Some Studies of Through Space
Functional Group - Arene Interactions

A Thesis Presented by

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Abstract

This thesis is divided into three chapters.

The first chapter is a review, which brings together the available information about the through space aromatic ring interactions from experimental, biological, and theoretical chemistry.

The second chapter describes the syntheses of series of novel 9,10[1',4']-benzenoanthracenes and 9,10-propanoanthracenes. Different spectroscopic techniques are used to characterise the behaviour of the title compounds both in solution and in the solid phase. The rigid skeleton of the 9,10[1',4']-benzenoanthracenes allows the position of substituents to be determined unequivocally. However, 9,10-propanoanthracenes have a flexible bridge which can flip over the aromatic moiety and thus interactions between the aromatic rings and different functional groups can be compared. A preliminary study of the influence of solvation on the conformational equilibria were also performed.

A variety of spectroscopic techniques are used to characterise the interactions. These results have given some insight into hydrogen bonding to an aromatic system. The role of a through space interaction on $^1$H and $^{13}$C NMR spectra was also investigated.

Chapter three provides a formal description of experimental results and procedures.
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Particular thanks go to Dr. Edgar Anderson, Dr. Michael Abraham, Dr. Henry Rzepa, and Dick Sheppard for their helpful discussions of the strange "water doublet" and other phenomena.

I am very grateful to Dr. Alfred Bader who made all this possible by founding the Alfred Bader Research Studentship.

Most importantly, I would like to thank my wife Sylva and my parents for their constant love and encouragement.
Abbreviations

Ac  acetyl
APT  attached proton test
b.p.  boiling point
d  doublet
d  secondary or quaternary carbon
dd  doublet of doublets
ddd  doublet of doublets of doublets
dt  doublet of triplets
CI  chemical ionisation
DAST  diethylaminosulfur trifluoride
DCM  dichloromethane
DMAP  4-dimethylaminopyridine
DMF  dimethylformamide
DMSO  dimethylsulfoxide
EI  electron impact ionisation
Et  ethyl
FAB  fast atom bombardment ionisation
H-ar.  aromatic protons
h  hour
J_{XY}  coupling constant between atoms X and Y
M^+  molecular ion
m  multiplet
m  medium
min.  minutes
mol.eq.  molar equivalents
m.p.  melting point
m-CPBA  3-chloroperbenzoic acid
<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDA</td>
<td>lithium diethylamine</td>
</tr>
<tr>
<td>LW</td>
<td>line width</td>
</tr>
<tr>
<td>NMR</td>
<td>nuclear magnetic resonance</td>
</tr>
<tr>
<td>NOE</td>
<td>nuclear Overhauser effect</td>
</tr>
<tr>
<td>PCC</td>
<td>pyridinium chlorochromate</td>
</tr>
<tr>
<td>s</td>
<td>singlet</td>
</tr>
<tr>
<td>s</td>
<td>strong</td>
</tr>
<tr>
<td>T</td>
<td>temperature (K)</td>
</tr>
<tr>
<td>THF</td>
<td>tetrahydrofuran</td>
</tr>
<tr>
<td>TLC</td>
<td>thin layer chromatography</td>
</tr>
<tr>
<td>TMS</td>
<td>trimethylsilyl</td>
</tr>
<tr>
<td>t</td>
<td>triplet</td>
</tr>
<tr>
<td>w</td>
<td>weak</td>
</tr>
<tr>
<td>u</td>
<td>primary or tertiary carbon</td>
</tr>
<tr>
<td>ΔG</td>
<td>difference in energy (kJ mol(^{-1}))</td>
</tr>
<tr>
<td>δ(_C)</td>
<td>carbon chemical shifts in ppm</td>
</tr>
<tr>
<td>δ(_H)</td>
<td>proton chemical shifts in ppm</td>
</tr>
<tr>
<td>(v_{\text{max}})</td>
<td>peak frequencies in infrared spectra</td>
</tr>
</tbody>
</table>
Chapter One

REVIEW

THROUGH SPACE AROMATIC INTERACTIONS
1.1. Introduction

In recent years, many vital and varied aspects of noncovalent bonding have attracted considerable interest. Knowledge of such intermolecular interactions is necessary in many areas including the rational development of efficient drugs, sensors, asymmetric catalysts, and new materials.

The vast majority of organic compounds contain at least one aromatic or heteroaromatic moiety. Originally, aromatic rings were viewed as a scaffold on which functional groups, responsible for effectiveness of interactions, were positioned. However, as we shall see, recent evidence has shown, that they play a much more active role.

Several reviews have been published on some of the aspects of aromatic ring interactions. Thus, hydrogen bonding to an aromatic ring\(^1-^4\), aromatic-aromatic\(^4-^9\) and CH-\(\pi\) interactions\(^10,^11\), experimental\(^12,^13\) and theoretical\(^14\) studies of dimers and small clusters, and the complexation of neutral molecules by cyclophanes\(^15,^16\) and calixarenes\(^17,^18\) all form the subjects of recent reviews. Several facets of intermolecular interactions including aromatic systems were discussed by Schneider\(^19\) and the compilation of thermodynamic and kinetic data for macrocycle interactions with neutral molecules by Izatt et al\(^20\) also contains many aromatic hosts. The early work on \(\pi\)-molecular complexes was summarised by Mulliken and Person\(^21\) and by Foster\(^22\). Aromatic rings are very often encountered in crystal engineering studies. However, these studies are not mentioned in this review since many examples can be found in recent publications\(^23,^24\).

At this time, an overview, which would bring together information from different fields of chemistry is still lacking; the closest approach to this aim being a paper by Burley and Petsko\(^4\). The objective of this review is an introductory attempt to fill this gap.
Interactions between aromatic rings are of paramount importance as they regularly occur both in biological\textsuperscript{4} and synthetic\textsuperscript{15-18,25} molecules. In recent years, evidence has accumulated that aromatic rings are rarely found in the traditionally conceived face-to-face π-stacked geometry, but that they occur either in the T-shaped or offset stacked geometries (Figure 1).

Since charge-transfer interactions are optimised by maximum overlap of the orbitals involved, the charge-transfer theory cannot explain these orientation preferences. A different theoretical explanation is thus required.

Several authors have suggested\textsuperscript{4,9,14,26-29}, that the quadrupolar moment of participating aromatic systems is responsible for their orientation behaviour. Electrostatic forces between the quadrupoles and other charged entities are substantially more directional and decay more slowly than dispersion forces. Thus, while the dispersion interaction energy is proportional to \(r^{-6}\), the distance dependence of the energy of the quadrupole interactions is as follows\textsuperscript{4,28}: charge-quadrupole \(\propto r^{-3}\), dipole-quadrupole \(\propto r^{-4}\), quadrupole-quadrupole \(\propto r^{-5}\), where \(r\) is the distance between two interacting particles.

In 1980, Vrbancich and Ritchie\textsuperscript{26} determined the quadrupole moments of several aromatics from studies of the electric field-gradient birefringence (Table 1). The authors then used these moments to explain the structures of aromatic dimers. They wrote: "It is of interest that the vapour-phase 1,3,5-trifluorobenzene dimer has the
parallel-plane configuration, in contrast to the dimers of benzene and hexafluorobenzene. Our measurements indicate that it has a near zero quadrupole moment, so that quadrupole moments are unlikely to be significant in the dimer. We expect it to have a symmetrically staggered arrangement of the F-atoms, which would maximise the stabilising interaction of local C-F dipoles on one molecule with the polarizable C-H and C-C bonds on the other. ... It should be recognised that when the centres of the interacting molecules are in such proximity it may be unwise to place too much reliance on the notion of interacting quadrupole moments. Higher-order multipole moments could be significant and the multipole representation itself of questionable validity.”

Table 1: The quadrupole moments of some aromatic molecules

<table>
<thead>
<tr>
<th>Compound</th>
<th>$10^{-40}$ C m$^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>benzene</td>
<td>-33.3±2.1</td>
</tr>
<tr>
<td>1,3,5-trimethylbenzene</td>
<td>-32.1±2.7</td>
</tr>
<tr>
<td>hexamethylbenzene</td>
<td>-24.1±1.9</td>
</tr>
<tr>
<td>1,3,5-trifluorobenzene</td>
<td>+3.1±0.4</td>
</tr>
<tr>
<td>hexafluorobenzene</td>
<td>+31.7±1.7</td>
</tr>
</tbody>
</table>

Some time later Pawliszyn et al$^{27}$ demonstrated in their theoretical study of benzene and s-tetrazine dimers that simple considerations of the quadrupole moments of the investigated aromatic molecules led to the correct predictions of the geometry of the complexes.

The importance of the quadrupole moments of aromatic rings was also discussed by Burley and Petsko$^4$. "Charge-quadrupole interactions occur in the form of negatively charged oxygen-aromatic interactions. Dipole-quadrupole interactions occur in the form of $\partial^-$ oxygen-aromatic and sulphur aromatic interactions, which can also be
said to represent a type of "hydrogen bond" with a carbon atom as the hydrogen donor. Dipole-quadrupole interactions also occur in the form of $\partial^+$ amino-aromatic interactions. Finally, the aromatic-aromatic interaction is an example of a quadrupole-quadrupole interaction. Both the aromatic-aromatic interaction and the $\partial^+$ amino-aromatic interaction can also be described as "hydrogen bonds". The $\partial^+$ amino group interacting with an aromatic ring can be said to act as a "hydrogen bond donor," and the $\pi$-electron cloud of the remaining aromatic ring can be said to act as the "hydrogen bond acceptor" group. Although we do not favour such terminology, it does serve to underscore the similarity between these interactions and the more strongly polar conventional hydrogen bond."

In a recent review, Luhmer$^9$ has argued for the importance of quadrupolar interactions in molecular recognition processes involving a phenyl group. A comparison of the molecular parameters of benzene and cyclohexane (Table 2) reveals, that the only substantial difference between these molecules exists in their quadrupole moments. As their polarizabilities differ only slightly, both molecules should give rise to very similar dispersion and dipole-induced dipole interactions. The difference in their behaviour should therefore stem mainly from the quadrupole moments.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Benzene</th>
<th>Cyclohexane</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular Volume (Å³)</td>
<td>148.4</td>
<td>180.6</td>
</tr>
<tr>
<td>Molecular Surface (Å²)</td>
<td>135.6</td>
<td>154.5</td>
</tr>
<tr>
<td>Polarizability (Å³)</td>
<td>10.4</td>
<td>11.2</td>
</tr>
<tr>
<td>Polarizability Anisotropy (Å³)</td>
<td>-3.7 (or -5.6)</td>
<td>1.7</td>
</tr>
<tr>
<td>Dipole moment (C m)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Quadrupole moment (10⁻⁴⁰ C m²)</td>
<td>-29.0 ± 1.7</td>
<td>3.0 ± 1.0</td>
</tr>
</tbody>
</table>
Interactions between aromatic rings

This viewpoint was also reinforced by Hunter and Sanders\textsuperscript{30} who performed simple electrostatic calculations of benzene dimers, in which benzene was input essentially as a quadrupole. Preferences were found for the T-shaped and offset-stacked geometries of the benzene rings. They expressed their results in the following set of rules:

\textbf{Rule 1}: $\pi$-$\pi$ repulsion dominates in a face-to-face $\pi$-stacked geometry.

\textbf{Rule 2}: $\pi$-$\sigma$ attraction dominates in an edge on or T-shaped geometry.

\textbf{Rule 3}: $\pi$-$\sigma$ attraction dominates in an offset $\pi$-stacked geometry.

\textbf{Rule 4}: for interactions between highly charged atoms, charge-charge interactions dominate.

\textbf{Rule 5}: a favourable interaction with a neutral or weakly polarised site requires the following $\pi$-polarisation: (a) a $\pi$-deficient atom in a face-to-face geometry

(b) a $\pi$-deficient atom in the vertical T-group in the edge-on geometry

(c) a $\pi$-rich atom in the horizontal T-group in the edge-on geometry.

\textbf{Rule 6}: a favourable interaction with a neutral or weakly polarised site requires the following $\sigma$-polarisation: (a) a positively charged atom in a face-to-face geometry

(b) a positively charged atom in the vertical T-group in the edge-on geometry

(c) a negatively charged atom in the horizontal T-group in the edge-on geometry.

Reversing the polarisation in rules 5 and 6 leads to repulsion.

Although the parameters chosen for their calculations were almost arbitrary, and a small change in them leads to different results\textsuperscript{28}, these rules are valid and very useful for molecular design.
An elegant example of the application of these rules for the synthesis of a receptor is provided by macrocycle 1\textsuperscript{31}. This host complexed benzoquinone in deuterated chloroform. \textsuperscript{1}H NMR studies have shown, that the quinone is buried deep in the cavity with its hydrogens aiming towards the aromatic rings of the host (T-shaped geometry). No complexation could be detected with a large excess of tetramethylbenzoquinone, tetrachlorobenzoquinone, and anthraquinone, although these bulkier quinones fit into the cavity of 1.

\begin{itemize}
  \item 2a \(X = \text{OCH}_3\)
  \item 2b \(X = \text{CH}_3\)
  \item 2c \(X = \text{H}\)
  \item 2d \(X = \text{Cl}\)
  \item 2e \(X = \text{CO}_2\text{CH}_3\)
  \item 2f \(X = \text{NO}_2\)
\end{itemize}

\begin{itemize}
  \item 3a \(X = \text{OCH}_3, \ Y = \text{H}\)
  \item 3b \(X = \text{Cl}, \ Y = \text{H}\)
  \item 3c \(X = \text{NO}_2, \ Y = \text{H}\)
  \item 3d \(X = \text{OCH}_3, \ Y = \text{OCH}_3\)
  \item 3e \(X = \text{OCH}_3, \ Y = \text{COOCH}_3\)
  \item 3f \(X = \text{COOCH}_3, \ Y = \text{COOCH}_3\)
  \item 3g \(X = \text{OCH}_3, \ Y = \text{NO}_2\)
  \item 3h \(X = \text{NO}_2, \ Y = \text{COOCH}_3\)
\end{itemize}
A group of Italian and American workers\textsuperscript{32,33} have devised an ingenious method for the estimation of the role which electron charge transfer plays in aromatic-aromatic interactions. They have prepared a series of 1,8-diarylnaphthalenes 2 and 3 and measured the barriers to rotations of the aryl moieties (Table 3).

**Table 3**: The barriers to rotations of the aryl moieties in 1,8-diarylnaphthalenes 2 and 3\textsuperscript{32,33}

<table>
<thead>
<tr>
<th>Compound</th>
<th>$\Delta G^\circ$ (kJ mol$^{-1}$)</th>
<th>Compound</th>
<th>$\Delta G^\circ_{\text{syn-anti}}$ (kJ mol$^{-1}$)</th>
<th>$\Delta G^\circ_{\text{anti-syn}}$ (kJ mol$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2a</td>
<td>58.2</td>
<td>3d</td>
<td>100.4</td>
<td>103.8</td>
</tr>
<tr>
<td>2b</td>
<td>60.2</td>
<td>3e</td>
<td>102.1</td>
<td>105.9</td>
</tr>
<tr>
<td>2c</td>
<td>61.5</td>
<td>3f</td>
<td>103.8</td>
<td>106.7</td>
</tr>
<tr>
<td>2d</td>
<td>64.9</td>
<td>3g</td>
<td>103.3</td>
<td>107.1</td>
</tr>
<tr>
<td>2e</td>
<td>70.7</td>
<td>3h</td>
<td>106.3</td>
<td>109.6</td>
</tr>
<tr>
<td>2f</td>
<td>72.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3a</td>
<td>103.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3b</td>
<td>107.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3c</td>
<td>109.2</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

They have argued, that the energy of the transition states should not depend on the nature of the substituents X and Y, and a stabilisation or a destabilisation of the ground state should be responsible for differences in the barriers to rotations. If the charge transfer interaction was dominant, the barrier would be smallest with $X =$ electron acceptor and $Y =$ electron donor. On the other hand, if through space coulombic interaction between the phenyl groups (a repulsion of two $\pi$-clouds) was important, then the rotation would be fastest with two electron withdrawing groups and would slow down with an increase in the electron richness of one or both aromatic
Interactions between aromatic rings

rings. Since all measurements made have shown monotonically increasing barriers on passing from the electron donating to the electron withdrawing substituents (Table 3) the authors were able to conclude that the contribution from the charge transfer interaction between two aromatic systems is not important, at least for the system in hand.

Recently this group\textsuperscript{34} prepared a series of compounds 4 containing a perfluorinated phenyl ring. The barriers to rotation found are summarised in Table 4 and show a decrease with increasing electron donating capability of the substituent on the aromatic ring. This trend is the reverse of that for phenyl derivatives 2 and 3, and supports the theory that quadrupolar interaction is the determining force in the interactions of aromatic rings. As pointed out by the authors, perfluorinated arenes can be potentially efficient in the binding of aromatic compounds, and as such a vast area has been opened up for exploration.

Table 4: The barriers to rotations of the aryl moieties in 1,8-diarylnaphthalenes 4\textsuperscript{34}

<table>
<thead>
<tr>
<th>Compound</th>
<th>( \Delta G^\neq ) (kJ mol(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a</td>
<td>19.5</td>
</tr>
<tr>
<td>4b</td>
<td>19.8</td>
</tr>
<tr>
<td>4c</td>
<td>20.2</td>
</tr>
</tbody>
</table>
An interesting model system for studying π-π interactions was proposed by Gang and Moore\textsuperscript{35} who synthesised phenyl acetylene macrocycles 5 and measured their association in CDCl\textsubscript{3}. The rigidly held planar geometry of these compounds promotes co-operative π-π interaction between several pairs of aromatic rings in the neighbouring molecules in the offset stacked geometry and so magnifies otherwise weak interaction between a pair of aromatic rings. Rather surprisingly the highest association constant at 20°C ($K_{assoc} = 60 \text{ M}^{-1}$) was found for 5a. Compounds 5b and 5c are attracted less ($K_{assoc} = 18 \text{ M}^{-1}$ and 26 M\textsuperscript{-1}, respectively), no evidence for dimerisation of molecules 5d and 5e was observed. $K_{assoc}$ varies significantly with temperature. According to van't Hoff analyses, macrocycle 5b shows a slightly higher enthalpy of dimerisation then 5a, but the entropic cost of formation of the dimer is substantially higher and so at ambient temperature the entropic effect dominates and the compound 5a self-associates to a higher extent.
Interactions between aromatic rings

Wilcox et al\textsuperscript{36} have recently tested the strength of the edge-to-face aromatic interactions by preparing esters 6 and investigating their conformational equilibria. The X-ray structure of a crystal of para-nitrophenyl ester 6e confirmed that the phenyl groups are suitably oriented for edge-to-face stacking to the aromatic ring which forms the base in conformation A and this stacking survives in solution, as evidenced by \textsuperscript{1}H NMR. The conformation ratio for the phenyl ester 6a was unchanged in chloroform, nitromethane, dimethylsulfoxide, benzene, carbon tetrachloride, tetrachloroethylene, and tetrachloroethane. The results are summarised in Table 5. The stabilisation energy from the stacking is rather weak (1-2 kJ mol\textsuperscript{-1}), with the highest preference being achieved for electron deficient 6d and 6e. The same effect was observed with the highly polarizable iodine substituent in 6f. Nonaromatic esters 6g and 6h exhibited a similar preference for conformation A and so, at least in this system, aromatic face to edge stacking seems to be of the same magnitude as aromatic-alkyl interactions.
Table 5: Conformational equilibria of esters 6 in CDCl₃

<table>
<thead>
<tr>
<th>Ester</th>
<th>% of A</th>
<th>ΔG (kJ mol⁻¹)</th>
<th>Ester</th>
<th>% of A</th>
<th>ΔG (kJ mol⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6a</td>
<td>60</td>
<td>-1.0</td>
<td>6g</td>
<td>65</td>
<td>-1.5</td>
</tr>
<tr>
<td>6b</td>
<td>65</td>
<td>-1.5</td>
<td>6h</td>
<td>80</td>
<td>-3.4</td>
</tr>
<tr>
<td>6c</td>
<td>60</td>
<td>-1.0</td>
<td>6i</td>
<td>50</td>
<td>0.0</td>
</tr>
<tr>
<td>6d</td>
<td>75</td>
<td>-2.7</td>
<td>6j</td>
<td>60</td>
<td>-1.0</td>
</tr>
<tr>
<td>6e</td>
<td>75</td>
<td>-2.7</td>
<td>6k</td>
<td>35</td>
<td>1.5</td>
</tr>
<tr>
<td>6f</td>
<td>75</td>
<td>-2.7</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The complexation of 2,6-disubstituted naphthalenes 7 with the hosts 8 in several solvents has been studied by Diederich et al.³⁷⁻³⁹.

In this case binding was strongest when both X and Y were electron acceptors, intermediate when X was an acceptor and Y a donor, and weakest when X and Y were
both electron donors. The thiomethoxy group deviated from this trend. Thus, the binding constant of 2,6-dithiomethoxynaphthalene \(7f\) was substantially higher than the binding constant of either 2,6-dimethoxynaphthalene \(7d\) or 2,6-dimethylnaphthalene \(7e\).

Table 6 The association constants for binding of 2,6-disubstituted naphthalenes with macrocycle \(8d\) in CD$_3$OD$^{38}$

<table>
<thead>
<tr>
<th>Guest</th>
<th>(K_a) (M$^{-1}$)</th>
<th>Guest</th>
<th>(K_a) (M$^{-1}$)</th>
<th>Guest</th>
<th>(K_a) (M$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(7a)</td>
<td>20±5</td>
<td>(7i)</td>
<td>117±10</td>
<td>(7q)</td>
<td>216±15</td>
</tr>
<tr>
<td>(7b)</td>
<td>23±5</td>
<td>(7j)</td>
<td>119±10</td>
<td>(7r)</td>
<td>272±15</td>
</tr>
<tr>
<td>(7c)</td>
<td>27±5</td>
<td>(7k)</td>
<td>134±25</td>
<td>(7s)</td>
<td>&lt;10</td>
</tr>
<tr>
<td>(7d)</td>
<td>53±5</td>
<td>(7l)</td>
<td>167±20</td>
<td>(7t)</td>
<td>29±5</td>
</tr>
<tr>
<td>(7e)</td>
<td>67±5</td>
<td>(7m)</td>
<td>64±10</td>
<td>(7u)</td>
<td>40±5</td>
</tr>
<tr>
<td>(7f)</td>
<td>162±10</td>
<td>(7n)</td>
<td>109±10</td>
<td>(7v)</td>
<td>91±10</td>
</tr>
<tr>
<td>(7g)</td>
<td>105±15</td>
<td>(7o)</td>
<td>188±10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(7h)</td>
<td>111±10</td>
<td>(7p)</td>
<td>210±15</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The complexation of benzene derivatives by macrocycle \(8e\) was also studied in a variety of solvents of differing polarity$^{37,39}$. Complexation is enthalpically driven in these instances and usually accompanied by an unfavourable entropic term. A large part of the favourable enthalpy change results from a solvent-specific contribution.
A striking example of the fact that the enthalpic and entropic terms can differ dramatically for complexation in solvents in which similar binding free energies are measured is provided by the complexation of pyrene by macrocyclic host 9. In acetone and dimethylsulfoxide, the binding is strongly enthalpy driven (\( \Delta H = -27.2 \text{ kJ mol}^{-1} \)) and entropically unfavourable (\( T\Delta S = -10.0 \text{ kJ mol}^{-1} \)). On the other hand, the enthalpy of formation in N,N-dimethylacetamide is substantially smaller (\( \Delta H = -8.4 \text{ kJ mol}^{-1} \)), but this is compensated by a favourable entropic term (\( T\Delta S = +10.0 \text{ kJ mol}^{-1} \)).

Molecular cleft 10\(^{40}\) was used for the transport of aromatic aminoacids between two water layers separated by a chloroform interface. The relative rates of the transport of the aminoacids decrease in the order: tryptophane > tyrosine methyl ether > phenylalanine >> leucine, indicating that aromatic-aromatic stacking obviously operates in this system. Interestingly, the aminoacids are transported in a termolecular complex which uses two molecules of the cleft. The same receptor also binds \( \beta \)-arylethylamines.

Rebek later synthesised a series of molecules 11 and 12\(^{41-43}\) and investigated their binding affinity towards a series of adenine derivatives. The association constants for binding of 9-ethyl adenine 13 in CDCl\(_3\) are summarised in Table 7.
Interactions between aromatic rings = 22 =

11a R = NH-phenyl
11b R = NH-2-naphthyl
11c R = NH-2-anthryl

11d W = N, Y = NH, X = Z = H
11e W = CH, Y = O, X = Z = H
11f W = CH, Y = O, X = Z = \text{tBu}
11g W = CH, Y = CH\text{CH}_2\text{CH}_2\text{O}, X = Z = F
11h W = CH, X = Br, Y = O, Z = H

12a Y = CO, R = phenyl
12b Y = CO, R = 2-naphthyl
12c Y = CO, R = 2-anthryl
12d Y = CO, R = 2-(3-methoxy)anthryl
12e Y = CO, R = 2-(3-hydroxy)anthryl
12f Y = SO, R = 2-naphthyl

12g R =

12h R =

13
Table 7: The association constants for binding of 9-ethyl adenine with hosts 11 and 12 in CDCl₃⁴¹,⁴²

<table>
<thead>
<tr>
<th>Compound</th>
<th>Kₐ (M⁻¹)</th>
<th>Compound</th>
<th>Kₐ (M⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>11a</td>
<td>101</td>
<td>12a</td>
<td>100</td>
</tr>
<tr>
<td>11b</td>
<td>220</td>
<td>12b</td>
<td>170</td>
</tr>
<tr>
<td>11c</td>
<td>440</td>
<td>12c</td>
<td>260</td>
</tr>
<tr>
<td>11d</td>
<td>120</td>
<td>12d</td>
<td>140</td>
</tr>
<tr>
<td>11e</td>
<td>90</td>
<td>12e</td>
<td>260</td>
</tr>
<tr>
<td>11f</td>
<td>125</td>
<td>12f</td>
<td>8.4</td>
</tr>
<tr>
<td>11g</td>
<td>79</td>
<td>12g</td>
<td>100</td>
</tr>
<tr>
<td>11h</td>
<td>64</td>
<td>12h</td>
<td>420</td>
</tr>
</tbody>
</table>

As anticipated, ethyl adenine was hydrogen bonded to the imide part of the receptors with both Watson-Crick and Hoogsteen modes operating. Differences in complexation constants can be explained on the basis of π-π stacking. An increase in the size of the arene favourably affects the enthalpy of the interaction; this effect is partially compensated by a decrease in the entropy. The phenyl and anthryl groups differ by ca 4 kJ mol⁻¹ in the strength of their stacking interaction. A comparison of the complexation in different solvents indicates a constancy of the stacking effect. The stronger binding of t-butyl naphthalene derivative 11g in comparison to unsubstituted receptor 11f is attributed by the authors to the polarizability contribution of the added t-butyl groups. The change from the electron-rich aromatics in series 11 to the electron-poor in series 12 led to a lowering of the affinity for adenine. The strong affinity of imido derivative 12h is probably due to preorganisation which follows on from its rigidity.
Interactions between aromatic rings

A beautiful example of the $\pi-\pi$ stacking interaction in complexation of adenosine derivatives is provided by “scorpion” receptors, e.g. 14$^{44}$. When 9-ethyladenine is added to a solution of 14, the receptor undergoes reorganisation and the pendant chain closes the cavity with complexed ethyladenine.

Very strong binding of 9-propyl adenine has also been achieved with "tweezers" 15$^{45}$. In this instance, it is noteworthy how a single hydrogen bond and two stacking interactions can lead to a very strong binding.
Interactions between aromatic rings

The use of rigid molecular tweezers 16 has demonstrated that the electronic properties of the aromatic rings can be of paramount importance. 2,4,7-trinitrofluorenone 17 is bound 5 times more strongly by the electron rich host 16a than by the alkyl substituted congener 16b. Zimmerman and Saionz have recently succeeded in the preparation of HPLC stationary phases with similarly shaped molecules. The enthalpies for binding of different guests with tweezer’s hosts were estimated from the retention times and found to correspond to those derived from solution measurements.
Interactions between aromatic rings

Hamilton's 'molecular hinge' 18\(^\oplus\) is another receptor using stacking interactions for the recognition of nucleic bases. The X-ray structure of macrocycle 18 shows an open conformation with the naphthalene poised away from the pyridine ring at an inter-plane angle of 127.5\(^\circ\). A 1:1 complex is formed, when crystals are grown in the presence of 1-butyl thymine 19. The naphthalene lies approximately parallel (14\(^\circ\)) to the plane of the thymine substrate and the angle between the pyridine and naphthalene planes is now 161.6\(^\circ\). \(^1\)H NMR studies confirmed that the same structural complex persists in deuterochloroform solution.

\[
R =
\]

Schneider and Wang have studied the association of porphyrins 20 with a variety of aromatic compounds in water\(^\text{49,50}\). It was shown in previous studies\(^\text{51}\) that the attraction between charges amounts to 5±1 kJ mol\(^{-1}\) per salt bridge and it is practically independent of the size of the ions. This knowledge enabled these authors to separate the contribution of the aromatic systems to the overall binding. Reasonably consistent results were obtained: viz. 7.2±1.5 kJ mol\(^{-1}\) for the benzene, 15.8±1.8 kJ mol\(^{-1}\) for the naphthalene, and 18.5±0.5 kJ mol\(^{-1}\) for the phenanthrene derivatives leading to an increment of 1.4±0.15 kJ mol\(^{-1}\) per \(\pi\)-electron. Especially noteworthy is a comparison of the association between terephthalate 21 (\(\Delta G = -13.1\) kJ mol\(^{-1}\)) and cyclohexanedicarboxylate 22 (\(\Delta G = -8\) kJ mol\(^{-1}\)) with porphyrins 20.
Interactions between aromatic rings

The hydrophobic effect cannot account for the difference in the binding energy, as the surface areas of these compounds are similar. When copper(II) is complexed by porphyrin 20a, approximately the same association energies are found, whereas introduction of zinc leads to a decrease in the binding energy by ca. 3.4 kJ mol\(^{-1}\).

The enthalpy of the interaction between two porphyrin moieties with complexed zinc\(^{52}\) amounts to 48±10 kJ mol\(^{-1}\).

L’Esperance et al\(^{53}\) have studied the conformational effects in the crystal structures of 9,14-diphenylbenzo[b]triphenylenes 23. They found, that the influence of substituents X on the nonbonded repulsion of the \(\pi\)-electron clouds is small in comparison with the crystal packing forces.
Nolte's group has demonstrated\textsuperscript{54,55} that aromatic-aromatic interactions alone are sufficient for complexation. Their host \textbf{24}, binds electron deficient aromatics (nitrobenzenes, cyanobenzenes) in CDCl\textsubscript{3}. The molecule exists in three conformations interconverting by nitrogen inversion (\textbf{Figure 2}). In the absence of a guest, conformer \textbf{B} predominates (89.6\%) and conformers \textbf{A} (7.7\%) and \textbf{C} (2.7\%) are populated substantially less. When a guest is bound to the host, the relative amount of the \textbf{C} conformer increases.
The authors suggested that the guests are sandwiched between the naphthalene walls in the offset geometry. When the naphthalene rings are connected with monoazapolyethyleneglycol bridges, an allostere effect operates in the host. The addition of a potassium salt into a solution of this receptor lead to a marked increase in the binding of dinitrobenzene.

Receptor 25 proved to be very efficient in the selective recognition and separation of isomeric and partially hydrogenated arenes in water. Thus, phenanthrene 26 and acenaphthylene 27 are complexed by 25 while anthracene 28 and acenaphthene 29 are not.
Newcomb et al\textsuperscript{58} have synthesised compounds 30 and studied their intramolecular stacking interactions in water. Although no evidence for stacking was detected in the case of binaphthyl derivative 30a, biadenyl compound 30b is stacked; however this intramolecular association does not survive in DMSO solution. Mixed derivative 30c also stacks to a considerable extent in water. The authors ruled out the classical hydrophobic effect as stacking in compound 30a would also be expected in such a case, and proposed instead that the attraction between partial positive and negative charges in the neighbouring aromatic groups is responsible for the observed stacking in molecules 30b and 30c.

Crystallographic studies in which some kind of aromatic-aromatic interaction was detected are very numerous. Crystal packing of aromatic compounds, and the use of the information which can be gained from this approach for the design of receptors was discussed by Plebe and Diederich\textsuperscript{59}. A rather successful model for the prediction of crystal structures of fused-ring aromatic hydrocarbons was recently proposed.\textsuperscript{60-62}

Gas-chromatographic studies\textsuperscript{63} have shown that the strength of the interaction between a phenyl group in a stationary liquid and a benzene molecule in a sample is significantly altered when a methyl group is introduced into a benzene ring in the sample. Methyl, ethyl, chloro, trichloromethyl, dimethylamino, methoxymethyl, and methoxy substituents were compared in the publication.

The benzene-benzene interaction, as a prototype of the aromatic-aromatic interaction, has attracted much attention from experimental physical chemists\textsuperscript{64-72}. Most measurements suggest that T-shaped structure for the dimer is preferred\textsuperscript{70-73}. The rotational spectrum is consistent with a T-shaped symmetric top\textsuperscript{73}, but there is some evidence that this top is not the ground state of the dimer. Mass selected hole-burning experiments even indicate the presence of three different ground state structures\textsuperscript{74}. The hexafluorobenzene dimer is also T-shaped\textsuperscript{71}, but the benzene-hexafluorobenzene dimer possess a stacked structure\textsuperscript{71}, in accordance with the reasoning of the quadrupolar model. The T-shaped structures are very common in the crystals of simple aromatics\textsuperscript{75}.
The binding energies of neutral benzene dimers, as estimated by different experimental techniques, are summarised in Table 8. The discrepancy in the observed energies is caused by difficulties connected with the individual experimental techniques\(^{26,77}\).

**Table 8: Binding energies of the neutral benzene dimers\(^{64}\)**

<table>
<thead>
<tr>
<th>Binding energy (kJ mol(^{-1}))</th>
<th>Reference</th>
<th>Binding energy (kJ mol(^{-1}))</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.8±1.0</td>
<td>64,78</td>
<td>10.6</td>
<td>67</td>
</tr>
<tr>
<td>2.8</td>
<td>65</td>
<td>10.0</td>
<td>68</td>
</tr>
<tr>
<td>9.6</td>
<td>66</td>
<td>2.5</td>
<td>69</td>
</tr>
</tbody>
</table>

Krause *et al*\(^{79}\) have measured binding energies for small benzene clusters. The dissociation energies found for neutral and charged clusters are as follows: dimer = 6.8 (charged dimer 63.7), trimer = 19.3 (26.1), tetramer = 9.6 (12.5), pentamer ≤5.8 (≤12.5) kJ mol\(^{-1}\). These results support a stable triangular structure for the neutral benzene trimer. The cyclic structure of the trimer is also supported by laser induced photodissociation studies of benzene clusters\(^{80}\).

**Table 9: Dissociation energies of the neutral dimers measured by resonance-enhanced two-photon ionisation\(^{13,78}\)**

<table>
<thead>
<tr>
<th>Dimer</th>
<th>dissociation energy (kJ mol(^{-1}))</th>
<th>Dimer</th>
<th>dissociation energy (kJ mol(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>benzene-benzene</td>
<td>6.8±1.0</td>
<td>benzene-toluene</td>
<td>14.5±1.0</td>
</tr>
<tr>
<td>benzene-cyclohexane</td>
<td>7.7±2.0</td>
<td>p-DFB*-p-DFB</td>
<td>8.7±2.0</td>
</tr>
<tr>
<td>toluene-toluene</td>
<td>14.5±1.0</td>
<td>benzene-p-DFB</td>
<td>7.7±2.0</td>
</tr>
</tbody>
</table>

\(^*\)p-difluorobenzene
Dissociation energies of several aromatic dimers were measured by Ernstberger et al.\textsuperscript{13,78} (Table 9). Toluene clusters were shown to be considerably stronger bound; the energetic differences between the other clusters were within experimental error.

Benzene cluster ions are particularly stable when they contain 14, 20, 24 or 27 molecules; this is a possible indication of the icosahedral packing about the central dimer ion\textsuperscript{81,82}.

Calculation of the benzene dimer as a prototypical aromatic cluster has attracted considerable attention\textsuperscript{28,83-91}. The earlier calculations agreed on the fact, that the face-to-face geometry is not energetically advantageous, and predicted that the T-shaped geometry is the most stable one. It is therefore rather surprising, that the highest quality calculations\textsuperscript{28} performed thus far contradict the preference for a T-shaped geometry. Hobza et al.\textsuperscript{28} have used high quality basis sets and corrected their results for the basis set superposition error. The investigated structures are depicted in Figure 3 and the calculations summarised in Table 10.
Interactions between aromatic rings

![Diagram of benzene dimers and interaction structures]

Figure 3

Table 10: Calculated interaction energies for structures of benzene dimer$^{28}$ depicted in Figure 3

<table>
<thead>
<tr>
<th>Structure</th>
<th>DZ+2P* (kJ mol$^{-1}$)</th>
<th>DZ+2P (kJ mol$^{-1}$)</th>
<th>R (Å)**</th>
</tr>
</thead>
<tbody>
<tr>
<td>a)</td>
<td>-7.9</td>
<td>-8.8</td>
<td>5.00</td>
</tr>
<tr>
<td>b)</td>
<td>-6.9</td>
<td></td>
<td>5.10</td>
</tr>
<tr>
<td>c)</td>
<td>-2.9</td>
<td>-3.7</td>
<td>6.22</td>
</tr>
<tr>
<td>d)</td>
<td>-8.0</td>
<td>-8.8</td>
<td>5.05</td>
</tr>
<tr>
<td>f)</td>
<td>-8.3</td>
<td>-9.5</td>
<td>3.85</td>
</tr>
<tr>
<td>g)</td>
<td>-3.6</td>
<td></td>
<td>3.90</td>
</tr>
</tbody>
</table>

* polarisation functions on carbons only

** distances between the centres of both rings
The most stable structure found was the parallel-displaced f), followed respectively by the displaced T-shaped d), and T-shaped a) and b). Parallel-sandwich g) was considerably less stable, but still more stable than T-shaped c). Structures a), c), d), and f) were confirmed to be the energetic minima. The authors have predicted that the stabilisation energies are underestimated by approximately 20% and after correction for the zero-point energy, the stabilisation enthalpy of the dimer was estimated to be 10.0 kJ mol⁻¹.

Caution should be exercised when considering the results of molecular ab Initio calculations involving benzene and other aromatic molecules. Benzene is a computationally large molecule and so only comparatively small basis sets can be used in the calculations; 6-31G** or 6-31+G* are the highest quality sets commonly used. It was demonstrated¹⁴,²⁸ that the 6-31G* basis set does not furnish the correct quadrupolar moment of benzene, 6-31+G* affords reasonable quadrupolar moment and total polarizability, but it gives considerably larger stabilisation energies for the benzene dimer than high quality sets, and so even this basis set is not sufficiently reliable.

The maximum strength of a phenyl-phenyl interaction in water and chloroform is expected to be ca 4 kJ mol⁻¹ from Monte Carlo studies⁹²; the optimal gas-phase interaction is considerably damped out by the solvent and the entropy effect. The benzene dimer prefers to adopt the T-shaped geometry and stacked structures become more favourable with increasing size of the arenes used. Molecular dynamic calculations⁹³ indicate that two benzene molecules prefer the T-shaped geometry as opposed to the face-to-face stacked dimer in water, although the latter has much smaller surface area exposed to water. The offset-stacked and T-stacked geometries were not however compared in this paper.

Aromatic-aromatic interactions were shown to play an important role in the determination of the three dimensional structures of proteins⁹⁴ and nucleic acids⁹⁵,⁹⁶, in the stabilisation of the structure of zinc fingers⁹⁷-¹⁰⁰, in the binding of NADPH in
Interactions between aromatic rings

= 35 =

dihydrofolate reductase\(^{101}\), in cell-cell adhesion\(^{102}\), and in systems connected with immunological responses\(^{103,104}\).

Studies of protein crystal structures\(^{105,106}\) and phenyl containing molecules\(^{107}\) have demonstrated that phenyl rings are very rarely found in the face-to-face stacked geometry and that the T-shaped and offset-stacked modes are much preferred.

Burley and Petsko have surveyed the crystal structures of 34 proteins and 4 peptides\(^{104}\). They found that on average about 60\% of aromatic side chains are involved in forming aromatic pairs, 80\% of which form networks of three or more interacting aromatic residues. The aromatic aminoacids are notably absent in the regions where the polypeptide chain is disordered. These authors have made the interesting proposition that the aromatic-aromatic interactions may form nucleation sites in the protein folding pathway.

The energetic difference between an aromatic pair in the folded protein relative to solvated aromatic rings by water in an unfolded protein amounts to 5.4 kJ mol\(^{-1}\), as follows from double mutant cycle analysis\(^{108}\). Tyrosine-tyrosine and phenylalanine-phenylalanine interactions were shown to make identical contributions to protein stability, tyrosine being preferred on the solvent exposed surface.

Brocchieri and Karlin\(^{106}\) have studied the relative spatial disposition of side chain planar groups in 186 proteins. When planes are randomly distributed in space, the probability of finding two planar groups in a near perpendicular position is much higher than for a nearly parallel configuration. In the investigated proteins the search found a quite uniform, and so significantly nonrandom, distribution of the aromatic rings. The parallel geometries are therefore preferred; the rings are only rarely fully stacked, but they are mostly positioned in the displaced stacking mode. The edge-to-edge and edge-to-centre geometries were found to be the most commonly encountered arrangements of planar residues in protein structures.

\(\pi-\pi\) Stacking is often evoked in order to explain diastereoselective preferences in asymmetric synthesis\(^{109-111}\). However, some care should be taken, as high
Interactions between aromatic rings
diastereoselectivities can be explained without invocation of these interactions. The interactions between ligand's aromatic rings are important in metal complexes, especially in displacing an equilibrium among complex species, even in organic solvents.

As the preceding discussion demonstrated, understanding of intra- and intermolecular interactions between aromatic rings has improved considerably in recent years. The notion of an aromatic ring as a quadrupole is very useful for qualitative considerations, and as such the reason why complexes of two similar aromatic rings prefer offset stacked and T-shaped geometries becomes obvious. If an aromatic system is heavily substituted with electronegative substituents such as fluorine, the sign of the quadrupole can be reversed and thus, for example the complex between benzene and hexafluorobenzene exhibits stacked geometry.

The importance of the contribution of aromatic-aromatic interactions to the binding energies in host-guest complexes and their biological significance is still disputed. While some authors consider these interactions to be of great importance, others disagree and claim that these interactions are too weak for really sizeable effects. Unfortunately, the quantitative data are rather scarce and caution has to be taken before reaching some definite conclusions. The strength of these interactions obviously depends on many factors such as steric accessibility and the electronic properties of the rings, and so the significance of these interactions should not be dismissed out of turn. The foregoing discussion has indeed demonstrated that they can play an important role.

It would be very useful to be able to predict whether a T-shaped or an offset stacked geometry would be adopted by the aromatic rings in a particular system. Unfortunately, it is exceedingly difficult to provide a definitive solution to this problem. Obviously, the steric considerations would be very important for any particular complex, as the energetic difference between the T-shaped and offset stacked configurations is rather weak; as such the offset stacked geometries would be expected to become more dominant with the increasing size of an arene. The contact area
between two aromatic rings is larger in the offset stacked than in the T-shaped geometry, and so attractive dispersion forces become dominant with increasing size of the arene
1.3. Alkyl - Aromatic Ring Interactions

The existence of an attractive interaction between alkyl groups and π-systems is well documented in the literature. Many examples of these interactions can be found in recent reviews\textsuperscript{10,11,13} and so only one representative example will be given here.

\begin{align*}
31a & \quad X = (CH_3)_2N, Y = CH_3 \\
31b & \quad X = H, Y = CH_3 \\
31c & \quad X = NO_2, Y = CH_3 \\
31d & \quad X = H, Y = H \\
31e & \quad X = H, Y = COOCH_3
\end{align*}

Japanese workers\textsuperscript{114} have studied the conformational equilibria in a series of substituted triptycenes 31 (Table 11). The ratio of conformers depends on the electronic properties of the methyl and benzyl groups; the preference for the synclinal conformers A, B is substantially higher than that expected on simple steric grounds alone.
Table 11: Conformational equilibria in triptycenes 31

<table>
<thead>
<tr>
<th>Compound</th>
<th>X</th>
<th>Y</th>
<th>K = (A+B) / C</th>
</tr>
</thead>
<tbody>
<tr>
<td>31a</td>
<td>(CH$_3$)$_2$N</td>
<td>CH$_3$</td>
<td>2.87±0.1</td>
</tr>
<tr>
<td>31b</td>
<td>H</td>
<td>CH$_3$</td>
<td>2.30±0.04</td>
</tr>
<tr>
<td>31c</td>
<td>NO$_2$</td>
<td>CH$_3$</td>
<td>1.52±0.04</td>
</tr>
<tr>
<td>31d</td>
<td>H</td>
<td>H</td>
<td>2.22±0.06</td>
</tr>
<tr>
<td>31e</td>
<td>H</td>
<td>COOCH$_3$</td>
<td>4.09±0.16</td>
</tr>
</tbody>
</table>

Some type of attractive interaction can be expected on the basis of the quadrupolar moment of an aromatic ring. The methyl C-H bond is weakly polarised, with a partial positive charge being developed on the hydrogen. This polarisation is magnified if an electronegative substituent is introduced in the vicinity of the C-H bond in question. Some electrostatic attraction between this charge and the negative part of the ring quadrupole is therefore expected. The dispersion interactions will be of course the main contributors to the interaction potential.
1.4. Hydrogen Bonding to Aromatic Rings

In their famous monograph\(^1\), Pimentel and McClellan asked the question: "Do aromatics form a hydrogen bond?" and answered as follows: "In conclusion, the data support strongly the existence of complex formation between acids and aromatics acting as bases. Since there is ample evidence that the proton of the acid is specifically involved in the interaction, it can properly be called a H bond". Their evidence was based on following facts: a) the frequency of the A-H stretching mode (A = O, S, N, halogen) is shifted to lower frequencies, when the hydrogen bond donor is transferred from inert solvent to aromatics. At the time of the book's publication, such cases were demonstrated for phenol, water, amides, amines, alcohols, hydrogen chloride and pyrrole.

b) in \(^1\)H NMR studies, an interaction of aromatics with chloroform and water shifts the proton resonance to higher fields due to diamagnetic anisotropy of the aromatic \(\pi\)-electrons

c) solubility data (hydrogen chloride in aromatics, water in benzene) and freezing point diagrams (hydrogen chloride or chloroform with aromatics) reveal association of some kind, which could be hydrogen bonding.

In the following years, spectroscopic evidence for the formation of these hydrogen bonds accumulated, especially thanks to the work of Oki and Iwamura\(^{115,116}\), so that in 1965 Tichy\(^3\) could cite over two hundred molecules in which infrared spectroscopy indicated the presence of intramolecular hydrogen bonding to an aromatic ring.
Some of the bonds were observed to be particularly strong; for example the intramolecular hydrogen bonds in diphenylmethanes 32 were preserved even in solution in pyridine, a strong hydrogen bond acceptor\textsuperscript{117}. An X-ray study\textsuperscript{118} later confirmed the presence of the bond in a crystal of diphenylmethane 32 (R=CH\textsubscript{3}).

Crystallographic studies later gained in importance in the detection of hydrogen bonds to unsaturated systems\textsuperscript{119-122}. Perutz\textsuperscript{2} has recently written a review on the role of aromatic rings as hydrogen bond acceptors, with the main emphasis based on evidence from crystal structures, particularly those of proteins.

A very interesting example of intermolecular hydrogen bonding to an aromatic ring was revealed in the crystal structures of both enantiomerically pure (S), and racemic 2,2,2-trifluoro-1-(9-anthryl)ethanol 33\textsuperscript{123}. In a crystal of the optically active (S) isomer, two anthracene rings are nearly parallel to each other and the hydroxyl group of each molecule is directed towards the aromatic ring of the second. This example can be considered as a violation of the Etter rules\textsuperscript{124} for hydrogen bonding, as the strongest conceivable hydrogen bond (between the two hydroxyls) in this case is not formed. A similar hydrogen bonding pattern was also found in the crystal structure of silanol 34\textsuperscript{121}. 

![Chemical structures](image-url)
Hydrogen bonding to an aromatic ring

Water can also form a hydrogen bond to aromatic rings. Water is imbedded inside the cavity of crystalline calixarene 35a; the hydrogen atoms of water being directed towards the opposite aromatic groups.

A comprehensive study of the crystal structures of tetraphenylborates with organic ammonium cations revealed a variety of normal, bifurcated and trifurcated N-H...π bonds as well as OH...π bonds to the phenyl groups of the anion. It was of particular interest that these bonds were formed even although this resulted in unfavourable bonding geometry.

Hanton and Hunter have published a very interesting crystal structure of diamine 36. This compound is deficient in hydrogen bond acceptors and this fact has a profound influence on the packing of the molecule. Two nitrogen atoms, which appear to be chemically equivalent are in fact different in the crystalline state. One of them is sp\(^2\) hybridised and forms a hydrogen bond with the second nitrogen of another
molecule, which is sp\(^3\) hybridised. The sp\(^3\) nitrogen, a weaker hydrogen donor than the sp\(^2\) one, then forms a hydrogen bond to the aromatic ring containing the sp\(^2\) nitrogen (the nitrogen lone pair is delocalised over the whole ring giving an electron rich \(\pi\)-system).

The fact that both sides of an aromatic ring can be simultaneously hydrogen bonded was documented in crystal structures of toluene-hydrogen chloride and mesitylene-hydrogen chloride complexes\(^{128}\), and was also revealed by both X-ray and \(^1\)H NMR spectroscopy in bovine pancreatic trypsin inhibitor\(^{129}\).

Knowledge of the stabilisation energy which is gained upon the formation of these hydrogen bonds and how this energy is influenced by substitution of the aromatic ring is obviously important for many applications. Oki and Iwamura\(^{115}\) have shown, that the strength of hydrogen bonds in a series of aryl phenols depends on the electronic properties of both aromatic rings (Figure 4).

\[
\begin{align*}
\text{OH} & \quad \text{OH} \\
\text{NO}_2 & \quad \text{O}_2\text{N} \\
\Delta H = 4 \text{ kJ mol}^{-1} & \quad \Delta H = 6 \text{ kJ mol}^{-1} & \quad \Delta H = 10 \text{ kJ mol}^{-1}
\end{align*}
\]

**Figure 4**

The dependence of the strength of the OH-aromatic bond on the ring substituents was also observed in the complexes of hydrogen chloride and hydrogen bromide with simple aromatics in hexane solution\(^{130}\); the enthalpy of formation increased from 12.7 kJ mol\(^{-1}\) for the benzene-hydrogen chloride complex to 14.1 kJ mol\(^{-1}\) for the mesitylene-hydrogen chloride complex.

An infrared study of the interactions between N-tert-butylformamide\(^{131}\) and alkyl-substituted benzenes in tetrachloromethane revealed an increase of the binding enthalpy with increasing methyl substitution of the benzene ring (the enthalpy ranged from \(\Delta H = 5 \text{ kJ mol}^{-1}\) for benzene to 6.7 kJ mol\(^{-1}\) for hexamethylbenzene). A similar
trend in binding energies was also observed in the binding of N-cyclohexylformamide\textsuperscript{132}. The heat of formation of the benzene-aniline and benzene-N-methylaniline complexes was estimated to equal \(-6\) kJ mol\(^{-1}\) by overtone infrared spectroscopy\textsuperscript{133}.

Yoshida and Ōsawa\textsuperscript{134} have investigated the hydrogen bonding of phenol to the \(\pi\)-electron system of aromatics, heteroaromatics, fulvenes and azulenes. The latter two classes of compounds proved to be especially strong hydrogen bond acceptors.

\begin{align*}
&37a \quad X = Y = CH \\
&37b \quad X = N, Y = CH \\
&37c \quad X = CH, Y = N \\
&37d \quad X = N-O, Y = CH \\
&37e \quad X = CH, Y = N-O \\
&38a \quad X = Y = CH \\
&38b \quad X = N, Y = CH \\
&38c \quad X = CH, Y = N \\
&38d \quad X = N-O, Y = CH \\
&38e \quad X = CH, Y = N-O
\end{align*}

Takasuka \textit{et al}\textsuperscript{135} have measured the hydroxyl stretching bands of both exo-alcohols 37 and endo-alcohols 38. Intramolecular hydrogen bonds were detected in endo-series 38, the frequency shift being highest for benzene analogue 38a, intermediate for pyridine analogues 38b and 38c, and smallest for pyridine N-oxides 38d and 38e. This order agrees with the expected \(\pi\)-electron donor capabilities of the investigated rings. Comparison of the photoelectron spectra of benzobicyclo[2,2,1]hepten-2-ols 37a and 38a reveals an increase in the ionisation potential of the aromatic \(\pi\)-system and a decrease of the ionisation potential of the oxygen lone pair in endo-isomer 38a relative to exo-alcohol 37a. This behaviour is typical of the formation of a hydrogen bond\textsuperscript{136}.

A matrix isolation study\textsuperscript{137} of the interaction between water and alkyl benzenes also indicates that the complexes formed are progressively more stable on going from benzene to hexamethylbenzene. Molecular beam studies\textsuperscript{138} of benzene, 1,3,5-
Hydrogen bonding to an aromatic ring

trifluorobenzene and hexafluorobenzene complexes with hydrogen fluoride have shown, that hydrogen fluoride forms a complex less easily with increasing fluorine substitution. The benzene-hydrogen fluoride complex in solid argon\textsuperscript{139} was investigated by infrared spectroscopy; and is probably weaker than either acetylene-hydrogen fluoride or ethene-hydrogen fluoride complexes. Fluoro-, chloro-, and bromobenzene each form complexes with hydrogen fluoride in an argon matrix\textsuperscript{140}. While in the case of fluorobenzene only one 1:1 complex was identified, which was assigned as a complex with hydrogen fluoride bonded to fluorine, chloro- and bromobenzene form two discrete types of 1:1 complexes with hydrogen fluoride hydrogen bonding either to the halogen or to the $\pi$-system.

![Diagram of hydrogen bonding to aromatic ring](image)

Figure 5

Oki and Iwamura\textsuperscript{141} and Ueji\textsuperscript{142} studied the effects of solvents on the infrared and $^1$H NMR spectra of intramolecular hydrogen bonds to aromatic rings in 2-arylphenols and 2,6-diarylphenols. The strength of the hydrogen bond increased with the increase of the dihedral angle $\Phi$ (Figure 5).

Perutz has carried out simple energy calculations (Leonard-Jones potential + coulombic interaction) for the interaction between an N-H group and an aromatic ring\textsuperscript{143}. The calculations predict that the N-H interaction is strongest when both nitrogen and hydrogen lie on the C$_6$ axis of benzene. Rotating the N-H group so that the H atom moves off the ring axis while the N atom stays on it, makes the interaction less favourable. Even larger effects were exhibited upon rotation of the entire group off the ring axis, while keeping the N-H directed towards the ring centre.

Gas phase studies have also played an important role in studies of hydrogen bonding to aromatic rings. The lower and upper boundaries for ground state binding
Hydrogen bonding to an aromatic ring

Energy $D_0$ of several benzene complexes were estimated from resonance-enhanced multiphoton ionisation\textsuperscript{144} (Table 12). The value for the water-benzene dimer agrees well with the one from dispersed fluorescence measurement\textsuperscript{145}. Recently, the threshold photoionisation difference method\textsuperscript{146} gave a dissociation energy value of 2.25±1.2 kJ mol\textsuperscript{-1} for the water-benzene dimer. The dissociation energy of the benzene-hydrogen chloride complex as estimated from dissociation photoionisation (20 kJ mol\textsuperscript{-1}) is outside the limit\textsuperscript{147}. Microwave spectra\textsuperscript{148} of the benzene-hydrogen chloride dimer are consistent with a complex, in which hydrogen chloride lies on the $C_6$ axis of benzene.

Table 12: The ground state binding energies $D_0$(kJ mol\textsuperscript{-1}) of benzene complexes\textsuperscript{144}

<table>
<thead>
<tr>
<th>Complex</th>
<th>$D_0$(kJ mol\textsuperscript{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>benzene-HCl</td>
<td>$7.5 &lt; D_0 &lt; 15.9$</td>
</tr>
<tr>
<td>benzene-CHCl$_3$</td>
<td>$8.4 &lt; D_0 &lt; 19.2$</td>
</tr>
<tr>
<td>benzene-H$_2$O</td>
<td>$6.7 &lt; D_0 &lt; 17.6$</td>
</tr>
<tr>
<td>benzene-CH$_3$Cl</td>
<td>$6.3 &lt; D_0 &lt; 14.2$</td>
</tr>
<tr>
<td>benzene-CCl$_4$</td>
<td>$10.0 &lt; D_0 &lt; 13.4$</td>
</tr>
</tbody>
</table>

Complexes of water\textsuperscript{149} and ammonia\textsuperscript{150} with benzene were recently detected in the gas phase. Gutowsky\textsuperscript{151} has measured the rotational spectra of benzene-water dimers. The water is hydrogen bonded to one face of benzene; the potential minimum is shallow and isotropic enabling free rotation of the water.

Multiphoton ionisation studies of clusters of benzene with water\textsuperscript{145,152,153}, water-methanol\textsuperscript{154} and methanol\textsuperscript{155} indicate that clusters are formed on one side of the benzene ring. As the effective temperatures are near absolute zero, the entropic contribution to the free energy is insignificant. Molecular mechanics studies\textsuperscript{156} of the structures and stabilities of benzene- (water)$_2$-12 clusters presented the water-water attraction as the force dominating conformational preferences. In multiphoton ionisation of mixed benzene-water-methanol clusters the complex formation between methanol and benzene was strongly enhanced, when a single water molecule was preadsorbed\textsuperscript{157}. Infrared spectroscopy\textsuperscript{158} of water solutions in aromatics indicated that the water molecule was bound through a single hydrogen to the aromatic ring. A water molecule tended to have one hydrogen pointed towards benzene in a molecular
dynamics study of a diluted aqueous solution of benzene\textsuperscript{159}. However, the effect was not strong enough to disturb the integrity of the hydrogen-bonded network and the hydration of benzene was essentially similar to that of nonaromatic alkanes. Benzene also interacts as a hydrogen bond acceptor with ice\textsuperscript{160}.

It is of interest to compare these results with the thermodynamics of transfer of aromatic and aliphatic hydrocarbons from the gas phase into water\textsuperscript{161}. The Gibbs energy of hydration of aromatics was found to be negative and so the mechanism causing the hydrophobicity of aromatic compounds should be different from that for aliphatic hydrocarbons, i.e. a much stronger interaction between aromatic compounds in the liquid phase than between their aliphatic counterparts. The enthalpy of interaction between water and benzene or toluene was estimated to be approximately 6 kJ mol\textsuperscript{-1}.

It was recently found\textsuperscript{162}, that N-alkyl indoles form vesicles in water solution. The ability of the aromatic moiety to function as a head group comes as a surprise and many interesting results might well be expected on the basis of this observation in the near future. Indole constitutes the side chain of the amino acid tryptophane and so this finding may have important biological implications.

Several theoretical studies have been published on interactions between hydrogen donors and aromatic rings.\textsuperscript{83,92,143,149,156,159,163-173}

Hydrogen-bonded complexes involving benzene as a hydrogen bond acceptor were theoretically studied by Cheney\textsuperscript{163}. The results are summarised in Table 13. The subunits in the benzene-AH\textsubscript{n} complexes undergo wide amplitude oscillations on potential surfaces that are best described as broad shallow valleys in the $\pi$-hydrogen bonding region.
Table 13: Calculated binding energies of hydrogen bonded benzene dimers

<table>
<thead>
<tr>
<th>benzene dimer with</th>
<th>Binding energy (kJ mol⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HF 3-21 G*</td>
</tr>
<tr>
<td>HF</td>
<td>18.8</td>
</tr>
<tr>
<td>HCl</td>
<td>13.0</td>
</tr>
<tr>
<td>H₂O</td>
<td>14.2</td>
</tr>
<tr>
<td>H₂S</td>
<td>6.7</td>
</tr>
<tr>
<td>NH₃</td>
<td>4.6</td>
</tr>
</tbody>
</table>

Brédas has studied the benzene-hydrogen fluoride complex using the MP2-6-31G*/3-21G level of theory and obtained the binding energies for different conformations as depicted in Figure 6.164

\[
\begin{align*}
\text{F} & - \text{H} \\
\text{F} & - \text{H} \\
\text{F} & - \text{H} \\
\text{H} & - \text{F-H} \\
21.5 \text{ kJ mol}^{-1} & 20.1 \text{ kJ mol}^{-1} & 18.8 \text{ kJ mol}^{-1} & 8.6 \text{ kJ mol}^{-1}
\end{align*}
\]

Figure 6

These calculations indicate that the hydrogen fluoride molecule should move rather easily on the top of the aromatic ring. A flat potential was also found for benzene-water and benzene-formic acid complexes167; this potential became even flatter with an increase in the aromatic surface167. A comparison of benzene-water and benzene-pyrene complexes167 predicts an increase in binding energies on moving from benzene to large aromatic compounds. An experimental confirmation of the flat aromatic potential came from a matrix isolation study of the benzene-water dimer174. Two or more energy states are accessible for water at 11-17K. Molecular mechanics
Hydrogen bonding to an aromatic ring

calculations of the benzene-water complex\textsuperscript{166} suggest that hydrogen bond exchange is a very low energy process.

The binding energy between water and benzene was calculated\textsuperscript{167} to amount to 15.9 kJ mol\(^{-1}\) (MP2/6-31G*//3-21G); the authors estimated that upon increasing the correlation contributions and taking account of zero point energy, the actual binding energy should be in the order of 6.3-8.4 kJ mol\(^{-1}\). Similar results have been obtained by other authors.\textsuperscript{149,163,168}

Calculations for the benzene-ammonia complex\textsuperscript{167,168} (MP2/6-31G*//HF/3-21G(*)) show a preference (approx. 4 kJ mol\(^{-1}\)) for ammonia to approach towards the edge of the benzene ring, a result contradicting experimental finding\textsuperscript{150}.

\textit{Ab initio} calculations\textsuperscript{169} (MP2/6-31G*//3-21G*, uncorrected for zero-point energy and basis set superposition error) of complexes of benzene with formamide and methanethiol found four different minima for the formamide-benzene complex (Figure 7) and five for the methanethiol-benzene complex (Figure 8).

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure7}
\caption{Figure 7}
\end{figure}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure8}
\caption{Figure 8}
\end{figure}
The effects of neighbouring charge on the strength of benzene-methanethiol interaction were investigated by point-charge calculations and these effects were found to be significant. The authors proposed that a change in the local electric field may serve as a switch to promote structural reorganisation of the aromatic and sulphur-containing residues during the cycle of activity of an enzyme.

Benzene-hydrogen chloride and toluene-hydrogen chloride complexes have been studied using both fluorescence and multiphoton ionisation detection\textsuperscript{175}. The hydrogen bond seems to dramatically increase the rate of intersystem crossing. After ionisation of the aromatic compound the complex is very efficiently destroyed\textsuperscript{144,175}. In the dimer, the acidic hydrogen points toward the π-electron cloud. Upon ionisation of the aromatic molecule, this proton is now in the vicinity of the positive charge and the complex is dramatically destabilised.

The role which hydrogen bonding from amidic protons to aromatic rings plays in the determination of the structure of proteins is the subject of recent controversy. Some authors\textsuperscript{143} argue that this interaction can significantly affect the conformations of proteins. A survey\textsuperscript{176,177} of protein structures has shown that the majority of above ring amino-aromatic contacts involved stacking of the planar amidic nitrogens above their aromatic partners. However, hydrogen bonds were found in only 3\% of all the amino-aromatic interactions.

A preference for amino groups and aromatic rings to form van der Waals contacts and for the amino group to be above the plane of the aromatic ring was found in the crystal structures of 52 proteins\textsuperscript{178}, but geometrical evidence did not support the suggestion that aromatic-amino hydrogen bonds are common in proteins.
A very interesting example of how a hydrogen bond to an aromatic ring can influence the properties of an enzyme is provided by the isoenzyme 3-3 of glutathione transferase. In this enzyme, the pH of the bound glutathione is lowered by almost three units due to a stabilising effect of the tyrosine residue on the glutathione anion (Figure 9). When the hydroxyl group of threonine was removed by mutation, the pK of glutathione increased by 0.7 units corresponding to an increase in proton affinity of 4 kJ mol⁻¹. A model computational study (MP2/6-31+G*/3-21G*) performed with methanol, p-cresol, and methanethiol, with and without the methanol binding to the face of the p-cresol ring has shown a decrease of methanethiol deprotonation energy by 6.3 kJ, when the hydrogen bond between the aromatic ring and methanol is formed. Preliminary kinetic experiments with the native enzyme and its mutants indicate that the threonine hydrogen bond significantly enhances the nucleophilic reactivity of the glutathione anion. The authors suggested that the on-face hydrogen bond and perhaps a cation-π interaction can act as electronic substituents on aromatic systems that are analogous to covalent ortho, meta, and para substituents. They proposed to call this effect nephotic (from the Greek nephos [cloud]).

Through space interactions between two aromatic rings were demonstrated in small cyclophanes. A substituent on one aromatic ring regulates the reactivity of the other ring.

Monte Carlo and molecular dynamic calculations of the denaturation of proteins by chaotropic agents such as urea or guanidinium ion suggest that hydrogen
bonding to aromatic rings substantially contributes to these processes. It was computationally demonstrated\textsuperscript{171} that the attraction for urea increases with increasing size of the arene. This finding is corroborated by the experimental fact that urea has a greater solubilizing effect on naphthalene than toluene\textsuperscript{185}.

The existence of hydrogen bonds towards aromatic rings has been proved. Although these bonds are weaker than classical hydrogen bonding, they are still of a considerable strength, with their strength depending on the substituents of the aromatic ring; electron donating substituents increase hydrogen bond accepting capacity of the rings while electron withdrawing substituents decrease the hydrogen bond accepting capacity of the rings. On the other hand, when a hydrogen bond is formed towards a ring, the properties of ring's substituents are also influenced. The hydrogen atom prefers to aim towards the centre of the ring, but the attractive potential is rather flat and so a more sidewise approach is common.
1.5. Interactions between Aromatic Rings and Charged Species

The interactions between charges and aromatic systems has of course attracted a great deal of attention. The pioneering measurements of complexes of ammonium ions with different π-donors such as benzene in a high-pressure mass spectrometer\textsuperscript{186,187} demonstrated, that these dimers are of considerable stability, with the interaction energies being as large as 92 kJ mol\textsuperscript{-1}.

![Chemical structures]

In the late 80's, macrocycles 39\textsuperscript{188-190} were demonstrated to be efficient hosts for ammonium cations. The macrocycle 39a possess such a strong affinity for cations that even in water 1-trimethylammonium-4-t-butyl benzene is complexed with its charged ammonium group buried in the cavity and the hydrophobic t-butyl group extruding out towards water. The best complexation was achieved with host 39a. A replacement of the phenyl rings by furan or thiophene in 39e and 39f decreased the host's affinity for cations. The binding of the cations was found to be predominantly enthalpically driven\textsuperscript{191}. Interestingly, the entropic contribution to binding is small in CDCl\textsubscript{3} at 298K, although binding of neutral guests with these highly preorganised hosts is entropically costly\textsuperscript{42,192}. 

39a R = H, X = 1,4-phenyl
39b R = Br, X = 1,4-phenyl
39c R = H, X = 2,5-dimethoxy -1,4-phenyl
39d R = Br, X = 2,5-dimethoxy -1,4-phenyl
39e R = H, X = 2,5 - furanyl
39f R = H, X = 2,5 - thienyl
39g R = H, X = 1,3-phenyl
39h R = H, X = 1,4-cyclohexyl
Table 14: The association energies for binding of electron deficient guests by hosts 39a and 39h in D$_2$O.$^{193}$

<table>
<thead>
<tr>
<th>Guest</th>
<th>Macrocycle 39a $\Delta G_{assoc}$ (kJ mol$^{-1}$)</th>
<th>Macrocycle 39h $\Delta G_{assoc}$ (kJ mol$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>40a</td>
<td>22.6</td>
<td>24.7</td>
</tr>
<tr>
<td>40b</td>
<td>23.0</td>
<td>24.3</td>
</tr>
<tr>
<td>40c</td>
<td>25.9</td>
<td>25.1</td>
</tr>
<tr>
<td>40d</td>
<td>26.4</td>
<td>26.4</td>
</tr>
<tr>
<td>40e</td>
<td>26.8</td>
<td>2.4</td>
</tr>
<tr>
<td>40f</td>
<td>17.6</td>
<td>18.0</td>
</tr>
<tr>
<td>40g</td>
<td>18.8</td>
<td>20.1</td>
</tr>
<tr>
<td>40h</td>
<td>31.8</td>
<td>26.4</td>
</tr>
<tr>
<td>40i</td>
<td>30.1</td>
<td>25.1</td>
</tr>
</tbody>
</table>
Macrocycles 39a and 39h\textsuperscript{193} bind electron deficient quinolines 40a,b,c and isoquinolines 40d,e more tightly than electron rich indoles 40f,g, although the latter are substantially less water soluble (Table 14). It was also noted that while hosts 39a and 39h complexed neutral guests with similar affinity, an exchange of the phenyl group for the cyclohexyl moiety considerably diminished the binding of charged guests.

Calixarenes are also capable of cation binding. An X-ray study of a complex of tetraphenol p-tert-butylcalixarene 35b with caesium cation has shown that the cation is surrounded by the four aromatic rings of the calixarene, the metal being in much closer proximity to the aromatic carbons than to the phenolic oxygens\textsuperscript{194}. Ion transport experiments\textsuperscript{195} and \textsuperscript{133}Cs NMR spectroscopy\textsuperscript{196} corroborate that caesium cation complexation occurs inside the cavity. Ammonium cations can be similarly complexed\textsuperscript{197-199} and mass spectrometry\textsuperscript{200} can be used for detection of these complexes.

Calix[4]arenes which are fixed in the 1,3-alternate conformation 42 are more efficient in cation binding than cone conformers 41\textsuperscript{201,202}. Some calixarenes show considerable discrimination between alkali metal cations\textsuperscript{201,203-207}. Silver cation can easily tunnel through the cavity of 1,3-alternate calixarenes 42\textsuperscript{201} and an approach towards the synthesis of nano-tubes with a π-hole for metal tunnelling from 1,3-alternate calixarenes has also been reported\textsuperscript{208}. Ammonium cations\textsuperscript{209} are also bound by resorcinol derived macrocycles.
Cryptophanes \(43^{10}\) bind acetylcholine and other ammonium ions in water. The interaction energy strongly depends on the size of the cavity; host \(43b\) is a much more potent receptor than \(43a\). The authors expressed the idea that, besides other factors, a loose association is required in order to achieve a strong binding of quaternary ammonium species to their receptors in water, possibly due to the enthalpy-entropy compensation.

Macrobicycle \(44b\) was prepared in a single synthetic step from 1,3,5-tris(bromomethyl) benzene and dimethyl methylenedisalicylate in the presence of
caesium carbonate in 23 % yield without the necessity for high dilution conditions\textsuperscript{211}. Hydrolysis of 44b provided hexacarboxylate host 44a, which proved to be very efficient in complexation of quaternary ammonium compounds in water. The bowl shaped cyclophane 45a is also an efficient host\textsuperscript{212}.

\begin{figure}
\centering
\includegraphics[width=\textwidth]{images/46_47.png}
\caption{Cyclophane 46 and cavitand 47.}
\end{figure}

It is also of significance that the parent hydrocarbons without any heteroatom can also bind cations. Thus cyclophane 46 and especially cavitand 47 can efficiently, and selectively extract silver cation from water to chloroform\textsuperscript{213}.

Interactions between positive charges and electron rich aromatics have been explored in the development of high yielding syntheses of catenanes\textsuperscript{214,215}.

\begin{figure}
\centering
\includegraphics[width=\textwidth]{images/48a_49_50.png}
\caption{Catenanes 48a, 49, and 50.}
\end{figure}

Schneider\textsuperscript{216} has estimated that an average value for an interaction between an N\textsuperscript{+} charge and a phenyl ring is approximately 3 kJ mol\textsuperscript{-1} in their work on the
complexation of benzene, naphthalene, di(p-aminophenyl)methane and diphenylamine with receptors 48, 49 and 50. Both hydrophobic cavity effects and induced dipole-dipole interactions were evoked in the publication to explain the results.

51a $X = \text{OH}, R_1 = \text{H}, R_2 = \text{CH}_3$
51b $X = \text{OH}, R_1 = \text{CH}_3, R_2 = \text{H}$
51c $X = \text{COO}^-, R_1 = R_2 = \text{H}$
51d $X = \text{CH}_2\text{COO}^-, R_1 = R_2 = \text{H}$
51e $X = \text{OH}, R_1 = \text{H}, R_2 = \text{CH}_3$
51f $X = \text{OH}, R_1 = \text{CH}_3, R_2 = \text{H}$
51g $X = \text{COO}^-, R_1 = R_2 = \text{H}$
51h $X = \text{CH}_2\text{COO}^-, R_1 = R_2 = \text{H}$
51i $X = \text{H}$
51j $X = \text{OH}$
51k $X = \text{H}$
51l $X = \text{OH}$
51m
Guests with a saturated framework\textsuperscript{217} are bonded substantially less by macrocycle 48\textsuperscript{a} then their aromatic counterparts. In the case of macrocycle 48\textsuperscript{b}, with its charged groups at a greater distance from the cavity, the difference in binding is smaller.

\textbf{Table 15} Complexation free enthalpies at ambient temperature with 48\textsuperscript{a}

<table>
<thead>
<tr>
<th>Compound</th>
<th>$\Delta G$ (kJ mol$^{-1}$)</th>
<th>Compound</th>
<th>$\Delta G$ (kJ mol$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>51\textsuperscript{a}</td>
<td>10.0 (7.5)*</td>
<td>51\textsuperscript{h}</td>
<td>11.7</td>
</tr>
<tr>
<td>51\textsuperscript{b}</td>
<td>11.3 (6.7)*</td>
<td>51\textsuperscript{i}</td>
<td>16.7</td>
</tr>
<tr>
<td>51\textsuperscript{c}</td>
<td>16.3*</td>
<td>51\textsuperscript{j}</td>
<td>16.3</td>
</tr>
<tr>
<td>51\textsuperscript{d}</td>
<td>15.9</td>
<td>51\textsuperscript{k}</td>
<td>13.0</td>
</tr>
<tr>
<td>51\textsuperscript{e}</td>
<td>3.3 (4.2-7.1)*</td>
<td>51\textsuperscript{l}</td>
<td>11.3</td>
</tr>
<tr>
<td>51\textsuperscript{f}</td>
<td>2.1-4.6 (3.8-6.3)*</td>
<td>51\textsuperscript{m}</td>
<td>6.7</td>
</tr>
<tr>
<td>51\textsuperscript{g}</td>
<td>10.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* in brackets are complexation free enthalpies with host 48\textsuperscript{b}

In another paper, Schneider\textsuperscript{218} has studied the equilibria of 10 ion pairs with aromatic units in either one or in both of the ions in water. The complexation strength linearly increased with the number of aryl groups in the complexes. The authors estimated that a stabilisation of approximately 2 kJ mol$^{-1}$ results from an interaction of either a cation or an anion with a phenyl ring located in a suitable vicinity. A confirmation of similar effects of both negative and positive charges comes from measurements of the association free energies of complexes 52\textsuperscript{219}. 
The major contribution to this stabilisation was attributed to the charge-induced dipole interaction.

Schwabacher\textsuperscript{220} has studied complexation by macrocycles 53 and 54 in D\textsubscript{2}O. The complexes can adopt two principal binding conformations A and B. (Figure 10)

The most common binding conformation A, places the host charge towards the edge but near a node in the electrostatic potential surface. It would then be predicted to have a
small effect on binding as observed. The ring junction charge would be expected to play a large role in conformation B, commonly seen with large guests. An ion-quadrupole interaction stabilises binding in conformation B for anionic 54 and destabilises binding in conformation B for cationic 53.

Very interesting host 55 named Kyuphane was synthesised$^{221}$ and found to bind chloroform very strongly. Indeed, it took 18h of heating at 100°C/ 0.05 torr to entirely remove chloroform from the 1:1 crystalline complex. Kyuphane was dissolved in acidic medium (as a tetracation) and its binding properties towards neutral 56 and anionic 57 guests were also examined (Table 16).

\[
\begin{align*}
56a & \quad X = Y = Z = H \\
56b & \quad X = N(CH_3)_2, \ Y = Z = H \\
56c & \quad X = Z = OH, \ Y = H \\
56f & \quad X = NH\text{-phenyl}, \ Y = Z = H \\
56g & \quad Y = NH\text{-phenyl}, \ X = Z = H
\end{align*}
\]
57a $X = SO_3^-$, $A = B = C = D = Y = H$
57b $Y = SO_3^-$, $A = B = C = D = X = H$
57c $X = D = SO_3^-$, $A = B = C = Y = H$
57d $Y = B = SO_3^-$, $A = C = D = X = H$
57e $Y = C = SO_3^-$, $A = B = D = Y = H$
57f $D = SO_3^-$, $X = N(CH_3)_2$, $A = B = C = Y = H$
57g $C = SO_3^-$, $Y = NH-p$-tolyl, $A = B = D = X = H$
57h $A = SO_3^-$, $X = NH$-phenyl, $B = C = D = Y = H$
57i $A = C = SO_3^-$, $X = -N=N$-phenyl, $Y = OH$, $B = D = H$

**Table 16:** The association constants for binding of guests 56 and 57 with Kyuphane

<table>
<thead>
<tr>
<th>Compound</th>
<th>$K$ (M$^{-1}$)</th>
<th>Compound</th>
<th>$K$ (M$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>56a</td>
<td>3000</td>
<td>57b</td>
<td>150</td>
</tr>
<tr>
<td>56b</td>
<td>27000</td>
<td>57c</td>
<td>100</td>
</tr>
<tr>
<td>56c</td>
<td>no complexation</td>
<td>57d</td>
<td>1400</td>
</tr>
<tr>
<td>56d</td>
<td>5600</td>
<td>57e</td>
<td>150</td>
</tr>
<tr>
<td>56e</td>
<td>710</td>
<td>57f</td>
<td>43000</td>
</tr>
<tr>
<td>56f</td>
<td>88000</td>
<td>57g</td>
<td>420000</td>
</tr>
<tr>
<td>56g</td>
<td>69000</td>
<td>57h</td>
<td>160000</td>
</tr>
<tr>
<td>57a</td>
<td>100</td>
<td>57i</td>
<td>440000</td>
</tr>
</tbody>
</table>

The first enzyme, in which the importance of the aromatic-cation interaction was unequivocally demonstrated was acetylcholinesterase.²²²-²²⁵ Sussman *et al.*²²² have discussed the effects which the aromatic binding site can have on the function of the enzyme. Thus, in the first instance the hydrophobicity of the aromatic gorge would produce a low local dielectric constant, which could result in a higher effective local charge than might be predicted from the small number of acidic groups nearby. Secondly, the aromatic lining may permit the use of a mechanism involving initial
absorption of acetylcholine to low affinity sites followed by two-dimensional diffusion to the active site. It would explain the high rate for ligand binding by acetylcholinesterase, and by the same means, rapid removal of the reaction product, choline, can be achieved.

Aromatic residues have also been proposed to play an important role in potassium ion channels, for the functioning of cationic neurotransmitter receptors, and in the binding of S-adenosylmethionine in methyltransferases.

Kumpf and Dougherty have published Monte Carlo computational studies of the interactions of benzene with alkali metal cations both in the gas phase and in water. In the gas phase, the expected order of the stability of the complexes was found (Li+ > Na+ > K+ > Rb+). In water this order depends on whether 1:1 complexes (Li+ > K+ > Na+ > Rb+) or 2:1 complexes (K+ > Rb+ > Na+ > Li+) are formed. In the optimised [benzene-M+-benzene] interaction, the benzene-benzene distance for Li+ is so small that no water molecules (which are about the size of K+) can solvate the Li+. In the [benzene-K+-benzene] complex there is some space for direct aqueous solvation. These results could explain the selectivity in potassium channels for K+, providing that the walls of the channel are formed by aromatic residues. It is known, that quaternary ammonium ions inhibit K+ channels by binding within the ion conduction pore. Mutation studies suggest that the binding site for the tetraethylammonium ion in Shaker K+ channel is formed by aromatic residues. Kerr and Sansom have proposed that tyrosine in the potassium ion channel signature sequence in the P region (a highly conserved stretch of eight amino acids which seems to contribute to channel selectivity) is important for the selectivity of these channels. Mutation studies however did not confirm this hypothesis.
Macrocycles $39a$ and $39h^{188}$ catalyse $S_N2$ reactions. The Menschutkin reaction between quinoline $58$ and methyl iodide in water proceeded 80 times faster in the presence of macrocycle $39a$ and 20 times faster in the presence of $39h$. Demethylation of dimethylphenylsulfonium tetrafluoroborate $59$ was also accelerated. Thus, reactions which develop positive charge in the transition state and reactions which destroy positive charge are catalysed. The former observation can be explained by the ability of the hosts to bind cations through the cation-π interaction. In the second case, however, the charge is diminishing on going from the charged ground state to the partially charged transition state. The authors suggested that the high polarizability of the transition states is well matched to the very polarizable host and that this contributes to the catalysis.

Such stabilisation of charged transition states by the aromatic-cation interactions was proposed as the explanation for the action of 2,3-oxidosqualenelanosterol cyclase$^{234}$, the enzyme which catalyses the complex cyclization/rearrangement reactions leading from the acyclic terpenoid polyene to lanosterol. These reactions are electrophilic in nature and the cyclases from different species contain unusually large numbers of tryptophane and tyrosine residues.

Another role of aromatic residues in proteins was demonstrated in the enzyme barnase$^{235}$. An aromatic-histamine interaction stabilises the protonated form of histidine
relative to the nonprotonated form by 3.3-4.2 kJ mol\(^{-1}\) and, thereby, increases its pK\(_a\) value. The interaction is not masked by high salt concentrations and decreases in the series histidine-tryptophane > histidine-tyrosine > histidine-phenylalanine.

\[
\begin{align*}
60a & \quad X = \text{OCH}_3 \\
60b & \quad X = \text{H} \\
60c & \quad X = \text{Cl} \\
60d & \quad X = \text{NO}_2
\end{align*}
\]

\[
\begin{align*}
61a & \quad X = \text{OCH}_3 \\
61b & \quad X = \text{H} \\
61c & \quad X = \text{Cl} \\
61d & \quad X = \text{NO}_2
\end{align*}
\]

\[
\begin{align*}
62a & \quad X = \text{OCH}_3 \\
62b & \quad X = \text{H} \\
62c & \quad X = \text{Cl} \\
62d & \quad X = \text{NO}_2
\end{align*}
\]

Change of pK\(_a\) caused by through space interaction with an aromatic ring have been demonstrated in a series of bicyclo[2,2,1]heptenes 60, 61, and 62\(^{236}\)(Table 17)

Table 17: pK values of carboxylic acids 60, 61, and 62\(^{236}\)

<table>
<thead>
<tr>
<th>Compound</th>
<th>pK(_a)</th>
<th>Compound</th>
<th>pK(_a)</th>
<th>Compound</th>
<th>pK(_a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>60a</td>
<td>6.34</td>
<td>61a</td>
<td>6.33</td>
<td>62a</td>
<td>6.77</td>
</tr>
<tr>
<td>60b</td>
<td>6.28</td>
<td>61b</td>
<td>6.28</td>
<td>62b</td>
<td>6.69</td>
</tr>
<tr>
<td>60c</td>
<td>6.17</td>
<td>61c</td>
<td>6.13</td>
<td>62c</td>
<td>6.58</td>
</tr>
<tr>
<td>60d</td>
<td>5.89</td>
<td>61d</td>
<td>5.84</td>
<td>62d</td>
<td>6.08</td>
</tr>
</tbody>
</table>

Whether the inductive or the through-space electrostatic field effect is important is discussed in reference\(^{237}\)
A similar effect was found in a series of carboxylic acids. The $pK_A$ values gradually increased with increasing electron donating power of substituents from $pK_A = 5.87$ ($X = OAc, Y = H; X = H, Y = OAc$) to $pK_A = 6.61$ ($X = OCH_3, Y = H; X = H, Y = OCH_3$). That the hydrogen bonding capacity of the carboxyl is also dependant on the nature of the substituents was demonstrated by binding of ethyl adenine. As the conjugation of the aromatic rings is prohibited due to steric reasons, the phenyl groups seem to exert their influence through space.

Several factors can contribute to the increase in $pK_a$ of these acids; a hydrogen bond to the aromatic system can stabilise the protonated form and a repulsion between carboxylate anion and $\pi$-electrons destabilise the unprotonated form. The substituent effects are expected to work in the same direction. Decreasing the electron density of the aromatic ring weakens the hydrogen bond as well as diminishes the repulsion.

Aromatic side chains in proteins interact with arginine in a planar stacking fashion, with the guanidinium group directly over the ring and the two planes nearly parallel. This configuration leaves the three nitrogen atoms free to engage in hydrogen bonding.

An arginine residue positioned over the aromatic ring is statistically favoured. A preference for the guanidinium group of arginine to reside over aromatic rings was also found by Flocco. The planes of an aromatic ring and the group are arranged almost parallel, so that the nitrogen's hydrogen atoms are free to engage in hydrogen bonding.

A statistically significant preference for the positively charged amino groups of lysine, arginine, asparagine, glutamine and histidine to be located within 6 Å of the ring centre of phenylalanine, tyrosine and tryptophane has been found in 33 protein crystal structures by Burley and Petsko. The authors have suggested that the packing of both polar and nonpolar atoms with aromatic side chains in the hydrophobic core of a protein is determined by at least two requirements: viz. the need to exclude water molecules, and also the formation of a large number of enthalpically favourable, weakly
polar interactions that are almost certainly electrostatic in origin. The free energy contribution from aromatic-quaternary ammonium interaction was estimated to be 8-16 kJ mol$^{-1}$ from mutation studies$^{223}$. The effect of volume occlusion caused by the favourability of oxygen-nitrogen interactions should also be considered$^{242}$, as aromatic carbons, methyl carbons and aliphatic carbons all show a preference for stacking above the face of arginine.

The interaction between phenylalanine and a positively charged histidine was shown to be efficient in stabilising an $\alpha$-helix in proteins$^{243}$. Weak stabilisation can be detected even when histidine is uncharged$^{243}$.

Complexes between aromatic cations and a second aromatic molecule are substantially stabilised by charge delocalisation over both molecules$^{69,244-246}$. This stabilisation decreases with increasing difference between ionisation potentials of the two molecules.

Recently a theoretical study of binding forces between aromatic rings and quaternary amines was published$^{247,248}$. The authors studied complexes of tetramethylammonium and ammonium cations with benzene using the MP2 6-311+G** level of theory. The calculations support the notion that the important binding forces arise from the charge-quadrupole and charge-polarizability interaction.

In accordance with the quadrupolar model of an aromatic ring, aromatics interact strongly with cations. This fact was elegantly used in the design of many hosts for cation complexation, and the great significance of aromatic residues for the stabilisation of positive charge in the catalytic sites of enzymes was conclusively demonstrated.

The preference for the cation to approach the centre of the ring should be much more pronounced than in the case of hydrogen bonding. It is also important to stress that the attractive force between a charge and a quadrupole decays much more slowly with distance than in the case of typical attractive van der Waals interactions. This fact will influence not only the thermodynamics but the kinetics of investigated systems. In
a vacuum, the rate of formation of cation - aromatic complexes is expected to be faster than that of their neutral counterparts. The situation in a solution is much less obvious, as the solvent has to be reorganised during complex formation. Under such conditions the ions are solvated more and their solvation sphere is held more tightly than it is in neutral molecules, and this will slow down the complexation. The final result will be then determined by the sum of these opposing effects. As complexation kinetics are very important in catalysis, there is considerable scope for experimental work in this area.

The understanding of anion-aromatic interactions is much less developed, and much experimental and theoretical work is clearly required. Speculations based on the quadrupolar model of the aromatic ring suggest exciting possibilities. If the quadrupolar moment of the aromatics is reversed by electronegative substituents then an attraction between the aromatic system and an anion can be envisaged. The answer to questions such as "will perfluorinated Dougherty's macrocycle or perchlorinated calixarenes bind anions?" will be hopefully be found in the future. The implications of such a discovery are obvious.
Molecular complexes of halogens with aromatic compounds have attracted considerable attention\(^{249-257}\). A charge transfer band is formed when halogens are dissolved in aromatic solvents\(^{254,255}\). Raner \textit{et al}\(^{255}\) noticed that while the charge-transfer band for an iodine atom correlated linearly with the vertical ionisation potential of the corresponding arene, no such correlation was found for chlorine and bromine atoms. Interestingly, a molecular dynamics simulation\(^{258}\) of an iodine solution in benzene did not find any evidence for the presence of a well-defined complex in solution.

Fredin and Nelander\(^{250}\) noted, that upon complexation of benzene with chlorine, bromine and iodine monochloride in a matrix that a symmetry forbidden vibration of benzene appeared, indicating that the complex should be of a low symmetry. The results were interpreted as evidence for an oblique complex structure, with the halogen molecule interacting mainly with one of the \(\text{C} = \text{C}\) bonds. A complex of low symmetry was also formed with a bromine atom\(^{251}\). The benzene-iodine complex in a nitrogen matrix is axial, in contrast to other halogens\(^{259}\). Solution spectra of iodine and bromine in benzene\(^{260}\) and bromine with hexadeuterobenzene\(^{261}\) indicate an axial \(C_{6v}\) structure of the halogen benzene complexes.

Chains of alternating halogen and benzene molecules in the axial configuration were found in crystal structures of benzene-chlorine\(^{262}\) and benzene-bromine\(^{263}\) (1:1) addition compounds. Person \textit{et al}\(^{264}\) later measured the infrared spectra of the crystals, which indicated formation of 1:1 complexes in the crystals and discussed the apparent discrepancy between their results and X-ray measurements.

Several examples of complexation of halogenated compounds by aromatic hosts have appeared in the literature\(^{221,265-269}\), although the contribution of the halogen-aromatic interaction is unclear.
The enthalpy of formation of the iodine-benzene complex in the vapour phase was estimated to be -10.2 kJ mol\(^{-1}\) at 450K from P-V-T data\(^{270}\), -8.4\(^{271}\) and -9.9\(^{272}\) kJ mol\(^{-1}\) from spectrophotometric measurements. The complexes between atomic iodine and aromatics are stronger than between molecular iodine and aromatics\(^{273}\).

In proteins, oxygen\(^{29,106,240,274}\) and sulphur\(^{275}\) atoms are found preferentially in the plane of the aromatic rings and no case of a carboxylate oxygen straight over the aromatic ring (angle >80°) has been found\(^{240}\). The sulphur aromatic contacts occur slightly more frequently than expected\(^{275}\). In proteins containing positively charged side chains, this preference becomes even more pronounced\(^{276}\). Morgan \textit{et al}\(^{277}\) have found regions in eight globular proteins in which the side chains of sulphur-containing amino acids alternated in space with side chains of aromatic amino acids. The authors proposed, that this chain is involved in the conduction of electrons, as all the relevant proteins are connected with electron transfer, and in each of them the sulphur-aromatic ring chain included the prosthetic group.

Dimethylsulfide forms 1:1 complexes with aromatic compounds in carbon tetrachloride\(^{278}\); the heat of formation of these complexes has been estimated to be approximately 4 kJ mol\(^{-1}\). It was shown\(^{279}\) that such an interaction can be reproduced with a suitably parameterised molecular mechanics program. Sulphur-aromatic interactions were also demonstrated using NMR studies of small peptides\(^{280,281}\).

Complexes of oxygen with benzene and hexafluorobenzene were detected by Grover\(^{282}\) in the gas phase.

![Diagram](image.png)
An interesting interaction between an aromatic ring and a phosphorus atom was discovered by Pasca. The proton decoupled $^{13}$C NMR spectrum of cyclophane 64 shows spin-spin coupling between phosphorus and all the aromatic carbons. The basal methine carbon is a doublet with $J_{PC} = 7.5$ Hz; the coupling is greater than to most of the aryl carbons of the triarylphosphine part of the molecule. No coupling between phosphorus and the bridging methylene atom is visible. The $^{31}$P NMR spectrum shows a single peak at $\delta = 5.0$, substantially down field from the resonance of precursor 65 ($\delta = -26.7$), the shift being in the opposite direction to that which would result from simple ring-current effects. The authors asked the question whether this effect could be interpreted as a demonstration of the donation of phosphine electron density to the basal ring.

F-F coupling can be transmitted through the plane of an intervening phenyl group. The magnitude of $J_{1,8}$ coupling in 1,5,8-trifluoro-9,10-diphenylanthracene 66 ($J_{1,8} = 6.4$ Hz; $J_{1,5} = 1.3$ Hz; $J_{5,8} = 23.0$ Hz) is significantly larger than in 1,5,8-trifluoroanthracene 67 ($J_{1,8} = 1.1$ Hz; $J_{1,5} = 1.1$ Hz; $J_{5,8} = 22.8$ Hz).

The preference of chalcogens to approach towards the edge of the aromatic ring is again in accordance with the quadrupolar model. Chalcogens are strongly electronegative, and as such possess a partial negative charge themselves. The negative charge is then attracted towards the positive hydrogens of the ring. Similar considerations should be valid for halogens, especially fluorine and chlorine. The
apparently anomalous behaviour of molecular iodine, bromine and chlorine which are found above the ring is in fact simply explained by the formation of charge transfer complexes with donation of $\pi$-cloud electron density to the halogen-halogen $\sigma^*$-orbital.
1.7 Conclusions

Sometimes rather heated debate occurs, as to whether a molecular fragment has or has not some special interaction with aromatic rings. In our view, some of these questions are more semantic than real. Such problems are typical of weak interactions, for even the definition of the prototypical weak interaction, the hydrogen bond, is difficult to agree on\textsuperscript{285}, and indeed the same might be said of the definition of aromaticity\textsuperscript{286}.

The role of the aromatic rings should be considered in context. Probably the most logical way to assess the importance of aromatic systems is to compare their behaviour with saturated analogues (e.g. benzene against cyclohexane, naphthalene against trans-decaline, and so on). This comparison is not flawless of course, as the steric demands are slightly different in both classes of compounds.

Investigations of series of model systems play a major role in unravelling the underlying principles of these interactions. The major problem with this approach lies in the virtual impossibility of changing just one factor when similar compounds are compared; changes in distances and angles between groups of interest are also difficult to achieve in small steps. The evaluation of the role of the solvent is also far from simple.

\textit{Ab initio} calculations will doubtless contribute significantly to investigations. It should of course be kept in mind, that aromatics are computationally large molecules and so many approximations have to be made in the calculation (with the improvement of computers, more precise results can be expected, but due to the so called \(n^4\) catastrophe - the number of integrals that has to be calculated increases with the fourth power of the number of the functions used to describe the system - many molecules of practical interest will stay out of reach of precise calculations). Semiempirical and molecular mechanics calculations therefore remain the most useful theoretical technique for larger systems. They are very useful in exploiting trends and in reaching
qualitative conclusions, but their use for quantitative work and for the search of underlying physical principles is more problematic.

The experimental studies of small clusters in gas phase and matrix isolation investigations are indeed very important. They are most useful for small symmetric molecules, where many details of complex structure can be gained.

It was demonstrated that some properties of the aromatic systems can be explained on the basis of their quadrupolar moments. As the aromatic rings usually contain one or more substituents, dipole interactions also come to play. This is especially true for heteroaromatic molecules.

Much research has to be done of course, before the bonding properties of aromatic compounds can be predicted with a reasonable confidence. Distance and angular dependence of the aromatic interactions have to be investigated much more, especially when several substituents and/or heteroatoms are introduced into the aromatic rings.
1.8. References


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References


Chapter Two

SOME STUDIES OF THROUGH SPACE FUNCTIONAL GROUP - ARENE INTERACTIONS
2.1. Introduction

As the preceding review has demonstrated, even in spite of a considerable body of information, our knowledge and understanding of the noncovalent interactions of aromatic compounds is far from complete. In particular, little is known about the interactions between different functional groups and aromatic rings, with the exception of hydrogen bonding.

It appeared to us that 9,10[1',4']-benzenoanthracenes 1 and 9,10-propanoanthracenes 2 are well suited for the study of these interactions. Both the aromatic rings and the functional groups are spatially confined in these molecules. Benzenoanthracenes 1 have rigid skeletons, and the position of the substituents can, in principle, be easily controlled and determined.

Any difference in the spectral characteristics of their two aromatic rings should be caused by a through-space interaction with a functional group. Any contribution from a through-bond interaction to this difference can be practically excluded, as the functional group has a very similar connectivity framework.
Propanoanthracenes 2 exist as a mixture of two easily interconvertible conformers. The relative abundance of each conformer in solution can therefore provide a measure of the interaction energy between functional groups and aromatic rings. It has been demonstrated by molecular mechanics calculations, that the precise conformation of the bridge in the parent bicyclo-[3,2,2]-nonane is determined largely by the substituents present rather than by the carbon skeleton.

The distance $d$ between the functional group $Y$ and the aromatic quaternary carbons varies from 2.8 Å (for $Y = F$) to 3.2 Å (for $Y = S$) as indicated by molecular mechanics calculations (Macromodel®, MM3 force field). This distance is sufficiently close to the sum of the van der Waals radii of the aromatic carbons and the appropriate atoms to make the results useful for other systems.

A similar approach has been used by a group of Japanese workers, who examined derivatives of 1,10-benzeno-[2.2]-orthocyclophane 3 and 1,11-benzeno-[2](4,5)-tropolonophane 4 in their investigation of through space $\pi-\pi$ interactions. The equilibrium constants were determined by $^1$H NMR spectroscopy from the magnitude of the coupling constants between aliphatic hydrogens.
2.2 Synthesis of 9,10[1',4']Benzenoanthracenes

With the above considerations in mind, we therefore embarked upon the synthesis of the required carbocyclic skeletons. Thus, photochemical [4+4] cyclization of anthracene and 1,3-cyclohexadiene\(^5\) gave 9,10,11,12,13,14-hexahydro-9,10[1',4']-benzenoanthracene 5.

Since the dimerisation of anthracene itself occurs readily under photochemical conditions a large excess of relatively expensive 1,3-cyclohexadiene was needed. Another problem in this reaction is the low solubility of anthracene and so a large
amount of solvent is also required even for relatively small scale reactions. Nevertheless, using this protocol it was possible to prepare 1.5g batches in a routine manner.

The adduct was then reduced with palladium on charcoal to afford the known compound $^6$ 9,10,11,12,13,14,15,16-octahydro-9,10[1',4']-benzenoanthracene 6 in 84% yield, which provided the standard against which the spectra of novel compounds could be compared.

Exo-12,13-epoxy-9,10,11,14,15,16-hexahydro-9,10[1',4']-benzenoanthracene 7 was prepared by meta-chloroperbenzoic acid epoxidation of the alkene 5 in 67% yield. Since one face of the double bond is shielded by the aromatic ring only the exo-isomer was formed. Attempts to prepare the endo-epoxide via a bromohydrin intermediate were however unsuccessful and addition of hypobromous acid, generated in situ from N-bromosuccinimide and water in dimethylsulfoxide solution onto the alkene 5 resulted in an intractable mixture of products. It is perhaps appropriate to note that the simple parent bicyclo[2,2,2]octene undergoes a variety of rearrangements when subjected to similar conditions. Our system seems to behave in an analogous fashion.

Base catalysed rearrangement of the epoxide 7 with butyl lithium afforded a complex mixture of products, from which 9,10,11,13,14,15,16-heptahydro-9,10[1',4']-benzenoanthracene-12-one 8 was nevertheless isolated in 33% yield. When LDA was used instead of butyl lithium no reaction occurred. In this instance, the base has to approach the epoxide from the side hindered by the aromatic ring and LDA seems to be too bulky for such a purpose.

In an alternative sequence addition of borane to the alkene 5, followed by oxidative work up furnished exo-9,10,11,13,14,15,16-heptahydro-12-hydroxy-9,10[1',4']-benzenoanthracene 9 in 51% yield. The exo-alcohol 9 was then oxidised with PCC to furnish ketone 8 in 70% yield.
Since the cycloaddition reaction of anthracene with 1,3-cyclohexadiene could not be easily scaled up, and the overall yield for the transformation of alkene 5 to ketone 8 was quite low, an alternative route to the ketone was highly desirable.

![Chemical structures and reactions]

Our attention therefore turned to the possibility of another photochemical [4+4] cycloaddition reaction. These have received some attention within the last three decades and their synthetic potential is tremendous, since an eightmembered ring is formed in a single step. The choice of substrates is however severely limited because rather strict
Synthesis of benzenoanthracenes

Electronic and conformational boundary conditions have to be fulfilled for the reaction to occur.

We envisaged that easily available 2-(1,3-cyclohexadienyloxy)-trimethylsilane 10 could be used in such [4+4] cycloaddition. Indeed it reacted with anthracene under standard conditions to afford 9,10,11,12,13,14-hexahydro-12-trimethylsilyloxy-9,10[1',4']-benzenoanthracene 11, which was transformed, without isolation, to the required ketone 8. Reduction of the ketone 8 with diisobutylaluminum hydride furnished endo-9,10,11,13,14,15,16-heptahydro-12-hydroxy-9,10[1',4']-benzenoanthracene 12 in 78% yield. Since the aromatic ring shields one side of the ketone, the endo-alcohol was formed as the exclusive product.

\[
\begin{align*}
\text{12} & \quad \text{Ac}_2\text{O}, \text{DMAP} \quad 77\% \\
\text{13} &
\end{align*}
\]

\[
\begin{align*}
\text{9} & \quad \text{Ac}_2\text{O}, \text{DMAP} \quad 75\% \\
\text{14} &
\end{align*}
\]

Both the endo-alcohol 12 and the exo-alcohol 9 could be acetylated under standard conditions using dimethylaminopyridine as catalyst to give endo-12-acetoxy-9,10,11,13,14,15,16-heptahydro-9,10[1',4']-benzenoanthracene 13 and exo-12-acetoxy-9,10,11,13,14,15,16-heptahydro-9,10[1',4']-benzenoanthracene 14 in 77% and 75% yields, respectively.
2.3 Synthesis of 9,10-Propanoanthracenes

With an appropriate route to the 9,10[1',4']-benzenoanthracenes in hand, we then tackled the problems posed in construction of the propano bridge. 9,10-dihydro-9,10-propanoanthracen-12-one 15 was identified as a suitable starting material for the preparation of the series of propanoanthracenes. In 1992, Hoffmann and Karama published a paper describing the reaction of anthracene and tetrabromoacetone with zinc/copper couple and chlorotrimethylsilane, which afforded this ketone in 22% yield. In this reaction the oxoallyl carbocation 16 is formed and then undergoes a [4+3] cycloaddition with anthracene to give 11,13-dibromo-9,10-dihydro-9,10-propanoanthracen-12-one 17. Dibromopropanoanthracenone 17 is then reduced in situ to the product propanoanthracenone 15.

In our hands, however, the reaction gave very poor yields (<3%) and since a considerable amount of polymeric material was formed during the reaction, purification...
of ketone 15 was not trivial. On several occasions, the unreduced dibromopropanoanthracenone 17 could be detected. At a later stage during the course of our work Hoffmann’s group published another paper\textsuperscript{10}, describing a reaction under almost identical conditions, in which the dibromopropanoanthracenone 17 was formed as the major product in 15% yield. The dibromoketone was then reduced to the parent ketone with zinc and ammonium chloride.

However, as we required propanoanthracenone 15 in multigram quantities and of high purity, a new route to the ketone was obviously needed. In this respect, we were inspired by a communication\textsuperscript{11} from the Corey group on cycloaddition reaction of 2-bromo-2-propenal 18. This paper described a rearrangement of 1-hydroxy-1-formyl-bicyclo[2,2,2]octane 19 generated \textit{in situ} from 1-bromo-1-formyl-bicyclo[2,2,2]octane 20, using an aqueous solution of potassium carbonate, to afford 1-hydroxy-bicyclo[3,2,2]nonan-2-one 21. We reasoned that the addition of two aromatic rings to the bicyclic skeleton would not change the course of such a reaction, and that the resulting hydroxyketone 22 could be deoxygenated to give the desired propanoanthracenone 15.

Accordingly, the Diels-Alder addition of 2-bromo-2-propenal 18 to anthracene was carried out and furnished the known\textsuperscript{12} 11-bromo-9,10-dihydro-11-formyl-9,10-ethanoanthracene 23. In the original procedure for the preparation of 2-bromo-2-propenal 18\textsuperscript{13}, 2,3-dibromo-2-propanal is dehydrobrominated during steam distillation. In practice however, we found it to be more convenient to use triethylamine as a dehydrohalogenation reagent.
Since aldehyde 23 is a water insoluble solid, different reaction conditions for its rearrangement had to be found. When aldehyde 23 was dissolved in ethanol and an aqueous solution of sodium carbonate was added, the hydroxyketone 22 could be isolated. Unfortunately, several by-products were formed; and a $^1$H NMR spectrum of the most abundant of these revealed that an ethyl group had been incorporated into the molecule. When acetone was used instead of ethanol, most of the starting aldehyde 23 was recovered unchanged. When potassium hydroxide was used as a base, although the rearrangement was substantially accelerated, aldolization of acetone became the major process and the purification of the product became very difficult.
We found that the rearrangement proceeded best when THF was used as a co-solvent and potassium hydroxide as a base. In this case, extraction followed by a single crystallisation from ethyl acetate and petrol afforded 9,10-dihydro-11-hydroxy-9,10-propanoanthracen-12-one 22 in very good purity in 58% yield. 9,10-dihydro-12-hydroxy-9,10-propanoanthracen-11-one 24 could also be isolated from this reaction by flash chromatography from the mother liquor.

Interestingly, this reaction only gave the pure product when conducted under an air atmosphere. When a nitrogen atmosphere was used, a yellow polymeric material was formed and, even more importantly, the desired ketone 22 always crystallised out with a substantial amount of isomeric hydroxyketone 24. The equilibrium mixture of ketones 22 and 24 is produced in this reaction. This fact was confirmed by the transformation of ketone 24 to the mixture of ketones in a water/THF/KOH system.

Attempts to prepare ketone 15 by the acid catalysed rearrangement of 9,10-dihydro-11-formyl-9,10-ethanoanthracene 25 failed. Thus, the aldehyde was recovered unchanged after 12 hours from its solution in either acetic acid or formic acid while methanesulfonic acid caused extensive decomposition. Refluxing of the aldehyde for 3 min in a 45% solution of HBr in acetic acid gave starting material and traces of an alkene.

Zinc in acetic acid, hydriodic acid in acetic acid, and red phosphorus with iodine in carbon disulphide have all been successfully used in the transformation of α-hydroxyketones to ketones. However, in our case all of these reagents failed. We were eventually able to remove the hydroxyl group with samarium diiodide in good yield (69 %) and the desired ketone 15 was obtained in excellent purity after crystallisation from ethyl acetate and petrol. A comparison of the melting point of our ketone (m.p. 236-236.5 °C) with that reported by Hoffmann and Karama (m.p. 220 °C) suggests, that these authors were unable to obtain a completely pure product, probably because of the presence of polymeric impurities.
With an effective route to the desired propano bridged system now established, we then set about the preparation of the functionalised derivatives required for our study. Ketone 15 was smoothly reduced with sodium borohydride in tetrahydrofuran-methanol to give 9,10-dihydro-12-hydroxy-9,10-propanoanthracene 26. The reaction of propanoanthracenone 15 with methyl magnesium bromide gave a 1:1 mixture of 9,10-dihydro-12-hydroxy-12-methyl-9,10-propanoanthracene 27 and the starting ketone. When ethylmagnesium bromide was used, a 3:1 mixture of the ketone and 9,10-dihydro-12-ethyl-12-hydroxy-9,10-propanoanthracene was detected in the crude mixture by $^1$H-NMR spectroscopy. Our suspicion that the Grignard reagents also function as a base was confirmed by quenching the reaction with deuterium oxide. A $^1$H-NMR spectrum of the recovered ketone 15 revealed the incorporation of one deuterium into the molecule.

The use of alkyl cerium reagents, which have recently proved to be very efficient in addition reactions to readily enolizable carbonyl compounds, provided a convenient solution to this problem. Both methyl cerium and n-butyl cerium reagents
were prepared according to a literature procedure\textsuperscript{17}, and their reaction with ketone 15 afforded 9,10-dihydro-12-hydroxy-12-methyl-9,10-propanoanthracene 27 and 12-butyl-9,10-dihydro-12-hydroxy-9,10-propanoanthracene 28 in 93% and 75% yields, respectively.

\[
\text{HO} \quad \xrightarrow{\text{DIBAL-H, 86\%}} \quad \text{HO} 
\]

Reduction of hydroxyketone 22 with diisobutylaluminum hydride furnished 9,10-dihydro-\textit{cis}-11,12-dihydroxy-9,10-propanoanthracene 29 in 86\% yield. When sodium borohydride was used as a reductant, a by-product was formed, which was inseparable either by chromatography or crystallisation. Although the identity of this product could not be definitively established, the position of peaks in the \textsuperscript{1}H and \textsuperscript{13}C NMR spectra are consistent with the formation of 9,10-dihydro-\textit{trans}-11,12-dihydroxy-9,10-propanoanthracene. Attempts to alkylate the hydroxy group of hydroxyketone 22 failed.

Trialkyloxonium salts are commonly used for the preparation of ethers from alcohols. Surprisingly, in our case, the reaction of trimethyloxonium tetrafluoroborate with alcohol 27 did not give the expected methyl ether, but instead afforded 9,10-dihydro-12-methyl-9,10-propenoanthracene 30 in 86\% yield.
Synthesis of propanoanthracenes

\[
\begin{align*}
27 & \quad R = \text{CH}_3 \\
28 & \quad R = (\text{CH}_2)_3\text{CH}_3 \\
31 & \quad R = \text{CH}_3 (84\%) \\
32 & \quad R = (\text{CH}_2)_3\text{CH}_3 (81\%)
\end{align*}
\]

Purdie methylation with iodomethane and silver(I)oxide, freshly prepared from silver(I)nitrate and sodium hydroxide in acetonitrile also failed and the starting material was recovered. 9,10-Dihydro-12-methoxy-12-methyl-9,10-propanoanthracene 31 and 12-butyl-9,10-dihydro-12-methoxy-9,10-propanoanthracene 32 were however finally prepared by the deprotonation of the alcohols with potassium hydride and subsequent reaction of the resultant anions with dimethyl sulfate in DMSO solution in 84 and 81% yields, respectively.

A reaction of propanoanthracenone 15 with methylenetriphenylphosphorane using a deuterium oxide quench gave a mixture of 9,10-dihydro-12-methylene-9,10-propanoanthracene 33 (34%) and recovered ketone (50%), in which a deuterium atom had been incorporated, testifying once again to the acidity of the protons adjacent to the carbonyl group.

The Lombardo reagent, prepared from zinc, titanium tetrachloride and a dihalomethane and introduced in the late seventies for the preparation of methylene compounds from easily enolizable ketones proved to be more successful in our case and the alkene 33 was thus prepared in 60% yield.
Epoxidation of this alkene with *meta*-chloroperbenzoic acid then furnished 9,10-dihydro-12,14-epoxy-12-methylene-9,10-propanoanthracene **34** in 64% yield.

Attempts at the direct preparation of the S,O-acetal **35** from ketone **15** and mercaptoethanol proved to be problematical and are summarised in **Table 1**.

**Table 1: Attempts at the direct preparation of the S,O-acetal **35** from ketone **15****

<table>
<thead>
<tr>
<th>Run</th>
<th>mercaptoethanol (mol. eq.)</th>
<th>catalyst</th>
<th>solvent</th>
<th>temp. °C</th>
<th>time h</th>
</tr>
</thead>
<tbody>
<tr>
<td>119</td>
<td>2</td>
<td><strong>BF</strong>₃<strong>Et</strong>₂<strong>O</strong> (1)</td>
<td>diethylether</td>
<td>35</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>1.5</td>
<td>p-toluenesulfonic acid (0.2)</td>
<td>1,4-dioxane</td>
<td>100</td>
<td>6</td>
</tr>
<tr>
<td>320</td>
<td>co-solvent *</td>
<td><strong>BF</strong>₃<strong>Et</strong>₂<strong>O</strong> (co-solvent)</td>
<td>acetic acid</td>
<td>20</td>
<td>18</td>
</tr>
<tr>
<td>4</td>
<td>solvent *</td>
<td><strong>BF</strong>₃<strong>Et</strong>₂<strong>O</strong> (co-solvent)</td>
<td>mercaptoethanol</td>
<td>157</td>
<td>1</td>
</tr>
</tbody>
</table>

* mercaptoethanol polymerises under reaction conditions

In all of the above cases, only starting material could be detected in the reaction mixtures. 2-Aminoethanol also failed to give a reaction with ketone **15** at 80°C using p-toluenesulfonic acid as a catalyst. Another strategy was therefore needed. Trimethylorthoformate is a very efficient reagent for acetalizations of hindered ketones²¹. It proved to be successful in our case and 9,10-dihydro-12,12-dimethoxy-9,10-propanoanthracene **36** was prepared in 59% yield; 9,10-dihydro-12-methoxy-9,10-propenoanthracene **37** was also isolated as a by-product (20%) from this reaction. Transacetalisation of the dimethylacetal **36** with mercaptoethanol then furnished 9,10-
dihydro-12,12-ethylenethio-oxy-9,10-propanoanthracene 35 in 51% yield. Attempts to extend this protocol for preparation of the N,O-acetal 38 were however unsuccessful and alkene 37 was the only isolable product when acetal 36 was reacted with 2-aminoethanol in the presence of p-toluenesulfonic acid.

Fluorination of the tertiary alcohol 27 with the popular Middleton reagent, diethylaminosulfur trifluoride, furnished 9,10-dihydro-12-fluoro-12-methyl-9,10-propanoanthracene 39 in 71% yield.

Preparation of the corresponding tertiary halides 9,10-dihydro-12-chloro-12-methyl-9,10-propanoanthracene 40 and 9,10-dihydro-12-bromo-12-methyl-9,10-propanoanthracene 41 was also attempted. A high yielding method for the preparation
Synthesis of propanoanthracenes

of tertiary chlorides from alcohols has been described by Carman and Shaw and involves stirring a suspension of tertiary alcohol, phosphorus pentachloride, and calcium carbonate in chloroform for several minutes, and then filtering off the solid phase and evaporating the solvent to give the pure chloride in an almost quantitative yield. When these conditions were applied to alcohol 27, the $^1$H NMR spectrum of the crude reaction mixture revealed that a clean 1:1 mixture of alkene 30 and a compound with a $^1$H NMR spectrum which was consistent with the expected spectrum for the chloride 40 had been formed. Attempts to purify this latter compound failed. The presumed chloride was unstable both on silicagel and on an alumina column. When the reaction was performed in the absence of base, the alkene was not detected but several other compounds were formed in addition to the chloride. Attempts to find some more suitable hydrogen chloride quench have failed thus far. Reaction of the alcohol 27 with phosphorus pentabromide gave alkene 30 as the major product, although some bromide seemed also to be formed on the basis of the $^1$H NMR spectrum of the crude product mixture. Attempted bromination of the alcohol 27 with hexamethyldisilane and pyridinium bromide perbromate gave only an intractable mixture of products. It might be necessary to perform the halogenation reactions on a large scale and purify these products by crystallisation.
The evidence from the halogenation reactions, together with the previously mentioned facile enolisation of ketone 15 in both the Grignard and Wittig reactions, indicate that the formation of a double bond in the bridge of propanoanthracenes is an easy process. It is difficult to assess whether the primary reason for this fact is the removal of steric interactions between the C-12 substituents and the aromatic ring, or whether some interaction between the double bond and the aromatic rings has a stabilising effect. Thus, the task of functionalising propanoanthracenes appears to be deceptively simple, but the propensity for double bond formation presents rather formidable synthetic challenges.

As mentioned in the introductory review, the quadrupolar moment of aromatic rings can be reversed by the introduction of electronegative substituents. Almost nothing is known about the interactions of such a ring and so we attempted to prepare octachlorinated propanoanthracenes to investigate the changes caused by the reversal of the quadrupolar moment.

Both aromatic rings in hydroxyketone 22 could be fully chlorinated with a mixture of sulfuryl chloride, sulfur monochloride and aluminum chloride to give 9,10-dihydro-11-hydroxy-1,2,3,4,5,6,7,8-octachloro-9,10-propanoanthracen-12-one 42 in 32% yield. This reagent mixture, firstly described by Silberrad in 1922 and then rediscovered by Ballester at the 50's, is a very powerful chlorinating agent. Thus far, it has been mostly used for the preparation of polychlorinated aromatic and alkylaromatic compounds. In the latter case, the alkyl chain is also at least partially chlorinated. We were pleased to find that only the aromatic part of the molecule was attacked in our case, with the bridge surviving unchanged. Unfortunately however, when the parent ketone 15 was used as a substrate, a complex inseparable mixture of products was formed.
Attempts to remove the hydroxyl group from the hydroxyketone with samarium diiodide failed. The hydroxyketone 42 is only sparingly soluble in most solvents and so the deoxygenation procedure had to be changed. Toluene was used as a co-solvent and the reaction conducted at 0°C. The perchlorinated aromatic rings are electron poor and may interfere with electron transfer from samarium diiodide.

The free radical deoxygenation of alcohols via reaction of their thiono esters with tri-n-butylstannane is an important synthetic procedure. To the best of our knowledge, this method has never been used in the case of an α-hydroxy ketone substrate. A reaction of hydroxyketone 42 with 1,1'-thiocarbonyldiimidazole 43
furnished expected thionoester 44, but only in 20% yield, with a substantial part of the starting ketone being recovered. Very surprisingly the further product of the reaction, which was isolated in approximately the same quantity as the thionoester, had spectral properties which would be consistent with the deoxygenated ketone 45. Unfortunately, this product could not be isolated in sufficient purity, which would permit a conclusive identification, as another by-product was eluted simultaneously on column chromatography purification. This reaction was performed in several solvents (benzene, toluene, dimethylaminoformamide) and at several temperatures (50-85 °C), but always most of the starting ketone was recovered. It was observed that during the reaction a product was formed which appeared as the largest spot on an analytical TLC plate, but it always suffered decomposition on the column.

The direct elimination of a thionoester without the use of some radical reducing agent such as tributyltin hydride has never been observed so far, so this reaction deserves further investigation and other α-hydroxy ketones should be studied.
2.4 Spectral Characteristics of 9,10[1',4']Benzenoanthracenes and 9,10-Propanoanthracenes

With the preparation of a useful series of compounds for study now accomplished, it was therefore appropriate to carry out their detailed spectral characterisation. The molecular structures of all relevant compounds are collected in Appendix 4 (page 167).

2.4.1 Infrared Spectra

The frequencies of the O-H stretching vibrations of the synthesised alcohols are collected in Table 2. The infrared spectra of alcohols 9 and 26, with their hydroxyl groups pointing away from the ring, show hydroxylic stretching around 3624 cm⁻¹ in tetrachloromethane and 3609 cm⁻¹ in chloroform and carbon disulfide solutions. Several peaks appear in this region in carbon disulfide (Figure 1 and 2).

Table 2: The O-H stretching vibrations of alcohols in cm⁻¹

<table>
<thead>
<tr>
<th>Compound</th>
<th>CHCl₃</th>
<th>CCl₄</th>
<th>CS₂</th>
<th>Pyridine</th>
<th>KBr</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>3609</td>
<td>3625</td>
<td>3609 multiplet</td>
<td>3397</td>
<td>3557</td>
</tr>
<tr>
<td>12</td>
<td>3563</td>
<td>3577</td>
<td>3576</td>
<td>3567</td>
<td>3582</td>
</tr>
<tr>
<td>26</td>
<td>3606</td>
<td>3623 multiplet</td>
<td>3609 multiplet</td>
<td>3257</td>
<td>3298</td>
</tr>
<tr>
<td>27</td>
<td>3581</td>
<td>3595</td>
<td>3593</td>
<td>3586</td>
<td>3562</td>
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<tr>
<td>28</td>
<td>3581</td>
<td>3596</td>
<td>3587</td>
<td>3344</td>
<td>3590</td>
</tr>
</tbody>
</table>
Figure 1: The infrared spectrum of alcohol 9 in carbon disulfide
Figure 2: The infrared spectrum of alcohol 26 in carbon disulfide
The formation of a hydrogen bond in alcohols 12, 27, and 28 is clearly demonstrated by the shift of this vibration to lower frequencies. These peaks are sharp and concentration independent (Figure 3 and 4). The intramolecular hydrogen bond in these alcohols partially survives even in pyridine, a strong hydrogen bond acceptor (Figure 5 - 9).

In the exo-alcohols 9 and 26 one strong absorption peak appears in the 800-1400 cm\(^{-1}\) region of their spectra, which can be assigned to a vibration mode with a major contribution from the O-C stretching vibration. On the other hand, the endo-alcohols 12, 27, and 28 have two peaks in this region, which are shifted to higher frequencies in comparison with their relevant exo-alcohol counterparts (Table 3). A typical demonstration of this effect is provided by the spectra of alcohols 9 (Figure 1) and 12 (Figure 3) in carbon disulfide.

Table 3: The C-O stretching vibrations of alcohols in cm\(^{-1}\)

<table>
<thead>
<tr>
<th>Compound</th>
<th>CHCl(_3)</th>
<th>CCl(_4)</th>
<th>CS(_2)</th>
<th>KBr</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>1001</td>
<td>1002</td>
<td>1004</td>
<td>1009</td>
</tr>
<tr>
<td>12</td>
<td>1074</td>
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<td>1077</td>
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<td></td>
<td>1051</td>
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</tr>
<tr>
<td>26</td>
<td>1048</td>
<td>1037</td>
<td>1037</td>
<td>1041</td>
</tr>
<tr>
<td></td>
<td>1031</td>
<td></td>
<td></td>
<td>1031</td>
</tr>
<tr>
<td>27</td>
<td>1108</td>
<td>1111</td>
<td>1110</td>
<td>1110</td>
</tr>
<tr>
<td></td>
<td>1060</td>
<td>1057</td>
<td>1055</td>
<td>1084</td>
</tr>
<tr>
<td>28</td>
<td>1052</td>
<td>1053</td>
<td></td>
<td>1052</td>
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<tr>
<td></td>
<td>1030</td>
<td>1031</td>
<td></td>
<td>1030</td>
</tr>
</tbody>
</table>

The solid state spectrum of the endo-alcohol 12 resembles its solution spectra. In this instance, the hydroxyl prefers the intramolecular binding mode to the intermolecular one, as expected on steric grounds. Surprisingly, the spectrum of the
Figure 3: The infrared spectrum of alcohol 12 in carbon disulfide

Figure 4: The infrared spectrum of alcohol 27 in carbon disulfide
Figure 5: The infrared spectrum of alcohol 9 in pyridine

Figure 6: The infrared spectrum of alcohol 12 in pyridine
Figure 7: The infrared spectrum of alcohol 26 in pyridine

Figure 8: The infrared spectrum of alcohol 27 in pyridine
**Figure 9:** The infrared spectrum of alcohol 28 in pyridine

*ex*o-alcohol 9 ([Figure 10](#)) indicates that the hydroxyl group does not engage in a hydrogen bond to the hydroxyl of the second molecule, but forms a hydrogen bond to an aromatic ring in a violation of the Etter rules\(^{27}\) which states that the strongest conceivable hydrogen bond should be formed. Nevertheless, an X-ray crystal structure determination of 9 would be required for definitive proof. Such types of bonding have also been previously described in crystals of 2,2,2-trifluoro-1-(9-anthryl)ethanol\(^{28}\) and in the crystal structure of silanol\(^{29}\). In these cases, however, dimers were formed in the solid state.

The solid state spectrum of alcohol 28 is consistent with an intramolecular hydrogen bond to the aromatic system ([Figure 11](#)).
Figure 10: The solid state infrared spectrum of alcohol 9 in KBr

Figure 11: The solid state infrared spectrum of alcohol 28 in KBr
Alcohol 27 is different. Two peaks appear in the spectrum, one typical of strong binding to oxygen, the second in a position characteristic of an OH...π hydrogen bond (Figure 12).

The carbonyl stretch of the endo-acetate 13 (1717 cm\(^{-1}\)) is shifted by 5 cm\(^{-1}\) to lower frequency in comparison with the exo-acetate 14 (1722 cm\(^{-1}\)). In the solid state, the carbonyl vibration of endo-acetate 13 is split into a doublet; and so implying the non-equivalence of the molecules in the crystal lattice.

Figure 12: The solid state infrared spectrum of alcohol 27 in KBr
2.4.2 $^1$H NMR Spectra

The spectra of 9,10[1,4]-benzenoanthracene derivatives are rather complex due to the presence of long range couplings and the non-equivalence of the geminal hydrogens. Thus, coupling constants could be found only after a series of decoupling experiments and in several instances were not attainable at all.

![Diagram of 9,10[1,4]-benzenoanthracene](image.png)

The coupling constants $J_{9,14}$ and $J_{10,11}$ in benzenoanthracenes vary from 11 to 12 Hz; *endo*-compounds have $J_{9,14}$ higher then $J_{10,11}$, in accordance with the presumed larger twisting effect of the functional group on the dihedral angle between the closer protons H-10 and H-11. In the *exo*-compounds $J_{10,11}$ is higher then $J_{9,14}$. Rather large through space W-coupling can also be detected in the spectra; in the case of *exo*-alcohol 9 and *exo*-acetate 14 long range coupling constants larger than 3 Hz were identified.

The hydroxylic hydrogen of the *endo*-alcohol 12 is coupled to H-12 with $J = 11.5$ Hz at room temperature, $J = 11.2$ Hz at 55°C and $J = 12.2$ at -55°C. These coupling constants indicate that the dihedral angle between H-12 and the hydroxylic hydrogen is close to 180°, a value which is consistent with the hydrogen atom pointing towards the center of the aromatic ring. The chemical shift of the hydroxylic hydrogen was shifted to lower field with decreasing temperature. A rather strong hydrogen bond is obviously formed in this molecule, as supported by the infrared evidence. The strength of this interaction is not sufficient to immobilize the hydroxylic proton however, as witnessed by the strong saturation transfer to water upon irradiation of the hydroxyl and by the fact, that upon addition of a drop of D$_2$O the hydroxylic signal immediately disappeared. In comparison, a typically broad hydroxylic signal is present in the
spectrum of the *exo*-alcohol 9. The stereochemistry of the hydroxylic group also substantially influences the chemical shift of the bridgehead hydrogen H-9. Thus, while in the *exo*-alcohol 9 the chemical shifts of protons H-9 and H-10 are 4.16 and 4.30 ppm, respectively; both bridgehead hydrogens absorb at 4.29 ppm in the *endo*-alcohol 12.

The aromatic part of the spectrum also provides some interesting information. One of the aromatic resonances is shifted by 0.2 ppm downfield from the rest of the aromatic signals in the spectrum of the *endo*-alcohol 12. When this resonance was irradiated, three peaks appeared in the aliphatic region of the NOE difference spectrum; the peak corresponding to the H-9,10 frequency, the hydroxyl proton doublet and the water peak (Figure 13). When the peaks due to the hydroxyl hydrogen and H-13*endo* were irradiated, the intensity of the isolated aromatic multiplet was increased. This evidence supports the assignment of this multiplet as H-4. By way of contrast, the aromatic resonances of the *exo*-alcohol 9 are much closer to each other.

The signal due to H-4 is also similarly separated in the spectrum of the *endo*-acetate 13. The assignment of this proton as H-4 was confirmed by the presence of a NOE effect upon irradiation of the methyl group (Figure 14). When H-4 was irradiated, peaks due to the methyl group and H-10 were present in the NOE difference spectrum (Figure 15). The H-4 proton is also distinct from the rest of the aromatic hydrogens in the *exo*-acetate 14. Irradiation of H-12 increases the intensity of this proton (Figure 16). Saturation of this single aromatic resonance strongly enhanced the absorption of proton H-10 (Figure 17).

The aromatic signals are clearly separated in the spectrum of epoxide 7. The signals due to α and β aromatic protons underneath the epoxide moiety absorb at lower field in comparison with the second ring by 0.07 ppm and 0.04 ppm, respectively. The assignment of the signals was based on NOE evidence (Figure 18 and 19). These shifts are consistent with some removal of electron density by through space interaction between the epoxide group and the aromatic ring.
Figure 13: The NOE difference spectra of alcohol 12
Figure 14: The NOE difference spectrum of *endo*-acetate 13
Figure 15: The NOE difference spectrum of *endo*-acetate 13
Figure 16: The NOE difference spectrum of *exo*-acetate 14
Figure 17: The NOE difference spectrum of exo-acetate 14
Figure 18: The NOE difference spectrum of epoxide 7
Figure 19: The NOE difference spectrum of epoxide 7
An interesting example of how dangerous the assignment of the resonances based only on chemical shift arguments can be is provided by alcohols 9 and 12, and their acetates 14 and 13. The chemical shifts of their protons H-13 are summarized in Table 4. At first sight, the signals due to the H-13 protons seem to appear in the same region for all of the compounds. Detailed analysis of the coupling patterns and especially the long range W coupling between $H_{13}^{\text{endo}}$ and $H_{15}^{\text{endo}}$ shows however that this perception is wrong. $H_{13}^{\text{endo}}$ absorbs at lower field then $H_{13}^{\text{exo}}$ in exo-compounds 9 and 14 but at higher field in endo-compounds 12 and 13. This assignment is also corroborated by NOE difference spectra after irradiation of H-12 (Figure 16).

Table 4: The chemical shifts ($\delta$) of protons H-13 in selected benzenoanthracenes

<table>
<thead>
<tr>
<th>Protons</th>
<th>Alcohols</th>
<th>Acetates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>9</td>
<td>12</td>
</tr>
<tr>
<td>H-$13^{\text{endo}}$</td>
<td>1.80</td>
<td>1.03</td>
</tr>
<tr>
<td>H-$13^{\text{exo}}$</td>
<td>1.12</td>
<td>2.01</td>
</tr>
</tbody>
</table>

The second order nature of the spectra of propanoanthracenes and the influence of the bridge flipping on the coupling constants are discussed in Appendix 1 and 2.

The hydroxylic signal of the alcohol 27 appears as a broad singlet, as commonly encountered in the spectra of alcohols. However, this resemblance is only superficial, as the broadening of the signal is not caused by fast exchange but is due to a complex coupling pattern. The methyl group of the alcohol is coupled to the hydroxylic proton with a coupling constant $J = 1.0 \text{ Hz}$. The hydroxyl proton is also coupled to the H-11,13
hydrogens since upon irradiation of H-11\textsuperscript{trans}, 13\textsuperscript{trans}, the hydroxyl signal changes to a multiplet whose shape is compatible with a split quartet.

In attempts to minimize amount of any impurities present in the solvent, deuterochloroform was distilled straight into an NMR tube via Teflon tubing under an atmosphere of nitrogen. Unfortunately, it proved to be very difficult to completely remove water by this procedure, a small baseline water peak could usually be detected. These experiments although unsuccessful in their original aim, paid a surprising and totally unexpected dividend. When a solution of alcohol 27 was prepared in this way, the residual water peak appeared as a doublet (Figure 20). Irradiation of the hydroxyl proton led to saturation transfer to the water peaks, which were now clearly visible in the difference spectrum. Upon addition of a drop of deionised water, the signal gained in intensity, but collapsed into a singlet.

A water saturated chloroform solution of the alcohol was therefore prepared by adding a drop of deionised water to deuterochloroform and then distilling this into the NMR tube containing the alcohol. A cloudy solution resulted from this distillation and three hydroxyl signals appeared in the \textsuperscript{1}H NMR spectrum, the bulk water at δ = 4.80, hydroxyl signal at δ = 1.18 and the dissolved water peak at δ = 1.59, again appearing as a doublet. Integration of the doublet upon acquiring just one scan gave an approximately 1:1 ratio between dissolved water and the alcohol (Figure 21).

When deuterochloroform was distilled in an atmosphere of air, sufficiently intense water peaks resulted and the problem with condensing water was removed. At least ten samples were prepared which exhibited this effect, using different batches of deuterochloroform as well as of the alcohol. The water peak collapsed into a singlet after several hours. Slight decomposition of chloroform probably took place. Rather fast disappearing of coupling information caused by chloroform decomposition was observed by Pearce and Sanders\textsuperscript{30} in their study of coupling from hydroxyl protons in diluted deuterochloroform solutions. The chemical shift difference between two water signals varied between samples, the maximal detected one was 1.8 Hz. Splitting of the
Figure 20: Two water peaks in the spectrum of alcohol 27
Figure 21: The spectrum of alcohol 27 in water saturated deuterochloroform
A water peak was also observed in a solution of the butyl alcohol derivative 28, but was never detected with alcohols 26 and 12.

As such behavior of water is very unusual, this system was thoroughly investigated. All protons of the alcohol were gradually decoupled, but the splitting of the water signal remained unchanged. The water peak appeared as a singlet, when the measurement was done at 200 MHz. It could not be caused by poor resolution of the instrument, as the doublet due to the methyl group (J = 1.0 Hz) was resolved almost to the baseline. The presence of the splitting was confirmed by 400 MHz instrument before and after this measurement.

When the solution of the alcohol was gradually cooled down, no increase in separation between two water signals was observed. Heating of the solution at 50°C resulted in the collapse of the two peaks into a single signal. When this solution was cooled to 20°C, the two signals did not reappear and so it is impossible to conclude whether a genuine transition to a fast exchange limit occurred or whether a decomposition of chloroform was the cause of this collapse.

Rationalisation of this behavior is difficult. Some kind of a complex between the alcohol and a water molecule seems to be formed, with a lifetime sufficiently long to be detectable on the $^1$H NMR time scale. Such a long lifetime is several orders of magnitude longer than would be expected. The geometry of this postulated complex is also very difficult to disentangle. The hydroxy group pointing towards the aromatic ring seems to be crucial for observation of two water signals as only in the alcohols 27 and 28 is this effect observed. We can conceive a formation of a classical hydrogen bond between water and the hydroxyl moiety together with a creation of a hydrogen bond between the aromatic ring and one of water protons. In this case, of course, the magnetic anisotropy of the aromatic ring should cause a dramatic shift of the water signal towards higher field, but this is not corroborated by the experimental finding. Other binding geometries are even more difficult to defend. The investigation of the
It follows from the above discussion that the appearance of two water peaks in the spectra is poorly understood. The question remains whether we are witnessing the formation of some unusually strong complex or whether some unexpected NMR effect is in operation. In both cases this problem deserves further attention as solvation phenomena are currently a major topic of scientific research and seemingly strange effects often help to uncover basic principles.

Protons $H_A$ and $H_B$ absorb accidentally at the same frequency in the spectrum of epoxide 34. The spectrum shows a doublet due to these protons and a triplet due to $H_C$. This $AA'B$ spectrum was simulated on the computer for plausible values of coupling constants. The simulation has shown that for $J_{AB}$ substantially larger than $J_{AC}$ and $J_{BC}$ the apparent coupling constant of the signals is always equal to the half of the sum of $J_{AC}$ and $J_{BC}$ and does not depend on the particular values of these coupling constants.

The spectrum of the S,O-acetal 35 reveals that the two possible conformers are unequally populated at room temperature. Unfortunately, in this case NOE experiments failed to distinguish between these conformers. Irradiation of the methylene group next to the oxygen in the five-membered ring gave approximately the same NOE effect to both protons $H_A$ and $H_B$ (Figure 22). The conformer with oxygen aiming towards the aromatic ring was tentatively assigned to be the more populated one.

However, conformers could be unequivocally assigned in the case of the ethers 31 and 32 on the basis of their NOE difference spectra (Figure 23 and 24). A signal due to $H_A$ but not $H_B$ was present when the methoxy protons were irradiated.

The aromatic resonances due to the aromatic ring underneath the hydroxylic moiety in alcohols 27 and 28 are shifted towards lower field by approx. 0.1 ppm in comparison to the second ring. The difference between both rings in alcohol 26 is negligible. The aromatic hydrogens are also clearly separated in the spectrum of epoxide 34 and S,O-acetal 35.
Figure 22: The NOE difference spectrum of S.O acetal 35
Figure 23: The NOE difference spectrum of ether 31
Figure 24: The NOE difference spectrum of ether 32
An unusual effect was observed in the spectrum of hydroxyketone 24. The coupling between $H_B$ and $H_C$ is clearly visible in the $H_B$ signal but not in the $H_C$ signal (Figure 25). Irradiation at the frequency of $H_C$ leads to the collapse of $H_B$ into a quartet. This effect is not caused by the fast relaxation of proton $H_C$. The inverse-recovery experiment confirmed that proton $H_B$ relaxes faster than $H_C$. 
Figure 25: The $^1$H NMR spectrum of hydroxyketone 24
2.4.3. $^{13}$C NMR Spectra

No unexpected effect was found when the aliphatic part of the spectrum of 9,10[1,4]-benzeneanthracenes were compared with the spectra of bicyclo[2,2,1]heptanes and bicyclo[2,2,2]octanes. More interesting results were provided by the aromatic portion of the spectra.

The chemical shifts of the quaternary aromatic carbons are markedly influenced by the position of the substituent. Unfortunately, these carbons could not be assigned, as $^{13}$C-$^{13}$C correlation experiments are prohibitively time demanding and the spectra are unsuitable for simpler techniques. Nevertheless, even with this restriction, some interesting information could be gained. The quaternary carbons of the parent compound 6 absorb at 144.58 ppm. Introduction of the double bond in alkene 5 only slightly distinguishes between the pairs of quaternary carbons. The presence of the epoxide moiety in 7 has a more profound influence, and 1.6 ppm is the difference between the shifts. The introduction of a carbonyl moiety as in ketone 8 has a considerable influence. The stereochemistry of the substituent in alcohols 9 and 12, and ester 14 and 13 also play an important role.

The chemical shifts of the quaternary aromatic carbons in 9,10-propanoanthracenes also depend strongly on the position of the bridge. These carbons have not yet been assigned. The nondecoupled carbon spectra of alcohols 26 and 28 were acquired (Figure 26 and 27) and it was found that the coupling pattern of quaternary aromatic signals is substantially different. It is hoped that the analysis of the coupling could help with assignment, but unfortunately, we do not have an appropriate program at our disposal yet.
Figure 26: The quaternary aromatic signals of alcohol 26
Figure 27: The quaternary aromatic signals of alcohol 28
2.4.4. Mass Spectra

The cation of molecular weight 178 is the dominant peak in the mass spectra of the 9,10[1,4]-benzoanthracenes, corresponding to the fragment 46.

Attempts to detect the molecular ion by EI or FAB of the alkene 5 were unsuccessful, the fragment 46 was the major cation detected. A retro[4+4] cycloaddition therefore seems to be the dominant fragmentation pathway.

The endo-alcohol 12 and the exo-alcohol 9 behave differently under ionization. Thus, while the exo-alcohol 9 gives a rather strong molecular ion M⁺ upon electron impact ionization and ten times smaller M⁺ - H₂O, the molecular ion of the endo-alcohol 12 was not detected under the same conditions. The weak signal due to M⁺ could be detected in the FAB spectrum, with the M⁺ - H₂O signal being five times more intense than M⁺. On the other hand, the spectra of endo- and exo-acetates 13 and 14 are very similar.

The spectra of the 9,10-propanoanthracene derivatives are rather similar, the most notable difference is a very substantial increase in the intensity of peaks with mass 191 and 192, one of these peaks sometimes being the strongest peak in the spectrum. An explanation for the marked persistence of these ions could be that rearrangement to the aromatic cation 47 (mass = 191) occurs.
In contrast with benzenoanthracenes, no marked difference was detected between alcohol 26, with its hydroxyl group pointing away from the ring, and intramolecularly hydrogen bonded alcohols 27 and 28.
2.5 Thermodynamics of Interactions

A comparison of the interaction energies between different functional groups and the aromatic ring is one of the main aims of this work. The way the equilibrium ratios and the difference in the interaction energies were estimated is discussed in Appendix 2 and 3. The results are summarised in Table 5 with the more populated conformer being the one depicted in Figure 28.

![Chemical structures](Figure 28)
Table 5: Equilibrium ratios and the energetic difference between conformers of 9,10-propanoanthracenes in CDCl₃

<table>
<thead>
<tr>
<th>Compound</th>
<th>Jₐb (Hz)</th>
<th>Jₐc (Hz)</th>
<th>Ratio</th>
<th>ΔG (kJ mol⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>26</td>
<td>7.2</td>
<td>1.2</td>
<td>&gt;95:5</td>
<td>&gt;7.2</td>
</tr>
<tr>
<td>27</td>
<td>6.7</td>
<td>1.3</td>
<td>&gt;95:5</td>
<td>&gt;7.2</td>
</tr>
<tr>
<td>28</td>
<td>6.7</td>
<td>1.3</td>
<td>&gt;95:5</td>
<td>&gt;7.2</td>
</tr>
<tr>
<td>31</td>
<td>5.4</td>
<td>2.8</td>
<td>72:28</td>
<td>2.3</td>
</tr>
<tr>
<td>32</td>
<td>6.5</td>
<td>1.7</td>
<td>91:9</td>
<td>5.8</td>
</tr>
<tr>
<td>39</td>
<td>6.2</td>
<td>1.8</td>
<td>91:9</td>
<td>5.8</td>
</tr>
<tr>
<td>35</td>
<td>5.8</td>
<td>2.6</td>
<td>77:23</td>
<td>2.9</td>
</tr>
</tbody>
</table>

The equilibrium ratios of these compounds were also predicted using molecular mechanics (Macromodel®, MM2 and MM3 force fields) and semiempirical quantum chemistry calculations (PM3). The results are summarised in Table 6. If several energetic minima were available for the molecule because of a rotation of its functional group only the lowest minimum was used for the equilibrium calculation. The inspection of both tables reveals that both experimental and theoretical results predict the same preferred conformer in all investigated cases.
Thermodynamics of interactions

Table 6: The energetic difference (kJ mol$^{-1}$) and equilibrium ratios between conformers of 9,10-propanoanthracenes as estimated by molecular mechanics and semiempirical quantum chemistry calculations

<table>
<thead>
<tr>
<th>Compound</th>
<th>MM2</th>
<th>MM3</th>
<th>MM3 (CHCl$_3$)</th>
<th>PM3</th>
</tr>
</thead>
<tbody>
<tr>
<td>26</td>
<td>-5.1 (89:11)</td>
<td>-21.4 (100:0)</td>
<td>-11.1 (99:1)</td>
<td></td>
</tr>
<tr>
<td>27</td>
<td>-8.5 (97:3)</td>
<td>-10.2 (99:1)</td>
<td>-9.8 (98:2)</td>
<td>-9.9 (98:2)</td>
</tr>
<tr>
<td>31</td>
<td>-7.2 (95:5)</td>
<td>-7.7 (96:4)</td>
<td>-5.5 (91:9)</td>
<td></td>
</tr>
<tr>
<td>32</td>
<td>-10.6 (99:1)</td>
<td>-9.7 (98:2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>35</td>
<td>-4.0 (84:16)</td>
<td>-6.6 (94:6)</td>
<td>-6.7 (94:6)</td>
<td></td>
</tr>
<tr>
<td>39</td>
<td>-24.8 (100:0)</td>
<td>-14.9 (100:0)</td>
<td>-11.2 (99:1)</td>
<td>-3.1 (78:22)</td>
</tr>
<tr>
<td>34</td>
<td>-0.5 (55:45)</td>
<td>-6.8 (94:6)</td>
<td>-7.6 (96:4)</td>
<td></td>
</tr>
</tbody>
</table>

In all of the investigated alcohols, only one conformer is observed experimentally. The energetic difference between two conformers has to be higher, therefore, than 7 kJ mol$^{-1}$. In the alcohol 26 the hydroxyl group points away from the ring. A hydrogen bond which can be formed in the second conformation is not strong enough to compensate for the larger van der Waals radius of oxygen in comparison with hydrogen.

Alcohols 27 and 28 however are fixed in the opposite conformation. The smaller van der Waals radius of oxygen in comparison with the methyl group and the formation of the hydrogen bond now act in the same direction. The importance of the contribution of the hydrogen bond can be judged from the comparison of alcohol 27 with the fluoroderivative 39, in which both the $endo$- and $exo$-isomers are significantly populated at ambient temperature (ratio 91:9). The fluorine atom is smaller than oxygen and so considerations based solely on steric grounds would anticipate a greater conformer ratio in the fluoride than in the alcohol. The molecular mechanics calculations indeed predict such a trend as the force fields used (MM2 and MM3) are
not parametrised for hydrogen bonding towards an aromatic ring. On the contrary, semiempirical calculations predicted the observed results.

Hydroxyketone 22 exists predominantly in the conformation in which the hydroxyl moiety points away from the aromatic ring. The position of the 11-hydroxyl group is reversed in diol 29. The more "sidewise" approach of this hydroxyl in comparison with the 12-hydroxy group is obviously preferable.

In the remainder of the compounds both conformers are significantly populated. The preferred conformation for the ethers 31 and 32 is the one with the ether moiety aiming towards the aromatic ring. Because of the rotation around the C₁₂-O bond, two energetic minima for the ether moiety are predicted to occur in the endo-conformer by the molecular mechanics calculations. The minimum with a CMe or BuC₁₂OCH₃ dihedral angle of around 65° is predicted to be preferred against the periplanar alternative by approximately 20 kJ mol⁻¹.

The energetic difference between the two conformers of S,O acetal 35 amounts to approximately 3 kJ mol⁻¹. Unfortunately, all attempts to determine experimentally which conformer predominates failed. On the basis of steric arguments and the molecular mechanics calculation it can be expected with a reasonably high probability that the conformer depicted in Figure 28 is the more populated one.

Epoxide 34 was also synthesised. Unfortunately, this molecule was not amenable to conformational analysis by our method. Calculations predict that oxygen will project away from the ring. The plane defined by the two hydrogens and the carbon of the epoxide methylene group is almost parallel to the aromatic ring and so the hydrogens do not dramatically interact with the ring.

Since the dependence of intermolecular interactions on solvation is a topic of extensive research, we have investigated the influence of solvent on the equilibrium constant in the ether 31, the fluoride 39 and the S,O-acetal 35. The results are summarised in Table 7.
The ratio of conformers in the ether 31 is not markedly influenced by solvent. The given values for all solvents are inside experimental error. The solvent dependence is however more profound in the cases of the other two molecules. While the equilibrium constants are similar in carbon tetrachloride, carbon disulfide and benzene, they are substantially changed in more polar acetonitrile and chloroform. The origin of this shift is difficult to explain. It cannot be explained on the basis of different solvation of the functional groups. Fluorine and oxygen should be more solvated in polar solvents than either the methyl group or the sulfur atom. Thus, the conformer which exposes them more to the solvent should be relatively more populated in chloroform and acetonitrile than in other solvents. The experimental facts contradict this theory. Other effects have obviously to be considered, but they are difficult to uncover at this stage of the work.

Table 7: The equilibrium ratios of 9,10-propanoanthracenes 31, 39, and 35 in several solvents

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Equilibrium ratio (ΔG (kJ mol⁻¹))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>31</td>
</tr>
<tr>
<td>CDCl₃</td>
<td>72:28 (2.3)</td>
</tr>
<tr>
<td>CCl₄*</td>
<td>69:31 (1.9)</td>
</tr>
<tr>
<td>CS₂*</td>
<td>72:28 (2.3)</td>
</tr>
<tr>
<td>C₆D₆</td>
<td>67:33 (1.8)</td>
</tr>
<tr>
<td>CD₃CN</td>
<td>71:29 (2.2)</td>
</tr>
</tbody>
</table>

* contained cca 8% C₆D₆
2.6 Conclusions

This research project was initiated with the aim of assessing the usefulness of 9,10[1',4']-benzoanthracenes and 9,10-propanoanthracenes as model systems for the investigation of through space interactions between different functional groups and aromatic rings. This work was undoubtedly successful in this respect.

The advantage of using benzoanthracenes for these studies in having both the investigated and the reference aromatic ring in the same molecule, was especially demonstrated by $^1$H NMR spectroscopy. Epoxide 7 is a nice example of this fact; all aromatic hydrogen atoms could be unequally assigned in this molecule and some removal of the electron density from the ring beneath the epoxide moiety was demonstrated. Alcohols 9 and 12, and acetates 14 and 13 also exhibited substituent dependant change in their $^1$H NMR spectra. It remains to be seen, if the chemical reactivity of both rings also substantially differs. This will be ascertained by further investigation. Alcohol 12 forms a strong hydrogen bond towards its aromatic ring. This bond partially survives even in pyridine and it shows a marked orientational preference as witnessed by the small temperature dependence of the coupling constant of the hydroxyl proton.

Propanoanthracenes function as torsion balances with which the interaction energies between aromatic rings and different functional groups can be compared. Although considerable synthetic difficulties hampered their exploration, several interesting compounds were nevertheless prepared and their investigation confirmed the usefulness of our approach.

The differences in interaction energies between functional groups investigated so far were substantial and demonstrated that these interactions can be of great importance in complex formations and other phenomena. The significance of hydrogen bonding was particularly clearly illustrated.

Propanoanthracenes are also suitable for research of solvation phenomena. The effect of solvent on conformational equilibria is sufficiently great to be discernible. The
observation of two water peaks in the spectrum of 9,10-dihydro-12-hydroxy-12-methyl-9,10-propanoanthracene 27 is especially intriguing, but the data are not yet sufficient to explain this phenomenon.

Although development of synthetic procedures was not the aim of this work, two reactions described here deserve a special comment. Successful [4+4] cycloaddition reaction 2-(1,3-cyclohexadienyloxy)-trimethylsilane 10 demonstrated the suitability of this diene as a reactant in these reactions. As the product of the cycloaddition contains an unsymmetrical double bond which can be cleaved to give an eight member ring with two different substituents, 2-(1,3-cyclohexadienyloxy)-trimethylsilane can find its place in the synthesis of these hardly accessible systems.

The successful chlorination of hydroxyketone 22 to give 9,10-dihydro-11-hydroxy-1,2,3,4,5,6,7,8-octachloro-9,10-propanoanthracen-12-one 42 is also remarkable. It demonstrated that some substituents can survive the harsh conditions of this reaction. As it is our opinion that the reversal of quadrupolar moment of an aromatic ring by electronegative substituents will play an important role in the near future, the significance of this finding is obvious.
Appendix 1: Computer Simulation of AA'BB'CC' Spectrum

12-(un)substituted-9,10-propanoanthracenes are of Cs symmetry. The protons related by the plane of symmetry are chemically but not magnetically equivalent and so protons $H_A$, $H_B$, and $H_C$ form second order AA'BB'CC' system.

As the correct evaluation of the coupling constant was crucial for the success of this work, this system was simulated on a spectrometer computer. The chemical shifts and coupling constant used in the calculation are typical of the propanoanthracene series.

Simulation conditions:
Chemical shifts: $H_A = 150$ Hz; $H_B = 0$ Hz; $H_C = 550$ Hz
Coupling constants: $J_{AB} = 15$ Hz; $J_{AC} = 5$ Hz; $J_{BC} = 3$ Hz; $J_{AA'} = 2$ Hz
Line width: $LW = 0.5$ Hz

The simulated spectra fortunately showed that the coupling constants can be read directly from the 400 MHz spectrum without the necessity to resort to computer iterations. (Figure 29)
Figure 29: The simulated 400 MHz $^1$H NMR spectrum of a typical propanoanthracene
Figure 29: The simulated 400 MHz $^1$H NMR spectrum of a typical propanoanthracene
Appendix 2: Determination of Equilibrium Constants.

The flipping of the bridge in the 9,10-propanoanthracenes is a fast process on the NMR time scale at room temperature and so only average chemical shifts and coupling constants are observed in their spectra. The spectrum of 9,10-dihydro-12-methoxy-12-methyl-9,10-propanoanthracene 31 measured in carbon disulfide at -110 °C was still in a fast exchange limit.

The expected value for the coupling constant between protons A and C can be calculated from the following equation, if the relevant coupling constants in both conformations and the equilibrium ratio of conformers are known.

\[ J_{AC} = J'''_{AC} \cdot x + J''_{AC} \cdot (1 - x) \]

- \( J_{AC} \): average coupling constant between protons \( H_A \) and \( H_C \)
- \( J'''_{AC} \): coupling constant between protons \( H_A \) and \( H_C \) in conformation A
- \( J''_{AC} \): coupling constant between protons \( H_A \) and \( H_C \) in conformation B
- \( x \): proportion of time spent in conformation A

\[ J_{BC} = J'''_{BC} \cdot x + J''_{BC} \cdot (1 - x) \]

- \( J_{BC} \): average coupling constant between protons \( H_B \) and \( H_C \)
- \( J'''_{BC} \): coupling constant between protons \( H_B \) and \( H_C \) in conformation A
- \( J''_{BC} \): coupling constant between protons \( H_B \) and \( H_C \) in conformation B
- \( x \): proportion of time spent in conformation A

These equations can be easily rearranged to give the formula for the calculation of \( x \).
While \( J_{AC} \) and \( J_{BC} \) are experimental values, \( J_L \) and \( J_S \) can not be determined from the spectrum of the given compound, unless a slow exchange limit is reached by cooling down the solution. As the flipping of the bridge is a very facile process, this strategy could not be adopted in this work. Another possibility is to measure the appropriate coupling constants in a similar compound with an overwhelming preference for one conformer.

The coupling constants between the corresponding protons in several investigated compounds as predicted by Macromodel® are summarised in Table 8. If several energetic minima were available for the molecule because of a rotation of its functional group only the lowest minimum is listed.

Table 8: Calculated coupling constants in selected 9,10-propanoanthracenes

<table>
<thead>
<tr>
<th>Compound</th>
<th>( J_L' ) [Hz]</th>
<th>( J_S' ) [Hz]</th>
<th>( J_L'' ) [Hz]</th>
<th>( J_S'' ) [Hz]</th>
</tr>
</thead>
<tbody>
<tr>
<td>26</td>
<td>6.3</td>
<td>1.4</td>
<td>6.9</td>
<td>1.1</td>
</tr>
<tr>
<td>27</td>
<td>6.4</td>
<td>1.4</td>
<td>6.4 (6.6)*</td>
<td>1.4 (1.3)*</td>
</tr>
<tr>
<td>31</td>
<td>7.2</td>
<td>1.1</td>
<td>6.6</td>
<td>1.3</td>
</tr>
<tr>
<td>35</td>
<td>6.9</td>
<td>1.2</td>
<td>6.9</td>
<td>1.2</td>
</tr>
<tr>
<td>39</td>
<td>6.9</td>
<td>1.2</td>
<td>6.7</td>
<td>1.3</td>
</tr>
</tbody>
</table>

* the coupling constants in the second conformer of similar energy

It follows from the table that coupling constants \( J_L' \) and \( J_L'' \) (\( J_S' \) and \( J_S'' \)) are not generally equal. The functional groups introduce some twisting into the bridge and the extent of this twist is dependant on the nature of the group. The assumption of the equality would of course help us with the evaluation of the experimental spectra,
because in such a case the sum of coupling constants $J_{AC}$ and $J_{BC}$ does not depend on the actual ratio of conformers:

$$J_{AC} + J_{BC} = J'_L \cdot x + J'_S \cdot (1 - x) + J''_L \cdot x + J''_S \cdot (1 - x) = (J'_L - J''_L + J'_S - J''_S) \cdot x + (J''_L + J''_S)$$

if $J'_L = J''_L$ and $J'_S = J''_S$ then

$$J_{AC} + J_{BC} = J'_L + J'_S$$

Because the coupling constants $J_S$ vary much less than $J_L$, we could get the coupling constant $J_S$ from some reference compound which would be fixed in one conformation and the constant $J_L$ from the equation:

$$J_L = (J_{AC} + J_{BC}) - J_S$$

Several numerical experiments were therefore performed to investigate the plausibility of this approach and to assess the magnitude of errors in the estimations. The results of one of these calculations for $J'_L = 6.3$ Hz, $J'_S = 1.4$ Hz, $J''_L = 6.9$ Hz, $J''_S = 1.1$ Hz are summarised in Table 9.
Table 9: Comparison between calculated conformational ratio for $J_L' = 6.3$ Hz, $J_S' = 1.4$ Hz, $J_L'' = 6.9$ Hz, $J_S'' = 1.1$ Hz and for approximate coupling constants

<table>
<thead>
<tr>
<th>$J_{AC}$ [Hz]</th>
<th>$J_{BC}$ [Hz]</th>
<th>ratio</th>
<th>$J_L$ [Hz]</th>
<th>$J_S$ [Hz]</th>
<th>ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.81</td>
<td>1.68</td>
<td>90:10</td>
<td>6.29 (6.19)</td>
<td>1.20 (1.30)</td>
<td>91:9 (92:8)</td>
</tr>
<tr>
<td>5.32</td>
<td>2.26</td>
<td>80:20</td>
<td>6.38 (6.28)</td>
<td>1.20 (1.30)</td>
<td>80:20 (81:79)</td>
</tr>
<tr>
<td>4.83</td>
<td>2.84</td>
<td>70:30</td>
<td>6.47 (6.37)</td>
<td>1.20 (1.30)</td>
<td>69:31 (80:20)</td>
</tr>
<tr>
<td>4.34</td>
<td>3.42</td>
<td>60:40</td>
<td>6.56 (6.46)</td>
<td>1.20 (1.30)</td>
<td>59:41 (59:41)</td>
</tr>
<tr>
<td>3.36</td>
<td>4.58</td>
<td>40:60</td>
<td>6.74 (6.64)</td>
<td>1.20 (1.30)</td>
<td>39:61 (39:61)</td>
</tr>
<tr>
<td>2.87</td>
<td>5.16</td>
<td>30:70</td>
<td>6.83 (6.73)</td>
<td>1.20 (1.30)</td>
<td>30:70 (29:31)</td>
</tr>
<tr>
<td>2.38</td>
<td>5.74</td>
<td>20:80</td>
<td>6.92 (6.82)</td>
<td>1.20 (1.30)</td>
<td>21:79 (20:80)</td>
</tr>
<tr>
<td>1.89</td>
<td>6.32</td>
<td>10:90</td>
<td>7.01 (6.91)</td>
<td>1.20 (1.30)</td>
<td>12:88 (11:89)</td>
</tr>
</tbody>
</table>

Inspection of the table reveals that this approach is indeed plausible the maximum error being three units. The experimental data indicate that this calculated example has probably higher discrepancies between values of $J_L$ and $J_S$ then the real systems and so it presents the upper error estimation.

Alcohols 26 and 27 provided us with the standard. The conformer with the hydroxyl group pointing away from the ring is much more energetically favourable then the other one in alcohol 26, the opposite is true for alcohol 27. The values $J_S$ were therefore assigned to be either 1.2 Hz ($J_{AC} + J_{BC} > 8.0$ Hz) or 1.3 Hz ($J_{AC} + J_{BC} \leq 8.0$ Hz).
Appendix 3: Determination of Energy Difference between Conformers

If the ratio of conformers is known, difference in their energy at given temperature can be calculated according to the following equation:

\[ \Delta G = RT \ln K \]

\( \Delta G \)...........energy difference between conformers (J mol\(^{-1}\))

\( R \).............universal gas constant \((R = 8.314 \text{ J K}^{-1}\text{mol}^{-1})\)

\( T \).............temperature (K)

\( K \)............equilibrium constant

A correlation chart which was constructed according to this equation is depicted in Figure 30.

The estimation of the error in the measurement of conformation equilibria is rather difficult, but after several calculations of these values with slightly changed parameters of \( J_L \) and \( J_S \) as well as \( J_{AC} \) and \( J_{BC} \) it can be quite safely concluded that the error margin is smaller than three points in the determination of the equilibrium. It means that e.g. in the case of a calculated value 72:28, these margins are from 69:31 to 75:25.

The effect which an error in the determination of equilibrium constants can have on the precision of the calculated energetic differences strongly depends on the value of the equilibrium constant as demonstrated in Figure 31. This graph compares \( \Delta G \) for given ratio of conformers \( x : y \) with the one for ratio \((x+1) : (y-1)\). So, e.g. the difference between ratios 61:39 and 60:40 amounts to only 0.1 kJ mol\(^{-1}\), while the difference between ratios 91:9 and 90:10 is 0.3 kJ mol\(^{-1}\).
Correlation chart between ratio of conformers and difference in their energy at 293 K

Figure 30
The correlation chart between conformational ratios and energy differences

Figure 31
Appendix 4: Molecular structures of compounds mentioned in chapters 2.4 and 2.5.

Benzenoanthracenes:
Propanoanthracenes:
Chapter Three

Experimental
General Procedures.

$^1$H NMR spectra were recorded at 400 MHz on a Varian VXR-400 instrument and at 200 MHz on a Varian XL-200 instrument. The residual protic solvent was taken as an internal standard. $^{13}$C NMR spectra were recorded at 100.6 MHz and the $^{19}$F NMR spectrum at 376.3 MHz on a Varian VXR-400 instrument. The fluorine spectrum was referenced toward fluorotrichloromethane. The solutions for NOE measurements were degassed via four "freeze-pump-thaw" cycles viz., the NMR tube was immersed into a liquid nitrogen bath under a static nitrogen atmosphere and then placed under oil pump vacuum for 1 min. When the solution froze, it was left to thaw under the nitrogen atmosphere. The spectra (4000 - 6000 datapoints) were acquired with the decoupler off during acquisition, and using 90° transmitter pulse width. The irradiation frequencies were changed after 16 scans; two scans without acquisition were performed after each change. The time of irradiation varied from 4 to 6 seconds and ca. 100 transients were usually acquired before difference spectra were calculated. Spin simulations were performed with the program LAME, available in a software package for the VXR-400 instrument. Carbon types were distinguished on the basis of APT experiments.

Infrared spectra were recorded on a FT-IR Perkin-Elmer 1605 spectrometer at ± 2 cm$^{-1}$ resolution. Elementary analyses were performed by University College Chemistry Department microanalytical laboratory. Melting points were taken on a Reichert hot stage and are uncorrected. Mass spectra were recorded on a VG ZAB instrument under electron impact, chemical ionisation and fast atom bombardment conditions. In the spectra of polychlorinated compounds only the most intense peak in the isotopic cluster is quoted, except in the case of the molecular ion.

Petrol refers to light petroleum ether (b.p. 40-60 °C) which was distilled before use. Diethyl ether, THF, toluene and benzene were distilled under nitrogen from sodium benzophenone-ketyl. DCM, chloroform, and tetrachloromethane were distilled under nitrogen from phosphorous pentoxide. DMSO, DMF and chlorotrimethylsilane
were distilled from calcium hydride at reduced pressure and stored over 4 Å molecular sieves. Triethylamine and pyridine were distilled from potassium hydroxide and stored over potassium hydroxide. 1,4-Dioxane was distilled from lithiumhydride. Methanol was distilled from magnesium methoxide. 2-Mercaptoethanol was distilled from 4 Å molecular sieves. Acrolein (90% water solution) was dried with anhydrous copper sulfate and distilled. A solution of 1,2-diiodoethane in DCM was washed with a water solution of sodium thiosulfate, and DCM evaporated in vacuo prior to use. P-Toluenesulfonic acid was dried at 120 °C under vacuum. Zinc dust was acid washed and dried under vacuum. Preparative column chromatography was performed at low positive pressure on Merck Kieselgel 60 (230-400 mesh). Preparative column chromatography was performed at low positive pressure on Merck Kieselgel 60.

Analytical thin layer chromatography was performed on pre-coated glass backed plates (Merck Kieselgel 60 F\textsubscript{254}) and visualized with ultraviolet light (245 nm), iodine, potassium permanganate [add 62.5 g Na\textsubscript{2}CO\textsubscript{3} in water (1.25 l) to 12.5 g KMnO\textsubscript{4} in water (1.25 l)], acidic ammonium molybdate (IV) [conc. H\textsubscript{2}SO\textsubscript{4} (250 ml), ammonium molybdate tetrahydrate, water (2.25 l)].

Water sensitive reactions were carried out in flame-dried glassware under a nitrogen atmosphere. The ultraviolet light was provided by an Osram 400W medium pressure lamp.
Preparation\textsuperscript{5} of 9,10,11,12,13,14-hexahydro-9,10[1',4']-benzenoanthracene (5)

A solution of anthracene (2g, 11 mmol) and cyclohexadiene (15ml) in benzene (400ml) was irradiated for 15h with ultraviolet light. Benzene was evaporated \textit{in vacuo}. Purification of the residue by flash chromatography (silica gel; petrol-0.5% AcOEt) gave 9,10,11,12,13,14-hexahydro-9,10[1',4']-benzenoanthracene 5 (2.1g) as yellow crystals, which were recrystallised from diethyl ether to give white crystals (1.4g). An analytic sample was recrystallised from AcOEt/petrol.

m.p. = 204-204.5 °C (AcOEt / petrol); lit\textsuperscript{5} 197-200°C

ν\textsubscript{max} (CHCl\textsubscript{3}) 3071m, 3039s, 2939s, 2870m, 1473s, 1462m, 1455s cm\textsuperscript{-1}

ν\textsubscript{max} (KBr) 3065w, 3035s, 2952s, 2865m, 1470s, 1453s, 769m, 747s, 721s, 666s, 624s cm\textsuperscript{-1}

δ\textsubscript{H} (400 MHz, CDCl\textsubscript{3}) 7.07-7.21 (8H, m, H-ar.), 5.67-5.70 (2H, m, H-15,16), 4.22 (2H, d, H-9, 10), 3.14-3.18 (2H, m, H-11,14), 1.38-1.54 (4H, m, H-12,13)

assigned couplings: J\textsubscript{9,14} = J\textsubscript{10,11} = 11.1 Hz

δ\textsubscript{C} (100.6 MHz, CDCl\textsubscript{3}) 145.01d, 144.76d, 134.05u (C-15,16), 128.10u, 126.14u, 125.58u, 125.38u, 51.89u (C-9,10), 40.33u (C-11,14), 24.90d (C-12,13)
Preparation of 9,10,11,12,13,14,15,16-octahydro-9,10[1',4']-benzenoanthracene (6)

A solution of 9,10,11,12,13,14-hexahydro-9,10[1',4']-benzenoanthracene 5 (78mg, 0.30 mmol) in DCM (10ml) was stirred for 2h with palladium on charcoal (10%) (19mg). The catalyst was filtered off and DCM was removed in vacuo. Purification of the residue by flash chromatography (silica gel; petrol-0.5%AcOEt) gave 9,10,11,12,13,14,15,16-octahydro-9,10[1',4']-benzenoanthracene 6 (65mg, 84 %) as white crystals.

m.p. = 234-235 °C

νmax (CHCl₃) 3071w, 2939s, 2920s, 2863m, 1489w, 1476s, 1455s cm⁻¹
νmax (KBr) 3065w, 3013w, 2947s, 2936s, 2899s, 2861s, 1473s, 1452s, 767s, 744s, 712s cm⁻¹

δH (400 MHz, CDCl₃) 7.21-7.26 (4H, m, H-1,4,5,8), 7.12-7.17 (4H, m, H-2,3,6,7), 4.24 (2H, d, H-9,10), 2.76 (2H, m, H-11,14), 1.24-1.32 (8H, m, H-12,13,15,16)

assigned couplings: J₉,₁₄ = J₁₀,₁₁ = 11.2 Hz

δC (100.6 MHz, CDCl₃) 144.58d, 127.47u, 125.35u, 50.12u (C-9,10), 38.82u (C-11,14), 24.61d (C-12,13,15,16)

m/z (El) 260 (M⁺, 4%), 179 (85), 178 (100), 176 (37), 152 (18), 151 (14), 86 (11), 84 (18), 81 (10), 56 (10), 50 (12), 47 (28), 38 (15), 36 (11)
Preparation of \textit{exo}-12,13-epoxy-9,10,11,14,15,16-hexahydro-9,10[1',4']-benzenoanthracene (7)

3-Chloroperoxybenzoic acid (Aldrich; 50-60\%\%) (0.8 g) was added as a single portion to a stirred solution of 9,10,11,12,13,14-hexahydro-9,10[1',4']-benzenoanthracene 5 (0.3 g, 1.2 mmol) in DCM (50 ml). After 2 h, the reaction mixture was poured into a solution of sodium thiosulfate and extracted with DCM (3x). The combined dichloromethane extracts were washed with a solution of sodium bicarbonate, brine, and then dried (\(\text{MgSO}_4\)) before being concentrated \textit{in vacuo}. Purification of the residue by flash chromatography (silica gel; petrol-4\%AcOEt) gave \textit{exo}-12,13-epoxy-9,10,11,14,15,16-hexahydro-9,10[1',4']-benzenoanthracene 7 (0.22 g, 67\%) as white crystals. An analytical sample was recrystallised from ethanol.

\textit{m.p.} = 238-240 °C (ethanol)

\(v_{\text{max}}\) (CHCl\(_3\)) 3071w, 3020s, 2940s, 2866w, 1488m, 1474s, 1463s, 1440w, 1433w, 983s cm\(^{-1}\)

\(v_{\text{max}}\) (KBr) 3063w, 3031w, 2956m, 2937s, 1473s, 1459m, 979s, 847s, 817s, 781s, 761s, 728s 587s cm\(^{-1}\)

\(\delta_H\) (400 MHz, CDCl\(_3\)) 7.28 (2H, m, H-1,4), 7.21 (2H, m, H-5,8), 7.16 (2H, m, H-2,3), 7.12 (2H, m, H-6,7), 4.32 (2H, d, H-9,10), 3.00-3.03 (2H, m, H-11,14), 2.62-2.63 (2H, m, H-12,13), 1.46-1.50 (2H, m, H-15\textit{exo}, 16\textit{exo}), 0.94-0.99 (2H, m, H-15\textit{endo}, 16\textit{endo})

assigned couplings: \(J_{9,14} = J_{10,11} = 11.0 \text{ Hz}\)

decoupling experiments: irradiation frequency (changed signals): 4.32 (3.02); 3.02 (4.32, 1.48, 0.96)

NOE: irradiation frequency (NOE): 2.62 (7.28, 4.32, 3.02); 0.96 (7.21, 3.02, 1.48)
Experimental : benzenoanthracenes

δC (100.6 MHz, CDCl₃) 144.07d, 142.44d, 128.06u, 126.80u, 126.07u, 125.76u, 56.02u (C-12,13), 48.44u (C-9,10), 38.29u (C-11,14), 22.02d (C-15,16) m/z (EI) 274 (M⁺, 6%), 215 (11), 202 (20), 191 (21), 179 (79), 178 (100), 165 (11), 152 (32), 139 (6), 96 (15) Found: C, 87.31; H, 6.58. C₂₀H₁₈O requires C, 87.54; H, 6.61%.

Preparation of \textit{exo}-9,10,11,13,14,15,16-heptahydro-12-hydroxy-9,10[1',4']-benzenoanthracene (9)

\begin{center}
\includegraphics[width=0.5\textwidth]{diagram}
\end{center}

A 1M solution of borane (1.8mmol) in THF was added dropwise over 5 min to a stirred solution of 9,10,11,12,13,14-hexahydro-9,10[1',4']-benzenoanthracene 5 (0.40g, 1.4mmol) in THF at -78 °C. The mixture was stirred for 20 min at -78 °C, then slowly warmed up to room temperature and stirred for another hour. A solution of hydrogen peroxide (3ml) and sodium carbonate (0.4g) in water (10ml) was added at once and after 30 min sodium sulphite was added. The mixture was diluted with water and extracted with diethyl ether (3x). The combined organic extracts were washed with brine, dried (MgSO₄) and evaporated \textit{in vacuo}. Purification of the residue by flash chromatography on silica gel (petrol-20%AcOEt) gave \textit{exo}-9,10,11,13,14,15,16-heptahydro-12-hydroxy-9,10[1',4']-benzenoanthracene 9 (0.22g, 51%) as white crystals. m.p. = 182-185 °C

ν\textsubscript{max} (CCl₄) 3625w (multiplet), 3070w, 3023w, 2923s, 1476s, 1463m, 1456s, 1002s cm\(^{-1}\)
ν\textsubscript{max} (CHCl₃) 3609m, 3454w (disappears upon dilution), 3070m, 3010s, 2939s, 2923s, 2913s, 2868m, 1476s, 1456s, 1001s cm\(^{-1}\)
Experimental: benzoanthracenes

$\nu_{max} (CS_2)$ 3612w, 3609w, 3606w, 3602w, 3599w, 3067w, 3019w, 2919s, 1004m, 761s, 745s, 718s cm$^{-1}$

$\nu_{max}$ (pyridine) 3397 (broad) cm$^{-1}$

$\nu_{max}$ (KBr) 3557s, 3064s, 3021s, 2955s, 2857s, 1474s, 1454s, 1240m, 1009s, 762s, 746s, 721s, 598s cm$^{-1}$

$\delta_H$ (400 MHz, CDCl$_3$) 7.12-7.21 (8H, m, H-1-8), 4.30 (1H, d, H-10), 4.16 (1H, d, H-9), 3.67-3.70 (1H, m, H-12), 2.77-2.82 (1H, m, H-14), 2.64-2.69 (1H, m, H-11), 1.75-1.83 (1H, m, H-13$^{endo}$), 1.65-1.74 (1H, m, H-16$^{exo}$), 1.60 (1H, bs, OH), 1.37-1.46 (1H, m, H-15), 1.22-1.32 (1H, m, H-15), 1.13-1.18 (1H, m, H-16$^{endo}$), 1.09-1.14 (1H, m, H-13$^{exo}$)

assigned couplings: $J_{10,11} = 11.8$ Hz, $J_{9,14} = 11.5$ Hz, $J_{12,13-end} = 9.3$ Hz, $J_{11,12} = J_{12,13-exo} = 2$–2.5 Hz, $J_{12,16-end} = 3.1$ Hz, $J_{13-end},13-exo = 14.9$ Hz, $J_{13-exo},14 = 5.3$ Hz

decoupling experiments: irradiation frequency (changed signals): 4.30 (2.66), 4.16 (2.79), 3.69 (2.67, 1.80, 1.16, 1.11), 2.79 (4.16, 1.80, 1.41, 1.27, 1.11), 2.66 (4.30, 1.80, 1.69)

NOE: 3.68 (2.66, 1.80)

$\delta_C$ (100.6 MHz, CDCl$_3$) 144.95d, 144.77d, 143.38d, 142.87d, 127.77u, 127.63u, 127.48u, 127.38u, 125.67u, 125.56u, 125.49u, 125.42u, 67.67u (C-12), 49.73u, 48.23u, 46.79u, 38.06u (C-14), 36.15d (C-13), 23.90d (C-15), 17.67d(C-16)

m/z (EI) 276 (M$^+$, 22%), 258 (2), 215 (7), 202 (14), 191 (16), 179 (100), 178 (100), 165 (8), 152 (24), 139 (5), 115 (5), 97 (14)

Found: C, 86.82; H, 7.31. C$_{20}$H$_{20}$O requires C, 86.92; H, 7.29%.
Experimental: benzenoanthracenes

Preparation of 9,10,11,13,14,15,16-heptahydro-9,10[1',4']-benzenoanthracene-12-one (8) from exo-12,13-epoxy-9,10,11,14,15,16-hexahydro-9,10[1',4']-benzenoanthracene (7)

A 2.5M solution of butyllithium (0.5mmol) in hexanes was added dropwise over 3 min. to a stirred solution of exo-12,13-epoxy-9,10,11,14,15,16-hexahydro-9,10[1',4']-benzenoanthracene 7 (30 mg, 0.11mmol) in heptane (5 ml) and diethyl ether (9 ml) at -78 °C. After 10 min., the mixture was warmed to room temperature and stirred for 20 h. The solution was then poured into water and extracted with DCM (3x), washed with brine, dried (MgSO₄) and evaporated in vacuo. Purification of the residue by flash chromatography (silica gel; petrol-20%AcOEt) gave 9,10,11,13,14,15,16-heptahydro-9,10[1',4']-benzenoanthracene-12-one 8 (10 mg, 33%) as light yellow crystals (ca.90% purity by 1H NMR, a further purification was difficult due to a presence of several by-products).

Preparation of 9,10,11,13,14,15,16-heptahydro-9,10[1',4']-benzenoanthracene-12-one (8) from exo-9,10,11,13,14,15,16-heptahydro-12-hydroxy-9,10[1',4']-benzenoanthracene (9)

A solution of exo-9,10,11,13,14,15,16-heptahydro-12-hydroxy-9,10[1',4']-benzenoanthracene 9 (45 mg, 0.16mmol) in DCM (5 ml) was added at once to a stirred
Experimental: benzenoanthracenes

A suspension of PCC (53mg, 0.24mmol) in DCM (5ml). Diethyl ether was added after 2h and the solid was filtered off and thoroughly washed with DCM. The filtrate was evaporated in vacuo. Purification of the residue by flash chromatography on silica gel (petrol-20% AcOEt) gave 9,10,11,13,14,15,16-heptahydro-9,10[1',4']-benzenoanthracene-12-one 8 (31mg, 70%) as white crystals.

Preparation of 2-(1,3-cyclohexadienyloxy)-trimethylsilane (10)

Diisopropylamine (15.5ml, 0.11mol) and a 2.5M solution of butyllithium (0.11mol) in hexanes were added to THF (200ml) cooled with an ice-methanol bath and stirred for 10 min. 2-Cyclohexenone was added dropwise over 7 min, and the mixture stirred for 10 min, then trimethylsilyl chloride was added, the cooling bath removed and the mixture stirred for 2.5 h. THF was then partially evaporated in vacuo, petrol (300ml) was added and the solution washed with a saturated solution of sodium bicarbonate (2x30ml; cooled to 0°C). The filtrate was dried (MgSO₄) and evaporated in vacuo. Distillation of the residue gave 2-(1,3-cyclohexadienyloxy)-trimethylsilane 10 (16g, 91%).

b.p. = 54-60 ºC / 7torr; lit. b.p. = 56-58 ºC / 6torr

ν_max (neat) 3048w, 2959m, 2937m, 2825m, 1649s, 1401s, 1251s, 1199s, 911s, 845s cm⁻¹
 δ_H (400 MHz, CDCl₃) 5.85 (1H, m, H-4), 5.69 (1H, m, H-3), 4.88 (1H, m, H-1), 2.08-2.19 (4H, m, H-5, 6), 0.20 (9H, s, Si-(CH₃)₃)
Preparation of 9,10,11,13,14,15,16-heptahydro-9,10[1',4']-benzeno anthracene-12-one (8) from anthracene and 2-(1,3-cyclohexadienyloxy)-trimethylsilane (10)

A photochemical vessel was charged with 2-(1,3-cyclohexadienyloxy)trimethylsilane (10) (13.6g, 81mmol), anthracene (2.5g, 14 mmol) and benzene (400ml) and irradiated for 17h with ultraviolet light at 30°C. Some white crystals were deposited on the bottom of the reaction vessel after the irradiation. Benzene was evaporated in vacuo, then diene 10 was removed by distillation (7g) and the remaining yellow oil was dissolved in DCM and stirred with an aqueous solution of NaF (1.7g). The aqueous phase was extracted with DCM (3x), the combined extracts were washed with brine, dried (MgSO₄) and evaporated in vacuo. Purification of the residue by flash chromatography (silica gel, gradient elution; petrol-10% AcOEt → petrol-20% AcOEt) gave 9,10,11,13,14,15,16-heptahydro-9,10[1',4']-benzeno anthracene-12-one 8 (2 g, 70%) as light yellow crystals of ca. 90% purity by ¹H NMR. These crystals were recrystallised from ethanol to give white crystals (1.5g). Analytical sample was recrystallised from ethyl acetate.

m.p. = 198-198.5 °C (ethyl acetate)

$\nu_{\text{max}}$ (CHCl₃) 3011m, 2942m, 2872w, 1707s, 1476m, 1455w, 1401w, 1118w cm⁻¹

$\nu_{\text{max}}$ (KBr) 3044w, 2965m, 2940m, 2866m, 1709s, 1476s, 1450s, 1396s, 767s, 756s, 744s cm⁻¹
Experimental: benzenoanthracenes

$\delta_{H}$ (400 MHz, CDCl$_3$) 7.15-7.32 (8H, m, H-ar.), 4.40 (1H, d, H-9), 4.36 (1H, d, H-10), 3.30 (1H, dt, H-11), 3.02-3.07 (1H, m, H-14), 1.82-1.95 (2H, m, H-13), 1.53-1.61 (2H, m, H-16), 1.36-1.42 (2H, m, H-15)

assigned couplings: $J_{9,14} = 11.5$ Hz, $J_{10,11} = 12.0$ Hz
decoupling experiments: irradiation frequency (changed signals): 3.30 (4.36, 1.57), 3.05 (4.40, 1.88, 1.39), 1.57 (3.30, 1.39)

$\delta_{C}$ (100.6 MHz, CDCl$_3$) 214.47d (C-12), 144.54d, 141.72d, 141.06d, 140.6d, 128.56u, 127.81u, 127.48u, 127.40u, 126.99u, 126.86u, 126.37u, 125.92u, 55.38u, 49.02u, 47.19u, 42.47d (C-13), 35.72u (C-14), 23.69d, 22.25d

m/z (El) 274 (M+, 14%), 215 (9), 203 (23), 202 (30), 191 (40), 189 (28), 179 (71), 178 (100), 176 (68), 165 (20), 152 (65), 139 (15), 126 (14), 115 (14), 89 (13), 76 (12), 68 (24), 55 (73)

Found: C, 87.61; H, 6.68. C$_{20}$H$_{18}$O requires C, 87.54; H, 6.61%.

Preparation of endo-9,10,11,13,14,15,16-heptahydro-12-hydroxy-9,10[1',4']-benzenoanthracene (12)

A 1.5M solution of diisobutylaluminum hydride (1 ml, 1.5 mmol) in toluene was added over 1 min to a solution of 9,10,11,13,14,15,16-heptahydro-9,10[1',4']-benzenoanthracene-12-one (8) (0.32g, 1.2mmol) in benzene (40 ml). The mixture was stirred 2h, then poured into an aqueous solution of ammonium chloride. The aqueous phase was extracted with diethyl ether (3x). The combined organic extracts were washed with brine, dried (MgSO$_4$) and evaporated in vacuo. Purification of the residue by flash chromatography on silica gel (petrol-20%AcOEt) gave endo-.
9,10,11,13,14,15,16-heptahydro-12-hydroxy-9,10[1',4']-benzenoanthracene 12 (0.25g, 78%) as white crystals, the analytic sample was sublimed to give white crystals.
m.p. = 233-234 °C. (sublimation)
\( \nu_{\text{max}} (\text{CCl}_4) 3577 \text{s}, 3071 \text{w}, 3023 \text{w}, 2924 \text{s}, 2864 \text{m}, 1475 \text{s}, 1463 \text{s}, 1403 \text{m}, 1075 \text{s}, 1054 \text{s} \text{ cm}^{-1} \)
\( \nu_{\text{max}} (\text{CHCl}_3) 3563 \text{m} \text{ (no change upon dilution)}, 3071 \text{w}, 3011 \text{s}, 2936 \text{s}, 2866 \text{m}, 1475 \text{s}, 1455 \text{s}, 1406 \text{m}, 1074 \text{s}, 1051 \text{s} \text{ cm}^{-1} \)
\( \nu_{\text{max}} (\text{CS}_2) 3576 \text{m} \text{ (singlet)}, 3068 \text{w}, 3021 \text{w}, 2919 \text{s}, 2859 \text{w}, 1074 \text{s}, 1053 \text{s}, 751 \text{s}, 714 \text{s} \text{ cm}^{-1} \)
\( \nu_{\text{max}} (\text{pyridine}) 3567 \text{ (sharp)}, 3303 \text{ (broad) cm}^{-1} \)
\( \nu_{\text{max}} (\text{KBr}) 3582 \text{s}, 3064 \text{w}, 3014 \text{w}, 2959 \text{s}, 2926 \text{s}, 2862 \text{m}, 1473 \text{s}, 1452 \text{s}, 1077 \text{m}, 1051 \text{m}, 1029 \text{m}, 759 \text{s}, 752 \text{s}, 712 \text{s} \text{ cm}^{-1} \)
\( \delta_H (400 \text{ MHz, CDCl}_3) 7.44-7.48 \text{ (1H, m, H-4)}, 7.12-7.28 \text{ (7H, m, H-1,2,3,5,6,7,8)}, 4.29 \text{ (1H, d, H-10)}, 4.29 \text{ (1H, d, H-9)}, 3.72 \text{ (1H, m, H-12)}, 2.95-3.01 \text{ (1H, m, H-11)}, 2.83-2.89 \text{ (1H, m, H-14)}, 2.01 \text{ (1H, ddd, H-13\text{exo})}, 1.12-1.28 \text{ (4H, m, H-15,16)}, 1.04 \text{ (1H, d, OH)}, 0.99-1.06 \text{ (1H, m, H-13\text{endo})} \)
assigned coupling: \( J_{9,14} = 11.5 \text{ Hz}, J_{10,11} = 11.2 \text{ Hz}, J_{12,13\text{-exo}} = 10.8 \text{ Hz}, J_{12,13\text{-endo}} = 5.3 \text{ Hz}, J_{11,12} = 4.8 \text{ Hz}, J_{13\text{-exo}, 13\text{-endo}} = 15.3 \text{ Hz}, J_{13\text{-endo}, 15\text{-endo}} = 2.1 \text{ Hz}, J_{13\text{-exo}, 14} = 6.5 \text{ Hz}, J_{12,\text{OH}} = 11.5 \text{ Hz} \)
decoupling experiments: irradiation frequency (changed signals): 3.72 (2.98, 2.01, 1.04, 0.99-1.06), 2.99 (4.29, 3.72, 1.12-1.28), 2.86 (4.29, 2.01, 1.12-1.28, 0.99-1.06)
NOE: 7.46 (7.20, 4.29, 1.04), 3.72 (2.98, 2.01), 2.01 (3.72, 2.86, 0.99-1.06), 1.03 (7.46, 2.01)
\( \delta_C (100.6 \text{ MHz, CDCl}_3) 145.79 \text{d}, 144.56 \text{d}, 143.78 \text{d}, 142.78 \text{d}, 128.08 \text{u}, 128.02 \text{u}, 127.19 \text{u}, 127.04 \text{u}, 126.83 \text{u}, 126.36 \text{u}, 125.69 \text{u}, 125.65 \text{u}, 71.75 \text{u} \text{ (C-12)}, 50.04 \text{u}, 47.51 \text{u}, 46.01 \text{u}, 39.06 \text{u} \text{ (C-14)}, 37.32 \text{d} \text{ (C-13)}, 24.90 \text{d}, 23.05 \text{d} \)
m/z (FAB) 275 (M\text{+}, 5%), 259 (11), 258 (14), 191 (15), 179 (63), 178 (70), 165 (14), 149 (52), 55 (100)
Found: C, 86.59; H, 7.31. C\text{20}H\text{20}O requires C, 86.92; H, 7.29%.
Preparation of *endo*-12-acetoxy-9,10,11,13,14,15,16-heptahydro-9,10[1',4']-benzenoanthracene (13)

A solution of *endo*-9,10,11,13,14,15,16-heptahydro-12-hydroxy-9,10[1',4']-benzenoanthracene 12 (62mg, 0.22mmol), 4-(dimethylamino) pyridine (37mg, 30mmol) and acetic anhydride (0.050ml, 53mmol) in DCM (20ml) was stirred for 24h. The reaction mixture was then poured into water and extracted with DCM (3x), the combined organic extracts were washed with sodium bicarbonate and brine, dried (MgSO₄) and evaporated *in vacuo*. Purification of the residue by flash chromatography on silica gel (petrol-5%AcOEt) gave the *endo*-12-acetoxy-9,10,11,13,14,15,16-heptahydro-9,10[1',4']-benzenoanthracene 13 (55 mg, 77%) as a colourless oil, which crystallised upon standing.

m.p. = 144-147°C

\( \nu_{\text{max}} (\text{CHCl}_3) \) 3071w, 3011m, 2868w, 1717s, 1476m, 1465w, 1456m, 1384w, 1368m, 1263s, 1244s, 1032m cm\(^{-1}\)

\( \nu_{\text{max}} (\text{KBr}) \) 3073w, 3042w, 2961m, 2936m, 2869w, 1728s, 1719s, 1474w, 1253s, 1026s, 762m, 745m, 722s cm\(^{-1}\)
Experimental: benzenoanthracenes

\( \delta_H (400 \text{ MHz}, \text{CDCl}_3) 7.35-7.38 (1\text{H, m, H-4}), 7.24-7.27 (1\text{H, m, H-1}), 7.10-7.19 (6\text{H, m, H-2,3,5,6,7,8}), 4.72 (1\text{H, dt, H-12}), 4.25 (1\text{H, d, H-9}), 4.23 (1\text{H, d, 11.2 Hz, H-10}), 2.98-3.02 (1\text{H, m, H-11}), 2.82-2.85 (1\text{H, m, H-14}), 1.97 (1\text{H, ddd, H-13}^{\text{endo}}), 1.85 (3\text{H, s, O-CO-CH}_3), 1.18-1.32 (4\text{H, m, H-15,16}), 1.10-1.15 (1\text{H, m, H-13}^{\text{endo}}) \)

assigned coupling: \( J_{9,14} = 11.5, J_{10,11} = 11.2, J_{12,13}^{\text{endo}} = 10.6 \text{ Hz, } J_{12,13}^{\text{exo}} = 5.3 \text{ Hz, } J_{11,12} = 5.2 \text{ Hz, } J_{13,13}^{\text{exo}}, J_{13,13}^{\text{endo}} = 15.1 \text{ Hz, } J_{13,13}^{\text{endo}}, J_{15,15}^{\text{endo}} = 2.9 \text{ Hz, } J_{13,13}^{\text{exo}}, J_{14,14} = 6.5 \text{ Hz} \)

decoupling experiments: irradiation frequency (changed signals): 3.00 (4.72, 4.23, 1.25), 2.84 (4.25, 1.97, 1.25, 1.13)

NOE: irradiation frequency (NOE): 7.37 (7.13, 4.25 or 4.23, 1.85), 4.72 (3.00, 1.97), 1.97 (4.72, 2.83, 1.12), 1.85 (7.37, 7.13)

\( \delta_C (100.6 \text{ MHz}, \text{CDCl}_3) 170.52 \text{d (O-CO-CH}_3) , 144.69 \text{d, 144.51d, 144.09d, 143.14d, 129.36u, 128.00u, 126.90u, 126.52u, 125.75u, 125.56u, 125.51u, 124.82u, 73.44u (C-12), 49.90u, 47.66u, 42.74u, 38.49u, 33.24d (C-13), 24.15u, 23.05d, 21.32u (O-CO-CH}_3) \)

m/z (EI) 318 (M\(^+\), 5\%), 258 (46), 217 (14), 191 (8), 179 (85), 178 (99), 167 (9), 149 (28), 140 (13), 111 (12), 97 (41), 81 (27), 71 (34), 69 (32), 56 (64), 54 (44), 41 (100), 38 (46)

Found: C, 82.66; H, 7.15. C\(_{22}\)H\(_{22}\)O\(_2\) requires C, 82.99; H, 6.96%.

Preparation of \textit{exo-12-acetoxy-9,10,11,13,14,15,16-heptahydro-9,10[1',4']-benzenoanthracene (14) \[ \text{C}_{22}\text{H}_{22}\text{O}_{2} \]}

A solution of \textit{endo-9,10,11,13,14,15,16-heptahydro-12-hydroxy-9,10[1',4']-benzenoanthracene 9 (50mg, 0.18mmol), 4-dimethylamino pyridine (31mg, 25mmol)
and acetic anhydride (0.045ml, 47mmol) in DCM (12ml) was stirred for 24h. The reaction mixture was then poured into water and extracted with DCM (3x), the combined organic extracts were washed with sodium bicarbonate and brine, dried (MgSO₄) and evaporated in vacuo. Purification of the residue by flash chromatography on silica gel (petrol-10% AcOEt) gave the ketone 8 (44 mg, 75%) as a colourless oil, which crystallised upon standing.

m.p. = 110-113 °C

ν_max (CHCl₃) 3072w, 3023m, 2940m, 2866w, 1722s, 1477m, 1464m, 1456m, 1381w, 1367m, 1020m, 973w cm⁻¹

ν_max (KBr) 3068w, 3000w, 2956m, 2944m, 2912m, 2870w, 1726s, 1476w, 1456w, 1437w, 1378m, 1366m, 1254s, 1244s, 1019s, 771s, 747m, 728s cm⁻¹

δ_H (400 MHz, CDCl₃) 7.34-7.37 (1H, m, H-4), 7.20-7.24 (3H, m, H-1, 5, 8), 7.12-7.18 (4H, m, H-2, 3, 6, 7), 4.61-4.65 (1H, m, H-12), 4.33 (1H, d, H-10), 4.18 (1H, d, H-9), 2.75-2.84 (2H, m, H-11, 14), 1.94 (3H, s, CO-CH₃), 1.75-1.83 (1H, m, H-13_endo), 1.53-1.63 (1H, m, H-16exo), 1.35-1.44 (1H, m, H-15exo), 1.24-1.33 (1H, m, H-15_endo), 1.15-1.21 (1H, m, H-13exo), 1.08-1.14 (1H, m, H-16_endo)

assigned couplings: J₁₁₃_endo,₁₃_exo = 15.3 Hz, J₁₀,₁₁ = 11.9 Hz, J₉,₁₄ = 11.5 Hz, J₁₂,₁₃_endo = 9.3 Hz, J₁₃_endo,₁₅_endo = 3.2 Hz, J₁₁,₁₂ ≡ J₁₂,₁₃_endo ≡ J₁₂,₁₆_endo ≡ 2-2.5 Hz, J₁₃_endo,₁₄ ≡ 3.2 Hz
decoupling experiments: irradiation frequency (changed signals): 4.63 (2.80, 1.78, 1.18, 1.11); 1.78 (4.63, 2.80, 1.28, 1.18)

NOE: irradiation frequency (NOE): 7.35 (4.33), 4.63 (7.35, 1.78), 1.55 (2.80, 1.11)

δ_C (100.6 MHz, CDCl₃) 170.50d (O-CO-CH₃), 144.75d (two carbons), 143.26d, 142.35d, 128.11u, 127.78u, 127.39u, 126.12u (two carbons), 125.70u, 125.59u, 71.50u (C-12), 49.70 u (C-9 or C-10), 47.99u (C-9 or C-10), 43.21u (C-11 or C-14), 37.85u (C-11 or C-14), 33.13d (C-13), 23.85d (C-15), 21.51u (O-CO-CH₃), 18.54d (C-16)
m/z (EI) 318 (M⁺, 44%), 258 (8), 217 (4), 179 (49), 178 (100), 140 (6), 97 (8), 81 (10), 56 (8), 41 (34)

Found: C, 82.72; H, 7.01. C₂₂H₂₂O₂ requires C, 82.99; H, 6.96%.
Preparation of 9,10-dihydro-9,10-propanoanthracen-12-one (15) from anthracene and tetrabromoacetone

\[
\text{\begin{align*}
\text{\includegraphics[width=0.5\textwidth]{anthracene+tetrabromoacetone.png}}
\end{align*}}
\]

A three-necked flask was charged with anthracene (5g, 28 mmol) and 1,4-dioxane (70 ml) and heated to 85°C. When anthracene had dissolved, zinc dust (7g, 112 mmol) and copper(I)chloride (1.2 g, 11.2 mmol) were added. The mixture was stirred for 10 min., then chlorotrimethylsilane (7ml, 56 mmol) was added as a single portion. A solution of 1,1,3,3-tetrabromoacetone (20.9 g, 56 mmol) in 1,4-dioxane (15 ml) was added dropwise over 1h. The mixture was stirred for 6h at 85°C, then the zinc was removed by filtration and the residue evaporated \textit{in vacuo} to give a dark red oil. The oil was chromatographed twice (silica gel, DCM) to give yellow crystals (0.48g) that contained a substantial amount of a polymer. Their sublimation gave slightly impure white crystals (0.18g) of 9,10-dihydro-9,10-propanoanthracen-12-one 15.

Preparation of 2-bromo-2-propenal (18)

\[
\text{\begin{align*}
\text{\includegraphics[width=0.5\textwidth]{acrolein+bromine.png}}
\end{align*}}
\]

A solution of bromine(38ml, 0.74 mol) in tetrachloromethane (60 ml) was added dropwise to a stirred solution of acrolein (50 ml, 0.74 mol) in tetrachloromethane (500ml) at 0°C. Then triethylamine (103 ml, 0.74 mol) was added dropwise with vigorous stirring. The mixture was stirred for 2 h. The formed salt was filtered off and the residue concentrated \textit{in vacuo} to give an oil, which was dried with molecular sieves.
Experimental: propanoanthracenes

(3 Å). Distillation of the oil furnished 2-bromo-2-propenal 18 (53.8 g, 40%) as a colourless oil.

b.p. = 38-39 °C / 17 torr; lit.13 46-48°C / 28 torr

Preparation of 11-bromo-9,10-dihydro-11-formyl-9,10-ethanoanthracene12 (23)

Anthracene (25 g, 0.28 mmol), 2-bromo-2-propenal 18 (38 g, 0.28 mmol), potassium carbonate (4 g), and hydroquinone (0.4 g) were stirred in toluene (250 ml) for 4 days at 100 °C. The solution was cooled, filtered and evaporated to give a brown oil. Purification of the residue by flash chromatography (silica gel, petrol-10% ethyl acetate) afforded yellow crystals which were recrystallised from ethyl acetate/petrol to give 11-bromo-9,10-dihydro-11-formyl-9,10-ethanoanthracene 23 as white crystals, containing ca. 5% of anthracene. An analytical sample was recrystallised from petrol/ethyl acetate.

m.p. = 133-134 °C (petrol-ethyl acetate); lit.12 129-130 °C (cyclohexane)

$\nu_{\text{max}}$ (CDCl$_3$) 3074w, 3027w, 2957w, 2830w, 1728s, 1460m cm$^{-1}$

$\delta_H$ (400 MHz, CDCl$_3$) 9.32 (1H, d, J = 0.7 Hz, CHO), 7.09-7.46 (8H, m, H-ar.), 4.73 (1H, s, H-10), 4.38 (1H, t, J = 2.7 Hz, H-9), 3.02 (1H, ddd, J = 14.2; 2.8; 0.9 Hz, H-11), 2.20 (1H, m, H-11)

$\delta_C$ (100.6 MHz, CDCl$_3$) 189.04 (CHO), 143.03, 142.78, 138.60, 137.81, 127.66, 127.13, 126.51, 126.23, 126.03, 125.14, 123.89, 123.50, 68.86 (C-11), 52.46 (C-10), 43.89 (C-9), 38.22 (C-11)
Preparation of 9,10-dihydro-11-hydroxy-9,10-propanoanthracen-12-one (22)

A 3M solution of potassium hydroxide in water (200 ml) was added to a solution of 11-bromo-9,10-dihydro-11-formyl-9,10-ethanoanthracene 22 (13.3g, 42 mmol) in THF (500ml) under air atmosphere, the mixture was vigorously stirred for 2.5 h and then neutralised with 2M HCl. THF layer was separated and the aqueous phase extracted with DCM (3x). The combined organic extracts were washed with brine, dried (MgSO₄) and evaporated in vacuo. Crystallisation of the residue from ethyl acetate/petrol gave 9,10-dihydro-11-hydroxy-9,10-propanoanthracen-12-one 22 (6.1g, 58%) as white crystals. An analytical sample was recrystallised from ethyl acetate.

m.p. = 186-187 °C (ethyl acetate)

ν max (CHCl₃) 3471w, 3075w, 2934w, 2857w, 1702s, 1477m, 1458m, 1090m, 1066s cm⁻¹

δH (400 MHz, CDCl₃) 7.50-7.52 (1H, m, H-ar.), 7.38-7.40 (2H, m, H-ar.), 7.28-7.30 (3H, m, H-ar.), 7.18-7.22 (2H, m, H-ar.), 4.38 (1H, d, H-10 ), 4.30-4.32 (2H, m, H-9 and H-11 ), 3.98 (1H, d, OH), 3.16 (1H, dd, H-13 cis ), 2.83 (1H, m, H-13 trans)  

coupling constants: J₉,₁₃ cis = 6.7 Hz, J₁₀,₁₁ = 2.1 Hz, J₁₁,OH = 2.5 Hz,

J₁₃ cis,₁₃ trans = 15.3 Hz

The signal at 3.98ppm disappeared upon addition of D₂O.

decoupling experiments: irradiation frequency (changed signals): 4.31 (3.98, 3.16, 2.83), 3.16 (4.31, 2.83), 2.83 (4.31, 3.16)
Experimental: propanoanthracenes

\[ \delta_C (100.6 \text{ MHz, CDCl}_3) \]

\begin{align*}
208.25d \text{ (C-12, 143.24d, 139.82d, 139.23d, 138.11d, 138.11u,} \\
127.96u, 127.53u, 127.33u, 126.92u, 126.87u, 125.96u, 125.50u, 81.30u \text{ (C-11), 52.07d} \\
(C-13), 49.88u \text{ (C-10), 43.47d (C-9)}
\end{align*}

\[ m/z (\text{EI}) \]

250 (M+, 0.1%), 203 (7), 191 (36), 189 (42), 179 (100), 178 (100), 139 (22),
128 (13), 126 (18), 115 (19), 98 (12), 87 (20), 77 (19), 63 (48), 51 (35), 43 (91)

Found: C, 81.73; H, 5.74. CHO requires C, 81.58; H, 5.64%.

Chromatography of the mother liquid and subsequent recrystallisation from ethyl acetate provided isomeric 9,10-dihydro-12-hydroxy-9,10-propanoanthracen-11-one 24.

m.p. = 186-190 °C (ethyl acetate)

\[ \nu_{\text{max}} (\text{KBr}) \]

3479s, 3450m, 3034w, 2943w, 2917w, 2852w, 1707s, 1476m, 1456m,
1077s, 1043m, 784m, 763m, 755m, 699m, 652m cm\(^{-1}\)

\[ \delta_H (400 \text{ MHz, CDCl}_3) \]

7.45-7.43 (2H, m, H-ar.), 7.23-7.36 (6H, m, H-ar.), 4.86 (1H, s, H-10), 4.28 (1H, d, H-9), 4.12 (1H, dt, H-12), 3.33 (1H, d, OH), 3.00 (1H, ddd, H-13),
1.83 (1H, ddd, H-13)

coupling constants: \( J_{9,13} \text{trans} \) = 6.9 Hz, \( J_{9,13} \text{cis} \) = 1.2 Hz, \( J_{13} \text{cis,13-trans} \) = 12.8 Hz, \( J_{12,13} \text{trans} \) = 9.0 Hz, \( J_{12,13} \text{cis} \) = 9.8 Hz, \( J_{12,\text{OH}} \) = 3.3 Hz

\[ \delta_C (100.6 \text{ MHz, CDCl}_3) \]

204.56d (C-11), 143.01d, 139.29d, 136.60d, 134.38d, 128.28t,
128.23t, 127.64t, 126.88t (2 carbons), 125.52t (2 carbons), 125.91t, 72.75t (C-12),
60.39t (C-10), 43.90t (C-9), 42.82d (C-13)

\[ m/z (\text{EI}) \]

250 (M+, 0.6%), 234 (0.3), 203 (5), 202 (5), 191 (20), 189 (22), 179 (99), 178 (100), 176 (73), 165 (12), 152 (42), 139 (10), 89 (34), 76 (31)
Experimental: propanoanthracenes

Preparation of 9,10-dihydro-9,10-propanoanthracen-12-one (15) from 9,10-dihydro-11-hydroxy-9,10-propanoanthracen-12-one (22)

A solution of 1,2-diiodoethane (9.3g, 30 mmol) in THF (40 ml) was added dropwise to a stirred suspension of samarium powder (5g, 33 mmol) in THF (40 ml) at 0°C. The dark blue mixture was stirred for 2.5h at room temperature, then cooled at -78°C and a solution of 9,10-dihydro-11-hydroxy-9,10-propanoanthracen-12-one 22 (4g, 16 mmol) in THF (60 ml) was added dropwise. When about 80% of the hydroxyketone was added the solution turned yellow. The mixture was warmed to room temperature and turned again blue. The rest of the hydroxyketone was then added. The solution was poured into a solution of potassium carbonate and extracted with DCM (3x), washed with brine, dried (MgSO₄) and evaporated in vacuo. Crystallisation of the residue from ethyl acetate/petrol gave 9,10-dihydro-9,10-propanoanthracen-12-one 15 (2.6g, 69%) as white crystals. An analytical sample was recrystallised from ethyl acetate.

m.p. = 236-236.5°C (ethyl acetate)

\( \nu_{\text{max}} (\text{CHCl}_3) 3077\text{w}, 3017\text{s}, 2929\text{w}, 1691\text{s}, 1478\text{w}, 1458\text{w}, 988\text{w} \text{ cm}^{-1} \)

\( \nu_{\text{max}} (\text{KBr}) 3037\text{w}, 2927\text{m}, 2891\text{m}, 1685\text{s}, 1477\text{s}, 1454\text{s}, 1400\text{s}, 1331\text{s}, 1116\text{s}, 985\text{s}, 772\text{s}, 765\text{s}, 709\text{s}, 683\text{s}, 592\text{s} \text{ cm}^{-1} \)

\( \delta_{\text{H}} (400 \text{ MHz, CDCl}_3) 7.36-7.38 (4\text{H, m, H-1,4,5,8}), 7.22-7.38 (4\text{H, m, H-2,3,6,7}), 4.29 (2\text{H, t, H-9,10}), 2.87 (4\text{H, d, H-11,13}) \)

coupling constants: \( J_{9,13} = J_{10,11} = 3.9 \text{ Hz} \)

\( \delta_{\text{C}} (100.6 \text{ MHz, CDCl}_3) 209.31\text{d} (\text{C-12}), 141.74\text{d}, 127.02\text{u}, 125.95\text{u}, 51.05\text{d} (\text{C-11, 13}), 43.42\text{u} (\text{C-9, 10}) \)
**Experimental: propanoanthracenes**

m/z (EI) 234 (M⁺, 54%), 215 (33), 202 (8), 191 (100), 189 (65), 178 (63), 176 (46), 165 (53), 163 (18), 151 (30), 139 (16), 115 (14), 89 (13), 75 (18), 63 (34), 51 (31), 42 (86), 39 (43)

Found: C, 86.92; H, 5.95. CHO requires C, 87.15; H, 6.02%.

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**Preparation of 9,10-dihydro-12-hydroxy-9,10-propanoanthracene (26)**

Sodium borohydride (1g, 26 mmol) was added as a single portion to a solution of 9,10-dihydro-9,10-propanoanthracen-12-one 15 (0.7g, 2.8 mmol) in THF (25 ml) and methanol (15 ml). The solution was stirred for 18h, then poured into water and extracted with DCM (3x), washed with brine, dried (MgSO₄) and evaporated *in vacuo*. Purification of the residue by flash chromatography (silica gel; petrol - 25% ethyl acetate) gave 9,10-dihydro-12-hydroxy-9,10-propanoanthracene 26 (0.65g, 92%) as white crystals. An analytical sample was recrystallised from ethyl acetate/petrol.

m.p. = 127-128 °C (ethylacetate /petrol), lit.¹⁰ 114-116 °C

\[
\begin{align*}
\nu_{\text{max}} (\text{CCl}_4) & \text{ 3623w (multiplet), 3479w (broad), 3077w, 3046w, 3024m, 2927s, 2857w,} \\
& \text{1492w, 1474s, 1458s, 1037s cm}^{-1}
\end{align*}
\]

\[
\begin{align*}
\nu_{\text{max}} (\text{CHCl}_3) & \text{ 3606m, 3435w (broad, disappears on dilution), 3071w, 3012s, 2929s,} \\
& \text{2857s, 1492m, 1474s, 1458s, 1048s, 1031s cm}^{-1}
\end{align*}
\]

\[
\begin{align*}
\nu_{\text{max}} (\text{CS}_2) & \text{ 3612w, 3608w, 3605w, 3602w, 3598w, 3594w, 3067w, 3021m, 2926s,} \\
& \text{2852w, 1037s cm}^{-1}
\end{align*}
\]

\[
\begin{align*}
\nu_{\text{max}} (\text{pyridine}) & \text{ 3257 (broad) cm}^{-1}
\end{align*}
\]

\[
\begin{align*}
\nu_{\text{max}} (\text{KBr}) & \text{ 3298s (broad), 3030m, 3049m, 3020m, 2924s, 2855m, 1473s, 1456s, 1049s,} \\
& \text{1041s, 1031s, 761s, 746s, 665s, 595s cm}^{-1}
\end{align*}
\]
Experimental: propanoanthracenes

$\delta_H$ (400 MHz, CDCl$_3$) 7.25-7.30 (4H, m, H-1,4,5,8), 7.15-7.20 (4H, m, H-2,3,6,7), 4.13 (2H, dd, H-9,10), 3.26-3.34 (1H, m, H-12), 2.41-2.48 (2H, m, H-11$^{\text{trans}}$, 13$^{\text{trans}}$), 1.54 (2H, ddd, H-11$^{\text{cis}}$, 13$^{\text{cis}}$), 1.20 (1H, s, OH)

coupling constants: $J_{9,13-\text{trans}} = J_{10,11-\text{trans}} = 7.2$ Hz, $J_{9,13-\text{cis}} = J_{10,11-\text{cis}} = 1.2$ Hz,
$J_{11-\text{cis},11-\text{trans}} = J_{13-\text{cis},13-\text{trans}} = 13.1$ Hz, $J_{11-\text{cis},12} = J_{13-\text{cis},12} = 10.3$ Hz,
$J_{11-\text{trans},12} = J_{13-\text{trans},12} = 6.1$ Hz, $J_{11-\text{trans},13-\text{trans}} = 1.2$ Hz

$\delta_C$ (100.6 MHz, CDCl$_3$) 144.24d, 140.60d, 126.42u, 126.33u, 125.56u, 125.37u, 68.26u (C-12), 44.01u (C-9,10), 39.29d (C-11,13)

m/z (EI) 236 (M+, 40%), 219 (18), 217 (32), 218 (100), 203 (19), 192 (49), 191 (51), 189 (18), 178 (72), 176 (8), 165 (9), 152 (6), 139 (2), 115 (2)

Found: C, 86.74; H, 6.91. C$_{17}$H$_{16}$O requires C, 86.40; H, 6.82 %.

Preparation of 9,10-dihydro-12-hydroxy-12-methyl-9,10-propanoanthracene (27)

Cerium(III)chloride heptahydrate (3.3g, 8.6 mmol) was ground in a mortar and placed in a 250 ml flask. The flask was evacuated (0.1 torr) and immersed in an oil bath (140-150 °C) for 3h. While the flask was still hot, nitrogen gas was introduced and the flask was cooled in an ice bath. Cold THF (20 ml) was added all at once with vigorous stirring, the ice bath was removed and the suspension was stirred for 2h. The flask was cooled to -78°C and a 1.4M solution of methyl lithium (6 ml, 8.4 mmol) in diethyl ether was added dropwise and the light yellow suspension was stirred for 1h. A solution of 9,10-dihydro-9,10-propanoanthracen-12-one 15 (1.0g, 4.3 mmol) was added dropwise. The mixture was stirred for 2h, then warmed up to 0°C, poured into 1M HCl and extracted with ethyl acetate (3x). The combined ethyl acetate extracts were washed with
brine, and dried (MgSO₄). Evaporation of the solution in vacuo gave 9,10-dihydro-12-hydroxy-12-methyl-9,10-propanoanthracene 27 (1.0 g, 93%) as white crystals, pure by $^1$H NMR spectroscopy. An analytical sample was recrystallised from ethyl acetate-petrol.

m.p. = 128-129 °C (ethyl acetate-petrol)

$\nu_{\text{max}}$ (CCl₄) 3595s, 3074w, 3050w, 3024m, 2974m, 2931s, 2914s, 1474s, 1456s, 1377s, 1288m, 1224m, 1111s, 1057s cm$^{-1}$

$\nu_{\text{max}}$ (CHCl₃) 3581s, 3074m, 2932s, 1476s, 1456s, 1379m, 1107s, 1060s cm$^{-1}$

$\nu_{\text{max}}$ (pyridine) 3586 (sharp), 3303 (broad) cm$^{-1}$

$\nu_{\text{max}}$ (CS₂) 3592.9m, 3068w, 3021w, 2969w, 2928m, 1110m, 1055m, 762s, 747m cm$^{-1}$

$\delta_{\text{H}}$ (400 MHz, CDCl₃) 7.37-7.42 (2H, m, H-1,4), 7.27-7.31 (2H, m, H-5,8), 7.22-7.26 (2H, m, H-2,3), 7.15-7.20 (2H, m, H-6,7), 4.14 (2H, dd, H-9,10), 2.32 (2H, m, H-11cis, 13cis), 1.96 (2H, dd, H 11trans, 13trans), 1.17 (1H, m, OH), 0.95 (3H, d, CH₃)

coupling constants: $J_{9,13-\text{cis}} = J_{10,11-\text{cis}} = 6.7$ Hz, $J_{9,13-\text{trans}} = J_{10,11-\text{trans}} = 1.3$ Hz,

$J_{11-\text{cis},11-\text{trans}} = J_{13-\text{cis},13-\text{trans}} = 14.5$ Hz, $J_{11-\text{cis},13-\text{cis}} = 1.9$ Hz, $J_{\text{OH},\text{CH}_3} = 1.0$ Hz

decoupling experiments: irradiation frequency (changed signals): 1.17 (0.95)

NOE: 4.14(7.40, 7.29, 2.32, 1.96)

$\delta_{\text{C}}$ (100.6 MHz, CDCl₃) 144.23d, 141.61d, 126.95u, 126.43u, 126.24u, 125.25u, 72.72d (C-12), 44.94u (C-9,10), 44.65d (C-11,13), 32.83u (CH₃)

m/z (El) 250 (M⁺, 17%), 232 (60), 217 (62), 203 (5), 192 (85), 191 (54), 178 (70), 165 (10), 105 (13)

Found: C, 86.23; H, 7.34. C₁₈H₁₈O requires C, 86.36; H, 7.25%.
Experimental: propanoanthracenes

Preparation of 12-butyl-9,10-dihydro-12-hydroxy-9,10-propanoanthracene (28)

Cerium(III)chloride heptahydrate (2.5g, 6.7 mmol) was ground in a mortar and placed in a 250 ml flask. The flask was evacuated (0.1 torr) and immersed in an oil bath (140-150 °C) for 4h. While the flask was still hot, nitrogen gas was introduced and the flask was cooled in an ice bath. Cold THF (15 ml) was added all at once with vigorous stirring, the ice bath was removed and the suspension was stirred for 2h. The flask was cooled to -78°C and a 1.9M solution of butyllithium (3.5 ml, 6.7 mmol) in hexanes was added dropwise and the yellow suspension was stirred for 1h. A solution of 9,10-dihydro-9,10-propanoanthracen-12-one 15 (0.8g, 3.4 mmol) was added dropwise. The mixture was stirred for 3h, then poured into 1M HCl and extracted with DCM (3x). The combined dichloromethane extracts were washed with brine, dried (MgSO₄) and evaporated in vacuo. Purification of the residue by flash chromatography (silica gel; petrol-10% ethyl acetate) gave 12-butyl-9,10-dihydro-12-hydroxy-9,10-propanoanthracene 28 (0.75g, 75%) as white crystals. An analytical sample was recrystallised from ethyl acetate.

m.p. = 103-105 °C (ethyl acetate)

$\nu_{\text{max}}$ (CCl₄) 3596s, 3073w, 3045w, 3024m, 2953s, 2934s, 2915s, 2873m, 2843w, 1492w, 1474s, 1469m, 1456s, 1053s, 1031s cm⁻¹

$\nu_{\text{max}}$ (CHCl₃) 3581s, 3071w, 3010s, 2937s, 2873m, 2864m, 1475s, 1456s, 1052s, 1029s cm⁻¹

$\nu_{\text{max}}$ (pyridine) 3587 (sharp), 3345 (broad) cm⁻¹

$\nu_{\text{max}}$ (KBr) 3590s, 3071w, 3021w, 2960s, 2932s, 2908s, 2861s, 1477s, 1467s, 1456s, 1052s, 1030s, 771s, 600s, 533s cm⁻¹
Experimental: propanoanthracenes

\[ \delta_H (400 \text{ MHz}, \text{CDCl}_3) \]
\[
7.35-7.40 (2 \text{H, m, H-1,4}), 7.24-7.28 (2 \text{H, m, H-5,8}), 7.20-7.24 \\
(2 \text{H, m, H-2,3}), 7.13-7.17 (2 \text{H, m, H-6,7}), 4.12 (2 \text{H, dd, H-9,10}), 2.29 (2 \text{H, ddd, H-11cis, 13cis}), 1.88 (2 \text{H, dd, H-11trans, 13trans}), 1.14-1.18 (6 \text{H, m, H-butyl}), 1.04 (1 \text{H, s, OH}), 0.80-0.83 (3 \text{H, m, H-butyl})
\]

Coupling constants: \( J_{9,13\text{cis}} = J_{10,11\text{cis}} = 1.3 \text{ Hz, } J_{9,13\text{trans}} = J_{10,11\text{trans}} = 1.3 \text{ Hz, } \)

\( J_{11\text{cis,11trans}} = J_{13\text{cis,13trans}} = 14.5 \text{ Hz, } J_{11\text{cis,13cis}} = 1.9 \text{ Hz} \)

\[ \delta_C (100.6 \text{ MHz}, \text{CDCl}_3) \]
\[
144.41d, 141.69d, 126.93u, 126.39u, 126.22u, 125.20u, 74.29d \\
(\text{C-12}), 45.60d (\text{C-1'}, 44.93u (\text{two carbons, C-9,10}), 43.61d (\text{two carbons, C-11,13}), \\
24.55d, 23.08d, 14.00p (\text{C-4'})
\]

\( m/z (\text{EI}) \)
\[
292 (M^+, 3%), 274 (10), 235 (35), 217 (22), 192 (45), 178 (83), 165 (6), 86 (10), 84 (16), 49 (45), 28 (100)
\]

Found: C, 86.06; H, 8.25. \( \text{C}_{21}\text{H}_{24}\text{O} \) requires C, 86.26; H, 8.27%.

**Preparation of 9,10-dihydro-cis-11,12-dihydroxy-9,10-propanoanthracene (29)**

A solution (1.5M) of diisobutylaluminum hydride (0.67 ml, 1 mmol) in toluene was added as a single portion to a solution of 9,10-dihydro-11-hydroxy-9,10-propanoanthracen-12-one 22 (0.1g, 0.4 mmol) in THF (10 ml) at -78 °C. The solution was slowly warmed to ambient temperature and stirred for 0.5 h, then poured into 1M HCl and extracted with DCM (3x), washed with brine, dried (MgSO\(_4\)) and evaporated in vacuo. Purification of the residue by flash chromatography (silica gel; petrol-50% ethyl acetate) gave 9,10-dihydro-cis-11,12-dihydroxy-9,10-propanoanthracene 29 (0.26g, 86%) as white crystals. An analytical sample was recrystallised from ethyl acetate.
Experimental: propanoanthracenes

m.p. = 201-202 °C (ethyl acetate)

$\nu_{\text{max}}$ (KBr) 3518s, 3390s, 3065m, 3033m, 2936s, 2919s, 2855m, 1476s, 1455s, 1047s, 
989s, 772s, 754s, 701m, 678s, 597s cm$^{-1}$

$\nu_{\text{max}}$ (CHCl$_3$) 3613w, 3546m, 2931m, 2861w, 1475m, 1456w, 1388w, 1056s, 
1047(shoulder of the previous peak), 950w cm$^{-1}$

$\delta_{H}$ (400 MHz, CDCl$_3$) 7.38-7.41 (1H, m, H-ar.), 7.17-7.33 (7H, m, H-ar.), 4.37 (1H, d, 
H-10), 4.11-4.16 (2H, m, H-9,11), 3.30 (1H, m, H-12), 2.32 (1H, m, H-13$^{\text{trans}}$), 1.96 
(1H, d, C$^{12}$-OH), 1.57-1.64 (2H, m, H-13$^{\text{cis}}$, C$^{11}$-OH)

coupling constants: $J_{9,13-\text{trans}}$ = 7.0 Hz, $J_{9,13-\text{cis}}$ = 1.5 Hz, $J_{10,11} = 7.0$ Hz,

$J_{11,12} = 10.2$ Hz, $J_{11,C11-OH} = 8.6$ Hz, $J_{12,13-\text{cis}} = 10.2$ Hz, $J_{12,13-\text{trans}} = 6.2$ Hz,

$J_{12,C12-OH} = 9.8$ Hz, $J_{13-\text{cis,13-trans}} = 13.5$ Hz

The signals at 1.96 and 1.58 ppm disappeared upon addition of D$_2$O.

decoupling experiments: irradiation frequency (changed signals): 3.30 (4.14, 2.32, 1.96, 
1.60)

$\delta_{C}$ (100.6 MHz, CDCl$_3$) 144.65d, 140.26d, 138.14d, 136.44d, 128.83u, 127.77u, 
127.25u, 126.61u, 126.46u, 126.36u, 126.01u, 125.46u, 69.64u (C-11 or C-12), 69.56 
(C-11 or C-12), 50.97u (C-10), 43.95u (C-9), 35.04d(C-13)

m/z (El) 252 (M$^+$, 6%), 234 (11), 216 (5), 192 (18), 191 (16), 179 (59), 178 (100),
165 (3), 152 (3)

Preparation of 9,10-dihydro-12-methyl-9,10-propenoanthracene (37)

To a stirred suspension of trimethylxonium tetrafluoroborate (45 mg, 0.3 mmol) in
DCM (3 ml) was added solid 9,10-dihydro-12-hydroxy-12-methyl-9,10-
Experimental: propanoanthracenes

propanoanthracene 27 (50mg, 0.2 mmol) as a single portion. The suspension was stirred for 14h, then poured into 1M HCl and extracted with DCM (3x), washed with brine, dried (MgSO₄) and evaporated in vacuo. Purification of the residue by flash chromatography (silica gel; petrol-3%ethyl acetate) gave 9,10-dihydro-12-methyl-9,10-propanoanthracene 37 (40 mg, 86%) as white crystals.

m.p. = 162-166 °C

υ max (KBr) 3019w, 2970w, 2933m, 2908m, 2883m, 1473m, 1446m, 1291m, 1173m, 949m, 764s, 687s, 595s, 473s cm⁻¹

δH (400 MHz, CDCl₃) 7.34-7.39 (2H, m, H-ar.), 7.21-7.25 (2H, m, H-ar.), 7.13-7.19 (4H, m, H-ar.), 6.07 (1H, m, H-11), 4.19 (1H, d, H-10), 4.12 (1H, t, H-9), 2.41 (2H, m, H-13), 1.44 (3H, m, CH₃)

coupling constants: J9,13 = 3.7 Hz, J10,11 = 8.5 Hz, J11,13 = 1.8 Hz, J11,CH₃ = 1.5 Hz, J13,CH₃ = 0.9 Hz

δC (100.6 MHz, CDCl₃) 146.06d, 141.34d, 132.26d (C-12), 125.90u, 125.86u, 123.85u, 45.95u (C-9,10), 38.03d (C-13), 25.18u (CH₃)

m/z (EI) 232 (M⁺, 100%), 217 (99), 215 (30), 203 (10), 202 (21), 191 (24), 189 (14), 178 (14), 165 (8), 152 (4), 139 (2), 115 (3)

Preparation of 9,10-dihydro-12-methoxy-12-methyl-9,10-propanoanthracene (31)

To a stirred suspension of potassium hydride (14 mg, 0.35 mmol) in DMSO (3 ml) was added solid 9,10-dihydro-12-hydroxy-12-methyl-9,10-propanoanthracene 27 (60mg, 0.24 mmol) as a single portion. The mixture immediately turned dark red. The suspension was stirred for 20 min, then dimethyl sulfate(0.045 ml, 0.48 mmol) was
added dropwise. The solution became light yellow and was further stirred for 15 min.,
then poured into water and extracted with DCM (3x), washed with brine, dried
(MgSO₄) and evaporated in vacuo. Purification of the residue by flash chromatography
(silica gel; petrol - 5%AcOEt) gave 9,10-dihydro-12-methoxy-12-methyl-9,10-
propanoanthracene 31 (53 mg, 84%) as white crystals.
m.p. = 115-116 °C
νmax (CHCl₃) 2973m, 2937m, 1476m, 1456m, 1115s, 1083s, 1067m cm⁻¹
δH (400 MHz, CDCl₃) 7.25-7.30 (4H, m, H-ar.), 7.13-7.18 (4H, m, H-ar.), 4.07 (2H, dd,
H-9,10), 2.74 (3H, s, OCH₃), 2.31 (2H, m, H-11cis,13cis), 1.84 (2H, dd, H-11trans,
13trans), 0.74 (3H, s, CH₃)
coupling constants: J₉,₁₃-cis = J₁₀,₁₁-cis = 5.4 Hz, J₉,₁₃-trans = J₁₀,₁₁-trans = 2.8 Hz,
J₁₁-cis,₁₃cis = 1.5 Hz, J₁₁-cis,₁₁-trans = J₁₃-cis,₁₃-trans = 14.5 Hz
δH (400 MHz, CCl₄ - C₆D₆ - 12:1)
coupling constants: J₉,₁₃-cis = J₁₀,₁₁-cis = 5.0 Hz, J₉,₁₃-trans = J₁₀,₁₁-trans = 3.0 Hz,
J₁₁-cis,₁₁-trans = J₁₃-cis,₁₃-trans = 14.3 Hz
δH (400 MHz, CS₂ - C₆D₆ - 12:1)
coupling constants: J₉,₁₃-cis = J₁₀,₁₁-cis = 5.4 Hz, J₉,₁₃-trans = J₁₀,₁₁-trans = 2.8 Hz,
J₁₁-cis,₁₁-trans = J₁₃-cis,₁₃-trans = 14.3 Hz
δH (400 MHz, C₆D₆)
coupling constants: J₉,₁₃-cis = J₁₀,₁₁-cis = 5.1 Hz, J₉,₁₃-trans = J₁₀,₁₁-trans = 3.1 Hz,
J₁₁-cis,₁₁-trans = J₁₃-cis,₁₃-trans = 14.3 Hz
δH (400 MHz, CD₃CN)
coupling constants: J₉,₁₃-cis = J₁₀,₁₁-cis = 5.4 Hz, J₉,₁₃-trans = J₁₀,₁₁-trans = 2.9 Hz,
J₁₁-cis,₁₁-trans = J₁₃-cis,₁₃-trans = 14.6 Hz
δC (100.6 MHz, CDCl₃) 144.17d, 142.85d, 126.09u, 125.79u, 125.32u, 124.93u, 76.38d
(C-12), 47.92u (OCH₃), 44.71u (C-9,10), 39.94u (C-11,13), 27.96u (CH₃)
m/z (EI) 264(M⁺, 35%), 249 (14), 232 (50), 217 (62), 192 (100), 178 (73)
Found: C, 86.47; H, 7.58. C₁₉H₂₀O requires C, 86.32; H, 7.63%.
Preparation of 12-butyl-9,10-dihydro-12-methoxy-9,10-propanoanthracene (32)

To a stirred suspension of potassium hydride (14 mg, 0.35 mmol) in DMSO (3 ml) was added solid 12-butyl-9,10-dihydro-12-hydroxy-9,10-propanoanthracene 28 (60 mg, 0.2 mmol) as a single portion. The mixture turned orange. The suspension was stirred for 20 min., then dimethyl sulfate (0.045 ml, 0.48 mmol) was added dropwise. The solution became light yellow and was further stirred for 15 min, then poured into water and extracted with DCM (3x), washed with brine, dried (MgSO₄) and evaporated in vacuo. Purification of the residue by flash chromatography (silica gel; petrol - 5% AcOEt) gave 12-butyl-9,10-dihydro-12-methoxy-9,10-propanoanthracene 32 (51 mg, 81%) as colourless oil.

\[ \text{\textit{v}}_{\text{max}} (\text{CHCl}_3) \ 2936\text{s}, \ 2875\text{m}, \ 1602\text{m}, \ 1474\text{w}, \ 1456\text{m}, \ 1121\text{w}, \ 1113\text{w}, \ 1077\text{s}, \ 1026\text{w} \ \text{cm}^{-1} \]

\[ \delta_{\text{H}} (400 \text{ MHz, CDCl}_3) \ 7.23-7.30 \ (4\text{H, m, H-ar.}), \ 7.10-7.16 \ (4\text{H, m, H-ar.}), \ 4.03 \ (2\text{H, dd, H-9,10}), \ 2.63 \ (3\text{H, s, OCH}_3), \ 2.38 \ (2\text{H, m, H-11}_{\text{cis}},13_{\text{cis}}), \ 1.68 \ (2\text{H, dd, H-11}_{\text{trans}},13_{\text{trans}}), \ 1.05-1.17 \ (6\text{H, m, H-1', 2', 3'}), \ 0.81 \ (3\text{H, t, H-4'}) \]

coupling constants: \[ J_{10,11}_{\text{cis}} = J_{9,13}_{\text{cis}} = 6.5 \text{ Hz}, \ J_{10,11}_{\text{trans}} = J_{9,13}_{\text{trans}} = 1.7 \text{ Hz}, \ J_{11}_{\text{cis}},13_{\text{cis}} = 1.9 \text{ Hz}, \ J_{11}_{\text{cis}},1_{\text{trans}} = J_{13}_{\text{cis}},13_{\text{trans}} = 14.8 \text{ Hz} \]

\[ \delta_{\text{C}} (100.6 \text{ MHz, CDCl}_3) \ 145.04\text{d}, \ 142.53\text{d}, \ 125.97\text{u}, \ 125.69\text{u}, \ 125.08\text{u}, \ 124.86\text{u}, \ 78.05\text{u} \ (C-12), \ 47.63\text{u} \ (OCH}_3), \ 44.79\text{u} \ (\text{two carbons; C-9,10}), \ 39.43\text{d} \ (C-1'), \ 38.17\text{d} \ (\text{two carbons; C-11,13}), \ 24.23\text{d}, \ 22.96\text{d}, \ 14.00\text{u} \ (C-4') \]

\[ m/z \ (\text{FAB}) \ 306 \ (M^+, \text{6}%), \ 275 \ (63), \ 249 \ (68), \ 217 \ (41), \ 191 \ (100), \ 178 \ (88) \]

Found: C, 86.08; H, 8.49. \( \text{C}_{22}\text{H}_{26}\text{O} \) requires C, 86.23; H, 8.55%.
Preparation of 9,10-dihydro-12-methylene-9,10-propanoanthracene (33)

A mixture of zinc powder (2.5g, 38 mmol), diiodomethane (1.8 ml, 22 mmol) and THF (40 ml) was stirred for 30 min., then cooled to 0°C and a solution (1 M) of titanium tetrachloride in dichloromethane (4.3 ml, 4.3 mmol) was added in 10 min. The dark brown mixture was stirred for 30 min at room temperature. A solution of 9,10-dihydro-9,10-propanoanthracen-12-one (15) (1g, 4.3 mmol) in THF (20 ml) was added dropwise and the mixture was stirred 1.5 h, then poured into 1M HCl and extracted with DCM (3x). The combined dichloromethane extracts were washed with brine, dried (MgSO₄) and evaporated in vacuo. Purification of the residue by flash chromatography (silica gel; petrol-3%ethyl acetate) gave 9,10-dihydro-12-methylene-9,10-propanoanthracene 33 (0.6g, 60%) as white crystals.

m.p. = 159-160°C

ν_max (KBr) 3070m, 3039m, 3019m, 2976m, 2937s, 2898s, 1637s, 1476s, 1454s, 1424s, 1115s, 992s, 895s, 767s, 697s, 598s, 500s cm⁻¹

δ_H (400 MHz, CDCl₃) 7.25-7.29 (4H, m, H-1,4,5,8), 7.16-7.19 (4H, m, H-2,3,7,8), 4.46 (2H, quintet, H-14), 4.09 (2H, t, H-9, 10), 2.61 (2H, dt, H-11,13)
coupling constants: J_{9,13} = J_{10,11} = 4.1 Hz, J_{11,14} = J_{13,14} = 1.1 Hz

δ_C (100.6 MHz, CDCl₃) 144.83d (C-12), 142.93d, 126.15u, 125.52u, 115.48d (C-14), 45.93u (C-9,10), 41.64u (C-11,13)
m/z (EI) 232 (M⁺, 100%), 217 (57), 203 (6), 202 (7), 191 (17), 179 (12), 178 (77), 176 (11), 165 (5), 152 (8), 151 (5), 139 (2), 126 (1)

Found: C, 92.90; H, 7.01. C₁₈H₁₆ requires C, 93.06; H, 6.94%.
Preparation of 9,10-dihydro-12,14-epoxy-12-methylene-9,10-propanoanthracene (34)

3-chloroperoxybenzoic acid (Aldrich; 50-60%) (0.25 g) was added as a single portion to a stirred solution of the 9,10-dihydro-12-methylene-9,10-propanoanthracene 33 (0.1 g, 0.4 mmol) in DCM (5 ml). After 2h, the reaction mixture was poured into a solution of sodium thiosulphate and extracted with DCM (3x). The combined dichloromethane extracts were washed with a solution of sodium bicarbonate and with brine, dried (MgSO₄) and evaporated in vacuo. Purification of the residue by flash chromatography (silica gel; petrol-10%ethyl acetate) gave 9,10-dihydro-12,14-epoxy-12-methylene-9,10-propanoanthracene 34 (68 mg, 64%) as white crystals. An analytical sample was recrystallised from ethyl acetate.

m.p. = 169-170°C (ethyl acetate)

\( \nu_{\text{max}} \) (KBr) 3032w, 2947m, 2922m, 2857w, 1492m, 1478m, 1456m, 1175m, 1114m, 1015s, 896m, 796m, 764s, 753m, 715m, 594s cm⁻¹

\( \delta_{\text{H}} \) (400 MHz, CDC\(_3\)) 7.32-7.36 (2H, m, H-1,4 or H-5,8), 7.27-7.32 (2H, m, H-1,4 or H-5,8), 7.18-7.25 (4H, m, H-2,3,6,7), 4.19 (2H, t, H-9,10), 2.07 (2H, s, H-14), 2.03 (4H, d, H-11,13)

coupling constants: \( J_{9,13} = J_{10,11} = 4.1 \) Hz

\( \delta_{\text{C}} \) (100.6 MHz, CDC\(_3\)) 142.91d, 142.27d, 126.51u, 126.43u, 125.72u, 125.64u, 56.78d (C-12), 54.68 (C-14), 44.67u (C-9,10), 40.91d (C-11,13)

m/z (EI) 248(M⁺, 26%), 229(10), 217(23), 215(14), 193(65), 191(35), 179(27), 178(100)

Found: C, 87.25; H, 6.43. C\(_{18}\)H\(_{16}\)O requires C, 87.06; H, 6.49%.
Preparation of 9,10-dihydro-12, 12-dimethoxy-9,10-propanoanthracene (36) and 9,10-dihydro-12-methoxy-9,10-propenoanthracene (37)

A solution of 9,10-dihydro-9,10-propanoanthracen-12-one 15 (0.3 g, 1.2 mmol) and p-toluenesulfonic acid (0.3 g, 1.7 mmol) in trimethyl orthoformate (15 ml) and methanol (15 ml) was refluxed for 1 h. The reaction mixture was then poured into a solution of sodium carbonate and extracted with ethyl acetate (3x), washed with brine, dried (MgSO₄) and evaporated in vacuo. Purification of the residue by flash chromatography (silica gel; petrol-5% ethyl acetate) afforded in the order of elution 9,10-dihydro-12-methoxy-9,10-propenoanthracene 37 (65 mg, 20%) as white crystals.

m.p. = 203-205 °C

υmax (KBr) 3074w, 3037w, 2998w, 2939m, 2906m, 2890m, 2821m, 1648s, 1462s, 1455s, 1201s, 1152s, 774s, 769s, 762s, 745s, 732s, 707s, 593s cm⁻¹

δH (400 MHz, CDCl₃) 7.37-7.40 (2H, m, H-ar.), 7.25-7.28 (2H, m, H-ar.), 7.15-7.19 (4H, m, H-ar.), 5.40 (1H, d, H-11), 4.32 (1H, d, H-10), 4.23 (1H, t, H-9), 3.35 (3H, s, OCH₃), 2.57 (2H, d, H-13)

coupling constants: J₉,₁₃ = 3.7 Hz, J₁₀,₁₁ = 9.1 Hz

δC (100.6 MHz, CDCl₃) 153.63d (C-12), 146.48d, 141.04d, 126.11u, 125.94u, 125.85u, 123.76u, 100.62u (C-11), 53.46u (OCH₃), 44.91u (C-9 or C-10), 43.19u (C-9 or C-10), 36.56d (C-13)

m/z (EI) 248 (M⁺, 72%), 234 (47), 215 (87), 202 (15), 191 (100), 178 (27), 165 (14), 105 (32)

and 9,10-dihydro-12,12-dimethoxy-9,10-propanoanthracene 36 (210 mg, 59%) as white crystals. An analytical sample was recrystallised from ethyl acetate-petrol.
Experimental: propanoanthracenes

m.p. = 152-155 °C (ethyl acetate-petrol)

$\nu_{\max}$ (KBr) 3064w, 3034m, 2975m, 2941s, 2923s, 2824m, 1476s, 1454m, 1361m, 1101s, 1049s, 1008s, 967s, 768s, 749s, 680s, 598s, 576s cm$^{-1}$

$\delta_{H}$ (400 MHz, CDCl$_3$) 7.26-7.30 (4H, m, H-1,4,5,8), 7.13-7.18 (4H, m, H-2,3,6,7), 4.11 (2H, t, H-9,10), 2.85 (6H, s, OCH$_3$), 2.19 (4H, d, H-11,13)

coupling constants: $J_{9,13} = J_{10,11} = 4.1$ Hz

$\delta_{C}$ (100.6 MHz, CDCl$_3$) 143.14d, 126.07u, 125.07u, 101.30d (C-12), 47.02u (CH$_3$), 43.62u (C-9,10), 38.24d (C-11,13)

m/z (El) 280 (M+, 44%), 265 (17), 249 (74), 234 (49), 217 (74), 215 (71), 205 (30), 192 (81), 191 (85), 178 (79), 165 (25), 152 (16), 105 (21)

Found: C, 81.52; H, 7.08. C$_{19}$H$_{20}$O$_2$ requires C, 81.40; H, 7.19%.

Preparation of 9,10-dihydro-12,12-ethylenethio-oxy-9,10-propanoanthracene (35)

A solution of 9,10-dihydro-12, 12-dimethoxy-9,10-propanoanthracene 36 (50 mg, 0.18 mmol) and p-toluenesulfonic acid (50 mg, 0.28 mmol) in 2-mercaptoethanol (5 ml) was heated at 80°C for 5h. The reaction mixture was poured into an aqueous solution of sodium hydroxide, extracted with ethyl acetate (3x), washed with the solution of sodium hydroxide (2x) and brine, dried (MgSO$_4$) and evaporated in vacuo. Purification of the residue by flash chromatography (silica gel; petrol-5% AcOEt) afforded 9,10-dihydro-12,12-ethylenethio-oxy-9,10-propanoanthracene 35 (28 mg, 51%) as white crystals.

m.p. = 147-149 °C
Experimental: propanoanthracenes = 203 =

v\text{max} (KBr) 3062\text{w}, 3025\text{w}, 2929s, 2916s, 2906s, 2875s, 1472s, 1455s, 1426m, 1071s, 1006s, 974s, 791m, 768s, 686s, 596s cm\textsuperscript{-1}

δ\text{H} (400 MHz, CDCl\textsubscript{3}) 7.33-7.37 (2H, m, H-1,4), 7.26-7.29 (2H, m, H-5,8), 7.22-7.25 (2H, m, H-2,3), 7.17-7.14 (2H, m, H-6,7), 4.17 (2H, dd, H-9,10), 3.91 (2H, t, H-1'), 2.82 (2H, t, H-2'), 2.68 (2H, dd, H-1\textsuperscript{trans},13\textsuperscript{trans}), 2.35 (2H, dd, H-1\textsuperscript{cis},13\textsuperscript{cis})

coupling constants: J\textsubscript{9,13-trans} = J\textsubscript{10,11-trans} = 5.8 Hz, J\textsubscript{9,13-cis} = J\textsubscript{10,11-cis} = 2.6 Hz,

J\textsubscript{11-cis,11-trans} = J\textsubscript{13-cis,13-trans} = 14.0 Hz, J\textsubscript{11-trans,13-trans} = 1.5 Hz, J\textsubscript{1',2'} = 5.8 Hz

δ\text{C} (100.6 MHz, CDCl\textsubscript{3}) 143.83d, 141.72d, 126.78u, 126.51u, 126.23u, 125.34u, 95.58d (C-12), 68.96d (C-1'), 46.17d (C-11,13), 44.47u (C-9,10), 33.61 (C-2')

m/z (EI) 294 (M\textsuperscript{+}, 9%), 234 (57), 215 (20), 191 (96), 179 (94), 178 (100), 165 (14), 152 (12), 105 (12)

Found: C, 77.57; H, 6.29, S, 11.26. C\textsubscript{19}H\textsubscript{18}O\textsubscript{5}S requires C, 77.53; H, 6.16., S, 10.87 %.
Preparation of 9,10-dihydro-12-fluoro-12-methyl-9,10-propanoanthracene (39)

Diethylaminosulfur trifluoride (0.066 ml, 0.5 mmol) was added as a single portion to a solution of 9,10-dihydro-12-hydroxy-12-methyl-9,10-propanoanthracene 27 (60 mg, 0.24 mmol) in THF (2 ml) at -78 °C. The reaction mixture was stirred for 1.5 h, then warmed to room temperature, poured into water and extracted with DCM (3x), washed with brine, dried (MgSO₄) and evaporated in vacuo. Purification of the residue by flash chromatography (silica gel; petrol-2% ethyl acetate) afforded 9,10-dihydro-12-fluoro-12-methyl-9,10-propanoanthracene 39 (43 mg, 71%) as white crystals.

m.p. = 108-112 °C

ν_max (KBr) 3024 w, 2966 m, 2929 m, 2915 m, 1755 m, 1379 m, 1127 s, 1082 s, 854 s, 828 s, 769 s, 745 s, 596 s, 495 s cm⁻¹

δ_H (400 MHz, CDCl₃) 7.27-7.33 (4H, m, H-1,4,5,8), 7.15-7.21 (4H, m, H-2,3,6,7), 4.10 (2H, dd, H-9,10), 2.46 (2H, m, H-11 cis,13 cis), 1.97 (2H, ddd, H-11 cis,13 trans), 1.08 (3H, d, CH₃)

coupling constants: J_9,13 cis = J_{10,11 cis} = 6.2 Hz, J_{9,13 trans} = J_{10,11 trans} = 1.8 Hz, J_{11 cis,11 trans} = J_{13 cis,13 trans} = 15.1 Hz, J_{F,11 cis} = J_{F,13 trans} = 34.5 Hz, J_{F,11 cis} = J_{F,13 cis} = 20.2 Hz, J_{11 cis,13 cis} = 1.8 Hz, J_{F,CH₃} = 21.2 Hz

δ_H (400 MHz, CCl₄ - C₆D₆ - 12:1)

coupling constants: J_{9,13 cis} = J_{10,11 cis} = 5.8 Hz, J_{9,13 trans} = J_{10,11 trans} = 2.2 Hz, J_{11 cis,11 trans} = J_{13 cis,13 trans} = 14.8 Hz, J_{F,11 cis} = J_{F,13 trans} = 30.6 Hz, J_{F,11 cis} = J_{F,13 cis} = 20.0 Hz, J_{11 cis,13 cis} = 1.8 Hz, J_{F,CH₃} = 20.6 Hz
Experimental: propanoanthracenes

\[ \delta_H (400 \text{ MHz, } C_6D_6) \]

coupling constants: \( J_{9,13-\text{cis}} = J_{10,11-\text{cis}} = 5.9 \text{ Hz}, J_{9,13-\text{trans}} = J_{10,11-\text{trans}} = 2.0 \text{ Hz}, \]
\( J_{11-\text{cis},11-\text{trans}} = J_{13-\text{cis},13-\text{trans}} = 14.9 \text{ Hz}, J_{F,11-\text{trans}} = J_{F,13-\text{trans}} = 31.9 \text{ Hz}, \)
\( J_{F,11-\text{cis}} = J_{F,13-\text{cis}} = 20.1 \text{ Hz}, J_{11-\text{cis},13-\text{cis}} = 1.8 \text{ H}, J_{F,CH_3} = 20.8 \text{ Hz} \)

\[ \delta_H (400 \text{ MHz, } CD_3CN) \]

coupling constants: \( J_{9,13-\text{cis}} = J_{10,11-\text{cis}} = 6.2 \text{ Hz}, J_{9,13-\text{trans}} = J_{10,11-\text{trans}} = 1.8 \text{ Hz}, \)
\( J_{11-\text{cis},11-\text{trans}} = J_{13-\text{cis},13-\text{trans}} = 15.3 \text{ Hz}, J_{F,11-\text{trans}} = J_{F,13-\text{trans}} = 35.1 \text{ Hz}, \)
\( J_{F,11-\text{cis}} = J_{F,13-\text{cis}} = 20.4 \text{ Hz}, J_{11-\text{cis},13-\text{cis}} = 2.0 \text{ H}, J_{F,CH_3} = 21.2 \text{ Hz} \)

\[ \delta_C (100.6 \text{ MHz, } CDCl_3) 144.07d, 141.86d, 126.31u, 126.17u, 125.55u, 125.34u, 96.39d \]
\( (d, J = 167.6 \text{ Hz, C-12}), 44.43u (C-9,10), 42.29d (d, J = 21.3 \text{ Hz, C-11,13}), 30.62u (d, J = 24.3 \text{ Hz, CH}_3) \)

\[ \delta_F (376.3 \text{ MHz, } CDCl_3) -123.0 \text{ (multiplet) ppm} \]

m/z (El) 252 (M+, 100%), 232 (24), 231 (16), 218 (10), 217 (57), 192 (47), 191 (97), 189 (17), 179 (8), 178 (51), 165 (7), 152 (3), 139 (2), 128 (1)

Found: C, 85.81; H, 6.92. C_{18}H_{17}F requires C, 85.68; H, 6.79 %.

Preparation of 9,10-dihydro-11-hydroxy-1,2,3,4,5,6,7,8-octachloro-9,10-propanoanthracen-12-one (42)

Aluminum chloride (1.7g, 13 mmol) was added as a single portion to a solution of 9,10-dihydro-11-hydroxy-9,10-propanoanthracen-12-one 22 (1g, 4 mmol) in sulfuryl chloride (50 ml) and sulfur monochloride (8 ml). The reaction mixture turned red and was refluxed for 1h. The solvents were evaporated in vacuo. An aqueous solution of
Experimental: propanoanthracenes

potassium carbonate was added to the residue and the mixture extracted with toluene (3x250 ml). Organic extracts were washed with brine, dried (MgSO₄) and evaporated in vacuo. Crystallisation of the residue from xylene gave 9,10-dihydro-11-hydroxy-1,2,3,4,5,6,7,8-octachloro-9,10-anthracen-12-one 42 (0.67 g, 32%) as yellow crystals.

m.p.: the compound decomposes at temperatures >250 °C without melting

ν<sub>max</sub> (CDCl₃) 3482 w, 2958 w, 1712 s, 1372 s, 1328 w, 1232 w, 1176 w, 1079 m cm⁻¹

δ<sub>H</sub> (400 MHz, CDCl₃) 5.83 (1H, d, H-10), 5.56 (1H, dd, H-9), 4.28 (1H, t, H-11), 3.94 (1H, d, OH), 3.26 (1H, dd, H-13<sub>cis</sub>), 2.80 (1H, ddd, H-13<sub>trans</sub>)

coupling constants: J₁₀,₁₁ = 2.3 Hz, J₉,₁₃<sub>cis</sub> = 6.6 Hz, J₉,₁₃<sub>trans</sub> = 1.7 Hz,

J₁₁,OH = 2.7 Hz, J₁₃<sub>cis</sub>,₁₃<sub>trans</sub> = 15.8 Hz
decoupling experiments: irradiation frequency (changed signals): 5.83 (4.28), 5.56 (3.26, 2.80), 4.28 (5.83, 3.94, 2.80)

δ<sub>C</sub> (100.6 MHz, CDCl₃) 205.58d (C-12), 139.74d, 136.82d, 136.50d, 136.08d, 133.01d, 132.99d, 132.89d, 132.84d, 132.41d, 130.93d, 130.10d, 129.83d, 80.56u (C-11), 47.10u (C-10), 45.71s (C-13), 38.96u (C-9)
m/z (CI-ammonia) 550(19), 549(28), 548(12), 547(44), 546(17), 545(51), 544(18), 543(46), 542(4), 541(22) (M+NH₃⁺ - isotopic cluster, %), 508(21), 454 (100), 420 (96)
m/z (EI) 454 (M⁺ - 2 Cl, 85), 418(36), 384 (26), 350 (16), 314 (21), 279 (100), 256(52)
Preparation of 9,10-dihydro-11-(imidazol-1-yl-thiocarbonyloxy)-1,2,3,4,5,6,7,8-octachloro-9,10-propanoanthracen-12-one (44)

A solution of 9,10-dihydro-11-hydroxy-1,2,3,4,5,6,7,8-octachloro-9,10-propanoanthracen-12-one 42 (50 mg, 0.1 mmol) and 1,1'-thiocarbonyldiimidazole 43 (36 mg, 0.2 mmol) in benzene (5 ml) was stirred at 70°C for 8 h. The solution was directly transferred to a column. Flash chromatography (silica gel, gradient elution; petrol-4% AcOEt → petrol-30% AcOEt) gave in order of elution presumed 9,10-dihydro-1,2,3,4,5,6,7,8-octachloro-9,10-propanoanthracen-12-one 45 (8 mg) as yellow crystals, recovered hydroxyketone 42 (29mg), and 9,10-dihydro-11-(imidazol-1-yl-thiocarbonyloxy)-1,2,3,4,5,6,7,8-octachloro-9,10-propanoanthracen-12-one 44 (12 mg, 20%) as yellow crystals.

\( \nu_{\text{max}} (\text{CDCl}_3) 2928\text{s}, 2855\text{m}, 1709\text{s(broad)}, 1602\text{m}, 1483\text{s cm}^{-1} \)

\( \delta_H (400 \text{ MHz, CDCl}_3) 7.57 (1H, s, H-imidazol), 7.11 (1H, s, H-imidazol), 6.82 (1H, s, H-imidazol), 5.93 (1H, d, H-10), 5.58 (1H, dd, H-9), 5.10 (1H, d, H-11), 3.30 (1H, dd, H-13\text{cis}), 2.41 (1H, dd, H-13\text{trans}) \)

coupling constants: \( J_{9,13\text{cis}} = 5.9 \text{ Hz}, J_{9,13\text{trans}} = 1.9 \text{ Hz}, J_{10,11} = 3.4 \text{ Hz} \)

\( J_{13\text{cis},13\text{trans}} = 15.7 \text{ Hz} \)

\( \delta_C (100.6 \text{ MHz, CDCl}_3) 184.67 (C=S), 139.99, 135.22, 134.57, 133.70, 132.80, 131.76, 131.73, 131.41, 131.22, 130.53, 130.1, 84.08\text{u} (C-11), 44.03\text{u} (C-10), 38.13\text{u} (C-9), 37.02\text{d} (C-13) \)
4. References


