Design and synthesis of coronene-based and other novel inclusion compounds.

by

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Dedication.

To my mother and father.

Acknowledgements.

Firstly, my sincere thanks to Dr. David D. MacNicol for his continual support throughout the period of my research, and his careful proof reading of this thesis.

Secondly, I must thank friends from Labs. 313 and 168 for helping me retain my sanity at the more stressful points of my research. They include: John Maguire, Greg Bradley, Djamel Khelifi, Stuart Rowan, Martin Lear and others too numerous to mention. Also Dr. D.G. Morris for his helpful discussions during my term in both Labs, Kerr Jamieson for his friendly service as the Chemistry Branch Librarian, and Betty Forbes for dealing with my Australian correspondence.

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Finally, I wish to acknowledge BASF for their gift of coronene; Professor Watanabe and his colleagues at Kyoto University for supplying perfluoro-perhydrocoronene, and SERC for their support, which allowed me to research such an interesting topic.

To be a philosopher is not to merely have subtle thoughts, or even to found a school, but so to love wisdom as to live according to its dictates, a life of simplicity, independence, magnanimity and trust. It is to solve some of the problems of life, not only theoretically, but practically.

Thoreau, "Walden".

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RESULTS AND DISCUSSION

Chapter 6

Design of coronene-based hosts

Chapter 7

Fine-tuning within the spider-host series.

Chapter 8

A novel fluorocarbon reaction - study of new substrates

Summary

Chapters 1-4 present an overview of the development of clathrate chemistry; from its early origins, involving purely chance discoveries, to the present day, where new concepts are deliberately employed in the design of new clathrate systems. In addition, Chapter 5 describes some illustrative applications of the host molecules discussed.

The research contained in Chapter 6 details the specific use of one of the key concepts for the design of new host series, this being the consideration of molecular symmetry. The coronene unit, with its C_3 axial symmetry, was successfully employed as core building block for a new series of per-substituted sulphur-bases coronene hosts. Dodecakis(3,5-dimethylphenylthio)coronene, prepared by dipolar aprotic solvent-promoted substitution of perchlorocoronene, proved to be the most versatile host. The structure of the 1,4-dioxane clathrate of this host has been established by CPMAS NMR and single-crystal X-ray analysis. Systematic design work was carried out to define the relationship between the structure of side-chain moiety and clathration ability in related sulphur-based systems, and the results are described.

Members of a new class of molecule, dodecakis(aryloxy)coronenes, have been prepared for the first time, and also found to form crystalline inclusion compounds. These hosts are characterised by lower stability and higher guest content compared with their sulphur-based counterparts, dodecakis(3,5-

dimethylphenoxy)coronene, for example, incorporating *ca.* six 1,4-dioxane guest molecules per host.

Chapter 7 describes the optimisation of inclusion versatility in the octa-substituted naphthalene host series (spider-host) using the concept of identification of a favoured side-chain moiety in design. Using this approach the most versatile spider-host known to date, octa(3,4-dimethylphenylthio)-naphthalene, was synthesised. This host has been found to form clathrates with over twenty guest species ranging in size from ethanol to isobutyrophenone. In the case of the toluene adduct, single-crystal X-ray analysis has established a unique (with respect to clathrate design) cubic form, space group $Pn\bar{3}$. Also discussed are related new octaethers; reinforcing the difference in inclusion characteristics observed for the oxygen- and sulphur- spider-hosts.

Chapter 8 describes a further study of a novel reaction of saturated fluorocarbons, previously defined for perfluorodecalin, and now extended to substrates perfluoroperhydroacenaphthene and perfluoroperhydrocoronene. Both reactions met with success; the latter is particularly noteworthy since this substrate led to the versatile host molecule dodecakis(3,5-dimethylphenyl-thio)coronene, referred to above, via a novel process involving aromatisation of all seven six-membered rings.

CHAPTER 1.

CLASSICAL HOSTS

1.1 General background and nomenclature

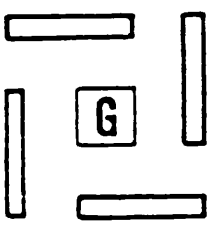
Inclusion compounds can be divided into two separate groups : complexes and clathrates. The complexes are defined as host-guest aggregates which are derived from a coordination between the host and guest components. Usually only one host molecule is involved in the aggregate, hence such complexes are known as unimolecular hosts.

On the other hand, the term clathrate is used for host-guest aggregates where the guest is retained by steric barriers formed by the host lattice (crystal lattice forces). These hosts are termed multimolecular, as more than one host molecule is involved in the aggregate.

The subject for discussion will be limited solely to clathrates as the research contained herein involves the design of such species and not complexes. The main purpose of the review will be to illustrate how clathrate hosts have evolved over the past 150 years, from the accidental discovery of classical hosts, to the rational design of a new host series. This chapter sets the scene by describing a representative number of classical hosts which formed the basis of clathrate chemistry as we know it today. The emphasis is placed mainly on the structures of the classical hosts, particularly because of their influence on the subsequent design of new host series. Chapter 2 then takes clathrate chemistry

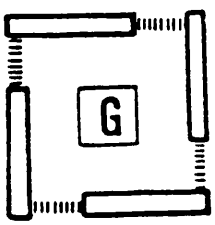
one step further with the introduction of the first concept[1] in host design: the modification of a classical host. Chapters 3 and 4 conclude the discussion on the evolution of the clathrate by illustrating the two concepts representing the pinnacle of host design, namely, design by analogy[2] and design using molecular symmetry[3]. The final chapter then concentrates on the properties and applications of some of the hosts discussed.

However before progressing any further, it would be worthwhile examining the classification of clathrates in order to facilitate further discussion. Clathrates in general can be categorised into four types according to their host-guest interaction:-

(a) 

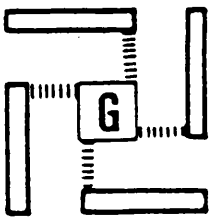
G = Guest.

without any coordinative interaction ("true" clathrate).

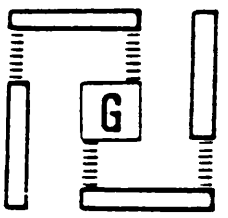
(b) 

Coordinative host-host interaction (coordination assisted clathrate host lattice).

(classical clathrates).

(c) 

coordinative host-guest interaction only (coordinato-clathrate).

(d) 

both coordinative host-host and host-guest interaction(coordinato-clathrate in a coordination-assisted host lattice).

A further classification involves the topology of the host-guest aggregate. More specifically, the topology of the cavity encapsulating the guest. Only two types of cavity are of relevance within this discussion:- the open channel cavity (tubulate) and the totally enclosed cage structures (cryptates). The distinction between the two is not always clear cut : in some clathrates the channels markedly narrow at regular intervals and thus could be regarded as cryptate structures.

The final classification involves numerical considerations dealing with the total number of individual components in a chemical sense e.g. ternary (t) etc, and with the number of particles [host, guest separately e.g. monomolecular (1m), binuclear (2n) respectively] are also practicable. Emphasis though will mainly be placed on the type of interaction and host-guest topology when characterising the distinct clathrates.

Some workers involved with clathrate nomenclature[4] tend to become over involved with unhelpful details relating to the terminology, generally leading to

confusion for the reader, hence the reason for a more simplified version.

Finally, to avoid further confusion, the term clathrate will often be replaced with adduct or, even, complex.

1.2 Hydroquinone

Most early clathrates were discovered purely by chance. These crystalline adducts are comprised of a guest component, normally taken up from the recrystallisation solvent, and a host compound, early discovered examples of which are now widely known as classical hosts.

The first classical host of any significance was the H_2S adduct of hydroquinone, discovered in 1849 by Wöhler.[5] The clathrate merely aroused curiosity, until that is the 1940s, when Powell's excellent X-ray study revealed the complex structure behind such a simple clathrate.[6]

X-ray studies demonstrated that hydroquinone can exist in three crystal forms designated α, ß and γ.[6,7,8,9,10] The versatile ß-form was solved first establishing three crystallographically distinguishable kinds of ß-hydroquinone host lattice, Types I-III, all having the same general formula $3C_6H_4(OH)_2xG$, where G represents the encaged guest molecule and x is a site occupancy factor between zero and one. The H_2S clathrate corresponds to the Type I situation for ß-hydroquinone, where cavities having $\bar{3}$ symmetry are present. Fig. 1.1

shows a stereoview of such a centrosymmetric cage of the unsolvated form.

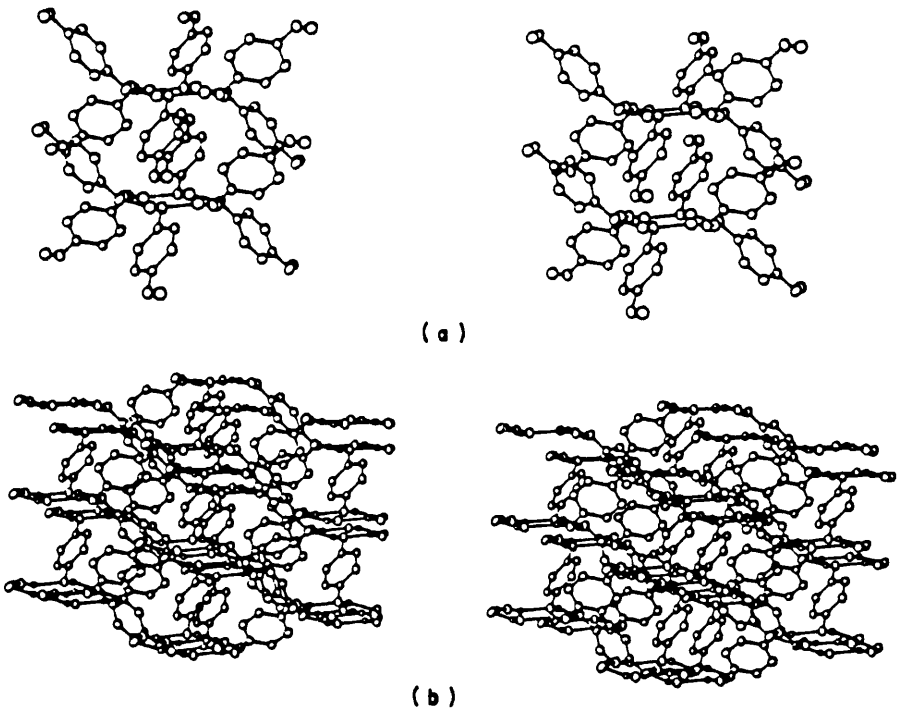


Fig. 1.1. (a) Stereoview illustrating a single cage of the unsolvated form of the ß-hydroquinone host lattice (b) interpenetrating networks of ß-hydroquinone.

As can be seen, the top and bottom of the void are formed by hexagons of hydrogen-bonded oxygen atoms; an ordered arrangement of hydrogen atoms is apparent in the $[OH]_6$ rings and the host molecules point alternately above and below the mean plane of the (nearly planar) six oxygen atoms. The hexameric

units forming the ceiling and floor of a given cage (Fig. 1.1b), belong to two identical, but displaced, three-dimensional interlocking networks.

In Type II clathrates, such as those formed by hydroquinone with SO_2, MeOH and CH_3NC, a lowering of space group from $R\bar{3}$ to $R3$ is found, and guest accommodation is provided in cages which are still trigonal, though no longer centrosymmetric. For the relatively long guest molecule, methyl isocyanide, the cage length is markedly increased compared to type I systems (Fig. 1.2).[11]

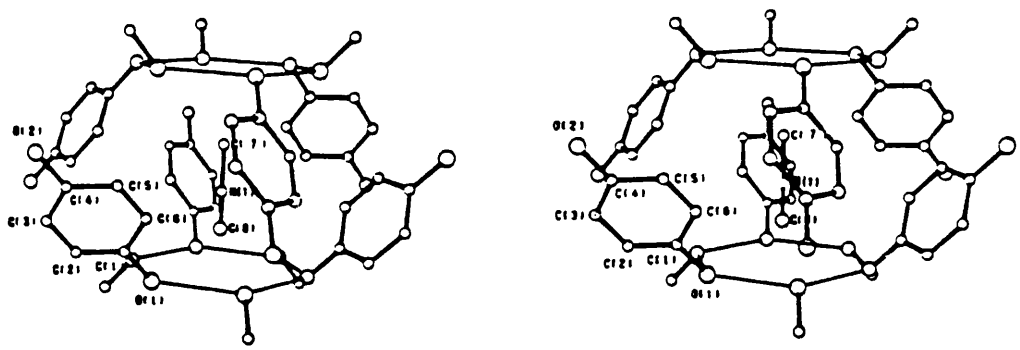


Fig. 1.2. A stereo-drawing showing a CH_3NC guest molecule trapped inside a cage.

An X-ray analysis of the methanol clathrate has revealed the hydroxyl group of the methanol interacts with three phenolic oxygen atoms of the adjacent $[OH]_6$ ring (Fig. 1.3). It has been proposed that this interaction causes the lowering of space group symmetry to $R3$, found in Type II clathrates. Hence,

formation of Type II ß-hydroquinone clathrates is favoured by guest molecules of appropriate sizes which can interact appreciably with specific sites in the walls of the clathration cavity.

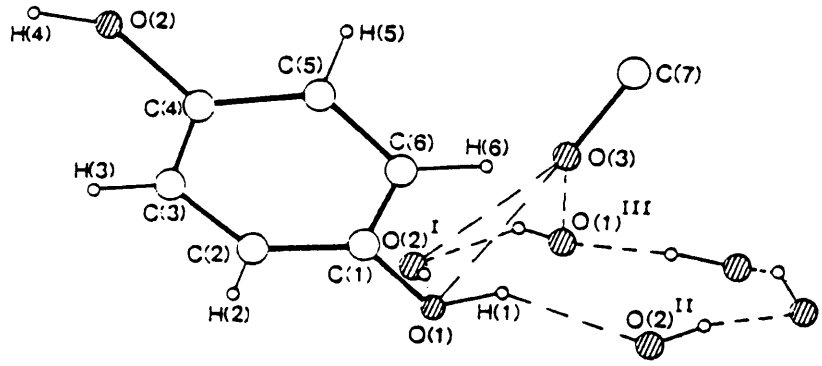


Fig. 1.3. Host-guest interactions in the methanol clathrate of hydroquinone.

The Type III system involves a further lowering of symmetry from rhombohedral lattice to space group *P*3. Only acetonitrile forms an adduct with hydroquinone to give this Type III system. As shown in Fig. 1.4, the three symmetry-independent acetonitrile molecules fit snugly inside three distinct cavities, where one guest molecule is aligned in the opposite sense to the other two.[9]

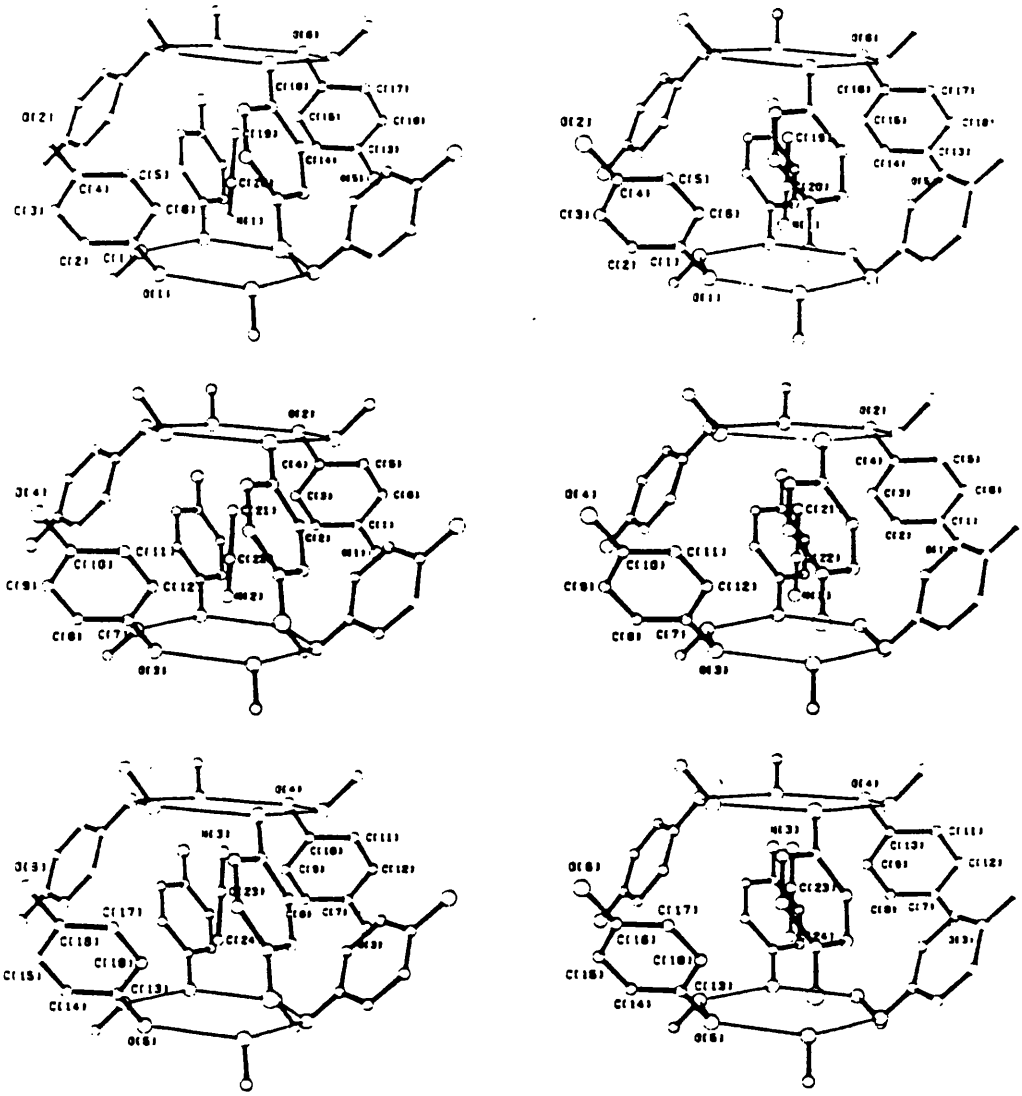


Fig.1.4. Type III. Hydroquinone clathrate trapping acetonitrile.

The main difference between CH_3CN and CH_3NC adducts appears to be the greater acidity and reduced effective molecular length of the former, resulting in different systems for both guests within the hydroquinone network. Both adducts are markedly unstable and rapidly lose guest in air.

Until recently only these three types of ß-hydroquinone were known to exist. Then in 1991 Ermer succeeded in producing an additional form.[12] Having noticed the role of host-guest interactions in determining the type of lattice formed by ß-hydroquinone, Ermer proposed that a single ß-hydroquinone network offered a favourable geometry for the inclusion of the topical[13] and voluminous buckminsterfullerene (C_{60}) as a guest. Furthermore he expected that complex formation would be supported by the π electron donating properties of hydroquinone as C_{60} had been shown to be an unusually strong electron acceptor.

Crystallisation duly gave the $(HQ)_3\ C_{60}$ complex with space group $R\bar{3}m$; even higher symmetry than the Type I ß-hydroquinone clathrate. Complex $(HQ)_3\ C_{60}$ confirmed Ermer's postulate by possessing a single host lattice of hydroquinone enclathrating the C_{60} molecule. Within the complex the C_{60} molecules exhibited orientational disorder. In contrast, the hydroquinone host molecules were ordered and structurally well-defined. The structural characteristics of the hydrogen-bonded architecture of the $(HQ)_3C_{60}$ complex are illustrated in Fig. 1.5.

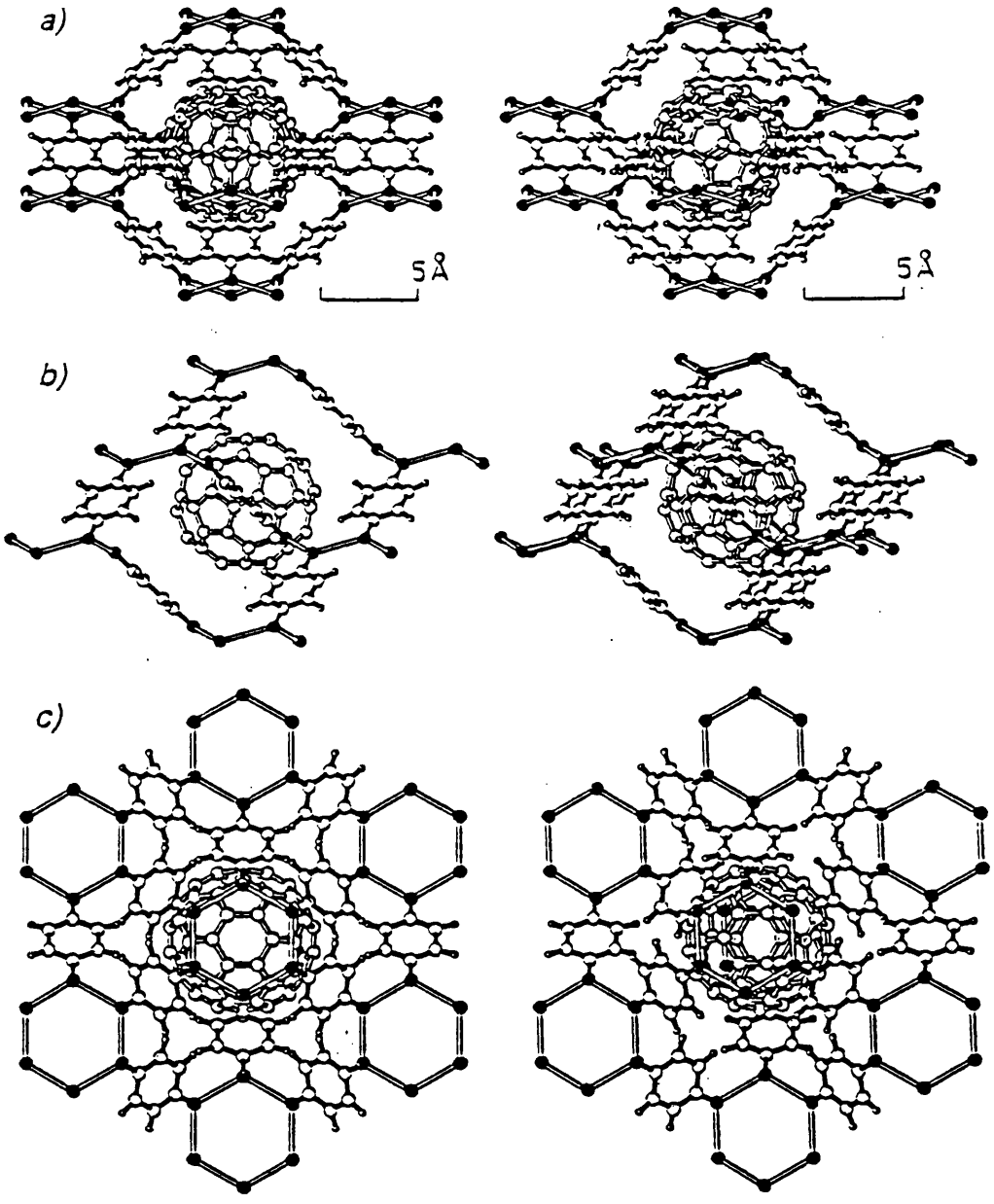


Fig. 1.5. Ball-and-stick stereoviews of the super-polonium architecture of $(HQ)_3C_{60}$. The representation of C_{60} is based on constructed atomic coordinates. The bridging hydrogen atoms of the $(OH)_6$ rings are omitted, and the O(H)O bridges are drawn as white bands; note the pronounced chair-like puckering of the $(OH)_6$ rings.

Hydroquinone = HQ.

The considerable trigonal elongations in the $(HQ)_3C_{60}$ complex is reflected in the geometry of the hydrogen-bonded $(OH)_6$ rings, which are highly puckered in the present complex (Fig. 1.5a,b) yet almost flat in the doubly interpenetrating ß-hydroquinone structures. This puckering is a consequence of the elongation of the lattice in $(HQ)_3C_{60}$ when compared to those of other forms of hydroquinone. The elongation resulting in a 20.5% increase in unit cell volume, compared to a hypothetical undistorted single ß-HQ lattice.

The large C_{60} molecules have a molecular mass 2.2 times larger than that of three hydroquinone molecules, and occupy 50% of the crystal volume. Therefore, the $(HQ)_3C_{60}$ clathrate represents one of the rare inclusion compounds with more guest than host material, and constitutes the fourth type of ß-hydroquinone.

Wallwork and Powell carried out further work on hydroquinone in the 1960's, managing to elucidate the structure of α-hydroquinone.[14] The stable α form crystallised in the $R\bar{3}$ space group with 54 molecules of hydroquinone in the hexagonal unit cell, and, correspondingly, 3 molecules in the asymmetric unit. Of the three crystallographically independent hydroquinone molecules in the asymmetric unit, two are involved forming two interpenetrating, open, hydrogen-bonded cageworks similar to those found in the structure of ß-hydroquinone and capable of clathrating small molecules,[9,15,16] whereas the third forms double helices consisting of hydrogen-bonded chains of molecules round the threefold

screw axes, one of which is denoted by a continuous line at the left side of Fig. 1.6a.

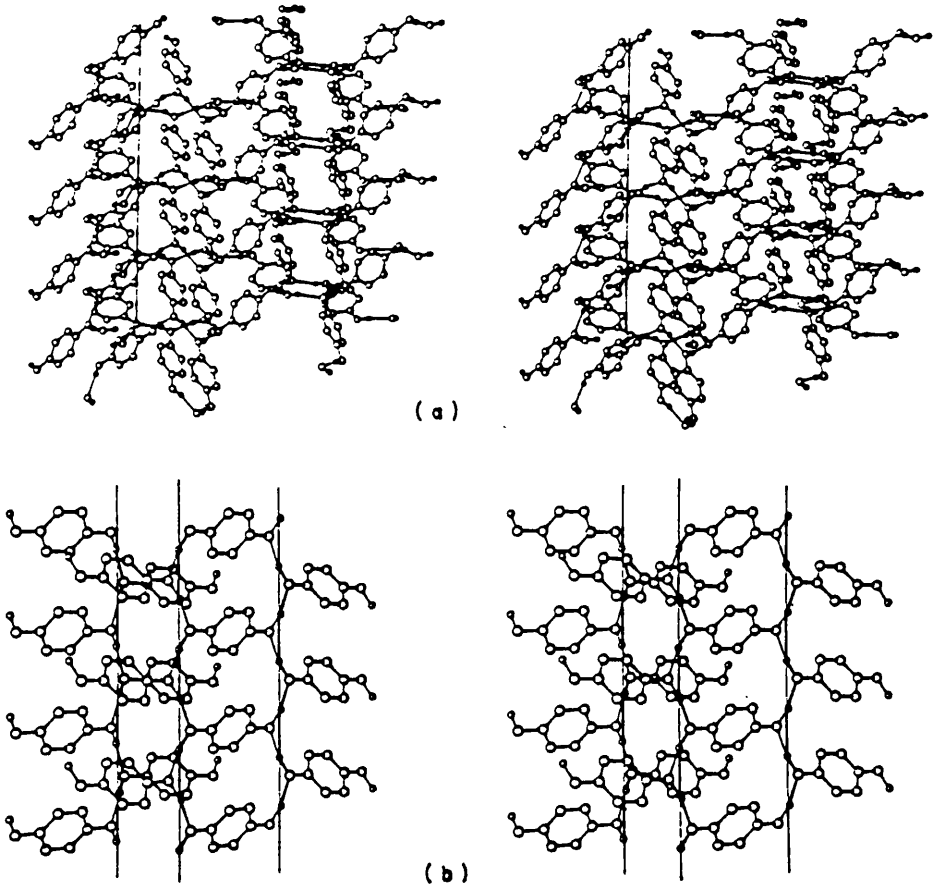


Fig. 1.6. (a) Stereoview illustrating the structure of α-hydroquinone and (b) the structure of γ-hydroquinone (the parallel lines represent two-fold screw axes).

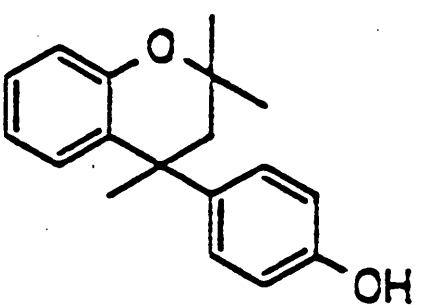
The cageworks and helices are hydrogen-bonded together in such a way that the interpenetrating cageworks are connected (unlike the ß form) and the two strands of the double helix are connected. The local density for the helical region is high for an organic structure consisting only of light atoms and confirms that this part of the structure cannot include guest molecules. Thus, there are

three cages (of $\bar{3}$ symmetry) similar in size to those of the ß form and 54 molecules of hydroquinone per unit cell, the minimum ratio expected for α hydroquinone clathrates is 18:1 against 3:1 for the ß hydroquinone clathrates.

The γ form, shown in Fig. 1.6b, has no hydrogen-bonded hexameric units and no known inclusion properties; the structure[17] is built up from sheets of hydrogen-bonded hydroquinone molecules, 2-fold screw axes, relating centrosymmetric molecules of hydroquinone, denoted by parallel lines in figure 1.6b. The instability and cleavage of the γ form is due to weak van der Waals forces holding the sheets together.

1.3 Dianin's compound

A host molecule bearing a close resemblance to ß-hydroquinone, at least in space group $R\bar{3}$ and hexameric hydrogen-bonded host unit, is 4-*p*-hydroxy-phenyl-2,2,4-trimethylchroman (1), first prepared by a Russian chemist A.P. Dianin in 1914.[18]



(Dianin)

(1)

He obtained the chroman by the gaseous HCl-catalysed condensation of phenol and mesityl oxide. Its propensity for inclusion was soon realised, forming adducts with guests as diverse as argon,[19,20] sulphur dioxide,[20] ammonia[20], decalin[21] glycerol,[22] sulphur hexafluoride,[23,24] di-*t*-Butyl nitroxide[25] and chloroform[26]. Most adducts crystallised in the space group $R\bar{3}$ with a host-guest ratio of 6:1. Like ß hydroquinone the matrix is held together by hydrogen-bonded hexamers; Fig. 1.7 shows the unsolvated form.

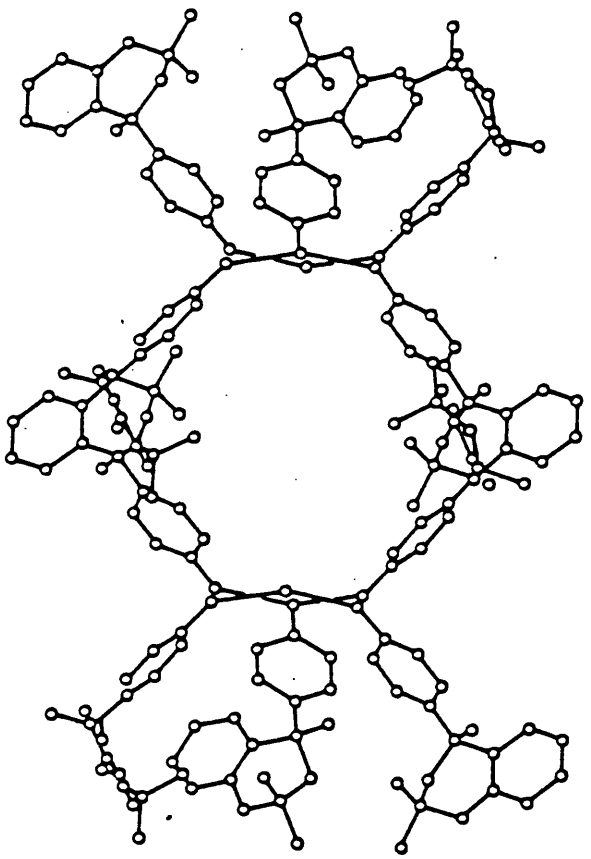


Fig. 1.7. Illustration of the unsolvated form of Dianin's compound (1), viewed normal to the *ac*-plane. Two molecules of (1) which lie above and below the cavity as viewed in this direction have been excluded (apart from their hydroxyl oxygen atoms) to show the cage more clearly.

At the top and bottom of each cage there are puckered hexagons of six hydroxyl oxygen atoms, linked by a network of hydrogen bonds, and three molecules of one configuration point upwards, with three of the opposite configuration pointing downwards. Each particular column is infinite in content and runs parallel to the *c*-axis; it is surrounded efficiently by six other identical columns related by three-fold screw axes (parallel to *c*), such that no significant spaces are left between columns. The dove-tailing involved in the lateral packing is illustrated in Fig. 1.8, the projection in one column fitting neatly into the indentation of its neighbour.

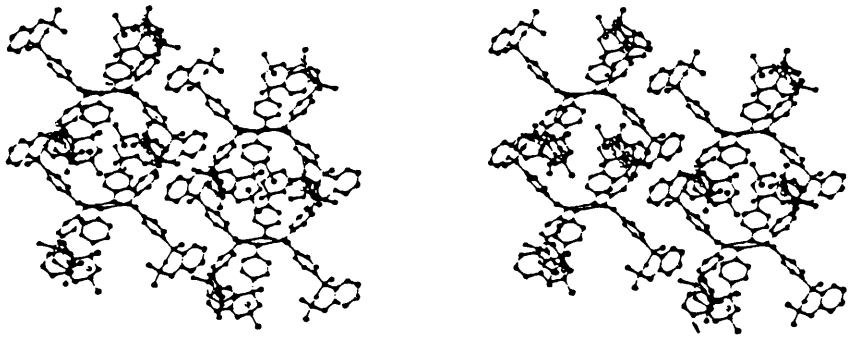


Fig. 1.8. An illustration of the dove-tailing involved in the lateral packing of columns, infinitely extended along *c* in unsolvated (1).

1.4 Urea

It was Bengen in 1940, who, purely by chance, found that urea could form a crystalline adduct with octyl alcohol. Subsequent work revealed that inclusion compounds were readily formed with *n*-alkanes and *n*-alkenes provided the

hydrocarbon has six or more carbon atoms.[27,28] For example, *n*-hexane forms an adduct, whereas no such stable compound is formed with *n*-pentane. Urea forms a vast number of inclusion compounds with a variety of different guests, including hydrocarbons and their alcohols, esters and ether derivatives, also with aldehydes, ketones, carboxylic acids, amines, etc., provided that their main chain consists of six or more carbon atoms.

Normally pure urea crystallises tetragonally (Fig. 1.9), however the

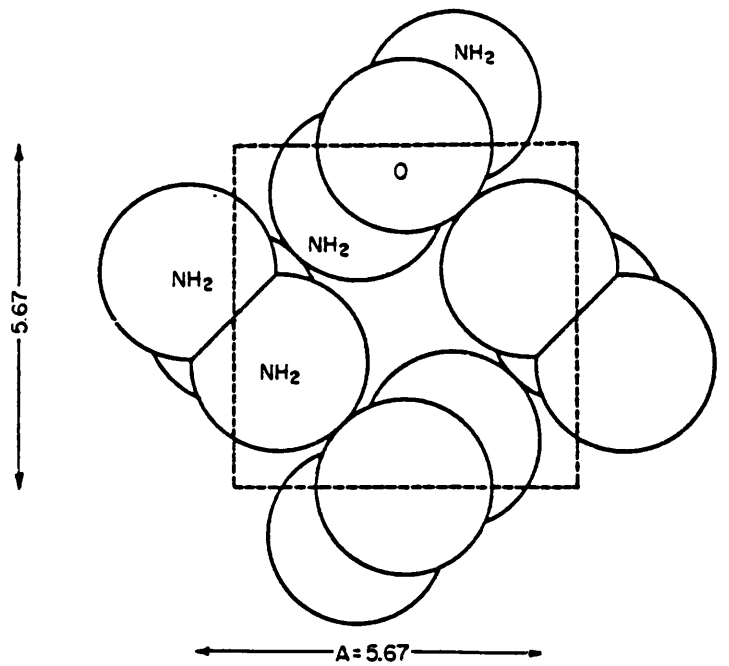


Fig. 1.9. The tetragonal urea structure.

clathrates crystallise to give a hexagonal crystal structure (Fig. 1.10).[29,30]

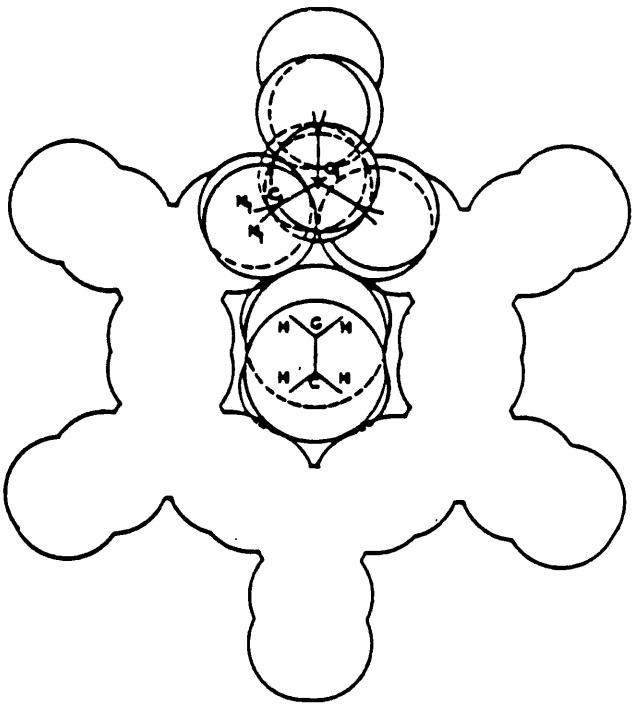


Fig. 1.10. The hexagonal crystal structure of urea adducts.

The clathrates are similar to those formed by Dianin's compound and hydroquinone, in that they form a coordination-assisted clathrate host lattice, involving hydrogen bonding between host molecules. From the X-ray analysis[30] it appears that the lattice of "hexagonal urea" has channel-like cavities with a diameter of only 5.2Å, explaining why usually only linear guests are included (sufficiently long branched-chain compounds are also included).

A fundamental feature of the channels in the urea lattice is the fact that the urea molecules making them up are aligned either in left-handed or right-handed helices, which are related as image and mirror image. The achiral urea

therefore spontaneously crystallises into two enantiomorphic lattices (Fig. 1.11): a property utilised in the resolution of racemic guest molecules (see Chapter 5).[31]

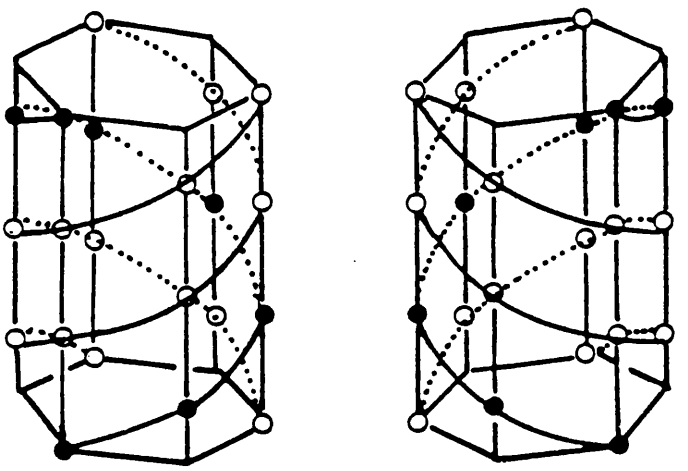


Fig. 1.11. A representation of the arrangement of urea molecules in the hexagonal lattice.

1.5 Thiourea.

In 1947, Angla, reported that thiourea also formed adducts with a variety of organic compounds.[32] The clathrates were in general rhombohedral crystals of the coordination-assisted type, similar to urea. The thiourea host lattice however has a channel diameter of approximately 6.1Å compared with 5.2Å for the urea host lattice. As a consequence, thiourea forms channel-type clathrates with highly branched hydrocarbons, e.g. trimethyl pentane and larger cyclic compounds such as cyclopentane, cyclohexane and decalin. On the other hand,

linear n-paraffins cannot form inclusion compounds with thiourea because of their loose fit in the large thiourea channels.

The arrangement of thiourea molecules in the crystals is not dissimilar to that of urea molecules in the urea inclusion lattice. Figure 1.12 compares these lattices.[33] Unlike urea, however, no spontaneous resolution is observed with thiourea.

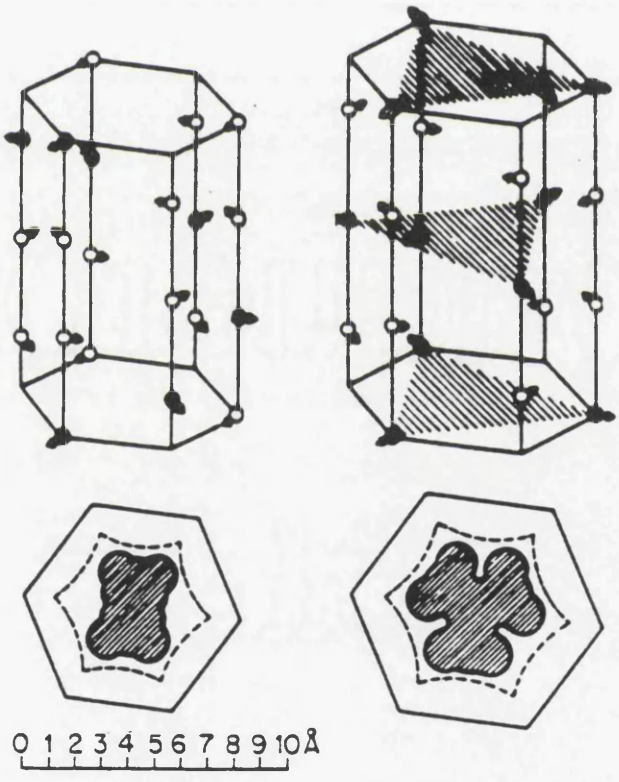


Fig. 1.12. Fundamental lattices of urea and thiourea inclusion compounds.

1.6 Trimesic acid.

The final coordination-assisted host relevant to this discussion is benzene 1,3,5-tricarboxylic acid (trimesic acid, TMA). TMA, like hydroquinone, has 3 polymorphs designated α, ß and γ. ß- and γ-TMA are both high-temperature polymorphs. The ß-form, however, cannot be quenched and has a limited lifetime at high temperature, thus preventing the determination of its structure. Both the α- and the γ-TMA have had their structures elucidated.[34,35] The common structural motif is the infinite hexagonal network of hydrogen-bonded TMA molecules (Fig. 1.13) and the way these networks are linked.

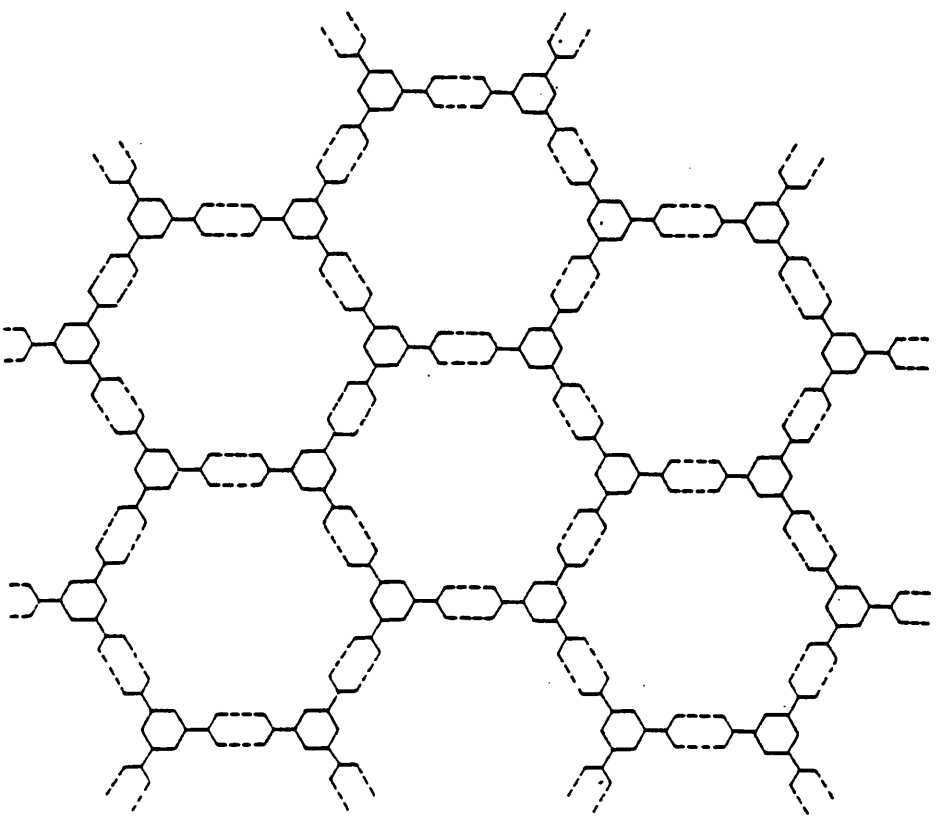


Fig. 1.13. Basic chicken-wire motif in hydrogen-bonded TMA.

Each central hole in Fig. 1.13 is threaded by three similar hexagonal arrangements, each parallel to the others (Fig. 1.14).

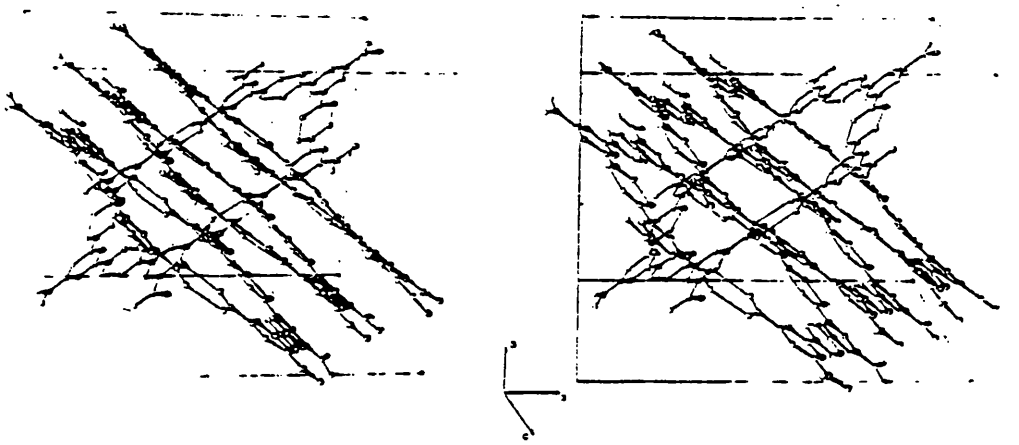


Fig. 1.14. Catenation of the hexagonal TMA networks.

Therefore the hexagonal network is triply catenated by the other three interlaced networks. These in turn are catenated by the original network and by two other parallel networks on either side of the original one.

Thus a three-dimensional matrix is formed consisting of two sets of three parallel networks, each set being triply catenated by the other. While each network is internally hydrogen bonded, there is no hydrogen bonding between the three networks of a set, nor between one set and another. The descriptions now diverge for the two polymorphs.

The simpler γ-TMA has hexagonal networks which are all essentially

planar and thus the two interlaced sets of parallel triplets cannot fill space efficiently but leave inclusion channels with axes along *c* (Fig. 1.14). The channels along *c* are filled with the appropriate polyhalide anions formed in inclusion compounds TMA $0.7H_2O.HI_5$ and TMA $0.7H_2O.0.103\ HBr_5$; both having space group I_{222}. Presumably the water molecule and associated proton must also reside within these channels.

In α-TMA the networks are planar only for intervals of three hexagonal units (Fig. 1.15).

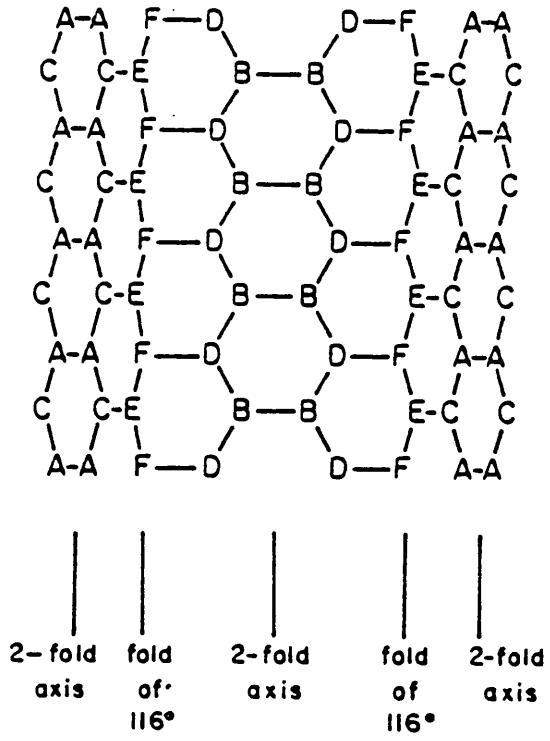


Fig.1.15. α-TMA : structure of the network repeat unit, shown here schematically. The molecules F,D and B in this figure are essentially coplanar; however the hexagonal network undergoes an abrupt fold between F and E with an angle of 116° between the mean planes.

Then, there is an abrupt change in the direction of the hexagonal network which arises from both rotation and displacement from the benzene ring planes of hydrogen-bonded carbonyl groups joining the molecules denoted as E and F. This fold or pleat can only occur in the flanking hexagons of each catenated triplet and hence does not appear in the partial structure shown in Fig. 1.16 below, where only central hexagons are shown. Two types of cavity are shown in the region of local triple catenation, one larger and one smaller. The interstitial Br_2 molecules of the TMA.$^1/_6Br_2$ adduct, are found in the larger of these voids in disordered fashion; the adduct crystallising in the space group *C*2/*c*.

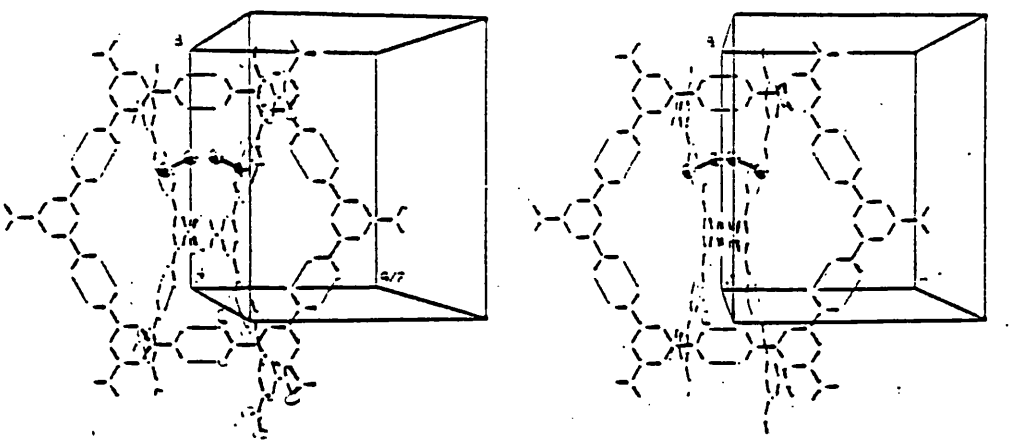


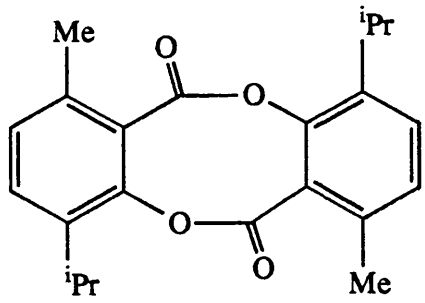
Fig. 1.16. α-TMA.$^1/_6Br_2$ stereodiagram showing part of the structure around the two-fold axis along 0,y,¼. Only the central member of each of the two triple networks of hydrogen-bonded TMA molecules is shown, and only one of the disordered Br_2 orientations.

α-TMA has also been shown to include acetone, resorcinol and hydroquinone in such channels.

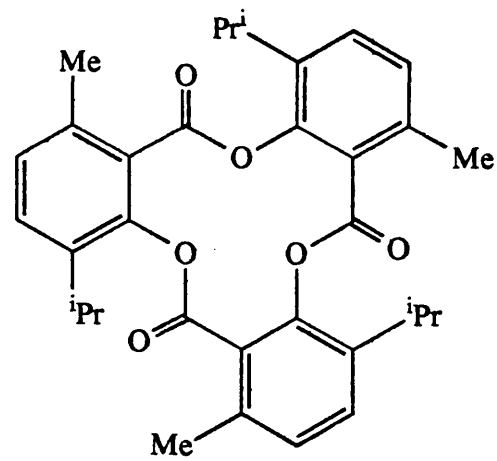
TMA may also incorporate H_2O or DMSO molecules in its hexagonal network. The DMSO molecules participate in the building of the lattice, with the sulphur and two methyl groups occupying the channel like gaps.

1.7 Tri-*ortho*-thymotide (TOT)

Following Spallino and Provenzal's[36] investigation in 1909 on the dehydration of 2-hydroxy-6-methyl-3-isopropylbenzoic acid (*o*-thymotic acid), Baker, Gilbert and Ollis succeeded in 1952 in separating, by fractional crystallisation, the di-*o*-thymotide(2) and tri-*o*-thymotide(3) produced during this reaction.[37]



(2)



(3)

The latter was found to include n-hexane, ethanol, methanol, (*dl*)-bromobutane, benzene, carbon tetrachloride, chloroform, 1,4-dioxane and *trans* stilbene. All clathrates had a host:guest ratio of 2:1, with the exception of benzene which has

a 2:2.5 host-guest ratio. In this case, the matrix interactions involve only van der Waals forces, hence TOT can be regarded as a true clathrate. Like urea, TOT clathrates spontaneously resolve on crystallisation, allowing resolution of racemic guest molecules (see Chapter 5).[37,39,42,151,152.]

Generally, in the solid state, TOT forms two types of enantiomorphous clathrates which can be differentiated by the topology of the cavity:

Type (a). The guest molecules are enclosed in discrete cages and are not in mutual contact. This is the more common form of TOT clathrate. The adducts normally crystallise in the space group $P3_121$, and are formed with guests of length not greater than 9Å e.g.(*dl*)-2-bromobutane or ethanol.

Type (b). The guest molecules are accommodated in continuous "linear" channels running through the crystal along characteristic crystallographic directions. The guest components are generally, but not always, in contact with each other in the channels. The adducts crystallise in three space groups, $P6_1$, $P6_2$ and $P6_3$. The guests are mainly long chain-like molecules.

The cage-type clathrate cavity is comprised of eight TOT molecules related in a pairwise manner about a crystallographic twofold axis that typifies the dissymmetry of the cage (Fig. 1.17).[40,41,42] The special location of the cages limits their number to three in each unit cell, with their centres separated by an average distance of *ca.* 13Å

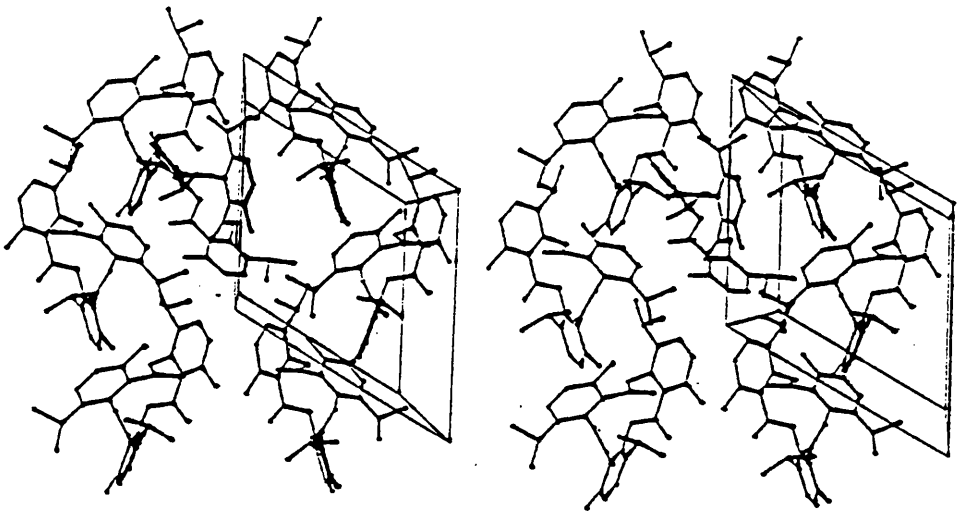


Fig.1.17. Stereoview of the packing of TOT molecules in a cage-type clathrate (space group $P3_121$). For clarity the top host molecule has been removed. A unit cell is outlined to indicate the crystallographic axial directions. A crystallographic two-fold axis runs parallel to the *a* axis.

The overall van der Waals contour of the cage resembles that of a deformed ellipsoid. The regions of the cage at both ends of the two-fold axis intercept differ from one another in shape and nature. At one end, a cluster of four isopropyl groups contributes to the formation of a bulge (e.g. near the origin of Fig. 1.17) which acts as a local receptor for bulky guest substituents. All guests containing a heteroatom, for example, are locked in that particular area close to the crystallographic two-fold axis. At the opposite end, two crystallographically equivalent carbonyl oxygen atoms point into the cage and may be in contact with the guest molecule.

With larger guests such as benzene[43] and *trans*-stilbene[44] the nature of the voids is different. In this case the clathrates are characterised by independent channels. The benzene adduct crystallises in the space group $P\bar{1}$ and contains three distinct channels in which the guest molecules reside : channels T_1 and T_3 are parallel to the *a* axis (Fig. 1.18) whilst channel T_2 is parallel to the *b* axis (Fig. 1.19).

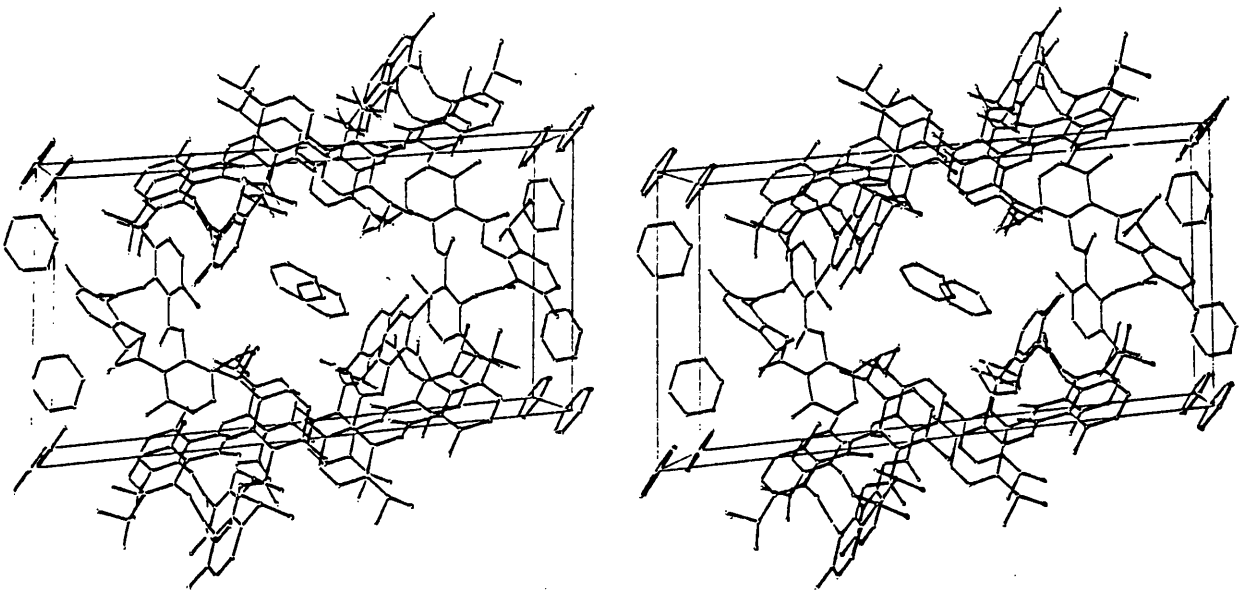


Fig. 1.18. Stereoview of the molecular packing of the TOT/benzene clathrate along the *a* axis. The benzene molecule at ¼, ½, ½ is located in channel T2. Channel T3 is centred around the *a* axis with a benzene ring in special position at 0,0,0 in the upper left corner. Channel T2 runs vertically along the *b* axial direction.

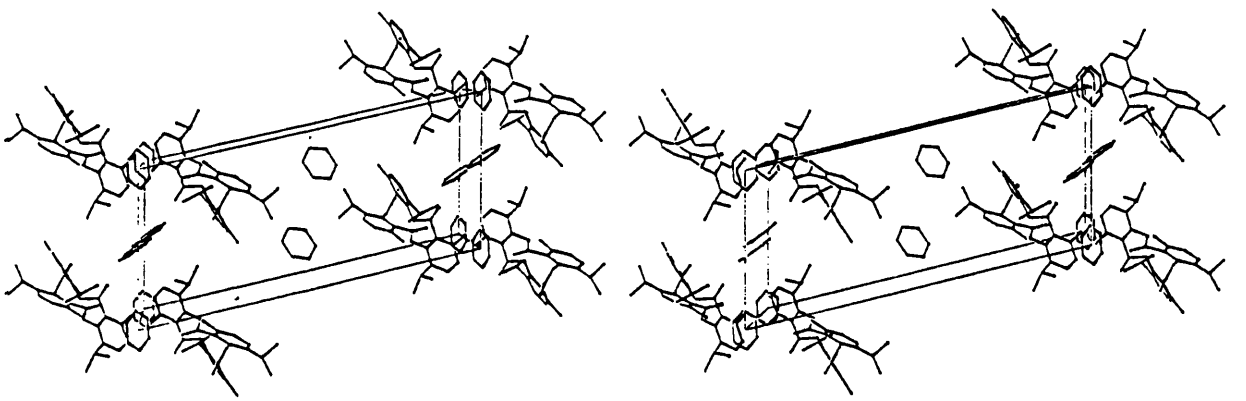


Fig. 1.19. Stereoview down the *b* axis of the channel T_2 in the TOT/benzene clathrate.

In the *trans*-stilbene adduct, the host-guest interactions and TOT's inherent flexibility combine to give a modified lattice architecture. In this case channels T_1 and T_2 remain, but channel T_3 completely disappears (Fig. 1.20).

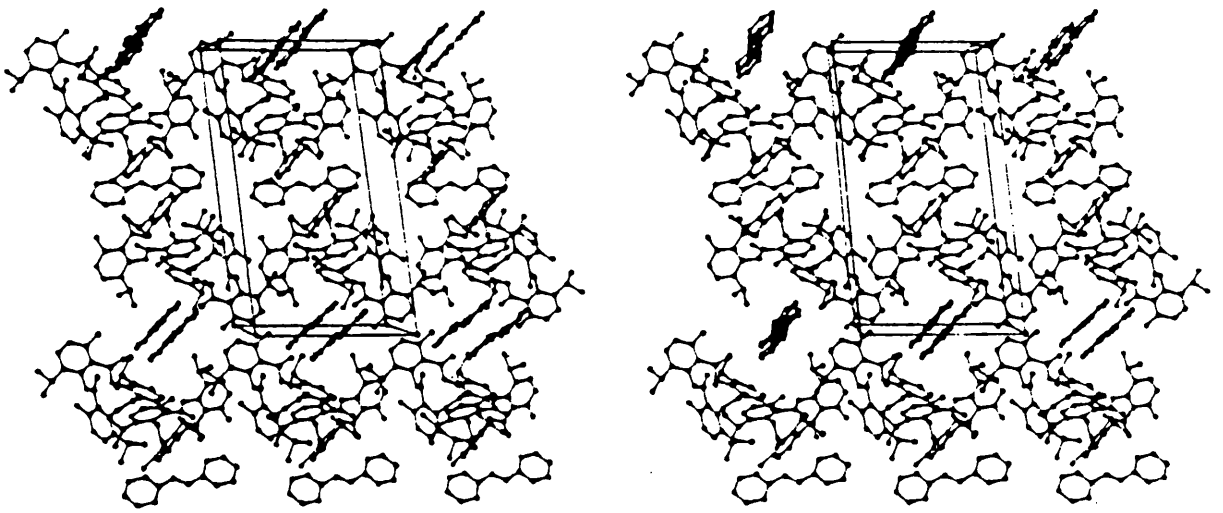
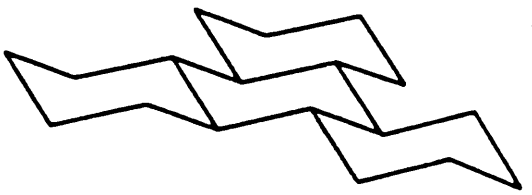


Fig. 1.20. Stereoview of TOT/trans-stilbene adduct structure.The *a,b,c* axes respectively point towards observer, to the right and upwards. Channel T_1 accommodates the *trans*-stilbene centred at 0 ,½ ,0.

1.8 Perhydrotriphenylene

trans, anti, trans, anti, trans-Perhydrotriphenylene (PHTP) (4) was synthesised by Farina in 1963[45] during research into low molecular weight models for optically active polymers.



PHTP

(4)

The molecule was prepared by hydrogenation of dodecahydrotriphenylene, $C_{18}H_{24}$, which in turn had been obtained from cyclohexanone according to

Mannich[46] or from tetralin and 1,4-dichlorobutane according to Reppe.[47]

As PHTP possesses $\underline{D}_3$ molecular symmetry, the host can exist in two enantiomeric forms (see Chapter 5), however, in initial studies, only racemic PHTP was used in the formation of clathrates.

The molecule's propensity for inclusion was discovered while recrystallising PHTP from *n*-heptane. Further investigation by Farina revealed its versatility. Examples of various types of guest forming clathrates with PHTP are linear compounds such as aliphatic hydrocarbons; mono- and di-carboxylic aliphatic acids and their esters; branched compounds such as 2,2,4-trimethyl pentane; cyclic molecules, specifically, benzene, toluene, 1,4-dioxane and guests of roughly spherical shape, such as carbon tetrachloride, chloroform and bromoform.[48-50]

In general, the adducts are non-stoichiometric as the arrangement of guest molecules inside the channels follows the criterion of total filling of available space. Again, like TOT, the host-guest and host-host interactions are purely van der Waals in nature, resulting in the classification of PHTP adducts as true clathrates.

The flexibility in crystal packing modes of PHTP, allowing accommodation of such varied guests, was further illustrated by the X-ray analysis of some PHTP clathrates.

The linear adduct with *n*-heptane crystallised in the $P6_3/m$ space group. The host structure is comprised of stacks of superimposed PHTP molecules arranged in the hexagonal unit cell (Fig. 1.21).[48-50] At the vertices of the cell there are channel-type cavities, the diameter of which is about 5Å. The guest molecules in these channels are not arranged in fixed positions.

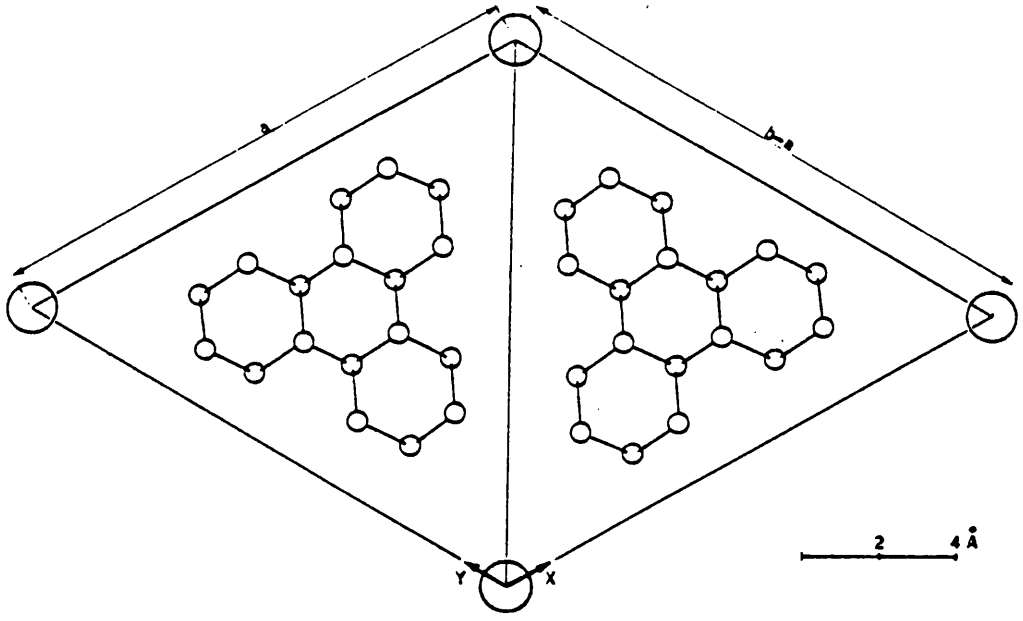


Fig. 1.21. *x-y* Projection of the crystal cell of the inclusion compound PHTP-*n*-heptane.

To accommodate bulkier guests, e.g. 2,4,4-trimethylpentane the host lattice simply expands by 0.3Å along the *a* and *b* axes of the crystal cell.[49,50]

Roughly spherical guests such as chloroform, give rise to a crystal cell of

quite different dimensions, with a cell volume typically three times that of the linear adduct.[49,51] The host lattice, though, closely resembles that of the *n*-heptane adduct (Fig. 1.22).

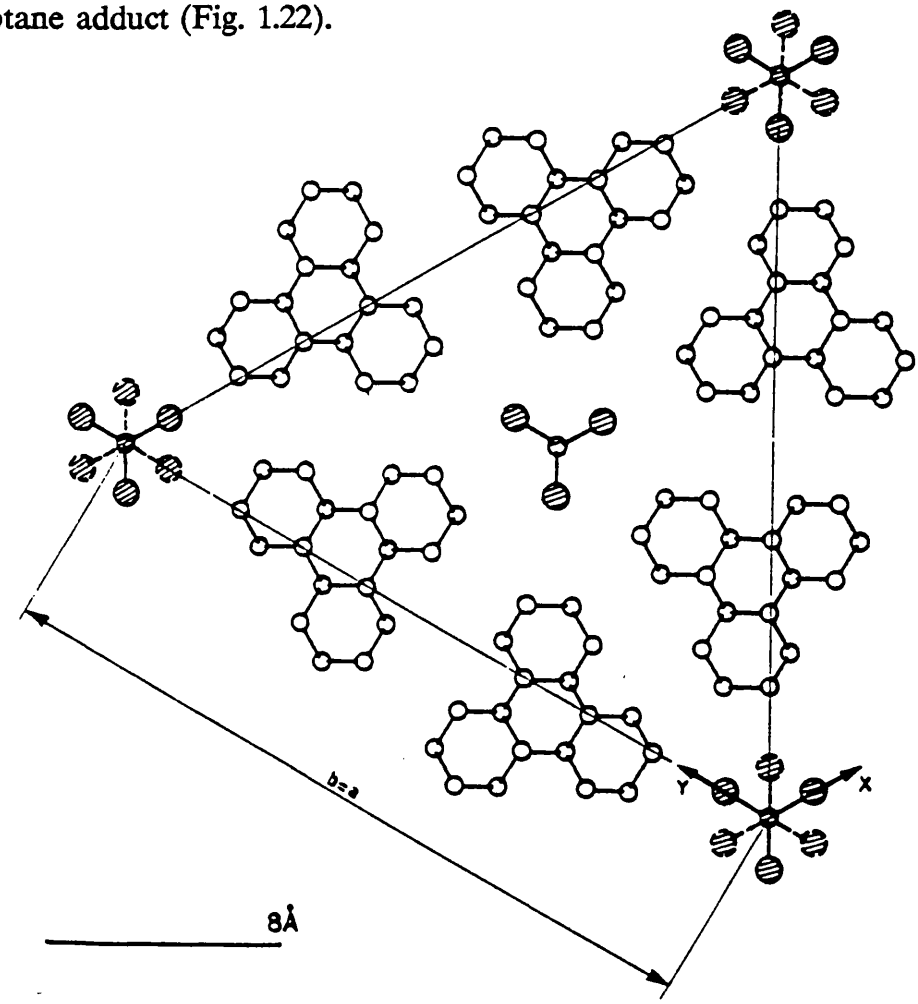


Fig. 1.22. *x-y* Projection of a part of the crystal cell of the inclusion compound PHTP-chloroform showing the different symmetry of the two channels. Guest molecules are shaded.

The host-guest ratio is exactly 6:3, yet the guest molecules do not occupy equivalent sites in the cell : two of them are located on the three-fold axes and one on the six-fold hexagonal axis at the vertex of the cell. The chloroform molecules along this axis are rotated by 60° and follow each other statistically in

such a way as to simulate hexagonal symmetry. In this inclusion compound there are therefore two different types of channel with different symmetries and dimensions.

A third and more complex type of architecture is found in the inclusion compound of PHTP with cyclohexane.[49,52] The adduct crystallises in the $R\bar{3}$ space group with a host-guest ratio of 54:21. The dimensions of a and b are close to those of the inclusion compound with $CHCl_3$, whilst the c axis is exactly 9 times greater. The cell of the PHTP-cyclohexane adduct (Fig. 1.23) shows PHTP molecules stacked in a slightly displaced manner on the horizontal plane, in such a way that their centre of gravity describes a 9/1 helix with a 0.4Å radius around the ternary crystallographic axis.

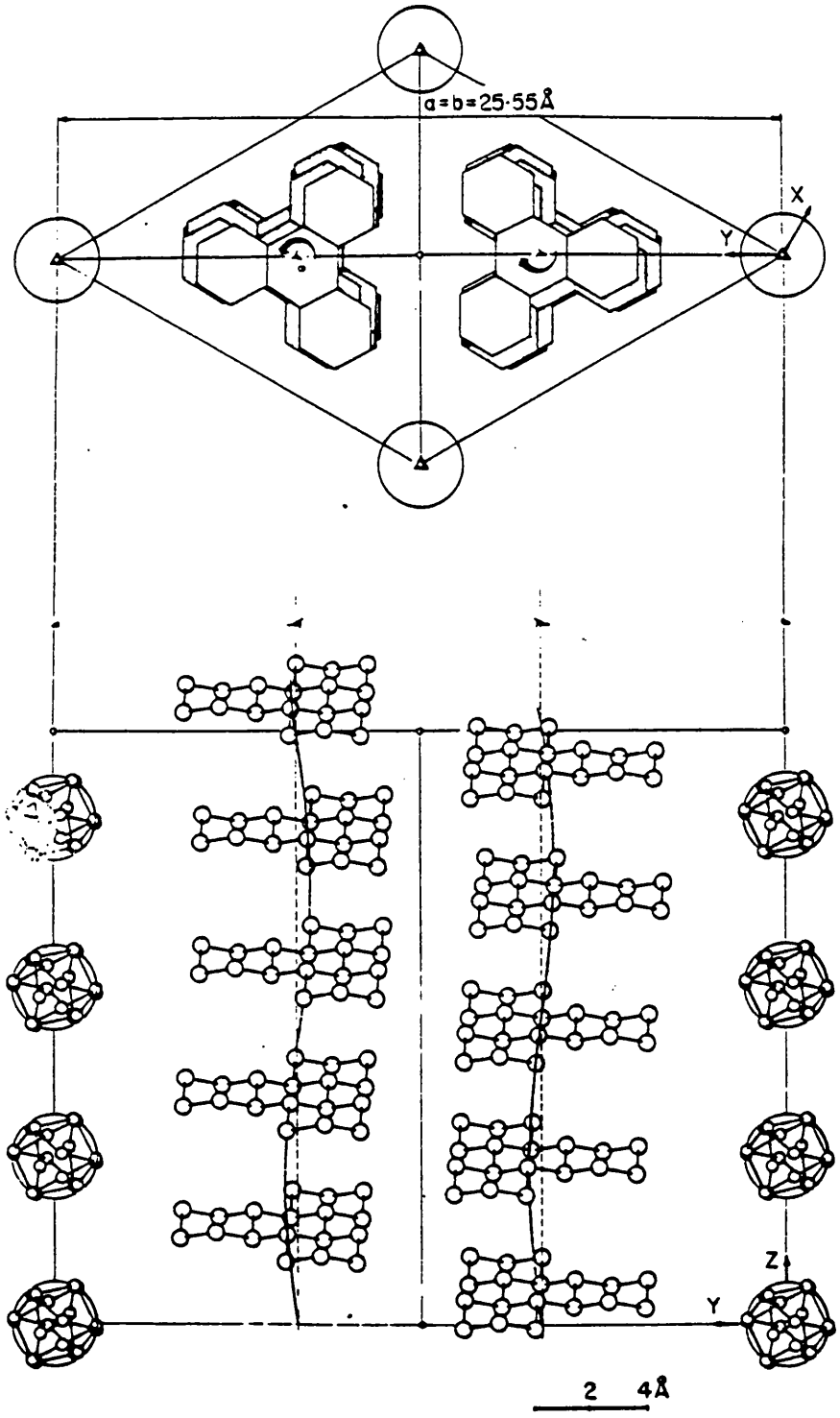


Fig. 1.23. Top and front view of the crystal cell of the inclusion compound PHTP-cyclohexane.

In addition to its 54 PHTP molecules, the cell contains 21 cyclohexane molecules in three equivalent channels, properly interlocked with the PHTP molecules and statistically arranged in many orientations.

PHTP's packing versatility also lends itself to the inclusion of macromolecular guests.[48,49,53,54] In particular, molecules such as polyethylene and 1,4-*trans*-polybutadiene.[55] This ability to include macromolecular guests led to an in-depth study of the polymerisation of various unsaturated monomers included in PHTP (see Chapter 5).

All of the classical hosts mentioned above were selectively chosen to illustrate the different topological and interactive relationships of a classical clathrate host matrix. These are summarised in Table 1, shown below.

Table 1. Classification of representative chance-discovered hosts.

MATRIX	MATRIX INTERACTION	
TOPOLOGY	HYDROGEN BONDING	VAN DER WAALS BONDING
Cage-type	hydroquinone	tri-*o*-thymotide
	Dianin's compound	
Channel	urea	perhydrotriphenylene
	thiourea	
	trimesic acid	

Key points of interest are: (a) the role that matrix interaction plays in determining the selectivity of the host. The true clathrates, involving only van der Waals bonding, tend to accommodate guests of varying size and shape, whereas those hosts utilising hydrogen bonding were less conformationally flexible, restricting their guests to a certain size or shape, as for urea and thiourea, for example;

(b) the various types of molecular architecture, particularly those of TMA and Dianin's compound;

(c) the role of host-guest interactions in altering the molecular architecture (e.g. the adduct of ß-hydroquinone with C_{60});

(d) the prominence of three-fold molecular symmetry in such classical hosts as TMA, PHTP and TOT;

(e) the host-guest stoichiometry and its relationship with the host-guest topology. For example, a non-stoichiometric ratio normally suggests the presence of channels rather than cages within the clathrate.

CHAPTER 2.

CONCEPT 1 : DESIGN BY MODIFICATION OF A CLASSICAL HOST MOLECULE.

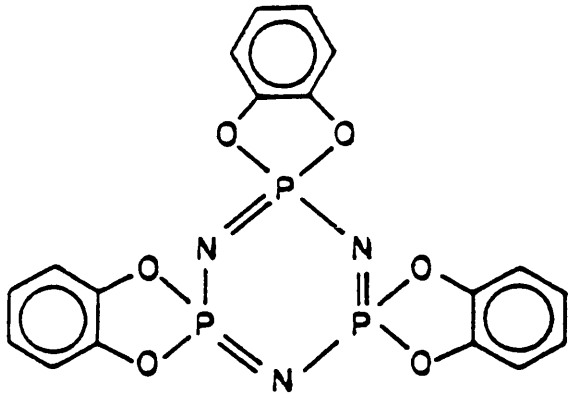
2.1 Spirocyclophosphazenes

Progress within this particular branch of inclusion chemistry would have been severely limited if one relied solely upon chance discoveries. To rectify this a new approach or concept was required.

The turning point occurred in the 1950's when Baker and McOmie[1] proposed a concept which would be used by the majority of inclusion chemists in the design of new host series. Primarily this involved modification of a chance discovery to see if new host properties were realised. They applied this concept to the well known classical host molecule Dianin's compound. Unfortunately their endeavours did not meet with success; however, in the late sixties MacNicol and co-workers[56] managed to synthesise a new series of hosts based on Dianin's compound.

The first successful modification of a chance discovery was, in fact, carried out by Allcock in 1963 while working on cyclophosphazenes in connection with high polymer research.[57]

By reacting catechol with hexachlorocyclotriphosphazene, Allcock prepared tris(*o*-phenylene-dioxy)cyclotriphosphazene (5).[57,58]



(5)

After recrystallising (5) from benzene he discovered from subsequent analysis that benzene had been included. Further crystallisations led to the uptake of many guests from aliphatic and aromatic hydrocarbons to olefins, ethers, chlorocarbons, ketones etc; host-guest ratios varying from 1:0.6 to 1:0.03. Small guests such as CS_2 or methanol can easily diffuse through the lattice at room temperature, whereas bulky guest molecules e.g. cumene, *o*-xylene and norbornadienes form extremely stable clathrates.

The clathrates formed by (5) belong to the "true" clathrate category and involve only van der Waals bonding. Two crystal types were established for (5) : the hexagonal modification, when acting as a host lattice, and the monoclinic

close-packed variant which is found when the system is freed from guest molecules.

The benzene adduct[59] of (5) crystallises in the $P6_3/m$ space group with a host-guest ratio of 1:1; the host framework consists of alternating layers of molecules, with a separation of 5Å between the layers (Fig. 2.1).

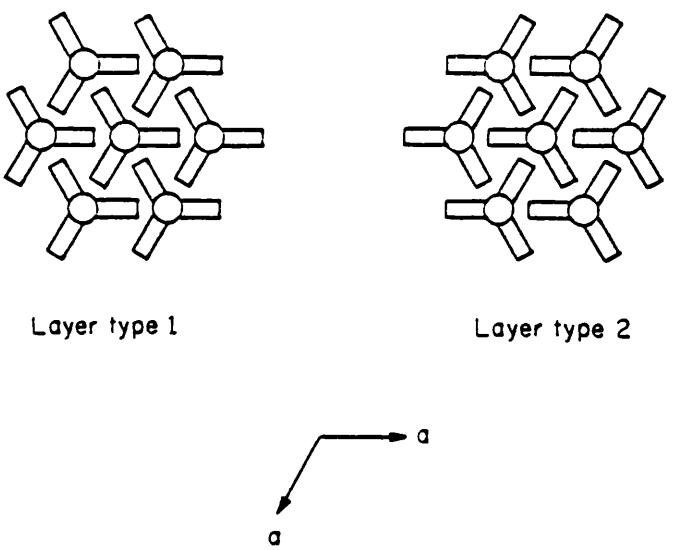


Fig. 2.1. Diagrammatic representation of molecules in the hexagonal crystal form in the plane of the *a*-axis; the circles represent the phosphazene rings and the radial arms depict the *o*-(phenylenedioxy) side groups.

The separation between the layers is too small to allow guest molecules to be sandwiched between the layers, hence the guests must occupy the spaces between the side groups of (5). Each molecule of (5) has a "paddle wheel" shape with the arylene dioxy side groups oriented at right angles to the plane of the phosphazene ring.[59,60]

Superimposition of the two layer types leads to an arrangement shown in Fig. 2.2, allowing one to establish the location of channels between the van der Waals boundaries.

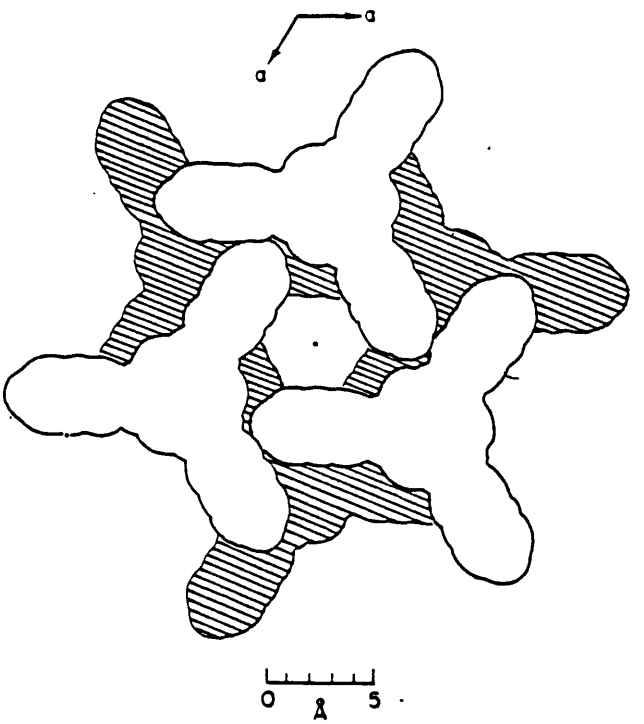
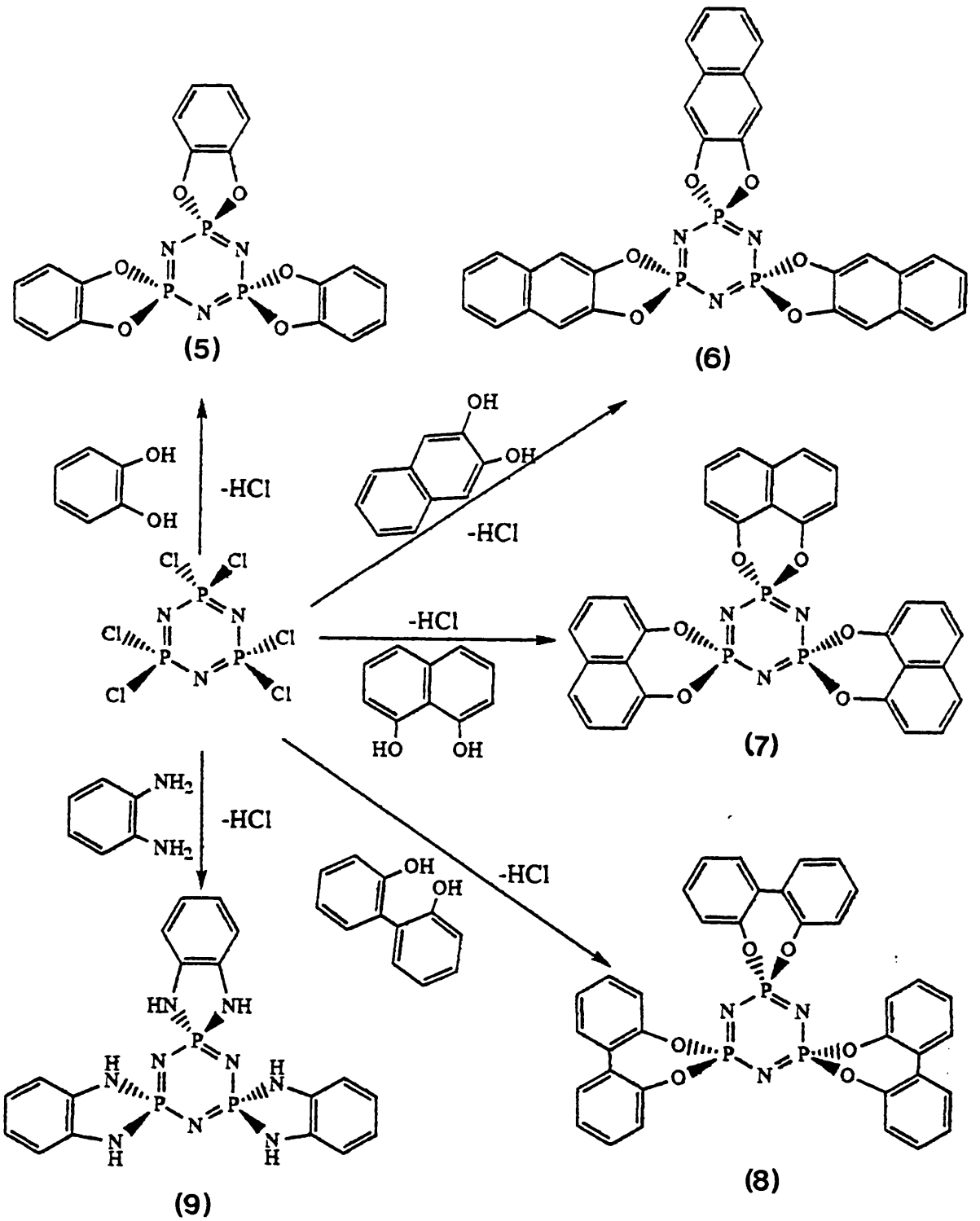


Fig. 2.2. van der Waals boundaries of molecules in the hexgonal inclusion adduct. The 4.5-5.0Å diameter tunnel is clearly visible.

At the narrowest point the channel has diameter 4.5-5Å; sufficiently wide to accommodate a wide variety of organic guests and allow migration of small guest molecules along the channel.

Having established the inclusion behaviour of (5) Allcock proposed that related phosphazene derivatives should behave in a similar manner,[58] as the inclusion behaviour seemed to be due to the "paddle wheel" like nature of the molecule. His strategy involved the synthesis of four new prospective host molecules (6) to (9) by the route mapped out in Fig. 2.3.

Fig. 2.3



Molecule (6), tris(2,3-naphthalenedioxy)cyclotriphosphazene behaves in a similar manner to (5), by forming clathrates with same types of guest molecules.[58,61]

The benzene adduct[61] crystallised in the $P6_3/m$ space group and possessed a host-guest ratio of 1:2. On this occasion larger quantities of guest are incorporated into the lattice of (6) : the longer radial "arms" of (6) increase the channel diameter to ≈ 10Å resulting in a greater uptake of the guest molecule, but reducing the stability of the adduct.

The similarity in structure and behaviour is, however, not maintained in the following hosts. Molecule (7), tris(1,8-naphthalenedioxy)cyclotriphosphazene, forms completely stable adducts unlike the previous two hosts.[62] This striking difference in clathrate behaviour reflects the different packing in the crystal structure of (7).

The *p*-xylene adduct of (7) has a triclinic unit cell space group $P\bar{1}$ and host-guest ratio of 2:1. Again, the guest molecules are packed between the side group of the phosphazene molecules but the channels are severely constricted at certain points along their length. Indeed, the *p*-xylene molecules appear to be trapped in cavities rather than channels. These differences have their origin in the different molecular conformation assumed by host (7). Whereas molecules (5)

and (6) possess radial side groups that are essentially linear when viewed down the *c*-axis, the side arms in (7) are bent (Fig.2.4).

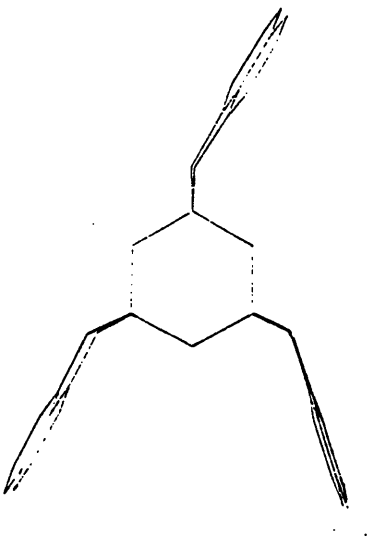


Fig. 2.4. Molecular conformation of tris(1,8-naphthalenedioxy)-cyclotriphosphazene (7).

This conformation produces a more efficient packing between the side groups and the *p*-xylene guest molecule (Fig. 2.5).

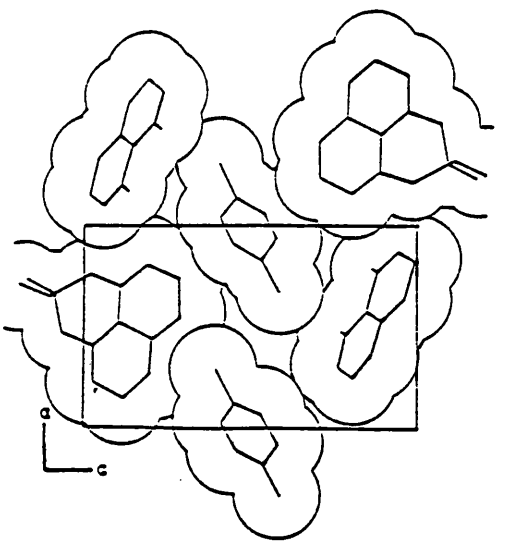


Fig. 2.5. van der Waals boundaries of the *p*-xylene and naphthalenedioxy side group of (7).

The packing now appears to offer opportunities for coplanar side group interactions which help explain the stability of the adduct.

The last two spiro compounds in the series, (8) and (9), do not approach the inclusion ability of the previous three hosts. In fact, compound (8), tris(2,2 - biphenylenedioxy)cyclotriphosphazene, failed to form any inclusion adducts at all.[63] Why this should be so, was answered by the X-ray analysis of molecule (8) (space group *C*2/*c*). The existence of the seven-membered spiro ring in (8) causes the side group to be twisted in a propeller-like arrangement. One of the side groups is twisted in the opposite direction to the other causing a complete loss of the channel and the molecule's inclusion properties.

Compound (9), tris(*o*-phenylenediamino)cyclotriphosphazene, has shown only limited inclusion ability[58] , forming an adduct solely with methyl ethyl ketone.

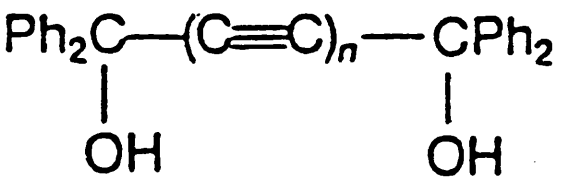
In common with most newly designed host series in this chapter, the initial inspiration for design came from the X-ray evidence from the first clathrate. From this evidence Allcock surmised that the inclusion behaviour was due to the "paddle wheel" nature of the molecule. His strategy involved synthesising closely related molecules to realise new inclusion behaviour. This logical approach was proved effective in the development of a new host series.

2.2 Coordinato-clathrates : The "Wheel-and-axle" and "Scissor" hosts.

As mentioned in the introduction the coordinato-clathrate is characterised by direct hydrogen bonding between the host and guest only.

The expansion of this area in clathrate chemistry was due mostly to work by Toda and Weber. Although they have developed many new types of coordinato-clathrates, the most interesting are, the "wheel-and-axle" and the "scissor" host series. Both illustrated clearly the logical progression involved in the creation of a new host series.

Toda's interest in the field of inclusion chemistry began in 1968 with his chance discovery of two new diol host molecules, 1,1,6,6-tetraphenylhexa-2,4-diyne-1,6 diol (10) and 1,1,4,4-tetraphenylbut-2-yne-1,4-diol (11).[64,65] Both molecules formed inclusion adducts with a wide variety of guest molecules. Owing to their elongated nature and the voluminous groups on each of the terminal sp^3 carbons the above diols were termed "wheel-and-axle" host compounds.



(10), n = 2 (11), n = 1

The X-ray study of the acetone complex of (10)[66], (Fig. 2.6) showed that the acetone inclusion is mediated by the formation of hydrogen bonds and also by the surrounding of the guest species by phenyl groups of (10).

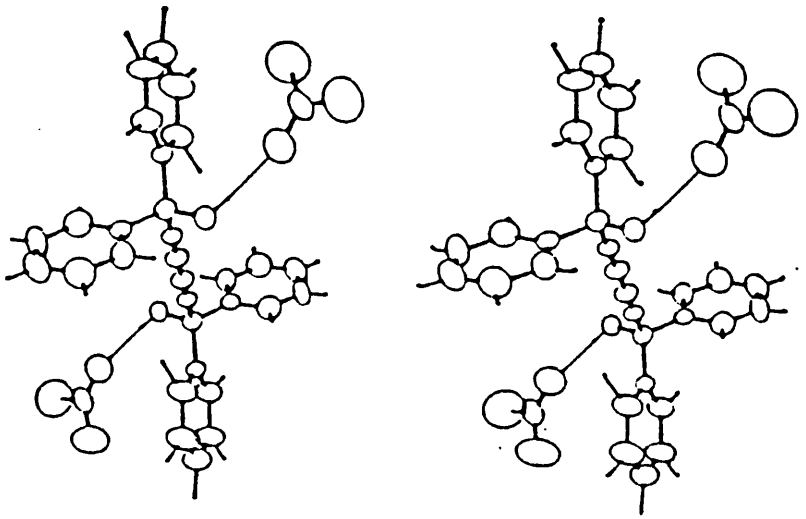
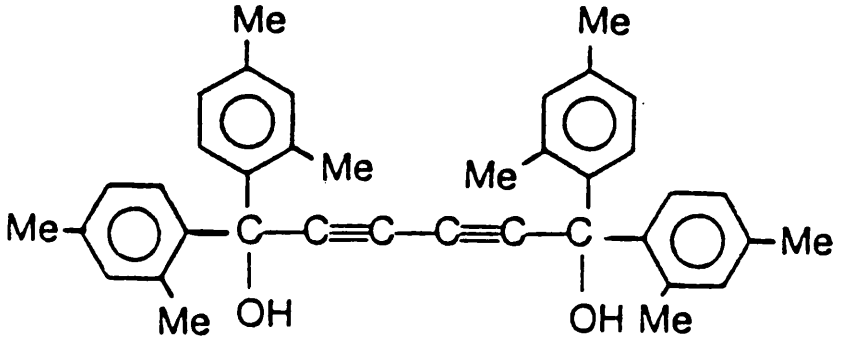


Fig. 2.6. Stereodrawing of the 2:1 acetone crystal inclusion of (10) (thin lines represent H-bond contacts).

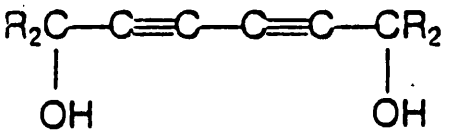
Also of interest is the anti-alignment of the hydroxy groups within the structure.

Toda then modified (10) by replacing the phenyl groups with 2,4-dimethyl-phenyl groups, giving a diacetylenic alcohol (12)[67] of even higher inclusion ability than either (10) or (11).



(12)

Moving in the opposite direction, by reducing the bulk at either end of the diol, Toda found a complete loss or a marked reduction in the inclusion properties. For example, both the tetramethyl (13a) and tetraethyl (13b) analogues of (10) show no inclusion ability. Similarly, the tetra-*t*-butyl analogue (14) formed only a few inclusion compounds.[68]

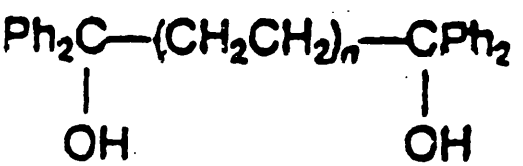


(13a) R = Me

(13b) R = Et

(14) R = Bu^t

Allied to the bulk factor, the rigidity of the host molecule seemed to play an integral part in the formation of a stable crystalline lattice. This was substantiated by the finding that 1,1,6,6-tetraphenylhexane-1,6 diol (15) does not form any inclusion compounds.[68]



(15) n = 2

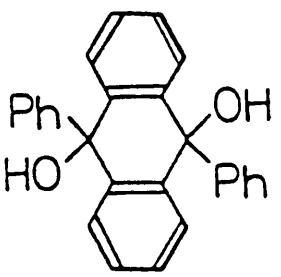
In the light of this newly accumulated information on diol host molecules, Toda devised a strategy for the design of new coordinato-clathrates. In essence they must possess the following features:

(a) Some form of diol or dicarboxylic acid functionality capable of participating in hydrogen bonding; this must correspond to an *anti* arrangement.

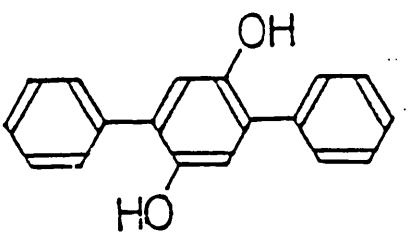
(b) Rigidity built into the backbone of the host molecule to facilitate the formation of a crystalline lattice;

(c) A degree of bulk, which should also contribute to a less close-packed host lattice.

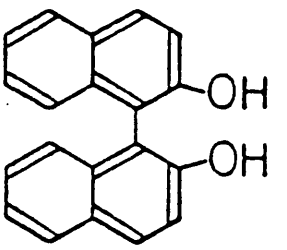
Following this strategy Toda chose to examine three molecules for host potential, specifically : 9,10-dihydroxy-9,10-diphenyl-9,10-dihydroanthracene (16) ; 2,5-(diphenyl)hydroquinone (17) and 2,2′-dihydroxy-1,1′-binaphthyl (18).[69] All three were found to be good hosts forming highly crystalline inclusion compounds.



(16)



(17)



(18)

Molecule (18)[70] particularly interested Toda, mainly because of its ability to include a vast range of guest molecules. Weber also noted the molecule's close resemblence to a pair of tailors scissors, and subsequently called the molecule a scissor host (Fig. 2.7).

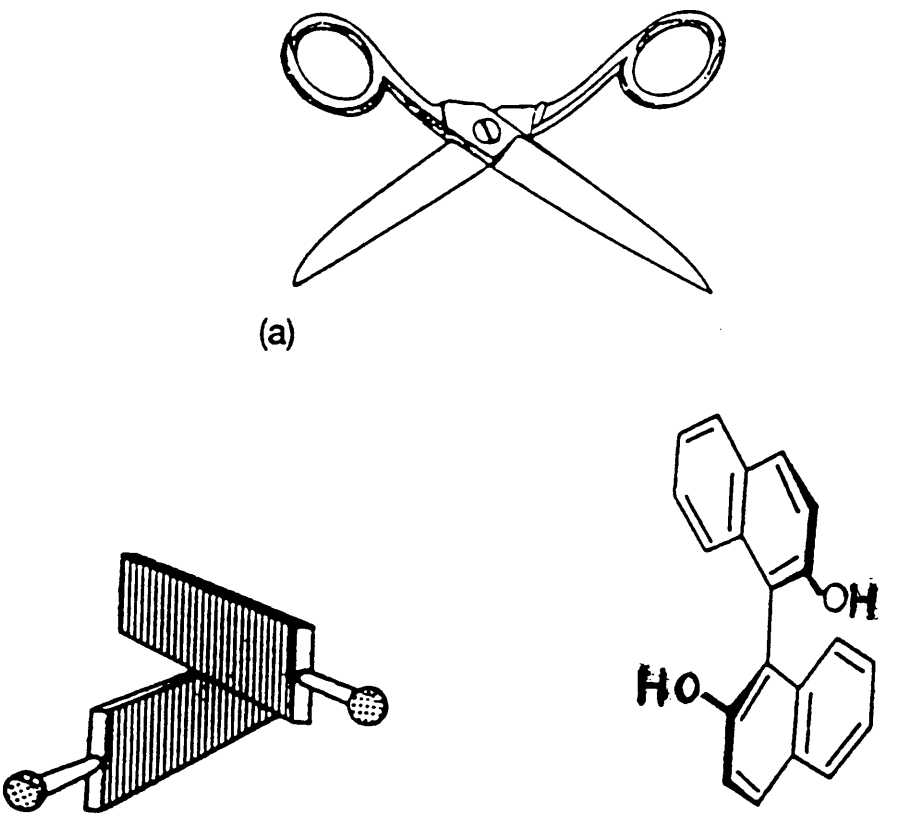


Fig. 2.7. The scissor host.

From Fig. 2.7 it is evident that scissor host (18) possesses a C_2 axis of symmetry implying exploitable chirality and hence the existence of an enantiomeric pair. As the racemic host and the separated optically active hosts crystallise in different lattices, they must consequently have different inclusion

properties.

The racemic molecule (18) was shown to form adducts with many different compound classes[71-79] including : alcohols, amines, carboxylic acids, amides, dipolar aprotic and rather apolar solvents. The clathrate, as expected, involves coordinative hydrogen bonding interactions between functional groups of host and guest. The guest molecules, depending on their functionality and size, dictate the form of the lattice and the different stoichiometries.

From Table 2 one can also see a marked preference for certain functionalities by racemic host (18). Amines such as primary and secondary aliphatic, alicyclic, heterocyclic and aromatic amines are preferred as guests, usually in a stoichiometric ratio of 1:1.[71]

Table 2. Inclusion compounds of racemic host (18).

Guest Compound	Host:guest mol ratio[a]
methanol	1:2
cyclopentanol	1:2
ethylene gylcol	2:3
lactic acid	1:2
cyclopentylamine	1:1
diisopropylamine	1:1
di-*t*-butylamine	2:3
dicyclohexylamine	1:1
2,5-diamino-2,5-dimethylhexane	1:1
4-chlorobenzylamine	1:1
4-hydroxybenzylamine	1:1
3-methylaniline	1:1
3,5-dimethylaniline	1:1
2,6-dimethylaniline	1:1
3-hydroxyaniline	1:2
2-amino-6-methylpyridine	1:1
imidazole	1:2
piperidine	1:1
pyridine	1:2
dimethylformamide	2:3
dimethyl sulphoxide	1:2
acetone	1:1
acetylacetone	1:2
cyclohexanone	1:1
γ-butyrolactone	1:2
dioxane	1:2
tetrahydrofuran	1:2
$LiOH.H_2O$	1.5:3:8[b]
$NaOH.H_2O$	1.5:3:8[b]
$KOH.H_2O$	1.5:3:8[b]
$CsOH.H_2O$	1:1:6[b]
NH_3.MeOH	2:2:1[c]

[a] Determined by NMR integration.
[b] Host : $MOH:H_2O$ mol ratio
[c] Host : NH_3:MeOH mol ratio

Owing to the weakly acidic nature of hydroxy groups, the amine inclusion compounds of (18) are not expected to have salt character. Proof of this can be

found from the X-ray structure of the adduct between (18) and imidazole (Fig. 2.8). The host molecule adopts ideal two-fold symmetry. The imidazole molecules are linked into an infinite spiral with host molecules as hydrogen bond donor or acceptors. The tetragonal crystal lattice consists of hosts of the same chirality (i.e. spontaneous resolution has occurred), hence the structure falls into the inclusion compounds of the optically resolved host (18).

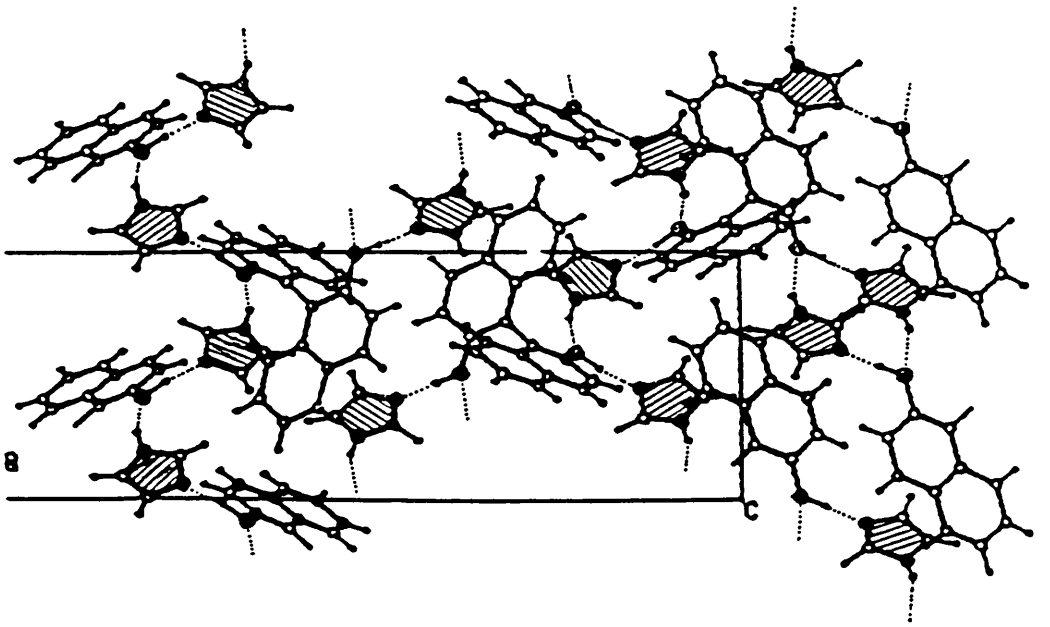


Fig. 2.8. Crystal structure of the imidazole (1:2) inclusion compound of optically resolved host (18). The imidazole rings are distinguished by hatching.

Also inclusion compounds between racemic (18) and typical inorganic species such as alkali hydroxides and ammonia have been noted (Table 2). The ternary complex's packing[74] is illustrated in Fig. 2.9. The phenolic groups, ammonia and methanol molecules are interlinked by hydrogen bonds to form columns with a hydrophilic interior and hydrophobic exterior.

The crystal lattice is itself built up by lateral packing of such infinite columns.

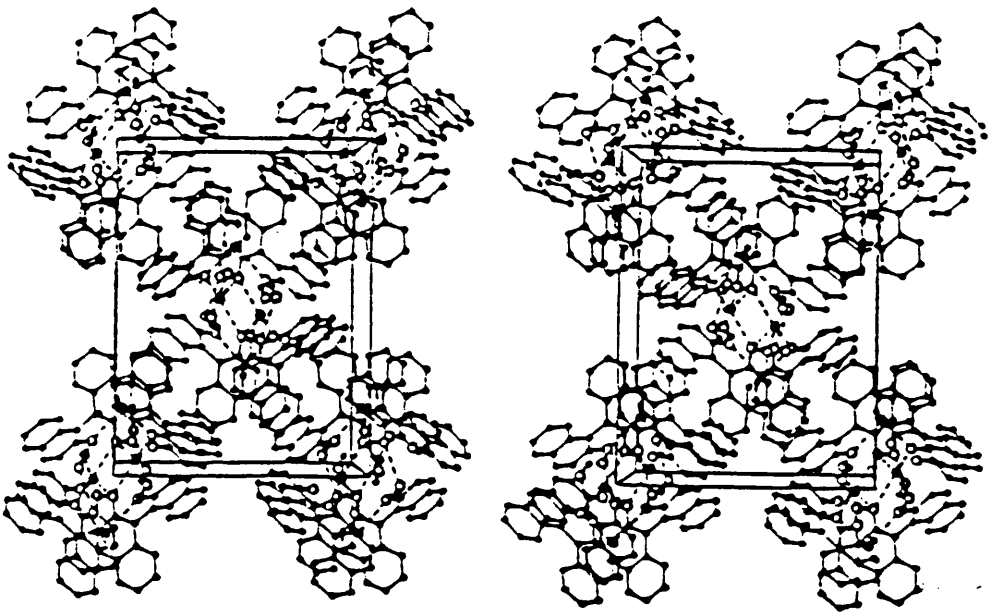
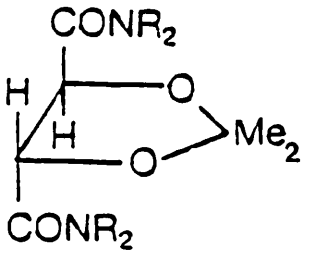


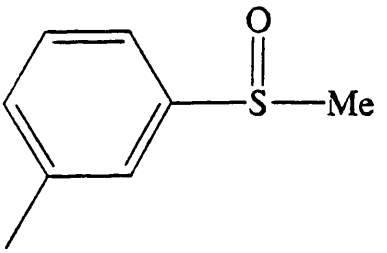
Fig. 2.9. Crystal structure of the (18) NH_3,MeOH ternary inclusion compound; stereoscopic packing illustration. Bold dots and open circles represent N and O atoms, respectively.

Optically resolved (18) was then isolated to compare its inclusion properties with that of the racemic host.

Resolution of the host is no trivial matter, usually effected by inclusion complex formation with optically active methyl *m*-tolyl sulphoxide[80] or by fractional recrystallisation of the cinchonine salt of binaphthyl phosphoric acid.[81] Toda found both methods either cumbersome or expensive, hence he developed

a chiral tartaric acid derivative (19)[82] (see Chapter 5).





(19) R = Me (20)

Resolution of (18) was accomplished by simple complexation with compound (19). The crystalline adduct contained the (*S*)-(-) form of (18) only. The (*R*)-(+) form could then be recovered from the solution in 100% e.e.

During inclusion studies optically pure (18) was shown, either in the (*R*)-(+) or (*S*)-(-) form, to be effective in the optical resolution of racemic guests. Such guests include sulphoxides, selenoxides, phosphine oxides and phosphinates.[83] An example of resolution by complexation is shown by the 1:1 inclusion compound between (*R*)-(+)-(18) and (*R*)-(+)-(20) (Fig. 2.10).[83]

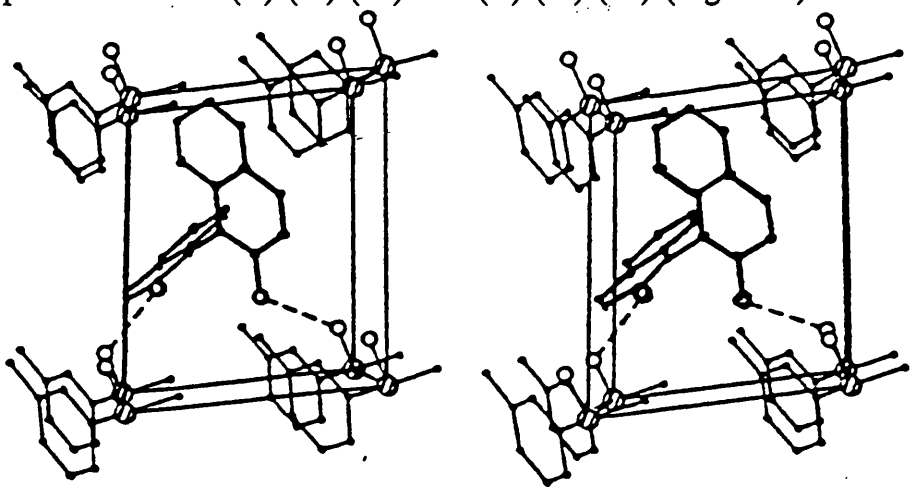
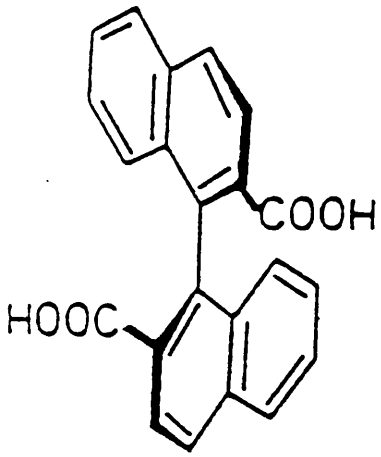


Fig.2.10. Crystal structure of the (*R*)-(+)-(18),(*R*)-(+)-(20) inclusion compound

Paralleling Toda's success with compound (18), Weber found that 1,1′-binaphthyl-2,2′-dicarboxylic acid (21)[81,84] behaved in a similar fashion.



(21)

The molecule (21) also possesses C_2 molecular symmetry, pointing to exploitable chirality, hence both racemic and optically pure (21) were tested for inclusion properties. The presence of carboxylic acid groups for hydrogen bonding facilitated the formation of coordinato-clathrates with most non-basic guests. Examples of the various adducts formed by racemic (21) are shown in Table 3.

Table 3. Representative adducts formed by inclusion compounds of racemic host (21) : stoichiometries and thermal stability characterization.

Entry	Guest Compound	Host:guest mol ratio[a]	Thermal dec. (°C)[b]
1	methanol	1:2	146(+82)
2	ethanol	1:2	88(+10)
3	1-propanol	2:1	75(-22)
4	2-propanol(isopropanol)	1:2	86(+ 4)
5	1-butanol	1:1	72(-46)
6	2-butanol(*sec*-butanol)	1:1	92(- 7)
7	2-methyl-1-propanol(isobutanol)	1:1	71(-37)
8	2-methyl-2-propanol(*t*-butanol)	1:1	141(+58)
9	1-pentanol	1:2	123(-15)
10	2-methyl-1-butanol	2:1	135(+ 7)
11	2-methyl-2-butanol	1:2	164(+62)
12	4-methyl-1-pentanol	1:1	154(- 9)
13	benzyl alcohol	1:1	120(-85)
14	trichloroethanol	1:1	117(-34)
15	ethylene glycol	1:1	165(-32)
16	propylene glycol	1:1	149(-66)
17	acetic acid	2:3(1:1)	115(- 3)
18	propionic acid	2:1	139(- 2)
19	lactic acid	1:1	140(-)[e]
20	formamide	1:2	136(-74)
21	*N*-methylformamide	1:2	108(-75)
22	*N,N*-dimethylformamide	1:2	117(-35)
23	dimethyl carbonate	2.1[c]	<25
24	diethyl carbonate	d	<25
25	acetylacetone(2,4-pentanedione)	1:1	64(-70)
26	acetonitrile	1:1	119(+38)
27	nitromethane	1:1	126(+25)
28	dimethyl sulphoxide	1:1	155(-34)
29	diethyl ether	d	<25
30	bromobenzene	1:1	116(-40)

[a] Determined by NMR integration after a drying period of 12 h at 0.5 torr for each compound.
[b] Value indicates the beginning of the clathrate decomposition(either onset of opacity or release of the gaseous components). Specification in parentheses gives the relative thermal stability (difference between the decomposition point of the clathrate and the boiling point of the respective neat guest solvent at atmospheric pressure).
[c] Decomposes under vacuum drying at ambient temperature.
[d] Unstable at atmospheric pressure.
[e] No boiling point for the neat guest solvent in the literature.

The basic structure pattern which is observed in the crystal packing of the alcohol inclusion compounds of racemic (21) is a channel matrix formed by the host (Fig. 2.11).[84]

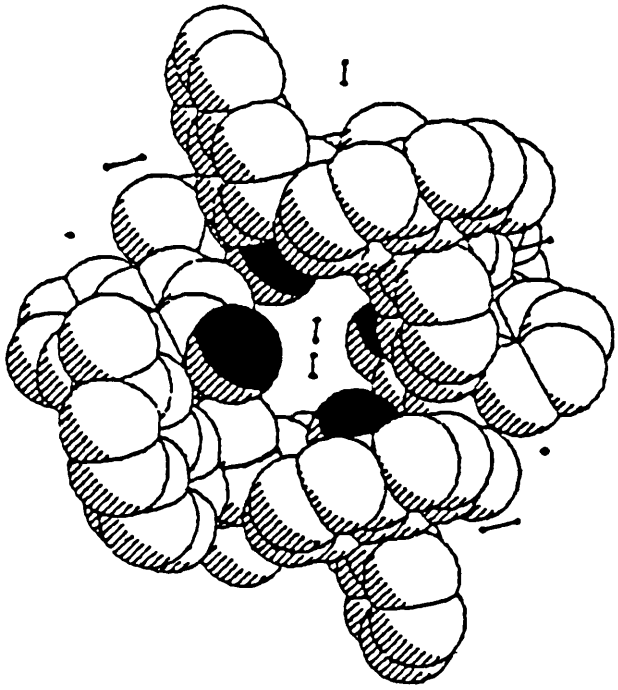


Fig. 2.11. Inclusion channel in (21).MeOH (1:2). Space filling illustration; view down the channel axis; methanol molecules represented as small sticks.

The walls of these channels are regularly interrupted by protruding carboxyl groups, at the polar ends of which the guests are located (Fig. 2.12a). How frequently this occurs is closely related to the nature of the guest molecules, and the size and shape of the hydrophilic cavities (Figs. 2.12 b-e).[71]

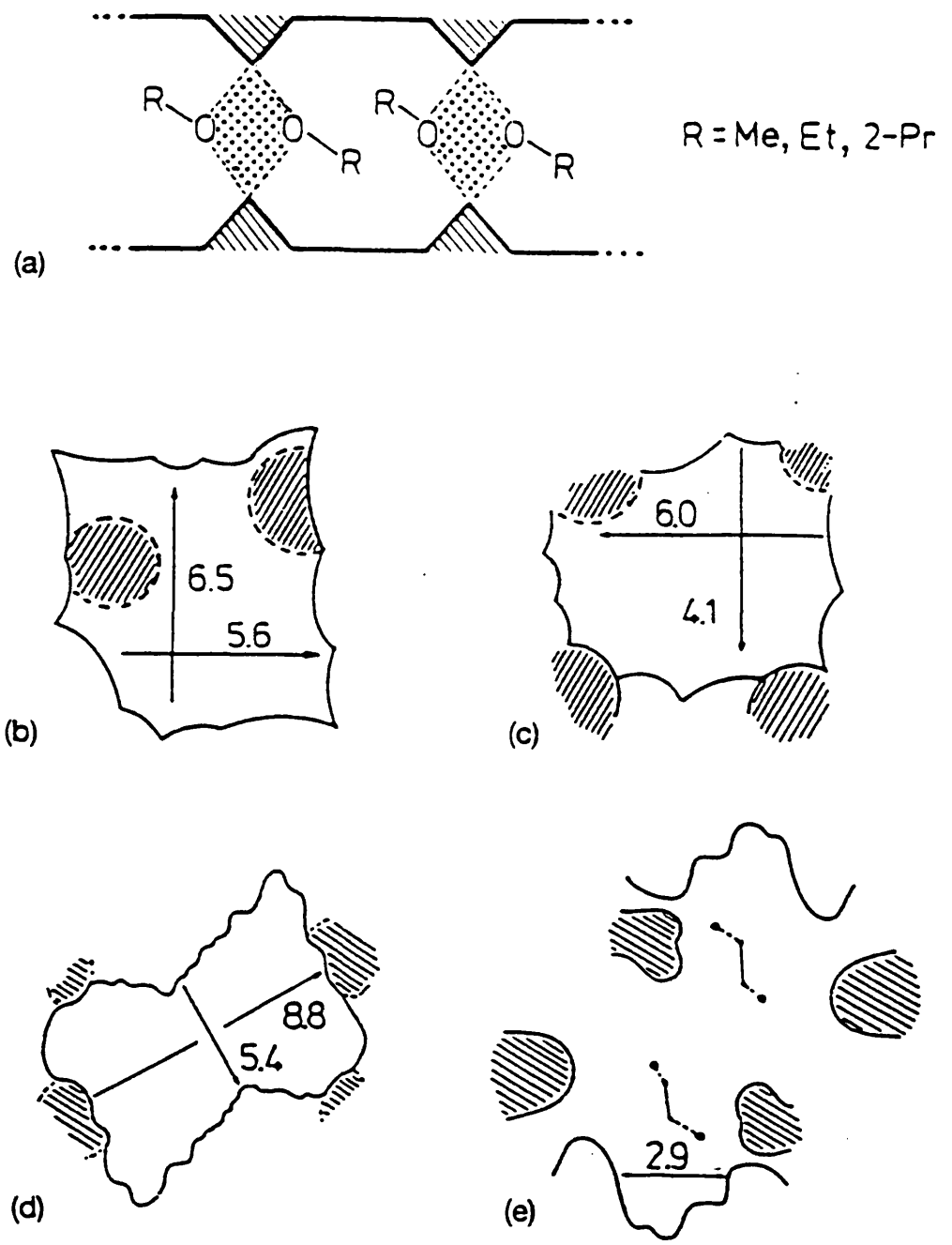


Fig. 2.12. Channel characteristics of inclusion compounds of (21) with alcohols. (a) Longitudinal cross-section of the inclusion channel for the simple alcohol inclusions of (21) (schematic representation); hatched triangles and dotted squares represent polar areas, while the rest is of an apolar character. (b-e) Approximation of the van der Waals cross-sections of inclusion channels in the inclusion compounds of (21) (b) with MeOH (1:2) (c) with 2-PrOH (1:2) (d) with 2-BuOH (1:1) (e) with ethylene glycol (1:1). Dimensions are in Å; hatched regions represent O atoms of the matrix; continuous solid lines indicate surfaces with an apolar attribute; non-zero electron density contours in (d) and (e).

In the methanol clathrate, the dimensions of the cleft formed by the surrounding groups are 6.5Å (height) and 5.6Å (width). On accommodating larger guests such as ethanol or 2-propanol, the width of the cage is increased to 6Å with a depth of 4Å (Fig. 2.12c). With 2-butanol as guest the walls of the participating naphthyl moieties are no longer parallel, giving rise to a parallelopiped-shaped cavity with dimensions shown in Fig. 2.12d. The depth of the cleft in the 2-butanol adduct is twice as large as in the methanol or 2-propanol inclusion compounds. Finally, the ethylene glycol inclusion compound of (21) forms a hydrophilic cavity intra- rather than inter-molecularly. The guest molecule, which has a relatively small lipophilic surface, fits partly into a preformed void of the host molecule (Fig. 2.12e). The result is a non-channel or cavity-type structure which is more compact.

The above study merely reinforces what has already been mentioned; that the crystal architecture of the adducts is to a great extent influenced by subtle host-guest interactions. Further evidence of this was obtained by examining the adducts of (21) with acetic acid[71,85] DMF[86] or DMSO.[86] Perhaps the most interesting was the adduct formed between (21) and bromobenzene.[86] Here one encounters a lattice-stabilised type of clathrate, involving host-host interactions, but with no specific binding contact between host and guest. Therefore bromobenzene has forced the host to adopt the coordination-assisted type host lattice.

The building principle of this inclusion crystal is the formation of infinite chains of hydrogen-bonded, carboxylic group-dimerised, host molecules of alternating chirality (Fig. 2.13).

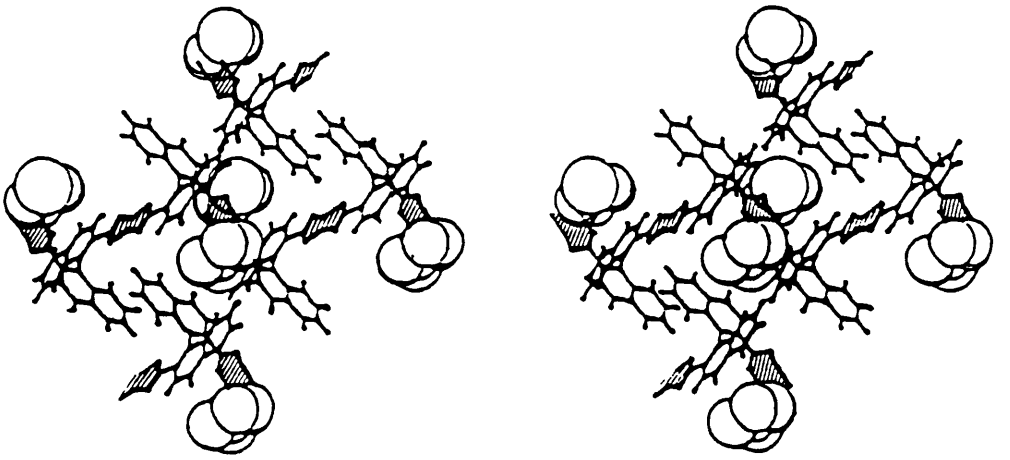


Fig. 2.13. Crystal structure of (21) bromobenzene (1:1) inclusion compound.

Owing to the shape of the host, the chain consists of segments in a zig-zag-like arrangement which offers the possibility of having the guest molecules included in the apolar clefts found between these chains. The loose attachment of the bromobenzene molecule in the lattice void gives rise to the disorder observed for this guest species.

Racemic (21) also exhibits remarkably selective inclusion behaviour from solvent mixtures (Table 4); selective inclusion behaviour is derived from steric factors as well as from chemical functionality.

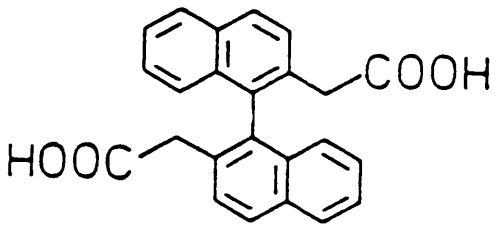
Table 4. Representative preference of guest binding of racemic host (21) from a two-component solvent system.

Entry	Recrystallisation solvent compound mixture (equimol.ratio)[a]	Relative guest excess, % g.e.[b]
1	methanol/*ethanol*	46
2	methanol/*t-butanol*	91
3	*methanol*/toluene	14
4	*ethanol*/2-propanol	79
5	*ethanol*/t-butanol	92
6	ethanol/*benzyl alcohol*	20
7	ethanol/*ethylene glycol*	>95
8	*ethanol*/acetic acid	>95
9	ethanol/*dimethylformamide*	>95
10	*ethanol*/acetonitrile	>95
11	1-propanol/*2-propanol*	29
12	1-butanol/*t-butanol*	74
13	isobutanol/*t-butanol*	78
14	acetonitrile/*dimethyl sulphoxide*	>95
15	*acetonitrile*/toluene	42

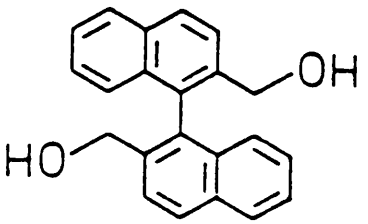
[a] Solvents printed in italics refer to those preferentially enclathrated.
[b] Determined by NMR integration of the isolated crystals after a drying period of 12 h at 0.5 torr.

Weber then optically resolved (21)[87] to see if his original proposal, that racemic and optically pure (21) should form inclusion compounds, was true. Unfortunately, optically resolved (21) showed very limited inclusion ability.[88]

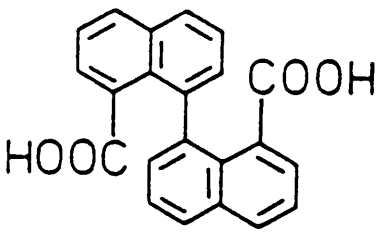
With the undisputed success of both (18) and (21) to act as host molecules, Weber, quite logically, wondered if changing the position of the functional groups or varying the skeleton itself would result in new types of host molecule. Weber then proposed the modified molecules (22),(23) and (24) as potential new host molecules.



(22)



(23)



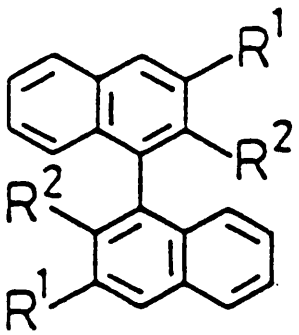
(24)

Obviously, compounds (22)[89] and (23)[87] represent homologues of parent compounds (21) and (18) respectively, with one methylene unit inserted between the skeleton and each functional group. This structural modification however, resulted in complete loss of inclusion behaviour, at least for the racemic species, to which his studies were restricted. Evidently the additional methylene units neighbouring the functional groups allow too much conformational flexibility, in a way that may facilitate functional group dimerisation and dense crystal packing, which is contrary to the general idea of coordinato-clathrate formation.

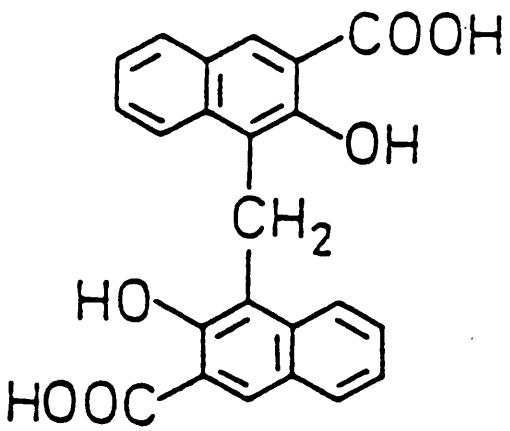
On the other hand compound(24), 1,1′-binaphthyl 8,8′-dicarboxylic acid[90], is a constitutional isomer of (21). As a consequence of the differing carboxyl group positions, Weber thought that the molecules should pack in a different fashion within the crystal and thus change the inclusion properties. The change

was, however, too drastic, and molecule (24) could only form salt-type associations with basic molecules such as pyridine.[91]

Undeterred by this apparent lack of success, Weber examined other structurally modified binaphthyls for new inclusion behaviour: namely compounds (25), (26), (27), (28) and (29).



(25) $R^1 = COOH$, $R^2 = OH$
(26) $R^1 = COOH$, $R^2 = OMe$
(27) $R^1 = COOMe$, $R^2 = OH$
(28) $R^1 = COOMe$, $R^2 = OMe$



(29)

Racemic compound (25)[92] showed only very limited coordinato-clathrate behaviour[89] since it should have a natural tendency to hydrogen bond intramolecularly rather than coordinatively with guest molecules. Only the DMF adduct of (25) had a defined stoichiometry, with a host-guest ratio of 1:2.

Replacing the hydroxyl function with methoxy reduces the possibility of intramolecular hydrogen bonding, thus increasing the tendency for host-guest binding. This strategy met with success as racemic molecule (26)[93] formed adducts with dimethylsulphoxide (DMSO), acetone, bromobenzene and toluene.[89]

Further application of this idea involved examining racemic (27)[94] and (28)[93] for inclusion properties. No coordinato-clathrate activity was detected; possibly due to the lack of protonic functions available to bind the guest. (*R*)-(+)-(27)[94] did however form a "true" clathrate with bromobenzene as guest. The interactions are purely van der Waals in nature allowing bromobenzene molecules to fill the space between the sheets formed by the binaphthyl groups (Fig. 2.14).

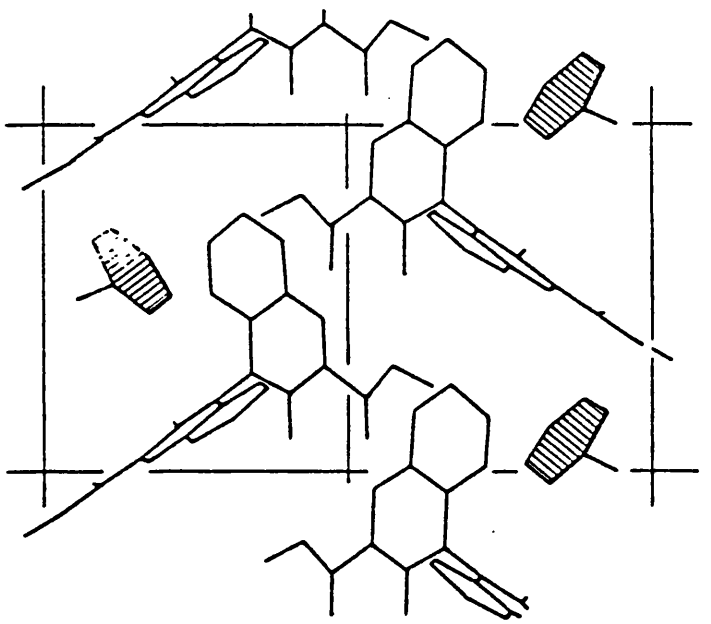
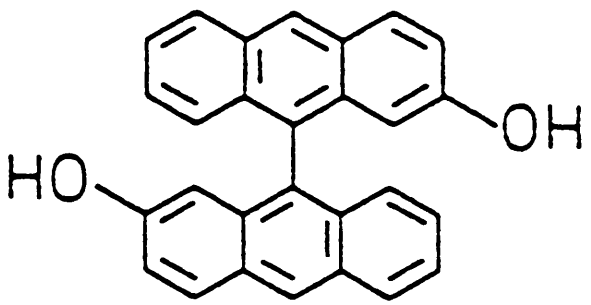


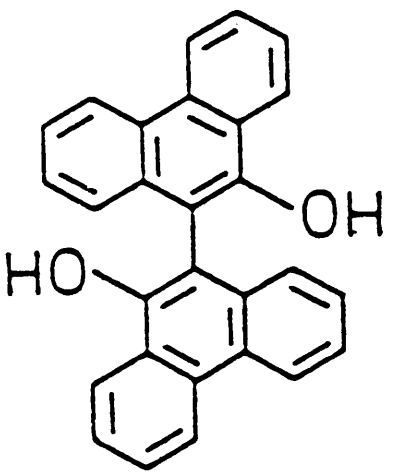
Fig. 2.14. Crystal structure of the (*R*)-(+)-(27).bromobenzene (1:1) inclusion compound.

Finally, Weber examined compound (29)[95], primarily to determine the effect of geometrical distortion relative to compound (25). Only one adduct, with DMF, was detected.

After Weber had essentially exhausted many attractive possibilities for new binaphthyl-based scissor hosts, Toda sought to further expand the scissor-host idea using his empirically derived strategy. This involved determining the inclusion properties of similar, but bulkier, bisaryl diols. The bulk of the aromatic groups should control the lattice assembly of the molecules and thus influence their clathrate properties. Such an enlargement of the basic skeleton is displayed by 9,9′-bianthryl (30)[72] and 9,9′-biphenanthryl (31).[96]



(30)



(31)

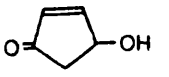
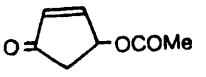
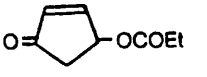
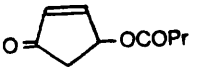
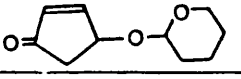
Both molecules are constitutional isomers of one another and form inclusion compounds with the same solvents, mainly of the dipolar aprotic type.[72,73] The range of inclusion properties, though, is limited when compared to the parent racemic diol (18) (Table 5).

Table 5. Inclusion compounds of bianthryl and biphenanthryl hosts (racemic).

Host	Guest Compound	Host:guest mol ratio
(30)	ethanol	1:2
	dimethylformamide	1:2
	dimethyl sulphoxide	1:2
	acetone	1:2
	tetrahydrofuran	1:2
	dioxane	1:1
(31)	methanol	1:1
	1-phenylethylamine	1:1
	dimethylformamide	1:2
	dimethyl sulphoxide	1:2
	acetonitrile	1:2
	acetone	1:1
	cyclopentanone	1:1
	cyclohexanone	1:2
	nitrobenzene	1:1
	pyridine	1:2
	tetrahydrofuran	1:2
	carbon tetrachloride	1:1

Optically resolved (31) exhibited similar inclusion properties to that of optically pure (18).[73] The (*S*)-(-)-(31) enantiomer was found to form a number of inclusion compounds with optically active propionic acid, butyric acid and cyclopentanone derivatives; some of the guests are incorporated in an enantiomerically pure form into the crystal lattice from a racemic mixture (Table 6).

Table 6. Inclusion formation of optically resolved host (31) [(*S*)-(-)-(31)][a]

Guest compound	Host : guest mol ratio	Yield (%)[b]	Guest configuration[c]	Optical purity (% *ee*)[d]
Me−CHCl−COOMe	1 : 1	75	(−)	69.4[e]
Me−CH(OPh)−COOMe	1 : 1	86	(−)	100[f]
Me−CH(OH)−CH_2−COOEt	1 : 1	86	(+)	92.7[e]
$ClCH_2$−CH(OH)−CH_2−COOMe	1 : 1	57	(−)	95.3[e]
MeOOC−CH(OH)−CH_2−COOMe	1 : 1	81	(+)	60.0[e]
Me−CH(NH_2)−CH_2−COOEt	1 : 1	85	(−)	58.0[g]
	1 : 1	h	(−)	2.2[f]
	1 : 1	45	(−)	100[g]
	1 : 1	28	(−)	100[g]
	1 : 1	51	(−)	100[g]
	1 : 1	51	(−)	100[g]

[a] Analogous inclusion complexes involving opposite guest configuration were obtained with (*R*)-(+)-(31)
[b] Isolated yield based on racemic guest used.
[c] Determined after decomposition of the clathrate.
[d] Determined by comparison with reported $[\alpha]_D$ values.
[e] Repeated inclusion complexation with (*S*)-(-)-(31) yielded 100% ee of the guest.
[f] One complexation process.
[g] After recrystallisation of the complex.
[h] Not reported.

The differences in enantioselectivity can be rationalised by inspecting the crystal structure of selected adducts. For example, the 1:1 inclusion compounds of (*S*)-(-)-(31) with (*S*)-(-)-methyl-2-chloropropionate and (*S*)-(-)-(31) with (*S*)-(-)-methyl-4-chloro-3-hydroxybutyrate have guest optical purities of 69.4 and 95.3 respectively from racemic mixtures.

Apparently the mode of hydrogen bonding between host and guest determines how the molecules pack and, as a consequence, the enantioselectivity. The propionate inclusion compound (Fig. 2.15a) involves one hydrogen bond per host molecule, whereas in the butyrate inclusion compound (Fig. 2.15b) each host molecule maintains two hydrogen bonds. Therefore, the former adduct uses discrete host-guest units in the crystal lattice packing, whilst the latter is built of infinite chains of alternating host and guest molecules.

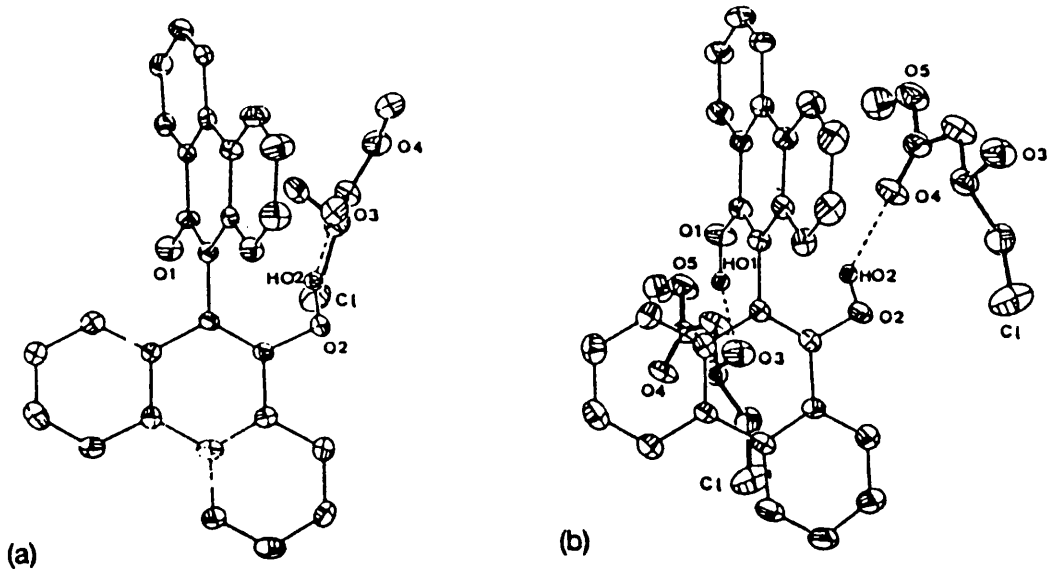
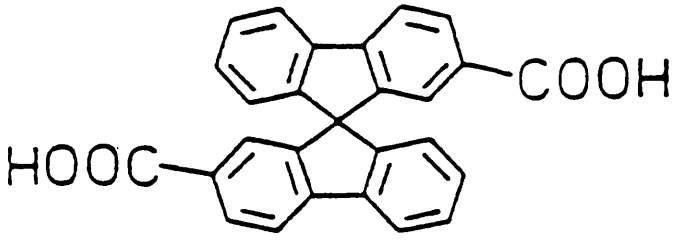


Fig. 2.15. Crystal structure of (a) the (*S*)-(-)-(31) (*S*)-(-)-methyl 2-chloropropionate (1:1) inclusion compound and (b) the (*S*)-(-)-(31) (*S*)-(-)-methyl 4-chloro-3-hydroxy-butyrate (1:1) inclusion compound; molecular structures. The host molecule is indicated by bold lines.

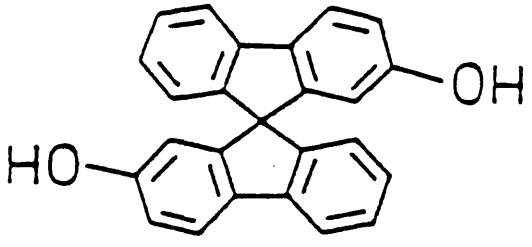
Whilst the biaryls are flexible with reference to the central bond, the flexible hinge is not applicable to the final type of scissor host : the spiro compound. A scissor-like shape is opened up via the spiro linkage, which fixes

the edges of the molecular scissors at an angle of 90°. This gives rise to lower spatial adaptability of the host molecule, which should be reflected in distinct inclusion properties.

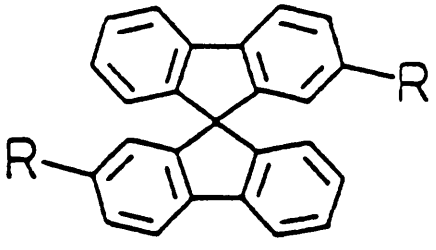
To test this theory, Weber selected four spiro compounds for analysis, namely (32)[97], (33)[72], (34a)[97] and (34b)[98].



(32)



(33)



(34a) $R = COCH_3$
(34b) $R = CH_2OH$

Again, the molecules belong to chiral point group $\underline{C}_2$ and both racemic and resolved host molecules were examined for inclusion behaviour.[72,89,98,99] In general, though, the adducts were formed by racemic host molecules, with the singular exception of (34b) which only formed an adduct in the optically pure state.[98] A summary of this inclusion behaviour is found in Table 7.

Table 7. Inclusion compounds of functional spiro-type hosts (racemic).

Host	Guest Compound	Host:guest mol ratio
(32)	ethanol	2:1
	2-propanol	1:1
	dimethylformamide	1:2
	dioxane	1:1
	benzene	1:1
(33)	cyclopentanone	1:2
	benzene	1:2
(34a)	tetrahydrofuran	2:1
	benzene	1:1
	1-bromopentane	2:3
(34b)[a]	benzene	1:1

[a] Optically resolved host (*R*)-(+).

The building principles of such spiro-type inclusion compounds can be deduced from two of the above crystal structures, specifically those of racemic (32).DMF (Fig.2.16)[99] and (*R*)-(+)-(34b).benzene (Fig. 2.17).

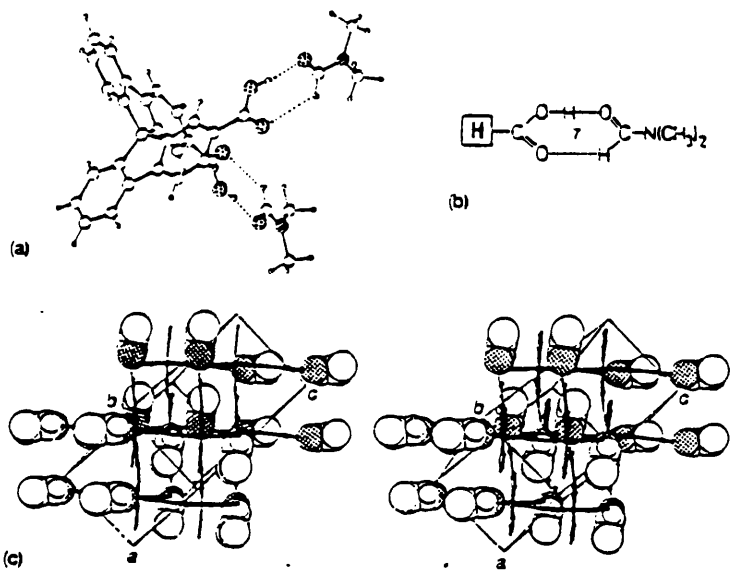


Fig. 2.16. Crystal structure of (32) DMF (1:2) inclusion compound: (a) molecular structure, (b) scheme of H bonds involved (c) packing illustration (stereoview). In (c), the host molecules are represented in a stick style, the guest molecules are in a space filling representation (with 3/4 of the van der Waals radii of the composing atoms; oxygen atoms shaded).

In the former case the host-guest aggregate preserves perfect two-fold molecular symmetry in the crystal lattice. The formamide moiety acts as a hydrogen bond acceptor from a carboxylic group of the host and also serves as a donor making a C-H....O type of interaction[100] possible (Fig. 2.16b). Consequently a seven-membered closed ring of hydrogen bonds is formed from both carboxylic groups of the host. The crystal packing of this inclusion compound (Fig.2.16c) revealed that the orientation of the guest molecules is largely dictated by the rigid angle-shaped host framework. Such a guest-orientating effect certainly contributes to the pattern for recognition of the solvent and explains the particular inclusion properties of (32).

A certain similarity between the binaphthyl and the spiro molecules is seen by comparing the structures of (*R*)-(+)-(34b).benzene (Fig. 2.17) and

(21).bromobenzene (Fig. 2.13). Both adducts are of the coordinative-assisted clathrate type. The host molecules in the two adducts are bound into infinite zig-zag chains by hydrogen bonds, the disordered benzene molecules appearing interstitially placed between such chains.[98]

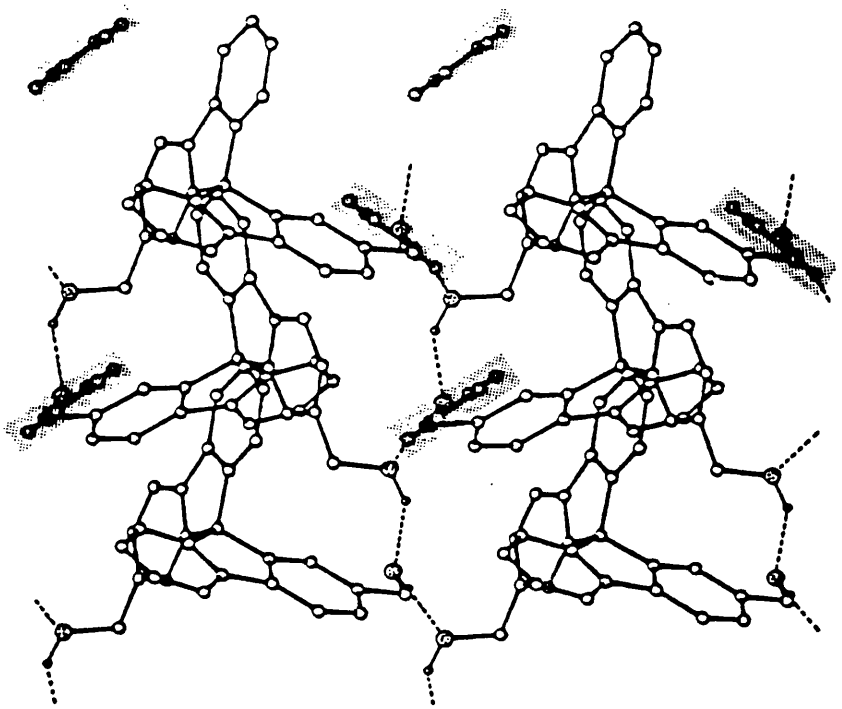
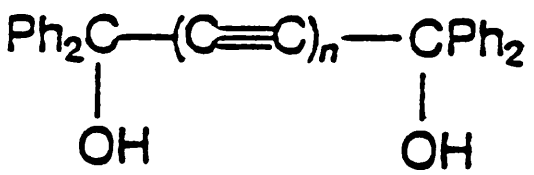


Fig. 2.17. Crystal structure of the (*R*)-(+)-(34b).benzene (1:1) inclusion compound; packing illustration. The guest molecules are indicated by shading.

For Toda one question remained unanswered : was the presence of a diol or dicarboxyl group a necessary prerequisite to the formation of a scissor host? This question arose from two detailed observations. Firstly, from work carried out by Hart[101] on 1,6-dihydroxy-1,1,6,6-tetraphenylhexa-2, 4-diyne (10), and secondly, from the packing in the adduct formed between 1,2-dihydroxy-1,1,2,2-tetraphenylethane (35) and *p*-xylene. In the former case Hart replaced the hydroxy functionality with a third aryl group, i.e. phenyl, *p*-biphenyl or

4-methoxyphenyl as substituents. Depending on the type of the aryl residue, inclusions of benzene, toluene, xylene and chloroform were observed.



(35) n=o

In the latter, the crystal structure (Fig.2.18) showed that the guest molecule was trapped by the surrounding phenyl groups of (35) only, with hydrogen bonding playing no role. On the basis of these observations Toda suggested that non-polar hydrocarbon analogues of (35) should also form inclusion compounds.

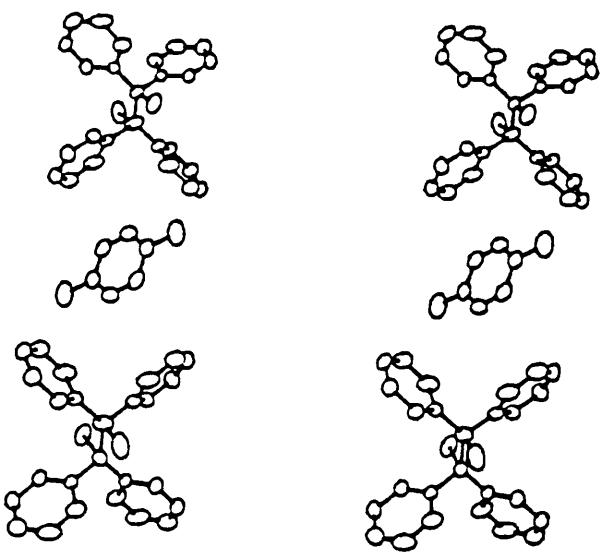
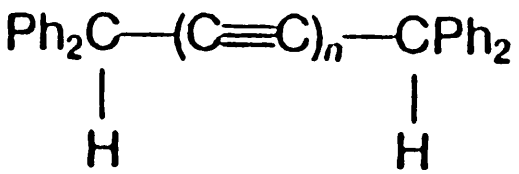


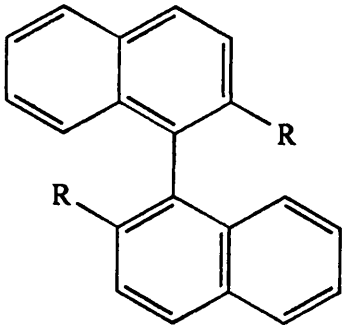
Fig. 2.18. A stereodrawing of the 1:2 complex of *p*-xylene with (35).

This was borne out by the fact that 1,1,2,2-tetraphenylethane (36) formed a similar complex to that observed for (35).[102] Also 1,1,6,6-tetraphenylhexa-2,4-dyne (37) and 1,1,4,4-tetraphenylbut-2-yne (38) were shown to form inclusion compounds with guests mainly of a non-polar nature.[102]

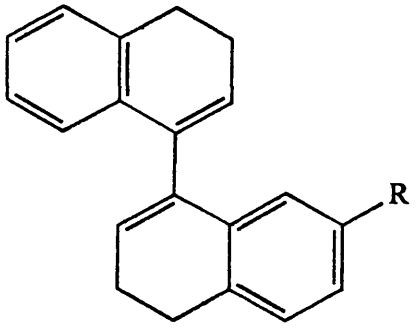


(36) n = 0 (37) n = 2 (38) n = 1

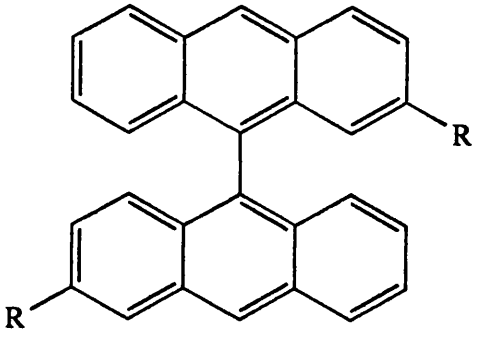
Applying the same strategy to the scissor hosts, Toda and Weber designed "true" clathrate-type scissor host molecules, some of which are shown below.



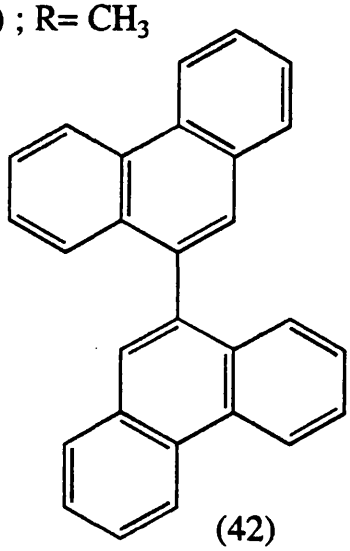
(39a) ; R= H
(39b) ; R= CH_3



(40a) ; R= H
(40b) ; R= CH_3



(41a) ; R= H
(41b) ; R= Cl



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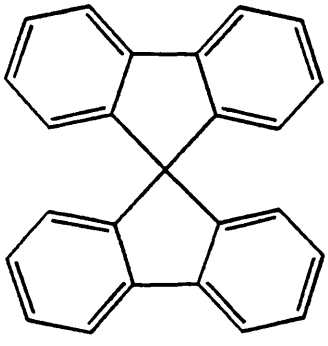
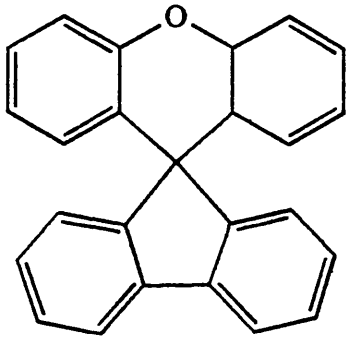
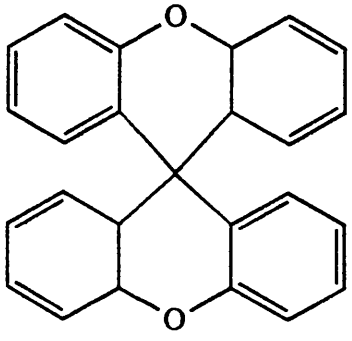


(43)



(44)



(45)

The binaphthyls, biphenanthryls, bianthryls and spiro-bifluorenes all formed numerous inclusion compounds.[104] Interestingly, the spirobifluorene (43)[97] proved to be more versatile than its coordinato-clathrate analogue, forming twenty one adducts with cyclic guests of varying polarity, from cyclohexane to γ-butyrolactone.[72,103]

Of particular interest were the adducts formed by (39a)[105], mainly because of the range in polarity of the included guests - from methanol to cyclohexene.[71]

Toda gave two explanations for the existence of the methanol adduct : either a weak intermolecular hydrogen bridge exists between OH groups and aromatic π systems[105] or one can imagine a cluster formation of two or more guest molecules which mutually mask their hydrophilic sites so as to be compatable with the apolar host lattice.

The packing of non-polar scissor host molecules is illustrated by the crystalline inclusion compound between (41a) and benzene (Fig. 2.19).[103]

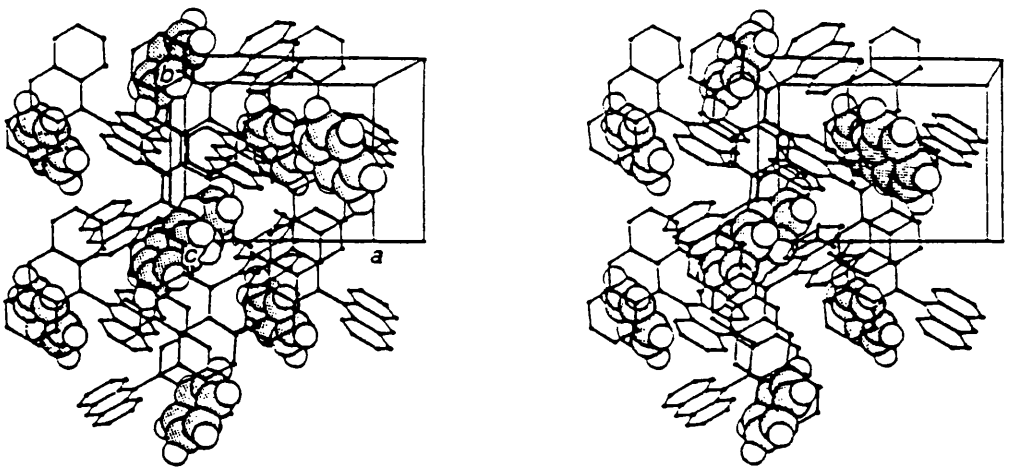


Fig. 2.19. Crystal structure of the (41a) benzene (1:1) inclusion compound : stereoscopic packing illustration. The host molecules are represented in a stick style (H atoms omitted), the guest molecules are in a space filling representation (with about half of the van der Waals radii of the composing atoms; C atoms shaded).

The guest molecule is perfectly ordered within the crystal. This is explained by the tight fit of the pair of benzene guests occupying almost completely closed cages which are formed by the flat surfaces from eight contributing host molecules. The cage structure of the host matrix and the extremely good spatial fit between host molecules and guest are responsible for the pronounced selectivity behaviour of (41a) (Table 8).

Table 8. Selective guest inclusions of host (41a) from two-component solvent systems (complete discrimination unless otherwise stated).

Host	Recrystallisation solvent compound mixture (I/II)[a]	Host:I:II mol ratio[b]
(41a)	toluene/benzene	1:x:y[c]
	toluene/*o*-,*m*-xylene	1:x:y[c]
	toluene/pyridine	1:0:1
	toluene/dioxane	1:0:1
	toluene/cyclohexane	1:0:1
	cyclohexane/ *o*-,*m*-,*p*-xylene	1:1:0
	cyclohexane/pyridine	1:1:0
	pyridine/tetrahydrofuran	1:1:0
	pyridine/*n*-heptane	1:1:0
	pyridine/chloroform	1:1:0
	pyridine/ dimethylformamide	1:1:0

[a] Equimolar mixture.
[b] Determined by NMR integration.
[c] No clear discrimination in favour of I or II.

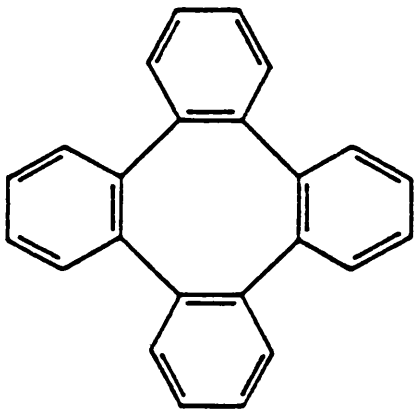
In conclusion, Toda's chance discovery and observation of the crystal packing of molecule (10) with various guests led to the formulation of an empirically derived strategy for host design.

Development of a new host series, called the scissor host series, subsequently followed. Within the series both Toda and Weber demonstrated a very logical approach to design, introducing new hosts to the series based on previous experimental observations. This was highlighted by Toda's discovery of non-functionalised scissor host molecules.

The latter addition to the scissor series rather reduced the credibility of his original strategy. For in the light of their discovery the only salient features a host must now possess are bulk and rigidity. Perhaps the additional requirement of molecular symmetry could have been added to his list of features required for host formation, as C_2 molecular symmetry is present, without fail, in all the hosts discovered by Toda and Weber. Both, in fact, referred to the C_2 symmetry when discussing the chirality of the host molecule, but not as an integral part of their overall design strategy. This relevance of symmetry to design was later proven by MacNicol while working on the design of 3-fold molecular hosts.[3]

2.3 Tetraphenylene and related host molecules.

Interest in tetraphenylene (46) began with its synthesis and accidental discovery of the molecule's inclusion behaviour in 1943 by Rapson.[107] However in the early forties clathrate chemistry was still in its infancy, hence no one thought it of sufficient interest to pursue the matter further. Until, that is, the mid seventies, when MacNicol's new concept stressing the importance of 3-fold molecular symmetry in design of inclusion compounds, managed to renew interest in tetraphenylene, particularly for Mak and Wong. These workers then decided to investigate more thoroughly the adducts formed by tetraphenylene[108,109] and examine the role played by C_2 molecular symmetry[108,110] in the formation of such adducts.



(46)

The inclusion compounds formed by (46) conform to the general formula $2C_{24}H_{16}G$, where G is a guest species ranging in size from methylene chloride to cyclohexane (Table 9).

Table 9. Crystal data for clathrate inclusion of tetraphenylene $2C_{24}H_{16}G$

Guest Solvent G	*a*(Å)	*c*(Å)	Volume(Å)^3 Unit cell	Cavity
CH_2Cl_2	9.892(5)	18.46(1)	1806	77.7
acetone	9.902(2)	18.491(6)	1813.0	81.2
tetrahydro furan	9.906(1)	18.503(5)	1815.7	82.6
CH_2Br_2	9.935(2)	18.546(6)	1830.6	90.0
$CHCl_3$	9.925(2)	18.593(3)	1831.5	90.5
1,4-dioxane	9.968(1)	18.553(5)	1843.5	96.5
2-bromo propane	9.973(1)	18.633(5)	1853.3	101.4
1-bromo propane	10.004(1)	18.647(4)	1866.2	107.8
CCl_4	9.930(2)	18.932(6)	1866.8	108.2
benzene	10.069(1)	18.431(5)	1868.6	109.0
cyclo-hexane	10.073(1)	18.712(2)	1898.6	124.1

The adducts tend to be unstable, losing their guest components on standing in air at room temperature. They all constitute an isomorphous series belonging to space group $P4_2/n$ and are morphologically distinguishable from the pure host (46) which crystallises in the space group $C2/c$. As expected, all intermolecular interactions are of van der Waals type; the host molecules form a cavity, oblate spheroidal in shape, in which the guest resides. Like the classical hosts TOT and PHTP, the cavity size undergoes significant changes as the host cagework adapts itself to the steric requirements of various guests.

From their in-depth study of the varying crystalline structures of the clathrates of (46), and in the light of the prominence now given to molecular symmetry within host design, Mak and Wong proposed a new strategy allowing them to synthesise a new host series derived from tetraphenylene.

For host (46), they reasoned that a secondary $\underline{C}_2$ axis passing through the centres of a pair of opposite carbon-carbon single bonds, which gives the molecule its twisted shape, was responsible for the inclusion behaviour of (46), rather than the principle $\underline{C}_2$ axis of the $\underline{D}_{2d}$ molecular point group (Fig. 2.20).

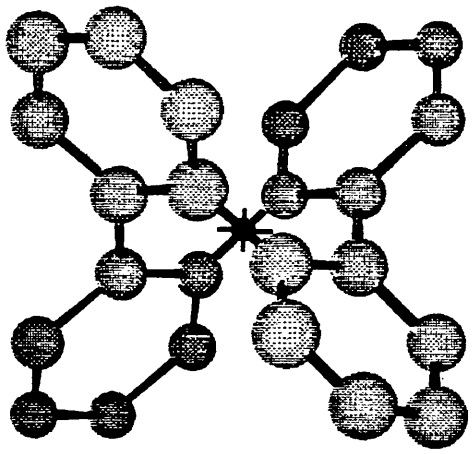
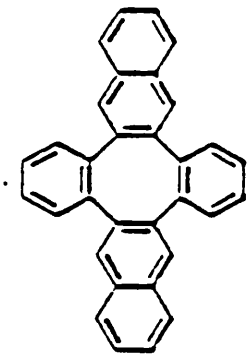
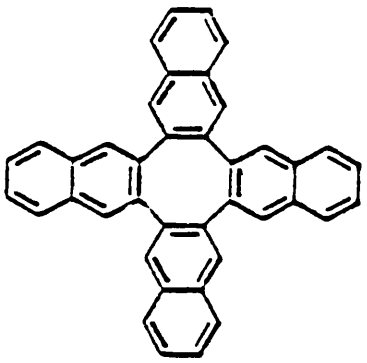


Fig. 2.20. Tetraphenylene, indicating a key C_2 axis.

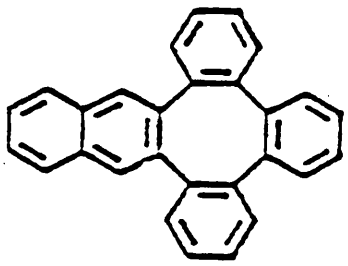
In order to test this notion Mak and Wong synthesised[111] a new series of benzo-fused tetraphenylenes for clathration of larger guest molecules.



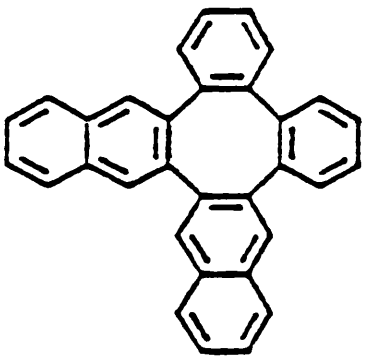
(47)



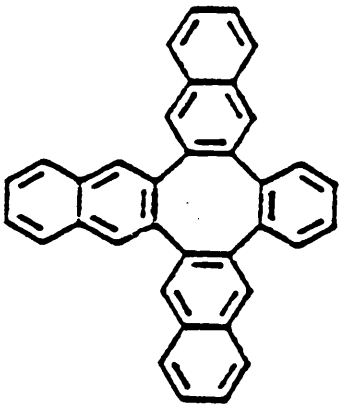
(48)



(49)



(50)



(51)

In conformity with their assertion, (47), (49) and (51), none of which possesses a secondary $\underline{C}_2$ axis, exhibited no inclusion behaviour. On the other hand (48) and (50) both of which contain a secondary $\underline{C}_2$ axis (Fig. 2.21) behave as effective hosts for benzene, *p*-xylene and 1,2,4-trimethylbenzene.[112]

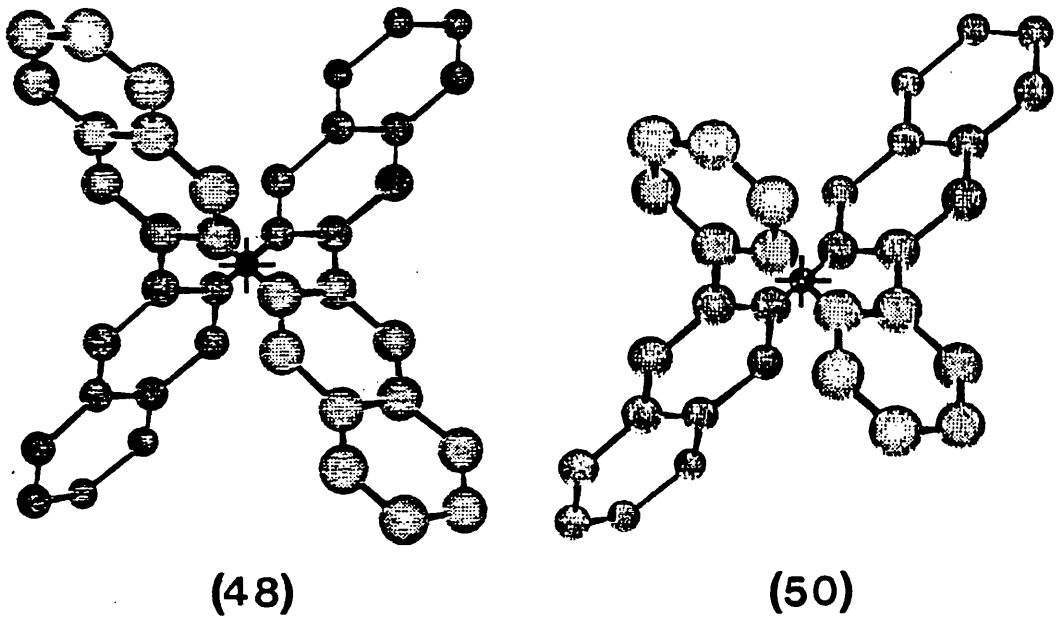


Fig. 2.21. Molecules (48) and (50), indicating the key $\underline{C}_2$ axis.

The new clathrates differed markedly from the tetraphenylene clathrates in regard to tenacity of retention, mode of accommodation, and the degrees of order or disorder of the guest species.

Figure 2.22 shows the molecular packing of the (48) *p*-xylene 1:1 adduct.[112] In this case the guest molecules are well-ordered and enclosed in a cavity surrounded by six host molecules, whilst the symmetry of the molecule is close to D_{2d}.

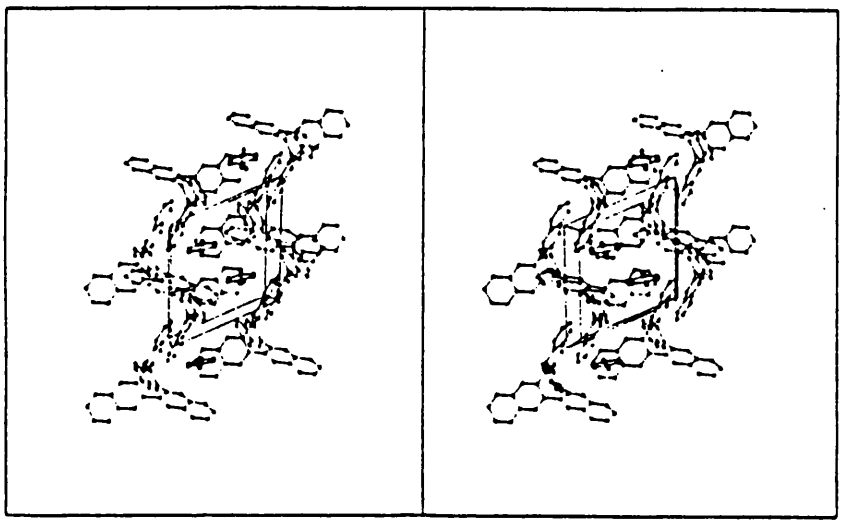


Fig. 2.22. Crystal structure of (48). *p*-xylene adduct.

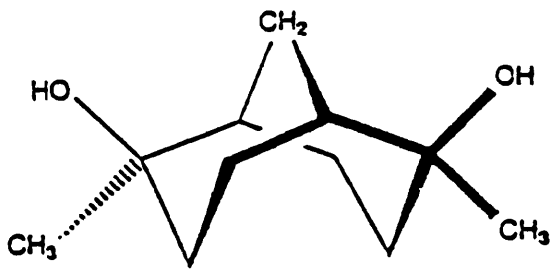
Unlike tetraphenylene, the host-guest ratio does vary with the various inclusion compounds of (48) and (50), suggesting a variety of mutual host-guest adaptions with interesting variations of cage geometry. Unfortunately, Mak and Wong have not yet made an in-depth study of the crystal structures of such clathrates which would have allowed one to examine these changes of geometry in detail.

What they have accomplished, though, is the successful design and synthesis of a limited series of host compounds, using the concept of molecular symmetry. Although rigidity and bulk are present in the above host molecules,

these factors seem to play a less important role than symmetry in the design of such host molecules. Evidence for this lies in the fact that molecules (47), (49) and (51) were completely devoid of inclusion activity. Therefore, Mak and Wong have taken this form of design one step on from Toda and Weber's work by noting the relevance of C_2 molecular symmetry.

2.4 Alicyclic diol hosts.

The occurrence of canals or channels is a relatively common feature in inclusion chemistry and is encountered across a range of quite different host structures.[113] Channel *helicity* is, however, encountered less often in the inclusion field[114] though is exhibited by the classical host urea. In 1979 Bishop discovered a new host with such a helical packing topology, namely, the alicyclic diol *exo*-2, *exo*-6-dihydroxy-2,6-dimethylbicyclo[3.3.1]nonane (52).[115] The new host molecule was observed to form solid inclusion adducts when crystallised from a wide range of common solvents, including ethyl acetate, toluene, acetone, chloroform and 1,4-dioxane. In most cases the adducts were found to be very stable.



(52)

The X-ray crystal structure of the inclusion compound of (52)[115,116] with ethyl acetate (host-guest ratio 3:1) revealed that the material crystallised in the space group $P3_121$ (or its enantiomorph $P3_221$), although the original diol comprised a racemic mixture of the two enantiomeric forms of (52). That is the material had undergone spontaneous resolution in forming each crystal, and a mixture of chiral crystals[112] had been produced.

The projection view of the crystal structure (Fig. 2.23) shows a very open network of diol molecules, with large tubes of approximately triangular cross section, where the guest molecules reside. The host molecules are linked by hydrogen bonding in the form of tight helical spines. There are six spines and six diol molecules surrounding each of the triangular tubes, with each diol molecule functioning as a double hydrogen bond donor and double hydrogen bond acceptor.

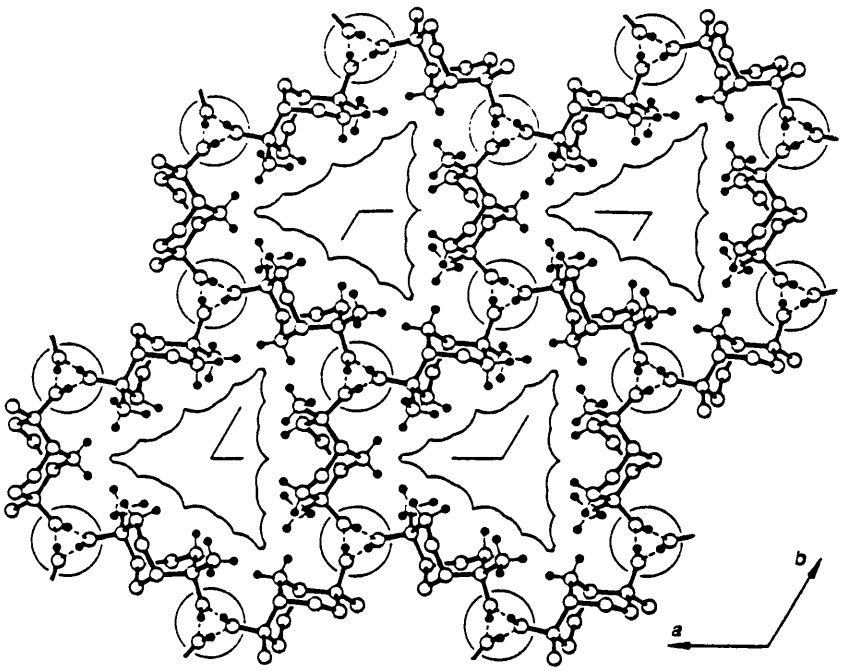


Fig. 2.23. Projection view, parallel to the threefold screw axes, of the diol host network in (52). Hydrogen bonds are marked as broken lines, and the helical spines of hydrogen bonds are circled. Selected hydrocarbon hydrogen atoms are included with their van der Waals radii, defining the triangular projected cross-section of the canals.

The chain of six diol molecules surrounding each tube has a pitch of 2*c*, and as a consequence of the *c* repetition of diol molecules, the complete helix of

the host lattice is comprised of two separate helical chains without direct hydrogen bonding between the helices (Fig. 2.24).

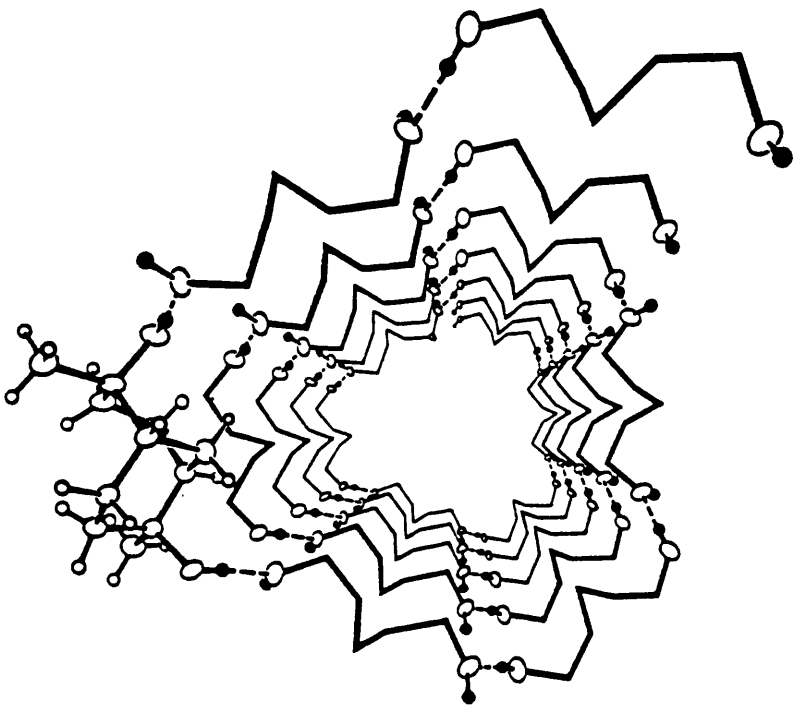


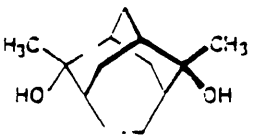
Fig. 2.24. Perspective view of the double helical sequence of hydrogen bonded diol molecules in one tube of (52). All diol molecules except one are represented diagrammatically as the bridges linking the two OH groups.

The walls of the tubes are lined only by the hydrophobic parts of the molecule, whilst the diol OH functions are located in the tight spines which are inaccessible to guest molecules. Hence, unlike the coordinato-clathrates, no formal hydrogen bonding is found between the host and guest molecules, allowing

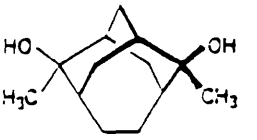
classification of this type of host as coordination-assisted clathrate, or, more specifically, tubulato-clathrate. Bishop, on the other hand, favours the term helical tubuland, to describe such systems.

Having established the novel architecture of (52) in detail, Bishop felt that such a molecule could be successfully modified to produce new hosts with a similar molecular architecture; maintaining the C_2 symmetry and at the same time the diol functionality, as well as the in built rigidity of the parent host molecule (52).

Implementation of this strategy led to the synthesis[114,115,118-121] of a complete familty of novel alicyclic diols shown below.



(53)



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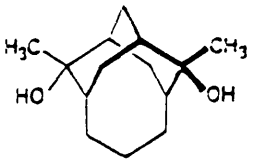

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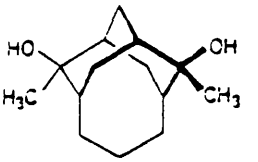
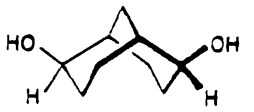


(56)



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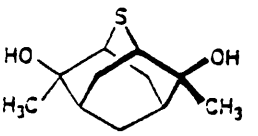

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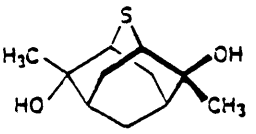

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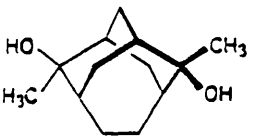

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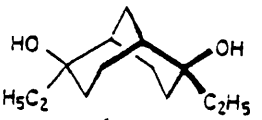

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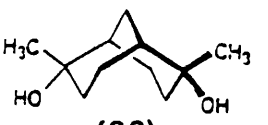

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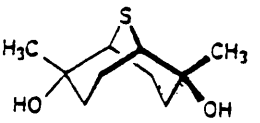

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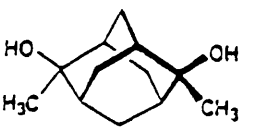

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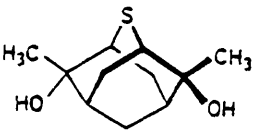

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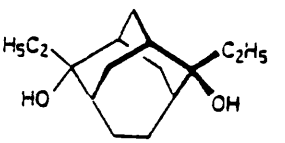

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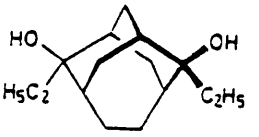

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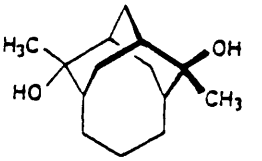


(68)

Only molecules (53) and (55) of the newly synthesised diols actually formed inclusion compounds. The reason for this can be established by examining the crystal structures of all the diol molecules.

The diols can be separated into three separate groups according to their dimensional ordering within the crystal.

The first group consists of molecules (52)-(56) which crystallise in the space group $P3_121$ (or its enantiomorph). Hence all adopt the helical tubuland arrangement[118,119] of the parent molecule (52). A more quantitative examination revealed two subsets of this helical tubuland family:- Set A included molecules (52), (54) and (56); whilst Set B consists of diols (53) and (55). The feature necessitating such a division was the strength of the hydrogen bonding within the crystal structures of the diols. In Set A the molecules have shorter hydrogen bonds, which is reflected in the cross sectional area of the channel accommodating the host molecule, with values ranging from 22.4Å^2 for (52) to 4.7Å^2 and 2.7Å^2 for (54) and (56), respectively. Such a narrowing is clearly evident from Fig. 2.25 showing the projection of diol (56). In this case the newly introduced propylene bridge occupied most of the cavity, reducing the space available for including guest molecules.

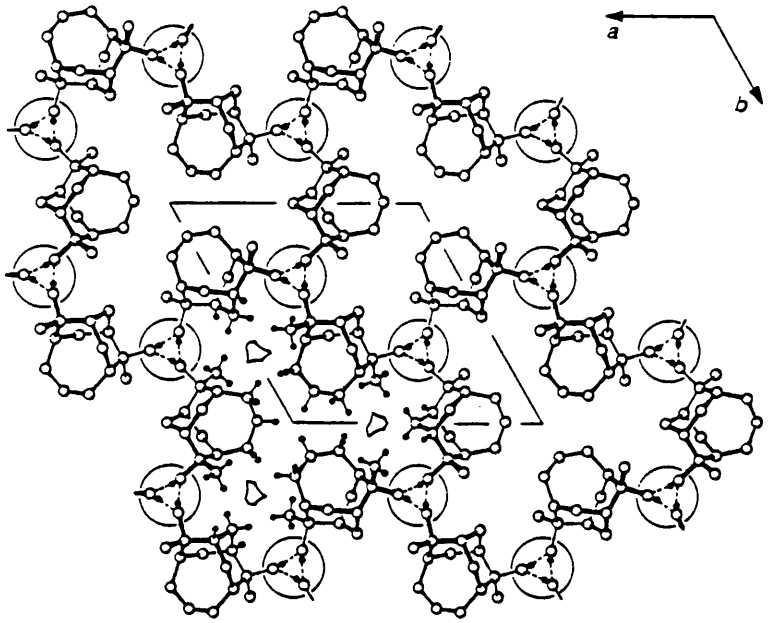


Fig. 2.25. Projection view of the host diol network in the crystal structure of (56).

Molecules in Set B are characterised by having longer hydrogen bonds within their crystal structures.

This is reflected in the cross sectional area of the channels for (53) and (55) which are 30.2Å^2 and 34.7Å^2, respectively. By addition of the bridge on the same size of the molecule, one alters the packing slightly, a consequence of which is the formation of a larger cavity. This is illustrated by the projection view of host diol (55) (Fig. 2.26).

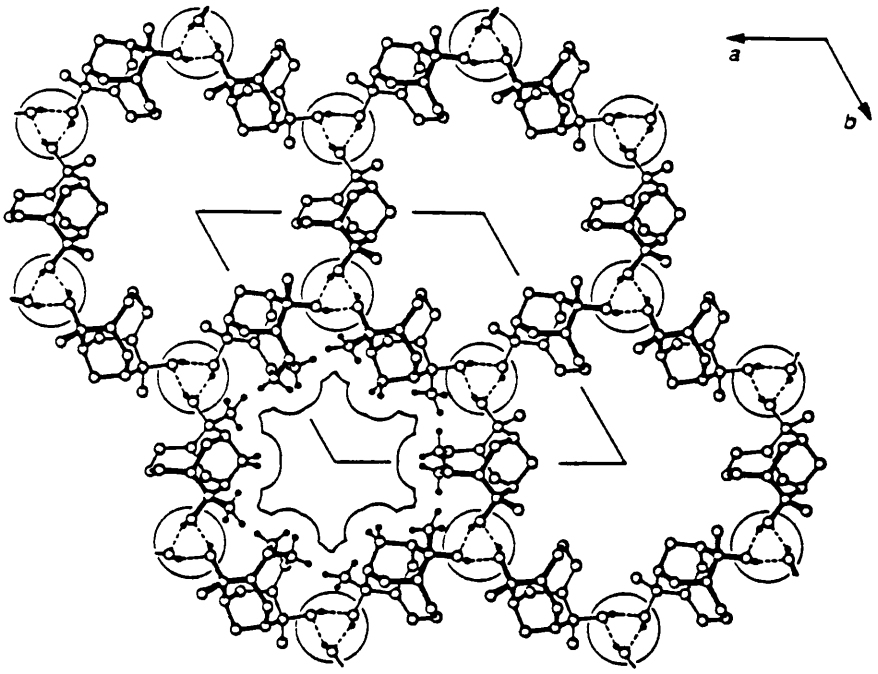


Fig. 2.26. Projection view of the host diol network in the crystal structure of (55).

Bishop's initial expectation that such novel architecture should persist throughout all the host molecules was not, however, realised. Diols (57) to (60)[118,119] were found to have crystal structures distinctly different from that of the helical tubuland structure, and constitute the second group of alicyclic diols.

The packing of such diols is typified by molecule (58), crystallising in the space group $P4_1$. The helical hydrogen bonding in the crystal is distinctly different from that of the helical tubuland structures in that half of the hydroxy hydrogen atoms in these structures are not involved in hydrogen bonds : each hydroxy group is involved as a hydrogen donor *or* as a hydrogen acceptor in a hydrogen bond (Fig. 2.27).

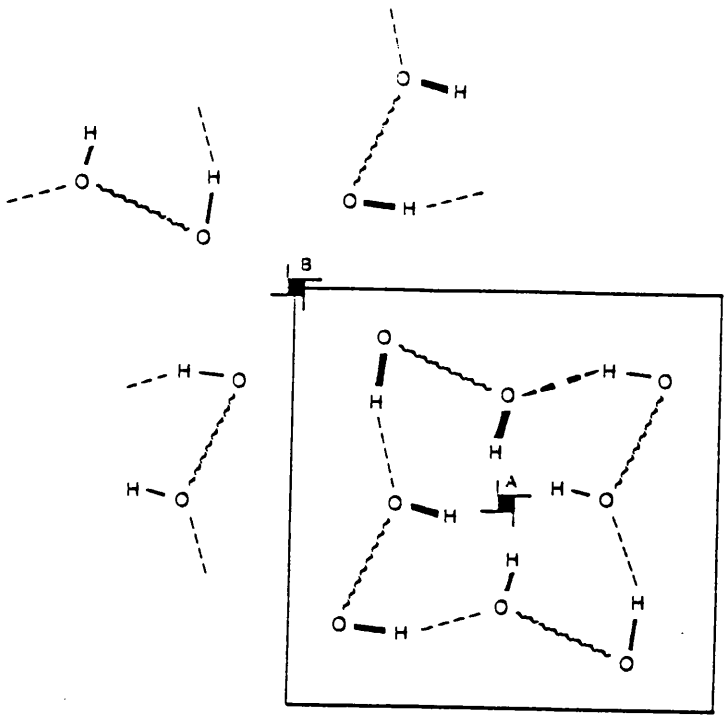


Fig. 2.27. Projection along the tetragonal axis of (58).

There are two types of 4_3 screw axis in the structure : that marked A in Fig. 2.27 is surrounded by a helix of hydrogen-bonded diols, whereas the diols around the 4_3 axis B are not connected by hydrogen bonds. There is no room for guest inclusion around either axis.

The final group constitutes those diols (61) to (68).[120] All these have cyclic hydrogen-bonded sequences, leading to layer arrangements instead of a helical tubuland structure. Again, the close packing prevents any adduct formation.

From this experimental evidence Bishop[122] was able to construct a set of guidelines or determinants, specifying requirements for helical tubuland

formation:-

(1) The diols must have C_2 molecular symmetry.

(2) The alicyclic structure must be capable of a small degree of flexibility. This allows the molecules to assume the helical tubuland form in the crystal lattice.

(3) A molecular bridge on the opposite side to the hydroxy groups (the *anti*-face) is not a necessary prerequisite for tubuland formation, as diols (52), (54) and (56) all form tubulands.

(4) A molecular bridge on the same side as the hydroxy groups (the *syn* face) is essential, since diols (63) and (64) crystallised, not as the helical tubulands, but as layer structures.

(5) The alcohol groups must be tertiary, and must have a methyl substituent. All other types of substituent have led to non-tubuland crystal structures.

Molecules with the above characteristics may in general adopt the helical tubuland form; an exception to the rule is molecule (53), which also forms a tetragonal crystal structure[121] with benzene guest molecules located in hydrocarbon-lined ellipsoidal cavities (Fig. 2.28).

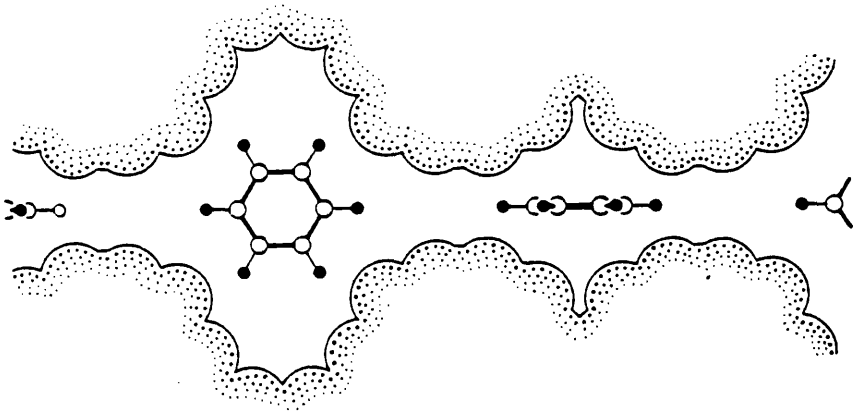


Fig. 2.28. Cross-sectional representation of the cavities in the (53).C_6H_6 adduct, linked along crystallographic two-fold axes parallel to *c*, showing the van der Waals surface due to hydrogen atoms of the host molecules and the orientation of the benzene guest molecules.

Unlike the tubulands, this structure involves hydrogen-bonded helices of both enantiomers of the diol.

Such variation in structural form is not found in those diols with tight hydrogen bonding. Diol molecules (52), (54) and (56) all maintain the helical tubuland structure even in the absence of guest molecules. This is unique in tubuland clathrates, since all the previously discussed tubulands (e.g. urea, thiourea) require the presence of a guest to stabilise the tubular crystalline lattice.

In conclusion, Bishop's work could be described as the optimisation of the first strategy in host design, judicious modification of a known host. Not only did he recognise the importance of structure and functionality but also the siginificance of molecular symmetry in the design of a new host series. His detailed research has revealed the structural principles underlying the formation of these multimolecular assemblies, allowing one to foresee the possibility of new host systems.

CHAPTER 3.

CONCEPT 2 : DESIGN BY ANALOGY.

3.1 Hexa-host systems

The previous section dealt with chance discoveries of new host molecules, and their subsequent modification leading to completely new host systems. The design followed a strategy developed from the analysis of the chance discovery. The question now arises as to how one might design a new host series without this initial input. The answer was provided by MacNicol in the 1970's when he proposed that new hosts could be rationally designed using a concept called the hexa-host analogy.[2]

The concept was essentially derived from the packing modes of such classical hosts as hydroquinone, phenol and, especially, Dianin's compound (1). In Chapter 1 the packing of such hosts was discussed in detail, and revealed that the molecules packed in the form of a hydrogen-bonded hexamer (Fig. 3.1).

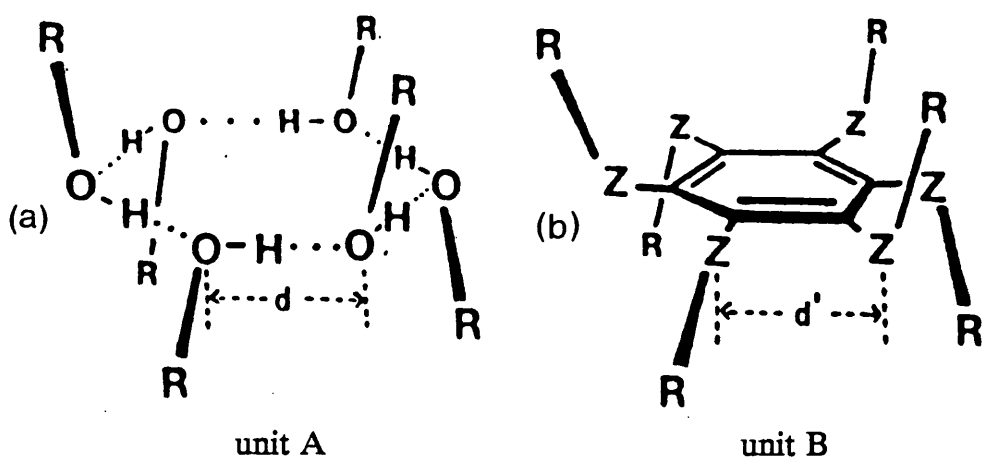
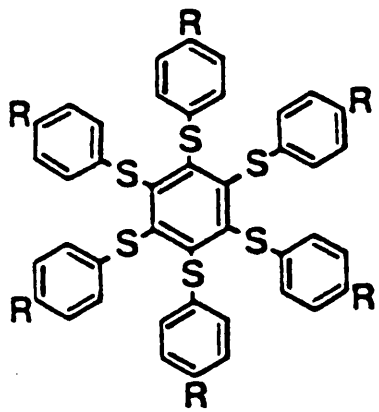


Fig. 3.1. Comparison of (a) hydrogen-bonded hexamer unit with (b) hexasubstituted benzene analogue.

This hydrogen-bonded grouping, which plays a key role in maintaining the "open" clathrate structure is however, of a temporary nature. MacNicol noticed that a parallel existed between this temporary unit (A) and the structure of a suitably hexasubstituted benzene B (Fig. 3.1), and reasoned that molecules of the latter type might possess a greatly increased tendency to crystallise forming non-close-packed structures with inclusion properties. MacNicol also noted the favourable correspondence of overall geometric aspects and hexamer dimensions of units (A) and (B). The strategy involved synthesising a series of such hosts, termed hexa-hosts, by substituting hexachlorobenzene with various thiophenolate, phenolate or selenophenolate nucleophiles. The first hexa-host (69) was initially prepared in moderate yield, using phenylthiocopper[123] (PhSCu) to provide the benzenethiolate nucleophile and was found to include CCl_4, CCl_3CH_3 and other chlorine-containing molecules.[2]



(69) R=H

The inclusion compounds crystallised in the $R\bar{3}$ space group with three host molecules and six guest molecules in the hexagonal unit cell. The packing[26,124]

diagram (Fig. 3.2) shows the "true" clathrate nature of the adduct; the host molecules completely encapsulating the guest molecules by van der Waals interaction.

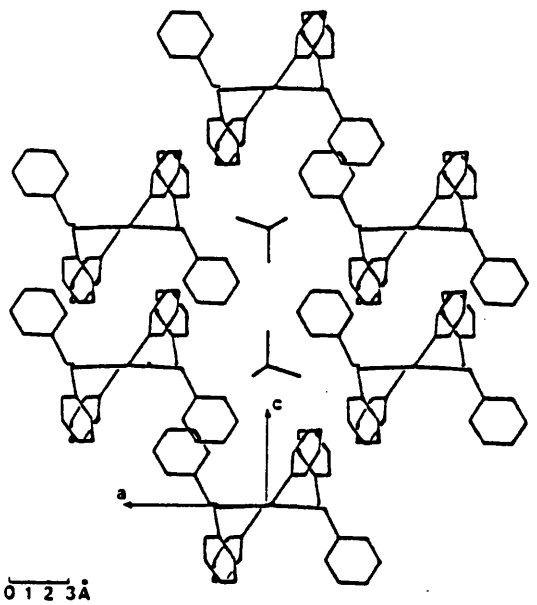
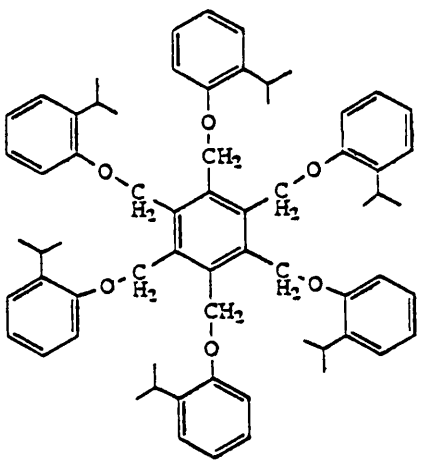


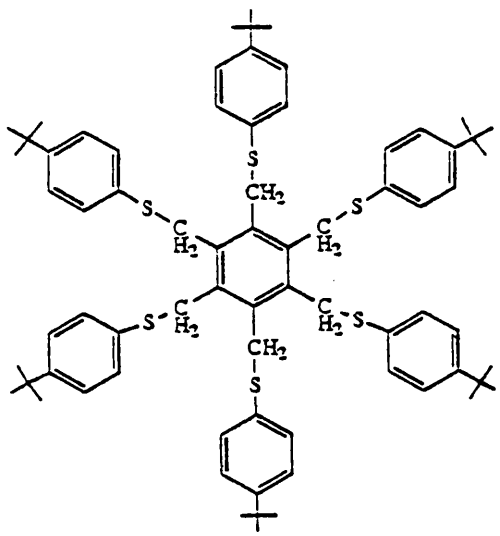
Fig. 3.2. An illustration of the host-guest packing in the crystal of the CCl_4 clathrate of hexakis(phenylthio)benzene (69), as viewed onto the *ac* plane. Two host-molecules which lie above and below the cavity as viewed in this direction have been excluded to show the guest molecules more clearly.

To prove this was no isolated discovery of a host compound MacNicol decided to extend the series of hexa-hosts to remove any doubt. Synthetic difficulties prevented a further extension of the one-atom link hexa-host series at this time (the atom link refers to the number of atoms between the benzene nucleus and the substituted aryl group). Therefore MacNicol modified his

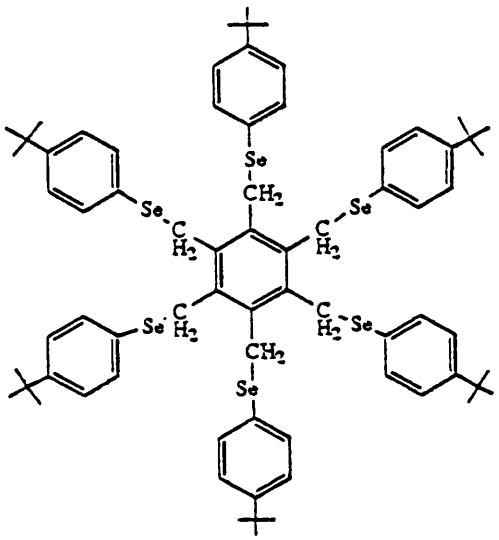
strategy slightly by forming a two-atom link hexa-host series.[2] This involved substituting hexakis(bromomethyl)benzene, $C_6(CH_2Br)_6$, with the aforementioned nucleophiles as well as nitrogen-based nucleophiles. The result was a remarkable series of new oxygen-, sulphur-, selenium- and nitrogen-based hexa-hosts, all too numerous to mention. The two link hexahosts had the general formula $C_6(CH_2X\text{-}Ar)_6$ where X defines the heteroatom O, S, Se or N and Ar represents a side-chain aromatic moiety. Typical examples of two link hexa-hosts include the molecules shown below, (70), (71), (72) and (73).[2, 124]



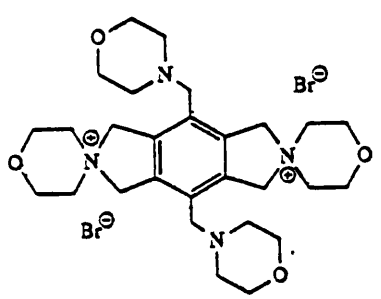
(70)



(71)



(72)



(73)

Of particular interest is molecule (71) which formed an inclusion compound with such large guests as the triterpene squalene, $C_{30}H_{50}$. This squalene adduct crystallises in the $P\bar{1}$ space with a host-guest ratio of exactly 2:1. On this occasion the guest is situated not in a cage, but in continuous channels running through the crystal (Fig. 3.3).[125]

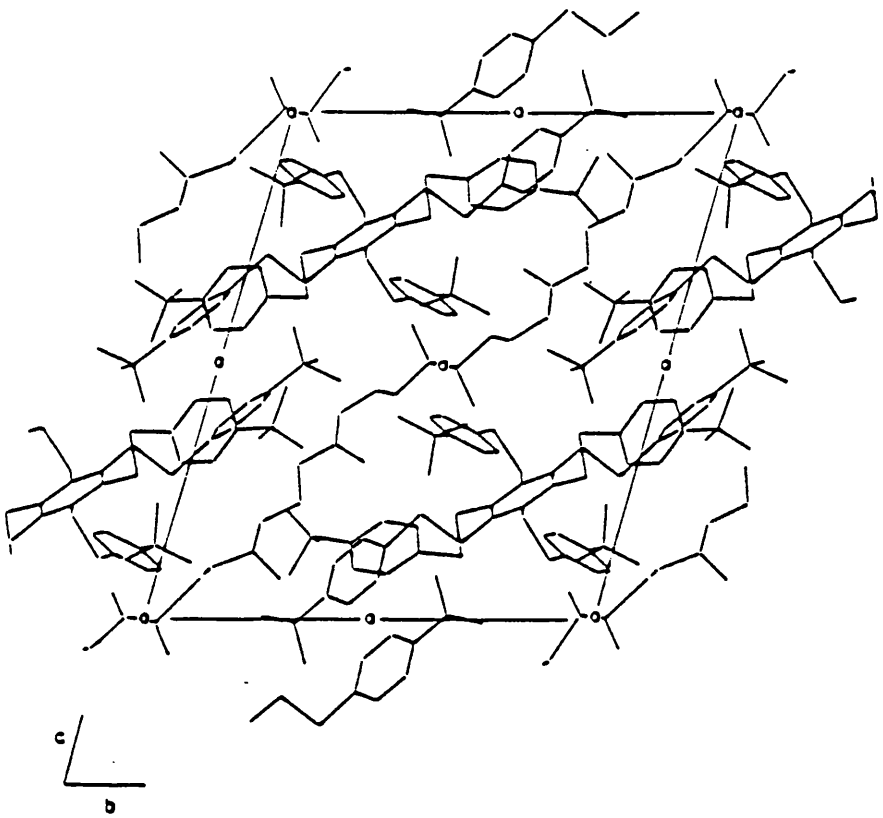


Fig. 3.3. A view looking onto the *bc* plane illustrating the host-to-guest packing in the adduct of hexakis(*p*-*t*-butylphenylthiomethyl)benzene (71) with squalene.

It can be seen from Fig.3.3 that the disordered squalene exists as a pair of enantiomeric conformations belonging to the point group C_1, and appears as a

continuous chain.

On the other hand, compound (73) represents a novel bis-quaternary dispiro system formed by reaction of hexakis(bromomethyl)benzene with morpholine.[126] No inclusion behaviour has as yet been found for (73), but this molecule represents a novel and interesting type of potential host molecule. A view of the structure[126] in the crystal shows the centrosymmetric molecule located on a point of $\bar{1}$ symmetry (Fig. 3.4). The two independent morpholine rings both have chain conformations, and the quaternary nitrogen atoms are displaced above and below the plane of the central benzene ring.

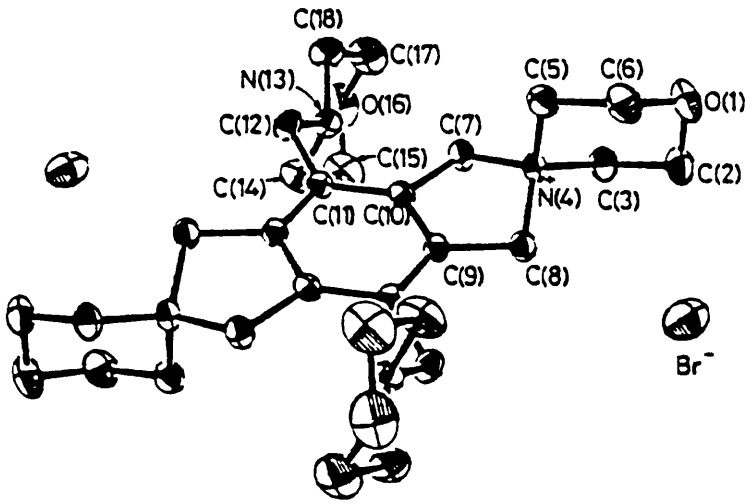
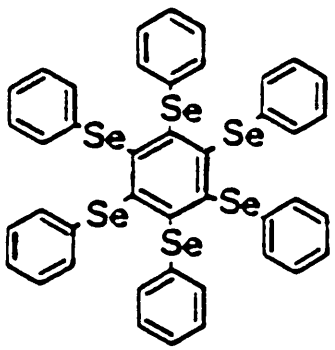
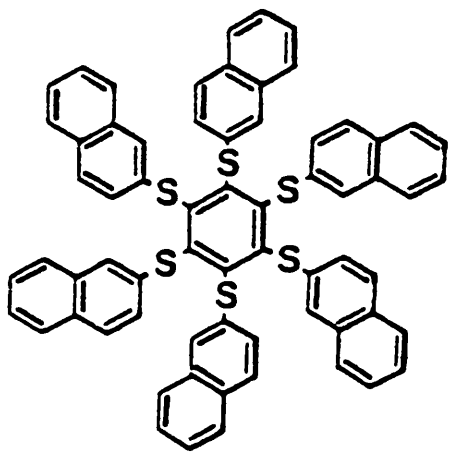


Fig. 3.4. A view of the molecular structure of (73) in the crystal looking onto the *ab* plane.

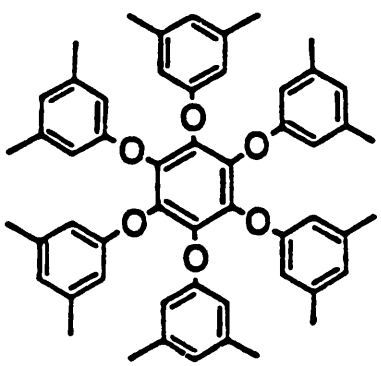
Having established a vast new two atom-link hexa-host series MacNicol then tried to expand his one-link hexa-hosts by circumventing the synthetic problem. This was accomplished by employing 1,3-dimethylimidazolidin-2-one (DEMU)[127,128] as the reaction medium. The resulting promotion of aromatic nucleophilic substitution consequently led to the facile synthesis of many one-atom link hexa-hosts.[129] Typical examples are molecules (74)-(76).



(74)



(75)



(76)

Compound (74)[129] forms an adduct with CBr_4; the host-guest ratio being 1:2. The adduct has a cage structure similar to that of the CCl_4 clathrate of (69).[130]

The novel hexakis(aryloxy)benzenes were not obtained before the discovery of the use of DEMU as solvent, because of the reduced nucleophility of the phenoxide when compared to thiophenoxide. Their synthesis revealed a completely new series of host molecules, some with interesting properties (see Chapter 5). A typical example of an oxygen-based hexa-host is molecule (76), which forms a 1:1 adduct with acetonitrile.[131] The crystal packing of the adduct, $P\bar{1}$ space group, is revealed in Fig. 3.5.

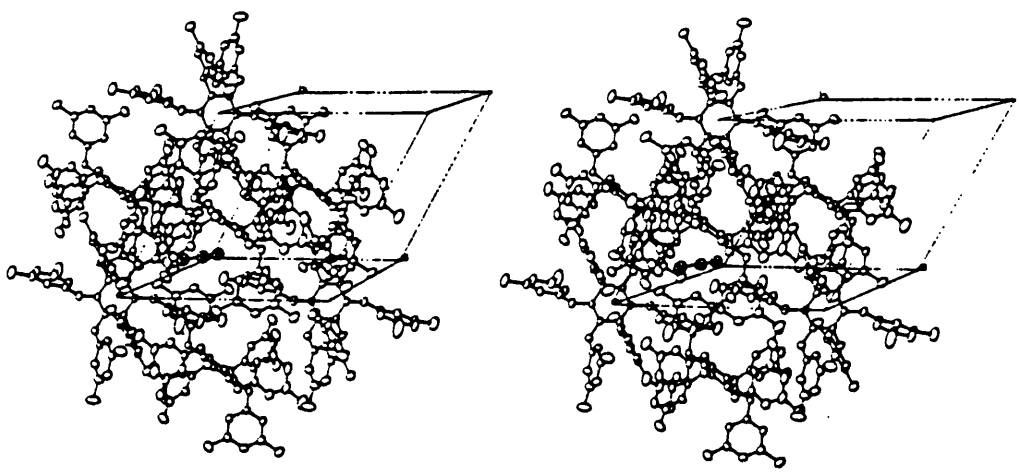


Fig. 3.5. An illustration of the structure of the (1:1) inclusion compound of hexakis(3,5-dimethylphenyloxy)benzene (76) with acetonitrile as guest. Crystallographically non-equivalent host molecules are located at (0,0,0) and (½,½,½) and there are two $CH_3C{\equiv}N$ guest molecules in each unit cell, one of which is shown.

In the acetonitrile adduct there are two crystallographically distinct host molecules and both of these, located at points of $\bar{1}$ symmetry, are constrained to

be centrosymmetric. The two acetonitrile guest molecules occupy enantiomerically related general positions in the unit cell. Additionally, the acetonitrile guest molecule interacts with a host molecule, methyl....O distances of 3.252Å and 3.366Å being found.

In short, MacNicol's work represents a new level of design within inclusion chemistry. Purely by observing the packing modes of classical host molecules, he was able to design an extensive and interesting series of new inclusion compounds. The concept of design by analogy requires both imagination and logic in its application, and therefore constitutes an intellectual progression from the design by modification concept.

3.2 Diamondoid inclusion systems.

A similar, although more tenuous application of the design by analogy concept was conceived by Ermer in the late eighties. His interest also lay with the packing of classical host molecules, specifically trimesic acid (TMA). The TMA crystal packing influenced Ermer greatly, with its four interpenetrating sets of open-stacked, folded hexagonal "chicken wire" nets of trimesic acid molecules held together by pairs of hydrogen bonds. Ermer envisaged that a similar 3-dimensional organic system should exist, having in mind as an analogy the formal structural transformation of graphite into diamond.

His choice of potential host compound was influenced by observing the

packing of certain organometallic species. In particular $Cd(SC_6H_5)_2$, which tends to adopt a three-dimensional non-molecular polyadamantoid structure (Fig.3.6),[132] suggesting that adamantane would be a particularly favourable building block in

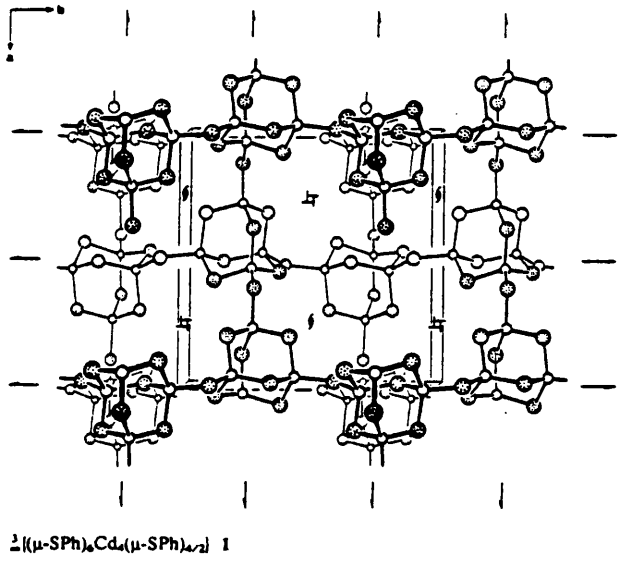
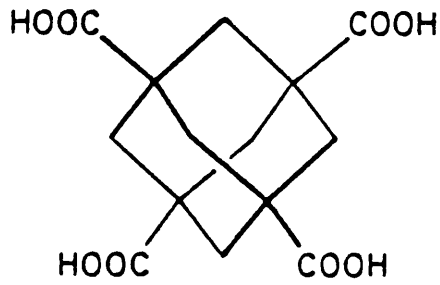


Fig. 3.6. The polyadamantoid framework in crystalline $Cd(SPh)_2$ (drawn with all phenyl groups omitted). The larger dotted circles are the sulfur atoms.

any lattice. In addition, adamantane's in-built rigidity and similarity to the diamond lattice itself made it the obvious candidate for the development of diamondoid-type structures. He proposed to link the adamantane units via hydrogen bonding using carboxyl groups oriented in a tetrahedral fashion, similar to the oxygen atoms in the diamond-like cubic SiO_2 structure.

Ermer duly synthesised his proposed molecule, adamantane 1,3,5,7-tetra-carboxylic acid (78). The X-ray structure of compound (78) revealed a novel diamondoid architecture, containing no less than five interpenetrating hydrogen-bonded diamondoid lattices.[133]



(78)

The molecule (78) has S_4 symmetry in the crystal, which has space group $I4_1/a$. Fig. 3.7 shows a single super-diamondoid lattice formed by the pairwise hydrogen-bonding of (78).

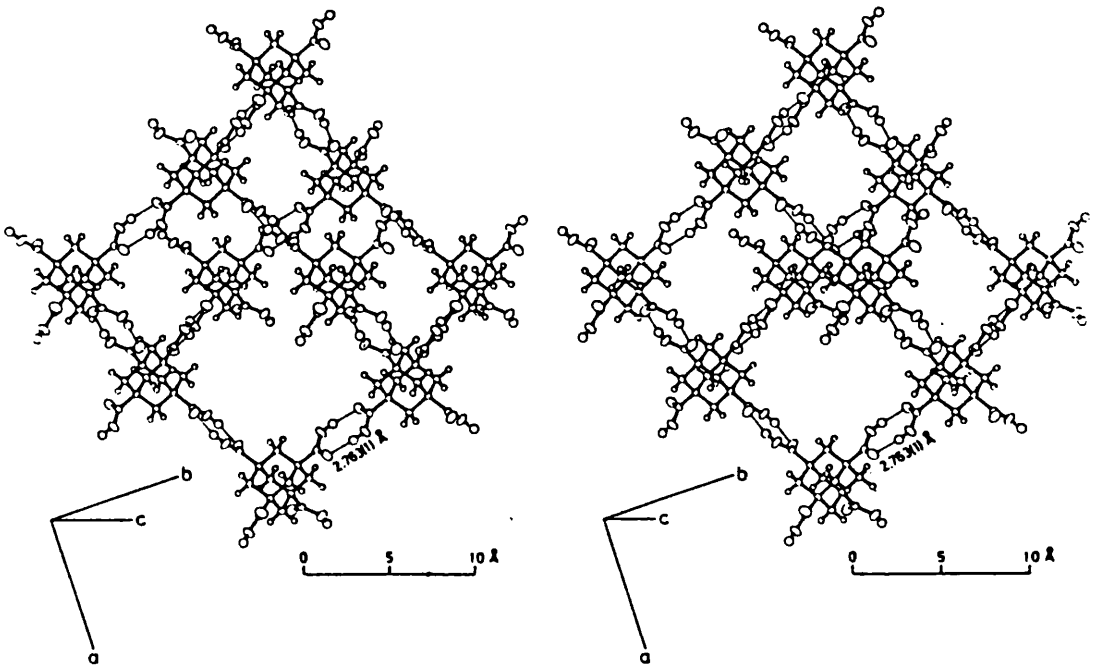


Fig. 3.7. Stereoview of a hydrogen-bonded super-adamantane framework of (78) cut out of an individual diamondoid lattice with O(H)...O distance of the hydrogen bonds. Note the large central cavity, which is filled by four interpenetrating equivalent diamondoid frameworks. The view is very roughly along the tetragonal axis, *c* as indicated.

The open spaces of this architecture are clearly evident from the drawing and are filled in the crystal by four other symmetry-equivalent super-diamond lattices. Hydrogen bonding occurs only within a particular diamondoid lattice but not between different lattices. A pictorial impression of how the five diamondoid lattices are interwoven can be seen in Fig. 3.8.

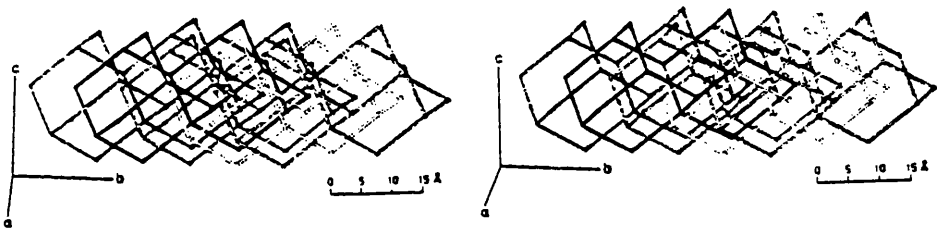
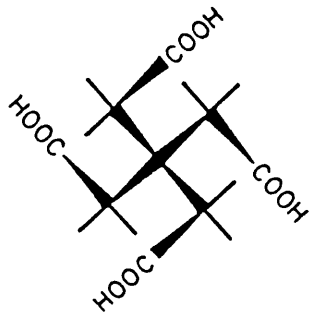


Fig. 3.8. Impression of five diamondoid lattices (stereoview).

The above work demonstrated rather beautifully that tetrafunctional organic molecules with tetrahedral directed substituents are, under suitable conditions, capable of building large hollow diamond-like lattices in the crystal Obviously the five-fold interpenetration of the diamondoid lattices precludes formation of any adduct, though, the molecule could be termed a 'self-inclusion' compound.

As a step toward a more systematic exploration of the packing modes of tetracarboxylic acids with tetrahedrally oriented carboxyl groups, Ermer chose to analyse methane tetraacetic acid (79).[134]



(79)

This time the degree of interpenetration is three-fold, such that (79) has a distorted triple-diamond structure.[135] Fig. 3.9 shows a hydrogen-bonded superadamantane unit of the diamondoid network of (79). The large central cavity is filled in the crystal by two equivalent, interpenetrating diamondoid networks. Once again, no inclusion was exhibited because of the close-packed nature of the crystal.

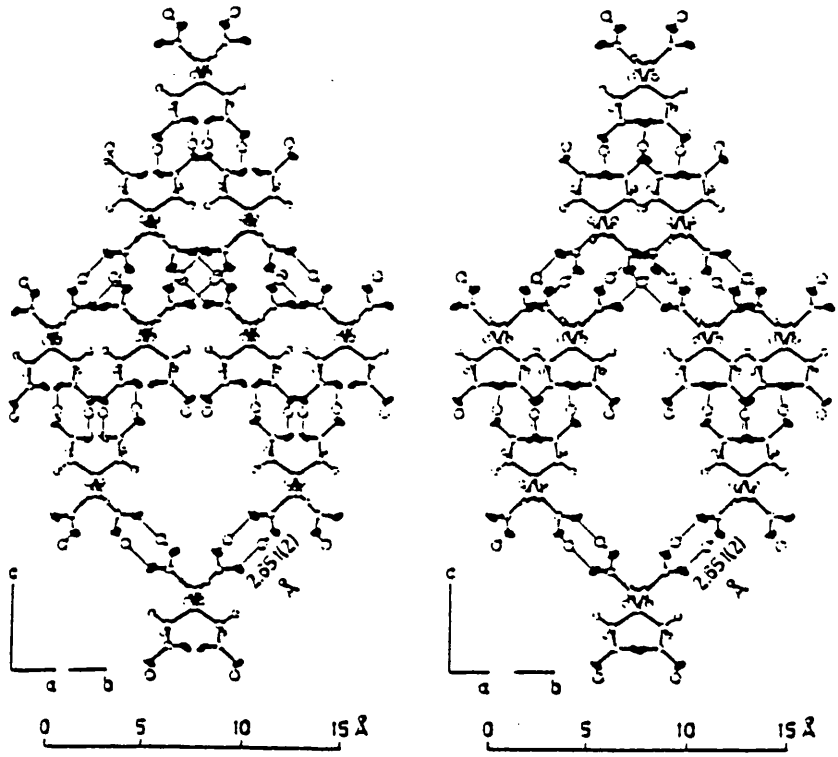


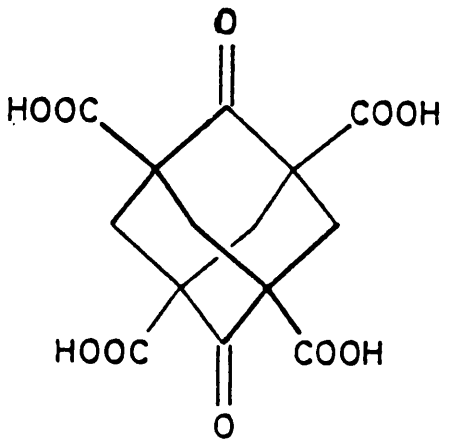
Fig. 3.9. Stereoview (perpendicular to *c* axis) of a hydrogen-bonded superadamantane unit of a diamondoid network of (79). Note the tetragonal elongation along *c* and the large central cavity, which is filled in the crystal by two equivalent, interpenetrating diamondoid networks.

Although the mode of the interpenetration is different, both of the aforementioned tetracarboxylic acids crystallise in the same space group $I4_1/a$.

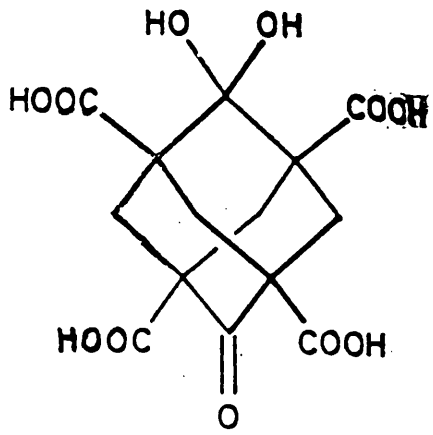
Ermer proposed that either of the two compounds should have guest inclusion potential if the degree of interpenetration could be lowered. The strategy involved accomplishing this by modifying the structure of either (78) or (79). For further investigation Ermer chose to modify (78) rather than (79), because of the latters unfavourable conformational flexibility.

A small modulation of the adamantane core was then effected to see if his

reasoning was correct. Ermer duly synthesised 2,6-dioxoadamantane-1,3,5,7-tetracarboxylic acid (80).[136] No inclusion ability was shown by (80), however



(80)



(81)

the hydrate (81) did include acetic acid in a host-guest ratio of 1:1.[136] A novel type of inclusion compound was formed, consisting of three interpenetrating super-diamond networks, which accommodated acetic acid guest molecules in triple-helical channels (Fig. 3.10).[136]

The guest acid molecules exist in the dimeric form within the channels.

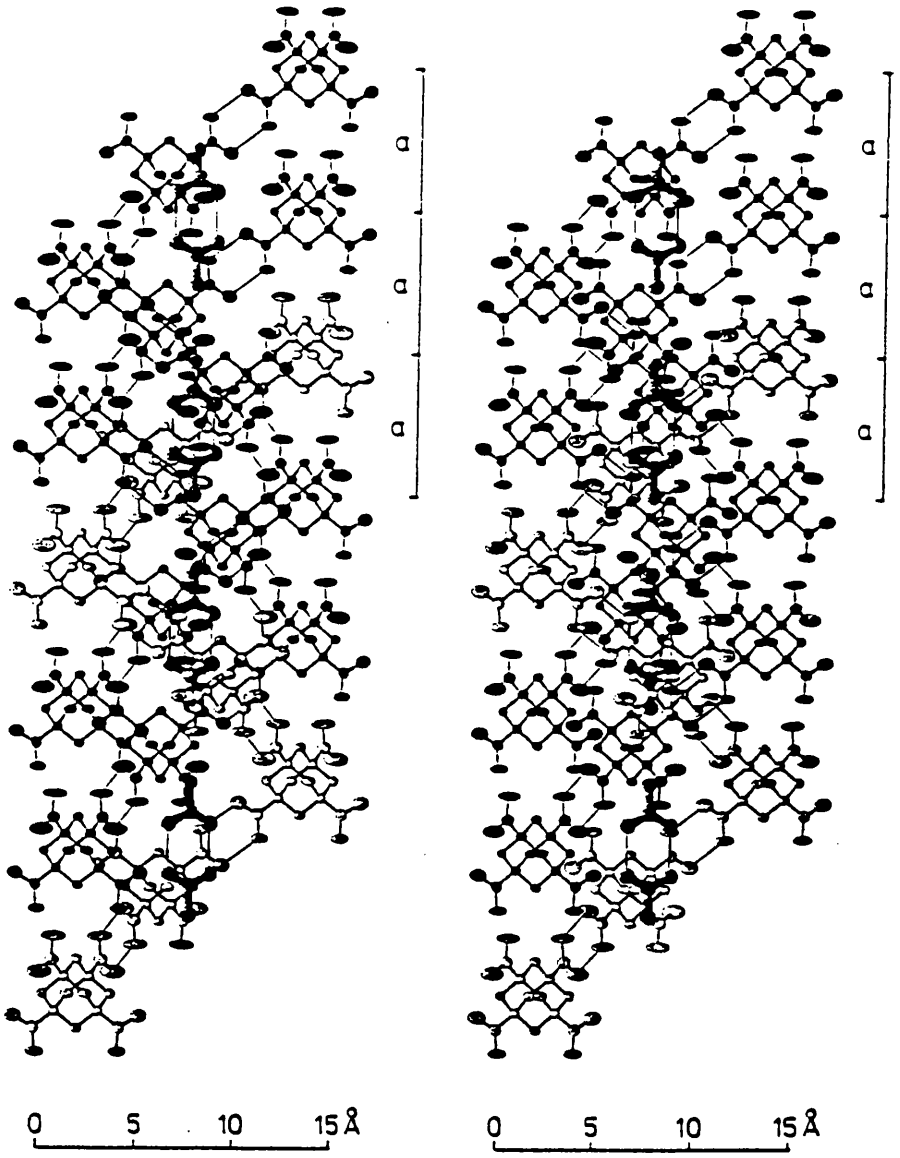
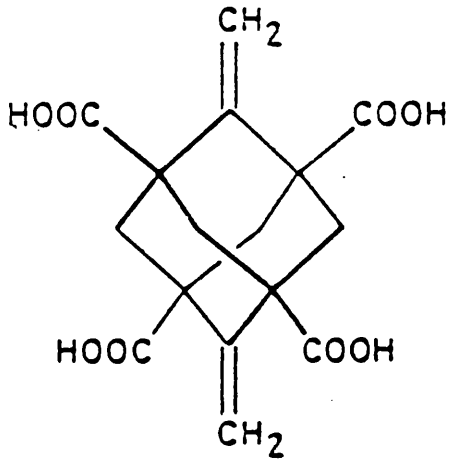


Fig. 3.10. Three-fold helical architecture of the channels in the 1:1 adduct of acetic acid and (81).

Accordingly,the complex is at the same time a genuine inclusion compound and a self-inclusion compound. Obviously, molecule (81) is not a versatile host as it includes only the above guest; however, it did confirm Ermer's postulate.

Encouraged by this result Ermer sought to further modify the structure of (80) and form an even more voluminous double-diamond-like architecture. He conjectured that by changing from dioxo to the larger dimethylidene functionality, to give 2,6-dimethylideneadamantane-1,3,5,7-tetracarboxylic acid(82)[137], one should observe a novel double diamondoid architecture.



(82)

The expected propensity of (82) to include molecular guests was quickly confirmed by the isolation of the monohydrate complex (82).H_2O [137] from the reaction medium. Of all the adducts formed by (82), the H_2O adduct possessed the most complex structure. The monohydrate, (82).H_2O, crystallised in the centrosymmetric space group $P\bar{1}$, with 4 molecules of (82) and four water molecules in the unit cell; the crystal structure being completely ordered.[137] The low symmetry of the adduct indicated that the pattern of hydrogen bonding would be rather complex. Instead of pairwise hydrogen bonds, the four COOH groups of every tetra-acid molecule are connected to the COOH groups of four

different tetra-acids in a severely distorted tetrahedral fashion, by means of single hydrogen bonds (Fig. 3.11).

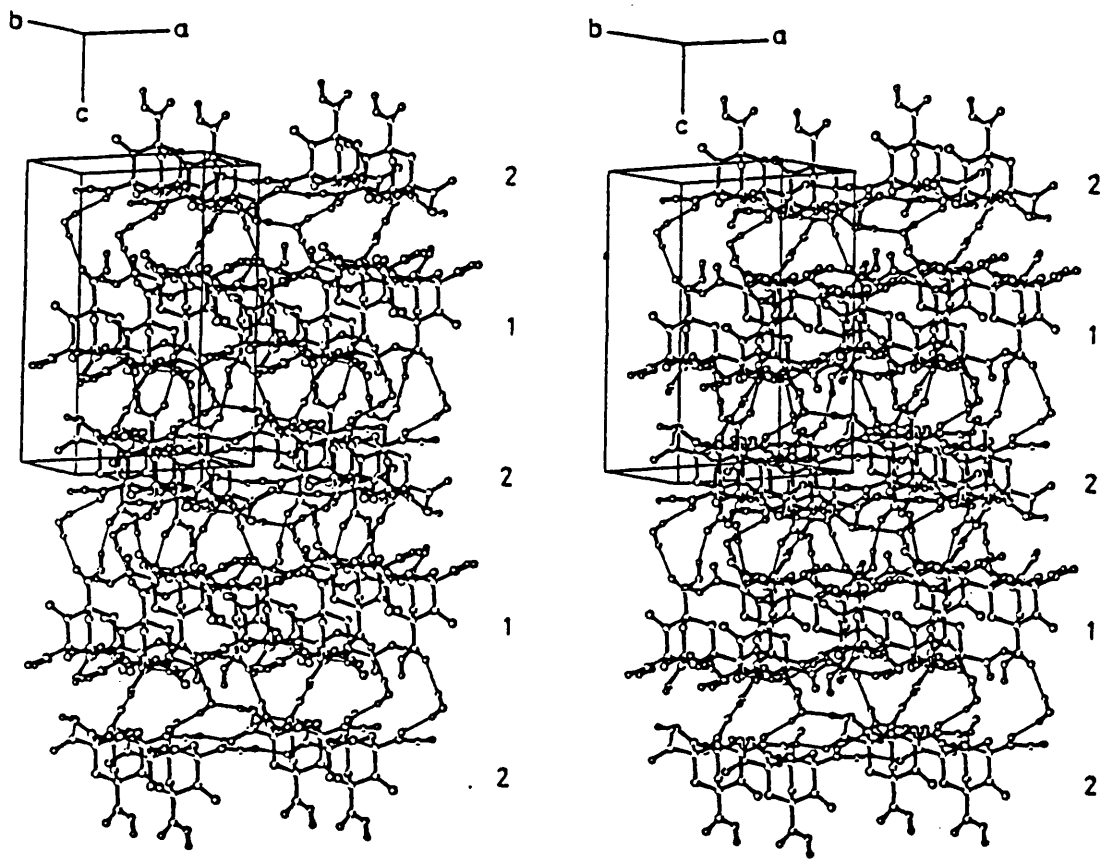


Fig. 3.11. Crystal-packing stereodiagram of (82).H_2O. The contents of 8 unit cells are shown, and the two types of symmetry-independent tetra-acid and H_2O molecules building up the two likewise different kinds of double layers parallel to the *a,b* plane are differentiated by the labels 1 and 2, respectively, in the right column.

Ermer proposed two interpretations of such a complex hydrogen bonded architecture:- Either (a) the three dimensional network of hydrogen-bonded tetra-acid and water molecules of (82).H_2O may be characterised in terms of a distorted double-diamond super-zincblende architecture (Fig. 3.12).

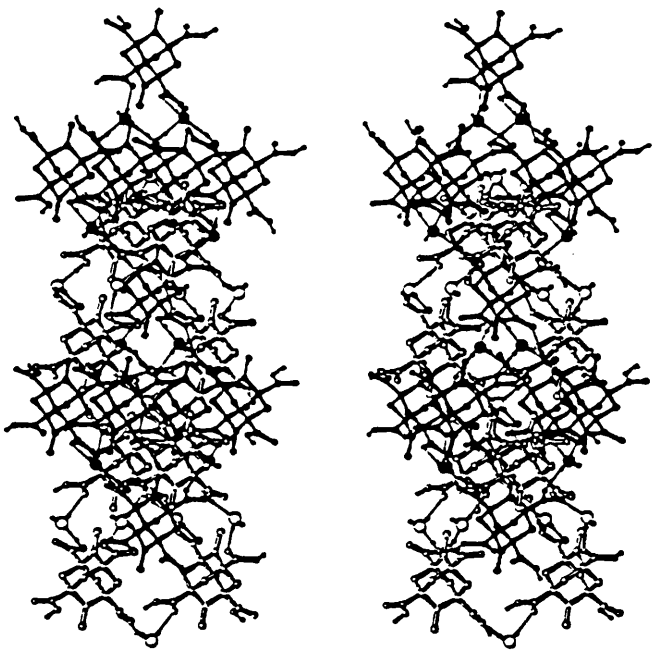


Fig. 3.12. Double super-zincblende description of the H-bonded crystal structure of (82).H_2O. Ball-and-stick representation. All H-bonds drawn (thin lines), water O-atoms enlarged for better recognition.

or (b) the hydrogen-bonded tetra-acid molecules may be grouped into two, four-connected two-dimensional networks interpenetrating each other and leaving open cavities which accommodate water molecules (Fig. 3.13).

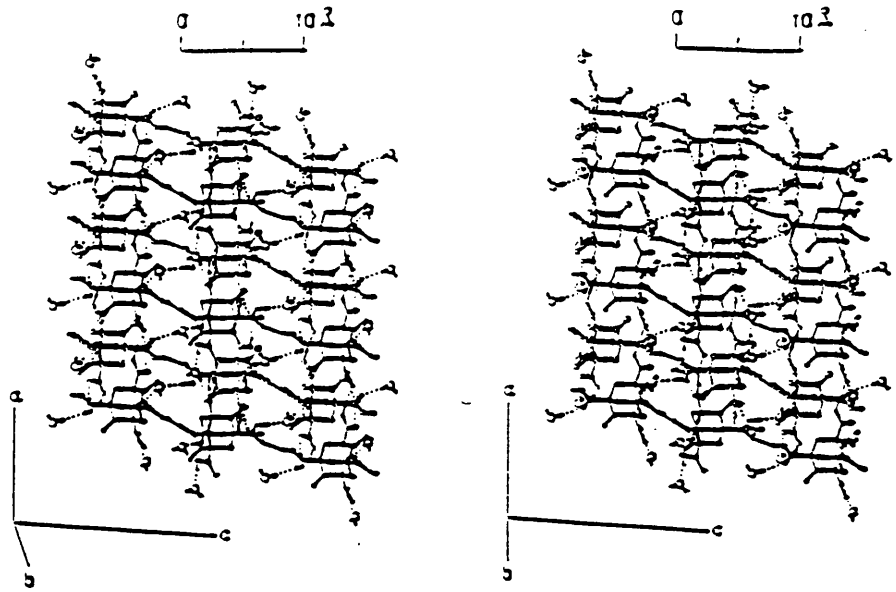


Fig. 3.13. Double interpenetrating layer description of the H-bonded structure of (82).H_2O

Fortunately such a structural dichotomy was not retained when Ermer sought to expand the guests included by (82).

Crystallisation of the (82).H_2O adduct from acetone in the presence of P_2O_5 to remove the water gave a surprising result. The new adduct did not have acetone as guest, but a mixture of 4-methylpent-3-en-2-one (MP), 2,6-dimethylhepta-2,5-dien-4-one (DMH) and mesitylene (M), in a host-guest ratio of 1:(0.6:0.1:1.1).[137] The guest molecules are volatile condensation products of acetone.

The new inclusion compound crystallised in the tetragonal space group $P4_2/nnm$. Accordingly, the tetra acid molecules have rather high symmetry, $\underline{D}_{2d}$

The guest molecules present in the new clathrate are disordered, however the host architecture was well refined.[137] The host molecules join to form two symmetrically interpenetrating super-diamondoid networks, linked via pairwise hydrogen bonds between the carboxyl groups. The diamond-like networks are somewhat compressed tetragonally; both interpenetrating networks are translationally equivalent and can be merged into one another by elementary translations. A stereo representation of the double diamond host architecture is shown in Fig. 3.14.

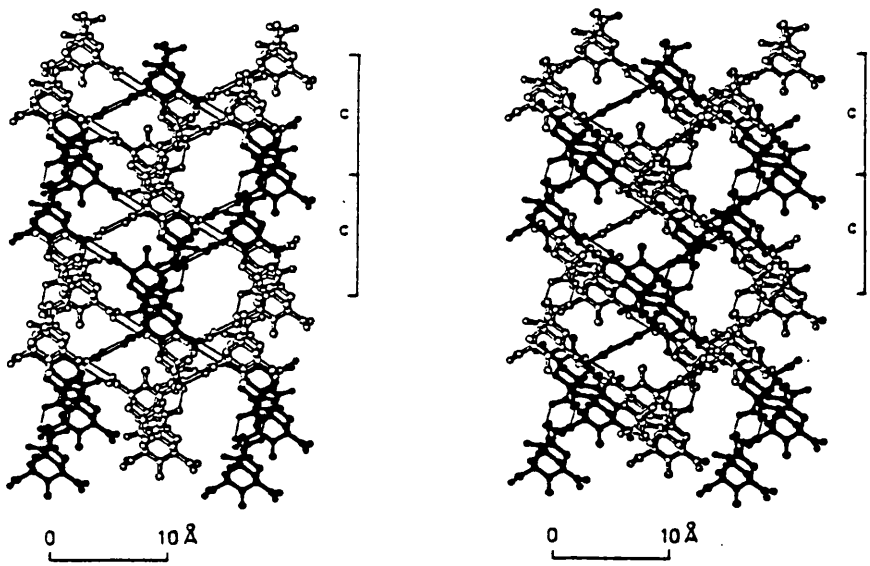


Fig. 3.14. Double-diamond-like host architecture of (82)-(MP-DMH-M). Ball-and-stick representation of the two interpenetrating super-diamond networks (*c*-axis approximately vertical, hydrogen atoms omitted). A hydrogen bonded super-adamantane unit and some additional elements of each network are shown. Note that the C=C bonds joining the exo-methylidene groups and the adamantane cores are directed along the tetragonal *c* axis.

It may be noted that both diamond-like host networks have no close van der Waals contacts (Fig. 3.15) and are evidently almost totally embedded in the disordered guest molecules, functioning much like a glassy matrix.

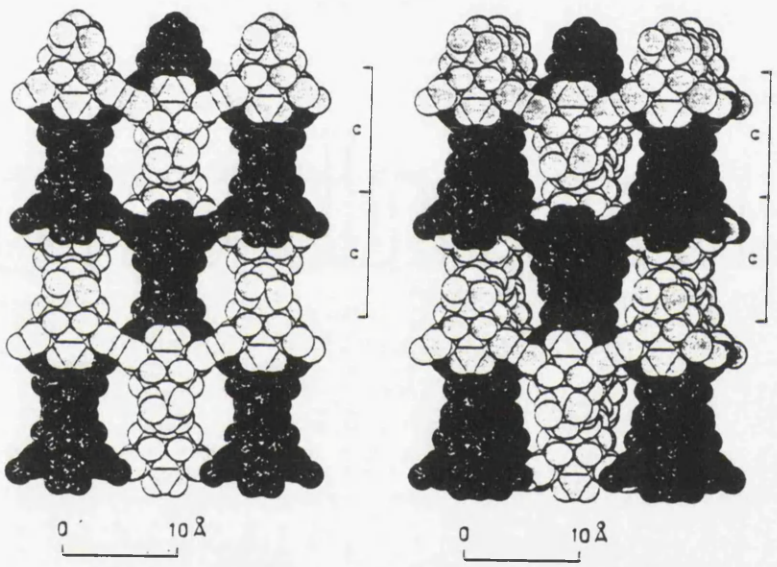


Fig. 3.15. Space-filling stereoview along bisector between *a* and *b* axes for left member of pair *c* axis vertical. The cavities are occupied by the guest species MP, DMH and M which are disordered and could not be seen in the electron-density maps. Note that the two interpenetrating super-diamond networks have no van der Waals contacts.

This is in contrast to the inclusion compound (81).AcOH which is

characterised by triply helical host channels accommodating chains of acetic acid guest molecules.[136]

The third inclusion compound of (82) involved mesitylene only as the guest; formed by crystallising (82).H_2O solely from mesitylene. The complex (82).M_2[137], like (82):(MP:DMH:M) crystallises tetragonally in the $I4_1/acd$ space group. As $I4_1/acd$ is a sub-group of $P4_2/nnm$, the symmetry of the host lattice in (82)(MP:DMH:M) is higher than in (82).M_2

Once again the tetra-acid molecules of the present complex build up two equivalent symmetrically interpenetrating super-diamond networks via pairwise hydrogen bonds between the COOH groups. On this occasion the diamondoid lattices are not translationally equivalent, being related by 4_1 screw axes or by $\underline{C}_2$ axes directed along *a* or *b* (Fig. 3.16).[137]

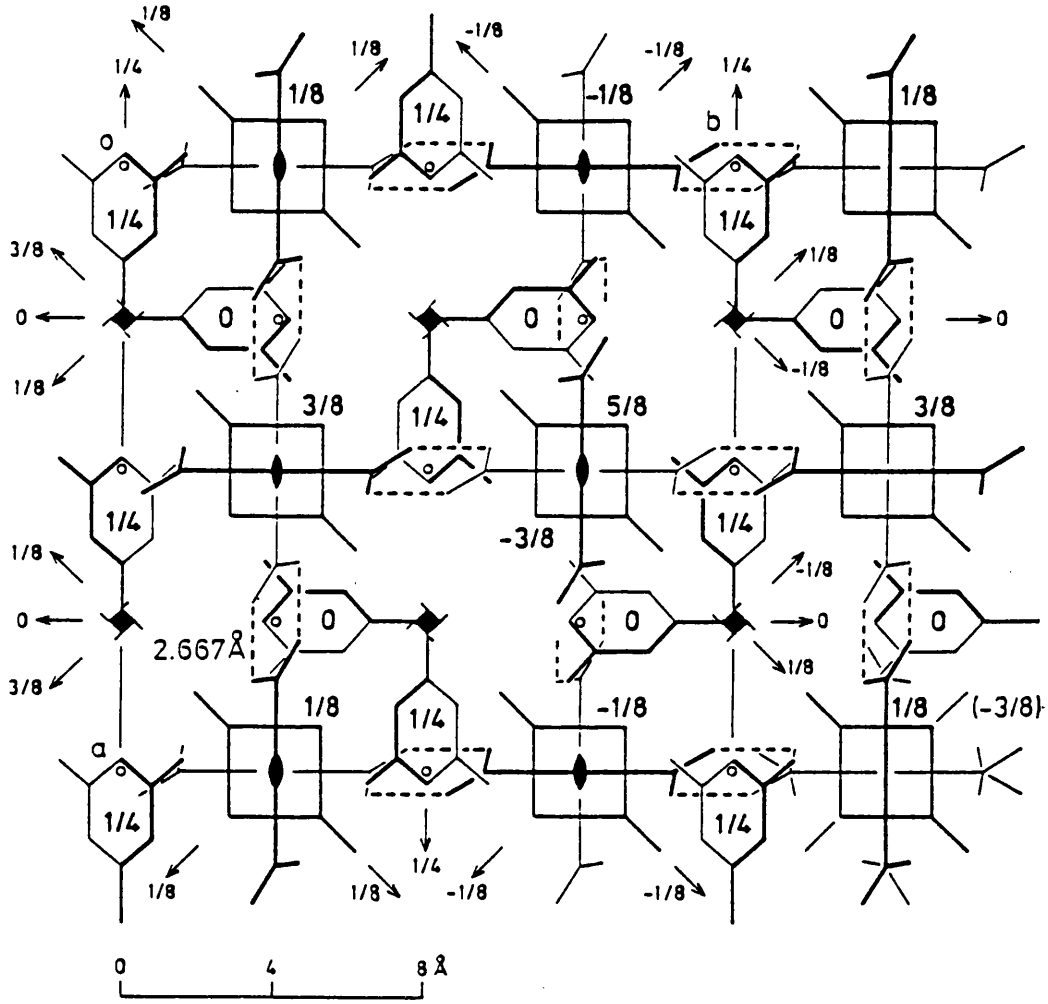


Fig. 3.16. Illustration of space-group symmetry ($I4_1/acd$) diagram of (82).M_2 projected along tetragonal c axis. Note that in (82).M_2 the exocyclic C-C bonds are perpendicular to the c axis. An additional tetra-acid molecule is drawn in light lines (lower-right corner) in order to point out the new translational equivalence and the orthogonality of the C=C bonds of the two networks. Note also that the chains of guest molecules running along the a and b axes, respectively are antiparallel.

With regard to the guest molecules, their deposition may be characterised in two ways : (a) the mesitylene molecules may be grouped into helices of alternating chirality winding about the 4_1 screw axes. There are four mesitylene molecules per turn, and the rise of the helix per turn is equal to the cell edge *c*, and thus equal to the distance between two opposite centres of a super-adamantane unit of the host (Fig. 3.16); (b) the mesitylene molecules may, alternatively, be grouped onto orthogonal chains running along the $\underline{C}_2$ axes (parallel to the cell edges *a* and *b*) on which the guest species are located (Fig. 3.17 a,b).

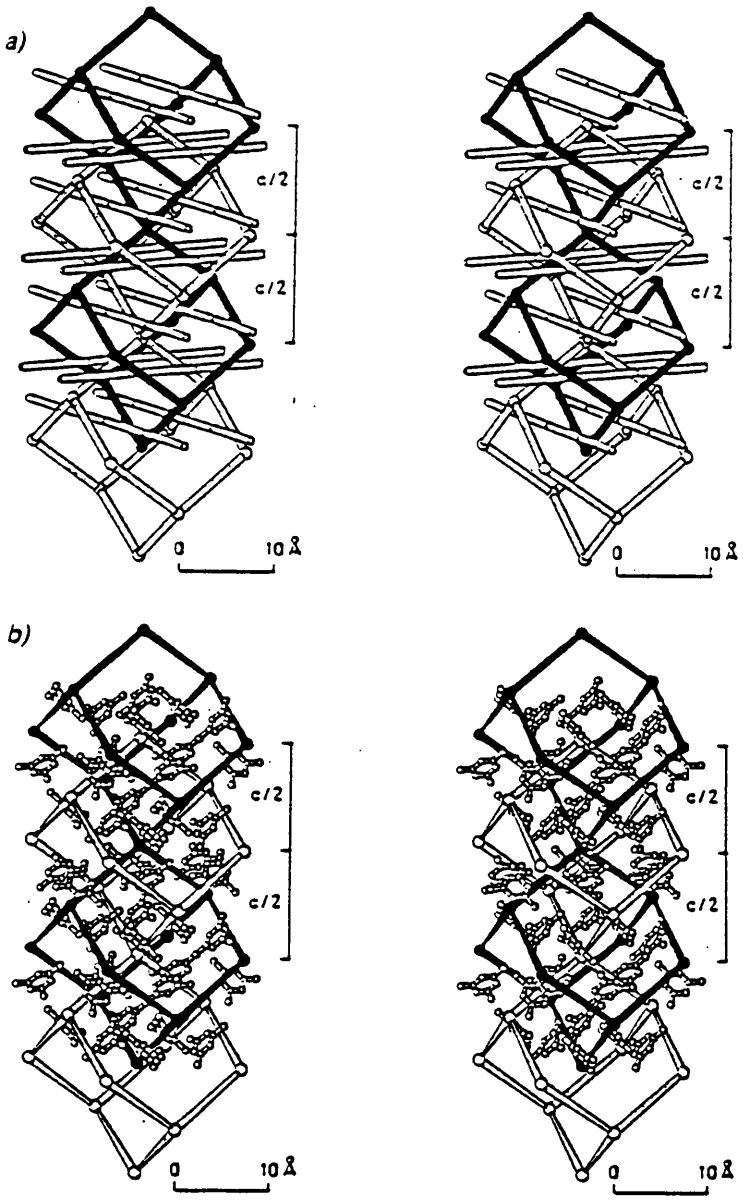


Fig. 3.17. Host-guest architecture of (82).M_2 (a) Diagrammatic stereoview of the double-diamond-like host structure. The system of interpenetrating, mutually orthogonal twofold axes is shown (white rods) on which the guest molecules reside. (b) Same view as (Fig. 3.17a) with the interpenetrating two-fold axes replaced by the actual mesitylene guest molecules.

It may also be seen from Fig. 3.18, showing the complete host-guest architecture, that the mesitylene guests fit singly between the two super-diamond networks of the tetra-acid host. The individual mesitylene chains are obviously polar, but the polarity of neighbouring parallel chains is opposite as required by the centrosymmetric space group.

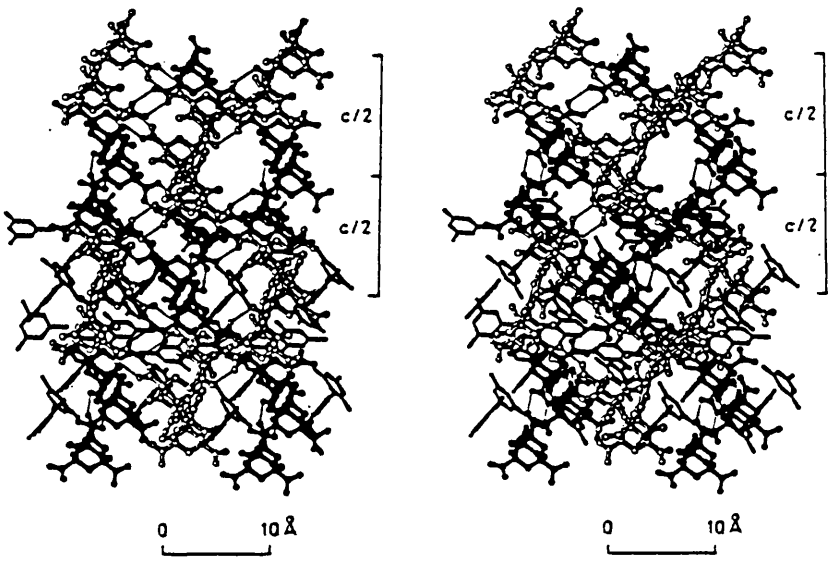


Fig. 3.18. Ball-and-stick stereorepresentation of complete host-guest architecture. In the upper part of the drawing, the mesitylene guest molecules are removed in order to visualise the host cavities.

As a whole, the host-guest complex (82).M_2 displays a rather intricate pattern of multiple interpenetration consisting of the two interlaced super-diamond host networks, which are themselves interpenetrated by two sets of non-intersecting mesitylene chains crossing each other at right angles. Again, the two host networks of (82).M_2 have no van der Waals contacts and are totally "solvated" by aromatic guest molecules sandwiched in between. However, contrary to the previous adduct, the intercalating three-dimensional array of guest molecules is ordered in the crystals of (82).M_2

The above adduct compares favourably with one already mentioned, namely the Bishop's dimethylhomoadamantane diol (53) benzene adduct.[121] This adduct crystallises in the same space group $I4_1/acd$ as (82).M_2. The intramolecular tetrahedral linkages are made up of O(H)-OH bonded macrocyclic diol tetramers of S_4 symmetry bridged by pairwise hydrogen bonds (across C_2 sites) to form two symmetrically interpenetrating super-diamond networks (Fig. 3.19) much as in (82) M_2.

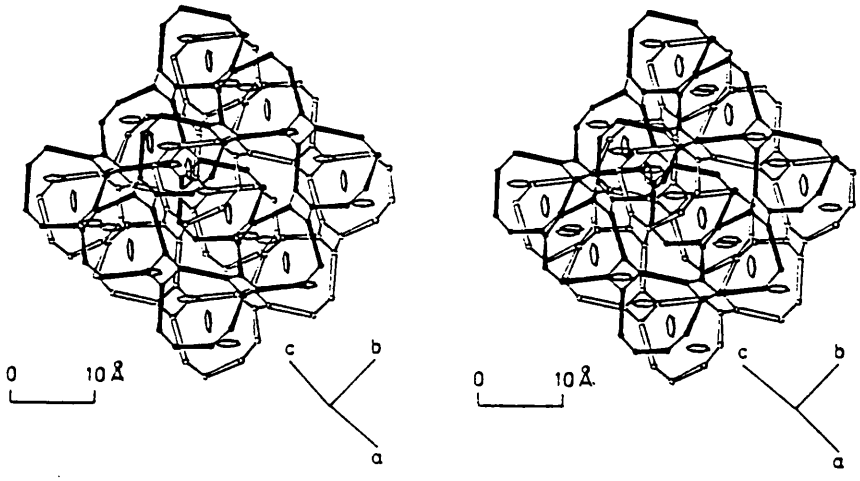


Fig. 3.19. Stereoview of the crystal structures of (53)benzene with space group $I4_1/acd$. The double-diamond structure of an inclusion compound of a dimethylhomoadamantanediol with benzene guest molecules. Two symmetrically interpenetrating super-adamantane units (black and white, respectively) are shown diagrammatically as well as 9 chains of benzene guest molecules; the latter are partially disordered in the actual structure. The diol host molecules are represented by their O-atoms only, joined by thick rods, which stand for the hydrocarbon core. Thin lines connecting the O-atoms symbolize O(H)O-H bonds, The tetrahedral building blocks of the super-diamond networks consist of H-bonded cyclic diol tetramers; these tetramers are interlinked by pairwise additional H-bonds in tetrahedral fashion. The crystal axes shown indicate directions only.

By crystallising (82).H_2O from a 1:1 mixture of (MP) and (M) Ermer obtained the new adduct (82).(MP.M) in the ratio 1:(0.4:1.6). This fourth inclusion compound of (82) is structurally very similar to (82).M_2 crystallising in the same space group $I4_1/acd$ and therefore was of limited interest.

Having established the existence of host molecules with a double-diamondoid architecture, Ermer wanted to take this one step further and form a single-diamondoid lattice. His strategy involved the use of host-guest interactions rather than host structural modification, to produce this novel architecture. Precedent for this lay in his work with hydroquinone and C_{60}[12] where he used the voluminous C_{60} guest to disrupt the doubly interlocking lattice of hydroquinone (see Chapter 1). In this case he selected *tert*-butylbenzene (TBB) as guest. Unfortunately the actual crystal structure analysis of (82).TBB revealed that the guest still existed within a less hollow double-diamond-like host architecture[137]; the adduct crystallising in the $F2/d$ space group with a host-guest ratio of approximately 1:1.7. In the (82).TBB complex the steric bulk, which is increased by the *t*-butyl group, causes an asymmetric interpenetration of the host (Fig. 3.20a). In this way, the previously even (symmetric) distribution of hollow host spaces between the two diamond lattices is broken, such that one half of the cavities grow at the expense of the other half. In fact, one half of the cavities vanishes altogether, that is, the two super diamond networks attain van der Waals contact (Fig. 3.20b).

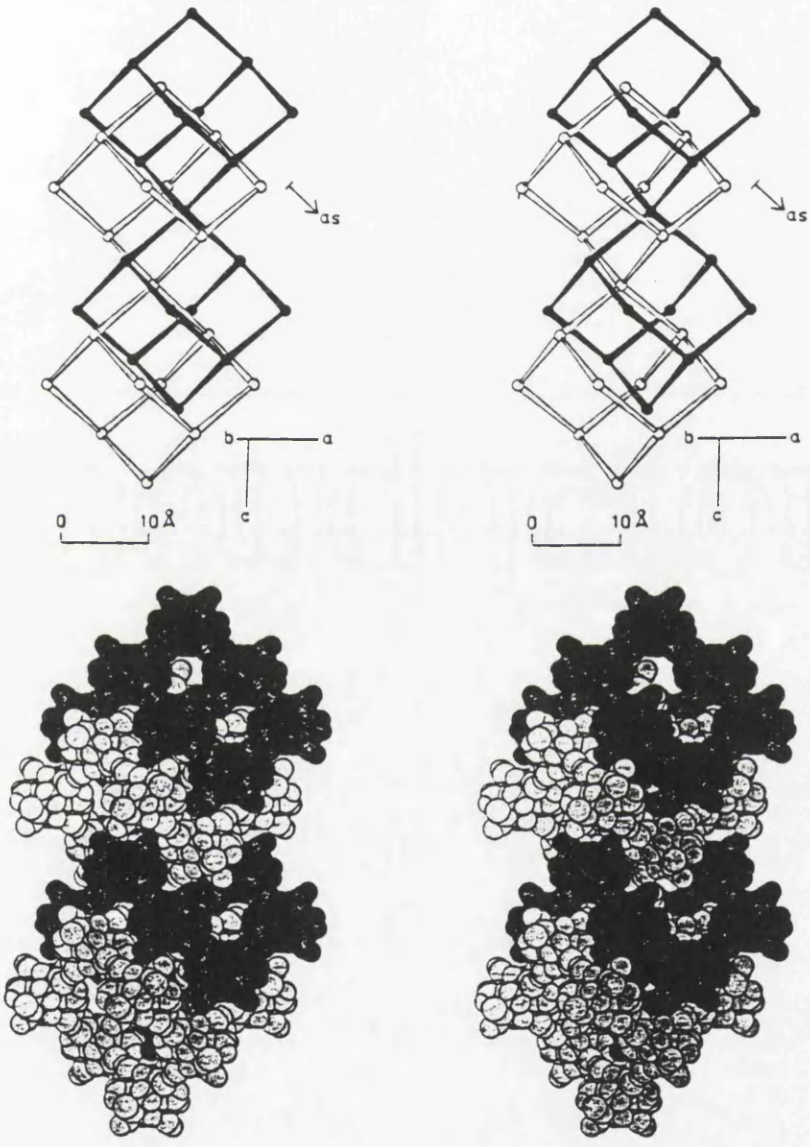


Fig. 3.20a. View approx. along *b* axis showing the asymmetry shift vector (*as*) to run essentially parallel to the *a*,*c* bisector.

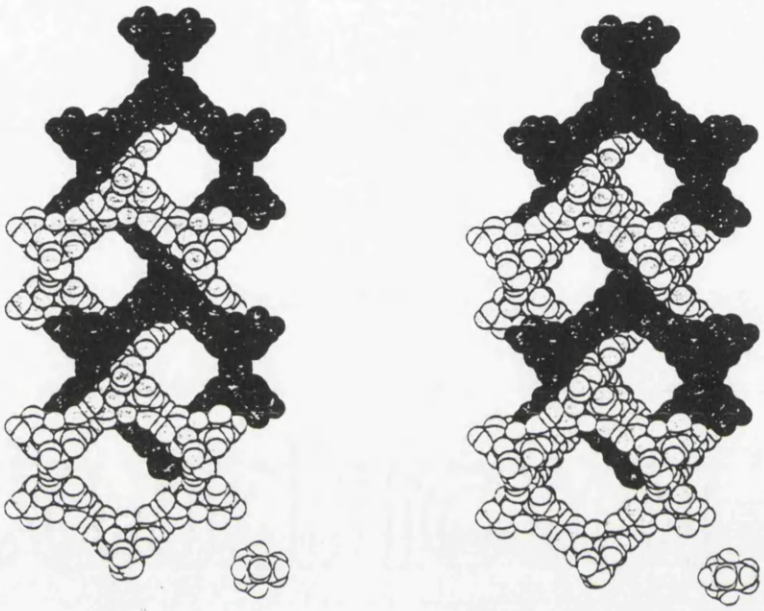


Fig. 3.20b. View perpendicular to *as* vector and *b* axis. Visualisation of the widened host channels as a consequence of the asymmetry shift.

The asymmetry shift of the two diamond-like lattices in (82).TBB is therefore maximal, and follows an all or nothing principle; the interstices are either large enough to house molecular guests or they vanish completely. In addition, the cell dimensions of the (82).TBB complex indicated that the asymmetry of interpenetration enforced by TBB guest molecules does not lead to any pronounced distortion of the two individual super-diamond host lattices. Close inspection of the above space filling view (Fig. 3.20b) reveals that the wide

host channels in (82).TBB involve bottle-necks of some size, which are represented by the bulky adamantane cores of the molecules of (82).

In summary, Ermer like MacNicol, has shown an effective understanding of crystal packing. This understanding led him to design a molecule possessing a novel diamondoid architecture. By a series of systematic structural modifications he then realised a new series of diamondoid host molecules. In addition, his elegant X-ray work revealed in detail this novel host architecture and how it was changed by structural modification of the host. Also, Ermer demonstrated the use of more subtle host-guest interactions to modify the host architecture. Although not an extensive series when compared to the hexa-hosts, the diamondoid hosts represent a form of crystal engineering which had not been previously witnessed within clathrate chemistry. This is borne out by Ermer's ability to alter, almost at will, the interpenetration of the lattices : culminating in the formation of new inclusion compounds. Therefore, Ermer, along with MacNicol, can justifiably represent the unique group of chemists involved in clathrate design by analogy.

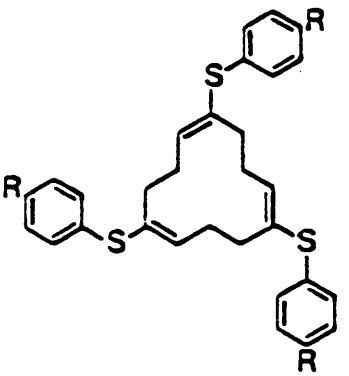
CHAPTER 4

CONCEPT 3 : DESIGN OF HOSTS USING MOLECULAR SYMMETRY.

4.1 Cyclododecatriene-based hosts

Trigonal molecular symmetry is a prominent feature in a number of classical host molecules e.g. TOT and PHTP. In the multimolecular inclusion compounds formed by these hosts the surrounding lattice is normally consolidated by van der Waals forces alone, and not by hydrogen bonding.

With this in mind MacNicol proposed the third concept. This detailed the use of trigonal symmetry as a key element in the synthesis of new host molecules. His second strategy, therefore involved preparing molecules with 3-fold molecular symmetry. To establish a new clathrate series of cyclododecatriene-based host molecules, (83) and (84) were duly prepared.[138]

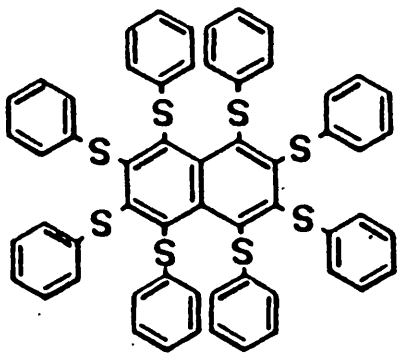


(83) R = H
(84) R = Me

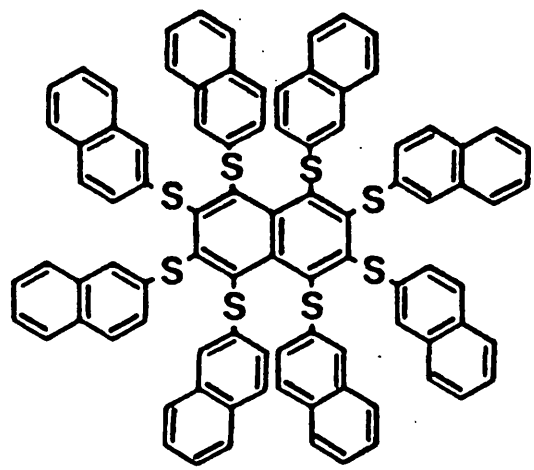
Both hosts were found to form adducts with numerous guest molecules, normally included in the host-guest stoichiometric ratio of 2:1.[138] No X-ray study of any adduct has yet been reported, however. Of particular interest is the ability of (84) to form stable inclusion compounds with such volatile species as *t*-butylacetylene and 2,2- and 2,3-dimethylbutane.

4.2 Octa-hosts (spider-hosts)

Admittedly, the above represents a rather limited exploration of the use of trigonal symmetry within host design. MacNicol, though, devised a more fruitful approach which involved examining the use of two-fold molecular symmetry within host design.[111] His strategy exploited the 2-fold symmetry of octasubstituted naphthalenes and involved reaction of octafluoronaphthalene with the appropriate arene thiolate nucleophiles, generating, for example, host molecules such as (85) and (86).[139]



(85)



(86)

Significantly, both (85) and (86) form crystalline inclusion compounds on recrystallisation from 1,4-dioxane, thus establishing (85) and (86) as members of a new class of eight-legged, or "spider" hosts. Interestingly, two forms of (85) were obtained, a yellow form (from DMF at room temp) and a red form (from anisole at 50°C). The origin of the different colour was established by X-ray analysis of both forms (Fig. 4.1).

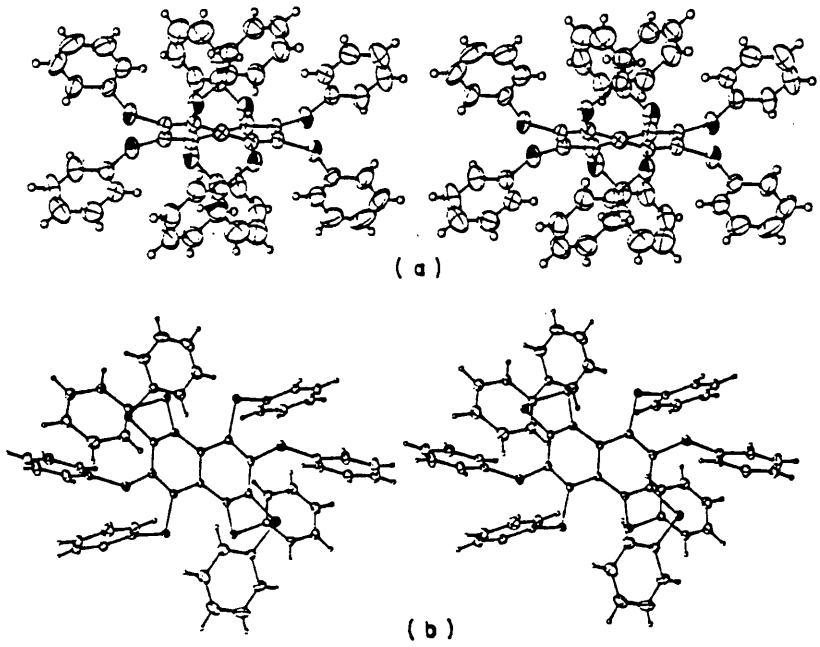


Fig. 4.1. Stereoviews showing the molecular structure of octakis(phenylthio)-naphthalene (85) in (a) the yellow unsolvated crystal; and (b) the red unsolvated crystal.

The yellow form is monoclinic space group $I2/c$ and contains a very pronounced twist around the bond at ring fusion, whereas the red form, triclinic space group $P\bar{1}$, has the central region not far from planar. Fascinatingly, the

transformation between the two forms can be accomplished when one presses crystals of the yellow form on a glass slide, producing red crystals at the point of application of pressure. However, it should be pointed out that the red form produced by pressure is not necessarily the same red form as that produced by crystallisation from anisole at 50°C. In line with the strategy used to expand the hexa-host series, MacNicol and co-workers have also developed an interesting oxygen-based series of spider-hosts.[140]

In the light of the above work by MacNicol, molecular symmetry is now regarded as an integral feature of any design strategy. The influence of symmetry was particularly relevant in all the clathrates covered in this discussion, whether of scissor-type host, hexa-host or other examples.

Hopefully this review has presented all the key features of design in a simplified fashion allowing the reader to foresee, perhaps, new inclusion possibilities in a complex, but interesting, field of organic chemistry.

CHAPTER 5.

PROPERTIES AND APPLICATIONS OF MULTIMOLECULAR INCLUSION COMPOUNDS.

The design and subsequent structure elucidation of a new inclusion series is a challenge and an education to any person working within the inclusion field. Unfortunately industry would only deem such academic endeavours as worthwhile if the compounds possess certain properties or applications. However identification of such properties has not appeared to be a priority among researchers in general, although some, particularly Toda, are now stressing the importance of applications.

Recognition of these applications began with classical hosts followed eventually by newly designed clathrates. The purpose of this chapter is to illustrate these properties and applications.

5.1 Inclusion polymerisation.

Interest in inclusion polymerisation began to develop in the late fifties, as an alternative method to Ziegler-Natta coordination polymerisation to obtain highly stereoregular polymers. The addition polymerisation was carried out within channel-type inclusion compounds, producing linear macromolecules with complete elimination of by-products. The reaction generally proceeds via a chain mechanism whereby a small number of initiation reactions, commonly caused by radiation, give rise to a large number of reactions between guest molecules (propagation reaction). The ratio between polymer yield and initiation

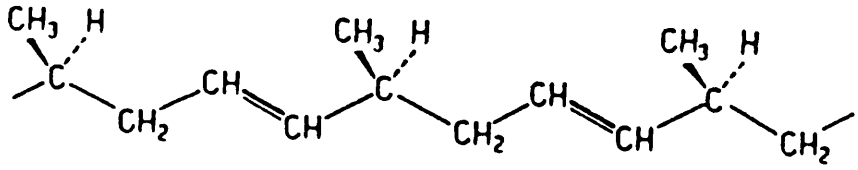
reaction may thus reach very high values. The macromolecular nature of the product facilitates separation between host and guest by selective dissolution or by sublimation.

In 1956 Clasen[141] reported the first example of inclusion polymerisation with 2,3-dimethylbutadiene included in thiourea. No initiating agent was used and the polymerisation took months to go to completion. Brown and White then continued the work using urea and thiourea with up to thirty monomers as guest molecules.[142,143] In this case the polymerisation process was initiated by high energy radiation (such as ß, γ or X-ray) giving polymers with considerable chemical and steric regularity.

Subsequently, more hosts were found to exhibit this property, specifically the *trans-anti-trans-anti-trans* stereoisomer of perhydrotriphenylene (PHTP) (see Chapter 1).

Members of the Natta group, in 1963, were able to demonstrate that PHTP formed flexible channels, allowing accommodation of both linear and bulky monomers, unlike urea or thiourea which form channels which are rigid and less accommodating. As well as including a wider range of guests, PHTP had the additional property of rapid complex formation; urea and thiourea both take days or weeks to form adducts whereas PHTP requires only a few minutes.[144-146] A further example of PHTP's versatility was illustrated by the first synthesis of a

highly isotactic polymer, 1,4-*trans*-isotactic polymer (87), by polymerising 1,3-*trans*-pentadiene.



(87)

As PHTP belongs to the point group $\underline{D}_3$ the molecule (87) is chiral. The inclusion adducts of a single enantiomer of PHTP have a crystal lattice which is chiral, with space group $P6_3$. As a consequence, PHTP was considered for asymmetric polymerisation. The first example recorded, involved polymerisation of 1,3-*trans*-pentadiene in optically active PHTP, yielding an isotactic polymer endowed with weak optical activity, from which optically active substituted succinic acid was obtained by oxidative cleavage (see Scheme 1).

Scheme 1.

(*R*)(−)PHTP + 1,3-*trans*-pentadiene →

$$-CH_2-CH=CH-CH(CH_3)-CH_2-CH=CH-CH(CH_3)-CH_2-CH=CH-CH(CH_3)-$$

(*S*) (+) polypentadiene $|\alpha|_D = +2.7$

→ $HOOC-CH(CH_3)-CH_2-COOH$

(*S*) (−) methylsuccinic acid $|\alpha|_D = -1.2$

Though it can hardly be considered to be a method suitable for large scale preparation of polymers, inclusion polymerisation has been quite thoroughly studied during the past quarter of a century because of the particular structural properties of the polymers obtained, and as a versatile example of a solid state reaction.

5.2 Chromatographic separation.

From the vast range of purely organic multimolecular inclusion compounds available, only thiourea and urea have lent themselves to chromatographic separations.

The separation process involves using the selective inclusion behaviour of both urea and thiourea. As mentioned earlier, urea forms stable inclusion compounds preferentially with straight chain hydrocarbons, whereas thiourea forms stable inclusion compounds only with branched substances. Utilising these properties under liquid chromatographic conditions one is able to separate branched molecules from linear molecules.

An example is the use of a urea adduct in the separation of branched and linear fatty acids.[147] In this case the branched molecules were eluted first as the linear fatty acids tend to form transient inclusion compounds with the urea adduct.

Thiourea, on the other hand, allows elution of linear compounds before branched. The adduct was particularly useful as a stationary phase for the separation of a mixture of fluoroderivatives of pentene.[148] Both applications involve the use of adducts as the stationary phase, since the absence of guest molecules would lead to close packed structures for both urea and thiourea, rendering them inoperative with regard to their chromatographic applications.

5.3 Enantiomeric selectivity

The most extensively studied field as regards applications of clathrates appears to be that of enantiomeric selectivity. Classical hosts have proven useful, although they have been superseded by the newly designed coordinato-clathrates of Toda.

The ubiquitous urea, again proved of use in resolution of guest molecules. Schlenk, in fact, was the first to carry out optical resolution work using urea as the host molecule.[149] The asymmetry of the hexagonal lattice of urea made it an attractive candidate for resolving racemates. Schlenk's work proved that adducts of homologs have the same configuration and the same lattice structure. Correlations between homologous α-methyl-, α-chloro-, α-bromo-, α-amino-, and α-mercaptocarboxylic acids and between ß-methyl- and ß-chlorocarboxylic acids were shown. He found that in the series of L-ß-chlorocarboxylic acids, the optical resolution is (+) up to L-ß-chlorovaleric but (-) from L-ß-chlorocaproic acid onwards.[150]

The observed enantiomeric enrichment was rather poor for urea with typical values of 5-15% ee. These values could be improved upon by use of a chiral auxiliary such as an asymmetric surface or optically active co-solutes giving ee values of up to 96%.

A marked improvement on this enantioselective behaviour was found by

Gerdil who selected tri-*ortho*-thymotide (TOT) as his host. The TOT molecule can exist in two helical propeller-shaped conformers which at room temperature rapidly interconvert. In the absence of appropriate guest molecules, TOT crystallises in an achiral crystal lattice of the space group $Pna2_1$ which contains molecules of the P-(plus) and M-(minus) helical configuration. However, if TOT crystallises in the form of a clathrate spontaneous racemate resolution occurs. Hence the TOT single crystals consist of P or M host molecules respectively, which because of their chirality have enclosed one of the enantiomers preferentially. This peculiarity of the crystallisation behaviour allows the resolution of racemic guest molecules. Crystals containing TOT in the P or M configuration are then used separately as seed crystals to grow larger single crystals.

Gerdil, Arad Yellin and others subsequently attempted the resolution of a number of guests.[38,39,41,151,152] The ee's values reflected a marked improvement in resolution compared with the urea clathrates, with an optimum of 83% ee in the absence of a chiral auxiliary. All the data shown were obtained from racemic solutions of guest (see Table 10).

Table 10. Guest enantiomeric excess and host-guest correlation of configuration in (P)-(+)-TOT clathrates.

Guest	Guest e.e.(%)[a]	Guest configuration
Cage-type		
2-chlorobutane	32,45	(S)-(+)
2-bromobutane	34,35	(S)-(+)
2-iodobutane	<1	-
ethyl methyl sulfoxide	83	(S)-(+)
methyl methanesulfinate	14	(R)-(+)
2-butanol	<5	(S)-(+)[b]
2-aminobutane	<2	-
1,2-dibromopropane	<2	-
trans-2,3-dimethyloxirane	47	(SS)-(-)
trans-2,3-dimethylthirane	30	(SS)-(-)
trans-2,4-dimethyloxetane	38	-
trans-2,4-dimethylthietane	9	-
2,3,3-trimethyloxaziridine	7	-
propylene oxide	5	(R)-(+)
2-methyltetrahydrofuran	2	(S)-(+)
Channel-type		
2-chlorooctane	4	(S)-(+)
2-bromooctane	4	(S)-(+)
3-bromooctane	4	(S)-(+)
2-bromononane	5	(S)-(+)
2-bromododecane	5	(S)-(+)

[a] Single crystals grown from racemic solutions of guests.
[b] Grown from optically pure guest

From these results several factors which seemed to determine a higher enantiomeric selectivity, were identified specifically:-

(a) Cavity symmetry and guest symmetry:- *trans*-2,3-dimethyloxirane and *trans*-2,3-dimethylthirane have $\underline{C}_2$ molecular symmetry which is also the symmetry of the cavity when they are located in the crystal[153]; these guests were found to exhibit

high enantiomeric selectivity, suggesting that the coincidence of guest and cavity symmetry favours discrimination.

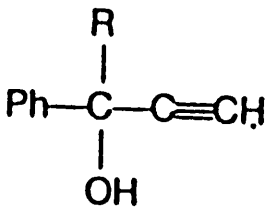
(b) The absolute configuration of the preferred guest enantiomer is such that homologous atoms or groups in related molecules occupy similar positions in space. This behaviour is very reminiscent of that for urea.

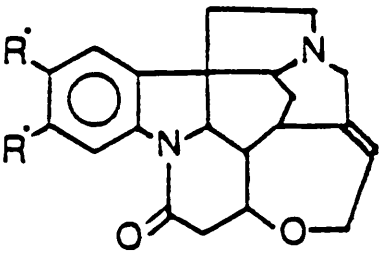
(c) The guest's size is an important factor; the smallest molecule studied and the largest, 2-methyltetrahydrofuran, exhibit the smallest discrimination.

The above conditions would allow one to select specific guests for optimal resolution in TOT. As yet, however, neither urea nor TOT have been able to resolve completely a racemic guest solution.

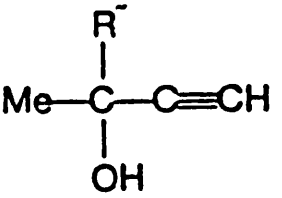
Toda then revolutionised enantioselective inclusion by employing optically active hosts which resolve by forming coordinato-clathrates with a favoured enantiomer from racemic guest. The only limitations are that the guest must have capacity for hydrogen bonding, and be able to form a stable adduct.

An example of resolution by such complexation involved the use of brucine (88) in the resolution of tertiary acetylenic alcohols. After two recrystallisations with brucine, 4,4-dimethyl-3-phenyl-1-pentyn-3-ol (89) was completely resolved into the (+) form with a yield of 78%.[154-156] In a similar vein, Toda resolved a complete series of closely related acetylenic alcohols (Table 11).[155,156] Consequently, by critically examining the experimental results, Toda was able to establish trends which lead to the isolation of optically pure guests in high yields.





(89) R = Bu^t (97) R = CH_2Cl (88) R = OMe
(90) R = Am^t (98) R = CF_3
(91) R = Bu^n (99) R = Me
(92) R = Pr^n (100) R = H
(93) R = Pr^i (101) R = *o*-Br—C_6H_4—
(94) R = Et (102) R = *o*-Cl—C_6H_4—
(95) R = CCl_3 (103) R = *o*-F—C_6H_4—
(96) R = $CHCl_2$ (104) R = *o*-Me—C_6H_4—



(105) R = Bu^t
(106) R = Et

Table 11. Yields and $[\alpha]_D$ values of (89)-(97) and (101)-(104) of 100% ee obtained by optical resolution utilizing complexation with (88).

(88)	Complexation time.	$[\alpha]_D$	Yield (%)
89	2	+0.9	47
90	1	+10.5	84
91	2	+12.4	77
92	2	+4.5	29
93	3	+1.1	19
94	2	+7.2	36
95	4	+13.8	33
96	2	-3.4	70
97	3	+11.1	39
101	3	-134	63
102	8	-135	10
103	3	-59.1	14
104	6	-53.7	21

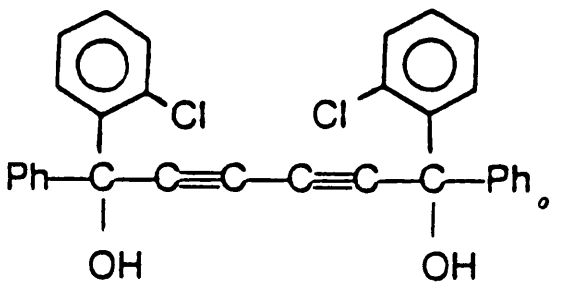
Even after several complexations compounds (98)-(100) were still poorly resolved, inferring that the R group should be larger than a methyl group for efficient resolution with brucine. Furthermore, since neither (105) nor (106) formed a complex with brucine, the presence of at least one aryl group[155] seemed to be essential for resolution. Significantly, a cyclohexyl-substituted *tertiary* acetylenic alcohol also did not form a complex with brucine, implying that the cyclic nature of the substituent is not important for the complexation. Toda suggested that the planarity of the aryl ring or an interaction with the π system could be two factors which facilitate complexation.[155]

His choice of guest is particularly useful, as optically active acetylenic alcohols are useful synthons for the preparation of various chiral compounds,

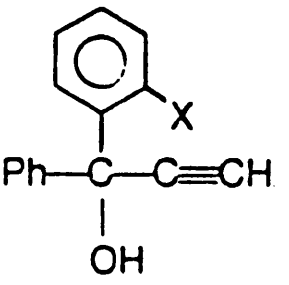
since they have two functional groups.

As well as naturally occurring hosts, Toda was able to employ his own discoveries with considerable success: he prepared the chiral host compound 1,6-bis(o-chlorophenyl)-1,6-diphenylhexa-2,4-diyn-1,6-diol (107), by oxidative coupling of optically active (108) which had been resolved by complexation with brucine (88).[157]

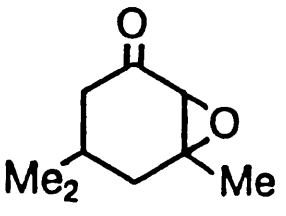
Using the enantiomer (-)(107) as the complexing host facile resolution of 2,3-epoxycyclohexanones, (109) and (110) was accomplished, giving (+)-(109) and (+)-(110) of 100% ee in 31 and 18 per cent yields, respectively.[158]



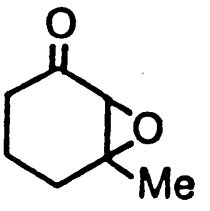
(107)



(108) X = Cl



(109)

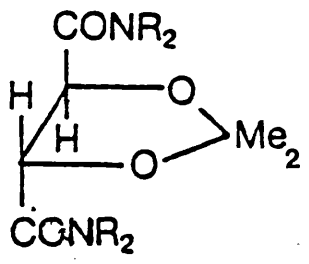


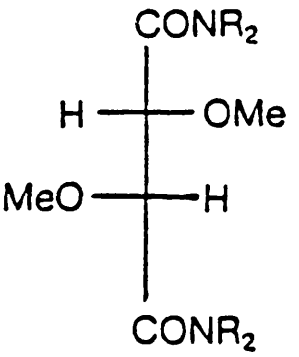
(110)

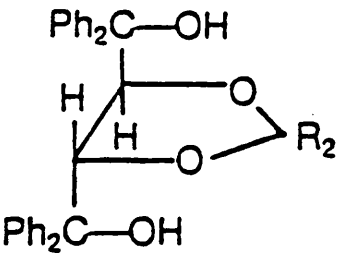
Key intermediates in prostaglandin synthesis were also resolved, for example, optically active 6-oxabicyclo[3.3.0]oct-2-en-7-one was obtained in good yields by using (107) as the resolving agent.[159]

In line with his coordinato-clathrate strategy, Toda suggested that suitable hosts containing amide functionality should also form coordinato-clathrates, owing to their ability to form host-guest hydrogen bonds. Application of this concept to enantioselective resolution involved the synthesis of chiral tartaric acid derivatives (111) and (19).[82] Toda used both in the resolution of the binaphthyl and biphenanthryl scissor hosts (Chapter 2)[82] which proved useful when ascertaining the host properties of the optically active hosts.

The idea for the design of such compounds came from an accidental discovery by Seebach, who synthesised the chiral tartaric acid derivative (112) called $\alpha,\alpha,\alpha,\alpha$-tetraaryl-1,3-dioxolane-4,5-dimethanol (TADDOL).[160-163] Quite by accident

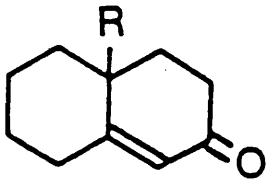




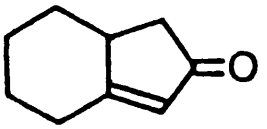


(19) R = Me (111) R = Me (112) R = Me

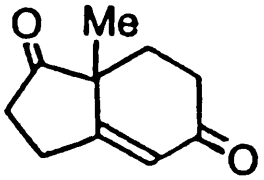
he discovered the inclusion ability of (112) by isolating the CCl_4 adduct.[162-164] Toda realised that such a chiral molecule should also be effective with regard to optical resolution by complexation. Indeed, optically active (112) was particularly efficient in the resolution of bicyclic enones. By complexation with (-)(112) optically pure (113), (114), (115), (116) and (117) were obtained in 62, 43, 80, 50 and 70% yields respectively.[165]



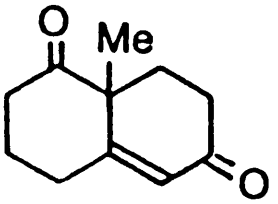
(114) R = Me
(113) R = Et



(115)



(116)

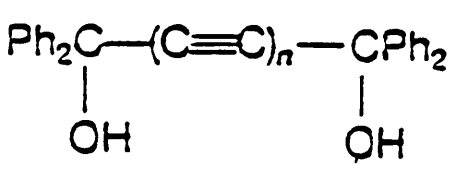


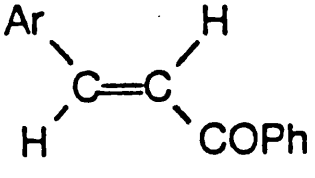
(117)

5.4 Photoreactions in inclusion chemistry.

Photoreactions usually produce many setbacks for the synthetic chemist. For example during the process of olefin polymerisation in solution a complex mixture of all the possible stereoisomeric photodimers is normally produced. To overcome these problems the reaction can be carried out in the solid state. Even in the pure crystal form, though, the molecules may assume an unfavourable orientation preventing them from reacting. In addition to the correct orientation the reacting molecules must also pack within a distance of 4.2Å (Schmidt rule[166]).

A solution to such problems again lay with Toda's coordinato-clathrate host molecules. He predicted that the host would form a coordinato-clathrate with the reactant molecule and hold it in the correct geometry for reaction.[167] This was illustrated by the irradiation of a 1:2 host-guest complex of 1,1,6,6-tetra-phenylhexa-2,4-diyne-1,6-diol (10) and chalcone (118).





(10) $n = 2$ (118) $Ar = C_6H_5$

After six hours the *syn*-head-to-tail dimer was formed in 90% yield.[168,169] The X-ray analysis (Fig. 5.1) revealed that the packing of the complex would only allow the formation of the *syn*-head-to-tail dimer.

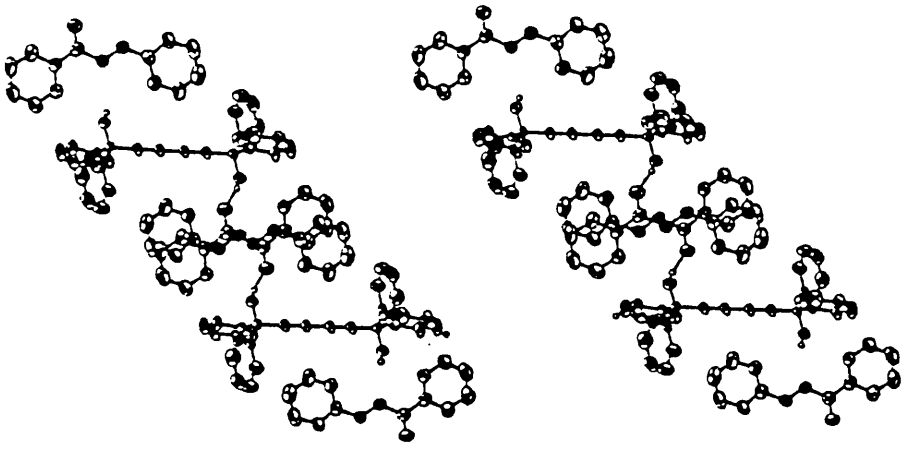
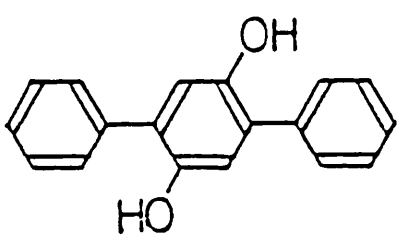
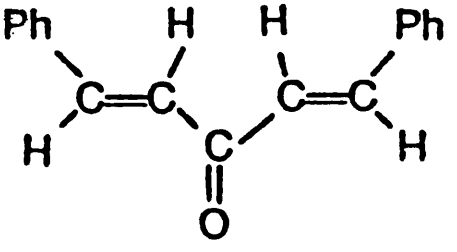


Fig. 5.1. Stereoscopic view of the 1:2 inclusion compound of (10) and (118).

Similarly, photodimerisation of benzylidene acetone (119) is also difficult both in solution[170] and the solid state.



(17)



(119)

However, when a 1:2 inclusion complex of 2,5-diphenylhydroquinone (17) and reactant molecule (119) is irradiated in the solid state, the *syn*-head-to-tail dimer is obtained in 70% yield.[169]

The same reaction carried out in solution in the absence of a host molecule, gave the *anti*-head-to-tail dimer in 30% yield. The hydrogen bonding in the former case makes the packing tight (Fig. 5.2), allowing the double bonds to approach a reacting distance of 3.8Å (Fig. 5.3)[171]

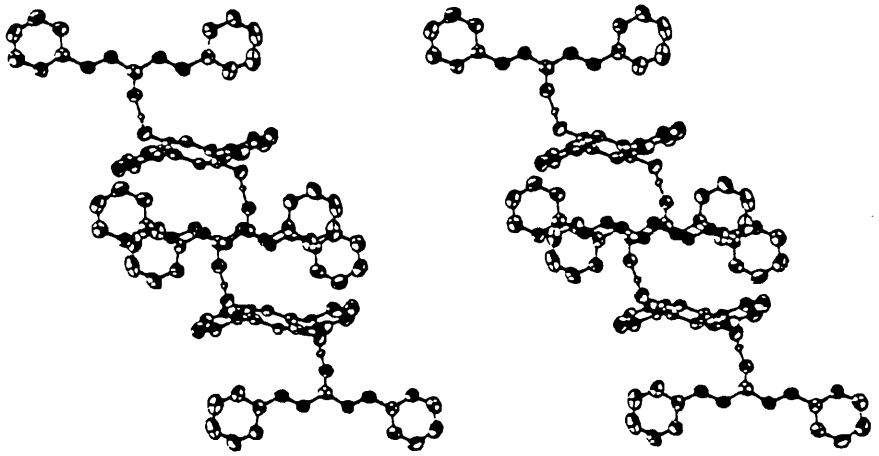


Fig. 5.2. A stereoscopic view of the 1:2 inclusion compound of (17) and (119).

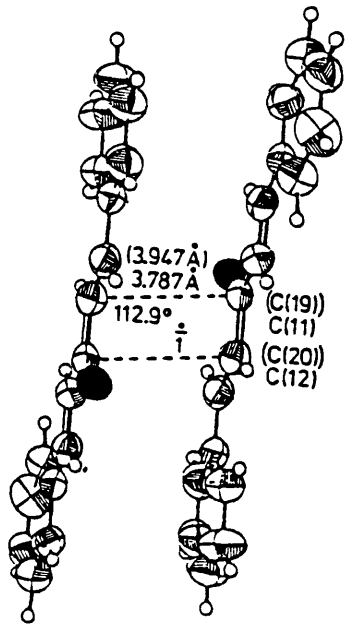
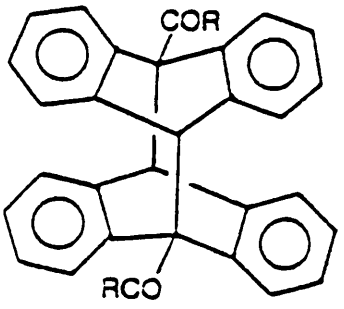


Fig. 5.3. The mutual relationship and geometrical parameters of the reacting centres of the pair of (119) molecules.

Another example of the influence of host molecules on photoreactions is the irradiation of 9-formylanthracene while complexed to host molecule (10). In solution, irradiation for 24 hours gave the *anti*-photocyclo addition product (120) in low yield;[172] however, irradiation of a 1:2 inclusion complex of (10) and 9-formylanthracene in the solid state for 8 hours gave the *anti*-product in 86% yield.[169]



(120) R = H

X-ray study again explained why this should be so. Both molecules of 9-formylanthracene are situated between two molecules of host (10), with the juxtaposition of the guest molecules controlled by the direction of host-guest hydrogen bonds (Fig. 5.4).

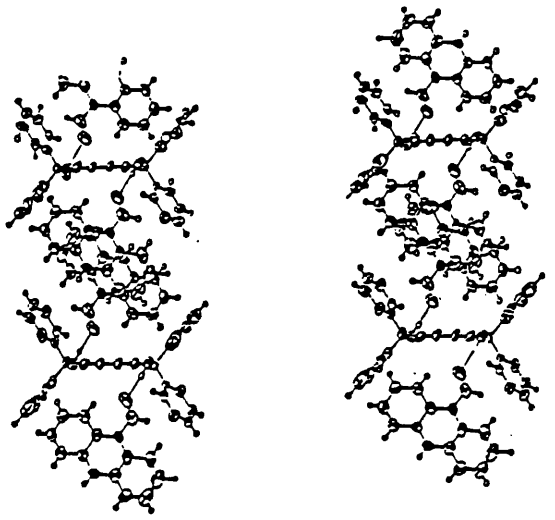
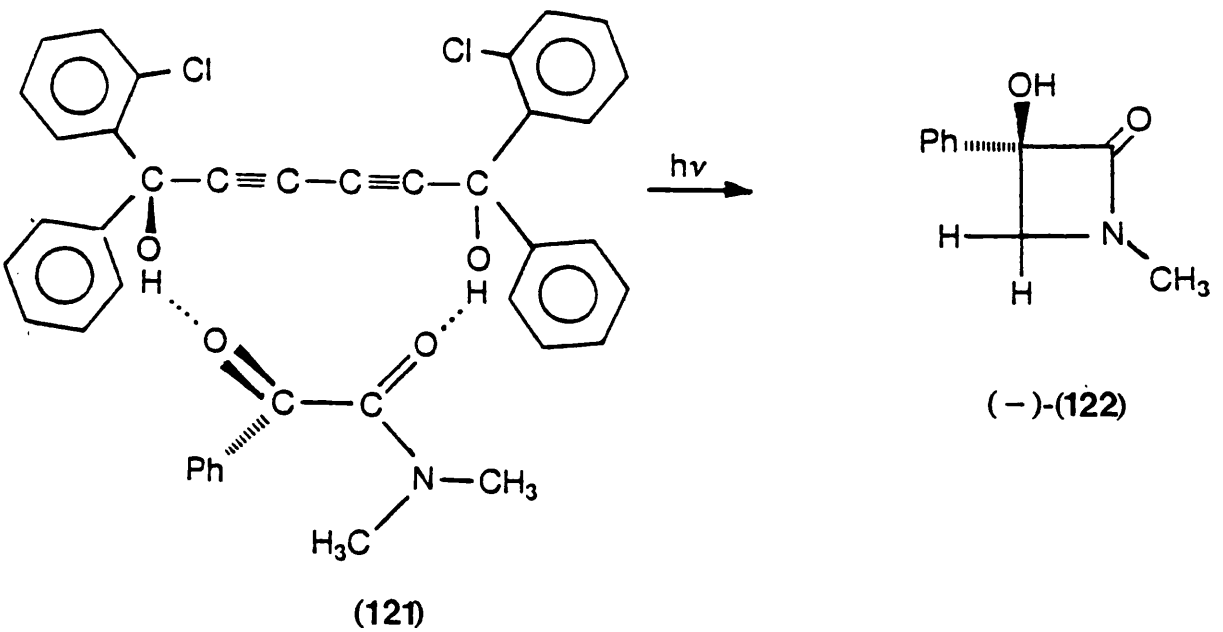


Fig. 5.4. Stereoscopic view of the 1:2 inclusion compound of (10) and 9-formylanthracene.

This guest arrangement leads to the *anti*-dimer (120) on photodimerisation; the distance between the two reaction centres being short enough (4.0Å) to allow reaction to occur readily.[173]

5.5 Enantioselective photoreactions.

Normally, the enantiocontrol of photoreactions, even in the presence of host molecules, is rather poor with ee values of up to 60%. Typically, though, Toda found a select few examples that gave very promising results. The first example relates to the enantioselective photocyclisations of the α-oxoamide (121) to the ß-lactam (122) in the presence of chiral host molecule (-)(107) (Fig. 5.5).



(121)

(−)-(122)

Fig. 5.5. A schematic illustration of the enantioselective photocyclisation of (121) in its inclusion compound with (-)(107).

Irradiation of the 1:1 inclusion compound of (121) and (-)(107) (Fig. 5.6) in the solid state for 8 hours gave (-)(122) of 100% ee in 90% yield.[174,175] The complexed guest molecule (121) is arranged unsymmetrically and therefore chirally, by twisting around the bond between two carboxyl groups; explaining the high value of both yield and optical purity.

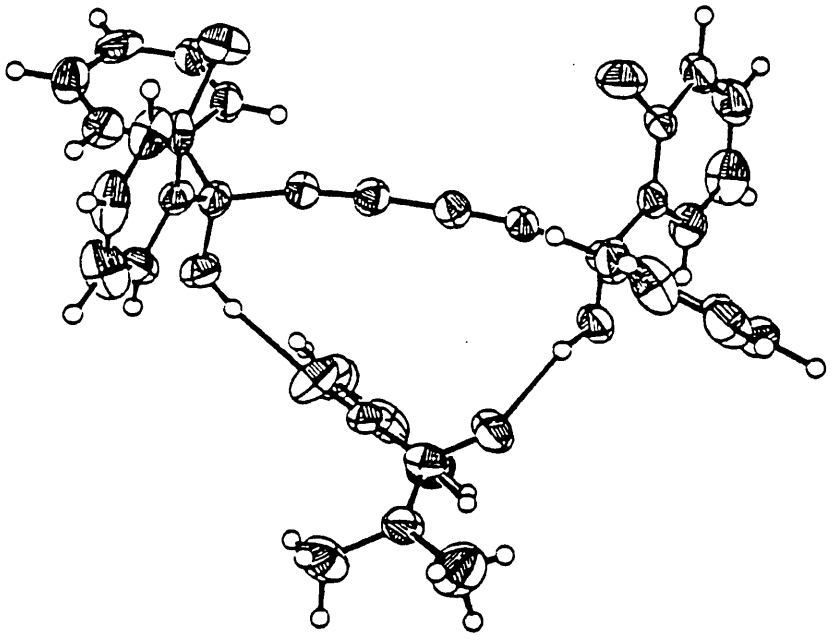


Fig. 5.6. Stereoscopic view of the 1:1 inclusion compound of (-)(107) and (121).

A further successful application of chiral host molecule (107) was in the enantioselective photocyclisation of a 1:1 complex with guest molecule (123), which gave (-)(124) of 100% ee in 50% yield.[176]

An explanation for this occurrence can be found from Fig. 5.7, illustrating the coordinato-clathrate complex between (123) and host (-)(107).

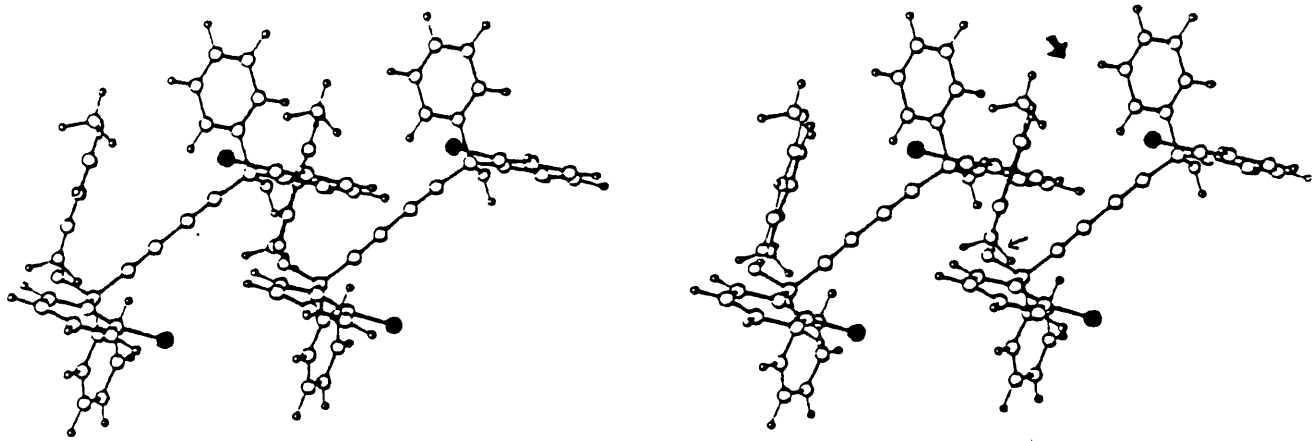


Fig. 5.7. A stereoscopic view of the 1:1 inclusion compound of (-)(107) and (123).

The methoxy group of (123) is in close van der Waals contact with the benzene ring indicated by the thick arrow, hence disrotatory ring closure of (123) cannot occur in the direction of the thick arrow but can only occur in the opposite direction to give (-)(124).[177] Fig. 5.8 demonstrates this more vividly, showing

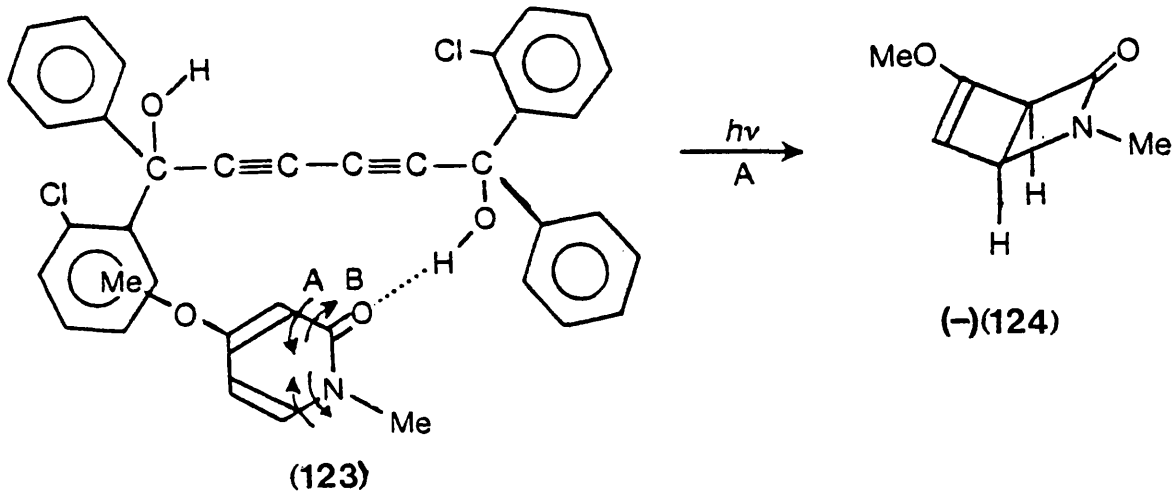


Fig. 5.8. A schematic illustration of the enantioselective photocyclisation of (123) in its inclusion compound with (-)(107).

5.6 Stabilisation of strained conformers.

In a few instances the guest molecules in a clathrate many assume a strained conformation that is beneficial to the overall stability of the clathrate lattice. Or conventionally, the host lattices may be considered as media for stabilising normally unstable guest conformations.[178] Three hosts which have exhibited this property are thiourea, TOT and hexahost (71) (Chapter 3).

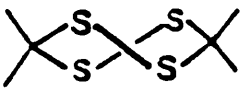
IR and Raman spectroscopic studies of thiourea inclusion compounds of monohalocyclohexanes[179] have shown the predominance of axial conformers in the cavities. This is in contrast with the preferred equatorial conformation in the liquid on gaseous phases.

The TOT clathrates have also exhibited this property; specifically with chlorocyclohexane, bromocyclohexane and 2-chlorotetrahydropyran as guest molecules.[180]

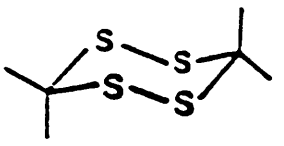
The crystal structure of the TOT/chlorocyclohexane at 158° K has been interpreted as the inclusion of two energetically disfavoured conformations of guest : an axial-chlorine chair and an axial-chlorine boat conformation distributed statistically in the ratio 2:1 over the available sites.

In a similar manner hexahost (71) has trapped guests in disfavoured conformations; specifically squalene and 3,3,6,6-tetramethyl-*s*-tetrathiane (125).[181]

The latter guest is trapped in the less favoured chair form (126), rather than the twist-boat form (125), normally predominating in the absence of host constraints.



(125)

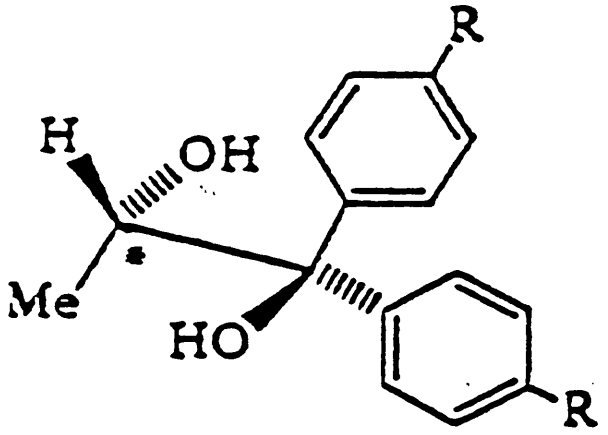


(126)

MacNicol suggested[181] that the trapping of guests in such novel conformations offer the possibility of specific guest reactions.

5.7 Organic clathrates as highly selective chemical sensors.

The need for chemical sensors[182] is great, applications[183] ranging, for example, from concentration analysis for medical purposes, industrial process control, warning and safety systems, and environmental analysis. Until recently, among the organic inclusion compounds, only monomolecular hosts have found application. Weber then discovered clathrate forming compounds (127) and (128), which are bulky derivatives of natural lactic acid, and as expected display enantioselective clathration.



(127) R = H
(128) R = CMe_3

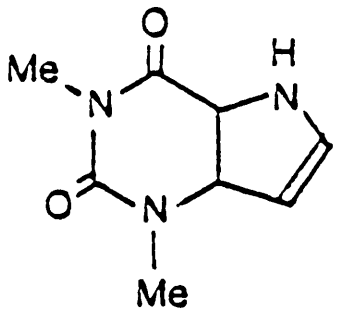
He found that the crystalline substances also proved to be highly selective sorbents for organic solvent vapours.[184] A quartz oscillator coated with either (127) or (128) can detect the solvent vapour by a shift in its basic frequency due to clathrate formation. Crystalline (128) as a sensor coating showed a pronounced affinity for 1-butanol. In spite of higher polarities and smaller

spatial demands, acetone, methanol, and 2-propanol gave much smaller signals even when larger quantities were used. Compound (127) on the other hand, demonstrated a high selectivity for 1,4-dioxane. Strangely, though, cyclohexane, which has a similar structure to 1,4-dioxane, gave only small signals.

Therefore the selectivity of the sensor coating depends on the structure of the host molecule, which could be widely varied to reveal different guest selectivities.

5.8 Isolation of natural products.

Normally extraction of caffeine (129) is a time-consuming process : Gatterman's extraction consists of more than seven experimental procedures.

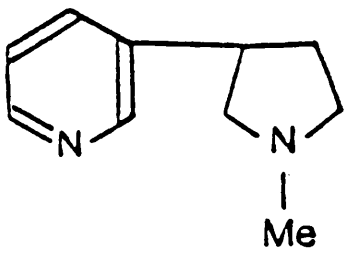


(129)

Toda improved upon this method by using host-guest complexation. He simply boiled the leaves in methanol for 8 hours, after which time the solution is concentrated. Host molecule (10) was then added to the solution, and

immediately formed a 1:2 host-guest complex with the caffeine in solution. Further recrystallisation from acetone gave a 1:2 complex of (10) and acetone. After filtration of the newly formed complex, the acetone solution was evaporated to give pure caffeine.[185]

In a similar way, Toda managed to isolate nicotine (130) from tobacco leaves as a 1:1 complex with (10).[186] The X-ray structure revealed the nature of the complex (Fig. 5.8).



(130)

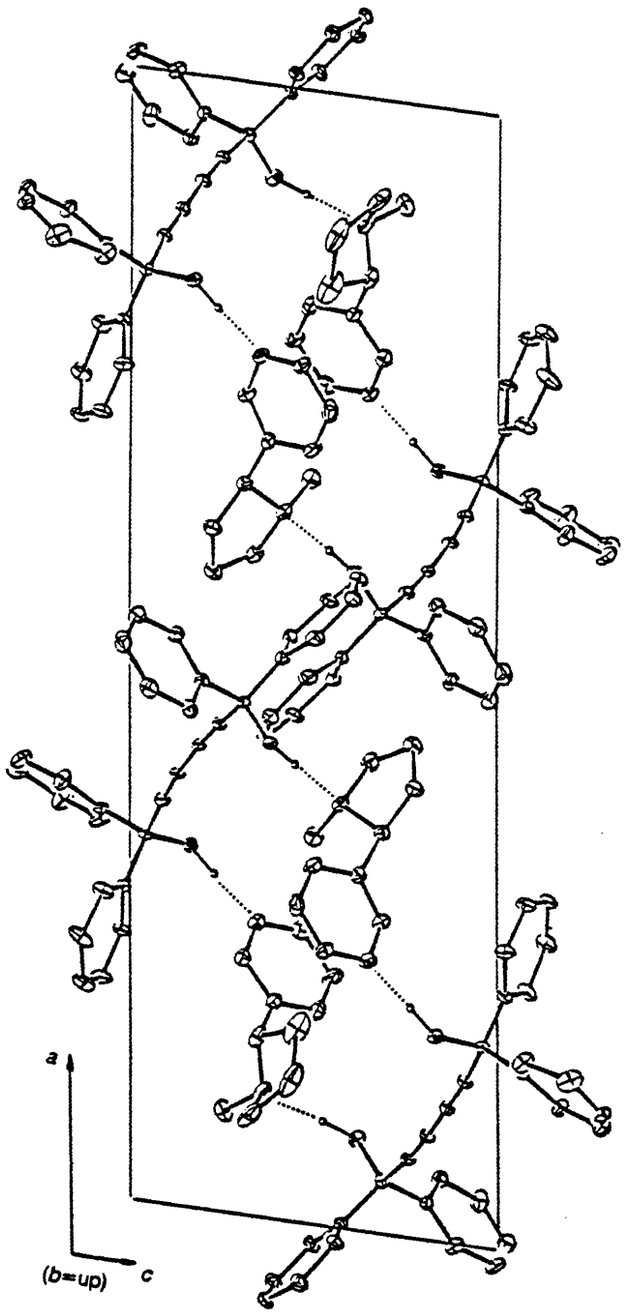
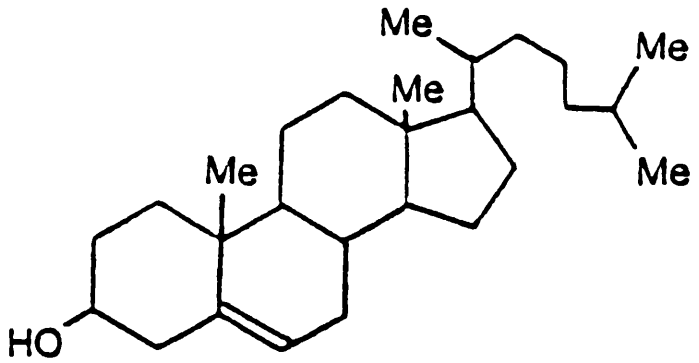
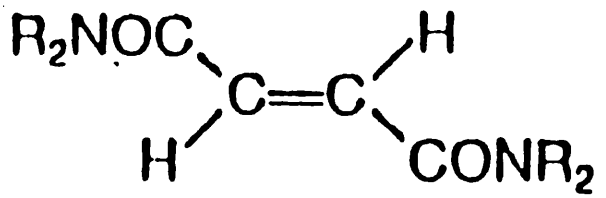


Fig. 5.8. A packing diagram for the cyclic 2:2 complex of (10) and nicotine (130)

Two molecules of (10) are bound to two molecules of nicotine by four O-H...N hydrogen bonds to form a cyclic 2:2 complex. Cholesterol (131) has also been isolated in the pure state from gallstones by complexation with host molecule (132).[185]



(131)

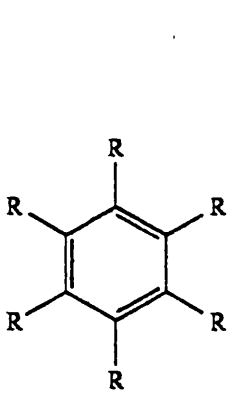


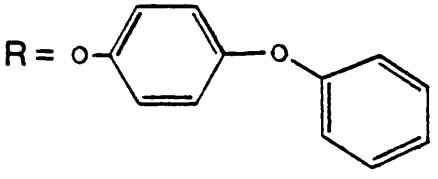
(132) R = cyclohexyl.

5.9 Storage of volatile and reactive reagents.

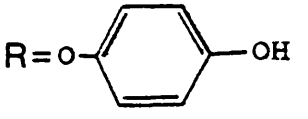
For a long time clathrates have been proposed as storage containers for volatile reagents or radioactive waste e.g., the enclathration of Kr^{85} in hydroquinone.[187] Currently, there are signs of a renewed interest in these applications.

A recent example of a clathrate specifically designed for the storage of phosgene, $COCl_2$ and thiophosgene, $CSCl_2$, relates to host molecule (133).[188]





(133)



(134)

Host molecule (133) forms a beautifully crystalline adduct (Fig. 5.9), host-guest ratio 1:1, allowing safe handling of this toxic guest. Also, host (134), which crystallises analogously to ß-hydroquinone (from ethanol which is not included), has been prepared[189] with a view to storing hydrogen, helium and argon.

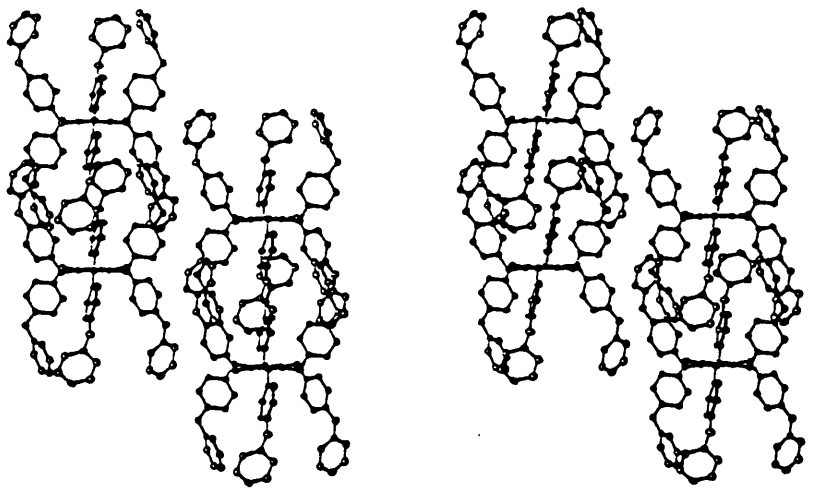


Fig. 5.9. A stereoview illustrating the efficient packing of adjacent columns which extend infinitely along *c* in the 1:1 $COCl_2$ clathrate of 2. The disordered phosgene molecule has been omitted for clarity.

To expand this particular area of host molecule application, and for that matter, all the others contained within this chapter, requires an even deeper understanding of the way in which host molecules pack. This would allow one to engineer specifically tailored host-molecules for a targetted guest. At the moment, however, this form of crystal engineering requires further development, but promises many useful further applications.

RESULTS AND DISCUSSION

CHAPTER 6

DESIGN OF CORONENE-BASED HOSTS.

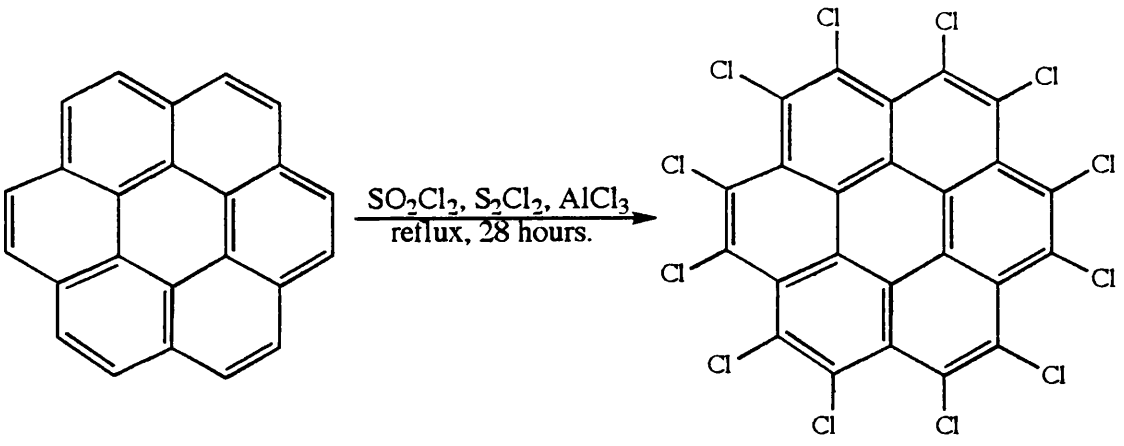
6.1 Perchlorocoronene - a host precursor

Design of new crystalline host lattices still presents a major challenge at the present time. As discussed in the foregoing chapters, many important classes of crystalline inclusion compound are formed by self-assembly, in the presence of suitable guests, of individual host molecules which possess a 2-fold or 3-fold rotation axis. A salient example of a C_2 axis as molecular host determinant is provided by the work of Mak and Wong, and also by that of Bishop (Chapter 2).

Trigonal symmetry is a common feature of a number of important host molecules; examples being cyclotriphosphazines, perhydrotriphenylene, cyclododecatriene-based hosts (Chapter 4) and hexa-hosts (Chapter 3).

In the present chapter the successful design and synthesis of new types of trigonal, coronene-based host molecules are described. The starting material perchlorocoronene (135) was prepared by chlorination of coronene under SO_2Cl_2-S_2Cl_2-$AlCl_3$ conditions (Scheme 2).[190]

Scheme 2.



(135)

The structure of this molecule has been established by single - crystal X-ray crystallographic and high-resolution electron microscopy studies (Fig. 6.1).[191] Fig. 6.2 also illustrates the markedly non-planar form of (135) which reflects pronounced *peri*-interactions.

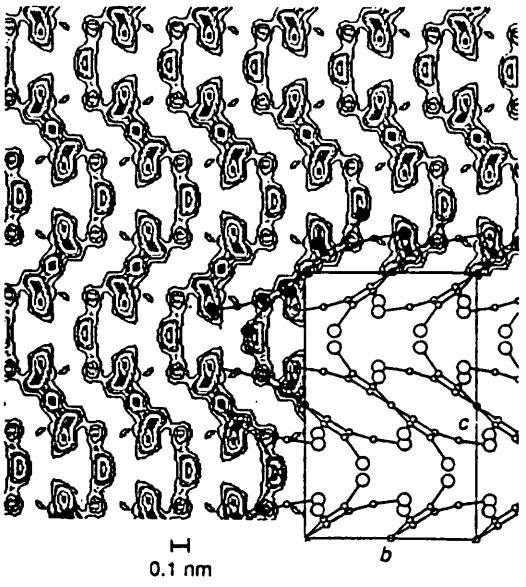


Fig. 6.1. Centroid map from mode 53 of the phasing tree. Inset : molecular array on the b-c face of the unit cell.

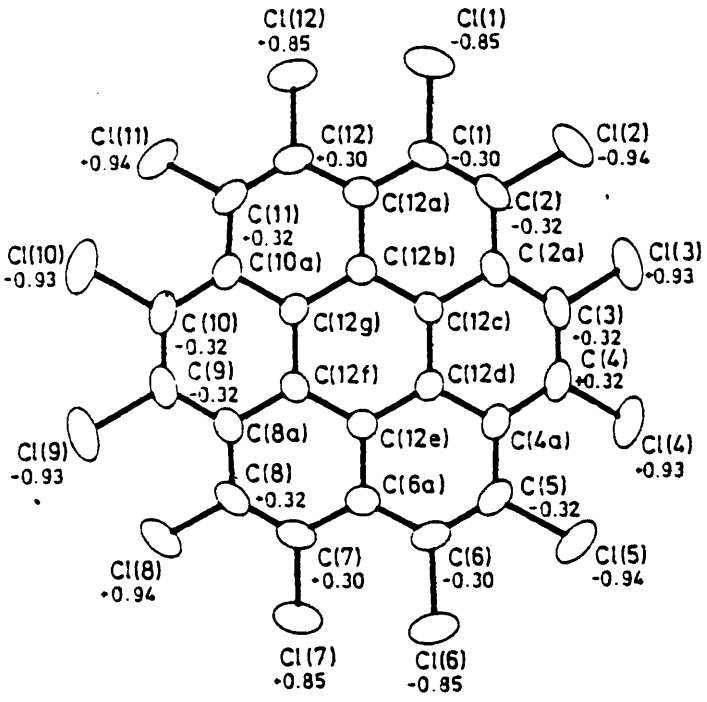


Fig. 6.2. Atomic numbering scheme and displacement (Å) of atoms of (135) from the mean plane of the carbon atoms. Atoms for which no displacements are given (the central ring and directly-attached carbon atoms) do not deviate significantly from planarity.

This conformation, close to $\underline{D}_{3d}$, may be described as *aabbaabbaabb* (*a* = above, *b* = below), and two concave faces, back-to-back, are evident from the stereoview in Fig. 6.3.

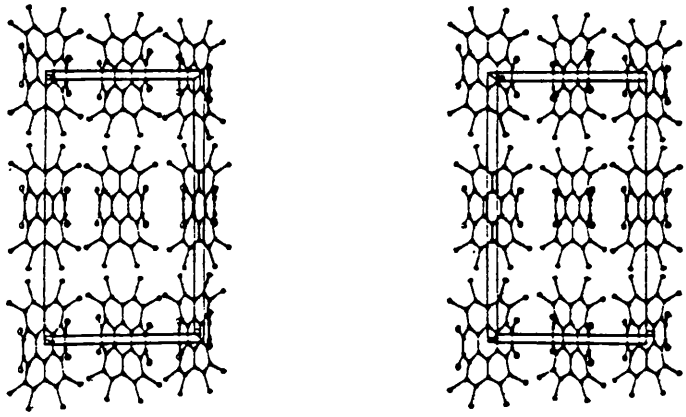


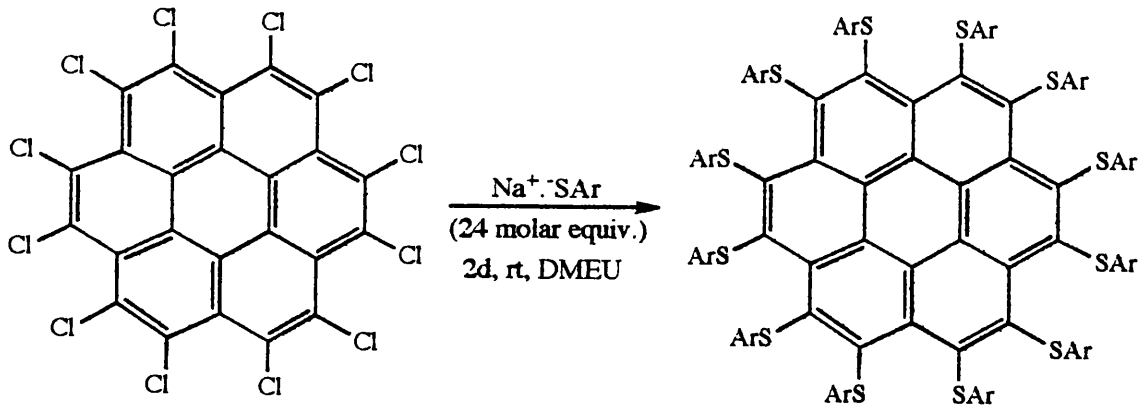
Fig. 6.3. Stereoview illustrating the non-planar nature of perchlorocoronone.

Following the line of argument that identification and introduction of suitable side-chain components could lead to analogous conformations, with extended and opposing concave faces, back-to-back, a range of compounds was synthesised. As will be seen, suitable side-chain moieties are critical with respect to crystallinity and stability of the inclusion compound formed. It may be stressed that features of critical importance are the C_3 axis (assuming an *aabbaabbaabb* is achieved in reality) normal to the central coronene core; and the overall molecular shape possessing two concave faces, back-to-back. In a sense this may be considered a higher order analogue of a hexa-host in which pairs of side-chain moieties alternate regularly above and below the central aromatic core, unlike a typical hexa-host which possesses a single side-chain moiety displaying an alternating arrangement.

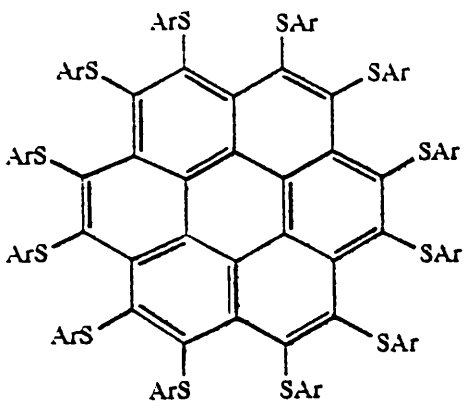
6.2 Discovery of a novel sulphur-based coronene host

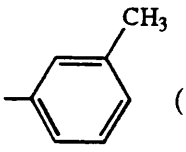
The dodeca-substituted sulphur-based coronenes were readily prepared in excellent yields (Experimental) by treatment of perchlorocoronene with the appropriate arenethiolate, in the solvent DMEU, employed to promote complete displacement of the chlorine atoms (Scheme 3). For these runs, reaction times were typically 2 days and 24 molar equivalents of arenethiolate were used, a 100% excess. Purification of the sulphur-containing coronenes proved difficult. Conventional columning on silica was ruled out because of a tendency to oxidation on the column. Therefore, all sulphur-based coronenes were purified by crystallisation from suitable solvents.

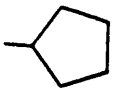
Scheme 3.

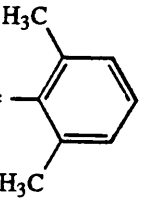


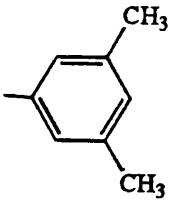
In view of brief preliminary studies[192] it was apparent that judicious selection of side-chain moiety would be required to obtain highly crystalline adducts;previously it was known that coronenes per-substituted by thiolates such as benzene thiolate, *p*-methoxybenzene thiolate, *p-t*-butylbenzenethiolate and ß-naphthalene thiolate all failed to produce material with well-defined inclusion properties. Although, it may be noted that dodecakis (*p-t*-butylphenylthio) coronene[192] had shown some promise, forming an adduct with diethylsuccinate on very slow crystallisation from this solvent. The study was initiated by using thiolates, generated from commercially available thiols which were thought to present a favourable overall shape. Following the procedure outlined above, compounds (136)-(139) were synthesised.



(136) ; Ar= 

(137) ; Ar= 

(138) ; Ar= 

(139) ; Ar= 

Compound (136), dodecakis (3-methylphenylthio)coronene was synthesised in 87% yield. Purification was accomplished by crystallisation from 1,4-dioxane / methanol solvent mixture. The *meta*-tolylthio moiety had proven successful in the formation of a particularly versatile octa-host,[193] octakis(*m*-tolylthio) naphthalene, however, in the present case, no inclusion was detected for host molecule (136) from chlorinated, aromatic or aliphatic solvents.

In a similar fashion, compound (137), dodecakis(cyclopentylthio)coronene was prepared, yield 60%. The low yield was a result of successive recrystallisation from an isopropanol/1,4-dioxane solvent mixture, used to remove cyclopentyl mercaptan impurities which could hinder formation of any crystalline adducts. Crystallisation of (137) from many varied solvents gave a close-packed orange compound, containing no solvent as guest.

Compound (138) possessed *ortho* methyls, introduced in the hope of "locking" the molecule into the desired *aabbaabbaabb* conformation. Analysis of the end product from the reaction revealed however that the substitution was incomplete, probably due to sterically hindered attack of incoming nucleophiles at adjacent centres on the coronene unit. No further investigation of the synthesis of (138) was carried out.

On the other hand, reaction of the 3,5-dimethylbenzenethiolate nucleophile did produce the fully substituted molecule (139), dodecakis (3,5-dimethylphenyl-thio)coronene. A blood-red oil, isolated from the reaction mixture was recrystallised from a 1,4-dioxane/methanol mixture to give a crop of purple crystals, 85% yield, m.p. 275-278°C (1,4-dioxane adduct).

The 200 MHz ^{1}H NMR spectrum indicated inclusion of 1,4-dioxane in a host-guest ratio of 1:2. Inclusion of other guests; specifically *N*-methyl-morpholine, 1,4-thioxane, tetrahydrofuran, tetrahydrothiophene, cyclohexanone, cycloheptanone and DMEU was also found, with a common host-guest ratio of 1:2. In contrast, cyclopentanone and 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidone (DPEU) were not included.

Host molecule (139) was then recrystallised twice from 1,4-dioxane at 50°C (in an oven) to give X-ray quality crystals.

X-ray study of host molecule (139)

The X-ray analysis initially proved problematical. At room temperature very few reflections were observed, consistent with the view that the host molecules were undergoing pronounced thermal motion within the crystal. To obviate this problem, the data were collected at low temperature (120 K). Accordingly, a full data set was obtained and the structure was solved using direct methods and refined to a final R factor of 9%.

The highly crystalline 1,4-dioxane adduct is triclinic, space group $P\bar{1}$ with a = 17.094(6), b = 17.489(6), c = 23.987(6)Å; α = 74.63(2), ß = 71.72(3) and γ = 60.53(3) Z = 2 (host) and 4 guest molecules. Similar unit cell dimensions were found for the 1,4-thioxane adduct.

Fig. 6.4 shows a view of the dodecakis(3,5-dimethylphenylthio)coronene host molecule (139) viewed normal to the central coronene core.

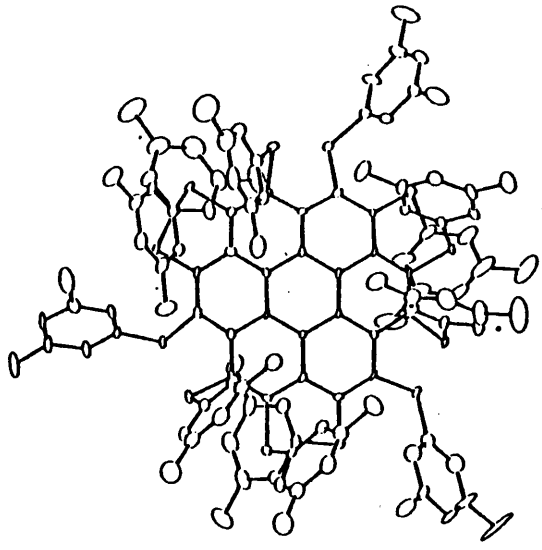


Fig. 6.4. A view of the host molecule dodecakis(3,5-dimethylphenylthio)coronene (139) in its 1,4-dioxane adduct.

Satisfyingly, the geometry of the nucleus of (139) has been translated faithfully from the favoured perchlorocoronene conformation (Fig. 6.2), alternating pairs of sulphurs adopting the desired *aabbaabbaabb* conformation (Fig. 6.5).

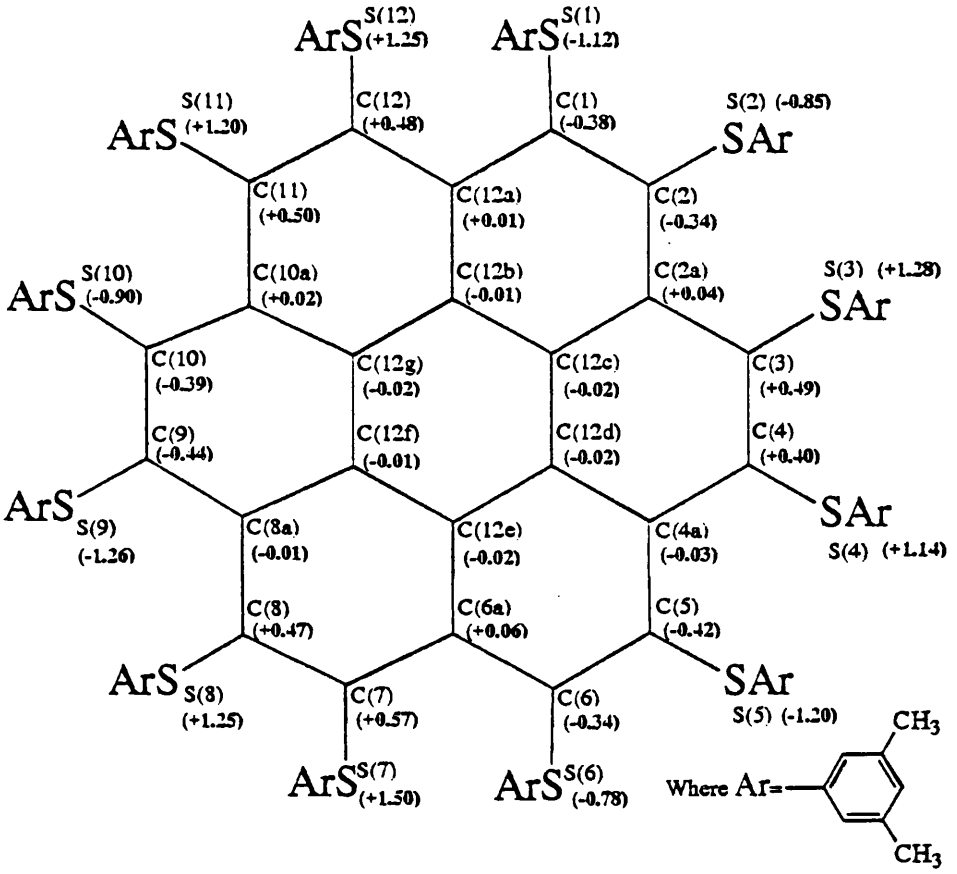


Fig. 6.5. Atomic numbering scheme and displacement (Å) of atoms of (139) from the mean plane of the carbon atoms.

Fig. 6.6 shows a stereoview illustrating the overall conformation of the host molecule. In this, the non-planarity of the central coronene core is clearly apparent. An extremely novel conformation is found, and pairs of legs are indeed shown to alternate above and below the mean plane of the aromatic core, as planned.

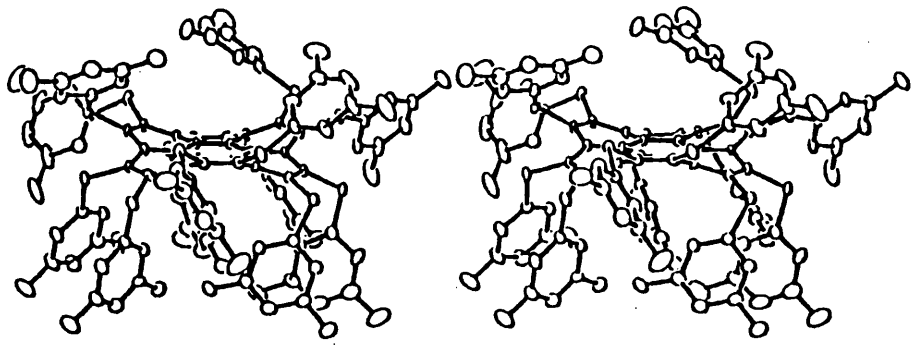


Fig. 6.6. A stereoview illustrating the molecular conformation of host (139) in its 1,4-dioxane adduct.

A key feature of the molecule is an approximate C_3 axis normal to the central coronene core (*vide infra*), that is, the molecule has non-crystallographic symmetry, C_3. Corresponding to this, there are two types of pairs of legs : parallel or splayed (above and below, respectively, in Fig. 6.6). This is noteworthy because the molecule occupies a general position in the triclinic unit cell, which does not require the molecule to adopt a symmetrical conformation. This led to careful checking of the unit cell, which was substantiated by deviation from exact C_3 symmetry and the ordered arrangement of the 1,4-dioxane guest in one of its two crystallographically distinct locations. Significantly, prolonged scrutiny of a number of adjacent triclinic cells shows that the host packing approximates to a rhombohedral packing mode, corresponding roughly to space

group $R\bar{3}$, with the host molecule located on the (approximate) three-fold proper rotation axis. This packing is reflected in the (non-crystallographic) C_3 symmetry of the host molecule of (139). The exact triclinic packing, space group $P\bar{1}$, is illustrated in Fig. 6.7, the stereoview looking down the *a* axis.

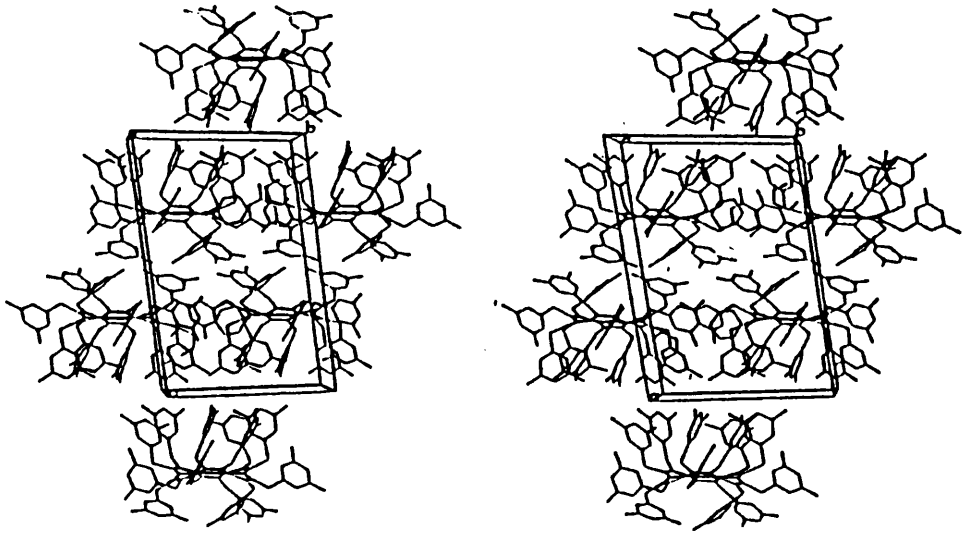


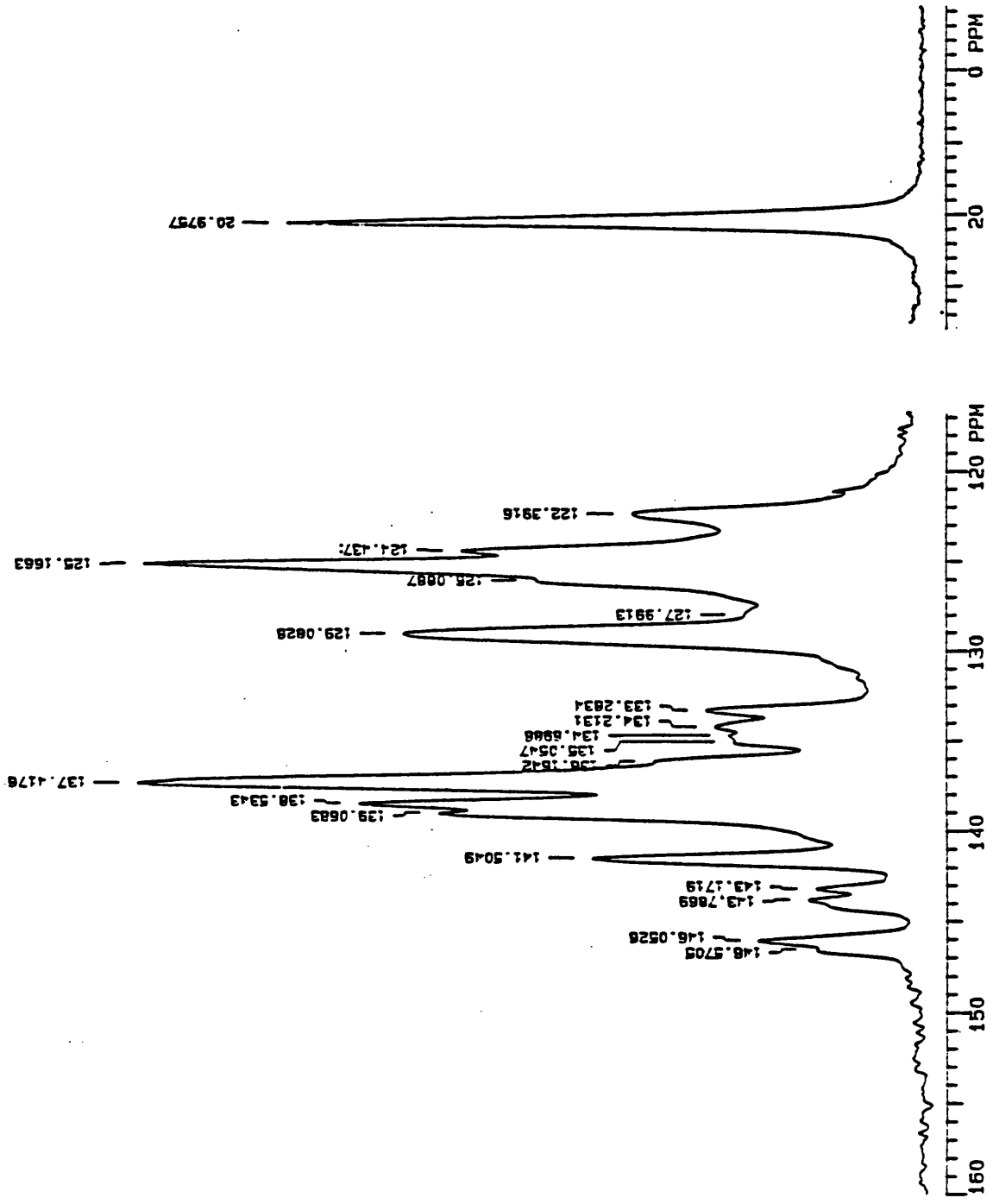
Fig. 6.7. A stereoview showing the host-guest packing in the 1,4-dioxane adduct of host (139).

Two guest locations are indicated, one guest molecule being fully resolved, but only five atoms of the disordered guest were found. The ordered 1,4-dioxane is closest to the centre of the cell in Fig. 6.7, whilst the disordered guest may be seen (in part) round the front left corner of the cell. By contrast, in the 1,4-thioxane adduct (not shown) the guest closer to (½,½,½) is disordered and the other guest, close to the bottom left hand front corner of the cell, is ordered.

Solid State ^{13}C NMR of (139)

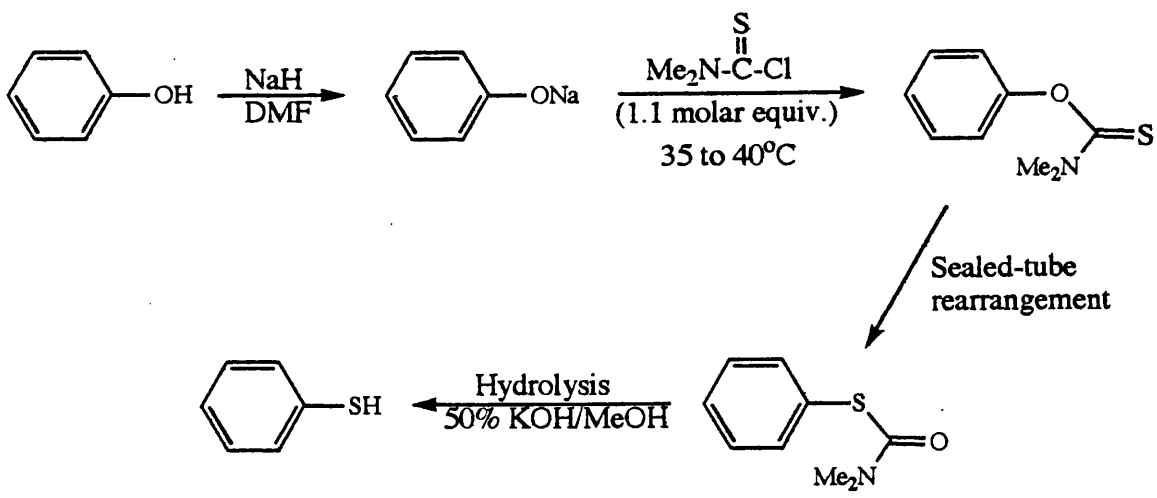
The cross polarisation magic angle spinning (CPMAS) and non-quaternary suppression (NQS) concur with the observed deviation from ideal symmetry. The central coronene core carbons conform to C_3 symmetry with only two signals as expected, observed at 124.4 and 122.3 δ_C (Fig. 6.8). However the outer carbons of the coronene core not attached to *S*-aryl moieties do not correspond to the two expected for C_3 symmetry; they display several signals from 135.5 to 133.4 δ_C. Also, those carbons of the coronene core directly attached to the *S*-aryl moieties are represented by six signals from 146.6 to 143.2 δ_C, instead of the four expected if exact C_3 symmetry were present.

Fig. 6.8. Solid-state ^{13}C CPMAS spectrum of dodecakis(3,5-dimethylphenylthio)-coronene (139).



6.3 Synthesis of new thiols by Newman-Karnes method

To continue study of the design of sulphur-based coronene hosts new arene thiols were required. The synthetic method used was that of Newman and Karnes[194] (Scheme 4).



Scheme 4.

The phenoxide salt, formed by reaction of the phenol with NaH, was reacted with *N,N*-dimethylthiocarbamoyl chloride. By simple nucleophilic displacement one obtains the *O*-aryl dimethylthiocarbamate. The *O*-aryl thiocarbamate was then rearranged to the more stable *S*-aryl thiocarbamate in a vacuum-sealed pyrolysis tube. The temperature required for the rearrangement was dependent upon the activating groups or deactivating groups attached to the phenyl ring. The *S*-aryl dimethylthiocarbamate was then simply hydrolysed under an inert atmosphere of nitrogen and the thiol subsequently isolated. Thiol (144) *p*-methylsulphonylbenzenethiol was prepared initially from 4-(methylmercapto)-phenol (Experimental) and also thiol (148), *p*-adamantylthiophenol, was prepared from adamantane.[195] Interestingly, *p*-adamantylphenol was found to possess clathrating ability; it forms adducts with methanol, nitromethane and 1,4-dioxane, with host-guest ratios of 3:2, 3:1 and 6:1, respectively. The methanol and nitromethane adducts were completely stable to guest loss, whereas the 1,4-dioxane adduct lost all guest component over a period of 24 hours. A possibility is that these adducts might have a host packing analogous to that of Dianin's compound clathrates, though this has not yet been established.

Thiols (148), (149) and (150) have previously been synthesised[194,195,196] by the Newman-Karnes method. Table 12 catalogues these thiols and those newly synthesised by this method.

Table 12. Thiols synthesised by the Newman-Karnes method.

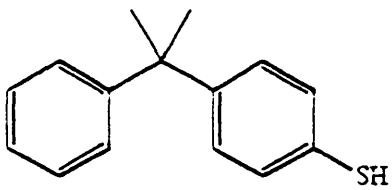
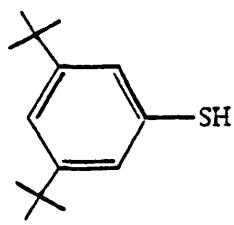
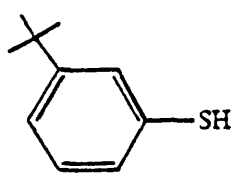
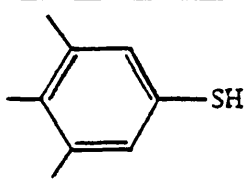
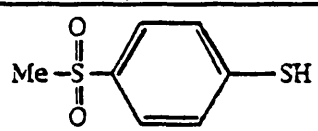
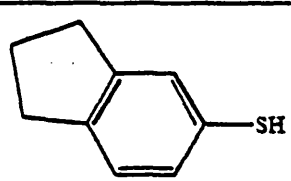
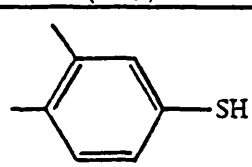
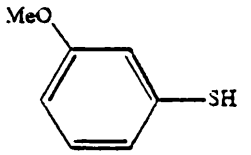
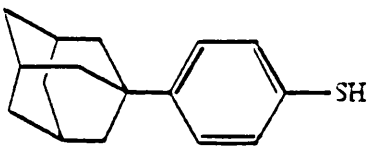
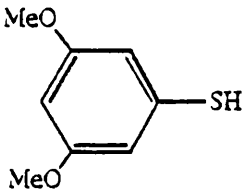
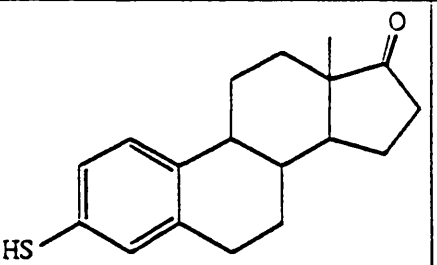
Thiol synthesised	*Rearrangement temperature of O-aryl*	m.p./b.pt.
 (140)	275°C	43-44°C
 (141)	300°C	52-53°C
 (142)	285°C	68°C/0.005mm
 (143)	300-305°C	65°C/0.005mm
 (144)	255-260°C	68-69°C
 (145)	300°C	66-68°C/0.005mm
 (146)	285°C	56°C/0.005mm

Table 12. (continued)

 (147)	300°C	72-74°C/0.005mm
 (148)	300°C	104-105°C
 (149)	265°C	92°C/0.005mm
 (150)	300°C	138-140°C

Problems encountered during the synthesis of the above thiophenols were : (a) cleavage of the *O*-aryl dimethylthiocarbamate in step 2 when the temperature is raised above 40°C; (b) the presence of small amounts of water in the pyrolysis tube, promoting hydrolysis of the *O*-aryl compound; and (c) production of disulphide if extreme care was not taken to expel oxygen from the system.

The thiols were then reacted in the form of their thiolate salts to produce a new series of prospective host compounds (Table 13).

Table 13. A listing of newly synthesised sulphur-based dodecahosts.

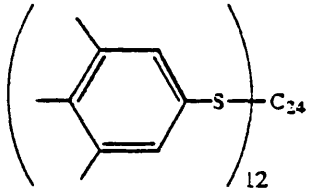
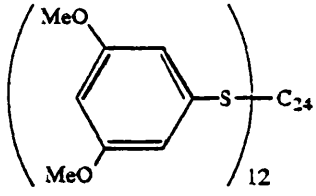
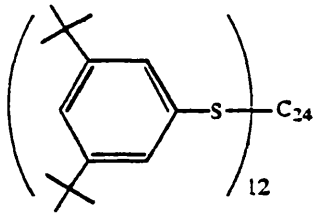
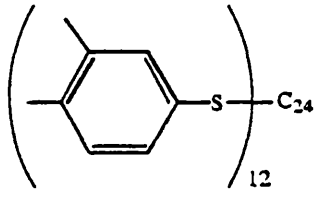
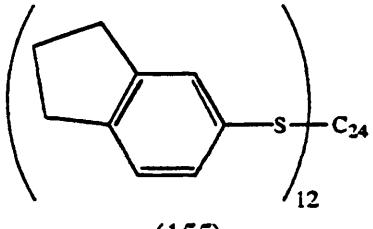
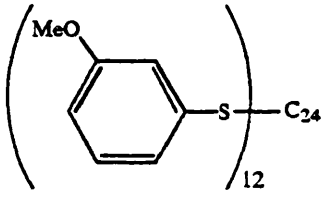
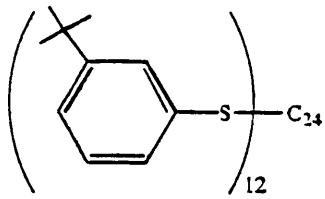
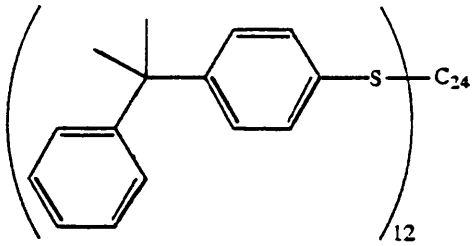
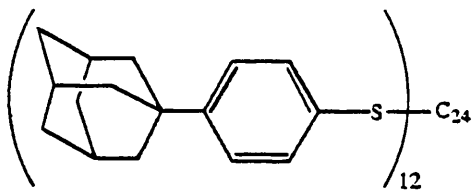
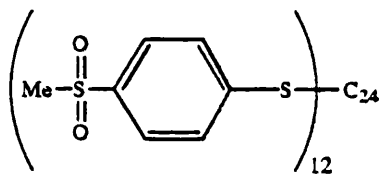
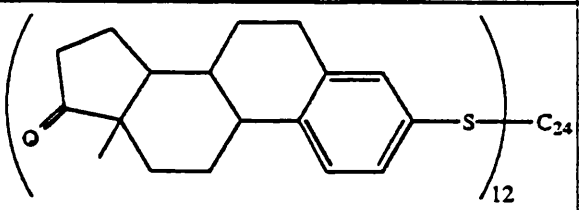
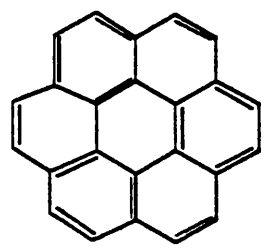
Dodeca-host	% Yield
 (151)	92
 (152)	75
 (153)	87
 (154)	94
 (155)	72.9
 (156)	88.7

Table 13. (continued)

 (157)	91.9
 (158)	88.9
 (159)	89.7
 (160)	94.1
 (161)	71.1

C_{24} = coronene unit,  .

6.4 Design of new sulphur-based coronene hosts

Having discovered the 3,5-dimethylphenylthio group to be a favoured moiety with regard to formation of sulphur-based coronene clathrates, the design strategy now adopted involved concentrating on moieties with related shape and structure features, the aim being optimisation of clathrating ability.

With this in mind, compound (151), dodecakis(3,4,5-trimethylphenylthio)-coronene was synthesised. It was hoped that the presence of the extra methyl in the 4 position would alter the packing in such a fashion that ideal C_3 symmetry would be observed within the clathrate's architecture.

A deep red powder, compound (151), was isolated from the reaction medium by triturating the red oil from the work-up with 1,4-dioxane. The extra methyl on each leg, increased the hydrocarbon bulk of the compound, thus preventing crystallisation from the polar solvent 1,4-dioxane.

Compound (151) was found to be sparingly soluble in tetrahydrofuran and pentamethylene sulphide, including both as guests in a host-guest ratio of 1:2 (determined by ^{1}H NMR). The highly crystalline form of (151) was obtained by crystallising (151) from tetrahydrothiophene at 45°C, host-guest ratio 1:2, m.p. > 310°C. The crystals of (151) appear monoclinic (or triclinic) in shape differing from the approximate hexagonal habit of (139). Host molecule (151) also formed more stable adducts than (139). Host (139) was found to lose half a mole of guest over a six month period, whereas no such loss occurred for host (151).

As yet no X-ray analysis has been carried out on the tetrahydrothiophene clathrate of (151) to establish the actual mode of host-guest packing in this adduct.

Continuing the theme of utilising a 3,5-disubstituted moiety within design, compound (152), dodecakis(3,5-dimethoxyphenylthio)coronene was formed. Purification of the resultant black/purple oil was effected by crystallisation from a mixture of 1,4-dioxane and methanol. Inclusion experiments from many solvent types, for example, toluene, benzene, dichloromethane, 1,4-dioxane and isopropanol failed to reveal any evidence for a new clathrate system. The polarity and angularity of the methoxy groups were obviously not ideal attributes compatable with crystalline adduct formation.

Resorting to hosts with more hydrocarbon character, whilst maintaining the favoured shape and substitution pattern of side-chain moiety, led to the synthesis of compound (153), dodecakis(3,5-di-*t*-butylphenylthio)coronene. Trituration with 1,4-dioxane gave a pure material by reverse-phase TLC. The host (153) was found to be insoluble in all non-polar and polar aliphatic solvents; sparingly soluble in dichloromethane, and very soluble in chloroform and aromatic solvents.

Attempted recrystallisation of (153) from any single solvent, for example, CH_2Cl_2 or $CHCl_3$ or toluene failed to yield any adduct, hence solvent mixtures were employed. Inclusion behaviour was eventually noted from a 1:2:2 mixture of chloroform, isopropanol, and carbon disulphide. The ^1H NMR revealed the selective inclusion of five molecules of chloroform and one molecule of isopropanol, to one of the host molecule. The crystals were hexagonal in shape, of X-ray quality and stable to guest loss.

Having effectively exhausted the various thiols with substituents at the 3,5-positions, a search for an optimised coronene host was pursued by examining different side-chain moieties, having only one *meta* position substituted.

To test the relevance of the 'second' methyl in the 5-position with regard to formation of non-close packed host molecules, compound (154), dodecakis(3,4-dimethylphenylthio)coronene was synthesised. Surprisingly, compound (154) was only sparingly soluble in 1,4-dioxane, unlike (139), hence purification was

accomplished by triturating using the aforementioned solvent.

Again no inclusion was noted from any single solvent, consequently solvent mixtures were used. Crystallisation from a 4:1 mixture of 1,4-dioxane and dichloromethane gave an adduct with inclusion of 1,4-dioxane only, in a host-guest ratio of 1:4. Hence the versatility of the host is markedly reduced by omission of the methyl in the 5 position.

Altering the moiety slightly by the formal introduction of a bridging methylene group between the methyls gave the 5-indanethio side-chain analogue. The fully substituted compound however, dodecakis (5-indanethio)coronene (155), behaved in a similar manner to (154). Inclusion was only noted by crystallising (155) from a 1:1 mixture of dichloromethane and 1,4-dioxane, the adduct consisting of 3 molecules of 1,4-dioxane and 1 molecule of dichloromethane to one of host (155).

Omitting substitution at the 4-position and concentrating on purely *meta*-substituted moieties revealed a similar reluctance to form open crystalline structures.

Compound (156) dodecakis(*m*-methoxyphenylthio)coronene, forms clathrates from solvent mixtures only. Crystallisation of (156) from a 1:2 mixture of chloroform and 1,4-dioxane gave an adduct containing chloroform and 1,4-

dioxane; host-guest ratio 2:(7:2) respectively. The above crystallisation mixture was used to purify crude (156). X-ray quality crystals were obtained from a 1:1:1 mixture of isopropanol, chloroform and dichloromethane, the adduct consisting of four molecules of chloroform and one of isopropanol, to one of the host (156).

To conclude design using *meta*-substituted moieties compound (157) dodecakis (*m-t*-butylphenylthio)coronene was synthesised. Purification of (157) was effected by trituration with 1,4-dioxane. As before, no inclusion was noted by recrystallising (157) from any single solvent. Recrystallisation from a 1:1:1 mixture of carbon disulphide, isopropanol and chloroform gave highly symmetrical deep-purple crystals with 7 molecules of chloroform and one molecule of isopropanol to two host (157) molecules.

Therefore, from the above results, one can state quite categorically that a singly *meta*-substituted side-chain moiety appears to be disfavoured with respect to design of a versatile sulphur-based coronene host. This leaves *para*-substituted moieties as the only possible practical route left to explore. As mentioned earlier, the *p-t*-butylphenylthiolate-derived host had shown some promise, with the isolation of a single adduct. Perhaps by increasing the bulk of the *para*-substituent one would discover new inclusion properties.

In accord with this idea, dodecakis(*p*-cumylphenylthio)coronene (158) was prepared. Purification was accomplished this time by crystallisation from a

carbon tetrachloride/isopropanol mixture. Crystallisation of (158) from single solvents and from solvent mixtures failed to reveal any new inclusion properties corresponding to *para*-substitution.

Similarly, compound (159), dodecakis(*p*-adamantylphenylthio)coronene failed to show inclusion ability. In this case (159) was only soluble in carbon disulphide. Subsequent attempted recrystallisations from solvent mixtures produced an amorphous glassy material with no inclusion of any solvent noted.

Continuing design utilising a *para*-substituted moiety, attempted to exploit the renowned ability of sulphones to form materials of high crystallinity. In order to mimic the shape of the *p*-*t*-butylphenylthio side-chain moiety, compound (160), dodecakis(*p*-methylsulphonylphenylthio)coronene was synthesised. The orange compound, purified by trituration with 1,4-dioxane was found to be soluble in only three solvents:- DMEU, DPEU and DMSO. Preliminary investigations, though, suggest that compound (160) is unlikely to be a particularly versatile host.

Finally, to conclude design of new sulphur-based coronene hosts, attention was focussed purely on the bulk of the side-chain moiety; specifically using an estrone-related thiolate salt for substitution of the coronene core. The fully substituted orange compound (161) was purified by crystallisation from a 1,4-dioxane/methanol mixture. A very unusual deep-purple, clear glassy material was obtained, interestingly trapping 5 molecules of 1,4-dioxane to one of the host.

Further attempted recrystallisations from other single solvents again failed to yield any inclusion adducts. No further search for inclusion properties from host (161) was carried out, because of the low yield of pure material.

Obviously, the pursuit of the strategy of using bulkier moieties may have to run the gauntlet of materials that are non-crystalline. In the present case, however, the glassy adduct formed by (161) is not without interest.

The experimental results described above give firm support for the original premise, that the shape of the side-chain moiety is critical in determining the versatility of the host molecule. With coronene, the 3,5-dimethylphenylthio side-chain turned out to be the prime candidate.

This poses the question : why was the 3,5-substituted leg so successful? Presumably when problems of solubility are overcome, a determining factor in crystal formation must lie with the conformation favoured by the host molecule. Hexa-host and naphthalene-based spider-host clathrates show a marked preference for select conformations during crystal growth. In the hexa-host series, although eight conformations are possible, only two are, in fact, favoured with regard to clathrate formation. Correspondingly, the spider-hosts favour three conformations, selected during adduct formation from a possible 14.

Considering coronene hosts, 8 conformations are possible (Fig. 6.9).

Fig. 6.9. Possible conformations of a dodeca-substituted coronene in solution.

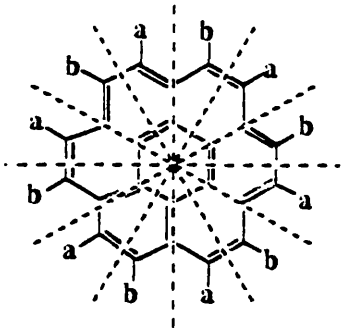
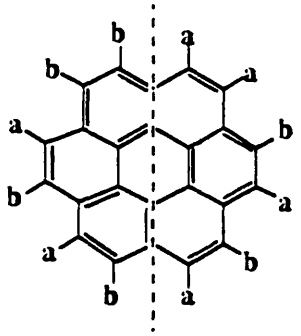
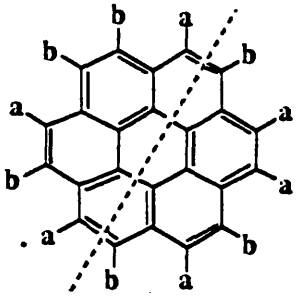
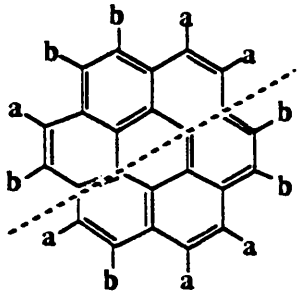
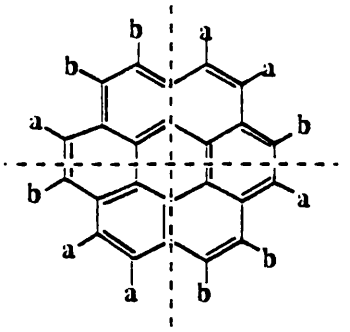
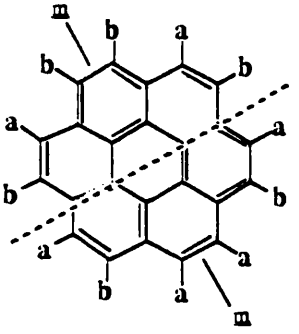
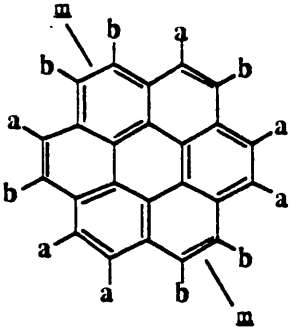
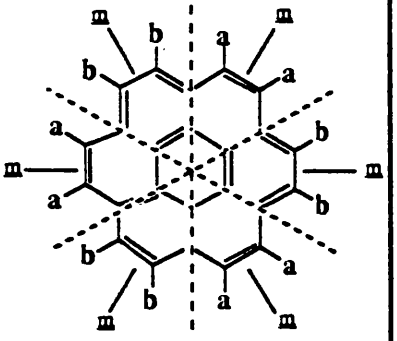
Structure representation assuming up/down 'peri' disposition (a= above plane; b= below plane)	Alternative symbolic representation*	$\phi^{+\cdot}$ note (i)	No. of N.E.C.s note (ii)	No. of switches	Point group
 Type I	U U U U U U	1	3	0	D_6
 Type II	M U U U	6	14	1	C_2
 Type III	M M U U	6	12	2	C_2
 Type IV	M U U W	6	14	2	C_2

Fig. 6.9. (continued)

 Type V	U U M U U M	3	7	2	D_2
 Type VI	U U M M M M	3	7	3	C_{2h}
 Type VII	U U M U U M	6	12	3	C_s
 Type VIII	U U M U U M	1	3	3	D_{3d}

* U= one (local) chirality;
M= opposite (local) chirality.

Notes: (i) ϕ^+ = the number of different legs or moieties;
(ii) N.E.C.= non-equivalent carbons.

From structural data of perchlorocoronene and host (139) only the *aabbaabbaabb* conformation has been detected. One can tentatively assume that this conformation must be the sole favoured form required for formation of crystalline inclusion compounds.

For uniform crystal growth of a clathrate one appropriate conformation must be present in sufficient concentration to allow crystal nucleus formation; and this conformation, assuming there are several present, must be replenished by sufficiently rapid conformational interconversion. If this conformation, here *aabbaabbaabb*, is present in too low a concentration the solubility product corresponding to crystallisation of a different conformation in a close-packed mode may occur leading to formation of an unsolvated crystal. In intermediate situations, co-precipitation may occur or, where another conformation can be randomly incorporated into the growth adduct crystal, an adduct exhibiting poor crystallinity may be formed.

Clearly, for dodecakis(3,5-dimethylphenylthio)coronene (139), for example, an optimal situation has been achieved, where the efficiency of packing in the clathrates is matched by 'clean' crystallisation of the *aabbaabbaabb* conformation, present in sufficient concentration in solution to exceed the adduct's solubility product without exceeding that of any other possible crystal form.

It may be that increasing the bulk of the side-chain moiety leads to a

greater number of less rapidly interconverting conformations, further complicating crystal growth. Significantly for more bulky side-chains, as in compounds (153), (157), (158), (159) and (161) exchange among different conformations is not yet at limiting fast exchange on the NMR time scale at room temperature, adding some credence to the possibility that the rate of conformational interconversion may be important. Fig. 6.10 and Fig. 6.11 show ^{1}H NMR spectra for (153) in toluene-d_8 as solvent at room temperature and 100°C respectively. There is an obvious sharpening of the *t*-butyl signal at 100°C, though rapid leg displacement is still not yet occurring, as is evident from the signal width.

Accordingly, with such a number of possible conformations, one may therefore offer a rationalisation for poor crystal growth. Indeed this was found in a number of cases, resulting in very little inclusion activity. Highlighted particularly by compounds (159) and (161), is the possible influence of low packing coefficients. These on deposition both form amorphous glassy materials from some solvents.

The lack of inclusion ability noted for compound (152) containing the 3,5-dimethoxyphenylthio side-chain moiety could be attributed to either the subtle change in shape, destabilising the adduct structure, incurred by introduction of the angular methoxy groups or, reflecting the more polar nature of the molecule, a different conformational distribution in solution.

Fig. 6.10. ^{1}H NMR spectrum of dodecakis(3,5-di-*t*-butylphenylthio)coronene (153) in toluene-d_8 as solvent at room temperature.

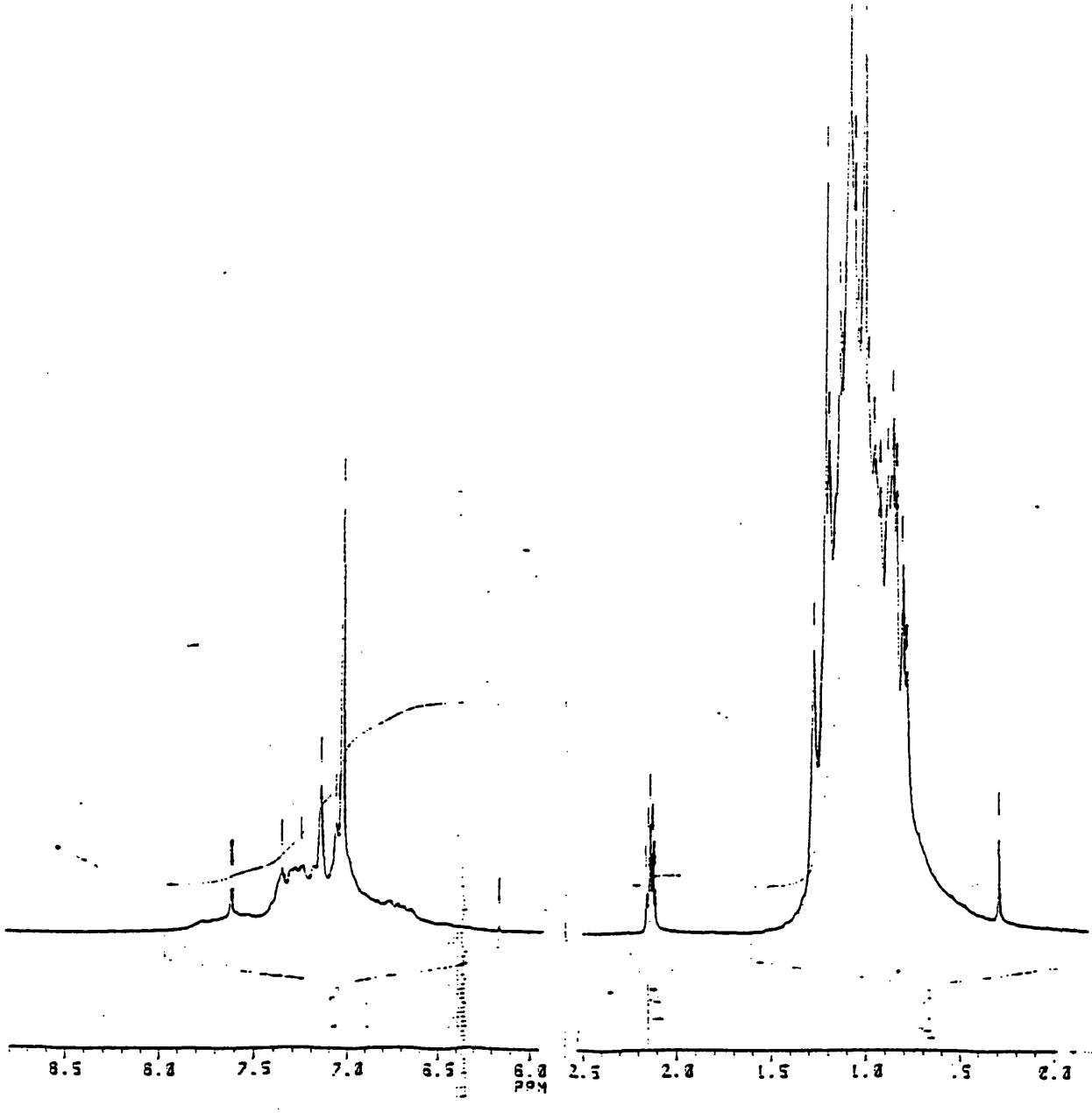
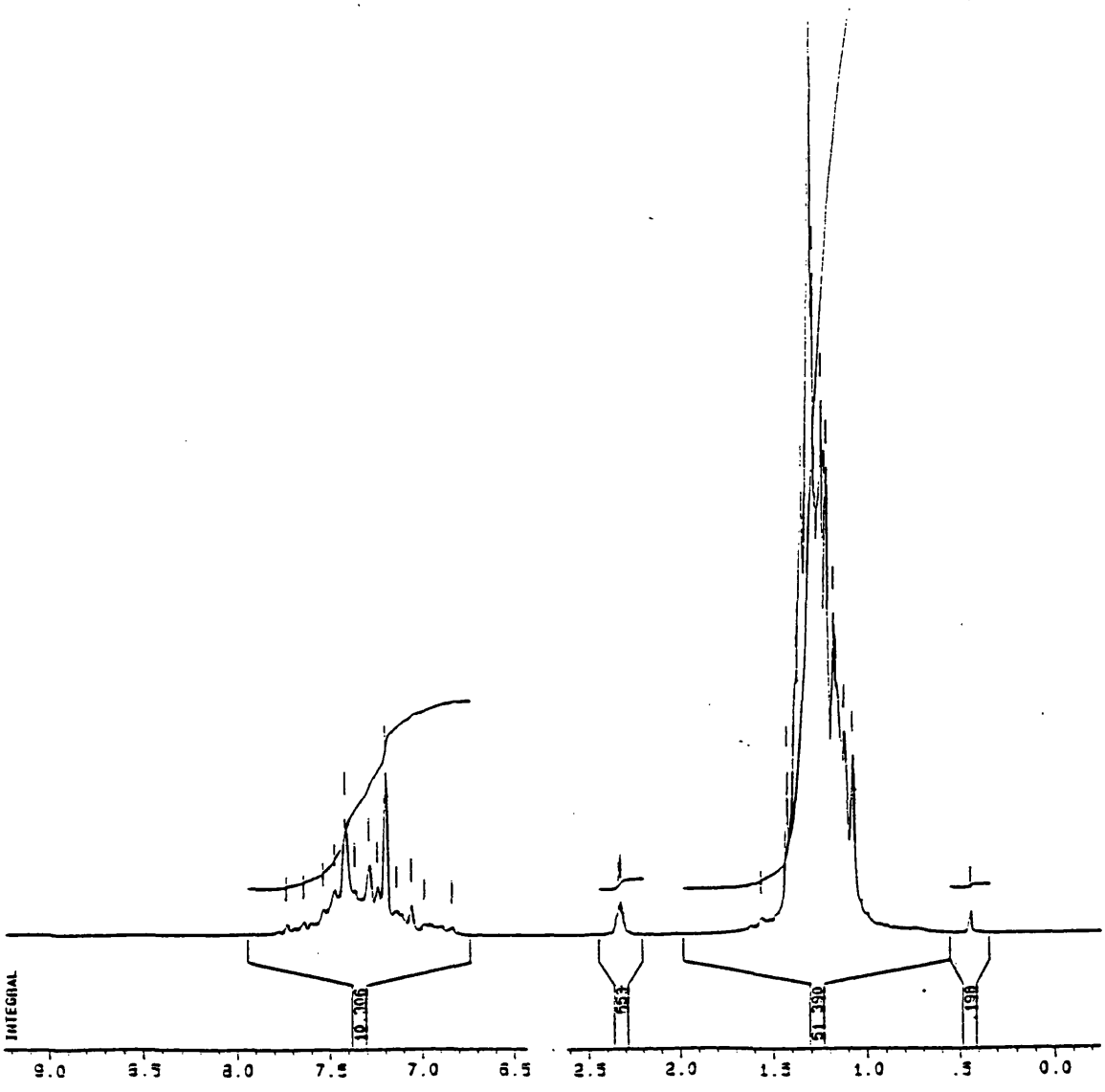


Fig. 6.11. ^{1}H NMR spectrum of dodecakis(3,5-di-*t*-butylphenylthio)coronene (153) in toluene-d_8 as solvent at 100°C.



In general most side-chain moieties, can be used to construct new clathrates. However, the coronene series proved more problematical, possibly for the reasons already mentioned.

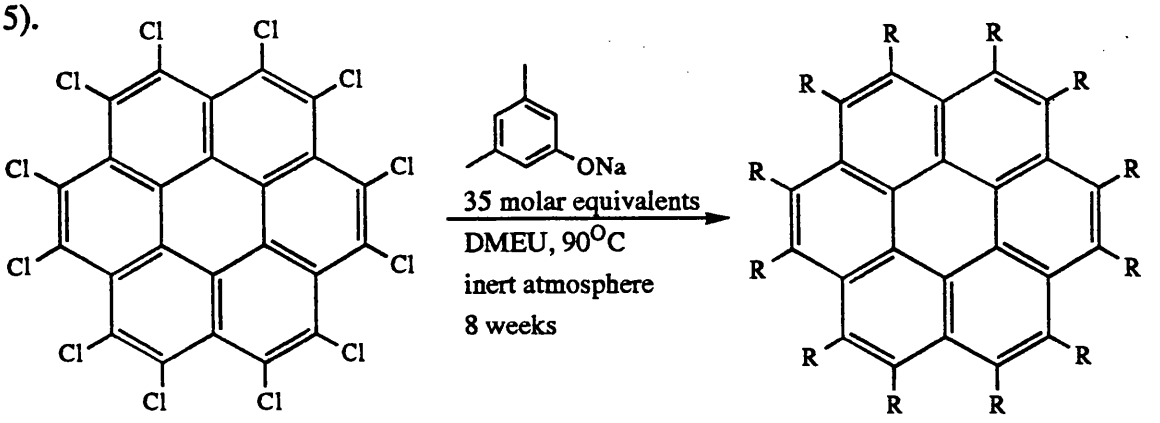
On the other hand, an initial optimisation of inclusion ability is less dependent upon design than on systematic screening. Having achieved a suitable "lead", one can then set about the deliberate design of an even more versatile clathrate by subtle modification of the favoured leg-shape. On this occasion, however, the first lead compound happened to be the most prolific inclusion compound.

6.5 Oxygen-based coronene hosts.

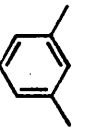
The extension to oxygen-based coronene hosts would seem the most obvious path to follow considering the successful development of oxygen-based hexa-host and spider-host series. An apparent stumbling block to this was the supposed "inertness" of perchlorocoronene to substitution by phenoxide nucleophiles.

An experimental finding, however, provided evidence to the contrary. It was discovered that reaction of perchlorocoronene with an impure thiophenolate salt, containing one-third ethoxide (in molar terms), gave a coronene partially substituted by ethoxide. This observation therefore suggested that under appropriate conditions perchlorocoronene should undergo complete substitution by phenoxide nucleophiles.

Using a procedure similar to that used in formation of spider-host[140] and hexa-host molecules[197], a new oxygen-based coronene host was prepared (Scheme 5).



Scheme 5.

(162) ; R = O- 

With the unparalleled success of the 3,5-dimethylphenyl moiety in the design of sulphur-based coronene hosts, a favoured nucleophile, 3,5-dimethylphenoxide was employed in the synthesis of prime candidate (162), a prospective oxygen-based coronene host.

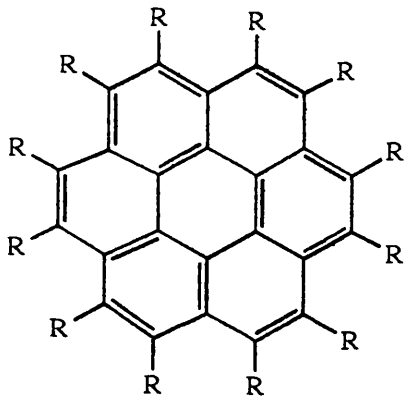
After 8 weeks the reaction mixture had assumed a dark brown colour. The work-up led to isolation of a dark green/brown fluorescent oil which by column chromatography gave a bright yellow fluorescent oil, compound (162).

Crystallisation of the material from 1,4-dioxane produced cube-like crystals, m.p. 291-292°C, containing 1,4-dioxane in a host-guest ratio of 1:5.5 (determined by ^{1}H NMR). The adduct was found to be unstable losing the guest completely over a period of 24 hours when left standing in air at room temperature. Further examination of the molecules inclusion behaviour was prevented by the low yield of pure product (18% yield), and the need to retain back-up crystals for an X-ray study of the clathrates' architecture.

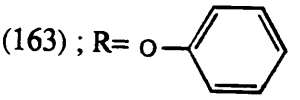
A preliminary X-ray investigation has so far furnished only unit cell dimensions.

The crystalline 1,4-dioxane adduct is monoclinic, with a = 16.430(10), b = 16.453(4), c = 24.420(10)Å, ß = 100.94(3)°, Z = 2 (host), and *ca.* 11 guest molecules.

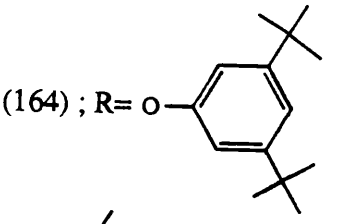
To expand the series, synthesis of new hosts containing favourable moieties was then attempted.



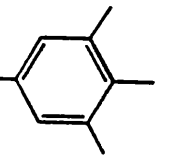
(163) ; R= O



(164) ; R= O



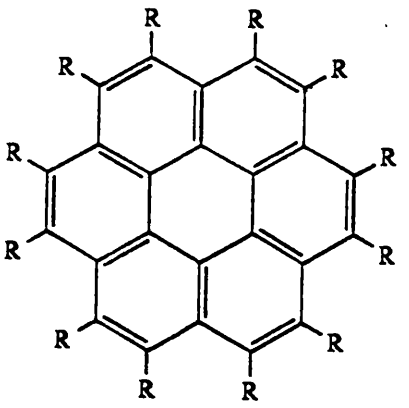
(165) ; R= O

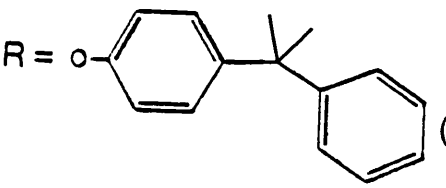


As a consequence of laboratory reorganisation the synthesis of compounds (163)-(165) had to be conducted over a 14 week period. This would have been of no consequence, had the reaction course paralleled phenoxide substitution of hexahalobenzene or octahalonaphthalene substrates. However, the fully substituted coronene appears sensitive to cleavage, hence a mixture of fully substituted and cleavage products was obtained. The mixtures proved too difficult to separate, therefore no further analysis was carried out.

Cleavage may also have occurred during the synthesis of host (162), though to a much smaller extent, accounting for the low yield.

To confirm that the isolation of host (162) had been no fortuitous occurrence, oxygen-based host (166) was prepared.





(166)

Reaction of sodium *p*-cumylphenoxide with perchlorocoronene under the usual conditions with a slightly reduced reaction time (see Experimental) gave (166), dodecakis(*p*-cumylphenoxy)coronene, yield 30%, m.p. >300°C.

Feather-like crystals were obtained after crystallisation from 1,4-dioxane and *N*-methylmorpholine; however recrystallisation of (166) from acetone produced rod-shaped crystals containing acetone in a host guest ratio of 1:10 (by ^{1}H NMR). Again, the adduct was found to be unstable losing all the guest component over 24 hours when left standing at room temperature.

An X-ray analysis was attempted at 120K : although the crystal was strongly diffracting, its unit cell dimensions were too large for accurate measurement, hence this study had to be terminated.

Lack of time prevented a further expansion of the oxygen-based host series.

In many ways, though, the oxygen-based hosts should prove to be a more extensive host series than their sulphur-based counterparts.

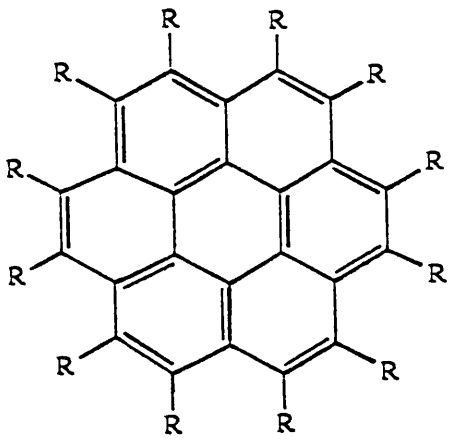
This is illustrated by the ability of compound (166) to act as a host - in contrast to its sulphur-based analogue (159).

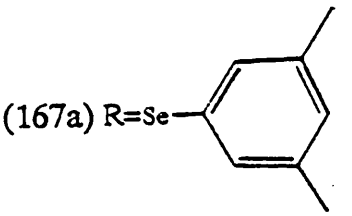
From this limited investigation it is not obvious which side-chain moiety produced the most versatile clathrate, however it is apparent that oxygen-based hosts have distinctly different inclusion characteristics from their sulphur-based analogues. This is evident from the host-guest ratios and the stability of the adducts. This dependence on chalcogen link atom, oxygen or sulphur, is also found in the hexa-host and spider-host series.

A full X-ray study, to be completed in the near future, should reveal a novel and exciting architecture for the 1,4-dioxane adduct of host (162). In addition, if the synthetic problem can be mastered then design of a more extensive series should be possible, facilitated by their case of purification.

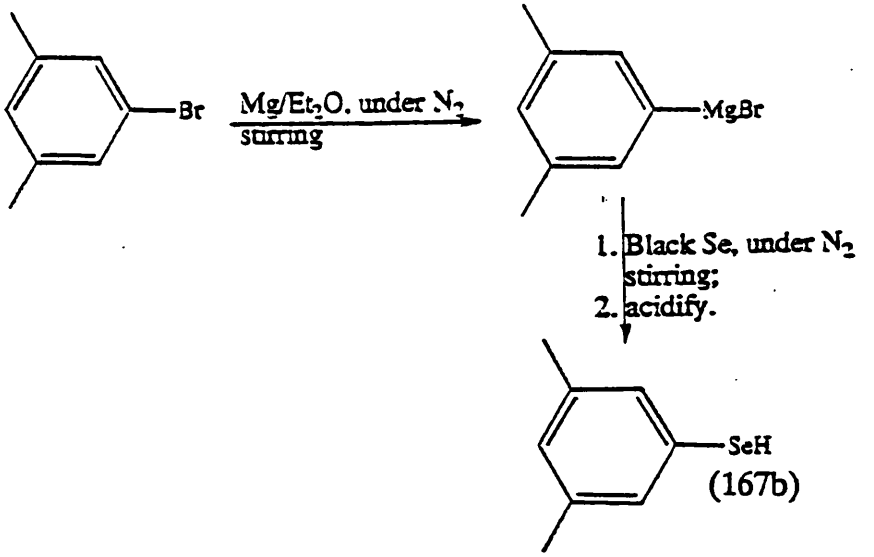
6.6 Attempted synthesis of dodecakis(3,5-dimethylphenylseleno)coronene (167a)

Following the success of the 3,5-dimethylphenylthio and 3,5 dimethylphenoxy side-chain moieties in host formation, an attempted synthesis of the attractive selenium analogue (167a) was initiated.





The selenol (167b) was prepared accordingly to a method developed by Forster[198] (Scheme 6).



Scheme 6.

Reaction of the selenophenolate under conditions similar to those used for sulphur-based coronenes (see Experimental), gave a promising red oil. Reverse-phase TLC, however, indicated the presence of many by-products; presumably cleavage products. Purification of this mixture by silica column chromatography proved unsuccessful - the selenium derivatives possibly being more susceptible to oxidation than the sulphur-based coronene hosts.

Other attempts at synthesis of compound (167a) included : reducing the number of molar equivalents of salt used; running the reaction in the absence of light and reducing the reaction time (see Experimental). On each occasion a mixture, probably comprised of cleavage products and the fully substituted compound, was obtained.

Isolation of the desired product was attempted by crystallisation from various solvents; hoping, by judicious choice of solvent, to obtain solely the fully substituted compound, possibly as an adduct. In all cases, however, the impure oil went rapidly into solution and subsequently gave no crystals; this was the case for solvents of polarity varying from cyclohexane to 1,4-dioxane. Purification by precipitation using solvent mixtures also proved to be unsuccessful.

The problematical isolation of the fully substituted compound (167a), prevented even a preliminary study of the molecule's inclusion properties, hence, regrettably, the work was discontinued. Selenium analogue (167a) still

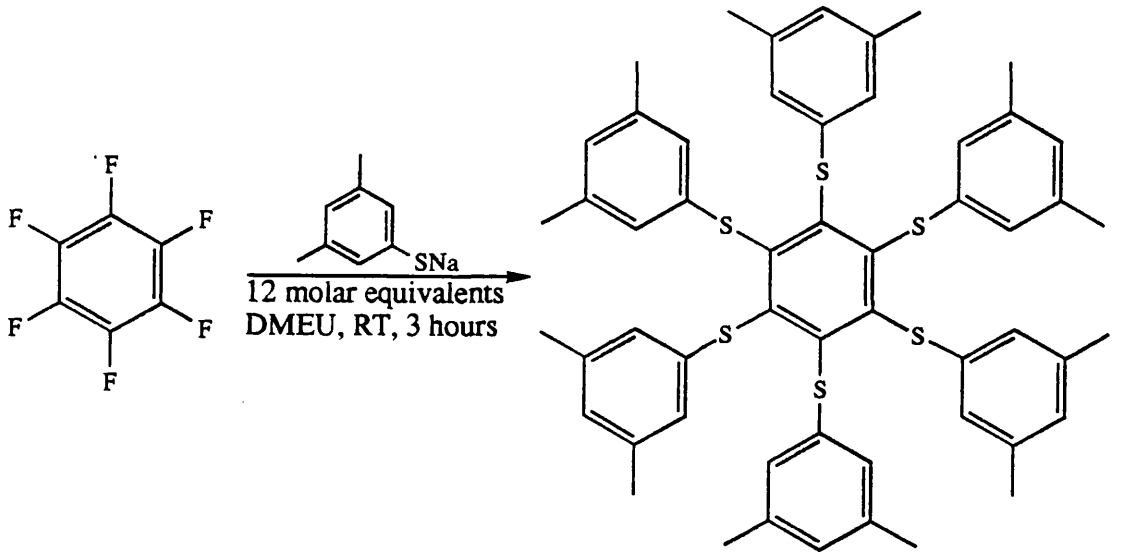
presents an attractive target, not only to complete the series but to see if exact crystallographic trigonal symmetry is realised in its potential adducts.

6.7 Hexa-hosts - how do these compare with side chain-related coronene hosts?

The similarity between hexa-host and coronene-based hosts has been discussed earlier, an important feature being that both central cores possess 3-fold symmetry.

The aim of the research at this point was to identify, if possible, any correspondence in crystal packing or inclusion properties between two separate host series; specifically between members of the hexa-host and coronene-based species possessing a common side-chain. Accordingly, having established the packing for the 3,5-dimethylphenylthio moiety on coronene, the hexa-host containing the same side-chain moiety was synthesised and its inclusion ability was investigated.

Synthesis of hexakis(3,5-dimethylphenylthio)benzene (168) was in accord with the procedure outlined below (Scheme 7).

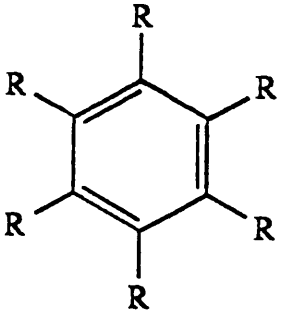


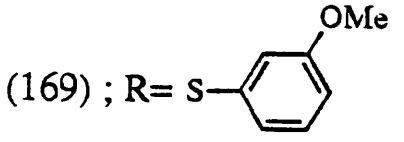
(168)

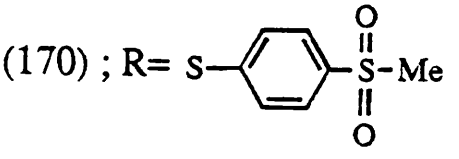
Scheme 7.

Following isolation and purification of (168) a number of inclusion experiments were carried out. Though the crystals themselves were highly crystalline, no inclusion was observed for (168). Disappointingly, an X-ray study of (168) was not possible, ruling out a more detailed analysis of the molecule's architecture.

Extending the investigation to *meta*- and *para*-substituted moieties, compounds (169) and (170) were synthesised.







As before, no inclusion was noted for either compound after crystallisation from different solvents. A marked reduction in crystallinity, though, was evident for both (169) and (170).

Such a brief investigation can only hint at possible similarities, or differences, between the hexa-host and coronene-based host molecule series; that

is, only comparison of crystalline nature and crystal habit is possible at present. However, when the results of further X-ray analyses become available patterns may emerge relating the structure of side-chain moiety to the versatility of trigonal host molecules.

CHAPTER 7

FINE-TUNING WITHIN THE SPIDER-HOST SERIES.

7.1 Design of a versatile sulphur-based octa-host

The spider-host series was established by MacNicol, Robertson and coworkers in the mid-eighties, and consolidated the relevance of molecular symmetry in design of new host molecules (Chapter 4).

The object of the present research was to optimise spider-host design by using subtle variations in "leg" shape, leading to more versatile hosts.

Synthesis of sulphur-based spider-hosts employing selected side-chain moieties had highlighted the *m*-tolylthio group as a "leg" presenting an ideal shape for inclusion design[193], the host forming tetragonal adducts with a range of different guest molecules.

The question remained as to whether this moiety or a closely related one, or, alternatively, a distinctly different one, would prove the most successful with respect to host versatility. Consequently the following compounds were synthesised (Table 14).

Table 14. A listing of newly synthesised sulphur-based octa-hosts.

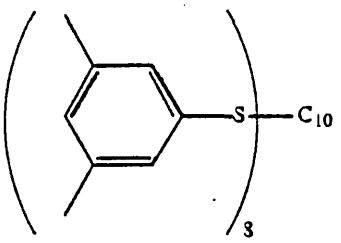
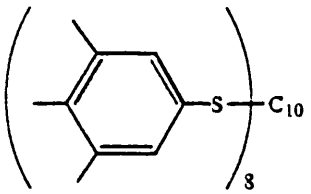
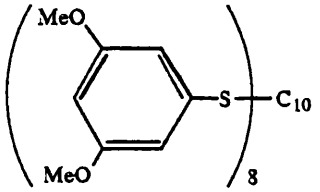
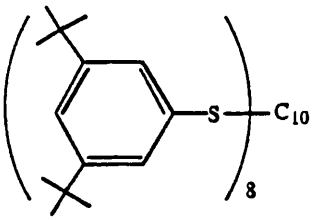
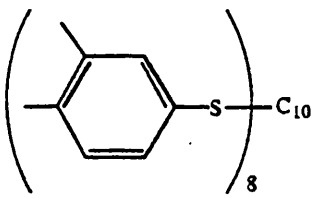
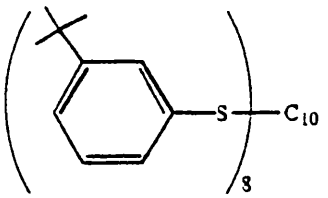
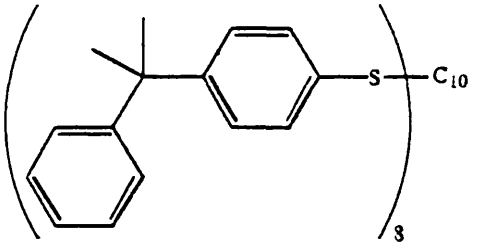
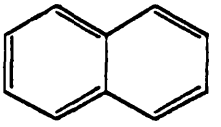
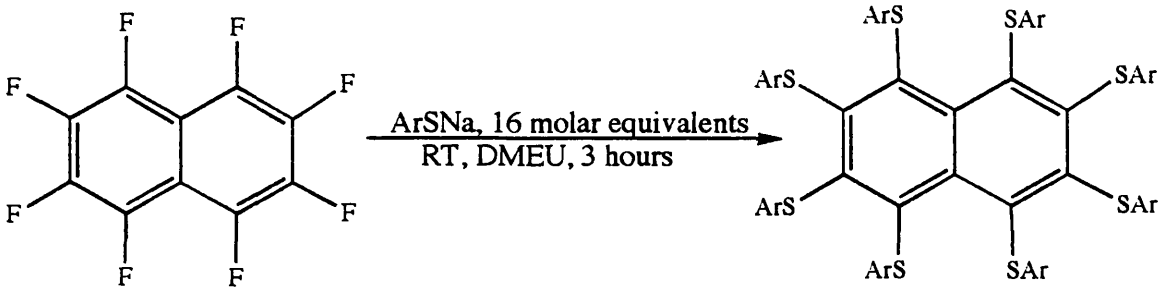
Octa-host	% Yield
 (171)	87.6
 (172)	93
 (173)	92.3
 (174)*	----
 (175)	82.2

Table 14. (continued)

 (176)	83
 (177)	81.2

C_{10} = naphthalene unit, 

Previously, reaction times of approximately 2 days were normally employed; however, it has now been found that reactions go to completion after a period of only 3 hours (Scheme 8).



Scheme 8.

The compounds all had ^{1}H and ^{13}C NMR, mass spectral and micro-analytical data fully in accord with their proposed structures, with the exception of compound (174), [see Experimental].

Compound (171), octakis(3,5-dimethylphenylthio)naphthalene, was purified by column chromatography and recrystallised from a 1,4-dioxane/methanol mixture to give unsolvated red crystals with well-defined morphology. Subsequent recrystallisations from toluene, dichloromethane, chloroform and numerous cyclic and acyclic aliphatic solvents revealed a complete absence of inclusion behaviour for (171). In most cases a red powder-like microcrystalline material was produced.

Similarly, compound (172), octakis(3,4,5-trimethylphenylthio)naphthalene, purified by triturating with diethyl ether, exhibited no guest incorporation. As before, crystallisation from the usual solvents led to formation of a close-packed unsolvated material.

Again, following this trend, octakis(3,5-dimethoxyphenylthio)naphthalene (173), purified by column chromatography, gave unsolvated orange microcrystalline material from a range of solvents, for example, cyclohexane, 1,4-dioxane, *N*-methylmorpholine, acetone, chloroform, dichloromethane and isopropanol.

To conclude this investigation pertaining to the relevance of 3,5 disubstituted moieties in design of versatile spider-hosts, a synthesis of compound (174), octakis(3,5-di-*t*-butylphenylthio)naphthalene, was attempted. After approximately 3 hours, a single yellow spot was recorded by TLC (silica). With no observable change noted for a further 2 hour reaction period, the reaction was adjudged to have gone to completion and was therefore terminated. Purification by column chromatography gave a yellow oil, which upon crystallisation from a 2:1 1,4-dioxane/methanol mixture produced crystals, possibly monoclinic or triclinic from their morphology, including 1,4-dioxane in a host-guest ratio of 1:4. The adduct was unstable, losing the guest over a period of 48 hours at room temperature.

The yellow colour of the product did not seem to concur convincingly with the fully substituted naphthalene, for substitution with other 3,5-disubstituted side-chain moieties had produced compounds red or orange in colour. Perhaps, though, the bulkier moiety could have forced the molecule into a conformation similar to the parent spider-host (Chapter 4).

The ^{1}H, ^{13}C and ^{19}F NMR data proved much more enlightening. The ^{1}H NMR spectrum Fig. 7.1, shows an aromatic region clearly identifying three distinctly different types of side chain moieties.

This is not compatible with a fully substituted spider-host but is fully consistent with three distinct pairs of side-chain in a hexa-substituted counterpart (174').

(174')

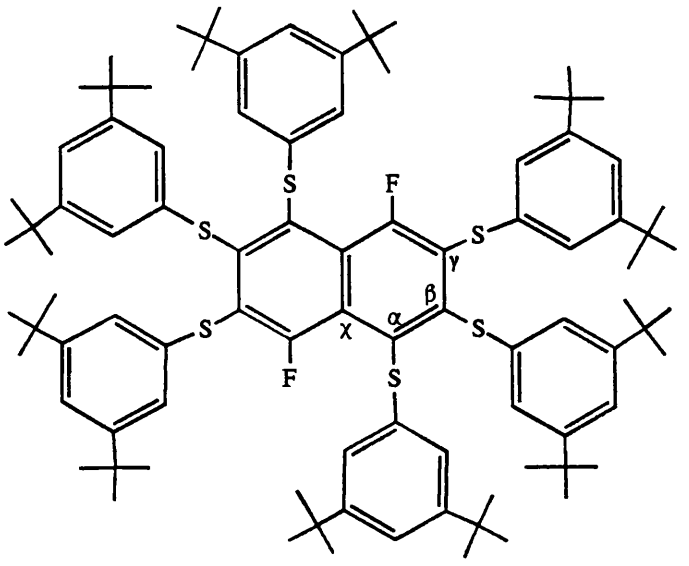
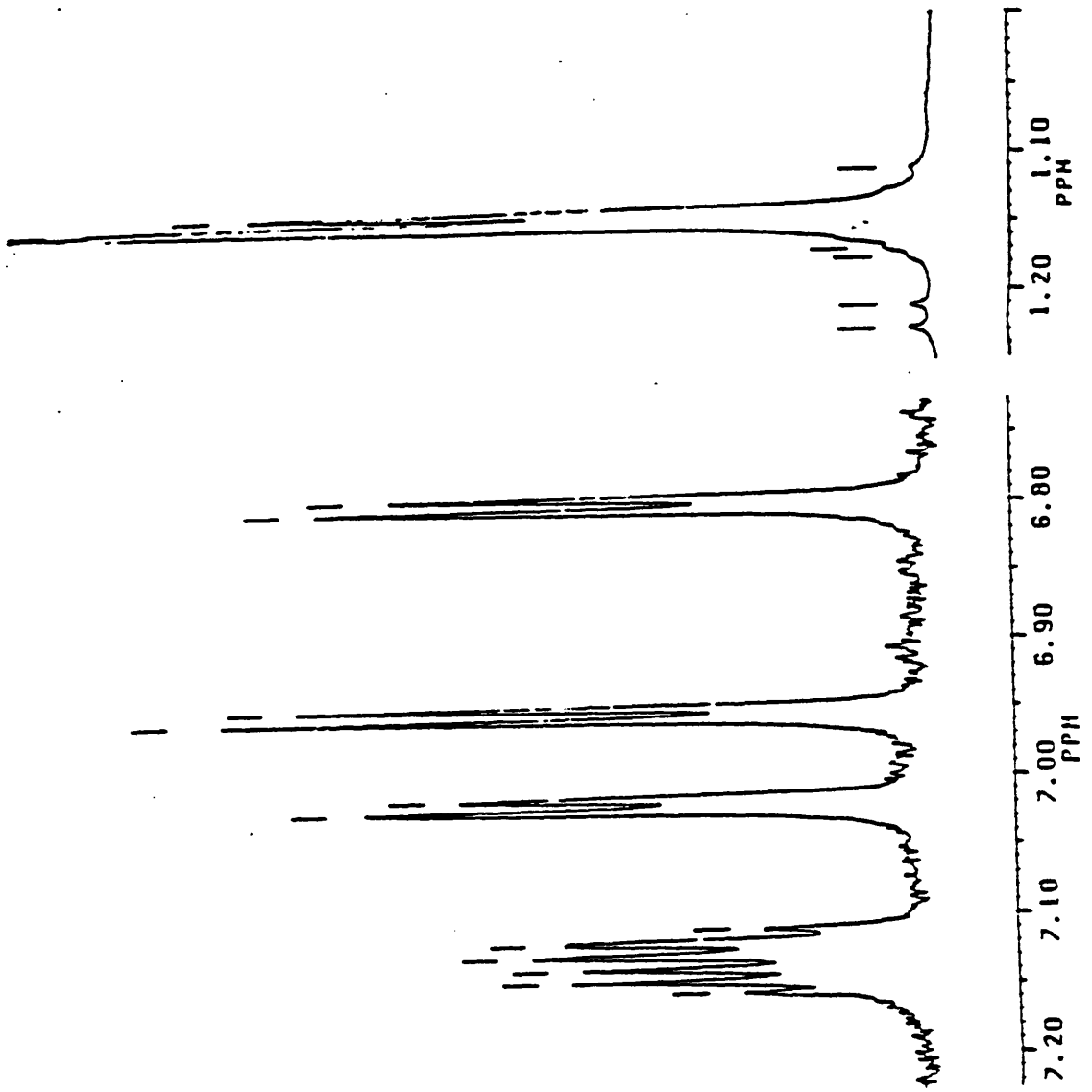


Fig. 7.1. ^{1}H NMR spectrum of partially substituted host molecule (174')



The ^{13}C NMR spectrum, Fig. 7.2, also shows the presence of three distinct moieties with three related signals at 123.53, 122.70, 122.19; and at 120.92, 120.34 and 120.09, δ_C, assigned respectively to the carbons *ortho* and *para* to sulphur on the side-chain moiety. A comparison of the central naphthalene core carbons for (174′) and the other spider-hosts show a non-conformity in shift values (Table 15). The χ carbon resonance is found at high field at 126, δ_C, entirely in agreement with the structure for (174′). Both the α and ß resonances at 136.9 and 135.9 show definite splitting consistent with coupling to fluorine, ^{19}F. The presence of a partially substituted host was confirmed by observation of a single fluorine resonance at -92.44 ppm in the ^{19}F NMR spectrum.

NMR evidence is consistent with the view that two (hindered) centro-symmetrically related *peri*-positions are unsubstituted as in (174′). In effect, the product could be regarded as an extended hexa-host.

However, it should also be pointed out that alternative structures having the fluorine atoms in the 2- and 6-positions or, the 2- and 7-positions or the 1- and 8-positions of the naphthalene cannot be discounted.

Fig. 7.2. ^{13}C NMR spectrum of partially substituted host molecule (174')

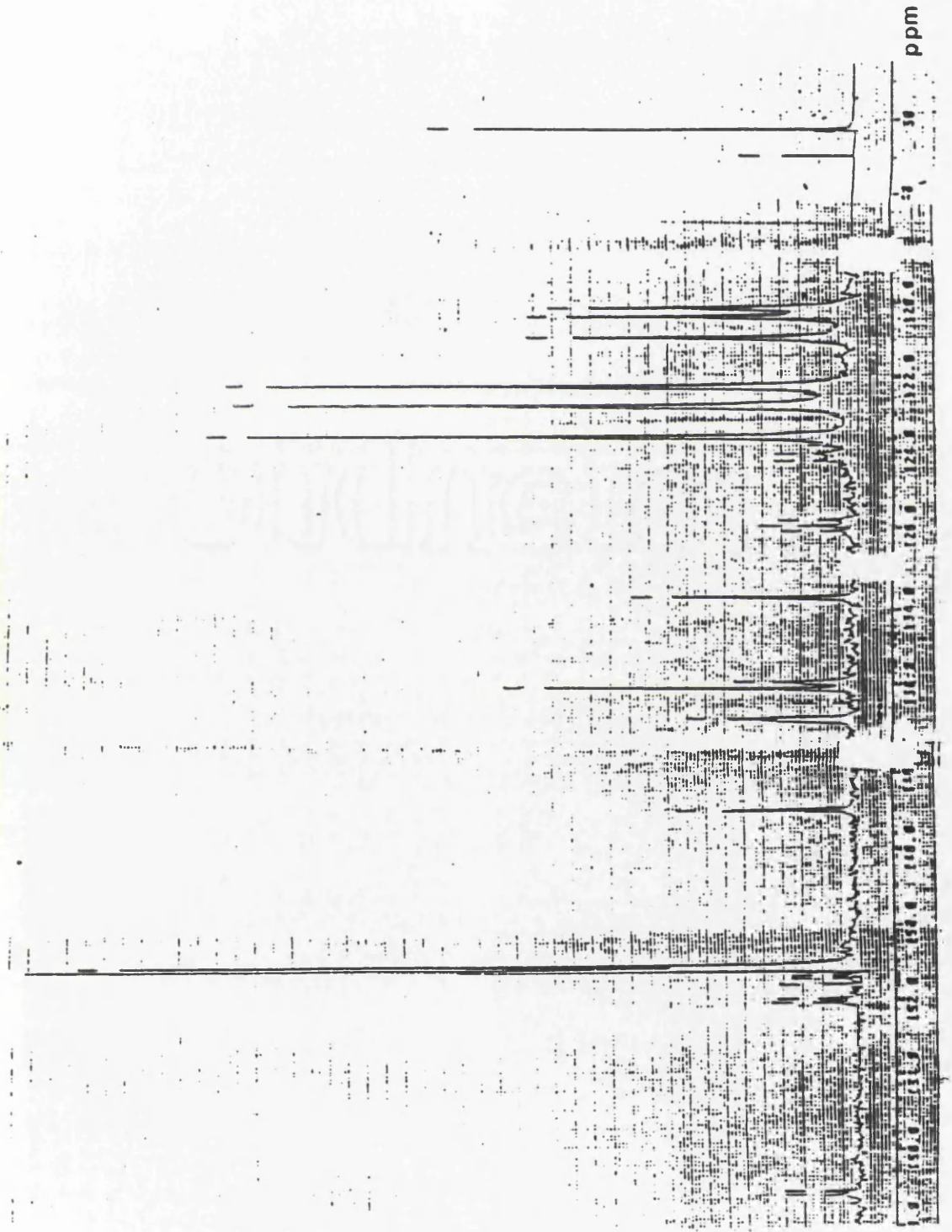
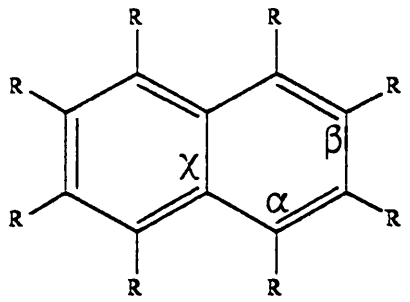


Table 15 : δ_C-Naphthalenes



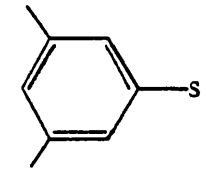
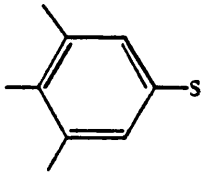
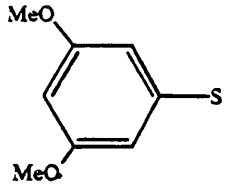
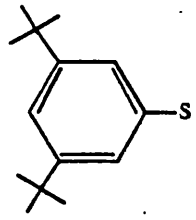
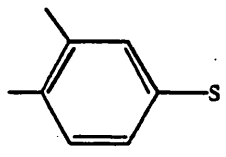
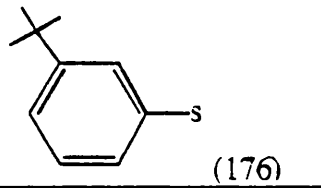
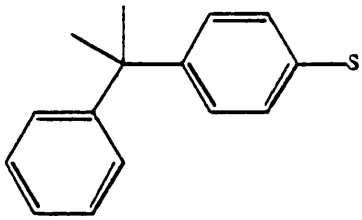
R	δ_C-χ	δ_C-α	δ_C-β	Solvent
H	133.9	128.3	126.1	$CDCl_3$
F	107.5	142.4	137.6	$CDCl_3$
 (171)	146.93	143.32	139.89	$CDCl_3$
 (172)	146.81	143.46	138.62	$CDCl_3$
 (173)	147.92	143.51	141.96	$CDCl_3$
 (174')*	124.10	136.90	135.90	$CDCl_3$
 (175)	144.69	140.35	139.86	$CDCl_3$

Table 15. (continued)

 (176)	144.76	140.75	140.18	$CDCl_3$
 (177)	143.64	139.55	135.65	$CDCl_3$

*Shift values corresponding to hexa-substituted naphthalene.

Returning to the true spider-hosts, it is apparent that the 3,5-disubstituted moieties present entirely the wrong side-chain shape for inclusion in general, let alone optimisation of inclusion behaviour.

A further exploration of the spider-host series involved focussing attention on moieties with a shape close to that of the *m*-tolylthio group. Consequently, octakis(3,4-dimethylphenylthio)naphthalene (175) was synthesised, m.p. 131-133 °C. The inclusion behaviour of (175) was immediately confirmed following purification by silica column using diethyl ether/40-60° petrol and diethyl ether/60-80° petrol as eluents. Overnight, fractions from both columns produced red cubic crystals containing 40-60° and 60-80° petrol fractions as guests. To probe the versatility of host (175), several inclusion experiments were undertaken, the results of which are shown in Table 16.

Table 16. Results of Inclusion Experiments for Spider-host (175).

Expt. No.	Solvent(s) of recrystallisation	Host-guest ratio †
1.	1,4-dioxane	1:1.9
2.	1,4-thioxane	1:1.9
3.	benzene	1:1.4
4.	toluene	1:1.4
5.	pyridine	1:1.5
6.	benzyl Alcohol	1:1.2
7.	*o*-xylene	1:1.2
8.	*m*-xylene	1:1.1
9.	*o,m,p* xylenes(equimolar mixture)	1:(0.33:0.33:0.33)
10.	*N*-methyl morpholine	1:1.3
11.	1,1,1-trichloroethane	1:1.6
12.	40-60° petrol/diethyl ether(10/1)	40-60° petrol incl.
13.	60-80° petrol/diethyl ether(10/1)	60-80° petrol incl.
14.	isopropanol/CS_2 (1/1)	1:1 Δ (isopropanol only)
15.	ethyl acetate	1:1
16.	DMF	1:1.5
17.	methyl ethyl ketone	1:1.2
18.	THF	1:1.4
19.	triethyl orthoacetate*	2:1
20.	triethyl orthoformate*	2:1
21.	isobutyrophenone	1:1
22.	H.M.P.A.	1:0.33

† Host-guest ratios determined by ^{1}H NMR.

Δ Inclusion of isopropanol determined by ^{1}H NMR and IR.

* In both cases, recrystallisation resulted in hydrolysis of the proposed guest. Crystallisation from triethyl orthoformate led to complete hydrolysis and inclusion of ethanol and ethyl formate in a host-guest ratio of 2:(0.667:0.33). Crystallisation from triethyl orthoacetate led to inclusion of ethanol, ethylacetate and triethyl orthoacetate.

All adducts reported for host (175) were highly crystalline, the crystals being cubic in shape and stable to guest loss.

Without doubt, compound (175) must represent the most versatile spider-host discovered to date. The *m*-tolyl spider-host, for example, crystallises unsolvated from toluene; whilst host (175) retains this solvent as guest with a host-guest ratio of 1:1.4. Recrystallisation of (175) from an equimolar mixture of *o*-, *m*-, and *p*-xylene produced no evidence for pronounced selective guest inclusion by (175); all three xylene isomers being trapped in roughly equal proportions.

The inclusion evidence so far does, however, suggest that molecule (175) could be an excellent candidate for storage of volatile materials (*cf.* Chapter 5).

X-ray study of host (175)

The highly crystalline toluene adduct is cubic, space group $Pn\bar{3}$, with a = 22.544Å. The structure was refined to a final R-factor of 9%, though the disordered guest was not located.

Within this adduct the host molecule (175) adopts the *aabbaabb* conformation (Fig. 7.3), the same conformation as that found for octakis(*m*-tolylthio) naphthalene in its 1,4-dioxane adduct (and the isomorphous unsolvated crystal).

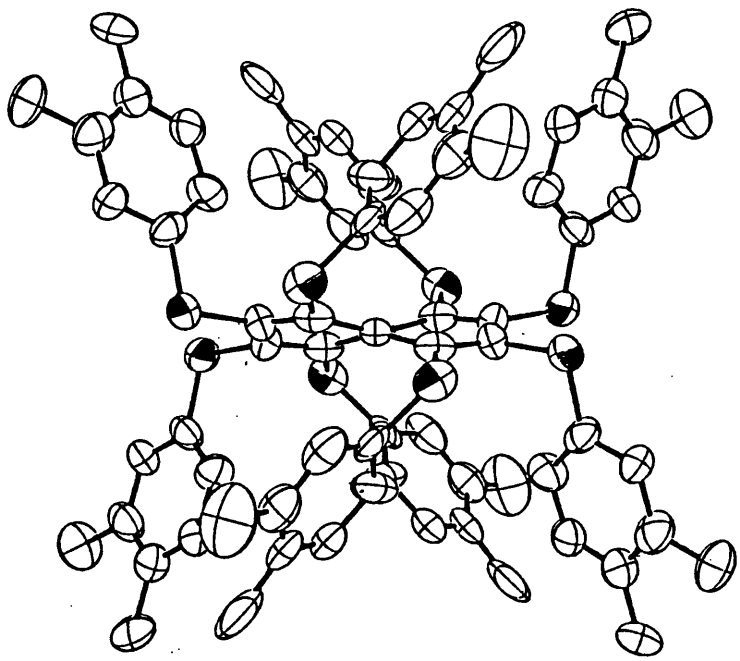


Fig. 7.3. View illustrating the molecular structure of host (175) in the solvated cubic crystal.

On the other hand, the crystal packing in the toluene adduct of (175) is quite distinct from that in the 1,4-dioxane adduct of its *m*-tolyl spider counterpart. The latter has a sheet-type host packing, with separate molecules approaching each other edge-on as shown in Fig. 7.4.[193]

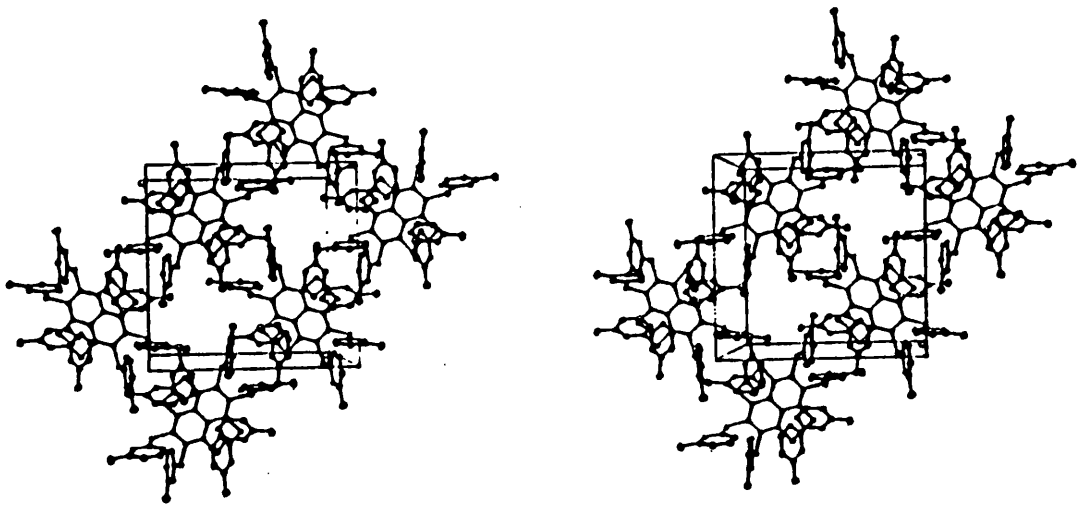


Fig. 7.4. A stereoview, looking down *c* showing the molecular packing of octakis (*m*-tolylthio)naphthalene in its empty-cage form.

In contrast, for (175), adjacent molecules of the host do not approach each other with the above relative disposition. This can be appreciated by careful inspection of the stereoview of the toluene adduct (Fig. 7.5). The packing in this case, appears to be dense around (½ ,½ ,½); therefore the disordered guest is probably located along a 3-fold axis, approaching (0,0,0).

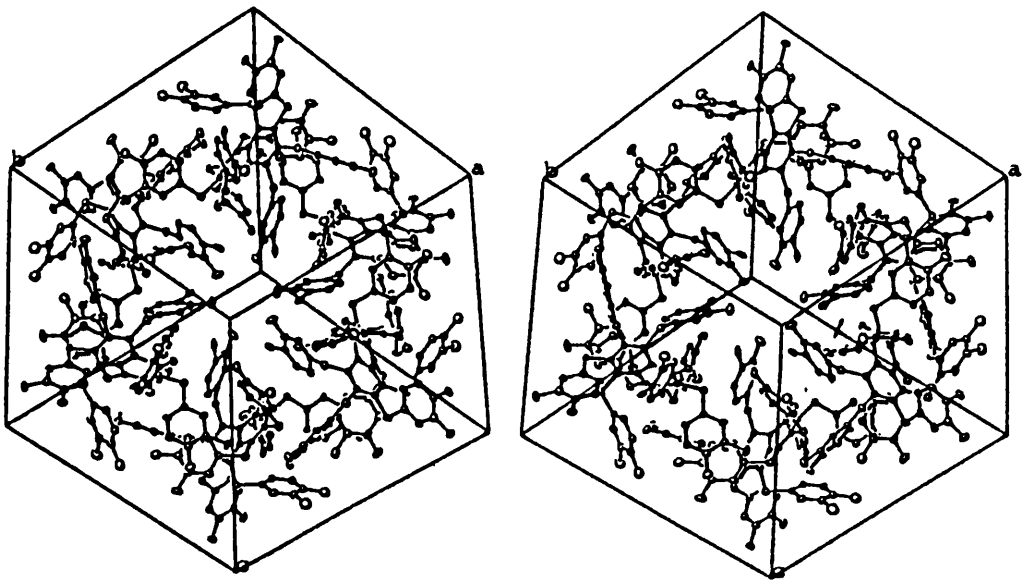


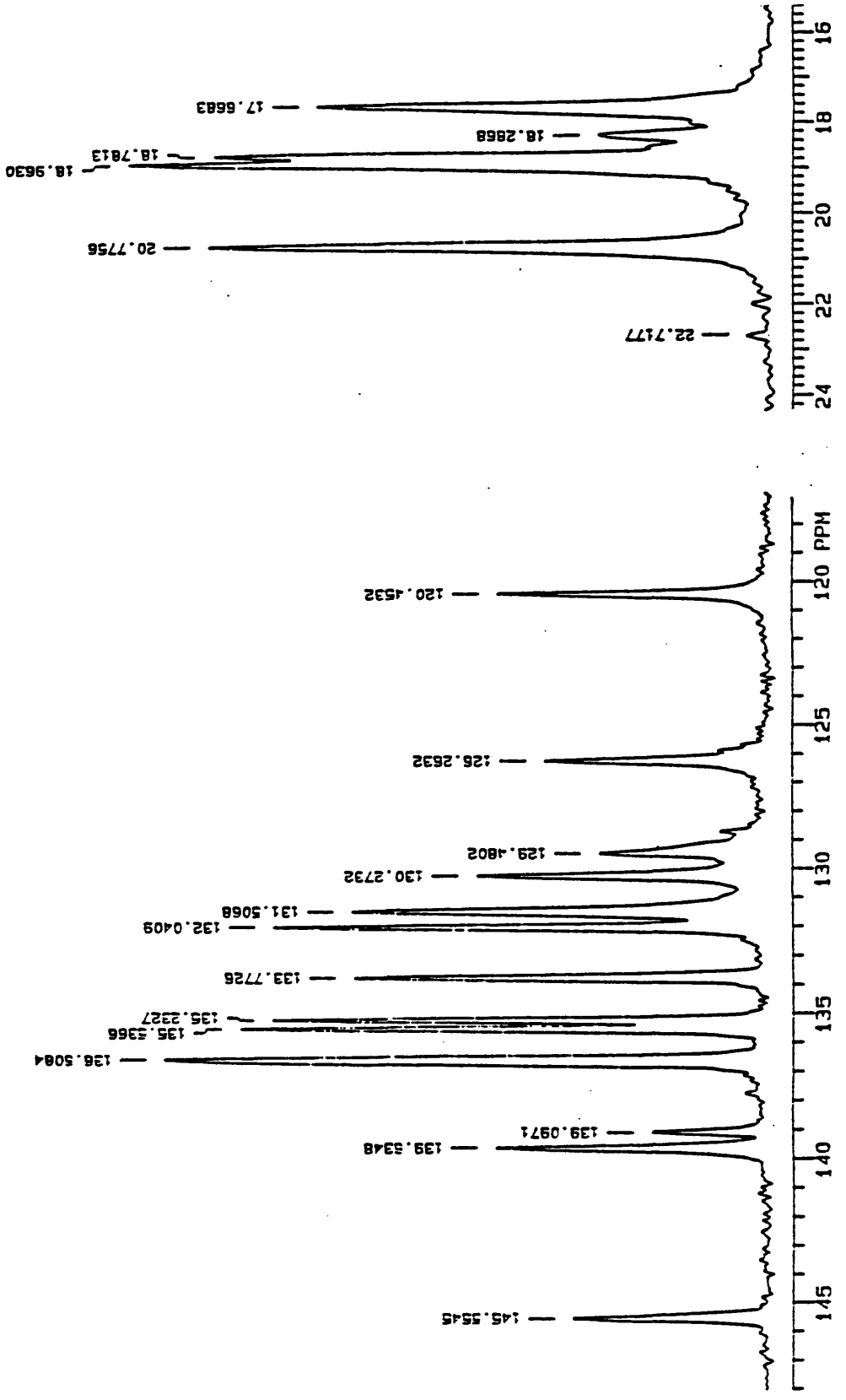
Fig. 7.5. A stereoview showing the molecular packing of host molecule (175)

Solid-state ^{13}C NMR spectra of the toluene and 1,4 dioxane adducts of (175)

Solid-state ^{13}C NMR studies are entirely consistent with the X-ray data for host (175), as $\underline{D}_2$ symmetry figures prominently in the host resonances.

For the toluene adduct of (175), five methyl signals are noted (Fig. 7.6). The additional methyl signal at δ_C, 18.3, may indicate the presence of unfilled cavities as expected from the non-stoichiometric host-guest ratio (Table 16). Six protonated carbon signals are observed in the range 120.4 - 131.5 δ_C; also, the carbon atoms of the central naphthalene core α, ß and ring-fusion type, are found as singlets at 139.6, 139.1 and 145.5 δ_C respectively. All of this evidence corresponds with the $\underline{D}_2$ conformational symmetry of host molecule (175).

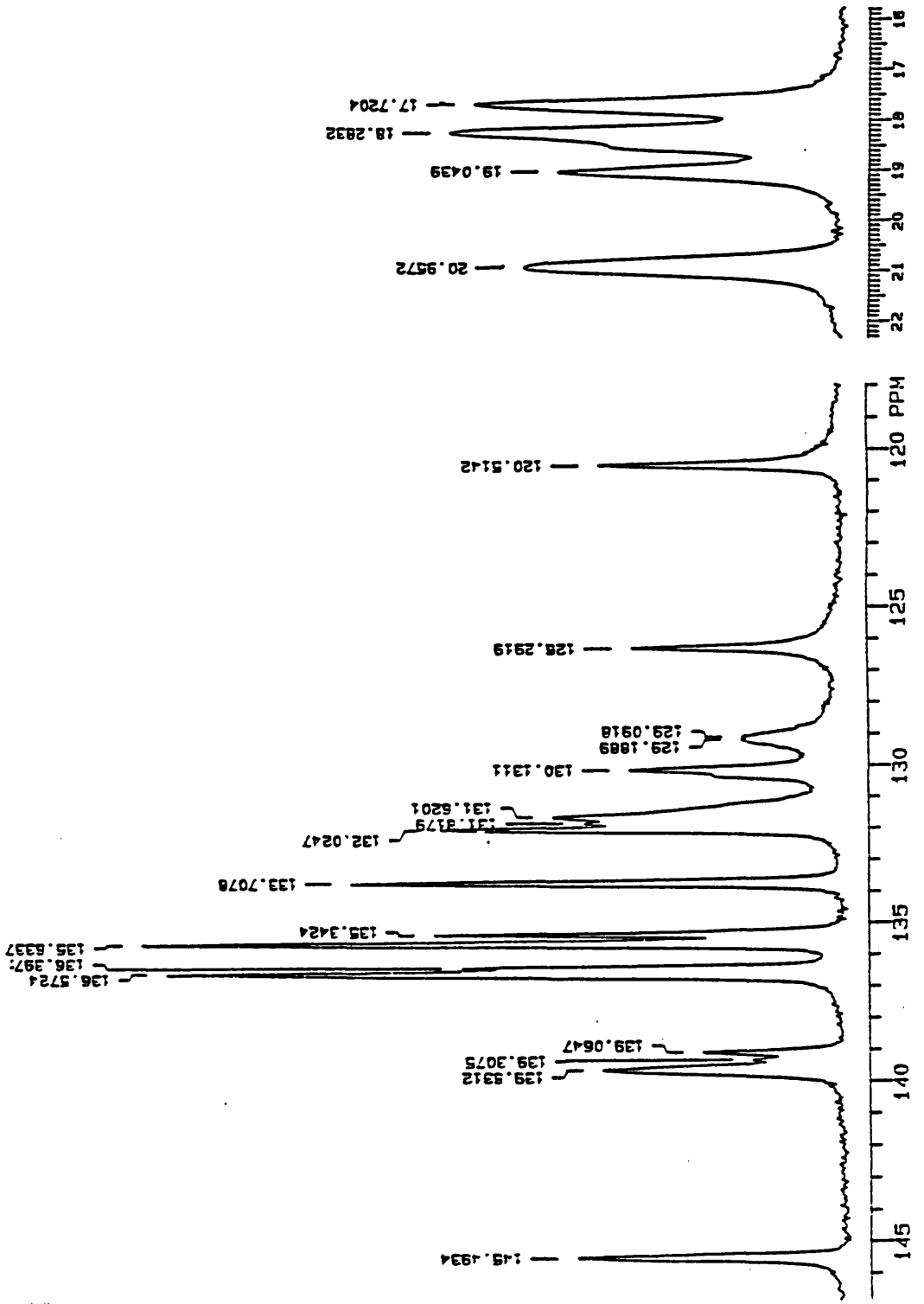
Fig. 7.6. ^{13}C Solid state CPMAS spectrum of octakis(3,4-dimethylphenylthio)-naphthalene (175) (toluene adduct).



A similar pattern is found in the ^{13}C solid-state NMR spectrum of the 1,4-dioxane adduct of (175) (Fig. 7.7). Better definition is evident in this spectrum, probably owing to a higher guest occupancy. In this case, only a small shoulder is found on the signal at δ_C , 18.3, almost certainly reflecting fewer unfilled cavities in the 1,4-dioxane clathrate of (175) (Table 16).

In both spectra a strong γ effect can be seen for one of the carbons *ortho* to the sulphur in (175); this results in a strong upfield shift to 120, δ_C. Thus, the above assignments are in good agreement with exact $\underline{D}_2$ symmetry for the host molecule octakis(3,4-dimethylphenylthio)naphthalene (175) in its toluene and 1,4-dioxane clathrates.

Fig. 7.7. ^{13}C Solid-state CPMAS spectrum of octakis(3,4-dimethylphenylthio)naphthalene (175) (1,4-dioxane adduct).



The uniqueness of host molecule (175) is characterised by the space group, $Pn\bar{3}$, of the adducts formed. In general, those hosts which form adducts of high symmetry (space group commonly $R\bar{3}$), for example, hydroquinone or Dianin's compound (Chapter 1), tend to be extremely versatile hosts.

The clathrates formed by (175) possess the highest crystal symmetry of any purely organic inclusion compounds discovered thus far; also this host includes a wide range of guests. Additionally, host molecule (175) was not discovered by chance, but was obtained by structurally directed synthesis.

To underline the extent to which inclusion behaviour depends on side-chain shape, a recent synthesis[199] of a spider-host containing the 5-indanethio side-chain led to complete loss of inclusion behaviour. Therefore by formal introduction of a bridging methylene group between the methyls of (175), one loses the open crystalline architecture of (175) and hence its inclusion capacity.

The following two hosts, (176) and (177), concluded the design work on the spider-host series, and further strengthened the concept of the premier importance of side-chain shape within design.

Octakis(*m*-*t*-butylphenylthio)naphthalene (176), contains a bulky moiety in favoured *meta* position. Only *N*-methylmorpholine was found to form an adduct with (176); an observation which is in total agreement with design work

on sulphur-based coronene hosts: that is, an increase in the bulk of the side-chain moiety consequently reduces the crystal-forming ability.

Similarly, octakis(*p*-cumylphenylthio)naphthalene (177) gave unsolvated feather-like crystals after recrystallisation from solvents such as 1,4-dioxane, chloroform, dichloromethane and *N*-methylmorpholine. However, from a dilute solution of acetone, compound (177) did give a 1:1 inclusion compound with this solvent.

To summarise, the results here mirror those obtained in design of coronene hosts. That is to say, selected side-chain moieties are key determinants for the formation of open crystalline structures, since these structural components favour certain conformations during crystal growth, and, presumably disfavour alternative low-energy, close-packed packing modes.

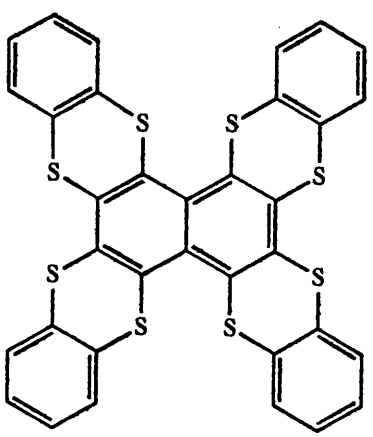
The optimisation of inclusion ability, in this case, was by design rather than by chance, with the favoured moiety corresponding to a 3,4-substitution pattern in the side-chain.

In contrast, the 3,5 dimethylphenylthio side-chain, corresponds to a compound completely devoid of inclusion ability. All of which leads to a crude caveat relating to a prediction concerning optimisation of host properties.

This is : a highly favoured side-chain for one series cannot be blindly assumed to be highly effective in another. For example, whilst the 3,4-dimethylphenylthio side chain is highly favoured in the C_2 naphthalene series, it is the 3,5-dimethylphenylthio moiety which is the most effective in the C_3 coronene series, this latter side-chain being totally ineffective in the spider-host context.

7.2 Attempted synthesis of the novel naphthalene host (178).

The most versatile spider-hosts, containing the *meta*-shaped moieties, form adducts which crystallise in the *aabbaabb* conformation. Presumably if one could enforce such a conformation by employing suitable substitution, then inclusion should be favoured. An attractive building block appeared to be benzene-1,2-dithiol, as its sodium salt. The synthesis of (178) proved rather more difficult than expected, however.



(178)

Using normal conditions for spider-host formation, no colour change was observed over a period of 10 days. This indicated that the nucleophilicity of the dithiolate anion must be markedly less than that of a monothiolate anion. One possible explanation for this is that chelation of the two sulphur anionic centres to the sodium cation could lead to tight ion pairing, which would reduce nucleophilic power.

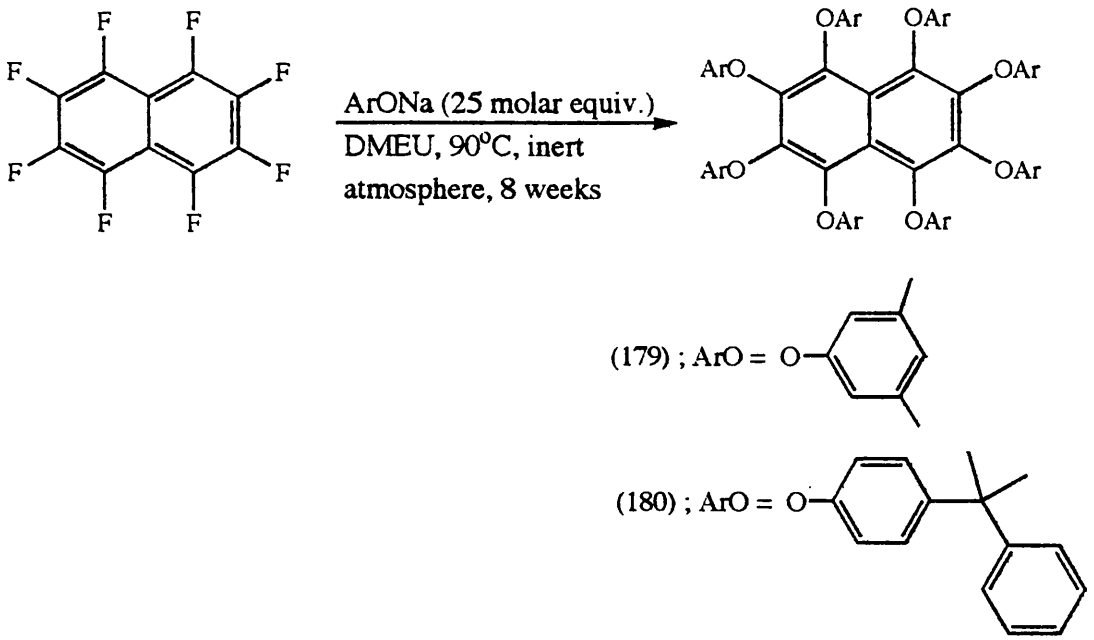
To overcome this problem more severe conditions were chosen; the reaction temperature was increased to 65°C and double the quantity of salt used (Experimental). After approximately 5 weeks the reaction mixture had attained a yellow colour. Isolation of the product was then accomplished by extracting with copious amounts of toluene. The yellow sand-like material recovered had a melting point > 300°C and was found to be insoluble or at best, very sparingly soluble in all the many solvents tried. A strong parent ion was found by mass spectroscopy, *m/e* 680 and a single spot by TLC (silica); the microanalysis was not, however, in good agreement with the proposed structure. The insolubility of this compound, favoured structure (178), prevented any ^{1}H NMR analysis.

In light of the above, the identity of the product cannot be taken to be established with certainty, though its mass spectrum indicates that it has structure (178) or one isomeric with this. To date, this compound has shown no evidence of adduct formation.

7.3 Oxygen-based spider-hosts.

A brief excursion into design of oxygen-based spider-hosts was made in order to elucidate further the differing inclusion properties of ether-hosts compared to their thioether counterparts. Evidence for such a dependence on link atom, O or S, has already been uncovered during design of coronene-based hosts (Chapter 6).

Two key moieties were selected for synthesis of new spider-hosts (179) and (180), to demonstrate this difference in host characteristics (Scheme 9).



Scheme 9.

Octakis(3,5-dimethylphenoxy)naphthalene (179) was purified by recrystallisation from 1,4-dioxane. Subsequent recrystallisations from 1,4-dioxane

gave colourless crystals (possibly monoclinic or triclinic from their crystal habit) containing 1,4-dioxane with host-guest ratio of 1:1. This adduct was unstable, losing all of the guest component over a 48 hour period at room temperature. A further brief investigation of the inclusion ability of (179) failed to uncover any new adducts.

Octakis(*p*-cumylphenoxy)naphthalene (180) was isolated in a similar manner by recrystallisation from a 1,4-dioxane/methanol mixture. Examination of the inclusion ability of (180) led to isolation of adducts with 1,4-dioxane, *N*-methylmorpholine and toluene. The first two adducts had a host-guest ratio of 1:4, whilst the latter had a host-guest ratio of 1:2. The crystals of all adducts were of X-ray quality, but were unstable in air, losing all guest component over 2 days at room temperature. The morphology of these adducts appeared consistent with monoclinic or triclinic crystal systems.

Once again, the results here for (179) and (180), confirm the pronounced difference between sulphur- and oxygen-containing host molecules for two distinct host series. Compound (179), forming a clathrate readily with 1,4-dioxane unlike its octathioether analogue (171), and (180), demonstrating a significantly greater versatility than its sulphur counterpart (177), establish the point in question.

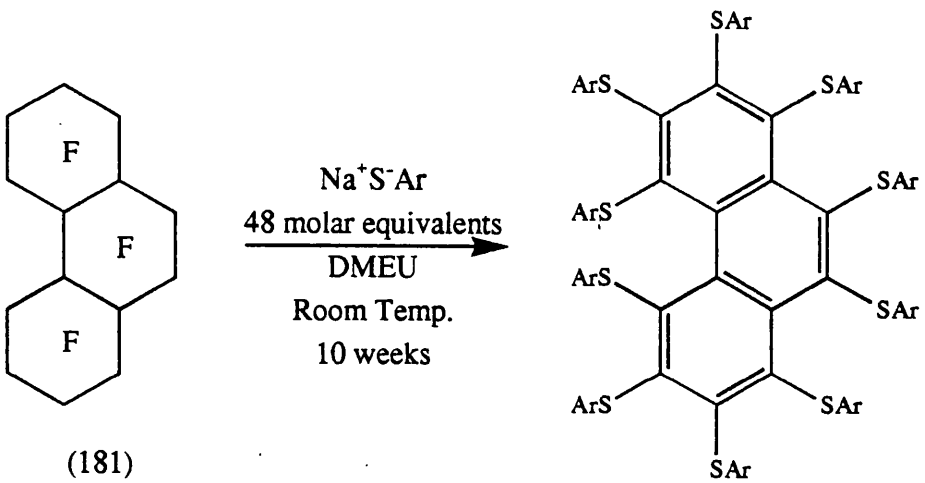
CHAPTER 8.

A NOVEL FLUOROCARBON REACTION - STUDY OF NEW SUBSTRATES.

8.1 Background to novel fluorocarbon reaction

Prior to 1986, saturated fluorocarbons were regarded as almost totally inert materials - reactions were found to occur only under very extreme conditions, for example, at 500°C with molten sodium. This property led to many applications from non-stick surfaces to blood substitutes.[200]

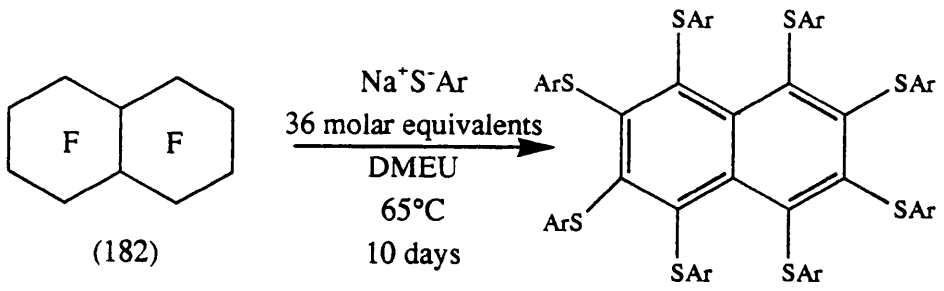
The inertness was more or less accepted until MacNicol and McGregor in 1986[201] found by chance that perfluoroperhydrophenanthrene (181) was completely, albeit slowly, aromatised and persubstituted by arene thiolate nucleophiles in DMEU (Scheme 10). This discovery of a novel reactivity was confirmed spectroscopically but no X-ray work was attempted at this time.



(181)

Scheme 10.

MacNicol and Robertson then extended study of this novel reactivity to perfluorodecalin (182),[202] reasoning that aromatisation and substitution should occur to produce a spider-host by a very novel route. Experimental results, backed by a single-crystal X-ray analysis, proved this to be the case. Optimal reaction conditions are shown below (Scheme 11).



Scheme 11.

Limitations to the reaction were noted from a more extensive investigation : (a) the fluorocarbon must possess a tertiary centre otherwise no reaction will occur, for example, perfluorocyclohexane was found to be completely inert; (b) the temperature must not be raised above 70°C, to prevent decomposition of the product by side-chain cleavage.

To explain this novel reactivity, three reaction mechanisms were considered (Fig. 8.1). The initial stage, proceeding to a possible monoolefin intermediate,

could occur by three distinct routes:-

(a) S_N2 attack at carbon, $S_N2(C)$.

(b) S_N2 attack at fluorine, $S_N2(F)$.

(c) Single electron transfer (SET).

Normally, fluorinated systems are resistant to $S_N2(C)$ attack; displacement of fluoride from CF_3 or CF_2H by attack at carbon with an external nucleophile has not been unambiguously established.

Similarly, no examples exist for direct $S_N2(F)$ attack when fluorine is attached directly to carbon in any fluorinated molecule.

The most likely mechanism is of the SET-type, favoured particularly by the high electron affinities of cyclic saturated fluorocarbons.

Initiation of the reaction is envisaged to occur at the tertiary centre possessing the greatest electron affinity. Two modes of electron transfer are possible leading to the intermediate bridgehead anion (Fig. 8.1). The mono olefin is then formed; immediately followed by aromatisation and persubstitution to produce a new spider-host by a novel route (Fig. 8.2).

Fig. 8.1. Novel reactivity of perfluorodecalin : alternative pathways to proposed intermediate perfluoroalkene.

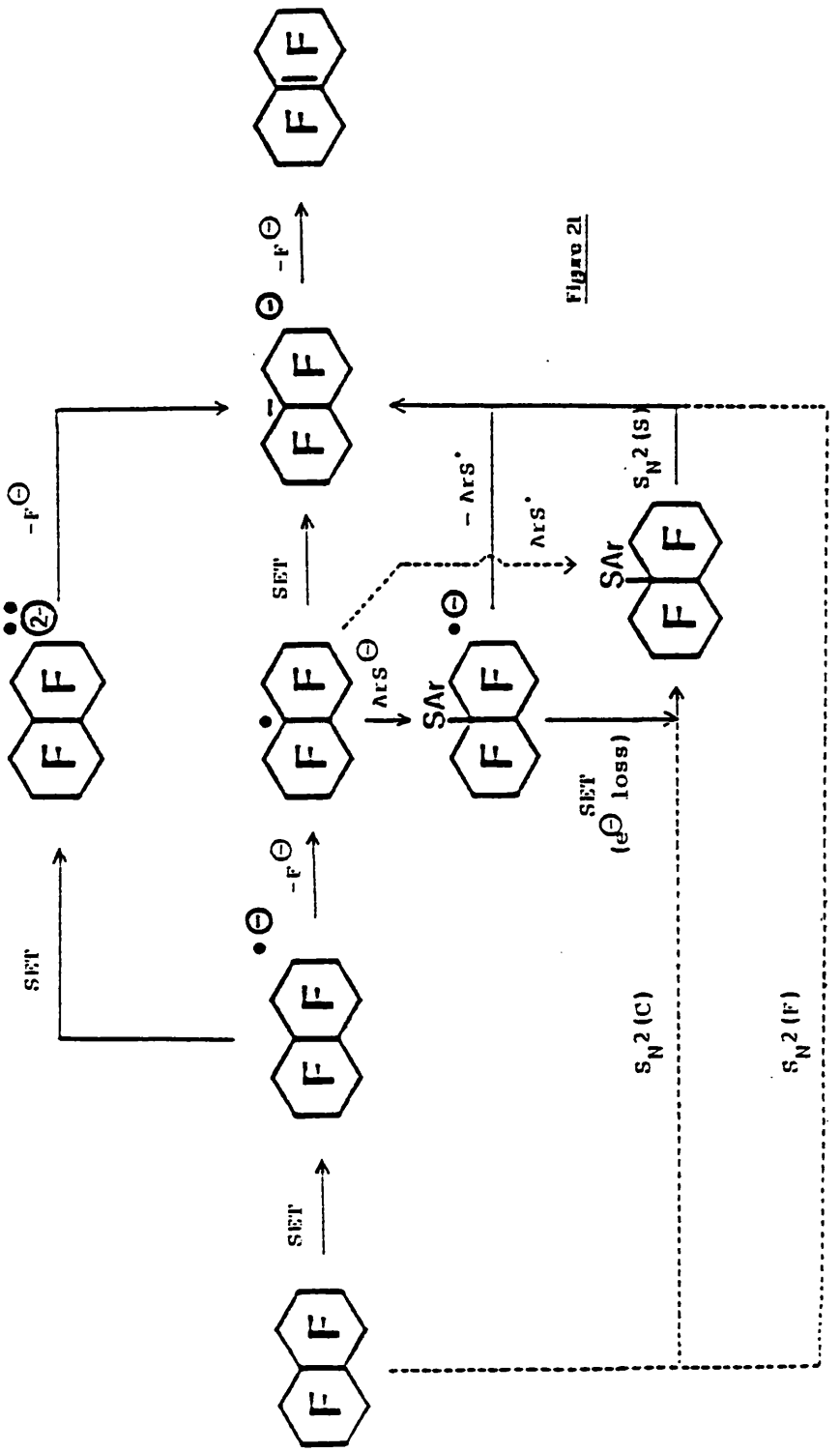
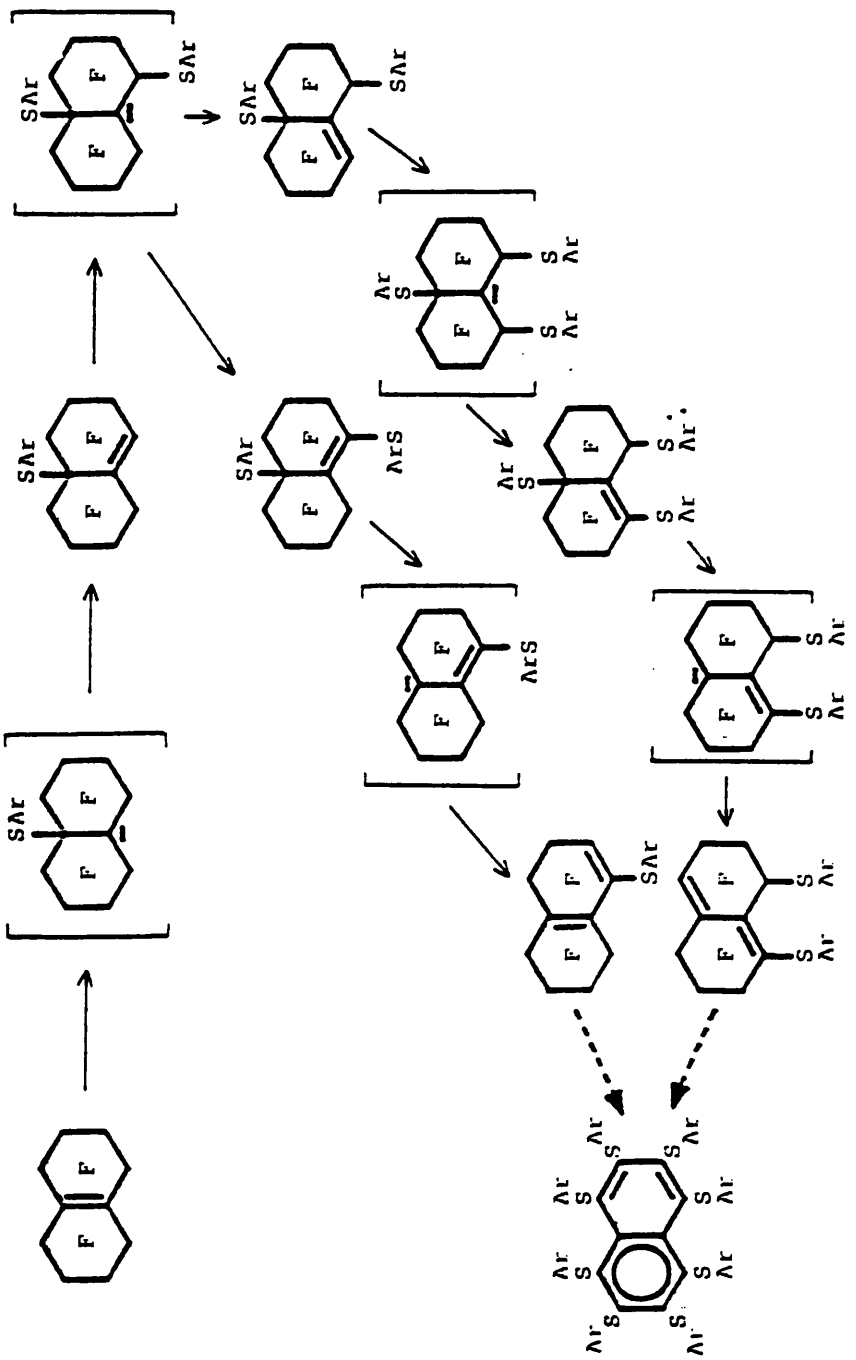
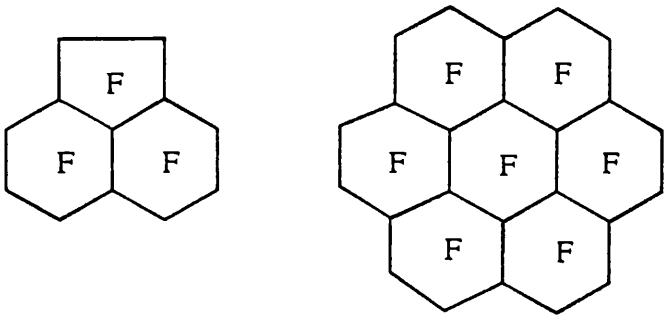


Fig. 8.2. Outline of some possible initial steps for the aromatisation of proposed intermediate alkene : subsequent steps (not shown) also involve combined addition-elimination, continued *ipso* substitution, and progressive reduction.



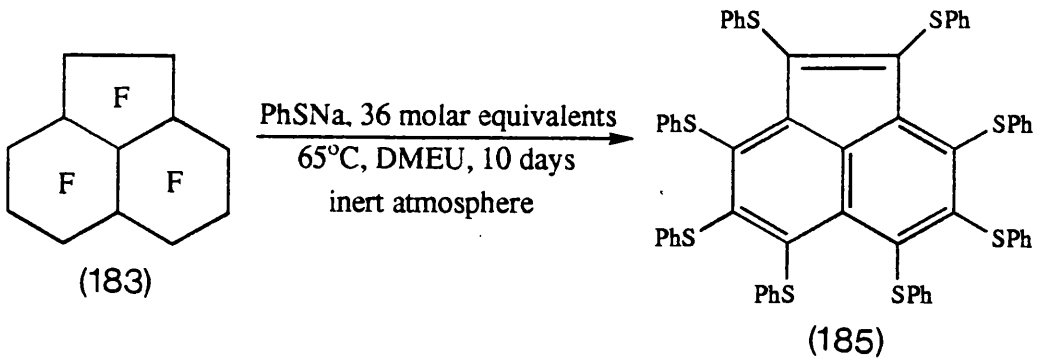
The research contained within this chapter follows on from the above work, and now addresses extension of the scope of the reaction to substrates perfluoroperhydroacenaphthene (183) and perfluoroperhydrocoronene (184).



(183) (184)

8.2 Perfluoroperhydroacenaphthene as substrate.

Initially, perfluoroperhydroacenaphthene (183) was proposed as a nucleus for creation of a new host series : it may be noted that the C_2 molecular symmetry of (183) presents a favourable molecular determinant with potential for achieving this objective. By employing the same reaction conditions used for perfluorodecalin substitution, synthesis of octakis(phenylthio)acenaphthylene (185) was attempted (Scheme 12).



(183) (185)

Scheme 12.

On addition of the thiophenolate salt to the reaction medium, a purple colour was observed. This colour intensified over 2 hours, finally giving a deep black/purple solution. Analysis of the solution after ten days by TLC silica revealed six different compounds. Milder conditions were then sought.

Consequently, a reduction in the excess number of molar equivalents of salt was made, and stirring was carried out at room temperature for 2 days (Experimental) : this reduced the number of compounds to three.

Purification of the mixture by column chromatography on silica led to isolation of the fully substituted compound (185) containing the phenylthio side-chain moiety, yield 13.6% m.p. 222-223°C.

Preliminary inclusion experiments failed to produce evidence for inclusion compound formation by (185), and the low yield prevented a more comprehensive study.

Attempts to optimise the reaction conditions did not meet with success; even after 10 minutes at 0°C, cleavage products of the fully substituted acenaphthylene were observed. Running the reaction in a different solvent, for example DMF, failed to allow isolation of the desired product. Changing the nucleophile, using anions such as *p*-methylbenzenethiolate, *m*-methylbenzenethiolate or 3,5-dimethylbenzenethiolate, also gave complex mixtures; hence, no further study of perfluoroperhydroacenaphthene (183) as a starting material for new inclusion compounds was carried out.

The research, though, was not completely in vain as it did reveal an unusually high reactivity for the saturated fluorocarbon (183). Why then should the reaction proceed at such a vastly different rate to that of perfluorodecalin?

Although no definite reason can be given at present for the significantly faster reaction of (183) compared to perfluorodecalin, a factor worthy of consideration is the relative electron affinities of the two substrates. In conclusion, both substrates yield fully sp^2 hybridised cores, albeit at different rates; the favoured mechanism, involving SET, is summarised in Fig. 8.1 and Fig. 8.2. As can be seen, the aromatisation process involves a series of addition-

elimination, *ipso*-substitution, and progressive reduction steps.

8.3 Perfluoroperhydrocoronene as substrate.

To establish further the range of applicability of this novel reaction, perfluoroperhydrocoronene (184) was then considered.

Only 200 mgs of this extremely scarce starting material was available,(synthesised by Watanabe, Katoh and Nakajima[203]), so a judicious choice of reaction conditions was critical. A suitable choice of nucleophile was important, to allow ready identification of the fully substituted coronene, assuming, of course, that the above substrate would undergo complete aromatisation and substitution. From information gained earlier, the ideal nucleophile was 3,5-dimethylbenzenethiolate as the product hoped for, (139), was already completely characterised (Chapter 6).

A 100% excess of this thiolate salt was then reacted with (184) in DMEU at 65°C (Experimental). After one week no red or orange spot, characteristic of the fully substituted compound was observed by reverse-phase TLC; only a large fluorescent spot along with four others were evident. The reaction mixture was left for a further four weeks and then analysed again by reverse-phase TLC. No noticeable change had occurred so the reaction was terminated.

Still eager to isolate the desired compound, more extreme conditions were employed. In this case a 700% excess of 3,5-dimethylbenzenethiolate salt was reacted at 65°C with (184). Analysis of the reaction mixture by reverse-phase TLC after four weeks revealed a faint red spot, at high Rf, as well as a more intense yellow spot at lower Rf, along with numerous others including the same fluorescent spot found in the first investigation. Continuation of the reaction for a further four weeks led to an intensification of both the yellow and red spots, with a diminution of the previously large fluorescent spot.

Lack of time meant the reaction had to be taken off, then analysed. Purification by flash column chromatography (to prevent oxidation) on silica, eluting with diethylether/40-60° petrol gave 10 mgs of a red/orange oil which produced two coloured spots by reverse-phase TLC. The red spot of the two, on co-spotting, was found to correspond exactly to that from an authentic specimen of (139) prepared from perchlorocoronene (135).

FAB mass spectrometry was chosen as a suitable method to establish that compound (139) had indeed been formed. The FAB mass spectrum of the above mixture showed a strong peak from $(M+H)^+$ at *m/e* 1933, as required for (139). Further peaks from the mass spectrum corresponded to the known fragmentation pattern of dodecakis(3,5-dimethylphenylthio)coronene (139). This evidence indicates that fluorocarbon (184), the largest substrate studied so far, does indeed undergo complete aromatisation and per-substitution, albeit at a

slower rate than that of perfluorodecalin.

Taking account of the slower nature of the reaction, a mechanistic rationalisation can be proposed (Fig. 8.3).

Essentially the same method for initiation is proposed; only two single electron transfer leading to the generation of the anion (186) are shown here. This may then, by elimination of fluoride ion, form the mono olefin (187), analogous to that proposed as an intermediate in the perfluorodecalin reaction, which may subsequently undergo a series of addition-elimination, continued *ipso*-substitution and progressive reduction steps leading to compound (139).

Fig. 8.3. Proposed mechanism for aromatisation and persubstitution of perfluoroperhydrocoronene (184) by arene thiolate nucleophiles.

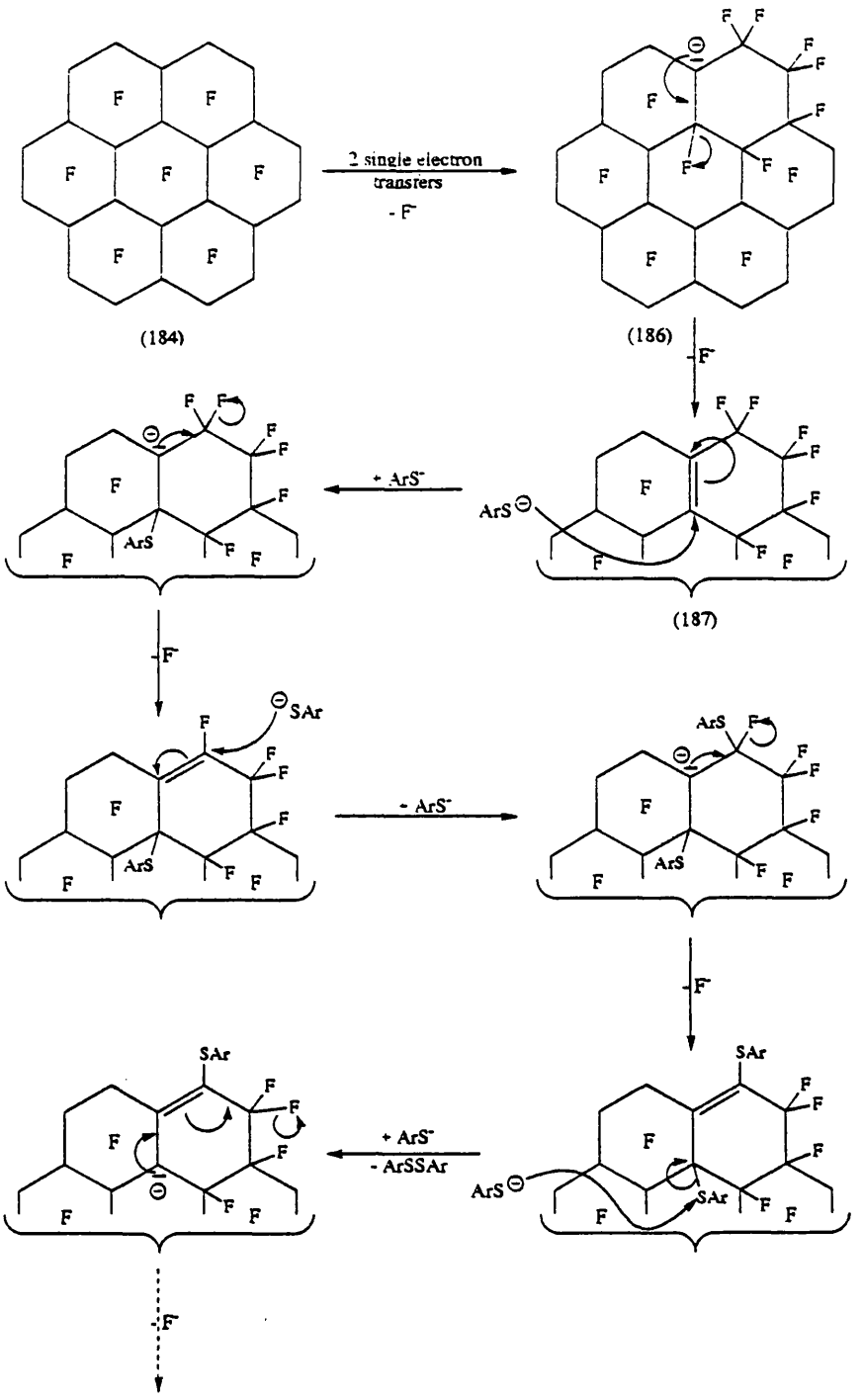
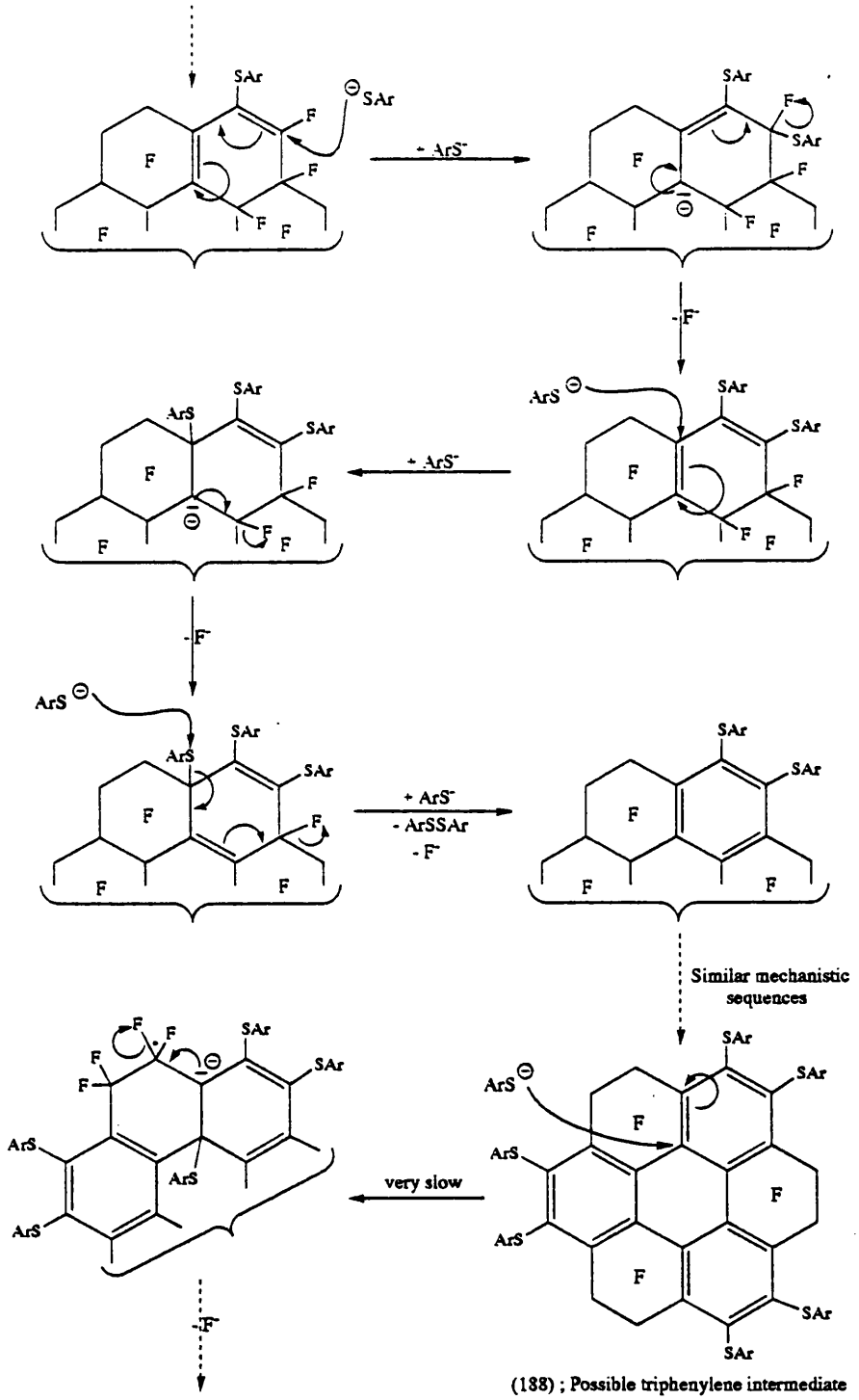
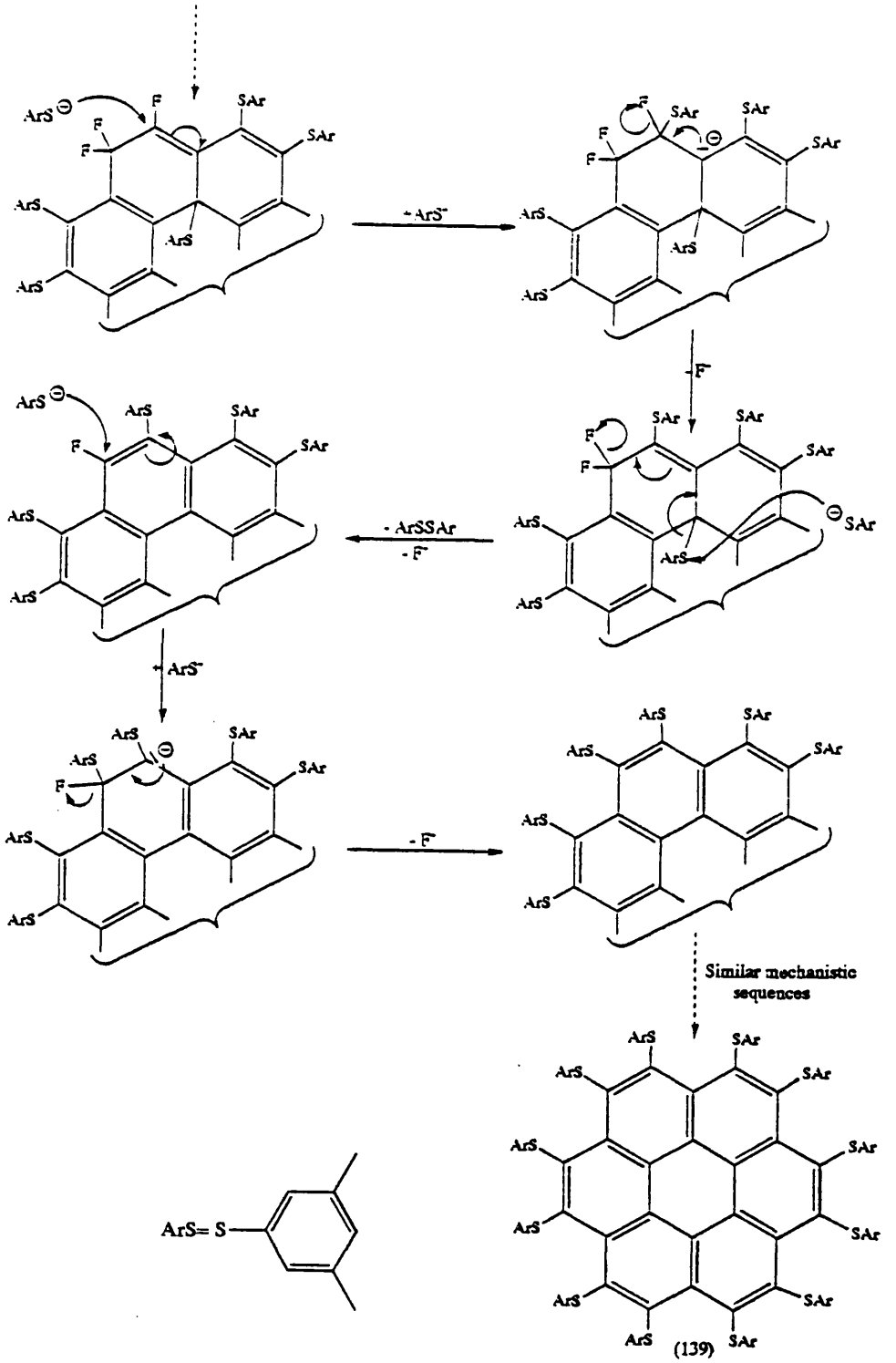


Fig. 8.3. (continued)

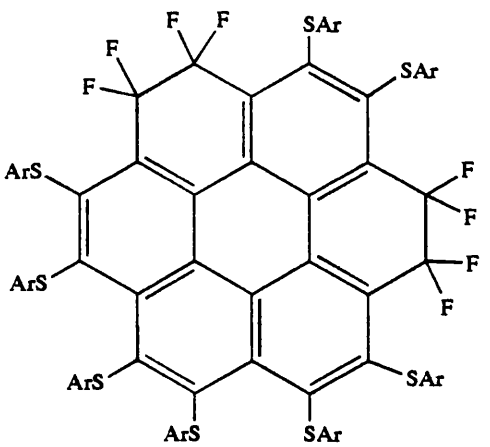


(188) ; Possible triphenylene intermediate

Fig. 8.3. (continued)



Interestingly, though, the reaction may proceed through a relatively stable aromatic intermediate (188), from which it may reluctantly react to give the end product. This stable intermediate (188) could account for a decrease in the overall reaction rate. An indication for the presence of (188) is a peak at 1539 in the FAB mass spectrum corresponding roughly to that of compound (189) ($M+H^+$ = 1536.5). This peak was not detected in the FAB mass spectrum of (139). Allied to this evidence was observation of strange electrical behaviour on the probe consistent with the presence of fluorinated material.



(189)

Another mechanism (not shown) is also possible, by-passing the intermediate (188); however, as in the above mechanism, hindrance to nucleophilic attack may equally lead to a slow overall reaction rate.

In conclusion, the results provide strong evidence that the reaction is applicable to even such large saturated fluorocarbons as (184). To increase the yield of product (139) from (184) as starting material, use of ultrasound is an attractive possibility worthy of consideration. A more detailed investigation should also focus attention on the intermediates involved in the reaction : such a study may well establish (188) as a key intermediate.

The above results, as a whole, establish that the novel saturated fluorocarbon reaction with arenethiolates is not limited to perfluorodecalin but that many substrates can be expected to react and that the reaction rate will depend on the structure of the specific fluorocarbon substrate. Many applications can be envisaged, for example, since the arenethiolate acts as a reducing agent and the fluorocarbon as an oxidising agent, a suitable configuration of these components should be of interest with respect to possible battery application.

EXPERIMENTAL : General Procedures, instruments and selected materials.

Melting points (m.p.) were determined on a Kofler hot-stage apparatus and are uncorrected. Infra-red spectra were recorded on a Perkin-Elmer 983 spectrophotometer as potassium bromide discs (unless otherwise stated). The following abbreviations are used: s-strong, m-medium, w-weak, br-broad. Units for I.R. were in cm^{-1}.

Proton nuclear magnetic resonance (NMR) spectra were determined on a Perkin Elmer R32 (90MHz) and Varian EM390 (90MHz) spectrometers using tetramethylsilane (TMS) as internal standard and both Brüker WP200SY (200MHz) and Brüker AM200SY (200MHz) spectrometers using the deuterated solvent as reference signals.

Carbon NMR spectra were determined on the latter two instruments at 50MHz; signals relative to the deuterated solvent and proton noise decoupled. The fluorine NMR spectrum was determined on the Brüker AM200SY (188MHz) spectrometer using $CFCl_3$ at 0ppm as internal standard. Solid-state carbon NMR spectra were obtained through the SERC service at Durham University. The following abbreviations are used: s-singlet, d-doublet, t-triplet, q-quartet and m-multiplet.

Routine mass spectrometry (< 900 amu) was determined using a VG/Kratos MS 12 spectrometer. Mass spectrometry for compounds > 900 amu was provided by the SERC fast atom bombardment (FAB) mass spectrometry

service, Swansea College. Host-guest ratios were determined by ^1H NMR solution spectra signal ratios.

All microanalyses were determined on a Carlo Eerba elemental analyser, model 1106.

Column chromatography was performed using Fluka Kieselgel HF_{254} and, for flash chromatography, Merck Kieselgel 60 230-400 mesh. Preparative thin layer chromatography (TLC) was performed using 20 x 20 cm glass plates precoated with 2mm of Merck Kieselgel 60 F_{254} (No. 5717). Qualitative reverse-phase TLC was performed using Macherey-Nagel Duren nanosilica C18 $100UV_{254}$ 0.20mm plates. Merck 0.2mm precoated aluminium foil (No. 5554) was also used.

Coronene was supplied by BASF, and perfluoroperhydrocoronene was synthesised by N. Watanabe, S. Katoh and T. Nakajima at Kyoto University.

SYNTHESIS OF STARTING MATERIALS.

Thiol Syntheses

Example 1 : Preparation of *O*-(*p*-cumylphenyl)dimethylthiocarbamate.

To a cooled solution of *p*-cumylphenol 25g (0.118 moles) in 200ml of dry dimethylformamide (DMF) contained in a 500ml 3-necked flask equipped with condenser and nitrogen bleed, was added in small proportions, 95% sodium hydride 2.98g (0.124 moles). The cooling bath was removed and the mixture stirred under a continuous nitrogen flow until no further bubbles were observed. Dimethylthiocarbamoyl chloride 16.06g (0.13 moles) was then added and the reaction temperature raised to 40°C. The reaction was continued for a further 2 hours with stirring under nitrogen flow; then the mixture was added to 300ml of water in a separating funnel and extracted twice with 400ml portions of toluene/petroleum ether (40-60°) 4/1. The organic extracts were washed with water, 5% potassium hydroxide solution (500ml) and saturated sodium chloride solution (500ml) and filtered through anhydrous magnesium sulfate. Upon concentrating to dryness 30.6g of the desired *O*-aryl dimethylthiocarbamate was obtained. Recrystallisation from methanol gave 25g (83.6% yield) of pure white material, m.p. 112-113°C. Found : C, 72.17; H, 7.02; N, 4.53%. $C_{18}H_{21}SNO$ requires C, 72.24; H, 7.02; N, 4.68%; δ_H (200 MHz, $CDCl_3$). 7.32-6.92 (m, 9H), 3.45 (s,3H), 3.30 (s,3H), 1.69 (s,6H); *m/e* 299, M^+.

2. Preparation of *S*-(*p*-4-cumylphenyl)dimethylthiocarbamate.

Pure dry *O*-(*p*-4-cumylphenyl)dimethylthiocarbamate 7.3g (24.4 mmoles)

was heated in an evacuated pyrolysis tube at 275°C in a Wood's metal bath for 1.5 hours. The resultant pale yellow gum was then recrystallised from methanol giving 6.4g of the *S*-aryl compound as colourless needles, m.p.102-103°C, yield 87%. Found: C, 72.16; H, 7.06; N, 4.56%. $C_{18}H_{21}SNO$ requires C, 72.24; H, 7.04; N, 4.68%; δ_H (200 MHz, $CDCl_3$) 7.40-7.12 (m,9H), 3.05 (s,6H), 1.67 (s,6H); υ max (KBr) 3050 (w), 3020 (w), 2980 (m), 2960 (m), 2918 (w), 1659 (s), 1592 (w), 1490 (m), 1462 (w), 1440 (m), 1361 (s), 1310 (m), 1102 (m), 1090 (s), 1070 (m), 1025 (w), 1015 (m), 907 (m), 832 (s), 762 (s), 702 (s), 682 (s); *m/e* 299, M^+.

3. Preparation of *p*-cumylthiophenol (140).

80ml of methanol was purged using a nitrogen bleed for approximately ten minutes then added to a 3 necked flask equipped with stirring bar, condenser and nitrogen bleed. 6.3g (0.021 mols) of the *S*-aryl was added against a slow countercurrent of nitrogen. A 70ml, 50% potassium hydroxide solution was then prepared and purged under nitrogen for ten minutes. Addition of the potassium hydroxide solution to the flask resulted in precipitation of the *S*-aryl from solution. The reaction mixture was refluxed under nitrogen flow with vigorous stirring until the precipitate had disappeared (~ 2 hours). The mixture was refluxed for a further 30 minutes to ensure hydrolysis was complete. Cooling of the reaction mixture under a nitrogen atmosphere, followed immediately by addition of concentrated hydrochloric acid to pH1, deposited a yellow oily film on the surface of the solution. The reaction mixture was then transferred to a

separating funnel containing 300 ml of water. Extraction of the thiol (140) was accomplished using 2 x 300ml of toluene. The organic extracts were then washed with brine, and concentrated to dryness under reduced pressure to give 4.5g of a yellow solid, crude (140), m.p. 40-46°C. Distillation of the crude thiol at 125°C, 0.005mm gave 3.6g (75% yield) of a white crystalline material. m.p. 43-44°C. Found: C, 78.78; H, 7.15%. $C_{15}H_{16}S$ requires C, 78.9; H, 7.02%; δ_H (200 MHz, $CDCl_3$) 7.27-7.07 (m,9H), 3.38 (s,1H), 1.64 (s,6H); υ max (KBr) 3082 (m), 3059 (m), 3012 (w), 2970 (s), 2940 (m), 2870 (w), 2560 (s), 2540 (m), 1600 (m), 1495 (s), 1470 (m), 1445 (m), 1400 (m), 1386 (w), 1365 (m), 1235 (m), 1120 (m), 1101 (m), 1072 (m), 1030 (m), 1020 (m), 825 (s), 769 (s), 730 (m), 720 (m), 702 (s); *m/e* 228, M^+ and 213 $[M\text{-}CH_3]^{+\cdot}$

4. Preparation of *O*-(3,5-di-*t*-butylphenyl)dimethylthiocarbamate.

Sodium 3,5-di-*t*-butylphenoxide was made from 3,5-di-*t*-butylphenol 20.1g (97.6 mmoles) and 95% sodium hydride 2.46g (0.102 moles) according to the method of Example 1. It was then reacted with dimethylthiocarbamoyl chloride 13.2g (0.107 moles) in DMF at 40°C, and the reacted material also isolated according to the method of Example 1. Crystallisation of the crude product from methanol gave 26.5g (92.7% yield) of the desired *O*-aryl, m.p. 117-119°C. Found: C, 69.73; H, 9.30; N, 4.63%. $C_{17}H_{27}SNO$ requires C, 69.62; H, 9.21; N, 4.77%; δ_H (200 MHz, $CDCl_3$) 7.28 (t,J=1.7Hz, 1H), 6.91 (d, J=1.7 Hz, 2H), 3.47 (s,3H), 3.43 (s,3H), 1.32 (s,18H); υ max (KBr) 2960 (s), 2901 (w), 2864 (m), 1609 (m), 1588 (m), 1522 (s), 1480 (m), 1420 (m), 1387 (s), 1360 (m), 1300 (m),

1270 (s), 1241 (w), 1200 (s), 1190 (s), 1165 (w), 1140 (s), 1000 (w), 980 (w), 905 (m), 898 (w), 868 (m), 702 (m); *m/e* 293, M^+.

5. Preparation of *S*-(3,5-di-*t*-butylphenyl)dimethylthiocarbamate.

7.5g of *O*-(3,5-di-*t*-butylphenyl)dimethylthiocarbamate was heated in an evacuated pyrolysis tube at 300°C in a Wood's metal bath for 1.5 hours. The gummy off-white product was recrystallised from methanol to give 6.8g (90.7% yield) of the corresponding *S*-aryl compound m.p. 104-107°C. Found: C, 69.69; H, 9.30; N, 4.71%. $C_{17}H_{27}SNO$ requires C, 69.02; H, 9.21; N, 4.77; δ_H (200 MHz, $CDCl_3$) 7.43 (t, J=1.8Hz, 1H), 7.32 (d, J=1.8Hz, 2H), 3.07 (s,6H), 1.32 (s,18H); υ max (KBr) 2960 (s), 2860 (m), 1665 (s), 1589 (m), 1570 (w), 1475 (m), 1455 (w), 1425 (m), 1392 (m), 1360 (s), 1350 (s), 1251 (s), 1241 (m), 1200 (w), 1085 (s), 1045 (w), 902 (m), 875 (s), 856 (w), 703 (s), 680 (s), 650 (m); *m/e* 293, M^+.

6. Preparation of 3,5-di-t-butylthiophenol (141).

6.7g (22.9 mmoles) of *S*-(3,5-di-*t*-butylphenyl)dimethylthiocarbamate was hydrolysed using the same method and conditions as Example 3. Isolation by the method of Example 3 gave 4.7g of crude thiol. Distillation at 110°C, 0.005 mm, produced 4.1g, (83.2% yield) of (141), m.p. 52-53°C. Found: C, 75.62; H, 9.74. $C_{14}H_{22}S$ requires C, 75.67; H, 9.91; δ_H (200 MHz, $CDCl_3$), 7.21 (t, J=1.7Hz, 1H), 7.12 (d,J=1.7Hz, 2H), 3.43 (s,1H), 1.29(s,18H); υ max (KBr) 2960 (s), 2900 (w), 2870 (w), 2560 (w), 1590 (m), 1570 (s), 1520 (w), 1467 (m), 1428 (w), 1410 (w), 1388 (w), 1355 (s), 1280 (m), 1242 (s), 1200 (m), 1135 (w), 890 (w), 860 (s),

852 (s), 775 (m), 701 (s); *m/e* 222, M^+.

7. Preparation of *O*-(*m*-*t*-butylphenyl)dimethylthiocarbamate.

Sodium *m*-*t*-butylphenoxide was made from *m*-*t*-butylphenol 22g (0.146 moles) and 95% sodium hydride 3.6g (0.154 moles) according to the method of Example 1. It was reacted with dimethylthiocarbamoyl chloride 19.8g (0.161 moles) and the reacted material also isolated according to the method of Example 1. Recrystallisation of the crude product from methanol gave 27g (77.6% yield) of the desired *O*-aryl as white needles, m.p. 60-63°C. Found: C, 65.68; H, 8.13; N, 5.86%. $C_{13}H_{19}SNO$ requires C, 65.82; H, 8.02; N, 5.90%. δ_H (200MHz, $CDCl_3$) 7.36-7.32 (m,2H), 7.08-7.06 (m,1H), 6.92-6.86 (m,1H), 3.46 (s,3H), 3.34 (s,3H), 1.32 (s, 9H); υ max (KBr) 2955 (s), 2860 (w), 1711 (w), 1603 (m), 1580 (m), 1530 (s), 1480 (m), 1420 (w), 1409 (w), 1387 (s), 1360 (w), 1287 (s), 1260 (s), 1191 (s), 1165 (w), 1130 (s), 1105 (v.w), 1075 (w), 1001 (m), 962 (m), 891 (s), 870 (m), 820 (w), 796 (s), 701 (m), 695 (s); *m/e* 237 M^+.

8. Preparation of *S*-(*m*-t-butylphenyl)dimethylthiocarbamate.

8.5g (35.9 mmoles) of *O*-(m-t-butylphenyl)dimethylthiocarbamate was heated in an evacuated pyrolysis tube at 285°C in a Wood's metal bath for 1.5 hours. On crystallising the resultant gum from methanol 7.8g of the corresponding *S*-aryl was obtained (91.7% yield) m.p. 89-91°C. Found: C, 65.98; H, 8.19; N, 5.96%. $C_{13}H_{19}SNO$ requires C, 65.82; H, 8.02; N, 5.90%; δ_H (90MHz, $CDCl_3$) 7.5-7.2 (m,4H), 3.05 (s,6H), 1.3 (s,9H); υ max 2964 (s), 2905

(w), 2868 (w), 1655 (s), 1626 (w), 1587 (m), 1477 (s), 1456 (w), 1404 (m), 1363 (s), 1257 (s), 1128 (w), 1097 (s), 1082 (m), 1053 (w), 904 (m), 891 (s), 792 (s), 698 (s), 688 (s); *m/e* 237, M^+.

9. Preparation of *m-t*-butylthiophenol (142).

7.5g (31.6 mmoles) of *S*-(*m-t*-butylphenyl)dimethylthiocarbamate was hydrolysed using the same method and conditions as noted in Example 3. Isolation of the reacted material by the method of Example 3 gave 5.3g of a yellow, pungent scented liquid, compound (142). Distillation at 60°C, 0.005 mm gave 4.5g of (142) as a colourless liquid, yield 85.8%. Found: C, 72.45; H, 8.22%. $C_{10}H_{14}S$ requires C, 72.29; H, 8.43; δ_H (90 MHz, $CDCl_3$) 7.31-7.15 (m,4H), 3.43 (s,1H), 1.32 (s,9H); υ max (thin film) 2960 (s), 2900 (w), 2860 (m), 2560 (w), 1588 (s), 1565 (m), 1477 (s), 1455 (w), 1401 (m), 1390 (w), 1361 (s), 1282 (m), 1261 (s), 1200 (m), 1160 (w), 1125 (w), 1103 (w), 1082 (m), 995 (w), 915 (m), 876 (m), 856 (m), 782 (s), 761 (w), 699 (s); *m/e* 166, M^+.

10. Preparation of *O*-(3,4,5-trimethylphenyl)dimethylthiocarbamate.

Sodium 3,4,5-trimethylphenoxide was made from 3,4,5-trimethylphenol 20g (0.137 moles) and 95% sodium hydride 3.46g (0.144 moles) according to the method and conditions of Example 1. It was reacted with dimethylthiocarbamoyl chloride 18.6g (0.151 moles) and the reacted material also isolated according to the method of Example 1. (Excess DMF (~ 100ml) was employed to counter the saponifying effect of the phenoxide salt). On crystallising the crude material

from methanol 26.5g of the required *O*-aryl compound was obtained as white crystals (yield 73.3%) m.p. 84-85°C. Found: C, 63.77; H, 7.37; N, 6.71. $C_{12}H_{17}SNO$ requires C, 64.57; H, 7.62; N, 6.27; δ_H (90MHz, $CDCl_3$) 6.72 (s,2H), 3.40 (s,3H), 3.28 (s,3H), 2.28 (s,6H), 2.15 (s,3H); *m/e* 223, M^+.

11. Preparation of *S*-(3,4,5-trimethylphenyl)dimethylthiocarbamate.

9.8g (43.9 mmoles) of *O*-(3,4,5-trimethylphenyl)dimethylthiocarbamate was heated in an evacuated pyrolysis tube at 300-305°C in a Wood's metal bath for 2 hours. On crystallising the crude product from methanol 8.4g of the corresponding *S*-aryl compound was obtained (yield 85.7%) m.p. 72-73°C. Found: C, 64.31; H, 7.76; N, 6.27%. $C_{12}H_{17}SNO$ requires C, 64.57; H, 7.62; N, 6.27%; δ_H (200MHz, $CDCl_3$) 7.15 (s,2H), 3.05 (s,6H), 2.28 (s,6H), 2.16 (s,3H); υ max (KBr) 2978 (s), 2920 (s), 2862 (w), 1655 (s), 1473 (m), 1458 (m), 1444 (m), 1406 (w), 1398 (w), 1361 (s), 1257 (m), 1153 (w), 1132 (w), 1101 (s), 908 (m), 856 (m), 688 (s); *m/e* 223, M^+.

12. Preparation of 3,4,5-trimethylthiophenol (143).

8.3g (37.2 mmoles) of *S*-(3,4,5-trimethylphenyl)dimethylthiocarbamate was hydrolysed using the same method and conditions as in Example 3. Isolation of the reacted material by the method of Example 3 gave 5.3 g of crude (143). The pungent smelling liquid was then distilled at 65°C, 0.005 mm to give 4.6g of pure (143), yield 81.3%. Found: C, 71.02; H, 7.62%. $C_9H_{12}S$ requires C, 71.05; H, 7.89%; δ_H (90MHz, $CDCl_3$) 6.93 (s,2H), 3.27 (s,1H), 2.21 (s,6H), 2.11 (s,3H); υ max 2970 (w), 2940 (s), 2905 (s), 2860 (s), 2560 (m), 1625 (m), 1588 (s), 1565

(w), 1470 (s), 1450 (w), 1440 (w), 1401 (w), 1375 (m), 1310 (w), 1255 (w), 1195 (s), 1140 (m), 1007 (m), 998 (m), 932 (w), 885 (s), 850 (s), 700 (s); *m/e* 152, M^+.

13. Preparation of *p*-methylsulphonylphenol.

30g (0.214 moles) of *p*-(methylmercapto)phenol was reacted with a six-fold excess of 30% hydrogen peroxide by stirring in 200ml of glacial acetic acid for 24 hours at room temperature. The product was deposited around the edge of the round bottomed reaction flask and 25g was collected by filtration, yield 67.9%, m.p. 97-98°C. Found: C, 48.56; H, 4.60%. $C_7H_8O_3S$ requires C, 48.83; H, 4.65%; δ_H (200MHz, D_6-DMSO) 10.61 (s,br,1H), 7.73 (AA'BB' aromatic, 2H) 6.95 (AA'BB' aromatic, 2H), 3.12 (s,3H); υmax (KBr) 3379 (s,br), 3285 (s), 3018 (m), 2997 (m), 2928 (m), 2918 (m), 1604 (s), 1589 (s), 1502 (m), 1456 (m), 1410 (w), 1381 (m), 1327 (m), 1304 (s), 1284 (s), 1251 (s), 1176 (w), 1145 (s), 1107 (w), 1089 (s), 981 (m), 972 (m), 966 (m), 844 (s), 827 (s), 769 (s), 709 (w), 648 (w), 628 (m); *m/e* 172, M^+.

14. Preparation of *O*-(*p*-methylsulphonylphenyl)dimethylthiocarbamate.

Sodium *p*-methylsulphonyl phenoxide was made from *p*-methylsulphonyl-phenol 21g (0.122 moles) and 95% sodium hydride 3.08g (0.128 moles) according to the method and conditions of Example 1. It was reacted at 40° for 2 hours with dimethylthiocarbamoyl chloride 16.57 g (0.134 moles) and the reacted material also isolated according to the method of Example 1. Recrystallisation of the crude product from methanol gave 24.5g of the *O*-aryl compound, yield

77.5%, m.p. 185-187°C. Found: C, 46.12; H, 5.12; N, 5.18%. $C_{10}H_{13}O_3S_2N$ requires C, 46.33; H, 5.02; N, 5.41%; δ_H (200 MHz, $CDCl_3$) 7.97 (AA'BB' aromatic, 2H), 7.28 (AA'BB' aromatic, 2H), 3.46 (s, 3H), 3.37 (s, 3H), 3.09 (s, 3H); *m/e* = 259, M^+.

15. Preparation of *S*-(*p*-methylsulphonylphenyl)dimethylthiocarbamate.

O-(*p*-methylsulphonylphenyl)dimethylthiocarbamate 9.2g (35.5 mmoles) was heated in an evacuated pyrolysis tube at 255-260°C in a Wood's metal bath for 2 hours. On crystallising the crude material from methanol, 8.7g of the corresponding S-aryl compound was obtained, yield 94.6%, m.p. 142-144°C. Found: C, 46.44; H, 4.89; N, 5.23%, $C_{10}H_{13}O_3S_2N$ requires C, 46.33; H, 5.02; N, 5.40%; δ_H (200 MHz, $CDCl_3$) 7.93 (AA'BB'aromatic, 2H), 7.70 (AA'BB' aromatic, 2H), 3.11 (s, 6H), 3.06 (s, 3H); υ max (KBr) 3018 (w), 2998 (w), 2910 (m), 1665 (s), 1578 (w), 1467 (w), 1409 (w), 1382 (m), 1369 (m), 1360 (m), 1321 (w), 1302 (s), 1280 (w), 1257 (m), 1142 (s), 1105 (w), 1089 (s), 1012 (m), 960 (s), 901 (m), 828 (s), 776 (s), 735 (m), 710 (m), 680 (s), 652 (m); *m/e* 259 M^+.

16. Preparation of *p*-methylsulphonylthiophenol (144).

S-(*p*-methylsulphonylphenyl)dimethylthiocarbamate 8.4g (32.43 mmoles) was hydrolysed using the same method and conditions of Example 3. Isolation of the product by the method of Example 3 gave 5.4g of crude thiol (144) as a solid. Distillation at 125°C/0.005 mm gave 4.7g of pure (145) m.p. 68-69°C, yield 77.1%. Found: C, 44.64; H, 4.00. $C_7H_8O_2S_2$ requires C, 44.68; H, 4.25; δ_H

(200 MHz, D_6-DMSO) 7.67 (AA'BB'aromatic, 2H), 6.85 (AA'BB'aromatic, 2H), 4.51 (s, 1H), 2.93 (s, 3H); υ max (KBr) 3020 (w), 3000 (w), 2920 (w), 2560 (m), 1580 (s), 1470 (m), 1399 (s), 1320 (w), 1290 (s), 1270 (s), 1188 (m), 1149 (s), 1120 (w), 1100 (s), 1086 (s), 1010 (m), 960 (s), 932 (m), 820 (s), 775 (s), 731 (m); *m/e* 188, M^+.

17. Preparation of *O*-(5-indanyl)dimethylthiocarbamate.

Sodium 5-indanoxide was made from 5-indanol 22.3g (0.166 moles) and 95% sodium hydride 4.2g (0.175 moles) according to the method and conditions of Example 1. It was reacted at 40°C for 2 hours with dimethylthiocarbamoyl chloride 22.6g (0.183 moles) and the reacted material also isolated according to the method of Example 1. Recrystallisation of the crude product from methanol gave 27.6g of the desired *O*-aryl compound, m.p. 68-71°C, yield 75.2%.
Found: C, 64.98; H, 6.83; N, 6.24%. $C_{12}H_{15}SNO$ requires C, 65.15; H, 6.79; N, 6.33%; δ_H (200 MHz, $CDCl_3$), 7.19 (d, J=8Hz, 1H), 6.89 (s, 1H), 6.79 (m, 1H), 3.42 (s, 3H), 3.29 (s, 3H), 2.89 (m, 4H), 2.07 (quintet, J=7.2Hz, 2H); υ max (KBr) 2950 (s), 2920 (s), 2862 (w), 2840 (m), 1605 (w), 1590 (w), 1535 (s), 1480 (s), 1436 (m), 1403 (m), 1391 (s), 1320 (w), 1285 (s), 1230 (s), 1170 (a), 1140 (s), 1078 (m), 1050 (w), 1000 (w), 962 (m), 911 (m), 902 (m), 855 (m), 825 (s), 703 (m), 670 (w); *m/e* 221, M^+.

18. Preparation of *S*-(5-indanyl)dimethylthiocarbamate.

O-(5-indanyl)dimethylthiocarbamate 9.8g (44.34 moles) was heated in an

evacuated pyrolysis tube at 300°C for 3 hours in a Wood's metal bath. Crystallisation of the crude material from methanol gave 8.8g of the corresponding *S*-aryl, yield 89.8%, m.p. 47-49°C. Found: C, 65.08; H, 6.98; N, 6.19%. $C_{12}H_{15}SNO$ requires C, 65.16; H, 6.79; N, 6.33%; δ_H (200MHz, $CDCl_3$) 7.34 (s, 1H), 7.23 (s, 2H), 3.04 (s, 6H) 2.90 (m, 4H), 2.09 (quintet, 2H); *m/e* 221, M^+.

19. Preparation of 5-indanethiol (145).

S-(5-indanyl)dimethylthiocarbamate 8.6g (38.91 mmoles) was hydrolysed using the same method and conditions of Example 3. Isolation of the product by the method of Example 3 gave 5.3g of crude liquid, thiol (145). Distillation at 66-68°C/0.005 mm gave 4.5g of pure (146), yield 77.1%. Found: C, 72.08; H, 6.40%. $C_9H_{10}S$ requires C, 72.00; H, 6.66%; δ_H (200 MHz, $CDCl_3$) 7.37-7.01 (m, 3H), 3.38 (s, 1H), 2.83 (m, 4H), 2.03 (quintet, 2H); υ max 3050 (w), 3010 (m), 2942 (s), 2860 (m), 2840 (s), 2559 (m), 1597 (s), 1565 (m), 1472 (s), 1431 (s), 1405 (m), 1309 (w), 1302 (w), 1288 (w), 1257 (m), 1175 (m), 1100 (m), 1035 (w), 873 (m), 860 (m), 808 (s); *m/e* 150, M^+.

20. Preparation of *O*-(3,4-dimethylphenyl)dimethylthiocarbamate.

Sodium 3,4-dimethylphenoxide was made from 3,4-dimethylphenol 21.4g (0.175 moles) and 95% sodium hydride 4.43g (0.185 moles) according to the method and conditions of Example 1. It was reacted at 40°C for 2 hours with

dimethylthiocarbamoyl chloride 23.8g (0.192 moles) and the reacted material also isolated according to the method of Example 1. Recrystallisation of the crude product from methanol gave 28.1g of the *O*-aryl compound m.p. 89-91°C, yield 76.8%. Found: C, 63.17; H, 7.28; N, 6.53%. $C_{11}H_{15}OSN$ requires C, 63.16; H, 7.18; N, 6.69%. δ_H (200 MHz, $CDCl_3$) 7.13 (d, J=8Hz, 1H), 6.81 (m, 2H), 3.44 (s, 3H), 3.31 (s, 3H), 2.25 (s, 3H), 2.24 (s, 3H); υ max (KBr) selected 2940 (m,br), 1530 (s), 1495 (s), 1448 (w), 1410 (w), 1387 (s), 1290 (s), 1270 (m), 1240 (s), 1190 (m), 1169 (s), 1155 (s), 1135 (s), 1105 (m), 1050 (w), 1010 (m), 914 (m), 865 (m), 810 (m); *m/e* 209 M^+.

21. Preparation of *S*-(3,4-dimethylphenyl)dimethylthiocarbamate.

O-(3,4-dimethylphenyl)dimethylthiocarbamate 9.5g (45.45 mmoles) was heated in an evacuated pyrolysis tube at 285°C in a Wood's metal bath for 1.5 hours. The product was recrystallised from methanol to give 8.4g of the corresponding *S*-aryl compound, yield 93.7%. δ_H (90MHz, $CDCl_3$) 7.32-7.22 (m, 3H), 3.09 (s, 6H), 2.3 (s, 6H).

22. Preparation of 3,4-dimethylthiophenol (146).

S-(3,4-dimethylphenyl)dimethylthiocarbamate 7.4g (35.41 mmoles) was hydrolysed using the same method and conditions of Example 3. Isolation of the product by the method of Example 3 gave 5.2g of crude thiol (146) as a liquid. Distillation at 56°C/0.005mm gave 4.3g of pure (146), yield 80.9%. Found: C, 69.59; H, 6.99%. $C_8H_{10}S$ requires C, 69.56; H, 7.25%. δ_H (200 MHz, $CDCl_3$)

7.05 (s, 1H), 7.0-6.96 (m, 2H), 3.34 (s, 1H), 2.19 (s, 6H); υ max (thin film) 3010 (m), 2960 (m), 2939 (s), 2918 (s), 2860 (m, br), 2560 (m), 1595 (s), 1660 (w), 1489 (s), 1448 (s), 1392 (w), 1380 (m), 1188 (s), 1140 (m), 1127 (m), 1100 (m), 1020 (m), 990 (m), 920 (m), 879 (s, br), 806 (s); *m/e* 138, M^+.

23. Preparation of *O*-(m-methoxyphenyl)dimethylthiocarbamate.

Sodium *m*-methoxyphenoxide was made from *m*-methoxyphenol 23g (0.185 moles) and 95% sodium hydride 4.67g (0.195 moles) according to the method and conditions of Example 1. It was reacted at 40°C for 2 hours with dimethylthiocarbamoyl chloride 25.13g (0.204 moles) and the reacted material also isolated according to the method of Example 1. The crude component on this occasion could not be recrystallised from methanol; each recrystallisation producing a gummy material. A distinct smell of amine was also present from the crude product; its presence confirmed by ^1H NMR. The crude material was then purified by dissolving in toluene (200ml) and washing twice with 10% hydrochloric acid solution (2x300ml) with a final wash with brine. On evaporation of the organic layer to dryness a gum-like material was present. δ_H (90MHz, $CDCl_3$) 7.28-7.2 (m, 1H), 6.84-6.6 (m, 3H), 3.74 (s, 3H), 3.40 (s, 3H), 3.25 (s, 3H).

24. Preparation of *S*-(m-methoxyphenyl)dimethylthiocarbamate.

O-(*m*-methoxyphenyl)dimethylthiocarbamate 8.7g (41.23 mmoles) was heated in an evacuated pyrolysis tube at 300°C in a Wood's metal bath for 2

hours. Crystallisation of the gummy product from methanol produced a gum corresponding to the *S*-aryl compound. Purification by tritrating with cold methanol gave 8.4g of the gummy material. δ_H (90MHz, $CDCl_3$) 6.4-6.1 (m, 4H), 3.71 (s, 3H), 3.07 (s, 6H).

25. Preparation of *m*-methoxythiophenol (147)

S-(*m*-methoxyphenyl)dimethylthiocarbamate 8.1g (38.39 mmoles) was hydrolysed using the same method and conditions of Example 3. Isolation of the product by the method of Example 3 gave 5.2g of crude thiol (147). Distillation at 72-74°C/0.005mm gave 4.5g of pure (147), yield 83.7%. Found: C, 60.07; H, 5.72%. C_7H_8OS requires C, 60.00; H, 5.71. δ_H (200 MHz, $CDCl_3$) 7.16 (m, 2H), 6.80-6.66 (m, 2H), 3.74 (s, 3H), 3.39 (s, 1H); υ max (selected) 3080 (w), 3015 (m), 2980 (m), 2960 (m), 2850 (m), 2565 (m), 1591 (s), 1577 (s), 1481 (s), 1464 (w), 1429 (s), 1286 (s), 1250 (s), 1234 (s), 1161 (m), 1109 (m), 1099 (m), 1041 (s), 856 (s), 843 (s), 771 (s), 684 (s); *m/e* 140, M^+.

26. Preparation of *p*-adamantylthiophenol (148)

Compound (148) was prepared according to the method detailed in ref. 195 overall yield 25%, m.p. 104-105°C (lit. 105-106°C). Analysis of thiol (149). Found: C, 78.40; H, 8.27%. $C_{16}H_{20}S$ requires C, 78.69; H, 8.20%. δ_H (200 MHz, $CDCl_3$) 7.23 (s, 4H), 3.38 (s, 1H), 2.08 (s,br, 3H), 1.88 (m, 6H), 1.76 (m, 6H); υ max (KBr) (select) 2899 (s), 2847 (s), 2554 (w), 1662 (m), 1495 (s), 1446 (m), 1402 (m), 1107 (w), 1097 (m), 1010 (m), 800 (s); *m/e* 244, M^+.

The rearrangement of the *O*-aryl compound was found to occur at 300°C over a 2 hour period, instead of 275°C, as quoted in ref 195. Inclusion was noted, by chance, for *p*-adamantylphenol. Including methanol, nitromethane and 1,4-dioxane in host-guest ratios of 3:2, 3:1 and 6:1 respectively.

27. Preparation of 3,5-dimethoxythiophenol (149)

Compound (149) was prepared according to the method detailed in ref 196 Overall yield 32%, m.p. 31°C. Analysis of thiol (150)-Found: C, 57.65; H, 6.18%. $C_8H_{10}SO_2$ requires C, 56.47; H, 5.88%. δ_H (200 MHz) 6.67 (d, J=2.2Hz, 2H), 6.26 (t, J=2.2 Hz, 1H), 3.76 (s, 6H), 3.46 (s, 1H); υ max (thin film, selected) 3001 (m), 2961 (m), 2939 (m), 2835 (m), 2560 (m), 1585 (s), 1456 (s), 1421 (s), 1332 (m), 1317 (m), 1298 (s), 1282 (s), 1205 (s), 1157 (s), 1107 (m), 1064 (s), 1043 (s), 862 (m), 854 (m), 825 (s); *m/e* 170 M^+.

28. Preparation of thioestrone (150).

Compound (150) was prepared according to the method detailed in ref 194. Overall yield 15% m.p. 138-140°C. δ_H (200 MHz, $CDCl_3$) 7.18-7.04 (m, 3H), 3.36 (s, 1H), 2.87 (m, 2H), 2.58-1.94 (m, 10H), 1.62-1.45 (m, 5H), 0.91 (s, 3H); υ max (KBr, select) 3061 (w), 2988 (w), 2964 (s), 2932 (s), 2868 (s), 2545 (vw), 2361 (m), 2343 (w), 1736 (s), 1483 (m), 1452 (m), 1404 (m), 1371 (m), 1255 (w), 1215 (w), 1182 (w), 1082 (m), 1051 (m), 1006 (m), 814 (m); *m/e* 286, M^+.

29. Preparation of 3,5-dimethylbenzeneselenol (167b).

The entire apparatus was set up under subdued light. In a 500ml, 3-necked round-bottomed flask equipped with condenser, magnetic stirring bar and nitrogen balloon was placed magnesium 3.4g (0.141 moles) and a crystal of iodine. 40ml of the solution consisting of 3,5-dimethylbromobenzene 26g (0.141 moles) in dry diethyl ether (200 ml) was added via a pressure equilibrated dropping funnel to initiate formation of the grignard. The remainder of the 3,5-dimethylbromobenzene was added dropwise over a 45 minute period with continual stirring at room temperature. After a further fifteen minutes the dropping funnel was replaced by an addition flask containing dry black selenium 9.48g (0.12 moles). The selenium was then added over 30 minutes with vigorous stirring. The stirring was continued for another 30 minutes, at which point the reaction mixture was quickly transferred to a large crystallising dish containing 200g of ice. Concentrated hydrochloric acid (70 ml) was added immediately and the contents were then transferred to a 2L separating funnel by filtering through a conical funnel packed with glass wool to remove unwanted solids. A small amount (100ml) of diethyl ether was used to remove any residual selenol attached to the glass wool. The selenol was then extracted using diethyl ether (2 x 400ml), washed with brine and quickly passed through a sinter containing dry Na_2SO_4. Evaporation of the organic extracts gave a pungent smelling yellow oil, which was distilled at 80°C/0.1mm to give 20g of the desired selenol as a liquid (76.7% yield). Found: C, 51.82; H, 5.59%. $C_8H_{10}Se$ requires C, 51.90; H, 5.41%; δ_H (90 MHz, $CDCl_3$) 6.96 (s, 2H), 6.79 (s, 1H), 2.20 (s, 6H), 1.41 (s, 1H); υ max

(thin film) 3035 (w), 3002 (w), 2980 (w), 2950 (w), 2920 (s), 2870 (m), 2310 (w, Se-H stretch), 1600 (s), 1580 (s), 1452 (s,br), 1382 (m), 1260 (m), 1120 (w), 1038 (m), 840 (s), 818 (s), 680 (s).

30. Synthesis of Perchlorocoronene (135).

A single-necked 3 litre round-bottomed flask containing stirring bar was fitted with a 3-necked adaptor, to which was attached a pressure equilibrated dropping funnel, a dry-cold condenser and a stopper. Aluminium trichloride ($AlCl_3$) was then added along with 300ml of sulphuryl chloride (SO_2Cl_2). A distillation take-off with condenser leading to a collecting flask was connected to the dry-cold condenser. This enabled efficient containment of the volatile and corrosive SO_2Cl_2. The above solution was brought to reflux, and a mixture of sulphur monochloride 89.6g (0.664 moles), SO_2Cl_2 (100ml) and coronene 2.5g (8.3 mmoles) added dropwise over a period of 40 minutes. Upon addition of the mixture, a blue/black colour was observed in the reactant flask. A further 1.2 litres of SO_2Cl_2 was added to wash all the coronene into solution. The reaction volume was then maintained at a constant 1.5 litres, with continual reflux and stirring for 28 hours. Typically, the SO_2Cl_2 had to be replenished every 20 minutes, even with dry-cold apparatus. After a 28 hour reaction period, the sulphuryl chloride was allowed to evaporate off to a volume of 100 ml. The remaining SO_2Cl_2 was removed under reduced pressure until a dry solid remained. The residue was treated carefully with 200ml of water and solid sodium bicarbonate added gradually till no more gas evolution took place. The

mixture was then heated on a steam bath with stirring for 1 hour, and strongly acidified with excess concentrated hydrochloric acid. The solid yellow product, perchlorocoronene, was collected by filtration and washed with water and methanol. Purification by recrystallisation from chlorobenzene gave 4.9g of pure perchlorocoronene, m.p. >300°C, yield 82.7%. υmax(KBr,select) 1545(s), 1452(w), 1408 (w), 1304 (w), 1257 (s), 968 (s), 924 (w), 771 (m), 723 (m); *m/e* 714, M^+.

Synthesis of Sulphur-link Coronene Hosts.

31. Preparation of Dodecakis(*m*-methylphenylthio)coronene (136)

Sodium 0.56g (23 mmoles) was added directly to a 3-necked flask containing dry absolute alcohol and stirred. When the sodium had completely disappeared, indicating complete formation of ethoxide, *m*-toluenethiol 3.1g (25 mmoles) was added at room temperature under an atmosphere of N_2. The solution was stirred vigorously at room temperature for a further 20 minutes, then evaporated to dryness, producing the crude *m*-toluenethiolate salt. Purification of the salt was effected by washing on a sinter with dry diethyl ether. The salt was quickly transferred to a 100ml round bottomed flask and dried at reduced pressure (oil pump). Having dried the salt, it was stored permanently under vacuum.

20ml of dry DMEU was then added to a 100ml quick-fit conical flask containing a magnetic stirring bar, rubber septum and perchlorocoronene 0.2g (0.28 mmoles). The mixture was degassed for 20 minutes then the *m*-toluenethiolate salt 0.98g (6.72 mmoles) was added. The complete reaction mixture was degassed and left to stir at room temperature for two days. At the end of the two day period the contents of the flask were transferred to a separating funnel containing 250 ml of toluene. The organic layer was washed 10 times with an equivalent volume of water then evaporated to dryness, giving a red oil, which upon crystallisation from a 1,4-dioxane/methanol mixture produced 0.42g (0.24 mmoles) of compound (136), yield 85%, m.p. 215-217°C.

δ_H (200MHz, $CDCl_3$) 6.77 (m, 24H), 6.59 (s, 12H), 6.16 (s, 12H), 2.09 (s, 36H)

δ_C (50 MHz, $CDCl_3$) 139.95 (s), 139.65 (s), 137.79 (s), 133.67 (s), 128.35 (d), 126.92 (d), 125.94 (d), 124.11 (s), 123.46 (d).

32. Preparation of Dodecakis(cyclopentylthio)coronene (137).

To a 3-necked 100ml round-bottomed flask, equipped with condenser and nitrogen bleed, was added cyclopentyl mercaptan 3g (29 mmoles) and dry tetrahydrofuran (THF) 35ml. The solution was purged with nitrogen for 20 minutes while being stirred continually. The nitrogen flow was then stopped and 95% sodium hydride 0.73g (31 mmoles) added. After 20 minutes evolution of hydrogen had ceased, indicating complete formation of the thiolate salt. The solution was evaporated to dryness under reduced pressure, to give the crude salt. This was immediately transferred to a glass sinter washed with dry diethyl ether and quickly added to a 100ml round bottomed flask, then dried and also stored under vacuum.

The sodium cyclopentylthio salt 0.83g (6.7 mmoles) was reacted with perchlorocoronene 0.2g (0.28 mmoles) in 20ml of dry DMEU at room temperature and the reacted material also isolated according to the method of Example 31. Purification of the product by recrystallisation from isopropanol/1,4-dioxane gave 0.25g of (137) as an orange/red powder, yield 60%, m.p. 206-211°C; one spot by reverse-phase TLC. δ_H (200 MHz, $CDCl_3$) 3.90 (m, 12H), 2.31-1.25 (m, 96H); δ_C 50.37 (d,br), 33.35 (t,br), 24.86 (t,br).

33. Attempted preparation of dodecakis(2,6-dimethylphenylthio)coronene (138)

Sodium 2,6-dimethylbenzenethiolate was made from 2,6-dimethylbenzenethiol 0.93g (6.7 mmoles) and sodium 0.15g (6.7 mmoles) according to the method of Example 31. It was reacted with perchlorocoronene 0.2g (0.28 mmoles) in 20ml of DMEU for 2 days at room temperature and the reacted material also isolated according to the method of Example 31. Reverse-phase TLC of the crude product revealed the presence of 4 different compounds. No further analysis was carried out.

34. Preparation of dodecakis(3,5-dimethylphenylthio)coronene (139).

Sodium 3,5-dimethylbenzenethiolate was made from 3,5-dimethylbenzenethiol 0.99g (7.2 mmoles) and sodium 0.16g (7.2 mmoles) according to the method of Example 31. It was reacted with perchlorocoronene 0.25g (0.3 mmoles) in 20ml of dry DMEU for 2 days at room temperature, and the reacted material also isolated according to the method of Example 31. The crude product was purified by crystallisation from a 1,4-dioxane/methanol mixture to give 0.52g (0.27 mmoles) of (139), yield 89.7%, m.p. 275-278°C (1,4-dioxane adduct). δ_H (200 MHz, $CDCl_3$) 6.55 (s, 12H), 6.25 (s, 24H) 1.69 (s, 72H): δ_C (50 MHz, $CDCl_3$) 139.74 (s), 138.84 (s), 137.54 (s), 134.35 (s), 127.12 (d), 124.36 (d), 123.62 (s), 21.11 (q); υ max (KBr, selected) 3026 (s), 2914.8 (s), 2855 (s), 2727 (w), 2361 (m), 1734 (w), 1616 (s), 1599 (s), 1579 (s), 1545 (m), 1508 (m), 1456 (s,br), 1375 (m), 1250 (s), 1116 (m), 1035 (m), 835 (s), 680 (s); FAB accurate mass, *m/e* 1933.52±0.17, $(M+H)^+$

35. Preparation of dodecakis(3,4,5-trimethylphenylthio)coronene (151).

Sodium 3,4,5-trimethylbenzenethiolate was made from 3,4,5-trimethylbenzenethiol 1.17g (7.7 mmoles) and 95% sodium hydride 0.19g (8.1 mmoles) according to the method of Example 32. It was reacted with perchlorocoronene 0.23g (0.32 mmoles) in dry DMEU for 2 days at room temperature and the reacted material also isolated according to the method of Example 31. Purification of the crude product by trituration with 1,4-dioxane gave 0.62g (2.9 mmoles) of compound (151), yield 92%, M.P. > 310^{O}C. Tetrahydrothiophene clathrate . Found: C, 75.35; H, 6.45%. $C_{132}H_{132}S_{12}$ requires C, 75.42; H, 6.28%(empty form); δ_H (200 MHz, $CDCl_3$) 139.85 (s), 136.00 (s), 135.30 (s), 134.50 (s), 131.71 (s), 126.25 (d), 123.39 (s), 20.26 (q), 14.87 (q).

36. Preparation of dodecakis(3,5-dimethoxyphenylthio)coronene (152)

Sodium 3,5-dimethoxybenzenethiolate was made from 3,5-dimethoxybenzenethiol 1.31g (7.7 mmoles) and sodium 0.18g (7.7 mmoles) according to the method of Example 31. It was reacted with perchlorocoronene 0.23g (0.32 mmoles) in dry DMEU for 2 days at room temperature, and the reacted material also isolated according to the method of Example 31. Purification of the crude product by crystallisation from 1,4-dioxane/methanol gave 0.56g (0.24 mmoles) of compound (152) as a black/purple powder, yield 75%, m.p.211-216°C. δ_H (200 MHz, $CDCl_3$) 6.05 (s, 12H), 5.78 (s, 24H), 3.33 (s, 72H); δ_C (50 MHz, $CDCl_3$) 160.45 (s), 140.76 (s), 135.19 (s), 123.64 (s), 114.87 (s), 104.56 (d), 98.44 (d), 54.86 (q).

37. Preparation of dodecakis(3,5-di-*t*-butylphenylthio)coronene (153).

Sodium 3,5-di-*t*-butylbenzenethiolate was made from 3,5-di-*t*-butylbenzenethiol 1.86g (8.4 mmoles) and 95% sodium hydride 0.21g (8.8 mmoles) according to the method of Example 32. It was reacted with perchlorocoronene 0.25g (0.35 mmoles) in dry DMEU at room temperature for 2 days and the reacted material also isolated according to the method of Example 31. Purification of the crude product by trituration with 1,4-dioxane gave 0.89g (0.3 mmoles) of (153) as a red powder, yield 87% m.p. 256-259°C. δ_H (200 MHz, $CDCl_3$) 7.38-6.54 (m, 36H), 1.52-0.61 (m, 216H). δ_C (50 MHz, $CDCl_3$) broad resonances observed at 150.63, 136.8, 122.54, 119.63, 34.55 and 31.19.

38. Preparation of dodecakis(3,4-dimethylphenylthio)coronene (154).

Sodium 3,4-dimethylbenzenethiolate was made from 3,4-dimethyl-benzenethiol 0.98g (7.1 mmoles) and sodium 0.16g (7.1 mmoles) according to the method of Example 31. It was reacted with perchlorocoronene 0.21g (0.29 mmoles) in dry DMEU for 2 days at room temperature, and the reacted material also isolated according to the method of Example 31. Purification of the crude product by trituration with 1,4-dioxane gave 0.53g (0.27 mmoles) of (154) as a fine red powder, yield 94%, m.p. 195-197°C. δ_H (200 MHz, $CDCl_3$) 6.51 (d, J=8Hz, 24H), 6.06 (dd, J=8Hz; J=1.5 Hz, 12H), 2.10 (s, 36H), 1.93 (s, 36H); δ_C (50 MHz, $CDCl_3$) 139.98 (s), 136.23 (s), 133.14 (s), 129.66 (d), 127.84 (d), 124.19 (d), 123.86 (s), 19.61 (q), 19.36 (q); FAB MS, *m/e* 1933, $(M+H)^+$.

39. Preparation of dodecakis(5-indanylthio)coronene (155).

Sodium 5-indanylthiolate was made from 5-indanethiol 1.26g (8.4 mmoles) and sodium 0.19g (8.4 mmoles) according to the method of Example 31. It was reacted with perchlorocoronene 0.25g (0.35 mmoles) in 20 ml of dry DMEU at room temperature for 2 days, and the reacted material also isolated according to the method of Example 31. Purification of the crude product by crystallisation from dichloromethane/1,4-dioxane gave 0.53g of compound (155) as brown/red crystals, yield 72.9% m.p. 193-194°C. δ_H (200 MHz, $CDCl_3$) 6.70 (d, J=8Hz, 12H), 6.53 (s, 12H), 6.29 (d, J=8Hz, 12H), 2.76 (t, J=7.1Hz, 24H), 2.55 (t, J=7.1Hz, 24H), 1.93 (quintet, J=7.1Hz, 24H); δ_C (50 MHz, $CDCl_3$) 144.10 (s), 141.10 (s), 140.03 (s), 137.19 (s), 133.43 (s), 124.92 (d), 124.21 (d), 123.92 (s), 122.78 (d), 32.65 (t), 32.42 (t) and 25.29 (t).

40. Preparation of dodecakis(*m*-methoxyphenylthio)coronene (156).

Sodium *m*-methoxybenzenethiolate was made from *m*-methoxybenzenethiol 1.13g (8.1 mmoles) and sodium 0.19g (8.1 mmoles) according to the method of Example 31. It was reacted with perchlorocoronene 0.24g (0.34 mmoles) in 20 ml of dry DMEU at room temperature for 2 days and the reacted material also isolated according to the method of example 31. Purification of the crude product by crystallisation from chloroform/1,4-dioxane gave 0.59g of compound (156) as purple crystals, yield 88.7%, m.p. 217-218°C. δ_H (200 MHz, $CDCl_3$) 6.79 (t, J=8 Hz, 12H), 6.58 (dd, J=7.8 Hz, J=1.8 Hz, 12H), 6.35 (s, 12H), 5.92 (d, J=8 Hz, 12H), 3.55 (s, 36H); δ_C (50 MHz, $CDCl_3$) 159.33 (s), 140.89 (s), 140.15 (s),

133.72 (s), 129.36 (d), 124.16 (s), 122.25 (s), 119.13 (d), 111.67 (d), 55.02 (q); FAB MS, *m/e* 1957, $(M+H)^+$.

41. Preparation of dodecakis(*m-t*-butylphenylthio)coronene (157).

Sodium *m-t*-butylbenzenethiolate was made from *m-t*-butylbenzenethiol 1.39g (8.4 mmoles) and 95% sodium hydride 0.21g (8.8 mmoles) according to the method of Example 32. It was reacted with perchlorocoronene 0.25g (0.35 mmoles) in 20ml of dry DMEU at room temperature for 2 days, and the reacted material also isolated according to the method of Example 31. Purification of the crude product by trituration with 1,4-dioxane gave 0.73g of (157) as a red powder, single spot by reverse-phase TLC, yield 91.9%, m.p. 223-224°C. δ_H (200 MHz, $CDCl_3$) 7.11 (d, 12H), 6.97 (t, 12H), 6.40 (broad resonance, 24H), 1.03 (broad resonance, 108H); δ_C (50 MHz, $CDCl_3$) 151.60 s, 139.96 (s), 129.13 (s), 124.62 (s), 124.06 (d), 123.44 (d), 122.64 (d), 34.80 (s), 31.27 (q).

42. Preparation of dodecakis(*p*-cumylphenylthio)coronene (158)

Sodium *p*-cumylbenzenethiolate was made from *p*-cumylbenzenethiol 1.85g (8.1 mmoles) and sodium 0.19g (8.1 mmoles) according to the method of Example 31. It was reacted with perchlorocoronene 0.24g (0.34 mmoles) in 20ml of dry DMEU at room temperature for 2 days, and the reacted material also isolated according to the method of Example 31. The crude product was purified by crystallisation from carbon tetrachloride/isopropanol to give 0.91g of a red microcrystalline material, single spot by reverse-phase TLC, yield 88.9%, m.p. 196-

201°C. δ_H (200 MHz, $CDCl_3$) broad resonances at 7.17, 6.71, 6.46, 1.46; δ_C (50 MHz, $CDCl_3$) 150.54 (s), 127.99 (d), 126.75 (d), 125.55 (d), 42.56 (s), 30.58 (q,br).

43. Preparation of dodecakis(*p*-adamantylphenylthio)coronene (159)

Sodium *p*-adamantylbenzenethiolate was made from *p*-adamantylbenzenethiol 1.88g (7.7 mmoles) and sodium 0.18g (7.7 mmoles) according to the method of Example 32. It was reacted with perchlorocoronene 0.23g (0.32 mmoles) in 20ml of DMEU at room temperature for 2 days and the reacted material also isolated according to the method of Example 31. Purification of the crude product by triturating with 1,4-dioxane gave 0.92g of a purple microcrystalline material, one spot by reverse-phase TLC, yield 89.7%, m.p. >300°C. δ_H (200 MHz, CS_2) 6.81 (d, J=8Hz, 24H), 6.32 (d, J=8Hz, 24H), 1.93 (s,br,36H), 1.67 (s,br, 144H); δ_C (50 MHz, CS_2) 147.97 (s), 147.49 (s), 136.12 (s), 135.46 (s), 127.5 (d br), 125.6 (d br), 42.83 (t), 36.82 (t), 35.65 (s), 29.16 (d).

44. Preparation of dodecakis(*p*-methylsulphonylphenylthio)coronene (160)

Sodium *p*-methylsulphonylbenzenethiolate was made from *p*-methyl sulphonylbenzenethiol 1.52g (8.1 mmoles) and sodium 0.19g (8.1 mmoles) according to the method of Example 31. It was reacted with perchlorocoronene 0.24g (0.34 mmoles) in 20ml of dry DMEU at room temperature for 2 days, and the reacted material also isolated according to the method of Example 31. Purification of the product by trituration with 1,4-dioxane gave 0.81g of an orange powder, one spot by reverse-phase TLC, yield 94.1%, m.p 279-282°C. δ_H (200

MHz, D_6-DMSO) 7.56 (d, J=8.2 Hz, 24H), 6.81 (d, J=8.2 Hz, 24H), 3.11 (s,36H); δ_C(50 MHz, D_6-DMSO) 144.69 (s), 138.22 (s), 128.15 (d), 127.47 (d), 125.10 (s), 43.3 (q); FAB MS *m/e* 2533, $(M+H)^+$

45. Preparation of dodecakis(estronethio)coronene (161)

Sodium estronethiolate was made from estronethiol 0.918g (3.4 mmoles) and 95% sodium hydride 86 mgs (3.6 mmoles) according to the method for Example 32. It was reacted with perchlorocoronene 0.1g (0.14 mmoles) in 10ml of dry DMEU at room temperature for 4 days and the reacted material also isolated according to the method of Example 31. Purification of the crude product by crystallisation from 1,4-dioxane/methanol gave 0.35g of an amorphous purple glass, one spot by reverse-phase TLC, yield 71.1%, m.p. > 320°C (glass). δ_H(200 MHz, $CDCl_3$) extremely broad resonances observed at 7.0-6.1 and 2.8-0.6.

Synthesis of Oxygen-link Coronene Hosts.

46. Preparation of dodecakis(3,5-dimethylphenoxy)coronene (162)

3,5-Dimethyl phenol 2g (16.4 mmoles) was added to a 100ml 3-necked flask equipped with condenser, nitrogen bleed, magnetic stirring bar and containing 35ml of dry diglyme. The solution was purged with nitrogen for 10 minutes, then sodium 0.38g (16.4 mmoles) added, and the mixture warmed to 90° with stirring. After approximately 3 hours under a nitrogen atmosphere the sodium had disappeared indicating the complete formation of the phenoxide salt. The solution was quickly transferred to a 100 ml quick-fit round-bottomed flask

and evaporated on the rotary evaporator. Residual diglyme was removed under oil pump vacuum with heating. The dry salt (2.3g) was stored under vacuum.

Sodium 3,5-dimethylphenolate 1.41g (9.8 mmoles) was then added to a 100ml quick-fit conical flask containing 20 ml of degassed DMEU, perchlorocoronene 0.2g (0.28 mmoles), a rubber septum, and magnetic stirring bar. The mixture was degassed for a further 20 minutes then placed in a pre-equilibrated oil bath at 90°C for 8 weeks with stirring.

At the end of the 8 week reaction period, the reacted material was transferred into a 1L separating-funnel containing 250 ml of toluene, and washed with ten 250 ml portions of water. Evaporation of the organic layer gave a brown oil which was purified on silica by column chromatography (eluent 60-80° petrol/diethyl ether 97/3), giving 88mgs of compound (163) as a yellow powder, yield 18.1%, m.p. 291-292°C. δ_H (200 MHz, $CDCl_3$) 6.40 (s, 12H), 6.04 (s, 24H), 1.99 (s, 72H); FAB MS, *m/e* 1741, $(M+H)^+$.

47. Attempted preparation of compound (163), dodecakis(phenoxy)coronene

Sodium phenolate was made from phenol 0.92g (9.8 mmoles) and sodium 0.23g (9.8 mmoles) according to the method of Example 46. It was reacted with perchlorocoronene 0.2g (0.28 mmoles) in 20 ml of dry DMEU at 90°C for 14 weeks, and the reacted material also isolated according to the method of Example 46. Analysis of the crude brown oil isolated revealed the presence of six different compounds by TLC (silica).

48. Attempted preparation of dodecakis(3,5-di-*t*-butylphenoxy)coronene (164).

Sodium 3,5-di-*t*-butylphenolate was made from 3,5-di-*t*-butylphenol 2.2g (10.8 mmoles) and sodium 0.25g (10.8 mmoles) according to the method of Example 46. It was reacted with perchlorocoronene 0.22g (0.31 mmoles) in 20ml of dry DMEU at 90°C for 14 weeks, and the reacted material also isolated according to the method of Example 46. Analysis of the product by TLC (silica) revealed the presence of 5 different compounds.

49. Attempted preparation of dodecakis(3,4,5-trimethylphenoxy)coronene (165).

Sodium 3,4,5-trimethylphenolate was made from 3,4,5-trimethylphenol 1.3g (9.8 mmoles) and sodium 0.23g (9.8 mmoles) according to the method of Example 46. It was reacted with perchlorocoronene 0.2g (0.28 mmoles) in DMEU at 90°C for 14 weeks and he reacted material also isolated according to the method of Example 46. The final crude product analysed as 5 different compounds by TLC (silica).

50. Preparation of dodecakis(*p*-cumylphenoxy)coronene (166).

Sodium *p*-cumylphenolate was made from *p*-cumylphenol 2.29g (10.8 mmoles) and sodium 0.25g (10.8 mmoles) according to the method of Example 46. It was reacted with perchlorocoronene 0.22g (0.31 mmoles) in 25ml of dry DMEU for 7 weeks at 90°C, and the reacted material also isolated according to the method of Example 46. Purification of the crude product by column chromatography on silica (eluent 60-80° petrol/diethyl ether, 98/2), gave 0.26g of

compound (166) as a yellow powder, yield 29.7%, m.p.>300°C. δ_H(200 MHz, $CDCl_3$) 7.18-7.12 (m,60H), 6.78 (AA BB system, aromatic,24H), 6.30(AA BB system, aromatic,24H), 1.52 (s,72H); δ_C(50MHz, $CDCl_3$), 156.26 (s), 150.96 (s), 143.29 (s), 141.63 (s), 127.82 (d), 126.87 (d), 126.71 (d), 125.41 (d), 120.98 (s), 120.05 (s), 114.79 (d), 113.50 (s), 42.26 (s), 30.94 (d); FAB MS *m/e* 2821, $(M+H)^+$.

51. Attempted synthesis of dodecakis (3,5-dimethylphenylseleno)coronene (167a)

(a) Sodium 3,5-dimethylbenzeneselenolate was made from 3,5-dimethylbenzeneselenol 1.55g (8.4 mmoles) and 95% sodium hydride 0.21g (8.8 mmoles) according to the method of Example 32. It was reacted with perchlorocoronene 0.25g (0.35 mmoles) in 20ml of dry DMEU for 2 days and the reacted material also isolated according to the method of Example 31. The crude product analysed as 5 different compounds by reverse-phase TLC.

(b) Procedure as in (51a) above; the reaction run in the absence of light. Crude product analysed as 5 different compounds by reverse-phase TLC.

(c) Procedure as in (51b) with 18 molar equivalents of sodium 3,5-dimethylbenzeneselenolate used instead of the normal 24. Crude product analysed as 4 different compounds by reverse-phase TLC.

(d) Procedure as in (51c) with a 12 hour reaction period. Reacted material analysed as 4 spots by reverse-phase TLC.

Synthesis of Sulphur-link Hexa-hosts

52. Preparation of hexakis(3,5-dimethylphenylthio)benzene (168).

Sodium 3,5-dimethylbenzenethiolate was made from 3,5-dimethylbenzenethiol 2.67g (19.4 mmoles) and sodium 0.44g (19.4 mmoles) according to the method of Example 31. It was then added to a 100ml quick conical flask equipped with stirring bar, rubber septum and 30ml of dry degassed DMEU. The contents of the flask were then degassed for a further 15 minutes before addition of perfluorobenzene 0.3g (1.6 mmoles). The reaction was carried out with stirring at room temperature for 3 hours under a nitrogen atmosphere (degassing after addition of perfluorobenzene may result in removal of this low boiling reagent from solution). The reacted material was then isolated in accord with the method of Example 31. Purification by column chromatography on silica (eluent 60-80° petrol/diethyl ether 10/1) gave 1.2g of compound (168) as a green fluorescent microcrystalline material, yield 83.9%, m.p.203-205°C. δ_H (200 MHz, $CDCl_3$), 6.67 (s, 6H), 6.55 (s, 12H), 2.15 (s, 36H); δ_C (50 MHz, $CDCl_3$) 148.59 (s), 138.19 (s), 139.69 (s), 127.68 (d), 125.51 (d) and 21.31 (q).

53. Preparation of hexakis(*m*-methoxyphenylthio)benzene (169).

Sodium *m*-methoxybenzenethiolate was made from *m*-methoxybenzenethiol 2.89g (20.6 mmoles) and sodium 0.47g (20.6 mmoles) according to the method of Example 31. It was reacted with perfluorobenzene 0.32g (1.7 mmoles) in 35ml of dry DMEU for 3 hours at room temperature according to the method of

Example 52. The reacted material was then isolated according to the method of Example 31. Purification of the crude material by column chromatography (silica) gave 1.35g of compound (169) as yellow/green crystals, 87.7% yield, m.p. 141-142°C. δ_H (200 MHz, $CDCl_3$) 7.08 (t, J=8.2H, 6H), 6.66 (ddd, J=8.4 Hz; J=1.4 Hz; J=1 Hz, 6H), 6.52 (m, 12H), 3.68 (s, 18H); δ_C (50 MHz, $CDCl_3$) 160.42 (s), 148.71 (s), 139.38 (s), 130.18 (d), 120.15 (d), 113.51 (d), 112.10 (d) and 55.50 (q).

54. Preparation of hexakis(*p*-methylsulphonylphenylthio)benzene (170).

Sodium *p*-methylsulphonylbenzenethiolate was made from *p*-methylsulphonylbenzenethiol 3.03g (16.3 mmoles) and sodium 0.37g (16.3 mmoles) according to the method of Example 31. It was reacted with perfluorobenzene 0.26g (1.4 mmoles) in 40ml of dry DMEU at room temperature for 3 hours according to the method of Example 52, and the reacted material also isolated according to the method of Example 31. Purification of the crude product by column chromatography (silica; eluent acetone/CH_2Cl_2 4/1) gave 1.45g of compound (170) as a fine yellow powder, yield 86.7%, m.p. 181-184°C. δ_H (200 MHz, D6-DMSO) 7.76 (AA'BB' aromatic, 12H), 7.30 (AA'BB' aromatic, 12H), 3.16 (s, 18H); δ_C (50 MHz, D6-DMSO) 147.49 (s), 143.61 (s), 138.29 (s), 127.86 (d), 126.86 (d), 43.45 (q).

Synthesis of Sulphur-link Octa-hosts

55. Preparation of octakis(3,5-dimethylphenylthio)naphthalene (171)

Sodium 3,5-dimethylbenzenethiolate was made from 3,5-dimethylbenzenethiol 2.03g (14.7 mmoles) and sodium 0.34g (14.7 mmoles) according to the method of Example 31. It was reacted with perfluoronaphthalene 0.25g (0.92 mmoles) in 30ml of dry DMEU for 3 hours and the reacted material also isolated according to the method of Example 31. Purification of the crude product by crystallisation from 1,4-dioxane/methanol gave 0.98g of compound (171) as red crystals, yield 87.6%, m.p. 180-181°C. δ_H (200 MHz, $CDCl_3$) 6.63 (2 peaks, 8H), 6.48 (s, 8H), 6.37 (s, 8H), 2.05 (2 peaks, 48H). δ_C (50 MHz, $CDCl_3$) 146.93 (s), 143.32 (s), 139.89 (s), 138.33 (s), 137.97 (s), 137.95 (s), 137.17 (s), 127.68 (d), 127.27 (d), 124.53 (d), 124.43 (d), 21.25 (q), 21.16 (q).

56. Preparation of octakis(3,4,5-trimethylphenylthio)naphthalene (172).

Sodium 3,4,5-trimethylbenzenethiolate was made from 3,4,5-trimethylbenzenethiol 2.06g (13.5 mmoles) and 95% sodium hydride 0.34g (14.2 mmoles) according to the method of Example 32. It was reacted with perfluoronaphthalene 0.23g (0.85 mmoles) in 30ml of dry DMEU at room temperature for 3 hours, and the reacted material also isolated according to the method of Example 31. Purification of the crude product by trituration with diethyl ether gave 1.05g of compound (172) as a red microcrystalline material, yield 93%, m.p.143-145°C. δ_H (200 MHz,$CDCl_3$) 6.49 (s, 8H), 6.42 (s, 8H), (2 peaks, 2.00 and 1.98, 72H). δ_C (50 MHz, $CDCl_3$) 146.81 (s), 143.46 (s), 138.62 (s), 136.53 (s), 136.46 (s),

133.52 (s), 132.43 (s), 132.11 (s), 126.82 (d), 126.17 (d), 20.56 (q), 20.42 (q) and 14.98 (q).

57. Preparation of octakis(3,5-dimethoxyphenylthio)naphthalene (173).

Sodium 3,5-dimethoxybenzenethiolate was made from 3,5-dimethoxybenzenethiol 2.5g (14.7 mmoles) and sodium 0.34g (14.7 mmoles) according to the method of Example 31. It was reacted with perfluoronaphthalene 0.25g (0.92 mmoles) in 30ml of dry DMEU for 3 hours at room temperature, and the reacted material also isolated according to the method of Example 31. Purification of the crude product by column chromatography (silica) gave 1.25g of compound (173) as a fine orange powder, yield 92.3%, m.p. 157-159°C. δ_H (200 MHz, $CDCl_3$) 6.13 (m, 8H), 6.07 (d, J=2.1 Hz, 8H), 5.94 (d, J=2.1 Hz, 8H), 2 peaks 3.57, 3.55, 48H; δ_C (50 MHz, $CDCl_3$) 160.74 (s), 160.6 (s), 147.92 (s), 143.51 (s), 141.96 (s), 139.09 (s), 138.25 (s), 105.49 (d), 104.29 (d), 98.64 (d), 98.11 (d), 55.1 (q).

58. Attempted preparation of octakis(3,5-di-t-butylphenylthio)naphthalene (174).

Sodium 3,5-di-*t*-butylbenzenethiolate was made from 3,5-di-*t*-butylbenzenethiol 3.26g (14.7 mmoles) and 95% sodium hydride 0.37g (15.5 mmoles) according to the method of Example 32. It was reacted with perfluoronaphthalene 0.25g (0.92 mmoles) in 35ml of DMEU for 5 hours, and the reacted material also isolated according to the method of Example 31. Purification of the crude product by column chromatography (silica) gave a 0.71g of a bright yellow

compound, one spot by TLC (silica), m.p. 243-4°C. δ_H (200 MHz, $CDCl_3$), 7.14 (m), 2 related peaks at 7.02 and 7.01, 2 related peaks at 6.95 and 6.94, 2 related peaks at 6.80 and 6.79, 3 related peaks at 1.14, 1.13 and 1.11; δ_C (50 MHz, $CDCl_3$) 2 related peaks at 151.1 and 151.0 (s), 146.93 (s), 136.1 (s), 133.66 (s), 3 related signals at 123.53, 122.70 and 122.19 (d); 3 related signals at 120.92, 120.34 and 120.09 (d), 37.74 (s), 31.27 (q); δ_F (188 MHz, $CDCl_3$), -92.45 (s).

59. Preparation of octakis(3,4-dimethylphenylthio)naphthalene (175).

Sodium 3,4-dimethylbenzenethiolate was made from 3,4-dimethylbenzenethiol 2.11g (15.29 mmoles) and sodium 0.35g (15.29 mmoles) according to the method of Example 31. It was reacted with perfluoronaphthalene 0.26g (0.96 mmoles) in 30ml of DMEU for 3 hours, and the reacted material also isolated according to the method of Example 31. Purification of the crude product by column chromatography on silica (eluent petrol 40-60 or 60-80°/diethyl ether 10/1) gave 0.96g of compound (175) as red cube-like crystals, yield 82.2%, m.p. 131-133°C (clathrate). δ_H (200 MHz, $CDCl_3$) 6.82 (m, 8H), 6.65 (m, 8H), 6.44 (dd, J=8Hz, J=1.9 Hz, 4H), 6.18 (dd, J=8Hz; J=1.9Hz, 4H), 4 peaks at 2.17, 2.09, 2.08 and 2.00 corresponding to two different moieties on the fully substituted spider-host (176), 48 H; δ_C (50 MHz, $CDCl_3$) 144.69 (s), 140.35 (s), 139.86 (s), 136.83 (s), 136.51 (s), 136.09 (s), 134.35 (s), 134.11 (s), 133.80 (s), 129.87 (d), 129.79 (d), 129.72 (d), 129.06 (d), 125.74 (d), 125.02 (d), 19.70 (q), 19.57 (q), 19.47 (q), 19.34 (q); υ max (KBr, select) 2960 (m), 2920 (m,br), 2860 (w,br), 1592 (s), 1483 (s), 1442 (s), 1380 (m), 1300 (w,br), 1225 (w), 1182 (m),

1140 (w,br), 1020 (w), 990 (m), 950 (w), 878 (s), 818 (s), 802 (s), 700 (w); FAB MS *m/e* 1216, M^+.

60. Preparation of octakis(*m-t*-butylphenylthio)naphthalene (176).

Sodium *m*-t-butylbenzenethiolate was made from *m-t*-butylbenzenethiol 2.44g, (14.71 mmoles) and 95% sodium hydride 0.37g (15.48 mmoles) according to the method of Example 32. It was reacted with perfluoronaphthalene 0.25g (0.92 mmoles) in 30ml of dry DMEU for 3 hours at room temperature and the reacted material also isolated according to the method of Example 31. The crude material was purified by crystallisation from 1,4-dioxane/methanol to give 1.1g of compound (176) as an orange powder, yield 83%, m.p. 203-205°C. δ_H (200 MHz, $CDCl_3$), 7.36-6.88 (m, 24H), 6.34 (d, J=7.7Hz, 4H), 6.12 (d, J=7.7Hz, 4H), 2 peaks at 1.71 and 1.21 corresponding to the *m-t*-butyl methyls of 2 distinct moieties. δ_C (50 MHz, $CDCl_3$), 151.48 (s), 151.35 (s), 144.76 (s), 140.75 (s), 140.18 (s), 138.68 (s), 137.24 (s), 128.46 (d), 127.94 (d), 126.83 (d), 125.54 (d), 124.94 (d), 124.43 (d), 122.97 (d), 122.97 (d), 122.78 (d), 34.69 (s), 34.60 (s), 31.20 (q), 31.16 (q).

61. Preparation of octakis(*p*-cumylphenylthio)naphthalene (177).

Sodium *p*-cumylbenzenethiolate was made from *p*-cumylbenzenethiol 3.4g (15.29 mmoles) and sodium 0.35g (15.29 mmoles) according to the method of Example 31. It was reacted with perfluoronaphthalene 0.26g (0.96 mmoles) in 40ml of DMEU for 3 hours and the reacted material also isolated according to

the method of Example 31. Purification by column chromatography (silica) gave 1.51g of compound (177) as an orange/red microcrystalline material, yield 81.2%, m.p. 161-162°C. Found: C, 80.52; H, 6.29%. $C_{130}H_{120}S_8$ requires C, 80.57; H, 6.20%. δ_H (200 MHz, $CDCl_3$) 7.23-7.04 (m, 40H), 6.89-6.63 (m, 32H), two peaks at 1.52 and 1.49 corresponding to methyls of two different side-chain moieties, 48H. δ_C (50 MHz, $CDCl_3$), 150.47 (s), 150.13 (s), 148.91 (s), 148.37 (s), 143.64 (s), 139.55 (s), 135.65 (s), 134.76 (s), 128.87 (d), 128.08 (d), 127.98 (d), 127.47 (d), 127.40 (d), 126.85 (d), 126.71 (d), 126.61 (d), 125.66 (d), 125.615 (d), 42.62 (s), 30.68 (q).

62. Attempted preparation of compound (178).

(a) Bis-sodium benzenedithiolate was made from 1,2-benzenedithiol 0.63g (4.41 mmoles) and sodium 0.2g (8.82 mmoles) according to the method of Example 31. It was reacted with perfluoronaphthalene 0.15g (0.55 mmoles) in 15ml of dry DMEU for 10 days at room temperature, and the reacted material also isolated according to the method of Example 31. Surprisingly, no product formation was noted by TLC (silica).

(b) Bis-sodium benzenedithiolate was made from 1,2-benzenedithiol 1.25g (8.82 mmoles) and sodium 0.41g (17.64 mmoles) according to the method of Example 31. It was reacted with perfluoronaphthalene 0.15g (0.55 mmoles) in 15ml of DMEU for 5 weeks at 65°C, and the reacted material also isolated according to the method of Example 31, using 1 litre of toluene to extract the

product.

Purification by trituration from 1,4-dioxane gave 0.2g of a light yellow product as a fine powder, m.p. > 320°C. *m/e* 680, M^+. One spot by TLC (silica).

Oxygen link Spider-hosts.

63. Preparation of octakis(3,5-dimethylphenoxy)naphthalene (179).

Sodium 3,5-dimethylphenolate was made from 3,5-dimethylphenol 2.69g (22.05 mmoles) and sodium 0.51g (22.05 mmoles) according to the method of Example 46. It was reacted with perfluoronaphthalene 0.25g (0.92 mmoles) in 25 ml of DMEU for 8 weeks at 90°C and the reacted material also isolated according to the method of Example 31. Purification of the crude product by crystallisation from 1,4-dioxane gave 0.67g of compound (179) as a white powder, yield 66.9%, m.p.197-198°C. δ_H (200 MHz, $CDCl_3$) 2 peaks at 6.50 and 6.45 corresponding to the proton para to sulphur on two different moieties, 8H; 6.16 (s, 16H); 2 peaks at 2.14 and 2.11 corresponding to methyl groups on two different moieties; δ_C (50 MHz, $CDCl_3$) 158.46 (s), 157.22 (s), 141.54 (s), 140.13 (s), 138.26 (s), 138.04 (s), 123.88 (d), 122.94 (d), 120.74 (s), 113.84 (d), 113.12 (d), 21.31 (q), 21.21 (q).

64. Preparation of octakis (*p*-cumylphenoxy)naphthalene (180).

Sodium *p*-cumylphenolate was made from *p*-cumylphenol 4.86g (22.94 mmoles) and sodium 0.53g, (22.94 mmoles) according to the method of Example 46. It was reacted with perfluoronaphthalene 0.26g (0.96 mmoles) in 50 ml of dry DMEU for 8 weeks at 90°C and the reacted material also isolated according to the method for Example 31. Purification of the crude material by crystallisation from 1,4-dioxane/methanol gave 1.21g of compound (181) as a white microcrystalline material yield 69.7%. m.p. 101-103°C. δ_H (200 MHz,

$CDCl_3$), 7.24-7.12 (m, 40H), 6.87 (t,J=9 Hz, 16H), 6.40 (d, J=9 Hz, 16H), 2 peaks at 1.56 and 1.54 corresponding to methyls on two different moieties; δ_C (50 MHz, $CDCl_3$), 156.22 (s), 154.85 (s), 150.93 (s), 150.91 (s), 144.39 (s), 143.52 (s), 140.99 (s), 139.94 (s), 127.87 (d), 127.84 (d), 127.12 (d), 127.09 (d), 126.75 (d), 126.66 (d), 125.50 (d), 125.44 (d), 120.25 (s), 115.26 (d), 114.57 (d), 42.30 (s), 30.93 (q), 30.83 (q); FAB MS *m/e* 1809, $(M+H)^+$.

Novel fluorocarbon reactions.

65. Attempted synthesis of octakis(phenylthio)acenaphthylene (185).

Sodium benzene thiolate was made from benzene thiol 1.26g (11.45 mmoles) according to the method of Example 31. It was reacted with perfluoroperhydroacenaphthene (183) 0.15g (0.29 mmoles) in 20ml of dry DMEU at 60°C for 10 days, and the reacted material also isolated according to the method for Example 31. TLC (silica) analysis of the crude product revealed the presence of six different compounds.

66. Preparation of octakis(phenylthio)naphthalene (185)

Sodium benzenethiolate was made from benzene thiol 0.94g (8.59 mmoles) and sodium 0.2g (8.59 mmoles) according to the method of Example 31. It was reacted with perfluoroperhydroacenaphthene (182) 0.15g (0.29 mmoles) in 20ml of dry DMEU at room temperature for 2 days, and the reacted material also isolated according to the method of Example 31. The crude product analysed as 3 different compounds by TLC (silica). Purification by column chromatography

gave 40 mgs of compound (184) as a black/purple microcrystalline material yield 13.6%, m.p.222-223°C. δ_H (200 MHz,$CDCl_3$) 7.15-6.75 (m 40H); δ_C(50MHz, $CDCl_3$), 148.81 (s), 141.72 (s), 141.45 (s), 139.91 (s), 139.53 (s), 138.61 (s), 137.82 (s), 137.15 (s), 136.51 (s), 133.25 (s), 131.88 (s), 128.87 (d), 128.73 (d), 128.66 (d), 128.54 (d), 128.32 (d), 128.15 (d), 127.83 (d), 127.55 (d); FAB MS *m/e* 1016 M^+.

67. Attempted optimisation of the reaction of sodium benzenethiolate with perfluoroperhydroacenaphthene.

(a) Procedure as in Example 66; reaction time of 10 minutes at O°C in DPEU as solvent. The reacted material analysed as 4 different compounds by TLC (silica).

(b) Procedure as in Example 66 with DMF employed as reaction solvent. Crude product analysed as 3 compounds by TLC (silica).

68. Reaction of perfluoroperhydroacenaphthene with different nucleophiles.

(a) Procedure as in Example 66 with *p*-methylbenzenethiolate employed as reagent. Analysis by TLC (silica) revealed the presence of 5 different compounds.

(b) Procedure as in Example 66 with *m*-methylbenzenethiolate employed as reagent. Analysis by TLC (silica) revealed presence of 4 different compounds.

(c) Procedure as in Example 66 with 3,5-dimethylbenzenethiolate employed as reagent. Analysis by TLC (silica) revealed presence of 5 different compounds.

69. Reaction of perfluoroperhydrocoronene (184) with sodium 3,5-dimethylbenzenethiolate.

(a) Sodium 3,5-dimethylbenzenethiolate was made from 3,5-dimethylbenzenethiol 0.82g (5.92 mmoles) and sodium 0.14g (5.92 mmoles) according to the method for Example 31. It was reacted with perfluoroperhydrocoronene (184) 0.08g (0.08 mmoles) in 15ml of dry DMEU at 65°C for 5 weeks, and the reacted material also isolated according to the method of Example 31. Analysis of the crude product by reverse-phase TLC revealed 5 different compounds were present, none of which were coloured.

(b) Sodium 3,5-dimethylbenzenethiolate was made from 3,5-dimethylbenzenethiol 3.55g (22.72 mmoles) and sodium 0.59g (25.72 mmoles) according to the method of Example 31. It was reacted with perfluoroperhydrocoronene (184) 0.1g (0.1 mmole) in 40ml of dry DMEU at 65°C for 8 weeks and the reacted material also isolated according to the method of Example 31. Purification by flash chromatography (silica) gave an orange/red oil (10mgs) which analysed as two compounds by reverse-phase TLC. FAB MS indicated presence of desired compound (139) with *m/e* 1933, $(M+H)^+$ Also observed peaks at *m/e* 1795 and 1676 - fragmentation peaks of compound (139) made by normal route. Peak at *m/e* 1539 corresponding approximately to compound (189).

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