Synthesis of Sumanene Hexatrifluoromethanesulfinate and exploring the extent of chemical reactivity of Sumanene and Hexakis(bromomethyl) Sumanene

A Thesis

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Certificate

This is to certify that this dissertation entitled “Synthesis of Sumanene Hexatrifluoromethanesulfinate and exploring the extent of chemical reactivity of Sumanene and Hexakis(bromomethyl) sumanene” towards the partial fulfillment of the BS-MS dual degree program at the Indian Institute of Science Education and Research, Pune represents study/work carried out by Shashank Verma at Department of applied chemistry under the supervision of Prof. Hidehiro Sakurai, Department of chemistry, during the academic year 2024-2025.

Professor Hidehiro Sakurai

Department of chemistry

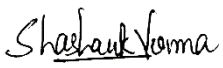
Osaka University

This thesis is dedicated to?

This thesis is dedicated to my family members who supported me through all the difficult phases that came across me and my friends who guided me and motivated me all the time.

Declaration

I hereby declare that the matter embodied in the report entitled “Synthesis of Sumanene Hexatrifluoromethanesulfinate and exploring the extent of chemical reactivity of Hexakis(bromomethyl) sumanene” are the results of the work carried out by me at the Department of Applied Chemistry, Osaka University, under the supervision of Prof. Hidehiro Sakurai, and the same has not been submitted elsewhere for any other degree. Wherever others contribute, every effort is made to indicate this clearly, with due reference to the literature and acknowledgement of collaborative research and discussions.



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Abstract:

Sumanene is a very interesting molecule especially owing to its unique structure. The extent of the chemical reactivity that the sumanene molecule can show is still a topic that is being heavily researched in the field of research of curved polyaromatic compounds. In this research thesis, the chemical reactivity of the sumanene molecule has been studied including the chemical reactivity of the benzylic and aromatic positions. Trails have been made to synthesize a molecular cage which includes the two sumanene bowls linked together by a diamino linker. However, due to the high complexity of the conditions that were required to be optimized, the attempt to synthesize it failed. Moving ahead with the hexaphosphonate derivative of sumanene, an opportunity appeared to try if a coupling reaction namely Horner–Wadsworth–Emmons reaction, which produces E and Z alkenes can be performed on it. When the reaction was tried with a strong base, competitive deprotonation of the benzylic proton was found along with the alpha proton adjacent to the phosphonate group. This result implied the fact that further attention should be paid to the acidity of those two protons and the basicity of the base used. Finally, the substitution reaction was tried on hexa-bromo sumanene in which the six bromo groups were substituted with six sulphate groups and the pure product was isolated in a decent yield followed by a trail to perform [2+1] cycloaddition of the formed product to the C_{60} fullerene.

Acknowledgment:

I want to thank my supervisor, Professor Hidehiro Sakurai, who made this work possible with his guidance, knowledge, experience, and constant support. I would also like to thank Professor Yuta Uetake and Professor Yumi Yakiyama for their constant input which helped me in improving my research work. I would also like Professor Boopathy Gnanaprakasam to give valuable input during the mid-year evaluation. I would also want to thank Sakurai Laboratory and Osaka University for provide me this opportunity to complete my master thesis at their prestigious institute. Thanks to all my fellow lab mates and seniors who helped me with their constant support and help that they provided me at regular periods of time.

Finally, I would like to thank my family and friends for providing me with constant motivation and invaluable support.

CHAPTER 1: Introduction

For a long period, a group of molecules known as polycyclic aromatic hydrocarbons (PAHs) have been in continuous talks and have also gained a keen interest in different scientific communities around the world. Polycyclic aromatic hydrocarbons have been known for their diverse application in different fields of science and technology (Alvi, S.; Ali, R., 2020). On the other hand, polycyclic aromatic hydrocarbons are prevalent pollutants found in the environment that are mostly created when organic resources such as coal, oil, and wood are not fully burnt (Hussein I. Abdel-Shafy, Mona S.M. Mansour, 2016). There are many examples of polycyclic aromatic hydrocarbons (PAHs) that vary in the number and arrangement of their rings such as naphthalene, biphenyl, fluorene, anthracene, phenanthrene, etc as shown in figure:1.1.

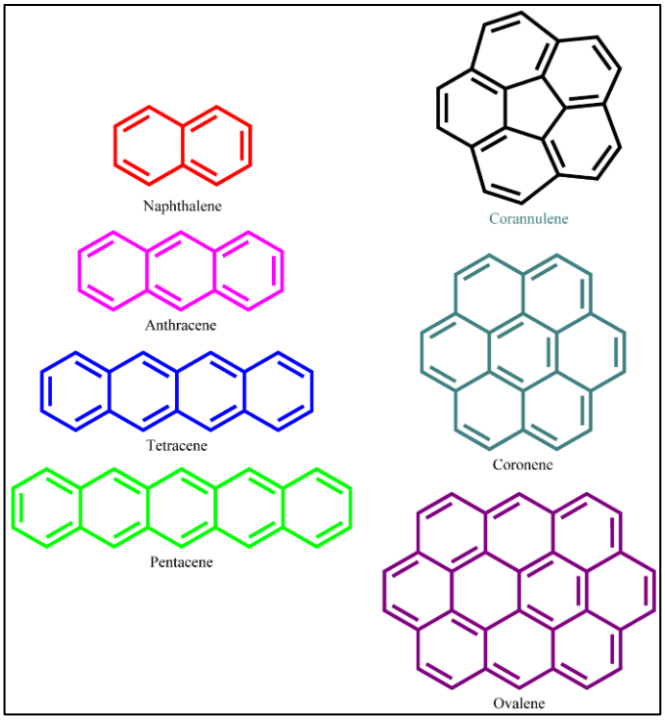


Figure: 1.1(different variety of polycyclic aromatic hydrocarbons)

Among a vast variety of polycyclic aromatic hydrocarbons (PAHs) that have been discovered and studied in detail, a new class of PAHs emerged known as curved aromatic species or curved polycyclic aromatic hydrocarbons. It is well known that the curved and bowl-shaped surfaces in nature are very universal for example the curvature possessed by our planets and atomic orbitals, for instance, typically influences the charge-transport, redox, self-assembly, and optical characteristics of bowl-shaped π-conjugated systems (Alvi, S.; Ali, R, 2020). Similar to this, the physical and chemical characteristics of curved aromatic compounds or curved PAHs substantially alter. Curved aromatic compounds, sometimes known as curved PAHs, present an alluring mix of basic issues, synthetic difficulties, and visual appeal in

chemistry. Among the variety of interesting properties that are offered by the curved aromatic compounds, some properties gained keen interest. As contemporary hydrocarbon research has evolved during the modern era, there has been a great deal of interest in the connection between π-electron conjugation and molecular geometry which was also observed in the case of curved aromatic species. During the extensive research on aromatic molecules, the tendency of aromatic compounds to be planar was identified early on, and deviations from this structural paradigm have subsequently been sought in a variety of settings, producing groundbreaking findings in the chemistry of cyclophane, circulene, and helicene. The discovery of curved carbon allotropes, such as fullerenes and carbon nanotubes (CNTs), has catalyzed a fresh surge of research into non-planar aromatics, leading to significant progress over the past thirty years (Marcin Stepien, Marcin A. Majewski, 2018).

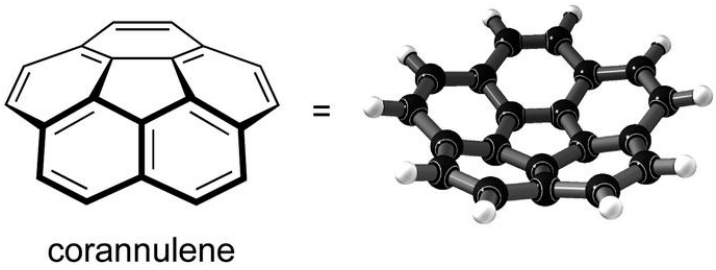


Figure: 1.12 (Curved structure of corannulene)

This extensive research gave rise to a new group of molecules known as bucky bowls. These are the group of molecules that have a bowl-like curved structure and an extended conjugation present within the structure. These molecules are often described as the smallest fragment of the fullerene C_{60}. C_{60} or the buckybowl has been studied by many researchers around the world for many reasons such as their unique physical appearance and chemical properties. One of the most exciting opportunities was to study it as a possible precursor for the chemical bottom-up synthesis of C_{60}. Fullerene is an allotrope of carbon that involves the carbon atoms connected to each other by single and double bonds to form a closed or partially closed molecule or structure, with rings of either five to six atoms. These molecules may have shapes of hollow spheres, elliptical, and tubes. Corannulene is a very well-known bucky bowl molecule and is often described as the smallest fragment of fullerene C_{60} which retains a curved molecular structure (Stuparu MC, 2021). Corannulene ($C_{20}H_{10}$) is a polycyclic hydrocarbon in which five six-membered rings surround a central five-membered ring to construct a bowl-like aromatic structure (as shown in the figure: 1.12) (Muzammil, E.M., Halilovic, D. & Stuparu, M.C, 2019).

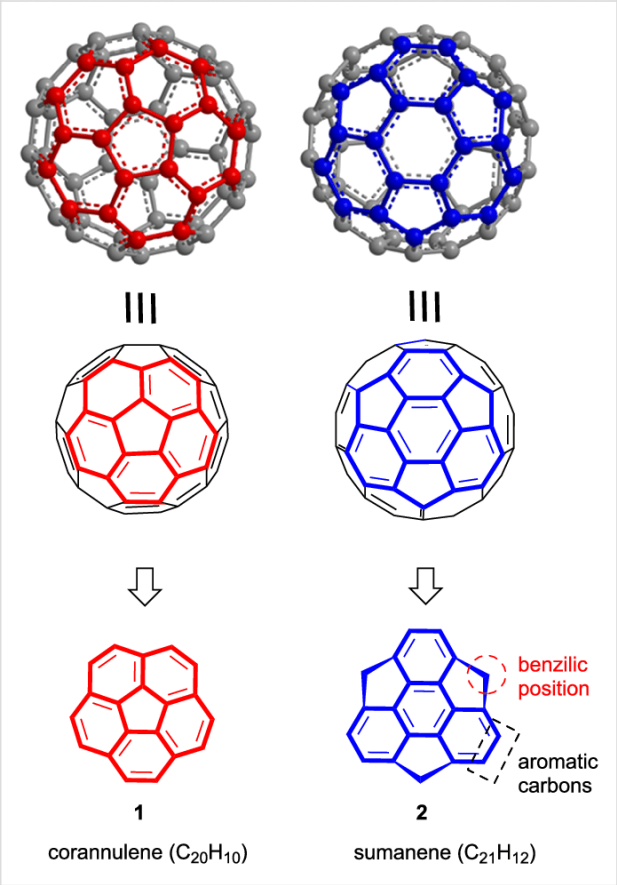


Figure: 1.13 (Bucky bowl structure of sumanene and corannulene)

Very similar to the shape and physical appearance of corannulene, Sumanene is another bucky bowl molecule that is known for its curved surface and other unique properties. Unlike corannulene, sumanene has 4 six-membered rings involving one at the center and 3 five-membered rings (as shown in Figure 1.13).

The discovery of fullerene C_{60} and the small fragments that different C_{60} having different combinations of five and six-membered rings that can emerge from them made a large group of researchers curious to achieve the synthesis of those fragments and further study the physical and chemical properties of those curved bucky bowl molecules. On the contrary, the task of reaching the complete synthesis of non-planar aromatic compounds is very difficult. While working with curved aromatic compounds one must deal with the curvature and the strain associated with the molecule. Spherical curvature (Gaussian-positive) is ascribed to fullerenes and various bowl-shaped aromatics. Conversely, saddle-shaped, and helical structures can be viewed as hyperbolically (negatively) curved. In order to quantify the curvature associated with the curved aromatic compounds geometrical measures such as bond torsions, pyramidalization angles, and ring puckering coordinates are generally used. Another

important aspect that needs attention is molecular strain as it is difficult to synthesize highly strained molecules. Curved aromatic molecules are generally strained molecules so it becomes important to minimize the strain as much as possible. The strain present in complex molecules is generally quantified using computational methods rather than experimental methods ((Marcin Stepien, Marcin A. Majewski, 2018). The strain present in a curved aromatic molecule determines the degree of curvature that it will hold.

Talking about the synthetic strategies to synthesize curved aromatic molecules, some synthesis techniques can be utilized to induce curvature to a molecule. The synthetic strategies to synthesize a curved aromatic species can be grouped into three categories which are namely: cyclization reactions, reactions involving eliminations and finally ring contraction reactions.

Starting with the cyclization reactions, there are four specific cyclization reactions that can be used for the curved aromatic molecule synthesis which are: Direct Macrocyclization, Cyclooligomerization, Multiple Annulation (stitching), Tandem and template-assisted macrocyclization (as shown in figure 1.14). Moving further to elimination reactions, the different kinds of elimination reactions that can be utilized for the synthesis of curved aromatic compounds are: Sub-unit masking and other elimination reactions. Finally moving on to the ring contraction reactions, the group of ring contraction reactions that can assist in the synthesis of the curved aromatic molecules is: Peripheral contraction, Transannular contraction: the fold-in method, and Extrusions from metallacycles. The methods mentioned before are some of the very well-studied and researched routes for the synthesis of curved aromatic species.

The first attempts towards the synthesis of sumanene were made by Prof. Mehta and his group which was reported in J. Chem. Soc. Chem. Commun. in 1993 (Goverdhan Mehta, Shailesh R. Shah, K. Ravikumar, 1993). However, in that journal, it was reported as a failure as Prof. Mehta was not able to achieve the complete synthesis of sumanene via retrosynthesis. Before the attempt to synthesize sumanene by Prof. Mehta's team, the first attempt at the synthesis of curved strained molecule was made by Wayne E. Barth and Richard G. Lawton in 1966 in which they published the article regarding the synthesis of corannulene (Wayne E. Barth, Richard *G.* Lawton, 1970).

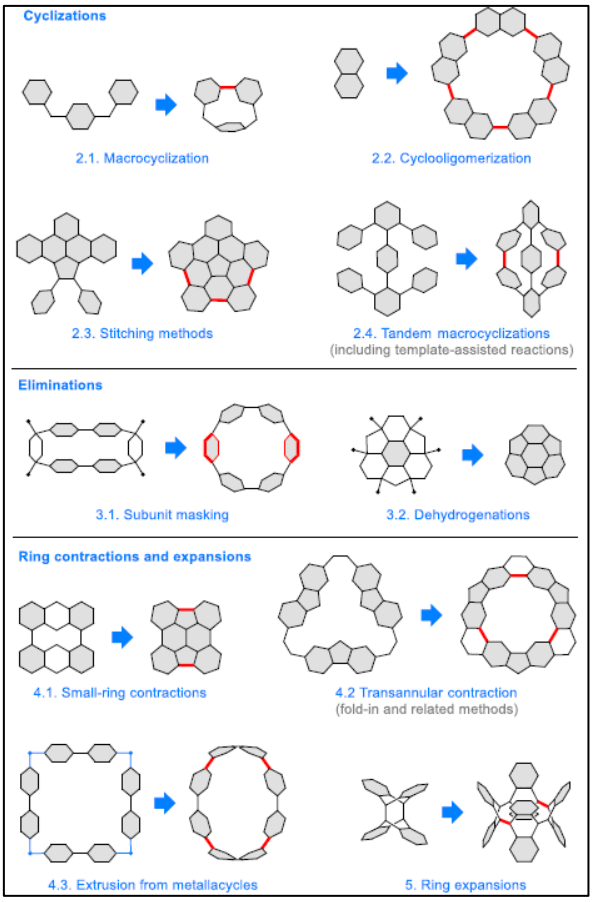


Figure: 1.14 (Variety of cyclization reactions)

Following the steps of Wayne E. Barth and Richard G. Lawton and working on the previous work done by Prof. Mehta and his team on the retrosynthesis of sumanene, Prof. Hidehiro Sakurai of Osaka University established himself in sumanene and aza-sumanene chemistry from 1993 to 2014. The first attempt was started with the outlining of the retrosynthesis for the synthesis of sumanene in 1993 followed by confirming the final draft of the retrosynthesis scheme in 1996.

The research attempt to achieve the synthesis of sumanene starts with cyclotrimerization of the norbornene unit according to the retrosynthesis scheme. Following the synthesis of two well-reported methods the first one involves the direct trimerization of α-bromocuprio-norbonadiene species from the corresponding deprotonated intermediate of the Schlosser base, on the other hand, the second method involves the trapping of the same intermediate as a Me_3Sn derivative, which was further followed by (2-thiophene carboxylate) (CuTC)-mediated cyclotrimerization. But in both cases, the undesired anti-product was the major product in addition to it the isolation of it was a serious issue. So, it was clear that it was necessary to develop a new method for syn-selective cyclotrimerization (Hidehiro Sakurai, 2021). Several attempts were made to achieve the trimerization of norbornanone derivatives but it was observed that it is difficult to achieve because of steric problems. During the revaluation of the reaction conditions and optimization of the methods it was found out that

Prof. Sakurai's group was facing issues and was restricted due to the high toxicity of Me_3Sn, So, in order to deal with it Me_3Sn was replaced with Bu_3Sn. Using Bu_3Sn in the place of Me_3Sn resulted in a better yield of 75% to form product 4 (figure 1.15). A similar reaction was conducted using the CuTC method which also gave a decent yield. It was hypothesized that the route of converting 3 to 2 (figure 1.15). would be the most complicated step, but it was found that compound 3 was completely stable under ozonolysis conditions. This observation motivated Prof. Sakurai's group to work further on this scheme using the tandem ROM-RCM route because as we discussed above tandem and template-assisted macrocyclization are a set of reactions that are very efficient in achieving curved aromatic molecules. Moving further to get compound 2 (figure 1.15) from compound 2, it was observed that compound 3 (figure 1.15) contains three benzonorbornadiene units which are said to be highly reactive towards ROMP. To deal with these issues, the reaction was conducted under ethylene atmosphere. Also, in addition to its first-generation Grubbs catalyst was used to avoid the heat generated which can further generate coordinatively unsaturated species. The progress of the reaction was monitored using NMR and after analyzing the NMR it was found that there were no patterns of terminal vinyl proton was observed there. There was the direct formation of 2 (hexahydrosumanene). From these patterns, it can be inferred that compound 2 has a thermodynamically favored as well as less strained structure. So, after all the confirmatory analysis it was confirmed that the conversion of compound 3 to compound 2 was successfully achieved through the ROM-RCM method. With the formation of compound 2, only the final aromatization step was left to yield the final compound 1 (sumanene). The final aromatization step was straightforward which can be achieved using DDQ oxidation. The product formed was analyzed using 1HNMR, and the final target molecule compound 1 (figure 1.15) (sumanene) was confirmed (synthesis route shown as in figure 1.15). After confirming sumanene formation, the next step was scaling up the sumanene production which was successfully achieved after some years of hard work (Hidehiro Sakurai, 2021).

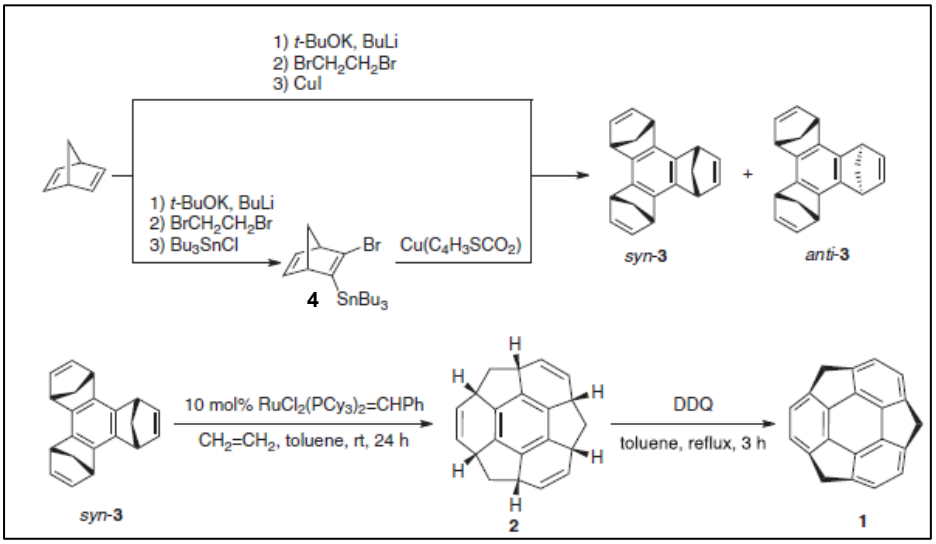


Figure: 1.15 (Complete synthesis scheme of sumanene)

In the domains of chemistry and materials science, sumanene is a special polycyclic aromatic hydrocarbon (PAH) with several distinctive characteristics. Its distinctive qualities are some of these:

- **Molecular structure:** With three fused benzene rings, sumanene has a unique tricyclic structure. This molecule has a "U"-shaped structure and is very symmetrical and flat. Its special electrical characteristics come from this shape.

- **High stability:** Sumanene is a polycyclic aromatic hydrocarbon, however because of its special three-ring structure, it is exceptionally stable. It can withstand chemical processes that would normally harm other PAHs because of the conjugation of π-electrons in its structure.

- **Aromaticity:** According to Hückel's rule, sumanene is aromatic because of its conjugated π-electron system across the fused benzene rings. Its stability and distinct chemical behavior are influenced by this characteristic.

- **Electron-deficient nature:** Since the molecule's three-ring arrangement gives it a distinct electron-deficient area, it is a great option for interacting with molecules that have a lot of electrons. This makes it particularly promising for application in sensors and molecular electronics.

- **Optical properties:** Sumanene is useful for use in organic light-emitting diodes (OLEDs) and other photonic devices because of its intriguing optical characteristics, which include fluorescence.

- **Potential for functionalization:** Sumanene is a promising candidate for further functionalization because of its planar structure and electrical characteristics, which will enable it to be modified for a variety of materials science applications, including molecular devices and nanomaterials.

- **Small bandgap:** In contrast to other polycyclic aromatic hydrocarbons, sumanene possesses a comparatively narrow electrical bandgap. Because of this, it is a material that shows promise for use in organic electronics and semiconductors, among other electronic applications.

- **Low symmetry breaking:** Because of the molecule's strong symmetry, there is less symmetry breaking, which can be important for the consistency and effectiveness of devices that use sumanene.

Because of these characteristics, sumanene is a fascinating chemical for study in many scientific domains, including material science, organic electronics, and nanotechnology.

Sumanene can be a very productive molecule but regardless of a bunch of distinctive properties that sumanene shows, working on sumanene is challenging because of its unique structure and properties. When researching or creating sumanene, some of the main challenges that researchers encounter are as follows:

1) **Synthesis complexity:**

- **Synthetic Difficulty**: Sumanene is difficult to synthesize, particularly in large quantities, due to its tricyclic structure. It takes advanced synthetic methods to create the fused aromatic rings in a regulated way, which frequently leads to complicated reaction conditions or low yields.

- **Starting materials:** Sumanene synthesis requires beginning material which is also known as starting material, which might be costly or hard to get. This may increase the overall intricacy and expense of the study.

2) **Purification and isolation:**

- **Purification challenges:** Following the synthesis, it may be challenging to separate sumanene from contaminants or other byproducts. Sumanene's molecular structure makes it difficult to separate with high purity, necessitating the use of sophisticated chromatographic methods or challenging circumstances.

- **Stability under harsh conditions:** Even while sumanene is more stable than other polycyclic aromatic hydrocarbons, it can nevertheless break down in hostile environments (such as high temperatures or exposure to oxidizing agents), which makes storage and purification challenging.

3) **Functionalization:**

- **Limited Functionalization:** Sumanene can be functionalized, although because of its aromatic character and the electrical effects of the fused rings, it can be difficult to add functional groups to its structure. Compared to more straightforward aromatic molecules, this makes controlled functionalization more difficult.

- **Selective Functionalization**: It may be quite difficult to add functional groups to molecules at the correct locations without affecting their stability or aromaticity. The same goes for the case of the sumanene. It could be necessary to precisely regulate the reaction conditions in order to achieve the required degree of selective functionalization.

4) **Electronic Property Control**:

- **Tuning Electronic Properties**: Although sumanene's special electrical characteristics such as its tiny bandgap and electron-deficient nature, make it valuable for some applications, it can be challenging to manage or adjust these characteristics for particular purposes. Significant fine-tuning may be necessary to get the optimal electrical characteristics for certain applications, which is not always simple.

- **Charge Transport**: The molecule's relatively poor symmetry and the possibility of flaws in larger-scale manufacture make it difficult to ensure effective charge transfer in organic electronics and semiconductor applications, despite sumanene's promising potential.

5) **Characterization**:

- **Advanced Techniques Needed**: Sumanene's tiny size and distinct structure make it challenging to characterize using standard methods (such as NMR or IR spectroscopy). To completely describe the molecule's structure and characteristics, complicated methods like high-resolution mass spectrometry or X-ray crystallography could be required.

- **Unusual Physical Properties**: Sumanene may behave differently chemically and physically than more common aromatic compounds due to its unique molecular geometry and aromaticity. This makes it more challenging to predict how it will behave in different settings or systems without conducting a lot of testing.

6) **Cost and Scale-Up:**

- **Expensive Materials:** Reagents and starting materials needed for sumanene synthesis might be expensive. Therefore, without major improvements in synthetic processes or cost reduction, it may become economically impossible to scale up production for commercial or practical purposes.

- **Scalability:** A major obstacle to scaling up sumanene manufacturing for commercial or large-scale uses is the synthesis's complexity and the requirement for extreme accuracy.

7) **Environmental and Safety Concerns:**

- **Toxicity and Environmental Impact:** Like many polycyclic aromatic hydrocarbons, sumanene's toxicity and potential effects on the environment may be a worry, particularly when it comes to large amounts of waste byproducts from its manufacture.

- **Handling in Laboratory Settings:** Advanced laboratory safety procedures and cautious handling are necessary for some of the potentially dangerous chemicals and intermediates utilized in the synthesis of sumanene.

Facing these obstacles, new techniques for the synthesis, functionalization, and use of sumanene and related compounds are progressively being developed, and research into these molecules is still progressing. However, at the moment, these challenges pose serious obstacles to industrial-scale applications and broad utilization.

In the past decade, there has been great progress in the field of exploring the chemical reactivity of sumanene especially in the field of organic chemistry, to see the different substituents that can be made on the aromatic periphery of the sumanene molecule. One of those efforts resulted in the successful synthesis of 2,3,5,6,8,9 Hexakis (bromomethyl)sumanene which is also known as Hexakis bromomethyl sumanene by Prof. Sakurai's group reported successfully in 2022. Prior research provides compelling evidence that the hexa-substituted sumanene derivatives help create the distinctive supramolecular structures that are derived from sumanene's symmetric nature (C3v) and bowl structure. Due to the poor reactivity, only two techniques have been documented for the complete hexa-substitution of the aromatic perimeter of sumanene. But regardless of the previous findings, Prof. Sakurai's group worked on the hexabromination of sumanene which resulted in the formation of hexabromosumanene. Hexabromosumanene proved very useful as various reactions such as cross-coupling and S_NAr reactions were carried out. Its exceedingly poor solubility, however, limited hexabromosumanene's wider use in synthetic chemistry. The halomethylation of aromatic compounds is resistant to steric limitation, and aromatic compounds with a halomethyl moiety (C_{sp3}-X, X=Cl, Br, or I), like benzyl bromide, are among the usual molecules exhibiting high reactivity to nucleophilic substitution process. Following this, the halomethyl group substitution could drastically improve the solubility of the formed substituted molecule. Prof. Sakurai's group successfully produced 2,3,5,6,8,9 Hexakis(bromomethyl)sumanene (6Br) by employing an excess of 1,3,5-trioxane and HBr-AcOH. It expanded the range of synthesizable hexa-substituted sumanene derivatives by making it easier to introduce functional groups like OAc, H, Cl, I, OMe, and SAc by straightforward nucleophilic substitution due to its strong stability in air and outstanding solubility for different 6Br solvents. According to a single crystal X-ray structural investigation of 6Br, a dimer structure with significant contact was formed, mostly due to Br···π interaction inside dimers (H. Nakazawa, 2022). With the successful synthesis of the hexakisbromomethyl sumanene further reactivity scopes of these molecules have started to be discovered as hexakisbromomethyl sumanene has a way better chemical reactivity if compared to the other substituted derivative of sumanene.

The main aim of my master's thesis project is to study the extent of chemical reactivity of hexakisbromomethyl sumanene in the field of organic chemistry. Some of the previous research those have been done on hexakisbromomethyl sumanene has inspired some new

fascinating research ideas to work on. Starting with the attempt to form molecular cages from pentagon fused derivatives of hexakisbromomethyl sumanene. While investigating the possibility of the bottom-up synthesis of aza-sumanene, it came across that it is possible to further functionalize the alkyl bromine moiety of the hexakisbromomethyl sumanene molecule which can help in the modification of the necessary functional groups for convergent synthesis-oriented dimerization of the two pieces by forming a six-membered ring, resulting in the formation of sumanenyltriamine (H. Nakazawa et al., 2023). Also, it was observed that the introduction of Cs (cesium ion) in a mixture having sumanene derivative led to the aggregation of those derivatives. After calculating and predicting the interaction energy of different aggregation complexes, it was found that the interaction energy of the sandwich-type complexes was the highest and closest to be found in this case. So, there is a possibility of the formation of a sandwich-type cage complex when cesium ion is introduced in the system, which can help in the formation of a capsule-like cage structure when the attacking ligand is introduced in the system (12 equivalent of cesium ions needed to be introduced). Once those derivatives (hexakisbromomethyl sumanene molecule) get aggregated in the reaction system, a diamine can be introduced in the same reaction system which will react with both hexakisbromomethyl sumanene molecules to form two pentagon fused moieties, joining the two hexakisbromomethyl sumanene molecules resembling molecular cage-like structure.

Another very interesting research idea was to try the Horner–Wadsworth–Emmons reaction (HWE reaction) with the phosphite derivative of the sumanene molecule. The phosphite derivative can be prepared from the sumanene molecule by simply reacting its hexa-bromo methyl derivative with triethyl phosphite under specific conditions. The Horner-Wadsworth-Emmons (HWE) reaction is a chemical process that produces a combination of E and Z alkenes, but primarily E-alkenes when stabilized phosphonate carbanion reacts with aldehydes (or ketones) in organic chemistry. So, performing an HWE reaction on the phosphite derivative of sumanene can lead to the formation of sumanene derivatives which have a long-extended conjugation. Finally, the research that was very fascinating was that the synthesis of the trifluoromethane sulfinate derivative of the sumanene molecule, as a trifluoromethane sulfinate derivative molecule, can be further attached to a carbon nanotube (CNT) which can serve great utility. The synthesis of the trifluoromethane sulfinate derivative is
So, for my master's thesis, my main focus is to explore the scope and range of the chemical reactivity of sumanene and hexakisbromomethyl sumanene at different positions in the molecule such as benzylic and aromatic positions.

CHAPTER 2: Synthesis Section

2.1 materials:

2-Thiophene carboxylic acid was purchased from BLD pharma tech, copper (1) oxide, 1,1-diphenylprop-2-yn-1-ol, dichloromethane, and triethyl phosphite were purchased from Wako chemicals. Potassium tert-butoxide, Caesium carbonate, and 2,5-norbornadiene were purchased from Sigma Aldrich. n-butyl lithium (n-BuLi), Sodium trifluoromethane sulfinate, and sodium sulphate were purchased from Kanto Chemicals. Dibromoethane, n-tributyltin chloride tricyclohexylphosphine, DDQ (2,3-Dichloro-5,6-dicyano-1,4-benzoquinone). 1,3,5-trioxane, HBr (in acetic acid), Caesium chloride, potassium carbonate, Ethylene diamine, 2,2-Dimethyl-1,3-propanediamine, and C_{60} fullerene were purchased from Tokyo Chemical Industry (TCI). Apart from all these reagents solvents like acetonitrile, toluene, methanol, hexane, diethyl ether, tetrahydrofuran (THF), Dimethylformamide (DMF), chloroform, Dimethyl sulfoxide (DMSO) and ODCB (Ortho Dichlorobenzene) were also used which were purchased locally.

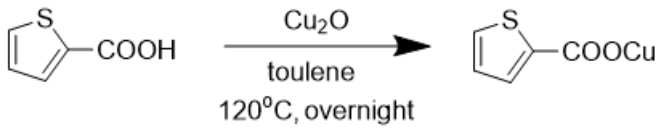
2.2 methods:

All manipulations of moisture or air-sensitive reactions were performed by standard Schlenk techniques in anhydrous solvents under a nitrogen atmosphere using flame-dried glassware. Joel 400Hz NMR spectrophotometer was used to record the NMR spectra for 1H and 13C experiments. $CDCl_3$, DMSO-d6, D_2O, and $CDCl_3$ containing TMS as an internal standard were used as solvents for recording the NMR spectra. IR experiments were performed while using chloroform (CHCl3) as a solvent medium and done using Jasco FT/IR-4100 instrument. Medium-pressure liquid chromatography (MPLC) was performed using Yamazen smart flash instrument to purify impure crude products using a mixture of solvents such as a mixture of chloroform and methanol or a mixture of ethyl acetate and hexane. In order to dry up the excess moisture and solvent present in the extracted product was desiccated using a vacuum sample drying oven. The mass analysis of the obtained products was done using APCI-MS which was performed by Acquity ultra-performance LC (SQ detector). At last, the solvent present with the product was evaporated using Eyela digital water bath SB-1000 rotatory evaporator.

2.3 synthesis procedures:

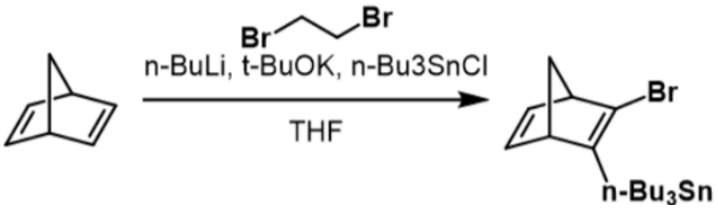
2.31) Sumanene synthesis:

a) Copper TC synthesis:



Take a clean and dry 1 litre 2-necked round bottom flask, add 125g (0.975 mol, 100 mol%) of 2-Thiophene carboxylic acid with 42g (0.294 mol, 30 mol%) of copper (1) oxide to the flask and purge the flask with nitrogen gas efficiently after sealing all the openings. Once the nitrogen gas is nicely purged, with the help of a syringe add 450mL of toluene as a solvent and let the reaction mixture stir with reflux for 8 hours at 120ºC. Filter the reaction mixture using a vacuum filter and wash it using methanol, hexane, and diethyl ether. Once filtered dry the obtained product (reddish brown) in desiccator overnight at 80ºC.

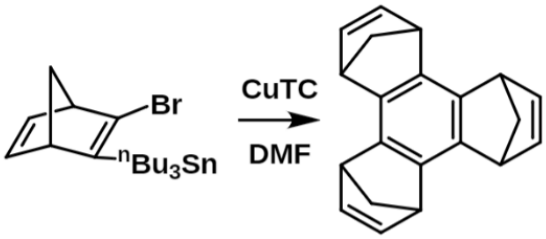
b) Sumanene first:



Take a clean and flame dry 1 litre 3-necked round bottom flask, add 28g of potassium tert-butoxide (250 mmol, 200 mol%), and purge the flask with nitrogen gas efficiently. Once the flask is purged with nitrogen, using a clean syringe add 50mL of 2,5-norbornadiene (500 mmol, 400 mol%) followed by 380 mL of THF as a solvent. Cool the reaction mixture to -80ºC and once the reaction mixture cools down add 100 mL of n-BuLi to it. After the addition of n-BuLi the color of the reaction mixture changes from brown to orange. Once the color changes, move the reaction mixture to -40ºC for 30 minutes and add 10.8 mL of dibromoethane to it, and let it stir for 90 minutes at -40ºC. After 90 minutes add 40.7mL of n-tributyltin chloride with a syringe and let the reaction mixture stir at room temperature for 1 hour. Once the reaction is completed, quench the reaction with water and extract the organic layer with a mixture of hexane and ethyl acetate (with a ratio of 1:1). Wash the mixture with brine and water (3*200 mL) and extract the organic layer again and dry it over sodium

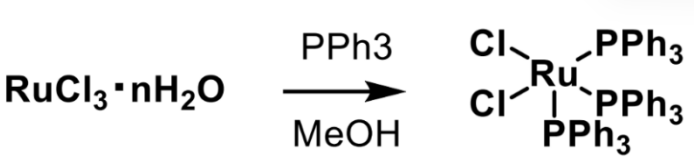
sulphate. Dry the obtained organic layer by vacuum evaporation and purify the obtained product further by a short column to get the pure product (yellow oil). (Hidehiro Sakurai *et al.,* 2003)

c) Sumanene second:



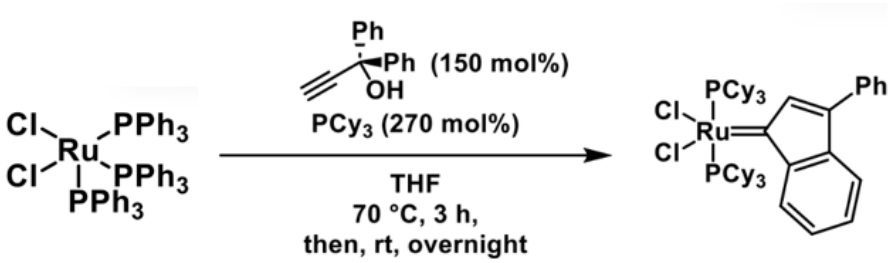
Take a clean and flame dry 1 litre 2-necked round bottom flask and add prepared Copper TC (96 mol%) catalyst to it and purge the flask with nitrogen gas. Once the nitrogen gas is purged nicely to the flask, add DMF using a clean syringe (the solution will turn green) and cool the reaction mixture to -40^{o}C. Once cooled, add the synthesized sumanene first (100 mol%) to the solution dropwise and stir the resulting reaction mixture for 1 hour at -20^{o}C (the reaction mixture will turn brown). After that move the reaction mixture to room temperature and let it stir overnight (the color of the reaction mixture will change to orange). Once the reaction is completed, quench the reaction with 300 mL 30% aqueous ammonia solute. Extract the organic layer with a 7:3 solution of hexane and ethyl acetate (5*200 mL), and further extract the layer after washing with water (3*200 mL) and dry it over sodium sulphate followed by the vacuum evaporation of the solvent. Once the crude product is obtained, purify the crude product using MPLC (hexane: toluene = 60:40) and collect the pure product which is a pale brown solid. (Hidehiro Sakurai *et al.,* 2003)

d) Grubbs first:



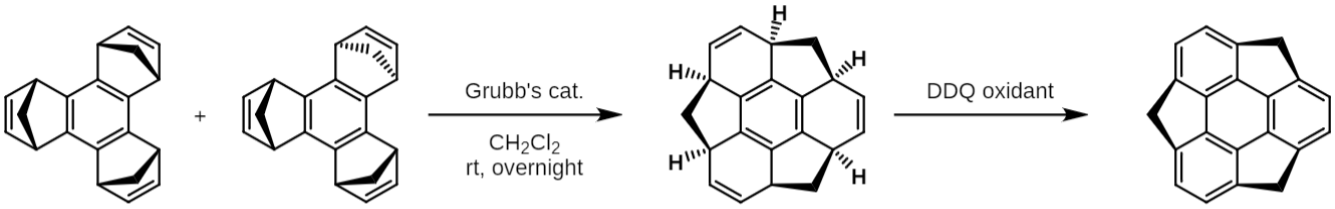
Take a clean and dry 3-litre 3-necked flask and add 8g (38.6 mmol, 100 mol%) of $RuCl_3.nH_2O$ and 54.8g (209 mmol, 542 mol%) of PPh_3 and purge nitrogen gas into the flask and further add 1-litre methanol as a solvent into the flask. Stir the reaction mixture with reflux at 70ºC for 3 hours. Once the reaction is completed cool the mixture to room temperature and filter the solution using a vacuum filter by washing it with diethyl ether (200 mL) and evaporate the solvent using a rotatory evaporator to obtain the final product which is brown in color.

e) Grubbs second:



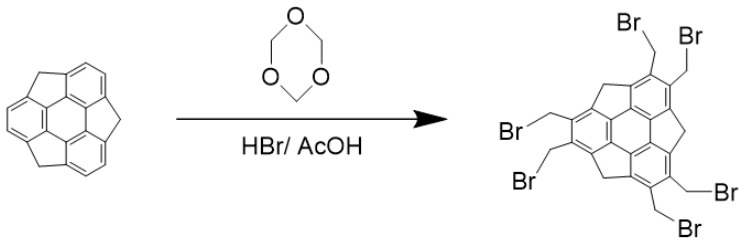
Take a clean and dry 1 litre 3-necked round bottom flask and add 17g (17.7 mmol, 100 mol%) of prepared Grubbs first as a starting material followed by 5.7g (27.5 mmol, 155 mol%) of 1,1-diphenylprop-2-yn-1-ol and purge nitrogen gas carefully into the flask. Add 600 mL of THF as a solvent into the flask using a clean syringe and stir the solution at 70ºC for 3 hrs with reflux. Take another 1 litre round bottom flask which is completely vacuumed and purged with nitrogen. Add 91 mL (47.9 mmol, 270 mol%) of tricyclohexylphosphine to it with the content of the previous flask into this one and let it stir overnight at room temperature. Once the reaction is completed (progress of the reaction is monitored with TLC), evaporate the excess solvent and filter the content of the reaction mixture by washing them with hexane and diethyl ether. Dry the filtrate using rotatory evaporation and collect the product (red-colored product).

f) Sumanene third:



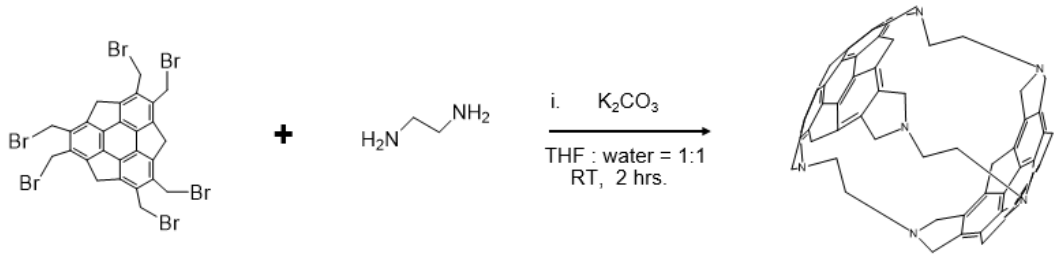
Take a clean and dry 1 litre 3-necked round bottom flask and add 5.8g (21.5 mmol, 100 mol%) of sumanene third as the starting material the purge the flask with ethylene gas efficiently. Once the ethylene gas is purged add 430 mL of dichloromethane using a clean syringe followed by 3g (3.23 mmol, 15 mol%) of Grubbs catalyst and let the solution stir at room temperature overnight. Once the reaction is completed, collect the crude product and perform a short column with a 1:1 mixture of hexane and dichloromethane. Once the short column is completed evaporate the excess solvent using a rotatory evaporator. Collect the resulting product add it to another round bottom flask and add 430 mL of dichloromethane to it. Cool down the reaction mixture in the flask to 0^{o}C and add 14.6 g (64.4 mmol, 300 mol%) of DDQ (2,3-Dichloro-5,6-dicyano-1,4-benzoquinone) and stir the solution for about minutes at room temperature. Once the reaction is completed perform a short column to purify the crude product using a 4:1 mixture of hexane and dichloromethane. Collect the filtrate and evaporate the solvent using a rotatory evaporator and collect the pure product (sumanene) which will be a white or pale-yellow solid. (Hidehiro Sakurai *et al.,* 2003)

2.32) Synthesis of Hexakis(bromomethyl) sumanene:



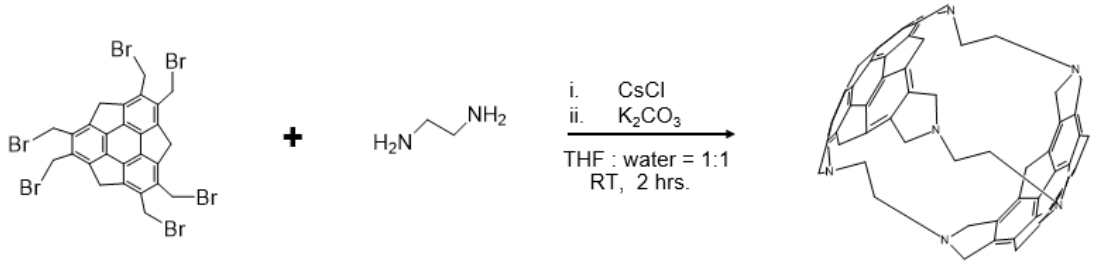
Take a clean and flame dry test tube and add 101.5 g sumanene (0.384 mmol, 100 mol%) and 414 mg (4.55 mmol, 1200 mol%) 1,3,5-trioxane to it and purge nitrogen gas to it. Once nitrogen gas is purged to the test tube, add 5 ml HBr (in acetic acid) and let the mixture stir at 120^{o}C overnight. Once the reaction is completed cool the reaction mixture to room temperature. Once cooled, a light-yellow precipitate will start to appear in the test tube. Filter the precipitate using a membrane filter by washing it with water (20mL). Once collected, dissolve the crude product in chloroform and give it a wash with water (3*50 mL) and dry it over sodium sulphate. Evaporate the solvent and collect the crude product. Purify the crude product by a short column with a 1:1 mixture of hexane and chloroform. Collect the filtrate and evaporate the solvent to obtain a pure product (260.5 mg, 83% yield) (yellow powder)(H. Nakazawa, 2022).

2.33) Sumanene cage synthesis with ethylene diamine (EDA):



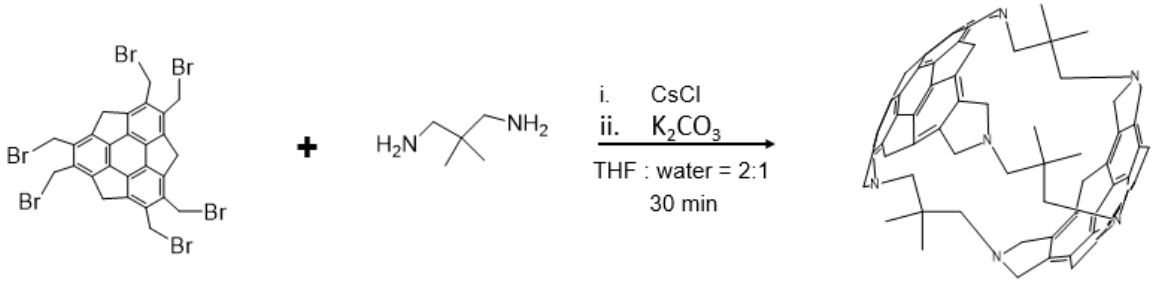
Take a clean and flame-dry test tube and add Hexakis-bromomethyl sumanene (100 mol%) and THF as a solvent to it. After adding these add ethylene diamine (150 mol%) to the reaction mixture dropwise slowly and let the reaction mixture stir for 30 minutes. Check the progress of the reaction via TLC and once the reaction is completed with the total consumption of starting material, extract the organic layer with chloroform by giving washes with water and brine, also add 1ml of 1M of solution of K_2CO_3 in water and then finally extract the organic layer. Evaporate the solvent using a rotatory evaporator.

2.34) Sumanene cage synthesis with ethylene diamine and cesium chloride:



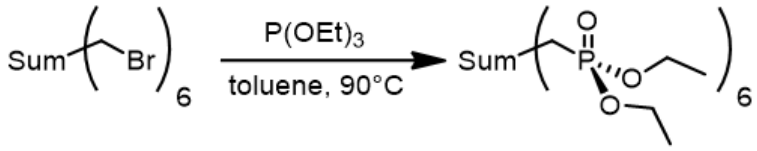
Take a clean and flame-dry test tube and add Hexakis-bromomethyl sumanene (100 mol%) and THF as a solvent to it. After adding these add Caesium chloride (100 mol%) (dissolved in a 1:1 solution of THF and water) followed by ethylene diamine (150 mol%) to the reaction mixture dropwise slowly and let the reaction mixture stir for 30 minutes. Check the progress of the reaction via TLC and once the reaction is completed with the total consumption of starting material, extract the organic layer with chloroform by giving washes with water and brine also add 1ml of 1M of solution of K_2CO_3 in water and then finally extract the organic layer. Evaporate the solvent using a rotatory evaporator.

2.35) Sumanene cage synthesis with 2,2-Dimethyl-1,3-propanediamine (DPDA) and caesium chloride:



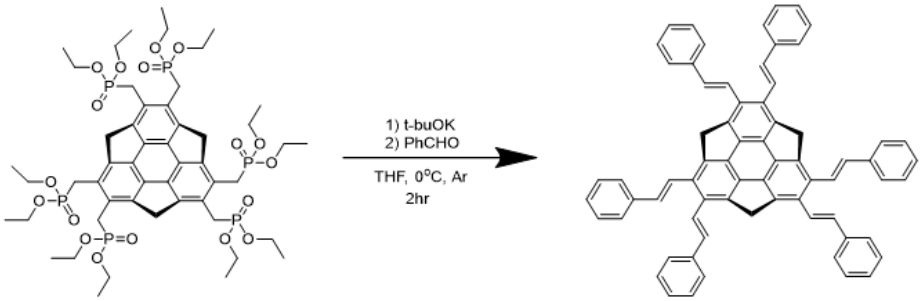
Take a clean and flame-dry test tube and add Hexakis-bromomethyl sumanene (100 mol%) and THF as a solvent to it. After adding these add Caesium chloride (100 mol%) (dissolved in a 1:1 solution of THF and water) followed by DPDA (150 mol%) to the reaction mixture dropwise slowly and let the reaction mixture stir for 30 minutes. Check the progress of the reaction via TLC and once the reaction is completed with the total consumption of starting material, extract the organic layer with chloroform by giving washes with water and brine also add 1ml of 1M of solution of K_2CO_3 in water and then finally extract the organic layer. Evaporate the solvent using a rotatory evaporator.

2.36) Sumanene hexamethyl phosphonate synthesis:



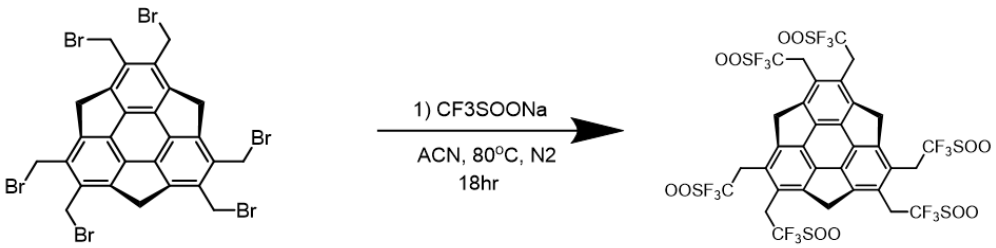
Take a clean and flame dry test tube and add 15mg (0.0182 mmol, 100 mol%) of Hexakis bromomethyl sumanene as a starting material followed by 40uL (0.219 mmol, 1200 mol%) triethyl phosphite to it. Once the materials are added, purge nitrogen gas to the test tube efficiently. After nitrogen gas is purged, add 2 mL of toluene to the test tube as a solvent and let the reaction mixture stir for 72 hours at 90ºC. Once the reaction is completed which was tracked by TLC, collect the product layer by PTLC with a 97:3 solution of chloroform and methanol. After collecting the product, extract the organic layer by chloroform with washes of water and brine. Evaporate the solvent by a rotatory evaporator to obtain the pure product in the form of yellow oil (7 mg, 34% yield).

2.37) Horner–Wadsworth–Emmons reaction (HWE) reaction using benzaldehyde:



Take a clean and flame-dry test tube and add sumanene phosphite (100 mol%) as a starting material followed by THF as a solvent and purge argon gas into the test tube. After purging argon gas add the equivalent amount of base (600 mol%) (depending upon the requirement of the intensity of the base starting with potassium tert-butoxide and followed by n-butyl lithium) to the reaction mixture, at a suitable temperature (maximum yield was found out to be at room temperature) and let the reaction mixture stir at room temperature for 24 hours. Once the reaction is completed (which was being tracked by TLC), extract the organic layer by chloroform and obtain the final product by evaporating the solvent.

2.38) Synthesis of Sumanene Hexatrifluoromethanesulfinate:



Take a clean and flame dry test tube and add 20 mg (0.024 mmol, 100 mol%) of Hexakis bromomethyl sumanene as a starting material followed by 45.5 mg (0.291 mmol, 1200 mol%) of Sodium trifluoromethane sulfinate and purge the test tube with nitrogen gas. Once the nitrogen gas is purged, add 2.5 mL of acetonitrile as a solvent and let the mixture stir for 24 hours at 80°C. Once the reaction is completed (monitored with TLC), extract the organic layer with ethyl acetate and give washes with water and brine. Once the organic layer is obtained, perform PTLC to obtain pure product as a light-yellow solid (10.2 mg, 36.77% yield).

2.39) Synthesis of [2+1] Sumanene Hexatrifluoromethanesulfinate cycloadded molecule to C_{60}:

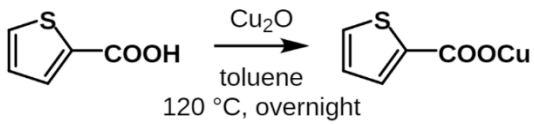
Take a clean and flame-dry test tube and add 9 mg (0.0079 mmol, 100 mol%) of starting material which was sumanene Hexatrifluoromethanesulfinate in this case followed by 2 ml of DMSO as a solvent with 34.2 mg (0.095 mmol, 1200 mol%) Cs_2CO_3 (cesium carbonate) as a base and purge the test tube with nitrogen gas. Once the nitrogen gas is purged, let the reaction mixture stir for 1 hour at 27°C. After 1 hour add 6.31 mg (0.0079 mmol, 100 mol%) of C_{60} fullerene dissolved in ODCB (Ortho Dichlorobenzene) (2 ml) to the reaction mixture and let the reaction mixture stir for another 6 hours and check the progress of the reaction via TLC with a solvent mixture of methanol and chloroform in a ratio of 1:5. Once the reaction is completed quench the reaction with water and give the wash with brine. Finally, extract the organic layer with chloroform and evaporate the present solvent using a rotatory evaporator. The boiling point of ODCB is high and cannot be evaporated by a rotatory evaporator. So, the remaining ODCB is removed by centrifugation with ethanol as a secondary solvent (15*2 ml). Once ODCB was removed, the product was collected (1.9 mg).

CHAPTER 3: Results and discussion

3.1) Sumanene synthesis:

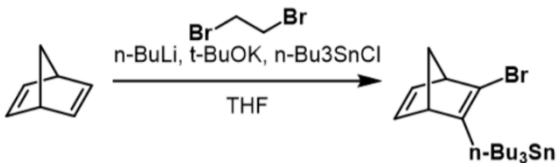
The synthesis of sumanene is well known and I followed the complete procedure to synthesize my first batch of sumanene [4]. The synthesis of sumanene involves the following steps:

a) Synthesis of CuTC:



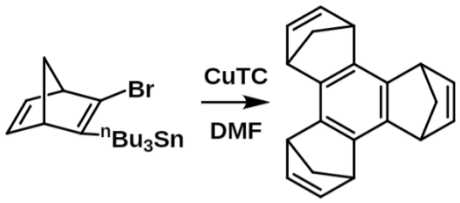
Yield: 43%

b) Synthesis of Sumanene first:



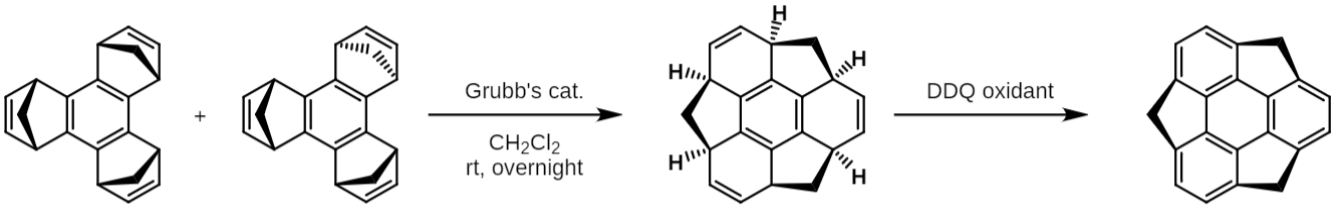
Yield: 63.6%

c) Synthesis of sumanene second:



Yield: 7.3%

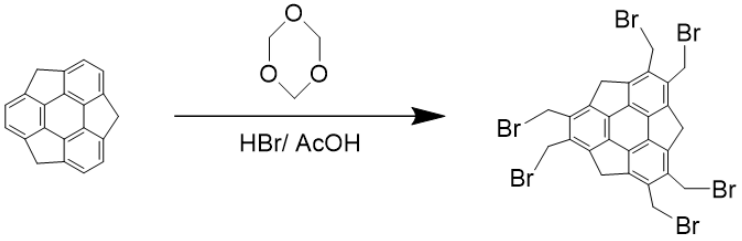
d) Synthesis of sumanene third:



Yield: 1.625%

3.2) Synthesis of Hexakis(bromomethyl) sumanene:

The synthesis of sumanene and Hexakis(bromomethyl) sumanene is well known and I followed the complete procedure to synthesize my first batch of Hexakis(bromomethyl) sumanene.

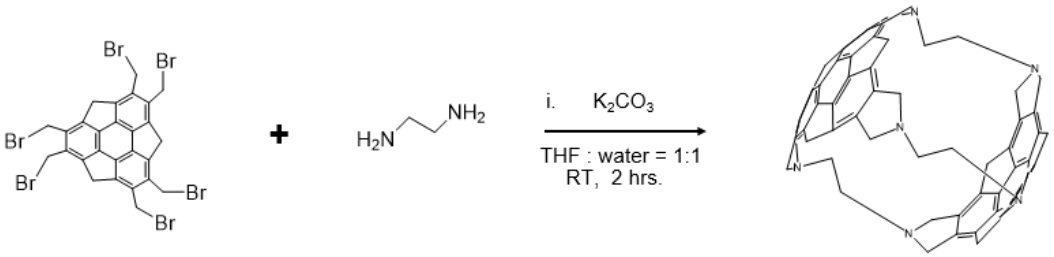


Yield: 85%

<u>Remarks and observation:</u>

The results of the sumanene synthesis and the synthesis of Hexakis(bromomethyl) sumanene were compared with the previous results when the synthesis was done by the previous members of the laboratory as these reactions were already standardized and optimized and I needed to follow the synthetic routes. I just collected the analytical data and did a comparative analysis.

3.3) Synthesis of cage complex with Ethylene diamine (EDA):



S no.	Temperature (°C)	Starting Material quantity	observation
1	60	5 mg	precipitation
2	0	5 mg	precipitation
3	RT	1 mg	No instant Precipitation

Table:3.11

Remarks and observation:

The product obtained after the reaction which was performed under all the conditions mentioned in table:1 was a bright yellow solid that was completely amorphous and did not have any crystalline properties at all. Also, the solid was insoluble in all the available solvents which have been mentioned below. (refer table:3.11).

Solvent	Solubility
Water	Very poor
Hexane	Very poor
DCM	Very poor
Chloroform	Very poor
Methanol	Very poor
DMSO	Very poor
Ethyl acetate	Very poor

Table:3.12

Because of the insolubility of the obtained product, it was not possible to get the liquid phase NMR (refer to Figure 3.11) and perform any further purification steps. As can be seen in the NMR it was not possible to get a D_2O NMR because of its insolubility in any solvents (refer table:3.12).

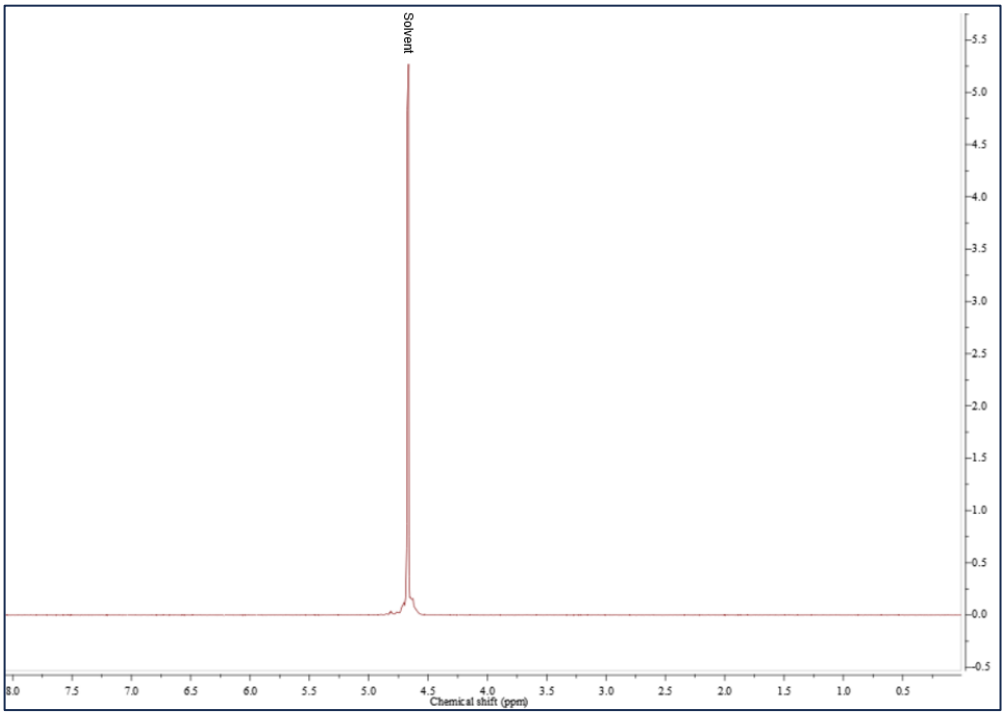


Figure:3.11 (NMR of the obtained product in D_2O is just giving the solvent peak)

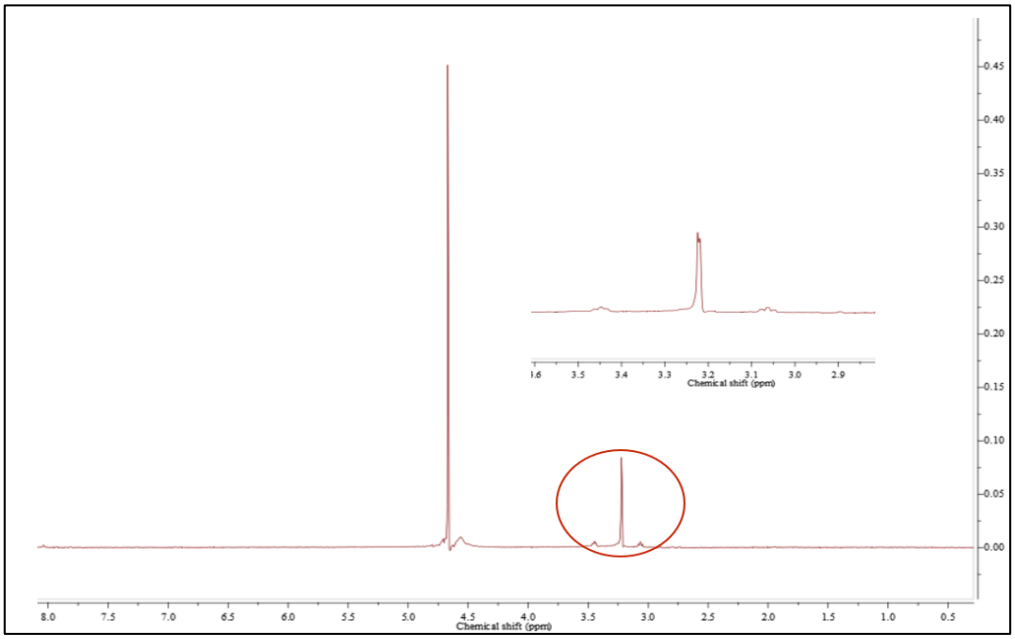
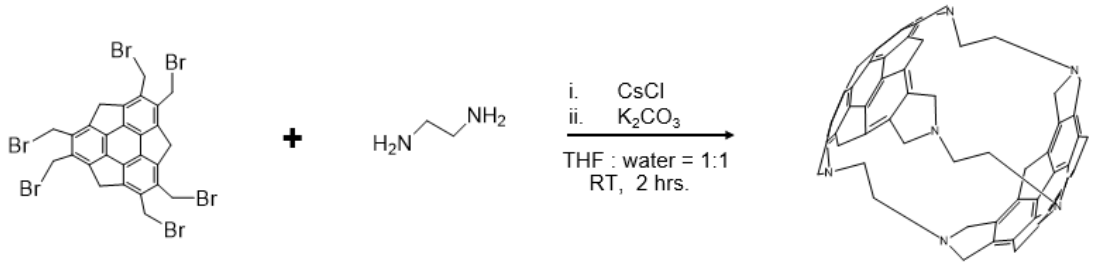


Figure:3.12 (NMR of the obtained product in D_2O giving the solvent and EDA peak)

During the analysis of the crude product after the second batch trail, D_2O NMR was taken again and it was found that a singlet peak was there in the NMR plot which corresponds to the unreacted ethylene diamine which was present there with the crude product (refer figure:3.12). The unreacted ethylene diamine present was removed by multiple water washes because of the high solubility of it in water. But because of the insolubility of the obtained product caused trouble in characterizing the crude product that was obtained after performing the reaction, as most of the characterization experiments require the product to be in a dissolved solution phase. Because of this issue, the further continuation of these reaction conditions was not possible.

3.4) Synthesis of cage complex with Ethylene diamine (EDA) and CsCl:



S no.	Starting Material amount (mg)	CsCl amount (eq.)	Addition of base	Temperature (°C)
1	1	0.5	Before rxn	RT
2	1	0.5	Before rxn	60
3	1	0.5	Before rxn	0
4	1	1	Before rxn	RT
5	1	2	Before rxn	RT
6	1	0.5	After rxn	RT
7	1	0	After rxn	RT
8	5	0.5	After rxn	RT
9	7	0.5	After rxn	RT

Table:3.13

Remarks and observation:

For the next set of reactions, the amount of the starting material was significantly reduced to a scale of 1 mg, and a CsCl (cesium salt) was introduced into the reaction system. The solvent system used for this set of reactions was a mixture of water and THF in a ratio of 1:1 for the proper dissolution of CsCl and the organic starting material. There was no precipitation while the ethylene diamine was being added dropwise slowly and even after the completion of the reaction and the organic layer was extracted using chloroform and was dried. All the reaction conditions mentioned in Table 3.13 were tried. The crude NMR of the product showed that the product has a

lot of impurities and contains a lot of undesired and unknown side products as well (refer to figure 3.15).

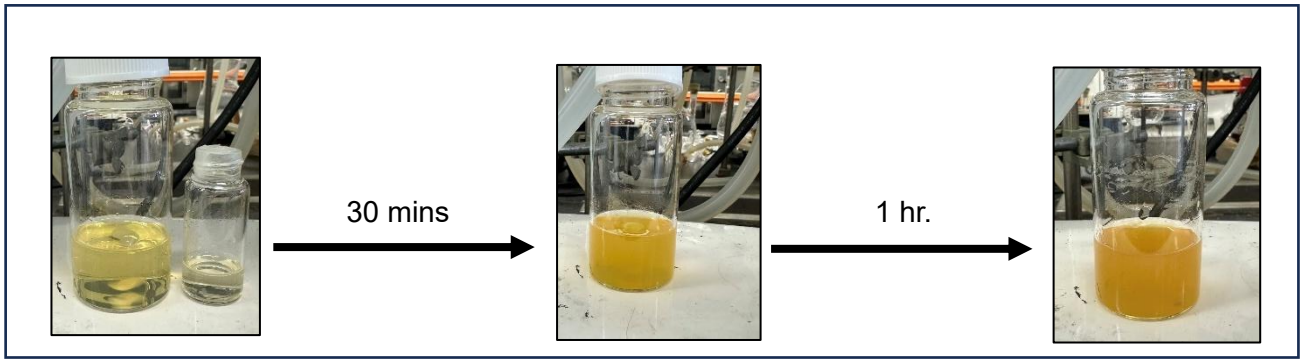


Figure:3.13 (Colour change during the progression of reaction)

To resolve the issue of product impurity, I focused on the optimization of the TLC conditions so that I could perform some polarity-based separation methods such as MPLC, PTLC, or short column to purify the crude product. But while trying certain combinations of different solvents and polarity, it was found that the polarity of the extracted compound was so high that it was not able to move on TLC after trying multiple solvent conditions (refer to figure:3.14).

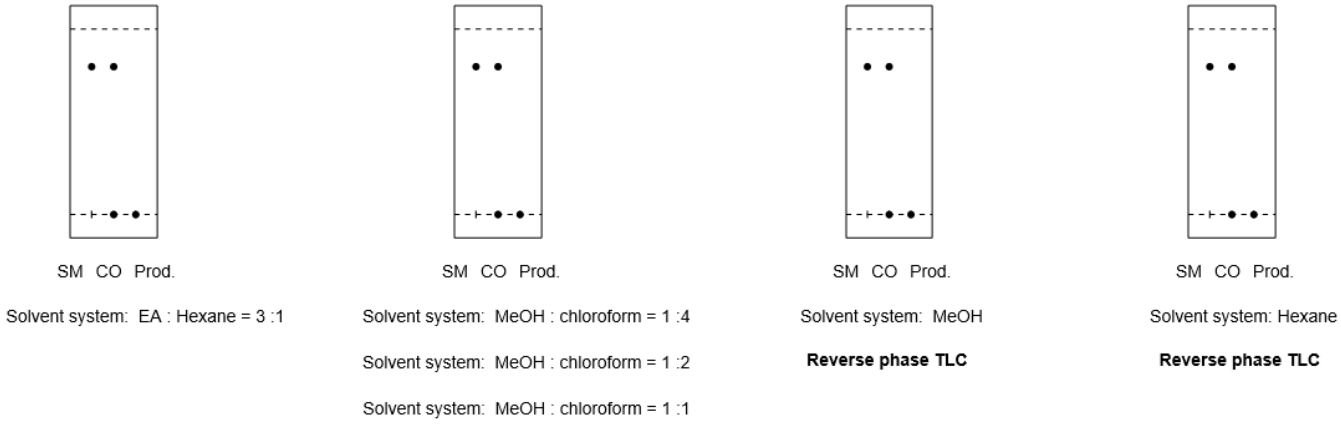


Figure:3.14 (Different solvent systems tested for the extracted compound)

A crude NMR of the unpurified product was also taken to see the extent of impurities present in the product (refer to Figure 3.15). The crude NMR clearly showed that there is a major number of impurities and the classification of the target product peaks was very hard.

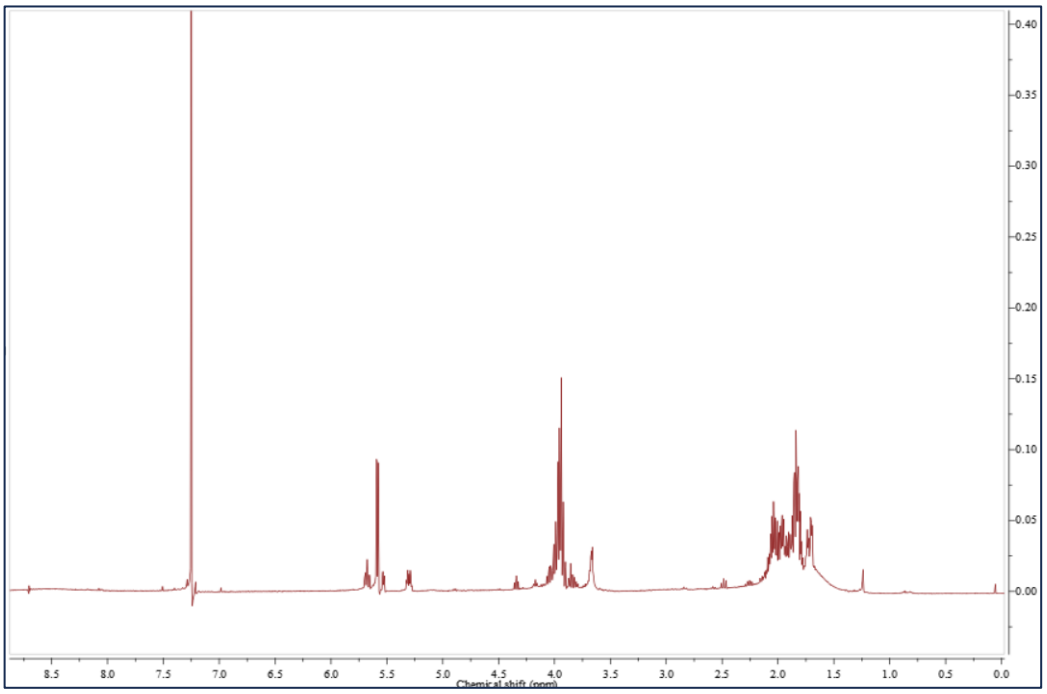


Figure:3.15 (Crude proton NMR of the product obtained)

Also, the crude NMR of the final product obtained after trying different temperature conditions were tracked to see if there is any difference which can be seen in the Dcrude NMR (refer figure:3.16).

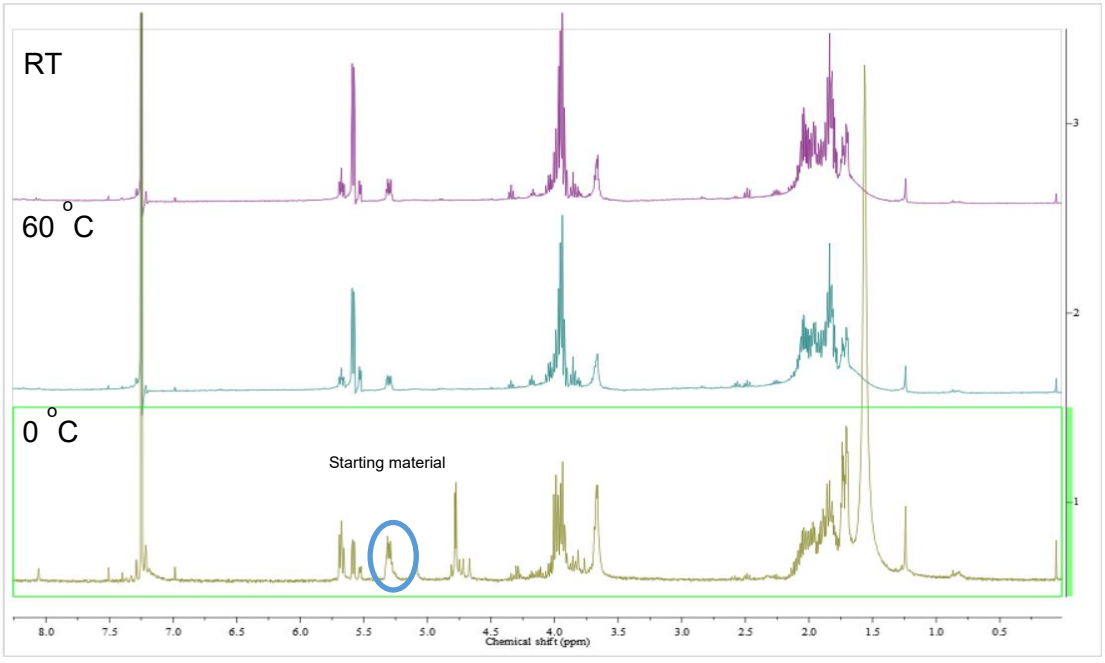


Figure:3.16 (Comparative crude proton NMR at different temperatures)

From the above NMR, it can be said that the crude product obtained after the reaction completion was almost the same. Just the difference that can be seen was in the case of 0ºC, where the consumption of the starting material was not completed even after increasing the reaction time of the mixture.

To check if there is any fragment that matches the mass of my target compound APCI mass spectra were collected at different temperatures. However, I was not able to detect any fragment which was having a mass near my target compound even after increasing the temperature (refer figure:3.17 and 3.18). The mass of the target was 816.

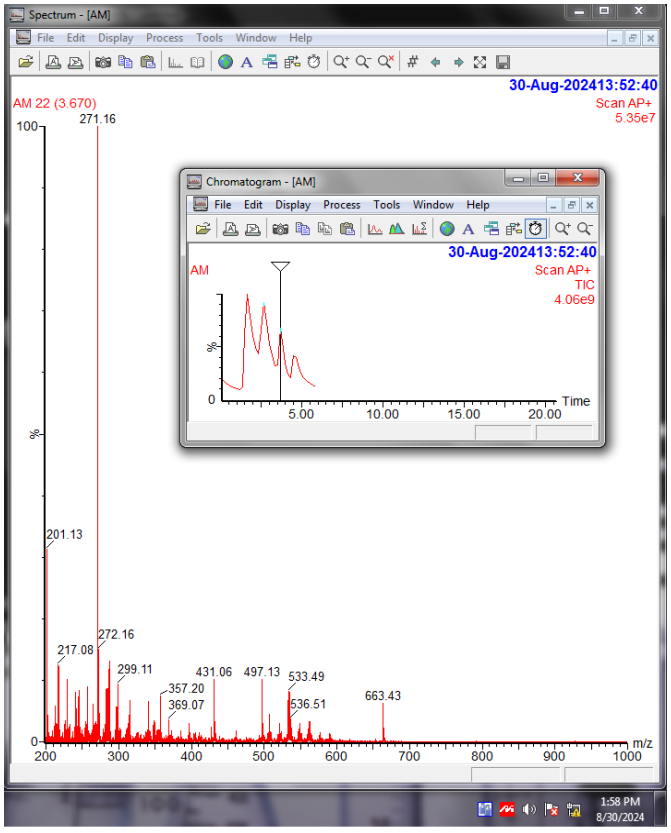


Figure:3.17 (APCI Measurement temperature: 250ºC)

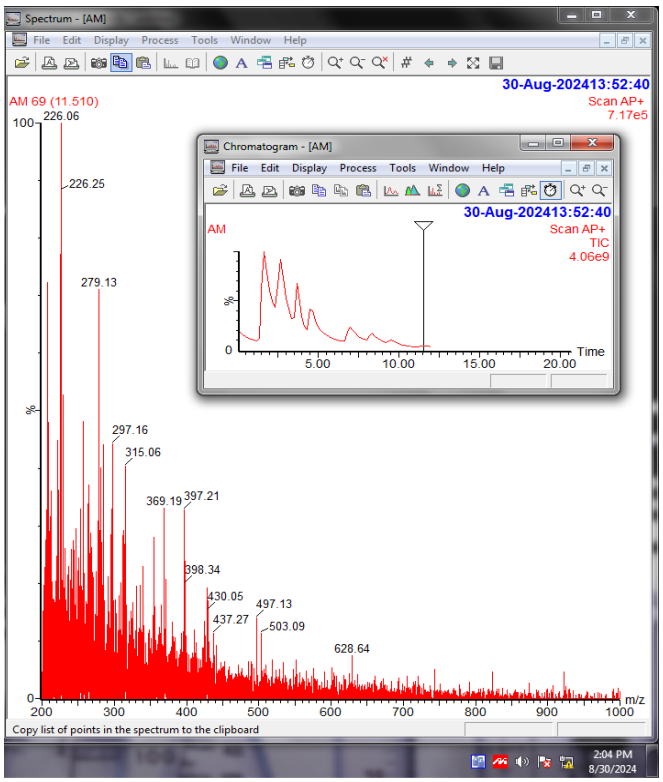
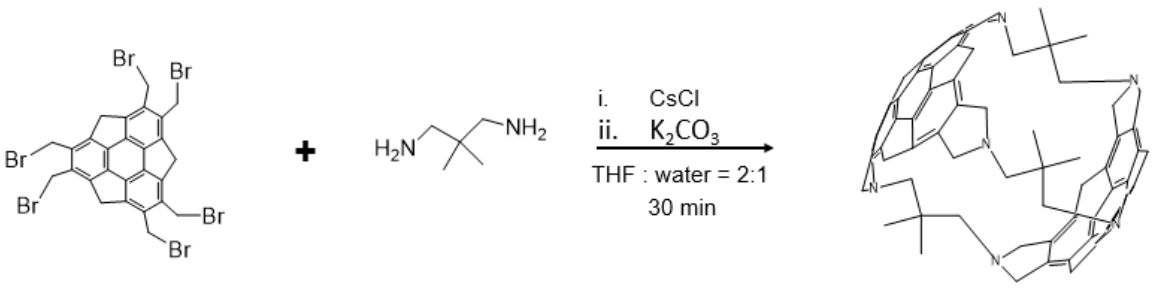


Figure:3.18 (APCI Measurement temperature: 400°C)

The characterization of the product was becoming an issue because of the high impurity concentration in the crude product. However, because of the dissolution problem further purification of the crude product was not possible, even the purification of this crude product with GPC was not possible because of its big enough size which can damage the GPC machine. So, moving forward some different synthesis techniques need to be applied to achieve the desired product.

3.5) Synthesis of cage complex with 2,2-Dimethyl-1,3-propanediamine (DPDA) and Cscl:



S no.	Starting Material amount (mg)	Cscl amount (eq.)	DPDA amount (eq.)	Temperature (°C)
1	2	2	6	RT
2	3	2	3	RT
3	3	2	1.5	RT

Table:3.14

Remarks and observation:

The next set of reactions (refer table:3.14) involved the change of the attacking ligand from EDA to DPDA (which is a more strained attacking ligand as compared to EDA, as the attacking amino groups in DPDA have comparatively lower bond angle than EDA), increase in amount of starting material used in the beginning of the reaction and also the change in ratio of the solvent system (refer table:3.15) for the better dissolution of the reagents.

WATER: THF	Dissolution issue
1:1	Yes
1:2	No
1:3	CsCl dissolution issue

Table:3.15

The organic layer was extracted by chloroform and the crude product was obtained after evaporating the solvent. The crude product that was obtained showed the same characteristics as in the previous reaction involving the polarity issue. The crude product that was obtained again had a very high polarity which made it seriously difficult to separate the impurities from the crude product and purify it. Again, different solvent combinations were tried to standardize and find the perfect solvent system for the obtained crude product (refer to figure 3.19).

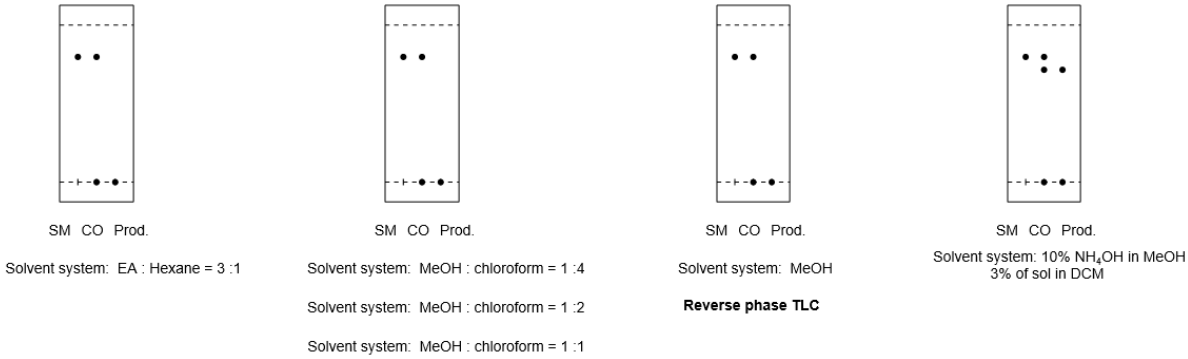


Figure:3.19 (Different solvent systems tested for the extracted compound)

The only solvent system in which the spot of the crude was able to move and give some separation was a solution of 10%NH_4OH in MeOH and 3% of that solution in DCM. The only issue with this solvent system was its very high polarity. Using this solvent system PTLC was done to collect the pure compound but when PTLC was done using this solvent system (refer figure:3.2), the spots were not moving up properly and were getting dragged.

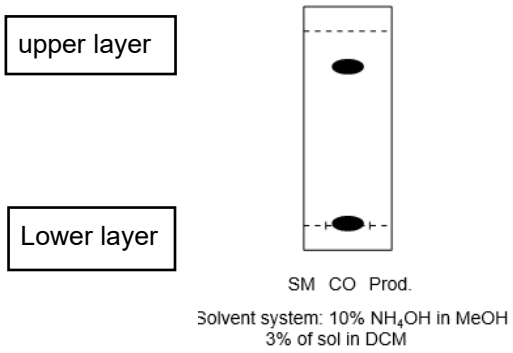


Figure:3.2 (Product and impurity spots on a PTLC plate)

The upper spot that appeared on the PTLC plate was collected and the NMR of the product present in that solvent was checked it was found that the NMR obtained from that spot did not have any peaks in the sumanene region which would correspond to the target compound (refer to Figure:3.21).

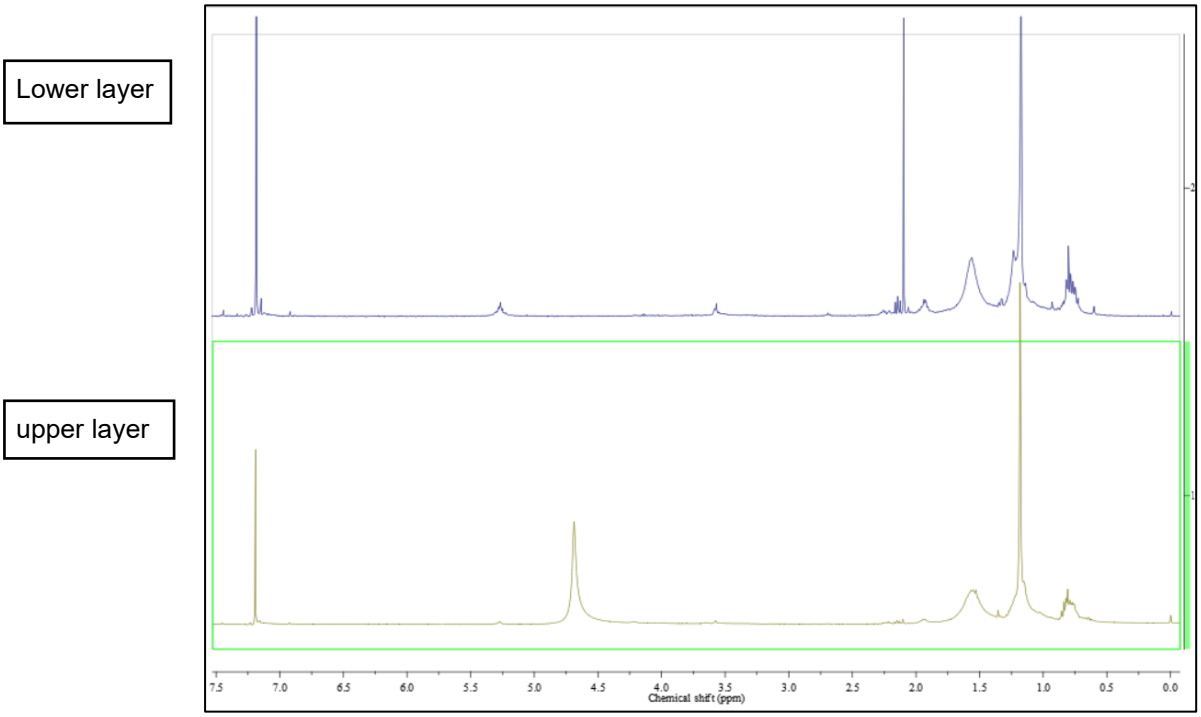


Figure:3.21 (Proton NMR of the two spots obtained from PTLC)

Further on the remarks and suggestions I decided to make some changes to the amount of DPDA that I am using while doing the reaction to see if there is any effect of changing the amount of the linking reagent (refer to table 3.16).

Case number	Amount of DPDA used (ul)
1	5.5
2	11
3	16.5

Table:3.16

Looking at figure we can clearly see that the change in the amount of the linking reagent DPDA was having a slight impact on the crude product formation but it was hard to say what was reason behind it (refer to figure 3.22).

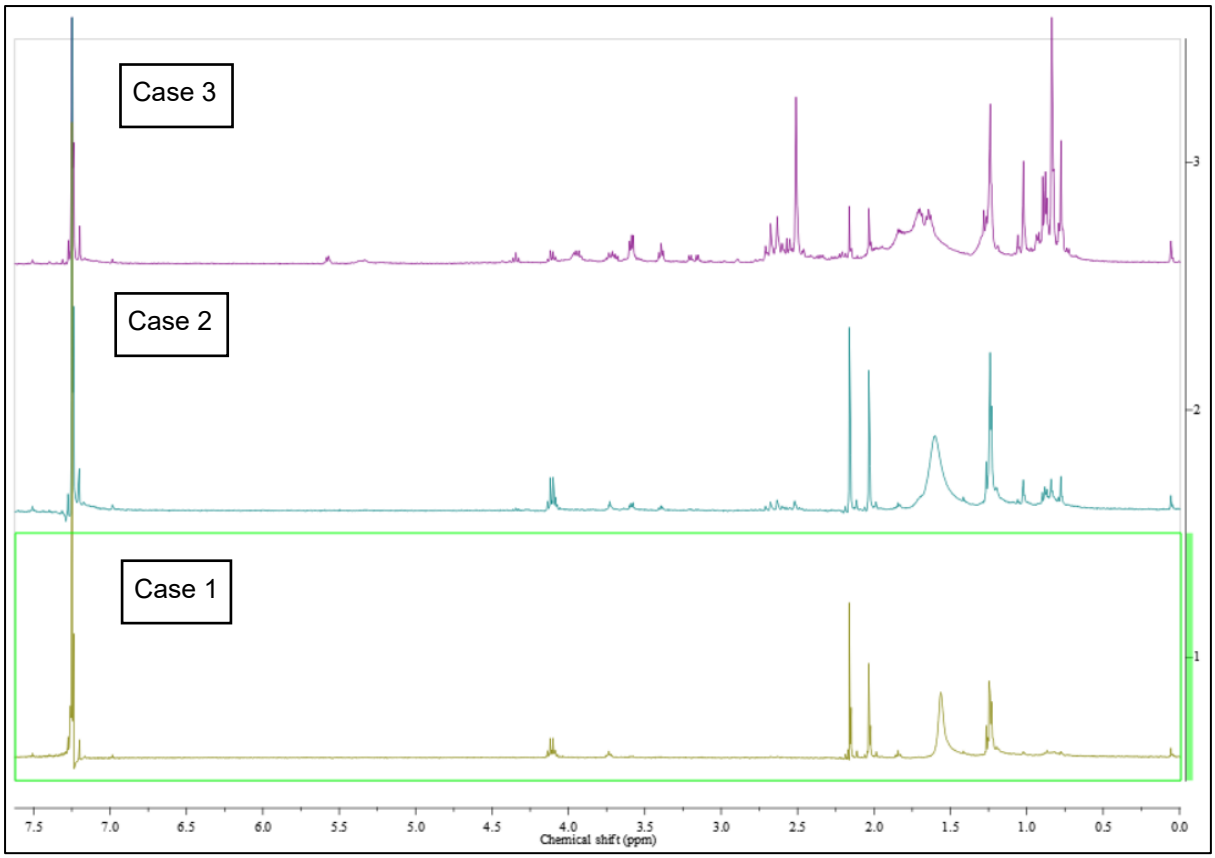
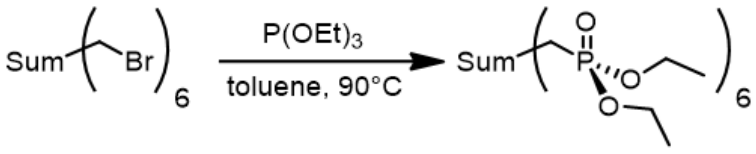


Figure:3.22 (Proton NMR of the three DPDA cases)

It can also be seen that there are no peaks in the NMR of cases 1 and 2 that are present in the sumanene region so they could not contain any possible target compound. On the other hand, in case 3 there were some peaks in the sumanene region but it also contains a huge number of impurities within it. So, with a huge number of impurities that were present in the crude product and those impurities could not be separated with the available methods, I was not able to continue this project further because of lack of any encouraging data, time, and possible future direction.

3.6) Sumanene hexamethyl phosphonate synthesis:



Remarks and observation:

After trying the possibility of synthesizing molecular cages utilizing sumanene molecule, it was clear that it would require a lot of thought process and a very specific synthesis route. For the second project, I started with the synthesis of sumanene hexaphosphonate. It was a very straightforward reaction which was already tried by one of my lab mates but this reaction was not optimized. So, I took the opportunity to further properly optimize the reaction and purification of the sumanene hexaphosphonate.

Serial number	Reaction time (hrs)	Final Yield (%)
1	24	28
2	48	31
3	72	34

Table:3.17

The reaction time of the reaction mixture was increased eventually for better product formation and it was observed that with the increase of reaction time, it was observed that the yield of the reaction also increased (refer table:3.17). Moving further for better purification of the crude product the solvent system for PTLC was changed from a mixture of chloroform and methanol in ratio of 95:5 was changed to 99.5:0.5, which gave a better separation. After the pure compound was obtained, the purity of the compound and its characterization were done by using proton NMR. Looking at the proton NMR it was clear that the product obtained after PTLC was very pure without any impurity or contamination giving the doublet of the benzylic proton at 4.60 ppm and 4.65 ppm, also the proton of carbon f (as in figure:3.23) appeared as a multiplet at 1.33 ppm. The protons of carbon g appear at a triplet at 1.09 ppm. Finally, the protons of carbons b, c, and d appear as multiplet and a doublet of doublet between 4.06 ppm and 3.46 ppm. So, using the proton NMR the formation of sumanene hexaphosphonate was confirmed (refer figure:3.23).

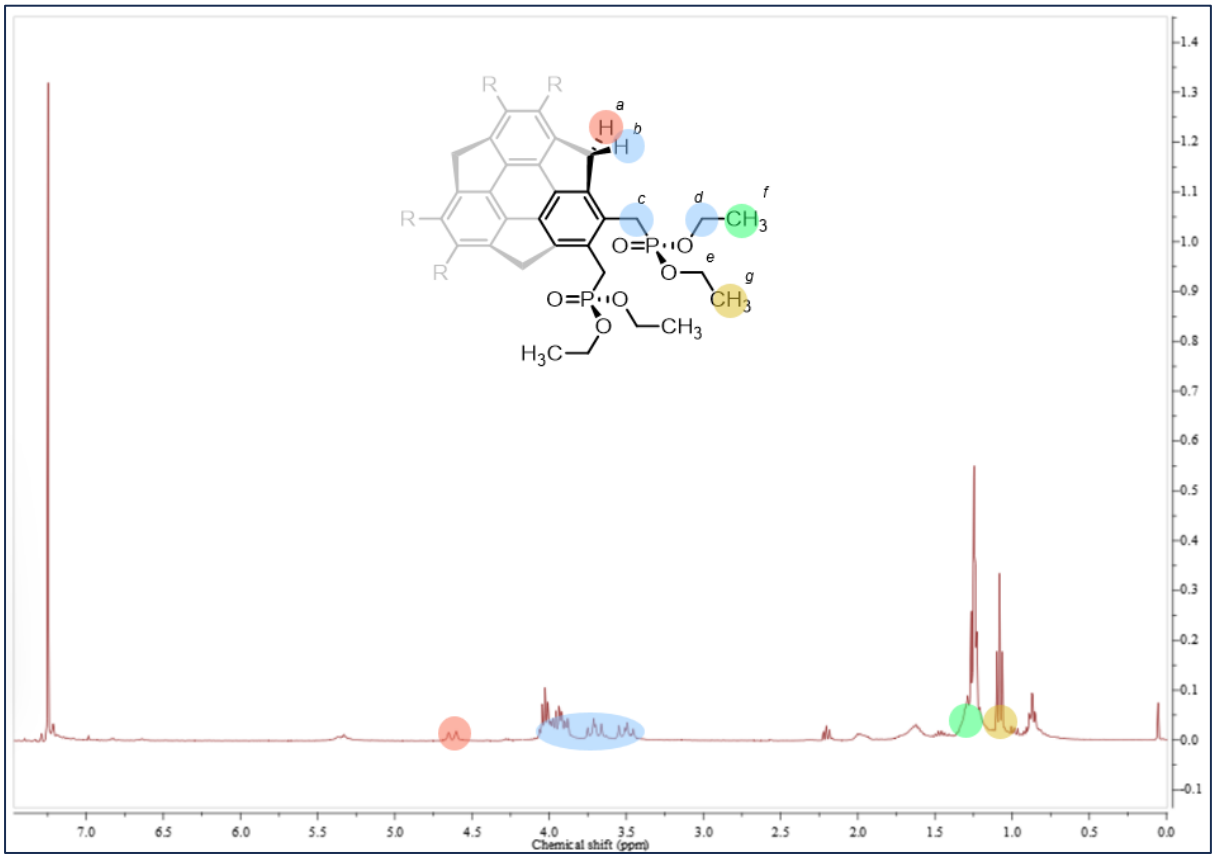
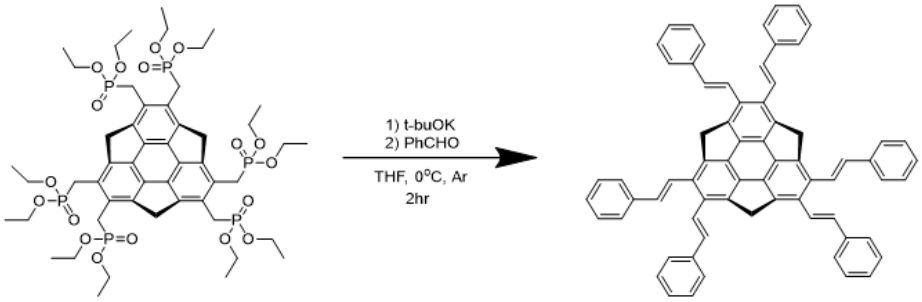


Figure:3.23 (Proton NMR of the obtained pure compound)

3.7) Horner–Wadsworth–Emmons reaction with benzaldehyde:



The Horner–Wadsworth–Emmons reaction is a very well-known reaction that involves the stabilization of the phosphonate carbanions with the help of aldehydes to finally produce a mixture of Z and E alkenes. In my case, I will be using sumanene hexaphosphonate as a target molecule on which the base can attack to form the corresponding ylide. The formed ylide then further reacts with the available aldehyde which is benzaldehyde in my case to

form the desired alkene in the form of a mixture of Z and E alkenes which proceeds via a concerted step. But the most difficult aspect of this reaction was to choose a suitable base that could deprotonate the alpha proton next to the phosphonate group selectively and not affect the benzylic proton present on the sumanene hexaphosphonate molecule.

To begin my set of reactions, I started with potassium tert-butoxide which is not a very strong base. The reaction conditions that I tried are shown in Table 3.18.

S No.	t-BuOK eq.	Addition temp.	PhCHO eq.	Stirring temp.(°C)	Stirring time (hr.)	SM recovered (%)
1	9	RT	6	RT	3	88.57
2	20	RT	12	RT	24	89.03
3	20	RT	12	40	48	90.75
4	40	RT	24	60	48	85.22

Table:3.18

While tracking the reaction progress via TLC it was observed that there was no product spot observed on it. Also, the proton NMR of the crude product obtained showed only the peaks of the starting material and benzaldehyde and no new product formation (refer figure:3.24)

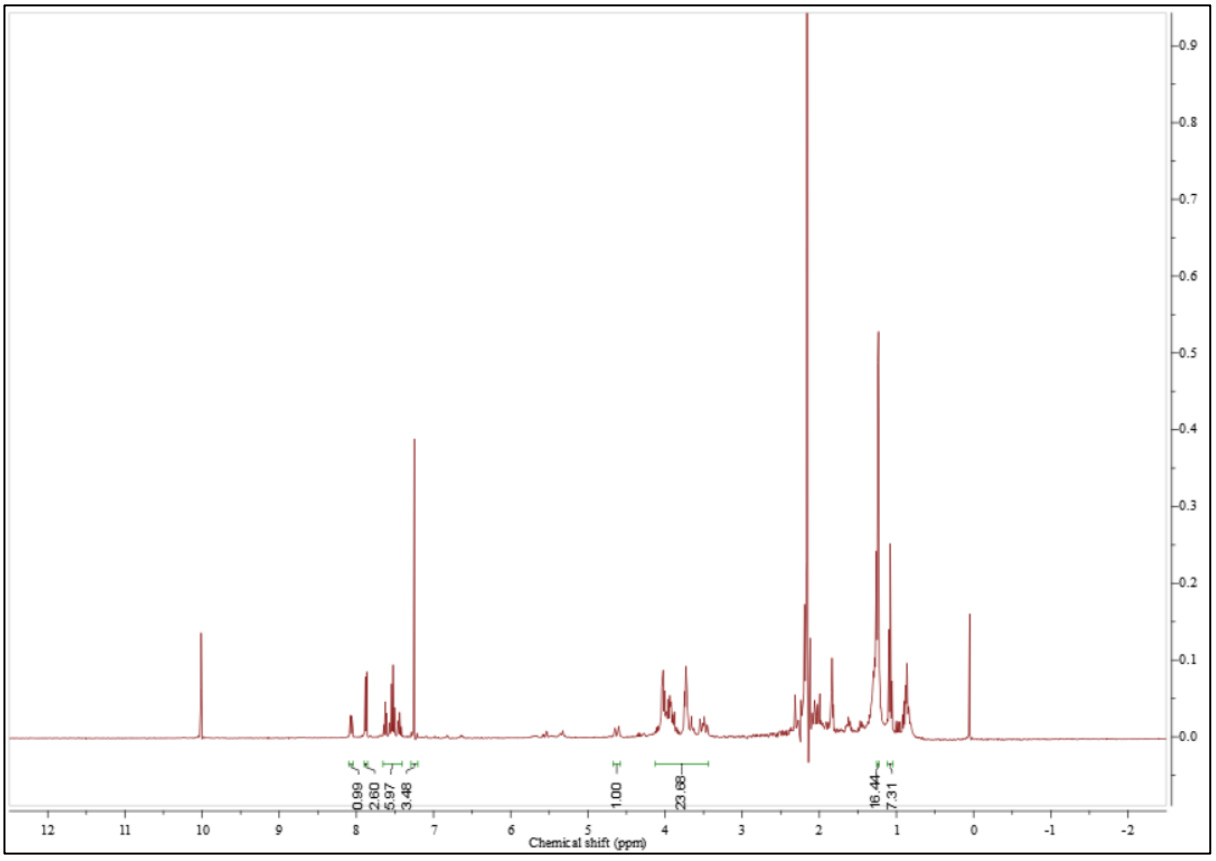


Figure:3.24 (Crude proton NMR of the obtained product)

The unconsumed starting material was recovered from the crude product using PTLC each time (as shown in Figure 3.25) and the percentage of the starting material recovered was also calculated and noted in order to see if there was any consumption of starting material actually happening or not. In the case of using potassium tert-butoxide as a base, the percentage of starting material recovered was always over 85% which indicates that the starting material was not getting consumed.

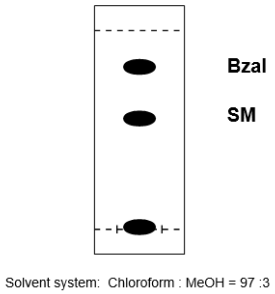


Figure:3.25 (PTLC plate and spots of the crude product)

So, I decided to change the base to a stronger base which is n-BuLi, so that the alpha proton near the phosphonate group can be deprotonated. The reaction conditions mentioned in Table 3.19 were performed.

S No.	n-BuLi eq.	Addition temp. (in ^{o}C)	PhCHO eq.	Stirring temp. (in ^{o}C)	Stirring time (hr.)	SM recovered (%)
1	10	-78	6	-95	5	91
2	20	-78	12	-78	18	89
3	30	-80	12	-78	24	85
4	40	-80	24	-40	24	73
5	40	-80	24	0	4	-
6	40	-80	24	RT	24	-
7	40	-80	24	RT	56	-
8	40	-80	24	RT	76	0
9	40	-80	24	30	24	0

Table:3.19

After trying certain temperature combinations to see at which temperature the starting material starts to get consumed. When the temperature gets lower down to -40^{o}C from -95 ^{o}C, a certain reduction in the recovered amount was observed indicating the consumption of starting material. It can be seen from the figure:3.26 that the starting material (red region) and benzaldehyde (blue region) are still present. When the temperature of the reaction mixture

gets lower to 0ºC and the stirring is increased to 24 hours, complete consumption of starting material is observed. The crude product was obtained after doing the workup.

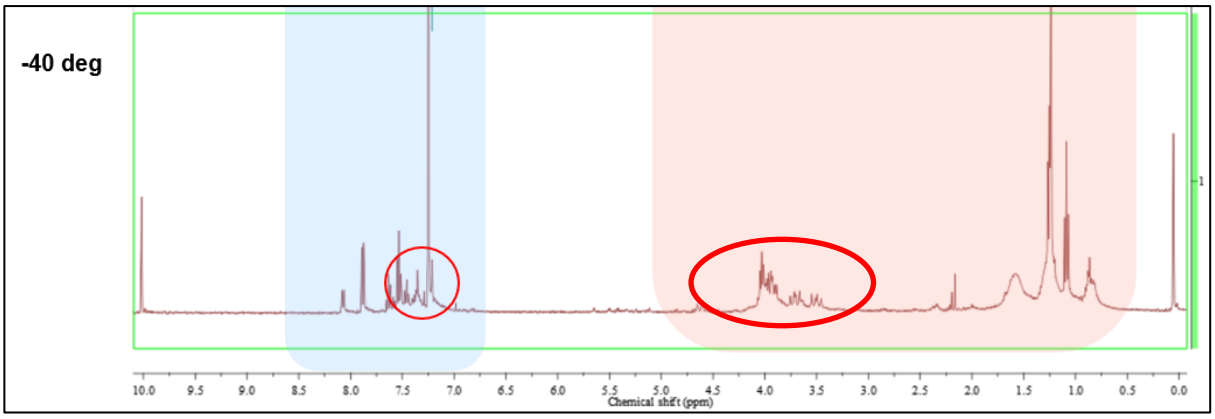


Figure:3.26 (Crude proton NMR of the product when reaction done at -40ºC)

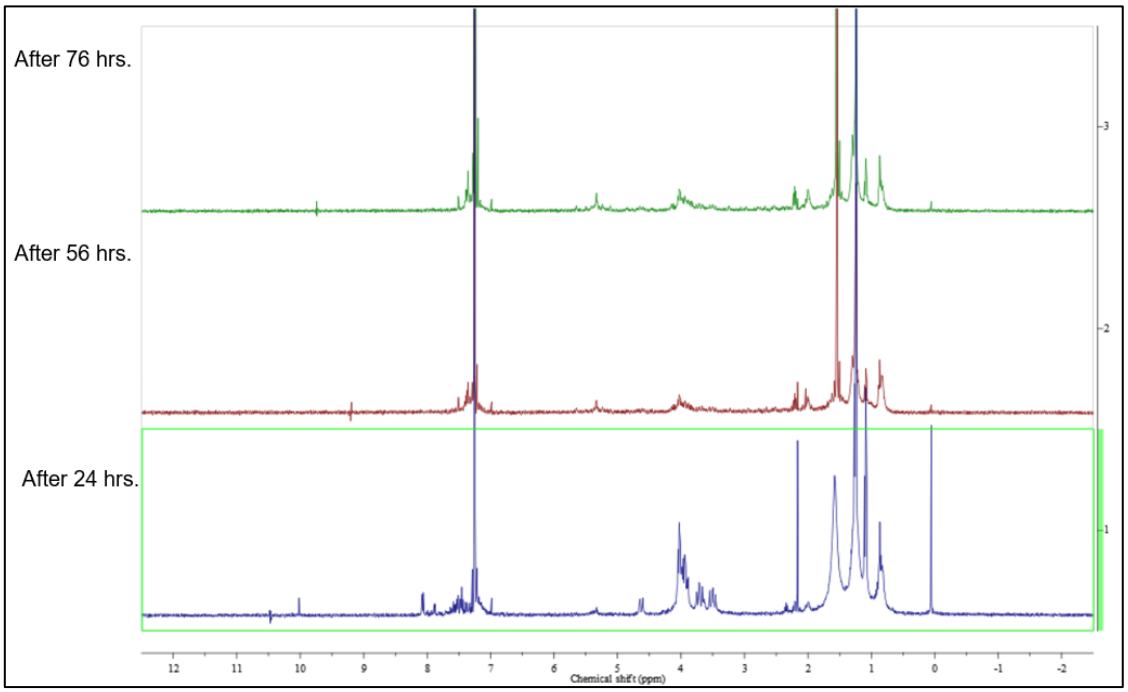


Figure:3.27 (Crude proton NMR of the product after different time spans)

The crude proton NMR showed that the benzaldehyde and the starting material were completely consumed and some new peaks have emerged (refer figure:3.28). The crude product was purified and the product spot was obtained using PTLC. Proton NMR of the purified compound was taken and it shows certain peaks in the aromatic region which corresponds to the benzene moiety attached to the starting compound but the issue was the unknown impurities and side products present with it which were hard to separate.

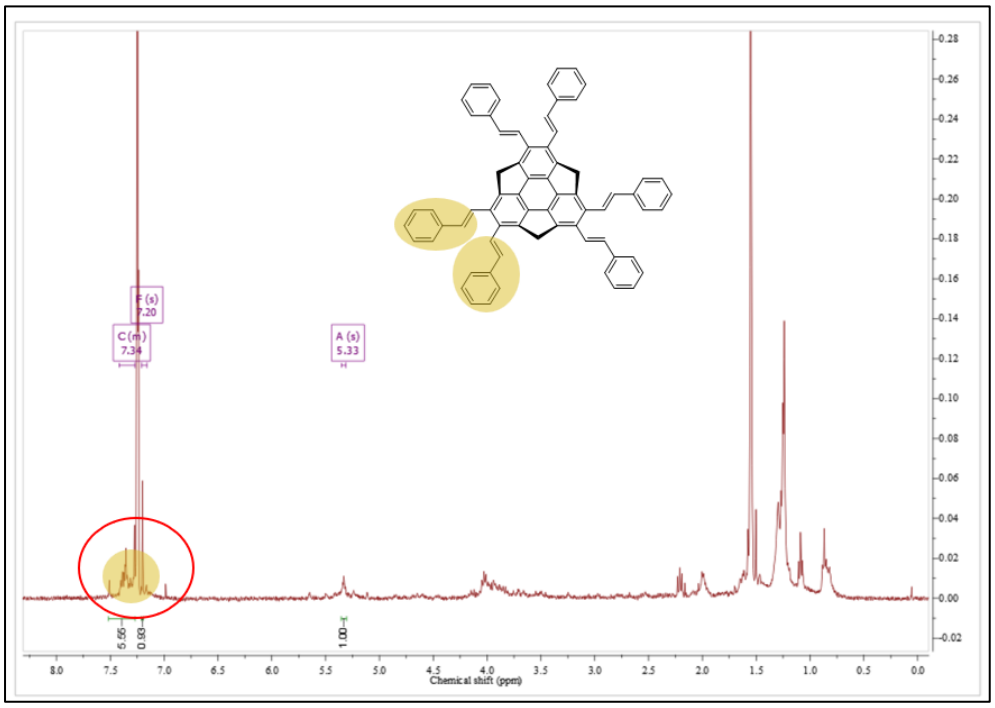


Figure:3.28 (Proton NMR of the pure product obtained after PTLC)

This issue was arising due to the fact that I was using a very strong base which was n-BuLi. It attacked the alpha protons adjacent to the phosphonate group as well as the benzylic protons on the sumanene backbone which would have resulted in the formation of undesired side products rather than the main targeted molecule. In order to synthesize the target molecule, we have to be really careful about the acidity of both types of protons and choose a perfect base that can deprotonate the alpha proton adjacent to the phosphonate group selectively. But paying attention to all these conditions and achieving the selective deprotonation would be a time-consuming task and because of the shortage of time, I decided to move to a different project.

3.8) Sumanene Hexatrifluoromethanesulfinate synthesis:

In this project, my main aim was to successfully synthesize a Hexatrifluoromethanesulfinate derivative of sumanene. The synthesis of this particular derivative was a relatively very straightforward reaction that involved the sulphonation of the bromomethyl group present on the sumanene backbone. The crude product obtained was purified using PTLC in which the solvent system was finalized after trying a variety of different combinations to see which solvent system gave the best separation as shown in table 3.2.

Serial number	Solvent system
1	5:95 (methanol: chloroform)
2	10:90 (methanol: chloroform)
3	10:90 (ethyl acetate: Hexane)
4	25:75 (ethyl acetate: Hexane)

Table:3.2

Among all these tried solvent systems 25:75 (ethyl acetate: Hexane) was found to be giving the best separation and PTLC was done using that to obtain the pure compound (refer figure:3.29).

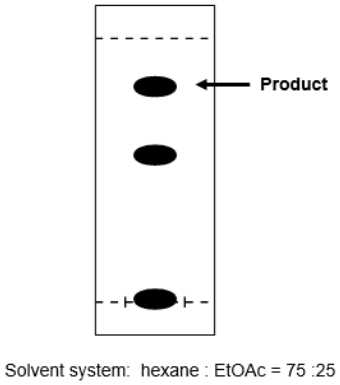


Figure:3.29 (PTLC plate and spots of the crude product)

Once the pure product was obtained the proton NMR was obtained to confirm the formation of the product and check if there are any unwanted impurities or side product present with it or not. The product obtained after PTLC looked really clean with clear and clean peaks of the target molecule with just some solvent residue peaks of ethyl acetate.

From the proton NMR of the purified product, the target molecule can be properly confirmed. The doublet of doublet peaks at a chemical shift of 4.2 ppm and 5.0 ppm represents the benzylic protons of the sumanene backbone. On the other hand, the doublet of a doublet at 4.85 ppm and 5.15 ppm represents the two alpha protons adjacent to the trifluoro sluphinate group. This result was also confirmed by analyzing the peaks by checking the coupling constant of the peaks. The coupling constant of the doublet of doublet peaks at 4.85 ppm and 5.15 ppm was found to be 14.18 Hz each while the coupling constant of the doublet of doublet peaks at a chemical shift of 4.2 ppm and 5.0 ppm was found to be 19.21 Hz and 19.67 Hz which are very similar so can be termed as a doublet of double (refer figure:3.3).

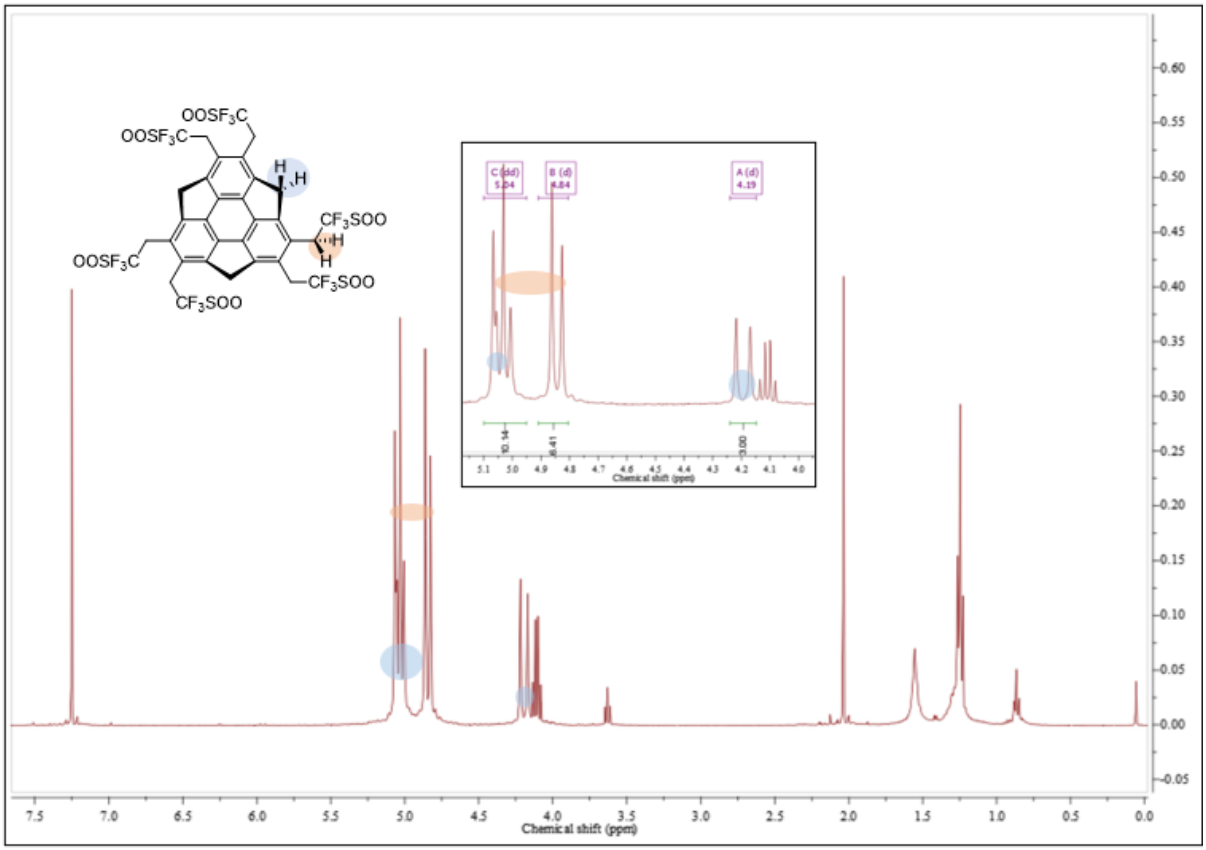


Figure:3.3 (Proton NMR of the purified product)

After confirming the proton NMR, The ^{13}C NMR was taken to further characterize the target molecule. The carbon NMR of the obtained molecule looked clean with clear peaks. The peaks corresponding to each carbon can be found in the NMR spectra (refer to Figure 3.31).

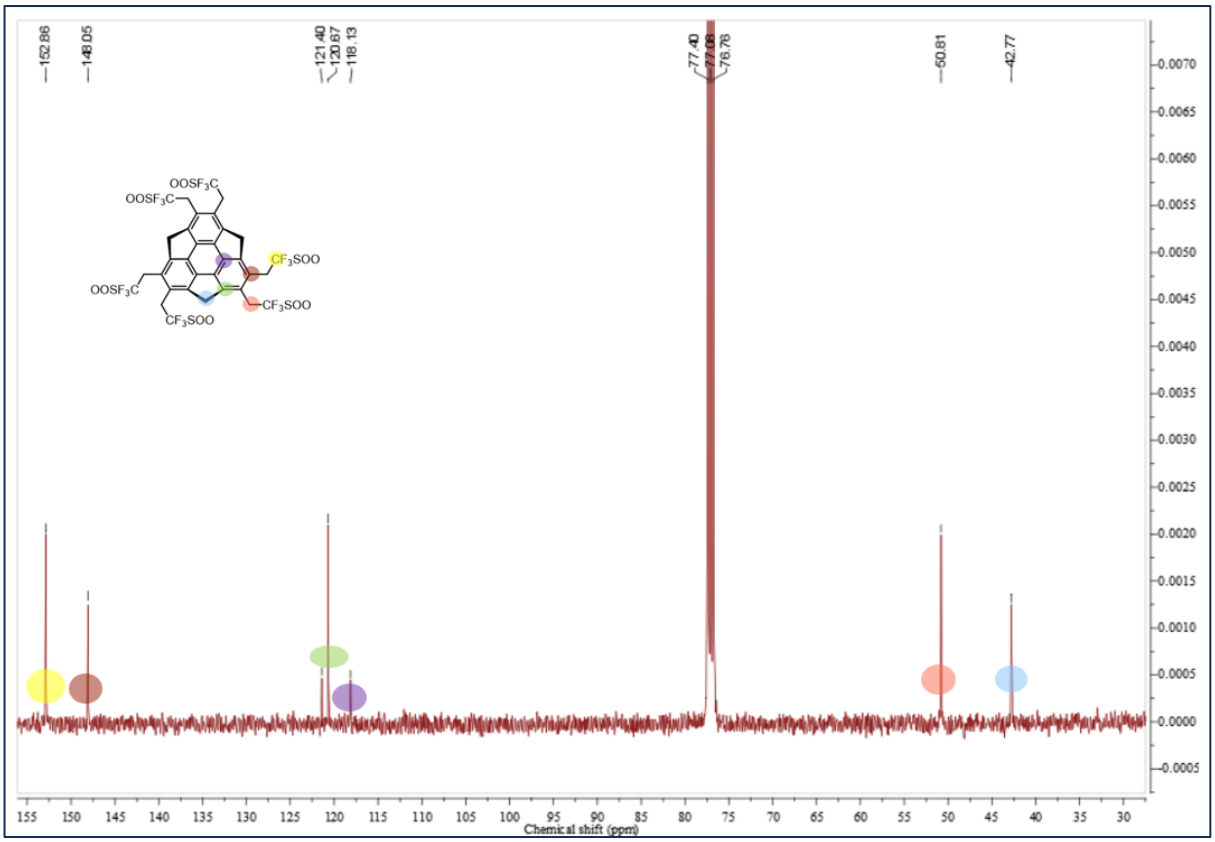


Figure:3.31 (13C NMR of the purified product)

For other confirmatory tests, an IR analysis experiment was also conducted (refer to Figure 3.32).

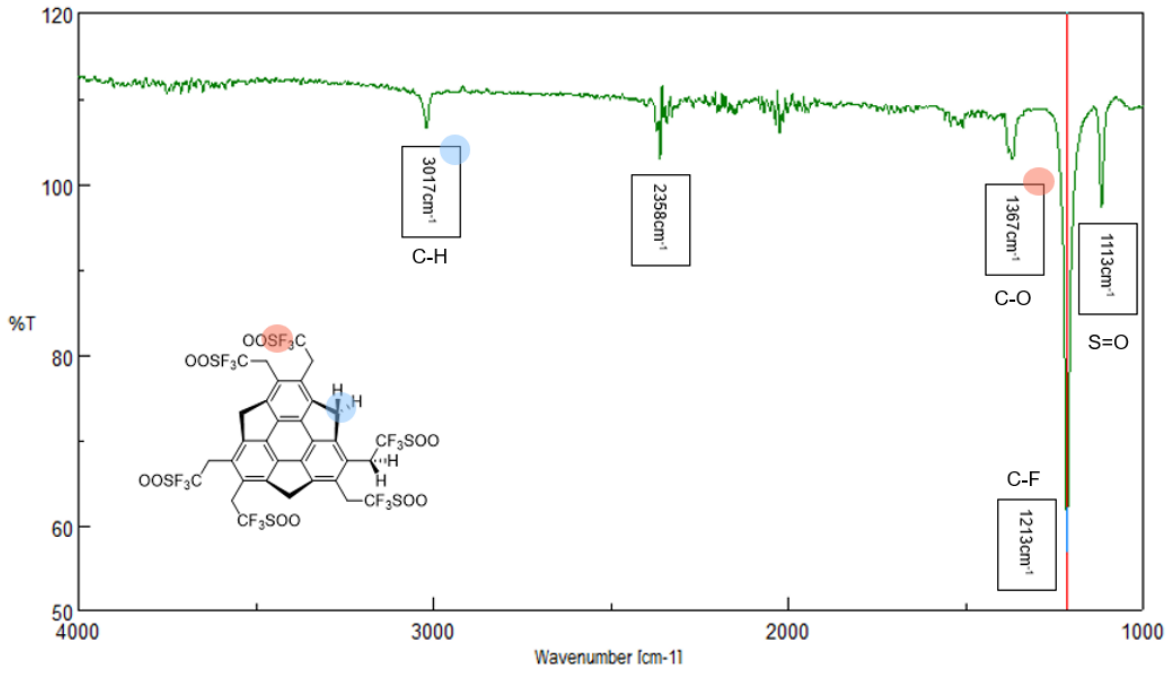


Figure:3.32 (IR plot of the obtained pure compound)

From the IR analysis the stretching frequencies of some of the characteristic bonds such as C-F, C-C, C-H and S-O bonds present in the purified target molecule. From the obtained IR spectra of the synthesized molecule we can infer that the peaks at 1113cm^{-1} represent the S=O double bond stretching frequency. The long peak at 1213cm^{-1} represents the C-F bond stretching frequency which confirms the presence of the C-F bond in the target molecule. On the other side, the peaks at 1367cm^{-1} and 3017cm^{-1} correspond to the C-O and C-H (benzylic) stretching frequencies respectively which helped in the further characterization of the synthesized target molecule.

With the confirmation of the target molecule, this molecule (Sumanene Hexatrifluoromethanesulfinate) can be utilized for various purposes among which can be utilized for further reactions.

3.9) Synthesis of [2+1] Sumanene Hexatrifluoromethanesulfinate cycloadded molecule to C_{60}:

With the available time left, after the successful synthesis of Sumanene Hexatrifluoromethanesulfinate, an opportunity to try a [2+1] cycloaddition of it on the C_{60} molecule appeared. Sulfinate derivative molecules are very well known for their ability to undergo [2+1] cycloaddition on the C_{60} molecule.

With the available 9 mg of the starting material (Sumanene Hexatrifluoromethanesulfinate), two batches of reactions were set up to rest this reaction. For the first batch, 4 mg of the starting material was used to set up the reaction but I failed in recovery of the final product during the centrifugation step. The main reason behind this would be the very low concentration of the product in the centrifugation tube.

In the second batch where 5 mg of the starting material was utilized, the crude product was obtained nicely via centrifugation. The crude product obtained was analyzed via proton NMR and 13C carbon NMR.

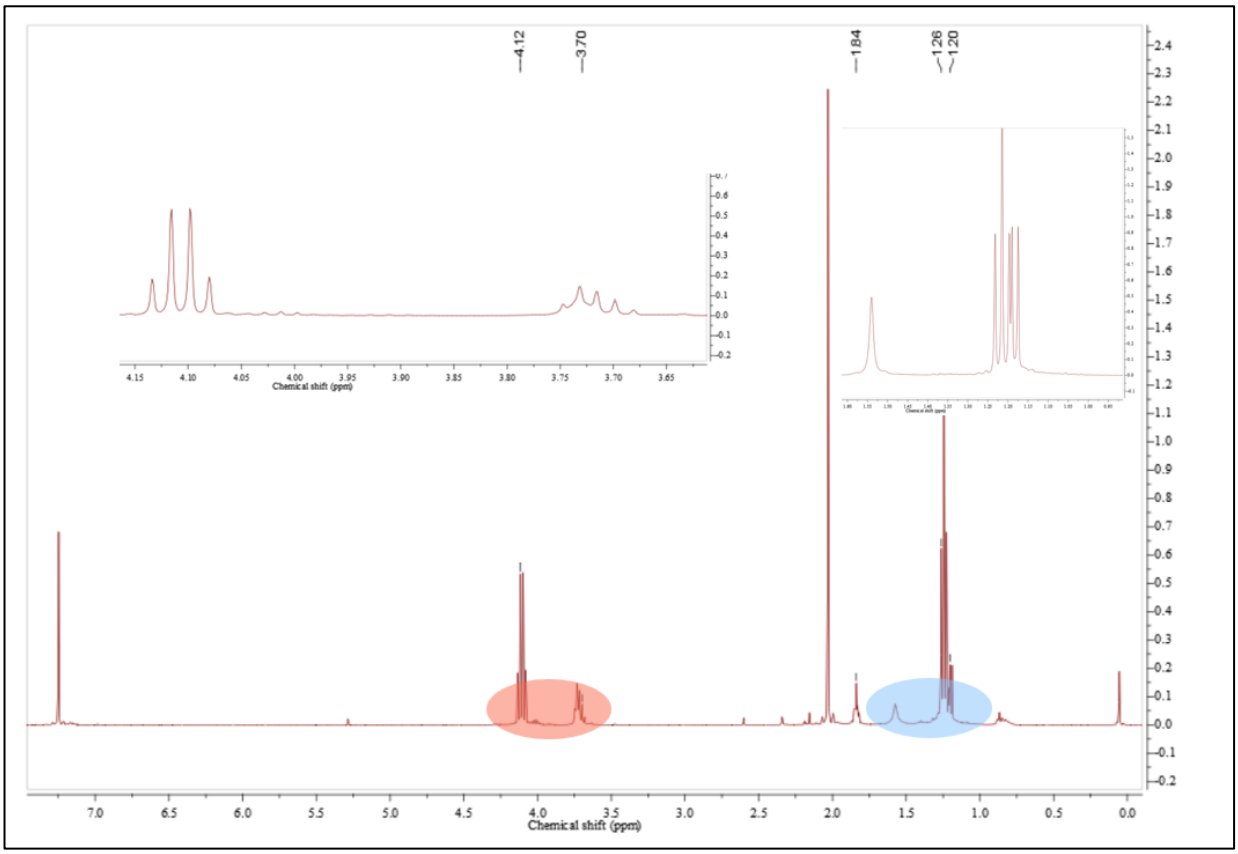


Figure:3.33 (Proton NMR of the purified product)

The peaks appearing in the proton NMR of the crude product correspond to a lot of solvent impurities that involve ethyl acetate and ethanol contamination. Apart from the solvent contaminant peaks, peaks appearing at 1.20 ppm (doublet), 1.85 ppm (singlet), and 3.70 (multiplet) represent the formed products. Also, the peaks corresponding to the starting material were not visible in the crude NMR.

The major observation was that the peaks that represent the benzylic protons on the sumanene moiety were not visible on the crude NMR, which tells us that during the addition of the base the benzylic protons of the sumanene moiety were also deprotonated with the alpha proton adjacent to the sulfinate group, which eventually led to a formation of an unwanted product giving an unconventional proton NMR.

The same observations were observed with the carbon NMR (13C NMR) as the solvent peaks were so dominant that even the C_{60} peak was not visible. Another possible explanation for this observation could be the very low concentration of the crude product because of the small-scale synthesis attempt.

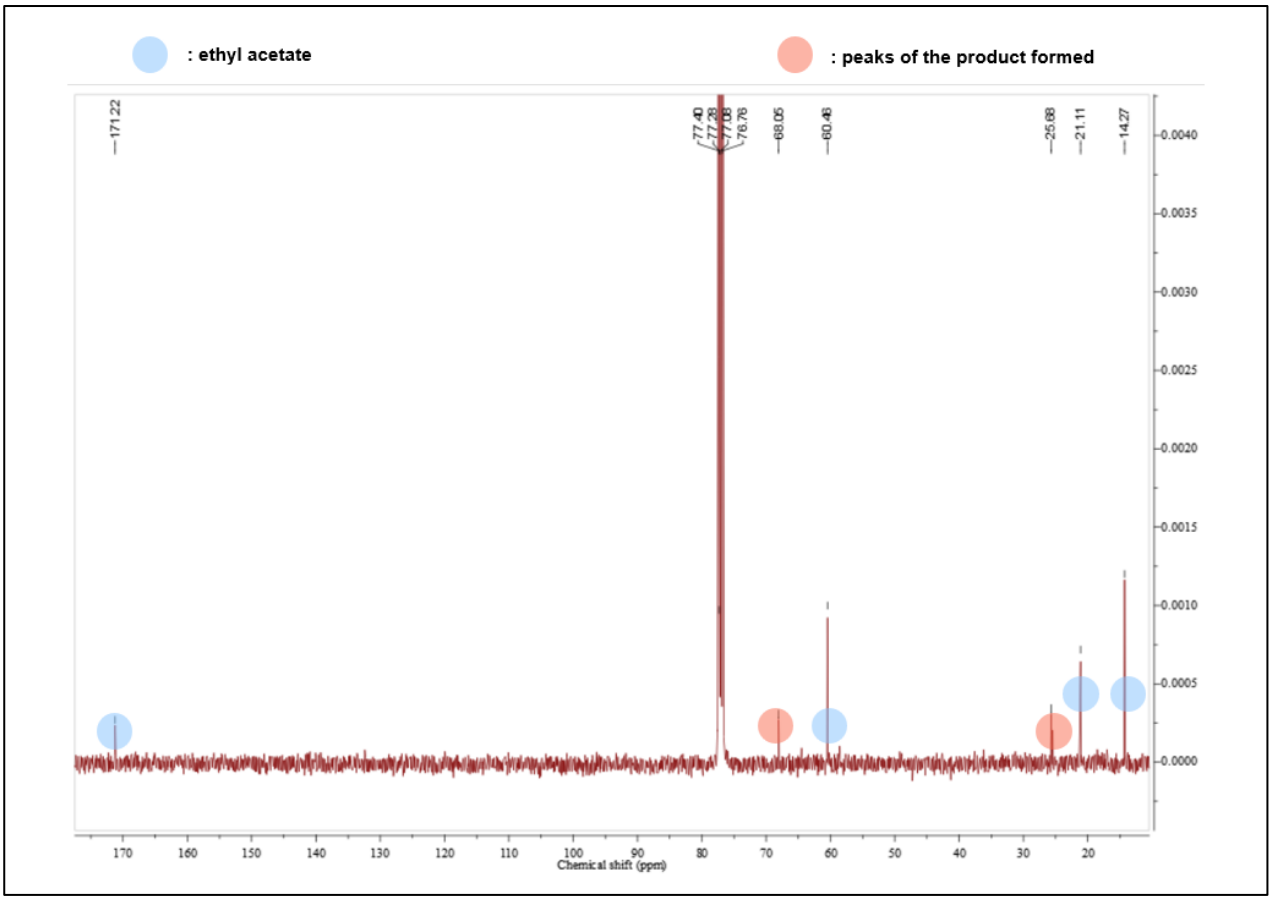


Figure:3.34 (13C NMR of the crude product)

For future trials of this reaction, a relatively large-scale reaction can be set up to give a good amount of product, also the equivalents of the reagents that were being added to the reaction mixture could be altered especially the amount of cesium carbonate for the selective deprotonation of the alpha proton adjacent to the sulfinate group rather than the benzylic protons to prevent the formation of any other unwanted product formation, also the equivalents of C_{60} fullerene should be increased to 300 mol%.

CHAPTER 4: Conclusion

The main aim of my master's project was to inspect the chemical reactivity of the sumanene molecule over trials with different reaction conditions. Sumanene is a significantly reactive molecule. Talking about the reactivity of sumanene, the periphery of the molecule (the aromatic and benzylic region) shows the most reactivity of the molecule. The main reason behind it is the presence of the availability of acidic protons on its periphery which can be deprotonated to pave the way for the attack of different substituent groups. Bases of different reactivity ranging from mild bases such as potassium tert-butoxide to relatively strong bases such as n-butyl lithium are utilized for deprotonation purposes. Once deprotonated, various types variety of reactions can be performed on the molecule to obtain new molecular derivatives. Sumanene because of its unique design has always been a very interesting molecule to study because of its special and unique structure.

Despite its unique structural properties, sumanene proved to be a very difficult molecule to work upon mainly because of its unique structure and different deprotonation sites also including its sensitivity towards basic conditions. This difficulty led to a vast number of synthetic failures and successful synthesis of some characterizable derivative compounds including Sumanene Hexatrifluoromethanesulfinate during the span of this master thesis.

Apart from all this Sumanene proves itself to be a versatile molecule. Also, with the successful synthesis of the Sumanene Hexatrifluoromethanesulfinate molecule, its reactivity scope can be stretched further.

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