Design, Synthesis, Characterization and Redox Properties of Planar and Non-planar Macrocycles Derived from Thiophene Subunits

A Thesis

Submitted in Partial Fulfillment of the Requirements

For the Degree of

Doctor of Philosophy

By

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Dedicated to

My Parents

ShriRamNarain Gaur &Smt. Indravati Gaur,

My Sisters

Renu&Neha,

And

My All Teachers

IISER PUNE

Certificate

Certified that the work described in the thesis entitled**"*Design, Synthesis, Characterization and Redox Properties of Planar and Non-planar Macrocycles Derived from Thiophene Subunits*"**Submitted by Mr. Rakesh Gaur was carried out by the candidate, under my supervision. The work presented here or any part of it has not been included in any other thesis submitted previously for the award of any degree or diploma from any other university or institution.

Date:07.10.2019

V. G. Anand

Research Supervisor

Declaration

I hereby declare that thesis contains original research work which represents my ideas in my own words and wherever other's ideas have been included, I have adequately cited and referenced the original sources. I also declare that I have adhered to all principles of academic honesty and integrity and have not misrepresented or fabricated or falsified any idea/data/fact/source in the submission. I understand that violation of the above will result in disciplinary actions by the Institute and can also evoke penal action from the sources, which have thus not been properly cited or from whom appropriate permission has not been taken when needed.

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Contents

Chapter-3.B: Synthesis & Characterization of Ortho-Phenylene-Bridged Hepta and Octathiophene Macrocycles

The thesis entitled "***Design, Synthesis, Characterization and Redox Properties of Planar and Non-planar Macrocycles Derived from Thiophene Subunits***" describes planar and non-planar macrocycles by modification in thiophene based cyclizing units, which were found to resemble antiaromatic isophlorin framework. Generally antiaromaticity is considered to destabilize π electrons delocalization in comparison to their aromatic analogs. This thesis presents the successful attempts at the synthesis of stable antiaromatic thiophene based macrocycles which belongs to the class of core-modified expanded isophlorins. The first 18π macrocycle similar to [18]annulene came suggested by Woodward during the synthesis of an 18π porphyrin ring, through the oxidation of an unstable antiaromatic 20π intermediate, termed as "isophlorin". It was discovered while attempting the synthesis of Vitamin B_{12}. Since then, there have been continuous efforts to isolate the unstable 20π intermediate for exploring the chemistry of anti-aromatic molecules. Porphyrin and its higher analogs are classical examples of macrocycles with extended conjugation. Large expanded porphyrins derived from pyrroles and other heterocycles such as furan/thiophene/selenophene have been widely reported in literature.

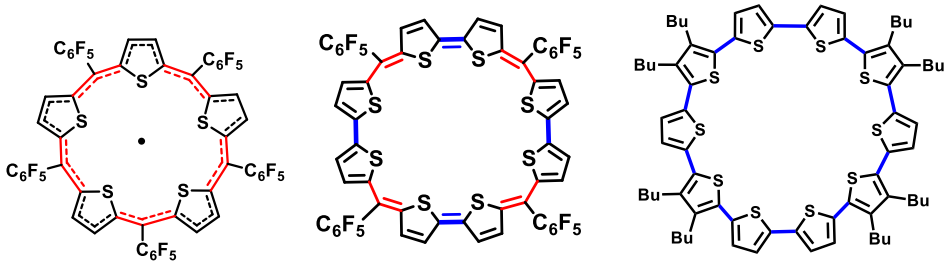
In chapter one, provides a brief introduction to one pot synthesis of porphyrinoids bearing four to twelve pyrroles having corresponding number of meso carbons by reacting pyrrole with pentafluorobenzaldehyde under modified Lindsey conditions. However, for the better understanding of π conjugation in giant conjugated systems it is necessary that it flows through sp^2 carbon framework. Possible ways to avoid the interference of N in the conjugation can be achieved if we have amine like N in the conjugated molecules or by replacement of all pyrrole subunits by small aromatic units like benzene, thiophene and furan. Later, the first thiophene derived annulene with three sulfur. Similarly, higher analogues of 18π annulene such as tetrathia[20]annulene[2,0,2,0] and hexathia[30]annulene[2,0,2,0,2,0] were synthesized by McMurry coupling of 2,2'-bithiophene-5,5'dicarboxaldehyde under high dilution conditions. The chemical shift values observed for the protons of these macrocycles bear resemblance to the protons of unsubstituted thiophene. Therefore the ^1H NMR spectrum revealed lack of effective delocalization of π electrons, in spite of complete conjugation in the macrocycles. The first neutral aromatic annulene which was derived from thiophene was the tetrathia [22]annulene[2,1,2,1]. It was synthesized using multistep procedure. In comparison to the above described thiophene derived annulenes, this macrocycle bears additional meso carbon bridges which facilitates the macro-cyclization of all the four thiophenes in the same plane. Presence of methine carbon bridges plays a very important role in enabling macrocycle to gain a planar structure and hence enhanced the conjugation between the thiophene sub units. Enlarging the conjugation by introducing

methane carbon bridge, offers a unique way to synthesize macrocyclic conjugated oligothiophenes. But invariably the realization of such giant macrocycles has been tedious due to the multi-step synthetic approach.

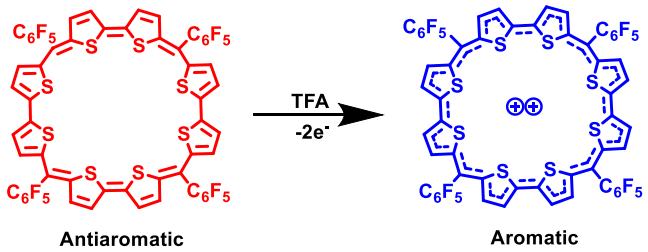
Later attempts were made to synthesize octaethyltetrathia isophlorin having methane bridges in between thiophene subuits. Similarly one-pot synthesis of pentathiaisophlorin having meso carbon linked with pentaflorobenzene showing cationic, anionic and radical character was achieved from commercially available thiophene and pentafluoro benzaldehyde. Bauerle and co-workers have successfully synthesized cyclco[n]thiophenes, bearing ten to thirty-five thiophene subunits. The same group later reported a series of cyclo(n)thiophenes bearing 12, 14 and 16 thiophene units. Similar such macrocycles were also synthesized by Iyoda and co-workers, in which the acetylene linked thiophenes were used as oligomers. The ^{1}H NMR spectrum of these macrocycles did not reveal significant ring current effects indicating the benzenoid nature of the macrocycles. This asserts the lack of effective π orbital overlap between adjacent thiophene unit and hence the absence global aromatic features for the macrocycles.

Most of these syntheses mentioned above account for multiple step synthesis which hampers the further investigation of these expanded thiophene based macrocycles. Here in this thesis aims to develop simple synthesis of thiophene based macrocycles which are having *alpha alpha* coupled thiophene units in combination with methane bridges to achieve effective delocalization of π electrons. In a quick analysis of the initial work it has been observed that these cyclic molecules even after having complete conjugation tend to loose planarity. They generally adapt to different morphologies which are generally classified as twisted shape, saddle shape and figure-eight configurations. In this thesis, the first V-shaped macrocycle for an expanded core-modifies isophlorin with 32π electrons will be discussed. Also these macrocycles with thiophene units are found to be stable and anti-aromatic macrocycles which display interesting redox properties.

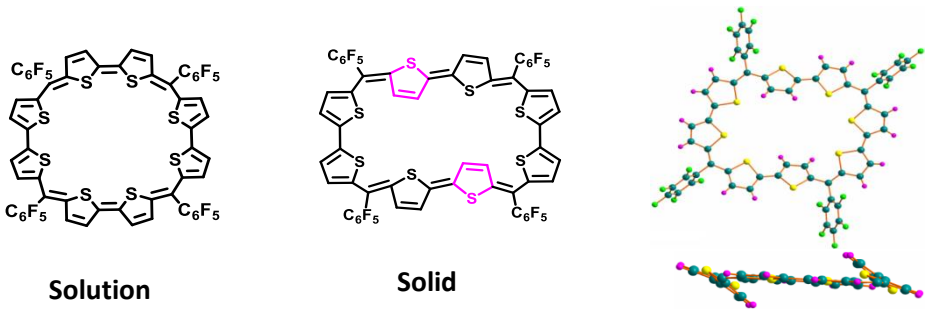
As mentioned above synthesis octaethyl tetrathia & pentathia isophlorin having methane bridges in between thiophene subuits and the one-pot synthesis of pentathiaisophlorin having meso carbon linked with pentaflorobenzene showing cationic, anionic and radical character was achieved from commercially available thiophene and pentafluoro benzaldehyde. These macrocycles are having meso carbon bridge between every two thiophene units, whereas Bäuerle & co-workers reported sunthesis of oligothiophenes ranging from ten to thirty two no of thiophene which are completely ∝-∝ connected. These two structural differences motivated us to synthesize oligothiophene which may have both *meso* carbon and ∝-∝ connection alternatively in the same macrocycle.



In 2008 it was shown that 2-pentafluorophenylhydroxymethyl furan undergoes self condensation by an acid-catalyzed reaction, followed by $FeCl_3$ oxidation resulting in the formation of 20π tetraoxaisophlorin. In the similar way we also designed our simple one pot synthesis, where bi-thiophene mono-ol undergoes self-condensation in presence of acid, followed by oxidation employing DDQ. A range of aromatic, antiaromatic and unstable radical were identified in the reaction mixture. Significantly, a 36π conjugated macrocycle with eight thiophene and four meso carbons was isolated from column chromatography. Appropriate analysis enabled to confirm this macrocycle as a antiaromatic system. It could be easily oxidized to 34π aromatic system. This molecule was comprehensively studied by spectroscopic techniques such as ^1H NMR, Uv-Vis absorption and single crystal X-ray diffraction along with computational studies.

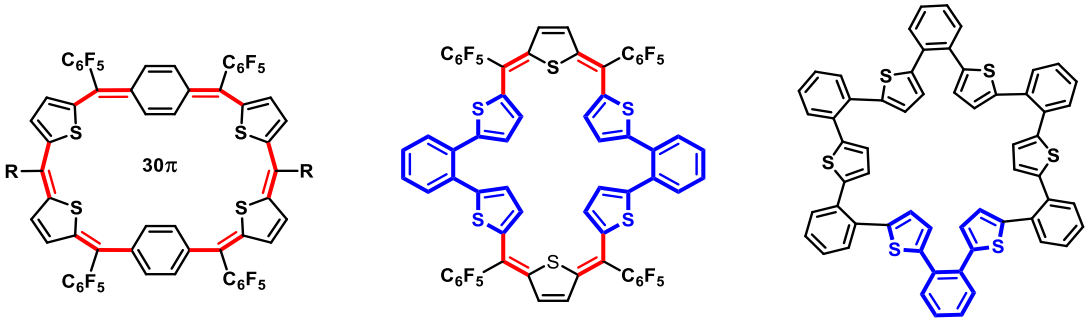


In the above studies it was found that molecule is displaying different types of conformation in solution and solid state.

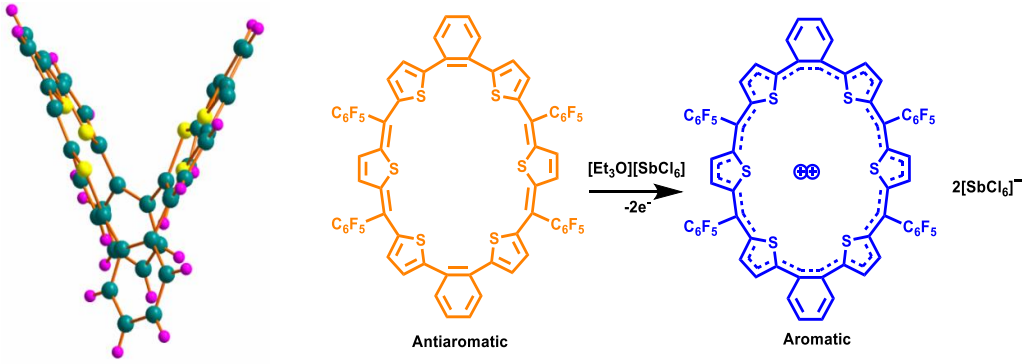


Similar such macrocycles with six, ten and twelve thiophene were also identified in the reaction mixture. However, low yields of hexa thiophene and dodeca thiophene system and the instability of deca thiophene hampered the further analysis of these macrocycles.

In continuation on these studies, introduction of benzene into the π circuit of such conjugated systems is expected to display interesting structural and electronic properties. It is reported that 30π conjugated system with *meso* carbon between every subunits in macrocycles shows global conjugation. In an another report, Osuka and co-workers successfully avoided the bridging carbons in between and connected the thiophenes ortho to each other on the benzenes. These nanorings displayed a highly twisted conformation. Keeping these two different successful studies, we planned our synthesis with the thiophenes connected ortho to each other on the benzenes and *meso* carbons in the macrocycle.



In third chapter, by amalgamating above two concepts, a simple synthetic strategy was designed by employing acid catalyzed condensation of dithienyl-benzene and thiophene-di-ol and further oxidized using DDQ. This condensation results in the formation of single 32π conjugated macrocycle with six thiophene units, two benzene and four meso carbons and further purified by coloum chromatography. Suitable analysis enabled to confirm this macrocycle as a antiaromatic system. It could be easily oxidized to a 30π aromatic dicationic system. This molecule was analyzed by spectroscopic techniques such as ^{1}H NMR, Uv-Vis absorption and single crystal X-ray diffraction along with computational studies.



In the next section of chapter three, expansion of conjugation in the macrocycle was exhaustively attempted by increasing the number of thiophene in the monomers and following the same methodology. Condensation of bithiophene-diol and terthiophene-diol with dithinyl-benzene

resulted in 2:2 and 1:2 condensation owing to the formation of 40π antiaromatic and 34π aromatic system respectively. These systems easily undergo two electron oxidation to give dicationic species, found to be reversible on addition of triethylamine. 40π macrocycle displayed a complex ^{1}H NMR and COSY probably due to its highly non-planar structure. Further it was analyzed through HRMS, Uv-Vis absorption. A 34π macrocycle was also characterized through variable temperature along with the above mentioned spectroscopic techniques.

Chapter-1

Introduction

Aromaticity is one of the most interesting and vastly explored areas due to the strong π electron delocalization in a cyclic molecular framework. Based on Huckel's rule, these molecules are broadly classified as aromatic if they bear (4n+2)π electrons and anti-aromatic molecules, if they account for (4n) number of π electrons along the conjugated pathway respectively[1]. In this context, annulenes represent fine examples for studying the concept of ring current effects induced by π electron delocalization. Systems containing 12 to 18 π-electrons in the conjugated pathway proved the validity of Huckel rule without exception (figure-1). But higher order annulenes having 22 or more π-electrons were found to be insoluble in common organic solvents, thereby hindering further study on larger conjugated systems[2]. Cyclic conjugated systems have attracted considerable attention for their opto-electronic properties, structural intricacy, and synthetic challenges.

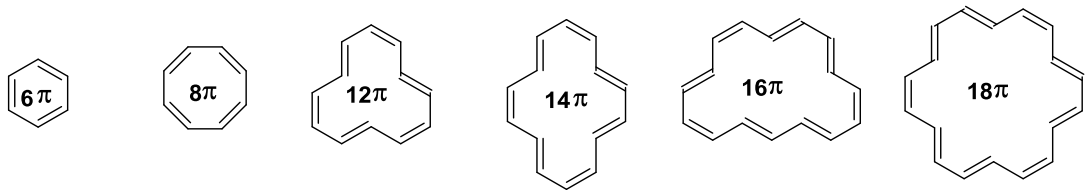
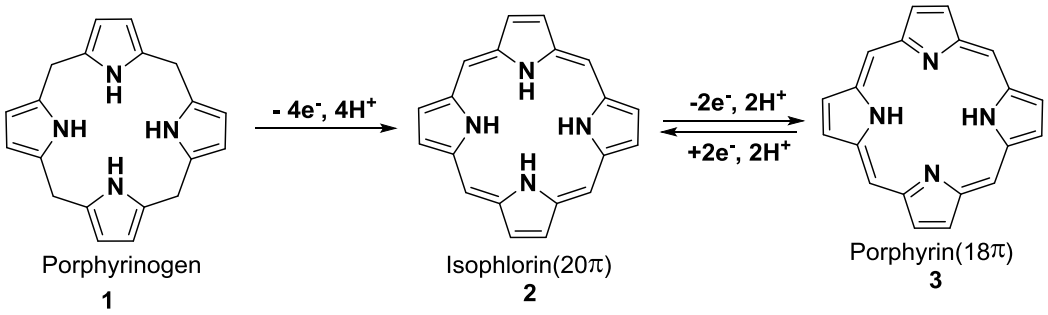


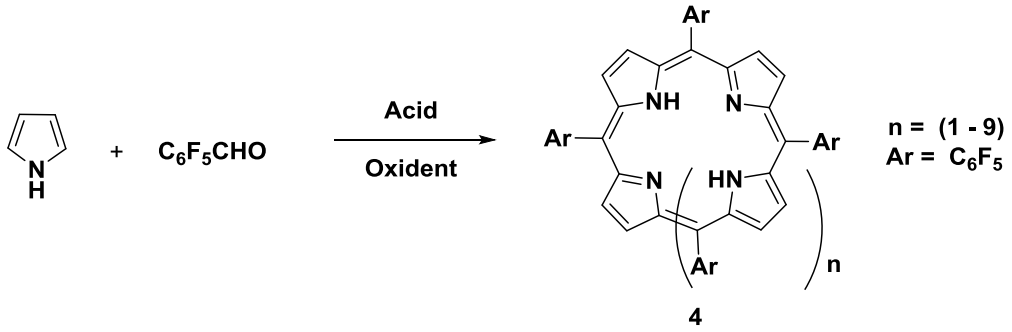
Figure **1**: Annulenes from 6π - 18π system.

Moving toward higher order hetero-annulenes leads to onset of conformational flexibility, which results in the loss of planarity resulting from weak π electron delocalization and consequently displays non-aromatic behavior. Even though 18π annulene satisfies physical criteria of aromaticity, but it also shows similar reactivity as polyenes. In comparison to [18]annulene bridged annulenes, such as 1,6-methano[10]annulene[3], clearly indicates that the rigidity of the ring skeleton is an essential prerequisite for the stability of [4n+2] annulenes where n > 1.

A 18π macrocycle similar to [18]annulene[4] came into picture when Woodward suggested the formation of an 18π porphyrin ring, **3**, through the oxidation of an unstable antiaromatic 20π intermediate, termed as "isophlorin", **2**. It was discovered while attempting the synthesis of Vitamin B_{12}. Since then, there have been continuous efforts to isolate the unstable 20π intermediate for exploring the chemistry of anti-aromatic molecules.



Porphyrin and its higher analogs are classical examples of macrocycles with extended conjugation. Large expanded porphyrins derived from pyrroles and other heterocycles such as furan/thiophene/selenophene have been widely reported in literature[5-9]. In the last two decades, significant advancements in methodologies to synthesize molecules with extended conjugation and their studies resulted in the multidimensional application of these molecules in the area of molecular electronics, molecular recognition and medicines[10-13]. Synthesis of conjugated systems with predetermined size and number of π electrons can be achieved either by increasing the number of conjugated double bonds in between the four pyrrole rings or by increasing the number of pyrrole rings in the macrocycle. In 2001, Osuka and coworkers reported[14] a one pot synthesis of porphyrinoids having four to twelve pyrroles with corresponding number of meso carbons by reacting pyrrole with pentafluorobenzaldehyde under modified Lindsey conditions (scheme-1).

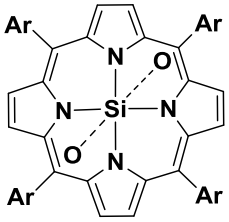


Scheme-**1**:Acid catalyzed condensation of pyrole and pentafluoro-benzaldehyde.

These porphyrinoids can be viewed similar to larger unknown annulenes and therefore are also known as aza-annulenes due to incorporation of N atom along the conjugated pathway. However, for a better understanding of π conjugation in giant conjugated systems it is necessary that it flows through sp^2 carbon framework. Possible ways to avoid the interference of N in the conjugation can be achieved with amine like nitrogen in the

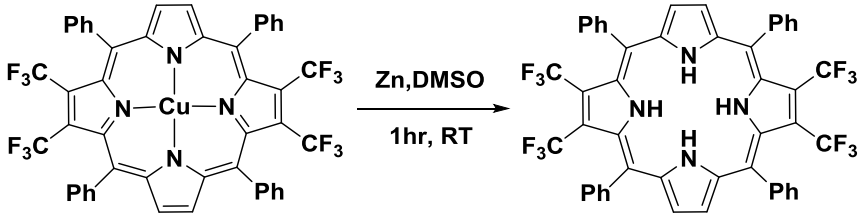
conjugated molecules or by replacement of all pyrrole subunits by small aromatic units like benzene, thiophene and furan.

In 2005, a silicon complex of antiaromatic porphyrin was reported by Vaid and coworkers[15], who described the synthesis of Si(IV)porphyrin, **5**, by the reduction of $Si(TPP)Cl_2$ with two equivalents of Na/Hg in THF (TPP is Tetraphenylporphyrinto). A detailed analysis lead to the identification of macrocycle in -4 oxidation state upon complexation with silicon. Single crystal X- ray diffraction studies revealed that though there is a unique C-C bond length alteration along the periphery, it also clearly indicated the flow of conjugation through carbon framework. However, the structure of molecule was highly ruffled in nature.



5

Later, in 2007, a serendipitous discovery of β-tetrakis(trifluoromethyl)-meso-tetraphenylporphyrin **7** was achieved[16] upon the addition of activated Zinc powder into a DMSO solution of Cu (II) β-tetrakis(trifluoromethyl)-*meso*-tetraphenylporphyrin under inert conditions (scheme-2). Single crystal X-ray diffraction analysis of the isolated product, **7**, revealed it as a 20π isophlorin with a nonplanar saddle conformation.

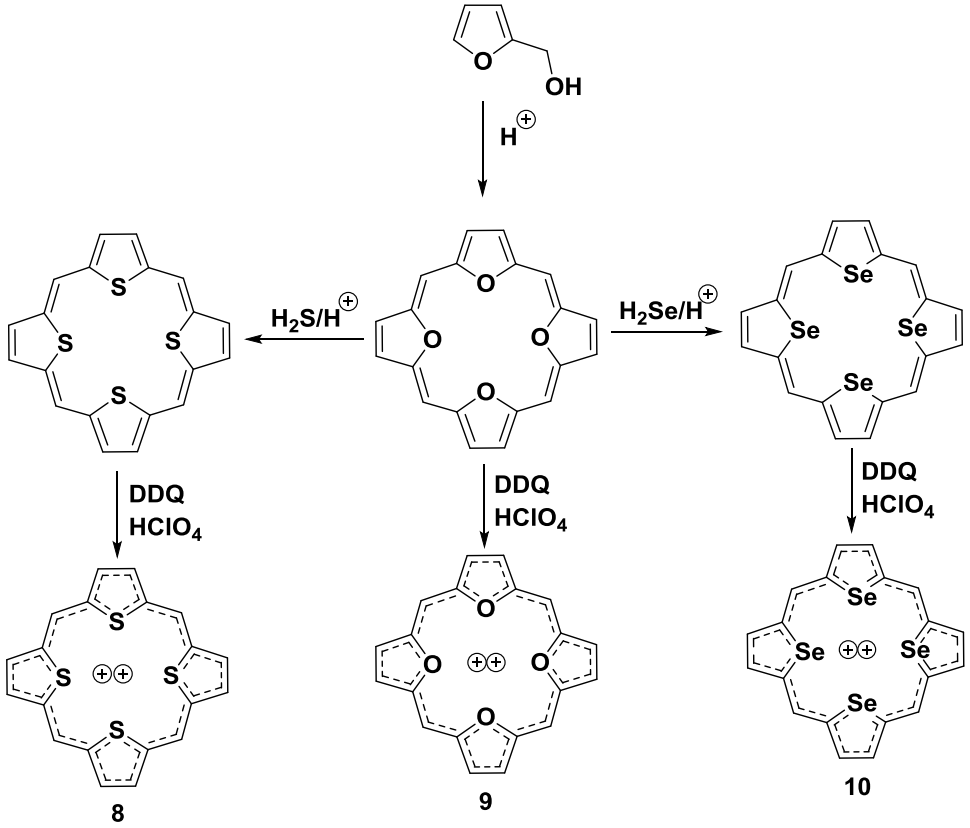


6 **7**

Scheme-**2**: Demetalation of Cu (II) Beta-tetrakis(trifluoromethyl)-meso-tetraphenylporphyrin.

In past, many attempts were made to prepare isophlorins having subunits other than pyrrole and their redox studies displayed interesting results not familiar to porphyrin. Vogel and coworkers pioneered the synthesis of macrocycles with thiophene, furan or selenophene as their subunits[17]. These molecules resemble the 20π isophlorin, 2, in their

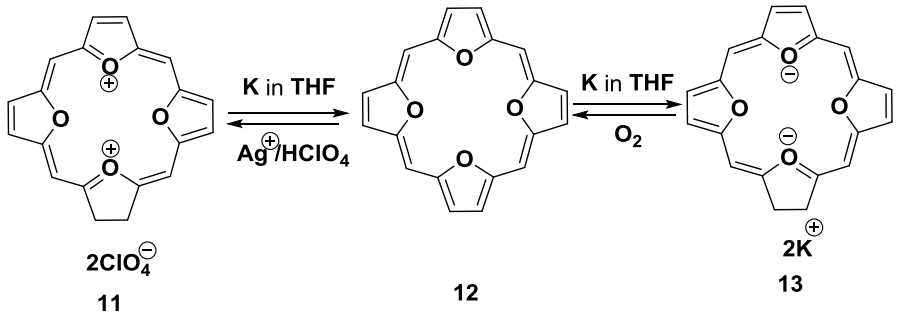
neutral state and undergo two-electron oxidation easily to yield 18π porphyrin dication[17b]. They reported the porphyrin analog of a tetrathia-porphyrin **8**, dication having meso carbon between adjacent thiophene units[17c], similarly they also synthesized porphyrin analog of tetraoxa-porphyrin **9**, dication in three steps from furfuryl alcohol(scheme-3). Single crystal X-ray diffraction of these two cationic species revealed the displacement of thiophene rings from the mean plane of macrocycle, where as in another case it was found to be planar. The reason for this is attributed to difference in the Vander-wall radii between oxygen and sulphur atoms.



Scheme-**3**: Synthesis of macrocycles derived from thiophene/furon/selenophene from furfuryl alcohol and their oxidation.

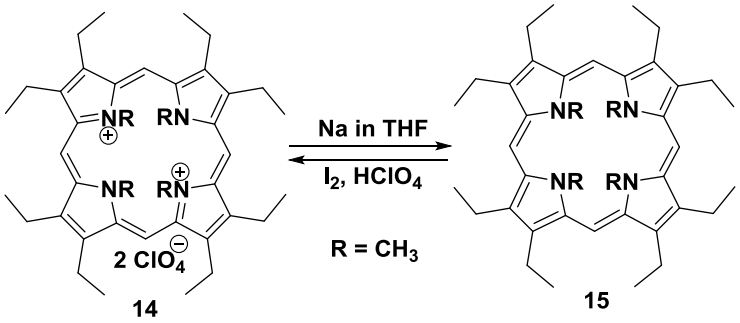
The synthesis of unsubstituted tetraoxaporphyrin was achieved by a two electron reduction of its corresponding dication using potassium in THF under anhydrous conditions.[18] The reaction easily proceeds further resulting in the formation of dianion of tetraoxaporphyrin, **11**. The neutral tetraoxaporphyrin was isolated as black air sensitive crystals (stored at -78°C) by two-electron oxidation of its dianion. The *meso* proton of **12** was found to resonate at -0.3 ppm in its ^{1}H NMR spectrum suggesting a strong paratropic

ring current effect. Single crystal X- ray diffraction confirmed a planar structure for **12**, but the nature of bonding along the periphery was inconclusive due to static and dynamic disorder.



Scheme-**4**: Synthesis of neutral tetraoxaisophlorin by two-electron reduction of corresponding dication which further reduce to its dianion in presence of potassium.

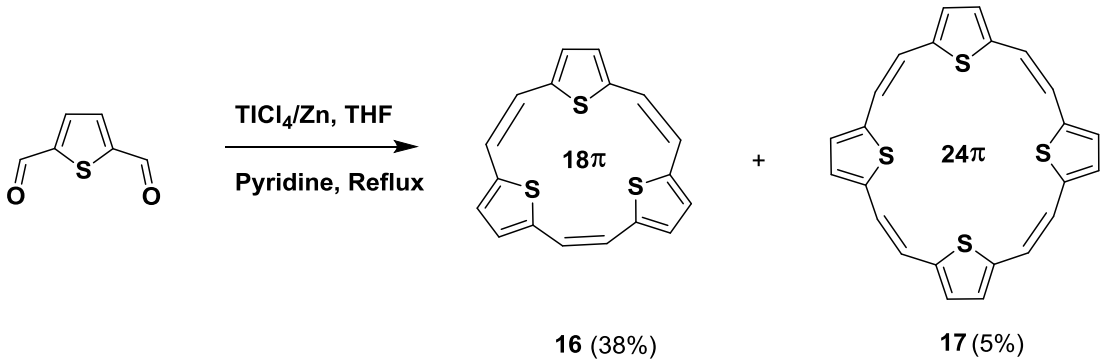
A little later, the octaethyl derivative of neutral N,N',N",N'"-tetramethylisophlorin **15** was synthesized by a two-electron reduction of N,N',N",N'"-tetramethyl-octaethylporphyrin dication, **14**, using sodium in THF (scheme-5).[17d] In comparison to the highly reactive tetraoxaisophlorin, it was found to be moderately stable when exposed to air. The *meso* proton resonated at 4.95 ppm in its ^{1}H NMR spectrum, and down field shifted by 5.3 ppm in contrast to tetraoxaisophlorin. This shift implied the structure induced loss of paratropism for this macrocycle. Solid state study of this molecule i.e. single crystal X-ray diffraction displayed a saddle shaped conformation with *syn, anti, syn, anti*-arrangements of the N-methyl groups.



Scheme-**5**: Synthesis of neutral N,N',N",N'"-tetramethylisophlorin by a two-electron reduction of its corresponding dication.

In 1964, the first thiophene derived annulene **16**, heterocyclic derivative of [18]annulene with three sulfur bridges was reported by Badger & coworkers.[20] Its single crystal X-ray diffraction analysis revealed that all three thiophene units were pushed out of the mean

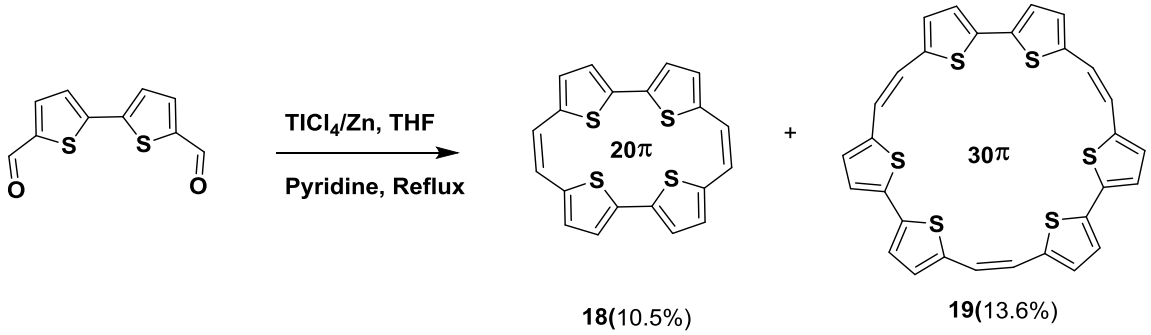
macrocyclic plane leading to loss of planarity. Despite being (4n+2)π electrons system, no significant ring current effect was observed in this 18π annulene as inferred from its spectroscopic properties and hence considered as non-aromatic in nature. Kauffmann and coworkers synthesized a cross-conjugated cyclo[4] and cyclo[6]thiophene by employing bithiophene as precursors. Due to ∝,β - or β,β -linkages of the thiophene units, these systems were found to be faintly conjugated. Later, in 1977 the [24]annulene, tetrasulfide **17**, a higher analog of **16**, was synthesized by using low temperature Witting reaction.[21] In this case too, no ring current effects were observed even though it accounted for 4nπ electrons. It indicated that even though these annulenes have alternate single and double bonds throughout the macrocycle, but it lacked effective conjugation due to unfavorable alignment of π electron orbitals. These two thiophene based annulenes **16** and **17** were synthesized earlier through multistep procedures in low yield. However, Cava and coworkers devised an alternate synthetic methodology (scheme-6) through the McMurry coupling of 2,5- thiophenedicarboxaldehyde[22].



Scheme-**6**: Synthsis of thiophene based annulenes employing McMurry coupling of 2,5-thiophenedicarboxaldehyde.

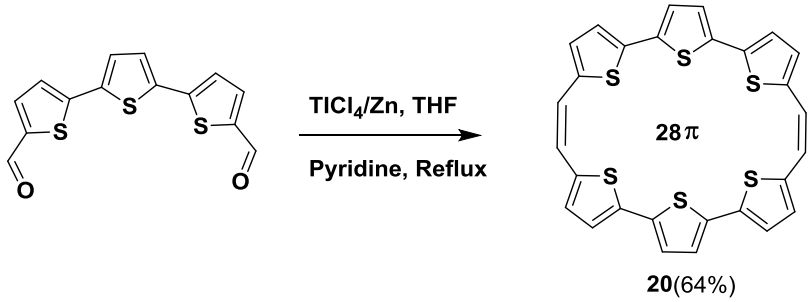
Similarly, higher analogues of 18π annulene such as tetrathia[20]annulene[2,0,2,0] **18** and hexathia[30]annulene[2,0,2,0,2,0] **19** were synthesized by McMurry coupling of 2,2'-bithiophene-5,5'dicarboxaldehyde (scheme-7) under high dilution conditions[22]. These thiophene based macrocycles, **18** and **19**, were separated and found to be stable under ambient conditions. ^{1}H NMR analysis revealed an unexpected aspect of conjugation in these macrocycles. In **18**, three sets of protons were observed as a singlet at δ 6.70 ppm along with two doublets of AB type system at 6.99 ppm and 6.78 ppm, indicative of a symmetrical structure devoid of ring current effects. Similarly, **19** displayed three sets of signals in its ^{1}H

NMR spectrum. They appeared as two doublets at δ 7.05 ppm and 6.98 ppm and a singlet at δ 6.60 ppm. These signals appeared very similar to the chemical shift values observed for the protons in unsubstituted thiophene. Therefore, the ^{1}H NMR spectrum revealed lack of effective delocalization of π electrons, in spite of complete conjugation in the macrocycles.



Scheme-**7**: Synthsis of thiophene based annulenes employing McMurry coupling of 2,2'-bithiophene-5,5'dicarboxaldehyde.

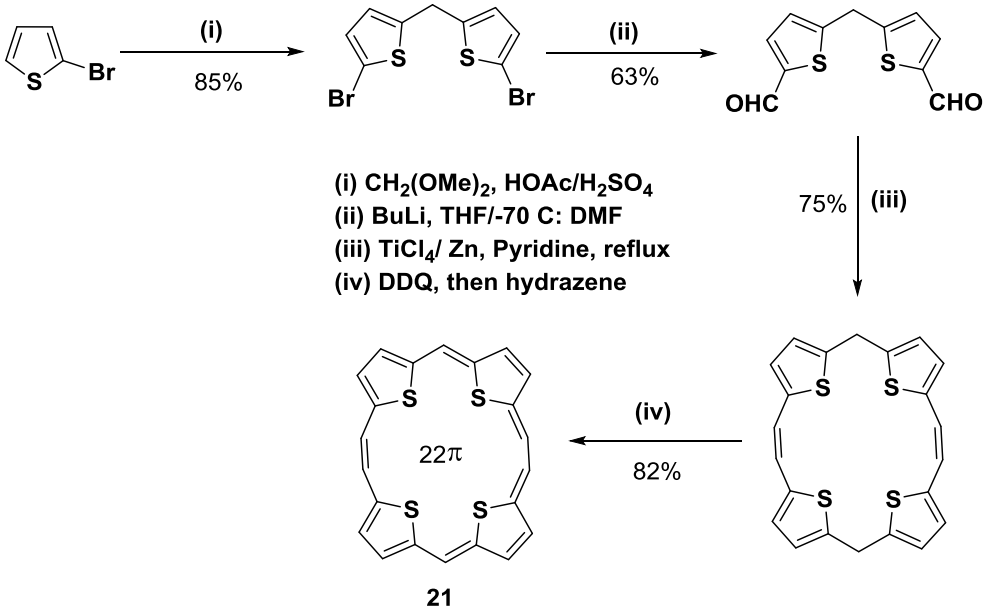
The hexathiahomoporphycene **20** was isolated as the only higher homologue of tetrathiaporphycene in the McMurry coupling of 5,5'-terthiophenedicarboxaldehyde (scheme-8). This macrocycle was found to be moderately stable and displayed two singlets in the range of δ 6.94 to 6.26 ppm suggestive of weak conjugation. Despite the fact that this system accounts for 4nπ electrons, it was considered to be non-aromatic rather than anti aromatic in nature. Therefore, annulenes consisting of thiophene units and *cis* double bonds were perceived to lack effective delocalization of π electrons.



Scheme-**8**: Synthsis of thiophene based annulenes employing McMurry coupling of 5,5'-terthiophenedicarboxaldehyde.

The first neutral aromatic annulene which was derived from thiophene was the tetrathia [22]annulene[2,1,2,1], **21**. It was synthesized by employing a multistep procedure[22] as described in scheme-9. This molecule exhibited two singlets at δ 12.34 and 11.36 ppm corresponding to the protons of methylene and ethylene protons, while thiophene protons

were observed at δ 10.86 and 10.84 ppm. In comparison to the above described thiophene based annulenes(**18**,**19** and **20**), this macrocycle bears additional *meso* carbon bridges which facilitates the macro-cyclization of all the four thiophenes in the same plane. Presence of methine carbon bridges plays a very important role in enabling the macrocycle to gain a planar structure and hence enhances the conjugation between the thiophene sub units.

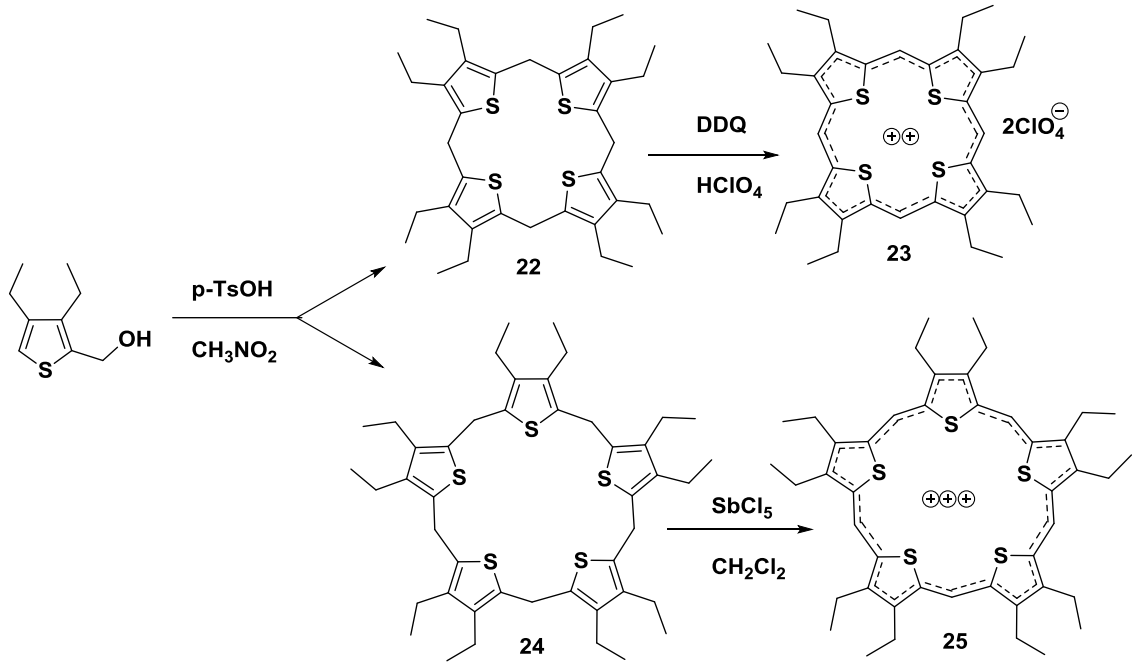


21

Scheme-**9**: Multistep synthesis of tetrathia [22]annulene with additional meso carbon bridges.

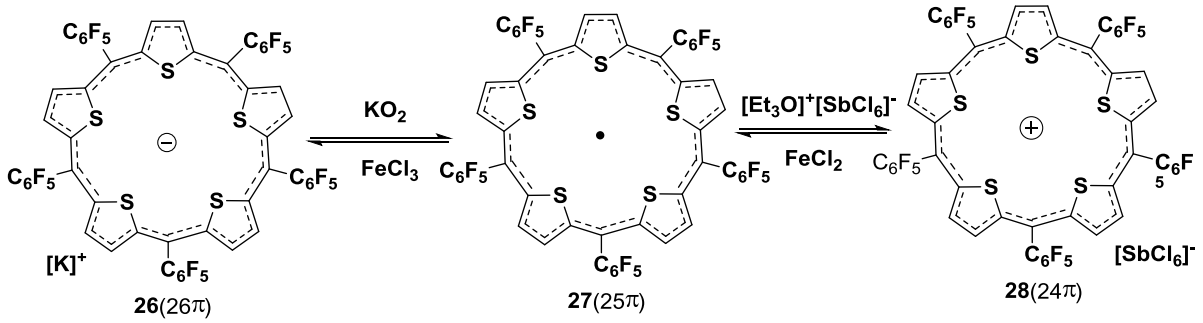
Expanding the conjugation of **21** offers a unique path to synthesize macrocyclic conjugated oligothiophenes. But invariably the realization of such giant macrocycles has been tedious due to the multi-step synthetic approach.

Later, attempts were made to synthesize octaethyltetrathia isophlorin[23] having methylene bridges in between thiophene subuits. The acid catalyzed self-condensation of 3,4-diethyl-2-(hydroxymethyl) thiophene resulted in the formation of tetrathia-porphyrinogen **22** along with pentathia-porphyrinogen **24** (scheme-10). Oxidation of octaethyl tetrathia-porphyrinogen with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in acetic acid and 70% perchloric acid led to the formation of octaethyltetrathiaporphyrin dication **23**. Oxidation of decaethylpentathiaporphyrinogen with antimony pentachloride in dichloromethane yielded aromatic 24π decaethylpentathia porphyrin trication **25**.[23]



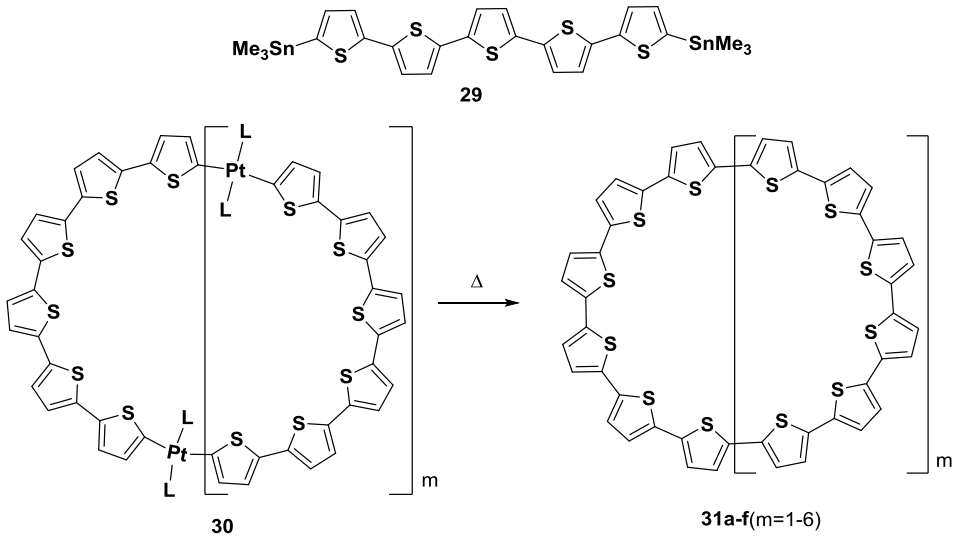
Scheme-**10**: Synthesis of tetrathia and pentathia isophlorins in their dicationic and tricationic form respectively.

Similarly, one-pot synthesis of pentathiaisophlorin having *meso* carbon linked with pentaflorobenzene[23,24] showing cationic, anionic and radical character was achieved from commercially available thiophene and pentafluoro benzaldehyde (scheme-11).[24] This reaction is similar to modified Rothemund's synthesis of porphyrin but the nature of the products isolated from this reaction was much different from what was observed in the case of pyrrole. A range of π-conjugated macrocycles such as aromatic, antiaromatic, non-aromatic, non-antiaromatic and neutral radicals were observed in reaction mixture. A reasonably good yield of a π conjugated macrocycle with five thiophene subunits was isolated from column chromatography. A detailed analysis concluded it as a neutral 25π electron radical **27**. The radical nature of this macrocycle was further confirmed by one-electron redox reaction. **27** could be either oxidized to 24π antiaromatic macrocycle **28** or could be reduced to 26π aromatic macrocycle **26** easily. All the three states of this macrocycle were comprehensively characterized by spectroscopic techniques such as ^{1}H NMR, ESR, UV-Vis absorption, cyclic voltammetry and single crystal X-ray diffraction along with computational studies.



Scheme-**11**: Reduction and oxidation of 25π stable radical to 26π anion and 24π cation respectively.

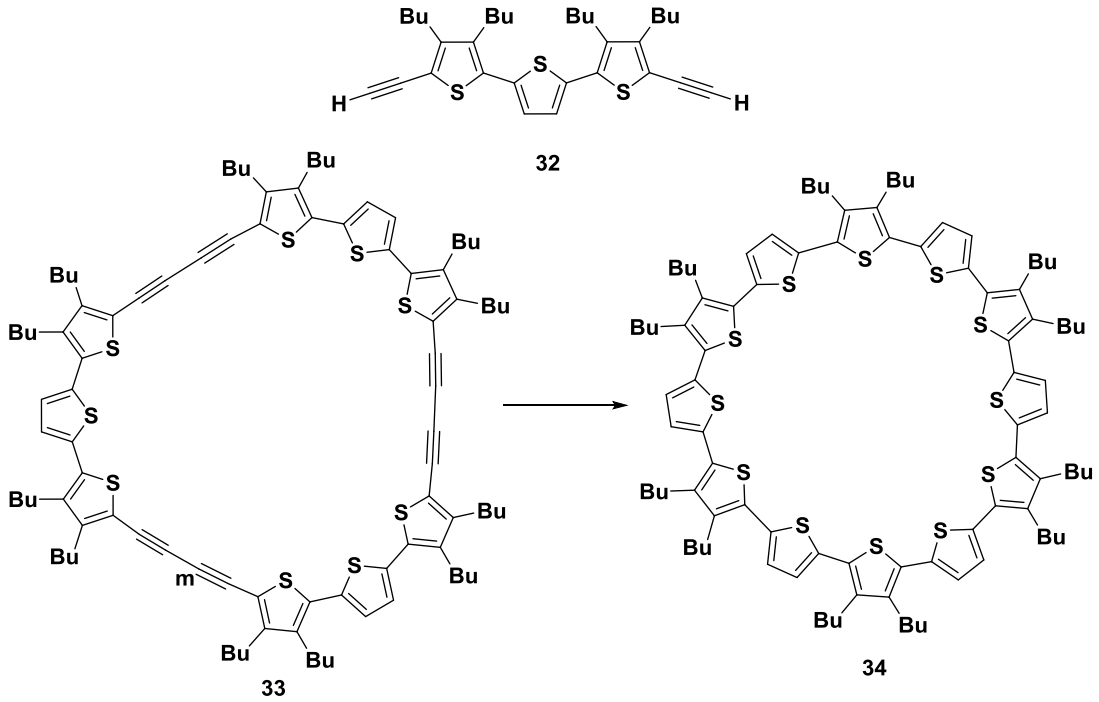
Bauerle and co-workers[25] have successfully synthesized cyclco[n]thiophenes, bearing ten to thirty five thiophene subunits (scheme-12). They exploited a one- pot synthesis of platinum assisted cyclization /coupling reaction of stannyl substituted oligothiophenes, **29**. A metalla-macrocycle, **30**, was generated in this process of organometallic reactions involving ligand exchange reactions with platinum, to facilitate C-C bond formation by reductive elimination of the metal by thermal activation. The macrocycles were separated by size exclusion chromatography. The yields of the macrocycles varied from 1.5% to 25% depending on the size of the macrocycle. The thirty-five membered macrocycle was found to form in major yields.



Scheme-**12**: Reductive elimination of metalla-macrocycle by thermal activation.

The same group later reported a series of cyclo(n)thiophenes bearing 12, 14 and 16 thiophene units (scheme-13). In this synthesis they employed Sonogashira-Hagihara coupling reaction between diiodo-oligothiophenes and trimethylsilylacetylene to

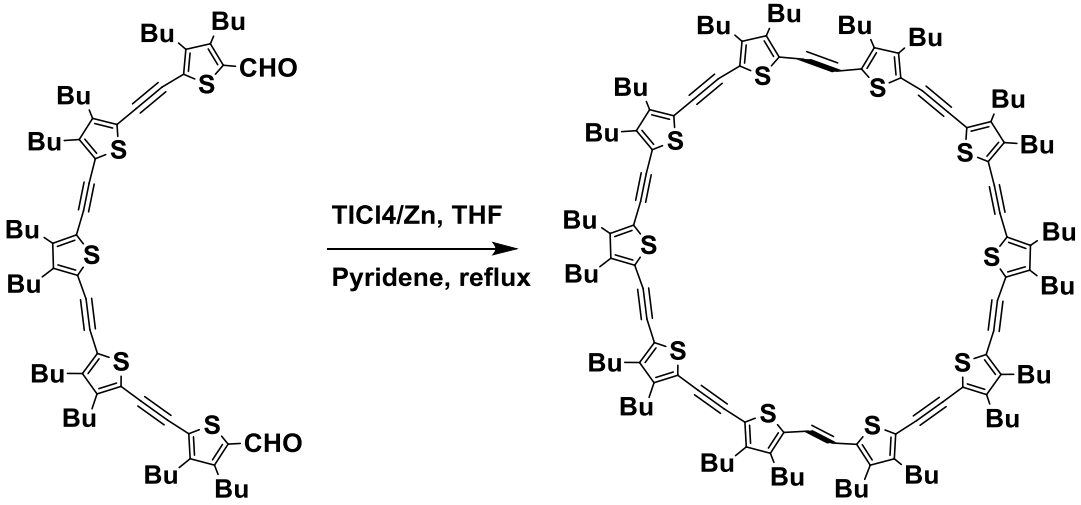
generate di-acetylene a substituted oligothiopohene, **32**. This was followed by Glaser reaction of the corresponding deprotected acetylenes to synthesize macrocyclic oligothiophenes with two consecutive acetylenes in between the short oligothiophenes, **33** (scheme-13). The reaction of these macrocycles with sulfur nucleophiles in methanol converted the two acetylene bridges into an individual thiophene heterocycle. In this method they were able to create multiple thiophene sub-units upon the formation of macrocycle, **34**. This procedure was found useful to synthesize size specific macrocycles but with low yields. Even though all the macrocycles could be considered as 4nπ antiaromatic macrocycles, no obvious ring current shifts were observed in their respective ^{1}H NMR spectrum. As spectroscopic investigations, suggested lack of effective delocalization of π electrons, they are considered to be benzeniod in character rather than annulenoid type conjugated systems.



Scheme-**13**: Conversion of two acetylene bridges into an individual thiophene in macrocycle after its reaction with sulfur nucleophiles in methanol.

Similar such macrocycles were also synthesized by Iyoda[26] and co-workers, in which the acetylene linked thiophenes were used as oligomers (scheme-14). Bisformylation of oligothiophenes followed by McMurry coupling yielded the ethylene bridged giant

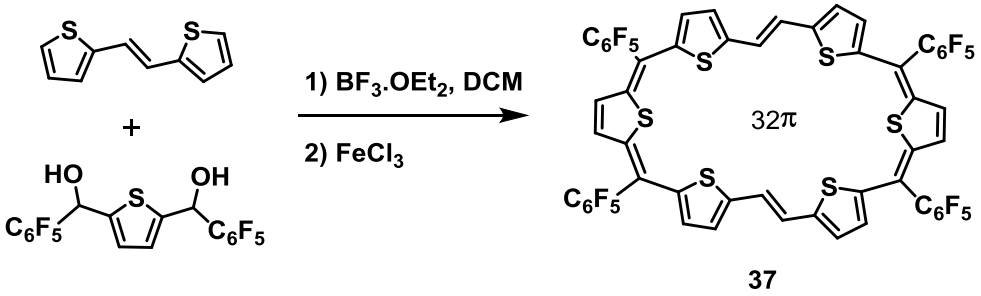
macrocyclic oligothiophenes bearing twelve to thirty subunits. They were separated by gel permeation chromatography. The presence of ethylene bridges gave rise to regional isomers with respect to *E* and *Z* configurations. The macrocycle with twelve thiophene subunits was found to have three different isomers in the form of *E*, *E*; *E*, *Z* and *Z*, *Z* with respect to the ethylene bridges. Amongst these three, the *E*, *E* isomer was formed in highest yields and was also characterized by single crystal x-ray crystallography. Out of the twelve thiophenes in the macrocycle, two diagonally opposite thiophenes were found to be inverted such that the sulphur of these thiophene rings were pointing towards the outside of the macrocycle. The electronic properties of these macrocycles as estimated by electronic spectroscopy displayed a gradual red shift and they were found to absorb in the visible region between 450 – 500 nm. The ^{1}H NMR spectrum of these macrocycles did not show any significant ring current effects indicating the benzenoid nature of the macrocycles. This asserts the lack of effective π orbital overlap between adjacent thiophene unit and hence the absence global aromatic features for the macrocycles.



Scheme-**14**: Synthesis of ethylene bridged giant macrocyclic oligothiophenes by McMurry coupling.

It can be concluded that expansion of π-electron conjugation could be achieved either by involving more heterocyclic units or by inserting more carbon bridges in between the heterocyclic units. Recently Anand and coworkers[27] have synthesized core-modified expanded isophlorins by replacing methine bridges with ethylene bridges. In this synthesis

a bis-thienyl ethylene was employed as a precursor and acid catalysed condensation was employed with appropriate diols of thiophene/ furan/selenophene, which resulted in the formation of macrocycles having ethylene as well as methine bridges (scheme-15). Macrocycles were separated by column chromatography and characterized through appropriate analytical techniques. The isolated molecules accounted for 32π electrons conjugation and hence antiaromatic in nature. The expected paratropic ring current effects were observed through ^{1}H NMR spectroscopy and further validated through the estimated NICS values. Single crystal X-ray analysis confirmed the planar structure of this macrocycle. This macrocycle undergoes reversible two-electron oxidation to form 30π dicationic species. In the same reaction mixture along with 32π system formation of its higher analog 48π system was also observed in MALDI-TOF mass spectrum.



37

Scheme-**15**: Synthesis of core-modified expanded isophlorins with ethylene bridges.

From the above mentioned examples of thiophene based macrocycles, it can be easily concluded that macrocyclic structures can be achieved by more than one possible way. A small increment in the number of heterocyclic units can be accomplished by employing short chain oligomeric hetrocyclic units as precursors or by the introduction of ethylene, acetylene bridges. It was also learned that the presence of methine bridges in between the heterocyclic units facilitates the flow of conjugation in these cyclic structures. Several examples described above reveals the variety of combinations to couple thiophene units with ethylene acetylene or methine bridges and their utility attractive building blocks in the synthesis of large π-conjugated macrocycles.

The Aim of this thesis:

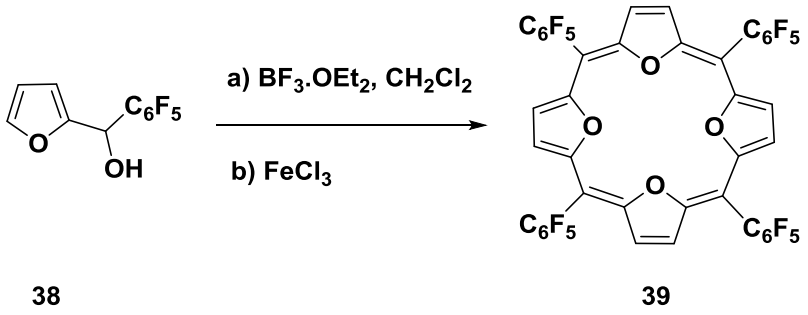
Most of these syntheses discussed above account for multiple step synthesis which hampers the further investigation of these expanded thiophene based macrocycles. Here, in this thesis a chief aim is to develop simple synthetic methodology of thiophene based macrocycles which are having *alpha alpha* coupled thiophene units in combination with methine bridges to achieve effective delocalization of π electrons. In a quick analysis of the initial work it has been observed that these cyclic molecules even after achieving complete conjugation tend to lose planarity. They generally adapt to different topologies which are generally classified as twisted shape, saddle shape and figure-eight configurations. In this thesis, the first V-shaped macrocycle for an expanded core-modified isophlorin with 32π electrons will be discussed. Also these anti-aromatic macrocycles with thiophene units are found to be stable and display interesting redox properties.

Chapter-2

One pot synthesis of S8, S10 & S12 Macrocyclic Oligothiophenes

II.1: Introduction

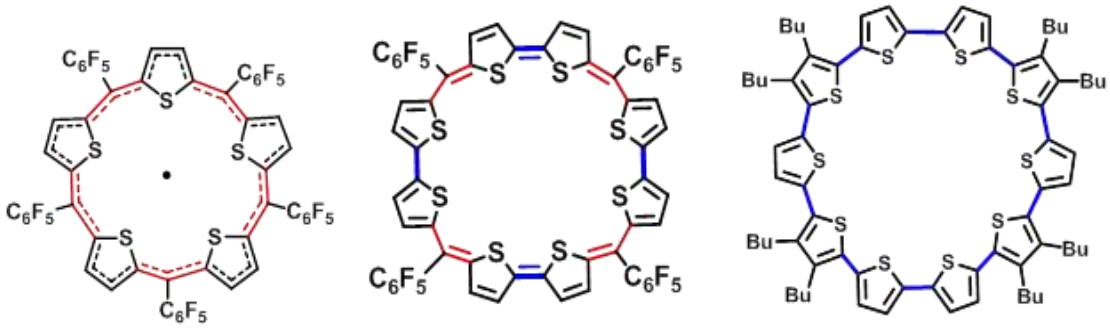
Porphyrins and higher homologs of porphyrins represent some of the finest examples for the study of aromatic and antiaromatic behavior of molecules with complete π-conjugation. These molecules exhibit attractive electronic, structural, and redox properties with potential for various applications. Their coordination chemistry is equally rich and opens the way for their application in the areas of functional dyes, nonlinear optical materials, ion receptors,[28,29,30&31] or as stable radicals. Porphyrins with different substituents on *meso* carbon atoms and β positions of the pyrrole rings can be synthesized in a one-pot synthesis by employing Lindsey conditions.[32] In 2008 it was shown that 2-pentafluorophenylhydroxymethyl furan **38** undergoes self-condensation by an acid-catalyzed reaction, followed by $FeCl_3$ oxidation (scheme-16) resulting in the formation of 20π tetraoxaisophlorin[33].



38 **39**

Scheme-**16**: Acid catalyzed self-condensation of Pentafluoro-furan-mono-ol.

As mentioned in previous chapter octaethyltetrathia & pentathiaisophlorin having methane bridges in between thiophene subuits and the one-pot synthesis of pentathiaisophlorin having meso carbon linked with pentaflorobenzene showing cationic, anionic and radical character was achieved from commercially available thiophene and pentafluoro benzaldehyde. These macrocycles are having meso carbon bridge in between two thiophene units, whereas Bäuerle & co-workers reported the synthesis of oligothiophenes ranging from ten to thirty two units of thiophenes which are completely ∝-∝ connected. These two structural differences motivated the synthesis of an oligothiophene which can have both meso carbon and ∝-∝ connection alternatively in the same macrocycle.



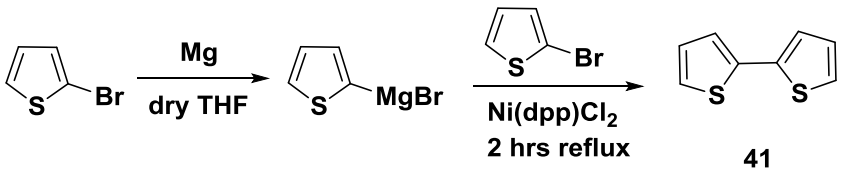
27 40 34

It can be envisaged that oligothiophenes might also yield macrocycles with similar structural and electronic properties. This chapter describes the attempts to employ[2,2'-bithiophen]-5-yl(perfluorophenyl)methanol, instead of pentafluorophenylhydroxymethyl furan, to synthesize the homologs of thiaisophlorin having both alpha-alpha linkage and meso carbon in between, as shown above.

II.2: Synthesis

Synthesis of monomers:

2,2'-Bithiophene: **41**



41

Scheme-**17**: Synthesis of 2,2'-Bithiophene.

Activated Mg (1.5 g, 62 mmol) and a pinch of iodine were stirred in 40 ml dry tetrahydrofuran (THF) under inert atmosphere until the color of solution changed to light brown. Then, 2-bromothiophene (6ml, 62mmol) dissolved in dry THF (10ml) was added slowly and stirring continued for few minutes till the color of solution turned to colorless. Vigorous bubbling was observed, and the color further changed to dark brown whilst most of the Mg turnings were found to be dissolved. 2-Bromothiophene (5.01ml, 51.6mmol) was added at 0°C and temperature was maintained till Ni(dpp)Cl_2 (0.336gm, 0.62mmol) was added as slowly as possible, as a suspension in THF. The mixture was allowed to warm up to room temperature and then was refluxed at 90°C for 3hrs (scheme-17). The reaction

was quenched with dilute hydrochloric acid (dil. HCl) while maintaining it in ice cold conditions due to the exothermic reaction. The organic layer was separated and the aqueous layer extracted with diethyl ether (Et_2O) (4 x 100 ml), dried over sodium sulphate (Na_2SO_4), and evaporated under reduce pressure. The resulting mixture was chromatographed on silica (hexane). The desired product 2,2'-Bithiophene, **41** was obtained as colorless viscous liquid. Yield 8.54 g (83%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, 5.7 Hz, 2H), 7.26 (d, 3.6Hz, 2H), 7.10 (dd, 2H).

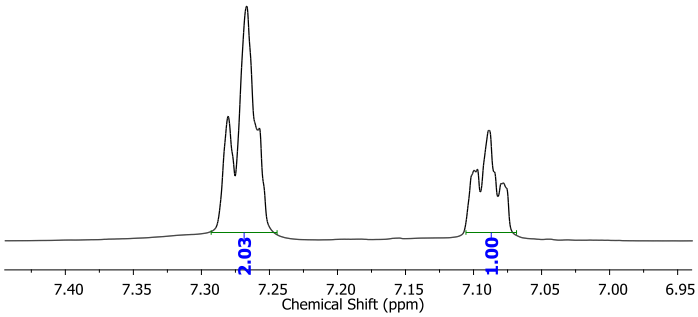
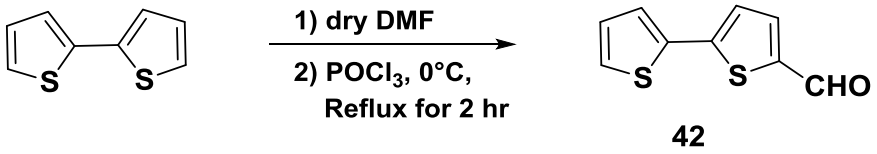


Figure **2**: Partial ^{1}H NMR of 2,2'-Bithiophene, **41**.

2,2'-Bithiophene-5-carboxaldehyde: **42**



Scheme-**18**: Synthesis of 2,2'-Bithiophene-5-carboxaldehyde.

$POCl_3$ (0.95 ml, 10 mmol) was added at 0°C to a stirred solution of 2,2'-bithiophene (0.83 g, 5 mmol), **41**, and dry dimethyl formamide (DMF) (1.2 ml, 15 mmol) in 20 ml of 1,2-dichloroethane under argon. After 2 hours of refluxing (scheme-18), the mixture was cooled to room temperature and neutralized with 10 ml of a 1M aqueous solution of sodium acetate. The organic layer was separated, and the aqueous layer extracted with 3x15 ml of DCM. The combined extracts were washed with water, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by column

chromatography (silica gel, CH_2Cl_2) to give 0.87 g (89 %) of product as a yellowish solid. ^1H NMR (400 MHz, $CDCl_3$): δ 9.85(s,1H), 7.66(d, 4Hz, 1H), 7.37-7.35(m, 1H), 7.34(s,1H), 7.23(s,1H) ,7.07-7.05(m,1H).

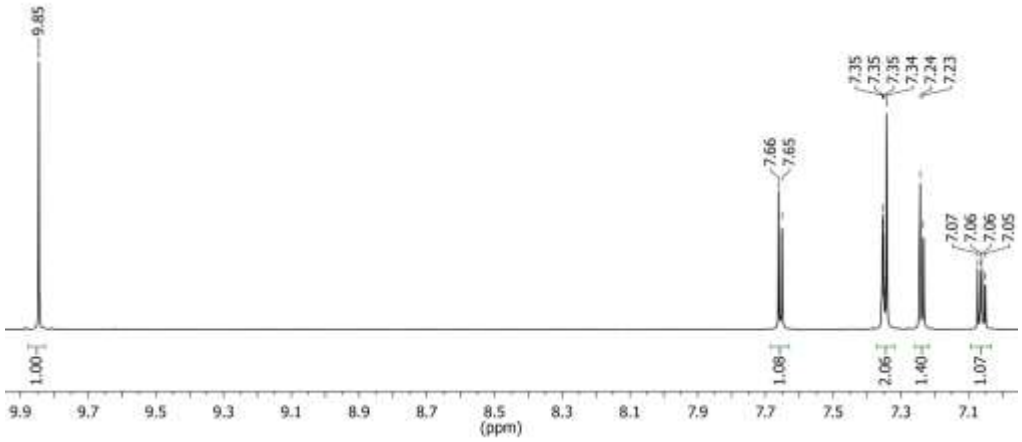
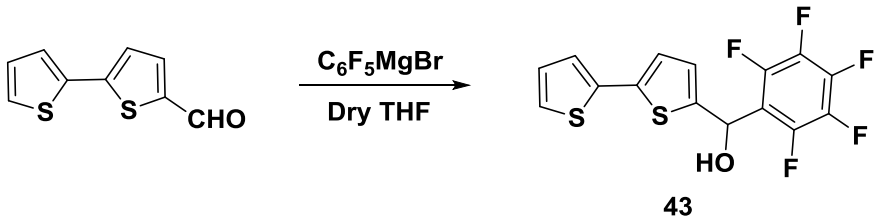


Figure **3**: Partial ^1H NMR of 2,2'-Bithiophene-5-carboxaldehyde, **42**.

[2,2'-bithiophen]-5-yl(perfluorophenyl)methanol: **43**



43

Scheme-**19**: Synthesis of [2,2'-bithiophen]-5-yl(perfluorophenyl)methanol.

Activated Mg (0.169 g, 6.95 mmol) and pinch of iodine were stirred in dry THF (25ml) for 2 minutes under an inert atmosphere. Then, pentafluorobromide (0.859 ml, 6.7 mmol) was added slowly and color of solution turned dark brown and was allowed to stir for two hours. To the Grignard reagent derived from pentaflorobromide was added to the aldehyde, **43**, dissolved in THF at 0°C and allowed to reach room temperature (scheme-19). Consumption of aldehyde was confirmed by TLC analysis. Then the reaction mixture was quenched after 3 hours and the organic layer was extracted with Et2O. The combined organic layers were washed with water and brine solution. After drying over Na2SO4, the

solvent was evaporated under vacuum to yield the pure compound**,** as white solid. Yield: 62%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (d, 4 Hz, 1H), 7.12 (d, 4 Hz, 2H), 7.01-6.99(m, 1H), 6.98 (d, 4Hz, 1H), 6.80(d, 4Hz, 1H), 6.35 (d, 4Hz, 1H), 3.89(d, 4Hz, 1H).

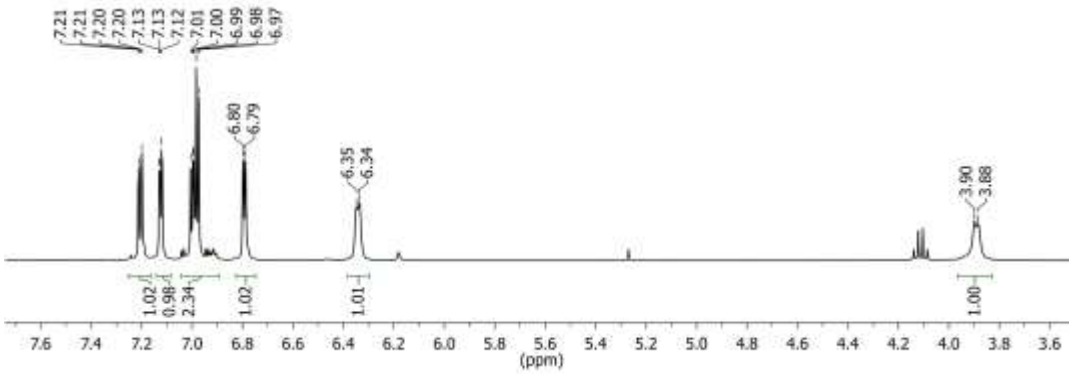
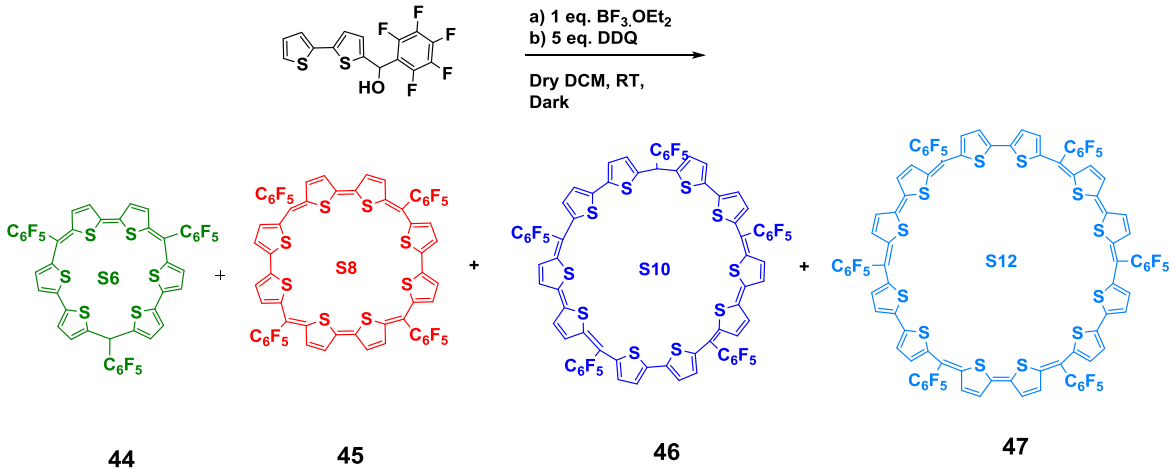


Figure **4**: Partial ^{1}H NMR of [2,2'-bithiophen]-5-yl(perfluorophenyl)methanol, **43**.

Synthesis of macrocycles:

Bis-thiophene -mono-alcohol (500 mg, 1.37mmol), **42**, was dissolved in 500 ml of dry dichloromethane and in the absence of light. After addition of $BF_3.OEt_2$ (0.17 ml, 1.37mmol), the solution was stirred for additional two hours at room temperature. DDQ (1.56g, 6.89mmol) was then added, and the solution left open to air for an hour (scheme-20), before passing the reaction mixture through a short pad of basic alumina. The formation of macrocycles was confirmed from MALDI –TOF/TOF mass spectrometry.



Scheme-**20**: Identification of macrocyclic oligothiophenes macrocycles bearing eight, nine and ten thiophene sub-units.

Apart from the expected macrocycle, the MALDI-TOF mass spectrum of this reaction indicated the formation of macrocycles containing eight, ten and twelve thiophene subunits (figure-5).

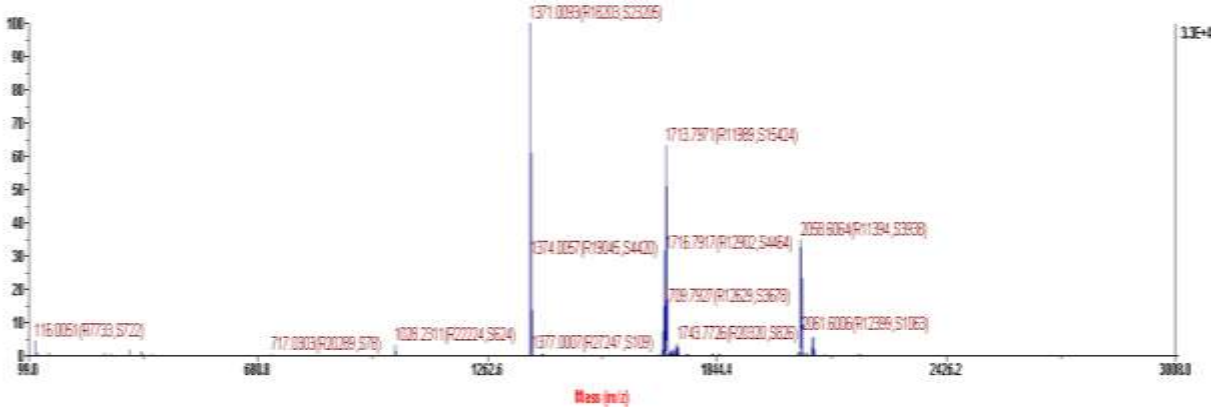


Figure **5**: MALDI-TOF/TOF mass spectrum of reaction mixture as described for scheme-20.

II.3: Isolation & Characterizations of Octathiaisophlorin

Silica-gel column chromatography led to separation of 36π octathiaoctaphyrin (**45)** in 7.5% yields. Separation of 44π decathiadecaphyrin(**46)** was achieved while passing through basic alumina. A macrocycle with ten thiophene units (**46)** and six thiophene **(44)** were also detected in the mass spectrum (figure-5) but due to unconjugated in nature because of presence of sp^3 could not be isolated. Macrocycle with twelve thiophene **(47)** was found to have very poor yields because of its very large size. Octaphyrin was expected to be a completely conjugated macrocycle as it was containing even number of carbon atoms in the conjugated pathway. Whereas decaphyrin was expected to be semi-conjugated due to the odd number of carbon atoms. A red colored fraction that eluted with CH_2Cl_2/Petroleum ether (1:10) displayed m/z 1371.7515 in its MALDI-TOF/TOF mass spectrum (1371.8744) (figure 6). It displayed a symmetrical ^{1}H NMR spectrum in deuterated chloroform at room temperature. Only two doublets, corresponding to equal number of protons, were found to resonate at δ 7.07 and 6.71 ppm (figure-7). As the macrocycle accounts for 38π electrons along its conjugated pathway, it can be considered to exhibit anti-aromatic characteristics. The observation of just two doublets in the ^{1}H NMR spectrum suggested a highly symmetrical structure of the macrocycle. Generally,

expanded isophlorins display fluxional structures and hence adopt either ring inverted or figure-of-eight non-planar structure. Therefore, its ^{1}H NMR was recorded even at low temperature up to 223K (figure-8). As no significant difference was observed in its spectrum, it suggested that the macrocycle was not fluxional in character. In tune with its extended conjugation, it displayed an intense absorption band at 550 nm (Є = 31,959) and a higher energy band at 464 nm (figure-11).

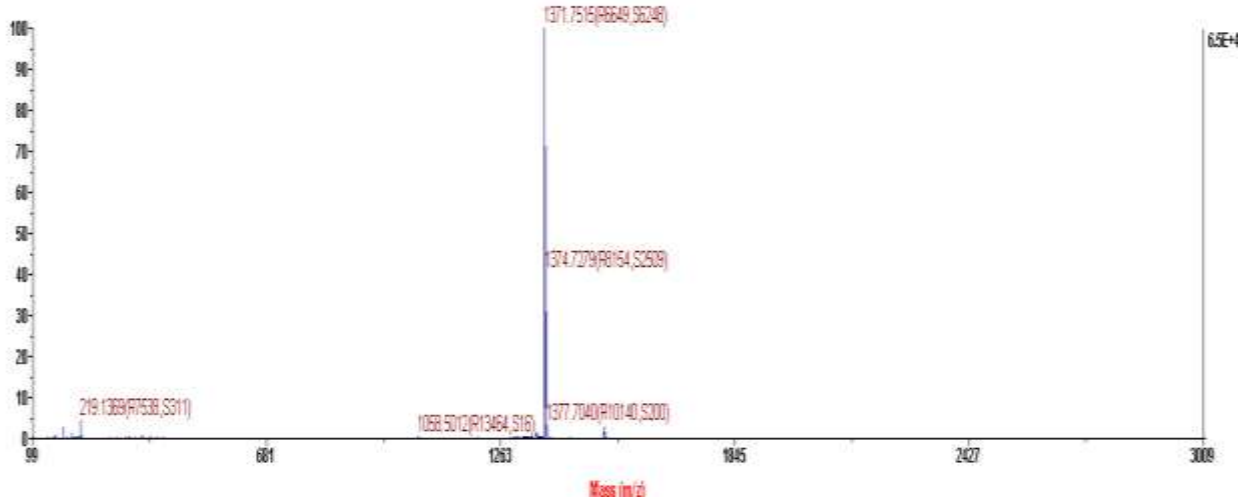


Figure **6**: MALDI-TOF/TOF mass spectrum of the purified sample of S8 (**45**).

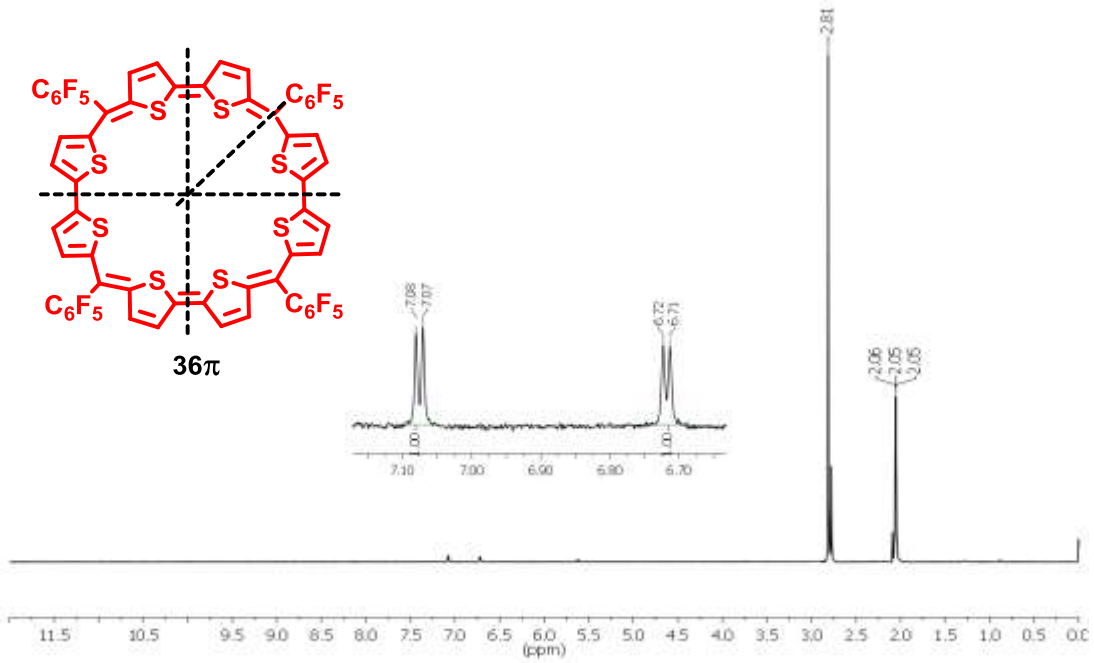


Figure **7**: ^{1}H NMR spectrum of Macrocycle 45 in Acetone-d_6 at RT**.**

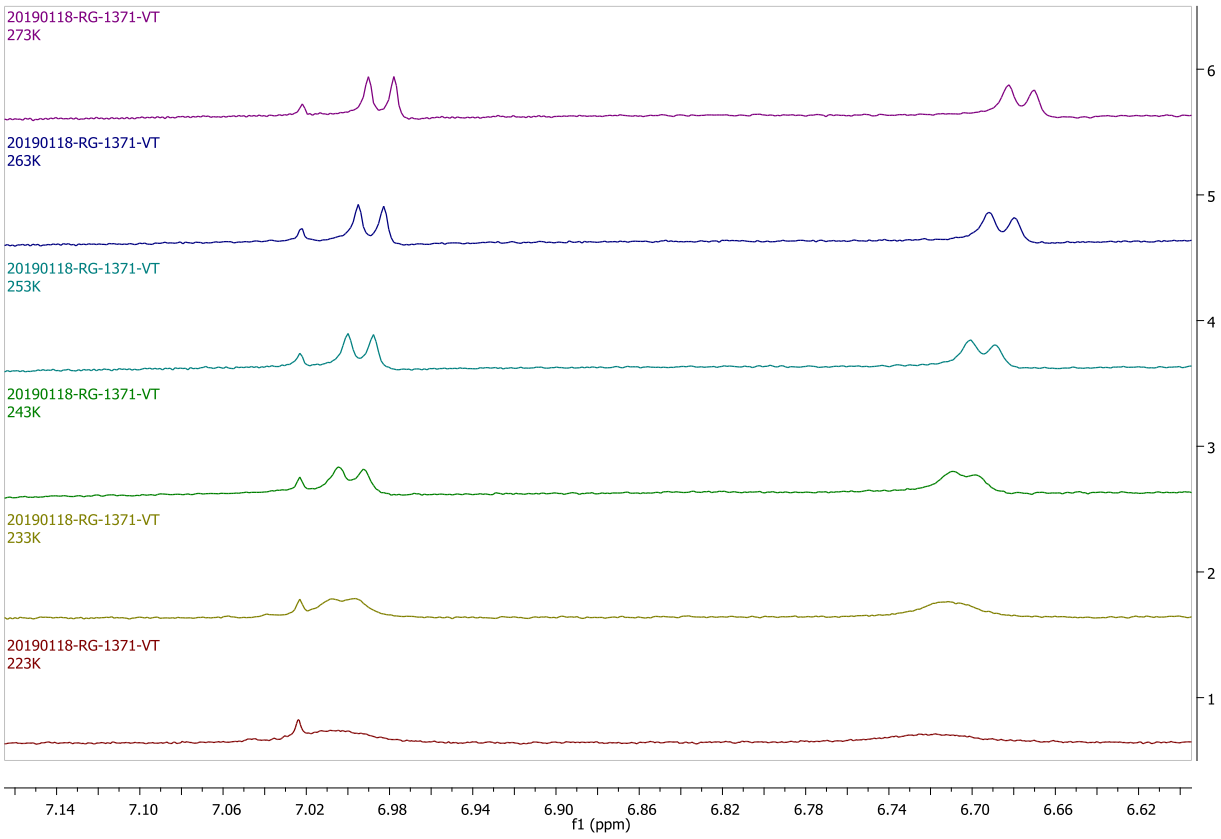


Figure **8**: Variable temperature ^{1}H NMR of **45** in Acetone-d_6.

Broadening of signals is generally observed due to rotational energy barrier of certain chemical bonds at lower temperature. A molecule can have two different conformations at two different temperatures. So when temperature of solution containing molecules is reduced slowly, the molecule attains a stable conformation due to restricted rotation. However, in this case, the broadening of signals can be attributed either to aggregation or due to poor solubility in this solvent at lower temperatures.

II.4: Molecular Structure of 45

A number of attempts were required to grow good quality crystals of octathiaoctaphyrin (**45)**. Fortunately, good quality crystals were obtained through slow evaporation method using benzene as the solvent. It crystallized in Triclinic system with P-1 space group and displayed a planar structure with respect to eight thiophenes. It shows that the six

thiophene rings are aligned such that the sulphur atoms are pointing towards center of the macrocycle and two of the diagonally opposite thiophenes are pointing away from the center due to ring inverted structure (figure-9). However, ^{1}H NMR spectrum convincingly supports a planar structure with all sulfur atoms within the core of the macrocycle. In contrast, the molecule adopts a rectangular shape instead of the expected symmetrical square as analyzed by single crystal X-ray diffraction analysis. The orientations of pentafluorophenyl rings are almost orthogonal to the macrocycle, which prevents any kind of π-stacking due to steric hindrance. As this cyclic system is having 36π-electrons (4nπ) in its conjugated pathway, it is expected to exhibit anti-aromatic characteristics.

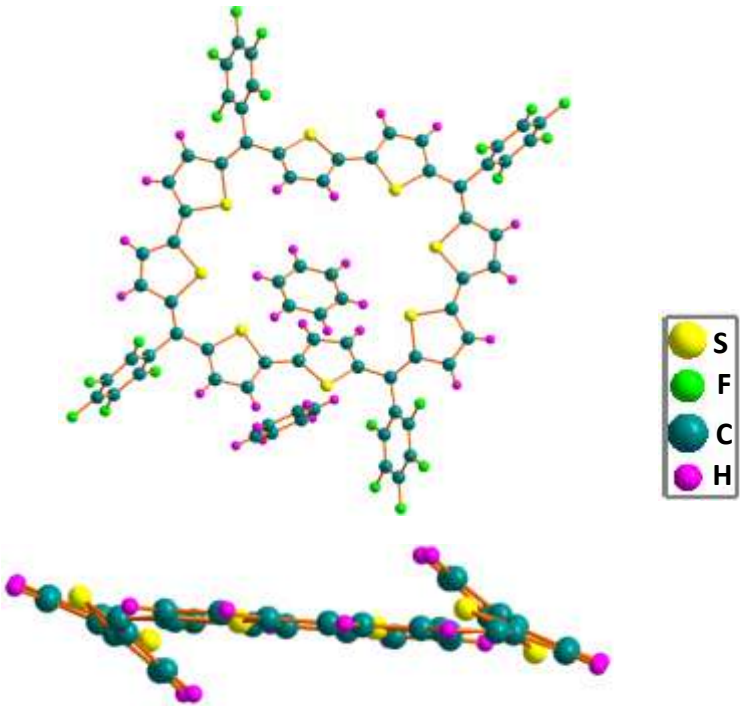


Figure **9**: a) Top view of the molecule **45**, with two molecules of benzene, b) Side view of the molecule **45** without benzene molecules.

Structure of molecule **45** in solution and solid-state are found to be different. ^{1}H NMR shows only two signals, indicating that the molecule is highly symmetrical and possibly have a planar structure having all the thiophene pointing towards center in the solution state (figure-10). However, the molecular structure found after crystallization displayed the flipping of two diagonally opposite thiophene resulting in the decrease of symmetry.

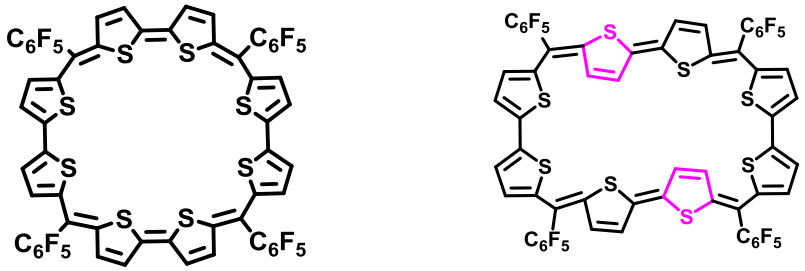
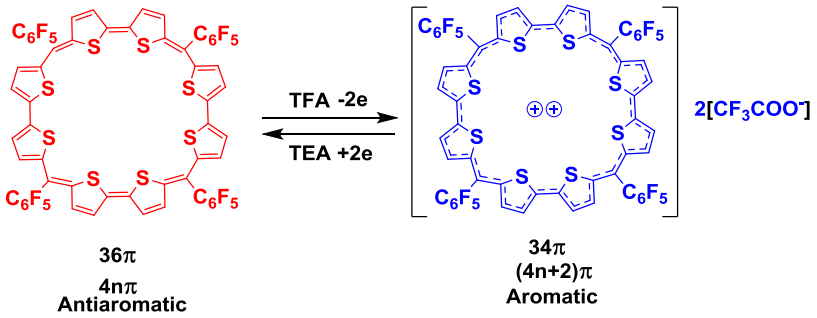


Figure **10**: Macrocycle **45** showing different structure in the solution and the solid state.

II.5: Two electron oxidation of 45

Antiaromatic macrocycles undergo facile two-electron oxidation to yield the corresponding dicationic aromatic species.[34] As the octa-thiophene (**45)** accounts for a formal 36π electron along its conjugated pathway, it can be expected that this macrocycle can also be oxidized to its 34π dicationic species. Addition of Meerwein salt $[Et_3O]^+[SbCl_6]^-$ or $NOBF_4$ or trifluoroacetic acid (TFA) to antiaromatic systems are known to oxidize the 4nπ species to the corresponding dicationic species.[35] Addition of TFA to a dichloromethane solution of octa-thiophene induced a subtle change in the color from red to a bluish colored solution. Similar observation was made upon the addition of TFA to (**45**) in dichloromethane (scheme-21). This bluish solution displayed an intense absorption band at 665 nm (Є = 76,815) followed by weak and broad absorptions (figure-11), in the region between 900-1200 and at 1900 nm. A phenomenal red shift by more than 100 nm for the most intense band suggested the two-electron ring oxidation of the octathiophene (**45)**. This dicationic species could be easily reduced back to the free base octathiophene (**45**) molecule upon addition of base like triethylamine.



Scheme-**21**: Two electron oxidation of **45** Macrocycle.

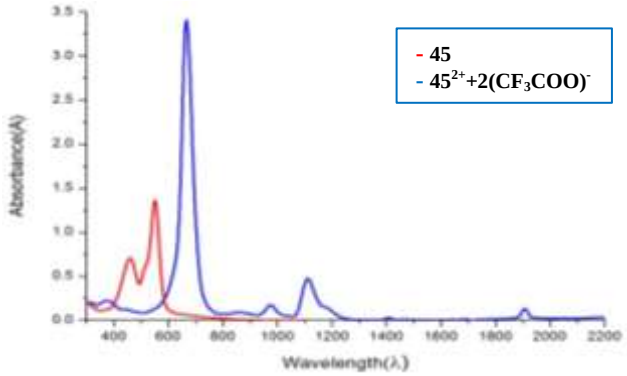


Figure **11**: Absorption changes observed upon the addition of TFA to **45** in dichloromethane.

^{1}H NMR of this new molecule was obtained by addition of TFA to the solution of S8 (**45**) in $CDCl_3$. The room temperature spectrum displayed two singlet's at δ 13.01 and 14.37 ppm corresponding to an equal number of protons (figure-12). A similar pattern of the ^{1}H NMR spectrum with respect to the free base form of the macrocycle suggested no untoward changes in the topology of the macrocycle upon oxidation. Interestingly, these signals are downfield shifted by at least 7 ppm with respect to the free base chemical shift values (figure-13), due to diatropic ring current effect. Such significant shifts can be attributed only to the oxidation of the macrocycle to the corresponding 34π dicationic species which is expected to be aromatic in nature. As it sustains a planar topology, the downfield shifts are appropriate enough to justify the expected diatropic ring currents of the planar aromatic dication.

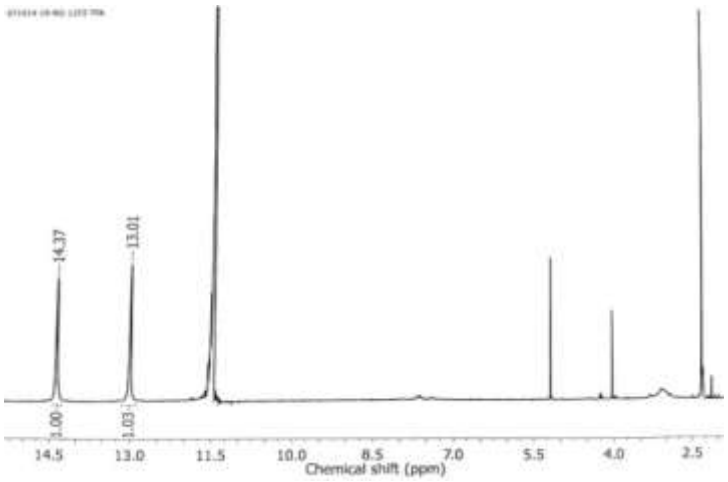


Figure **12**: Partial ^{1}H NMR of Dicationic Species of Macrocycle 45 in $CDCl_3$ at RT.

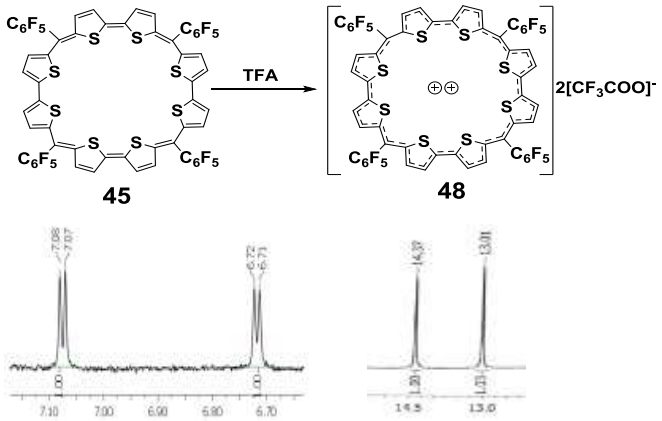


Figure **13**: Comparative depiction of partial ^{1}H NMR of **45** and **48**.

The above figure shows the drastic change in the ^{1}H NMR of octathiophene, **45**, before and after addition of TFA, which conforms conversion of the antiaromatic molecule to the corresponding aromatic species.

II.6: Quantum mechanical Calculations

To obtain more insight into molecular orbitals and to quantify the aromaticity of the oxidation states of **45**, Quantum mechanical calculations were performed using the Gaussian09 rev D program suite.[36] All the theoretical calculations were carried out by employing Density Functional Theory (DFT) with Becke's three-parameter hybrid exchange functional and the Lee-Yang- Parr correlation functional (B3LYP) and 6-31G(d,p) basis set for all the atoms that were employed in the calculations. The molecular structures derived from single crystal analysis were good enough to carry out these calculations. Hence, the single crystal data was employed to obtain the geometry-optimized structures through Gaussian 09 program.[36] Among diverse methods are explored to quantify the aromaticity of conjugated systems[37], Nucleus Independent Chemical Shift (NICS) is one of the most successful parameters to quantify aromaticity.[38]

NICS	Aromaticity
Negative	Aromatic
Positive	Antiaromatic
Around Zero	Non-Aromatic

Table **1**: Sign for NICS value in different cases.

Schleyer was the first to introduce magnetic criterion as a measure of aromaticity and antiaromaticity (or non-aromaticity). He defined it as "Absolute magnetic shielding's, computed at *ring center,* non-weighted mean of the heavy atom coordinates) or at another interested point of molecule, which was done by placing a dummy atom. To correspond to the familiar NMR chemical shift convention, the signs of the computed values are reversed".

II.6.1: NICS calculations

NICS values were obtained with gauge independent atomic orbital (GIAO) method based on the optimized geometries. The global ring centers for the NICS (0) values were designated at the non-weighted mean centers of the macrocycles.

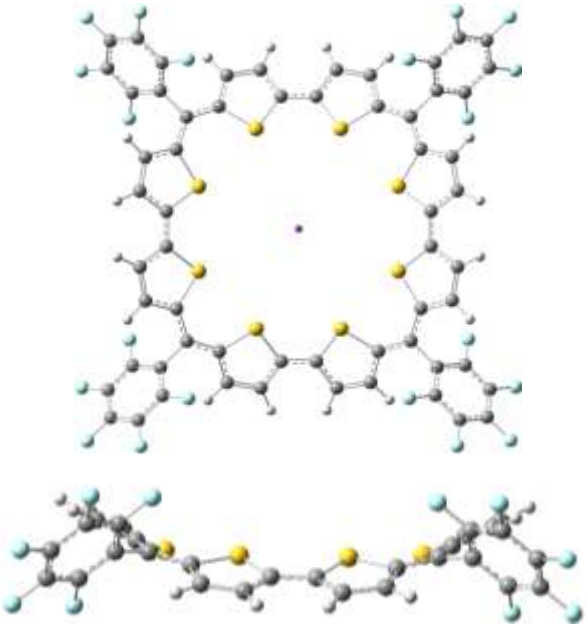


Figure **14**: Top and side view of optimized **45** for NICS calculation of neutral and dicationic states.

Figure-14 represents the optimized structure of the expected structure in the solution state, obtained by using Gaussview & Gaussian to estimate the NICS(0) value for macrocycle **45** and its dication. The estimated NICS(0) value for the neutral macrocycle was found to be +8.33 ppm whereas for the dicationic species shift was found to be -13.52 ppm. These calculations lead to the conclusions that the octathiophene **45** is weakly antiaromatic in its free base form and undergoes facile two-electron oxidation to yield the corresponding aromatic dication.

As the crystal structure of the molecule shows the flipping of two diagonally opposite thiophene ring away from the center, the alternate structure was also studied after optimizing its geometry for the estimation of NICS(0) in the freebase and for it dication species. The optimization of the structure with diagonally inverted thiophenes was also done for theoretically derived structure (using Gaussview & Gaussian), to compare the observed and theoretical NICS(0) values obtained.

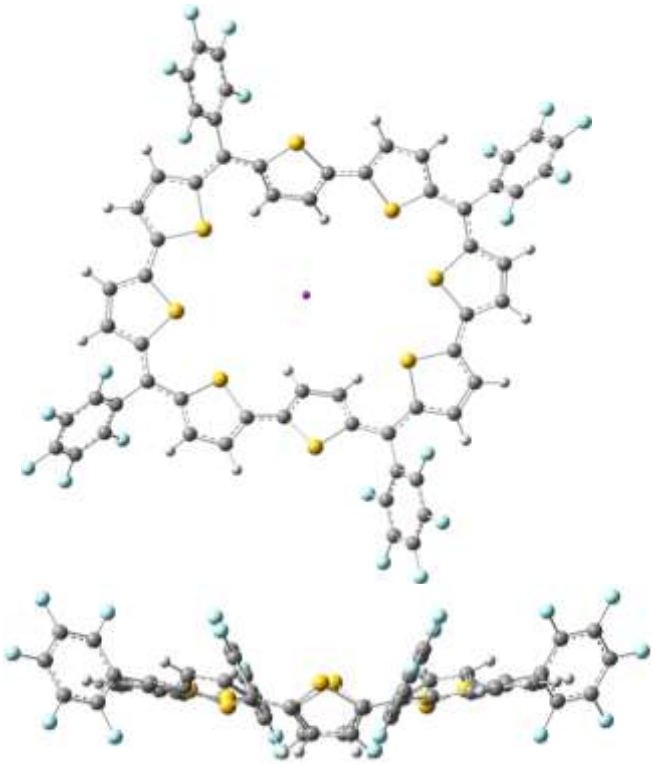


Figure **15**: Top and side view of optimized geometry for **45** with two diagonally opposite flipped thiophene for NICS calculation of neutral and dicationic states.

As depicted in the figure-15, the optimized structure with ring inverted thiophenes displayed NICS(0)values of +4.92 ppm and -13.04 ppm for the freebase and the dication respectively, for the theoretically obtained structure. Whereas NICS(0) values for the optimized structure of crystal structure was found to be +4.45ppm and -11.4 ppm for the freebase and the dication respectively. The value does not vary significantly for the freebase, but a variation of nearly +1.64 ppm was observed in the dicationic form. Therefore it can be inferred that the NICS(0) value estimated for the computed structure is and the molecular structure obtained on crystallization are comparable with each other's ring current effects.

II.6.2: ACID calculations

The Anisotropy of the Current-Induced Density (ACID)[39] was also plotted to visualize the ring current effect due to delocalized π electrons. The ACID plots display the magnitude and direction of the induced ring current when an external magnetic field is applied orthogonal to the macrocycle plane. Current density plots were obtained by employing the continuous set of gauge transformations (CSGT) method to calculate the current densities, and the results were plotted using POVRAY 3.7 for Windows. Similar to NICS method, clockwise ring currents represent aromatic molecules whereas anticlockwise ring currents are representative of antiaromatic molecules. Apart from the direction of ring currents, it also aids in determining the path of the delocalized π-electrons.

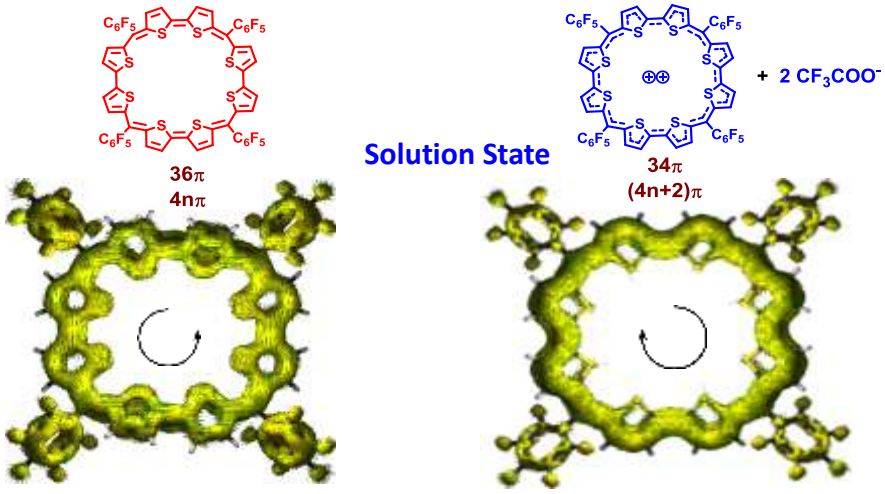


Figure **16**: ACID Plot of **45** & **48.**

The above structure is as expected in the solution state. Figure-16 (left side) represents the ACID plot of octathiophene **45** and depicts the anti-clockwise direction of electron flow confirming antiaromatic characteristic of the macrocycle. Similarly, ACID plot of dicationic species **48** was also derived as shown in the figure above, on the right. The direction of electron flow is clockwise direction confirming that the molecule is aromatic in nature. In the plot (figure-16), it can be seen that the path of flow of electrons was through carbon perimeter only.

Similar plots (figure-17) were derived for the thiophene inverted macrocycles as observed in its structure after crystallization and in all these plots the flow of pi-conjugation is predominantly through the carbon atoms alone and hence they represent the expanded version of the isophlorin skeleton structure.

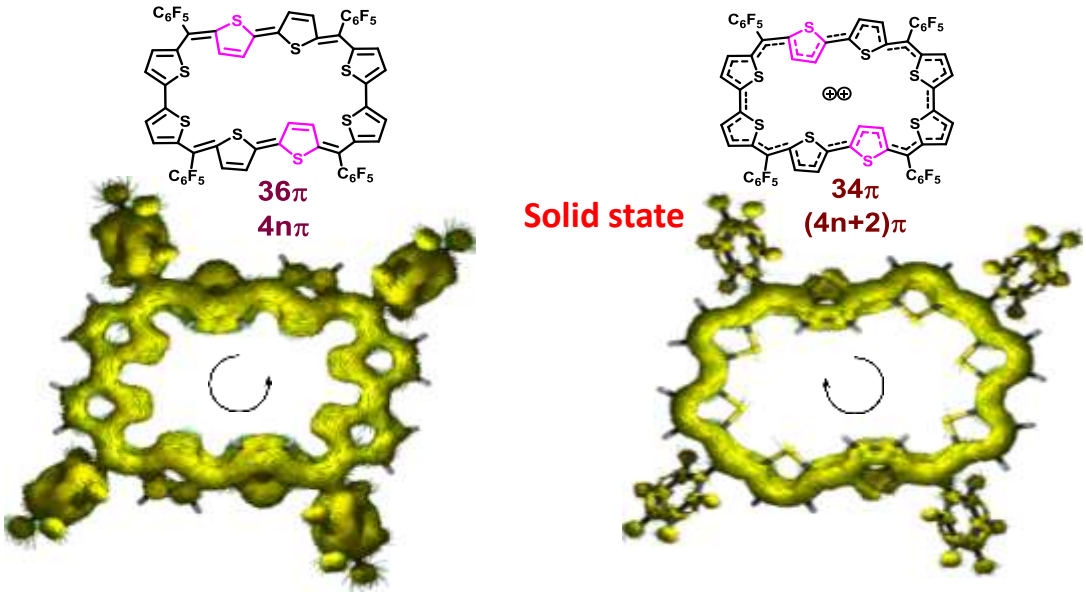
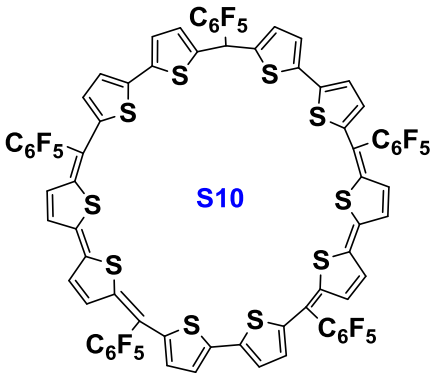


Figure **17**: ACID Plot of **45** and **48** with two flipped thiophenes (solid state).

II.7: Isolation of Decathiaisophlorin:

In the same reaction (scheme-20), the formation of decathiadecaphyrin **46** was observed from MALDI-TOF/TOF mass spectrum. However, this macrocycle contains odd no of meso carbons and hence leads to incomplete conjugation. The decathiadecaphyrin was separated while neutralizing the reaction mixture by passing through basic alumina column. It was isolated as a blue color fraction by employing dichloromethane and petroleum ether in the

proportion of 2:10 in less than 1% yields. Its mass spectrum (figure-19) it displayed an m/z value of 1715.3223 corresponding to incomplete oxidation of the macrocycle. In its ^{1}H NMR decaphyrin displayed eleven signals which were observed at 6.13, 6.35, 6.59, 6.63, 6.70, 6.93, 6.95,7.02, 7.08, 7.11 and 7.15 ppm. These signals further validate the presence of a sp^3 meso carbon which obstructs the complete conjugation of the macrocycle. However, this molecule was not found to be stable for long periods and hence only limited characterization of this macrocycle was successful. It can be envisaged that it can lead to the formation of a radical species, however all efforts to obtain its radical species turned futile and lead to the oxidative loss of the macrocycle to products which could not be characterized satisfactorily.



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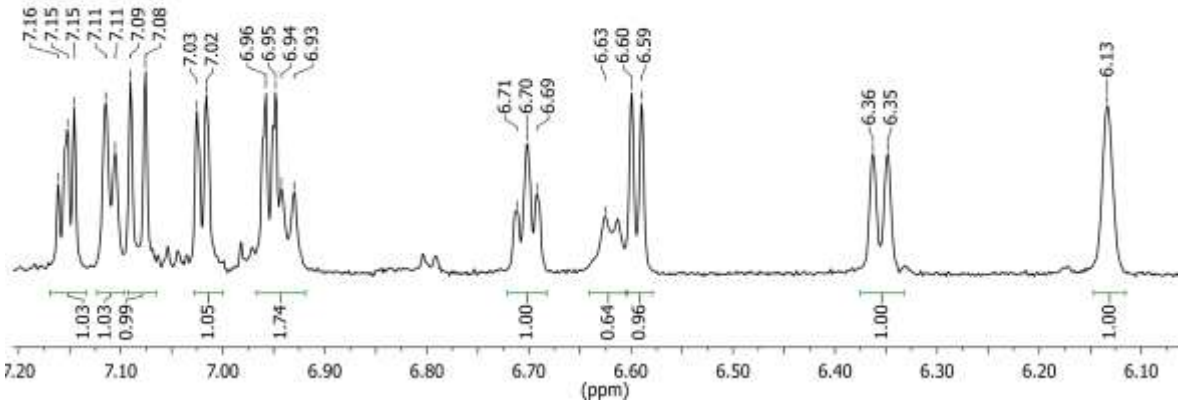


Figure **18**: Partial ^{1}H NMR of Decathiaisophlorin S10 (**46**) in chloroform-*d* at RT.

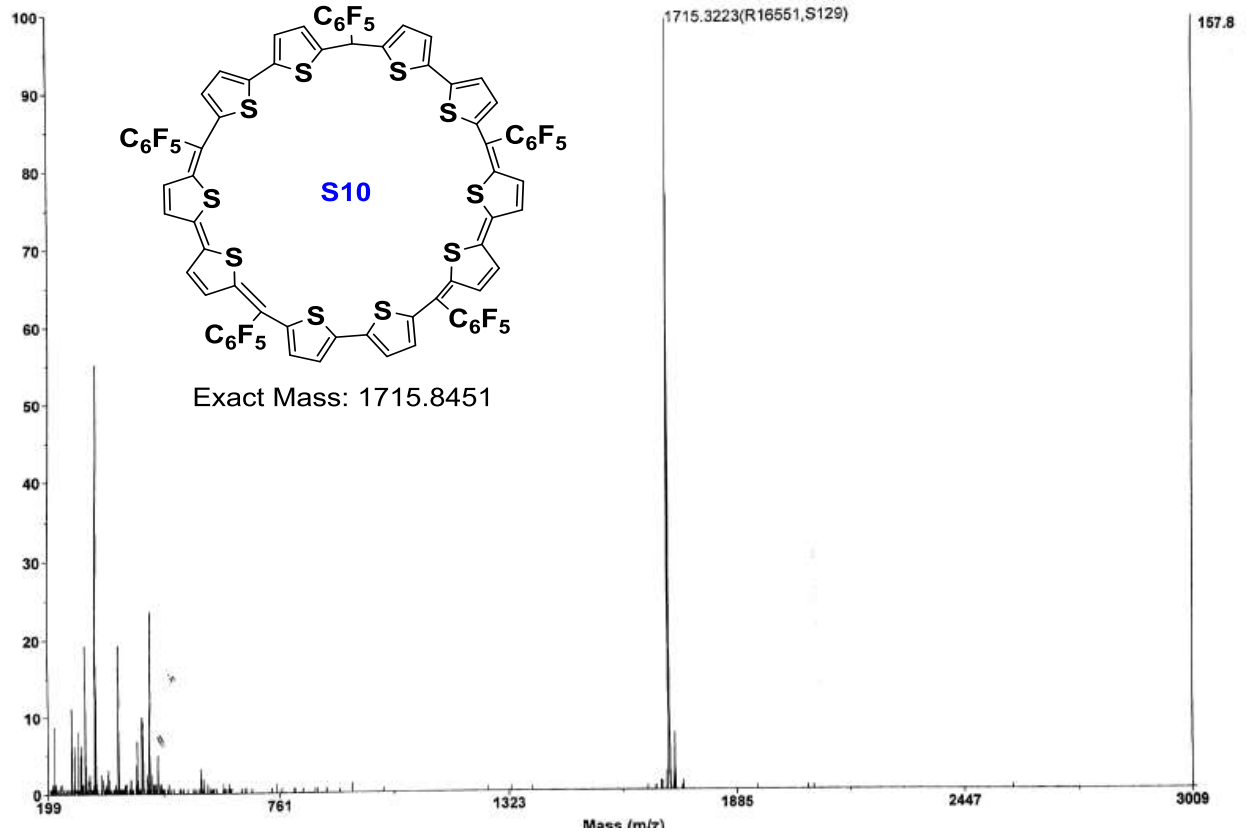


Figure **19**: MALDI-TOF/TOF spectrum of S10 (**46**).

Decathiaisophlorin was found in low yield, and even after several trials this molecule is found to be unstable due to the probable inherent radical nature. Optimization of theoretically generated revealed figure-8 configuration, for which Calculation of NICS value is not of so much value.

II.8: Conclusions

Bi-thiophene mono-ol undergoes self-condensation under oxidative conditions to yield π-conjugated macrocycles bearing eight, ten, and twelve thiophene units with carbon bridges in between. Depending on the length of the conjugation the formal π electron count varies from 36π electrons in the octa thiophene macrocycle **45** to 54π electrons in the dodeca thiophene macrocycle **47**. The nature of the products is dependent on the number of π electrons in the respective macrocycle. The macrocycles obtained in this reaction resemble the skeletal frame-work of isophlorins and hence they can be considered as expanded

isophlorins. The pyrrole's ability to inter-convert the nitrogen between imine and amine forms makes the nitrogen to be a part of the π-conjugated network and hence such pyrrole based macrocycles resemble porphyrin. Studies on octathiaisophlorin reveal that it's an anti-aromatic system which can be easily oxidized to aromatic system by addition of Meerwien salt/$NOBF_4$/TFA as oxidizing agent. Crystallography studies indicate that even though the molecule is highly symmetrical, but on crystallization it leads to a modified geometry in the solid state. Computational studies revealed that dicationic species preferred the carbon frame-work for conjugation to flow. To conclude, bithiophene appears to be suitable building block for the synthesis of variety of antiaromatic macrocycles. It can be observed that the properties and the reactivity of antiaromatic macrocycles vary significantly in contrast to aromatic molecules. However, more such macrocycles would be required to generalize the reactivity of antiaromatic system.

Chapter-3:A

Section-A: Synthesis & Characterization of Ortho-Phenylene-Bridged Hexathiophene Macrocycle

III.1.1 INTRODUCTION

In the previous chapter, synthetic details of expanded isophlorins derived from thiophene sub-units were described along with their structural characterization. It was envisaged that the length of the conjugated pathway in macrocyclic oligothiophenes could be extended by incorporation of benzene in the macrocycle.[40] However the participation of benzene π electrons in the conjugated pathway of smaller macrocycle was not observed in the case of 20π conjugated system. In contrast it was observed in the aromatic 30π conjugated system (figure-20). The presence of *meso* carbons in between every unit of heterocycle unit plays an important role in global delocalization of π electrons.

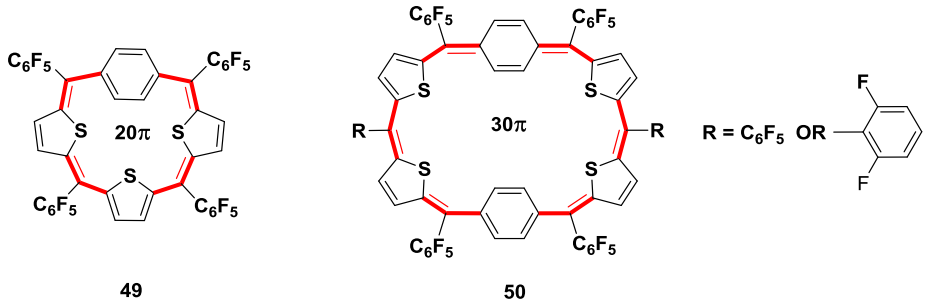


Figure-**20**: Benzene incorporated isophlorinoids.

Another example of benzene appended macrocycles was recently reported[41] by Osuka & coworkers. They highlighted the synthesis of hybrid nanorings by employing strategic cross-coupling reactions (figure-21). Through this reaction, they successfully avoided the bridging carbons in between and the thiophenes were connected ortho to each other on the benzenes. Molecular structures of these nanorings displayed a highly twisted conformation as analyzed through single crystal X-ray diffraction.

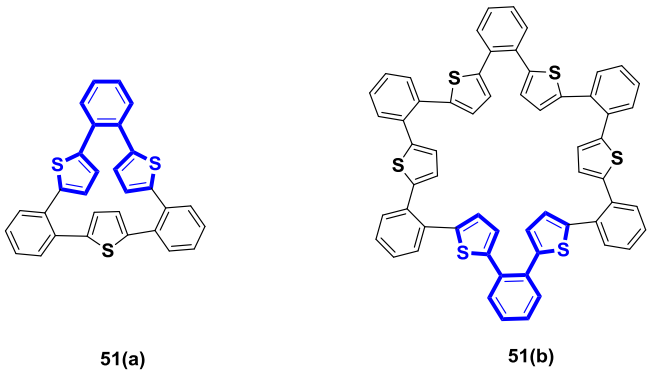
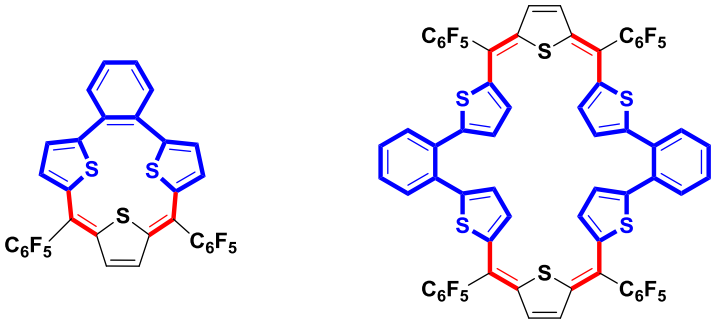


Figure-**21**: ortho-phenylene-bridged hybrid nanorings.

By blending these two synthetic strategies, the synthesis of macrocycles having a combination of *meso* carbons and ortho-phenylene bridge was targeted (figure-22), through a simple synthetic strategy.



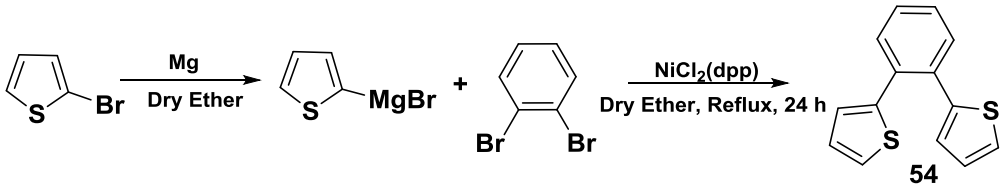
52 53

Figure-**22**: macrocycles having ortho-phenylene-bridge and meso carbons in between.

III.1.2 SYNTHESIS

Synthesis of monomers:

1, 2-Di(thiophen-2-yl)benzene: **54**



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Scheme-**22**: Synthesis of 1,2-Di(thiophen-2-yl)benzene.

Under inert atmosphere using dry diethyl ether (15 ml) as a solvent, thienyl magnesium bromide was prepared from 9.8 g of 2-bromothiophene and 1.5 g of magnesium. 1,2-dibromobenzene (5.7 g) was added after 2 hours and $NiCl_2$ [dppp] (0.32 g) suspended in anhydrous ether was added very slowly at 0^0C (scheme-22). After stirring for 24 hrs under reflux, aqueous ammonium chloride was added to the reaction mixture and the crude product was extracted into ethyl acetate. The crude product was purified by column chromatography using hexane, to obtain 4.5 g of 1,2-dithienylbenzene, **54**, in 65% yield. ^{1}H NMR (400 MHz, $CDCl_3$, 298K): δ 6.98(dd, J = 4Hz, 2H), δ 7.04(dd, J = 4Hz, 2H), δ 7.34(dd, J = 4Hz, 2H), δ 7.44(dd, J = 4Hz, 2H), δ 7.60(dd, J = 4Hz, 2H).

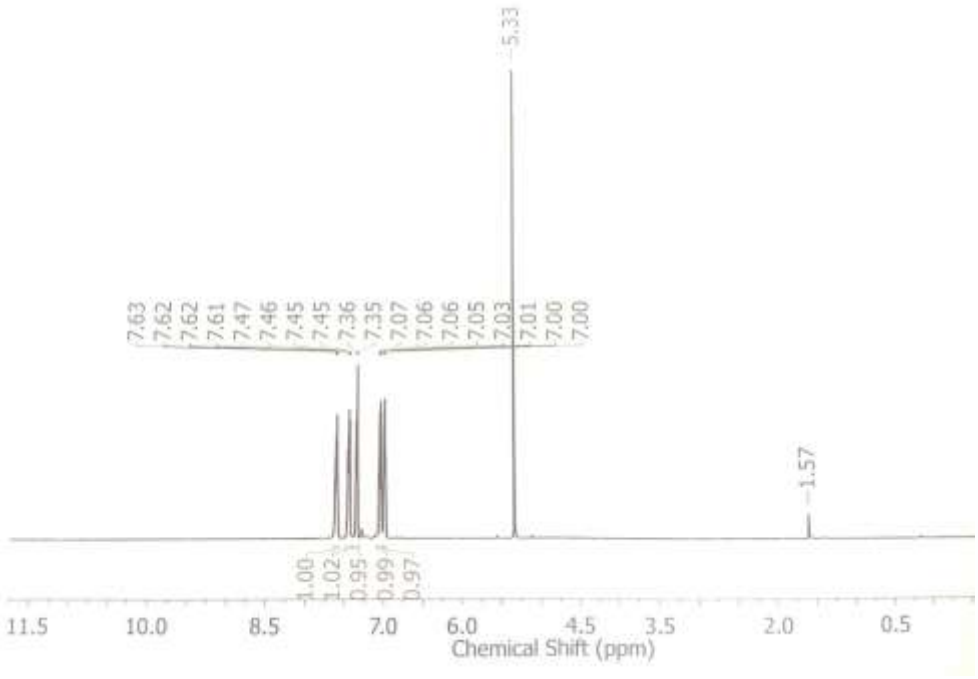
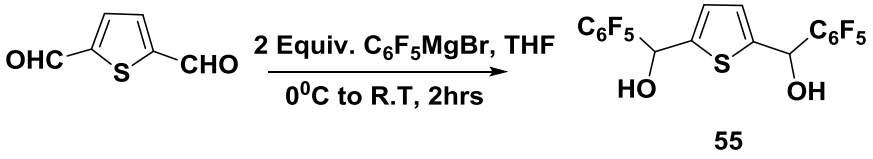


Figure-**23**: ^{1}H NMR of 1, 2-Di(thiophen-2-yl)benzene.

2, 5-bis(pentafluorophenylhydroxymethyl) thiophene: **55**



Scheme-**23**: Synthesis of 2, 5-bis(pentafluorophenylhydroxymethyl) thiophene.

Freshly prepared two equivalents of Grignard reagent (C_6F_5MgBr, 15 mmol) was added to a stirred solution of 2,5-diformylthiophene, II.1, (7.5 mmol, 1.05g in 15 ml THF) under argon atmosphere at 0◦C (scheme-23). Stirring was further continued to attain room temperature, and the reaction mixture was quenched with saturated NH_4Cl solution. The aqueous layer was extracted three times with diethyl ether and the combined organic layers was washed with water and brine solution. After drying over Na_2SO_4, the solvent was evaporated under vacuum to yield the pure compound, as a white solid in 65% yields. ^{1}H NMR (300 MHz, CDCl3, 298K): δ 6.76(s, 2H), δ 6.33(d, J = 8.1Hz, 2H), δ 2.84(d, J = 8.1Hz, 2H).

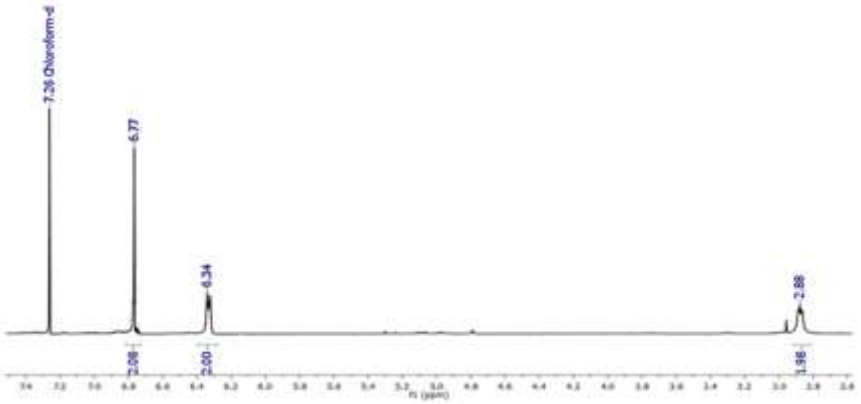
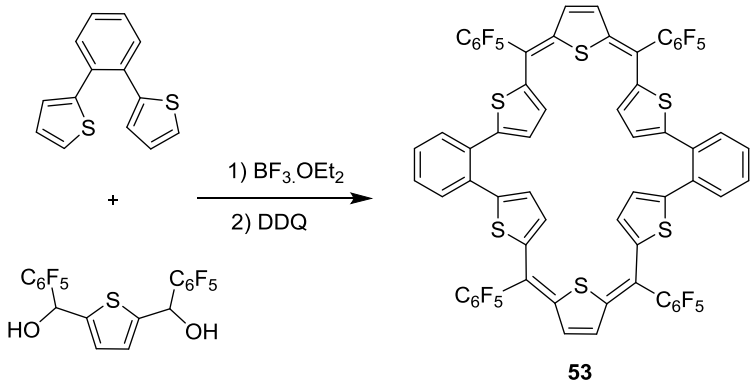


Figure-**24**:^{1}H NMR of 2,5-bis(pentafluorophenylhydroxymethyl) thiophene, **55**.

Synthesis of macrocycle 53:



Scheme-**24**: Synthesis of Macrocycle **53**.

Macrocycle **53** was prepared by mixing **54** (121mg) and **55** (237.8mg) in 150 ml of dichloromethane under dry conditions and in absence of light. $BF_3.OEt_2$ (70.86 mg) was added by micro syringe and the reaction was constantly stirred for further two hours at room temperature. DDQ (283.34 mg) was added and the reaction was now opened to air with continuous stirring for another one hour (scheme-24). The formation of macrocycle **53** was confirmed by MALDI-TOF/TOF Mass spectrum of reaction mixture (figure-25). The reaction mixture was passed through a short pad of basic alumina and the desired product was purified by silica gel chromatography. This macrocycle was further characterized by mass spectrometry, ^{1}H NMR and single crystal X-ray diffraction analysis.

Figure-**25**: MALDI-TOF/TOF Mass spectrum of reaction mixture.

III.1.3: Isolation of macrocycle 53

After neutralizing the reaction mixture by passing through basic alumina, column chromatography led to separation of macrocycle in 10% yields. Purification of this 32π macrocycle was achieved through column chromatography. A deep orange color fraction eluted with CH_2Cl/Petroleum ether(1:20) and displayed an intense absorption at 468 nm (Є = 59,514). MALDI-TOF/TOF: Obsd.: 1361.0181; Calcd: 1359.9570 (**53**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.30 (s,4H), δ 6.98 (d, J = 4Hz, 4H), δ 7.12 (d, J = 4Hz, 4H), δ 7.42 (dd, J = 4Hz, 4H), δ 7.55 (dd,J = 4Hz, 4H).

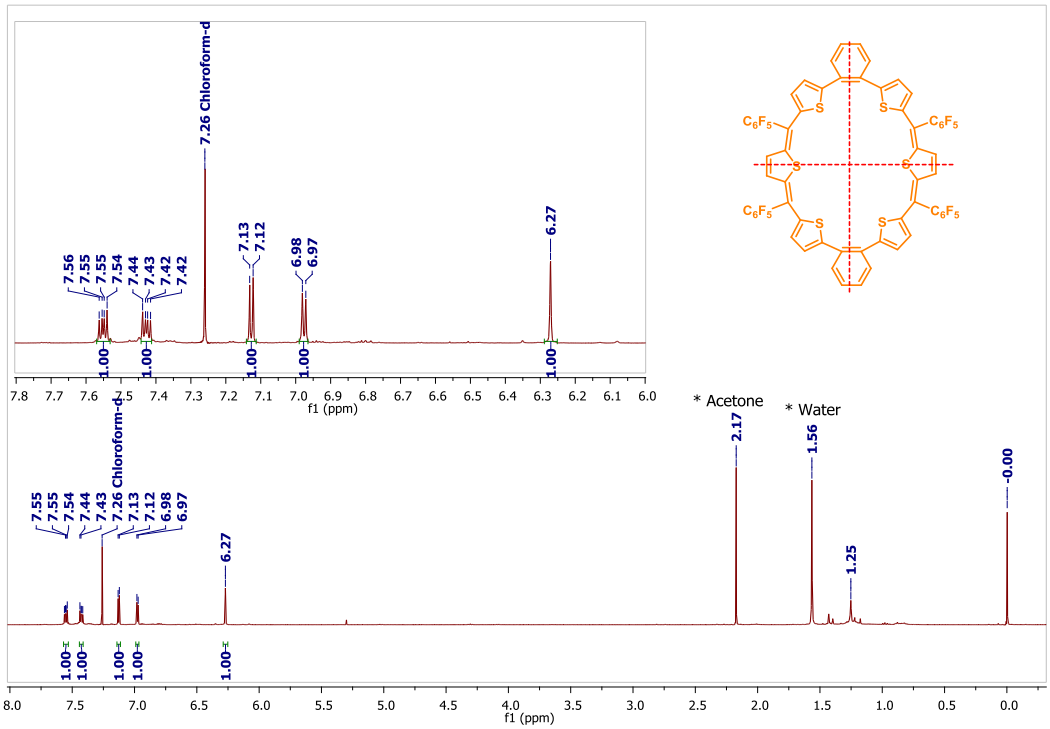


Figure-**26**: ^{1}H NMR of Macrocycle **53** in Acetone-d_6 at RT.

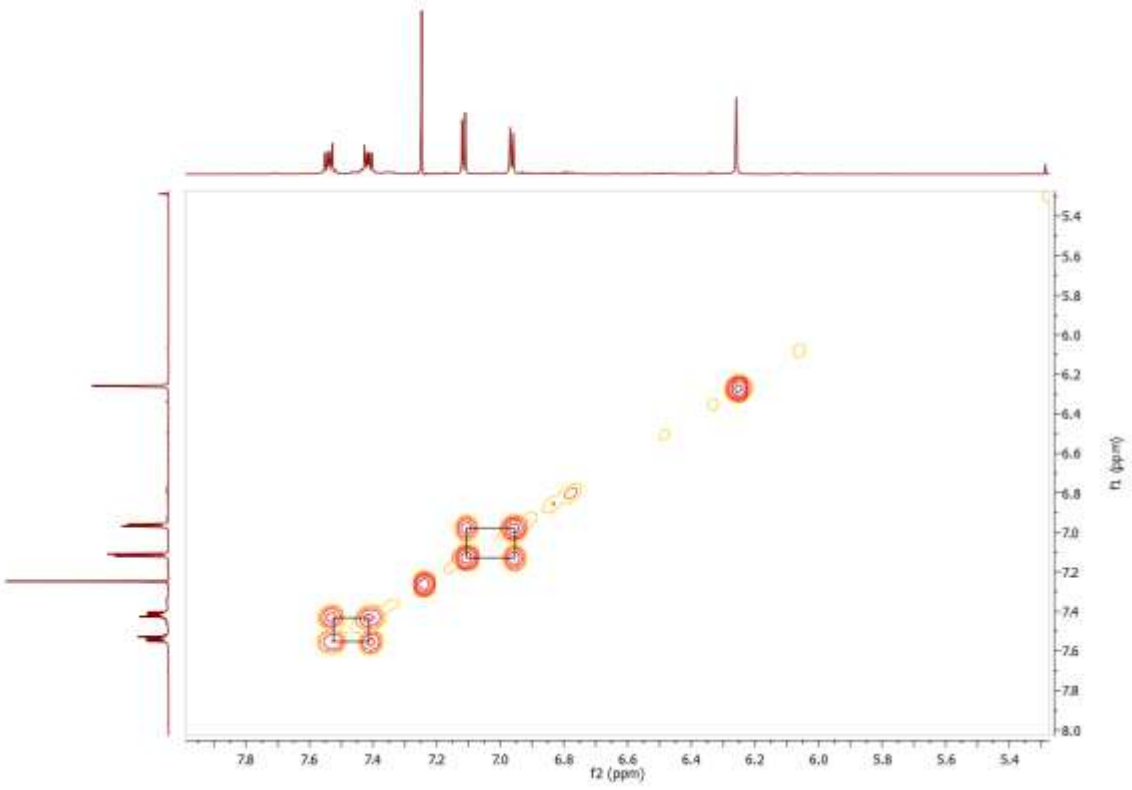


Figure-**27**: 2D COSY of Macrocycle **53** in Acetone-d_6 at RT.

The exact mass of the macrocycle was further confirmed by high resolution mass spectrometry (calculated: 1359.9570 and observed: 1359.9584), shown in figure-28. Further characterization from NMR spectroscopy revealed well resolved spectrum at room temperature. Overall it revealed a symmetric spectrum as observed by two doublets at δ 6.98 and 7.12 ppm, doublet of doublets at 7.42 and 7.55 ppm and one singlet at 6.30 ppm (figure-26). A ^{1}H - ^{1}H COSY revealed two different correlations between the signals. A pair of signals (at δ 6.98 & 7.12; and 7.42 & 7.55 ppm) corresponding to the thiophene and benzene protons were identified respectively (figure-27). The doublet of doublets corresponded to the benzene protons, while the two different doublets were ascribed to the thiophene rings.

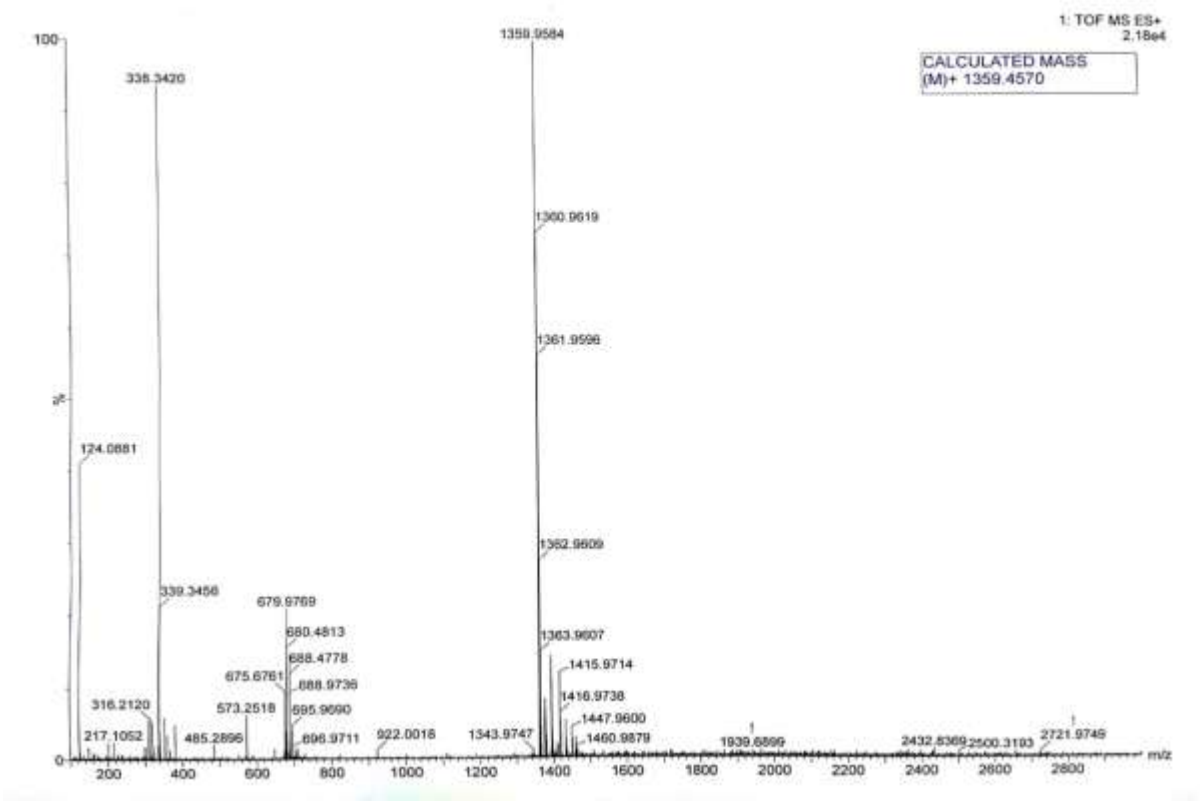


Figure-**28**: HRMS of macrocycle **53**.

III.1.4: CRYSTAL STRUCTURE

Further confirmation of the structure was obtained from single crystal X-ray diffraction analysis. Good quality red crystals were grown through solvent diffusion method using dichloromethane and hexane as solvent systems. The macrocycle crystallized in monoclinic system with C2/c space group and was found to adopt a V-shaped molecule (figure-29).

Viewing along **X**-axis (which pass through the centre of two benzene rings), the macrocycle can be perceived to adopt a butterfly type structure. Both the wings are same but the thiophene units adjacent to benzene shows opposite orientation, in support of the five signals observed in its ^{1}H NMR spectrum.

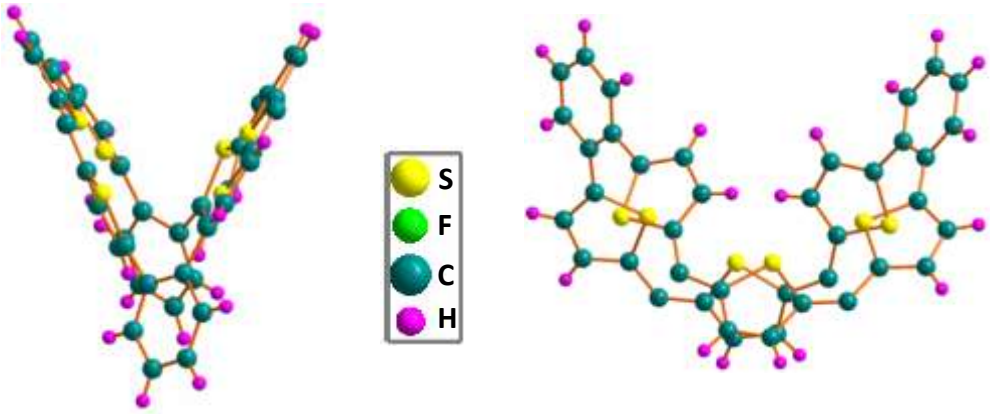


Figure-**29**: a) V-shaped view of the macrocycle **53**. b) Side view of the macrocycle **53**.

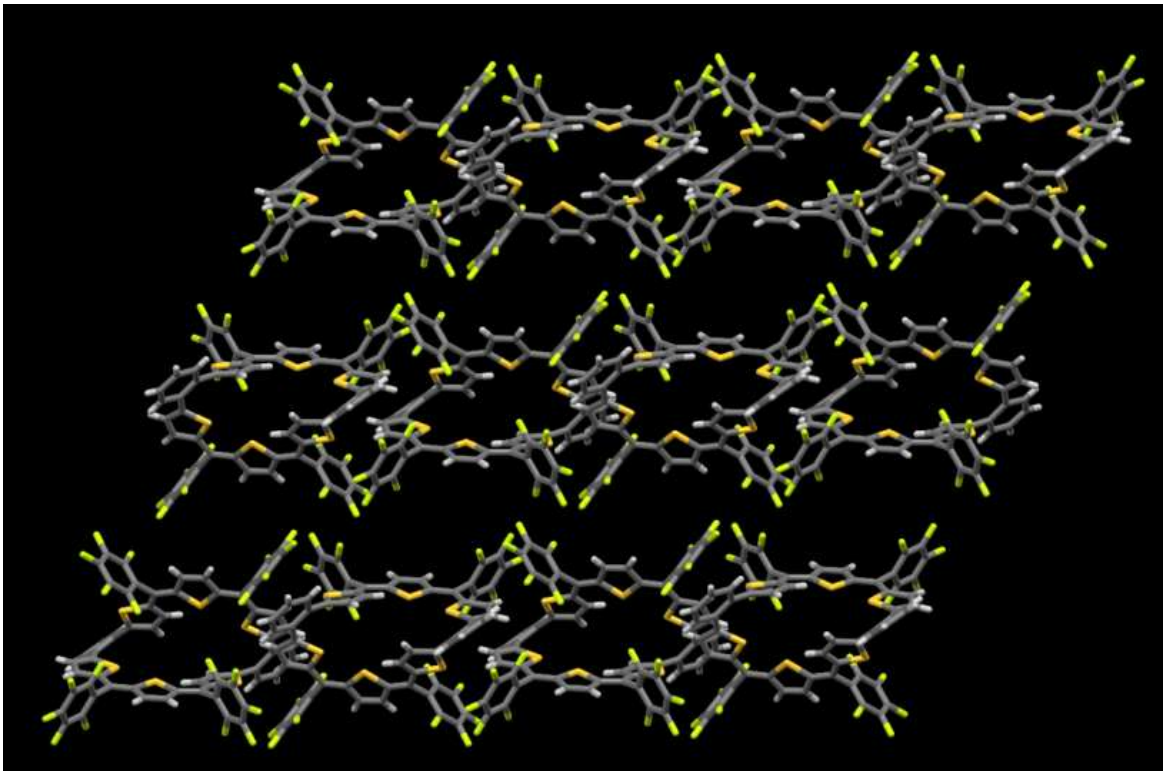


Figure-**30**: Packing of macrocycle **53** in the crystal.

The molecular packing of **53** was found to exhibit a variety of non-covalent interactions in its V- shaped structure. The interaction was observed as the molecules arrange themselves in a linear fashion (figure-30). Packing also revealed few interactions between these linear wires. Inter molecular *C-F---H-C and C-F---* π (3.55 Å) interactions between two pentafluro-benzene of adjacent molecule and between pentafluro-benzene and benzene of adjacent molecule were observed in the crystal packing. Apart from this there is *C-F---H-C* (2.88 Å, 118.71°) between pentafluro-benzene and benzene of adjacent molecule, this clearly shown in the figure below.

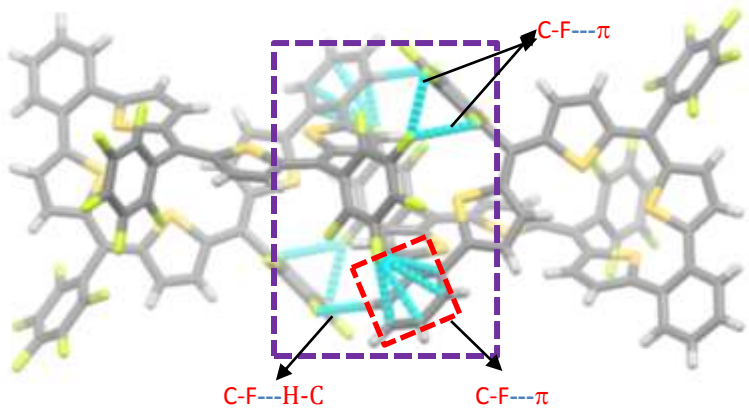


Figure **31**: Non-covalent interaction between two adjacent molecule in crystal array.

A few more inter-molecular interactions between the linearly arranged molecules also, these are *C-F---F-C* (4.33 Å) and *C-F*---π interactions (4.46 Å and 3.91 Å) between two pentafluro-benzene from different linear array. This interaction is indicated in the figure below.

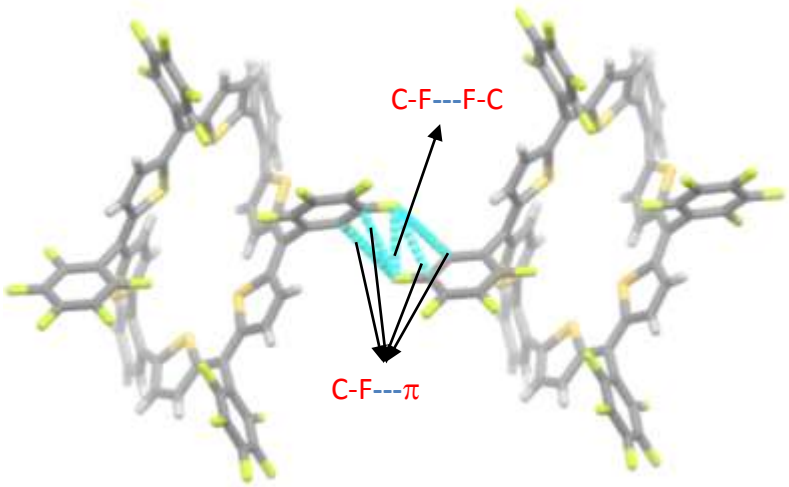


Figure **32**: Non-covalent interaction between two molecules aligned in different linear array.

III.1.5.: Distance between non-covalently interacting units

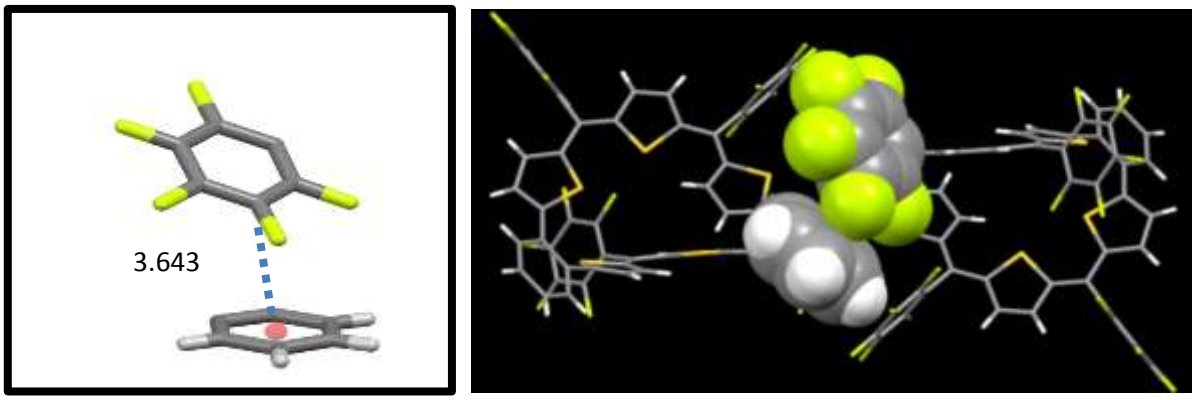


Figure-**33**: Interactions between pentafluorophenyl and phenyl ring of adjacent molecules of macrocycle **53**.

The fluorine nearest to the plane of phenyl ring is having *C-F---π* interactions with the π electron cloud above the phenyl ring (figure-33). The distance between the carbon of the pentafluorophenyl and the center of phenyl ring was found to be 3.64 Å suggestive of *π - π* interactions.

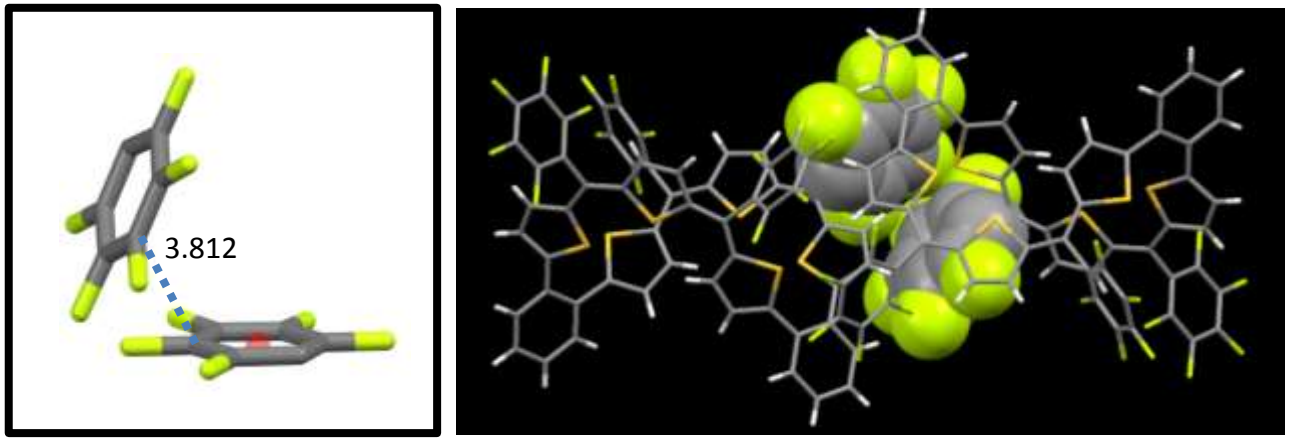


Figure-**34**: Interactions between two pentafluorophenyl rings of adjacent molecules of macrocycle **53**.

As explained earlier in figure: 31 it was shown that *C-F--- π* interactions are observed between the two pentafluorophenyl rings (figure-34). The distance between the two nearest carbons of two different phenyl rings was found to be 3.81 Å.

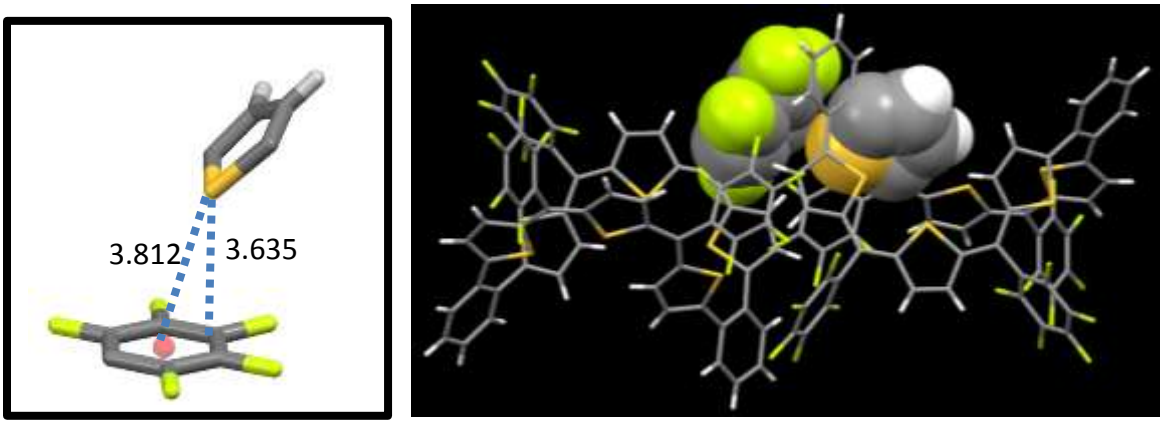


Figure-**35**: Interactions between pentafluorophenyl and thiophene ring of adjacent molecules of macrocycle **53**.

Medium range non-covalent interaction was observed between the pentafluorophenyl ring and the sulphur of the thiophene ring (figure-35). The distance between the sulphur and the center & nearest carbon of pentafluorophenyl is 3.812Å and 3.635Å respectively.

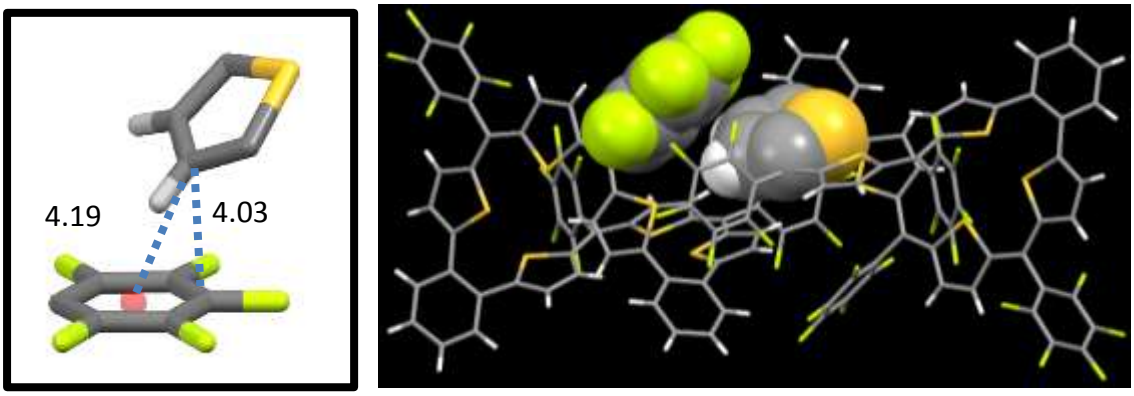


Figure-**36**: Interactions between pentafluorophenyl and thiophene ring of adjacent molecules of macrocycle **53**.

Further, possible weak non-covalent interaction between pentafluorophenyl ring and the thiophene aligned in the direction away from it was also identified in the crystal lattice (figure-36). The distance between nearest carbon of thiophene and center & nearest carbon of pentafluorophenyl ring is 4.19 Å and 4.03 Å.

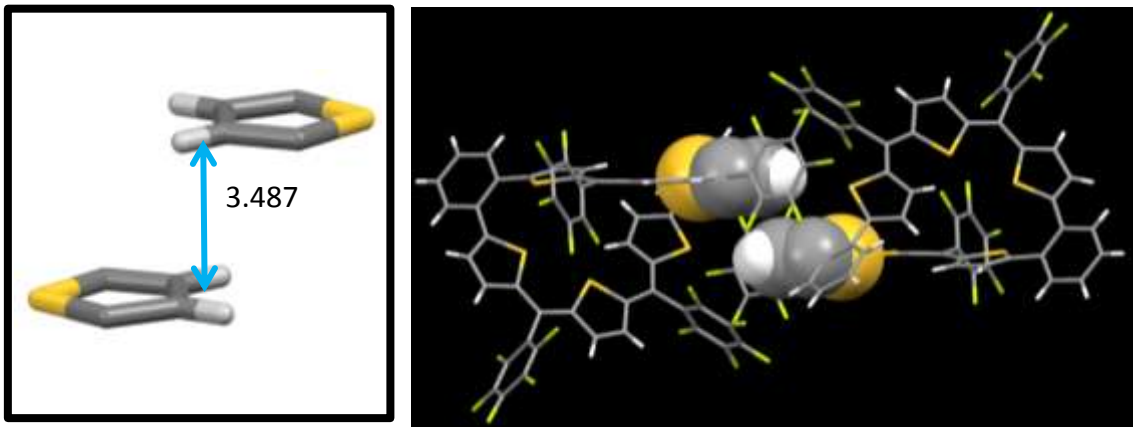


Figure-**37**: Interactions between two thiophene ring of adjacent molecules of macrocycle **53**.

It was very interesting to observe a very strong π- π stacking where it is showing slipped as well as antiparallel kind of stacking with a measured distance between plane of these two thiophene of 3.487Å (figure-37).

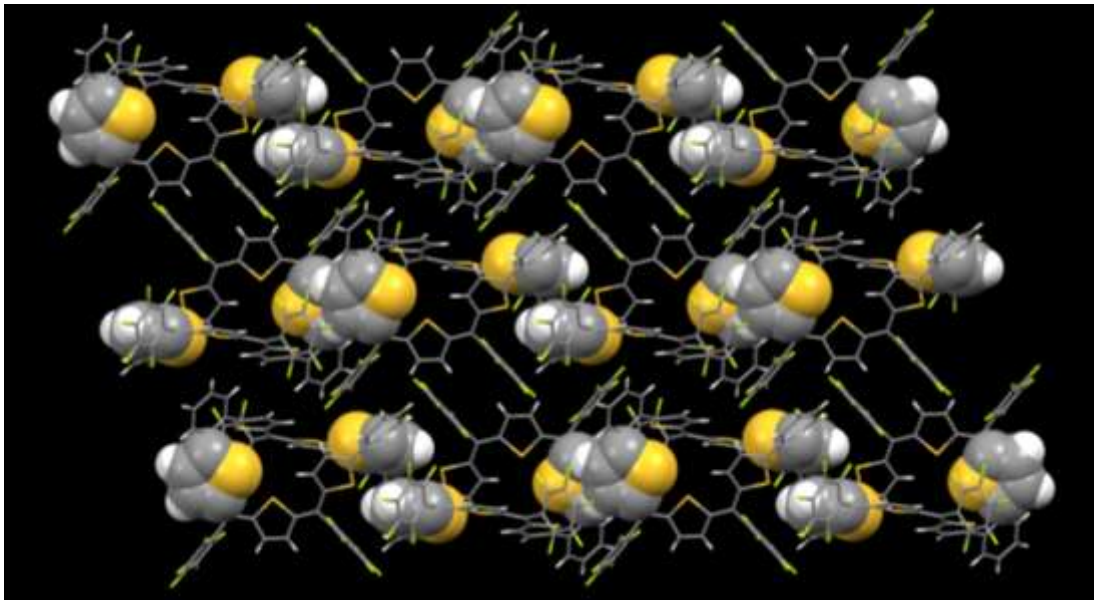
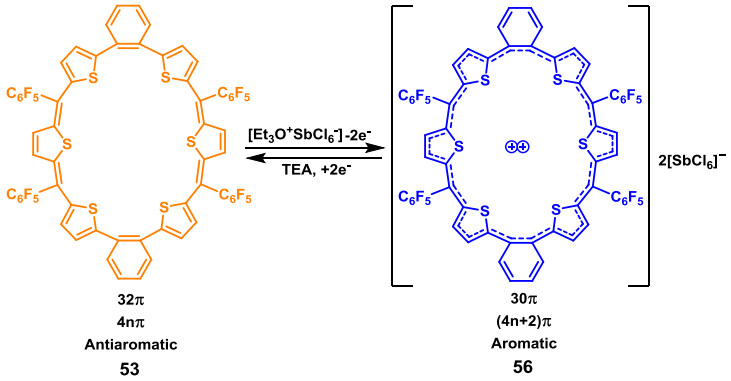


Figure-**38**: Stacking between two thiophene rings in the crystal.

We can easily observe that the stacking of thiophene in the crystal array is both in horizontal and vertical fashion alternatively (figure-38).

III.1.6: Two electron oxidation of 53

Meerwein salt ($[Et_3O]^+[SbCl_6]^-$) acts as an effective ring oxidizing agent for π-conjugated systems. Addition of Meerwein salt to **53** in dichloromethane (scheme-25) immediately induced a color change from orange to bluish colored solution. This bluish solution displayed a red shifted absorption from 468 nm (Є = 59,514) to 674 nm (Є = 90,290) with a relative increase in the intensity, followed by characteristic weak and broad absorption (figure-39), in the region between 900-1000nm, suggesting the strong aromatic character of cationic species **56**. This dicationic species can be easily be converted to the neutral macrocycle upon addition of triethylamine.



Scheme-**25**: Conversion of Macrocycle **53** to its Dication **56.**

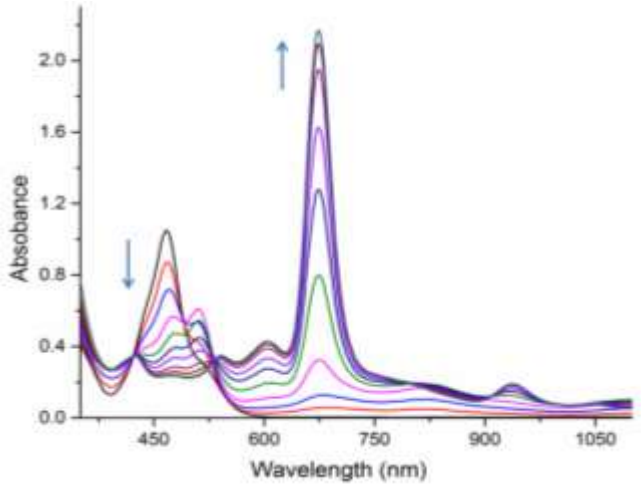


Figure-**39**: Absorption changes observed upon the addition of Meerwein's salt to **53** in dichloromethane.

Even after many trials, it was not possible to isolate the dicationic species **56,** suggestive of its unstable characteristics. Therefore the decaying of dicationic species was recorded over 12 hours at an interval of every two hrs as displayed in figure-40.

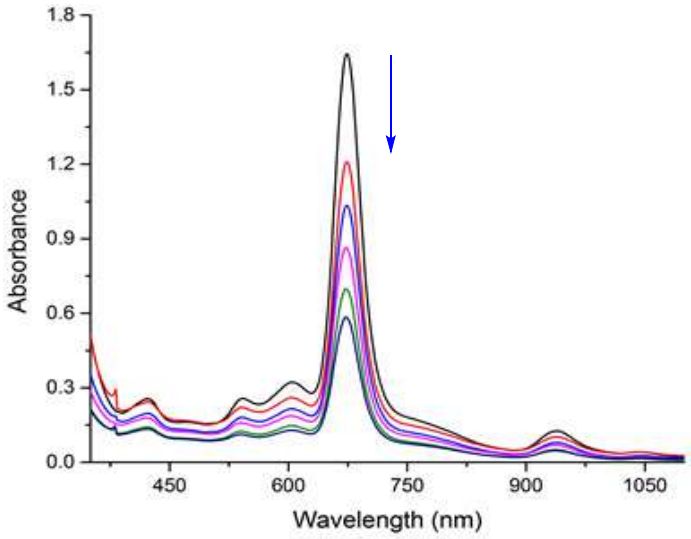


Figure-**40**: Absorption changes showing the decaying of dicationic species **56,** observed after every 2 hrs.

III.1.7: Quantum mechanical Calculations

The non-aromatic character of 32π expanded isophlorin was confirmed by Nucleus Independent Chemical Sift (NICS) calculations at global ring centres. The estimated Nucleus Independent Chemical Shift (NICS)[38] value for this structure was found to be + 1.0 ppm and in support of the non-antiaromatic features of the macrocycle. The ACID[39] plots did not yield definitive direction of the ring current, supporting the lack of π-delocalization in this macrocycle (figure-41).

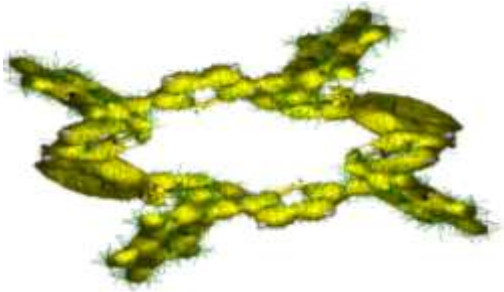


Figure-**41**: ACID plot of **53** at an isosurface value of 0.05.

Macrocycle **53** is non-antiaromatic due to 32π electrons. However, upon oxidation by Meerwein salt, it undergoes a two-electron oxidation to yield the 30π dicationic macrocycle, **56**. Therefore the dication is expected to aromatic due to (4n+2)π electrons. Unfortunately, the dicationic species was not stable under ambient conditions to elucidate its structure either in solid or solution states. However, a strong and intense red shifted electronic absorption suggested the formation of an aromatic species. The estimated Nucleus Independent Chemical Shift (NICS) value for 53 was found to be + 1.0 ppm (as mentioned) and in support of the non-antiaromatic features of the macrocycle.

To simulate the steady-state absorption spectra, time-dependent TD-DFT calculation were employed on the optimized structures. Simulated absorption spectra for the **53**, matched the experimental observed spectrum (figure-42). The estimated values for HOMO – LUMO energy gap is comparable to the earlier reported 32π macrocycles and hence it supports the two-electron oxidation as observed through electronic absorption spectroscopy.

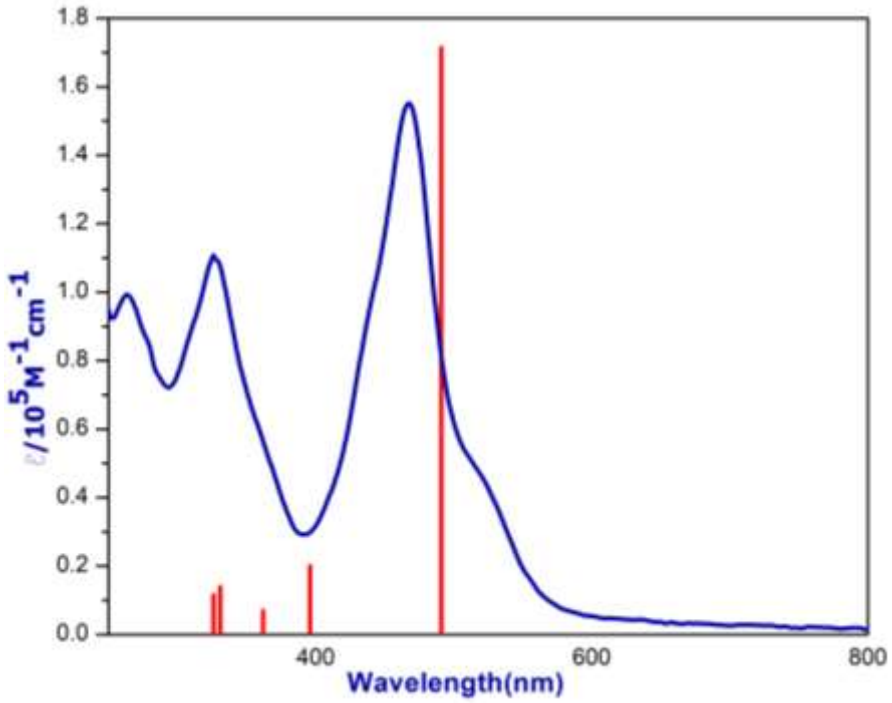


Figure-**42**: UV-Vis absorption spectra of **53** (blue) recorded in CH_2Cl_2 at room temperature along with theoretical vertical excitation energies (red) obtained from TD-DFT calculations carried out at the B3LYP/6-31G(d,p) level.

III.1.8: Conclusions:

Most of the isophlorin-type macrocycles characterized prior to this study are supposed to have planar, twisted, figure-8 and some distorted structures. The introduction of benzene in the macrocycle has shown the formation of V-shaped molecule, which is first of its own kind. Due to presence of pentafluorobenzene and benzene, on crystallization macrocycle **53** displayed a variety of non-covalent interactions. This molecule on crystallization also shows π- π stacking, where two thiophene rings are positioned anti-parallel to each other in slipped stacking. In the next section we have tried to expand macrocycles by increasing number of thiophene in the monomers.

Chapter-3:B

Synthesis & Characterization of Ortho-Phenylene-Bridged Hepta and Octathiophene Macrocycles

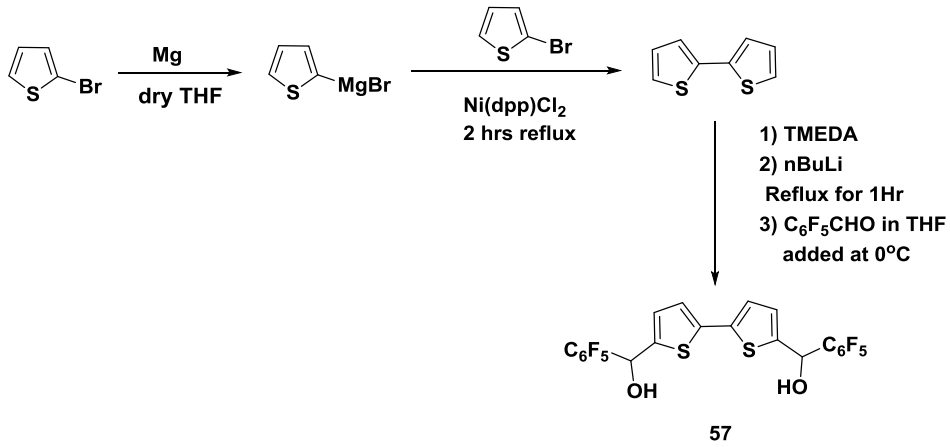
III.2.1: INTRODUCTION

To further explore the structural diversities that can be achieved by incorporation of ortho-phenylene bridge in the macrocycles, a synthetic strategy was designed to increase the number of thiophenes in the macrocycle. Following a similar methodology 1,2-di(thiophen-2-yl)benzene was condensed with bi-thiophene diol and terthiophene diol to obtain higher homologues of the V-shaped macrocycle, 53.

III.2.2: Synthesis

Synthesis of monomers:

Bithiophene diol: **57**



Scheme-**26**: Synthesis of Bithiophene-diol.

N- butylithium (20 ml, 1.6 M solution in hexane, 32 mmol) was added to solution of N,N,N',N'-tetramethylenediamine (TMEDA, 4.8 ml, 32 mmol) in dry n-hexane (50 ml), followed by addition of bithiophene (2.66 g, 16 mmol) under nitrogen. The reaction mixture was heated under reflux for one hour. As the reaction proceeded, a white turbid solution formed indicating the formation of the 5,5' –dilithiated salt of bithiophene. The reaction mixture was cooled to 0°C in an ice bath and a solution of pentaflurobenzaldehyde (31 mmol) in THF (32 ml) was added. The reaction mixture was stirred at 0°C for 15 min and then warmed to room temperature (scheme-26). An ice-cold saturated NH_4Cl solution (50 ml) was added and the reaction mixture was extracted with ether. The organic layer was then washed with brine and dried over anhydrous Na_2SO_4. After removing the solvent under reduced pressure, the crude product is purified by

column chromatography on silica gel using 1:4 ethylacetate/petroleum ether as eluent. The product was collected as a pale yellow powder in 66 %yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.83 (d, J = 4Hz,2H), 6.35 (d, J = 4Hz, 2H), 6.80 (d, J = 4Hz, 2H), 6.98 (d, J = 4Hz, 2H).

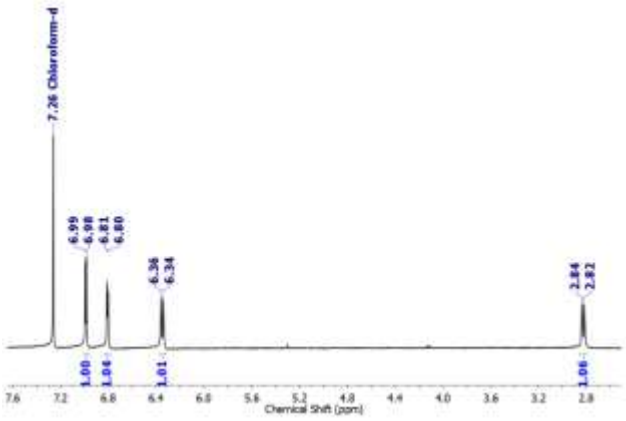
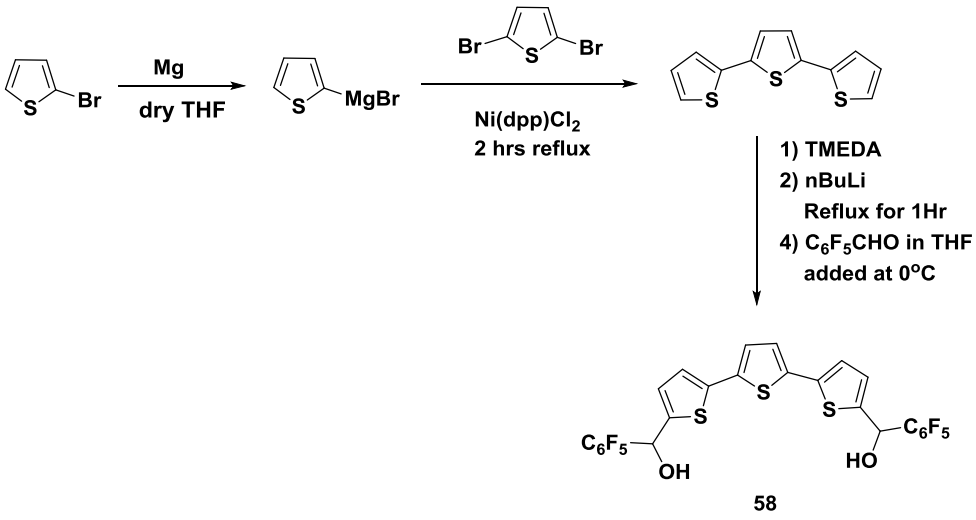


Figure-**43**: ^{1}H NMR of Bithiophene-diol.

Trithiophene-diol: **58**



Scheme-**27**: Synthesis of Bithiophene-diol.

N- butylithium(15 ml, 1.6 M solution in hexane, 24 mmol) was added to a solution of N,N,N',N'-tetramethylenediamine (TMEDA, 3.8 ml, 24 mmol) in dry n-hexane (50 ml), followed by addition of terthiophene (2.5 g, 12 mmol) under nitrogen. The reaction mixture was refluxed for one hour. As the reaction proceeded, a white turbid solution formed indicating the formation of the 5,5' –dilithiated salt of terthiophene. The reaction mixture

was cooled to 0°C in an ice bath and a solution of pentaflurobenzaldehyde (11 mmol) in THF (24ml) was added. The reaction mixture was further stirred at 0°C for 15 min and then warmed to room temperature (scheme-27). An ice-cold saturated NH_4Cl solution (50 ml) was added and the reaction mixture was extracted with ether. The organic layer was then washed with brine and dried over anhydrous Na_2SO_4. After removing the solvent under reduced pressure, the crude product is purified by column chromatography on silica gal using 1:6 ethylacetate/petroleum ether as eluent. Product was collected as pale yellow powder in 56% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 2.84(d, J = 4Hz, 2H), δ 6.36(d, J = 4Hz, 2H), δ 6.81(d, J = 4Hz, 2H), δ 7.00(d, J = 4Hz, 2H), δ 7.05(s, J = 4Hz, 2H).

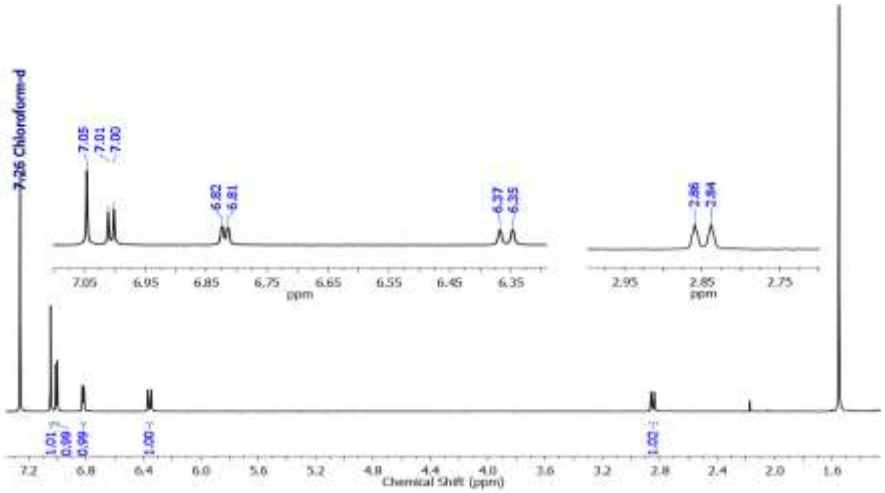
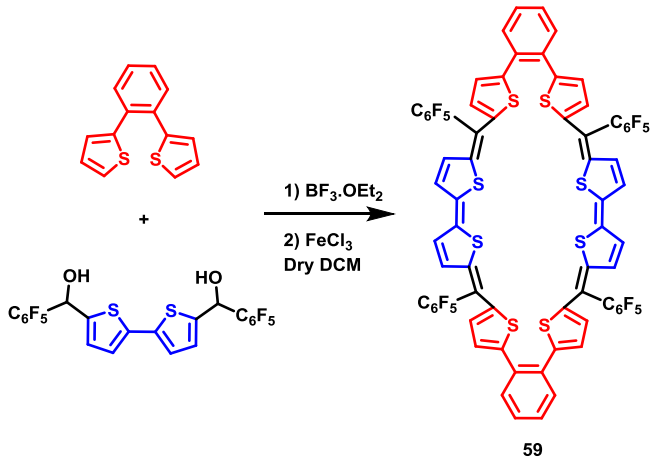


Figure-**44**: ^1H NMR of Terthiophene-diol.

III.2.3: Synthesis of Octathiophene 59:



Scheme-**28**: Synthesis of macrocycle **59**.

1,2-di(thiophen-2-yl)benzene (100 mg, 0.41 mmol), **54**, and bithiophene-diol (230 mg, 0.41 mmol), was dissolved in 100 ml of dry DCM under inert conditions and in absence of light $BF_3.OEt_2$ (0.05 ml, .041mmol) was added by micro syringe and left for constant stirring for 2 hr at room temperature. $FeCl_3$ was added, left open for one hour and basic workup was done by passing reaction mixture through basic alumina. MALDI-TOF/TOF spectrum of reaction mixture was displayed a peak at m/z 1523 indicating to the formation of macrocycle **59**, through a 2+2 condensation of the reactants. The same spectrum also displayed a low intensity peak at m/z 2286 suggesting the formation of macrocycle **60,** by a 3+3 condensation of the precursors (figure-45).

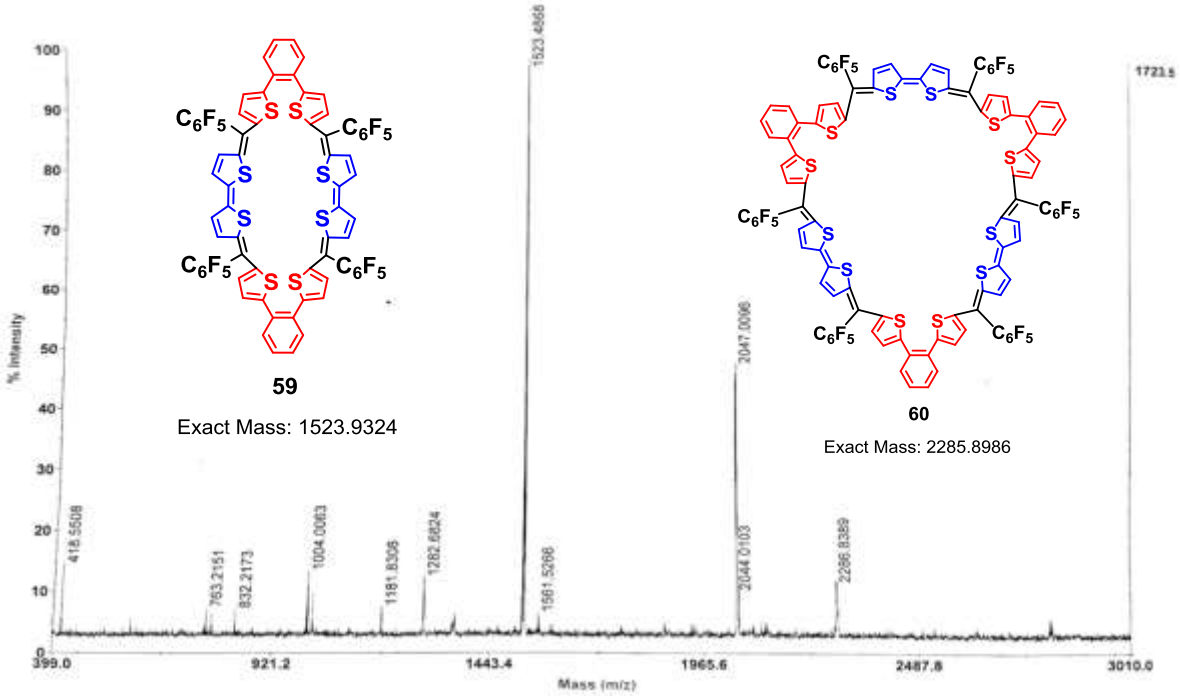


Figure-**45**: MALDI-TOF/TOF Mass spectrum of reaction mixture.

III.2.4: Isolation and characterization of macrocycle 59

After neutralizing the reaction mixture by passing through a short pad of basic alumina, column chromatography was employed for the purification of macrocycle **59**, but it was found that macrocycle was susceptible to decomposition in silica-gel column. Therefore, its purification was achieved using basic alumina as the separating medium, with yield of 2%.

A deep blue color fraction eluted with CH_2Cl_2/petroleum ether (1:4) displayed an intense absorption at 610 nm (Є = 28,284).

In its high resolution mass spectrum it displayed peak at m/z 1524.5728, corresponding to the calculated mass ($C_{72}H_{24}F_{20}S_8$) 1523.9324 (figure-46). As the macrocycle is expected to have exact mass of 1523.9324 instead of the observed 1525.9463, it suggested the possibility of protonated species under mass spectrometric conditions.

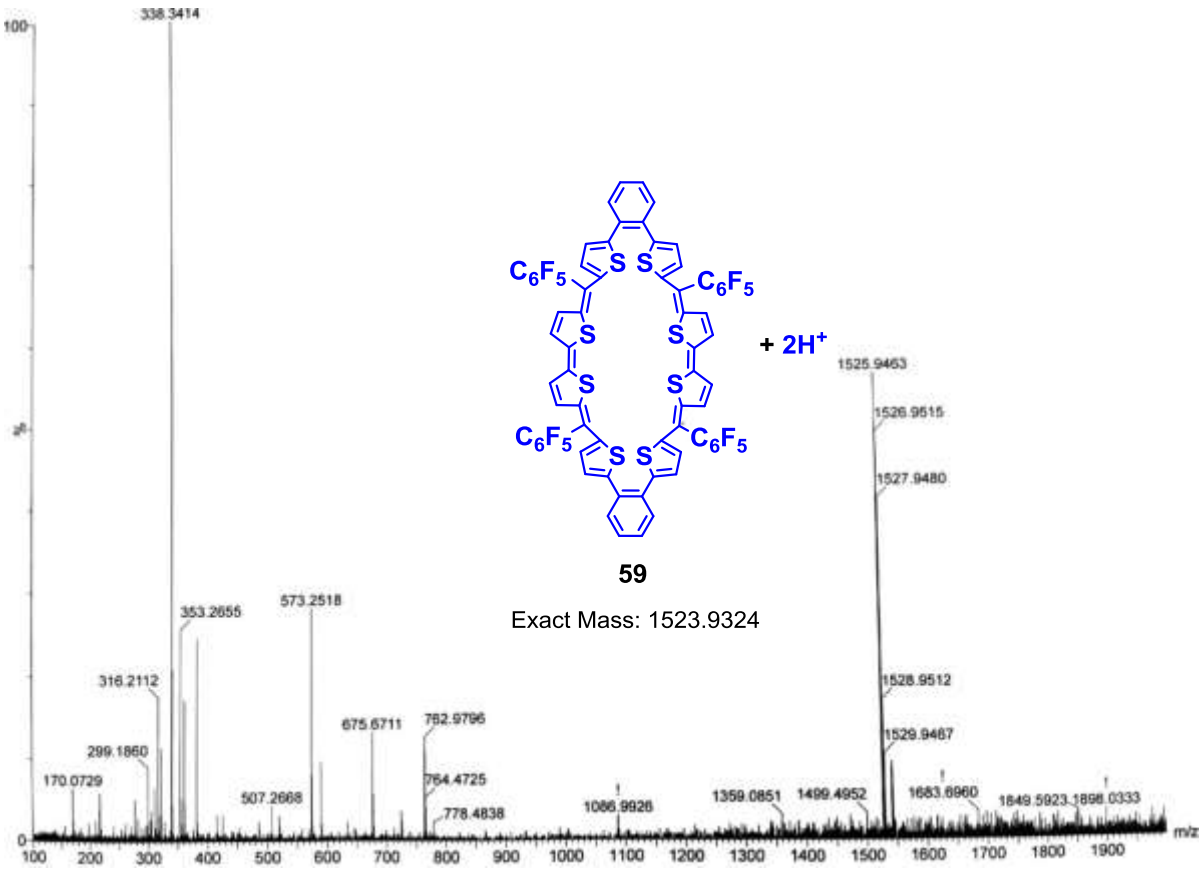


Figure-**46**: HRMS of Macrocycle **59**.

59 was further characterized by ^{1}H NMR spectroscopy and it was expected to display six different signals. However, its ^{1}H NMR spectrum displayed more than the expected number of signals in the region δ 6.0 – 8.0 ppm (figure-47). These chemical shift values and the increased number of signals strongly suggested a non-planar structure devoid of any ring current effects. However, its NMR spectrum recorded at 203K did not reveal any significant difference from the room temperature spectrum (figure-48). Even though ^{1}H-^{1}H COSY recorded at 203K revealed multiple correlations but did not yield conclusive evidence about the structure of this macrocycle (figure-49).

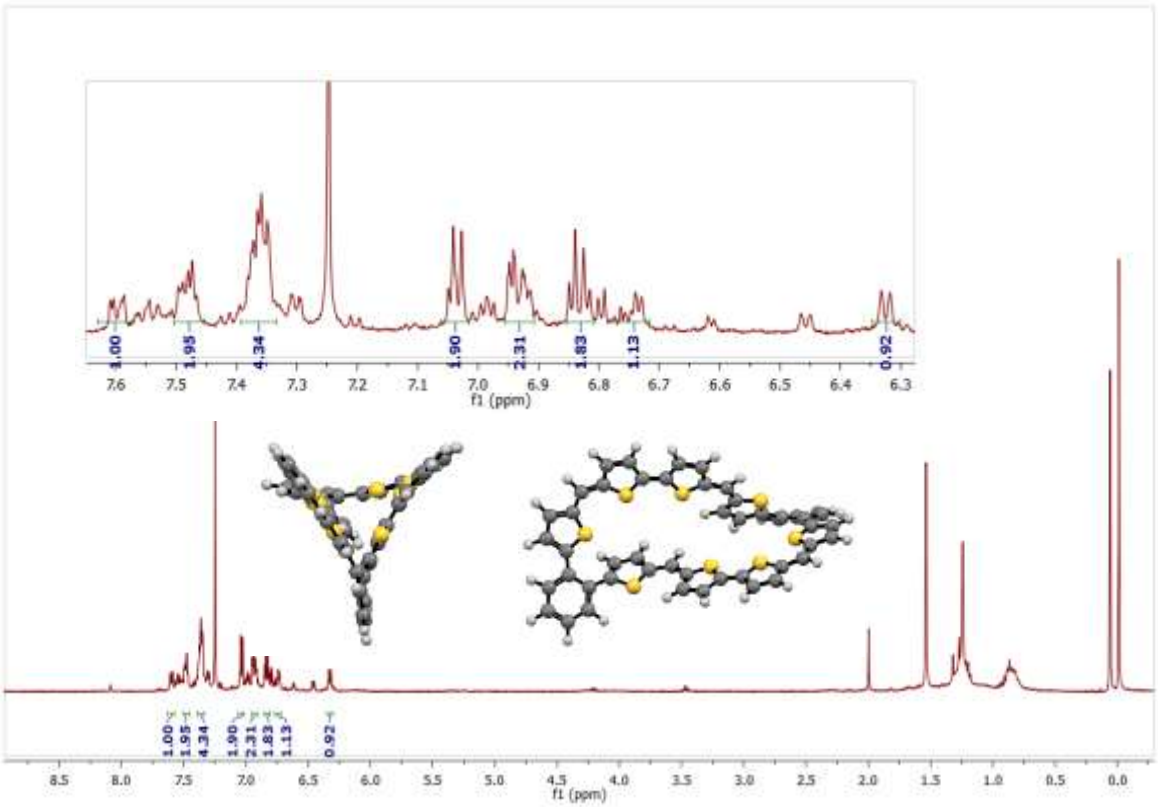


Figure-**47**: ^{1}H NMR of **59** at RT in Chloroform-*d*, with energy optimized structure.

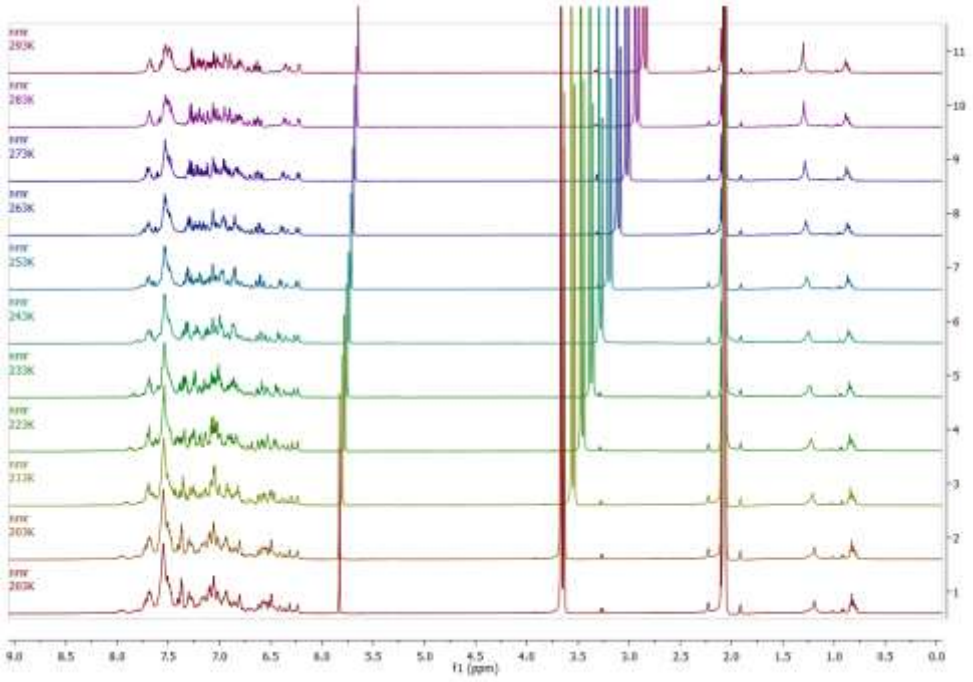


Figure-**48**: Variable temperature ^{1}H NMR of Macrocycle 59 in Acetone-d_6.

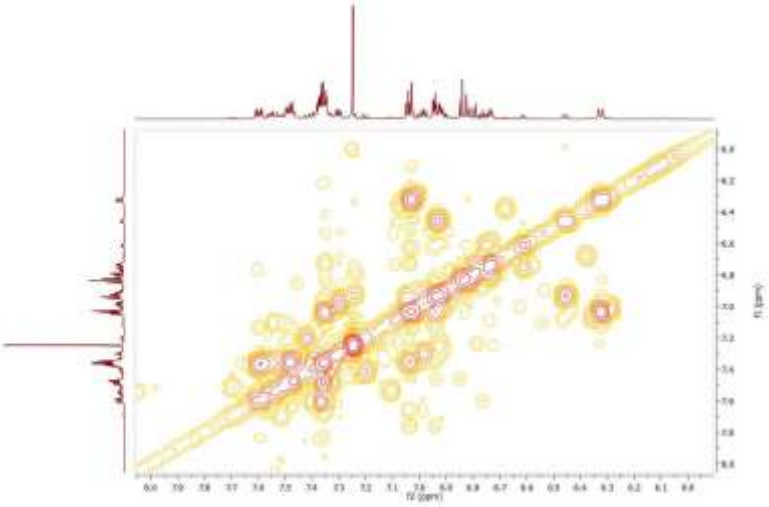
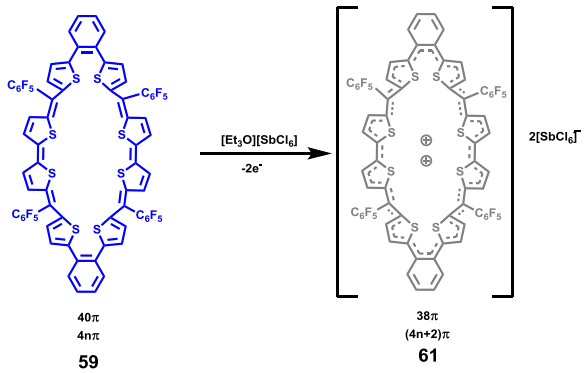


Figure-**49**: 2D-COSY of **59** in Chloroform-*d* at RT.

III.2.5:Two electron oxidation of 59

Owing to its expected anti-aromatic character due to the 40π electrons along its conjugated circuit, it can be expected to undergo two-electron oxidation with suitable oxidizing agents like Meerweins salt ($[Et_3O]^+[SbCl_6]^-$) which acts as an effective two electron-oxidizing agent for 4nπ systems. Addition of Meerweins salt to **59** in dichloromethane (scheme-29) immediately induced a color change from bluish to a grayish colored solution. The gray colored solution displayed a red shifted absorption from 610 nm (Є = 28,284) to 915 nm (Є = 47,059) with relatively increased intensity, followed by weak and broad absorptions (figure-50), in the region between 900-1000nm, suggesting the formation of dicationic species **61**. This dicationic species was easily reduced back to the neutral macrocycle upon the addition of triethylamine.



Scheme-**29**: Conversion of Macrocycle **59** to its Dication **61**.

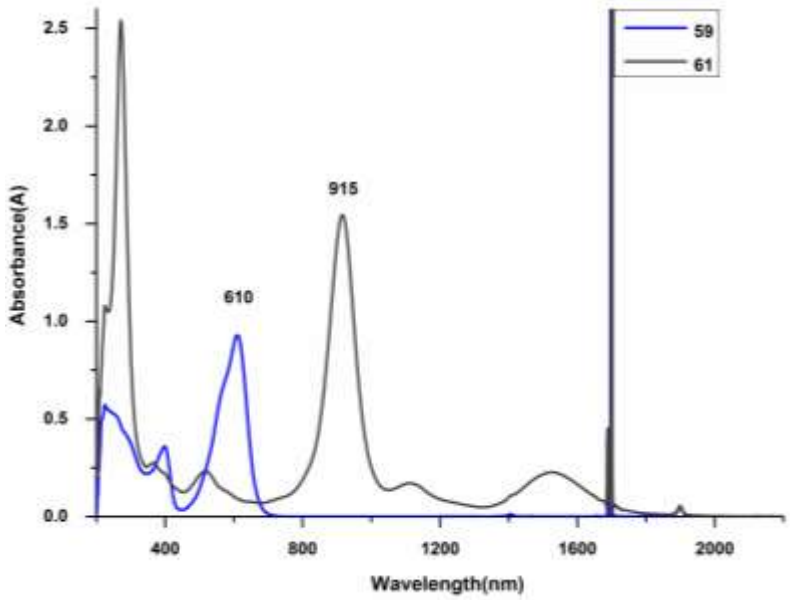


Figure-**50**: Absorption spectrum of **59** and its dication **61** after addition of Meerwein's salt.

High resolution mass spectrum displayed signal at m/z 761.9629 corresponding to the expected m/z at 761.9662 for the dicationic species (figure-51). This observation is found to be in agreement with the calculated species for the dicationic macrocycle expected from the oxidation of the 40π macrocycle **61**.

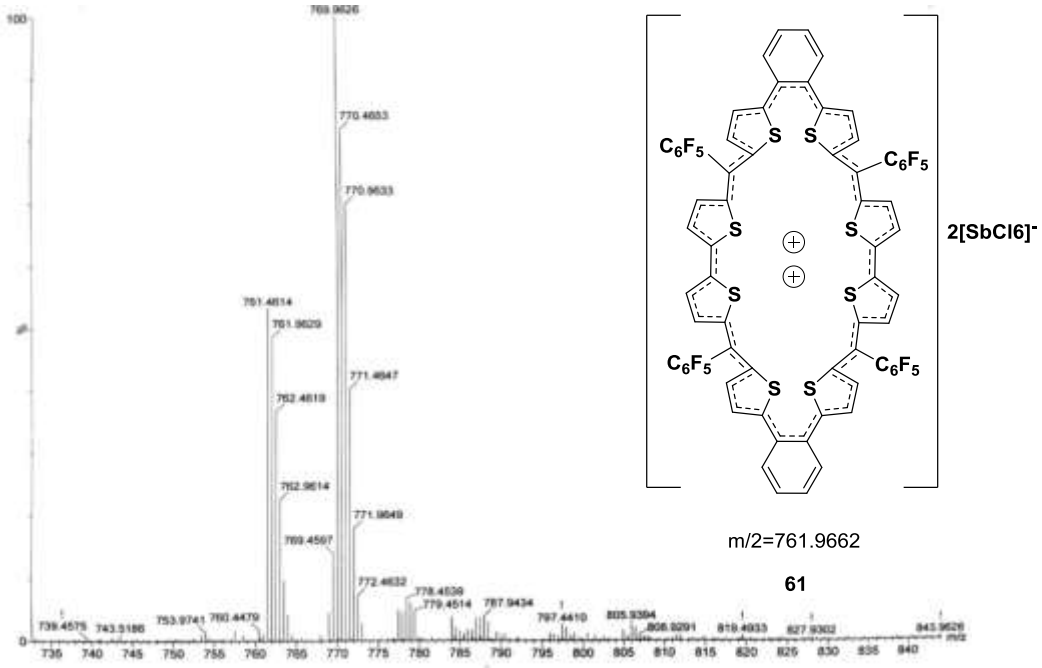
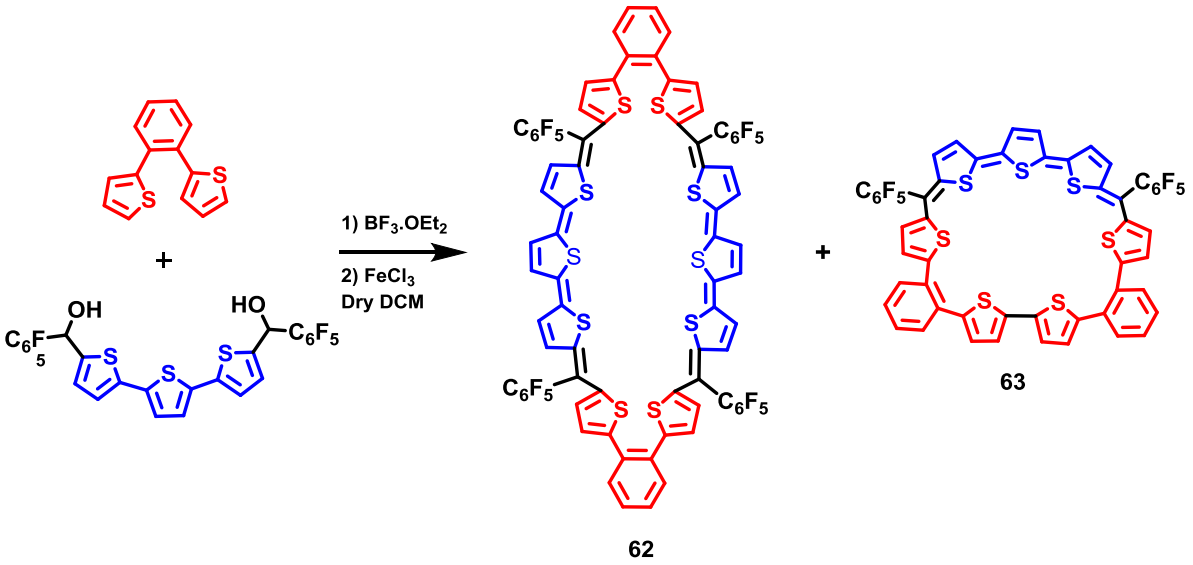


Figure-**51**: HRMS of Dication **61**.

All attempts to crystallize this macrocycle went futile and hence its portable structure was attempted by computational studies. Assuming that the macrocycle was planar, the energy optimization of such a conformation actually yielded non-planar structure with two ring inverted thiophenes. However, the macrocycle tends to lose its planar conformation and hence the ring current effect as observed in its ^{1}H NMR spectrum.

III.2.6: Synthesis of Macrocycle: 63

Based on the synthesis of the macrocycle **59**, a similar reaction was attempted by condensing 1,2-di(thiophen-2-yl)benzene, **54**, with terthiophene diol, **58**, under similar reaction conditions as described in scheme-28.



Scheme-**30**: Synthesis of macrocycle **63**.

2-di(thiophen-2-yl)benzene (100 mg, 0.41 mmol), **54**, and terthiophene-diol (264 mg, 0.41 mmol), **58**, were dissolved in 100 ml of dry DCM under inert condition and in absence of light. $BF_3.OEt_2$ (0.05 ml, .041mmol) was added by micro syringe and left for constant stirring for two hours at room temperature. $FeCl_3$ (167 mg, 2.065 mmol) was added , and the reaction micture was left open to air for one hour (scheme-30). A mild basic workup was provided by passing reaction mixture through a short pad of basic alumina. MALDI-TOF/TOF mass spectrum of the reaction mixture displayed the formation of two different macrocycles corresponding to 2:1 and 2:2 ratio of the precursors (figure-52). However, the

attempted purification of the macrocycles from column chromatography resulted in the decomposition of the expected macrocycle. Nevertheless, the separation was aided when it was attempted on basic alumina column. One of the macrocycles resulted due to 2:1 condensation, in which two molecules of 1,2-di(thiophen-2-yl)benzene, **54**, was condensed with one molecule of terthiophene diol. The higher analogue with 2:2 condensation was also observed but in very low yields.

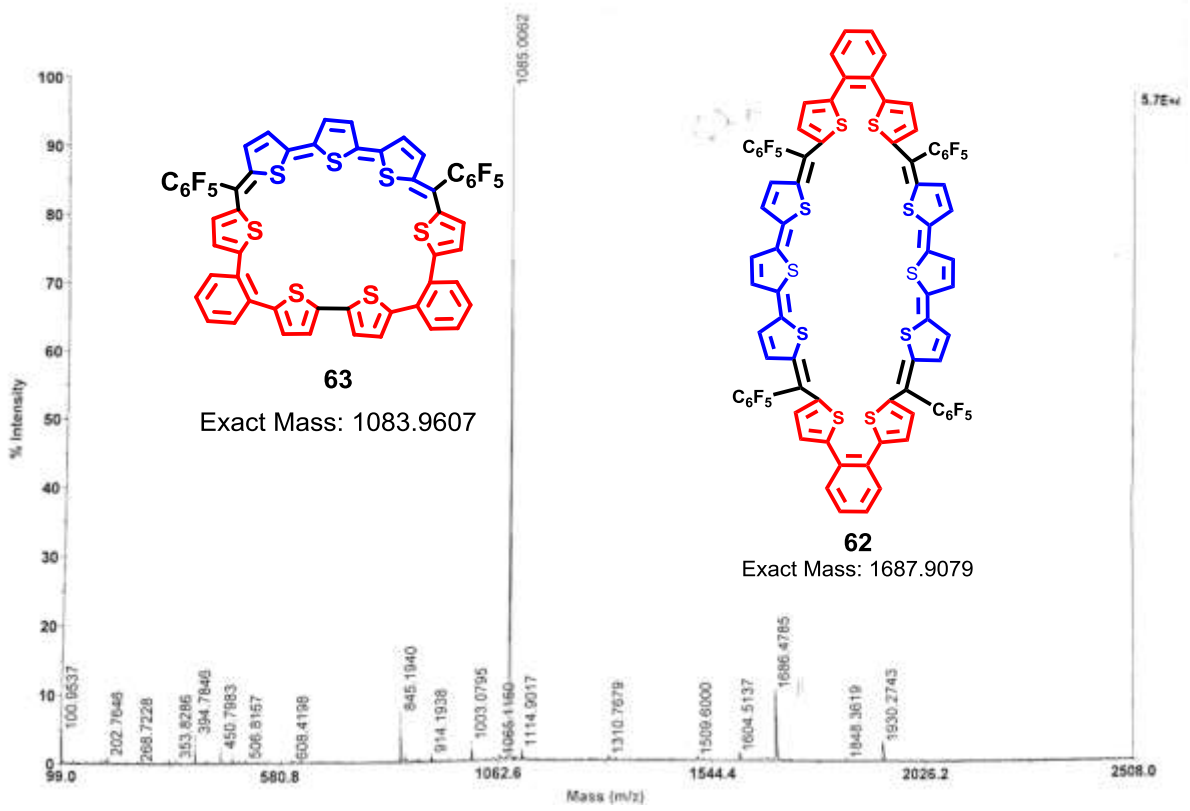


Figure-**52**: MALDI-TOF/TOF Mass spectrum of reaction mixture.

III.2.7: Isolation and characterization of Heptathiophene

After neutralizing the reaction mixture by passing through a short pad of basic alumina, column chromatography was used for purification of macrocycle **63**, Purification of this 34π macrocycle was achieved by repeated chromatographic separation on basic alumina column in 3.5% yield. Seperation was confirmed by MALDI-TOF/TOF Mass spectrum (figure-53), which on further purification gives a deep green colored fraction in CH_2Cl_2/Petroleum ether(1:5), displayed m/z 1085.9761 in its high resolution mass spectrum (figure-54). The

calculated mass value of 1083.9607 corresponds to ($C_{54}H_{22}F_{10}S_7$). A mass difference of almost two units, as mentioned before may be attributed to the diprotonated macrocycle under mass spectrometeric conditions.

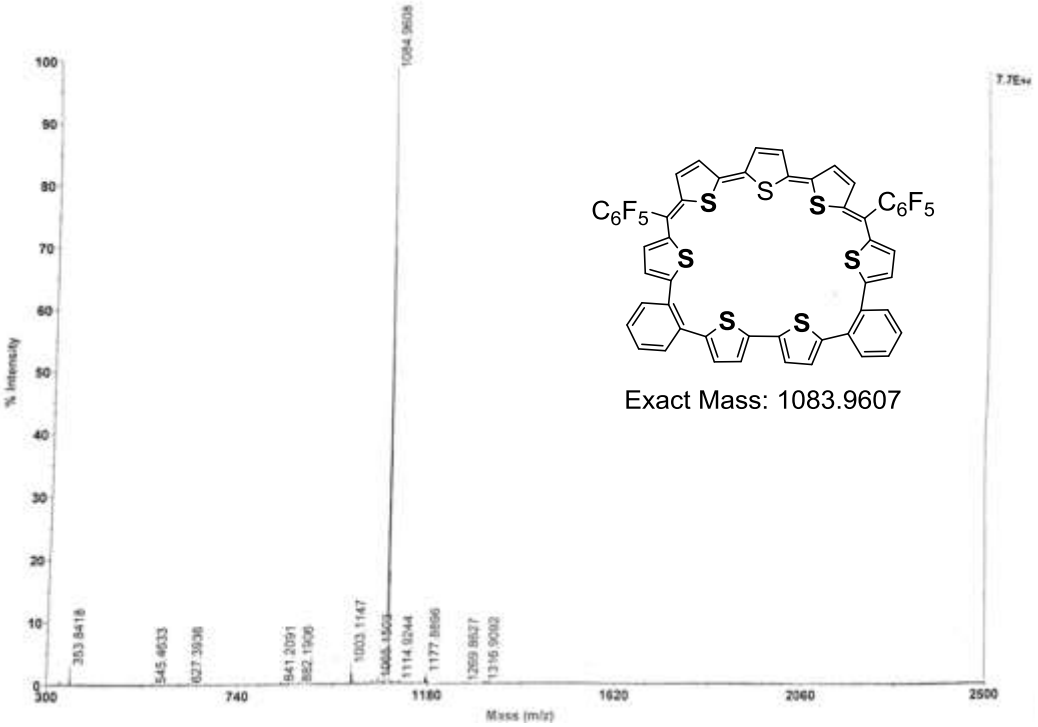


Figure-**53**: MALDI-TOF/TOF Mass spectrum of Macrocycle **63**.

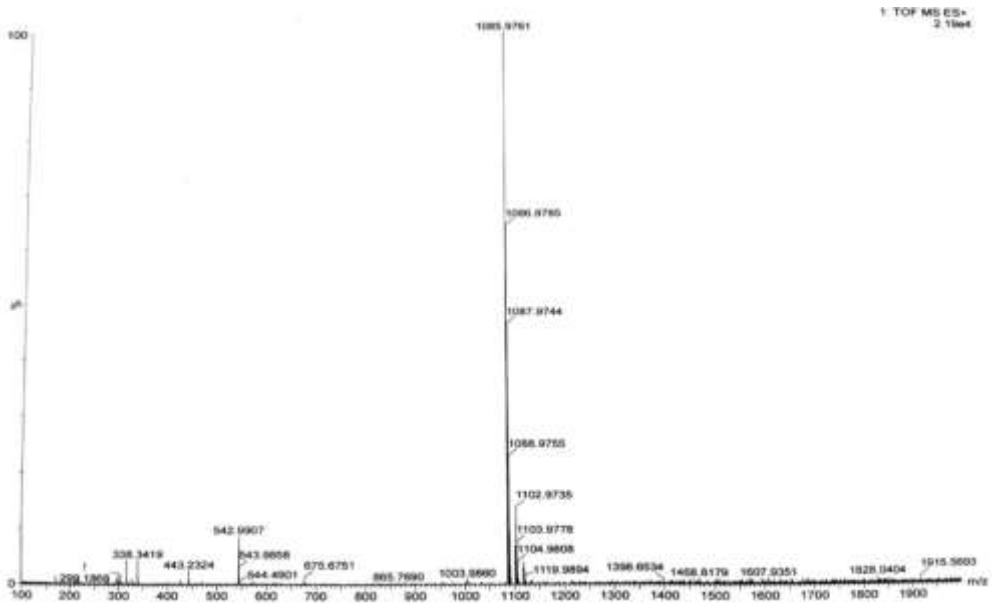


Figure-**54**: HRMS of **63**.

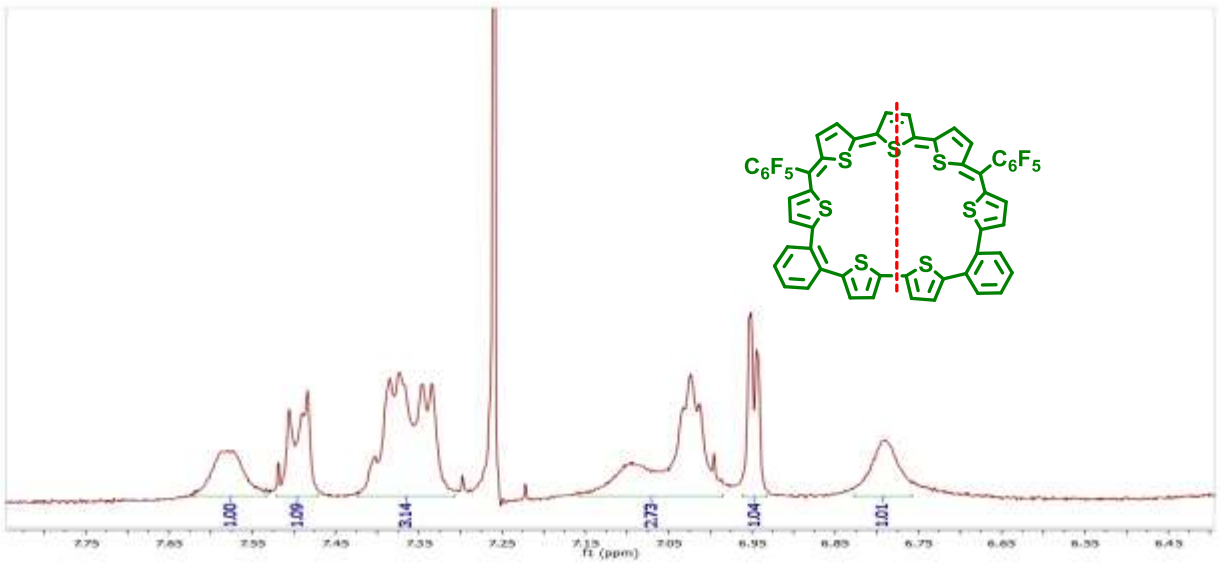


Figure-**55**: ^{1}H NMR of **63** at RT in $CDCl_3$.

Attempts were made to characterize this macrocycle through ^{1}H NMR spectroscopy. However, an unresolved NMR spectrum was observed at room temperature (figure-55) and therefore spectrum was recorded at lower temperatures. The spectrum appeared to resolve better upon decreasing the temperature and a resolved spectrum was observed at 253K (figure -56). Overall eight signals were observed in the region between δ 6.5 to 8.0 ppm. A multiplet could be ascribed to the benzene protons as they appear similar to the pervious described macrocycle, **59**. The rest of doublets correspond to the protons of the thiophene units. As these values do not reflect the expected ring current effect from the 34π aromatic system, **63**, it was suspected that the macrocycle loses its aromaticity due to a non-planar structure. The increased number of signals in comparison to the expected C_2 symmetrical structure further supports the possibility of structure-induced loss of planarity for **63**. All efforts to crystallize this macrocycle went futile and hence its probable structure was deduced through computational studies. The energy optimized structure for the expected planar topology was found to be less favorable in comparison to the non-planar macrocycle (figure-57). The obtained energy minimized structure supports the loss of aromatic features and the unsymmetrical feature as observed from the NMR spectroscopy.

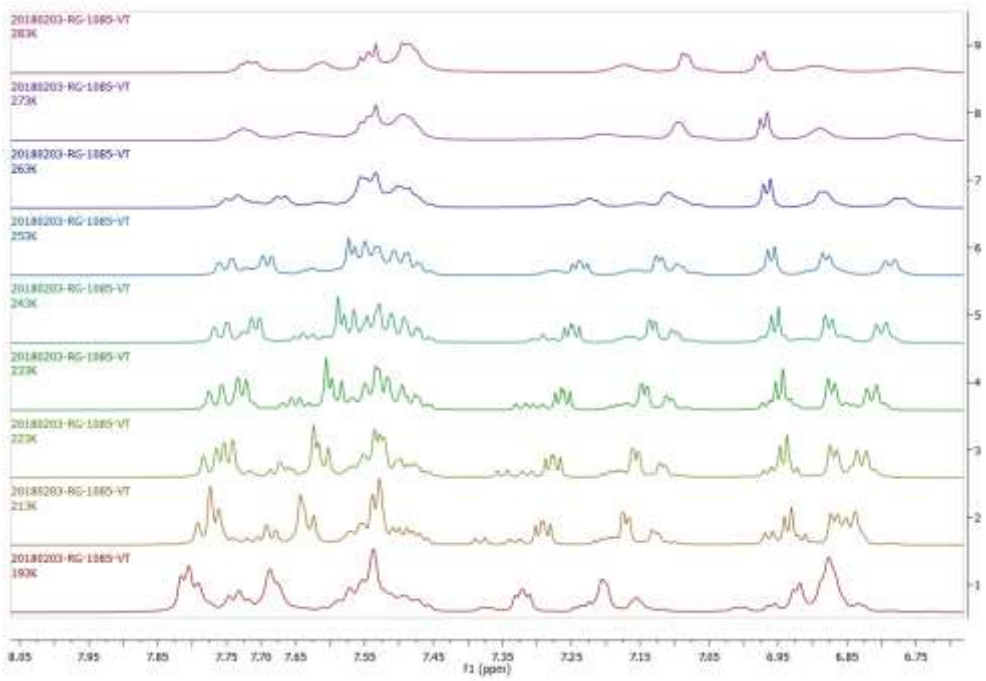


Figure-**56**: Variable temperature NMR of **63** in Acetone-d_6.

Heptathiophene, **63**, can be divided into two equal halfs on the basis of symmetery and expect signals for eleven protons. All the doublets corosponds to thiophene proton whereas multiplets corosponded to benzene protons. ^{1}H NMR (400 MHz, C_3D_6O) δ 6.78(d, J = 4Hz,2H), δ 6.88(d, J = 4Hz, 2H), δ 6.95(d, J = 4Hz, 2H), δ 7.11(m, J = 4Hz, 2H), δ 7.24(m, J = 4Hz, 2H), δ 7.55(d, J = 4Hz, 4H), δ 7.72(d, J = 4Hz, 2H).

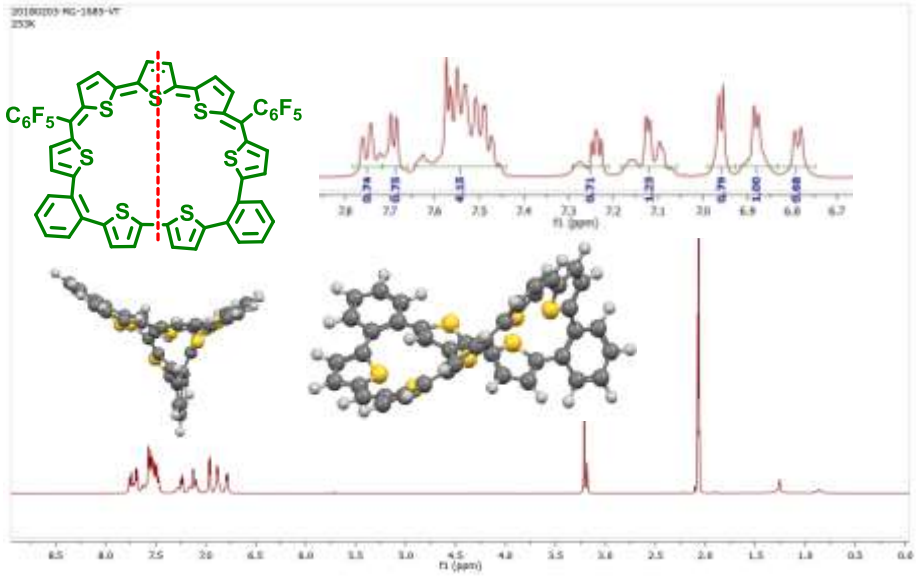
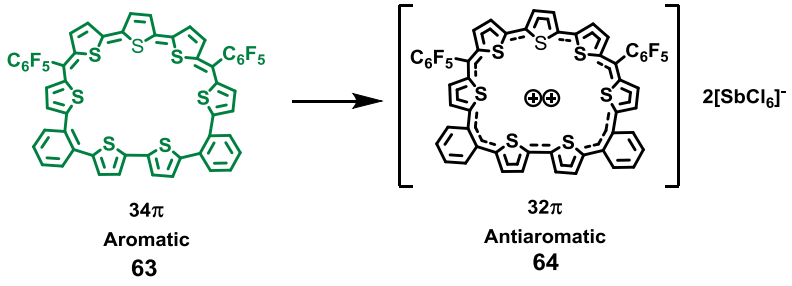


Figure-**57**: ^{1}H NMR of **63** at 253K, with twisted Chem 3D structure.

III.2.8: Two electron oxidation of Heptathiophene

As non-planar aromatic systems are prone to two-electron oxidation, it can be expected that **63** can also lose two-electrons to yield the corresponding anti-aromatic dication. Meerwein salt was employed as an oxidizing agent for the 34π macrocycle. Addition of Meerwein's salt to **63** in dichloromethane (scheme-31) immediately induced a color change from green to a dark colored solution. This green solution displayed a red shifted absorption from 708 nm (Є = 37,071) to 930 nm (Є = 43,864) with relatively comparable intensity (figure-58), sugestive of formation of dicationic species **64**.



Scheme-**31**: Conversion of Macrocycle **63** to its Dication **64**.

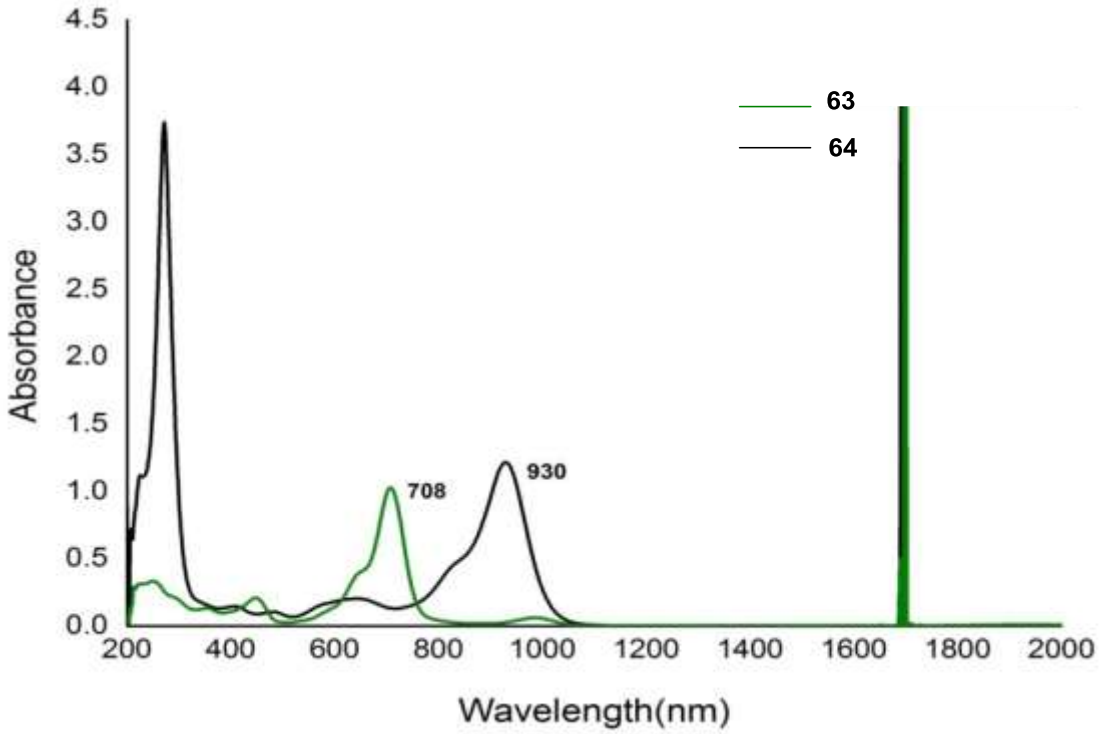


Figure-**58**: Absorption spectrum of **63** and its dication **64**, after addition of Meerweins salt.

However, this 32π dicationic species was found to be unstable under ambient conditions and hence it could not be characterized completely. However, the formed dication undergoes a quick and a facile two-electron reduction to yield the neutral 34π macrocycle in quantitative yields.

III.2.9: Conclusion

In the previous section, the introduction of benzene in the macrocycle has shown the formation V-shaped molecule, which is first of its own kind. Here in this section on increasing the number of thiophene rings in the macrocycle, it was found that on cyclization the reaction is favoring the formation of 2:2 condensation due to the reduced (two) number of thiophene in monomer whereas on increasing number of thiophene from two to three in monomer, the reaction favoured a 2:1 condensation instead of 2:2 condensation. Macrocycles obtained by these synthetic protocols are found to be both aromatic and anti-aromatic due to (4n+2)π and 4nπ-number of electrons respectively. However they tend to lose planarity and are easily susceptible for two-electron oxidation to yield the corresponding dicationic species.

The thesis describes the design, synthesis, characterization and redox properties of planar and non-planar macrocycles derived from thiophene subunits. From the synthetic view point, the one pot synthesis of expanded isophlorins from bithiophene diol through acid catalyzed self-condensation yields π-conjugated aromatic, antiaromatic and unstable radical cyclic systems. Appropriate analysis of the isolated macrocycle was done in the terms of structural features, electronic and redox properties. One of the most important aspect of this thesis is existence of two different conformations of 36π octathiophene in solution and solid state. This was confirmed when the octathiophene showing only two signals in ^{1}H NMR in solution state displayed flipping of two diagonally opposite thiophene units in its molecular structure on crystallization. The structure was found to be almost planar. Moreover this macrocycle easily undergoes two electron oxidation.

Introduction of benzene in such type of expanded isophlorins results in the loss of planarity of macrocycles. The third chapter describes the synthesis of a dibenzi expanded 32π isophlorin through a simple methodology. It adopts a unique V-shape not observed in that class of macrocycles. In accordance with the loss of planarity, it is not found to be antiaromatic in nature. This result reveals the role of different aromatic sub-units on the structure of the macrocycles. The non antiaromatic nature of the macrocycle was confirmed through NICS calculation, which was estimated to be +1ppm, indicating very weak antiaromatic nature of macrocycles. Moreover ACID plots displayed random direction of dipole moment in the molecule due to non-planar structure. This macrocycle also very easily undergoes facile two electron oxidation to yield 30π dicationic species, which was found to be unstable in nature. Studies are in progress to explore the effect of fused aromatic rings on such antiaromatic macrocycles.

In conclusion, this thesis presents the unexplored facets of isophlorin and its higher derivatives in particular, which can be extrapolated to antiaromatic systems in general. It is always considered that antiaromatic molecules are unstable in nature, this presumption is proved wrong through the work of this thesis. It can easily be concluded that anti aromatic macrocycles easily undergoe two electron oxidation in comparison to their aromatic

counterpart. Introduction of benzene in such π conjugated system shows interesting structural properties to be explored in future.

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Publication

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