APPROACHES TO BRIDGED ANNULENES USING BOTH CLASSICAL AND REACTIVE INTERMEDIATES. THE SYNTHESIS OF THE FIRST DIATROPIC BRIDGED THIAANNULENE AND SEVERAL FUSED DIHYDROPYRENES

by

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A Dissertation Submitted in Partial Fulfilment of
the Requirements for the Degree of

DOCTOR OF PHILOSOPHY

in the Department of Chemistry

We accept this dissertation as conforming
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ABSTRACT

The successful synthesis of the first bridged thia[13]annulene, *trans*-9b,9c-dimethyl-9b,9c-dihydrophenyleno[1,9-bc]thiophene, **120**, was achieved in 11 steps, starting from 3-methylthiophene, **111**. Using the external and internal proton chemical shifts of **120**, it was shown unambiguously to be the first diatropic bridged thia annulene. From the proton chemical shifts of **120**, its diatropicity was estimated to be about 35-40% that of dimethyldihydropyrene **12**. Synthesis of the potential intermediate 2,4-bis(bromomethyl)-3-methylthiophene, **110**, is expected to lead to syntheses of a variety of new bridged annulenes.

Synthesis of the *quasi*-biphenylene, **155**, was attempted. The precursor to **155**, 1,3-bis(methoxymethyl)-2-methylbiphenylene, **170**, was synthesised from 1,2-dibromobenzene, **82**, in 4 steps. Attempts to convert **170** into the corresponding dibromide were unsuccessful.

The synthesis of *trans*-14b,14c-dimethyl-14b,14c-dihydro-benzo[1",2":3,4]cyclobuta[1,2-*b*]naphtho[2,1,8-*fgh*]anthracene, **192**, was achieved from the oxa[17]annulene **63**. A detailed nmr analysis of **192** was made using 1D and 2D nmr techniques together with a bond order-chemical shift correlation for **192**. From the ^{1}Hnmr data of **192**, using Mitchell's method, the diatropicity of biphenylene was estimated to be 50-55% that of benzene.

The adduct **209**, from cycloheptatriene and oxa[17]annulene **63**, was obtained in in 60% yield, but attempted dehydration/deoxygenation reactions were unsuccessful.

The cyclopropene adduct **224**, was obtained in 41% yield from the oxa[17]annulene **63**. Attempted synthesis of the benzocyclopropene fused dihydropyrene **218** gave partial success. The proton nmr data obtained from the reaction mixture seem to indicate the lack of Mills-Nixon effect in benzocyclopropene, **181**.

Some attempted reactions of the dihydropyryne **62**, did not yield any of the expected products.

A new synthesis of symmetrical 1,2-diketones from Grignard reagents was developed. 1,2-Bis(2'-methyl-3'-methoxymethylphenyl)ethanedione, **241**, was synthesised using this method. *anti*-9,25-Dimethylquinoxalino[10,11-*b*]-2-thia[2.3]metacyclophane-10-ene, **287**, was synthesised from the diketone **241**. An X-

ray crystal determination showed its anti geometry. The unstable *trans*-14c,14d-dimethyl-14c,14d-dihydrotribenzo[*abc*]phenazine, **279**, was synthesised from the thiacyclophane **287**. The proton nmr spectrum of **279**, revealed its similarity to the naphtho[e]dihydropyrene **58**.

From the proton chemical shifts of **279**, the diatropicity of quinoxaline was estimated to be the same as that of naphthalene.

The teraryl **281** and the thiophene dioxide **296** were synthesised. Exploratory model reactions of **296**, resulted in various teraryls. Complexation of the thiophene dioxide **296** resulted in the complex **297**. An X-ray crystal determination of **297** showed it have a syn geometry. Barrier to rotation in the teraryls obtained in this work was studied by variable temperature nmr. The results are rationalised in terms of varying ring size of arenes.

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LIST OF ABBREVIATIONS

Ar, Arom	aromatic ring
bp	boiling point
n-BuLi	*n*-butyllithium
t-Bu	*t*-butyl
$CDCl_3$	chloroform-d
CD_2Cl_2	dichloromethane-d_2
^{13}Cnmr	carbon-13 nuclear magnetic resonance
m-CPBA	*m*-chloroperoxybenzoic acid
decomp.	decomposition
DIBAH	diisobutylaluminiumhydride
DMF	dimethylformamide
DMSO	dimethylsulfoxide
EtOH	ethanol
^{1}Hnmr	proton magnetic resonance
IR	infrared spectrum
LiTMP	lithium 2,2,6,6-tetramethylpiperide
LDA	lithium diisopropylamide
Me	methyl
MeOH	methanol
mp	melting point

MS	mass spectrum
CI	chemical ionisation
EI	electron impact
NMP	1-methyl-2-pyrrolidinone
NMR	nuclear magnetic resonance
s	singlet
d	doublet
t	triplet
dd	doublet of doublets
m	multiplet
ppm	parts per million
Ph	phenyl
RE	resonance energy
REPE	resonance energy per electron
THF	tetrahydrofuran
TMEDA	N,N,N,N-tetramethylethylenediamine
UV	ultraviolet spectrum
VT	variable temperature

ACKNOWLEDGEMENTS

I would like to express my sincere thanks to Professor R. H. Mitchell first for introducing me to the chemistry of annulenes and cyclophanes and secondly the freedom to explore various aspects of this chemistry during my stay here. I am also very grateful to Professor Mitchell for his encouragement, patience and support during the course of this work.

I wish to thank Professor W. J. Balfour for reading and correcting part of this thesis and his kind help during the final year.

I am grateful to many faculty members of this department for their encouragement and help, in particular: Professor T. E. Gough for his timely rescues, Dr. T. W. Dingle for calculating the π-SCF bond orders reported in this thesis and Professor A. Fischer for some valuable discussions during the early part of this work. I would like to thank Mrs. C. Greenwood for her help in recording the nmr spectra, Dr. D. McGillivray for recording the mass spectra and K. A. Beveridge for the X-ray determinations.

I am grateful to the University of Victoria and the department of chemistry for the financial support which financed my study at this University.

I am very thankful to all my friends and colleagues for their help and support.

I would also like to express my gratitude to all my family for their loving encouragement and patient support.

To my mother

who cared and suffered to give me an excellent education.

CHAPTER ONE

INTRODUCTION

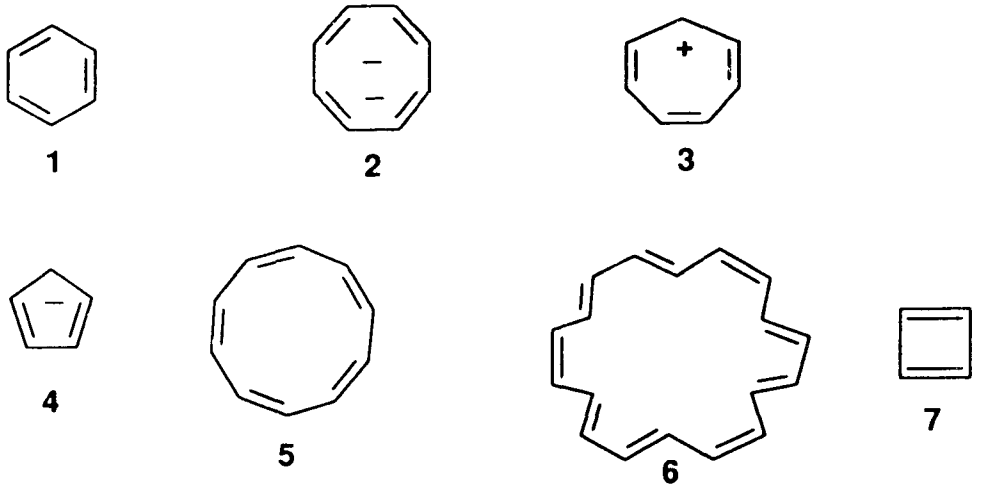
1.1 Prologue

Aromatic compounds constitute a broad class of chemicals and are connected to a wide range of topics, starting from the chemical evolution of life[1] to carcinogenicity.[2] Yet, aromaticity is one of the most difficult and hard to define concepts among bonding theories. After the discovery of benzene by Faraday in 1825,[3] and the subsequent growth of the chemistry of benzene derivatives, the definition of aromaticity has undergone several changes.[4,5] Kekulé's intuitive idea of the structure of benzene and its derivatives,[6] gave some understanding of the constitution of these compounds, and greatly aided the invention of new dyes which helped the establishment of several chemical industries based on coal-tar.

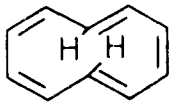
Aromatic compounds, though they fall under the broad category of unsaturated compounds, have several distinct characteristics such as higher thermal stability and lower chemical reactivity. Hückel's molecular orbital (HMO) theory made the first successful attempt to account for such stability based on their π-electron configuration.[7] According to Hückel theory, planar, monocyclic, conjugated molecules having (4n+2) π-electrons (where n is an integer) will be more stable, and those having (4n) π-electrons will be less

stable than a conjugated acyclic polyene. It follows from this prediction that the molecules which do not satisfy all three criteria, namely planarity, fully conjugated π-electrons and monocyclic, will be of intermediate stability. Later, the planar, monocyclic, conjugated molecules with (4n+2) π-electrons were termed as aromatic, those with (4n) π-electrons as antiaromatic and the rest nonaromatic.

The popularity of HMO theory among synthetic chemists led to the syntheses of several non-natural cyclic systems such as tropylium cation,[8] cyclooctatetraenyl dianion[9] and several neutral systems. Such molecules, e.g., **2-6**, along with known compounds, like benzene **1**, were found to behave in accordance with HMO theory. The 4π-system, cyclobutadiene, **7**, was shown to be highly reactive and could not be studied under normal conditions.[10] Only recently, under special surroundings, could a ^{1}Hnmr spectrum of **7** be obtained at room temperature.[11]



Conformational mobility in the case of larger cyclic compounds, called the annulenes, such as the [10]annulene **8** (the number 10 refers to the number of peripheral atoms in the ring) and the [14]annulene **9**, renders them non-planar at normal temperature and hence non-aromatic.[12] This problem was overcome in two different ways. One approach was due to Sondheimer and Nakagawa, who introduced large substituents and triple bonds to make the large annulene rings rigid and planar.[13] For example, the annulenes **10** and **11** are aromatic.



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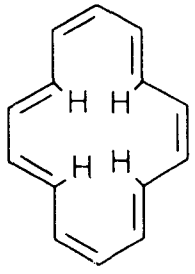

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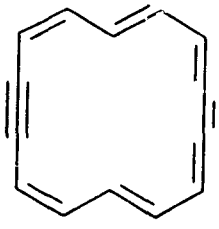

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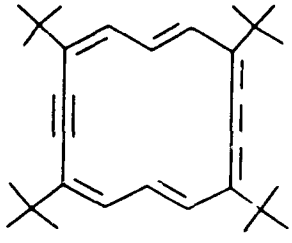

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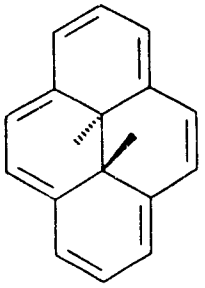
The other approach was through the efforts of Boekelheide and Vögel and employs the strategy of using saturated internal bridges to introduce rigidity and to arrest the conformational mobility. The [14]annulene, *trans*-10b,10c-dimethyl-10b,10c-dihydropyrene (DMDHP), **12**, synthesised by Boekelheide[14] and the [10]annulene, 1,6-methano[10]annulene, **13**, made by Vögel[15] are rigid conjugated systems.



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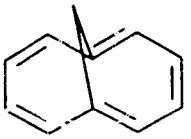

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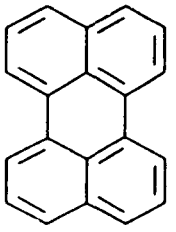
While HMO theory could explain and predict the stabilities of monocyclic conjugated hydrocarbons, it fails to account for the behaviour of several cross conjugated systems and nonalternant systems. Modifications of the HMO theory can explain the properties of conjugated heterocyclic compounds.[16]

Polyacenes such as perylene, **14**, non-Hückel systems such as **15**, and non-planar systems such as **16**, can now be considered as aromatic, according to Randic's conjugated circuit theory.[17] It states that regardless of the total π-electron count, systems that possess only (4n+2) conjugated circuits are aromatic and those with only (4n) conjugated circuits are antiaromatic.



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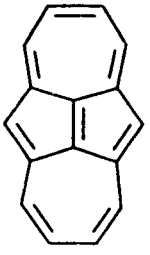

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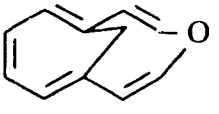

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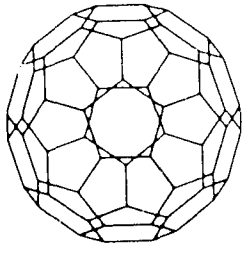
Predictions as to whether a system will be aromatic or antiaromatic can also be made on the basis of a graph theoretical approach.[17]

1.2 Detection of aromaticity

The interplay of theory and practice in aromatic chemistry has led to syntheses and discoveries of a rich variety of compounds. One of the recent discoveries, guided by theoretical prediction, being the fullerene (C_{60}) **17**.[18] This is a stable, spherical aromatic compound for which new theories had to be developed to account for its chemical and physical behaviour.[19,20]



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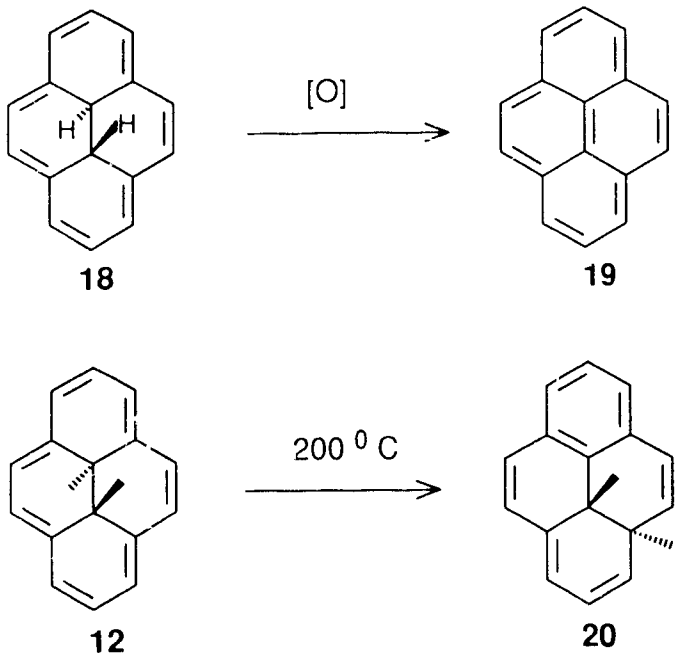
With such new and complex molecules being added to the class of aromatic compounds from time to time, the means of detecting the aromatic character through a single property becomes difficult. We shall now briefly consider some of the means of detecting aromatic character.

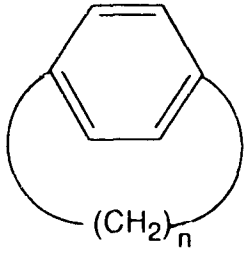
Chemical and thermal stabilities, although indicators of aromatic character, cannot be applied as universal criteria. For example, let us consider the [14]annulenes **18** and **12**. The dihydropyrene **18** is oxidised easily into

pyrene **19** by air[21] and DMDHP **12**, though resistant to air oxidation, undergoes thermal rearrangement to **20**.[22] Yet both are now considered aromatic by other criteria.



Data can be obtained from X-ray measurements, for example, the equal bond lengths observed in benzene derivatives and the only small deviations from planarity led to consideration of lack of bond alternance and planarity as criteria for aromaticity. Benzene is planar and has equal C-C bond lengths of 1.398 Å. The tendency towards coplanarity of the π-system atoms is due to the fact that the colinearity of the axes of the *p* orbitals for their maximum overlap is achieved thus leading to the lowest energy of the molecule. Introduction of strain generally leads to deviation from planarity.

For example, in the strained [n]paracyclophanes **21**[23] and **22**[24], the benzene ring is distorted into a boat form with a deviation of 15-17° from planarity when n = 7, and 20-21° when n = 6.



21 = n = 6

22 = n = 7

Despite the strain, the bond lengths in the benzene ring of **21** and **22** remain almost equal and suggest along with other criteria that the aromaticity in the benzene ring is not lost. The necessity to grow single crystals of X-ray quality and the sometimes misleading information that can be obtained due to steric factors makes this method difficult to apply as a general criterion of aromaticity. Also carbon-carbon bond lengths cannot be compared to bond lengths involving heteroatoms. It should be noted that fused systems such as napthalene, show bond alternation, and thus interpretation of this as a direct measurement of aromaticity needs care. We shall consider this later.

The concept of bond order (ρ), is a theoretical one that depends on the valency multiplicities between atoms in molecules, and is related to bond length.[25] The quantity ρ has a physical significance that is associated with the binding power of a bond since the product of the coeffcients of adjacently

bonded atoms may be considered as a bond electron density.

$$\rho_{rs} = \Sigma_j n_j c_{jr} c_{js} \quad (1)$$

where

n = number of electrons in the j^{th} molecular orbital

c_{jr} = coefficient of atom r in the j^{th} molecular orbital

Benzene has a bond order of 0.667, while in a perfectly delocalised [14]annulene, the value is 0.642 and thus the value depends on the ring size. The bond orders of the 1-2 and 2-3 bonds in naphthalene have values of 0.725 and 0.603, respectively, indicating bond alternation. Although, it is difficult to determine a range of bond orders by which a system may be classified as aromatic,[26] bond orders can be used (as are bond lengths) as indicators of bond fixation, which is related to aromaticity. The more unequal or alternating are the bonds in a system, the less aromatic is it.

Whilst all aromatic compounds give ultra-violet spectra, which are convenient classification tools, the spectra obtained result from the energy differences between the ground and the excited states of the molecules, and thus do not distinguish the presence or absence of aromaticity.

Aromatic hydrocarbons have very distinct magnetic properties. Experimental work done in the late 1920s, revealed the higher magnetic exaltation and pronounced anisotropic behaviour of aromatic compounds.[27]

This led Raman and Krishnan to resurrect an earlier hypothesis of Ehrenfest to rationalise the anomalous diamagnetic behaviour.[28] Based on this work, Pauling, using the then available quantum mechanical theory, gave a theoretical explanation.[29] Pauling's model, like the Ehrenfest hypothesis, assumes Larmor precession of the electrons in benzene to account for its pronounced diamagnetic behaviour and it formed the basis for the popular "ring current" theory, discussed below.

1.2.1 Ring current theory and aromaticity

With the advent of nuclear magnetic resonance (nmr) spectroscopy, Pauling's model for benzene under the influence of an applied magnetic field, gained attention and was first used by Pople,[30] in a classical sense, to explain proton chemical shifts. Later, improvements by other workers, gave rise to the "ring current" theory of which a comprehensive review has appeared.[31]

In the ring current model, a planar aromatic molecule assumes a perpendicular orientation to the applied magnetic field. The applied field is assumed to "induce" a "ring current" in the π-electrons of the molecule. This will produce a secondary magnetic field which is against the applied magnetic field at the centre of the molecule, and with the applied field on the outside of the molecule. As a result of this, the external protons of the molecule experience a strong deshielding and would appear in the low field region of the nmr spectrum. Any protons present inside the ring experience a strong

shielding and would appear in the high field region of the spectrum. The ring current model for benzene is illustrated in Figure 1.

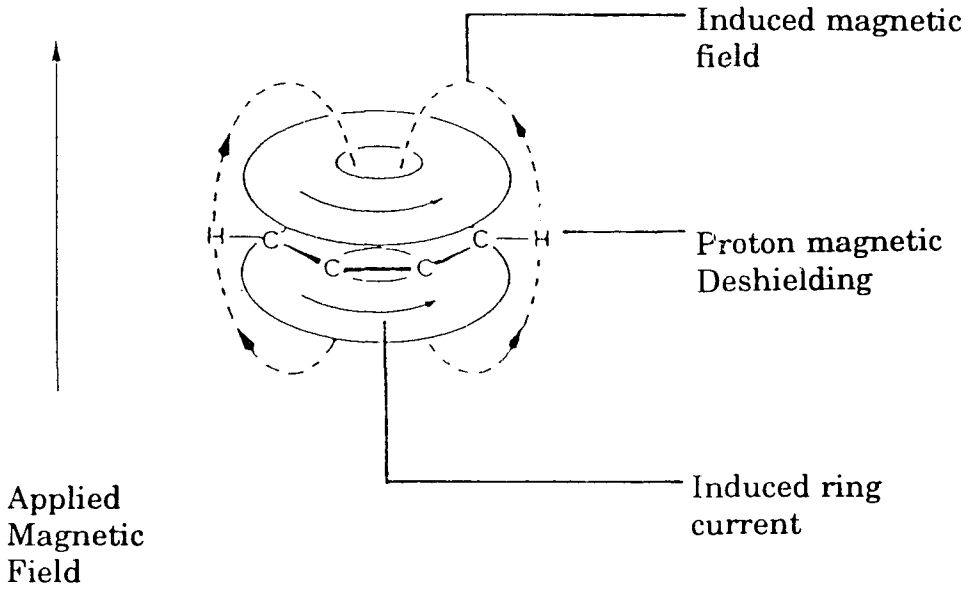
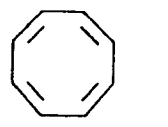


Figure 1 Induced ring current and proton magnetic deshielding in benzene.

Although there is no proof that ring currents exist, the ring current theory does adequately explain the chemical shifts of annulenes, and it has become a widely accepted concept. In (4n+2) annulenes, the external protons are deshielded due the ring current and are termed diatropic. In (4n) annulenes, the external protons are shielded due to what is called "a paramagnetic ring current" and such (4n) annulenes are called paratropic. Those annulenes which do not show delocalisation of the π-electrons are called atropic.

Numerous examples of diatropic and paratropic annulenes are known.

Table 1 lists some examples of neutral, charged and hetero versions of (4n+2) and (4n) annulenes with the chemical shifts of their inner and outer protons.



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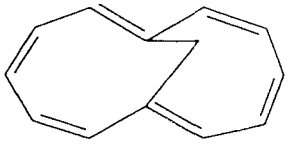

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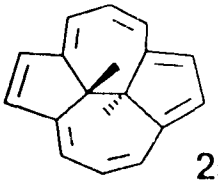

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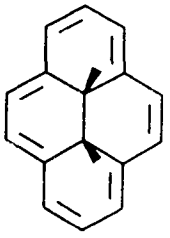

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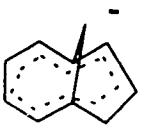

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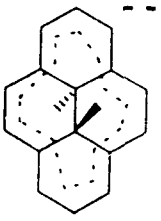

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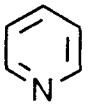

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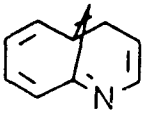

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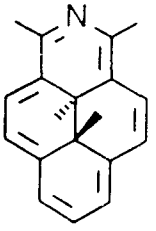

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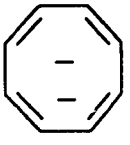

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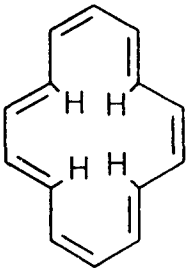

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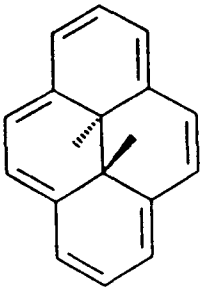

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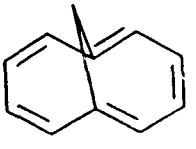

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Table 1 ^{1}Hnmr chemical shifts (δ) of selected annulenes in ppm.

Compound	π e	δ Outer protons	δ Inner protons	Ref
1	6	7.27	---	32
23	8	5.70	---	33
13	10	7.27-6.35	-0.52	34
24	12	5.5-5.2	6.06	35
9	14	7.88	-0.61	36
25	14	8.77-8.04	-4.53	37
12	14	8.67-7.98	-4.25	38
26	14	8.74-7.50	-2.06	39
27	2	11.1	---	40
2	10	5.70	---	41
28	10	6.8-5.4	-0.7,-1.2	42
29	16	-3.19- -3.96	21	43
30	6	8.5-7.46	---	44
31	6	7.7-6.05	---	45
32	10	8.23-6.5	0.65- -0.4	46
33	14	9.5-8.7	-3.75,-3.80	47

From Table 1, it is evident that the (4n+2) annulenes are diatropic. We shall now briefly discuss some aspects which affect the shielding and deshielding of protons.

Among the neutral annulenes, the protons of benzene, **1**, which is considered by some schools as 'the real aromatic molecule', resonate at 7.27 ppm, about 1.5 ppm downfield from a normal olefin. This additional deshielding indicates the presence of a ring current. In the [14]annulene **9**, the inner protons are shielded due to the ring current and appear at -0.61 ppm. Whereas, in the isoelectronic bridged annulenes **25** and **12**, the shielding of the inner protons is stronger. This difference is attributed to the rigidity and near planar periphery of the bridged annulenes. Any deviation from planarity leads to a reduction of ring current. The bridge protons of the methano annulene **13**, appear at -0.52 ppm and are thus not so strongly shielded. This molecule has a bent periphery. The *cis*-dmdhp **26**, has its internal methyl protons at -2.06 ppm, a marked reduction in shielding compared to **12**. The internal methyls in **13** point away from the π-network and the overall geometry of the molecule is like that of a saucer. When an annulene suffers a total lack of planarity, the delocalisation of the π-electrons is disrupted. As a result, there is no ring current and hence it is atropic. For example, cyclooctatetraene **23**, is tub shaped. Its protons are not shielded (as would be expected for a 4n annulene), indicating an absence of a ring current. On the other hand, in the near-planar [12]annulene **24**, the inner protons are more strongly shielded than the outer

protons. This paratropic behaviour is quite dramatic in case of the paratropic dianion **29**, whose internal methyl protons appear some 25 ppm downfield from those of the diatropic **12**.

The protons of the [2]annulene, cyclopropenium cation, resonate downfield at 11.1 ppm. In this case the positive charge also deshields the protons. An upfield shift is experienced by protons in a negatively charged system. The chemical shift of the aromatic cyclooctateraenyl dianion is the same as that of the nonaromatic cyclooctatetrene.

In heterocycles, the chemical shift differences depend on the dipole moments. The isoelectronic pyridine **30**, and pyrrole **31**, have a difference of about 1 ppm in the chemical shift of their protons. This is due to the direction of the dipoles in these systems. The direction of the dipole is towards nitrogen in pyridine and away from nitrogen in pyrrole.

31 **30**

These chemical shift differences, resulting from charge and/or dipole moments, do not reflect the true shielding or deshielding of protons due to ring current. Vogler has derived an equation relating the observed shielding (σ) to

the shielding due to ring current and other factors.[48] This is given in equation 2.

$$\sigma = \sigma^{RC} + \sigma^{LA} + \sigma_{\mu}^{0} + \sigma_{v}^{q} \quad (2)$$

Where σ^{RC} = Shielding due to ring current

σ^{LA} = Shielding due to the local anisotropy

σ_{μ}^{0} = The zero of the chemical shift scale

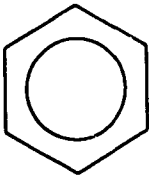
σ_{v}^{q} = Shielding due to excess π-electron density

So, interpretation of the chemical shifts in annulenes has to be carried out with extreme caution, especially in the case of charged systems and heterocycles where the shielding arising due to local anisotropic contributions and excess π-electron density are of equal importance.[49] Nevertheless, the diatropicity of an annulene can be considered as a criterion for aromaticity, provided that the above mentioned factors (which can be calculated theoretically) are taken into consideration.

Another magnetic property of conjugated systems, diamagnetic susceptibility, has been related to aromaticity through the empirical quantity, diamagnetic susceptibility exaltation (DSE).[50]

1.2.2 Resonance and aromaticity

Although recently new insights have been offered about the origin of the stabilisation in aromatic compounds,[51, 52, 53] it is believed that the delocalisation of π-electrons lowers the total energy of the aromatic molecule relative to the hypothetical bond localised structure. A theoretical parameter, called resonance energy (RE), has been attributed to the lowering of energy due to delocalisation and it has beer suggested as a suitable criterion for determining the aromaticity of a compound. Taking benzene, **1**, as an example, if the calculated energy of the structure **34** was the same as the experimental value within experimental deviation, then structure **34** would very well represent benzene. If the experimental val ıe of the energy of benzene is greatly different from the calculated energy of the structure **34**, the structure **34** would then be a poor representation of the real molecule. This energy difference may be attributed to the resonance structure **1**.



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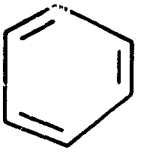

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Theoretical calculations can be performed to estimate the resonance energy of a given molecule. However, the choice of a model is very critical. Earlier problems encountered in HMO theory, using ethene or cyclohexene as

models, have been overcome by Dewar, who using the Pople-Pariser-Parr approximation (PPP), derived more reasonable values termed Dewar Resonance Energies (DRE).[54] Other modifications by Hess and Schaad,[55] Herndon,[56] Aihara,[57] and Trinajstic[58] are also available.

Table 2: REPE (in β units) of selected conjugated compounds

Number	Compound	Hess-Schaad[55]	DRE	TRE[58]
7	Cyclobutadiene	-0.268	-0.136	-0.307
1	Benzene	0.065	0.120	0.046
30	Pyridine	0.058	0.110	0.038
31	Pyrrole	0.039	--	0.040
35	Thiophene	0.032	--	0.033
4	Cyclopentadienyl	-----	--	0.094

Hess and Schaad suggested the use of the term resonance energy per (π) electron (REPE) as a more suitable parameter than the total resonance energy. REPE is a convenient parameter to compare systems with different numbers of π-electrons. However, it must be pointed out that the REPE does not reflect the overall stability of a molecule and strictly refers to the extent of stabilisation or destabilisation due to conjugation. Table 2 contains the

REPE's for a few systems as calculated by Hess and Schaad using the HMO method and by Trinajstic by the graph theoretical method (topological resonance energy or TRE).

Aromatic compounds have a positive REPE, antiaromatic compounds have a negative REPE and nonaromatic compounds possess an REPE close to zero.

Among the criteria we alluded to in the preceding pages, none can be exclusively related to aromaticity, and none when violated are good enough to discount the property. Based on the present consensus among chemists,[59] and that of Garratt's "definition",[60] one might say: *an aromatic compound is a cyclic diatropic system with a positive Dewar resonance energy (≥3 kcal/mol) in which all the contributing atoms are involved in a single conjugated system.*

1.3 Estimation of aromaticity

Because of the difficulties one encounters in defining and detecting aromaticity, any experimental "measurement" of it is futile. One could only hope to get an estimate of aromaticity, relative to a well studied molecule such as benzene.

Thermochemical estimates of resonance energy suffer from the same draw back as the theoretical estimate of resonance energy itself. Both need a suitable, hypothetical model to arrive at the resonance energy. Two methods are used to estimate the resonance energy of a molecule using thermochemical

data. One method is to use the heat of atomisation of a compound. For example, a simple calculation of the heat of atomisation for cyclohexatriene **34** would be to sum the bond energies of six C-H, three C-C and three C=C bonds. Then one can derive the resonance energy of benzene either as (i) 46.7 kcal/mol by taking the bond energy of ethylene as the double bond in the calculation or as (ii) 35.3 kcal/mol by taking the bond energy of a cis-disubstituted ethylene double bond (i.e. cyclohexene) in the calculation (Table 3).

Table 3 Calculations of the RE of benzene (kcal/mol)

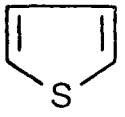
	C-H	C-C	C=C	ΔH_a °(**34**)	ΔH_a °(**1**)	RE
CALC.(i)	6(98.5)	3(83.1)	3(143.7)	1271.4	1318.1	46.7
CALC.(ii)	6(98.5)	3(83.1)	3(147.5)	1282.8	1318.1	35.3

Another method is to use hydrogenation data. For example, the heat of hydrogenation for cyclohexatriene **34** can be calculated as 85.8 kcal/mol by multiplying that of cyclohexene by 3, i.e., 3 x 28.6 = 85.8 kcal/mol. Comparison of this value with the experimental value of heat of hydrogenation of benzene (49.8 kcal/mol) gives the resonance energy of benzene as 36 kcal/mol.

Recently, using the same principle described above, an attempt has been made to estimate the DRE of heterocycles from thermochemical data (Table 4).[61]

Table 4 DRE of some heterocycles from thermochemical data in kcal/mol[61]

Compound	Number	RE
Pyridine	**30**	35.2
Pyridazine	**36**	30.1
Pyrrole	**31**	26.5
Furan	**37**	20.8



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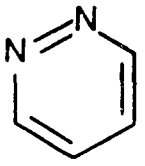

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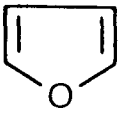

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Very recently, Katritzky and coworkers have made an attempt to quantify aromaticity in heterocycles, using principal component analysis of several properties.[62] Since, each property used itself is a result of many approximations, and the method used to arrive at the results was purely analytical, it is difficult to comment on the reliability of this approach. This paper also lists the recent theoretical attempts to estimate aromaticity.

1.3.1 Mitchell's method of estimation of aromaticity

Twenty years ago, Mitchell's group started their work on annelated dmdhps. *trans*-10b,10c-Dimethyl-10b,10c-dihydropyrene (DMDHP), **12**, is a relatively stable compound which is strongly diatropic. It has a near planar, rigid skeleton, held by the ethano bridge, and is little strained. With nearly equal peripheral bond lengths it acts as a stereochemically fixed, 'perfect' Hückel, [14]annulene. DMDHP bears its methyl substituents within the 14 π-electron cloud, placing them in the centre of the diamagnetic current. The internal hydrogens are well insulated from the π-network (by 3 σ bonds) and their chemical shift is not affected appreciably upon substitution with a variety of groups in a number of positions (Table 5).

Figure 2 shows selected bond lengths and angles from an X-ray crystal determination[63] of DMDHP, **12**. The space filling model of DMDHP is depicted in Figure 3, and Table 5 lists the internal methyl chemical shifts of a number of derivatives of **12**.

It can be seen from Table 5 in compounds **38-47** that the internal methyl proton chemical shift of **12** is not affected very much by external substituents. The protons of **12** itself appear at δ -4.25 ppm, some 5.2 ppm shielded from those of the atropic model **48**.

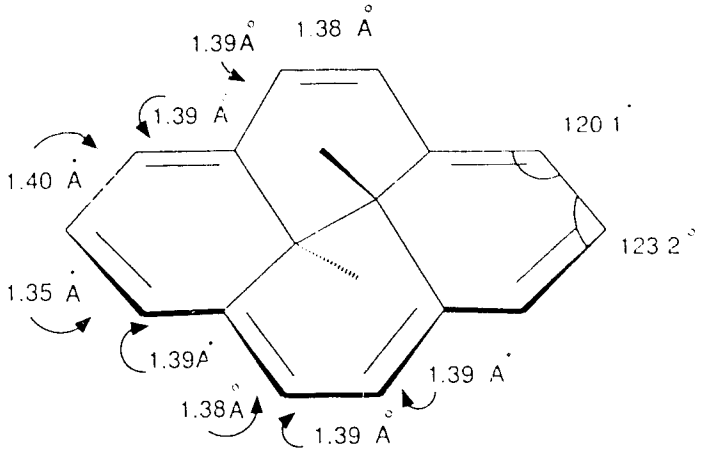


Figure 2 Selected bond lengths and angles of **12**.

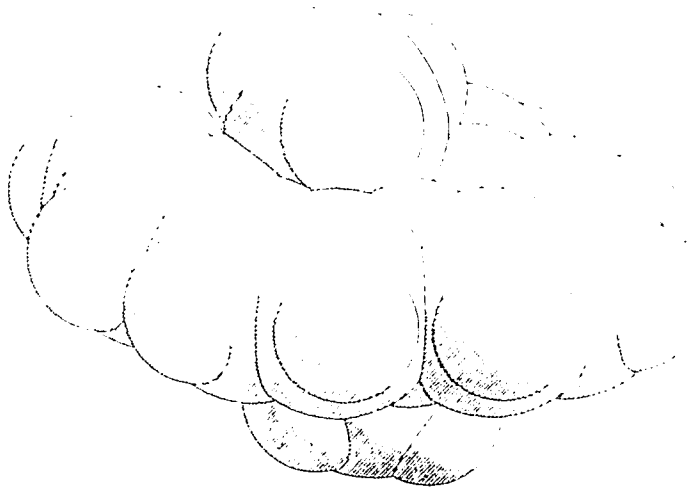
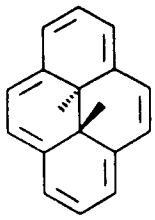
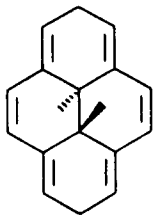


Figure 3 Space filling model of **12.**



δ -4.25 ppm

12



δ +0.97ppm

48

Table 5 Chemical shifts (δ) of internal CH_3 protons for substituted DMDHP in ppm.

Compound	Substituent(s)	Position	δ (ppm)	Ref
38	Br	2	-4.07,-4.08	64
39	$COCH_3$	2	-4.03	65
40	$C(Ph)_3$	2	-3.92,-4.03	65
41	NO_2	2	-4.03	65
42	2-DMDHP	2	-3.68,-3.77	66
43	CH_3	2,7	-4.09	67
44	Br	2,7	-4.02	68
45	$COOCH_3$	2,7	-3.92	67
46	*t*-Bu	2,7	-4.06	69
47	$OCOCH_3$	2,4,7	-3.83	70

The above mentioned features make DMDHP a good probe to detect changes in delocalisation caused by annelation.

1.3.1.1 Benzannelation studies on DMDHP

Benzannelation of an annulene was primarily used by Sondheimer,[71] Staab[72] and Nakagawa[73] to bring about stability and increase the rigidity of

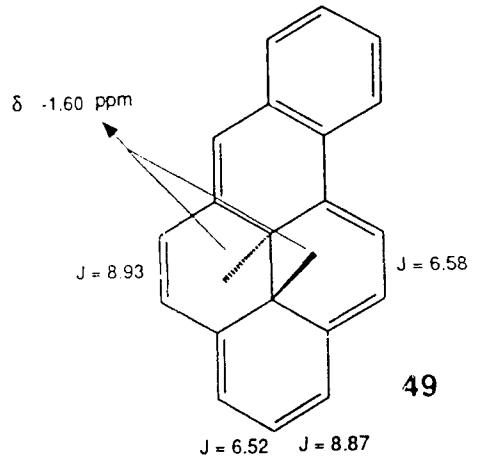
macrocyclic annulenes. Studies done by Staab,[72] Boekelheide[74] and Mitchell[75] on annelated bridged annulenes provided additional information on the changes that occur due to annelation, as discerned from the ^{1}Hnmr data. An excellent review on benzannelated annulenes is available.[76]

Some of the changes which occur on fusion of benzene to DMDHP, which are similar to the changes in any annulenoannulene, are the following:

1. Benzannelation leads to bond alternation in both the benzene and the DMDHP rings.

2. As a result, the bond orders, ρ, change from a fully delocalised value, and thus so do the vicinal coupling constants of the protons on the molecule.

3. The shielding caused by the ring current, experienced by the internal methyl protons in DMDHP is reduced, and is reflected by a lower field chemical shift of the internal methyl protons. For example, in the benzo-DMDHP **49**,[77] the internal methyl protons resonate at -1.60 ppm, showing a downfield shift of 2.65 ppm from that of the parent DMDHP. Also the vicinal coupling constants in the molecule vary between 6.52-8.93 Hz.



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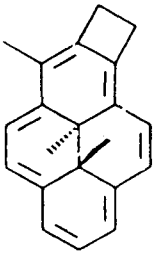
These changes in chemical shift of the internal protons and the coupling constants of the external protons are brought about only by the fusion of a ring with a cyclic array of π-electrons. In compounds **50**, **51**, and **52**, where the fused ring is atropic, the internal methyl chemical shifts are not very different from those of the parent DMDHP, **12** (Table 6).

Table 6 Internal methyl chemical shifts of some fused derivatives of DMDHP, in ppm.

Number	δ (ppm)	Ref
12	-4.25	14
50	-4.23	78
51	-3.72, -3.73	79
52	-4.15, -4.16	80



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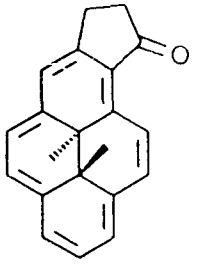

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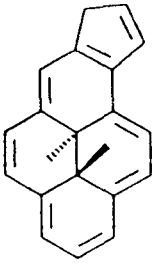

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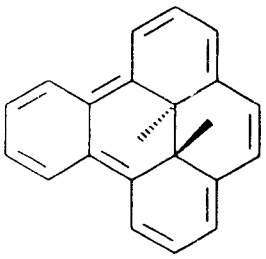
Examination of the chemical shift values given in Tables 5 and 6, clearly show that any change in the internal methyl chemical shifts brought about by substitution or by the fusion of an atropic ring on the DMDHP ring is not very significant. Mitchell and coworkers have shown that the average deviation of the bond orders in the DMDHP fragment of benzannelated DMDHPs correlates linearly with the change in the internal methyl chemical shifts.[82] The bond orders can be calculated either using the π-SCF method or from the vicinal coupling constants ^3J, using equation 3.[83] This equation originally derived by Günther by plotting ^3J values of benzenoid hydrocarbons against the corresponding calculated π-SCF values,[83] was used by Mitchell and coworkers in their earlier work. Better correlations relating ^3J and calculated π-SCF bond orders for the DMDHP derivatives were obtained, recently by Zhou, and we will use these correlations in our work and also show the advantage of these improved correlations over that of Günther's
in detail in chapter 3.

$$\rho_{mn} = 0.104\ {}^3J_{mn} - 0.120 \qquad (3)$$

A plot of Δr, the average deviation in the bond order from the expected Hückel value of 0.642, for a perfectly delocalised [14]annulene for each macrocyclic ring of **49**, **53**, **54**, **55**, against the chemical shift shielding Δδ, gave a straight line, from which equation 4 was obtained:[84]



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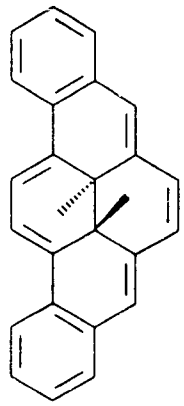

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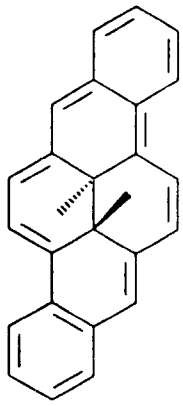

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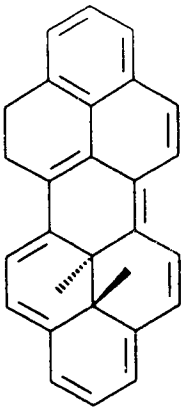

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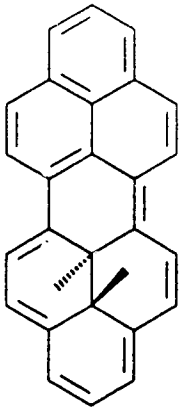

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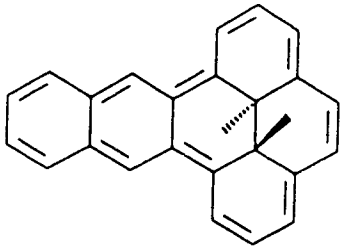

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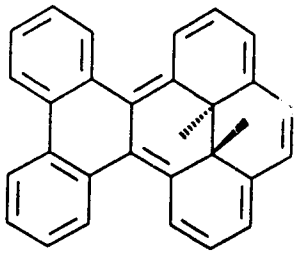


59

$$\Delta\delta = 5.533 - 27.52\ \Delta r \qquad (4)$$

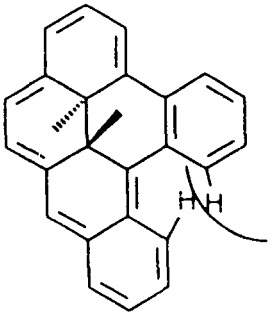
This correlation is valuable in two respects. First, if bond orders can be calculated either by using equation 3 or π-SCF calculations, then the chemical shift shielding can be predicted. Secondly, a measured chemical shift can be used to comment on the average bond order deviations and hence on the shielding changes due to annelation. The chemical shifts of all the protons can also be calculated according the method of Vogler.[85] Table 7 includes some of the predicted and observed chemical shift values for the internal methyl group protons for a number of benzannelated DMDHPs.

Table 7: Predicted and observed internal methyl proton chemical shifts for some fused DMDHPs, in ppm.

Compound	δCH_3(predicted)	δCH_3(observed)	Ref
56	-2.75	-2.78	86
57	-3.97	-4.19,-4.28	87
58	-1.25	-0.74	88
59	-3.84	-3.32	89

From the table, it can be seen that there is a good agreement between the observed and the predicted values. It is assumed that the

DMDHP and the annelating rings are not deformed very much due to annelation. Due to the lack of availability of any X-ray structure information, force-field calculations have been used to calculate the geometry of the molecules and these calculations indicate that the geometry indeed is not altered very much.[75] Vogler calculates that even in the case of extremely crowded molecules such as **60**, the chemical shift change due to deformation is negligible.[85]



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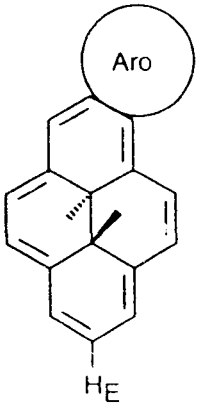


61

Zhou, using the Haigh-Mallion equation, has shown that the through space anisotropy effect of the annelating benzene rings, is very small.[90] In the molecule **61**, proton E is the farthest from the annelating ring and is thus least affected by anisotropy and geometry changes. Recently,[91] a quantitative correlation has been derived that relates the internal methyl ring current chemical shift, δ_{RCM}, to that of the ring current chemical shift of proton E, δ_{RCH}, for a number of annelated DMDHP derivatives. The following equation, which represents a straight line plot, was obtained:

$$\delta_{RCM} = -2.60\ \delta_{RCH} - 0.029 \quad (5)$$

where

$\delta_{RCM} = 0.97 - \delta CH_3$, and

$\delta_{RCH} = 6.13 - \delta_E$

δ_E = Observed chemical shift of proton E

The value of 0.97 is the chemical shift for the model **48** and 6.13 is that of a conjugated polyene in the absence of any ring current effect.[92,93]

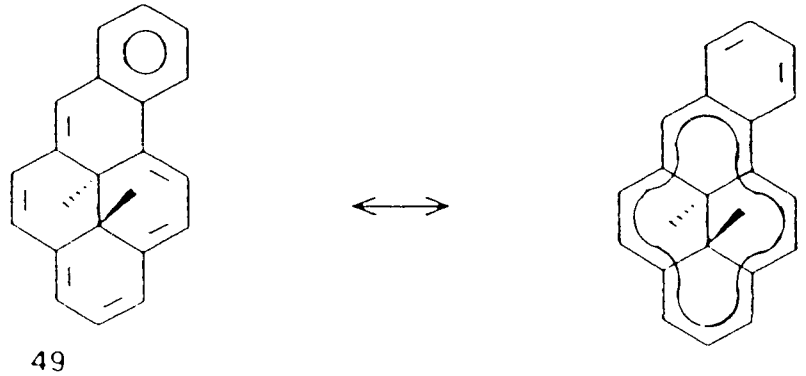
The values of chemical shift shieldings thus obtained have been related to Dewar resonance energies (DRE) of the annelating fragments.[94] For the 14π-system to fully delocalise in **49**, the delocalisation of benzene must be interrupted, leaving only a *cis*-butadiene residual. The loss of RE then is approximately that of benzene. By analogy, for the dibenzannelated analogue **54**, the loss of RE is twice that of **49**. For the naphth-fused DMDHP, **56**, a styrene is left when the 14π-system delocalises. Here, the loss of RE approximates to the difference between that of naphthalene and styrene. By plotting the calculated REs of various residuals and the corresponding shielding changes (Δ) in the internal methyl chemical shifts (δ), Venugopalan obtained the following equation (equation 6).

$$\Delta = 2.5366\ RE^{*} + 0.2141 \quad (6)$$

(Correlation coefficient = 0.9905)

where $\Delta = |-4.25 - \delta|$ and

RE^{*} = RE of the annelating ring - RE of the residual



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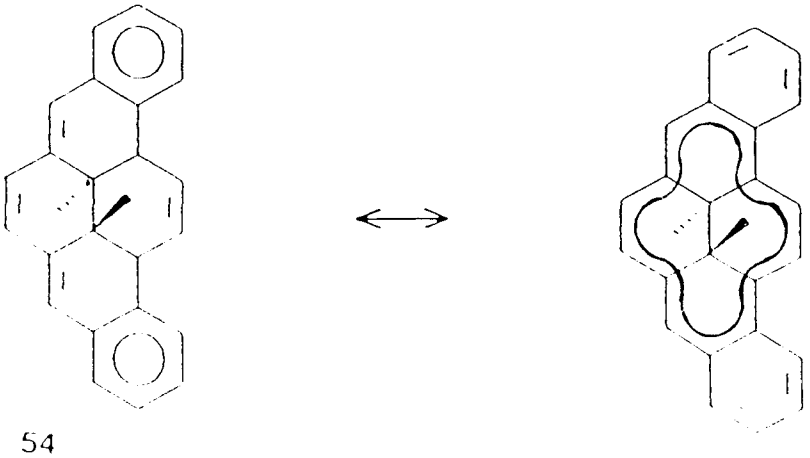

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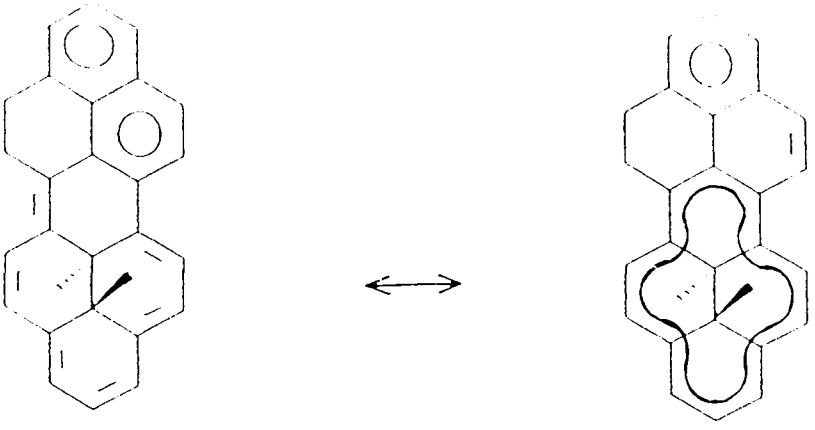


56

Equation 6 demonstrated the linear relationship between change in the chemical shift shielding and the resonance energy and thus further substantiated the validity of using the internal methyl chemical shifts to estimate the aromaticity of various aromatic rings.

Another, simple and direct approach was developed by Mitchell who used the chemical shift changes of the internal and external protons of an annelated DMDHP with respect to those of the benzo[a]DMDHP, **49**.

$$\text{"Aromaticity"} = [\delta(CH_3)\text{Ring} - \delta(CH_3)\mathbf{12} \,/\, \delta(CH_3)\mathbf{49} - \delta(CH_3)\mathbf{12}] \quad (7)$$

Equation 7 gives a relative measure of the aromaticity of an annelating ring with respect to that of benzene based on its bond fixing ability in the annelated DMDHP. Due to its simplicity, it is very easy to get an estimate of the relative aromaticity of a molecule with respect to that of benzene by simply measuring the chemical shift of the internal methyl protons.

Thus, the DMDHP molecule is a good nmr probe for aromatic rings and one could comment on the extent of aromatic character of any aromatic compound by fusing it to the DMDHP ring.

1.4 Synthetic routes to DMDHP and its derivatives

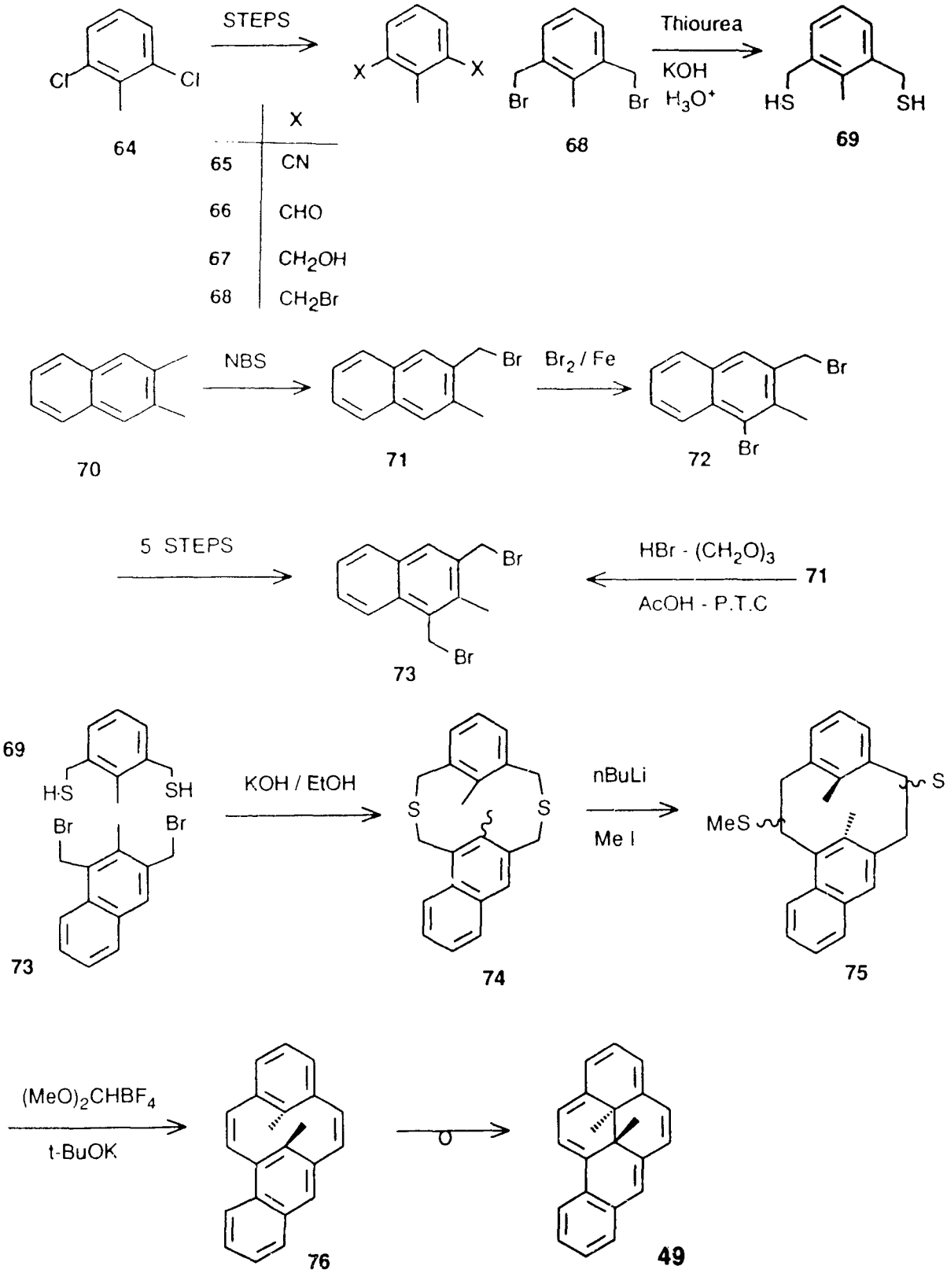
Boekelheide and coworkers developed several synthetic methods to DMDHP.[95] Among those known routes, *the dithiacyclophane route*, invented by Mitchell and Boekelheide is the most convenient and practical one.[96] Mitchell and Zhou have shown that the dihydropyryne **62** (page 36), could be generated and trapped with various furans, leading to several benzo-fused DMDHPs.[97] Mitchell and Zhou have also synthesised the oxa[17]annulene **63** (page 36), which could be used as a synthon for various fused DMDHPs.[98] Mitchell and coworkers have used the thiacyclophane route to synthesise [e]annelated DMDHPs, starting from the appropriately substituted *o*-teraryls.[99] Since this thesis is mainly concerned with the utilisation of the existing synthetic pathways to make annelated DMDHPs and the possible exploration of complementary new synthetic strategies, it is appropriate here to discuss briefly the known methodologies in the following pages.

1.4.1 The dithiacyclophane route

We shall illustrate the dithiacyclophane strategy by using the synthesis of benzo[a]DMDHP **49** as the example. The synthesis is shown in Scheme 1.

This strategy involved the construction of a macrocyclic ring by coupling the dithiol **69**, with the dibromide **73**, under high dilution conditions. The resulting syn/anti mixture of the thiacyclophanes **74**, were then ring contracted by means of a Wittig rearrangement and the thiolates formed were methylated

Scheme 1


STEPS
Thiourea
KOH
H_3O^+
64
65 CN
66 CHO
67 CH_2OH
68 CH_2Br
68
69
NBS
Br_2 / Fe
70
71
72
5 STEPS
HBr - $(CH_2O)_3$
AcOH - P.T.C
73
69
KOH / EtOH
nBuLi
Me I
73
74
75
$(MeO)_2CHBF_4$
t-BuOK
76
49

with MeI to yield the *anti*-cyclophanes **75**. The S-methylated [2,2]cyclophanes **75**, were further methylated with Borsch reagent and the resultant sulphonium salts, upon treatment with base, eliminated Me_2S to yield the cyclophanediene **76**. The cyclophanediene formed, rearranged, *in situ*, to the benzo[a]DMDHP **49**. The key synthons, the dibromide **73**, and the dithiol **69**, were synthesised from the commercial 2,3-dimethylnaphthalene **70**, and 2,6-dichlorotoluene **64**, using standard transformations, as shown in Scheme 1.

From the example given, it is clear that the essential intermediates in this methodology are a 1,2,3-substituted arene and 2,6-bis(mercaptomethyl)toluene, **69**. Though the bis(bromomethyl)naphthalene **73**, is now accessible in two steps from 2,3-dimethylnaphthalene, via our phase transfer catalysed bromomethylation procedure,[100] the synthesis of such intermediates is not trivial and is often time consuming. Even the synthesis of the dibromide **68**, involves four steps. So, it was our intention to find a shorter route to 2,6-bis(bromomethyl)toluene and an appropriately substituted diene synthon which could lead to various fused 1,2,3-substituted benzenes via Diels-Alder reactions.

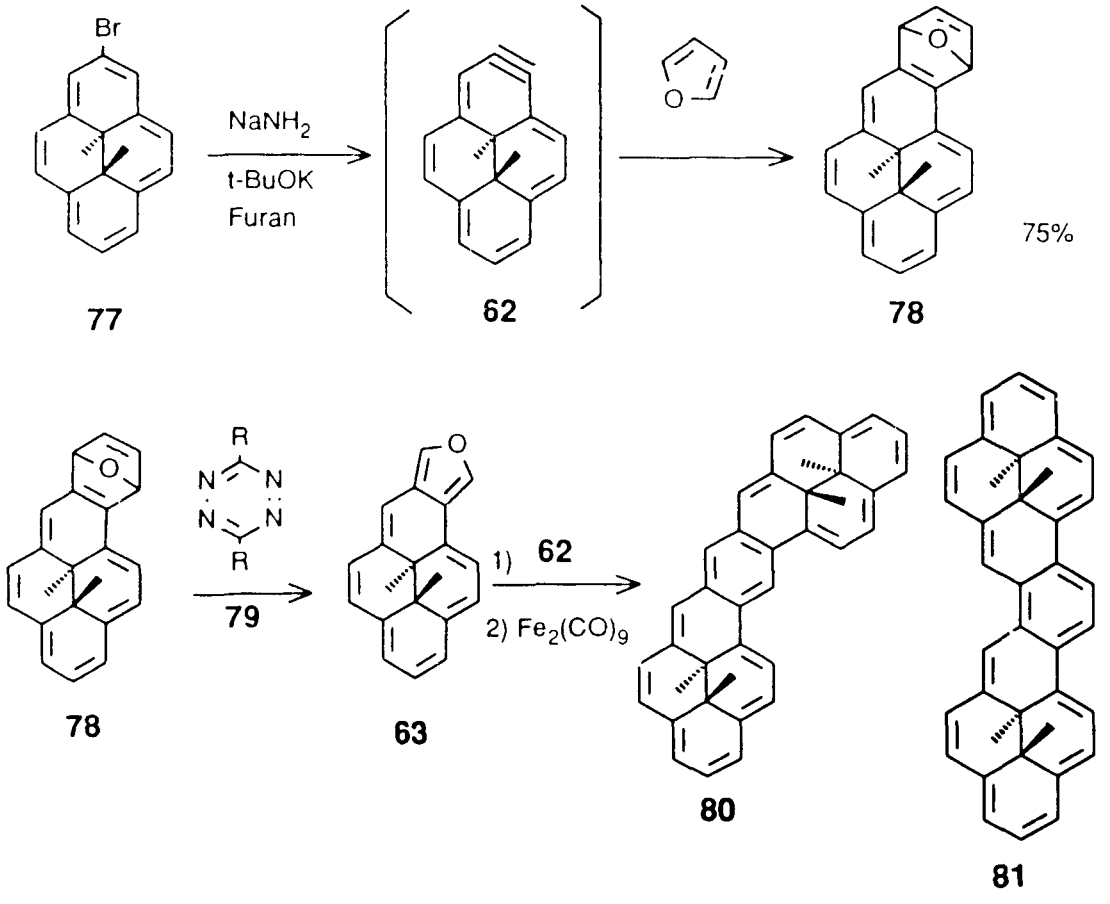
1.4.2 The dihydropyryne/oxa[17]annulene route

The dihydropyryne, **62**, could be generated by the action of sodamide and a catalytic amount of *t*-BuOK on the bromoDMDHP **77**, in the presence of a trapping agent. For example, the adduct **78**, can be obtained in 75% yield

by trapping of the aryne **62**, with furan.

Although Zhou has utilised this method to synthesise several benzannelated DMDHPs, the potential of this very useful intermediate has not been fully explored. Hence, we were interested in finding other possible uses of this aryne intermediate.

The oxa[17]annulene **63**, obtained by the reaction of the tetrazine **79**, with the furan adduct, is a relatively stable compound to handle. This has been shown to cyclo-add to arynes to give adducts which on deoxygenation lead to benzannelated DMDHPs. For example the mixture of [a]annelated DMDHPs **80** and **81** were synthesised from the oxa[17]annulene in two steps.[98]



1.4.3 Syntheses of [e]fused DMDHPs

Mitchell and coworkers had developed a methodology based on the aryl-aryl coupling reaction between a Grignard reagent and a bromoarene mediated by transition metal catalysts.[99] For example, the benzo[e]DMDHP was synthesised as shown in Scheme 2. The salient features of this strategy are: (i) The Ni(0) mediated coupling of the mono-Grignard derived from 2,6-dichlorotoluene and 1,2-dibromobenzene to yield the *o*-teraryl **84**.

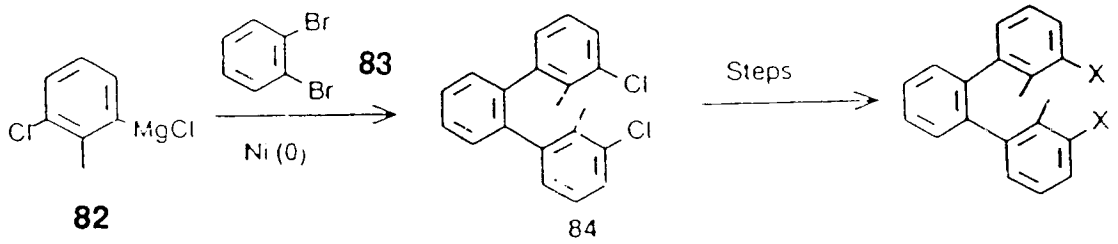
(ii) High dilution coupling of the dibromide **89**, with Na_2S which resulted in the *anti*-cyclophane **90**.

(iii) Wittig rearrangement, stepwise methylation of the ring contracted cyclophane, followed by the Hofmann elimination of the resultant sulphonium salt provided the benzo[e]DMDHP **53**.

This methodology, although reliable, needs a 1,2-dibromoarene. The synthesis of which is often difficult, as there are no general, convenient methods available to synthesise 1,2-dibromoarenes. For example, the synthesis of anthraceno[e]DMDHP **94**, would require 2,3-dibromoanthracene, **93**, and the *o*-teraryl obtained would be subjected to four functional group transformations (from chloro to bromomethyl), making the synthesis long and tedious.

Hence, we decided to explore possibilities to find and synthesise a common intermediate which would lead to various, properly substituted, *o*-teraryls.

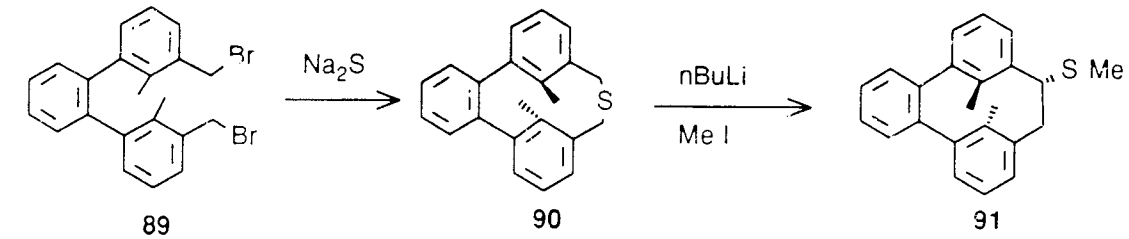
Scheme 2



82

84

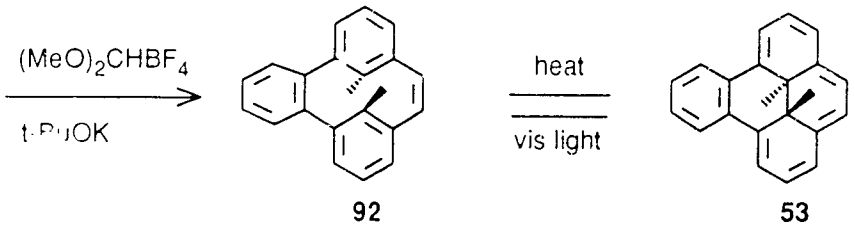
	X
85	CN
86	CHO
87	CH_2OH
88	CH_2Br



89

90

91



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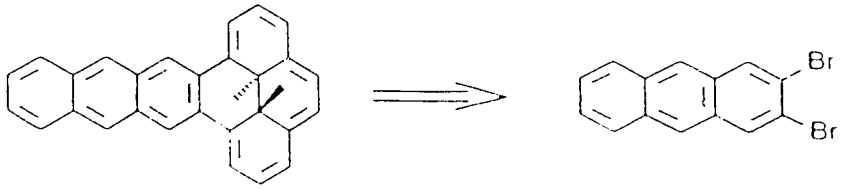
53



94

93

CHAPTER TWO

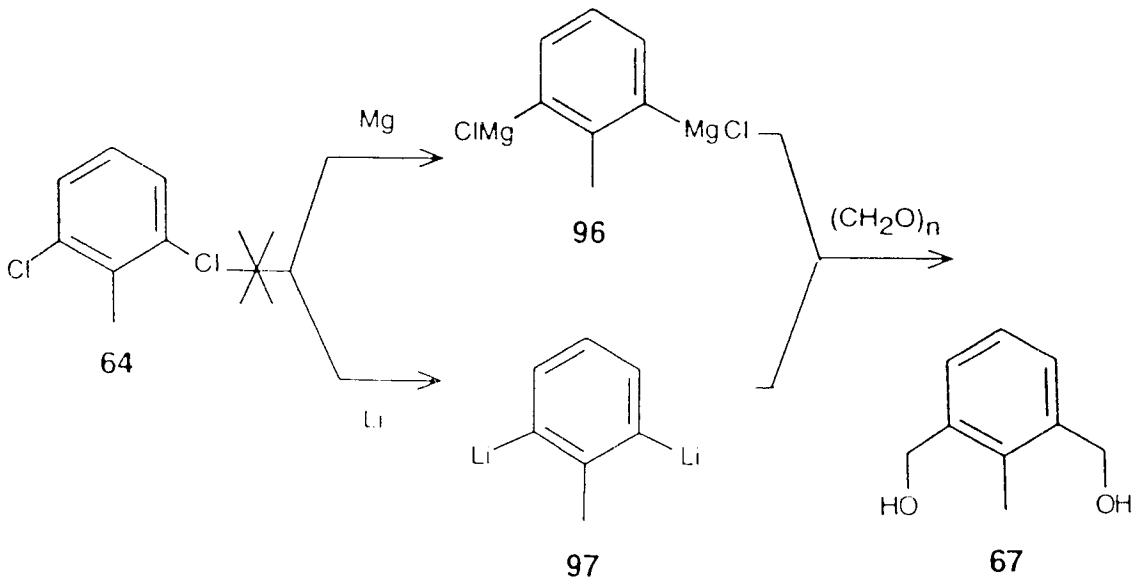
SYNTHESES USING THE DITHIACYCLOPHANE STRATEGY

2.1 Introduction

In this chapter, we will describe our efforts to devise a strategy to synthesise a properly substituted diene as a common precursor to various [a] fused DMDHPs. The synthesis of the first diatropic bridged thia[13]annulene will be described next, together with estimates of its diatropicity based on the chemical shifts of its internal and external protons and on coupling constant-chemical shift correlations. Synthesis of 1,3-bis(methoxymethyl)-2-methylbiphenylene from 1,2-dibromobenzene, in four steps, will be described next. An account of the attempted conversion of this bis-ether into 1,3-bis(bromomethyl)-2-methylbiphenylene, *en route* to the synthesis of a quasi-biphenylene-DMDHP will be given. A summary of possible future syntheses of [a] fused DMDHPs and heteroDMDHPs based on the intermediates derived in this project will be presented. But first, we will outline our results on the bis-bromomethylation of 4-*t*-butyltoluene and the conditions for this efficient bromomethylation procedure.

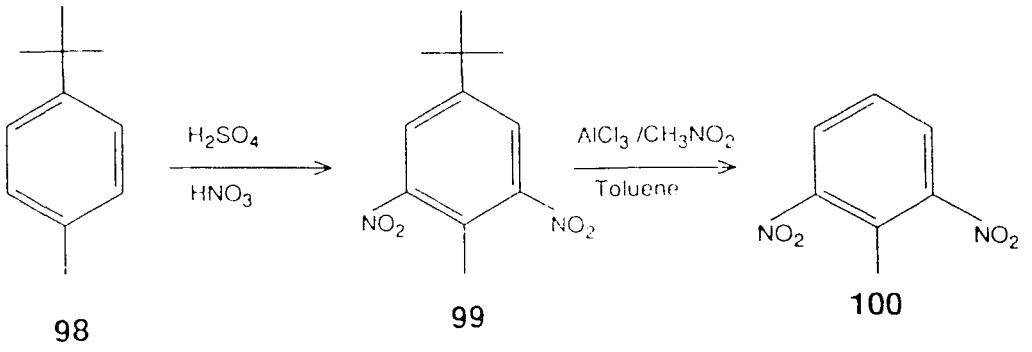
2.2 Bromomethylation of arenes

As seen from Scheme 1, one of the key synthons for the construction of the DMDHP nucleus, 2,6-bis(bromomethyl)toluene, **68**, can be synthesised from commercial 2,6-dichlorotoluene, **64**, in four steps. All attempts to shorten this synt· ›is through the bis-Grignard reagent **96** or the dilithio derivative **97** have so far been unsuccessful.[101]



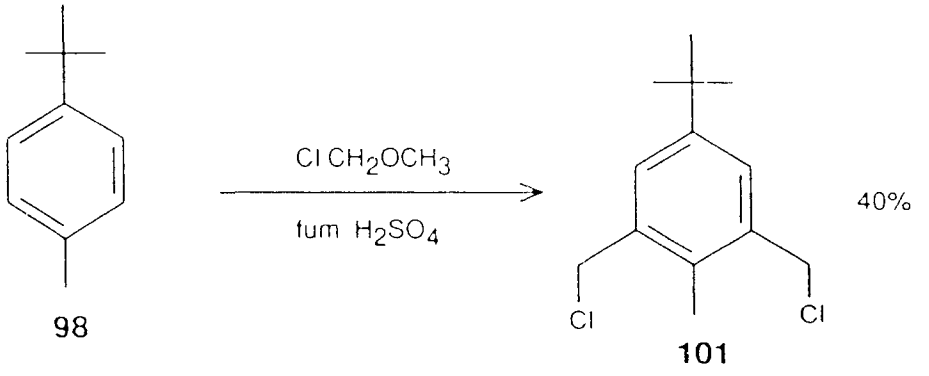
Tashiro *et al.* have used the *t*-butyl group as a block for electrophilic substitution reactions on arenes.[102] After the substitution, the *t*-butyl group is removed, leaving the specifically substituted arene. For example, 4-*t*-butyltoluene, **98**, on nitration yields the dinitrotoluene **99** which on de-*t*-butylation with an $AlCl_3/CH_3NO_2$/toluene system provides 2,6-dinitrotoluene,

100.[103]



98 99 100

Tashiro's group has also shown that 4-*t*-butyltoluene can be bis-chloromethylated, albeit in low yields, to give the bis-chloromethyl compound **101**.[104]

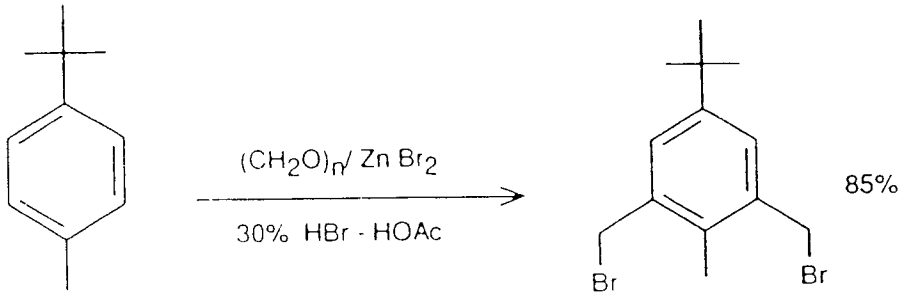


98 101

This procedure requires a large excess of the expensive and highly toxic, chloromethylmethylether as the chloromethylating agent. The harsh conditions necessary to bring about this reaction also lead to undesirable Friedel-Crafts (F-C) alkylation products, thus lowering the yield of the expected **101**.

Our realisation that the bromomethyl group is less reactive than the

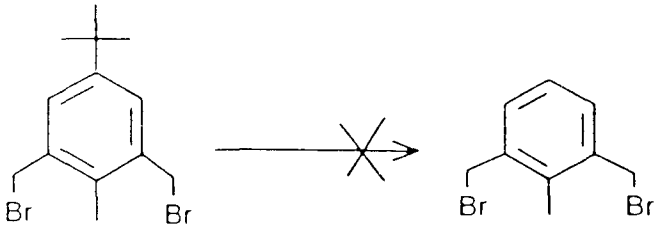
chloromethyl group in the F-C alkylation reaction,[105] coupled with the fact that HBr is a stronger acid than HCl, led us to invesitigate the bromomethylation of 4-*t*-butyltoluene.[100] Although our initial attempts were unsuccessful, we found that the reaction proceeds cleanly at 80-85°C with $(CH_2O)_3$ and *anhydrous* HBr in glacial acetic acid as the bromomethylating system and freshly prepared $ZnBr_2$ as a catalyst. Thus, the bisbromomethyltoluene **104** colorless needles, mp 95-96°C, could be obtained in 85% yield as the only product from 4-*t*-butyltoluene.



98 **104**

This procedure is superior to any other bromomethylation conditions known so far and appears to be a very general method of bromomethylation of arenes which are difficult to react under other conditions. This process is very selective, the extent of bromomethylation is controlled simply by varying the amount of trioxane used and no undesired side products due to F-C alkylation are produced.

However, de *t*-butylation of **104**, using all known procedures,[105] failed to give any of the desired **68**.



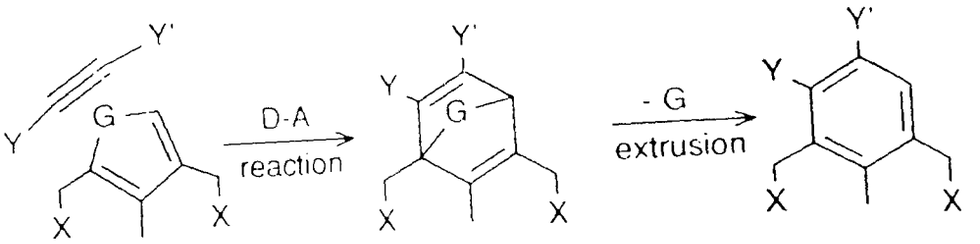
104 68

Since we wished to prepare the fused DMDHPs without any substituents, we made **68** by the reported route, starting from 2,6-dichlorotoluene.

2.3 Search for a 1,2,3-substituted diene synthon

Thus far [a]annelated DMDHPs have been synthesised from 1,2,3-substituted arenes as discussed in section 1.4.1. A general route to 1,2,3-substituted arenes from a common precursor would thus be desirable. A possible sequence which might achieve this is using a D-A reaction in which a diene with an extrudable group, such as **105**, is reacted with an alkyne to give the arene as shown in Scheme 3. Similar transformations utillising this D-A strategy has been used in the synthesis cis-DMDHP derivatives by Mitchell, Williams and others (Scheme 4).[106] There are several possible candidates for this diene, some are shown in Scheme 3. The cyclic diene has several advantages over an "open" diene: 1) The substituents could be put on a cyclic compound and hence the construction of such a synthon could be feasible. 2) The cyclic diene should be relatively stable and easy to handle.

Scheme 3



105

G = Extrudable group

Y,Y' = Substituents or Ring

X = Br, OH, OAc, etc

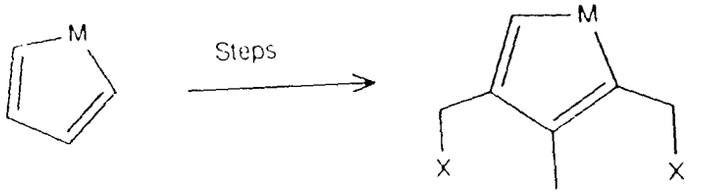
G = $-O-$ = 105

$-SO_2-$ = 106

$-CO-$ = 107

$-CO-O-$ = 108

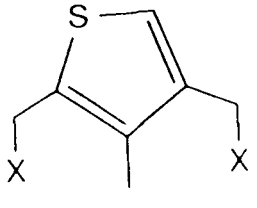
$-CO-CO-$ = 109



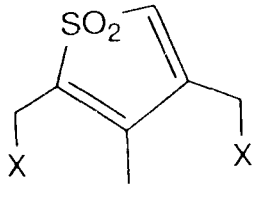
M = O, S, etc

3) The extrudable group as part of the diene will act as a masked double bond and would allow the synthesis of the product in one pot.

Examination of the possible dienes **105-109**, indicated that the furan **105** and the thiophenedioxide **106**, rank among the better candidates. The cyclopentadienone **107**, could be expected to be prone to dimerisation. The α-pyrone **108**, and the *o*-quinone **109**, may require long syntheses. Although there are several routes to substituted furans,[107] there are no general methods available for the synthesis of 2,3,4-substituted furans. Manipulation of the furan ring is not easy, as it is not very stable to electrophilic substitution reactions. Thiophene on the other hand is more robust, as it can be subjected to electrophilic substitution and metallation reactions. This makes the functionalisation of the thiophene ring easier.[108] There are several mild reagents known for the oxidation of thiophene to thiophene dioxide,[109] and substituted thiophene dioxides are known to be stable. Hence, we chose to synthesise 2,4-bis(bromomethyl)-3-methylthiophene, **110**, as the precursor to the diene synthon, **106**.



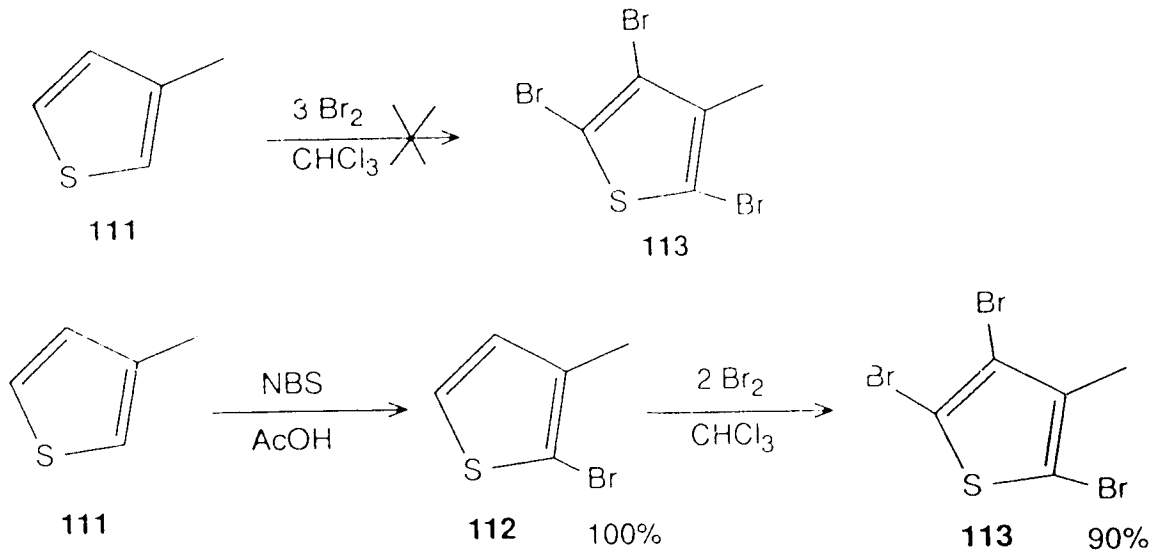
110



106

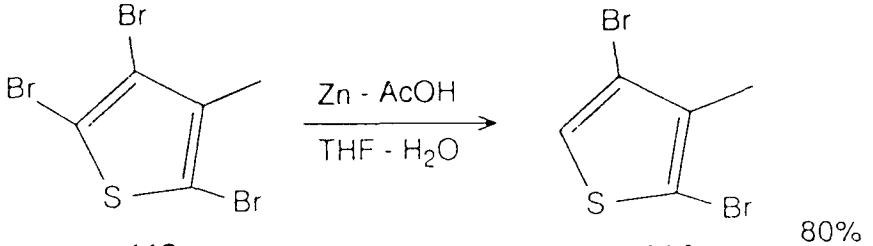
2.4 Synthesis of 2,4-bis(bromomethyl)-3-methylthiophene, 110

We decided to synthesise, **110**, starting from commercial 3-methylthiophene, **111**. 2,4-dibromo-3-methylthiophene, **114**, is a known compound and can be obtained in two seemingly simple steps from **111**. Perbromination of 3-methylthiophene is reported to proceed smoothly by the reaction of bromine on **111**.[110] However, we found that this bromination can not be performed on a large scale (>0.1 mole) as polymeric products ensue.[111] Hence, we mono-brominated **111**, with the NBS-AcOH system, according to the procedure of Kellog and coworkers[112], to obtain **112** in near quantitative yield. The monobromide **112** on treatment with two moles of bromine, resulted in the tribromide **113** in 90% yield.



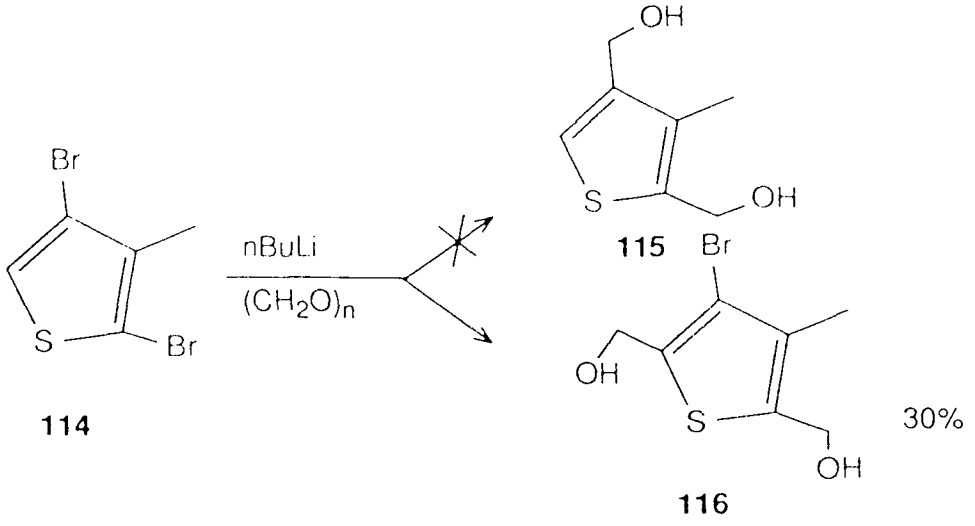
The tribromothiophene **113** is a low melting solid (mp 29-31°C)[113] and is a liquid at room temperature when ~5% THF is introduced as an impurity. This liquid mixture, when reduced with a stoichiometric (1:1) amount of Zn

dust in AcOH-H_2O, gave the dibromide **114** in 80% yield, as the only product. The nature of the solvent system seems to be very crucial to ensure the selectivity and high yield of the product. Recently, a report has appeared describing this selective transformation by electrochemical means.[114]



113 **114** 80%

With the required 2,4-dibromo-3-methylthiophene in hand, we proceeded to synthesise the dibromide **110**. Repeated attempts to produce the dialcohol **115** by dilithiation with various reagents (*n*BuLi, *n*BuLi/TMEDA, LiTMP) followed by quenching with paraformaldehyde did not yield any of the expected **115**. The major product was instead the bromo-dialcohol **116**.



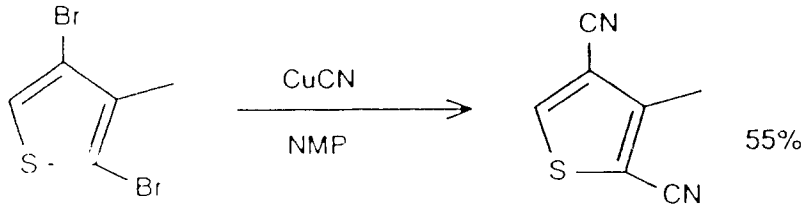
114 30%

116

This dialcohol **116**, mp 87-89°C, showed no aromatic protons in its ^{1}Hnmr spectrum and an absence of any aromatic CH carbons in its ^{13}Cnmr

spectrum. Its molecular ion peaks (M^+ 238, 236) and elemental analysis indicated the presence of one bromine atom in the molecule. Why there is a preference for lithiation of the thiophene ring at the 5-position over the 4-position is not obvious.[115]

The failure to lithiate **114** selectively at the 2 and 4 positions, led us to investigate an alternate route to the dibromide **110**. Cyanation of the dibromide **114**, with excess of CuCN in NMP at 140°C, readily yielded the dicyanide **117** in 55% yield.



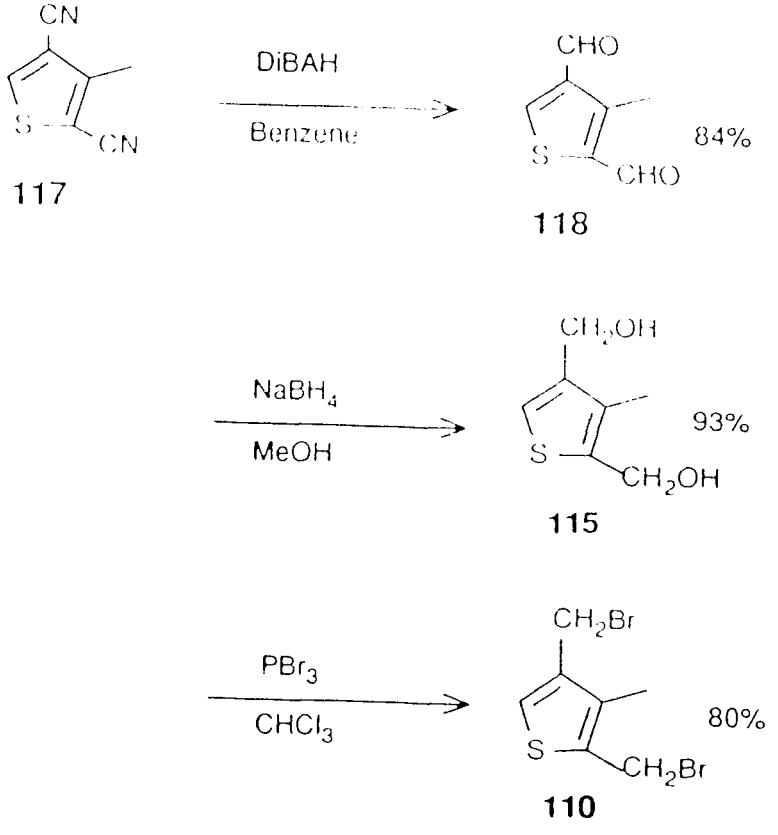
114 117

Colorless crystals of pure **117**, mp 134°C, were obtained by direct sublimation, under vacuum, of the crude product from the cyanation reaction. The dicyanide **117**, showed the correct molecular ion (M^+ 148) in its mass spectrum and a characteristic -CN band at 2210 cm^{-1}, in its IR spectrum. In the ^{13}Cnmr spectrum the -CN carbons were present at 113.6 and 108.0 ppm.

Reduction of the dicyanide **117**, with excess DIBAH, followed by sublimation of the crude product, resulted in the dialdehyde **118**. The structure of this dialdehyde, mp 106-108°C, was confirmed from its molecular ion (M+1 155) and strong IR bands for aldehyde carbonyl groups at 1649 cm^{-1} and 1643 cm^{-1}. In the ^{1}Hnmr spectrum the aldehyde protons appeared at 10.10

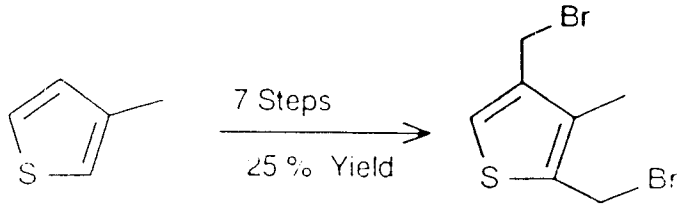
and 9.97 ppm, the aromatic proton at 8.87 ppm and the methyl protons at 2.78 ppm as singlets. In the ^{13}Cnmr spectrum, the carbonyl carbons appeared at 185.4 and 182.3 ppm. Further reduction of **118** with $NaBH_4$ and *careful* work up of the reaction mixture, gave the dialcohol **115**, mp 95-97°C, in 93% yield. The methylene protons of the dialcohol **115**, appeared as singlets at 4.61 and 4.45 ppm, in its ^{1}Hnmr spectrum. This compound also showed the correct molecular ion (M^+ 158) in its mass spectrum and a satisfactory elemental analysis. The dialcohol **115**, decomposed into gummy materials when exposed to strong acids and hence should be handled with care. Conversion of the diol **115** to the dibromide **110**, with PBr_3 proceeded smoothly to afford **110**, in 80% yield (Scheme 4).

Scheme 4



The structure of the dibromide **110** (colorless microscopic crystals, mp 112-115°C (decomp)), was confirmed from its molecular ion peaks in the mass spectrum and a satisfactory elemental analysis. The methylene protons of **110** appeared at 4.64 and 4.39 ppm as singlets in the ^{1}Hnmr spectrum. Compound **110** is quite unstable as it decomposed to black tarry materials within three days, in the solid state, even under argon. Hence, it should be made fresh immediately preceeding further reaction.

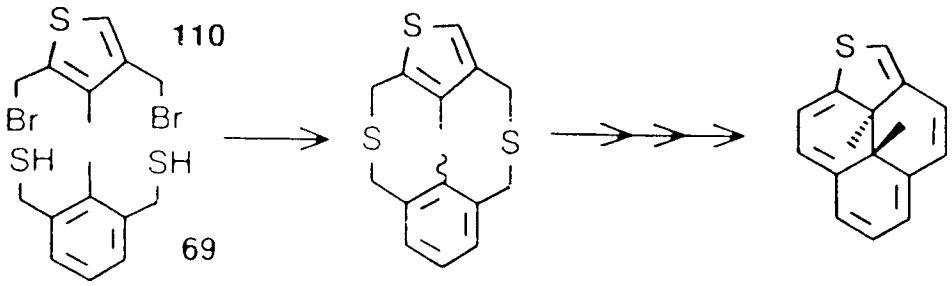
Thus, we achieved the synthesis of the dibromide **110**, starting from 3-methylthiophene, in seven steps and an overall yield of 25%.



111 110

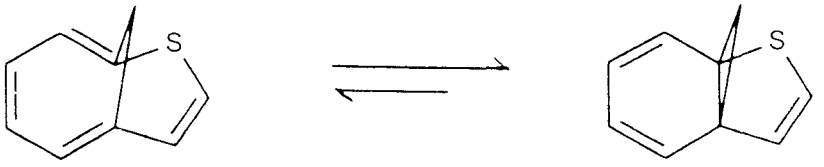
2.5 Synthesis of the first diatropic bridged thiaannulene 120

The dithiacyclophane route we described earlier in section 1.4.1., offered new possibilties for the bis-bromomethylthiophene **110**. Compound **110** was a direct precursor to the unknown bridged thiaannulene **120**.



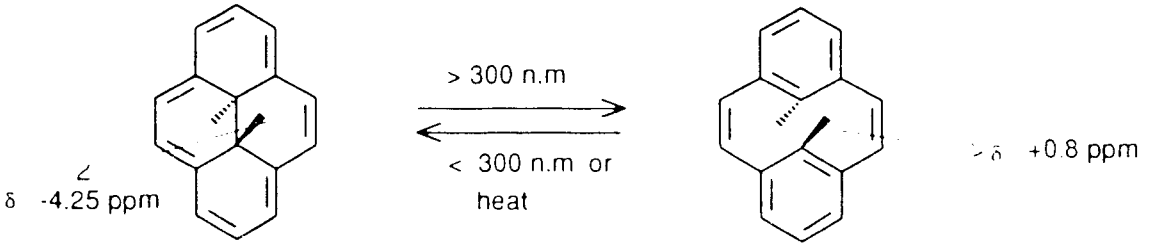
123 120

Very few bridged heteroannulenes have been synthesised so far.[116] Okazaki *et al.* have described the synthesis of the methanothia[9]annulene **121**.[117] Unfortunately, due to the rapid equilibrium between **121** and its valence isomer **121a**, they were unable to conclude whether **121** is diatropic or not, especially since the bridge protons of both **121** and **121a** appear at approximately the same chemical shift.



121 **121a**

The possibility of encountering a difficulty such as the rapid interconversion of valence isomers and negligible difference in the chemical shifts of the methyl protons of the valence isomers **120** and **120a** can be evaluated by comparison of the chemistry of DMDHP, **12**, and its isomer **12a**.



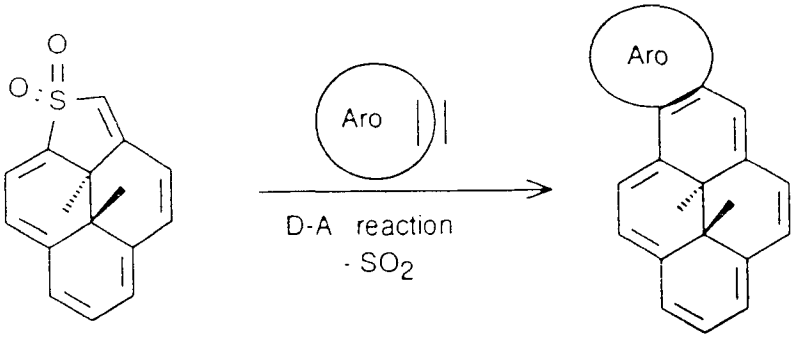
12 **12a**

120 **120a**

Since, in the DMDHP system, this isomerisation process can be driven either towards **12** or **12a** photochemically,[118] one could expect to overcome this problem. The chemical shift difference of the methyl protons of **120** and **120a**, should be significant even in the complete absence a ring current in **120**, and hence enable us to distinguish between them, unlike the case of **121** and **121a** above.

The thiaannulene dioxide **122**, if it could be synthesised, would serve as an immediate precursor to various [a]fused DMDHPs, through D-A reactions (Scheme 5). Also, we were interested to find out whether the thiacyclophane chemistry, which is reliable for aromatic hydrocarbons, can be applied successfully to heterocyclic systems as this success would pave the way to the syntheses of several other bridged heteroannulenes.

Scheme 5

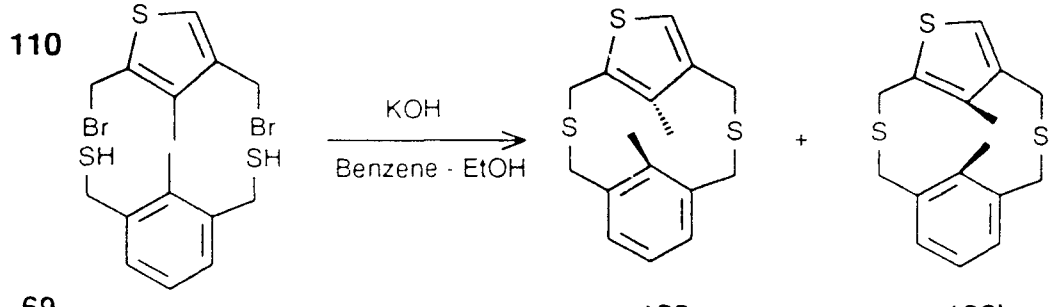


122 Fused DMDHPs

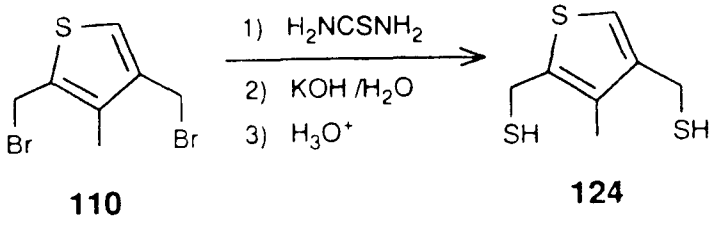
Hence, we directed our attention to the synthesis of the thia[13]annulene **120**.

2.5.1 Synthesis of the dithiacyclophanes 123

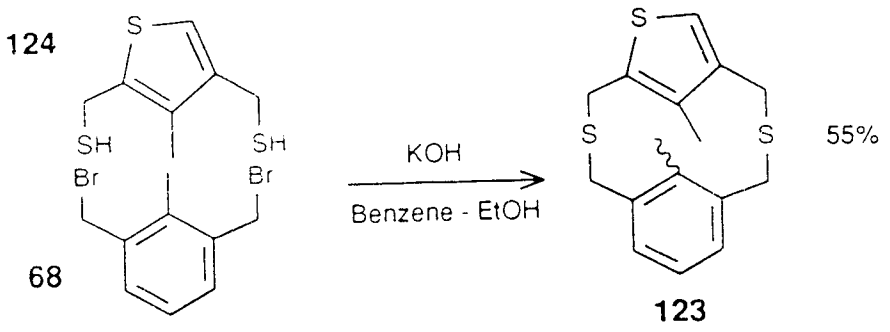
Coupling of the dibromide **110**, with the dithiol **69**, under high dilution conditions, yielded the expected dithiacyclophanes as a mixture of *anti*-**123a** and *syn*-**123b** isomers, in 71% yield. The mixture gave the correct molecular ion (MH^+ 337) and satisfactory elemental analysis. The *anti*/*syn* ratio was determined to be 2.6/1 from the ratio of ^{1}Hnmr chemical shifts of the methyl protons. The syn methyl protons appeared as two singlets at 2.36 and 2.33 ppm and the anti methyl proton signals were at 1.88 and 1.21 ppm.



In order to find out whether there would be any change in the *anti*/*syn* ratio and/or the total yield, we tried the alternate coupling, that is the coupling of the dithiol **124** with the dibromide **68**. The dithiol **124** was obtained as a low melting solid, from the dibromide **110**, through its dithiouronium salt and the base treatment of the latter.



The dithiol, **124**, was found to be very prone to polymerisation even under an inert atmosphere. The coupling of **124**, with the dibromide **68**, under conditions analogous to those used for the previous coupling also produced the thiacyclophanes **123**, in the same anti/syn ratio, but in lower yields (55%). The lower yield may be due to the propensity of the dithiol to polymerise.



2.5.2 *anti*-9,17-Dimethyl-2,11,-dithia[3]metacyclo[3](2,4)thiophenophane

Unlike the anti/syn mixture of the thiacyclophanes **74**,[119] the two isomers **123a** and **123b**, proved inseparable under a variety of chromatographic conditions. However, we took advantage of the slight difference in solubilities between **123a** and **123b** to achieve separation. The anti isomer **123a** is less soluble in toluene-anhydrous EtOH (1:1) than *syn*-**123b**. Ten, careful fractional recrystallisations of the anti/syn mixture gave a pure sample of *anti*-**123a**.

Figure 4 250 MHz ($CDCl_3$) ^{1}Hnmr spectrum of **123a**

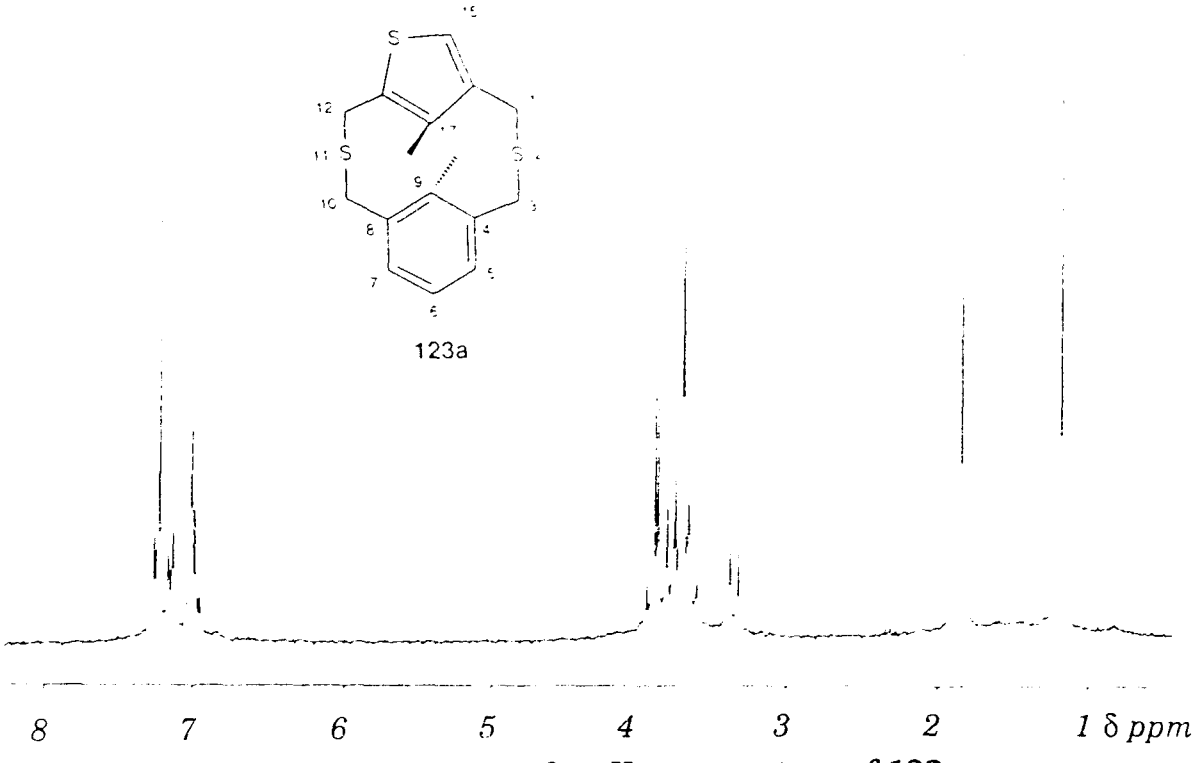
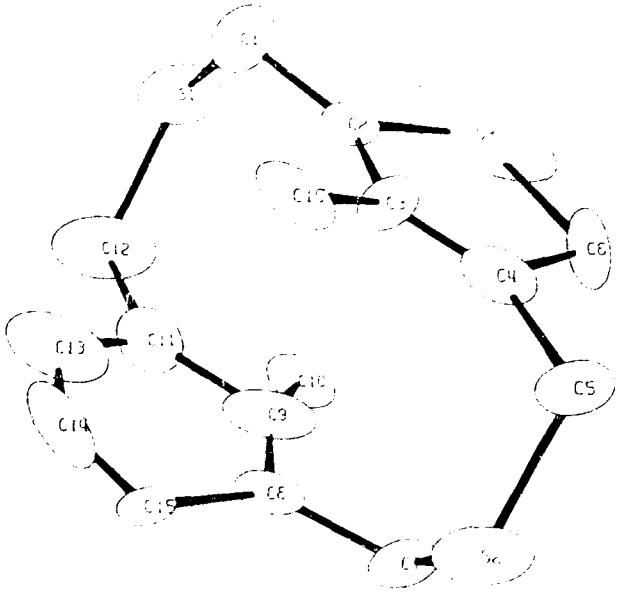


Figure 5 ORTEP diagram of an X-ray structure of **123a**



The *anti*-isomer, **123a**, (colorless crystals, mp 228-230°C (decomp)) showed, in its ^{1}Hnmr spectrum, Figure 4, a multiplet at 7.27-6.97 ppm due to the phenyl ring protons and a singlet at 7.03 ppm due to the thiophene ring proton. The bridge methylene protons appear as four overlapping AB's at 3.98-3.36 ppm. Two singlets, due to the methyl protons appear at 1.88 and 1.21 ppm. The singlet at 1.21 ppm is assigned to the thiophene methyl protons because these protons are situated above the phenyl ring and experience a strong shielding. The phenyl methyl protons are assigned the lower shift as the shielding experienced by them comes from thiophene which has a weaker ring current than benzene and thus the shielding should be less. We attempted an X-ray crystal structure determination of **123a**. Single crystals, grown by the slow evaporation of a dilute solution (solvent system toluene-EtOH, 1:1), were subjected to X-ray crystal determination by Kathy Beveridge at the University of Victoria. The crystal structure clearly showed the carbon skeleton, but due to disorder could not be refined further to locate the hydrogens. An ORTEP diagram of *anti*-**123a** is shown in Figure 5. The crystal parameters are collected in the appendix.

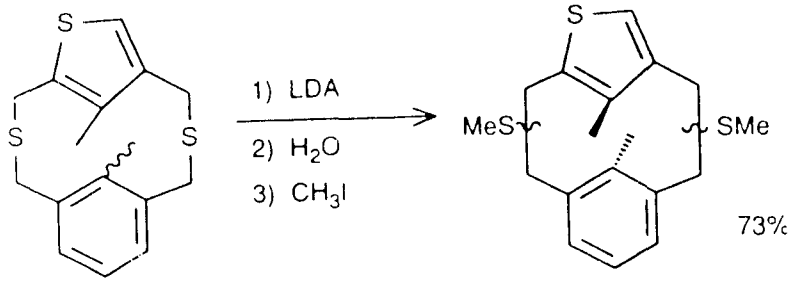
From the ^{1}Hnmr spectrum of the anti/syn mixture, the notable differences were in the chemical shifts of the thiophene ring proton and the methyl protons of *syn*-**123b**. The thiophene ring proton in *syn*-**123b** resonates at 6.32 ppm, an upfield shift of 0.7 ppm relative to that of the thiophene ring proton in *anti*-**123a**. This is due to the shielding effect of the phenyl ring. The

methyls appear as singlets at 2.36 and 2.33 ppm, values very different from those in *anti*-**123a** (see above), as they do not experience any shielding from the aryl rings. The syn and anti isomers of **123** can also be readily distinguished by their ^{13}Cnmr spectra as the chemical shifts of all the corresponding carbons were different. For example, the bridge methylene carbons of **123a** resonate at 33.0, 31.2, 28.7 and 27.2 ppm whereas those of **123b** appear at 36.9, 34.9, 31.6 and 31.1 ppm.

2.5.3 Synthesis of *trans*-9b,9c-dimethyl-9b,9c-dihydrophenyleno[1,9-bc]thiophene, 120.

Wittig rearrangement of a syn/anti mixture of dithiacyclophanes, often converts some of the syn isomer to the corresponding ring contracted anti-cyclophane.[120] The syn/anti mixture of the thiacyclophanes **123** when subjected to Wittig rearrangement with LDA, followed by methylation with CH_3I of the dithiolates formed, resulted in a complicated mixture of compounds from which the expected anti-cyclophane **125** could not be isolated in a pure form. Since, an excess of base is usually used to bring about the Wittig rearrangement, we reasoned that the excess LDA present might be deprotonating the thiophene ring proton, H-14, of the thiacyclophane thus yielding a complex mixture of products. In order to eliminate any such possibility, the reaction of the thiacyclophanes after treatment with excess LDA, was quenched with water and the products methylated with CH_3I. This

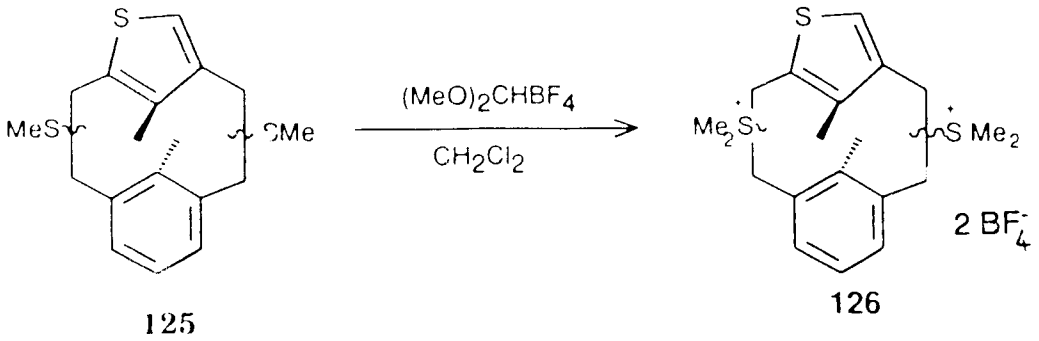
process cleanly yielded the anti-cyclophanes **125**, in 73% yield. No syn isomer could be detected by ^{1}Hnmr.



123 **125**

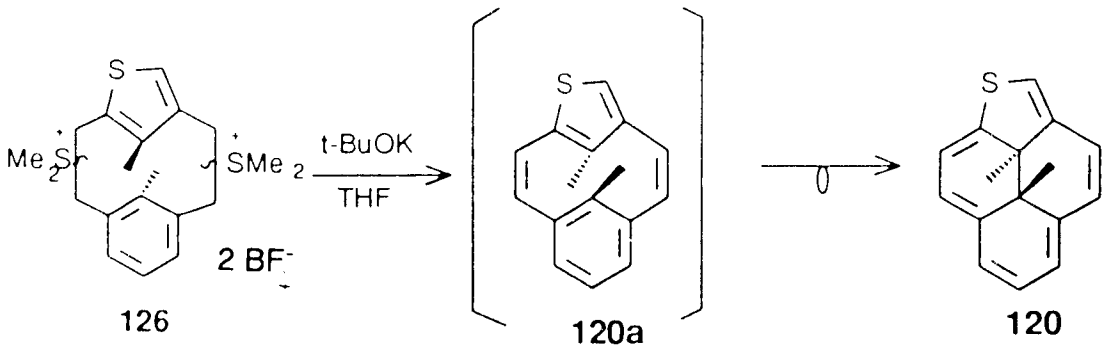
The structure of this cyclophane was confirmed by the molecular ion (M^+ 334, base peak) in its mass spectrum and correct elemental analysis. The anti configuration was evident from the ^{1}Hnmr spectrum with chemical shifts of the methyl protons attached to benzene and thiophene rings appearing strongly shielded at 1.57 and 0.71 ppm respectively. The S-methyl groups appear as two singlets at 2.25 and 2.11 ppm. The ^{13}Cnmr of **125**, showed several peaks for the S-methyl carbons and thus indicated the presence of a variety of isomers of **125** with the different orientations of the S-methyl groups on the ring. Two major peaks due to the bridge carbons attached to the S-methyl groups appear at 51.9 and 51.6 ppm.

The cyclophanes **125** were then S-methylated with an excess of Borsch reagent to yield the bis-salt **126**, in near quantitative yield. The off-white salt was quite unstable, turning increasingly grey within hours. An attempt to measure its melting point resulted in decomposition at ~60-65°C.



125 126

Treatment of a suspension of the crude bis-salt **126**, with an excess of *t*-BuOK, at 80°C in the dark, led to the formation of the thia[13]annulene, **120**.



126 120a 120

The Hofmann elimination of **126** resulted in the direct formation of the thia[13]annulene **120**, presumably via the cyclophanediene **120a**. Isolation of compound **120** proved to be a difficult task as it was found to be very light-sensitive. So, the work up and the chromatographic separation were carried out in the absence of light to obtain the thia[13]annulene **120**, as a reddish orange solid in 30% yield. A pure sample was obtained by recrystallisation from degassed methanol as orange-red plates, mp 70-71°C (decomp). The gross structure of **120** was identified from its mass spectrum [M^+ 238, M-15 223, M-

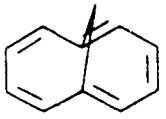
30 208 (base peak)] and a satisfactory elemental analysis. The nmr spectra of **120** are discussed, in detail, in the next section. It was freely soluble in many common solvents, the solutions were stable when diethylether was present, for up to three days in the absence of light and oxygen. In the solid state, compound **120** was stable for a week at -20°C. The decomposition products were quite polar and poorly soluble even in methanol.

2.5.4 The first diatropic bridged thiaannulene

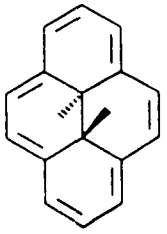
2.5.4.1 Introduction

Heteroannulenes have received considerable attention in the literature,[121] particularly because of an interest in the aromaticity relative to that of benzene of such molecules as furan, thiophene, pyrrole and pyridine. Going by the Hückel π-electron count, the bridged annulenes **13** and **12** can be considered as homologues of benzene, **1**.

1 [6]



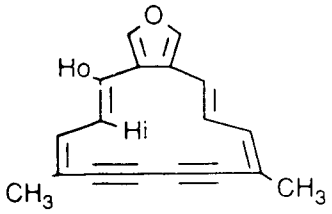
13 [10]



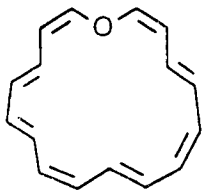
12 [14]

When it comes to heteroannulenes, this homologation is not as straight forward because the electronic and chemical nature of heteroatoms are considerably different from that of carbon. For example, nitrogen is more

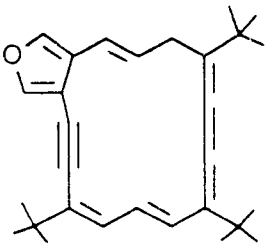
electronegative than carbon and is tri- or pentavalent. Introduction of heteroatoms in annulene structures, in general, is more difficult because of these differences. The detection and estimation of diatropicity of heteroannulenes is difficult if they are not made rigid through bridging, and especially so for the weakly diatropic compounds. For example, in **128**, a measure of the aromaticity is taken as the difference in chemical shift between the inner (H_i) and outer (H_o) protons.[122] However, such protons are subject to severe anisotropic effects from the neighbouring acetylenic groups and in addition they are conformationally mobile. The molecule **129**, is quite floppy, nonplanar and nonaromatic.[123] In more rigid annulenes such as **130**, the anisotropy problems are not solved.[124]



128



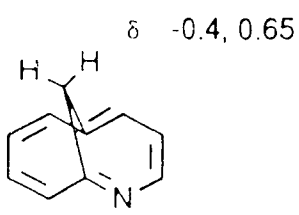
129



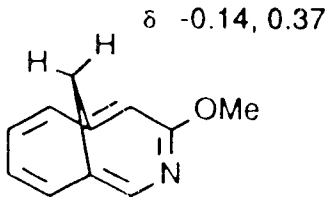
130

Bridging could overcome the problems of rigidity and anisotropic effects created by triple bonds. The aza[10]annulenes **131** and **132** made by Vögel and coworkers, and by others, show strong diatropic behaviour. However, due to the close proximity of one of the bridge protons to the N atom, a fairly large anisotropic effect is observed as is shown by the difference in

their chemical shifts.



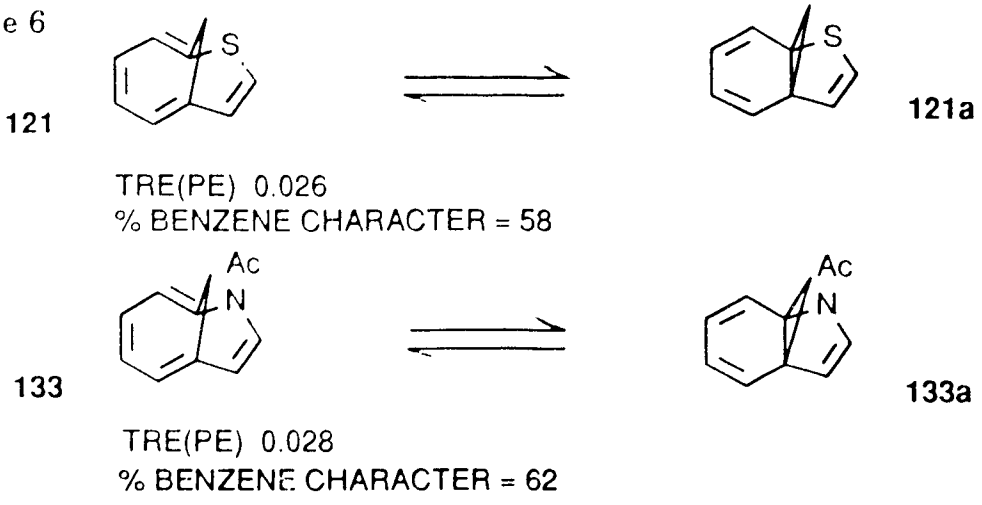
131



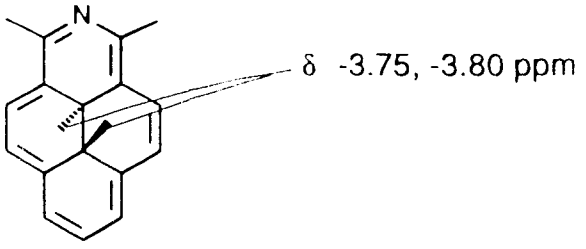
132

In the bridged hetero[9]annulenes, another unexpected problem was encountered. Due to the methanoannulene-norcaradiene valence isomerisation problem, the heteroannulenes themselves are difficult to observe. Even though the methanothia[9]annulene, **121**,[125] and the methanoaza[9]annulene, **133**,[126] are predicted to have strong aromatic character by topological resonance energy estimates,[127] both are shown to be in equilibrium with their corresponding norcaradiene valence isomers (Scheme 6). It is particularly interesting to note that the theoretically "more aromatic" azaannulene **133**, exists solely in the tricyclic form and no evidence could be found for the presence of a fully conjugated structure.

Scheme 6



However, though no theoretical estimates are available, the azaDMDHP **33** is strongly diatropic as shown by the strong shielding of its internal methyl protons.



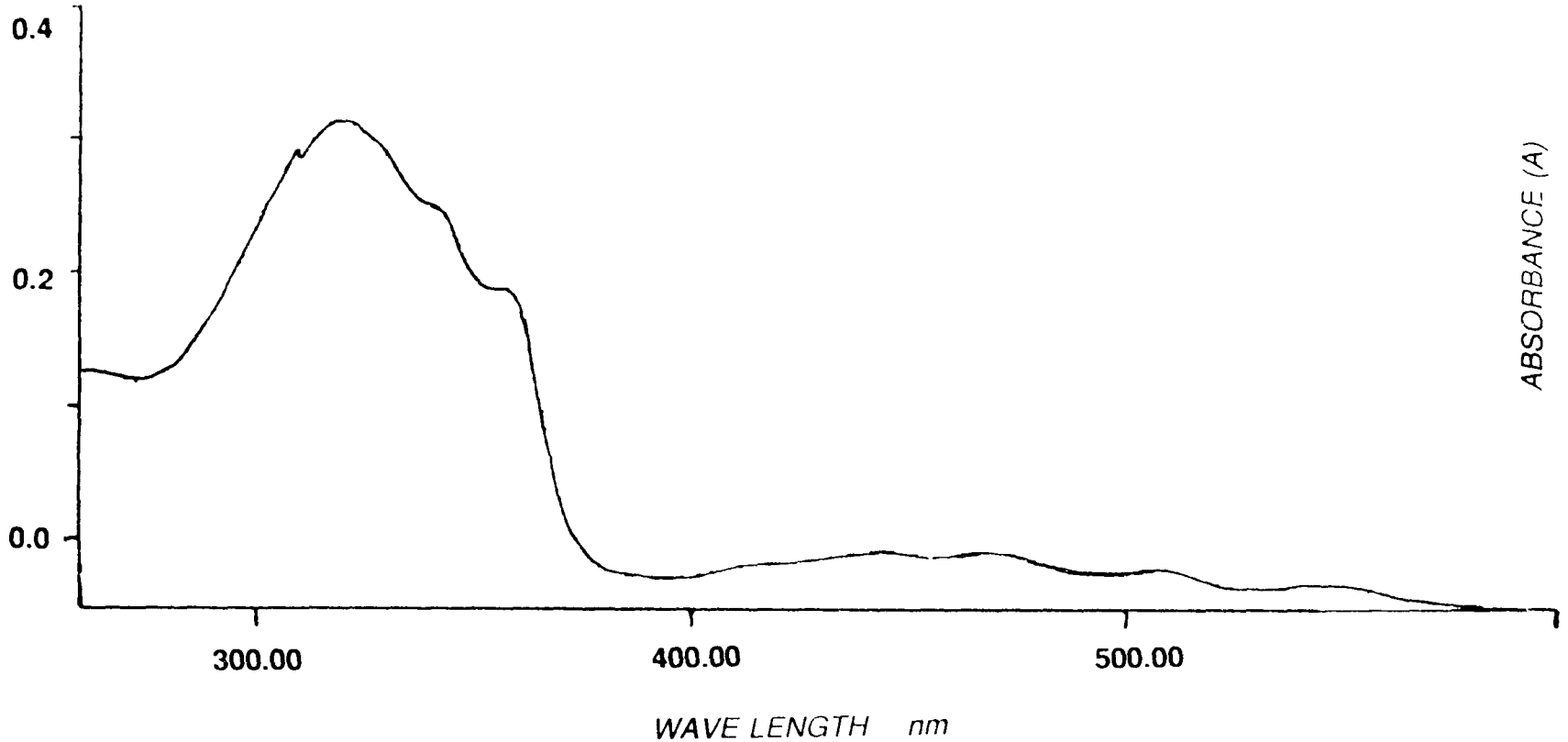
33

We shall examine the spectral data of the thia[13]annulene **120**, in the following pages in detail and compare them with those of other thiaannulenes and heteroDMDHPs and present an experimental estimate of the aromaticity of **120**, based on its ring current.

2.5.4.2 UV-Vis spectrum of 120

The red thiaannulene **120** shows absorption maxima at 320, 443, 470, 505, 550 nm. A UV-Vis spectrum of **120** in cyclohexane is shown in Figure 6. Comparison of the absorption maxima at the longest wavelength of the related systems **12**, **33** and **63** with that of **120** shows that the λ_{max} of the thiaannulene **120** lies in between that of the strongly diatropic DMDHP, **12**, and azaDMDHP **33** and the weakly diatropic oxa[17]annulene **63** (Table 8). When a degassed solution of **120** was irradiated with visible light, the color of the solution was bleached immediately and the absorption maxima were shifted to lower

Figure 6. U.V-Vis spectrum of **120** in cyclohexane



wavelengths, presumably due to either first the photochemical valence isomerisation of **120** to **120a** and then decomposition, or to the direct decomposition of **120**. The process was found to be irreversible as irradiation of the bleached solution with UV light did not result in the restoration of the red color, and TLC and ^{1}Hnmr analysis of the bleached solution indicated the presence of some unknown polar compounds.

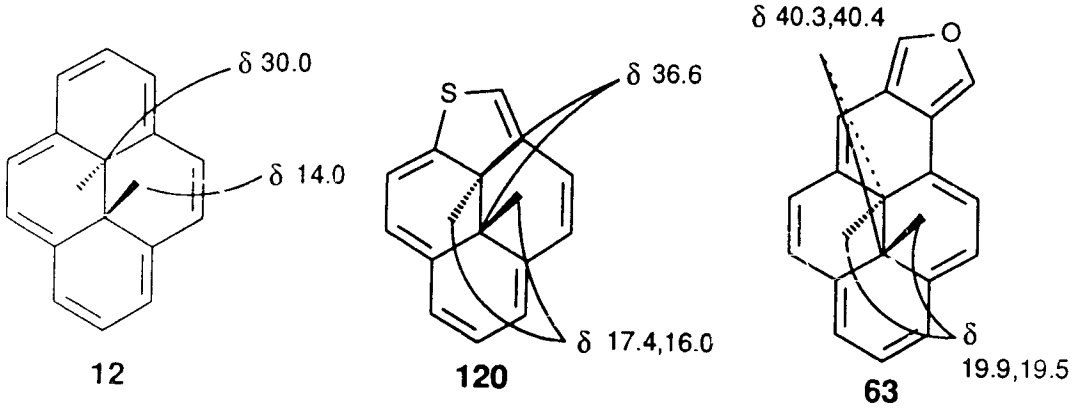
Table 8 Comparison of the longest λ_{max} of **120** and related annulenes

Compound	λ_{max}nm	logε_{max}
12	651	2.52
33	655	3.25
120	550	2.27
63	494	3.83

2.5.4.3 NMR spectra of the thiaannulene, 120

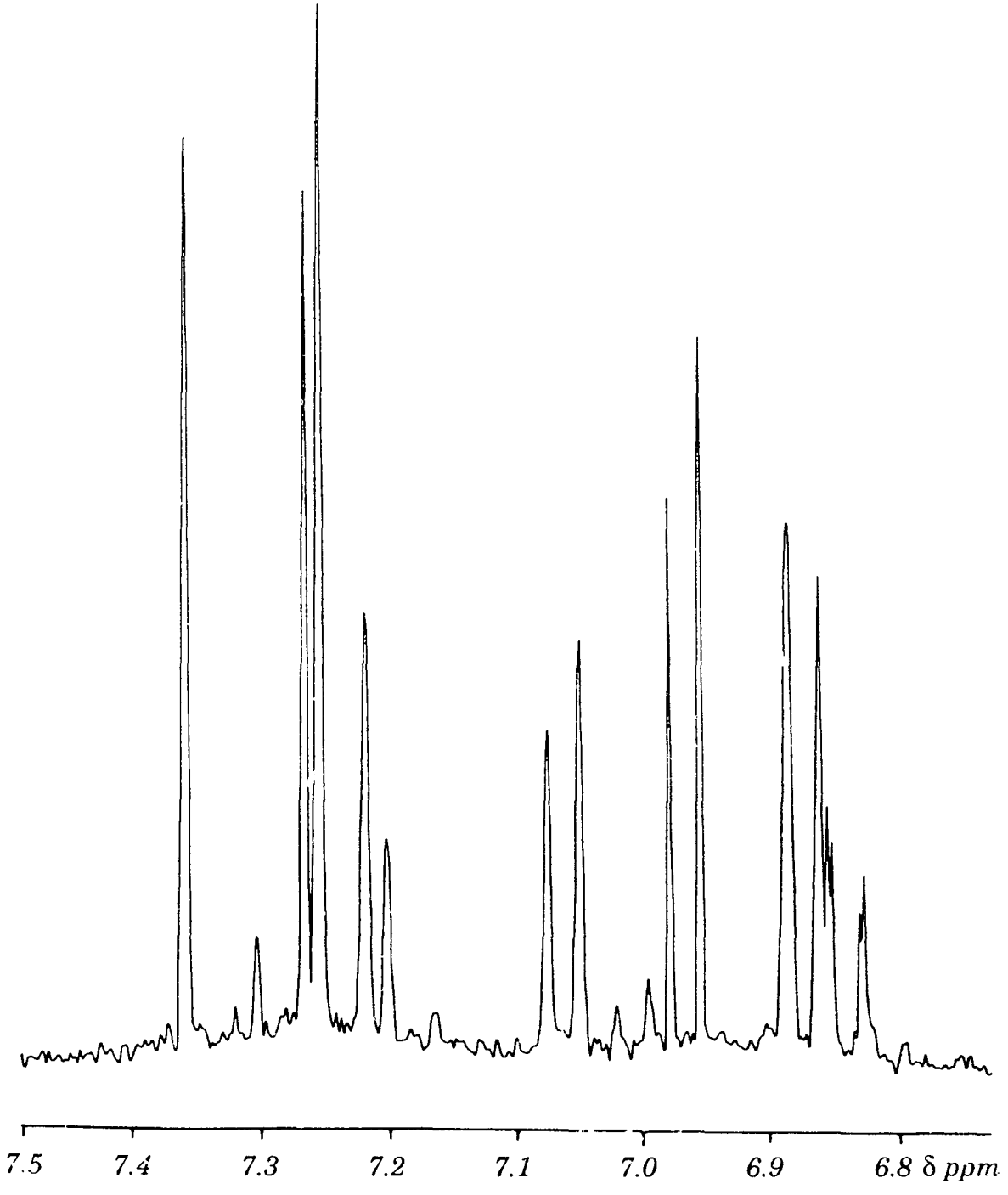
^{13}C chemical shifts of internal methyl carbons, although they cannot be used reliably to estimate shielding or deshielding due to ring current changes, are good indicators of the presence of a ring current.[128] The peripheral carbons of **120**, occur between 130.0 - 120.8 ppm (aryl quarternary) and 126.1 - 114.2 ppm (aryl CH) which are in the normal aromatic/alkene

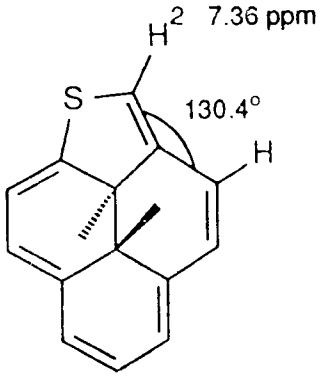
region comparable to the corresponding carbon shifts of **12** and **63**. The bridge carbons and the methyl carbons, which can be assigned easily, also resonate in the same shielding region as those of **12** and **63**. The shielding experienced by the methyl and the bridge carbons of the thiaannulene lies in between that of **12** and **63**.



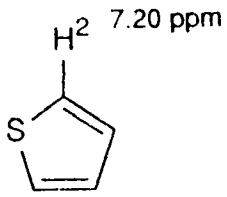
The ^{1}Hnmr spectrum of **120**, is more informative. The internal methyl protons of **120** appear as two singlets at -1.16 and -1.32 ppm, showing a strong shielding due the presence of a ring current, while the external protons resonate between 7.36 - 6.83 ppm and are deshielded. Thus, the thia[13]annulene **120**, is clearly diatropic. Figure 7 shows the partial (aryl region) ^{1}Hnmr spectrum of **120**. Note that the protons H^2 of **120** and H^2 of thiophene have almost the same chemical shift. Assuming all other contributions we mentioned in equation 2, such as local anisotropy and excess π-electron density are equal in both cases the shifts of these protons at 7.36 ppm and 7.20 ppm for **120** and thiophene, respectively, indicate the extent of ring current contributions in **120** and **34**.

Figure 7 250MHz ^{1}Hnmr spectrum of **120** in CD_2Cl_2 (aryl region only)



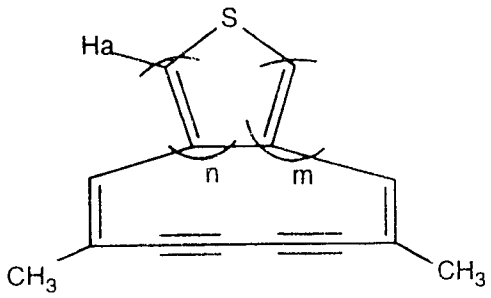


120



34

Such a comparison could be considered reasonable here because the peripheral bond angle next to H2 of the carbon periphery of **120**, is quite wide (130.24°) meaning any chemical shift change of H^2 due to peri interactions between H^2 and H^3 should be very small. We would like to point out here that similar comparisons are not applicable to Sondheimer's thia[13]annulene, **134**, and its homologues made by Ojima and coworkers.[138] The chemical shifts of the external proton H_a and methyl protons of compounds **134 - 140** are collected in Table 9.



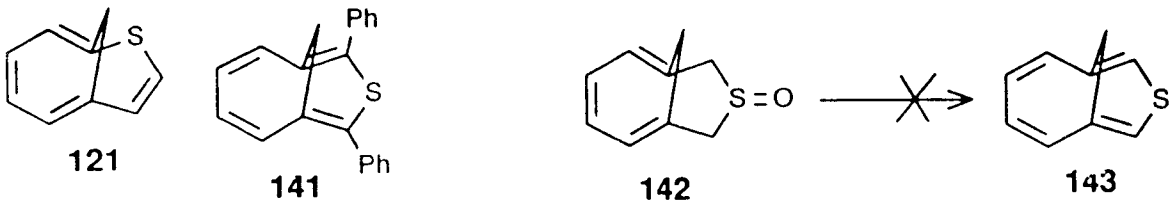
134 - 140

Table 9 Chemical shifts (δ) of H_a and CH_3 of some thiaannulenes in ppm.

Compd	No π e^{-1}	n	m	δ H_a	δ (CH_3)	Ref
134	14	1	1	5.51	2.29	129
135	16	1	2	6.4-5.8	1.61,1.57	129
136	18	2	2	5.66	2.22	130
137	20	3	4	6.04	1.71,1.69	131
138	22	4	4	5.87	2.18	132
139	24	4	5	6.03	1.82,1.81	132
140	26	5	5	6.53	2.13	132

From Table 9, it can be seen that δ H_a values range from 5.51 to 6.53 ppm, and do not well reflect the extent of the paratropic or diatropic nature of the ring current present. Ojima,[133] drew attention to the higher field resonances of the external methyl protons of the [4n] annulenes compared to the lower field shifts of the methyl protons of the [4n+2] annulenes as indicators of paratropicity and diatropicity respectively. It is worth noting, however, that the observed differences (~0.5 ppm) are very small. A nice comparison of the external proton chemical shift of **120** would have been with the corresponding protons of the thia[9]annulenes **12a** and **141**. But, as we mentioned earlier, due to an isomerisation problem, ^{1}Hnmr analysis of the

external protons of **121** was not possible. The other thia[9]annulene, **141**, has phenyl groups flanking sulfur. Attempts made by Vögel's group to synthesise **143**, from the sulfoxide **142**, were not successful.

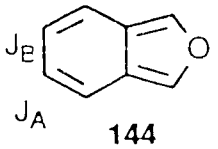


121 **141** **142** **143**

2.5.4.4 A look at vicinal coupling constants, geometries and comparison with other bridged heteroannulenes

The vicinal coupling constants (^3J) in the thia[13]annulene, **120**, show considerable variation (Figure 7). Sardella and coworkers have used the ratio of vicinal coupling constants as an indicator of bond alternation in the benzene ring part of isobenzofuran type heterocycles **144** - **147** (Table 10). This ratio (J_A/J_B) for compounds **144** - **147** is almost invariable (0.70 - 0.74) and is comparable in value to that of the *nonaromatic* moieties such as **148** and **149**. This similarity led Sardella to conclude that the major contributing structure in such molecules is **151** and the 'aromaticity' of the heterocycles such as **144** should essentially be that of the corresponding five membered ring heterocycle (in the case of **144**, it is furan). Kato et al., have calculated the J_A/J_B ratio for their methanohetero[9]annulenes and from the values obtained, contended that

they are also as aromatic as the corresponding heterocycles. From Table 10, major discrepancies could be noted. The hypothetical cyclooctatetraene conformer **148**, *o*-xylylene **149**, isobenzofuran, **144**, thiophene, **35**, and the methanoannulenes **141** and **152**, all have the almost the same J_A/J_B ratio as that of the nonaromatic **153**. While Sardella's argument supports his contention that **151** is the major contributor in heterocycles such as isobenzofuran, it actually works against Kato's conclusion that is the methano thia[9]annulene **141** and related systems are aromatic!



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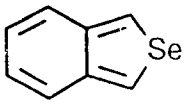

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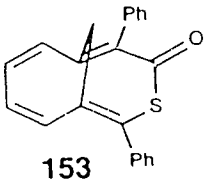

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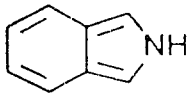

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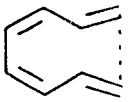

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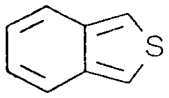

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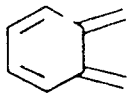

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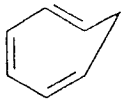

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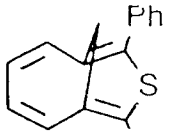

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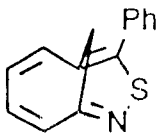

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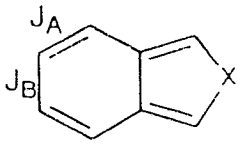

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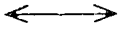
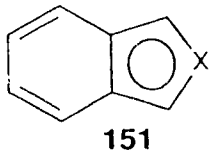




151

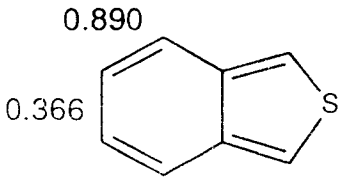
Table 10 Comparison of J_B/J_A ratios of **141** and related systems

Compound	J_B/J_A	Ref	TRE/e (% benzene character)	Ref
144	0.70	134	0.011 (25)	139
145	0.75	134	0.032 (71)	139
146	0.72	134	0.029 (63)	139
147	0.74	134	-	-
148	0.70*	135	-	-
149	0.70*	136	-	-
35	0.71	137	0.033 (71)	140
141	0.74	138	0.020 (44)	140
152	0.76, 0.74	138	-	-
153	0.74, 0.71	138	-	-

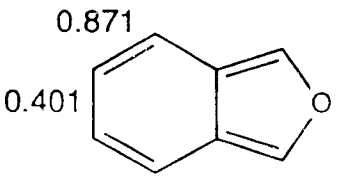
* From bond orders

Though the topological resonance energy estimates put the TRE(PE) of **141**, as having 44% of benzene character, no positive evidence has been obtained from ^{1}Hnmr studies to show the definitive presence of a ring current

in **141**. To add an interesting complication to the bond alternation value for thianaphthene **146** (0.72), obtained from the J_A/J_B ratio, recent calculations of Glidewell and Lloyd,[141] show considerably different values. These calculated ratios (from bond orders) are indicative of a much higher bond alternation in such systems than found earlier and are in contradiction with Sardella's conclusions. We shall not get into this controversial area to comment on which theoretical or experimental result or conclusion is correct. But, from what we have shown, it is very clear that a reliable proof for the existence of diatropicity in the methanothia[9]annulene, **141**, is still lacking.



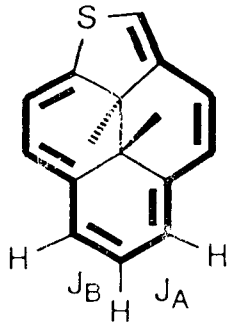
ρ_1/ρ_2 = 0.41



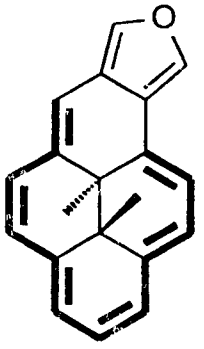
ρ_1/ρ_2 = 0.46

One of the major problems in discerning the tropicity of methanoannulenes is due to their geometry. Even the parent methano[10]-annulene, **13**, has a bent periphery. So, reasonable estimates of ring current are difficult. To check whether the thia[13]annulene, **120**, is comparable to the parent DMDHP and related systems, and due to problems in obtaining a stable single crystals of **120**, we implemented molecular mechanics (MM) calculations on the thia[13]annulene, **120**, and the oxa[17]annulene, **63**. Some of the salient features of the results obtained, together with the J_A/J_B values are

given in Table 11.



120



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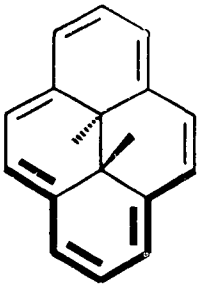


12

Table 11 Comparison of some MM results and J_A/J_B ratio of **120**, **63** and **12**.

Compd	Average deviation of peripheral bond angles[@]	S_E(kcal/mol)	J_A/J_B
120	3.4	48	0.68
63	3.1	56	0.58
12	2.0	26	1.00

[@] from 120°

The MM calculation of the average deviation of the peripheral carbon bond angles for compounds **120**, **63** and **12** are consistent with the calculated strain energies. The geometries of the peripheral carbon skeleton of **120** and

63 are almost identical to that of DMDHP, **12**. The notable feature is that the average deviations (from 120°) of the peripheral carbon bond angles for **120** and **63** are almost the same as that of DMDHP itself. Since, the geometries are very similar and the hetero atoms are far removed from the bottom protons, a comparison of the vicinal coupling constants could be made. The J_A/J_B ratios indicate that the degree of bond alternation is in the order **63** > **120** > **12**. Even the weakly diatropic oxa[17]annulene, **63**, has been shown to be diatropic by Mitchell.[142] These results along with the upfield chemical shifts of the internal methyl protons of **120**, clearly show that it is diatropic.

Next, we shall estimate the diatropicity present in the thia[13]annulene, **120**, using Mitchell's approach and compare it with other heteroDMDHPs and DMDHP itself.

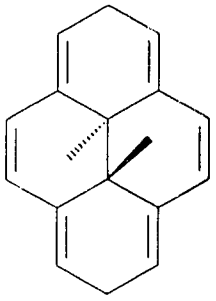
2.5.4.5 Estimation of diatropicity in the thia[13]annulene, 120

As we showed in the introduction, Mitchell's method of estimation of aromaticity of a fused DMDHP uses the reduction in diatropicity in the macro ring. This reduction is estimated from the change in coupling constants (bond alternation) and the internal methyl proton chemical shifts (ring current reduction) which correlate linearly with each other. Equations 4 and 5 can be recalled here to be used in our discussion.

Equation 4 is only dependent on the changes in the average deviation of bond orders ($\Delta\nu$). The atropic model **48** used to obtain shielding changes,

can be used here as well because of the similarities in the geometries of the concerned molecules. Hence a prediction of the internal methyl chemical shift can be made using bond orders.

Equation 5 can be used to calculate the ring current magnitude of the external proton H_D. Since this proton is quite distantly located from the sulfur atom in **120**, the local anisotropic effect of sulfur on the chemical shift of H_D should be small. The shielding due to excess π-electron density would affect the values of $\delta(CH_3)$ and δH_D. The $\delta(CH_3)$ value would indicate a higher ring current in **120**, due to increased shielding arising from the excess π-electron density and the reduced area. Haddon has shown that ring current (RC) is directly proportional to the area (A) of a ring for a given number of electrons.[143]



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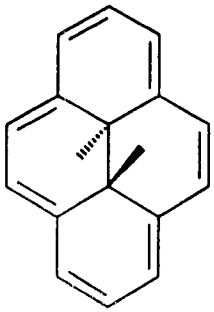

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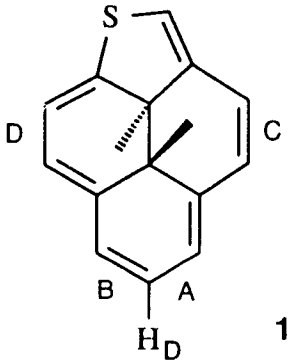


120

The bond orders in the thia[13]annulene can be calculated from the coupling constants us.. g the empirical equations 8 and 9. Equation 8 was

obtained for bonds A and B of DMDHP derivatives and equation 9 for C and D bonds.

$$\rho = 0.0765\ J + 0.0642 \tag{8}$$

$$\rho = 0.0643\ J + 0.147 \tag{9}$$

These equations should give values closer to the π-SCF values than equation 3 which was derived for benzene derivatives. We will make use of these equations in estimating the diatropicity of the thia[13]annulene, **120**.

The π-bond orders derived using equations 8, 9 and 3 and from the π-SCF calculations, together with the corresponding coupling constants are listed in Table 12. The average deviation of both π-SCF and those bond orders obtained through equations 8 and 9 ($\Delta\nu$) are very close to each other in value.

The good agreement between the calculated and observed chemical shifts of the internal methyl protons of **120** means that the shielding of the internal methyl protons is due to the strength of the ring current present.

Table 12 Coupling constant and bond order data for compound **120**.

Bond	J_{expt}	J_{corr}^{*}	$\rho_J^{\P}$ x 10^3	$\rho_J^{\S}$ x 10^3	ρ_{SCF} x 10^3	$\lvert \rho x10^3\text{-}642 \rvert$
A	4.40	4.32	445	395	518	197,247,124
B	6.51	6.43	664	556	762	22,87,120
C	9.31	9.23	961	740	815	31,98,173
D	6.02	5.94	614	529	501	28,113,141
$\Delta\nu$			141.7	136.0	139.5	

δ (CH_3)	using $\rho_J^{\P}$	-0.66
δ (CH_3)	using $\rho_J^{\S}$	-0.82
δ (CH_3)	using ρ_{SCF}	-0.72
δ (CH_3)	experimental	-1.16, -1.32

$\rho_J^{\P}$ obtained using equation 3; $\rho_J^{\S}$ obtained using equations 5 and 6; ρ_{SCF} from π-SCF output; * a naphthalene type correction (subtraction of 0.08 Hz from the experimental J)

Thus, the ratio of the change in chemical shift shielding of the internal methyl protons of **120** to the change in the chemical shift shielding of the internal methyl protons of the parent DMDHP can be taken as a measure

of the extent of diatropicity, as follows:

$$\% \text{ diatropicity} = [\Delta\delta(CH_3)\ \mathbf{120} / \Delta\delta(CH_3)\ \mathbf{12}] \times 100 \qquad (10)$$

where $\Delta\delta(CH_3)\ \mathbf{120} = \delta(CH_3)\ \mathbf{120} - \delta(CH_3)\ \mathbf{48}$ and

$\Delta\delta(CH_3)\ \mathbf{12} = \delta(CH_3)\ \mathbf{12} - \delta(CH_3)\ \mathbf{48}$

We get a value of -1.24 ppm for the average of $\delta(CH_3)$ of **120**. From the $\delta(CH_3)$ values of DMDHP, **12**, and the model **48** at -4.25 and +0.97 ppm respectively and using the relationship above, we get the $\Delta\delta(CH_3)$ **120** and $\Delta\delta(CH_3)$ **48** as 2.21 and 5.22 respectively. Substituting these values in equation 10, we get a measure of diatropicity of the thia[13]annulene **120** to be 42% that of the parent DMDHP.

$$\% \text{ Diatropicity of } \mathbf{120} \text{ relative to } \mathbf{12} = 2.21 / 5.22 \times 100 = 42\%$$

Consideration of the two different $\delta(CH_3)$, -1.16 and -1.32 observed for **120**, this approach would give estimated values of diatropicity for **120** as 40 and 44% respectively.

Using equation 5 (page 30), the chemical shift value of the external proton H_D

of **120** can be calculated. Rearranging equation 5, we get;

$$\delta_D = [\delta_{RCM} + 0.029 / -2.60] - 6.13$$

$$\delta_{RCM} = 0.97 - \delta(CH_3)$$

$$= 0.97 - 1.22 = 2.19$$

$$\therefore \delta_D = 6.98 \text{ ppm}$$

This calculated value of δ_D is in excellent agreement with the experimentally observed value of 6.84 ppm for **120**. Hence, we can use this chemical shift value to get another estimate of the diatropicity of the thia[13]annulene **120**. The ratio of the change in chemical shift of H_D with respect to the atropic model to that of DMDHP, **12**, should then reflect the extent of diatropicity in thia[13]annulene **120** with respect to the diatropicity of DMDHP, **12**. Thus we can calculate the extent of diatropicity in **120**, using H_D values as:

$$\text{Diatropicity of } \mathbf{120} = (\delta H_D \mathbf{120} - \delta H_D \text{ Model}) / (\delta H_D \mathbf{12} - \delta H_D \text{ Model})$$

$$= (6.84 - 6.13) / (8.14 - 6.13)$$

$$= 0.35$$

This indicates that the diatropicity of the thia[13]annulene **120** is about 35% of the diatropicity of DMDHP, **12**.

The discrepancy in the measure of diatropicity using internal and external proton chemical shifts (~10%) may be due to a number of factors affecting the magnitude of chemical shifts of internal and external protons, such as the ring size, excess π-electron density, etc. Nevertheless, it is fair to say that the thia[13]annulene **120** is undoubtedly diatropic and has a diatropicity of about 35-42% of that of DMDHP, **12**.

2.5.4.6 Comparison of the diatropicity of 120 with other hetero-DMDHPs

The diatropicity of the thia[13]annulene **120** could be compared with that of other hetero-DMDHPs. The only other [14]-π hetero-DMDHP known is the azaDMDHP **33**. We will include the recently synthesised oxa[17]annulene **63** also in the discussion as this is the only diatropic bridged oxaannulene known. Diatropicity of each annulene was estimated using the internal methyl proton chemical shifts {$D(CH_3)$} and the chemical shift of the external proton H_D {$D(H_D)$}, as shown above for **120**. The values obtained are listed in Table 13.

Table 13 Comparison of diatropicities of **12**, **120**, **63**, and **33**, from the chemical shifts of their external and internal protons.

Compound	$\delta(CH_3)$ppm	δH_Dppm	$D(CH_3)^1$	DH_D[1]
12	-4.25	8.14	100	100
120	-1.16, -1.32	6.84	42	35
63	+0.15,+0.13	6.35	16	11
33	-3.75, -3.80	~8.1[2]	91	98

[1] Diatropicity (D) expressed as % diatropicity of DMDHP, **12**.

[2] Approximate value from ref. 47.

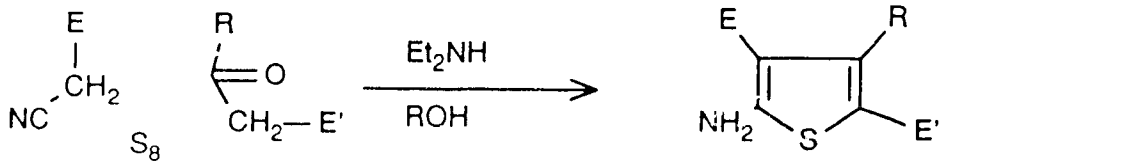
The diatropicity values obtained from $\delta(CH_3)$ are very close to those obtained from the corresponding δH_D values (5-7% difference). From Table 13, the annluenes compared could be listed diatropic in the order **12>33>120>63**. The azaDMDHP **33** is as strongly diatropic as the parent DMDHP, **12**. The thia[13]annluene **120** is about 35-42% diatropic with respect to **12**. While the oxa[17]annluene being the weakest diatropic system in the series is about 11-16% as diatropic.

This comparison though very limited in number, is the first of its kind, which using chemical shifts alone, reliably sets up an experimental diatropicity scale. Syntheses of other hetero-DMDHPs would be expected to result in more information on their diatropicities relative to that of DMDHP.

2.6 A short synthesis of 2,4-bis(bromomethyl)-3-methylthiophene, 110

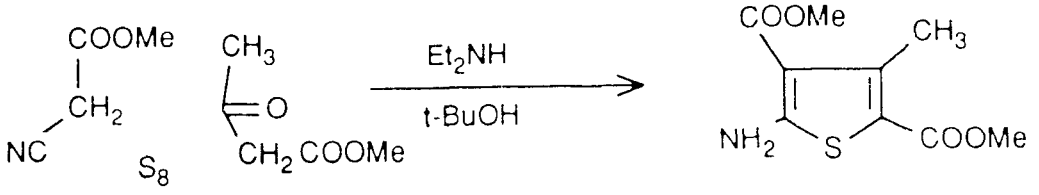
After achieving the synthesis of the thia[13]annulene **120**, we sought to synthesise the precursor dibromide **110**, by a shorter route. We looked for an alternate route which did not involve the use of 3-methylthiophene because of the failure of selective lithiation of **114**. Gewald synthesis of tetra substituted thiophenes[144] seemed to be a viable option. In this method, two different active methylene group containing compounds are condensed with elemental sulfur in the presence of a base to yield a substituted thiophene (Scheme 7).

Scheme 7



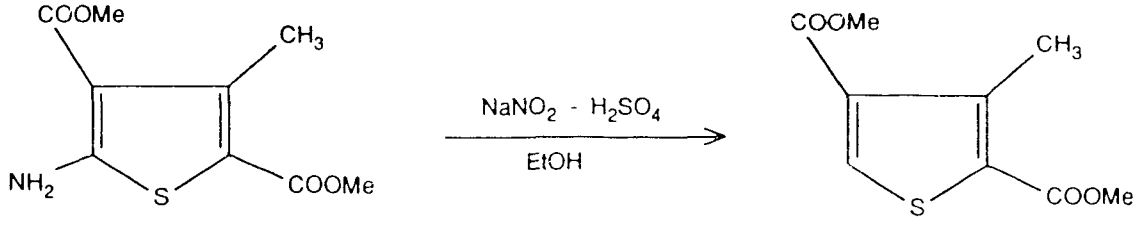
154 E, E' = electron withdrawing groups

Since this method would lead to a thiophene with the desired substitution pattern, we decided to make use of this strategy. The only initial concern was the removal of the amino group as aminothiophenes are generally very reactive and their chemistry is relatively unexplored.[145] Condensation of an equimolar amount of cyanomethyl acetate with methylaceto acetate and sulfur with diethylamine as the base, resulted in the formation of the product, **155**, in 40-60% yield.



155

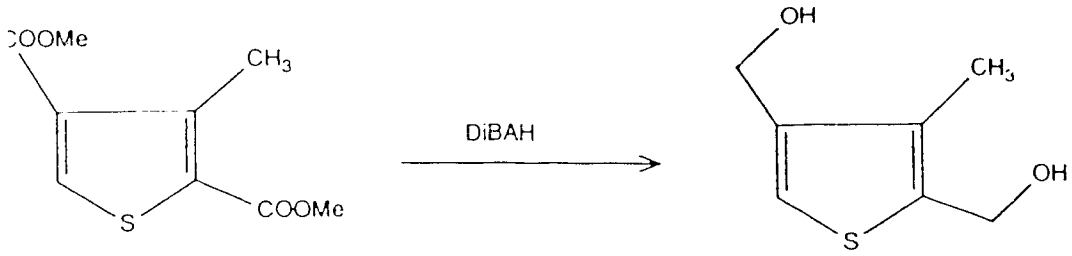
The yield was higher (>60%) when the reaction was performed on the 0.5 mole scale. *t*-BuOH was used as the solvent rather than the usual ethanol to avoid any trans-esterification reactions. The structure of the amino diester **155**, mp 126-127°C, was confirmed from its molecular ion in its mass spectrum (M^+ 229, base peak) and a satisfactory elemental analysis. The carbonyl carbons appeared at 166.4 and 166.3 ppm in the ^{13}Cnmr spectrum. Two NH stretches were observed, at 3400 and 3300 cm^{-1}, in the IR spectrum while a strong carbonyl stretch was present at 1718 cm^{-1}. Deamination of **155** by diazotization with $NaNO_2/H_2SO_4$ in ethanol, much to our delight, yielded the required diester **156**, as the only product, in 77% yield.



155 **156**

The success of this deamination, perhaps, is due to the presence of two powerful electron withdrawing ester groups in **155** which moderates the reactivity of the intermediate diazonium salts.[146] Colorless crystals of pure **156**, mp 102-104°C, were obtained by sublimation of the chromatographed product. The carbonyl carbons of **156** were present at 162.9 and 162.5 ppm in the ^{13}Cnmr spectrum and two carbonyl stretches were observed at 1731 and 1705 cm^{-1} in the IR spectrum. The diester **156** also gave the correct molecular ion (M$^+$ 214) in its mass spectrum and a satisfactory elemental analysis.

Reduction of this diester **156** with DiBAH gave the dialcohol **115** identical in all respects to a previously obtained sample.



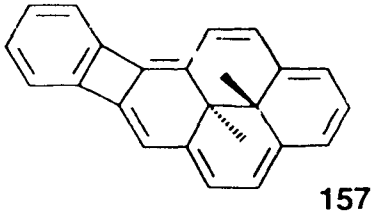
156 **115**

This dialcohol can be converted to the dibromide **110** in 80% yield, as mentioned earlier. The overall yield of **110** in this four step synthesis, is 22-24%, comparable to the 25% yield in the seven step sequence described in section 2.2. However, this new sequence has reduced the number of steps to just four and is cost and time effective.

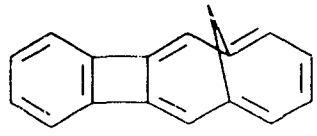
2.7 Attempted synthesis of the *quasi*-biphenylene 157.

2.7.1 Introduction

As part of our programme directed towards syntheses of [a] fused DMDHPs, we wished to synthesise the *quasi*-biphenylene-DMDHP, **157**. Biphenylene is a theoretically interesting molecule with surprising thermodynamic stability, in spite of its total π-electron count being twelve- a [4n] number.[147] It would be interesting to find out about the bond fixation and the effect of [4n] contribution through the DMDHP probe. Also, it will make an interesting comparison to the methanoannulene **158**, synthesised by Garratt and Vollhardt.[148]



157

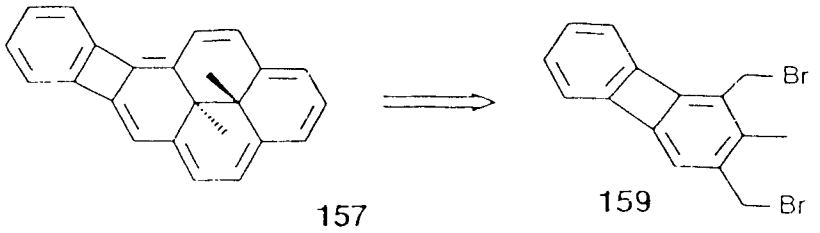


158

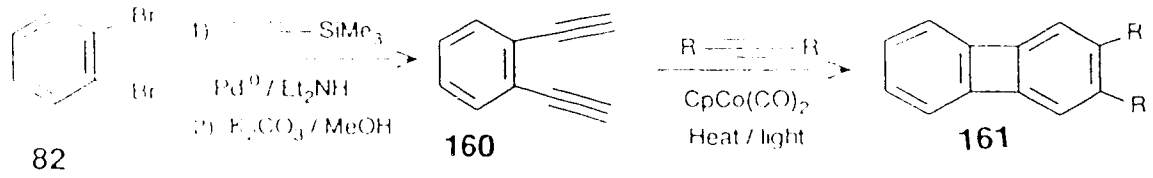
2.5.2 Retrosynthetic analysis of 157.

The thiacyclophane route to DMDHPs indicated the dibromide **159** as a precursor to **157**. Among the syntheses of substituted biphenylenes known to date, Vollhardt's cobalt mediated synthesis of biphenylenes is the most versatile.[149] Vollhardt's synthesis starts from an *o*-dibromoarene. Substitution of aryl bromides with acetylenes using palladium catalysts and subsequent cobalt mediated cyclisation of the resulting *o*-diyne with an alkyne, readily yields the substituted biphenylene (Scheme 8).

Scheme 8



157 159

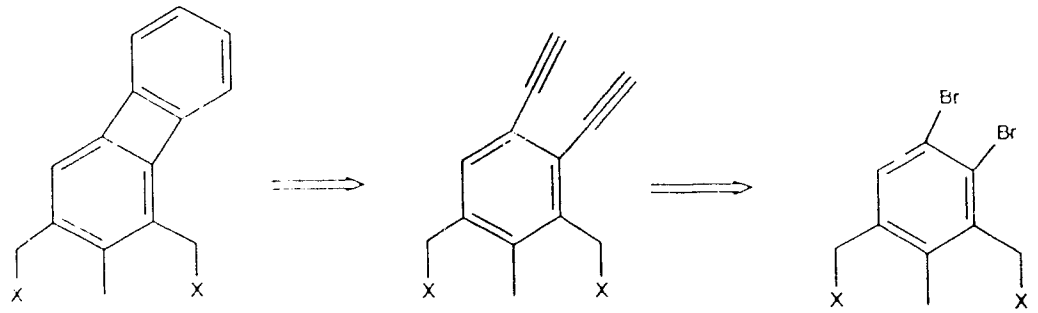


82 160 161

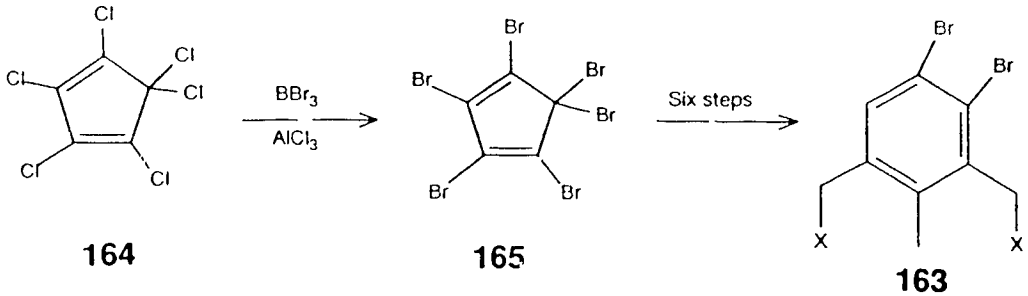
Based on this strategy, two approaches to construct the precursor biphenylene **159** could be envisaged (Scheme 9).

Scheme 9

Approach A

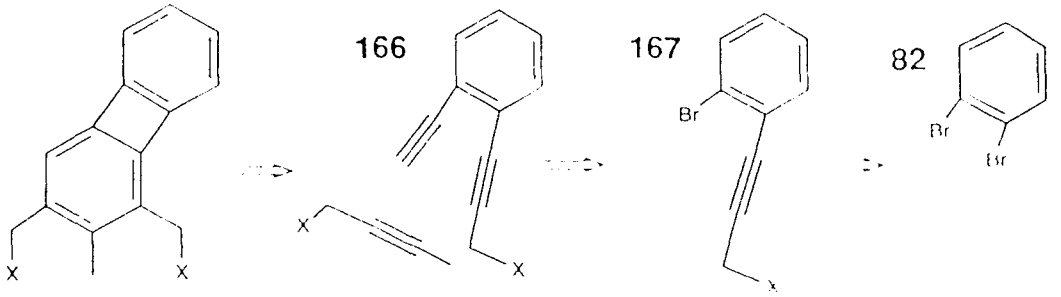


159 162 163



164 165 163

Approach B



157

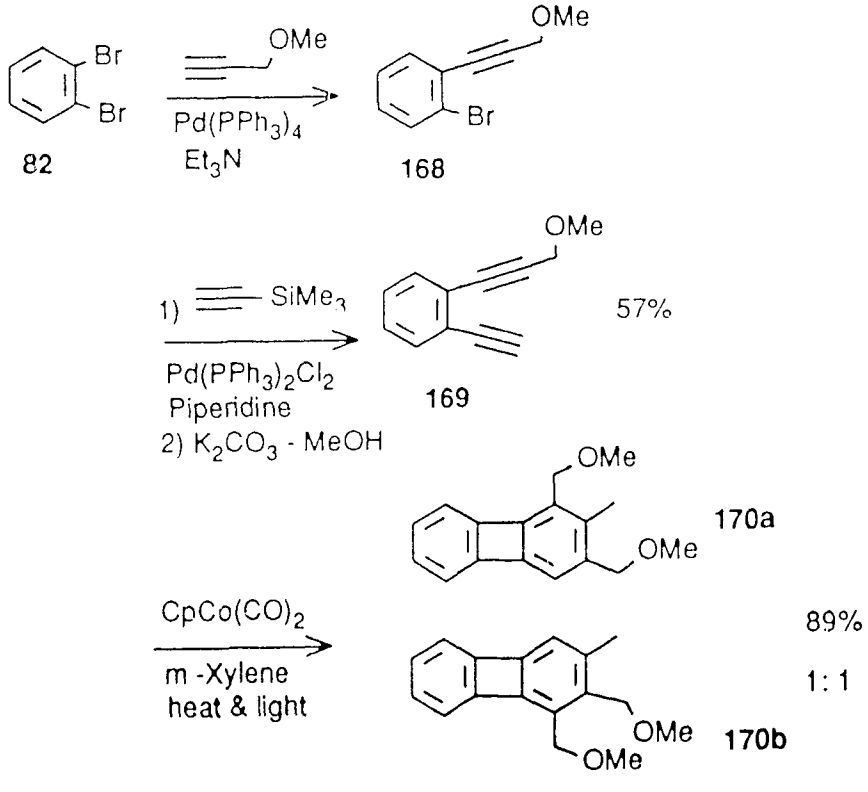
Approach A would require the *o*-dibromoarene **163**. The dichloro analog of **163** has been synthesised from hexachlorocyclopentadiene by Mitchell, Williams and others.[150] However, aryl chlorides do not react very well in Heck type ethynylation reactions. The *o*-dibromo compound **163**, would require a long synthesis from the expensive hexabromocyclopentadiene which can be made from hexachlorocyclopentadiene and a large excess of BBr_3, by West's procedure.[151] Approach B, on the other hand, would lead to **159** from the relatively inexpensive and commercially available *o*-dibromobenzene and readily available alkynes, in only four steps. Hence, we decided to pursue the second approach.

2.7.3 Synthesis of 1,3-bis(methoxymethyl)-2-methylbiphenylene

The alkyne synthons required for the synthesis of **159** were easily prepared from propargyl alcohol, according to the procedures of Brandsma.[152] Reaction of *o*-dibromobenzene, **82**, with propargylmethylether under Heck type ethynylation conditions yielded the alkyne **168** in 71% yield. The colorless liquid **168**, bp 80-82°C/0.05mm, is stable indefinitely under argon at -15°C. Ethynylation of **168** with trimethylsilylacetylene proceeded readily as shown by the ^{1}Hnmr of the crude product. But the resultant product was inseparable from the unreacted starting material **168**. So, the crude product was treated with K_2CO_3 in MeOH to remove the trimethylsilyl group and the desilylated product was isolated pure by chromatography in 57% yield. The diyne **169**, bp 100°C/0.4mm, was identified by its molecular ion (M^+ 170) in its mass spectrum. In its ^{1}Hnmr spectrum, the aryl protons appeared as a multiplet at 7.45-7.23 ppm, the methylene protons as a singlet at 4.36 ppm, the methoxymethyl protons as a singlet at 3.46 ppm and the lone alkyne proton as a singlet at 3.29 ppm. A chemical analysis of a sample of the diyne **169**, although it gave a good analysis for hydrogen, would not give a satisfactory analysis for carbon. This may be because of the lack of availability to do extended combustion on the analytical sample. The diyne **169**, was quite unstable and polymerised within two days. Hence it was used immediately in the next step. A mixture of this diyne, a large excess of 1-methoxy-2-butyne and a catalytic amount of $CpCo(CO)_2$ in degassed xylene, when subjected to

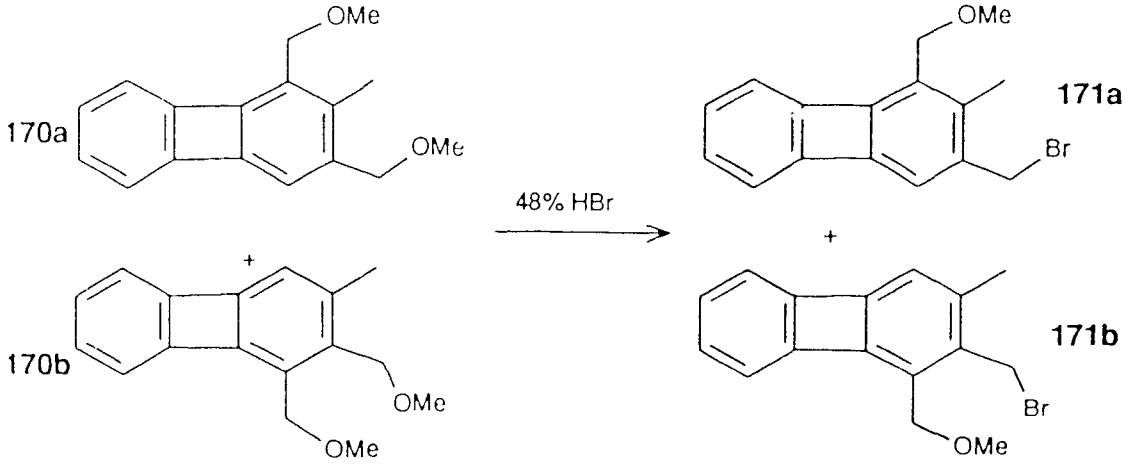
Vollhardt cyclisation conditions, readily yielded the expected bisether **170a** along with its isomer **170b** in combined yield of 89%. The two isomers **170a** and **170b** were present in a 1:1 ratio, as discerned from the ^{1}Hnmr spectrum. The desired isomer **170a** could not be separated from **170b** by chromatography or by distillation. The ^{1}Hnmr of the mixture showed a multiplet at 6.85-6.75 ppm for the protons H5-H8, a singlet each for H4 of **170a** and **170b** at 6.60 and 6.45 ppm, three singlets for the methylene protons at 4.45, 4.35 and 4.28 ppm, two singlets at 3.40 and 3.35 ppm for the methoxy protons and two singlets for the methyl protons at 2.20 and 2.05 ppm. The compounds also gave the correct molecular ion (M^+ 254) in their mass spectrum and a satisfactory exact mass measurement.

Scheme 10



2.7.4 Attempted synthesis of the bis-bromides 159

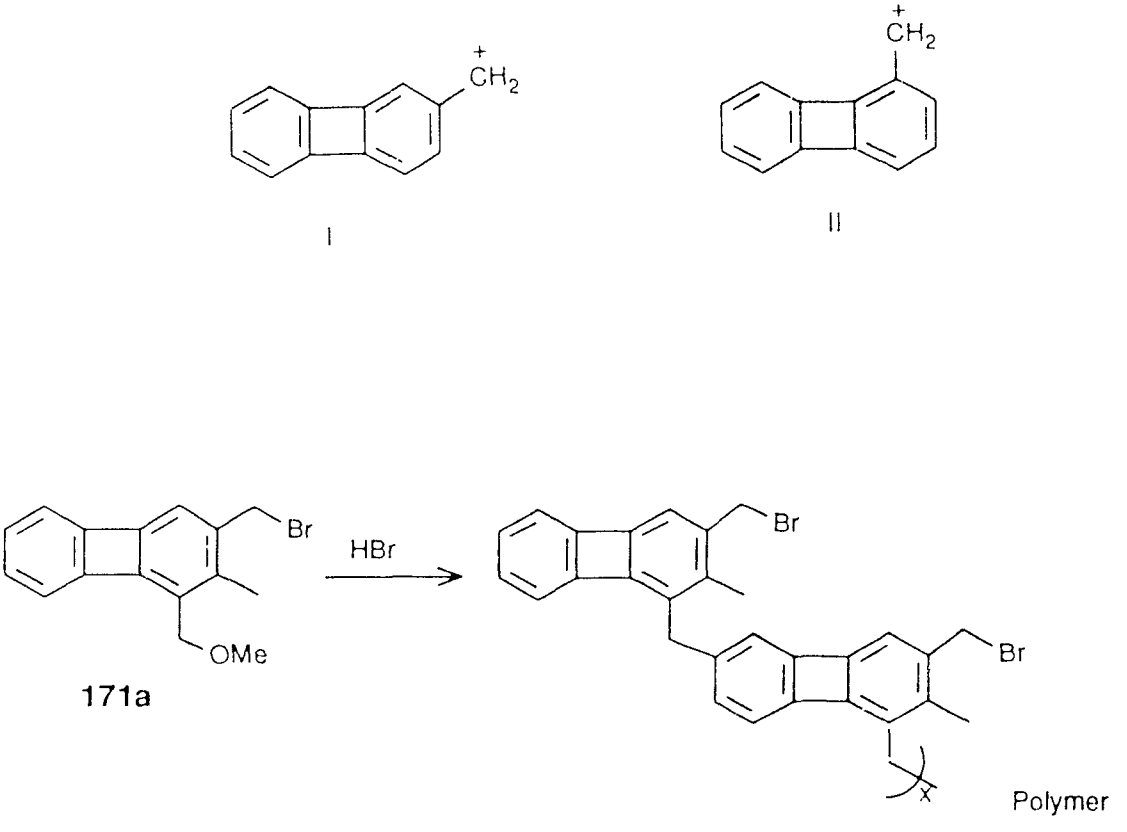
The methoxyethers **170a** and **170b** obtained as shown above were then subjected to different reaction conditions and reagents in order to obtain the corresponding bisbromomethyl compounds. Reaction of a mixture of **170a** and **170b** with 48% HBr at room temperature resulted in the mixture of the mono bromides **171a** and **171b** in 60% yield. The gross structures of the monobromomethyl compounds were confirmed from the correct molecular ions (M^+ 304, 302)- indicating the presence of only one bromine, and a satisfactory chemical analysis.



Upon longer reaction time with HBr, compounds **170a** and **170b** decomposed into polymeric materials and no bisbromomethyl compounds could be detected. Attempts made with the milder reagent, BBr_3, at -70°C also did not yield any of the expected products. This failure may be due to the difference in the stabilities of the cations of type **I** and **II**. AM-1 calculations[152]

indicate that **I** is more stable than **II** by about 4 kcal/mol. This would explain the ready formation of the monobromides **171a** and **171b**. During the longer reaction time needed to cleave the methoxymethyl group at the 2 position of the biphenylene ring, presumably the F-C alkylation by biphenylene is a competing reaction, leading to polymer formation (Scheme 11).

Scheme 11



2.8 Thiophene-1,1-dioxides in syntheses

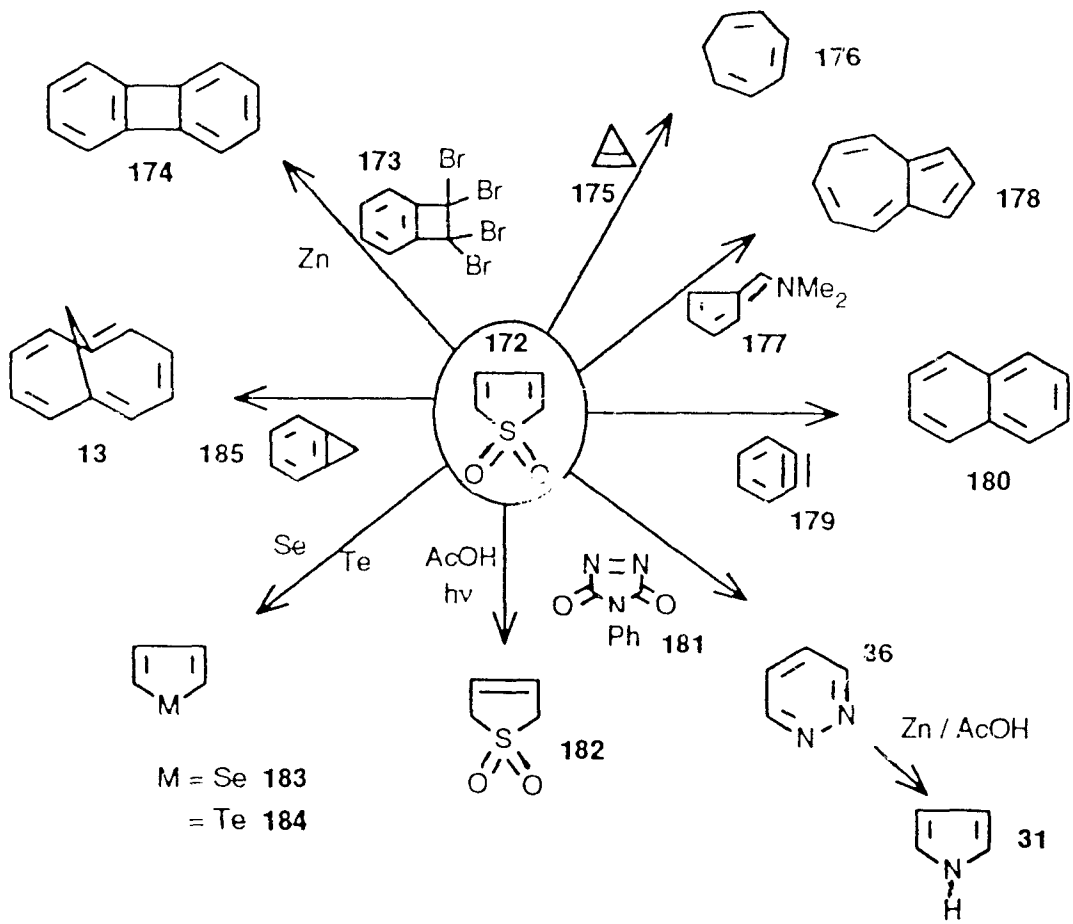
The reason for our alternate, shorter synthesis of the dibromide **110**, is because it is a direct precursor to the thiophenedioxide, **106**. The need for a common precursor diene to construct various DMDHP precursor was further stressed by the failure to achieve the synthesis of the bisbromomethyl-biphenylene **159**. We outline some of the known transformations of thiophene-1,1-dioxides below, for future reference.

Thiophene dioxides undergo cycloaddition reactions, leading to a variety of cyclic compounds. Some of these reactions might lead to construction of new DMDHP precursors in the future. The [4+2] D-A type reaction of thiophene- dioxides with cyclopropene, followed by extrusion of SO_2, leads to cycloheptatrienes in near quantitative yields.[154] Reaction with 6,6-dimethyl-aminofulvene results in the formation of azulene.[155] Dienophiles such as benzyne and DMAD react with thiophenedioxides to yield useful products.[156] Dibromobenzocyclobutadiene upon reaction with thiophenedioxides leads to biphenylenes.[157] Recently, Neidlein and coworkers have shown that benzocyclopropene reacts with thiophenedioxides resulting in the direct formation of methano[10]annulenes.[158] Complexes of thiophenedioxides could be made with $Fe(CO)_5$[159] and reduced photochemically to dihydro-thiophenedioxides[160] which should serve as useful dienes.[161] Heterocycles can also be derived from thiophenedioxides. Reaction with the dienophile **181**, leads to 1,2-diazines.[162] 1,2-Diazines can in turn be transformed into pyrroles

by Zn/HOAc.[163] Finally, through one of the most unusual transformations, thiophenedioxides can be converted to selenophenes or tellurophenes by simply heating them with selenium or tellurium powder respectively.[164]

These transformations are shown in Scheme 12 and, for related reactions, more details are given in Chapter IV.

Scheme 12



2.9 Summary

We started the synthesis of the dibromide **110**, as an approach to various [a]fused DMDHPs. We accomplished the synthesis of **110**, initially from commercial 3-methylthiophene in seven steps and later by Gewald synthesis in four steps. This compound is a direct precursor to the thia[13]annulene, **120**. To detect and estimate the diatropicity of this homologue of thiophene, we synthesised **120**, in four steps from the dibromide **110**. The thia[13]annulene **120**, was shown to be diatropic and its diatropicity was estimated to be 35-42% of the diatropicity of DMDHP.

Synthesis of the quasi-biphenylene-DMDHP **157** was attempted through the dibromide **159**. The biphenylene bisether **170** was constructed from readily available materials, using Heck type ethynylation and Vollhardt's cyclisation as key reactions, in four steps. Unfortunately, due to the difference in the reactivity of the methoxymethyl groups, the required dibromide **159** could not be made. This further emphasises the use of a common diene synthon such as **105** in the construction of various rings.

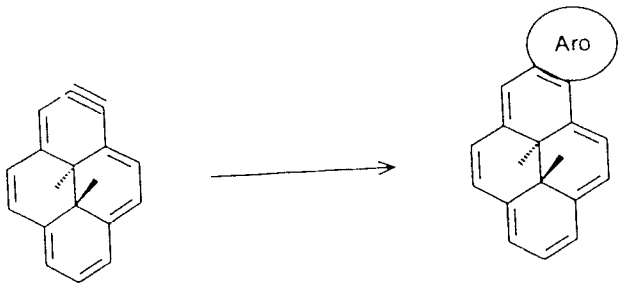
CHAPTER THREE

SYNTHESES USING REACTIVE INTERMEDIATES

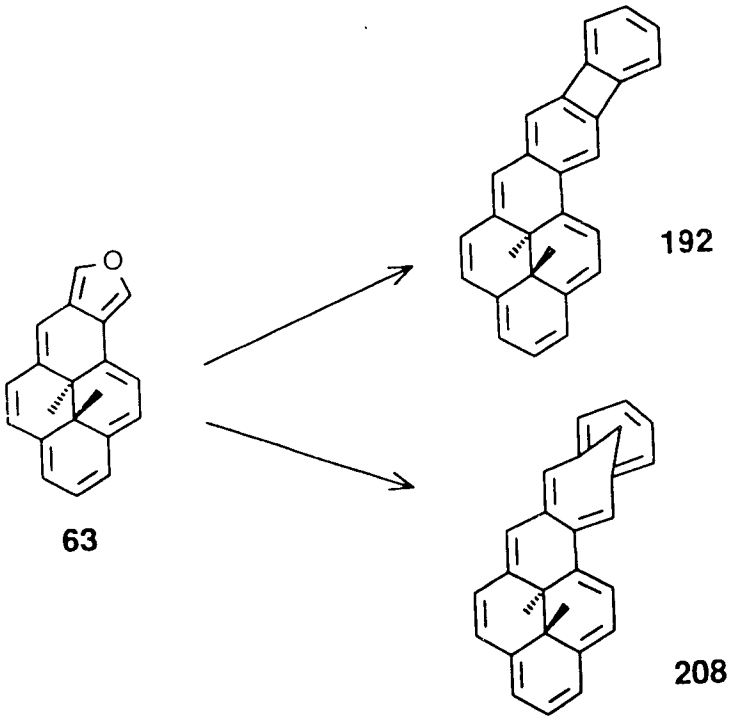
3.1 Introduction

In this chapter we shall describe our results on the syntheses of several [a] fused DMDHPs using the intermediates, oxa[17]annulene **63** and dihydropyryne **62**. As we showed in the general introduction, the oxa[17]annulene and the dihydropyryne had been used by Zhou to synthesise several benzo[a]DMDHPs.[98] Several unexplored possibilities for these two intermediates exist. Hence, we pursued some of the avenues for the syntheses of a few interesting fused DMDHPs. We chose the biphenylene fused DMDHP **192** and the methano[10]annulene fused DMDHP **208** as targets through the oxa[17]annulene intermediate. Both biphenylene and methano[10]annulene are extremely interesting molecules from a theoretical point of view, the former being a 12 π system and the latter as a Hückel [10] π-annulene. Use of DMDHP as a probe would unravel the diatropicities of these molecules which could be compared to the theoretical estimates. From a synthetic point of view, these two systems should be accessible via cycloaddition reactions by analogy with the reactions of isobenzofuran. The oxa[17]annulene **63** can be construed as a homologue of isobenzofuran. The aryne **62** could be put to use in [4+2] D-A type reactions for the construction of heterocycles and in the syntheses of other rings using cycloaddition reactions (Scheme 13).

Scheme 13



62 61



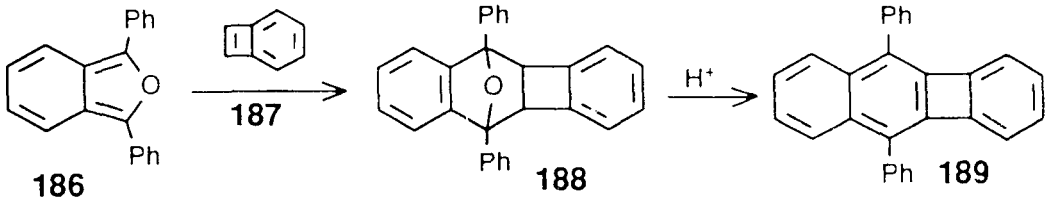
63 192 208

3.2 Syntheses using oxa[17]annulene

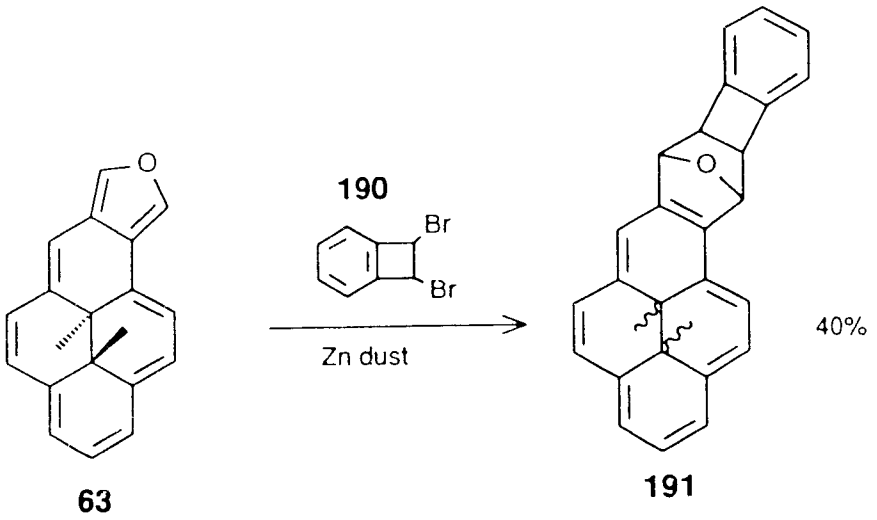
3.2.1 Synthesis of the biphenylene fused DMDHP, 192

Cava and coworkers have demonstrated the utility of isobenzofuran derivatives in the syntheses of several novel aromatics.[165,166] Isobenzofuran **186** reacts with benzocyclobutadiene, generated *in situ*, to give the adduct **188**, which upon dehydration gave the benzobiphenylene, **189** (Scheme 14).[165]

Scheme 14



This sequence could be expected to provide the biphenylene DMDHP **192** when the oxa[17]annulene **63** is used instead of isobensofuran. The required oxa[17]annulene **63** was synthesised from 2,6-dichloroannulene, in a linear sequence consisting of 13 steps, according to known procedures.[98] Reaction of **63** with a large excess of 1,2-dibromobenzocyclobutene and Zn dust at 40°C, gave the adduct **191** in 40% yield.



3.2.1.1 Structure of the adduct 191

The gross structure of the compound **191** was identified from its molecular ion (M+1 373) in its mass spectrum and a satisfactory elemental anayıisis. Two isomers due to different orientations of the internal methyl groups with respect to the orientation of oxygen were present, according to the ^{1}Hnmr spectrum with the methyl protons appearing at -4.06,-4.11 and -4.08, -4.13 ppm as singlets. From the integration of the methyl signals, the ratio of the two isomers were found to be 1:2. The stereochemistry of the bridge position where the cycloaddition has taken place, was determined from the ^{1}Hnmr spectrum, as follows.

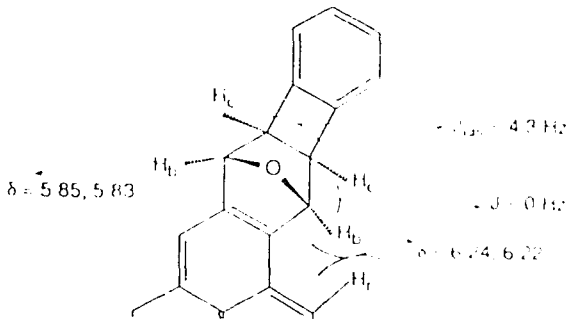


Figure 8a

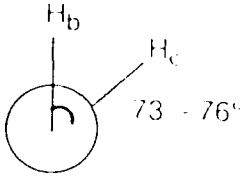


Figure 8b

First, the bridge protons H_b and $H_{b'}$ appear as singlets at 6.42/6.22 and 5.85/5.83 ppm, respectively. A pair of singlets for H_b and $H_{b'}$ are observed because two isomers with different orientations of the methyl groups were present. The H_b proton, experiencing a steric compression from the DMDHP proton H_r, resonates at a lower field compared to the $H_{b'}$ proton. There is no coupling between protons H_b and H_c or $H_{b'}$ and $H_{c'}$, suggesting a staggered configuration these protons (Figure 8a and 8b). To verify this, models of *exo*-**191** and *endo*-**191**, were generated using the Alchemy drawing program. The structures, along with some selected data of **191** are shown in Figure 9 and 10. The H_b-C-C-H_c and the $H_{b'}$-C-C-$H_{c'}$ dihedral angles for the *exo* isomer are 73° and 76° respectively, while the corresponding values of the same protons of the *endo* isomer being 32°. The absence of coupling between protons H_b and H_c suggest an *exo* orientation for the compound **191** as the value of dihedral angles from 73-76° is more consistent with the observed absence of coupling between these two protons. The *endo* isomer with dihedral angle values at 32° would have resulted in a H_b-H_c coupling of ~7 Hz.[167]

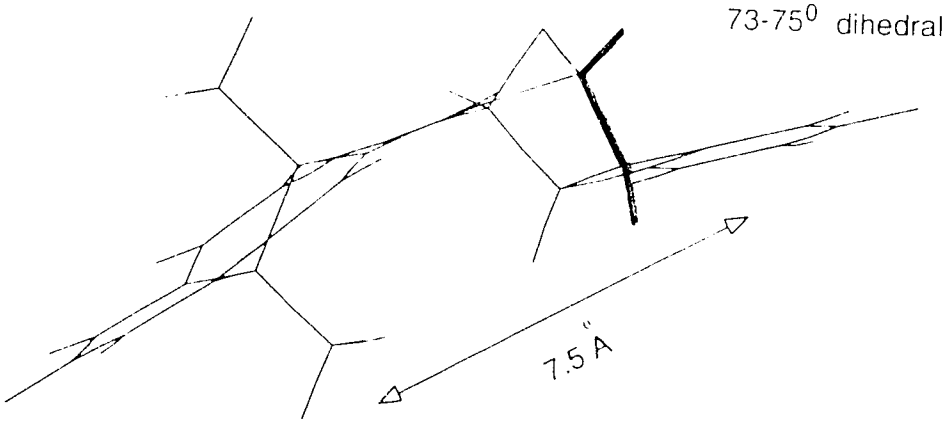


Figure 9 Structure of *exo*-**191**

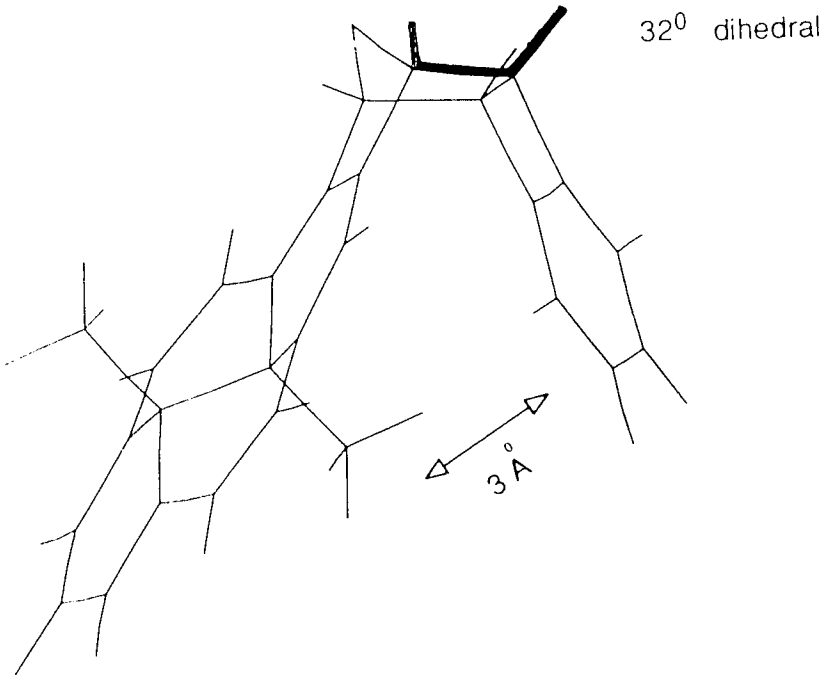
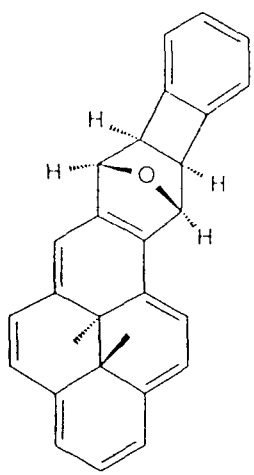
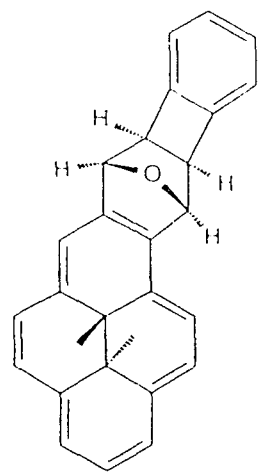


Figure 10 Structure of *endo*-**191**

Secondly, the models clearly show that the average distance of the internal methyl protons (situated almost on top of the benzene plane) from the benzene moiety in the *endo* i mer is ~3Å. Using Haigh-Mallion tables[168] an additional shielding of the internal methyl protons due to the orientation of the benzene ring can be calculated to be ~0.8 ppm. Since no methyl proton signals above -4.13 ppm were observed, the *endo* structure can be ruled out. On the other hand, in the *exo*-configuration, the methyl proton-benzene distance is about ~7.5Å, a value sufficiently large to make the shielding-deshielding effects of the benzene ring negligible. It should also be noted that the benzene ring in *exo*-**191** is arranged almost parallel to the DMDHP plane. Thirdly, the ^{13}C nmr spectrum of **191** showed only one signal each for C_b, $C_{b'}$ and C_c, $C_{c'}$ at 80.45, 78.18 and 52.62, 51.10 ppm - indicating the presence of only one isomer, namely the *exo*-**191**.



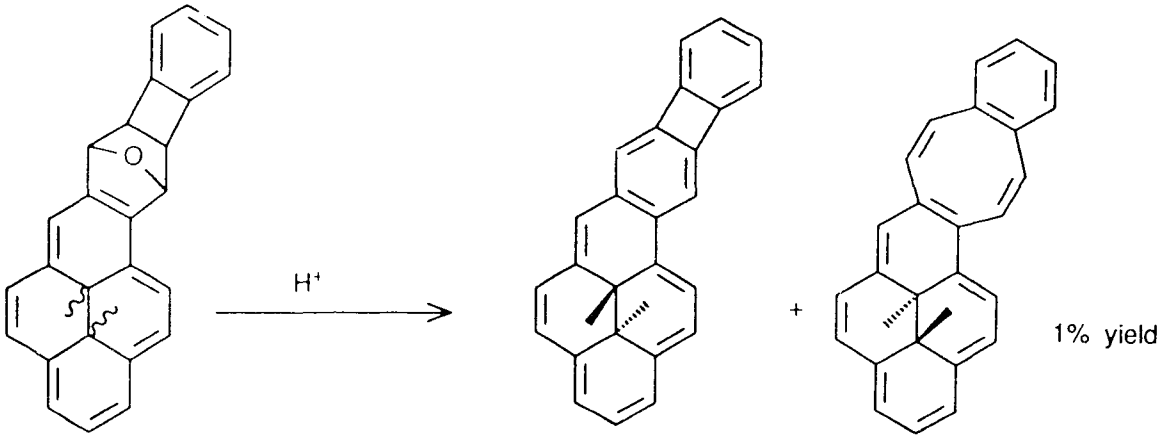
191a



191b

3.2.1.2 Attempted dehydration reactions on 191

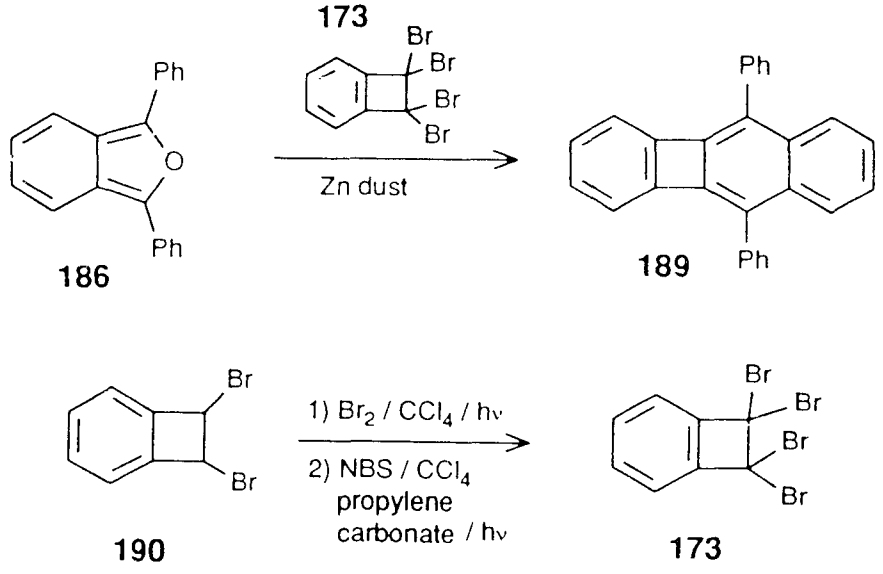
Having determined the stereochemistry of **191**, we proceeded to attempt the dehydration of the adduct with acids in order obtain the biphenylene **192**. DMDHP, is electron rich and is readily protonated.[169] So, only mild acids were tried first. But unfortunately, despite several attempts, the dehydration of **191** resulted in extensive decomposition and only a minuscule amount of non-polar products were obtained (see experimental for the various conditions tried).



191 **192** **193**

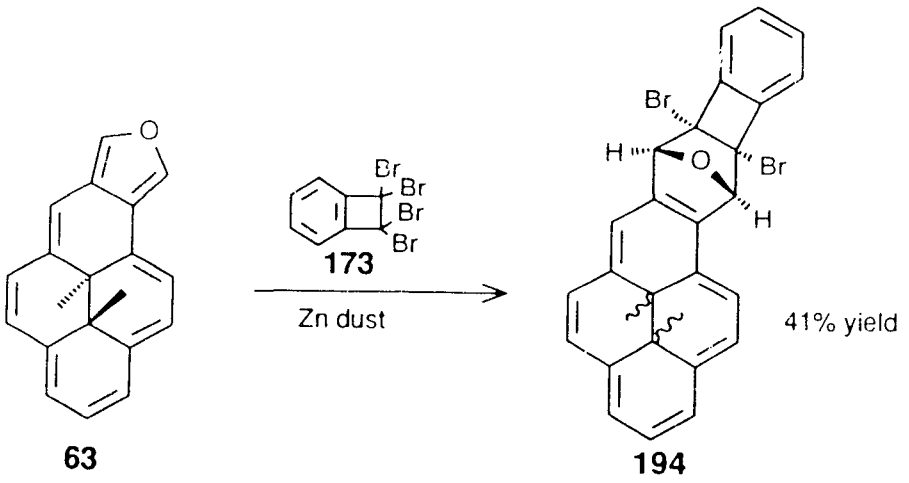
The products obtained in the above reaction, which could not be purified further, are probably a mixture of compounds **192** and **193**. A ^{1}Hnmr spectrum of the crude product showed singlets at -2.76, -2.77 and at -4.1 and -4.4 ppm. The signals at -2.76 and -2.77 ppm were later shown to be those of the methyl protons of the DMDHP **192**. The singlets at -4.1 and -4.4 ppm are tentatively assigned to the methyl protons of **193**.

The sensitivity of the DMDHP ring to acids, led us to investigate other possibilities for the construction of the biphenylene ring in **192**. Cava and coworkers have shown that the isobenzofuran **186** on reaction with the tetrabromide **173**, and Zn dust gives the benzobiphenylene **189**. Since this reaction does not require any acids, we decided to implement this strategy for our system.



3.2.1.3 Synthesis of *trans*-14b,14c-dimethyl-14b,14c-dihydrobenzo[1",2":3,4]cyclobuta[1,2-b]naphtho[2,1,8-*fgh*]anthracene, 192.

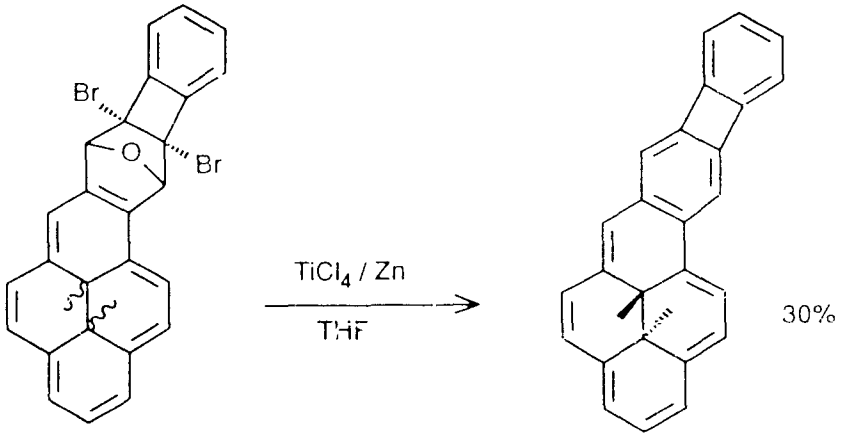
Action of Zn dust on a mixture of the oxa[17]annulene **63** and an excess of the tetrabromide **173** proceeded slowly to give the dibromoadduct **194** in 41% yield. Under the conditions employed, the biphenylene ring is not created directly in this sequence thus enabling us to isolate the intermediate **194**.



63 194

Here again, only the exo isomer was formed. By analogy with the dihydroadduct **191**, this dibromoadduct was assigned the exo configuration. In the ^{1}Hnmr spectrum, the benzylic bridge protons of **194** appear at 6.3 and 5.8 ppm as singlets. This compound was identified by its molecular ion (M^+ 534) and a satisfactory exact mass measurement. The tetrabromide **173**, used in the above reaction, was prepared from the corresponding dibromide **190** using a modified procedure of Cava.

The dibromoadduct **194** on attempts using activated Zn dust under various conditions, did not yield any of the expected biphenylene **192**. Hence we tried a low valent titanium system to accomplish this conversion. Reduction of the dibromide **194** using a green titanium species generated from $TiCl_4$-Zn, yielded the biphenylene **192** in 30% yield. It should be noted that other titanium species generated from reagents such as $TiCl_3$-LAH, $TiCl_4$-Zn (reflux), or $TiCl_4$-nBuLi-Et_3N, resulted only in extensive decomposition of the starting material.



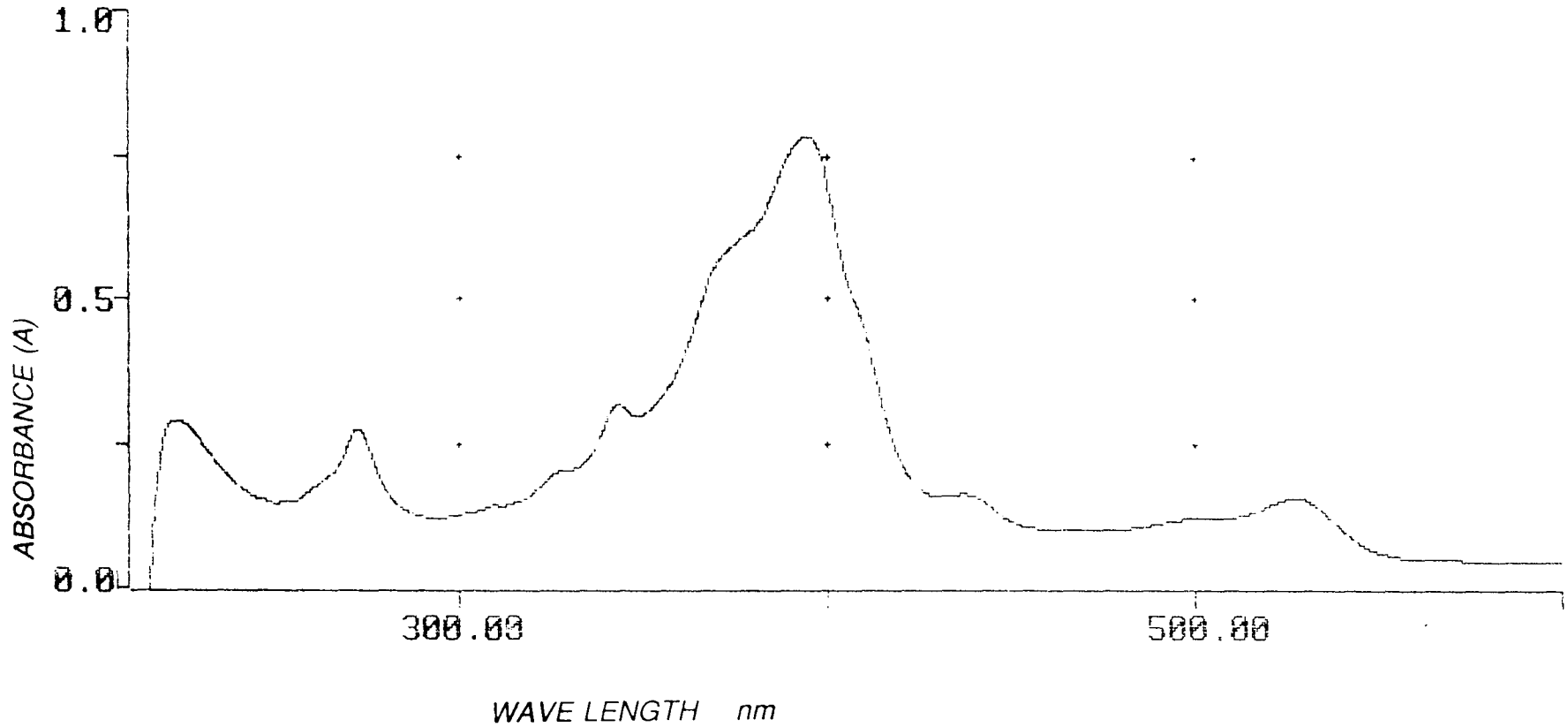
194 **192**

3.2.1.4 Properties of the biphenyleno DMDHP 192.

The biphenylene **192** was obtained as dark-red (almost black) needles, mp 190°C, from cyclohexane. Its gross structure was confirmed from its molecular ion (M^+ 356) in its mass spectrum and a satisfactory analysis. Compound **192** is very stable and readily soluble in all common organic solvents. The mass spectrum cleavage pattern was characteristic of most DMDHP's, with a strong molecular ion at m/e 356 and two peaks at m/e 341 and 326, showing the successive loss of the internal methyl groups.

The deep-red colored compound **192**, in its UV-Vis spectrum, had three major bands with the strongest absorption at 390 nm (log ε_{max} 5.4). This is a typical region for biphenylene and its derivatives. The DMDHP ring in **192**, causes absorption at longer wavelengths tailing up to 650 nm. A U.V-Vis spectrum of **192** in cyclohexane is shown in Figure 11.

Figure 10 UV-Vis spectrum of **192** in cyclohexane

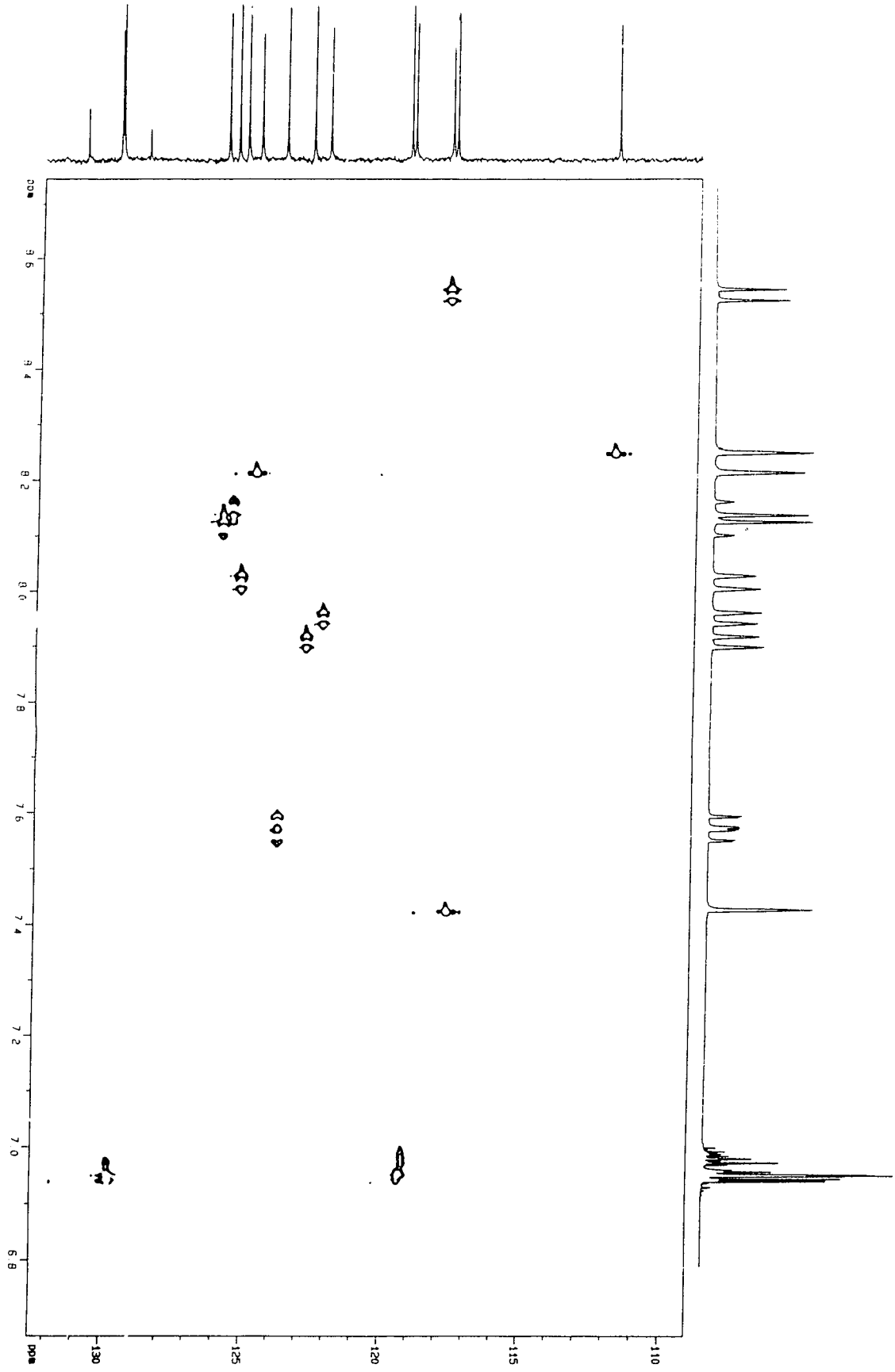


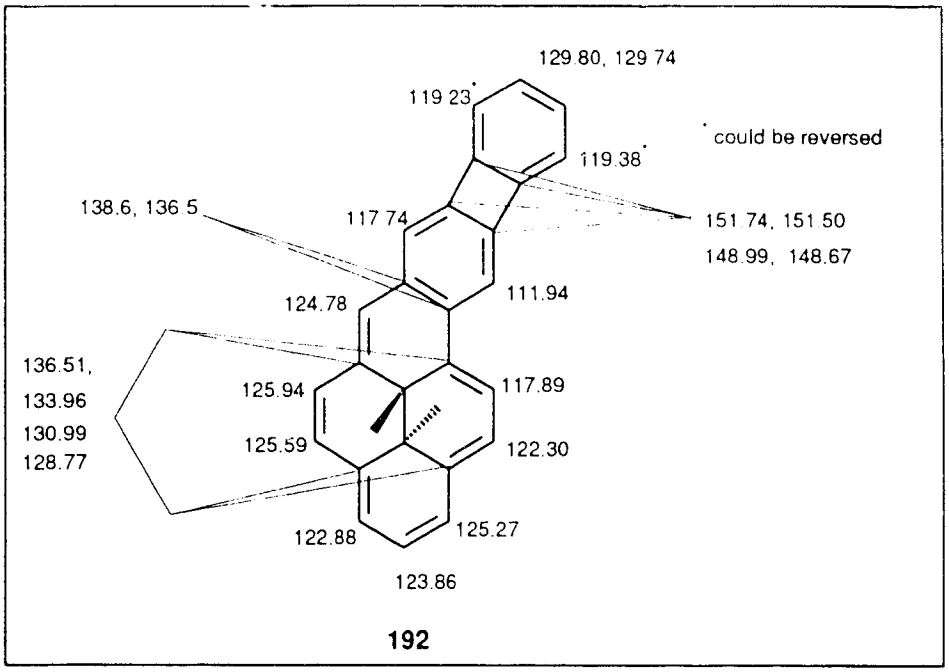
The nmr spectra of the biphenylene **192**, were more informative and with the help of 2D-nmr spectra, the ^{13}C and ^{1}H assignments were made with certainty. These are discussed next.

3.2.1.5 ^{13}Cnmr spectrum of 192

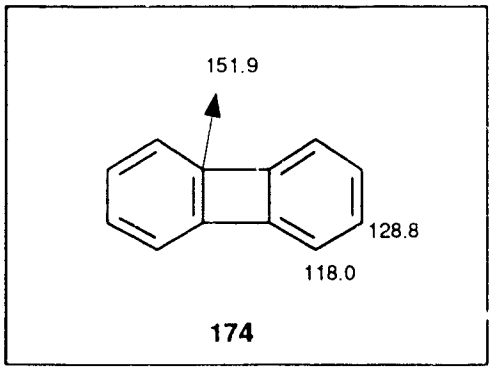
The ^{13}C assignments were made mainly based on a HetCorr (C-H) spectrum of **192** (Figure 12). The CH carbons could be assigned from the coupling between the carbon attached to a specific proton which were assigned using a COSY-H spectrum (see later). The quarternary carbons of the biphenylene ring were assigned the lowest field shifts in accordance with the assignments for the corresponding carbons in the parent biphenylene **174**.[170] These carbons experience a further downfield shift (~10 ppm) due to the paramagnetic ring current of the central four membered ring. The two quaternary carbons bridging DMDHP and biphenylene were assigned the values 138.6 and 136.5 ppm, by analogy of the corresponding carbon chemical shifts in benzo[b]biphenylene **195**.[171] The four remaining quarternary aromatic carbons were assigned the values of the remainder of the quarternary aromatic carbon peaks (136.51, 133.96, 130.99 and 128.77 ppm). The bridging aliphatic quarternary carbons have the chemical shift values of 33.96 and 33.65 ppm and the internal methyl carbons resonate at 16.16 and 16.25 ppm.

Figure 12 ^{13}C-^{1}H Hetcorr spectrum of **192** (aryl region)

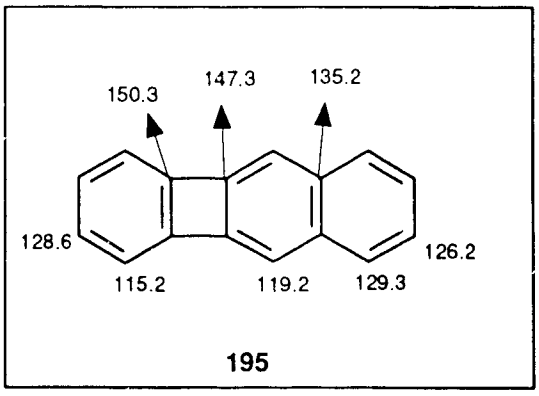



129.80, 129.74
119.23
could be reversed
119.38
138.6, 136.5
117.74
151.74, 151.50
148.99, 148.67
111.94
124.78
136.51,
133.96
130.99
128.77
125.94
117.89
125.59
122.30
122.88
125.27
123.86

192


151.9
128.8
118.0

174


150.3
147.3
135.2
128.6
126.2
115.2
119.2
129.3

195

A comparison of the chemical shifts of the bridge quarternary carbons, and the internal methyl carbons of **192** with those of the atropic model **47**, DMDHP, **12**, and of the benzo[a]DMDHP **49** could be made. The data are collected in Table 14.

Table 14 Comparison of ^{13}C chemical shifts of **47**, **12**, **192**, and **49**.

	internal bridge carbon			internal methyl carbon		
No	δ	Δδ	%Δδ of **12**	δ	Δδ	%Δδ of **12**
47	39.2			23.6		
12	30.0	-9.2	100	14.0	-9.6	100
192	33.6,33.9	-5.6,-5.3	61,58	16.1,16.2	-7.5,-7.4	78,77
49	35.5,36.0	-3.7,-3.2	40,35	17.0,17.7	-6.6,-5.9	69,61

The strength of the ring current magnitude present in the macroring is reflected by the chemical shifts of the internal carbons. The larger the ring current magnitude, the stronger the shielding and thus the lower the chemical shift value. From Table 14, it is evident that the ring current magnitude (Δδ) of the macroring in **192** is intermediate in value to those of **12** (strongest) and **49** (lowest).

3.2.1.6 ^{1}Hnmr spectrum of 192

In the ^{1}Hnmr spectrum of **192**, the internal methyl protons appear at -2.76 and -2.77 ppm as singlets. From the chemical shifts of the internal methyl protons, it is evident that a strong ring current is present in the macroring. The extent of diatropicity of the macroring and the diatropicity of the annelating biphenylene fragment were estimated using Mitchell's method. This is discussed, in detail, in the next section.

The aromatic region of the spectrum was interpreted using a regular ^{1}Hnmr spectrum (Figure 13) and a COSY-H (Figure 14) spectrum. The biphenylene protons, H-8, H-9, H-10 and H-11, appeared as a complex ABCD multiplet from 6.99 - 6.93 ppm with not enough observable lines and hence could not be analysed. The singlet at the highest field, at 7.42 ppm, is attributed to the biphenylene proton H7, by analogy with the corresponding protons in biphenylene, **174**, and the benzobiphenylene **195**. The lowest field singlet at 8.25 ppm is assigned to H-12 of the biphenylene ring. Due to phenanthrene type steric compression with H-13, proton H-12 resonates at a lower field than H-7. One branch of an AB multiplet at 8.53 ppm, which also showed a small coupling in the COSY-H spectrum with H-12, is assigned to the proton, H-13. The proton, H-14, shows a strong coupling with H-13 and resonates at 7.95 ppm. The remaining AB multiplet is assigned to H-4 and H-5 which resonate at 8.12 and 8.15 ppm respectively.

Figure 13 360 MHz spectrum (CD_2Cl_2) of **192** (aryl region)

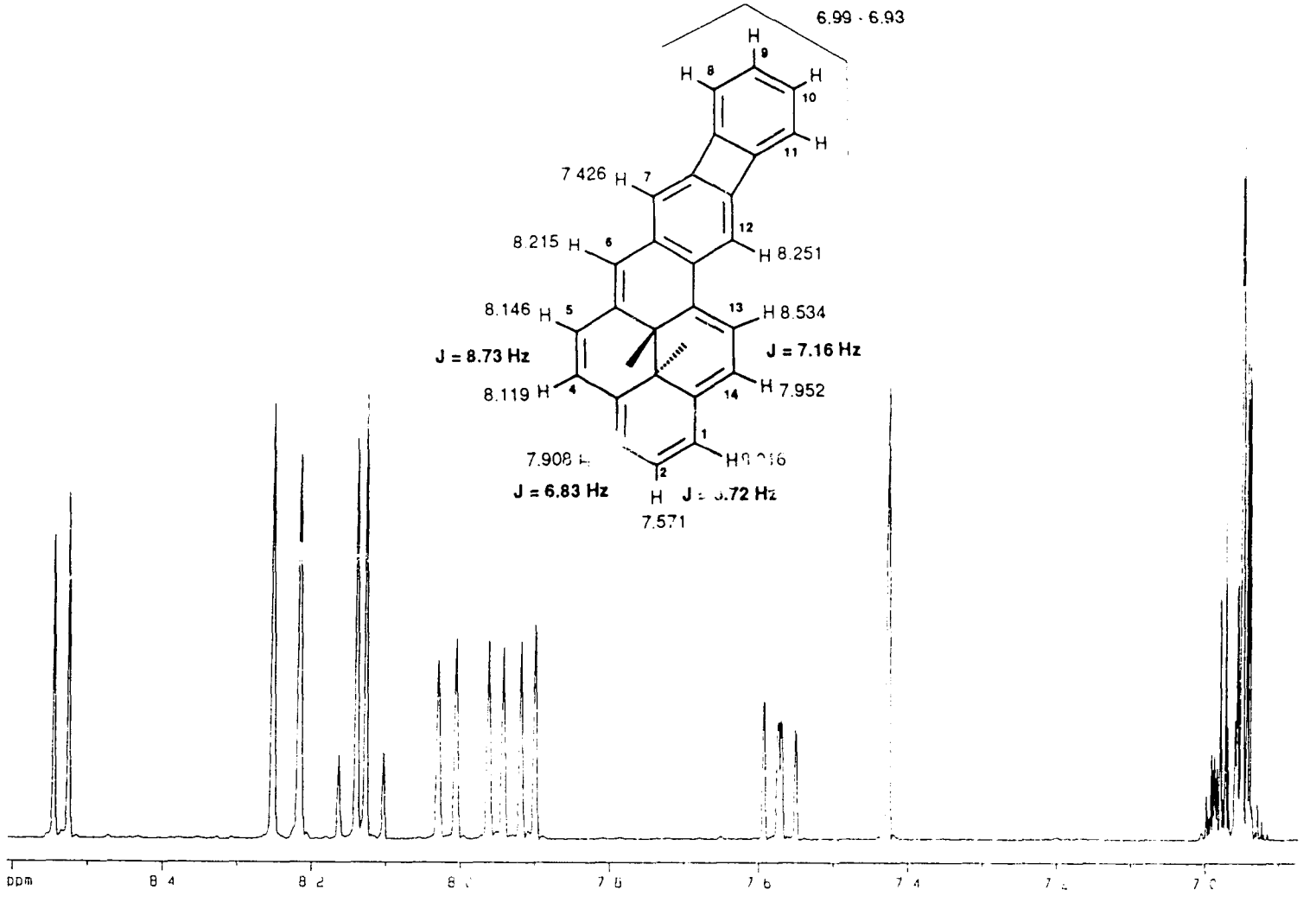
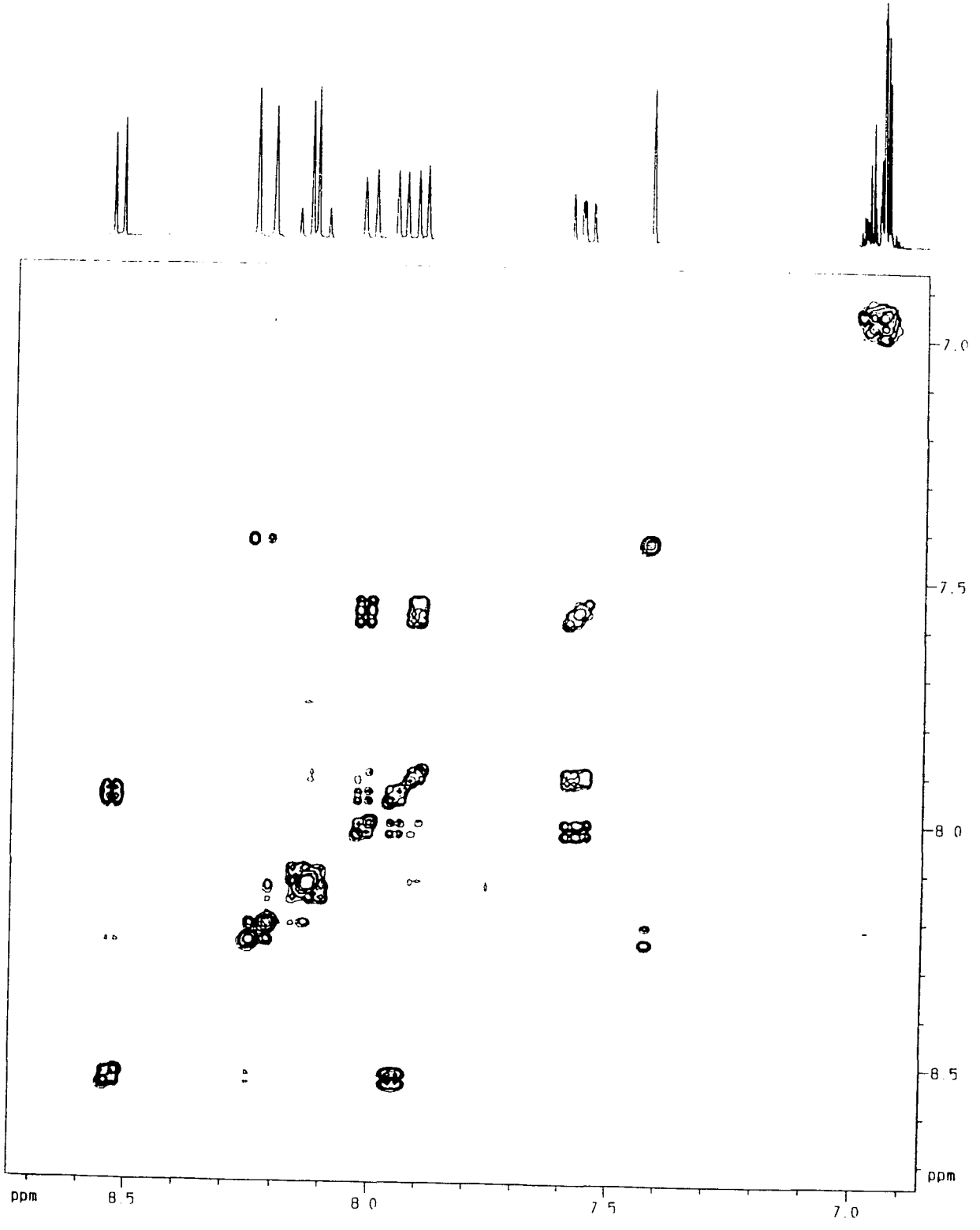


Figure 14 COSY-H spectrum of **192** (aryl region)



The protons H-1, H-2, and H-3 showed a typical ABC pattern in the spectrum. H-2 appeared as a doublet of a doublet centred at 7.57 ppm. Protons H-1 and H-3 resonate at 8.02 and 7.91 ppm respectively.

3.2.1.7 Coupling constant-bond order correlations in 192

In order to evaluate the bond alternation in the DMDHP ring, the coupling constants from the macroring protons were used to derive bond orders using Günther's empirical relationship and these values inturn can be compared with the π-SCF bond orders. The ratio of vicinal coupling constants and/or of the vicinal bond orders reflect the extent of bond alternation in a molecule (see page 76). The ratio of vicinal coupling constants in **192** are J_A/J_B = 0.78 and J_C/J_D = 0.79 and the corresponding ratios from the π-SCF bond orders being 0.83 and 0.79. These values besides indicating bond alternation in the macroring, also reflect the lack of alteration of the macroring geometry due to annelation. The ratios (or Q values) would have been very different if there was a significant alteration in the geometry which affects the value of the coupling constant. As we showed earlier, in chapter two, Günther's empirical relationship of coupling constants and π-SCF bond orders were derived from the coupling constants of acenes. So, we used the equations derived for annelated DMDHPs by Zhou (equations 8 and 9) which give a better correlation.

Table 15 Comparison of π-SCF bond orders and bond orders derived from ^3J's.

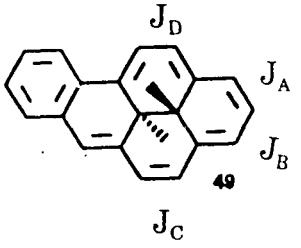
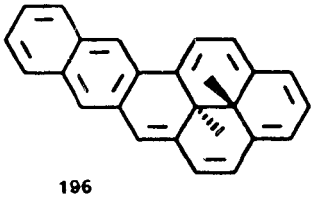
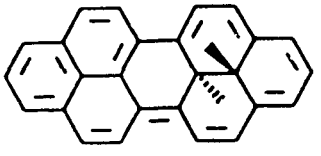
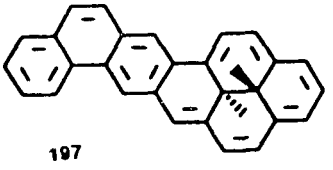
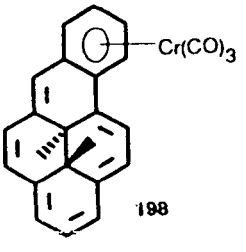
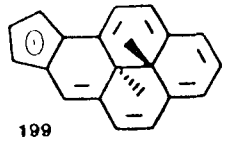
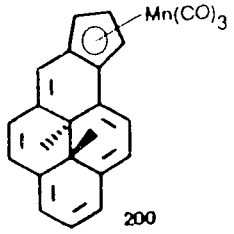
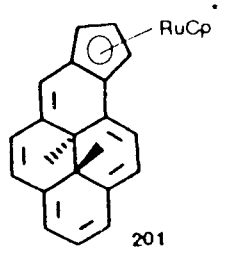
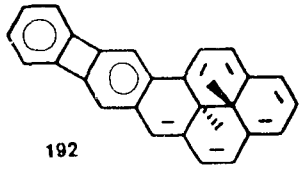
Compound	$J_{1,3}$ (Hz)*	ρ^1	ρ^2	ρ-SCF
 49	J_A 8.79	0.794	0.737	0.717
	J_B 6.44	0.550	0.557	0.573
	J_C 8.67	0.782	0.704	0.731
	J_D 6.20	0.525	0.546	0.552
 196	J_A 9.00	0.816	0.753	0.733
	J_B 6.23	0.528	0.541	0.554
	J_C 8.92	0.808	0.721	0.750
	J_D 6.11	0.515	0.540	0.529
	J_A 8.71	0.786	0.731	0.693
	J_B 7.24	0.633	0.618	0.599
	J_C 8.41	0.755	0.688	0.702
	J_D 6.94	0.602	0.593	0.583
 197	J_A 8.86	0.801	0.742	0.730
	J_B 6.00	0.504	0.523	0.558
	J_C 8.87	0.802	0.717	0.745
	J_D 6.16	0.521	0.543	0.535
 198	J_A 8.97	0.719	0.750	0.719
	J_B 6.30	0.546	0.546	0.546
	J_C 9.24	0.759	0.741	0.759
	J_D 6.53	0.553	0.567	0.553

Table 15 continued,

 199	J_A 7.87	0.698	0.666	0.706
	J_B 6.78	0.585	0.583	0.577
	J_C 8.33	0.746	0.683	0.710
	J_D 7.05	0.613	0.600	0.573
 200	J_A 8.85	0.825	0.741	----
	J_B 6.08	0.513	0.529	----
	J_C 9.09	0.800	0.731	----
	J_D 6.41	0.547	0.559	----
 201	J_A 8.74	0.789	0.733	----
	J_B 6.25	0.537	0.542	----
	J_C 8.76	0.791	0.710	----
	J_D 6.25	0.530	0.549	----
 192	J_A 8.64	0.778	0.725	0.705
	J_B 6.75	0.582	0.580	0.586
	J_C 8.65	0.779	0.703	0.717
	J_D 6.86	0.593	0.588	0.570

* corrected for steric interactions; ρ^1 obtained using equation 3; ρ^2 obtained using equations 7 and 8

Comparison of these values with those obtained using equation 3 and the values obtained from π-SCF output, for a series of [a]-annelated DMDHPs, could be made (Table 15). From Table 15, it can be seen that the bond orders derived using equation 7 and 8 compare very well to the values obtained from

π-SCF output. We will use these values to calculate chemical shift of the internal methyl protons of **192**. The bond orders were calculated using the equations 7 and 8 and the corrected coupling constants (0.3 Hz for J_D and 0.08Hz for J_A, J_B and J_C-phenanthrene and naphthalene type corrections respectively).

Using equation 4, the value of the internal methyl proton chemical shift of **192** was then calculated (Table 16). The value of δ obtained using π-SCF bond orders was -2.72 ppm which agrees well with the experimental values of δ at -2.76 and -2.77 ppm. Even better agreement was found by using the values obtained from bond orders derived from equations 7 and 8. The predicted value of δ here was -2.77 ppm, exactly that of the experimentally found. The calculated value of δ using bond orders obtained from equation 3, on the other hand, was -1.92 ppm which is 0.85 ppm off the experimental value. Thus, it is worth noting that the bond order-chemical shift correlations in annelated DMDHPs using coupling constants is better done using the values obtained from equations 7 and 8.

Table 16 Coupling constant, Bond order and Chemical shift data for compound **192**.

Bond	J_{expt}	J_{corr}	$\rho_J^{\P} \times 10^3$	$\rho_J^{\S} \times 10^3$	$\rho_{SCF} \times 10^3$	$\lvert \rho x10^3\text{-}642 \rvert$
A	8.72	8.64[i]	778	725	705	136,63,83
B	6.85	6.75[i]	582	580	586	60,56,62
C	8.73	8.65[i]	779	703	717	137,75,61
D	7.16	6.86[ii]	593	588	570	49,72,54
Δν			95.5	65	67	

δ (CH_3)	using $\rho_J^{\P}$	-1.92
δ (CH_3)	using $\rho_J^{\S}$	-2.77
δ (CH_3)	using ρ_{SCF}	-2.72
δ (CH_3)	experimental	-2.76, -2.77

[i] naphthalene type correction; [ii] phenanthrene type correction; [¶] from equation 3

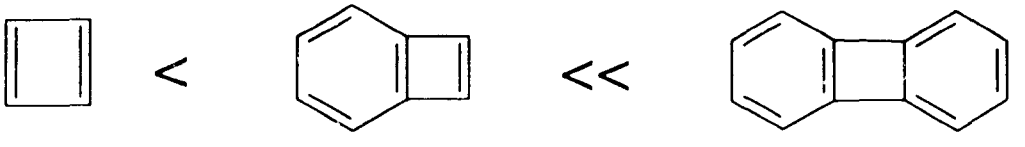
[§] from equations 7 and 8.

The calculated and experimental δ values of the internal methyl protons in **192** are in excellent agreement. Hence we can conclude that the bond alternation in **192** follows the bond order-chemical shift linear

relationship developed earlier for benzannelated DMDHPs. This also indicates that the bond fixing ability of biphenylene is similar to that of acenes. The bond fixing ability of an annulene has been related to its aromaticity and resonance energy. Thus we can now calculate the diatropicity of biphenylene with respect to that of benzene.

3.2.1.8 Estimation of diatropicity of biphenylene from 192

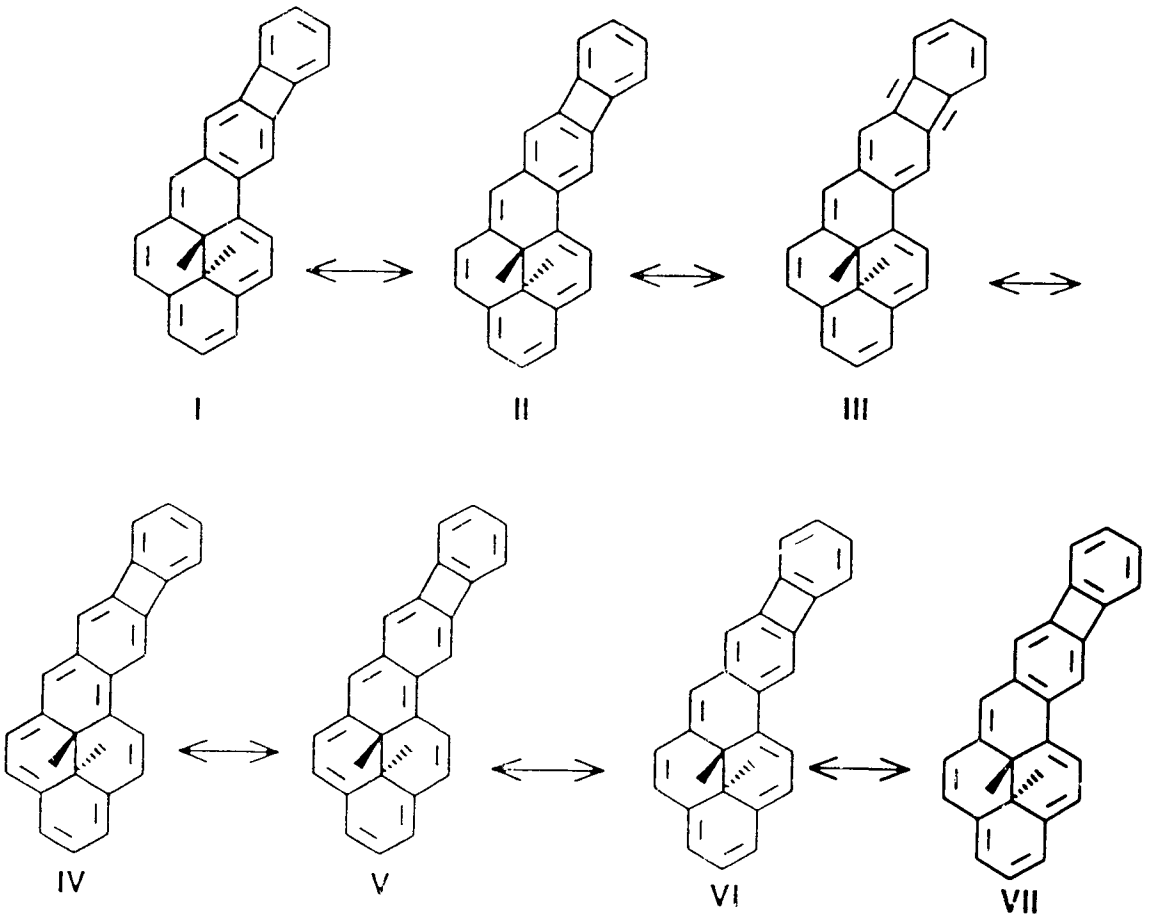
Biphenylene shows significant bond alternation, as discerned from X-ray crystal data.[172] This bond alternation could be rationalised from the bond fixation view point. Biphenylene can be considered as dibenzocyclobutadiene. Benzannelation leads to bond fixation and this is revealed by the bond alternation in the molecule. Due to bond fixation in biphenylene, the paramagnetic ring current of the central four membered ring is quenched and hence the overall stability of the molecule is increased. This is reflected in the order of stability of **7**, **202**, and **174**.[173]

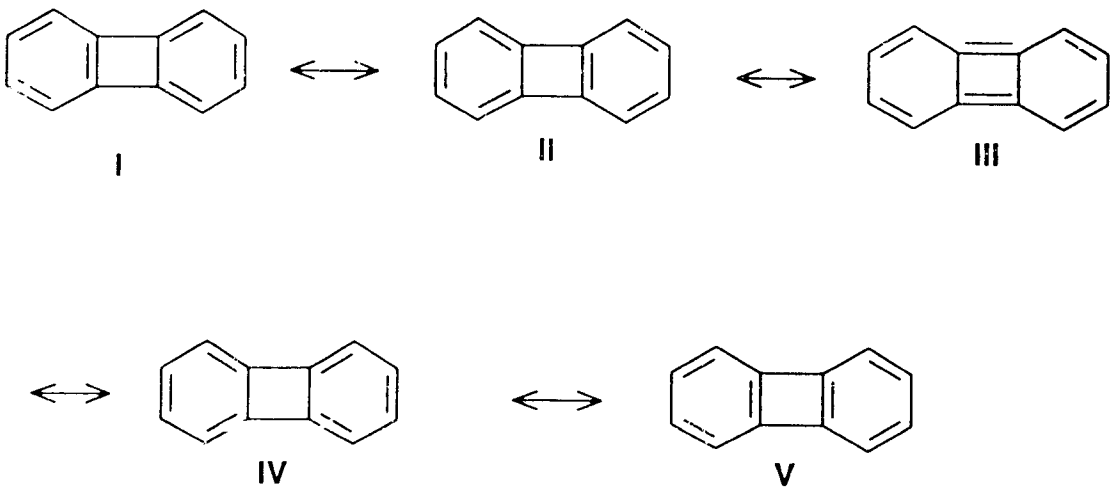


7 **202** **174**

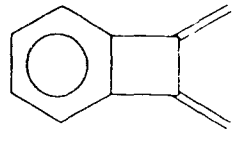
Six resonance structures, as shown in Scheme 15, can be drawn for **192**. Biphenylene itself has five limiting structures of which structure **IV** is the major contributor.

Scheme 15



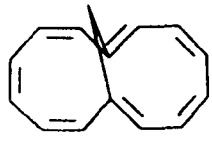


Among the resonance contributors of **192**, structures **IV** and **V** are less favoured based on the experimental coupling constants. Structure **III** would be a paratropic [24]-π system, and thus contributes even less to the overall structure, based on the observed chemical shifts of the external and internal protons. Structures **I**, **II**, **VI** and **VII** contribute most to compound **192**, which indicates the fusion of a [14]-π system to the bis(methylene)-benzocyclobutane, **203**.

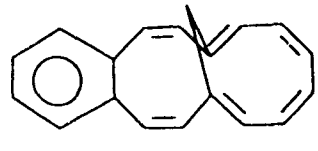


203

It must be pointed out here that Scott has shown, based on experimental coupling constants, benzannelation induces the same amount of bond fixation in [4n] annulenes as it does in [4n+2] annulenes.[174] The paramagnetic ring current in the methano[12]annulene, **204**, is reduced by 50% upon benzannelation. This has been shown based on the change in internal methylene proton chemical shifts and coupling constants of **204**, and **205**. Since the changes in bond alternation due to annelation is the same here, we can apply Mitchell's method to estimate the diatropicity of **192**



204



205

Using the change in the chemical shift of **192** from that of the parent DMDHP, **12**, the ratio of change in diatropicity of the macroring of **192** to the change in the diatropicity of the macroring of the benzo[a] DMDHP, **49**, is taken as the diatropicity of the annelating ring biphenylene, relative to that of benzene.

i.e., % diatropicity (benzene scale) = $\Delta\delta(CH_3)$ **192** / $\Delta\delta(CH_3)$ **49** x 100

where $\Delta\delta(CH_3)$ **192** = $\delta(CH_3)$ **192** - $\delta(CH_3)$ **12**

and $\Delta\delta(CH_3)$ **49** = $\delta(CH_3)$ **49** - $\delta(CH_3)$ **12**

Using the experimental values of $\delta(CH_3)$ for compounds **192**, **12**, and **49** (-2.77, -4.25 and -1.60 respectively) in the above expressions, we get the $\Delta\delta(CH_3)$ **192** and $\Delta\delta(CH_3)$ **49** as 1.48 and 2.65 respectively and thus:

% diatropicity of biphenylene = 1.48 / 2.65 x 100 = 56%

This estimate of diatropicity of biphenylene relative to that of benzene is in good agreement with the calculated relative estimate of 43% from REPE values.[175]

Using equation 5, the chemical shift value of the external proton H-2 of **192** can be calculated. The rearranged form of equation 5 is;

$$\delta = [\delta_{RCM} + 0.029 / 2.60] + 6.13$$

δ_{RCM} = 0.97 - $\delta(CH_3)$

= 0.97 - 2.77 = 3.74

δ = 7.579 ppm

This calculated value of δH_2 is in excellent agreement with the experimentally observed value of 7.571 ppm for **192**. We will use this chemical shift value to obtain a further estimate of the diatropicity of the biphenylene fragment in **192**. The ratio of the change in chemical shift of H_1 with respect to the benzo[a] DMDHP **49** to that of the parent DMDHP, **12**, reflects the extent of diatropicity of biphenylene with respect to the diatropicity of benzene. Thus we can calculate the relative diatropicity of biphenylene with respect to benzene as:

Diatropicity of biphenylene = (δH_2 **192** - δH_D **49**) / (δH_D **12** - δH_D **49**)

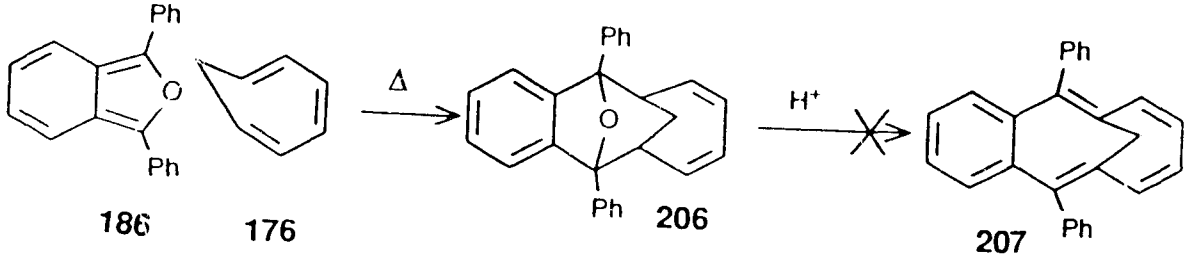
= (7.57 - 7.13) / (8.14 - 7.13)

= 0.44

This indicates that the diatropicity of biphenylene with respect to that of benzene is about 44%. Again, comparison of the theoretical estimates from REPE values are in good agreement with that found using chemical shift values. The discrepancy in the estimate of diatropicity using internal and external proton chemical shifts (12%) may be due the factors affecting the magnitude of chemical shifts of internal and external protons. Thus we find that biphenylene is about 44-56% diatropic as benzene.

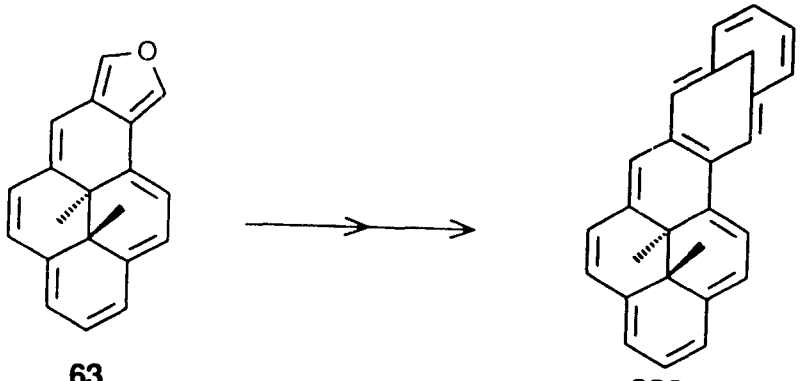
3.2.2 Attempted synthesis of the methano[10]annuleno dihydropyrene 208

The [6+4] cycloaddition of cycloheptatriene, **176**, with the isobenzofuran **186** leads to the adduct **206**, and has been known for some time.[176] However, attempted dehydration of the adduct **206** did not yield any of the benzomethano[10]annulene, **207**.[176]



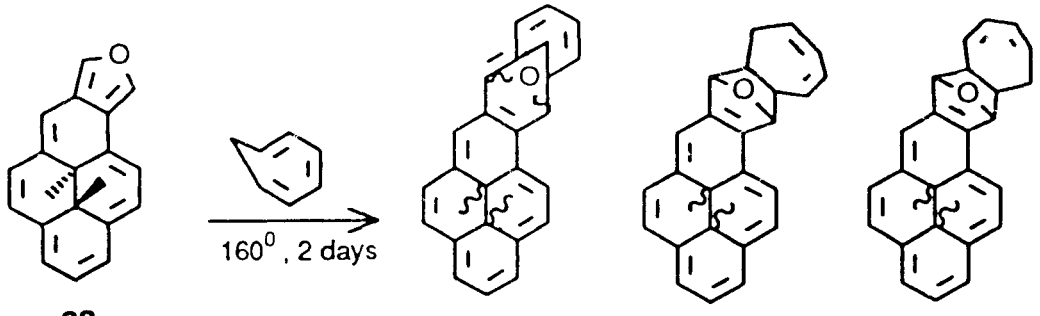
186 176 206 207

We wondered whether such a [6+4] type cycloaddition reaction between the oxa[17]annulene **63**, and cycloheptatriene **176** is possible at all, and in the event the reaction does proceed, whether the resultant cycloadducts could be dehydrated with mild acids to yield the annulenoannulene, **208**.



63 208

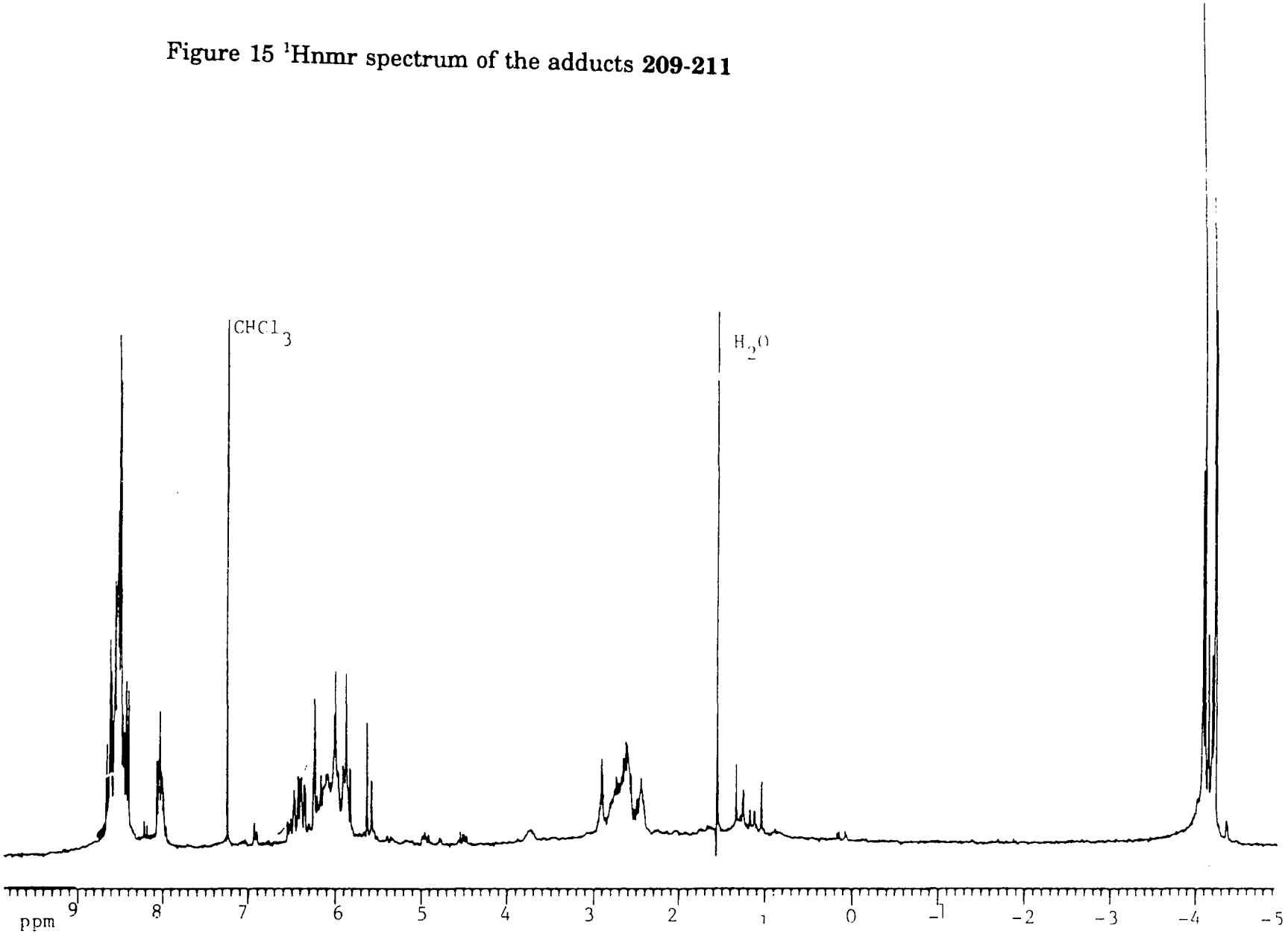
Unlike isobenzofuran, much to our surprise, the oxa[17]annulene **63**, proved to be very reluctant to react with cycloheptatriene. Refluxing the oxa[17]annulene **63**, in neat cycloheptatriene, even for a week, resulted only in the recovery of the starting materials. No dimerisation of the oxa[17]annulene, a process which occurs readily when isobenzofuran is heated at 80°C,[177] was observed. However, the reaction could be performed successfully by heating a degassed mixture of **63** and a large excess of cycloheptatriene in a sealed tube at 160°C for two days to yield a mixture of 1:1 adducts in 60% yield.



63 **209** **210** **211**

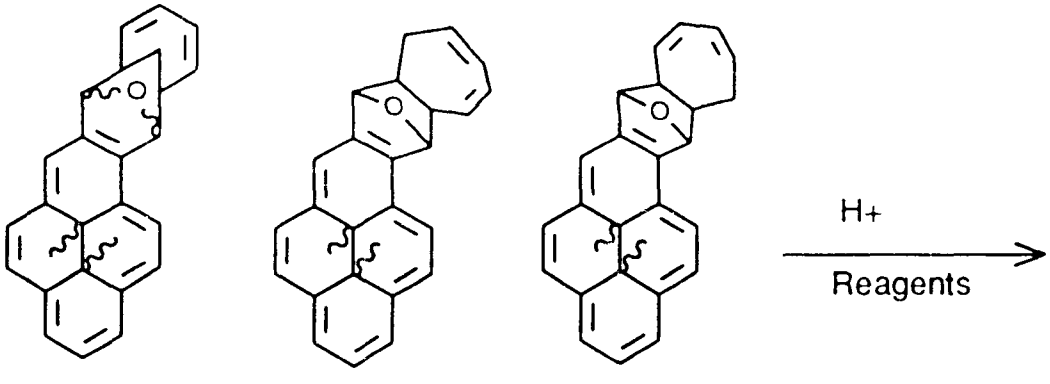
The green isomeric mixture could not be separated into its components by chromatography. That the products obtained from this reaction were a result of a 1:1 cycloaddition reaction between the oxa[17]annulene, **63**, and cycloheptatriene was clear from the mass spectrum which showed the correct molecular ion (M^+ 364) and the absence of any higher molecular weight peaks in its mass spectrum. The ^{1}H nmr of the mixture showed eight signals

Figure 15 ^{1}Hnmr spectrum of the adducts **209-211**



Probably the mixture constituted all the possible eight isomers. The fact that the integrity of the DMDHP nucleus was preserved even after heating for two days at 160°C is indeed noteworthy (the parent DMDHP, **12**, decomposes ~150°C) and should be very useful in future syntheses involving thermal cycloaddition reactions.

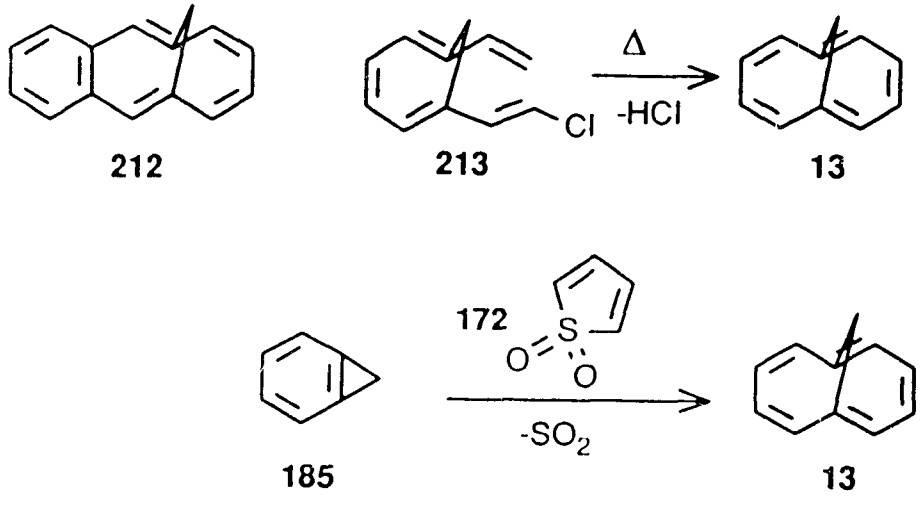
Next, the deoxygenation and dehydration reactions of the cycloadducts **209-211** was tried. The attempts made are listed in the table in the experimental section, and all the attempts made failed to produce any expected product and instead led to the recovery or the total decomposition of the starting material. We abandoned this scheme because of this setback and due to the knowledge gained from the dehydration attempts made on the adduct **191**, which indicated the propensity of the DMDHP ring to get protonated easily, perhaps leading to the failure of these reactions. Hence, an alternate strategy was sought.



3.3.2.1 Attempted synthesis of the cyclopropabenzo[a]dihydropyrene 218

A search for various pathways for the construction of the methano[10]annulene skeleton revealed that the non-angular benzomethano[10]annulene **212** is unknown. The best analogy we could find is in the synthesis of the parent methano[10]annulene **13** itself. Two syntheses of **13** are shown in Scheme 16. The first one involves an electrocyclisation-dehydrohalogenation sequence[178] and the second a [4+2] cycloaddition-extrusion protocol.[179]

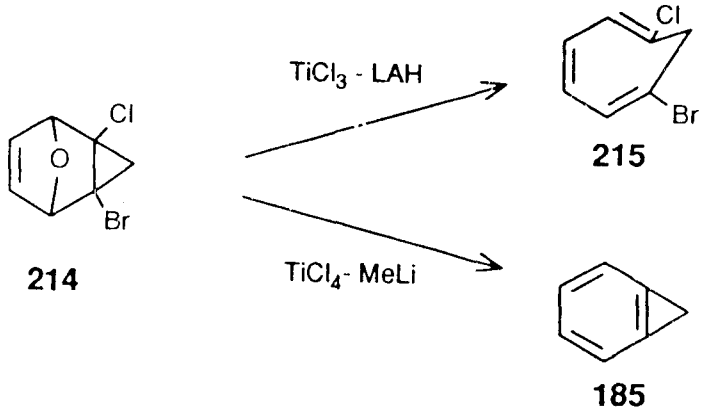
Scheme 16



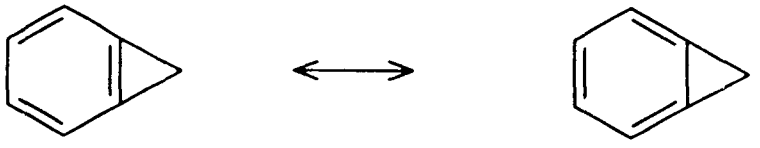
These two sequences suggest to us that a benzocyclopropene or a cycloheptatriene should be intermediates - both accessible from furans. Müller and coworkers, in their syntheses of various cycloproparenes, have used the

Diels-Alder reaction between furans and cyclopropenes which were then converted into cycloproparenes or cycloheptatrienes, depending on the reaction conditions.[180] For example, the dihalocycloheptatriene **215** and cyclopropabenzene **185** were obtained from the adduct **214** (Scheme 17).[180]

Scheme 17

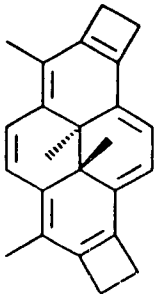


Thus, synthetically, it is feasible to obtain these useful moieties fused to DMDHP from the oxa[17]annulene, **63**. Cyclopropabenzene **185** is yet another theoretically interesting molecule with a strain energy of 68 kcal/mol.[181] In addition to that, the so called Mills-Nixon effect which is presumed to operate in small ring annelated arenes is a topic of much discussion in the literature.[182] The Mills-Nixon effect in cyclopropabenzene **185**, for example, is presumed to cause bond localisation in the benzene ring thus favouring the kekule structure **185b** over **185a**.

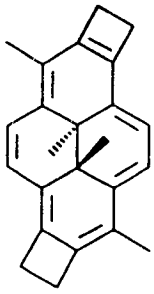


185a **185b**

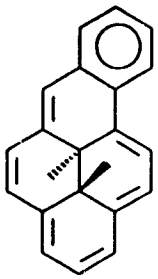
Although there were several attempts to prove or disprove the existence of such an effect,[183,184,185] so far, there is no conclusive evidence for the presence or the absence of bond fixation and the controversy continues unabetted.[186] Mitchell and coworkers have used the DMDHP probe earlier to show the absence of any such bond fixation that might arise due to butannelation of DMDHP.[187] Compounds **216** and **217** showed no bond fixation as evidenced by the magnitude of the internal methyl proton chemical shifts. The $\delta(CH_3)$ of **216** and **217** are almost the same in value, clearly indicating the absence of any bond fixation.



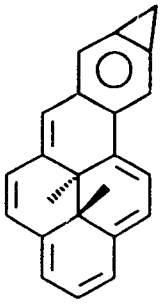
216



217



49

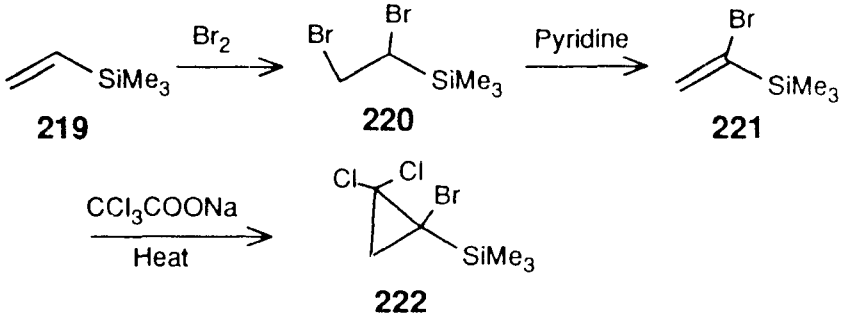


218

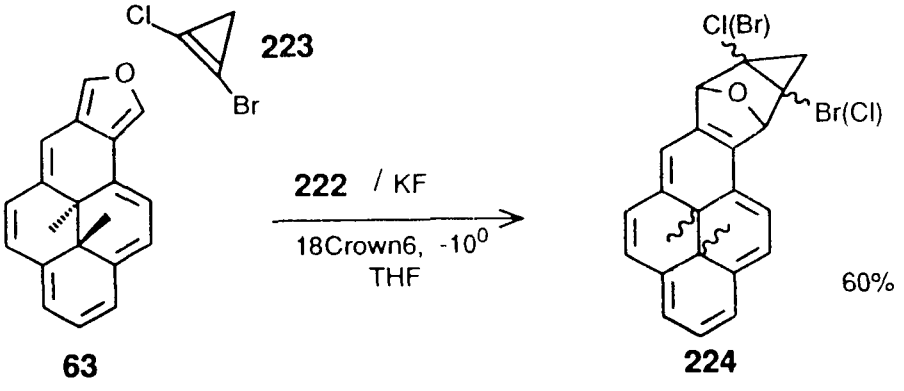
The cyclopropabenzo[a]DMDHP **218** would provide information regarding the presence or absence of a Mills-Nixon effect by comparing the value of $\delta(CH_3)$ of **218** with that of the known benzo[a]DMDHP **49**. A more localised benzene ring would result in a more bond fixed DMDHP moiety and hence a less shielded internal methyl proton. Hence, we decided to synthesise the fused DMDHP **218**. The required cyclopropene precursor **222** was made from commercial vinyltrimethylsilane, **219** in a three step synthesis by

reported procedures (Scheme 18).[188,189]

Scheme 18

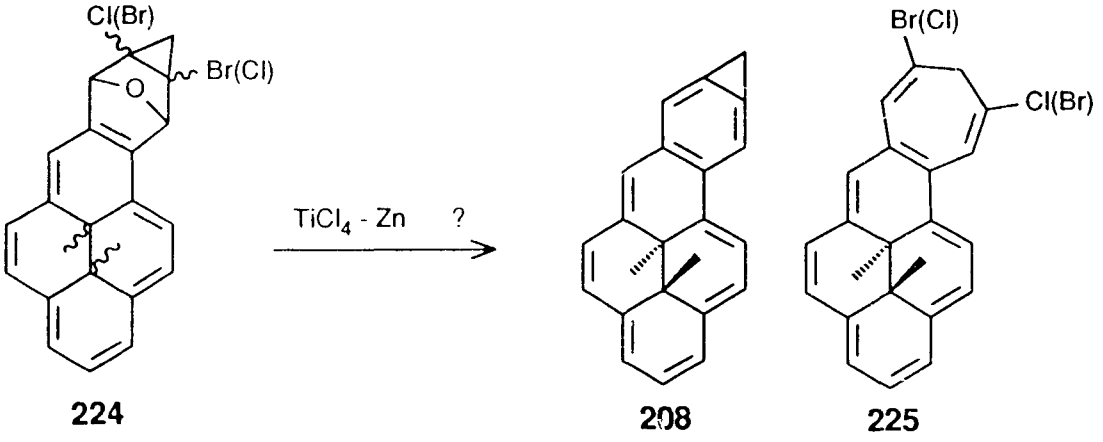


Reaction of the unstable cyclopropene **223**, generated in situ from the precursor **222**, with the oxa[17]annulene **63** led to the formation of the cycloadducts **224** in 60% yield. The adduct obtained was a mixture of several isomers.



The mixture, which was inseparable by chromatography or by recrystallisation, gave a satisfactory elemental analysis and the correct molecular ion (M^+ 426 for $C_{23}H_{18}{}^{79}Br_1{}^{37}Cl_1O_1$) in its mass spectrum. A ^{1}Hnmr

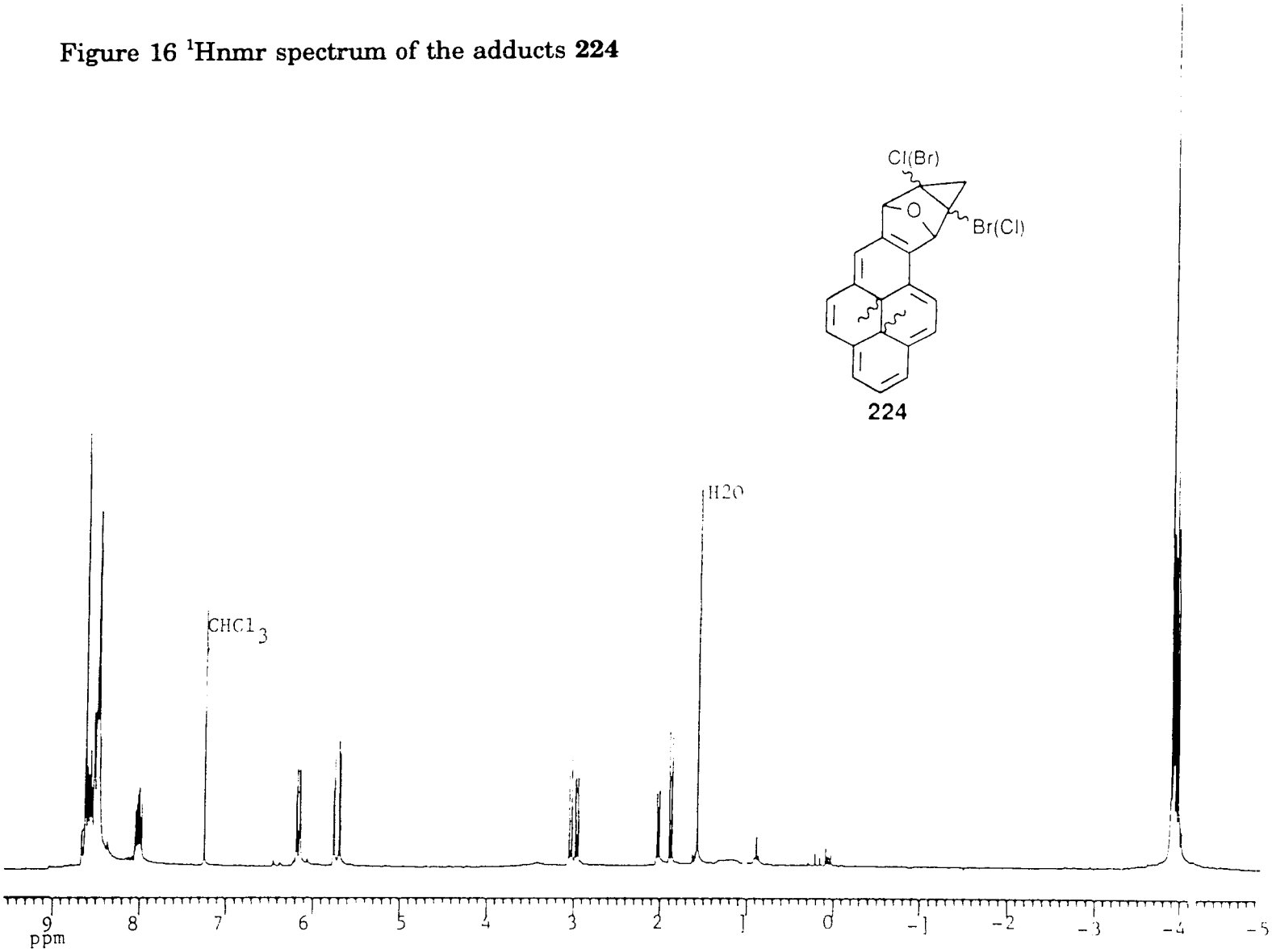
spectrum (Figure 16) of the green adducts showed several peaks for the internal methyl protons between -3.9 and 4.2 ppm and several peaks for the internal methyl carbons in the ^{13}Cnmr spectrum, indicating the presence of several isomers. Reaction of the adducts with titanium reagents was attempted next. Action of a "green titanium" species generated from $TiCl_4$-Zn on the cycloadducts **224** proceeded very slowly. The reaction mixture after two days showed a non-polar, TLC unstable, reddish-brown compound. The mixture was worked up carefully and chromatographic separation was attempted.



224 **208** **225**

The products were very unstable to silica gel. Hence, they were chromatographed under argon using a chromatotron. A strong smelling red-brown band was isolated from the mixture. It gave the ^{1}Hnmr spectrum

Figure 16 ^{1}Hnmr spectrum of the adducts **224**



shown in Figure 17.

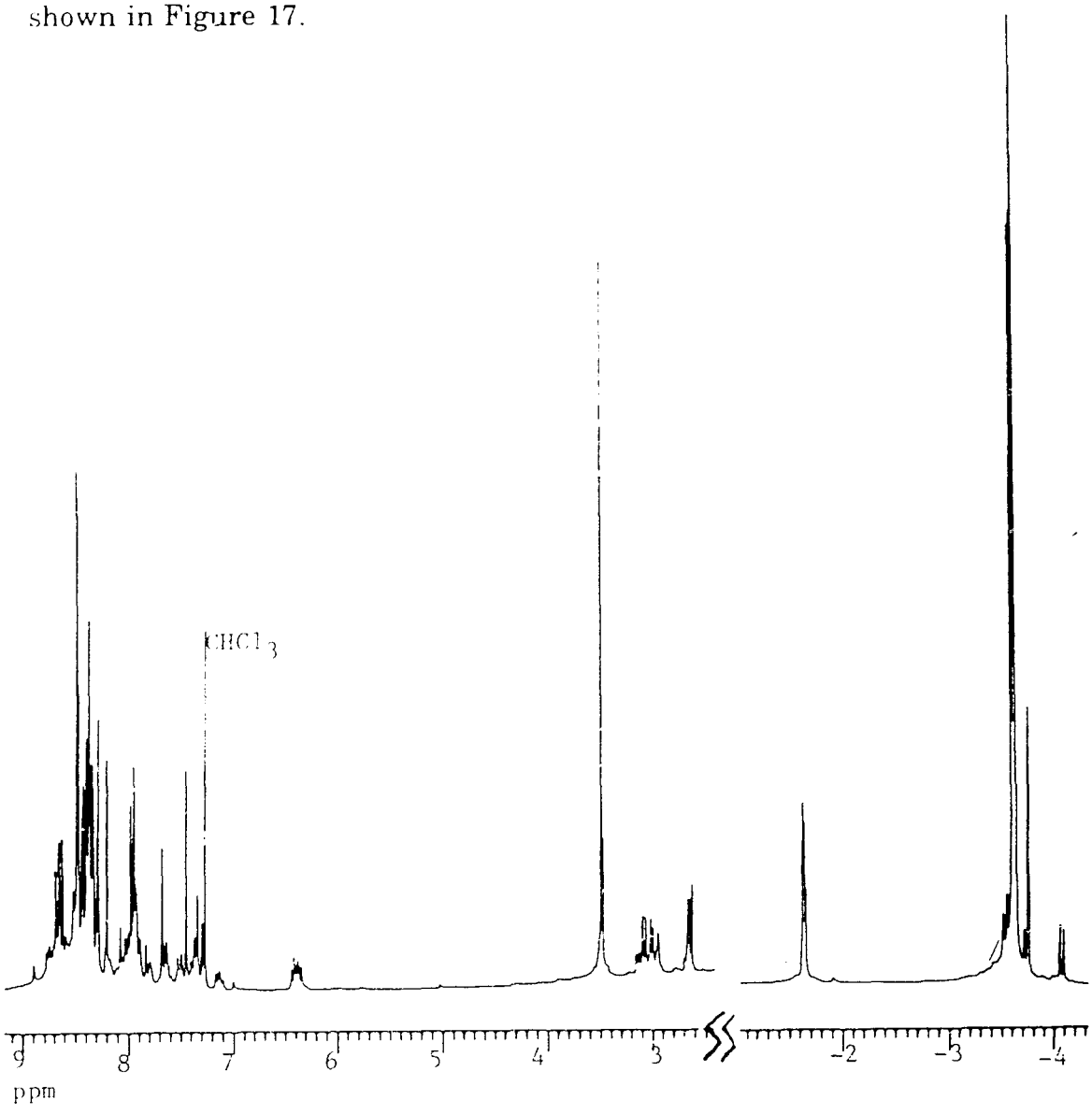


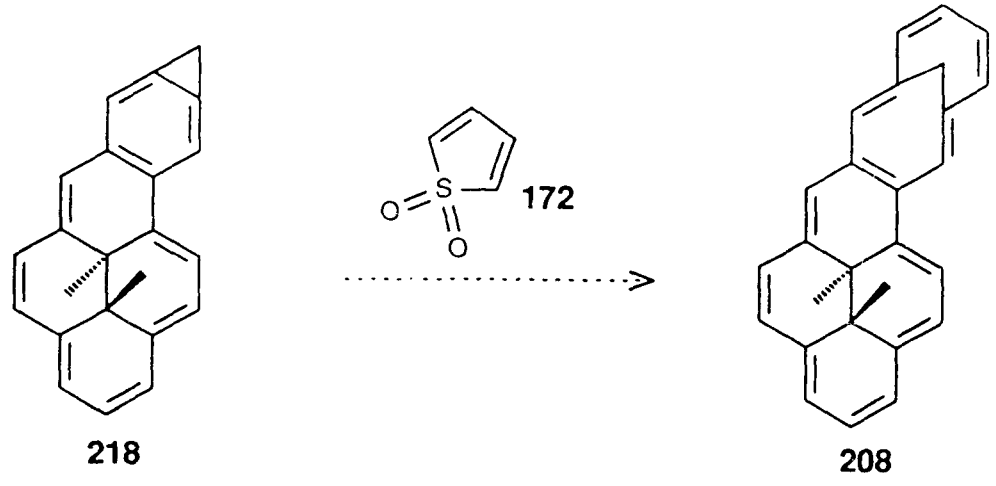
Figure 17 ^{1}Hnmr spectrum of the product(s) from reaction of **224** with Ti(0)

From the ^{1}Hnmr spectrum obtained, we tentatively assign the structures **218** and **225** to the product mixture. There are two singlets present at 3.4 and 3.3 ppm in the ^{1}Hnmr spectrum which are assigned to the -CH_2-

protons of **225** and **218** respectively. Two methyl proton signals were present at -1.62 and -3.9 ppm. The ratio of $-CH_2-$ and $-CH_3$ signals indicated that the compounds **218** and **225** were present in a 1:5 ratio. The chemical shifts of the internal methyl protons of the product mixture obtained (**218** and **225**) is worth noting. The chemical shift $\delta(CH_3)$ of compound **218** at -1.62 ppm is almost the same as that of the methyl protons of the benzo[a]DMDHP **49**! This would indicate that there is no additional bond fixation in **218** due to propannelation and that the Mills-Nixon effect is absent.

Unfortunately, during and after chromatography, the mixture proved to be very unstable and a mass spectrum could not be obtained. Attempts to generate the benzocyclopropene **218** using a $TiCl_3$-MeLi system resulted in total decomposition of the adduct **224** (into at least 20 compounds!).

Additional work and structural proof are needed to substantiate these findings. Due to the unstable nature of the product mixture, the next reaction to produce **208** could not be tried.

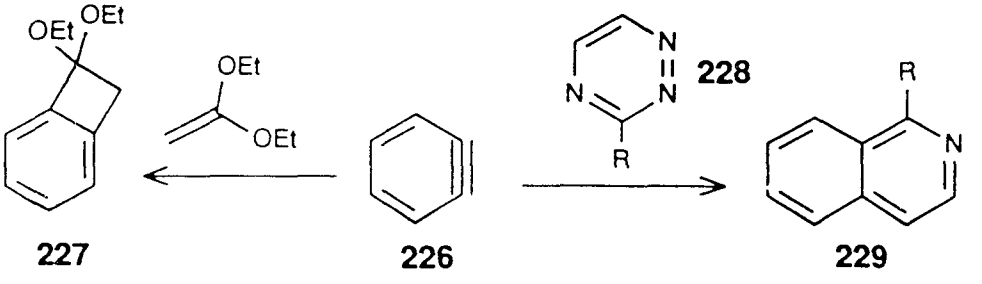


218 **208**

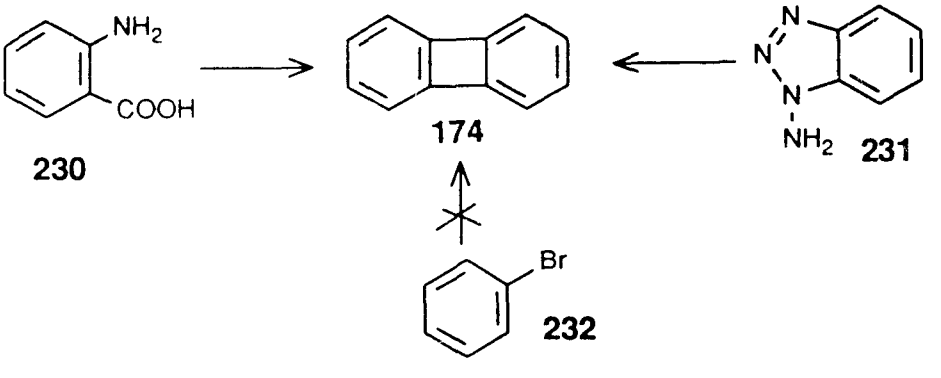
3.3 Syntheses using arynes

Arynes are versatile intermediates which lead to a variety of products.[190,191] Benzyne, **226**, for example, leads to acenes and other fused benzene derivatives through D-A reactions (Scheme 19).

Scheme 19



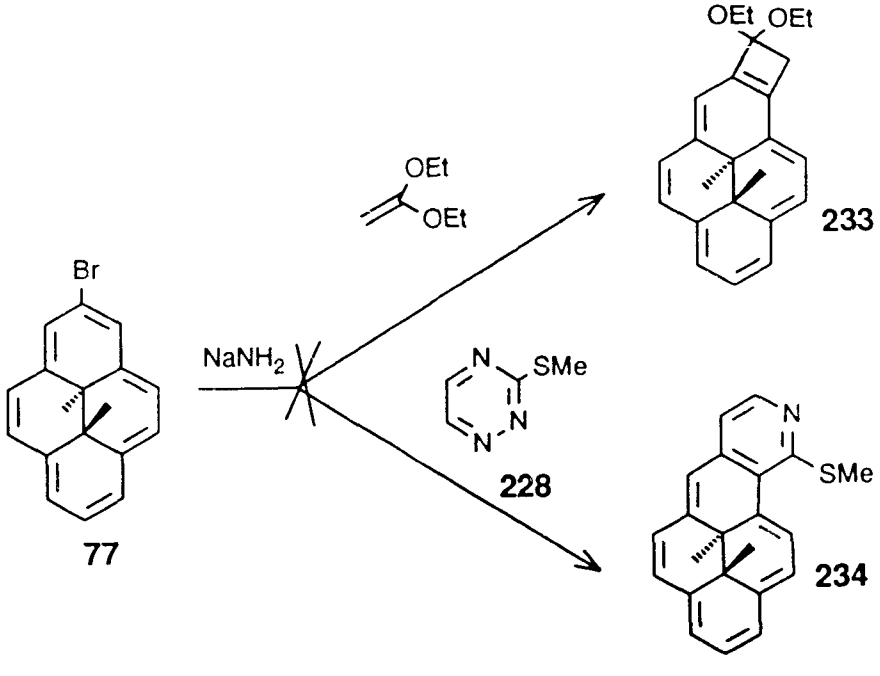
However, the method of generation of benzyne is very critical to the success of a given reaction. Usually, benzyne generated from anthranilic acid, **230** or the benzotriazole **231** take part in most of the reactions. For example, biphenylene, **174**, is obtained in a reasonable yield from benzyne generated from **230** and **231** but not from bromobenzene, **232**.[192]



Zhou's efforts to synthesise a precursor of anthranilic acid type for the generation of the aryne **62** did not bear any fruit. However, he has demonstrated that the aryne **62** could be generated and trapped with furans in high yields.

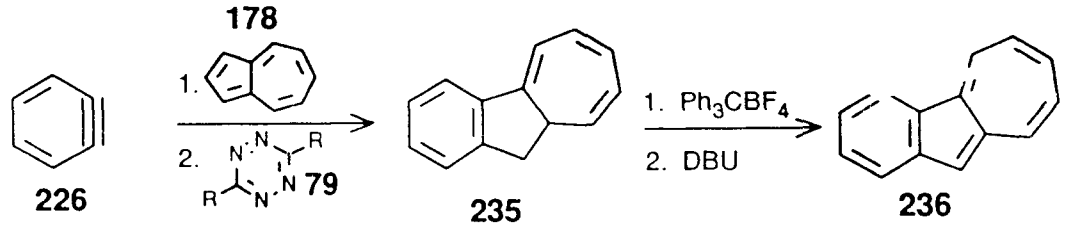
We wondered whether this aryne could be trapped with any other reactants to create some interesting fused DMDHPs. We describe our attempts, which were not successful, here. Benzyne generated from bromobenzene/sodamide system has been trapped with 1,1-dialkoxyethenes to yield 2+2 adducts.[193] For example, the adduct **227**, was obtained in 70% yield. We wished to try this reaction on our aryne **62** since this would lead to a variety of other compounds.[194]

Scheme 19

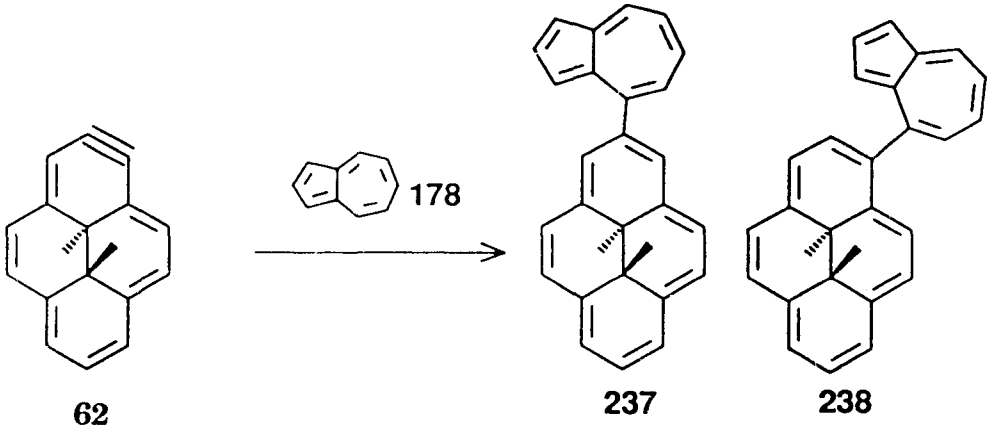


However, when this reaction was tried, no adducts were isolated. The same fate was met with in the reaction of aryne **62** and the triazine **228**.

Reaction of benzyne generated from anthranilic acid has been reported to give a [6+2] adduct with azulene.[195] This adduct **235** was subsequently transformed into the benzoazulene **236** in two steps.



When the aryne **62** was generated in the presence of excess azulene, the only products isolable, in low yield, were the biaryls **237** and **238**.



One of the biaryls from the mixture was isolated pure after careful fractional crystallisation. It was identified by its molecular ion (M^+ 358) in its

mass spectrum. The internal methyl protons of the biaryl **237** appeared as singlets at -3.98 and -4.10 ppm. The U.V-Vis spectrum, showed a broad long wave length band at 512 nm ($\log\varepsilon_{max}$ 2.85), characteristic of azulene. These biaryls are formed presumably through an ene reaction of the electron rich aryne **62** with azulene, **178**.

3.4 Summary

In this project, involving the reactive intermediates **62** and **63**, we attempted the syntheses of several fused DMDHPs using various methodologies and strategies. We successfully synthesised the biphenylene fused DMDHP, **192** from the oxa[17]annulene in two steps. A thorough analysis of the nmr spectra of **192** was carried out using 2-D nmr spectra. Using Mitchell's method of estimation of aromaticity, we estimated the diatropicity of biphenylene, **174**, to be about 44-56% of benzene which compares favourably with the theoretical estimates. Attempts were made to synthesise the methano[10]annuleno DMDHP, **208**. Although unsuccessful, new insights were gathered about the reactivity and stability of the oxa[17]annulene **63**, and the interesting DMDHP derivative, **224** was obtained. This adduct is a potential precursor to the unknown cyclopropabenzo-DMDHP, **218**. Preliminary studies indicate the absence of Mills-Nixon effect in cyclopropabenzene. Attempted syntheses of several fused DMDHPs using the aryne **62** were unsuccessful.

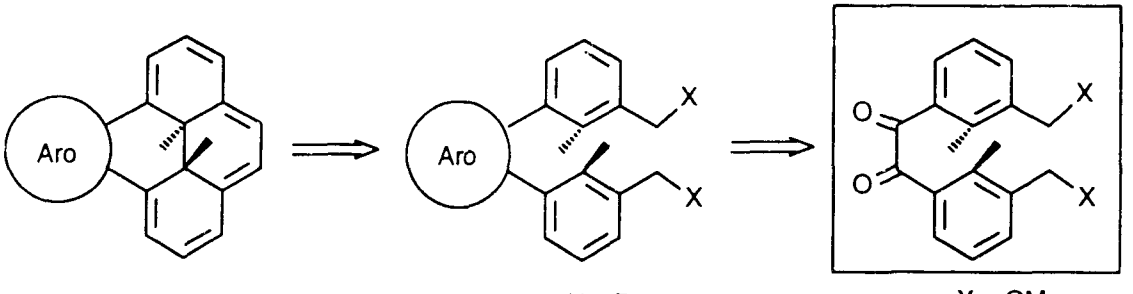
CHAPTER FOUR

SYNTHESES USING CLASSICAL INTERMEDIATES- APPROACHES TO [e]-ANNELATED DMDHPs

4.1 Introduction

In the general introduction (section 1.4.3) we saw the reported syntheses of [e] fused DMDHPs from substituted *o*-teraryls. The major drawback in that sequence is that the synthesis requires a 1,2-dibromoarene, synthesis of which is not always trivial. Examination of an *o*-teraryl intermediate needed for the synthesis of an [e] fused DMDHP showed the fragment which is common for all *o*-teraryls (Scheme 20). This intermediate **240**, in turn, led to a diketone **241** as a potential intermediate.

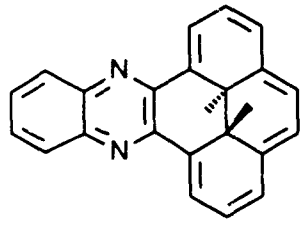
Scheme 20



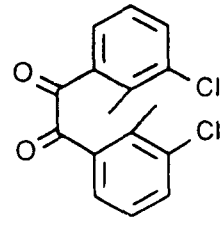
239 X = Br **240** X = OMe **241**

1,2-diketones are very versatile intermediates from which a wide variety of rings can be constructed using well documented reactions. Hence we chose the diketone **241** as the common intermediate and directed our attention to its synthesis.

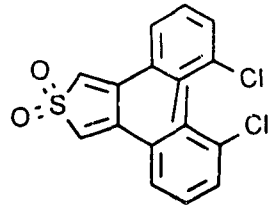
In this chapter, we will describe our model studies directed towards the synthesis of the dione **241**, our discovery of a new synthesis of symmetrical 1,2-diones from Grignard reagents and the synthesis of the quinoxalino DMDHP, **279**. We will also describe the synthesis of some model *o*-teraryls using the model dione **249** and the synthesis and utility of another potential intermediate, the thiophenedioxide **296**.



279



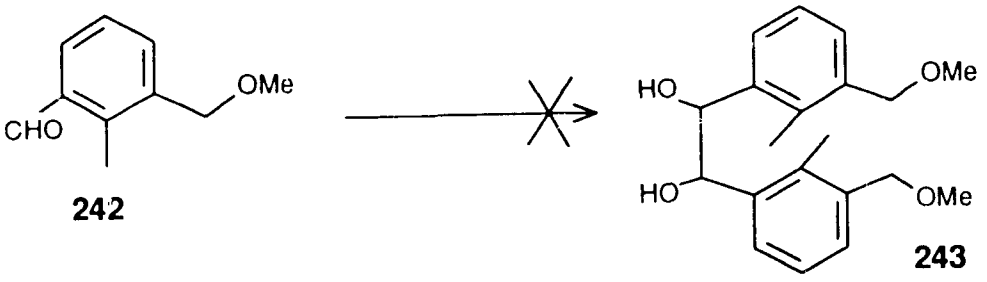
249



296

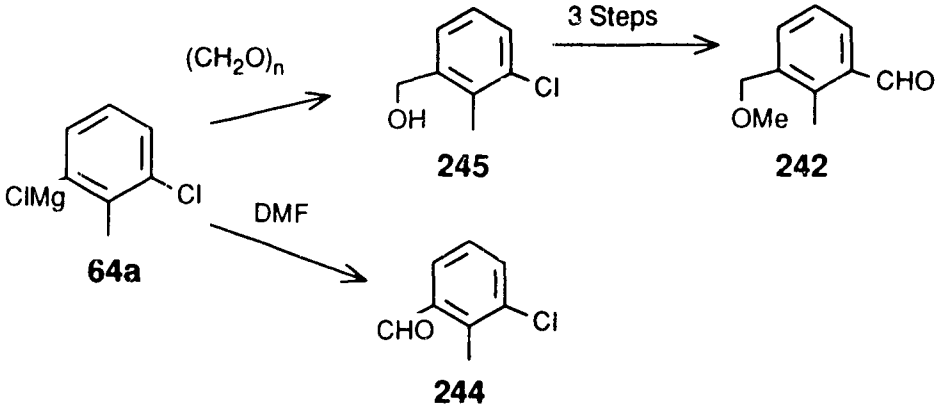
4.2. Model studies using 2,6-dichlorotoluene, 64

Symmetric 1,2-diketones can be prepared in many different ways.[196] In principle, benzoins are easy to prepare from formyl arenes and can be readily oxidised to benzils (1,2-diketones).[197,198] When we tried benzoin condensation on the aldehyde **242**, the expected benzoin **243** could not be obtained.

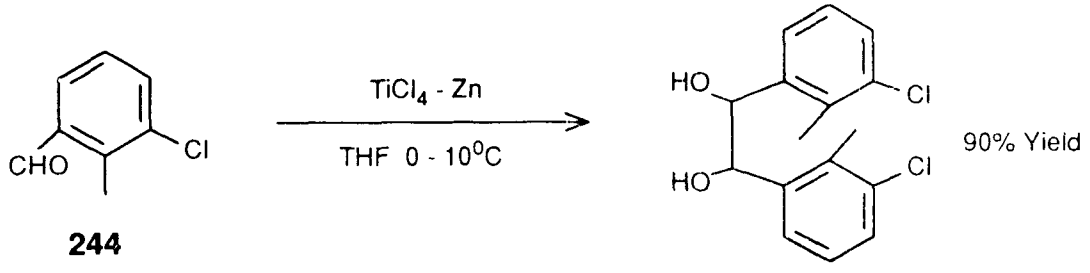


This difficulty we encountered initially, prompted us to use the relatively inexpensive aldehyde **244** as a model for reactions leading to the diketone **241**. The required aldehydes **242** and **244** were made from 2,6-dichlorotoluene by reported procedures (Scheme 21).[199]

Scheme 21



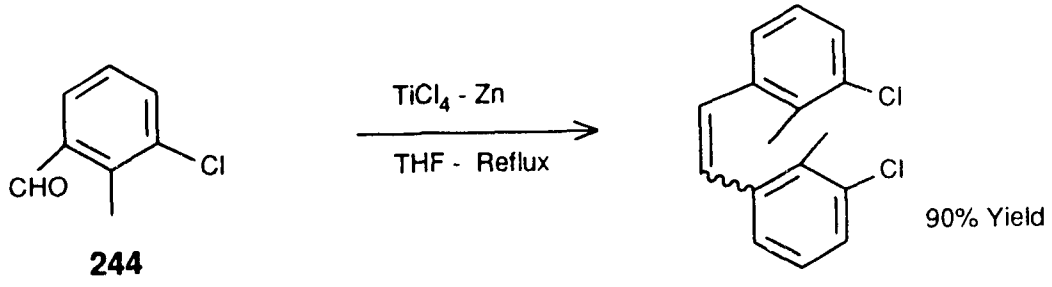
Titanium mediated coupling of aldehydes is known to lead to either 1 2-diols[200] or alkenes[201] depending on the conditions used. Reaction of the aldehyde **244** with $TiCl_4$ - Zn dust under Mukaiyama conditions yielded the diol **246** as a mixture of two isomers in 90% yield.



244 **246**

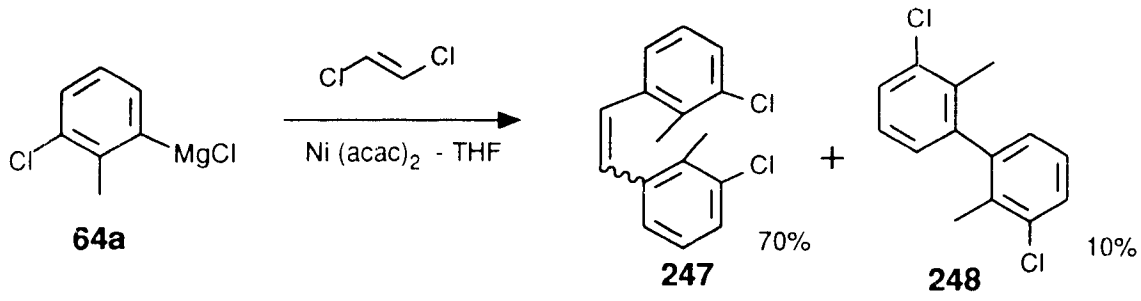
The diol **246** was identified from its mass spectrum (M/2 156, base peak) and nmr spectra. The ^{1}Hnmr spectrum of **246** showed two singlets at 4.93 and 4.65 ppm for the -CH-O- proton of the two isomers and a singlet at 2.35 ppm for the methyl protons. Fractional recrystallisation did not result in the separation of the isomers and the diol decomposed on attempted chromatography. Hence, no further attempt was made to separate the isomers.

When the aldehyde **244** was coupled using the $TiCl_4$/Zn system under McMurry conditions, the stilbene **247** was obtained as a mixture of *cis* and *trans* isomers in a combined yield of 90%.



244 **247**

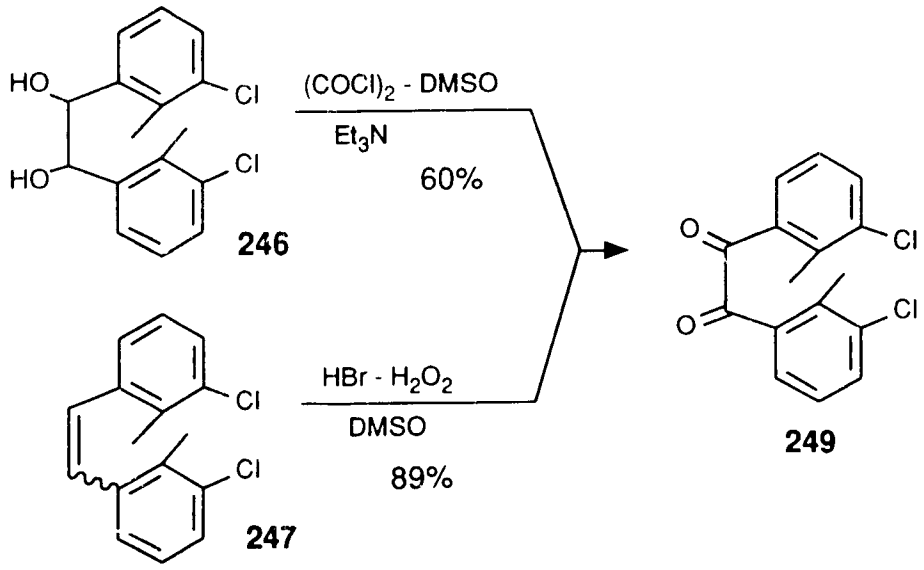
The same stilbene **247** was also obtained in a 70% yield from the Grignard reagent **64a** and 1,2-dichloroethene, through a nickel mediated coupling reaction. The known biaryl **248**[202] was formed as a side product in about 10% yield.



64a **247** **248**

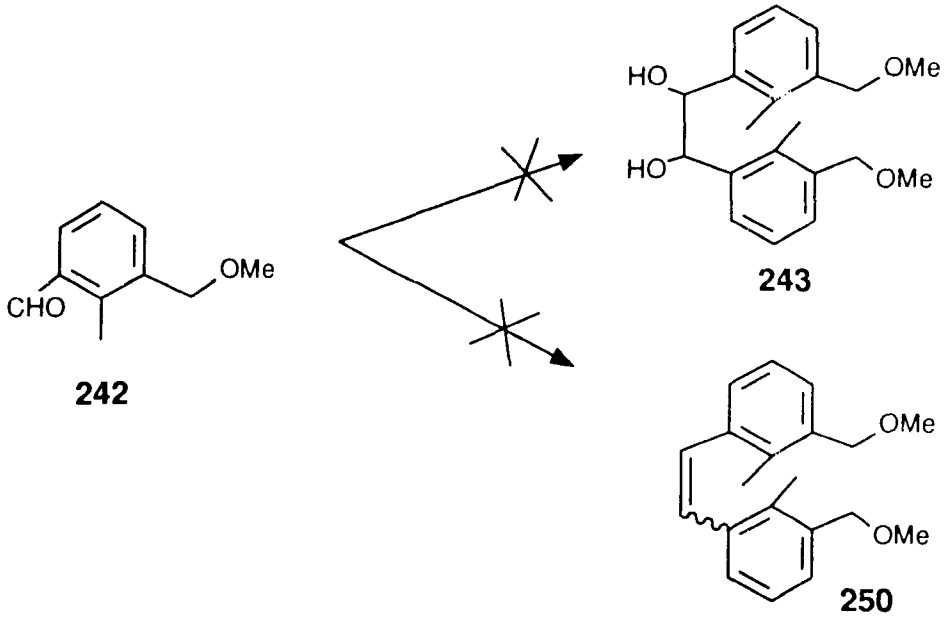
A pure sample of the *trans* isomer **247a**, mp 146-148°C, was obtained by recrystallisation of the isomeric mixture from ethanol. The stilbene **247** gave the correct molecular ion (M^+ 276) in its mass spectrum and a satisfactory elemental analysis.

The diol **246** and the stilbene **247** were then oxidised by $(COCl)_2/Et_3N/DMSO$[203] and $HBr/H_2O_2/DMSO$[204] systems respectively in to the diketone **249**.

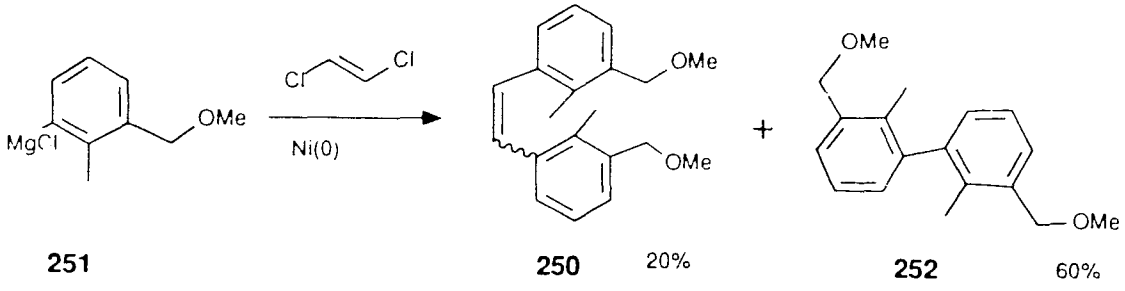


The diketone **249** was obtained as yellow needles from ethanol, mp 122-124 C. Its structure was confirmed from the correct molecular ion (M^+ 306, 308, 310) in the mass spectrum and a satisfactory analysis. In its ^{13}Cnmr spectrum, the carbonyl carbon appeared at 194.9 ppm and a strong carbonyl stretch was observed at 1687 cm^{-1} in its IR spectrum.

The synthesis of the model diketone **249** from the aldehyde **244** through the diol **246** or the stilbene **247** could thus be achieved by selective oxidations. We then turned our attention to the synthesis of the diketone **241**. The conditions under which the aldehyde **244** underwent coupling, did not work for the aldehyde **242** and no expected products could be isolated.



The Ni(0) mediated coupling of the Grignard reagent **251** with dichloroethene gave the stilbene **250** in only ~20% yield. The major product in this reaction was the unwanted biaryl **252**.



251 **250** 20% **252** 60%

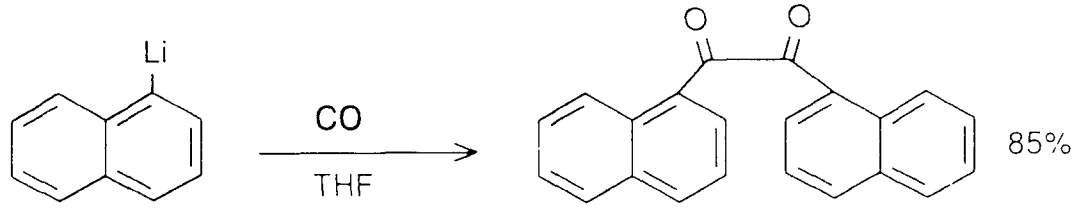
The presence of the stilbene **250** in the reaction mixture was identified from the ^{1}Hnmr spectrum and comparison with the reported ^{1}Hnmr values.[205] The product mixture from the above reaction when treated with HBr/H_2O_2/DMSO system resulted in a complicated mixture of compounds from which the presence of the desired diketone **241** could not be detected. These failures led us to look for means to synthesise the diketone which does not involve the aldehyde **242**.

4.3 Search for a direct synthesis of 1,2-diketones

We next searched for a direct synthesis of 1,2-diketones from a haloarene as this would avoid the use of the aldehyde **242** and give access to the diketone via an organometallic reagent. If such a reaction is feasible, the diketone **241** would be directly accessible from the Grignard reagent **251**.

Kollonitsch has reported some success in obtaining diketones from *purified* organo cadmium reagents and oxalyl chloride.[206a] But the major disadvantage of this procedure is that it requires the organo cadmium reagent to be free of any magnesium or lithium salts which is usually very difficult.

So, this approach was not considered. Nudelmann had succeded in reacting organolithium reagents, derived from iodoarenes, and carbon monoxide to yield diketones.[206b] For example, the diketone **254** was obtained, in 85% yield, from 1-lithionaphthalene, **253**.

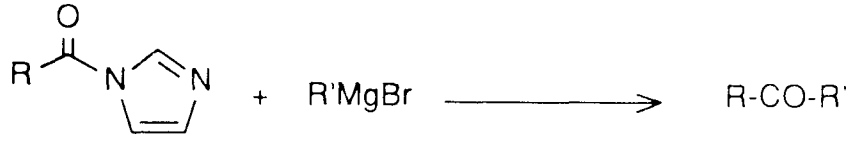


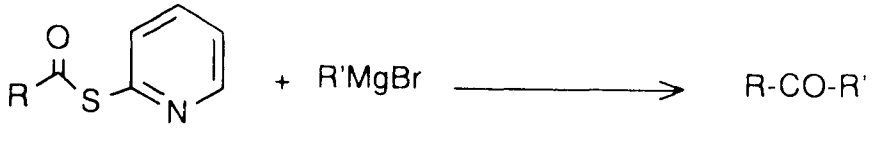
253 **254**

When this reaction was tried on our model, the Grignard reagent **64a**, no reaction was evident and the known alcohol **245** was obtained from the reaction mixture after quenching with $(CH_2O)_n$ and work up.

Next we turned our attention to the synthesis of ketones from Grignards to look for analogies. There are several methods available for the preparation of ketones from Grignard reagents.[207, 208, 209] Staab's method[207, 210] involves the use imidazolides while Mukaiyama's procedure[208] makes use of thio esters (Scheme 22).

Scheme 22



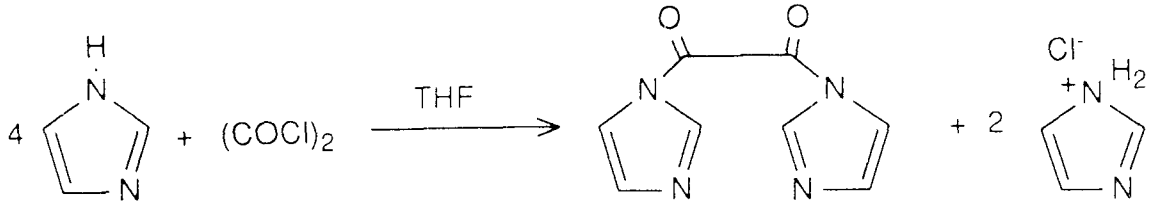


We wondered whether such a transformation could be applied for the synthesis of 1,2-diketones, starting from an oxalyl derivative and a Grignard reagent. We describe our results towards this goal, next.

4.4 A new synthesis of symmetrical 1,2-diketones

1,1'-Oxalylimidazole, **259**, is a known compound, first prepared by Murata.[211] It has been used for a variety of functional group transformations.[212] Gill and Kiefel have used this reagent as a "dicarbonyl synthon" in their synthesis of Grevillin.[213] Since the preparation of **259** is easy and as it can be made from inexpensive imidazole and oxalyl chloride, we decided to use this as a source of the dicarbonyl fragment in our diketone synthesis.

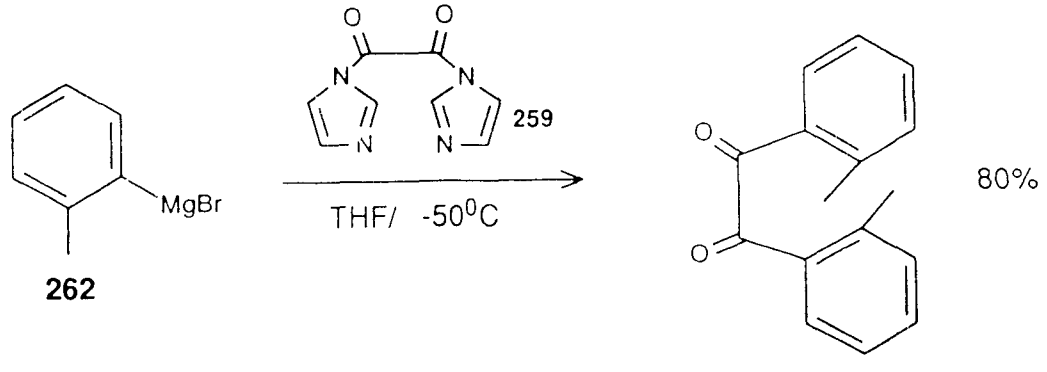
Reaction of four equivalents of imidazole with one equivalent of oxalyl chloride in dry THF at -10°C, followed by the filtration of the precipitated imidazole hydrochloride, readily yielded a solution of 1,1'-oxalylimidazole, **259**. A small portion of this solution on evaporation of the solvent, gave the imidazolide **259**, as a pale yellow powder. This sample gave the correct molecular ion (M^+ 190) in its mass spectrum and had a carbonyl stretch at 1595 cm^{-1} in its IR spectrum. 1,1'-Oxalylimidazole is very hygroscopic and hence should be handled under dry conditions or used immediately following its preparation.



259

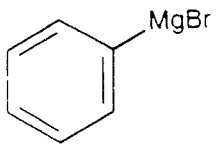
It could also be made, more conveniently, by reacting two equivalents of imidazole with one equivalent of oxalyl chloride in presence of diisopropylethylamine as the base in dry THF. Diisopropylethylamine hydrochloride is less hygroscopic than imidazole hydrochloride and hence it is easier to exclude moisture during the filtration of the reaction mixture. It was found necessary to wash the precipitate with plenty of dry THF to dissolve most of the product, **259**, because it is not very soluble in THF.

We next tried a model reaction of a Grignard reagent with **259**, expected to result in a 1,2-diketone. When the Grignard reagent **262** was reacted with half an equivalent of 1,1'-oxalylimidazole at -50°C, it resulted in the immediate formation of the diketone **263** in 80% yield.



262 **263**

The utility of this new method was tested for a few other Grignard reagents. The yields of the 1,2-diketone products obtained are listed in Table 17.



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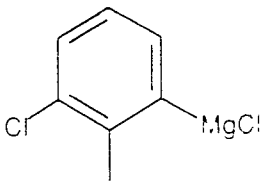
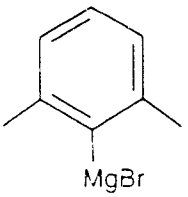
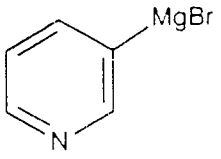


64a



262



264

Table 17 Synthesis of 1,2-diketones from Grignard reagents.

Grignard	Temp (°C)	Time (min)	Yield (%)
256	-70	5	60
264	-70	5	60
262	-30	10-15	70
64a	-80	5	65

The yields are consistently in the range of 60-75%. In the case of unhindered Grignard reagents, such as **256**, 5-10% of keto alcohols of the type $Ar_2CH(OH)COAr$ were also isolated. This might be a result of further addition of Grignard to the 1,2-diketone formed. The yield is affected drastically if a precipitate formation is observed during the addition of the reagent to the Grignard, consistent with Mukaiyama's observations.[208] It is essential that the temperature should be controlled carefully to get the optimum yields.

In general, this new 1,2-diketone synthesis from Grignard reagents

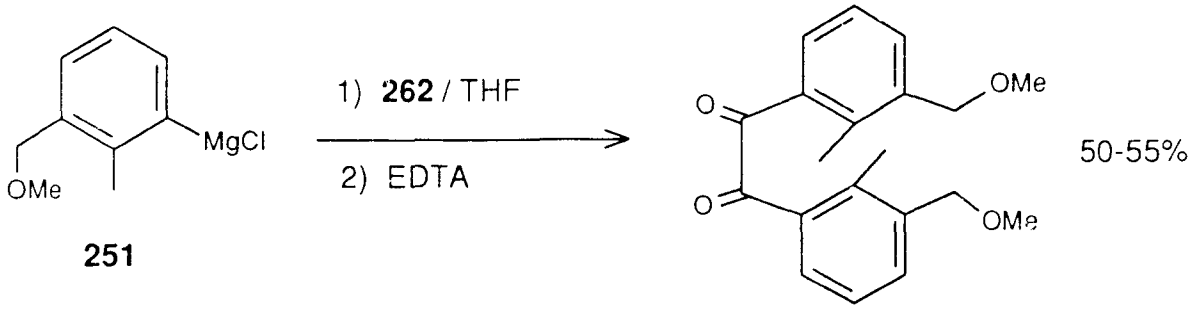
is a simple and direct method of synthesis of symmetric diketones which works particularly well for very hindered aryl Grignards. Recently, two similar syntheses of 1,2-diketones[214, 215] which are complimentary to our method[216] have been reported in the literature.

4.4.1 Synthesis of 1,2-bis(3'-methoxymethyl-2'-methylphenyl) ethanedione, 241.

When we next implemented this new synthesis of diketones for our synthon **241**, a varying yield of the diketone was obtained as the only product. The diketone **241** was obtained as yellow needles, mp 69°C, from methanol. The structure of the diketone was confirmed from its molecular ion (MH^+ 327, weak, M1/2 163, 100%) in its mass spectrum and a correct elemental analysis. The diketone **241** exhibited a strong carbonyl stretch at 1674 cm^{-1} in its IR spectrum and its carbonyl carbon appeared at 196.8 ppm in the ^{13}Cnmr spectrum.

Initially, the variable yield was quite puzzling and could not be explained. This problem was solved as follows. First, the mass balance of the product mixture after chromatography was checked carefully and the unreacted starting material accounted only for 10-20% of the total mass with the rest being the expected diketone product. When the reaction mixture was

worked up and the diketone isolated by direct recrystallisation, a white, waxy material was also isolated. This material gave a ^{13}Cnmr spectrum which had the same number of peaks as that of the diketone but with very different chemical shifts (See Figures 18 and 18a for the authentic nmr spectra of **241**). A satisfactory analysis or a mass spectrum could not be obtained for this material. We reasoned that the excess magnesium used to generate the Grignard reagent **251** (two equivalents of Mg are used[217]), which results in the formation of excess of magnesium salts, might have led to the complexation of the product formed and the waxy material may be a complex of the dione **241** and magnesium salts of an unknown composition. The yield of the dione product from the reaction mixture improved to a consistent level of 50-55% when solid ethylenediaminetetraacetic acid was used to quench the reaction. Use of $MgSO_4$ as a drying agent must be avoided to dry the organic extracts of the product mixture, as this leads to the loss of the product.



251 **241**

Thus, the useful synthon, the dione **241**, was obtained in a reasonable yield and in only three simple steps from 2,6-dichlorotoluene.

Figure 18 ^{1}Hnmr spectrum of **241**

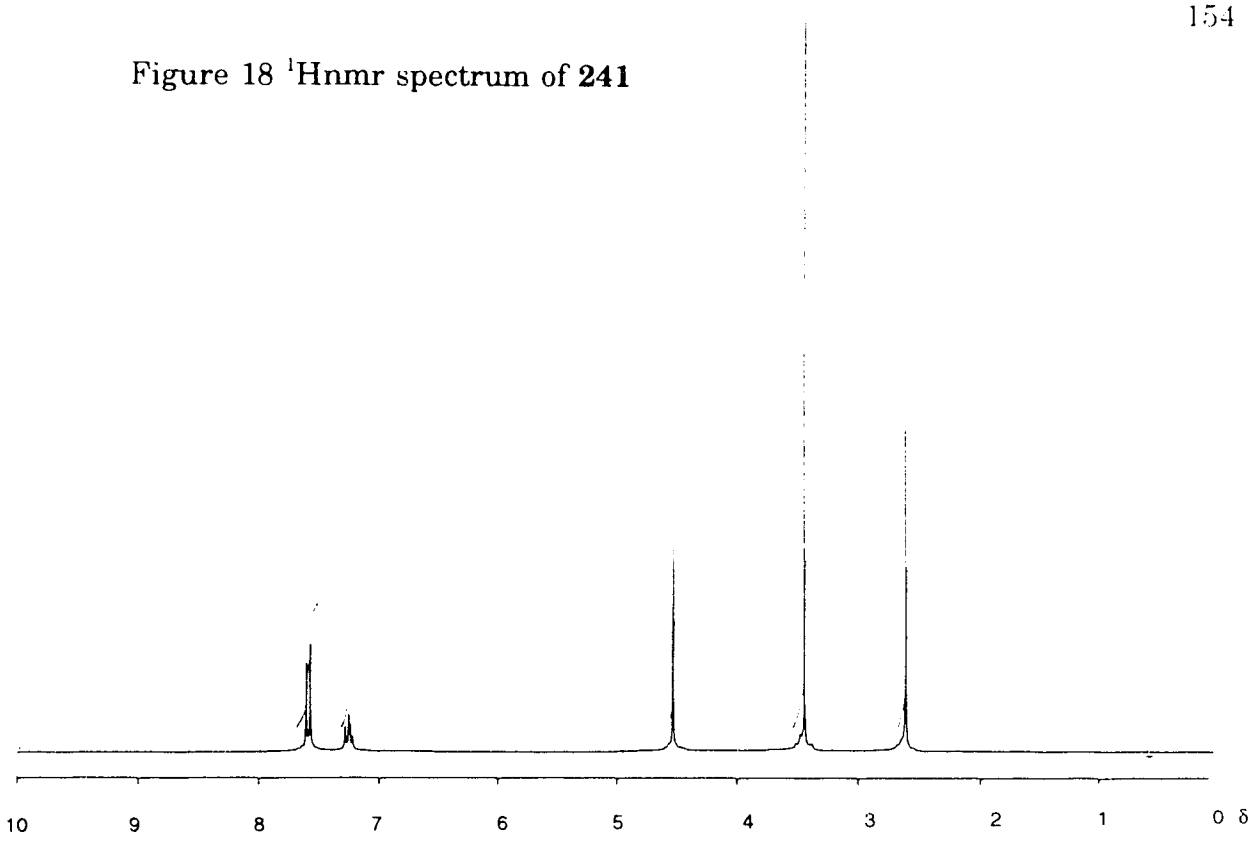
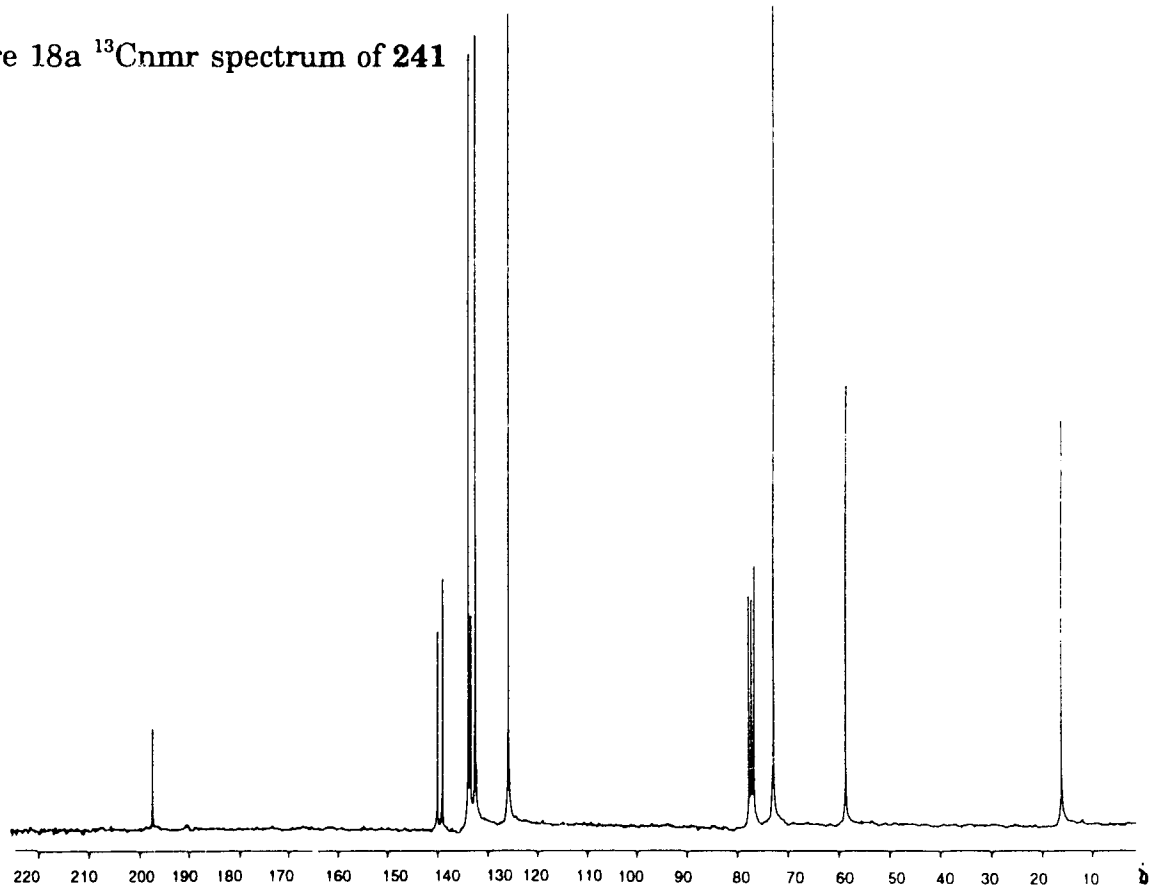


Figure 18a ^{13}Cnmr spectrum of **241**

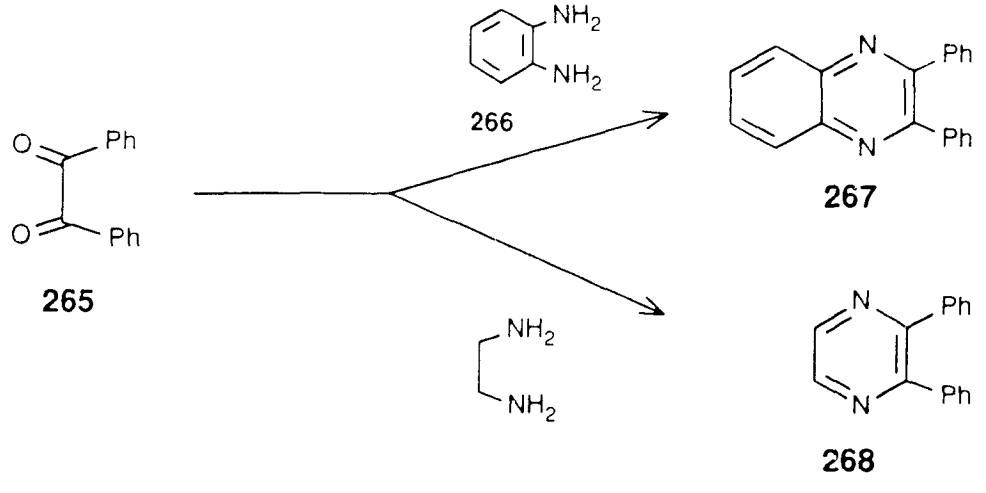


4.5 Significance of the diketone synthon 241

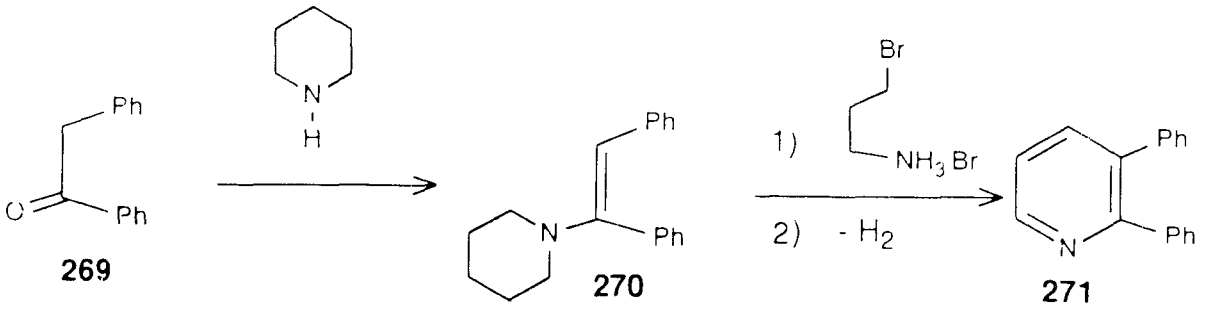
In the general introduction, we referred to a possible common intermediate for the syntheses of various [e]fused DMDHPs. In the previous sections, we described how we achieved the synthesis of the dione intermediate **241**. Before we describe our results on the use of this synthon in the synthesis of the quinoxalino DMDHP **279** it is appropriate to list some of the numerous possible uses of this diketone intermediate. We will use the parent compound, benzil, **265**, as the example for the reactions indicated below.

4.5.1 1,2-diketones in the synthesis of various aromatic rings

Nitrogen heterocycles such as pyrazines and quinoxalines are obtained easily by condensation of ethylenediamine and *o*-phenylenediamine respectively with a dione.[218]

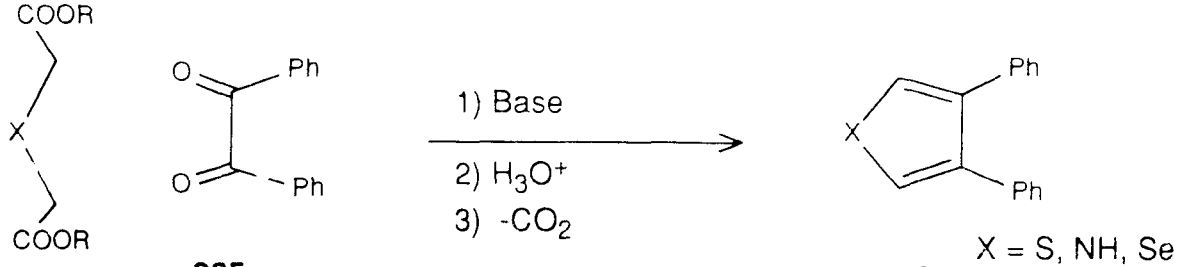


In a related sequence, a pyridine ring[219] could be constructed from desoxybenzene which in turn is easily obtained from a benzil.[220]



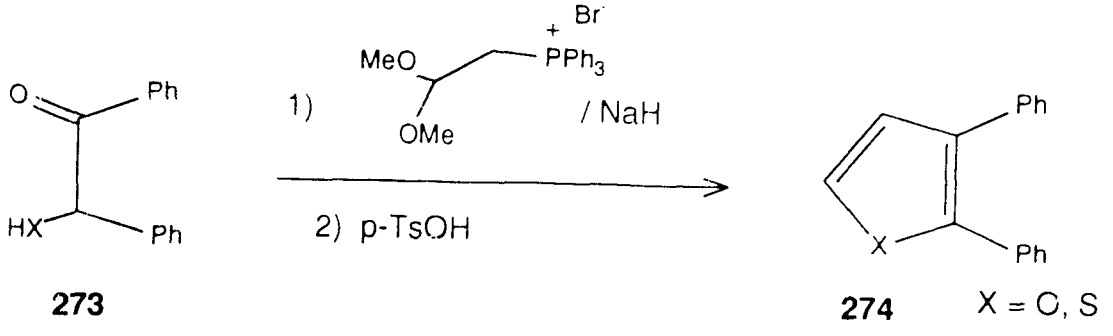
269 270 271

Aldol type condensation reactions of diones with appropriate esters result in 3,4-substituted five membered ring heterocycles.[221]



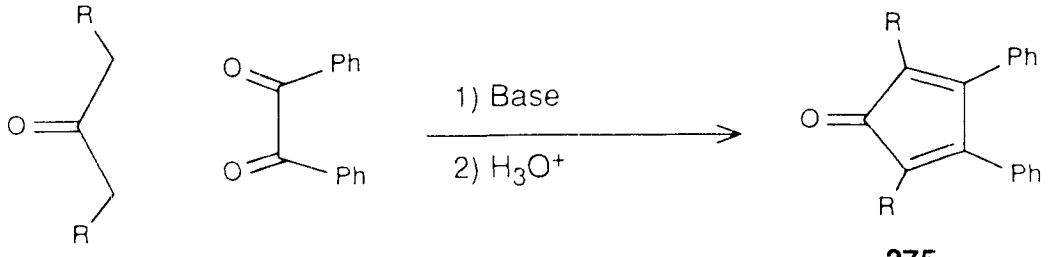
265 272

Benzoins which can be obtained by the reduction of the corresponding benzils[222] are useful in the syntheses of 2,3-substituted heterocycles.[223]



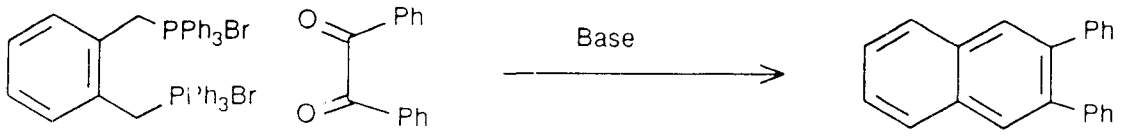
273 274

An useful electron deficient diene, cyclopentadienone, can easily be obtained from a 1,2-diketone.[224]



265 **275**

Polyacenes are also available from benzils through a double Wittig sequence, albeit in low yields.[225]

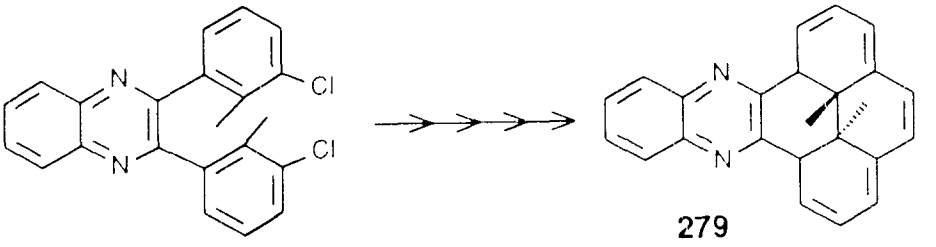


276 **265** **277**

The possible transformations of 1,2-diketones and their derivatives we have outlined above, involve only one or two steps and are generally high yielding. Many useful intermediates such as cyclopentadienes and thiophenedioxides can be obtained from 1,2-diketones and used in several subsequent reactions. We shall describe some of the model reactions we performed using the easily accessible dione **249** next.

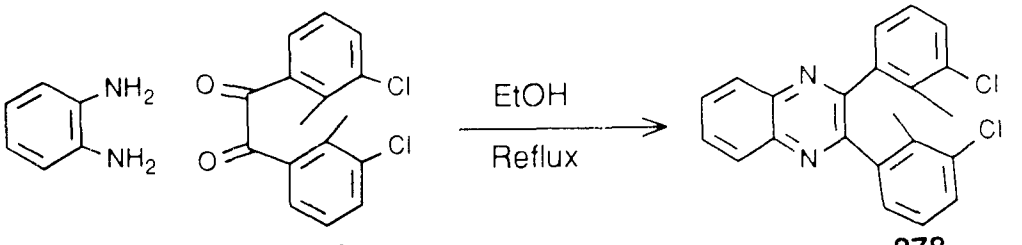
4.5.2 Some model ring syntheses using the dione 249

To demonstrate the feasibility of the 1,2-diketone intermediates in the syntheses of [e] fused DMDHPs, a couple of model syntheses were carried out using the readily available dione **249**. Condensation of 1,2-phenylenediamine with **249** proceeded readily to afford the quinoxaline teraryl **278**.



278 279

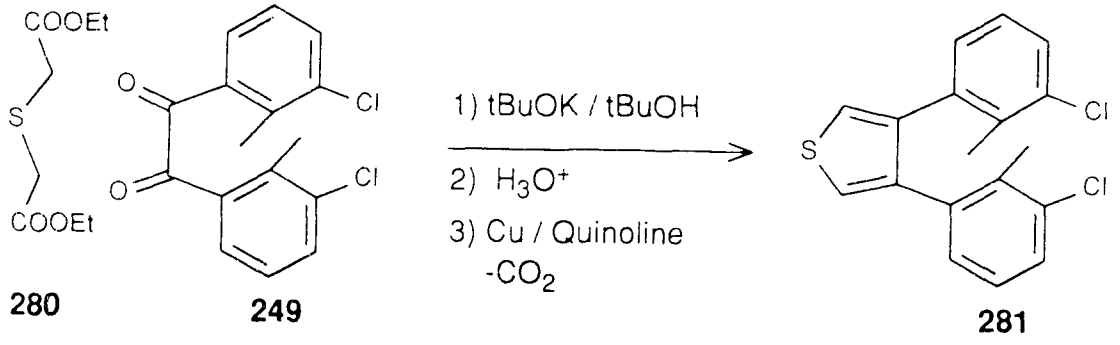
White crystals of **278**, mp 171-172°C, gave the correct molecular ion (M^+ 379) in the mass spectrum and a satisfactory analysis. In the ^{1}Hnmr spectrum, only a singlet was observed for the methyl protons at δ 2.17 ppm, at ambient temperature. We will discuss the V-T nmr experimental results in section 4.8. This teraryl **278** can be considered as a precursor to the [e] fused DMDHP **279** based on the earlier synthesis of the benzo[e]DMDHP, **53**, from the teraryl **84** (Scheme 2, page 38).



266 249 278

The thiophene teraryl **281** was synthesised through a Hinsberg synthesis[221b] of thiophenes. Thus, condensation of the thiodiacetate **280** with one equivalent of the dione **249** in the presence of *t*-BuOK, gave a dark, gummy solid which on heating in dry quinoline in the presence of copper

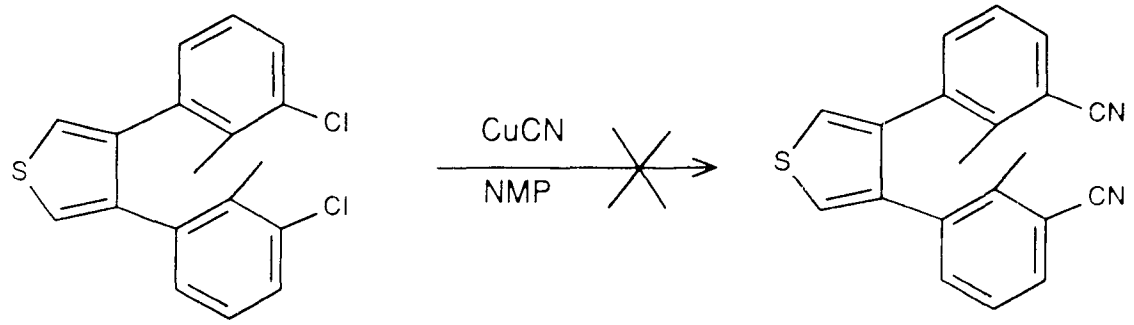
powder, resulted in the *o*-teraryl **281** in 30% yield.



280 **249** **281**

The teraryl **281** formed colorless needles, mp 152-153°C, from hexanes. It showed the correct molecular ions (M^+ 336, 334, 332) in the mass spectrum and also gave a satisfactory elemental analysis. In the ^{1}Hnmr spectrum, the methyl protons appeared as a singlet at 2.09 ppm at ambient temperature.

When an attempt was made to convert the dichloride **281** into the dicyanide **282**, it resulted only in the formation of a deep-blue, polar solid which could not be characterised by spectroscopic means due to its extreme insolubility in many common solvents.

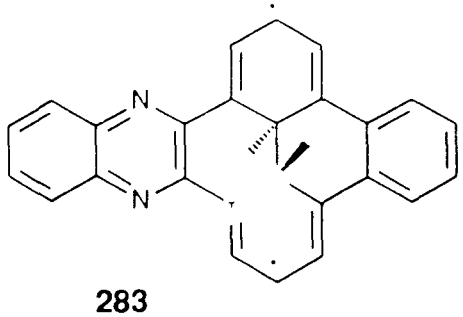


281 **282**

This result further emphasises the importance of the diketone **241** as an important intermediate which would eliminate the need for transformations involving harsh conditions.

4.6 Utility of 1,2-diketone 241 - synthesis of the quinoxalino dihydropyrene, 279

We chose to synthesise the quinoxalino DMDHP **279** to demonstrate the utility of the diketone synthon **241**. In addition to this we were interested to find out whether the chemical properties of this dihydropyrene **279** would compare with those of the isoelectronic naptho[e]dihydropyrene **58**.[94] The quinoxaline fused dihydropyrenes **283** and **284**, synthesised by Mitchell and Weerawarna[226] decomposed upon generation presumably because of their biradicaloid nature.[227] Hence, the synthesis of the dihydropyrene **279** was undertaken.



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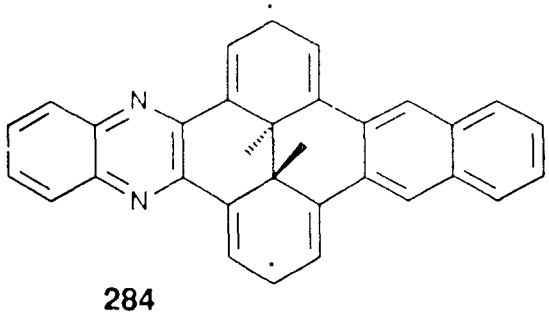
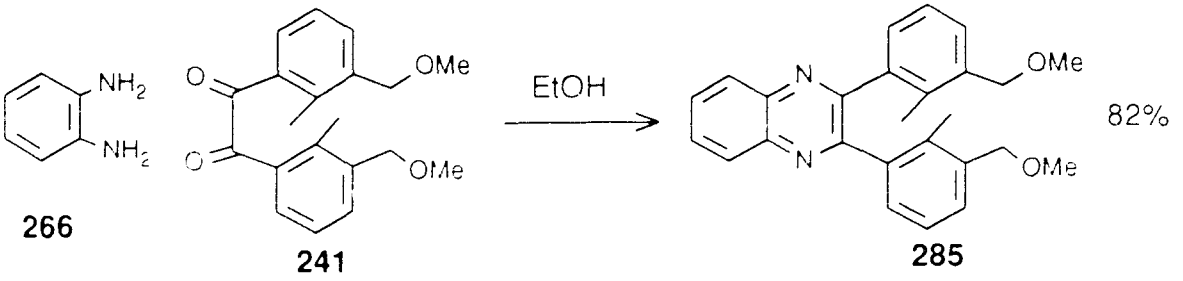


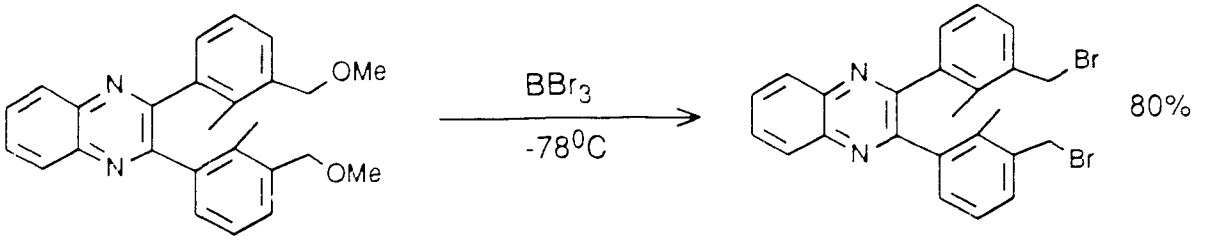
284

Condensation of the diketone **241** with excess *o*-phenylenediamine in dry EtOH yielded the *o*-teraryl **285** in 82% yield.



266 241 285

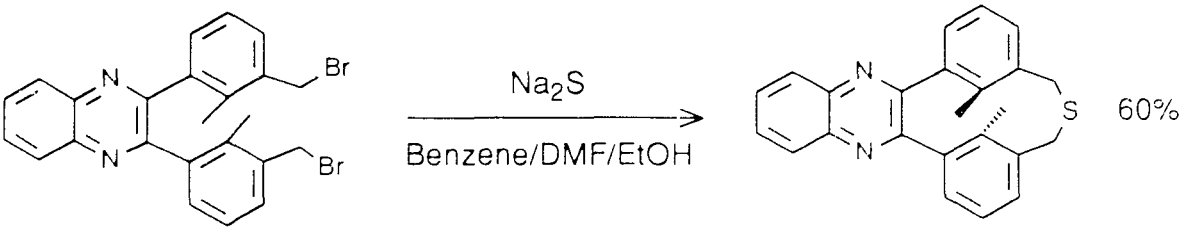
This compound **285**, mp 151°C, gave the correct molecular ion (M^+ 398) in its mass spectrum and a satisfactory elemental analysis. In its ^{1}Hnmr spectrum, the aryl protons of the quinoxaline moiety appear as multiplets centred at 8.18 ppm (H-5, H-8) and 7.81 ppm (H-6, H-9) and the aryl protons of the benzene ring appear as a multiplet at 7.27 - 7.02 ppm. The methylene protons appear as a singlet at 4.40 ppm whereas the methoxymethyl protons resonate at 3.27 ppm and the methyl protons at 2.08 ppm respectively as singlets. A total of ten carbon signals were obtained for the aryl carbons in the ^{13}Cnmr spectrum. The methylene carbon appeared at 72.8 ppm, the methoxymethyl carbon at 57.7 ppm and the methyl carbon at 15.8 ppm. The teraryl **285** was then converted into the corresponding dibromide **286** by treatment with BBr_3 at -78°C in 80% yield.



285 286

The gross structure of this dibromide **286**, mp 250-251°C, was determined from the correct molecular ion peaks (M^+ 498, 496, 494) in its mass spectrum and a satisfactory elemental analysis. In the ^{1}Hnmr spectrum, the protons of the bromomethyl group in compound **286** appeared as a singlet at 4.44 ppm. In the ^{13}Cnmr spectrum, the methylene carbon ($-CH_2Br$) appears at 32.2 ppm and the methyl carbon resonates at 16.0 ppm.

Coupling of the dibromide **286** with Na_2S, under high dilution conditions, resulted in the formation of the thiacyclophane **287**, in 60% yield. In this reaction, no dimer formation was observed.

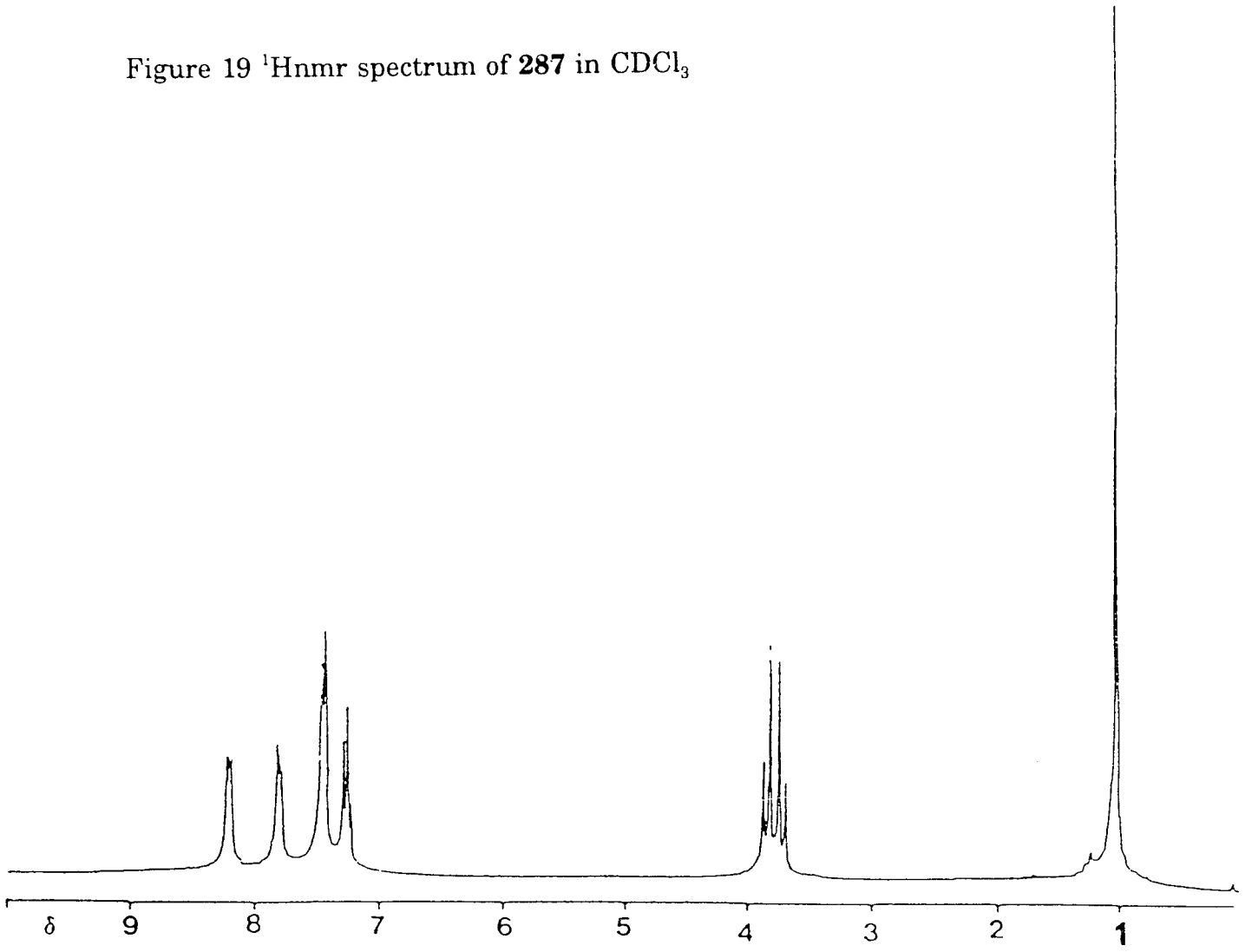


286 **287**

4.6.1 The structure of the thiacyclophane 287.

The gross structure of the thiacyclophane was confirmed from the correct molecular ion (M^+ 368) and a satisfactory analysis. Compound **287** formed bright-yellow needles from toluene-EtOH and melted at 233-234°C with decomposition. The *anti* configuration of **287** was determined from its nmr spectra and an X-ray crystal determination.

Figure 19 ^{1}Hnmr spectrum of **287** in $CDCl_3$



In the ^{1}Hnmr spectrum (see Figure 19), an AA'BB' multiplet centred at 8.2 ppm and 7.8 ppm, was observed for H-7,10 and H-8,9 protons of the quinoxaline ring. The phenyl ring protons appeared as a multiplet centred at 7.3 ppm. The bridge protons appear as a AB multiplet at 3.83 and 3.72 ppm with J_{AB} = 13 Hz. This AB pattern remained unchanged even when a solution of **287** in CS_2-CD_2Cl_2 (1:1 v/v), was cooled to -100°C, indicating that the sulphur wobbling was present even at that temperature. The methyl protons appeared as a singlet at 1.02 ppm showing appreciable shielding due to the *anti* orientation. Nine carbon signals were observed for the aryl carbons of the cyclophane in the ^{13}Cnmr spectrum. The bridge carbon appeared at 30.6 ppm and the methyl carbon at 17.6 ppm.

To further confirm the *anti* configuration of **287**, a single crystal X-ray structure determination was undertaken. Single crystals of **287** were grown from a toluene-EtOH (1:1 v/v) solvent system by slow evaporation and the crystal structure determination was carried out by Kathy Beveridge at the University of Victoria. An ORTEP diagram of the structure of **287** is shown in Figure 20.

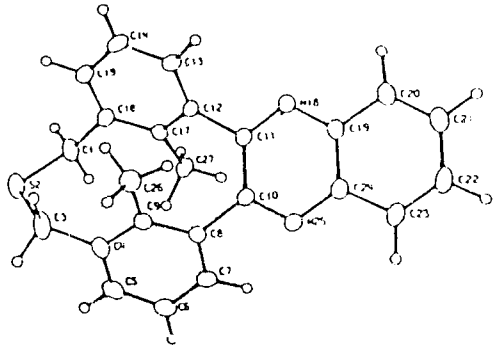
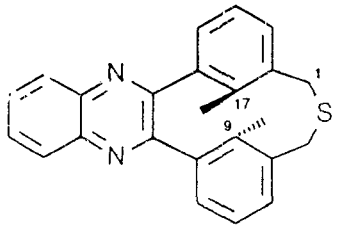


Figure 20. ORTEP diagram of an X-ray structure of **287**.

The X-ray structure clearly revealed the *anti*-stepped geometry of the thiacyclophane **287** in the solid state. As seen in other *anti*-[2_2] and [3_2]metacyclophanes,[228] the aromatic rings are bent outward in a slightly distorted boat shape. Deviations of the inner carbons (C9 and C17 in **287**, C9 and C17 in **288**,[228] C9 and C18 in **289**,[230] C8 and C16 in **290**[229]) from their basal planes (α) are observed to be much larger than those of the outer carbons (β) in these molecules (see Figure 21). Clearly, the largest steric compression occurs between the two inner carbons which are very close to one another in space and this is reflected in the large deviation of the inner carbons from the basal plane of the phenyl rings. As observed by Zhang,[228] the deviations of the inner carbons from their corresponding basal planes were inversely proportional to the corresponding distances between the two inner carbons (Table 18).



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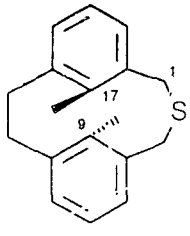

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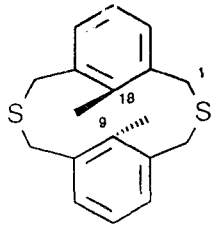

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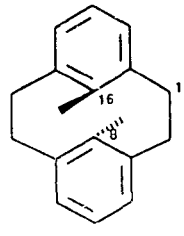


290

Table 18 Comparison of deviations in cyclophanes **287**, **288**, **289** and **290**

Compound	Distances (Å)		Angles (°)		Distance (Å)
	d_1	d_2	α	β	between inner C
290	0.187	0.088	15.4	7.3	2.68
287	0.132	0.055	10.4	4.8	2.88
288	0.126	0.041	10.2	3.3	3.01
289	0.077	0.029	6.4	2.6	3.24

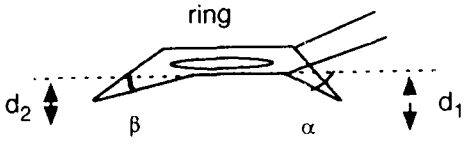


Figure 21. Description of α, β, d_1 and d_2

From Table 18, it can be seen that the deviation of the inner carbons increases when the distance between the inner carbons is reduced. The inner carbon distance in turn depends on the bridge length of the cyclophane. Thus, among the four cyclophanes, the [2_2]metacyclophane **290** is the most strained because of the shortest bridge length while the [3_3]thiacyclophane **289** is the least strained due the longest bridge length. Cyclophane **287** is more strained than the [2_3]metacyclophane **288** due to the presence of a shorter two carbon bridge formed by sp^2 carbons in **287**. In cyclophane **288**, the C_{10}-C_{11} bond

length is 1.54Å while it is 1.37Å in cyclophane **287**. The inner carbon distance in **288** is 2.88Å indicating that the strain is felt mostly by the inner carbons due to steric crowding. This distance is lower than that in **288** (3.01Å) because of the constriction brought about by the shortening of one of the bridges in **287**. In addition to the bond length factor, the strain imparted on the phenyl rings due to the twisting of the phenyl rings seems to be higher. The more pronounced phenyl-phenyl sliding in **287** is reflected by the dihedral between the phenyl planes in **287** (16.1°) which is higher than the corresponding dihedral (11.9°) in **288**. One other interesting comparison between the [2$_3$]metacyclophanes **287** and **288** is the plane projected distances of their internal methyl carbons (Figure 22).

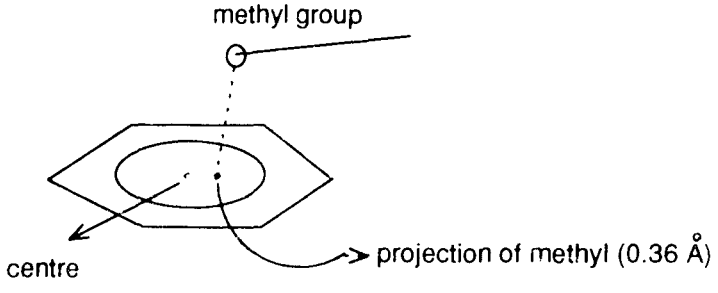


Figure 22 Plane projection of internal methyl on to the opposite ring.

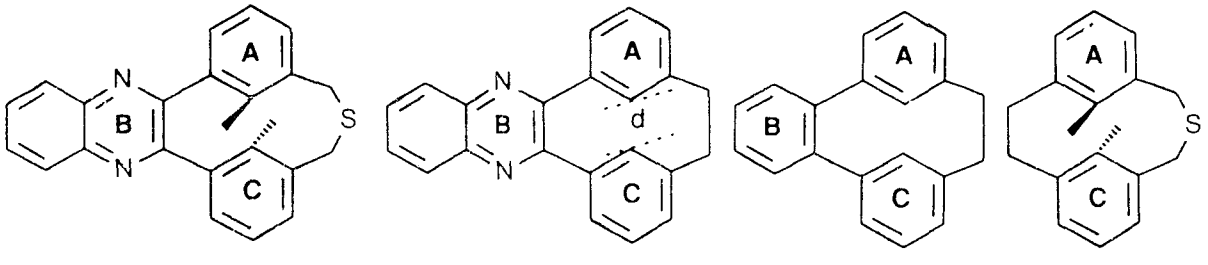
The C26-plane distance in **287** is 3.03Å with the C26 carbon at 0.36Å off the centre of the phenyl ring. The corresponding values for **288** are 3.13Å and 0.35Å,[228] almost identical to those of **287**. The value of the methyl proton chemical shifts of **287** and **288** are 1.02 ppm and 0.85 ppm respectively,

indicating that the *anti* geometry is maintained in the solution state as well by these molecules.

Comparison of the torsional angles (Table 19) of the ABC planes in **287**, **288**, **291**[231] and **292**,[231] revealed that the extent of twisting of the planes in **287** is higher than that in the others. This implies that the helicity of **287** is more pronounced than ethano bridged cyclophane **291** with internal hydrogens. This may be due to the presence of methyl groups which act as an extension of the A and C planes in **287** and thus bring about an increased twist in the helix. The torsion angle between the B and C planes in **287** is 49° which higher than the corresponding value in the [2_2]cyclophane **291** (40°).

Table 19 Comparison of torsional angles in **287**, **291**,[231] **292**[231] and **288**.

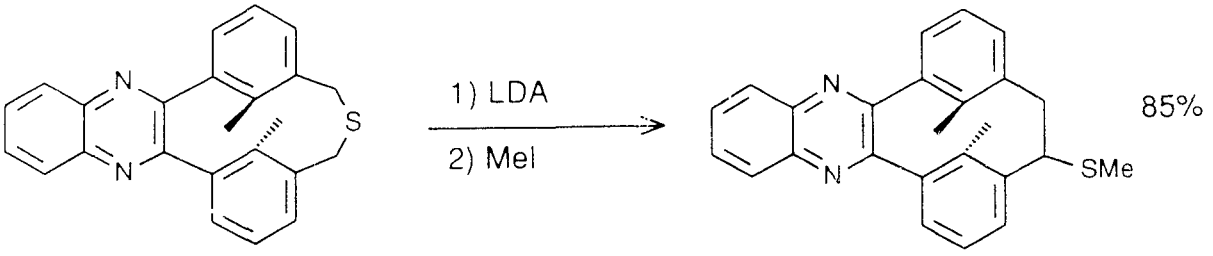
Compound	**287**	**291**	**292**	**288**
Torsion angle ABC (°)	16.1	3.6	11.0	11.9
Torsion of B and C from plane A (°)	49	40	48	--
Inner carbon distance d (Å)	2.88	2.58	2.58	3.01



287 **291** **292** **288**

4.6.2 Synthesis of the dihydropyrene 279

The *anti*-thiacyclophane **287**, upon Wittig rearrangement with excess LDA followed by methylation with CH_3I, produced a single isomer, **293**, of the ring contracted cyclophane.



287 **293**

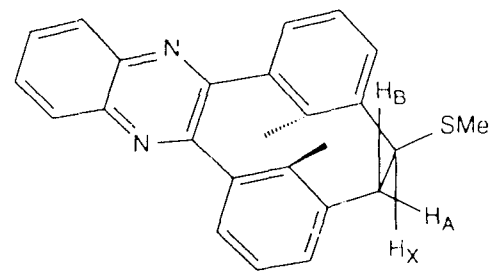
The gross structure of the cyclophane **293**, mp 122-124°C, was confirmed from its molecular ion peak (M' 354) in the mass spectrum and a satisfactory analysis. The isomer **293** was assigned the pseudoequatorial structure based on its ^{13}Cnmr and ^{1}Hnmr spectra. The ^{13}Cnmr spectrum showed only one $-SCH_3$ peak at 15.9 ppm with the internal methyl carbons appearing at 17.3 and 17.2 ppm. The $-CH_2-$ and the -CH- carbons of the bridge appear at 45.1 ppm and 54.2 ppm respectively. This indicated the presence of only one isomer. In the ^{1}Hnmr spectrum, a singlet for the $-SCH_3$ at δ 2.19ppm, together with a singlet for the internal methyl protons at δ 0.75ppm, indicated it to be a pseudoequatorial isomer, where neither internal methyl group is deshielded from the other, as would be the case if the $-SCH_3$ group were pseudoaxial.[38] In the case of the benzo and naphtho analogs of **293**, also a single isomer is formed.[202, 94] This formation has been rationalised in terms of

unfavourable interaction between an axial -S- and the aromatic methyl group.[202]

H_X δ 3.87 J_{XB} = 11Hz, J_{XA} = 3Hz

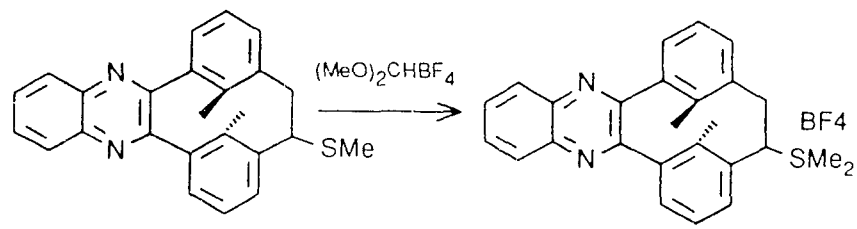
H_A δ 3.27 J_{AB} = 12Hz, J_{AX} = 3Hz

H_B δ 2.56 J_{BA} = 12Hz, J_{BX} = 11Hz



293

Conversion of **293** to the salt **294** was achieved with Borch's reagent, in 80% yield. Treatment of the unstable **294** with excess *t*-BuOK in dry THF at 50°C, in the absence of light, yielded the green DMDHP **279**.



293 **294**

Rapid chromatography of the crude reaction mixture on deactivated SiGel, under argon, gave a ~10% yield of the DMDHP, as a green, unstable semisolid which decomposed at ~80°C. The compound gave the correct molecular ion (M^+ 334) in the mass spectrum and showed a base peak at 304 due to the successive loss of two methyl groups. The characteristic internal methyl protons of the dihydropyrene appear at δ - 0.72 ppm as a singlet. A pure sample of **279** could not be obtained as it decomposed very rapidly. A solution of **279** in degassed CD_2Cl_2 was moderately stable and a proton nmr

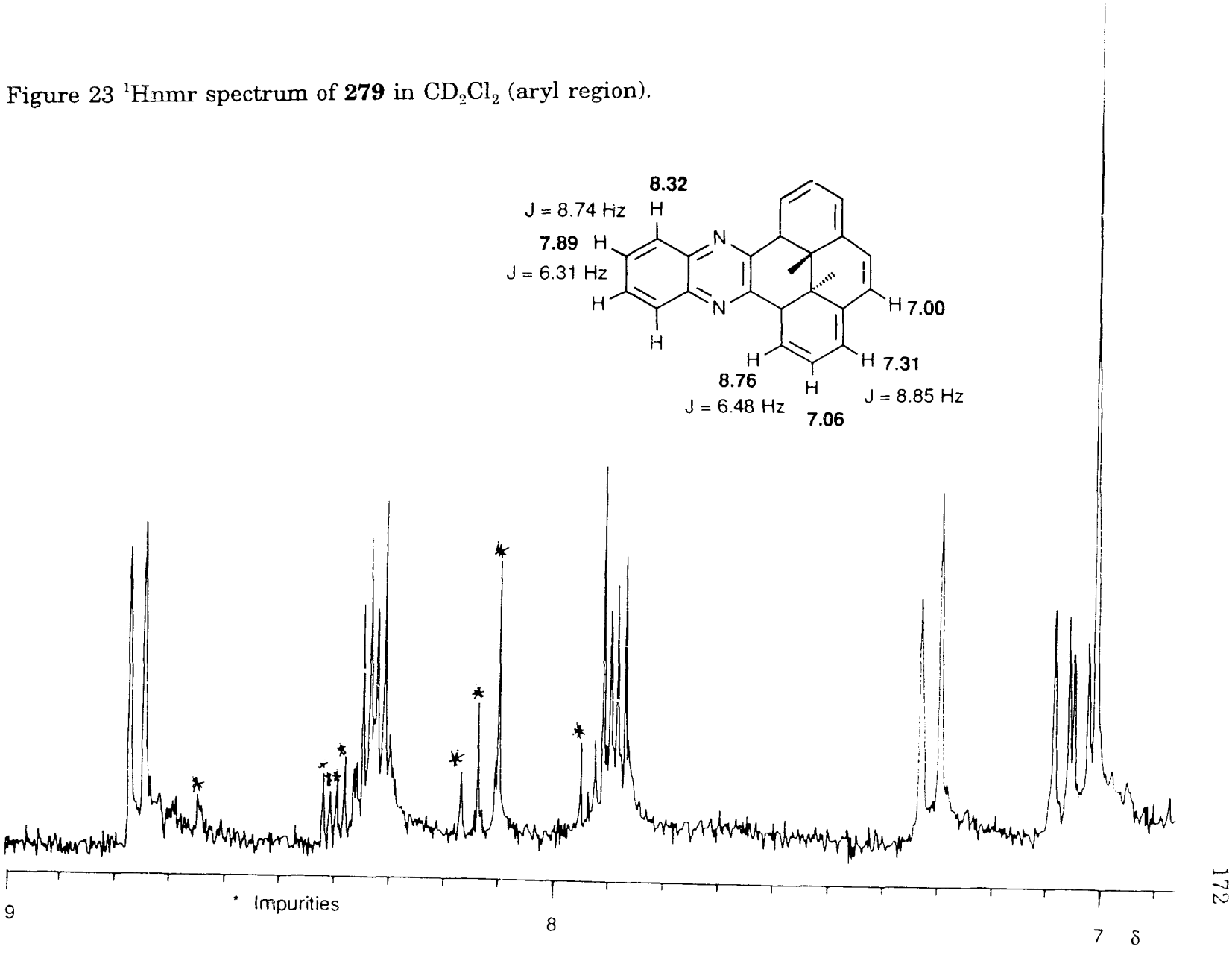
spectrum of **279** together with a small amount of an unknown impurity could be recorded.

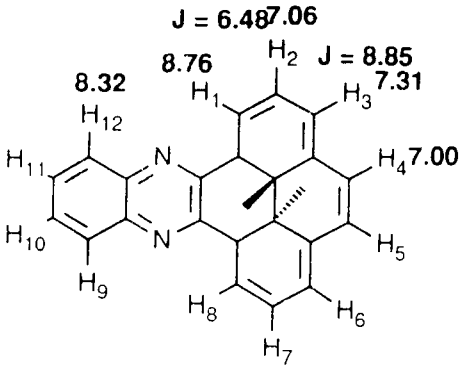
4.6.3 ^{1}Hnmr spectrum of the dihydropyrene 279 and comparison with the naphtho[e]dihydropyrene 58

The aryl region of the ^{1}Hnmr spectrum of **279** in CD_2Cl_2 is shown in Figure 23, together with the assignments. The protons are assigned on the following basis: H-4,5 (see page 172) appear, as expected, as a singlet at δ 7.00. The bay protons of **279**, H-1,8 appear as a doublet at δ 8.76 and are the most deshielded protons. H-1,8 experience an additional deshielding from the adjacent nitrogens on the quinoxaline ring. H-9,12 are seen as part of a AA'XX' multiplet centred at δ 8.32. The other part of the AA'XX' multiplet, corresponding to H-10,11 is observed at δ 7.89. The signal corresponding to H-3,6 is as expected a doublet and appears at δ 7.31, J = 8.85 (coupled to H2,7, respectively), with the *meta* coupling to H-1,8, respectively, too small to be observed. The doublet of doublets which would be expected for H-2,7 is observed at δ 7.06 and the signal due to H-4,5 appears close to the most upfield peak of the doublet of doublets at δ 7.00.

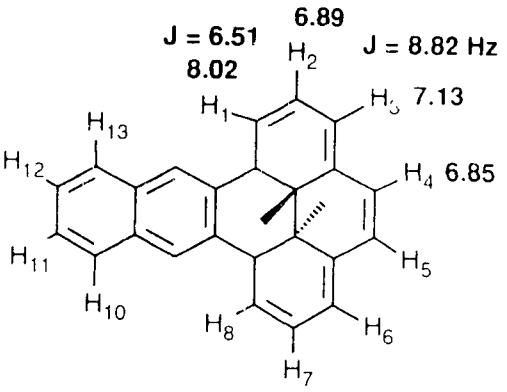
There is a striking resemblence between the ^{1}Hnmr data of **279** and that of the naphtho[e]dihydropyrene **58**. The structures of **279** and **58** together with their ^{1}Hnmr data are shown in Figure 24.

Figure 23 ^{1}Hnmr spectrum of **279** in CD_2Cl_2 (aryl region).





279



58

Figure 24 ^{1}Hnmr data of **279** and **58**.

The ^{1}Hnmr spectrum of **58** has been predicted by Vogler by means of semiempirical quantum chemical procedures.[85] Comparison of the predicted and experimentally obtained chemical shifts for **58** has been made by Venugopalan.[94] The predicted chemical shifts of the external protons and those observed (in $CDCl_3$) for **58** and the observed chemical shifts of the corresponding protons of **279** are presented in Table 20. For clarity, only the data for the external protons of the macro ring are compared. As can be seen, there is general aggreement between the predicted and the observed shifts. The only deviation from Vogler's prediction (in terms of the order in which the protons appear downfield from TMS) involves the protons H-4,5. While H-2,7 are predicted to be the more shielded protons, H-4,5 are observed to be more shielded. This discrepancy has been rationalised in terms of the deviation of H-4,5 from the mean molecular plane which is the largest observed for the protons affected by the inclusion of the bridge carbons.[94] The additional shielding experienced by H-1,8 of **279** due to the nitrogens on the quinoxaline

ring would account for the large difference (1.04 ppm) between the calculated and observed chemical shifts.

Table 20 Comparison of predicted and observed chemical shifts of **58** and **279**

Proton	Predicted[85] shifts δ	Observed[94] δ **58**	Observed δ **279**
2,7	7.06	6.89	7.06
3,6	7.09	7.13	7.31
4,5	7.19	6.85	7.00
1,8	7.72	8.02	8.76

A bond order-chemical shift correlation incorporating the internal methyl chemical shift for **279** was made and the results are presented in Table 21. As can be seen from the Table, there is a good corelation between the predicted and observed chemical shifts. This reflects a good agreement between the change in chemical shift shielding of the internal methyls with the change in the bond orders of the macro ring. The π-SCF bond orders calculated for **58**[94] are used. The observed internal methyl chemical shift for **279**, at δ -0.72 is almost identical to that of **58**, which occurs at δ -0.74. This indicates the bond fixing ability of the quinoxaline ring is exactly the same as that of naphthalene.

Table 21 Coupling constants, Bond orders and calculated Chemical shifts for **279**.

Bond	J	$\rho_J \times 10^3$	$\rho_{\pi SCF} \times 10^3$
A	8.85	804	747
B	6.48	540	528
Δr		132	120
$\Delta\delta_{calc}$		1.91	2.22
$\delta_{calc} = 0.97-\Delta\delta_{calc}$		-0.94	-1.25

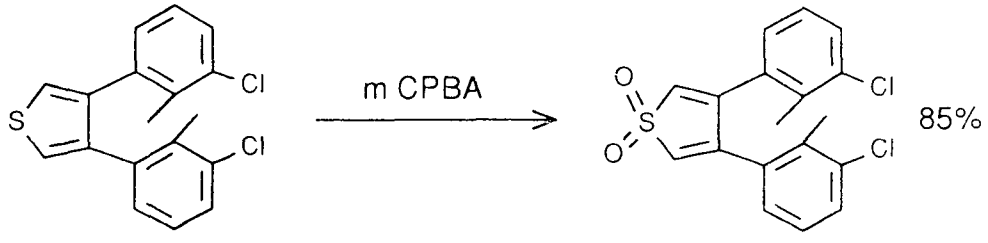
From the linear correlation of the chemical shift shielding and the RE of the annelating ring, obtained by Venugopalan[94], we can conclude that the resonance energy of quinoxaline is almost the same as that of naphthalene. This is in fair agreement with the values obtained by other methods.[62] The effect of nitrogens on the ring current of the quinoxaline moiety being the same as those of carbon atoms.

The unstable nature of **279** could be due to the anthracene like structure of **279** which promotes biradicaloid nature in acenes. In addition the presence of two nitrogens in **279**, would make it more prone to protonation and subsequent decomposition of the compound.

4.7 Syntheses using thiophene-1,1-dioxide- Formation and some reactions of the thiophenedioxide 296.

As shown in section 4.5.2, the thiophene teraryl **281** can be synthesised easily, using the Hinsberg synthesis. We wanted to explore the possibility of oxidising **281** to the dioxide **296**, and its use in the syntheses of some novel aromatic ring systems.

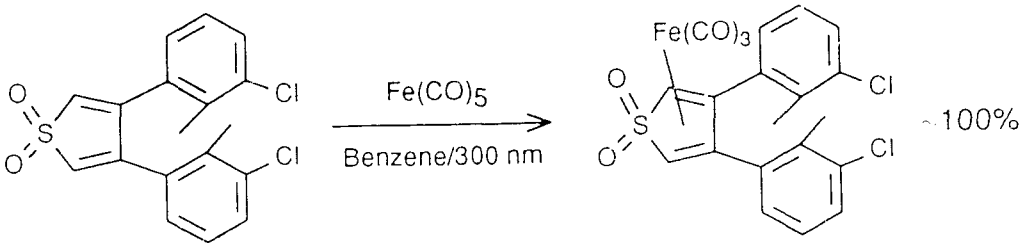
Oxidation of the thiophene **281** with excess of *m*-CPBA, in 1,2-dichloroethane, produced the thiophenedioxide **296** in 85% yield.



281 **296**

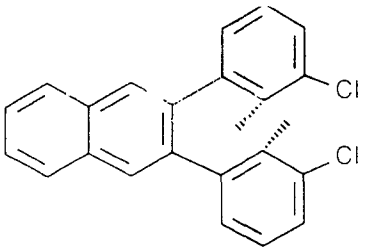
The dioxide **296** formed colorless crystals and melted, with decomposition, at 171-173 °C. Its structure was confirmed from its molecular ion peaks (MH$^+$ 368, 366) in its mass spectrum and a satisfactory elemental analysis. In the ^{1}Hnmr spectrum, the methyl protons of **296** appear as a singlet at 2.13 ppm. This compound is indefinetly stable at room temperature but decomposes at > 100 °C in solution or at > 170 °C in the solid state.

The thiophenedioxide **296**, when reacted with $Fe(CO)_5$ in benzene using 300 nm light, gave the iron tricarbonyl complex **297** in quantitative yield.

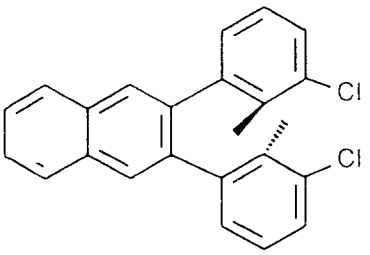


296 **297**

The complex **297** was obtained as yellow needles from the reaction mixture by direct recrystallisation. This complex melted at 250-252 C with decomposition. Its structure was determined from the molecular ion peaks (MH^+ 507, 505) in its mass spectrum and correct elemental analysis. The ^{1}Hnmr spectrum of **297** exhibited a multiplet at 7.33-6.92 for the phenyl protons, a doublet at 4.33 ppm (J = 1.7 Hz) for the thiophene protons and a singlet at 2.52 ppm for the methyl protons. In the ^{13}Cnmr spectrum, the carbonyl carbons appeared at 205.9 ppm and the methyl carbons at 17.8 ppm. Both the ^{1}Hnmr and ^{13}Cnmr spectra of **297** showed no variation in the chemical shift of the methyls with temperature, indicating no rotation of the phenyl rings in the molecule. This was very interesting because all the related teraryls such as **298**, synthesised so far, showed variable temperature nmr behaviour. As well, a crystal structure determination of the teraryl **298** had shown the presence of both *syn* **298a** and *anti* **298b** in the unit cell.[91]



298a



298b

We thus decided to determine the solid state structure of the complex **297**. Single crystals for X-ray structure were grown using a toluene-CH_2Cl_2 (5:1) solvent system under a nitrogen atmosphere. The structure determination was carried out by Kathy Beveridge at the University of Victoria. An ORTEP diagram of **297** is shown in Figure 25.

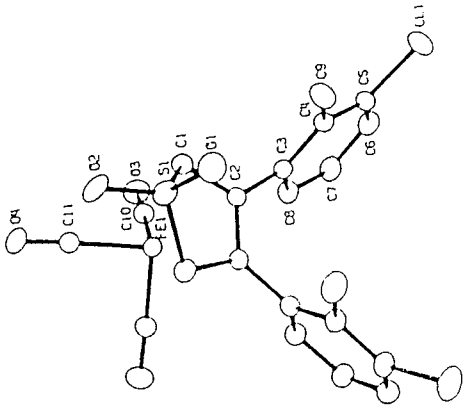
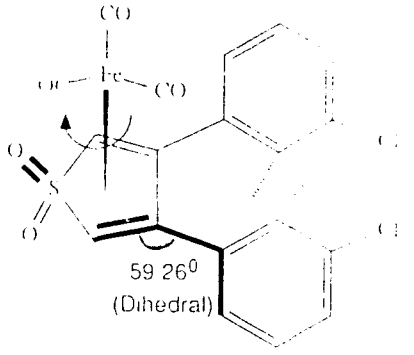


Figure 25 ORTEP diagram of an X-ray structure of **297**.

The X-ray structure clearly showed a *syn* conformation for the the complex **297**. The phenyl rings are twisted at angle of 59.26° with respect to the thiophene ring. The methyl groups point away from the iron tricarbonyl moiety because of steric reasons. The rotation of the iron tricarbonyl moiety seems to win over the rotation of the phenyl rings, thus fixing the conformation of **297** as *syn*.



297

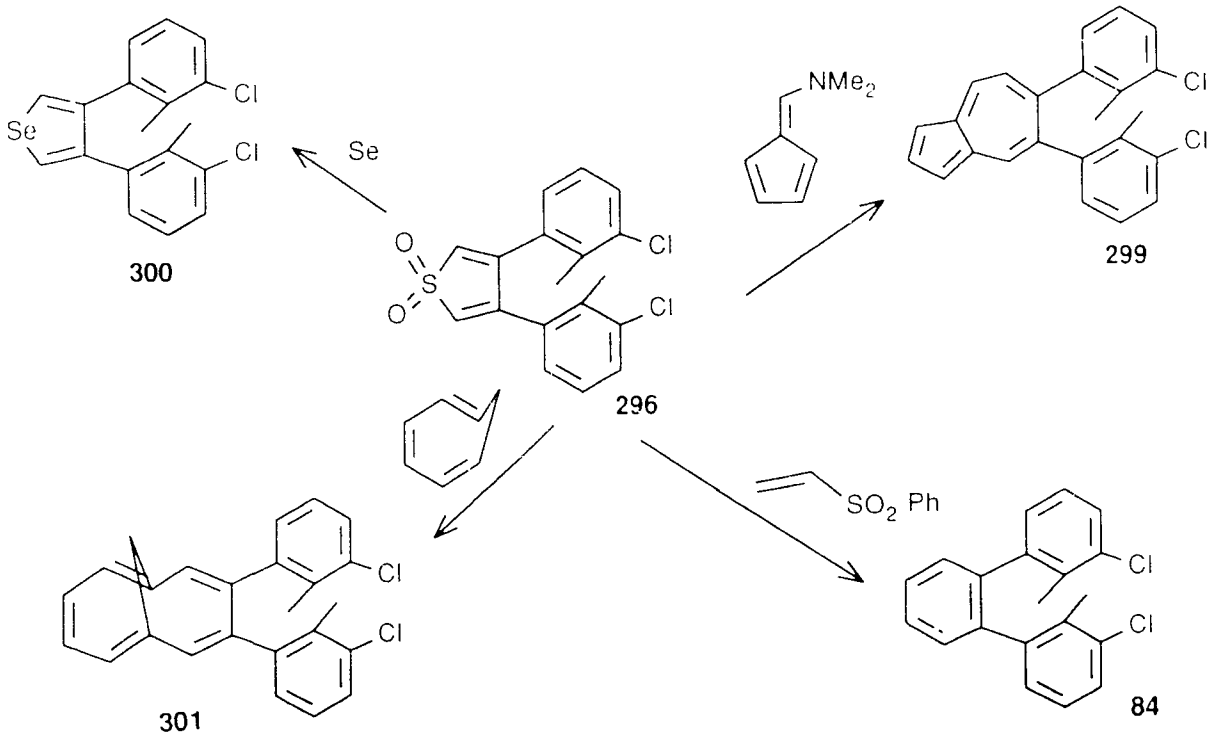
The crystal parameters and data for the bond lengths and angles for **297** are collected in the appendix.

Several other model reactions of the thiophenedioxide **296** resulted in the formation of various aromatic rings as shown in Scheme 23.

Reaction of N,N-dimethyaminofulvene with **296** resulted in the formation of the blue azulene **299** in 8% yield. The structure **299** was identified from the molecular ion peaks in its mass spectrum, and a characteristic U.V. band at 550 nm for azulene. The ^{1}Hnmr spectrum of this azulene teraryl showed two sets of singlets at 2.22, 2.20/2.13, 2.07 ppm (2:1 ratio) for the methyl protons, indicating the presence of both *anti* and *syn* conformers of **299** at ambient temperature.

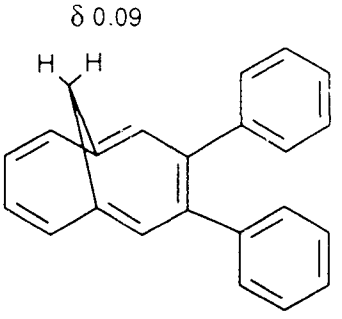
Heating the thiophenedioxide **296** with phenylvinylsulphone, in xylene, yielded the known teraryl **84** in 80% yield. The reaction involves a D-A reaction followed by SO_2extrusion and sulfinic acid elimination to give the product. Compound **84** thus obtained was found identical in all respects to an authentic sample.[99]

Scheme 23



When a mixture of **296** and excess of selenium powder was pulverised and heated to 200°C, the selenophene **300** was obtained as the only product in 50% yield. The selenophene **300** formed colorless needles (mp 182-185°C) which turned grey over a few days. In the ^{1}Hnmr spectrum, the H2 proton appeared as a singlet at 2.07 ppm. The mass spectrum showed several molecular ion peaks (MH^+ 384, 383, 381, 379, 377, 375) due the presence of several isotopes of selenium.

In a preliminary experiment, a sample of the thiophenedioxide **296** was heated, at reflux, in neat cycloheptatriene which resulted in a yellow gum. This product was considerably nonpolar with respect to the thiophenedioxide. It was not purified further. The ^{1}Hnmr spectrum of the gummy material showed the presence of aryl protons and a singlet at 0.097 ppm. In comparison with the chemical shift of the methylene protons of the methanoannulene **302**, which occur at 0.09 ppm, the presence of **301** in the product mixture was discerned.



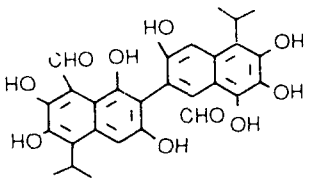
302

4.8 Barrier to rotation in *o*-teraryls

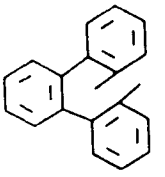
4.8.1 Introduction

The non-coplanar arrangement of the two benzene rings in biphenyl and its derivatives was recognised several decades ago.[232] The theory of restricted rotation about single bonds joining the two benzene rings matured only twenty years later.[233] Atropisomerism in numerous substituted biphenyls, evident from the optical resolution of enantiomers, has become an extensively investigated area.[234] Many biaryl derivatives are of paramount chemical[235] and

biological[236b] importance. For example, the binaphthyl, gossipol (below) is being evaluated as a potential male oral contraceptive.[236b]



GOSSIPOL



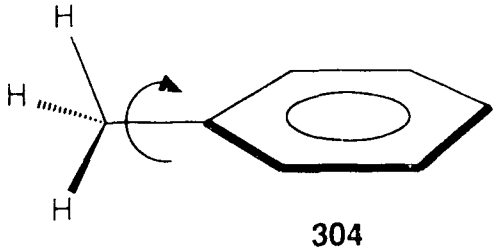
303

Restricted rotation is also expected to be observed in polyphenyl systems,[237] for example, in *o*-teraryls, leading to the existence of rotational isomers when appropriate substituents are present in the aryl rings. This phenomenon has been demonstrated in the conformational studies of 1,2-di-*o*-tolylbenzene **303**. In 1980, Mitchell and Yan reported the barrier to rotaion for a series of 2',2"-dimethyl-*o*-terphenyls to be in the range of 69-75 kJ/mol.[238] Recently, Lai and coworkers have reported the barrier to rotation in similar diphenylphenanthrene derivatives as 115-158 kJ/mol.[239] The presence of the methyl groups, which act as a ^{1}Hnmr handle, allows the rotational process to be followed, easily by ^{1}Hnmr.

In the foregoing sections, we described the syntheses of the *o*-teraryls **278**, **281**, **299** and **300** as models towards the syntheses of various [e]annelated dihydropyrenes. These compounds will allow the study of their general conformational behaviour.

4.8.2 Rotational isomerism and experimental estimation

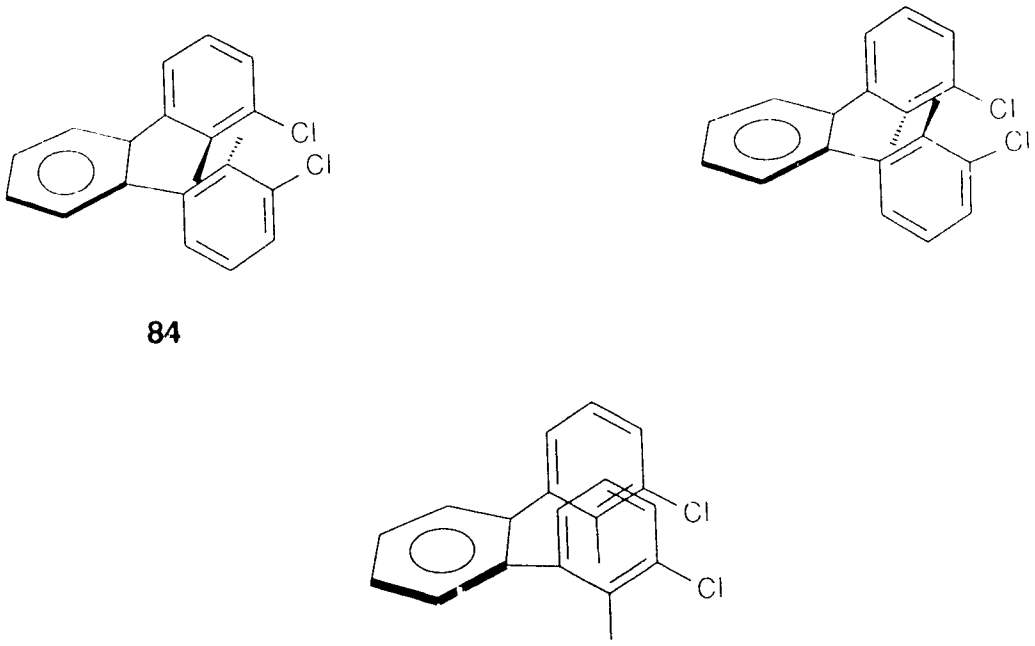
The two types of methyl protons in the *syn*-isomer **303a** and the *anti*-isomer **303b** are in different magnetic environment and thus would be expected to appear at different chemical shifts. The observation of two well resolved singlets, in the ^{1}Hnmr spectrum (at -80°C), for the methyl protons at the 2', 2''-positions of **84**, has been attributed to the presence of syn and anti isomers.[238] In addition, as we mentioned earlier, the presence of syn and anti isomers of **298** has been demonstrated, at least in the solid state.[94] The C-C rotation about the C_{Phenyl}-CH_3 bond can be neglected as this rotation is too fast to be observed by nmr. For example, in toluene, **304**, no change in the methyl proton signals could be observed even at -100°C.[240]



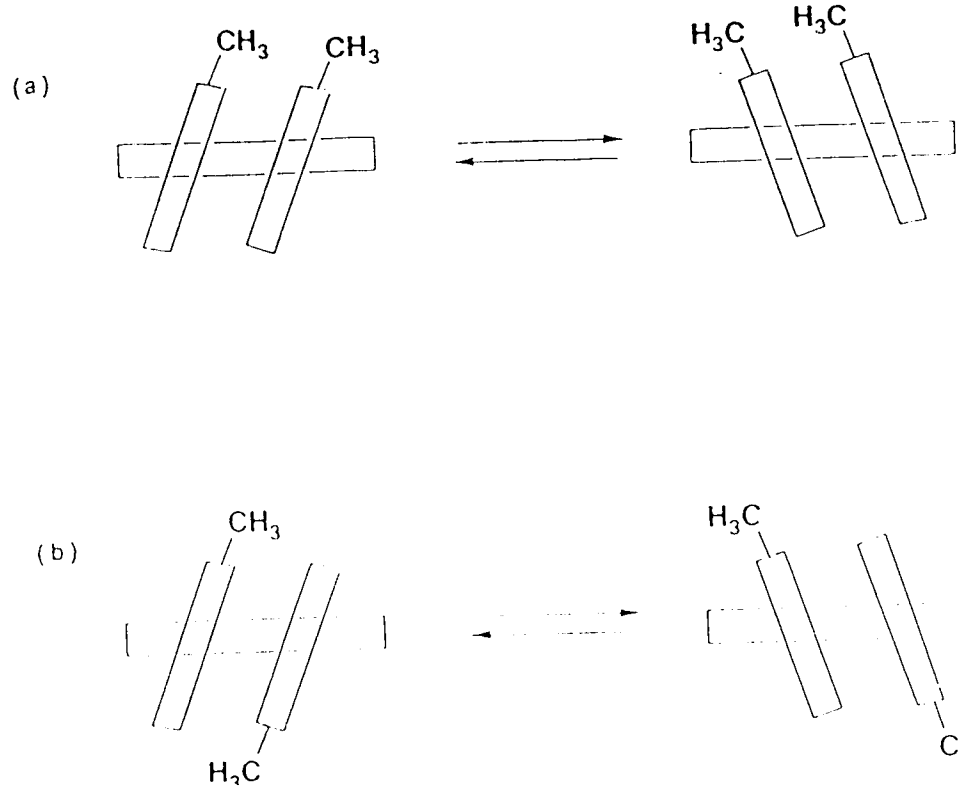
304

The two tolyl rings in **84** are expected to tilt at an angle to the benzene ring, similar to biphenyl systems.[241] Flipping process[242] of the tolyl rings could then occur as shown in Figure 26. The presence of a mixture of these conformers would, in principle, result in several methyl signals in the ^{1}Hnmr spectrum. It is, however, believed that there are no substantial barriers[243] to these processes and thus the equilibria should be fast within the NMR time scale. The rapid interconversions will then result in two averaged singlets for the methyl groups of the *syn* and *anti*-isomers of **84**, respectively.

Figure 26 Flipping processes in *o*-teraryls.



84



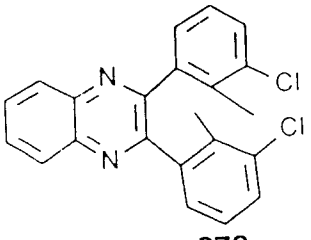
These methyl signals are observed at ~0.2-0.4 ppm upfield from the methyl signal of toluene (δ 2.37),[241] presumably due to a small shielding effect of the opposite tolyl ring and/or the benzene ring. However, an unambiguous assignment of the two singlets to the syn and anti isomers of **84** based on the chemical shift difference would be impossible.

An estimation of the energy barrier for the interconversion process between syn and anti described above could be obtained using the coalescence temperature (T_c) method.[245] In this study, a dilute (5%) solution of the respective teraryl in a mixture (1:1 v/v) of $CDCl_3$-CD_2Cl_2 were used to record the ^{1}Hnmr spectrum. The frequency of separation ($\Delta\nu$) was determined at the lowest temperature and using the T_c the transition state free energy at coalescence, $\Delta G^{\ddagger}$, was then calculated from the following equation:[245, 246]

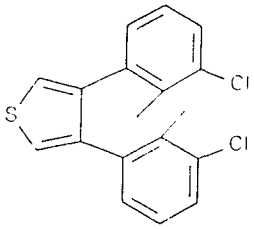
$$\Delta G^{\ddagger} = 0.019T_c (9.972 + \log T_c/\Delta\nu) \text{ kJ mol}^{-1}$$

This equation applies only to equally intense exchanging sites. In the compounds used in this study with the exception of compound **299** (two sets of methyl signals in a ratio of 2:1 is observed for **299**), the ratio of peaks for the rotational isomers observed were equal. The $\Delta S^{\ddagger}$ value for the rotational isomerism in the closely related compounds **278**, **298**, **281**, **299** and **300** is also expected to be approximately constant and thus the $\Delta G^{\ddagger}_c$ values obtained could be reasonably compared in order to indicate the relative energy barrier for the

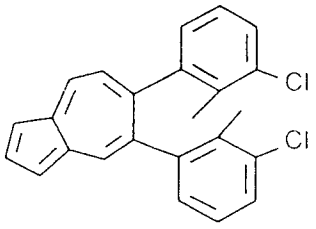
syn ↔ anti interconversion processes. The dynamic NMR results for the compounds examined in this work are summarised in Table 22.



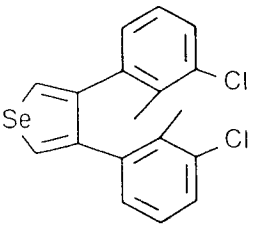
278



281



299



300

Table 22 Thermodynamic data for the barrier to rotation in 3',3''-dichloro-2',2''-dimethyl-*o*-teraryls

Compound	Δν (Hz)	T_c (°C)	$\Delta G^{\ddagger}_c$ (kJ/mol)
278	8.3	54	72.1
298[94]	29.0	86	76.0
281	7.5	22	64.8
300	7.0	44	70.0
299	18.0	>180*	>98.0

* T_c (in d_6-DMSO) could not be determined. Assuming T_c to be 180°C, gives a value of $\Delta G^{\ddagger}_c$ = 98 kJ/mol.

The $\Delta G^{\ddagger}$ values obtained for compounds **278-300** are in the range of 65 to >98 kJ/mol. The barrier to rotation in compound **281** is the lowest while the corresponding barrier in **299** is the highest, at >98 kJ/mol. Compound **299** could not be heated at high temperatures for long periods of time as this led to its decomposition. Hence, the coalescence temperature could not be determined. The ΔG value for **298** is about 4 kJ/mol higher than the value for **278**. The absence of peri protons in **278**, probably leads to a lesser steric interaction with the methyl group of the rotating tolyl rings, thus lowering the barrier to rotation. Comparison of the values for **281**, **300**, **278**, **298** and **299** show an increasing value of barrier to rotation in these teraryls. This can be accounted for when the geometries of the various rings involved are considered. As shown in Figure 27, the angle between the interacting tolyl planes with respect to the centre of the aryl ring decreases when the ring size is increased.

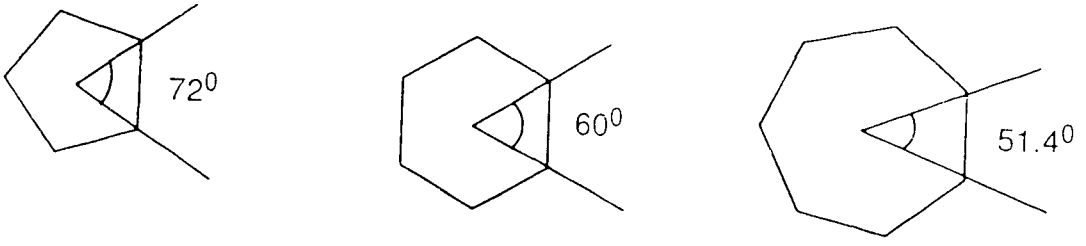


Figure 27 Description of angles in rings of varying size.

This would lead to further constriction of the tolyl rings and thus would increase the energy barrier to rotation. This would account for the

increased barrier in compound **299**. However, other effects such as dipolar interactions[217] cannot be ruled out

4.9 Summary

A new synthesis of symmetrical 1,2-diketones from Grignard reagents and 1,1'-oxalylimidazole was developed. The model diketone **249**, synthesised by several different routes was used in the precursor teraryls **278** and **281**. The synthesis of the diketone **241**, identified as a common precursor to various [e]fused dihydropyrenes was achieved in 50-55% yield. Using the diketone **249**, the thiacyclophane **287** was synthesised. An X-ray crystal analysis of **279** showed it to have an *anti* configuration. Comparison of the crystal data for **287** with related systems revealed the extent of strain present in **287**. The unstable quinoxalinodihydropyrene **287**, was synthesised from the thiacyclophane **287**. ^{1}Hnmr analysis of **279** showed its similarity to the naphthodihydropyrene **58**. The model thiophenedioxide **296** was prepared. Several model reactions using **296** were carried out. Complexation of the thiophenedioxide **296** yielded the complex **297**. An X-ray structure of **297** revealed syn geometry. The barrier to rotation in various teraryls obtained in this study was investigated.

CHAPTER FIVE

CONCLUSIONS

We have successfully synthesised the first bridged thia[13]annulene **120** in 11 steps from 3-methylthiophene, **111**. Using the internal methyl chemical shifts and the chemical shift of the external proton H_D, we have shown that the thia[13]annulene **120** is diatropic. This represents the first *unambiguous* example of a diatropic bridged thiaannulene. Using the internal and external proton chemical shift values, the diatropicity of **120** was estimated to be about 35-42% of that of DMDHP, **12**.

From inexpensive and commercially available starting materials, an efficient synthesis of the diol **115** was achieved in 4 steps in an overall yield of 25%. This compound **115** should pave way for the syntheses of a variety of [a]fused dihydropyrenes and many bridged annulenes.

The synthesis of the *quasi*-biphenylene **157**, was attempted. The synthesis of the precursor biphenylene **170a** was achieved in 4 steps from 1,2-dibromobenzene, **82**. Attempted conversion of **170** into the dibromide **159** resulted in polymer formation. A slight variation in the protecting group in compound **170** is expected to lead to the successful synthesis of the dibromide **159** and subsequently the *quasi*-biphenylene **157**.

Bis-bromomethylation of 4-*t*-butyltoluene, **98**, was successfully carried out in 85% yield using a new bromomethylating system. This procedure which

is potentially a general one should be useful in the syntheses of several [a]fused dihydropyrenes.

We successfully synthesised the biphenylene fused dihydropyrene **192**, from the oxa[17]annulene **63**, in two steps. A detailed analysis of the ^{1}H and ^{13}Cnmr spectra of **192** was carried out using 1D and 2D nmr techniques. A bond order-chemical shift correlation of **192** was carried out which indicated the extent of bond fixation in the macro ring due to the annelation of biphenylene. Using Mitchell's method, the diatropicity of biphenylene was estimated to be about 50-55% that of benzene, **1**.

Synthetic utility of the oxa[17]annulene **63** was explored. The oxa[17]annulene **63** was found to be stable up to 160°C. Thermal reaction of the oxa[17]annulene **63** with cycloheptatriene resulted in the 1:1 cycloadducts **209-211**, in a combined yield of 60%. Attempted acid catalysed dehydration/ deoxygenation reactions of the adducts **209-211** did not yield any of the expected annulenoannulene **208**.

Synthesis, isolation and characterisation of the benzocyclopropene fused dihydropyrene **218**, from the oxa[17]annulene **63**, was attempted next. We succeeded in isolating the adducts **224** from a reaction between the oxa[17]annulene **63** and the cyclopropene **223**, in 41% yield. The synthesis of **218** from the adducts **224** was attempted using low valent titanium reagents, which resulted in a very unstable product mixture. From the ^{1}Hnmr of the isolated product mixture, the major products were tentatively identified as

benzocyclopropene fused DMDHP **218** and the cycloheptatriene fused DMDHP **225**. The internal methyl chemical shift of **218** (δ -1.62), seems to indicate the lack of a Mills-Nixon effect in benzocyclopropene.

Attempted syntheses of some [a]fused dihydropyrenes from the dihydropyryne **62** were unsuccessful.

We succeeded in finding a new direct method of synthesis of 1,2-diketones from Grignard reagents and 1,1'-oxalyimidazole, **259**. This diketone synthesis yields diketones in 50-85% yield and is complimentary to two recently reported syntheses. We successfully synthesised the diketone **241** using this new method. The diketone **241**, was identified as a common precursor to various [e]-fused dihydropyrenes.

Using this diketone synthon **241**, we synthesised the thiacyclophane **287**. An X-ray structure determination of the thiacyclophane **287** revealed its anti geometry. Comparison of the structural data for **287**, with the data for related cyclophanes revealed the strain present in the cyclophane **287**. The highly unstable dihydropyrene **279** was synthesised from the thiacyclophane **287**. A ^{1}Hnmr analysis of **279** showed its similarity to the naphtho[e]dihydropyrene **58**.

From the model diketone **249**, the teraryls **278** and **281** were synthesised. Conversion of **281** to the thiophene dioxide **296** was achieved in 85% yield. The thiophene dioxide **296** was complexed with ironpentacarbonyl to yield the complex **297**, in quantitative yield. An X-ray structure of this

complex **297** showed it to have a syn geometry.

Model reactions carried out using the thiophene dioxide **297** resulted in the formation of the teraryls **84**, **299**, **301** and **300**.

A variable temperature nmr study of the teraryls obtained in this study revealed the increase in barrier to rotation due to the change in the ring size.

As outlined in the preceding chapters, a plethora of fused dihydropyrenes and new bridged annulenes await syntheses using the new methodology and intermediates reported in this thesis.

CHAPTER SIX

EXPERIMENTAL

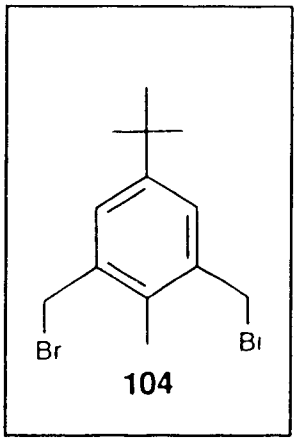
Instrumentation

Melting points were determined on a Reichert 7905 melting point apparatus integrated to an Omega Engineering Model 199 Chromel-alumel thermocouple. Infrared spectra, calibrated with polystyrene, were recorded on a Bruker IFS25 FT-IR spectrometer and only the major bands are reported. UV-Visible spectra were recorded on a Cary 5 UV-VIS-NIR spectrometer using cyclohexane as solvent. Proton magnetic resonance spectra of solutions in chloroform-d (unless otherwise specified) were recorded on a Perkin-Elmer R-32 (90 MHz) using tetramethylsilane as internal standard, or a Bruker WM 250 (250 MHz) spectrometer, or a Bruker AMX 360 (360 MHz), using the chloroform peak at 7.24 ppm for calibration. Carbon nuclear magnetic resonance spectra were recorded on a Bruker WM 250 (62.9 MHz) using solutions in chloroform-d, and the solvent peak at 77.0 ppm was the calibrant. Variable temperature experiments were done on a Perkin-Elmer R-32 (90 MHz) instrument, using $CDCl_3$-CD_2Cl_2 solutions. Mass spectra were recorded on a Finnigan 3300 gas chromatography-mass spectroscopy system using methane as a carrier gas for chemical ionisation. Exact mass measurements were done on a Kratos Concept-H instrument using perfluorokerosene as the

standard. Elemental analyses were performed by Canadian Microanalytical Services Ltd., Vancover, B.C. X-ray structure determinations were carried out by Kathy Beveridge on a Picker 4 circle diffractometer automated with a PDP 11/10 computer. All the solvents used in the reactions were purified and distilled according to standard procedures.[248] All evaporations were carried out under reduced pressure on a rotary evaporator. SiGel refers to silicagel.

Experimental Procedures

2,6-Bis(bromomethyl)-4-*tert*-butyltoluene, 104.



104

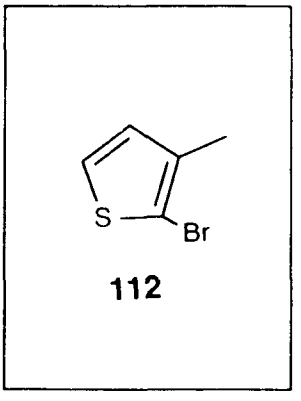
4-*tert*-butyltoluene (22.2 g, 0.15 mol) was added to a mixture of trioxane (11.3 g, 0.12 mol, excess) and zinc bromide (3.4 g, 0.015 mol, catalyst, freshly prepared from zinc dust and 1,2-dibromoethane in dry THF, followed by the removal of THF under high vacuum) in 30% HBr in glacial acetic acid (100 mL, 0.47 mol, Aldrich), containing acetic anhydride (~5 mL). The whole mixture was heated at 80-85°C with magnetic stirring for 22 hours. After that period, it was cooled to ~25°C and poured into ice (500 g). The solid was then extracted with hexanes (2x250 mL) and the combined hexane extracts were washed

successively with water (2x100 mL), 10%$NaHCO_3$ (2x50 mL), satd. NaBr (100 mL) and dried over $MgSO_4$. The solvent was evaporated to leave a light brown residue which on recrystallisation from hexanes gave **104** as colorless needles (43.5 g, 86%), **mp** 92-93°C; **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 7.32 (s, 2H, Aryl-H), 4.55 (s, 4H, -CH_2Br), 2.42 (s, 3H, Ar-CH_3), 1.33 (s, 9H, -C(CH_3)$_3$); **^{13}Cnmr** (62.9 MHz, $CDCl_3$) δ 149.2, 136.3, 133.6 (Aryl quaternary C), 127.9 (Aryl CH), 34.2 (-<u>C</u>(CH_3)$_3$), 32.9 (-CH_2Br), 31.1 (-C(<u>C</u>H_3)$_3$), 13.8 (Ar-CH_3); **ms** (EI) m/e(%): 336 (M^+, 4), 334 (M^+, 9), 332 (M^+, 5), 255 (100), 253 (98), 159 (30).

Anal Calcd. for: $C_{13}H_{18}Br_2$ C 46.74 , H 5.43

Found C 46.72 , H 5.44

2-Bromo-3-methylthiophene, 112.

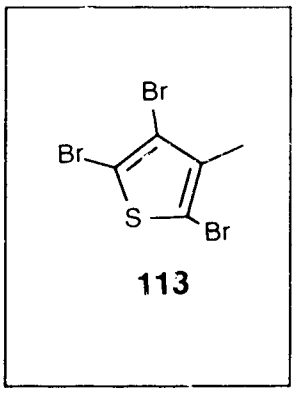


112

2-Bromo-3-methylthiophene was prepared by the method of Kellog.[112] A slurry of NBS (178 g, 1.0 mol) and a 50:50 (v/v) mixture of $CHCl_3$-AcOH (500 mL) was added (*Caution! Exothermic Reaction!*) to a mechanically stirred solution of 3-methylthiophene (98g, 1.0 mol) in a 50:45:5 (v/v/v) mixture of $CHCl_3$-AcOH-DMF (500 mL) over 30 minutes. The mixture was stirred for an additional 30 minutes. The reaction was quenched by the addition of ice-water (500 mL), the organic layer was separated, washed with water (4x250 mL), satd. $NaHCO_3$ (2x100 mL),

satd. NaCl (2x200 mL) and dried over Na_2SO_4. Removal of the solvent gave the product **112** as a pale yellow liquid (178 g, ~100%). It was pure by ^{1}Hnmr; **bp** 62-64°C/10mm (lit[112] **bp** 63-65°C/10mm); **^{1}Hnmr** (90 MHz, $CDCl_3$) δ 7.0 (d, 1H, J=5.5 Hz, H-5), 6.7 (d, 1H, J=5.5 Hz, H-4), 2.2 (s, 3H, -CH_3). The crude product was used directly in the next step.

2,4,5-Tribromo-3-methylthiophene, 113.

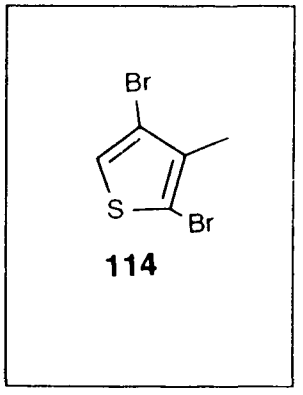


113

In a three necked 1 litre flask, fitted with a mechanical stirrer, double walled condensor (leading to a funnel immersed in water), and an addition funnel, are placed the product from the above reaction (178 g, 1.0 mol) dissolved in chloroform (50 mL). The flask was immersed in a deep pan through which cold tap water was running. Bromine (320 g, 2.0 mol) was added dropwise to the well stirred reaction mixture over 10 hours. When the addition was completed, the cold water pan was replaced with a heating mantle and the mixture refluxed for 10 hours. After cooling the mixture to 25°C, KOH (100 g) in 95%EtOH (500 mL) was added very cautiously (*HIGHLY EXOTHERMIC!*) to the mixture and it was refluxed for an additional 4 hours. The mixture was then poured in to ice-water (3 L), the aqueous layer removed, the dark-brown organic layer taken up in chloroform (500 mL), washed with water and dried over $MgSO_4$. Removal of chloroform gave a dark-brown solid which was extracted with hot

heptane (600 mL). The heptane extracts were filtered through a short column of neutral alumina (50 g) and the solvent evaporated from the filtrate to give the pure product **113** (302 g, 90%) as colorless needles. **mp** 29-31°C (lit[113, 111] **mp** 27-28.5, 33°C); **^{1}Hnmr** (90 MHz, $CDCl_3$) δ 2.15 (s, $-CH_3$); **ms** (EI) m/e(%): 339 (M^+,31), 337 (M^+,94), 335 (M^+,100), 333 (M^+,47), 286 (14), 284 (29), 282 (16), 258 (31), 256 (59), 254 (30).

2,4-Dibromo-3-methylthiophene, 114.

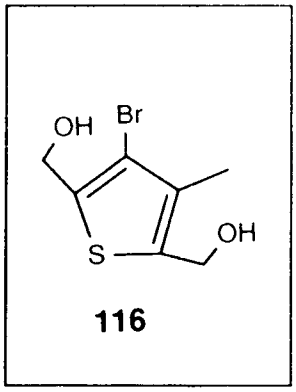


114

Zinc dust (9.70 g, 0.149 mol) was added to a vigorously stirred mixture of glacial AcOH (26 mL), water (70 mL) and THF (10 mL) and the mixture was brought to a gentle reflux and then the heat was removed. 2,4,5-tribromo-3-methylthiophene (50.0 g, 0.149 mol) in THF (5 mL) was then added dropwise at such a rate that the reaction mixture kept refluxing. After the addition was complete (~30 minutes) the mixture was refluxed for 10 hours then cooled to 25°C and extracted with $CHCl_3$ (250 mL). The $CHCl_3$ layer was washed with water (3x50 mL), 10% $NaHCO_3$ (2x50 mL), satd. NaCl (2x50 mL), dried over $MgSO_4$. Removal of the solvent and distillation at 0.3mm of the crude product gave 2,4-dibromo-3-methylthiophene **114** (30 g, 79%) as a clear liquid, **bp** 62-64°C/0.3mm (lit[114] **bp** 80°C/10mm); **^{1}Hnmr** (90 MHz, $CDCl_3$) δ 7.20 (s, 1H, Ar-H), 2.18 (s, 3H, $-CH_3$); **ms** (EI) m/e(%): 259 (M^+,45), 257 (M^+,92), 255

(M^+,51), 206 (41), 204 (42), 179 (22), 178 (100), 176 (100).

Attempted synthesis of 2,4-Bis(hydroxymethyl)-3-methylthiophene from 115 *via* metallation. Formation of 2,5-bis(hydroxymethyl)-4-bromo-3-methylthiophene 116.



116

n-BuLi (44 mL, 2.5M solution in pentane, 0.11 mol) was added dropwise to a stirred solution of 2,4-dibromothiophene (12.25 g, 50 mmol) in dry THF (100 mL), at -80°C (dry ice-Acetone), under argon. The addition was controlled in such a manner that there was no appreciable rise in the internal temperature of the reaction mixture (+/- 2°C, ~30-40 minutes). The solution turned from colorless to light brown, then to dark brown, during the course of the addition. The mixture was stirred for 3 hours at -80°C (The solution was an off-white suspension at the end). Paraformaldehyde (3.30 g, 0.11 mol, pulverised and dried over P_4O_{10} under *vacuo* overnight) was added, in portions, to the reaction mixture under a blanket of argon. The cooling bath was removed and the stirring continued for 12 hours at 25°C. The reaction was quenched with the addition of satd. NH_4Cl (20 mL), and the organic layer was separated and dried over $MgSO_4$. Removal of the solvent gave a dark-yellow, foul smelling oil which on trituration with $CHCl_3$ and cooling gave a white-crystalline

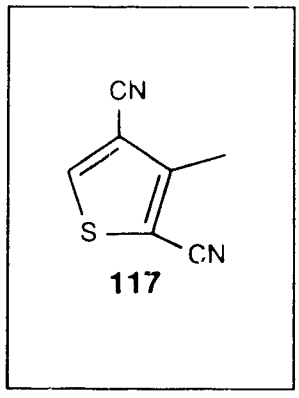
precipitate. The precipitate was recrystallised from ethyl acetate/hexane to yield colorless needles of **116** (3.6 g, 30%), **mp** 87-89°C; **^{1}Hnmr** (250 MHz, CD_3CN) δ 4.64, 4,62 (s, 2H each, -$\underline{CH_2}$OH), 3.54, 3.46 (broad s, 1H each, -OH), 2.26 (s, 3H, -CH_3); **^{13}Cnmr** (62.9 MHz, CD_3CN) δ 138.4, 133.4, 120.9, 111.4 (C 1,2,3,4), 59.5, 59.8 (-CH_2OH), 13.9 (-CH_3); **ms** (EI), m/e (%): 238 (M^+,48), 236 (M^+,46), 222 (10), 220 (10), 192 (15), 190 (16), 158 (40), 112 (80), 100 (100); **IR** (KBr, cm^{-1}): 3250(-OH), 2948, 2872, 1442, 1380, 1354, 1178, 1128, 977, 714.

Anal Calcd. for: $C_7H_9BrSO_2$ C 35.46 , H 3.83

Found 35.92 , H 3.79

Use of LDA and *n*-BuLi/TMEDA as the metallating agents also resulted in the formation of **116** as the major product and did not yield any **115**.

2,4-Dicyano-3-methylthiophene, 117.



117

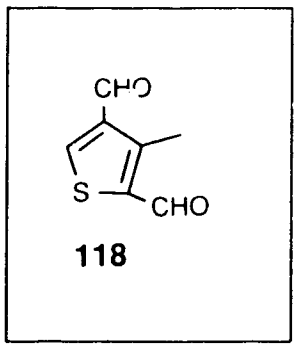
CuCN (17.5 g, 0.19 mol) was added, in small portions with vigorous stirring, to a warm (~60°C) solution of 2,4-dibromo-3-methylthiophene (42.0 g, 0.16 mol) in N-methylpyrrolidinone (100 mL) and the whole mixture was heated to 140-160°C. After 3 hours, it was cooled to about ~80°C and CuCN (17.5 g, 0.19 mol) was added in small portions and the mixture was again heated to 140-160°C for an additional 4 hours. It was then cooled to ~60°C and poured into a 50:50 v/v mixture of ammonia and water (600 mL), stirred well for 3 hours and filtered.

The residue was washed with CH_2Cl_2 (400 mL) and the filtrate extracted with CH_2Cl_2 (5x100 mL). The CH_2Cl_2 extracts were combined and the solvent was evaporated. The residue obtained was taken up in ether (500 mL) and washed well with water (5x100 mL) and dried over $MgSO_4$. Removal of the ether gave the crude product as a dark-brown solid which upon sublimation (80°C/0.1mm) gave the product as colorless needles (13 g, 54%), **mp** 134°C (sublimes); **^{1}Hnmr** (90 MHz, $CDCl_3$) δ 8.05 (s, 1H, Ar-H), 2.55 (s, 3H, -CH_3); **^{13}Cnmr** (62.9 MHz, $CDCl_3$) δ 150.4, 112.8, 112.0 (C-1,2,3), 139.5 (C-4), 113.6, 108.0 (-CN), 14.5 (-CH_3); **ms** (CI), m/e (%): 189 (M+41,4), 177 (M+29,10), 151 (5), 150 (10), 149 (M+1,100); (EI), m/e(%): 148 (M,94), 147 (100), 121 (49), 94 (5), 70 (19), 69 (6), 51 (4), 45 (17); **IR** (KBr, cm^{-1}): 3086, 2210 (-CN), 1643, 1442, 1391, 1101, 877, 835, 475.

Anal	Calcd. for:$C_7H_4N_2S$	C 56.74 , H 2.72 , N 18.91
	Found	C 56.41 , H 2.83 , N 18.28

2,4-Bis(formyl)-3-methylthiophene, 118.

DiBAH (70 mL, 1M solution in hexanes, 70 mmol, excess) was added dropwise to a mechanically stirred solution of the dicyanide **117** (5.0 g, 33.7 mmol) in dry benzene (70 mL) over one hour, under argon. The solution was stirred for an additional hour and then was quenched with the sequential addition of MeOH (10 mL), 50:50 v/v mixture of



118

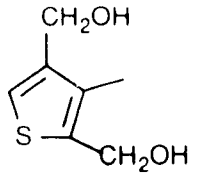
MeOH:water (20 mL) and 10%HCl (25 mL). The mixture was then extracted with ether (4x75 mL), the ether extracts washed well with water (3x50 mL) and dried over $MgSO_4$. Removal of ether gave the crude product **118** as an orange-yellow solid which was sublimed (90°C/0.1mm) to give the pure dialdehyde **118** (4.36 g, 84%) as colorless needles, **mp** 106-108°C; **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 10.10, 9.97 (s, 1H each, -CHO), 8.37 (s, 1H, Ar-H), 2.78 (s, 3H, -CH_3); **^{13}Cnmr** (62.9 MHz, $CDCl_3$) δ 185.4, 182.3 (-CHO), 146.2, 141.8, 140.3 (C-1,2,3), 144.8 (C-4), 13.2 (-CH_3) ; **ms** (CI), m/e (%): 183 (M+29,9), 157 (4), 156 (8), 155 (M+1,100); **IR** (KBr, cm^{-1}): 3075, 1693 (-CHO), 1643 (-CHO), 1530, 1405, 1350, 1241, 1090, 814, 701, 676.

Anal Calcd. for $C_7H_6O_2S$: C 54.23 , H 3.92

Found C 54.06 , H 3.74

2,4-Bis(hydroxymethyl)-3-methylthiophene, 115.

$NaBH_4$ (380 mg, 10 mmol, excess) was added to a solution of the dialdehyde (2.0 g, 13 mmol) in MeOH (80 mL). The mixture was stirred at 25°C for 3 hours, 36%HCl (4-5 drops) was added to quench the reaction and the solvent was evaporated. The solid residue was extracted with ether (100 mL) and the ether evaporated to yield the crude product which was recrystallised from heptane to give the diol **115** (1.9 g, 93%) as colorless needles, **mp** 95-97°C; **^{1}Hnmr** (250 MHz,



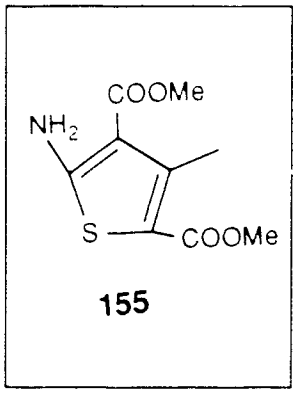
115

CD_3CN) δ 7.08 (s, 1H, Ar-H), 4.61, 4.45 (s, 2H each, $-CH_2O$), 2.60 (broad s, 2H, -OH), 2.10 (s, 3H, $-CH_3$); **^{13}Cnmr** (62.9 MHz, CD_3CN) δ 143.6, 139.9, 133.5 (C-1,2,3), 118.4 (C-4), 59.9, 57.9 ($-CH_2OH$), 11.9 ($-CH_3$) ; **ms** (CI), m/e (%): 159 (M+1,1), 158 (M$^+$,3), 157 (2), 151 (1), 141 (100), 111 (15); **IR** (KBr, cm^{-1}): 3274 (-OH), 2885, 1454, 1404, 1320, 1190, 1090, 1010, 1002, 864, 777, 676.

Anal Calcd. for $C_7H_{10}O_2S$: C 53.14 , H 6.37

Found C 53.11 , H 6.32

2,4-Dimethyl 2-amino-3-methylthiophene-2,4-dicarboxylate, 155.



155

Diethylamine (73 g, 1 mol) was added to a stirred mixture of methyl cyanoacetate (99 g, 1 mol), methyl acetoacetate (116 g, 1 mol) and sulphur (32 g, 1 mol), in *t*-BuOH (500 mL) at 40°C under nitrogen. The resulting dark-red reaction mixture was heated at 70-75°C for 2 days. Then the solution ***(EXTREME CAUTION SHOULD BE EXERCISED! ALL THE PRODUCTS RESULTING FROM THIS REACTION ARE FOUL SMELLING AND STICK TO CLOTHING, HAIR AND SKIN EASILY!!)*** was concentrated in vacuo, filtered through a short column of SiGel (500 g) and chromatographed over SiGel (2 kg, elution with 1:1 $CHCl_3$:hexanes) to give a foul smelling yellowish brown solid which upon recrystallisation from $CHCl_3$/hexane gave pure **155** as colorless crystals (92 g, 40%), **mp** 126-127°C; **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 6.59 (broad s, 2H, -

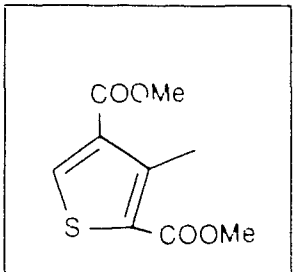
NH_2), 3.80, 3.75 (s, 3H each, $-COOCH_3$), 2.64 (s, 3H, $-CH_3$); **^{13}Cnmr** (62.9 MHz, $CDCl_3$) δ 166.4, 166.3 (-<u>CO</u>OCH_3), 163.2, 148.2, 108.3, 108.0 (C-1,2,3,4) 51.4, 50.9 (-COO<u>CH_3</u>), 15.9 ($-CH_3$); **ms** (CI, m e (%): 270 (M+41,weak), 258 (M+29,4%), 230 (M+1,100), 229 (M⁺,10), 198 (60); (EI) m e (%): 229 (M⁺,100), 198 (30), 197 (90), 166 (60); **IR** (KBr, cm^{-1}): 3400 ($-NH_2$), 3300 (NH_2), 1718 (-<u>CO</u>OMe), 1655, 1605, 1530, 1442, 1291, 1228, 1090, 1053, 1005.

Anal Calcd. for $C_9H_{11}NO_4S$: C 47.15 , H 4.84 , N 6.11

Found C 46.99 , H 4.77 , N 6.04

When this reaction was performed on half the scale described in the above procedure, the yield of **155** was consistently ~62-65%.

2,4-Dimethyl 3-methylthiophene-2,4-dicarboxylate, 156.



156

An ice-cold solution of sodium nitrite (8.0 g, 0.116 mol) in water (10 mL) was added dropwise, *via* a syringe whose tip was kept below the surface (*this is essential to ensure the proper mixing of the reactants without raising the internal temperature of the reaction mixture*) of a solution of **155** (25.0 g, 0.109 mol) and conc.H_2SO_4 (25 mL) in anhydrous EtOH (175 mL), with vigorous stirring, at -2°C (ice-NH_4Cl mixture, *internal temperature*). The solution was stirred at -2 - 0°C for 30 minutes, gently warmed to 40°C and heated at 40-50°C for one hour. After the

evolution of [illegible] the reaction mixture was cooled to 25°C and neutralised with $NaHCO_3$, then extracted with ether (5x100 mL). The combined ether extracts were washed with water (5x75 mL), 10%$NaHCO_3$ (2x50 mL), satd. NaCl (2x50 mL), dried briefly over $MgSO_4$ and the solvent evaporated to yield a dark-red solid. The crude product was chromatographed over SiGel (elution with 3:7 ether:hexanes) to give the diester **156** as shiny white needles (18.0 g, 77%). A small portion was further purified by sublimation at 100°C/0.1mm, **mp** 102-104°C; **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 8.17 (s, 1H, Ar-H), 3.84, 3.82 (s, 3H each, -$COOCH_3$), 2.77 (s, 3H, -CH_3); **^{13}Cnmr** (62.9 MHz, $CDCl_3$) δ 162.9, 162.5 (-$\underline{CO}OCH_3$), 146.9, 133.2, 128.3 (C-1,2,3), 137.6 (C-4), 51.8, 51.6 (-COO$\underline{CH_3}$), 14.5 (-CH_3); **ms** (CI), m/e (%): 255 (M+41, weak), 243 (M+29,5), 215(M+1,100), 214(M^+,4), 183 (10); (EI),m/e(%); 214 (M^+,60), 183 (100), 182 (40); **IR** (KBr, cm^{-1}): 3111, 1731 (-COOMe), 1705 (-COOMe), 1530, 1430, 1379, 1266, 1228, 1053, 1015, 764.

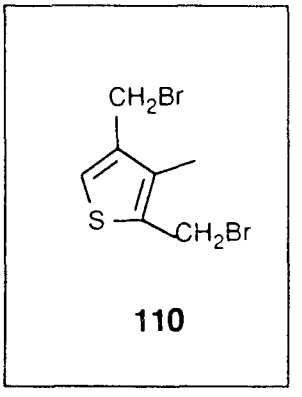
Anal	Calcd. for:$C_9H_{10}O_4S$	C 50.46 , H 4.71
	Found	C 50.46 , H 4.59

Synthesis of 2,4-bis(hydroxymethyl)-3-methylthiophene from the diester 156.

DiBAH (14 mL, 1.6M solution in hexanes, 22 mmol) was added dropwise to a mechanically stirred solution of the diester **156** (2.14g, 10 mmol) in dry ether (100 mL) at 0°C under argon. After the solution has been stirred at 25°C

for 4 hours it was quenched with MeOH (10 mL, *caution!*). The reaction mixture was evaporated to dryness to leave a solid residue. The residue was sohxlet extracted with ether, the solvent removed from the ether extract and the residue was recrystallised from heptane to yield the diol **115** (0.87g, 55%), identical in all respects to the previously made sample.

2,4-Bis(bromomethyl)-3-methylthiophene, 110.



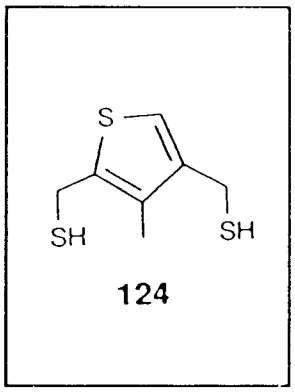
110

PBr_3 (1.2 mL, 13 mmol, excess) was added dropwise to stirred solution of the diol **115** (1.8 g, 11.4 mmol) in dry $CHCl_3$ (50 mL, refluxed over P_4O_{10} and distilled to remove EtOH) containing 2 drops of pyridine at 0°C. The mixture was allowed to warm to 25°C and stirred for 4 hours. It was then quenched with the addition of ice-water (10 mL), and the organic layer was separated, washed with water (2x20 mL), 10%$NaHCO_3$ (2x20 mL), satd. NaBr (2x10 mL) and then was dried over $MgSO_4$. The solvent was evaporated to leave a brown gummy residue which on *immediate* recrystallisation from hexane gave the dibromide as an unstable, colorless microcrystalline solid (2.6 g, 80%), **mp** 112-115°C (decomp), which decomposed within three days; **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 7.25 (s, 1H, Ar-H), 4.64, 4.39 (s, 2H, -CH_2Br), 2.21 (s, 3H, -CH_3); **^{13}Cnmr** (62.9 MHz, $CDCl_3$) δ 137.8, 136.5, 134.8 (C-1,2,3), 125.1 (C-4), 26.7, 25.5 (-CH_2Br), 11.8 (-CH_3); **ms** (CI), m/e (%): 327 (M+41, weak), 325 (M+41, weak), 323 (M+41, weak), 315

(M+29, 1), 313 (M+29, 2), 311 (M+29, 1), 287 (M+1, 3), 285 (M+1, 6), 283 (M+1, 3), 205 (95), 203 (100).

Anal	Calcd. for $C_7H_8Br_2S$:	C 29.60 , H 2.84
	Found	C 30.02 , H 2.87

2,4-Bis(mercaptomethyl)-3-methylthiophene, 124.



124

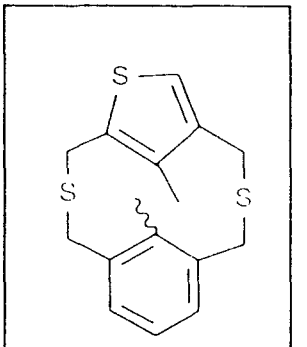
Thiourea (1.53 g, 20.2 mmol) was added to a stirred solution of the dibromide **110** (2.84 g, 10 mmol) in a 1:1 v/v mixture of dry THF and EtOH (50 mL). The mixture was refluxed for 2 hours under argon, cooled to 25°C, and the crystalline thiouronium salt obtained was filtered. After drying the thiouronium salt over-night under vacuum, it was added to an argon purged solution of KOH (5.2 g, 85%, 40 mmol) in water (25 mL). The mixture was refluxed for 3 hours under argon, then cooled to ~5°C, acidified with 20%H_2SO_4, and extracted with ether (3x25 mL). The combined ether extracts were dried over $MgSO_4$ and evaporation of the solvent gave the crude dithiol **124**. The crude product was recrystallised from $CHCl_3$ under argon to yield the pure dithiol as off-white crystals (1.71 g, 90%), **mp** ~18°C, which were stable under nitrogen but polymerised rapidly upon exposure to air; **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 6.96 (s, 1H, Ar-H), 3.83, 3.61 (d, 2H each, J=7Hz, -CH_2-), 2.16 (s, 3H, -CH_3), 1.88, 1.66 (t, 1H each, J=7Hz, -SH); **^{13}Cnmr** (62.9 MHz, $CDCl_3$) δ 140.7, 138.4, 132.3 (C-1,2,3), 119.7 (C-4),

22.8, 21.7 (-CH_2SH), 11.9 (-CH_3), **ms** (CI), m/e (%): 219 (M+29, 5), 191 (M+1, 10), 190 (M^+, 5), 156 (100).

Anal Calcd. for:$C_7H_{10}S_3$ C 44.17 , H 5.30

Found C 43.83 , H 5.03

9,17-Dimethyl-2,11-dithia[3]metacyclo[3](2,4)thiophenophane, 123.

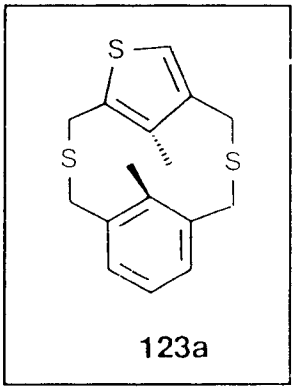


123

A solution of the dibromide **110** (2.00 g, 7 mmol) and the dithiol **69** (1.30 g, 7 mmol) in argon purged benzene (500 mL) was added to a mechanically stirred solution of KOH (0.925 g, 85%, 14 mmol) in argon purged 95%EtOH (1000 mL) contained in a morton flask *via* a precision addition funnel over 24 hours. The experimental setup was kept under a positive pressure of argon throughout the course of the addition. After the addition was over, the solvents were removed under vacuum, the solid residue was extracted with CH_2Cl_2 (200 mL) and water (100 mL). The CH_2Cl_2 extract was washed with water (2x50 mL), dried over $MgSO_4$ and evaporated to yield the crude cyclophanes **123** (1.90 g, 89%) which were essentially pure by nmr. The crude products thus obtained were purified by chromatography on SiGel (elution with 1:1 CH_2Cl_2:pentane) to give the pure thiacyclophanes **123** (1.50 g, 71%). The isomers syn **123a** and anti **123b** could not be separated by column chromatography, but a small portion of the pure anti **123a** could be obtained by repeated (*ten!*) fractional

recrystallisations from toluene/EtOH. The initial ratio of the anti/syn isomers was determined to be 2.6/1 by **^{1}Hnmr**. Coupling of the dithiol **124** with the dibromide **68** also resulted in the thiacyclophanes **123** in the same anti/syn ratio but in lower yields (55%).

***anti*-Thiacyclophane 123a**



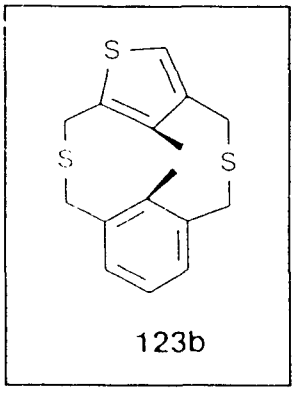
123a

mp 228-230°C(decomp); **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 7.27-6.97 (m, 3H, H-5,6,7) 7.03 (s, 1H, H-14), 3.98-3.36 (m, 8H, H-1,2,3,4,8,9,10,11), 1.88 (s, 3H, 9'-CH_3), 1.21 (s, 3H, 17'-CH_3); **^{13}Cnmr** (62.9 MHz, $CDCl_3$) δ 138.1, 137.1, 136.9, 135.6, 134.0 (C-4,8,9,13,16,17), 130.6, 129.6, 125.1, 123.2 (C-5,6,7,14), 33.0, 31.2, 28.7, 27.2 (C-1,3,10,12), 15.7, 12.1 (C-9',17'); **ms** (CI), m/e (%): 347 (M+41,1), 335 (M+29,5), 307 (M+1,100), 306 (M^+,20), 275 (1), 261 (3), 124 (30); (EI), m/e(%): 306 (M^+,20), 124 (100): **IR** (KBr, cm^{-1}): 3075, 2885, 1460, 1404, 1216, 1160, 914, 790, 720, 588; U.V (Cyclohexane) λ_{max}nm(logε): 280 (3.15, shldr), 260 (3.67, shldr), 220 (4.52).

***syn*-Thiacyclophane 123b (by subtraction of the peaks due to anti 123a)**

^{1}Hnmr (250 MHz, $CDCl_3$) δ 7.13-6.85 (m, 3H, H-5,6,7), 6.32 (s, 1H, H-14),

4.25-3.60 (m, 8H, H-1,2,3,4,8,9,10,11), 2.36, 2.33 (s, 3H each, $-CH_3$); **^{13}Cnmr** (62.9 MHz, $CDCl_3$) δ 136.9, 136.6, 135.9, 135.1 (C-4,8,9,13,16,17), 130.1, 128.7, 125.3, 124.4 (C-5,6,7,14), 36.9, 34.9, 31.6, 31.1 (C-1,3,10,12), 16.8, 13.6 (C-9',17').



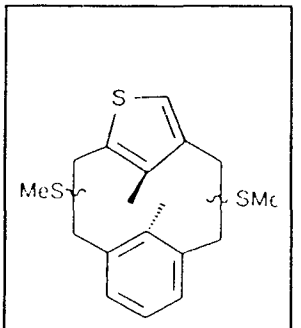
123b

Anal(*anti*) Calcd. for $C_{16}H_{18}S_3$: C 62.70 , H 5.92

Found C 62.44 , H 5.81

Wittig rearrangement of the thiacyclophane 123.

LDA (0.5 mL, 2.5M solution in cyclohexane, Aldrich, 1.2 mmol, excess) was injected by a syringe into a stirred solution of the thiacyclophane **123** (100 mg, 0.32 mmol) in dry THF (10 mL) under argon at -10°C. The color of the solution changed from colorless to dark-brown. The solution was allowed to warm to 25°C over 30 minutes, when water (100 μL) was added. The color of the reaction mixture was bleached to pale yellow, and then CH_3I (1 mL, large excess) was added to the reaction and the stirring continued for 3 hours. The solvent was then evaporated, the residue extracted with CH_2Cl_2, the extracts dried over $MgSO_4$ and the solvent removed to yield the crude product. This was chromatographed on SiGel (elution with 7:3 pentane:CH_2Cl_2) to give **125** as a mixture of many isomers (80 mg, 73%); **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 7.72-



125

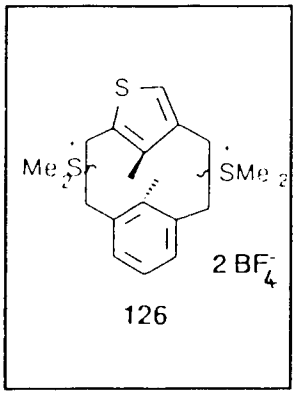
6.84(m, 4H, Aryl-H), 4.41-2.02 (m, 6H, bridge-H), 2.25, 2.11 (s, 3H each, -SCH_3), 1.57, 0.71 (s, 3H each, internal-CH_3); **^{13}Cnmr** (62.9 MHz, $CDCl_3$) δ (major peaks) 144.5, 143.8, 140.2, 137.3, 136.3, 136.2 (Aryl quarternary), 128.7, 125.0, 124.1, 121.6 (Aryl CH), 51.9, 51.6 (-CHSMe), 42.6, 38.1 (-CH_2-), 17.8, 12.7 (-CH_3), 15.8, 15.3 (-SCH_3) ; **ms** (CI), m/e (%): 363 (M+29,weak),335 (M+1,40), 334 (M^+,30), 287 (100), 239 (5); (EI),m/e(%): 334 (M^+,100), 287 (14), 286 (40), 271 (60).

Anal Calcd. for $C_{18}H_{22}S_3$: C 64.62 , H 6.63

Found C 64.50 , H 6.50

Synthesis of the thia[13]annulene 120.

A. Formation of the bis-salt 126.

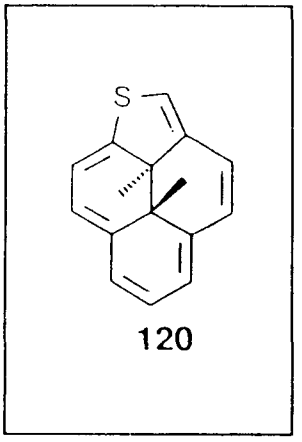


126

Borsch reagent (345 mg, ~80% oil, 1 mmol, excess) was added, as a suspension in dry CH_2Cl_2 (5 mL), to a stirred solution of the cyclophane **125** (80 mg, 0.24 mmol) in CH_2Cl_2 (10 mL) under argon at -30°C (dry ice-acetone). After the addition, the cooling bath was removed and the solution allowed to warm to 25°C over 3 hours. Ethyl acetate (10 mL) was added and the stirring was continued for another 24 hours. An off-white crystalline

precipitate formed and it was fitered under suction, washed with dry ethyl acetate (10 mL) and dried overnight under vacuo. The salt **126** (152 mg, ~100%) was quite unstable hence it was used directly in the next step. It decomposed at ~60-65°C.

B. Synthesis of *trans*-9b,9c-Dimethyl-9b,9c-dihydrophenyleno[1,9-bc]thiophene 120.



120

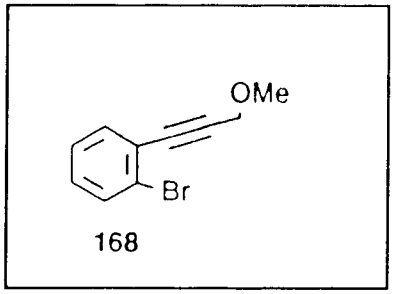
t-BuOK (100 mg, 95%. 0.78 mmol) was added to a stirred suspension of the bis-salt **126** (152 mg, 0.24 mmol) in dry THF (10 mL) under argon. The reaction flask was protected from light by means of aluminium foil. The reaction mixture was heated to a gentle reflux for 30 minutes, cooled to 25°C and quenched with degassed satd. NH_4Cl (5 mL). The organic layer was separated, washed with degassed satd. NaCl (5 mL) and evaporated to leave a dark-brown residue. The residue was chromatographed rapidly (SiGel, deactivated with 10% water, elution with pentane under argon), in the absence of light to give the thia[13]annulene as a reddish orange solid (17 mg, 30%). Recrystallisation from degassed methanol gave orange-red plates, **mp** 70-71°C(decomp): **^{1}Hnmr** (250 MHz, CD_2Cl_2) δ 7.36 (s, 1H, H2), 7.26 (d, 1H, J= 9.36 Hz, H3), 7.23 (d, 1H, J= 9.36 Hz, H4), 7.19 (d, 1H, J= 6.51 Hz, H7), 7.04 (d, 1H, J = 1.40 Hz, H5), 6.94 (d, 1H, J= 6.02 Hz, H9), 6.85 (d, 1H, J= 6.02 Hz, H8), 6.85 (dd, 1H, H6); **^{13}Cnmr** (62.9 MHz, CD_2Cl_2) δ 138.0, 136.7, 122.9, 120.8

(Aryl quarternary), 126.1, 125.0, 124.0, 121.1, 120.2, 119.5, 118.5, 114.2 (Aryl CH), 36.6 (Bridge quarternary), 17.4, 16.0 (Internal -CH_3) ; **ms** (CI), m/e (%): 238 (M^+, 8), 223 (15), 208 (100); U.V (Cyclohexane) λ_{max} nm (log ε_{max}): 505 (2.52), 470 (2.67), 443 (2.68), 389 (2.40), 320 (3.63), 272 (3.30).

Anal Calcd. for $C_{16}H_{14}S$: C 80.63 , H 5.92

Found C 80.23 , H 5.90

2-bromo-1-(3'-methoxymethylpropynyl)benzene, 168.



168

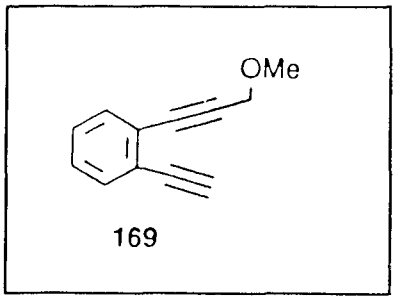
1,2-dibromobenzene (23.6 g, 0.10 mol) was added to a stirred mixture of 3-methoxypropyne[150a] (21.0 g, 0.16 mol), copper(I)iodide (900 mg, 4.7 mmol), tetrakis(triphenylphosphine)palladium(0) [150b] (5.0 g, 4 mmol, 4 mol%) in dry, degassed triethylamine (200 mL). The well stirred mixture was heated to a gentle reflux under argon and refluxed for 14 hours. It was then cooled to 25°C, quenched with satd. NH_4Cl and extracted with ether (200 mL). The ether layer was washed with 10%HCl (4x100 mL), water (2x100 mL),10% $NaHCO_3$ (2x50 mL), satd. NaCl (50 mL), dried over $MgSO_4$ and the solvent evaporated to leave the crude product as a dark-brown liquid. The crude product upon flash chromatography on SiGel (elution with 9:1 pentane:ether) gave unreacted 1,2-dibromobenzene (6.6 g, 28% of the starting amount) followed by the product **168** (12.0 g, 53%, 71% based on the recovered 1,2-dibromobenzene). The

product thus obtained was distilled under vacuum, with an argon leak to give the pure product **168** as a colorless liquid, **bp** 80-82°C/0.05mm ; **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 7.56-7.11 (m, 4H, Ar-H), 4.35 (s, 2H, -CH_2-), 3.47 (s, 3H, -OCH_3); **^{13}Cnmr** (62.9 MHz, $CDCl_3$) δ 133.2, 132.0, 129.3, 126.7 (Aryl CH), 125.1, 124.5 (Aryl quarternary), 89.6 (C-1'), 84.6 (C-2'), 59.9 (-CH_2), 57.3 (-OCH_3); **ms** (EI), m/e(%):227 (M^+,7), 225 (M^+,9), 195 (70), 193 (68), 145 (100), 114 (43), 102 (89); **IR** (neat, cm^{-1}): 3061, 2986, 2935, 2885, 2822, 1580, 1560, 1475, 1429, 1367, 1356, 1279, 1240, 1190, 1100, 1055, 1026, 997, 967, 945, 902, 751, 711, 651, 588, 535.

Anal Calcd. for $C_{10}H_9BrO$: C 53.36 , H 4.03

Found C 53.22 , H 4.09

2-Ethynyl-1-(3'-methoxypropynyl)benzene, 169.



169

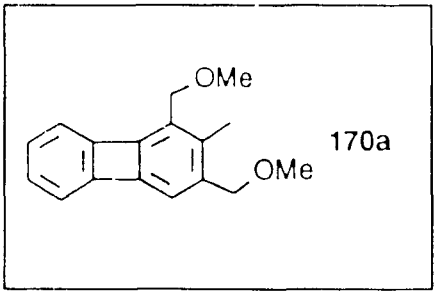
The alkyne **168** (10.00 g, 44 mmol) was added to a magnetically stirred mixture of trimethylsilylacetylene (11.00 g, 112 mmol, Aldrich), copper(I)iodide (0.57 g, 3 mmol), dichlorobis(triphenylphosphine)palladium(II)[150b] (1.54 g, 2.2 mmol, 5mol%) and triphenylphosphine (1.31 g, 5 mmol) in dry diethylamine (100 mL), under argon. The mixture was then heated at 70°C for 14 hours, cooled to 25°C, and the solvent removed. Ether (200 mL) and satd. NH_4Cl (50 mL) were added to the residue and the ether layer washed with

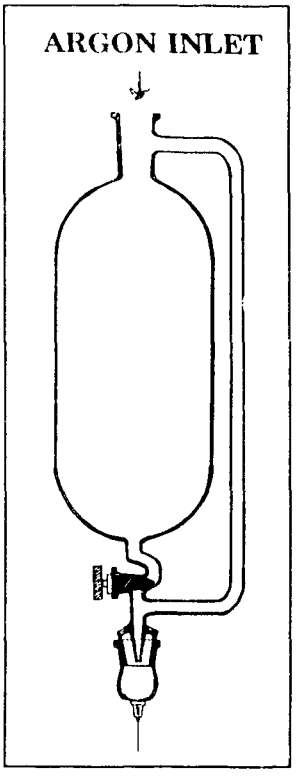
5%HCl (25 mL), water (25 mL) and dried over $MgSO_4$. TLC analysis of the crude product showed the product was inseparable from the starting material **168** (the presence of the product was deduced from the presence of Me_3Si- group in the **^{1}Hnmr** spectrum). Hence, the crude product (after the removal of ether) was dissolved in dry MeOH (200 mL) and K_2CO_3 (2.5g) was added and the mixture stirred at 25°C for 3 hours. The mixture was filtered to remove the solids and the solvent removed to yield a dark-brown oil. Flash chromatography on SiGel (elution with ether:pentane 9:1) gave first unreacted **168** (3.0 g, 30%), followed closely by the desilylated diyne **169** (3.0 g, 57%, based on the recovered starting material) as a light-brown oil. It was distilled immediately under vacuum, with an argon leak, to give the pure diyne as a colorless oil, **bp** 100°C/0.4mm. The diyne decomposed within a day even under an argon atmosphere and hence it had to be used immediately, in the next step; **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 7.45-7.23 (m, 4H, Ar-H), 4.36 (s, 2H, -CH_2-), 3.46 (s, 3H, -OCH_3), 3.29 (s, 1H, Alkyne CH); **^{13}Cnmr** (62.9 MHz, $CDCl_3$) δ 132.4, 131.9, 128.4, 128.0 (Aryl CH), 125.6, 124.5 (Aryl quarternary), 89.0 (C-1'), 84.6 (C-2'), 82.0 (C-5'), 80.9 (C-6'), 60.2 (-CH_2-), 57.4 (-OCH_3); **ms** (EI), m/e (%): 170 (M^+,34), 169 (3), 155 (13), 142 (6), 141 (67), 140 (50), 139 (100), 127 (40), 126 (21), 115 (24), 87 (17), 75 (17), 74 (18), 63 (30).

Anal*	Calcd. for $C_{12}H_{10}O$:	C 84.68 , H 5.92
	Found	C 83.51 , H 5.84

* Facility to do extented combustion was not available

Synthesis of the biphenylenes 170a and 170b





A mixture of the diyne **169** (3.5 g, 20 mmol), 1-methoxy-2-butyne (19.5 g, 0.23 mol), cyclopentadienyldicarbonylcobalt (1 g, 5 mmol, Strem, 25mol%) in argon purged m-xylene (250 mL, freshly distilled from sodium under argon) was added dropwise via a syringe tip (see diagram. This setup was an alternative to a syringe-pump and allowed the spraying of the reactants as an aerosol.) over 12 hours to refluxing m-xylene (500 mL), while it was being irradiated with a 600 watt halogen lamp (at a distance of ~1 meter. The lamp was cooled by a fan). After the addition was over, reflux was continued for an additional 12 hours. The mixture was cooled and the solvent removed under vacuum to leave a dark solid residue. Flash chromatography of the residue on SiGel (elution with 9:1 pentane:ether), gave the biphenylenes **170** as a dark-yellow oil (5 g, 98%). This oil upon bulb to bulb distillation at 0.1mm gave the products (4.5 g, 89%) as a bright yellow oil, **bp** 190-200°C/0.1mm. The two isomers were not separable by chromatography or by distillation. **^{1}Hnmr** (90 MHz, $CDCl_3$) δ 6.85-6.75 (m, 8H, Ar-H), 6.60, 6.45 (s, 1H each, Ar-H), 4.45, 4.35, 4.28(s, 8H total, -CH_2-), 3.35, 3.40 (s, 6H

each, -OCH_3), 2.20, 2.05 (s, 3H each, -CH_3); **ms** (EI), m/e (%): 254 (M^+,40), 253 (14), 224 (5), 223 (13), 222 (100), 206 (4), 190 (6), 178 (38), 162 (9), 138 (5), 137 (15); **IR** (KBr, cm^{-1}): U.V (Cyclohexane) λ_{max} nm (log ε_{max}): 364 (3.55), 347 (3.40), 310 (2.51, shldr), 256 (4.65), 251 (4.46, shldr), 248 (4.48), 228 (4.14, shldr).

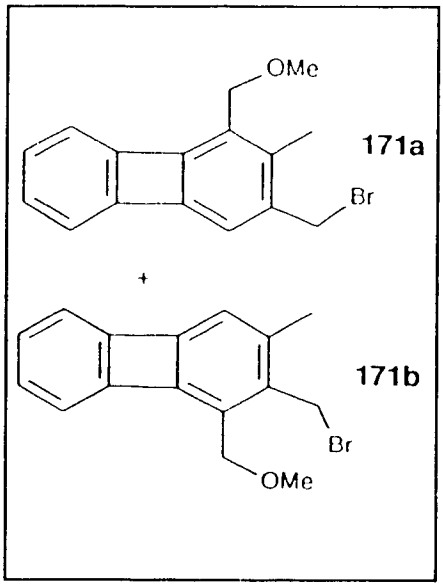
Anal Calcd. for $C_{17}H_{18}O_2$: C 80.28 , H 7.13

Found C 79.74 , H 7.02

Attempted conversion of the bis-ethers 170 to the dibromides 159.

1) Short reaction time: Formation of the mono-bromides 171.

HBr (10 mL, 48% aqueous solution, large excess) was added to the bis-ethers **170** (0.508g, 2 mmol) and the resulting blue colored mixture was magnetically stirred at 25°C for 2 hours. The mixture was poured onto crushed ice and extracted with ether (100 mL). The ether extract was washed with water (50 mL), 10% $NaHCO_3$ (25 mL), satd. NaBr (25 mL)



and dried over $MgSO_4$. Removal of ether resulted in a dark-yellow gum which upon trituration with heaxane gave the mono-bromides **171** as a light yellow solid (364 mg, 60%). **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 6.74-6.63 (m, 8H, Ar-H), 6.51, 6.44 (s, 1H each, Ar-H), 4.45, 4.43, 4.35, 4.34 (s, 2H each, $-CH_2Br$), 3.42, 3.41 (s, 3H each, $-OCH_3$), 2.22, 2.11 (s, 3H each, $-CH_3$) ; **ms** (CI), m/e (%): 304 (M^+,5), 302 (M^+,5), 273 (6), 271 (5), 224 (4), 223 (100).

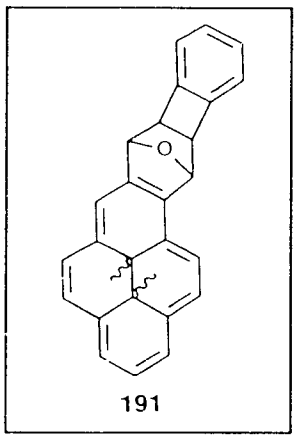
Anal Calcd. for $C_{16}H_{15}BrO$: C 63.38 , H 4.99

Found C 63.48 , H 4.89

2) Longer reaction time: decomposition

HBr (10 mL, 48% aqueous solution, large excess) was added to the bis-ethers **170** (0.508g, 2 mmol) and the resulting mixture was stirred magnetically for 2 days at 25°C. The mixture was filtered and the solid dark-brown residue was extracted with CH_2Cl_2 (50 mL). The CH_2Cl_2 extract upon removal of the solvent gave a red-brown gum which gave a spectrum consistent with the dibromide structure but the mass spectrum indicated the molecular weight to be more the 600. Treatment of the bis-ethers with BBr_3 at -70°C also resulted in polymer formation.

Reaction of the oxa[17]annulene 63 with benzocyclobutadiene.


191

Zinc dust (1g, large excess) was added in one portion to a solution of 1,2-dibromobenzocyclobutene[165] (0.600 g, 2.3 mmol) and the oxa[17]annulene[98] **63** (0.200 g, 0.73 mmol) in dry THF (50 mL). The mixture was then heated to 40°C with magnetic stirring under argon. After 12 hours the mixture was cooled to room temperature, filtered to remove inorganic solids and the filtrate concentrated. The crude material upon SiGel chromatography (elution with 9:1 pentane:ether), gave the olive green exoadducts **191** (0.125 g, 46%). **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 8.64, 8.63 (s, 1H total, H6), 8.60-8.54 (m, 6H, H1-5, H16), 8.09-8.04 (m, 1H, H15), 7.38-7.27 (m, AMBX system, 4H, H9-12), 6.24/6.22 (s, 1H total, H14), 5.85/5.83, (s, 1H total, H7), 3.63 (d, 1H, J = 4.3 Hz, H14), 3.48 (d, 1H, J = 4.3 Hz, H8), -4.06,-4.11/-4.08,-4.13 (s. 6H total, internal $-CH_3$); **^{13}Cnmr** (62.9 MHz, CD_2Cl_2) δ 141.6, 137.1, 136.8, 128.4, 127.3, 124.6, 123.7, 123.2, 122.1, 122.4, 119.6, 115.6 (Aryl C), 80.4, 78.1 (Bridge O-CH-), 52.6, 51.1 (Bridge -CH-), 31.9, 30.9 (Bridge quarternary C), 14.5, 14.4 ($-CH_3$); **ms** (CI), m/e (%): 375 (M+1,93), 374 (M^+,100), 359 (32), 347 (2), 346 (4), 345 (22), 331 (30), 316 (5), 315 (6), 216 (11).

Anal Calcd. for $C_{28}H_{22}O$: C 89.81 , H 5.92

Found C 89.38, H 5.88

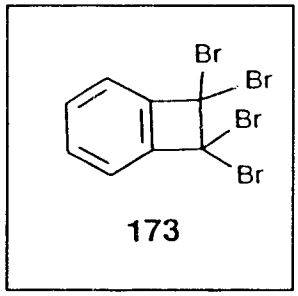
Attempted dehydration of the exo adducts 191.

As detailed in the following table, an acid (0.1 mmol) in solvent (1 mL) was added to exo adducts **191** (10 mg) at the stated temperature. The runs were conducted until some change in the starting material occured (monitored by TLC). All the attempted reactions led to extensive decompositon of the starting material and only trace formation of products, which were identified from the spectrum as **192** and **193**. The internal methyls at δ -4.1 and -4.4 are assigned to those of **193**. These two compounds were inseparable under a variety of conditions.

No	Temperature °C	Solvent	Acid
1	0 - 25	AcOH	36% HCl
2	0 - 25	Benzene	HCl (gas)
3	-50 - 25	None	H_2F_2 (liquid)
4	-10 - 25	Benzene	47% HI
5	-10 - 25	AcOH	HCl (gas)
6	-10 - 50	THF	$TiCl_4$
7	-10 - 50	THF	$SnCl_4$

8	0 - 25	Et_2O	$BF_3.Et_2O$
9	80	Benzene	Al_2O_3
10	25 - 55	CH_2Cl_2	Nafion-H
11	25	Benzene	Nafion-H, light

Synthesis of 1,1,2,2-Tetrabromobenzocyclobutene 173.

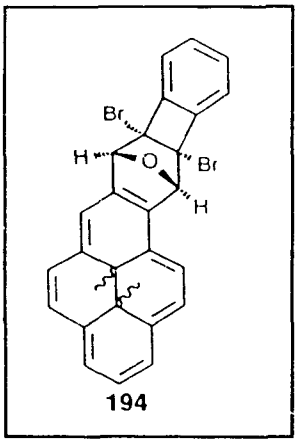


173

The mixture of 1,2-dibromobenzocyclobutenes, **190,** obtained by the procedure of Cava and coworkers[165] were purified (*This purification is essential*) according to the procedure of Barton and coworkers.[157] To the dibromide thus obtained (5.62 g, 20 mmol) was dissolved in CCl_4 (100 mL) was added NBS (17.80 g, 0.1 mol) and proplyenecarbonate (10 mL) and then AIBN (~10 mg, catalyst) was added to the mixture, which was then refluxed with good stirring and irradiation with two 250 watt sunlamps for 12 hours. The mixture was cooled to 25°C and filtered under suction. The residue was washed with dichloromethane (50 mL) and the combined filtrates were washed well with water (5x25 mL), 10% sodium bisulphite (3x25 mL), Satd. NaCl, dried over $MgSO_4$ and evaporated to leave an orange oil. Trituration of this oil with pentane gave white cubic crystals of **173** (5.44 g, 60%). **mp** 117-118°C(lit[165] **mp** 117-118°C).

^{1}Hnmr (250 MHz, $CDCl_3$) δ 7.64-7.51 (m, 2H, H-1,4), 7.34-7.29 (m, 2H, H-2,3).

Synthesis of the dibromobenzocyclobutene adduct 194.



194

Zinc dust (1 g, large excess) was added to a solution of the oxa[17]annulene **63** (200 mg, 0.73 mmol) and the tetrabromide **173** (600 mg, 1.4 mmol) in dry THF (50 mL). The mixture was then heated to 40°C with magnetic stirring under argon. After 6 hours, an additional amount of the tetrabromide (600 mg, 1.4 mmol) was added and the reaction continued for another 6 hours. The reaction mixture was cooled to 25°C and filtered. The solid residue was washed with diethylether (50 mL) and the combined filtrates were evaporated to give a green residue which on chromatography on SiGel (elution with pentane:ether, 9:1) gave the green adduct **194** (159 mg, 41%). **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 8.77-8.54 (m, 7H, H1,3,4,5,6,13,14), 8.10-8.03 (m, 1H, H2), 7.55-7.36 (m, 4H, H8-11), 6.34, 6.32 (s, 1H total, H7), 5.90, 5.89 (s, 1H total, H12), -4.00, -4.01, -4.02, -4.03 (s, 6H total, $-CH_3$); **^{13}Cnmr** (62.9 MHz, $CDCl_3$) δ 142.5, 142.2, 137.9, 137.7, 137.5, 136.3, 136.7, 136.0, 134.4, 132.3, 131.0, 130.7, 129.7, 129.3, 129.2, 128.6, 126.0, 125.5, 125.0, 124.7, 123.9, 123.8, 123.6, 123.5, 123.3, 122.6, 121.7, 121.5, 121.0, 120.5, 119.2, 118.2, 116.4 (Aryl Carbons), 91.4, 89.4, 84.6, 84.0, 82.2, 81.9 (-CH-O-), 71.3, 71.2, 71.0, 70.5, 66.4,

65.6 (-C-Br), 33.5, 31.8, 31.6, 30.7, 29.6, 29.0, 28.6 (bridge quarternary C), 14.3 (broad, internal -CH_3); **ms** (EI), m/e (%): 534 (M^+,14), 532 (M^+,44), 530 (M^+,20), 438 (31), 437 (30), 436 (40), 408 (11), 357 (57), 356 (46), 342 (78), 313 (67), 171 (62), 149 (60); **IR** (KBr, cm^{-1}): 3023, 2961, 2923, 1429, 1367, 1329, 1203, 1141, 1027, 990, 927, 855, 751, 660, 610; U.V (Cyclohexane) λ_{max} nm (log ε_{max}): 513 (3.62), 473 (3.97), 420 (3.82, shldr), 380 (4.58), 366 (4.30, shldr), 342 (4.92), 286 (3.92).

Anal Calcd. for $C_{28}H_{20}Br_2O$: C 63.18 , H 3.79

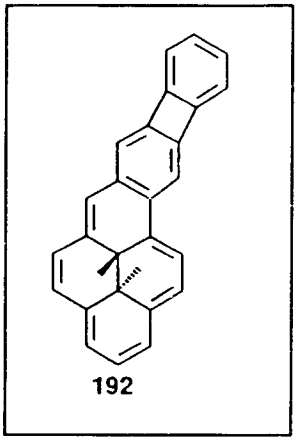
Found C 62.98 , H 3.79

HRMS Calcd. for $C_{28}H_{20}{}^{81}Br_2O$: 533.9869

Found 533.9869

Synthesis of *trans*-14b,14c-dimethyl-14b,14,c-dihydro-benzo[1",2":3,4]cyclobuta[1,2-*b*]naphtho[2,1,8-*fgh*]anthracene, 192.

$TiCl_4$ (0.5 mL, 4.5 mmol) was injected by syringe in to a stirred suspension of zinc dust (2 g, large excess) in dry THF (20 mL) under argon at room temperature. After stirring for 3 hours (the suspension was dark green in color) at 25°C, the solid dibromide **194** (100 mg, 0.18 mmol) was added at once to the suspension and the stirring was continued for an additional 4 hours. The



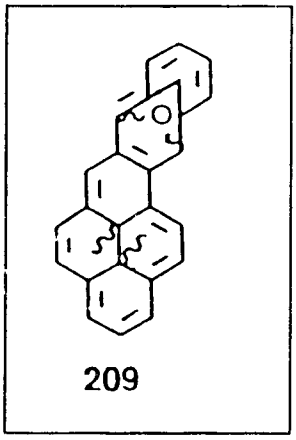
192

reaction was then quenched with ice-water (10 mL). Diethylether (50 mL) was added and the organic layer separated. The ether layer was washed with satd. $NaHCO_3$ solution (2x25 mL), satd. NaCl (2x25 mL), dried over $MgSO_4$ and evaporated leave a dark red residue. This residue was taken up in pentane (50 mL) and filtered through SiGel (5 g). The pentane solution after evaporation and recrystallisation from pentane gave dark-red (almost black) crystals of **192** (20 mg, 31%). **mp** 190°C, ($CDCl_3$, 360 MHz) δ 8.53 (AB, 1H, J = 7.16 Hz, H13), 8.25 (s, 1H, H12), 8.22 (s, 1H, H6), 8.15, 8.12 (AB, 2H, J = 8.73 Hz, H4, H5), 8.02 (ABM, 1H, J = 8.72 Hz, H1), 7.95 (AB, 1H, J = 7.16 Hz, H14), 7.91 (ABM, 1H, J = 6.83 Hz, H3), 7.57 (ABM, 1H, H2), 7.43 (s, 1H, H7), 6.99 - 6.93 (AMBX, m, 4H, H8-11), -2.76, -2.77 (s, 3H each, $-CH_3$). See text for the proton assignments based on 1H-COSY45 experiment. **^{13}Cnmr** (62.9 MHz, $CDCl_3$) δ 151.74, 151.50, 148.99, 148.67 (quaternary C in biphenylene), 138.6, 136.5 (quarternary C in biphenylene-DHP junction), 136.51, 133.96, 130.99, 128.77 (quarternary C in DMDHP), 129.80, 129.74 (C9,10), 125.94 (C5), 125.59 (C4), 125.27 (C1), 124.78 (C6), 123.86 (C2), 122.88 (C3), 122.30 (C14), 117.89 (C13), 117.74 (C7), 111.94 (C12), 33.9, 33.6 (bridge quaternary), 16.2, 16.1 (internal - CH_3); **ms** (EI), m/e (%): 356 (M^+,23), 342 (15), 341 (40), 327 (27), 326 (100), 324 (13), 163 (37); **IR** (KBr, cm^{-1}): U.V (Cyclohexane) λ_{max}nm(logε): 590 (4.74, shldr), 526 (5.26), 467 (5.08), 393 (5.99), 347 (5.56, shldr), 342 (5.59), 309 (5.26), 292 (5.17, shldr), 271 (5.53), 249 (5.25), 222 (5.55).

Anal Calcd. for $C_{28}H_{20}$: C 94.34 , H 5.66

	Found	C 93.93 , H 5.65
HRMS	Calcd. for $C_{28}H_{20}$:	356.1594
	Found	356.1594

Reaction of the oxa[17]annulene 63 with cycloheptatriene - Synthesis of 209-211.



The oxa[17]annulene, **63** (100 mg, 0.365 mmol) was dissolved in a 1:1 (v/v) mixture of degassed benzene and cycloheptatriene (10 mL, large excess of cycloheptatriene). This solution was placed in a thick walled tube and the tube was sealed under argon. It was then heated at 160°C(+/- 2°C) for 48 hours after which it was allowed to cool to room temperature and with caution the tube was opened. The volatile contents of the tube were evaporated to leave a dark-green residue and the residue was chromatographed on SiGel (elution with 9:1, pentane:ether) to give the green adducts **209-211** (80 mg, 60%). **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 8.65-8.42 (m, 8H, H1,3,4,5,6,15,16), 8.39-7.99 (m, 1H, H2), 6.41-5.55 (m, 6H, H7,9,10,11,12,14), 2.89-2.43, 1.31-1.02 (m, 4H, H8,13, -CH_2-), -4.09,-4.12, -4.16, -4.20, -4.23, -4.24 (s, 6H total, -CH_3); **ms** (CI), m/e (%):405 (M+41,1), 393 (M+29,1), 366 (10), 365 (M+1,38), 364 (M^+,24), 349 (1), 347 (1), 301 (2), 287 (1), 273 (28), 272 (13), 257 (3), 242 (1), 121 (4), 107 (1), 95 (1), 93 (100), 91 (26), 79 (9).

Anal Calcd. for $C_{27}H_{24}O$: C 88.97 , H 6.64

Found C 88.45 , H 6.50

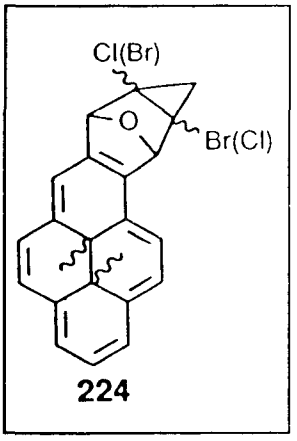
Attempted dehydration/deoxygenation of the cycloheptatriene adducts 209-211.

The cycloheptatriene adduct **209-211** (10 mg, 0.02 mmol) was dissolved in a solvent (1 mL), and this solution was treated with a deoxygenating/or dehydrating agent. The reaction conditions of these experiments are detailed in the following table.

No	Temperature °C	Solvent	Reagent
1	0 - 25	AcOH	36% HCl
2	25	Benzene	P_4S_{10}
3	-10 - 25	CH_2Cl_2	BF_3-Et_2O
4	0	Et_2O	HPF_6
5	-20 - 25	CH_2Cl_2	$TiCl_4$
6	0 -25	THF	$TiCl_4$ - Zn

7	-5 - 25	THF	$TiCl_4/Zn/EtN_3$
8	80	Benzene	$Fe_2(CO)_9$
9	25 - 60	CH_3CN	Me_3SiCl/NaI

Synthesis of the cyclopropene adducts 224.



224

Solid KF (116 mg, 2 mmol) was added to a solution of the oxa[17]annulene **63** (100 mg, 0.36 mmol), 1-Bromo-2,2-dichloro(trimethylsilyl)cyclopropane **222**[189] (0.525 mg, 2 mmol) and 18-Crown-6 (1.05 g, 4 mmol) in dry THF (10 mL) under argon at -10°C. The solution was stirred magnetically for 6 hours at the same temperature and an additional portion of KF (116 mg, 2 mmol) and the cyclopropane **222** (0.525 mg, 2 mmol) were added and the stirring continued for another six hours. After 12 hours water (10 mL) and ether (50 mL) were added to the reaction mixture, the ether layer separated, washed with satd. NaCl (3x10 mL), dried over $MgSO_4$ and the solvent evaporated to give a dark green gummy residue. This residue upon chromatography over SiGel (elution with 8:2 pentane:ether) gave the cyclopropene adducts **224** (64 mg, 41%) as a mixture of many isomers (see text) which were not separable by fractional recrystallisation or by chromatography. **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 8.61-8.01

(m, 7H, H1,3,4,5,6,11,12), 7.99-7.96 (m, 1H, H2), 6.17-6.12 (m, 1H, H10), 5.74-5.66 (m, 1H, H7), 3.50-2.02 (m, 2H, $-CH_2-$), -3.90, -3.93, -3.94, -3.96, -3.99, -4.00 (s, 6H total, $-CH_3$); **^{13}Cnmr** (62.9 MHz, $CDCl_3$) δ 138.30, 138.05, 137.78, 137.57, 137.47, 136.84, 136.68, 135.78, 135.66, 133.96, 129.33, 128.33, 125.19, 124.91, 124.81, 124.39, 123.75, 123.61, 123.37, 123.22, 120.54, 120.25, 120.16, 119.89, 118.24, 118.12, 117.65, 117.56, 115.74 (Aromatic carbons), 88.89, 83.93, 83.49, 82.65, 82.24, 81.63, 81.51, 80.36, 80.30 (-CH-O-), 65.83, 52.67, 52.31, 51.76, 43.82, 43.25, 42.79, 42.72 (quaternary -C-Cl and -C-Br), 31.98, 31.77, 31.30, 30.92, 30.61, 30.50 ($-CH_2-$), 15.25, 14.36 ($-CH_3$); **ms** (EI), m/e (%): 428 (M^+,13), 426 (M^+,40), 424 (M^+,28), 418 (5.6), 413 (8.7), 412 (7.4), 411 (13.6), 409 (16.5), 332 (6.6), 330 (43), 329 (10), 315 (12), 294 (22), 286 (43), 267 (19), 266 (100); **IR** (KBr, cm^{-1}): 3026, 2987, 2958, 2919, 2860, 1445, 1367, 1337, 1279, 1220, 1152, 1064, 986, 908, 859, 830, 810, 717, 673; U.V (Cyclohexane) λ_{max}nm(logε): 513 (3.64, shldr), 475 (4.28), 418 (4.05), 380 (4.95), 366 (4.60, shldr), 342 (5.33), 286 (4.25).

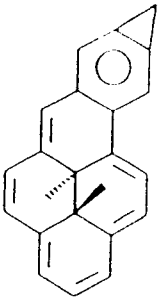
Anal Calcd. for $C_{23}H_{18}BrClO$: C 64.89 , H 4.26

Found C 64.70 , H 4.30

HRMS Calcd. for $C_{23}H_{18}{}^{79}Br_1{}^{37}Cl_1O_1$: 426.0196

Found 426.0196

Attempted synthesis of the benzocyclopropene 218.



218

1 Reaction with a $TiCl_4$-Zn system

$TiCl_4$ (0.1 mL, 0.5 mmol) was syringed in to a well stirred suspension of zinc dust (200 mg, large excess) in dry THF (10 mL), under argon at 25°C. The stirring was continued for an additional 3 hours after which period the suspension was dark-green in color. The cyclopropane adduct **224** (50 mg, 0.12 mmol) in dry THF (1 mL) was then added dropwise to the above green supension. The stirring continued for 2 days at 25°C. Then the reaction mixture was quenched by the addition of satd. $NaHCO_3$ (5 mL), the organic layer separated, washed with satd. NaCl (2x5 mL), dried over $MgSO_4$ and the solvent evaporated to leave a filmy residue which upon rapid radial chromatography (Silica gel plates made with Merck7749 silica gel with binder and indicator; elution with 9:1 pentane:ether under nitrogen) gave a trace of red-brown products tentatively identified from the spectrum as the ring opened **225** and the benzcyclopropene **218** (5:1 ratio from the integration of the internal methyl protons). This product mixture was highly unstable after the isolation, the solutions of which had a very unpleasant odour causing severe headaches and rapidly decomposed into deep-red polar products which could not be further characterised spectroscopically. The products from the red-brown band had the following peaks;

^{1}Hnmr (250 MHz, $CDCl_3$) δ 8.87-7.27 (complex multiplet, aryl and vinyl protons), 3.47, 3.45 (singlets, -CH_2- of **225** and **218** respectively in a 5:1 ratio), -1.64, -1.65, -1.66, -1.67 (singlets, -CH_3 of **218**), -3.60, -3.62, -3.63, -3.64 (singlets, -CH_3 of **225**).

Eluted next was the unreacted starting compound **224** (20 mg, 40%).

2 Reaction with a $TiCl_4$/MeLi/Et_3N system

MeLi (10 µL, 1.0 M solution, 0.44 mmol) was syringed into a stirred solution of **208** (50 mg, 0.12 mmol), $TiCl_4$ (44 µL, 0.40 mmol) and Et_3N (55 µL, 0.43 mmol) in dry THF (20 mL) under argon, at -70°C. The reaction mixture was stirred at the same temperature for 6 hours during which period, the color of the mixture gradually changed from dark-green to dark-red. Then it was warmed up to -30°C and quenched with water (5 mL), the organic layer separated, washed with satd. NaCl (2x10 mL), dried quickly over $MgSO_4$ and the solvent evaporated under low pressure (0.1mm) without heat. **^{1}Hnmr** spectrum of the crude product (20 mg) indicated that it was a mixture of *at least 20 different compounds!* All attempted purification of this mixture resulted in further decomposition of the products and no useful information could be obtained from any spectroscopic measurements.

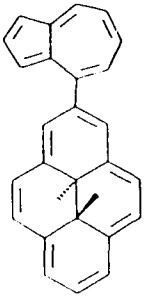
Attempted reaction of the dihydropyryne 62 with 1,2,4-triazine.

$NaNH_2$ (63 mg, 1.6 mmol) and a catalytic amount of t-BuOK (5 mg) were added to a solution of the bromodihydropyrene[98] **77** (100 mg, 0.32 mmol) and 3-methylthio-1,2,4-triazine (500 mg, large excess) in dry THF (5 mL) under argon. The mixture was stirred magnetically at room temperature for 16 hours, and it was tested periodically by TLC. At the end, the mixture was decomposed with methanol and the solvent evaporated. The residue, after chromatography on SiGel, gave the unreacted bromide, DMDHP and the unchanged triazine amounting to 90% of the total mass of the reactants and no other new products.

Attempted reactions of the dihydropyryne with neat ethylvinylether, 2,3-dihydrofuran, and toluene solution of 1,2 diethoxyethene[193] under similar conditions also led to the recovery of the starting materials and DMDHP.

Reaction of dihydropyryne 62 with Azulene.

$NaNH_2$ (63 mg, 1.6 mmol) and a catalytic amount of t-BuOK (5 mg) were added to a solution of the bromide **77** (100 mg, 0.32 mmol) and azulene[155] (600 mg, 4.6 mmol) in dry THF (5 mL), under argon. The mixture was stirred magnetically at room temperature for 3 hours and quenched with methanol. The residue after evaporation of the solvent was subjected to sublimation



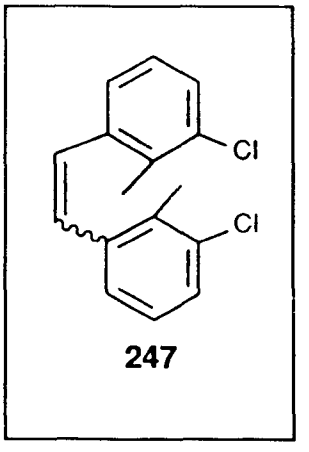
237

at 60 C and 1 mm pressure. This removed most of the unreacted azulene. The residue after sublimation was chromatographed on SiGel. Elution with pentane gave a trace of unreacted azulene, DMDHP (50 mg) and a mixture of the biaryls **237** and **238** (5 mg, 4.4%). Repeated fractional crystallisation from heptane gave one of the isomers pure. **mp** 156-158°C (decomp); **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 9.00 - 7.15 (16H, complex multiplets, aromatic protons), -3.88, -3.96 (3H each, singlets, internal methyls). U.V. (cyclohexane) λ_{max} nm (ε_{max}) 620 (1.96, shldr), 512 (2.85), 429 (2.12, shldr), 387 (3.18), 361 (2.93, shldr), 341 (3.31), 295 (2.69, shldr), 268 (3.04), 251 (2.97, shldr) ; **ms** (EI), m/e (%): 358 (M^+,31), 344 (20), 343 (45), 329 (27), 328 (100), 327 (22), 326 (47), 172 (18), 164 (13.3), 163 (33).

HRMS Calcd. for $C_{28}H_{22}$: 358.1753

Found 358.1767

1,2-Bis(3-chloro-2-methylphenyl)ethene, 247.



247

1) Ni(0) mediated coupling of the Grignard 64a.

About 1 mL of a solution of 2,6-dichlorotoluene (80.5 g, 0.5 mol) in dry THF (150 mL) and 1,2-dibromoethane (~0.5 mL, activator) were added to a warm (~40°C),

stirred mixture of magnesium (12.5 g, 0.51 mol) in dry THF (300 mL) under nitrogen. After the reaction started, the remainder of the 2,6-dichlorotoluene solution was added dropwise to the magnesium (~1 hour), and the reaction mixture refluxed for 3 hours. It was cooled to 25°C and transfered (under nitrogen) to a dropping funnel.

The Grignard reagent thus prepared was added dropwise to a mechanically stirred solution of trans-1,2-dichloroethene (23 g, 0.24 mol), and (2.5 mmol, 5 mol%, catalyst) in dry THF (250 mL) at -30°C at such a rate that the temperature was kept between -15- -20°C. After the addition was over (~2 hours), the reaction mixture was *cautiously* heated to a reflux and refluxed for 6 hours. The mixture was cooled to 25°C and poured over crushed ice (500 g). It was then extracted with CH_2Cl_2 (3x200 mL). The combined extracts were washed with 10%HCl (100 mL), water (100 mL), satd. NaCl (100 mL) and dried over $MgSO_4$. The solvent was removed under vacuum to leave a dark-brown oil which upon chromatography over SiGel (elution with 9:1 hexanes:CH_2Cl_2) gave the biaryl **248** first (6.25 g, 10%, identical to an authentic sample[202]). Eluted next were the stilbenes **247** (48.0 g, 70%, mixture of cis and trans isomers). The two isomers were not separable by chromatography but recrystallisation from 95%EtOH gave a pure sample of the trans isomer as colorless needles. **mp** 146-148°C **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 7.46-7.11(m, 3H, Ar-H),7.15(s, 1H, =CH), 2.45(s, 3H, -CH_3); **ms** (CI), m/e (%):319 (M+41,1), 317 (M+41,2), 309 (M+29,1), 308 (M+29,2), 307 (M+29,15),

306 (M+29,4), 306 (M+29,23), 281 (M+1,10), 280 (M+1,12), 279 (M+1,64), 278 (M+1,28), 277 (M+1,100), 276 (M^+,18), 257 (37), 243 (43); (EI) m/e(%): 280 (M^+,10), 279 (M^+,10), 278 (M^+,61), 277 (M^+,18), 276 (M^+,100), 241 (20), 226 (42), 206 (67), 191 (24), 190 (15), 189 (26); **IR** (KBr, cm^{-1}):

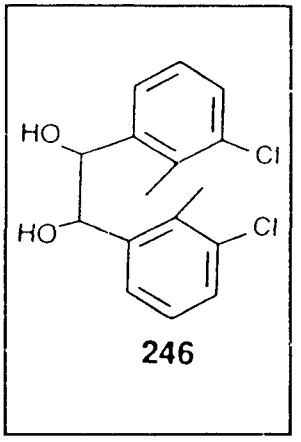
Anal Calcd. for:$C_{16}H_{14}Cl_2$ C 69.33 , H 5.09

Found C 69.08 , H 5.01

2) Ti(0) mediated coupling of the aldehyde 244

$TiCl_4$ (3.7 g, 19.5 mmol) was added to a stirred suspension of Zinc dust (2.6 g, excess) in dry THF (50 mL) under argon. The mixture was brought to a reflux and refluxed for 1 hour. After cooling to 25°C, the aldehyde **244**[199] (2.0 g, 13 mmol) in THF (25 mL) was added dropwise to the grey suspension. After the addition was over, the mixture refluxed for 3 hours, cooled to 25°C and quenched with satd. Na_2CO_3. The organic layer was separated, the aqueuos layer extracted with ether (2x50 mL) and the combined organic layers washed with satd. NaCl and dried over $MgSO_4$. Removal of the solvents and recrystallisation of the crude product gave colorless needles of the trans-stilbene (1.6 g, 90%), identical to the previously obtained sample.

1,2-Bis(3-chloro-2-methylphenyl)-1,2-dihydroxyethane, 246



246

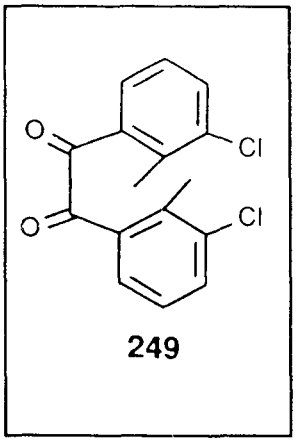
$TiCl_4$ (9.25g, 49 mmol) was added dropwise to the aldehyde **244** (5g, 32.5 mmol) in dry THF (100 mL) at -10 C under argon. Zinc dust (6.4g, excess) was added to the stirred mixture, in small portions. The color of the reaction mixture turned from dark-yellow to pale green. After stirring for 3 hours without further cooling, the reaction was quenched with satd. Na_2CO_3. The organic layer separated, the aqueous layer extracted with ether (3x50 mL) and the combined organic layers dried over $MgSO_4$. Removal of the solvents gave the diols **246** as a white solid. The solid was recrystallised from CH_2Cl_2/heptane (4.55 g, 90%). **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 7.49-7.07 (m, 6H, Ar-H), 4.93, 4.65 (s, 1H each, -CH-O), 4.79 (s, 2H, -OH), 2.35 (s, 6H, $-CH_3$); **^{13}Cnmr** (62.9 MHz, $CDCl_3$) δ 140.3, 139.5, 135.0, 134.9, 133.9 (Aryl quarternary C), 128.8, 126.6, 126.5, 125.8, 125.7 (Aryl CH), 74.8, 63.5 (-CHOH), 15.1 ($-CH_3$).

Anal Calcd. for $C_{16}H_{16}Cl_2O_2$: C 61.75 , H 5.15

Found C 60.95 , H 5.18

1,2-Bis(3-chloro-2-methylphenyl)ethanedione, 249

1) Oxidation of the stilbene 247



249

H_2O_2 (14mL, 30% aqueous solution, excess) was added catiously ***(CAUTION: Exothermic reaction! An over sized vessel must be used to avoid foaming!)*** to a stirred suspension of the stilbene 11 (5.54 g, 20 mmol) and 48% HBr (15 mL) in DMSO (80 mL). An exothermic reaction commenced immediately. After 30 minutes the mixture was cautiously heated to 110-120°C for 15 hours. It was then cooled to 25°C, poured into crushed ice (500 g) and the precipitate filtered. The crude product upon recrystallisation from 95% EtOH gave the unreacted stilbene 11 (3.05 g, 55%). Concentration of the mother liquor gave the dione 11 (2.46 g, 40%, based on starting stilbene, 89%, based on the recovered stilbene) as yellow needles. **mp** 122-124°C; **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 7.62-7.19 (m, 3H, Aryl-H), 2.67 (s, 3H, $-CH_3$); **^{13}Cnmr** (62.9 MHz, $CDCl_3$) δ 194.9 (CO), 138.7, 137.2, 134.1 (Aryl quarternary C), 134.3, 130.7, 136.7 (Aryl CH), 17.3 ($-CH_3$) ; **ms** (CI), m/e (%): 337 (M+29,3), 335 (M+29,4), 311 (M+1,2), 309 (M+1,18), 308 (M+1,5), 307 (M+1,28), 305 (M^+,1), 173 (25), 172 (9), 171 (77), 157 (22), 156 (10), 153 (100); (EI) m/e(%): 308 (M^+,weak), 306 (M^+,weak), 170 (4), 156 (2), 155 (33), 154 (18), 153 (100), 152 (16); **IR** (KBr, cm^{-1}): 3080, 1687 (C=O), 1560, 1442, 1379, 1291, 1128, 1180, 1130, 777, 739,

733, 695, 664.

Anal	Calcd. for $C_{16}H_{12}Cl_2O_2$:	C 62.56 , H 3.94
	Found	C 62.28 , H 3.93

2) Oxidation of the diols 246

DMSO (1.7 mL, 22 mmol) was added dropwise to a stirred solution of oxalyl chloride (1 mL, 11 mmol) in dry CH_2Cl_2 (25 mL) under nitrogen at -30°C. After 2 minutes the diol **246** (0.44g, 1.42 mmol) in THF (5 mL) was added at once to the mixture and the stirring was continued for 30 minutes. Triethylamine (7 mL, 50 mmol) was then added to the mixture and after 30 minutes at -30°C, the mixture was allowed to warm up to 25°C over 2 hours. Ether (100 mL) was added to the reaction mixture, which was then washed sucessively with water (2x25 mL), 10%HCl (25 mL), water (25 mL), 10%$NaHCO_3$ (25 mL) and dried over $MgSO_4$. Removal of solvent gave the crude product as an oily solid which upon recrystallisation from CH_2Cl_2/heptane gave the dione **249** (0.262 g, 60%) as yellow plates, identical to the previously obtained sample.

Attempted Ti(0) coupling of 3-methoxymethyl-2-methylbenzaldehyde

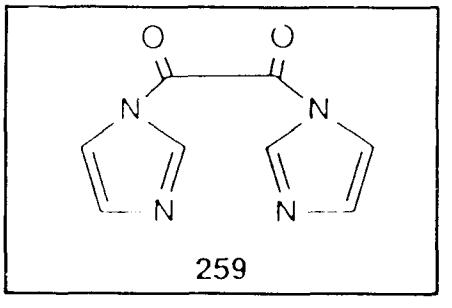
3-Methoxymethyl-2-methylbenzaldehyde[199] was reacted with the $TiCl_4$/Zn system as described for the reaction of 3-chloro-2-methylbenzaldehyde. No expected products (diol or stilbene) could be obtained. Only gummy materials of high molecular weights were obtained.

Attempted benzoin condensation of 242

3-methoxymethyl-2-methylbenzaldehyde **242** (3.54 g, 22 mmol) was added to a solution of NaCN (0.24 g, 4.9 mmol, catalyst) in 95%EtOH (100 mL). The mixture was heated first at 40°C (2 hours) and then at reflux (6 hours). TLC analysis indicated no reaction and work-up of the reaction mixture led to the recovery of **242** (90%).

1,2-diketone syntheses

1,1'-Oxalylimidazole, 259.



259

1) From oxalyl chloride and imidazole

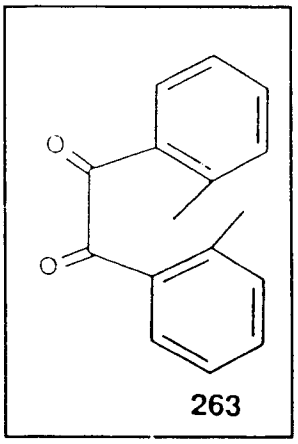
Freshly distilled oxalyl chloride (12.7 g, 0.1 mol) in dry THF (25 mL) was added dropwise to a well stirred solution of imidazole (27.2 g,

0.4 mol, dried overnight under vacuum) in dry THF (300 mL) under argon at 0°C. After the addition was over (~30 minutes), the cooling bath was removed and the stirring continued at 25°C for 4 hours. Then the mixture was filtered under a blanket of argon, the precipitate washed with dry THF (100 mL) and the filtrates combined. A small portion of the filtrate on evaporation gave a very hygroscopic, off-white solid. **ms** (CI), m/e(%): 231 (M+41,1), 219 (M+29,1), 191 (M+1,13), 109 (8), 97 (24), 70 (100); (EI),m/e(%): 190 (M^+,3), 163 (4), 120 (4), 95 (11), 69 (7), 68 (100), 67 (9). **IR** (KBr, cm^{-1}): 3110, 2980, 2800, 2590, 1595 (C=O), 1420, 1300, 1080, 1060, 900, 880, 830, 760, 630.

2) From oxalyl chloride, imidazole and diisopropylethylamine

Oxalyl chloride (6.60 g, 0.1 mol) in dry THF (25 mL) was added dropwise to a stirred solution of imidazole (7.07 g, 0.05 mol) and diisopropylethylamine (18.36 mL, 0.1 mol) in dry THF (200 mL) at 0°C under argon. After the addition was over the mixture was stirred at 25°C for 1 hour and filtered under a blanket of argon. The precipitate was washed with dry THF (50 mL) and the combined filtrates were used directly for the next reaction.

1,2-Bis(2-methylphenyl)ethanedione, 263



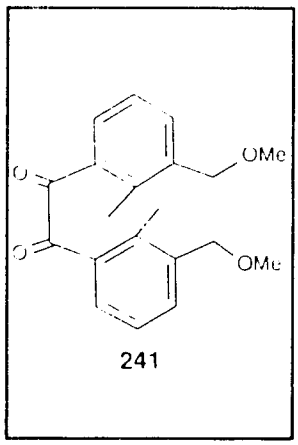
263

2-Bromotoluene (3.42 g, 20 mmol) in dry THF (20 mL) was added, under argon, to a warm, stirred mixture of magnesium turnings (480 mg, 0.02 g atm) and dry THF (30 mL) at such a rate that the mixture kept refluxing. After the addition was over the mixture was refluxed for an additional hour and gradually cooled to -50°C. 1,1'-oxalylimidazole, **259** (1.80 g, 9 mmol) in dry THF (50 mL) was added dropwise to the cooled Grignard reagent while maintaining the internal temperature of the mixture between -45 and -40°C. After the addition was over, the mixture was stirred for an additional 15 minutes without further cooling and quenched with satd. NH_4Cl. The organic layer was removed, the solvent evaporated to leave a yellow oily residue. This was passed through a small column of SiGel to give the dione **263** as yellow crystals (1.32 g, 80%). **mp** 92-94°C (lit[249]. mp 92-94°C); **^{1}Hnmr** (90 MHz, $CDCl_3$) δ 7.70-7.15 (m, 4H, Ar-H), 2.75 (s, 3H, $-CH_3$); **ms** (CI), m/e (%): 279 (M+41,weak), 267 (M+29,12), 239 (M+1,8), 237 (1), 119 (100); (EI), m/e (%): 119 (M1/2, 100), 91 (49), 65 (24).

The dione **249** was prepared as described above in 70% yield. It was found identical in all respects to a sample made by the oxidation of **246**. Other diones made from Grignards **262** and **264** were identical to the compounds reported in the literature (1,2-bis(2',6'-dimethylphenyl)ethanedione[250] and 1,2-

bis(3'-pyridyl)ethanedione[251]). The reaction conditions and the product yields are listed in Table 17.

1,2-Bis(3-methoxymethyl-2-methylphenyl)ethanedione, 241



241

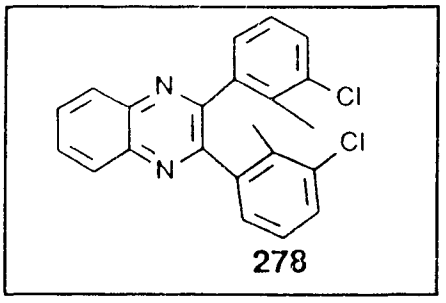
1,1'-Oxalylimidazole (52 mmol, solution in THF, prepared from oxalylchloride/diisopropylethylamine/ imidazole as described above) was added dropwise to the solution of the Grignard **251** (prepared from 18.0 g, 105 mmol of the ether as described in Ref. 199) at -40 - -35°C, under argon. After the addition was over it was stirred for 15 minutes, solid EDTA (~10 g) was added to the reaction mixture and it was allowed to warm upto 25°C. satd. NH_4Cl (50 mL) was then added to the mixture and the organic layer separated. The aqueous layer was extracted with ether (2x100 mL) and the combined organic layers were dried over $\mathbf{Na_2SO_4}$. After the removal of the solvents the crude product was chromatographed on SiGel (elution with 8:2 pentane:ether) to give the unreacted ether (3 g, 17%) followed by the yellow dione **241** (8.1 g, 50%). It was recrystallised from MeOH to give pure **241** as yellow needles. **mp** 69°C; **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 7.59-7.21 (m, 3H, Ar-H), 4.51 (s, 2H, -CH_2), 3.43 (s, 3H, -OCH_3), 2.60 (s, 3H, -CH_3); **^{13}Cnmr** (62.9 MHz, $CDCl_3$) δ 196.8 (CO), 139.6, 138.6, 132.9 (Aryl quarternary C), 133.4, 132.1, 125.5 (Aryl CH), 72.6 (-CH_2-O), 58.4 (-OCH_3), 15.8 (-CH_3) ; **ms** (CI), m/e (%): 355(M+29,weak), 327

(M+1, weak), 326 (M$^+$,1), 295 (9), 164 (10), 163 (M1/2,100), 121 (23); **IR** (KBr, cm^{-1}): 645, 725, 743, 784, 913, 930, 970, 1116, 1193, 1225, 1312, 1376, 1450, 1461, 1582, 1674 (C=O), 2819, 2858, 2992.

Anal Calcd. for $C_{20}H_{22}O_2$: C 73.59 , H 6.79

Found C 73.38 , H 6.71

2,3-Bis(3-chloro-2-methylphenyl)quinoxaline, 278.



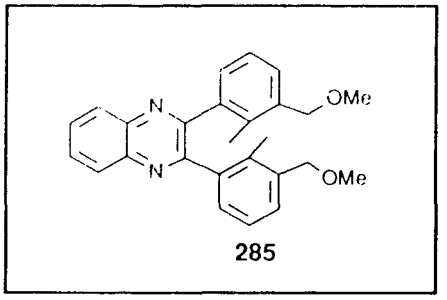
278

A mixture of 1,2-phenylenediamine (1.6 g, 14.8 mmol) and the dione **249** (4.0 g, 13.0 mmol) in MeOH (200 mL) was refluxed for 6 hours under nitrogen. The mixture was cooled to 25°C and the solvent evaporated to leave a brown solid. This was chromatographed on SiGel (elution with 8:2 hexanes:$CHCl_3$) to yield the teraryl **278** (4.43 g, 90%) as white crystals. A sample was recrystallised from 95%EtOH. **mp** 171-172°C ; **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 8.21-8.14 (m, 2H, H-5,H-8), 7.87-7.80 (m, 2H, H-6,H-7), 7.35-6.98 (m, 6H, H-4',5',6'), 2.17 (s, 6H, -CH_3); **^{13}Cnmr** (62.9 MHz, $CDCl_3$) δ 154.1, 140.9, 139.6, 135.4, 134.5 (C-2,C-3,C-9,C10,C-1',C-2',C-3'), 130.5, 129.6, 129.2, 128.3, 126.3 (C-5,C-6,C-7,C-8,C-4',C-5',C-6'), 17.6 (-CH_3); **ms** (CI), m/e (%): 412 (M+29, 12), 420 (M+29, 20), 384(M+1, 11), 383 (M+1, 65), 382 (M+1, 20), 382 (M+1,

100).

Anal	Calcd. for $C_{22}H_{16}Cl_2N_2$:	C 69.67 , H 4.25 , N 7.39
	Found	C 69.67 , H 4.27 , N 7.36

2,3-Bis(3-methoxymethyl-2-methylphenyl)quinoxaline, 285



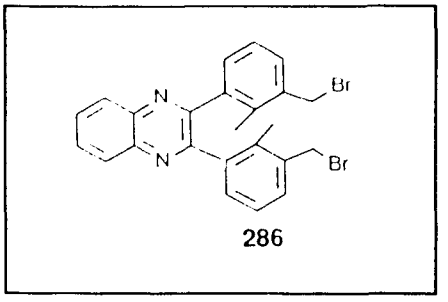
285

A mixture of 1,2-phenylenediamine (320 mg, 2.96 mmol) and the dione **241** (600 mg, 1.84 mmol) in dry EtOH (150 mL) containing 4Å molecular sieves (~5 g) was refluxed for 30 hours under nitrogen. The mixture was then cooled to 25°C, filtered to remove the molecular sieves and the solvent removed. The solid residue was chromatographed on SiGel (elution with 7:3 hexanes:ethylacetate) to give the teraryl 11 as a pale-viscous oil, which upon trituration with ethyl acetate yielded colorless crystals of pure **285** (601 mg, 82%). **mp** 151°C; **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 8.20-8.17 (m, 2H, H-5,H-8), 7.82-7.79 (m, 2H, H-6,H-9), 7.27-7.02 (m, 6H, H-4',5',6'), 4.40 (s, 4H, $-CH_2O$), 3.27 (s, 6H, $-OCH_3$), 2.08 (s, 6H, $-CH_3$); **^{13}Cnmr** (62.9 MHz, $CDCl_3$) δ 155.4, 140.9, 138.6, 136.7, 134.7 (C-2,C-3,C-9,C-10,C-1',C-2',C-3'), 130.0, 129.5, 129.2, 128.6, 125 (C-5,C-6,C-7,C-8,C-4',C-5',C-6'), 72.8 ($-CH_2O$), 57.7 ($-OCH_3$), 15.8 ($-CH_3$).

Anal	Calcd. for $C_{26}H_{26}N_2O_2$:	C 78.36 , H 6.57 , N 7.02

Found C 78.43 , H 6.58 , N 7.02

2,3-Bis(3-bromomethyl-2-methylphenyl)quinoxaline, 286.



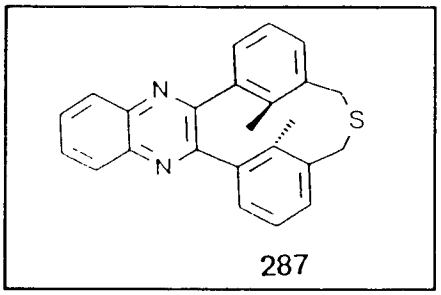
286

The teraryl **285** (1.00 g, 2.5 mmol) in dry CH_2Cl_2 (15 mL) was added to a stirred solution of BBr_3 (2.50 g, 10 mmol, excess) in dry CH_2Cl_2 (100 mL) at -70 °C under argon. The solution turned orange in color. The mixture was allowed to warm upto 25 °C and stirred for 10 hours. It was then quenched with the addition of ice cold water (20 mL). A solution of K_2CO_3 was added to bring the pH of the aqueous layer to 8. The organic layer was separated, dried over $MgSO_4$ and the solvent removed to yield the crude product. It was recrystallised from CH_2Cl_2/heptane to yield the pure dibromide **286** (1.00 g, 80%) as colorless needles. **mp** 250-251°C; **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 8.22-8.18 (m, 2H, H-5,H-8), 7.85-7.81 (m, 2H, H-6,H-7), 7.27-7.06 (m, 6H, H-4',5',6'), 4.44 (s, 4H, $-CH_2Br$), 2.15 (s, 6H, $-CH_3$); **^{13}Cnmr** (62.9 MHz, $CDCl_3$) δ 154.9, 140.9, 139.1, 136.5, 135.6 (C-2,C-3,C-9,C-10,C-1',C-2',C-3'), 130.8, 130.5, 130.3, 129.2, 125.7 (C-5,C-6,C-7,C-8,C-4',C-5',C-6'), 32.2 ($-CH_2Br$), 16.0 ($-CH_3$); **ms** (EI), m/e (%): 498 (M', 5), 496 (M', 10), 494 (M', 5), 417 (100), 415 (98), 336 (28).

Anal Calcd. for $C_{24}H_{20}Br_2N_2$: C 58.09 , H 4.06 , N 5.65

Found C 58.08 , H 4.05 , N 5.66

***Anti*-9,25-Dimethylquinoxalino[10,11-*b*]-2-thia[2,3]metacyclophan-10-ene, 287.**



287

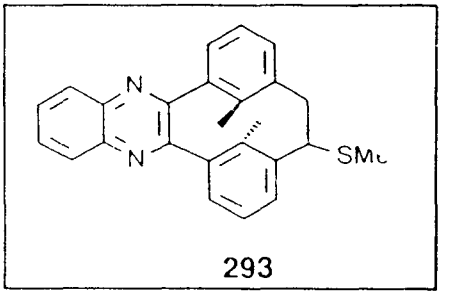
A solution of the bis-bromide **286** (1.40 g, 2.8 mmol) in dry benzene:95%EtOH:DMF (55:35:5 v:v:v mixture, 100 mL, thoroughly purged with argon) was added through one dropping funnel at the same rate as a solution prepared by dissolving $Na_2S.9H_2O$ (0.67 g, 2.8 mmol) in argon purged H_2O (20 mL) and then adding argon purged 95%EtOH (80 mL) in a second addition funnel, to a vigorously stirred, 95%EtOH (300 mL) under argon, over 6 hours. The mixture was stirred for a further 12 hours and then the solvents were evaporated. The residue was extracted with CH_2Cl_2 (300 mL) and water (100 mL). The CH_2Cl_2 layer was separated, dried over $MgSO_4$, and then evaporated to yield the crude product. The crude product upon chromatography on SiGel (elution with 7:3 pentane:$CHCl_3$) gave the thiacyclophane **287** (0.62 g, 60%). A sample was recrystallised from toluene/95%EtOH to give bright-yellow needles. **mp** 233-234°C; **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 8.22-8.18 (m, 2H, H13,16), 7.81-7.77 (m, 2H, H14,15), 7.46-7.22 (m, 6H, H5-7, H21-23), 3.83, 3.72 (AB, 8H, J=13 Hz, -CH_2-S-), 1.02 (s, 6H, -CH_3); **^{13}Cnmr** (62.9 MHz, $CDCl_3$) δ

155.3, 141.5, 139.4, 136.2, 134.7 (C4,24, C9,25, C8,20, C10,19, C12,17), 131.7, 129.8, 129.2, 126.5 (C5,23, C6,22, C7,21, C13,16, C14,15), 30.6 (-CH_2-S-), 17.6 (-CH_3); **ms** (CI), m/e (%): 409 (M+49,1), 397 (M+29,10), 371 (5), 370 (30), 369 (M+1,100), 368 (M^+,8); U.V (CH_3CN) λ_{max}nm(logε_{max}): 349 (5.02), 246 (5.58).

Anal Calcd. for $C_{24}H_{20}N_2S$: C 78.22 , H 5.47 , N 7.60

Found C 78.07 , H 5.48 , N 7.57

Wittig rearrangement of the thiacyclophane 287



293

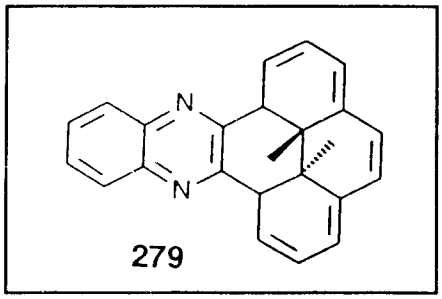
LDA (0.4 mL, 1.5M solution in cyclohexane, excess) was added dropwise to a stirred solution of the thiacyclophane **287** (100 mg, 0.27 mmol) in dry THF (10 mL) at 0°C, under argon. The solution turned deep-brown immediately. After stirring at 25°C for 15 minutes, MeI (0.8 mL, excess) was added, in one portion, to the solution and the stirring continued for an additional 3 hours. It was then quenched with water (10 mL) and extracted with $CHCl_3$ (3x100 mL). The combined $CHCl_3$ extracts were washed with satd. NH_4Cl (50 mL), water (50 mL), satd. NaCl (50 mL), dried over $MgSO_4$ and the solvent evaporated. The resulting brown solid was chromatographed on SiGel (elution with 8:2 pentane:$CHCl_3$) to give the cyclophane **293** (88 mg, 85%). It was recrystallised from toluene/EtOH as light yellow crystals. **mp** 122-124°C; **^{1}Hnmr** (250 MHz, CD_2Cl_2) δ 8.19-8.14 (m, 2H, H), 7.82-7.76 (m, 2H, H), 7.92-

7.89, 7.46-7.13 (m, 6H, H), 3.87 (dd, 1H, CHSMe, J_{XB} = 11 Hz, J_{XA} = 3 Hz), 3.27 (dd, 1H, H_A of bridge CH_2, J_{AB} = 12 Hz, J_{AX} = 3 Hz), 2.56 (dd, 1H, H_B of bridge CH_2, J_{BA} = 12 Hz, J_{BX} = 11 Hz), 2.19 (s, 3H, -SCH_3), 0.75 (s, 6H, -CH_3); **^{13}Cnmr** (62.9 MHz, CD_2Cl_2) δ 156.3, 156.2, 141.9, 141.1, 137.3, 136.9, 136.2, 135.9 (Aryl quarternary C), 131.4, 130.7, 130.6, 130.1, 129.6, 126.9, 126.7, 126.4 (Aryl CH), 54.2 (-CH-SMe), 45.1 (-CH_2-), 17.3, 17.2 (internal -CH_3), 15.9 (-SCH_3); **ms** (CI), m/e (%): 423 (M+41, Weak), 411 (M+29, Weak), 383 (M+1, 100), 382 (M$^+$, 8), 336 (30).

Anal Calcd. for:$C_{25}H_{22}N_2S$ C 78.50 , H 5.80 , N 7.32

Found C 78.12 , H 5.74 , N 7.21

Synthesis of *trans*-14c,14d-dimethyl-14c,14d-dihydrophenanthro[4,5-*abc*]phenazine, 279.



279

A) Salt formation

Borsch reagent (150 mg, ~80%, excess) in dry CH_2Cl_2 (5 mL) was added to a stirred solution of the cyclophane **293** (80 mg, 0.2 mmol) in dry CH_2Cl_2 (25 mL) at -30°C, under argon. The reaction mixture was then stirred without further cooling for 12 hours. Ethyl acetate (20 mL) was added to the mixture and the stirring continued for a further 12

hours. The greenish precipitate formed was filtered, and washed with ethylacetate (20 mL) to give the crude salt **294** (85 mg, 90%). The salt was quite unstable and hence was used immediately in the next reaction. It decomposed at ~100°C.

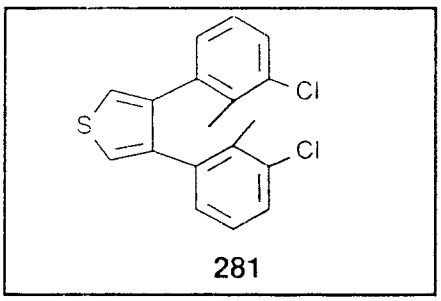
B) Hofmann elimination of 294

t-BuOK (117 mg, 95%, 1 mmol) was added to a stirred suspension of the salt **294** (80 mg, 0.15 mmol) in dry THF (50 mL) at 25°C, under argon. The reaction mixture was then brought to a reflux and refluxed for 6 hours. It was cooled to 25°C and extracted with ether (100 mL, thoroughly purged with argon) and degassed water (25 mL). The organic layer was washed with degassed water (25 mL), degassed satd. NaCl (25 mL), dried over $MgSO_4$ and the solvent evaporated without heat. The solid residue was dissolved in ether (2 mL) and quickly chromatographed on SiGel (deactivated with 10% H_2O, elution with degassed ether. Both the solvent and the SiGel slurry were purged well with argon), in the absence of any fluorescent light. The green fraction was evaporated to yield the dihydropyrene **279** (5 mg, 10%) as a green solid. It decomposed very rapidly in the presence of light and oxygen, resulting in many polar products (atleast 10, by TLC). Solutions of **279** in degassed chlorinated solvents were moderately stable.

mp ~70°C (decomp); **^{1}Hnmr** (250 MHz, CD_2Cl_2) δ 8.76 (d, 2H, H3,8, J = 6.54 Hz), 8.32 (AA'XX', 2H, H4,7), 7.89 (AA'XX', 2H, H5,6), 7.31 (d, 2H, H1,10, J

= 8.85), 7.06 (dd, 1H, H2,9), 7.00 (s, 2H, H11,12), -0.72 (s, 6H, internal methyl); **ms** (EI), m/e (%): 336 (M^+, 10), 321 (40), 306 (100).

3,4-Bis(3-chloro-2-methylphenyl)thiophene, 281.



281

A mixture of the dione **249** (3.07 g, 10 mmol) and diethyl thiodiacetate (2.06 g, 10 mmol, freshly distilled) was added to a solution of *t*-BuOK (1.35g, 12 mmol, freshly prepared by dissolving potassium in dry *t*-BuOH) in dry *t*-BuOH (100 mL) at 30 C, under argon. The mixture was stirred for 1 hour and acidified with 10% HCl. The solution was concentrated under vacuum to remove most of the *t*-BuOH and extracted with ether (4x100 mL). The combined ether extracts were dried over $MgSO_4$ and evaporated to leave a dark, tarry residue. This residue proved to be very difficult to purify and hence was used directly in the next step.

Copper powder (1g, catalyst) was added to a solution of the residue (4.5 g, dried over P_4O_{10} under vacuum, overnight) in quinoline (20 mL, dried over KOH pellets and redistilled) at ~130°C. After 15 minutes, it was heated to 240°C for 3 hours and most of the quinoline was distilled out using an air condenser. The residue was cooled to 25°C, extracted with ether (200 mL) and 10%HCl. The ether extracts were washed with 10%HCl, water (2x50 mL),

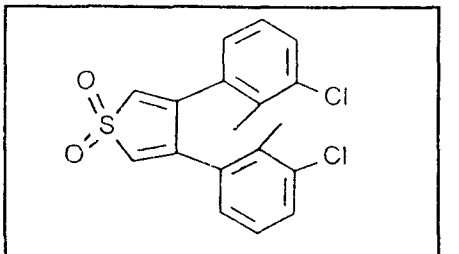
10%$NaHCO_3$ (2x25 mL), satd. NaCl (50 mL) and dried over $MgSO_4$. Removal of solvent yielded a black residue which was chromatographed over SiGel (elution with 9:1 pentane:CH_2Cl_2) to give the teraryl **281** (1 g, 30%). It was recrystallised from hexanes to give colorless needles. **mp** 152-153 C; **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 7.25-6.91 (m, 6H, H-4',5',6'), 7.20 (d, 2H, H-2,4, J=1.1 Hz), 2.09 (s, 6H, $-CH_3$); **^{13}Cnmr** (62.9 MHz, $CDCl_3$) δ 141.4, 137.8, 134.9, 134.5 (C-3,1',2',3'), 129.0, 128.2, 125.9, 124.2 (C-2,4',5',6'), 17.7 ($-CH_3$); **ms** (CI), m/e (%):364 (M+29, 12), 362 (M+29, 20), 336 (M+1, 11), 335 (M+1, 66), 334 (M+1, 21), 333 (M+1, 100), 171 (3), 86 (5), 84 (20); EI m/e : 334, 332 (M^+); **IR** (KBr, cm^{-1}): 3105, 3055, 2992, 2942, 2904, 1586, 1561, 1435, 1373, 1323, 1059, 1021, 864, 802, 783, 707, 607;

Anal Calcd. for $C_{18}H_{14}Cl_2S$: C 64.87 , H 4.23

Found C 64.70 , H 4.30

3,4-Bis(3-chloro-2-methylphenyl)thiophene-1,1-dioxide, 296.

*m*CPBA (2 g, 85%, 10 mmol, excess) was added to a solution of the teraryl **281** (1 g, 3 mmol) in 1,2-dichloroethane (100 mL). The mixture was heated at 80-85°C for 14 hours. Then it was cooled to 25°C, the precipitate filtered under suction, washed with $CHCl_3$ (200 mL), the combined filtrates



296

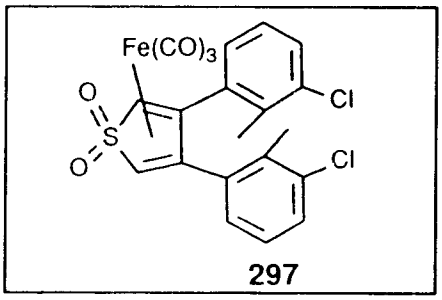
and the washings were washed with water (2x100 mL), 10%$NaHCO_3$ (2x100 mL), satd. NaCl (50 mL) and dried over $MgSO_4$. Evaporation of the dark-red organic layer gave the crude product as a dark-red oily solid, which upon recrystallisation from CH_2Cl_2 gave the thiophene dioxide **296** as colorless needles (0.93 g, 85%). **mp** 171-173°C(decomp); **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 7.32-6.84 (m, 6H, H-4',5',6'), 6.57 (d, 2H, H-2,4, J = 0.7 Hz), 2.13 (s, 6H, -CH_3); **^{13}Cnmr** (62.9 MHz, $CDCl_3$) δ 144.5, 135.5, 133.9, 132.6 (C-3,1',2',3'), 130.4, 128.7, 127.2, 126.5 (C-2,4',5',6'), 18.0 (-CH_3); **ms** (CI), m/e (%):408 (M+41, 3), 406 (M+41, 5), 396 (M+29, 13), 394 (M+29, 19), 368 (M+1, 69), 366 (M+1, 100); **IR** (KBr, cm^{-1}): 3092, 2992, 2954, 2916, 1561, 1536, 1435, 1310, 1272, 1222, 1184, 1122, 1009, 936, 846, 795, 701, 676, 563.

Anal Calcd. for $C_{18}H_{14}Cl_2O_2S$: C 59.19 , H 3.82

Found C 58.72 , H 3.86

Complexation of the thiophene dioxide 296

A solution of the dioxide **296** (500 mg, 13.6 mmol) and $Fe(CO)_5$ (4.9 g, 25 mmol) in argon purged, dry benzene (200 mL) was irradiated with 300 nm light in a Rayonet photoreactor, under argon. TLC analysis of the reaction mixture indicated that the reaction was complete after 1 hour.



297

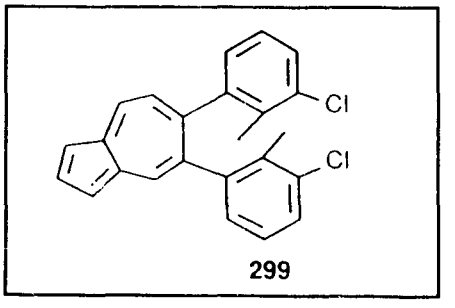
The mixture was then evaporated to leave a dark-brown residue. It was extracted with CH_2Cl_2 (100 mL) and the solvent removed to give the complex **297** (686 mg, ~ 100%). It was recrystallised from toluene/EtOH to give bright-yellow needles. **mp** 250-252 C(decomp); **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 7.33-6.99 (m, 6H, H-4',5',6'), 4.38 (d, 2H, H-2,4, J=1.7 Hz), 2.52 (s, 6H, $-CH_3$); **^{13}Cnmr** (62.9 MHz, $CDCl_3$) δ 205.9 (CO), 137.0, 136.0, 130.4 (C-1',2',3'), 131.6, 130.6, 125.9 (C-4',5',6'), 105.7, 68.0 (C-3,C-2), 17.8 ($-CH_3$) ; **ms** (CI), m/e (%): 507 (M+1, 64), 505 (M+1, 100), 97 (17), 93 (56), 83 (13) ; **IR** (KBr, cm^{-1}): 3061, 2088, 2019, 1555, 1436, 1392, 1279, 1228, 1184, 1150, 1109, 1040, 848, 795, 720, 689, 620, 595, 576, 507.

Anal Calcd. for $C_{21}H_{14}Cl_2O_2SFe$: C 49.93 , H 2.79

Found C 49.59 , H 2.85

5,6-Bis(3-chloro-2-methylphenyl)azulene, 299.

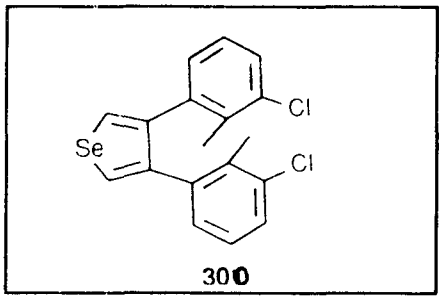
Dimethylaminofulvene[155] (90 mg, 0.74 mmol) was added to the thiophene dioxide **296** (260 mg, 0.71 mmol) in dry THF (100 mL), under argon. The mixture was refluxed for 3 hours. It was then evaporated to leave a dark-



299

blue residue which was chromatographed on SiGel (elution with pentane) to give the blue azulene **299**, as a mixture of syn and anti isomers (20 mg, 8%). **mp** (range) 70-85 C; **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 8.34-8.24 (m, 2H, H7,8), 7.95 (m, 1H, H2), 7.45-7.36 (m, 2H, H1,3), 7.23-6.76 (m, 7H, H4,1'-6', 1"-6"), 2.22, 2.20, 2.13, 2.07 (s, 6H, $-CH_3$); **^{13}Cnmr** (62.9 MHz, $CDCl_3$) δ 149.24, 146.26, 139.64, 139.10, 138.98, 138.38, 138.32, 138.13, 134.83, 130.45, 129.49, 128.00, 127.94, 127.80, 127.34, 126.24, 125.83, 125.76, 125.57, 125.31, 125.08, 119.54, 119.43, 118.64, 118.56 (aromatic carbons), 18.47, 18.24 ($-CH_3$); **ms** (CI), m/e (%):407 (M+29, 10), 405 (M+29, 6), 380 (M+1, 20), 379 (M+1, 80), 378 (M+1, 40), 377 (M+1, 100), 376 (M^+,10).

3,4-Bis(3-chloro-2-methylphenyl)selenophene, 300.

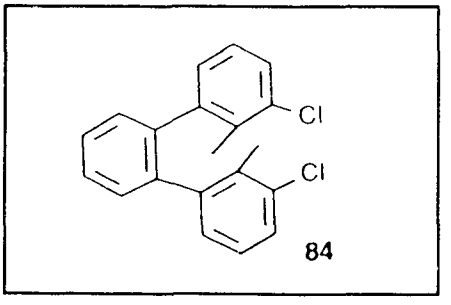


300

Selenium (0.2 g, 2.5 mmol, excess) was mixed with the thiophene dioxide **296** (0.1 g, 0.26 mmol) and the mixture was pulverised to a fine powder. The mixture was then placed in a test tube and heated to 200-210°C in a sand bath, under argon for 6 hours. It was cooled to 25°C, the residue was powdered and extracted with hot acetone (5x25 mL). The combined extracts were evaporated to leave a foul smelling residue which on chromatography on SiGel (elution with pentane) gave the selenophene **300** (10 mg, 10%). It was

recrystallised from hexanes as colorless needles which turned grey over a few days. **mp** 182-185 C; **^{1}Hnmr** (250 MHz, $CDCl_3$) δ 7.82 (s, 1H, H-3), 7.28-7.10 (m, 3H, H-4',5',6'), 2.07 (s, 3H, $-CH_3$); **ms** (CI), m/e (%): 413 (M+29, 2.8), 411 (M+29, 18.4), 409 (M+29, 29), 407 (M+29, 12.9), 405 (M+29, 3.2), 384 (M+1, 14.9), 383 (M+1, 66.1), 381 (M+1, 100), 379 (M+1, 49.2), 377 (M+1, 20.4), 375 (M+1, 2.2), 355 (2.2), 349 (3), 347 (8.7), 345 (6.8), 333 (2.7), 329 (7), 327 (14), 307 (11), 305 (6).

1,2-Bis(3-chloro-2-methylphenyl)benzene, 84.



84

Phenylvinylsulphone (51 mg, 0.3 mmol, Aldrich) was added to a stirred solution of the thiophene dioxide **296** (100 mg, 0.26 mmol) in *m*-xylene (10 mL). The mixture was refluxed for 3 hours and cooled to 25°C. It was then washed with 10%$NaHCO_3$ (10 mL) and the solvent evaporated to leave the crude product **84**. It was recrystallised from hexanes to give the pure **84** (60 mg, 70%), identical to an authentic[99] sample.

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APPENDIX

The completed results of π-SCF, AM-1 and PCMODEL/MMX calculations of the compounds mentioned in this thesis are available on request at the following address:

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X-ray crystal data of *anti*-123a

Formula	$C_{17}H_{18}S_3$
Formula weight	336.50
Temperature (°C)	20
System	Monoclinic
Space group	P_c (No. 7)
a	7.575(4)
b	12.246(7)
c	8.315(5)
β	109.09
V	739.6
Z	1
D_c	1.38 g cm^{-3}
D_m	1.38 g cm^{-3}
No. of reflections	1695
I=2.5σ(I)	1076
Radiation	Mo. K_α
R	0.13

X-ray crystal data of 287

Formula	$C_{24}H_{20}N_2S_1$
Formula weight	368.5
Temperature (°C)	20
System	Monoclinic
Space group	$P2_1/a$ (No. 14)
a	8.159(1)
b	12.801(2)
c	17.594(4)
α	90°
β	91.29(2)°
γ	90°
V	1837.1
Z	4
D_c	1.332 g cm^{-3}
D_m	1.331 g cm^{-3}
Crystal dimensions (mm)	0.34 x 0.67 x 0.62
μ	1.45 cm^{-1} (ABSB02)
Standards	00 11, 0 80, 6 00
2Θ range	0 - 50°
No. of reflections	3229
I=2.5σ(I)	2538
Radiation	Mo.K_α 0.71069
Max. shift/esd	0.011
Residual electron density	0.24
R	0.0485
R_w	0.0495

Fractional atomic coordinates and temperature parameters.

Atom	x/a	y/b	z/c	Ueq
S(2)	82083(10)	-10242(7)	54576(4)	727(3)
N(18)	4700(2)	1974(1)	8465(1)	43(1)
N(25)	3442(2)	-36(1)	8760(1)	46(1)
C(1)	9119(3)	-206(2)	6204(2)	55(1)
C(3)	6132(4)	-1404(3)	5711(2)	71(1)
C(4)	5810(3)	-1528(2)	6553(1)	49(1)
C(5)	6467(3)	-2370(2)	6956(2)	58(1)
C(6)	6227(3)	-2474(2)	7726(2)	55(1)
C(7)	5486(3)	-1675(2)	8112(2)	46(1)
C(8)	4886(3)	-801(2)	7726(1)	39(1)
C(9)	4893(3)	-777(2)	6926(1)	41(1)
C(10)	4428(3)	131(2)	8188(1)	39(1)
C(11)	5128(3)	1156(2)	8056(1)	37(1)
C(12)	6235(3)	1355(2)	7407(1)	38(1)
C(13)	5803(3)	2161(2)	6913(1)	49(1)
C(14)	6508(3)	2233(2)	6208(2)	55(1)
C(15)	7546(3)	1454(2)	5978(1)	51(1)
C(16)	8066(3)	671(2)	6478(1)	41(1)
C(17)	7527(3)	678(2)	7228(1)	37(1)
C(19)	3651(3)	1803(2)	9045(1)	42(1)
C(20)	3184(3)	2656(2)	9502(1)	51(1)
C(21)	2220(3)	2495(2)	10114(1)	57(1)
C(22)	1676(3)	1493(3)	10287(2)	61(1)
C(23)	2078(4)	656(2)	9847(2)	59(1)
C(24)	3071(3)	800(2)	9209(1)	45(1)
C(26)	3877(4)	12(2)	6488(2)	54(1)
C(27)	8354(3)	22(2)	7834(1)	45(1)
H(1A)	1005(3)	5(2)	600(2)	6(1)'
H(1B)	953(3)	-66(2)	662(2)	6(1)'
H(3A)	535(5)	-81(3)	545(2)	12(1)'
H(3B)	604(4)	-211(3)	550(2)	8(1)'
H(5)	717(3)	-288(2)	671(2)	7(1)'
H(6)	661(3)	-305(2)	796(1)	5(1)'
H(7)	543(3)	-168(2)	864(1)	5(1)'
H(13)	497(3)	265(2)	702(1)	6(1)'
H(14)	613(3)	274(2)	587(2)	6(1)'
H(15)	795(3)	144(2)	548(1)	6(1)'
H(20)	360(3)	335(2)	937(1)	6(1)'
H(21)	193(3)	309(2)	1044(2)	6(1)'
H(22)	93(3)	135(2)	1073(2)	6(1)'
H(23)	165(3)	-1(2)	991(2)	7(1)'
H(26A)	316(4)	-35(2)	616(2)	7(1)'
H(26B)	313(4)	43(2)	685(2)	7(1)'

H(26C)	445(3)	52(2)	618(2)	6(1)'
H(27A)	784(3)	14(2)	833(2)	6(1)'
H(27B)	844(3)	-73(2)	771(1)	5(1)'
H(27C)	944(4)	26(2)	788(2)	6(1)'

Estimated standard deviations are given in parentheses.

Coordinates x 10^n where n = 5,4,4,4, for P,O,N,C

Temperature parameters x 10^n where n = 4,3,3,3, for P,O,N,C.
U_{eq} = the equivalent isotropic temperature parameter.
$U_{eq} = 1/3 \sum_i \sum_j U_{ij} a_i^* a_j^* (a_i . a_j)$
Primed values indicate that U_{iso} is given
$T = \exp-(8\pi^2 U_{iso} \sin^2 \theta/\lambda^2)$

Hydrogen atom fractional atomic coordinates and isotropic temperature parameters.

Atom	x/a	y/b	z/c	Uiso
H(1A)	1005(3)	5(2)	600(2)	6(1)
H(1B)	953(3)	-66(2)	662(2)	6(1)
H(3A)	535(5)	-81(3)	545(2)	12(1)
H(3B)	604(4)	-211(3)	550(2)	8(1)
H(5)	717(3)	-288(2)	671(2)	7(1)
H(6)	661(3)	-305(2)	796(1)	5(1)
H(7)	543(3)	-168(2)	864(1)	5(1)
H(13)	497(3)	265(2)	702(1)	6(1)
H(14)	613(3)	274(2)	587(2)	6(1)
H(15)	795(3)	144(2)	548(1)	6(1)
H(20)	360(3)	335(2)	937(1)	6(1)
H(21)	193(3)	309(2)	1044(2)	6(1)
H(22)	93(3)	135(2)	1073(2)	6(1)
H(23)	165(3)	-1(2)	991(2)	7(1)
H(26A)	316(4)	-35(2)	616(2)	7(1)
H(26B)	313(4)	43(2)	685(2)	7(1)
H(26C)	445(3)	52(2)	618(2)	6(1)
H(27A)	784(3)	14(2)	833(2)	6(1)
H(27B)	844(3)	-73(2)	771(1)	5(1)
H(27C)	944(4)	26(2)	788(2)	6(1)

Estimated standard deviations are given in parentheses.

Coordinates x 10^n, temperature parameters x 10^n.
$T = \exp-(8\pi_2 U_{iso} \sin^2 \theta/\lambda^2$

Anisotropic temperature parameters (&2).

Atom	U11	U22	U33	U23	U13	U12
S(2)	855(5)	815(6)	521(4)	-222(4)	279(4)	-121(4)
N(18)	45(1)	42(1)	42(1)	0(1)	5(1)	1(1)
N(25)	49(1)	43(1)	48(1)	5(1)	16(1)	3(1)
C(1)	47(1)	71(2)	47(1)	-5(1)	10(1)	3(1)
C(3)	68(2)	95(2)	51(2)	-26(2)	8(1)	-10(2)
C(4)	46(1)	51(1)	50(1)	-14(1)	6(1)	-9(1)
C(5)	51(1)	47(1)	77(2)	-17(1)	12(1)	3(1)
C(6)	50(1)	37(1)	79(2)	4(1)	7(1)	5(1)
C(7)	44(1)	43(1)	51(1)	6(1)	5(1)	-1(1)
C(8)	35(1)	36(1)	45(1)	0(1)	6(1)	-4(1)
C(9)	38(1)	42(1)	44(1)	-3(1)	1(1)	-8(1)
C(10)	38(1)	41(1)	37(1)	3(1)	4(1)	4(1)
C(11)	38(1)	40(1)	34(1)	2(1)	3(1)	3(1)
C(12)	43(1)	36(1)	35(1)	1(1)	4(1)	-4(1)
C(13)	56(1)	40(1)	50(1)	8(1)	8(1)	5(1)
C(14)	64(2)	53(2)	49(1)	20(1)	7(1)	-1(1)
C(15)	53(1)	62(2)	38(1)	7(1)	9(1)	-7(1)
C(16)	36(1)	48(1)	39(1)	0(1)	6(1)	-6(1)
C(17)	38(1)	37(1)	37(1)	3(1)	3(1)	-7(1)
C(19)	42(1)	48(1)	37(1)	-1(1)	3(1)	3(1)
C(20)	53(1)	52(2)	47(1)	-7(1)	4(1)	4(1)
C(21)	56(2)	69(2)	45(1)	-11(1)	4(1)	13(1)
C(22)	61(2)	79(2)	43(1)	3(1)	18(1)	16(1)
C(23)	64(2)	57(2)	56(2)	10(1)	23(1)	7(1)
C(24)	46(1)	48(1)	42(1)	2(1)	10(1)	7(1)
C(26)	52(1)	58(2)	51(1)	4(1)	-12(1)	-5(1)
C(27)	39(1)	53(2)	44(1)	5(1)	1(1)	1(1)

U values $x10^n$ where n = 4,3,3, for S,C,N

$T = \exp -2\pi^2(U_{11}h^2a^{*2} + \ldots + 2U_{23}klb^*c^* + \ldots)$

Bond angles (d).

Atoms	Angle	Atoms	Angle
C(3) -S(2) -C(1)	110.0(1)	C(12) -C(11) -C(10)	121.5(2)
C(19) -N(18) -C(11)	117.2(2)	C(13) -C(12) -C(11)	117.1(2)
C(24) -N(25) -C(10)	117.4(2)	C(17) -C(12) -C(11)	122.4(2)
C(16) -C(1) -S(2)	115.7(2)	C(17) -C(12) -C(13)	119.9(2)
C(4) -C(3) -S(2)	116.6(2)	C(14) -C(13) -C(12)	120.4(2)
C(5) -C(4) -C(3)	120.4(3)	C(15) -C(14) -C(13)	119.1(2)
C(9) -C(4) -C(3)	119.6(3)	C(16) -C(15) -C(14)	121.1(2)
C(9) -C(4) -C(5)	120.0(2)	C(15) -C(16) -C(1)	120.2(2)
C(6) -C(5) -C(4)	120.9(2)	C(17) -C(16) -C(1)	120.2(2)
C(7) -C(6) -C(5)	119.1(3)	C(17) -C(16) -C(15)	119.5(2)
C(8) -C(7) -C(6)	120.8(2)	C(16) -C(17) -C(12)	117.9(2)
C(9) -C(8) -C(7)	119.7(2)	C(27) -C(17) -C(12)	120.8(2)
C(10) -C(8) -C(7)	117.8(2)	C(27) -C(17) -C(16)	121.2(2)
C(10) -C(8) -C(9)	122.1(2)	C(20) -C(19) -N(18)	118.9(2)
C(8) -C(9) -C(4)	118.1(2)	C(24) -C(19) -N(18)	121.5(2)
C(26) -C(9) -C(4)	121.1(2)	C(24) -C(19) -C(20)	119.6(2)
C(26) -C(9) -C(8)	120.8(2)	C(21) -C(20) -C(19)	120.0(3)
C(8) -C(10) -N(25)	116.7(2)	C(22) -C(21) -C(20)	120.3(3)
C(11) -C(10) -N(25)	121.1(2)	C(23) -C(22) -C(21)	121.1(2)
C(11) -C(10) -C(8)	122.1(2)	C(24) -C(23) -C(22)	119.8(3)
C(10) -C(11) -N(18)	121.3(2)	C(19) -C(24) -N(25)	121.2(2)
C(12) -C(11) -N(18)	116.9(2)		
C(23) -C(24) -N(25)	119.7(2)		
C(23) -C(24) -C(19)	119.1(2)		

Estimated standard deviations are given in parentheses.

TABLE 3S.

Bond angles involving H atoms (d).

Atoms	Angle	Atoms	Angle
H(1A) -C(1) -S(2)	104.7(18)	H(15) -C(15) -C(16)	117.4(16)
H(1A) -C(1) -C(16)	110.6(18)	H(20) -C(20) -C(19)	118.0(15)
H(1B) -C(1) -S(2)	108.5(16)	H(20) -C(20) -C(21)	122.0(15)
H(1B) -C(1) -C(16)	113.0(16)	H(21) -C(21) -C(20)	119.2(16)
H(1B) -C(1) -H(1A)	103.3(23)	H(21) -C(21) -C(22)	120.5(15)
H(3A) -C(3) -S(2)	104.5(21)	H(22) -C(22) -C(21)	122.2(15)
H(3A) -C(3) -C(4)	112.0(22)	H(22) -C(22) -C(23)	116.7(15)
H(3B) -C(3) -S(2)	102.6(18)	H(23) -C(23) -C(22)	123.8(17)
H(3B) -C(3) -C(4)	104.7(19)	H(23) -C(23) -C(24)	116.0(18)
H(3B) -C(3) -H(3A)	116.6(29)	H(26A)-C(26) -C(9)	108.1(17)
H(5) -C(5) -C(4)	120.6(17)	H(26B)-C(26) -C(9)	110.3(16)
H(5) -C(5) -C(6)	118.3(17)	H(26B)-C(26) -H(26A)	105.4(23)
H(6) -C(6) -C(5)	118.9(16)	H(26C)-C(26) -C(9)	117.4(16)
H(6) -C(6) -C(7)	121.9(16)	H(26C)-C(26) -H(26A)	107.6(24)
H(7) -C(7) -C(6)	121.1(16)	H(26C)-C(26) -H(26B)	107.3(22)
H(7) -C(7) -C(8)	118.0(16)	H(27A)-C(27) -C(17)	110.7(14)
H(13) -C(13) -C(12)	122.5(16)	H(27B)-C(27) -C(17)	114.9(14)
H(13) -C(13) -C(14)	117.0(16)	H(27B)-C(27) -H(27A)	112.0(20)
H(14) -C(14) -C(13)	118.7(16)	H(27C)-C(27) -C(17)	106.9(16)
H(14) -C(14) -C(15)	121.2(16)	H(27C)-C(27) -H(27A)	106.7(21)
H(15) -C(15) -C(14)	121.5(16)	H(27C)-C(27) -H(27B)	105.0(21)

Estimated standard deviations are given in parentheses.

Interatomic distances (A).

Atoms	Distance	Atoms	Distance
C(1) -S(2)	1.824(3)	C(11) -C(10)	1.452(3)
C(3) -S(2)	1.827(3)	C(12) -C(11)	1.494(3)
C(11) -N(18)	1.322(3)	C(13) -C(12)	1.389(3)
C(19) -N(18)	1.365(3)	C(17) -C(12)	1.405(3)
C(10) -N(25)	1.320(3)	C(14) -C(13)	1.383(3)
C(24) -N(25)	1.368(3)	C(15) -C(14)	1.375(4)
C(16) -C(1)	1.500(3)	C(16) -C(15)	1.394(3)
C(4) -C(3)	1.519(4)	C(17) -C(16)	1.401(3)
C(5) -C(4)	1.390(4)	C(27) -C(17)	1.505(3)
C(9) -C(4)	1.393(3)	C(20) -C(19)	1.414(3)
C(6) -C(5)	1.379(4)	C(24) -C(19)	1.399(3)
C(7) -C(6)	1.375(3)	C(21) -C(20)	1.362(4)
C(8) -C(7)	1.391(3)	C(22) -C(21)	1.393(4)
C(9) -C(8)	1.408(3)	C(23) -C(22)	1.366(4)
C(10) -C(8)	1.495(3)	C(24) -C(23)	1.412(3)
C(26) -C(9)	1.508(4)		

Estimated standard deviations are given in parentheses.

Interatomic distances for the hydrogen atoms (Å).

Atoms	Distance	Atoms	Distance
H(1A) -C(1)	0.904(28)		
H(1B) -C(1)	0.985(28)		
H(3A) -C(3)	1.092(41)		
H(3B) -C(3)	0.981(33)		
H(5) -C(5)	0.980(29)		
H(6) -C(6)	0.899(25)		
H(7) -C(7)	0.927(25)		
H(13) -C(13)	0.949(27)		
H(14) -C(14)	0.927(27)		
H(15) -C(15)	0.944(26)		
H(20) -C(20)	0.984(27)		
H(21) -C(21)	0.983(27)		
H(22) -C(22)	1.022(28)		
H(23) -C(23)	0.926(28)		
H(26A)-C(26)	0.933(31)		
H(26B)-C(26)	1.039(31)		
H(26C)-C(26)	0.968(29)		
H(27A)-C(27)	0.989(26)		
H(27B)-C(27)	0.991(26)		
H(27C)-C(27)	0.935(28)		

Selected intermolecular distances (Å).

Atoms	Distance	Sym	Tx	Ty	Tz
S(2) ...S(2)	4.269	-1	2	0	1
C(1) ...S(2)	4.008	-1	2	0	1
C(26) ...S(2)	4.003	-1	1	0	1
C(14) ...S(2)	3.694	2	1	0	1
C(20) ...N(18)	3.376	-2	0	1	0
C(21) ...N(18)	3.582	-2	0	1	0
C(9) ...C(5)	3.668	-2	0	0	0
C(7) ...C(6)	3.690	-2	0	0	0
C(22) ...C(7)	3.613	-1	1	0	2
C(15) ...C(13)	3.566	-2	1	1	0
C(16) ...C(13)	3.634	-2	1	1	0
C(15) ...C(14)	3.658	-2	1	1	0
C(21) ...C(19)	3.546	-2	0	1	0
C(21) ...C(20)	3.446	-2	0	1	0
C(22) ...C(20)	3.322	-2	0	1	0

The symmetry positions are for the second atom.
They are defined:
A negative symmetry position denotes inversion.
The translations (T) are applied finally.

X-ray crystal data of 297

Formula	$C_{21}H_{14}S_1O_5Cl_2Fe_1$
Formula weight	505.15
Temperature (°C)	20
System	Orthorhombic
Space group	P_n2_1a (No. 33)
a	15.098(4)
b	16.666(5)
c	8.422(2)
α	90°
β	90°
γ	90°
V	2119.1
Z	4
D_c	1.583 g cm^{-3}
D_m	1.567 g cm^{-3}
Crystal dimensions (mm)	1.08 x 0.40 x 0.31
μ	10.96 cm^{-1} (ABSB02)
Standards	10 0 0, 0 06, 0 14 0
2Θ range	0 - 50
No. of reflections	1926
I=2.5σ(I)	1744
Radiation	Mo.K_α 0.71069
Max. shift/esd	0.1
Residual electron density	0.5
R	0.054
R_w	0.057

Fractional atomic coordinates and temperature parameters.

Atom	x/a	y/b	z/c	Ueq
Fe(1)	16049(5)	0(1)	12562(9)	331(3)
Cl(1)	6590(35)	-22965(38)	82749(61)	741(12)
Cl(2)	6975(33)	23245(3[illegible]	82978(70)	767(13)
S(1)	-2260(10)	107(42)	16161(20)	473(5)
O(1)	-954(3)	13(11)	2745(6)	63(1)
O(2)	-504(3)	78(8)	-3(6)	59(1)
O(3)	2879(7)	1286(6)	756(11)	54(2)
O(4)	2863(8)	-1342(6)	915(13)	66(2)
O(5)	1115(4)	20(9)	-2101(5)	67(1)
C(2)	602(7)	757(9)	2025(13)	40(2)
C(3)	1123(8)	416(8)	3320(14)	38(2)
C(4)	1092(7)	-434(7)	3454(12)	25(2)
C(5)	613(9)	-701(7)	2069(16)	42(2)
C(6)	1489(8)	-917(8)	4657(14)	40(2)
C(7)	932(9)	-1313(7)	5713(15)	37(2)
C(8)	1288(6)	-1806(7)	6934(13)	37(2)
C(9)	2268(8)	-1886(7)	7114(13)	43(2)
C(10)	2760(6)	-1432(8)	6021(14)	41(2)
C(11)	2448(10)	-959(8)	4789(14)	55(2)
C(12)	1506(8)	979(7)	4619(14)	35(2)
C(13)	943(10)	1425(7)	5664(16)	44(2)
C(14)	1429(10)	1831(8)	6856(14)	61(2)
C(15)	2252(11)	1858(10)	7031(18)	78(2)
C(16)	2864(11)	1472(10)	6027(16)	66(2)
C(17)	2409(8)	1031(7)	4848(12)	38(2)
C(18)	-89(10)	-1308(11)	5546(18)	65(2)
C(19)	-64(9)	1279(9)	5621(18)	55(2)
C(20)	2426(6)	828(7)	976(12)	29(2)
C(21)	2353(9)	-751(9)	1098(14)	49(2)
C(22)	1297(5)	30(11)	-810(7)	45(1)

Estimated standard deviations are given in parentheses.

Coordinates x 10^n where n = 5,4,4,4, for P,O,N,C

Temperature parameters x 10^n where n = 4,3,3,3, for P,O,N,C.
U_{eq} = the equivalent isotropic temperature parameter.
U_{eq} = 1/3 $\sum_i\sum_j U_{ij} a_i^* a_j^* (a_i.a_j)$
Primed values indicate that U_{iso} is given
T = $\exp-(8\pi^2 U_{iso} \sin^2 \theta/\lambda^2)$

Interatomic distances (Å).

Atoms	Distance	Atoms	Distance
S(1) -Fe(1)	2.781(2)	C(4) -C(3)	1.422(9)
C(2) -Fe(1)	2.074(12)	C(12) -C(3)	1.553(16)
C(3) -Fe(1)	2.008(12)	C(5) -C(4)	1.443(17)
C(4) -Fe(1)	2.133(10)	C(6) -C(4)	1.426(18)
C(5) -Fe(1)	2.019(12)	C(7) -C(6)	1.389(18)
C(20) -Fe(1)	1.869(10)	C(11) -C(6)	1.454(18)
C(21) -Fe(1)	1.692(15)	C(8) -C(7)	1.422(16)
C(22) -Fe(1)	1.802(7)	C(18) -C(7)	1.548(19)
C(8) -Cl(1)	1.686(11)	C(9) -C(8)	1.493(15)
C(14) -Cl(2)	1.835(12)	C(10) -C(9)	1.405(16)
O(1) -S(1)	1.453(5)	C(11) -C(10)	1.386(17)
O(2) -S(1)	1.431(5)	C(13) -C(12)	1.431(18)
C(2) -S(1)	1.796(12)	C(17) -C(12)	1.380(17)
C(5) -S(1)	1.776(14)	C(14) -C(13)	1.415(20)
C(20) -O(3)	1.043(13)	C(19) -C(13)	1.540(20)
C(21) -O(4)	1.259(17)	C(15) -C(14)	1.252(22)
C(22) -O(5)	1.122(8)	C(16) -C(15)	1.408(24)
C(3) -C(2)	1.460(18)	C(17) -C(16)	1.413(18)

Estimated standard deviations are given in parentheses.

Anisotropic temperature parameters (&2).

Atom	U11	U22	U33	U23	U13	U12
Fe(1)	324(4)	344(4)	326(4)	17(11)	4(3)	0(11)
Cl(1)	1047(23)	700(21)	477(17)	143(17)	23(18)	-320(20)
Cl(2)	903(22)	745(22)	654(21)	-346(19)	87(19)	207(19)
S(1)	301(8)	599(10)	520(9)	20(23)	-88(7)	-27(20)
O(1)	28(2)	95(3)	66(2)	-14(3)	3(2)	13(3)
O(2)	54(2)	68(3)	56(2)	-2(3)	-25(2)	-5(3)
O(3)	51(3)	54(3)	56(3)	4(3)	-5(3)	7(3)
O(4)	74(3)	42(3)	82(3)	0(3)	17(3)	21(3)
O(5)	102(3)	62(2)	38(2)	3(3)	-13(2)	24(3)
C(2)	21(3)	72(3)	27(3)	-13(3)	-6(2)	-6(3)
C(3)	35(3)	49(3)	31(3)	-7(3)	3(3)	-7(3)
C(4)	16(3)	28(3)	31(3)	4(3)	7(2)	-13(2)
C(5)	45(3)	21(3)	59(3)	-9(3)	2(3)	-15(3)
C(6)	31(3)	49(3)	40(3)	-19(3)	8(3)	-23(3)
C(7)	40(3)	31(3)	39(3)	0(3)	-3(3)	5(3)
C(8)	23(3)	46(3)	42(3)	-2(3)	-10(3)	-12(3)
C(9)	59(3)	30(3)	40(3)	-1(3)	8(3)	-8(3)
C(10)	21(3)	56(3)	45(3)	-9(3)	-5(3)	3(3)
C(11)	60(3)	53(3)	52(3)	-5(3)	-38(3)	16(3)
C(12)	45(3)	26(3)	36(3)	-12(3)	-4(3)	-17(3)
C(13)	54(3)	38(3)	41(3)	3(3)	8(3)	14(3)
C(14)	119(4)	32(3)	33(3)	-13(3)	32(3)	3(3)
C(15)	93(3)	78(3)	61(3)	7(3)	-49(3)	-50(3)
C(16)	87(3)	63(3)	47(3)	-19(3)	-8(3)	-23(3)
C(17)	35(3)	44(3)	36(3)	-5(3)	21(3)	2(3)
C(18)	45(3)	103(3)	48(3)	23(3)	0(3)	2(3)
C(19)	34(3)	60(3)	70(3)	-6(3)	6(3)	27(3)
C(20)	21(3)	31(3)	36(3)	4(3)	13(2)	-13(3)
C(21)	56(3)	45(3)	46(3)	-1(3)	5(3)	-8(3)
C(22)	59(3)	36(2)	41(2)	-9(3)	3(2)	4(3)

Estimated standard deviations are given in parentheses.

U values $x10^n$ where n = 4,3,3, for S,C,N

$T = \exp-2\pi^2(U_{11}h^2a^{*2} + \ldots + 2U_{23}klb^*c^* + \ldots)$

Bond angles (d).

Atoms	Angle	Atoms	Angle
C(2) -Fe(1) -S(1)	40.2(3)	C(4) -C(3) -Fe(1)	74.7(8)
C(3) -Fe(1) -S(1)	62.8(4)	C(4) -C(3) -C(2)	115.4(13)
C(3) -Fe(1) -C(2)	41.9(5)	C(12) -C(3) -Fe(1)	133.1(9)
C(4) -Fe(1) -S(1)	63.0(3)	C(12) -C(3) -C(2)	119.5(12)
C(4) -Fe(1) -C(2)	70.7(5)	C(12) -C(3) -C(4)	123.9(13)
C(4) -Fe(1) -C(3)	40.0(2)	C(3) -C(4) -Fe(1)	65.3(8)
C(5) -Fe(1) -S(1)	39.6(4)	C(5) -C(4) -Fe(1)	65.5(6)
C(5) -Fe(1) -C(2)	72.8(3)	C(5) -C(4) -C(3)	105.1(12)
C(5) -Fe(1) -C(3)	68.8(5)	C(6) -C(4) -Fe(1)	130.9(8)
C(5) -Fe(1) -C(4)	40.6(5)	C(6) -C(4) -C(3)	127.2(13)
C(20) -Fe(1) -S(1)	131.9(4)	C(6) -C(4) -C(5)	127.6(10)
C(20) -Fe(1) -C(2)	94.3(5)	S(1) -C(5) -Fe(1)	94.0(5)
C(20) -Fe(1) -C(3)	95.4(5)	C(4) -C(5) -Fe(1)	74.0(6)
C(20) -Fe(1) -C(4)	126.9(4)	C(4) -C(5) -S(1)	109.0(8)
C(20) -Fe(1) -C(5)	164.1(5)	C(7) -C(6) -C(4)	118.0(11)
C(21) -Fe(1) -S(1)	132.6(5)	C(11) -C(6) -C(4)	120.0(10)
C(21) -Fe(1) -C(2)	164.2(6)	C(11) -C(6) -C(7)	122.0(13)
C(21) -Fe(1) -C(3)	124.5(6)	C(8) -C(7) -C(6)	120.6(12)
C(21) -Fe(1) -C(4)	93.4(5)	C(18) -C(7) -C(6)	122.8(12)
C(21) -Fe(1) -C(5)	95.4(6)	C(18) -C(7) -C(8)	116.4(11)
C(21) -Fe(1) -C(20)	95.4(3)	C(7) -C(8) -Cl(1)	123.5(8)
C(22) -Fe(1) -S(1)	81.3(2)	C(9) -C(8) -Cl(1)	116.5(8)
C(22) -Fe(1) -C(2)	95.5(5)	C(9) -C(8) -C(7)	119.9(10)
C(22) -Fe(1) -C(3)	137.1(5)	C(10) -C(9) -C(8)	114.2(10)
C(22) -Fe(1) -C(4)	138.9(5)	C(11) -C(10) -C(9)	128.2(11)
C(22) -Fe(1) -C(5)	98.7(6)	C(10) -C(11) -C(6)	115.0(12)
C(22) -Fe(1) -C(20)	91.7(6)	C(13) -C(12) -C(3)	121.7(11)
C(22) -Fe(1) -C(21)	96.7(6)	C(17) -C(12) -C(3)	120.3(10)
O(1) -S(1) -Fe(1)	145.4(2)	C(17) -C(12) -C(13)	117.9(10)
O(2) -S(1) -Fe(1)	100.9(2)	C(14) -C(13) -C(12)	112.2(12)
O(2) -S(1) -O(1)	113.7(3)	C(19) -C(13) -C(12)	119.3(12)
C(2) -S(1) -Fe(1)	48.2(4)	C(19) -C(13) -C(14)	127.1(12)
C(2) -S(1) -O(1)	113.5(7)	C(13) -C(14) -Cl(2)	111.8(11)
C(2) -S(1) -O(2)	109.4(6)	C(15) -C(14) -Cl(2)	120.2(12)
C(5) -S(1) -Fe(1)	46.4(4)	C(15) -C(14) -C(13)	127.9(13)
C(5) -S(1) -O(1)	113.6(7)	C(16) -C(15) -C(14)	124.3(12)
C(5) -S(1) -O(2)	117.8(6)	C(17) -C(16) -C(15)	110.0(13)
C(5) -S(1) -C(2)	85.7(3)	C(16) -C(17) -C(12)	127.6(11)
S(1) -C(2) -Fe(1)	91.6(6)	O(3) -C(20) -Fe(1)	177.0(10)
C(3) -C(2) -Fe(1)	66.7(7)	O(4) -C(21) -Fe(1)	178.3(12)
C(3) -C(2) -S(1)	104.4(10)	O(5) -C(22) -Fe(1)	177.5(16)
C(2) -C(3) -Fe(1)	71.5(7)		

Estimated standard deviations are given in parentheses.

Selected intermolecular distances (Å).

Atoms	Distance	Sym	Tx	Ty	Tz
O(1) ...Fe(1)	3.781	3	-1	0	0
O(5) ...Cl(1)	3.934	1	0	0	-1
Cl(2) ...Cl(1)	3.595	2	0	0	2
C(2) ...Cl(1)	3.771	2	0	0	1
O(3) ...Cl(1)	3.866	4	0	0	-1
C(16) ...Cl(1)	3.815	4	0	0	-1
O(5) ...Cl(2)	3.907	1	0	0	-1
C(22) ...Cl(2)	4.001	1	0	0	-1
C(5) ...Cl(2)	3.852	2	0	-1	1
O(4) ...Cl(2)	3.700	4	0	-1	-1
C(10) ...Cl(2)	3.871	4	0	-1	-1
C(11) ...S(1)	4.043	3	0	0	0
O(3) ...O(1)	3.034	3	0	0	0
O(4) ...O(1)	3.093	3	0	0	0
C(11) ...O(1)	3.606	3	0	0	0
C(20) ...O(1)	2.999	3	0	0	0
C(21) ...O(1)	3.018	3	0	0	0
C(11) ...O(2)	3.547	3	0	0	0
C(16) ...O(2)	3.495	3	0	0	0
C(17) ...O(2)	3.530	3	0	0	0
C(15) ...O(3)	3.413	1	0	0	1
C(19) ...O(3)	3.316	3	-1	0	0
C(8) ...O(3)	3.560	4	0	-1	0
C(9) ...O(3)	3.261	4	0	-1	0
C(9) ...O(4)	3.446	1	0	0	1
C(18) ...O(4)	3.328	3	-1	0	0
C(14) ...O(4)	3.323	4	0	0	0
C(15) ...O(4)	3.148	4	0	0	0
C(6) ...O(5)	3.195	1	0	0	1
C(7) ...O(5)	2.897	1	0	0	1
C(8) ...O(5)	3.161	1	0	0	1
C(12) ...O(5)	3.245	1	0	0	1
C(13) ...O(5)	3.016	1	0	0	1
C(14) ...O(5)	3.179	1	0	0	1
C(15) ...O(5)	3.587	1	0	0	1
C(18) ...O(5)	3.482	1	0	0	1
C(19) ...O(5)	3.354	1	0	0	1
C(22) ...C(8)	3.601	1	0	0	-1
C(22) ...C(14)	3.594	1	0	0	1

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Title of Thesis/ Dissertation: **APPROACHES TO BRIDGED ANNULENES USING BOTH CLASSICAL AND REACTIVE INTERMEDIATES. THE SYNTHESIS OF THE FIRST DIATROPIC BRIDGED THIAANNULENE AND SEVERAL FUSED DIHYDROPYRENES.**

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12 July 1994

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