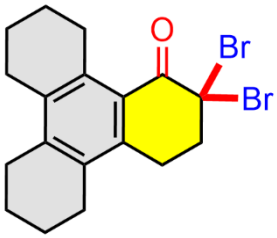
To a stirred solution of cycloalkanones **48** or **50** (2 mmol) in 10 mL dry Et_2O, a solution liquid Br_2 (1 mL) in 5 mL of dry Et_2O added dropwise in ice bath. Reaction was stirred in ice bath at for 1.5 hour, then after it was quenched 25 mL of water. Mixture was extracted by 2 x 20 mL portions of diethyl ether. Combined organic layers were washed 25 mL saturated solution of sodium bicarbonate, 25 mL of saturated solution of sodium thiosulphate and 25 mL of brine respectively. Organic phase was dried by sodium sulfate and evaporated by rotary evaporator and purify by column chromatography on a silica gel column using light petroleum and ethyl acetate.

2,2-dibromo-2,3,4,5,6,7,8,9-octahydro-1H-cyclopenta[*e*]-*as*-indacen-1-one **181**



Orange crystals, 67% yield, mp 131 °C, R*f*: 0.45 (5:1, Pet. Ether:EtOAc); **IR (KBr, cm^{-1})** 2948, 1716, 704; **^{1}H NMR (500 MHz, CDCl$_3$)** δ 4.16 (s, 2H), 3.26 (t, *J* = 7.5 Hz, 2H), 2.90 (t, *J* = 7.5 Hz, 2H), 2.83 (t, *J* = 7.5 Hz, 4H), 2.19 (pd, *J* = 7.5, 2.1 Hz, 4H); **^{13}C NMR (126 MHz, CDCl$_3$)** δ 192.90, 150.30, 144.50, 141.89, 140.82, 138.60, 122.89, 58.83, 51.49, 32.19, 31.17, 30.60, 29.83, 25.37, 25.10; **HRMS (ESI)** *m/z* calculated for $C_{15}H_{15}OBr_2$ $[M+H]^+$: 368.9490, found 368.9484.

2,2-dibromo-3,4,5,6,7,8,9,10,11,12-decahydrotriphenylen-1(*2H*)-one **182**



White powder, 92% yield, mp 168 °C, R*f*: 0.4 (5:1, Pet. Ether:EtOAc); **IR (KBr, cm^{-1})** 2927, 1689, 787; **^{1}H NMR (500 MHz, CDCl$_3$)** δ 3.11 (t, *J* = 6.2 Hz, 2H), 3.03 (t, *J* = 6.0 Hz, 2H), 2.90 (t, *J* = 6.0 Hz, 2H), 2.70 – 2.50 (m, 6H), 1.85 – 1.75 (m, 6H), 1.75 – 1.69 (m, 2H); **^{13}C NMR (126 MHz, CDCl$_3$)** δ 185.88, 142.84, 139.62, 139.60, 138.71, 135.84, 132.17, 124.39, 70.09, 44.91, 29.95, 27.73, 27.26, 27.14, 26.79, 22.97, 22.54, 22.49, 22.46; **HRMS (ESI)** *m/z* calculated for $C_{18}H_{21}OBr_2$ $[M+H]^+$: 410.9959, found 410.9943.

4.5 Conclusion

In this chapter, the carbonyl functionality has been exploited to synthesize 2-arylidenecycloalkanones, caprolactone and α,α-dibromoketones of decahydrotriphenylene-1-one **48** and trindanone **50** using simple methodologies. Without the influence of temperature or the nature of the substituents, all arylaldehydes containing EWG/EDG were well-tolerated for the synthesis of 2-arylidenetrindanones **165-176** in high yields. Additionally, the synthesis of 2-benzylidenedecahydrotriphenylenone **179** was sequentially accomplished using NaOEt in THF at ambient temperature. Benzo-fused lactone **180** was obtained by Baeyer-Villiger oxidation reaction. The synthesis of α,α–dibromoketones **181** and **182** were furnished *via* bromination. The synthesis of library of aesthetic carbocyclic derivatives of trindane **35** and dodecahydrotriphenylene **36** with diverse functionalities have been described under mild conditions and shorter reaction times with good to excellent yields.

4.6 References

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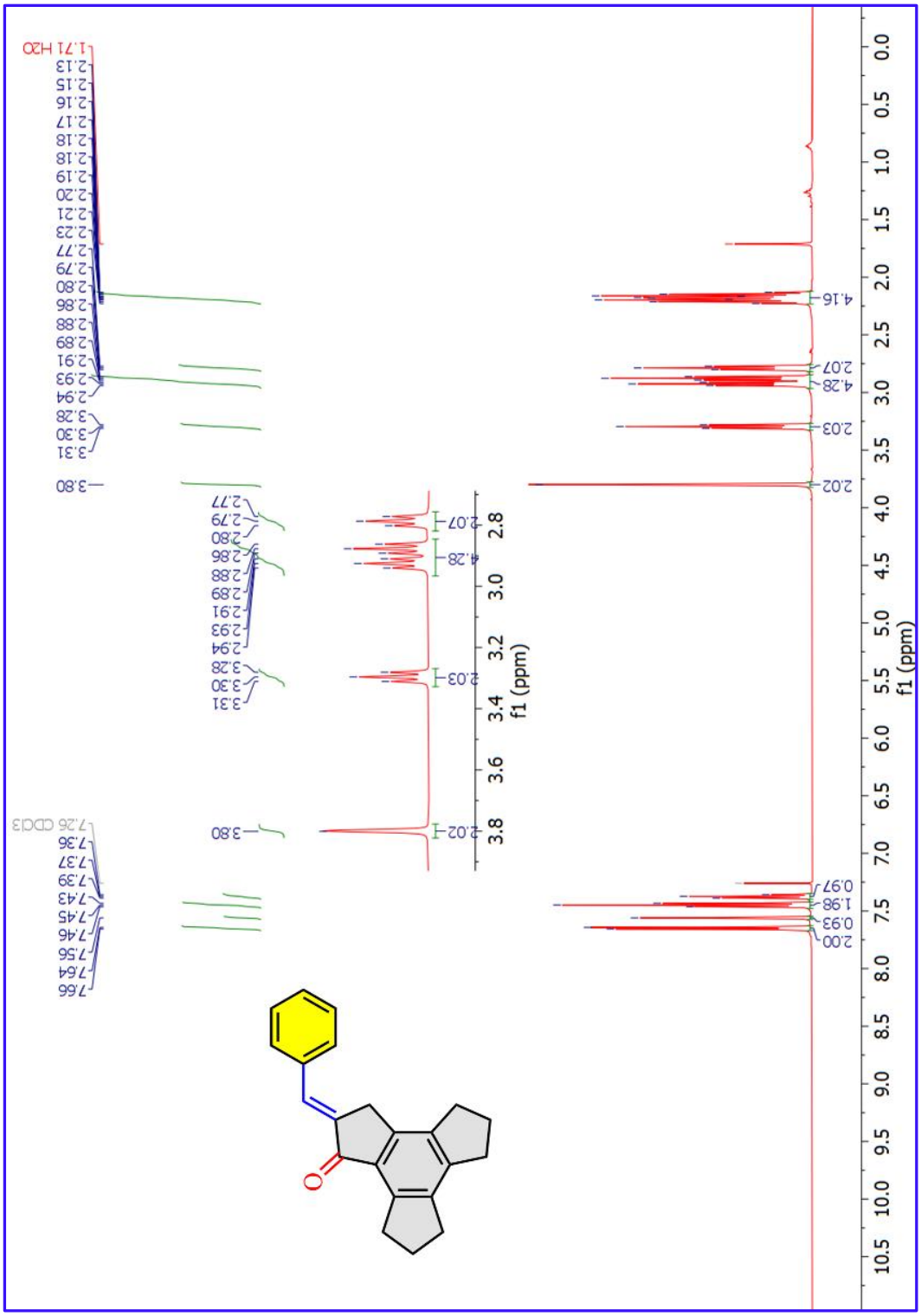
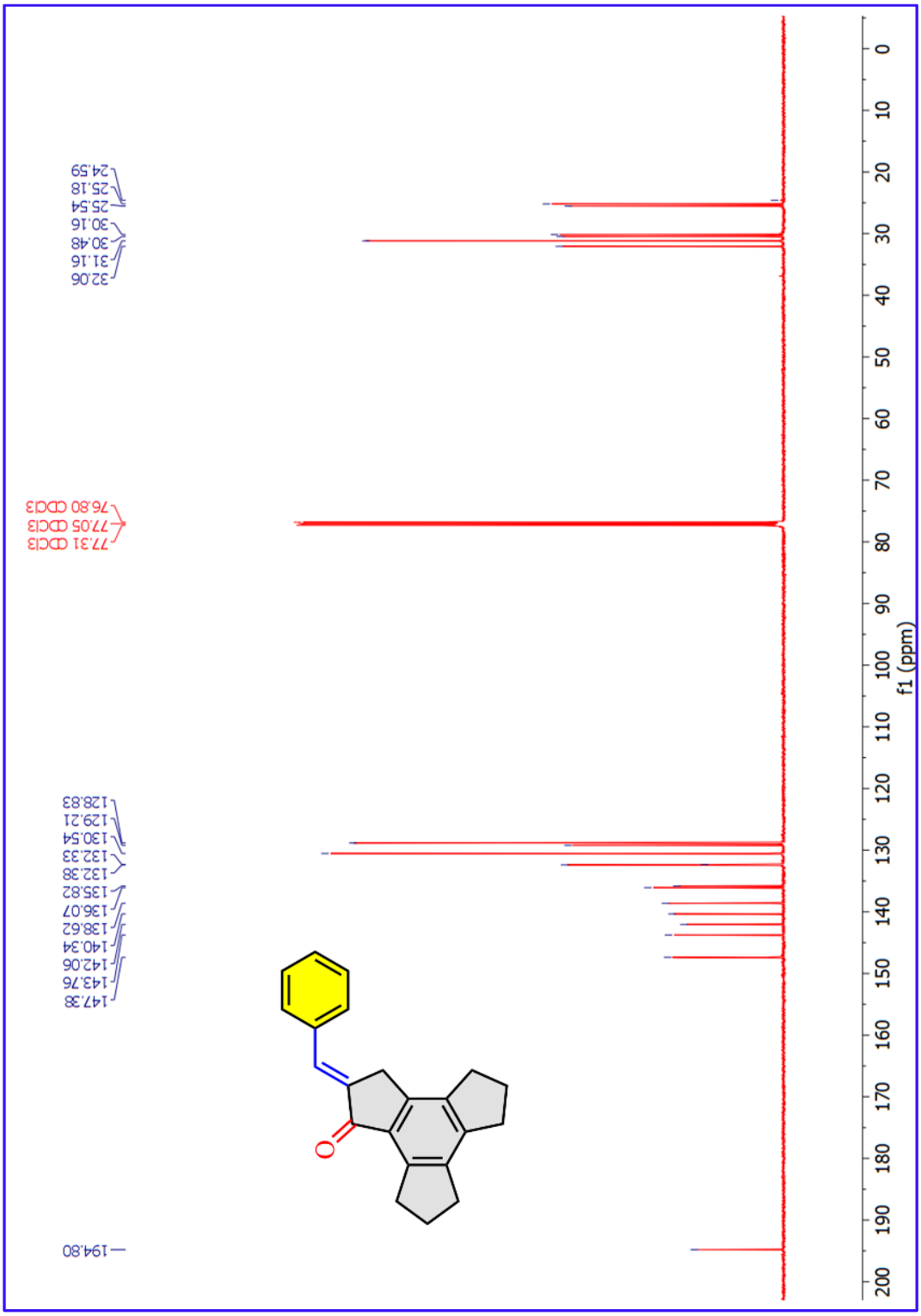
4.7 Spectral data of compounds

4.7.1 *^{1}H and ^{13}C NMR spectra and HRMS of products*

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129.21
130.54
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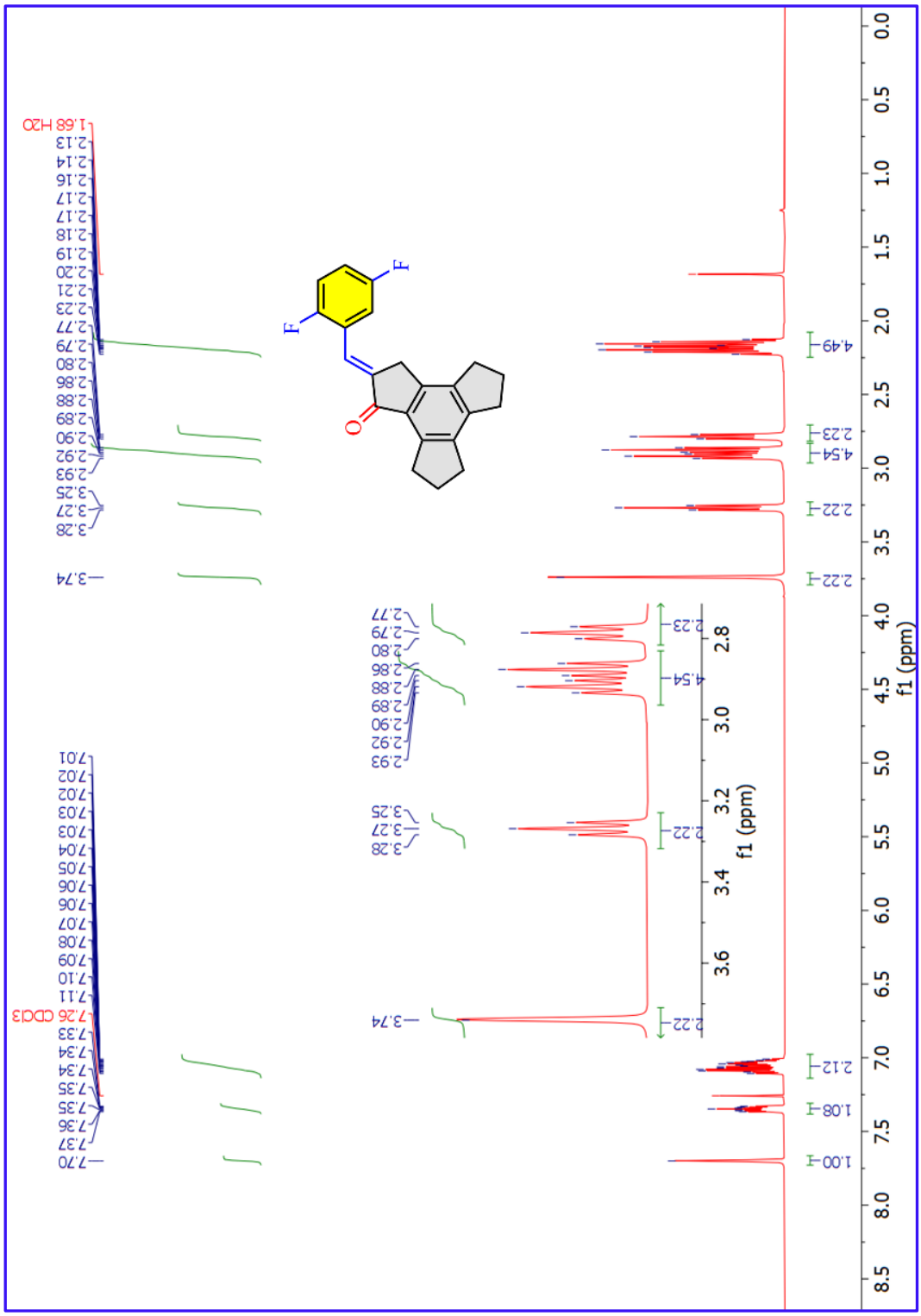
194.80
O
f1 (ppm)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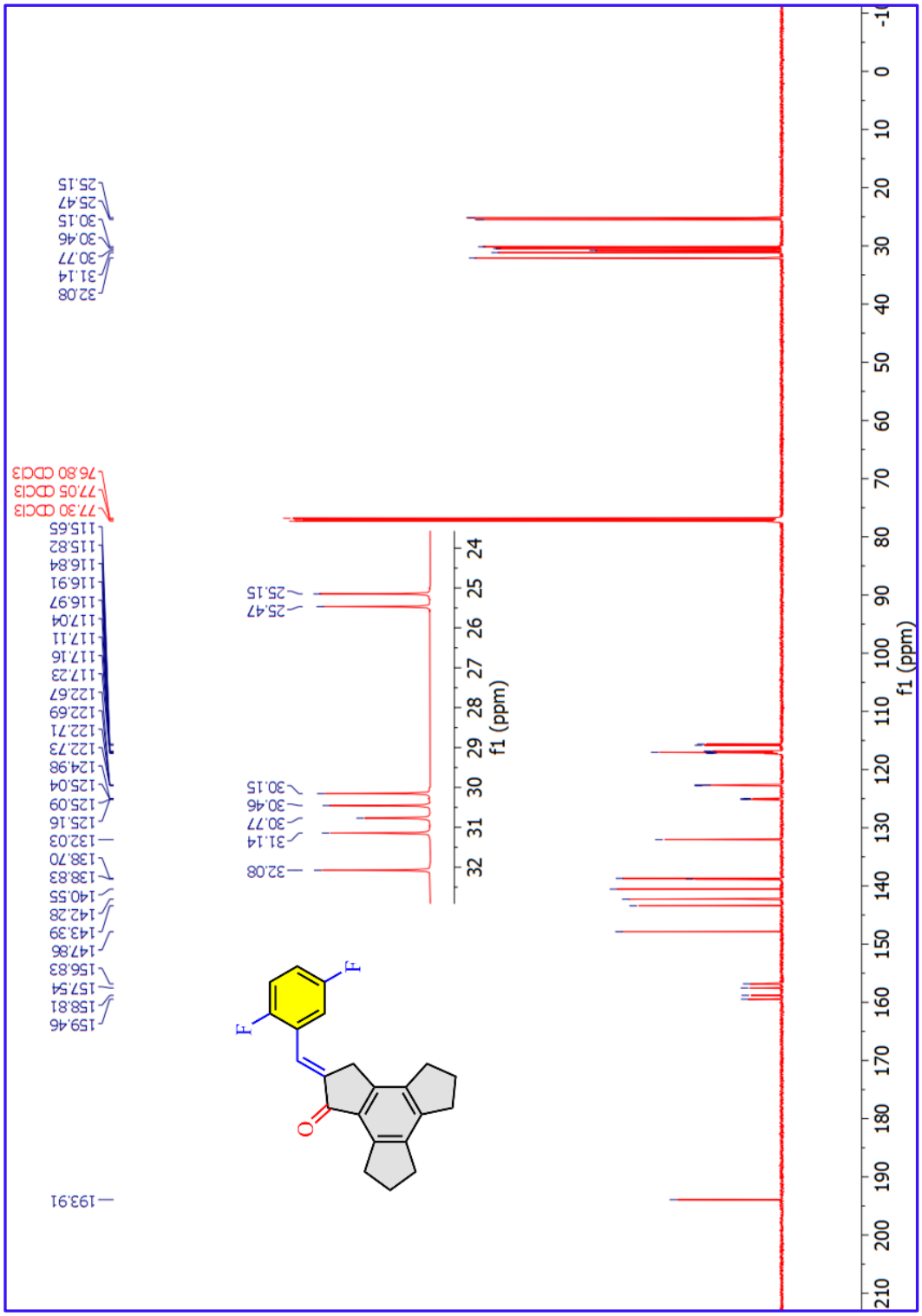
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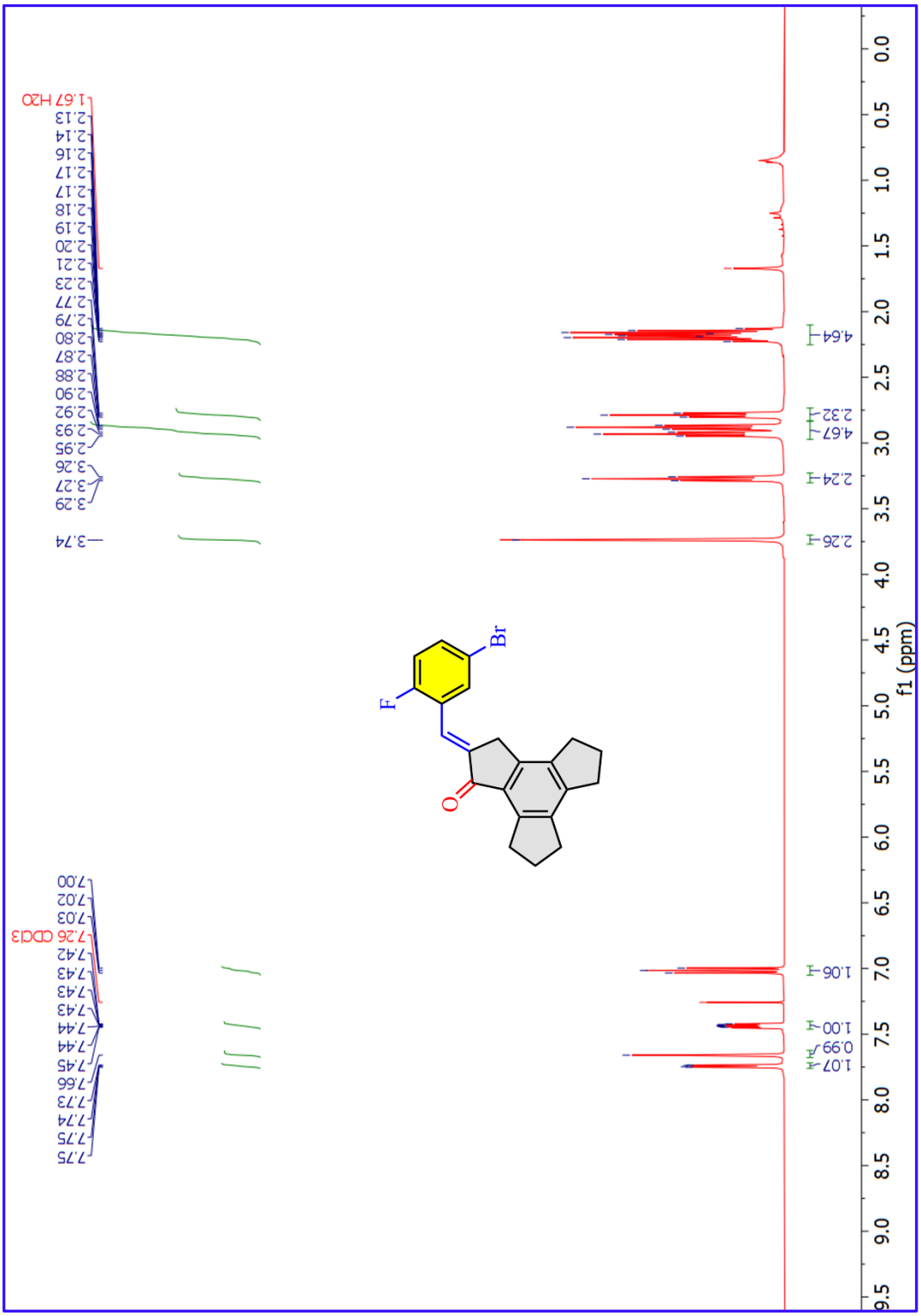
O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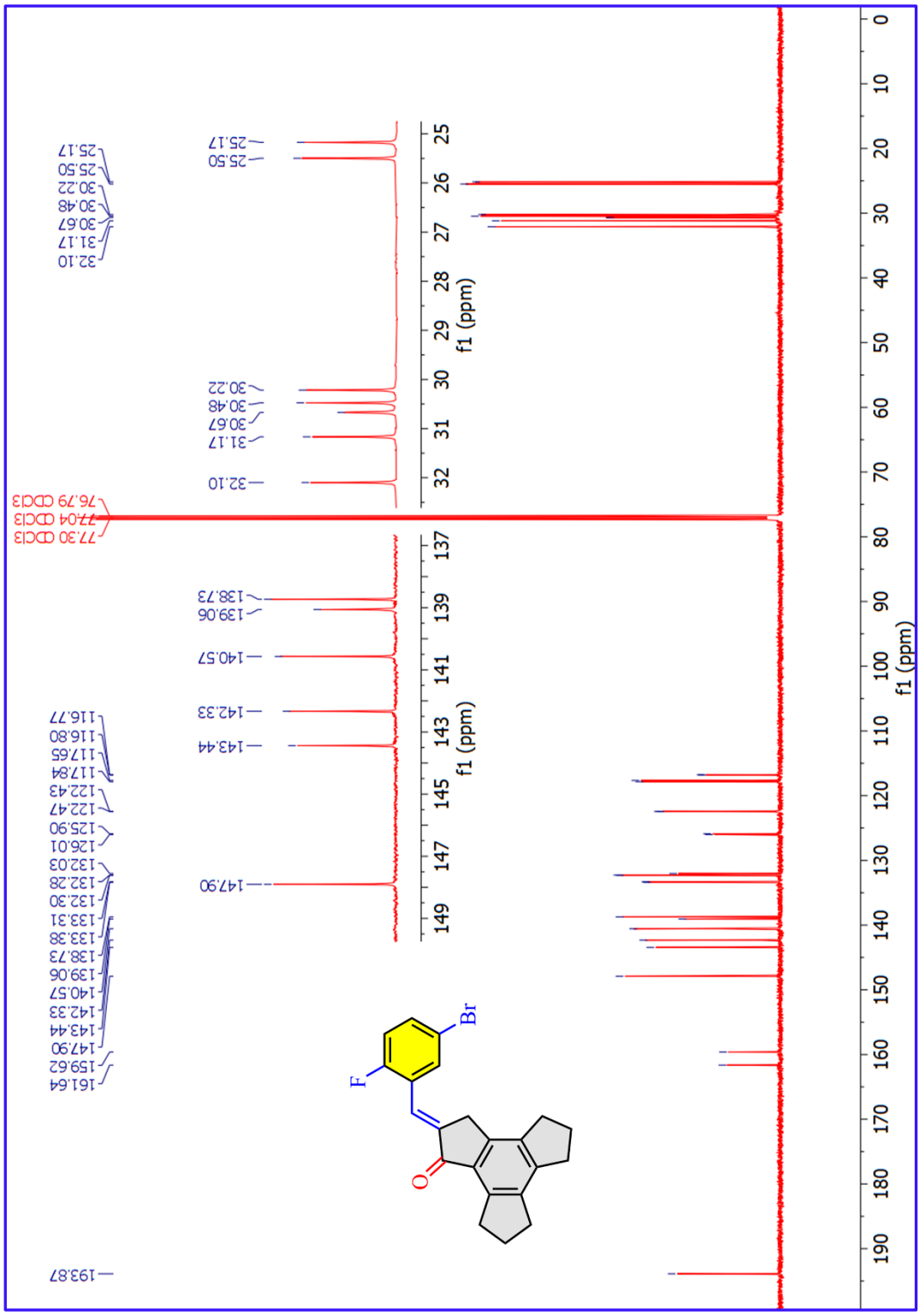
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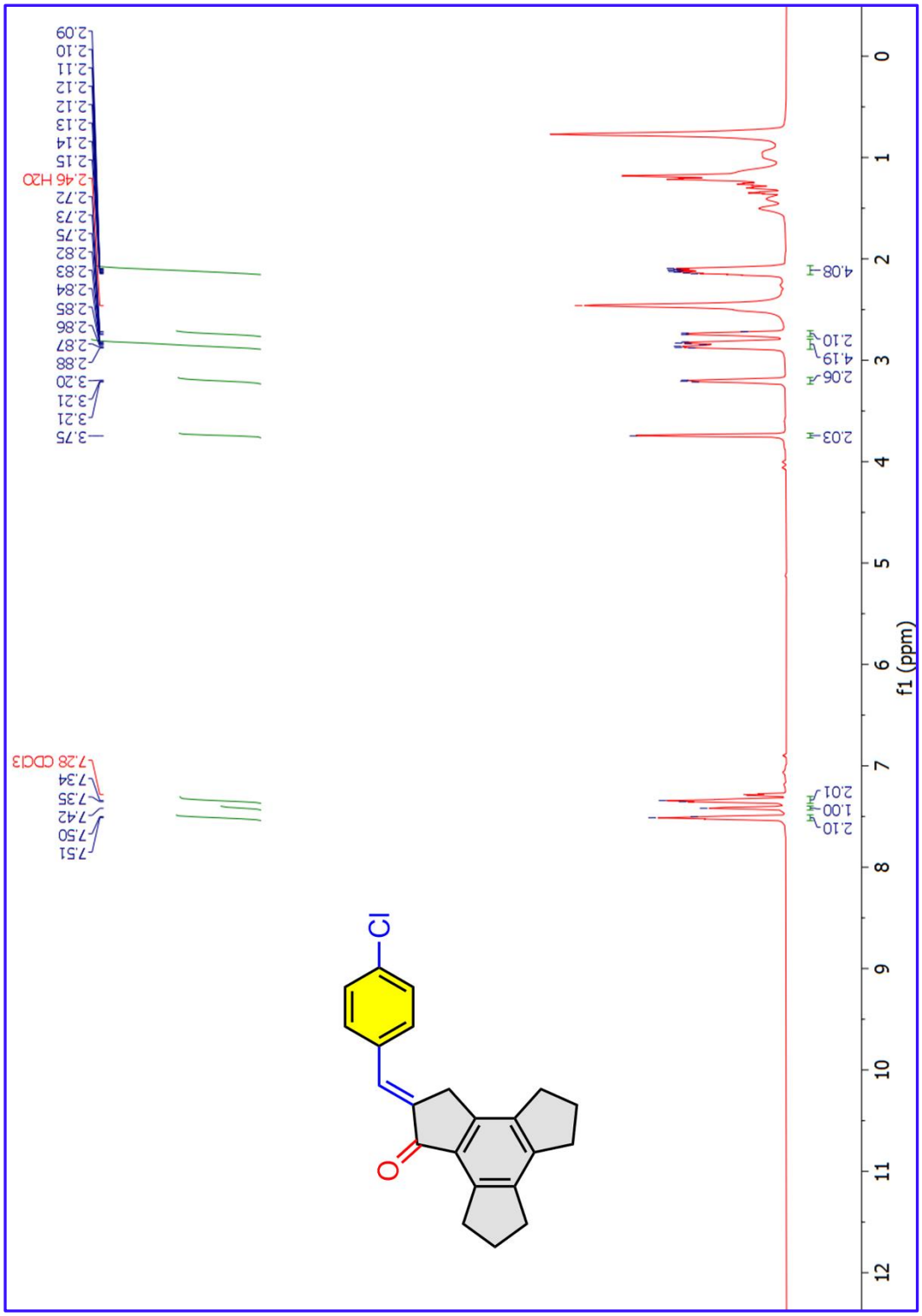
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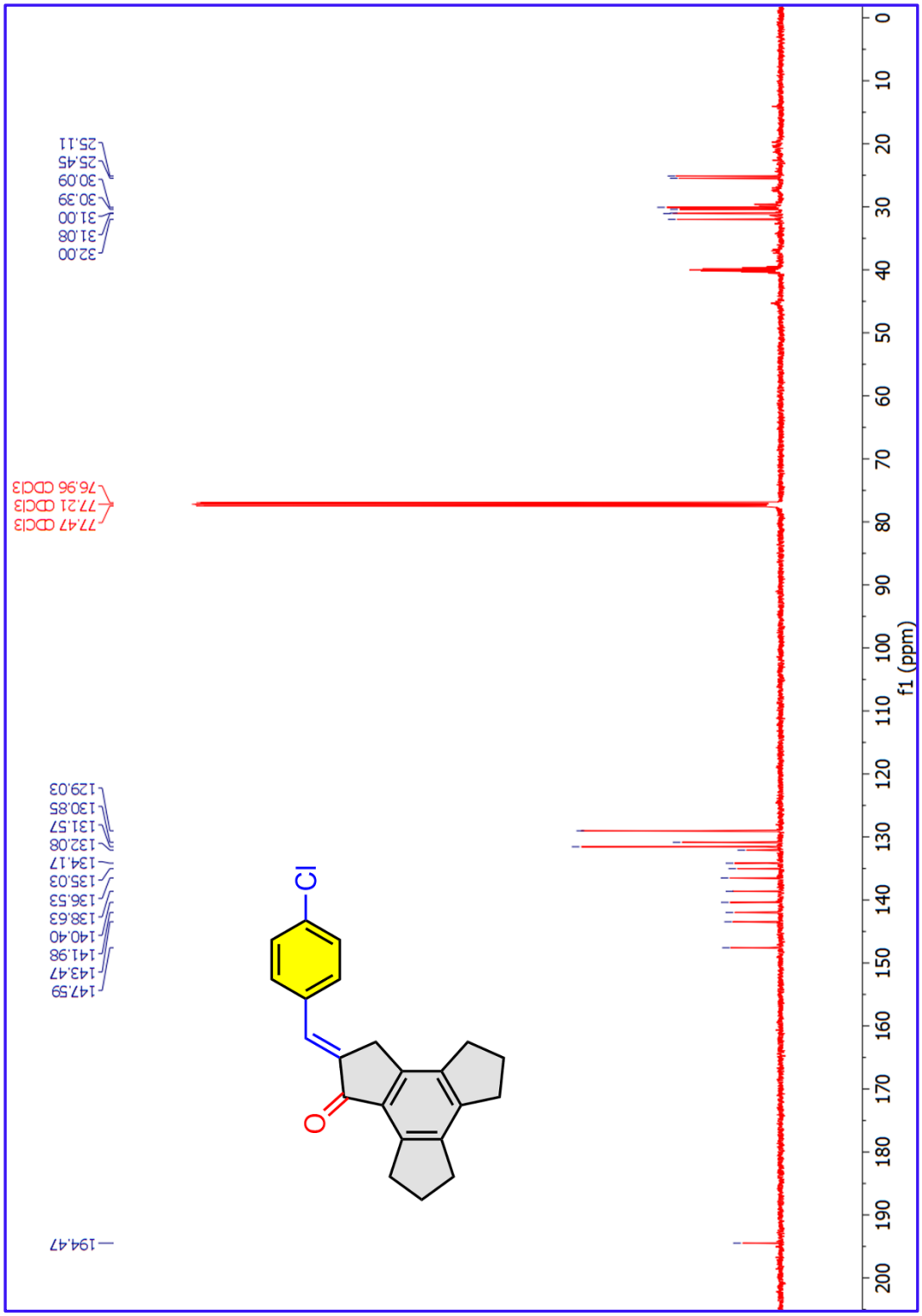
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31.08
32.00
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130.85
131.57
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147.59
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Cl
O
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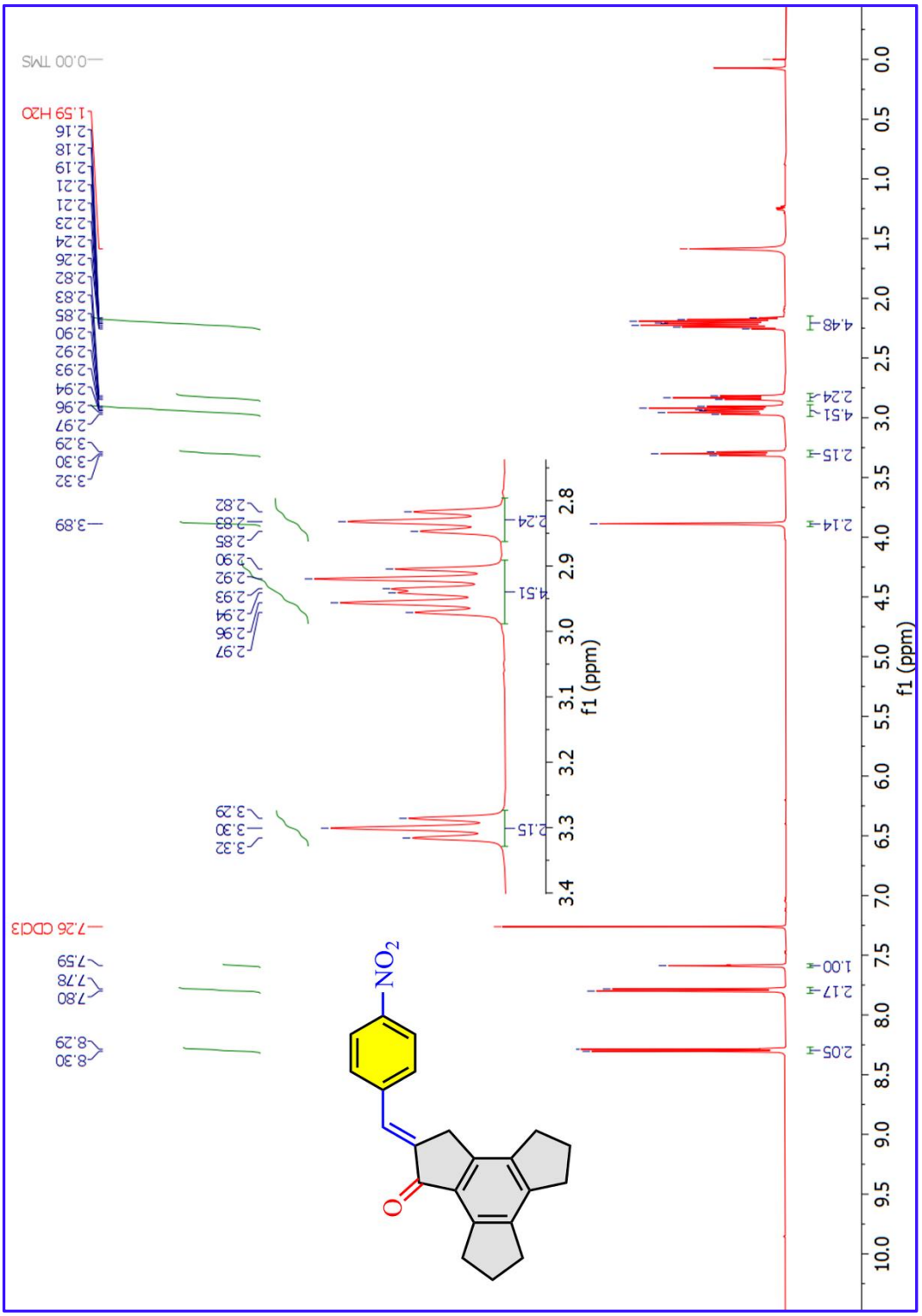
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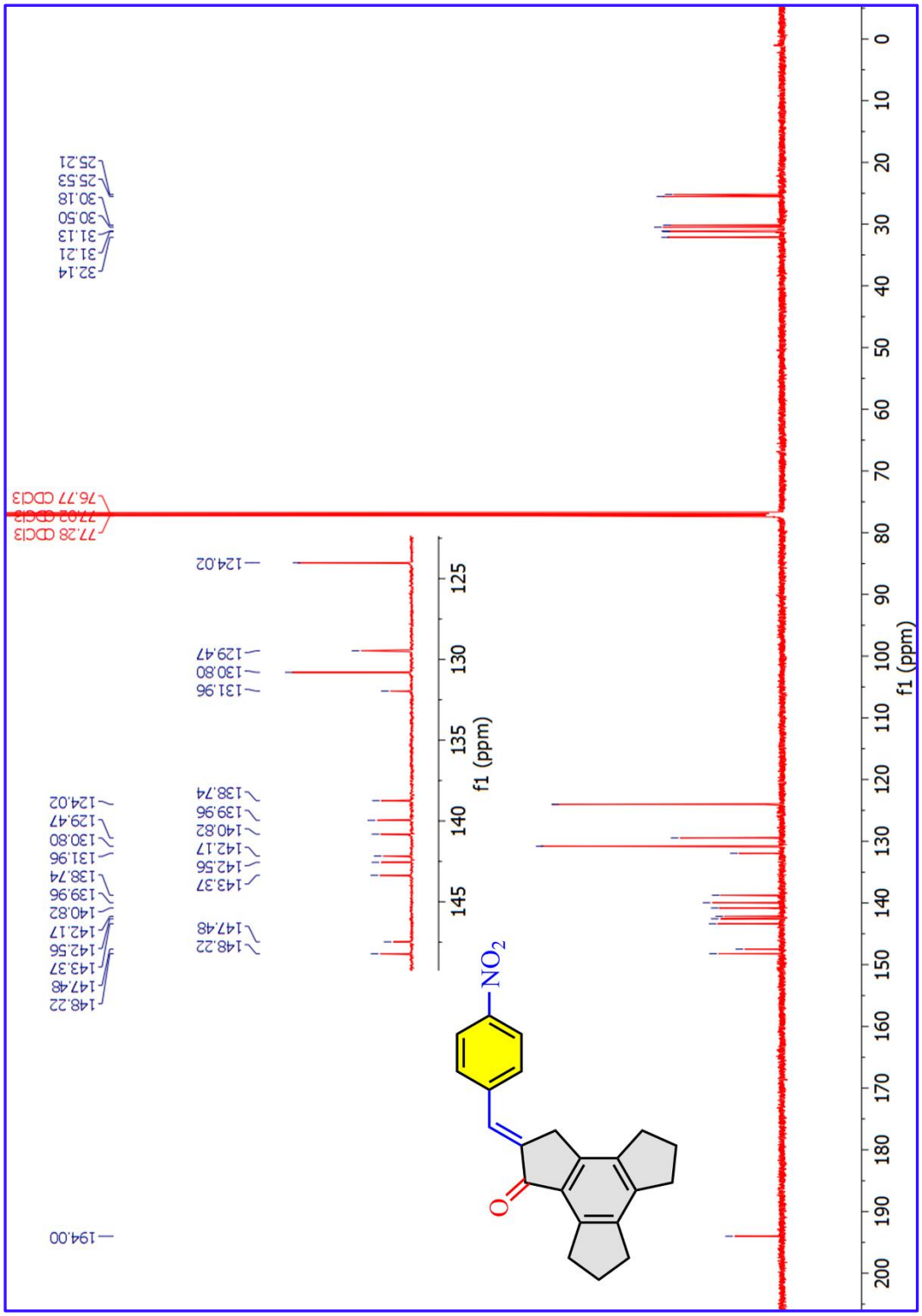
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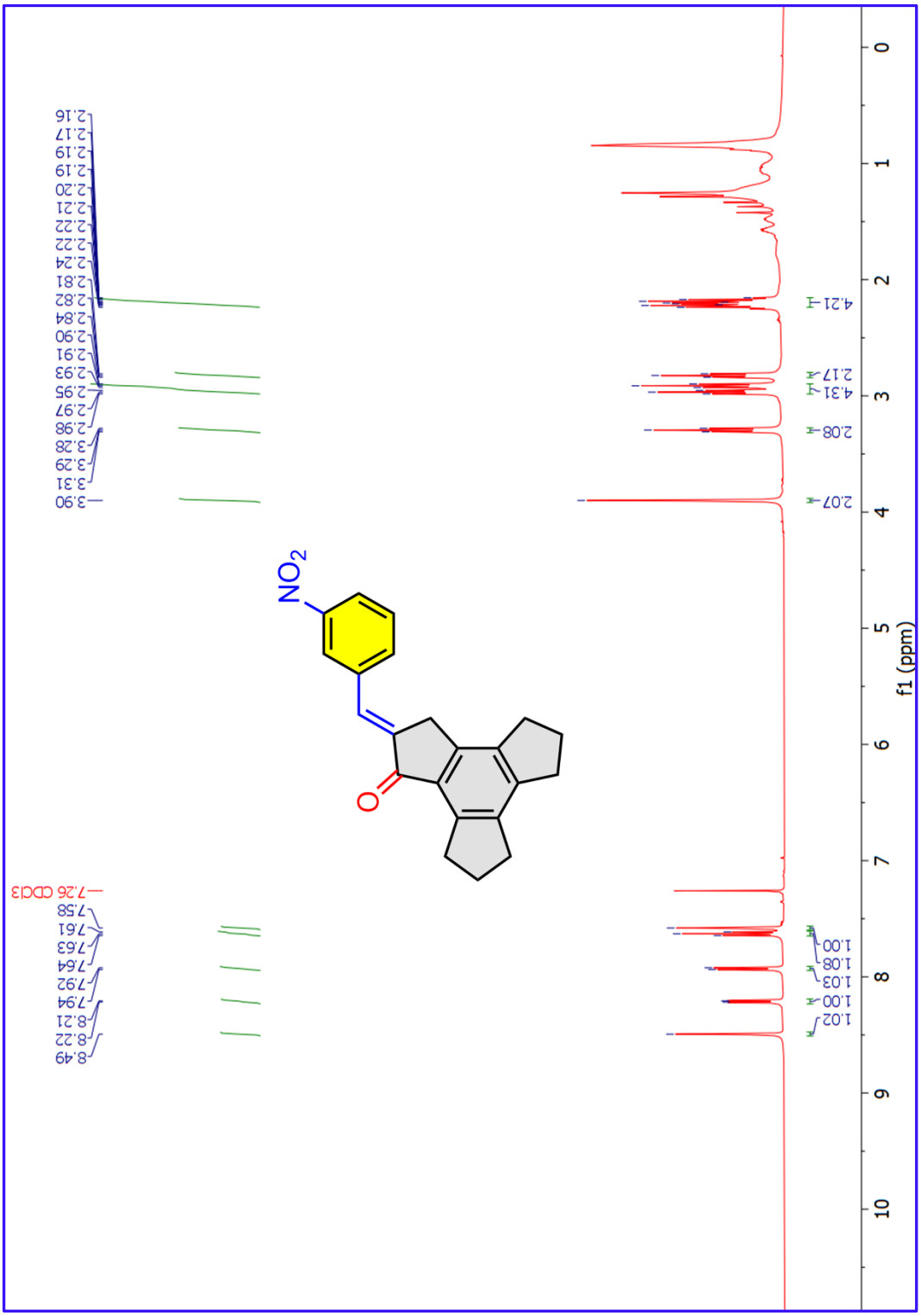
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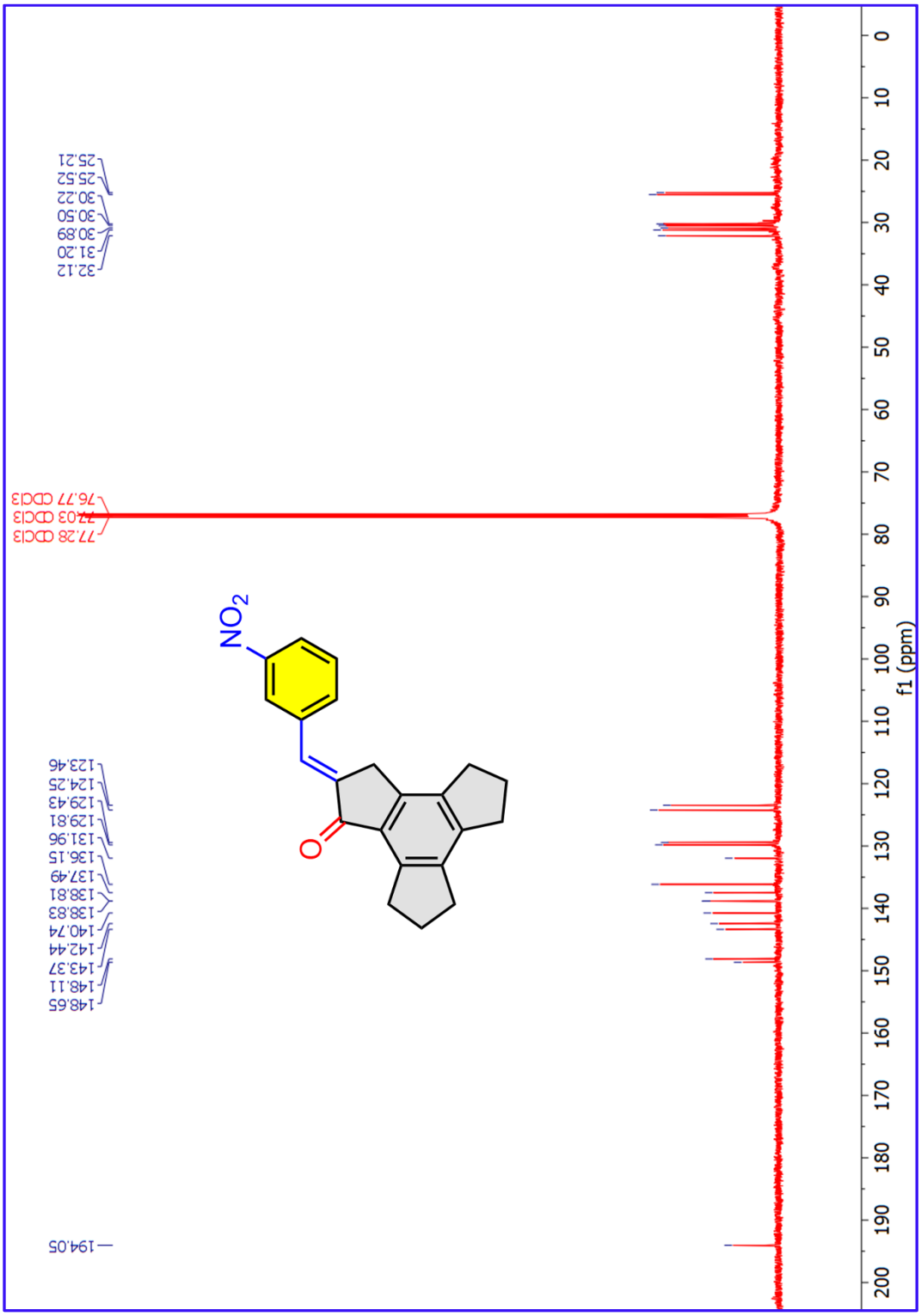
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124.25
129.43
129.81
131.96
136.15
137.49
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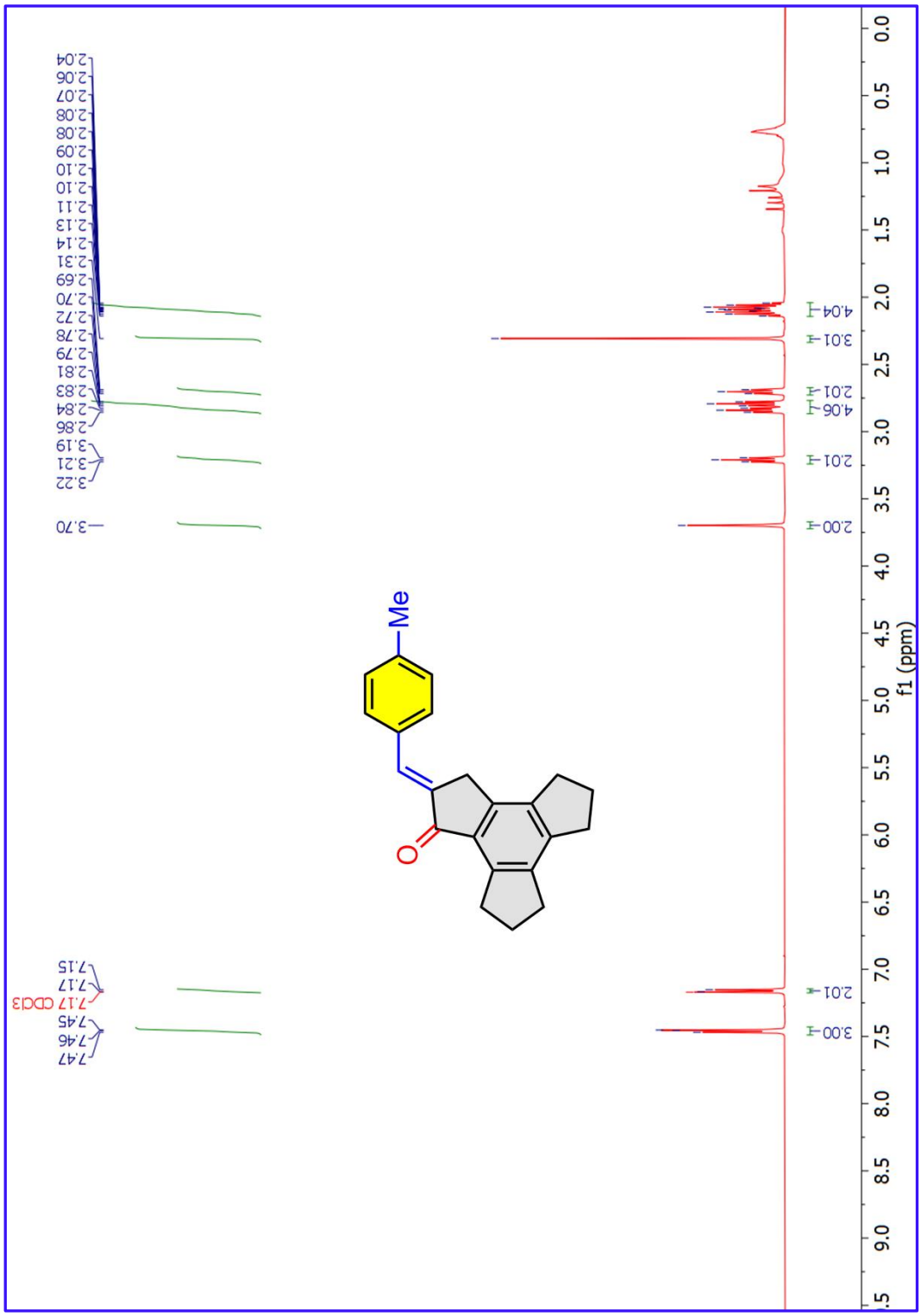
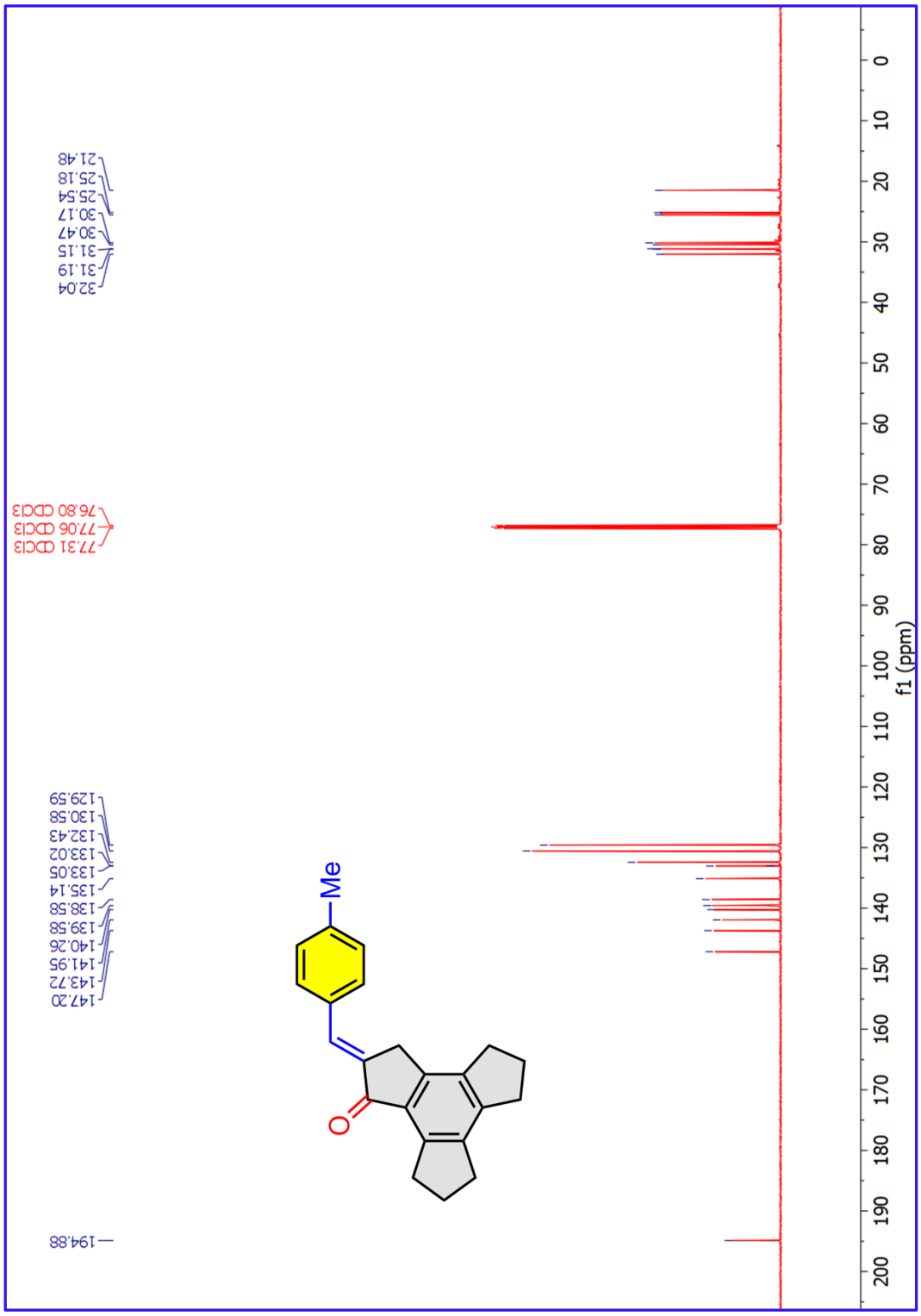
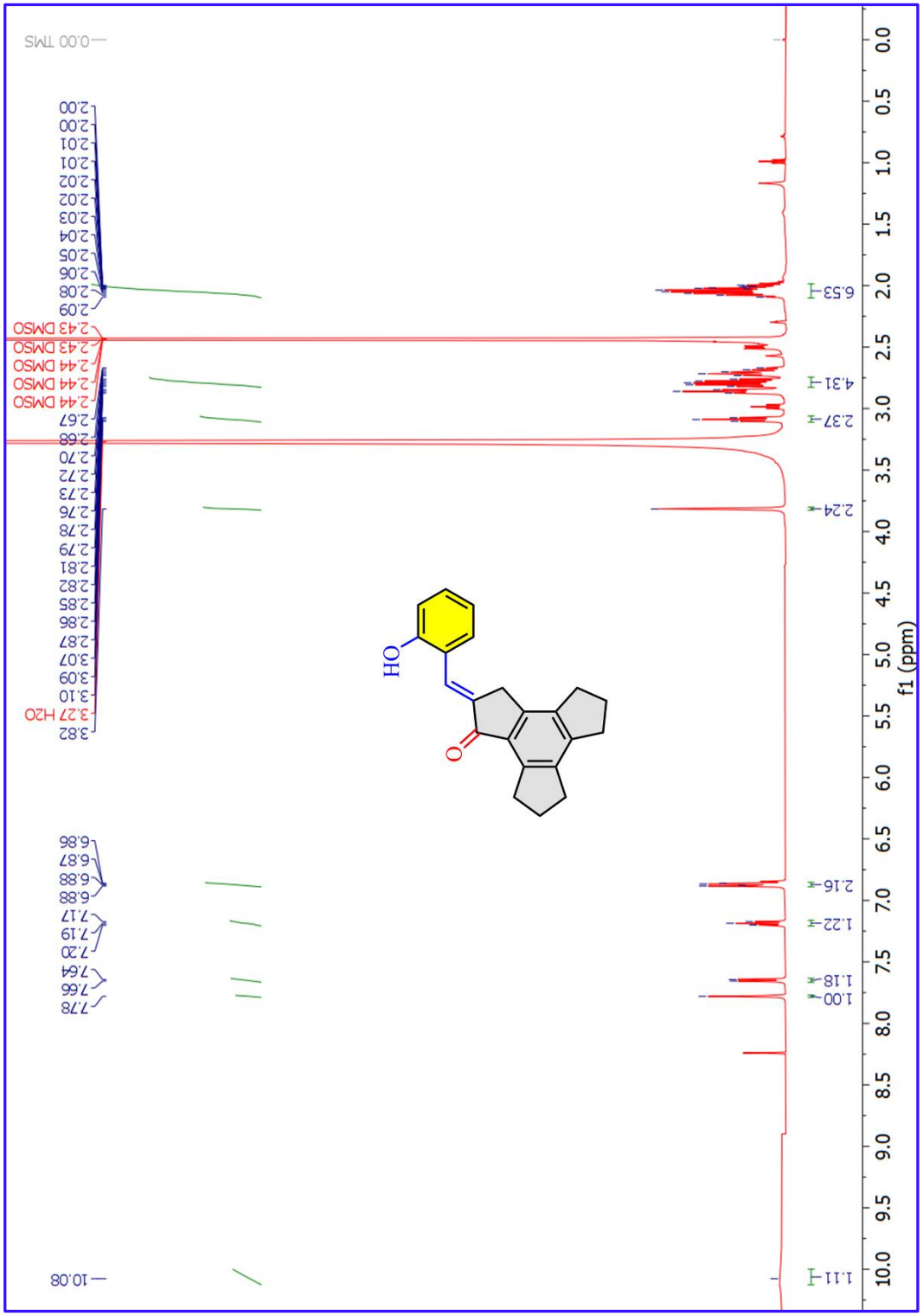
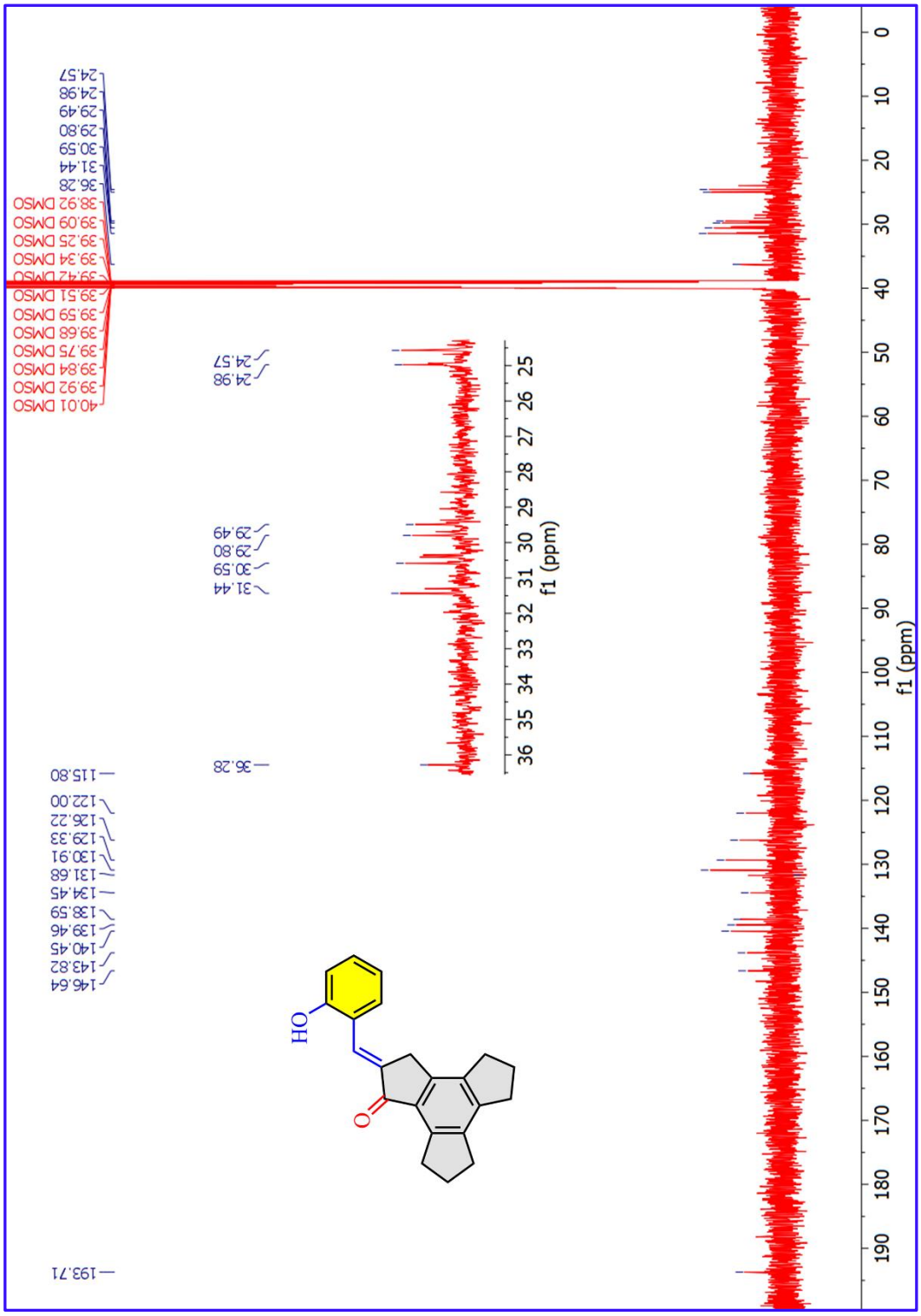
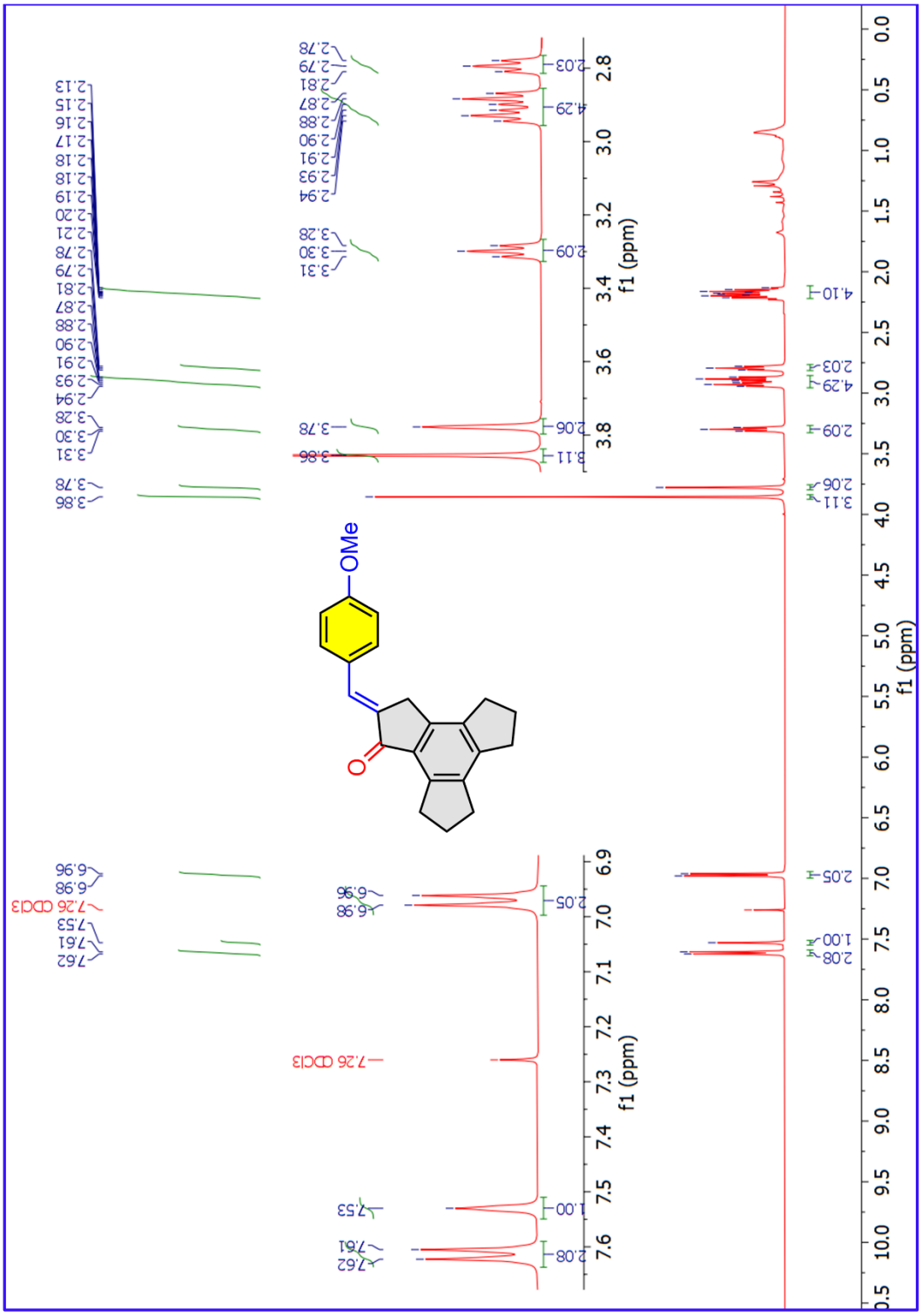
138.83
140.74
142.44
143.37
148.11
148.65
194.05
NO2
O
f1 (ppm)

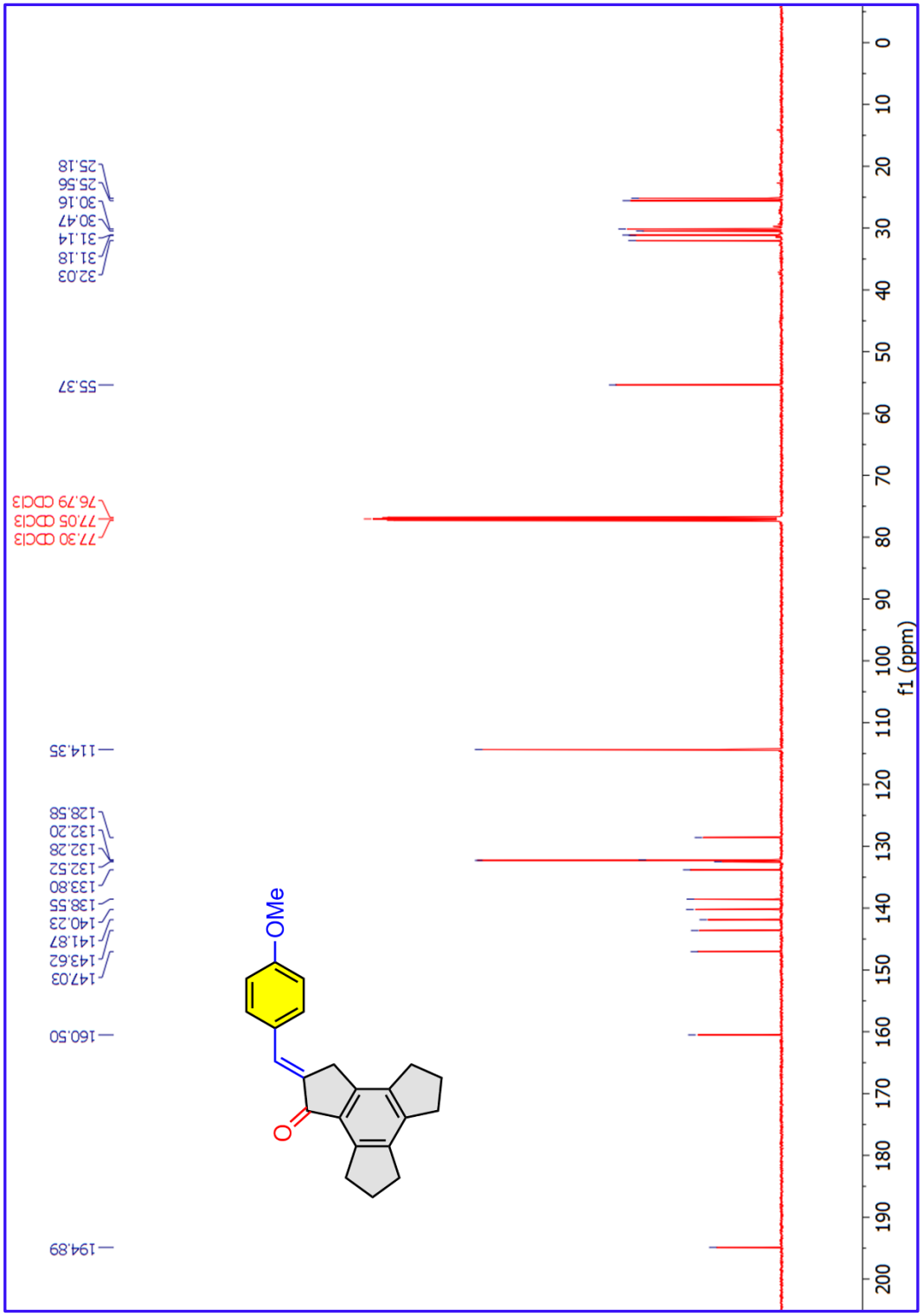

Me
O
f1 (ppm)

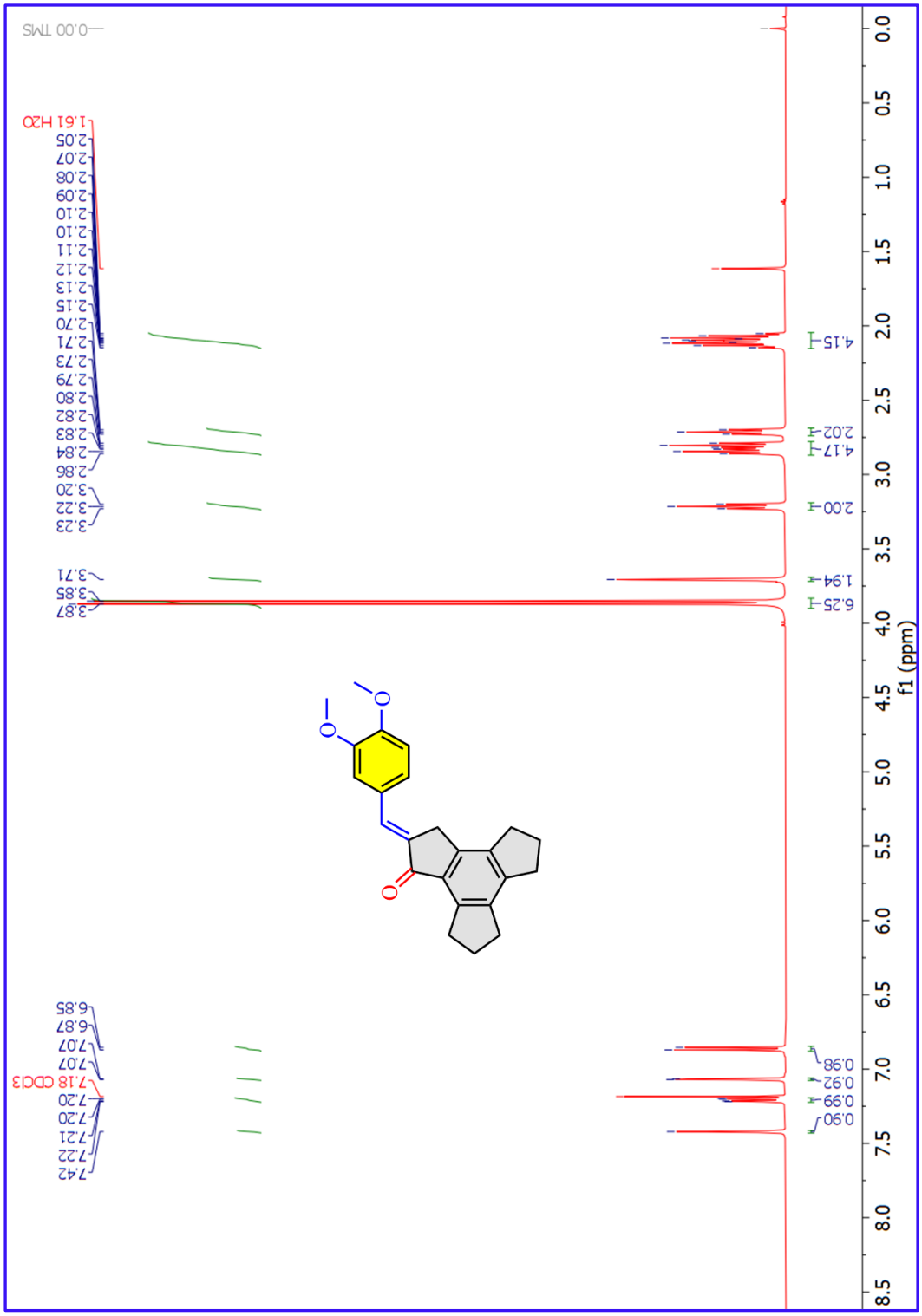

Me
O
194.88
147.20
143.72
141.95
140.26
139.58
138.58
135.14
133.05
133.02
132.43
130.58
129.59
77.31 CDCl3
77.06 CDCl3
76.80 CDCl3
32.04
31.19
31.15
30.47
30.17
25.54
25.18
21.48
f1 (ppm)

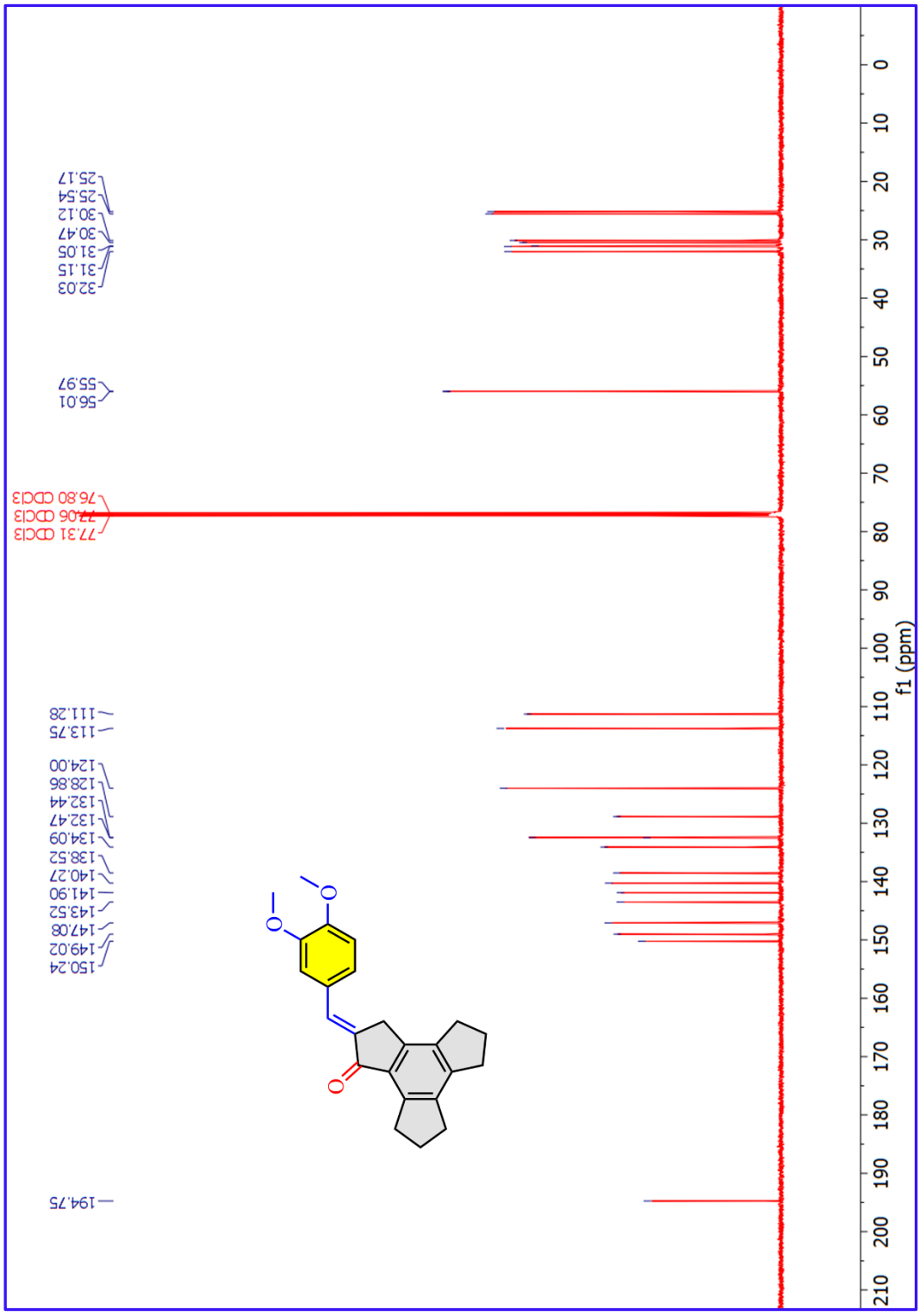

HO
O
f1 (ppm)

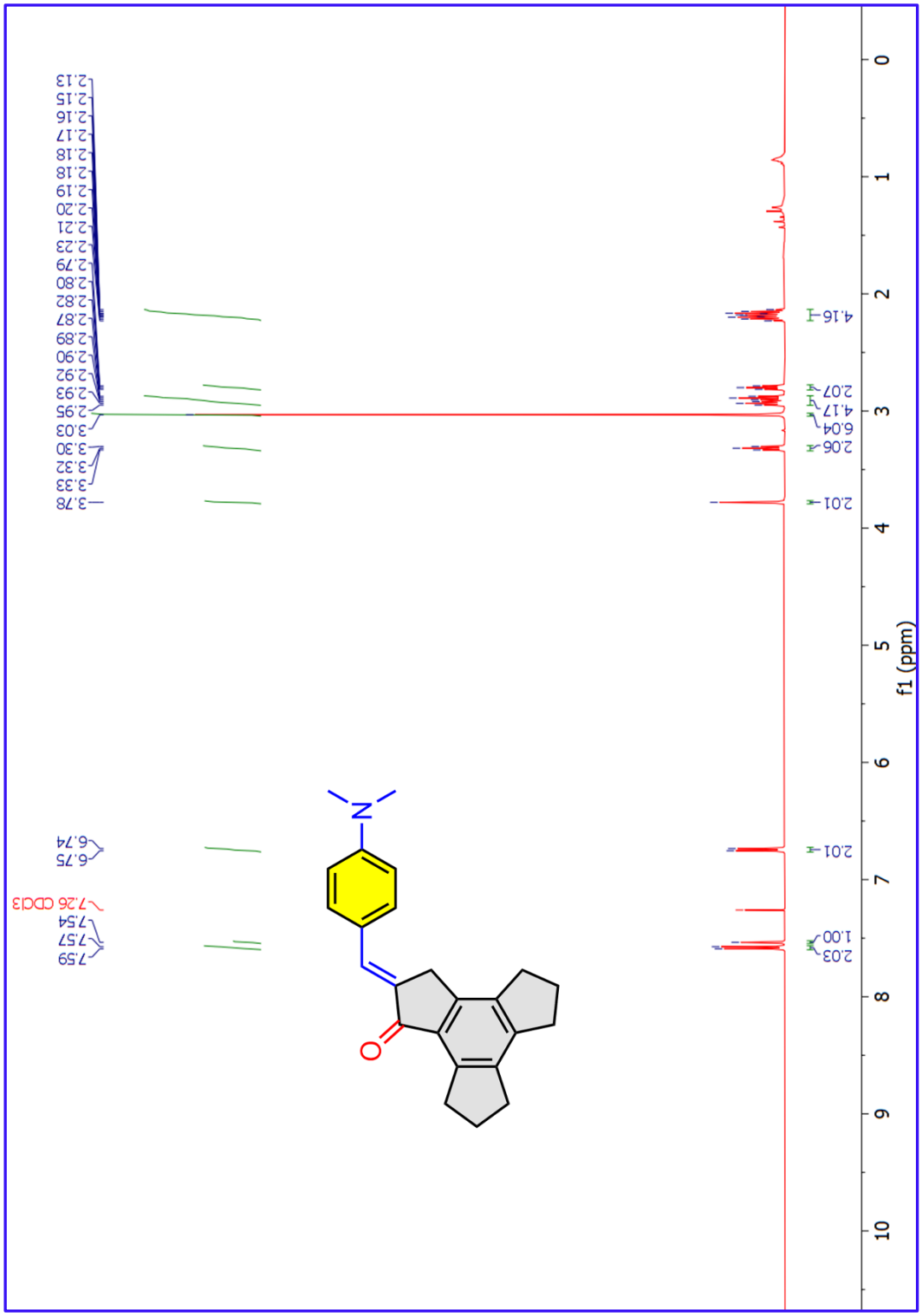

HO
O
f1 (ppm)
f1 (ppm)

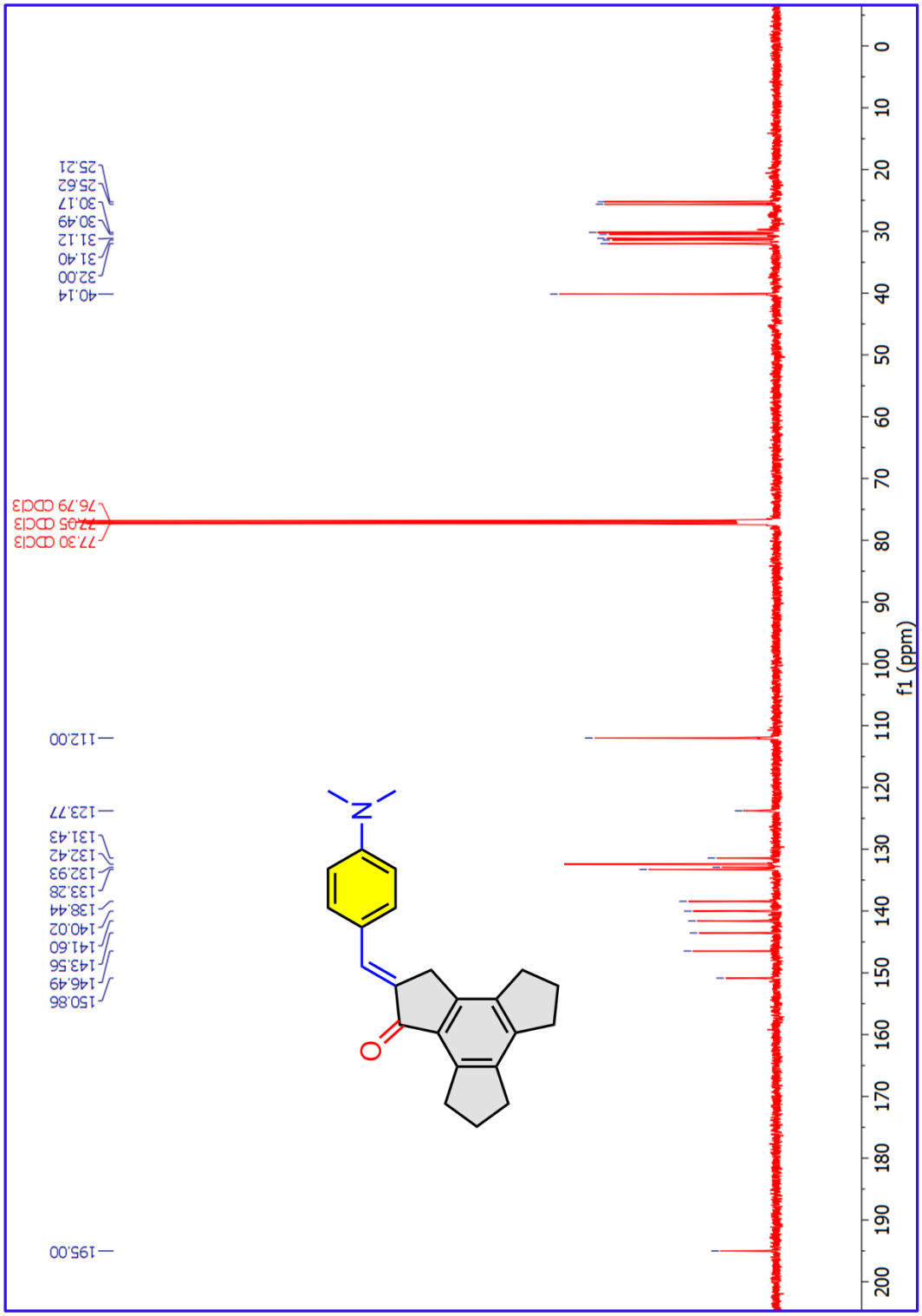

OMe
O
f1 (ppm)
7.26 CDCl3

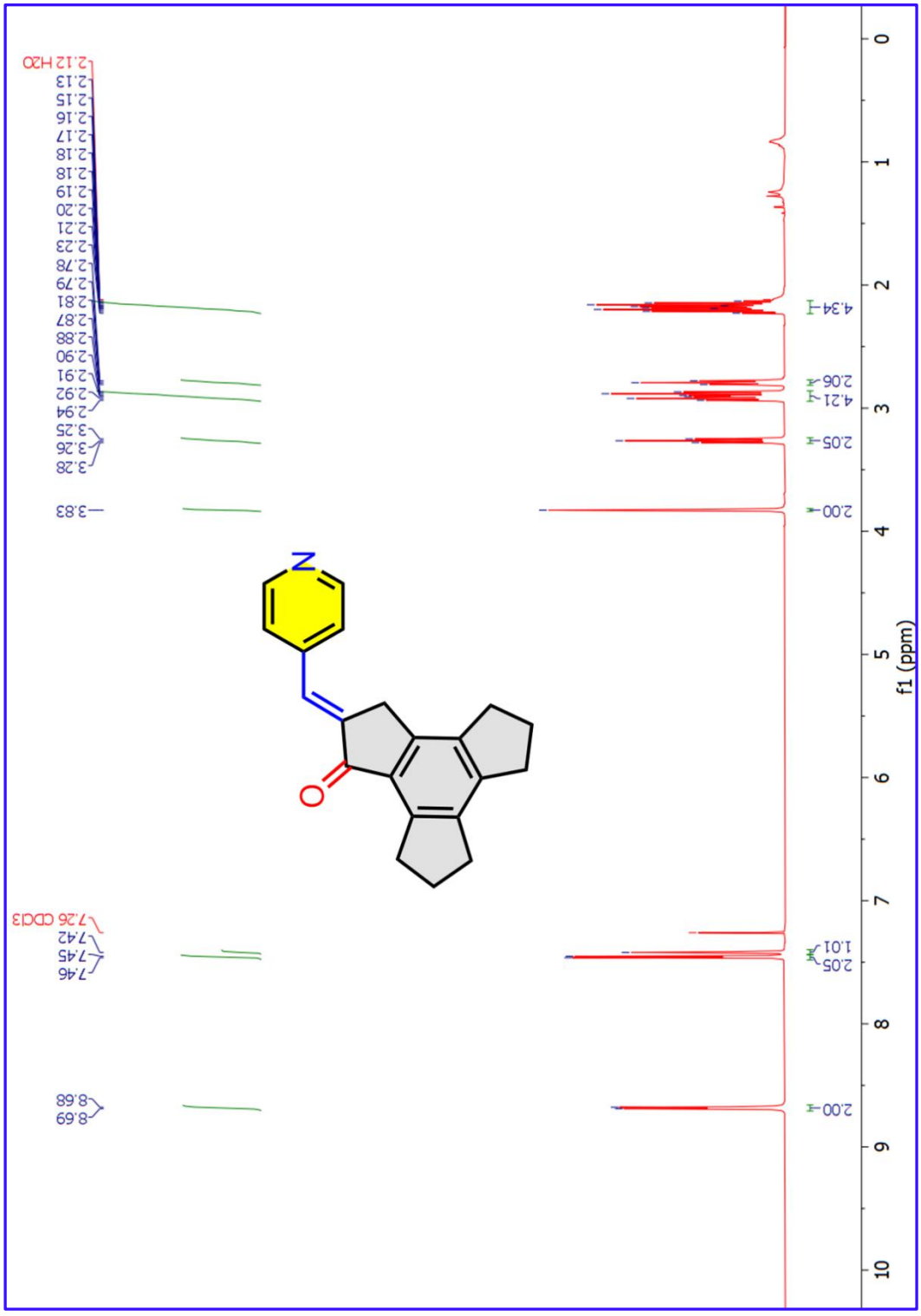

25.18
25.56
30.16
30.47
31.14
31.18
32.03
55.37
76.79 CDCl3
77.05 CDCl3
77.30 CDCl3
114.35
128.58
132.20
132.28
132.52
133.80
138.55
140.23
141.87
143.62
147.03
160.50
194.89
OMe
O
f1 (ppm)

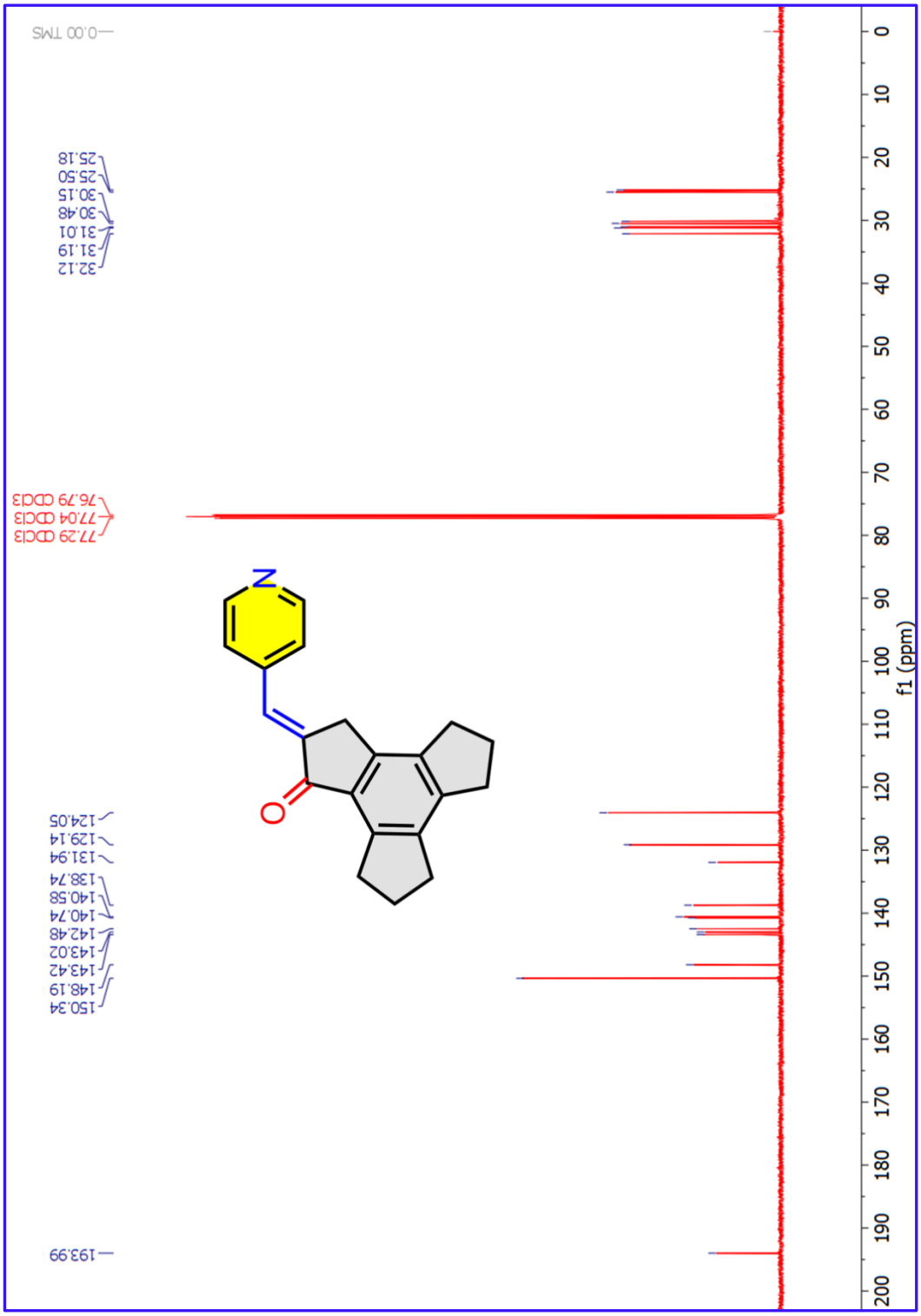

TMS 0.00
H2O 1.61
CDCl3 7.18
4.15
2.02
4.17
2.00
1.94
6.25
0.98
0.92
0.99
0.90
f1 (ppm)

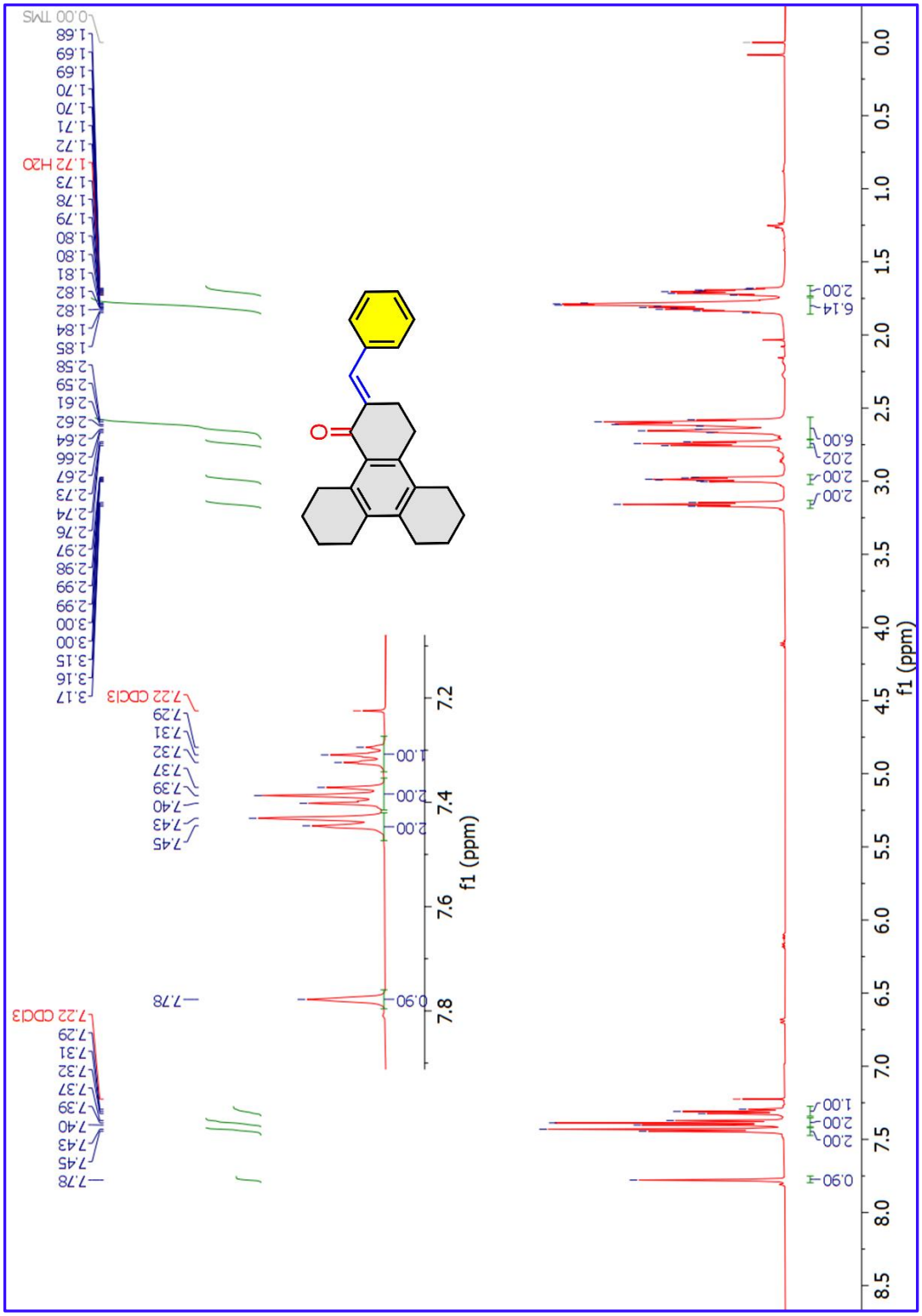

194.75
150.24
149.02
147.08
143.52
141.90
140.27
138.52
134.09
132.47
132.44
128.86
124.00
113.75
111.28
77.31 CDCl3
77.06 CDCl3
76.80 CDCl3
56.01
55.97
32.03
31.15
31.05
30.47
30.12
25.54
25.17
f1 (ppm)

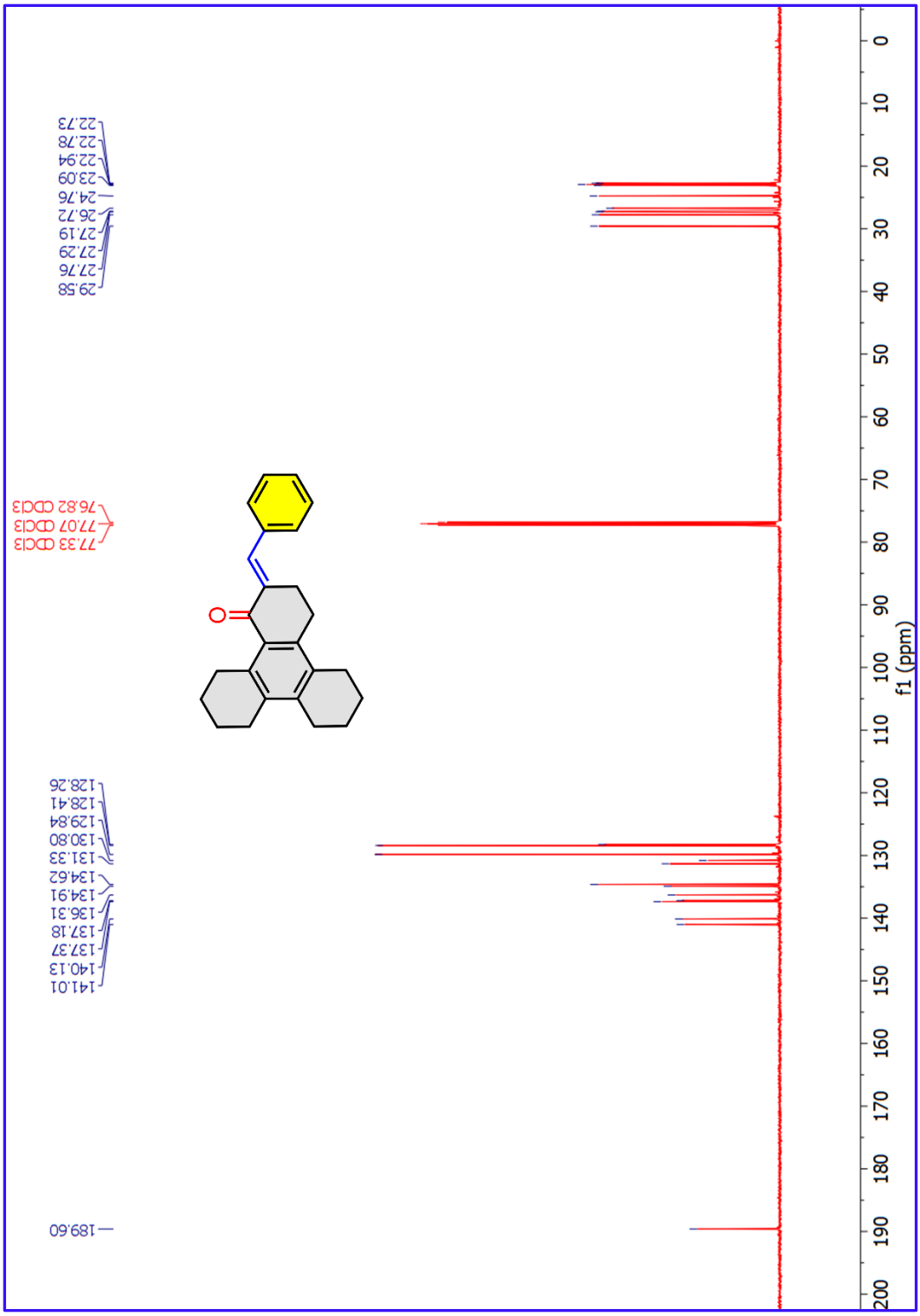

f1 (ppm)
0
1
2
3
4
5
6
7
8
9
10
4.16
2.07
4.17
6.04
2.06
2.01
2.01
2.03
1.00
7.26 CDCl3
7.59
7.57
7.54
6.75
6.74
3.78
3.33
3.32
3.30
3.03
2.95
2.93
2.92
2.90
2.89
2.87
2.82
2.80
2.79
2.23
2.21
2.20
2.19
2.18
2.18
2.17
2.16
2.15
2.13
N
O

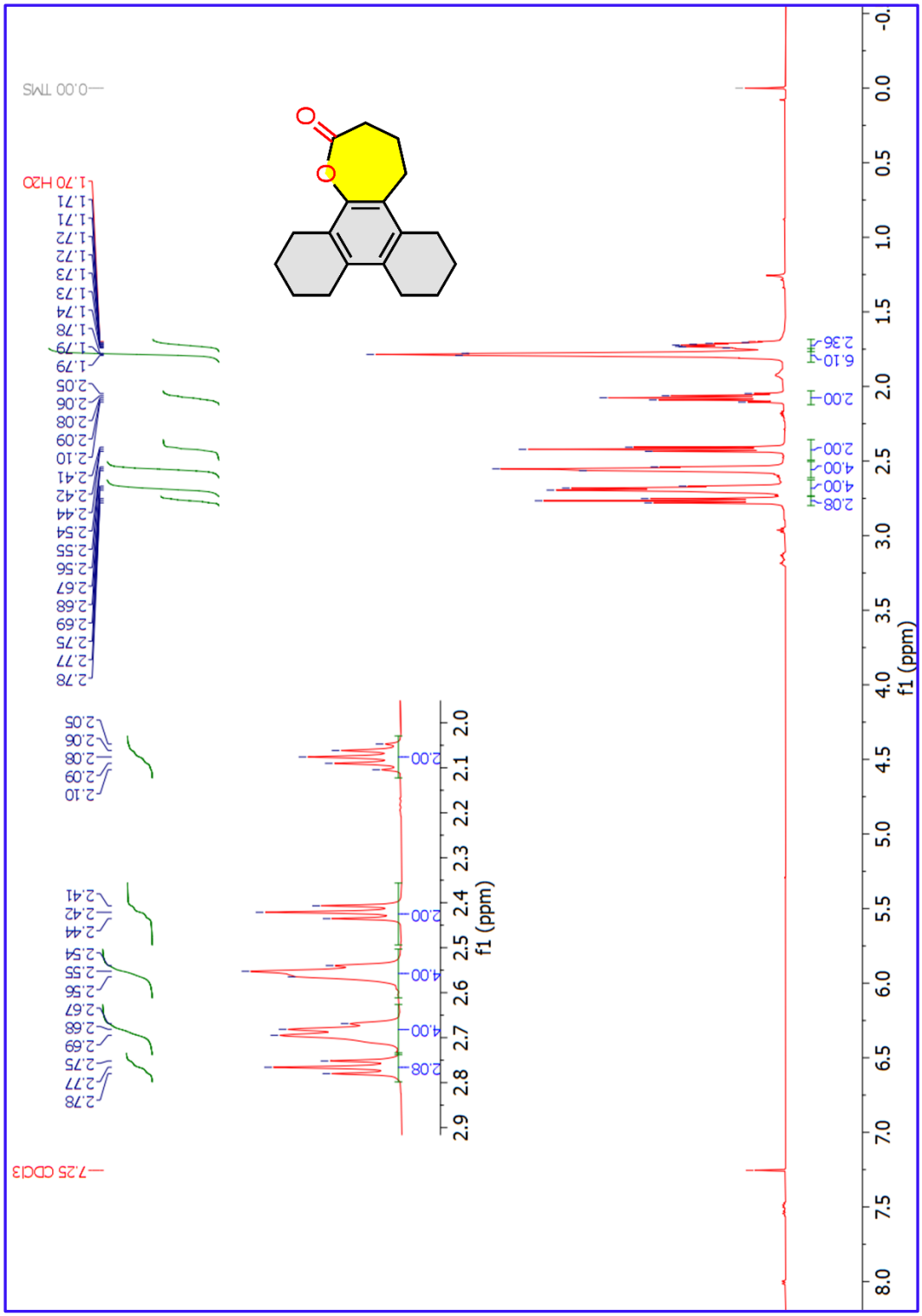

25.21
25.62
30.17
30.49
31.12
31.40
32.00
40.14
76.79 CDCl3
77.05 CDCl3
77.30 CDCl3
112.00
123.77
131.43
132.42
132.93
133.28
138.44
140.02
141.60
143.56
146.49
150.86
195.00
f1 (ppm)

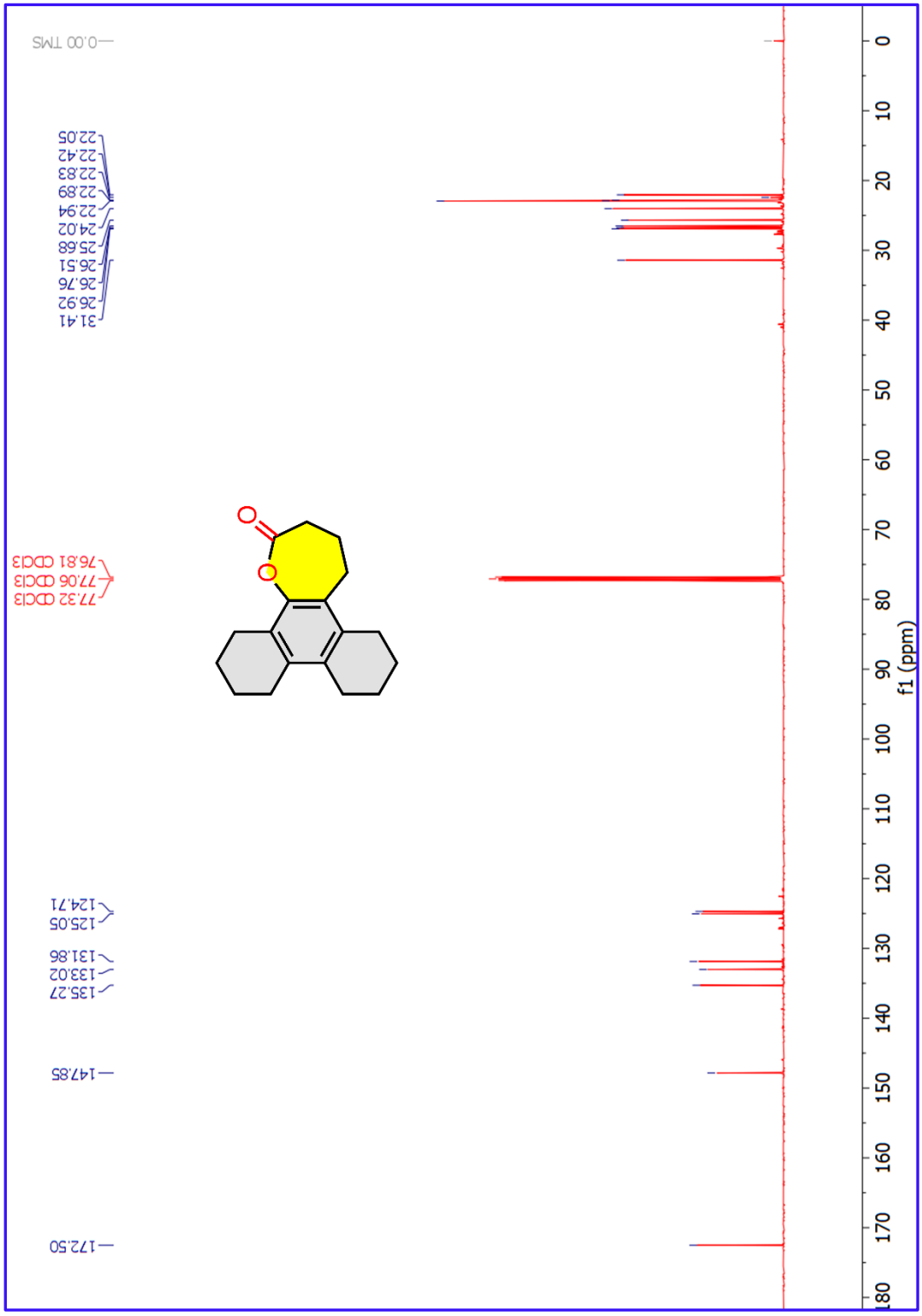

2.12 H2O
2.13
2.15
2.16
2.17
2.18
2.18
2.19
2.20
2.21
2.23
2.78
2.79
2.81
2.87
2.88
2.90
2.91
2.92
2.94
3.25
3.26
3.28
3.83
7.26 CDCl3
7.42
7.45
7.46
8.68
8.69
4.34
2.06
4.21
2.05
2.00
1.01
2.05
2.00
N
O
f1 (ppm)

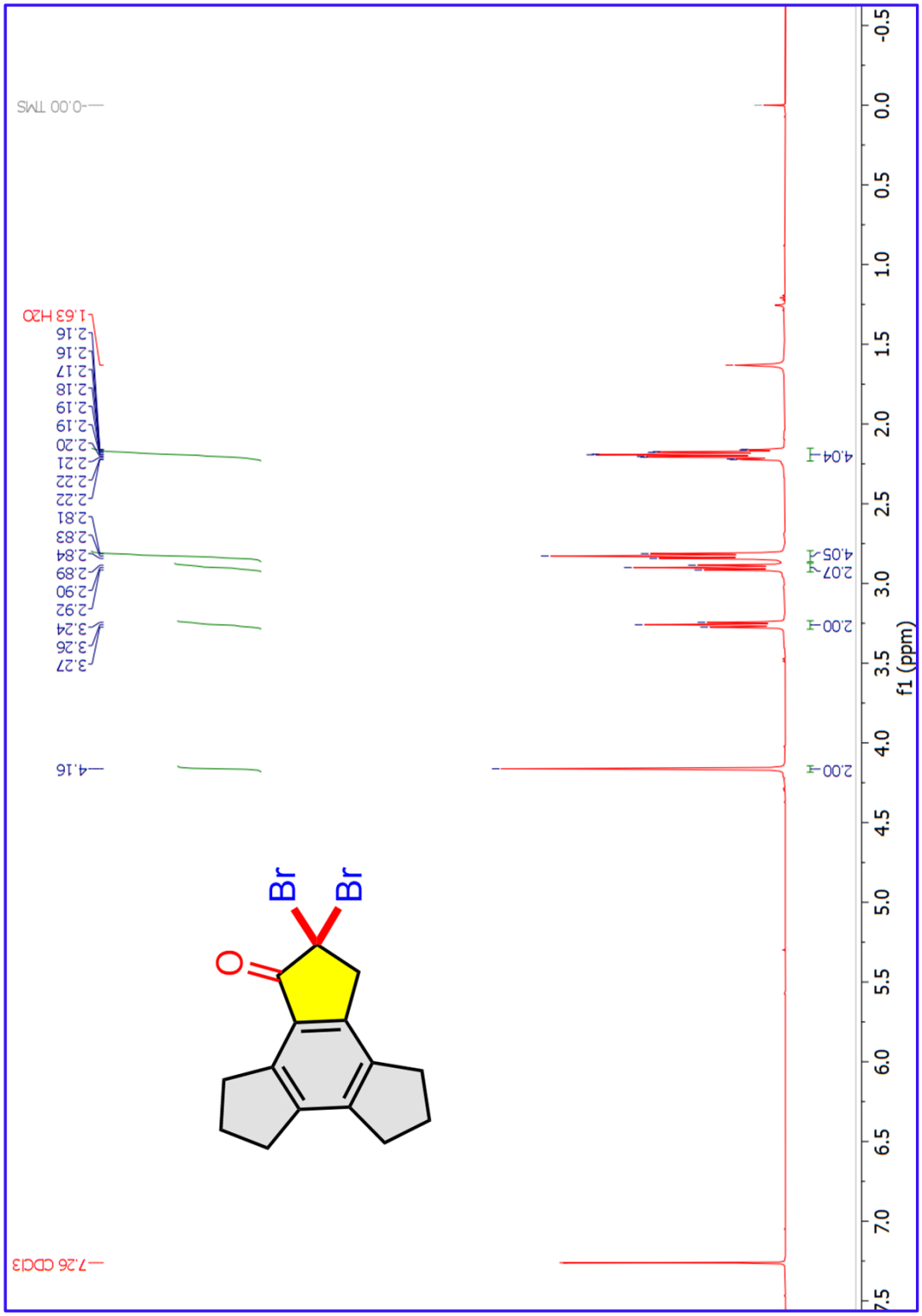

0.00 TMS
25.18
25.50
30.15
30.48
31.01
31.19
32.12
76.79 CDCl3
77.04 CDCl3
77.29 CDCl3
124.05
129.14
131.94
138.74
140.58
140.74
142.48
143.02
143.42
148.19
150.34
193.99
O
N
f1 (ppm)

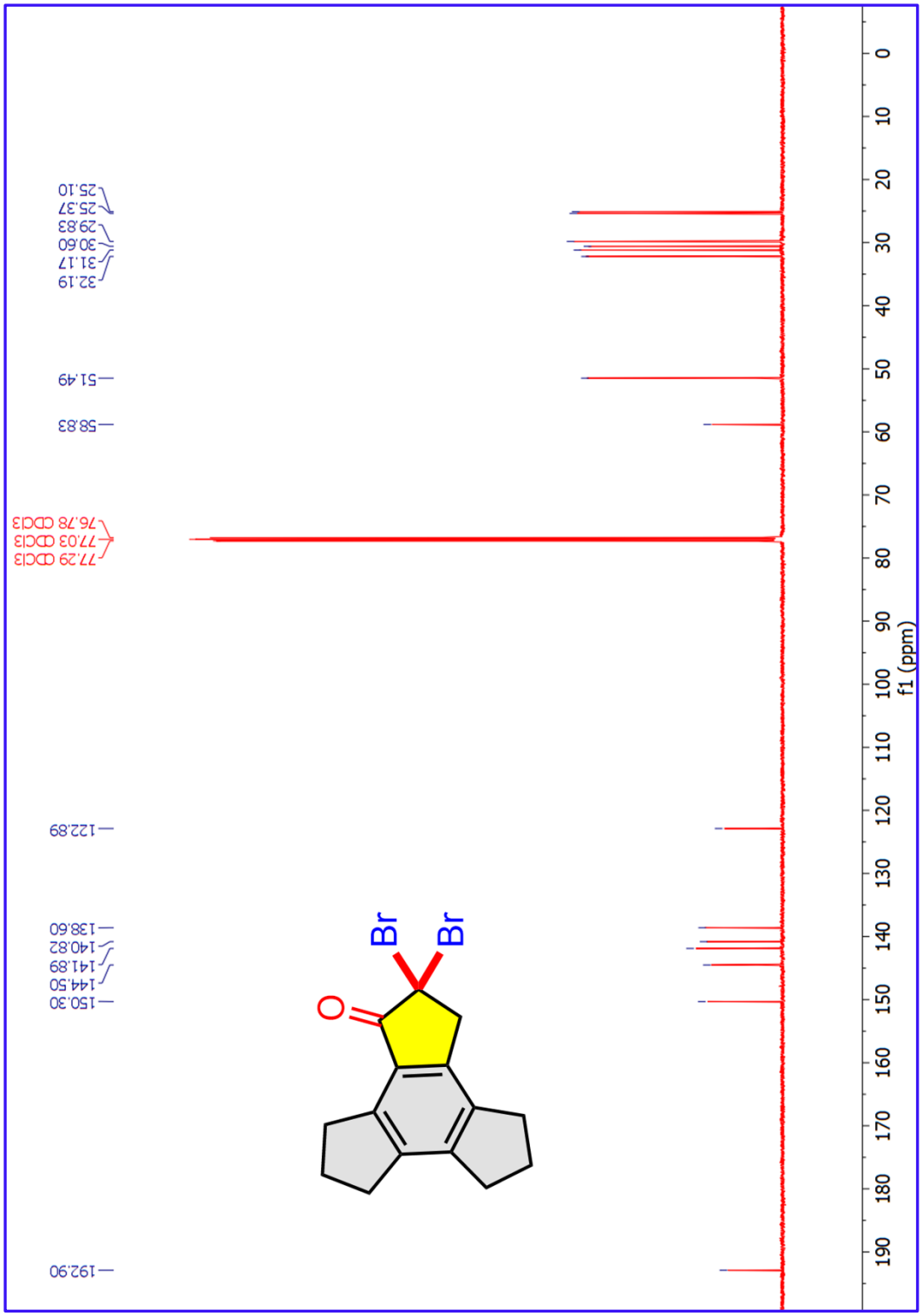

f1 (ppm)
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
2.00
6.14
6.00
2.02
2.00
2.00
1.00
2.00
0.90
7.2
7.4
7.6
7.8
1.00
2.00
2.00
0.90
O
0.00 TMS
1.68
1.69
1.69
1.70
1.70
1.71
1.72
1.72 H2O
1.73
1.78
1.79
1.80
1.80
1.81
1.82
1.82
1.84
1.85
2.58
2.59
2.61
2.62
2.64
2.66
2.67
2.73
2.74
2.76
2.97
2.98
2.99
2.99
3.00
3.00
3.15
3.16
3.17
7.22 CDCl3
7.29
7.31
7.32
7.37
7.39
7.40
7.43
7.45
7.78
7.78
7.45
7.43
7.40
7.39
7.37
7.32
7.31
7.29
7.22 CDCl3

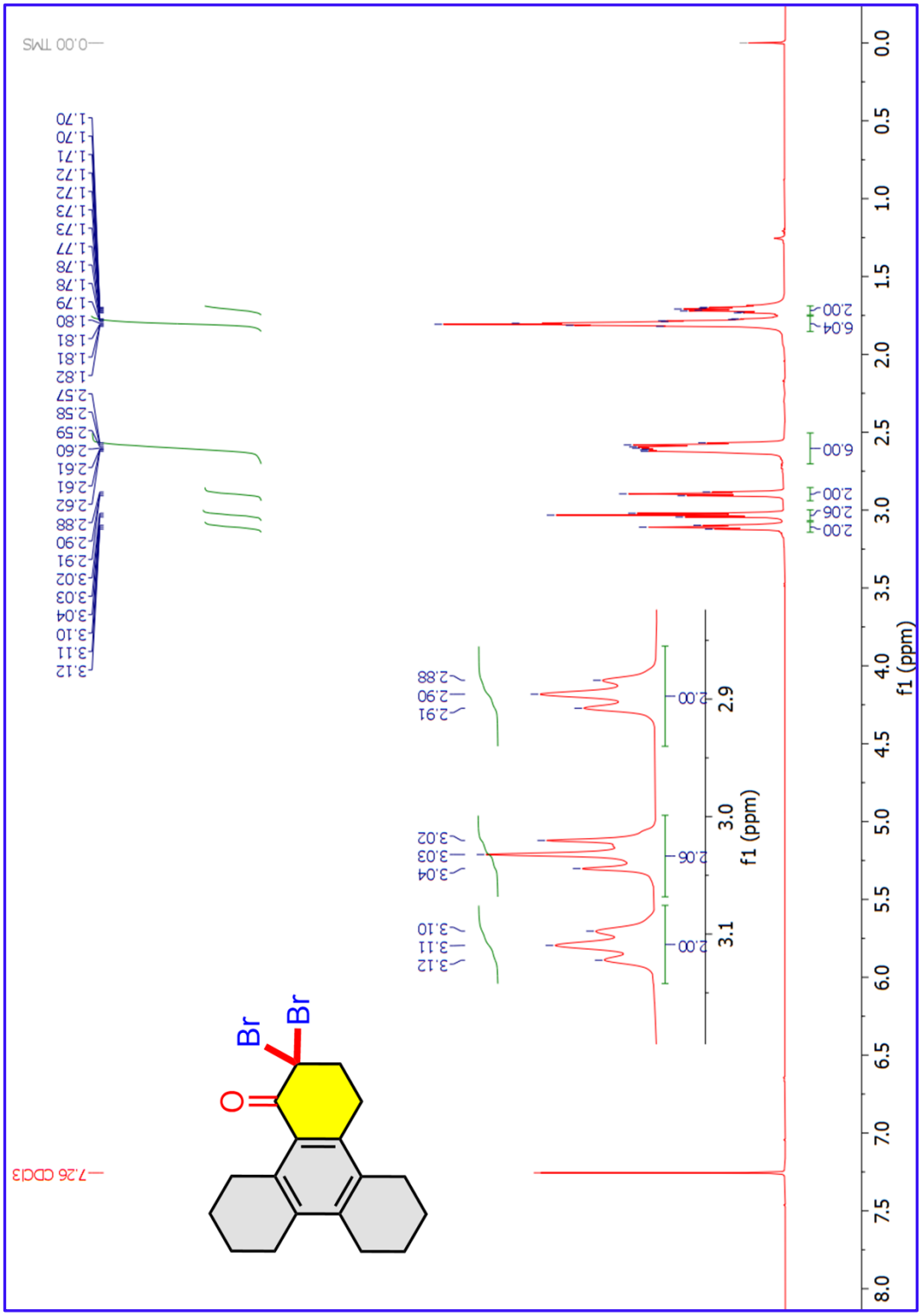

22.73
22.78
22.94
23.09
24.76
26.72
27.19
27.29
27.76
29.58
76.82 CDCl3
77.07 CDCl3
77.33 CDCl3
128.26
128.41
129.84
130.80
131.33
134.62
134.91
136.31
137.18
137.37
140.13
141.01
189.60
f1 (ppm)

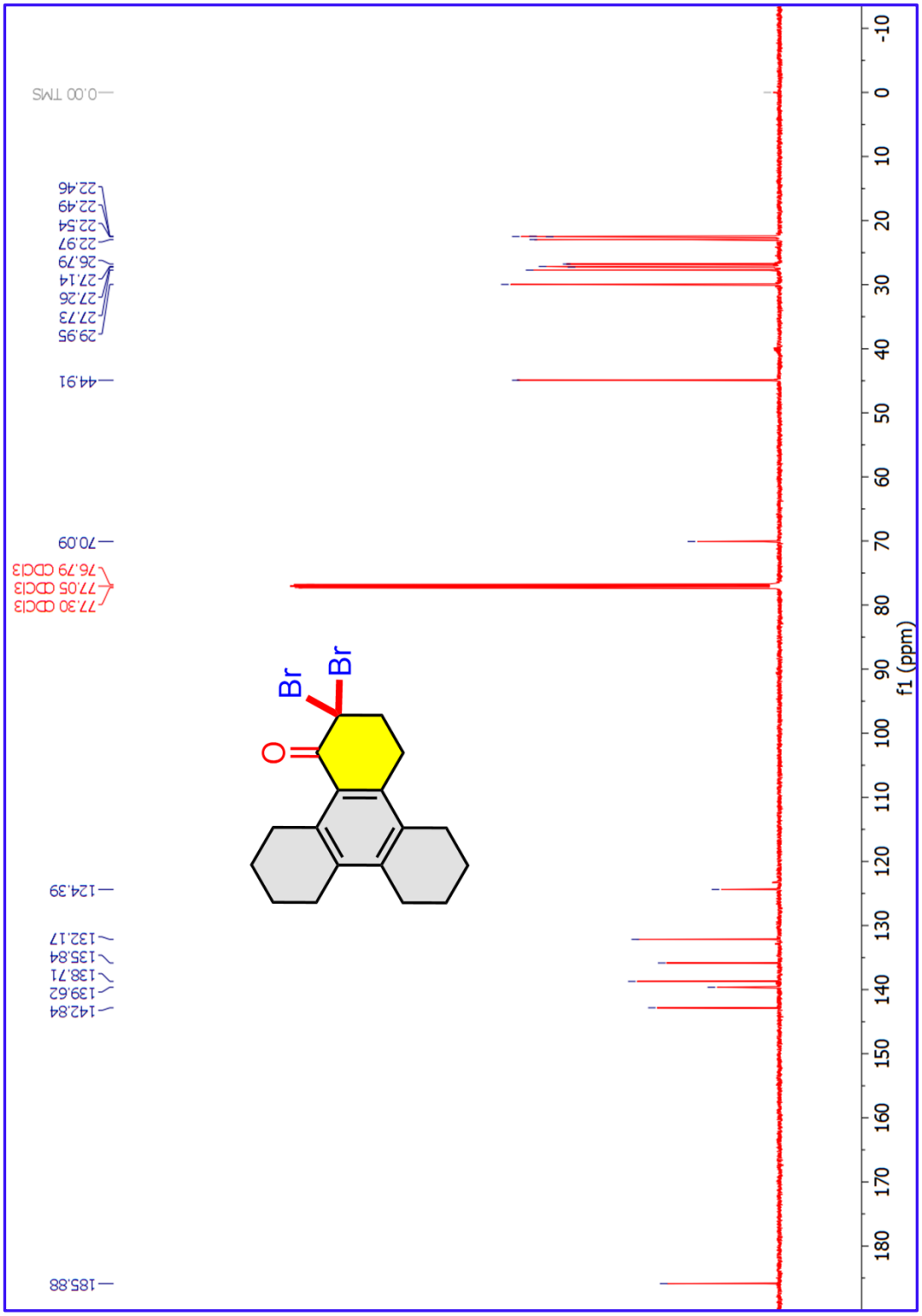

TMS 0.00
H2O 1.70
CDCl3 7.25
f1 (ppm)

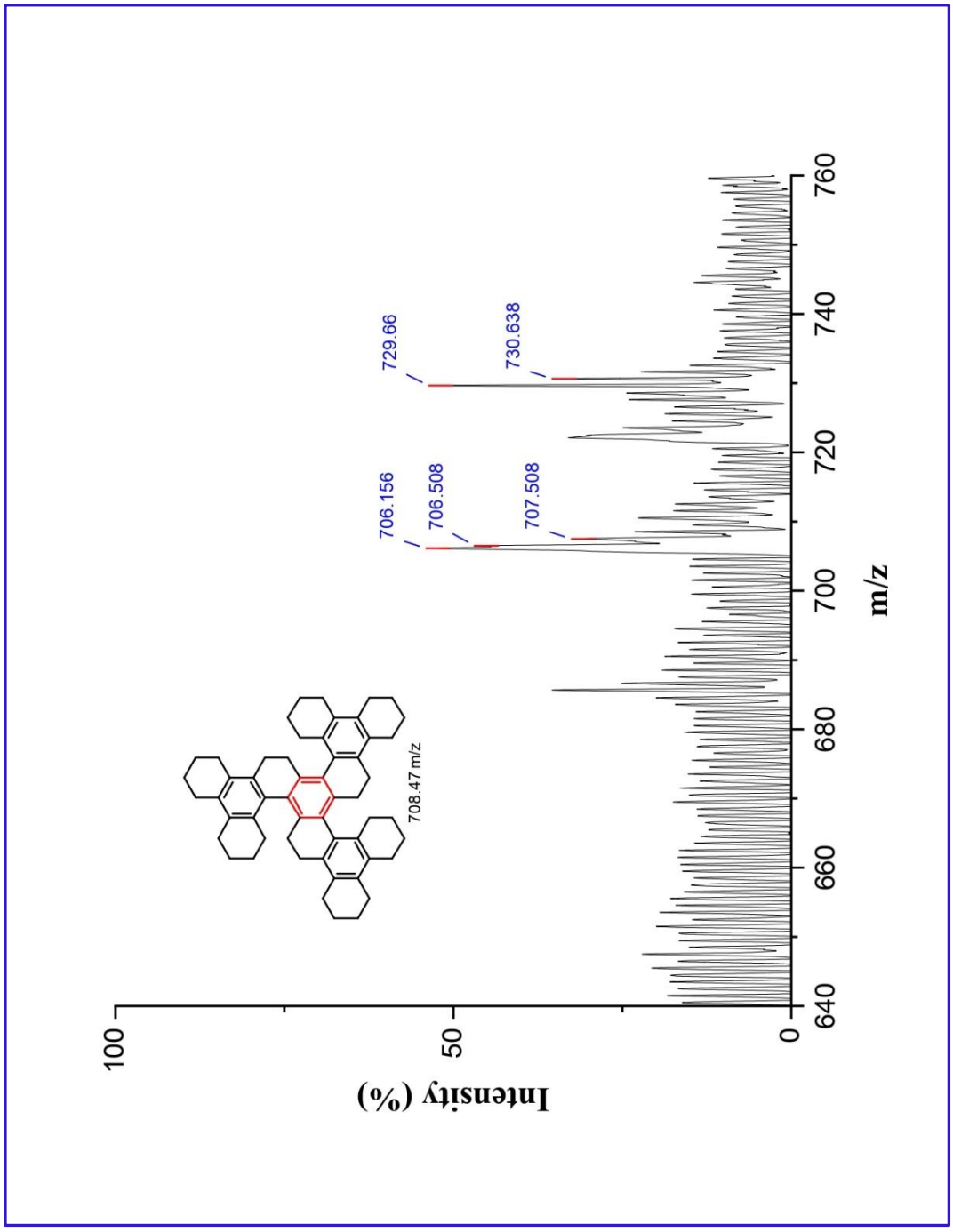

0.00 TMS
22.05
22.42
22.83
22.89
22.94
24.02
25.68
26.51
26.76
26.92
31.41
76.81 CDCl3
77.06 CDCl3
77.32 CDCl3
124.71
125.05
131.86
133.02
135.27
147.85
172.50
f1 (ppm)


TMS 0.00
1.63 H2O
2.16
2.16
2.17
2.18
2.19
2.19
2.20
2.21
2.22
2.22
2.81
2.83
2.84
2.89
2.90
2.92
3.24
3.26
3.27
4.16
7.26 CDCl3
4.04
4.05
2.07
2.00
2.00
Br
Br
O
f1 (ppm)


25.10
25.37
29.83
30.60
31.17
32.19
51.49
58.83
76.78 CDCl3
77.03 CDCl3
77.29 CDCl3
122.89
138.60
140.82
141.89
144.50
150.30
192.90
Br
Br
O
f1 (ppm)


TMS 0.00
7.26 CDCl3
1.70
1.70
1.71
1.72
1.72
1.73
1.73
1.77
1.78
1.78
1.79
1.80
1.81
1.81
1.82
2.57
2.58
2.59
2.60
2.61
2.61
2.62
2.88
2.90
2.91
3.02
3.03
3.04
3.10
3.11
3.12
6.04
2.00
6.00
2.00
2.06
2.00
2.88
2.90
2.91
2.00
3.02
3.03
3.04
2.06
3.10
3.11
3.12
2.00
f1 (ppm)
Br
Br
O


0.00 TMS
22.46
22.49
22.54
22.97
26.79
27.14
27.26
27.73
29.95
44.91
70.09
76.79 CDCl3
77.05 CDCl3
77.30 CDCl3
124.39
132.17
135.84
138.71
139.62
142.84
185.88
Br
Br
O
f1 (ppm)

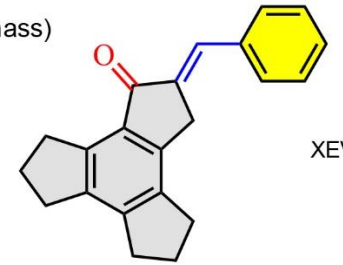

Intensity (%)
100
50
0
640
660
680
700
720
740
760
m/z
706.156
706.508
707.508
729.66
730.638
708.47 m/z

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
20 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-22 H: 0-21 O: 0-3 Br: 0-2

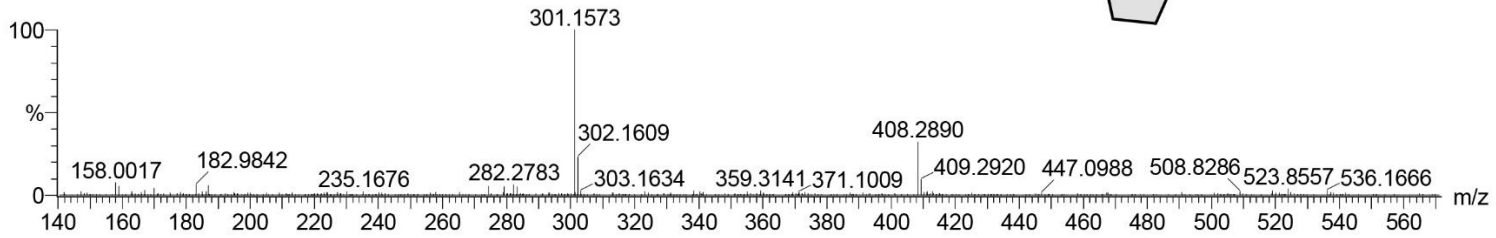


231122_GB072 16 (0.177)
Test Name :
1: TOF MS ES+

IITRPR

XEVO G2-XS QTOF
GB072

1.91e+006



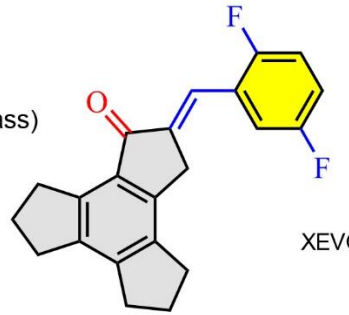
Minimum:				-1.5				
Maximum:		5.0	10.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
301.1573	301.1592	-1.9	-6.3	12.5	1050.0	n/a	n/a	C22 H21 O

Elemental Composition Report

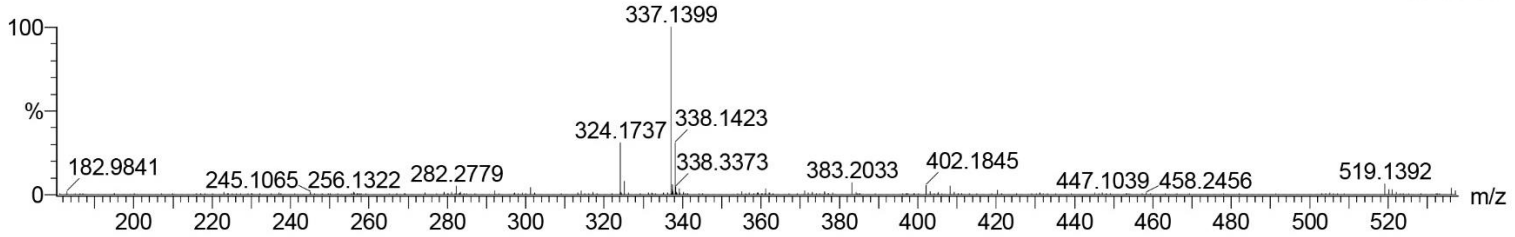
Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
55 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-22 H: 0-21 O: 0-3 Br: 0-2 F: 0-2



231122_GB073 13 (0.151) IITRPR XEVO G2-XS QTOF
Test Name : GB073
1: TOF MS ES+ 1.24e+007



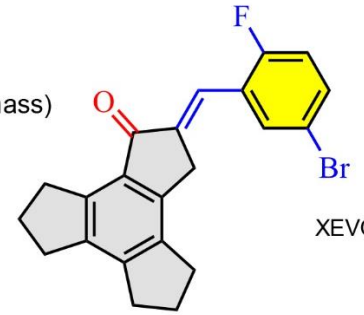
Minimum:				-1.5				
Maximum:		5.0	10.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
337.1399	337.1404	-0.5	-1.5	12.5	1058.6	n/a	n/a	C22 H19 O F2

Elemental Composition Report

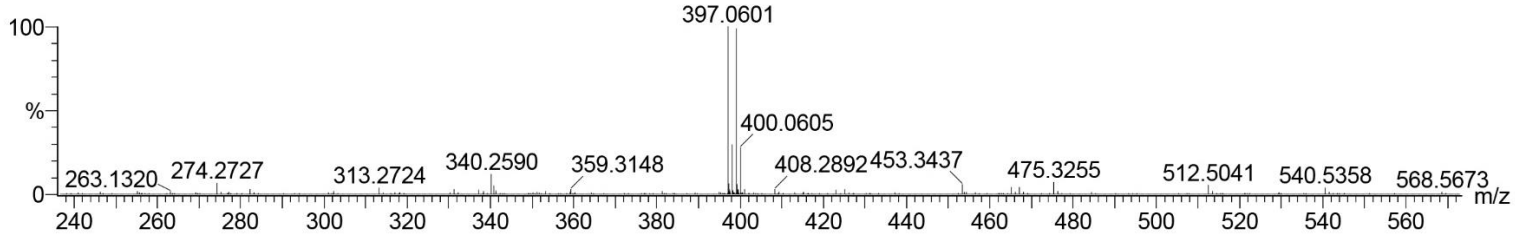
Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
31 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-22 H: 0-21 O: 0-3 F: 0-1 Br: 0-2



231122_GB_074 14 (0.160) IITRPR XEVO G2-XS QTOF
Test Name : GB_074
1: TOF MS ES+ 2.27e+007

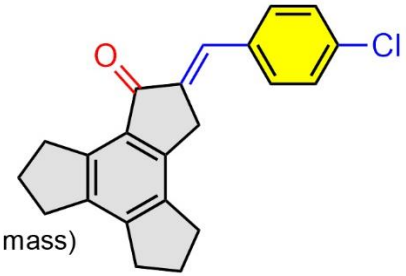


Minimum:				-1.5				
Maximum:		5.0	10.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
397.0601	397.0603	-0.2	-0.5	12.5	1074.8	n/a	n/a	C22 H19 O F Br

Elemental Composition Report

Single Mass Analysis

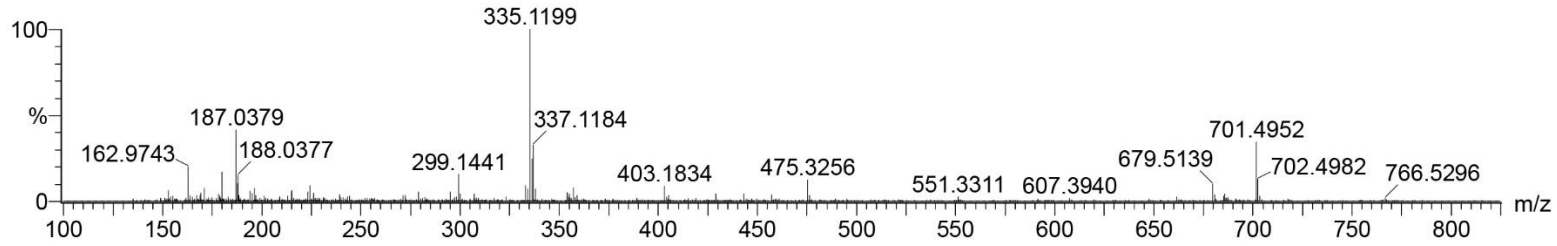
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3



Monoisotopic Mass, Even Electron Ions
13 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-22 H: 0-100 O: 0-2 Cl: 0-1

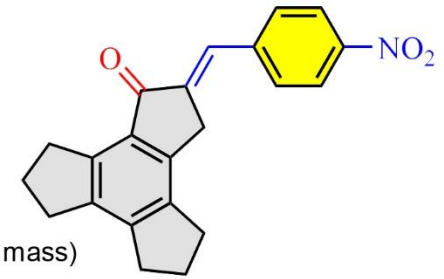
010323_GB_077 25 (0.277) IITRPR XEVO G2-XS QTOF
Test Name : 010323_GB_077
1: TOF MS ES+

5.02e+005



Minimum:				-1.5				
Maximum:		5.0	10.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
335.1199	335.1203	-0.4	-1.2	12.5	855.5	n/a	n/a	C22 H20 O Cl

Elemental Composition Report

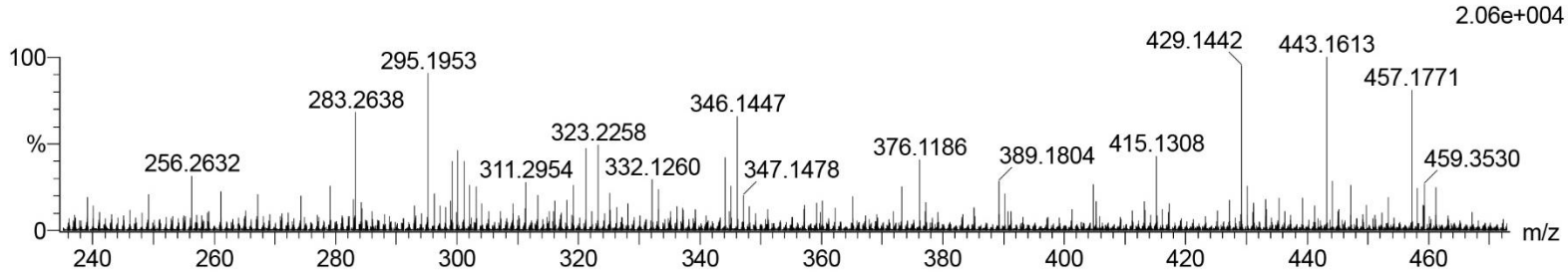


Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
22 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-22 H: 0-100 N: 0-2 O: 0-3

010323_GB_078 25 (0.277) IITRPR XEVO G2-XS QTOF
Test Name : 010323_GB_078
1: TOF MS ES+



Minimum:				-1.5				
Maximum:		5.0	10.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
346.1447	346.1443	0.4	1.2	13.5	734.9	n/a	n/a	C22 H20 N O3

Elemental Composition Report

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

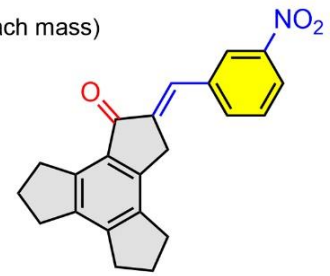
Monoisotopic Mass, Even Electron Ions
20 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-22 H: 0-50 N: 0-2 O: 0-3

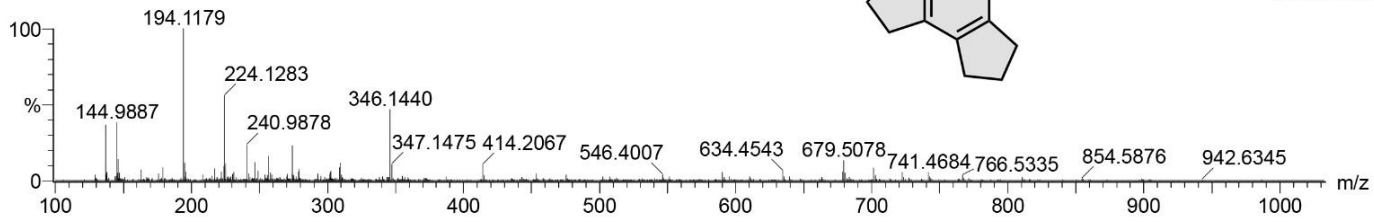
180423_GB_082 26 (0.285)
Test Name :
1: TOF MS ES+

IITRPR

XEVO G2-XS QTOF
180423_GB_082

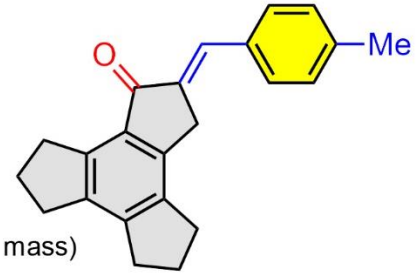
5.97e+005





Minimum:				-1.5				
Maximum:		5.0	20.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
346.1440	346.1443	-0.3	-0.9	13.5	777.9	n/a	n/a	C22 H20 N O3

Elemental Composition Report



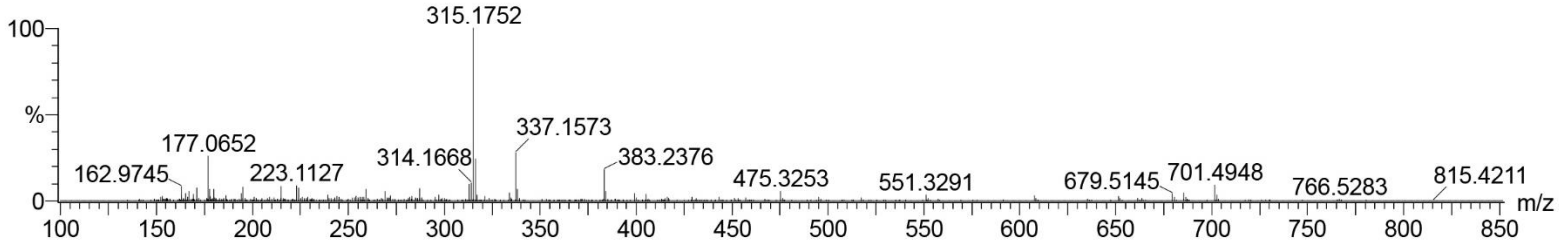
Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
13 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-23 H: 0-100 O: 0-3

010323_GB_080 28 (0.303) IITRPR XEVO G2-XS QTOF
Test Name : 010323_GB_080
1: TOF MS ES+

8.46e+005



Minimum:				-1.5				
Maximum:		5.0	10.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
315.1752	315.1749	0.3	1.0	12.5	901.1	n/a	n/a	C23 H23 O

Elemental Composition Report

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

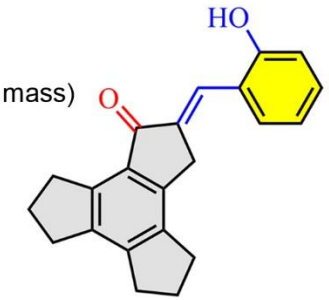
Monoisotopic Mass, Even Electron Ions
24 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-22 H: 0-50 N: 0-2 O: 0-2

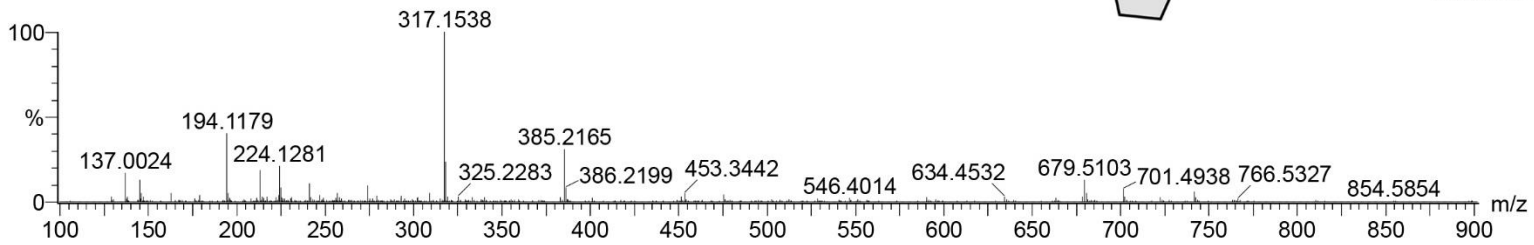
180423_GB_079 24 (0.257)
Test Name :
1: TOF MS ES+

IITRPR

XEVO G2-XS QTOF
180423_GB_079

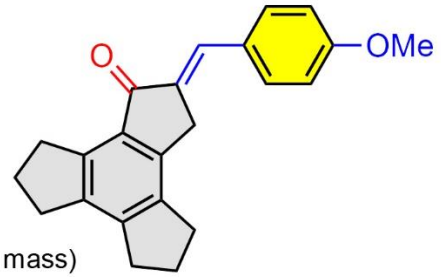
1.27e+006





Minimum:				-1.5				
Maximum:		5.0	20.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
317.1538	317.1542	-0.4	-1.3	12.5	883.0	n/a	n/a	C22 H21 O2

Elemental Composition Report



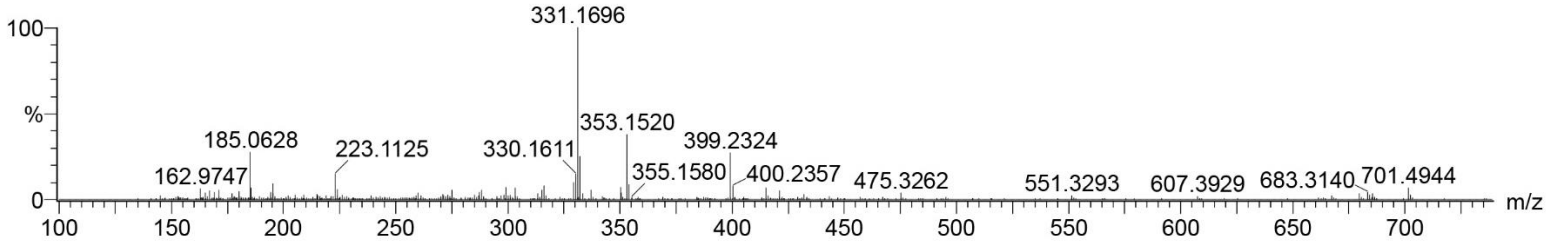
Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
6 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-23 H: 0-100 O: 0-2

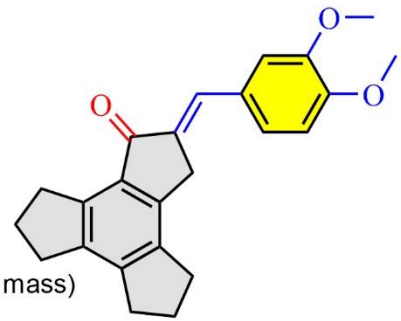
010323_GB_075 26 (0.285) IITRPR XEVO G2-XS QTOF
Test Name : 010323_GB_075
1: TOF MS ES+

1.29e+006



Minimum:				-1.5				
Maximum:		5.0	10.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
331.1696	331.1698	-0.2	-0.6	12.5	960.6	n/a	n/a	C23 H23 O2

Elemental Composition Report



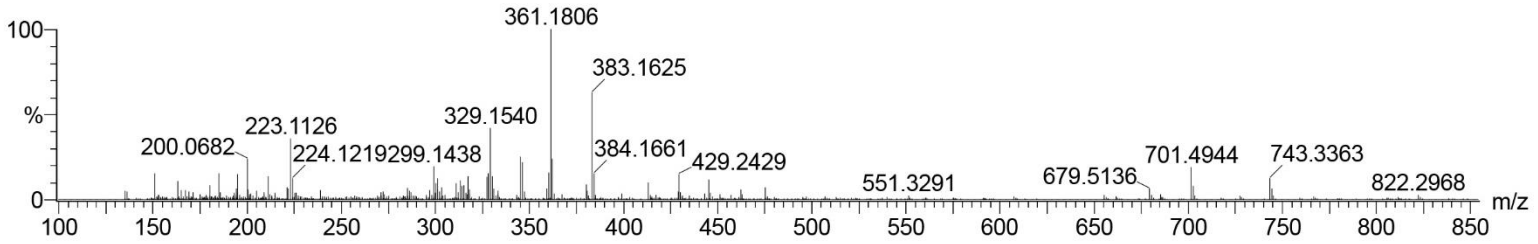
Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
7 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-24 H: 0-100 O: 0-3

010323_GB_081 28 (0.303) IITRPR XEVO G2-XS QTOF
Test Name : 010323_GB_081
1: TOF MS ES+

6.27e+005



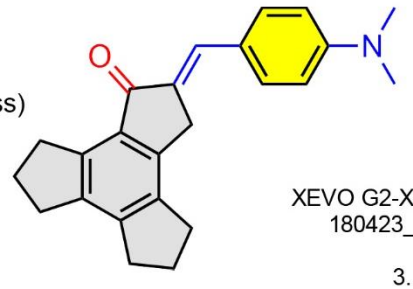
Minimum:				-1.5				
Maximum:		5.0	10.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
361.1806	361.1804	0.2	0.6	12.5	896.4	n/a	n/a	C24 H25 O3

Elemental Composition Report

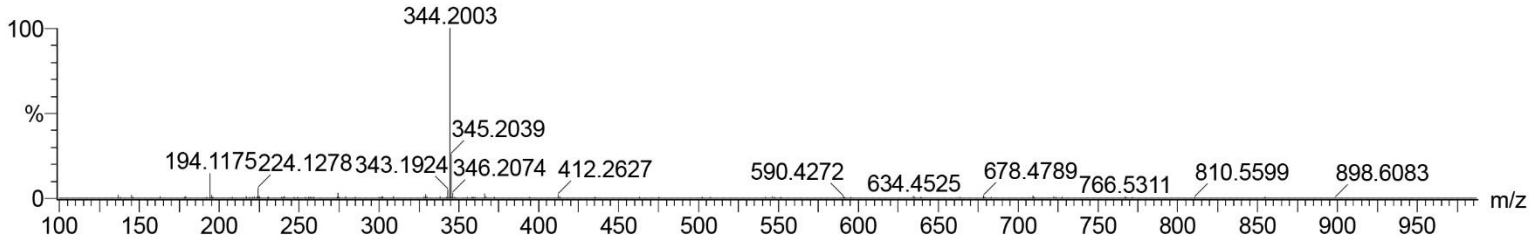
Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
34 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-24 H: 0-50 N: 0-2 O: 0-3



180423_GB_083 40 (0.417) IITRPR XEVO G2-XS QTOF
Test Name : 180423_GB_083
1: TOF MS ES+
3.14e+006



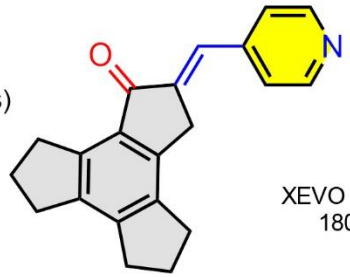
Minimum:				-1.5				
Maximum:		5.0	20.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
344.2003	344.2014	-1.1	-3.2	12.5	948.0	n/a	n/a	C24 H26 N O

Elemental Composition Report

Single Mass Analysis

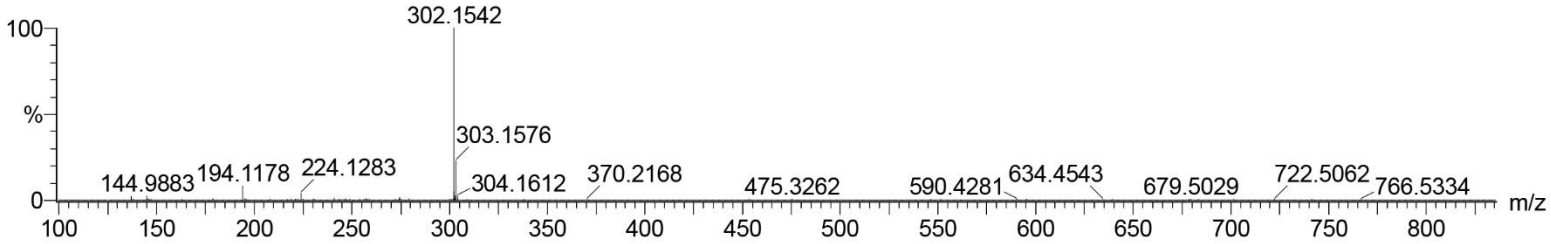
Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
48 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-24 H: 0-50 N: 0-2 O: 0-3



180423_GB_085 25 (0.277) IITRPR XEVO G2-XS QTOF
Test Name : 180423_GB_085
1: TOF MS ES+

6.48e+006



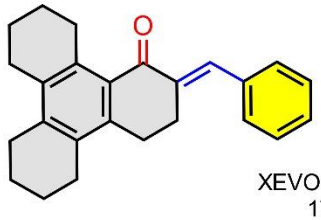
Minimum:				-1.5				
Maximum:		5.0	20.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
302.1542	302.1545	-0.3	-1.0	12.5	1021.6	n/a	n/a	C21 H20 N O

Elemental Composition Report

Single Mass Analysis

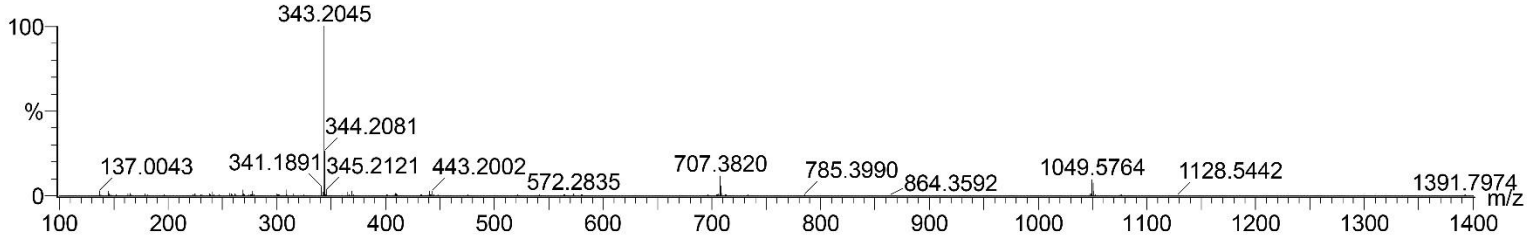
Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
7 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-25 H: 1-100 O: 1-2



170623_GB086 27 (0.294) IITRPR XEVO G2-XS QTOF
Test Name : 170623_GB086
1: TOF MS ES+

4.93e+006



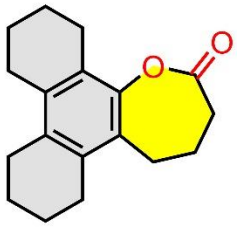
Minimum:				-1.5				
Maximum:		5.0	20.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
343.2045	343.2062	-1.7	-5.0	12.5	885.3	n/a	n/a	C25 H27 O

Elemental Composition Report

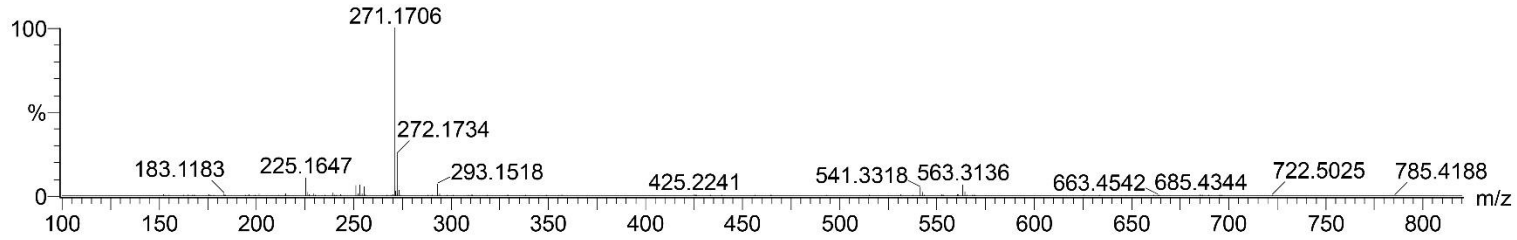
Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
3 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 1-18 H: 1-100 O: 1-2



260623_SD_05 32 (0.337) IITRPR XEVO G2-XS QTOF
Test Name : 260623_SD_05
1: TOF MS ES+
9.64e+006



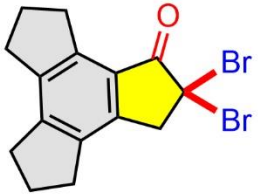
Minimum:				-1.5				
Maximum:		5.0	20.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
271.1706	271.1698	0.8	3.0	7.5	1126.2	n/a	n/a	C18 H23 O2

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
12 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-20 H: 0-15 O: 0-3 Br: 0-2

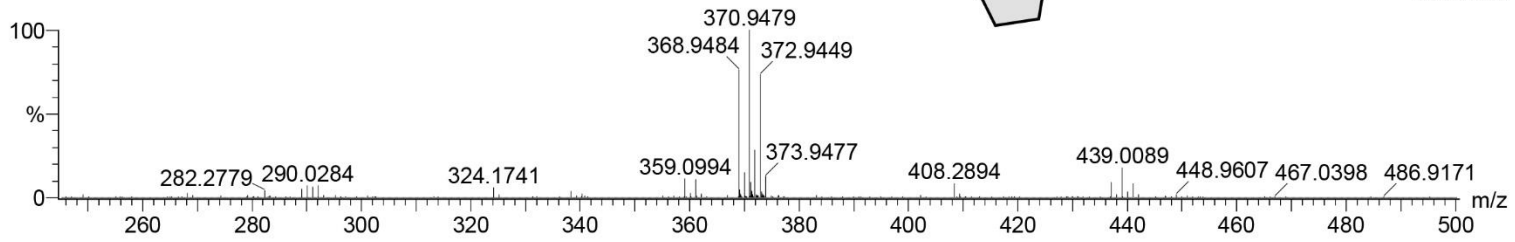


231122_GB065 15 (0.168)
Test Name :
1: TOF MS ES+

IITRPR

XEVO G2-XS QTOF
GB065

1.92e+007



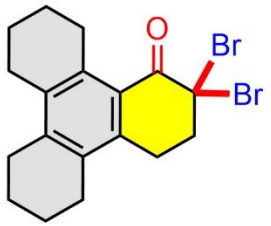
Minimum:				-1.5				
Maximum:		5.0	10.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
368.9484	368.9490	-0.6	-1.6	7.5	1097.8	n/a	n/a	C15 H15 O Br2

Elemental Composition Report

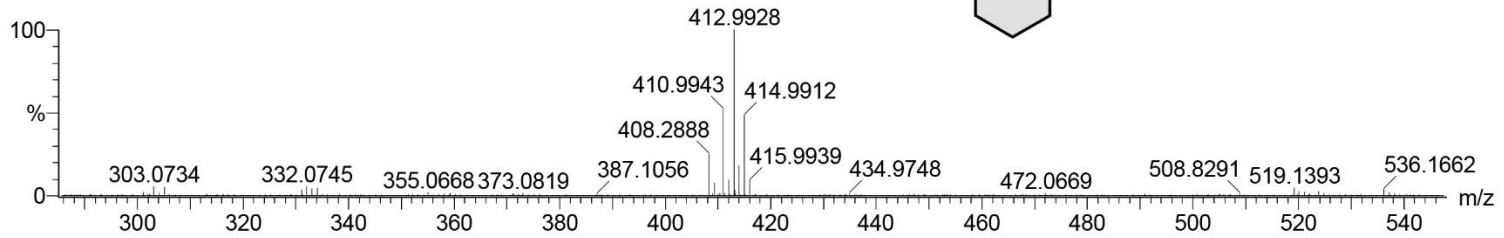
Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
14 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-20 H: 0-21 O: 0-3 Br: 0-2



231122_GB067 18 (0.205) IITRPR XEVO G2-XS QTOF
Test Name : GB067
1: TOF MS ES+ 2.81e+006



Minimum:				-1.5				
Maximum:		5.0	10.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
410.9943	410.9959	-1.6	-3.9	7.5	997.3	n/a	n/a	C18 H21 O Br2