SYNTHESIS AND CONFORMATIONAL STUDIES OF NOVEL AROMATIC COMPOUNDS

by

WILLEM ANKER

B. Sc., University of Leiden, 1972
M. Sc., University of Leiden, 1977

A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

in the Department of Chemistry

we accept this dissertation as conforming to the required standard

G. R. Branton R. H. Mitchell
C. E. Picciotto F. P. Robinson
C. D. Scarfe R. J. Scheffer

WILLEM ANKER, 1982
UNIVERSITY OF VICTORIA
March 1982

All rights reserved. This dissertation may not be reproduced in whole or in part, by mimeograph or other means, without the permission of the author.
Supervisor: Dr. R.H. Mitchell

ABSTRACT

The synthesis of anti-15-phenyl-16-methyl-dihydropyrene, a molecule having an aromatic π-electron cloud within and more or less perpendicular to another π-system, has been achieved. $^1$Hmr. data indicate the phenyl ring to be freely rotating and, furthermore, the ortho protons of the phenyl substituent to be the most shielded aryl protons known today. No interaction could be detected between the two π-electron systems of the aforementioned dihydropyrene, either by UV or ESR (ENDOR) spectroscopy.

Ring current shielding calculations, based on the Johnson-Bovey tables, have been performed for the phenyl protons of this dihydropyrene using one to four current loops in the annulene skeleton. A four current loop model was shown to give a fair correlation between calculated and observed shielding values.

Four new 2,11-dithia[3.3]metacyclophanes with one or two internal phenyl substituents have been synthesized and shown to undergo a dynamic process of phenyl ring twisting. Although these thiacyclophanes were obtained as syn and anti conformers, only one conformer was found for the dithiacyclophane with both a phenyl group and a hydrogen atom as internal substituents. Based on an X-ray crystallographic structure determination, this thiacyclophane was shown to exist in the crystalline state as the syn conformer. The phenyl substituent underwent a similar dynamic process as described above. This fluxional process was also found in three new [2.2]metacyclophanes.
with internal phenyl substituents.

The barrier to the fluxional process in these systems has been determined using the coalescence temperature method. The twisting process of the internal phenyl substituent in the metacyclophanes is thought to be restricted by the non-bonded interaction between the ortho protons of the phenyl group and the methylene bridge protons.

Furthermore, it was shown that 2,11-dithia[3.3]metacyclophane (internal hydrogens) possessed the syn conformation in the solid state as well as in solution. Based on this observation many simple dithia[3.3]metacyclophanes have been reassigned the syn conformation.

A search for new synthetic methods to eliminate sulfur from thiametacyclophanes, in order to prepare the labile metacyclophane-dienes was so far unsuccessful that no improvements over existing methods were found.

EXAMINERS:

G.R. Branton
C.E. Picciotto
C.D. Scarfe

R.A. Mitchell
F.P. Robinson
R.J. Scheffer
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Abstract</th>
<th>ii</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table of Contents</td>
<td>iv</td>
</tr>
<tr>
<td>List of Tables</td>
<td>vii</td>
</tr>
<tr>
<td>List of Figures</td>
<td>ix</td>
</tr>
<tr>
<td>Acknowledgement</td>
<td>xi</td>
</tr>
<tr>
<td>A Glossary of Terms</td>
<td>xii</td>
</tr>
</tbody>
</table>

## PART ONE

### CHAPTER ONE

**Introduction**

1.1 Aromaticity: not a fragrant concept at all  
1.2 Ring Currents as a Criterion for Aromaticity  
1.3 Quantitative Aspects of the Ring Current Concept

### CHAPTER TWO

**Results and Discussion**

2.1 Possible synthetic Approach  
2.2 Synthesis of 2,6-Bis(bromomethyl)toluene  
2.3 Synthesis of 2,6-Bis(bromomethyl)-1,1'-biphenyl  
2.4 Synthesis of trans-15-Phenyl-16-methyldihydropyrene  
2.5 Photoisomerization of  
2.6 Possible Interaction between the π-cloud of the Phenyl Substituent and the π-cloud of the Annulene Ring in  
2.7 Assessment of Ring Current Models for
TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.7.1 Existing Models</td>
<td>76</td>
</tr>
<tr>
<td>2.7.2 Single Current Loop Model for 51</td>
<td>78</td>
</tr>
<tr>
<td>2.7.3 Multiple Current Loop Model for 51</td>
<td>81</td>
</tr>
<tr>
<td>CHAPTER THREE</td>
<td></td>
</tr>
<tr>
<td>Conformational Behaviour of Metacyclophanes</td>
<td>87</td>
</tr>
<tr>
<td>3.1 Introduction</td>
<td>87</td>
</tr>
<tr>
<td>3.2 [2.2]metacyclophanes</td>
<td>91</td>
</tr>
<tr>
<td>3.3 2,11-Dithia[3.3]metacyclophanes</td>
<td>104</td>
</tr>
<tr>
<td>PART TWO</td>
<td></td>
</tr>
<tr>
<td>CHAPTER ONE</td>
<td>124</td>
</tr>
<tr>
<td>Introduction</td>
<td></td>
</tr>
<tr>
<td>1.1 The Pitfalls of the Hofmann Elimination in Cyclophane Chemistry</td>
<td></td>
</tr>
<tr>
<td>CHAPTER TWO</td>
<td>130</td>
</tr>
<tr>
<td>Sulfur Eliminations with Double Bond Formation</td>
<td></td>
</tr>
<tr>
<td>2.1 Introduction</td>
<td>130</td>
</tr>
<tr>
<td>2.2 Rapberg-Bäcklund Rearrangement</td>
<td>130</td>
</tr>
<tr>
<td>2.3 Eliminations of Sulfoxides and Sulfones</td>
<td>133</td>
</tr>
<tr>
<td>2.4 Sulfilimines</td>
<td>135</td>
</tr>
<tr>
<td>2.5 Trithiocarbonates</td>
<td>136</td>
</tr>
</tbody>
</table>
TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.6 Thiol Elimination by Mercuric Acetate</td>
<td>137</td>
</tr>
<tr>
<td>2.7 Attempted Substitution of the Sulfur Group</td>
<td>138</td>
</tr>
<tr>
<td>2.8 Possible Olefin Formation by Double Benzyne</td>
<td>140</td>
</tr>
<tr>
<td>Stevens Rearrangement</td>
<td></td>
</tr>
<tr>
<td>2.9 Elimination of Trimethylsilanethiol</td>
<td>141</td>
</tr>
<tr>
<td>2.10 Elimination via Ester stabilized Sulfur Ylids</td>
<td>142</td>
</tr>
<tr>
<td>2.11 Some Mechanistic Considerations</td>
<td>143</td>
</tr>
<tr>
<td>2.12 Application of these Findings to the Metacyclophane System</td>
<td>145</td>
</tr>
<tr>
<td>CHAPTER THREE</td>
<td></td>
</tr>
<tr>
<td>Possible Future Work</td>
<td>147</td>
</tr>
<tr>
<td>Experimental</td>
<td>148</td>
</tr>
<tr>
<td>References</td>
<td>166</td>
</tr>
<tr>
<td>Appendix</td>
<td>182</td>
</tr>
</tbody>
</table>
LIST OF TABLES

<table>
<thead>
<tr>
<th>TABLE</th>
<th>PAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$^1$Hmr $\delta$ values of [4n+2]annulenes and [8]annulenes</td>
</tr>
<tr>
<td>2</td>
<td>Free energy of activation and coalescence temperature for the ring inversion process of some [4n+2]annulenes, as obtained by $^1$Hmr</td>
</tr>
<tr>
<td>3</td>
<td>$^1$Hmr $\delta$ values of some didehydro- and tetrahydro-[4n+2]annulenes</td>
</tr>
<tr>
<td>4</td>
<td>$^1$Hmr $\delta$ values of bridged [4n+2]annulenes.</td>
</tr>
<tr>
<td>5</td>
<td>$^1$Hmr $\delta$ values of annulenes and their dianions and tetraanions</td>
</tr>
<tr>
<td>6</td>
<td>$^1$Hmr (CDCl$_3$, 250 MHz) $\delta$ values and coupling constants (J) for assigned protons 118A, 118B and 119</td>
</tr>
<tr>
<td>7</td>
<td>$^1$Hmr (CDCl$_3$, 250 MHz) $\delta$ values and coupling constants (J) for dihydropyrene 51 and 38</td>
</tr>
<tr>
<td>8</td>
<td>$^{13}$Cmr $\delta$ values for dihydropyrene 51 and 38</td>
</tr>
<tr>
<td>9</td>
<td>UV $\lambda_{\text{max}}$ (nm) and $\varepsilon$ for some trans-dihydro- pyrenes</td>
</tr>
<tr>
<td>10</td>
<td>ENDOR frequencies (MHz) and hyperfine coupling constants $a_H$ (Gauss) for the radical anion of trans-15-phenyl-16-methyldihydropyrene 51</td>
</tr>
<tr>
<td>11</td>
<td>Shielding calculations for the single current loop model of 51</td>
</tr>
<tr>
<td>12</td>
<td>Shielding calculations for the four current loop model of 51</td>
</tr>
<tr>
<td>12</td>
<td>$^{13}$Cmr $\delta$ values for selected carbon atoms of 51 and</td>
</tr>
</tbody>
</table>
possible reference compounds; calculated shielding
\(\Delta\delta\) for these carbon atoms of 51 87
14 Activation parameters for phenyl substituted [2.2]
metacyclophanes 102
15 250 MHz \(^1\)Hmr \(\delta\) values and coupling constants (J) for
the aromatic protons of the cyclophane rings 59,
and 192 115
16 Activation parameters for phenyl substituted di-
thia[3.3]metacyclophanes 118
LIST OF FIGURES

FIGURE PAGE
1 Magnetically induced electron circulation and proton magnetic deshielding on benzene 6
2 $^1$Hmr (250 MHz) of 118A, 118B and 119; internal methyl and thiomethyl protons are not shown 51
3 $^1$Hmr (250 MHz) of dihydropyrene 38 and 51; internal methyl protons are not shown 55
4 $^{13}$Cmr (62.9 MHz) of dihydropyrene 51; only the aromatic region is shown 56
5 Ultraviolet and visible absorption spectra of trans-15-phenyl-16-methyldihydropyrene 51 (large spectrum) and trans-15, 16-dimethyldihydropyrene 38 68
6 ESR (top) and ENDOR spectrum (bottom) for the radical anion of trans-15-phenyl-16-methyldihydropyrene 51 72
7 Correlation of the upfield shifts due to the ring current in 38, 48, 49 and 51 78
8 Four current loop model for ring shielding calculation of dihydropyrene 51 83
9 Variable temperature $^1$Hmr (CDCl$_3$/CD$_2$Cl$_2$) of 119 99
10 Variable temperature $^1$Hmr (CDCl$_3$) of anti-59 112
11 Variable temperature $^1$Hmr (CDCl$_3$) of syn-59A 113
12 Variable temperature $^1$Hmr (CCl$_4$) of anti-192 116
13 Dynamic process of ring twisting of the phenyl
LIST OF FIGURES

FIGURE  PAGE

substituent of 2,11-dithia[3.3]metacyclophanes 119

14 Variable temperature $^1$Hmr (CDCl$_3$/CD$_2$Cl$_2$) of 119 120
I would like to thank my supervisor, Dr. R.H. Mitchell, for his guidance and encouragement throughout the course of this work. The support from members of the department is also gratefully appreciated.
GLOSSARY OF TERMS AND ABBREVIATIONS

13Cmr carbon-13 magnetic resonance (spectrum)
DIBAL diisobutylaluminium hydride
DMF N,N-dimethylformamide
DMSO dimethylsulfoxide
1Hmr proton magnetic resonance (spectrum)
HOAc acetic acid
ir infrared absorption spectroscopy
Me methyl
ms mass spectrum
NaBH₄ sodium borohydride
NBS N-bromosuccinimide
NMP 1-methyl-2-pyrrolidinone
Ph phenyl
ppm parts per million
THF tetrahydrofuran
PART I

SYNTHESIS AND CONFORMATIONAL BEHAVIOUR
OF A DIHYDROPYRENE AND SOME
METACYCLOPHANES WITH INTERNAL
PHENYL SUBSTITUENTS
CHAPTER ONE

INTRODUCTION

1.1 Aromaticity: not a fragrant concept at all.

If asked "what was the first aromatic compound ever isolated", most chemists would probably answer "benzene", crediting Faraday's detection of benzene\(^1\) as a pyrolysis product of oil in 1825. Yet slightly earlier, dipotassium croconate\(^1\), an aromatic compound of a totally different sort, was prepared by Gmelin\(^2\).

\[
\text{\ce{[\text{K}^+\text{OOC-C6H4-OOC-K}^+]}^2}^\text{H}
\]

However, benzene has to be credited for the development of the concept of aromaticity\(^3\).

The designation "aromatic" was first applied to a group of natural products such as methyl salicylate\(^2\) (oil of winter green); ane-thole\(^3\) (aniseed), vanillin\(^4\) (vanilla beans) but also compounds like menthol\(^5\) (peppermint oil) or camphor\(^6\) (camphor laurel), on account of their characteristic odours or flavours.

When it was recognized (Kekulé (1865)\(^4\)) that many of these substances were derivatives of benzene, the classification acquired a structural significance and the "aromatic" series implied "benzene and its derivatives".
Soon, however, the concept of aromatic character changed into a chemical criterion and became identified with the unique stability of the phenyl group and its preference for reacting by substitution rather than addition. As a consequence it was the properties of the transition state which were chiefly considered.

Although some justification of benzene-like stability was gained in the principle of the aromatic sextet\(^5\) (1925), the necessary theoretical basis was provided by Hückel\(^6\) in the early 1930's in terms of the Molecular Orbital (MO) theory. His conclusions have been summarized in the now familiar Hückel rule which states that monocyclic systems with \((4n+2)\pi\)-electrons will be aromatic, whereas those with \((4n)\pi\)-electrons will not. More recently the periphery modification of Platt\(^7\) and the polycyclic modification of Volpin\(^8\) have been put forward to broaden the existing Hückel rule.

MO theory also provided a way to calculate resonance energies, a property of the ground state of the molecule. This resonance energy, defined as the difference between the total \(\pi\)-electron energy of a given conjugated molecule and of a corresponding hypothetical reference structure, has often been utilized, with variable success, for understanding and predicting aromatic stability\(^9\). Redefinition of the
reference energy by Dewar\textsuperscript{10} in 1965, led to what is now known as Dewar resonance energies, considered to be the "aromaticity" values available.

Later modifications of resonance energy (RE) calculations (based on different definitions of the hypothetical reference energy) were made by Hess and Schaad\textsuperscript{11} (RE from \(\pi\)-bond energies), Herndon\textsuperscript{12} (RE from Kekulé structures) and independently by Aihara\textsuperscript{13} and the Zagreb group\textsuperscript{14} (RE from graph theory). The use of graph theory for resonance energy calculations has an advantage over Dewar's method in that it can be applied to ions and radicals. A graph theoretical approach has also been used by Herndon (RE from photoelectron spectra\textsuperscript{15} or bond orders\textsuperscript{16}) and Randić\textsuperscript{17} (enumeration of conjugated circuits). It should be pointed out that all these different methods for calculating resonance energies make use of or compare their values with the ones obtained by Dewar. A close fit is then considered to be proof of the validity of the new method.

Aromatic compounds are not only characterized by their resonance energy but also by, for instance, the anisotropy of their diamagnetic susceptibility and changes in bond lengths and charge distribution related to the delocalization of the \(\pi\)-electrons.

So there has thus been a continuous process of transforming the meaning of aromaticity from the chemical definition, which emphasizes the energy content of the molecule in the excited state, to the physical viewpoint, which underlines the properties of the molecules in the ground state.
1.2 Ring Currents as a Criterion for Aromaticity.

Since the calculation of resonance energies is strongly dependent on the chosen degree of accuracy and on the personal selection of standards, the idea of defining aromaticity by the physical concept of ring currents found wide application.

The introduction of this concept can be attributed to the free electron model of Pauling who calculated the diamagnetic anisotropy of benzene on the hypothesis that the abnormally large diamagnetic susceptibility in the direction perpendicular to the basal plane arises from the Larmor precession of the six \( \pi \)-electrons in orbits including many nuclei. This idea was later used by Pople to explain the NMR deshielding of the benzene ring proton with respect to the ethylene proton. According to this model, an applied magnetic field \( H^0 \), perpendicular to the plane of a benzene ring, will induce a circulation of the \( \pi \)-electrons, called a diamagnetic ring current. This ring current will then generate a second magnetic field \( H^1 \), opposed to \( H^0 \) (figure 1), which will have the effect of increasing the magnetic field outside the plane of the ring (deshielding), while the apparent field inside the ring is decreased (shielding). This simple ring current model led to a new definition of aromaticity as being the ability to sustain a magnetically induced ring current of \( \pi \)-electrons.

Ring current effects on proton shifts have played a crucial part in elucidating the chemistry of the annulenes. Initially, the only neutral annulene known was benzene \( \text{[6]} \)annulene), as the severely
FIGURE 1. Magnetically induced electron circulation and proton magnetic deshielding in benzene.

non-planar cyclooctatetraene 8 ([8]annulene) may be excluded from consideration. More annulenes soon became available 23; and at first their proton shifts 24 seemed to disagree with simple ring current theory. However, gross discrepancies disappeared when the conformational mobility of some of these compounds was realized and low temperature spectra were obtained where necessary. The higher homologs of benzene, the [4n+2]annulenes, have very low field absorptions for outer ring protons, and very high field absorptions for inner protons, as compared to the normal value of δ5.70* for the non-aromatic [8]annulene 8 (see table 1). The only exceptions to this rule are the

*All δ values in ppm from tetramethylsilane (TMS) as internal standard.
[6]annulene

[8]annulene

[10]annulenes

[14]annulenes

[18]annulene

[22]annulene

[30]annulene
TABLE 1: $^1$Hmr 6 values of [4n+2]annulenes and [8]annulene.

<table>
<thead>
<tr>
<th>Annulene</th>
<th>Inner H</th>
<th>Outer H</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>[6] - 7</td>
<td>5.67$^a$</td>
<td>7.27</td>
<td>25</td>
</tr>
<tr>
<td>[8] - 8</td>
<td>4.14$^a$</td>
<td>5.70</td>
<td>26</td>
</tr>
<tr>
<td>[10] - 9A</td>
<td>-</td>
<td>5.67</td>
<td>27$^f$</td>
</tr>
<tr>
<td>[10] - 9B</td>
<td>-</td>
<td>4.14</td>
<td>27$^f$</td>
</tr>
<tr>
<td>[14] - 10A</td>
<td>-0.61$^b$</td>
<td>7.88$^b$</td>
<td>29$^a$</td>
</tr>
<tr>
<td>[14] - 10B</td>
<td>3.55$^c$</td>
<td>6.82$^c$</td>
<td>29$^a$</td>
</tr>
<tr>
<td>[18] - 11</td>
<td>-2.88$^d$</td>
<td>9.25$^d$</td>
<td>29</td>
</tr>
<tr>
<td>[22] - 12</td>
<td>-0.40, -1.20$^e$</td>
<td>9.65 - 9.30$^e$</td>
<td>30</td>
</tr>
<tr>
<td>[30] - 13</td>
<td>no $^1$Hmr obtained</td>
<td>9.10 - 8.50$^e$</td>
<td>32</td>
</tr>
</tbody>
</table>

$^a$Spectrum taken at -40°C. $^b$Spectrum taken at -126°C.
$^c$Spectrum taken at -155°C. $^d$Spectrum taken at -60°C.
$^e$Spectrum taken at -90°C.

[10]annulenes$^{27}$. Spectroscopic evidence led to the proposed structures 9A and 9B for the two isolated isomers of [10]annulene$^{27f}$. This assignment turned out to be consistent with theoretical calculations$^{28}$. Considering the higher [4n+2]annulenes, controversy still exists about the ground state structure of [18]annulene$^{11}$, whereas [26]annulene has not been prepared yet. Unfortunately, the "aromaticity" of [30]annulene$^{13}$ could not be tested by $^1$Hmr$^{32}$.

Although the [4n+2]annulenes, possessing 14 to 22 carbon atoms, are fluxional (see table 2), they all show a diamagnetic ring current effect, i.e., the outer protons absorbing to low field, the inner protons to high field. Compounds exhibiting this phenomenon are now
TABLE 2. Free energy of activation and coalescence temperature for the ring inversion processes of some [4n+2]annulenes, as obtained by ^1Hmr.

<table>
<thead>
<tr>
<th>Annulene</th>
<th>( \Delta G^# ) (kJmol(^{-1}))</th>
<th>( T ) (coa.°C)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>[14] - 10A</td>
<td>42.4 (0°C)</td>
<td>-44°C</td>
<td>29a</td>
</tr>
<tr>
<td>[14] - 10B</td>
<td>30.1 (0°C)</td>
<td>ca. -110°C</td>
<td>29a</td>
</tr>
<tr>
<td>[18] - 11</td>
<td>60.1 (0°C)</td>
<td>41°C</td>
<td>29b</td>
</tr>
<tr>
<td>[22] - 12</td>
<td>53.6 (20°C)</td>
<td>20°C</td>
<td>30</td>
</tr>
</tbody>
</table>

called *diatropic*, while those with the reversed, paramagnetic ring current are called *paratropic*.^33^

Since the degree of \( \pi \)-electron delocalization is related to the planarity of the conjugated system, stronger "ring currents" are expected in more rigid annulenes. One such group are the dehydroannulenes, prepared by Somdheimer \(^23\) and Nakagawa \(^34\), where the acetylene unit(s) increases the rigidity of the \( \pi \)-system.

An interesting example is 1,8-didehydro[14]annulene \(^{14}\) \(^{35}\) for which identical Kekulé structures can be drawn, as in the case of benzene. The rigidity of \(^{14}\) is indicated by the high field \(^1Hmr\) absorption of its inner protons: \( \delta -5.48 \). This implies a much larger
"ring current" for $14$ than for the flexible $[14]annulene\ 10A$.
Nakagawa has reported an efficient synthesis of the tetra substituted derivative of $14$ as well as the higher homologs of the didehydro-$[4n+2]annulenes\ 15\ \text{36}$. Unlike the various $[4n+2]annulenes$ (table 1),

all these didehydro- and tetradehydroannulenes have essentially the same geometry. This makes it possible to study the effect of increasing the value of $n$ in aromatic $(4n+2)\pi$-electron systems, keeping the geometry largely unchanged. It can be seen from the $^1$Hmr data (see table 3) that the diamagnetic shielding of the inner protons becomes progressively less as the value of $n$ increases. However, the ring current is still evident in the didehydro[30]annulene $15\ (m=5)$. This observation increases the uncertainty about the prediction $^{10a,37}$ that bond length equalization, a criterion for $\pi$-electron delocalization, is going to fail for large polyenes (somewhere between 22- and 26-membered rings).

Other constraints, apart from the acetylene-cumulene type bonds, for increasing the planarity of the annulene rings, have been put forward by Vogel $^{39}$ and Boekelheide $^{40}$. 
### TABLE 3. $^1$Hmr δ values of some didehydro- and tetrahydro-$[4n+2]$annulenes.

<table>
<thead>
<tr>
<th>Didehydro-annulenes 15</th>
<th>Inner H</th>
<th>Outer H</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>[14] m=1</td>
<td>-4.39</td>
<td>9.42</td>
<td>38</td>
</tr>
<tr>
<td>[18] m=2</td>
<td>-3.61</td>
<td>9.82, 9.32</td>
<td>38</td>
</tr>
<tr>
<td>[22] m=3</td>
<td>-0.83</td>
<td>9.16, 8.76</td>
<td>38</td>
</tr>
<tr>
<td>[26] m=4</td>
<td>αα. 1.9</td>
<td>8.23, 7.93</td>
<td>38</td>
</tr>
<tr>
<td>[30] m=5</td>
<td>3.5</td>
<td>7.5</td>
<td>38</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tetrahydro-annulenes 16</th>
<th>Inner H</th>
<th>Outer H</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>[18] m=1</td>
<td>-4.89</td>
<td>9.86</td>
<td>38</td>
</tr>
<tr>
<td>[22] m=2</td>
<td>-3.44</td>
<td>10.16, 9.67</td>
<td>38</td>
</tr>
</tbody>
</table>

Vogel noticed that, if the conformational mobility of the [10]annulene ring (9A and 9B) is locked by a bridging methylene group, the resulting molecule does exhibit aromatic character, whereas the open form is extremely reactive and not diatropic at all (table 1). The $^1$Hmr chemical shift data for some of these methano bridged annulenes are given in table 4.

These annulenes also constitute a group of compounds well suited for the correlation of the diamagnetic ring current of a $(4n+2)$ system with changes in geometry of the carbon framework. The stepwise bending of the carbon periphery of the syn-bridged [14]annulenes can be monitored by the increased shielding of the outer ring protons in the series (see table 4). From these data it is apparent that

*For X-ray data of methano bridged annulenes see reference 42.*
The relatively high degree of bending, achieved in this series, does not reduce the extent of \( \pi \)-electron delocalization significantly.

The same approach of a systematic departure from planarity has been used for the benzene ring in cyclophanes. For instance, for the \([n]\)paracyclophanes 28 and 29, although aromatic, an out of plane bending of the benzene ring has been reported of 9° and 17° respectively. Even the \([6]\)paracyclophane 30, in spite of a calculated
deviation of 22° from coplanarity of the benzene ring, is still "aromatic" by the ring current criterion. The Dewar isomers of [4]- and [3]paracyclophane (32 and 33 respectively) have also been isolated, but no isomerization to the corresponding paracyclophanes has been detected. So it seems that the still elusive [5]paracyclophane will form the crossover boundary between stability of benzene and Dewar benzene valence isomers, and therefore define the limit of aromaticity in the [n]paracyclophane series.

Comparison of syn-18 and anti-20 of the dimethano[14]annulenes shows a decrease in diatropicity for 20, as judged from the chemical shift values of the ring and bridge protons. X-ray data indicate bond length alternation for the carbon framework of 20, not because of deviation from planarity, but mainly due to the increased torsion angles (up to 75°) which prevent effective p-orbital overlap. However, for the comparable dioxo compound 22 no bond length alternation or increased torsion angles can be detected, so that, based on geometrical parameters, anti-22 is aromatic. On the other hand, 1 Hmr data show an increase shielding for the ring protons of 22 compared to 21 (same increase in shielding can be noticed in going from 18 to 20), which, together with chemical behaviour, implies an olefinic
nature for 22. This is a problem reminiscent to the controversy about the [18]annulene structure.\(^{31}\)

Vogel's methano bridged [10]annulene is not the only rigid, 10 π-electron system known. Recently, the tricyclic [10]annulene has been prepared, and chemical, as well as \(^1\)Hmr data indicate it to be aromatic.\(^{51}\)

Boekelheide, in his synthesis of trans-15,16-dimethyldihydro-pyrene, used an ethano bridge, instead of methylene bridges,
TABLE 4. $^{1}$Hmr $\delta$ values of bridged [4n+2]annulenes.

<table>
<thead>
<tr>
<th>Annulene</th>
<th>Inner H</th>
<th>Outer H</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>[10] - 17</td>
<td>-0.5</td>
<td>7.5 - 6.8</td>
<td>41</td>
</tr>
<tr>
<td>[14] - 18</td>
<td>0.9, -1.2</td>
<td>8.0 - 7.0</td>
<td>52a</td>
</tr>
<tr>
<td>[18] - 19</td>
<td>1.32, 0.53, -0.45</td>
<td>7.70 - 6.70</td>
<td>52b</td>
</tr>
<tr>
<td>[14] - 20</td>
<td>2.48, 1.88</td>
<td>6.33 - 6.20</td>
<td>52c</td>
</tr>
<tr>
<td>[14] - 21</td>
<td>---</td>
<td>8.53 - 7.81</td>
<td>52d</td>
</tr>
<tr>
<td>[14] - 22</td>
<td>---</td>
<td>7.78 - 6.85</td>
<td>52e</td>
</tr>
<tr>
<td>[14] - 23</td>
<td>---</td>
<td>8.95 - 8.30</td>
<td>58</td>
</tr>
<tr>
<td>[14] - 24</td>
<td>-1.82</td>
<td>8.17 - 7.82</td>
<td>52f</td>
</tr>
<tr>
<td>[14] - 25</td>
<td>-0.61, -1.16</td>
<td>7.88 - 7.55</td>
<td>52g</td>
</tr>
<tr>
<td>[14] - 26</td>
<td>0.52, -0.96</td>
<td>7.86 - 7.12</td>
<td>52h</td>
</tr>
<tr>
<td>[14] - 27</td>
<td>0.55, -0.11</td>
<td>8.10 - 6.95</td>
<td>52i</td>
</tr>
<tr>
<td>[14] - 34</td>
<td>---</td>
<td>8.08 - 7.90</td>
<td>58</td>
</tr>
<tr>
<td>[14] - 37</td>
<td>-2.06</td>
<td>8.74 - 7.50</td>
<td>55</td>
</tr>
<tr>
<td>[14] - 41</td>
<td>-1.67</td>
<td>7.92 - 7.53</td>
<td>51</td>
</tr>
</tbody>
</table>

to constrain the [14]annulene in a more or less planar structure, this type of bridging is based on the geometry of pyrene $^{34}$. Within this system, the internal hydrogens of $^{trans-15,16}$-dimethylidihydropyrene $^{40,54}$ appear in the $^{1}$Hmr at $\delta$-5.49, the highest value obtained so far for the [14]annulenes. However, the absolute record for any type of neutral annulene is held by hexahydrocoronene $^{43,56}$, where two of the
internal hydrogens resonate as high as $6.78$. Spectroscopic\textsuperscript{58} and theoretical\textsuperscript{17} findings suggest that pyrene $34$ and the two symmetrical isopyrenes $23$ and $35$, can be described as planar, vinyl-bridged $[14]$annulenes with perimeter type conjugation and, thus, as precursors of the annulenes $36 - 39$. There exists, therefore, a remarkable geometrical parallel between these three types of bridged $[14]$annulenes. The anthracene perimeter of $cis-36$ is slightly bent\textsuperscript{60} (saucer shaped), comparable to the curved shape of $cis$-dimethyldihydropyrene $37$, whereas the C-14 peripheries of $trans-38$\textsuperscript{61} and $trans-39$\textsuperscript{57} are both planar. A comparison of the $^1$Hmr chemical shift data for $36 - 37$ and $38 - 39$ (table 4) show that all three systems sustain a diamagnetic ring current equally well. However, Vogel’s system (methano bridged annulenes like $18$) is probably only suitable for $cis$-type $[14]$annulenes, since the $trans$ isomer of $36$, if synthesized, will be a very reactive species (c.f., anti-$20$).

Compared with these $[4n+2]$annulenes, the $[4n]$annulenes show a complete opposite magnetic effect, i.e., the outer protons absorb to high field, the inner protons to low field. This implies a paramagnetic ring current\textsuperscript{62}, flowing in the opposite direction to the diamagnetic ring currents found in the $[4n+2]$annulenes. In principle, it should be possible to convert a $[4n+2]$annulene into a $[4n]\pi$-system by adding or subtracting two electrons (and \textit{vice versa}). This change in total $\pi$-electrons should lead then to opposite ring currents in the neutral and charged species, and manifests itself from chemical shift values.
This type of transformation was first realized with cyclooctatetraene \( \text{8}^{63} \) (a [4n]annulene). However, the \(^1{\text{H}}\text{mr} \) of the dianion was almost identical to the neutral species, indicating that the deshielding effect of the diamagnetic ring current is balanced by the shielding due to the excess electron density. Also the paramagnetic ring current of \( \text{8} \) is impaired due to the non-planar (tub-shaped) structure of \( \text{8} \).

As was indicated before, trans-dimethyldihydropyrene \( \text{38} \) has a planar perimeter and is therefore an excellent candidate for testing the postulated ring current reversal. In fact the conversion of the neutral [14]annulene \( \text{38} \) to its dianion \( \text{38}^{2-} \) involves the transformation of a strongly diatropic to a strongly paratropic system, as indicated by the shift of the internal methyl protons: from \( \delta=4.25 \) to \( \delta=21.00^{64} \).

As examples for the reversed case, where a paratropic [4n]annulene is changed into a diatropic (4n+2)\( \pi \)-system, one can use 1,7-methano[12]annulene \( \text{44}^{65a} \) and the bridged [16]annulene \( \text{45}^{67} \). The crystal structure of \( \text{44} \) shows it to be nearly planar, but with complete bond alternation, due to increased torsion angles \( \delta^{66} \). On the other hand, compound \( \text{45} \) is expected to have a puckered perimeter \( \delta^{67} \). However, their respective dianions are diatropic (see table 5). For instance, the bridge methylene protons of \( \text{44} \) undergo an upfield shift from \( \delta=6.04 \) in the neutral molecule to \( \delta=4.44 \) in the dianion \( \delta^{65b} \).

Since a two-electron reduction of a [4n+2]annulene generates a paratropic species, further reduction to the tetraanion should then
provide the next higher homolog of the \([4n+2]\)annulene, and therefore restore the diatropicity of the system. This effect can clearly be seen from the dianion and tetraanion of pyrene 34 (table 5). The added electron density in the tetraanion \(34^-\), however, increases the shielding of the ring protons and therefore opposes the effect of the diamagnetic ring current. Acepleiadylene 46, which, like pyrene 34, can be described as a vinyl-bridged \([14]\)annulene \(^7\), shows a similar pattern for its dianion and tetraanion.

An interesting example of a peripheral ring current can be found in the di- and tetraanion of \([2_4]\)paracyclophanetetraene \(^7\). Whereas the neutral molecule 47 shows chemical shifts typical for aromatic and olefinic protons, the dianion \(47^-\) shows absorption of the internal benzene protons at \(6-7.07\). This implies a destruction of the
TABLE 5. $^1$Hmr $\delta$ values of annulenes and their dianions and tetraanions.

<table>
<thead>
<tr>
<th>Annulene</th>
<th>Inner H</th>
<th>Outer H</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>[8] - $^8$</td>
<td>---</td>
<td>5.70$^a$</td>
<td>63</td>
</tr>
<tr>
<td>[10] - $^8^2$-</td>
<td>---</td>
<td>5.70$^a$</td>
<td>63</td>
</tr>
<tr>
<td>[12] - $^{44}$</td>
<td>6.04</td>
<td>5.54 - 5.12</td>
<td>65b</td>
</tr>
<tr>
<td>[14] - $^{44^2}$-</td>
<td>-6.44</td>
<td>7.16 - 6.28</td>
<td>65b</td>
</tr>
<tr>
<td>[14] - $^{38}$</td>
<td>-4.25</td>
<td>8.67 - 7.98</td>
<td>64</td>
</tr>
<tr>
<td>[16] - $^{38^2}$-</td>
<td>21.60</td>
<td>-3.19 - 3.96</td>
<td>64</td>
</tr>
<tr>
<td>[16] - $^{45}$</td>
<td>4.81</td>
<td>4.50 - 0.59</td>
<td>67</td>
</tr>
<tr>
<td>[18] - $^{43^2}$-</td>
<td>-5.91,-5.99</td>
<td>8.53 - 6.68</td>
<td>67</td>
</tr>
<tr>
<td>[14] - $^{34}$</td>
<td>---</td>
<td>8.08 - 7.90</td>
<td>58</td>
</tr>
<tr>
<td>[16] - $^{34^2}$-</td>
<td>---</td>
<td>2.22 - 0.01</td>
<td>58</td>
</tr>
<tr>
<td>[18] - $^{34^4}$-</td>
<td>---</td>
<td>5.68 - 4.40</td>
<td>68</td>
</tr>
<tr>
<td>[14] - $^{46}$</td>
<td>---</td>
<td>8.33 - 6.89</td>
<td>69</td>
</tr>
<tr>
<td>[16] - $^{46^2}$-</td>
<td>---</td>
<td>1.53, -2.05</td>
<td>69</td>
</tr>
<tr>
<td>[18] - $^{46^4}$-</td>
<td>---</td>
<td>5.96 - 3.56</td>
<td>69</td>
</tr>
<tr>
<td>$^{47}$</td>
<td>7.37</td>
<td>7.37 , 6.48</td>
<td>71</td>
</tr>
<tr>
<td>[26] - $^{47^2}$-</td>
<td>-7.07</td>
<td>9.56 , 9.26</td>
<td>71</td>
</tr>
<tr>
<td>[28] - $^{47^4}$-</td>
<td>12.76</td>
<td>4.48 , 2.09</td>
<td>71</td>
</tr>
</tbody>
</table>

$^a$Signals of $^8$ and $^8^2$ are only 0.005 ppm apart$^63$; 65.70 taken from reference 26.

$\pi$-electron delocalization in the benzene rings of $^{47}$ in favor of a perimeter conjugation in the dianion. Further reduction to the tetra-anion $^{47^4}$- generates a paratropic species that can be considered as a [28]annulene, with the internal benzene protons resonating at 612.76.

The concept of a $\pi$-electron ring current in planar conjugated systems has clearly been of value in interpreting $^1$Hmr spectra. From
the data, obtained in the field of annulene chemistry, it can be con-
cluded that, in general, diatropicity gives a good qualitative picture
of the aromaticity of the system considered. However, diatropicity is
not the only magnetic property of conjugated (aromatic) systems that
has been related to "aromaticity".

Dauben, for instance, proposed the diamagnetic susceptibility
exaltation as a criterion for aromaticity. Although this method is
related to a theoretically well defined quantity, the London diamag-
etism, it is still empirical in character. Closely related is the
Faraday effect, proposed as a measure for aromaticity by Labarre.
Yet another ring current related approach is the determination of
bond alternation from \(^1\)Hmr coupling constants, based on the correla-
tion between ortho coupling constants and \(\pi\)-bond orders of benzenoid
hydrocarbons. However, partly due to the simple experimental
procedure, the use of \(^1\)Hmr chemical shift values as an indication of
aromaticity strongly outnumbers any of the above mentioned methods.

1.3 Quantitative Aspects of the Ring Current Concept.

Ever since Elvidge and Jackman, in 1961, proposed to use the
\(^1\)Hmr chemical shift as a quantitative measure of the ring current,
and consequently of aromaticity, much effort has been put into
deriving a mathematical equation that would relate the ring current
to the other, frequently used, aromaticity criterion, the resonance
energy. Although the existence of such a relation has been
questioned, Haddon recently showed that, indeed, for [4n+2]-
annulenes, a direct analytical relationship exists between ring current (RC), ring area (S) and resonance energy (RE).

\[ RC = \frac{3S}{2} \cdot RE \]  

(1)

Later, a slight modification of this formula was published by Aihara. This author also found a simple relationship to exist between the London diamagnetism, i.e., the contribution of ring currents to the magnetic susceptibility, and the resonance energy.

In order to obtain a quantitative assessment of the ring current, it is necessary to calculate the induced diamagnetic field (\( \mathbf{H}^* \) in figure 1), due to the \(-\)electron circulation, at any position in and around a molecule. A semi-empirical approach, based on the free electron model of Pople, has been described by Waugh and Fessenden (1957). They calculated the secondary field for benzene by assuming two circular current loops placed above and below the plane of the ring. This method has been put into graphical and tabular form by Johnson and Bovey. In 1972, Haddon pointed out that the use of line currents has distinct advantages over the Johnson Bovey method when applied to annulenes, for the carbon skeletons of annulenes larger than benzene are most often not circular at all. A further unique feature of Haddon's approach is that individual ring current intensities are not calculated, or even assumed, but are, instead, deduced from a statistical comparison with experimental \(^1\)Hmr shifts.

A quantum mechanical formulation of the ring current for benzene,
based on the London theory, was developed by McWeeney (1958). Later extension of this theory, to include protons located outside the plane of the benzene ring, led to the Haigh-Mallion tables (1972), which have a similar format to the earlier ones by Johnson and Bovey.

Although the Johnson-Bovey (JB) method and the Haigh-Mallion (HM) approach agree qualitatively with each other, in a quantitative sense there are some distinct differences. The JB tables overestimate the proton deshielding in or near the plane of the benzenoid hydrocarbons, while there is now sufficient evidence to show that the HM tables, although quite good in the deshielding region, underestimate the proton shielding above the plane of a benzene ring.

Boekelheide has shown that the $^1$Hmr and $^{13}$Cmr shift data for the alkylated dihydropyrenes correlate fairly well with the JB calculations. These comparisons, however, have been made under the assumption of a fixed conformation for the alkyl side chain in solution, which is not very likely.

\[38: R = \text{CH}_3\]
\[48: R = \text{CH}_2\text{CH}_3\]
\[49: R = \text{CH}_2\text{CH}_2\text{CH}_3\]
\[50: R = \text{Ph}\]
Our interests, therefore, went out towards a dihydropyrene with a more rigid substituent in the \( \pi \)-cavity, compared to the flexible alkyl chains in 48 and 49. We thought that a phenyl group would serve our purpose very well, better than, e.g., a tertiary butyl group or acetylene unit. The reason is that the phenyl group will give us three types of hydrogens at different levels above the plane of the dihydropyrene ring, whereas the other groups will only give one type of hydrogen at a fixed distance from the ring. Since it is possible that a molecule like 50, with two internal phenyl substituents, may have a different ring current intensity compared to 38, due to a change in geometry or magnetic effects by the phenyl groups, we decided to leave one methyl substituent in place. This would give us then the asymmetrically substituted dihydropyrene 51, where the internal methyl group serves as a reference to other substituted dihydropyrenes (e.g., 38, 48, 49) and the internal phenyl as a probe for the mapping of the
ring current effect above the ring of these dihydropyrenes. Apart from a synthetic challenge, it would also be of interest to see if there is any interaction between the π-cloud of the dihydropyrene ring and the π-cloud of the phenyl substituent, which is within and more or less perpendicular to the first one.
CHAPTER TWO
RESULTS AND DISCUSSION

2.1 Possible synthetic Approach.

Since dihydropyrene $51$ is the valence isomer of the metacyclophe
phanediene $51A$, it is not surprising that synthetic routes to the
dihydropyrene derivatives have evolved through $[2.2]$metacyclophanes
and $[2.2]$metacyclophehenedienes.

From the time of Pellegrin $^{90}$ (1899) until the late 60's the only
useful synthesis of $[2.2]$metacyclophanes was via the Würtz reaction,
involving dimerization of $m$-xylylendibromides by means of alkali
metals. Even with improved methods $^{91}$ this coupling reaction proceeds
in yields of only 20–30%, and furthermore, no useful methods were
available for converting the so obtained $[2.2]$metacyclophanes into the
corresponding dienes $^{92}$.

The breakthrough came in 1969, when Vögtle introduced the concept
of preparing dithiacyclophanes followed by oxidation and extrusion of
sulfur dioxide as a method of synthesizing $anti-[2.2]$metacyclophanes $^{93}$.
However, Mitchell and Boekelheide $^{94}$ should be credited with the first
useful synthesis of anti-[2.2]metacyclopahanedienes, which spontaneously
valence tautomerize to the trans-15,16-dihydropyrenes. Their approach involved the Stevens rearrangement of a dithiacyclophane followed by a Hofmann elimination. Later, the Wittig rearrangement was put forward as an alternative method for the ring contraction of dithiacyclophanes. A representative outline of these synthetic routes is shown in scheme 1.

![Scheme 1](image)

For the synthesis of dithiacyclophanes two routes are used extensively: the sodium sulfide coupling of a dibromide and the cyclization between a dibromide and a dithiol (see scheme 2).

To highlight the importance of the dithiacyclophanes and the subsequent ring contraction steps in the synthesis of dihydropyrenes, a comparison has been made in scheme 3 between the first synthesis of trans-15,16-dimethyldihydropyrene via a stepwise Wurtz coupling (route a) and that via the thiol-bromide cyclization (route b).
Apart from increased yields, the dithiacyclophane route has the further advantage that now for the first time syn- and cis-isomers respectively of [2.2]metacyclophanes and dihydropyrenes became accessible, because of the existence of anti- and syn-isomers in the thiacyclophanes. The thiol-bromide coupling made it also possible to obtain asymmetrically substituted [2.2]metacyclophanes and dihydropyrenes, of which our target molecule 51 is an example.

We therefore propose the synthetic pathway outlined in scheme 4.
as our route towards the synthesis of trans-15-phenyl-16-methylidihydropyrène 51. We predicted that a higher yield of 59 would be obtained using thiol 61 and bromide 54 rather than bromide 60 and thiol 55, because in the attacking nucleophile 61 the sulfur atoms are farther removed from the very bulky phenyl substituent than are the methylene carbons (the electrophile) in bromide 60. This increased distance between the phenyl substituent and the reactive center should then decrease the steric inhibition to coupling between 54 and 61 as compared to the coupling between 55 and 60.

2.2 Synthesis of 2,6-Bis(bromomethyl)toluene 54.

The bromide 54 was obtained via three different routes. The first two routes, both starting from dichloride 58, differ only in the conversion of the dicyanide 62. In one case di(isobutyl)aluminium hydride (DIBAL) was used to obtain 63\(^7\) whereas the other route involved basic hydrolysis followed by esterification with ethanol to yield diester 64\(^{92a}\). The conversion of dialcohol 65 to 54 proceeded much easier by using 48% aqueous HBr than by using \(\text{PBr}_3\).
The third route towards the synthesis of dibromide 54 involved a novel approach of starting with non-aromatic precursors and constructing a 1,2,3-trisubstituted benzene by a Diels-Alder reaction.

Early work by Hochf suggested that isophthalic acid derivative 70 was available by the sequence illustrated below. However, identification of the acid 70 was somewhat tenuous. The structure was mainly assigned by its melting point (305-306°C) as phthalic acids tend to melt below 200°C and the 4,6-dichloroisophthalic acid was known to
melt at 286°C.

In view of the simplicity and economy of this sequence further investigation by our group was warranted. It was reasoned that by using methyl crotonate \( \text{72} \) instead of ethyl acrylate \( \text{67} \) the desired diacid \( \text{71} \) would be obtained. Indeed, cycloaddition of \( \text{66} \) (prepared in 86% yield by addition of MeOH/KOH to hexachlorocyclopentadiene\(^1\)) and \( \text{72} \) gave a 60% yield of the Diels-Alder adduct \( \text{73} \) as a mixture of endo and exo isomers. Subsequent treatment with conc. sulfuric acid gave an almost quantitative conversion to the ketone \( \text{74} \) from which the diacid \( \text{71} \) could be obtained. However, treatment of ketone \( \text{74} \) with sodium methoxide in methanol gave directly the desired diester \( \text{75} \) in 70% yield. The removal of both chlorine atoms in \( \text{75} \) proceeded nearly quantitatively with Raney nickel (W-7). The dimethyl ester \( \text{76} \) can then be subjected to the same sequence of reactions as in the case of the diethyl ester \( \text{64} \) to yield \( \text{54} \).
The proposed mechanism for the rearrangement of 74 to 75 is outlined in scheme 5. As can be seen, intermediate 77 can open to give either 77A or 77C. However, it was established by the phthalein test that the final product was not a phthalic acid derivative which shows that the preferred way of ring opening occurs via 77A. From this point two possible allylic rearrangements can take place to give either 77B or 77D, which would then aromatize to give 75 or 78 respectively. The
\textsuperscript{1}Hmr of the final product showed a one proton singlet at 67.98, two singlets at 63.88 and 63.84 for the methyl esters and another singlet at 62.43 for the methyl group. This, together with the \textsuperscript{13}Cmr that clearly showed six different aromatic carbons, indicated 75 to be the final product since the symmetrical 78 will only give one signal for the methyl esters in the \textsuperscript{1}Hmr and only four aromatic carbons in the \textsuperscript{13}Cmr. This, therefore, indicates a mechanistic pathway via 77A and 77B as seen in scheme 5.

2.3 Synthesis of 2,6-Bis(bromomethyl)-1,1'-biphenyl 60.

Although bromide 60 was a known compound we attempted first to find a better route than the literature.\textsuperscript{103}

Since the above described cycloaddition of 66 and methyl crotonate 72, followed by ring opening of the adduct, turned out to be an economic way of preparing 75, we thought that the biphenyl ester 82 could be obtained in a similar fashion by using methyl cinnamate 79.
instead of 72 as dienophile. Conversion of 82 to bromide 60 will then be trivial (see conversion of 75 to 54).

Thus heating of diene 66 and dienophile 79 for four days at 160°C afforded 80. Since purification of 80 was problematic it was directly converted to ketone 81 by means of conc. sulfuric acid. This was then purified by column chromatography over silica gel. The first compound eluted from the column was a white solid that easily recrystallized from methanol to give colorless crystals in 20-30% yield, mp 112-113°C. This compound was assigned structure 84 based:
on the following spectroscopic data. The $^1$Hmr showed only one singlet at δ3.70. This, together with a C=O stretch at 1730 cm$^{-1}$ and a C=C stretch at 1610 cm$^{-1}$ in the ir spectrum, indicates an α,β-unsaturated methyl ester. A strong absorption in the ir spectrum at 715 cm$^{-1}$ is indicative for C-Cl stretch. The presence of chlorine is corroborated by its mass spectrum where the weak molecular ion at m/e 400 ($^{35}$Cl$_7$) showed the characteristic isotope pattern for a heptachloride; the fragmentation pattern is consistent with the loss of seven chlorine atoms each showing the correct isotope pattern.

A rationale for the formation of 84 can be found in the possible self-condensation of 66 where one molecule serves as a diene and another molecule as a dienophile. This then leads to the Diels-Alder adduct 83 (depicted as endo-adduct) which, on treatment with conc. sulfuric acid can give ketone 83A. Loss of carbon monoxide, followed by formation of hemiketal 83C can give, after elimination of hydrogen chloride, the fully aromatized heptachloro ester 84.

The second compound isolated from the reaction mixture of 66 and 79 was obtained in 40-50% yield (mp 158–159°C) and assigned structure 81A. This compound showed the standard isotope pattern for four
chlorine atoms in its mass spectrum with the molecular ion at m/e 378 ($^{35}\text{Cl}_4$). The $^1\text{Hmr}$ for 81A consisted of a multiplet at 67.43-7.11 for the five aromatic hydrogens, a doublet at 64.77 (J=9.5 Hz) for H-3, a singlet at 63.79 for the methyl ester and another doublet at 63.74 (J=9.5 Hz) for H-2. In the $^{13}\text{Cmr}$ the C-7 carbonyl appeared at 6187.1 and the ester carbonyl carbon at 5166.7.

According to the $^1\text{Hmr}$ as well as the $^{13}\text{Cmr}$ only one isomer of 81 is present. Since trans-methyl cinnamate 79 was used in the cycloaddition with 66, the Diels-Alder adducts 80 and 81 therefore should also have both substituents in a trans arrangement. It is known that a phenyl group is sterically more demanding than a carbomethoxy group. This then leads us to the indicated stereochemistry of 81A, where the phenyl substituent is placed in the endo position.

Having established the structure of ketone 81 as being 81A, it was then treated with sodium methoxide in methanol in order to give the expected biphenyl 82. Although, after column chromatography, the $^1\text{Hmr}$ of the first fraction indicated the presence of the desired compound 82, by showing three singlets at 68.02, 63.56 and 63.53 in the ratio of 1:3:3 plus a multiplet around 67.4, the main product, however, was assigned the structure 85 on the basis of its $^1\text{Hmr}$, $^{13}\text{Cmr}$ and mass spectrum. The $^1\text{Hmr}$ of 85 showed the expected multiplet at 67.42-7.11 for the aromatic protons, but furthermore there were two 1H doublets (J=8.5 Hz) at 64.69 and 63.48 respectively and three 3H singlets at 63.75, 63.64 and 63.50. The $^{13}\text{Cmr}$ showed three methyl carbons (quartet), two methine carbons (doublet), a carbonyl carbon at 6191.5 and a carbonyl ester at 6168.0. In the mass spectrum, the molecular ion at m/e
370 ($^{35}\text{Cl}_2$) showed an isotope pattern for two chlorine atoms. A strong signal at m/e 208 occurs in the mass spectrum of 85 and supports the proposed structure, since this mass number corresponds with the retro Diels-Alder fragment 2,5-dichloro-3,4-dimethoxycyclopentadienone 86.

The apparent substitution of the vinylic chlorine atoms in 81A by methoxy groups is not unprecedented in norbornene systems. Davies, for instance, reported that treatment of 87 with sodium methoxide yielded a mixture of the mono- and di-substituted norbornenes 88 and 89$^{105}$. The same reaction with 90 as substrate gave a 1:1 mixture of 91 and 92$^{106}$. However, the existence of a structure like 92 for our new compound 85 is not likely since this would give one extra proton.
signal. Further, the geminal dimethoxy group would not be stable towards strong acid whereas 85 was recovered unchanged after acid treatment.

Mechanistically these reactions of 87 and 90 can occur via an addition-elimination mechanism. However, homoconjugation between the double bond and the carbonyl in norbornene systems like 81A can invoke the participation of a non-classical ion like 93 in the substitution of the vinylic chlorides by methoxy groups. This type of conjugation is of course not possible in 87 and 90.

Spectroscopic evidence for the non-classical structure 93 can be found in 13Cmr where a strong upfield shift of the carbonyl carbon, in going from 94 to 95, is indicative for a structure like 93.
Thus a mechanism for the 1,2-substitution in 81A is much easier to envisage by using a non-classical structure like 93 than by using a direct addition-elimination mechanism, as proposed for 87 and 95. So we can conclude that spectroscopic and chemical data, as well as mechanistic considerations, are in support of the proposed structure 85.

Since the Diels-Alder approach for the synthesis of bromide 60 did not give the anticipated products an alternative synthesis involving biphenyl 100 was planned, which should give 60 on bromination with
N-bromosuccinimide (NBS). A Grignard coupling between \textsuperscript{96} and \textsuperscript{99} or between \textsuperscript{97} and \textsuperscript{98} could be expected to give the biphenyl \textsuperscript{100}. Because of steric reasons the first coupling would probably be preferred.

Naphthols\textsuperscript{108b,c} and phenols\textsuperscript{108a} have been converted directly to the corresponding bromides by the action of triphenylphosphine dibromide (\(\text{Ph}_3\text{PBr}_2\)), even \(\alpha\)-cresol \textsuperscript{101} gave a 72\% yield of the bromide \textsuperscript{102} via this method\textsuperscript{108b}. However, reacting 2,6-dimethylphenol \textsuperscript{103} with \(\text{Ph}_3\text{PBr}_2\), either in DMF or NMP or neat, did not yield the required bromide \textsuperscript{98}.

\[ \text{OH} \quad \rightarrow \quad \text{Br} \quad \rightarrow \quad \text{Br} \quad \rightarrow \quad \text{OH} \]

\textsuperscript{101} \textsuperscript{102} \textsuperscript{98} \textsuperscript{103}

Bromide \textsuperscript{98} was subsequently obtained by the diazotization\textsuperscript{109} of 2,6-dimethylaniline \textsuperscript{104}. The conversion of diazonium salt \textsuperscript{105} with 48\% aqueous HBr and CuBr gave a 62\% yield of bromide \textsuperscript{98}. This was then converted to the Grignard reagent \textsuperscript{99} and coupled with bromobenzene \textsuperscript{96}. Although biphenyl \textsuperscript{100} was formed, the yield (<10\%) necessitated that a more practical route to \textsuperscript{100} be devised.

\[ \text{NH}_2 \quad \rightarrow \quad \text{N}_2\text{Br} \quad \rightarrow \quad \text{Br} \]

\textsuperscript{104} \textsuperscript{105} \textsuperscript{98}

Vögtle\textsuperscript{103} had previously synthesized bromide \textsuperscript{60} by reaction of 2,6-dimethylcyclohexanone \textsuperscript{106} with phenyllithium to give alcohol \textsuperscript{107}.
which was then dehydrated by phosphoric acid, and then dehydrogenated with 10% palladium on charcoal to give biphenyl 100 in a claimed 44% overall yield.

However, we found this sequence required some modification. Thus cyclohexanone 106 with the Grignard reagent 97 (prepared from bromobenzene 96) gave alcohol 107. Subsequent dehydration of 107 proved to work better with p-toluenesulfonic acid than with phosphoric acid to yield the cyclohexene derivative 108. Both products, 107 and 108, were purified by vacuum distillation. Vogtle's next step, however, turned out to be problematic. Dehydrogenation of 108 using palladium on charcoal (10% or 30%) gave in our hands always a mixture of compounds containing 100, based on the strong singlet at δ1.96 in its $^1$Hmr and a molecular ion at m/e 182 in its mass spectrum. The mass spectrum also showed a molecular ion at m/e 188. This, together with multiplets at δ2.75-2.45 and δ0.80-0.50 in the $^1$Hmr, led us to the conclusion that the second compound in the mixture was in fact the cyclohexyl derivative 109. This implies that a disproportionation has taken place in the dehydrogenation of 108, where some part of the molecules serve as hydrogen donors while others function as acceptors. Since we were unable to separate 100 from 109, either by chromatography or distillation, we looked for different methods to oxidize 108 to 100.
The tendency of 108 to aromatize should increase upon the incorporation of an extra double bond in the cyclohexene unit. This was accomplished by the addition of bromine to 108 to form the dibromide 110 followed by dehydrobromination with potassium t-butoxide. The so obtained cyclohexadiene derivative 111 aromatized with 10% palladium on charcoal and gave us, after column chromatography, biphenyl 100 in 54% yield.

An even better yield of 100 was obtained when a quinone was used as an oxidizing agent for 108. It has been reported that 112 gave a 72% yield of 113 on dehydrogenation with p-chloranil 114 in refluxing xylene. We thus first tried dehydrogenation of 108 to 100 with quinone 116 (DDQ), the most powerful quinone reagent in routine use; this occurred smoothly in refluxing benzene. Economic reasons, however,
made us choose \( \beta \)-chloranil 115 for use on large scale. This quinone, although it has a greater reactivity than \( p \)-chloranil 114, has a lower oxidation potential than 116 and thus gave a reaction which was too slow in benzene but acceptable in xylene. Thus by using the reaction sequence indicated in scheme 6 we were able to increase the overall yield of 100 from the reported 44% to 64%.

Conversion of biphenyl 100 to the desired bromide 60 proceeded smoothly by adding N-bromosuccinimide in portions to a refluxing solution of 100 in carbon tetrachloride in the presence of catalytic amounts of benzoyl peroxide. However, recrystallization of 60 from methanol, as reported by Vögtle 103, gave only a 20% yield of bromide 60. The bulk of the crude material had been converted to the corresponding dimethyl ether 117 as indicated by its \( ^1 \)Hmr that, apart from
the usual aromatic protons at $\delta 7.40$, showed two singlets in the ratio of 2:3 at 64.11 and 63.20 respectively. A molecular ion at $m/e$ 242 in its mass spectrum was further proof for the existence of 117. Recrystallization from cyclohexane solved this problem and bromide 60 was subsequently obtained in 61% yield (mp 116-117°C). Therefore the low yield reported by Vögtle$^{103}$ (34%) for the NBS bromination of 100 may be explained by the formation of 117 during the recrystallization of 60 from methanol.

The normal procedure of converting bromide 60 into thiol 61 is by the action of thiourea in boiling ethanol followed by basic hydrolysis of the intermediate isothiouronium salt$^{97}$. Following this sequence Vögtle$^{103}$ obtained a 43% yield of thiol 61. However, keeping in mind the easy substitution of the bromine atoms of 60 by methanol to form 117, we decided to use tetrahydrofuran (THF) instead of ethanol as the solvent for the conversion of 60 into 61. This way we obtained thiol 61 in 94% yield (mp 66-68°C).

Thus, starting from 2,6-dimethylcyclohexanone 106 we have considerably improved the synthesis of dithiol 61 from the reported$^{103}$ 6% to a 37% overall yield.
2.4 Synthesis of trans-15-Phenyl-16-methyldihydropyrene 51.*

Coupling of bromide 54 and thiol 61 under high dilution conditions at room temperature, using potassium hydroxide in ethanol-benzene, gave, after chromatography over silica gel, a 20% yield of the desired dithiacyclophane as a mixture of anti-59 and syn-59A in the ratio of 7:1 (based on $^1$Hmr). 

To verify our statement (page 28) that the coupling between bromide 54 and thiol 61 would be more successful than the coupling of thiol 55 and bromide 60, we proceeded to attempt the coupling of 55 and 60 under the same conditions as described above. This time, however, the yield of the dithiacyclophane was only 6%, again as a mixture of anti-59 and syn-59A in the same ratio as obtained above. This proves that steric hindrance in the approach of the thiolate

* The Chemical Abstract now calls 51: trans-10b-phenyl-10c-methyl-10b,10c-dihydropyrene
nucleophile towards the methylene electrophile (of the bromide) is far less by using thiol 61 and bromide 54 than by using bromide 60 and thiol 55.

The yield of the dithiacyclophanes 59 and 59A could be further increased by coupling the bromide and thiol in refluxing ethanol instead of at room temperature. This yielded 59 and 59A in the ratio of 4:1 (based on $^1$Hmr) in about 40% overall yield. The separation of the anti- and syn-isomer 59 and 59A was quite tedious. Repeated column chromatography over silica gel gave pure anti-59 which, after recrystallization from benzene, yielded colorless crystals, mp 165°C. Those fractions from the column chromatography that showed (by $^1$Hmr) the presence of both isomers 59 and 59A with more of the syn-isomer 59A, were again chromatographed over silica gel to increase the yield of pure 59A. This was then repeatedly recrystallized from benzene/hexane to give 86 mg (0.6%) of pure syn-59A as colorless crystals, mp 170°C. Both isomers, 59 and 59A, showed a molecular ion at m/e 362 in their mass spectra and gave correct elemental analyses. The structure assignment of the pure anti- and syn-isomers 59 and 59A is based on their $^1$Hmr as compared with the $^1$Hmr of the anti- and syn-dimethyl-dithiacyclophanes 52 and 52A, which are not spontaneously interconvertible. In the $^1$Hmr, the protons of the internal methyl groups of 52 show an upfield shift due to the ring current of the opposite aromatic ring and appear as a singlet at 61.30, whereas the internal methyl protons of 52A are comparable with those of thiol 55 and appear at 62.54. In addition, the aromatic protons of 52 show the normal
anti-metacyclophane pattern at 67.4-7.0, whereas the aromatic protons of 52A are shifted upfield to 66.66, a common consequence of superimposing two parallel aromatic rings. The syn-conformation of 52A was later confirmed by X-ray crystallography.

In the $^1$H NMR for 59, we find a singlet at 61.56 for the internal methyl protons whereas the aromatic protons of the thiacyclophane are in the range of 67.46-7.02. The $^1$H NMR of 59A shows a singlet at 62.41 for the methyl protons whereas the aromatic protons are shifted
upfield to 66.99-6.75 as compared to 59. Thus comparison of these data with the ones given for thiacyclophanes 52 and 52A makes the assignment of the anti-conformation to 59 and the syn-conformation to 59A straightforward. It may be argued that the internal methyl group of 59A should experience a strong upfield shift because of the neighbouring phenyl substituent. However, from data that will be discussed in Chapter 3, we know that the phenyl group is not rigid but undergoes a partial rotation around the biphenyl bond. Therefore the methyl group experiences only a minor shielding by the phenyl substituent.

The next step towards the synthesis of dihydropyrene 51 is the ring contraction of thiacyclophane 59. This was done by the Wittig\textsuperscript{95} as well as the Stevens rearrangement\textsuperscript{94}, the latter giving better results.

Thus Wittig rearrangement of thiacyclophane 59 in dry THF using lithium diisopropylamide or n-BuLi, at 0°C or room temperature, followed by the addition of methyl iodide gave 118 as a mixture of isomers in

\[
\begin{align*}
\text{59} & \xrightarrow{\text{WITTIG}} \text{118} \\
\text{59} & \xrightarrow{\text{STEVENS}} \text{118}
\end{align*}
\]
37% yield. Alternatively, treatment of 59 with dimethoxycarbonium fluoroborate \(^{115}\) gave the Stevens salt \(^{59S}\) as a white powder in 96% yield. This salt \(^{59S}\) underwent a Stevens rearrangement upon treatment with potassium t-butoxide in dry THF and gave a 64% yield of \(^{118}\), again as a mixture of isomers. For its use in the Hofmann elimination reaction the mixture of isomers corresponding to \(^{118}\) need not be separated. However, careful chromatography of \(^{118}\) over silica gel gave the principal component in a pure state. Recrystallization from hexane afforded colorless needles, mp 157-158°C; its mass spectrum gave a molecular ion at m/e 390. This isomer has been assigned structure \(^{118A}\) based on its \(^{1}\)Hmr signals for the methylene-methine bridges of the [2.2]metacyclophane. Because we are dealing with the anti-conformation for \(^{118A}\), based on the upfield shift of the internal methyl protons at 60.87, the bridge protons are arranged in pseudoaxial or pseudoequatorial positions. Therefore; from the magnitude of the two coupling constants (\(J=4\) Hz, \(J=11.5\) Hz) found in both methine proton signals (H-1 and H-9) we can safely deduce that both thiomethyl groups are in the pseudoequatorial position. As a consequence, two of
the aromatic protons are strongly deshielded by these neighbouring sulfur atoms. The technique of double resonance was used to probe the coupling pattern for the bridge protons. This way, we were able to separate the six $^1H$ signals into two sets of coupled spin systems. Although the assignment of axial and equatorial protons in each set, based on the splitting patterns, is trivial, the correct assignment of H-1 and H-9 had to await the characterization of another isomer of 118, which we assigned structure 118B. Isomer 118B was obtained as a mixture of isomers from the same chromatography experiment that yielded 118A. Rechromatographing, followed by recrystallization from hexane, gave us 2 mg (0.3%) of 118B as white crystals, mp 162-163°C. Since the $^1H$mr showed only three $^2H$ signals for the bridge protons, it was obvious that we were dealing with a symmetrical structure like 118B or 118C where both thiomethyl groups are again in the pseudo-equatorial position, as indicated by coupling constants.

\[ \text{MeS} \quad \text{SMe} \]
\[ \text{118B} \]

\[ \text{MeS} \quad \text{SMe} \]
\[ \text{118C} \]

From mass spectral data of 118A and the desulfurized isomer 119, we can deduce that the preferred fragmentation pathway for these phenyl substituted [2.2]metacyclophanes is by symmetrical splitting of the
bridges as indicated by the dashed line for 118B. Thus, in the mass spectrum of 118B we find, apart from a molecular ion at \( m/e = 390 \), a strong signal (100%) at \( m/e = 211 \) corresponding to the fragment shown in 118B (see scheme 6). This implies that we are dealing with structure 118B instead of 118C.

Now, by simply comparing the chemical shifts of the methine protons H-1 and H-9 in 118A with H-1 in 118B, we can confidently assign the low field signal of the bridge protons in 118A to H-1 (64.26, see figure 2 and table 6). The assignment of some of the aromatic protons has been done by comparison between 118A, 118B and 119, and is straightforward, keeping in mind the deshielding effect of a neighbouring sulfur atom. The previously mentioned [2.2]metacyclophane 119 was obtained from 118A by desulfurization with Raney Nickel (W-7). Recrystallization from hexane gave colorless crystals of 119 (98%), mp 147°C. Its mass spectrum showed a molecular ion at \( m/e = 298 \). No efforts were made to solve the ABCD spin system for the bridge methylene protons in 119 (see figure 2).

The mixture of isomers 118 was subjected to a Hofmann elimination
FIGURE 2. $^1$Hmr (250 MHz) of 118A, 118B and 119; internal methyl and thiomethyl protons are not shown. Solvent (*) is CDCl$_3$. 
by, firstly, methylation with dimethoxycarbonium fluoroborate to give in 67% yield the anti-bis(sulfonium) salt, 120 which was then reacted with potassium t-butoxide in dry THF. This gave, after isolation and

![Chemical structure](image-url)
purification, pure \(trans\)-15-phenyl-16-methyldihydropyrene 51 in 41% yield. Recrystallization from cyclohexane gave dark green crystals, mp 159-160°C. The structure of 51 was confirmed by elemental analysis, \(^1\)Hmr and by its mass spectrum that showed a molecular ion at \(m/e\) 294 (16%) with peaks at 279 (30%) and 217 (22%), indicating the loss of a methyl or a phenyl group respectively, plus a peak at 202 (100%) which indicated the loss of both substituents leaving the stable pyrene 34 nucleus behind.

Our compound 51 is not the first dihydropyrene with different internal substituents at the C-15 and C-16 positions. Boekelheide\(^{118}\) reported the synthesis of 121, 122 and 123, where one substituent is kept as methyl while the other position is taken by a linear four atom chain. In the \(^1\)Hmr, the internal methyl group absorbs at \(\delta-4.25\) for 122 and at \(\delta-4.30\) for 121 and 123. Since the internal methyl group of 38 absorbs at \(\delta-4.25\), we can safely deduce from this that increasing the length of the substituent, with or without a remote functionality, does not noticeably alter the ring current effect and therefore the geometry of the dihydropyrene skeleton. It may be argued that the

\[
\begin{align*}
38: R &= \text{CH}_3 \\
51: R &= \text{Ph} \\
121: R &= \text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3 \\
122: R &= \text{CH}_2\text{CH}_2\text{CH}=\text{CH}_2 \\
123: R &= \text{CH}_2\text{CH}_2\text{OCH}_3
\end{align*}
\]
stereic requirements close to the annulene ring will be the same for a methyl group as for a n-butyl group so that no distortion of the annulene skeleton is expected by changing from \(38\) to \(121\). On the other hand, incorporation of a phenyl group, as in \(51\), may lead to some distortion because of the closer proximity of the ortho protons to the annulene perimeter. However, the \(^1\)Hmr of \(51\) shows the internal methyl protons to absorb at \(\delta-4.30\) so that we can conclude that also for \(51\) a normal dihydropyrene ring current is present.

The outstanding feature of the \(^1\)Hmr of \(51\) is the appearance of the ortho protons of the phenyl substituent at \(\delta2.80\), the most shielded aryl protons known today. Also the meta protons (\(\delta5.87\)) and para proton (\(\delta6.20\)) are shifted upfield, with respect to normal aryl protons, because of the dihydropyrene ring current. The \(^1\)Hmr \((250\text{ MHz})\) of \(51\) also shows two \(\text{AB}_2\) and one \(\text{AB}\) spin system for the annulene ring protons (the \(^1\)Hmr \((250\text{ MHz})\) of \(51\) and \(38\) are compared in figure 3 and table 7). The upfield triplet (\(\delta8.15\)) was assigned to H-9. This is reasonable when one assumes a geometry for \(51\) more or less identical with \(38\), which means that the phenyl group is not perpendicular to the plane of the annulene ring but slightly tilted towards H-9. This will induce, on average, a greater shielding for H-9 than for H-2. By using selective homo- and heteronuclear decoupling techniques, we were able to assign all the proton and carbon signals for \(51\) (for \(^1\)Cmr of \(51\) see figure 4 and table 8). In general, nonproton-bearing carbons are exempted from being assigned by single-frequency decoupling. However, these carbons are often subjected to long-range \(^1\)C-H couplings. Selective irradiation of a particular proton not only removes the one-bond
FIGURE 3. $^1$H NMR (250 MHz) of dihydropyrene 38 and 51; internal methyl protons are not shown.
FIGURE 4. $^{13}$Cmr (62.9 MHz) of dihydropyrene 51; only the aromatic region is shown.
### TABLE 7. $^1$H NMR (CDCl$_3$, 250 MHz) $\delta$ values and coupling constants ($J$) for dihydropyrene 51 and 38.$^a$

<table>
<thead>
<tr>
<th>Proton</th>
<th>51 $J$ (Hz)</th>
<th>38 $J$ (Hz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>H-2</td>
<td>8.31 J$_{2-3}=7.85$</td>
<td>8.12 J$_{2-3}=7.69$</td>
</tr>
<tr>
<td>H-3</td>
<td>8.69</td>
<td>8.61</td>
</tr>
<tr>
<td>H-5</td>
<td>8.66 J$_{5-6}=7.63$</td>
<td>8.65 J$_{5-6}=7.65$</td>
</tr>
<tr>
<td>H-6</td>
<td>8.51</td>
<td>8.65</td>
</tr>
<tr>
<td>H-8</td>
<td>8.75 J$_{8-9}=7.81$</td>
<td>8.61 J$_{8-9}=7.81$</td>
</tr>
<tr>
<td>H-9</td>
<td>8.15</td>
<td>8.12</td>
</tr>
<tr>
<td>CH$_3$-16b</td>
<td>-4.30</td>
<td>-4.24</td>
</tr>
<tr>
<td>H-2'</td>
<td>2.80</td>
<td>-</td>
</tr>
<tr>
<td>H-3'</td>
<td>5.87</td>
<td>-</td>
</tr>
<tr>
<td>H-4'</td>
<td>6.20</td>
<td>-</td>
</tr>
</tbody>
</table>

$^a$ $\delta$ values and coupling constants obtained by computer simulation, where necessary.

### TABLE 8. $^{13}$C NMR $\delta$ values$^a$ for dihydropyrene 51 and 38.$^b$

<table>
<thead>
<tr>
<th>Carbon</th>
<th>51$^b$</th>
<th>38$^c$</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-2</td>
<td>124.4</td>
<td>122.9</td>
</tr>
<tr>
<td>C-3</td>
<td>122.95</td>
<td>123.3</td>
</tr>
<tr>
<td>C-4</td>
<td>139.0</td>
<td>136.7</td>
</tr>
<tr>
<td>C-5</td>
<td>125.8</td>
<td>123.3</td>
</tr>
<tr>
<td>C-6</td>
<td>122.9</td>
<td>123.3</td>
</tr>
<tr>
<td>C-7</td>
<td>135.3</td>
<td>136.7</td>
</tr>
<tr>
<td>C-8</td>
<td>124.8</td>
<td>122.3</td>
</tr>
<tr>
<td>C-9</td>
<td>122.5</td>
<td>122.9</td>
</tr>
<tr>
<td>C-10</td>
<td>36.6</td>
<td>30.1</td>
</tr>
<tr>
<td>C-11</td>
<td>29.1</td>
<td>30.1</td>
</tr>
<tr>
<td>C-16b</td>
<td>14.9</td>
<td>14.1</td>
</tr>
<tr>
<td>C-1'</td>
<td>136.7</td>
<td>-</td>
</tr>
<tr>
<td>C-2'</td>
<td>124.1</td>
<td>-</td>
</tr>
<tr>
<td>C-3'</td>
<td>125.3</td>
<td>-</td>
</tr>
<tr>
<td>C-4'</td>
<td>125.0</td>
<td>-</td>
</tr>
</tbody>
</table>

$^a$ $\delta$ CDCl$_3$ = 77.0 ppm taken as reference point.

$^b$ Operating frequency: 62.9 MHz.

$^c$ Values taken from ref. 89 and corrected for $\delta$ CDCl$_3$ = 77.0 ppm, operating frequency: 25.2 MHz.
coupling but also all long-range couplings to carbon in which this proton is involved. The result is a line narrowing and therefore an increase in intensity for those quaternary carbons that exhibit long-range coupling with the irradiated proton. This way, we were able to assign carbons C-4 and C-7 as indicated in figure 4.

In the $^1$H NMR of 5 (figure 3) only one signal for the ortho protons of the phenyl group is present; this situation does not change between $+100 \, ^\circ \text{C}$ and $-100 \, ^\circ \text{C}$. On this basis, a structure like $\text{B}$, where the plane of the phenyl ring is parallel to the C$_{15}$-C$_{16}$ bond, can be ruled out because the two ortho protons ($H_o$) would experience two different magnetic environments, which would lead to separate chemical shifts for both protons. Therefore a situation like structure $\text{A}$, where the plane of the phenyl ring is perpendicular to the C$_{15}$-C$_{16}$ bond, or a freely rotating phenyl group, is more in line with the observation of only one signal for both ortho protons in the $^1$H NMR. However, we believe that the phenyl group undergoes free rotation for the following reasons.
Again assuming the same geometry for 51 as for 38 than, by using the X-ray data of 38, and taking the standard benzene bond lengths and bond angles for the phenyl group, we calculate the minimum distance of H\textsubscript{O\textsubscript{O}} to the mean plane of the annulene ring as 1.77 Å. From the \textsuperscript{1}Hmr of [2.2]metaparacyclophane-1,9-diene 124,\textsuperscript{119} we know that the meta-bridged benzene ring undergoes a fast ring inversion rendering the four protons of the para-bridged benzene ring into a singlet. Only below -100°C two separate signals are observed for these protons (coalescence temperature: T\textsubscript{c} = -96°C). During this easy process of ring inversion (\(\Delta G^\ddagger = 34.7 \text{ kJmol}^{-1}\)), H-8 penetrates into the aromatic \(\pi\)-electron cloud of the para-bridged benzene ring. The crystal structure of 124\textsuperscript{120} showed the two benzene rings to be inclined towards each other at an angle of 41°. In this position, the distance of H-8 to the plane of the para-bridged benzene ring is 2.16 Å. Now, if the meta-bridged ring is brought perpendicular to the para-bridged ring, but without otherwise distorting bond angles or bond lengths, this distance becomes 1.59 Å. Thus, taking collectively into account our calculated value of 1.77 Å for the distance of the ortho hydrogens to the plane of the ring in 51, the easy process of conformational flipping for 124 and the invariability of the \textsuperscript{1}Hmr of 51 between
+100°C and -100°C, we conclude that the phenyl substituent in dihydropyrene 51 is freely rotating.

Having successfully synthesized trans-15-phenyl-16-methylidihydropyrene 51, we turned our attention towards the preparation of the cis-isomer 128. This dihydropyrene 128 should be accessible by a similar route as the one used for the synthesis of trans-51, the only difference being that syn-59A instead of anti-59 has to be used. Mitchell and Boekelheide55 reported that Stevens rearrangement of syn-52A, followed by Hofmann elimination, gave 37 (as well as 38), the first example of a cis-substituted dihydropyrene. The formation of both 37 and 38 from 52A implies that a

![Diagram of Stevens and Hofmann rearrangements](image)

conformational inversion has taken place during the Stevens rearrangement of 52A. This is in accord with the postulated diradical mechanism for this type of rearrangement of sulfonium ylids 121. However, no inversion took place during the Stevens rearrangement in the recently reported 122 syntheses of the annelated cis-dimethyl-dihydropyrenes 125 and 126. On the other hand, Wittig rearrangement of syn-52A gave almost 100% inversion 95, so that after Hofmann...
elimination, only trans-38 will be obtained. We therefore subjected syn-59A to the sequence of Stevens rearrangement and Hofmann elimination, hoping to isolate cis-128. Thus, reaction of 59A with dimethoxyxycarbonium fluoroborate gave 88% of the sulfonium salt which on treatment with potassium t-butoxide gave 11 mg (24%) of rearranged product 127 that, based on $^1$Hmr, closely resembled 118 (no separation of isomers was attempted). This implies that an inversion from syn to anti has taken place during the rearrangement of 59A. However, subsequent treatment of the bis(sulfonium) salt of 127 with potassium t-butoxide in dry THF (Hofmann elimination) at 0°C did not yield
any identifiable products. Decreasing the temperature of the Hofmann elimination to -30°C did not change this result. Since the amount of pure syn-59A was limited, subsequent tries were done with 1:1 mixtures of 59 and 59A. However, the outcome was invariably the same: only trans-51 was obtained, no cis-dihydropyrene 128 could be detected.

2.5 Photoisomerization of 51.

One of the interesting aspects of dimethylidihydropyrene 38 is its reversible photochemical valence tautomerization into the [2.2] metacyclophane-1,9-diene 38A. This can be viewed as a specialized example of the more general cis-stilbene to 4a, 4b-dihydrophenanthrene isomerization 124. The tautomerization between 38 and 38A, as well as in many derivatives of 38, has been well studied by Blattmann and Schmidt 125. Apart from 38, this type of tautomerization has also been found in 48 123b and 49 123c and in the benzannelated 129 126 whereas for 130 127 and 131 122 no diene could be detected on irradiation with visible light. The dark reaction is very sensitive to the nature of the internal substituent and is, for instance, six times faster for 48 than for 38 123c. However, the correlation of the rate to the bulk of the internal substituent is not consistent, for the rate of the dark
reaction for 49 lies intermediate between 38 and 48. Since the protons of the open form (the diene) do not overlap with those of its isomeric dihydropyrene, $^1$Hmr can be used to monitor this process of valence tautomeration. However, irradiation of a solution of 51 in C$_6$D$_6$ with a tungsten lamp (General Electric, model MG, 650 Watt) did not result in any change in the $^1$Hmr of 51. Based on the mechanism of the Hofmann elimination, diene 51A will be formed first and will then rapidly isomerize to 51. And indeed, column chromatography in the dark of the Hofmann elimination product gave, in the first fraction, a mixture of 51 and 51A as based on $^1$Hmr. The presence of 51A is indicated in the $^1$Hmr by a singlet at 61.70 for the internal methyl protons, an AB quartet ($J=13$ Hz) at 66.69 and 66.35 for the bridge olefinic protons and by further signals around 67.05–6.45.
Efforts to separate 51A from 51 were unsuccessful because of the easy isomerization of 51A to 51. Irradiation of this mixture of 51 and 51A with visible light (30 seconds) led to a quantitative conversion of 51A to 51 based on the complete disappearance of the above mentioned signals in the $^1$Hnmr. Since the phenyl group in 51A is not able to rotate freely as in 51, we can state that 1) the relief of steric interaction of the bulky substituents with the metacyclophane ring in 51A, 2) the loss of strain energy of the twisted double bonds and 3) the gain of a planar (14 $\pi$-electron system more than offsets the loss of delocalization energy of the two benzene rings in 51A on isomerization to 51.

2.6 Possible Interaction between the $\pi$-cloud of the Phenyl Substituent and the $\pi$-cloud of the Annulene Ring in 51.

The interaction of non-conjugated $\pi$-electron systems has attracted great theoretical and experimental interest. It is clear that in neutral molecules experimental evidence for such interactions should be sought in spectral and ionization properties.
As was already reported by Cram, the face to face crowding of the benzene rings in [m.n]paracyclophanes resulted in a shift to longer wavelength (bathochromic), accompanied by a loss of fine structure, in the electronic spectrum of these compounds as compared to the open chain analog 136. For instance, [4,4]paracyclophane 132 still showed the same features in its UV spectrum as the open form 136, whereas for [4,3]paracyclophane 133, a bathochromic shift and a marked decrease in fine structure were already noticeable. This shift in wavelength and loss of fine structure became even more pronounced in 134 and 135.

These phenomena can be attributed, in part, to the concomitant bending of the benzene rings upon shortening the bridges, since [8]paracyclophane 28 showed a minor bathochromic shift and loss of fine structure as compared to the higher [n]paracyclophanes. This trend continues for 29 and 30; the bathochromic shifts, however, are smaller than in the case of the [m.n]paracyclophanes.

The same wavelength shift and structure loss can be seen in the UV spectrum of 137, as compared to 138, where the endo carbomethoxy group restricts the rotation of the two phenyl groups.

\[
\begin{align*}
&\text{132: } m=n=4 \\
&\text{133: } m=4, n=3 \\
&\text{134: } m=n=3 \\
&\text{135: } m=n=2 \\
&\text{136}
\end{align*}
\]
The more interesting cases, however, are those where the two \( \pi \)-systems are perpendicular and in close proximity to each other, since this is in fact the situation we encounter in our dihydropyrene 51. Two ways of obtaining mutually perpendicular \( \pi \)-electron systems are via spiro systems like A or via tricyclic systems like B. In "spiropolyenes" like A, the orbital interaction is through-space 129 and this leads to a new kind of homoconjugation called spiro-conjugation 130. This type of interaction manifests itself in the electronic spectra of spiro compounds where normally a bathochromic shift is observed as compared to the non-spiroannelated compound. A similar through-space orbital effect is evident in norbornadiene 139 which also shows a bathochromic shift in its UV spectrum as compared to the monoenne 140.
Gleiter explained the strong bathochromic shift in the UV spectrum of 141 ($\lambda_{\text{max}}$: 300 nm) as compared to 142 ($\lambda_{\text{max}}$: 220 nm), by a strong through-bond interaction between the π-orbitals of the double bond and the σ-bonds of the cyclobutane ring. The strong bathochromic and hyperchromic shift observed for 143, as reported by Mitchell and Sondheimer, can therefore be explained by a similar type of through-bond interaction. Thus, in case there is an interaction between the two perpendicular π-systems of 51, we may expect a shift to longer wavelength in the electronic spectrum with a possible loss of fine structure as compared to the spectrum of dimethyldihydro- pyrene. In figure 5, the spectra of 51 and 38 have been depicted whereas in table 9 a comparison of the absorption maxima and extinction
FIGURE 5. Ultraviolet and visible absorption spectra of trans-15-phenyl-16-methyldihydropyrene $51$ (large spectrum) and trans-15,16-dimethyldihydropyrene $38$ (insert; spectrum taken from reference 98b).
Table 9. UV absorption (nm) and € for some fluorophosphates.

<table>
<thead>
<tr>
<th>Substance</th>
<th>λ (nm)</th>
<th>ε (M^(-1) cm^-1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclohexane</td>
<td>240</td>
<td>530</td>
</tr>
<tr>
<td></td>
<td>250</td>
<td>480</td>
</tr>
<tr>
<td></td>
<td>260</td>
<td>430</td>
</tr>
<tr>
<td></td>
<td>270</td>
<td>380</td>
</tr>
<tr>
<td></td>
<td>280</td>
<td>330</td>
</tr>
<tr>
<td></td>
<td>290</td>
<td>280</td>
</tr>
<tr>
<td></td>
<td>300</td>
<td>230</td>
</tr>
<tr>
<td></td>
<td>310</td>
<td>180</td>
</tr>
<tr>
<td></td>
<td>320</td>
<td>130</td>
</tr>
<tr>
<td></td>
<td>330</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>340</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>350</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>360</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>370</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>380</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>390</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>400</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>410</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>420</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>430</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>440</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>450</td>
<td>0.0005</td>
</tr>
<tr>
<td></td>
<td>460</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td>470</td>
<td>0.00005</td>
</tr>
<tr>
<td></td>
<td>480</td>
<td>0.00001</td>
</tr>
<tr>
<td></td>
<td>490</td>
<td>0.000005</td>
</tr>
</tbody>
</table>

Note: The values represent typical UV absorption data for cyclohexane.
coefficients of a series of trans-dihydropyrenes has been made. From figure 5 we see that no loss of fine structure is evident for 51 as compared to 38. Furthermore, a comparison of the absorption maxima (table 9) shows that the whole spectrum of 51 is shifted ca. 4 nm to longer wavelength with the exception of the peak at 481 nm which is shifted 18 nm to longer wavelength as compared to the corresponding maximum in the spectrum of 38 (463 nm). This single shift may therefore be related to a possible interaction of the two π-clouds in 51. However, when we compare 51 with the other known asymmetrically substituted dihydropyrenes, i.e., 121, 122, and 123, we see (table 9) that these three compounds have a comparable absorption maximum in their electronic spectra (481 - 485 nm) as the one already mentioned for 51 (481 nm). Therefore, the observed bathochromic shift of this peak (481 nm in 51) with respect to the one in the spectrum of 38 (463 nm) may be simply due to the increased size of the substituent rather than to π-π interaction, since 121, 122, and 123 do not have a chromophore close to the annulene ring system.

Another technique that may shed some light on the possible interaction between the two π-clouds of trans-15-phenyl-16-methyldihydropyrene...
pyrene 51 is ESR spectroscopy. For this purpose, the radical anion 51\(^{−}\) was prepared by reduction of 51 with potassium metal using 1,2-dimethoxyethane (DME) as solvent. Since direct exposure of the DME solution of 51 to the surface of potassium may lead to a two electron reduction to form the dianion, the reduction was carried out in two steps. Firstly, generation of solvated electrons in DME and, secondly, reaction of 51 with these solvated electrons. Both steps have to be carried out at low temperature (−80°C). The ESR-spectrum obtained thereupon is shown in figure 6. Increasing the temperature stepwise from −80°C to +20°C did not alter the observed signal, i.e., no fine structure could be detected. The overall triplet shape of the spectrum (figure 6) is due to electron spin coupling with H-2 and H-9 which should be of comparable magnitude (ca. 5.5 G*). This assignment was borne out by the large hyperfine splittings of 5.46 G and 5.48 G found for the H-2 protons of the radical anions of 38\(^{136}\) and 40\(^{137}\) respectively. Coupling constants to other hydrogens in these two systems were smaller than one. Unambiguous assignment of the 5.46 G coupling to H-2 in 38 was made by preparation of the radical anion of the 2,9-dideutero derivative of 38\(^{136}\). The featureless structure of the ESR spectrum of 51 is not too surprising when we consider the theoretical number of lines possible for 51\(^{−}\). Assuming a delocalization of the odd electron over both π-systems, a total of 23,328 lines can be found for 51\(^{−}\) whereas for 38\(^{−}\), only 525 lines are theoretically available. Even by ignoring interactions of the electron with the two substituents

* hyperfine coupling constants are expressed in Gauss (G).
FIGURE 6. ESR (top) and ENDOR spectrum (bottom) for the radical anion of \textit{trans}-15-phenyl-16-methyldihydropyrene 51. The numbers above the ENDOR spectrum refer to the frequencies listed in Table 10. Both spectra recorded at \(-80\, ^\circ\mathrm{C}\) on a Bruker ER 200 tt.
in $51^-$, we still calculate the number of lines in the ESR spectrum of $51^-$ to be more than four times as great as for $38^-$. 

As in $^{1}Hmr$, the technique of double resonance can be used to simplify ESR spectra. For this reason, the electron nuclear double resonance (ENDOR) spectrum of $51^-$ was recorded (figure 6). The ENDOR spectrum consists of a series of doublets centered around the free proton frequency ($v^p_n$). The number of lines to highfield of $v^p_n$ is equal to the number of sets of equivalent protons that undergo interaction with the odd electron in the radical anion. As can be seen from figure 6, seven lines are recorded in the ENDOR spectrum of $51^-$ indicating seven different types of protons. In table 10, the observed ENDOR frequencies and coupling constants for $51^-$ are tabulated.

<table>
<thead>
<tr>
<th>ENDOR frequencies</th>
<th>Line position</th>
<th>$a_H$ (Gauss)</th>
<th>Proton</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.82</td>
<td>5'</td>
<td></td>
<td>CH$_3$</td>
</tr>
<tr>
<td>13.26</td>
<td>4'</td>
<td>0.22</td>
<td></td>
</tr>
<tr>
<td>13.44</td>
<td>3'</td>
<td>0.51</td>
<td></td>
</tr>
<tr>
<td>13.63</td>
<td>2'</td>
<td>0.65</td>
<td>H-3,5,6,8</td>
</tr>
<tr>
<td>14.03</td>
<td>1'</td>
<td>0.78</td>
<td></td>
</tr>
<tr>
<td>14.35</td>
<td>$v^p_n$</td>
<td>1.10</td>
<td></td>
</tr>
<tr>
<td>14.66</td>
<td>1</td>
<td>5.08</td>
<td>H-2,7</td>
</tr>
<tr>
<td>15.07</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15.26</td>
<td>3</td>
<td>5.65</td>
<td></td>
</tr>
<tr>
<td>15.44</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15.89</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21.47</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22.27</td>
<td>7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
In Scheme 7, a comparison has been made between the coupling constants found in the three known dihydropyrène radical anions 40', 38', and 51'. A correct assignment of the observed coupling constants for 51' at this stage is not possible. From the ENDOR data, it is immediately obvious that there is no direct spin density on the phenyl substituent. However, there is still the possibility of long-range proton hyperfine interaction between the odd electron in the annulene perimeter and the ortho proton of the phenyl substituent.

Two mechanisms have been invoked for obtaining spin density at a nucleus separated by two or more \( \sigma \)-bonds from some principal center containing a significant portion of the electron spin density. One such mechanism, called spin polarization, is purely a through-bond effect where spin density is induced through the bonding electrons. This mechanism decreases rapidly when the number of intervening \( \sigma \)-bonds increases. The second mechanism is that of spin delocalization (some-
times referred to as hyperconjugation) and is a through-space effect. For instance, the large coupling of 19.1 G found in 40 for the internal hydrogens has been explained by spin delocalization\textsuperscript{137}. Since the ortho hydrogen of the phenyl group (H-1') is four bonds removed from the nearest electron center (C-4), the effect of spin polarization will be negligible. As for the possibility of spin delocalization from the annulene perimeter onto the ortho hydrogen, molecular models indicate a favorable arrangement between H-1' and C-3 or C-5. However, from MO calculations\textsuperscript{136} as well as from the observed coupling constants for 51, we can infer a small spin density on carbons C-3 and C-5 as opposed to C-2 and C-4. Therefore, the effect of spin delocalization from C-3 (C-5) to H-1' will be even smaller than the observed coupling constants for H-3 and H-5. Our previously made assumption of a freely rotating phenyl group will decrease a possible spin delocalization even more. To make sure that no coupling constants smaller than 0.22 G were overlooked, an expanded ENDOR scan (1MHz width), was made around the free proton frequency. However, no extra coupling constants could be detected. We therefore conclude that there is no direct π-orbital overlap between the two π-systems in 51 and further that, probably because of rotation, no through-space delocalization of spin density onto the phenyl ring has taken place. However, to use the words of Russell\textsuperscript{138}, "It is considerably more reliable to make inferences based on the observation of long-range couplings rather than the lack of them". Thus both UV and ESR seem to support the idea that 51 consists of two non-interacting orthogonal π-electron systems.
2.7 Assessment of Ring Current Models for 51.

2.7.1 Existing Models.

The phenomenon of the aromatic ring current in NMR spectroscopy has been the subject of much interest and investigation since the original suggestion of a ring current shift in benzene by Pople. The most widely used approach today, to explain ring current shifts, is that based on the classical current loop model of Johnson and Bovey (JB), probably because of the easy access to their tabulated shielding-deshielding contributions of the benzene ring. The JB model for benzene consists of a current loop with radius 1.39 Å (standard benzene bond length). The parameters, Z and ρ, are used to determine any position in space around the benzene ring; Z denotes the vertical distance above the plane of the ring whereas ρ gives the in-plane distance from the center of this ring, both parameters are tabulated as 0.1 increments of the benzene ring radius (1.39 Å).

![Diagram of JB model](image)

Boekelheide adopted the JB model in his attempt to rationalize the observed chemical shifts of the alkyl protons and carbons in 38, 48 and 49. The dihydro derivatives 144, 145 and 146 were used as reference (no ring current present), since it is believed that the geometry of these compounds is almost the same as that for the
corresponding dihydropyrenes.

For the purpose of comparing the observed chemical shift difference $\Delta\delta$ with the calculated shielding contribution $\Delta\sigma$, due to the ring current, Boekeleheide assumed the conformation of the alkyl side chain in 48 and 49 to be as shown in A. Furthermore, the variation of the in-plane distance $\rho$ for the carbons and hydrogens of the side chain was neglected. Although the plot of the observed shift difference $\Delta\delta$ versus $Z$ (out of plane distance) showed a similar curve as the theoretical graph (JB method), fairly large deviations (2-5 ppm) can be observed (see figure 7).

* $Z$ measured from Dreiding models for 38, 48 and 49.
Because of the above mentioned approximations in the assessment of the ring current of dihydropyrenes we hoped that by making allowance for the variation in $\sigma$, our compound 51 with the non-flexible phenyl substituent, would serve as a better model.

2.7.2 *Single Current Loop Model for 51.*

The chemical shift of the aromatic protons of toluene ($\delta 7.20$) was taken as reference for the phenyl protons of 51 in the hypothetical case that the aromatic ring current would be absent; local anisotropy effects on the phenyl protons will not be considered yet. Compound 144 was used as reference for the internal methyl protons of 51.

To calculate the out of plane distance ($Z$) and the in-plane distance
(ρ) for the different hydrogens above the plane of the annulene ring of 51, we used the data from the crystal structure of 38. This gave us the basic annulene skeleton as well as the angle between the substituent and the plane of the ring (83.5°). The C15–C1 bond length was taken as 1.52 Å whereas standard benzene bond lengths (1.39 Å) and bond angles (120°) were used for the phenyl substituent; the C–H bond was taken as 1.1 Å for benzene. Since we consider both substituents in 51 as freely rotating, the in-plane distance (ρ) was averaged over four positions for the phenyl hydrogens whereas six positions were used to describe the methyl group.

To compare the values of Δδ observed for 51 with Boekelheide's ring current model, we have added our values to figure 7; the numerical comparison between Δδ (observed) and Δα (calculated) is made in Table 11.

<table>
<thead>
<tr>
<th>Proton</th>
<th>δ(ref)</th>
<th>δ(0)</th>
<th>Δδ</th>
<th>Δα</th>
<th>Δβ</th>
<th>Δδ</th>
<th>Δα</th>
</tr>
</thead>
<tbody>
<tr>
<td>H-2'</td>
<td>7.20</td>
<td>2.80</td>
<td>-4.40</td>
<td>-4.67</td>
<td>-0.45</td>
<td>-3.74</td>
<td>-4.42</td>
</tr>
<tr>
<td>H-3'</td>
<td>7.20</td>
<td>5.87</td>
<td>-1.33</td>
<td>-0.60</td>
<td>-0.30</td>
<td>-1.19</td>
<td>-1.31</td>
</tr>
<tr>
<td>H-4'</td>
<td>7.20</td>
<td>6.20</td>
<td>-1.00</td>
<td>&lt;-0.30</td>
<td>&lt;-0.27</td>
<td>-1.01</td>
<td>-1.11</td>
</tr>
<tr>
<td>CH₃</td>
<td>1.00</td>
<td>-4.30</td>
<td>-5.30</td>
<td>-3.55</td>
<td>-2.46</td>
<td>-7.59</td>
<td>-7.99</td>
</tr>
</tbody>
</table>

*a ring radius R in Å; b all δ, Δδ and Δα values in ppm; c toluene taken as reference; d δ(0) taken from reference 89.

Although the calculated value of Δα for the ortho protons (H-2') is very close to the observed value of 8, the strong deviation
between $\Delta_\sigma$ and $\Delta_\sigma$ for the other protons makes reconsideration of this model obvious. For comparison $\Delta_\sigma$ was calculated for the same ring current model but now with the in-plane distance included ($\rho \neq 0$). It is, of course, obvious that such a simple model must be far removed from actual size and shape of the current loop in the annulene ring, for a current loop with radius 1.39 Å is situated far inside the perimeter of the annulene. Furthermore, the actual shape of this loop will probably resemble an ellipse rather than a circle. As was already mentioned in chapter 1, Haddon reported that a direct relation exists between the ring current ($R_C$) and the resonance energy ($R_E$) of the aromatic system (equation 1). In the same paper the ring current was shown to be proportional with the ring area ($S$) and inversely proportional with the number of $\pi$-electrons ($N$); $E$ represents the total $\pi$-energy of the system (equation 2).

$$R_C = \frac{3S}{\pi} R_E \quad (1)$$
$$R_C = \frac{ES}{2N^2} \quad (2)$$

Using the resonance energies calculated by Haddon, Aihara or the Zagreb group we found that by applying equation 1, the ring current for the [14]annulene is ca. 1.6 times greater than for benzene, whereas application of equation 2 gave a factor of 1.5-1.7, depending on the value taken for $E$.

A simple way of increasing the ring current is by expanding the radius of the current loop and subsequently expressing $Z$ and $\rho$ in
units of this new radius; the shielding contributions can then again be calculated from the JB tables.

Since the \( \text{para} \) proton (\( H-4' \)) has a fixed position with respect to the annulene ring it can be used to calibrate the size of the ring current. As can be seen from table 11, a ring current with radius 2.16\( \text{Å} \) results in a calculated \( \Delta \sigma = -1.01 \), perfectly in line with the observed \( \Delta \delta = -1.00 \). However, the calculated shielding contributions (\( \Delta \sigma \)) for \( H-2' \) and \( H-3' \) are too small. Increasing the ring radius to 2.23\( \text{Å} \) (1.6 times the size of benzene) gave a near perfect match between \( \Delta \sigma \) and \( \Delta \delta \) for the phenyl protons. However, in this model the internal methyl protons are too strongly shielded (\( \Delta \sigma = -8.0 \)). To obtain the correct shielding contribution of \( \Delta \sigma = -5.30 \) for the methyl protons a ring radius of 1.85\( \text{Å} \) had to be used. This, however, strongly underestimated the \( \Delta \sigma \) values for the phenyl protons. Although minor changes in the ring radius resulted in major changes for the shielding contributions of \( H-2' \) and the methyl protons (see table 11), we were not able to find a set of \( \Delta \sigma \) values that resembled the observed \( \Delta \delta \) values for the four types of protons in 51.

2.7.3 Multiple Current Loop Model for 51.

Since a single current loop, placed in the center of the annulene ring, was not able to describe the observed shielding effects in 51 satisfactorily, we tried to improve our calculated values of \( \Delta \sigma \) by summation over two or more circular current loops. We thought that two current loops, centered at C-15 and C-16 respectively, would give
a better description of the more elongated ring current in the annulene ring of 51. However, even variation of the ring radius of these loops between 1.39Å and 1.85Å did not yield a set of Δσ values that was in agreement with the observed Δσ values.

Although the best ring current model for dihydropyrenes would be the line current model used by Haddon, this would also require a full mapping of the shielding-deshielding contributions around the ring. We, therefore, resorted to a simpler approximation.

Our next model is based on the observation by Pople who showed that the proton chemical shifts of some polycyclic aromatic hydrocarbons could be calculated under the assumption that essentially the same current, equal to the benzene-ring current, is induced in each benzene hexagon of the polycyclic system. The same approach was later used by Abraham to calculate the observed proton chemical shifts in porphyrin systems.

We therefore placed four current loops in the annulene ring, each one located in the center of one of the four hexagons. For instance, for hexagon A, where five of the six carbons participate in the overall ring current (figure 8A), we approximated the contribution of the total ring current for this hexagon by a small circular current centered in hexagon A (figure 8B). The same approximations were used for the three remaining hexagons B, C and D (figure 8C).

For calculation purposes we further assumed the two substituents in 51 to be perpendicular to the plane of the annulene ring instead of making an angle of 83.5°; apart from this the same bond lengths and
bond angles were used as mentioned in section 2.7.2.

For our model we took the standard benzene ring current loop for the hexagons A and D (figure 8), whereas the ring radius for the current loops in B and C were simultaneously varied between 1.62Å and 1.72Å. The pertinent shielding calculations are reported in table 12:

**TABLE 12. Shielding calculations for the four current loop model of 51.**

<table>
<thead>
<tr>
<th>Proton</th>
<th>$\delta$(obs)</th>
<th>$\delta$(ref)$^b$</th>
<th>$\Delta\delta$</th>
<th>$\Delta\sigma^a$</th>
<th>$\Delta\sigma$</th>
<th>$\Delta\sigma$</th>
<th>$\Delta\sigma$</th>
</tr>
</thead>
<tbody>
<tr>
<td>H-2'</td>
<td>2.80</td>
<td>7.20</td>
<td>-4.40</td>
<td>-2.97</td>
<td>-3.14</td>
<td>-3.30</td>
<td>-3.52</td>
</tr>
<tr>
<td>H-3'</td>
<td>5.87</td>
<td>7.20</td>
<td>-1.33</td>
<td>-1.48</td>
<td>-1.52</td>
<td>-1.57</td>
<td>-1.62</td>
</tr>
<tr>
<td>H-4'</td>
<td>6.20</td>
<td>7.20</td>
<td>-1.00</td>
<td>-0.99</td>
<td>-1.02</td>
<td>-1.07</td>
<td>-1.13</td>
</tr>
<tr>
<td>CH$_3$</td>
<td>-4.30</td>
<td>1.00</td>
<td>-5.30</td>
<td>-5.36</td>
<td>-5.52</td>
<td>-5.67</td>
<td>-5.92</td>
</tr>
</tbody>
</table>

$^a$R stands for $R_B=R_C$ (Å), the ring radius of the current loop in hexagons B or C (see figure 8).

$^b$R stands for $R_B=R_C$ (Å), the ring radius of the current loop in hexagons B or C (see figure 8).
We believe that the combination of two benzene ring currents for the hexagons A and D \((R_A = R_D = 1.39\AA)\) and two current loops of radius \(1.68\AA\) each for the hexagons B and C \((R_B = R_C = 1.68\AA)\) gives the best description of the ring current in \(61\), although it may seem that the difference between \(\Delta\sigma\) and \(\Delta\delta\) for H-2' is too large. However, no corrections for local anisotropy contributions to \(\delta\) (ref) have been made so far.

If we look at the chemical shifts for the ethyl-side chain in \(145\) we notice that the methyl protons absorb at \(80.63\), whereas a value of \(80.95\) is normally found for the methyl protons in straight alkanes. This means that the ethyl side chain in \(145\) experiences an upfield shift of at least 0.3 ppm due to the local anisotropy of the double bonds. This effect is still noticeable in \(146\) where the methyl protons \((\gamma)\) of the side chain absorb at \(80.82\). Boekelheide interpreted the AA'XX' spin system of the \(\alpha\)- and \(\beta\)-methylene protons of the n-propyl group in \(49\) either in terms of a preferred conformation or as restricted rotation about the carbon-carbon bond between the \(\alpha\)- and \(\beta\)-methylene carbons. This interpretation was supported by the fact that the \(\text{Hmr of } 49\) did not show any temperature dependence over the range of \(-80^\circ\) to \(+80^\circ\).
If indeed these alkyl side chains in 48 and 49 have a preferred conformation like the one depicted above, we can say that the α-methylene protons will experience a smaller shielding from the double bonds in 145 or 146 than the *ortho* protons (H-2') of the phenyl group in the so far hypothetical molecule 147. This is because the *ortho* protons will be pushed farther over the double bonds in 147 during the rotation of the phenyl group than the comparable β-protons in 147.

Their "fixed" conformation as in 145 and 146. Since the γ-protons in
146 experienced a similar but smaller shielding from the double bonds we can say that also for the meta protons (H-3') in 147 a small up-field shift can be expected due to the olefinic system. We therefore believe that the reference chemical shift for H-2' and H-3' should be smaller than the 67.20 value quoted in tables 11 and 12. However, it has to be seen if the chemical shift for H-2' in 147 will be as high field as 66.20 which is the shift value that would give a very good match between A6 and A0 (table 12). It would therefore be of considerable help if compound 147 were available. Unfortunately, our efforts to synthesize 147 have been without success so far.

Although the ring current effect for protons has been well established and, in many instances, successfully applied, the picture is less clear for heavier elements like carbon. For instance, Boekelheide concluded, based on his data represented in figure 7, that "for the same position in space relative to the mean plane of delocalization of the aromatic π-electron cloud, the magnitude of the ring-current effect on chemical shifts is essentially the same for carbon-13 as for protons and follows the theoretical curve predicted by Johnson and Bovey". On the other hand, extensive investigation of the 13Cmr of bridged annulenes led Günther to a totally different conclusion. According to his opinion: "It is evident that the dominance of local atomic contributions to the shielding constant prevents the carbon nucleus from being a probe for ring current effects; this is,

* for a different graph of the data from figure 7 see reference 40.
however, no disadvantage, since $^1$Hmr will take care of ring currents and there is no need to duplicate these results".

In Table 13 the $^{13}$Cmr $\delta$ values are reported for the phenyl and methyl substituents of 51 together with values for possible reference compounds.

<table>
<thead>
<tr>
<th>Carbon</th>
<th>$\delta$(51)</th>
<th>$\delta$(144)$^a$</th>
<th>$\delta$(146)$^b$</th>
<th>$\delta$(149)$^b$</th>
<th>$\delta$(150)$^b$</th>
<th>$\delta$(151)$^b$</th>
<th>$\Delta\delta$</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-1'</td>
<td>136.7</td>
<td>-</td>
<td>137.8</td>
<td>144.3</td>
<td>148.8</td>
<td>150.9</td>
<td>-11.2</td>
</tr>
<tr>
<td>C-2'</td>
<td>124.1</td>
<td>-</td>
<td>129.3</td>
<td>128.4</td>
<td>125.6</td>
<td>125.4</td>
<td>-5.1</td>
</tr>
<tr>
<td>C-3'</td>
<td>125.3</td>
<td>-</td>
<td>128.5</td>
<td>128.6</td>
<td>128.0</td>
<td>128.3</td>
<td>-2.5</td>
</tr>
<tr>
<td>C-4'</td>
<td>125.0</td>
<td>-</td>
<td>125.7</td>
<td>125.9</td>
<td>126.1</td>
<td>125.7</td>
<td>-1.9</td>
</tr>
<tr>
<td>CH$_3$</td>
<td>14.9</td>
<td>23.6</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-10.5</td>
</tr>
</tbody>
</table>

$^a$Reference 89; $^b$Reference 148; $^c$Based on four current loop model with $R_A=R_D=1.39$ Å and $R_B=R_C=1.65$ Å (Figure 8).

As can be seen from Table 13, the calculated shielding contributions ($\Delta\delta$) do not really match with the "observed" shift differences ($\Delta\delta$); the best values for $\Delta\delta$ are obtained by taking ethylbenzene 149 as reference compound for the carbon chemical shift values of the phenyl ring of 51 in the absence of a ring current.
Although we are lacking a good reference model for our observed carbon chemical shift values of $^{51}$, we can state that the proton is indeed a far better nucleus to probe a possible ring current effect than the carbon. Our proposed four current loop model (figure 8) gives a good qualitative picture of the ring current in dihydropyrene $^{51}$ and is expected to be close to quantitative if reference compound $^{147}$ becomes available. A further test for this model would be the synthesis of dihydropyrene $^{152}$ where one substituent is a t-butyl group. This group is expected to undergo free rotation, for the same reason as the phenyl group does. Therefore, this t-butyl group does not suffer from the shortcomings of the linear alkyl chains in $^{48}$ and $^{49}$ which may or may not undergo free rotation. Furthermore, the protons of the t-butyl group will extend further over the dihydropyrene ring and are therefore even closer to the edge of the current loop in hexagons B and C (figure 8), the area where the shielding-deshielding contributions are changing fastest.
3.1 Introduction.

The term 'cyclophane' was first introduced by Cram in 1951 and was later defined as a general name for a family of compounds containing any number of benzene rings joined by chains in the para, meta and/or ortho positions. An increasingly greater interest has arisen in these bridged molecules during recent years resulting in many bizarre new structures. To accommodate the need for a systematic way of naming all these new compounds a general nomenclature was developed to name all bridged molecules containing any number and type of aromatic rings.

As far as metacyclophanes are concerned, the most common are the [n]metacyclophanes and [m.n]metacyclophanes (m≠n or m=n); both series show interesting conformational changes. Dithiametacyclophanes, used extensively as precursors for the corresponding meta-cyclophanes, show similar conformational processes. However, the
longer C-S bond, and therefore lower bending energy of a C-S-C bridge provides more conformational flexibility in the dithiametacyclophanes than in their metacyclophane counterparts, thus resulting in lower conformational energy barriers.

During the course of this work it was discovered that the phenyl substituent of the otherwise rigid thiacyclophanes 59 and 59A underwent a dynamic process of ring twisting.

At low temperatures we were able to 'freeze out' this process on the NMR time scale. Subsequently it was found that this process of ring twisting of the phenyl substituent was also present in the more closely packed [2.2]metacyclophanes 118A, 118B and 119.
In the following sections we have limited the discussion of metacyclophanes to two main classes of compounds: [2.2]metacyclophanes (section 3.2) and dithia[3.3]metacyclophanes (section 3.3).

3.2 [2.2]metacyclophanes.

The parent [2.2]metacyclophane 153, which was first synthesized by Pellegrin in 1899, has been shown from $^1$Hmr and X-ray studies to exist in a 'stepped' conformation (anti), in solution as well as in the solid state. Ring inversion between 153A and 153B can be ruled out since the methylene protons of 153 did not show any temperature dependence in the $^1$Hmr between $-80^\circ$ and $+190^\circ$. Further evidence of the rigid conformation of the [2.2]metacyclophane system was provided by the isolation of stable optical isomers such as 154A and 154B.
Since 153 does not show a ring inversion process, it is of course clear that any substituted [2.2]metacyclophane will therefore have the same rigid structure as the parent 153. However, if the benzene nuclei in 153 are replaced by pyridine rings as in 155, the rigidity of the [2.2]metacyclophane system is lost and an inversion process of the type 153A \(\rightarrow\) 153B must be assumed on the basis of the temperature dependent \(^1\text{Hmr}\) 151a. On the other hand, 156 showed again the rigid [2.2]metacyclophane structure 151b. It was therefore concluded that

![Chemical Structures](image)

the space occupied by the lone pair of electrons on the nitrogen atom of pyridine is smaller than that occupied by a hydrogen atom attached to an aromatic nucleus. Further \(^1\text{Hmr}\) studies have confirmed these results 152.

The internal protons of 153 absorb at 64.25 whereas a value of ca. 67.1 is found for \(m\)-xylene. This strong upfield shift (\(\Delta \delta = 2.85\)) was adequately explained \(88c\) by the ring current model of Johnson and Bovey 151a. The internal protons of 156 151b and 157 153 absorb at slightly lower field (64.40 and 64.51 respectively), as might be expected for an electron withdrawing group.
For the methyl derivative 160, we find the internal methyl protons at 60.56, considerably shielded from those of 1,2,3-trimethylbenzene (62.15). The difference in shielding from their respective models of the internal protons in 153, Δδ=1.59, can be explained with the help of the X-ray data for 153 and 160. These data show, firstly that the vertical distance between the benzene ring planes is greater in 160 than in 153 and, secondly, the distortion of the benzene ring into a boat shape is more pronounced for 160 than for 153. The methyl group in 160 will therefore be farther removed from the benzene ring than the internal proton is in 153. Also the extra distortion of the benzene ring may contribute to the smaller Δδ value found for 160 as compared to 153.

Introduction of a double bond into one or both of the bridges of 153 or 160, has a rather dramatic effect on the chemical shift of the internal protons as can be seen in Scheme 8 (δ values refer to the
internal substituent). This deshielding effect, which is much greater for an internal hydrogen (153, 159) than for an internal methyl group (160, 162), has been explained as an anisotropy effect of the double bond. However, from the crystal structure of 153, 158, and 159 we can see a decrease of the interplanar distance of the benzene rings together with a flattening of the stepped structure in going from 153 to 159.

In 153 the internal proton is deeply immersed in the shielding zone of the opposite benzene ring whereas for 159 this proton is located right on the edge of the benzene ring (based on X-ray data), i.e., the region of space where the magnetic field is changing rapidly. It is therefore possible that the internal proton moves from the shielding zone (as in 153) to the deshielding zone (as in 159) of the opposite benzene ring. Because of the bulky methyl groups no major flattening of the [2.2]metacyclophane ring can take place on going from 160 to 162. This implies that the position of the methyl group with respect to the opposite benzene ring does not change much in 160 and 162 which reflects the minor changes in the observed chemical shifts for 160-162 as compared to those for 153, 158 and 159.

Comparable shift variations for the methyl group can be seen in 119 (δ=0.84) and 51A (δ=1.70). We therefore believe that not the anisotropy of the double bond alone but more the ring current of the opposite benzene ring, explains the observed deshielding of the internal protons of the [2.2]metacyclophanes upon introduction of double bonds.
Changing one of the internal protons of 153 for a larger group has a pronounced effect on the chemical shift of the remaining \( H_1 \) as can be seen from scheme 9.

<table>
<thead>
<tr>
<th>R</th>
<th>( \delta H_1 )</th>
<th>reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>4.37</td>
<td>93a</td>
</tr>
<tr>
<td>Cl</td>
<td>3.94</td>
<td>93a</td>
</tr>
<tr>
<td>CH(_3)</td>
<td>3.72</td>
<td>155</td>
</tr>
<tr>
<td>Ph</td>
<td>3.57</td>
<td>157</td>
</tr>
</tbody>
</table>

**SCHEME 9**

From these data it can be deduced that, generally speaking, the bigger the \( R \) group the more \( H_1 \) is pushed towards the \( \pi \)-cloud of the benzene nucleus resulting in an increased shielding. Based on the \(^1\)H\(_{\text{mr}}\) data of the [2.2]metacyclophanes reported so far we can visualize three possible geometries for the metacyclophane ring system, these are depicted in scheme 10.
Which geometry, A, B, or C, would be preferred would then depend on the size of the R-group as well as on the hybridization of the bridge carbons. With a large R-substituent, such as chlorine (164), methyl (165) or phenyl (166), geometry B will be preferred resulting in the observed upfield shifts of the internal protons as compared to the value of 64.25 for 153. As was mentioned before, the internal protons for [2.2]metacyclophane-1-ene 158 and -1,9-diene 159 are considerably less shielded than for 153, which may reflect a structure like C.

Whereas the [2.2]metacyclophanes described so far, according to the spectroscopic findings, have the anti conformation with staggered benzene rings, the existence of a syn form for a [2.2]phane has also been detected. Mitchell and Boekelheide, for instance, have reported 167\(^{97}\) and 168\(^{55,94}\), the thiomethyl derivatives of the still elusive syn forms of 153 and 160 respectively.

The existence of both syn structures 167 and 168 was based on \(^{1}\)Hmr;
the internal protons of 167 absorbed at δ7.3 whereas a value of δ2.0 was found for the internal methyl protons of 168:

Subsequently 169A, a syn-[2.2]phane without thiomethyl groups on the bridges, was synthesized and shown to undergo a quantitative conversion to the anti form 169, indicating the greater stability of this type of conformation. As a last example of syn-[2.2]metacyclophanes the two difluoro compounds 170 and 171 deserve mentioning. The assignment of the syn conformation for 170 and 171 is not obvious from Hmr, and since Fmr is not established yet in cyclophane chemistry, the authors resorted to dipole moment measurements to
Since the ring structure of [2.2]metacyclocphanes has been shown to be rigid, the only dynamic behaviour in this class of compounds can be found in suitably substituted [2.2]phanes. Whereas for 160, 165 and 172-174 the internal methyl-, ethyl- and even n-propyl group did not give an indication in their $^1$Hmr of hindered rotation, the $^1$Hmr of the internal phenyl group in 119 showed a remarkable temperature dependence as shown in figure 9. From the $^1$Hmr of 119, as seen in figure 9, it is obvious that we are dealing with a dynamic process of ring twisting of the phenyl substituent. Molecular models show that a complete rotation of the phenyl group is unlikely. Since 119 will have a structure represented by A (scheme 10) only the ortho protons (H-2',6') of the substituent will experience a stronger shielding than normal from the opposite benzene ring. At -20°C this process of ring twisting is still fast enough to equilibrate both ortho protons resulting in only one signal in the $^1$Hmr. The coalescence temperature ($T_C$) is reached at -59°C. Further cooling will slow down the ring twisting even more so that
FIGURE 9. Variable temperature $^1$H NMR (CDCl$_3$/CD$_2$Cl$_2$) of 119.
eventually two separate signals can be observed for H-2' and H-6'.

The high field signal (H-2') is well separated in figure 9.

However, the signal due to H-6' is obscured by the aromatic protons of the metacyclophane skeleton. This problem was solved by obtaining a low temperature (-80°C) 250 MHz $^1$Hmr which clearly showed both protons H-2' and H-6'.

To calculate the activation parameters for dynamic processes, like the one encountered for 119, either line shape analysis or the $T_c$ method can be used. Reasonably accurate (+1kJ/mol) $\Delta G^\neq$ values can be obtained by either method, even when the error in temperature estimation is up to 8°C. We have employed the $T_c$ method for our calculations. The only two parameters necessary to derive $\Delta G^\neq$ at the coalescence temperature $T_c$ are $T_c$ (in K) itself and the low temperature separation $\Delta v$ (in Hz) of the two exchanging protons. The free energy of activation at the coalescence temperature is then obtained from 161:

$$\Delta G^\neq = 2.3RT_c (10.32 + \log T_c - \log k_c)$$

where

119
Equation (4) is only valid for uncoupled equally populated exchanging sites, but is often used for more complex cases to obtain approximate values of $\Delta G^\ddagger_c$.

The correct exchange rate $k_c$ for coupled (AB) nuclei is calculated as follows:

$$k_c = \frac{\pi}{\sqrt{2}} (\Delta \nu^2 + 6J^2)^{1/2}$$  \hspace{1cm} (5)

where $J$ (in Hz) is the coupling constant between the two exchanging nuclei. Since the coupling between H-2' and H-6' in 119 is only the order of 1-1.5 Hz, and the shift difference $\Delta \nu$ for all our systems is greater than 35 Hz, the error introduced by using equation (4) instead of (5) is negligible. At the slow exchange limit for 119 we find H-2' at 66.42 and H-6' at 66.93 (based on $\Delta \nu = 46.2$ Hz obtained from 250 MHz spectrum and corrected for 90 MHz data).

A similar process of ring twisting is observed for the two isomeric thiomethyl derivatives 118A and 118B. At the low temperature limit H-2' and H-6' for 118A absorb at 66.26 and 66.67 respectively. Because of solubility problems for 118B at low temperature (-85°C) the 'frozen' conformation was not obtained but the chemical shifts for H-2' and H-6' are estimated as 66.42 and 66.82, based on the similarity of the coalescence process of 118B with that for 118A. The activation parameters for 118A, 118B and 119, calculated via the $T_c$ method are reported in table 14.

From these data we can see that 118A and 119 show an energetically

<table>
<thead>
<tr>
<th>Phanes</th>
<th>$\Delta G^\circ$ (kJ/mol)</th>
<th>$T_c$</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>118A</td>
<td>43.1</td>
<td>-63°C</td>
<td>this work</td>
</tr>
<tr>
<td>118B</td>
<td>40.0</td>
<td>-77°C</td>
<td>this work</td>
</tr>
<tr>
<td>119</td>
<td>43.5</td>
<td>-59°C</td>
<td>this work</td>
</tr>
<tr>
<td>166</td>
<td>54</td>
<td>0°C</td>
<td>157</td>
</tr>
</tbody>
</table>

similar behaviour, whereas 118B has a slightly lower activation energy for this process of ring twisting. An explanation can be found in the varying degrees of interaction between H-6' and H-9 as depicted below.

The twisting of the phenyl ring is severely hindered by the interaction of the two ortho protons (H-2', 6') with the two axial bridge protons H-2 and H-9. As we have shown before, the thiomethyl groups in 118A and 118B are placed in equatorial positions and are therefore subjected to a 1,3-diaxial interaction with the neighbouring aromatic proton. To relieve this non-bonded interaction the thiomethyl group will have to move out of the plane of the benzene ring thereby changing...
the location of H-2 and H-9, whereas this effect works in opposite
directions for the substituents in 118A, resulting in no net change
compared to 119 (see table 14), in the symmetrically substituted
118B this out of plane bending of the thiomethyl groups increases
the distance between H-2,9 and H-2',6' slightly. In geometric terms
(page 96) this results in a small change from structure A towards
the more elongated structure C (based on molecular models).

Recently Vögtle reported that [2.2]phane 166 showed a similar
process of ring rotation as the compounds mentioned above. The free
energy of activation for this process is also reported in table 14.
From this we see that for 166 we are dealing with a higher energy
barrier than for 119. This implies an increased non-bonded interaction
between H-2,9 and H-2',6'. Based on the 3.57 value reported for the
internal proton of 116 we did assign geometry B (page 96) to 166.
Since the phenyl ring can undergo a larger bond rotation in a geometry
like B than in A (page 96), H-2' will be pushed deeper in the
cloud of the benzene ring and therefore be subjected to an increased
shielding; this is supported by the observed shifts for H-2' (5.29)
and H-6' (66.55) in the slow exchange range. As a result of the
bending of the metacyclophane structure (geometry B as depicted for
166) the protons H-2,9 and H-2',6' are placed closer together,
resulting in the higher ΔG_C value of 166 as compared to 119. Whether
we are dealing with a free rotation of the phenyl group of 166 at
higher temperatures, as implied by Vögtle, remains to be seen.
3.3 2,11-Dithia[3.3]metacyclophanes.

Insertion of a sulfur atom into the middle of the bridges of the [2.2]metacyclophane system leads to the 2,11-dithia[3.3]metacyclophanes. Whereas the former are rigid the latter can undergo several dynamic processes such as syn-anti isomerization (A → B), wobbling of the bridges* (C → D → E) or scissoring of the benzene rings.

The first observation of stable anti and syn isomers in this thiacyclophane series was reported by Vögtle\textsuperscript{96b} for the dichloro compound 172, however, no separation of the individual isomers was mentioned. In the case of 52, Mitchell and Boekelheide\textsuperscript{94} reported the isolation of syn-52A and anti-52 (page 46). Although the large size of the internal substituents of 52\textsuperscript{112} and 172\textsuperscript{96b} prevents

* Depicted for the syn conformation; bridge wobble in anti conformation leads mainly to ring scissoring (according to molecular models)
isomerization of the type $A \leftrightarrow B$ (no change in $^1$Hmr up to 180°C), the parent compound 173 has always been assumed to undergo a rapid interconversion of the syn and anti form based on the temperature independent $^1$Hmr. The observed chemical shift for the internal protons of 173 (66.82, CDCl₃) was thus considered to be an average for all contributing conformers, though it was quite clear from these and subsequent papers that the anti conformer of 173 was generally thought to be in excess. As a result of an investigation to attempt to resolve an apparent anomaly of melting points of 173, we undertook an X-ray structure determination of this compound. This showed that in the crystalline state 173 exists as the syn
conformer. To determine the preferred conformation of $\text{173}$ in solution suitable models for $\text{sym-173}$ and $\text{anti-173}$ have to be found. The $\text{sym}$-tris-bridged cyclophane $\text{175}$, with the aromatic proton ($H_1$) at 66.91\textsuperscript{164} (66.90\textsuperscript{165}), provides an excellent model for $H_1$ of $\text{sym-173}$, whereas at that time $\text{174}$, with $H_1$ at 65.59\textsuperscript{112} (65.50\textsuperscript{166}), was taken as a model for $\text{anti-173}$. Clearly $H_1$ for $\text{173}$ (66.82) is almost identical in chemical shift to that of $\text{175}$. Also the remaining aryl hydrogens of $\text{173}$ at 66.91 are clearly shielded from normal benzene hydrogens. This evidence points to the fact that at room temperature 2,11-dithia[3.3]-
metacyclophane 173 exists in solution, as in the crystalline state, as the syn-conformer. We could not find evidence for participation of the anti-conformer. Related thiacyclophanes with internal protons have therefore been reassigned to the syn-conformer based on \(^1\)Hmr data\(^{163}\). Although we were not able to detect any ring inversion (\(\Delta \rightleftharpoons \Xi\)) for 173 we did notice a collapse of the \(^{13}\)Cmr signal due to the bridging methylenes at ca. -100°C in CD\(_2\)Cl\(_2\). Unfortunately, however, we were not able to find a solvent in which 173 retained some solubility at lower temperatures, and hence could not determine whether a freezing out was occurring of the bridge wobbling process (\(\Gamma \rightleftharpoons \Phi \rightleftharpoons \Xi\)). We believe that the freezing out of this wobbling was observed in the case of 176\(^{162}\). The internal protons (H\(_i\)) of 176 appeared at 66.58 at -55°C, whereas the methylene protons showed a singlet (63.58) at room temperature and an AB quartet (63.65 and 63.51) at -55°C (\(T_C = -41^\circ\)C). Although the room temperature shift value for H\(_i\) of 176 was not reported we believe that it should be very close to the reported value of 6 6.63\(^*\) for H\(_i\) of 173\(^{162}\).

We therefore assume H\(_i\) of 176 to be temperature independent, which implies that no ring inversion has taken place. The 'freezing out' of the bridge wobble should be in favor of structure \(\Gamma\) since \(\Xi\) as well as \(\Phi\) experiences an 1,3-diaxial interaction between one of the methylene protons and a methyl substituent, structure \(\Gamma\) was also

\(^*\) Sato\(^{162}\) recorded the \(^1\)Hmr of 173 and 176 in d\(_6\)-toluene. His value of 66.63 for H\(_i\) of 173 is therefore lower than our value of 66.82 in CDCl\(_3\); this behaviour in different solvents is normal\(^{163}\).
found in the crystal structure of 173.

Prior to the structure determination of 173, Vogtle\textsuperscript{96b,103} had undertaken a large study of the size effect of internal substituents of 2,11-dithia[3,3]metacyclophanes on the conformational mobility of the ring system. Whereas the dichloro compound 172 consisted of distinct non-interconvertible \textit{syn} and \textit{anti} isomers, the smaller difluoro 177 was formed as a single isomer, later proven to be \textit{syn}\textsuperscript{159}, that showed coalescence of the AB quartet of the bridge protons at 157°C. This collapsing of the bridge protons can be a result of either ring inversion (\textit{A} \rightleftarrows \textit{B}) or a fast bridge wobble (\textit{C} \rightleftarrows \textit{D} \rightleftarrows \textit{E}). We believe that the former situation is occurring. Cyclophanes 178 and 179 both showed a temperature independent \textsuperscript{1}Hmr, however, for 180 coalescence of the bridge AB-system was reached at 185°C\textsuperscript{96b}. We have reasons to believe that all three compounds 178–180, prefer the \textit{syn} conformation.

Firstly, for 181–185 \textsuperscript{1}H\textsubscript{1} was reported\textsuperscript{103} between 67.45–7.26 indicating, on our arguments, a high preference for the \textit{syn} conformation.

![Diagram of cyclophane compounds](attachment:diagram.png)

<table>
<thead>
<tr>
<th></th>
<th>X</th>
<th>Y</th>
</tr>
</thead>
<tbody>
<tr>
<td>172</td>
<td>Cl</td>
<td>Cl</td>
</tr>
<tr>
<td>177</td>
<td>F</td>
<td>F</td>
</tr>
<tr>
<td>178</td>
<td>H</td>
<td>Br</td>
</tr>
<tr>
<td>179</td>
<td>H</td>
<td>Cl</td>
</tr>
<tr>
<td>180</td>
<td>H</td>
<td>F</td>
</tr>
</tbody>
</table>
Furthermore, for 186 $H_1$ appeared between 67.15-6.85 whereas the methoxyl group absorbed at 63.70; no change with temperature was observed. Based on the shift values of the methoxyl group of the syn- and anti-isomers of 187 (63.55 and 63.25 respectively), 186 was also assigned the syn form. Secondly, the position of $H_1$ for a syn conformation of 178-180 will be around 66.8-7.3 which is also the area for the other aromatic protons of a syn cyclophane. Since the $^1H$mr of 178-180 were recorded at 60 MHz no separation between $H_1$ and the other aromatic protons may have been possible. If, in the case of 180 we are dealing with a ring inversion ($\Delta = B$) at higher temperatures, we expect $H_1$ to shift upfield to obtain an averaged position for a syn- and anti-conformer. However, the high temperature $^1H$mr of 178-180 have been recorded in diphenyl ether so that any shift of $H_1$ will be obscured by the solvent peak and/or spinning side bands. Reinvestigation of the $^1H$mr of 180 at higher field strength is recommended.

Whereas only the syn isomer was present for 188 (OCH$_3$ at 63.58;
of 178), both isomers were found for 189, although the syn isomer was in excess (2:1). In the case of 189 there is no doubt that at elevated temperatures a fast ring inversion (A ⇌ B) is taking place (T_C = 110°C), as judged from the coalescence of the methyl signals.

Taking all these data into account, the picture emerges that as long as one internal substituent in the 2.11-dithia[3.3]metacyclophanes is small (i.e., H or F) the syn conformation is favored independent of the size of the other internal substituent. The only obvious discrepancy to this observation is 190 where H appears at 55.0 (also temperature independent). Anomalous behaviour is also found for 174, where H absorbs at 55.59 and the internal methyl group at 82.14. If we compare this latter value with those for anti-189 (61.49) and syn-189 (62.42) it is tempting to assume a preferred syn conformation for 174. However, we believe that 174 behaves more like a pendulum, an inversion reminiscent to that of [2.2]metaparacyclophanediene 124. It would be interesting to know what conformation 174 adopts in the crystal state.
Although syn-anti inversion is not possible for thiacyclophane 59, because of the size of the internal substituents, it does undergo the same dynamic process of phenyl ring twisting (partial rotation) as observed in the [2.2]metacyclophanes 118A, 118B and 119.

Thus, in the $^1$Hmr of anti-59 (figure 10) we see, on cooling, a collapse of the broad 'singlet' at 66.74, representing the two ortho protons H-2' and H-6', followed by the appearance of two doublets at 67.11 (H-6') and 66.62 (H-2') respectively. The upfield shift of H-2' is caused by the shielding of the opposite benzene ring of the thia-cyclophane. The same process of phenyl ring twisting occurs also in syn-59A. At ambient temperature the five protons of the phenyl substituent form a broad singlet at 67.37, indicative for a syn conformation. In the 'frozen' conformation (-50°C) we see (figure 11) the two ortho protons at 68.29 (H-2') and 66.72 (H-6'). The downfield shift for H-2' is probably caused by steric compression with the methyl group. Double resonance was used to assign the other phenyl ring protons in the low temperature 250 MHz $^1$Hmr of syn-59A (see figure 11). Since we expect the two unhindered protons H-4' and H-5' to absorb around 67.35 (a normal benzene value). The downfield shift of H-3' (67.60) corroborated the assignment of H-2'.

Prior to the synthesis of 59 and 59A, the only successful preparation of a thiacyclophane having an internal phenyl group also had a small co-substituent, a hydrogen atom, 191103. At that time, Vogtle103 reported that compound 192, with two internal phenyl groups

* Based on 250 MHz $^1$Hmr of 59 at -55°C (see figure 10).
FIGURE 10. Variable temperature $^1$Hmr (CDCl$_3$) of anti-59.
FIGURE 11. Variable temperature $^1$Hmr (CDCl$_3$) of syn-59A.
could not be obtained from the cyclization of 2,6-bis(bromomethyl) biphenyl 60 and 2,6-bis(thiomethyl)biphenyl 61. However, we have successfully isolated \textit{anti}-192 as well as \textit{syn}-192A from this reaction, albeit in very low yields.

Recently, Kellogg reported the use of cesium carbonate (Cs$_2$CO$_3$) instead of KOH, as base for the bromide–thiol coupling, leading to vast improvements in the yields of the cyclic dithia compounds. However, application of this method to the coupling of bromide 60 and thiol 61 did not give anticipated yield increase for 192.

The assignment of an \textit{anti} and \textit{syn} conformation to the thiacyclophane 192 was not as simple as for 59, where the internal methyl group made the characterization of \textit{anti} and \textit{syn} conformers straightforward. Both \textit{anti}-192 and \textit{syn}-192A showed, in their $^1$Hmr, an AB quartet for the bridge methylene protons and an AB$_2$ system for the aromatic protons of the cyclophane ring (table 15). The only difference was that for 192A the aromatic protons of the phenyl substituent appeared more or less as a singlet at 67.23^*.

* Based on 250 MHz $^1$Hmr for 192 and 192A.
TABLE 15. 250 MHz $^1$Hmr $\delta$ values and coupling constants (J) for the aromatic protons of the cyclophane rings of 59 and 192.

<table>
<thead>
<tr>
<th>Phane</th>
<th>Proton</th>
<th>$\delta$(ppm)</th>
<th>J(Hz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>anti-59</td>
<td>H-5</td>
<td>7.47</td>
<td>7.6</td>
</tr>
<tr>
<td></td>
<td>H-6</td>
<td>7.29</td>
<td></td>
</tr>
<tr>
<td></td>
<td>H-14</td>
<td>7.20</td>
<td>-7.5</td>
</tr>
<tr>
<td></td>
<td>H-15</td>
<td>7.02</td>
<td></td>
</tr>
<tr>
<td>syn-59A</td>
<td>H-5</td>
<td>6.92*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>H-14</td>
<td>7.01*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>H-6,15</td>
<td>6.77</td>
<td>7.7</td>
</tr>
<tr>
<td>anti-192</td>
<td>H-5</td>
<td>7.25</td>
<td>7.6</td>
</tr>
<tr>
<td></td>
<td>H-6</td>
<td>6.96</td>
<td></td>
</tr>
<tr>
<td>syn-192A</td>
<td>H-5</td>
<td>7.33</td>
<td>7.6</td>
</tr>
<tr>
<td></td>
<td>H-6</td>
<td>6.99</td>
<td></td>
</tr>
</tbody>
</table>

* a reversed assignment can not be excluded.

(cf. 59A), whereas for 192 these protons appeared in two separate regions, a broad singlet at $\delta$7.03* (ortho Protons) and a multiplet at $\delta$7.35-7.20*. These data indicate an anti conformation for 192 and a syn conformation for 192A. The above assignments were further supported by the likeness of the variable temperature $^1$Hmr of 192 (figure 12) and 192A as compared to the ones for 59 (figure 10) and 59A (figure 11). In the 'frozen' conformation, the two ortho protons of the phenyl substituent of 192 absorbed at $\delta$7.22* (H-6') and $\delta$6.66 (H-2'), comparable to the values found for anti-59 ($\delta$7.11 and $\delta$6.62 respectively).

* Based on 250-MHz $^1$Hmr for 192 and 192A.
FIGURE 12. Variable temperature $^1$Hmr (CCl$_4$) of anti-192.
In the low temperature $^1$Hmr of 192A the two ortho protons absorbed at 67.93 and 66.62, similar shifts were observed for syn-59A (68.29 and 66.72 respectively).

Whereas for 59A the assignment of H-2' (58.29) and H-6' (56.72) is fairly simple, the picture is less clear for 192A. H-2' of 192A probably lies partly in the shielding zone of the other phenyl substituent and can therefore be assigned the shift 56.62. The downfield shift of H-6' (67.93) can then be explained by steric compression with H-1,10. However, a reversed assignment (as in 59A) cannot be excluded.

Undeniable proof of the anti conformation of 192 was obtained by X-ray determination of the crystal structure, which will, of course, also be the conformation in solution. From these X-ray data it can be seen that the phenyl substituents have undergone a partial bond rotation of ca. 54°, furthermore, it is obvious that no full rotation of the phenyl group will be possible. The crystal structure *to be published.*
also showed that the benzene rings of the cyclophane skeleton are slightly overlapping; the angle Cl'-C9-C18 is ca. 116°.

The activation parameters for the dynamic process of ring twisting of the phenyl group in thiacyclophanes 59, 59A, 192 and 192A are given in table 16.

<table>
<thead>
<tr>
<th>Phane</th>
<th>$\Delta G^#$ (kJ/mol)</th>
<th>$T_c$</th>
<th>Solvent</th>
</tr>
</thead>
<tbody>
<tr>
<td>anti-59</td>
<td>55.1</td>
<td>-5°C</td>
<td>CDCl$_3$</td>
</tr>
<tr>
<td>syn-59A</td>
<td>52.0</td>
<td>-8°C</td>
<td>CDCl$_3$</td>
</tr>
<tr>
<td>anti-192</td>
<td>50.8</td>
<td>-24°C</td>
<td>CCl$_4$</td>
</tr>
<tr>
<td>syn-192A</td>
<td>42.7</td>
<td>-55°C</td>
<td>CDCl$_3$/CD$_2$Cl$_2$</td>
</tr>
</tbody>
</table>

We believe that a similar process of ring twisting occurs in these thiacyclophanes as in the previously mentioned [2.2]metacyclophanes 118A, 118B and 119, i.e. rotation is hindered by the non-bonded interactions between the ortho protons of the phenyl substituent and the bridge methylene protons, as shown below in figure 13 (only anti conformers shown).

In 191 (internal phenyl and hydrogen) the rotation of the phenyl substituent presents an interesting problem. Whereas for 59, 59A, 192 and 192A the ortho protons H-2' and H-6' can be seen clearly at low temperature, albeit at high field strength (250 MHz), this is not the
case for 191. Vögtle reported that 191 is not temperature dependent. However, we observed that H-2' can be seen at 66.70 and H-6' at ca. 66.90, with $H_1$ at 65.49. As the temperature was lowered (figure 14) H-2' and $H_1$ both steadily moved upfield reaching, at $-100^\circ$C, 65.82 and 54.60 respectively. The shift difference ($\Delta \delta$) between H-2' and $H_1$ stayed constant (ca. 1.22 ppm) over the temperature range of $+40^\circ$C to $-110^\circ$C. The high field value of $H_1$ can be explained by an anti as well as a syn conformation, since in both cases $H_1$ is shielded by a benzene ring. We have, however, carried out an X-ray structure determination on this compound which showed it to be the syn isomer.

* to be published
FIGURE 14. Variable temperature $^1$H NMR (CDCl$_3$/CD$_2$Cl$_2$) of 191.
This, therefore, supports the observation that, as long as one internal substituent is small (H or F), the syn conformation is preferred over the anti.

We interpret the observed dynamic behaviour of 191 (figure 14) as being analogous to that for 95 or 192 (figure 13) except that at temperatures below +60°C the system is 'frozen' in one conformation. We believe that, as the temperature is lowered, the phenyl substituent rotates slightly thereby increasing the angle between the biphenyl rings (78.5° in crystal structure) and moving H-2' into the shielding region between the two phane rings. This probably also allows the dihedral angle between the two phane rings (20° in crystal structure) to increase such that H_1 also gets progressively more shielded.

Above 40°C H-2' disappears in the aromatic multiplet so that no possible coalescence of these two protons can be observed. For the disulfone 193, however, H-2' (66.10) and H-6' (66.70) coalesced at 167°C (ΔG_c =91.3 kJ/mol). Since the internal proton H_1 of 193 (65.9) absorbs in the same region as H_1 of 191 (65.49); one can argue that 193 also prefers the syn conformation and not the anti conformation, as assumed by Vögtle 157.
In conclusion, we have shown that the internal phenyl substituent of 2,11-dithia[3.3]metacyclophanes with the other internal substituent larger than hydrogen undergoes a twisting process (partial bond rotation), with respect to the phane ring, that can be 'frozen out' at low temperatures. We believe that this twisting process is restricted by the non-bonded interaction between the ortho protons of the phenyl group and the methylene bridge protons.
PART II

SULFUR ELIMINATIONS
1.1 The Pitfalls of the Hofmann Elimination in Cyclophone Chemistry.

Thiacyclophanes are now regarded as being useful intermediates in the preparation of many novel conjugated aromatic systems. One of the more important steps in such a synthesis of aromatic compounds is the transformation of a carbon-sulfur-carbon linkage in the thiacyclophanes to a carbon-carbon bond.

\[
\begin{align*}
\text{C} & \quad \text{S} \\
\text{C} & \quad \text{H}
\end{align*}
\rightarrow
\begin{align*}
\text{C} & \quad \text{C} \\
\text{C} & \quad \text{H}
\end{align*}
\]

Whereas this sequence has now been achieved by a variety of methods, most of which extrude sulfur or a small neutral group containing sulfur, e.g. \( \text{SO}_2 \), the direct conversion of a C-S-C linkage to a carbon-carbon double bond is more difficult to achieve. This is particularly important in the metacyclophane series, since it is not possible to functionalize the bridge methylenes of [2.2]metacyclophanes directly which could lead to the desirable cyclophone-1,9-dienes (precursors to the dihydropyrenes).

This problem was partially overcome when a method was found to ring contract a thiacyclophane and leave a substituent on the bridge. The latter could subsequently be eliminated to introduce the unsatura-
ration in the bridge and so give the desired diene 195.

\[
\begin{array}{c}
\text{194} \\
\text{R} \quad \text{R} \\
\text{X} \\
\rightarrow \\
\text{195} \\
\text{R} \quad \text{R} \\
\text{X}
\end{array}
\]

The ring contraction step was effected by means of firstly the Stevens rearrangement, and subsequently by the more easy to carry out Wittig rearrangement or benzyne induced Stevens rearrangement, both of which avoided the preformation of a sulfonium salt.

\[
\begin{array}{c}
\text{S-CH}_3 \\
\text{SCH}_3
\end{array}
\]

Stevens rearrangement

\[
\begin{array}{c}
\text{S} \\
\text{CH}_3
\end{array}
\]

Wittig rearrangement

\[
\begin{array}{c}
\text{S} \\
\text{SPh}
\end{array}
\]

Benzyne-Stevens rearrangement
For the elimination of the remaining thio-substituent on the bridge a Hofmann elimination has most often been used.

\[
\begin{align*}
\text{SCH}_3 & \quad \xrightarrow{\text{Base}} \quad \text{Hofmann elimination} \\
\text{S(CH}_3)_2 &
\end{align*}
\]

Although this elimination works very well in some cases, the yield and nature of the product is strongly dependent on the geometry of the molecule under investigation, as well as the base-solvent system used. For instance, mixed isomers of the bis(sulfonium) salt 196 with t-BuOK/THF at reflux gives an 85% yield of dihydropyrene 38.

\[
\begin{align*}
196 & \quad \xrightarrow{\text{Me}_2\text{S}} \quad 38 \\
197 & \quad \xrightarrow{\text{Me}_2\text{S}} \quad 159
\end{align*}
\]

Whereas bis(sulfonium) salt 197, which is analogous to 196 but has internal hydrogen atoms instead of methyl groups, only gives 35% of [2.2]metacyclophane-1,9-diene 159 after treatment with t-BuOK/THF at 0°C.
Whereas in these simple systems the yields are at least fair, in more complex cases the yields have often been very poor. The erratic behaviour of the Hofmann elimination becomes quite obvious if we consider, for example, the naphthalenophanes. Reiss has reported the synthesis of \( [2.2] (2,7) \text{naphthalenophane-1,11-diene} \) from the corresponding bis(sulfonium) salt, in 21% yield by using KOH in EtOH. The elimination was unsuccessful using NaH or potassium 2,6-di-t-butylphenoxide in THF (only products derived from a second Stevens rearrangement were obtained).

Boekelheide reported the synthesis of the \((2,6; 2', 7')\text{naphthalenophanediene} \) in only 6% yield using KOH/EtOH. In contrast to these results stands the chiral \((2,6)\text{naphthalenophanediene} \) that has been prepared by Staab in 41% yield from the sulfonium salt by using t-BuOK/THF. The Hofmann elimination failed completely in the synthesis of \( [2.2] (3,6) \text{phenanthro-(2,7)naphthalenophane-1,11-diene} \) (KOH/EtOH gave only a second Stevens rearrangement) and \( [2.2] (2,7) \text{pyrenophane-1,9-diene} \).

An alternative method to generate a C-C double bond in meta-cyclophanes would thus be of considerable use, particularly if it were found successful in one or more of these more difficult systems.
This part of the project thus had as its goal, the conversion of 2,11-dithia[3.3]metacyclophe 173 into the diene 159 by an alternate route to that used above.

This system was chosen to study first since the Hofmann elimination of the bis(sulfonium) salt 197 only gave a 35% yield of diene 159 and further because this diene 159 rapidly converted to pyrene 34 at temperatures above 60°C. Thus not only an alternative way of generating the double bonds of 159 was required which would improve the yield (>35%) but also the reaction must proceed at room temperature or less to prevent the valence tautomerization of diene.
159 to the dihydroxyrene 40. The latter rapidly forms pyrene 34

at higher temperatures or by oxidation. It is then hoped that a successful method for the formation of diene 159 could be used in other problematic systems such as mentioned in reference 146.
CHAPTER TWO
SULFUR ELIMINATIONS WITH DOUBLE-BOND FORMATION

2.1 Introduction.

The objective of this project was to find an alternative to the well-known sequence of Stevens/Wittig rearrangement followed by the Hofmann elimination to change the C-S-C linkage in thiacyclophanes into a C-C double bond.

In the following pages a list of possibilities for the above mentioned conversion is given and the application of some of these reactions to metacyclophanes is discussed.

2.2 Ramberg-Bäcklund Rearrangement.

The halogen atoms of α-halosulfones, in contrast to halogen atoms α to other electron-withdrawing groups, show marked resistance to nucleophilic substitution. However, the same α-sulfonyl halogen atoms are capable of facile intramolecular 1,3-elimination, leading to replacement of the sulfonyl group by a C-C double bond with loss of halide ion. This extrusion process, frequently referred to as the α-halosulfone or Ramberg-Bäcklund rearrangement, has
found broad utility in olefin synthesis and can be depicted as follows:

\[
\text{H} \quad \text{C} \quad \text{SO}_2 \quad \text{Base} \quad \text{C} \quad + \text{SO}_2 + "HX"
\]

\( \alpha \)-halosulfone:

Application of this rearrangement in the cyclophane series has been successful in a few cases, e.g. in the synthesis of \([n+1]\)para-cyclophane-1,n-dienes 203\(^{180}\) and \([2.n]\)paracyclophane-1-enes 204\(^{181}\).

\[
\begin{array}{c}
\text{203} \\
\text{204}
\end{array}
\]

However, the reaction has proven unsatisfactory when applied to thia-cyclophane systems having two C-S-C bridges, possibly because of, firstly, severe conformational restraints that impede the intramolecular displacement and, secondly, problems in the chlorination step of the sulfide where quite often the dichloride instead of the monochloride was obtained. For instance, pyridinophane 205 on treatment with KOH/CCl₄ (in situ generation of \(\alpha\)-chlorosulfone\(^{182}\)) failed to give the ring contracted product\(^{183}\). Similar results were obtained in other metacyclophane systems such as thia-cyclophane 173\(^{184}\).
Staab et al. were only marginally successful in ring contracting metacyclophane via a modified Ramberg-Bäcklund rearrangement, where the yield of the pyrene derivative was only 0.9%.

Mitchell has reported the successful conversion of the C-S-C linkage in α-chlorosulfides to C-C double bonds without preparing the sulfones, as is required in the Ramberg-Bäcklund rearrangement. Although this method worked very well in open chain sulfides subsequent attempts with thiametacyclophane and its para analog did not yield pyrene or [2.2]paracyclophane-1,9-diene respectively. Reiss was also unsuccessful in his attempts to ring contract thiacyclophane to the diene system via this method.
2.3 Eliminations of Sulfoxides and Sulfones.

Double bond formation by thermal elimination of sulenic acids from sulfoxides was first reported by Cram in 1960, and has, since then, found wide application in organic chemistry. For instance, the previously mentioned [2,n]paracyclophane-1-enes have also been prepared by the thermolysis of the corresponding methylsulfoxide derivatives. Boekelheide, however, was the first to apply this procedure to [2,2]cyclophanes, prepared from the thiacyclophanes via the benzyne induced Stevens rearrangement. He found that sulfoxide 210 gave a 37% yield of pyrene on pyrolysis in vacuum. We found, however, that the yield could be made quantitative by thermolysis of the methylsulfoxide 211 in xylene rather than pyrolysis of the phenylsulfoxide 210. Due to the high temperatures employed in these reactions only pyrene and no diene was obtained in the case of metacyclophanes 210 and 211.

As an alternative to pyrolysis Mitchell and Yan investigated the base induced sulfinate elimination, first reported by Ingold, for the benzannelated example 212. This successfully gave the benzdi-
Thus we further investigated this approach. However, treatment of the [2.2]metacyclophane sulfones 213 and 214 with t-BuOH in THF either at room temperature or at reflux, did not give the expected diene 159. Even when using the strongly electron withdrawing 2,4-dinitrophenyl group (2,4-DNP) as in 215, no diene 159 could be detected. However, we found that the methylsulfone 214 with t-BuOK in DMF or DMSO at 55°C yielded 41% of pyrene 34 (no reaction occurred at room temperature).

Whilst this was disappointing it was reasoned that the trifluoromethylsulfone 216 would improve the reaction since trifluoromethylsulfinate should be a better leaving group than the ones already mentioned. However, Wittig rearrangement of 2,11-dithia[3.3]metacyclophane 173 followed by addition of trifluoriodomethane (CF₃I) at -50°C (CF₃I: bp -22°C) gave only a very low yield of the trifluoromethylsulfide 217).

Moreover, oxidation to the sulfone 216 as well as direct elimination of the CF₃S group in 217 were unsuccessful. While it was known that CF₃I undergoes easy homolytic fission of the carbon-iodine bond both...
under thermal and photolytic conditions, the polarization of the carbon-iodine bond in CF₃I is not as obvious as it is for methyl iodide CH₃⁻⁻, and hence may be responsible for the poor yield of the desired product 217.

2.4 Sulfilimines.

A further group of sulfur derivatives that have been used in pyrolytic double bond formations are the sulfilimines, also known as sulfimides. Their general structure can be represented by 218. Spectroscopic studies suggest that the sulfur-nitrogen bond in N-tosylsulfilimines 219 is of greater dipolar nature than the sulfur-oxygen bond in sulfoxides.

It was thus expected that sulfilimines such as 219 with a δ-hydrogen would undergo a similar, and perhaps more facile, cis-elimination than sulfoxides.

Indeed, experiments showed that the pyrolysis of N-tosyl-
sulfilimines 219 was much more facile than the corresponding sulf-
oxides 195. However, the temperature applied (>80°C) was expected to
limit the usefulness of this method in the synthesis of metacyclophane-
diene 159.

2.5 Trithiocarbonates.

It was pointed out by Corey and Winter 196 that reaction of the
cyclic 1,2-trithiocarbonates 220 with trialkylphosphite gave alkenes
via a stereospecific cis-elimination.

\[
\begin{array}{c}
\text{S} & \text{S} & \text{S} \\
\text{S} & \text{S} & \text{S} \\
\end{array}
\xrightarrow{(\text{RO})_3\text{P}} \Delta \\
\text{S} & \text{S} & \text{S} \\
\text{S} & \text{S} & \text{S} \\
\text{S} & \text{S} & \text{S} \\
\end{array} + \text{CS}_2 + (\text{RO})_3\text{PS}
\]

In contrast to these cyclic trithiocarbonates 220, the open chain
derivatives have not been well studied either on thermolysis or on
treatment with base. However, by analogy to the Chugaev reaction 197,
where a methylxanthate 221 yields an olefin on pyrolysis, the

\[
\begin{array}{c}
\text{O} \\
\text{SMe} \\
\text{S} \\
\end{array}
\xrightarrow{\Delta} \\
\text{SMe} \\
\text{S} \\
\end{array} + \text{COS} + \text{MeSH}
\]

reaction of a trithiocarbonate 222 was thought worth investigating.

Thus Wittig rearrangement of 2,11-dithia[3.3]metacyclophane 173
followed by addition of CS$_2$ and CH$_3$I respectively gave trithiocarbonate 225 in 63% yield. Then 225 was treated with t-BuOK in THF at 0°C, 25°C, and at reflux, also direct pyrolysis in xylene and in 2,6-lutidine were tried. However, no diene 159 or pyrene 34 could be detected in any of these experiments.

We also attempted a number of conversions not based on pyrolysis. These are listed below.

2.6 Thiol Elimination by Mercuric Acetate.

The successful elimination of a thiol group in a substituted cyclopentane 223, by the action of mercuric acetate in acetic acid, has been mentioned by de Mayo$^{198}$ . Good yields of the corresponding cyclopentene 224 were claimed. However, a reaction procedure or cross-reference was not mentioned, either in this paper or in any previous or subsequent papers.

Treatment of dithiol 226 with mercuric acetate in THF or HOAc
(under N₂) at 10°C, 30°C or 80°C did not yield the expected diene 159 or pyrene 34.

Substitution of an ethylthio group in 229 for an acetate group 230 by the action of mercuric acetate in THF was mentioned in an earlier report 199.

However, when we reacted methylthio derivative 227 with mercuric acetate in THF at 25°C or at reflux no acetate 231 could be detected.

2.7 Attempted Substitution of the Sulfur Group in 226 and 227 by Halogen or Oxygen.

Dibromotriphenylphosphorane (Ph₃PBr₂) has been found to effect the cleavage of a variety of ethers under essentially neutral conditions

\[ R-O-R' + \text{Ph}_3\text{PBr}_2 \rightarrow R-\text{Br} + R' - \text{Br} + \text{Ph}_3\text{OH} \]
Unfortunately alkyl sulfides are essentially inert to this reagent. However, dibenzylsulfide gave a 51% yield of benzylbromide on treatment with $\text{Ph}_3\text{PBr}_2$. The same reagent has also been used successfully for the conversion of primary and secondary thiols to the corresponding bromides.

However, our attempted conversion of dithiol 226 and methylthio derivative 227 into the metacyclopheane bromide 232 by reaction with $\text{Ph}_3\text{PBr}_2$ did not give any products that could be identified. Treatment of dithiol 226 with triphenylphosphine and $\text{CCl}_4$, which is a known method for the substitution of a hydroxyl group by a chlorine, also failed to give the desired metacyclopheane chloride 233.

Heterocyclic thiols have been converted to the corresponding chlorides by a number of methods. For example, reaction with aqueous sodium hypochlorite or treatment with sulfurylchloride. However, when these methods were tried on dithiol 226 no chloride 233 was obtained.

At this point we attempted a different approach in which the functionality of the system of the carbon bearing the sulfur substituent is changed, e.g. by conversion to a carbonyl. This would be...
effected by means of an α-chlorosulfide, which, on subsequent

\[
\begin{align*}
\text{SR} & \rightarrow \text{ClSR} \rightarrow \text{C} = \text{O} \\
\end{align*}
\]

hydrolysis\textsuperscript{205} or treatment with mercuric oxide in BF\textsubscript{3}-etherate\textsuperscript{206}, might give the carbonyl group, from which several reactions might find success in forming the final double bond.

A very large number of sulfides have been converted to α-chlorosulfides by both N-chlorosuccinimides (NCS)\textsuperscript{207} and sulfury chloride\textsuperscript{208}. However, we were surprised to find that methylthio derivative \textsuperscript{227} and phenylthio derivative \textsuperscript{228} both failed to α-chlorinate with the above reagents.

2.8 Possible Olefin Formation by Double Benzyne Stevens Rearrangement.

It was noted that on treatment of 2,11-dithia[3.3]metacyclophane\textsuperscript{173} with benzyne (benzyne induced Stevens rearrangement\textsuperscript{171}) not only the expected phenylthio derivative \textsuperscript{228} was formed but also diphenylsulfide \textsuperscript{234}. A possible explanation for the presence of diphenyl sulfide \textsuperscript{234} can be that after the first benzyne Stevens rearrangement a second benzyne molecule reacts with one side of the ring contracted phenylthio derivative \textsuperscript{228} to yield, after abstraction of a β-hydrogen from the bridge, diphenylsulfide \textsuperscript{234} and an olefin.

To verify this hypothesis and test whether the olefinic product
could be made more significant, phenylthio derivative 228 was tested with 2.2 equivalents of benzyne. Unfortunately, however, only a small amount of pyrene 34 could be detected.

\[ \text{PhS} \quad \text{SPh} \quad \text{PhS} \quad \text{PhSi} \quad \text{PhSPh} \]

2.9 Elimination of Trimethylsilylanethiol.

Walter and Lüke\textsuperscript{209}, in their synthesis of masked enamines, reported that the addition of trimethylsilylchloride to the lithium salt 235 resulted in the spontaneous decomposition of the postulated intermediate 236 by elimination of unstable trimethylsilylanethiol 237 with concomitant double bond formation to 238.

\[ \begin{align*}
\text{SLi} & \quad \text{H-C-N(Si(\text{Me})_3)_2} \\
& \quad \text{CH}_2\text{R} \\
\text{(Me)}_3\text{SiCl} & \quad \text{H-C-N(Si(\text{Me})_3)_2} \\
\text{H-C-R} & \quad \text{H} \\
\text{(Me)}_3\text{SiSSi(\text{Me})_3} & \quad \text{2x} \\
\text{H}_2\text{S} & \quad \text{2x} \\
\text{(Me)}_3\text{SiSH} & \quad \text{2x} \\
\text{C} & \quad \text{C} \\
\text{H} & \quad \text{H} \\
\text{N(Si(\text{Me})_3)_2} & \quad \text{2x} \\
\text{235} & \quad \text{236} \\
\text{237} & \quad \text{238}
\end{align*} \]

However, treatment of the lithium salt of dithiol 226 with trimethylsilylchloride led only to recovered dithiol 226.
2.10 Elimination via Ester Stabilized Sulfur Ylids.

An elegant procedure to effect double bond formation by sulfide elimination was put forward by Vedesj\textsuperscript{210}. This procedure involved the fragmentation of an ester stabilized sulfur ylid (e.g. 241) which was prepared by alkylation of a sulfide with trifluoromethane sulfonates (triflates\textsuperscript{211}) of e.g. \( \alpha \)-hydroxyesters, ketones or nitriles, followed by deprotonation of the resulting sulfonium salts (e.g. 240). Ylid fragmentation at room temperature then yielded the olefin. For instance lactone 239 gave sulfonium salt 240 on alkylation with triflate 245 (alkylation time: 2 days).

\[
\text{MeS} \quad 239 \quad \text{EtO} \quad 240
\]

Subsequent treatment with base gave the ester stabilized ylid 241 from which the \( \alpha,\beta \)-unsaturated lactone 242 was obtained in 94\% yield (reaction time: 10 min.). Examples with phenylthio groups instead of a methylthio group as in 239 were also reported.

Thus the trifluoromethanesulfonate ester of ethylglycolate 245
(representative of triflates derived from α-hydroxyesters) was conveniently prepared in 72% yield by slow addition of ethyldiazoacetate to trifluoromethanesulfonic acid in liquid SO$_2$ at -78°C.

\[ \text{CF}_3\text{SO}_2\text{H} + \text{N}_2\text{CHCO}_2\text{Et} \rightarrow \text{CF}_3\text{SO}_2\text{CH}_2\text{CO}_2\text{Et} \]

Alkylation of the metacyclophane sulfides and with triflate was complete in 15 h. Subsequent treatment of these sulfonium salts with base (triethylamine or 1,5-diazabicyclo[5.4.0]-undec-5-ene (DBU)) should have given the ester stabilized sulfur ylids, which could then have undergone fragmentation, as indicated before, to form an olefin. However, none of the expected diene or pyrene could be detected, even when the reaction was warmed to 60°C.

2.11 Some Mechanistic Considerations.

Most examples of the elimination reactions discussed above are 6-eliminations in which two groups are lost from adjacent atoms. There are two ways for this to happen.

From a conformation such as (anti-periplanar) anti elimination occurs, whereas from conformation (syn-periplanar) syn elimination
is the result.

It has been noted that the presence of free or ion-paired base can alter the mode of elimination (anti versus syn). For example, the case of cyclopentane 249, where the phenyl and tosylate group are trans to each other, there are two types of β-hydrogens, one of which is more acidic (H-2) and leads to 250 via syn elimination. Loss of the less acidic proton (H-5) will give the non-conjugated cyclopentane 248 via an anti elimination. With t-BuOK in t-BuOH (50°C) 92% of 250 and 8% of 248 were formed, which indicated a high preference for syn elimination in this system.

\[ \text{t-BuOK} \quad \text{t-BuOH} \]

"crown-ether"

However, addition of the crown ether dicyclohexyl 18-crown-6 (this ether selectively removes K⁺ from the t-BuO⁻⁻⁻⁻⁻K⁺ ion pair and thus leaves t-BuO⁻⁻⁻⁻⁻ as a free base) changed the product composition to 70% of 248 and 30% of 250 which indicates a preference for anti elimination.

\[ \text{R-O-K} \]
From this and other studies, the picture emerged that for neutral leaving groups (e.g. tosylate, halide) syn elimination is favored by ion-paired bases, via a transition state like 251 whereas the free base favors anti elimination.

For positively charged leaving groups (e.g. trimethylammonium) it was predicted that free base should be more effective than ion-paired base in promoting syn elimination, because electrostatic interaction of the negatively charged base and the positive leaving group would put the base into a favorable position for attack on a syn β-hydrogen. This would lead to a transition state like 252. This view was corroborated by Saunders' work.

\[2,12\] Application of these Findings to the Metacyclophane System.

Molecular model studies of sulfonium salt 197 showed us that an anti-periplanar arrangement was very unlikely, this would put the leaving group in the sterically more hindered pseudo-axial position. Therefore, the Hofmann elimination of 197 was assumed to follow a syn pathway. Since we have a positively charged leaving group in 197,
syn elimination will be promoted by free base. Apart from adding a

crown ether, the free base concentration can also be increased by
using DMSO instead of THF, since the former solvates cations more
effectively than the latter. Still another way of increasing the free
base concentration is by addition of a quaternary ammonium salt that cannot itself undergo elimination.

Treatment of sulfonium salt 197 with t-BuOK in DMSO at room temperature yielded pyrene 34 in 43% yield. Addition of tetramethylammonium bromide did not improve the elimination. The effect of added ammonium salt was also negligible in the t-BuOK/THF system. Hofmann elimination of 197 in t-BuOK/THF with crown ether 18-crown-6, to promote the free base, was in so far successful that mainly cyclophanediene 159 was obtained, as opposed to the other reactions where pyrene 34 was formed instead. The yield, however, was only 10%.

Unfortunately, no new or improved method for sulfur elimination with double bond formation was found during the course of this research.
CHAPTER THREE
POSSIBLE FUTURE WORK

Since ring contraction of thiacyclophanes via Wittig or Stevens rearrangement, followed by reaction with methyl iodide, yields a mixture of thiomethyl isomers, it is possible that only certain of these isomers can successfully undergo the Hofmann elimination of the corresponding sulfonium salts.

It has been noticed\textsuperscript{122} that the isomer ratio of the thiomethyl derivative 254 depends on the temperature at which the Wittig rearrangement of thiacyclophane 253 is executed.

If this variation in isomer ratio with reaction temperature turns out to be a general phenomenon for thiacyclophanes, separation of these isomers from the mixture followed by Hofmann elimination of the sulfonium salts then will give valuable information about, firstly, which isomer(s) eliminates preferentially and secondly, how to enrich the product mixture with this isomer(s).
EXPERIMENTAL

All melting points were determined on a Kofler hot stage and are uncorrected. The $^1$Hmr spectra were determined in CDCl$_3$ (unless otherwise stated) on a Perkin-Elmer R12B (60 MHz), R32 (90 MHz) or Bruker WM-250 (250 MHz) spectrometer and are reported in ppm downfield from tetramethylsilane as internal standard. The variable-temperature $^1$Hmr studies were carried out on a R32 (90 MHz) spectrometer, using CDCl$_3$, CD$_2$Cl$_2$, or CDCl$_3$:CD$_2$Cl$_2$ (1:1) as solvent for variable temperature (-100°C to +60°C) studies. $^{13}$Cmr spectra were determined in CDCl$_3$ on a Nicolet TT-14 Fourier Transform spectrometer operating at 15.1 MHz or on a Bruker WM-250 operating at 62.9 MHz and are reported in ppm with δCDCl$_3$=77.0 ppm as reference point.

UV spectra were recorded on a Cary-17 spectrophotometer or a Beckmann DU-8 spectrophotometer.

Mass spectra were determined on a Hitachi Perkin-Elmer RMU-7E or Finnigan 3300 mass spectrometer at 70 eV using electron impact (EI) or chemical ionization (CI) (M$^+$ = molecular ion in mass spectra).

Microanalyses were performed by Canadian Microanalytical Service Ltd. (Vancouver, B.C.). All evaporations were carried out under reduced pressure on a rotary evaporator at ca. 40°C. All organic layers were washed with water (unless otherwise stated) and dried over anhydrous sodium sulfate or magnesium sulfate.
1. 2-Bromo-1,3-dimethylbenzene 98.

(a) Diazotization of 2,6-dimethylaniline 104.

48% aq. HBr (35 ml, 310 mmol) was added slowly to 2,6-dimethylaniline 104 (15 g, 123.8 mmol) at 0°C. Then a solution of sodium nitrite (8.54 g, 122.8 mmol) in H₂O (15 mL) was added rapidly, with stirring, the temperature being kept below 10°C.

(b) Conversion of diazonium salt into 98.

The above prepared cold diazonium solution (see (a)) was added dropwise to a refluxing mixture of CuBr (9.77 g, 68.1 mmol) and 48% aq. HBr (8.4 mL, 74.3 mmol) over a period of 30 min. After cooling the mixture was extracted with benzene. The combined organic layers were washed, dried and evaporated. The residual dark red liquid was chromatographed over silica gel using pentane as eluant to yield 2-bromo-1,3-dimethylbenzene 98, 14 g (62%), bp 205-206°C (lit. bp 206°C).

Hmr, δₗ (CDCl₃, 60 MHz), 6.90 (s, 3H, Ar-H) and 2.34 (s, 6H, Ar-CH₃).

2. 2,6-Dimethyl-1-phenylalloehexanol 107.

A portion (1 mL) of a solution of bromobenzene (68.43 g, 435.8 mmol) in dry THF (500 mL) was added to magnesium (10.7 g, 440 mg-atom) in dry THF (100 mL) at 35°C under N₂.

A few drops of 1,2-dibromoethane were added to initiate the reaction and then the remainder of the solution of bromobenzene was added dropwise at a rate to maintain gentle reflux. After the addition the mixture was further heated at reflux for 30 min.
2,6-Dimethylcyclohexanone 106 (50g, 396 mmol) was then added drop-wise to the hot Grignard reagent. After the addition, heating at reflux was continued for 9 h. The reaction mixture was then cooled and concentrated under reduced pressure. Benzene was added and the organic extracts were washed with dilute HCl and H2O. The organic extracts were combined, dried and evaporated to give a clear yellow liquid. Vacuum distillation yielded colorless alcohol 107, 67.32g (83%), bp 158°C/18 Torr (Lit. bp 134-135°C/15 Torr); 1Hmr, δ, (CCl4, 60 MHz), 7.25 (m, 5H, Ar-H), 1.56 (m, 9H, -CH3) and 0.57 (d, J=6Hz, 6H, -CH3).

3. (2,6-Dimethyl-1-cyclohexen-1-yl)benzene 108.

p-Toluenesulfonic acid (1.4g, 8.14 mmol) was added to a solution of alcohol 107 (67.2g, 329.4 mmol) in toluene (25 mL). The mixture was heated at reflux for 6 h. with azeotropic removal of water (Dean-Stark apparatus). Vacuum distillation yielded the cyclohexene 108 as a colorless liquid. 52.24g (85%), bp 64°C/0.5 Torr (Lit. bp 91-92°C/1.5 Torr), 1Hmr, δ, (CCl4, 60 MHz), 7.07 (m, 5H, Ar-H), 2.40-1.20 (m, 7H, -CH2), 1.46 (s, 3H, -CH3) and 1.80 (d, 3H, J=6Hz, -CH3).

4. 2,6-Dimethyl-1,1'-biphenyl 100.

(a) From the Grignard of 2-bromo-1,3-dimethylbenzene 98.

A portion (1 mL) of a solution of 98 (4g, 21.6 mmol) in dry THF (15 mL) was added to magnesium (530 mg, 21.8 mg-atom) in dry THF (15 mL).
at 35°C under N₂. Then a few drops of 1,2-dibromoethane were added
to initiate the reaction and then the remainder of the solution of 98
was added dropwise at a rate to maintain gentle reflux. After the
addition, the mixture was heated at reflux for an additional 2 h. at
which time most magnesium had disappeared.
The mixture was then cooled to -78°C and a solution of bromobenzene
(3.58g, 22.8 mmol) in dry THF (25 mL) was added dropwise, followed
by Ni (acac)₂ (ca. 5 mg).
The reaction mixture was then allowed to warm to room temperature
over 1 h. and subsequently was heated at reflux for 15 h. This mixture
was then cooled and benzene was added and the organic extracts were
washed with dilute aqueous HCl and H₂O. The organic layer was dried
and evaporated to give a brown liquid which was chromatographed
over silica gel using pentane as eluant.
From the methyl proton resonances in the ¹H mr spectra (60 MHz) the
presence of m-xylene (δ2.26, s, Ar-CH₃), 2-bromo-1,3-dimethylben-
zen e 98 (δ2.32, s, Ar-CH₃) and 2,6-dimethylbiphenyl 100 (δ2.00, s,
Ar-CH₃) was indicated.
Vacuum distillation of this eluate then yielded two main fractions.
The first (bp ca. 80°C/50 Torr) contained mainly m-xylene. The second
fraction (0.53g) still showed, by ¹H mr, some bromide 98 to be present
together with the desired product (in the ratio by ¹H mr 1:3). Subse-
quently 100 was obtained pure by the alternate route C described be-
low.
(b) From (2,6-dimethyl-1-cyclohexen-1-yl) benzene 108 via bromination, dehydrobromination followed by dehydrogenation.

A solution of Br₂ (3g, 18.75 mmol) in CCl₄ (20 mL) was added dropwise to a solution of 108 (2g, 10.75 mmol) in CCl₄ (25 mL) at 0°C. The addition was stopped as soon as the bromine colour persisted. The reaction mixture was then washed successively with aqueous NaHSO₃ and H₂O, dried and evaporated to give a pale yellow liquid.

Dry THF (40 mL) and t-BuOK (2.4g, 21.4 mmol) were then added to this liquid and the mixture was heated at reflux for 4 h. under N₂. After cooling, dichloromethane and dilute HCl were added to the reaction mixture. The organic layer was separated, washed, dried and evaporated to give a dark brown liquid. This was then chromatographed over silica gel using pentane dichloromethane (1:1) as eluant to give an orange liquid.

Benzene (25 mL) and 10% Pd/C (2g) were then added to this orange liquid. This mixture was heated at reflux for 12 h., while N₂ was bubbled through the solution. After cooling, the mixture was then filtered with celite and the filtrate was evaporated to give a brown liquid. Subsequent chromatography over silica gel using pentane as eluant yield biphenyl 100, 1.06g (54%), identical to the next sample (c).

(c) From (2,6-dimethyl-1-cyclohexen-1-yl) benzene 108 via direct dehydrogenation.

A solution of cyclohexene 108 (30g, 161.3 mmol) and α-chloranil 115
(95.2 g, 387.2 mmol) in dry m-xylene (200 mL) was heated at reflux for 3 h. under N₂.

Tetrachlorohydroquinone was then removed by hot filtration and the filtrate was distilled under vacuum. The fraction with boiling range 60-80°C/2-3.10⁻¹ Torr was then collected and subsequently chromatographed over silica gel, using pentane as eluant to give 2,6-dimethylbiphenyl 100 as a colorless liquid, 18.58 g (63%), bp 66-70°C/2-3.10⁻¹ Torr (Lit bp 129°C/14 Torr), ¹Hmr, δ (90 MHz), 7.40-6.93 (m, 8H, Ar-H) and 1.96 (s, 6H, Ar-CH₃); ms peaks (EI) at m/e (relative intensity) 182 (M⁺, 100), 181 (46), 167 (92), 166 (32), 165 (58) and 152 (20); ¹³Cmr, δ, (62.9 MHz), 141.8 (C-1), 141.1 (C-1'), 136.0 (C-2), 129.0, 128.4, 127.3 (C-3, C-2', C-3'), 127.0, 126.7 (C-4, C-4') and 20.8 (Ar-CH₃).

Note: For preparative purposes biphenyl 100 was obtained from 2,6-dimethylcyclohexane 106 without the isolation of alcohol 107 and cyclohexene 108. The overall yield was 64% based on the cyclohexane 106.

5. 2,6-Bis(bromomethyl)-1,1'-biphenyl 60.

N-bromosuccinimide (37.2 g, 209 mmol) and benzoylperoxide (5 mg) were added, in four equal portions, over a period of 2 h., to 2,6-dimethylbiphenyl 100 (18.5 g, 101.6 mmol) in refluxing CCl₄ (125 mL) with concomitant irradiation (200 W. lamp).

After the addition the mixture was irradiated under reflux for an additional 1.5 h. The reaction mixture was then cooled and the
succinimide was removed by filtration. The filtrate was evaporated and gave a tan colored solid. This was then stirred with pentane for 10 min; filtration yielded white bromide 60. Evaporation of the filtrate, followed by washing with pentane, was repeated to increase the yield of bromide 60, 21.2 g (61%), a sample was recrystallized from cyclohexane as white crystals, mp 116-117°C, (Lit. 103 mp 116-117°C), 1Hmr, δ, (CDCl3, 90 MHz), 7.37 (road s, 8H, Ar-H) and 4.10 (s, 4H, -CH2Br); 13Cmr, δ, (62.9 MHz), 141.6, 136.4 (C-1, C-1'), 136.6 (C-2), 130.5, 129.2, 128.2 (C-3, C-2', C-3'), 128.4, 127.9 (C-4, C-4') and 31.7 (-CH2Br).

6. 2,6-Bis(mercaptomethyl)-1,1'-biphenyl 61.

Thiourea (5.5 g, 72.4 mmol) was added to a solution of 2,6-bis(bromomethyl)biphenyl 60 (10 g, 29.4 mmol) in dry THF (200 mL). After the addition the mixture was heated at reflux for 3 h. under N2. Then a solution of KOH (3.88 g, 69.3 mmol) in H2O (50 mL) was added to the hot mixture and heating at reflux was continued for another 3 h. The mixture was then cooled and acidified with 6M aqueous H2SO4, and the whole was extracted with benzene. The benzene extract was washed, dried and evaporated to give a pale yellow oil which solidified on standing. Subsequent chromatography of the solid over silica gel using pentane (400 mL) and pentane/dichloromethane (200 mL, 9:1) as eluants yielded white dithiol 61, 6.82 g (94%), mp 66-68°C. (Lit. 103 mp 64-66°C), 1Hmr, δ, (90 MHz), 7.48-7.22 (m, 8H, Ar-H), 3.42 (d, 4H, J=5 Hz, -CH2SH) and 1.55 (t, 2H, J=5 Hz, -CH2SH); 13Cmr, δ,
(62.9 MHz), 139.9 (C-2), 139.8, 137.9 (C-1, C-1'), 129.4, 128.4,
127.6 (C-3, C-2', C-3'), 128.4, 127.6 (C-4, C-4') and 26.9 (-CH₂SH).


A solution of the dithiol 61 (10g, 40.6 mmol) and the dibromide 54 (11.3g, 40.6 mmol) in nitrogen purged benzene (900 mL) was added dropwise to a well stirred solution of KOH (5.7g, 101.8 mmol) in nitrogen purged 95% EtOH (2500 mL) at 60°C under nitrogen. When the addition was complete (2.5d) the solution was cooled and concentrated. Dichloromethane and water were added to the residue as well as dilute aqueous HCl to neutralize the solution. The dichloromethane extract was washed, dried and evaporated. The residue was then preadsorbed on celite and chromatographed over silica gel using benzene/pentane (1:1) as eluant. The chromatography gave two fractions: The first consisted of a mixture of anti and syn thiacyclophanes 59 and 59A 5.7g (39%), while the second contained products of higher molecular weight.

Note: when the bromide-thiol coupling was done at room temperature lower yields of dimer 104 were obtained (20%).

(a) anti-9-phenyl, 18-methyl-2,11-dithia[3.3]metacyclophane 59.

The mixture of the anti- and syn-dithiacyclophanes 59 and 59A, obtained from the first fraction from the chromatography experiment above, was rechromatographed over silica gel using benzene/pentane (1:4) as eluant. The first fraction of this chromatography contained
the pure anti-isomer 59, while later fractions contained increasing amounts of the syn-isomer 59A.

The mixture of the anti- and syn-isomer obtained in these later fractions was repeatedly recrystallized from benzene to give pure crystals of anti-isomer 59. The crystals of 59 obtained by chromatography (see above) were also recrystallized from benzene. The combined yield of anti-isomer 59 was 2.66g (18%) of colorless crystals, mp 165°C, 1Hmr, δ, (90 MHz), 7.46 (AB^2, 2H, H-5), 7.35-7.13 (m, 6H, Ar-H), 7.02 (AB^2, 1H, H-15), 6.74 (br. s, 2H, H-2', 6'), 3.79 and 3.66 (AB quartet, 4H, J=14.3 Hz, -CH=CH-S-), 3.70 and 3.46 (AB quartet, 4H, J=13.6 Hz, -CH=CH-S-) and 1.56 (s, 3H, Ar-CH);

ms peaks (EI) at m/e (relative intensity) 362 (M^+, 9), 212 (15), 211 (24), 179 (100), 178 (49), 165(38), 152 (17), 149 (13), 148 (12), 135 (17), 134 (16), 118 (28), 117 (60), 91 (45) and 77 (23);

^13Cmr, δ, (1511 MHz), 143.0 (C-9), 137.9 (C-1'), 136.8 (C-18), 135.6, 134.9 (C-4, C-13), 130.7 (C-2'), 130.1, 129.9, 126.8 (C-5, C-14, C-3'), 127.0, 126.8, 125.0 (C-6, C-15, C-4'), 32.5, 31.1 (C-1, C-3) and 15.8 (Ar-CH).

Anal. Calcd. for C_{23}H_{22}S_2 : C 76.19, H 6.11

Found : C 76.09, H 6.16

(b) syn-9-phenyl, 18-methyl-2,11-dithia[3.3]metacyclophane 59A.

The mixtures of anti and syn thiacyclophanes 59 and 59A that showed the syn-isomer to be the major component, obtained from chromatography or from recrystallization as described in (a), were
repeatedly recrystallized from a benzene/hexane mixture (1:9) to yield 86 mg (0.6%) of \( \text{59A} \) as colorless crystals, mp 170°C, \(^1\)Hmr, δ, (90 MHz), 7.37 (br. s, 5H, Ar-H), 6.99 (AB\(_2\), 2H, J=7Hz, H-5 or H-14), 6.90 (AB\(_2\), 2H, J=7Hz, H-5 or H-14), 6.75 (AB\(_2\), 2H, J=7Hz, H-6, H-15), 4.19 and 3.68 (AB quartet, 4H, J=7Hz, -CH\(_2\)-S-) and 2.41 (s, 3H, Ar-CH\(_3\));

ms peaks (EI) at m/e (relative intensity) 362 (M\(^+\), 37), 211 (27), 179 (100), 178 (52), 165 (33), 149 (12), 148 (11), 134 (11), 117 (37), 115 (24), 91 (26) and 77 (15);

\(^{13}\)Cmr, δ, (15.1 MHz), 139.1 (C-9), 136.2, 134.2 (C-18, C-1'), 136.1, 135.2 (C-4, C-13), 131.7 (C-2'), 130.3, 129.4, 127.7 (C-5, C-14, C-3'), 128.2, 127.0, 125.8 (C-6, C-15, C-4'), 36.1, 34.9 (C-1, C-3) and 17.9 (Ar-CH\(_3\)).

Anal. Calcd. for \( \text{C}_{23}\text{H}_{22}\text{S}_2 \) : C 76.19, H 6.11

Found : C 76.87, H 6.13

8. Wittig rearrangement of anti-dithiacyclophane \( \text{59} \) to \( \text{118} \).

n-BuLi(268.8 mg, 4.2 mmol) in hexane (4mL) was added by syringe to a stirred solution of dithiacyclophane \( \text{59} \) (648 mg, 1.79 mmol) in dry THF (45 mL) under nitrogen at room temperature. The initially colorless solution turned dark red and was stirred for an additional 5 min. Methyl iodide (0.5 mL, 8.0 mmol) was then added upon which the solution turned pale yellow. The mixture was then acidified with aqueous HCl and extracted with dichloromethane. The organic extract was washed with water, until neutral, dried and evaporated to give a
yellow oil. This was then chromatographed over silica gel using benzene as eluant to give 258 mg (37%) of 118 as a mixture of isomers.

9. Anti-Bis(sulfonium) salt 59S of anti-dithiacyclophane 59.

A solution of thiacyclophane 59 (1.76g, 4.86 mmol) in dry dichloromethane (50 mL) was added slowly with stirring to a suspension of dimethoxycarbonium fluoroborate (3.42g, 80% as oil, 16.8 mmol) in dry dichloromethane (5 mL) held at -30°C under a nitrogen atmosphere. When the addition was complete, the mixture was allowed to warm to room temperature and was stirred for another 4 h. Then ethyl acetate (35 mL) was added and the mixture was stirred for 5 h. This filtration gave the bis(sulfonium) salt 59S as white powder (2.63g, 96%). This was employed directly in the next step.

10. Stevens Rearrangement of 59S to give 118.

Potassium t-butoxide (2.0g, 17.86 mmol) was added to a stirred suspension of sulfonium salt 59S (2.63g, 4.65 mmol) in dry THF (130 mL) under a nitrogen atmosphere. The mixture was then stirred for 1h. at room temperature after which aqueous HCl and dichloromethane were added. The organic layer was separated, washed with water, dried and evaporated. The yellow residue was then preadsorbed on silica gel and chromatographed over silica gel, using pentane as eluant to give 1.16g (64%) of 118 as a mixture of isomers.

(a) anti-1,9-Bis(methylthio)-8-phenyl-16-methyl[2.2]metacyclophane 118A.
The mixture of isomers \[ \text{118} \] (747 mg, 192 mmol) was carefully rechromatographed over silica gel, using pentane as eluant, to separate the individual components. The first fractions provided a crystalline solid \[ \text{118A} \] which, after recrystallization from hexane, gave 182 mg \( (24\%) \) of colorless needles, mp 157-158°C. \[^1\text{Hmr}, \delta, \text{(90 MHz)}\], 8.00 (dd, 1H, J=7Hz, H-6), 7.70 (dd, 1H, J=6Hz, J=2Hz, H-14), 7.39 (dd, 1H, J=7Hz, H-4), 7.22-6.87 (m, 6H, Ar-H), 6.48-6.34 (m, 2H, H-2',6'), 4.26 (dd, 1H, J=4Hz, J=11.5Hz, H-1(ax)), 3.82 (dd, 1H, J=4Hz, H-9(ax)), 3.29 (dd, 1H, J=4Hz, J=11.5Hz, H-10(eq)), 2.70 (t, 2H, J=11.5Hz, J=11.5Hz, H-2(ax)), 2.16 (s, 3H, (S-CH\_3)-9), 2.12 (s, 3H, (S-CH\_3)-1), and 0.87 (s, 3H, Ar-CH\_3); ms peaks (EI) at m/e (relative intensity) 390 (M\(^+\), 7), 225 (31), 179 (16), 178 (17), 165 (100), 149 (13), 147 (11), 115 (12), 91 (6) and 77 (7); \[^13\text{Cmr}, \delta, \text{(62.9 MHz)}\], 147.2 (C-8), 143.3 (C-16), 137.9 (C-1'), 137.1, 136.3, 135.9, 134.9 (C-3, C-7, C-11, C-15), 130.7 (C-2',6'), 126.7 (C-3',5'), 129.3, 128.4, 126.9, 126.4, 125.9, 124.8, 124.7 (C-4, C-5, C-6, C-12, C-13, C-14, C-4'), 53.2 (C-9), 52.9 (C-1), 43.2 (C-2), 42.5 (C-10), 16.2 (Ar-CH\_3), 15.6 (1 S-CH\_3) and 15.1 (9 S-CH\_3).

Anal. Calcd. for \( \text{C}_{25}\text{H}_{26}\text{S}_2 \): C 76.87, H 6.71

Found : C 76.40, H 6.38

(b) \( \text{ant}^{\text{a}},\text{1,10-bis(methylthio)-8-phenyl-16-methyl[2.2]metacyclophane} \)

\[ \text{118B} \].

Later fractions of the above mentioned chromatograph (see (a)) showed, based on \[^1\text{Hmr}\], an increase in a second isomer which we.
assigned as 118B. These fractions were again chromatographed over silica gel using pentane as eluant to give 118B as a waxy solid. Repeated recrystallization from hexane gave 2 mg (0.3%) of 118B as white crystals, mp 162-163°C, $^1$Hmr, $\delta$, (90 MHz), 7.62 (d, 2H, J=8Hz, H-12), 7.36 (d, 2H, J=7Hz, H-4), 7.12-6.86 (m, 5H, Ar-H), 6.65-6.52 (m, 2H, H-2',6'), 4.15 (dd, 2H, J=4Hz, J=11Hz, H-1(ax)), 3.32 (dd, 2H, J=4Hz, J=12Hz, H-2(eq)), 2.77 (t, 2H, J=11Hz, J=12Hz, H-2(ax)), 2.11 (s, 3H, S-CH$_3$) and 0.93 (s, 3H, Ar-CH$_3$); ms peaks (EI) at m/e (relative intensity) 390 (M$,^+$, 29), 211 (100), 191 (21), 178 (22), 165 (32), 163 (21), 147 (37), 115 (14), 91 (11) and 77 (13);

$^1$Cmr, $\delta$, (62.9 MHz), 146.5 (C-8), 143.6 (C-16), 137.8 (C-1'), 136.6, 135.7 (C-3, C-11), 131.2 (C-2'), 129.1, 126.7, 125.4 (C-4, C-12, C-3'), 126.8, 125.8, 125.2 (C-5, C-13, C-4'), 52.5 (C-1), 44.0 (C-2), 16.4 (Ar-CH$_3$) and 15.5 (Ar-CH$_3$).


A solution of the mixture of isomers 118 (1.03g, 2.64 mmol) in dry dichloromethane (10 mL) was added to a stirred suspension of dimethoxycarbonium fluoroborate (2.14g, 80% as oil, 10.6 mmol) in dry dichloromethane (5 mL) held at -30°C under nitrogen. When the addition was complete, the mixture was allowed to warm to room temperature and was stirred for another 4 h. Then ethyl acetate (35 mL) was added and stirring was continued for 0.5 h. The solvent was removed by
The oily residue was triturated with ethyl acetate effecting the separation of 1.05 g (67%) of the bis(sulfonium) salt 120 as an off-white powder. This was employed directly in the next step.

Anhydrous potassium t-butoxide (0.79 g, 7.05 mmol) was added to a stirred suspension of the bis(sulfonium) salt 120 (1.05 g, 1.77 mmol) in dry THF (35 mL) under nitrogen. The mixture was then stirred for 1 h. at reflux. After cooling of the reaction mixture, benzene was added and the mixture was acidified with aqueous HCl. The organic layer was then separated, washed, dried and evaporated. The dark green residue was preadsorbed on celite and chromatographed over silica gel, using pentane as eluant, and gave 213 mg (41%) of 51.

Recrystallization from cyclohexane gave dark green crystals, mp 159-160°C, $^1$Hmr, δ, (90 MHz), 8.77-8.03 (m, 10H, Ar-H), 6.20 (t, 1H, J=7.5Hz, H-6'), 5.85 (t, 2H, J=7.5Hz, H-3'), 2.81 (d, 2H, J=7.5Hz, H-2') and -4.30 (s, 3H, -CH$_3$).

ms peaks (EI) at m/e (relative intensity) 294 (M$^+$, 16), 279 (30), 217 (22) and 202 (100);

UV, cyclohexane $^\text{max}$\(_{\text{max}}\) (ε) 341 nm (86.000), 357.5 (24.000), 383 (46.000), 443 (5.000), 461 (6.200), 481 (6.500), 540 (215), 590 (217), 603 (264), 615.5 (296), 631 (244) and 645.5 (325);

$^{13}$Cmr, δ, (62.9 MHz), 139.0 (C-4), 136.7 (C-1'), 135.3 (C-7), 125.8 (C-5), 125.3 (C-3'), 125.0 (C-4'), 124.8 (C-8), 124.4 (C-2), 124.1 (C-2'), 122.9 (C-3), 122.9 (C-6), 122.5 (C-9), 36.6 (C-15), 29.1 (C-16) and 14.9 (C-16b).
A solution of 118A (182 mg, 0.466 mmol) in 100% ethanol (40 mL) containing W-7, Raney Nickel116 (6g) was heated at reflux for 6 h. After removal of the catalyst and solvent, the residue was taken up in dichloromethane and chromatographed over silica gel. This gave 136.4 mg (98%) of anti-8-phenyl-16-methyl[2.2]metacyclophane 119. Recrystallization from hexane gave colorless crystals, mp 147°C, 1Hmr, δ, (CCl₄, 90 MHz), 7.26-7.18 (d (AB₂), 2H, Ar-H), 7.0-6.6 (m, 7H, Ar-H) 6.51-6.38 (m, 2H, H-2',6'), 3.05-2.65 (m, 8H, -CH₂-CH₂-) and 0.79 (s, 3H, Ar-CH₃); ms peaks (EI) at m/e (relative intensity) 298 (M⁺, 7), 180 (21), 179 (100), 178 (21), 165 (9), 119 (16), 117 (10), 91 (7) and 77 (5); 13Cmr, δ; (62.9 MHz), 146.8 (C-8), 143.0 (C-16), 138.9 (C-1'), 137.4, 136.3 (C-3, C-11), 130.8 (C-2'), 128.3, 127.2, 126.3 (C-4, C-12, C-3') 126.30, 125.8, 124.0, (C-5, C-13, C-4'), 37.0, 36.7 (C-1, C-2) and 15r8 (Ar-CH₃).

Anal. Calcd. for C₂₃H₁₈ : C 93.84, H 6.16
Found : C 93.63, H 6.35

12. Raney Nickel Desulfurization of 118A.

A solution of 118A (182 mg, 0.466 mmol) in 100% ethanol (40 mL) containing W-7, Raney Nickel116 (6g) was heated at reflux for 6 h. After removal of the catalyst and solvent, the residue was taken up in dichloromethane and chromatographed over silica gel. This gave 136.4 mg (98%) of anti-8-phenyl-16-methyl[2.2]metacyclophane 119. Recrystallization from hexane gave colorless crystals, mp 147°C, 1Hmr, δ, (CCl₄, 90 MHz), 7.26-7.18 (d (AB₂), 2H, Ar-H), 7.0-6.6 (m, 7H, Ar-H) 6.51-6.38 (m, 2H, H-2',6'), 3.05-2.65 (m, 8H, -CH₂-CH₂-) and 0.79 (s, 3H, Ar-CH₃); ms peaks (EI) at m/e (relative intensity) 298 (M⁺, 7), 180 (21), 179 (100), 178 (21), 165 (9), 119 (16), 117 (10), 91 (7) and 77 (5); 13Cmr, δ; (62.9 MHz), 146.8 (C-8), 143.0 (C-16), 138.9 (C-1'), 137.4, 136.3 (C-3, C-11), 130.8 (C-2'), 128.3, 127.2, 126.3 (C-4, C-12, C-3') 126.30, 125.8, 124.0, (C-5, C-13, C-4'), 37.0, 36.7 (C-1, C-2) and 15r8 (Ar-CH₃).

Anal. Calcd. for C₂₃H₂₂ : C 92.57, H 7.43
Found : C 92.41, H 7.23

13. 9,18-Diphenyl-2,11-dithia-[3,3]metacyclophane 192.

A solution of the dithiol 61 (5.0g, 20.32 mmol) and the dibromide 60 (6.91g, 20.32 mmol) in deoxygenated benzene (900 mL) was added dropwise to a well stirred solution of potassium hydroxide (3.4g,
61 mmol) in deoxygenated 95% ethanol (100 mL) at reflux under nitrogen. When the addition was complete (3 days), the solvent was removed under reduced pressure. The residue was then acidified with aqueous HCl and extracted with dichloromethane (500 mL). The organic layers were combined and washed with water, dried and evaporated. The white residue was preadsorbed on silica gel and chromatographed over silica gel using pentane (1000 mL) and pentane/dichloromethane (1:1) as eluants. This yields 58 mg (0.6%) of 192 as a mixture of syn- and anti-isomers.

In a comparable experiment, dicesium carbonate (3 equivalents) was used as the base instead of potassium hydroxide. However, the yield of the syn and anti mixture of 192 was not improved, 43 mg (0.5%).

(a) anti-9,18-Diphenyl-2,11-dithia[3.3]metacyclophane 192.

The mixture of isomers 192, described above, was again preadsorbed, this time on celite, and chromatographed over silica gel using pentane as eluant. The first fractions were enriched in the anti-isomer. Recrystallization from dichloromethane gave 9 mg of anti-192 as colorless crystals, mp 248-249°C, [Lit. mp 220-226°C], $^1$Hmr, $\delta$, (90 MHz), 7.34-7.19 (m, 12H, Ar-H), 7.15-6.86 (m, 6H, H-6, H-2'), 4.22 and 3.57 (AB quartet, 8H, J=15Hz; -CH$_2$-S-);

$^{13}$Cmr, $\delta$, (CD$_2$Cl$_2$, 15.1 MHz), 139.4 (C-9), 137.6 (C-1'), 135.7 (C-4), 133.2 (C-2'), 130.6, 127.7 (C-5, C-3'), 128.7, 127.4 (C-6, C-4') and 35.0 (C-1).
Anal. Calcd. for C_{28}H_{24}S_{2} : C 79.20, H 5.70
Found : C 79.11, H 5.79

(b) syn-9,18-Diphenyl-2,11-dithia[3.3]metacyclophane 192A

The later fractions of the above mentioned chromatography experiment (see (a)) showed, by $^1$HMR, enrichment in the syn-isomer. These syn-isomer enriched fractions were combined and evaporated to dryness. Dichloromethane (5 mL) was then added and the solid was dissolved by heating. Subsequent cooling to 0°C followed by filtration gave, after two repetitions, 2.5 mg of pure syn-192A, mp 174-176°C, $^1$HMR, $\delta$, (90 MHz), 7.42 (AB$_2$, 4H, J=7 Hz, H-5), 7.29 (s, 10H, Ar-H), 7.07 (AB$_2$, 2H, J=7 Hz, H-6), 3.74 and 3.58 (AB quartet, 8H, J=13 Hz, $-\text{CH}_2$-$S-$); ms peaks (EI) at m/e (relative intensity) 424 (M$^+$, 26), 211 (39), 180 (35), 179 (100), 178 (33), 165 (42) and 152 (16); $^{13}$CMR, $\delta$, (62.9 MHz), 141.7 (C-9), 136.8 (C-1'), 134.9 (C-4), 132.3, 130.7, 126.9 (C-5, C-2', C-3'), 127.2, 127.0 (C-6, C-4') and 32.7 (C-1).


A solution of the dithiol 61 (429 mg, 2 mmol) and $\alpha,\alpha'$-dibromo-m-xylene (538 mg, 2 mmol) in nitrogen purged benzene (400 mL) was added dropwise to a well stirred solution of potassium hydroxide (320 mg, 5.7 mmol) in nitrogen purged 95% ethanol (500 mL) at 60°C under nitrogen. When the addition was complete (30 h), the solution
was stirred at 60°C for an additional hour. The solvent was then removed under reduced pressure. The residue was acidified with aqueous HCl and extracted with dichloromethane. The organic extract was washed with water until neutral, dried and evaporated. The residue was then preadsorbed on celite and chromatographed over silica gel using pentane (500 mL) and pentane-dichloromethane (200 mL, 9:1) as eluants.

Recrystallization from cyclohexane gave colorless crystals of the di-thiacyclophane 191, 276 mg (40%), mp 144°C [Lit. mp 134°C], \(^1\)Hmr, \(\delta\), (90 MHz), 7.34-7.05 (m, 7H, Ar-H), 6.99-6.83 (m, 3H, Ar-H), 6.70 (br s, 1H, H-2'), 5.49 (s, 1H, H-18), 3.70 and 3.53 (AB quartet, 4H, J=13Hz, \(-\text{CH}_2\text{-S}\)-), 3.62 and 3.55 (AB quartet, 4H, J=16Hz, \(-\text{CH}_2\text{-S}\)-); ms peaks (EI) at m/e (relative intensity) 348 (M^+, 50), 211 (19), 180 (24), 179 (100), 178 (57), 165 (21), 135 (10), 104 (10), 91 (12) and 78 (9);

\(^{13}\)Cmr, \(\delta\), (62.9 MHz), 143.4 (C-9), 137.7 (C-1'), 139.6, 135.0 (C-4, C-13), 130.4, 126.5 (C-5, C-14), 130.1 (C-2'), 129.5 (C-6'), 128.6 (C-18), 128.3, 127.7, 127.4 (C-6, C-15, C-4'), 127.3 (C-3',5'), 35.3 and 34.2 (C-1, C-3).

Anal. Calcd. for C\(_{22}\)H\(_{20}\)S\(_2\) : C 75.82, H 5.78

Found : C 75.70, H 5.92
REFERENCES


3. (a) Aromaticity - An International Symposium held at Sheffield (1966), Special Publication No. 21, The Chemical Society (1967);


6. E. Hückel, Z. Physik., 70, 204 (1931); (b) ibid., 72, 310 (1931); (c) ibid., 76, 628 (1932); (d) Z. Electrochem., 42, 752 (1937).


19. (a) P. Ehrenfest, Physika, 5, 388 (1925); (b) Z. Physik., 58, 219 (1929).


33. P.J. Garratt, in ref. 3e, page 177.


44. (a) D.J. Cram, C.S. Montgomery and G.R. Knox, J. Am. Chem. Soc., 88, 515 (1966); (b) A.D. Wolf, V.V. Kane, R.H. Levin and
M. Jones, Jr., *ibid.*, 95, 1680 (1973).


59. E. Vogel, private communication to M.D. Bierbaum and W. Anker.


61. A.W. Hanson, Acta Cryst., 18, 599 (1965).


100. R.V. Williams, post-doctoral report, University of Victoria (1980).


104. see reference 3g, Chapter 4.


120. A.W. Hanson, Acta Cryst. (B), 27, 197 (1971).


184. V. Boekelheide and C.H. Tsai, unpublished results.


204. M. Pesson and D. Richer, Comptes Rendus, 260, 603 (1965).


216. (a) J.K. Borchardt and W.H. Saunders, Jr., J. Am. Chem. Soc., 96, 3912, 3918 (1974); (b) A.F. Cockerill and R.G. Harrison, in


173 191 \textit{anti-192} \\
\textit{syn-192A}
VITA

Surname: ANKER  Given Names: WILLEM

Place of Birth: ALPHEN, THE NETHERLANDS  Date of Birth: June 9, 1951

Educational Institutions Attended, with Dates of Entering and Leaving:

UNIVERSITY OF LEIDEN, LEIDEN, THE NETHERLANDS  1969 to 1972

UNIVERSITY OF LEIDEN, LEIDEN, THE NETHERLANDS  1974 to 1977

UNIVERSITY OF VICTORIA, VICTORIA, B.C., CANADA  1977 to 1982

Degrees, Diplomas, Etc., Awarded, with Dates and Names of Institutions:

B. Sc.  1972  UNIVERSITY OF LEIDEN, LEIDEN, THE NETHERLANDS

M. Sc.  1977  UNIVERSITY OF LEIDEN, LEIDEN, THE NETHERLANDS

Honors and Awards:

UNIVERSITY OF VICTORIA GRADUATE FELLOWSHIP, 1977/78, 1979/80

PUBLICATIONS.

1. The crystal and molecular structure of syn-2,11-dithia-
[3.3]metacyclophane.
   Willem Anker, Gordon W. Bushnell, and Reginald H. Mitchell,

2. The synthesis and conformational behaviour of 2,11-dithia-
[3.3]metacyclophanes with internal phenyl substituents.
   Reginald H. Mitchell and Willem Anker, Tetrahedron Letters,

3. The synthesis of an unusual dihydropyrene containing one
aromatic π-cloud within and perpendicular to a second.
   Reginald H. Mitchell and Willem Anker, Tetrahedron Letters,
   5139 (1981).
PARTIAL COPYRIGHT LICENSE

I hereby grant the right to lend my thesis or dissertation (the title of which is shown below) to users of the University of Victoria Library, and to make single copies only for such users or in response to a request from the library of any other university, or similar institution, on its behalf or for one of its users. I further agree that permission for extensive copying of this thesis for scholarly purposes may be granted by me or a member of the University designated by me. It is understood that copying or publication of this thesis for financial gain shall not be allowed without my written permission.

Title of Thesis/Dissertation

SYNTHESES AND CONFORMATIONAL STUDIES OF NOVEL AROMATIC COMPOUNDS

Author

Signature

WILLEM ANKER

Date