UNPRECEDENTED REACTIVITY OF FLUOROCARBONS AND THE SYNTHESIS OF NEW INCLUSION COMPOUNDS

by

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DEDICATION

For Mum

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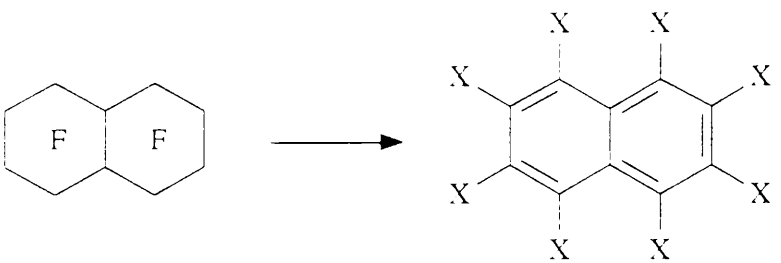
CONTENTS

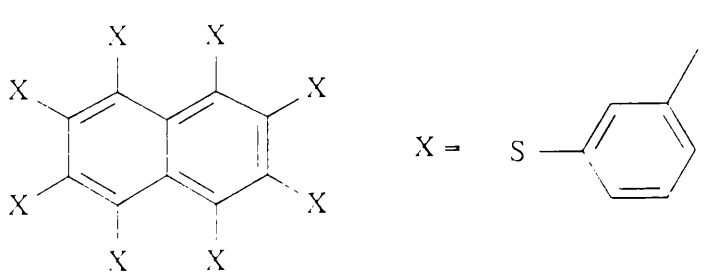
SUMMARY

A new and unprecedented reactivity of saturated fluorocarbons has been discovered. Application of this reaction to perfluorodecalin at ambient temperature and above is used to synthesis members of the 'octa-host' series.



The mechanism of the reaction and its extension to analogous reactions, including different substrates (unsaturated fluorocarbons or other saturated fluorocarbons, particularly those with a tertiary carbon centre) and different nucleophiles is investigated. A Single Electron Transfer (SET) pathway is favoured.

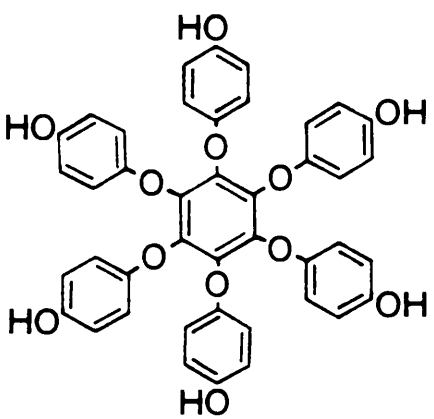
The 'octa-host' series itself, an extension of the 'hexa-host' series, is further investigated and new host inclusion discovered. A new class of host materials, octakis(aryloxy)naphthalenes, is synthesised. Structural investigation of six octa-hosts by X-ray single-crystal diffraction is used to elucidate their inclusion properties; uniquely one of the octa-hosts, octakis(m-tolylthio)-naphthalene has a 'clathrate' open-packed structure as a non-solvate, with no stabilisation other than by van der Waals forces.



Another, octakis(cyclohexylthio)naphthalene, contains an axial C-S cyclohexyl bond conformation. These two solid-structures are also investigated by magic angle spinning ^{13}C solid state n.m.r.

Other 'octa-host'-like variants were investigated, including routes to 'deca-hosts', anthracene based systems, both through classical synthesis routes and using the newly discovered reactivity of saturated fluorocarbons.

More structural tuning of the 'hexa-host' concept was investigated by the synthesis and solid-state structure elucidation of hexakis - (p-hydroxyphenyloxy)benzene, a potential β-Hydroquinone analogue.



Chiral legs for 'hexa-' and 'octa-hosts' were briefly investigated.

The role of symmetry in partnership with molecular conformation and shape is analysed for the 'octa-hosts', C_2 equivalents of the C_3 'hexa-hosts', and general principles discussed.

Fluorocarbon chemistry is summarised and recent progress in the directed design of inclusion compounds reviewed.

"L'étude des composés fluorés réserve encore bien des surprises".

H. Moissan

"In the field of observation, chance favours only the prepared mind".

L. Pasteur.

INTRODUCTION

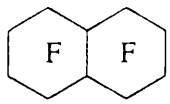
1. Fluorocarbons[1-7]

1.1 Nomenclature and background[1,2,8]

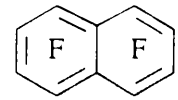
As in the term 'hydrocarbon' the name 'fluorocarbon' is self-explanatory, meaning a compound containing only carbon and fluorine. The tremendous growth in organofluorine publications has, however, almost totally devalued this definition to include compounds containing residual hydrogens, other atoms, e.g. ether or amine links, and even halogens. (In organofluorine chemistry it is practice to exclude fluorine itself from the group name halogens: halofluorocarbons, e.g. chlorofluorocarbons (CFCs) are indeed a major and topical class in their own right). A flexible naming system which makes such differences clear is the use of the prefix 'perfluoro'. This, prefixed to all of, or the relevant part of, a standard designation, indicates the replacement of all hydrogens with fluorine atoms unless the hydrogen atom is integral to the functionality.

In this way all the compounds in Figure 1, loosely described as fluorocarbons, are satisfactorily named without ambiguity. 'Perfluoro' nomenclature is adopted in this thesis and 'fluorocarbon' used in its original sense. The use of a capital F in a ring is equivalent in structural terms to perfluoro substitution of that system.

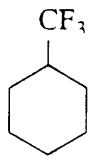
Organofluorine compounds now command an important position in chemistry and in commercial applications. Fluorocarbons themselves have a considerable and growing role in this respect because of their unique mix of chemical and physical properties. Unsaturated and aromatic fluorocarbons are of wide theoretical interest and synthetic utility, and saturated fluorocarbons and their derivatives are dominant in industrial usage.



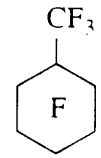
perfluorodecalin (1)



perfluoronaphthalene (2)



(perfluoromethyl)cyclohexane (3)



perfluoromethylcyclohexane (4)

$CF_3\,CO_2H$

perfluoroethanoic acid (5)

$CF_3\,CF_2\,O\,CF_2\,CF_3$

perfluoroethyl ether (6)

Figure 1

The history of saturated fluorocarbons is that of their synthesis, properties and applications with little exception since it is from their almost total lack of chemical reactivity that their use has grown. Organic fluorides are rare in nature. All known fluorocarbons are synthetic and most perfluoro analogues are already a reality - a measure of modern advancement.[8]

1.2. Synthesis

Early developments[1,9]

Industrial production of fluorocarbons and derivatives was founded on halogen exchange reactions and late 1930's-40's developments on the control of exhaustive fluorination, spurred on by American requirements to contain the UF_6 needed to make an atomic bomb - the Manhattan project.[10]

Early organofluorine chemistry was limited by the problems surrounding the production, handling and reactivity of elemental fluorine and hydrogen fluoride, and a lack of alternative reagents. Aromatic carbon-fluorine bond synthesis progressed through the use of diazonium salts and the Balz-Schiemann improvement,[11] although decreasing in use towards the forties. Isolation of elemental fluorine by Moissan in 1886 had not advanced the art (despite his valiant efforts). His claim to have made the first fluorocarbon, perfluoromethane, was later discredited. He had, however, quickly established that fluorine reacts violently with organic material even at low temperature because of the large exothermic heat of reaction caused by easy fluorine homolytic cleavage (158.8 kJ mol^{-1}) and very strong C-F formation (414-519, average 485 kJ mol^{-1}).[3,8,9] The energy released by this facile fluorination is more than sufficient to rupture C-C bonds and can manifest itself in fires and explosions.

Meanwhile, the first substantial progress in polyfluorocarbons was achieved by Swarts. Using various antimony halides, he prepared and documented a series of poly(halofluoro)aliphatic compounds by halogen exchange, in which he noted general stability, especially in C-F bonds, and unusual physical properties. In particular he transformed aromatic bound CCl_3 groups to CF_3. Exploitation of his work, by Midgley, led to the large-scale manufacture of chlorofluorocarbons as refrigerants, thus establishing the first major industrial fluorine technology.

In 1926 Lebeau and Damiens isolated perfluoroethane as the first fluorocarbon as an electrolysis of product at a carbon anode and then in 1930 Swarts recorded perfluoroethane from electrolysis of perfluoroethanoic acid. In the thirties, the use of better-designed reactors and inert diluents allowed direct fluorination of carbon to perfluoromethane, which Ruff and Bretschneider converted in an arc to perfluoroethane and the new perfluoroethene.

Saturated fluorocarbons[1,8,9,10]

The breakthrough arrived in 1937 after an experimental mistake allowed Simons and Block to observe that mercury smoothly catalysed the synthesis of higher fluorocarbons from fluorine and carbon at high temperatures due to in situ mercuric fluoride formation. The range of saturated fluorocarbons produced was C_1-C_7, including the cycles C_5F_{10} (7) b.p. 23°C, C_6F_{12} (8) b.p. 51°C and C_7F_{14} (9) b.p. 80°C.

Thus began the first significant work with fluorocarbons, indicating the possibility of cyclic and chain fluorocarbons of any size, their weak intermolecular forces, and their outstanding thermal and chemical stability.

Soon after, Bigelow isolated perfluorocyclohexane (8) as the main product from direct fluorination of vaporised benzene in copper gauze, and no aromatics were observed. Also at this time was the accidental discovery of poly(tetrafluoroethylene)(10) - PTFE - by Plunkett at Du Pont.

The Manhattan project led to the discovery of catalytic vapour phase fluorination of hydrocarbons by Cady and Grosse with Cu-Ag and Cu-Au the favoured systems. Substrates successfully tackled included anthracene (43% conversion), toluene (85%) and n-heptane (62%). This approach was overshadowed by two processes developed concurrently.

From the knowledge that certain transition metal high valency fluorides are fluorinating agents, Fowler and colleagues invented a process which effectively split the overall heat of reaction into halves.[2,10] The metal fluoride salt is regenerated during the reaction with a fluorine feed and cobalt trifluoride has remained the preferred choice:

$$C\text{-}H + 2\ CoF_3 \rightarrow C\text{-}F + HF + 2\ CoF_2 \qquad \Delta H = -52\ kcal\ mol^{-1}$$

$$2\ CoF_2 + F_2 \rightarrow 2\ CoF_3 \qquad \Delta H = -52\ kcal\ mol^{-1}$$

This proved to be a highly effective and reliable operation, remaining today the route to many of the specialist fluorocarbon chemicals marketed.[12]

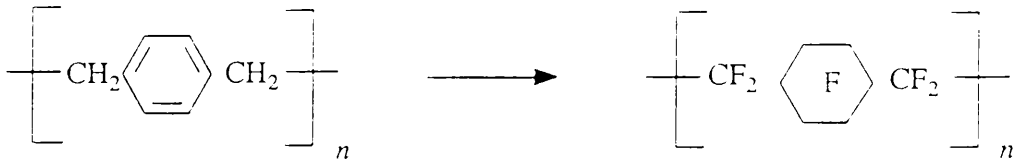
In response to the large quantities of expensive fluorine required in this route, McBee and co-workers utilised halogenation - halogen exchange chemistry to provide substrates giving overall cheaper fluorination.[10] Polyhalofluorocarbons are a major source of precursors to fluorocarbons, particularly the unsaturates.[8]

The other advance in exhaustive fluorination was again due to Simons[13] through his electrochemical fluorination technique (ECF).[8,14] In this, an organic substrate dissolved in anhydrous hydrogen fluoride is electrolysised at low voltage to yield the perfluorinated material and hydrogen gas. The process now provides most commercial fluorocarbon derivatives since much functionality is retained.[15] Hydrocarbons themselves are only sparingly soluble in hydrogen fluoride, thus rendering ECF unsuitable for fluorocarbon production.

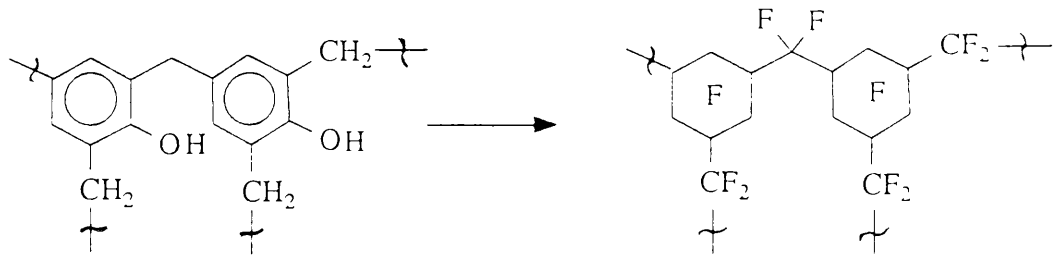
Not all (necessarily) saturated fluorocarbons or their derivatives, (particularly those containing weak bonds, including higher systems), can be either commercially produced or accessed by the above exhaustive fluorination techniques. This is most often attributable to the high monetary costs in energy, fluorine-wasteful methods and the expense of alternative fluorine sources, and the poor and complex yields associated with the skeletal rearrangements and fragmentations from the redox and radical based routes respectively.

Recent work has shown how these problems can be overcome in the facile direct fluorination of substrates by strict control of reaction conditions, particularly in the first stages, to give clean, high-yielding transformations. The two best methods currently are LaMar fluorination, developed by Lagow,[16] and Adcock's aerosol fluorination.[17] Both processes have been successful on the gram-quantity level with extensive types of substrate, and each predicts the realisation of scaling up in the near future.[8] The LaMar process is a batch cryogenic fluorination, performed over many hours, using infinite to zero dilution of fluorine gas in a multi-zone reactor packed with metal turnings.[18] In the continuous heterogeneous aerosol process, substrate adsorbed onto fine sodium fluoride particles is carried quickly in gas streams through an optimised temperature and fluorine gradient before final photochemically induced fluorination.[19] This can produce very cleanly from the reactor, for example, (8) in 30% yield from cyclohexane, and perfluoro(1,2 dimethoxyethane) (36%).[20] By use of the LaMar process, tetrakis-(perfluorocyclohexyl)methane, a compound containing weak bonds (see 1.3) has been made in 96% yield,[21] and perfluoro- (crownethers), e.g. perfluoro(18-Crown-6), 34% yield.[22] Of industrial importance has been the demonstrated use of LaMar fluorination on preformed polymers to produce the perfluoropolymer. It has long been known that direct fluorination of polymer surfaces imparts useful properties of inertness.[23,8] If suitably small polymer particles are used, Lagow has effected complete molecular fluorination.[24] Examples, (Figure 2), include poly-p-xylylene, polyisobutylene, phenol-formaldehyde resin and polyesters (completed using sulphur tetrafluoride to fluorinate carbonyl groups), to yield in the last case perfluoropolyether.[25] Perfluoro(polyisobutylene) cannot be made directly from the perfluoromonomer. Perfluoropolyethers are important materials.[15a,16,26]

A number of other techniques have been explored to control the fluorination of organic materials,[8,27a] including photofluorination in an inert solvent solution under a fluorine atmosphere.[27b] Other, less general routes are available for the synthesis of saturated fluorocarbons from more reactive fluorocarbons and fluorocarbon intermediates (Figure 3).



poly-p-xylylene



phenol-formaldehyde resin

Figure 2 (adapted from ref.24)

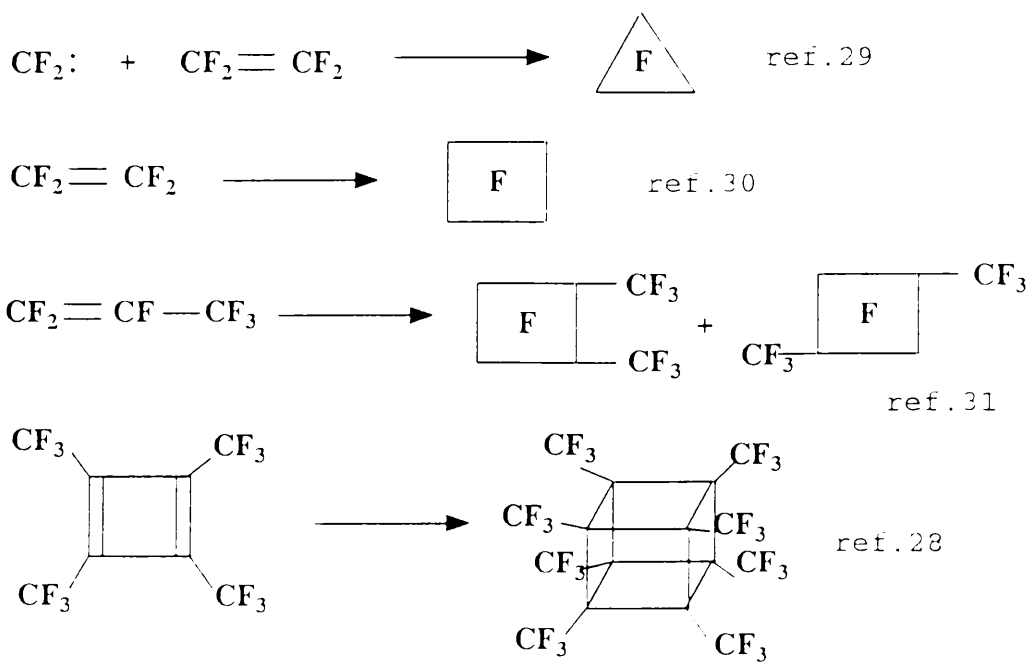


Figure 3

Three-membered rings are accessed from the readily-formed difluorocarbene and a perfluoro-olefin, whilst easy, preferred, [2+2] cycloadditions of perfluoro-olefins leads to four-membered rings.[28,3]

Addition of (elemental) fluorine to unsaturated fluorocarbons has not been extensively used and only a few examples are recorded, e.g. perfluoropropane from perfluoropropene.[32,33] Recent work in this field has, however, led to the discovery of intermediate radicals stable in solution, even heated, under air or with hydrogen- donating solvents.[34] Some work has been done on fluorination of oligmers of $CF_2 = CF_2$ with CoF_3.[35] Surprisingly little has been done to quench perfluorocarbanions with an electrophilic fluorine source, achieved by Banks for the perfluoroisopropyl anion with perfluoro-N-fluoropiperidine.[36]

Aromatic fluorocarbons[8] (Figure 4)

Since fluorination of aromatic hydrocarbons almost invariably leads to addition products, their fluorocarbon counterparts cannot normally be made directly. Two procedures are the preferred laboratory and commercial method to overcome this, saturation-aromatisation[37-40] and fluoride exchange of perhaloaromatics (Halex reaction).[45]

The first synthesis in this field is attributed to Désirant, who pyrolysed tribromofluoromethane to give perfluorobenzene,[46] though this compound was first published by McBee (made from hexachlorobenzene using Swarts chemistry and zinc dehalogention in miserable yield).[47]

Tatlow and co-workers found that cyclic saturated fluorocarbons, or partially unsaturated systems,[37-40] could be aromatised at ca. 500°C over nickel or iron. Unfortunately, the yields rapidly decrease with more complex systems.

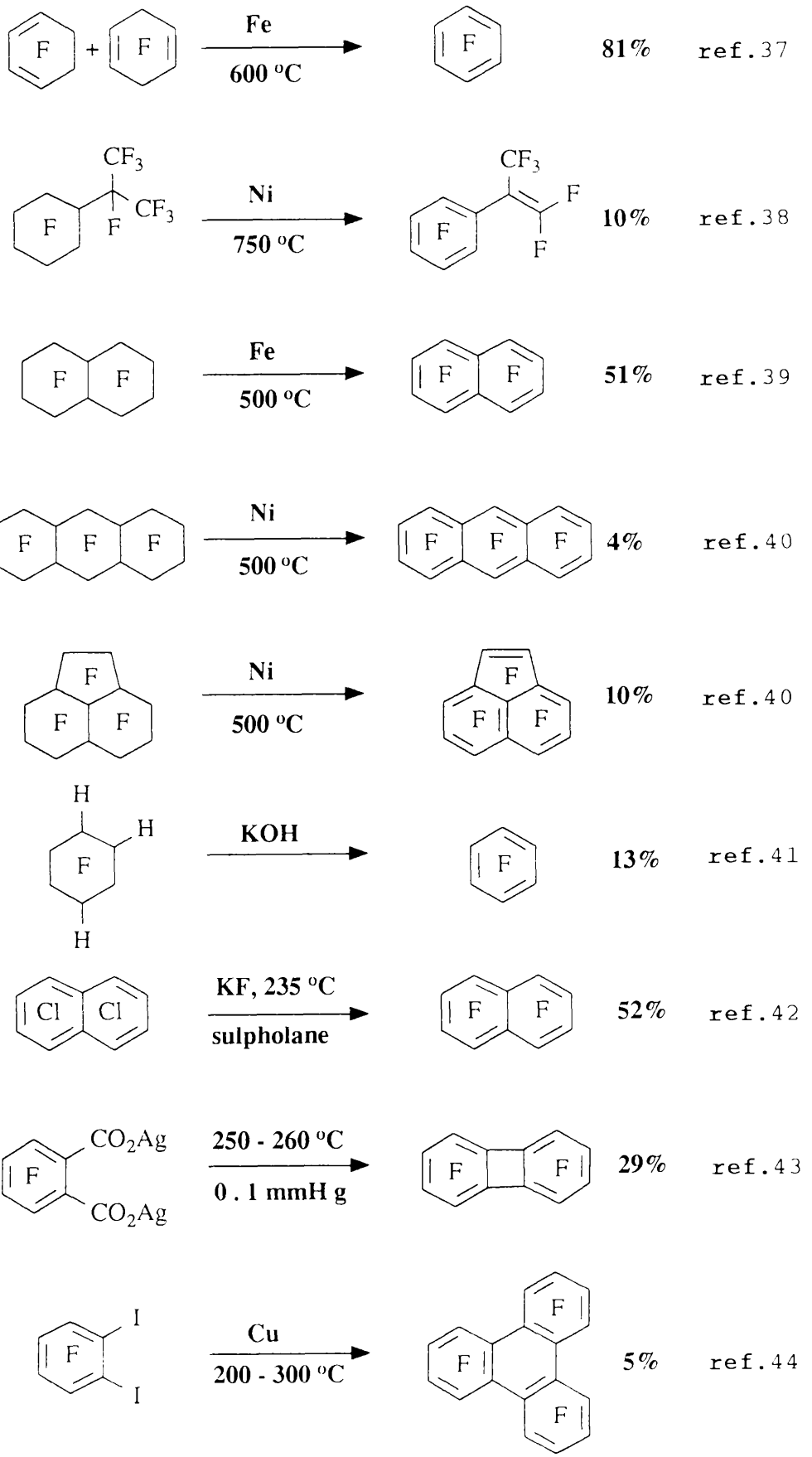

Fe
600 °C
81%
ref.37
Ni
750 °C
10%
ref.38
Fe
500 °C
51%
ref.39
Ni
500 °C
4%
ref.40
Ni
500 °C
10%
ref.40
KOH
13%
ref.41
KF, 235 °C
sulpholane
52%
ref.42
250 - 260 °C
0 . 1 mmH g
29%
ref.43
Cu
200 - 300 °C
5%
ref.44

Figure 4

It was found that using a milder fluorinating agent like CeF_4 or $KCoF_4$, or by running the CoF_3 fluorination at lower temperature,[48] incomplete reaction was achieved leaving residual hydrogen[49] and/or unsaturation.[50] Indeed, with some salts (such as the potassium tetrafluorocobalt) the aromatic system may remain intact and the products may contain some of the perfluoroaromatic itself.[51] Products with suitable numbers and placement of hydrogen can then be dehydrofluorinated with strong base,[41] taking care not to allow the base to react nucleophilically with the aromatic fluorocarbon product. A more recent improvement of this reaction has been published also.[52]

The second approach is to displace halide, chloride normally, from perhaloaromatics with fluoride in a dipolar aprotic solvent, or if necessary at higher temperature in an autoclave with solvent or alternatively in an electrolytic melt.[42,45,53]

More complex aromatic fluorocarbon systems have been synthesised using conventional techniques (e.g. arynes), with suitable derivatives,[43,7] and perfluoro(hexakismethylbenzene) resulted from trimerisation of perfluoro(bismethylacetylene).[54]

Unsaturated fluorocarbons (Figure 5)

Perfluoro-olefins also cannot normally be synthesised directly, except again with some mild high valency metal fluoride processes[55] and additionally one case of complete one-step halogen exchange.[56] Normally, these materials are made from polyfluorocarbons with a structural feature suitable for creating unsaturation. These processes - dehydrofluorination,[57,58] dehalogination,[61,62] defluorination[59,60] and decarboxylation[63] - are formally those of 1,2-elimination.

Suitable substrates are furnished by techniques already mentioned - incompletely fluorinated hydrocarbons, halogen exchange products, fluorinated hydrocarbons and ECF of carboxylic acids respectively.

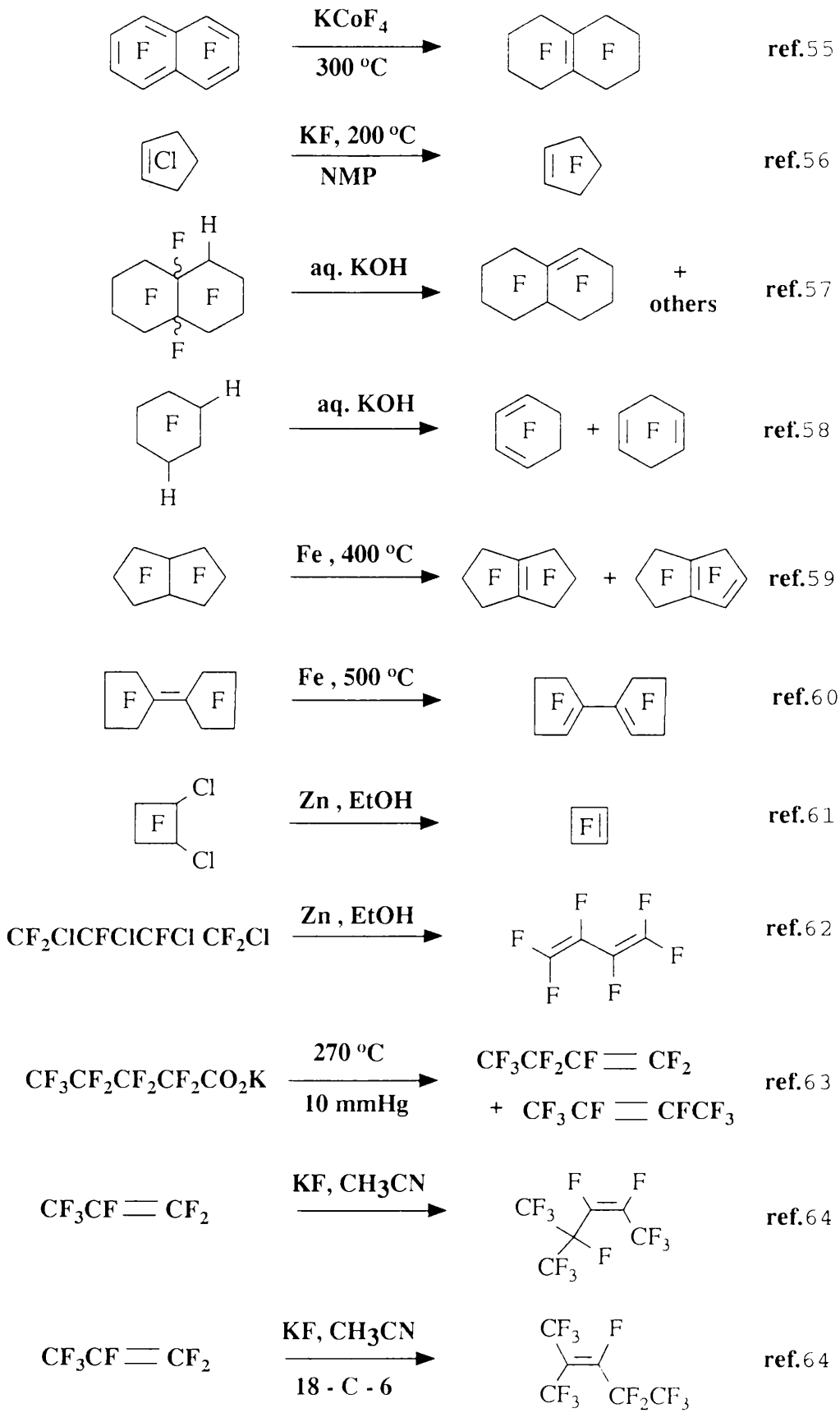

KCoF4
300 °C
ref.55
KF, 200 °C
NMP
ref.56
aq. KOH
+
others
ref.57
aq. KOH
ref.58
Fe , 400 °C
ref.59
Fe , 500 °C
ref.60
Zn , EtOH
ref.61
CF2ClCFClCFCl CF2Cl
Zn , EtOH
ref.62
CF3CF2CF2CF2CO2K
270 °C
10 mmHg
CF3CF2CF = CF2
+ CF3CF = CFCF3
ref.63
CF3CF = CF2
KF, CH3CN
ref.64
CF3CF = CF2
KF, CH3CN
18 - C - 6
ref.64

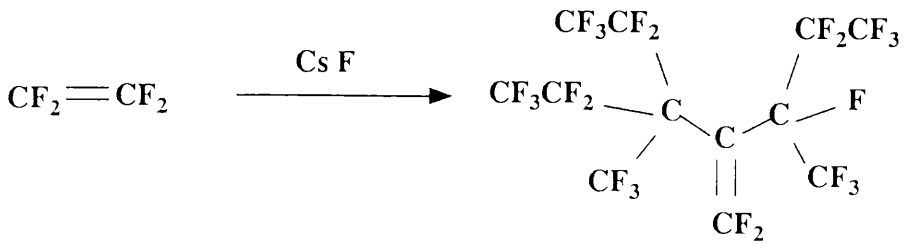
Figure 5

Dehydrofluorination is limited by product control and separation after fluorination, and defluorination by specificity (usually leading to an aromatic product). Dehalogination has been widely used to form many acyclic and cyclic perfluoro-olefins and decarboxylation leads to both terminal and internal unsaturation directly or induced by isomerisation.

Pyrolysis of fluorocarbons also leads to unsaturation arising from C-C bond cleavage, and PTFE is a convenient laboratory source of lower olefins, the exact composition of which depends on temperature and pressure. TFE can be produced almost exclusively by PTFE pyrolysis at ca. 610°C in vacuo.[65]

Perfluoro-olefins can be synthesised variously from other perfluoro-olefins, e.g. pyrolysis, photochemically, isomerisation, carbene addition, coupling (of Iodo derivatives), and the most successful source of new perfluoro-olefin systems in recent years has been through fluoride induced oligmerisations.[64]

Since Miller's discovery that perfluorocarbons could be generated from perfluoro-olefins and fluoride in dipolar aprotic solvents, much work has been carried out, particularly concerning the oligmerisation of perfluoroethylene and proprene, and more recently cyclic olefins.[3,66] Olefins are produced by the β-elimination of a fluoride from the growing chain. Because isomerisation to more stable internal unsaturation and regiospecific attack to give tertiary carbanions is preferred, the products tend to be highly branched. Propylene usually yields only dimers and trimers, controllable by the method of generation, though more recent conditions allow production of hexamers. The more active perfluorethyl carbanion easily yields the hexamer (11) with product distribution dependant on fluoride/CF_2CF_2 ratio.[67]



(11)

Perfluoro polymers and telomers[8,68]

The first, and still the foremost, fluorocarbon to find a large commercial outlet was a polymer - poly(tetrafluoroethylene)(PTFE). Discovered by Plunkett in 1938 after accidental spontaneous radical polymerisation of tetrafluoroethylene(TFE), its properties were soon recognised and developed, spawning large research effort into other polymers and helping to found organofluorine chemistry as a subject due further investigation.

Fabrication difficulties have led to a search for similar materials retaining the qualities of PTFE but in more manageable form.[69] Most of these are polyfluoropolymers, e.g. Viton A, but one other fluorocarbon polymer is in widespread use, FEP (fluorinated ethylene propene), a co-monomer of TFE and HFP (hexafluoropropane). HFP, higher fluoro-olefins and di-olefins were found difficult to homopolymerise to high molecular weights. Aromatic fluoropolymers have also been investigated.[70] Normal polymerisation techniques are used to make these materials.

Related compounds of high synthetic and industrial value are TFE telomers, initiated by attack of other radicals, particularly R_fI species, on the perfluoro alkene.[15b,71] Control of length and side products has been investigated and a recent paper describes the more controlled, efficient, low temperature and time production of these chains by a copper-mediated reaction.[72]

1.3 Chemical reactivity of fluorocarbons[8]

Saturated fluorocarbons

In a recent review, Tatlow reported "It is almost too well known to need stating that saturated fluorocarbons have few reactions and even these require extreme forcing conditions".[73] The carbon chain in saturated fluorocarbons is protected by a close fit of fluorines, very strongly bonded (see 1.4), the surface of which is a sea of electrons - described by Simons as "hearts of diamonds and skins of rhinoceros hide".[74a] Reactions are resisted even when thermodynamics would dictate otherwise.[75] Boiling concentrated acids and alkalis, molten alkalis, oxidising and reducing agents under usual conditions and other highly reactive systems are all ineffectual in breaking down saturated fluorocarbons,[74b] which do not hydrolyise below 500°C[76] but are slowly decomposed in liquid ammonia - sodium.[77] Decomposition does occur in the presence of hot molten alkali or above 500°C with glass or silica, thus providing methods of elemental analysis[78]. Cyclic saturated fluorocarbons can be defluorinated by iron or nickel at ca. 500°C (see Figure 4 & 5), the only useful chemical modification. Unspecified reaction at elevated temperature is reported with anhydrous aluminium chloride.[73]

The weakness in saturated fluorocarbons is the carbon-carbon bonds which can be homolytically cleaved in the region of 900°C for perfluorinated n-alkanes (cf. CF_4, stable to 2000°C).[1,67] Tertiary-tertiary carbon bonds can be cleaved at lower temperatures (Figure 6)[79] and quaternary-tertiary bonds may break at less than 300°C.[9] Perfluorocyclopropane, the only strained system, decomposes at 170°C to give difluorocarbene.[80]

Pyrolysis can be used as a source of other, usually unsaturated, fluorocarbons, especially with PTFE (see 1.2).[81] Similarly, both saturated fluorocarbon molecules and polymers can be degraded (synthetically or otherwise) by high energy radiolysis, e.g. electron beams, to give alkanes and alkenes.

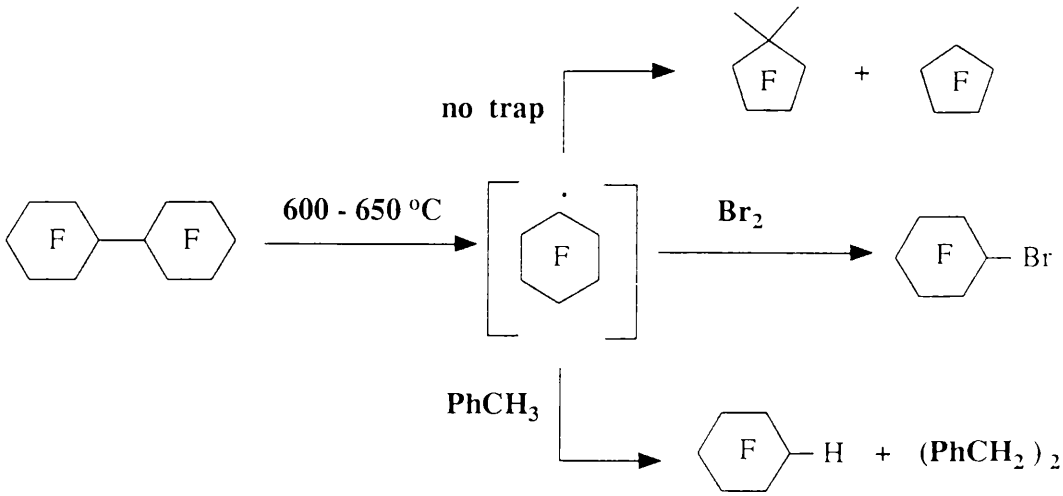


Figure 6 (adapted from refs.67 & 79)

In the former case, products of both higher and lower size are formed, and with a higher degree of branching, providing an alternative synthetic source. The radicals produced during this process can be long-lived spectroscopically and recently stable radicals have been generated from individual alkanes containing a tertiary or quaternary carbon.[82] A defluorination of alkanes by this method to alkenes (as intermediates to surfactants) has been patented.[83]

Capture of thermal electrons has been well studied, indicating increasing ability to form the parent ion rather than fragmentation as size and unsaturation increase. Cyclic saturated perfluorocarbons, and especially those with trifluoromethyl groups, are excellent at capturing low energy electrons non-destructibily[84]. This is very useful in negative ion mass spectrometry[85] and the analytical detection of such molecules in their use as tracers (to 1 part in 10^7 atmospherically)[12b]. The higher and the cyclic perfluoroalkanes have positive electron affinities[86] but whilst displaying excellent capture characteristics of free electrons do not, in the gas phase, behave in electron transfer equilibria and it is suggested that this is because of the extremely large geometry changes inherent between parent and parent anion.[87]

Perfluoropolymers[8,68]

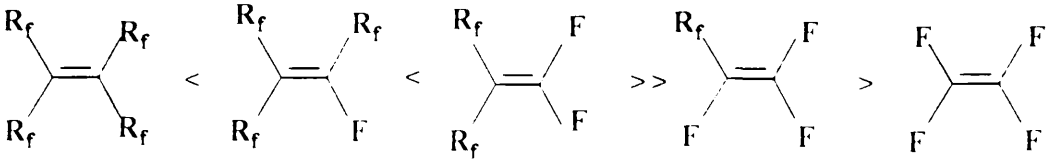
Of course, PTFE itself has the definitive polymer chemical stability, being attacked only by molten alkali metals and ClF_3 or F_2 at elevated temperature and pressure. It is not attacked at all by solvents (in a working range from 260° to about absolute zero) and does not degrade below 400°C. As noted previously it can be degraded with high energy radiation.

Aromatic fluorocarbons[88a,1,7,8]

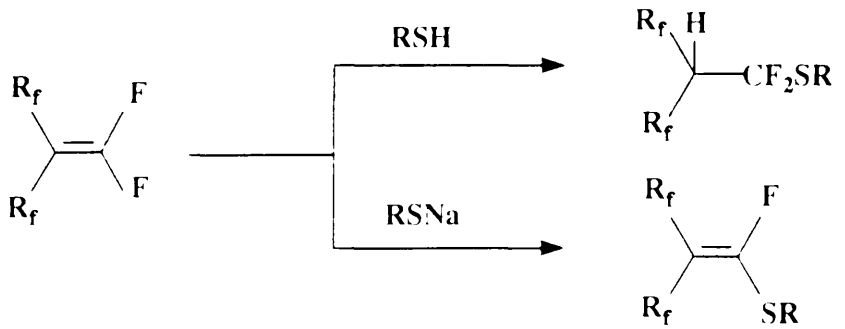
The chemistry of aromatic fluorocarbons[3,88a] is dominated by aromatic nucleophilic substitution reactions, of which a vast amount of literature is available and many of these derivatives are commercially available. Radical substitution, electrophilic addition and carbene addition are reported but the other major field of work is photochemical additions and valence isomerisations.

Unsaturated fluorocarbons[88b,1,7,8]

The double bond in perfluoro-olefins is highly activated to nucleophilic attack, the result of which can be overall addition, vinylic substitution or allylic substitution resulting from the intermediate carbanion. Consideration of the nature of the alkene and the different pathways followed has established the following observations. Attack is preferential at a terminal difluoromethylene and the rate is greatly enhanced by replacement of (destabilising) fluorine substitutions with perfluoroalkyl groups which stabilise the carbanion.[3] The electrophilicity of the double bond is, however, reduced as fluorine is then replaced with more perfluoroalkyl groups.[89] The relative reactivity of olefinic fluorocarbon centres is as follows:



For these reasons, perfluoro-isobutylene has become the model for nucleophilic reactions despite its very high toxicity. It is substituted by alcohols at room temperature without base.[88c] Nucleophilic attack on TFE and other low-order systems usually results in an overall addition, but in higher systems, which offer more carbanion stabilisation, substitution tends to predominate, especially with cyclic olefins where addition is rare.[88b,89b] Reaction conditions may dictate the outcome, particularly with regard to sources of electrophile, including solvent :[90]



Vinylic substitution is normally preferred to allylic substitutions, consistent with the difficulties of displacing fluoride from highly-fluorinated carbon centres. Small cyclo-olefins give little allylic substitution but perfluorocyclohexene gives large amounts. Carbanions derived from internal olefins prefer to eliminate from adjacent CF_2 than CF_3 groups[91]. Such carbanion reactivity is the only unambiguous case for fluoride displacement from a perfluoroalkyl group,[3] although intramolecular examples have been suggested (see results and discussion 1.2). Facile aqueous hydrolysis of CF_2 in activated systems, e.g. perfluorocycloheptatriene to perfluorotropone[92] and acid hydrolysis of perfluorocylohex-1-3-diene to perfluoroquinone,[93] may be direct allylic substitution rather than through attack on double bond.

Production of a new vinylic fluorine often results in further substitution at this more reactive centre. The elimination products arising from cyclic olefins have been rationalised in terms of a transient carbanion with retained stereochemistry and the characteristics of the newly formed bond.[94]

Thus allylic substitution, stereochemically favoured, competes with elimination of the weaker vinyl fluorine, and is encouraged by an electron-withdrawing nucleophile-derived substituent: an amine which weakens the bond through its lone pair exclusively favours vinylic substitution. Subsequent addition of a nucleophile to the 1-substituted perfluoro-olefin is found to favour allylic substitution even more strongly.

As previously mentioned, perfluoro-olefins add fluoride itself to provide useful precursors for many reactions and isomerisms by elimination of allylic fluorine. They also react with free radicals or carbenes and undergo facile cyclo-additions. Some electrophilic additions are also known, many catalysed by hydrogen fluoride or antimony pentafluoride.[88b,3]

1.4 Physical Properties and Applications

Saturated fluorocarbons and perfluorpolymers[95,68,74b]

Saturated fluorocarbons have remarkable physical strength: the average bond dissociation energy in perfluoromethane is 385 kJ mol^{-1}. Bond strength increases in the series mono-, di-, tri-, and perfluoromethane as bond length decreases (1.385Å CFH_3, 1.317Å CF_4), typical of trends caused by progressive fluorination (which are not, however, always regular). Carbon-carbon bonds also shorten and strengthen (stronger by 36 kJ mol^{-1} in PTFE than polyethylene). Although the size of fluorine allows persubstituion (van der Waal radii (Å) F 1.35, H 1.20, Cl 1.8, C 1.70), it does lead to restricted conformational interconversion, causing a helical twist in carbon backbones rather than a zig-zag, and makes the surface of the chain cylindrical in form. Fluorocarbons are extremely similar and good separation became possible only with the advent of g.l.c.

Their physical properties are abnormal, and extreme. Most fluorocarbons are colourless liquids at room temperature (C_5-C_{15} b.p. 30-250°C), following b.p. values and a trend very similar to that of hydrocarbon analogues, belying their mass because of minimal intermolecular interaction. They have low critical temperatures and pressures, are very dense, will wet any surface because of their low surface tensions, display high co-efficients of expansion, have the highest refractive indices of all organic compounds and some of the highest liquid compressibilities with commensurate low acoustic velocities. Their range of electrical properties, e.g. low dielectric constants, makes them superb insulators. They possess interesting solubility characteristics, being immiscible or poorly soluble in most solvents, requiring similar compounds also with low internal pressures to mix. They do exhibit a large capacity for dissolved gas. Allied to their properties of being chemically inert, non-flammable, non-toxic and excellent at fast electron capture, these exceptional properties are finding many uses for fluorocarbons in industry, where boiling point then usually becomes the main consideration in choosing the desired molecule.

The main uses of fluorocarbons are in the microelectronics[96] and electrical field, but a developing and high profile use is as blood substitutes.[97] As well as applications in the electrical (silicon-chip eluting, leak testing, burn-in, thermal shock and steady-state testing, hot-spot location, dewpoint determination, condensation soldering dielectric fluid, liquid banner and cooling) and medical fields (red blood-cell substitute and organ storage), other uses are with heat pipes, atmospheric and explosives tagging, lubricants, laser cooling, liquid springs and acoustic-optical.[12b]

More generally, there is an even bigger market met by perfluoro-compounds requiring retention of the above properties in the presence of other functionality. The drawback of all these compounds is their expense, which has limited their use to specialised high value and military products.

The most abundant and well-known fluorocarbon is still PTFE (1985 value $1000 million),[98] which despite its cost is often the most economical after other factors are included - replacements, maintenance, safety, environmental and complexity of operations requiring reliability. PTFE has physical characteristics comparable with the molecular systems making it the ultimate material (so far) and is by far the biggest fluoropolymer. Its use is still growing - non-stick linings, artificial limbs, glass coating, optical-fibre coating, fabrics, mechanical and electrical components. The uses of fluorocarbons envisaged at its birth are being fulfilled as interesting, and unique, high performance, high value products.

Unsaturated and aromatic fluorocarbons

Unsaturated and aromatic fluorocarbons are endowed with similarly abnormal properties but they are unsuitable for common use because of their high toxicity. They do however have great value as chemical intermediates.

2. A Decade of Inclusion by Design

2.1 Inclusion chemistry : an introduction

Inclusion chemistry[99] is an imprecisely defined field with boundaries that extend into other areas. An exact definition of what constitutes an inclusion compound is not available - far less a reliable guide as to what design of molecule will lead to inclusion. This however has not prevented its rise to that of a major science, now recognised from undergraduate to Nobel laureate levels[100], fuelled perhaps by the very visual and appealing concept suggested by its name and influencing the chemist's way of thinking in determining his work and view of it. The subject also neatly reflects the rise in interdisciplinary research and the synthesis of chemical systems (as opposed to single entities).

The basis for inclusion is the use of one molecular system to encapsulate another in a chemical box, either by purely physical imprisonment or additionally using forces to chemically associate species other than by formal (covalent and ionic) bonding (i.e. involving weaker forces such as ion-ion dipole, hydrogen bonding, van der Waals forces). Most inclusion compounds published utilise only partial containment but, in a specific fit, the idea of lock-and-key pairs has been adopted successfully.[101] Pre-requisite for the phenomena is a space created by the encapsulating 'Host' within which the 'Guest' can be included. This space may not exist in the absence of the guest. Voids, which require concave host topology, are not commonly encountered in non-biological systems.

Focusing on the 'space' necessary for allowing 'Host-Guest' chemistry, it is apparent that a complementary relationship, sometimes uniquely so, exists, and this causes common, often diagnostic, effects attributable to inclusion principles. This relationship is akin to that of molecular recognition, the main goal responsible for advancing the field.

The perceived future of this approach is controlled chemical reactivity in vitro (solution and solid-state) by means and with results comparable to in vivo chemistry, as typified by Lehn's description of supramolecular assemblages and devices whose shape in space leads to non-random action.[100a] Other important theoretical and applied ends are also achievable, and achieved, through inclusion.

In short, inclusion chemistry involves groupings of non-covalently bonded components in constrained geometrical partnerships due to the physical and chemical forces defined by the topology of the host presenting the spatial vacancies.

More generally, different views exist amongst researchers on what constitutes and what does not constitute inclusion. All potential expressions of the phenomena are, however, adequately conveyed by pictorial representation of the molecular event and thus the subject is well served and advanced through modern research aids such as solid-state n.m.r., X-ray crystallography, computer graphics and modelling.[102] Recent progress has been achieved using such aids in the consideration of the structures of old and potential new hosts. This is easy for unimolecular hosts, but not so for clathrates and related hosts. Whereas the geometric parameters associated with macrocycles can be arrived at by computations, even before undertaking X-ray diffraction studies,[102a] solid-state intermolecular forces and cavities are not yet accessible in this manner.

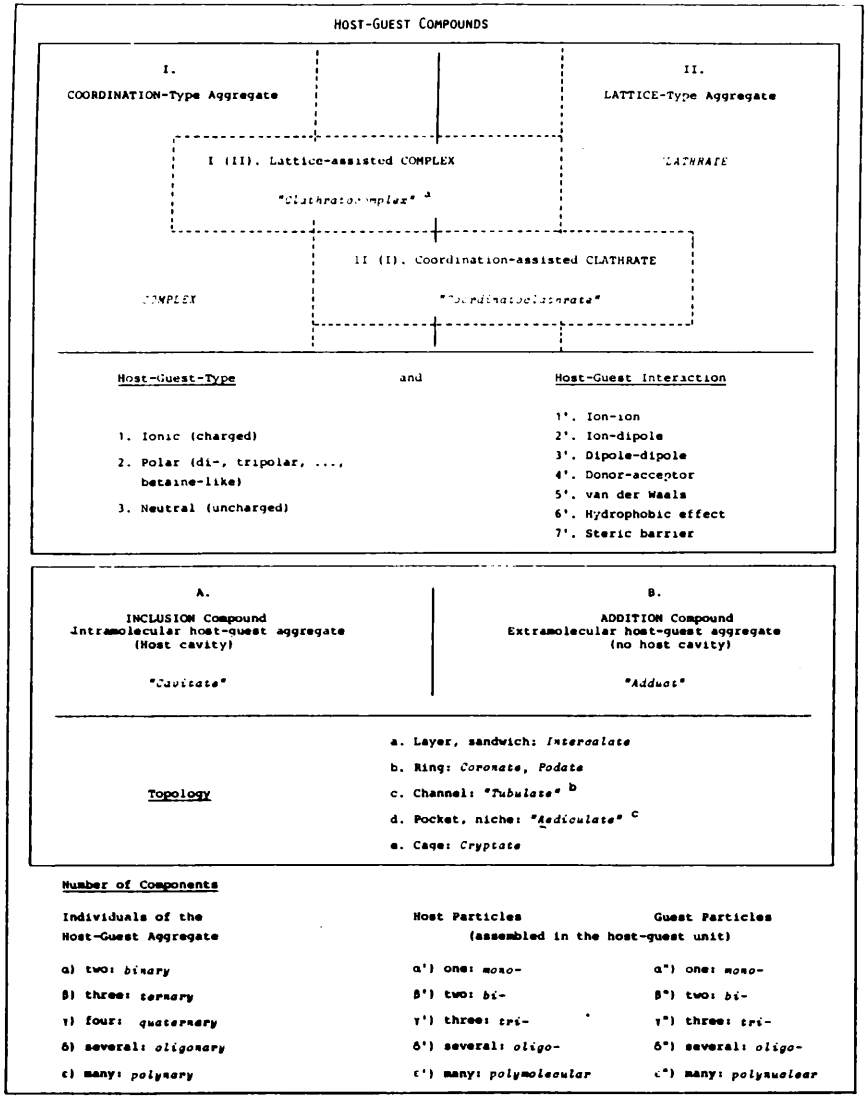
For this reason, design of lattice-inclusion hosts involves the blacker, less-well-developed, art of incorporating advantageous design elements - in only one case has the packing structure, and consequently inclusion, been fully related to host molecular structure and host-host interactions.[103] A further undervalued, intriguing, and as yet mysterious aspect of such host design is the question of symmetry.[104]

Inclusion research tends to involve pictorial representation accompanied by descriptive but often trivial nomenclature. A systematic nomenclature based on topological features of the inclusion compound has been proposed (Figure 7).[105] Despite wide acknowledgement, it is little used. One feature not listed in the classification is symmetry considerations; this could possibly be incorporated in future where appropriate.

The development of inclusion chemistry can be represented effectively by the course of progress in host design, with emphasis on the last decade. For this purpose, a division into two sections will in general be broadly followed:

1) unimolecular hosts (acting in solution),
and
2) multimolecular hosts (operating in the solid-state).

This approach is neither complete nor mutually exclusive in contribution but covers the two main threads. A notable exception is the 'liquid clathrate' family of hosts.[106]



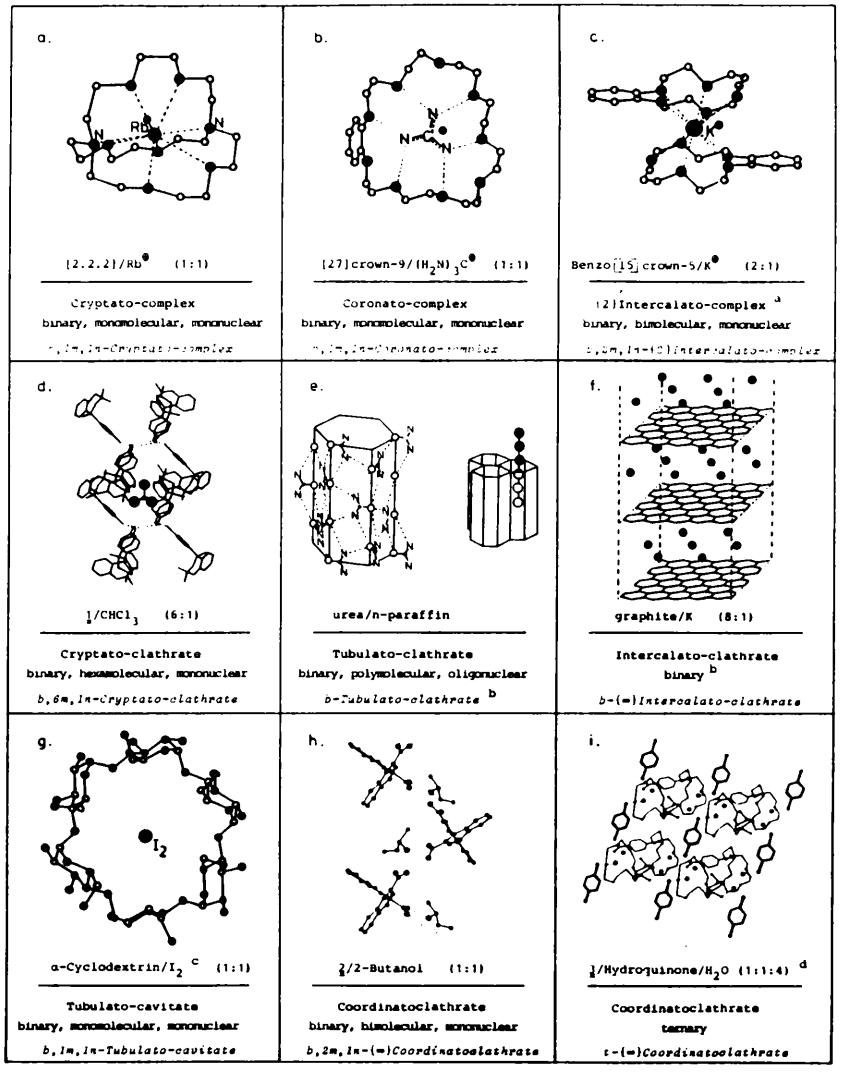


Figure 7 - A Proposal for the classification and nomenclature of host-guest type compounds (ref. 105)

2.2 Unimolecular hosts[107]

Modern inclusion chemistry was largely stimulated by Pedersen's[107b] discovery of crowns and their remarkable abilities to bind strongly and with specific metal cations, which came in the same period as the discovery of natural ionophores.[108] Previously crowns, cyclodextrins[109] and other hosts such as calixarenes[110] existed but with very limited recognition of their worth.

Generally, unimolecular hosts offer a cavity, or the possibility of one, with a favourable environment (e.g. hydrophilic or hydrophobic) for the guest. This is achieved by an array of suitable host donor units stabilising the guest, these usually in the form of a ring, and which may be further enhanced by other similar arrays and geometric spacer groups linking up to increase the coverage afforded to the guest by the host cavity and improve the definition of cavity shape. The limit of this kind of increasing structural complexity and 'information' is reached with cavitands which are essentially unimolecular hollow spheres.[111]

As hosts become larger, guests similarly rise in level from small ions to small molecules, complex ions, large molecules and collections of guests. Designing hosts for specific guests and multi-topic hosts has initiated large areas of research.

Much attention is also currently given to the inclusion of neutral molecules; since these are bigger and have lower binding energies, the challenge is far greater than with, for example, alkali metals ions.

Two simple theories recurrent in unimolecular host design are the principles of Complementarity and Pre-organisation. Together they dictate that the most specific and strongest inclusion of guest is achieved with hosts which exactly match them in every way, at all points, and which are already arranged to do so before the inclusion compound is formed.[112, 102f]

Both of these principles relate to the thermodynamics of inclusion.[113,102f] The influence of the dynamics of host and guest is less well summarised and, hence, incorporated in design.[114,102f]

Development of crown-like hosts and other macrocyclic hosts is covered separately, each with representative examples:

Crowns[115]

Uncomplexed crowns (macrocyclicpolyethers) have no cavity but their flexibility enables them to turn their oxygen donors inwards to a suitable electrophilic guest, e.g. K^+, to encapsulate and bind it. A geometric size recognition occurs, rendering the partnership more than mere ligand and centre. The guest organises the host to the best co-ordinating conformation. Guests other than metal cations and ammonium ions are less strongly held and 'perch' on the side of simple crowns.

Crown chemistry has developed in many directions. Elaboration of the basic structural unit, (CH_2CH_2O), by varying length and type of backbone, the number, type and distribution of donors, changing ring size, incorporating backbone and donors into structural features, and appending other groups has led to a multitude of coronands and macrocycles that need not necessarily have any similarity to simple crowns such as 18-C-6 (12). 'Crowns' have diversified into noncyclic (podands) and polycyclic systems (e.g. cryptands). They have been co-operatively attached to other host structural units, as whole or parts, and have been immobilised on membranes and polymers.[116] They are reagents and catalysts, transport carriers and resolving agents (when chiral).[117] Guests are now also Lanthanides and transition metals, complex cations, anions and neutral molecules. Papers on crowns, podands, coronands and crown-like macrocycles abound. Only a brief look at some representative current activity is possible.

a) Subunits

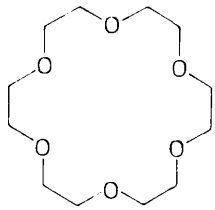
Crowns are used in conjunction with other sub-units to modify activity, e.g. redox potentials, of neighbouring centres, and vice-versa.[118] As an example, three research groups independently synthesised the tetra 15-C-5 phthalocyanine(13), each stressing different aspects of its use; as a water or solvent soluble phthalocyanine;[119a] a quantitative colorimetric determination of K^+ to 10^{-8}M;[119b] and as a potential catalytic centre.[119c] Similarily crowns are being used in biochemistry to design radiotracers.[120]

b) Chirality

Two main approaches to chiral crowns are used. The first is from resolved bis-aromatics[121] (after Cram's classical work) and the second by incorporating sugar and amino acid residues into the ring.[122] Some other approaches have been used mainly based on other C_2 subunits.[123]

c) Guests

Design for selectivity has required consideration of cavity size, donor types and distribution, and lipophilicties for transport in particular.[124] In the search for lithium ion selective crowns, good discrimination against sodium ion was required and most successfully found in 12-C-4 based systems.[125] The best K^+ ionophore found is a podand (14) with an appearance distinctly reminiscent of naturally occurring systems.[126]



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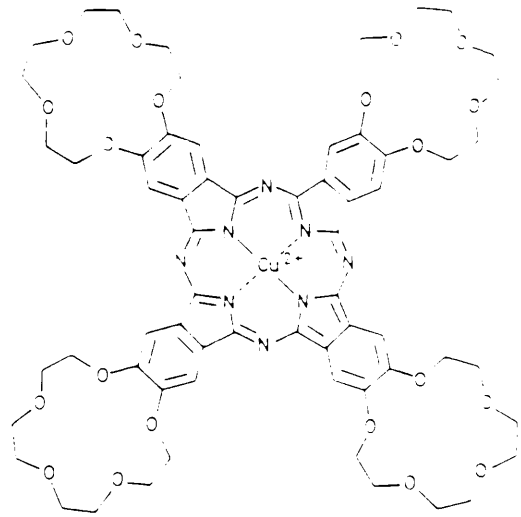

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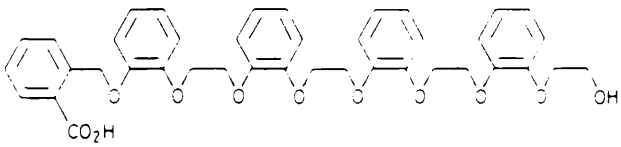

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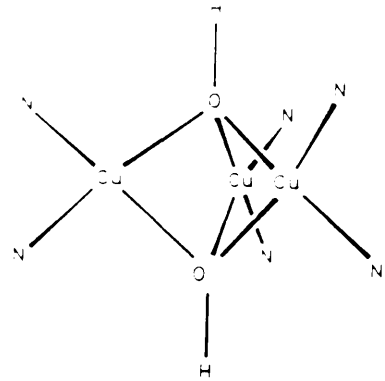

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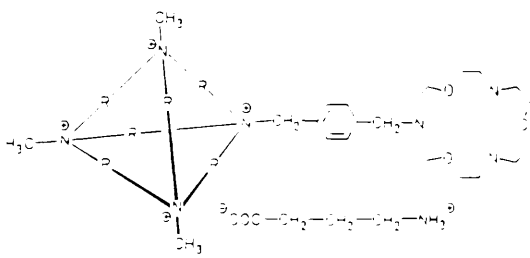

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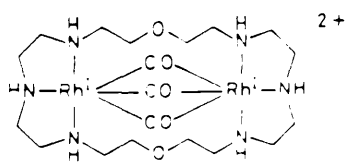

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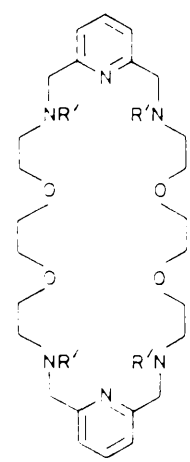


R′=H

(18)[132]

More complex cationic guests, especially copper-based, such as (15), have been included.[127] Anions have been included, mainly by polyamine cations, and even large complexes like $Co(CN)_6^{3-}$ are afforded protection (from photo-induced dissociation) in this manner.[128] The principles of cation and anion binding can be incorporated into one molecule. Schmidtchen has designed ditopic molecules based on two independent host components to recognise broad groups of guest solely by the end group interactions without the constraints imposed by developing rigid cavities (16).[129] Other flexible ditopic cages are available.[130] Polytopic macrocycles allow entry to systems with potential as controlled chemical systems. In the $Rh_2(CO)_3$ inclusion compound (17) a very short rhodium-rhodium bond was observed.[131] Natural processes may also be modelled, e.g. reduction of O_2 -> H_2O with Cu_2^{II} guest in host (18).[132] Crowns have been used to complex guests already attached at other centres - 2nd sphere co-ordination, e.g. the anti-tumour molecule cisplatin.[131] These observations led Stoddart to synthesise a series of dibenzocrowns and related hosts which show remarkable binding with paraquat and diquat. Here the guest is completely encapsulated in the folded crown and held by π-π charge transfer, colambic attraction, hydrogen bonding and dispersion forces.[134] Changing the components responsible for these interactions allows modifications of interactions, evaluation of their relative importances, and differential guest behaviour. This has in turn led to other receptors, using different interplays of interactions.[135]

d) Complexes with neutral guests[136]

Crown complexes with neutral guests have only recently received attention even though they were observed by Pedersen in his original work and later used as purifying techniques. At present, most of the host design and understanding is related to the solid-state and chance discoveries - but the situation is now changing rapidly.

Where it is necessary to draw on solid-state X-ray diffractions studies, care must be taken to avoid wrongly interpreting inclusion that is dependent on lattice (intermolecule) factors. Symmetry would appear to be more important for neutral guests than for charged ones, perhaps not unconnected with lower stabilisation energies.[137]

In inclusion complexes of crowns with neutral molecules, many common features exist. 18-C-6, the most common host in this area, adopts the symmetric conformation D_{3d}, which has the lowest torsional strain but has high-energy dipole interactions. These are relieved by electron-accepting guests which form symmetric 1:2 complexes by packing perpendicularly to the crown.[138,45f] Guests are small, have permanent dipoles, and are CH, NH or OH acidic; they are not encapsulated, as in the case of metal ions. Bifurcated hydrogen bonds are always present, occurring between non-adjacent host donor sites to double donor guest sites (or via a linking water molecule for acidic OH guests).[139] The importance of configurational as well as constitutional factors has been noted.[140]

Alcohols are not guests, and amines rarely. Aza analogues are poorer hosts (possibly attributable to lowered symmetry or strong intra-annular bonding). Crowns incorporating benzo units normally do not give enhanced properties despite the occasional case where the increased bulkiness and rigidity provides an ideal cavity (probably generally of clathrate type). The poorer donor atoms cause weaker interactions with neutral guest in solution.

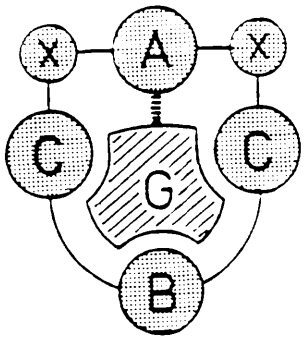
In his study of crowns and malonitrile guest in solution, Reinhoudt found that 18-membered rings formed the strongest complexes and enthalapy gains were offset by entropy losses in a linear fashion.[141] This is related to the strength of hydrogen bonds involved and the amount of host re-organisation required. Additional binding sites, if non-sterically interacting, enhance hydrogen bonding but intra-annular hydrogen bonding, as with 2,6-pyridino-crowns, is unfavorable despite the preferential use of this binding site.

Hydrogen bonding in solution has been observed elsewhere using ^{1}H n.m.r. and i.r. measurements but this represents the first thermodynamic findings for such systems.[142]

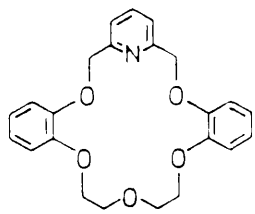
The discovery that pyridino-based crowns resulted in complexation of a wide range of guests, including now alcohols, has led Weber to an extensive exploration of directed host design for related crowns.[143] The parent host (19) was analysed as being composed of different subunits performing different structured roles. (The pyridino unit is used in hydrogen bonding and is necessary for any alcohol inclusions).

These units were varied (Figure 8) to produce new hosts, some without a pyridino unit. The resulting solid-state inclusions show similarities to clathrate inclusion, even when intramolecular, such as excellent guest discrimination and tight structural demands on guest. Hosts are generally highly conformationally rigid, being 18- to 24-membered, and produce molecular conformations with niches at the binding site, e.g. 'dentist's chair', which often have crystallographic mirror symmetry.

Vögtle and Newkome have demonstrated pyridino-crowns to include water. It would appear this occurs because of interaction between water and part of the polyethylene chain able to fold like 18-C-6, with water encapsulated in a space created by the aromatic portion.[144] Despite 18-C-6 being hydroscopic, no direct evidence of a water inclusion compound for it has been found. Other notable water inclusion compounds are formed with hosts (20) and (21).[145] In the former case the host-guest complex adopts crystallographic C_2 symmetry, with water straddling the twofold axis; and in the latter, the water is totally encapsulated in near perfect tetrahedral geometry by a host conformation almost identical to that of its free form. One non-pyridino-crown inclusion compound has been structurally defined where an alcohol is (weakly) hydrogen bonded to the host, the bicyclic isomer (22) with methanol.[146] The guest would appear perfectly to fill up a small niche in the conformation belonging virtually to the free host. Furthermore, unusually the methanol does not act as a hydrogen bond acceptor.



A = H-bond-mediating (basic) section of the host skeleton; dashed line represents H-bond interaction;
B = handle-type section;
C = flanking group;
X = linkage position;
G = guest inclusion.



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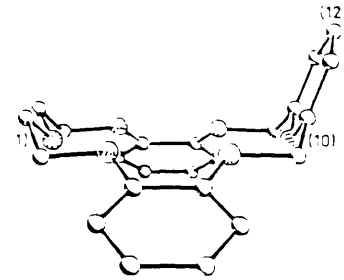
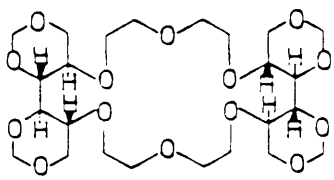


'Dentists Chair'

Figure 8 (adapted from ref. 143)



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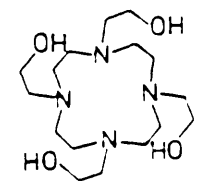

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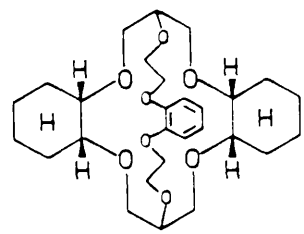

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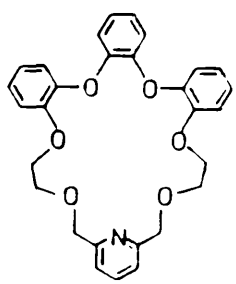

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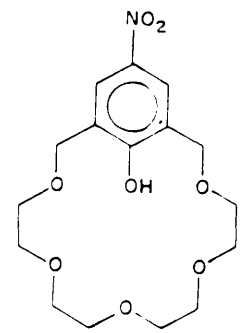


(24)[115]

The most recent and best example of this strategy occurs with the first inclusion of nitromethane, by host (23).[147] The nitromethane (and only nitromethane) fits neatly into an intramolecular hole, hydrogen bonding to all catechol-derived oxygens and the pyridino subunit, and is further held tightly in the packing as it is encapsulated in a near-spherical hole defined by neighbouring hosts.

A different approach to the binding of neutral molecules has been followed by Reinhoudt[148] wherein the guest, e.g. water or urea, is effectively bound as its cation (much stronger binding) by complexing the neutral molecule to protonated crowns containing, e.g. pyridinium or intra-annular carboxylic groups (24), or by using an electrophilic lithium ion. This has been extended to the binding of a metal centre and a molecule separately, where the molecule (urea) is additionally co-ordinated to the covalently bonded metal, e.g. a nickel or uronium centre.

e) 'Armed crowns'

A significant development in unimolecular inclusion chemistry has been the development of armed macrocycles, particularly the armed crowns (Lariat ethers) studied by Gokel, e.g. (25). He has shown that 'hole- size' or 'cavity-size' is only a first approximation to explain the binding strength and selectivity trends shown by flexible unimolecular hosts.[149] In such cases the cation guest organises the host donor atoms towards the optimum array (not necessarily the same as the macrocycle's best geometry) and the number type and topological relation of the donors is responsible for the behavioural trends. This can be expressed in terms of an effective ionic-radius fit. Kollman has shown flexibility and electrostatic attraction important in crowns.[102c] The placement of an additional donor in the arm of the crown has a large effect on stabilities- about an order of ten - and optimally requires apical interaction. This competes with solvent co-ordination, and less successfully if too long an arm.

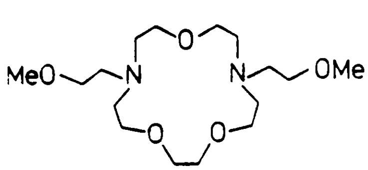
Nitrogen is preferred to carbon as a pivot because it is more flexible.[150] Hancock recently demonstrated with bridged aza cycles that as a host rigidity increases the hole size relationship strengthens.[151] The relationship between lariat ethers and cryptands has also been observed elsewhere in design of good selective carriers.[152] The greater flexibility of the double-armed crown allows for better rates, retaining the dynamics of the natural ionophores and the inclusion abilities related to cryptands.

f) Cryptands[152] - higher crowns

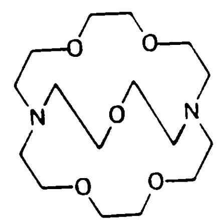
Originally Lehn invented cryptands, e.g. (26) - [2,2,1] cryptand, three dimensional crowns with aza bridgeheads, for selective total encapsulation of metal ions based on cavity size. Similar carbon bridgehead ligands were known (Stoddart) but were not nearly as strong complexing agents due to greater flexibility and absence of endo nitrogen lone pair donors. As the most powerful ligands (~ 10^8 better than crowns and even orders of magnitude better than natural ionophores), cryptands found widespread use.[154] The underlying principle involved was ascribed to the macrobicylic effect - greater pre-organisation of the donors and greater shielding.

However it has been recognised that cryptands are flexible and this with other factors such as solvent interactions, anion interactions, thermodynamic contributions of ΔH and ΔS, and type of metal ion, all contributes to stabilities and selectivities not directly dependent on cavity size to cation radius agreements, and indeed these do not necessarily correlate with trends in transport and extraction.[113b]

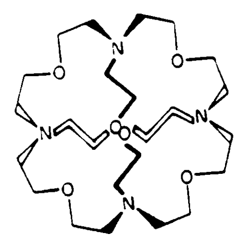
The dominant thermodynamic factor is found to be ΔH,[155a] but ΔS can determine selectivities in some cases,[155b] especially for small, rigid cryptands. When the radius of the ion is bigger than the cavity size, a discontinuity in trends occurs.[156]



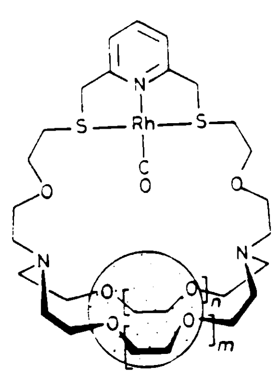
(25)[115]



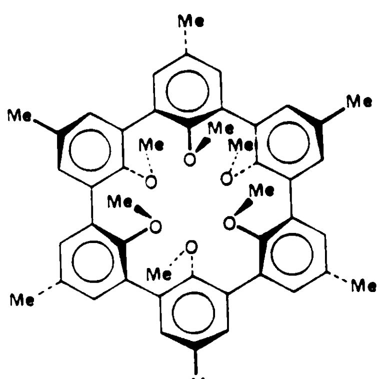
(26)[115]



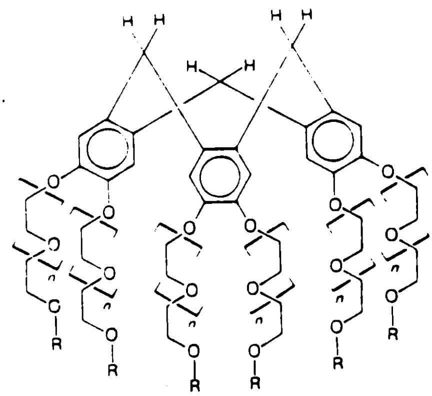
(27)[102g]



(28)[161]



(30)[102g]



(29)[115]

Ions can by cryptated or complexed (less strongly) outside, or both depending on relative sizes.[157] Ions bigger than the cavity size can also be accommodated inside with distortion of the host and less complete encapsulation (NB, even with complete encapsulation however, the cryptate must be considered as a charged species, unlike natural ionophores which hide both the ion and its charge). Endo lone-pairs are prevalent and lead to superior oxygen-metal interactions, although exo conformations are more important in larger, more flexible cryptands and in decomplexation.[113b]

Metal cations from all over the periodic table have now been cryptated and other spherical cations of a more surprising nature such as halogen cations have been included.[158] By suitable design other species can be successfully 'recognised' by cryptands, e.g. the azide anion, through complementarity (in size, shape, and the type and position of the interacting host functionality).[159,100a] Like crowns, cryptands have been developed with higher degrees of topology and different donor structural features; the spherical macrotricylic (27) is designed to the highest level of complementarity for NH_4, resulting in the highest stability and selectivity observed for this guest.[160] Any small change in host design greatly reduces these properties. Dinuclear cryptands, e.g. (28), have received interest similarly because of their potential as biomimetic chemical systems.[161] Removing the donors from one arm of a cryptand still leads to a cryptate effect but also uniquely opens the face of metal centres to external approach.[162]

Cryptates are under directed design towards the harnessing of photochemical conversions of a metal centre in the presence of absorbing donors in the host.[163]

Cryptate complexes of diammonium species have been extensively used to observe the relationship giving best matching within host and guest pairs. Rigidity increases recognition, and in the direction of bonding is essential for good selectivity; however, flexibility perpendicular to this direction can be used to strengthen binding.[164]

Increasing the scope of possible guests and other important dynamic properties, e.g. allostery and exchange, does require built-in flexibility, though this is difficult to design. Structural complementarity of host and guest has been tested by n.m.r. methods, looking at dynamic coupling and chemical shift data.[165]

g) Flexible crown-like hosts[166]

Many varieties of poly-flexiarmed rings have been developed, e.g. tentacle molecules,[166a] trigapus,[166b] hexapus (29),[166c] octapus,[166d,e] with 3-8 arms. These offer adjustable micellar hydrophobic interiors which can solubilise and protect guests from hydrolysis and chlorination for example. Not surprisingly, they are non-selective and the nature of interactions and binding is less well understood, though electrostatic interactions are favourable with charged species. Rates of transport and solubilising power are greater than for 18-C-6.

The nature and number of arms can determine the effectiveness of the host, but the central structure must be rigid.[161] Design has been extended to give catalytic reaction of guest in the hydrophobic pocket.

h) Spherands[168]

Spherands are the family of hosts designed by Cram on which the principles of pre-organisation in particular and complementarity have been best developed by design.[112] They consist of protected rigid spherical arrays of donor groups from a cyclic covalent linking of 4-8 donor units. The donor unit is typically a meta-linked anisole but others such as cyclic ureas vary immensely the possible hosts.[102g] Related compounds can be designed by incorporating elements of other host systems, such as cryptands, in addition to or in place of donor units.

In the parent spherand (30) the rigidity is so enforced that the host is absolutely pre-organised for binding - that is, it does not change conformation upon binding and its cavity is unsolvated prior to binding. When combined with the guest of perfect complementarity, a lithium ion, there arises the strongest binding recorded - despite the poor ligand nature of the donors.[169]

Using many examples of donor unit, numbers of unit, mixed units and guests, Cram has demonstrated the order of pre-organisation matches that of binding strength, i.e. ΔG^0 (binding) spherand > cryptahemispherand > cryptand > hemispherand > coronand > podand > solvent. Maximum selectivity follows a similar pattern but requires design to take more account of complementarity of guests to be disparate, and this best selectivity is not usually at maximum complementarity.[170,112g]

The role of models to predict results is stressed in Cram's design work. Molecular mechanics has also been used to predict correctly the structure prior to X-ray diffraction analysis.[102a]

Functionalised spherands have been used as enzyme mimics, and with chromogenic groups as analytical complexing agents.[171] Unfortunately, the size of cavity possible with spherands is both small and restricted.

Macrocycles to cavitands[172,111]

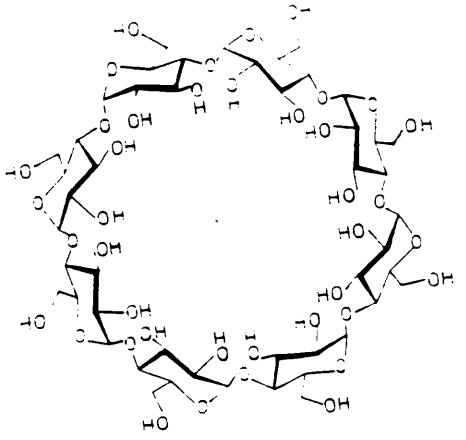
There is a rapidly growing interest in macrocycles that have a large protected inner concave surface able to fully include small molecules intramolecularly in solution, particularly neutral ones where only weak interactions are involved. These molecules are cavitands and require greater topological definition than that offered by simple coronand-based macrocycles. The most extensively studied group comprise the cyclodextrins (CD), the first to be studied, and also naturally host occurring materials.[109]

They are macrocyclic oligosaccharides with well-defined hydrophobic cavities - 'bucket' or truncated-cone shape with upper and lower hydrophilic rims.

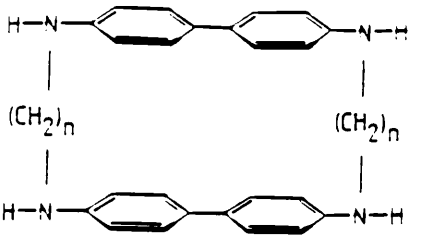
The bulk of research on cyclodextrins pertains to the α and β forms, but γ-cyclodextrin (31) is now being investigated. This has shown γ-CD to possess a cavity large enough to accommodate two aromatic guests simultaneously, leading to a better binding than with one guest because of the closer fit (complementarity). The second guest can be a different species from the first, and can be chosen to correctly reshape the cavity.[173] Indeed it may be covalently attached to the cyclodextrin rim.[174] Inside the cavity, the two molecules, e.g. pyrene, may adopt a chiral disposition, form excimers, or, if two halves of a larger molecule, show induced conformational change.[175] The importance of complementarity is shown by the complete preference of a naphthalene group covalently attached to γ-CD to reside in β-CD.[176]

β-CD has itself been modified in the presence of surfactants such that association constants of β-CDs with pyrene and naphthalene are altered up and down respectively due to the changing roles of hydrophobicity and size fittings.[177] γ-CD can include 12-C-4 (a proposed ion-transport membrane model), and ternary complexes are observed.[178] The thermodynamics of benzene inclusion have been measured by vapour pressure measurements, indicating γ-CD to have a good entropy contribution but poor overall binding, consistent with steric fitting.[179] With a larger guest like ferrocene, γ-CD can orientate it to give the best fitting.[180] Binding and orientation of guest have been studied with ^{13}C MAS n.m.r., ^{2}H solid echo n.m.r., luminescene, fluorescene, ^{13}C n.m.r. and induced circular-dichroism methods.[181]

The use of CDs as enzyme models and vehicles for reactions has been pursued by many groups.[182] Using the hydrophobic stereo-regulated cavities for reaction of two guest components has been investigated, e.g. a Diels-Alder reaction showing the first example of enzyme-analogue saturation kinetics (using β-CD).[183]

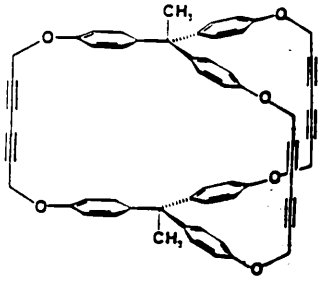


(31)[172b]

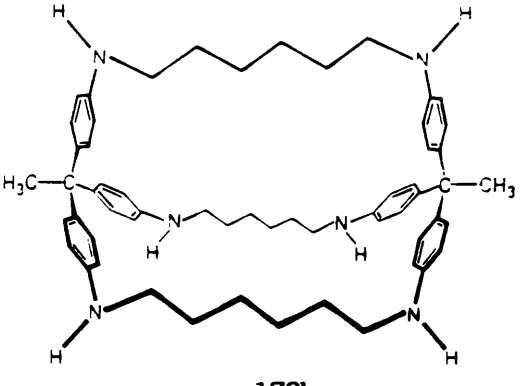


n = 3, 4

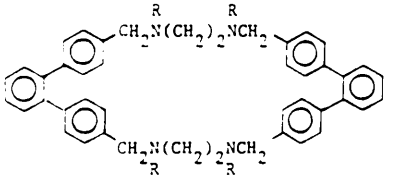
(32)[172b]



(33)[193]

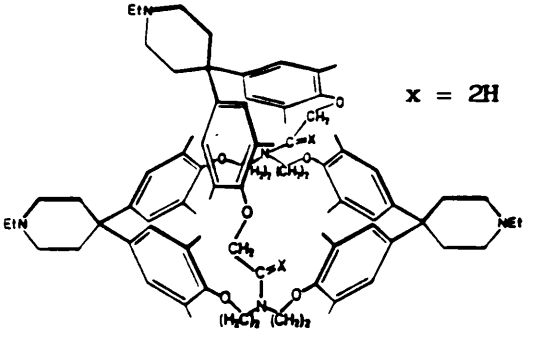


(34)[172b]



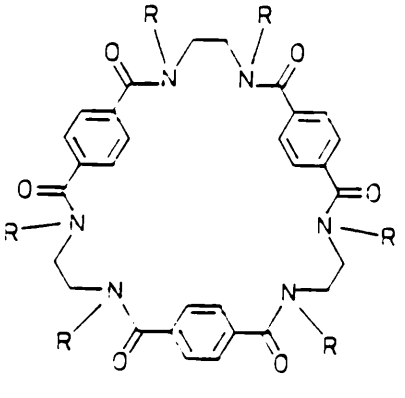
R = CH_2Ph

(36)[172c]



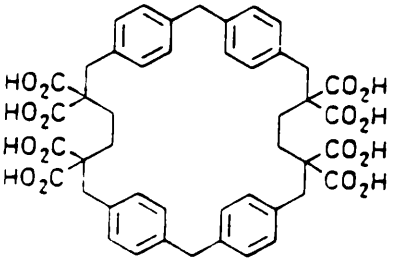
x = 2H

(35)[197]



R = CH_2Ph

(37)[172b]



(38)[172b]

Binary complexes have been used to give 100% carboxylation at the para position, to modify electrode reactions and in reaction with halogen gases, even to 100% ee.[184]

Modification of CDs to alter inclusion properties through steric and binding control has mainly been approached through selective capping and the use of regio-isomeric sulphonate intermediates; capping with an aza crown reversed Na^+/k^+ selectivity.[185] By altering the cavity and using guests of tailored geometry, rates of reactions were accelerated by 10^6. With the correct fit, a guest may be induced into a transition-state-like change.[186]

When modifying a CD cavity with other functionality to promote specific binding, it is observed that the magnitude of the effect depends on how the hydrophobicity is affected. Methylated CDs and CDs in membranes can even be used to transport substituted benzenes with some selectivity.[187] Cyclodextrin inclusion compounds have also led the way in applying inclusion to drug delivery systems and second-harmonic generation.[188] Despite these advances the CDs suffer from a lack of versatility, precluding substantial redesign of the cavity shape and size, and hence synthetic cavities become attractive propositions in pursuit of better and more-understood cavitate inclusion.

An inspirational starting point in this direction was the crystalline inclusion compounds discovered by Stetter in 1955, whose inclusion ability was so related to the potential cavity size of the macrocyclic tetramine (32) that these were until recently considered prime examples of intramolecular inclusion. An X-ray diffraction analysis proved differently.[189] This highlights the difficulties of obtaining information of the type of association occurring, without recourse to X-ray diffraction. In solution, the main methods of investigation are changes in fluorimetric, u.v. and n.m.r. spectroscopic measurements. In the solid-state, the only unambiguous methods available are neutron diffraction and X-ray diffraction (where suitable crystals are obtained) in determining whether the inclusion is intramolecular as required, $(HG)_n$, or lattice inclusion (H_nG_m).

The translation of results in solid-state to solution-states even with proven cavitate formation is not necessarily straightforward.

The first direct evidence of cavitate inclusion was furnished by Koga, using a macrocycle similar to Stetter's where biphenyl is replaced by diphenylmethane. Importantly, this change provides ready-made corners in a box-shape within which the (durene) guest is totally encapsulated.[190] The principles important in good design in the area are becoming better established. Necessarily there must be a size and shape fit between the host and guest pair but also required is a complementarity of interactions to allow strong and selective inclusion. Hydrophobicity is the major driving force to cavitate formation, but this is lost in non-aqueous systems and smaller energy interactions must be used. Again, the principle of pre-organisation is the vital design consideration.

In cyclophane cavities, inwardly-facing aromatic groups form the walls and are joined by spacer groups. Unless the macrocycle has some rigidity, no inclusion is observed and thus the spacers must maintain the cavity shape to some extent, otherwise special 'guest-sticky' interactivty attractive forces are required.[191] The role of flexibility is under debate. Flexibility has been declared "the enemy" by Breslow and most designs centre on rigid pre-formed cavities,[192] but value has been placed on its role and in a most recent case it was stated "an excess of rigidity is perhaps not for the best".[191c] Indeed Breslow has designed a tricyclic host (33) which twists shut to encapsulate benzene as guest.[193]

The study of hydrophobic guests in aqueous solution requires water-soluble hosts.

This has been achieved by incorporating hydrophilic moieties into the macrocyclic ring, as substituents on the aromatic groups and as functionality built onto the ring - best results are obtained when they are extracavity, ensuring retention of binding (hydrophobicity) and possible enhancement even with suitable guests though polar and ionic interactions.[194]

The correct hydrophilic functionality allows solubility in neutral as well as acidic conditions. Cavities can be extended and inclusion enhanced by adding side arms of substituents (e.g. methyl groups and hydrophilic bridges), to enhance hydrophilic or hydrophobic interactions, which may be more usefully flexible. In addition, chemical systems which avoid host-host or guest-guest hydrophobic aggregations must be found to study inclusion properties.[172a]

Utilising these ideas led to the first example of transport of aromatic guests through an aqueous phase by a host.[195] Many guests have been solubilised in water, some to surprising degrees and stabilities. A host (34) with a spherical cavity has been used to solubilise adamantane; its out-in isomer has a much smaller cavity and consequently different inclusion properties.[196]

In organic solvents the hydrophobic driving force is lost and inclusion is mainly an enthalopic process. Now solvent molecules can compete for the cavity so complementarity and well defined cavities are vital. A spherical analogue (35) of Diederich's host is not only an excellent host in aqueous medium, for perylene especially, but will operate in organic solvents, even benzene, to form complexes with the highest association constants of this type yet recorded.[197] Here, as others have noted in similar cases, the cavity is highly pre-organised and utilises a common geometry of binding in various solvents. Optimum complementarities of van der Waals fitting correlate with binding - perylene has the best fit. Another host which includes smaller aromatic guests in the crystalline phase (X-ray diffraction with one guest proved intramolecular inclusion) shows a direct relationship of size to thermal stability - notably the strongest complex was formed with benzene which also has a templating action in the host synthesis.[198a] A similar observation has been made elsewhere.[198b]

Some groups have noted that with neutral guests CPK models predict too large a guest as optimum fit, e.g. CH_2Cl_2 <u>versus</u> $CHCl_3$. Such a small change in guest size can have a very large effect in the lattice energies for the crystalline inclusion compounds also.[199]

Other hosts designed by Vögtle exemplify the versatility and potential in cyclophane hosts. The use of flexible aromatic side-arms to shape a hydrophobic cavity can lead to cavities requiring exacting guest-size fitments with small neutral molecules.

The host (36) can selectively include cyclohexane from benzene, although such complexes are not yet proven intramolecular.[200] Similarly designed polylactam-based cyclophanes complex many aromatic and aliphatic guests in acidic solution. The inclusion of chloroform by one such hexalactam (37) is so strong the guest is not removed under chromatography, recrystallisation or drying *in vacuo*, even though dichloromethane is not included.[201] This perfect complementarity has been exploited in a cheap, solid-state sensor device, able to measure atmospheric chloroform to 1 in 10^{12} parts. Other successes are the first large carbocyclic host (38),[202] including aromatic ammonium ions, and the incorporation of the correct donor units (catechol) into the arms of a bicyclic cage (39) design to furnish a synthetic siderophile (ferric chelator) better than enterobactin, Natures best, and an intermolecular clathrate host with the hexamethyl ether (40).[203]

The contribution of other factors, apart from hydrophobicity and ion-ion interactions, has been examined.[192a] Despite being small effects, both electron donor-acceptor and ion-dipole interactions are valuable contributions to good design, even allowing the inclusion of quite water-soluble guests. Not surprisingly, with electron-rich cyclophane hosts it was found that disubstituted naphthalenes were more strongly bound in the substituent pair order of acceptor-acceptor > acceptor-donor > donor-donor, and such interactions can serve to orientate a guest specifically. Favourable ion-dipole interactions resulting from both guest or host ionic residues are also noted. Hydrogen bonding too has been observed as a strong directional interaction with acidic guests.

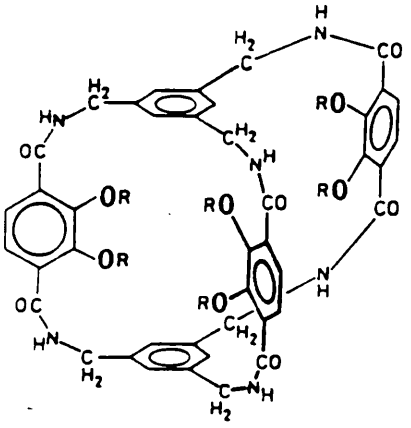
Chirality has been introduced into related hosts. Diederich has very successfully used computer modelling to design chiral spacers and predict requirements for inclusion.[204]

Some design has been undertaken to build molecular belts and boxes like paracyclophanes using other rigid cyclic building blocks.[205] Cram has linked substituted dibenzofuran(41) [206] and Stoddart mixed six-membered rings (42) [207] to give hosts that show inclusion properties, but whose crystal complexes collapse very quickly. Cucurbituril (43) is a fascinating collar of six methano linked glycoluril units with C_6 symmetry which exhibits host characteristic properties in solution which are borne out by X-ray diffraction analysis of crystals.[208] In acidic solution, amines of many structurally diverse types are guests, up to the size of para-substituted benzene. Charge dipole effects are greater than hydrophobicity in these cases. Mock has also included neutral guests, but these are less stable, and has investigated the dynamics of the inclusion.[114e]

Some similar cavitand structures using the glycoluril building block have been reported, of which a C_3 cavity built in partnership with hydroquinone link walls appears promising.[209]

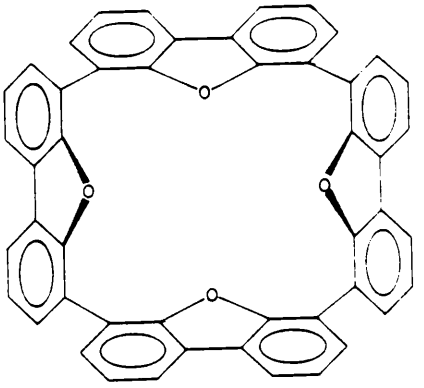
Busch has developed various vaulted cyclidene structures which offer a rigid hydrophobic pocket.[210a] In conjunction with the presence of metal centres this allows a ternary inclusion compound of butanol and molecular oxygen; the butanol fits the hydrophobic pocket and trails the alcoholic functionality outside the cavity, and the oxygen is bound to the Ni centre.[210b]

Rebek Jr. has investigated easily-assembled molecular clefts, e.g. (44) built from two molecules of a triacid and a spacer group[211,102g]. This approach is very different to the cyclophane host designs. Unlike macrocycle design, functionality convergent on the cavity is easily introduced and the synthesis is more straightforward, not requiring a ring design of the normally required thirty or so atoms. The hydrophilic cleft can be used to recognise diacids and aminoacids in particular.

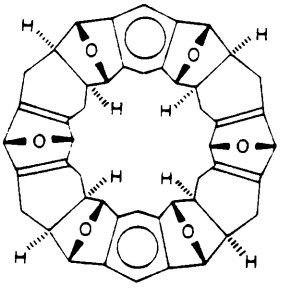


(39) R = H [107a]

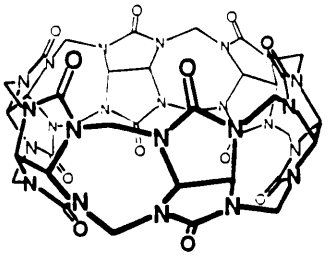
(40) R = Me



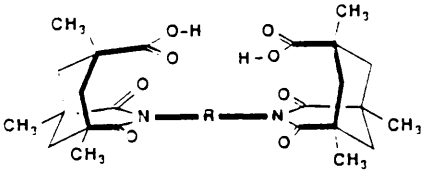
(41) [102g]



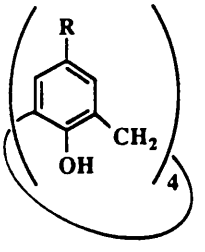
(42) [102g]



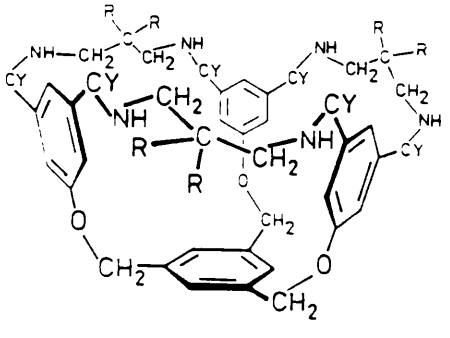
(43) [114e]



(44) [102g]

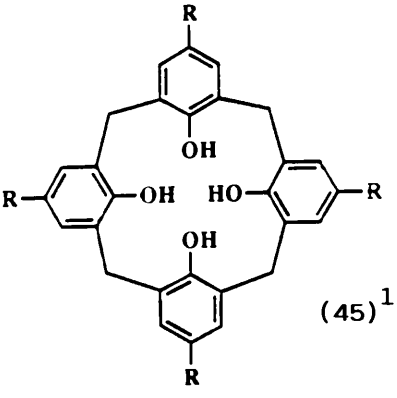


(45) [110a]



R = CH_3; Y = 2H

(46) [172b]



(45) [110a]

In addition to hydrogen bonding, large contributions to binding arise from ionic interactions and notably aromatic-stacking interactions. One problem in the cleft design was achieving optimal interatomic distances and it was suggested that complicated enzyme structure were a response to the discontinuous size of spacer groups available.[211b]

Rebek's receptors have been developed to investigate DNA-like base-pairing recognition. Hamilton has used a macrocyclic host, described as a molecular hinge, to similar purpose operating through hydrogen bonding and π-π interactions also.[211c] Designed host pockets based on vancomycin hydrogen bonding interactions have also been explored as peptide receptors.[211d]

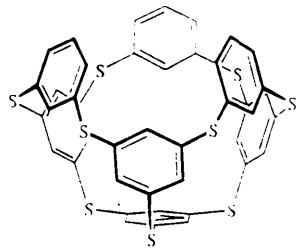
Metacylophanes give rise more easily than paracyclophanes to pockets with topologies for building cavitand structures. One of the most recently studied hosts of this class are the calixarenes, developed mainly by Gutsche.[110] In connectivity, they are related to paraycyclophanes and spherands, but in operational appearance resemble cyclodextrins, having a cone-shaped hydrophobic cavity with a hydrophilic rim.[212]

Potentially, they are much more versatile as the number and type of phenol units may be varied. Although conformationaly dynamic, in host-guest complexes the cone shape is always observed for the common Calix-4-arenes (45) and surprisingly the larger calixarenes are not conformationally loose. Calixarenes have been made more rigid by bridging, silylating and binding to transition metals. X-ray crystallography has shown oxygen binding to alkali metals in cone conformation with simultaneous guest encapsulation.[212c] Water-soluble calixarenes have been synthesised and hexasulphonated Calix-6-arenes show useful properties including stabilisation of aromatic diazonium salt in water and a host which is the most selective uranophile yet from amongst the many hosts designed for UO_2^+ (ascribed to binding geometry).[212d] Transport of alkali metals favours Cs^+ in a manner inconsistent with hole-size arguments, although transport and selectivity have been ascribed to this function in other cases.

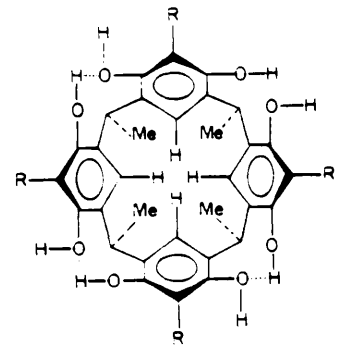
Because of the phenolic functionality, the transport is of a different nature to that of crown systems. Asymmetrically built and chirally substituted calixarenes have now also been described.

Vögtle has synthesised tricyclic 'basket' metacyclophanes to have a floored and walled cavity.[213] THF can be included in water by host (46). Another basket metacyclophane (47) forms a clathrate with the guest (chloroform) in the bowl. The host is similar to hexa-host cavity with the 'lid-off'; no solution inclusion behaviour is yet observed.[214] Schneider has shown that the metacyclophane (48) has an open-bowl-shaped cavity, and despite its not affording great encapsulation strongly binds guests that participate in ion-ion pairing. [215]

Cram has elaborated the phenolic functionality to give first unimolecular cavitand[111] 'baskets' with methyl groups as 'feet', e.g. (49), and then completely enclosed cavities called carcerands, e.g. (50)[216,102g] The 'baskets' all have large internal concave surface area but only those which cannot self-fill their cavities give intramolecular inclusion compounds; the others, however, yield lattice inclusion compounds. Unusually, these hosts have C_4 molecular symmetry and at least near C_2 symmetry is seen in each crystal structure. Complementarity is highest with guests containing a dipole. When bridged with dialklysilanes the basket has a very narrow opening through which the solvent is not generally admitted and only CS_2, CH_3CCH and O_2 can form inclusion compounds. With these inclusion compounds the only driving force is the residual dipole-dipole interaction, all other energies being equal, and ΔG^o of formation is now only ca. -1 kcal. When two of the more open 'baskets' are closed to form a shell despite the fact that the cavity is of size suitable for, say, DMF or benzene, these guests can only be entrapped if present during shell closure. After that, only H_2O and O_2 are small enough to enter. Interestingly Cs^+, present at the final chloride elimination step, is trapped inside and trace freons which seem highly complementary are also scavenged. Two cavitand baskets dimerise face to face in solvent when they have a large lipophilic open surface despite the lack of any binding force, e.g. pole-dipole.[217]

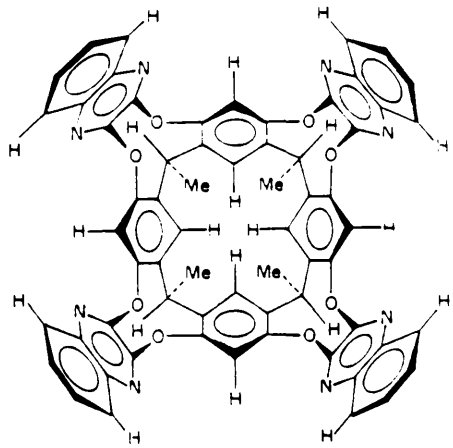


(47)[214]

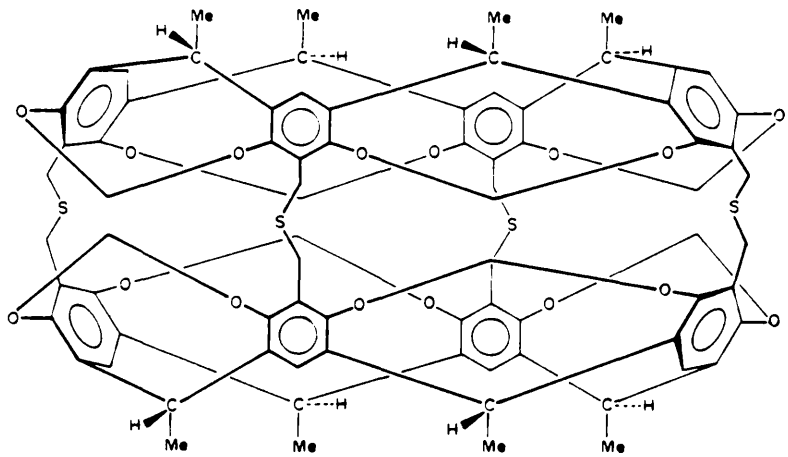


R = H

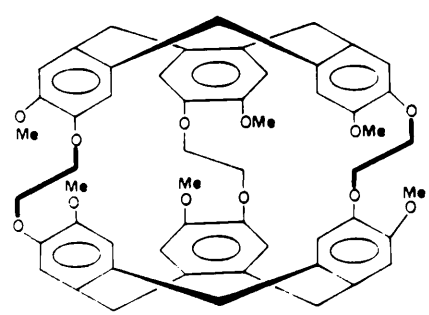
(48)[102g]



(49)[102g]



(50)[102g]



(51)[102g]

A similar approach, by Collet, based on the bowl-shaped ortho-cyclophane CTV, produced the elegant cryptophanes, e.g. (51) which include tightly small lipophillic molecules of correct size. Highly complementary fittings account for excellent guest specificity which has been combined with the host chirality to provide an n.m.r. determination of the $[\alpha]_D$ for CFHBrCl and resolved inclusion compounds.[218a] When the hosts are made water soluble the extra hydrophobic energy gains allows for the scavaging of very small traces of chloroform.[218b]

Collet's and Cram's cavitands represent the best unimolecular hosts - totally complementary guest inclusion with pre-organised fully encapsulating cavities of small neutral organic molecules from organic solvents.

A future source of cavitands may lie in the carbospheres suggested as space dust constituents and synthesised by laser evaporation of graphite surfaces. The proposed predominant C_{60} species which has the 'soccerball' design of a trunctated icosahedron (52), includes lanthanum ions.[219]

2.3 Multimolecular solid-state hosts[99]

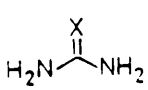
Historical perspective[220,99]

Solid-state inclusion compounds where the guest is trapped extramolecularly in the voids of a multimolecular host lattice, rather than intramolecularly, are the subject of this section. Host lattices represent the oldest known examples of inclusion despite being generally little understood at the time, often described only as non-stoichimetric.[221] Examples[99a] (Figure 9) include gas hydrates, ureas (53), phenols, e.g. quinol (54) and Dianin's compound (55) and cholic acids, e.g. deoxycholic acid (DCA) (56). The insight was provided by Powell's X-ray crystallographic studies on β-hydroquinone inclusion compounds, in which he identified the guests as being sterically imprisoned in the host lattice.[222] He thus termed these compounds (as) "clathrates", a description used now to classify all extramolecular inclusion lattices involving only physical containment of guest[222b]; host molecules may, however, interact chemically. Those lattices that additionally have significant host-guest interactions have been recently classified as coordinatoclathrates.[105] Previously only the varying topology of the free space defined by the physical barriers of the host lattices has been stressed, but this is not necessarily helpful. The three idealised forms are, however, cavities, channels and layers, of which cavities truly represent Powell's classical clathrate. Such lattice inclusion generally relies on non-close-packed host structures resulting from poor space filling by concave (and bulky groups) and/or open networks supported by intermolecular interactions. Hydrogen bonding is of special interest with regard to these classical open networks. In the absence of strong intermolecular forces, such as hydrogen bonding or ionic bonds, the non-close-packed host structure is supported by the presence of the guest.

Other hosts[99a] of importance discovered (Figure 9) were triphenylmethane (TPM) (57), perhydrotriphenylene (PHTP) (58), tri-o-thymotide (TOT) (59)[223a] and the related trianthranilides, cyclotriveratrylene (CTV) (60) and analogues, and cyclophosphazenes, e.g. (61).

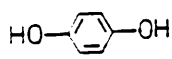
These molecules are all conformationally bulky and possess idealised 3-fold symmetry and they pack with only van der Waals forces between hosts. In crystal structures the phane regions are responsible for space creation and the lattice symmetry is trigonal or close to trigonal. Study of inorganic hosts such as Hoffman-types, Werner complexes, intercalation compounds and zeolites as well as the solid-state inclusion of cyclodextrins and cyclophanes contributed to development of the subject.[99a,172]

Current awareness in inclusion, mainly represented by macrocycles, coupled with interest in the study of systems with weak intermolecular forces, biological-related properties, or lattice-controlled resolutions, separations, reactions and storage, together with improved and accessible solid-state techniques, (e.g. X-ray crystallography, ^{13}C MAS n.m.r., i.r.) has made multimolecular hosts a sizeable subject. Without question, the major obstacle to rapid advancement is the discovery of new hosts.

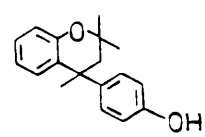


X = O,S,Se

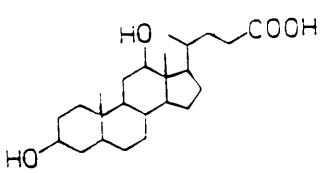
(53)



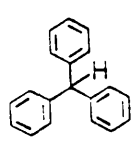
(54)



(55)



(56)



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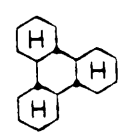
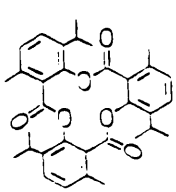


(58)



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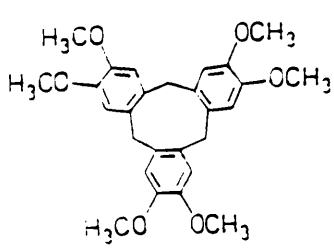
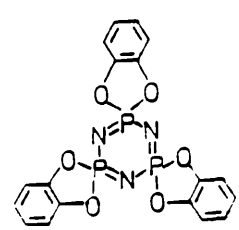


(60)



(61)

Figure 9 (adapted from ref. 223b)

New host discovery[223b]

The hosts described have been found by chance, as are many new types. Examination of the literature for unrecognised, or undeveloped, cases of inclusion is still a productive source of new hosts. Even simple modifications of host molecules normally destroys their inclusion properties. Unlike the reliable, predictive, molecular modelling programs for unimolecular hosts, similar packages have not yet been developed for designing host lattices. This arises from the relative complexity of intermolecular forces compared to the strong, directional, covalent bonds. In the near future another, hybrid, route could be to design lattices where cavities are intramolecular (unimolecular) and the host intermolecular packing can be well defined. A modified host retaining inclusion properties may even have an entirely different lattice structure - a single host may also adopt different structures with different guests.

Limited success in modifying hosts to alter the size and shape of lattice space came from work on urea and the cyclophosphazenes.[99a] The first extensive study into producing new host lattices and understanding the fundamentals of the inclusion properties came from structural changes/modification of Dianin's compound (55), resulting in significant adaptions of cavities.[224]

In 1976 MacNicol[225a] published the first identification of a major family of new hosts structurally unrelated to any previous, based on the 'hexa-host' strategy (section c). Recognition of the predominance of trigonal symmetry in host lattices further led MacNicol to synthesise new compounds and prove them to be effective hosts.[225,104]

Other groups have since developed different routes to finding and developing new host families, and these are discussed first, followed by other recent discoveries and developments and then finally the 'hexa-host' family.

a) New design rationale and host families[226]

Inclusion properties of acetylenic diols (62) first reported in 1968[227] have later led Toda and Hart to design many new hosts, originating from their 'wheel and axle' analogy.[228] This shape, to which the host molecules were compared, was predicted to pack preferentially to leave channels between parallel 'axles' separated by adjacent 'wheels'. Suitably large 'wheels' compensate for lengthened 'axles' or 'axle' functionality that may otherwise cause (unfavourable) host-host interactions. It was recognised that earlier hosts (63) may be structurally related.[229]

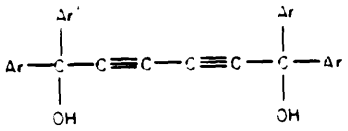
Key features amongst the hosts are:

1) bulky hydrophobic groups
2) rigid construction
3) commonly, strong hydrogen bonding to complementary guest functionality
4) often symmetry, particularly C_2.

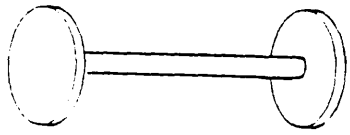
'Wheels' are normally (substituted) phenyl groups but other aromatic systems or alkyl groups of sufficient size have been successful. The 'axle' has been varied widely (in functionality), thus increasing or eliminating host-guest interactions, increasing or decreasing length, and changing the rigidity.

This demonstrates co-ordinato-interactions to improve stabilities and rigidity crucial for wide inclusion properties. Thus (64) is a general host and true clathrate, (65) forms only a toluene inclusion compound and (66) many co-ordinatoclathrates.

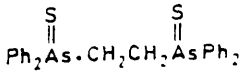
The important initial design feature is poorly packing end groups supported by non-self-interacting linear rigid spacing. Hart has shown that while the combination of trityl groups with the strongly co-ordinating urea centre makes ditritylurea (DTU) (67) an excellent host,[230] N-tritylurea (NTU) (68) is indeed an effective clathrate due to completely shielded inter-host hydrogen bonding.[231]



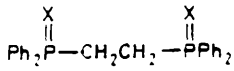
(62)[228]



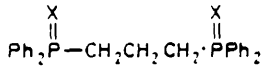
"wheel and axle"[223b]



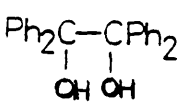
(63a)[229]



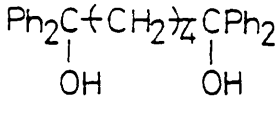
(63b, X = S,Se)[229]



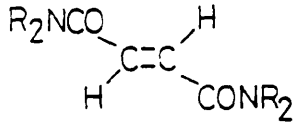
(63c, X = S,Se)[229]



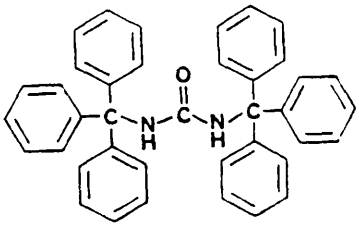
(64)



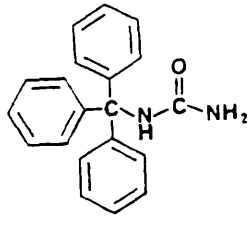
(65)[234]



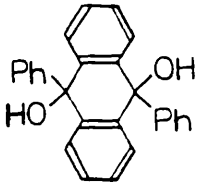
(66)[234]

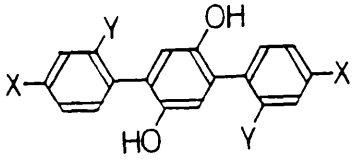


(67)[226b]

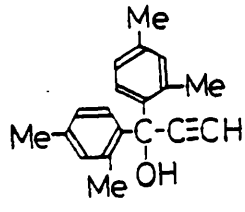


(68)[226b]

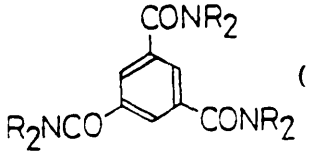




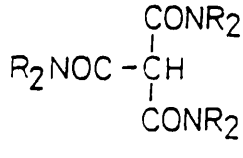
(69a,b)[234]



(70)[234]



(71a,b)[234]



This leaves poorly packing, well organised, rows of trityl groups, highlighting the role of bulkyl groups left with few freedoms of association.

Further noting that planar aromatic groups were always mutually twisted and presenting anti-diol conformations prompted design of 'no-wheel-and-axle' hosts, e.g. (69),[232] related to the cordinato-clathrates of Weber.[233b] This change, to covalently predict the necessary conformation expected in the lattice structure, is (perhaps) an expression of the principle of pre-organisation applied to the multi-molecular situation. The alcohols of structure $R^{I}R^{II}R^{III}COH$, e.g. (70), where R^{I}, R^{II} are bulkyl hydrophobic groups and R^{III} linear and rigid, are also hosts displaying the same packing features of parallel disposed aromatic groups, rods and hydroxyls of adjacent molecules.[233] Significantly, lattice centrosymmetry relates two of these hosts so that they appear structurally similar to one larger acetylenic diol, so that now symmetry rather than covalent bonding or hydrogen bonding is responsible for a favourable organisation of host molecules.

Recognition of the role of small amides as strong co-ordino-clathrate guests has led, by role reversal, to Toda's amide hosts[234] as well as DTU and NTU. The 'non-wheel-and-axle' amide hosts, e.g. (71), show notably both uses of aromatic rings, as rigid anchors and favoured C_3 propeller cup-shape. A conceptual reversing of host and guest roles using alkaloids has been useful, leading to optical resolution.[235] Resolutions, lattice phase reactions and separations (e.g. isomers, alcohols from water) have been dominant applications of Toda's hosts.[234,236] Recently Toda has formed inclusion compounds from solid host and guest components.[237] These still demonstrate properties such as enantiomeric and tautomeric selectivity but can now be run as continuous processes. The stoichimetry of guests with hosts may be different from that obtained by crystallisation. The solid-solid reaction, unlike a well established case, does not rely on sublimable components, nor does it show charge-transfer or heat-forming characteristics.

The specific shape dimension implicit in inclusion is well demonstrated by calculating theoretically the preference of hosts for ROH over H_2O resulting from non-bonded interactions rather than functional interaction.[238]

Lattice symmetry is observed to play an interactive part with key structural elements, namely host molecular shape (idealised point group symmetry), cavities and hydrogen bonding patterns).[239]

Host molecules are observed on 2 or $\bar{1}$ lattice sites where permissible, even if independent molecules or sets of molecules exist. Circuits of hydrogen bonding often involve 2 hosts and 2 guests, and are commonly around an inversion centre, as are clathrate cavities. As previously described, lattice symmetry is also implicated in constructing from smaller hosts wider associations reminiscent of bigger, more symmetric hosts, in an operation potentially related to hydrogen bonding requirements.

Weber[223a] has used explicitly the concept of co-ordinatoclathration by designing hosts containing functionality for the purpose of guest complexation by hydrogen bonding on the premise that this should yield more general and stronger inclusion properties than sole reliance on non-bonded interactions. Necessarily (to produce lattice voids), the host contains an allied structural feature. Again here angular aromatic groups and systems are used, in either the 'roof' or 'scissors' analogy (Figure 10).[240] This concept has been exploited particularly well with 1,1´-binaphthyl-2,2´-dicaboxylic acid (72), for which more than fifty guests and many X-ray structures are reported.[241] As with other 'new' hosts, the literature shows precedent, unrecognised at the time, for these inclusion properties.

(72) also shows remarkable selectivity even amongst homologous guests. The cause of both is illustrated in the range of structures found for the different guests, where the co-ordination response is tailored to meet guest requirements.

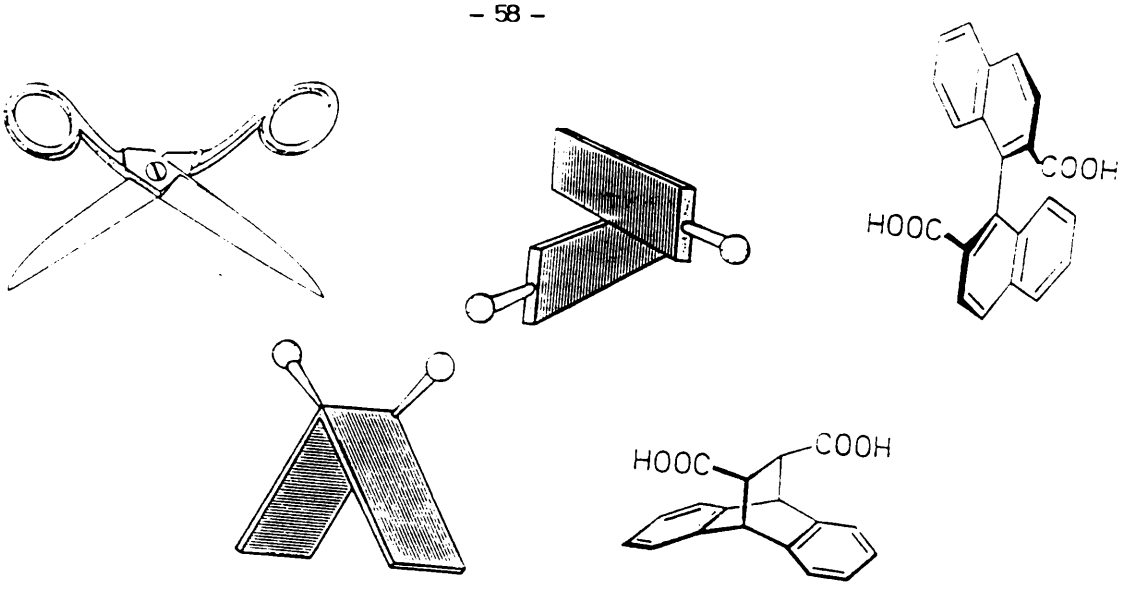
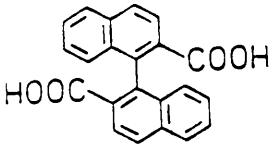
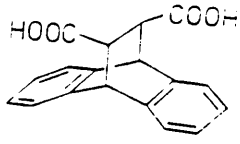


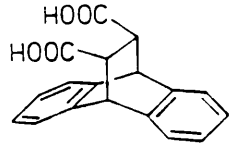
Figure 10 "scissors and roof" (adapted from ref. 240a)



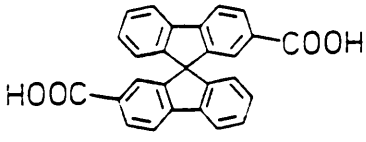
(72)[240a]



(74a)[240a]



(74b)[240a]



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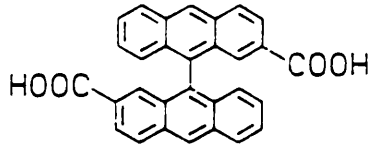
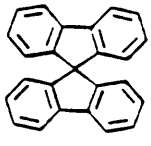
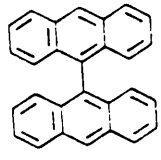


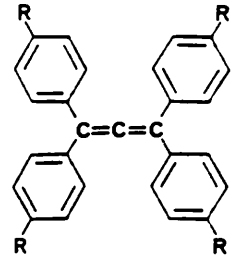
(73b)



(75)[240a]



(76)[240a]



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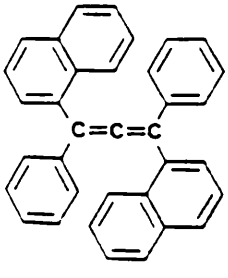

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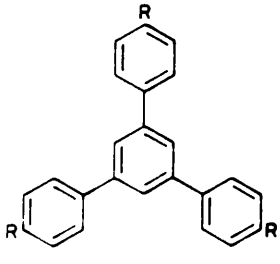
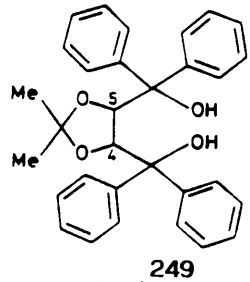


(83)[250]



(82)[249]

In a series of guest alcohols, different planar homodromic closed loops of hydrogen bonds, with participation to full donor acceptor potential, are observed, with the hydrophobic guest body disordered in the intermolecular voids.

For lower alcohols a twelve membered ring containing two host and two guest hydroxyl groups, on a symmetry inversion centre, is found. Change is made to a two-host and one-guest containing ten-membered ring for the bigger sec-BuOH, where the inversion centre is now between two guests and the binaphthyl hinge is at its most distorted from C_2. The ethylene glycol adduct used a 24 membered ring, built by four hosts and two guests, with the small hydrophobic portion easily accommodated almost intramolecularly. Host lattices tend to use 2-fold symmetry to coincide with molecular C_2 elements, and often orthogonal glide planes. Dimethylformide (DMF) does not utilise full hydrogen bonding, ascribed to a packing problem, and two independent DMF guests exist.[242] One joins in a seven membered ring, the co-ordinates only to one host site. Dimethylsulphoxide, which has acceptor sites only, acts to form infinite chains. The firm basis of the clathration properties for the host is revealed with bromobenzene guest, where now only host-host interactions are possible, and these, typical diacid groupings, occur on inversion centres. Changing the chemical functionality of the 'sensor' group from a carboxylic acid to an amide or ester has uncovered more (limited) hosts.[240a]

Other systems developed on the co-ordinoatoclathrate principle are the spirobifluorene (73a)[243] and anthraceno compound (74a).[244] Each structure has built on the C_2 symmetry of the host in the lattice and indeed the related host (74b) with C_h molecular symmetry has diminished inclusion properties. In the acetic acid clathrate of (74a) the only interactions are host-host and guest-guest pairings with the structure propogated by glide plane n almost perpendicular to the molecular symmetry.[244]

9,9'-Spirobifluorene (75) is a clathrate-forming hydrocarbon giving good selectivities on strict structural requirements for many non-polar guests. The similarly shaped hydrocarbon 9,9'-bianthryl (76) forms clathrates with a closely matching lattice structure, but these are fewer and weaker. Weber has related this to the rigidities of the molecular hosts.[245] Both do make use of bigonal symmetry, as do the allenes, e.g. (77) R= t-Butyl , which form similarly demanding clathrates showing good guest separations. The substituents must be more bulky than simple phenyl groups. The non C_2 allene (78) only includes benzene; unfortunately its C_2 isomer is not reported.[246] Some more recent inclusion has been achieved with C_2 and C_S substitution of larger spacer groups, with or without co-ordinating groups, onto cyclopropane and cyclobutane, e.g. (79).[247] These demonstrate linear arrays of hydrogen bonding and true clathrate structures respectively.

Further new examples of matching angular phane groups with C_2 or C_3 symmetry and co-ordinating groups are found with tartaric acid derived host compounds, e.g. (80), and triphenylmethanol (81)[248] (an extension of the clathrate properties of TPM (57)). With (82) and related compounds the racemic, resolved (R,R) and meso compounds are all inclusion compounds.[249]

In summary the most common features of Weber's hosts are:

1) bulky hydrophobic aromatic groups, angularly dispositioned
2) strong host-guest co-ordinative interactions
3) loops with full donor-acceptor participation
4) molecular C_2 symmetry (expressed in lattice 2 symmetry).

Weber has also described a series of hosts based on 1,3,5-tris(aryl)benzenes,[250] minimalistic hexa-hosts, e.g. (83), R= CO_2H,. These require bulk substituent of 'legs', preferably para, and to be rigid, or substituted to give coordinatoclathrates. A crystal structure of (83) .3 DMF has demonstrated 3 crystallographic structure and 'piedfort' packing (see Results and Discussion, section 2.11).

Mak has also remarked on the role of C_2 symmetry in hosts.[251] His recent investigations into the saddle-shaped hydrocarbon host o-tetraphenylene (84) have concluded the molecule uses only C_2 (and not full D_{2d}) lattice symmetry.[252]

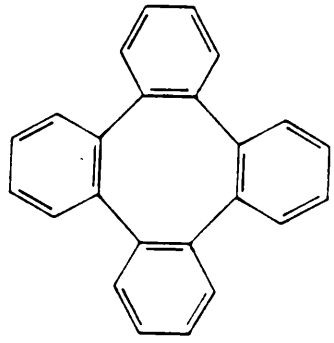
The C_2 axis runs across bonds 1,1' and 12,12' in a conformation distorted from the idealised (Figure 11). Cavity size correlates well to guest requirements. (85) cannot obtain this crystallographic C_2 symmetry and is not a host; its isomer (86) is not reported.

The expanded derivative (87) can, and is a host.[253] In the p-xylene adduct the host molecule attains C_{2d} point symmetry but packs differently (in $P\bar{1}$). Two inversely related xylene guests fill the cavity and like other clathrates of (87) are much more stable than those of the parent host (84). Another clathrate of (87) with a different structure has also been recognised.

The range of inclusions offered by coordinoclathrates over van der Waals consolidated clathrates has been surpassed by the onium hosts.[254] No host-guest interactions operate and the lattice is held together by electrostatic charges. This permits strong clathration, enough stability to allow large host conformational flexibility, and proves a high 'hit rate' in design. Required characteristics for the hosts are:

1) Bulky rigid groups ('arms')
2) rigid molecular 'anchor'
3) limited flexibility 'arm joints'
4) optimal regiosubstitution of 'arms'
5) symmetry.

Flexible arms, extended arm joints and other substitutions on the molecular framework are all to be avoided. The counter-anions serve only to consolidate the lattice; however, smaller anions shrink cavity sizes and limit the maximum guest size correspondingly.[255a]



(84)[253b]

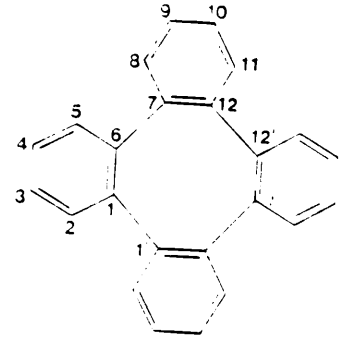
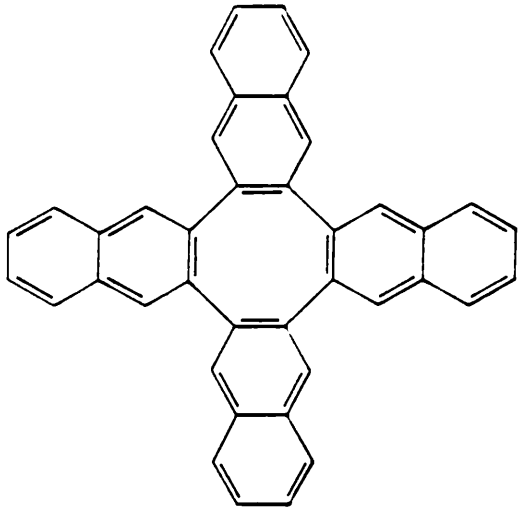


Figure 11 (C_2 numbering)[253b]



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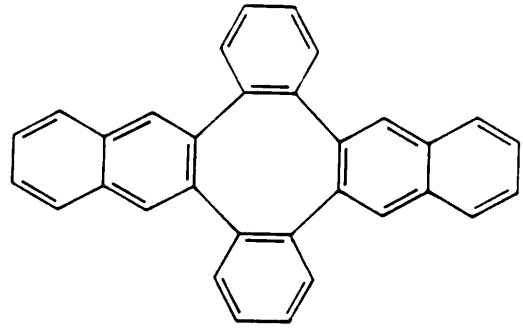

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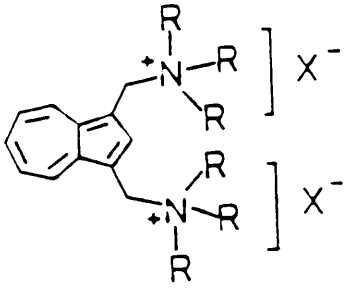
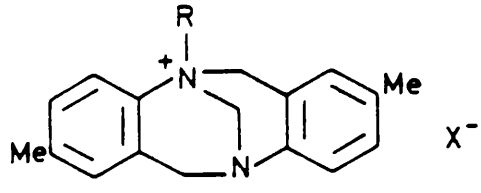


R = Me, X = I

(88)[223b]



R = Me, X = I

(89)[257]

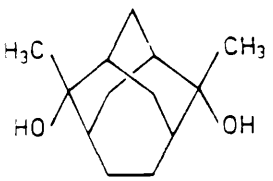
A single host has the ability to respond to different guests by radically changing its conformation, e.g. (88) may be transoid (with methyl iodide) or cisoid (with butanol). Even an apparently ideal opportunity for isostructural replacement of disorded butanol by butan-1,4-diol produces a new packing.[255b]

Quaternised alkaloid bases make good (chiral) hosts.[256] Those derived from Troger's base, e.g. (89), have excellent rectangular cavities due to the cation's hinge shape.[257] Other onium compounds, e.g. phosphoniums, show evidence of inclusion.

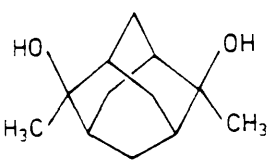
Bishop has discovered an excellent family of hosts in which to conduct a thorough investigation into the design requirements displayed through one single lattice structure. These form helical tubulands with inclusion in the canals. Beginning from the parent bicyclic diol (90) [258], he subsequently established that inclusion was dependent on the following characteristics[259]:

1) There is packing in the space group $P3_121$ (or $P3_221$ - spontaneous resolution).
2) R^1,R^3 or R^2,R^4 are cis-related hydroxyl groups, and
3) R^2,R^4 or R^1,R^3 are cis-related methyl groups (91).
4) A bridge exists on the face containing the hydroxyls (n>o) but,
5) a bridge on the other face is optional.
6) C_2 molecular symmetry exists, not necessarily attained in the lattice.
7) There is a small degree of molecular flexibility (related to hydrogen bonding ability).
8) No other molecular substitution is permitted.

Thus molecules (92), (93) and (94) fail to be hosts (on rules 7,3 and 4), whereas for example compound (95) is.[260]

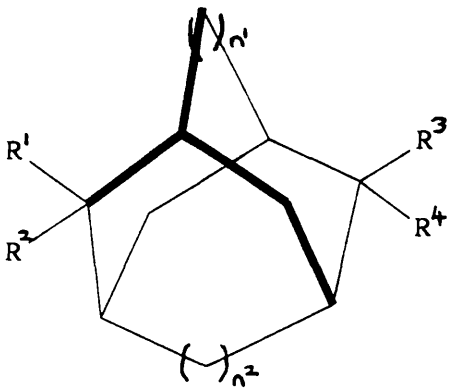


(95)[262]



(92)[262]

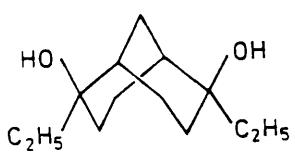
(94)[262]



(91)

(93a)[262]

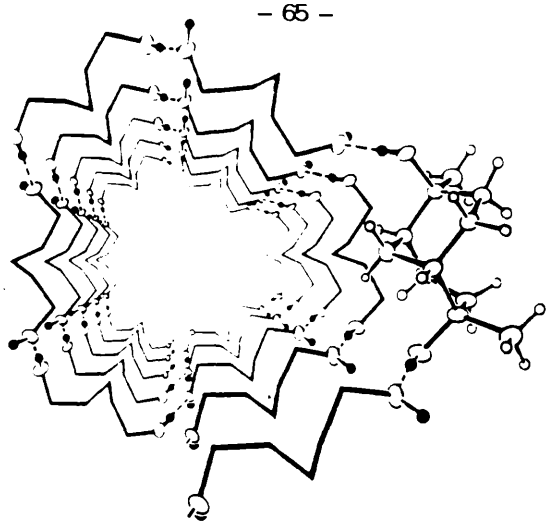
(90)[262]



(93b)[262]

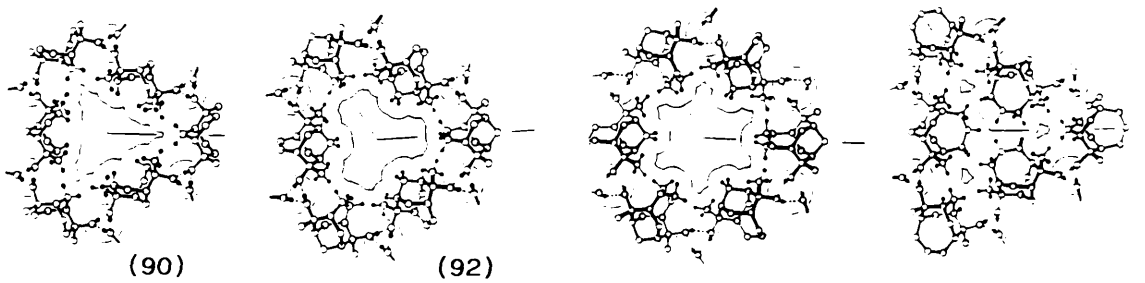
The structure adopted by the hosts is shown in Figure 12a. This is of two identical sets of intercoiled helices of pitch 2c, each formed of six host molecules per turn, connected by enclosed spines of hydroxyl groups with maximised hydrogen bonding and leaving hydrophobic canals of various shapes, ideally, the length of the crystal.

Guests (e.g. ethylacetate, dioxan, toluene) are not located and show no interactions with the host but they are tightly bound in the tubuland structure. Examining each symmetry element in the space group, and the movement available to the host molecules under these restrictions, Bishop identified the key structural variation and its consequences for void shapes, and then related it to the molecular shape and the fundamental non-bonded interactions underlying this.[103]



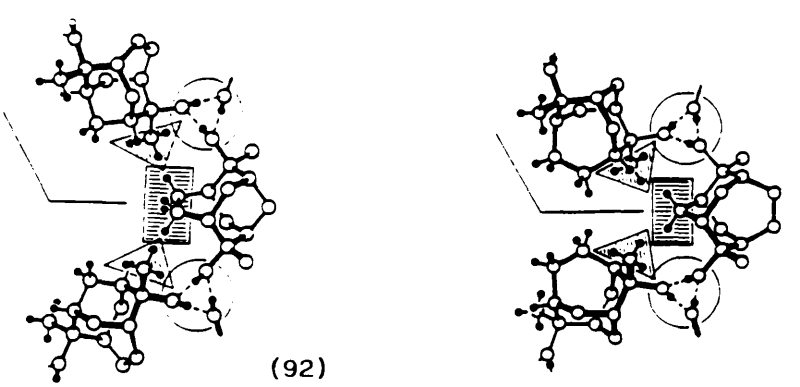
(90)

a) Exaggerated perspective view of the helical sequence of hydrogen-bonded diol molecules in one canal; all except one diol molecule are represented diagrammatically as the bridge linkage of the two OH groups



(90) (92)

b) Comparative projections along the *c* axis of the diol molecules and the canals they enclose. The bond thickening signifies depth in individual molecules only, because the helical characteristic is absent from these projections of the lattice. The canal boundaries are marked as the intersecting projected van der Waals spheres of the hydrogen atoms which line the canals. All five diagrams are presented on the same scale. Significant hydrogen atoms are marked as filled circles, and the spines are circled



(92)

c) Projections along the *c* axis of details of structures with ethano and methano *syn* bridges (cross-hatched rectangle), respectively. The differing proximity of the *syn* bridge to the methyl substituents (cross-hatched triangles) on the flanking *anti* walls of the canal are apparent

Figure 12a–c structural detail of diol tubulands

(adapted from ref. 262)

The variable proves to be the radius measured from the canal centre to the face opposite the hydroxyls, brought about by translation along the a-axis. Changes occur in the cross-sectional area (CSA) of the channel and the orientation of the projected hydrogen-bond spines, in turn also leading to different unobstructed channel areas (and hence the free space topology) (Figure 12b). A further consequence is varying hydrogen bond lengths, and corresponding shifts in the lattice strength (as reflected by melting points). Bishop observes the pitch to be invariant and related to the molecular width (and so unlikely to be made variable) but proposes the length of molecule, and hence CSA, amenable to change.[103] The non-bonded interaction on which the structures ultimately 'rest' is between the methyl groups epimeric to the hydrogen-bonded hydroxyl groups (Figure 12c). When these are removed or changed the structure collapses. Although these hosts have the classical characteristics of being rigid C_2 diols forming open structures based on maximum host-host hydrogen bonding, they are different in using helical, not circular, interactions.

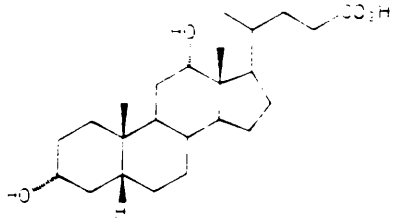
Interestingly, host (95) also crystallises in another space group ($I4_1/acd$) with benzene guest, based on a (non-helical) tubuland structure with uniquely S_4 rather than S_3 symmetry.[261] Design in this space group has not been pursued. Bishop has also observed that because of the very small asymmetric unit of the host and the high symmetry of the canals, guests cannot be complementary in symmetry and necessarily become disordered.[262] Bishop has rationally overcome some of the difficulties encountered in modifying known multimolecular hosts, i.e.

1) Establishing the basis of design and permissible variations for host properties.
2) Modelling of lattice structure from host molecular structure.

b) New developments and new hosts (and new significances)

Bile acids, particularly deoxycholic acid (DCA)(56), form many inclusion compounds.[263] The host molecular shape is crucial - an arched back with spaced lipophilic groups on one side and methyl substituents on the other (96). In the most common orthorhombic structures anti-parallel bilayers of host molecules related by 2_1 axes leave hydrophobic channels with 2_1 or 2 symmetry. The bilayers are held together by maximised interhost hydrogen bonding of adjacent opposite ends and centrally facing partners. Different guests are catered for by the'motifs' available from relative displacements of bilayers. Much work has been undertaken on regio-selective addition of the guests (normally tightly held and specifically orientated) to the channel walls[264] and on controlled self-polymerisation or cyclisation in pathways not available to the guest in solution.[265] In the related tetragonal form, 4_1 axes relate bilayers which use their small polar guests to link the hydrogen bonding in co-ordinoclathration. Similar to Bishop's compounds, the newer hexagonal structure is built on a 6_5 axis to generate helices, with polar groups pointing inwards to small continuous channels containing suitably sized co-ordinoclathrated guests. Overall, the drive to maximise hydrogen bonding of an awkwardly shaped molecule has led to a series of inclusion structures using both co-ordinative and steric properties of guests to fill cavities created by the symmetry propagation of the structure. Very recently methyl esters of some bile acids, in particular methyl cholic acid, have shown strong inclusion over a vast range of guests.[266]

In this case, the C_2-related host-host interactions are hydrophobic, allowing hydrophilic host-guest-host hydrogen bonding across channels.



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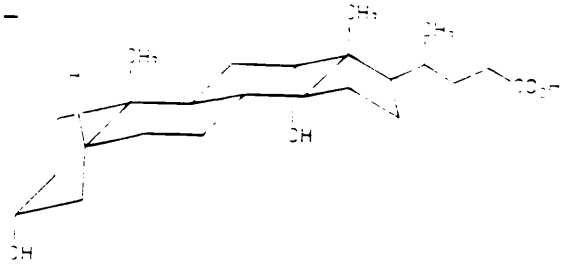

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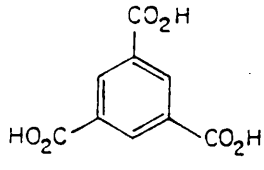

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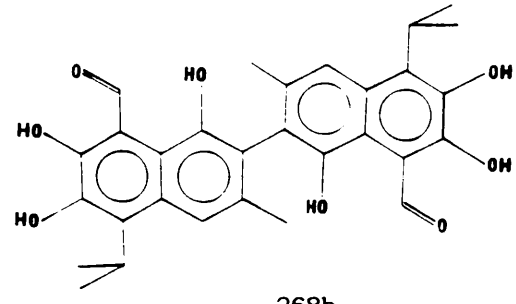

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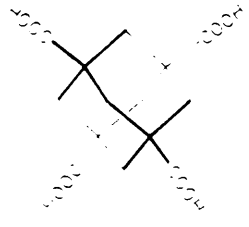

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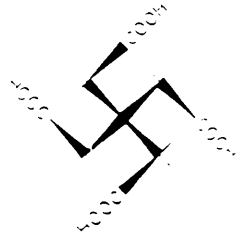

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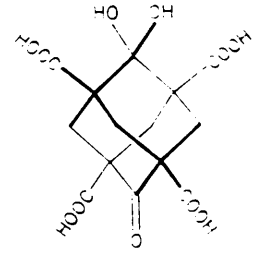

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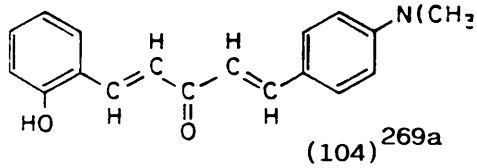

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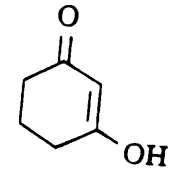

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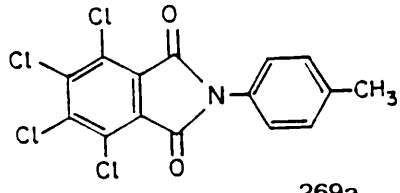

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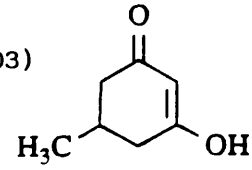
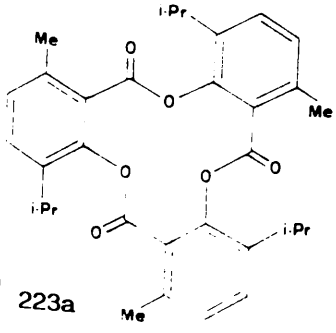
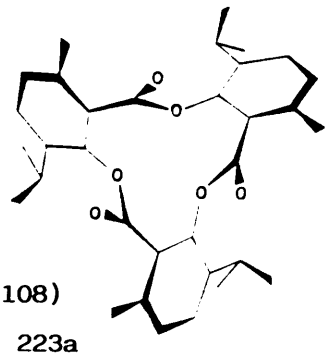
(103)





(59) 223a



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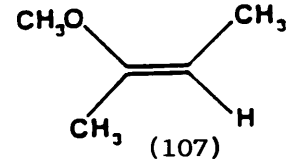

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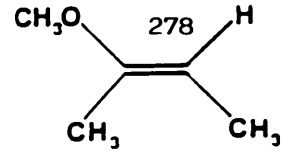


278

Other 'natural' hosts are known. In the isolation and structure elucidation of a natural pigment a fatty acid clathrate was formed whose composition was then established by making urea clathrates.[267] Gossypol (97), another pigment, has been shown to form many inclusion compounds, both clathrate and coordinato-clathrate. The host is C_2, restricted in the rotation of its rings (allowing enantiomers) and contains many sites for interactions.[268]

Trimesic acid (TMA) (98), which has C_3 symmetry, forms an open 'chicken-wire' 2D structure, potentially ideal for inclusion, where the correct orientation of maximally interacting functionality in a planar host has led to large voids. In the past, this structure has always been found in catenated forms, thus severely curtailing possible inclusion compounds; some non-catenated related structures are observed with both DMSO and water.[269] An equivalent situation for the 'three-dimensional' tetracarboxylic acids derived from adamantane (99) and tetramethyl methane (100). These molecules pack in a diamondoid structure with five and three fold interpenetrating structures respectively to fill their own lattice spaces.[270] These molecules have S_4 tetragonal symmetry.

Significantly perhaps, although no inclusion was found in these cases, the related <u>3-fold</u> diamondiod structure for (101) included guest - the host (disordered keto-hydro positions) here now has lower D_2 symmetry only.[271] Indeed, β-hydroquinone itself is two interpenetrating lattices. The first non-catenated 'chicken-wire' TMA structures have also now been reported, where C_{7-10} alcohols and hydrocarbons are guests. Despite different space groups (e.g. $P3_1$ and C2/c) they appear to be isostructural, with channels arising from stacked layers containing disordered guests (not refined).[272]

A new class of multi-molecular host is represented by the cyclamers (102) and (103). Again, a planar host structure with correctly orientated hydrogen bonding groups forms a 2-D network, but of discrete entities now.

These are cycles of six hosts leaving a hollow centre able to take only a specific sized guest (which is in cavities, not channels, because of offset adjacent layers). Benzene is fully incorporated, matching size and symmetry, however, thiophene can be partially incorporated with benzene as the major guest.[283]

The cyclamer ring in likened to a solid-state macrocycle using hydrogen bonds in place of covalent bonds - the reverse of the hexa-host situation. The cyclamer structure is, however, another example of $R\bar{3}$ lattice symmetry.

In a study of the Heilbron complexes of DHDK (E,E-1-[p-Dimethyl-aminophenyl]-5-[o-hydroxyphenyl]-penta-1,4-diene-3-one) Herbstein has identified the following points concerning the DHDK host structure as being important contributions to the known different lattice structures.[269a,274]

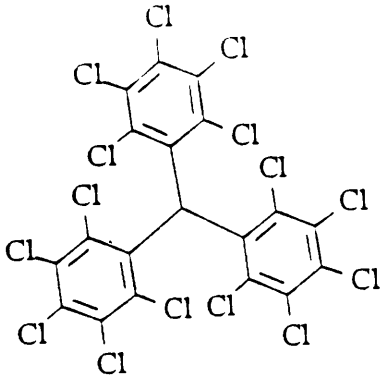
1) Conformational flexibility 2) Bulky groups
3) Hydrogen bond donor-acceptor 4) Electron donor-acceptor

In each of three different structures (1 - $CHCl_3$ in cavities, host-host hydrogen-bonded pairs; 2 - m-dinitrobenzene in channels, host-host hydrogen-bonded chains; 3 - p-dimethylaminobenzaldeyhyde coordinoclathrate, host-host dipole interactions) DHDK has a different conformation.

In the inclusion compounds of 2,5-Dichloro-5-carboxy benzenesulfonimide (105), three different packing of hosts in U-shaped C_2 conformations exist where host derived polar groups interact with guests.[275] Another (co-ordinoclathrating) host lattice using host C_2 symmetry is reported. Lattice 2 and 2_1 symmetry is used in the inclusion structure of N-(p-tolyl)tetrachlorophthalimide (TTP) (106) with aromatic guests. Van der Waals forces between anti-parallel host molecules leave the polar groups to form a channel with inclusion potentially capable of enantiomeric discrimination since the crystals are spontaneously resolved, built using a twisted (55^{o}) host structure. [269a]

Tri-ortho-thymotide, TOT (59) is a well-known host[223a] that spontaneously resolves on inclusion.[276] It can act as a host through either cavity or channel formation and uses many different space groups. In $P\bar{1}$, channels are formed from TOT molecules packing as if they were spheres although two different conformations exist. In the well studied P3,21 structure cavities are formed on 2_1 axes, in which guests are often distorted or in centrosymmetric related pairs, and guest-to-cavity volumes correlate well. TOT has been used as a medium for resolving guests and performing enantioselective reactions. Very high ee are possible with repeated crystallisations on non-racemic starting mixtures; molecules with two-fold symmetry often give rise to high discrimination.[277] The first example of a bimolecular heterogenous reaction in a chiral lattice host has been reported for the hyperoxidation of prochiral olefins.[278] In the ring-opening of epoxides (107) ee of 10% were found in favour of the product enantiomer which was the better guest.[279] In the attempted photo-isomerism of trans-stilbene, cis-stilbene which was the wrong symmetry for the channel was not formed.[280] It has been argued that either the static guest shape or its dynamic coupling (from ^{13}C MAS) van der Waals fit is responsible for good discrimination.[281] TOT never acquires full conformational C_3 symmetry in host lattices (though more so than for the guest free structure) but does always adopt a propeller shape rather than a helical conformation (108).

A new host family with propeller conformation and potential but unused C_3 symmetry are the perchlorotriphenylmethane based stable free radicals (109). Parallel disposed aromatics rings form channels with THF, dioxane or aromatic guests. Veciana has compared the structure with that of tris(1,8-naphthalenedioxy)-cyclotriphosazene. Host properties are retained with para ring substitution.[282]



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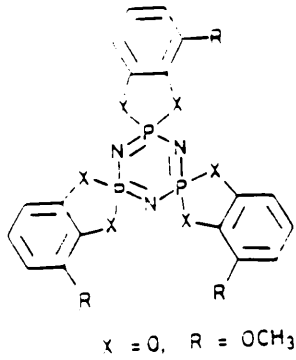

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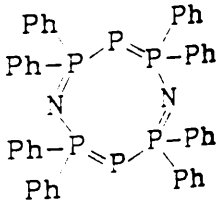

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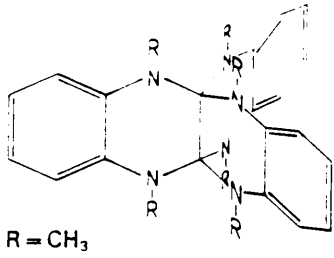

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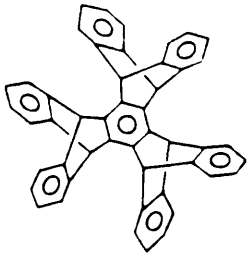

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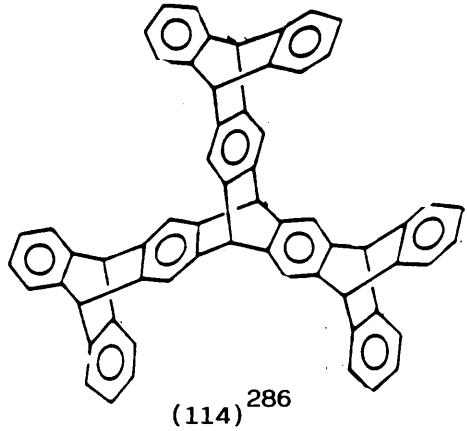

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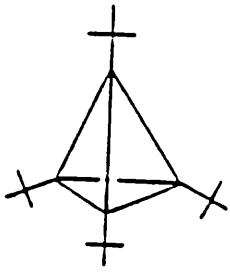

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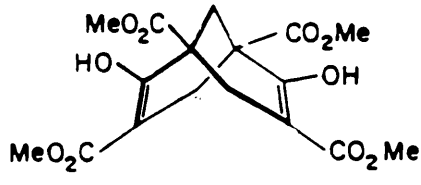
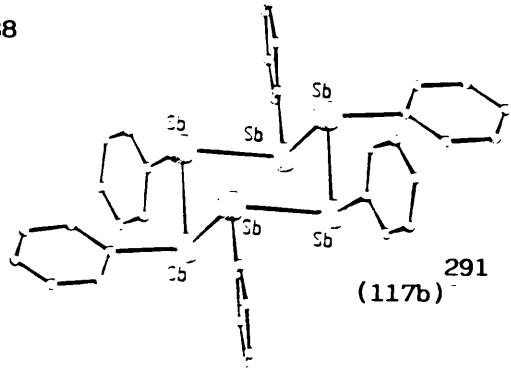


(116)[289]



(117b)[291]

A new spirocyclophosphazene (110) has been reported where a 3-methoxyl ring substituent still allows inclusion properties.[283] No X-ray structure has been undertaken but n.m.r. experiments show the substituents are conformationally locked all on one side. Octaphenyl-1,5,2 λ^5,3,4 λ^5,6 λ^5,7,8 λ^5-diazahexaphosphocine (111) is reported to retain solvent molecules but no structures for these potential C_2, cyclophosaphazene-like, adducts is given.[284] (112) was isolated as a host with 0.5 mole of disordered ethanol. The host has exact D_3 symmetry in the space group $Pa\bar{3}$.[285]

In the synthesis of hydrocarbon triptycene derivitive (113) a chlorobenzene inclusion compound was isolated. Although the structure was not fully resolved obvious shape and symmetry relations to cyclophosphazenes and other hosts are apparent.[286] Tritriptycene (114) forms an inclusion compound with acetone, the host using full D_3 symmetry in space group $P6_3/m$. Guests are disordered, in both channel position and occupancy, between almost parallel facing corners of aromatic rings from two molecules (similarly shaped C_2-hosts based on Tröger's base have been synthesised).[287] The same space group is found for the argon clathrate of tetra-tert-butyltetrahedrane (115), the first gas inclusion published with only host-host vdw forces.[288] The guest is trapped in an octahedral hole formed from a t-butyl group from each of six adjacent hosts.

The benzene clathrate of Meerwein's ester (116) is a complete contrast to these cases structurally, but still uses symmetry in packing.[289] The ester molecule (completely enolised) is located on a 2-fold rotation axis with two of the four stoichiometric benzene molecules on symmetry centres. Only benzene forms an inclusion compound. In the lattice each ester is surrounded by two neighbours and sixteen benzene molecules. It is not possible to define which is host and which is guest, with half of the weight due to the benzene.

Not surprisingly the structure is unstable. Dodecaphenylacyclohexagermane (117a) ·7 benzene is a similar case.[290]

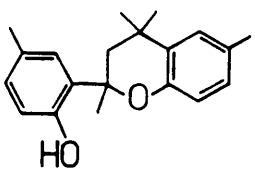
Another polyphenyl-substituted inorganic ring host is hexaphenylcyclohexastibane (117b) ·1 dioxane (or benzene). The host is an equatorial chair conformation, centrosymmetric and approximate P3d.[291] Seven structures of hydrate inclusion compounds built on polyhedral three-dimensional hydrogen-bonded networks were recognised until recently.[292] A further high pressure form with, for the first time, helium guest has been found while related to the ice II structure. This has $R\bar{3}$ symmetry built on alternately stacked layers of non-planar and almost planar rings each containing six fully hydrogen-bonded water molecules.[293]

The flavans, e.g. (118), which are structurally related to Dianin's compound, have been known for some time to form inclusion compounds. The first flavan host structures have now been published[294] and unlike Dianin's compound these have no hydrogen-bonded hexamers of host molecules, but, instead, participate in co-ordinatoclathration. In the dioxan adduct water bridges the phenolic hydroxyl to the dioxan (in hydrogen bonding) and is additionally hydrogen-bonded to the host ether oxygen. The structure is $P\bar{1}$ with the dioxan located on the inversion centre. An equivalent structure was found when the water-dioxan-water guest was (isostructurally) replaced by trans-1,4-bis(hydroxy-methyl)cyclohexane, although the guest was in the 'inverted' chair position.[295]

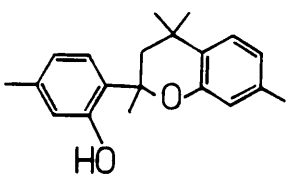
N,N´-dimethylpiperazine forms a similar inclusion compound with flavan (119). Common to both hosts is the angular disposition of the two, flat, aromatic rings and an outwardly facing phenolic hydroxy in a conformation arising from a half-chair in the hetero-ring, with eclipsed, or almost eclipsed, bonds about the phenol-ring bearing bond. Parallel facing aromatic groups dileanate the cavity.

In the benzene and cyclohexa-1,4-diene clathrates of host (120) in $P\bar{1}$ the guests are located on the inversion centres but the host retains near C_2 symmetry, the axis passing through the spirocarbon and the centres of the two perpendicular planar regions.[296]

Substitution of the desired C_3 triphenylene structure itself is expected to yield more hosts. O-(3,5-Dinitrobenzoyl) derivitives (121) appear promising as inclusion hosts where the substitution is a cyclic structure at an angle to the planar moiety; (121a) is indeed an $R\bar{3}$ clathrate.[297] Another $R\bar{3}$ clathrate structure is that of bistriphenylsilane (122). In this case the host was designed as an isostructural replacement of the TPM lattice structure, with great success.[298a] The host (123) forms clathrates, but perhaps not surprisingly these all pack in $P\bar{1}$ and not with the tetragonal symmetry of the free host.[298b]



(118)[223b]



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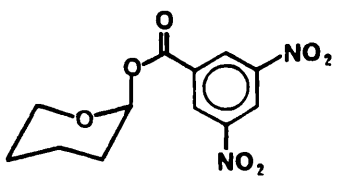
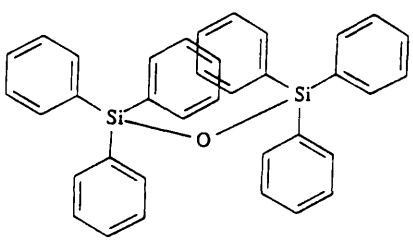


(121a)[297a]



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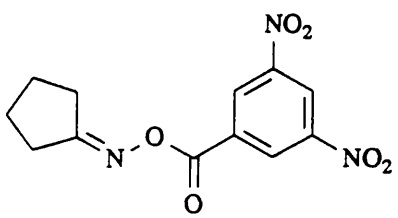


(121b)

c) The hexa-host analogy and related hosts[225,220b]

Attempting to discover new clathrates by design rather than chance, and with molecular structure unrelated to hosts previously encountered, MacNicol compared the hydrogen-bonded hexamer unit found in the well-known phenolic class of clathrate hosts (e.g. hydroquinone, phenol and Dianin's compound [Figure 13]) to that of a potentially isostructural hexasubstituted benzene: the 'hexa-host analogy' (Figure 14). The attraction of this replacement unit lay not only in its similar dimensions and dispositions of 'legs' (aryl or alkyl groups connected through a link atom), but also in the covalently fixed constructions of the component groups (in contrast to the temporary hydrogen-bonded unit of the phenolic hosts). The latter were often to be found adopting other non-inclusion structures, just as most phenols are not hosts.

Also notable was the trigonal symmetry inherent in hexasubstituted benzenes and promising reports of solvent retention by those examples synthesised earlier.[299]

A large number of hexa-hosts (Figure 15) were subsequently prepared from hexakis(bromomethyl)benzene and hexahalobenzenes using 'legs' derived from thiophenols, selenophenols, phenols and anilines and their extended benzyl or longer homologues, both to establish the analogy and to form the widest family of clathrate hosts known.

The first structural investigation of a hexa-host, (124).CCl_4, proved the clathrate nature of the inclusion, the alternate up and down disposition of 'legs' around the central benzene rings and, indeed, an $\bar{R}3$ space group. This constitutes the first rational new clathrate design.[300]

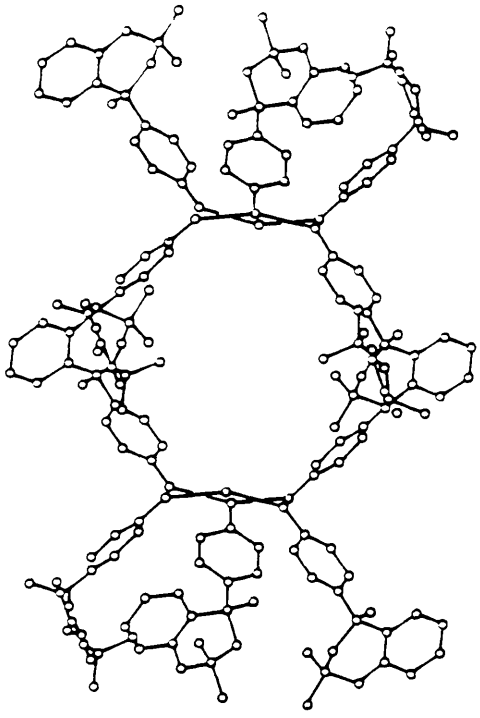
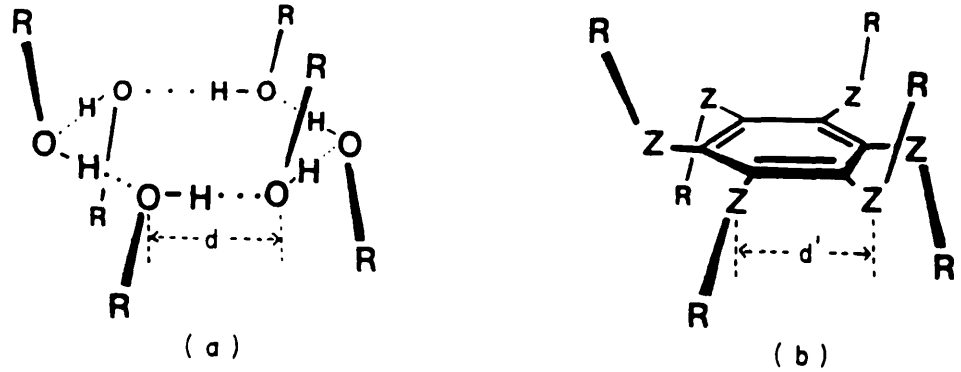


Figure 13

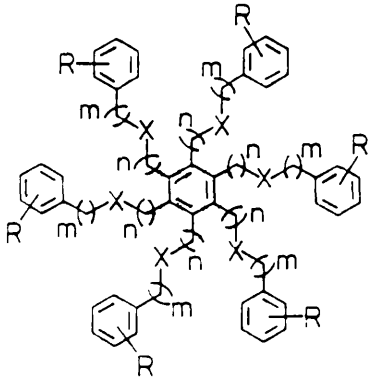
Structure of unsolvated Dianin's compound (55), viewed normal to the ac-plane. Two molecules of 55 which lie above and below the cavity as viewed in this direction have been excluded (apart from their hydroxyl oxygen atoms) to show the cage more clearly.

(adapted from Ref.224)



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

Figure 14 (adapted from Ref.225b)



X = S, O, Se, CH_2 , NR

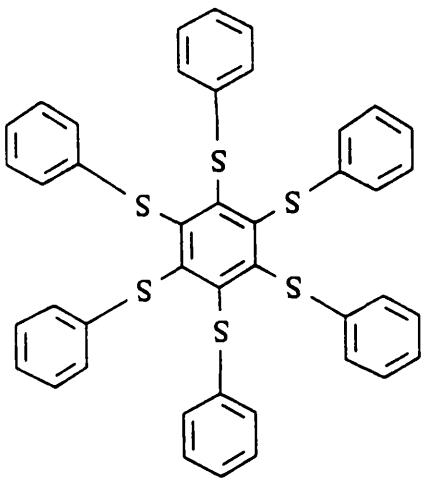
n, m, $\geq$ o

Figure 15 [223b]

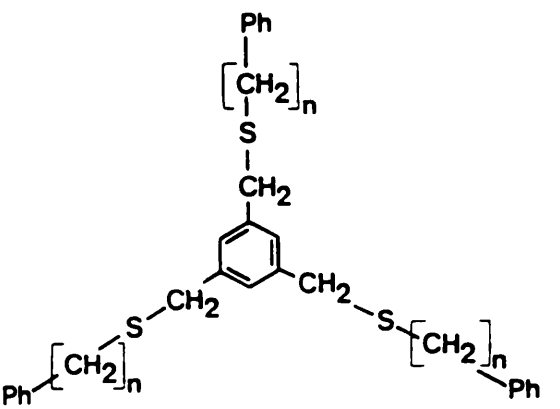
Inclusion ability of hexa-host molecules had the following general characteristics.

1) Inclusion more prevalent in sulphur link hexa-hosts.
2) Inclusion possible for saturated ring containing 'leg'.
3) Methyl and chlorine are good 'leg' ring substituents.
4) Ring substitution of rings most favourably <u>meta</u>, least favourable <u>ortho</u>.
5) Inclusion diminishes as leg lengthens - no inclusion for '5 link' molecules, (i.e. a five atom chain between the benzene and the (aryl) end group).

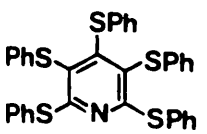
No inclusion properties were observed for the 1,3,5-trisubstituted benzenes (125), nor the parent pyridine based 'penta-host' (126); a by-product (127), is a host.[301]



(124)



(125)[225b]



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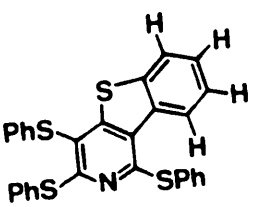
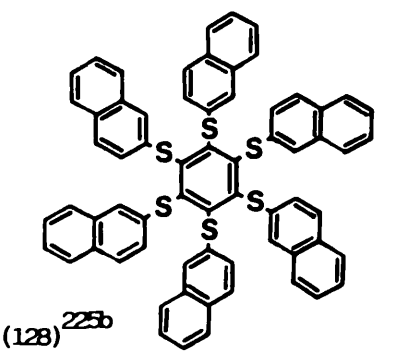


(127)[225b]



(128)[225b]

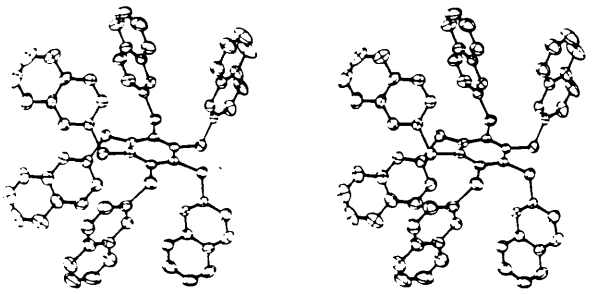
In the further structural investigations of hexa-host inclusion compounds the following points became apparent.

1) Other space groups occur, with trigonal lattice symmetry restricted (though further planned examples are currently emerging).[302]
2) Centrosymmetry of host is common.
3) Alternate disposition of legs is virtually exclusive.
4) Trigonal host symmetry is normally lost as the length of leg linkage increases (although it may be retained at the core).
5) Besides the columnar hexahost Dianin's packing, other different cavity and channel forming structures are possible.
6) As leg linkages increase the mean displacement of the leg above or below central benzene ring decreases.
7) A second type of conformation with approximate C_2 symmetry (Figure 16) not having alternate disposition of legs can still form inclusion compounds, i.e. (128).dioxan (Figure 17).[303]

Interesting information on guests generated by these investigations concerns the stabilisation of favoured conformations of squalene, 3,3,6,6-tetramethyl-s-tetrathiane, 2-N-n-butyl-N-methylformamide, and the first observation of dimeric acetic acid (in the first chiral hexa-host) (129).[304]

Hexa-host structures have been used by other groups as complexing unimolecular hosts[305] and potential liquid crystals.[316] Vögtle has synthesised 'dodecahosts', (130) but no structure of the inclusion compound is published.[307] Inclusion properties appear, however, very limited, perhaps because of a disc-like shape arising from overcrowding; since this does not represent the open structure of the hexa-hosts it may be nearer to the cyclophosphazene design.

Developing the rising identification of two-fold molecular symmetry in clathrate hosts, MacNicol prepared the octahosts (131) and (132) from octafluoronaphthalene, and found remarkable conformational interest in addition to inclusion.[308] Rather than adopt alternate leg displacements above and below the naphthalene core, other distributions were found. For the unsolvated host two different structures were observed by single-crystal X-ray diffraction, each producing crystals different in colour, one red and the other yellow. Applying pressure to the 'yellow' form produces red crystals, perhaps the same as the more dense 'red' form. This line of development of the hexa-host strategy appeared promising.



A stereoview showing the host molecule of hexakis-(β-naphthylthio)benzene in its 1,4-dioxan channel-type inclusion compound. All hydrogen atoms have been omitted for clarity. The molecule has approximate C_2 symmetry.

(adapted from Ref.225b)

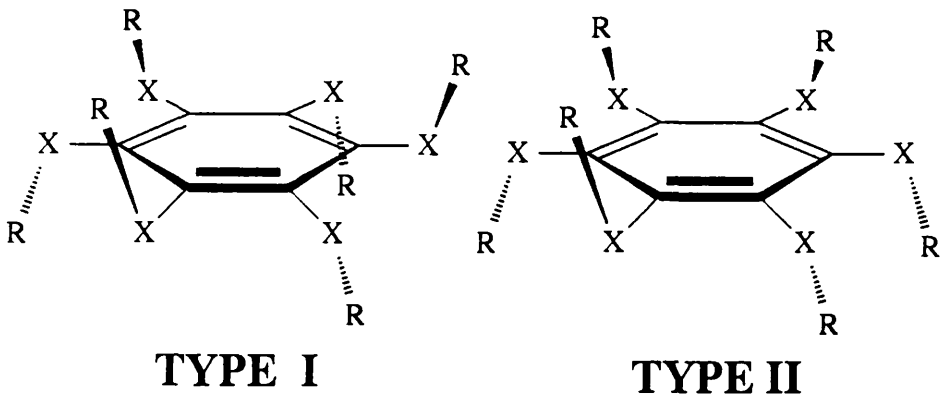
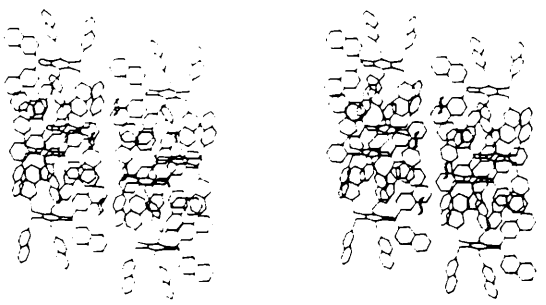
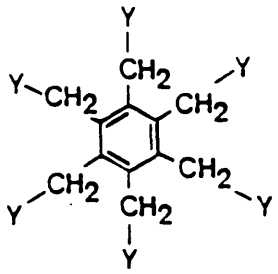


Figure 16

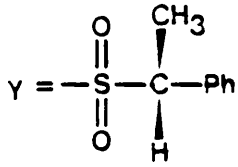


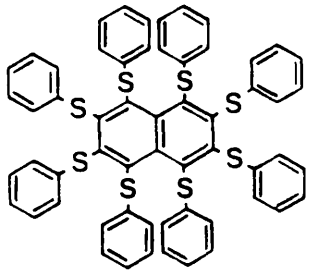
A stereoview showing the host-guest packing of the adduct of (128) with 1,4-dioxan as guest in the triclinic crystal. The chair-shaped 1,4-dioxan molecules can be seen to be located in continuous voids in the structure.

Figure 17 (adapted from Ref.225b)

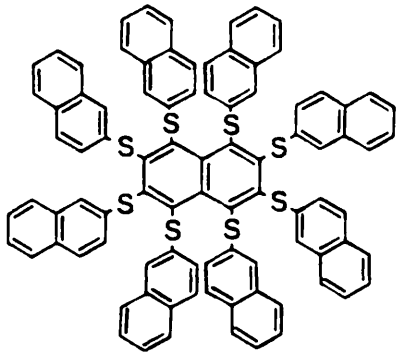


(129)[225b]

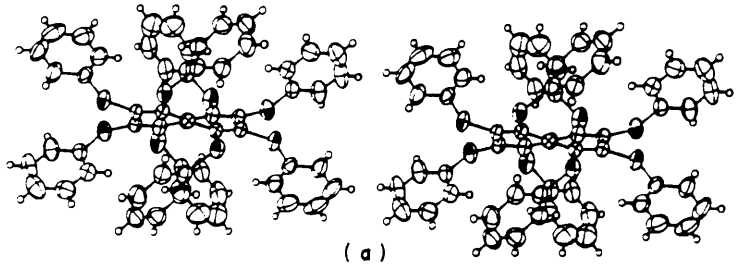


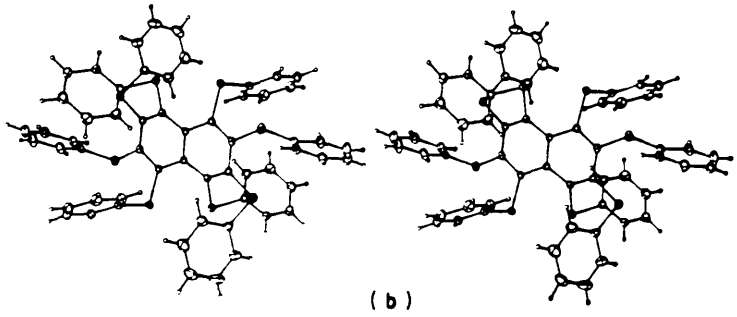


(131)[225b]



(132)[225b]





Stereoviews showing the molecular structure of (131) in (a) the yellow unsolvated crystal, and (b) the red unsolvated crystal.[308]

RESULTS AND DISCUSSION

A New Chapter in Fluorocarbon Chemistry

1.1. Perfluorodecalin - initial reactivity

Saturated fluorocarbons, distinguished by exceptional physical properties and minimal chemical interest, are widely recognised for their inertness. A great body of work has been accumulated on the chemistry of unsaturated fluorocarbons - almost entirely on addition-elimination type reactions with nucleophiles - but even this very rarely extends beyond allylic positions into perfluoroalkyl chains (and hence the widespread use of perfluoroalkyl groups as inert substituents in perfluorocarbon derivatives). The results obtained in the course of this investigation force a re-evaluation of this position, particularly for saturated fluorocarbons. In complete contradiction to previous expectation, a new mild, facile synthetic route to hexa- and octa-hosts starting from perfluoroalkanes and perfluoroalkenes, has been discovered. Other unknown potential hosts may also be accessible with this chemistry.

The octa-hosts octakis(phenylthio)naphthalene (131)[308], octakis-(m-tolylthio)naphthalene (134)[309] and octakis(m-methoxyphenylthio)-naphthalene (135) have been prepared from perfluorodecalin (1) in dipolar aprotic solvent (DMEU or DMF) using the appropriate arylthio sodium salt (route A).

These results are summarised in Table 1. The hosts obtained from this route are identical to those of the host products synthesised from perfluoronaphthalene (2) in an orthodox synthetic scheme, (route B), although in a poorer yield - up to 65% (unoptimised). The structures of hosts (131)[308] and (134)[309] (section 2.6) from the latter route have been unambiguously determined by X-ray single crystal diffraction.

Table 1

Reactions of perfluorodecalin (1) with aryl sulphur nucleophiles

Reagent*†	Solvent	Temperature	Time	Product	Yield# (%)
phenylthiolate	DMEU	ambient	several months		17‖
phenylthiolate	DMEU	60-70°C	10 days		65
phenylthiolate	DMF	60-70°C	10 days		55
m-tolylthiolate	DMEU	ambient	8 weeks		20‖
m-methoxy-benzenethiolate	DMEU	ambient	several months		5‖<

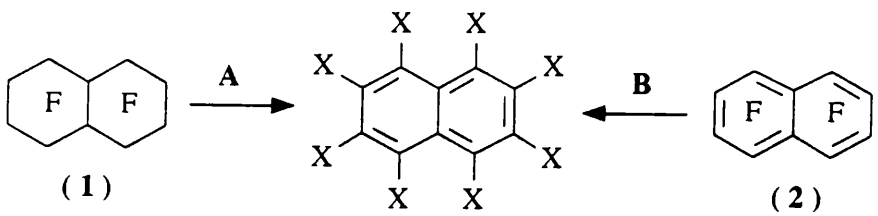
* With respect to (1), 36 molar equivalents were employed.

† The (sodium) salt was preformed and dried before use.

Yields based on (1) and not optimised.

‖ Most of (1) recovered untreated.

< Small amounts of related products were also isolated.



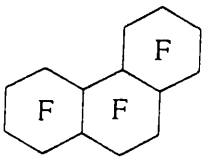
(1) (2)

(131), X = -S-C6H5

(134), X = -S-C6H4-CH3

(135), X = -S-C6H4-OCH3

The reaction of (1) with sodium thiophenolate in DMEU at room temperature was the first attempt to synthesise an octa-host by the new method. This was undertaken following an observation[310] that a compound with characteristics similar to those expected for the compound that would be formed from perfluorophenanthrene (136) with a thiophenolate was slowly formed over several weeks from a purchased sample of 'perfluorophenanthrene' which, on later investigation, appeared to be perfluoroperhydrophenanthrene (137) of unknown quality.



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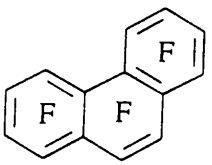
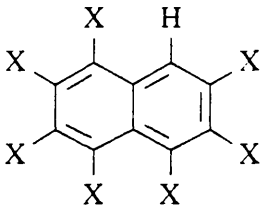


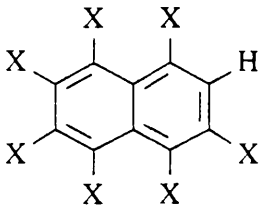
(136)

After a month, no evidence of the required colour change indicating the presence of octahost was visible. The reaction was left to stir and in the intervening period (the reaction) was repeated at 80-90°C over four weeks. The red product from this co-spotted with (131) on silica t.l.c. plates and had an indentical mass-spectrum. Under reverse phase conditions it separated into four products, all of similar but distinct R_f to that of (131). This mixture remains unidentified at present.

Eventually the room temperature reaction evolved a deep red colour and a white precipitate. After a total of eight months with unreacted (1) still apparent, a standard work-up produced (131) in low yield. The reaction was found not to be appreciably accelerated with UHF sonic treatment or gentle heating (up to 40°C), but at 60-70°C (bath temperature) colour was seen after five days and all the decalin visibly consumed after ten days. At 80°C two extra products were isolated, one orange and one yellow.

These additional compounds have mass spectrum, ^{1}H and ^{13}C n.m.r. consistent with reductive leg cleavage and are assigned structures (138) and (139); the isomers are not assigned although the more prevalent yellow compound has a simpler n.m.r. spectrum and shows easier leg loss under mass spectrometry.





(138),(139),X=SPh

The reaction was further established by formation of the octa-hosts (134) and (135) by this method.

By using an ion-selective electrode, it was established that the white precipitate was fluoride. Examination of the aqueous portions of reactions of perfluoro-aromatics, alkenes (section 1.3) or decalin by this technique gave molarities of <u>ca.</u> 10^{-2} -10^{-3}, compared to 10^{-6} background. Blanks and reactions with other inactive substrates, however, gave readings of 10^{-4} - 10^{-5}M and the method did not prove viable for determining potential partial reaction of other fluorocarbons.

The reaction also provided substantial amounts of diphenyl disulphide, equivalent to > 4 molar equivalents per mole of perfluorodecalin.

Repeating the reaction of (1) with sodium thiophenolate in DMF rather than DMEU gave only a moderate drop in yield (65% to 55%, unoptimised).

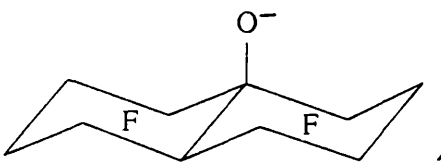
1.2. Reaction mechanism

Since there is no precedent for this reactivity of a saturated fluorocarbon, the mechanism is of immense interest. The initial stage is possibly one of the three following alternatives:

1) $S_N2(C)$
2) $S_N2(F)$
3) SET

An S_NI pathway is highly unlikely in view of the mild conditions and very strong bonds. The central carbon-carbon bond is in any case the weakest[67] (see introduction, section 1.3).

Highly fluorinated systems are exceptionally resistant to $S_N2(C)$ and indeed displacement of fluoride from CF_3 or CF_2H by attack at carbon with an external nucleophile is unknown[3]. A few intramolecular examples have been postulated[311-314] [Fig 18], for which only the first could plausibly proceed by a different mechanism although this does not appear to be the case. The only examples of nucleophilic attack at carbon in a similar situation are the ring opening of perfluoroepoxides, the ring closure of fluorocarbonhalohydrins to epoxides[3], and more recently the closure of anion (138) to give 9,10-epoxyperfluorodecalin (139).[315] Mechanistically, the process could be related to a previous unexpected chemical reactivity of similar compounds, that of halogenofluorocarbons.



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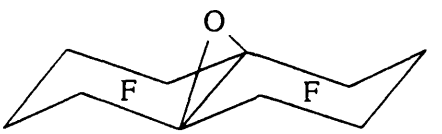

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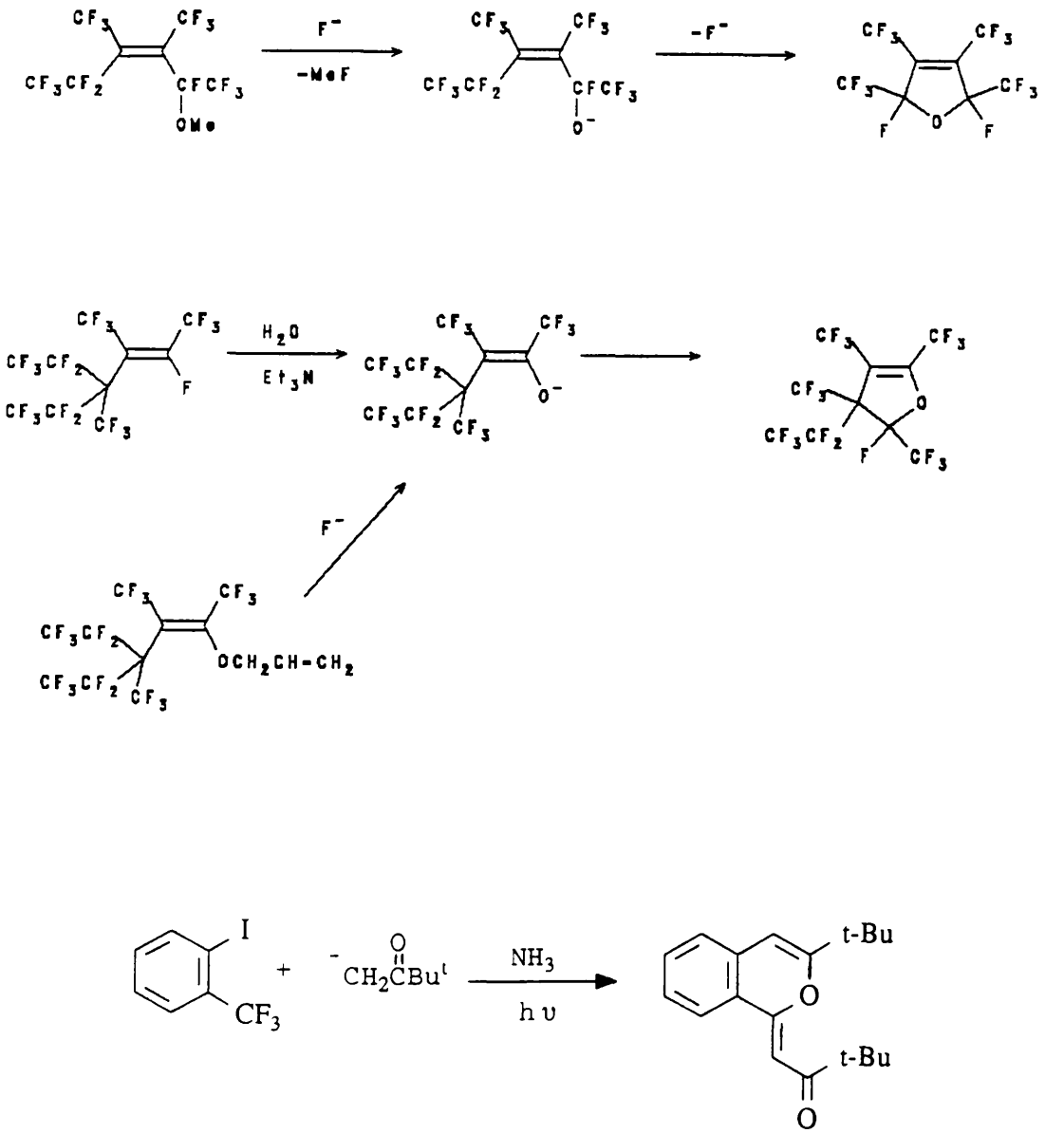
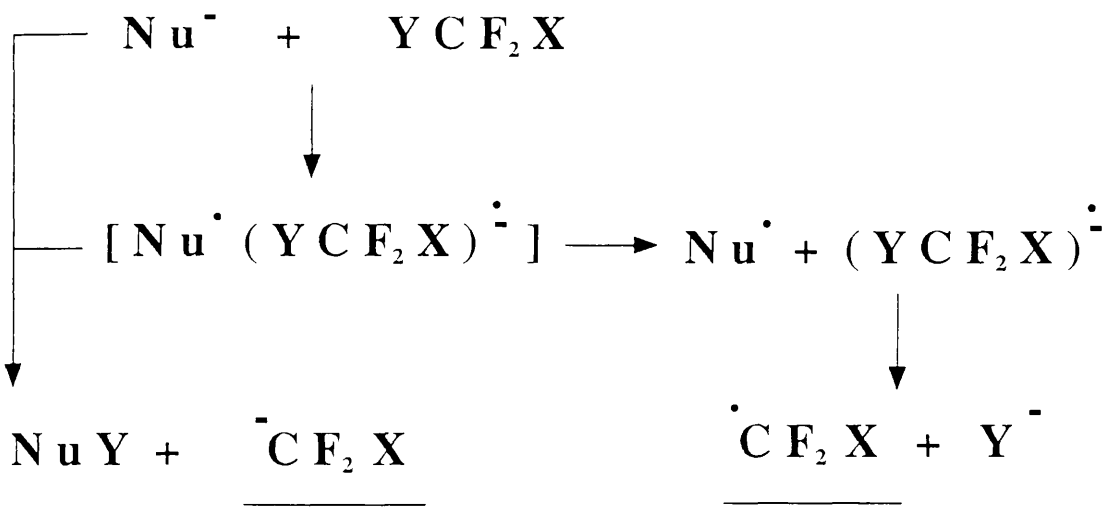


figure 18 : intramolecular $S_N2(C)$ & $S_{RN}1$

Halogenofluorocarbons (HFCs) (where 'halogeno' refers to bromine or chlorine) were considered inert or very unreactive until the 1970's, when halophilic attack by nucleophiles was established[316]. Iodocompounds are excluded since they are well-known reactive intermediates through both homolytic and hetereolytic bond cleavage in the presence of heat, light or nucleophiles[317]. It was known that chlorofluorocarbons could be destroyed by powerful nucleophiles[318], as could fluorocarbons in liquid ammonia/sodium amide[77]. Synthetic reactions of HFCs with many nucleophiles are now reported (e.g. P, S, Se, O, N and C based).[316,319,320] All published examples concerning chlorofluorocarbons (CFCs) involve methane and ethane systems, though a few other alkane systems are known for bromofluorocarbons. The mechanism of halophilic attack has been ascribed to both S_N2 and SR_N1 processes (Figure 19), sometimes occurring simultaneously. It is not yet clear what determines the choice of pathway and a common first step has been suggested[321]. In the case of thiophenoxide nucleophiles, the SR_N1 pathway appears correct with relatively small (and less reactive) molecules (e.g. CF_3Br, CF_3CF_2Br, CF_2Cl_2), and an anionic pathway (via carbenes with methanes and ethenes with ethanes) for larger ones, (e.g. CF_2Br_2, $BrCF_2CF_2Br$, $ClCF_2CFCl_2$). Indeed, the intermediate-sized compound $BrCF_2Cl$ reacts by both at once.[321]

All reactions with phenoxides[322] proceed by ionic intermediates. Equally, all reactions involving 1,2-halogeno substituted fluoroethanes react by the ionic route (Figure 20). CF_3CCl_3 also reacts in this way (for which fluoride elimination is now required) but a competing pathway exists under some conditions.[323] This is not an SR_N1 type, although a non-chain SET mechanism could not be discounted and evidence was presented for a proposed solvent-caged trapping of PhSCl by the relatively stable intermediate anion $CF_3CCl_2^-$. The reaction of Co^I 'supernucleophiles' with HFCs is also postulated to involve electron transfer[3]. In no case is halophilic attack thought to be at a fluorine centre[3].

$$Nu^- + YCF_2X \longrightarrow NuCF_2(X \text{ or } Y) + (Y \text{ or } X)^-$$



initiation of ionic or radical-anion chain mechanism (via possible common intermediate), then propagation:

IONIC CHAIN MECHANISM

$$\cdot CF_2X \longrightarrow CF_2{:} + X^-$$

$$Nu^- + CF_2{:} \longrightarrow NuCF_2^-$$

$$NuCF_2^- + XCF_2Y \longrightarrow NuCF_2Y + CF_2X^-$$

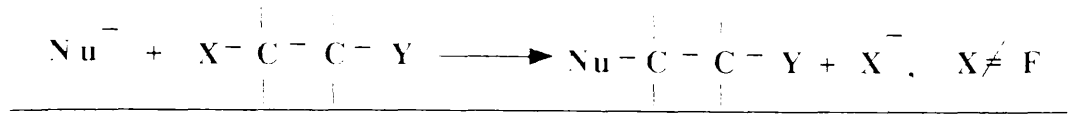
RADICAL-ANION CHAIN MECHANISM

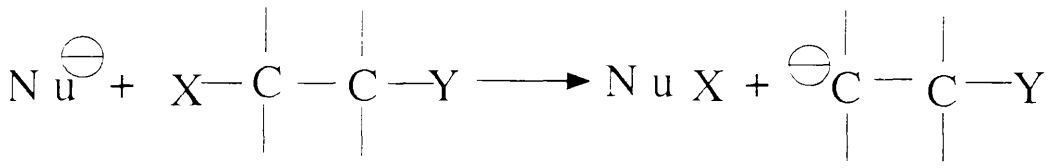
$$\cdot CF_2X + Nu^- \longrightarrow NuCF_2X^{\cdot -}$$

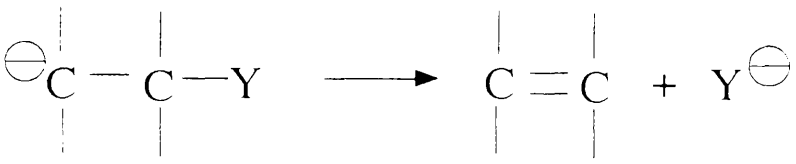
$$NuCF_2X^{\cdot -} + XCF_2Y \longrightarrow NuCF_2X + XCF_2Y^{\cdot -}$$

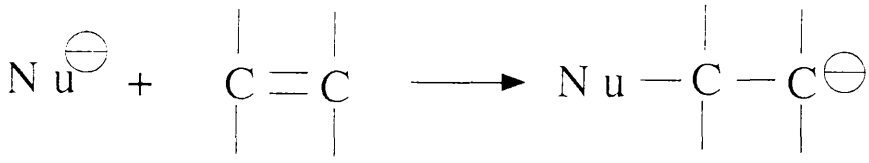
$$XCF_2Y^{\cdot -} \longrightarrow \cdot CF_2X + Y^-$$

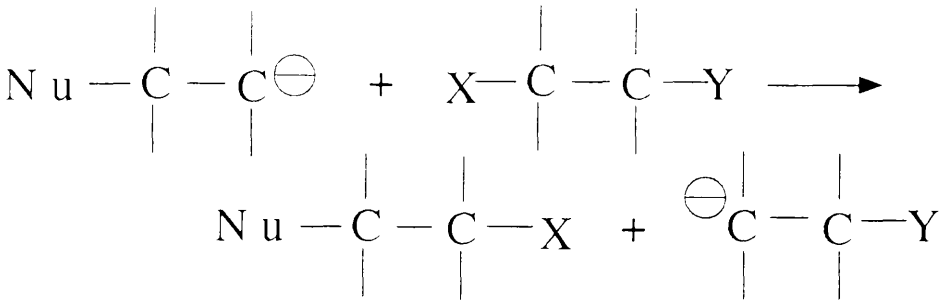
Figure 19 -Halophilic pathways



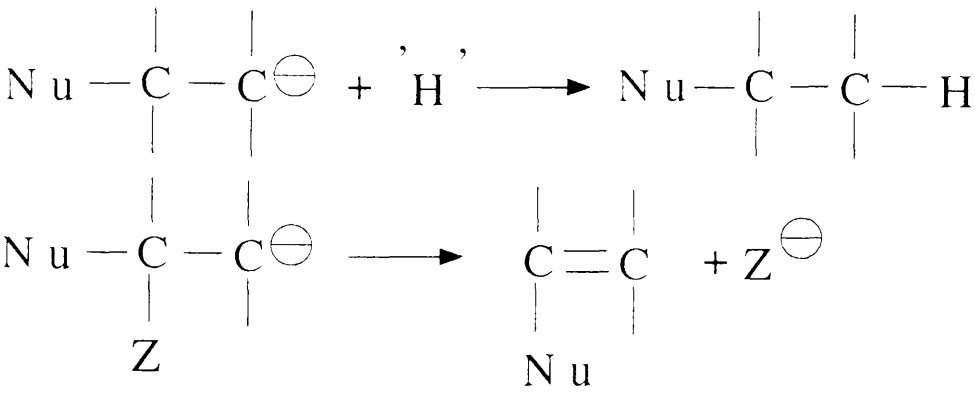








termination



CF_3CCl_3

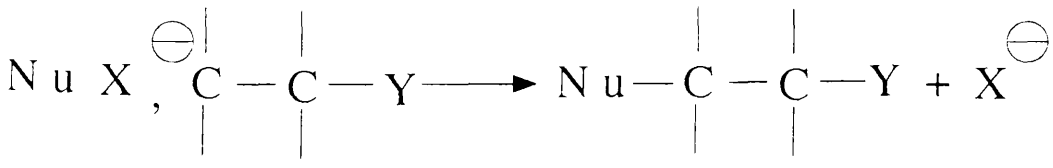


Figure 20 (adapted from ref.316)

Direct $S_N2(F)$ is known in a few cases[324]. The most common examples are the fluorination of nucleophiles by elemental fluorine. Fewer examples exist where fluorine is attached to other groups and none where the fluorine is attached to a carbon in a fluorocarbon or related system; N-fluoroperfluoromorpholine and N-fluoroperfluoropiperidine do deliver 'F^+' by $S_N2(F)$, even to a perfluorocarbanion.[325-327] Other 'F^+' sources are becoming more commonly used.[326]

An SET process is the more attractive pathway, either via a specific halophilic attack similar to the above HFC cases or through a more general approach into the fluorocarbon molecule.[328]

Although saturated fluorocarbons appear chemically impregnable, they have a potential Achilles heel in their great ability to capture electrons.[83] Analogous to SF_6, their electrical properties make them ideal inert atmospheres.[96] Branched and cyclic saturated fluorocarbons have even higher electron affinities than straight chain homologues. As the number of branches and rings or the size of molecule in a series of perfluoroalkanes increases, the electron attachment (measured by E.I. time of flight mass spectrometry) changes from a dissociative to an associative mechanism and the auto detachment lifetime of the parent radical anion is increased from 10^{-15}s to the order of 10^{-5}s.[329] Correspondingly, the electron affinity (EA) of fragment radicals and the lifetimes of fragment anions increase, whereas the simple one bond cleavage fragmentation of parent anion decreases. Molecular shape also contributes to anion lifetimes through effectiveness of energy dissipation. In the case of the cyclic alkane C_5F_{10}, fragmentation occurs only at higher energies, consistent with required breakage of a non-tertiary carbon fluorine bond, and is believed complex, leading to a neutral molecule with a double bond.[86]

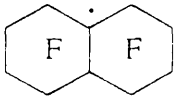
Perfluoromethylcyclohexane (4) has a high EA (1.06 $\pm$ 0.15 eV) very close to that of SF_6 (1.05 $\pm$ 0.1 eV) and like SF_6 the molecular anion did not participate in normal gas phase electron transfer equilibria.[87] Both also have similar negative ion mass spectra, consisting of the parent anion and a small peak at $[M - F]^-$. Entropy calculations, however, show that whereas SF_6 has a very different geometry to SF_6^-, this is not the case for $C_7F_{14}^-$ and C_7F_{14}.[330]

This reason was given to explain why destruction of the parent ion by positive ion recombination returned the parent molecule for C_7F_{14} but not for SF_6 (which gave an unknown product with no electron affinity). It cannot explain why, like SF_6, C_7F_{14} does not participate in the gas phase electron transfer equilibria. Liebman assumes no geometry change on electron attachment and has suggested that the captured electron may reside in a delocalised anti-bonding molecular orbital with perfluorocycloalkanes.[331]

Scherer has used chemical ionisation and found it to be more suitable for observing parent anions, with less fragmentation additionally, and applicable to many perfluorocompounds.[332]

With perfluorodecalin, no fluoride ion or much other fragmentation was seen and a very long-lived parent anion is formed. A very high EA, greater than that of C_6F_6, was indicated.[333] It is therefore reasonable to propose a small concentration of perfluorodecalin radical anion is able to exist in an equilibrium under the reaction conditions that lead to host formation.

HFC radical anions cleave to produce a halogen ion (not fluoride) and a radical[316,318,334]. Perfluorocarbon radicals are well-known intermediates from this reaction, e.g. CF_3Br^- -> $CF_3\cdot$ + Br^-, and others.[335] Some of these have surprising stabilities, e.g. formed in the radiolysis of perfluoroalkanes containing tertiary or quartnery carbons,[82] and when formed in the partial fluorination of perfluoroalkenes with elemental fluorine, or thermally or photochemically generated.[336] Scherer's radicals[336] are very notable, able to survive 100°C, to be produced in 88% concentration, or to last indefinitely in particular cases. The tertiary perfluorodecalin radical (140) is not persistent[6] and would be expected to oxidise a partner via SET and then expel fluoride ion from the resulting anion (141) to yield the 9,10-olefin (142).



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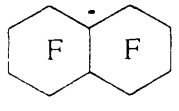

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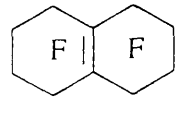


(142)

The anion (141) has been isolated and characterised, using the stable tris(dimethylamino)sulphonium (TAS) (143) salt-forming method of irreversible fluoride addition to perfluorolefins.[337]

Equally, the negative ion mass spectrometry findings suggest that although a small radical anion like CF_4^- fragments to form both F^- and CF_3^-, a larger perfluororadical anion is not likely to produce much fluoride[329a] and indeed with chemical ionisation of perfluorodecalin neither F^- nor $[M - F]^-$ was observed.

This suggests only complex fragmentations occur, [e.g. to give an olefin] and/or a second event is necessary to cause bond breakage of the very stable perfluorodecalin radical anion. Scherer has suggested that "a second electron transfer might be required to cause loss of fluoride ion", or that "the counter ion might turn out to play a role in fluoride loss".[333]

The presence of fluoride as a product (currently indistinguishable from further fluoride elimination) may support its formation during fragmentation, but there has not been a search for products resulting from radical fluorine loss. The two fluorines most likely to be expelled are those on the tertiary carbons, also resulting in formation of the (most stable) 9,10-alkene (142). Since the ratio of trans:cis isomers in unreacted substrate did not change after reaction of some perfluorodecalin, a common first step followed by step-wise loss of fluoride through a common planar intermediate is probable. Only tertiary perfluorocarbanions appear to be stable[337] and these show evidence for stabilisation by negative anionic hyperconjugation in which the 9,10-double bond could be favoured.[338]

In summary, each possible likely pathway, SET or other, leads to the key intermediate, an olefin almost certainly with the 9,10-double bond. The thioether (145) which arises directly from $S_N2(C)$, or after a possible (solvent caged) reaction of the anion with PhSF ($S_N2(F)$), or of the radical with PhS or PhS^- (after electron loss), will be attacked by further thiophenolate to give the olefin (142), via the anion or 1,2 elimination, with disulphide formation (see 1.3). This is shown in Figure 21. Further reaction of the intermediate olefin (142) is discussed later (see 1.3).

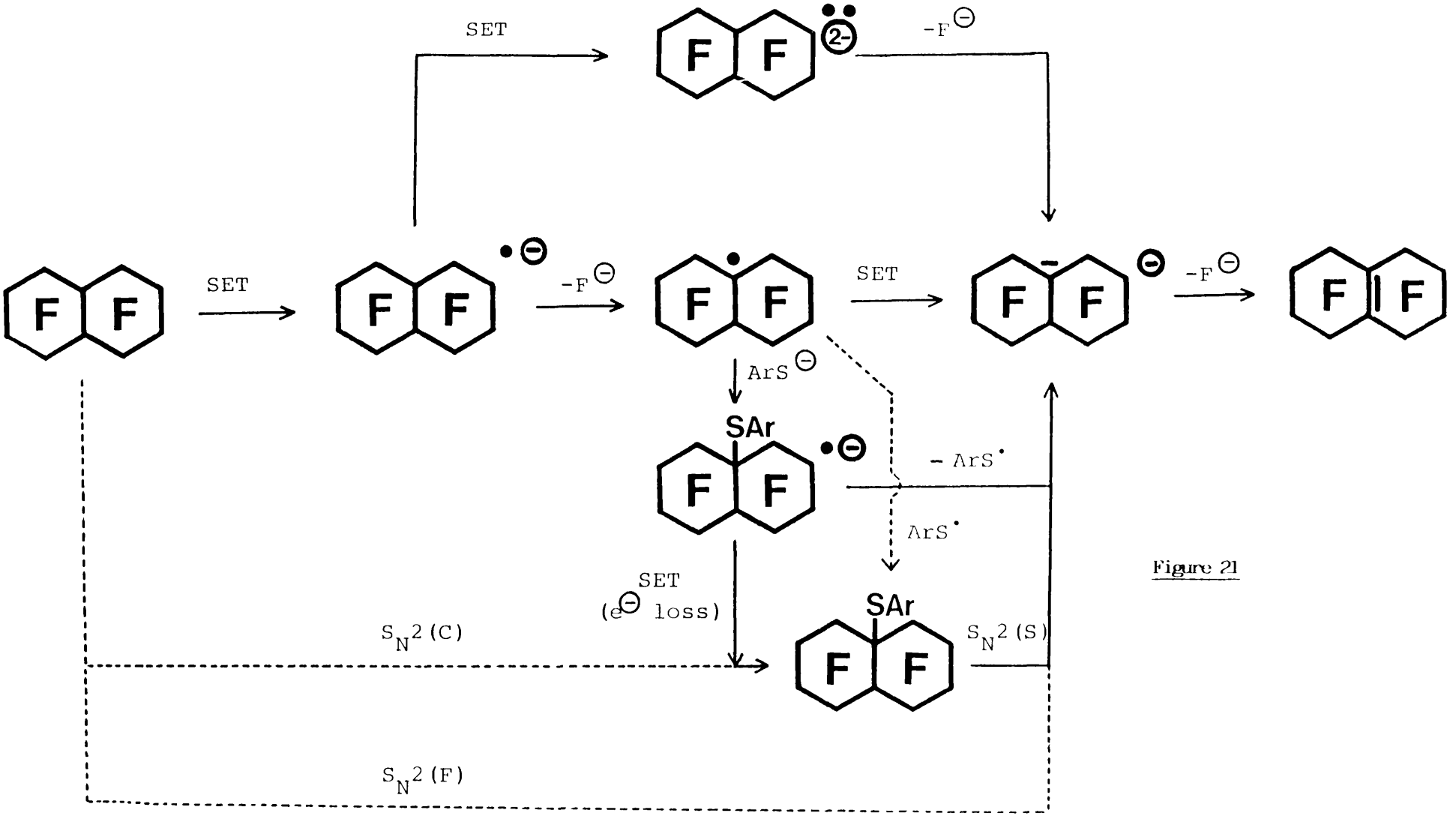


Figure 21

1.3. Perfluoro-olefins

Since no intermediate products are observed (by t.l.c.) in the course of the reaction, the further transformations must be much faster than the rate of olefin product. To test this, the reaction of perfluorocyclohexene (145), a model compound, was undertaken under analogous conditions at room temperature. This yielded 98% of the corresponding hexa-host hexakis(phenylthio)benzene (124) with immediate visible transformation of the perfluoroalkene (soluble in the system) to coloured product, comparable with the reaction rate of perfluorobenzene (146) under the same conditions. Again, substantial amounts of disulphide were formed and fluorine was eliminated as fluoride.

This result is new but can be explained by extrapolating from previous work.

The nucleophilic substitution of cyclic perfluoroalkenes takes place by an addition-elimination sequence in preference to electrophilic attack on the intermediate anion (see Introduction, section 1.3). In six-membered rings, displacement of an allylic fluorine competes with loss of fluoride from vinylic centre of attack, especially for a second nucleophile.[94] Reactions involving perfluoro-olefins and nucleophiles very often lead to polysubstituted products even with only equimolar amounts, although these are usually not identified and are ignored.[339] In the poly-addition of alkoxides acetal formation[340] may take place, and with amines, imine formation can lead to fluoride displacement.[341,340]

No thioacetals have been isolated but recent findings indicate a redox reaction (involving a disulphide-forming elimination from perfluorothioethers) leads to carbanions[342] which may then eliminate 1,4 to produce new unsaturation. Under conditions of excess thiophenoxide, significant polysubstitution has been observed in the reaction with perfluoropropene dimers arising from further additions to the reduced dienes formed in this way.[343] Similar reductions are possible electrochemically,[344] and perhaps with fluoride ion.[312,345]

Hence, the elimination of all fluorines from perfluorocyclohexene to give the hexa-substituted benzene and disulphide by-product, whilst unprecedented in extent of reaction, is entirely consistent with known chemistry, especially under the forcing conditions of excess (sulphur) nucleophile and an extremely good dipolar aprotic solvent. Further elimination of fluoride is now required only from CF_2 and not CF_3 groups, and so this is expected to be more facile[3] than in previous cases, and as substitution increases, intermediate carbanions should be more charge stabilised and products increasingly more soluble. Progressive reduction and substitution of the system presumably take place at similar rates.

The proposed 9,10-olefin (142) intermediate from perfluorodecalin (1) is relatively less reactive than perfluorocyclohexene (145) (see Introduction, section 1.3), but is still expected to be very reactive under these conditions (Figure 22). Indeed, in the reaction of (142) with methoxide in methanol, or with amines in ammonia, only polysubstituted products were isolated and even mild conditions with molar equivalents returned starting material in preference to monosubstitution.[345] This is consistent with the formation of more reactive double bonds after the initial addition-elimination.

In the reaction of (142) with methoxide, only three of the seven similar products formed were identified (Figure 23) corresponding to the expected initial bi- and tri- substituted olefins (reductions not being possible). Other products may involve acetal or ketone formation. Importantly, no products from protonation of intermediate carbanions were detected, and a higher degree of fluoride elimination from allylic positions was noted than for the cyclohexene system.

Under the conditions of excess thiophenolate in DMEU at room temperature, a sample of the intermediate olefin (142), 91% in strength by GC, clearly yielded octakis(phenylthio)naphthalene (131) with an immediate transformation. The saturated impurities, insoluble in the reaction, were not observed to react over 3 days.

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.

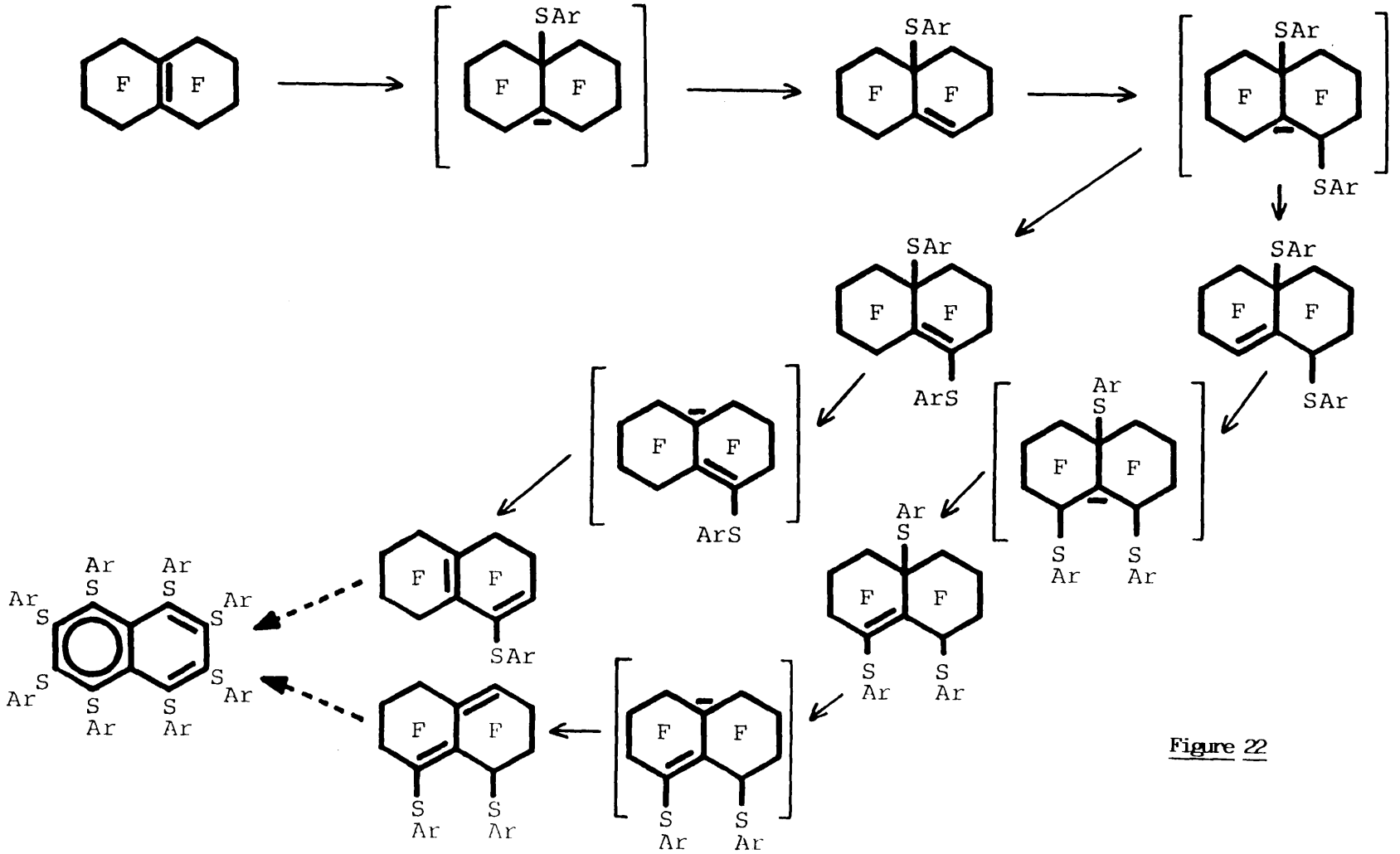


Figure 22

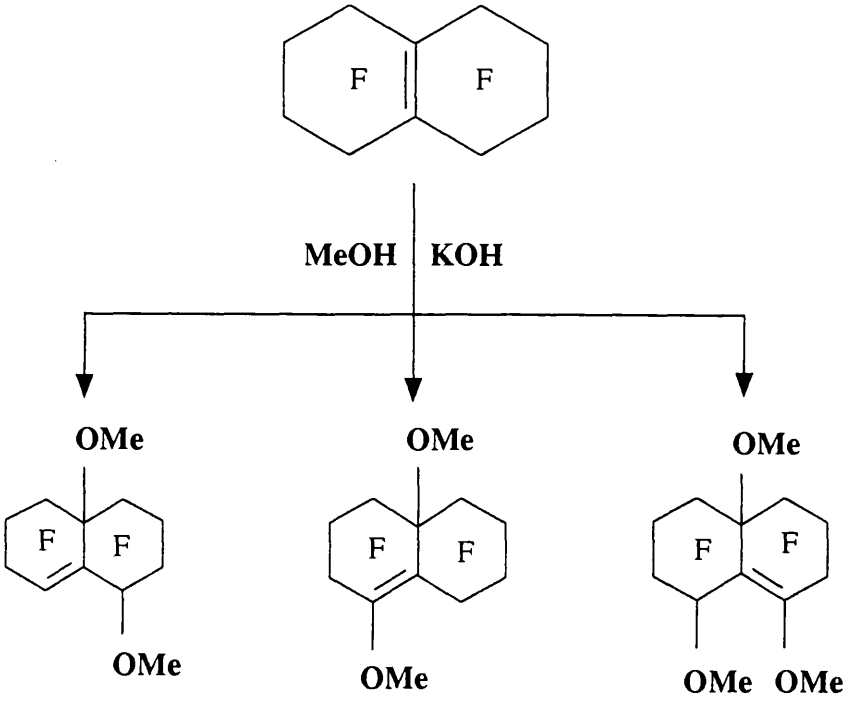


Figure 23

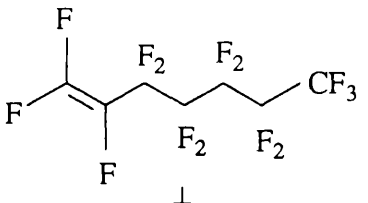
The yield of product after chromatography was 99%, based on the initial weight of alkene added, and no intermediates were observed by t.l.c. Again, the perfluoroalkene had reacted in a manner previously expected for a perfluoroaromatic substrate, with, additionally, production of large amounts of diphenyl disulphide.

Extension of the reaction to a linear substrate, perfluorohept-1-ene (147), gave a mixture of products at room temperature. Without separation, however, mass spectral analysis showed that the highest weight products corresponded to the expected structure for the fully-reacted substrate, $C_6(SAr)_7CF_3$; (148a) m/e 904 Ar= phenyl; (148b) m/e 1002 Ar= p-tolyl; and with further commensurate 'leg' losses. g.l.c. - m.s. on the mixture obtained using p-tolythiolate highlighted the lower weight products : m/e 898, 775, 652....; m/e 794,671, 548.....; m/e 832, 709, 586; m/e 728, 605.

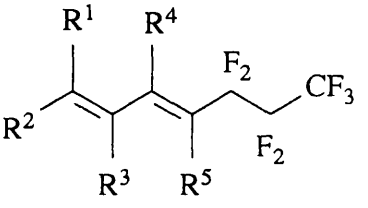
These series, marked by successive leg losses (123 a.m.u.), correspond to cases of incomplete substitution (heptatrienes) and incomplete reduction (heptadienes), respectively displayed in structures (149b)-(152b) (Figure 24) where it is assumed reaction occurs progressively from the original double bond along the chain towards the terminal trifluoromethyl group; a number of different pathways lead to the same products.

When thiophenolate was used, the corresponding structures (149a) (m/e 814), (150a) (m/e 724) as well as less substituted heptatrienes (m/e 634, m/e 544) and (151a) (m/e 762), (152a) (m/e 672), and also a more substituted heptadiene (m/e 852), were observed. This additional peak may correspond to an intermediate between heptadiene and heptratiene structures, e.g. (153). Another extra peak in this area, m/e 832, has not been identified.

Incomplete reduction of the linear alkene systems is in keeping with the greater preference of allylic substitution in cyclic systems, and the mixture of products is in keeping with that observed by Ishikawa and Maruta (Figure 25).[343a]

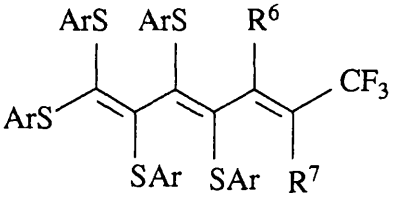


(147)



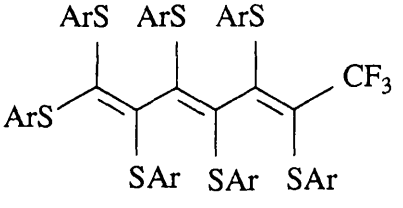
(152b), R^n = *p*-CH_3Ph , except R^1 or R^2 . . . or R^5 = F ; m/e 728

(151b), R^n = *p*-CH_3Ph ; m/e 832

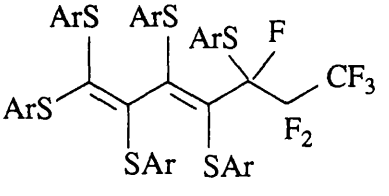


(150b), Ar = *p*-CH_3Ph ; R^6 = R^7 = F ; m/e 794

(149b), Ar = *p*-CH_3Ph ; R^6 , R^7 = F , *p*-CH_3Ph ; m/e 898



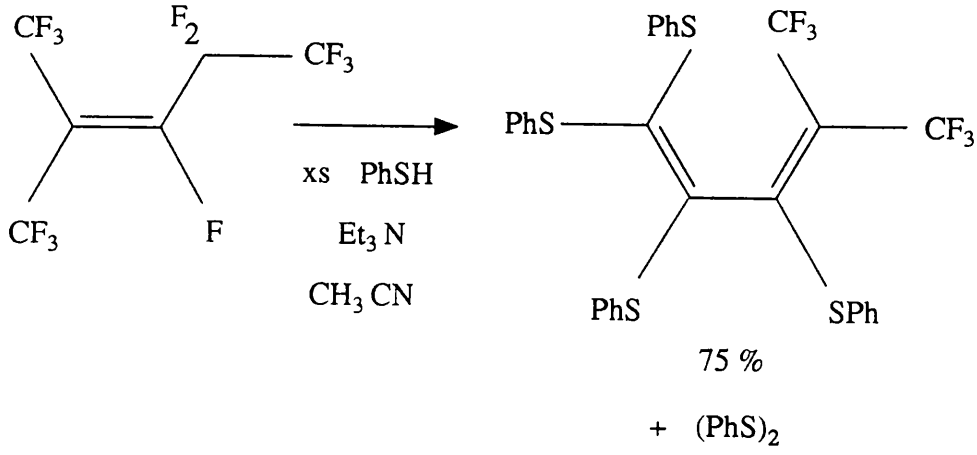
(148b), Ar = *p*-CH_3Ph ; m/e 1002



(153), Ar = Ph ; m/e 852

Figure 24

Figure 25



75 %

+ $(PhS)_2$

1.4. Perfluorodecalin - quality and analysis

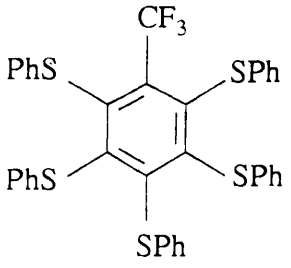
A small amount of unsaturated substrate in the perfluorodecalin could be responsible for some octa-host formation (although a yield of 65% requires a genuine reactivity of perfluoroalkane even if propagated by intermediates involving the presence of alkene in the starting material) and so it was decided to investigate spectroscopically what level, if any, existed. To this end also, the reaction was repeated using medical-grade decalin, which is necessarily free of the highly toxic alkene contaminants. These reactions proceeded as the previous sample of perfluorodecalin had. This was itself analysed by ^{1}H and ^{13}C n.m.r., and raman spectroscopy. At full expansions, no signals from alkene or hydrogen-containing material were observed. The material was also returned to its manufacturers and re-analysed, proving to be at 95.6% strength and conforming to quality specification. The balance is due to bond cleavages and reorganisations during CoF_3 fluorination and 1% piperdine fluoride, not to any unsaturated impurities.[346]

1.5. Saturated fluorocarbons

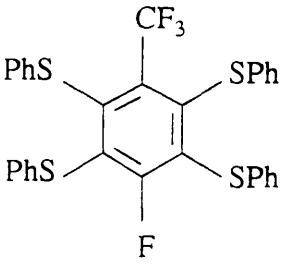
Other saturated fluorocarbons were investigated. The saturated, single, unsubstituted ring-system perfluorocyclohexane (8) did not react under analogous reaction conditions even when heated. Hexakis(phenylthio)benzene (124) was isolated in a 1% yield but the substrate contained ca. 2% perfluorocyclohexene (145) impurity and additionally the hexa-host was formed immediately even at room temperature. Equally, the saturated linear unbranched system perfluoro-n-hexane (154) did not react although it was found that the substrate was not observable after attempted reaction over relevant time periods (to the temperature) and some disulphide was formed. This may be the result of relative solubilities and oxygen content of the substrate, as no significant fluoride level was detected.

With the branched ring-system perfluoromethylcyclohexane (4), colouration due to reaction developed over many weeks at 50°C. The product finally isolated corresponded to only a small yield, ca. 1%, of substituted substrate. Mass spectrometry of the product, a mixture of similar materials by t.l.c., indicated the presence of the expected product m/e 686, pentakis(phenylthio)-trifluoromethylbenzene (155), and a greater detection at m/e 634, presumably tetrakis(phenylthio)di(trifluoromethyl)-cyclopentadiene from perfluorodimethylpentane (a likely contaminant caused by rearrangement during CoF_3 fluorination). The highest peak observed, though very minor, was at m/e 794. This peak is related to m/e 686 by 108amu, cf. PhS 109amu, and is of unidentified structure.

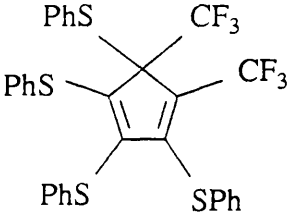
After further chromatographic purification, the main red product fraction showed peaks potentially belonging to three products; m/e 686 (155) and m/e 596, tetrakis(phenylthio)fluorotrifluoro-methylbenzene (156), the incompletely substituted product, were two. The largest peak, m/e 524 (and two large peaks for sequential leg loss), was unidentified ($C_5(CF_3)_2(SPh)_3$ = 525 amu). ^{19}F n.m.r. did indicate the presence of a number of different fluorine nuclei.



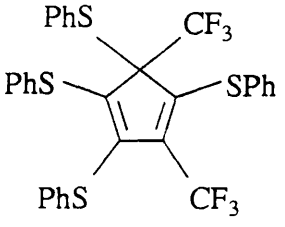
(155)



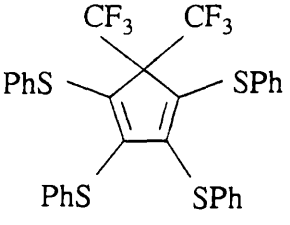
(156)



(157a)



(157b)



(158)

The reactivity involved in the perfluoromethylcyclohexane (4) case appears to be that of saturated systems because of the slow development of colour, although this is not conclusive. If only saturated systems are involved, then the dimethylcyclopentane perfluoro-substrate (as an assumed impurity) is much more reactive than the methylcyclohexane system, and this latter one is either unreactive or much less reactive than perfluorodecalin.

The lack of reactivity shown by perfluorohexane (154) and perfluorocyclohexane (8), and the apparent increase in reactivity in the sequence perfluoromethylcyclohexane (4), perfluorodimethyl-cyclopentane, perfluorodecalin (1) is consistent with the requirement for a tertiary carbon centre and a minimum electron affinity. Two adjacent tertiary carbons may be necessary.

A tertiary carbon in a cyclic system, rather than in a highly branched alicyclic, may perhaps be a necessity to achieve an effective electron affinity. The absence of an α-fluorine (a destabilising influence) at a potential radical or carbanion centre, and the relative bond strength (tertiary C-F < secondary C-F) favour reactivity residing preferentially at tertiary rather than secondary carbon centres. The requirement for a high enough electron affinity (compare perfluoromethylcyclohexane(4) to perfluorodecalin (1) reactivity) may indicate an electron transfer mechanism as more likely, rather than $S_N2(F)$ where the key step of carbon-fluorine bond breaking is influenced less directly by the electron affinity (of the leaving group). In the reaction where a perfluorodimethylcyclopentane is assumed to have been transformed, (157a,b) are likely products, from the 1,2- and 1,3- dimethyl isomers respectively.

Should (158) be present, arising from the 1,1-dimethyl substrate, there is clearly the situation of a sufficiently high electron affinity occurring without a tertiary centre being present. Under an SET mechanism further reaction may then be possible by fragmentation of the relatively weak spiro carbon-carbon bonds (leading to different types of products), whereas $S_N2(F)$ may be impossible.

One system not containing tertiary carbons but with an electron affinity that may be suitable for reaction is PTFE. If the important structural feature pertaining to reactivity is an 'ortho' relationship of adjacent tertiary centres, then the suggested mechanisms do not fully explain the reaction. It is assumed that after bond breakage by whatever mechanism, then expulsion of neighbouring β-fluorine is an easy step, not dependant on having a tertiary fluorine available. If the two adjacent centres were to be involved in a bond-breaking, rate determining step, then perhaps transfer of two electrons is required, producing two fluoride ions and an alkene after fragmentation. PTFE is known to produce alkenes by depolymerising under electron bombardment and it has no tertiary centres (see Introduction, section 1.3).

1.6. Perfluoropolymers

The reaction with poly(tetrafluoroethane) was tried, using a chromatographic packing as a convenient form with a high surface area. Although no fluoride ion formation was detected, the material was physically changed from granules to a single transparent film under the conditions of heating in DMEU or DMF with or without thiolate. One significant difference was detected in the presence of nucleophile:- under electron microscopy the surface was shown to be rippled in the presence of nucleophile but blank (smooth) otherwise.

Under examination by surface reflectance absorbance i.r. spectroscopy, material produced by heating only was similar to the starting material. The material exposed to thiolate, however, had absorbances at ν 3018.5, 3057, 3073, and 3084 $cm.^{-1}$ Two explanations for these observations are reaction of polymer with thiolate and absorbance of thiolate by polymer. Reaction would most likely be at polymer ends, however, particularly where unsaturated (from disproportionation in polymerisation). The range of other non C-C and C-F bond absorbances indicates the large amount of other materials present in the sample (plasticisers and other additives presumably) and their possible identities and roles have not been examined.

Using HMPA as a solvent and additionally [2,2,1] cryptand (26) as a promoter did not effect any more reactivity as observed by fluoride ion and polymer weight measurements. The use of polysulphide nucleophiles (Na_2S_2, Na_2S_4) was also unsuccessful.

FEP (fluorinated ethlyene proplyene) polymer in the form of tubing shavings (very low surface area) did not appear to show any effects at all in the reaction. The tertiary centres in this system do make it a more likely substrate (in the correct physical form) to react than PTFE.

1.7. Modification of Reactivity

The role of S.E.T. is central under the proposed mechanism. The two possible functions of the thiolate as a nucleophile and an electron source could be separated, and reactivity enhanced with a better electron source if a discrete SET step is occurring.

Electron source

Additions of sodium metal to the reaction increased the yield of octakis(m-tolylthio)naphthalene to 39% from 27% and to 46% from 14% when performed against an identical standard preparation, under 'cold' and 'hot' conditions respectively. Qualitatively, the reaction with sodium thiophenolate was also accelerated under ambient conditions. The results are not comprehensive and at present serve only to indicate a trend.

This rate and yield increase could be resulting from a drying effect by the sodium of the solvent, thus activating it. A reaction using sodium-dried solvent was found to be ineffective in promoting the reaction. The addition of iodide ions to the reaction also produced no enhancement. Other effective additives envisaged include aromatic anions, (e.g. naphthaldeide), electron-rich single electron oxidisers, (e.g. Co^{I} complexes), or ultimately 'naked' electrons such as using a cathode.

Conversely, under the SET mechanism proposals, an electron scavenger may adversely affect the reaction. With 10% nitrobenzene as a co-solvent, no reaction was observed at room temperature, and <1% at the elevated temperature under the conditions of the standard perfluorodecalin reactions with sodium thiophenolate. In the 'hot' reaction, however, with 10% toluene as a co-solvent, only a small decrease in yield against a standard was observed (from 14% to 10%). The nitrobenzene immediately produced a deep black charge transfer colour in the presence of thiolate ion.

These findings support the SET mechanism in the reaction of perfluorodecalin and indicate possible areas of versatility in development of the reaction. Sodium/HMPA has been shown to reduce similar products from thioethers to thiols.[347]

Nucleophile modification

Two other classes of nucleophile were tried in the reaction with perfluorodecalin :- sodium phenylselenide and sodium p-methoxyphenolate. Under the ambient conditions and in the dark, the selenide gave two products, the octa-host and the product from cleavage of 2 'legs', $C_{10}(PhSe)_6H_2$ (159), in a total yield of ca. 100%. Under the ambient conditions, the phenolate did not react, but, at 90°C in a sealed tube for 8 weeks, significant reaction took place as indicated by the fluoride ion measured and the ^{19}F n.m.r. spectrum of the product. t.l.c. indicated the presence of many individual products and ^{19}F n.m.r. indicated different fluorine sites. Structures of the types encountered by Tatlow et al, in the reaction of the perfluorodecalene (142) are to be expected, including the numerous unidentified products (Figure 23). Although acetal formation is likely in the reaction, the reduction of the bicylic ring is not directly possible in the manner available to the other chalcogen nucleophiles. Formation of ketones is a possible alternative. Cleavage of legs by a further SET mechanism, however, to give an anion which can then eliminate fluoride to leave unsaturation, may be possible in such an active system; similar crown ether promoted cleavage has been observed.[348]

Although the chemical shifts of fluorine nuclei are more varied and less predictable than hydrogen nuclei in the equivalent fluorocarbons to their hydrocarbon compounds respectively, and derivatives, the fluorine spectrum obtained from the 'hot' reaction is notable for a number of features. These are, first that the majority of peaks are in the same region as perfluorodecalin (1)[349a] but at different shifts δ (-111 - 141). Second, no peak is observed in the region of the tertiary fluorines in perfluorodecalin δ (-189).

Third, some peaks are also seen at δ (-80) and δ (-150) corresponding to possible allyl and vinyl positions respectively.[349b] This suggests favoured initial reaction at the tertiary sites followed by some limited further reaction.

1.8. Application to inclusion compounds and other areas

The new reactivity described can be further used in a number of ways. The array of bulky substituents around a central fixture has proved a useful approach to new clathrates. The simplest approach to such molecules relies on multiple nucleophilic substitution. Perfluoroaromatic compounds are ideal starting materials for this approach, as successfully demonstrated with the commercially available perfluorobenzene, -pyridine and -naphthalene substrates. Synthesis of larger perfluoroaromatics is more difficult. Specialist technology is required and yields are low, making their synthesis non-trivial in the laboratory and unattractive commercially. Routes to perfluoro (and perhalo) aromatics by other means are not often better.

In contrast, perfluorosaturates and olefins are readily available commercially and more accessible by a wider variety of means. Utilising such precursors should open many new systems to exploration for new clathrates of the type described (for example see section 2.8) and may even be a cheaper alternative to some already accessible.

The practical benefits gained from perfluorinated and polyfluorinated materials are manifest in their wide and expanding use in simple and sophisticated technological applications. In particular, PTFE is a highly successful material, used for its chemical and physical resistance. Nevertheless, these very properties render PTFE limited in use because it is difficult to incorporate both chemically, having no functionablity, and physically, since it is nearly unworkable. Whereas with smaller systems exhaustive fluorination can be achieved while leaving intact much functionality to produce directly fluorocarbon derivatives, this method cannot be easily applied to polymers. Lagow and others have shown how polymers of varied types can be fluorinated directly as small particles but these technologies are extremely difficult to operate and give very small through-puts.

Additionally, such products, although of greatly enhanced physical properties, are not identical in structure to parent polymer with considerable cross-linking being one often unwanted feature. At present, introduction of functionality into a pre-formed perfluoropolymer is not an attractive proposition.

The new reactivity described may be suitable for development for the controlled modification of preformed perfluoropolymers to give valuable site reactivity, (e.g. for adhesion properties, polymer reagents, chromatography supports and membrane materials), without sacrificing the benefits of a perfluoro-backbone.

Reactivity in fluorocarbons is almost the antithesis of requirements for current applications, but new chemicals with mixed properties might now be available by use of such reactivity, once it is fully understood and controlled. Synthetic utility may also be found in non-clathrate chemistry, particularly in protecting group methodology. The reactions described are certainly the first ever useful 'test-tube' reactions of saturated fluorocarbons, and as such open a new chapter in fluorocarbon chemistry contrary to all expectations.

The discoveries ask new questions of our understanding of chemical reactivity[350], and as such could have relevance in other non-related areas. One area of obvious importance in related systems is the destruction of halofluorocarbons[351], possibly by a similar reaction.

2. Extension of the 'Hexa-host' Concept

2.1 Octa-hosts : octakis(arylthio)naphthalenes

The first octa-hosts synthesised by MacNicol and co-workers were (series parent member) octakis(phenylthio)naphthalene (131) and octakis(β-Naphthylthio)naphthalene (132). These exhibited some inclusion properties and indicated interesting structural features in the solid state.[308] Following this, three isomeric 'tolylthio' octa-hosts were synthesised: octakis(o-tolylthio)-naphthalene (160), octakis(m-tolylthio)naphthalene (134) and octakis(p-tolylthio)naphthalene (161). These all showed some inclusion properties, of which (134) appeared the most general host.

Further investigation of some of these inclusion properties with a particular view to exploring the structure of the adducts of (134) was undertaken.

Octakis(m-tolylthio)naphthalene (134) was synthesised from octafluoronaphthalene (2). It was found that an extended reaction time (5 days) caused a poorer quality of product to be formed, presumably by leg cleavages with disulphide formation, and a lower yield. The reaction appeared to be complete within a few hours. The known dioxan clathrate and the empty structure obtained on recrystallisation from toluene were investigated by single-crystal X-ray diffraction (section 2.6).

It was already known that octakis(m-tolylthio)naphthalene (134) was a host for nitromethane (1.0), acetonitrile (0.9), dioxan (0.9) and benzene (0.5), but not for toluene, anisole, oxepan or acetone. The maximum guest occupancy per mole host was one mole, and some variance ($\pm$ 0.1) was observed. The host was recrystallised from other solvents to examine further the nature of the cavity size since for this host the structure of non-solvated material gave no visible sign of depending on the presence of a guest. Toluene was used as a co-solvent where host solubility prevented direct recrystallisation.

The level of acetonitrile included decreased as toluene co-solvent used increased. Thus at 50/50 and 75/25 v/v toluene-acetonitrile only 0.7 and 0.4 moles acetonitrile per mole (134) were included. The absence of a scavenging effect is in agreement with the forming crystal structure being independent of the solution composition. From a saturated toluene solution methanol was included at ca. 0.7 moles per mole.

Chloroform and methylene chloride were included using neat solvents at 1.0 moles per mole. Small molecules appear to be easily incorporated into the host structure, and lost only under forcing conditions or over a long time. The acetonitrile clathrates lost 10-50% of the solvent over 60 hours at 0.1mm Hg. The acetonitrile clathrate at maximum occupancy had lost almost all its guest after 1 year at atmospheric pressure, while the nitromethane clathrate was reduced to 0.15 mole per mole over the same period. Such results, although not indicative of full guest retention, and, more importantly, the X-ray crystal structures, indicated that small gases may also be held by this host. Methane gas was used to saturate a hot solution of toluene containing octakis-(m-tolylthio)naphthalene (134) and then the solution cooled. Crystals obtained from this experiment were placed in an n.m.r. tube with $CDCl_3$ and dissolved in situ by gentle heating. A small peak was observed at δ0.3 that persisted until all the crystals were dissolved and for a time thereafter, eventually disappearing. The same peak was observed in $CDCl_3$ saturated directly with methane gas. After three months, crystals from this experiment still displayed the same effect. The slow release of very small amounts of gases or other materials from crystals has technological applications.

Larger guests similar in size to benzene and toluene were tried. Furan (0.5) and THF (0.85) as well as piperidine (0.95) were included. s-Trioxane was included (0.7) from a saturated toluene solution. No selectivity was shown between dioxan and s-trioxane. In the series cyclohexane, cycloheptane, cyclo-octane inclusion diminished from 0.3 to 0.2 to 0.12 moles per mole respectively. Pyridine was not included.

Surprisingly, inclusion was found with m-xylene (0.75), mesitylene (0.35) and p-chlorotoluene (ca. 1). Ethylbenzene was not included. Examination of the unit cell dimensions of the mesitylene inclusion compound found little difference to those of the unsolvated host. The nature of the inclusion of these toluene-like guests is not known.

Octakis(o-tolylthio)naphthalene (160) also includes guests. New results, such as toluene inclusion (1:2) and ethyl acetate as not being included, show how these vary from the m-tolyl isomer (134) and that both inclusion and non-solvate structures may exist. Crystallisation from N-methylformamide at room temperature also gave inclusion of 1:2, but at lower temperature, 0-5°C, the inclusion was not always found. Conversely, inclusion of n-hexane, room temperature ca. 1:2 increased to ca. 1:6 at lower temperature. From a structural viewpoint this material is as interesting a subject as the m-tolyl isomer. Single crystal X-ray diffraction quality material could not, however, be achieved despite extensive efforts with the 1:2 dioxan clathrate. In contrast, good adduct crystals of octakis(p-tolylthio)naphthalene (161) with dioxan (1:2) were obtained.

Molecular structural change, even to isomers, normally precludes retention of clathrate properties, unless, as in this case, there is a good underlying design feature. However within the observed inclusion m-substitution in the octa-hosts appeared very favourable, especially since, as well as forming a good host with the m-tolylthio- leg, the non-solvate structure had a stable form with cavities (section 2.6).

Substitution proved useful with hexa-hosts and aryloxy octa-hosts (section 2.3), and the p-tolylthio- leg also led to inclusion. Ortho substitution is likely to be less favoured, especially for large groups, due to steric crowding. Further changes were attempted on these grounds.

Models indicated that a m-alkoxy or m-hydroxy substituent would give a potentially good binding site with the octa-host used in a multimolecular or unimolecular fashion. After synthesis of octakis(m-methoxyphenylthio)naphthalene (135) it was shown that the host included some guests. Methanol and Acetone were co-included from binary solvent mixtures at ca. 1 mole guest total, methanol 0.5 moles, Acetone 0.3 - 0.5 moles, but not from neat solvent. Methanol was included selectively from a mixture with cyclohexanone. Isopropanol was included from neat (0.5 moles), but not larger alcohols.

More impurities, however, were generated in its synthesis than with the tolylthio-isomers, and these had to be removed by repeated chromatography and recrystallisation. They were initially thought to be from incomplete reaction, or in situ demethylation, or leg displacement. Following isolation of the two main impurities, which were more orange than the red product (135), mass spectrometry showed nearly identical mass spectrum to (135), despite clean differentiation by t.l.c.; however, contamination of the samples was not fully verified on the scale undertaken. Octakis- (p-methoxyphenylthio)naphthalene (162) did not show inclusion on recrystallisation from dioxan, chloroform, toluene, methanol or acetone.

At this point synthesis of the potentially favourable leg 3,5-dimethoxythiophenol from the corresponding phenol was undertaken - on scale-up from a 0.5g to 25g preparation the reaction failed.[352]

Octakis(p-chlorophenylthio)naphthalene (163) synthesis was undertaken and the product had analysis and mass-spectrum in accord with expected values. It was, however, so high melting and insoluble that it could not be crystallised, except in small amount from dioxan.

De-methylation with boron tribromide[353] of octakis(m-methoxyphenylthio)naphthalene (135), containing some product impurities, gave a complementary product mix, which contained no methyl groups. This product was soluble in dilute sodium and potassium hydroxide and these solutions had different colours (yellow-orange and orange-red respectively) at similar concentrations. There may therefore be a preferentially binding effect.

2.2 Octa-hosts : octakis(alkylthio)naphthalenes

Octakis(alkylthio)naphthalenes have been investigated for liquid crystal properties ($C_{10}S_8R_8$: R = C_5H_{11}, $C_{12}H_{25}$, $C_{16}H_{33}$) without any inclusion being reported.[306b] The use of a cycloalkyl group should provide a better solid-state structural basis for inclusion. Octakis- (cyclohexylthio)naphthalene (164) was prepared as a free host on crystallisation from an n-hexane and toluene mixture. Benzene, dioxan and cyclohexane were observed on isolation to be present at variable low levels (0.1-0.25) moles of solvent per mole host and were slow to be removed in vacuo; these do not however appear to be fully crystalline adducts. In contrast, the chlorinated solvents methylene chloride (2 moles), 1,1,2,2-tetrachloroethane (4 moles), 1,4-dichlorobutane (4 moles) and 1,1,1-trichloroethane (1 mole) were all retained on recrystallisation. The quoted (approximate) guest ratio is determined by ^1H n.m.r. and accurate weight loss from a top-pan balance - these clathrates decomposed immediately on isolation in air, the crystals, initially highly crystalline, visibly crumbling to powder. The unsolvated crystals were stable in air and single crystal X-ray diffraction was used to determine the structure (see section 2.6).

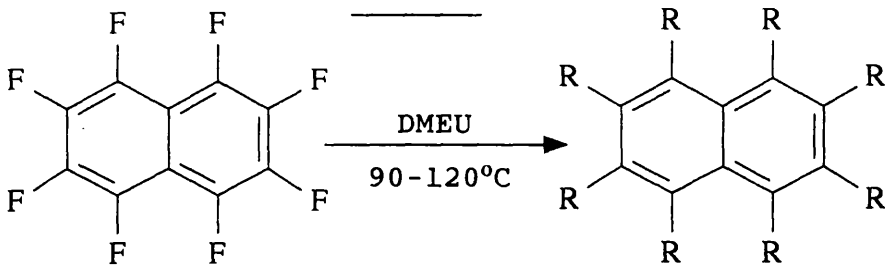
2.3 Octa-hosts : octakis(aryloxy)naphthalenes

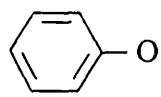
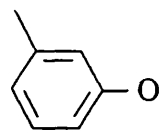
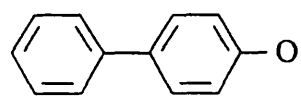
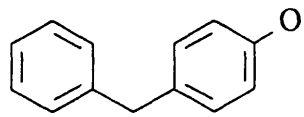
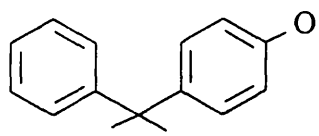
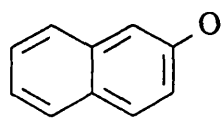
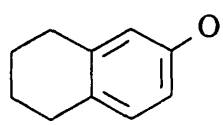
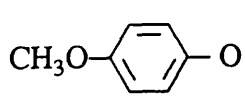
Preparation and identification

The oxygen analogues of the octakis(arylthio)naphthalene octa-host family were synthesised by heating a 24-32 mole equivalence of the sodium aryloxylate salt with octafluoronaphthalene at 90-120°C in DMEU, in a sealed tube, for several weeks (Table 2). The conditions are not optimised; yields of crude product in the range 30-91% were obtained. Products often contained impurities such as phenols and break-down by-products, commonly removed by trituration with ether or ethanol and then recrystallisation. Octakis-(aryloxy)naphthalenes were relatively insoluble in toluene and other solvents and initial isolation by precipitation from drowning out with water was usually preferred to an extraction process. Elemental analysis was generally poor but mass spectrometry and ^{13}C n.m.r. provided reliable identification. Analysis of stable clathrates when stoichiometric or host purified by inclusion gave better analysis. Mass spectrometry usually identified the parent peak, and partial and whole leg eliminations sequentially, although in some cases FAB technique was required. No peaks for the heptasubstituted compounds were observed. ^{13}C n.m.r. spectroscopy identified signals closely matching predicated values for phenol ethers, with the α- and β- legs usually differentiated at most centres. The central naphthalene core was relatively insensitive to the leg. Chemical shifts for the octakis(aryloxy)naphthalene series naphthalene nuclei are given in Table 3 in comparison to other octa-substituted naphthalenes, and as an example the full ^{13}C spectrum is shown in Table 4 for octakis(β-Naphthyloxy)naphthalene (165) in relation to β-Naphthol.[354]

The parent oxygen octa-host (166) was prepared in good yield despite the use of perishable teflon seals. Other octakis(aryloxy)-naphthalenes were synthesised in sealed glass tubes. In the preparation of octakis(p-methoxyphenyloxy)naphthalene (174) by both methods it was, however, observed that in perishable apparatus a mixed product was obtained, apparently from *in situ* demethylation, and a residue of an insoluble white crystallisation material was formed which did not melt up to 310°C and had an i.r. spectrum very similar to that of hexakis(p-hydroxyphenyloxy)benzene (168).

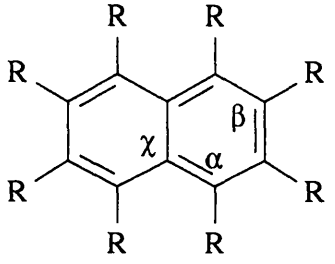
Table 2

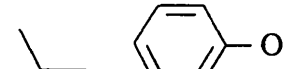
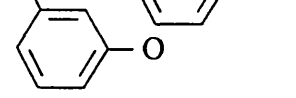
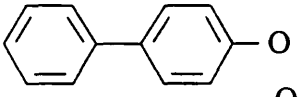
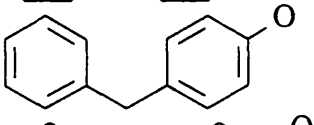
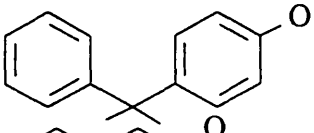
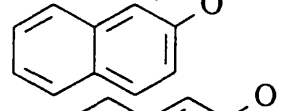
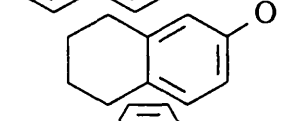
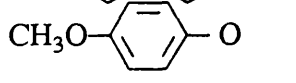
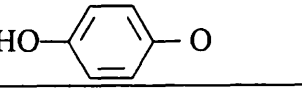
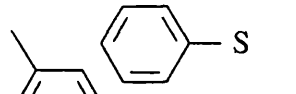
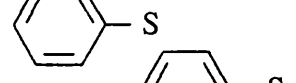
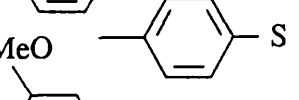
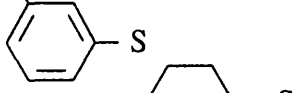
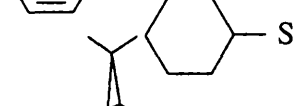
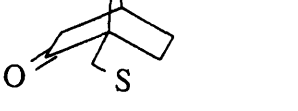


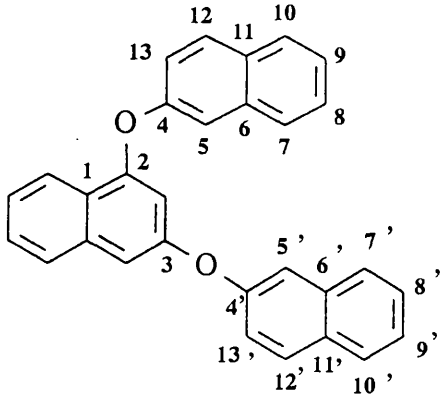
octa-host	yield % *	R
(166)	85	
(167)	72	
(170)	91 #	
(171)	57	
(172)	30	
(165)	55	
(169)	77	
(174)	70	

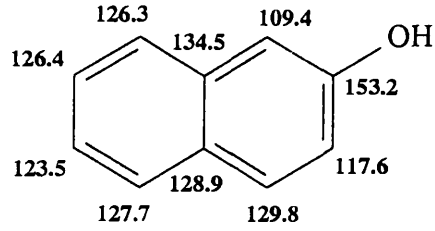
* crude ; # DMEU clathrate

Table 3 : δ_c-Naphthalenes



$\delta_c - \chi$	$\delta_c - \alpha$	$\delta_c - \beta$	solvent	R
133.9	128.3	126.1	$CDCl_3$	H
107.5	142.4	137.6	$CDCl_3$	F
120.6	141.3	140.1	$CDCl_3$	
121.0	141.4	140.1	$CDCl_3$	
120.6	141.3	140.1	$CDCl_3$	
120.7	140.5	139.8	D^6-DMSO	
120.3	141.1	140.0	$CDCl_3$	
121.6	141.0	140.3	D^6-DMSO	
120.8	141.9	140.5	$CDCl_3$	
120.8	142.0	140.5	$CDCl_3$	
120.7	141.3	140.2	D^6-DMSO	
142.9	140.9	139.1	$CDCl_3$	
144.2	140.1	139.9	$CDCl_3$	
143.2	140.5	139.1	$CDCl_3$	
144.9	140.6	140.0	$CDCl_3$	
143.1	137.7	137.7	$CDCl_3$	
137.2	144.5	140.9	$CDCl_3$	





C	type	δ (D^6 - DMSO)	C	type	δ (D^6 - DMSO)
1	s	121.6	9	d	124.4
2	s	141.0	9′	d	124.0
3	s	140.3	10	d	127.5
4	s	156.0	10′	d	127.5
4′	s	154.4	11	s	(129.3) *
5	d	110.1	11′	s	(129.0) *
5′	d	109.4	12	d	129.3 *
6	s	133.8	12′	d	129.0 *
6′	s	133.4	13	d	117.6
7	d	126.7	13′	d	117.0
7′	d	126.3			
8	d	126.8			
8′	d	126.5			

* Overlapping

Table 4 - δ_C (50 MHz),(165)

In the attempted preparation of hexakis(3,5-dimethoxyphenyloxy)-benzene and octakis(3,5-dimethylphenyloxy)naphthalene the products were so tarry that although the presence of the title compounds was confirmed by m.s. they could not be easily separated.

Inclusion properties

Octakis(phenoxy)naphthalene (166) was recrystallised from a number of solvents. Ethyl acetate and toluene were included at 2 moles guest per mole host, whereas acetone and dioxan were included at 1 mole guest (ratios measured by ^{1}H n.m.r. and TGA). The inclusion was variable in character, empty host crystals sometimes being formed, but consistent in quantity. Guest was lost on standing or *in vacuo*, e.g., ethylacetate removed in 24 hours at 1mm Hg. Acetonitrile, nitromethane, cyclohexane and hexane were not included. In all cases crystals were small and powdery. Chloroform and methylene chloride gave large but defective crystals which crumbled quickly in air and did not show signs of solvent inclusion. None of the crystals was suitable for single-crystal X-ray diffraction.

The oxygen analogue of the versatile octakis(*m*-tolylthio)-naphthalene (134) was disappointing. Octakis(*m*-tolyloxy)-naphthalene (167) gave no inclusion behaviour with dioxan, acetonitrile, *N*-methylformamide, acetone, chloroform or cyclohexane. An empty host structure, ex dioxan, was obtained for single-crystal X-ray diffraction (see section 2.6).

Octakis(*β*-naphthyloxy)naphthalene (165) is a versatile clathrate. Dioxan, benzene, acetone, ethylacetate, acetonitrile, nitromethane and *p*-xylene were included at a host-guest ratio of *ca*. 1/2; the ^{1}H n.m.r. ratio was substantiated for acetonitrile, benzene and acetone using TGA. The acetone inclusion compound was further investigated by single-crystal X-ray diffraction (see section 2.6). Toluene and mesitylene were included at *ca*. 1 mole guest per host, and from a 50:50 mixture of toluene/*n*-heptane 1 mole guest per host was included but in a ratio of 3/1 favouring *n*-heptane over toluene. The host was insoluble in neat *n*-heptane. Again chloroform and methylene chloride produced unstable crystal structures.

A slight structural change to octakis(1,2,3,4-tetrahydro-6-naphthyloxy)naphthalene (169) caused virtual loss of inclusion properties, dioxan, acetone, toluene, n-heptane, ethylacetate and hexane all being excluded. Host properties appeared to be present with cyclohexane or an isopropanol/cyclohexane mixture, this solvent being removed only after being left in vacuo for many days. On repeated recrystallisation, however, no inclusion occurred with the host material, perhaps due to an increase in purity of the system.

Octakis(p-phenylphenyloxy)naphthalene (170) was obtained as a 1:1 inclusion compound with DMEU on drowning-out during isolation. The highly insoluble green crystals could be dissolved only by boiling in DMSO, the host then being precipitated by addition of water. Inclusion testing of this material is imprecise, although some evidence exists for cyclohexane inclusion. The colour of the DMEU clathrate, its extreme insolubility and high melting point suggest formation of a clathrate involving some interaction.

Extending the distance between the two aryl rings in the leg produced materials also very insoluble, more difficult to purify or obtain crystals from and showing no inclusion. Thus octakis-(p-benzylphenyloxy)naphthalene (171) did not include ethylacetate, benzene, acetonitrile, acetone, isopropanol or cyclohexane, or mixtures of these.

Octakis(p-cumylphenoxy)naphthalene (172) was isolated in poor yield - it retained p-cumylphenol impurities and was difficult to purify. The product was rather insoluble and often gave oils on recrystallisation, even from crystalline starting material. No inclusion was seen with ethanol, cyclohexane, acetonitrile, dioxan or chloroform.

The mass spectral fragmentation and its material characteristics were parallel to those of the hexa-host analogue.[355]
Octakis(p-methoxyphenoxy)naphthalene (174) was prepared but no inclusion tests performed. It was clearly demethylated by BBr_3 analogous to the hexa-host (173) (section 2.9), on the evidence of n.m.r., but this material was not fully characterised.

2.4 Octa-hosts - interconversions and mixed structures

A desirable feature in clathrate design is to modify the cavity with a specific change whilst retaining the original packing. This might be achieved by differentiation of one or more legs of a poly-host. This is particularly relevant to octa-hosts, where a standard 'Dianin's' or hexa-host type I structure is not retained under systematic modification. Mixed poly-hosts also have potential as new and more sophisticated inclusion compounds and materials, e.g. introduction of chirality to poly-hosts may be economically achieved by the use of only one chiral leg.

Use of mixed perhaloaromatics such as 1,3,5-trifluoro-2,4,6-trichlorobenzene is a possible entry to these systems for hexahosts. The difference between fluorine and chlorine in this case appears inadequate for the purpose,[356] although fluorine and bromine were used successfully.[305c] Compounds of this nature would be more difficult to obtain for higher aromatic systems. A further problem may arise in subsequent unwanted leg replacement.

Another approach entails replacing legs in a preformed octa-host, and separating the products.

Octakis(phenylthio)naphthalene(131) and octakis(phenyloxy)-naphthalene(166) were both reacted with excess p-tolythiolate in DMEU and each was smoothly transformed to octakis(p-tolylthio)-naphthalene, monitored on C_{18} reverse-phase silica t.l.c. plates.

Reaction of octakis(p-tolylthio)naphthalene(161) with a vast excess of a different leg, sodium thiophenolate, in the manner of a standard synthesis was successful in substituting the original legs to give a product co-spotting octakis(phenylthio)-naphthalene on t.l.c. (normal and reverse phase). H.p.l.c. analysis (reverse phase) showed the product to be a mixture of the octa-host(131), as a minor product, a closely eluting major product - probably with seven legs the same - and two very minor broad peaks - probably isomeric six (and five) thiophenyl leg containing naphthalenes.

Use of 0.5-2.0 mole equivalents of sodium thiophenolate resulted in a very small degree of exchange to give a weak broad signal. Unlike the immediate reaction of octafluoronaphthalene with the thiophenolate salt, the exchange process was not recorded by t.l.c. after 30 minutes. In a similar experiment using octakis(phenyloxy)naphthalene (166) as the substrate, prolonged heating at 80°C was required to effect reaction (colour change to red), and a wider spectrum of intermediate products was observed by h.p.l.c. Normal phase h.p.l.c. did not separate mixed leg octa-hosts, but reverse phase h.p.l.c. is suitable both for reaction monitoring (e.g. of perfluorosubstrate substitution) and quantitative separation of the mixed octa-hosts.

A different approach to 'mixed' systems may be doping a structure of one octa-host with another, which will not then necessarily adopt the same conformation as in the one component crystal, but adopt that of its surroundings in a mixed crystal. Different conformations of a polyhost are likely to correspond to similar minima, as demonstrated by octakis(phenylthio)naphthalene (131).

2.5 Attempted preparation of other octahosts

The attempted synthesis of octakis(benzylthio)naphthalene gave a poor mixture of products consistent with debenzylation of substituted legs and none of the isolated fractions appeared to be the desired host. Re-benzylation was only briefly attempted. Similar problems were encountered in the attempted synthesis of octakis(2-pyridylthio)naphthalene, although some of the isolated fractions from chromatography indicated the presence of this material by mass spectrometry. Attempts to use benzyl sodium, phenyl lithium, sodium cyanide, and sodium benzenesulphinate salts as legs gave tars.

2.6 Solid-State crystal structure, molecular conformations and inclusion

Octakis(arylthio)naphthalenes - (134) and (161)

Octakis(m-tolylthio)naphthalene (134) was further purified by column filtration chromatography using lipidex 5000 phase, a 50% substituted (C_{15} average) alkoxy group derivitive of sephadex LH20, and recrystallised from toluene and dioxan to give the non-solvated and dioxan adduct (1:1) respectively. Interestingly on single-crystal X-ray diffraction analysis it was found that the two host crystal structures are identical save for the slight increase in cell dimensions and minor molecular conformation changes in the clathrate due to the presence of the disordered guest. The disordered guest is situated close to a four-fold proper rotation axis whilst the host molecule is located at a point of exact 222 (D_2) symmetry (Figure 26).

No other prior published case was found where the clathrate host structure is supported in the absence of guest by van der Waals packing-forces only, although one example has been published since.[288] This crystal structure arises from efficient edge-on packing of host molecules which all have the same conformational chirality within a given layer parallel to the ab plane. The cavities are of a true clathrate nature, as established by van der Waals section analysis and supported by 'tightness' of dioxan guest retention.

In the case of two other guests, acetonitrile and nitromethane, leakage was found with time. This may indicate a different crystal structure entirely, and indeed the morphologies are different, although this is not necessarily significant. The results indicating apparent 'partial occupancy ' of acetonitrile clathrates (section 2.1) do, however, support the non-solvate structure in this case despite guest loss. In contrast the effects seen with n.m.r. spectroscopy from attempted methane inclusion in crystals grown from toluene support strong retention of guest in that structure.

Two packing modes for one host arising from different molecular conformation types was previously noted with the parent octakis-(phenylthio)naphthalene (131).[308] These two distinct conformations were previously classified as 'yellow' and 'red' forms, based on the colour of the crystals, and indeed pressure applied to the 'yellow' form produced a 'red' form, one that is slightly more dense, assuming that it is identical to the first 'red' form (see Introduction, section 2.3c).

The molecular conformation of the octakis(m-tolylthio)naphthalene in the non-solvate and dioxan clathrate (Figure 27) is of a type previously encountered in the 'yellow' form based on consideration of leg displacements above and below the mean central core naphthalene unit. In this conformation there is considerable non-planarity at the core naphthalene unit, a torsion angle of 26(1)°C and 27(1)°C being observed for C(1) - C(9) - C(10) - C(4) in the non-solvate and dioxan clathrate respectively, while the atoms C(1) - C(4) are close to coplanar in each case. This compares to 31(1)° and 0(1)° for the equivalent torsion angles in the 'yellow' and 'red' forms of the parent host.

Since it was possible that the degree of torsion in the central ring was related to conformational type and to the u.v./visible spectrum of the solid-state, studies were undertaken with KBr disc preparations of various hosts to find a quicker, non X-ray diffraction method of establishing possible conformational type. These found no differences in either parent host or isomeric octakis(tolylthio)naphthalene hosts. The method was limited by the practical technique itself however, because of unsuitable equipment and the sample preparation - high pressure possibly leading to host conformational changes!

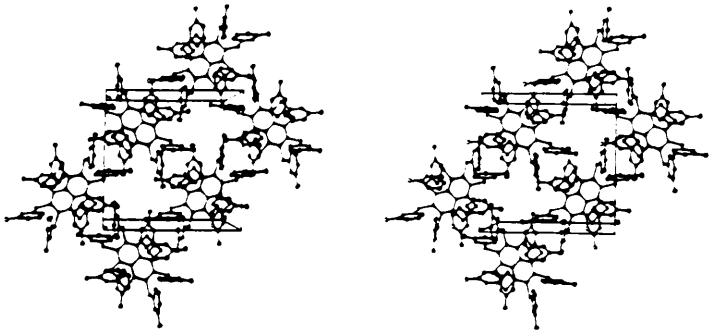


Figure 26

A stereoview showing the molecular packing of (134) in the non-solvate form.

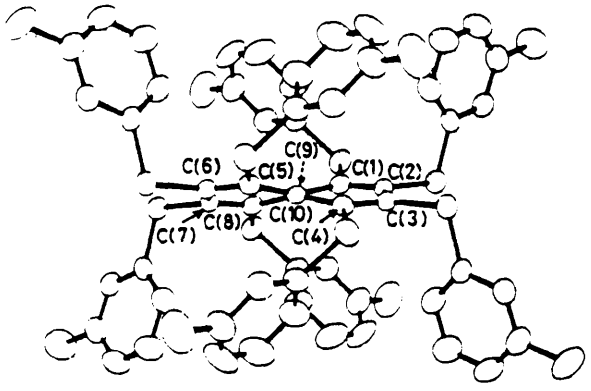


Figure 27

Molecular conformation of (134) in the non-solvate form.

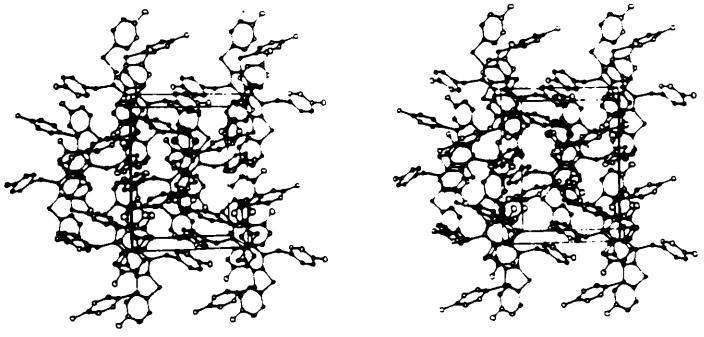


Figure 28

A stereoview showing the clathrate packing of (161)• dioxan.
The atoms of the guest are represented by filled circles.

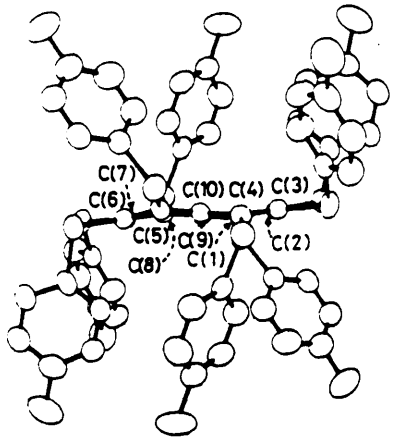


Figure 29

Molecular conformation of (161) in its 1,4-dioxane clathrate.

While as yet observing only one conformational type for the m-tolylthio-substituted host naphthalene, a further intriguing aspect was encountered. The mesitylene adduct of the host was regularly isolated on recrystallisation despite its apparent oversize for the cavity of the X-ray diffraction studied crystal form. The adduct (1:0.35) appeared identical to the non-solvate from toluene and gave the same unit cell measurements. These anomalous findings were not resolved.

Octakis(p-tolylthio)naphthalene (161) also gave a dioxan adduct (1:2) which was prepared for X-ray diffraction studies. Its crystal structure (Figure 28)is based on an entirely different and new molecular conformation, (Figure 29). The host has a central torsion angle of only $3(1)^{o}$ and is an orange crystal adduct, with the core naphthalene rings as shallow boat conformations.

The other isomeric host octakis(o-tolylthio)naphthalene (160) could also be prepared as a 1:2 dioxan adduct, but crystals suitable for X-ray diffraction were not obtained despite extensive purification and recrystallisation. In this case the crystals did not appear to lose dioxan and no purification overcame the crystal growth problem.

It was clear that inclusion properties were not necessarily related to one specific leg arrangement either for one host molecule or amongst closely related conformations. A consideration of the idealised maximum possible symmetry of the various leg conformations gave rise to a new classification system for the various types. Assuming a trans arrangement for peri-related groups, there are 14 possible types: these were classified primarily on the basis of symmetry, assuming achiral legs. The greatest weight is placed on proper rotation axes, in the order D_2, C_{2h}, C_2, C_s, C_i and C_1. Secondary ranking was decided by consideration of the degree of leg alternation, the most with highest weighting, and finally the third and lowest criterion required to differentiate fully all fourteen conformation types was chosen as maximum (non-exact) symmetry of the central six carbon atoms and the four α-substituted legs with a C(9) - C(10) bond on an exact C_2 axis outweighing other C_2 orientations.

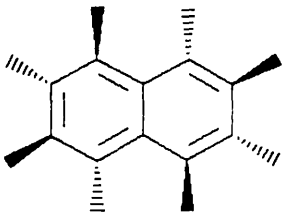
Under these criteria, the 14 types (Figure 30) are type I, ababab (D_2); type II, aabbaabb (D_2); type III, abbabaab (C_{2h}); type IV, aaaabbbb (C_{2h}); type V, ababaabb (C_2); type VI, aababab (C_2); type VII, aaababbb (C_2); type VIII, abbbabbb (C_2); type IX, abbabbbb (C_s); type X, abaababb (C_i); type XI, abababbb (C_1); type XII, abbabbab (C_1); type XIII, aabbabbb (C_1); type XIV, aababbbb (C_1), where a and b denote the leg as projecting relatively above or below the central naphthalene core.

According to this classification, the crystal structure molecular conformational types relating to the octakis(arylthio)naphthalene hosts are type II, aabbaabb (m-tolyl, phenyl 'yellow' form), type III, abbabaab, (p-tolyl) and type X, abaababb, (phenyl 'red' form). Significantly no type I, ababab, is observed in contrast to the hexa-hosts where the equivalent type I, ababab, is strongly preferred.

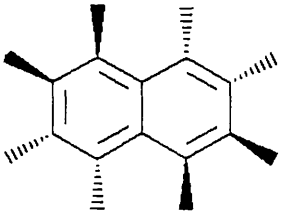
Octakis(aryloxy)naphthalenes - (165) and (167)

Crystal structures were determined for two of the octakis(aryloxy)-naphthalenes (Figures 31 & 32), one as an adduct and the other as a non-solvate. Octakis(m-tolyloxy)naphthalene (167) does not have the same conformation as its thio-analogue (134). It is another example of a type III and is also like the octakis(p-tolythio)naphthalene host structure in both central core naphthalene and (oxygen) linkages, although O(2) and O(6) are displaced by 0.172(5)Å from the mean naphthalene plane (Figure 33). The methyl substituents are orientated such that the plane of symmetry possible in type III cannot be used.

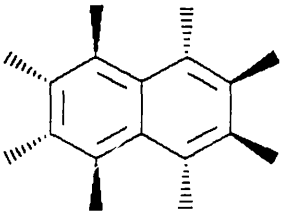
Octakis(β-naphthyloxy)naphthalene (165) does form inclusion compounds and the acetone adduct (1:2) was found to have a remarkable conformational type not previously encountered (Figure 34). This did not fit the classification of types I-XIV as in this case a unique cis-peri relationship of legs was found.



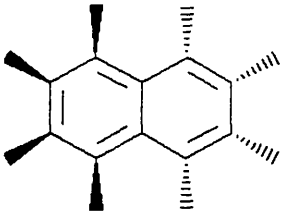
TYPE I , D_2



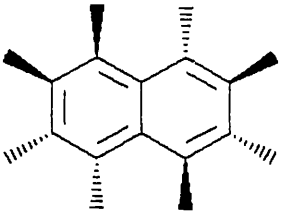
TYPE II , D_2



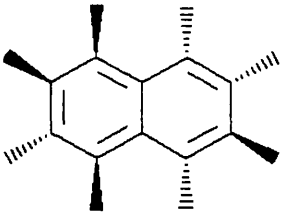
TYPE III , C_{2h}



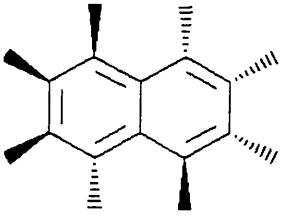
TYPE IV , C_{2h}



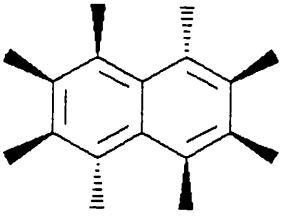
TYPE V , C_2



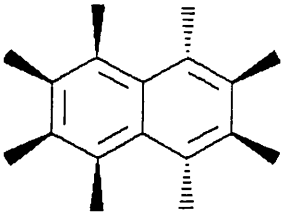
TYPE VI , C_2



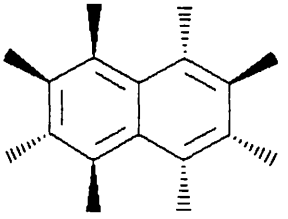
TYPE VII , C_2



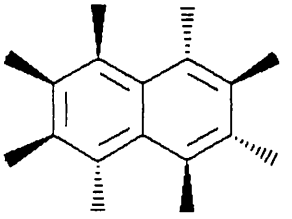
TYPE VIII , C_2



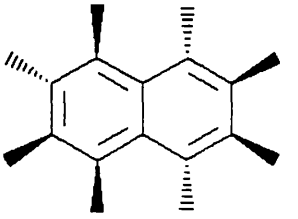
TYPE IX , C_s



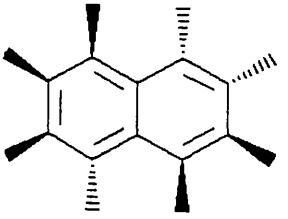
TYPE X , C_1



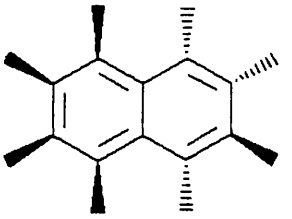
TYPE XI , C_1



TYPE XII , C_1

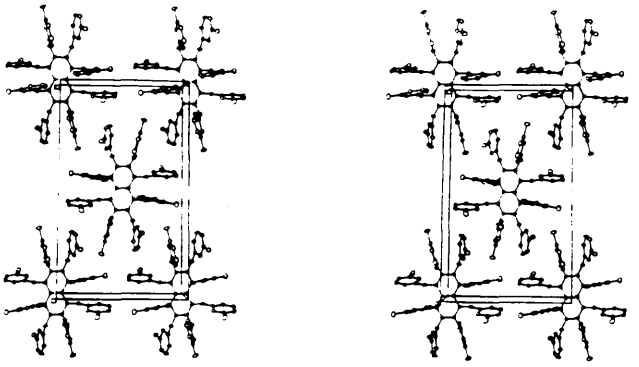


TYPE XIII , C_1



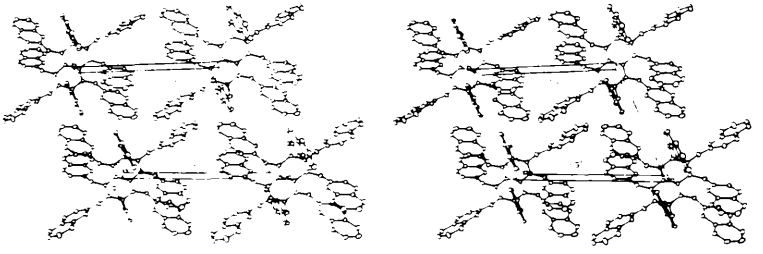
TYPE XIV , C_1

Figure 30 - Idealised octahost molecular conformational symmetry types assuming trans-peri interaction



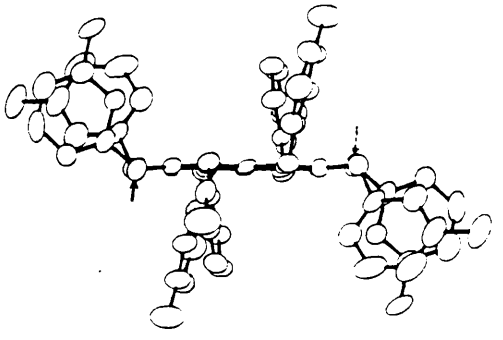
A stereoview of the molecular packing of (167) in the unsolvated crystal.

Figure 31



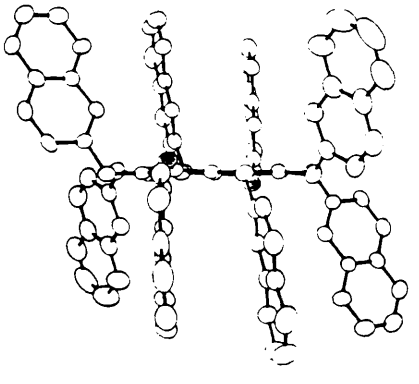
A stereoview of the (165). 2 acetone packing structure.
G and G^1 denote the approximate centres of two centrosymmetrically related guests.

Figure 32



The molecular conformation of (167) in the unsolvated crystal.
The atoms O(2) and O(6), indicated by arrows, are displaced by 0.172(5)Å from the central naphthalene plane.

Figure33



The host molecular conformation in the clathrate (165), 2 acetone, illustrating the unique cis-peri (type X) relationship of legs. The oxygen atoms O(1) and O(5), both shaded, have the largest displacements from the central naphthalene plane.

Figure 34

Not surprisingly this causes a greater degree of displacement of oxygen atoms from the central naphthalene's mean plane, particularly O(1) and O(5), at 0.326(4)Å and 0.219(4)Å respectively. The smaller oxygen link is evidently able to attenuate repulsion to accommodate such a unique peri relationship. This unclassified type (abbabbaba) is, like type III, C_{2h} idealised symmetry.

Octakis(cyclohexylthio)naphthalene (164)

The unsolvated form of the material was investigated by single crystal X-ray diffraction and another unexpected conformational feature was discovered (Figure 35). While existing in a type III conformation overall the two legs at C(1) and C(5) were found to have axial S-cyclohexyl ring conformation.

Interestingly, for a monosubstituted cyclohexane ring no equivalent situation was present in the Cambridge Data Bank. The crystal structure (Figure 36) was very dense and is not likely to be that in the inclusion adducts formed by the host. The presence of the axial substituents precludes the molecules' attaining the maximum non-crystallographic symmetry for type III of C_{2h} and they use exact C_i symmetry instead. Again, the central torsion angle is near 0^o with the six-membered ring having a shallow boat conformation and the two independent α-carbon atoms displaced by 0.14Å and 0.15Å from the mean plane of the central naphthalene core.

Octakis(phenylseleno)naphthalene (175)

The octa-host (175) was purified by column filtration chromatography and recrystallised unsolvated from toluene/chloroform. This material was found to have close packed structure and to be another example of a type X conformation (Figure 37). As with (131) 'red' form the central naphthalene core is near planar with the six-membered ring in a shallow boat. In this case a direct (non-solvate) solid-state structural chalcogen analogue has been found.

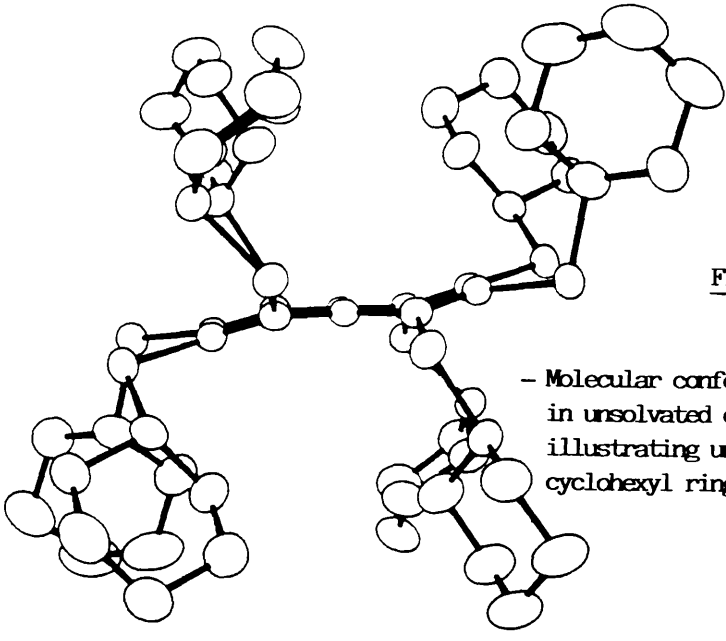


Figure 35

- Molecular conformation of (164) in unsolvated crystal, illustrating unique axial *S*-cyclohexyl ring.

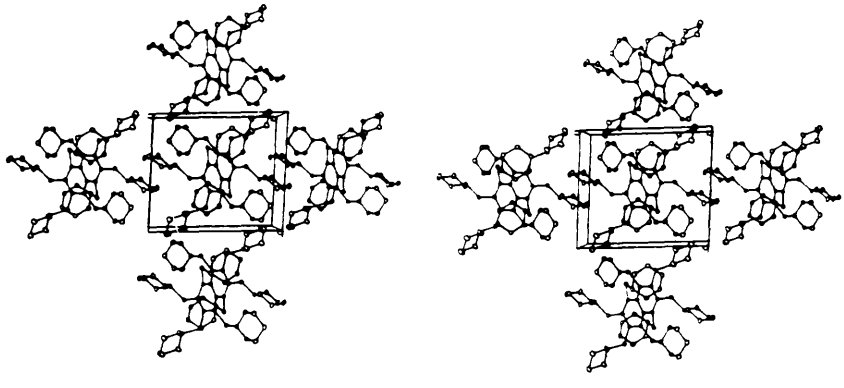


Figure 36 — Molecular packing in unsolvated crystal of (164)

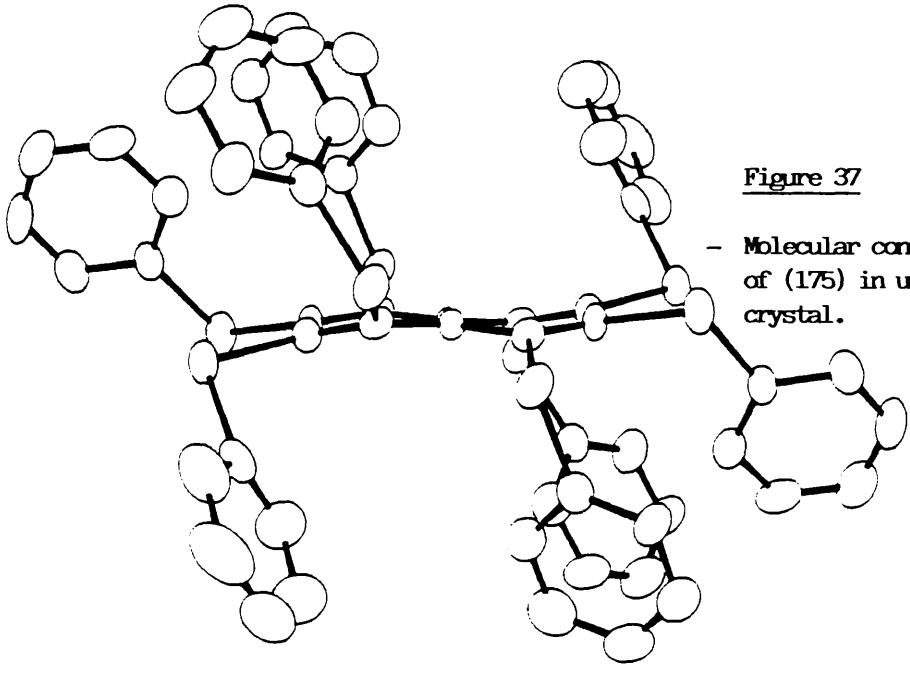


Figure 37

- Molecular conformation of (175) in unsolvated crystal.

Although type II structures appear to be more prevalent than the others and no type I 'hexahost' structure has yet been found, it is clear that inclusion is not the result of a particular conformational type or vice-versa. A given host is likely to exist as at least two types, one the non-solvate and the other(s) adducts. Octakis(m-tolylthio)naphthalene is indeed unique in forming an open-packed 'clathrate' structure as a non-solvate. The energy level differences between the crystal types must be small in some cases.

The classification of conformational types is ordered by symmetry elements since the experience of hexa-hosts and other clathrate systems indicates multi-molecular inclusion is likely to be a phenomenon associated with molecular symmetry (potential or fulfilled). This has been borne out by the findings so far. The observed conformations are of types II, III, and type X and one unclassified case. These represent maximum idealised molecular symmetry of D_2 (3 cases), C_{2h} (4 cases) and C_i (2 cases), but the actual findings indicate D_2 (2 cases), C_2 (1 case) and C_i (6 cases). In fact, two of the three centrosymmetric classified conformational types have now therefore been observed.

Unlike the C_2 symmetry considerations in the tetraphenylenes there does not seem to be a preferred C_2 axis. In the plane of the naphthalene core C_2 axes parallel and perpendicular to the C(9) - C(10) bond are equally represented. Since all the legs are equal however the crystal structure is not forced into differention and selective leg replacement may prove a favoured axis. A chiral leg would equally negate the possibility of the centrosymmetric structures currently prevalent.

Perhaps surprisingly, the type I conformation has not been found as yet. Complete C(1) - C(4) and C(5) - C(9) alternation has occurred in the case of the β-naphthyloxy leg, but with the unusual cis-peri relationship. The alternation may be due to a bigger leg pulled even closer in proximity by the smaller oxygen links. The thio-analogue is known but the structure not determined.

A large chiral leg may be sufficient to force the type I conformation. It may be that the type I is disfavoured by not being centrosymmetric - the hexa-host type I is centrosymmetric. In this sense the 'unusual' β-naphthyloxy leg octa-host is actually more akin to the hexa-hosts.

Obviously the central structural feature of the hexa-hosts in the solid-state molecular crystal, columnar packing with cavities directly above and below each central core benzene ring, is not repeated in the octa-hosts, which in any case are C_2 and not C_3 based molecules. In the octa-hosts, cavities are formed entirely in the space between legs of different hosts. There is one hexa-host analogy for this behaviour, where the clathrate of hexakis(β-naphthylthio)benzene (128) packs as in 'type II', C_2 non-centrosymmetric conformation enclosing the guest between legs (Figure 17, see Introduction, section 2.3c). Other non-clathrate hexa-host conformations are known where a low degree of alternation of legs is promoted by co-ordination.[305c]

There is no one packing description to cover the various host structures, although clearly the steric features of the leg - an angular 'link' and large flat 'wall' - are universal. These and the symmetry provide a basis for good host design.

In the non-solvated crystal structures, octakis(m-tolylthio)-naphthalene (134) excluded, the legs fill their own space in a normal close-packed fashion. Clearly however, they must be able to realign to include fairly large guests, e.g. octakis-(cyclohexylthio)naphthalene (164) includes a mole of CH_3CCl_3, in a, presumed more open, unstable structure. One common feature relating symmetry to structure is the central naphthalene C(1) - C(9) - C(10) - C(4) torsion angle. In type II structures where the legs are not centrosymmetrically related but have maximum D_2 symmetry the torsion angle is large, 26-31°. In types III, X, and the unclassified case, the legs are centrosymmetrically related and the torsion angle is now 0-3°. In the former case the other six-membered ring carbons are near planar whereas in the latter the six-membered ring now forms a shallow boat.

This observation is consistent with expectation from the perpendicular application of forces to a model naphthalene system. Interestingly there are three types where although the molecule is not centrosymmetric but either the α-carbon or β-carbon groups alone are. In types V and VII the outer, β-carbon, legs are centrosymmetric and in type XII the inner, α-carbon, legs are.

For the eleven conformational types not seen, some predictions, based on those so far observed, of the likelihood of finding these with octakis(arylthio)naphthalenes are as following: types I, V and VI are most likely, having symmetry, equal numbers of 'up' and 'down' legs and no more than two adjacent legs of the same directional 'sense'; type IV is centrosymmetric, and the only centrosymmetric conformational type not found, but is strongly disfavoured by having two rings each containing legs all of the same sense; types XI - XIV have no symmetry, mostly poor alternation and unequal distribution of legs and are unlikely to be found, or at least to occur frequently; types VII - IX have symmetry but also have poor alternation and unequal distribution of legs. Type VII however is disfavoured only by poor alternation and does have centrosymmetrically related outer legs, and is therefore next most likely in order after types I, V and VI. Of these three types, type V has centrosymmetrically related 'outer' legs and could be most favoured for non-chiral groups.

The non-classified type (U) observed in the host structure of (165) is unique amongst those of the '<u>cis</u>-<u>peri</u>' types in relation to the favoured type III and X conformations. That is it is centrosymmetric, has one pair less than full leg alternation and is described within the sequence <u>abbabaabab</u>babaab...etc., i.e. taking the eight symbols starting from the first symbol, and then the eight starting from the second symbol, and then from the third symbol, etc., this sequence describes types III, X, U, X, III, X, U, X....etc. 'Widening' the <u>peri</u> interaction, e.g. to give the pseudo-octa-hosts based on biphenylene (see section 2.9) may then allow observation of the type U with a 'thio-leg'. Types V and VI are similarly related to each other and another (non-centrosymmetric, C_1) '<u>cis</u>-<u>peri</u>' type. Type II is related in a similar fashion to C_{2v} '<u>cis</u>-<u>peri</u>' type.

2.7 Solid-state - magic angle spinning ^{13}C n.m.r.

The unique structural features found in the single-crystal X-ray diffraction studies of (134) and (164) made them ideal candidates for further investigations of octa-host crystal structure.

Octakis(m-tolylthio)naphthalene (134)

In the ^{13}C solid-state n.m.r. spectra of (134) as the non-solvate ex toluene (Figures 38 & 39) and the dioxan solvate (Figures 40 & 41), the key feature is the high-field methyl group signals. Where the non-solvate has two independent signals the clathrate structure is less well resolved but clearly shows more and different chemical shifts. This information fits entirely with the D_2 conformational assignment of the single-crystal X-ray structure of the non-solvate and importantly with the persistently less than molar guest occupancy of the clathrate. Should the cavities in the non-solvate structure not be completely filled then the number of independent methyl group signals should rise, as observed. Additionally the empty cavities within the dioxan clathrate may be expected to retain unchanged chemical shifts. Prominent in the dioxan clathrate solid-state n.m.r. spectrum is a residual signal at δ 20.4 from unfilled cavities; the second methyl signal of empty cavities is hidden by the methyl signal of a filled cavity. This situation, whereby the difference in chemical shifts and the structural sensitivity is a feature of the closely packed, and structurally vital, methyl groups, is analogous to that of the 'waist' methyl substituents in Dianin's compound and its analogues, where the presence of guest physically disturbs the adjacent methyl groups to influence the inclusion structure.[224] A similar interaction was found central to the host inclusion properties of the (hydrogen-bonded) tubulands (see Introduction, section 2.3).[262]

In the non-solvate, the low-field shifts of the two independent leg-bearing naphthalene carbons are both down-field of their solution-spectra values by 6ppm.

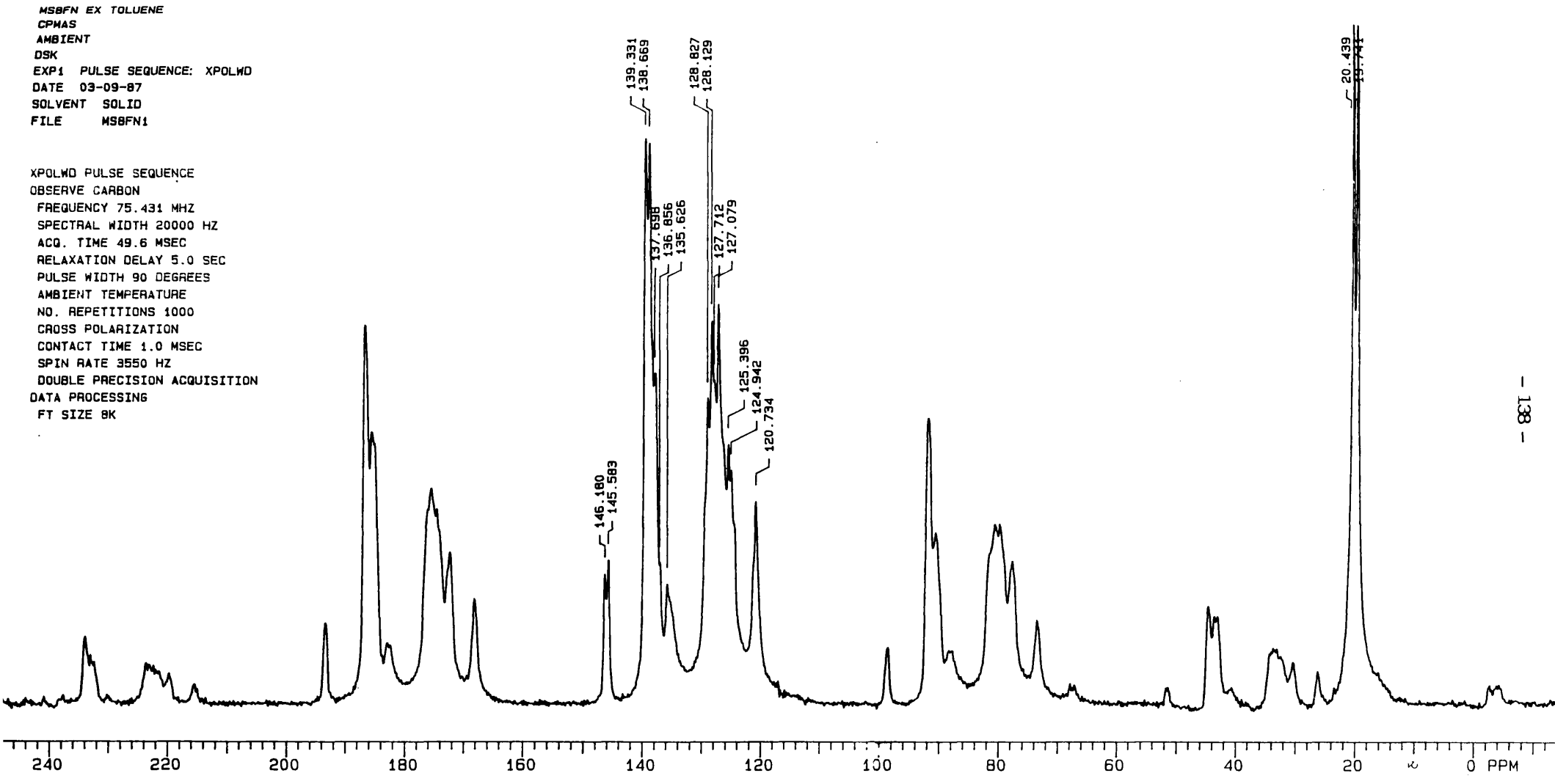


Figure 38 – Solid-State ^{13}C CPMAS n.m.r. of (134), unsolvated ex toluene

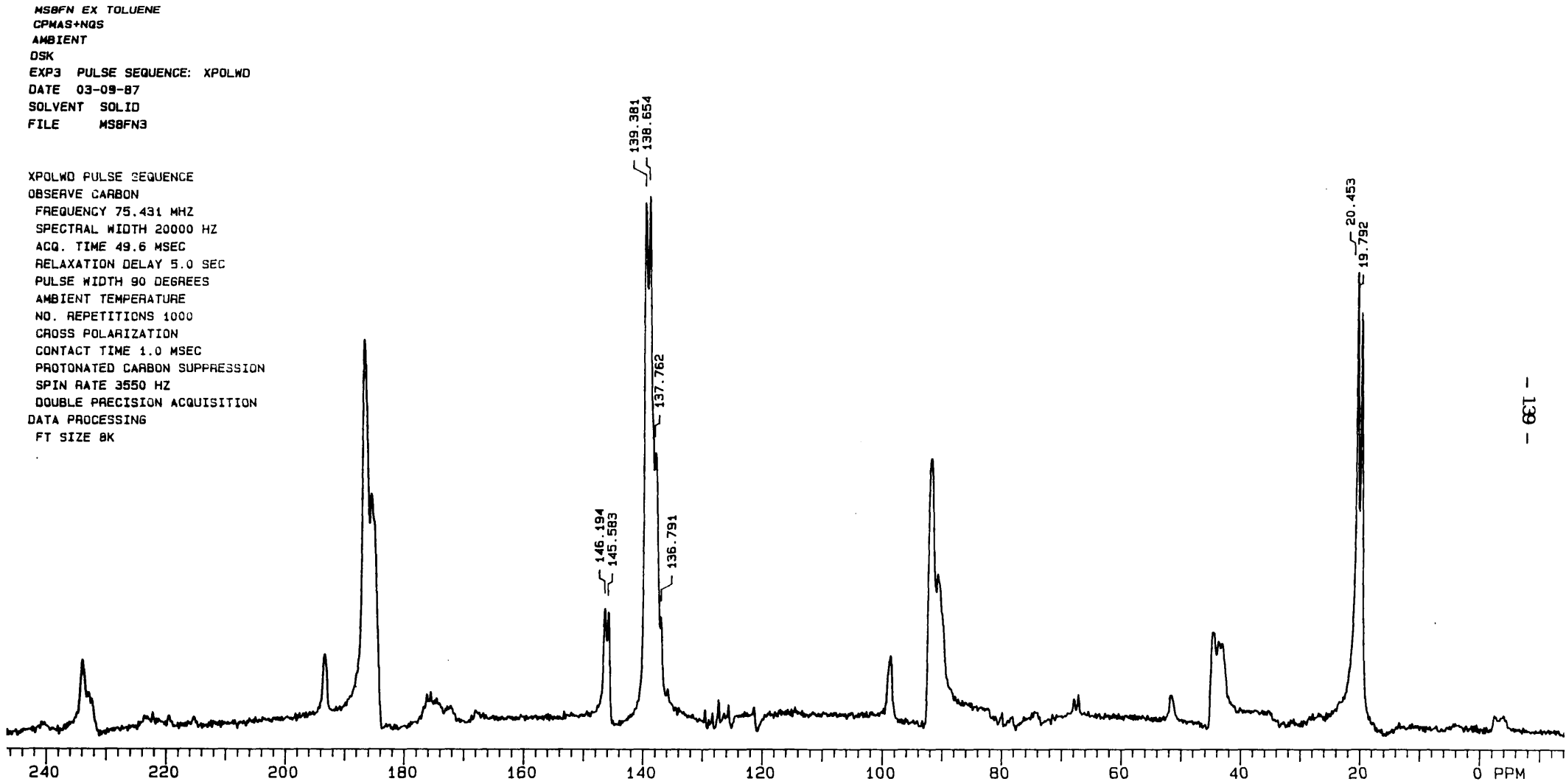


Figure 39 – Solid-state ^{13}C CPMAS + NQS n.m.r. of (134), unsolvated toluene

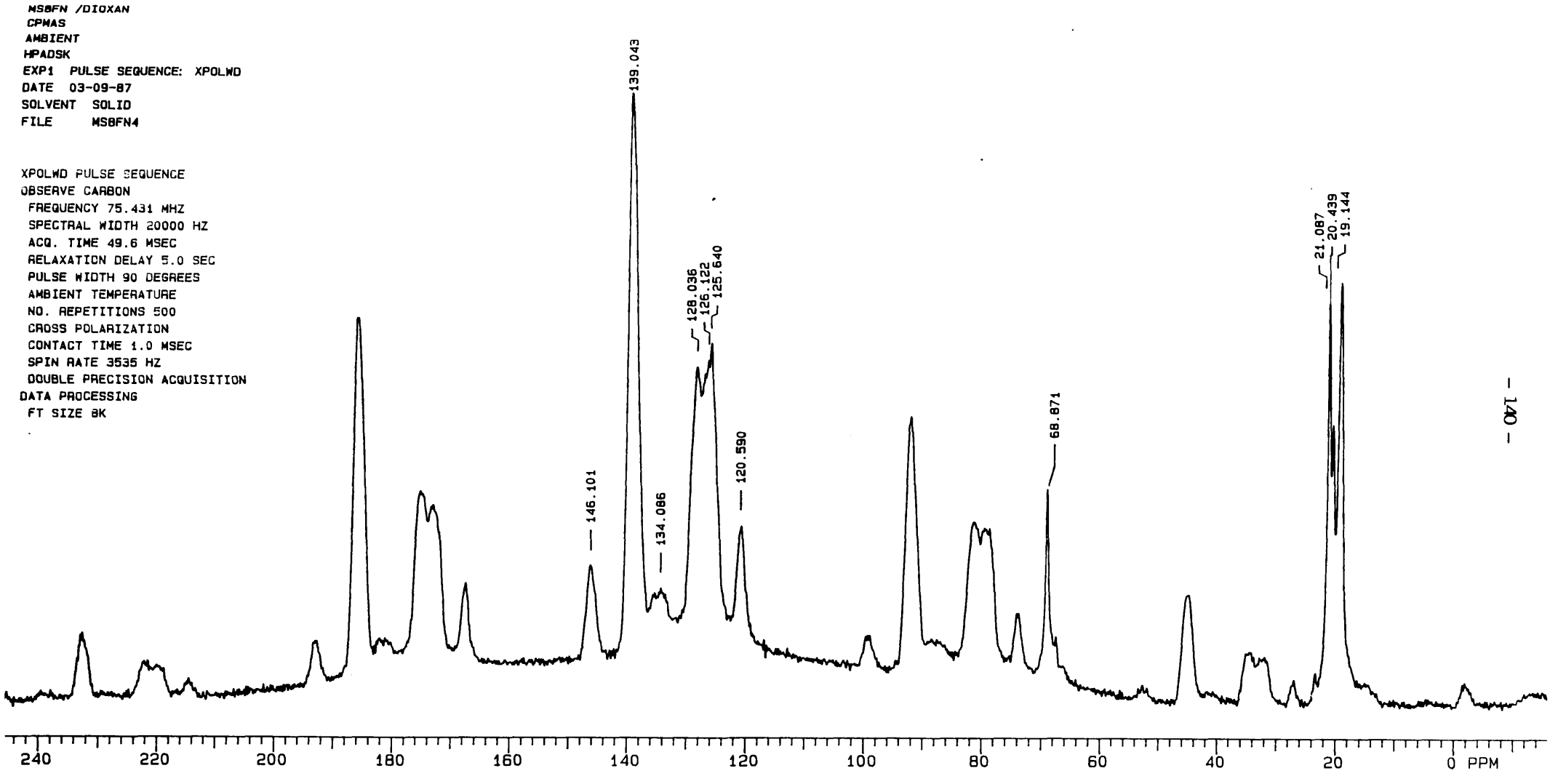


Figure 40 – Solid-state ^{13}C CPMAS n.m.r. of (134), dioxan clathrate

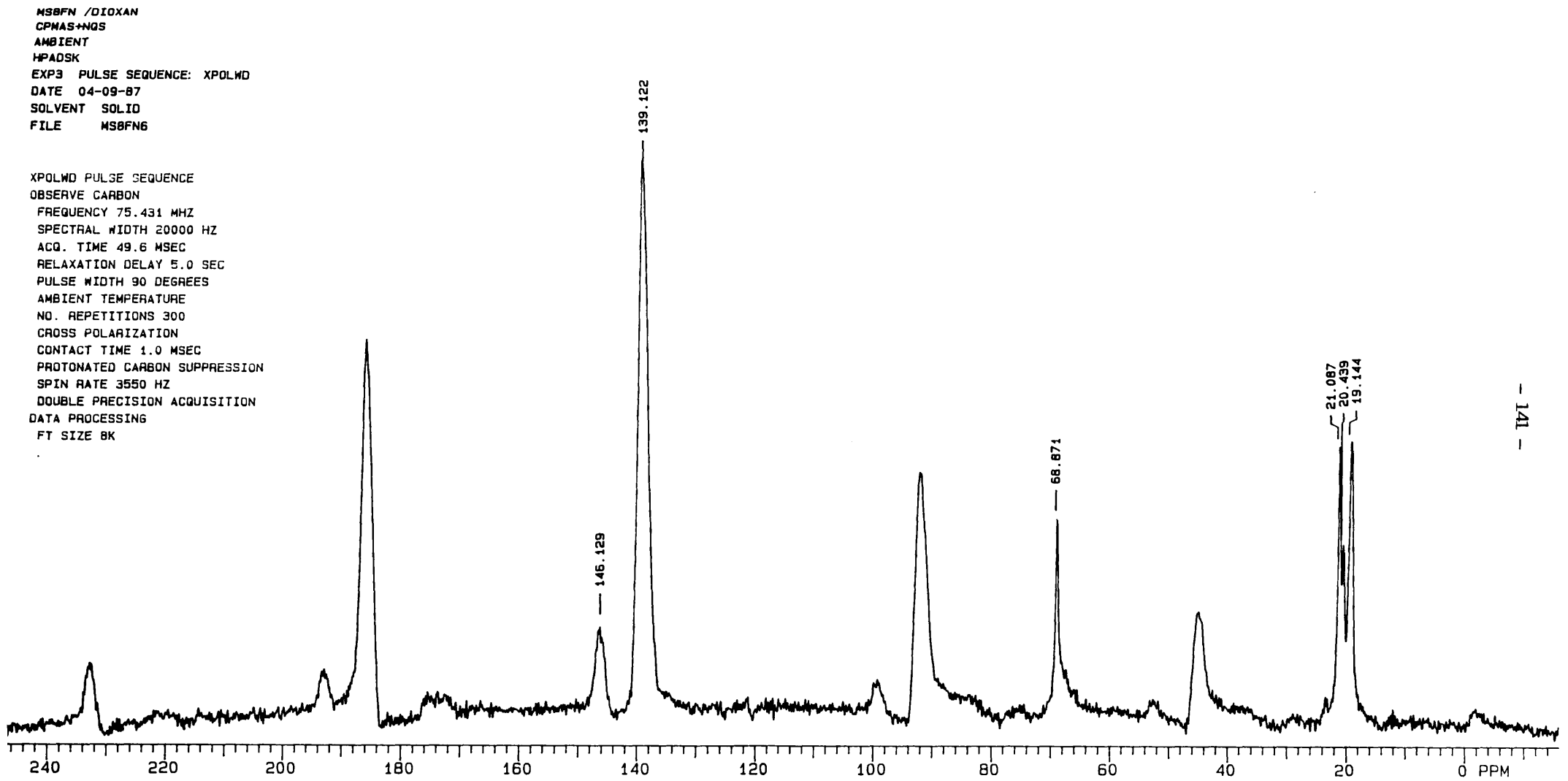


Figure 41 – Solid-state ^{13}C CPMAS + NQS n.m.r. of (134) dioxan clathrate

This is common to the related carbon centres in the octakis-(cyclohexylthio)naphthalene spectrum, and may prove to be a general feature of this class of compound, rather than due to the large central naphthalene ring twist for example. The unsubstituted central naphthalene carbon centres have moved from a distinct chemical shift of δ 144.2 in solution into an unresolved peak elsewhere, most likely amongst the the other quaternary carbons. These are found as a maximum of five signals (against a required minimum of five independent carbon centres). In fact the general low-field values of the two central naphthalene carbons (see following discussion) in solution spectra of octakis(aryl- or alkylthio)naphthalenes are in contrast to the up-field shift experienced in octakis(aryloxy)-naphthalenes and octafluoro-naphthalene from their value in naphthalene itself (δ 133.3).

The other low-field peaks belonging to the 8 independent aryl carbons on the legs are represented in the solid-state by seven signals, six poorly resolved and one well separated. The one marked by an up-field shifted value (δ 120.7) in comparison to the solution values may be due to one or both of the independent carbons ortho to the sulphur and para to the methyl groups that may be in the shielding region of the central naphthalene ring.

The dioxan clathrate is very similar to the non-solvate in its down-field carbon spectrum except for a general loss of resolution attributed to the partial occupancy of guest. The dioxan itself is represented by a fairly sharp signal. The aromatic carbons in the ring are more likely to experience effect of empty and full cavities on each side, and hence become less resolved.

Octakis(cyclohexyl)naphthalene (164)

The ^{13}C solid-state n.m.r. experiments with octakis(cyclohexyl)-naphthalene gave very distinct and clear evidence of the special conformation of the axially orientated legs at C(1) and C(5), and of the whole molecule in general (Figure 42). Immediately apparent is the number of independent low field core naphthalene carbon atoms, five in total.

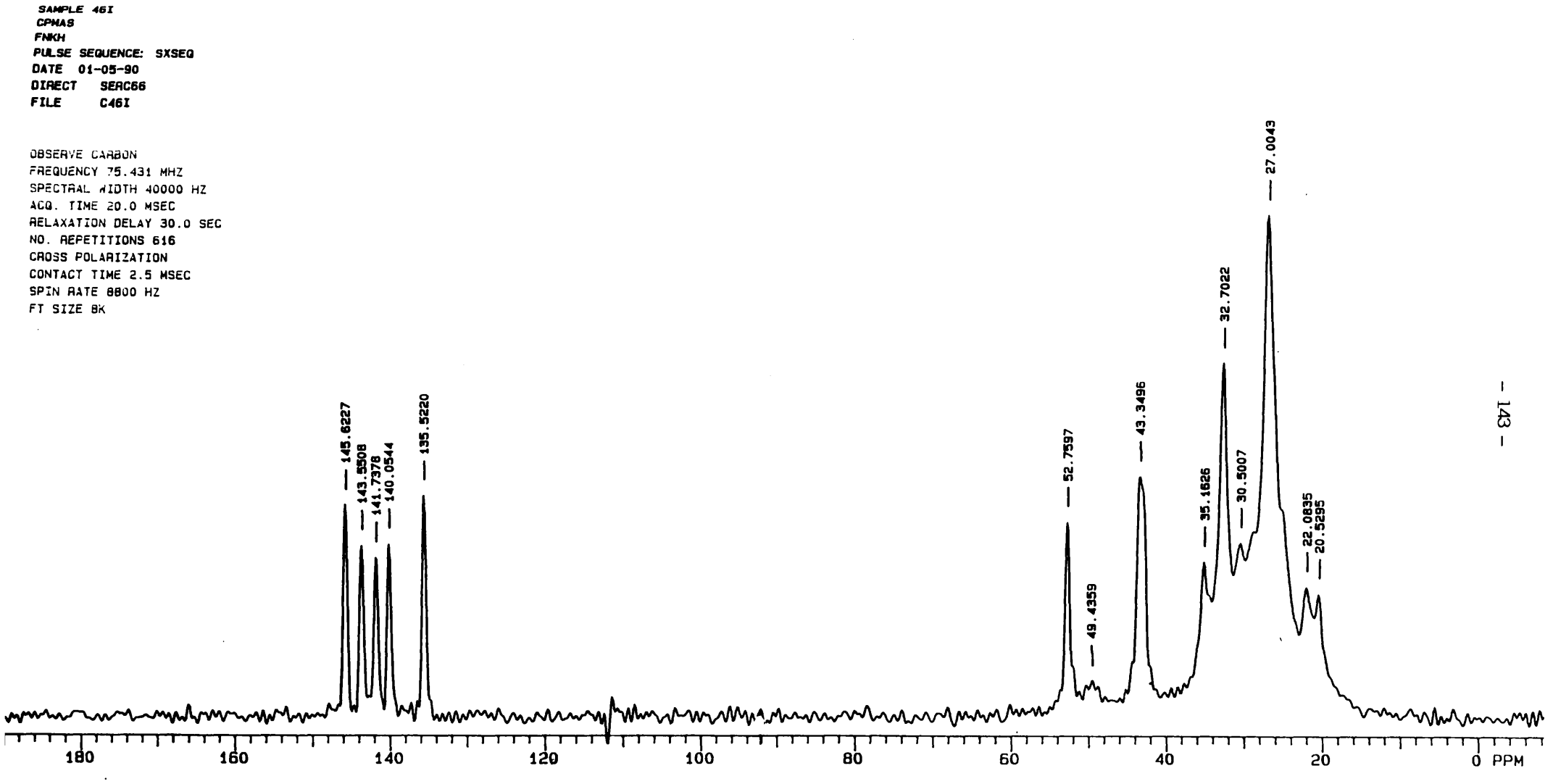
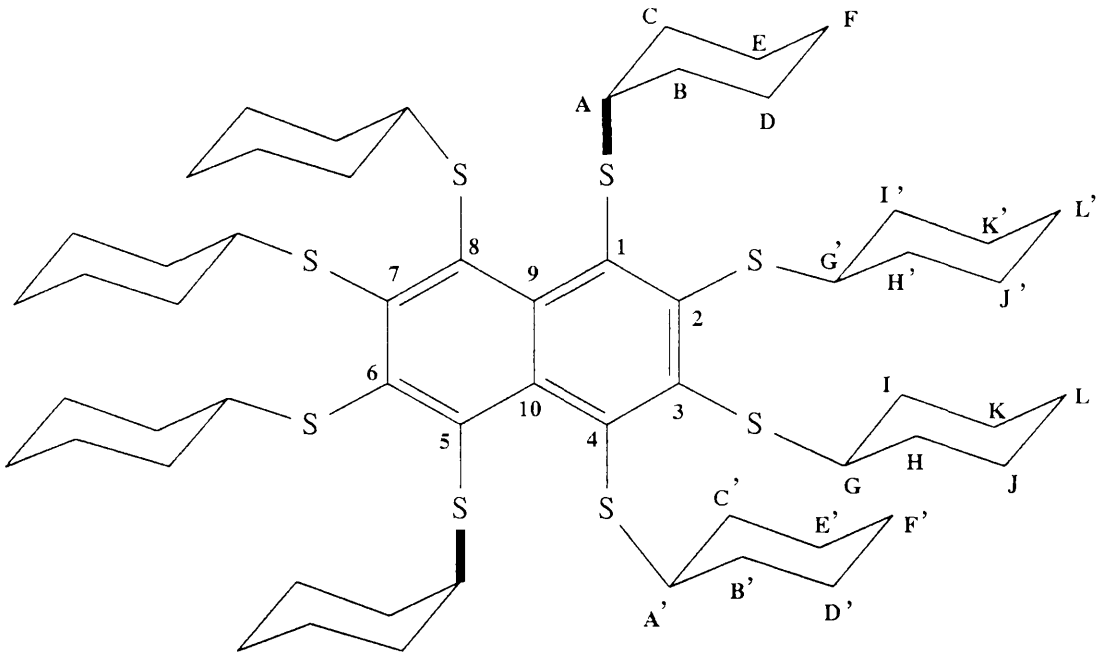


Figure 42 – Solid-state ^{13}C CPMAS n.m.r. of (164), unsolvated

This neatly corresponds to the lower than idealised centrosymmetric type III conformation of abbabaab, more accurately represented in this case as a'bbab'aab where a' and b' are the axial S-cyclohexyl legs, and C(1), C(2), C(3), C(4) and C(9) are the independent centres (Figure 43). There is also, however, a large move in the field strength values of the α and β positions, C(1) - C(8), and a possible shift in the central carbons C(9) and C(10), from their $CDCl_3$ solution values of δ 137.7 and δ 143.1 respectively. The highest field signal in the solid, δ 135.5, may be the C(1) axial S-cyclohexyl leg as this has the lowest torsion angle and hence should experience the highest expected γ- effect. The three 'equatorial' positions C(2) - C(4) are more likely to remain close in chemical shift. Alternatively, the signal at δ 135.5 could be the C(9) carbon, by analogy with the high-field shift assumed present from the solid-state values of (134).

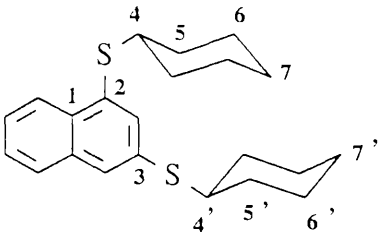
At least as interesting are the high-field signals, which also show remarkable resolution. These are tentatively assigned in the following way (Figure 43). The methine carbons are δ 52.8 for equatorial legs and δ 49.4 for the axial leg. The peaks at δ 43.3 and δ 32.7 are the next nearest carbon centres but with one side trans, anti-parallel and the other gauche, receiving a strong γ - effect from the naphthalene core. Similarly the peaks at δ 35.2 and δ 30.5 equate to the equivalent carbons on the axial leg, but with the gauche centre possibly not receiving such shielding from the naphthalene core, as observed in the X-ray crystal structure. Finally the peak at δ 27.0 is all the other centres unresolved except for the two crystallographically non-equivalent ring carbons in the axial leg receiving a γ - shielding effect from the axial sulphur (δ 22.1, 20.5).

These findings illustrate well the shielding effects in the solid-state lost in solution spectra (Table 5), particularly strong γ -effects, and the usefulness of solid-state n.m.r. as a technique in clathrate structure determination. The solid-state ^{13}C n.m.r. spectra of the 'red' and 'yellow' forms (type X and type II respectively) would make a good comparison.



δ_c	C
145.6 143.6 141.7 140.1 135.5	1,2,3,4,9
52.8	A′,G,G′
49.8	A
43.3	B′,H,H′
35.2	B
32.7	C′,I,I′
30.5	C
27.0	D′,J,J′,E′,K,K′,F,F′,L,L′
22.1 20.5	D,E

Figure 43 - assignment of δ_c in solid-state ^{13}C CPMAS n.m.r. (164). Unique S - cyclohexyl axial bond conformation is highlighted.

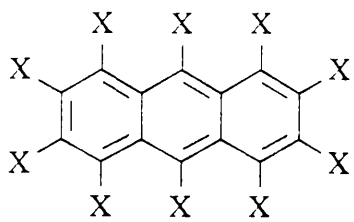


C	type	δ_C ($CDCl_3$)	C	type	δ_C ($CDCl_3$)
1	s	143.1	5	t	33.0
2	s	137.4	5'	t	33.0
3	s	137.4	6	t	26.1
4	d	50.0	6'	t	25.8
4'	d	49.6	7	t	25.7
			7'	t	

Table 5 - δ_c (25MHz),(164)

2.8 Deca-hosts - attempted preparation

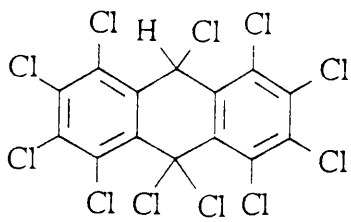
One aim of the work was to extend the 'hexa-host principle' further from the 'octa-hosts' to the 'deca-hosts', deca-substituted anthracenes (175). These molecules are expected to show inclusion behaviour analogous to that of the octa-host, but indeed have some greater interest. Not only is a similar series of leg conformations possible, but a greater degree of distortion may be envisaged from the central aromatic core, and with a ribbon-like twisting of the three rings leading to enantiomerically related helices.[357] The extended delocalisation on the 'deca-host' series may also lead to interesting electronic properties, e.g. colours[357] and secondary harmonic generation.[358] The higher molecular weight hosts may also be more stable and form 'tighter' clathrates. Furthermore 'deca-hosts' would be another step along the extended linear acene group where other even more interesting hosts and molecules may exist, particularly derivatives of the unstable higher parent hydrocarbon members. The most obvious route to deca-hosts is *via* perhaloanthracenes.



(175)

Literature preparations of decachloro- and decafluoroanthracene are available but perhalogenated higher members of the series of linear acenes are not known. Halogenation-dehalogenation syntheses involving the higher systems are very inefficient, even for anthracene. Perchloroanthracene, made from anthracene using BMC chlorination conditions and subsequent chemical dechlorination, was obtained by Ballester in a yield of 10% (compared to perchloronaphthalene, 58%).[359]

Following this procedure repeatedly gave an equivalent weight of a compound (176) with similar characteristics, believed to be 1,2,3,4,5,6,7,8,9,10,10-undecachloro-9,10-dihydroanthracene (177) or another $C_{14}HCl_{11}$ compound. This may be due to performing the reaction daily over two weeks, rather than continuously. Using stronger conditions gave a mixture, including other hydrogen-containing material, and at a much reduced yield.



(177)

Chemical dechlorination of the $C_{14}HCl_{11}$ material gave two compounds inseparable by recrystallisation or sublimation. Spectroscopic investigation suggested the formation of anthracenes with hydrogen present, and a thermochromicity similar to that for perchloroanthracene was observed.[359] Mass spectrometry revealed strong and weak signals corresponding to $C_{14}Cl_9$ and $C_{14}Cl_{10}$ ions respectively. Dechlorination (major) and dehydrochlorination (minor) are suspected.

Sublimation of the $C_{14}HCl_{11}$ compound mainly produced a material corresponding to one of the chemical dechlorination products. Thermal dechlorination is known in related cases.[359,360]

The classic route to perfluoroaromatics involves exhaustive fluorination of hydrocarbon followed by defluorination, using cobalt trifluoride (or similar high valency metal salt) and metal gauzes respectively. Anthracene is a very poor substrate, yielding less than 0.05% perfluoroanthracene (178).[40b] A route to octafluoranthra-9,10-quinone (179) from tetrachlorophthalic anhydride and potassium fluoride provides an alternative highly fluorinated precursor to perfluoroanthracene (Figure 44).[361]

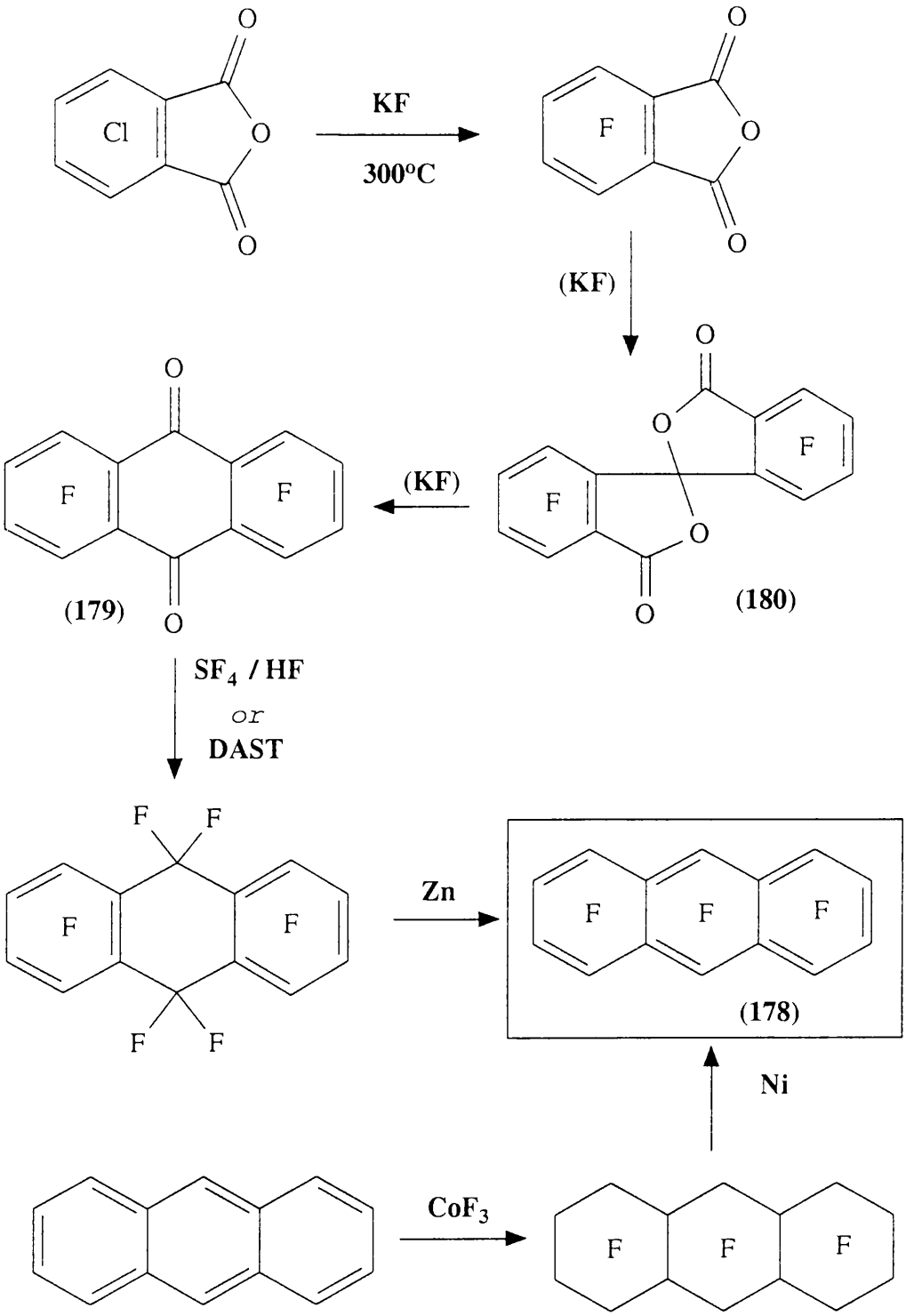
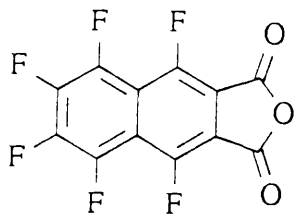


Figure 44 - Perfluoroanthracene syntheses

Similar conditions in an autoclave, with or without more severe heating, produced the intermediate lactone (180) predominantly, with the anthraquinone as a minor product.[362] Using pyrex glass according to the method of Inoue et al again gave mainly lactone.[363] The lactone was not converted to anthraquinone when recycled, or when heated in a sealed tube, although the mixtures could be repeatedly recrystallised to give the anthraquinone in very low yield. Perfluoroanthraquinone has become commercially available from a similar route, and in accordance with Inoue's observations it was observed that chlorine is left in some of the product (m/e 368). The reaction is most sensitive to the preparation of anhydrous fluoride.[363]

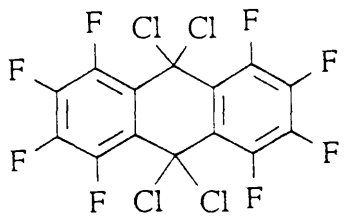
Hexafluoro-2,3-naphthalene dicarboxylic acid or its anhydride or hexachloro-analogus (181) are potential precursors to longer perfluoro-acenes. These materials might be accessible from perhaloanthracenes by analogy to perfluoronaphthalene chemistry.[364]



(181)

In the chlorination of hexachloro-1,4-naphthaquinone with phosphorous pentachloride perchloroanthracene was obtained directly.[365a] Chlorination of octafluoro-9-10-anthraquinone (179) to 9,9,10,10-tetrachloro-octafluoro-9-10-dihydroanthracene (181) was attempted. Mild treatment of (179) with phosphorous pentachloride returned essentially the starting material and some minor reaction products observed in the mass spectrum at m/e corresponding to $C_{14}F_xCl_{10-x}$, x = 4-8. Complete reaction of the anthraquinone in a sealed tube caused widespread halogen exchange.

Products could be crudely fractionated by sublimation or solubility, those with greater chlorine content requiring greater temperature or being less soluble respectively, and were characterised by mass spectrometry as losing Cl_2 (even m/e) when highly chlorinated and C_1 fluorine-containing species when lightly chlorinated (odd m/e). No peaks corresponding to $C_{14}X_{12}$ were observed despite a full range of $C_{14}F_xCl_{10-x}$, x = 0-10 species ($C_{14}C_{10}$ was the biggest peak in the sublimination residues). Elimination of chlorine to form an anthracene from the 9,10-dihydro species could be occurring in the reaction, during sublimination, or under mass spectrometric conditions. Product obtained before sublimination had a UV spectrum more consistent with perhalo-9-10-dihydroanthracene species. Chlorination of perfluoroketones has been shown to require forcing conditions.[365b]

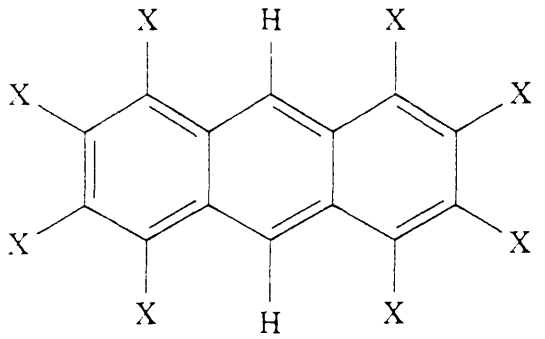


(181)

Treatment of octafluoroanthraquinone (179) with sulphur tetrachloride and anhydrous hydrogen fluoride produced only a loss of some starting material and a green salt believed to be nickel fluoride.[362c,363] Under more severe reaction conditions a greater amount of octafluoroanthraquinone was lost. The sulphur tetrafluoride was checked by i.r. spectroscopy and showed only very minor impurities.

Fluorination was attempted with diethylamino-sulphur trifluoride (182), (DAST) in chlorobenzene.[367] This returned mainly starting material again, although peaks were observed in the mass spectrum at m/e 374 and 390, possibly $C_{14}F_{10}O$ and $C_{14}F_9ClO$ respectively, and in the i.r. spectrum at 2880-2970, 1850, and 1020-1120 cm^{-1}; lit. ν (c=o), perfluoro-9-oxo-9,10-dihydroanthracene (183), 1705cm^{-1}.[362c] Prolonged heating with DAST at 80°C caused (179) to break-down, and no higher molecular weight products were observed.

After the failure to make any perhaloanthracenes some perfluoroperhydroanthracene (184) was obtained to try to make 'deca-hosts' by the new saturated perfluorocarbon reaction route. Treatment of (184) with sodium thiophenolate did not give the deca-host but instead the reduced 1,2,3,4,5,6,7,8,-octakis-(phenylthio)anthracene (185) in poor yield as the main product.



X = PhS (185)

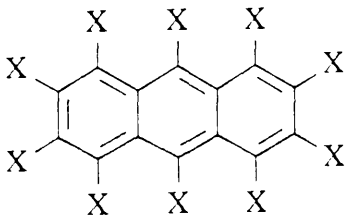
Although the starting material contained impurities (as is usually the case for such materials, the impurities are liable to be molecules containing rearrangement products, residual hydrogen or unsaturation), their total content is approximately 10% (crude material) at most but probably far less (recrystallised).[368] These are more likely to react under the conditions. Since the reaction product after purification was a minimum 22% yield on substrate charged and 30% on substrate reacted, this is clearly an actual product of the perfluoroperhydroanthracene. Reaction is hindered by the insolubility of the substrate. Elimination of the legs from the 9- and 10- positions is in agreement with expected steric-relief considerations. A second attempt using a bulkier leg, p-t-butylthiolate, did not prevent leg cleavage. This leg cleavage is occurring at temperatures lower than for the reduction observed in naphthalene-decalin system.

Finally it was decided to use the material isolated from sublimation of reaction products from PCl_5 and (179), as any perhalo- compound with the correct C_{14} skeleton could potentially give a deca-host, regardless of both the chloro- and fluoro-substitution pattern and the degree of unsaturation.

Treatment with sodium thiophenolate gave a high weight of highly coloured products similar to those from the perfluoroperhydroanthracene reaction, but not of identical t.l.c. R_f. Isolation by chromatography of the main product gave material that could not be crystallised or fully identified. The product appears to be an unsymmetrically substituted anthracene not containing low-field hydrogen or carbon as would be expected from an anthraquinone or leg cleavage product. This route to deca-hosts *via* perhaloanthracenes or 9,10-dihaloperhaloanthracenes requires further investigation.

2.9 Other poly-host systems

In addition to the naphthalene-based 'octa-hosts', other systems have potential as related structures retaining their symmetry. Examples are biphenylene (186), fulvalene (187) and anthracenes with no legs on the middle ring (188).[369] Biphenylene is equivalent to a leg distribution equal to naphthalene but now elongated to relieve the peri-interactions.



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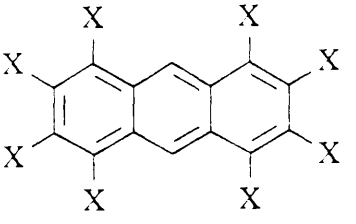

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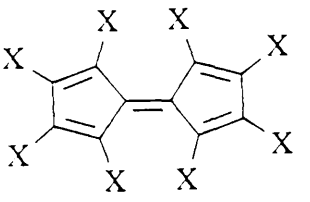

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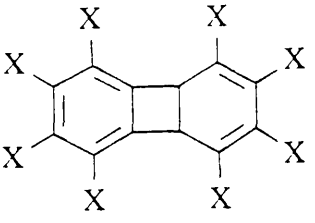

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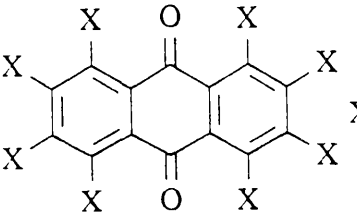
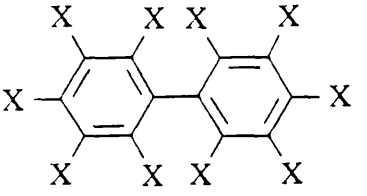
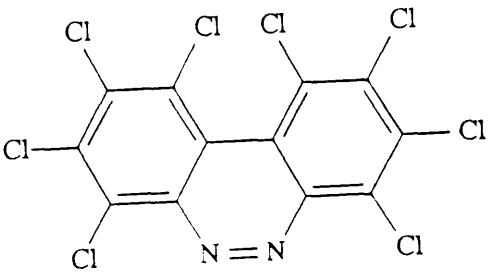


(179)



(194)

Octachlorobiphenylene (189) was synthesised by the pyrolysis of tetrachlorophthalic anhydride (190) according to the method of Brown et al.[370a] As observed by MacBride and Kanoktanapora in an alternative synthesis from octachloro-benzo[c]cinnoline (191), this material contains an impurity, probably isomeric, that could not be separated.[370b] It was, however, at a lower level than obtained by Brown et al (λ max 424 and 452 nm not as strong and ν max 1205cm^{-1} not strong).



(191)

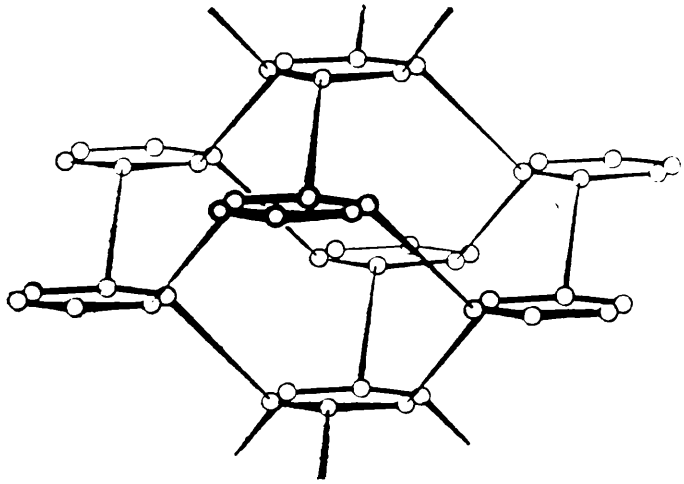
Reaction of (189) in DMEU with sodium thiophenolate at room temperature gave a mixture of products, with chlorine still present. Brief heating and isolation of products followed by column chromatography produced a low yield of purple crystalline material with a mass spectrum consistent with that expected for the pseudo-octa-host. The octachlorobiphenylene appeared unstable in this reaction, giving dark-coloured products and low yields. Complete substitution may, however, require more forcing conditions because of the less active chloro-substituents. This merits further investigation, and perhaps the use of octafluoro-biphenylene. Octachlorofulvalene(192) has been shown to break down under the mild conditions.[356]

A brief attempt at the reaction of (179,X = F) with sodium thiophenolate gave a mixture of products, chromatographic separation of which gave material with highest m/e corresponding to the substituted anthraquinone(193).

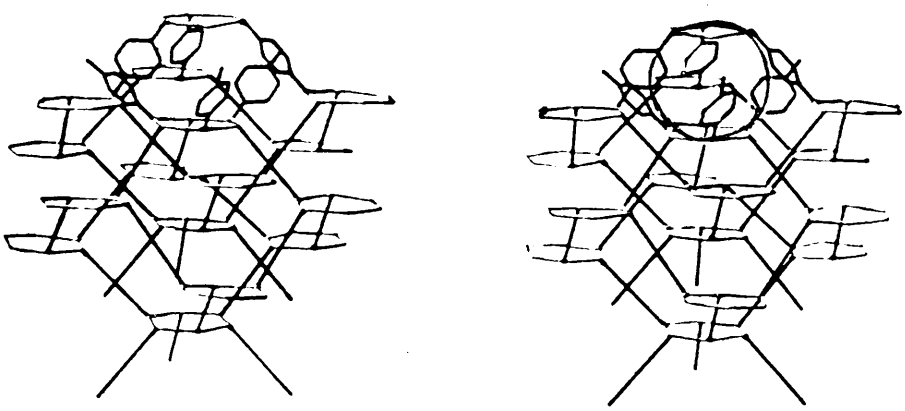
The non-planar biphenyl system is a candidate for persubstitution to give alternative 'deca-hosts' (194)[371]. Initial investigations showed that incomplete substitution is occurring at room temperature in DMEU with decafluorobiphenyl in the normal manner using phenylthiolate salt. The product has a mixed ^{19}F n.m.r. spectrum and analysis that indicates two or three positions are left unsubstituted, i.e. at least one per ring. Heating to 60°C eliminated fluoride - the use of a p-tolylthio leg again demonstrated a mixture of sites for the final substitution position. No low-field H-sites that may result from leg cleavage were observed. This system therefore although more stearically hindered, can be used for host investigations - the extra crowding around a tight core suggests that in this system p-substitution may be more favoured than m-substitution, both to allow deca-substitution and to give a structural framework with the potential to build cavities.

2.10 Hexakis(p-hydroxyphenyloxy)benzene : a potential analogue of β-hydroquinone

In the hexa-host analogy, there is a set of molecules which have a special significance because of a very close relationship to clathrate systems on which the analogy is based. These molecules are of the formula $C_6(OR)_6$ where ROH corresponds to a clathrate-forming phenolic molecule of the hexameric structure type, e.g. Dianin's compound and β-hydroquinone. To mimic Dianin's compound host structure to the full with a hexa-host would involve alternate substitution of (R) and (S) enantiomeric legs. The synthesis can be envisaged as occurring through selective substitution with a suitable mixed perhalocompound - more likely for thia-Dianin's - or selective trimerisation of a 1,2-(R),(S)-substituted [meso] ethyne; use of achiral Dianin's-type legs, e.g. p-cumylphenol, is a currently successful approach to structure investigation of hexa-host molecules.[356] The basic β-hydroquinone hexamer structure is directly parallelled by the simple hexa-ether hexakis- (p-hydroxyphenyloxy)benzene (168). Furthermore this hexa-ether is a building block theoretically capable of reproducing the infinite β-hydroquinone system (Figure 45) with alternate 'hexamers' of hydrogen-bonding and hexa-host types. Thus for every hexa-host central benzene ring the six adjacent ring structures are true hydrogen-bonded phenolic hexamers (each built from six hexa-host phenolic legs derived from six (different) hexa-host molecules), and, conversely, each hydrogen-bonded hexamer is adjacent to six hexa-host central benzenes. One further structural element is still required, however, for a complete β-hydroquinone mimic, and that is two independent interpenetrating lattices. This is less likely to happen for the bigger hexa-host unit than for the smaller quinol molecule, and one lattice alone would have to be very strong to overcome the very open packing. Bond angles and lengths are also not identical and therefore an exact iso-structural match would involve strain. Nevertheless, other interpenetrating 'chicken-wire' structures have been developed.[270,271]



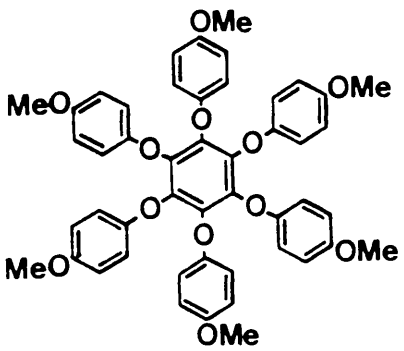
Hydrogen bonding structure of quinol molecules forming infinite three-dimensional cagework in β-Hydroquinone crystals. Each regular hexagon denotes six hydrogen bonds between oxygen atoms. The tapered lines represent the O-O axis of a quinol molecule.



Sterescopic representation of the interpenetration of two hydrogen-bonded cageworks (as above).
Benzene rings are shown by small hexagons on the upper part of the drawing and the roughly spherical space enclosed between the two cageworks is indicated.

Figure 45 (adapted from Ref.222a)

Hexakis(p-methoxyphenyloxy)benzene (173)[372] was prepared from p-methoxyphenol and hexafluorobenzene, and then demethylation of (173) was cleanly achieved using excess BBr_3,[373] 6 moles per leg in an overall yield of 72% for two steps. The hexa-quinol (168) is relatively insoluble but was found to dissolve in DMSO and pyridine with gentle heating. Recovered material from these solvents is, however, less pure. Oxidation is suspected. (168) could be recrystallised however from MeOH, in small quantities, in a sealed tube by heating to 200-360°C to give very small, pure, stable rhombohedral crystals. The hexa-quinol could be similarly dissolved in acetone but only oils were formed.



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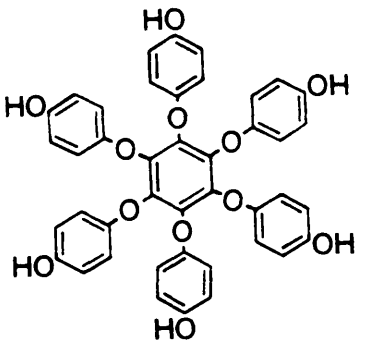
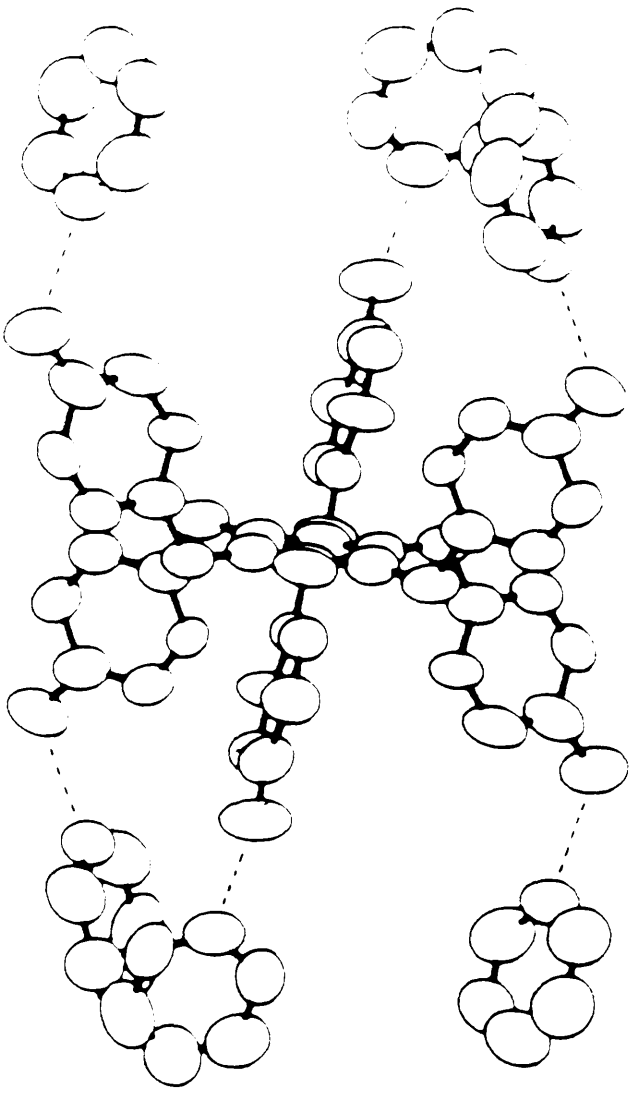


(168)

Use of nearer stoichiometric amounts of BBr_3 (0.5 mole per leg), resulted in material difficult to work up and containing residual methoxy substituents. Such material could not be retreated due to its insolubility. The unsolvated host charred on melting, but better behaviour was observed for solvates. Solvated (168) obtained after recrystallisation from MeOH appeared unaffected up to greater than 300°C, suggesting a rather more stable form than the apparently more amorphous parent, or the relatively weak DMSO or pyridine solvates. Material recrystallised from ethanol or isopropanol had no guest or enhanced thermal stability.

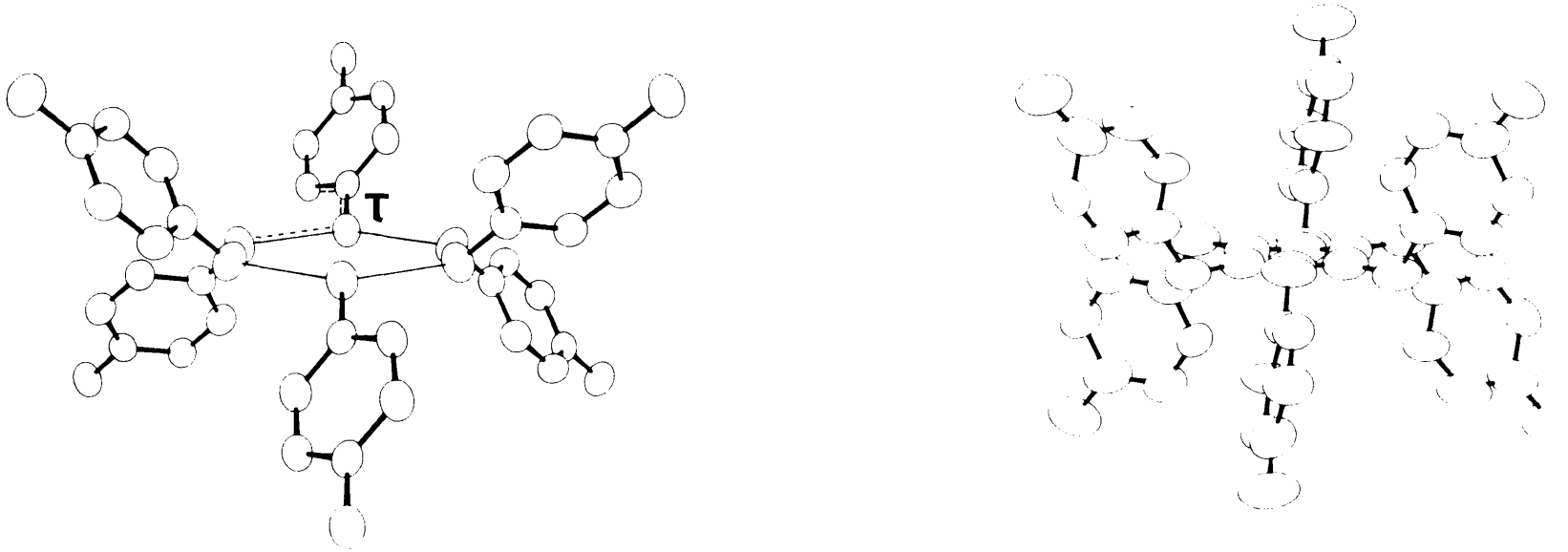
The adduct from pyridine has one molecule of guest hydrogen-bonded to each leg as shown by single crystal X-ray crystallography (Figure 46). The central hexa-host uses crystallographic 3 symmetry and corresponds to a β-hydroquinone hexameric unit, although torsion angles differ significantly (Figure 47). The extended host unit, including the six pyridine molecules, packs in columns in classic hexa-host fashion, giving a long c-axis as measured from one central benzene ring to the next (Figure 48).

Figure 46



A view of the host molecule (168) with its six associated pyridine molecules. All hydrogen atoms have been omitted, and hydrogen bonds between oxygen and nitrogen are denoted by broken lines.

Figure 47



A comparison of the hydrogen-bonded hexameric unit of β-hydroquinone (left) with the molecule of (168) in its pyridine adduct. In the former the torsion angle τ (denoted by the dotted line), -59^{o}C, is significantly smaller in magnitude compared to the corresponding angle for (168).

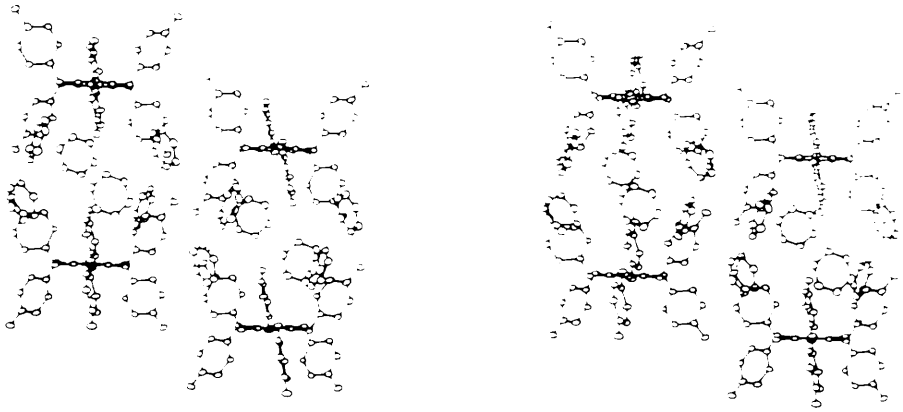


Figure 48 A stereoview normal to the c-axis of the pyridine adduct of (168). Included water is not shown.

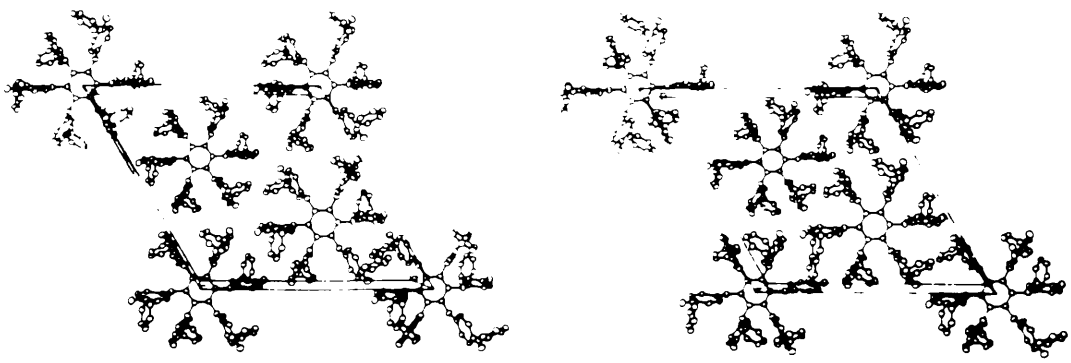


Figure 49 A stereoview looking down the c-axis of the pyridine adduct of (168). Included water is not shown.

The crystallographic measurements of this unit are very similar to those for Dianin's compound,[224] and indeed the pyridine resides at a perpendicular angle to the leg, parallelling that of the benzo moiety in Dianin's compound (Figure 49).

Attempts to grow crystals of the host from quinoline and isoquinoline solutions to give closer structural congruence appeared only to oxidise (168). The structure is also a true clathrate due to residual trapped water, also observed by 200 MHz ^{1}H n.m.r. Growing crystals from aqueous solutions did not change the water content (0.4 moles per mole host maximum) or crystal characteristics of the adducts. The pyridine guest was lost on standing. DMSO was also found to be included at the same level of six moles guest per host, but was even more unstable. The symmetric field of phenolic groups offered by the hexaquinol makes it an attractive coordinatoclathrate host; it may also be ideal for mixed host crystals, e.g. with crown ethers, for example 18-crown-6.[376]

The much stronger methanol-including form of the hexa-quinol, in which the guest was retained for a year without change (measured by TGA) and was not removed <u>in vacuo</u> (8 hrs), is likely to be a different structure in which the phenolic groups are hydrogen-bonded to other phenolic groups. Additionally, since methanol and not ethanol or isopropanol was included, this may well indicate a tight clathrate structure; alternatively (but much less probably) the methanol (1:1 host to guest by ^{1}H n.m.r. and TGA) may be involved in closed hydrogen-bonded loops with the phenolic functions. The i.r. spectra of the unsolvated material, the methanol inclusion compound and unsolvated material obtained by removing the methanol at 20°C during thermograviometry, were all identical, suggesting a similarity of hydrogen bonding using phenol groups only.

Hydrogen bonding patterns in the methanol, pyridine and dimethysulphoxide inclusion compounds were all slightly different, though all possessing an extended range of broad stretching frequencies at 3000-2500 cm^{-1} reminiscent of β-hydroquinone.[374]

The major ν(O-H) was observed at 3240, 3200, and 3140 cm^{-1} respectively for the three crystals. The Raman spectra of the methanol and pyridine structures were identical in this area. The methanol host-guest system showed no signs of water inclusion by either ^{1}H n.m.r. or TGA.

Further investigation of the structure of the methanol adduct to see whether it might have adopted a β-hydroquinone double lattice was undertaken with ^{13}C MAS n.m.r. spectroscopy.

Assuming $R\bar{3}$, a normal hexa-host structure would result in equivalent legs and full occupancy. A structure that is the direct analogue of β-hydroquinone with interpenetrating hydrogen-bonded lattices would result in equivalent hexa-host molecules each with two independent legs, and generate four cavities of 3 types for each hexa-host pair, potentially resulting in uneven partial occupancy.

In a rhombohedral R3 structure like this the lattice points are between adjacent stacking pairs of hexa-host and the cages (corresponding to spaces between permanent-permanent, permanent-hydrogen-bonded and hydrogen-bonded-hydrogen-bonded hexa-units) are of different sizes and polarities. A single non-interpenetrating structure would have equivalent legs and cavities but would probably be too open to hold the methanol guest.

The direct β-hydroquinone analogue described has a possible precedent in the structure of phenol clathrates.[375] Recent studies of β-hydroquinone methanol clathrates have also shown less than full occupancy of cages.[376]

The ^{13}C solid-state n.m.r. spectrum of hexakis(p-hydroxyphenoxy)-benzene 1:1 methanol clathrate (Figure 50) is relatively simple in agreement with a high symmetry and virtually constant over -50°C to 80°C in agreement with a tight, ordered structure. The methanol is observed as a sharp singlet. The rhombohedral classification and the long c-axis later found by powder X-ray diffraction studies[356] do not concur with a typical hexahost structure and an open-packed non-penetrating β-hydroquinone structure is very unlikely.

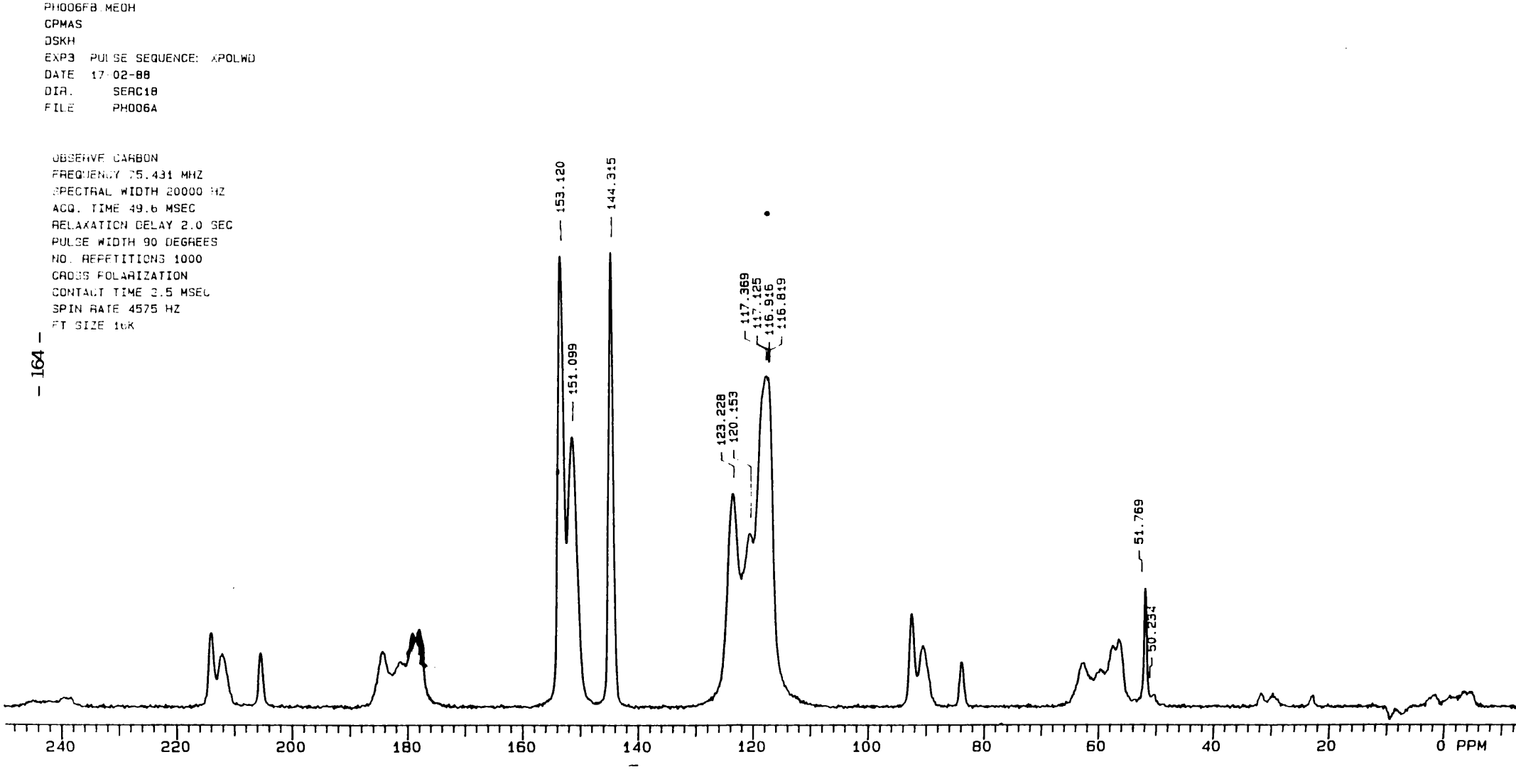


Figure 50 Solid-state ^{13}C n.m.r. of the (168).MeOH adduct.

The desired interpenetrating β-hydroquinone structure is therefore a strong candidate in this case. Such a structure would be in agreement with the solid-state n.m.r. spectrum if the methanol guest was highly localised to cavities between central benzene rings and hydrogen-bonded hexamers, for which two exist per pair of unit cell host molecules, rather than the non-equivalent pair of cavities between two central benzene rings and two hydrogen-bonded hexamers respectively, or any other combination. The sharp MeOH signal could then also indicate the methanol to be highly orientated, with the hydroxyl facing into the hydrogen-bonded hexamer. The c-spacing does allow for a great deal of flexibility in the relative size of the four cavities per pair of unit cell host molecules - the central benzene rings could be relatively close, though unlikely to approach van der Waals contact.

The carbon nuclei show a broad response, but particularly the hydrogen-bearing aromatic leg carbons and one of the oxygen-bearing aromatic ether carbons (presumed to be that of the central benzene ring, δ 151.1). This line broadening could be due to methanol's occupying only the 'temporary-permanent' cages. Within the broad band of hydrogen-bearing carbons is some resolution of the expected inequivalence, including some peaks shifted to lower field relative to the solution spectrum (Figure 51).

Overall, the information is supportive of the β-hydroquinone analogue structure. The non-solvated material (e.g. from larger alcohols) will be a different structure again in the absence of guest or the same structure without guest, depending on the role of methanol in stabilising the structure or otherwise.

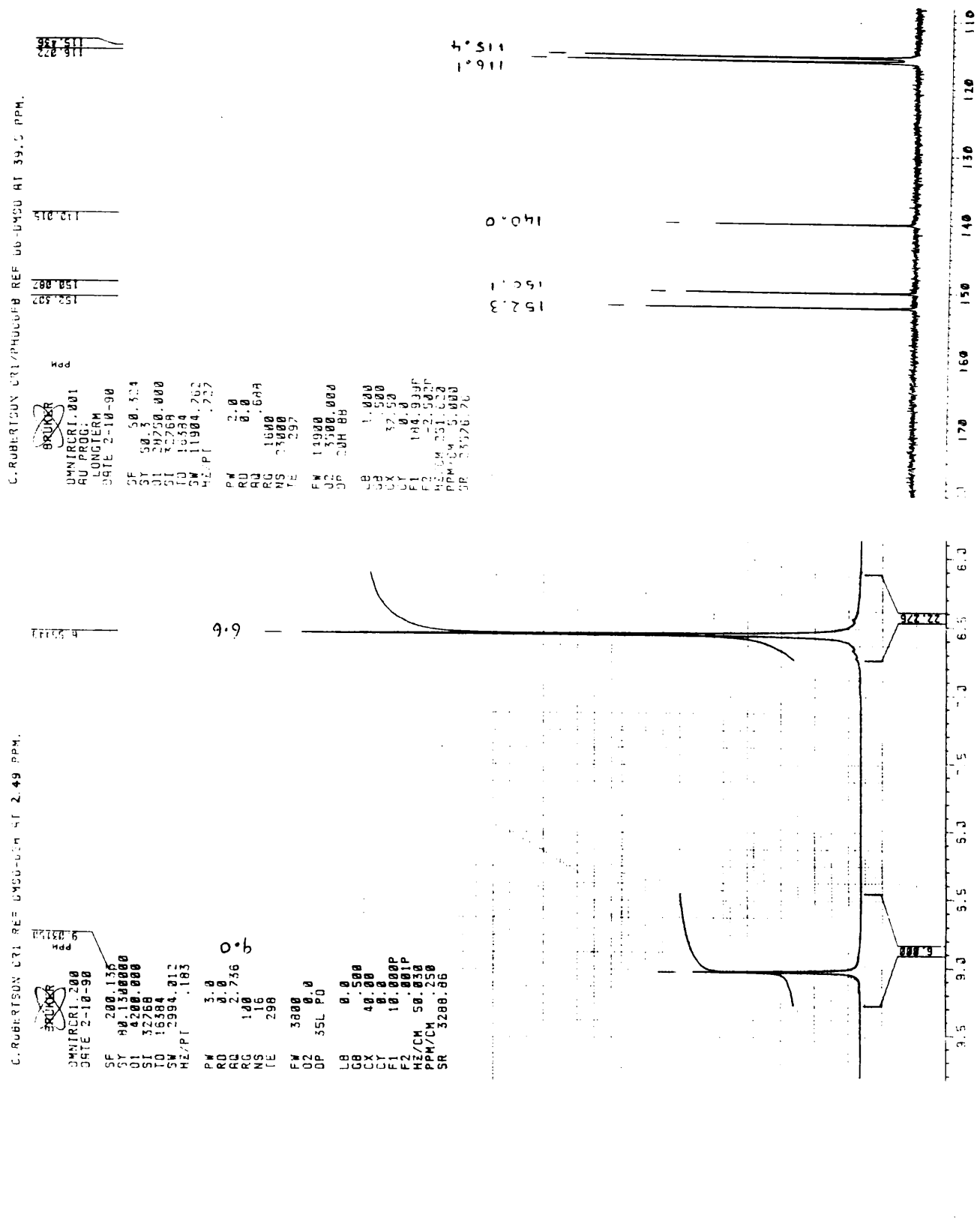


Figure 51 ^{1}H and ^{13}C n.m.r. of (168) in D^{6}-DMSO

Preparation of the thia-analogue of the hexaquinol (168), hexakis-(p-hydroxyphenylthio)benzene (195) was attempted by demethylation of the corresponding hexa-ether (196). Despite purification no crystals could be obtained, and details of the compound were subsequently published elsewhere in the literature : a high melting point, compared to the 3-hydroxy analogue particularly, suggests a strong clathrate may be possible with this compound.[305c] It was also found that uncharacterised material made previously by the direct, unprotected route, similar to the published synthesis, was a different, unidentified, material with a very different (Ar) C-S ^{13}C n.m.r. spectrum (central ring δ 144.3 and 143.6, leg δ 125.8). This may indicate a mixture of compound or two types of central carbon. Both central ring signals are up-field of the published value (lit. δ 148.0). The ^{1}H n.m.r. spectrum (90MHz, CD_3COCD_3) δ 8.50 (s,1H), 7.05 (d,2H), 6.75 (d,2H) was also different from the published spectra (see Experimental).

2.11 Chiral 'legs'

Chiral poly-hosts may occur either by the use of a chiral leg or fortuitous spontaneous resolution of enantiomeric crystals, as yet unseen. Use of a chiral leg has been achieved only once, by oxidation of the sulphur linkage to give a sulphone (129).[225b] A new chiral leg was required with the chirality resident close to the central core but with a normal linkage, and non-enolisable, and relatively large to induce or magnify chiral behaviour.

The terpeneol series appeared a good source of chirality, with fixed axial or equatorial substituents already observed with octakis(cyclohexylthio)naphthalene (164).

Neothiomenthol (197) was prepared according to the method of Beretta et al,[377] using the improved methyl xanthate substitution in DMF.[378] A lower yield was found of thiol, although other fractions of good purity gave a similar total yield, but the best material had a far higher optical rotation (+56.8° - 62.2) than that reported, +47.8°, using the DMF route. This figure is higher than reported in a later estimate from diasteriomeric resolutions (+53.2°)[379] and an alternative synthesis (53.9°)[380]. Use of DMEU instead of DMF did not improve the yield significantly, although the cruder fractions were less discoloured, but it did give rise to a more difficult separation under vacuum distillation.

Substitution of hexafluorobenzene with neomenthyl thiolate gave the 2,3,5,6 tetrasubstituted product (198). This product was particularly well characterised by m.s., ^{19}F and ^{13}C 50 MHz n.m.r. A simulated ^{13}C spectrum (PANIC) for the leg-bearing carbon was in close agreement to that found (Figure 52). Further substitution could not be effected even in HMPA and with cryptand (26), or by using the smaller thiophenolate leg. Reaction of the thiolate with octafluoronaphthalene gave an uncharacterised red oil containing many ^{19}F n.m.r. fluorine signals, suggesting a mixture of partly substituted products.

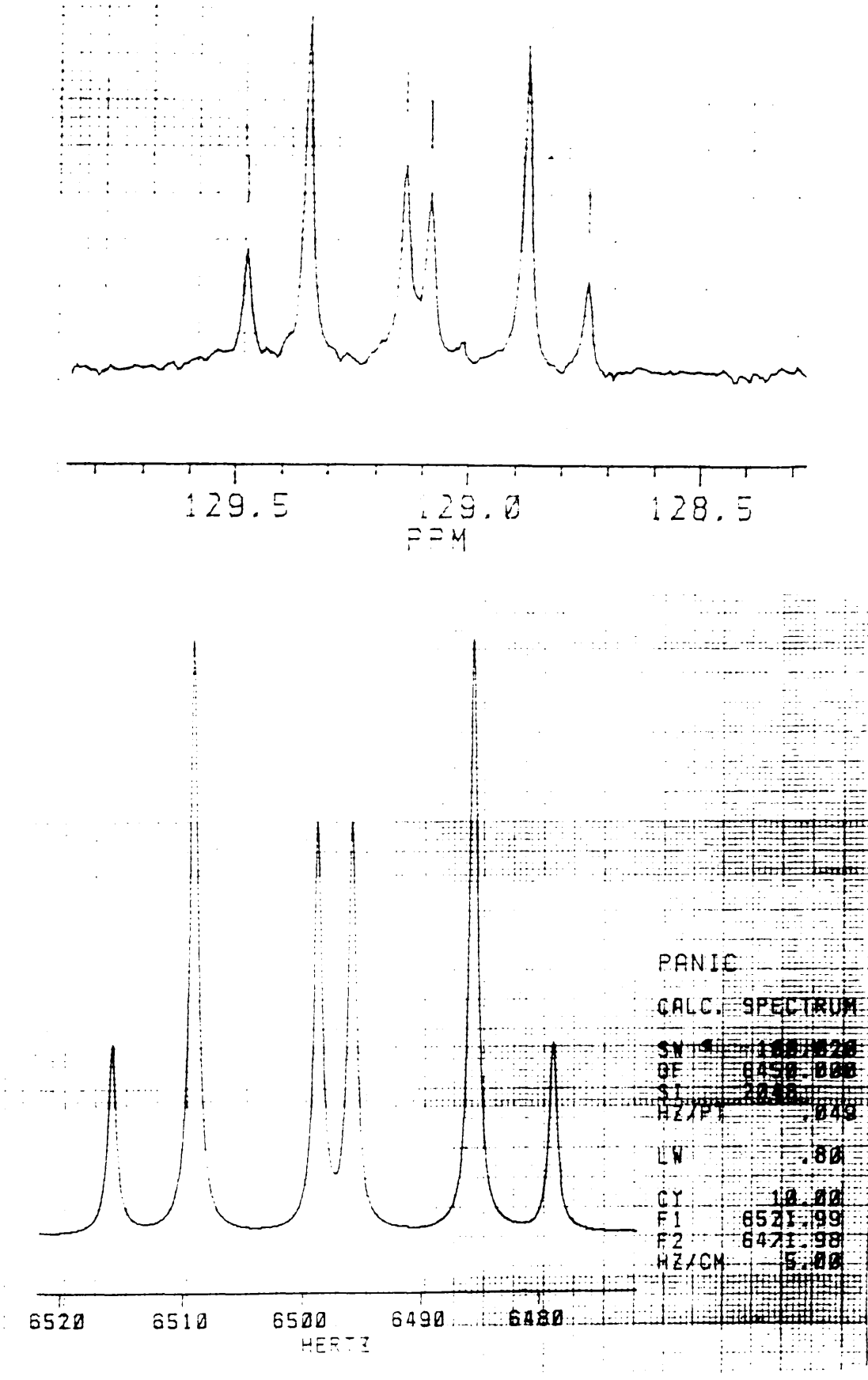
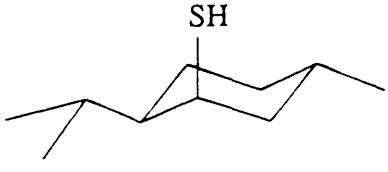


Figure 52 A comparison of the ^{13}C n.m.r. signal for the leg-bearing carbon in (198), above, with a PANIC simulation, below.

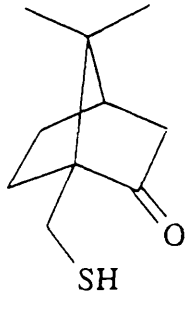
Preparation of other menthylthiols was abandoned as it was unlikely complete substitution would be possible. Substantial amounts of alkene by-product from elimination reactions would also tend to reduce yields even further in these syntheses (from axial substituents).

Despite its large size, reaction of the chiral salt leg derived from (1R)-(-)-10-thiocamphor (199) gives complete reaction with octafluoronaphthalene. Although the compound (200) needs full investigation, preliminary results indicate inclusion of sec-butanol, a racemic guest, at a 1:1 mole ratio. The crystals were too small for single-crystal X-ray diffraction and no attempt was made to see if either guest enantiomer was preferred. No other guests have been tried.

The large leg size and its chiral nature may make this inclusion compound an ideal type I conformation candidate since the chirality is both fairly close to the core naphthalene centre and permanent. A chiral induction effect in inclusion is likely.



(197)



(199)

2.12 Pre-organisation, complementarity, symmetry and new hosts

The general concepts of pre-organisation and complementarity and the specific clathrate symmetry rules are illustrated by the results obtained herein. Complementarity of guest (shape, size, dynamics, polarity, interaction, orientation, symmetry and chirality) to the cavity has occurred to varying degrees. Pre-organisation relates to those features enabling the lattice to choose a non-close-packing alternative, as with (134). Rigidity, good regiosubstitution and conformational directions of groups in the host molecule can pre-organise a required microstructure of the lattice. Functional interactions can also be viewed as a form of built-in pre-organisation (not unlike the special specificities associated with particular series of directed functional groups in biochemistry), if their molecular organisation is taken into account as with (168). Potential pre-organisation of cavities is implicit in strategies using molecular angularity and concavities, and aromatic groups are good 'pre-fabricated walls'. These features are provided by the legs used in poly-hosts and their correct regiosubstitution. An important factor associated with pre-organisation is the 'pre-elimination' of non-inclusion alternatives, i.e. the absence of non-usefully contributing features. In clathrates, symmetry can perhaps fulfil this role.

Undoubtedly symmetry is more prevalent in host molecules than in non-hosts. An obscuring factor may be the tendency to synthesise mainly symmetric cases and indeed, this is possibly compounded by the relative ease of synthesising symmetric molecules, particularly when large molecular structures are attempted.

The actual frequency with which symmetry occurs in host molecules and their lattices compared to non-inclusion molecules and lattices has, however, been shown to be pertinent by the results of an exploratory search of the crystallographic database amongst R3 and $R\bar{3}$ systems. By implication host molecular symmetry is valuable as a means of promoting crystallographic symmetry.

Symmetry in hosts may, then, be described as a 'pre-organised' method of amplifying the presence of a desirable feature and its regiochemistry, as well as of minimising unwanted features. A lattice structure could become favourable by the pre-organised propagation promoted by host symmetry and repetitious favourable interactions; indeed, non-host-derived lattice symmetry elements are equally valid in this respect, but less predictable. The type of symmetry and its nature of operation require further work. The roles of C_2 and C_3 symmetry are not necessarily equivalent; particular types of C_2 symmetry are perhaps more useful than others.[251] Centrosymmetric structures may offer advantages over non-centrosymmetric ones. Although symmetry may not appear as immediately important as good structural features, it may favour from amongst those possible structures of similar energy levels the selection of an open-packing or inclusion mode.

Ideas for host design can be linked to analysis of known lattice structures and pre-organisation. Identification of essential lattice units and their subsequent pre-organisation by incorporation into different molecules may lead to new, not necessarily chemically or structurally related, hosts. Liquid clathrates[106] are a good example of the first and the hexa-host concept is the major example of the latter line of thinking.[223b,225b] Advantageous conformational restriction of known hosts (Toda)[232] or linking of co-operating units (Weber)[240] is possible (see Introduction section 2.2). Pre-organisation by space-group restriction (Bishop) has been successful.[103] The opposite tack to pre-organising could be invoked, e.g. cyclamers (covalent bonds replaced by hydrogen bonds)[273] or acetylenic alcohols (cutting the unit in half)[233] are retrospective examples of replacing a bonded unit with smaller components still having the required complimentarity for organisation.

Having pre-organised a feature or special design element, other changes in molecular design can be attempted. Thus favourable features of the hexa-host concept design allow for useful development in the direction of octa-hosts and more extended linear systems, coronenes,[385] 'piedfort-type' hosts (pairs of 1,3,5-substituted benzenes, sandwiched at the central benzene ring) and the refinement of hexa-host legs to mimic and reconstruct the structures of the older clathrates such as hydroquinone.[356]

In the absence of suitable symmetry, shape or any other rationale, it is highly unlikely that even the smallest modification of a host would lead to retention of inclusion properties. Increasingly success in inclusion is not left to chance, but specifically designed and incorporated into (host) molecular features. Extension of the hexa-host concept has led to new hosts.

EXPERIMENTAL

General Procedures and Instruments

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, sh - shoulder. Ultra-violet spectra were recorded on a Pye Unicam SP8-100.

Proton nuclear magnetic resonance (n.m.r.) spectra were determined on a Perkin-Elmer R32 (90 MHz) spectrometer using tetramethylsilane (TMS) as internal standard and both Varian XL100 (100 MHz) and Bruker WP 200SY (200 MHz) spectrometers using the detuerated solvent as reference signals.

Carbon n.m.r. spectra were determined on the latter two instruments at 25 MHz and 50 MHz respectively, signals relative to the detuerated solvent and proton noise decoupled. Fluorine n.m.r. spectra were determined on the Varian XL100 (94 MHz) spectrometer using $CFCl_3$ at 0 ppm as an internal standard. Solid-state carbon n.m.r. spectra were obtained through the S.E.R.C. service at Durham University, and 360 MHz high field n.m.r. was provided by Dr. I. Sadler, Edinburgh University. The following abbreviations are used: s-singlet, d-doublet, t-triplet, q-quartet, m-multiplet, 2C - two overlapping carbon signals.

Routine mass spectrometry (<900 amu) was determined using a VG/Kratos MS 12 spectrometer and high resolution spectra were recorded on a VG/Kratos MS 9025 spectrometer. Mass spectrometry for compounds >900 amu was provided by the S.E.R.C. m.s. service, Swansea College.

Guest-Host ratios were determined (unless otherwise stated) by ^1H n.m.r. solution spectra signal ratio's. A Du-Pont Model 990 Thermal analyser with 951 TGA accessory was also used in measuring inclusion ratio's.

Column chromatography was performed using Fluka Kieselgel HF_{254} and, for flash chromatography Merck Kieselgel 60 230-400 mesh. Preparative thin layer chromatography (t.l.c.) was performed using 20 x 20 cm glass plates pre-coated with 2 mm of Merck Kieselgel 60 F_{254} (No.5717). Qualitative reverse-phase t.l.c. was performed using Macherey-Nagel Duren nanosilica C18 $100UV_{254}$ 0.20 mm plates. Merck 0.2mm pre-coated aluminium foil (No.5554) and plastic (No. 5735) plates were also used.

A Heat Systems Ultrasonics Model W-380 ultrasonic processor with a Model 431B cup horn accessory was used in UHF sonic experiments.

Starting Materials and Solvents

Perfluorodecalin (1) supplied by Fluorochem as a practical grade mixture of cis- and trans- isomers was used unless stated otherwise. It was re-analysised by the manufactures (ISC chemicals) and found to be of correct specification; content perfluordecalin 96.5% as 54.5% cis- and 41.9% trans-isomer by g.l.c. Additionally, no hydrogen or unsaturation was detected by Raman, F.T.I.R. (thick film), ^{1}H (100 MHz) NMR or ^{19}F (94 MHz) n.m.r. spectroscopy; all of these methods gave results in accord with the perfluorodecalin structure.

Perfluoromethylcyclohexane (4), perfluorohexane (154) and perfluoroheptene (140) were also supplied by Fluorochem and used as received.

Perfluorocyclohexane (98%) (8), perfluorocyclohexene (145), perfluorodecal-9,10-ene (91%) (142) and perfluoroperhydroanthracene (90%) (184) were supplied by the University of Birmingham (Dr. P.L. Coe and J. Burdon). Poly(tetrafluoroethane) was in the form of Fluoroport T (Teflon 6) column packing supplied by Applied Science Laboratories Inc. FEP (fluorinated ethylene propylene) polymer was in the form of shavings of tubing. (1R)-(-)-10-thiocamphor was available in the laboratory.

1,3-Dimethyl-2-imidazolidone (DMEU) was supplied by Fluka (Purum, > 99%) and Aldrich (AR, 99%) and dried over calcium hydride prior to distillation (0.5 mm Hg, 52.5°C) and storage over 4Å molecular sieves.

Dimethylformamide was similarly dried, distilled and stored. Hexamethylphosphoramide (HMPA) was dried over sieves before use. Tetrahydrofuran (THF) was dried by refluxing over sodium and benzophenone, and freshly distilled before use. Ethanol was dried with sodium and ethyl phthalate.[382] DMEU was recovered using a procedure for the cyclic urea homologue DMPU (N,N'-dimethyl-N,N'-propylene urea).

Preparation of Compounds

1. Preparation of sodium arylthiolate salts

a) example preparation of sodium benzenethiolate

In a flushed three-necked flask equipped with a condenser bearing a three-way tap with a balloon connected to an argon cylinder, rubber septum stoppers and a magnetic stirrer was placed sodium hydride 60% dispersion in oil, 7.422g (186mmol). The hydride was washed with 3 x 50ml aliquots of sodium-dried pentane and then dried at 0.1mm Hg). Under argon 15ml of freshly distilled THF was added and the contents cooled to -78°C. Thiophenol (97%), 21.46g (195 m moles) was dissolved in 45ml THF and injected, and then the reaction allowed to warm slowly to room temperature, allowing excess pressure to escape occasionally. The reaction was gently refluxed until all the hydride was reacted and then the solvent removed on a rotary evaporator. The product was dried *in vacuo* until no further weight loss occurred. ^{1}H n.m.r. (d^6- DMSO) of the sodium benzenethiolate (31.40g) determined the product to contain *ca* 2/3 mole THF per mole salt.

b) example preparation of sodium m-tolylthiolate

Under an argon atmosphere as described in example a) sodium 3.0 g (0.125 mmol) was dissolved in 50 ml ethanol (super-dry) and *m*-methylbenzenethiol 17.08 g (0.138 mmol added. After completion of reaction the solvent was removed on a rotary evaporator and the product washed with sodium-dried ether until odour-free. The sodium *m*-tolylthiolate was dried to constant weight and ^{1}H n.m.r. (d^6-DMSO) indicated no solvent to be present.

2. Preparation of octakis(phenylthio)naphthalene (131) from (1)

a) In a 100ml conical flask equipped with a rubber septum and a magnetic stirrer was placed sodium benzenethiolate complex with THF (example 1 a)), 6.633g (36.8mmol) and 30ml of de-gassed DMEU. The salt was dissolved and oxygen removed by stirring in vacuo (via a needle). Under argon, perfluorodecalin (1) 0.742g (1.61 mmol) was injected and the insoluble fluorocarbon stirred vigorously. After some weeks the colour deepened, and was deep red after 2 months; a white precipitate was present. T.l.c. of aliquots gave two spots only, corresponding to the product and diphenyldisulphide. After seven months a sample of unreacted perfluorodecalin was withdrawan and washed with DMEU. ^{19}F (94MHz) n.m.r. was identical to that of the starting material, showing no change in the isomeric ratio.[349C] A portion of the reaction mixture was dissolved in toluene, causing further precipitation. The white solid was washed with chloroform and dissolved in distilled water. A reading of 10^{-2} molar was obtained with a fluoride sensitive electrode. The solid did not melt on hot plate apparatus (320°C). The reaction mixture was dissolved in 30ml toluene and washed with distilled water (2 x 20ml) and then with tap water (8 x 50m).

The portion of distilled water washings was bubbled with oxygen until no more disulphide was formed, keeping the solution acidic, and then filtered, washed with chloroform and buffered (potassium hydrogen phthlate, sodium hydroxide). The fluoride content was measured with an ion-sensitive electrode at 3 x 10^{-3}M against a background of 1 x 10^{-6}M. The toluene and water were removed by azeotrope from the organic phase on a rotary evaporator to leave solid, 0.522g. This was dissolved in chloroform and diphenyl disulphide removed on a silica chromatography column (eluent petroleum ether-chloroform 4/1). The red product was transferred to a silica preparative t.l.c. plate and eluted twice (petroleum ether; petroleum ether-chloroform 1/1). The product after isolation from chloroform was 0.264g of octakis(phenylthio)-naphthalene (131), 17% yield. Recrystallisation from cyclohexane gave material with physical and spectroscopic properties fully in accord with that of the title compound prepared from octafluoronaphthalene and of structure unambigously determined by x-ray single crystal diffraction. Diphenyl disulphide, 0.231g, was recovered, corresponding to ca 4 moles per mole octakis-(phenylthio)naphthalene (131).

m.p. 205-206°C; ν max (selected) 3055(m), 1580(s), 1475(s), 1440(s), 1025(s), 735(s), 700(s) and 685cm^{-1}(s); δH (90MHz, ($CDCl_3$) 7.3-6.4 (m),; δC (25MHz, CCDCl3) 125.7(d), 146.5(d), 127.3(d), 128.5(d), 128.7(d), 129.6(d), 137.4(s), 138.7(s), 139.1(s), , 140.9(s), and 142.9(s); ^{19}F : no spectrum observed. (high res) 992.0901 [M^+] 884.0845 [M^+-SC_6H_4]; m/e 992 (linked scan) [M^+] 915.57;

b) A reaction mixture of 537mg (2.98 mmol) of sodium benzenethiolate complex and 22mg perfluordecalin (1) (0.048mmol) in 4ml DMEU, prepared according to the method of example 2a), was heated in an oil bath (temperature 60-70°C) for ten days; red colouration visible after five days. The reaction mixture was worked up according to the usual method to give 94mg product. Purification with silica preparative t.l.c. gave 31mg of product, 65% yield. The crystalline product (ex cyclohexane) was identical to that from example 2a).

c) In the manner of example 2b) 577mg sodium benzenethiolate complex and 26mg perfluorodecalin (1) in 4ml DMF gave product, 55% yield. The crystalline product (ex cyclohexane) was identical to that from example 2a).

d) In the manner of example 2b542mg sodium benzenethiolate complex and 23mg perfluorodecalin (1) was placed in an ultrasonic cuphorn 384 and adjusted to maximum tuning (ca. 40% power). The mixture was sonicated for 8 hours both on continuous and 50% pulsed. No colour was observed.

e) In the manner of example 2b) sodium benzenethiolate complex 2.66g (14.8 mmol) was reacted with 95mg perfluorodecalin (0.21 mmol) [Medical grade] in DMEU for 10 days at 70-80°C. After isolation and removal of diphenyl disulphide three products were present, separated by preparative silica t.l.c. (toluene-cyclohexane 3/1). In order of highest R_f the products were i) red, 6mg, ii) orange, 33mg, and iii) yellow, 59mg.

The red material had spectroscopic properties fully in accord with those of octakis(phenylthio)naphthalene (131) and co-spotted with authentic material under t.l.c. Yield 3%. The orange material had the following spectroscopic details, consistent with heptakis(phenylthio)naphthalene (138/139).

Yield 17%, δ_H (90MHz, $CDCl_3$) 7.9(s) 7.4-6.5 (m) [ratio of peaks ca 1:60] δC (25MHz, $CDCl_3$) 146.8-125.0 (many peaks); m/e 884 [M^+], 852 [M^+-32, 100%] 807 [M^+-77], and 776 [M^+-98].

The yellow material had the following spectroscopic details, consistent with heptakis(phenylthio)naphthalene (138/139). Yield 33; δ_H (100MHz, $CDCl_3$) 7.9(s), 7.35-7.0 (m), 6.7-6.6 (m); δC (25MHz, $CDCl_3$) 145.7-125.4 (many peaks); m/e 884 [M^+], 852 [M^+-32], 807 [M^+-77], and 776 [M^+-98 100%]. Total yield 53%.

3) Preparation of octakis(m-tolythio)naphthalene) (134) from (1)

Sodium m-tolylthiolate, 2.840g (19.5 mmol) was reacted with perfluorodecalin 200mg (0.433 mmol) in 15ml DMEU according to the method of example 2a. The red colour and white precipitate developed more quickly and the reaction was worked-up after eight weeks in the normal manner. The product was purified with silica using preparative t.l.c. plates (R_f 0.44, chloroform-petroleum ether 40-60^0 3/2) to give 93mg of (134), a 20% yield.

Crystals obtained on recrystallisation from toluene had properties fully in accord with octakis(m-tolylthio)naphthalene (134) prepared from octafluoronaphthalene (2) and structure unambiguously determined by X-ray single crystal diffraction, and co-spotted under t.l.c., m.p. 156-157°C; ν max (selected) 3030 (m), 2920(m), 1590(s), 1575(s), 1475(s), 1220(m), 1170(m), 1120(m), 1080(m), 1040(m), 1000(m), 875(m), 855(s), 780(s), 690(s), and 430CH^{-1}(m); δ_H(100MHz, $CDCl_3$) 2.15 (12H,s), 2.2 (12H,s), and 6.2-7.1 (32H, (m)); δ_F no spectrum observed; m/e 1104 [M^+], 981 [M^+-SC_7H_7], and 858 [M^+-2 (SC_7H_7)]; m/e (high res) 1104.2157.

4. Preparation of octakis (m-methoxyphenylthio)naphthalene (135)

Sodium m-methoxyphenylthiolate, 8.31g (51.3 mmol) was prepared according to the method of example 1, and reacted with perfluorodecalin(1) 0.567g (1.227 mmol) in 20 ml DMEU according to the method of example 2a. Colouration took place after two months and after seven months the product was isolated according to the normal method to give 136mg of coloured products and 700mg of diphenyl disulphide. T.l.c. in $CHCl_3$ gave the main product at R_f=0.34 and four other products at lower R_f; this pattern of products was identical to material isolated from octafluoronaphthalene as starting material.

The compounds were separated using preparative t.l.c. with chloroform eluent and the following fractions obtained:

a) red, 72mg, R_f=0.34
b) orange, 7mg, R_f=0.12
c) orange, 8mg, R_f=0.08
d) pink-orange, 4mg, R_f=0.06
e) various, 5mg, R_f<0.05

The main fraction had spectroscopic properties identical to those of the title compound made from octafluoronaphthalene purified and structure unambiguously determined by single crystal diffraction. Yield 5%, δ_H (90MHz, $CDCl_3$) 7.2-6.0, (32H), 3.63(12H), and 3.69(12H); δ_C (25MHz, $CDCl_3$) 159.8($2C_1$s), 144.9(s), 140.6(s), 140.3(s), 140.0(s), 138.8(s), 129.6(d), 129.5(d), 120.8(d), 119.9(d), 114.2(d), 113.2(d), 112.2(d), 111.9(d), 55.3(q), 55.1(q); m/e 1232 [M^+, 100%], 1218 [M^+-CH_2], 1202 [M^+-OCH_2], 1125 [$M^+-C_6H_4OCH_3$], and 1094 [$M^+-SC_6H_4OMe$, 56%].

The second fraction had the following spectroscopic properties, δ_H (100MHz, $CDCl_3$) 7.25-5.9 (m), and 3.74-3.66 (m) ratio 4H:3H; δ_C (25MHz, $CDCl_3$) 171.0-149.7 (various), 140.6-138.8 (various), 134.3-111.3 (various), and 55.6 and 55.2; m/e 1232 (56%), 1218, 1125, and 1094 (100%).

The third fraction had the following mass spectrum m/e 1232 (31%), 1218, and 1094 (100%).

5. Preparation of octakis(phenylseleno)naphthalene (175) and hexakis(phenylseleno)naphthalene (159) from (1)

Similar to the method of example 1a sodium benzeneselenoxide 1.54g (8.6 mmol) was reacted with perfluorodecalin (1), 0.188g (0.255 mmol) in DMEU in the dark at ambient temperature. After eight months all the decalin had reacted and the reaction mixture was worked-up in the normal manner. A yellow precipitate, 169mg, was filtered from the toluene solution of products, m.p.. 240-246°C. The organic phase gave 0.921g of red product which was purified by trituration with MeOH and then with silica using column chromatography (Petroleum ether 60-80°C-methylene chloride gradient) to give 170mg of red material.

The yellow material was recrystallised from carbon disulphide. Crystals m.p.. 244-246°C had the following spectroscopic properties in accord with the structure hexakis(phenylseleno)naphthalene. Yield 55%, δH (100MHz, $CDCl_3$) 8.05 (s,1H), and 7.5-6.6 (m,15H); m/e 1060[M^+]. The red material co-spotted under t.l.c. with authentic octakis(phenylseleno)-
naphthalene (175) prepared from octafluoronaphthalene and structure unambiguosly determined by single crystal X-ray analysis. Yield 49%. The material contained some solvent as evidence by ^1H n.m.r., δ_H (100MHz, $CDCl_3$) 6.6-7.7, and 0.7-1.7.

6. Enhanced preparation of octakis(m-tolylthio)naphthalene (134) from (1) using sodium metal at ambient temperatures

Two reaction mixtures A and B were prepared from the same sources of perfluorodecalin (1), DMEU and sodium m-tolylthiolate using the procedure of example 3 these being identical apart from the additional inclusion of ca. 0.5g sodium metal in small pieces to B. A and B were reacted simultaneously for eight weeks at ambient temperature before being worked up as described in example 3 with in the case of B additional removal and toluene washing of unreacted sodium from the toluene solution of product prior to water-washing the combined toluene solutions. In this manner A (containing 0.103g perfluorodecalin, 8ml DMEU and 1.30g sodium m-tolylthiolate gave 68mg of product (27% yield) whilst B (containing 0.108g perfluorodecalin, 8ml DMEU and 1.37g sodium m-tolylthiolate gave 101mg of product (39% yield), both products having m.p. 156-157°C and co-spotting under t.l.c. with authenticated samples of octakis(m-tolylthio)naphthalene(134).

7. Enhanced preparation of octakis(m-tolylthio)naphthalene (134) using sodium metal at elevated temperature

Two reaction mixtures A and B were prepared from the same sources of perflourodecalin (1), DMEU and sodium m-tolylthiolate using the procedure of example 3, these being identical apart from the additional inclusion of ca. 0.5g sodium metal in small pieces to B. A and B were reacted simultaneously in the same bath at 50-60°C for five days before being worked up as described in example three with in the case of B additional removal and toluene washing of unreacted sodium from the toluene solution of product prior to water-washing the combined toluene solutions. In this manner A (containing 0.125g perfluorodecalin, 10ml DMEU and 1.58g gave 42mg of product (14% yield), whilst B (containing 0.120g perfluorodecalin, 10ml DMEU and 1.52g sodiun m-tolylthiolate) gave 133mg product (46% yield), both products having m.p. 156-157°C and co-spotting under t.l.c. with authenticated sample of octakis(m-tolylthio)naphthalene.

8. Diminished preparation of octakis(m-tolylthio)naphthalene (134) from (1) in the presence of nitrobenzene

Two reaction mixtures A and B were prepared from the same sources of perfluorodecalin DMEU and sodium m-tolylthiolate using the procedure of example 3, these being indentical apart from an additional 10% v/v charge of toluene to A and of nitrobenzene to B. A and B were reacted simultaneously at 50-60°C for five days before being worked up as described in example three. In this manner A (containing 0.120g perfluorodecalin, 9ml DMEU, 1ml toluene and 1.67g sodium m-tolylthiolate) gave 29mg product (10% yield) whilst B (containing 0.144g decalin, 9ml DMEU, 1ml nitrobenzene and 1.82g sodium m-tolylthiolate) gave 2mg product (<1% yield) after removal of nitrobenzene on a silica chromatography column (petroleum ether-methylene chloride graded eluent). Both products had m.p. 156-157°C and co-spotted under t.l.c. with authenticated samples of octakis(m-tolylthio)naphthalene (134).

9. Preparation of hexakis(phenylthio)benzene (124) from (1)

Using the method described in example 2 sodium benzenethiolate complex 630mg (3.50mmol) was reacted with perfluorocyclohexene 7.5mg (0.029mmol) in 4ml DMEU at room temperature for 72 hours. The crude product, 23.5mg, obtained after the usual work-up and purification with silica preparative t.l.c. (40-60 Petroleum ether; chloroform) contained trace toluene (^{1}H n.m.r.) and was recrystallised from 1,1,1-trichloroethane to give 21mg of the 1:1 clathrate. Yield 96%. The crystals m.p. 185-186°C had spectroscopic properties identical with those of an authentic sample of hexakis(phenylthio) benzene (124) prepared from hexafluorobenzene and structure unambiguously determined by X-ray single crystal diffraction, and co-spotted on t.l.c. (SiO_2C_{18} R_f=0.21, MeOH; SiO_2 R_f=0.48,hexane/ chloroform); δ_C (25MHz, $CDCl_3$) 148.1(s), 137.7(s), 128.9(d), 128.2(d), and 126.2(d), (host); δ_H (90MHz, $CDCl_3$) 7.25-6.85 (m, 30H) and 2.75 (s, 6H), (clathrate); max selected 3070(m), 3010 (w), 3000(w), 2950(w), 1580(s), 1480(s), 1440(s), 1075(s), 1025(s), 7040(s), 7035(s), 700(s), and 690(s), (clathrate); m/e 726 (M^+), 650 (M^+-C_6H_4), and 616 (M^+-HSC_6H_5), (clathrate).

10. Preparation of octakis(phenylthio)naphthalene (131) from (142)

Using the method described in example 2 sodium benzenethiolate complex 1.49g (8.3 mmoles) was reacted with perfluorodecal-9-10-ene, 91%, 0.0775g (0.18 mmoles). After 72 hours at room temperature the reaction was worked up in the normal fashion and purified with silica chromatography (40-60° petroleum ether-methylene chloride graded eluent). The product, 163mg, 99% yield co-spotted under t.l.c. with authentic octakis(phenylthio)naphthalene. Recrystallisation from cyclohexane-methylene chloride gave 156mg of crystals m.p. 205.5-206.5 containing ca 1.5 moles methylene chloride guest and with spectroscopic properties identical to those of the title compound made from octafluoronaphthalene and structure unambiguously determined by X-ray single crystal diffraction.

11. Attempted Preparation of hexakis(phenylthio)benzene (124) from perfluorocyclohexane (8)

a) Using the procedures described in example 2 perfluorocyclohexane (containing 2% of perfluorocyclohexene), 0.103g (0.34 mmoles) was reacted in 5ml DMEU with 1.580g sodium benzenethiolate complex 18.77 mmoles at 60-70°C (bath temperature) for 10 days. After work-up and isolation 3mg of product co- spotting under t.l.c. with authenticated hexakis(thiophenyl)benzene (128) was obtained, m.p. 185-186°C (ex cyclohexane).

b) Similarly to example 11a) 0.084g perfluorocyclohexane (containing 2% of perfluorocyclohexene), 0.28 mmol, was reacted in 5ml DMEU with 1.22g (16.78 mmoles) sodium benzenethiolate complex at room temperature for 12 hours. 1mg of product co-spotting under t.l.c. with authenticated hexakis(phenylthio)benzene (128) was obtained.

12. Attempted reaction of perfluorohexane (154)

Perfluorohexane, 29mg, (0.87 mmoles) was reacted with 610mg (3.39 mmoles) sodium benzenethiolate complex in 6ml DMEU for 10 days at 60°C according to the method for example 2b. No fluorocarbon was recovered, no products were obtained and significant fluoride levels were not detected in the aqueous wash (4×10^{-5} M); some disulphide was formed.

13. Attempted reaction of perfluoroheptene (147)

a) Perfluoroheptene (147), 32mg, (0.091 mmoles) was reacted with 856mg (4.76 mmoles) sodium benzenethiolate complex in 10ml DMEU at room temperature for 14 days according to the method of example 2a. The product, a yellow oil which solidified on standing, weighed 105mg and was composed of many products according to t.l.c. (silica, 60-80 Petroleum ether- methylenechloride 2/1), with the main product of highest R_f. Mass spectral analysis m/e 904, 864, 852, 832, 814, 795, 775, 757, 743, 722, 705, 687 (100%), 671, 646, 634, 618, 610, 596, and 578.

b) Similarly to example 13a) perfluoroheptene (147), 29mg (0.083 mmoles) was reacted with 792mg (5.42 mmoles) sodium p-tolylthiolate in 10ml DMEU at room temperature for 14 days. The product, a brown oil, solidified on standing, weighed 109mg and was composed of many products according to t.l.c., with the main product of highest R_f. Mass spectral analysis m/e 1102 [M+] 898, 881, 850, 832, 814, 794, 775, 757, 728, 709, 687, 671 (100%), 653, 634, 605, 586, 561, 548, 530, 507, 497, 479, 457, 437, 425, and 406.

14. Reaction of perfluorodecalin (1) with sodium p-methoxyphenolate

a) Perfluorodecalin (1), 0.318g (0.69 mmoles) was reacted with 4.35g (29.8 mmoles) sodium p-methoxyphenolate in 20ml DMEU for 2 weeks at room temperature according to the method of example 2a. The isolated product, 273mg, contained no fluorine (^{19}F n.m.r.) and no naphthalene derivatives (13C n.m.r.); the first aqueous washes contained little fluoride ($3 \times 10^{-4}M$) ion and the perfluorodecalin was largely recovered (0.295g).

b) Perfluorodecalin (1), 0.738g (1.60 mmoles) was reacted with sodium p-methoxyphenolate, 7.22g (49.5 mmoles) in 50ml DMEU at 90°C for 2 weeks, similar to the method described in Example 2b. After isolation of black product ca 0.5 g, the first aqueous washes contained fluoride ion ($1.3 \times 10^{-3}M$) significantly higher than background readings ($10^{-6}M$) and only 501mg of perfluorodecalin was recovered. The product, containing many impurities similar to those products in example 14a), had a wide ^{19}F n.m.r. spectrum: δ_F (94 MHz, $CDCl_3$), (-78),(-77), (-81), (-103), (-111), (-141), and (-151) [decalin (1): (-177) - (-141), and (-189)][349C]; δ_H (90MHz, $CDCl_3$) 7.2-6.6 (m, 4H), and 3.9-3.6 (m, 3H).

15. Reaction of perfluoromethylcyclohexane (4)

Perfluoromethylcyclohexane (4), 0.434g (1.24 mmoles) was reacted with 5.88g (32.7 mmoles) sodium benzenethiolate complex in 20ml DMEU at 50°C for 16 weeks according to the method of example 2a. A red colouration developed after two weeks. After isolation of the crude product, 163mg, diphenyl disulphide was removed using chromatography (Petroleum ether) to leave ca. 5mg of a red solid shown by t.l.c. to comprise at least two major products. Mass spectrometry showed two parent peaks at m/e 686 and 634 corresponding to pentakis(phenylthio)trifluoromethylbenzene (155) and tetrakis(phenylthio)di(trifluoromethyl)pentadiene (157) respectively and a major peak at m/e 526 corresponding to loss of phenylthio from the latter product. Other leg losses were identifiable. Some small higher weight peaks were observed, highest m/e 794.

Further purification with silica (petroleum ether) isolated the main product fraction, 2mg, after two plates. Mass spectrometry showed parent peaks at m/e 686 (and related leg losses) and m/e 596 corresponding to tetrakis(phenylthio)fluorotrifluoromethylbenzene (156) and m/e 524 (not assigned); δ_H (100MHz, $CDCl_3$) 7.37-6.85 (m).

16. Attempted reactions of poly(tetrafluoroethane) ['teflon']

Teflon 6 was stirred in solvent (DMEU, DMF, or HMPA) with an eight fold excess per 'fluorine' of thiolate nucleophile (sodium benzenethiolate complex, or sodium polysulphides[385]) at room temperature for several months or at 60-80°C (over several days, and sometimes in the presence of [2,2,1] cryptand, similar to the method of example 2a). Reactions were drowned out into distilled water and the teflon washed with methylene chloride and water, then dried in vacuo over P_2O_5. The aqueous washings were treated as outlined in example 2a) and monitored with fluoride ion sensitive electrodes. [Blanks were performed corresponding to conditions of 'no time', 'no teflon', 'no salt', 'no solvent' and with added weights of fluoride ion]. The isolate teflon was generally of the same weight as starting material but physically changed into a single, transparent film. The aqueous washings did not produce fluoride readings higher than the blanks [10^{-5}-10^{-6}M]; added fluoride ion was traced at 70% recovered [10^{-3}-10^{-4}M].

Thus typically

1) 21.5mg teflon (0.43 mmol 'CF_2') was heated at 60-80°C for ten days in 8ml DMEU with 0.490g sodiumbenzenethiolate complex (2.7 m^2mol), and after isolation 20mg of product were obtained; Fluoride 10^{-6}M.
2) 13.3mg teflon was heated at 60-80°C for ten days in 4ml DMEU and 12.6mg of product were isolated; Fluoride 10^{-6}M.

Electron micrographs of teflon before reaction and after heating in DMEU showed a smooth surface. Electron micrograph of the teflon after reaction with sodium benzenethiolate showed a rippled surface. Reflectance absorbance infrared spectrometry showed that the surface after reaction contained new absorbances from ca ν max 390-3090 cm^{-1} (Figure 53).

17. Reaction of octakis(p-tolylthio)naphthalene (161) with sodium thiophenolate

a) 18.3mg (0.0166 mmoles) of octakis(p-tolylthio)naphthalene was dissolved in 0.5ml degassed DMEU with 1.8mg of sodium thiophenolate-THF (0.01 mmoles) and stirred for seven days. After being worked up in the manner of example 2a t.l.c. on SiO_2C_{18} plates showed no change from the starting material, R_f 0.09 (MeOH). H.p.l.c. of the product is described in part e).

b) As described above, a), 10.0mg (0.0091 mmoles) octakis-(p-tolylthio)naphthalene was reacted with 2.0mg of sodium thiophenolate-THF (0.11 mmoles). H.p.l.c. of the product is described in part e).

c) As described above, a), 9.93mg (0.0090 mmoles) octakis-(p-tolythio)naphthalene was reacted with 4.0mg of sodium thiophenolate-THF (0.22 mmoles). H.p.l.c. of the product is described in part e).

d) As described above, a), 26.0mg (0.0236 mmoles) octakis-(p-tolylthio)naphthalene was reacted with 3.79g (21.1 mmoles) of sodium thiophenolate complex in 15ml DMEU. After ½ hour t.l.c. on SiO_2-C_{18} plates showed no change from the starting material, R_f= 0.09 (MeOH).

After 3 days a single spot co-spotting with octakis(phenylthio)-naphthalene (131) was observed and the reaction worked-up. H.p.l.c. of the product is described in part e).

e) H.p.l.c.

H.p.l.c. was performed using a Perkin-Elmer series 100 pump with Tri-det detector and HS-3 C_{18} reverse phase analytical cartridge column in 100% MeOH. The solvent was eluted at 1ml/min and u.v. detection used to observe products, injected as solutions in ethylacetate.

Compound	Rt (min)
A) octakis(phenylthio)naphthalene	1.7 sharp
B) octakis(p-tolylthio)naphthalene	4.2 sharp
C) product, example a)	4.2 sharp
D) product, example b)	4.2 sharp strong + 3.6 weak, broad
E) product, example c)	4.2 sharp strong + 3.6 weak, broad multiplet
F) product, example d)	1.5 sharp, strong
	1.7 sharp, medium
	2.5 small, broad
	2.9 small, broad

18. Reaction of octakis(phenoxy)naphthalene (166) with sodium-thiophenolate

2mg (0.0023 mmoles) octakis(phenoxy)naphthalene was reacted with 0.5g of sodium thiophenolate-THF complex (2.78 mmoles) in 1ml degassed DMEU at ca. 80°C for 30 hours, in which time the solution turned red. After isolating in the normal manner as described in example 2a the product was dissolved in ethylacetate and run under the following h.p.l.c. conditions, as in example 17:

Step	Time(min)	Solvent composition		Comment
		% MeoH	%H_2O	
0	0.5	90	10	pre-wash
1	0.5	90	10	
2	5.0	100	0	linear rise
3	3.0	100	0	
4	1.0	90	10	linear fall
5	4.0	90	10	equilibration

Compound		Rt(min)	Relative height
A)	octakis(phenylthio)naphthalene	6.9	
B)	octakis(phenoxy)naphthalene	2.6	
C)	product	3.1	6
		5.5	12
		6.1	70
		6.9	24
		7.1	35
		8.6	11

19. Synthesis of oxygen link octahosts : octakis(ß-naphthyloxy-naphthalene (165)

β-Naphthol 9.742g (67.6 mmol) in freshly distilled tetrahydrofuran (THF) was added to a washed (isopentane) suspension of sodium hydride (2.704g 60% dispersion in oil, 67.6 mmol) in THF under argon atmosphere at -78°C. After warming to room-temperature the flask was refluxed on a water bath until no more hydride was visible. The solvent was removed after a fast transfer to the rotary evaporator, followed by pumping (0.1mmHg) to constant weight.

The salt was briefly crushed and the powder added into a long-necked tube with the bottom blown under flushing argon. The neck was narrowed and 0.8512 octafluoronaphthalene (3.13 mmol) added as a solution in DMEU, total 30ml. The tube was carefully evacuated (0.5mmHg) until no further bubbling took place and most of the salt had dissolved. The tube was finally refilled with argon and sealed before heating in an oven at 90°C for eighteen weeks with occasional shaking.

The reacted mixture was poured onto 200ml of ice-water and taken up in 60ml toluene. Eight further 150ml portions of water were used to wash the organic layer, with subsequent drying (sodium sulphate) and removal of solvent leaving 3.46g of a brown solid. This was repeatedly triturated with hot ethanol to remove most of the colour, leaving 2.16g of a white solid (1.71 mmols, 55%), as one spot R_f 0.85, [$CHCl_3$/Petroleum ether 40-60, 3/2] on silica. Pure material was obtained by soxhlet extraction of 1.000 g in acetonitrile for 5 hours, to leave 0.491g of the adduct.

The solvent-free title compound (165) m.p. 259-260°C was obtained by heating at 70°C, 0.5mm Hg. Found:C, 85.5%; H, 4.6%. $C_{90}H_{56}O_8$ requires C, 85.4%; H, 4.5%; νmax 3055(m), 3030(m), 1630(s), 1600(s), 1592(m), 1515(s), 1465(s), 1442(m), 1405(s), 1387(m), 1363(s), 1268(m), 1248(s), 1212(s), 1182(m), 1162(s), 1140(m), 1118(m), 1088(m), 1050(w), 1040(w), 1020(w), 982(m), 975(m), 917(m), 875(w), 840(m), 808(m), 770(w), 745(m), 623(w), and 470(m)cm^{-1}; δ_H (90MHz, $CDCl_3$) 7.1-7.8 (m 40H) and 6.65-7.05 (m 16H); δ_C (50MHz, d^6-DMSO) 156.0(s), 154.4(s), 141.0(s), 140.3(s), 133.8(s), 133.4(s), 129.3(2c), 129.0(2c), 127.5(2c), 126.8(d), 126.7(d), 126.5(d), 126.3(d), 124.4(d), 124.0(d), 121.6(s), 117.6(d), 117.0(d), 110.1(d), and 109.4(d); m/e 1264 [M^+], 1121 [M^+-OR] and 978 [M^+-$(OR)_2$] (R = $C_{10}H_9$).

20. Octakis(phenoxy)naphthalene (166)

Sodium phenoxide was prepared according to the method of Vogel[382] from phenol (Analar, 9.58g 0.10 moles) and sodium hydroxide solution (20ml, 5.00M, 0.10 moles). 10.1g, 87 mmoles, of the salt was degassed in ca 20ml DMEU with 1.012g, 3.72 mmoles, of octafluoronaphthalene (2) in a tube equipped with rotaflow teflon valve and heated at 120°C for nine weeks. The yellow-green solution was poured into water and washed with toluene. The toluene solution was washed ten times with water; the aqueous fractions were then filtered, washed with further water and the white crystalline solid precipitate dissolved in chloroform. The organic solutions were dried with anhydrous magnesium sulphate. T.l.c. (SiO_2; toluene) showed the chloroform solution to be essentially one spot; this material was concentrated and crude product, 2.73g, 85% yield, m.p. 197-208°C was obtained after crystallisation and drying.

The toluene solution was purified by preparative t.l.c. (SiO_2; toluene) to give a further 0.4g of impure material. The product (166) was recrystallised from ethylacetate and dried at 5mmHg for 24 hours, m.p. 209-210°C; T.l.c. (SiO_2:toluene) Rf=0.65; δ_H (200MHz, $CDCl_3$) 7.12-7.02 (m, 16H), 6.91-6.82 (m, 8H), and 6.60-6.54 (m, 16H); δ_C (50MHz, $CDCl_3$) 158.1 (s), 156.6 (s), 141.3 (s), 140.1 (s), 128.9 (2C) (d), 122.3 (d), 121.5 (d), 120.6 (s), 115.6 (d), and 115.1 (d); m/e 864 [M^+] and 771 [M^+-PhOH.

21. Octakis(m-methylphenoxy)naphthalene (167)

Sodium m-methylphenoxide was prepared from sodium (2.5g, 109 mmole) and m-cresol (AR, 14.71g, 112 mmoles) in dry ethanol under argon. The solvent was removed on a rotary evaporator and the product washed with sodium-dried ether prior to drying to constant weight.

6.0g (49 mmoles) of sodium m-methylphenoxide was reacted with octafluoronaphthalene, 0.58g 2.13 mmoles, at 120°C for 12 weeks and isolated according to the method of example 20. The product, a brown oil, was triturated with ether to give 1.50g of white powder, Yield 72%. Crystals were obtained from dioxan m.p. 150-152°C; R_f = 0.65 ($CHCl_3$ SiO_2); νmax selected 3040(m), 2960(m), 2920(m), 2860(m), 1700(w), 1610(s), 1590(s), 1490(s), 1460(s), 1410(s), 1370(s), 1250(s), 1185(s), 1150(s), 775(m), and 685(m); δ_H (200MHz, $CDCl_3$) 7.03-6.90 (m, 8H) 6.70-6.60(m, 8H) 6.45-6.35 (m, 16H), 2.18 (s, 12H) and 2.14 (s, 12H); δ_C (50MHz, $CDCl_3$) 158.3(s), 157.0(s), 141.4(s), 140.1(s), 138.7(d), 138.6(d), 128.4(d), 128.3(d), 123.0(d), 122.2(d), 121.0(s), 116.5(d), 116.2(d), 112.6(d), 112.1(q), 21.4(d), and 21.3(q). m/e 976 M^+ 961 M^+-CH_3.

22. Octakis(1,2,3,4-tetrahydro-6-naphthyloxy)naphthalene (169)

1,2,3,4-tetrahydro-6-Naphthol, 3.827g (25.8 mmoles) was reacted with 1.056g (26.4 mmoles) of sodium hydride (60% dispersion in oil) in the manner of example 19 to give on isolation a white salt. This was reacted with octafluoronaphthalene (2) 0.260g (3.13 mmoles) in DMEU in the manner of example 19 for 20 weeks at 90°C before working up as normal. The lightly coloured oil was boiled in 50ml ethanol and the white solid precipitate, 0.960g, filtered and dried; the material had melting point 200-205°C and was essentially one spot by t.l.c., corresponding to a 77% yield of crude. Recrystallisation twice from cyclohexane gave a clathrate containing ca 1 mole guest m.p. 206.5-208°C. Further recrystallisation gave unsolvated host. R_f = 0.30 (SiO_2-C_{18} MeOH/EA 2/1); Found : C, 85.5; H, 4.6; $C_{90}H_{56}O_8$ requires C, 85.4; H, 4.5; ν_{max} (selected) 2860 (m), 2840 (m), 1610 (m), 1585 (m), 1495 (s), 1450 (s), 1365 (s), 1350 (m), 1245 (s), 1225 (s), 1150 (m), 995 (m), 980 (m), 935 (m), 825 (m), and 800 (m) cm^{-1}; δ_H (90MHz $CDCl_3$) 6.85-6.60 (m, 8H), 6.45-6.20 (m, 16H), 2.8-2.4 (m, 32H) and 1.9-1.5 (m, 32H); δ_C (50MHz $CDCl_3$) 156.4 (s), 155.2 (s), 141.8 (s), 140.4 (s), 137.3 (s), 137.1 (s), 130.5 (s), 129.4 (s), 129.0 (d), 128.9 (d), 120.8 (s), 116.1 (d), 115.5 (d), 113.5 (d), 112.5 (d), 29.5 (t), 29.4 (t), 28.6 (2C)(t), 23.4 (t), 23.3 (t), 23.1 (t), and 23.0 (t); max (selected) 3060 (w), 3020 (w), 2930 (s), 2890 (m), m/e 1296 [M^+].

23. Octakis(p-phenylphenoxy)naphthalene (170)

Sodium p-phenylphenolate was prepared according to the method of example 19 from p-phenylphenol 11.32g, 66.5 mmoles and sodium hydride 60% dispersion 2.60g, 65 mmoles. The salt was reacted with 0.811g octafluoronaphthalene, 2.98 mmoles and isolated according to the method of example 19. The insoluble material gathered from the aqueous portions consisted of green crystals, was washed with water then acetone and dried at 80°C. This material 4.32g was shown to be the DMEU clathrate (1:1) m.p. 304-310°C, a yield of octakis(p-phenylphenoxy)naphthalene of 91%. The material gathered according to normal toluene extraction was very crude by t.l.c., and weighed 1.84g. The DMEU clathrate was dissolved by boiling in DMSO and precipitated with water. After drying in vacuo the white crystals had m.p. 305-306.5°C; R_f 0.50 SiO_2 -C_{18} MeOH/EA 2/1; Found: C, 85.40; H; 4.84; $C_{106}H_{92}O_8$ requires C, 86.39; H, 4.92; DMEU clathrate Found: C, 83.97; H, 5.18; N, 1.87; $C_{106}H_{72}O_8 . C_5H_{10}N_2O$ requires C, 83.97; H, 5.20; N, 1.76; ν max (selected) 3060 (w), 3035 (w), 1605 (m), 1590 (m), 1585 (m), 1515 (s), 1490 (s), 1455 (w), 1400, 1365 (s), 1220 (s), 1190 (m), 1270 (m), 1010 (m), 970 (m), 875 (m), 830 (m), 760 (s), and 700 (m) cm^{-1}; DMEU clathrate additional at 2940 (w), 2880 (w), and 1700 (m) cm^{-1}. δ_H (90MHz, $CDCl_3$) 7.5-7.2 (m, 56H), 6.8-6.6 (16H); DMEU clathrate (D^6-DMSO) 7.7-7.3 (m, 56H) 7.0-6.8 (18H), 3.29 (t, 4H) and 2.73 (s, 6H); δ_C (50MHz, $CDCl_3$) 158.0 (s), 156.7 (s), 141.8 (s), 140.8 (s), 140.5 (2c)(s), 135.8 (s), 135.0 (s), 128.7 (2c)(d), 128.3 (d), 127.8 (2)(d), 127.5(d), 126.9 (2c)(d), 120.9 (s), 116.2 (d), and 115.7 (d); m/e 1472 [M^+ weak]; (FAB, 3-nitrobenzyl alcohol) 1473, 1321 [M^+-$C_6H_4C_6H_4$] and 1305 [M^+- $OC_6H_4HC_6H_4$].

24. Octakis(p-benzylphenoxy)naphthalene (171)

Sodium p-benzylphenoxy was made from p-benzylphenol (95%) 10.09g, 52.1 mmole and sodium hydride (60% dispersion) 2.198g, 54.9 mmoles according to the method of example 19. It was reacted with 0.50g, 1.84 mmoles octafluoronaphthalene (2) in DMEU and isolated also according to the method of example 19. The crude product 6.1g was triturated with hot ethanol to give 1.67g of light-brown crystals, a yield of 57% crude material m.p. 137-138.5°C.

On recrystallisation from isopropanol the crystals had m.p.144-145°C; δ_H (200MHz, D^6-DMSO) 7.29-7.07 (m, 40H) 6.95-6.96 (m, 16H) 6.51-6.42 (m, 16H) 3.79 (5, 8H) 3.77 (s, 8H); 8_C (50MHz, D^6-DMSO) 156.5 (s), 155.0 (s), 141.34 (s), 141.26 (s), 150.5 (s), 139.8 (s), 135.0 (s), 134.0 (s), 129.3 (d), 129.2 (d), 128.6 (d), 128.5 (d), 128.3 (2c,d) 125.9 (2c,d) 120.7 (s), 115.1 (d), 114.8 (d), and 40.1 (2c,t) m/e 1584 [M^+].

25. Octakis(p-cumylphenoxy)naphthalene (172)

Sodium p-cumylphenolate was made according to the method of example 19; 4.98g (21.3 mmoles) was reacted with 0.308g octafluoronaphthalene (1.13 mmoles) at 120°C for 13 weeks and the product isolated similarly. The product, a brown oil, 3.75g, contained p-cumylphenol as a major impurity. Trituration with ethanol and recrystallisation from ethanol gave 0.61g of white crystals, 30% yield m.p. 148-155°C. Column chromatography of the ether solution did not give any crystalline material.

R_f= 0.75 SiO_2, $CHCl_3$; δ_H (100MHz, $CDCl_3$) 7.23-7.16 (m, 40H) 6.95-6.81 (m, 16H) 6.35-6.44 (m, 16H), 1.55 (s, 24H) and 1.57 (s, 24H); δ_C (25MHz $CDCl_3$) 156.3 (s), 154.8 (s), 151.0 (s), 150.8 (s), 144.5 (s), 143.6 (s), 141.1 (s), 140.0 (s), 127.9 (2C)(d), 127.1 (2C)(d), 126.4 (2C)(d), 125.5 (2C)(d), 120.3 (s), 115.4 (d), 114.7 (2C)(d), 42.4 (2C)(s), 30.9 (q); m/e 1808 [M^+] and 1596 [M^+ - 212].

26. Octakis(p-methoxyphenoxy)naphthalene (174) and Octakis-(p-hydroxyphenoxy)naphthalene

a) p-methoxyphenol was recrystallised from toluene over charcoal and 51.2g, 412mmoles, reacted with 60% sodium dispersion in oil, 16.50g, 413mmoles, according to the method of example 19. Sodium p-methoxyphenolate, 60.4g, was reacted with 3.19g octafluoro-naphthalene, 11.73 mmoles in 100ml DMEU at 90°C for eight weeks. The reaction was drowned into ice-water and the white solid filtered, washed with water and toluene then dried to give 6.73g product. The toluene washings were combined with toluene extractions of the aqueous, washed, dried and 2.35g of off-white solid product obtained. Total crude yield 70%. The material (174), was essentially one spot by t.l.c.; m.p. 215-216°C/ Sc (25MHz, $CDCl_3$) 154.8(s), 154.2(s), 152.7(s), 151.3(s), 142.0(s), 140.5(s), 120.8(s), 116.7(d), 115.9(d), 114.1(d,2c), 55.6(q); Under demethylation with BBr_3 by the method of example 39 a product was obtained δ_C (25MHz, D^6-DMSO) 152.3(s), 151.6(s), 151.4(s), 149.8(s), 141.3(s), 140.2(s),116.0(d), 115.5(d), 115.3(2c); m/e 1104 [M+].

27. Octakis(cyclohexylthio)naphthalene(164)

Sodium cyclohexylthiolate, 8.9g, was made from cyclohexylthiol (11.0ml, 10.45g, 87.2 mmol) and sodium (1.5g, 65.2 mmol) in dry ethanol according to the method of example 2b. This was reacted with octafluoronaphthalene (0.670g, 2.46 mmol) in 30ml degassed DMEU by addition over 30 minutes from a flexible sidearm and then further stirring for three days until no more colour change was observed (bright yellow).

The product, a single material by t.l.c. of an aliquot was isolated according to method of example in toluene. The crude material m.p. 234-242°C was recrystallised from hexane to give the title compound (164) in 87% yield, 2.23g, m.p. 250-252°C;νmax (selected) 2940(s), 2850(s), 2780(w), 2660(w), 1615(w), 1460(sh), 1445(m), 1335(m), 1295(w), 1260(m), 1225(w), 1195(w), 1175(w), 1115(w), 1090(w), 1050(w), 1025(w), 995(m), 940(w), 915(w), 885(w), 835(w), 815(w), 770(w), and 735(m) cm^{-1}; δ_H (100MHz, $CDCl_3$) 3.95-3.55 (M, 4H), 3.2-2.8 (m, 4H), 0.8-2.0 (m, 80H); δ_C (25MHz, $CDCl_3$) 143.08(s), 137.74(2(c)(s), 49.97(d), 26.11(t), 25.84 (2(c)(t), 25.72(t), 32.90(2(c)(t); m/e 1040 [M^+], 957 [M^+- (C_6H_{11})], 926 [M^+- $C_6H_{11}S$], and 874 [M^+- (C_6H_{11})].

b) In a similar experiment the salt and product were prepared according to the method of example 20. Thus sodium p-methoxyphenolate 1.40g 9.6 mmole and octafluoronaphthalene 0.129g 0.47 mmole gave 0.44g of product m.p. 204-213°C as a mixture by t.l.c. The mass spectrum was predominately m/e M^+ 792 $C_{10}F_6$ $(OPhOMe)_4$. Column chromatography (Silica, chloroform-pentadiene ether) gave 0.217g m.p. 214-215°C, with spectroscopic properties identical to those in 26a).

A small amount of insoluble material left after work-up as white solid was recovered m.p. >310°C. The material was soluble in dilute hydroxide, and had an i.r. (ν2950-3100cm^{-1}) similar to that of hexakis(p-hydroxyphenyl)benzene (168).

28. Pyrolysis of tetrachlorophthalic anhydride

a) Pyrolytic apparatus[386]

A horizontal silica tube (60cm x 2cm i.d.), with the middle portion (35cm) packed with 1cm lengths of 5mm i.d. silica tubing, was heated in an external cylindrical electric furnace under a dead-end pressure of 0.1 mmHg (measured at the oil rotary pump) equipped with two liquid nitrogen traps at the vapour outlet. The inlet was equipped with a small flask and a nitrogen bleed which reduced the pressure measured to 0.2-0.5 mmHg. The temperature profile of the tube and furnace was calibrated with a Comack thermocouple.

b) Pyrolysis of tetrachlorophthalic anhydride : octachlorobiphenylene (189)

4.91g of tetrachlorophthalic anhydride was carried by nitrogen into the tube (middle section 600-725°C) by sublimation from a small flask carefully heated with a bunsen burner. A black-green solid was quickly deposited at the vapour outlet and first trap, and black deposits were left in the tube. The tube and trap were washed with chloroform and the solid (3.91g) filtered off. This was washed with 60-80°C petroleum ether (10 times), benzene (6 times) and chloroform (8 times) until washings were colourless, to give 0.62g of yellow-green solid. The crude product was recrystallised twice from o-dichlorobenzene and dried in vacuo at 70°C for 12 hours to give 0.44g octachlorobiphenylene (189) as fine dark green needles m.p. 301-303°C (s.t.) (lit 296-298°C, 312-313.5°C)[370];

Found: C, 33.78; Cl 66.24; $C_{12}Cl_8$ requires C, 33.69; Cl, 66.31; ν max 1630(w), 1600(w), 1580(w), 1540(w), 1495(w), 1455(w), 1435(w) 1355(sh,w), 1340(m), 1325(s), 1305(s), 1290(s), 1270(m), 1250(sh,m), 1245(sh,m), 1230(s), 1205(m), 1180(w), 1155(s), 1145(s), 1120(w), 1105(w), 1040(w), 1030(w), 950(w), 915(w), 895(m), 850(w), 750(w), 690(w), 655(s), 545(w), and 510(m) cm^{-1}; λ max ($CHCl_3$) 269 (sh), 279, 290, 330, 352, 368 (sh), 373, 392, 420, and 453 nm (lit. 269 (sh), 279, 290, 333, 352, 369 (sh), 374, 393, 424, and 453 nm); m/e 424 [M^+], 389 [M^+-35], and 354 [M^+-70].

Octachlorobiphenylene (189) was reacted with sodium thiophenolate in DMEU until analysis by t.l.c. showed no starting material left and only one product spot remaining, (14 hours). R_f = 0.28 (S_1O_2, 60-80^{0}C Pet ether/$CHCl_3$), R_f = 0.18 ($S_1O_2C_{18}$, MeOH).

A portion was removed and worked-up by washing copiously with water in toluene, and removal of solvent to give a solid; analysis Cl 9%. The reaction was heated for a few hours at 80°C and a portion similarly removed. Analysis Cl nil. The bulk of the reaction was dissolved in toluene and washed with copiously with water, dried with anhydrous sodium sulphate and the solvent removed on a rotary evaporator. T.l.c. indicated the presence of 1 main spot and 2 other spots. The black-green product could not be crystallised and was separated on a silica column (2" long, 1" diameter) eluting first with petroleum ether the 60-80°C petroleum ether $CHCl_3$, 3/2. The coloured fractions were collected (red, purple, green, red, yellow in order of elution).

The second elution gave t.l.c. showing only one spot (δ_H (90 MHz, $CDCl_3$) 6.8-7.4(m); δ_C (25 MH_2, $CDCl_3$) 125-132 (s, various), 135(s) 138(s); m/e 1016 (M^+), 1084 (M+-32), 1007 (M+-109) consistent with the formula $C_{12}(SPh)_8$. Isolated weight solid 62mg. Total weight coloured fractions 150mg.

29. Attempted preparation of perchloroanthracene

a) Chlorination of anthracene; attempted preparation of perchloro-9,10-dihydroanthracene. According to the method of Ballester, anthracene (5.00g), aluminium trichloride (2.50g) and sulphur-monochloride (5.00g) were reacted in sulphuryl chloride (freshly distilled from P_2O_5), but over a period of two weeks operation, in the dark using a cardice condenser. After the prescribed work-up 3.95g of a white solid (177) m.p. 310-318°C (sub) (lit 355-7°C (dec)(sub)) was obtained, Found: C, 29.82; H, Nil or trace; Cl, 69.92; $C_{14}HCl_{11}$ requires C, 30.08; H, 0.18; Cl, 69.74; $C_{14}H_{12}$ requires C, 28.32, Cl, 71.68; ν max 3080(w), 2920(w), 1565(w), 1520(w), 1425(w), 1380(w), 1350(s), 1305(w), 1290(m), 1220(w), 1200(m), 1180(w), 1155(m), 1010(w), 990(w), 960(w), 900(w), 880(w), 840(w), 820(w), 780(w), 750(s), and 740(s) cm^{-1}; λ max (CCl_4) 266, 294(sh), 300(sh), 312(sh)nm (ϵ2400, 310, 290, 200); [lit. 297, 307(sh)nm (ϵ582 and 400)]; R_f = 0.48 (SiO_2, C6,H_{12}); m/e 520 (C_{14} Cl_{10} 518) weak, 486 [M^+ -34], 450 [M^+-70], 416 [M^+-104], 380 [M^+-140, (100%)].

b) Dechlorination of (177) Compound (177), described above, was dechlorinated according to the method of Ballester for perchloro-9,10-dihydroanthracene. Thus 0.40g (177) and stannous chloride (4.00g) in 250ml $CHCl_3$ (freshly distilled) under nitrogen in the dark gave 260mg of yellow crystals m.p. 150°-214°C (yellow to orange) (s.t.) ν max (selected) 3100(w), 2970(w), 1580(m), 1540(m), and 1370(s) cm^{-1}; max (C_6H_{12}) 222, 249, 300, 428, and 456 nm (ϵ18900, 14300, 79600, 5100, and 4600); δ_H (90MHz, $CDCl_3$) 8.65(s); δ_C (25MHz, $CDCl_3$) 134.1(s), 131.1(s), 130.1(s), 127.2(s), and 124.6(s); R_f 0.44, and 0.22 (SiO_2, C_6H_{12}). m/e 520 ($C_{14}Cl_{10}$ 518) weak, -34 (100%), -70, -104, -140.

c) Sublimation of (177). Compound (177), described above, sublimed at 1mmHg, 220-300°C, gave product R_f 0.44 (SiO_2, C_6H_{12}); λ max 285, 295, 416, and 444 (ϵ= 1.16, 1.26, 0.07, and 0.05).

d) Chlorination of anthracene; stronger conditions. 2.52g anthracene, 23.1g $AlCl_3$ and 50g S_2Cl_2 was refluxed for 8 hrs in the dark in 500ml sulphuryl chloride. After work-up as in a) 0.5g of crude product was obtained. A portion of recrystallised from chloroform produced 20mg of pale cream crystals m.p. 200-280°C and 320-325°C (sub); R_f 0.40, and 0.48 (SiO_2 (C_6H_{12}); δ_H (90MHz, $CHCl_3$) 6.9(s), 5.0(s).

Preparation of octachloroanthraquinone (179)

a) Tetrachlorophthalic anhydride (13g) and anhydrous potassium fluoride (130g) were dried in an oven for 24 hours at 130°C. The salt was further dried by grinding to a powder and heating for 48 hours at 150°C in vacuo. The mixture was placed in a glass beaker in an autoclave (1L) with bolts finger tight and then heated to 300°C over three hours and held for a further three hours. The crude yellow product (2.80g) was removed from the autoclave walls and sublimed at 230°C, 0.5mmHg to give 2.53g of product m.p. 177-281°C (lit. dilactone 176-177°C, anthraquinone 343-343°C); i.r. as published for octafluoroanthraquinone and also ν max 1825(s), 1320(w), 935(s), 895(m), 845(w), and 770(w) [dilactone lit. 1835 cm^{-1}].

2.50g of product was heated in a sealed tube with a further 1g of anhydrous potassium fluoride and heated at 300°C for 30 minutes. Sublimation at 10mm the product gave 89mg of yellow product with the correct i.r. for octafluoroanthraquinone and a small peak at 1825 cm^{-1}. Further sublimation produced 750mg of compound with similar mixed i.r.. T.l.c. (SiO_2 toluene) also showed a relative change in concentration from lactone (R_f 0.61) to anthraquinone (R_f 0.42).

8.0g of the product, recrystallised from chlorobenzene and dried in vacuo gave 0.31g of yellow crystals m.p. 240-243 with i.r. identical to that published. m/e 370, 368, 352 [M^+, 100%], 324 [M^+-CO], and 296 [M^+-$(CO)_2$].

b) In a claisen flask placed anhydrous potassium fluoride (50g) dried as described above in a) was heated under vacuum for 30 minutes with a bunsen and the dried tetrachlorophthalic anhydride (13g) added. The mixture was heated in an air bath at 370-400°C for 4 hours under nitrogen and then in vacuo to sublime out the product 2.85g, as a mixture similar to that in a). Recrystallisation from chlorobenzene gave 0.18g of crystals after drying in vacuo. with i.r. identical to octafluoroanthraquinone, and a weak peak at ν max 1750cm^{-1}.

31. Treatment of octafluoroanthraquinone with sulphur tetrafluoride and anhydrous hydrogen fluoride

a) Octafluoroanthraquinone (0.50g 1.42 mmol) was reacted with SF_4 (0.48g, 4.44 mmol) in AHF (1ml) in a monel metal bomb, 75ml capacity, at 160-180°C (electrical furnace temperature) for 24 hours. The products were poured into a plastic beaker and after evaporation of reagents the residue washed with water until washings neutral before drying in vacuo over P_2O_5. Vacuum sublimation yielded 0.37g of starting material.

b) Octafluoroanthraquinone (0.50g) was reacted with SF_4 (0.75g) in AHF (5ml) in a monel metal bomb, 10ml capacity, at 190°C for 18 hours then 210°C for 12 hours and worked up similar to a). From which 0.06g of starting material was recovered.

32. Treatment of octafluoroanthraquinone (179) with DAST

a) Octafluoroanthraquinone (71mg, 0.20 mmoles) was stirred at -78°C under nitrogen in 8ml of dried distilled chlorobenzene and DAST (0.07ml 0.53 mmoles) injected in. The reaction was allowed to warm to room temperature and then heated for 45 min. in a bath at 80°C, before stirring for a further 16 hours at ambient. The reaction material was dissolved in carbon tetrachloride, filtered, washed with water and then dried with anhydrous sodium sulphate before removal of solvent. A brown solid (52mg) was obtained after drying in vacuo over P_2O_5, i.r. identical to that of octafluoroanthraquinone except ν max 2880-2970 (sharp), 1805 (sharp) and 1020-1120 cm^{-1} (broad); m/e 352, 368, 374, 384 and 390. Sublimation produced 38mg of octafluoroanthraquinone.

b) Octafluoroanthraquinone (37mg) and DAST (0.7ml) in 8ml PhCl at 80°C for 18 hours, treated similar to a) except additionally product washed with weak bicarbonate solution, gave 4mg of product corresponding to starting material.

33. Preparation of (+) - Neothiomenthol (197)[377-380]

a) To (-)-Menthol, (29g, 186 mmoles; c5, EtOH $[\alpha]_D^{20}$ -48.9° (lit. -50°) in 150ml dry pyridine was added p-toluenesulphonylchloride (53.1g, 279 mmoles, m.p. 67-68°C) and the solution made up to 250ml with further pyridine. After four days stirring in a sealed flask water was added and the precipitate washed and dried over P_2O_5. The crude material (57g) was dissolved in hot hexane filtered and recrystallised three times to give (-)-menthyl-p-toluenesulphonate 44g, m.p. 93.5°C $[\alpha]_D^{20}$ 67.5° (cl., $CHCl_3$) (Lit. m.p. 94-95°C, $[\alpha]_D^{25}$ -67°); Found C, 65.85; H, 8.56; S,10.25; $C_{17}H_{26}O_3S$ requires C, 65.80; H,8.44; S,10.31; m/e 310 $[M^+]$.

b) (-)-menthyl p-toluenesulphonate (10g, 32 mmol) was reacted with potassium ethyl xanthate[382] (8.6g, 42mmol) in DMF (40ml) according to the method of van Leusen et al and the crude product cleared with 1,3-diaminoethane (15ml). The crude thiol (3.5g) was fractionally distilled to give (197) 1.52g (8.82 mmoles), 28% yield of (+)-neomenthane-3-thiol [(+)-neomenthylthiol] $[\alpha]_D^{20}$ (c=2.04 $CHCl_3$) + 62.2° [lit. 47.8°, c2.06, $CHCl_3$, 53.2°, 53.9°][378-380]; δ_C (25MH_z, $CDCl_3$) 48.4 (d), 44.2 (t), 40.2 (d), 35.4 (t), 30.4(d), 26.0 (d), 24.2 (t), 22.2(q), 20.9 (q), and 20.4 (q); m/e 172 $[M^+]$, 139, 138.

34. Attempted Preparation of Hexakis((+)-neomenthylthio)benzene (198)

a) (+)-neothiomenthol (2.26g, 13.1 mmoles) was reacted with sodium hydride (0.800, 13.3 mmoles) 40% dispersion in oil according to the method of example 1a and after isolation *in situ* 0.187g, 1.01 mmoles of hexafluorobenzene was added in 10ml DMEU, causing an immediate colour change to yellow. No change in t.l.c. of aliquots occurred from after 5 hours. After 5 days the product was isolated according to method of example 2a and 1.54g of a crude grey-blue crystals were isolated.

These were recrystallised twice from toluene to give 0.70g, 81% of a colourless solid m.p. 149-151°C, 1,4-difluoro-2,3,5,6-tetrakis-(neomenthylthio)benzene(198); ν max 2950(s), 2920(s), 2885(s), 2840 (s), 1640 (br) 1545 (w), 1475(m), 1455(m), 1445(m), 1375(s), 1355(m), 1320(m), 1300(m), 1280(m), 1240(m), 1230(m), 1190 (m), 1170, 1160 (w), 1140 (m), 1125(w), 1090(w), 1060(w), 1020(w), 1000(w), 985(w), 950(w), 935(w), 920 (w), 865, 850 (m), and 820 (w) cm^{-1}; δH (90 MHz, $CDCl_3$) 3.9-3.7(m), 2.2-0.6 (m); δC (50 MHz, $CDCl_3$) 160.21 (J CF 242.4 Hz; J CCCCF 3.8Hz), 129.11 (J CCF 22.3 Hz; J CCF 15.0Hz), 50.84, 26.77, 49.32, 25.50, 40.86, 22.18, 35.42, 21.25, 30.18, and 20.94; m/e 794 [M^+] 652 [$M^+-C_{10}H_{22}$], 510, 368, and 226; R_f 0.65 (SiO_2 $CHCl_3$/40-60 Pet. ether 3/12).

b) 0.142g of (198) was dissolved in 4.8ml dried HMPA and added to further thiolate (ex 0.151g thiol, 0.0371g NaH 40% disp.) prepared according to example 34a). No change was observed in products after 4 weeks or additionally after a further week at 40°C in the presence of sodium thiophenolate, as monitored by t.l.c.

35. Attempted Preparation of Octakis(+)-neomenthylthio)naphthalene

36mg 0.132 mmoles, of octafluoronaphthalene in 5ml DMEU was added to (+)-neomenthylthiolate prepared from 391mg thiol (2.27 mmol) and 0.101g NaH 40% disp in oil as in example 34a, giving a red solution immediately. A single product spot was observed and after 4 days the reaction was worked up as in example 2a to give 254mg crude product as a red oil; δ_F (94MHz, $CDCl_3$) -86.0, -96.4, -96.6, 98.1, -97.5, -99.1, -99.56, -99.74, -99.75, -99.81, -106.9; δ_C (25MHz, $CDCl_3$) 162.1, 161.6, 160.1, 160.0, 149.9, 149.7, and 148.9 (aromatic only);

36. Attempted preparation of decakis(phenylthio)anthracene

Perfluoroperhydroanthracene (90%) m.p. 80-85°C (lit 90-94°C) was recrystallised from diethyl ether to m.p. 88-93°C. To 10ml DMEU in a rubber sealed conical flask with magnetic stirring, previously degassed, was added 2.05g sodium thiophenolate (15.5 mmoles) and then the solution was degassed again. Perfluoroperhydroanthracene, 195mg (0.31mmoles) was added under nitrogen. The insoluble substrate was heated in the DMEU salt solution at 45-60°C for 7 days; the subliming substrate was regularly shaken back under the liquid surface. The solution quickly turned green-black but no other colour changes were observed beyond this.

The products were isolated in the normal manner in toluene. The unreacted substrate was recovered and recrystallised from toluene to give 51mg m.p. 92-98°C, on evaporation the toluene gave more, less pure, material. The reaction products, after the normal isolation and further column chromatography gave a mixture by t.l.c. of two red spots. These were separated with preparative t.l.c. to give a main band of 0.122g and a minor product, of lesser R_f, of 0.039g. The major product was recrystallised from cyclohexane to give 70mg m.p. 212-214°C, identified as 1,2,3,4,5,6,7,8-octakis(phenylthio) anthracene (185), yield 22% on substrate charged, 30% on substrate reacted. δ_H (100MHz, $CDCl_3$) 10.1 (s, 2H) 7.1-6.9 (m, 40H);

δ_C (25MHz, $CDCl_3$) 145.4(s), 142.1(s), 138.5(s), 137.1(s), 134.1(s), 130.0(d), 129.0(d), 128.9(d), 128.4(d), 127.8(d), 126.1(d), and 125.9(d); m/e 1042 [M^+] (FAB-EI).

37. Attempted preparation of decakis(p-t-Butylphenylthio)-naphthalene

Perfluorohydroanthracene, 167mg, 0.23mmole, m.p. 88-93°C, was reacted with sodium p-t-Butylphenylthiolate 2.20g, 11.7mmole according to the method of example 36. The product was isolated in the normal manner. The product similarly contained two hydrogen substituents on the anthracene (9,10 assignment).

38. Preparation of hexakis(p-methoxyphenoxy)benzene)

26.00g (210mmol) of p-methoxyphenol recrystallised from toluene and charcoal was reacted with 8.33g (208mmol) of sodium hydride 40% dispersion in oil according to the method of example 19, to give sodium p-methoxyphenolate 31.05g. This was reacted with 1.596g (8.56mmol) hexafluorobenzene according to the method of example 19. After eight weeks the reaction mixture was poured into 1L of ice-water. The insoluble white product was washed copiously with water and dried in vacuo over P_2O_5 to constant weight. The dried crude product, 6.50g, was recrystallised from chloroform (300ml)/acetone (100ml)/ dioxan (100ml) to give after drying 5.88g hexakis(p-methoxyphenoxy)benzene (173) 85% yield ; δ_H (90MHz, $CDCl_3$) 6.65 (s, 24H) 3.70 (s, 18H); m/e 810 [M+]

39. Preparation of hexakis(p-hydroxyphenoxy)benzene (168)

508mg (0.627mmol) of hexakis(p-methoxyphenoxy)benzene(173) was dissolved in 50ml CH_2Cl_2 under nitrogen and cooled to -78°C. Boron tribromide (ca. 2.2ml, 23mmol) was injected, the reaction allowed to rise slowly to room temperature and stirred for 12 hours. Anhydrous ether was slowly added, followed by analar, then moist ether until no further reaction was observed (vented through needle). The white precipitate was filtered, washed with water and then methanol before drying in vacuo over P_2O_5 to give 0.387mg hexakis(p-hydroxyphenoxy)benzene(168), 85% yield; m.p. 305°C (darkens) 320-325°C (dec);

ν max 3240(br,s), 3030(m), 2970(br,w), 2890(br,w), 2790(br,w), 2730(br,w), 2690(br,w), 2590(br,w), 2050(br,w), 1950(w), 1630(br,m), 1595(m), 1505(s), 1450(s), 1360(m), 1340(m), 1280(m), 1220(s), 1195(s), 1100(m), 1020(m), 995(s), 945(s), 855(m), 840(m), 830(m), 785(s), 720(w), 700(w), 675(br,w), 625(w), 540(w), 525(m), 495(w), 470(w), and 450(w)cm^{-1}; δ_H (200MHz, (d^6DMSO) 9.02 (s, 6H) 6.55 (s, 24H); δ_C (25MHz, d^6-DMSO) 152.3(s), 150.1(s), 140.0(s), 116.1(d), 115.4(d); m/e 726.1713 $C_{42}H_{30}O_{12}$ requires m/e 726.1737.

40. Hexakis(p-hydroxythiophenoxy)benzene

200mg hexakis(p-methoxythiophenoxy)benzene, δ_H (90MHz, $CDCL_3$) 6.9 (d, 2H), 6.65 (d, 2H), 3.75 (s, 3H) [lit. (d^6-acetone) 6.94 (d, 2H), 6.78 (d, 2H), 3.77 (s, 3H)]; δ_C (25HMz, $CDCl_3$) 158.4 (s), 147.8 (s), 131.4 (s), 128.8 (d), 114.4 (d), 55.2 (q) [lit. 148.0, central ring], was demethylated with boron tribromide (1.70g) in methylene chloride according to the method of example 39. The yellow precipitate (152mg) was shown by t.l.c. to be a mixture of compounds. The main product was isolated by preparative t.l.c. (Ethylacetate-acetic acid- 40-60 petroleum ether, 60-4-36, R_f 0.10). The yellow oil (86mg) could not be crystallised. δ_H (90MHz, CD_3COCD_3 8.4 (s, 1H) 6.9 (d, 2H), 6.6 (d, 2H) [lit. 8.45(s, 1H), 6.86 (d, 2H), 6.72 (s, 2H)]; δC (25MHz, CD_3COCD_3) 157.2(s), 148.7(s), 131.7(s), 128.4(d), 116.9(d) [lit. 148.0, central ring].

41. Preparation of Octakis((1R)-(-)-10-Camphorthio)naphthalene (200)

1R-(-)-10-thiocamphor, 0.663g, was reacted with sodium hydride and then octafluoronaphthalene, 0.058g, according to the method of example 2. After isolation the yellow product was re-crystallised from methanol to give (200), 200, 2.72g, 81% yield, m.p. > 315°C; R_f 0.48 (SiO_2C_{18}, methanol); δ_C (50MHz, $CDCl_3$) 216.5(s), 216.2(s), 144.5(s), 140.9(s), 137.2(s), 61.4(s), 61.2(s), 48.0(s), 47.7(s), 43.4(d), 43.3(d), 43.1(t), 42.9(t), 27.0(t), 26.8(t), 26.5(t), 26.4(t), 20.6(q), 20.4(q), 20.2(q), 20.1(q), 35.9(t), 35.8(t).

Crystal Data

A) Octakis(m-tolylthio)naphthalene, $C_{66}H_{56}S_8$, (134), unsolvated form: M = 1105.68, tetragonal, space group P4/ncc, a = 15.875(2), c = 23.654(3) Å, U = 5961.2 Å^3, Z = 4, D_c = 1.23 g cm^{-3}, $\mu(MoK_\alpha)$ = 3.25 cm^{-1}. Number of independent intensities: 3256 from red prism, 0.3 x 0.2 x 0.2 mm, mounted on fibre. Final R for 1492 reflections considered observed: 0.042; R' 0.034.

B) Octakis(m-tolylthio)naphthalene dioxan adduct, $C_{66}H_{56}S_8$, (134)·$C_4H_8O_2$: M = 1193.79, tetragonal, space group P4/ncc, a = 16.040(2), c = 23.793(2) Å, U = 6121.4 Å^3, Z = 4, D_c = 1.29 g cm^{-3}, μ(Mo-K_α) = 3.23 cm^{-1}. Number of independent intensities: 3512 from red prism, 0.3 x 0.3 x 0.2 mm, mounted in capillary. Final R for 1369 reflections considered observed: 0.045; R' 0.038.

C) Octakis(p-tolylthio)naphthalene bis-dioxan adduct, $C_{66}H_{56}S_8$, (161)· 2[$C_4H_8O_2$]: M = 1281.90, monoclinic, space group $P2_1/n$, a = 11.225(4), b = 14.602(2), c = 21.083(2) Å, β= 101.30(3)°, U = 3388.6 Å^3, Z = 2, D_c = 1.26 g cm^{-3}, μ(Mo-K_α) = 2.98 cm^{-1}. Number of independent intensities: 7363 from red prism, 0.7 x 0.2 x 0.2 mm, mounted in capillary. Final R for 3836 reflections considered observed; 0.066; R' 0.095.

D) Octakis(cyclohexylthio)naphthalene, $C_{58}H_{88}S_8$, (164): M = 1041.9, triclinic, space group $P\bar{1}$, a = 10.630 (1), b = 11.011 (4), c = 12.304 (2) Å, α = 86.82 (2), ß= 87.31 (2), γ = 89.32 (2)° . U = 1434 (1) Å^3, Z = 1, D_C = 1.21g cm^{-3}, T = 293K.

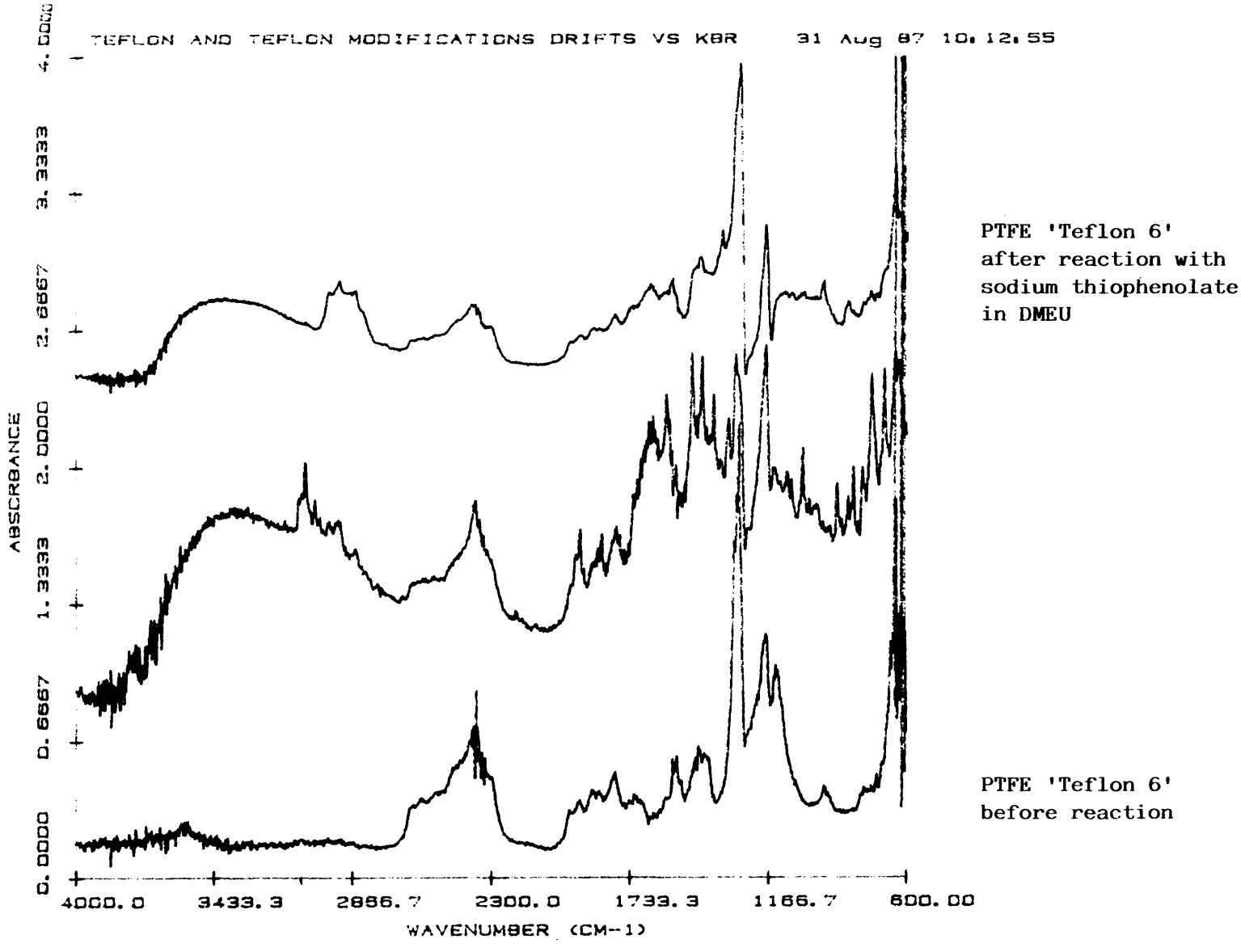
E) Octakis(phenylseleno)naphthalene, $C_{58}H_{40}Se_8$ (175) : M = 1368.64, triclinic, space group $P\bar{1}$, a = 9.288 (1), b = 11.301 (2), c = 12.737 (2) A, α = 101.10 (1), β = 95.39 (1), γ = 109.46 (1) °, U = 1219 (1) Å^3, 2 = 1, D_C = 1.86g cm^{-3}, T = 293k, R = 0.044 for 2451 indepedent reflections with $F_o^2 > 2\sigma(F_o^2)$.

F) Octakis(m-tolyloxy)naphthalene, $C_{66}H_{56}O_8$, (167): M = 977.2, monoclinic, space group $P2_1/n$, a = 7.831(1), b = 14.092(3), c = 23.934(3) Å, β = 96.97(1)°, U = 2622(1) Å^3, Z = 2, D_C = 1.24 g cm^{-3}, T = 293K, R = 0.058, R' = 0.070 for 1503 independent reflections with $F_o^2 > 2\sigma(F_o^2)$.

G) Octakis(β-naphthyloxy)naphthalene bis-acetone adduct, $C_{90}H_{56}O_8$ (165).2(C_3H_6O): M = 1381.6, triclinic, space group $P\bar{1}$, a = 11.064(3), b = 12.377(7), c = 15.975(9), Å, α = 117.09(4), β = 112.27(4), = 75.23(4) Å, U = 1793(1)A^3, Z = 1, D_C = 1.28 g cm^{-3}. T = 293K, R = 0.085, R' = 0.083 for 3109 independent reflections with $F_o^2 > 2\sigma(F_o^2)$.

H) Hexakis(p-hydroxyphenyloxy)benzene hexa-pyridine adduct, $C_{42}H_{30}O_{12}$ (158).$6C_4H_5N.xH_2O$, Formula weight = 1219.32 for x taken as 1, trigonal, $R\bar{3}$, $\underline{a}$ = 22.088(3), $\underline{c}$ 12.232(3) Å, $\underline{V}$ = 5168(2) $Å^3$, $\underline{Z}$ = 3, $\underline{D}_c$ = 1.18 g cm^{-3}, μ = 0.74 cm^{-1} for Mo-$\underline{K}_\alpha$ radiation, = 0.7107 Å. Number of independent reflections: 2503 from hexagonal needle, 0.6 x 0.2 mm, T = 293K. Final $\underline{R}$ for 537 reflections with $\underline{F}^2 > 2\sigma(\underline{F}^2)$: 0.094, $\underline{R}'$ 0.109.

X-ray intensity measurements were made by 2θ-w scan on a Nonius CAD4 diffractometer using graphite-monochromated Mo-K_α radiation. Unit cell parameters were determined by least-squares refinement of diffractometer setting angles. The principal computer programs used in structure solution and refinement are: MITHRIL, a computer program for the automatic solution of crystal structures from X-ray data. C.J. Gilmore, J.Appl.Crystallogr., 1984, 17, 42; the GX crystallographic Program System, P.R. Mallinson and K.W. Muir, J.Appl. Crystallogr., 1985, 18, 51. In structures A) and B) hydrogen atoms were located in difference- Fourier maps calculated during the anisotropic least-squares refinement, isotropic hydrogen parameters being included in subsequent refinement. In B) peaks associated with the guest were included in the calculations. In C) some of the methyl hydrogens were placed in theoretical positions. In H) the insufficiently large crystal limits precision and all aromatic host hydrogens and guest pyridine hydrogens were placed in theoretical positions. Two independent electron density peaks observed on and near the three-fold axis were ascribed to two types of statistically- disordered water molecule.


TEFLON AND TEFLON MODIFICATIONS DRIFTS VS KBR
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ABSORBANCE
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1166.7
600.00
WAVENUMBER (CM-1)
PTFE 'Teflon 6' after reaction with sodium thiophenolate in DMEU
PTFE 'Teflon 6' before reaction

Figure 53

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