STUDIES ON SYNTHESIS, STRUCTURES
AND REACTIONS OF SMALL MEMBER BRIDGED
AROMATIC COMPOUNDS

September 2012

Department of Energy and material Science
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STUDIES ON SYNTHESIS, STRUCTURES AND REACTIONS OF SMALL MEMBER BRIDGED AROMATIC COMPOUNDS

A Thesis Presented

By

Bigyan Sharma

Submitted to the Graduate School of Science and Engineering Saga University in partial fulfillment of the requirements for the degree of

DOCTOR OF PHILOSOPHY

Organic Chemistry

September 2012
DEDICATION

For my Parents

Late Tikaram Acharya & Late Mukhyarupa Acharya

For my

Wife Pramila

Son Ujwol & Daughter Yuki
ACKNOWLEDGEMENTS

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Thank you
ABSTRACT

STUDIES ON SYNTHESIS, STRUCTURES
AND REACTIONS OF SMALL MEMBER BRIDGED AROMATIC
COMPOUNDS

September 2012

Bigyan Sharma, Saga University, Japan
Directed by: Prof. Takehiko Yamato

The reaction route of strained small member bridged aromatic compounds having methyl group undergoes Iodine induced and Lewis acid catalyzed isomerization and transannular reaction to pyrene derivatives having alkyl groups played greater role of photo-physical properties in OLED materials. The recent and unique technique of isomerization product of pyrene derivative from [2.2]meta and [2.2]metaparacyclophane is the novel path to get highly fluorescence probes. The novel [3.3]pyrenophane compounds were first prepared and established their different conformer by applying spectroscopic technique. The 6,18-di-tert-butyl-9-methoxy[3.3]metacyclo(1,3) pyrenophane was shown as syn-conformation, which is the unique and novel conformer. In contrast, 17-tert-butyl-5,6,7,9-tetramethyl-2,11-dithia[3]metacyclo[3](1,3)pyrenophane was anti-conformer. The photooxygenated product of highly strained octamethyl[2.2]metacyclophane produced a mixture of mono- and bis-endoperoxides, while the corresponding octamethyl[2.2]metaparacyclophane afforded only the bis-endoperoxide. Finally, studies of a highly strained small members bridged aromatic compounds undergo Lewis acid catalysed and photooxygenation reaction is our final goal included in this thesis.
STUDIES ON SYNTHESIS, STRUCTURES
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AROMATIC COMPOUNDS

By
Bigyan Sharma

A thesis submitted in partial fulfillment of the requirements for the degree of

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Chapter 1

General Introduction

Small member bridged aromatic compounds

In this chapter general introduction of Small member bridged aromatic compounds (cyclophane) and their applications are presented, and brief introduction outline of present thesis are also discussed.
1. General introduction

1.1 Small member bridged aromatic compounds (cyclophane)

Small member bridged aromatic compounds (cyclophane) have been studied for more than one century and have been broadened dramatically. Cyclophane chemistry has both theoretical and practical use and plays an important role in the study of electronic interactions and system strain. It demonstrates that two or more closely placed π electron clouds have both steric and electronic interactions. Transannular interactions also play an important role in the stabilization of the cations and anions generated from cyclophanes.

According to Cram\(^1\) Schubert\(^2\) and Smith\(^3\) a cyclophane consist in principle of an aromatic core (arene ring) and an aliphatic chain that forms a bridge between two non-adjacent positions of the aromatic unit (Figure 1.1). Cyclophanes are a class of compounds which are made of bridged aromatic molecules. [n]Cyclophanes are among the simplest possible cyclophane structures. The most common of these consist of a phenyl ring, to which is attached an aliphatic "tether" of length equal to n methylene units. As with any disubstituted benzene, [n]cyclophanes may be meta-, para- or ortho- (left to right, Figure 1.1), although [n]orthocyclophanes are often considered to be simple fused-ring systems rather than true cyclophanes. Complicated cyclophanes are the [m.n] type’s cyclophanes molecules which contain two tethers with methylene chains of lengths m and n, respectively. Because of the added complexity of these molecules, many more permutations are possible than with the [n]cyclophanes. Once again, meta-, para-, and ortho- isomers are possible, in addition to adding the possibility of incorporating multiple tether and aromatic systems, as is the case with[m]para[n]metacyclophane 4, [m.n]paracyclophane 5 and [m.n]metacyclophane 6 (Figure1.2).
The nomenclature for this class of compounds was developed over a number of years, starting from 1930 by Wieland et al.\textsuperscript{4}, in the 1983, who recognised certain stereochemical relationships of dissymmetry in these cyclic systems and choose to name them as “Ansacompounds\textsuperscript{5}” [Ansas (Latin) meaning—handle] since the bridges looked like handles to the ring when portrayed in two dimensions.

![Fig.1.2: Some examples of [m,n]cyclophanes](image)

Vögtle and Neumann in 1970 contributed further to the cyclophane nomenclature. The first part of the phane nomenclature developed by the International Union of Pure and Applied Chemistry (IUPAC) was published in 1998.\textsuperscript{6} Cyclophanes have lead to a new field of research called host-guest chemistry or supramolecular chemistry. Donald J. Cram together with Charles J. Pedersen and Jean-Marie Lehn received the Nobel Prize for his pioneering work in the field of host-guest chemistry in 1987. Because of their cyclic structures, cyclophanes are usually be used as hosts in a host-guest system. Cyclophanes have interesting properties as synthetic receptors and are preorganized for binding guests of appropriate dimensions. The aromatic groups that encircle their binding cavities are often benzene rings, but they can also be condensed, and heteroaromatics that impart particular molecular recognition properties. The size, shape, charge, hydrophobicity, and π-donor/acceptor properties of these cavities are thus synthetically tunable, and so cyclophane hosts have been designed for a great variety of molecular guests.\textsuperscript{7-9}

![Scheme 1.1: (2,2)(1,3)cyclophane](image)
[2.2]Cyclophane is a relatively small cyclophane family of structures consisting of two benzene rings cyclically interconnected by carbon atoms or chains. In 1899 Pellegrin synthesized the first cyclophane [2.2] metacyclophane; (Scheme 1.1) by a Wurtz coupling, but the field we now know of as cyclophane chemistry probably started in 1949 with the synthesis of [2.2]paracyclophane by Brown and Farthing by simple pyrolysis of p-xylene (Scheme 1.2). In order to study the electronic interactions between “face to face” arranged aromatic systems, Cram and Steinberg synthesized the same cyclophane two years later by a designed synthetic strategy.

\[ \text{Scheme 1.2: [2.2](1,4) cyclophane} \]

A more recent example in this series of bridged benzene systems is the six cyclophane and superphane, which is completely bridged and was isolated by Boekelheide in 1979 (Figure 1.3). Presently all six possible [2,2]cyclophanes now are known. The [2,2]orthoparacyclophane(4), was first synthesized in 1992 by Tobe et al. These studies illustrated that the aromatic rings in cyclophanes are not planar but distorted out of planarity by bending. Boyd measured the heat of combustion of cyclophanes 8, 9, 10 (Figure 1.3), and determined their strain as 12, 31, 23 kcal/mol, respectively. The x-ray study unequivocally revealed that a benzene ring can be distorted into boat-, chair-, and twist-forms by
clamping or bridging them in cyclophanes. These aberrations led to unusual spectroscopic properties and chemical reactivities.

There has always been interest in relationships between structure and physical and chemical properties of aromatic hydrocarbons, which may additionally be strained or sterically hindered. Paracyclophane (9) is one such phane which has interested chemists, theoreticians and industrialists over many years and has been studied extensively. Paracyclophane is a multi-ton industrial product used as a monomer in polymer chemistry. Though the benzene rings of this sandwich structured molecule are bent (non planar) due to the short ethano-bridges, they still exhibit aromatic character as shown by spectral data and chemical reactivity studies. The strain caused by this molecular deformation produces strain energy of ca. 30 kcal/mol.

Cyclophane chemistry gives an opportunity to increase the distortion gradually and successively, which changes the chemical and spectroscopic properties of the aromatic units. Some interesting functionized units can be placed very close to the aromatic ring. For example, one can compare the transannular electronic effects and steric strain of multi-layered cyclophanes or heterocyclophanes with these in the parent hydrocarbon compounds. The chemistry of cyclophanes has received significant attention due to their numerous applications. In the beginning, research on the cyclophane systems was focused mainly on the development of newer synthetic methods and also on the investigation of their physical properties. Subsequently, the scope of the cyclophane chemistry has been extended to the incorporation of heterocycles into these molecules and later on to the synthesis of multibridged and multilayered cyclophanes.

The first practical application of the cyclophanes was found in the host-guest chemistry. Molecular recognition of ions and neutral molecules by the functionalized cyclophanes has been demonstrated through numerous examples. Cyclophane may serve as a building unit for nests, hollow cavities, ‘multi-floor’ structures, helices, macro-polycyclics, macro-hollow tubes, novel ligand systems, etc. Cyclophane chemistry also has importance in supramolecular chemistry, molecular recognition, and may be used as a building block for organic catalysts (novel ligand) and crown ethers.

1.2 Chapter wise description:

The synthesis of small member bridged aromatic compounds leads to the synthesis of potentially useful materials that could be used in different practical aspects of chemistry. Accordingly, inspired by intriguing applications in applied chemistry, the aim of this thesis is to design, synthesis and investigation of variety of [n.n]cyclophane with unique structural architectures with
distortion from planarity of aromatic compounds. The motivation of this thesis is to investigate and discuss complete structural properties using most modern techniques like $^1$H NMR, $^{13}$C NMR, NOESY, IR, UV-Vis, Florescence and single X-ray crystal analysis. The reminder of thesis is organized as follows. Chapter 2: provides a brief description of the existing literature concerning small member bridged aromatic compounds (Cyclophane) having different varieties like Pyrenophane, Aaulenophanes, Naphthalenophane, Anthracenophane, Pyridionphane, porphyrine and calixarenes etc. This chapter also provides physical and chemical properties of cyclophanes like Lewis acid catalysed reaction and Photooxygenation reaction. A number of applications for cyclophanes have been developed as precursors in chemical vapor deposition processes such as thin-film polymers and electronic coatings. Cyclophanes containing internal chelating sites such as the amine functional groups of compound have potential applications as ligands for single-site catalysts including the present propose of study.

Chapter 3 describes overall synthetic strategies of 8-methoxy[2.2]metacyclophanes from 9-methoxy-2,11-dithia[3.3]metacyclophane via bis-sulfoles by high-dilution method. Iodine induced and Lewis acid catalysed reaction of [2.2]metacyclphane suggest that the transannular and isomerization reaction routes might be useful for the preparation of pyrene derivatives having alkyl groups. By this synthetic way afforded the considerably less strained pyrene derivatives. The structures of compounds were fully characterized by $^1$H / $^{13}$C NMR, Mass spectroscopy, elemental analysis. Similarly a complete analysis of single crystal X-ray was presented.

Chapter 4 also describes total synthetic strategies of 8-methoxy[2.2]metaparacyclophanes from 9-methoxy-2,11-dithia[3.3]metaparacyclophane via bis-sulfoles by high-dilution method. Similarly, the preparation of [3.3]MPCP by coupling method and reduction of dione by Woulfkishner reduction method. X-ray diffraction study of 5-tertbutyl-8-methoxy[2.2]meta-paracyclopane is described. Lewis acid catalysed reaction of [2.2]metacyclphane suggest that the isomerization and transannular reaction routes might be useful for the preparation of pyrene derivatives having alkyl groups. By this synthetic way afforded the considerably less strained pyrene derivatives. The structures of compounds were fully characterized by $^1$H / $^{13}$C NMR, Mass spectroscopy, elemental analysis.

In Chapter 5, Synthesis, structure and properties of substituted (1,3)Pyreno [3.3]metacyclophane and various substituted 2,11-dithia[3]metacyclo[3](1,3)pyrenophanes are presented. Compounds are shown the anti- and syn-conformation depends upon the different substitution present in benzene ring. These findings suggest that the through-space interaction between the non-bonding
electron pairs of the oxygen atom of the methoxy group and the opposite pyrene π-electrons of the anti-conformer may disfavour the formation of the latter. The structures of compounds were fully characterized by $^1\text{H}/^1\text{C}$ NMR, Mass spectroscopy, elemental analysis. VT-NMR studies showed that the compound behave as different conformation depends upon the temperature change. Similarly photophysical properties of compounds were carefully examined in this chapter.

**Chapter 6** also describes total synthetic strategies of [2.2] meta- and metaparacyclophanes from 2,11-dithia[3.3]metaparacyclophane via bis-sulfones by high-dilution method. Photooxygenation of 4,5,6,8,12,13,14,16-octamethyl[2.2]metacyclophane, using a high pressure mercury lamp, produced a mixture of mono- and bis-endoperoxides, while the corresponding octamethyl[2.2]metaparacyclophane afforded only the bis-endoperoxide. Similar results were observed in the photooxygenation reaction of 4,5,6,12,13,15,16-hepta- methyl[2.2]metaparacyclophane, which led to endoperoxidation of only the para-benzene ring; this was attributed to the much larger degree of deformation of the para-benzene ring than of the meta-benzene ring. The structures of compounds were fully characterized by $^1\text{H}/^1\text{C}$ NMR, Mass spectroscopy, elemental analysis. Similarly a complete analysis of single crystal X-ray analysis was presented.

**1.3 References:**

19. F. Newmann, P., 1974; Vol. 48, 67.
Chapter 2
[n.n] cyclophane and present proposed study

Recent literature concerning synthesis, structure and conformation of [n.n]cyclophane and present proposed of study are presented in this chapter. From ancient development to the recent achievement towards the field of various kinds of cyclophane and their conformation, Lewis acid catalysed reaction and photooxygenation reaction are also discussed. Based on this literature reviews, the present propose of study are also discussed.
2.1. a [n.n]cyclophane

The cyclophane era is generally regarded as having begun with the description of di-p-xylylene by Brown and Farthing in 1949.¹ Their interest arose out of the experiments of Szwarc,² who showed that pyrolysis of p-xylene gave a linear polymer and extraction of such polymers led to their first isolation of di-p-xylylene.

Independently, Cram, and Steinberg³ had become interested in rigid molecules of known geometry for testing question of bonding, strain energies, and interactions of π-electron systems, and they prepared di-p-xylylene by design, via the intramolecular Wurtz coupling of 1,2-bis(4-bromomethylphenyl)ethane.

Cram and Steinberg also introduced the cyclophane nomenclature, now commonly used for this compounds⁴ by this nomenclature; cyclophane designates a molecule having a bridged aromatic ring. Each bridge is indicated by a number, corresponding to the number of bridge members, placed in a bracket before the name. The position of the bridges can be designated by the usual names of ortho, meta, and para or by numbers in parentheses following the brackets to indicate the positions of attachment on the aromatic ring.

The first synthesis of a cyclophane was that of Pellegrin,⁵ who prepared di-m-xylylene ([2.2]metacyclophane) by the Wurtz coupling of m-xylylene dibromide in 1899; the second was that of Baker, Banks, Lyons, and Mann,⁶ who prepared di-o-xylylene ([2.2]orthocyclophane) in 1945, again by a wurtz coupling reaction.

[2.2]Orthocyclophane is considered a dibenzocyclooctadiene rather than a typical cyclophane, since the properties of [2.2]orthocyclophane warrant no particular comment, inasmuch neither deformed benzene rings nor high-field inner protons are observed.

[2.2]Metacyclophane is well suited as a point of departure in the discussion of [2.2]phanes. The large assortment of its substitution products serves as ideal model systems to investigate benzene ring deformation, statistical and dynamic stereochemistry, and intramolecular and transannular steric and electronic effects. [2.2]metacyclophanes are also good model for the study of neighbouring groups, not necessarily directly bonded to functional groups, aromaticity of deformed benzene rings, transannular cyclizations and so on. The X-ray crystal structure of [2.2]metacyclophane reveals molecules with a center of symmetry, alternating axis, and a mirror plane. Both halves of the molecule are ordered in the form of steps. Because the benzene rings are not planar but distorted into boats, the steric overlap of the inner carbon atoms and their
attached hydrogens are diminished. The average C-C aromatic bond length is 138.6 pm, that of the aliphatic bonds is 154.3 pm. However, it is remarkable that such a strong distortion of the normally planar hexagonal benzene ring is not accompanied by substantial changes in the interatomic distances.

[2.2]Paracyclophane is attractive in its structure in which two benzene rings are close to each other and cofacial. A number of paracyclophane derivatives have been prepared and their physical properties, especially their optical and electronic properties due to the characteristic interactions between the two a novel extended π-electro systems.\(^7\)\(^9\) The Highest Occupied Molecular Orbital (HOMO) is higher than that of the corresponding alkyl benzene; the Lowest Unoccupied Molecular Orbital (LUMO) is lower than that in the open chain molecule. Thus, the energy gap between the HOMO/LUMO is much lower than the open chain compounds. The same type of interaction, albeit weaker, exists in the [3.3]cyclophane but is absent in the more widely separated [4.4]cyclophane, where the individual benzenes behave as separated π-electron systems. There are two essential characteristics of [2.2]paracyclophane: 1) the interaction between the π-electron systems of the two benzene-ring planes and 2) the deformation of the benzene rings. These characteristics are manifested in transannular directing effects in higher electrophilic substitution, neighbouring group effects of the isomerization and photochemical reactions of [2.2]paracyclophanes and their analogues.

2.1.b Other Cyclophanes

All of the cyclophanes discussed so far have been based on the simplest possible aromatic region, namely benzene. Cyclophanes containing variations in their aromatic regions are also known. [8] (2,7)pyrenophane 1 and [2]paracyclo[2](2,7) pyrenophane 2 (Figure 2.1) were synthesized by Bodwell and co-workers in 2000\(^1\)\(^0\). Interestingly enough, X-ray crystallography revealed that the pyrene moiety of both 1 and 2 proved to be significantly warped (as illustrated below). Even so the pyrene unit retains its aromatic character, an exception to the classic rules for aromaticity taught in undergraduate organic chemistry courses\(^1\)\(^1\)

![Fig.2.1: Cyclophanes synthesized by Bodwell and Colleagues 1-2](image-url)
Staab et al. synthesized [3.3]- and [4.4]pyrenophanes 3 and 4 (Figure 2.2) along with other pyrenophanes with different separations and orientations of the pyrene subunits. 12 These systems, consisting of two pyrene units each, show intramolecular excimer properties that are dependent on these parameters.

![Fig.2.2: Pyrenophanes, 3-4](image)

Tsuge et al. synthesized dithia[3.3]pyrenophanes 5 and 6 along with other pyrenophanes. 13 Pyrenophane 5 having methoxy group at the inner position exhibits a parallel within aromatic units. The amino group in 6 directed toward the π-cloud of the pyrene component with probably formation of hydrogen bonds. One of the pyrenophanes, [2.2](1,3) pyrenophane 7 (Figure 2.3), was reported by Misumi et al. 14 as well as a few “mixed,” “asymmetrical” pyrenophanes.

![Fig.2.3: Pyrenophanes, 5-7](image)

[2]Azuleno[2]phanes 8 and 9 (Figure 2.4) are 10π systems. 15,16 The C(9)-C(10) bond (azulene numbering) is elongated, and the azulene ring and benzene ring in compound 8 are distorted up to 9° and 13.8°, respectively. The distance between the single proton and the benzene rings in the intermediates for 8, 9 and 10 are estimated to be 1.50, 1.20, and 1.75 Å, respectively.
Fig. 2.4: Distances between two aromatic protons, 8-10

The cyclophanes with naphthalene rings and anthracene rings are of special interest, because naphthalene and anthracene have a more extensive aromatic core. It would be interesting to study the nature and extent of deformation of the naphthalene ring and anthracene ring, the strain energy, and static and dynamic stereochemistry, as well as charge transfer effects between neighboring aromatic units.

Naphthalenophane 11 was first synthesized in low yield from [2.2] paracyclophane by the annulation method in 1963 (Scheme 2.1) Then, Wasserman and Keehn reported the synthesis by coupling the \( p \)-xylene in situ from the pyrolysis of quaternary ammonium salt with silver oxide in 41% yield, which is an \textit{anti}- and \textit{syn}- mixture that can be separated by crystallization. The optimum procedure to produce 11 would be using the photochemical sulfur extrusion method with triethyl phosphate as a solvent.

Scheme 2.1: Synthesis of [2.2]naphthalenoparacyclophane, 11
A considerable number of investigations have been made into the chemistry of [2.2](1,4)naphthalenophanes. The syn- and anti- isomer 12 and 13 were first synthesized by elimination-cycloaddition of 4-methyltrimethylammonium hydroxide in 3% yield (Figure 2.5) each.\textsuperscript{20} The anti- configuration was confirmed by an alternate nine-step synthesis, in which only anti- isomer was generated. Wasserman and Keehn modified the procedure and got 40% anti- isomer and 4% syn- isomer.\textsuperscript{21} A highly efficient route to compound 25 was designed by Brown and Sondheimer,\textsuperscript{21} which involved the solvolysis of the corresponding ditosylate 14.

\begin{figure}[h]
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\includegraphics[width=0.7\textwidth]{figure2.5.png}
\caption{[2.2]anthracenophane and [2.2](2,5)heterophanes, 27-28}
\end{figure}

Anthracenophanes are virtually 1,4- or 9,10-disubstituted anthracenes, which have lower ionization potential than naphthalene or benzene. Golden first reported [2.2] (9,10)-anthracenophane (15) (Figure 2.6) in 1961.\textsuperscript{22} The synthesis and electronic absorption and emission spectra of five member ring incorporated anthracenophanes (16) were reported in 1977.\textsuperscript{23,24}

\begin{figure}[h]
\centering
\includegraphics[width=0.7\textwidth]{figure2.6.png}
\caption{[2.2]anthracenophane and [2.2](2,5)heterophanes, 15-16}
\end{figure}
In order to study the effect of transannular π-electron interactions in excimer fluorescence, photodimerization, and ESR phenomena, Misumi et al.\textsuperscript{25,26} have synthesized many cyclophanes which incorporate anthracenes. The first compound in this series was synthesized from dimerization of 1,4-anthraquinodimethane, in turn derived by a Hofmann elimination of a quaternary ammonium hydroxide (Scheme 2.2). The anti- isomer (17) was obtained in 14% yield.

Other cyclophanes, such as hetero- and meta-cyclophanes were also synthesized.\textsuperscript{27} Replacing benzene rings with pyridine rings results in [2.2](2,6)pyridinophane 18 (Figure 2.7).\textsuperscript{28} Porphyrine 19, which is very important in biological transformations, also has cyclophane characteristics and is considered a special cyclophane serial.\textsuperscript{29} Calixarenes 20 belong to the [1,α]cyclophane group; their basket-like shape was adapted to host-guest or receptor-substrate chemistry.\textsuperscript{27}
2.2 The Physical and Chemical Properties of Cyclophanes

Unusual structural features help chemists understand molecules and pursue their structural distortion limit. The works in this field provide useful information in developing, confirming, and refining the theoretical underpinnings of science. Cyclophane chemistry has provided insight into the ways in which molecules distribute strain, the effects of strain on molecular reactivity, transannular effects on chemical stability and spectroscopic properties, and as well as the criteria for aromatic stabilization.

The X-ray analysis of [2.2](1,4)paracyclophane reveals that the two benzene moieties are separated by a distance of 299 pm, which is much smaller than the usual π-system van der Waals contact distance of 340 pm between the two parallel aromatic rings in crystals. The bridged carbons are only 278 pm apart, and the center carbons are 309 pm, which means that the two aromatic rings are bent out of plane by an angle of 12.6°.

It is obvious that two π clouds pressed hard against each other should lead to additional steric repulsion between the two rings. One would intuitively assume that this steric repulsion would be relieved by lowering the number of interacting π-electrons. In contrast, the bending does not unambiguously increase or decrease the π electron ionization energies. The benzene system would be deformed and decrease its aromaticity due to lack of planarity, thus, ionization should
be facilitated. On the other hand, bending a $\pi$-system would localize its bond, i.e., forms a more polynenic type of structure which would increase the ionization energy.

Model calculations using localized orbitals have shown that out of plane deformations of ethylene have a negligible influence on its $\pi^{-1}$ ionization energy, as long as they do not exceed certain limits, typically about 20° for bending and/or twisting modes.\textsuperscript{31,32} The deformation results in decreasing ionization energy if it is not compensated by the necessary admixture of low-lying 2s atomic orbitals to accommodate the bulge, which would increase the ionization energy.

The study of $\pi$-electron energies in a series of cyclophanes by photoelectronic (PE) spectra indicates that ionization energies of $\pi$-electrons are affected by the substituent group in the benzene deck.\textsuperscript{19} The mean ionization energy for the two HOMOs of methyl substituted benzenes decreased by 0.5 eV. The cyclophanes had a smaller decrease in ionization energy. The ionization energy of superphane is not close to 6 eV as expected, but rather 7.5 eV. The monobromine substitution in the benzene ring has negligible influence on the PE spectra, while the amino group shifted the PE band towards the lower field. Bridge octafluoro paracyclophane (47) is an extreme example. The fluorine substitution induced the ionization energy shifts up field from 1.0 to 1.3 eV for the corresponding orbitals. The analysis of PE spectra leads to the recognition of a novel consequence of the “fluoro-effect”.

Cyclophanes involving higher aromatic systems have a lower ionization potential, especially cyclophanes with incorporated anthracene. The syn- and anti-isomers of [2.2](1,4)naphthalene -phanes\textsuperscript{17,33,34} (Scheme 2.3) can be interconverted by light. Irradiation of syn-isomer 12 in degassed benzene leads primarily to the anti-isomer 13, while continued irradiation of the 13 solution gives other products. Irradiation with light above 290 nm gives intermolecular rearrangement product 24, which rearomatizes to 13 at room temperature with a half life time of 76 s at 20°C, 24 is a kinetic product, because extended irradiation for 10 days at room temperature leads to the thermodynamically more stable product, dibenzoquinene 25, in 25-50 % yield. This compound is confirmed by x-ray, and presumably arises through two sequential $[2\pi + 2\pi]$ additions (22 first then 21). Normal naphthalene does not react with oxygen, but anti-[2.2]paracyclonaphthalene reacts with singlet oxygen to form transannular peroxide.\textsuperscript{18} This is due to the deformation of the naphthalene ring by the strain.
**Scheme 2.3**: photo reaction of [2.2]naphthalenophane

[2.2]Anthracenenophanes (*Scheme 2.4*) are fascinating compounds. Both the *anti*- and *syn*-isomers (17 and 27) are synthesized from the dimerization of 1,4-anthaquino-dimethane. The *syn*-isomer 27 can be rearranged thermally to the *anti*-structure 17. When light is used, the isomer 27 undergoes a rapid photo induced cyclization reaction to form cage compound 26, which is both thermally and photochemically reversible.

The transannular effect on the spectroscopy of cyclophanes has been utilized in the chemical luminescence polymer. π-Conjugated polymers having cyclophane derivatives as the key unit have been synthesized by Chujo et al. These polymers were soluble in common organic solvents, and self standing thin films exhibit strong blue photo-luminescence in solution and strong bluish-green photoluminescence in solid state.
2.2.a Lewis acid catalysed reaction:

For the further studies on the reaction of [2.2]metacyclophane (8) and derivatives have revealed three major reaction types (Scheme 2.5). These are substitution (path a), transannular dehydrogenation (path b and c), and transannular isomerization (path d). Due to ready transannular reactions the substitution reaction (path a) is rarely observed in metacyclophane compounds. Electrophilic, photolytic, and some radical reactions produced 4,5,9,10-tetrahydropyrene (28) in a good yield (path b and c). Further substitution or dehydrogenation was observed as a secondary process (e.g. 28 $$\rightarrow$$ 29 $$\rightarrow$$ 30). Treatment with iodine, on the other hand, gave 1,2,3,3a,4,5-hexahydropyrene (31) in a quantitative yield (path d).
The transannular reaction, Lehner and Langer obtained perhydropyrene on catalytic hydrogenation of 8. Dehydrogenation over Pd-C gave pyrene as reported by Baker et al. The same authors described the formation of 31 from 8 by the reaction of aluminum chloride. The detail studied of aluminum chloride reaction have revealed a new type of reaction giving rise to hydropyrenes and pyrene by disproportionation.

Cram et al. used AlCl₃-HCl for a skeletal rearrangement of [2.2]paracyclophane (32) to [2.2]metapara-cyclophane(33).

Yamato et al. used the Lewis and protic acid-catalyzed reactions of 5-tert-butyl-8-methoxy[2.2]MPCP-1,9-diene 34 was carried out under AlCl₃-MeNO₂ and TiCl₄ in
dichloromethane led to isomerization and transannular reactions to afford 2-tert-butylpyrene 35 (Scheme 2.6) within 1 min.

![Scheme 2.6: Isomerization and transannular reaction of [2.2]metaparacyclophane.]

Shimizu et al.\textsuperscript{47} used the AlCl\textsubscript{3}-MeNO\textsubscript{2}-catalysed trans-tert-butylation of 36 in benzene at 50°C for 3 h afforded metacyclophanes 38 and 39 along with the formation of tert-butylbenzene. None of the expected product 8,12,13,15,16-pentamethyl[2.2]MPCP 37 was detected under the conditions used. Prolonged reaction for 12 h under the same conditions gave only 39. This result suggests that 38 might be an intermediate in the formation of 39.

![Fig 2.9: [2.2]MPCP and [2.2]MCP]

2.2.b Photooxygenation reaction:

By the beginning of the twentieth century there were several reports\textsuperscript{48} describing the oxidation of organic and biological substrates in the presence of oxygen, light and a photosensitizer. It has become apparent during the last two decades that there are in fact two general classes of photooxidation\textsuperscript{49} In the first, called Type I, the sensitizer serves as a photochemically activated free-radical initiator. In its excited state the sensitizer reacts with a molecule of a substrate, resulting
in either hydrogen atom abstraction or electron transfer. The radicals thus formed react further with $^3$O$_2$ or other molecules. In the second class of reactions, Type II, the sensitizer triplet (sens$^3$), formed via intersystem crossing (ISC) of the excited singlet state sensitizer (sens$^1$*), interacts with oxygen, most commonly by transferring excitation, to produce $^1$O$_2$. The direct absorption of light by $^3$O$_2$ to produce $^1$O$_2$ from 30-46 kcal mol$^{-1}$ is a spin-forbidden process. Type II generally predominates with coloured sensitizers (dyes) which absorb visible light while Type I processes are favoured by high-energy UV absorbing sensitizers.

Furthermore, this research work on the basis of Type II, photooxygenation reaction to give endoperoxide compounds. Photochemically generated singlet oxygen ($^1$O$_2$) cycloadds to conjugated dienes and arenes to give endoperoxides. The endoperoxides are important intermediates in photo-oxidation reactions, but, in most cases, are too unstable to isolate in order to study their structure.

**Modes of reaction:**

The first of the singlet oxygen reaction modes is a [2 + 2]cycloaddition to a double bond to form a 1,2-dioxacyclobutane or dioxetane (Scheme 2.7). These cyclic peroxides are sometimes of moderate stability but readily cleave thermally or photochemically into two carbonyl-containing fragments. The cleavage is quite often accompanied by chemiluminescence.

![Scheme 2.7: [2+2] cycloaddition reaction](image)

The second mode bears a striking resemblance to the Alder 'ene' reaction.$^{50,51}$ In the $^1$O$_2$ ene reaction, olefins containing an allylic hydrogen are oxidized to the corresponding allylic hydroperoxides in which the double bond has shifted to a position adjacent to the original double bond (Scheme 2.8).
The third and final mode involves a [4 + 2] Diels-Alder-type addition of singlet oxygen to a diene producing endoperoxides (Scheme 2.9).

Polynuclear systems are likewise susceptible to the [2 + 4] mode of attack. For example, it has been known for more than half a century\(^{52}\) that the red rubrene 40 can be converted into its colourless transannular peroxide 41 by a self-sensitized photooxidation. Like the endoperoxides of other polynuclear arenes, this endoperoxide reverts thermally to \(^1\)O\(_2\) and the coloured starting material (Scheme 2.10)

Sawada et al. synthesized the endoperoxide 43 by irradiation of [2.2]metacyclophane 42 using high pressure mercury lamp. Although a no additional photosensitizer was added, the reaction leading to 43 is thought to proceed via \(^1\)O\(_2\). It may be possible that the [2.2]metacyclophane 42 itself acts as sensitizer in the reaction.\(^{53}\)
The similarly substituted hexamethylbenzene 44, itself is inert under the irradiation conditions mentioned above, although it has been reported that the formation of unstable endoperoxide 45 can be detected by $^1$H NMR spectroscopy in the reaction mixture, when methylene blue was used as a photosensitizer. Epidioxy hydroperoxide 46 is the final product via a subsequent ene-reaction of 45 (Scheme 2.12).\(^{54}\)

2.3 Application of cyclophanes:

A number of applications for cyclophanes have been developed. [2.2]Paracyclophanes have been used as precursors in chemical vapor deposition processes, such as thin-film polymers and electronic coatings. These coatings are used as inert barriers in such applications, very similar to the oiling of steel objects to prevent rust. 1,1,2,2,9,9,10,10-octafluoro[2.2]paracyclophane 47\(^{55}\) has seen use as a chemical vapor deposition polymer precursor, and is used in the microchip industry\(^ {56}\) as a protective barrier, similar to Teflon, for printed circuit boards. Cyclophanes containing internal chelating sites such as the amine functional groups of compound 48 have potential applications as ligands for single-site catalysts.\(^ {57}\)
2.4 References:

1915.


Chapter 3


The coupling reaction of the corresponding 2,6-bis(chloromethyl)benzenes and 1-methoxy-2,6-bis(sulfanylmethyl)benzenes under highly diluted conditions in 10% ethanolic KOH in the presence of a small amount of NaBH₄ afforded anti- and syn-9-methoxy-2,11-dithia[3.3]metacyclophanes are obtained, which were converted to the corresponding anti- and syn-conformation of 9-methoxy-2,11-dithia[3.3]metacyclophanes-2,2,11,11-tetraoxide by oxidation with excess m-CPBA. Further pyrolysis to afford the 8-Methoxy[2.2]metacyclophanes 5. X-ray diffraction study of 5-tert-butyl-8-methoxy[2.2]metacyclophane 5c is described. When 1-methoxy[2.2]metacyclophanes 5c are treated with Iodine in boiling benzene, the corresponding tetrahydropyrenes 6 are obtained in good yield. Lewis and catalyzed reactions of 8-substituted [2.2]metacyclophane 5 proceeded by transannular cyclization to afford the strainless pyrenes derivatives in good yields. Treatment of 5d with TiCl₄ in dichloromethane led to transannular reactions to afford transannular products 11a, 12 along with corresponding pyrene derivative 13 in almost quantitative yield. In contrast, similar treatment of 5e with AlCl₃-MeNO₂–catalysed trans-tertbutylation under the same reactions condition for same time afforded the transannular product 11b and very little amounts of 12 and 13. These findings strongly suggest that the 8-methoxy group might play an important role in the isomerization and transannular reactions.

3.1 Introduction:

For many years various research groups have been attracted by the structures of the [3.3]MCP ([3.3]MCP=[3.3]metacyclophane) skeleton.\textsuperscript{1,2} When both internal substituents of a [3.3]phane are H, the molecule may be mobile. Mitchell and coworkers\textsuperscript{3} have investigated the influence of large internal substituents upon the relative stability of the syn- and anti-conformers of 2,11-dithia[3.3]metacyclophanes. They demonstrated in 1970 that 9,18-dimethyl-2,11-dithia[3.3]MCP exists in syn- and anti-conformers (Figure 3.1), which do not interconvert below 200 °C.\textsuperscript{4} When a single tert-butyl group is present as an internal substituent (i.e. connected to C-9), only the syn-isomer is formed. A methyl group as the second internal substituent leads to a syn/anti mixture (6:4) and the presence of two internal tert-butyl groups allows the formation of only the anti conformer. Vogtle and Schunder\textsuperscript{5} have made extensive studies of syn-anti-conversions in their dithia[3.3]MCPs, especially in relation to the size of the substituents. When electron-withdrawing groups such as halo, nitro and cyano are present, the yields of the syn-isomers increase substantially. Very bulky groups, such as tert-butyl, decrease the yields of syn-isomers. Although the effect on the ratio of syn- and anti-conformers of dithia[3.3]MCPs was reported, it is still not clear what the effects are, not only with respect to the properties of the internal substituents, but also of having unsymmetrically substituted benzene rings arising from charge-transfer-type interactions between the two benzene rings as well as from the steric effects of the substituents at the 6- and 15-positions.

![Fig. 3.1 Syn- and Anti-conformation of thia-cyclophane](image-url)
All the previously studied compounds have been internally unsubstituted or methyl-substituted dithia[3.3]MCPs and it is surprising that there are very few reports on the preparation of 9-methoxy analogues. It is known that the inner substituent of the dithia[3.3]metacyclophanes has a great effect on their conformational mobility. In the previous related paper, we have focused on the dithia[3.3]metacyclophanes carrying no substituent at the inner position showing conformational flexibility. In order to obtain the fixed dithia[3.3] metacyclophane skeleton a bulky substituent has to be introduced at the inner position since an inner bulky group hampers rotation of the aromatic rings. Particularly, the dithia[3.3]metacyclophanes with several substituents were synthesized and the syn- or anti-isomers were isolated. In the case of H-substituent at the inner position, the syn and anti interconversion process is rapid at room temperature, whereas the syn and anti isomers can be isolated by introducing a bulky group such as Me at the 9 and 18 positions.

3.2 Result and Discussion

3.2.a Synthesis and Spectral properties

The synthesis and stereochemical assignments of 9-methoxy-2,11-dithia[3.3]MCPs. The substituent effects on the syn- and anti-conformations are also discussed. The cyclizations of 2-methoxy-5-substituted-1,3-bis(sulfanylmethyl)benzenes 1a-b with 4,6-dimethyl-2,5-disubstituted-1,3-bis(chloromethyl)benzenes 2a-c were carried out at high dilution in 10% ethanolic KOH and in the presence of a small amount of NaBH₄, giving mixtures of anti- and syn-2,11-dithia[3.3]MCPs were obtained. By careful column chromatography (silica gel, Wako C-300), two conformers, anti (anti-3) and syn-2,11-dithia[3.3]MCP (syn-3), were easily separated, anti-9-methoxy-2,11-dithia[3.3]MCPs 3b, 3d and 3e are 42, 47 and 39% yields and syn-9-methoxy-2,11-dithia[3.3]MCPs 3b, 3d and 3e are 14, 11 and 13% yields, respectively (Scheme 3.1). Similarly, 9-methoxy-2,11-dithia[3.3]MCPs 3a and 3e are 60 and 75% yields. The oxidation reaction of dithia[3.3]MCP 3a-e were carried out by adding an excess amount of m-CPBA to CHCl₃ solution at room temperature for 24 h under an argon atmosphere according to literature (Scheme 3.1). After the reaction, the mixture was washed with 10 % NaHCO₃ to quench the excess amount of m-CPBA. The crude product was purified by washing from ethanol to obtain the mixture of anti- and syn-2,11-dithia[3.3]MCP-2,2,11,11-tetraoxides as a white crystal solid. By careful column chromatography (silica gel, Wako C-300), two conformers, anti-2,11-dithia[3.3]MCP-2,2,11,11-tetraoxides (anti-4) and syn-2,11-dithia[3.3]MCP-2,2,11,11-tetraoxides (syn-4), were easily separated, anti-9-methoxy-2,11-dithia[3.3]MCP-2,2,11,11-tetraoxides 4b, 4d and 4e are 56, 20 and 50% yields and syn-9-methoxy-2,11-dithia[3.3]MCPs
4b, 4d and 4e are 14, 40 and 12% yields, respectively (Scheme 3.1). Similarly, 9-methoxy-2,11-dithia[3.3]MCP-2,2,11,11-tetraoxides 4a and 4c are 76 and 73% yields. Pyrolysis of bissulfones, 4a-e under reduced pressure (1 torr) at 465°C was carried out by a reported method\textsuperscript{11,12} to afford exclusively anti-5b, 5d and 5e are 60, 51 and 49% yields and syn-5e in 5% yields, respectively. Similarly, 9-methoxy [2.2]MCP 5a and 5c are 55 and 60% yields.

The structures of 3a, 3c and anti- and syn-conformations of 3b, 3d and 3e have been elucidated by elemental analyses and spectral data. The IR spectrum of 3a, 3c and anti- and syn-conformations of 3b, 3d and 3e show the absorption of the methoxy stretching vibration around 1690 cm\textsuperscript{-1}. The \textsuperscript{1}H NMR spectrum (in CDCl\textsubscript{3}) of anti-3b, 3d and 3e exhibits methoxy protons (3b. δ OMe= 3.11, 3d. δ OMe= 3.13 and 3e. δ OMe= 3.09) shielded by ring current of the opposite aromatic ring. Similarly internal methyl protons also shielded by ring current of the opposite aromatic ring (3b. δ Me=1.38, 3d. δ Me= 1.35 and 3e. δ Me= 1.35). But the aromatic protons of conformer anti-3 are observed much down field (3b. 7.00 and 7.31 ppm, 3d. 6.88 and 7.34 ppm and 3e. 7.34 ppm). In contrast, the methoxy protons of syn-3b, 3d and 3e are observed down field at 3.52 ppm for syn-3b, 3.52 for syn-3d and 3.52 for syn-3e. Similarly internal methyl protons also deshielded (Syn-3b. δ Me= 2.41, Syn-3d. δ Me= 2.41 and Syn-3e. δ Me= 2.43). Further, the benzene protons of Syn-3b, 3d and 3e can clearly be seen to be shielded (Syn-3b, 6.54 and 7.03 ppm, Syn-3d, 6.37 and 7.07 ppm and Syn-3e, 7.03 ppm) by the opposite benzene ring, a common consequence of face-to-face aryl rings.\textsuperscript{13} These observations strongly suggest that compound 3b, 3d and 3e adopts syn-conformation. The \textsuperscript{1}H NMR spectrum (in CDCl\textsubscript{3}) of 3a and 3c exhibits methoxy protons on 3a. δ OMe= 3.72 and 3c. δ OMe= 3.71 positions. Similarly internal benzene protons also found in normal positions. (3a. δ H= 6.57, and 3c. δ H= 6.52).
Scheme 3.1
Similarly, the structures of 4a-e have been elucidated by elemental analyses and spectral data. The IR spectrum of anti-4b, 4d and 4e and syn-4b, 4d and 4e as well as 4a and 4c shows the absorption of the methoxy stretching vibration around 1690 cm⁻¹. The ¹H NMR spectrum (in CDCl₃) of anti-4b, 4d and 4e exhibits methoxy protons (4b. δ OMe= 3.20, 4d. δ OMe= 3.22 and 4e. δ OMe= 3.17) shielded by ring current of the opposite aromatic ring.

Similarly internal methyl protons also shielded by ring current of the opposite aromatic ring (4b. δ Me= 1.26, 4d. δ Me= 1.30 and 4e. δ Me= 1.30). But the aromatic protons of conformer anti-4 are observed much down field (4b. 7.13 and 7.76 ppm, 4d. 7.04 and 7.78 ppm and 4e. 7.78 ppm). In contrast, the methoxy protons of syn-4b, 4d and 4e are observed down field at 3.55 ppm for 4b, 3.54 for 4d and 3.54 for 4e respectively. Similarly internal methyl protons also deshielded (syn-4b. δ Me= 2.53, 4d. δ Me= 2.51 and 4e. δ Me= 2.53). Further, the benzene protons of syn-4b, 4d and 4e can clearly be seen to be shielded (4b. 6.69 and 7.41 ppm, 4d. 6.59 and 7.61 ppm and 4e. 7.55 ppm) by the ring current of opposite benzene ring, a common consequence of face-to-face aryl rings.¹³ These observations strongly suggest that compound syn-4b, 4d and 4e adopt syn-conformation. The ¹H NMR spectrum (in CDCl₃) of 4a and 4c exhibits methoxy protons on 4a. δ OMe= 3.84 and 4c. δ OMe= 3.79 positions. Similarly internal benzene protons also found in normal positions. (4a. δ H= 6.78 and 4c. δ H= 6.71).

The pyrolysis products of 5a-e have been elucidated by elemental analyses and spectral data. The IR spectrum of 5a-e shows the absorption of the methoxy stretching vibration around 1700 cm⁻¹. The ¹H NMR spectrum (in CDCl₃) of anti-5b, 5d and 5e exhibits methoxy protons (5b. δ OMe= 2.86, 5d. δ OMe= 2.65 and 5e. δ OMe= 2.86) shielded by ring current of the opposite aromatic ring. Similarly internal methyl protons also shielded by ring current of the opposite aromatic ring (5b. δ Me= 0.57, 5d. δ Me= 0.54 and 5e. δ Me= 0.57). But the aromatic protons of conformer anti-5 are observed much down field (5a. 6.81 and 7.11 ppm, 5b. 6.61 and 7.11 ppm and 5e. 7.10 ppm). The ¹H NMR spectrum (in CDCl₃) of 5a and 5c exhibits methoxy protons (5a. δ OMe= 3.01 and 5c. δ OMe= 3.00) shielded by ring current of the opposite aromatic ring. Similarly internal methyl protons also shielded by ring current of the opposite aromatic ring (5a. δ H= 3.98, and 5c. δ H= 3.91).
[2.2]Meetacyclophane ([2.2]MCP) are distinguished by abnormal physical and chemical properties. Several qualitative explanations have been given for the origin of the abnormality: π-electron repulsion between the benzene rings,\textsuperscript{14-20} hyperconjugation with the bridging C-C bonds,\textsuperscript{21} nonplanarity of the benzene rings,\textsuperscript{22} and transannular π-π interaction between the benzene rings.\textsuperscript{23} Boschi and Schmidt\textsuperscript{23} suggested from the ionization energies and transannular π-π resonance integrals of [2.2]MCP that transannular π-π interaction may take place between C-1 and C-14. Later on, Sato and Takemura\textsuperscript{24} confirmed the transannular π-π interaction of [2.2]MCPs by comparison of the charged-transfer bands of cyclophane molecule with those of the corresponding acyclic models. [2.2]MCP showed only a moderate increase reflection decreased overlap between the two aryl groups, compared with the large enhancement in the π-basicity in the lower membered paracyclophanes. However, only the charge transfer bands of 1,14- unsubstituted[2.2]MCP and its alkyl derivatives were investigated.\textsuperscript{25}

3.2.b Iodine induced reaction:

We have reported\textsuperscript{26,27} the iodine-induced transannular cyclisation of 1-methoxy[2.2]MCPs to give 4,5,9,10-tetrahydropyrenes with remarkable ease and with high selectivity. The
cycloisomerisation was found to be strongly affected by the substituents at C-11 and proceeded involvement of the iodine molecule, possibly via $\pi$-complexation. These reaction are quite different from those of 1,14-unsubstituted.

**Table 3.1:** Iodine induced transannular reacton. $^a$ The product yields are determined by GC analyses. $^b$ Isolated yields are shown.

<table>
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<th>Substruct</th>
<th>$I_2$ (mol/mol)</th>
<th>Time (h)</th>
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<td>6(87)$^b$(79)$^b$</td>
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</tr>
</tbody>
</table>

[2.2]MCPs, which give 1,2,3,3a,4,5-hexahydropyrene$^{28,29}$ and might be attributed to the presence of the methoxy group at a position 1, which would increase the difference of the $\pi$-electron densities among the two benzene rings. These results prompted us to investigate the reaction of 1-monosubstituted[2.2]metacyclophanes with Iodine (Scheme 3.2). Thus there is substantial interest in investigating the Lewis acid transannular cyclisation reaction of 4-substituted-1-methoxy-10,12-dimethyl[2.2]MCP to give corresponding 4,5,9,10-tetrahydropyrenes with remarkable ease and with high selectivity.$^{30}$

The preparative route of 4-*substituted*-1-methoxy[2.2]metacyclophe` 5a and 5c are shown in Scheme 3.1. The preparation of 5a and 5c were prepared according to the sulphur methods. Compounds 5a and 5c were treated with Iodine in boiling benzene. The results are summarized in Table 3.1. As shown in Table 3.1, 5a and 5c gave the corresponding tetrahydropyrene 6 and 8 respectively.$^{26}$
3.2.c Acid catalysed reaction:

The Lewis acid-catalyzed reactions of 4-substituted 1-methoxy[2.2]MCP 5c was carried out under various conditions and the results are summarized in Table 3.2. Treatment of 5c with TiCl₄ in dichloromethane led to transannular reactions to afford transannular products 6 along with corresponing pyrene derivative within 30 minutes in almost quantitative yield. Similar treatment of AlCl₃-MeNO₂-catalysed trans-tertbutylation of 5c in benzene at 50°C for 30 minutes afforded
removal of the tert-butyl group to give 5a and 8 in 30 and 60 % yield along with tert-butyl benzene (9).

In contrast, similar treatment of 5c with TiCl₄-MeNO₂ in benzene under the same reactions condition for same time afforded the transannular product 6 and very little amounts of 7. These findings strongly suggest that the 1-methoxy group might play an important role in the isomerization and transannular reactions. A mechanism for the formation of the transannular product 6 and 8 from 5c and 5a are tentatively proposed in Scheme 3.3. Iodo cation attacks the ipso-position of 5c could afford the cation intermediate (A), which could produce 6 via cation intermediates B and C. Although the detailed mechanism of formation of 6 is not clear, one might assume the reaction pathway shown in scheme 3.3.

Table 3.2; Lewis acid catalysed trans tert-butylation reaction, a The product yields were determined by GC analyses. b Isolated yields are shown.

<table>
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<tr>
<th>Run</th>
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<th>Catalyst and condition</th>
<th>Time(h)</th>
<th>Product(%) a</th>
<th>Recovered(%) a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5c</td>
<td>TiCl₄/CH₂Cl₂/0°C</td>
<td>0.5</td>
<td>6(20)a</td>
<td>5c(66)</td>
</tr>
<tr>
<td>2</td>
<td>&quot;</td>
<td>&quot;</td>
<td>1.5</td>
<td>6(51)b(44)b</td>
<td>5c(12)</td>
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<td>&quot;</td>
<td>AlCl₃/MeNO₂/benzene/50°C</td>
<td>0.3</td>
<td>6(1)a</td>
<td>5c(99)</td>
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<td>4</td>
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<td>&quot;</td>
<td>2</td>
<td>6(52)a</td>
<td>5c(48)</td>
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<tr>
<td>5</td>
<td>&quot;</td>
<td>&quot;</td>
<td>3</td>
<td>6(61)b(56)b</td>
<td>5c(38)</td>
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<tr>
<td>6</td>
<td>&quot;</td>
<td>AlCl₃/MeNO₂/benzene/85°C</td>
<td>20</td>
<td>6(21)a</td>
<td>5a(54)b(50)b</td>
</tr>
<tr>
<td>7</td>
<td>&quot;</td>
<td>&quot;</td>
<td>48</td>
<td>6(18)a</td>
<td>5a(48)b(40)b</td>
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<tr>
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<td>&quot;</td>
<td>60</td>
<td>6(18)a</td>
<td>5a(54)b(45)b</td>
</tr>
<tr>
<td>9</td>
<td>6</td>
<td>AlCl₃/MeNO₂/benzene/50°C</td>
<td>3</td>
<td>8(74)b(66)b</td>
<td>6(80)a</td>
</tr>
<tr>
<td>10</td>
<td>&quot;</td>
<td>DDQ/benzene/85°C</td>
<td>1</td>
<td>7(20)a</td>
<td>-</td>
</tr>
<tr>
<td>11</td>
<td>&quot;</td>
<td>&quot;</td>
<td>4</td>
<td>7(85)a</td>
<td>-</td>
</tr>
<tr>
<td>12</td>
<td>8</td>
<td>&quot;</td>
<td>4</td>
<td>10(90)a</td>
<td>-</td>
</tr>
</tbody>
</table>

Dehydrogenation of 6 and 8 with DDQ in benzene afforded the corresponding pyrenes 7 and 10 in good yield. The trans tert-butylation of 7 in benzene did not afford any product. However, a similar reaction of 6 effected removal of the tert-butyl group to give 8 together with tert-
butylbenzene 9. The above results suggest that the reaction routes $5 \rightarrow 6 \rightarrow 8 \rightarrow 10$ might be useful for the preparation of pyrene derivatives having alkyl groups.26

The Lewis acid-catalyzed reactions of 5-tert-bugyl-9-Methoxy[2.2]metacyclophanes 5d and 5e were carried out under various conditions and the results are summarized in Table 3.3. Treatment of 5d with TiCl$_4$ in dichloromethane led to transannular reactions to afford transannular products 11a, 12 along with corresponding pyrene derivative (13) in almost quantitative yield. Interestingly, treatment of 5d with TiCl$_4$ in dichloromethane at 0°C to afford transannular products 12 along with corresponding pyrene derivative (13) within 8 hour in almost 78% yield. Similar treatment occurred at room temperature to afford corresponding pyrene derivative (13) about 40% yield within 9 h. Similarly, treatment of AlCl$_3$-MeNO$_2$--catalysed trans-tert-butylation of 5d in benzene at 50°C for 29 h. afforded 11a in 73 % yield. In contrast, similar treatment of 5e with AlCl$_3$-MeNO$_2$--catalysed trans-tertbutylation under the same reactions condition for same time afforded the transannular product 11b and very little amounts of 12 and 13.31 These findings strongly suggest that the 1-methoxy group might play an important role in the isomerization and transannular reactions.

![Scheme 3.5](image-url)
Table 3.3: Lewis acid catalysed trans tert-butylation reaction. \(^a\) The product yields were determined by GC analyses. \(^b\) Isolated yields are shown.

<table>
<thead>
<tr>
<th>Run</th>
<th>Substrate</th>
<th>Catalyst and condition</th>
<th>Time(h)</th>
<th>Product(%)(^a)</th>
<th>Recovered(%)(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>11a 12 13</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>5d</td>
<td>TiCl(_4)/CH(_2)Cl(_2)/0°C</td>
<td>0.5</td>
<td>5  -  -</td>
<td>90</td>
</tr>
<tr>
<td>2</td>
<td>&quot;</td>
<td>&quot;</td>
<td>1.0</td>
<td>3  2  -</td>
<td>83</td>
</tr>
<tr>
<td>3</td>
<td>&quot;</td>
<td>&quot;</td>
<td>2.5</td>
<td>4  13  -</td>
<td>70</td>
</tr>
<tr>
<td>4</td>
<td>&quot;</td>
<td>&quot;</td>
<td>5.5</td>
<td>-  48  8</td>
<td>41</td>
</tr>
<tr>
<td>5</td>
<td>&quot;</td>
<td>&quot;</td>
<td>8.5</td>
<td>-  (78)(^a)(68)(^b)</td>
<td>16  3</td>
</tr>
<tr>
<td>6</td>
<td>&quot;</td>
<td>&quot;</td>
<td>10</td>
<td>-  73  14</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>&quot;</td>
<td>TiCl(_4)/CH(_2)Cl(_2)/RT</td>
<td>1.5</td>
<td>5  15  -</td>
<td>61</td>
</tr>
<tr>
<td>8</td>
<td>&quot;</td>
<td>&quot;</td>
<td>3</td>
<td>3  35  11</td>
<td>14</td>
</tr>
<tr>
<td>9</td>
<td>&quot;</td>
<td>&quot;</td>
<td>6</td>
<td>4  34  43</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>&quot;</td>
<td>&quot;</td>
<td>9</td>
<td>3  38  (48)(^a)(34)(^b)</td>
<td>-</td>
</tr>
<tr>
<td>11</td>
<td>&quot;</td>
<td>&quot;</td>
<td>13</td>
<td>-  66  33</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>&quot;</td>
<td>AlCl(_3)/MeNO(_2)/benzene/50°C</td>
<td>1</td>
<td>11  -  -</td>
<td>80</td>
</tr>
<tr>
<td>13</td>
<td>&quot;</td>
<td>&quot;</td>
<td>4</td>
<td>19  -  -</td>
<td>75</td>
</tr>
<tr>
<td>14</td>
<td>&quot;</td>
<td>&quot;</td>
<td>29</td>
<td>(73)(^a)(64)(^b)</td>
<td>-  -</td>
</tr>
</tbody>
</table>

The structures of the products 5, 6, 7, 8, 10, 11, 12 and 13 were determined from their elemental analyses and spectral data. The \(^1\)H-NMR spectra of the [2.2]MCP 5c prepared in the present work show peaks due to the internal aromatic and methoxy protons at \(\delta\) 3.00 and 3.91 respectively. In \(^1\)H-NMR spectrum of transannular product 6, the signals for the bridge methylene protons of -CH\(_2\)CH\(_2\)- moieties as well as internal aromatic and methoxy protons disappeared, and new signals of the methylene protons appeared at 2.82 ppm as a singlet peak. Similarly, in \(^1\)H-NMR spectrum of oxidized product 7, the signal for the bridge methylene protons permanently disappeared, and new signals of the aromatic protons appeared within 7.70-8.18 ppm. These results suggest that the transannular product 6 was oxidized to corresponding pyrene 7.\(^{33}\) However, a similar reaction of 6 effected removal of the tert-butyl group to give 8 together with tert-butyl-\(\text{benzene}\) 9. Compound 8 was further oxidised to give corresponding pyrene derivative 10.
Lewis acid catalysed reaction of compound 5d and 5e was obtained to give compound 11a and 11b along with compound 12 and 13. The $^1$H-NMR spectra of the [2.2]MCP 5d prepared in the present work show peaks due to the internal methyl and methoxy protons at $\delta$ 0.54 and 2.89 respectively. In $^1$H-NMR spectrum of transannular product 11a (Figure 3.2), the signals for the bridge methylene protons of -CH$_2$CH$_2$- moieties as well as internal methyl and methoxy protons disappeared, and new signals of the methylene protons appeared within (2.40-3.14) ppm and methyl at 0.55 ppm.
Table 3.4; Lewis acid catalysed trans tert-butylation reaction, \(^a\) The product yields were determined by GC analyses. \(^b\) Isolated yields are shown.

<table>
<thead>
<tr>
<th>Run</th>
<th>Substrat</th>
<th>Catalyst and condition</th>
<th>Time(h)</th>
<th>Product(%)(^a)</th>
<th>Recovered(%)(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5e</td>
<td>AlCl(_3)/MeNO(_2)/benzene/50(^0)C</td>
<td>1.0</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>&quot;</td>
<td>&quot;</td>
<td>2.5</td>
<td>36</td>
<td>7</td>
</tr>
<tr>
<td>3</td>
<td>&quot;</td>
<td>TiCl(_4)/CH(_2)Cl(_2)/0(^0)C</td>
<td>5</td>
<td>(52)(^a)(45)(^b)</td>
<td>9</td>
</tr>
<tr>
<td>4</td>
<td>&quot;</td>
<td>&quot;</td>
<td>0.5</td>
<td>2</td>
<td>2</td>
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<tr>
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<td>&quot;</td>
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<td>6</td>
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<td>&quot;</td>
<td>3</td>
<td>50</td>
<td>(37)(^a)(25)(^b)</td>
</tr>
<tr>
<td>7</td>
<td>&quot;</td>
<td>&quot;</td>
<td>5</td>
<td>38</td>
<td>28</td>
</tr>
</tbody>
</table>

![Scheme 3.6](image-url)
The NOESY spectrum (Figure 3.3) clearly brought out strong connectivity between methyl protons (at position 12) and methylene bridge protons (at position 10) and also between the hydroxy proton (at position 8) and the methylene protons (at position 2 and 9) as well. Similarly, the $^1$H-NMR spectra of the [2.2]MCP 5e prepared in the present work show peaks due to the internal methyl and methoxy protons at $\delta$ 0.572 and 2.860 ppm respectively. In $^1$H-NMR spectrum of transannular product 11b, the signals for the bridge methylene protons of -CH$_2$CH$_2$- moieties as well as internal methyl and methoxy protons disappeared, and new signals of the methylene protons appeared within (2.46-3.32) ppm and methyl at 0.64 ppm (Figure 3.4). The NOESY spectrum (Figure 3.5) clearly brought out strong connectivity between methyl protons (at position 12) and methylene bridge protons (at position 10) and also between the hydroxy proton (at position 8) and the methylene protons (at position 2 and 9) as well. In $^1$H-NMR spectrum of transannular product 12, the signals for the bridge methylene protons of -CH$_2$CH$_2$- moieties as well as internal aromatic and methoxy protons disappeared, and new signals of the methylene protons appeared at 2.79 ppm as a singlet peak. Similarly, in $^1$H-NMR spectrum of oxidized product 13, the signal for the bridge methylene protons permanently disappeared, and new signals of the aromatic protons appeared within 7.98-8.29 ppm.

![Fig.3.4 $^1$H NMR spectrum of 11b in CDCl$_3$ at 25° C, 300 MHz, $\delta$ (ppm)](image-url)
Fig. 3.5 NOESY spectrum of compound 11b.
3.2.d X-ray analysis:

Conclusive evidence for the structure 5c was provided by a single-crystal X-ray structure determination. Figure 3.6 shows the molecular structure of 5c in a top view. The bond distances for 5c are listed in Table 3.5. The mean distance between mean geometric centres of rings of [2.2]MCP is equal to 4.00 Å and perpendicular distance between two benzene planes is 2.69 Å in figure 3.7.\(^\text{34}\) The two benzenes unit overlaps very slightly with their dihedral angle being only 5.64°. The benzene unit shows slight boat-type deformations with angles between C(14)-C(13)-C(9) and C(13)-C(12)-C(10)-C(9) as well as C(12)-C(11)-C(10) and C(13)-C(12)-C(10)-C(9) being 8.86 and 5.95° respectively. The another benzene unit shows strong boat-type deformations with angles between C(1)-C(6)-C(2) and C(6)-C(2)-C(3)-C(5) as well as C(4)-C(3)-C(5) and C(6)-C(2)-C(3)-C(5) being 11.30 and 5.38°, respectively. One of the methoxy groups which is located above the center of the benzene ring shows a remarkable deviation from the plane of the benzene ring.\(^\text{35}\) The bridging angles, C(2), C(16), C(15) and C(16), C(15), C(13) are 109.8 and 110.9°, respectively; however, for corresponding angles, C(6), C(7), C(8) and C(7), C(8), C(9) are appreciably smaller, being 109.2 and 110.6°, respectively.\(^\text{36}\) In the crystal-packing diagram of 5c (Figure 3.8), the intermolecular shortest distance within C12-H19C is 2.77 Å, which are shorter than the sum of the Van der Waals radii of the hydrogen (1.20 Å) and oxygen atoms (1.60 Å) or carbon atom (1.70 Å).\(^\text{37}\)
The UV-vis absorption spectra revealed that in compounds thiacyclophane \((3c)\) and its oxidized product \((4c)\) did not affect the \(\pi\) conjugation length within benzenes. But, the synthesis of the \([2.2]\) metacyclophane \((5c)\), Lewis acid catalysed transannular product \((6)\) and its corresponding pyrene \((7)\) were bathochromic shifted due to a \(\pi-\pi\) interaction between two opposite benzene rings. Next \(5c, 6\) and \(7\) compounds having same \(\lambda\)-max value noticed that they did not affect the \(\pi\) conjugation length within molecules (Figure 3.9).

**Fig.3.7** ORTEP drawing of the MCP 5c at the 50\% probability. Hydrogen atoms are omitted for clarity. The mean distance and perpendicular distance between two benzenes plane are given.

**Fig.3.8** Crystal packing diagram of two molecules of 5c and intermolecular shortest distance.
Table 3.5: The selected bond distances of compound 5c are listed.

<table>
<thead>
<tr>
<th>Bond</th>
<th>d</th>
<th>Bond</th>
<th>d</th>
<th>Bond</th>
<th>d</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1-O1</td>
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<td>C4-C18</td>
<td>1.529</td>
<td>C9-C10</td>
<td>1.389</td>
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<tr>
<td>O1-C17</td>
<td>1.434</td>
<td>C5-C6</td>
<td>1.384</td>
<td>C10-C22</td>
<td>1.515</td>
</tr>
<tr>
<td>C1-C2</td>
<td>1.392</td>
<td>C6-C7</td>
<td>1.515</td>
<td>C10-C11</td>
<td>1.394</td>
</tr>
<tr>
<td>C2-C3</td>
<td>1.396</td>
<td>C7-C8</td>
<td>1.560</td>
<td>C11-C12</td>
<td>1.396</td>
</tr>
<tr>
<td>C3-C4</td>
<td>1.394</td>
<td>C8-C9</td>
<td>1.514</td>
<td>C12-C23</td>
<td>1.512</td>
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<tr>
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<td>1.402</td>
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<td>1.396</td>
<td>C12-C13</td>
<td>1.399</td>
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<tr>
<td>C13-C15</td>
<td>1.514</td>
<td>C15-C16</td>
<td>1.569</td>
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<td>1.516</td>
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<tr>
<td>C18-C19</td>
<td>1.538</td>
<td>C18-C20</td>
<td>1.533</td>
<td>C18-C21</td>
<td>1.540</td>
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</table>

Fig. 3.9 UV-Vis absorption spectra of compounds 3c, 4c, 6 and 7 in dichloromethane at $1 \times 10^{-5}$ M concentration at 25°C, compared with that of compound 5c.
Table 3.6: Summary of crystal data of 5c

<table>
<thead>
<tr>
<th>Parameter</th>
<th>5C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empirical formula</td>
<td>C_{29}H_{30}O</td>
</tr>
<tr>
<td>Formula weight</td>
<td>322.49</td>
</tr>
<tr>
<td>Crystal system</td>
<td>triclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>P -1</td>
</tr>
<tr>
<td>a [Å]</td>
<td>9.229 (3)</td>
</tr>
<tr>
<td>b [Å]</td>
<td>9.412 (3)</td>
</tr>
<tr>
<td>c [Å]</td>
<td>12.278 (4)</td>
</tr>
<tr>
<td>α [°]</td>
<td>110.783 (17)</td>
</tr>
<tr>
<td>β [°]</td>
<td>96.531 (18)</td>
</tr>
<tr>
<td>γ [°]</td>
<td>103.008 (18)</td>
</tr>
<tr>
<td>Volume [Å³]</td>
<td>949.4 (5)</td>
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<tr>
<td>Z</td>
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</tr>
<tr>
<td>Dcalcd [Mg/m³]</td>
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</tr>
<tr>
<td>temperature [K]</td>
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</tr>
<tr>
<td>unique reflns</td>
<td>3334</td>
</tr>
<tr>
<td>obsd reflns</td>
<td>1766</td>
</tr>
<tr>
<td>parameters</td>
<td>223</td>
</tr>
<tr>
<td>R(int) σ</td>
<td>0.0525</td>
</tr>
<tr>
<td>R[I &gt; 2 (I)] a</td>
<td>0.0525</td>
</tr>
<tr>
<td>wR[I &gt; 2 (I)] b</td>
<td>0.0904</td>
</tr>
<tr>
<td>GOF on F²</td>
<td>1.004</td>
</tr>
</tbody>
</table>

[a] Conventional R on F_{hkl}: Σ|F_{o}| - |F_{c}|)/|σ|F_{o}|. [b] Weighted R on |F_{hkl}|²: Σ[w(F_{o}^{2} - F_{c}^{2})^{2}] / Σ[w(F_{o}^{2})]^{1/2}
3.3 Conclusion

In conclusion, the preparation of 8-methoxy[2.2]metacyclophane using the thiacyclophane method appears to be a useful route to such compounds. 9-methoxy[3.3]MCP adapted the syn- and anti-conformation in different proportion. X-ray diffraction study of 5-tertbutyl-8-methoxy[2.2]-metacyclophane 5c is described. Lewis acid catalysed reactions of 5c-e in benzene and dichloromethane led to the transannular cyclization and isomerization reactions affording the considerably less strained pyrenes derivatives in good yields. These reactions are strongly affected by the bulk and properties of the 8-substitutents as well as various methyl substitutents on meta-benzene rings, which increase the strain in the molecules.

3.4 Experimental:

All melting points are uncorrected. $^1$H NMR spectra were recorded at 300 MHz on a Nippon Denshi JEOL FT-300 NMR spectrometer in deuteriochloroform with Me$_4$Si as an internal reference. IR spectra were measured as KBr plates on a Nippon Denshi JIR-AQ20M spectrometer. Mass spectra were obtained on a Nippon Denshi JMSHX110A Ultrahigh Performance Mass spectrometer at 75 eV using a direct-inlet system. Elemental analyses were performed by Yanaco MT-5.

1. Preparation of 9-methoxy-14,16-dimethyl-2,11-dithia[3.3]metacyclophane (3a):

A solution of 1a (2g, 10 mmol) and 2a (2.02g, 10 mmol) in toluene (30 mL) was added drop wise over a period of 4h from a Hershberg funnel with stirring to a solution of potassium hydroxide (3.32 g, 71 mmol) and sodium borohydride (420mg) in ethanol (3.2 L). After addition the reaction mixture was concentrated and washed by water (30mL). The residue was extracted with CH$_2$Cl$_2$ (100mL×2). The CH$_2$Cl$_2$ extract was also washed by brine and dried by MgSO$_4$. The CH$_2$Cl$_2$ extract was concentrated and residue was chromatographed on silica gel (Wako C-300, 300g) (Hexane-ethyl acetate, 1:1 v/v, as eluent) to give a colourless solid. Recrystallization from hexane to gave 9-methoxy-14,16- dimethyl-2,11-dithia[3.3]metacyclophane(3a) as colourless prism (1g,30%), m.p.: 125-130°C $^1$H-NMR (300MHz, CDCl$_3$), δH 2.14 (6H, s, CH$_3$), 3.73 (3H, s, OCH$_3$), 3.50 (2H, d, J=14.4 Hz, CH$_2$), 3.71 (2H, d, J=1.5 Hz, CH$_2$), 4.31 (2H, d, J=14.1 Hz, CH$_2$), 6.57 (1H, s, Ar-H), 6.63 (1H, t, J=15.3 Hz, Ar-H), 6.88 (1H, s, Ar-H) and 6.96 (2H, d, J=7.71 Hz, Ar-H). m/z 330.51 (M$^+$) (Found: C, 68.10; H, 6.69 C$_{19}$H$_{22}$OS$_2$, required C, 69.05; H, 6.71).
2. Preparation of 9-methoxy-14,16,17,18-tetramethyl-2,11-dithia[3.3]metacyclophane (anti-3b and syn-3b):

A solution of 1a (565 mg, 2.82 mmol) and 2c (652 mg, 2.82 mmol) in toluene (10 mL) was added drop wise over a period of 4h from a Hershberg funnel with stirring to a solution of potassium hydroxide (3.32 g, 71 mmol) and sodium borohydride (210 mg) in ethanol (3.2 L). After addition the reaction mixture was concentrated and washed by water (30 mL). The residue was extracted with CH₂Cl₂ (100mL×2). The CH₂Cl₂ extract was also washed by brine and dried by MgSO₄. The CH₂Cl₂ extract was concentrated and residue was chromatographed on silica gel (Wako C-300, 100g) (Hexane-ethyl acetate, 1:1 v/v, as eluent) to give a colourless solid. Recrystallized from hexane to give 56% (573 mg) anti and syn mixture form. The two conformations were separated by PTLC method. Hexane and Dichloromethane in ratio of 1:1 was used as eluent in PTLC method to separate syn and anti conformation easily. Both conformations are recrystallized from Dichloromethane to gave 9-methoxy-14,16,17,18-tetramethyl-2,11-dithia[3.3]metacyclophane(3b) as colourless prism.

*Anti* conformation (anti-3b) was (429 g, 42%), m.p.: 165-168°C; ¹H-NMR (300MHz, CDCl₃), δH 1.38 (3H, s, CH₃), 2.28 (3H, s, CH₃), 2.44 (6H, s, CH₃), 3.11 (3H, s, OCH₃), 3.20 (2H, d, J= 14.4 Hz, CH₂), 3.63 (2H, d, J= 14.7 Hz, CH₂), 3.75 (2H, d, J= 12.0 Hz, CH₂), 3.90 (2H, d, J= 12.3 Hz, CH₂), 7.01 (1H, t, Ar-H) and 7.31 (2H, d, J= 5.7 Hz, Ar-H). δC (CDCl₃) 14.92, 16.62, 17.08, 25.60, 29.70, 61.76, 88.72, 115.17, 124.22, 127.51, 129.84, 131.91, 136.49 and 158.90.

*Syn* conformation (syn-3b) was (143 mg, 14%), m.p.: 189-192°C; ¹H-NMR (300MHz, CDCl₃), δH 1.97 (3H, s, CH₃), 2.16 (6H, s, CH₃), 2.41 (3H, s, CH₃), 3.42 (2H, d, J= 14.7 Hz, CH₂), 3.53 (2H, d, J= 15 Hz, CH₂), 4.42 (2H, d, J= 9.9 Hz, CH₂), 4.47 (2H, d, J= 9.9 Hz, CH₂), 6.54 (1H, t, Ar-H) and 7.03 (2H, d, J= 7.8 Hz, Ar-H). δC (CDCl₃) 15.95, 17.54, 23.92, 29.43, 30.97, 32.51, 88.06, 98.19, 120.12, 123.37, 128.49, 130.61, 132.70 and 134.05.

3. Preparation of 6-tert-butyl-9-methoxy-14,16-dimethyl-2,11-dithia[3.3] metacyclophane (3c):

A solution of 1b (3 g, 11.7 mmol) and 2a (2.37 g, 13.8 mmol) in toluene (45 mL) was added drop wise over a period of 12 h from a Hershberg funnel with stirring to a solution of potassium hydroxide (3.32 g, 71 mmol) and sodium borohydride (630mg) in ethanol (3.2 L). After addition the reaction mixture was concentrated and washed by water (30 mL). The residue was extracted with CH₂Cl₂ (150mL×2). The CH₂Cl₂ extract was also washed by brine and dried by MgSO₄. The
CH₂Cl₂ extract was concentrated and residue was chromatographed on silica gel (Wako C-300, 300g) (Hexane-ethyl acetate, 1:1 v/v, as eluent) to give a colourless solid. Recrystallization from hexane to give 6-tert-butyl-9-methoxy-14,16-dimethyl-2,11-dithia[3.3]metacyclophane (3c) as colourless prism (3.63 g, 75%), m.p.: 157°C. ¹H-NMR (300MHz, CDCl₃), δ H 1.08 (9H, s, t-Bu), 2.14 (6H, s, CH₃), 3.71 (3H, s, OCH₃), 3.45-4.35 (8H, m, CH₂), 6.52 (1H, s, Ar-H), 6.80 (1H, s, Ar-H) and 6.98 (2H, s, Ar-H).


A solution of 1b (3g, 11.69 mmol) and 2b (2.56g, 11.69 mmol) in toluene (15 mL) was added drop wise over a period of 4h from a Hershberg funnel with stirring to a solution of potassium hydroxide (3.32 g, 71 mmol) and sodium borohydride (630mg) in ethanol (3.2L). After addition the reaction mixture was concentrated and washed by water (30mL). The residue was extracted with CH₂Cl₂ (150mL×2). The CH₂Cl₂ extract was also washed by brine and dried by MgSO₄. The CH₂Cl₂ extract was concentrated and residue was chromatographed on silica gel (Wako C-300, 300g) (Hexane-ethyl acetate, 1:1 v/v, as eluent) to give a colourless solid. Recrystallized from hexane to give 58% (2.71g) anti and syn mixture. The two conformations were separated by PTLC method. Hexane and Dichloromethane in ratio of 1:1 was used as eluent in PTLC method to separate syn and anti conformation easily. Both conformation are Recrystallized from Dichloromethane to gave 6-tert-butyl-9-methoxy-14,16,18-trimethyl-2,11-dithia[3.3]metacyclophane (3d) as colourless prism.

Anti conformation (anti-3d) was (2.032g, 47%), m.p.: 142-144°C; ¹H-NMR (300MHz, CDCl₃), δ H 1.32 (9H, s, t-Bu), 1.33 (3H, s, CH₃), 2.44 (6H, s, CH₃), 3.13 (3H, s, OMe), 3.19-3.25 (2H, d, J= 15.6 Hz, CH₂), 3.65-3.72 (4H, m, CH₂), 3.85-3.89 (2H, d, J=12.3 Hz, CH₂), 7.88 (1H, s, Ar-H) and 7.34 (2H, s, Ar-H).

Syn conformation (syn-3d) was (0.67 mg, 11%), m.p.: 126-128°C; ¹H-NMR (300MHz, CDCl₃), δ H 1.159 (9H, s, t-Bu), 2.22 (6H, s, CH₃), 2.41 (3H, s, CH₃), 3.40-3.45 (4H, d, J=15.0 Hz, CH₂), 3.51 (3H, s, OMe), 4.38-4.42 (2H, d, J= 9.6 Hz, CH₂), 4.44-4.47 (2H, d, J= 9.6 Hz, CH₂), 6.37 (1H, s, Ar-H) and 7.07 (2H, s, Ar-H).

5. Preparation of 6-tert-butyl-9-methoxy-14,16,17,18-tetramethyl-2,11-dithia[3.3]metacyclophane (anti-3e and syn-3e):
A solution of 1b (3.3 g, 12.8 mmol) and 2c (3g, 12.8 mmol) in toluene (15 mL) was added dropwise over a period of 4h from a Hershberg funnel with stirring to a solution of potassium hydroxide (3.32 g, 71 mmol) and sodium borohydride (630mg) in ethanol (3.2L). After addition the reaction mixture was concentrated and washed by water (30mL). The residue was extracted with CH$_2$Cl$_2$ (150mL×2). The CH$_2$Cl$_2$ extract was also washed by brine and dried by MgSO$_4$. The CH$_2$Cl$_2$ extract was concentrated and residue was chromatographed on silica gel (Wako C-300, 300g) (Hexane-ethylacetate, 1:1 v/v, as eluent) to give a colourless solid. Recrystallized from hexane to give 52% (2.9g) anti and syn mixture. The two conformations were separated by PTLC method. Hexane and Dichloromethane in ratio of 1:1 was used as eluent in PTLC method to separate syn and anti conformation easily. Both conformation are Recrystallized from Dichloromethane to gave 6-tert-butyl-9-methoxy-14,16,17,18-tetramethyl -2,11-dithia[3.3]metacyclophane(3e) as colourless prism.

**Anti** conformation (**anti-3e**) was (2.1g, 75%), m.p.: 224°C; $^1$H-NMR (300MHz, CDCl$_3$), δ: 1.32 (9H, s, t-Bu), 1.35 (3H, s, CH$_3$), 2.44 (6H, s, CH$_3$), 3.09 (3H, s, OMe), 3.17-3.22 (2H, d, J=14.5 Hz, CH$_2$), 3.61-3.65 (2H, d, J=14.3 Hz, CH$_2$), 3.77-3.76 (2H, d, J= 11.93 Hz, CH$_2$), 3.85-3.89 (2H, d, J= 11.56 Hz, CH$_2$) and 7.34 (2H, s, Ar-H). m/z 414.67 (M$^+$) (Found: C, 72.19; H, 8.21, C$_{25}$H$_{34}$OS$_2$, required C, 72.41; H, 8.26).

**Syn** conformation (**syn-3e**) was (80 mg, 25%), m.p.: 201°C; $^1$H-NMR (300MHz, CDCl$_3$), δ: 1.10 (9H, s, t-Bu), 1.97 (3H, s, CH$_3$), 2.14 (6H, s, CH$_3$), 2.43 (3H, s, CH$_3$), 3.99-3.45 (2H, d, J=15.23 Hz, CH$_2$), 3.49-3.54 (2H, d, J=15.23 Hz, CH$_2$), 3.52 (3H, s, OMe), 4.41-4.42 (2H, d, J=1.65 Hz, CH$_2$), 4.46-4.47 (2H, d, J= 1.47 Hz, CH$_2$), 7.03 (2H, s, Ar-H). m/z 414.67(M$^+$) (Found: C, 72.16; H, 8.20, C$_{25}$H$_{34}$OS$_2$, required C, 72.41; H, 8.26).

6. **Preparation of 9-methoxy-14,16-dimethyl-2,11-dithia[3.3]metacyclophane-2,2,11,11-tetraoxide(4a):**

To a solution of 3a (800mg, 2.42mmol) in dry CHCl$_3$ (40 mL) was added m-chloroperbenzoic acid (2 g, 69-95%) purity at 0°C while stirring with magnetic stirrer. After the solution was stirred for 24 h in room temperature and argon atmosphere, the solvent was evaporated in vacuo to leave the residue which was washed with 10%NaHCO$_3$(75mL), water(30 mL) and ethanol to afford 9-methoxy-14,16 -dimethyl-2,11-dithia[3.3]metacyclophane-2,2,11,11-tetraoxide(4a): (726mg, 76%), m.p.: 273-275°C. $^1$H-NMR (300MHz, CDCl$_3$), δ: 2.28 (6H, s, CH$_3$), 3.84 (3H, s, OCH$_3$), 3.99 (2H, d, J=14.4 Hz, CH$_2$), 4.27-4.37 (4H, m, CH$_2$), 4.92 (2H, d, J=14.4 Hz, CH$_2$),
6.78 (1H, s, Ar-H), 6.90 (1H, t, J=18.4 Hz, Ar-H), and 7.40 (1H, s, Ar-H), 7.44 (2H, d, J=7.8 Hz, Ar-H). m/z 394.5 (M⁺) (Found: C, 56.59; H, 5.56. C₂₀H₂₄O₅S₂, required C, 57.85; H, 5.62).


To a solution of mixture of anti-3b and syn-3b (500mg, 1.39 mmol ) in dry CHCl₃ (25 mL) was added m-chloroperbenzoic acid (1.28 g, 6.78 mmol, 69-95% purity) at 0°C while stirring with magnetic stirrer. After the solution was stirred for 24 h in room temperature and argon atmosphere, the solvent was evaporated in vacuo to leave the residue which was washed with 10% NaHCO₃(100mL), water(50 mL) and ethanol to afford 6-tert-butyl-9-methoxy-14,16-dimethyl-2,11-dithia[3,3]metacyclophane 2,2,11,11-tetraoxide (4b), (0.470 mg, 79%) as a mixture of Syn and Anti conformation. The two conformations were separated by PTLC method. Hexane, Dichloromethane, Ethyl acetate in ratio of 2:2:1 was used as elutent in PTLC method to separate syn and anti conformation easily.

**Anti** conformation (anti-4b) was (376 g, 63 %), m.p.: 285°C, decompose; ¹H-NMR (300MHz, CDCl₃), δH 1.26 (3H, s, CH₃), 2.33 (3H, s, CH₃), 2.52 (6H, s, CH₃), 3.20 (3H, s, OMe) 3.81-3.85 (2H, d, J= 14.28 Hz, CH₂), 4.37-4.42 (2H, d, J=14.7 Hz, CH₂), 4.46-4.51 (2H, d, J= 14.4 Hz, CH₂), 4.66-4.71 (2H, d, J= 14.1 Hz, CH₂), 7.10-7.16 (1H, t, Ar-H), 7.75-7.77 (2H, d, J=7.5 Hz, Ar-H). m/z 422.56 (M⁺) (Found: C, 60.39; H, 6.96, C₂₁H₂₆O₅S₂, required C, 59.69; H, 6.20).

**Syn** conformation (syn-4b) was (94 mg, 16 %), m.p.: 283°C (decompose); ¹H-NMR (300MHz, CDCl₃), δH 2.04 (3H, s, CH₃), 2.28 (6H, s, CH₃), 2.525 (3H, s, CH₃), 3.55 (3H, s, OMe) 4.05-4.10 (2H, d, J=14.1 Hz, CH₂), 4.42-4.46 (2H, d, J=12.85 Hz, CH₂), 4.77-4.83 (2H, d, J=15.41 Hz, CH₂), 4.99-4.05 (2H, d, J=15.41 Hz, CH₂), 6.66-6.71 (1H, t, Ar-H), 7.52-7.55 (2H, d, J=7.52 Hz, Ar-H). m/z 422.56 (M⁺) (Found: C, 59.34; H, 6.68, C₂₁H₂₆O₅S₂, required C, 59.69; H, 6.20).


To a solution of 3c (1.00g, 2.58 mmol) in dry CHCl₃ (50 mL) was added m-chloroperbenzoic acid (2.57g, 10.4mmol, 69-95% purity) at 0°C while stirring with magnetic stirrer. After the solution was stirred for 24 h in room temperature and argon atmosphere, the solvent was evaporated in vacuo to leave the residue which was washed with 10% NaHCO₃(100mL), water(50 mL) and ethanol to afford 6-tert-butyl-9-methoxy-14,16-dimethyl-2,11-
dithia[3.3]metacyclophane-2,2,11,11-tetraoxide (4c): (0.850g, 73%), m.p.=266°C. \(^1\)H-NMR (300MHz, CDCl\(_3\)), \(\delta\)H 1.11 (9H, s, t-Bu), 2.28 (6H, s, CH\(_3\)), 3.79 (3H, s, OCH\(_3\)), 3.96-4.92 (8H, m, CH\(_2\)), 6.71 (1H, s, Ar-H), 7.17 (1H, s, Ar-H), and 7.50 (2H, s, Ar-H).


To a solution of mixture of anti-3d and syn-3d (1 g, 2.49 mmol) in dry CHCl\(_3\) (50 mL) was added m-chloroperbenzoic acid (2.57g, 10.4mmol, 69-95%) purity at 0°C while stirring with magnetic stirrer. After the solution was stirred for 24 h in room temperature and argon atmosphere, the solvent was evaporated in vacuo to leave the residue which was washed with 10% NaHCO\(_3\)(100mL), water(50 mL) and ethanol to afford 6-tert-butyl-9-methoxy-14,16,18-trimethyl-2,11-dithia[3.3]metacyclophane-2,2,11,11-tetraoxide(5b), (0.694 mg, 60 %) as a mixture of Syn and Anti conformation. The two conformations were separated by PTLC method. Dichloromethane and Ethyl acetate in ratio of 4:1 was used as eluent in PTLC method to separate Syn and Anti conformation easily.

Anti conformation (anti-4d) was (231 mg, 20%), m.p.: 300-302°C decompose; \(^1\)H-NMR (300MHz, CDCl\(_3\)), \(\delta\)H 1.30 (3H, s, CH\(_3\)), 1.34 (9H, s, t-Bu), 2.51 (6H, s, CH\(_3\)), 3.29 (3H, s, OMe) 3.83-3.88 (2H, d, J= 14.4 Hz, CH\(_2\)), 4.41-4.46 (4H, m, CH\(_2\)), 4.57-4.61 (2H, d, J= 14.1 Hz, CH\(_2\)), 7.048 (2H, s, Ar-H) and 7.26 (1H, s, Ar-H). \(\delta\)C (CDCl\(_3\)) 15.48, 21.12, 31.11, 34.60, 53.36, 62.371, 63.48, 119.80, 123.5, 130.43, 131.4, 140.551, 141.351, 147.0 and 156.51; (Found: C, 62.18; H, 6.99. C\(_{24}\)H\(_{32}\)O\(_5\)S\(_2\), required C, 62.04; H, 6.94).

Syn conformation (syn-4d) was (462 mg, 40%), m.p.: 295-298°C (decompose); \(^1\)H-NMR (300MHz, CDCl\(_3\)), \(\delta\)H 1.15 (9H, s, t-Bu), 2.35 (6H, s, CH\(_3\)), 2.51 (3H, s, CH\(_3\)), 3.54 (3H, s, OMe), 4.06-4.11 (2H, d, J= 14.7 Hz, CH\(_2\)), 4.26-4.31 (2H, d, J= 15.3 Hz, CH\(_2\)), 4.71-4.76 (2H, d, J= 15.3 Hz, CH\(_2\)), 4.50-5.05 (2H, d, J=15.0 Hz, CH\(_2\)), 6.59 (1H, s, Ar-H) and 7.62 (2H, s, Ar-H). \(\delta\)C (CDCl\(_3\)) 5.34, 21.27, 30.77, 42.40, 54.05, 54.29, 58.09, 91.63, 123.75, 128.17, 131.71, 139.41, 146.66, 154.28 and 164.62; (Found: C, 60.88; H,6.83, C\(_{24}\)H\(_{32}\)O\(_5\)S\(_2\), required C, 62.04; H, 6.94).

To a solution of mixture of anti-3e and syn-3e (1 g, 2.41 mmol) in dry CHCl₃ (50 mL) was added m-chloroperbenzoic acid (2.57 g, 10.4 mmol, 69-95%) purity at 0°C while stirring with magnetic stirrer. After the solution was stirred for 24 h in room temperature and argon atmosphere, the solvent was evaporated in vacuo to leave the residue which was washed with 10% NaHCO₃ (100 mL), water (50 mL) and ethanol to afford 6-tert-butyl-9-methoxy-14,16-dimethyl-2,11-dithia[3.3]metacyclophane-2,2,11,11-tetraoxide (4e), (0.715 mg, 62%) as a mixture of syn and anti conformation. The two conformations were separated by PTLC method. Dichloromethane and Ethyl acetate in ratio of 4:1 was used as eluent in PTLC method to separate syn and anti conformation easily.

Anti conformation (anti-4e) was (572 g, 50%), m.p.: 335°C, decompose; ¹H-NMR (300MHz, CDCl₃), δH 1.30 (3H, s, CH₃), 1.33 (9H, s, t-Bu), 2.31 (3H, s, CH₃), 2.51 (6H, s, CH₂), 3.17 (3H, s, OMe) 3.80-3.85 (2H, d, J=14.31 Hz, CH₂), 4.35-4.40 (2H, d, J=14.31 Hz, CH₂), 4.45-4.50 (2H, d, J=14.31 Hz, CH₂) and 7.78 (2H, s, Ar-H). δC (CDCl₃) 15.90, 16.94, 18.27, 31.11, 34.60, 53.26, 62.51, 63.85, 119.74, 123.42, 130.41, 135.13, 138.28, 139.01, 146.87 and 156.38; (Found: C, 62.56; H, 7.14. C₃₂H₃₄O₅S₂, required C, 62.73; H, 7.16).

Syn conformation (syn-4e) was (143 mg, 12 %), m.p.: 330°C (decompose); ¹H-NMR (300MHz, CDCl₃), δH 1.10 (9H, s, t-Bu), 1.33 (3H, s, CH₃), 2.01 (3H, s, CH₃), 2.27 (6H, s, CH₂), 3.544 (3H, s, OMe) 4.03-4.09 (2H, d, J=17.25 Hz, CH₂), 4.40-4.45 (2H, d, J=17.25 Hz, CH₂), 4.77-4.82 (2H, d, J=15.78 Hz, CH₂) and 7.55 (2H, s, Ar-H). δC (CDCl₃) 8.65, 19.01, 25.41, 28.49, 30.86, 54.15, 58.04, 63.18, 120.35, 123.70, 128.23, 136.54, 138.24, 139.65, 185.24 and 188.07; (Found: C, 61.80; H, 7.10. C₃₅H₃₈O₈S₂, required C, 62.73; H, 7.16).

11. Preparation of 8-methoxy 12,14 dimethyl[2.2]metacyclophane (5a):

500 mg (1.26 mmol) of 9-methoxy-12,14-dimethyl-2,11-dithia[3.3]metacyclophane-2,2,11,11-tetraoxide was pyrolyzed at 465 °C, analogously to the preparation of 8-methoxy-12,14-dimethyl[2.2] -metacyclophane(5a) yielding 65 mg (18%). During this reaction 25 mg of initial compound were recovered. Recrystallization of required compound from dichloromethane to a white crystal, m.p.: 42°C, ¹H-NMR (300MHz, CDCl₃), δH 1.78-1.86 (2H, m, CH₂), 2.29 (6H, s, CH₃), 2.50-2.26 (2H, m, CH₂), 2.660-2.724 (2H, m, CH₂), 3.21-3.28 (2H, m, CH₂), 3.01 (3H, s, OCH₃), 3.98 (1H, s, Ar-H), 6.79 (1H, s, Ar-H) and 7.05 (2H, s, Ar-H) and 7.25 (1H, s, Ar-H). (Found: C, 84.17; H, 8.32. C₁₉H₂₂O (266.38) required C, 85.67; H, 8.32).
12. Preparation of 8-methoxy-14,16,17,18-tetramethyl[2.2]metacyclophane (anti-5b):

Pyrolysis of dissulfone, anti-4b and syn-4b were carried out in an apparatus consisting of a horizontal tube (15 mm in diameter) passing through two adjacent tube furnace, each of which 20 cm long. The first furnace provided a temperature that would induce sublimation of the sulfone; the second was used at a higher temperature (465°C) that would assure pyrolysis. A vacuum pump was connected at the exit from the second furnace. 400 mg (0.947 mmol) of 9-methoxy-13,15,16,17-tetramethyl-2,11- dithia[3.3]metacyclophane-2,2,11,11-tetraoxide (anti-4b and syn-4b) were pyrolyzed at 465°C under reduced pressure (1 Torr) in the above apparatus as follows. The sample of disulfone was placed in the first furnace and small glass beads were packed into the second furnace. The product which sublimed was collected and chromatographed on silica gel (wako C-300, 100 g) (hexane as eluent) to give a colourless solid. Recrystallization from hexane gave 8-methoxy-12,13,14,16-tetramethyl[2.2]meta-cyclophane (anti-5b), yielding 167 mg (60%).

M. p.: 71-73°C, ¹H-NMR (300MHz, CDCl₃), δH 0.57 (3H, s, CH₃), 2.19 (6H, s, CH₃), 2.30 (3H, s, CH₃), 2.33-2.35 (2H, d, J=5.87 Hz, CH₂), 2.63-2.65 (2H, m, CH₂), 2.90-2.91 (2H, d, J=5.32, CH₃), 3.21-3.26 (3H, d, J=13.4 Hz, CH₂) and 6.78-6.83 (1H, t, Ar-H), 7.10-7.12 (2H, d, J=7.34 Hz, Ar-H). δC (CDCl₃) 15.64, 16.21, 16.40, 32.56, 33.11, 51.66, 59.60, 123.08, 128.63, 130.45, 131.41, 131.93, 133.48, 135.29 and 159.64; (Found: C, 84.27; H, 8.75. C₂₁H₂₆O, required C, 85.67; H, 8.90).

13. Preparation of 4-tert-butyl-1-methoxy-10,12-dimethyl[2.2]metacyclophane (5c):

500 mg (1.109 mmol) of 6-tert-butyl-9-methoxy-12,14-dimethyl-2,11-dithia[3.3]metacyclophane-2,2,11,11-tetraoxide (4c) was pyrolyzed at 465°C under reduced pressure (1 Torr). The product was collected and chromatographed on silica gel with hexane to yield the desired [2.2]metacyclophane. Recrystallization from dichloromethane afforded 193 mg (60%) of 4-tert-butyl-1-methoxy-10,12-dimethyl[2.2]metacyclophane (5c): colorless prisms (dichloromethane); m.p.: 58°C; IR (KBr) 2935, 2856, 2036, 1610,1469, 1459, 1357, 1284, 1213, 1201,1099, 1025, 944, 862, 860, 701, 603, 484 cm⁻¹, ¹H-NMR (300MHz, CDCl₃), δH 1.35 (9H, s, t-Bu), 2.29 (6H, s, CH₃), 2.49-2.58 (2H, m, CH₂), 2.62-2.70 (2H, m, CH₂), 3.19-3.91 (2H, m, CH₂), 3.00 (3H, s, OCH₃), 6.77 (2H, s, Ar-H) and 8.04 (2H, s, Ar-H). ¹³C-NMR (300MHz, CDCl₃), δC 18.814, 31.762, 33.319, 34.218, 37.638, 59.973, 124.183, 130.249, 132.952, 132.969, 133.686, 147.952, 159.919; m/z 322.48 (M⁺) (Found: C, 85.74; H, 9.28; O, 4.98. C₁₃H₁₉O₃ (322.26) required C, 85.66; H, 9.38; O, 4.96).
14. Preparation of 5-tert-butyl-8-methoxy-12,14,16-trimethyl[2.2]metacyclophane (anti-5d):

500 mg (1.109 mmol) of 6-tert-butyl-9-methoxy-14,16,18-trimethyl-2,11-dithia[3.3]metacyclophane-2,2,11,11-tetraoxide (anti-4d and syn-4d) were pyrolyzed at 510 °C, analogously to the preparation of 5-tert-butyl-8-methoxy-12,14,16-trimethyl[2.2]metacyclophane (anti-5d). The product was collected and chromatographed on silica gel (wako C-300, 100 g) (hexane as eluent) to give a yellowish oily liquid-202 mg (56%) as anti conformation, $^1$H-NMR (300MHz, CDCl$_3$), δH 0.54 (3H, s, CH$_3$), 1.29 (9H, s, t-Bu), 2.32 (6H, s, CH$_3$), 2.42-2.49 (2H, m, CH$_2$), 2.61-2.65 (4H, m, CH$_2$), 3.10-3.15 (2H, m, CH$_2$), 2.89 (3H, s, OMe), 6.61 (1H, s, Ar-H) and 7.11 (2H, s, Ar-H). δC (CDCl$_3$) 15.44, 19.32, 31.57, 32.08, 33.07, 34.04, 59.55, 125.64, 127.86, 130.64, 133.23, 133.88, 138.09, 145.99 and 158.82; (Found: C, 85.52; H, 9.54. C$_{24}$H$_{32}$O, required C, 85.66; H, 9.78).

15. Preparation of 5-tert-butyl-8-methoxy-12,13,14,16-tetramethyl[2.2]metacyclophane (anti-5e and syn-5e):

500 mg (1.109 mmol) of 6-tert-butyl-9-methoxy-14,15,16,18-tetramethyl-2,11-dithia[3.3]metacyclophane-2,2,11,11-tetraoxide (anti-4e and syn-4e) were pyrolyzed at 510 °C, analogously to the preparation of 5-tert-butyl-8-methoxy-12,13,14,16-tetramethyl[2.2]metacyclophane (5e), yielding-150mg (54 %). Recrystallization of required compound from hexane to a white crystal (anti-5e), m. pt.: 105-107°C. $^1$H-NMR (300MHz, CDCl$_3$), δH 0.57 (3H, s, CH$_3$), 1.29 (9H, s, t-Bu), 2.18 (3H, s, CH$_3$), 2.29 (6H, s, CH$_3$), 2.39-2.49 (2H, m, CH$_2$), 2.58-2.6 (4H, m, CH$_2$), 3.18-3.25 (2H, m, CH$_2$), 2.86 (3H, s, OMe) and 7.10 (2H, s, Ar-H). δC (CDCl$_3$) 15.63, 16.08, 16.39, 31.56, 32.61, 33.29, 34.00, 59.51, 125.50, 130.14, 130.66, 131.89, 133.44, 145.71, 158.56 and 183.18; (Found: C, 83.17; H,9.39. C$_{25}$H$_{34}$O, required C, 85.66; H, 9.78). Syn- conformation (syn-5e) was also produced in minimum amount as in mixture form.

Reaction of 5c with Iodine. Typical Procedure.

16. 2-tert-Butyl-6,8-dimethyl-4,5,9,10-tetrahydropyrene(6):

A solution of 50 mg (0.15 mmol) of 5c and 152 mg (0.60 mmol) of iodine in 4 mL of benzene was stirred for 120 h at 60°C. The reaction mixture was washed with 10 % sodium thiosulfate solution and then with water. The benzene solution was dried over Na$_2$SO$_4$ and concentrated to leave the mixture of 6 and 5c in 82.0 % and 2.0 % yields, respectively (The yields were determined by GLC analyses.).The mixture was taken up with dichloromethane and chromatographed over silica gel, using hexane as an eluent to give colorless solid, which was
recrystallized from dichloromethane to give 35.6 mg (79.0%) of 2-tert-Butyl-6,8-dimethyl-4,5,9,10-tetrahydropyrene (6), m. p.: 136-138°C; IR (KBr) 2938, 1602, 1450, 1355, 1282, 1224, 1012, 865, 734, 705, 611 cm⁻¹. ¹H-NMR(300MHz, CDCl₃), δ_H 1.35 (9H, s, t-Bu), 2.28 (6H, s, CH₃), 2.82 (8H, s, CH₂), 6.89 (1H, s, Ar-H) and 7.08 (2H, s, Ar-H). ¹³C-NMR (300MHz, CDCl₃), δ_C 19.259, 24.377, 28.613, 31.416, 34.506, 122.667, 128.617, 128.167, 130.488, 131.271, 132.244, 135.054, 149.823; m/z 290.44 (M⁺) (Found: C, 89.62; H, 8.93. C₂₂H₂₆ (290.21) required C, 90.98; H, 9.02)

Titanium Tetrachloride Catalysed Transannular Cyclization reaction of 5c

17. 2-tert-Butyl-6,8-dimethyl-4,5,9,10-tetrahydropyrene(6):

To a solution of 50 mg (0.155 mmol) of 5c and 4 mL of benzene was added a solution of 0.05 mL of MeNO₂ and also added 0.3 mL of TiCl₄ in 2 mL of benzene at 0°C. After the reaction mixture was stirred at 50°C for 1 h, it was poured into ice-water (5mL). The organic layer was extracted with CH₂Cl₂ (10 mL, 2 times). The extract was washed with water (5mL), dried (Na₂SO₄), and concentrated. The residue was column chromatographed over silica gel with hexane as an eluent to give 6 in 86.0% yields. (The yield was determined by GLC analyses). The crude mixture was taken up with dichloromethane and chromatographed over silica gel, using hexane as an eluent, to give colorless solid, which was recrystallized from dichloromethane to give 36.0 mg (81.0%) of 2-tert-butyl-6,8-dimethyl-4,5,9,10-tetrahydropyrene (6), m. p.: 136-138°C.

Aluminium Chloride Catalysed Trans-tert-butylation reaction:

18. 2-tert-Butyl-6,8-dimethyl-4,5,9,10-tetrahydropyrene(6)

To a solution of 60 mg (0.186 mmol) of 5c and 8 mL of benzene was added a solution of 0.023 mL of MeNO₂ and also added 8 mg of AlCl₃ in above solution at 0°C. After the reaction mixture was stirred at 50°C for 3 h, it was poured into ice-water (5mL). The organic layer was extracted with CH₂Cl₂ (10 mL, 2 times). The extract was washed with water (5mL), dried (Na₂SO₄), and concentrated. The residue was column chromatographed over silica gel with hexane as an eluent to give 61% of 6 as white solid crystal. Isolated yield was 56%.

19. Preparation of 1-methoxy-10,12-dimethyl[2.2]metacyclophane(5a):

To a solution of 60 mg (0.186 mmol) of 5c and 8 mL of benzene was added a solution of 0.023 mL of MeNO₂ and also added 8 mg of AlCl₃ in above solution at 0°C. After the reaction mixture
was stirred at 50°C for 4 h, it was poured into ice-water (5mL). The organic layer was extracted with CH₂Cl₂ (10mL, 2 times). The extract was washed with water (5mL), dried (Na₂SO₄), and concentrated. The residue was column chromatographed over silica gel with hexane as an eluent to give 30% of 5a as white crystalline solid. m.p.: 42°C, Isolated yield was 25%.; ¹H-NMR (300MHz, CDCl₃), δH 1.54 (6H, s, CH₃), 2.95 (8H, s, CH₂), 3.98 (3H, s, OCH₃), 7.17 (1H, s, Ar-H), 7.75 (1H, s, Ar-H) and 8.02-8.22 (3H, m, Ar-H). m/z 266.38 (M⁺) (Found: C, 84.17; H, 8.32, C₁₉H₂₂O, required C, 85.67; H, 8.32.

20. 6,8-dimethyl-4,5,9,10-tetrahydropyrene(8):

To a solution of 60 mg (0.186 mmol) of 5a and 8 mL of benzene was added a solution of 0.023 mL of MeNO₂ and also added 8 mg of AlCl₃ in above solution at 0°C. After the reaction mixture was stirred at 85°C for 24 h, it was poured into ice-water (5mL). The organic layer was extracted with CH₂Cl₂ (10mL, 2 times). The extract was washed with water (5mL), dried (Na₂SO₄) and concentrated. The residue was column chromatographed over silica gel with hexane as an eluent to give 21% of 6a and 54% of 8 as pale yellow oily liquid. Isolated yield was 48%.; ¹H-NMR (300MHz, CDCl₃), δH 2.29 (6H, s, CH₃), 2.75-2.88 (8H, m, CH₂), 6.92 (1H, s, Ar-H) and 7.05-7.14 (3H, m, Ar-H). ¹³C-NMR (300MHz, CDCl₃), δ 19.300, 24.237, 28.308, 125.667, 126.796, 130.439, 130.974, 131.156, 131.584, 132.384, 135.557.

Reaction of 6 with DDQ. Typical procedure:

21. 2-tert-Butyl-6,8-dimethylpyrene(7):

A solution of 26mg (0.08 mmol) of 6 and 36 mg of DDQ (90% purity) in 5 mL of benzene was refluxed for 4 h. After the reaction mixture was cooled and concentrated, the residue was extracted and chromatographed on silica gel with hexane/ethylacetate (1:1) as eluent to give 18 mg (77%) of 7, colourless prisms (dichloromethane): m.p.: 221-221.5 °C; λ max (KBr)/ cm⁻¹: 2950, 1600, 1450, 1380; ¹H-NMR (300MHz, CDCl₃), δH 1.51 (9H, s, t-Bu), 2.86 (6H, s, CH₃), 7.63 (1H,s,Ar-H), 7.98 (2H, d, J=10.1 Hz, Ar-H), 8.10 (2H, s, Ar-H) and 8.12 (2H, d, J=10.1 Hz, Ar-H); m/z 286.41 (M⁺). Anal. Calcd. for C₂₂H₂₂ (286.18): C, 92.26; H, 7.74. Found: C, 92.5; H, 7.6.²¹

22. 6,8-dimethylpyrene(10):
A solution of 50 mg (0.213 mmol) of 8 and 61 mg of DDQ (90% purity) in 10 mL of benzene was refluxed for 4 h. After the reaction mixture was cooled and concentrated, the residue was extracted and chromatographed on silica gel with hexane/ethylacetate (1:1) as eluent to give 44 mg (90%) of 10, colourless prisms (dichloromethane): m.p.: 142-143 °C.24

23. Preparation of 5-tert-butyl-8-hydroxy-12,14,16-trimethyl[2.2]metacyclophane (11a):

To a solution of 50 mg (0.148 mmol) of 5d and 8 mL of benzene was added a solution of 0.023 mL of MeNO₂ and also added 8 mg of AlCl₃ in above solution at 0°C. After the reaction mixture was stirred at 50°C for 29 h, it was poured into ice-water (20mL). The organic layer was extracted with CH₂Cl₂ (10mL, 2 times). The extract was washed with water (5mL), dried (Na₂SO₄), and concentrated. The residue was column chromatographed over silica gel with hexane as a eluent to give 73% of 11a as white crystalline solid. Isolated yield was 65%; m.p.: 107°C, ¹H-NMR (300MHz, CDCl₃), δH 0.55 (3H, s, CH₃), 1.22 (9H, s, t-Bu), 1.86 (1H, s, 8-OH), 2.30 (6H, s, CH₃), 2.40-2.48 (2H, m, CH₂), 2.63-2.68 (4H, m, CH₂), 3.10-3.14 (2H, m, CH₂), 6.67 (1H, s, Ar-H) and 7.01 (2H, s, Ar-H). δC (CDCl₃) 15.62, 19.31, 31.59, 32.27, 32.44, 32.68, 34.00, 65.51, 100.56, 124.99, 128.16 128.53, 128.58, 132.90, 134.37, 140.27, 145.40, and 152.45; m/z 322.48 (M⁺) C₂₃H₃₀O (323.22).

24. 5-tert-butyl-8-hydroxy-14,16,17,18-tetramethyl[2.2]metacyclophane (11b):

To a solution of 60 mg (0.170 mmol) of 5e and 7 mL of benzene was added a solution of 0.023 mL of MeNO₂ and also added 8 mg of AlCl₃ in above solution at 0°C. After the reaction mixture was stirred at 50°C for 5 h, it was poured into ice-water (20mL). The organic layer was extracted with CH₂Cl₂ (10 mL, 2 times). The extract was washed with water (5mL), dried (Na₂SO₄), and concentrated. The residue was column chromatographed over silica gel with hexane as an eluent to give 52% of 11b as white crystalline solid. Isolated yield was 48%; m.p.: 78°C, ¹H-NMR (300MHz, CDCl₃), δH 0.64 (3H, s, CH₃), 1.29 (9H, s, t-Bu), 1.83 (1H, s, 8-OH), 2.21 (3H, s, CH₃), 2.36 (6H, s, CH₃), 2.50-2.56 (2H, m, CH₂), 2.69-2.74 (4H, m, CH₂), 3.26-3.30 (2H, m, CH₂) and 7.08 (2H, s, Ar-H). δC (CDCl₃) 15.71, 16.20, 16.57, 30.12, 31.59, 32.27, 32.44, 32.68, 34.00, 65.51, 100.56, 124.99, 128.44, 128.53, 128.58, 132.90, 134.37, 140.27, 145.40, and 152.45; m/z 336.51 (M⁺) C₂₄H₃₂O (336.24).

25. 2-tert-Butyl-6,7,8-trimethyl-4,5,9,10-tetrahydropyrene(12):

To a solution of 50 mg (0.148 mmol) of 5d and 4 mL of dichloromethane and also added 0.3 mL of TiCl₄ in 2 mL of dichloromethane at 0°C. After the reaction mixture was stirred at 0°C for 8 h,
it was poured into ice-water (25mL). The organic layer was extracted with CH$_2$Cl$_2$ (10mL, 2 times). The extract was washed with water (5mL), dried (Na$_2$SO$_4$), and concentrated. The residue was column chromatographed over silica gel with hexane as a eluent to give 12 in 78.0% yields. (The yield was determined by GLC analyses.). The crude mixture was taken up with dichloromethane and chromatographed over silica gel, using hexane as an eluent, to give colorless solid, which was recrystallized from dichloromethane to give 36.0 mg (70.0%) of 2- tert-Butyl-6,7,8-trimethyl-4,5, 9,10-tetrahydropyrene (12), m.p.: 190-191°C. IR(KBr) 3040, 2960, 2900, 2850, 1600, 1430, 1360, 1280, 1230, 1200, 870, 715 cm$^{-1}$, $^1$HNMR (CDCl$_3$), $\delta_H$ 1.30(9H, s, t-Bu), 2.20 (6H, s, CH$_3$), 2.21 (3H, s, CH$_3$), 2.72-2.84 (8H, m, CH$_2$) and  7.01 (2H, s, Ar-H), Mass spectrum, m/e 304.47(M$^+$). Anal.Calcd. for C$_{23}$H$_{28}$: C, 90.73; H, 9.27. Found: C, C, 90.34; H, 9.51.

26. 2-tert-Butyl-6,7,8-trimethylpyrene (13):

To a solution of 50 mg (0.148 mmol) of 5d and 4 mL of dichloromethane and also added 0.3 mL of TiCl$_4$ in 2 mL of dichloromethane at 0°C. After the reaction mixture was stirred at room temperature (RT) for 9 h, it was poured into ice-water (25mL). The organic layer was extracted with CH$_2$Cl$_2$ (10mL, 2 times). The extract was washed with water (10mL), dried (Na$_2$SO$_4$), and concentrated. The residue was column chromatographed over silica gel with hexane as an eluent to give 13 in 48.0% yields. (The yield was determined by GLC analyses). The crude mixture was taken up with dichloromethane and chromatographed over silica gel, using hexane as an eluent, to give colorless solid, which was recrystallized from dichloromethane to give 18.0 mg (40.0%) of 2-tert-Butyl-6,7,8-trimethyl-4,5, 9,10-tetrahydropyrene (13), $^1$HNMR (CDCl$_3$) $\delta_H$ 1.57 (9H, s, t-Bu), 2.70 (3H, s, CH$_3$), 2.90 (6H, s, CH$_3$), 7.99 (2H, d, J=9.3Hz, Ar-H), 8.13 (2H, s, Ar-H) and 8.27 (2H, d, J=9.3 Hz, Ar-H).

3.5 References

Chapter 4

Synthesis and stereochemical Assignments of 8-methoxy[2.2] and 9-methoxy[3.3]metaparacyclophane, involved in Lewis-acid induced isomerisation and transannular reaction.

The preparation of methyl substituted 8-methoxy[2.2]metaparacyclophane 9 via thiacyclophane and its oxysdised products. Similarly, substituted-9-methoxy[3.3]metaparacyclophane 18 via coupling methods and its reduced by Wolff-Kishner reduction. X-ray difraction study of 5-tert-butyl-8-methoxy[2.2]metaparacyclophane 9b are described. Lewis acid catalysed reactions of 9b in various condition led to the isomerization and transannular cyclization reactions affording the considerably less strained pyrenes derivatives in good yields. These reactions are strongly affected by the bulk and properties of the 8-substitutents as well as various methyl substitutents on para benzene rings, which increased the strain in the molecules. But, Lewis acid catalysed reactions of 18 in various conditions led to tert-butylation product.

4.1 [2.2]metaparacyclphane:

4.1. a. Introduction

The meta-bridged benzene ring of [2.2]metaparacyclphane (MPCP=metaparacyclphane) (1) has been shown to undergo conformational flipping1-7 with a substantial energy barrier (ca.20 kcal mol\(^{-1}\)). According to X-ray crystallographic studies of 1,8 the deformations of benzene rings are similar to those of the corresponding rings in para- and meta[2.2]cyclophane, with para- and meta-bridged rings bent in a boat and a chair like form, respectively. The angle between the two aromatic planes defined by the carbon atoms, 3, 4, 6 and 7 on one hand, and 12, 13, 15 and 16 on the other, is about 13°. It should be noted that the angle between the 11,12,16-plane and 10,11-bond vector (or between13,14,15-plane and 1,14-bond vector) is even larger than the analogous angle in [2.2]paracyclphane. The para bridge moiety of 1 is thus more strongly tilted then those of the isomeric compound. Introduction of the substituents at the 8-position increases the strain in the molecule in comparison with the unsubstituted [2.2]MPCP (1); the deformation of para-benzen ring of 8-methyl[2.2]MPCP (2) was estimated to 15° by our previous X-ray crystallography.9 Thus introduction of methyl group to the para-benzene ring of [2.2]MPCP also increases the strain in the molecule. Therefore, there is substantial interest to prepare Polymethyl substituted [2.2]MPCPs to investigate the relationship between the strain and reactivity.10-11

![Fig. 4.1](image)

Previously we found that 8-methyl and 8-hydroxy[2.2]MPCPs9 can be conveniently prepared by AlCl\(_3\)-MeNO\(_2\)-catalysed trans-tert-butylation of the corresponding tert-butyl derivative. These
results suggest that 8,12,13,15,16-pentamethyl[2.2]MPCP (3) might be also prepared from corresponding tert-butyl group as a positional protective group on aromatic ring.\textsuperscript{12-16} We report here the convenient preparation of title compounds and their treatment with Lewis acid catalyst in a benzene solution.

\[ \text{Scheme 4.1} \]

\subsection*{4.1. b. Result and Discussion:}

The preparative route of 5-substituted polymethyl[2.2]MPCPs 9a-b are shown in Scheme 4.1. The preparation of 2,6-bis(sulfonomethyl)benzene 5a-b were prepared from bis(chloromethyl)benzene 4,\textsuperscript{9,12,17} 1,4-bis-(chloromethyl)-2,3,5,6-tetramethylbenzene 6 was prepared according the reported procedure.\textsuperscript{18} The cyclisation of bis(sulfonomethyl)benzene 5a-b and 1,4-bis(chloromethyl)-2,3,5,6-tetramethyl benzene 6 was carried out under highly diluted condition in 10% ethanoic KOH in the presence of small amount of NaBH\textsubscript{4}, giving the desired 2,11-dithia[3.3]MPCPs 7a and 7b in 58 and 60% yields respectively. Similarly, oxidation of 7a-b with m-chloroperbenzoic acid in CHCl\textsubscript{3} afforded the corresponding bisulfones 8a and 8b in 85, 90% yields respectively. Pyrolysis of bisulfones 8a-b under reduced pressure (1 torr) at 465°C
was carried out by a reported method,\textsuperscript{18,19} to afford exclusively 9a and 9b in 61 and 62\% yields, respectively.

The structures of 9a-b have been elucidated by elemental analyses and spectral data. For instance, the mass spectral data for 9b (9b. M+ = 350.4) strongly support for the formation of desired compounds. The IR spectrum of 9a-b shows the absorption of the methoxy stretching vibration around 1700 cm\textsuperscript{-1}. The \textsuperscript{1}H NMR spectrum (in CDCl\textsubscript{3}) of 9a and 9b show a singlet at \(\delta\) 1.69 and 1.72 ppm for methyl protons at 15,16-positions which is in a strongly shielding region of opposite \textit{meta}-bridged benzene ring and \(\delta\) 2.26, 2.27 ppm for external methyl protons at 17, 18-positions, respectively. On the other hand, the signals of the internal methoxy protons at 8-position and two types of aromatic protons for C-4, C-6 and C-5 were observed at upper field of \(\delta\) 3.21 ppm and 6.67, 7.29 ppm for 9a, \(\delta\) 3.19 ppm and 6.67 ppm for 9b which is in a strongly shielding region of opposite \textit{para}-bridged benzene ring.

\begin{center}
\includegraphics[width=\textwidth]{scheme_4_2.png}
\end{center}

\textsc{Scheme 4.2}
Table 4.1: Lewis acid catalysed isomerization and trans tert-butylation reaction. a The product yields were determined by GC analyses. b Isolated yields are shown.

<table>
<thead>
<tr>
<th>Run</th>
<th>Substract</th>
<th>Catalyst and condition</th>
<th>Time(h)</th>
<th>Product(%)</th>
<th>Recovered(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>9b</td>
<td>AlCl₃/MeNO₂/benzene/50°C</td>
<td>1.0</td>
<td>(47)³(34)b</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>&quot;</td>
<td>&quot;</td>
<td>2.0</td>
<td>20</td>
<td>74</td>
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<tr>
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<td>&quot;</td>
<td>&quot;</td>
<td>2.75</td>
<td>5</td>
<td>(88)³(75)b</td>
</tr>
<tr>
<td>4</td>
<td>TiCl₄/CH₂Cl₂/0°C</td>
<td>&quot;</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>TiCl₄/CH₂Cl₂/RT</td>
<td>&quot;</td>
<td>1</td>
<td>-</td>
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</tbody>
</table>

Attempted TiCl₄-catalysed trans-tert-butylation of 9b in benzene carried out under various conditions failed. Only the recovery of the starting compound 9b resulted. Interestingly, the AlCl₃-MeNO₂-catalysed trans-tert-butylation of 9b in benzene at 50°C for 1 h the afforded metacyclophanes 10 in 47% yields along with the formation of small amount of 11 and 12. The expected product 8-methoxy-12,13,15,16-tetramethyl[2.2]MPCP 9a was not detected from 9b under the conditions used. Prolonged reaction of 9b for 3 h under the same conditions gave 11 in 88% yields. This result suggests that 10 might be an intermediate in the formation of 11, 12 and 13 (Scheme 4.2). Thus, the present Lewis acid isomerisation was supposed to be much faster than trans-tert-butylation of [2.2]MCP.

A mechanism for the formation of the isomerisation products 10 from 9b is tentatively proposed in Scheme 4.3. Cram at. al. reported the AlCl₃-catalysed isomerisation of [2.2]paracyclophane
to the less strained [2.2]MPCP 1 along with transannular isomerisation products, 1,2,2a,3,4,5-hexahydropyrene and [2.2]metacyclophane.

The mechanism for the formation of the 9-hydroxy product 11 from 10 (Scheme 4.4) is tentatively proposed in Scheme 4.4.

In the case of 9b, the protonation of the ipso-position of ethylene bridge on the parabenzenne ring could afford the cation intermediate (A), which could isomerise to the strainless 5-tert-butyl-8-methoxy-12,13,14,16-tetramethyl[2.2]metacyclophane 10 via cation intermediates B and C. This novel isomerisation reaction might attributed to the methoxy groups at the 8-position of meta benzene ring and the methyl groups at the 12,13,15,16-positions of para benzene ring, which

![Scheme 4.4](image)

**Scheme 4.4**

The mechanism for the formation of the 9-hydroxy product 11 from 10 (Scheme 4.4) is tentatively proposed in Scheme 4.4.

**Fig.4.2** The molecular structure of 9b in a top view (left). The bond distances and the bond angles of methylene bridge of 9b are listed (right).
increase the strain in the molecule in comparison with the unsubstituted [2.2]MPCP 1 and 8-methyl[2.2]MPCP 2. We previously reported to the AlCl₃-MeNO₂ catalysed trans-tert-butylolation of 5-tertbutyl-8-methyl[2.2]MPCP afforded only the desired 8-methyl[2.2]MPCP 2. No present isomerisation product was observed under the conditions used. These results are attributed to the increase of degree of deformation of para-benzene ring, which was estimated to 17.87° by the X-ray crystallography study of 9b compared with that of 1 to 13° and 2 to 15°.

![Image of molecular structure](image_url)

**Figure 4.3** ORTEP drawing of the MPCP 9b at the 50% probability. Hydrogen atoms are omitted for clarity. The mean distance between two benzenes rings are given.

### 4.1. c. x-ray analysis:

Conclusive evidence for the structure 9b was provided by a single-crystal X-ray structure determination. Figure 4.2 shows the molecular structure of 9b in a top view. The bond distances for 9b are listed in Table 4.2. The mean distance between mean geometric centres of rings of [2.2]MPCP is equal to 3.27 Å in Figure 4.3. The two benzenes unit overlaps very slightly with their dihedral angle being only 15.22° in Figure 4.5. The meta bridge benzene unit shows slight boat-type deformations with angles between C(8)-C(9)-C(20) and C(8)-C(20)-C(6)-C(4) as well as C(5)-C(4)-C(6) and C(8)-C(20)-C(6)-C(4) being 12.19° and 5.96° respectively. The other para bridge benzene unit shows strong boat-type deformations with angles between C(17)-C(2)-C(10) and C(2)-C(10)-C(14)-C(7) as well as C(3)-C(7)-C(14) and C(2)-C(10)-C(14)-C(7) being 15.75 and 15.30° respectively. One of the methoxy groups which is located above the center of the benzene ring shows a remarkable deviation from the plane of the benzene ring. The bridging angles, C(17), C(22), C(16) and C(22), C(16), C(8) are 109.5 and 111.2° respectively; however, for corresponding angles, C(3), C(23), C(18) and C(23), C(18), C(20) are appreciably smaller and greater, being 108.8 and 111.9° respectively.
packing diagram of 9b (Figure 4.4), the intermolecular shortest distance within C26H56-H51C19 is 2.38 Å, which are shorter than the sum of the van der waals radii of the hydrogen (1.20 Å) and oxygen atoms (1.60 Å) or carbon atom (1.70 Å).  

Fig. 4.4 Crystal packing and short contact of [2.2]MPCP (9b).

X-ray crystallographic study of 9b shows that the compound is apparently conformationally more rigid than (1, R=H) because its methoxy substituent at 8-position is likely impinge upon the electron cloud of para-bridged one. It is quite interesting that the increase of degree of deformation of para-benzene ring, which was estimated to 17.87° of 9b compared with that of 2 to 15°.

Fig. 4.5 The two benzenes unit of 9b overlaps very slightly with their dihedral angle being only 15.22°.
Thus introduction of the methyl groups to the para benzene ring of [2.2]MPCP also increases the strain in the molecule in comparison with the unsubstituted 8-methyl [2.2]MPCP. It was also found the distortion angle of meta-benzene ring from planarity is 15.94° in comparison with that of 8,16-dimethyl[2.2]MCP (15.4).

### 4.2 [3.3]metaparacyclophane:

#### 4.2. a. Introduction:

The synthesis and stereochemical aspects of conformationally mobile [3.3]MCPs (MCP=metacyclophane) have been of interest during the past decade, with particular attention paid to dithia[3.3]MCPs, which possess an *anti*-stepped conformation. The pioneering work of the conformational investigation of 2,11-dithia[3.3]MCPs was reported by Vögtle et al. Shinmyozu and his co-workers have reported first preparation and conformational behavior in the carbocyclic [3.3]MCPs and their analogues. [3.3]MCP exists in the *syn*-geometry with a chair-chair arrangement of the trimethylene chains in the crystal state. The preferred geometry of [3.3]MCP in solution is also a *syn-*, on the basis of $^1$HNMR spectrum, in which [3.3]MCP shows strong temperature-dependent phenomenon at low temperature.

[3.3]MPCP (MPCP = metaparacyclophane) was first prepared by Shinmyozu and co-workers using (p-tolylsulfonyl) methyl isocyanide (TosMIC) as the cyclisation reagent, followed by Wolff–Kishner reduction. The *meta*-bridged benzene ring of [3.3]MPCP has been shown to
undergo conformational flipping\textsuperscript{34,35} with a significantly lower energy barrier than that in [2.2]MPCP (ca 80 kJ mol\textsuperscript{-1}).\textsuperscript{36} We reported the synthesis of 9-substituted \textsuperscript{3.3}MPCP-2,11-diones and conversion to the corresponding \textsuperscript{3.3}MPCPs by Wolff–Kishner reduction.\textsuperscript{37} The different orientation for the acetylation was observed depending on the substituent at C(9) position.

Interestingly, all of the compounds are internally unsubstituted \textsuperscript{3.3}MCP-2,11-diones and it is surprising that there are very few reports\textsuperscript{38,39} on the preparation of 9-methyl- or 9-methoxy-analogues despite the fact that the chemical shift of the internal substituents, such as methyl and methoxy group provides a convenient probe for \textsuperscript{1}H-NMR studies of any possible conformational changes.

We also reported the preparation of 2,11-dithia(1,4)naphthaleno\textsuperscript{3.3}MCPs and an internal substituent such as Me or OMe group is sufficient to allow the isolation of a discrete syn- or anti-isomer.\textsuperscript{40} Thus, there is substantial interest that employing a Polymethyl benzene ring instead of a naphthalene ring of the para-brided ring will provide good information about the $\pi-\pi$ interaction between the two stacking aromatic rings. Furthermore, the conformations of 9-substituted\textsuperscript{3.3}MCPs with a benzene skeleton having para-methylene bridge are so far not known in spite of the formation 6-tertbutyl-9-methoxy\textsuperscript{3.3}metaparacyclophane-2,11-diones. We describe here the synthesis of metaparacyclophane such as the titled MCPs using the above method, as well as studies of their conformation and distortion by the ring current interactions derived within two benzene rings.

\subsection*{4.2. b. Result and discussion:}

Vögtle reported\textsuperscript{41-43} the preparation of carbocyclic\textsuperscript{3n}MCPs using TosMIC\textsuperscript{44,45} as the cyclization reagent, which was applied in a new cyclization procedure without phasetransfer conditions\textsuperscript{46–50}. This strategy can be employed for the preparation of \textsuperscript{3.3}MCP containing two benzene rings. However, the preparation of \textsuperscript{3.3}MCPs using the TosMIC method is difficult because of its low yield as well as the difficulty of the product separation from the other macrocyclic oligoketones, \textit{i.e.} trimer and tetramer. Therefore, it has been very difficult to obtain sufficient amounts of the above compounds to investigate their chemical behavior.

The starting compound 2,6-bis(bromomethyl)-4-tert-butylanisole \textbf{15} was easily prepared from 4-tert-butylanisole \textbf{14} by using the tert-butyl group as a positional protecting group on the aromatic ring, followed by the cyclization of \textbf{15} and TosMIC carried out in dimethylformamide(DMF) with excess of sodium hydride to obtained the TosMIC adduct \textbf{16} as shown in Scheme 4.5.
The cyclic diketones 17 was synthesized by coupling the TosMIC-adduct 16 with 1,4-bis(chloromethyl)-2,3,5,6-tetramethyl benzenes 6 under highly diluted conditions in DMF with an excess of sodium hydride as shown in Scheme 4.6. We have improved the addition procedure in Vögtle's method\textsuperscript{41–43}. Thus, to a suspension of NaH in DMF was dropped a solution of 6 and TosMIC-adducts 16 in DMF at room temperature. This not only improves the yield of the desired ketones but also makes the handling of the base (solid NaH) easier. By careful column chromatography (silica gel, Wako C-300), 17 is separated as a white crystalline solid (54% yield).

The Wolff-Kishner reduction of diketone 17 afforded the desired 9-methoxy[3.3]MPCP (18) in 50% yields, respectively (Scheme 4.6).

The structures of 17 have been elucidated by elemental analyses and spectral data. For instance, the mass spectral data for 17 (M\textsuperscript{+} = 406.3) strongly supports cyclic structure. The IR spectrum of
17 shows the absorption of the carbonyl stretching vibration around 1697 cm\(^{-1}\). The \(^1\)H-NMR spectrum (in CDCl\(_3\)) of 17 exhibits four doublets at \(\delta\) 3.17 ppm (\(J= 11.4\) Hz), \(\delta\) 3.68 ppm (\(J= 15.3\) Hz), \(\delta\) 3.81 ppm (\(J= 11.7\) Hz) and \(\delta\) 3.98 ppm (\(J= 15.6\) Hz) for the ArCH\(_2\)CH\(_2\)CH\(_2\)Ar methylene protons and a singlet for the internal methoxy group at an upfield shift \(\delta\) 3.32 ppm from anisole (\(\delta\) 3.75 ppm) due to the ring current of the opposing aromatic ring\(^{49-51, 52-56}\). Further, the aryl hydrogens at 5,7-positions can clearly be seen to be shielded at \(\delta\) 6.88 ppm by the adjacent ring, a common consequence of a face-to-face benzene ring\(^{52-61}\). Also the tert-butyl protons were observed at \(\delta\) 1.21 ppm.

\[
\text{Scheme 4.7}
\]

Similarly, the structures of 18 have been elucidated by elemental analyses and spectral data. The IR spectrum of 18 shows the absorption of the carbonyl stretching vibration around 1710 cm\(^{-1}\). The \(^1\)H-NMR spectrum (in CDCl\(_3\)) of 18 exhibits four sets of multiplets at \(\delta\) 2.16, 2.34, 2.48, 2.73, 3.05 ppm respectively, for the ArCH\(_2\)CH\(_2\)CH\(_2\)Ar methylene protons and a singlet for the internal methoxy group at an upfield shift \(\delta\) 3.25 ppm from dione (17) (\(\delta\) 3.32 ppm) due to the ring current of the opposing aromatic ring. Further, the aryl hydrogens at 5,7-positions can clearly be seen to be shielded at \(\delta\) 6.67 ppm from dione (17) (\(\delta\) 6.88 ppm) by the adjacent ring, a common consequence of a face-to-face benzene ring\(^{52-61}\). Also the tert-butyl protons were observed at \(\delta\) 1.27 ppm.

4.2. c. Lewis acid catalysed reaction:

The Lewis acid-catalyzed reactions of 6-tert-butyl-9-methoxy[3.3]MPCP 18 was carried out under Lewis acid catalyzed and the results are summarized in Table 4.3. Treatment of AlCl\(_3\)-MeNO\(_2\) catalysed trans-tert-butylation of 18 in benzene at 50°C for 30 minutes afforded removal of the tert-butyl group to give 19 in 20 % yield along with tert-butyl benzene (21).
Table 4.3: Lewis acid catalysed trans tert-butylation reaction of 18. The product yields were determined by GC analyses. Isolated yields are shown.

<table>
<thead>
<tr>
<th>Run</th>
<th>Substrate</th>
<th>Catalyst and condition</th>
<th>Time(h)</th>
<th>Product(%)</th>
<th>Recovered(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>18</td>
<td>AlCl₃/MeNO₂/benzene/50°C</td>
<td>0.5</td>
<td>19(20)</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td>1.0</td>
<td>19(51)b</td>
<td>20(5)</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td>1.5</td>
<td>19(74)b</td>
<td>20(14)</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td>2.0</td>
<td>19(75)b</td>
<td>20(21)</td>
</tr>
</tbody>
</table>

Prolonged reaction for 1.5 h under the same condition gave 19 in 74% and 20 in 14% yields. Further prolonged the reaction for 2 h under the same condition gave 19 in 75% and 20 in 21% yields. This result suggests that 19 might be an intermediate in the formation of 20. Thus, the present Lewis acid tert-butylation was supposed to be much faster than isomerisation reaction.

4.3 Conclusion

In conclusion, the preparation of 8-methoxy[2.2]metaparacyclophane using the thiacyclophane method appears to be a useful route to such compounds. Similarly, the preparation [3.3]MPCP by coupling method and followed by oulf-kishner reduction method. X-ray diffraction study of 5-tert-butyl-8-methoxy[2.2]metaparacyclophane 9b is described. Lewis acid catalysed reactions of 9b and 18 in various condition led to the transannular cyclization and isomerization reactions affording the considerably less strained pyrenes derivatives in good yields. These reactions are strongly affected by the bulk and properties of the 8-substitutents as well as various methyl substitutents on para benzene rings, which increase the strain in the molecules. Further studies on the chemical properties of [2.2]MPCP and [3.3]MPCP are now in progress.

4.4 Experimental

All melting points are uncorrected. ¹H NMR spectra were recorded at 300 MHz on a Nippon Denshi JEOL FT-300 NMR spectrometer in deuteriochloroform with Me₄Si as an internal reference. IR spectra were measured as KBr plates on a Nippon Denshi JIR-AQ20M spectrometer. Mass spectra were obtained on a Nippon Denshi JMSHX110A Ultrahigh Performance Mass spectrometer at 75 eV using a direct-inlet system. Elemental analyses were performed by Yanaco MT-5.
1. Preparation of 9-methoxy-14,15,17,18-tetramethyl-2,11-dithia[3.3]metaparacyclophane (7a):

A solution of 5a (3.9 g, 13.2 mmol) and 6 (3.0 g, 13.2 mmol) in toluene (30 mL) was added dropwise over a period of 4 h from a Hershberg funnel with stirring to a solution of potassium hydroxide (3.32 g, 71 mmol) and sodium borohydride (630 mg) in ethanol (3.2 L). After the addition, the reaction mixture was concentrated and washed with water (50 mL). The residue was extracted with CH$_2$Cl$_2$ (100 mL x 3). The CH$_2$Cl$_2$ extract was also washed by brine and dried by MgSO$_4$. The CH$_2$Cl$_2$ extract was concentrated and residue was chromatographed on silica gel (Wako C-300, 300 g) (Hexane-ethyl acetate, 1:1 v/v, as eluent) to give a colourless solid. Recrystallization from chloroform gave 9-methoxy-14,15,17,18-tetramethyl-2,11-dithia[3.3]metaparacyclophane (7a) as colorless prism (2.4 g, 51 %), m.p.: 132-137°C; $^1$H-NMR (300 MHz, CDCl$_3$), $\delta$H 1.87 (6H, s, CH$_3$), 2.35 (6H, s, CH$_3$), 3.33 (3H, s, OCH$_3$), 3.19 (2H, d, J=15.3 Hz, CH$_2$), 3.46 (2H, d, J=13.2 Hz, CH$_2$), 3.84 (2H, d, J=15.3 Hz CH$_2$), 4.48 (2H, d, J=13.2 Hz, CH$_2$), 6.84 (1H, t, Ar-H) and 7.12 (2H, d, J=7.5 Hz, Ar-H). $\delta$C (CDCl$_3$) 16.01, 18.17, 26.34, 30.33, 122.45, 128.45, 131.90, 132.84, 133.42 and 153.27; (Found: C, 69.78; H, 7.35, C$_{21}$H$_{26}$O$_2$S$_2$, required C, 70.34; H, 7.31).


A solution of 5b (3.6 g, 13.8 mmol) and 6 (3.12 g, 13.8 mmol) in toluene (45 mL) was added dropwise over a period of 4 h from a Hershberg funnel with stirring to a solution of potassium hydroxide (3.32 g, 71 mmol) and sodium borohydride (630 mg) in ethanol (3.2 L). After the addition, the reaction mixture was concentrated and washed with water (30 mL). The residue was extracted with CH$_2$Cl$_2$ (150 mL x 2). The CH$_2$Cl$_2$ extract was also washed by brine and dried by MgSO$_4$. The CH$_2$Cl$_2$ extract was concentrated and residue was chromatographed on silica gel (Wako C-300, 300 g) (Hexane-ethyl acetate, 1:1 v/v, as eluent) to give a colourless solid. Recrystallization from chloroform gave 6-tert-butyl-9-methoxy-14,15,17,18-tetramethyl-2,11-dithia[3.3]metaparacyclophane (7b) as colorless prism (4.87 g, 79 %), m.p.: 128°C; $^1$H-NMR (300 MHz, CDCl$_3$), $\delta$H 1.295 (9H, s, t-Bu), 1.910 (6H, s, CH$_3$), 2.351 (6H, s, CH$_3$), 3.307 (3H, s, OCH$_3$), 3.19 (2H, d, J=15 Hz, CH$_2$), 3.445 (2H, d, J=13.2 Hz, CH$_2$), 3.81 (2H, d, J=15.6 Hz, CH$_2$), 4.511 (2H, d, J=13.5 Hz, CH$_2$) and 7.074 (2H, s, Ar-H). $\delta$C (CDCl$_3$) 16.01, 18.17, 26.34, 30.55, 31.70, 34.35, 62.48, 125.49, 131.46, 132.00, 132.54, 133.37, 144.68 and 151.16; m/z 414.67 (M$^+$) (Found: C, 72.46; H, 8.02. C$_{25}$H$_{34}$S$_2$, required C, 72.41; H, 8.26).

To a solution of 7a (1.5 g, 4.18 mmol) in dry CHCl₃ (75 mL) was added m-chloroperbenzoic acid (3.84 g, 69-95%) purity at 0°C while stirring with magnetic stirrer. After the solution was stirred for 24 h in room temperature and argon atmosphere, the solvent was evaporated in vacuo to leave the residue which was washed with 10% NaHCO₃ (100mL), water (50 mL) and ethanol to afford 9-methoxy-14,15,17,18-tetramethyl-2,11-dithia[3.3]metaparacyclophane-2,2,11,11-tetraoxide (8a): (1.49 g, 85 %), m.pt.>200°C, ¹H-NMR (300MHz, CDCl₃), δH 1.95 (6H, s, CH₃), 2.43 (6H, s, CH₃), 3.39 (3H, s, OCH₃), 3.86 (2H, d, J=14.4 Hz, CH₂), 4.48 (2H, d, J=15.0 Hz, CH₂), 4.69 (2H, d, J=15.9 Hz, CH₂), 4.86 (2H, d, J=14.7 Hz, CH₂), 6.93 (1H, t, Ar-H), and 7.70 (2H, d, J=8.4 Hz, Ar-H). δC (CDCl₃) 17.68, 18.62, 52.73, 60.71, 121.60, 123.30, 125.38, 129.03, 135.00 and 135.49.


To a solution of 7b (1 g, 2.49 mmol) in dry CHCl₃ (50 mL) was added m-chloroperbenzoic acid (2.57 g, 10.4 mmol, 69-95%) purity at 0°C while stirring with magnetic stirrer. After the solution was stirred for 24 h in room temperature and argon atmosphere, the solvent was evaporated in vacuo to leave the residue which was washed with 10% NaHCO₃ (100mL), water (50 mL) and ethanol to afford 6-tert-butyl-9-methoxy-14,15,17,18-tetramethyl-2,11-dithia[3.3]metaparacyclophane-2,2,11,11-tetraoxide (8b): (0.676 g, 58.3 %), m.pt.>200°C. ¹H-NMR (300MHz, CDCl₃), δH 1.30 (9H, s, t-Bu), 1.97 (6H, s, -CH₃), 2.43 (6H, s, CH₃), 3.37 (3H, s, OCH₃), 3.85 (2H, d, J=14.7 Hz, CH₂), 4.45 (2H, d, J=15.0 Hz, CH₂), 4.68 (2H, d, J=13.8 Hz, CH₂), 4.86 (2H, d, J=14.1 Hz CH₂) and 7.67 (2H, s, Ar-H). δC (CDCl₃) 0.00, 17.67, 18.62, 31.47, 34.90, 52.99, 60.55, 120.60, 125.25, 126.44, 134.99, 135.99, 146.11 and 153.38.

5. Preparation of 8-methoxy-12,13,15,16-tetramethyl[2.2]metaparacyclophane (9a):

500 mg (1.18 mmol) of 9-methoxy-14,15,17,18-tetramethyl-2,11-dithia[3.3]metaparacyclophane-2,2,11,11-tetraoxide (8a) was pyrolyzed at 465 °C, analogously to the preparation of 8-methoxy-12,13,15,16-tetramethyl[2.2]metaparacyclophane, yielding 212mg ( 61 %). Recrystallization from dichloromethane to a white crystal, m. p.: 106°C, ¹H-NMR (300MHz, CDCl₃), δH 1.69 (6H, s, CH₃), 2.27 (6H, s, CH₃), 2.31-2.36 (2H, m, CH₂), 2.82-2.90 (4H, m, CH₂), 3.12-3.17 (2H, m,
6. Preparation of 5-tert-butyl-8-methoxy-12,13,15,16-tetramethyl[2.2]metaparacyclophane (9b):

1 g (2.033 mmol) of 6-tert-butyl-9-methoxy-14,15,17,18-tetramethyl-2,11-dithia[3.3]metaparacyclophane-2,2,11,11-tetraoxide (9b) was pyrolyzed at 510 °C, analogously to the preparation of 5-tert-butyl-8-methoxy-12,13,15,16-tetramethyl[2.2]metaparacyclophane, yielding 459mg (62 %). Recrystallization from chloroform to a white crystal, m. p.: 88°C, \( ^1 \)H-NMR (300MHz, CDCl\(_3\)), \( \delta \)H 1.27 (9H, s, t-Bu), 1.722 (6H, s, CH\(_3\)), 2.270 (6H, s, CH\(_3\)), 2.778-2.943 (8H, m, CH\(_2\)), 3.189 (3H, s, OCH\(_3\)), and 6.670 (2H, s, Ar-H). \( \delta \)C (CDCl\(_3\)) 15.94, 16.16, 25.38, 29.49, 31.79, 34.05, 61.96, 124.36, 130.09, 131.96, 134.30, 134.66, 145.52 and 157.65; m/z 350.54 (M\(^+\)) (Found: C, 85.40; H, 9.73. \( C_{25}H_{34}O \) required C, 85.66; H, 9.78).

Aluminium Chloride Catalysed Isomerization reaction of (9b):

7. Preparation of 5-tert-butyl 8-methoxy-14,16,17,18-tetramethyl[2.2]metacyclophane (10):

To a solution of 60 mg (0.17 mmol) of 9b and 8 mL of benzene was added a solution of 0.023 mL of MeNO\(_2\) and also added 8 mg of AlCl\(_3\) in above solution at 0°C. After the reaction mixture was stirred at 50°C for 1 h, it was poured into ice-water (5mL). The organic layer was extracted with CH\(_2\)Cl\(_2\) (10mL, 2 times). The extract was washed with water (5mL), dried(Na\(_2\)SO\(_4\)), and concentrated. The yield was analysed by GC to give 47% of 10 as yellowish white crystalline solid along with 11 in 38% yield. Isolated yield of 10 was 40 %.; m. pt.: 105-107°C, \( ^1 \)H-NMR (300MHz, CDCl\(_3\)), \( \delta \)H 0.57 (3H, s, CH\(_3\)), 1.29 (9H, s, t-Bu), 2.18 (3H, s, CH\(_3\)), 2.29 (6H, s, CH\(_3\)), 2.39-2.49 (2H, m, CH\(_2\)), 2.58-2.6 (4H, m, CH\(_2\)), 3.18-3.25 (2H, m, CH\(_2\)), 2.86 (3H, s, OMe) and 7.10 (2H, s, Ar-H). \( \delta \)C (CDCl\(_3\)) 15.63, 16.08, 16.39, 31.56, 32.61, 33.29, 34.00, 59.51, 125.50, 130.14, 130.66, 131.89, 133.44, 145.71, 158.56 and 183.18; (Found: C, 83.17; H, 9.39. \( C_{25}H_{34}O \) required C, 85.66; H, 9.78).

8. 5-tert-butyl-8-hydroxy-14,16,17,18-tetramethyl[2.2]metacyclophane (11):

To a solution of 60 mg (0.17 mmol) of 9b and 8 mL of benzene was added a solution of 0.023 mL of MeNO\(_2\) and also added 8 mg of AlCl\(_3\) in above solution at 0°C. After the reaction mixture
was stirred at 50°C for 3 h, it was poured into ice-water (5mL). The organic layer was extracted with CH$_2$Cl$_2$ (10mL, 2 times). The extract was washed with water (5mL), dried (Na$_2$SO$_4$) and concentrated. The yield was analysed by GC to give 88% of 11 as yellowish crystalline solid along with very small amount of 12 in 6% yield. Isolated yield of 11 was 80 %.; m.p. 78°C, $^1$H-NMR (300MHz, CDCl$_3$), $\delta_H$ 0.64 (3H, s, CH$_3$), 1.29 (9H, s, t-Bu), 1.83 (1H, s, 5a-H), 2.21 (3H, s, CH$_3$), 2.36 (6H, s, CH$_3$), 2.50-2.56 (2H, m, CH$_2$), 2.69-2.74 (4H, m, CH$_2$), 3.26-3.30 (2H, m, CH$_2$), and 7.08 (2H, s, Ar-H). $\delta_C$ (CDCl$_3$) 15.71, 16.20, 16.57, 30.12, 31.59, 32.83, 32.89, 33.99, 53.47, 113.02, 124.84, 125.68, 129.12, 131.50, 133.87, 150.94 and 152.12; m/z 336.51 (M$^+$).

9. 2-tert-Butyl-6,7,8-trimethyl-4,5,9,10-tetrahydropyrene(12):

Colourless prisms (hexane); mp: 190-191°C; IR (KBr) 3040, 2960, 2900, 2850, 1600, 1430, 1360, 1280, 1230, 1200, 870, 715, cm$^{-1}$; $^1$H-NMR (300MHz, CDCl$_3$), $\delta_H$ 1.31(9H, s, t-Bu), 2.24 (9H, s, CH$_3$), 2.81 (8H, s, CH$_2$) and 7.02 (2H, s, Ar-H); mass spectrum, m/e 304.47(M$^+$). Anal. Calcd. for C$_{23}$H$_{28}$: C, 90.73; H, 9.27. Found: C, 90.34; H, 9.51.

10. 2-tert-Butyl-6,7,8-trimethylpyrene(13):

Colourless prisms (hexane); $^1$H-NMR (300MHz, CDCl$_3$), $\delta_H$ 1.57 (9H, s, t-Bu), 2.69 (3H, s, CH$_3$), 2.90 (6H, s, CH$_3$) and 7.99 (2H, d, J=9.3 Hz, Ar-H), 8.13 (2H, s, Ar-H) and 8.27 (2H, d, J=9.3 Hz, Ar-H). a

11. 2,6-bis[2-cyano-2-(toluenesulfonyl)ethyl]-4-tert-butylanisole (16) :

Preparation of the TosMIC adducts 16. Typical procedure: To a mixture of 20% aqueous NaOH (40 cm$^3$) and CH$_2$Cl$_2$ (50 cm$^3$) was added n-Bu$_4$NI (700 mg, 1.89 mmol) followed by a solution of TosMIC (8 g, 40.97 mmol) in CH$_2$Cl$_2$ (50 cm$^3$). After the reaction mixture was stirred at room temperature for 30 min, a solution of 2,6-bis(bromomethyl)anisole (4.0 g, 11.4 mmol) in CH$_2$Cl$_2$ (50 cm$^3$) was added dropwise for 1 h. The reaction mixture was stirred at room temperature for 2 h, quenched with water (50 cm$^3$), and was extracted with CH$_2$Cl$_2$ (50cm$^3$x3). It was washed with water (50 cm$^3$), dried with MgSO$_4$, and concentrated in vacuo to leave a residue. To this residue methanol (50 cm3) was added and left overnight in the refrigerator to give 2,6-bis[2-cyano-2-(toluenesulfonyl)ethyl]anisole (16) (4.9 g, 72%).

12. 6-tert-butyl-9-methoxy[3.3]metaparacyclophane-2,11-dione (17):
To a suspension of NaH (850 mg, 35.4 mmol) in DMF (62 mL) a solution of Tosmic adduct 16 (1.6 g, 2.84 mmol) and 1,4-bischloromethyl-2,3,5,6-tetra-methyl-benzene 6 (675 mg, 2.92 mmol) in DMF (14.4 mL) was added dropwise over a period of 6 h. After a suspension was stirred for an additional 5 h at room temperature, it was quenched with ice water (150 mL). The reaction mixture was extracted with CH₂Cl₂ (150 mL×2), washes with water (100 mL), dried with MgSO₄, and concentrated in vacuo to 30 mL. Concentrated HCl (5 mL) was added, and solution was stirred for 30 min. The organic layer was again extracted with CH₂Cl₂ (100 mL×2), wash with water (100 mL), and dried with MgSO₄. The solvent was removed and a small amount of acetone was added to the residue. Colorless prisms that precipitated after several hours were collected (yield 579 mg, 51%). M.p.:169°C. IR (KBr) : 3365, 2960, 2869, 2823, 2364, 1988, 1698, 1575, 1447, 1363, 1278, 1197, 1120, 1083, 1006, 883, 844, 590, 518, 451., ¹H-NMR (300MHz, CDCl₃), δH 1.21 (9H, s, tBu), 1.62 (6H, s, CH₃), 2.43 (6H, s, CH₃), 3.17 (2H, d, J=11.4 Hz, CH₂), 3.32 (3H, s, OCH₃), 3.68 (2H,d, J=15.3 Hz, CH₂), 3.81 (2H, d, J=11.7 Hz, CH₂), 3.98 (2H, d, J=15.6 Hz, CH₂) and 6.89 (2H, s, Ar-H); m/z Found. for C₂₇H₃₄O₃ (M+) 406.3, Calcd: 406.56 (Found: C, 79.75; H,8.39), requires, (C, 79.76; H, 8.43%).

13. 6-tert-butyl-9-methoxy[3.3]metaparacyclophane (18):

A mixture of 17 (40 mg, 0.09 mmol), 80% hydrazine monohydrate (0.02 mL, 0.59 mmol), triethylene glycol (3 mL), and KOH (33.11 mg, 0.59 mmol) was heated at 120 °C for 2 h, and cooled room temperature and stirred 1 h at argon atmosphere. Then the temperature was raised to 200 °C. The water generated during the reaction was removed by a Dean Stark condenser. Additional heating was continued for 3 h and then the mixture was cooled to room temperature and poured into ice water and acidified by adding 10% HCl solution. Then extracted twice with CH₂Cl₂ and the organic phase was washed with water and brine, and then dried with MgSO₄. The solvent was removed and the residue was purified from PTLC (Hexane-dichloromethane, 1:1 v/v as eluent). Colorless needles (18 mg, 55%), m.p.: 120°C. ¹H-NMR (300MHz, CDCl₃), δH 1.27 (9H, s, t-Bu), 1.72 (6H, s, CH₃), 2.31 (6H, s, CH₃), 2.16 (4H, m, CH₂), 2.34 (2H, m, CH₂), 2.48 (2H, m, CH₂), 2.73 (2H,m, CH₂), 3.05 (2H, m, CH₂), 3.25 (3H, s, OCH₃), and 6.67 (2H, s, Ar-H); δC (CDCl₃) 27.03, 31.68, 31.80, 34.07, 47.56, 62.73, 65.84, 97.15, 122.88, 130.71, 134.05, 134.31, 152.67 and 170.72. m/z for C₂₇H₃₈O (M+) 378.26 Calcd. 378.59.

Aluminium Chloride Catalysed Trans-tert-butylation reaction:

To a solution of 30 mg (0.08 mmol) of 18 and 4 mL of benzene was added a solution of 0.019 mL of MeNO2 and also added 6 mg of AlCl3 in above solution at 0°C. After the reaction mixture was stirred at 50°C for 2 h, it was poured into ice-water (5mL). The organic layer was extracted with CH2Cl2 (10mL, 2 times). The extract was washed with water (5mL), dried (Na2SO4), and concentrated. The residue was column chromatographed over silica gel with hexane as eluent to give 75% of 19 as white solid crystal. Isolated yield was 67%. m.p.: 89°C. 1H-NMR (300MHz, CDCl3), δH 1.69 (6H, s, CH3), 2.31 (6H, s, CH3), 2.18 (4H, m, CH2), 2.33 (2H, m, CH2), 2.51 (2H, m, CH2), 2.73 (2H, m, CH2), 3.07 (2H, m, CH2), 3.29 (3H, s, OCH3) and 6.71 (3H, m, Ar-H); δC (CDCl3) 16.04, 18.39, 24.97, 27.81, 31.74, 100.57, 122.06, 123.82, 125.89, 132.94, 134.37 and 135.01, m/z for C23H30O (M+) 322.48 Calcd. 322.25.

15. 9-hydroxy[3.3]metaparacyclophane (20):

To a solution of 30 mg (0.08 mmol) of 18 and 4 mL of benzene was added a solution of 0.019 mL of MeNO2 and also added 6 mg of AlCl3 in above solution at 0°C. After the reaction mixture was stirred at 50°C for 2 h, it was poured into ice-water (5mL). The organic layer was extracted with CH2Cl2 (10mL, 2 times). The extract was washed with water (5mL), dried (Na2SO4), and concentrated. The residue was column chromatographed over silica gel with hexane as eluent to give mixture of 20 with starting compound. 1H-NMR also found in mixture form.

4.5 References:

110, 7842.
33. L. Ernst., *Progress in Nuclear Magnetic Resonance Spectroscopy*, 2000, 37, 47.
Chapter 5

Synthesis, structure and spectral properties of substituted (1,3)pyreno[3.3]metacyclophane and substituted [2,11]dithia-[3](1,3)pyrenophanes. A New look using VT NMR and calculations.

The coupling reaction of the corresponding TosMIC-adducts 1a-b and 1,3-bisbromomethyl-7-tert-butylpyrene in the presence of NaOH and n-Bu₄NI in a mixture of CH₂Cl₂ and water under phase-transfer conditions afforded intermediate product, which were followed by acid treatment to afford the 6,17-ditertbutyl-9-substituted(1,3)pyreno[3.3]MCP-2,11-diones (3a-b). The Wolff-Kishner reduction of 6,17-ditertbutyl-9-substituted(1,3)pyreno[3.3]MCP-2,11-diones (3a-b) afforded the 6,17-ditertbutyl-9-substituted (1,3)pyreno[3.3]MCP(4a-b) in remarkable yield. By study the spectroscopic data, 3a exhibits the anti-conformation and 3b adopts syn-conformation. Similarly, the compound 4a and 4b show the syn-conformation. Variable-temperature NMR studies were carried out to determine the conformational behavior of Pyrenophane 3a-b and 4a-b. The preparation of poly-methyl substituted pyrenophane 14 and 15a-b via high-dilution method and its spectroscopic data were studied.
5. Synthesis, structure and spectral properties of substituted (1,3)pyreno[3.3]metacyclophane and substituted [2,11]dithia-[3](1,3)pyrenophanes. A New look using VT NMR and calculations.

5.1 (1,3)Pyreno[3.3]metacyclophane:

5.1.a Introduction

Supramolecular\(^1\) chemistry is based on the association of two or more building molecules through intermolecular interactions, in contrast to molecular chemistry, which is based on the covalent bonding of atoms. Cyclophanes, which are bridged aromatic molecules, have been expanding their interest in the field of supramolecular chemistry. Among them large-sized cyclophanes capable of forming the inner cavity have been playing a crucial role as synthetic receptors in molecular recognition which is one of the central topics of supramolecular chemistry.

On the contrary, small-sized cyclophanes characterized by the aromatic components which are fixed in close proximity to each other have not appeared so often in this field, however, they could be a good model for the study of weak interactions such as \(\pi-\pi\), CH–\(\pi\), or NH–\(\pi\) interactions based on \(\pi\)-electron system\(^2\)-\(^4\). Especially, cyclophanes composed of the pyrene unit are interesting because they have an extended \(\pi\)-electron system.

Although many cyclophanes having a pyrene skeleton and related compounds have been prepared\(^5\), there have been few investigations of their chemical nature in spite of a large number of reports on their spectroscopic properties. Umemoto et al.\(^5a\) first reported the synthesis of [2.2](1,3)pyrenophane and triple layered metacyclopyrenophanes in 1975; these are important as model compounds of transannular \(\pi\)-electronic interaction of excimer fluorescence\(^5b,5f\). Later on, Mitchell et al.\(^5g\) synthesized the internally substituted dithiametacyclophanes as precursors for the preparation of highly annulated trans-10b,10c-dimethyl-10b,10c-dihydropyrenes. Recently, Vogtle et al.\(^6\) also synthesized [2.2]cyclophane containing the pyrene unit in order to investigate their chiroptical properties.

In all the three above reports\(^5a,5g,6\), in order to construct the pyrene skeleton, the transannular reaction of 4,6-bis(bromomethyl)[2.2]metacyclophane with bromine is an important key step. The preparation of 1,3-disubstituted pyrene using regioselective electrophilic disubstitution seems to be quite difficult in spite of the fact that electrophilic substitution of pyrene itself occurs at the 1-, 3-, 6- and 8-position\(^7\)-\(^9\). For example, Harvey et. al.\(^10\) reported that acetylation of pyrene afforded 1,8-diacetylpynrene as a measure products along with 1,6 and 1,3-analogue. Therefore, the selective preparation of 1,3-disubstituted pyrene by direct electrophilic aromatic substitution was
very difficult because of their low yield as well as the difficult of their separation from the reaction mixture.

Such investigation has been limited, because the preparation pyrene having the substitutents at 1- and 3- positions is not easy. We were reported the AlCl$_3$-catalysed acetylation, of 2,7-di-tert-butylpyrene with acetyl chloride using the tert-butyl group as a positional protective group to afford only the 4,9 di-acetylated product, 4,9-diacetyl-2,7-di-tert-butylpyrene$^{11}$ and this strategy is also suitable for the preparation of 1,3-bridged benzenopyrenophane, 8-substituted [2]metacyclo[2](1,3)pyrenophanes.$^{12}$ Mitchell and his coworker have reported that 9,18-dimethyl-2,11-dithia[3,3]MCP (MCP= metacyclophane) exists in syn and anti-conformers, which don’t interconvert below 200°C.$^{13-17}$ Vogtle and Schunder$^{18}$ have made extensive studies of syn-anti- conversions in other dithia[3,3]MCPs, specially in the relation to the size of the substituent’s. Although the study on the syn and anti conformers of dithia[3,3]MCPs having an expanded π-congugated aromatic ring in spite of the much larger ring current interactions of π-conjugated system. Freezing conformational equilibrium, which is the common method of analysis, is often not effective in highly flexible molecules. Fukaawa et al.$^{18}$ developed a useful and very reliable method for the conformational analysis of flexible molecules using a combination of molecular mechanics calculations and chemical shift simulation of certain protons without the use of the freezing technique.

On the other hand, [3,3]MPCP (MPCP = metaparacyclophe) was first prepared by Shinmyozu and co-workers$^{19}$ using (p-tolylsulfonyl)methyl isocyanide (TosMIC) as the cyclisation reagent, followed by Wolff–Kishner reduction. The meta-bridged benzene ring of [3,3]MPCP has been shown to undergo conformational flipping$^{19,20}$ with a significantly lower energy barrier than that in [2.2]MPCP (ca 80 kJ mol$^{-1}$).$^{21}$ We reported the synthesis of 9-substituted [3,3]MPCP-2,11-diones and conversion to the corresponding [3,3]MPCPs by Wolff–Kishner reduction.$^{22}$ The different orientation for the acetylation was observed depending on the substituent at C (9) position.

We also reported the preparation of 2,11-dithia(1,4)naphthaleno[3,3]MCPs and an internal substituent such as Me or OMe group is sufficient to allow the isolation of a discrete syn- or anti-isomer.$^{23}$ Thus, there is substantial interest that employing a pyrene ring instead of a benzene ring of the para-bridged ring will provide good information about the π − π interaction between the two stacking aromatic rings. Furthermore, the conformations of 9-substituted[3,3]MCPs having a pyrene skeleton are so far not known in spite of the formation of two conformers, i.e. syn- and anti-conformers, being possible like 6,17-diterbityl-9-substituted(1,3)pyreno[3,3]metacyclo -
phane-2,11-diones and syn-conformers of 6,17-diterbutyl-9-substituted(1,3)pyreno[3.3] - metacyclopahne. We describe here the synthesis of pyrenophanes such as the titled MCPs using the above method, as well as studies of their conformation by the ring current interactions derived from pyrene ring.

5.1.b Result and discussion:

Vögtle reported the preparation of [3n]MCP-triones using (p-tolylsulfonfyl) methyl isocyanide (TosMIC) as the cyclisation reagent, which was applied in a new cyclisation procedure without phase-transfer conditions. This strategy can be employed for the preparation of 6,17-di-terbutyl-9-substituted(1,3)pyreno[3.3]MCP-2,11-diones containing two aryl rings. In fact, we have selected the stepwise cyclisation of TosMIC-adduct with 1,3-bis(bromomethyl)-7-tert-butylpyrene (2) to prepare the desired cyclic diketones as shown in Scheme 5.3. The starting compound, 2,6-bis(bromomethyl)-4-tert-butylanisoles (6a–b), was easily prepared from 4-tert-butylanisole by using the tert-butyl group as a positional protodcting group on the aromatic ring, followed by the cyclization of 6 and TosMIC carried out in dichloromethane and n-Bu₄NI with of 20% sodium hydroxide to obtained the TosMIC adduct (1a–b) as shown in Scheme 5.1. 1,3-bisbromomethyl-7-tert-butylpyrene 2 was prepared from pyrene using tert-butyl group as a positional protecting group on the aromatic ring as shown in scheme 5.2. The tert-butylpyrane was brominated with BTMABr in presence of dry dichloromethane, methanol and CaCO₃ to obtained 1,3-dibromo-7-tert-butylpyrene (10) in remarkable yield. Similarly, Formylation of compound 10 in presence of t-BuLi, freshly prepared THF, DMF, at -78°C to obtained the 7-tert-butyl-1,3-diformylpyrene (11). Further treatment of compound 11 with NaBH₄ in THF to
obtained the remarkable yield of 1,3-hydroxymethyl-7-tert-butylpyrene (12). Finally, Compound 12 was treated with PBr₃, dry ether, refluxed at 40°C to obtained the 1,3-bisbromomethyl-7-tert-butylpyrene in 90% yield (Scheme 5.2).

For the synthesis of 6,17-diterbutyl-9-substituted(1,3)pyreno[3.3]MCP-2,11-diones (3a-b), the (p-tolylsulfonyl) methyl isocyanide (TosMIC) method has been successfully employed in the critical coupling reactions. The key synthetic intermediates are the TosMIC-adducts 1a-b as well as 1,3-bisbromomethyl-7-tert-butylpyrene as given above. The 3a-b were synthesized by the coupling reaction between TosMIC-adducts 1a-b and the 1,3-bisbromomethyl-7-tert-butylpyrene in the presence of NaOH and n-Bu₄NI in a mixture of CH₂Cl₂ and water under phase-transfer conditions, followed by acid treatment to afford the 6,17-diterbutyl-9-substituted(1,3)pyreno[3.3]MCP-2,11-diones (3a-b) (Scheme 5.3).

The Wolff-Kishner reduction of 6,17-diterbutyl-9-substituted(1,3)pyreno[3.3]MCP-2,11-diones (3a-b) afforded the 6,17-diterbutyl-9-substituted(1,3)pyreno[3.3]MCP (4a-b) in remarkable yield (Scheme 5.3).

The structures of 3a-b have been elucidated by elemental analyses and spectral data. The IR spectrum of anti-3a and syn-3b show the absorption of the carbonyl stretching vibration around
1700 cm\(^{-1}\) for \(3a\) and the methoxy stretching vibration around 1695 cm\(^{-1}\) for \(3b\). The \(^1\)H NMR spectrum (in CDCl\(_3\)) of anti-\(3a\) exhibits two singlet peak at \(\delta\) H 3.37 ppm and 4.19 ppm for the ArCH\(_2\)COCH\(_2\)Ar methylene protons and two singlet for the aromatic-protons of H9 and H22 at strong upfield shift 4.97 and 6.38 ppm due to the ring current effect of the opposing aromatic ring.\(^{29}\) These observations strongly suggest that compound \(3a\) adopts the anti-conformation.

![Scheme 5.3](image)

In contrast, the methoxy protons of syn-\(3b\) are observed at \(\delta\) H 2.99 ppm. Further, the benzene protons (H5, H7) can clearly be seen to be shielded at \(\delta\) H 7.09 ppm by the adjacent pyrene ring, a common consequence of face-to-face aryl rings.\(^{29}\) Also the tert-butyl proton was observed at higher field, 1.16 ppm compared to that of the anti-\(3a\) at 1.36 ppm due to the strong shielding effect of the pyrene ring. These observations strongly suggest that compound \(3b\) adopts syn-conformation. These findings suggest that the through-space interaction between the non-bonding electron pairs of the oxygen atom of the methoxy group and the opposite pyrene \(\pi\)-electrons of the anti-conformer may disfavour the formation of the latter.
Similarly, the structures of 4a-b have been elucidated by elemental analyses and spectral data. For instance, the mass spectral data for syn-4a and syn-4b (for 4a, M+ = 472.26 and for 4b, M+ = 502.32) strongly supports cyclic dimeric structure. The IR spectrum of syn-4b shows the absorption of the methoxy stretching vibration around 1730 cm\(^{-1}\) for 4b. The \(^1\)H NMR spectrum (in CDCl\(_3\)) of reduction product syn-4a exhibits the benzene protons (H5, H7) can clearly be seen to be shielded at δ 6.23 ppm by the adjacent pyrene ring, a common consequence of face-to-face aryl rings.\(^{29}\) Also the tert-butyl proton was observed at higher field, δ 0.18 ppm due to the strong shielding effect of the pyrene ring. But, two singlet for the aromatic-protons of H9 and H22 at downfield shift δ 6.82 and 7.43 ppm due to no effect of ring current of the opposing aromatic ring,\(^{29}\) these findings suggest that compound 4a shows the syn-conformation.

Furthermore, the methoxy protons of syn-4b are observed at δ 3.67 ppm and the benzene protons (H5, H7) can clearly be seen to be shielded at 6.12 ppm by the adjacent pyrene ring, a common consequence of face-to-face aryl rings.\(^{29}\) Also the tert-butyl proton was observed at higher field, 0.01 ppm due to the strong shielding effect of the pyrene ring. These observations strongly suggest that compound 4b adopts syn-conformation. These findings also suggest that the through-space interaction between the non-bonding electron pairs of the oxygen atom of the methoxy group and the opposite pyrene π-electrons of the anti-conformer may disfavor the formation of the latter.

5.1. c. VT-NMR Spectral Properties:

To prevent the exchange of different peaks like axial and equatorial protons, the sample have to cool a sufficiently low temperature. At -90 °C, the axial and equatorial protons of cyclohexane no longer interchange and are resolved as two separate resonances. But as raise the temperature, the two peaks move together and broaden, indicating that there is some exchange (often called "slow exchange"). When the two peaks merge such that there is no distinguishable valley between them, i.e. the peaks have coalesced.\(^{30}\) As raise the temperature still more, the merged broad peak sharpens again. At this point, the lifetime of a species as axial or equatorial is much shorter than the timescale of the experiment (flipping the nuclear spin and observing the relaxation). Such a system is called "fast on the NMR timescale" or "high temperature limit".
Variable-temperature NMR studies were then undertaken to determine the conformational behavior of Pyrenophane 3a-b & 4a-b and to experimentally elucidate how the replacement of the hydrogen atoms in 9 position of benzene rings of pyrenophane 3a and 4a with the methoxy group of pyrenophane 3b and 4b. Consistent with the hypothesis of a conformationally unhindered ring-flipping process, the $^1$H NMR spectra of compound 3a-4b, recorded from room temperature (RT) to 140°C. Compound 3a showed two broad singlets for the methylene protons of the CH$_2$COCH$_2$ bridges at room temperature, the conformationally stable compound. The sharp singlets of the pyrene proton($\delta$ 8.00 ppm) and methylene proton($\delta$ 3.30 and 4.10 ppm) signals at 80°C suggest a rapid conformational isomerism on the NMR time scale, that is wobbling of the bridge and ring inversion of the pyrenophane ring. Conformation of compound 3a is anti-conformation at room temperature and 9-H is little bit tilted towards the pyrene core as an edge to face interactions. In contrast, conformation is slowly changed into parallel stalked arrangement with ring slide due to downfield shift of 9-H (4.85 to 4.98 ppm) as well as 5H and 7H (6.23 to 6.30 ppm) singlet proton signal by rising temperature up 80 to 140°C.$^{31-34}$
Interestingly, the broadening of the sharp pyrene doublet signals as the temperature was increased from 70 to 80°C is shown in Figure 5.1. The dramatically simplified and broad spectrum at 80°C indicated that this temperature is approaching the coalescence temperature (Tc) of conformational mobility. The very low value of Tc of both isomers of 3a (Tc < 90 °C) implied by this data makes any attempt at conformational freezing and its observation very difficult and highlights the rapidity of the rotation processes of 3a at ambient temperature as well as its limitless flexibility, which is in accordance with Vogtle's hypothesis.\(^{35}\) The simulation of the spectra at various temperatures showed that the line shape analysis could be performed by using a single set of rate constants.\(^{36}\) The energy barrier (\(\Delta G^\#\)) for the benzene ring-rotation from methylene bridge was estimated to be 18.9 kcal/mol (Tc = 80 °C), based on the AB system.\(^{37}\)

![Fig. 5.2. VT NMR spectroscopy of compound 4a.](image)

Similarly, Variable-temperature NMR studies were carried out to determine the conformational behavior of Pyrenophane 4a and to experimentally elucidate how the reduction of carbonyl carbon of pyrenophane 3a to obtained three-member pyrenophane compound. Compound 4a...
showed three broad singlets for the methylene protons of the \( \text{CH}_2\text{CH}_2\text{CH}_2 \) bridges at room temperature, the \textit{syn}-conformationally stable compound. The sharp singlets of the pyrene proton(\( \delta \) 7.85 ppm) and methylene proton(2.35, 2.75 and 3.35 ppm) signals at 90°C suggest a rapid conformational isomerism on the NMR time scale, that is wobbling of the bridge and ring inversion of the pyrenophane ring. Interestingly, benzene moiety closely proximity with pyrene cored at room temperature be confirmed by shielded proton signals at 6.23 and 6.83 ppm. In contrast, conformation is slowly changed in to parallel stalked arrangement within \textit{syn}-conformation due to repulse by pyrene core to out push the benzene ring, downfield shift of 9-H (6.69 to 7.00 ppm) as well as 5H and 7H(6.50 to 6.15 ppm) singlet proton signal by rising temperature up 30 to 60°C is shown in Figure 5.2. The simulation of the spectra at various temperatures showed that the line shape analysis could be performed by using a single set of rate constants.\(^{36} \) The energy barrier (\( \Delta G^\circ \)) for the benzene ring-pushing from pyrene core was estimated to be 20.2 kcal/mol (\( T_c = 100 \degree C \)), based on the AB system.\(^{37} \)

![Diagram](image)

**Fig. 5.3** VT NMR spectroscopy of compound 3b.

Similarly, Variable-temperature NMR studies were carried out to determine the conformational behavior of Pyrenophane 3b, which showed four pair doublets for the methylene protons of the
CH$_2$COCH$_2$ bridges at room temperature, the syn-conformationally stable compound. The mixing of doublet signals to get singlets of the pyrene proton(δ 7.92 ppm) and methylene proton(3.20 to 4.20 ppm) signals at 140°C suggest a rapid conformational isomerism on the NMR time scale, that is wobbling of the bridge and ring inversion of the pyrenophane ring. Conformation of compound 3b is syn-conformation at room temperature and 9-OMe (up field shifted at 2.92 ppm) is little bit tilted towards the pyrene core as an edge to face interactions. In contrast, conformation is slowly changed in to parallel stalked arrangement to tert-butyl-benzene is tilted towards the pyrene core with benzene ring deviation due to downfield shift of 9-OMe (2.92 to 3.00 ppm) and up field shift of 5H and 7H (6.92 to 6.85 ppm) as well as 6-tBu (1.00 to 0.90ppm) by rising temperature up 30 to 140°C (Figure 5.3). The simulation of the spectra at various temperatures showed that the line shape analysis could be performed by using a single set of rate constants.\(^{36}\)

The energy barrier ($\Delta G^\circ$) for the benzene ring-rotation from methylene bridge was estimated to be 19.54 kcal/mol ($T_c = 80 \ ^\circ C$), based on the AB system.\(^{37}\) The highly unstable transition state conformation was obtained at 140°C in which methylene bridge ring rotation energy barrier ($\Delta G^\circ$) was estimated to be 23.42 kcal/mol.

![Benzene ring slide](image)

**Fig.5.4.** Due to sliding of the benzene ring, all protons signal are downfield Shifted of compound 4b.
Similarly, Variable-temperature NMR studies were carried out to determine the conformational behavior of Pyrenophane 4b and to experimentally elucidate how the reduction of carbonyl carbon of pyrenophane 3b to obtained three-member pyrenophane compound. Compound 4b showed three broad multiplets signals for the methylene protons of the CH₂CH₂CH₂ bridges at room temperature, the syn-conformationally stable compound. The sharp multiplets of the pyrene proton (δ 7.60-7.99 ppm) and methylene proton (2.23-3.15 ppm) signals at 90°C suggest a rapid conformational isomerism on the NMR time scale, that is wobbling of the bridge and ring inversion of the pyrenophane ring. Interestingly, benzene moiety is diagonally proximity with pyrene core at room temperature be confirmed by shielded proton signals at 6.98 and 0 ppm for 5 and 7H of benzene and 7-trty-butyl group. In contrast, conformation is slowly changed in to parallel stalked arrangement within syn-conformation due to benzene ring slide over the pyrene core, up field shift of 9-OMe (6.70 to 6.65 ppm) as well as 5H and 7H (6.09 to 6.02 ppm) including 7-tert-butyl (0 to -0.10 ppm) singlet protons signal by rising temperature up 30 to 140°C (Figure 5.4). The simulation of the spectra at various temperatures showed that the line shape analysis could be performed by using a single set of rate constants. The energy barrier (ΔG°) for the benzene ring-sliding over pyrene core was estimated to be 20.67 kcal/mol (Tc = 140 °C), based on the AB system.37
### Table 5.1: Determination of thermodynamic parameters from VTNMR

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<th>Simulation 1/2 ΔH K.cal mol⁻¹</th>
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5.1. d. Photophysical properties:

The UV-Vis absorption and fluorescence spectroscopic data of novel [3.3]pyrenophane derived from [3.3]pyrenophaneidione in dilute dichloromethane solution at room temperature were measured and presented in Table 5.2 together with 7-tert-butyl-1,3-dimethylpyrene (5). The comparative UV-Vis absorption spectra of 3a-b (before reduction) and 4a-b (after reduction) are shown in Figure 5.5. For 7-tert-butyl-1,3-dimethylpyrene (5), the absorption spectra are almost identical compared with that of the parent pyrene with three well-resolved, sharp absorption bands observed in the region 300-350 nm. The slight bathochromic shift is ascribed to the increased electron density to the pyrene ring, arising from the electron-donating nature of tert-
butyl groups and methyl groups at the 7 and 1,3-positions respectively. The UV-Vis absorption spectra of compounds 3a-b (before reduction) and 4a-b (after reduction) with 5, all spectra are sharpened and the longest wave length hyperchromic absorption maximum of 3 and 4 occurs at 362 and 363 nm respectively (Table: 5.2), which are bathochromically red-shifted by 10-11 nm arising from 7-tert-butyl-1,3-dimethylpyrene (5).

![](image.png)

**Fig.5.5** Normalized UV-Vis absorption spectra of 3 and 4 recorded at ~ 10^{-7} M concentration at 25°C, with respect to 1,3-dimethyl-7-tert-butylpyrene (5)

Interestingly, anti-3a display little bit bathochromic shift by10 nm in the absorption bands, which could be attributed due to π-π interaction between two opposite benzene and pyrene rings. But, in syn-3b, 4a and 4b display more bathochromic shift by 11 nm in the absorption bands, which could be attributed due to strong π-π interaction between two face to face benzene and pyrene rings.

The fluorescence emission spectrum of 3a in dilute CH_{2}Cl_{2} solution at room temperature on excitation at 262 nm exhibited emission maxima at 395 and 408 nm in the visible blue region (Table 5.2 and Figure 5.6). Pyrenophane dione 3a has a big broad absorption band, which is centered at 401 nm. Similarly, fluorescence emission spectrum of 3b in dilute CH_{2}Cl_{2} solution at room temperature on excitation at 262 nm exhibited emission maxima at 397 and 410 nm in the visible blue region (Table 5.2 and Figure 5.6). It also has a big broad emission band, which is centered at 404 nm. Both compounds 3a and 3b have similar type of fluorescence broad emission band divided in to two equal halves. Among both, 3b is little bit bathocromic shifted due to syn-conformation(strong π-π interaction between two face to face benzene and pyrene rings) and present of electron donating methoxy group within molecule.
The reduction product of [3.3]pyrenophane (4a and 4b) obtained from [3.3]pyrenophanedione 3a and 3b are also similar type of broad fluorescence emission band are observed at 410 and 397 nm. Both florescence spectra of 4a and 4b are little bit blue shifted (6 nm) with compare to reference pyrene derivative due to syn-conformation (strong π-π interaction between two face to face benzene and pyrene rings). Among them, 4b is little bit bathocromic shifted due to present of electron donating methoxy group within molecule. Reference compound, 1,3-dimethyl-7-tert-butylpyrene (5) is sharper peak at (405 nm) with compare to other pyrenophane compounds.

**Table 5.2:** Optical absorption and emission spectroscopic data for 3a-b & 4a-b in CH$_2$Cl$_2$ (10$^{-6}$ to 10$^{-7}$M) at room temperature, compared with that of 5.

<table>
<thead>
<tr>
<th>Compd</th>
<th>Absorption$^{[b]}$ $\lambda_{abs}$ [nm]</th>
<th>Fluorescence$^{[c]}$ $\lambda_{abs}$ <a href="$%5Clambda_%7Bex%7D$">nm</a>$^{[d]}$</th>
<th>Stokes-shifts [nm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>361</td>
<td>395 (262)</td>
<td>34</td>
</tr>
<tr>
<td>3b</td>
<td>363</td>
<td>397 (262)</td>
<td>34</td>
</tr>
<tr>
<td>4a</td>
<td>363</td>
<td>410 (260)</td>
<td>47</td>
</tr>
<tr>
<td>4b</td>
<td>364</td>
<td>410 (260)</td>
<td>46</td>
</tr>
<tr>
<td>5</td>
<td>353</td>
<td>404 (252)</td>
<td>51</td>
</tr>
</tbody>
</table>

[a] all measurements were performed under degassed conditions.[b] ~ 10$^{-6}$ M in CH$_2$Cl$_2$, $\lambda_{abs}$ is absorption band appearing at the longest wavelength. [c] ~ 10$^{-6}$ M in CH$_2$Cl$_2$, $\lambda_{ex}$ fluorescence band appearing at the shortest wavelength. [d] wavelength of excitation.
5.2. 2,11-dithia[3]metacyclo[3](1,3)pyrenophanes

5.2. a. Introduction

Similarly, the preparation of 2,6-bis(chloromethyl)-1,3,4,5-tetramethylbenzene (19) has already been described previously.\(^{38,39}\) 2,6-Bis(sulfanylmethyl)-1,3,4,5-tetramethyl benzene (13) was prepared from 19 according to the reported procedure (Scheme 5.4).\(^{40}\) The compound 7a-c were also prepared form compound 6b-d according to the reported procedure (Scheme 5.1).\(^{40}\)

![Scheme 5.4](image)

5.2. b. Result and Discussion:

The cyclizations of 2,6-bis(sulfanylmethyl)-1,3,4,5-tetramethylbenzene (13) with 1,3-bis(bromomethyl) -7-tertbutylpyrene (2) was carried out at high dilution in 10% ethanolic KOH and in the presence of a small amount of NaBH\(_4\), giving anti-14 was obtained. By careful column chromatography (silica gel, Wako C-300), anti-14 easily purified to get 55% yields. Similarly, Cyclizations of 7a-c with 1,3-bis(bromomethyl)-7-tertbutylpyrene (2) was carried as same as above procedure, giving syn-15a-c. By careful column chromatography (silica gel, Wako C-300), syn-15a-c easily purified as a remarkable yields (Scheme 5.5).
H NMR Spectral Properties:

The structures of \textit{anti-14} and \textit{syn-15a-b} have been elucidated by elemental analyses and spectral data. The IR spectrum of \textit{syn-15a-b} shows methoxy stretching vibration around 1700 cm\(^{-1}\). The assignment of structure to \textit{anti-conformer 14} was readily apparent form its \(^1\)H NMR spectra (in CDCl\(_3\)). Thus, \textit{anti-14} exhibits two singlet peak at \(\delta\) 1.36 and 5.61 ppm for methyl protons and pyrene H22-proton, strong up-field shift due to the ring current effect of the opposing aromatic ring. These observations strongly suggest that compound \textit{anti-14} adopts the \textit{anti-}conformation.

In the case of \textit{syn-15a}, the methyl protons at 6-position appeared up-field shifts at \(\delta\) 0.97 ppm due to ring current effect of the opposite pyrene ring. The \(^1\)H NMR spectrum of CH\(_2\)SCH\(_2\) bridge of \textit{15a} showed a pair of doublets at \(\delta\) 3.52, 4.42 ppm (\(J=14.1\) Hz) and 4.29, 4.57 ppm (\(J=15.0\) Hz) at room temperature with increasing temperature in DMSO-d\(_6\), the doublets do not coalesce below 150\(^\circ\)C, respectively, and the energy barriers of flipping are both above 25 Kcal mol\(^{-1}\). These observations strongly suggest that the compound \textit{15a} also adopts rigid \textit{syn-}conformation.
However, the internal pyrene proton (H$_{22}$) and methyl protons at 9-position appeared at $\delta$H 5.61 ppm and 1.36 ppm different from those observed in 2,11-dithia[3]metacyclo[3](1,3)pyrenophanes 14. These finding might attributable to the different conformations between 14 and 15a. Similarly, the same up-field shift of the 5,7-aryl hydrogen’s was observed in syn-15b. Also, one of the tert-butyl protons of syn-15b was observed upfield, 0.10 ppm due to the strong shielding effect of the pyrene ring. These observations strongly suggest that compound 15b also adopt the syn-conformation.

5.3 Conclusion

The preparation of substituted (1,3)Pyreno[3,3]metacyclophane and various substituted 2,11-dithia[3]metacyclo[3](1,3)pyrenophanes are presente d. Compounds are shown the anti- and syn-conformation depends upon the different substitution present in benzene ring. VT-NMR studies of compounds 3 and 4 showed that the compound behave as different conformation depends upon the temperature change. Similarly photo-physical properties of compounds were carefully examined. The preparation of methyl substituted pyrenophane 14 and 15a-b via thiacyclophane and its spectroscopic data were studied.

5.4 Experimental part:

All melting points are uncorrected. $^1$H MMR spectra were recorded at 300MHz on a Nippon Denshi JEOL FT-300 NMR spectrometer in deuteriochloroform with Me$_4$Si as an internal reference. UV-Vis spectra were recorded on a Perkin Elmer Lambda 19 UV/VIS/NIR spectrometer. Mass spectra were obtained on a Nippon Denshi JMS-HX110A Ultrahigh performance Mass Spectrometer at a 75 eV using a direct-inlet system. Elemental analyses were performed by Yanaco MT-5.

1. 2-tertbutylpyrene(9):

Anhydrous AlCl$_3$ (7.24 g, 54.4mmol) was added in one portion to a stirred solution of pyrene (10 g, 49.44 mmol) and 2-chloro-2-methylpropane (5.77 mL, 52.35 mmol) in CH$_2$Cl$_2$ (100 mL) at 0°C. The resulting mixture was stirred for 3 h at room temperature and poured into a large excess of ice/water. The organic layer was extracted with CH$_2$Cl$_2$, dried over MgSO$_4$, filtered and evaporated to dryness. Column chromatography (SiO$_2$, hexane) gave 2-tertbutylpyrene (10.146g) in 79.45% yield as yellowish silver plates (m.p.: 110-112 °C). The $^1$H NMR spectrum completely agreed with the reported values.

2. 1,3-dibromo-7-tert-butylypyrene(10):
A solution of BTMABr$_3$ (4.0 g, 10.386 mmol) in dichloromethane (40 mL) was drop wise added in one portion of stirred solution of 2-tert-butylpyrene (1g, 3.87 mmol) in 30 mL of dichloromethane, 25 mL of MeOH and 500 mg CaCO$_3$ at 0°C. The resulting mixture was stirred for 24 h at 30°C. BTMABr$_3$ was neutralized with an aqueous 0.3 M Na$_2$S$_2$O$_3$ solution and extracted by CH$_2$Cl$_2$, washed by water and brine, dried over MgSO$_4$, filtered and evaporated to dryness. Recrystallization from pure cold hexane afforded 1,3-dibromo-7-tert-butylpyrene (932.5 mg) in 58.0% yield as white silver flakes. The $^1$H NMR spectrum completely agreed with the reported values.

3. 2-tert-butyl-6,8-diformylpyrene (11).

Bromopyrene derivative 10 (500 mg, 1.02 mmol) was placed in a 50 mL two-necked round-bottomed flask and mixed with dry THF (11 mL), then cooled to -78°C. After being added t-BuLi (1.6 M in pentane, 9.3 mL, 14.8 mmol) to this mixture, the reaction mixture was stirred at -78°C for 3 h. DMF (1.8 mL, 23.32 mmol) was added to this reaction mixture at one portion at -78°C. The reaction mixture was stirred at -78°C for overnight and then poured into a satd. aqueous NH$_4$Cl solution. The resulting solid was obtained by the filtration, and the organic filtrates were separated. The aqueous layer was extracted with ethyl-acetate, and then the combined organic extracts were washed with a saturated aqueous NaHCO$_3$ solution and a saturated aqueous NaCl solution, successively. The organic extracts were dried over Na$_2$SO$_4$, then filtered and concentrated under reduced pressure. The resulting solid was combined with the solid materials obtained by the filtration, and then recrystallized from benzene, to give diformylpyrene derivative 2 (307 mg, 81%) as a vivid yellow orange needles: m.p.: 267°C (dec.); $^1$H NMR (300MHz, CDCl$_3$) $\delta_h$ 1.63 (9H, s, t-But), 8.48 (2H, d, J=8.8 Hz, Ar-H), 8.49 (2H, s, Ar-H), 8.86 (1H, s, Ar-H), 9.52 (2H, d, J=8.9 Hz, Ar-H) and 10.80 (2H, s, CHO).

4. 2-tert-butyl-6,8-bis-hydroxymethylpyrene(12).

To a stirred solution of 2-tert-butyl-6,8-diformylpyrene(200 mg, 0.64 mmol) in THF (10 mL) was slowly added NaBH$_4$ (193 mg, 5.12 mmol) at 0°C, and the mixture was stirred for 3 h at room temperature. Then 5% HCl was added drop wise continuously to effervesce H$_2$ gas. The reaction mixture was poured into a large amount of ice-water and the resulting solid was obtained by the filtration, and the organic filtrates were separated. The aqueous layer was extracted with ethyl-acetate and then the combined organic extracts were washed with a satd. aqueous NaCl solution, successively. The organic extracts were dried over Na$_2$SO$_4$, then filtered and concentrated under reduced pressure. The resulting solid was combined with the solid materials obtained by the
filtration, and then recrystallized from THF to give 2-tert-butyl-6,8-bis-hydroxymethylpyrene (12) (164 mg, 80%) as a yellowish white solid:

5. 2,6-bis[2-cyano-2-(toluenesulfonyl)ethyl]-4-tert-butylanisole (1b):

Preparation of the TosMIC adducts 3:

To a mixture of 20% aqueous NaOH (40 cm³) and CH₂Cl₂ (50 cm³) was added n-Bu₄NI (700 mg, 1.9 mmol) followed by a solution of TosMIC (8 g, 41 mmol) in CH₂Cl₂ (50 cm³). After the reaction mixture was stirred at room temperature for 30 min, a solution of 2,6-bis(bromomethyl)anisole (2) (4.0 g, 11.4 mmol) in CH₂Cl₂ (50 cm³) was added dropwise for 1h. The reaction mixture was stirred at room temperature for 2h, quenched with water (50 cm³), and was extracted with CH₂Cl₂ (50 cm³ × 3). It was washed with water (50 cm³), dried with MgSO₄, and concentrated in vacuo to leave a residue. To this residue methanol (50 cm³) was added and left overnight in the refrigerator to give 2,6-bis[2-cyano-2-(toluenesulfonyl)ethyl]anisole (3) (4.9 g, 72%).

6. 1,3-bisbromomethyl-7-tertbutylpyrene (2):

A mixture of compound 12 (100 mg, 0.314 mmol) and freshly prepared dry. Ether (100 mL) in 100 mL reaction flask and kept rubber septum with continuous following of Argon gas. Charged PBr₃ by syringe at 0°C through septum. Changed the glass tab by continuous passing Argon gas. Refluxed with continues stirred within 12 hours and quenched by adding 150 mL water. Extracted by Ether (100 mL ×2) and washed by water (50 mL) and Brine (40 mL). Dried by MgSO₄, filtered and evaporated by vacue in reduced pressure (30°C/410 mmHg). Yellowish white compound was formed. The residue was recrystallized from hexane-benzene (1:1) which afforded dibromide 2 (136 mg, 98%) as pale yellow needles, m. p. 229-231 °C; V max (KBr)/cm⁻¹ 2950, 2900, 1590, 1380 and 1200; δH (CDCl₃) 1.59 (9H, s), 5.17 (4H, s), 7.98 (1H, s), 8.17 (1H, d, J=9.2), 8.30 (2H, s) and 8.31 (2H, d, J=9.2); m/z 446.22 (M⁺) (Found: C, 59.4; H, 4.54%)

7. 6,18-di-tert-butyl[3.3]metacyclo(1,3)pyrenophane-2,11-dione (3a):

A mixture of CH₂Cl₂ (28 mL), 40% aq. KOH (2 mL), and nBu₄NI (94 mg, 0.254 mmol) was heated under reflux (50°C) with vigorous stirring. To this mixture, a solution of 1a (274.4 mg, 0.50 mmol) and 2 (222.58 mg, 0.50 mmol) in CH₂Cl₂ (25 mL) was added drop wise over a period of 8 h. Additional heating and stirring were continued for 3 h. After cooling, the organic phase was separated and washed with water and brine and dried by MgSO₄. The solution was
concentrated to ca. 9 mL, conc. HCl (1.5 mL) was added and the mixture was stirred at room temperature for 2 h at room temperature. The organic phase was separated, washed with water and brine and dried with MgSO₄. The CH₂Cl₂ extract was concentrated and residue was chromatographed on silica gel (Wako C-300, 50 g) (Hexane-dichloromethane, 1:1 v/v and dichloromethane as eluent) to give a colourless solid. Recrystallization from dichloromethane gave 6,18-di-tert-butyl[3.3]metacyclo(1,3)-pyrenophane-2,11-dione as colourless prism (CH₂Cl₂), (120 mg, 48%), m.p. = 278°C; V max (KBr)/ cm⁻¹ 3021, 2960, 2865, 2370, 1698, 1598, 1475, 1415, 1361, 1228, 1157, 1122, 879, 808, 713, 605, 511., ¹H NMR (CDCl₃): δ H 1.36 (9H, s, 6-tBu), 1.60 (9H, s, 17-tBu), 3.66 (4H, s, CH₂), 4.19 (4H, s, CH₂), 4.97 (1H, s, 9-Ar-H), 6.38 (1H, s, 22-Ar-H), 7.177 (1H, d, J=1.47 Hz, 4,8-Ar-H), 8.091 (2H, d, J=9.18 Hz, 14, 20-Ar-H), 8.143 (2H, d, J=8.99 Hz, 15,19-Ar-H) and 8.27 (2H, s, 16,18-Ar-H); δ C (CDCl₃) 31.38, 31.49, 31.93, 34.75, 35.26, 48.94, 50.80, 122.79, 123.07, 123.19, 125.04, 125.19, 126.55, 128.82, 129.61, 130.83, 133.62, 135.66, 149.68, 152.59 and 207.97.

8. 6,18-di-tert-butyl-9-methoxy[3.3]metacyclo(1,3)pyrenophane-2,11-dione (3b):

A mixture of CH₂Cl₂ (28 mL), 40% aq. KOH (2 mL), and nBu₄NI (94 mg, 0.254 mmol) was heated under reflux (50°C) with vigorous stirring. To this mixture, a solution of 1b (290 mg, 0.50 mmol) and 2 (222.58 mg, 0.50 mmol) in CH₂Cl₂ (25 mL) was added dropwise over a period of 8 h. Additional heating and stirring were continued for 3 h. After cooling, the organic phase was separated and washed with water and brine and dried by MgSO₄. The solution was concentrated to ca. 9 mL, conc. HCl (1.5 mL) was added and the mixture was stirred at room temperature for 2 h at room temperature. The organic phase was separated, washed with water and brine and dried with MgSO₄. The CH₂Cl₂ extract was concentrated and residue was chromatographed on silica gel (Wako C-300, 50 g) (Hexane-dichloromethane, 1:1 v/v and dichloromethane as eluent) to give a colourless solid. Recrystallization from dichloromethane gave 6,18-di-tert-butyl-9-methoxy[3.3]metacyclo(1,3)pyrenophane-2,11-dione (130 mg, 49%), m.p. = 230°C; V max (KBr)/ cm⁻¹ 3033, 2863, 2354, 1700, 1596, 1484, 1363, 1272, 1224, 1103, 1000, 875, 808, 715, 653, 578, 507, ¹H NMR (CDCl₃): δ H 1.15 (9H, s, 6-tBu), 1.58 (9H, s, 17-tBu), 2.99 (3H, s, 9-OMe), 3.37 (2H, d, J=14.13 Hz, CH₂), 3.65 (2H, d, J=14.31 Hz, CH₂), 4.03 (2H, d, J=14.13, CH₂), 4.384 (2H, d, J=14.13 Hz, -CH₂), 7.090 (2H, s, 5,7-ArH), 8.063 (2H, d, J=9.18 Hz, 16,18-ArH) and 8.198 (5H, t, J=9.18 Hz, 14,15,19,20,22-ArH); δ C (CDCl₃) -13.94, 42.99, 61.39, 70.06, 100.57, 101.32, 109.97, 128.12, 135.19, 147.99, 162.61, 176.08, 190.16, 194.14, 200.56, and 211.53.
9. 6,18-di-tert-butyl[3.3]metacyclo(1,3)pyrenophane (4a):

A mixture of 3a (45 mg, 0.09 mmol), 80% hydrazine monohydrate (0.25 mL, 0.51 mmol), triethylene glycol (3 mL), and KOH (27.05 mg, 0.54 mmol) was heated at 120 °C for 2 h, and cooled room temperature and stirred 1 h at argon atmosphere. Then the temperature was raised to 200 °C. The water generated during the reaction was removed by a Dean Stark condenser. Additional heating was continued for 3 h and then the mixture was cooled to room temperature and poured into ice water and acidified by adding 10% HCl solution. Then extracted twice with CH₂Cl₂ and the organic phase was washed with water and brine, and then dried with MgSO₄. The solvent was removed and the residue was purified from PTLC (Hexane-dichloromethane, 1:1 v/v as eluent). Colorless needles (37 mg, 83%). m.p.: 213°C. \( V_{\text{max}} \) (KBr)/cm⁻¹ 3052, 2954, 2904, 2850, 2354, 1751, 1594, 1438, 1355, 1259, 1087, 1072, 875, 802, 707, 601, 487.¹H NMR (CDCl₃): \( \delta_H \) 0.176 (9H, s, 6-tBu), 1.550 (9H, s, 17-tBu), 2.35-2.41 (4H, m, CH₂), 2.79-2.83 (4H, m, CH₂), 3.43 (4H, s, CH₂), 6.23 (2H, s, 5,7-ArH), 6.82 (1H, s, 9-ArH), 7.43 (1H, s, 22-ArH), 7.88 (2H, d, J=9.00 Hz, 14, 20-ArH), 8.02 (2H, d, J=9.00 Hz, 15,19,-ArH), and 8.056 (2H, s, 16,18-ArH); m/z Calcd. for C₃₆H₄₀ (M+) 472.70. Found 472.3.

10. 6,18-di-tert-butyl-9-methoxy[3.3]metacyclo(1,3)pyrenophane (4b):

A mixture of 3b (45 mg, 0.085 mmol), 80% hydrazine monohydrate (0.25 mL, 0.51 mmol), triethylene glycol (3 mL), and KOH (28.61 mg, 0.51 mmol) was heated at 120 °C for 2 h, and cooled room temperature and stirred 1 h at argon atmosphere. Then the temperature was raised to 200 °C. The water generated during the reaction was removed by a Dean Stark condenser. Additional heating was continued for 3 h and then the mixture was cooled to room temperature and poured into ice water and acidified by adding 10% HCl solution. Then extracted twice with CH₂Cl₂ and the organic phase was washed with water and brine, and then dried with MgSO₄. The solvent was removed and the residue was purified from PTLC (Hexane-dichloromethane, 1:1 v/v as eluent). Colorless needles (21 mg, 49%). m.p.: 216°C. \( V_{\text{max}} \) (KBr)/cm⁻¹ 3037, 2958, 2919, 2850, 2819, 2356, 2028, 1901, 1739, 1592, 1481, 1359, 1294, 1261, 1201, 1103, 1024, 869, 802, 717, 646, 579, 484.¹H NMR (CDCl₃): \( \delta_H \) 0.00 (9H, s, 6-tBu), 1.49 (9H, s, 17-tBu), 2.19 (2H, m, CH₂), 2.372 (2H, m, CH₂), 2.52 (2H, m, CH₂), 2.97 (2H, m, CH₂), 3.14 (2H, m, CH₂), 3.68 (2H, m, CH₂), 3.66 (3H, s, 9-OMe), 6.12 (2H, s, 5,7-Ar-H), 7.76 (1H, s, 22-Ar-H), 7.79 (2H, d, J=9.36 Hz, 14, 20-Ar-H), 7.95 (2H, d, J=9.40 Hz, 15, 19-Ar-H) and 7.98 (2H, s, 16,18-Ar-H); m/z Calcd. for C₃₇H₄₂O (M+) 502.73. Found 502.3.

A solution of 13 (552.5 mg, 1.24 mmol) and 2 (281.6, 1.24 mmol) in toluene (20 mL) was added dropwise over a period of 5 h from a Hershberg funnel with stirring to a solution of potassium hydroxide (3.32 g, 71 mmol) and sodium borohydride (210 mg) in ethanol (3.2 L). After the addition the reaction mixture was concentrated and washed by water (30 ml). The residue was extracted with CH₂Cl₂ (100 ml x 2). The CH₂Cl₂ extract was also washed by brine and dried by MgSO₄. The CH₂Cl₂ extract was concentrated and residue was chromatographed on silica gel (Wako C-300, 100 g) (Hexane-dichloromethane, 1:1 v/v, as eluent) to give a colourless solid. Recrystallization from hexane-ethyl acetate 1:1 8(v/v) gave 17-tert-butyl-5,6,7,9-tetramethyl-2,11-dithia[3]metacyclo-(1,3)pyrenophane(14) as colourless prism (315 mg, 50%), m.p.: 188-190°C; ¹H-NMR (300 MHz, CDCl₃), δH 1.36 (3H, s, CH₃), 1.55 (9H, s, t-Bu), 2.19 (3H, s, CH₃), 2.47 (6H, s, CH₃), 3.69-3.44 (2H, d, J=15 Hz), 3.84-3.88 (2H, d, J=12.3 Hz), 4.11-4.15 (2H, d, J=12.3 Hz), 4.35-4.40 (2H, d, J=14.7 Hz), 5.61 (1H, s, Ar-H), 8.02-8.05 (2H, d, J=9.3 Hz), 8.19 (2H, s, Ar-H) and 8.17-8.20 (2H, d, J=9.0 Hz).


A solution of 7a (235 mg, 1.09 mmol) and 2 (487.7, 1.09 mmol) in toluene (20 mL) was added dropwise over a period of 5 h from a Hershberg funnel with stirring to a solution of potassium hydroxide (3.32 g, 71 mmol) and sodium borohydride (210 mg) in ethanol (3.2 L). After the addition the reaction mixture was concentrated and washed by water (30 ml). The residue was extracted with CH₂Cl₂ (100 ml x 2). The CH₂Cl₂ extract was also washed by brine and dried by MgSO₄. The CH₂Cl₂ extract was concentrated and residue was chromatographed on silica gel (Wako C-300, 100 g) (Hexane-dichloromethane, 1:1 v/v, as eluent) to give a colourless solid. Recrystallization from hexane-ethyl acetate 1:1 8(v/v) gave 17-tertbuthyl-9-methoxy-6-methyl-2,11-dithia[3]metacyclo-(1,3)pyrenophane(12) as pale yellow prism (MeOH), (15 mg, 38%), m.p.: 120-123°C; Vₘₐₓ(KBr)/ cm⁻¹ 2904, 1592, 1432, 1206, 1002 and 870; (300 MHz, CDCl₃), δH 0.97 (3H, s, 6-Me), 1.58 (9H, s, 17 t-Bu), 3.52 (2H, s, J=14.1 Hz, 1,12 CH₂), 3.72 (3H, s, J=9-OMe), 4.29 (2H, s, J=15.0 Hz, 3,10 CH₂), 4.42 (2H, s, J=14.1 Hz, 1,12 CH₂), 4.57 (2H, s, J=15.0 Hz, 3,10 CH₂), 6.39 (2H, s, 5,7 Ar-H), 7.65 (1H, s, 22A-rH), 8.01 (2H, d, J=9.2 Hz, 15,19 A-rH); m/z 496 (M+); HRMS (CI): m/z Calcd. for C₃₂H₃₂OS₂ (M+) 496.19. Found 496.19 (Found: C, 77.53; H, 6.37. C₃₂H₃₂OS₂, requires, 77.38; H, 6.49%).

A solution of 7b (96 mg, 0.373 mmol) and 2 (166 mg, 0.373 mmol) in toluene (20 mL) was added drop wise over a period of 5 h from a Hershberg funnel with stirring to a solution of potassium hydroxide (3.32 g, 71 mmol) and sodium borohydride (210mg) in ethanol (3.2 L). After the addition the reaction mixture was concentrated and washed by water (30ml). The residue was extracted with CH₂Cl₂ (100ml×2). The CH₂Cl₂ extract was also washed by brine and dried by MgSO₄. The CH₂Cl₂ extract was concentrated and residue was chromatographed on silica gel (Wako C-300,50g) (Hexane-dichloromethane, 1:1 v/v, as eluent) to give a colourless solid. Recrystallization from hexane-ethyl acetate 1:1 gave syn-6,17-di-tertbutyl-9-methoxy-2,11-dithia[3]metacyclo-(1,3)pyrenophane (3) as colourless prism (CH₂Cl₂), (65 mg, 32 %), m.p.: 241-244°C; Vₘₐₓ(KBr)/ cm⁻¹ 3050, 2950, 1590, 1480, 1260 and 880; ( 300MHz, CDCl₃), δH 0.10 (9H, s, 6-tBu), 1.56 (9H, s, 17-tBu), 3.54 (2H, d, J=14.3 Hz), 3.75 (3H, s, 9 OMe), 4.28 (2H, d, J=15.0 Hz, CH₂), 4.48 (2H, d, J=14.3 Hz, CH₂), 4.56 (2H, d, J=15.0 Hz, CH₂), 6.61 (2H, s, 5,7 A-rH), 7.64 (1H, s, 22 Ar-H), 7.95 (2H, d, J=9.2 Hz, 15,19 Ar-H), 8.12 (2H, s, Ar-H) and 8.17 (2H, d, J= 9.2 Hz); m/z 538(M+); C₃₅H₃₈OS₂. (Found: C, 77.95; H, 7.0, C₃₂H₃₂OS₂, requires, 78.02; H, 7.11%).

5.5 **References:**


20. L. Ernst, Progress in Nuclear Magnetic Resonance Spectroscopy, 2000, 37, 47.


35. F Vogtie and R Lichtenthaler, Z Naturforsch 1971, 26b, 872.

36. The simulation must take into account also how the populations change on changing the temperature (Boltzmann rule).


Chapter 6


Polymethyl substituted [2.2]meta- and [2.2]metaparacyclophanes were synthesized via the corresponding 2,11-dithia[3.3]meta- and -metapara-cyclophanes. Photooxygenation of 4,5,6,8,12,13,14,16-octamethyl[2.2]metacyclophane, using a high pressure mercury lamp, produced a mixture of mono- and bis-endoperoxides in quantitative yield, while the corresponding octamethyl[2.2]metaparacyclophane afforded only the bis-endoperoxide (on both the meta- and para-benzene rings). Similar results were observed in the photooxygenation reaction of 4,5,6,12,13,15,16-hepta-methyl[2.2]metaparacyclophane, which led to endoperoxidation of only the para benzene ring; this was attributed to the much larger degree of deformation of the para-benzene ring than of the meta-benzene ring. Structures of the novel [2.2]cyclophanes and photooxygenation products in solution and solid state (from X-ray analysis) are also discussed.

6.1 Introduction:

Photochemically generated singlet oxygen ($^1\text{O}_2$) cycloadds to conjugated dienes and arenes to give endoperoxides.\textsuperscript{1–3} The endoperoxides are important intermediates in photo-oxidation reactions, but, in most cases, are too unstable to isolate in order to study their structure. On the other hand, cyclophanes belong to one of the remarkable compound classes that has attracted extensive studies.\textsuperscript{4,5} It is known that strained aromatic rings in cyclophanes, such as in [2.2.2.2](1,2,4,5)cyclophane\textsuperscript{6} and [2.2]paracyclophane diene,\textsuperscript{7,8} readily undergo photocycloaddition with $^1\text{O}_2$ in the presence of photosensitizing dyes. Recently, it was reported that the photoirradiation of a mono-(Dewar benzene, bicyclo[2.2.0]-hexadiene) isomer of the [1.1]MCP (MCP= metacyclophane) gave the corresponding endoperoxide.\textsuperscript{9,10} In this case, no additional sensitizer was used. This result suggests that the strained MCPs are reactive in photocycloaddition reactions with $^1\text{O}_2$. Furthermore, introduction of methyl groups to the benzene ring of [2.2]MCP also increases the strain in the molecule. Therefore, there is substantial interest in preparing the polymethyl substituted [2.2]MCPs to investigate the relationship between the strain and reactivity. In this paper, we report the synthesis and structures of polymethyl substituted [2.2]MCPs and [2.2]MPCPs (MCP= metaparacyclophane). The first successful preparation and characterization of stable mono- and bis-endoperoxides of polymethyl substituted [2.2]MCPs and [2.2]MPCPs, using a high pressure mercury lamp, are also reported.

6.2 Results and Discussion:

The preparative route of 4,5,6,8,12,13,14-heptamethyl[2.2]-MCP (6a) and 4,5,6,8,12,13,14,16-octamethyl[2.2]MCP (6b) is shown in Scheme 6.1 and follows our previous reported procedure.\textsuperscript{11–16} The starting compounds, bis(chloromethyl)benzenes 2a and 2b were prepared in good yields by the chloromethylation of corresponding methylbenzenes 1a and 1b with chloromethyl methyl ether in the presence of zinc chloride.
Bis(chloromethyl)benzene 2b was converted to the bis- (sulfanylmethyl) derivative 3b in 72% yield according to the reported procedure. The desired 6a and 6b were prepared from the corresponding 2 and 3b via the disulfides 4 and bissulfones 5 according to reported methods. Thus, the cyclization of bis(chloromethyl)benzenes 2a and 2b with bis(sulfanylmethyl)benzene 3b was carried out under highly diluted conditions in 10% ethanolic KOH in the presence of a small amount of NaBH₄, giving anti-2,11-dithia[3.3]MCPs 4a and 4b in 80 and 72% yields, respectively. Oxidation of 4 with m-chloroperbenzoic acid (m-CPBA) in CHCl₃ afforded the
corresponding bissulfones anti-5 in almost quantitative yields. Pyrolysis of both bissulfones, 5a and 5b, under reduced pressure (1 torr) at 500°C was carried out via a reported method\textsuperscript{17,18} to afford, exclusively, the anti-6 products in 75 and 71% yields, respectively.

The assignments of structure for 6a and 6b were readily apparent from their \(^1\)H NMR spectra, which show the C8 methyl protons at \(\delta\) 0.45 and 0.44 ppm, respectively. The internal aromatic proton at the 16-position of 6a is also observed upfield (\(\delta\) 3.75 ppm). Since the internal methyl protons of the anti conformers have been shown to have an upfield shift due to the ring current of the opposite aromatic ring,\textsuperscript{4,5,17,18} our observations strongly indicate compounds 6a and 6b adopt the anti-conformation.

Fig. 6.1 Structures and numbering of [2.2]MCPs

The geometry of the [2.2]MCP skeleton, compound 7, Figure 6.1, is known in detail from an X-ray structural analysis.\textsuperscript{19} The crystal consists of discrete molecules, each of which has a centre of symmetry. The two halves of the molecule form a stepped system. It is interesting to note that the benzene rings are not planar, but are distorted towards a boat conformation, with the result that the molecule evidently avoids the steric interaction of the central carbon atoms C8 and C16, and of the attached hydrogen atoms, of the opposing ring. The C8···C16 distance is 2.689 Å. The average length of the aromatic C–C bonds was found to be 1.386 Å, and the aliphatic bond was 1.543 Å. It is remarkable that the normally hexagonal, planar benzene ring suffers such a pronounced deformation [11.9°] with no appreciable change in the interatomic distances.\textsuperscript{20,21} The X-ray structural analysis of 8,16-dimethyl[2.2]MCP 8 confirms the results obtained for the parent compound, 7\textsuperscript{22–34} with increased strain [15.4°]\textsuperscript{22} in 8 seen in particular in the C1-C2 bond distance (1.573 Å) and the distance between C8 and C16, increased to 2.819 Å in 8. We then wondered
how the introduction of methyl groups to all of the benzene ring sites, as in [2.2]MCP 6b, might affect the strain in the molecule.

**Fig. 6.2.** X-ray structure of 4,5,6,8,12,13,14,16-octamethyl[2.2]MCP 6b. The methyl group of C(41) is disordered in two distinct orientations. Thermal ellipsoids are shown at 50% probability.

An X-ray crystallographic study of 6b, *Figure 6.2*, shows that this molecule also lies about a centre of symmetry, with the *anti* conformation, with the two rings in a ‘step’ formation. This shows that the compound 6b is apparently conformationally less rigid than the parent [2.2]MCP, 7, because its methyl substituents at the 8,16 positions encroach on the electron clouds of the opposing meta-bridged rings; one methyl hydrogen atom, H(81c), lies directly over the centre of the opposing C6 ring, with H⋯C distances in the range 2.56–2.87 Å. It is interesting that the increase of degree of deformation [due to substitution of bulky electron donating CH₃ groups] of the meta-benzene rings, which was estimated at 17.63° for 6b, compares with that of 11.9° in [2.2]MCP 7. Introduction of the methyl groups at the 4,5,6,12,13 and 14 positions also increases the deformation of the meta-benzene ring. Thus introduction of methyl groups to the benzene rings of [2.2]MCP 7 increases the strain in the molecule in comparison with the unsubstituted [2.2]MCP, 7. It was also found the distortion angle of the meta benzene ring from planarity is 17.63° in 6b in comparison with that of 8,16-dimethyl[2.2]MCP, 8 (15.4°).²²,²³

Irradiation of 4,5,6,8,12,13,14-heptamethyl[2.2]MCP 6a in acetone, using a high pressure mercury lamp, produced endoperoxide 9a in 70% yield (*Scheme 6.2*).
Although no additional photosensitizer was added, the reaction leading to 9a is thought to proceed via $^1$O$_2$. Thus, the reaction was slowed remarkably by addition of 1,4-diazabicyclo[2.2.2]octane, a known $^1$O$_2$ quencher. It may well be possible that the [2.2]MCP 6a itself acts as sensitizer in the reaction. Furthermore, it is worth noting that the strain in the molecule of 6a might be released at the C8 carbon atom by a change in its hybridization mode from sp$^2$ to sp$^3$.

When irradiated under the same reaction conditions, 4,5,6,8,12,13,14,16-octamethyl[2.2]MCP 6b produced an inseparable mixture of mono-endoperoxide 9b and bis-endoperoxide 10b in quantitative yield in the ratio of 40 and 60%.

The similarly substituted hexamethylbenzene 11 is itself inert under the same irradiation conditions, although it has been reported that, when methylene blue was used as a photosensitizer, the formation of the unstable endoperoxide 12 can be detected by $^1$H NMR spectroscopy in the reaction mixture. Epidioxy-hydroperoxide 13 is the final product via a subsequent ene reaction of 12 (Scheme 6.3).
Endoperoxide 9a is stable enough to be recrystallized from acetone, whereas endoperoxide 12, which was not isolated, was reported to decompose completely at 40°C in 1 hour as measured by $^1$H NMR spectroscopy. Thermal deoxygenation of 9a was also monitored by $^1$H NMR spectroscopy. In fact, after heating a solution of 9a in CDCl$_3$ for 6 h, new signals derived from [2.2]MCP 6a were observed in the ratio of 15:85 (6a:9a) at 40°C and 45:55 (6a:9a) at 50°C. As a result, the thermal deoxygenation of 9a was shown to occur similarly to that of the endoperoxides of 1,4-dimethylnaphthalene and of 9,10-diphenylanthracene.$^{37}$

The structure of product 9a was determined on the basis of elemental analysis and from spectral data. Thus, the $^1$H-NMR spectrum of 9a shows five kinds of methyl resonances as singlets at $\delta$ 0.02 (3H), 1.26 (3H), 1.90 (3H), 2.17 (6H) and 2.24 (6H) ppm, in which one methyl proton (of C8) is shifted sharply upfield ($\delta$ 0.02 ppm) compared with that of [2.2]MCP 6a ($\delta$ 0.44 ppm) due to the ring current effect of the opposite benzene ring; by changing the carbon atom located on the internal 8-position from sp$^2$ to sp$^3$, the internal methyl group was located much closer to the opposite benzene ring. In contrast, the internal 16-proton appeared in the normal aromatic region, $\delta$ 6.53 ppm, (with no ring current effect, due to the transformation of the benzene ring to the endoperoxide) in comparison with that of 6a at $\delta$ 3.75 ppm.

We have assigned the $^1$H-NMR signals of 10b in a similar fashion. The methyl protons here were observed as singlets at $\delta$ 1.22 (6H), 1.51 (6H) and 1.85 (12H) ppm. No upfield shifts of the internal 8,16-methyl groups were observed. These findings strongly suggest that the both benzene
rings of 6b were photooxygenated and the structure of 10b is assigned the structure, 4,5,6,8,12, 13,14,16-octamethyl[2.2]MCP-5,8,13,16-bis-endoperoxide.

The meta-bridged benzene ring of [2.2]metaparacyclophane (MPCP = metaparacyclophane) (14) (Figure 6.3) has been shown to undergo conformational flipping\(^{38-43}\) with a substantial energy barrier (\(ca\) 20 kcal mol\(^{-1}\)). According to X-ray crystallographic studies of 14,\(^{44}\) the deformations of the benzene rings are similar to those of the corresponding rings in para- and meta[2.2]cyclophanes, with the benzene rings bent in a boat- and a chair-like form, respectively. The angle between the two aromatic planes (defined by the carbon atoms 3, 4, 6, and 7 vs 12, 13, 15, and 16) is about 13°. It should be noted that the angle between the 11, 12, 16-plane and 10-11 bond vector (and between the 13, 14, 15-plane and 1-14 bond vector) is even larger than the analogous angle (11.2°) in [2.2]paracyclophane.\(^{45}\) The para-bridged moiety of 14 is thus more strongly tilted within aromatic planes (41°) than those of the isomeric compound of [2.2]paracyclophane (0°) as well as [2.2]metacyclophane (0°).\(^{46}\) Introduction of the substituent at the 8-position increases the strain in the molecule in comparison with the unsubstituted [2.2]MPCP (14); the deformation of the para-benzene ring of 8-methyl[2.2]MPCP (15) was estimated at 15° from our earlier X-ray analysis.\(^{47}\) Introduction of methyl groups to the para benzene ring of [2.2]MPCP would also increase the strain in the molecule, and, therefore, we were interested in preparing the polymethyl substituted [2.2]MPCP 16b to investigate the relationship between the strain and the photooxygenation reactivity. The preparative route to the polymethyl substituted [2.2]-MPCPs 16a and 16b is shown in Scheme 6.4. The preparation of 2,6-bis(chloromethyl)toluenes 2a and 2b has been described above.\(^ {17,48}\) 1,4-Bis(sulfanylmethyl)-2,3,5,6-tetramethylbenzene 18 was prepared from the corresponding 1,4-bis(chloromethyl)- 2,3,5,6-tetramethylbenzene 17 according a reported procedure.\(^ {46}\)

Fig. 6.3
The cyclization reactions of the bis(chloromethyl)benzenes 2a, 2b with the bis(sulfanylmethyl) - benzene 18 were carried out under highly diluted conditions in 10% ethanolic KOH in the presence of a small amount of NaBH₄, giving the desired 2,11-dithia[3.3]MPCPs 19a and 19b in good yield. Photolysis of these products in triethylphosphate, with a high pressure mercury lamp (400W), was carried out according to the reported method⁴⁹,⁵⁰ to afford the corresponding [2.2]MPCPs 16a and 16b, respectively, in good yields.

Scheme 6.4

The structures of 16a and 16b were determined on the basis of elemental analyses and spectral data. The ¹H NMR spectrum of 16b in CDCl₃ shows a singlet at δ 1.61 ppm for methyl protons at the 15,16-positions (which are strongly shielded by the opposite meta-bridged benzene ring), and δ 2.31 ppm for the external methyl protons at the 12,13-positions. The signals of the internal methyl protons at the 8-position and two methyl protons at the 4,6-protons were observed upfield at δ 1.72 and 2.07 ppm which indicates these are in a region shielded by the opposite para-bridged benzene ring.
An X-ray crystallographic study of 16b, Figure 6.4, shows that this compound should be conformationally more rigid than 14 because its methyl substituent at the 8 position impinges upon the electron cloud of the para-bridged ring. The deformation of the para-benzene ring, estimated at 18.84° in 16b, has increased from 15° in 15; introduction of the methyl groups at the 12,13,15 and 16 positions increases the deformation of the para-benzene ring. Thus introduction of methyl groups to the para benzene ring of [2.2]MPCP 14 is also likely to increase the strain in the molecule in comparison with that in the unsubstituted 8-methyl[2.2]MCP 15.\(^{[47]}\) It was also found that the distortion angle of the meta benzene ring in 16b from planarity is 15.94°; in 8,16-dimethyl-[2.2] MCP 8, the angle is 15.4°.\(^{[36,37]}\)  

![Fig. 6.4. X-ray structure of 4,5,6,8,12,13,15,16-octamethyl[2.2]MCP 16b. The thermal ellipsoids are given at 50% probability.](image)

Irradiation of 4,5,6,12,13,15,16-heptamethyl[2.2]MCP 16a in acetone, using a high pressure mercury lamp for 6 h (under the same reaction conditions as for 6a and 6b, above) led to photooxygeneration only at the para-benzene ring to produce endoperoxide 20a in 62% yield (Scheme 6.5). Prolonged reaction for 12 h under the same conditions gave only 20a, in 65% yield; no formation of bis-endoperoxide 21a was observed under these conditions. On the other hand, the photoreaction of 4,5,6,8,12,13,15,16-octamethyl[2.2]MCP 16b under the same reaction conditions produced only the bis-endoperoxide 21b, in 57% yield.
However, bis-endoperoxide 21b was rather labile and readily decomposed to the original [2.2]MPCP 16b when heated at 80°C for 1 min. It is concluded that these photooxygeneration products are attributable to the larger degree of deformation of para-benzene ring in 16b than in [2.2]MPCP 14 and 8-methyl[2.2]MPCP 15 to 15°C.

The structure of product 20a was determined on the basis of elemental analysis and spectral data. Thus, the 1H-NMR spectrum of 20a shows six kinds of methyl resonances as singlets at δ 0.78 (3H), 1.00 (3H), 1.53 (3H), 2.02 (3H), 2.06 (3H, s), and 2.18 (6H) ppm, in which protons of two methyl groups, C15 and C16, have much larger upfield shifts (δ 0.78 and 1.00 ppm) than in [2.2]MPCP 16a (δ 1.61 ppm). This results from the change in form of the para ring; by changing the C16 carbon from sp² to sp³, an internal methyl group here would now be much closer to the opposite meta benzene ring. In contrast, the internal 8-proton, over the endoperoxide group, appeared at the normal aromatic region δ 5.95 ppm, whereas that of 16a, lying over the para benzene ring is at δ 5.08 ppm.

In contrast, the 1H-NMR signals of 21b were very complicated. The methyl protons were observed as 8 singlets at δ 1.31, 1.32, 1.41, 1.43, 1.51, 1.91, 1.92 and 2.01 ppm. No upfield shifts of the internal 8- and 16-methyl group protons were observed. This finding strongly suggests that
the both benzene rings of 16b were photooxygenated and that 21b is assigned the structure 4,5,6,8,12,13,15,16-octamethyl[2.2]MPCP-5,8,12,15-bis-endo-peroxide.

6.3 Conclusions

We have demonstrated that photooxygenation of 4,5,6,12,13,14,16-heptamethyl[2.2]MCP 6a using a high pressure mercury lamp produced exclusively mono-endoperoxide, while the photooxygenation of 4,5,6,8,12,13,14,16-octamethyl[2.2]MCP 6b forms a mixture of mono- and bis-endoperoxides in good yield; this latter reaction is strongly affected by the bulkiness of the methyl group in the 8-position which increases the strain in the molecule. Similar results were observed in the photooxygenation reaction of 4,5,6,12,13,15,16-heptamethyl[2.2]MPCP 16a which led to the mono-endoperoxidation of only the para benzene ring, compound 20a, whilst irradiation of 16b yielded only the bis-endoperoxide 21b. Further studies on the chemical properties of the photooxygenation products are now in progress.

6.4 Experimental Section

**General:** All mps (Yanagimoto MP-S1) are uncorrected. $^1$H NMR spectra (300 MHz) were recorded on a Nippon Denshi JEOL FT-300 NMR spectrometer with SiMe$_4$ as an internal reference; $J$-values are given in Hz. IR spectra were measured on samples as KBr pellets in a Nippon Denshi JIR-AQ2OM spectrophotometer. Elemental analyses were performed by Yanaco MT-5.

1. **Preparation of 2,6-bis(mercaptomethyl)-1,3,4,5-tetramethylbenzene (3b):**

A solution of 2b (9.25 g, 0.40 mmol) and thiourea (6.7 g, 88 mmol) in DMSO (50 mL) was stirred at room temperature under an atmosphere of nitrogen for 14 h. After the reaction mixture was poured into a solution of NaOH (20 g) in water (200 mL), the solution was stirred for 1 h, acidified with aqueous 10% HCl and extracted with CH$_2$Cl$_2$ (100 mL x 2). The CH$_2$Cl$_2$ extracts were washed with water (100 mL) followed by saturated aqueous NaCl (100 mL), then dried (Na$_2$SO$_4$) and evaporated in vacuo to leave a colourless solid. Recrystallization from hexane gave compound 3b as colourless prisms (6.5 g, 72%), m.p. 81–82°C; $v_{	ext{max}}$/cm$^{-1}$ (KBr) 3040, 2960, 2900, 2550, 1430, 1370, 1225, 1010, 790 and 675; $\delta$$_H$(CDCl$_3$) 1.54 (2H, t, $J$= 7.0 Hz, SH), 2.18 (3H, s, CH$_3$), 2.29 (6H, s, CH$_3$), 2.40 (3H, s, CH$_3$) and 3.76 (4H, s, CH$_2$); m/z 226 (M$^+$). (Found: C, 63.61; H, 8.13. C$_{12}$H$_{18}$S$_2$ (226.4) requires C, 63.66; H, 8.01%).

2. **Preparation of 5,6,7,9,14,15,16,18-octamethyl-2,11-dithia[3.3]meta-cyclophane (4b):**
A solution of \(2b \) (4.78 g, 20 mmol) and \(3b \) (4.52 g, 20 mmol) in benzene (100 mL) was added dropwise over a period of 12 h from a Herschberg funnel with stirring under nitrogen to a solution of potassium hydroxide (4.0 g, 71 mmol) and sodium borohydride (1 g) in ethanol (4 L). After the addition, the reaction mixture was concentrated and the residue was extracted with \(\text{CH}_2\text{Cl}_2 \) (200 mL \( \times \) 2). The \(\text{CH}_2\text{Cl}_2 \) extracts were concentrated and the residue was chromatographed on silica gel (Wako C-300, 400 g) (hexane-benzene, 1:1 v/v, as eluent) to give a colourless solid. Recrystallization from hexane/benzene 1:1 (v/v) gave compound \(4b \) as colourless prisms (5.57 g, 72%), m.p. >300°C; \(\nu_{\text{max}}/\text{cm}^{-1} \) (KBr) 3020, 2930, 1445, 1410, 1300, 1260, 1220, 1105, 1020, 805, 730; \(\delta_{\text{H}}\) (\(\text{CDCl}_3 \)) 1.16 (6H, s, \(\text{CH}_3 \)), 2.22 (6H, s, \(\text{CH}_3 \)), 2.41 (12H, s, \(\text{CH}_3 \)), 3.67 (4H, d, \(J = 13.7 \text{ Hz}, \text{CH}_2 \)) and 3.76 (4H, d, \(J = 13.7 \text{ Hz}, \text{CH}_2 \)); m/z 384 (M\(^+ \)) (Found: C, 75.05; H, 8.45. \(\text{C}_{24}\text{H}_{32}\text{S}_2 \) (384.64) required C, 74.94; H, 8.39).

The cyclization reaction of \(2a \) and \(3b \) was carried out using the same procedure as described above to afford 5,6,7,9,14,15,16-heptamethyl-2,11-dithia[3.3]metacyclophane \((4a) \) as colourless prisms (5.57 g, 72%), m.p. >300°C; \(\nu_{\text{max}}/\text{cm}^{-1} \) (KBr) 3050, 2950, 2900, 1430, 1370, 1280, 1215, 1060, 1000, 905, 785, 765, 740 and 720; \(\delta_{\text{H}}\) (\(\text{CDCl}_3 \)) 1.68 (3H, s, \(\text{CH}_3 \)), 2.10 (3H, s, \(\text{CH}_3 \)), 2.18 (6H, s, \(\text{CH}_3 \)), 2.30 (3H, s, \(\text{CH}_3 \)), 2.41 (6H, s, \(\text{CH}_3 \)), 3.01 (2H, d, \(J = 16.0 \text{ Hz}, \text{CH}_2 \)), 3.58 (2H, d, \(J = 12.0 \text{ Hz}, \text{CH}_2 \)), 4.04 (2H, d, \(J = 12.0 \text{ Hz}, \text{CH}_2 \)) and 4.48 (1H, broad s, Ar-H); m/z 370 (M\(^+ \)) (Found: C, 74.64; H, 8.24. \(\text{C}_{23}\text{H}_{30}\text{S}_2 \) (370.6) required C, 74.54; H, 8.16).

3. Preparation of 5,6,7,9,14,15,16,18-octamethyl-2,11-dithia[3.3]metacyclophane-2,2,11,11-tetraoxide (5b):

To a solution of \(4b \) (2.72 g, 7.1 mmol) in \(\text{CHCl}_3 \) (150 mL) was added \(m\)-chloroperbenzoic acid (3.40 g, 16.7 mmol, 85% purity) at 0°C while stirring with a magnetic stirrer. After the solution was stirred for 24 h at room temperature, the solvent was evaporated in vacuo to leave the residue which was washed with 10% NaHCO\(_3\) (100 mL), water (50 mL) and ethanol to afford \(5b \) as colourless prisms (3.20 g, 100%), m.p. >300°C; \(\nu_{\text{max}}/\text{cm}^{-1} \) (KBr) 3020, 2930, 2900, 1430, 1370, 1260, 1220, 1105, 1020, 805 and 730; \(\delta_{\text{H}}\) (\(\text{CDCl}_3 \)) 1.17 (6H, s, \(\text{CH}_3 \)), 2.26 (6H, s, \(\text{CH}_3 \)), 2.50 (12H, s, \(\text{CH}_3 \)), 4.53 (4H, d, \(J = 14.8 \text{ Hz}, \text{CH}_2 \)) and 4.62 (4H, d, \(J = 14.8 \text{ Hz}, \text{CH}_2 \)); m/z 320 (M\(^+ \)-2SO\(_2\)) (Found: C, 75.05; H, 8.45. \(\text{C}_{24}\text{H}_{32}\text{O}_4\text{S}_2 \) (448.64) required C, 64.25; H, 7.19).

Similarly, oxidation of \(4a \) with \(m\)-CPBA was carried out using the same procedure as described above to afford 5,6,7,9,14,15,16-heptamethyl-2,11-dithia[3.3]metacyclophane-2,2,11,11-tetraoxide \((5a) \) as colourless prisms (3.1 g, 100%), m.p. >300°C; \(\nu_{\text{max}}/\text{cm}^{-1} \) (KBr) 3050, 2930,
1410, 1300, 1150, 915, 850, 780, 725 and 700; δ_H (CDCl_3) 1.91 (3H, s, CH_3), 2.19 (3H, s, CH_3), 2.29 (6H, s, CH_3), 2.44 (3H, s, CH_3), 2.59 (6H, s, CH_3), 3.98 (2H, d, J = 15.2 Hz, CH_2), 4.24 (2H, d, J = 15.2 Hz, CH_2), 4.46 (1H, broad s, Ar-H), 4.66 (2H, d, J = 13.8 Hz, CH_2) and 4.80 (2H, d, J = 13.8 Hz, CH_2); m/z 306 (M^+ -2SO_2) (Found: C, 63.32; H, 6.96. C_{23}H_{30}S_2O_4 (434.60) required C, 63.56; H, 6.96).

4. Pyrolysis of disulfone 5b to give 4,5,6,8,12,13,14,16-octamethyl-[2.2]metacyclophane (6b):

Pyrolysis of disulfone 5b was carried out in an apparatus consisting of a horizontal tube (15 mm in diameter) passing through two adjacent tube furnaces, each 20 cm long. The first furnace provided a temperature that would induce sublimation of the sulfone; the second was used at a higher temperature (500°C) that would assure pyrolysis under reduced pressure (1 Torr); a vacuum pump was connected at the exit from the second furnace. The sample of disulfone 5b (1.14 g, 2.55 mmol) was placed in the first furnace and small glass beads were packed into the second furnace. The product which sublimed was collected and chromatographed on silica gel (Wako C-300, 100 g) (hexane as eluent) to give a colourless solid. Recrystallization from hexane gave compound 6b as colourless prisms (580 mg, 71%), m.p. >300°C; ν_{max}/cm^{-1} (KBr) 3050, 2960, 1440, 1410, 1365, 1320, 1180, 1060, 1040, 1000, 880, 800 and 740; δ_H (CDCl_3) 0.45 (6H, s, CH_3), 2.17 (6H, s, CH_3), 2.32 (12H, s, CH_3), 2.43 (4H, d, J = 9.6 Hz, CH_2) and 3.17 (4H, d, J = 9.6 Hz, CH_2); m/z 320 (M^+) (Found: C, 90.13; H, 10.19. C_{24}H_{32} (320.52) required C, 89.94; H, 10.06).

Pyrolysis of 5a was carried out using the same procedure as described above to afford, in 75% yield, 4,5,6,8,12,13,14-heptamethyl[2.2]metacyclophane (6a) as colourless prisms, m.p. 210–211°C; ν_{max}/cm^{-1} (KBr) 3017, 2970, 1460, 1440, 1410, 1370, 1325, 1180, 1060, 1020, 930, 880 and 745; δ_H (CDCl_3) 0.44 (3H, s, internal CH_3), 1.60–2.47 (4H, m, CH_2), 2.18 (3H, s, CH_3), 2.27 (6H, s, CH_3), 2.28 (6H, s, CH_3), 2.31 (6H, s, CH_3), 3.08–3.36 (4H, m, CH_2) and 3.75 (1H, broad s, Ar-H); m/z 306 (M^+) (Found: C, 90.37; H, 9.87. C_{23}H_{30} (306.47) required C, 90.13; H, 9.87).

5. Preparation of 1,4-bis(sulfanylmethyl)-2,3,5,6-tetramethylbenzene (18):

A solution of 1,4-bis(chloromethyl)-2,3,5,6-tetramethylbenzene 17 (9.25 g, 0.40 mmol) and thiourea (6.7 g, 88 mmol) in DMSO (50 mL) was stirred at room temperature under an atmosphere of nitrogen for 14 h. After the reaction mixture was poured into a solution of NaOH (20 g) in water (200 mL), the solution was stirred for 1 h, acidified with aqueous 10% HCl and extracted with CH_2Cl_2 (100 mL × 2). The CH_2Cl_2 extracts were washed with water (100 cm^3) and
saturated aqueous NaCl (100 mL), then dried (Na$_2$SO$_4$) and evaporated in vacuo to leave a colourless solid. Recrystallization from hexane gave compound 18 as colourless prisms (6.5 g, 71.8%), m.p. 113–114°C; $\nu_{\text{max}}$/cm$^{-1}$ (KBr) 3040, 2960, 2900, 2550, 1430, 1370, 1225, 1010, 790 and 675; $\delta$H (CDCl$_3$) 1.56 (2H, t, $J=6.6$ Hz, $\text{SH}$), 2.28 (12H, s, $\text{CH}_3$) and 3.80 (4H, d, $J=6.6$ Hz, $\text{CH}_2$); m/z 226 (M$^+$) (Found: C, 63.61; H, 8.13, C$_{12}$H$_{18}$S$_2$ (226.4) requires C, 63.66; H, 8.01%).

6. Preparation of 5,6,7,9,14,15,17,18-octamethyl-2,11-dithia[3.3]meta-paracyclophane (19b):

A solution of 2b (5.27 g, 20 mmol) and 18 (4.52 g, 20 mmol) in benzene (100 mL) was added dropwise over a period of 12 h from a Hershberg funnel with stirring under nitrogen to a solution of potassium hydroxide (4.0 g, 71 mmol) and sodium borohydride (1 g) in ethanol (4 L). After the addition, the reaction mixture was concentrated and the residue was extracted with CH$_2$Cl$_2$ (200 mL × 2). The CH$_2$Cl$_2$ extracts were concentrated and the residue was chromatographed on silica gel (Wako C-300, 400 g) (hexane-benzene, 1:1 v/v, as eluent) to give a colourless solid. Recrystallization from hexane-benzene 1:1 (v/v) gave compound 19b as colourless prisms (5.22 g, 54%), m.p. 207–208°C; $\delta$H (CDCl$_3$) 1.74 (3H, s, $\text{CH}_3$), 1.79 (6H, s, $\text{CH}_3$), 2.12 (3H, s, $\text{CH}_3$), 2.27 (6H, s, $\text{CH}_3$), 2.36 (6H, s, $\text{CH}_3$), 3.62 (2H, d, $J=16.2$ Hz, $\text{CH}_2$), 3.67 (2H, d, $J=13.7$ Hz, $\text{CH}_2$), 3.70 (2H, d, $J=16.2$ Hz, $\text{CH}_2$) and 4.34 (2H, d, $J=13.5$ Hz, $\text{CH}_2$); $\delta$C (CDCl$_3$) 16.05, 16.21, 16.73, 17.88, 18.44, 30.12, 30.66, 129.43, 131.72, 132.69, 133.28, 133.39, 133.44 and 133.60; m/z 384 (M$^+$) (Found: C, 75.05; H, 8.45, C$_{24}$H$_{32}$S$_2$ (384.64) required C, 74.94; H, 8.39).

The cyclization reaction of 2a and 18 was carried out using the same procedure as described above to afford 19a as colourless prisms (5.04 g, 68%), m.p. 147–148°C; $\delta$H (CDCl$_3$) 2.10 (3H, s, $\text{CH}_3$), 2.13 (6H, s, $\text{CH}_3$), 2.16 (12H, s, $\text{CH}_3$), 3.41 (4H, s, $\text{CH}_2$), 4.05 (2H, s, $\text{CH}_2$) and 5.19 (1H, s, Ar-H); $\delta$C (CDCl$_3$) 16.0, 16.2, 16.9, 31.0, 34.4, 126.3, 132.7, 133.3, 133.7 and 135.1; m/z 370 (M$^+$) (Found: C, 74.64; H, 8.24, C$_{23}$H$_{30}$S$_2$ (370.62) required C, 74.54; H, 8.16).

7. Photolysis of disulfide 19b to give 4,5,6,8,12,13,15,16-octamethyl-[2.2]metaparacyclophane (16b):

A solution of 19b (480 mg, 1.25 mmol) in triethylphosphate (100 mL) was irradiated with a 100 W high pressure mercury lamp (Riko Kagaku Sangyo Co.) for 6 h at room temperature in an argon atmosphere. A pyrex filter was used. After the reaction mixture was poured on to ice-10% NaOH solution (200 mL), it was stirred at room temperature for 3 h and extracted with CH$_2$Cl$_2$ (200 mL × 2). The CH$_2$Cl$_2$ extracts were washed with water (100 mL), and brine (100 mL), then
dried (Na$_2$SO$_4$) and evaporated in vacuo to leave a residue. This was chromatographed on silica gel (Wako C-300, 400 g) (hexane as eluent) to give a colourless solid. Recrystallization from hexane gave compound 16b as colourless prisms (304 mg, 71%), m.p. 187–189°C; $\delta_H$ (CDCl$_3$) 1.61 (6H, s, CH$_3$), 1.72 (3H, s, CH$_3$), 2.07 (3H, s, CH$_3$), 2.19 (6H, s, CH$_3$), 2.31 (6H, s, CH$_3$) and 2.60–3.18 (8H, m, CH$_2$); $\delta_C$ (CDCl$_3$) 15.83, 15.98. 16.07, 18.82, 26.85, 28.32, 129.38, 130.0, 130.5, 131.7, 133.9, 135.1 and 136.2; m/z 320 (M$^+$) (Found: C, 90.13; H, 10.19. C$_{24}$H$_{32}$ (320.52) required C, 89.94; H, 10.06).

Photolysis of 19a was carried out using the same procedure as described above to afford, in 76% yield, 4,5,6,12,13,15,16-heptamethyl[2.2]metaparacyclophane (16a), as colourless prisms, m.p. 176–178°C; $\delta_H$ (CDCl$_3$) 1.56 (6H, s, CH$_3$), 2.07 (3H, s, CH$_3$), 2.15 (6H, s, CH$_3$), 2.34 (6H, s, CH$_3$), 2.0–2.2 (2H, m, CH$_2$), 2.8–2.97 (4H, m, CH$_2$), 3.03–3.15 (2H, m, CH$_2$) and 5.08 (1H, s, Ar-H); $\delta_C$ (CDCl$_3$) 15.2, 15.7, 15.90, 15.92, 28.8, 31.9, 130.8, 130.9, 131.0, 131.7, 133.2, 135.3 and 135.6; m/z 306 (M$^+$) (Found: C, 90.21; H, 8.71. C$_{23}$H$_{30}$ (306.5) required C, 90.13; H, 9.87).

8. Photooxygenation of the [2.2]metacyclophane 6a:

A solution of 6a (100 mg, 0.33 mmol) in acetone (100 mL) was irradiated with a 100 W high pressure mercury lamp (Riko Kagaku Sangyo Co.) for 6 h at room temperature in air. A Pyrex filter was used. The reaction mixture was then evaporated under reduced pressure and the residue was chromatographed on silica gel (Wako gel C-300) using dichloromethane as eluent. The eluate was evaporated and the residue was recrystallized from acetone, giving 4,5,6,8,12,13,14-heptamethyl[2.2]metacyclophane-5,8-endoperoxide (9a) (77 mg, 70%), as colourless prisms (acetone), m.p. 80°C (decomp.); $\delta_H$ (CDCl$_3$) 0.02 (3H, s, CH$_3$), 1.26 (3H, s, CH$_3$), 1.90 (3H, s, CH$_3$), 1.88–1.95 (2H, m, CH$_2$), 2.17 (6H, s, CH$_3$), 2.24 (6H, s, CH$_3$), 2.36 (2H, ddd, J$=3.1$, 4.0 and 12.5 Hz, CH$_2$), 2.66 (2H, ddd, J$=3.1$, 3.6 and 12.7 Hz, CH$_2$), 3.03 (2H, ddd, J$=4.0$, 12.5 and 12.7 Hz, CH$_2$) and 6.53 (1H, s, Ar-H); m/z 338 (M$^+$) (Found: C, 81.24; H, 8.80. C$_{23}$H$_{30}$O$_2$ (338.49) required C, 81.61; H, 8.93).

9. Photooxygenation of the [2.2]metacyclophane 6b:

A solution of 6b (100 mg, 0.32 mmol) in acetone (100 mL) was irradiated and chromatographed similarly. The eluate was evaporated to afford a residue (100 mg) as a colourless solid which was found to be a mixture of endoperoxide 9b and bis-endoperoxide 10b in the ratio of 40:60 (Scheme 2) (determined from an $^1$H NMR spectrum). The residue was further chromatographed on silica gel (Wako gel C-300) using dichloromethane as eluent to give a colourless solid (95 mg). However, several attempts to isolate pure 9b and 10b failed.
4,5,6,8,12,13,14,16-Octamethyl[2.2]metacyclophane-5,8-endoperoxide 9b: δ<sub>H</sub> (CDCl<sub>3</sub>) 0.06 (3H, s, CH<sub>3</sub>), 1.47 (3H, s, CH<sub>3</sub>), 1.91 (6H, s, CH<sub>3</sub>), 1.79–1.86 (2H, m, CH<sub>2</sub>), 1.97 (3H, s, CH<sub>3</sub>), 2.22 (3H, s, CH<sub>3</sub>), 2.26 (6H, s, CH<sub>3</sub>), 2.30–2.40 (2H, m, CH<sub>2</sub>), 2.61 (2H, ddd, J = 3.1, 4.0 and 12.7 Hz, CH<sub>2</sub>) and 2.96 (2H, ddd, J = 4.0, 12.5 and 12.7 Hz, CH<sub>2</sub>.

4,5,6,8,12,13,14,16-Octamethyl[2.2]metacyclophane-5,8,13,16-bis(endoperoxide) 10b: δ<sub>H</sub> (CDCl<sub>3</sub>) 1.22 (6H, s, CH<sub>3</sub>), 1.51 (6H, s, CH<sub>3</sub>), 1.85 (12H, s, CH<sub>3</sub>), 2.12 (4H, d, J = 10.2 Hz, CH<sub>2</sub>) and 2.57 (4H, d, J = 10.2 Hz, CH<sub>2</sub>).

10. Photooxygenation of the [2.2]metaparacyclophane 16a:

A solution of 16a (100 mg, 0.33 mmol) in acetone (100 mL) was irradiated and chromatographed as for 6a above the resulting eluate was evaporated and the residue was recrystallized from acetone, giving 4,5,6,12,13,15,16-heptamethyl[2.2]metaparacyclophane-12,15-endoperoxide (20a) (69 mg, 62%), as colourless prisms (acetone), m.p. 90°C (decomp.); δ<sub>H</sub> (CDCl<sub>3</sub>) 0.78 (3H, s, CH<sub>3</sub>), 1.00 (3H, s, CH<sub>3</sub>), 1.53 (3H, s, CH<sub>3</sub>), 2.02 (3H, s, CH<sub>3</sub>), 2.06 (3H, s, CH<sub>3</sub>), 2.18 (6H, s, CH<sub>3</sub>), 2.35–3.20 (8H, m, CH<sub>2</sub>) and 5.95 (1H, s, Ar-H); m/z 338 (M<sup>+</sup>) (Found: C, 81.51; H, 8.97. C<sub>23</sub>H<sub>30</sub>O<sub>2</sub> (338.49) required C, 81.61; H, 8.93).


A solution of 16b (100 mg, 0.31 mmol) in acetone (100 mL) was irradiated and chromatographed as for 6a above the resulting eluate was evaporated and the residue was recrystallized from acetone, giving the mixture of 4,5,6,8,12,13,14,16-octamethyl[2.2]metaparacyclophane-5,8,13,16-bis(endoperoxide) (21b) in 57% yield with parent cyclophane 16b: δ<sub>H</sub> (CDCl<sub>3</sub>) 1.31 (3H, s, CH<sub>3</sub>), 1.32 (3H, s, CH<sub>3</sub>), 1.41 (3H, s, CH<sub>3</sub>), 1.43 (3H, s, CH<sub>3</sub>), 1.51 (3H, s, CH<sub>3</sub>), 1.91 (3H, s, CH<sub>3</sub>), 1.92 (3H, s, CH<sub>3</sub>), 2.01 (3H, s, CH<sub>3</sub>) and 2.0–2.8 (8H, m, CH<sub>2</sub>). However, several attempts to isolate pure 21b failed.

12. Crystallographic analysis of 6b:

C<sub>24</sub>H<sub>32</sub>, M = 320.5, triclinic, P-1 (no. 2), a = 7.9669(16), b = 8.3069(19), c = 8.6141(18) Å, α = 62.52(2), β = 64.37(2), γ = 65.64(2), V = 439.56(16) Å<sup>3</sup>, Z = 1, D<sub>c</sub> = 1.211 g cm<sup>-3</sup>, F(000) = 176, T = 140(1) K, μ(Mo-κα) = 0.067 mm<sup>-1</sup>, λ(Mo-κα) = 0.71073 Å.

Crystals are colourless prisms. One, ca 0.39 x 0.10 x 0.07 mm, was mounted in oil on a glass fibre and fixed in the cold nitrogen stream on an Oxford Diffraction Xcalibur-3 CCD diffractometer equipped with Mo-Kα radiation and graphite monochromator. Intensity data were
measured by thin-slice ω- and φ-scans. Total no. of reflections recorded, to θ\textsubscript{max} = 27.5°, was 7150 of which 2016 were unique (R\textsubscript{int} = 0.080); 1103 were ‘observed’ with I > 2σI.

Data were processed using the CrysAlisPro-CCD and –RED\textsuperscript{[51]} programs. The structure was determined by the direct methods routines in the SHELXS program\textsuperscript{[52]} and refined by full-matrix least-squares methods, on F\textsuperscript{2},s, in SHELXL\textsuperscript{[52]} The non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were included in idealised positions and their U\textsubscript{iso} values were set to ride on the U\textsubscript{eq} values of the parent carbon atoms. At the conclusion of the refinement, wR\textsubscript{2} = 0.103 and R\textsubscript{1} = 0.106\textsuperscript{[52]} for all 2016 reflections weighted w = [σ(F\textsubscript{o}\textsuperscript{2}) + (0.0430P)\textsuperscript{2}]\textsuperscript{1/2} with P = (F\textsubscript{o}\textsuperscript{2} + 2F\textsubscript{c}\textsuperscript{2})/3; for the ‘observed’ data only, R\textsubscript{1} = 0.049.

In the final difference map, the highest peak (ca 0.2 eÅ\textsuperscript{-3}) was close to C(8).

Scattering factors for neutral atoms were taken from reference\textsuperscript{[52]} Computer programs used in this analysis have been noted above, and were run through WinGX\textsuperscript{[54]} on a Dell Precision 370 PC at the University of East Anglia.

13. Crystallographic analysis of 16b:

C\textsubscript{24}H\textsubscript{32}, M = 320.52, monoclinic, P2\textsubscript{1}/n, a = 12.557(5), b = 8.833(3), c = 17.250(7) Å, β = 108.4873(16), V = 1814.4(13) Å\textsuperscript{3}, Z = 4, D\textsubscript{c} = 1.173 g cm\textsuperscript{-3}, μ (Mo-Kα) = 3.068 mm\textsuperscript{-1}, T = 296 K. Crystals are colourless prisms. Of 20741 reflections measured on a Rigaku Saturn CCD diffractometer, 4021 were independent, R\textsubscript{int} = 0.048; data were corrected for absorption on the basis of symmetry equivalent and repeated data (min and max transmission factors: 0.896, 0.997) and Lp effects. Structure solved by direct methods in Sir2002;\textsuperscript{[55]} refinement on F\textsuperscript{2} gave R\textsubscript{1} = 0.104 for 3757 data with F\textsuperscript{2} > 2σ(F\textsuperscript{2}), and wR\textsubscript{2} = 0.284 for all data, 218 parameters.

6.5 References:


52. G. M. Sheldrick, SHELX-97 - Programs for crystal structure determination (SHELXS) and refinement (SHELXL), Acta Crystallogr. 2008, A64, 112.
Summary

Small member bridged aromatic compounds have received widespread attention in organic chemistry as they are challenging targets for synthesis and have interesting physical properties. The chemical reactivity of small member bridged aromatic compound (Cyclophane) is strongly increased and quite unusual; sometimes, it is reminiscent of that of a localized cyclohexatriene-like system. The delocalization in benzene is due to the $\sigma$-system and counteracted by the $\pi$-system, it is proposed that bent benzene rings are full-fledged aromatics, i.e. olefin-like reactivity is predominantly a consequence of their high strain energy being dramatically relieved in the initial stages of such reactions. These properties of cyclophane took part in photo-oxygenation reaction with singlet Oxygen. The singlet oxygen reaction is a $[2 + 2]$ cycloaddition to an olefin-like double bond of benzene present of cyclophane to form an endoperoxide. These cyclic peroxides are sometimes of moderate stability but readily cleave thermally or photochemically into two carbonyl-containing fragments. Similarly, the reaction route from strained small member bridged aromatic compounds having methyl group undergoes iodine induced and Lewis acid catalyzed isomerization and transannular reaction to pyrene derivatives having alkyl groups played greater role of photo-physical properties in OLED materials.

Cyclophanes have also been used as intermediates in the total synthesis of complex natural products. In the last few decades much of the research on Cyclophanes has been focused on the inclusion of guest molecules into the cavity of the cyclophane and their conformational behaviour. Our work in this area has to do with the study of the effect of substituents on the conformational preferences of systems such as 8 and 16. In 8, good electron donating substituents favour syn-conformations and weak electron donating groups favour anti-conformations. Dipole effects appear to play an important role. On the other hand, the progressive increase in strain resulting from reduction in macrocycle ring size, or the introduction of additional conformational constraints, results in marked deviations from typical geometries. These strained cyclophane macrocyclic systems provide access to spatial orientations of functionality that would not be readily available in unstrained or acyclic analogs.

In this context, the present thesis entitled: “Synthesis, structure and reactions of small member bridged aromatic compounds” reports our efforts towards the design of a few noble cyclophane derivatives as probes for conformational analysis, endoperoxide reaction and OLED precursors. The motivation of this thesis is to investigate and discuss complete structural properties using
most modern techniques like $^1$H NMR, $^{13}$C NMR, NOESY, IR, UV-Vis, Fluorescence and single X-ray crystal analysis.

The first Chapter of the thesis briefly describes the recent literature concerning synthesis and development of small member bridged aromatic compounds and present proposed of study are presented.

In the second Chapter of the thesis provides a brief description of the existing literature concerning small member bridged aromatic compounds (Cyclopane) having different varieties. This chapter also provides chemical properties of cyclopanes like Lewis acid catalysed reaction and Photooxygenation reaction.

The third Chapter of the thesis describes overall synthetic strategies of [2.2]metacyclophanes from [3.3]metacyclophane via bis-sulfones by high-dilution method. Iodine induced and Lewis acid catalysed reaction of [2.2]metacyclphane suggest that the transannular and isomerization reaction routes might be useful for the preparation of pyrene derivatives having alkyl groups. Similarly a complete analysis of single crystal X-ray of [2.2]metacyclophanes was presented. Small-sized cyclophanes can be characterized by their aromatic components fixed in a forced proximity and their particular orientation. Considering their unique three-dimensional structure and conformational mobility, the small-sized cyclophanes possibly provide the fascinating supramolecular self-assembly upon coordination.

The fourth Chapter of the thesis briefly describes the total synthetic strategies of [2.2]metaparacyclophanes from dithia[3.3]metaparacyclophane via bis-sulfones by high-dilution method. Similarly, the preparation of [3.3]MPCP by coupling method and reduction of dione by woulfkishner reduction method. X-ray diffraction study of 5-tertbutyl-8-methoxy[2.2] - metaparacyclobaphane is described. Lewis acid catalysed reaction of [2.2]metacyclphane suggest that the isomerization and transannular reaction routes might be useful for the preparation of pyrene derivatives having alkyl groups. We studied the interactions of various bulgy groups with π-electrons clouds present on a benzene ring. It adopts unusual chemical conformations due to build-up of strain. Our work in this area has to do with the study of the effect of substituents on the conformational preferences of systems at 8-position. In MPCP, electron donating and electron withdrawing groups favor different conformations. Dipole effects appear to play an important role in conformation.

The fifth Chapter of the thesis describes the synthesis, structure and properties of substituted (1,3)Pyreno [3.3]metacyclophane and various substituted 2,11-dithia[3] metacyclo[3](1,3) -
pyrenophanes are presented. Compounds are shown the anti- and syn- conformation depends upon the different substitution present in benzene ring. These findings suggest that the through-space interaction between the non-bonding electron pairs of the oxygen atom of the methoxy group and the opposite pyrene π-electrons of the anti-conformer may disfavour the formation of the latter. VT-NMR studies showed that the compound behave as different conformation depends upon the temperature change. Similarly photo-physical properties of compounds were carefully examined in this chapter.

In the sixth Chapter of the thesis also describes total synthetic strategies of [2.2] meta- and metaparacyclophanes from 2,11-dithia[3.3]metaparacyclophane via bis-sulfones by high-dilution method. Photooxygenation of 4,5,6,8,12,13,14,16-octamethyl[2.2]meta-cyclophane, using a high pressure mercury lamp, produced a mixture of mono- and bis-endoperoxides, while the corresponding octamethyl[2.2]metaparacyclophane afforded only the bis-endoperoxide. Similar results were observed in the photooxygenation reaction of 4,5,6,12,13,15,16-heptamethyl[2.2]metaparacyclophane, which led to endoperoxidation of only the para benzene ring; this was attributed to the much larger degree of deformation of the para benzene ring than of the meta-benzene ring. The initial addition of singlet oxygen, through the concerted [4+2] cycloaddition by self sensitizer of cyclophane, forms an unstable endoperoxide. It will be used in photodynamic therapy. Similarly a complete analysis of single crystal X-ray analysis was presented.

In summary, many types of strained small member bridged aromatic compounds were selectively designed and synthesized. The design and synthetic methods for all compounds were fully presented. Lewis acid catalysed isomerization and transannular reaction routes are useful for the preparation of pyrene derivatives having alkyl groups. These results revealed that these materials like Polymethyl substituted pyrene are promising as host emitters for high efficiency OLEDs. On the other hand, we have synthesized pyrenophane compounds that the use of pyrene and benzene units with unique molecular architecture and the best way to studies the conformational changes of obtaining compound by using variable NMR technique. Chemical structures and photophysical properties for these compounds were determined by modern techniques and demonstrated. We have reported for the synthesis of poly methyl substituted [2.2]MCPs and [2.2]MPCPs, using higher pressure mercury lamp leading to the considerable extent compare to that of conventional methods. Synthesis and isolation of oxygenated octamethyl[2.2]-methacyclophane in laboratory condition are new result.