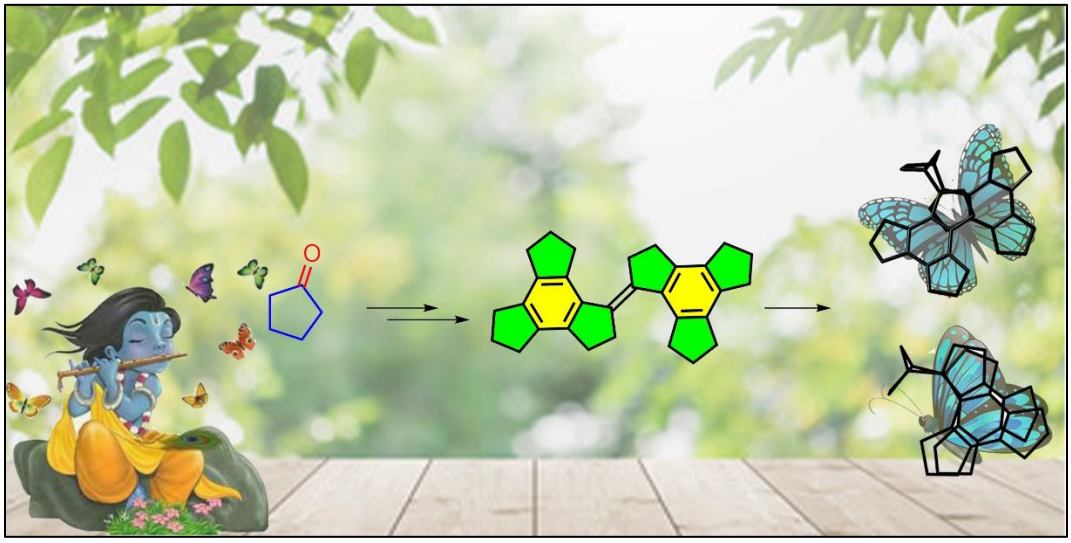
CHAPTER 3

Butterflyene: Synthesis of aesthetically appealing carbocycles resembling with the shape of a butterfly



3.1 Abstract

What makes molecules beautiful? Beauty can be due to their symmetry, simplicity, or complex carboskeleton. Sometimes beauty of the molecule remains concealed, waiting to be unveiled only after it has been envisioned and subsequently executed *via* a synthetic plan. An interesting molecular architecture, butterflyene resembling to the shape of a butterfly has been synthesized via a sequence of cyclocondensation, benzylic oxidation, McMurry coupling and Diels−Alder reaction (DAR) successively. The DAR of the tetrasubstituted double bond of a bicyclopentylidene moiety with various dienes has been performed to prepare the analogues of butterflyene. DFT calculations have also been used to analyse the structural optimization and reaction energies.

3.2 Introduction

Organic chemists have been fascinated by an array of intriguing molecular designs that resemble with various objects and some of them are even found to imitate the shape of the animals. As stated by Marcelin Berthelot[1] chemists often compare their work to that of the artists because, chemists also create their own molecular masterpieces. Roald Hoffmann also wrote an essay on chemical aesthetics elaborating into the nature of representation and aesthetics in chemistry.[2] Few examples from the plethora of compounds that resemble with the objects not only imagined but also successfully synthesized in laboratories such as basketane **98**,[3] pagodane **99**,[4] garudane **100**,[5] manxane **101**[6] are presented in **Fig. 3.1**.

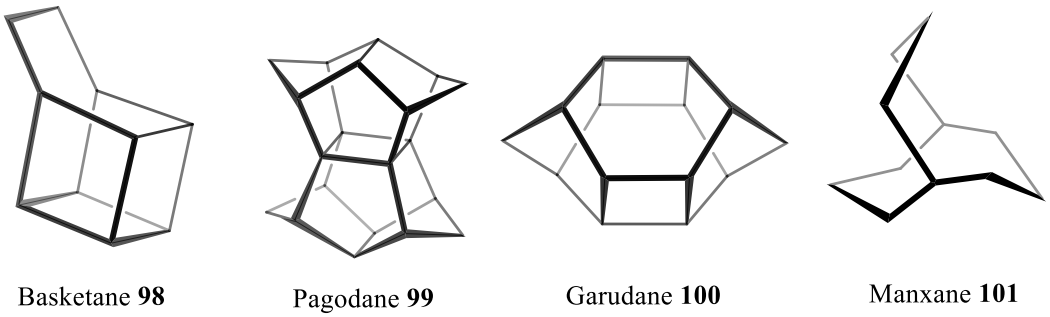
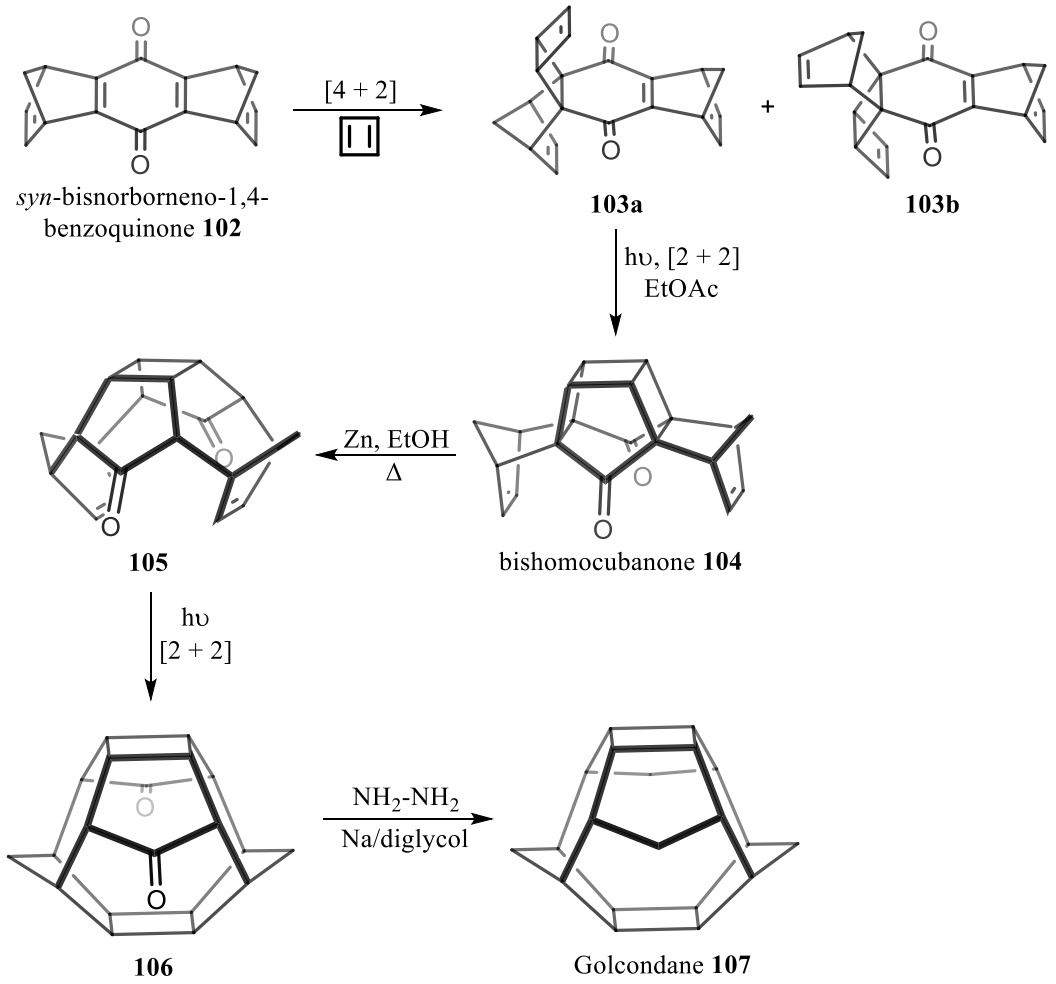


Figure 3.1 Some fascinating molecules having shapes resembling to familiar objects

Molecule golcondane **107** was named after "Golconda", the former name for Hyderabad city, by Goverdhan Mehta *et al.* in honor of the 400th anniversary of the establishment of Hyderabad, India.[7] The reaction of syn-bisnorborneno-1,4-benzoquinone **102** with cyclobutadiene afforded two [4 + 2] endo adducts **103a** and **103b** in 70% yield. Compound **103a** underwent smooth intramolecular [2 + 2] ring closure upon irradiation, forming annulated bishomocubanone diones **104** in 61% yield. In a one-pot reaction with Zn in EtOH, compound **105** was obtained from

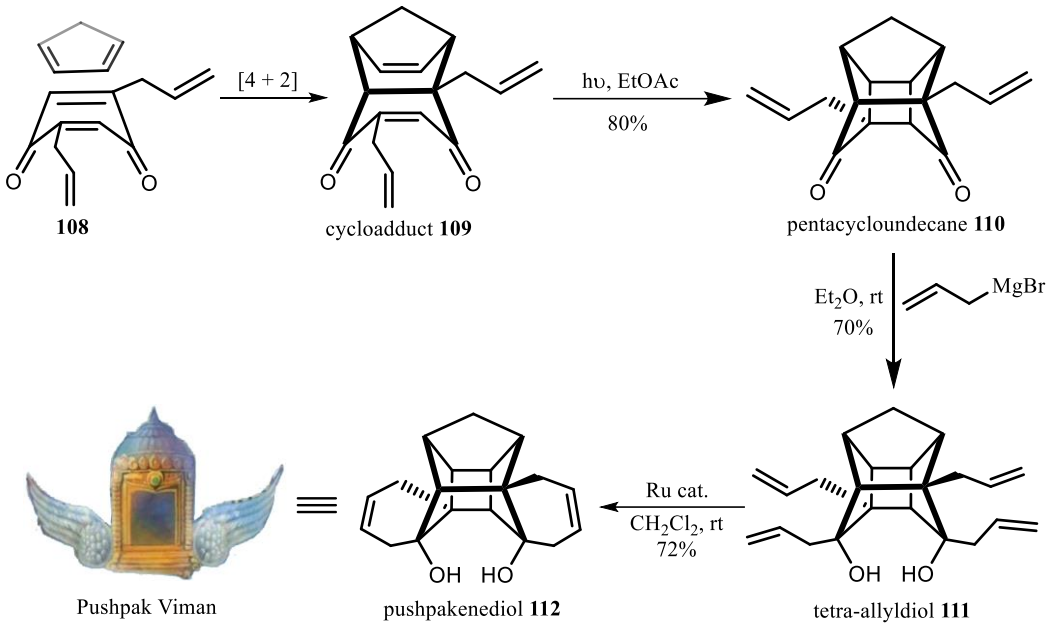
compound **104**. After further irradiation of **105**, the expected intramolecular [2 + 2] cycloaddition resulted in dione **106** which was then reduced to produce golcondane **107** *via* Wolff-Kishner reduction. (**Scheme 3.1**)



Scheme 3.1 Synthesis of golcondane **107**

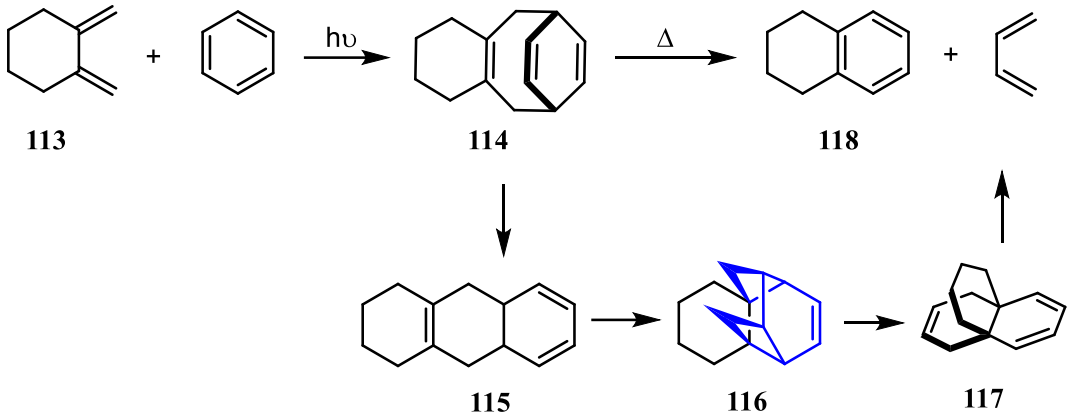
Other group have used an atom economical technique to build a complex caged molecular framework **112**.[8] A Diels-Alder reaction between cyclopentadiene and 2,5-diallyl-1,4-benzoquinone **108** produced cycloadduct **109**, which subsequently underwent [2 + 2] photocycloaddition to produce the cyclobutane ring **110**. Following that, the new tetra-allyldiol **111** was synthesized

by adding olefinic moieties to the pentacycloundecane **110** through alkenyl Grignard addition, followed by ring-closing metathesis of **111** afforded *bis*-annulated heptacyclic diol **112**. (**Scheme 3.2**) They coined the diol **112** as pushpakenediol because it was mimicking the historical old flying aircraft "Pushpak Viman" created by the popular ancient aeronautical engineer saint Bhardwaj.



Scheme 3.2 Synthesis of heptacyclic diol **112**

Gilbert *et al* at The University of Reading in England were able to produce tricyclic triene **114** by irradiating the mixture of 1,2-dimethylenecyclohexane **113** and benzene *via* [4 + 4] cycloaddition.[9] When they subsequently heated **114**, it produced tetralin **118** and 1,3-butadiene. They proposed a mechanism to explain these latter two products.[10] They proposed that triene **114** underwent a 1,3-sigmatropic shift to produce **115** and the convolution of **115** to **116** proceeds *via* intramolecular Diels-Alder reaction. The remaining two steps are retro Diels-Alder reactions. (**Scheme 3.3**)



Scheme 3.3 Synthesis of Felicine **5**

Gilbert and his research team engaged in a fun competition to come up with a name for this peculiar carbocycle **116**. One of his student, David Smith, ignored the left side ring and rotated and visualized core structure of **116**. A few more creative dives turned **116** into the face of grinning cat and hence "Felicene" was coined for **116** because Felis is Latin word for cat. (**Fig. 3.2**)

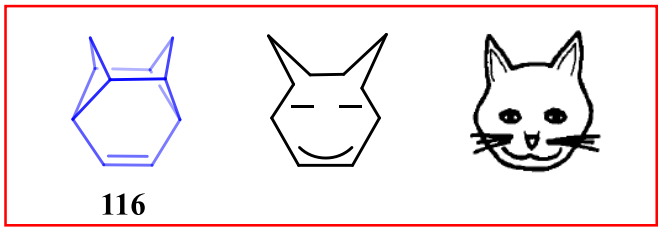
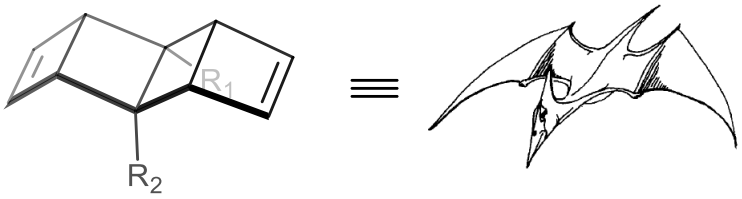


Figure 3.2 Graphical illustration of Felicene **116**

Not all animals that serve as naming inspiration can be found in forests or seas. Take the winged molecules **119**, commonly known as pterodactyladienes, which were synthesized from cyclobutadiene by Rowland Pettit from the University of Texas at Austin.[11] Their structural formations reminded him of the extinct flying creature, pterodactyli reptiles. In which, a wing edge is formed from

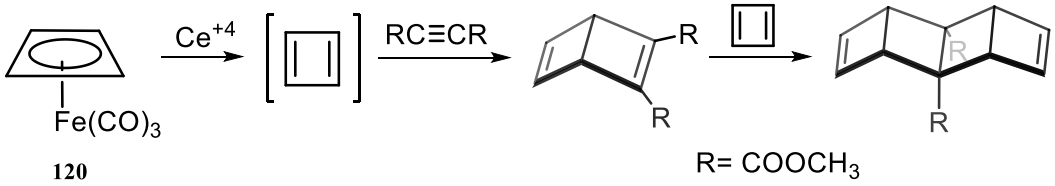
cyclobutene rings. The origins of this term are the Greek words pteron means wing and daktylos for finger. (**Fig. 3.3**)



119

Figure 3.3 Structural resemblance of **119** with pterodactyli

Pettit *et al.* have synthesized it from cyclobutadiene by freeing it from iron tricarbonyl complex **120** accompanied by the ceric ions and a suitable alkyne, two sequential cycloadditions produce the pterodactyladiene **119**. (**Scheme 2**)



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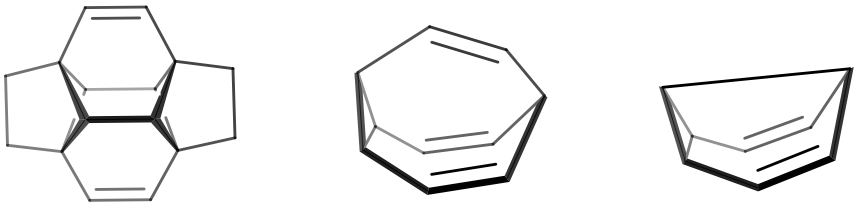
Scheme 3.4 Synthesis of pterodactyladiene **119**

In the discussions of animal shapes, the names equinene **121**, bullvalene **122**, and semibullvalene (calfene) **123** refer to two-legged creatures instead of four-legged ones. (**Fig. 3.4**) The Latin word *equus* refers to the horse for equinene **121** and here the horse turned out to be Harry Wasserman of Yale University. During his graduation at Harvard, Wasserman put in a lot of effort in laboratory, earning the moniker "Harry the Horse" from his PhD advisor, Robert B. Woodward.[12]



121 122 123

Figure 3.4 Shape of equinene **121**, bullvalene **122**, and semibullvalene **123**

The name bullvalene **122** is shrouded in secrecy and mysterious statements are often found in footnotes of the literatures. (15 in [13], 8 in [14]) Bullvalene was named, although, in honor of William Doering, who predicted several of its unique characteristics before it was synthesized.[15, 16] It seems that during early tenure of Professor Doering at Columbia University, his research students used to call him “The Bull” for unknown reason. The suffix "valene" may have evolved from "fulvalene," which was also synthesized by Professor Doering previously. As Calfene **123** is a partially grown bullvalene **122**, the name is meant to be ironic. Maynard Sherwin, a graduate student of Howard Zimmerman at the Wisconsin laboratory, synthesized calfene and labelled it.[17] However, literature more traditionally refers to calfene as semibullvalene **123**. This is how the story of these molecules involves a two-legged creature.

What if a molecule was given an animal part as its name? Professor Paquette has accomplished precisely that with **124**, which he named “snoutene.”[18, 19] This strange onomatopoeic phrase originated from Pinocchio, the small boy in the well-known children's tale whose nose got larger each time he spoke a lie. Prof. Paquette have also seen the crocodile snout in the flattened "nose." **124** can appear like a maybasket and a large scoop when viewed from different directions and therefore researchers from Ohio State University suggested "maybasketene" **124a** and "big scoupene" **124b** but "snoutene" ultimately triumphed by a nose. (**Fig. 3.5**)

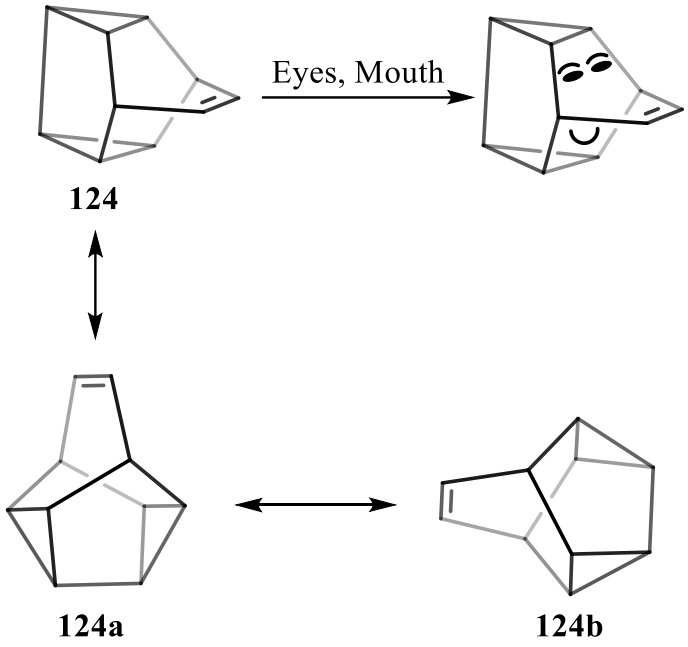
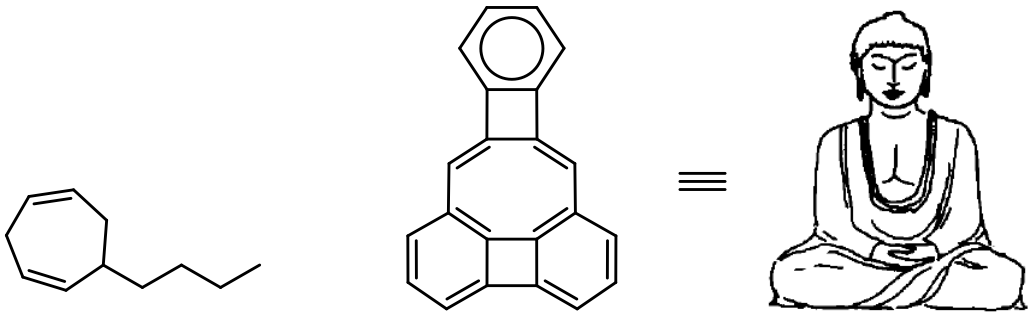


Figure 3.5 Different Shapes of **124** with different directions

Let's go a step farther and think of sperm as a part of an animal. Subramania Ranganathan, a scientist of Indian descent, from the Indian Institute of Technology, Kanpur humorously referred to **125** as "spermane." Nevertheless, **125** is a component of an essential oil from the genus *Dictyopteris* algae, and is thus also called as dictyopterine C in the articles.[20] (**Fig. 3.6**)

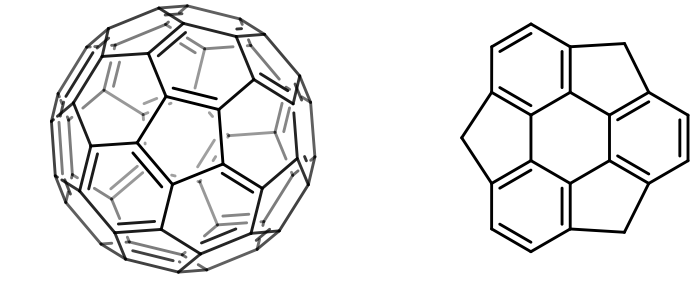
When Subramania Ranganathan read the article in which Charles Wilcox's team at Cornell University had synthesized **126**,[21] his imagination travelled far back into India's ancient history. The structure made him think of Buddha in meditation, who lived in India between 563 and 483 BC and was a founder of Buddhism.[22] (**Fig. 3.6**) He stated this in a monthly journal called *Current Highlights in Organic Chemistry*, a publication of abstracts written by him and his scientist wife Darshan and distributed by their institute.



125 126

Figure 3.6 Structural resemblance of molecules **125** and **126** referred by S. Ranganathan

Moreover, fullerene also received attention in designing new hydrocarbon architectures to construct wide variety of organic framework. The smallest stable fullerene known is buckminsterfullerene (C_{60}) **16** having twelve pentagonal and twenty hexagonal rings. Chemists have explored the peculiar reactivity and identified the functionalization characteristic of fullerene derivatives in order to use them in diverse fields from material science to medicine.[23] A smaller fragment of buckybowls namely sumanene **127** is easily discernible as structural motif of C_{60}. (**Fig. 3.7**)

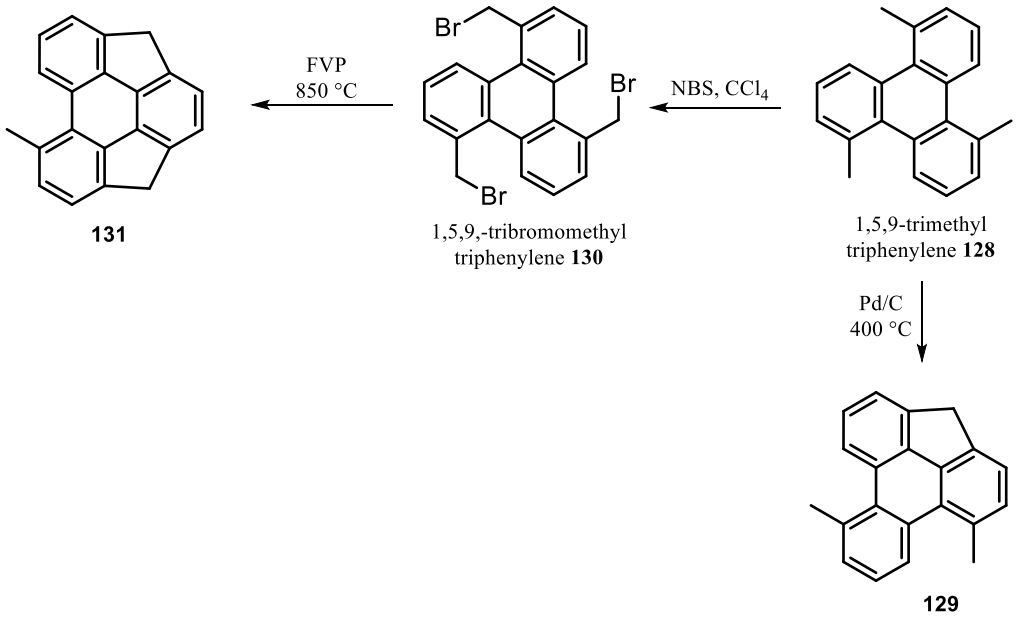


Buckminsterfullerene (C_{60}) **16** Sumanene(C_{21}) **127**

Figure 3.7 Bowl-shaped curved π-conjugated compounds

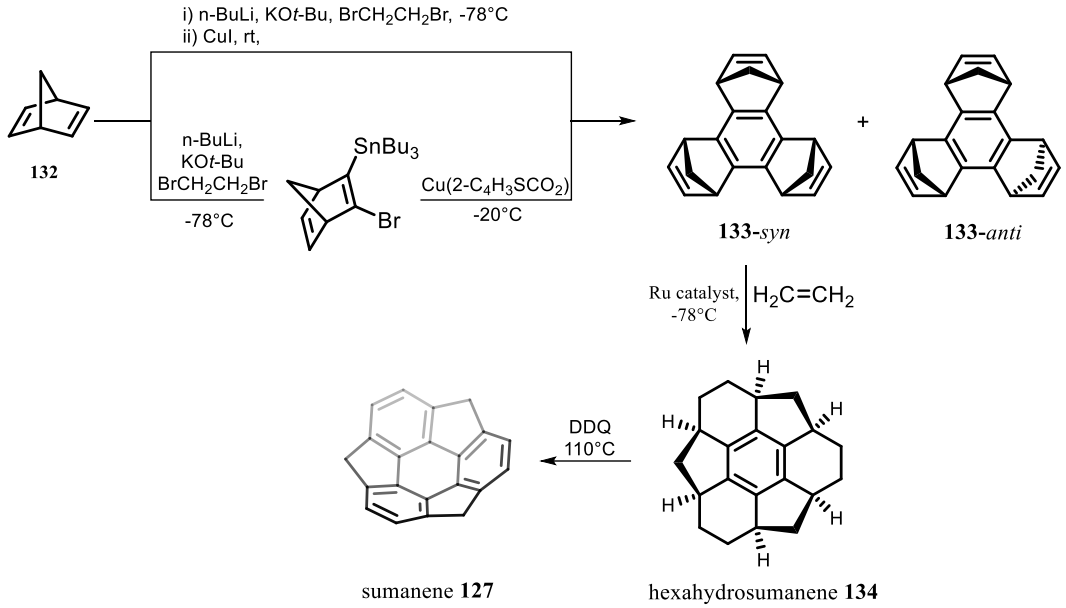
Sumanene **127**, a significant partial C_{3v} symmetric fullerene architecture, offers numerous advantages over corannulene derivatives, like the existence of three benzylic sites that could allow additional functionalization to produce novel bowl-shaped species. Professor Goverdhan Mehta from Indian Institute of Science, has dedicated his life in synthesizing aesthetically pleasing molecular entities. Mehta and coworkers designed the molecule **127** and the model shows that it has a flower-like structure, with the ring creating the petals.

They proposed trivial name "sumanene" for **127** as 'Suman' stands for flower in Sanskrit and Hindi. They used a trisubstituted triphenylene **128** in their approach to synthesized **127** *via* dehydrogenation step. They proceeded by using a direct cyclodehydrogenation approach using Pd/C catalyst, which produced a mono-bridged carbocycle **129** from prepared 1,5,9-trimethyltriphenylene **128**. In the second approach, they used flash vacuum pyrolysis (FVP) on previously prepared 1,5,9,-tribromomethyltriphenylene **130** at a higher temperature yielded a di-bridged carbocycle **131**. They were unable to produce sumanene **127** using any of the aforementioned approaches.[24] (**Scheme 3.5**)



Scheme 3.5 Attempted synthetic approaches towards sumanene **127**

Then, in 2003, Sakurai *et al*. used a nonpyrolytic strategy to synthesize sumanene **127**.[25] Their method of synthesis begins with the basic molecule norbornadiene **132**, which is transformed into cyclotrimers **133**. The **133**-*syn* isomer then experiences the tandem ring opening and ring closing metathesis by Ru-catalyst to form the vital intermediate hexahydrosumanene **134** *via* transferring the alkene bridges. The carbocycle **134** was then successfully oxidized with DDQ to form **127**. (**Scheme 3.6**)

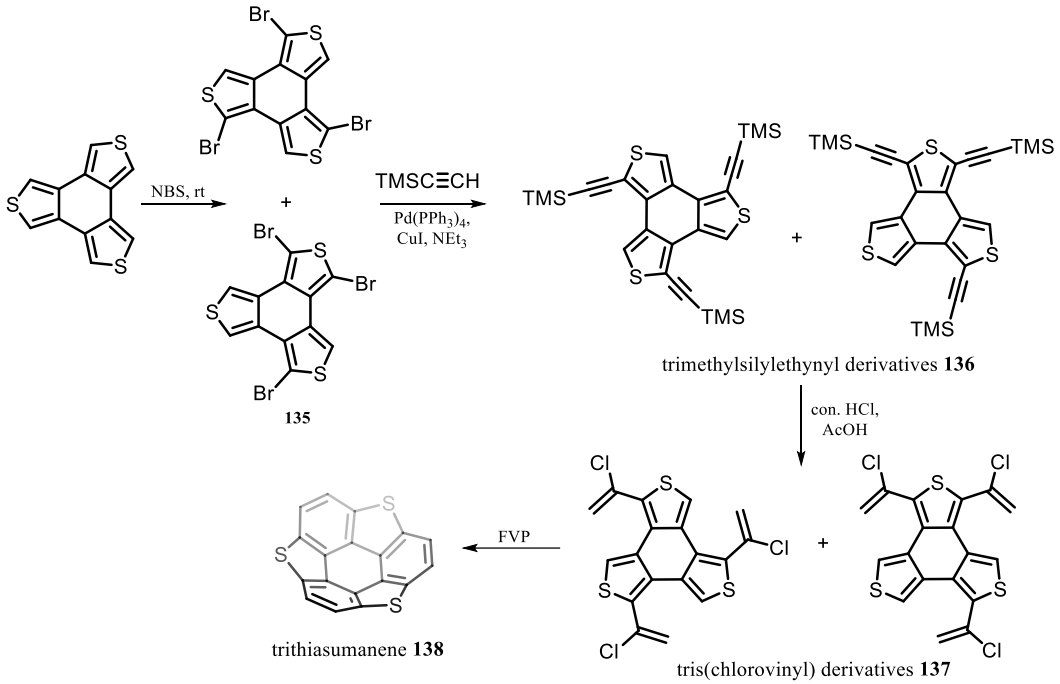


Scheme 3.6 Synthetic route towards sumanene **127** by Sakurai *et al*.[25]

The characterized data indicated that it has a rigid bowl-shaped architecture, which increases its attractiveness. While polycyclic heteroaromatics are also being pursued for the creation of highly functionalized, solution-processable derivatives for advanced materials.[26]

Otsubo *et al.* reported the first heteroaromatics with bowl curvature in 1999.[27] They successfully synthesized tribridged strained heteroaromatic system known as trithiasumanene **138** by inserting sulfur bridges on benzotrithiophene scaffold. The mixture of tribromo-derivatives **135** was first prepared using NBS,

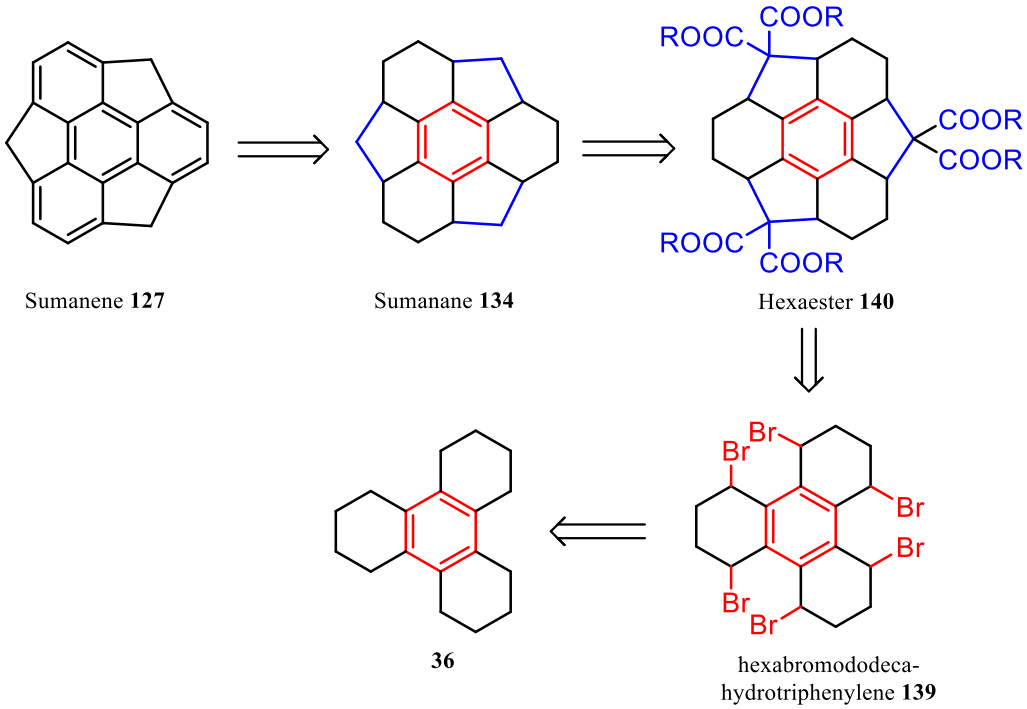
and then it was transformed into the trimethylsilylethynyl derivatives **136** by employing Sonogashira reaction. After that, conc. HCl was used to transform the trimethylsilylethynyl derivatives **26** into the tris(chlorovinyl) compounds **137**, which was subjected into FVP to yield sumanene type heteroaromatic system **138**. (**Scheme 3.7**)



Scheme 3.7 Synthesis of trithiasumanene **138**

A significant amount of experimental work has been done on the synthesis of sumanene and its derivatives, prompted us to explore novel synthetic route towards sumanene **127**.[28] Dodecahydrotriphenylene **36**, our standard scaffold, is what we've considered using to build sumanene **127** *via* sequential steps of photobromination, three-fold dialkylation, decarboxylation and oxidation. (**Scheme 3.8**) Usually the secondary halides are tagged with poor reactivity in eliminations, nonetheless we attempted an unsuccessful three-fold dialkylation as shown in **Scheme 3.8**. According to few reports, these typical bromoalkanes frequently undergo pyrolytic elimination at higher temperatures.[29, 30] We observed

during the reflux that hexabromo-DDHTP **139** readily decomposed at higher temperature and formed thermodynamically stable triphenylene **1** instead of the three-fold dialkylation reaction as anticipated.



Sumanene **127** Sumanane **134** Hexaester **140**

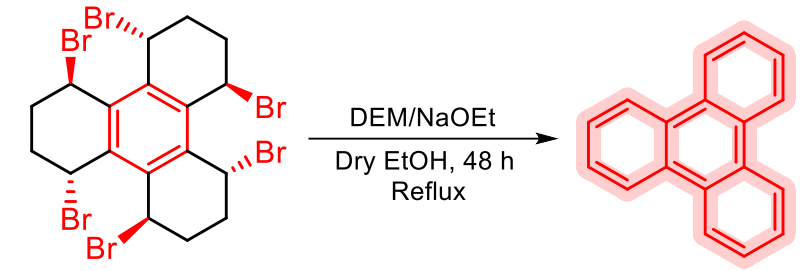
36 hexabromododeca-hydrotriphenylene **139**

Scheme 3.8 Retrosynthetic plan of sumanene **127**

Hexabromododecahydrotriphenylene **139** was firstly synthesized from photobromination of decahydrotriphenylene **36** with bromine under the illumination of a 300 W incandescent bulb as per reported procedure.[31] Then the attempt was made for the synthesis of hexacarboxylate **140**.[32] (**Scheme 3.9**)

Subsequently, the isolated compound was characterized using NMR analysis. The structure elucidation from ^{1}H and ^{13}C NMR analysis was against our hypothesis because we had got triphenylene **28** as a product in the end result. The ^{1}H NMR (500 MHz, $CDCl_3$) gave only two signals at δ 8.63 (dt, J = 6.2, 3.6 Hz, 6H) and 7.64 (dt, J = 6.3, 3.5 Hz, 6H) indicating the presence of twelve symmetric aromatic protons in the molecule. Its ^{13}C NMR (126 MHz, $CDCl_3$) spectrum

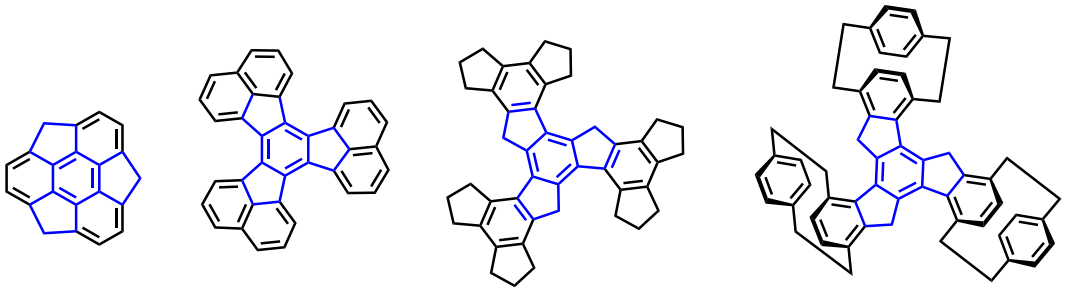
showed only three signals at δ 129.75, 127.18 and 123.27 at aromatic region confirms that all the aromatic carbons are presented symmetrically and the data was found to be consistent with the reported literature.[33]



Hexabromo-DDHTP **139** Triphenylene **1**

Scheme 3.9 Formation of triphenylene **1**

We then shifted our focus on trindane molecule **35** to construct new carbocyclic frameworks. Trindane **35** is one such promising scaffold which has been found to be present in various symmetrical carbocyclic frameworks as shown in **Fig. 7**. Our interest towards these scaffolds prompted us to explore new carbocycles possessing interesting architecture.



Sumanene **127** Decacyclene **13** Trimer of trindanone **51** Paracyclophane derivative **141**

Figure 3.8 Aesthetic architectures having trindane scaffold

Chemists have a distinct perspective on the world surrounding them. One day, I was admiring the beauty of a butterfly that was perched on my laptop. It was joyful to watch its wings start to flap as it flutters and flies away. The initial visuals by my closed eyes prompted me to imagine how trindane moieties would appear as the wings of the butterfly. The model gradually unraveled in front of my eyes, and to much of our delight and excitement, we set out to plan for its formation. Initially, we contemplated that the shape of an open–winged butterfly **3.9a** could be envisioned as **3.9b** in which one of the peripheral cyclopentane rings of two trindane units (held together by a small ring) overlapping with each other would appear just as shown in **Fig. 3.9**. On further simplification, the carbocyclic skeleton **3.9b** would furnish the structure as **3.9c**. We reckoned the wings of the butterfly as trindane moieties connected by a small bicyclic system as antennae located on the head of the butterfly. Similarly the close–winged butterfly **3.9d** was visioned as a molecule having **3.9e** framework in which both the trindane units completely overlap with each other giving a skeleton as **3.9f**.

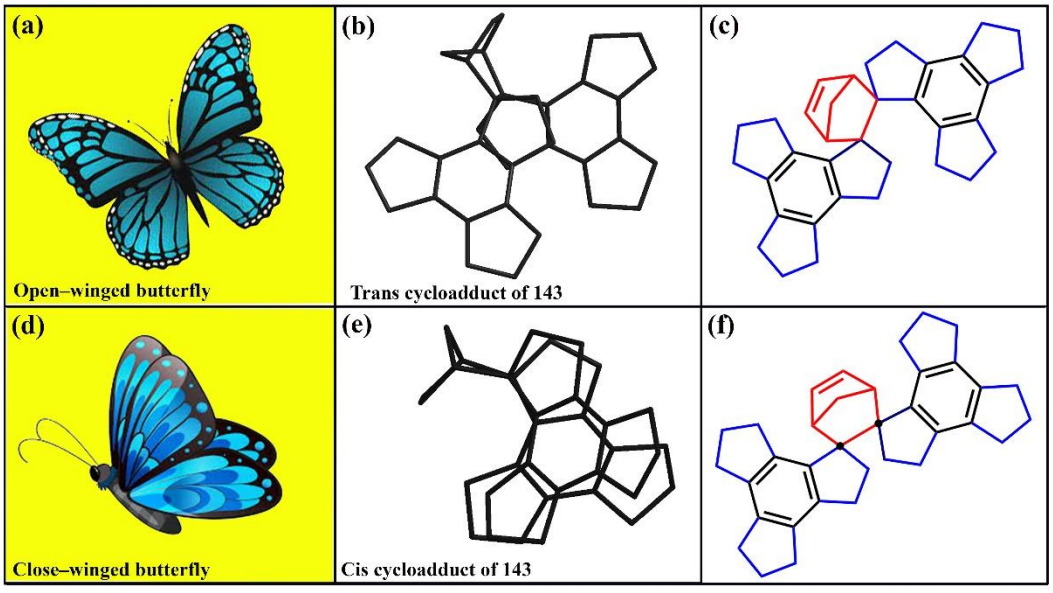


Figure 3.9 DFT Model Visualization of *cis*/*trans* cycloadducts of butterflyene

As shown in **Fig. 3.10**, this prototype decacyclic ring system was thought to be assembled *via* a Diels-Alder cycloaddition of **142** and a suitable diene. For this purpose, cyclopentadiene was chosen because of its easy accessibility and better reactivity in cycloaddition reactions. While the main body of the proposed butterfly was thought to be made up of two trindane rings connected by an olefinic bridge, the head part with the antennae was proposed to be assembled from a diene unit. The bitrindanylidene **142** was easily recognized as a McMurry dimer of the trindanone unit **50** which has been synthesized from cyclopentanone in two easy steps.[34]

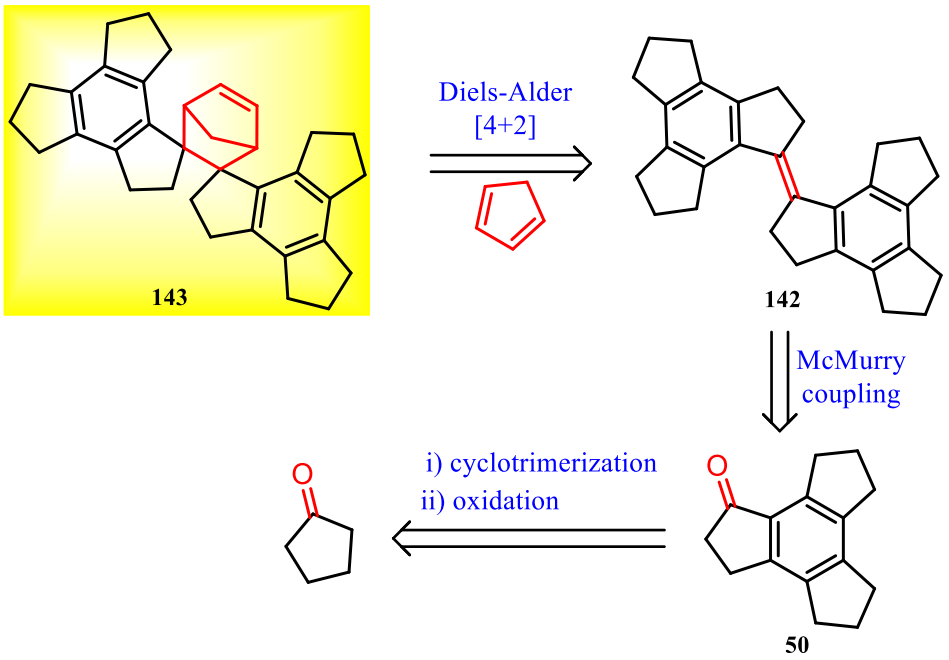
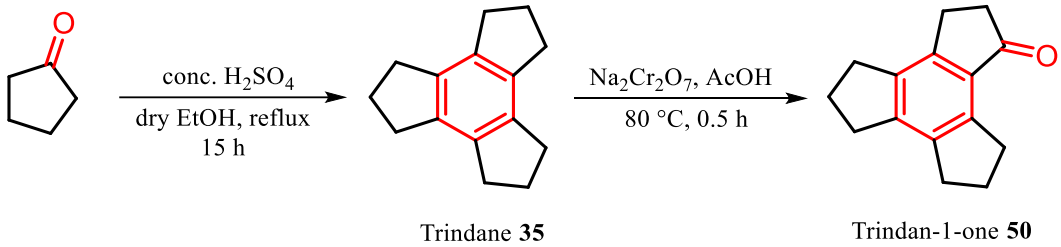


Figure 3.10 Retrosynthetic plan for proposed butterflyene **143**

3.3 Results and Discussions

At the outset, our synthetic efforts commenced with the preparation of trindane **35** by acid-catalyzed cyclocondensation of cylopentanone in dry ethanol

to deliver as a white solid in 32% yield.[34] The thus-obtained **35** was subjected to oxidation using sodium dichromate in glacial acetic acid to furnish its benzylic monoketone **50** (TLC). (**Scheme 3.10**)

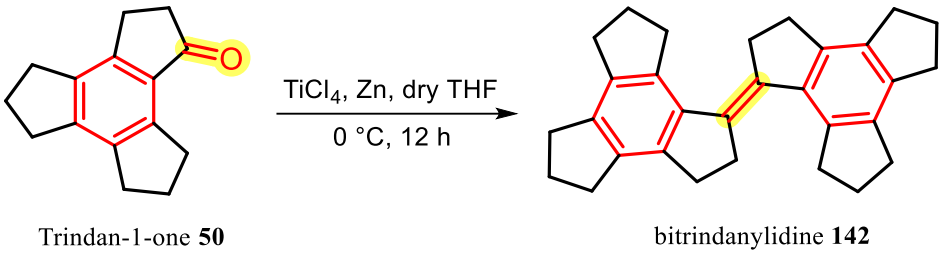


Trindane **35** Trindan-1-one **50**

Scheme 3.10 Synthesis of trindan-1-one **50**

This light yellow solid **50** was then chromatographed on a column of silica gel using light petroleum and ethyl acetate (98:2) to furnish it as white solid. Its ^{1}H NMR (600 MHz, $CDCl_3$) showed a triplet at δ 3.21 for methylene protons adjacent to carbonyl group among other proton signals. ^{13}C NMR (151 MHz, $CDCl_3$) of **50** showed signals at δ 207.71 indicating the presence of a carbonyl carbon along with six carbons of benzene ring at δ 149.53, 147.05, 141.39, 139.96, 139.18 and 131.49.

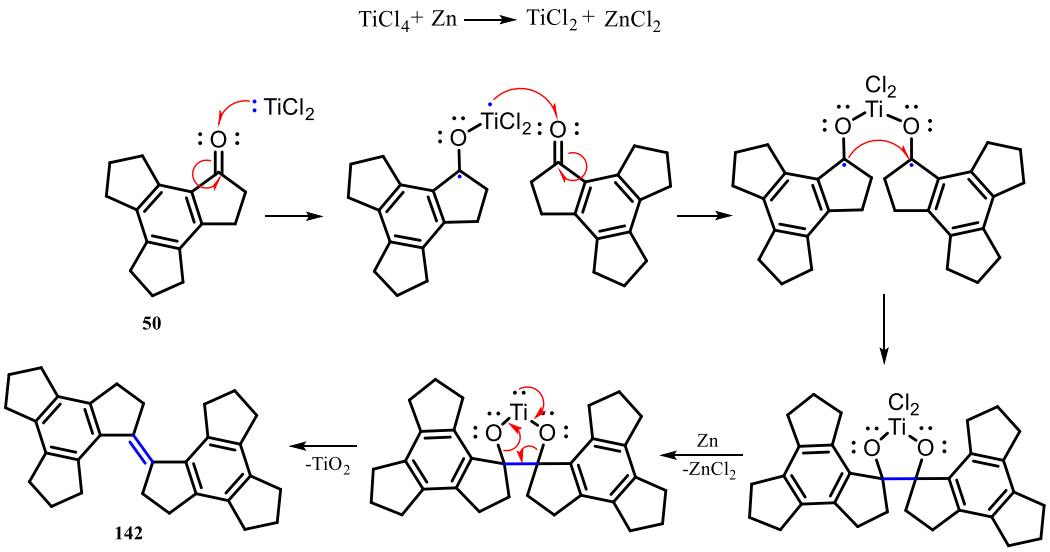
McMurry reaction[35] is a classic example of deoxygenative coupling of carbonyl compounds leading to the formation of alkenes, where low-valent titanium species have been found to promote the reaction of aldehydes/ketones to furnish alkenes *via* dimerization of ketyl radicals by one-electron reduction of the carbonyl groups. When McMurry discovered[36] in 1976 that $TiCl_3$ could be reduced with potassium in THF to produce a highly active Ti (0) reagent, he shortly introduced the employment[37] of $TiCl_3$/Li and then $TiCl_3$/Zn-Cu as safer substitutes. Numerous carbocycles have been accomplished by utilizing this C–C coupling approach, which can be exploited in both intra- and intermolecular manner. Accordingly, we attempted the synthesis of bitrindanylidine **142** by reductive dimerization of monoketo **50** using McMurry homocoupling reaction. (**Scheme 3.11**)



Trindan-1-one **50** bitrindanylidine **142**

Scheme 3.11 Synthesis of bitrindanylidine **142**

For this, low-valent titanium was initially prepared by the reduction of $TiCl_4$ using activated zinc dust in dry THF at 0 °C under argon blanket. (**Scheme 3.12**) Into the above mixture was introduced the solution of ketone **50** in THF slowly in drop wise manner. The reaction was stirred at ambient temperature for 12 h and was monitored by TLC. The subsequent workup and chromatography of the reaction mixture furnished the bitrindanylidine **142** as a white solid in 40% yield. The structure of the compound **142** was fully discernible from its spectral data.



Scheme 3.12 Plausible mechanism of action during the course of McMurry reaction

Thus, bitrindanylidine **142** exhibited bands at 1644 cm^{-1} indicating the aromatic C=C stretching in its IR spectrum. The proton NMR spectrum (600 MHz, $CDCl_3$) of **142** showed multiplets at δ 2.92 – 2.72 (m, 24H) confirming the presence of benzylic and allylic protons along with the homobenzylic protons between δ 2.20 – 2.02 (m, 8H). Its ^3C NMR (151 MHz, $CDCl_3$) displayed six signals at δ 140.24, 139.44, 139.19, 138.26, 137.76 and 137.22 for two aromatic rings along with one signal at δ 135.78 for olefinic exocyclic C=C bond. Additionally eight signals at δ 37.45, 34.69, 31.66, 31.40, 31.01, 30.56, 27.06 and 25.56 for a total of sixteen carbons on cyclopentane rings were also observed.

While proceeding towards the synthesis of the target molecule butterflyene **143**, we envisaged the difficulties associated with the Diels-Alder reaction (DAR) on a tetrasubstituted olefin. When we looked into the literature we found only a handful of examples of DAR on tetrasubstituted double bonds in *intra*- as well as *inter*-molecular fashion.[38, 39] There were no examples of DAR of bicycloalkylidenes except that of bicyclopropylidene **144** which was close to our system **142**.[40] Moreover the double bond in bicyclopropylidene **144** was reported to be reactive due to the strain involved in the cyclopropane rings. The reason for cycloaddition between **142** and $\mathbf{D_1}$ to form cycloadduct **143** was attributed to EWGs in the dienophile **146**.

Based on the above information, we anticipated a sluggish DAR of **142** as it is a relatively bulkier molecule. This may have a substantial bearing on the rate and outcome of its cycloaddition with the diene. It should be noted that the tetrasubstituted double bond in bitrindanylidine **142** has neither any type of strain like that present in a cyclopropane ring in **144** nor is it activated by any electron withdrawing group like that in **146** (**Fig. 3.11a** and **b**)

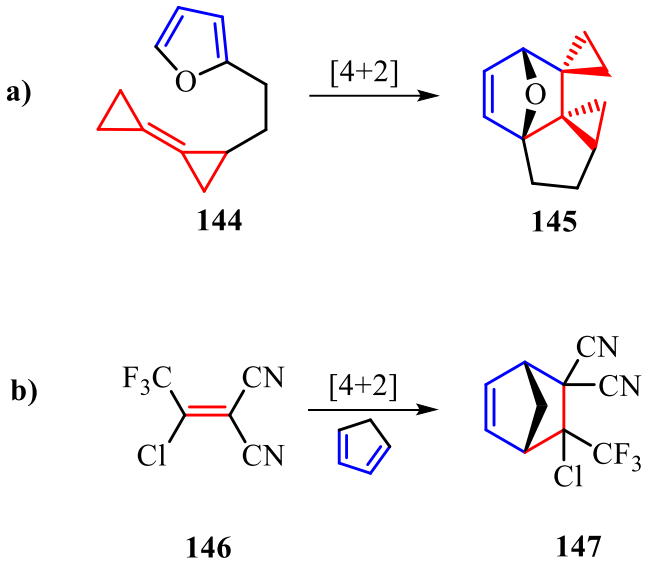
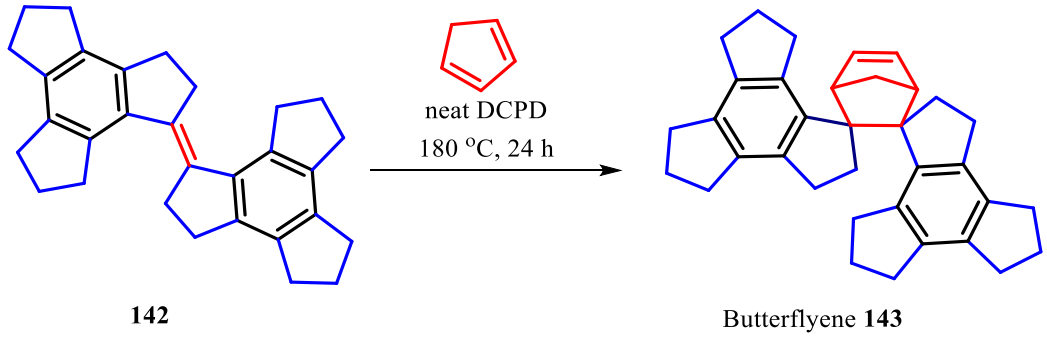


Figure 3.11 a) Intramolecular DAR of a strain-activated double bond in bicyclopropylidene **144**[40] **b)** Intermolecular DAR of a tetrasubstituted ethylene activated by EWGs **146**[41]

The DAR between **142** and freshly cracked cyclopentadiene, **D1** (with intermittent portion wise addition) in toluene under reflux met with no success as envisioned. Taking clue from this observation, we then attempted the DAR of **142** with neat dicyclopentadiene in a sealed tube at 180 °C for 24 h to furnish the cycloadduct **143** in 85 % yield. (**Scheme 3.13**)

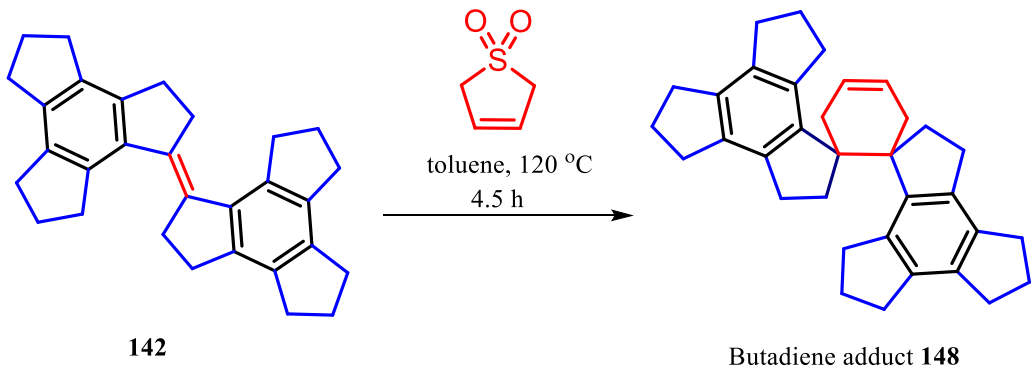


Scheme 3.13 Synthesis of Butterflyene **143**

Proton NMR spectra of butterflyene **143** indicated it to be a *cis* and *trans* mixture. It showed signals at δ 5.99, 5.61 and 5.44 indicating the presence of olefinic protons in the cycloadducts (as mixture) resulting from *cis*– and *trans*–isomers of **142** in the proportion of 79:21. The ^{13}C NMR (151 MHz, $CDCl_3$) of the compound **143** exhibited two signals at δ 137.22 and 132.31 and one signal at δ 131.16. Unfortunately, we could not separate the crystal of pure isomers of **143** from one another to obtain its SCXRD.

To the best of our knowledge this is the first report of a tetrasubstituted double bond in a bicyclopentylidene moiety undergoing DAR with a diene. It is noteworthy to observe that the **D_1** despite being a reactive diene, underwent cycloaddition with the tetrasubstituted olefin relatively under difficult condition. Prompted by this result, we examined the cycloaddition of the hindered dienophile **142** with some more dienes (**D_2-D_6**).

Fortuitously, we also succeeded in preparing the analogues of **143** such as butadiene adduct **148** and isoprene adduct **149**. Butadiene (**D_2**) gas was generated *in situ* using butadiene sulfone in toluene at 80 °C and bitrindanylidine **142** was added slowly while increasing the temperature to 120 °C. The reaction was complete after 4.5 h to furnish the butadiene adduct **148** as a white solid in 80 % yield. (**Scheme 3.14**)



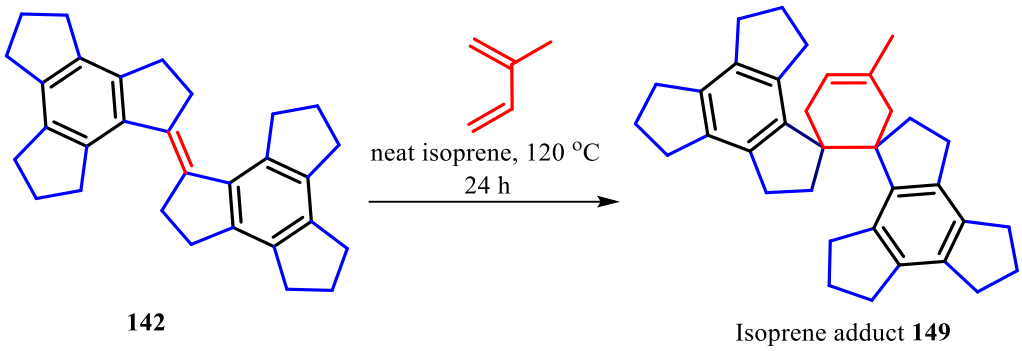
142

Butadiene adduct **148**

Scheme 3.14 Synthesis of butadiene adduct **148** of compound **142**

The structure of the compound **148** was deduced from its spectral features. Its proton NMR (500 MHz, $CDCl_3$) showed signals δ 5.54 and 4.52 for olefinic protons on cyclohexene ring in a percentage of 66:34 indicating it to be a mixture of *cis* and *trans* isomers as expected. Its ^{13}C NMR (151 MHz, $CDCl_3$) displayed signals at δ 147.36 - 134.10 revealing the presence of carbons of central benzene rings along with an additional signal at δ 127.11 confirming the presence of olefinic carbons of cyclohexene ring in **148**.

The isoprene adduct **149** was also prepared similarly from McMurry product **142** and isoprene (**D_3**) to furnish a white solid after column chromatography in 86% yield. (**Scheme 3.15**)



Scheme 3.15 Synthesis of isoprene adduct **149** of compound **142**

The proton NMR spectrum (600 MHz) of **149** showed signals at δ 5.52 and δ 4.49 for olefinic protons indicating it to be a *cis* and *trans* mixture in amount of 66:34 respectively. Moreover, ^{13}C NMR (151 MHz, $CDCl_3$) of **149** displayed resonances at δ 140.23 – 127.18 for fourteen aromatic and olefinic carbons and at δ 43.82 for one methyl carbon.

Interestingly, substantial difference in shielding of the olefinic protons in adducts **148** and **149** was observed in proton nuclear resonances as compared to that in **143**. This is presumably because of the rigidly locked conformation due to the methylene bridge in adduct **143** which is absent in **148** and **149**. In line with

magnetic anisotropies in the case of **148** and **149**, it is reasonable to surmise that one of the olefinic protons may experience magnetic deshielding arising from the central benzene rings of trindane moieties owing to the absence of the methylene bridge. It is also interesting to note that all the compounds (**142**, **1430**, **148**, **149**) showed highly abundant protonated molecular ion peaks $(M+H)^+$ as base peaks which may be due to high proton affinity and fragments corresponding to alkene cleavage were also highly stable.

As can be envisaged from the **Fig. 3.12**, the double bond in the *trans* isomer of **142** is relatively more hindered than that in the *cis* isomer. Further it is intriguing to observe that the addition with cyclic diene $\mathbf{D_1}$ in the DAR seems to be more difficult than that with acyclic dienes $\mathbf{D_2}$ and $\mathbf{D_3}$ due to the presence of the methylene group in $\mathbf{D_1}$ which perhaps makes the diene bulkier. The consequences of the above observations imply the formation of *cis* and *trans* product mixture. The cyclic diene $\mathbf{D_1}$ furnished the corresponding *cis* cycloadduct **143** in 79% while the corresponding *trans* adduct **143** in 21 %. On the other hand, the acyclic dienes $\mathbf{D_2}$ and $\mathbf{D_3}$ were found to be able to reach out to the hindered double bond in the *trans* isomer **142** to a better extent and thus furnished the corresponding *trans* cycloadducts in a higher proportion than that in case of $\mathbf{D_1}$ (34%). The acyclic dienes $\mathbf{D_2}$ and $\mathbf{D_3}$ furnished the corresponding *cis* cycloadducts as major products in 66%. The pictorial DAR is presented in **Fig. 3.12**. It is clearly evident that the DAR with all the dienes ($\mathbf{D_1}$-$\mathbf{D_3}$) is favored from the less hindered face from the opposite side of two trindane units in **142** to afford corresponding cycloadducts.

Next, we evaluated the scope of the DAR between **142** with dienes, *viz* 6,6-dimethylfulvene ($\mathbf{D_4}$), spiro[2.4]hepta-4,6-diene ($\mathbf{D_5}$) and anthracene ($\mathbf{D_6}$). We encountered difficulties upon first performing DAR under solvent conditions (Toluene and *o*-dichlorobenzene). We then turned our attempts under forcing condition (neat). However, it did not undergo cycloaddition with bitrindanylidine **142** perhaps due to the sterically bulkier size of the dienes.

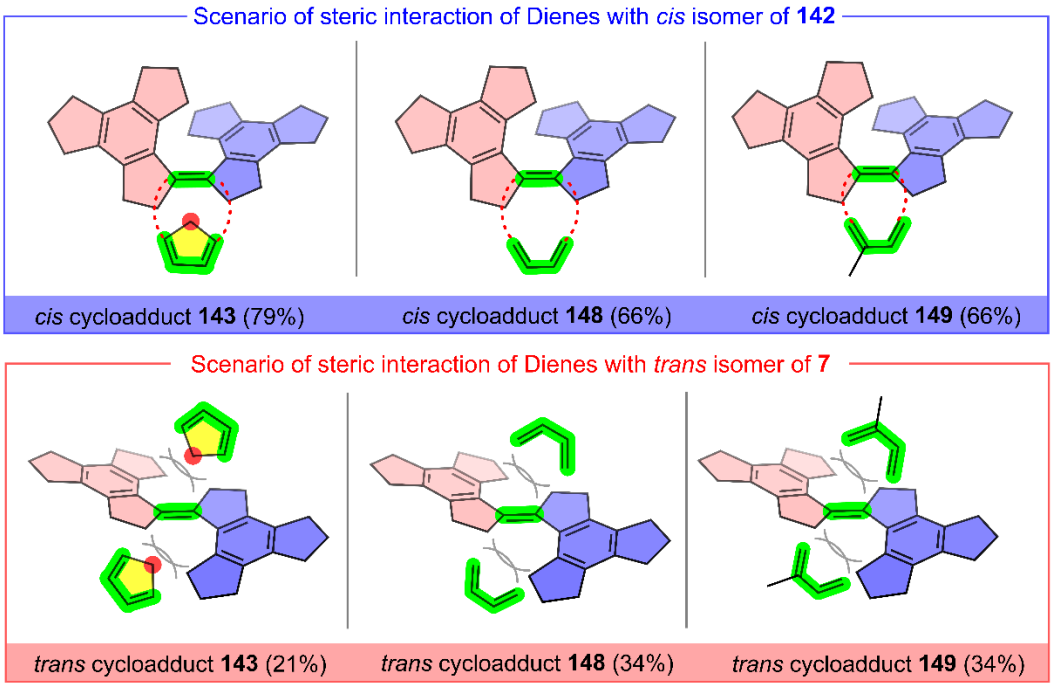


Figure 3.12 Interaction between *cis* and *trans* isomers of **142** with incoming dienes (Figures in parenthesis indicate percentage of relative olefinic peak intensities)

3.4 DFT Calculations

These interesting observations prompted us to study the selectivity of all the dienes (**D**$_1$-**D**$_6$) towards cycloaddition with **142** using Density Functional Theory calculations (DFT). The structural optimization, molecular orbitals and vibrational frequencies calculations were performed at M06-2X/6-311++G(d, p) level using the Gaussian09 Software package.[42, 43] It should be noted that the absolute value of the dihedral angle in **142** obtained from DFT studies is 177.38°. We have optimized all the cyclic and acyclic dienes such as 1,3-cyclopentadiene (**D**$_1$), 1,3-butadiene (**D**$_2$), isoprene (**D**$_3$), 6,6-dimethyl fulvene (**D**$_4$), spiro[2.4]hepta-4,6-diene (**D**$_5$) and anthracene (**D**$_6$). The energy gap of the dienes are in ascending order as follows: **D**$_3$ (2.164 eV) < **D**$_6$ (2.168 eV) < **D**$_4$ (2.796 eV) < **D**$_5$ (3.664 eV) < **D**$_1$ (3.743 eV) < **D**$_2$ (3.891 eV). The computed values for activation energy for all the cycloadducts are included in **Table 3.1**.

Table 3.1 Change in Gibbs free energy, enthalpy, and entropy in kcal mol^{-1} at 298.15 K

Cycloadducts of Dienes	Formation Energy	ΔG	ΔH	ΔS
D_1	–0.733	3.346	–13.455	–0.056
D_2	–1.599	–16.444	–33.045	–0.056
D_3	–1.723	–19.435	–35.509	–0.054
D_4	–0.377	10.989	–6.126	–0.057
D_5	–0.350	12.259	–5.391	–0.059
D_6	–0.396	10.890	–6.262	–0.058

The lowest value for Gibbs free energy is predicted for the isoprene adduct **149**, butadiene adduct **148** and butterflyene **143** (an adduct of **142** and cyclopentadiene **D_1**), which amounts to –19.435 kcal mol^{-1}, –16.444 kcal mol^{-1} and 3.346 kcal mol^{-1} respectively.

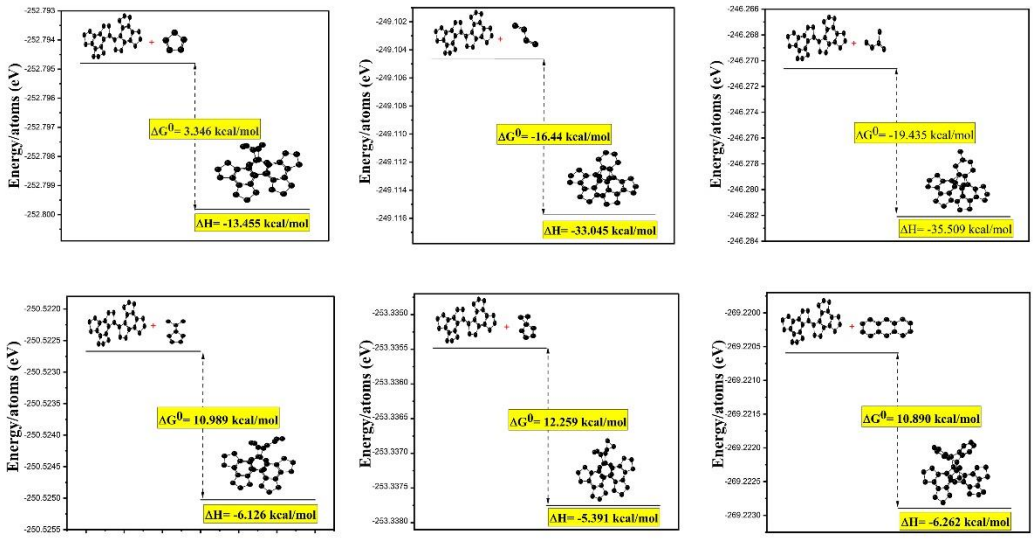
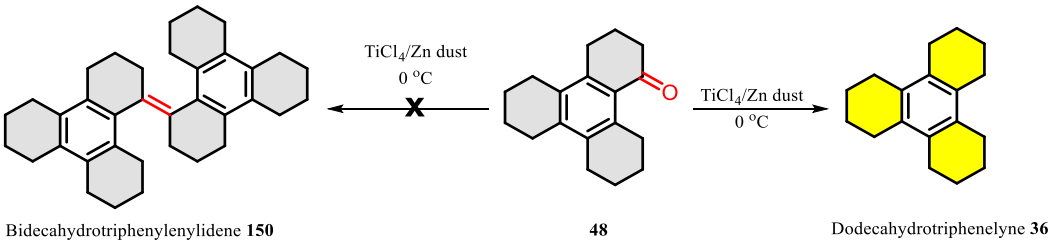


Figure 3.13 Reaction coordinate diagram of cycloadducts of various dienes **D_1-D_6**

These values are lower than all the remaining cycloadducts of the dienes (**D_4-D_6**) which did not undergo cycloaddition. These observations are in good agreement with the experimental results. We have also calculated the HOMO–LUMO gap of reactants as it gives the important parameters such as chemical potential (μ), global hardness (η), global electrophilicity index (ω) etc. These global parameters and frontier molecular orbit levels calculated are given in **Table 3.2**. The computed reaction energy diagram is indicated in **Fig. 3.13**. The HOMO energy of tetracyanoethene (TCE)[44] is –0.3486 au (–9.485 eV) and it is used to compute the global nucleophilicity (N') of diene, which can be express as $N'=E_{HOMO(diene)}–E_{HOMO(TCE)}$.

In context with our aforementioned trindane studies, we became interested to examine the McMurry homocoupling reaction of decahydrotriphenylen-1-one **48** under similar reaction condition as that of trindanone **50**.



Scheme 3.16 Attempted synthesis of McMurry dimer of **48**

Thus, when we treated **48** with titanium tetrachloride and zinc dust in dry THF under argon atmosphere at 0 °C. (**Scheme 13**), we observed and isolated a less-polar spot (TLC) and analyzed it from NMR. Its ^{1}H NMR (400 MHz, $CDCl_3$) showed only two signals at δ 2.57 (s, 12H) and 1.78 (s, 12H). The ^{13}C NMR (101 MHz, $CDCl_3$) of compound **43** gave three signals at δ 132.59, 26.82 and 23.07. These results clearly indicated the structure of dodecahydrotriphenylene **36**. The reaction of this ketone **48** did not yield the desired bidecahydrotriphenylenylidene

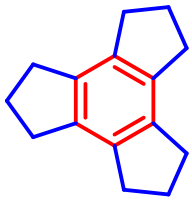
product **150**. Instead it went for the Wolff-Kishner type reduction and formed dodecahydrotriphenylene **36**.

Table 3.2 The Global parameter and Frontier molecular orbit levels calculated at M06-2X/6-311++G(d, p) level for the reactants

Diene/ Dienophile	HOMO (eV)	LUMO (eV)	η (eV)	μ (eV)	$\omega=\mu^2/2\eta$ (eV)	$\Delta N_{max}=-\mu/\eta$	N−1/ ω (eV)	N'	$HOMO_{diene}$–$LUMO_{dienophile}$	$HOMO_{dienophile}$–$LUMO_{diene}$
D_1	-7.535	-0.024	3.743	-3.779	1.908	1.010	0.524	1.950	-7.329	6.313
D_2	-7.953	-0.085	3.891	-4.019	2.075	1.033	0.482	1.532	-7.747	6.252
D_3	-6.515	-1.094	2.164	-3.804	3.344	1.758	0.299	2.970	-6.309	5.243
D_4	-7.279	-0.843	2.796	-4.061	2.949	1.452	0.339	2.206	-7.073	5.494
D_5	-7.343	-0.008	3.664	-3.675	1.844	1.003	0.542	2.142	-7.137	6.329
D_6	-6.719	-1.192	2.168	-3.955	3.608	1.824	0.277	2.766	-6.513	5.145
142	-6.337	-0.206	2.963	-3.271	1.806	1.104	0.554			

3.5 Experimental section

3.5.1 *Synthesis of trindane* **35**

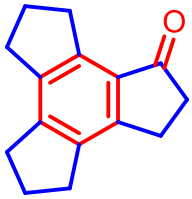


Cyclopentanone (16 ml, 180 mmol) and dry ethanol (18 ml) was taken in two-neck round-bottomed flask (100 mL) equipped with a condenser. A dropwise addition of concentrated sulfuric acid (8 ml, 150 mmol) into reaction mixture followed by refluxed for 15 h. After completion of reaction, mixture was poured on to ice, neutralized with sodium carbonate and extracted with ethyl acetate (3 x 30 ml). Organic layer was washed with water, brine and dried over Na_2SO_4. Removal of solvent under reduced pressure furnished a dark brown liquid which was chromatographed on a column of silica gel using light petroleum to furnished trindane as white solid (3.8 g, 32 %Yield); mp 90 °C (lit 95–97 °C)[34]

3.5.2 *Synthesis of trindan-1-one* **50**

Trindane **35** (2.50 g, 12.62 mmol) was dissolved in glacial acetic acid (25 mL) and the stirred solution was maintained at 80 ºC. Sodium dichromate dihydrate (4.50 g, 15.14 mmol, 1.2 equiv.) in glacial acetic acid (20 mL) was added dropwise at 80 ºC. After 30 min reaction mixture was poured into ice water and the precipitate which formed was separated, washed with water (2 × 10 mL) and dried under vacuum. Resulted light yellow solid was then chromatographed on a column of silica gel using light petroleum and ethyl acetate (98:2) to furnished trindan-1-one as white solid.

2,3,4,5,6,7,8,9-octahydro-*1H*-cyclopenta[*e*]-as-indacen-1-one **50**

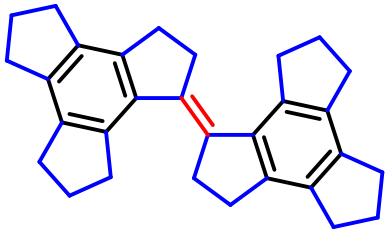


White solid, 1.5 g, 56% Yield, mp 115 ºC (lit 115 °C)[45], R*f*: 0.5 (4.5:0.5, Pet. Ether:EtOAc); **IR (KBr, cm^{-1})** 2953, 1703; **^{1}H NMR (600 MHz, CDCl$_3$)** δ 3.21 (t, *J* = 7.5 Hz, 2H), 3.00 – 2.95 (m, 2H), 2.88 (t, *J* = 7.5 Hz, 4H), 2.79 (t, *J* = 7.5 Hz, 2H), 2.68 – 2.64 (m, 2H), 2.19 – 2.12 (m, 4H); **^{13}C NMR (151 MHz, CDCl$_3$)** δ 207.71, 149.53, 147.05, 141.39, 139.96, 139.18, 131.49, 36.89, 31.96, 30.97, 30.39, 30.00, 25.55, 25.16, 24.59.

3.5.3 *Synthesis of Bitrindanylidine* **142**

Under an argon atmosphere, a three-necked pre-flamed dried round bottom flask equipped with a magnetic stirrer was charged with titanium tetrachloride (2.86 g, 15.08 mmol) and 30 ml of dry THF. The mixture was cooled to 0 °C. Then activated zinc dust (2.46 g, 37.71 mmol) was added slowly to the yellow suspension with the temperature kept at 0 °C. The suspension was then turned into dark brown immediately and stirred for 15 mins at 0 °C. The solution of trindan-1-one **6** (0.8 g, 3.77 mmol) in 30 ml of dry THF was added drop-wise over a period of 0.5 h. After addition, the reaction mixture was stirred at room temperature until **6** consumed (monitored by TLC). The reaction was quenched with 10% aqueous sodium bicarbonate and taken up in ethyl acetate. The organic layer was collected and concentrated. The dark brown crude was chromatographed on a column of silica gel using light petroleum to furnished 0.443 g of bitrindanylidine.

(*E*)-2,2',3,3',4,4',5,5',6,6',7,7',8,8',9,9'-hexadecahydro-1,1'-bi(cyclopenta[*e*]-*as*-indacenylidene) **142**



White solid, 0.443g, 30% Yield, mp 218 °C, R*f*: 0.8 (5:0, Pet. Ether:EtOAc); **IR (KBr, cm^{-1})** 2933, 1433; **^{1}H NMR (600 MHz, CDCl$_3$)** δ 2.92 – 2.72 (m, 23H), 2.20 – 2.02 (m, 8H), 1.56 (s, 1H); **^{13}C NMR (151 MHz, CDCl$_3$)** δ 140.24, 139.44, 139.19, 138.26, 137.76, 137.22, 135.78, 37.45, 34.69, 31.66, 31.40, 31.01, 30.56, 27.06, 25.56; **HRMS (ESI)** *m/z* calculated for $C_{30}H_{33}$ $[M+H]^+$: 393.2582, found 393.2581.

3.5.4 *General for synthesis of carbocyclic adducts* **143, 148** and **149**

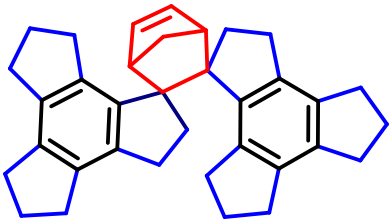
A three-necked pre-flamed dried round bottom flask equipped with A 50 ml three-necked round bottom flask was equipped with condenser and magnetic stirred under inert argon atmosphere. In RBF, bitrindanylidine **142** (100 mg, 0.25 mmol) was taken with/without 15 ml of dry toluene. Excess of various dienes (**D$_1$-D$_3$**) were injected in reaction mixture. The solution was then heated to reflux in an oil bath for several hours. After completion of reaction (monitored by TLC) the solution was then removed under vacuum distillation and the residues were purified by column chromatography on silica gel using light petroleum as eluent to afford cycloadducts **143, 148** and **149**.

Butterflyene adduct **143**

Bitrindanylidine **142** (100 mg, 0.25 mmol) in 10 ml of dicyclopentadiene was directly taken into the sealed tube. The reaction mixture was then heated up to

180 °C to generate cylopentadiene *in situ*. After completion of reaction (12 h), solution was removed using vacuum distillation and crude was chromatographed with column of silica gel using light petroleum to furnished **143** as a white solid.

2,2",3,3",4,4",5,5",6,6",7,7",8,8",9,9"-hexadecahydrodispiro[cyclopenta[*e*]-as-indacene-1,2'-bicyclo[2.2.1]heptane-3',1"-cyclopenta[*e*]-*as*-indacen]-5'-ene **143**



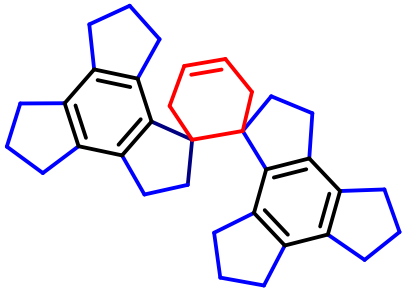
White solid, 90 mg, 85% Yield, mp >320 °C, R*f*: 0.95 (5:0, Pet. Ether:EtOAc); **IR (KBr cm^{-1})** 3046, 1449; **^{1}H NMR (600 MHz, CDCl$_3$)** δ 5.99 (s, 2H), 5.61 (d, *J* = 5.7 Hz, 1H), 5.44 (d, *J* = 5.6 Hz, 1H), 2.75 (s, 2H), 2.28 (d, *J* = 8.5 Hz, 3H), 2.20 (d, *J* = 17.5 Hz, 2H), 2.18 – 2.08 (m, 6H), 2.08 – 1.97 (m, 5H), 1.93 (dd, *J* = 16.3, 5.2 Hz, 3H), 1.90 (d, *J* = 4.7 Hz, 1H), 1.86 (dd, *J* = 19.3, 7.4 Hz, 2H), 1.68 (dd, *J* = 9.7, 4.9 Hz, 1H), 1.65 – 1.58 (m, 2H), 1.55 (s, 2H), 1.32 – 1.24 (m, 2H), 1.11 (t, *J* = 7.6 Hz, 2H), 0.94 (d, *J* = 10.2 Hz, 1H); **^{13}C NMR (151 MHz, CDCl$_3$)** δ 137.22, 132.31, 131.16, 55.68, 54.03, 47.64, 47.35, 47.07, 46.59, 44.41, 44.13, 43.90, 43.79, 43.59, 41.25, 40.83, 40.75, 39.50, 39.43, 37.38, 31.67; **HRMS (ESI)** *m/z* calculated for $C_{35}H_{39}$ $[M+H]^+$: 459.3052, found 459.3050.

Butadiene adduct **148**

Initially butadiene sulfone (300 mg, 2.55 mmol) was taken in 15 ml of dry toluene and heated the reaction mixture till 80 °C to form butadiene *in-situ*. Then bitrindanylidine **142** (100 mg, 0.25 mmol) was added into the reaction mixture and then it was refluxed. Small amount of sulfolene was added portion wise during the course of reaction. Reaction was completed after 4.5 h (TLC) and solvent was removed under reduced pressure to give yellow crude. It was then purified by

column chromatography on silica gel using light petroleum as eluent to furnished butadiene adduct **148** as a white solid.

2,2",3,3",4,4",5,5",6,6",7,7",8,8",9,9"-hexadecahydrodispiro[cyclopenta[*e*]-as-indacene-1,1'-cyclohexane-2',1"-cyclopenta[*e*]-*as*-indacen]-4'-ene **148**

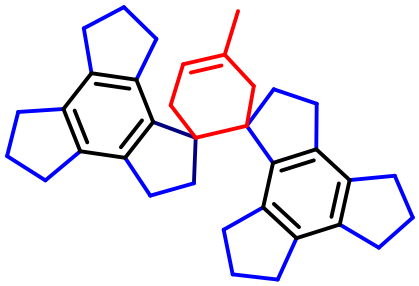


White solid, 90 mg, 80% Yield, mp 232 °C, R*f*: 0.90 (5:0, Pet. Ether:EtOAc); **IR (KBr, cm^{-1})**: 2946, 1446; **^{1}H NMR (500 MHz, $CDCl_3$)** δ 5.54 (s, 1H), 4.52 (d, *J* = 9.0 Hz, 1H), 3.31 (q, *J* = 6.9 Hz, 2H), 3.13 (d, *J* = 7.8 Hz, 2H), 2.97 – 2.81 (m, 14H), 2.65 (d, *J* = 7.5 Hz, 2H), 2.54 (dt, *J* = 12.4, 8.9 Hz, 1H), 2.22 (q, *J* = 5.2, 3.4 Hz, 2H), 2.10 – 1.97 (m, 2H), 1.58 (s, 1H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ 147.36, 139.17, 138.83, 138.46, 138.24, 138.05, 137.51, 136.71, 134.10, 127.11, 43.70, 35.88, 34.06, 31.63, 31.31, 31.19, 31.02, 30.88, 30.81, 29.21, 25.93, 25.51, 25.46; **HRMS (ESI)** Molecular ion peak at 447.30 $[M+H]^+$ was not observed in HRMS possibly because the compound **148** experienced a retro-Diels–Alder reaction during the analysis and peak displayed fragment ions at m/z 393.25 for $C_{30}H_{33}$.

Isoprene adduct **149**

Bitrindanylidine **142** (100 mg, 0.25 mmol) in 15 ml of isoprene was taken in sealed tube at 120 °C for 24 h. After completion of reaction (TLC), excess of isoprene was removed under reduced pressure and remaining crude was chromatographed using light petroleum as eluent to furnish 102 mg of **41** as a white solid.

4'-methyl-2,2",3,3",4,4",5,5",6,6",7,7",8,8",9,9"-hexadecahydrodispiro[cyclopenta[*e*]-as-indacene-1,1'-cyclohexane-2',1"-cyclopenta[e]-as-indacen]-4'-ene **149**



White solid, 102 mg, 86% Yield, mp 258-260 °C, R*f*: 0.95 (5:0, Pet. Ether:EtOAc); **IR (KBr, cm^{-1})** 2959, 1433; **^{1}H NMR (600 MHz, CDCl$_3$)** δ 5.52 (s, 1H), 4.49 (d, *J* = 8.8 Hz, 1H), 2.85 (dq, *J* = 26.2, 7.4, 6.7 Hz, 30H), 2.14 (dt, *J* = 11.1, 7.3 Hz, 9H), 1.54 (s, 3H); **^{13}C NMR (151 MHz, CDCl$_3$)** δ 140.23, 139.42, 139.16, 138.93, 138.25, 138.09, 137.73, 137.61, 137.20, 136.81, 135.77, 134.20, 131.04, 127.18, 43.82, 37.44, 35.98, 34.67, 34.19, 31.75, 31.64, 31.40, 31.30, 31.13, 30.99, 30.92, 30.55, 29.32, 27.03, 26.01, 25.60, 25.54; **HRMS (ESI)** *m/z* calculated for $C_{35}H_{41}$ $[M+H]^+$: 461.3208, found 461.3208.

3.6 Conclusion

In summary, we have imagined, retrosynthetically planned and executed the synthesis of a molecular framework **143** that has an appearance like a butterfly. The role of steric interactions of the dienes, butadiene **D$_2$** and isoprene **D$_3$** with **142** has also been investigated. The endgame of the synthesis consists of an unusual DAR on a tetrasubstituted double-bond in bicyclopentylidene moiety embedded in **142**. The DAR favoured dienes **D$_1$-D$_3$** from the less hindered face of **142** and in the case of the cyclic dienes **D$_4$-D$_6$**, steric considerations appear to decide the fate of the DAR. Theoretical calculations are also found to be in strong agreement. It is discovered that the estimated Gibbs free energy of the cycloadducts of dienes **D$_1$-D$_3$** is lower than that of the cycloadducts of dienes **D$_4$-D$_6$**, which is consistent with the experimental findings of the corresponding successful reactions.

3.7 References

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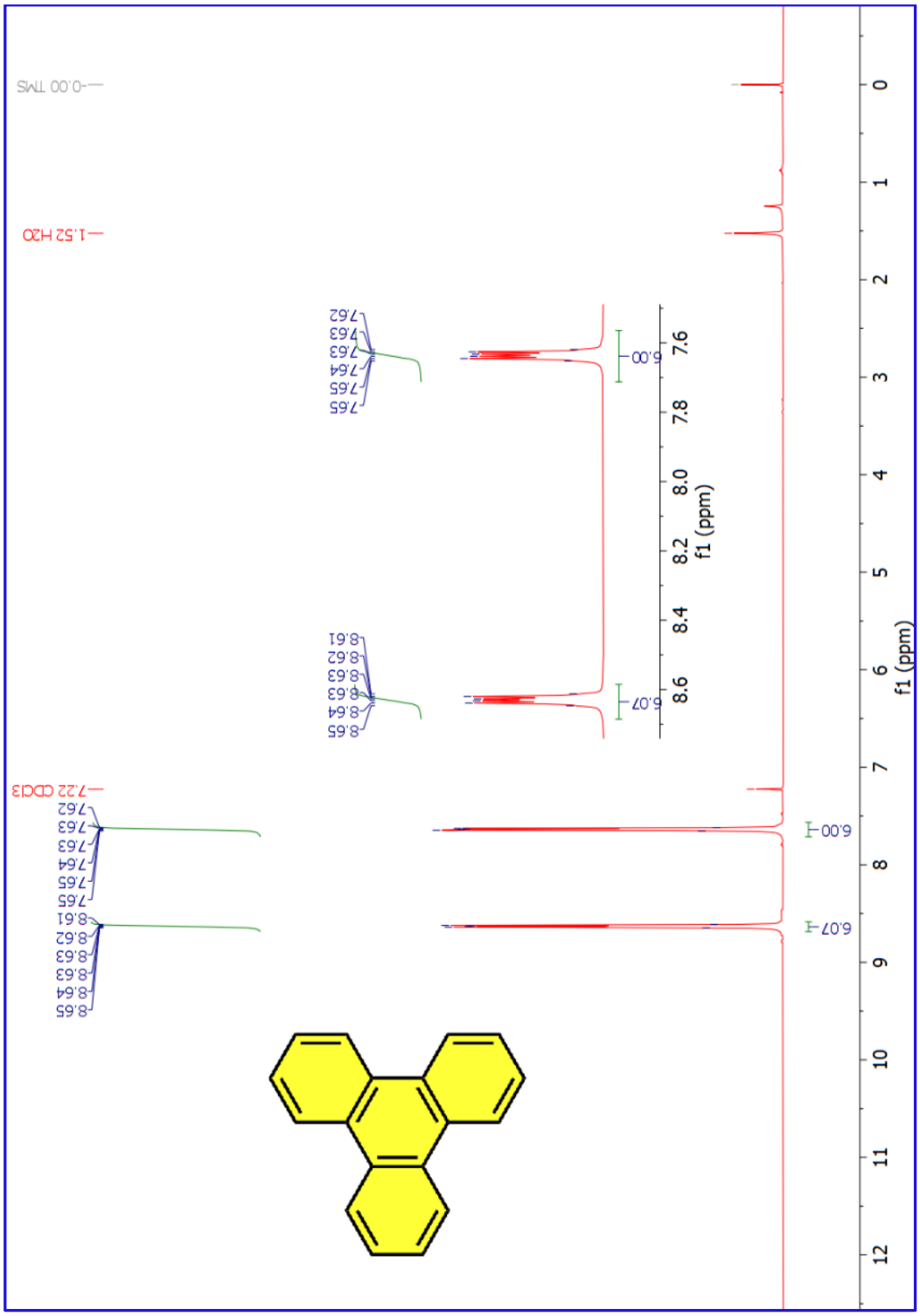
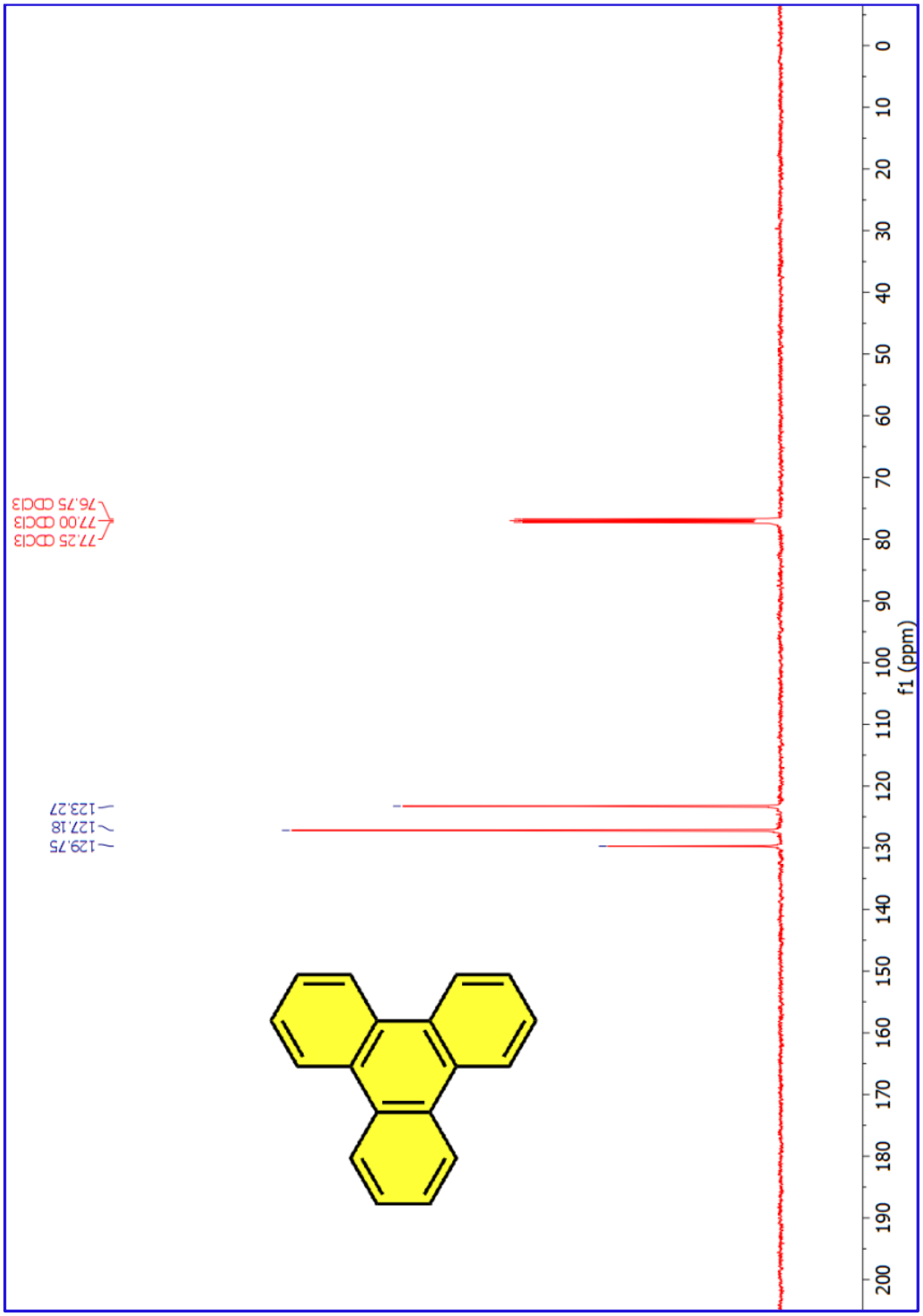
3.8 Spectral data of compounds

3.8.1 *^{1}H and ^{13}C NMR spectra and HRMS of products*

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127.18
123.27
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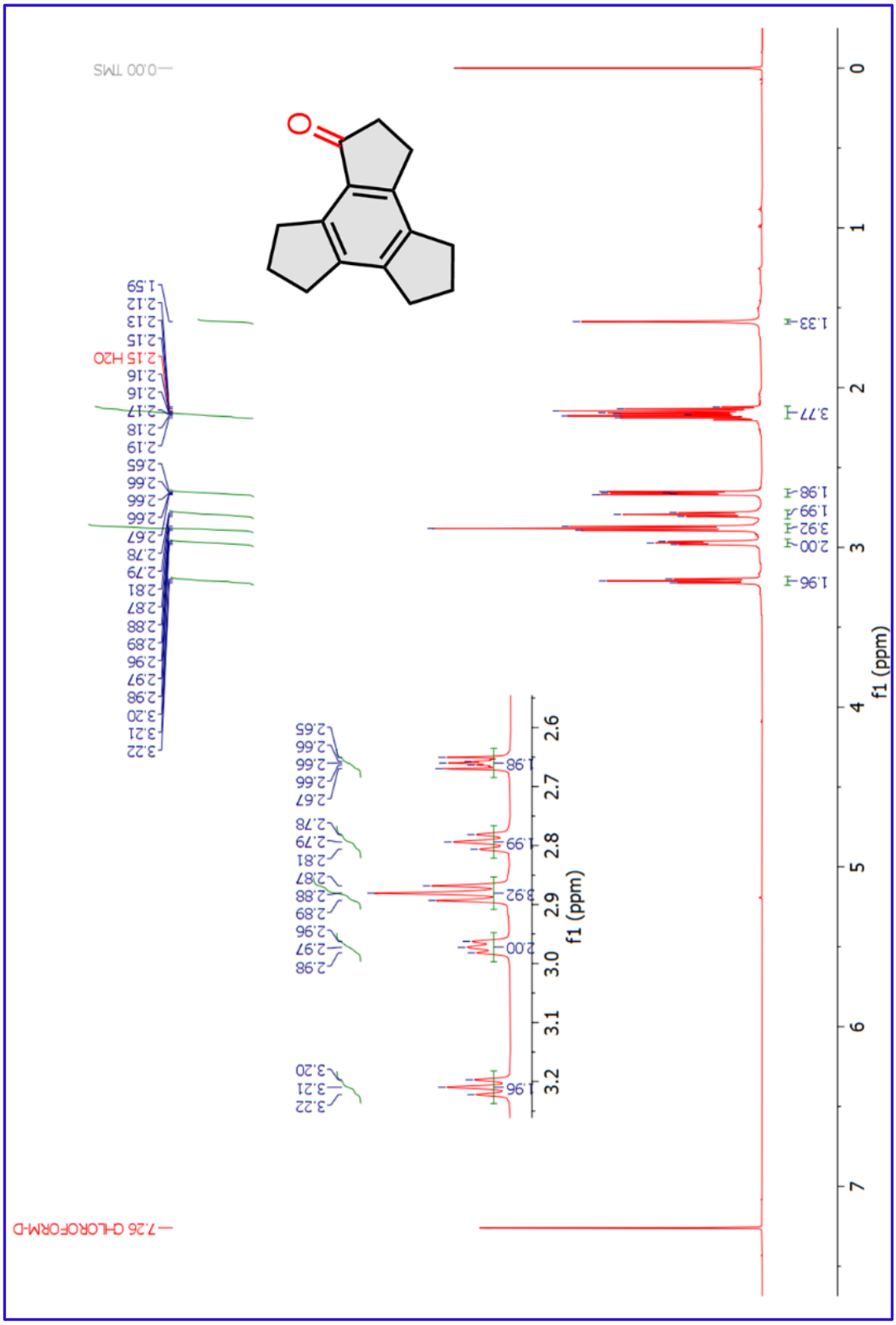
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H2O 2.15
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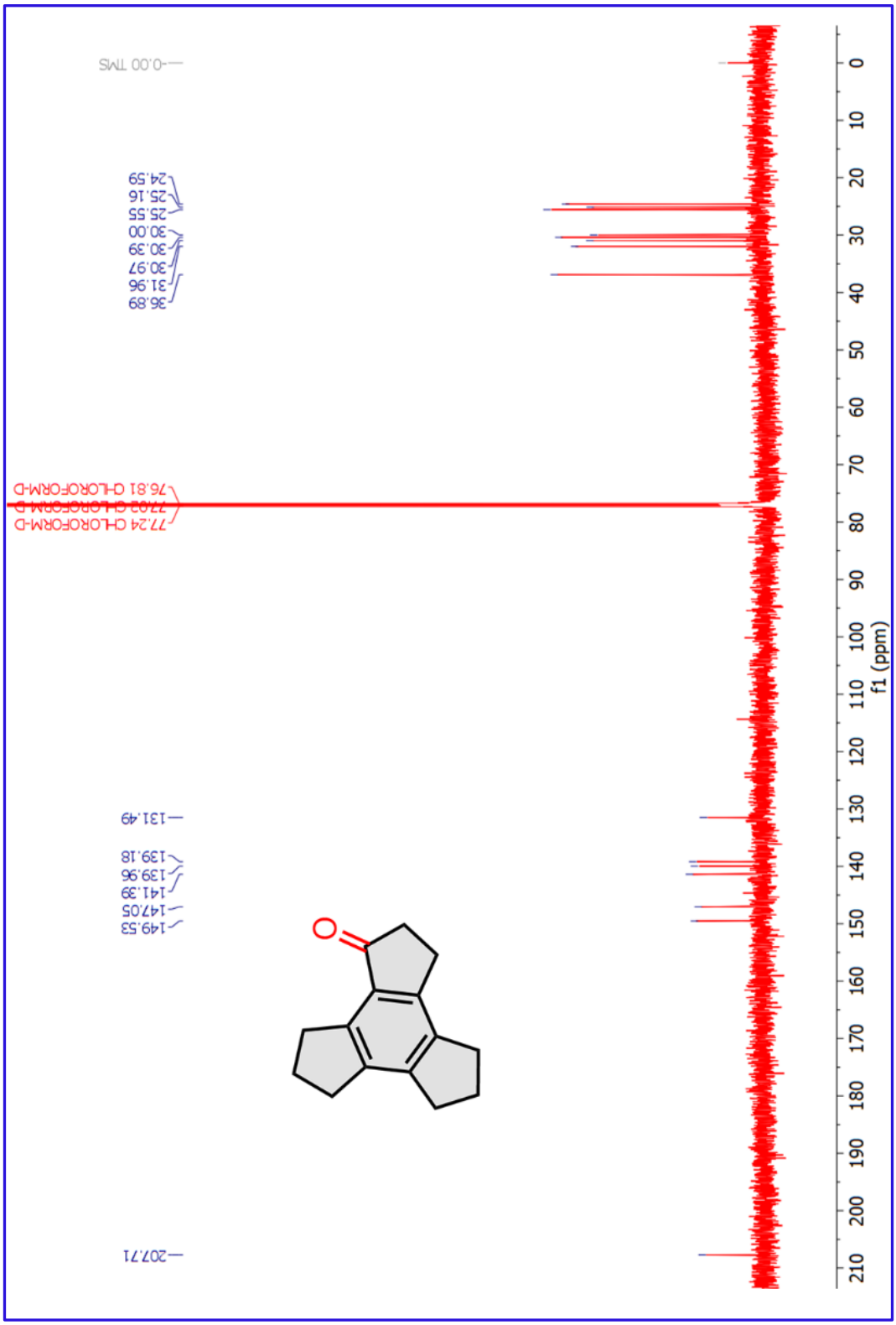
1.98
1.99
3.92
2.00
1.96
f1 (ppm)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31.96
36.89
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77.03 CHLOROFORM-D
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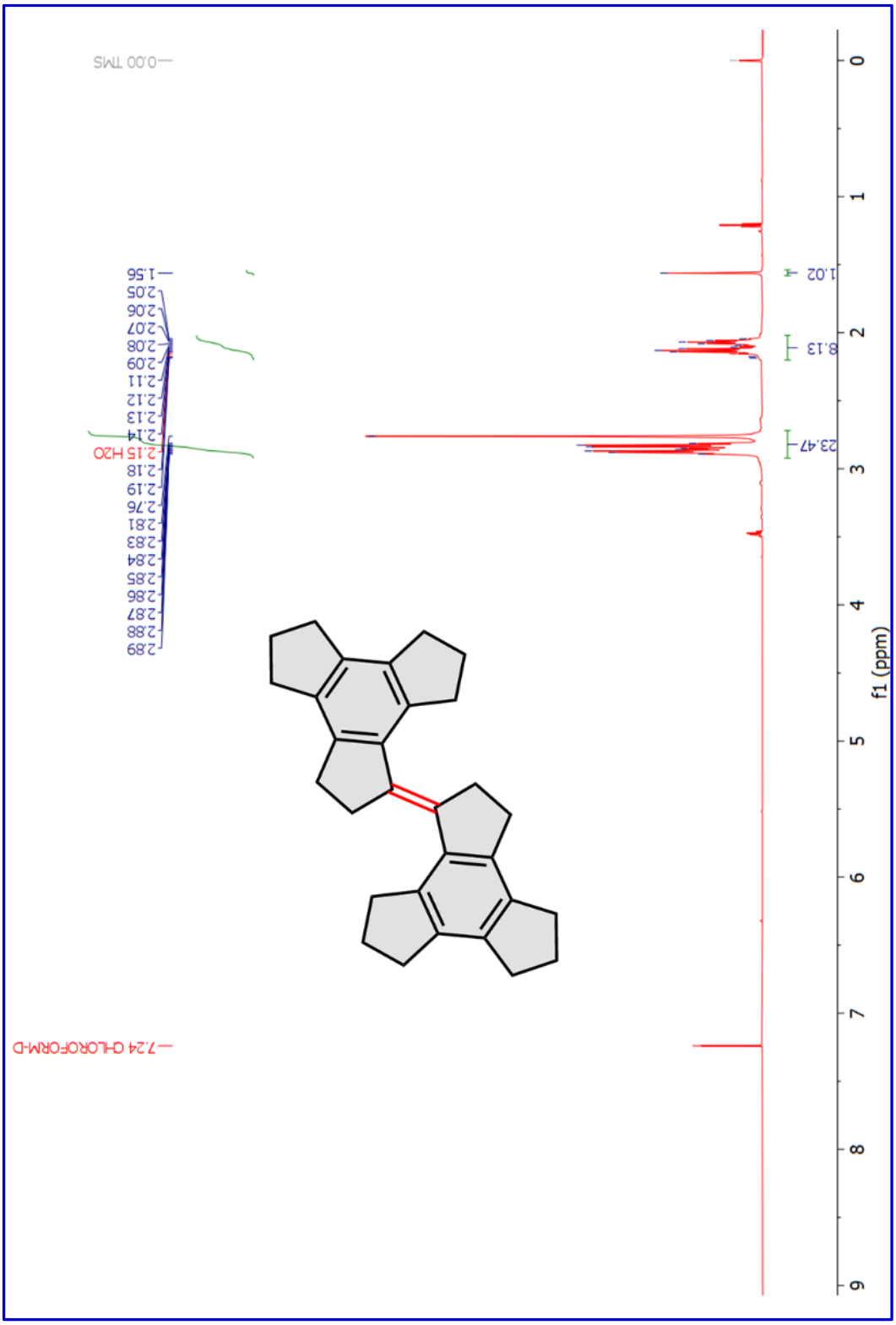
139.18
139.96
141.39
147.05
149.53
207.71
f1 (ppm)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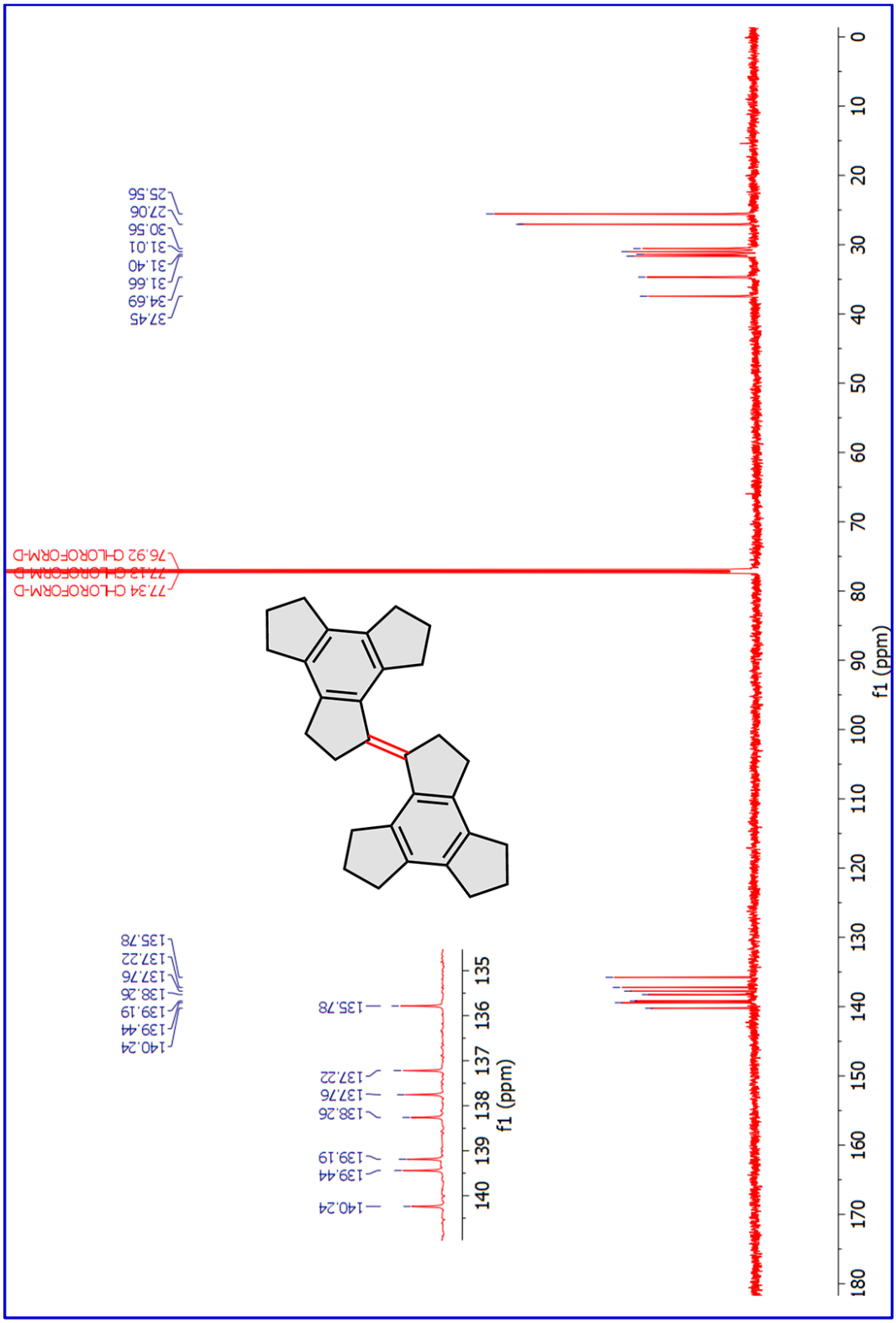
2.06
2.07
2.08
2.09
2.11
2.12
2.13
2.14
2.15 H2O
2.18
2.19
2.76
2.81
2.83
2.84
2.85
2.86
2.87
2.88
2.89
1.02
8.13
23.47
f1 (ppm)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77.13 CHLOROFORM-D
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31.66
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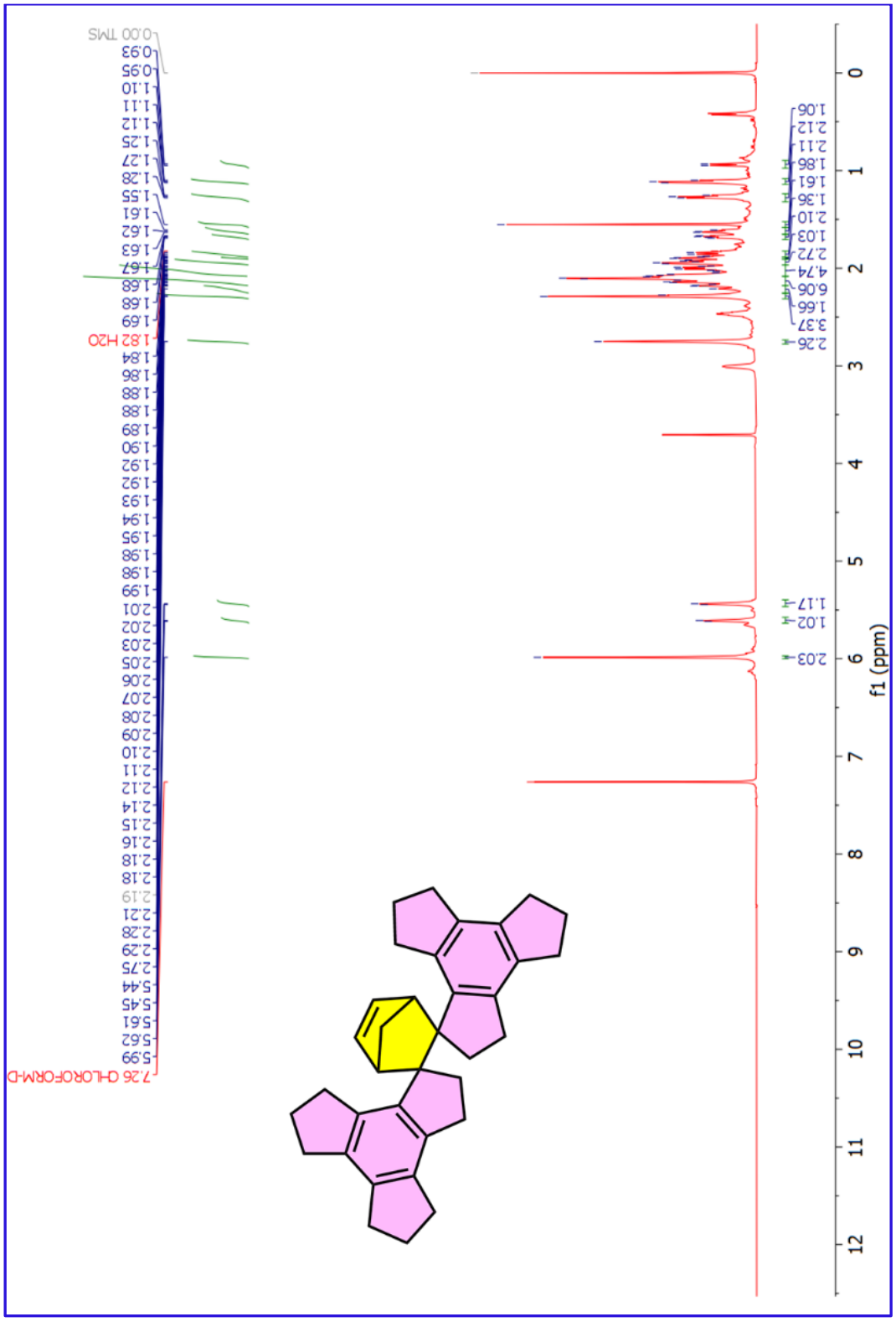
f1 (ppm)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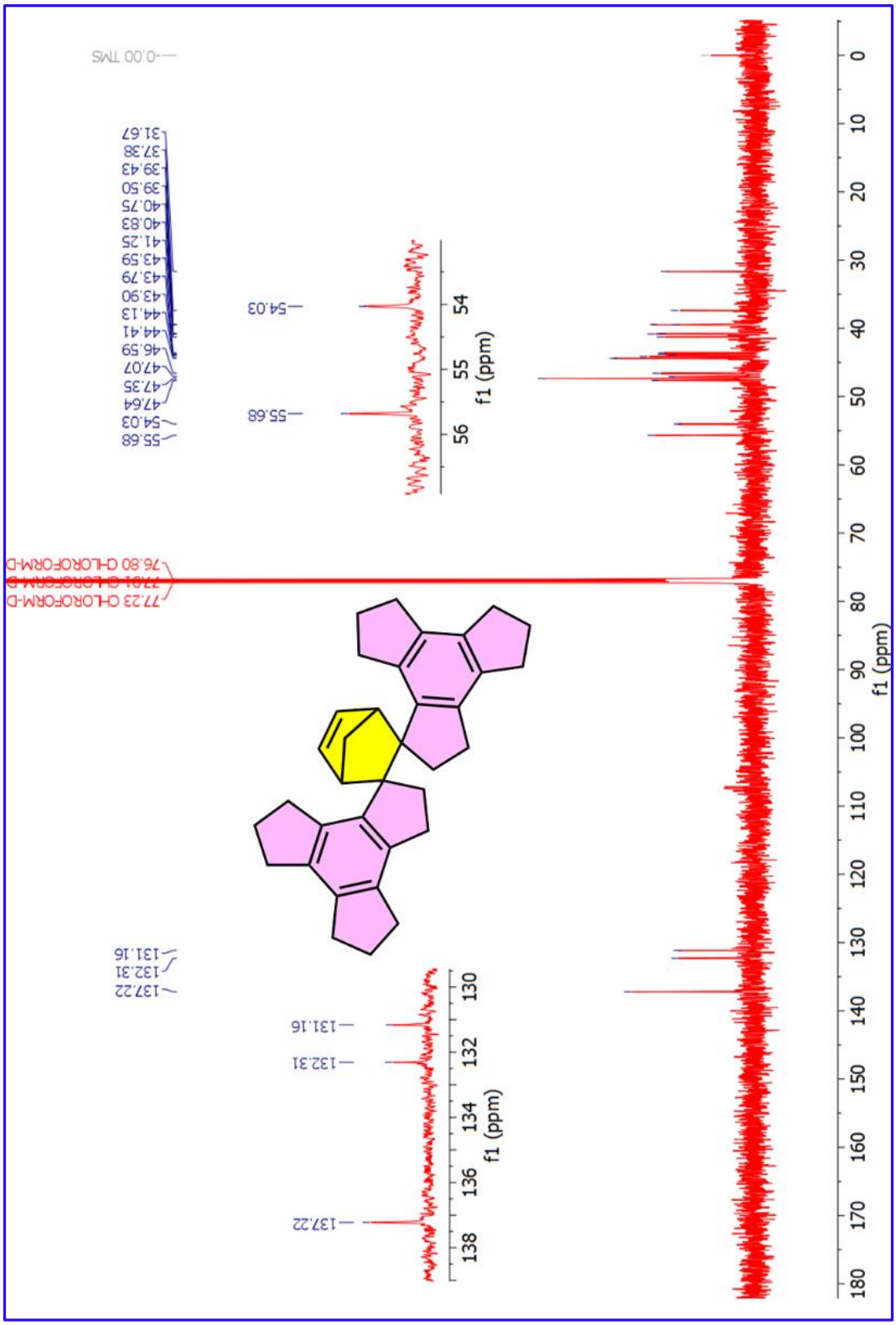
TMS
H2O
CHLOROFORM-D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44.41
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47.35
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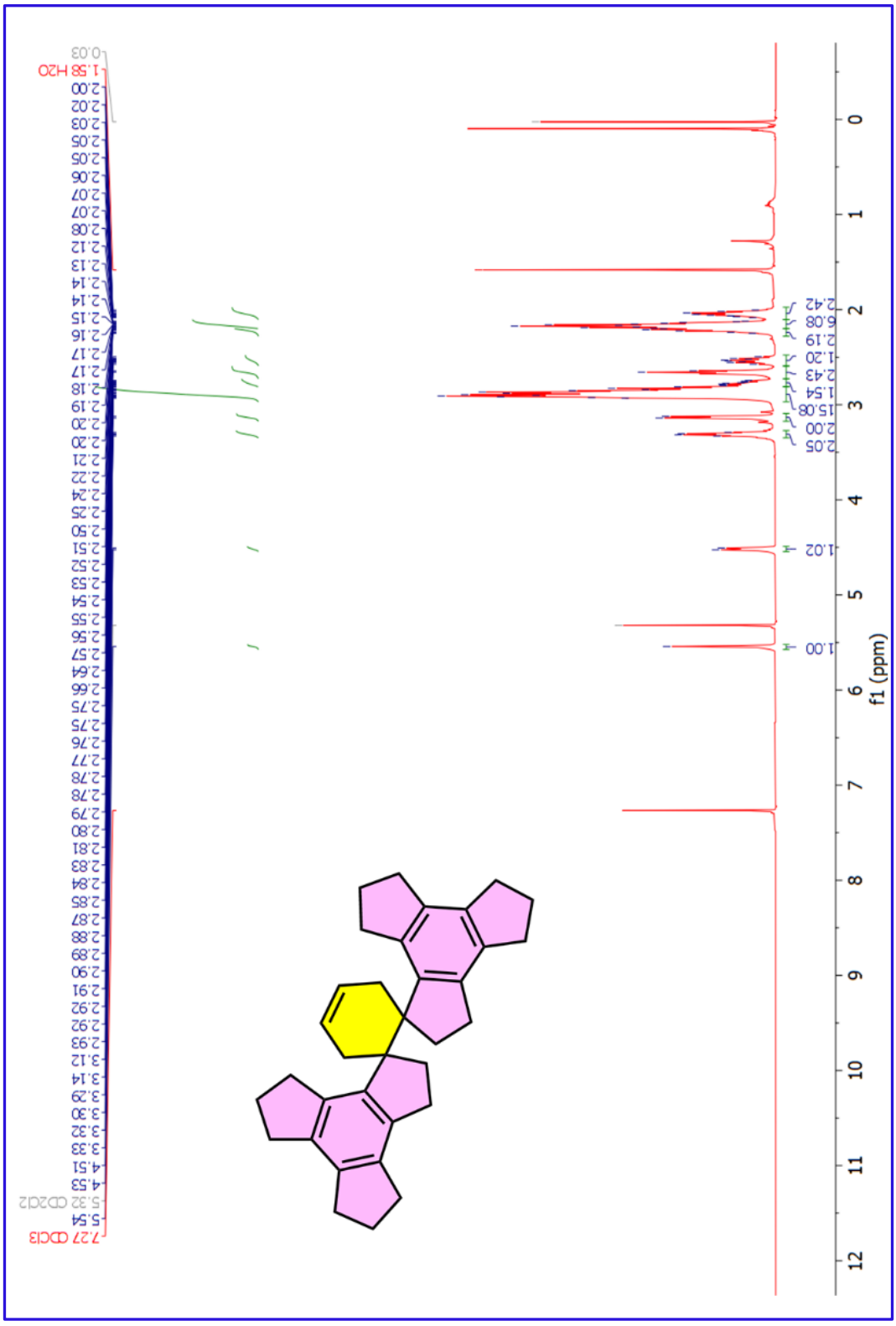
137.22
f1 (ppm)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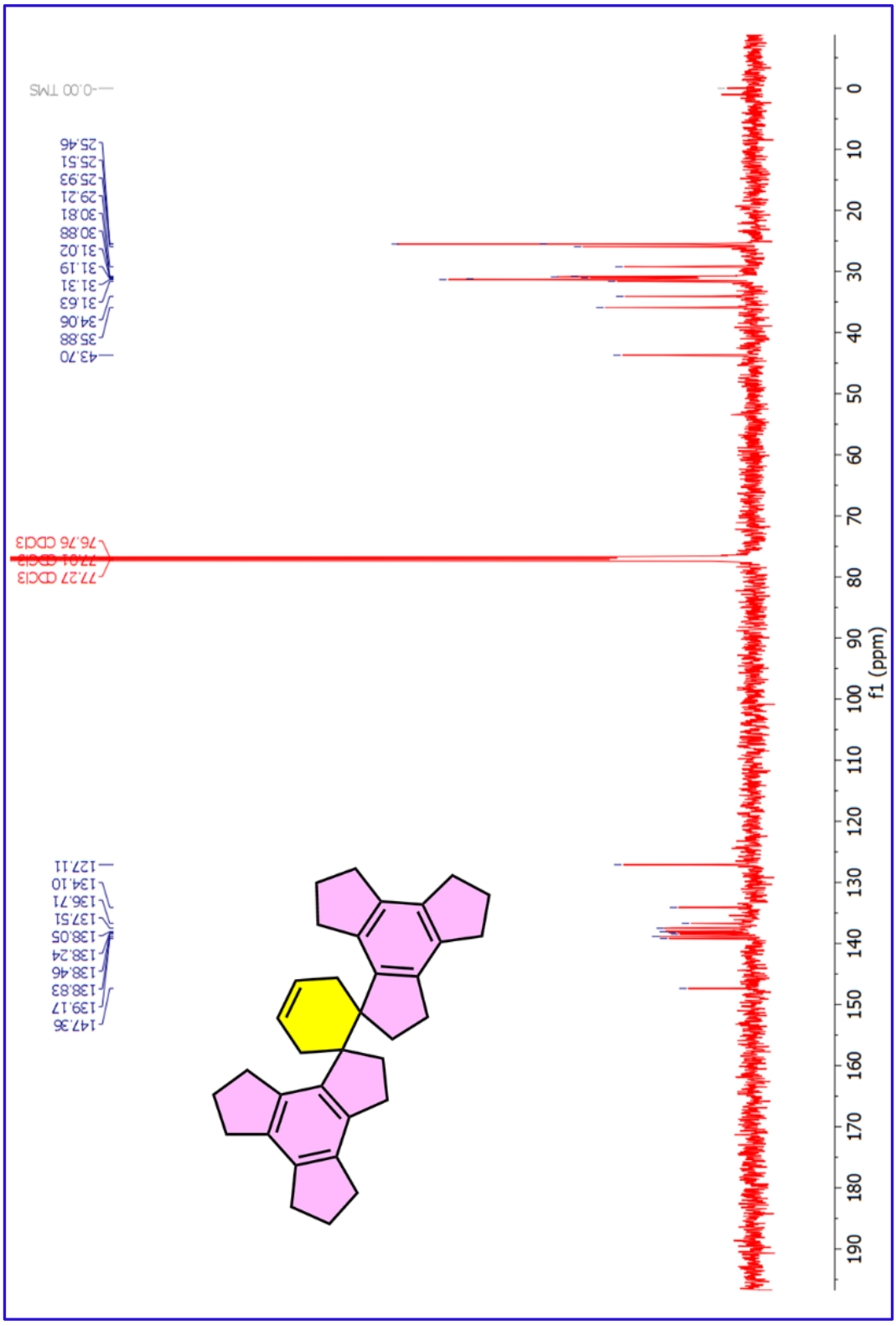
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35.88
43.70
76.76 CDCl3
77.01 CDCl3
77.27 CDCl3
127.11
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136.71
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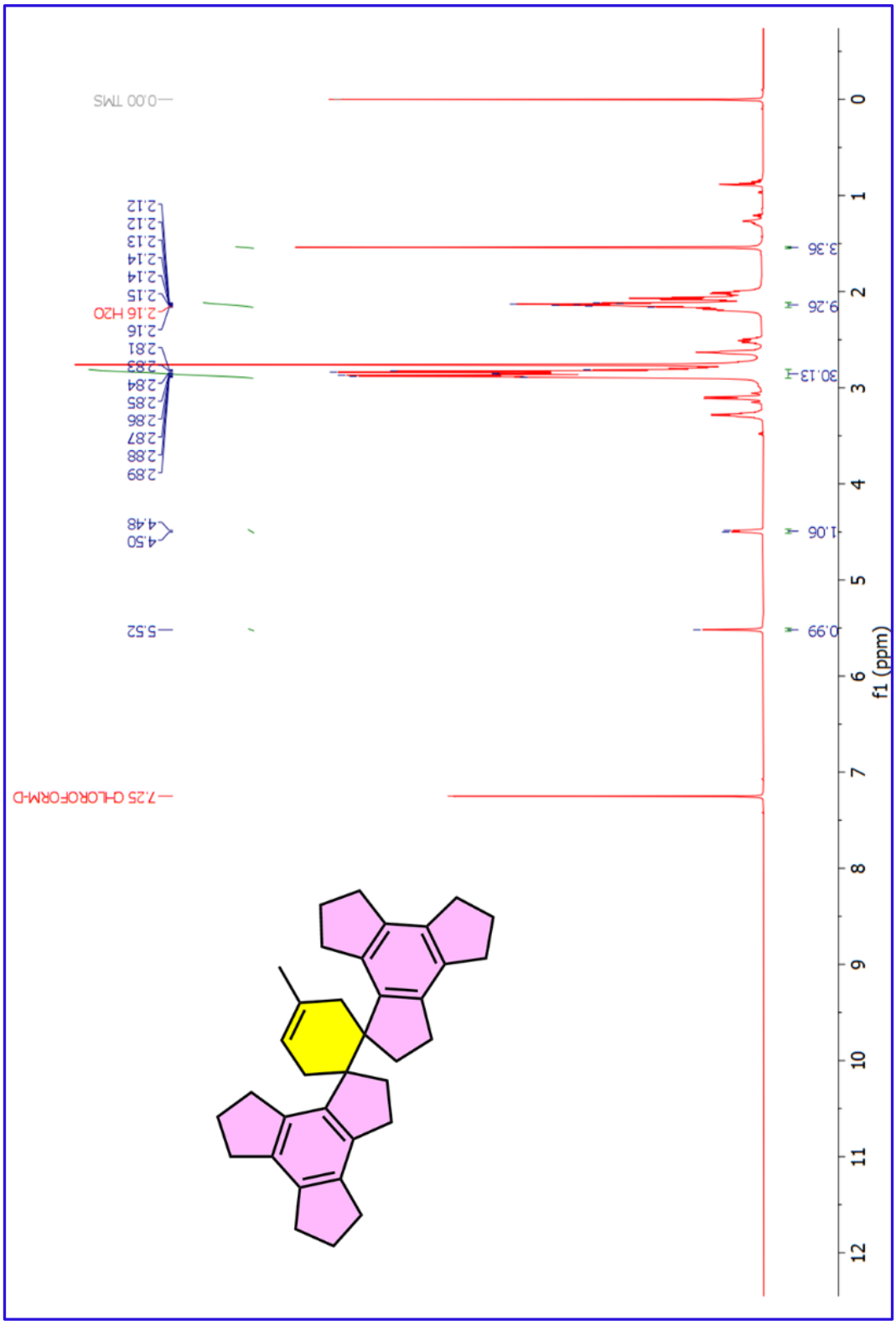
138.05
138.24
138.46
138.83
139.17
147.36
f1 (ppm)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2.87
2.88
2.89
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5.52
7.25 CHLOROFORM-D
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30.13
1.06
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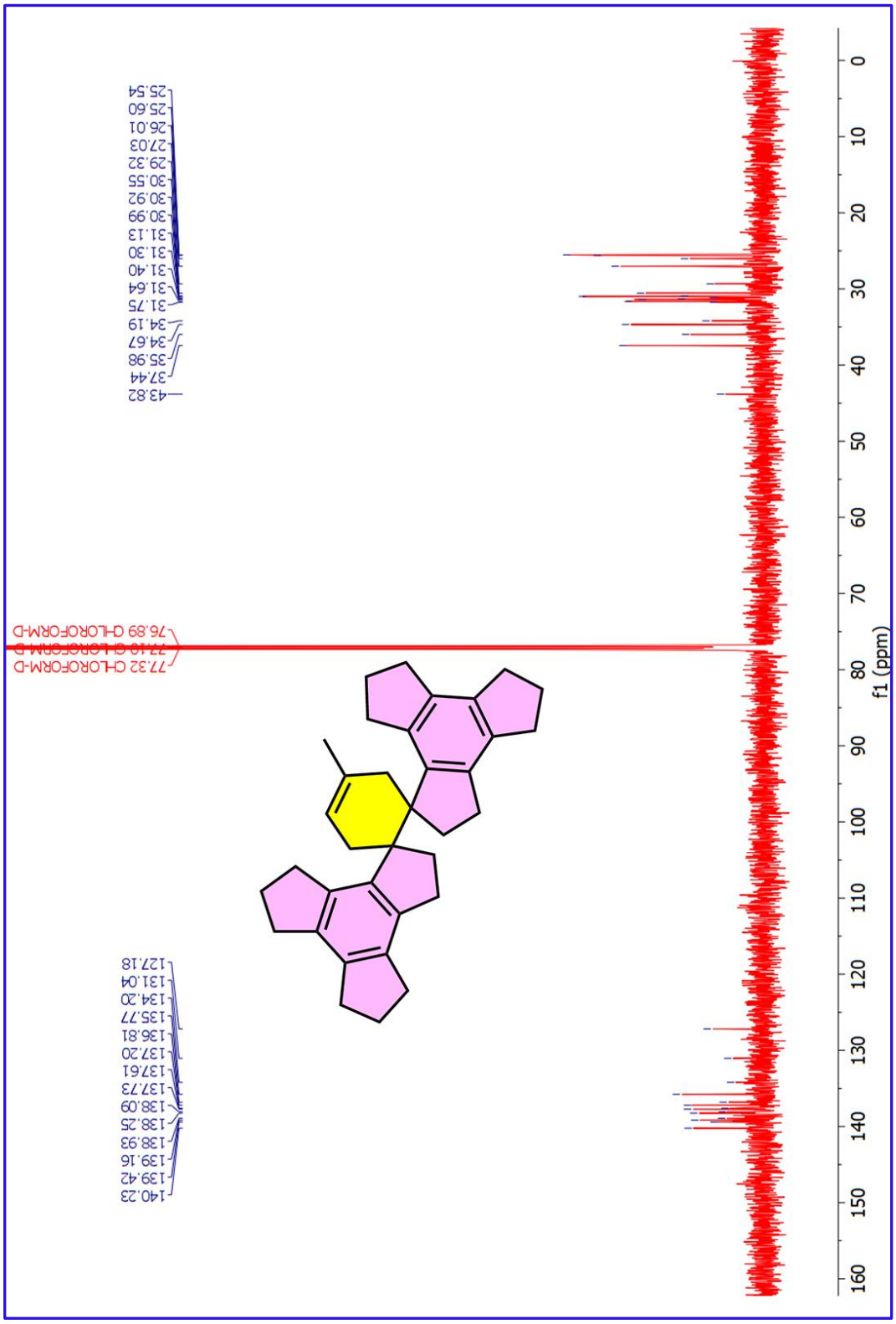
f1 (ppm)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50
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130
140
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25.60
26.01
27.03
29.32
30.55
30.92
30.99
31.13
31.30
31.40
31.64
31.75
34.19
34.67
35.98
37.44
43.82
76.89 CHLOROFORM-D
77.19 CHLOROFORM-D
77.32 CHLOROFORM-D
127.18
131.04
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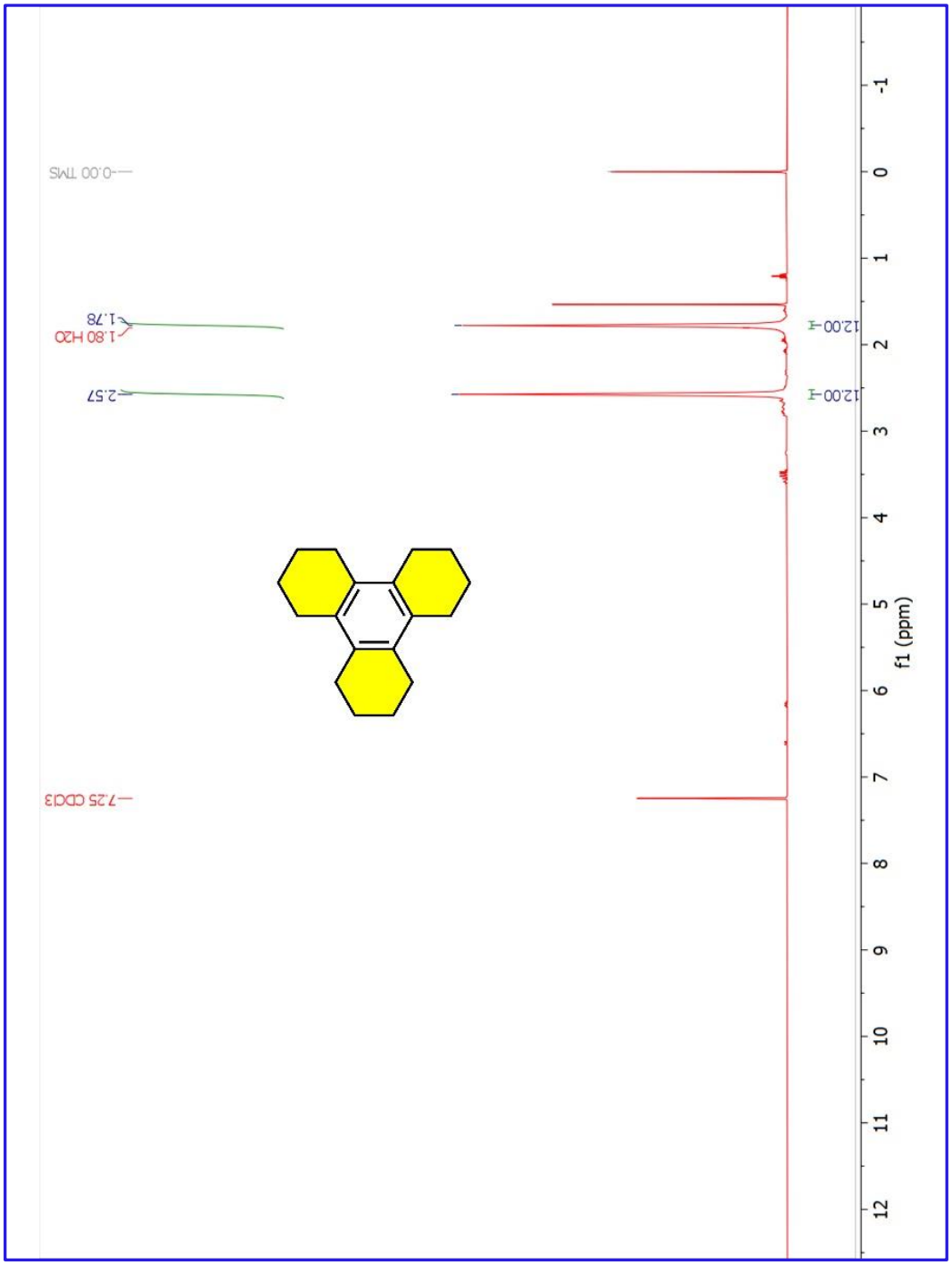
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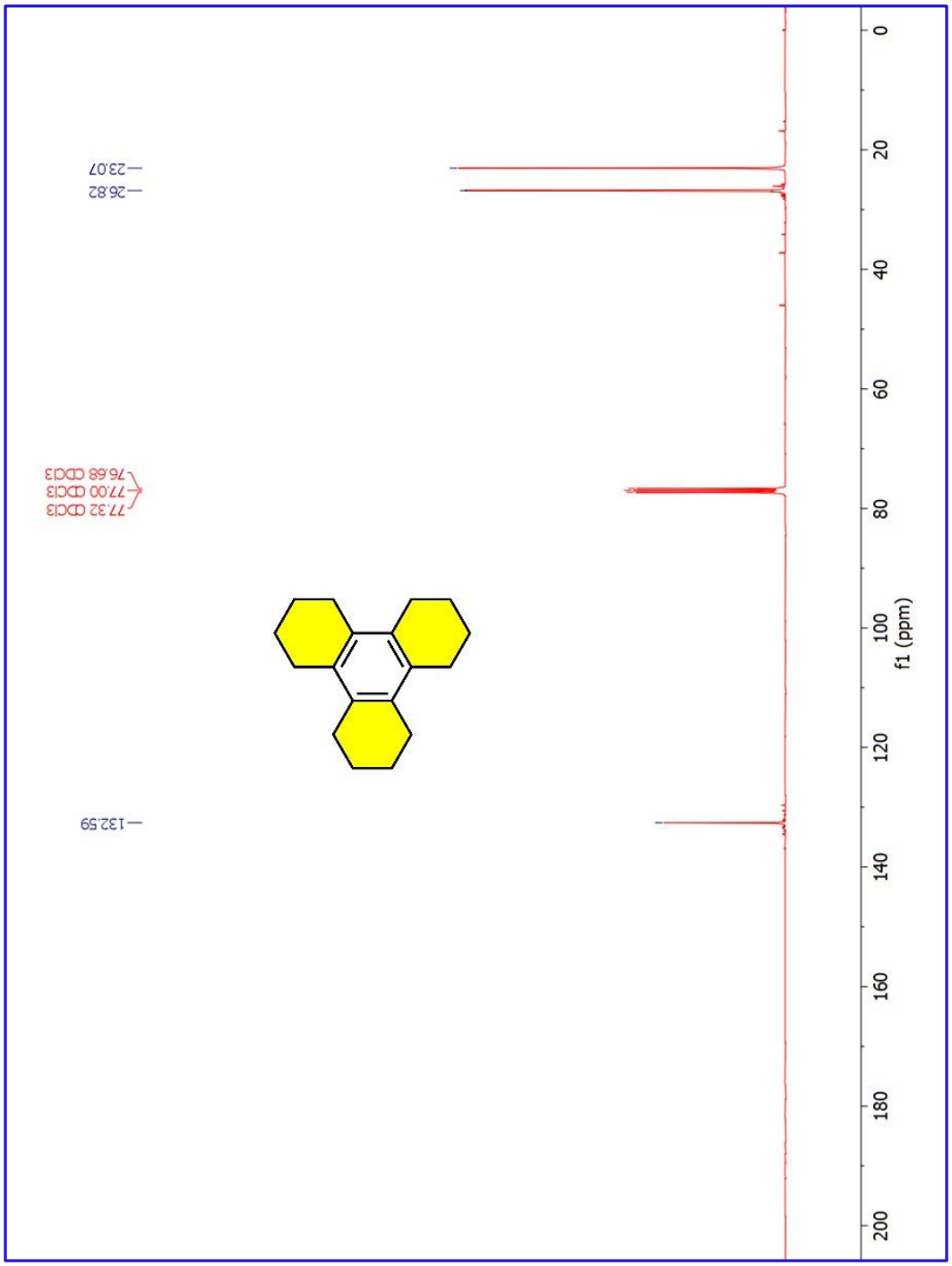
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26.82
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20
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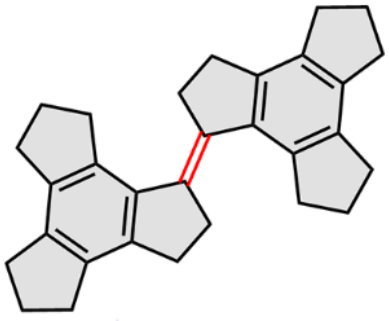
140
160
180
200
f1 (ppm)

Elemental Composition Report



Single Mass Analysis

Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 5

Monoisotopic Mass, Even Electron Ions
489 formula(e) evaluated with 5 results within limits (up to 1 closest results for each mass)
Elements Used:
C: 0-50 H: 0-50 N: 0-10 O: 0-10

Sample Name : GB042 IITRPR XEVO G2-XS QTOF
Test Name :
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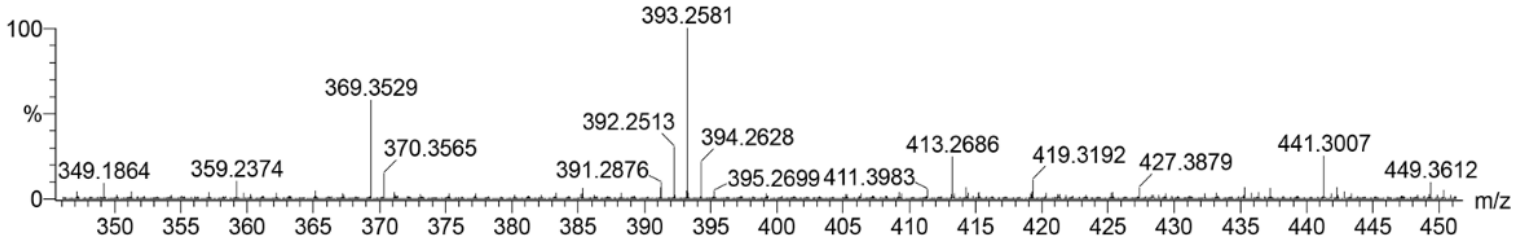
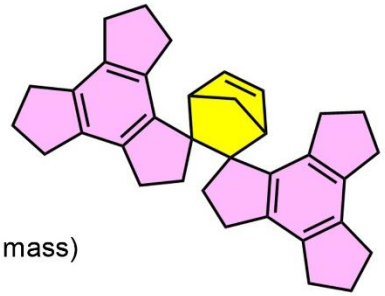
8.33e+004



Minimum:				-1.5				
Maximum:		2.0	10.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
393.2581	393.2582	-0.1	-0.3	14.5	1303.6	n/a	n/a	C30 H33

Elemental Composition Report



Single Mass Analysis

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Monoisotopic Mass, Even Electron Ions
516 formula(e) evaluated with 6 results within limits (up to 1 closest results for each mass)
Elements Used:
C: 0-50 H: 0-50 N: 0-10 O: 0-10

Sample Name : GB051 IITRPR XEVO G2-XS QTOF
Test Name :
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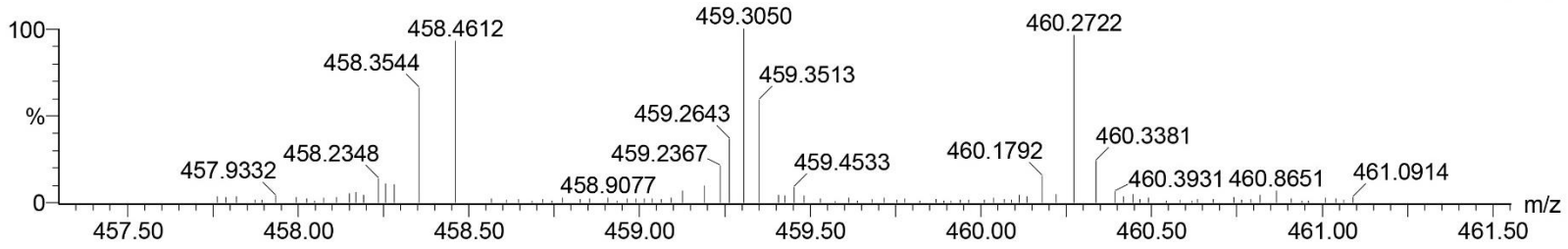
1.12e+004



Minimum:				-1.5				
Maximum:		2.0	10.0	50.0				
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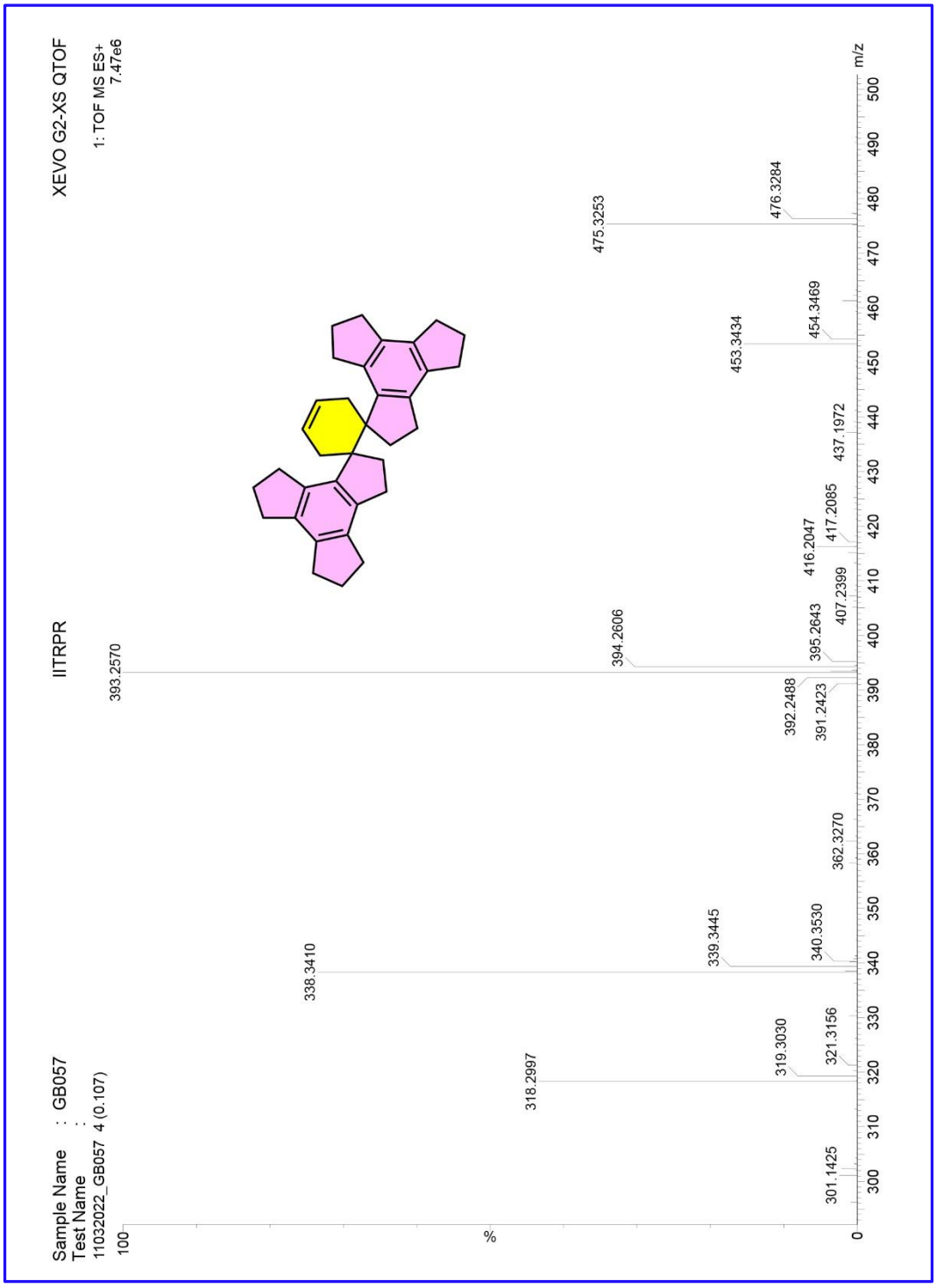
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1: TOF MS ES+
7.47e6
IITRPR
Sample Name : GB057
Test Name :
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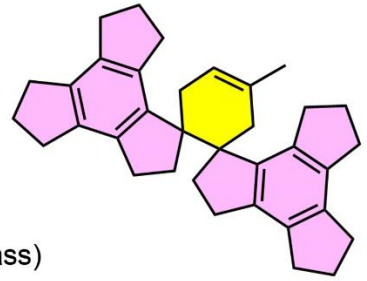
100
%
0
m/z
393.2570
394.2606
338.3410
318.2997
339.3445
475.3253
476.3284
453.3434
454.3469
392.2488
391.2423
395.2643
407.2399
416.2047
417.2085
437.1972
319.3030
321.3156
340.3530
362.3270
301.1425

Elemental Composition Report

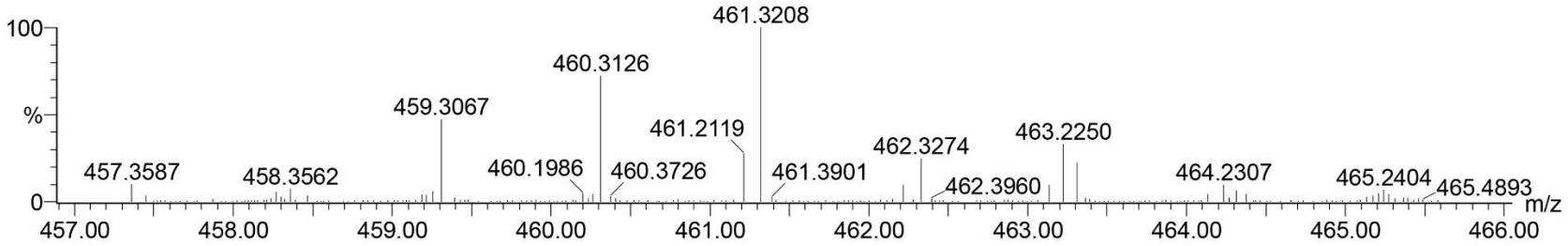


Single Mass Analysis

Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 5

Monoisotopic Mass, Even Electron Ions
517 formula(e) evaluated with 6 results within limits (up to 1 closest results for each mass)
Elements Used:
C: 0-50 H: 0-50 N: 0-10 O: 0-10

Sample Name : GB051 IITRPR XEVO G2-XS QTOF
Test Name :
11032022_GB053 3 (0.079) 1: TOF MS ES+
3.34e+004



Minimum:				-1.5				
Maximum:		2.0	10.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
461.3208	461.3208	0.0	0.0	15.5	1074.7	n/a	n/a	C35 H41