DESIGN AND SYNTHESIS OF NEW, MORE STRUCTURED, TRIGONAL HOST MOLECULES

Thesis submitted for the Degree of Doctor of Philosophy
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Finally I would like to thank the University of Glasgow for the Scholarship which made this work possible.

For my Parents.

"...the very point which appears to complicate a case is, when duly considered and scientifically handled, the one which is most likely to elucidate it."

(Sherlock Holmes in "The Hound of the Baskervilles, (Ch. 15), by Sir Arthur Conan Doyle.)

SUMMARY.

This thesis presents first a personal overview of the study of clathrate phenomena, over the past two decades. This is followed by a description of attempt to design, using logical principles, new trigonal host molecules. The first line of approach was to employ as suitable building blocks para-substituted phenols sharing some common structural features with Dianin's compound (p-hydroxyphenyl-2,2,4,-trimethylchroman): using salts of such phenols six-fold nucleophilic substitution of hexaflurobenzene was directed toward the production of new, more highly structured "hexa-host" molecules. A striking example of this approach is the tight inclusion of phosgene, scavenged from a 12.5% solution in toluene, within the closed clathrate cavities of hexakis(p-phenoxyphenoxy)benzene. An X-ray crystal structure analysis of this novel host lattice is presented. X-ray analysis of the iodomethane adduct of the same host reveals the iodine atom of the statistically disordered guest, close to the centre of the cavity. An isomorphous clathrate structure has also been defined for the CH_3CCl_3 adduct of hexakis(p-benzylphenoxy)benzene by X-ray methods. The similarity in the clathrate structures of the two hosts is highlighted along with their ability to include highly volatile and toxic guest molecules.

In addition, novel use of solid-state CPMAS ^{13}C NMR spectra is described; this provides evidence, independent of X-ray method, for the site-symmetry of hexakis(p-benzylphenoxy)benzene in its clathrates and its unsolvated forms. Parallel CPMAS studies are also reported

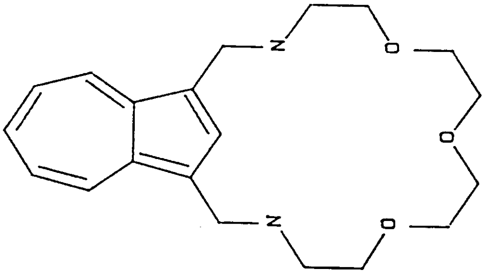
for hexakis(p-cumylphenoxy)benzene and hexakis(p-cumylphenoxymethyl)benzene.

A second strategy, termed the Piedfort concept (the name deriving from special coins struck at double thickness) is introduced for the first time. Two molecules of 2,4,6-tris(p-cumylphenoxy)-1,3,5-triazine are shown to undergo novel self-assembly to produce a composite unit (Piedfort unit), which acts as a single hexa-host molecule. The structure of this new unit, found both in the 1,4-dioxane inclusion compound of the above triazine and in its unsolvated crystal, has been elucidated by X-ray methods. The more highly structured 2,4,6-tris[p-(1-naphthyl)phenoxy]-1,3,5-triazine has also been synthesized; in this case the Piedfort units have almost certainly attained exact trigonal symmetry in the now rhombohedral adducts.

CONTENTS

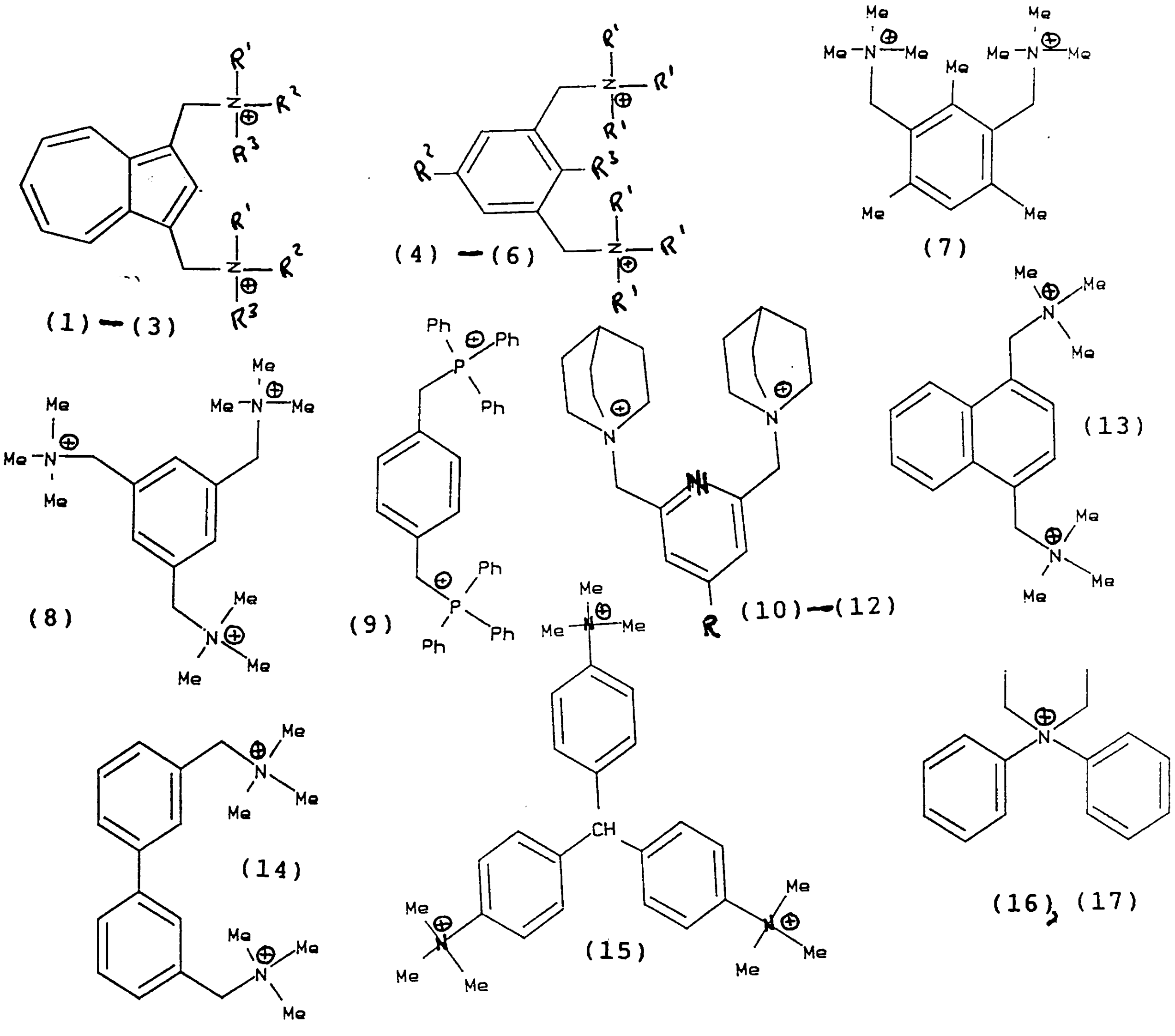
CHAPTER 1

Work carried out by Professor F. Vögtle, on onium salts is chosen to illustrate clathrates of an ionic type. Like many discoveries in inclusion chemistry the clathrate forming properties were discovered by chance[1]. In an attempt to synthesize compounds of type (A), crown ethers with azulene building blocks, some of the ammonium compounds discussed here of were prepared as intermediates. Compound (1) N,N-[1,3-azulenebis(methylene)] bis(trimethylammonium) diiodide (R = R = R' = Me) was prepared by methylation of the corresponding amine N,N-[1,3-azulenebis(methylene)] bis(dimethylamine) with excess iodomethane followed by recrystallisation from ethanol. It was subsequently found that some ethanol along with some iodomethane were retained in the resultant crystals. Further studies revealed an extensive range of inclusion behavior[2]. Investigations on other diammonium compounds of the type shown led to the series of hosts discussed below.



(A)

The planar and rigid azulene ring was recognised as the bulky group found in other clathrate-forming species[3]. Replacement of this unit by other planar and bulky "anchor" groups for example the naphthalene and anthracene rings and other aromatic systems along with modifications of the onium side arms led to production of compounds (1) - (30). It is their inclusion behaviour, structural features and adduct that are discussed here.

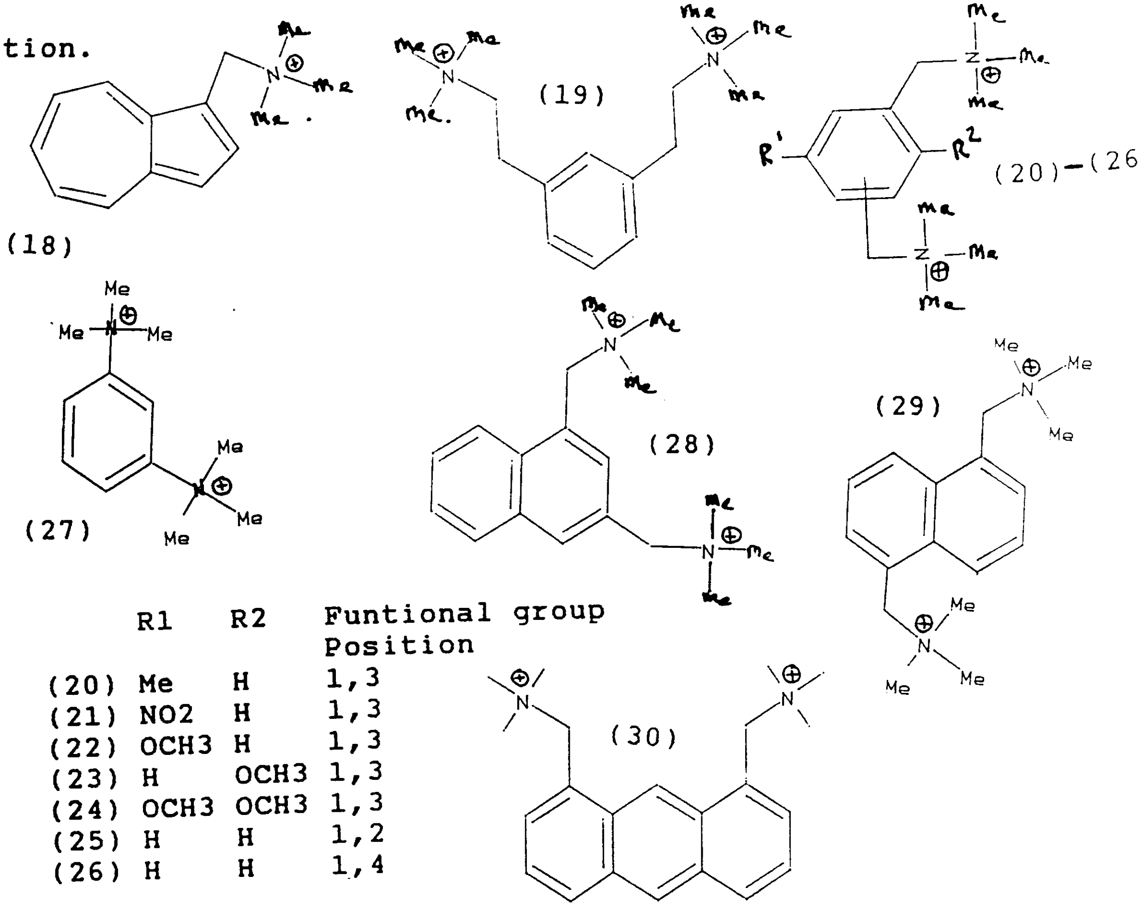


	R1	R2	R3
(1)	Me	Me	Me
(2)	Me	Me	Me
(3)	Me	Me	Et
(4)	Me	H	H
(5)	Me	tBu	H
(6)	Et	H	H

	Z	R
(10)	CH	H
(11)	CH	tBu
(12)	N	H
(16)	N	-
(17)	As	-

Figure 1. The set of clathrate forming ammonium salts

The compounds in Figure 1 were found to form inclusion compounds and comparison with the set of non-clathrate forming ammonium salts shown in Figure 2 can be used to give indications of the features necessary for clathrate formation.



	R1	R2	Funtional group Position
(20)	Me	H	1,3
(21)	NO2	H	1,3
(22)	OCH3	H	1,3
(23)	H	OCH3	1,3
(24)	OCH3	OCH3	1,3
(25)	H	H	1,2
(26)	H	H	1,4

Figure 2. The set of ammonium salts tested but not found to form adducts.

Comparison of the results for (1) and (2) where the iodide counter ion has been replaced with a bromide ion illustrates a considerable loss of inclusion ability along with the preference of (2) for smaller guest molecules as opposed to the much larger guests accommodated in clathrates of (1). This clearly indicates that the smaller counter ion corresponds to a tightening of the lattice structure resulting in reduced cavity space . Interestingly the use of triiodide as the counter ion leads to the total loss of inclusion ability, any cavity space being used to accommodate the very large anion.[4]

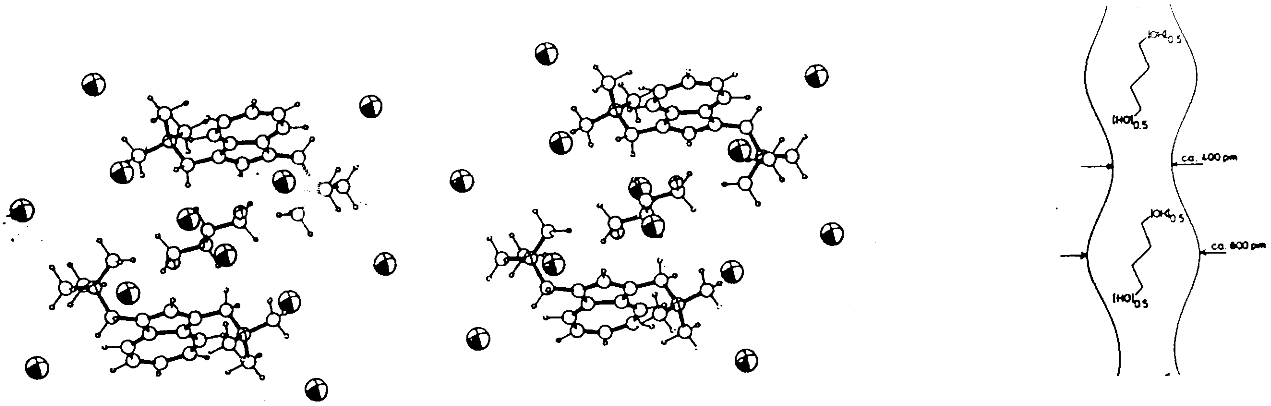
Similarly consideration of the molecular structures shown in Figures 1 and 2 gives hints at some generalisations about the structural moieties necessary for inclusion behaviour. It appears that both ionic groups are required, compare (1) and (4) with (18) and (27): the methylene "spacers" between the "anchor" group and the ionic group is present in most structures in Figure 1 its extension, in compound (19) or removal in compound (27) appears to lead to loss of or a lessening of clathrate forming properties. This is considered to result from the concept of optimum flexibility. A spacer group larger than the methylene allows the onium groups to much movement leading to the filling of any potential voids. Removal of the group removes the adaptability, necessary to accommodate a variety of guests: increasing the flexibility of the groups attached to the nitrogens of the onium groups appears to dramatically reduce host behaviour, compare (1)($R^1 = R^2 = R^3 =$ Me) and (3)($R^1 = R^2 =$ Me $R^3 =$ Et).

X-ray diffraction studies of several of the clathrates formed by the set of compounds shown in Figure 1 serves to confirm some of the theories presented above. Firstly a study of a number of clathrates of (1)[2] revealed no consistency in cavity dimensions. In fact it showed considerable adaptation of the host geometry to accommodate individual guests. Table 1 shows the crystal data for the structures discussed .

Table 1. Crystal data for some clathrates of (1)

Guest	Host:guest ratio	Lattice parameters	Space group	Cell Volumes	Crystal system	Z	[Ref.]
1-butanol	1:1	a = 16.477, b = 12.271, c = 13.485A ß = 109.94°	C2/c	2574 A3	monoclinic	4	[5]
1,4-butandiol	1:1	a = 7.85, b = 17.500, c = 9.700A ß = 96.50°	P21/m	1324 A3	monoclinic	2	[6]
iodomethane	1:1	a = 19.007, b = 17.305, c =7.555A	Pmna	2485 A3	orthorhombic	4	[1]

The variation represented in Table 1 is presented and discussed below. The structure of the (1).1-butanol clathrate[5] shown in Figure 3 revealed that the two onium side chains have a transoid relationship to the azulene "anchor" group. The guest molecules are located in tube-like cavities, fitted between alternating expansions and contractions in the tube shown schematically in Figure 3.



(a) (b)

Figure 3. (a) a stereoview of the crystal structure of the (1). 1-butanol adduct, observed in the direction of the a̲ - b̲ diagonal; (b) a schematic representation longitudinal section through the tube shaped cavity. Reproduced from reference [5].

The top and bottom of the tube are formed by the planar azulene rings, arranged in parallel layers, each layer containing molecules orientated in opposing directions. The lateral sides of the tube are formed from the onium groups projecting between the layers. The plane of the carbon atoms of the guest is almost parallel to that of the azulene rings; disorder in the position of the guest gives the apparent presence of a 1,4-butandiol molecule since the hydroxyl in the 1-butanol guest is found at either end of the pseudo cage. Leading to the conclusion that 1,4-butandiol would probably crystallise with an analogous structure. A full X-ray analysis of the (1).1,4-butandiol clathrate[6] however revealed a very different crystal structure. This result is difficult to explain since in neither case is there any obvious interaction between host and guest. Figure 4 shows some of the features present in this structure.

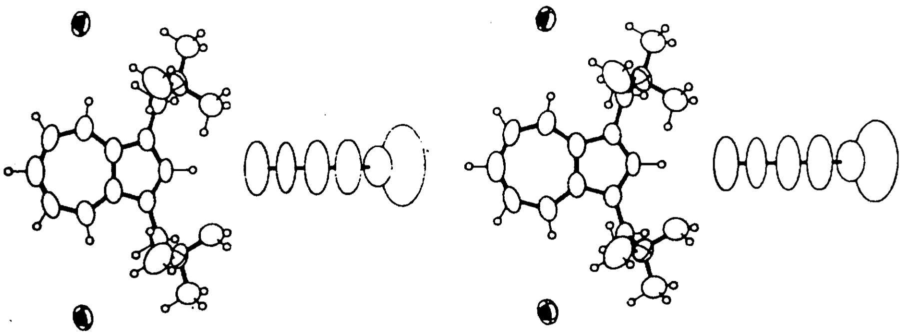


Figure 4. Stereoview of the crystal structure of the (1).1,4 butandiol clathrate. Reproduced from reference [6].

The onium groups in this case have a cisoid relationship to the azulene plane. The cavities are no longer tubular, the guest now being situated in a fully closed cage. As in the 1-butanol case, the top and bottom of the cage are formed by the azulene rings aligned in parallel layers, and the molecules are again orientated in opposite sense. The sides again by the onium groups and the cavities are aligned in a lateral direction. However the plane of the guest carbons is this time orientated nearly at right angles to the plane of the azulene rings. These differences illustrate that many subtle factors must be involved in the formation of these ionic host systems, a fact that obviously makes guest prediction difficult. The third structure is that of the (1).iodomethane clathrate[11]: see Figure 5 for some of the features of this structure.

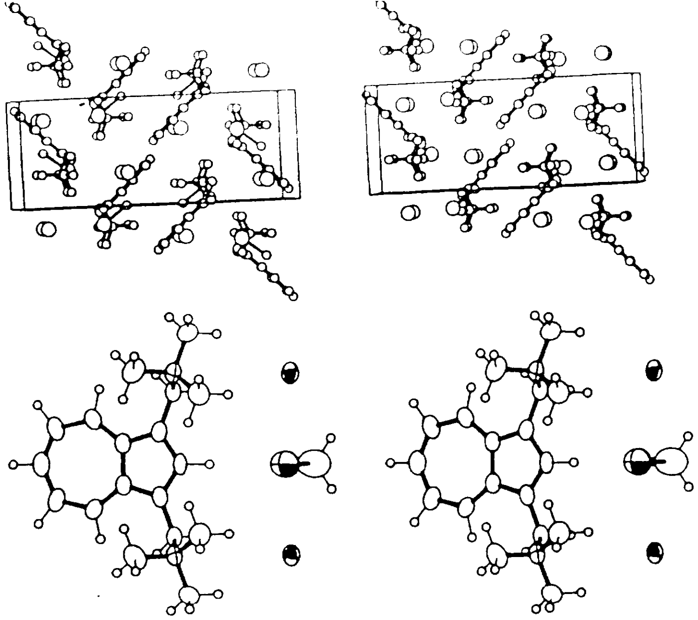


Figure 5. Crystal structure of the (1). iodomethane clathrate. (a) unit cell viewed across the azulene planes; (b) view perpendicular to the azulene plane. Reproduced from reference [1].

The guest is located in a cage, trapped between two onium groups, two iodide ions and a herring bone pattern of alternating stacks of layered azulene rings. Cell data for other clathrates of (1)[2] suggests different types of crystal structure, illustrating further the extraordinary ability of (1) to adapt to the geometry of its guest molecules.

Figures 6 and 7 show the unit cell of two clathrates which utilise as the "anchor" group t-butylbenzene[4]. The crystal data are given in Table 2.

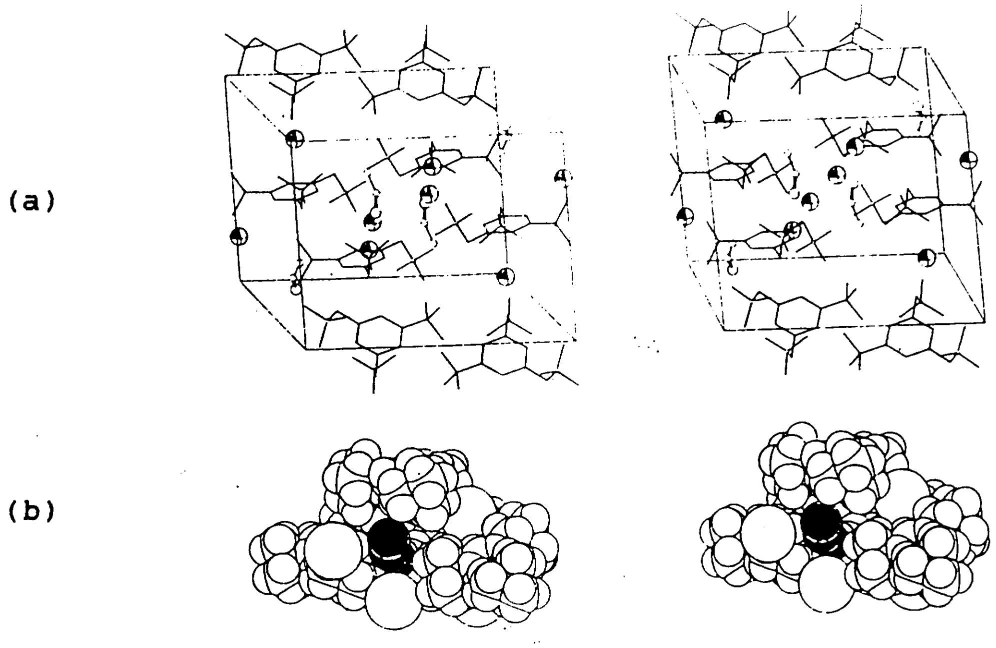


Figure 6. Crystal structure of the (5).ethanol adduct. (a) Unit cell stereoview; (b) space filling diagram (guest shaded). Reproduced from reference [4].

Table 3. Crystal data for the (5).ethanol and (11).isopropanol. water clathrates

Host	Host:guest ratio	Lattice Parameters	Space group	Cell Volumes	Crystal system	Z
(5)	1:1	a = 15.153, b = 12.023, c = 15.153A ß = 111.20°	C2/c	2618 A3	monoclinic	4
(11)	1:1	a = 14.696, b = 16.276, c = 12.659A	Pmna	3028 A3	orthrhombic	4

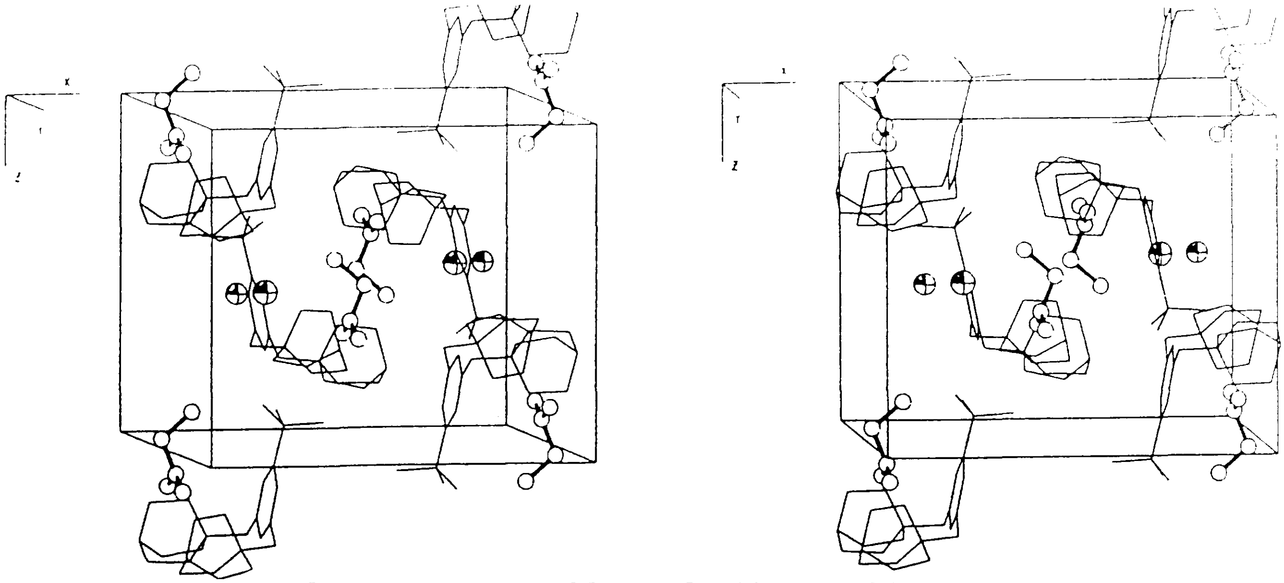


Figure 7. Unit cell of the (10).isopropanol.water clathrate. Reproduced from reference [4].

Figure 6 shows the (5).ethanol clathrate[4]. In this structure the onium groups are transoid with respect to the "anchor" group. Here the cavity boundaries however do not involve the use of the t-butylbenzene group. The true cage is lined with t-butyl groups and the onium side arms. Figure 7 shows the unit cell of the (11).isopropanol clathrate[6]. Here the much more bulky quinuclidinium ammonium groups are employed as the side arms with bromide as the counter ion. The arms exhibit cisoid arrangement, and the cavity, which contains two guests, is bounded by different parts of four host molecules. In addition to stoichiometric amount of isopropanol a molecule of water is also included at a fixed position in the unit cell. The distance of 3.48Å between a bromide ion and the water molecule indicates the presence of some hydrogen bonding between these species; a minimum distance of 4.1Å between water and the isopropanol molecules rules out any interaction between the different guest molecules. Figure 8 shows in detail the relationship of the positions of the host and isopropanol guest.

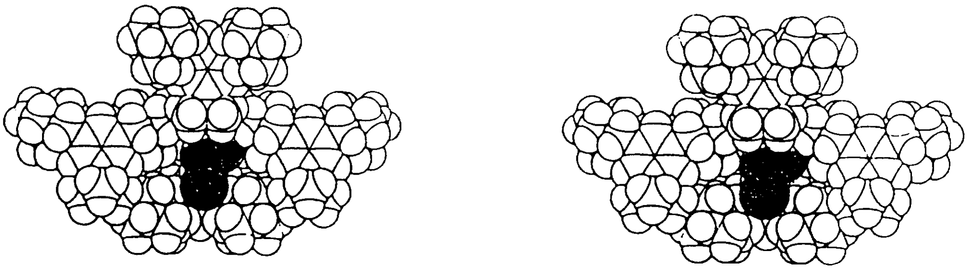


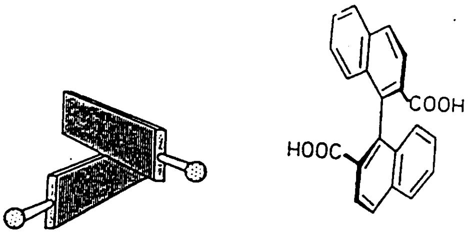
Figure 8. Illustration of the isopropanol adduct of (11). Guest is shown shaded in the cage type cavity. Reproduced from reference [6].

It has been shown in this chapter that a chance observation coupled to intelligent design, furthered by careful analysis of sucessful cases, can lead to the discovery of large and versitile host classes. These molecules also illustrate the ability of some host molecules to adapt their internal geometry to accommodate a large number of diverse guests. This perhaps indicates that clathrate minima offer, in the presence of suitable guests, the host, the possiblity of utilising low energy minima normally unable to exist in the crystalline state.

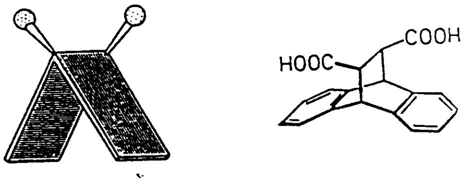
CHAPTER 2.

Moving from cases where the host lattice structure is comprised of an ionic network, to hosts which utilise hydrogen bonds between host molecules and between host and guest entities leads to the " Coordinatoclathrates", so named by a pioneer of these systems E. Weber[7]. Weber developed this concept in an attempt to pull together some accepted, if not definitely proven ideas about clathrate formation. Firstly the idea that molecular bulkiness and crystal inclusion are related and that polar groups on the host aid in structure formation specifically by hydrogen-bonded networks[8].

The coordinatoclathrate principle as utilised by Weber attempts to design guest specific host molecules by attaching polar sensor groups to planar aromatic anchor groups[9] with a "scissor" like or "roof" like structure. A further feature shared by the chosen molecules was the possession of C_2 symmetry, as shown schematically below.



"SCISSOR" (41)



"ROOF" (42).

It was hoped that these groups would not only aid in crystal structure formation by allowing polar interactions between individual host molecules but that by binding specifically with potential guest molecules could introduce a never before reported level of guest selectivity. The following chapter presents a summary of the work carried out in developing the above principle.

The principle grew out of a desire to select guest molecules using features other than their size as the discriminatory factor. It was felt that by using molecules of the type shown below a more subtle discrimination could be achieved, and that this would be facilitated by matching particular donor groups on the host with acceptor groups on the guest species and vice versa. Therefore it was projected that by using specifically polar interactions, e.g. dipole-dipole or H-bonds, this selectivity would be obtained.

The starting point for designing molecules with the features highlighted above was again a chance observation[10] that 1,1-binaphthyl-2,2-dicarboxylic acid (41), a compound normally obtained as an amorphous powder, gave colourless transparent crystals when recrystallised from ethanol. The included ethanol which was retained very strongly in stoichiometric quantities suggested clathrate formation. This molecule possesses the features outlined as necessary for "coordinatoclathrate" formation. The carboxy groups are the host sensors whilst the binaphthyl moiety provides the bulky anchor groups. A large number of "scissor" and "roof" compounds have been synthesised and their inclusion behaviour assessed. His study spectacularly confirmed his hypothesis. Weber has recently reviewed much of the work[11].

The investigation involved a detailed study of the crystal structures of adducts formed from these compounds. The study allowed Weber to identify several features which consistently turned up.

(i) Both enantiomers of the host molecules were always employed i.e no spontaneous resolution occurred.

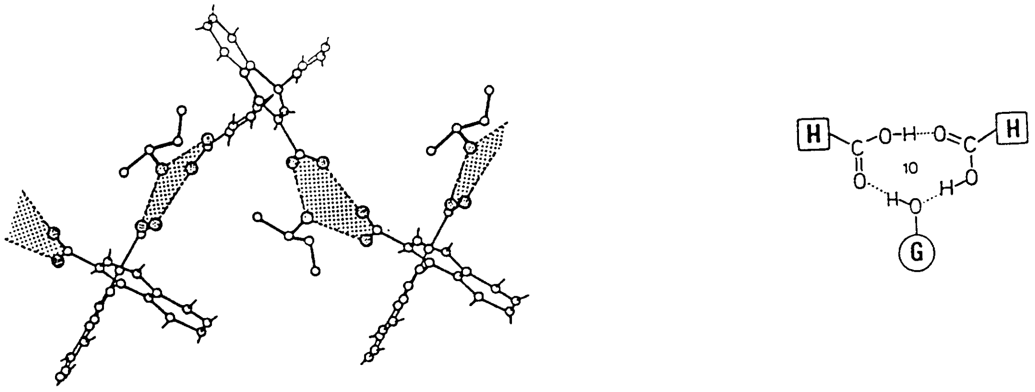
(ii) The structures contained closed rings of homodromic[12,13] hydrogen bonds

(iii) where applicable both enantiomers of racemic guests are included.

(iv) the full hydrogen bond donor/acceptor facilities of both host and guest are exploited.

(v) in the case where the guests are low molecular weight carboxylic acids, the acid often forms hydrogen bonded dimer pairs and therefore shows reduced host-guest interactions.

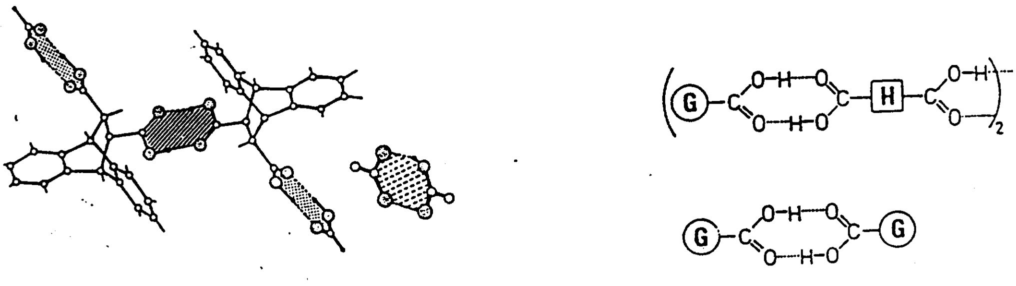
A number of crystal structures which illustrate the features discussed above will now be presented. The first example is that of the (41).2-butanol[7]. Figure 9 shows enatiomerically related host molecules separated by the homodromic hydrogen bonded ring containing a single guest molecule. A schematic of this arrangement is shown below along side the molecular diagram.



(a) (b)

Figure 9. (a) The molecular structure of the (41).2-butanol clathrate; (b) a schematic representation showing the hydrogen bonding present in the structure. Reproduced from reference [11].

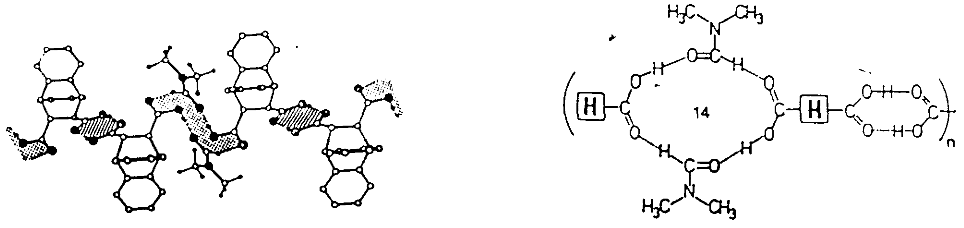
Figure 10 shows the formic acid adduct of the "roof" host trans-9,10-dihydro-9,10-etanoanthracene-11,12-dicarboxylic acid (42) [14]. Here two guest molecules are found centrosymmetrically related and hydrogen bonded to the two remaining carboxyl groups of a host dimer (MacNicol observed carboxylic acid guest dimers[15]). This host dimeric unit is formed by hydrogen bonding between the first pair of carboxyl groups. One half of one such entity is found in the asymmetric unit, along with a hydrogen-bonded guest dimer accommodated in channels formed by the repeating host-guest units. Again a schematic of the hydrogen bonding is shown in Figure 10.



(a) (b)

Figure 10. (a) The asymmetric unit of the (42).formic acid clathrate. (b) a schematic representation of the hydrogen bonding present in the structure. Reproduced from reference [11].

The hydrogen bonding features are also found in cases where aprotic solvents are included. This is illustrated by the (42).dimethylformamide clathrate[16]. Figure 11 reveals the structure of this host to be constructed of infinite chains of centrosymmetric hydrogen-bonded host dimers: the dimers are separated by 14 membered centrosymmetric, homodromic hydrogen-bonded rings containing two guest molecules.



(a) (b)

Figure 11. (a) The structure of the (42).dimethylformamide clathrate (b)a schematic representation of the hydrogen bonding present. Reproduced from reference [11].

A further strategy employed by Weber is the "propeller" model[17]. Here, molecules with potential trigonal symmetry and a variety of functional groups with hydrogen bonding potential were employed as suitable host candidates. This represented a change from the two-fold symmetry of the previous "roof" and "scissor" hosts. Figure 12 shows the structure of 1,3,5-tris(4-carboxyphenyl)benzene(43).3:dimethylformamide clathrate[17]. The host's molecular structure has exact three-fold symmetry (C_3) packing occuring in space group R3. However no host-host hydrogen bonding exists; and the hydrogen-bonding between host and guest does not utilise the full potential of either host or guest. i.e unlike in the cases represented above, here both the carboxy sensor groups of the host and the guest species are involved in only one hydrogen-bond. The unit cell shown in Figure 13 shows that individual host-guest units have self-assembled into centrosymmertic pairs at close to van der Waals separation between the central aryl units. Similar, but planned , centrosymmetric units, termed "Piedfort" units in true clathrate structures formed by more flexible triazines are described in the discussion section.

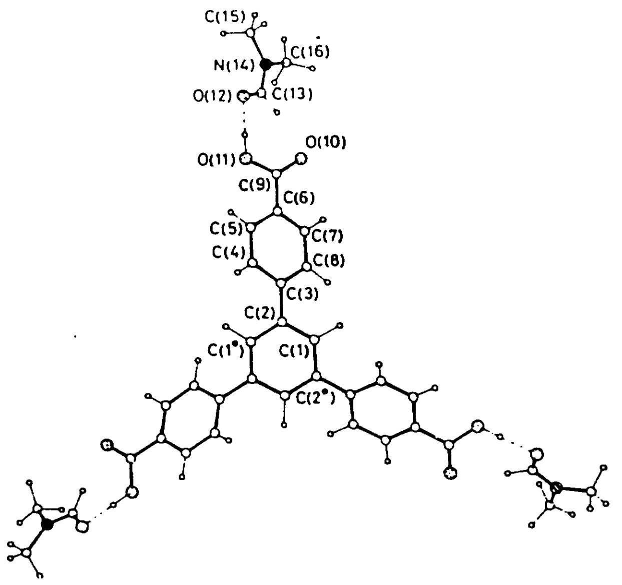


Figure 12. Top view of a host guest unit in the (43).3:dimethylformamide complex. Reproduced from reference [17].

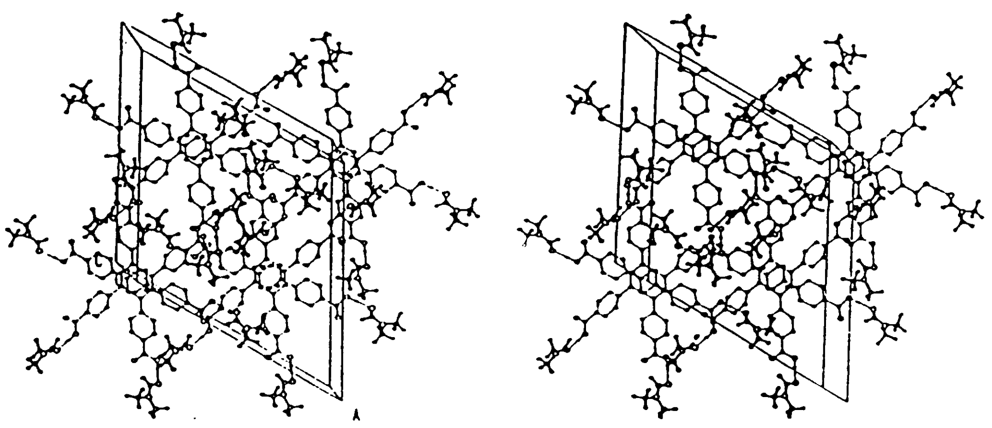
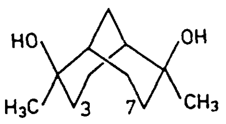


Figure 13. The unit cell showing molecular packing in the(43).3:dimethylformamide clathrate. The self assembled units can clearly be seen. Reproduced from reference [17].

Weber has shown that intelligent combination of molecular bulkiness and hydrogen bonding potential can lead to interesting new host systems. Further, that full use of potential symmetry elements is often displayed by the resulting host guest structures.

CHAPTER 3.

Following the observation that the bicyclic diol (44) exo-2, exo-6-dihydroxy-2,6-dimethylbicyclo[3.3.1]nonane [18] crystalised to give inclusion compounds from a number of solvents, an X-ray structural analysis of the (44).ethylacetate adduct revealed a helical "canal-host" structure. In this the individual host molecules, spontaneously resolved, pack in the space group $P3_121$ or its enantiomorph $P3_221$, and are found as part of two concentric helixes, which spiral round a crystallographic three-fold screw axis. The hydroxyl groups of the diol molecules are hydrogen bonded in sequence forming the double helixes (pitch 2c) as symmetry-related three-fold axes, or spines, six of which surround the central "canal" axis. A schematic illustration of this arrangement is shown in Figure 14 which also shows the symmetry features present in the structure. The walls of the resulting tube are lined with the hydrocarbon-like hydrogen atoms. These structural features were found in clathrates of a number of compounds from the list (45) - (53), synthesized[19] following the discovery of the clathrate forming properties of (44).



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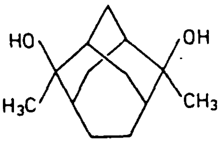

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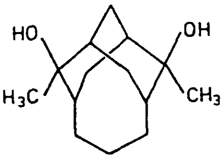

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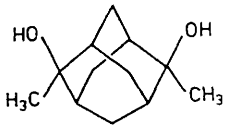

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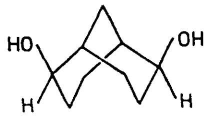

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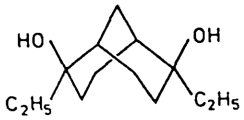

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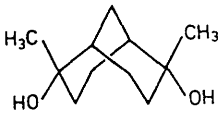

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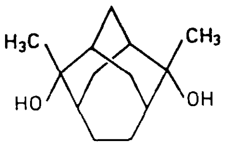

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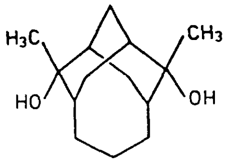

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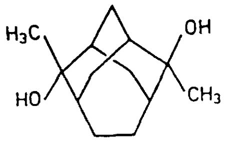


(53)

This chapter considers in detail the differences between the different helical canal inclusion compounds and attempts to relate these differences to the modifications made in molecular structures of the hosts. Some non-helical structures found in the series are also considered inorder to give a better insight into the molecular properties necessary for helical canal formation.

The helical canal feature was observed in the ethyl acetate clathrates of (44), (45), (46) and (51) and in the benzene clathrate of (52)[19] in all cases the spontaneous resolution had occurred and a common same space group is found. The schematic in Figure 14 gives the symmetry element of the $P3_121$ crystal space group. Theses are, three fold screw axes parallel to *c* at *X*, *Y* = 0,0; 1/3,2/3; and 2/3,1/3. Six two-fold axes perpendicular to *c*: two parallel to *a* at *Z* = 1/3,5/6; two parallel to *b* at Z = 1/6, 2/3 and two parallel to the *a*, *b* diagonal at = 0,1/2. Diol molecules which straddle the two fold axes at = 1/6, 1/2 and 5/6 only are hydrogen bonded around a tube in a spiral sequence (A) such that each diol molecule functions as a double hydrogen donor or a double acceptor in the sequence.

There is a translation of *c*/3 at each hydrogen bond and a complete turn of each spiral chain contains six diol molecules. The pitch is therefore 2*c* and the spiral is formed from two separate and identical helical chains without direct hydrogen between the individual helixes. It is worth noting here that for consistency the "*syn*" and "*anti*" terms used in describing the crystal structures presented here: refer to the bridge elements on the same "*syn*" or opposite "*anti*" side as the C-O bond directions. This does not always coincide with the "*syn*" and "*anti*" terms used in the systematic names. Where appropriate they refer to the hydroxyl functions relative to the larger of the bridges across the molecular two-fold axis. A summary of the crystallographic details for compounds (44), (45), (51) and (51) is given in Table 3.

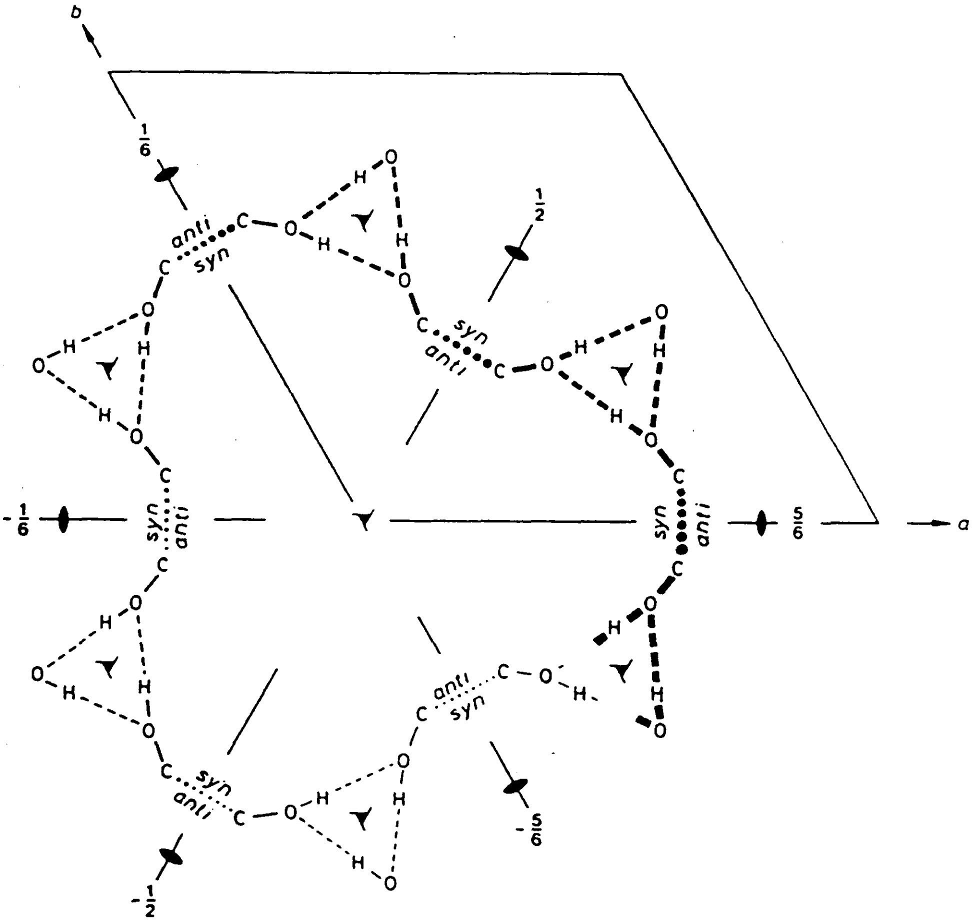


Figure 14. Diagrammatic representation of the sequence of hydrogen bonded diol molecules found in helical canal hosts. Reproduced from reference [20].

TABLE 3. Crystallographic data for shown compounds

	(44	(45)	(51)	(52)
Formula				
Formula mass	184	210	210	224
Space group	P3	*	P3 21	P3 21
a,b A	12.	11.905	13.192	13.740
c A	7.0	6.990	6.913	7.030
V A3	897	858.0	1041.98	1149.5
Z	3	3	3	3
m.p. °C	189	245-247	164-148	146.5-147

* Despite having the helical tube structure as well as trigonal lattice symmetry. The unit cell appears to only have two symmetry axes at *c*/2. The asymmetric unit expanded from one half molecule and a second molecule with pseudo two-fold symmetry.

In compound (52) the central methylene group of the propyl bridge is disordered equally between two conformations either side of a two-fold axis through the rest of the molecule[19]. There is consistency in all the lattices of the *c* spacing and therefore the pitch of the helix. Variations occurring in the *a* lattice parameter are consequently mainly responsible for changes in the cell volumes. It is shown below that these differences are not the result of differences in the inter-connection lengths of the diol between hydrogen bonded spines but are rather due to packing variations arising from the different diol shapes.

The intersecting of the van der Waals surfaces of the hydrocarbon-like hydrogen atoms which line the tube define the internal surface of the helical canal. A simple representation of the tube dimensions can be obtained from a projection of the unit cell along the *c*-axis showing the internal van der Waals radii. This yields a cross-sectional view of unobstructed area along the tube, which is therefore available for guest species without steric impediment. Such projections are shown in Figure 15 for compounds (44), (45), (51) and (52)[19].

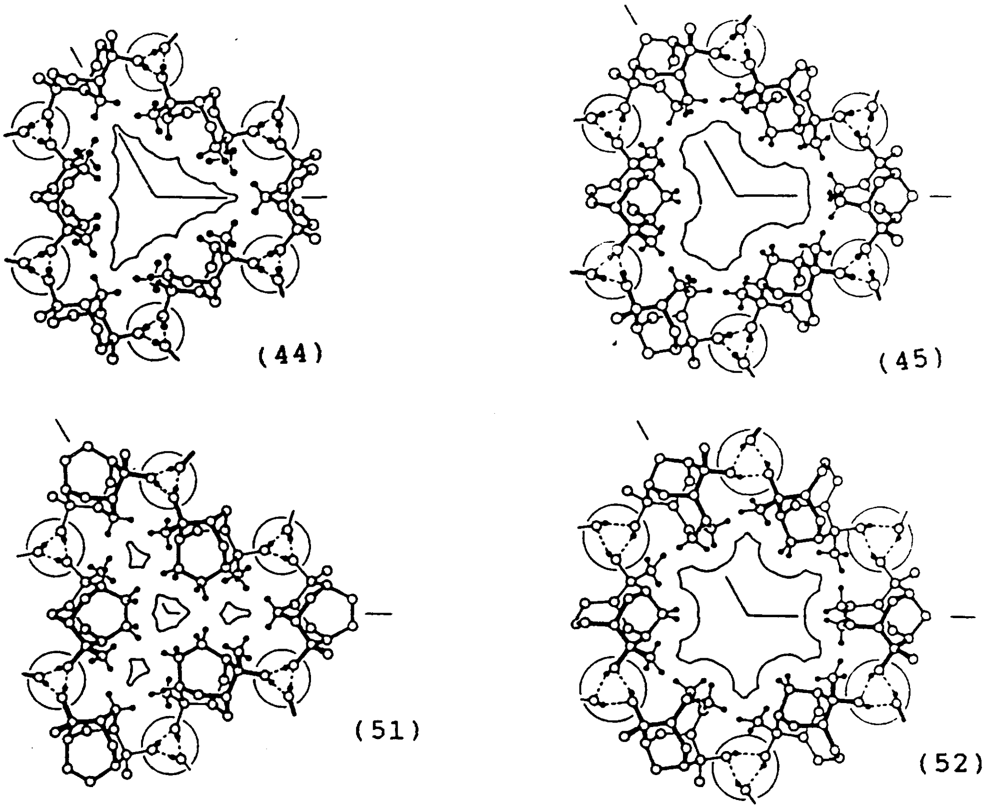

(44) (45) (51) (52)

Figure 15. Comparative projections along the *c*-axis showing the tubes enclosed for compounds (44), (45), (51), and (52). Reproduced from reference [19]

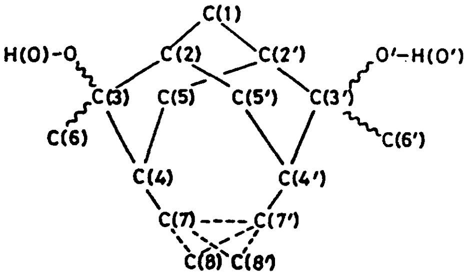
Table 4 shows the variation in the unobstructed areas associated with each compound.

Table 4. Free, unobstructed areas in the canals of the hosts

Compound	Unobstructed area Å2	Canal shape

(44)	22.4	Triangular
(45)	4.7	
(51)	30.2	Trilobed
(52)	34.7	Hexalobed

Consideration of the three dimensional tube shape will be presented later . Using the host numbering system given in scheme (B) some important intra-molecular dimensions are given in Table 5.



(B)

Scheme B

Little variation appears in these dimensions for all four compounds. The C(4) . . . C(4') distance varying as a result the different bridging groups. The relative orientation of the two C-O bonds is assessed by the notional bond angle C(3') . . . C(3)-O the spread of 122-126° reveals only slight variations. However considerable variations are observed in the notional torsion angle O-C(3) . . . C(3')-O, with lower values for the cases where the methylene bridging group is "<u>syn</u>" with respect to the C-O bonds. The higher values are found where the smaller bridging methylene is "<u>anti</u>" with respect to the C-O bonds. It is worth noting that in the cases of compound (46) where the methylene group is again in the "syn" orientation, a value of 71.3° is observed[19]. Further intra-molecular dimensions important in assessing the effect of molecular shape on lattice (and therefore canal) dimensions are given in Table 6[20].

Table 5. Some intra-molecular dimensions (from scheme (B))

Dimension (Å)	Compound			
	(44	(45)	(51)	(52)
O . . . . . O'	5.6	5.53	5.55	5.68
		5.53		
C(3) . . . C(3')	3.7	3.66	3.71	3.82
		3.67		
C(4) . . . C(4')	3.1	3.05	3.04	3.35
		3.06		
C(6) . . . C(6')	5.7	5.79	5.88	5.88
		5.80		
Angular Dimesions °				
C(3') . . . C(3)-O	126	124.8	122.3	123.0
		124.7		
		124.6		
O-C(3) . . C(3')-O	73.	78.9	94.3	97.2
		79.1		

Table 6. Values (A) of the radii defining the position of the host molecule along the two-fold axes.

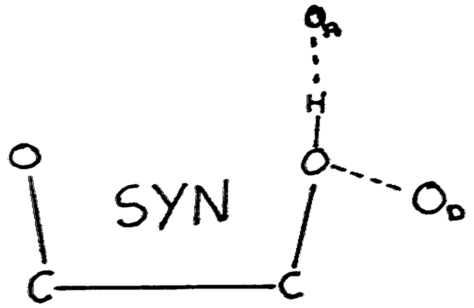
Radius	Compound			
	(44)	(45)	(51)	(52)
R anti (O . . . .O)	5.57	5.34	6.28	6.85
R syn (O . . . .O)	6.60	6.56	6.91	6.89
R anti (C . . . .C)	3.85	3.60	4.65	5.31
R syn (C . . . .C)	6.72	6.64	6.88	6.84

The displacement of the diol molecules along the two-fold axes are expressed by the radii R^{syn} (O . . .O) and R^{anti} (O . . .O).

These radii are defined as the distance of the intra molecular oxygen-oxygen vectors from the tube axis through the syn and anti faces. The sum of these R(O . . . O) radii gives tube size without consideration of any bridging group intrusions. While the ratio R^{syn}/R^{anti} correlates with the rotational twist of the projected triangular hydrogen bond spines and the directions of the hydrogen bonds relative to the host molecules. The second set of radii are relevant to the intrusions of the bridging groups into the tubes, being the distance between the vectors defined by C(2) . . . C(2') and C(4) . . . C(4') and the tube axis. They are labelled "syn" or "anti" depending on which face of the molecule they appear. Variations in R(O . . . O) radii are mostly in the R^{anti} values since the sum of these radii is the a dimension of the unit cell and the dimension is almost invariant. It can be shown that variations in the absolute area contained between the hydrogen bonded spines are the result of changes in theses R^{anti} values. The twist of each diol molecule about its two-fold axis can be expressed as the difference between the $\underline{z}$ co-ordinates of the two oxygen atoms. The respective values for (44), (45), (51) and (52) being 1.39, 1.42, 0.87 and 1.62Å. The angle of inclination of the C-O bonds to planes perpendicular to the spine axes are for (44), (45), (51) and (52) 13, 14, 21 and 8°, the variations being of no real significance. For the above condition to be meet and the pitch of the helixes, 2c, to remain unchanged requires large variations in the angle of approach of the C-OH group to its hydrogen bond spine. Table 7 shows hydrogen bonding distances and angles for the local environment (C).

Table 7. Hydrogen bond angles and distances around the triangular

spines	(44)	(45)			(51)	(52)
Dimesion						
O-H (Å)	0.81	0.81	0.85	0.89	0.76	0.87
C-O-H (°)	114	105	114	109	109	109
O . . . OA (Å)	2.81	2.84	2.84	2.83	2.98	3.08
C-O . . . OA (°)	108.4	106.6	106.4	106.4	108.1	112.1
O-H . . . OA (°)	170	170	162	171	172	173
C-O . . . OD (°)	128.2	132.3	132.5	132.8	130.4	120.2
OA . . .O . . . OD (°)	122.33	120.8	120.9	120.7	113.4	111.5



(C)

In all cases the acceptor O_A toward which the O-H bond is directed is on the "*syn*" face of the molecule. There is no apparent strain in the hydrogen bonds most, being close to ideal values. The C-O . . .O_A angle is close to tetrahedral (in all cases in the range 106-112°). The only significant variations in dimension between all four compounds appears in the O . . . O_A distance of (51) and (52). This increase indicates a weakening. This weakening appears to be the result of the increase in the R^{anti} (O . . .O) distance which is observed in (51) and (52). The size of the "*syn*" bridging functions clearly have an effect on the tube shape and therefore its capacity for guest inclusion. A useful expression of the intrusion into the tube are the R(C . . .C) radii given in Table 6. It can be seen that R^{anti}(C . . .C) is always less than R^{syn}(C . . .C). The general topological features of the tube wall are given in Figure 16[20].

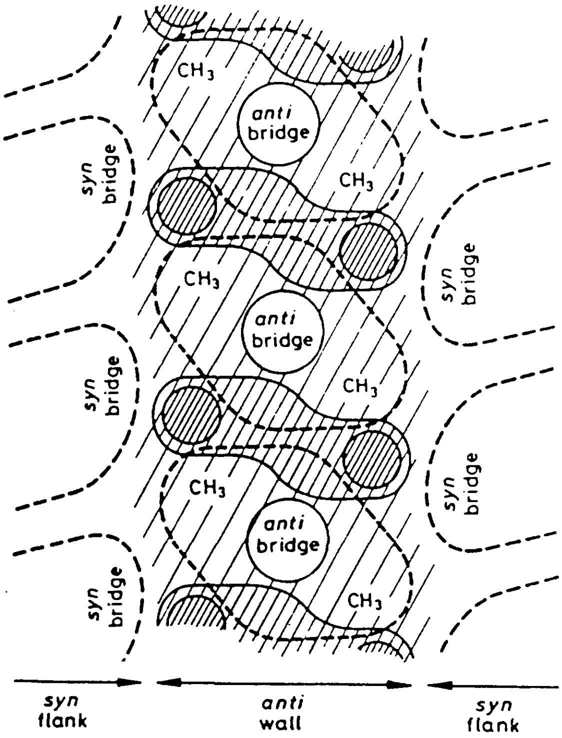


Figure 16 General topology of tube "*anti*" wall The degree

ofcross-hatching is proportional to the depth ito the wall accessible to guest. Reproduced from reference [20].

In compounds (45), (51) and (52) the anti bridge protrudes into the tube but because the bridges repeat approximately every 7Å (the pitch of the helix) there is considerable volume between these intrusions. A second region of moderate depth extends over the remainder of the anti wall. A deeper bent crevice extends across the wall. This contains even deeper tunnels through the walls. Whilst these tunnels cannot accommodate guests, the lateral crevices are in all cases sufficiently large to fit methyl groups or methylene/methine edges of any guest molecule. Hence the most obstructed case, in projection, (45) has these lateral crevices to the same extent as the others.

A summary can now be given of features necessary for helical canal behaviour.

(i) The diol must have C_2 rotation symmetry. Exact two-fold symmetry need not be adopted in the crystal structure.

(ii) The alicyclic structure must be capable of a small degree of flexibility. This allows the skeleton to twist slightly aiding the conformation imposed by the lattice. Thus the rigid adamantane analogue (47) adopts a very different crystal structure[22] as it lacks this flexibility.

(iii) A bridge on the opposite side of the molecule to the hydroxyl groups is optional. It can be removed or modified to control canal dimensions.

(iv) The two hydroxyl functions must separated by a molecular bridge: this buttresses the walls of the canal against collapse to a denser structure.

(v) The tertiary alcohol groups can only have a methyl substituent. This appears to have just the "correct" size, shape and rigidity to support the canal wall structure.

Figure 17 shows a projection diagram and a short set of data for Compound (46) which also meets the above set of conditions leading to helical canal host behaviour[23].

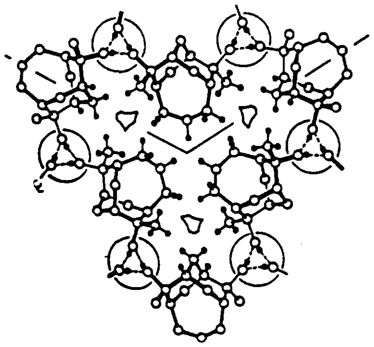


Figure 17. A projection diagram of a helical canal structure of compound (46). Reproduced from reference [23].

X-ray analyses of some of the other compounds shown above is worth consideration. Structures of compounds (48) and (49) show no clathrate behaviour or spontaneous resolution[24].

The asymmetric unit in the structure of (48) consists of two independent molecules while (49) has only one molecule per asymmetric unit in the orthorhombic space group Fdd2. Comparison of the intra molecular dimensions of (48), (49) and (44) revealed virtually identical distances. The different structures appeared to results from variations in the hydrogen bond networks found in the respective structures. In all cases the full hydrogen bond potential is utilised. Figure 18 a schematic projection of the crystal structure of (48) reveals that the diol molecules are stacked along the b̲ axis in a pseudo hexagonal array of stacks.

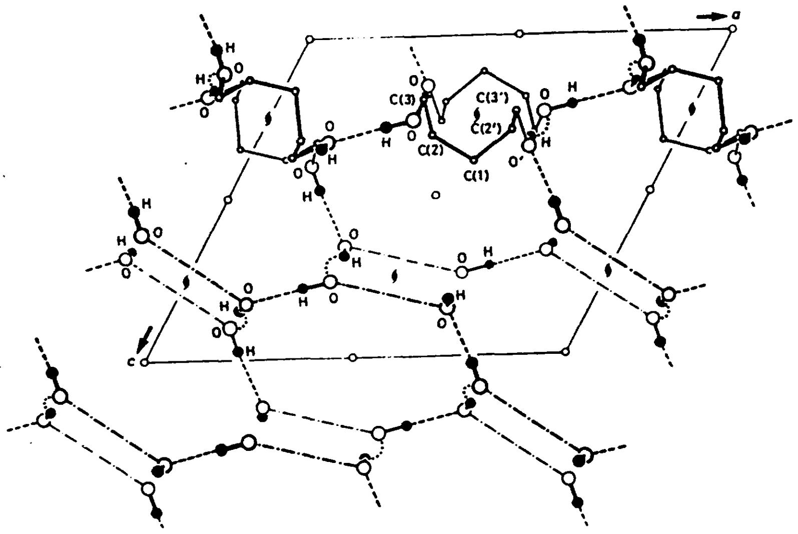


Figure 18. Diagramatic representation of (48) projected along the b̲ axis, showing the stacking of the molecules along the two-fold screw axes. Reproduced from reference [23].

The angle of cant between the stacking axis and each molecule excludes any similarity to canal structure of (44). The angle between the C(3)-O bond and the stacking axis in (48) is, for each independent molecule, 54.1° and 31.3°[24]. The analogous angle in (44) being 102.5°[19]. The hydrogen bond network in (48) consists of infinite connections in which the linkages alternate as inter and intra stack bonds extension occurring in glide operations. The arrangement of molecules linked along the direction by the Hydrogen bonded chain is shown in Figure 19(a). The diagram reveals that the chain loosely approximates to a spiral, however no similarity to the structure of (44) can be inferred. Figure 19(b) shows a schematic of the crystal structure of compound (49)[24]. Unlike all previous structures encountered the hydrogen bonding network here occurs as a four membered rings not infinite chains. The molecules are stacked along 2_1 screw axes parallel to the axes. The hydrogen bonds protrude from these stacks nearly at right angles to the 2_1 axes and provide links between four adjacent stacks arranged around a two-fold axis. The oxygen atoms of the four membered rings are displaced 0.47Å from the mean ring plane.

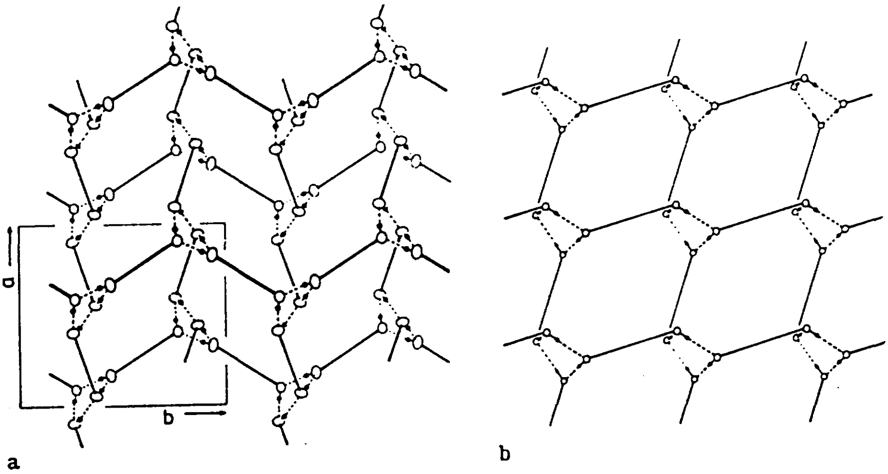


Figure 19 (a) a schematic diagram of the crystal structure of (48) (b) a schematic representation of the crystal structure of (49). Reproduced from reference [24].

Comparison of the internal angles of diols in a helical canal structure and those of diols which did not give this feature[25] revealed that any of the diols could adopt conformations which were able to be fitted into one of the helical canal crystal structures (except (49). It was therefore proposed that these structures may represent relatively shallow wells on the crystal free energy surfaces of the compounds. Evidence for this theory was obtained when it was found that on crystallisation from benzene (51), while still giving inclusion adopted an entirely different crystal structure to a helical canal[25]. This new structure having the tetragonal space group $I4_1/abc$ and a host:guest ratio of 4:1.

No spontaneous resolution occurs so the host structure is achiral. The structure is maintained by cyclic hydrogen bonds, seen in Figure 20 as dotted lines, in approximate squares which connect four host molecules.

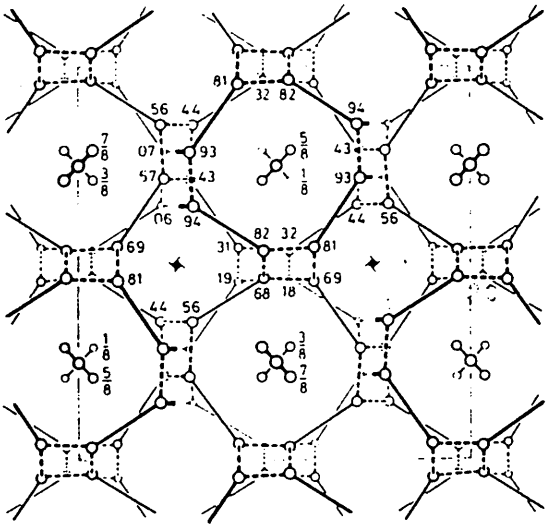


Figure 20. Schematic representation of the crystal structure of the (51).benzene clathrate viewed along the *c*-axis the host molecules are represented by solid lines and the hydrogen bonds by broken lines. Reproduced from reference [25].

Diol molecules, connected in cyclic quartets at the "level" edges of the squares, surround the channels of the linked guest cavities. Molecules connected *via* the "steep" edges occur in double spiralling chains around the 4_1 and 4_3 screw axes which are parallel to the axis. The crystal is racemic, with diol enantiomers aggregated around the left and right-handed screw axes. The host molecules surround hydrocarbon lined ellipsoidal cavities separated by c/2 along the crystallographic two-fold axis which is again parallel to the c-axis. The snug fit of the benzene guests in the resulting cavities can be seen in Figure 21[25]. Constriction in the canals make translation of benzene molecules along the canal impossible.

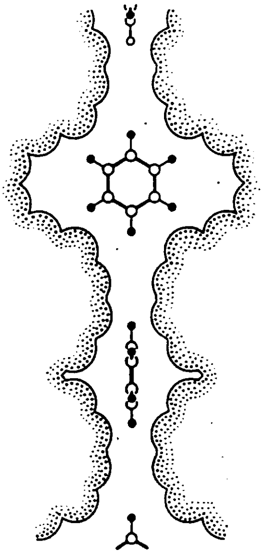


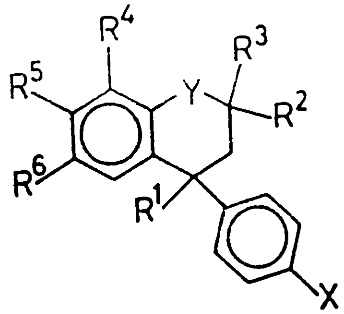
Figure 21 Cross-sectional representation of the cavities of the (51) .benzene clathrate The cavities are linked along two-fold axes parallel to the c-axis. Reproduced from reference [25].

Bishop's work represents again a situation where detailed structural analysis of existing hosts can give insights into the factors involved in their formation. This in turn aids more systematic design of new host molecules. However it is again apparent that even the most extensive analysis cannot always allow for the subtle forces at work in crystal formation. It is perhaps significant that the host species maintain a high degree of molecular as well as crystallographic symmetry on the formation of clathrates.

CHAPTER 4.

Summarised here will be the work of MacNicol and coworkers the further development of which was the aim of the work presented in this thesis. MacNicol's interest in the inclusion field began with attempts to produce new hosts with structures analogous to Dianin's compound (4-p-hydroxyphenyl-2,2,4-trimethylchroman)(54)[26,27,28] to this end firstly the thiachroman analogue[29] (55) (4-p-hydroxyphenyl-2,2,4-trimethylthiachroman) was synthesised. Following success with this compound, a large number of methyl-substituted analogues [such as (56 - 63)] were prepared. The compounds (56-60) giving host structures isomorphous with that of Dianin's clathrates, space group R$\bar{3}$.

Figure 22 illustrates this isomorphism well showing comparative stereo views of an unsolvated form of Dianin's compound[30], the clathrate of (55) and 2,5,5-trimethylhex-3-yn-2-ol[31] in Figure 22(b) and the 4-p-hydroxyphenyl-2,2,4,8-tetramethylthiachroman (56).cyclooctane[32] in . Figure 22(a) the unsolvated form of (54) shows the inter-column packing of the columnar stacks of hydrogen bonded hexamers. Figure 22(b) shows the corresponding molecular orientation of the thiachroman (55). However, as can be seen in Figure 22(c), the presence of the R^4 methyl group (56) caused the shortening and widening of the cavity between the hexameric units in order to accommodate the group in an iso-morphous structure.



R1 = R2 = R3 = Me, Y = O, X = OH (54)
R1 = R2 = R3 = Me, Y = S, X = OH (55)
R1 = R2 = R3 =R4 = Me, Y = S, X = OH (56)
R1 = R2 = R3 =R4 = Me, Y = S, X = OH (57)
R1 = R2 = R3 = Me, Y = Se, X = OH (58)
R1 = R2 = R3 = Me, Y = S, X = SH (59)
R1 = R2 = R3 =R5 = Me, Y = O, X = OH (60)
R1 = R2 = R3 =R5 = Me, Y = S, X = OH (61)
R1 = R2 = R3 =R6 = Me, Y = S, X = OH (62)
R2 = R3 = Me, Y = O, X = OH (63)
R1 = R3 = Me, Y = O, X = OH (64)
R1 = R2 = Me, Y = O, X = OH (65)

$R^1 \sim R^6 = H$ unless specified

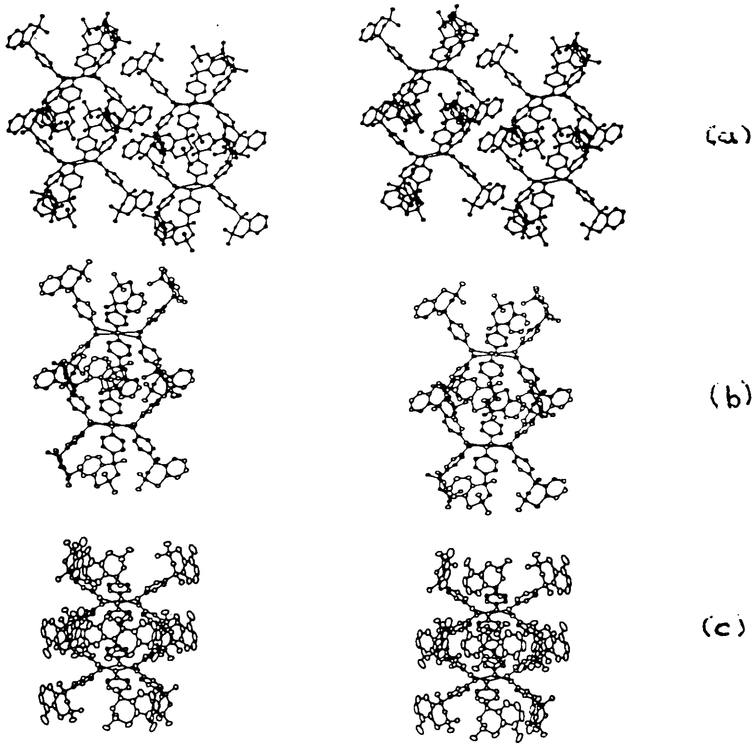


Figure 22 Dianin's and two iso-morphous structures. (a) Unsolvated form of Dianin's compound (54)(b) (55).2,2,5-trimethylhex-5-yn-2-ol clathrate. (c) (56).cyclooctane clathrate. Reproduced from references [30], [31] and [32].

Methyl substitution at $\underline{R}^5$ or $\underline{R}^6$ in both the chroman and thiachroman cases compounds (60), (61) and (62) lead to loss of inclusion behaviour the presence of methyl groups at these positions interrupts inter-column packing and forces the molecules to adopt alternative packing[33]. Interestingly chiral modification while forming clathrates failed to select single enantiomers from racemic guests[34].

The recurrence of the hexameric hydrogen-bonded structure found in the clathrates shown above and its presence in the clathrates of quinol (66)[35] and (67) phenol[36] led MacNicol and coworkers to synthesise compounds with a hexagonal core and six bulky substituents in the belief that this arrangement would also produce host behaviour. MacNicol saw the formation of the substituted benzene ring as the formal replacement of the labile hydrogen-bonded rings by permanent covalent bonds. This approach he called the "hexa-host" strategy[37]. Figure 23 shows a schematic representation of the "hexa-host" analogy.

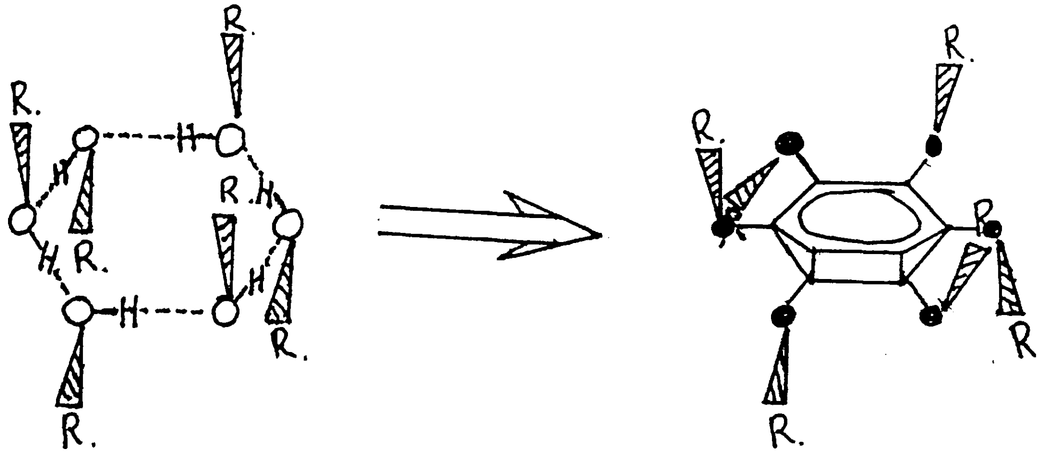


Figure 23. The "hexa-host" analogy.

The first compound of this new potential class of hosts [the "hexa-hosts"] Hexakis(thiophenoxy)benzene (68)[37] provided support this theory since it was indeed a versatile host. This led to the synthesis of an extensive set of new hosts[38], some of which are shown below in Figure 24.

(68) $C_6(SPh)_6$[36] (69) $C_6(SePh)_6$[39]

(70) $C_6(CH_2\text{-}S\text{-}[CH_2]_2\text{-}Ph)_6$[40]

(71) $C_6(CH_2\text{-}S\text{-}Ph(\underline{p}\text{-}Bu^t)_6$[41]

(72) $C_6(CH_2\text{-}N(COCF_3)\text{-}CH_2\text{-}Ph)_6$[42]

(72) $C_6(CH_2\text{-}O\text{-}Ph)_6$ [38]

Figure 24. Representative "hexa-hosts prepared by MacNicol and coworkers.

Many of the clathrates produced exhibit approximate trigonal symmetry and are centro-symmetric. The exact trigonal symmetry in Dianin's compound and its analogues, the clathrates of phenol and quinol along with other well known hosts systems such as (73)triphenylmethane[43], (74)PHTP[44], led MacNicol to design two new hosts, (76) Z,Z,Z,-1,5,9,-tris(thiophenoxy)-1,5,9,-cyclodecatriene and the p-mehtyl analogue (77)[45].

The X-ray structure of the hexakis-(selenophenoxy)benzene (69). 2 CBr_4 clathrate shown in Figure 25 is trigonal with space group $R\bar{3}$[39]; the view direction is towards the a, c plane. The cell shown is a rhombohedral cell where the c-axis of the trigonal cell has become the (vertical) diagonal of the rhomb. A directly analogous structure is found in the adduct of (68) with 2 CCl_4[37].

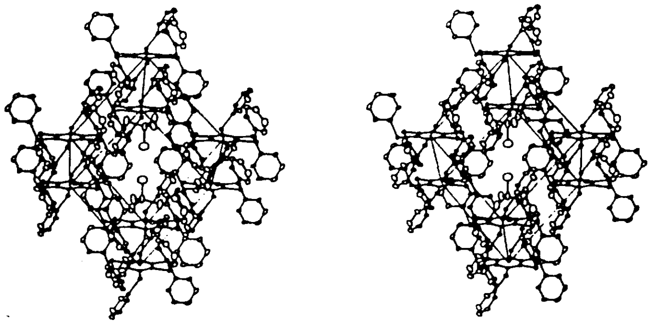


Figure 25 A stereoview showing the host guest packing in the crystal structure of the carbontetrabromide clathrate of (69). Reproduced from reference [39].

MacNicol also extended the idea of formal replacement of hydrogen bonds with covalent links. The flavan (78) 2'-hyroxy-2,4,4,7,4'-pentamethylflavan reported by Baker[46] to crystalise with a number of polar solvents, was later examined as the adduct with, 1,4-dioxane and water (2 : 1 : 2)[47]. Careful study of this structure suggested to MacNicol that *trans*-1,4-bis-(hydroxymethyl)cyclohexane (79), unlike the *cis* diastereoisomer, could specifically replace the dioxane : water guest assembly. This proved to be so[48] with the host almost exclusively trapping the *trans* isomer from a mixture (70% *trans*) of the two. The similarity of the structures produced can clearly be seen in Figure 26.

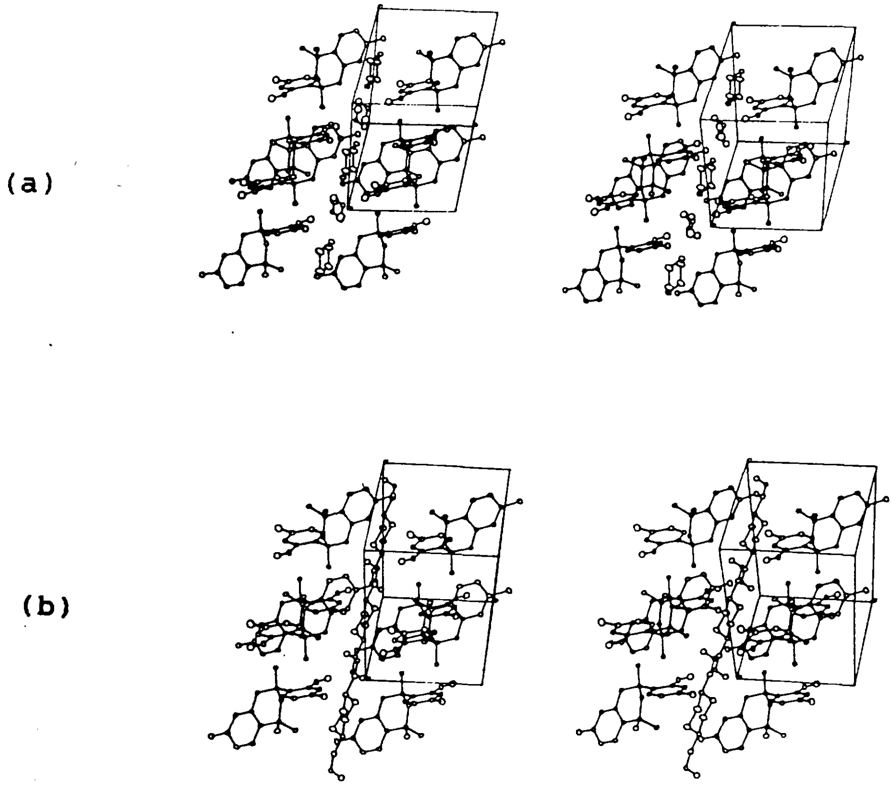
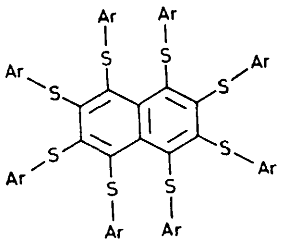


Figure 26. The structures of the (78). dioxane.2 water and (78). trans-1,4-bis(hydroxymethyl)cyclohexane(79) adducts. Reproduced from reference [48]

MacNicol's next development was made by replacing the central benzene moiety, of the "hexa-hosts" by the naphthyl group. This led to the successful new host group, named "spider" hosts[49], with the general structure shown below.



The first "spider" molecule (80) octakis(thiophenoxy)napthalene[49] did not give evidence of inclusion compound formation. However unperturbed MacNicol and coworkers went on to synthesis compounds (81-83)[50].

$C_8(SAr)_8$ (80) Ar = C_6H_5

(81) Ar = m-Me C_6H_4

(82) Ar = p-Me C_6H_4

(83) Ar = o-Me C_6H_4

All three proved to be host molecules. Figure 27 shows the structure of the (81) octakis(3-methylthiophenoxy)naphthalene.1,4-dioxane clathrate. In this structure the dioxane guest is statistically disordered about a four-fold axis is situated in a closed (true clathrate) cage.

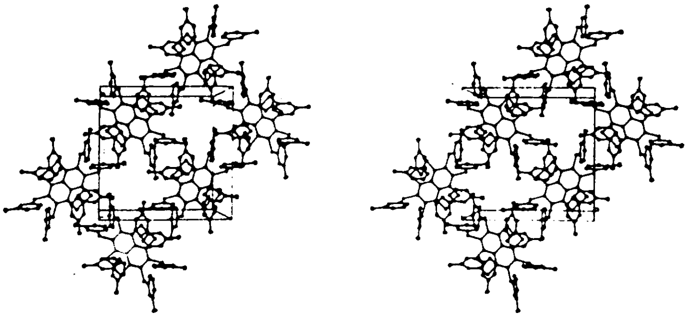


Figure 27. A stereoview looking down the c-axis, of the host-guest packing in the 1,4-dioxane clathrate of (81) the (disordered) guest molecule is not shown. The tetragonal adduct has space group P_4/ncc. Reproduced from reference [50].

MacNicol has consistently, since the discovery of the "hexa-hosts", used innovation rather than adaptation to produce novel host structures. This thesis describing new results hopes to further that tradition.

CHAPTER 5.

This chapter illustrates examples of mono-molecular hosts. It traces the development of a class of compounds, named cavitands[49] by their designer, Professor D. J. Cram. An interesting new type of mono-molecular host species the carcerands[50] is also discussed. Cram, one of the joint winners of the 1987 Nobel Prize for chemistry, has produced much chemistry relevant to the field of inclusion science[51]. Here, however, the compounds are limited mainly to those which do not have specific polar interactions between host and guest. Inclusion here relies on a pre-organised cavity built into the structure of the single molecule and this void is capable of accommodating a guest species in either crystal or solution states (and in some cases both). Thus one sees the major difference between mono-molecular and multi-molecular host systems: a multi-molecular system requires the organisation of a number of host molecules in order to enslave the guest whilst the mono-molecular host possesses a cavity within the single molecule suitable for guest accommodation. The guest is often a solvent molecule or, of potentially more practical use, a co-solute of the host.

The first cavitands synthesized by Cram[49] were formed from comformationally mobile cyclophanes of type (1) (B = 2H, A = H and R =Me) reported by Hõgberg[52]. These molecules are prepared by condensation of four resorcinol molecules with acetaldehyde[53], and have been reported since the nineteenth century (see references in [52]). Cram utilised these cyclophanes as host molecules in their own right[54]. However, since these involved host-guest hydrogen bonding they will not be discussed here. Compounds with the general structure shown have been synthesized by Cram as potential cavitand hosts. The nature of the pre-organised so called "bowl" cavity being immediately obvious.

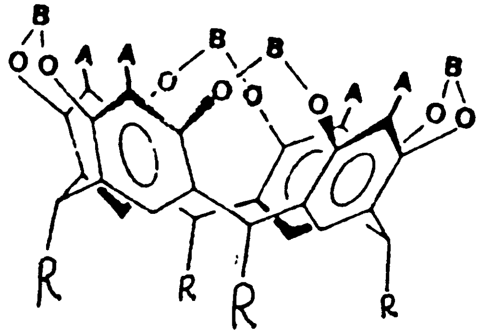
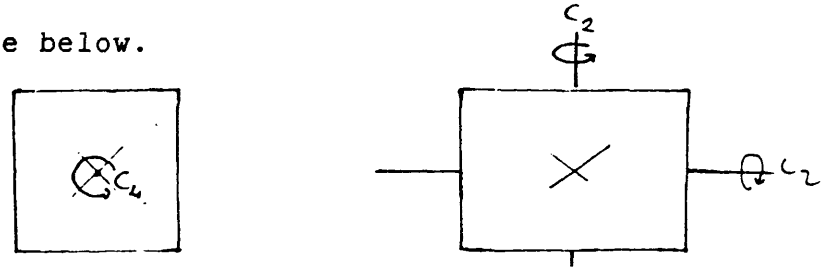


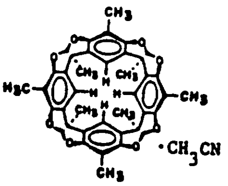
Figure 28. The general structure of cavitand hosts.

Cram synthesized a large number of compounds, varying the linking group B from methylene bridges[55] to substituted silyl groups[56], producing a wide range of host molecules. Taking the principle one step further Cram introduced a second pre-organised cavity by placing substituted phenyl groups in the R position, which had up till then been limited to methyl, producing the so called "box" and "bowl" hosts[57]. Molecules of the general type shown above are capable of possessing a perfect C_4 axis. Only (84).CH_3CN actually contains this symmetry element[55]. The rest of the structures have C_2 or approximate C_2 axes.

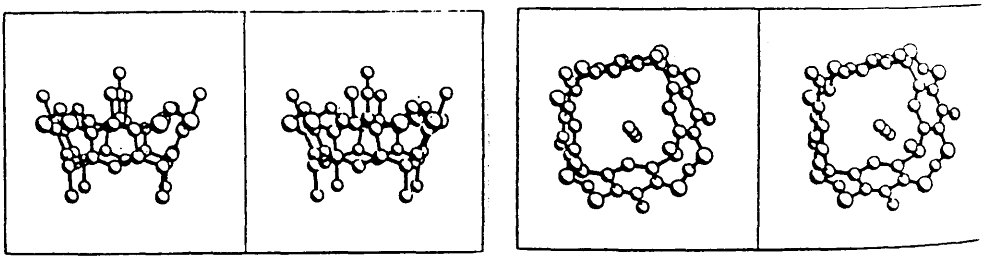
The phenyl rings which form the walls of the bowl-shaped cavity undergo adjustment in pairs, one pair moving out from, whilst the other is moved in, from the ideal "C_4" positions. This gives schematically a rectangle with "C_2" axes rather than a square arrangement with an exact "C_4" axis. See below.



X-ray structures of examples of the three types of cavitands mentioned are given below. Compound (84) where A = CH_3, B = CH_2 and R = CH_3 which on crystallisation from acetonitrile gives a molecular orientation possessing perfect four-fold symmetry the statistically disordered methyl end of the acetonitrile group penetrating deep into the bowl cavity leaving nitrogen atom nearly level with the hydrogens of the methylene groups linking the <u>ortho</u> carbons of the phenyl group. This can be seen in Figure 29.



(84)



(a) (b)

Figure 29. Two views of the X-ray structure of the (84). acetonitrile clathrate: (a) a side view; (b) a plan view of the molecule. Reproduced from reference [55].

Figure 30 shows an X-ray structure of a host in which a substituted silyl group was used to link the aryl groups[57] .In the case of (85), A = H, B = SiMe$_2$ and R = methyl. The presence of the methyl groups on the linking silicon atoms which point both toward and away from the cavity centre. Those pointing inward constricting the bowl entrance allowing only a slender linear host to enter. This can clearly be seen in the case of (85).CS$_2$ where the guest molecule appears to have "slipped" neatly into the small entrance left open by the intruding methyls. Careful consideration of the plan view also allows the reader to appreciate the loss of exact C$_4$ symmetry, the distance from the C(6) carbons of the phenyl groups at the top and bottom of the diagram being less than that between the equivalent carbons of those on either side.

Figure 30. The crystal structure of the carbondisulphide clathrate of (85). Reproduced from reference [57].

The (86)(A =Me, B = CH$_2$, R = Ph).benzene clathrate is a good illustration of a "bowl", "box" host[58]. Figure 31 shows a view of the general structure of these hosts, the bowl being formed by the linked resorcinol rings as before but now aryl groups attached at the R position of the general host form a second cavity capable of retaining a guest.

Cram realised that he could by suitably reacting together two cavitands he could possibly create "closed surface hosts with enforced interiors, large enough to imprison behind covalent bars guests the size of ordinary solvents."[59] He reported the creation of such a host formed by shell closure of two hemi-spherical cavitands producing a new host group he named the "carcerands"[59]. The synthesis of the first example involved placing reactive groups in the A position of cavitand molecules.

Cram synthesized compounds (87) A = methylenethiol, B = methylene and R = methyl (88) A = methylene chloride B = methylene and R = methyl coupling these under high dilution conditions using cesium carbonate in a mixture of dimethylformamide and tetrahydrofuran under an argon blanket. The compound formed (89) shown in Figure 32 proved intractable to usual spectral analysis due to its great insolubility. However using Fast Atom Bombardment Mass spectral analysis he identified a parent ion for (89) as well as ions indicating the inclusion of individual or combinations of elements from the reaction medium including to his surprise Argon which must have been dissolved in the reaction solvent.

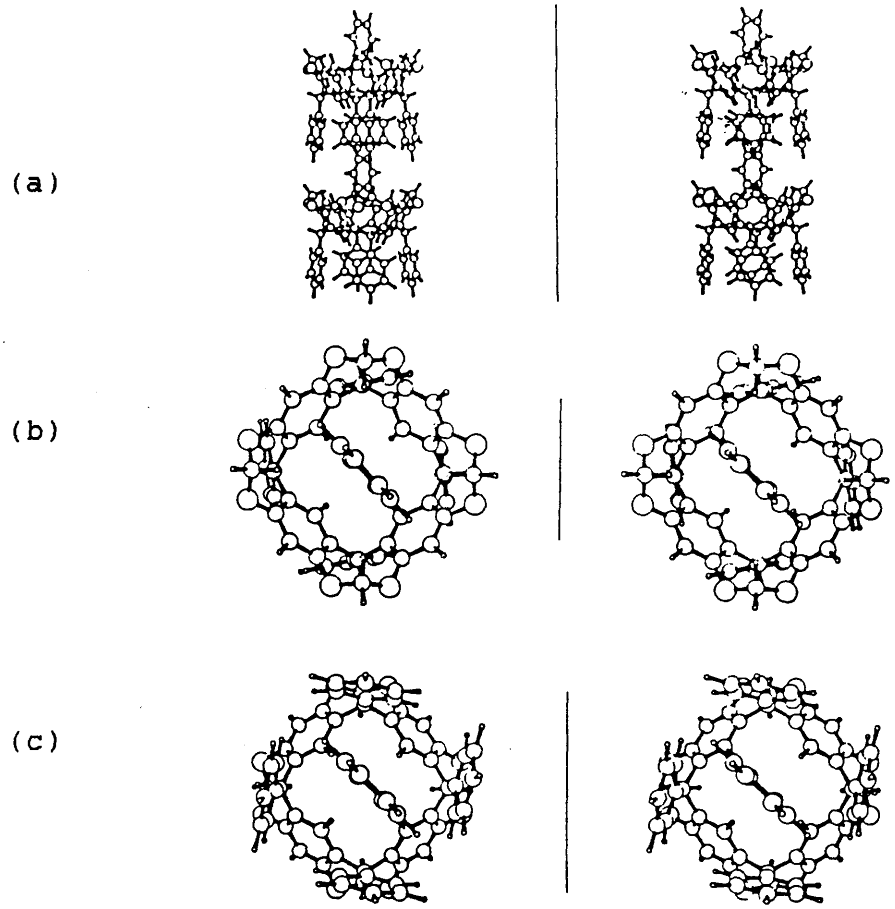
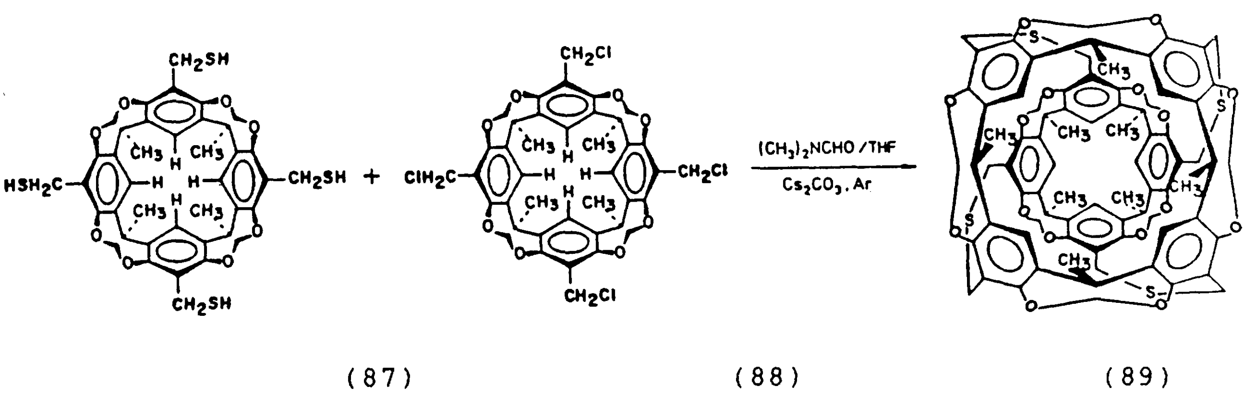


Figure 31. Three views of the "Box-Bowl" carcerand (86).(A = Me, R = Ph and B = CH_2) (a) aside view of the stacked host columns; (b) a plan view of the bowl cavity; (c) a plan view of the box cavity



(87) (88) (89)

Figure 32. The first "carcerand" host (89). reproduced from reference [59].

In a later paper Cram reported the synthesis of (90)[60], shown in Figure 33, by a similar technique of cavitand coupling claiming "Carcerand Interiors Provides New Phase of Matter"[60]. This material was soluble enough to allow n.m.r. analysis and a full assignment was possible.

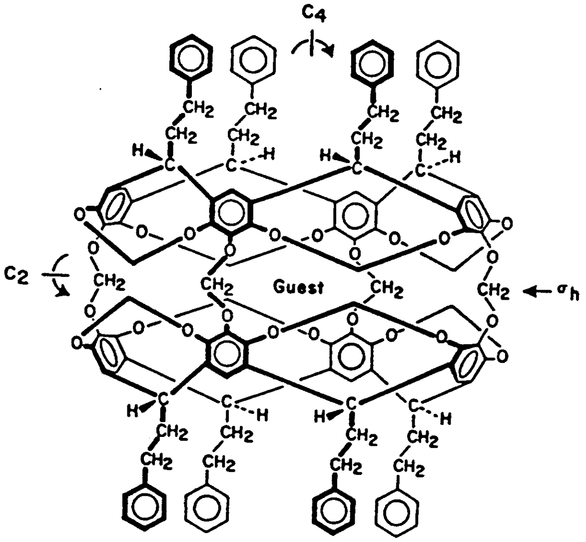
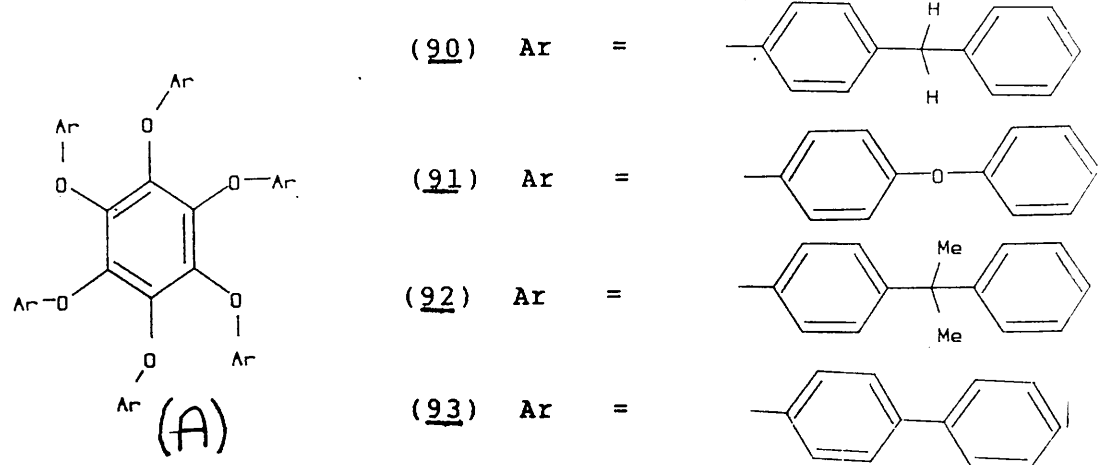


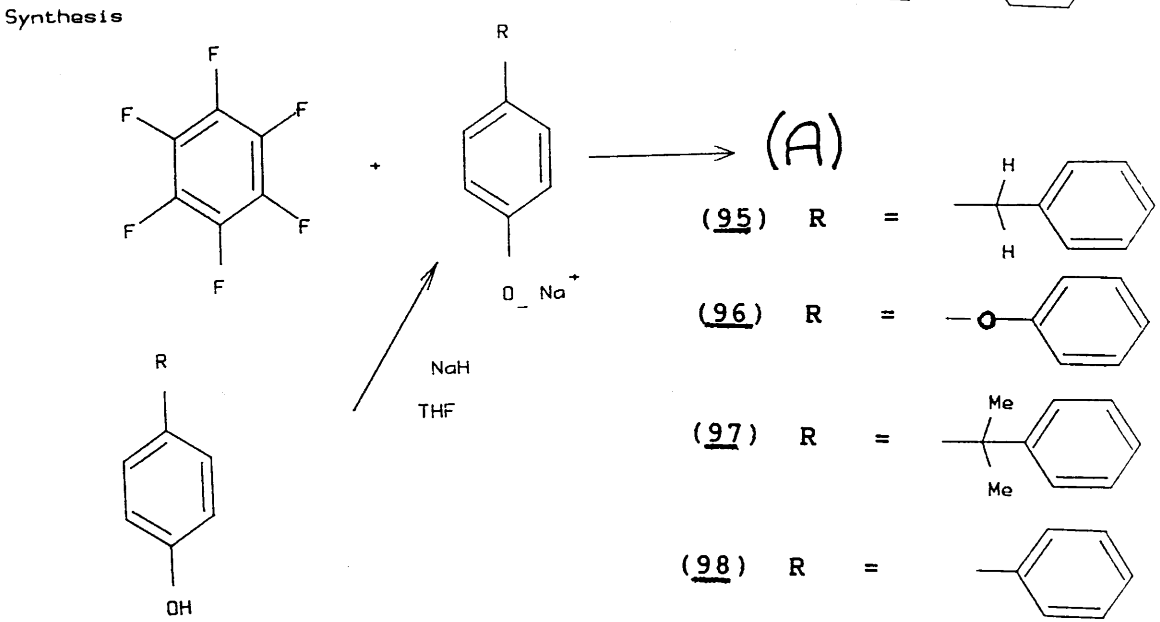
Figure 33. The soluble "carcerand" (89) Reproruced from reference [60].

The work presented represents only a very small fraction of the work carried out in the inclusion field by Cram but it shows that interesting and elegant new host molecules can be produced by the logical extension of a simple idea. That by pre-organising the potential for free space in the molecular level can stimulate nature to fill the resultant voids. It was for this intelligent use of chemical imagination that Cram shared in the 1987 Nobel prize for chemistry.

CHAPTER 6.

The compounds discussed in this chapter were synthesized because the *para* substituted phenols used in the six times substitution of hexaflurobenzene, satisfied criteria which it was considered would further the hexa-host principle by utilising more highly structured legs. Firstly, they bore a conceptual similarity to Dianin's compound (54) but, being achiral they avoided any synthetic difficulties which might be encountered in constructing a chiral analogue in which opposite enantiomers alternate around the central benzene moiety. In the cases of hexakis(*p*-benzylphenoxy)benzene (90) and hexakis(*p*-phenoxyphenoxy)benzene (91) as well satisfying the above criterion, the methylene and oxygen groups which link the outer and inner aryl groups of (90) and (91) can be considered to be a formal replacement by covalent linkages of the hydrogen bonds found in the pyridine clathrate of hexakis(*p*-hydroxyphenoxy)benzene (94)[61] . In the (94).6 pyridine clathrate where six pyridine molecules are hydrogen bonded to the six hydroxyl groups of the host giving the arrangement is as shown in Figure 34(d). The presence of trigonal symmetry in the resulting crystal structure strengthened the belief that (90) and (91) could also have trigonal host minima. The adduct structure possesses a significant cavity (residual electron density found in the X-ray structure of (94).6pyridine indicated partial occupancy, by water molecules, of this cavity [61]). The compounds shown below were synthesized, in good yield, from the sodium salts of the parent phenols (95-98) p-benzylphenol (95), p-phenoxyphenol (96), p-cumylphenol (97) and p-phenylphenol (98) and hexaflurobenzene by reaction, in a sealed tube for several weeks at 90° C using a nucleophile activating solvent, normally DMEU.





Both compounds (90) and (91) showed extensive inclusion ability which is shown in Tables 9 and 10. The host to guest ratio was assessed, where appropriate, by a combination of multiple integration of ^{1}H NMR microanalysis and thermalgravimetric analysis (TGA).

It must be noted however that on several occasions the host-guest ratio for an individual guest was in excess of that expected namely 1 : 1; e.g. as is shown in Table 9;

in two crystallisations of (90) from carbon tetrachloride both, microanalysis and TGA indicated a guest excess of approximately 20% However, crystallisation from a 1 : 1 mixture of carbon tetrachloride and acetonitrile gave a ratio of host to carbon tetrachloride of 1 : 1. The guest in all cases was only released from the clathrate on melting ca. 164° C. Similar situations were observed for other guest species in (90)parallel behaviour was also found for host (91). Full X-ray structural analysis of both hosts (presented later) showed that (i) the host structures possessed trigonal symmetry and (ii) the cavity in each case is only big enough to accommodate a single (small) guest molecule Since the tight inter-column packing rules out accommodation of any guest between the columns of host molecules an explanation for this variation in host-guest stoichiometry is not obvious. This phenomenon has been observed for other host systems[62] and the most likely hypothesis presented is that the extra guest molecules are found in macroscopic crystal defects deep in the crystal, since any guest remaining on the surface would be lost well below the melting point of the clathrate. Attempts were made to obtain a Nuclear Quadrapolar Spectrum of a sample of (90) crystalised from carbon tetrachloride having an excess of guest. It was reasoned that if the extra guests molecules were found in crystal defects, then the quadrapolar signal from macroscopic pockets(measured below the m.p. of CCl_4) would be significantly different from the individual guest molecules sequestered in the clathrate cages. Unfortunately, no adequate spectrum could be

Table 9. Inclusion data for compound (90)

Host	Guest	Host-Guest Ratio
(90)	CCl_4	1 : 1 b,c
Microanalysis: From 1:1 CCl_4:CH_3CN Found: C, 76.92, 77.28; H, 5.15, 5.00; Cl, 10.76 Theory: (H:G 1:1) C,77.03; H,4.98; Cl, 10.73 Thermalgravimetrograph Found: 11.5% Theory:11.63%		
(90)	CH_3Cl_3	1 : 1 b,c
Microanalysis: From 1:1 CH_3Cl_3:CH_3CN Found: C, 79.04, 79.06, H, 5.55, 5.43 Cl, 8.67 Theory: (H:G 1:1) C, 79.04; H, 5.29; Cl, 8.17 Thermalgravimetragraph Found:10.5% Theory: 10.24%		
(90)	CH_3I	1 : 1 a,c
Microanalysis: From CH_3I Found: C, 77.70, 77.99; H, 5.19, 5.37; I, 11.83, 11.88 Theory (H:G 1:1) C, 77.74; H, 5.26; I, 9.68		
(90)	Acetone	1 : 1 a
(90)	1,4-dioxane	1 : 1 a

a. Multiple integration of ^1H NMR spectra.
b. Thermalgravimetric analysis
c. Microanalysis

Table 10. Inclusion data for compound (91)

Host Guest Host-Guest Ratio
(91) CCl_4 1 : 2
Microanalysis:
Found: C, 65.39, 65.33; H, 3.73, 3.72; Cl, 18.33
Theory: (H:G 1:2) C,64.43; H,3.62; Cl, 19.06
Thermalgravimetrograph
Found: 19.5%
Theory: 20.67%

(91) CH_3CCl_3 1 : 1
Microanalysis:
Found: C, 69.61, 69.39; H, 4.25, 4.00; Cl, 13.72
Theory: (H:G 1:2) C, 67.37; H, 4.21; Cl, 14.95
Thermalgravimetrograph
Found: 16.00%
Theory: 15.00%

(91) CH_3I 1 : 1 a
Microanalysis:
Found: C, 69.02, 68.80; H, 4.12, 3.96; I, 12.38
Theory (H:G 1:1) C, 71.60; H, 4.30; I, 9.59

(91) $SOCl_2$ 1 : 1 b.
Microanalysis:
Found: C, 70.61, 70.61; H, 4.06, 3.92; Cl, 5.76;
Theory (H:G 1:1) C, 71.84; H, 4.15; Cl, 5.43
Thermalgravimetrograph
Found: 10.05%
Theory: 9.15%

(91) C_6H_6 1 : 1
Microanalysis:
Found: C, 80.18, 79.98; H, 4.73, 4.62
Theory (H:G 1:1) C, 80.00; H, 4.56
Thermalgravimetrograph
Found: 8.00%
Theory: 6.98%

(91) $CHCl_3$ 1 : 1
Microanalysis:
Found: C, 71.27; H, 3.91; Cl, 8.30
Theory (H:G 1:1) C, 72.84; H, 4.22; Cl, 8.18
Thermalgravimetrograph
Found: 11.05%
Theory: 9.18%

(91) CH_2Cl_2 1 : 1
Microanalysis:
Found: C, 73.80, 73.98; H, 4.43, 4.25; CL, 7.19
Theory (H:G 1:1) C, 74.82; H, 4.42; Cl, 5.60
Thermalgravumetrograph
Found: 7.5%
Theory: 6.72%

Table 10. Continued,

(91) $(CH_3)_2CO$ 1 : 1 a.b.

Microanalysis:
Found: C, 78.07, 78.22; H, 5.25, 4.99
Theory (H:G 1:1) C, 78.09; H, 5.08;
Thermalgravimetrograph
Found: 5.20%
Theory: 4.71%

(91) $CH_3COC(CH_3)_3$ 1 : 1 a.b.

Microanalysis:
Found: C, 78.86, 78.61; H, 5.12, 4.93
Theory (H:G 1:1) C, 78.63; H, 5.15;
Thermalgravimetrograph
Found: 7.0%
Theory: 7.8%

(91) $CH_3COCH_2CH_3$ 1 : 1 a.b.

Thermalgravimetrograph
Found: 6.5%
Theory: 5.4%

(91) $(CH_2CH_2)_2O$ 1 : 2

Microanalysis:
Found: C, 77.90, 77.79; H, 5.53, 5.53
Theory (H:G 1:2) C, 77.83; H, 5.27;
Thermalgravimetrograph
Found: 9.5%
Theory: 10.89%

(91) Cl_2CO 1 : 1 b.

Microanalysis:
Found: C, 74.06, 73.89; H, 4.37, 4.37; Cl, 5.01, 5.33
Theory (H:G 1:1) C, 74.00; H, 4.21; Cl, 5.52
Thermalgravimetrograph
Found: 5.05% (sample was lightly ground prior to measurement)
Theory:(for loss of one mole of phosgene) 7.7%

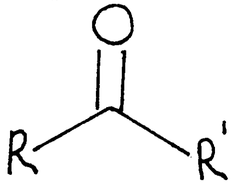
(91) Cl_2CS 1 : 2 b.

Microanalysis:
Found: C, 69.53, 69.46; H, 3.46, 3.69; Cl, 9.74; S, 3.92
Repeat after 10 months C, 69.63,69.75; H, 3.55, 3.37
Theory (H:G 1:2) C, 67.99; H, 3.82; Cl, 10.05; S, 4.53
Thermalgravimetrograph
Found: 16.0% (Repeat after 10 months 14.0%)
Theory:(H:G 1:2) 16.3%

(91) CH_3COCl 1 : 1 a.b

N.B. Host-Guest stoichiometries are closest fits to data available which is rarely exact.
a. Multiple integration of ^1H NMR spectra.
b. Infra. red analysis of adduct indicated guest presence.

obtained on the available equipment. The inclusion data for both hosts (90) and (91) and the size range of the guests indicates that the spatial fit of the guest into the available cavity is the dominant selective feature i.e. it is suggested the guest must lie within a specific size range in order to allow the trigonal molecular symmetry to be adopted. When the molecule is too small the "leg" moieties will have too much freedom of movement and will adopt a less symmetrical minimum. Similarly when the guest exceeds a critical size it pushes the host into an alternative minimum. On the basis of CPK model studies of the methyl iodide (MeI) clathrate of (91) it was predicted that guest species with the general structure shown below could be accommodated within the cavity observed provided R and R', taken together, were not too bulky.



On the basis of the model studies, pinacalone (3,3-dimethyl but-2-one) fitted into the cavity while hexachloroacetone could not be fitted without serious disruption to the host structure. Inclusion tests confirmed that pinacalone gave a highly crystalline adduct, host-guest ratio approximately 1:1. Hexachloroacteone lead to a white powder which contained no guest. The model studies also predicted that phosgene, thiophosgene and thionylchloride would fit into the available cavity space. The inclusion test for thionylchloride was carried out from the pure solvent by dissolving the host at high temperature in a sealed tube, while the tests for both phosgene, and thiophosgene were carried out by the sealed tube method from solutions of the potential guest in second solvents. In the case of phosgene from either a 12.5% solution of phosgene in toluene (supplied by BDH) or a 6.5% solution of phosgene in toluene made by diluting the 12.5% solution with spectroscopic grade toluene. The thiophosgene was tested from a 20% solution in mesitylene. Both were in fact included although the exact quantity of phosgene included appears to be to in doubt, microanalytical data indicated a perfect 1:1 host-guest ratio. The thermalgravimetrograph reproduced in Figure 35 however indicted less than full occupancy of the cavities although this is likely to have resulted from the sample's being lightly ground prior to the measurement, causing a slight loss of guest from the system due to cavity rupture. Infrared spectra of adducts from both the 12.5% and 6.0% solutions show a strong peak at 1803 cm^{-1} indicating the presence of phosgene. An experiment involving melting a sample of the adduct from the 6.0% toluene solution and collecting the released guest in a gas cell for infrared analysis confirmed the presence of phosgene in the adduct. The spectrum obtained and the appropriate sections of the adduct spectra are reproduced in Figure 36. The lack of peaks from toluene indicates that phosgene was the major guest component. Infrared analysis of other adducts identified the presence of all the ketone guests as well as thionyl chloride, phosgene and acetyl chloride interestingly the (C=O) (KBr disc) stretching frequencies observed in the phosgene (1803 cm^{-1}) and acetyl

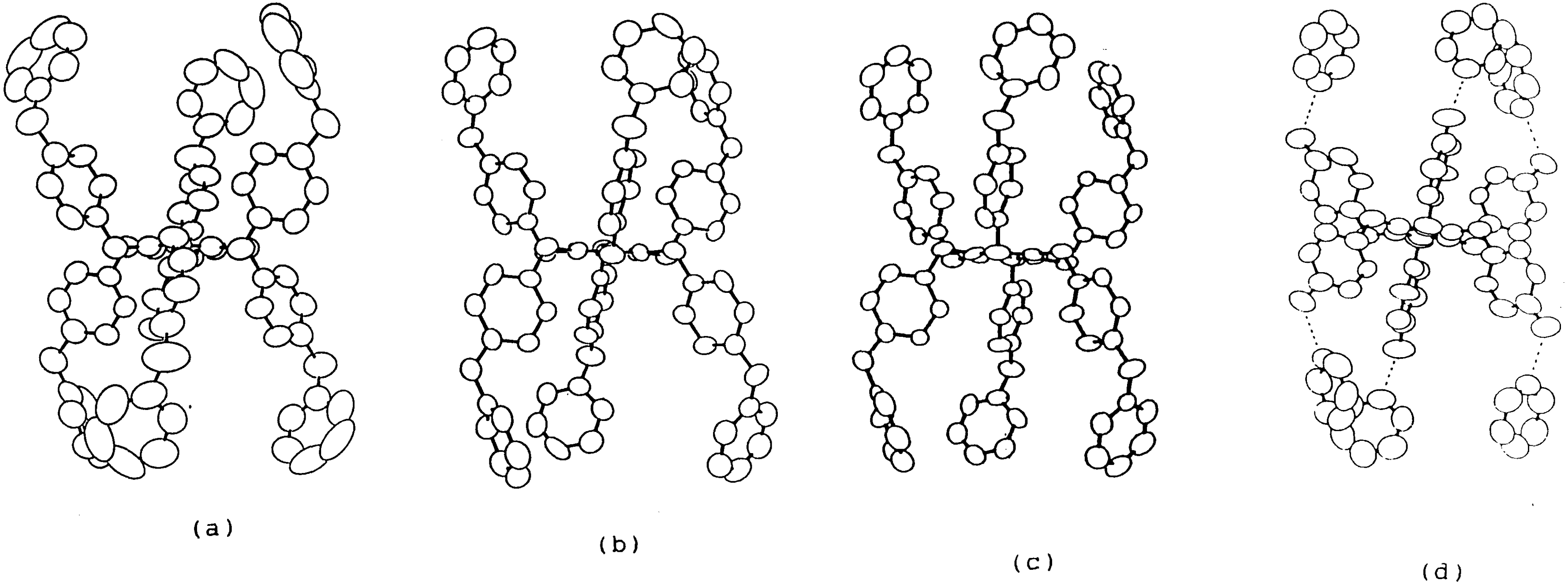


Figure 34. A comparison of single molecule structures of (a) the (90) adduct with 1,1,1-trichloroethane, (b) the phosgene adduct of (91), (c) the methyl iodide clathrate of (91) and (d) the 6 pyrdine adduct of (94). All viewed perpendicular to the c-axis.

chloride (1800 cm^{-1}) are shifted by similar amounts from the frequencies observed in CCl_4 at 1813 and 1806cm^{-1} indicating a possible weakly polar interaction between the guest and the cavity wall. Full X-ray structural analysis was carried out on the 1,1,1-trichloroethane clathrate of (90) and also both the methyl iodide and phosgene clathrates of (91). Figure 34 shows for comparison, single molecule views of the hosts in the 1,1,1-trichloroethane clathrate of (90) [Figure 34(a),] and the phosgene clathrate of (91) [Figure 34(b)]. The methyl iodide clathrate of (91) is illustrated in Figure 34(c) along with a single host molecule; and the six pyridine molecules found in the (94).6pyridine clathrate are apparent in Figure 34(d). The similarity among the four structures is remarkable: the inner phenyl rings of the new clathrates maintain analogous positions to the aryl sections of the hexaphenol (94) host molecule, whilst their outer phenyl rings take up orientations analogous to the pyridine guest molecules. The conformations around the central C-O bond in both adducts of (91) and in the CH_3Cl_3 adduct of (90) are similar to that found in the pyridine adduct of (94) such that the two ring planes, the central benzene moiety and the inner aryl group, are nearly at right angles. Careful inspection of the four molecular arrangements shows approximately constant mutual orientation of the two aromatic portions of the "leg", in the case of (90) and (91) the outer and inner aryl groups and in the clathrate case of (94) the plane of the host phenyl ring and the plane of the pyridine guests. These similarities are reflected in the unit cell dimensions observed for these structures represented in Figure 34. All possess the trigonal space group $R\bar{3}$ indicating that the structural analogy to Dianin's compound (54) may also be a useful guide to predicting future hexa-hosts. In the (90).1,1,1-trichloroethane clathrate the dimensions found are a = b = 23.144Å, c = 11.24Å with cell volume = 5217Å^3 and density D_c = 1.26 g cm^{-3} for Z = 3 , T = 293K , R = 0.100 for 851 independent reflections. The unit cell dimensions in the MeI clathrate of (91) are a = b = 22.311(94)Å, c = 11.005(91)Å with cell volume = 4744(91)Å^3 and density D_c = 1.39 g cm^{-3} for Z = 3 , T = 293K , R = 0.085 for 844 independent reflections. While in the phosgene clathrate of the same host the resulting dimensions are a = b = 22.300(7)Å, c = 10.980(3)Å with cell volume = 4729(91)Å^3 and density D_c = 1.35 g cm^{-3} for Z = 3 , T = 293K , R = 0.100 for 874 independent reflections. The dimensions found in the pyridine clathrate of (94)[61], differ significantly only in the c-axis dimension the values observed are a = b = 22.088Å, c = 12.232Å with cell volume = 5168Å^3 and density D_c = 1.16 g cm^{-3} for Z = 3(host) and 18 (guest), T = 293K , R = 0.06 for 1284 independent reflections. The decrease in the c axis dimension (of approximately 1.2Å) observed for the clathrates of compounds (90) and (91) reflects the formal replacement of the hydrogen bonds, length 2.71Å[61], found in the (94).6 pyridine clathrate with shorter covalent links a C-C bond in (90) and a C-O bond in (91). As discussed in the introduction MacNicol has already demonstrated, with the development of the hexa-host principle[37], that formal replacement of hydrogen bonds between host moieties can lead

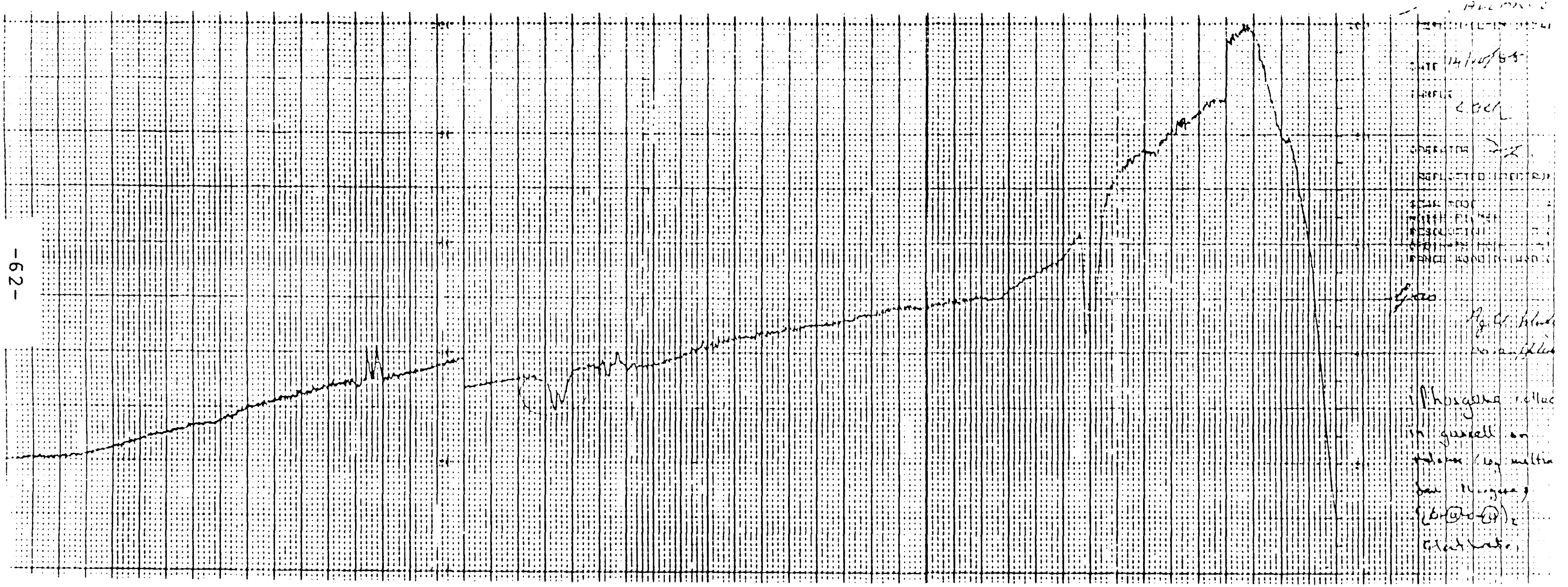


Figure 36(a). The infrared spectrum of the guest released from from the phosgene adduct of (91). Identified as phosgene by comparison with a spectrum of the gas.

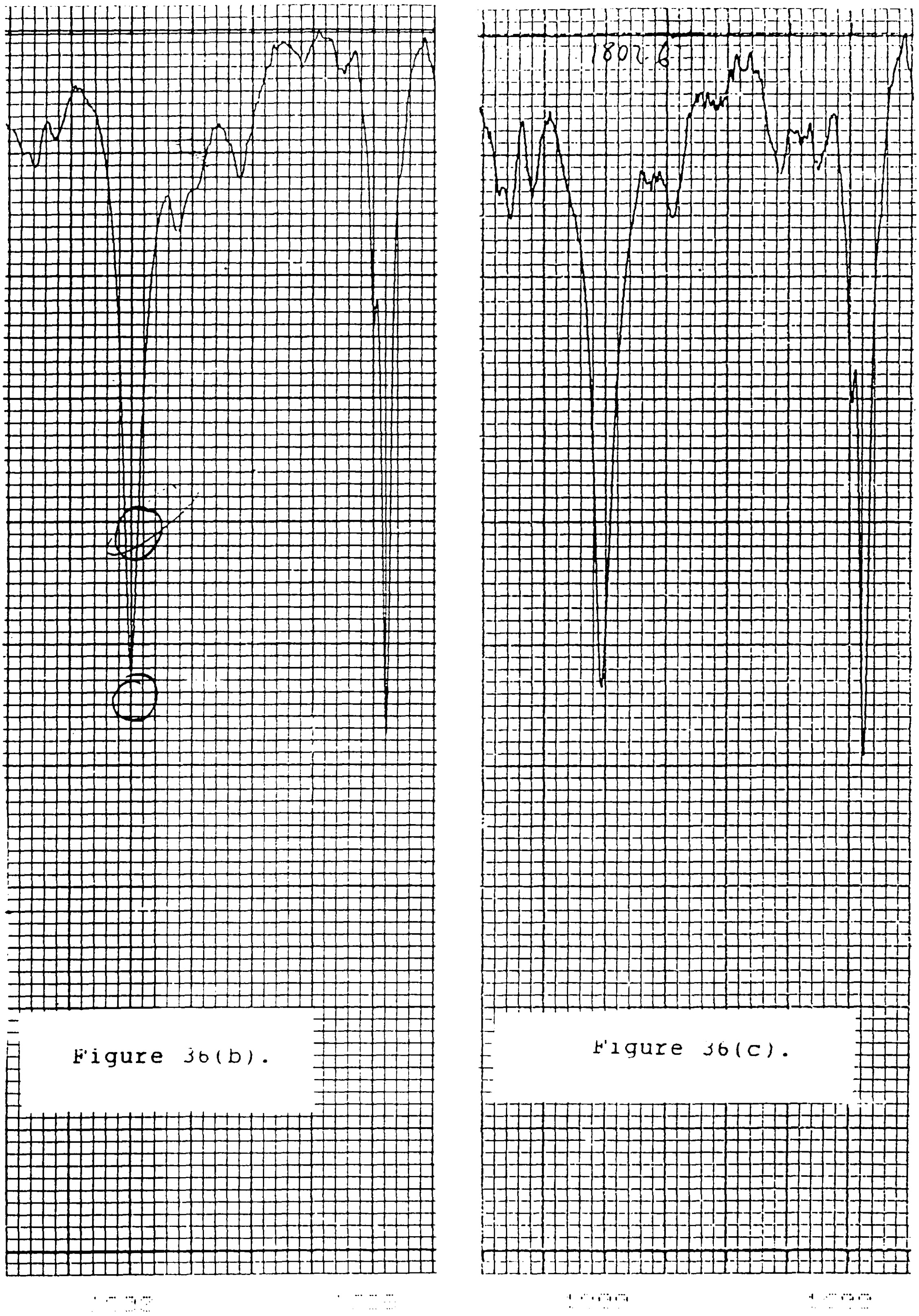


Figure 36(b). The section from the infrared spectrum of the acetyl chloroide adduct of (91) showing the carbonyl peak from the guest at 1800cm-1. Figure 36(c) a similarsection from the (91) phosgene adduct showing the phosgene carbonyl peak at 1803cm-1.

to new hosts and that in the cases of the (78) adducts with (i) dioxane and water (2:1:2) and (ii) trans-1,4-bis-(hyroxymethyl)cyclohexane (1:1) the formal replacement of hydrogen bonds between two different guest moieties can lead to new clathrates[48]. The adducts of (90) and (91) described here, convincingly demonstrate that this formal replacement has now been extended to replacement of hydrogen bonds between host and guest elements of a previously reported clathrate. Further examples of the similarities between the three structures are given in Figures 37 , 38 and 39. Figure 37 shows the inter-column packing present in the (91).$COCl_2$ compared with that found in the pyridine clathrate of (94).

The inter-column packing present in the (91).$COCl_2$; clathrate is tight, that is, there are no voids are available between columns formed by the infinite stacks of host molecules . Since near identical packing is observed in the MeI adduct this rules out the possibility that the slight excess of MeI is found in inter-column voids (CPK models show that only one MeI can be accommodated per cavity). As mentioned above, it is proposed that excess guest is situated in macroscopic crystal defects. This view is strengthened by the unit cell dimensions obtained for a CCl_4 adduct of (91) obtained from a small crystal from a sample which showed an excess of guest. Again the trigonal space group $R\bar{3}$ is found $\underline{a} = \underline{b} = 22.42(1)Å$, $\underline{c} = 11.030(2)Å$ with cell volume = $4806Å^3$. It is extremely unlikely that any different molecular arrangement would possess a near identical unit cell. CPK, space filling, model studies carried out on the CH_3CCl_3 adduct of (90) lead to the similar conclusions for this host where excess guest is often observed.

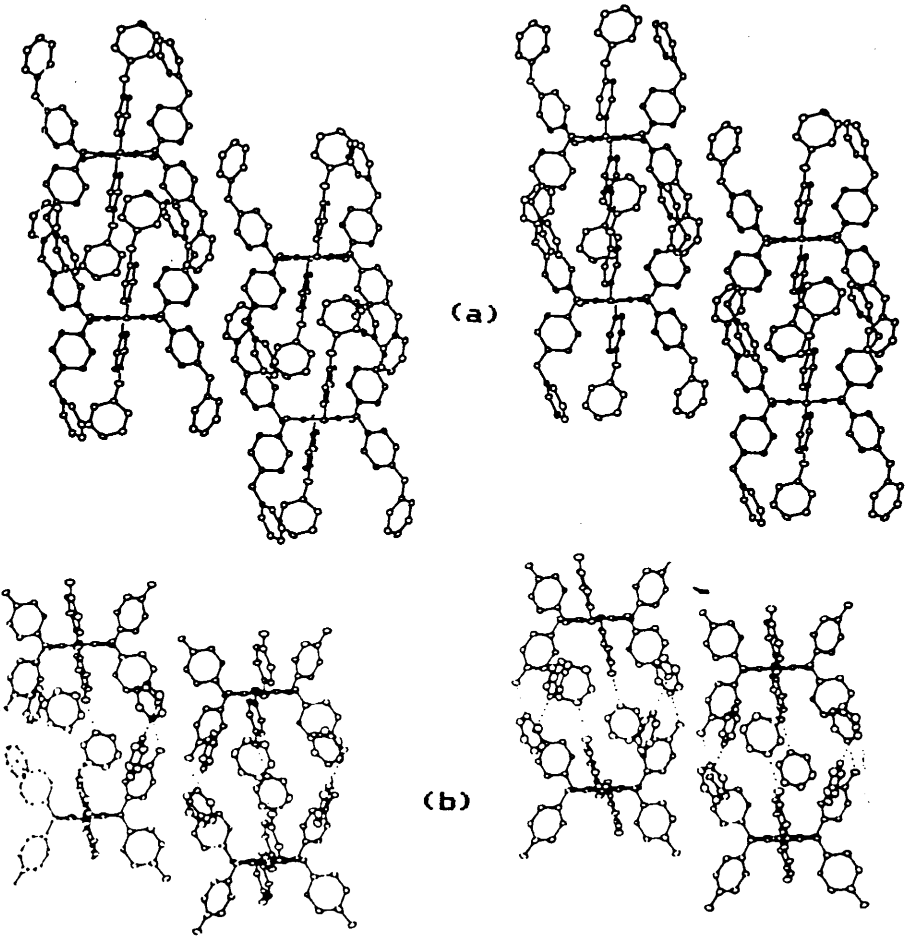


Figure 37. Inter column packing in (a) the (91). $COCl_2$, clathrate compared to that found in (b) the pyridine adduct of (94).

In all cases discussed host molecules are stacked along the c-axis forming the infinite chains mentioned above. Individual molecules and cages formed between pairs of host molecules possess exact C_{3i} ($\bar{3}$) symmetry. However only in the (91).MeI clathrate was iodine of the statistically disordered methyl iodide unambiguously located, close to the cage centre: this guest atom is shown in Figure 38. Electron density attributable to the phosgene molecule was observed but it was not possible to locate reliably any of the guest atoms. Figure 39 shows a final example of the good match between the new host structures and that of the pyridine adduct of (94) by showing views of the unit cells of this and the CH_3CCl_3 clathrate of (90) looking down the *c*-axis. Easily seen in both cases is the near right angles orientation of the planes of the "inner" and "outer" aryl moieties of their asymmetric units. A unit cell of an unsolvated form of (90) from acetonitrile was obtained. This was no longer trigonal but had triclinic space group $P\bar{1}$ and cell dimensions *a* =13.718Å, *b* = 15.312Å, *c* =15.814Å, α =102.19°, β =90.170°, γ =96.330° for *Z* = 2.

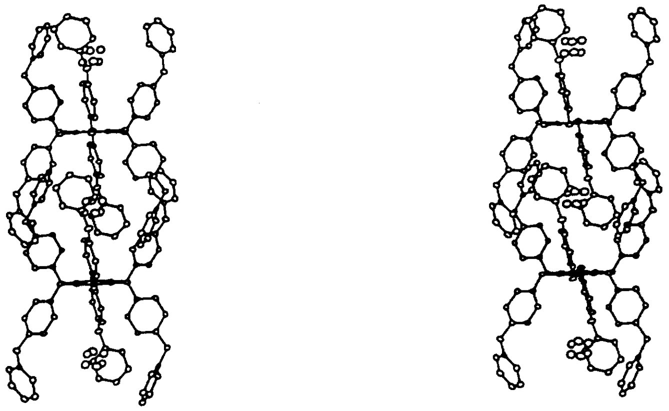


Figure 38. A view of the crystal structure of the (91).MeI clathrate showing the cage and including the statistically disordered iodines of the guest(near cage centre).

This finding indicated that at least in the case of (90) a second, non-clathrate, crystal minimum exists. It is therefore surely significant that rather than adopt this second minimum the compound prefers to adopt a highly symmetric orientation and facilitates this by incorporating a second, guest, element; also, that the minima adopted by the clathrates of (90) and (91) discussed here are very similar to that found in Dianin's compound (54) suggesting again that this is a "special" minimum for molecules with potential three-fold symmetry.

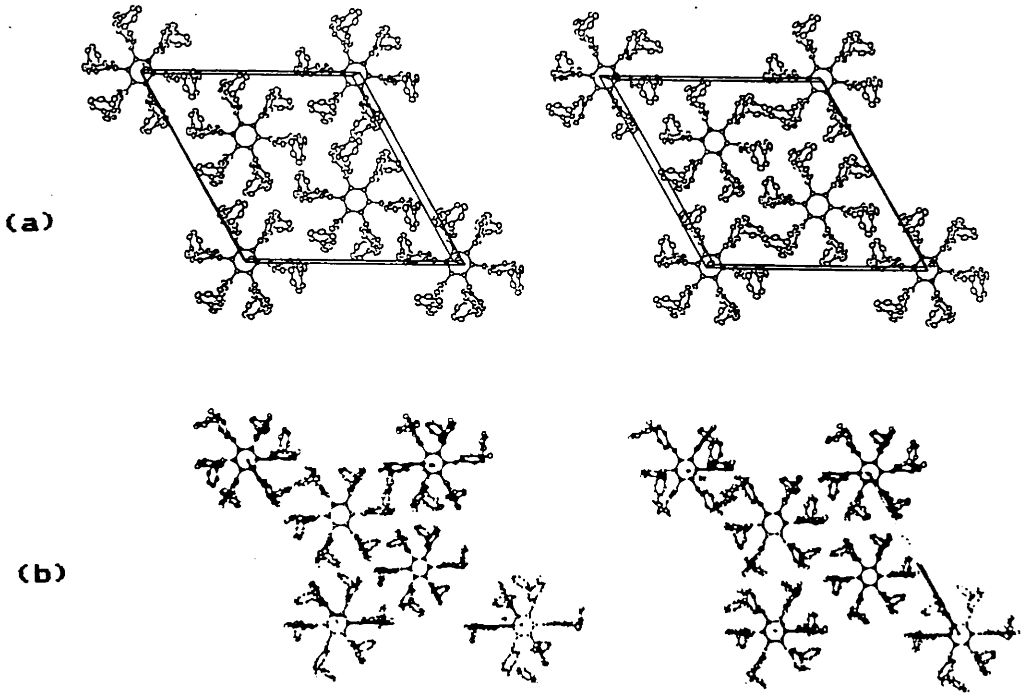


Figure 39. Views down the *c*-axis of (a) the unit cell of the (94) 6.pyridine adduct and (b) the unit cell of the (90). CH_3CCl_3 clathrate.

MacNicol and coworkers have now successfully synthesized a number of twelve-fold substituted corenenes and in at least one case the molecule forms a clathrates by adopting an orientation possessing close to three-fold symmetry.[63] Furthering the idea that building the potential for high symmetry into a compound can induce inclusion behaviour. Compounds (90) and (91) represent a successful extension to the hexa-host principle using logical design rather than molecular adaptation. Hosts (90) and (91) possess the ability to contain toxic and volatile guests, particularly in the case of (91) phosgene and thiophosgene, for long time periods. The thiophosgene adduct of (91) remained essentially unchanged for over a year and still contained a large percentage of its guest after nearly three years. This leads to possibility that these or, similar, hosts could be utilised in the transport and storage of the dangerous and corrosive materials. That the guest can be released without decomposing the host means that it could be reused many times, making the prospect commercially more attractive. The adducts are easily handled and could be transported without the extensive and expensive precautions required for the transport of neat phosgene or thiophosgene.

Compounds hexakis(p-cumylphenoxy)benzene (92) and hexakis(p-phenylphenoxy)benzene (93) were also synthesized as described above as potential hosts. In the case of (93) the lack of any atomic spacer between the directly linked phenyl groups of the "leg" naturally severely restricts the flexibility of the resulting compound and it was considered that this would reduce the prospects of clathrate formation. This may have proved to be the case since despite numerous recrystallisation tests from protic through dipolar aprotic to non-polar solvents no adducts were found. Compound (92) however proved to be interesting. Despite much effort no inclusion behaviour was observed, however the crystals obtained from acetonitrile were similar in appearance to crystals of Dianin's compound (54) adducts. For this reason a detailed X-ray crystal structure analysis was carried out. We were intrigued to find that the structure possessed the trigonal space group R$\bar{3}$ with unit cell dimensions *a* = *b* = 27.718(6)Å, *c* = 8.161(2)Å, cell volume = 5430(2)$Å^3$ and density D_c = 1.229 g cm^{-3} for *Z* = 3 , T = 293K , *R* = 0.1382 for 1459 independent reflections. The structure is an exact analogue of the clathrates described above. A view of a single molecule, shown in Figure 40, reveals however that in order to adopt this packing the outer phenyl group of the "leg" moiety is forced away from, rather than back toward, the three-fold axis along *c* as seen in the examples above.

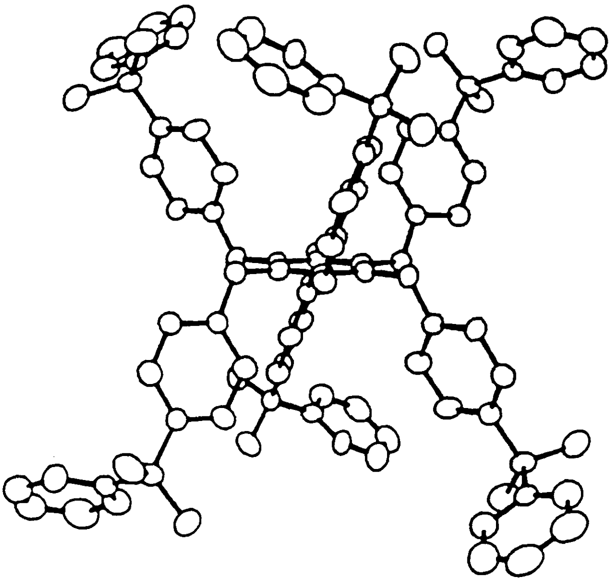


Figure 40. The single molecule of hexakis(*p*-cumylphenoxy)benzene (92), viewed perpendicular to the *c*-axis.

This conformational change probably reflects accommodation of the geminal dimethyl groups in positions which do not interfere with inter-column packing. (Figure 41 gives a view of the single molecule of (92) looking down the c-axis. This results in the increase in the a,b dimensions over those observed in the clathrates. As a consequence the increased space in the a,b plane allows the "leg" moieties to fit together more efficiently leaving only a small residual void between successive molecules in the columns. This void lacks sufficient dimensions to accommodate any guest a stereoview of the structure of (92) is shown in Figure 42. The trigonal minimum is here too "perfect" for clathrate formation since it is adopted with out requiring a second stabilising entity.

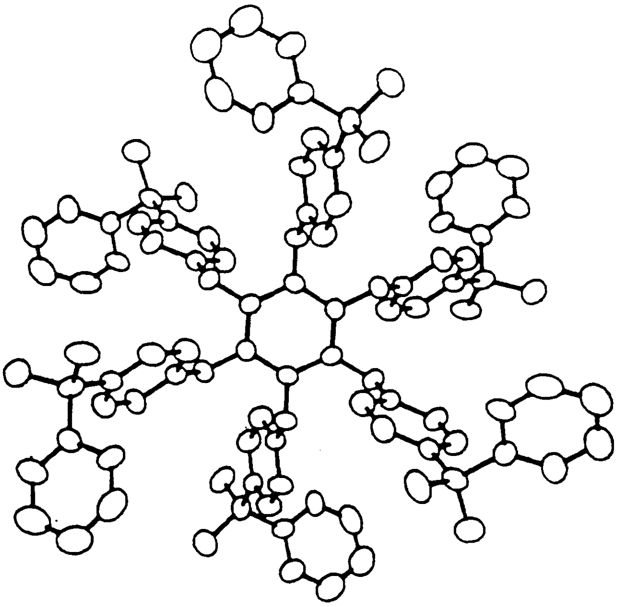


Figure 41. A single molecule of (92) viewed down the *c*-axis.

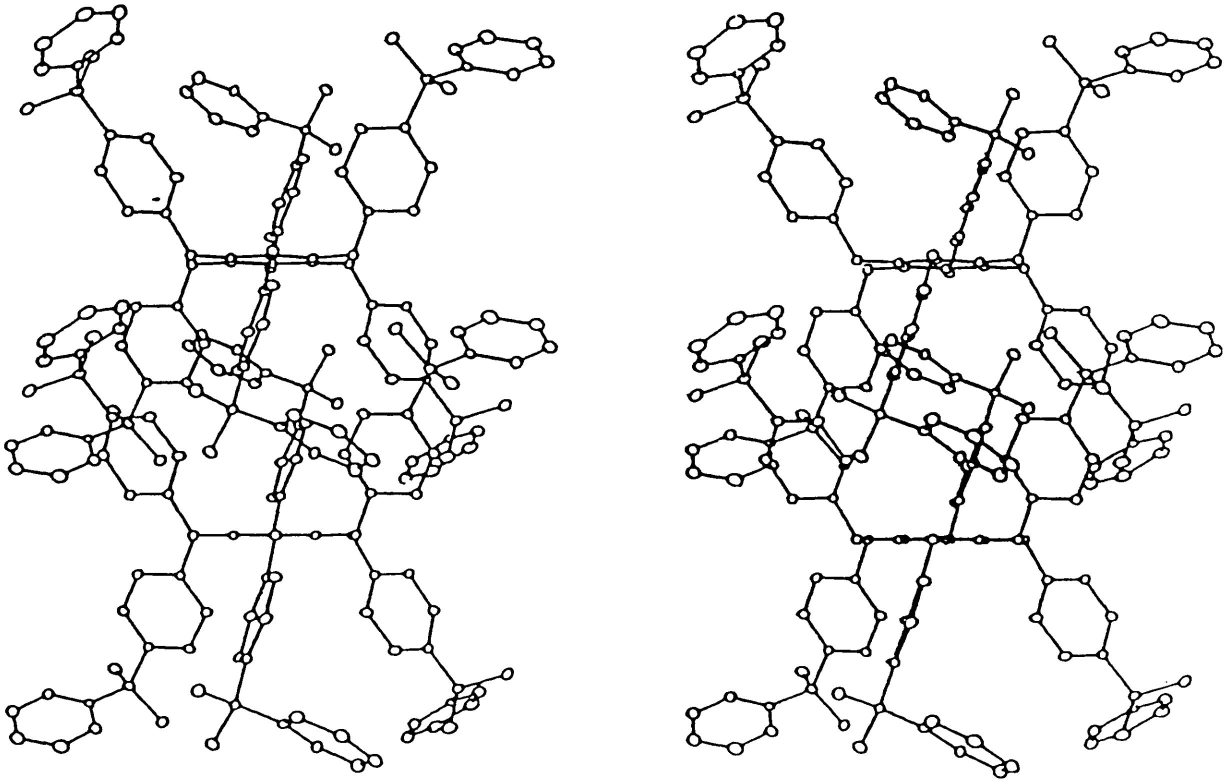


Figure 42. A stereoview of the structure of (92) showing two successive molecules from a column.

This unusual result led to the consideration that the parent phenol, *p*-cumyl phenol (97), would possess an analogous structure to that observed in (92). The central hexamer unit of in (92) being replaced by a hexamer of hydrogen bond similar to those observed in clathrates of Dianin's compound (54). This could have brought the hexa-host argument full circle with a new set of potential structured *phenolic* hosts based on evidence obtained from structured hexa-hosts. A full X-ray structural analysis was carried out on a crystal as supplied by Aldrich. It was greatly encouraging to discover that the structure possessed the trigonal space group $R\bar{3}$ with unit cell dimensions *a* = *b*, = 31.267(7)Å, *c* = 6.560(2)Å with cell volume = 5554(2)$Å^3$ and density D_c = 1.142 g cm^{-3} for *Z* = 18 , T = 293K , *R* = 0.143 for 1412 independent reflections. It was speculated that the phenol might have further widened the columns in order to accommodate the hydrogen bond hexamers. However the structure, on solution, proved to have adopted an entirely different trigonal minimum. Individual molecules of (97) are hydrogen bonded in infinite chains along three-fold screw axes found at 1/3, 1/3 (and 2/3, 2/3) in the unit cell. A stereoview of the unit cell looking down the *c*-axis is shown in Figure 43.

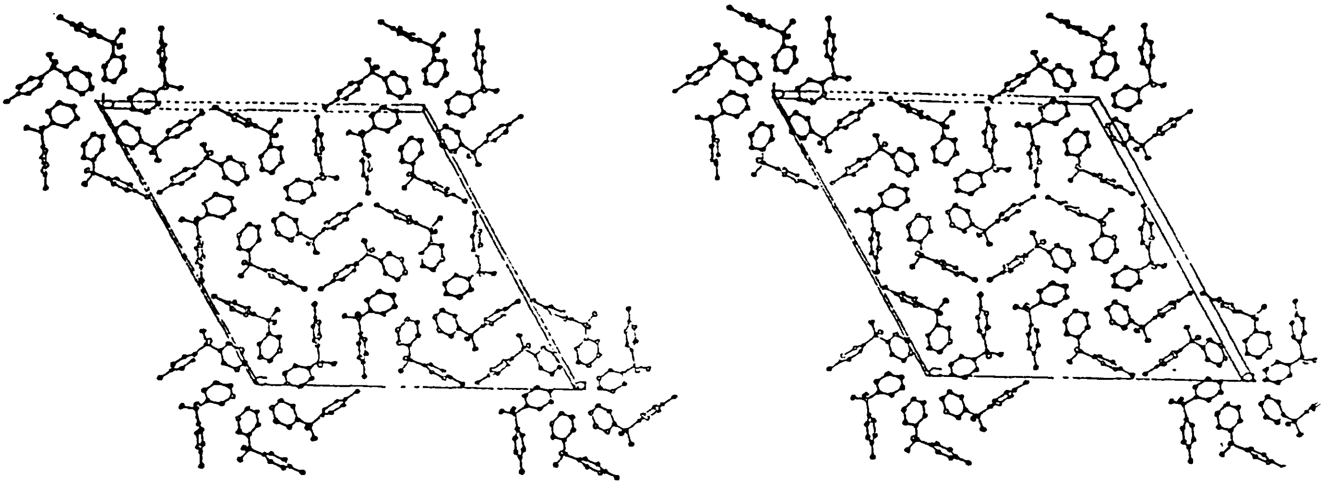


Figure 43. A stereoview of the unit cell of (97) viewed down the c-axis.

Clearly this represents a more favoured crystal minimum although its adoption of a high symmetry structure may indicate that the p-cumylphenyl moiety favours symmetrical crystal lattices. Finally a view of six molecules of (97) around the c-axis viewed down the same axis is shown Figure 44. The reversed nature of the hydrogen bonded structure relative to the hexameric benzene of (92) can clearly be seen, the hydrogen bonds forming away from the featured three-fold axis rather than around it.

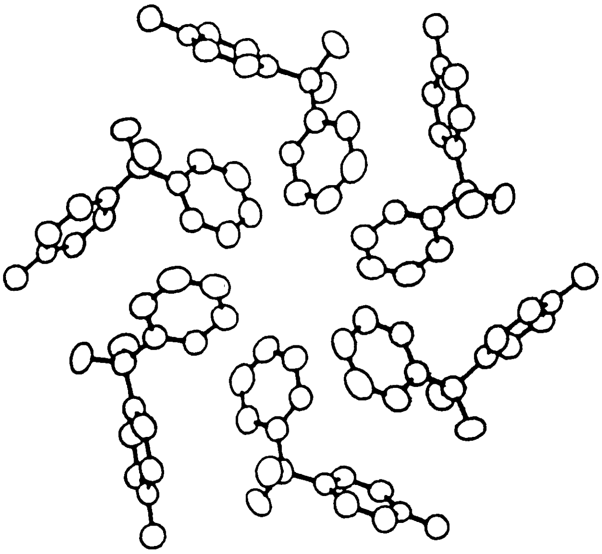


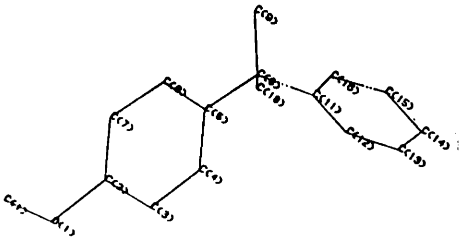
Figure 44. A view of six molecules of (97) around the c-axis viewed down this three-fold proper rotation axis.

Table 11 shows a comparison between the torsion angles around the propyl linking group in (92) and phenol

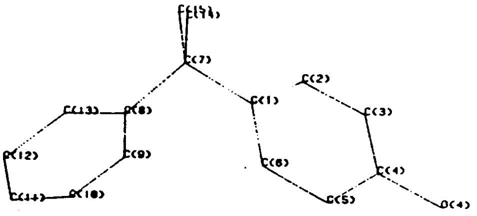
(97). It is clear that the molecular orientation in (97) and the p-cumylphenoxy moiety of (92) are quite different with individual torsion angles differing by as much as 28°. Anchoring the phenol to the central benzene group in (92) must restrict the options available. That both the minima found lead to trigonal structures suggests that an X-ray study on a series of selected phenols could generate new hexa-hosts.

Table 11 a comparison between the torsion angles of the p-cumyl moiety of (92) and those found in the phenol (97). Numbering systems as shown below.

Compound (92)		Compound (97)	
C(4)-C(5)-C(8)-C(11)	-62.2(7)	C(6)-C(1)-C(7)-C(8)	-48.6(6)
C(6)-C(5)-C(8)-C(11)	116.3(3)	C(2)-C(1)-C(7)-C(8)	135.6(7)
C(4)-C(5)-C(8)-C(10)	56.3(7)	C(6)-C(1)-C(7)-C(14)	75.4(6)
C(6)-C(5)-C(8)-C(10)	-125.2(8)	C(2)-C(1)-C(7)-C(14)	-100.4(7)
C(4)-C(5)-C(8)-C(9)	176.6(8)	C(2)-C(1)-C(7)-C(15)	17.0(6)
C(6)-C(5)-C(8)-C(9)	-5.0(6)	C(6)-C(1)-C(7)-C(15)	-167.1(7)
C(12)-C(11)-C(8)-C(5)	102.9(8)	C(13)-C(8)-C(7)-C(1)	130.0(7)
C(16)-C(11)-C(8)-C(5)	-73.7(7)	C(9)-C(8)-C(7)-C(1)	-51.6(6)
C(12)-C(11)-C(8)-C(10)	-15.4(7)	C(9)-C(8)-C(7)-C(14)	-171.4(8)
C(16)-C(11)-C(8)-C(10)	168.0(8)	C(13)-C(8)-C(7)-C(14)	10.2(6)
C(12)-C(11)-C(8)-C(9)	-134.4(9)	C(13)-C(8)-C(7)-C(15)	-108.8(7)
C(16)-C(11)-C(8)-C(9)	49.0(7)	C(9)-C(8)-C(7)-C(15)	69.7(6)



Numbering System for (92).



Numbering System for (97)

(97) It is clear from Table 11 that only very general similarities exist between the two torsion angle sets and that the angles differ by at least 12° from each other and as much as 28°. This result indicates that it is not a single rigid orientation of the p-cumylphenyl moiety that causes the adoption of the high symmetry crystal minima. It can therefore only be attributed to chance which seems an unsatisfactory explanation for such an unusual result.

CHAPTER 7.

This chapter introduces a further development from the hexa-host principle in which molecules in the group 2,4,6- tris(aryloxy)triazines were utilised as potential hosts. It was hoped that two molecules would undergo self-assembly to produce a composite unit which could act analogously to a single hexa-host molecule. This arrangement is referred to as the Piedfort unit*. A schematic representation of the proposed arrangement compared to a hexa-host molecule is shown in Figure 45 where Z represents a link atom or chain, and O and O outer groups.

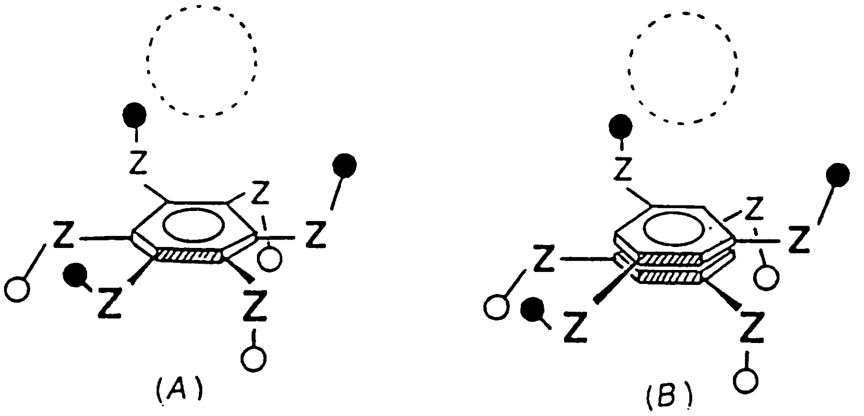
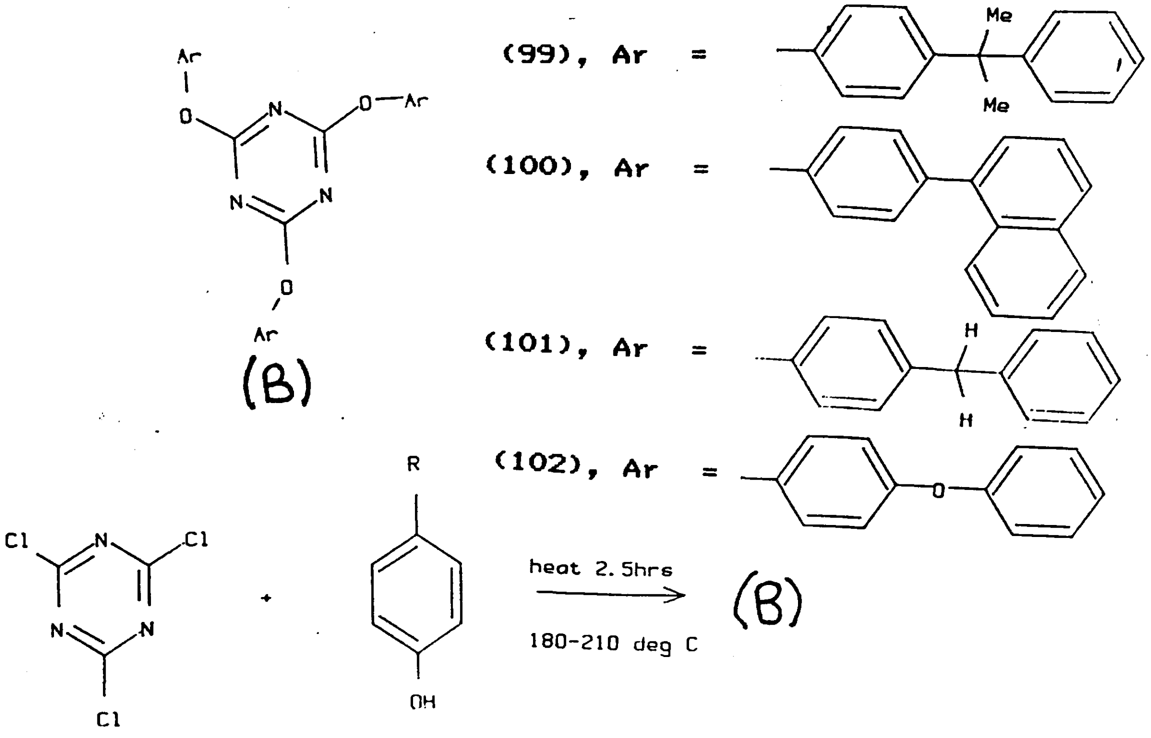


Figure 45 A schematic comparison of a hexa-host (A) with its Piedfort analogue (B). The light dotted circle is symbolic of the projected guest region in each case.

The following compounds (99-102) were synthesized by a literature route[64] from the parent phenols (95-97) and p-(1-naphthyl)phenol (103) and cyanuric chloride. The synthesis of (103) is described in a later chapter. The products obtained as off-white powders after trituration of excess phenol component with suitable solvent mixtures.

* Named for the specially minted double thickness Piedfort coins



The success of the Piedfort concept is illustrated by compound 2,4,6-tris(p-cumylphenoxy)-1,3,5-triazine (99) which forms a crystalline adduct with dioxane, host:guest ratio 1:2 established by ^{1}H NMR and thermogravimetric analysis (the thermograph obtained shown in Figure 46 illustrates the unstable nature of the adduct species the guest being lost well below its boiling point, 110^{o}C). In order to establish whether self-assembly had occurred in the Piedfort mode X-ray structure analysis of the adduct was carried out; for comparison a second structure for the unsolvated form was also obtained. The clathrate crystal being sealed in a thin walled capillary tube with a small amount of solvent to prevent crystal decomposition during data collection. Crystal data for both forms of (99) are given in Table 12

Table 12 crystal data for the (99).2:(1,4-dioxane) clathrate and the unsolvated form of (99)

(99) 1,4-dioxane clathrate

Space group lattice parameters

triclinic $P\bar{1}$ a = 13.906(3), b = 14.214(3), c = 14.604(2)Å,
α = 111.76(1), β = 106.82(1), Γ =
96.25(2)°, U = 2489(1) Å3, Z = 2,
Dc = 1.19 g cm-3

Unsolvated (99)

Space group lattice parameters

triclinic $P\bar{1}$ a = 13.041(3), b = 13.073(3), c = 13.463(2)Å,
α = 71.30(2), β = 84.98(2), Γ =
64.61(2)°, U = 1961(1) Å3, Z = 2,
Dc = 1.21 g cm-3

Figure 47(a) gives a general view of the host-guest packing in the 1,4-dioxane clathrate of (99): Figure 47(b) shows the packing in the molecular crystal of unsolvated (99).

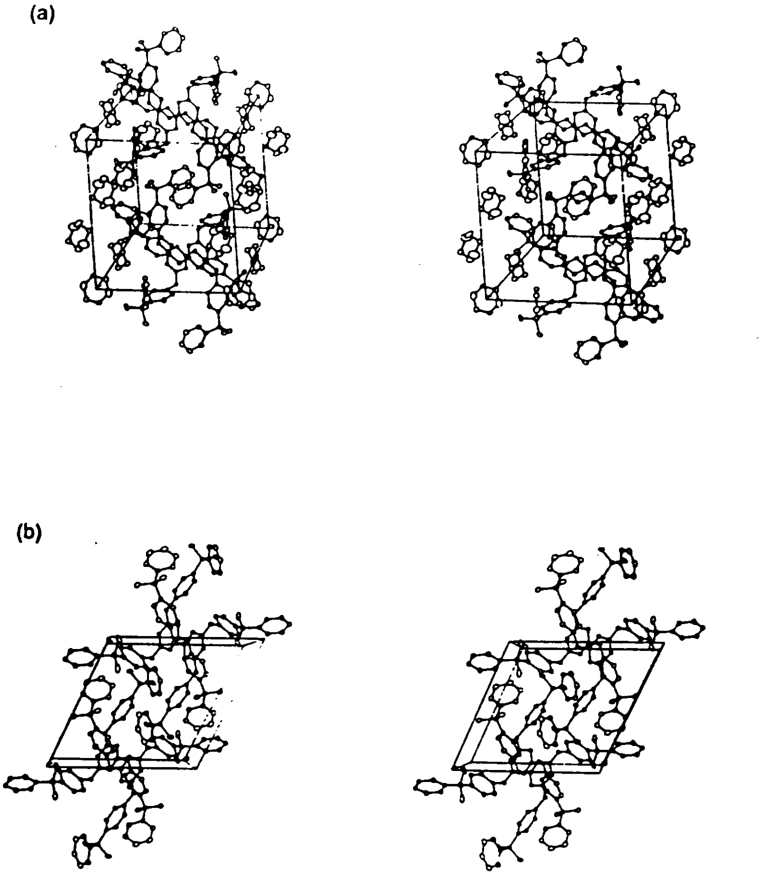


Figure 47. Stereoviews illustrating (a) the host-guest packing in the 1,4-dioxane inclusion compound of (99) and (b) the molecular packing in unsolvated (99).

In the adduct, pairs of host molecules are indeed found to be self-assembled as Piedfort units; furthermore, in the unsolvated crystals these units are also present. In each case two superposed molecules of (99), which are centro-symmetrically related, have their central rings essentially in Van der Waals contact(*vide infra*). The Piedfort unit, which possesses exact C_i symmetry, has, it may be noted the same staggered arrangement of nitrogen atoms as found by calculation[65] for the minimum energy form of the dimer of 1,3,5-triazine itself. The molecular structure of the dimer in the adduct is shown in Figure 48.

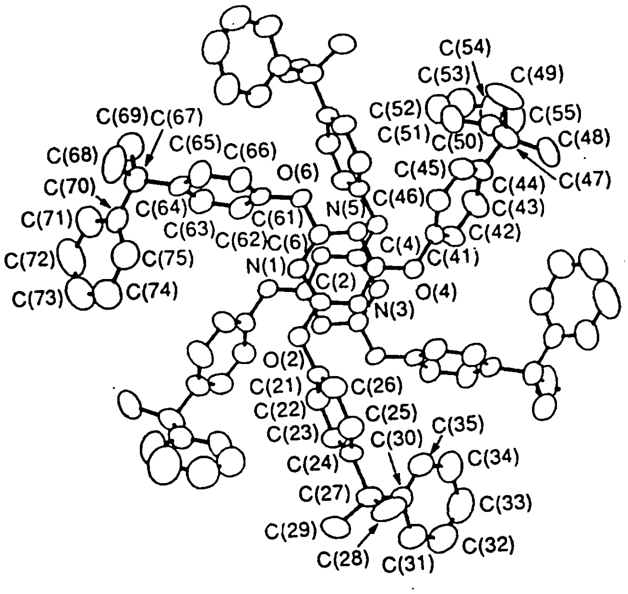


Figure 48. A view of the Piedfort unit in the 1,4-dioxane clathrate of compound (99), showing the atomic numbering scheme comon to this and the unsolvated form. The directon of view is inclined to the normal for clarity.

In the unsolvated crystal (atom labelling as in Figure 48) closest intermolecular contacts N(1)....C(4*), N(3)...C(6*), N(5)....C(2*) are 3.516(3), 3.549(3) and 3.546(3)Å respectively; whilst the corresponding values for clathrate are 3.458(6), 3.416(6) and 3.431(6)Å. These indicate a significantly closer approach of the central rings to exact Van der Waals contact on clathrate formation. The triazine ring is planar to ±0.01Å in each case, and the respective C-N-C and N-C-N ring angles have average values 112.1° and 127.9° for the unsolvated crystal and 111.9°, 128.2° in the clathrate. These angles are close to the corresponding unique values 113.2° and 126.8° found for the 1,3,5-triazine itself[66]. Interestingly, the dimeric unit in the clathrate possesses approximately trigonal symmetry, a non exact 3-fold proper rotation axis running normal to the central rings. The approach to C_{31} (3) symmetry may be seen in Figure 48, and sets of torsion angles for the crystallographically non-equivalent side chains: N(1)-C(2)-O(2)-C(21) (and related) -179°, 172°, 178°; C(2)-O(2)-C(21)-C(22) -105°, -114°, -77°; C(23)-C(24)-C(27)-C(30) 59°, 54°, 57°: C(24)-C(27)-C(30)-C(31) -160°, -135°, -142°. In contrast the Piedfort unit in the unsolvated crystal is much less symmetrical, although the central region retains some approximate trigonal character. The mean C-N, C-O(inner) and C-O(outer) bond lengths for (1), unsolvated and solvated respectively, are 1.323(2), 1.338(20, 1.413(2)Å; 1.324(3), 1.338(3), 1.410(3)Å. The C-N bond length can be compared to the that found in 1,3,5-triazine[66] of 1.319Å.

The stereoview Figure 47(a) illustrating the host-guest packing in the adduct reveals three crystallographically non-equivalent locations of the 1,4-dioxane guest molecule. All the dioxane guest molecules have a chair conformation; two being situated on centres of symmetry and the third occupies a general position, corresponding to the projected guest inclusion region (light dotted circle) in Figure 45(b). The structure exhibits interesting void geometry, with intersecting channels running along the b and c axial directions providing accommodation for the guest species.

The failure of the Piedfort unit to adopt trigonal symmetry appears to result from the "double" thickness of the central aromatic moiety allowing greater flexibility in the orientation of the torsion angles between the inner phenyl ring and the central moiety compared to that observed in hexakis(p-cumylphenoxy)benzene (92). Table 13 shows a set of important bond and torsion angles for the Piedfort clathrate, its empty form and for (92).

Analysis of Table 13 reveals that the "extra" spacing allowed by the Piedfort unit has had very little effect on the bond angles present in the leg units. But has led to the modifications in the torsion angles between the bonds of the central aromatic moieties and the carbon-oxygen bond from the inner phenyl group of the p-cumyl leg. In the Piedfort clathrate case, in all three independent legs, these torsion angles indicate near co-planarity with the central ring. The three pairs (the single values are given in Table 13) being for the O(2) linked "leg" -179.2 and 0.3°; the O(4) linked "leg" 172.1 and -7.9°; and the O(6) linked "leg" -3.4 and 177.7°. A very similar arrangement is found for the "empty" case the respective pairs being 175.4 and -5.0°; 169.5 and -11.2°; and -10.0 and 170.4°. In the hexamer case (92) the corresponding angles are near right angles , -102.8 and 77.7. Consideration of Table 13 further reveals that an exact trigonal is most nearly achieved in the dioxane clathrate, host orientation, with only the torsion angles between the outer phenyl group of the O(2) linked leg and the propyl linking group varying by more than 10° from equivalent angles in other legs. However, a much greater variation in corresponding torsion angles between the legs of the empty form is indicated; although it is worth noting that the most pronounced differences are found in the O(2) linked leg. This result lends support to the principle that higher symmetry is important in inclusion behaviour. There is significant similarity however, in the general orientation the *p*-cumyl groups in both Piedfort cases. However neither shows any similarity to the orientation of this group in the hexameric benzene case (92) , probably indicating that a large number of low energy orientations of the *p*-cumyl group exist. This could explain the extensive success of the use of this group in other new hosts synthesized in Glasgow[63] e.g. octakis (*p*-cumylphenoxy)napthalene and dodecakis(*p*-cumylphenoxy)corenene

The compound 2,4,6,-tris[*4*-(1-napthylphenoxy)]-1,3,5-triazine (100) was synthesized and tested for host properties. Encouragingly inclusion compounds are formed with both ethanol and 2-propanol; host-guest ratios are approximately 2:1 when crystallised at approximately 100°C in a sealed tube. The ratios were confirmed by both integration of ^{1}H NMR spectra and thermalgravimetric analysis, Figure 49 shows the thermalgravimetrograph of the ethanol clathrate of (100). On crystallisation from the same solvents at ambient temperatures unsolvated crystal forms are observed. Preliminary X-ray evidence indicates that the modification of the leg leads to a trigonal rather than triclinic host. Unit cell dimensions, for space group $R\bar{3}$, a = 24.828Å, b = 24.866Å and c = 89.016Å, are consistent with the presence of Piedfort units which have now attained exact three-fold

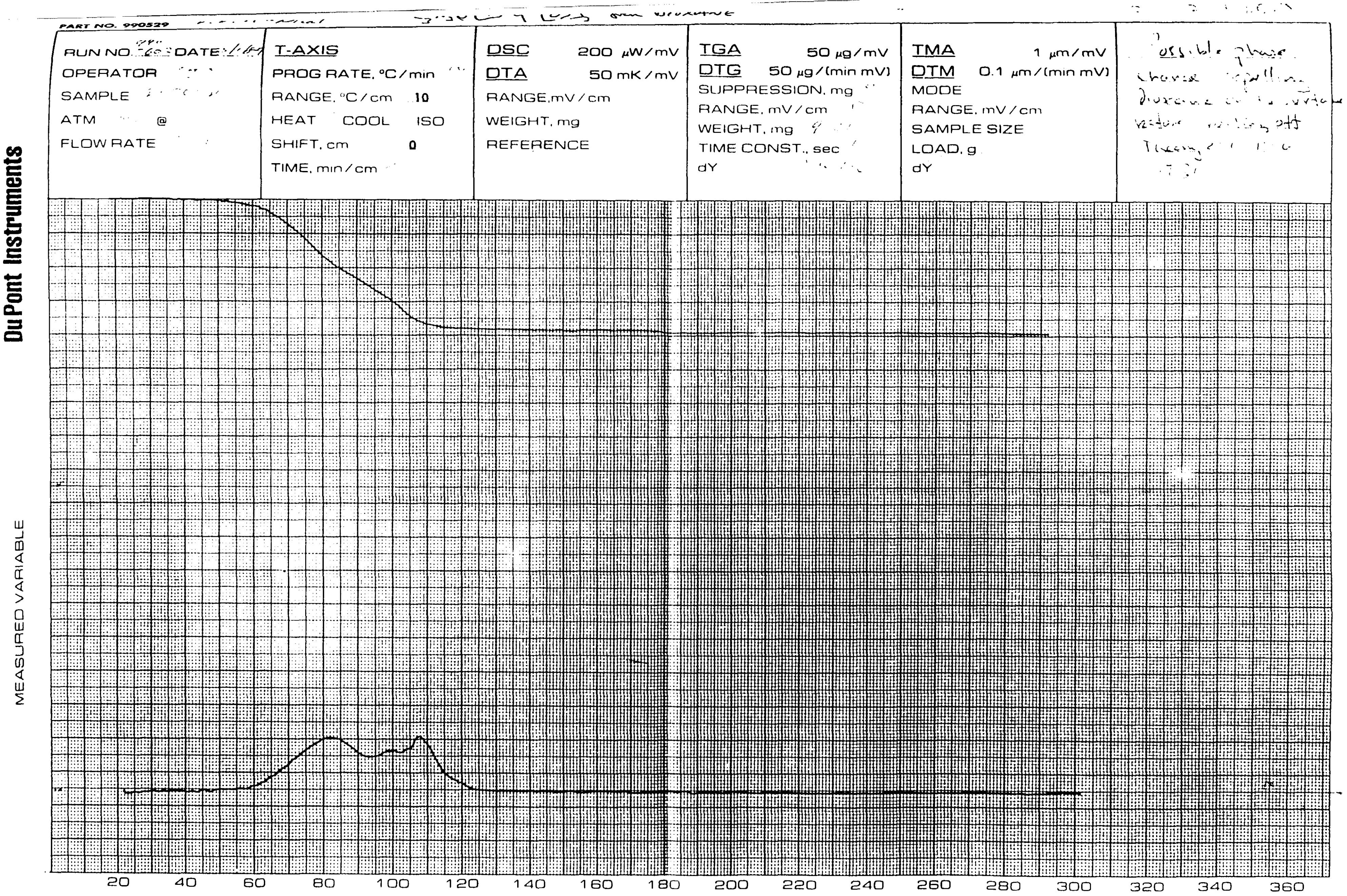


Figure 46. A thermalgravimetrograph of the (99).1,4-dioxane clathrate. Guest loss occurs below its boiling point between 55° and 100° C and indicates a host to guest ratio of 1:2.

Table 13. A comparison of the bond and torsion angles (°) found in the p-cumyl "legs" of (99).1,4-dioxane clathrate, an unsolvated form of (99) and the hexasubstituted benzene hexakis(p-cumylphenoxy)benzene (92).

(99) Clathrate

Bond angles (°)

leg (2)		leg (4)		leg (6)	
C(2)-O(2)-C(21)	119.4(5)	C(4)-O(4)-C(41)	120.5(4)	C(6)-O(6)-C(61)	119.6(5)
C(24)-O(27)-C(30)	109.5(6)	C(44)-O(47)-C(50)	108.3(6)	C(64)-O(67)-C(70)	110.4(6)
C(24)-O(27)-C(28)	112.3(6)	C(44)-O(47)-C(48)	109.3(7)	C(64)-O(67)-C(68)	111.9(7)
C(24)-O(27)-C(29)	106.9(7)	C(44)-O(47)-C(49)	111.2(6)	C(64)-O(47)-C(49)	108.8(8)
C(28)-O(27)-C(29)	107.7(6)	C(48)-O(47)-C(49)	109.9(7)	C(68)-O(67)-C(69)	107.5(9)
C(28)-O(27)-C(30)	110.9(7)	C(48)-O(47)-C(50)	110.6(7)	C(68)-O(67)-C(70)	106.2(7)
C(29)-O(27)-C(30)	109.6(7)	C(49)-O(47)-C(50)	107.5(6)	C(69)-O(67)-C(70)	112.2(8)

Unsolvated (99)

Bond angles

leg (2)		leg (4)		leg (6)	
C(2)-O(2)-C(21)	119.4(2)	C(4)-O(4)-C(41)	119.7(3)	C(6)-O(6)-C(61)	119.1(2)
C(24)-O(27)-C(30)	111.3(2)	C(44)-O(47)-C(50)	107.7(3)	C(64)-O(67)-C(70)	113.0(3)
C(24)-O(27)-C(28)	106.5(8)	C(44)-O(47)-C(48)	108.5(4)	C(64)-O(67)-C(68)	105.2(4)
C(24)-O(27)-C(29)	111.7(3)	C(44)-O(47)-C(49)	112.5(4)	C(64)-O(47)-C(49)	111.2(4)
C(28)-O(27)-C(29)	108.9(3)	C(48)-O(47)-C(49)	106.9(4)	C(68)-O(67)-C(69)	111.5(4)
C(28)-O(27)-C(30)	111.9(3)	C(48)-O(47)-C(50)	112.0(4)	C(68)-O(67)-C(70)	110.7(4)
C(29)-O(27)-C(30)	106.6(3)	C(49)-O(47)-C(50)	109.4(4)	C(69)-O(67)-C(70)	105.5(3)

(92)

Bond angles

C(2)-O(2)-C(21)	118.0(5)
C(24)-O(27)-C(30)	108.6(5)
C(24)-O(27)-C(28)	112.0(5)
C(24)-O(27)-C(29)	108.7(6)
C(28)-O(27)-C(29)	108.7(5)
C(28)-O(27)-C(30)	109.6(6)
C(29)-O(27)-C(30)	109.0(5)

Table 13. continued (Torsion angles o).

Torsion Angles

(99) Clathrate

leg(2)		leg(4)		leg(6)	
N(1)-C(2)-O(2)-C(21)	-179.2(7)	N(3)-C(4)-O(4)-C(41)	172.1(7)	N(1)-C(6)-O(6)-C(61)	-3.4(5)
N(3)-C(2)-O(2)-C(21)	0.3(5)	N(5)-C(4)-O(4)-C(41)	-7.9(5)	N(5)-C(6)-O(6)-C(61)	177.7(7)
C(2)-O(2)-C(21)-C(22)	-105.0(8)	C(4)-O(4)-C(41)-C(42)	-113.7(8)	C(6)-O(6)-C(61)-C(62)	-77.4(7)
C(2)-O(2)-C(21)-C(26)	79.6(7)	C(4)-O(4)-C(41)-C(46)	70.2(7)	C(6)-O(6)-C(61)-C(66)	108.7(7)
C(23)-C(24)-C(27)-C(28)	178.7(9)	C(43)-C(44)-C(47)-C(48)	-66.2(8)	C(63)-C(64)-C(67)-C(68)	174.7(9)
C(23)-C(24)-C(27)-C(29)	-61.1(8)	C(43)-C(44)-C(47)-C(49)	-172.3(9)	C(63)-C(64)-C(67)-C(69)	-66.6(9)
C(23)-C(24)-C(27)-C(30)	-59.1(7)	C(43)-C(44)-C(47)-C(50)	54.4(7)	C(63)-C(64)-C(67)-C(70)	56.7(7)
C(24)-C(27)-C(30)-C(31)	-160.4(9)	C(44)-C(47)-C(50)-C(51)	46.4(7)	C(64)-C(67)-C(70)-C(71)	-141.7(9)
C(24)-C(27)-C(30)-C(35)	25.8(7)	C(44)-C(47)-C(50)-C(55)	-138.3(9)	C(64)-C(67)-C(70)-C(75)	47.2(8)
C(28)-C(27)-C(30)-C(35)	-96.6(8)	C(48)-C(47)-C(50)-C(55)	-15.6(8)	C(68)-C(67)-C(70)-C(75)	-74.3(9)
C(29)-C(27)-C(30)-C(31)	-42.6(8)	C(49)-C(47)-C(50)-C(51)	-73.8(8)	C(69)-C(67)-C(70)-C(71)	168.7(11

Torsion Angles

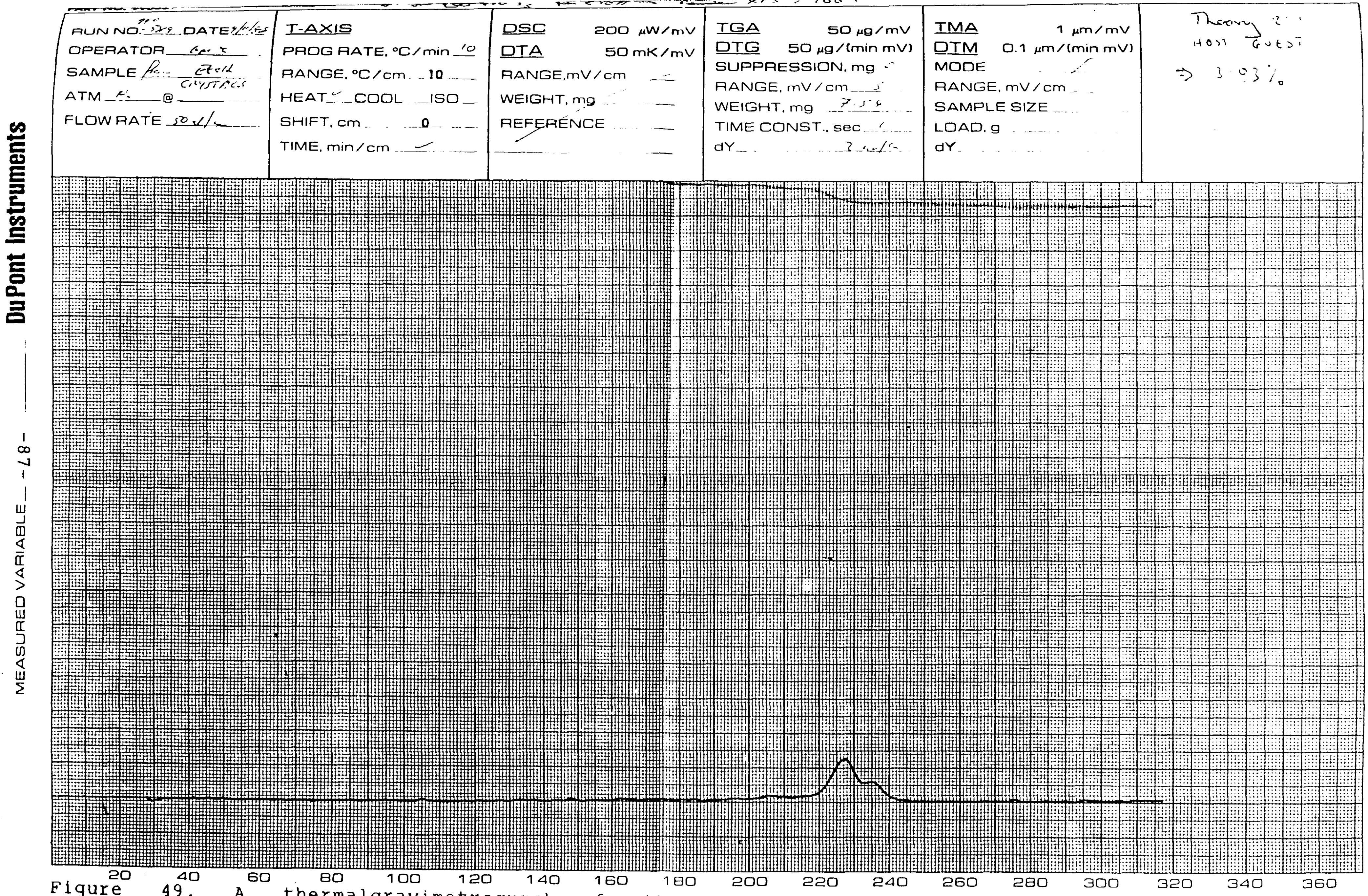
Unsolvated (99)

leg(2)		leg(4)		leg(6)	
N(1)-C(2)-O(2)-C(21)	175.4(3)	N(3)-C(4)-O(4)-C(41)	169.5(4)	N(1)-C(6)-O(6)-C(61)	-10.0(3)
N(3)-C(2)-O(2)-C(21)	-5.0(2)	N(5)-C(4)-O(4)-C(41)	-11.2(3)	N(5)-C(6)-O(6)-C(61)	170.4(3)
C(2)-O(2)-C(21)-C(22)	-110.8(3)	C(4)-O(4)-C(41)-C(42)	-90.7(4)	C(6)-O(6)-C(61)-C(62)	70.4(3)
C(2)-O(2)-C(21)-C(26)	75.1(3)	C(4)-O(4)-C(41)-C(46)	94.1(4)	C(6)-O(6)-C(61)-C(66)	-112.4(4
C(23)-C(24)-C(27)-C(28)	-100.6(7)	C(43)-C(44)-C(47)-C(48)	-59.4(4)	C(63)-C(64)-C(67)-C(68)	-67.4(4)
C(23)-C(24)-C(27)-C(29)	18.2(3)	C(43)-C(44)-C(47)-C(49)	-177.4(5)	C(63)-C(64)-C(67)-C(69)	172.1(5)
C(23)-C(24)-C(27)-C(30)	137.2(4)	C(43)-C(44)-C(47)-C(50)	62.0(4)	C(63)-C(64)-C(67)-C(70)	53.7(4)
C(24)-C(27)-C(30)-C(31)	143.4(5)	C(44)-C(47)-C(50)-C(51)	68.4(4)	C(64)-C(67)-C(70)-C(71)	157.6(4)
C(24)-C(27)-C(30)-C(35)	-39.9(3)	C(44)-C(47)-C(50)-C(55)	-111.7(5)	C(64)-C(67)-C(70)-C(75)	28.7(3)
C(28)-C(27)-C(30)-C(31)	24.4(3)	C(48)-C(47)-C(50)-C(51)	-172.4(6)	C(68)-C(67)-C(70)-C(71)	40.0(4)
C(29)-C(27)-C(30)-C(31)	-94.6(4)	C(49)-C(47)-C(50)-C(51)	-54.2(5)	C(69)-C(67)-C(70)-C(71)	80.7(4)

(92)

Torsion angles

C(1)-C(1)-O(2)-C(21)	-102.8(7)
C(1)-C(1)-O(2)-C(21)	77.7(7)
C(2)-O(2)-C(21)-C(22)	171.9(8)
C(2)-O(2)-C(21)-C(26)	-10.5(60
C(23)-C(24)-C(27)-C(28)	176.6(6)
C(23)-C(24)-C(27)-C(29)	56.3(7)
C(23)-C(24)-C(27)-C(30)	-62.2(7)
C(24)-C(27)-C(30)-C(31)	102.9(8)
C(24)-C(27)-C(30)-C(35)	-73.7(7)
C(28)-C(27)-C(30)-C(31)	134.4(9)
C(29)-C(27)-C(30)-C(31)	-15.4(7)



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TIME, min/cm

DSC 200 μW/mV
DTA 50 mK/mV
RANGE, mV/cm
WEIGHT, mg
REFERENCE

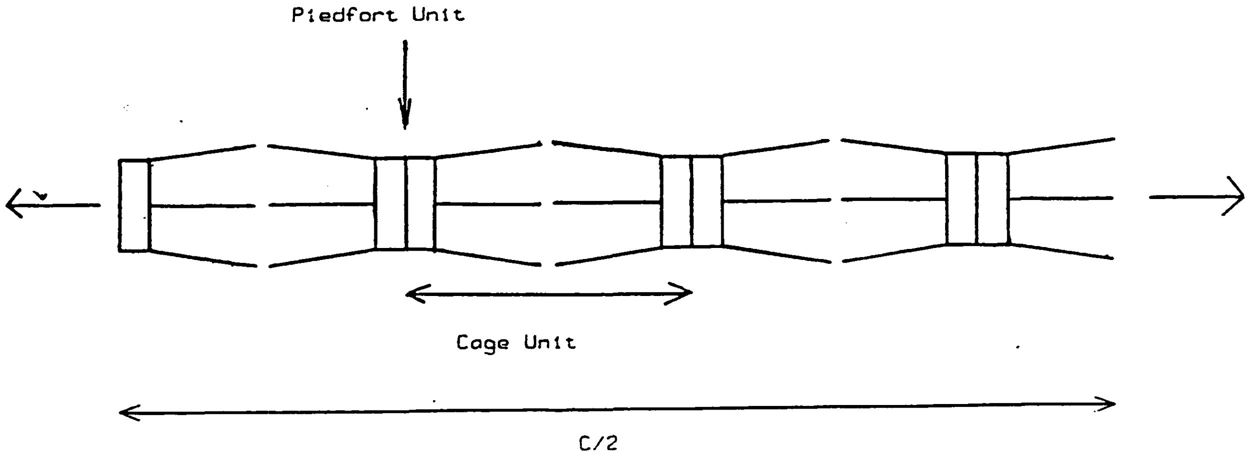
TGA 50 μg/mV
DTG 50 μg/(min mV)
SUPPRESSION, mg
RANGE, mV/cm 5
WEIGHT, mg 7.54
TIME CONST., sec
dY

TMA 1 μm/mV
DTM 0.1 μm/(min mV)
MODE
RANGE, mV/cm
SAMPLE SIZE
LOAD, g
dY

Theory 2:1
Host Guest
⇒ 3.03%

Figure 49. A thermalgravimetrograph of the (100).isopropanol clathrate. Guest loss occurs above 200° C and indicates a host to guest ratio of 2:1.

symmetry. The unusual feature of these unit cell dimensions is the exceptionally long c-axis dimension 89.01A. An explanation for this extended c-axis would be the arrangement of interlocking host pairs linked in the fashion shown in the scheme below.



Schematic view of a suggested packing mode of Piedfort units which would give a c-axial spacing of ca. 90 A.

The columnar stacking leaving individual cages between the Piedfort units. These cages would have a degree of freedom to rotate relative to each other like beads on an abacus. This mobility explaining the fact that the crystals do not give sufficient diffraction to allow full collection of the structure at room temperature. It is suggested that cooling the crystals with liquid nitrogen would eliminate this mobility and allow full crystal structure elucidation. It has not however been ruled out that the cooling process might lead to a phase change destroying the clathrate arrangement. Assuming a separation of approximately 12.5A between Piedfort units seven cages would be required to give the appropriate c-axis dimension. This gives an asymmetric unit equivalent two and half molecules made up from one third of seven independent molecules lying on the three-fold axis.

A Laué photograph, shown in Figure 50, provides further evidence for the extended c-axis. Analysis of the photograph by the method below leads to c dimensions of 112.83A and 102.81A for Y_1 and Y_2 which is in fairly good agreement with the value obtained by the cell programme.

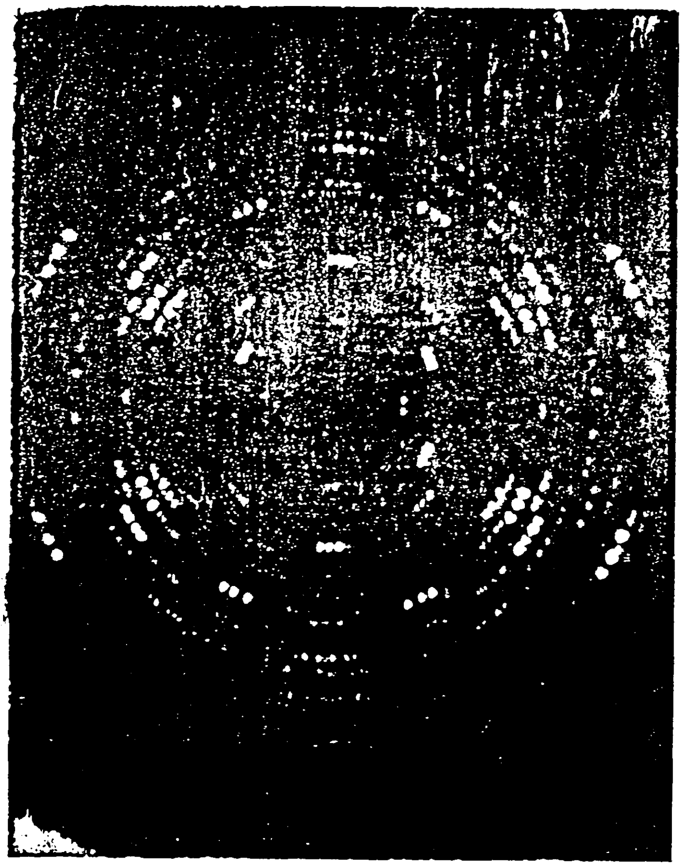


Figure 7 A Laué photograph of the (100).isopropanol clathrate.

The discovery of this new host group illustrates the use of structural analogy and imagination in the design of new hosts. The pronounced trigonal character found in the dioxane clathrate of (99) and the implied exact molecular three-fold axis in (100) indicates the strong part this symmetry plays in the host minima adopted. However the exact features necessary for host behaviour can still not be predicted accurately. Interestingly the two legs employed in the triazines which led to clathrate formation when used in hexa-substituted benzenes gave no inclusion behaviour. Thus the triazines 2,4,6-tris(p-benzylphenoxy)-1,3,5-triazine (101) and 2,4,6-tris(p-phenoxyphenoxy)-1,3,5-triazine (102), despite considerable effort failed to show any inclusion behaviour when crystalised from a large number of solvent systems at room temperature. In the cases of methanol, ethanol and 2-propanol experiments at both room temperature and at ca. 100° C were carried out . This is in stark contrast to the situation for their hexameric benzene analogues (90) and (91) which, as has been discussed earlier, both show extensive inclusion behaviour.

Analysis of the Laué Photograph giving the approximate c-dimensions mentioned above.

For Lamda = 0.7107A the wavelength of MoK_α radiation

$\underline{c} = n\ y/\sin\phi$ $\quad$ $\tan\phi_n = Y_n/v$ $\quad$ v = 190.5mm (crystal film distance)

$Y_1 = 1.2$mm $\quad$ $\tan\phi_1 = 1.2/190.5$ $\quad$ $\phi_1 = .3609^\circ$

$\underline{c} = .7107/\sin\phi_1$

$= 112.83$A

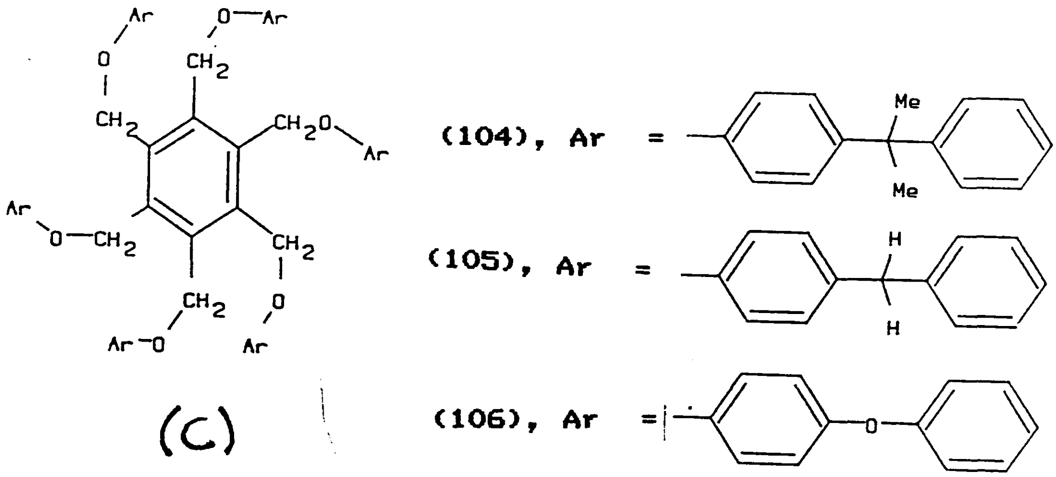
$Y_2 = 13.2$mm $\quad$ $\tan\phi_2 = 13.2/190.5$ $\quad$ $\phi_2 = 3.9638^\circ$

$\underline{c} = 07107 * 10/ \sin\phi_2$

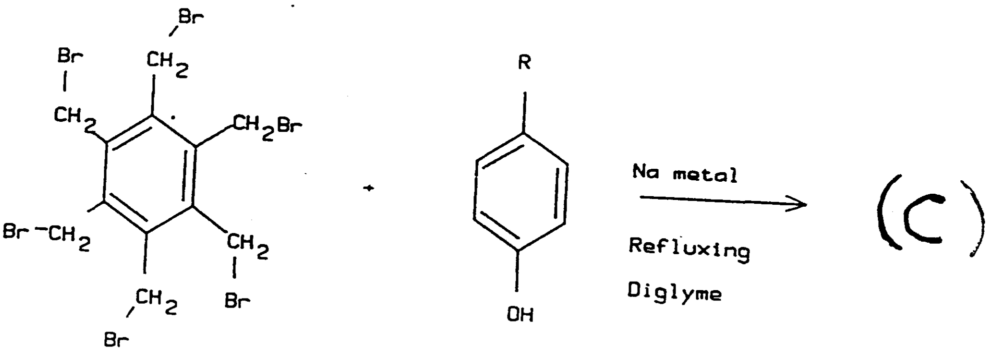
$= 102.81$A

CHAPTER 8.

This section deals with the synthesis of compounds (104-106) which are hexakis(*para*-substituted)phenoxymethylbenzenes, featuring a two-atom link between central and (first) aromatic side-chain ring.



(C)



(107)

The first in the series, hexakis(*p*-cumylphenoxymethyl) benzene (104), was synthesized following the discovery that hexakis(*p*-cumylphenoxy)benzene (92) adopted a trigonal structure on crystallisation without the necessity of a guest to stabilise the arrangement. It was reasoned that the introduction of a methylene group between the phenoxy group and central aromatic ring might open up the structure by increasing the distance spanned by the side-chain moieties A sketch of this is shown in Figure 51.

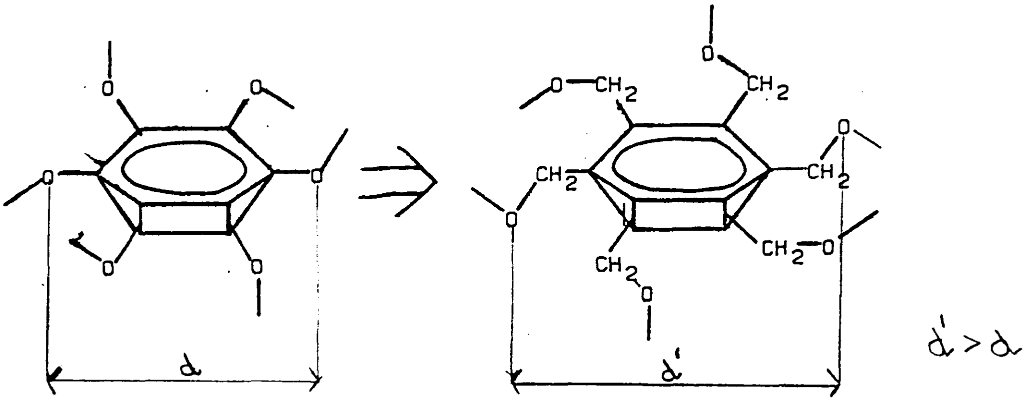


Figure 51. A sketch of the proposed effect of inserting a methylene group between the central and inner side-chain aryl moieties.

This, it was felt, might improve the chances of inclusion behaviour, possibly at the expense of loosing the high symmetry arrangement. A large number of phenoxy and thiophenoxy benzenes have reported by MacNicol and coworkers[67] as host molecules. (104) was made by reacting p-cumylphenol (97), dissolved in diglyme and treated with a molar equivalent of sodium metal, with hexakis(bromomethyl)benzene (107) by refluxing for 24 hours. The resulting product, an off-white solid, was insoluble at ambient temperatures, in most common organic solvents, making solution spectroscopy difficult. For this reason the presence of a guest was assessed by thermalgravimetric analysis and, where sufficiently prominent peaks existed, by infrared analysis. Inclusion experiments were carried out, as described earlier, employing heated sealed tubes. Thermogravimetric analysis results from these inclusion studies are presented in Table 14

Where easily identifiable infrared peaks existed infrared analysis was used to confirm guest identity. Figure 52 shows the appropriate sections of some of the the spectra obtained.

A second experiment designed to quantify as well identify the guest species was carried out for the dioxane clathrate. In this an accurately weighed sample of the adduct was placed in the bulb of the equipment shown in Figure 53. The bulb was connected to a vacuum tap and to a B10 quick fit female fitting which was modified with a long thin tube extension. An n.m.r tube fitted with a B10 male adaptor was fixed to this, the n.m.r tube was immersed in liquid nitrogen at -196°C, the whole system was then evacuated. The bulb section was then heated to melt the clathrate, the connecting glassware was also heated with an air blower to aid guest transfer. The system was heated for twenty minutes after melting to ensure full transfer of guest to the NMR tube section.

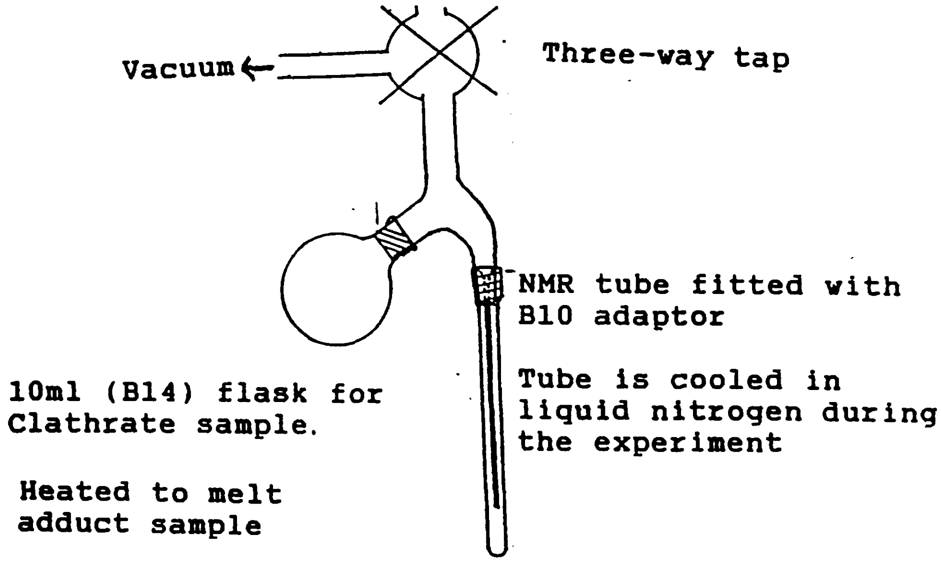


Figure 53. A sketch of the equipment used in the quantitative guest studies on some clathrates of (104).

On completion the ^{1}H NMR analysis was carried out using deuterated chloroform in which was dissolved an accurately weighed mass of mesitylene, the mass being approximately a molar equivalent to expected quantity of guest. The result of the procedure along with the experimental details is given in Figure 54. Integration of the resulting NMR signals confirmed the 1 : 1 host-to-guest ratio. The theoretical and obtained proton integration ratios of mesitylene methyl signals to dioxane methylenes for the experimental conditions given in Figure 54 are shown below.

Theoretical ratio	Found ratio
1.136 : 1	1.228 : 1

This is in good agreement with the TGA data shown in Table 14

TABLE 14

Thermalgraviometric analysis data for some clathrates of (104)

	% Weight loss		Temperature range
Guest molecule	Found	Theory	of loss in °C
		H:G 1:1	
toluene	5.21	6.07	193-245
trimethylsilane	6.04	6.20	
	(i) 2.00		130-175
	(ii)4.04		207-245
morpholine	6.01	5.76	185-240
acectonitrile	3.01	2.81	195-222
DMEU	7.21	6.63	195-240
carbontetrachloride	8.00	9.77	195-240
sulpholane	7.80	7.78	200-250
tetramethylurea	6.20	7.54	193-215
cyclohexane	6.00	5.58	183-250
dioxane	6.10	6.00	
	(i) 0.80		100-175
	(ii)5.30		193-250
dioxane repeat			
after 6 months	6.00	6.00	
	(i) 1.20		38-175
	(ii)4.80		200-250
		H:G 1:2	
methanol	4.00	4.30	192-227

The physical properties of (104) presented problems in confirming the proposed structure. Its extreme insolubility in solvents normally available in the deuterated form made solution NMR impossible. (A number of

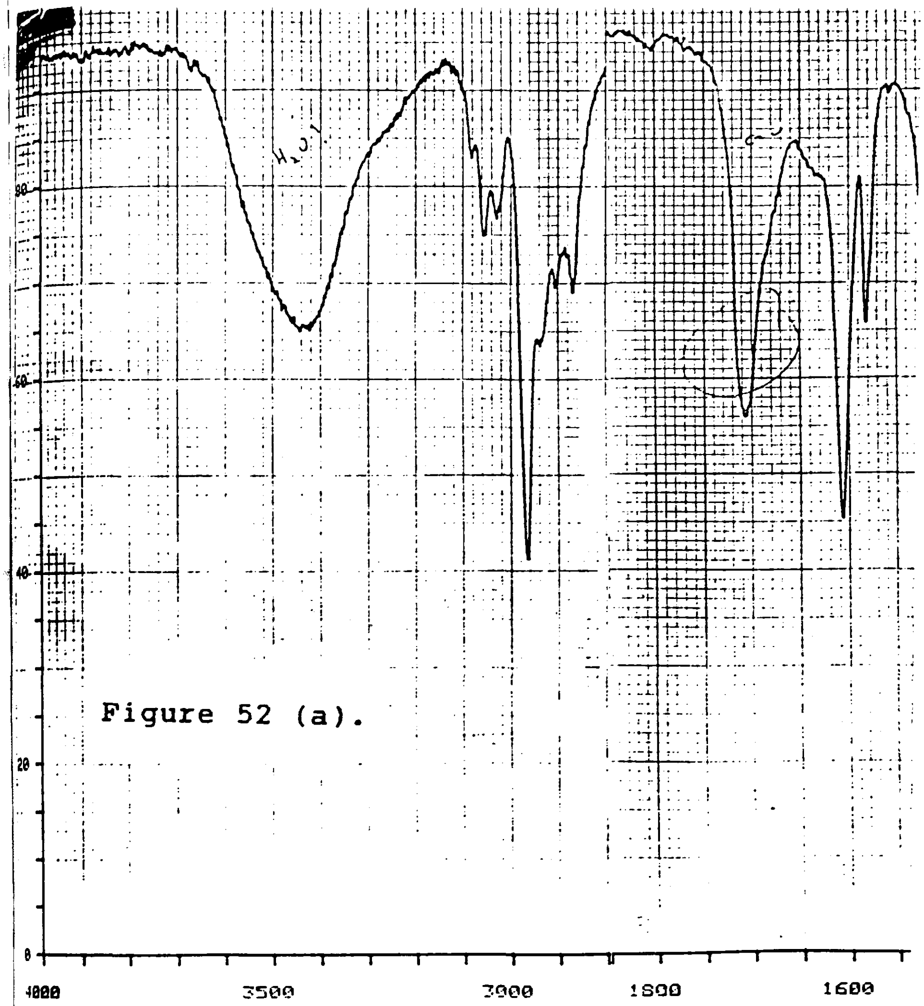


Figure 52 (a).

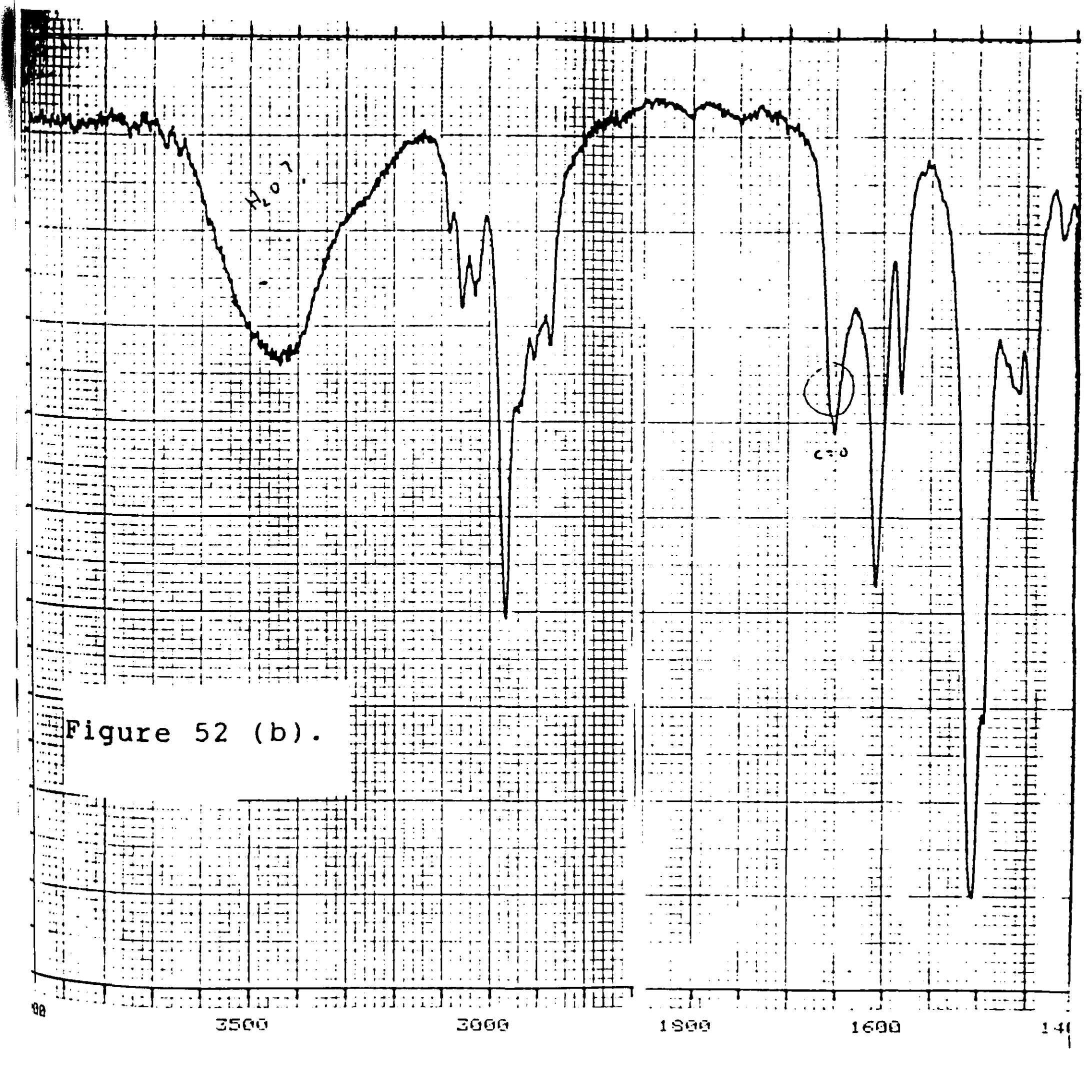


Figure 52 (b).

Figure 52. Showing the guest peaks in the infrared spectra of (104) clathrates guest peaks being ringed. (a)From showing the presence of water as well as the solvent showing the C=O and O-H stretching frequencies. (b) From tetramethylurea again water is present along with the solvent the C=O and O-H stretching frequencies again visible.

Experimental details of the guest quantification and identification experiment for the (104).1,4-dioxane clathrate.
Mass of clathrate = 53mg.
For 1:1 H:G ratio 3.088mg (0.0351 mmols) of guest expected.
Therefore to achieve 1:1 ratio of
1,4-dioxane to mesitylene in the n.m.r.
tube.
Requires theoretical mass
of 4.212mg(0.0351mmols) of mesitylene.
Actual weighed mass = 4.26mg (0.0355 mmols).
Expected H inetgration ratio
= 0.0351*8/0.0355*9 = 0.876.
Observed integration values
1,4-dioxane =116: Mesitylene = 142.5.
Ratio = 0.81.

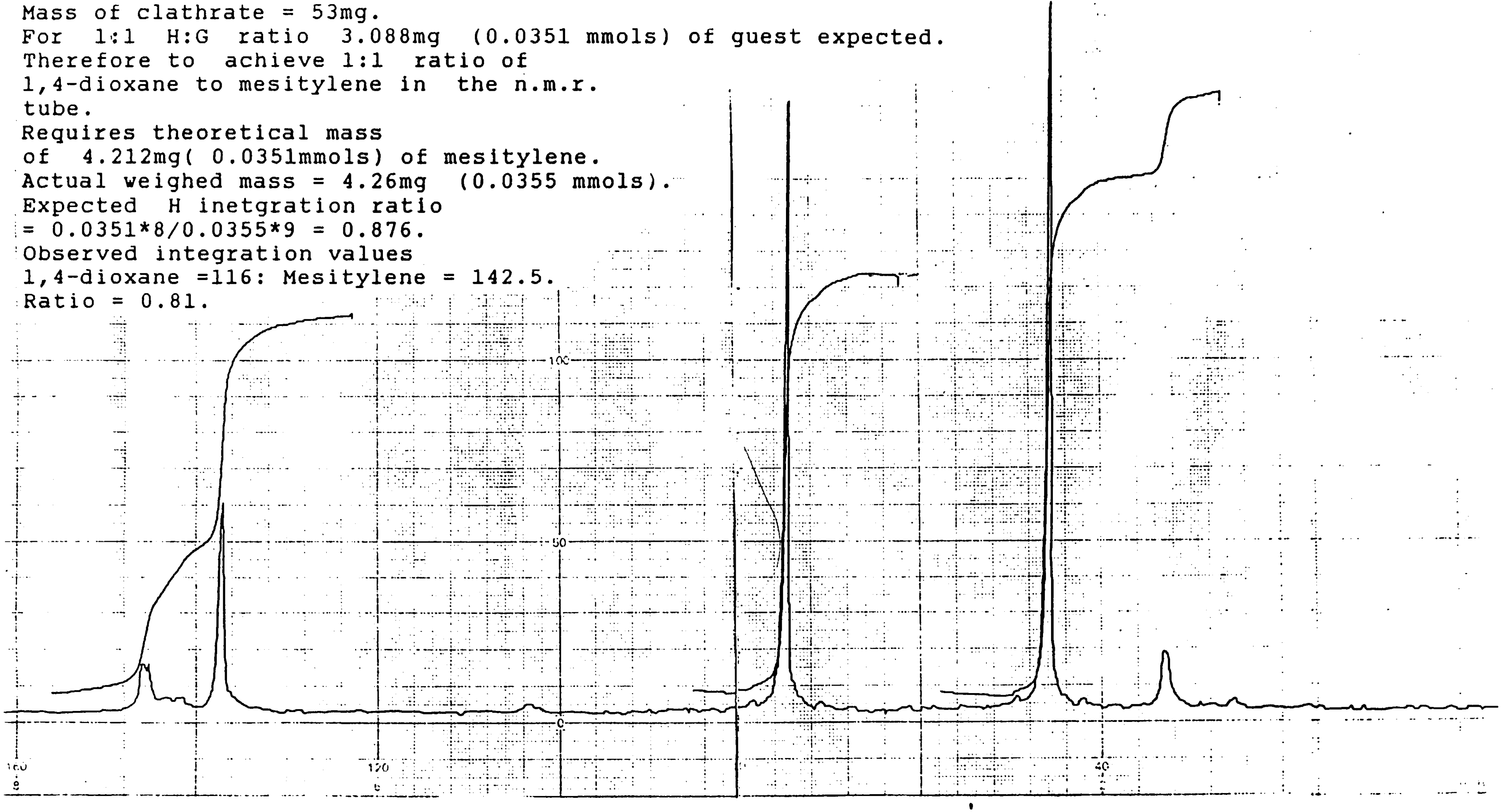
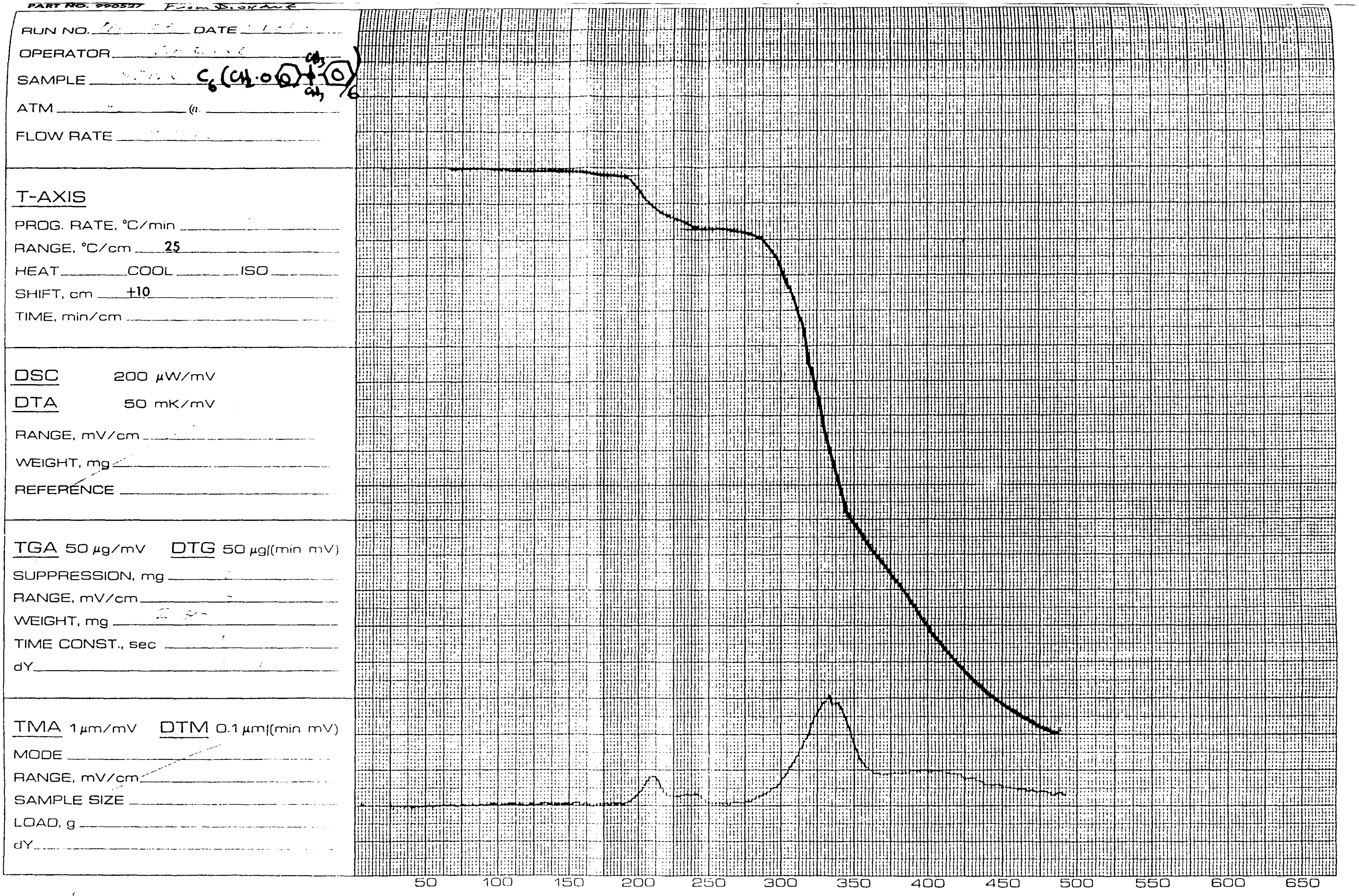


Figure 54. The ^1H NMR (100 MHz) spectrum from the guest quantification experiment carried out on the (104).1,4-dioxane clathrate along with the experimental details of this experiment.

attempts made to collect a solution ^{13}C spectrum, by overnight signal accumulation, in a heated, 40°C, mixture of d_8-toluene and d_2-dichloromethane, failed to yield an acceptable spectrum.) A number of mass spectral analyses carried out in Glasgow and at the S.E.R.C. mass spectral service at Swansea, involving both conventional and fast atom bombardment techniques resulted in no useful mass spectral evidence. The probable cause being the degradation of (104) at temperatures above 300° C, witnessed in the many thermalgravimetrographs of the clathrates of (104); for example see Figure 55. Also no X-ray quality crystals could be produced despite much effort.

As (104) is a versatile host molecule it was felt that some definitive spectral evidence was required. To this end samples of the (104) dioxane clathrate and an "unsolvated" sample (from chlorobenzene) were prepared for ^{13}C solid NMR analysis at Durham University. This technique has the added advantage of furnishing some information about the crystal structures of the samples, as the set of signals detected originates only from the crystalline asymmetric unit, all other molecular signals being symmetry related and therefore being in magnetically equivalent sites. Ripmeester[68] has already shown that the technique can be extremely useful in the analysis of clathrates. A study to establish the direct relevance to this case was carried out. This involved obtaining ^{13}C solid NMR spectra for a trigonal and non-trigonal forms of compound hexakis(p-benzylphenoxy)benzene (90). A single crystal X-ray analysis of the (90).1,1,1-trichloroethane clathrate



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SHIFT, cm +10
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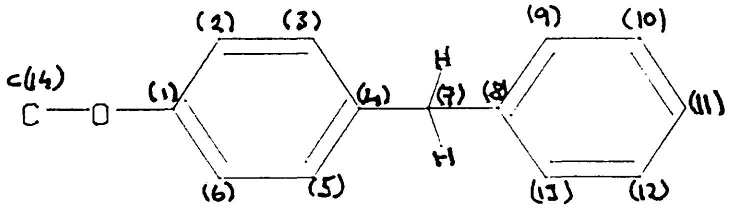
DSC 200 μW/mV
DTA 50 mK/mV
RANGE, mV/cm ____
WEIGHT, mg ____
REFERENCE ____

TGA 50 μg/mV DTG 50 μg/(min mV)
SUPPRESSION, mg ____
RANGE, mV/cm ____
WEIGHT, mg ____
TIME CONST., sec ____
dY ____

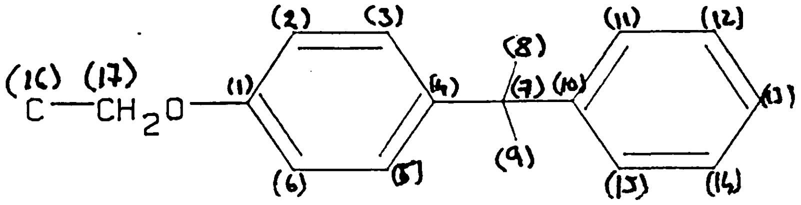
TMA 1 μm/mV DTM 0.1 μm/(min mV)
MODE ____
RANGE, mV/cm ____
SAMPLE SIZE ____
LOAD, g ____
dY ____

Figure 55. The thermalgravimetrograph of the (104).1,4-dioxane clathrate. Note the degradation of the host at temperatures above 250°C.

established, as described earlier a trigonal structure with space group R$\bar{3}$; whilst a partial structure obtained for the unsolvated form of (90) (from acetonitrile) gave a unit cell consistent with space group P$\bar{1}$. The spectrum of the trigonal clathrate showed a single set of peaks, most noticeably single peaks at 41.05 for the C(7) benzyl carbon and 156.17 for C(1). The spectrum of the triclinic, P$\bar{1}$ form shows two peaks of different intensities at 42.48 and 40.28 for C(7) and three peaks of equal intensity at 157.41, 156.97 and 156.31 for C(1), see Figure 56, confirming that solid state NMR can distinguish between two crystallographically distinct forms of the same compound. The numbering system used is shown below.



The spectroscopic results obtained for the two link compound (104) were also encouraging the dioxane clathrate giving the spectrum shown in Figure 57. This shows 13 strong signals, 17 would be the expected number for a molecular arrangement where the asymmetric unit was the section shown below, if all carbon atoms were in magnetically distinct environments. The posibility of near equivalence in the range between 125-130 seems likely.



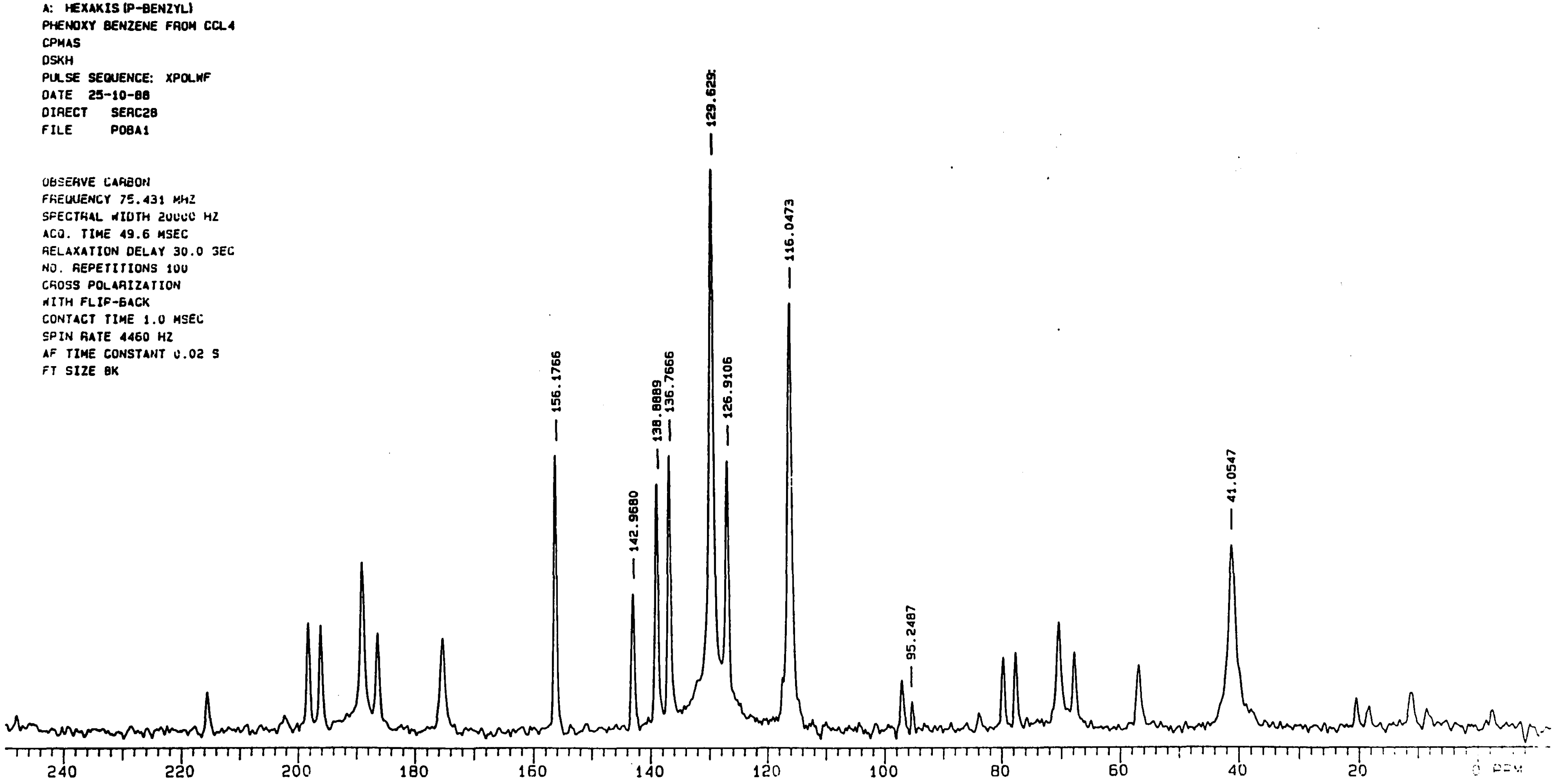
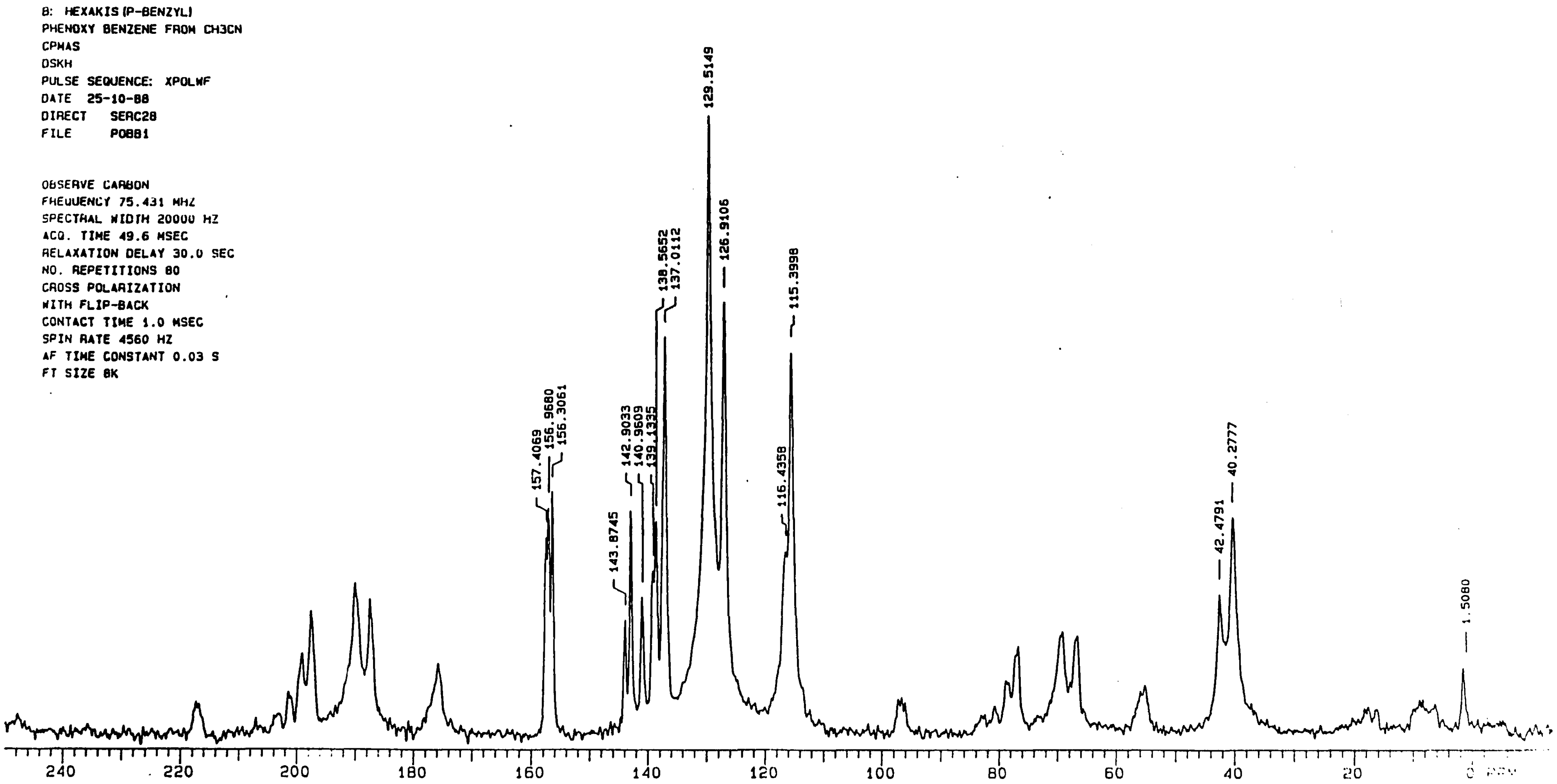


Figure 56(a). The solid-state CPMAS ^{13}C spectrum of the (90). CCl_4 clathrate, which is consistent with trigonal space group $R\bar{3}$.



```
B: HEXAKIS(P-BENZYL)
PHENOXY BENZENE FROM CH3CN
CPMAS
DSKH
PULSE SEQUENCE: XPOLWF
DATE  25-10-88
DIRECT   SERC28
FILE     P0881

OBSERVE CARBON
FREQUENCY 75.431 MHZ
SPECTRAL WIDTH 20000 HZ
ACQ. TIME 49.6 MSEC
RELAXATION DELAY 30.0 SEC
NO. REPETITIONS 80
CROSS POLARIZATION
WITH FLIP-BACK
CONTACT TIME 1.0 MSEC
SPIN RATE 4560 HZ
AF TIME CONSTANT 0.03 S
FT SIZE 8K
```

Figure 56(b). The solid-state CPMAS ^{13}C spectrum of the unsolvated form of (90) from acetonitrile , corresponding to the less symmetric space group P$\bar{1}$.

Clearly from the above evidence, if (104) adopted a lower symmetry form; a peak number much greater than 17 would almost certainly have been observed. Allowing for some signal overlap an interpretation of the spectrum is offered here. A non-quaternary suppression spectrum shown in Figure 58 reveals that the peaks at 156.83, 153.58, 139.79 and 137.59 result from quaternary carbons, the correct number for the proposed structure. Table 15 presents for comparison with the observed peaks some predicted shift values. These predictions were made using information presented in Tables of Spectral Data for Structure Determination of Organic Compounds some assumption made were that the cumyl group would be similar to a tertiary butyl and that the benzyl ether would induce shifts similar to those from a methoxy group, the limitation of this approach are obvious, primarily that the shifts are for solution spectra, but never the less the trends do appear to coincide.

Table 15. Predicted and observed peaks of (104)

Carbon No.	Predicted solution Peaks	Assigned Solid 13C
(1)	156.20	156.83
(2,6)	113.80	116.15,109.93
(3,5)	128.80	129.24* May inter-
(4)	140.50	139.79 change
(10)	148.60	153.59
(11,15)	126.50	126.97
(12,14)	128.50	128.77*
(13)	126.0	126.97
(7)	138.90	137.50

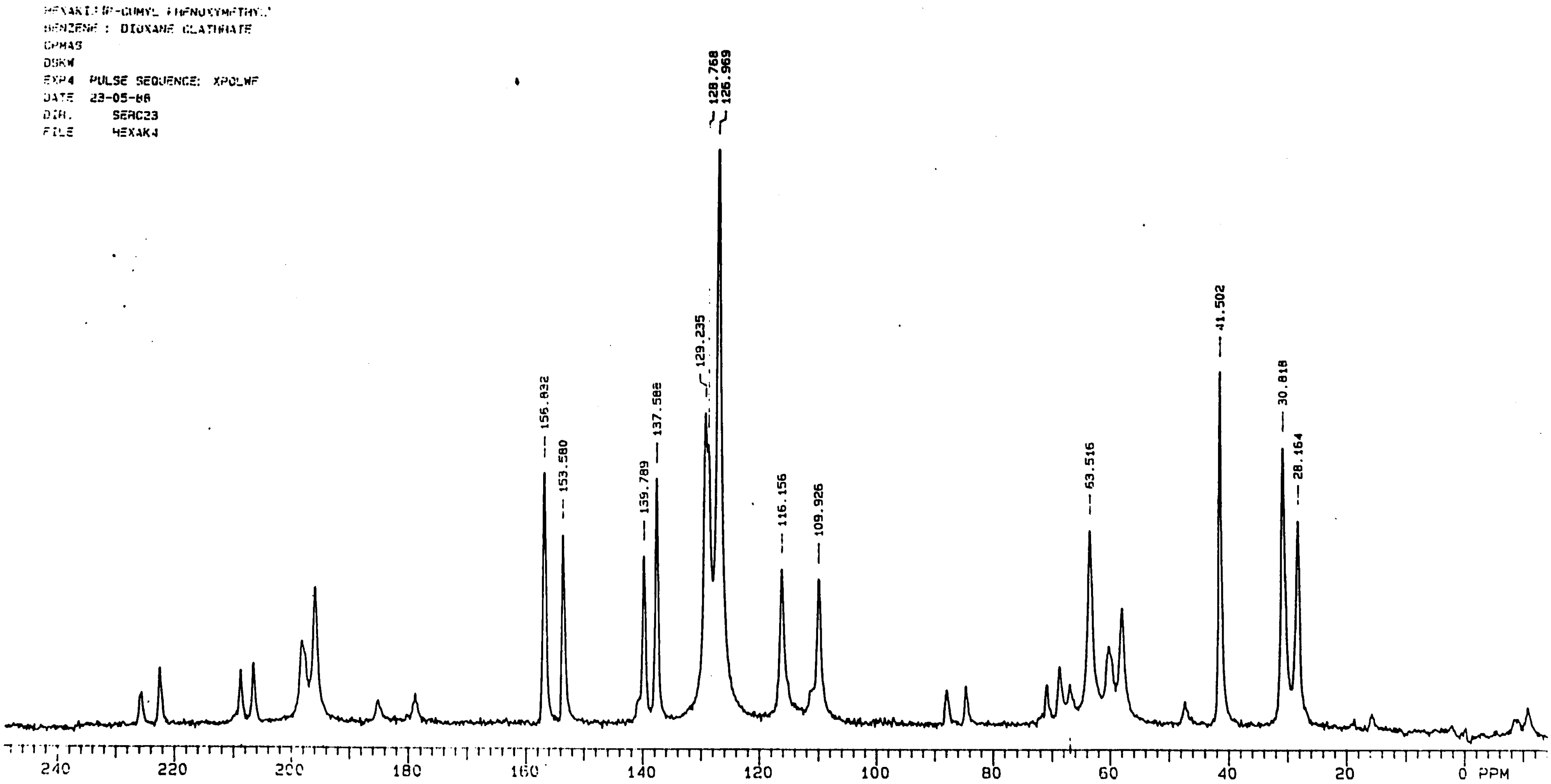


Figure 57. The solid-state CPMAS ¹³C spectrum of the (104).1,4-dioxane clathrate.

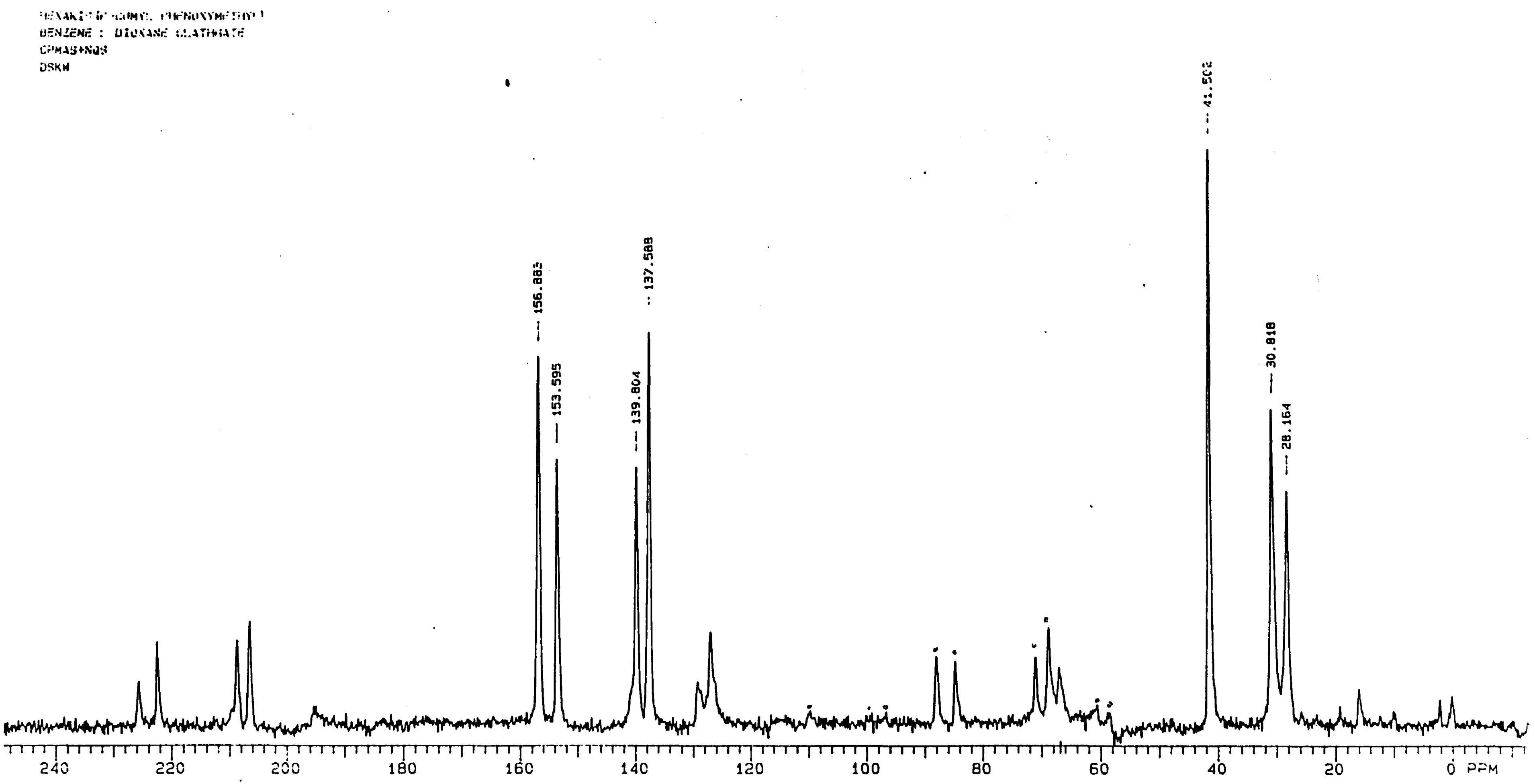


Figure 58. The non-quaternary suppressed solid-state CPMAS ^{13}C spectrum of the (104).1,4-dioxane clathrate.

Assignment of the non-aromatic peaks was done by comparison with the solution values obtained for hexakis(p-cumylphenoxy)benzene (92). The non-aromatic quaternary being assigned to the peak at 41.50, the value in (92) being 42.33, the cumyl methyl groups were assigned as the peaks at 28.16 and 30.82 their non-equivalence indicating that they lie in magnetically distinct environments; the methyls in the solution spectrum of (92) have the single value of 30.83. Further evidence for a high symmetry crystalline form is the presence of only two peaks assigned to carbons C(2) and C(6) in the Figure 57 above. It appears that the single signal which would be expected in a solution phase spectrum is now found as two distinct signals indicating that C(2) and C(6) are now in very different , but unique, environments. This phenomenon is observed in the solid phase ^{13}C spectrum of the known trigonal crystalline form of (92), see Figure 59, which contains the corresponding aromatic carbons shown in its asymmetric unit.

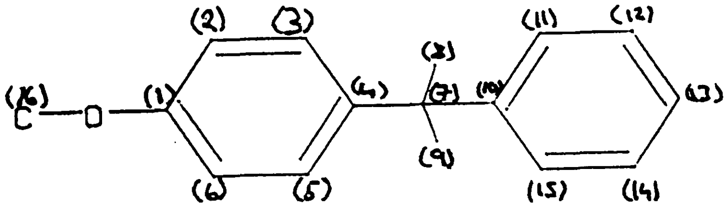


Table 16 shows the the ^{13}C assignment of C(2) and C(6) carbons of (104) and signals assigned to the C(2) and C(6) positions of (90) and (92) along with the solution ^{13}C NMR signals obtained for (90) and (92)

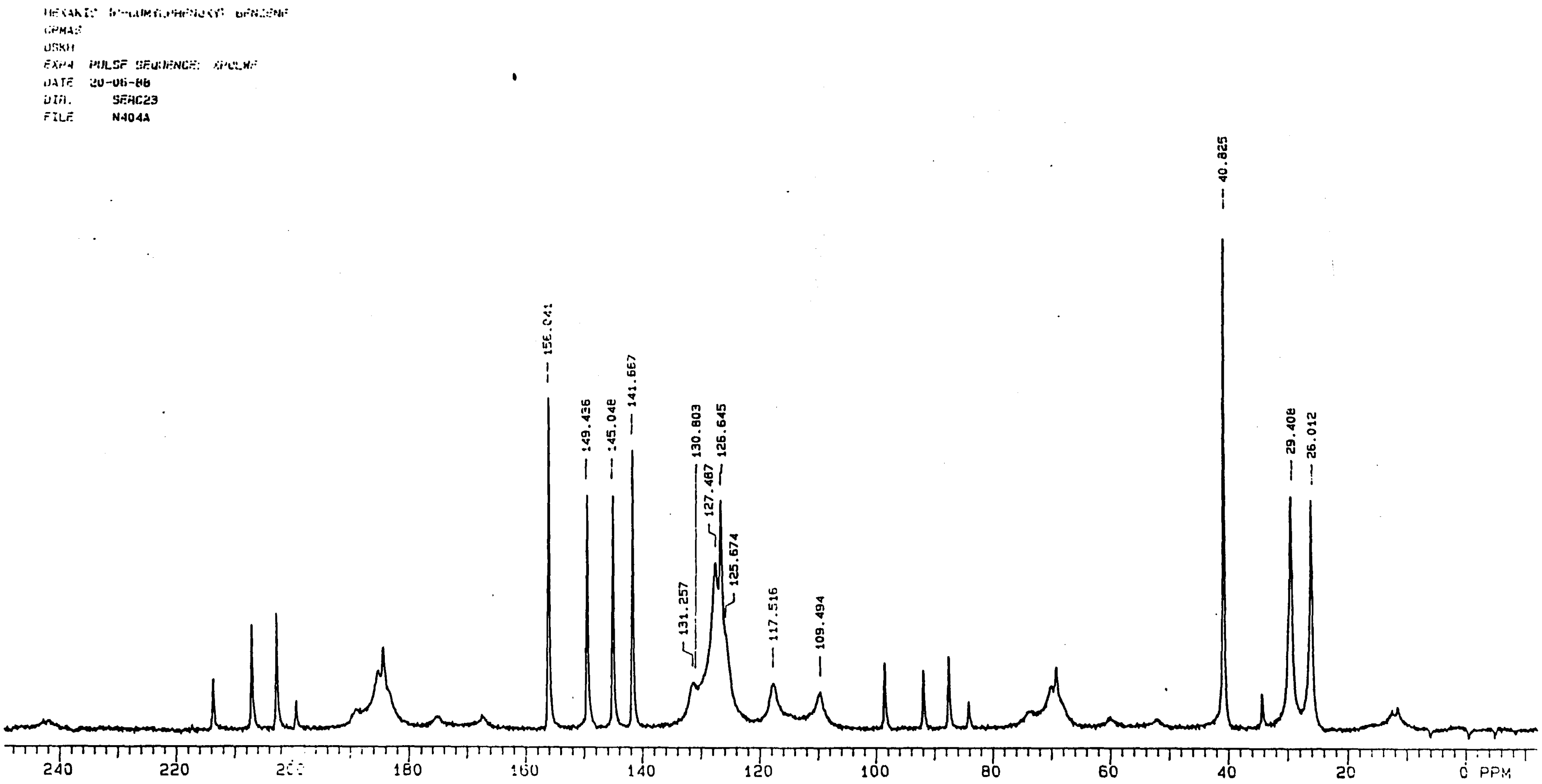


Figure 59. The solid-state CPMAS ^{13}C spectrum of the trigonal form, from acetonitrile, of hexakis(p-cumylphenoxy)benzene (92).

TABLE 16 Signal asignments in the solid and solution 13C spectra of the C(2) and C(6) positions for compounds (90), (92) and (104)

13C	Trigonal (92)	(104)	Trigonal (90)
CDCl3 Soln NMR	115.16	-*	115.65
Solid	117.52,109.49	116.16,109.93	116.05

* low solubility made measurement impossible.

The similarity between the chemical shifts for (92) and (104) is striking; this may result from nearly equal γ-gauche effects, to a central ring and methylene carbon respectively. Very interestingly this splitting is not observed in the trigonal from of (90) and the possibility of kenetic averaging cannot be ruled out. The observation of two distinct signal values is attributed to the values of the torsion angles around the carbon-oxygen bond between the central aromatic carbon and the linking oxygen causing the two ortho protons to experience different levels of shielding (γ-gauche effect predominating). The above argument indicates the strong likelihood that clathrates of (104) adopt a trigonal conformation. There are in fact a number of possible crystal structures which would give the asymmetric unit propossed above; the most likely, due to steric constraints in the host molecule, are however, C_{3i} or D_3 molecular symmerty. Further inspection of Figures 57 and 58 revealed the presence of a small broad peak at 67.2 which fits well with the published value of 67.4 for 1,4-dioxane, the guest in this case. MacNicol has already shown that magic angle NMR can be used to identify guest species in the case of the spider host octakis(m-methylthiophenoxy)naphthalene[69]. The presence

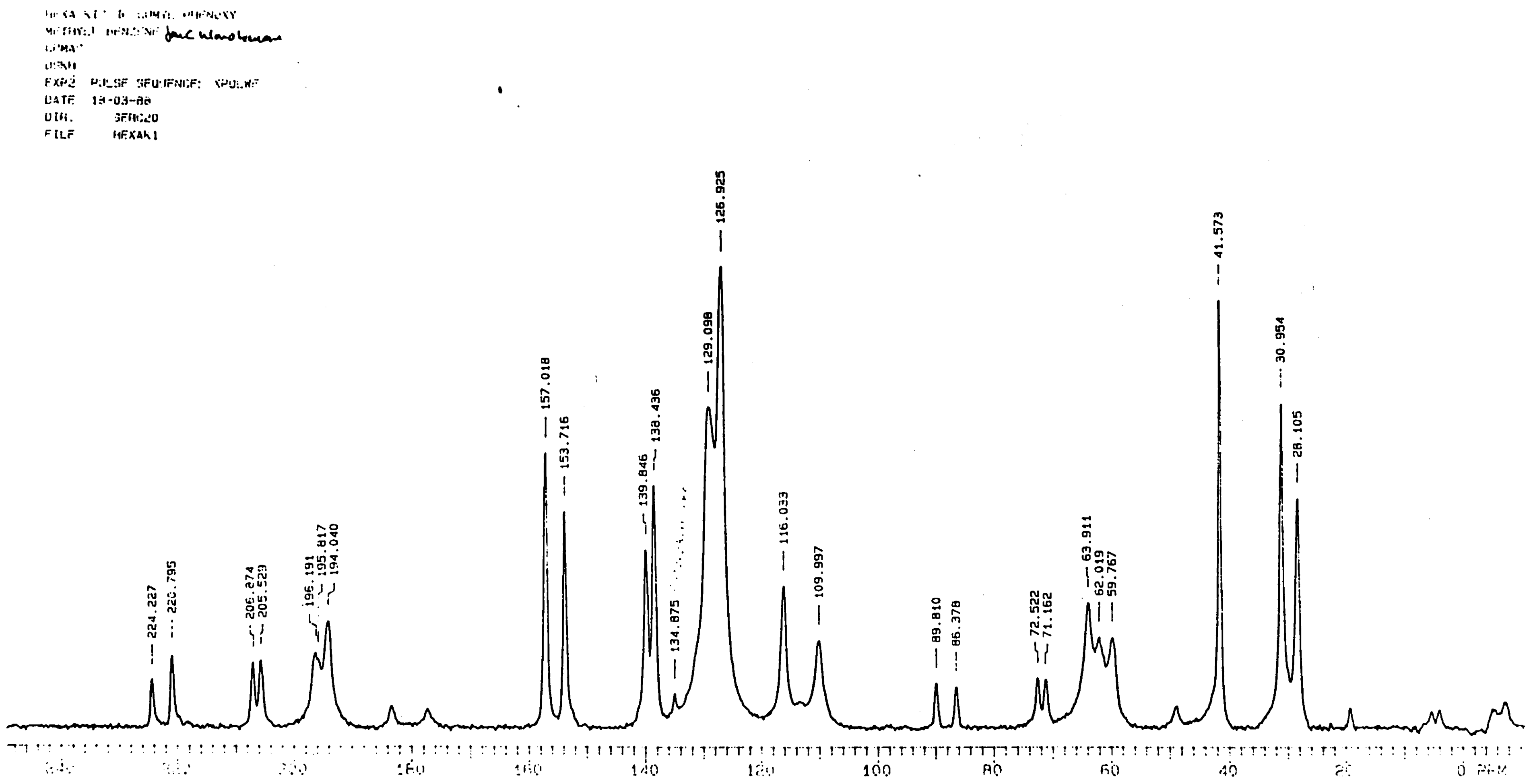


Figure 60. The solid-state CPMAS ^{13}C spectrum of (104) from chlorobenzene

of the guest peak in the N.Q.S., (non-quaterniary suppression spectrum) Figure 58 indicated that the guest was mobile within the cavity. The failure to suppress the methyls of the cumyl group showed that they must also be able to rotate freely.

The spectrum obtained for the sample of (104) crystallised from chlorobenzene, Figure 60, was nearly identical to that of the dioxane clathrate a comparison of the peak values is shown in Table 17.

Table 17. A comparison of the peak values obtained in the sample of (104) crystallised from both dioxane and chlorobenzene.

(104) DIOXANE CLATHRATE		(104) from CHLOROBENZENE	
	156.83	157.02	
	153.59	153.73	
	139.79	139.86	
	137.59	138.44	
129.24 Ave =			
128.77	129.00	129.00	*
	126.97	126.90	
	116.16	116.03	
	109.93	110.01	
	63.52	63.85	
	41.50	41.52	
	30.82	30.95	
	28.16	28.11	

* A broad peak is found at this site with a definite shoulder

The similarity represented above along with other evidence e.g. the presence of a hydroxyl stretching band in an infrared spectrum of (104) crystallised from chlorobenzene and the fact that a thermalgravimetrograph shown in Figure 61 shows a 2.6% weight loss; the loss being in two stages firstly a loss of 1.8% between 100 and 150°C probably surface chlorobenzene and secondly a loss of 0.8% being lost as the samples melts over the range 190 to 200°C. Which in light of the infrared evidence was considered to be water. This percentage water indicates partial cavity occupancy either two thirds containing one water molecule or one third containing two guest molecules or some other distribution. This partial occupancy may mean that the open host lattice, even with the cavity empty has some stability.

The solid phase NMR evidence presented above along with the thermal and infrared inclusion data lead to the proposition that (104), is not only a versatile host but that it adopts a trigonal conformation in its clathrate inclusion compounds. The most likely situation is that any guest, or hydrogen-bonded combination of guests, capable of fitting into the cavity of this versatile host structure will be included. It is worth noting here that trigonal or near trigonal crystal structures are observed in three different cases involving the p-cumylphenyl group. It may be that this group has a "special" affinity for high symmetry minima.

Compound (105) hexakis(p-benzylphenoxymethyl)benzene was produced analogously to (104) by treatment of

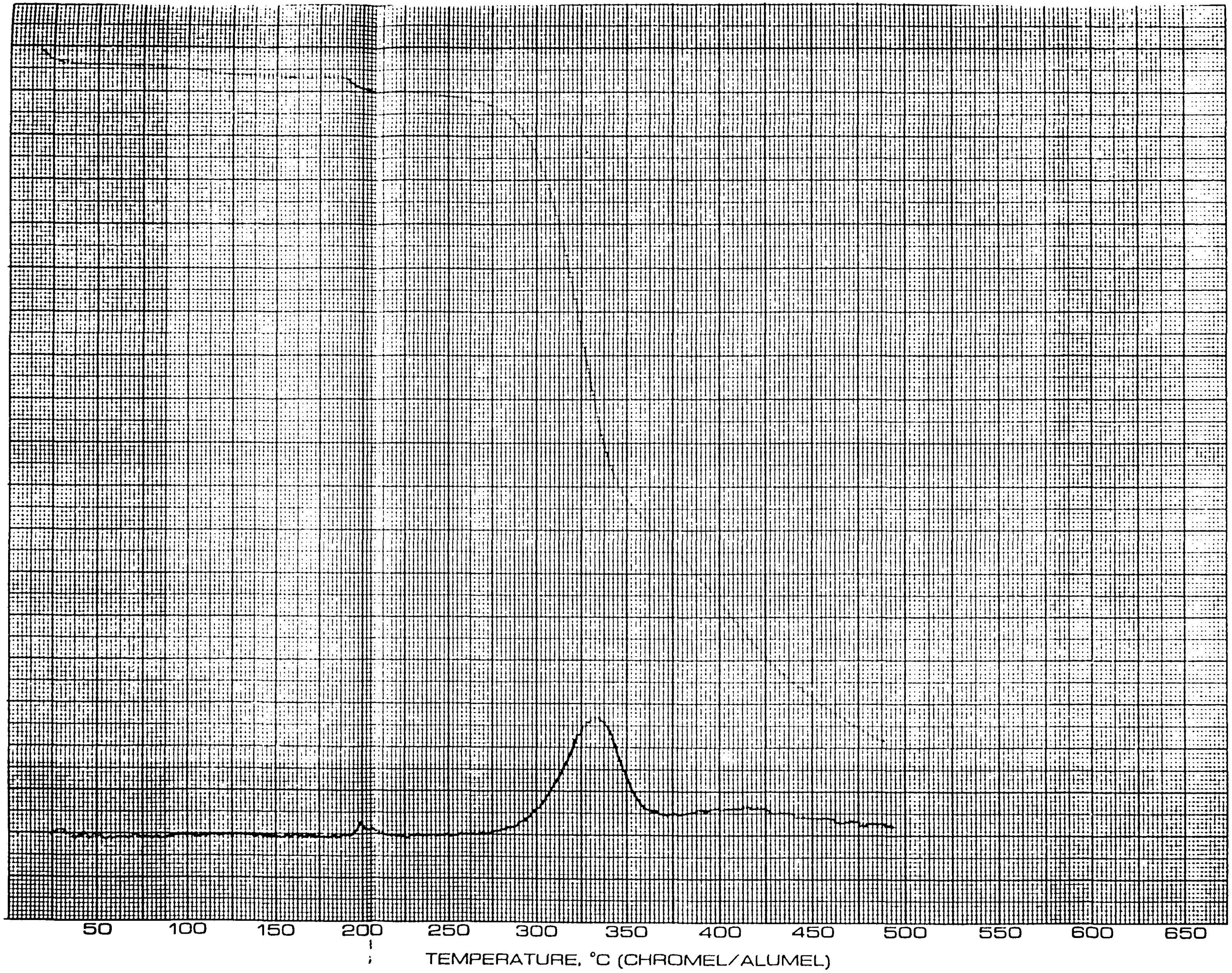


Figure 61. The thermalgravimetrograph of (104) crystallised from chlorobenzene showing that a small quantity of guest is lost around the melting point of the host.

p-benzylphenol (95) with sodium metal in refluxing diglyme followed by the addition of hexakis(bromomethyl)benzene (107). The material produced was again an off-white powder which, unlike (104) was very soluble in a large number of solvents. This made inclusion tests difficult since often very large quantities of (105) were required to achieve a saturated solution. Despite this crystallisations from solvents: methanol, ethanol, isopropanol, acetonitrile, ethylacetate, dioxane, cyclohexane, carbontetrachloride, and DMUE: revealed no inclusion behaviour; all samples, where possible, were examined by ^{1}H NMR, otherwise microanalysis or thermalgravimetric analysis were employed to look for evidence for clathrate formation.

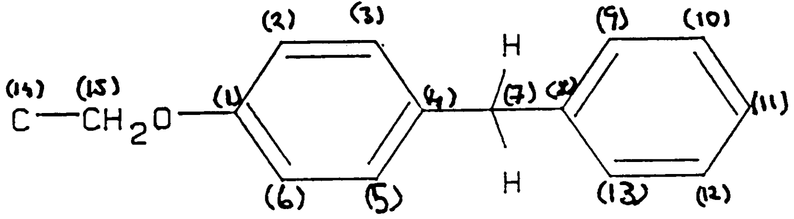
Identification utilised most modern spectral techniques, again however, no satisfactory mass spectrum could be obtained, indicating similar instability at temperatures above 300°C to those encountered with compound (104). Most useful in confirming the assigned structure of (105) was comparison of its ^{13}C spectrum with a solution spectrum for (90); and also comparison with a set of peaks predicted as described above (see reference[70]). The assignment and comparisons are shown in Table 18.

Table 18

Peak assignment for the ^{13}C NMR spectrum of (105)

Carbon No.	predicted peak	measured peak	peak from(90)
1	151.9	156.83	155.68
2,6	113.7	114.70	115.65
3,5	128.8	129.86	129.50
4	136.1	133.89	134.97
8	144.2	141.39	141.25
9,13	127.9	128.40	128.36
10,12	128.4	128.76	128.81
11	125.7	125.96	125.98
#14	138.9	137.83	140.20
7		40.98	40.97
15		63.57	

Assignment aided by presence of very similar peaks in the ^{13}C spectra of both (104) and (106). Numbering scheme is shown below.

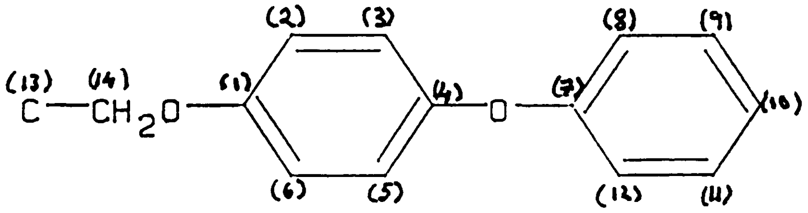


A final member of the series produced, analogously to the other compounds, from p-phenoxyphenol (96) and hexakis (bromomethyl)benzene, was hexakis(p-phenoxyphenoxymethyl)benzene (106). Again no useful mass spectral data could be obtained. Solution n.m.r spectra ^{1}H and ^{13}C were collected at 40°C in CD_2Cl_2. Table 19 shows peak assignments against the predicted values and peaks from compound (91).

Table 19. Assignment of solution ^{13}C NMR signals for (106), along with predicted peaks and an assignment for compound (91).

Carbon No.	predicted peak	measured peak	peak from(91)
1	153.4	156.83	154.78 or 153.5
2,6	114.1	116.44	120.63 or119.01 or 117.6
3,5	119.9	121.04	120.63 or119.01 or 117.6
4	149.5	151.49	154.78 or 153.5
7	157.6	158.72	159.42
8,12	119.0	118.24	120.63 or119.01 or 117.6
9,11	128.8	130.09	128.81
10	123.2	123.10	124.07
13	136.8	137.83	142.04
14		64.99	

Assumed numbering systems used in the assignments.



Numerous inclusion tests were carried out on (106), the resulting crystalline samples being subjected to thermalgravimetric analysis to assess if a guest was present. Solvent from all main classes -protic, dipolar aprotic and non-polar- were tested. However no clathrate formation was identified.

In line with the hypothesis that high symmetry is a

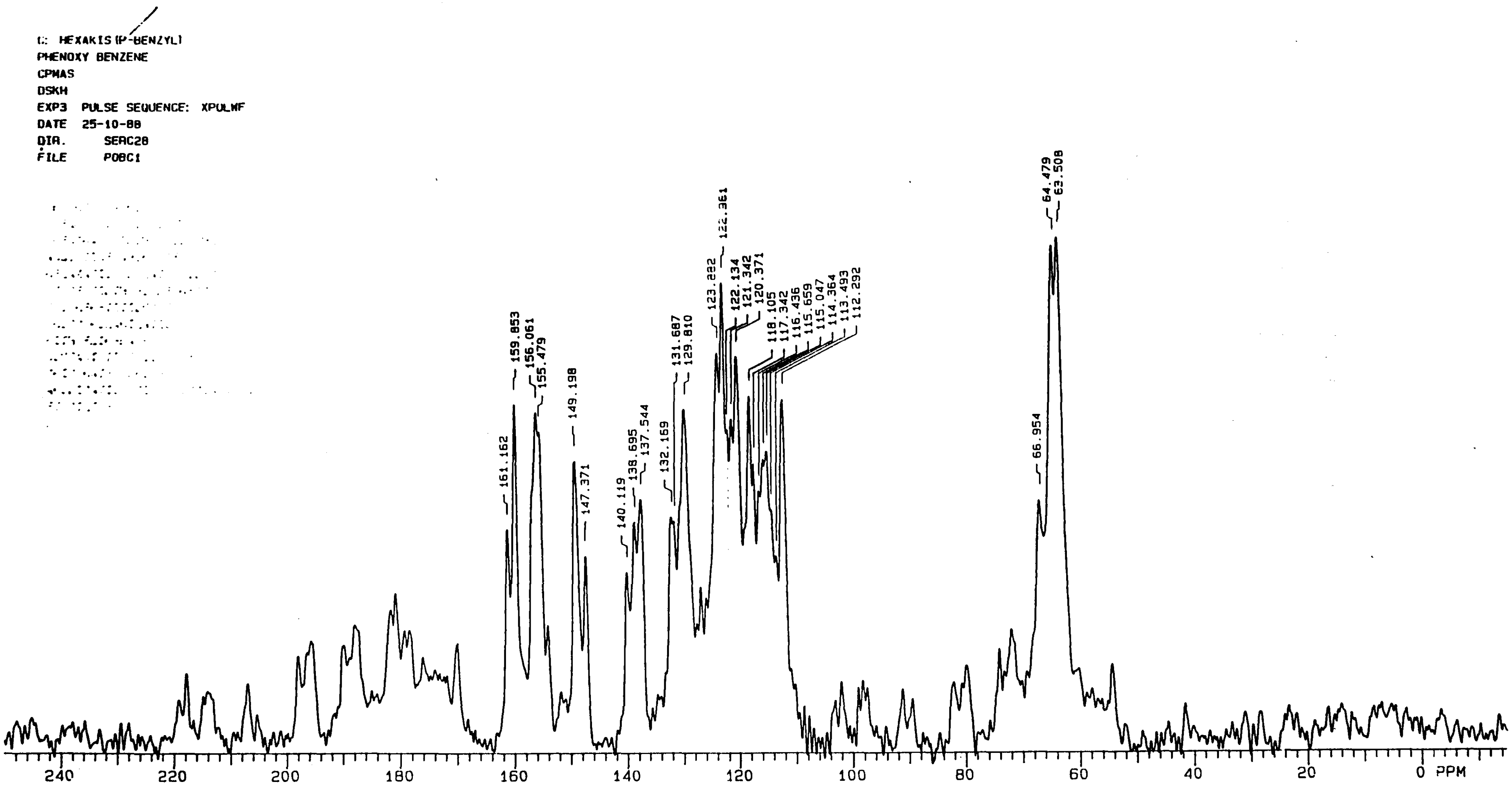
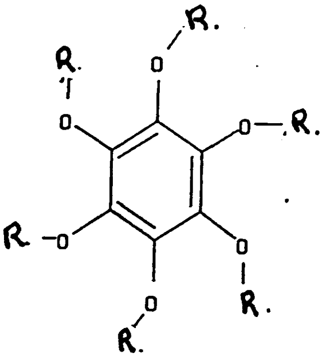


Figure 62. The solid-state CPMAS ^{13}C NMR spectrum of (106) from toluene. A low symmetry structure is assigned on the basis of the multiple signals observed for many carbaon positions.

feature of hexa-host behaviour, a sample of (106) was prepared for solid ^{13}C NMR spectroscopic analysis, by recrystallisation from toluene. No guest was observed in the thermalgravimetrograph of the sample. Lack of evidence in this case for a high symmetry molecular orientation not only strengthen the above hypothesis but also, by implication, lends weight to the previous interpretation presented in the case of compound (104). The spectrum obtained is shown in Figure 62. Clearly the large number of peaks rules out a high-symmetry molecular orientation in this case. Naturally, nothing can be said for samples from other inclusion tests but it is unlikely that crystallographically different unsolvated forms would exist: however this possibility cannot be dismissed completely. Brief consideration of the spectrum reveals the presence of three peaks in the region 62-67, at 66.95, 64.48, and 63.51 from methylene groups, (a single peak at 64.99 is found in the solution spectrum), which reside in magnetically non-equivalent environments. This establishes the existance of crystallographically distinct "leg" units for the hexa-substituted molecule (106). Peaks in the region assigned to quaternary carbons again show evidence of multiple "leg" orientations e.g. peaks at 161.16 and 159.85 corresond to the solution at 158.72; whilst peaks at 140.12, 138.70 and 137.54 correspond to the solution peak at 138.42. Tentatively location on a point of $\bar{1}$ symmetry is suggested [*cf*. the solis-state ^{13}C NMR of the unsolvated centrosymmetric molecule (90) shown in Figure 56(b)]. These compounds represent an extension to the large number of host molecules reported by MacNicol and coworkers[67] with the two-atom methyleneoxy linking moiety between the central benzene group and the "leg". However, the evidence presented here indicates that the present host, (104) is the first to adopt a high symmetry molecular conformation on clathrate formation which is probably related to the more structured nature of the "leg" moiety employed.

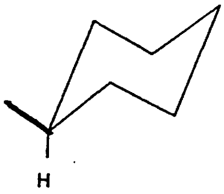
CHAPTER 9.

This chapter describes brief efforts toward synthesizing compounds in the structurally elegant group, the hexakis(cycloalkyloxy)benzenes.

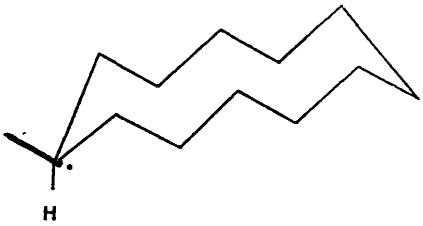


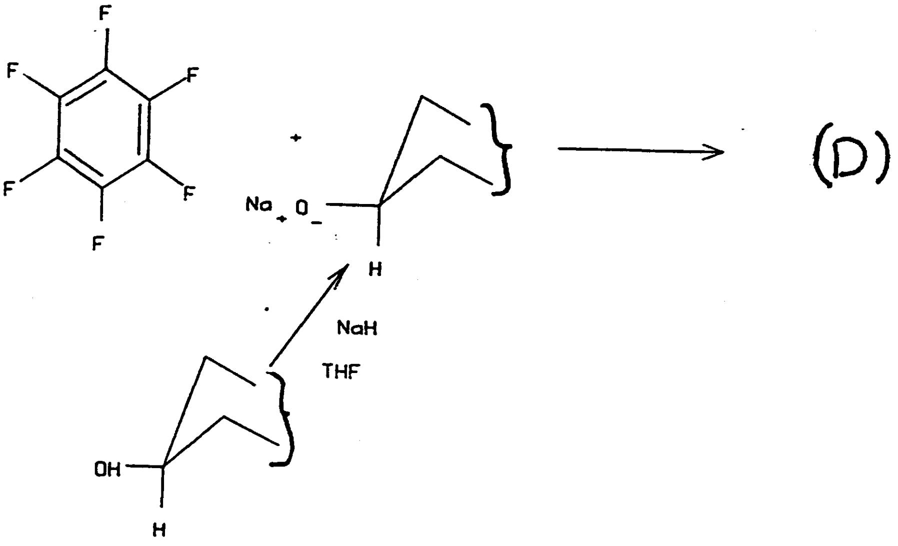
(D)

(108), R =

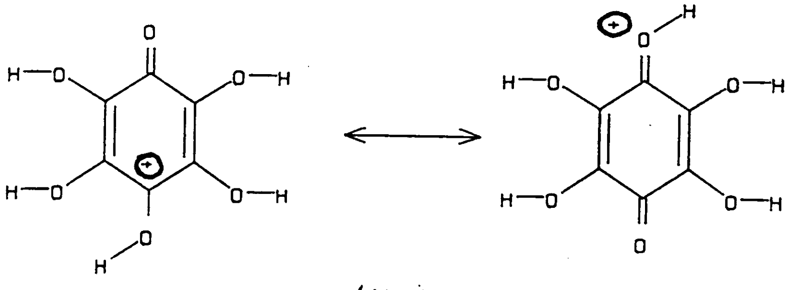


(109), R =





The compounds (108) hexakis(cyclohexyloxy)benzene and hexakis(cyclododecyloxy)benzene (109) were both produced by reacting the sodium salts of alcohols (obtained by reaction of the appropriate alcohol with 99% sodium hydride in freshly distilled tetrahydrofuran, -in both cases the salt did not easily form) with hexaflurobenzene in a nucleophile-activating solvent. Both (108) and (109) were obtained as white powders in low yields 15.3 and 3.6% respectively . Compound (108) was further purified by recrystallisation from chloroform giving excellent high purity crystals which degraded above 320°C without melting. An accurate mass spectral analysis gave an ion at M^+ = 666.439 identified as having the expected formula $C_{42}H_{66}O_6$, which is the formula of (108). A large peak at M^+ = 83 identified as being the C_6H_{11} cyclohexyl radical. Further evidence was the presence of small peaks at 584 from parent - 82,(cyclohexene), 502, parent -2 * 82 and peaks at positions corresponding to the loss of successive cyclohexenes up to loss of six. The most abundant peak was found at 173 identified as the 1-oxy, 2,3,4,5,6 pentahydroxy benzene cation (110) shown below.

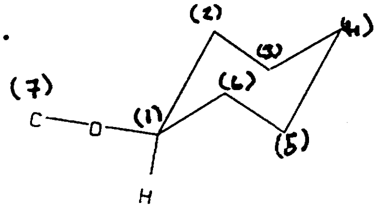


(110)

Comparison with the mass spectrum of model compound cyclohexyloxybenzene (111)[70], indicated that an expected major peak would be the hexahydroxybenzene, this being observed at 45% abundance as the major breakdown product from (110) ion. No peak at 83 is observed in the mass spectrum of (111) leading to the conclusion that its appearance in the spectrum of (108) results from its production from the plentiful supply of cyclohexene from the above fragmentation of (108).

Consideration of the ^{1}H and ^{13}C NMR spectra obtained for (108) also confirmed the proposed structure. The proton spectrum revealed a shift in the position of the methine proton from δ3.6 cyclohexanol[71] to δ4.0 for (108). A full assignment of the ^{13}C spectrum was achieved by comparison with published assignments for cyclohexanol (112)and methoxycyclohexane (113)[72]. Table 20 shows the peaks for spectra from reference [76] and the assignment for compound (108)

Table 20. Assignment of the ^{13}C NMR spectrum of (108). Numbering scheme as indicated below.



Carbon number	Cyclohexanol	Methoxycyclohexane	(108)
1	70.0	78.6	80.107
2,6	36.0	32.3	32.707
3,5	25.0	24.3	24.176
4	26.4	26.7	25.842
7			141.685

A number of inclusion tests were carried out on compound (108) from a variety of solvents, a list is given in Table 21

Table 21. Solvent used in inclusion tests on (108)

Test Solvent#

Dioxane

methanol

ethanol

ethanol\water*

acetonitrile

chloroform

* All tests carried out in heated sealed tubes.

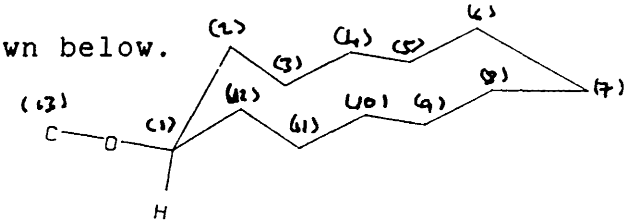
The mixture was used as it was considered that water might be a good guest; despite many efforts, even in a sealed tube, (108) resisted attempts to dissolve it in water alone.

The crystals resulting from the recrystallisation experiments were assessed by proton NMR for evidence of guest presence. However no inclusion of any guest was observed. Although X-ray quality crystals have been obtained , no X-ray diffraction analysis has yet been carried out on compound (108).

The analysis of compound (109) again indicated that the hexa-substituted product had formed, however (109) unlike the cyclohexyl compound (108)melted in the range 218 - 221°C before degradation. Mass spectral analysis gave peaks at M^{+} = 1171.18, the expected parent mass, identified as $C_{78}H_{138}O_6$. Some peaks corresponding to partial "leg" loss were observed at 1005.07, loss of 166 (cyclododecene); 838.09, loss of 332. The maximum abundance was found at 174.10; identified as hexahydroxybenzene radical cation. Further peaks were observed from cyclododecene radical $C_{12}H_{22}^{+}$ and its singly protonated partner $C_{12}H_{23}^{+}$ at 166.26

and 167.24, respectively. From the above it was concluded that (109) breaks down analogously to (108). Consideration of NMR data ^{1}H and ^{13}C supported the mass spectral evidence. In the proton spectrum the methine peak was centred at δ4.38 shifted from that of cyclododecanol[71] found at δ3.64. Assignment of the carbon spectrum was achieved by comparison with published assignment for cyclododecanol (114) and methoxycyclododecane (115)[73]. Comparisons are shown in Table 22.

Table 22. Assignment of the ^{13}C n.m.r spectrum of (109). Numbering as in the structure shown below.



Carbon number	Cyclododecanol	Methoxycyclo-dodecane	(109)
1	68.11	78.76	79.006
2,12	32.29	28.64	30.18
3,11	20.94	20.90	21.74
4,10	24.27	25.43	24.56
5,9	23.38	23.54*	23.74#
6,8	23.30	23.54*	23.74#
7	23.85	25.00	23.89
13	-	-	141.79

* observed as single peak. This was very important to the assignment of (109) since only seven peaks were observed from an expected eight. # Assignment made the basis of peak intensity.

Inclusion tests were carried out on (109) from the following solvents shown in Table 23.

Table 23. Solvent employed in inclusion tests on (109).

Test Solvent#
Dioxane
methanol
mesitylene
benzene
cyclooctatriene
chloroform

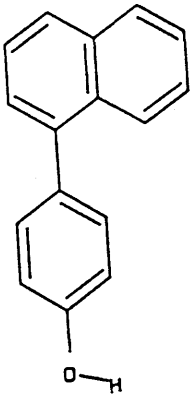
* All tests carried out in heated sealed tubes.

Again no inclusion behaviour was observed. The resulting crystals were assessed by 90MHz. NMR analysis where appropriate along with thermogravimetric analysis were no suitable proton signal existed. Here again excellent quality crystals were obtained but lack of time prevented X-ray diffraction analysis from being carried out. It would have been of interest to determine the number and type of comformations adopted by the substituted cyclododecane ring.

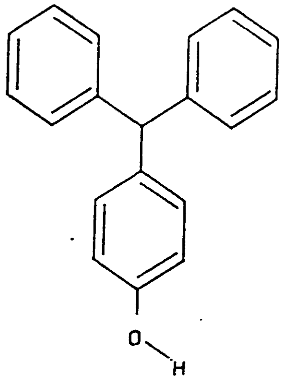
Whilst this short study did not lead to the discovery of new host species it extended the potential hexa-host range to include cycloalkoxy "legs", no compounds of this kind having been synthesized by any route previously. One further observation made for both (108) and (109) is that the crystals obtained from many of the inclusion tests clouded if left exposed to air. This is normally found when a guest is lost: since no evidence for inclusion was found it lead to the intriguing possibility that (108) and (109) were absorbing something from the air. Dale etal[74] observed the absorption of water in crystals of (116).

CHAPTER 10.

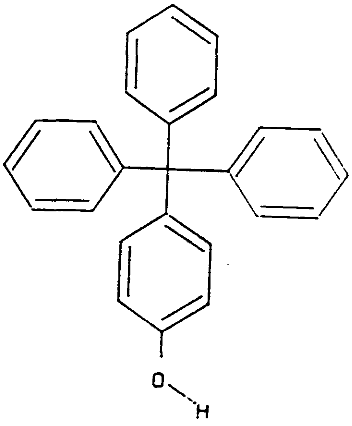
Consideration of the features present in the structure of Dianin's compound led to the selection of the following compounds (117) to (121) as a starting point in an atttempt to extend the "Hexa-host" principle by utilising more structured "leg" species. Efforts to synthesize these materials are described in this chapter along with some other synthetic studies aimed at creating new trigonal host compounds.



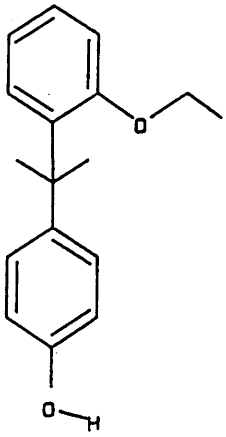
(117)



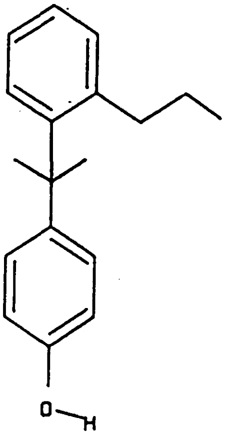
(118)



(119)



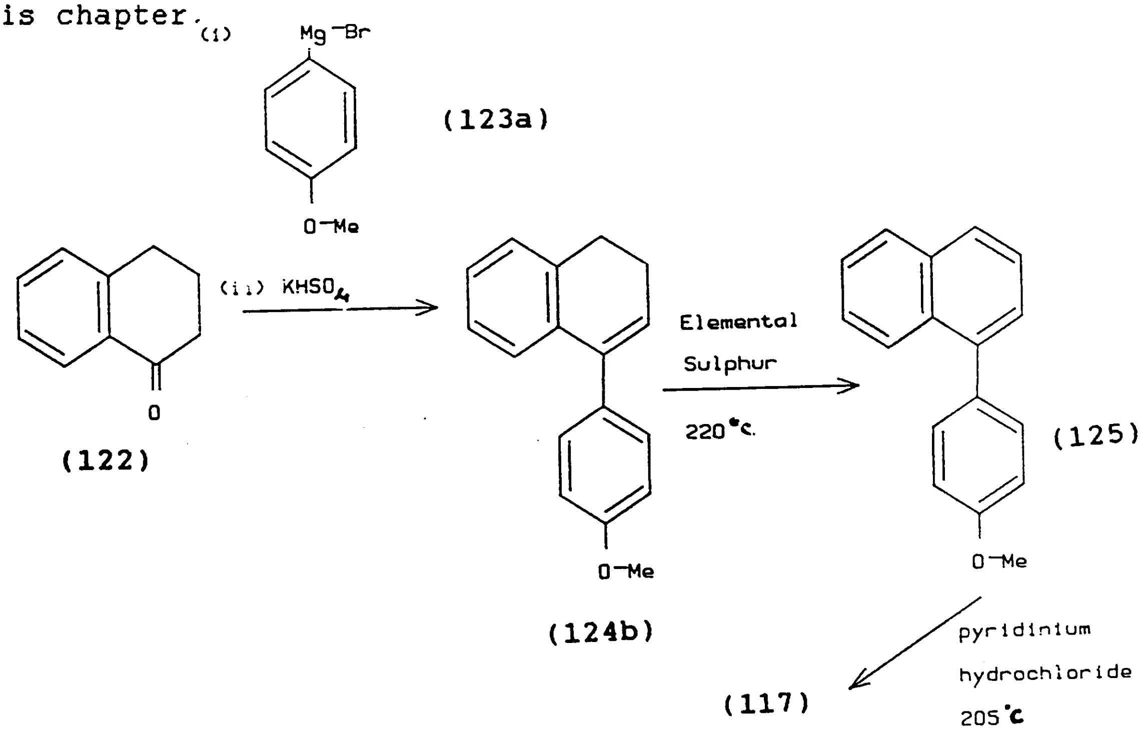
(120)



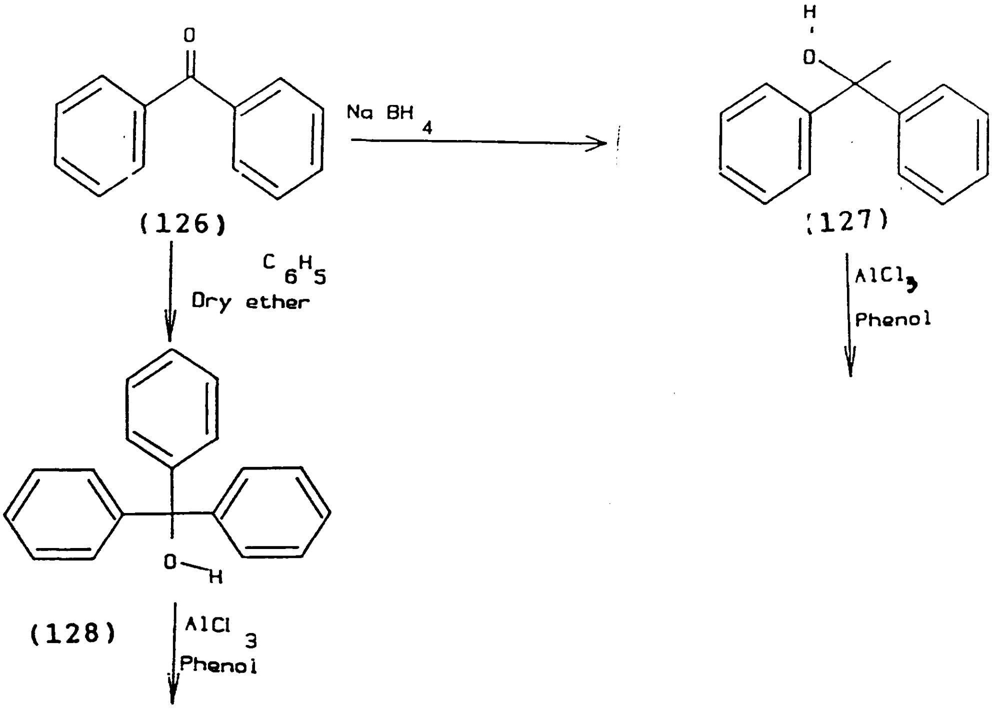
(121)

Compounds (117) - (120) are known in the litrature[75, 76] and their synthsis was achieved by the following methods. For p-(1-napthyl)phenol (117), redistilled tetralone (122) was added to the aryl Grignard

(123b)p-(methoxy)phenylmagnesium bromide, prepared by treatment of p-(bromo)anisole (123a), in sodium-dried diethylether, with magnesium turnings using crystalline iodine or methyl iodide as initiators. The crude product 1-(p-methoxyphenyl)-3,4- dihydronaphthalene (124b), obtained by distillation of the intermediate carbinol 1-hydroxy,-1-(p-methoxyphenyl) tetrahydronaphthalene (124a), was treated with elemental sulphur at 225° C yielding 1-(p-methoxyphenyl)naphthalene (125). This after recrystallisation from glacial acetic acid was heated to 205° C with an excess of pyridinium hydrochloride; work-up gave a brown oil which on recrystallisation from cyclohexane gave (117). Details of the hexa-substituted species generated from (117) and hexafluorobenzene are given later in this chapter.

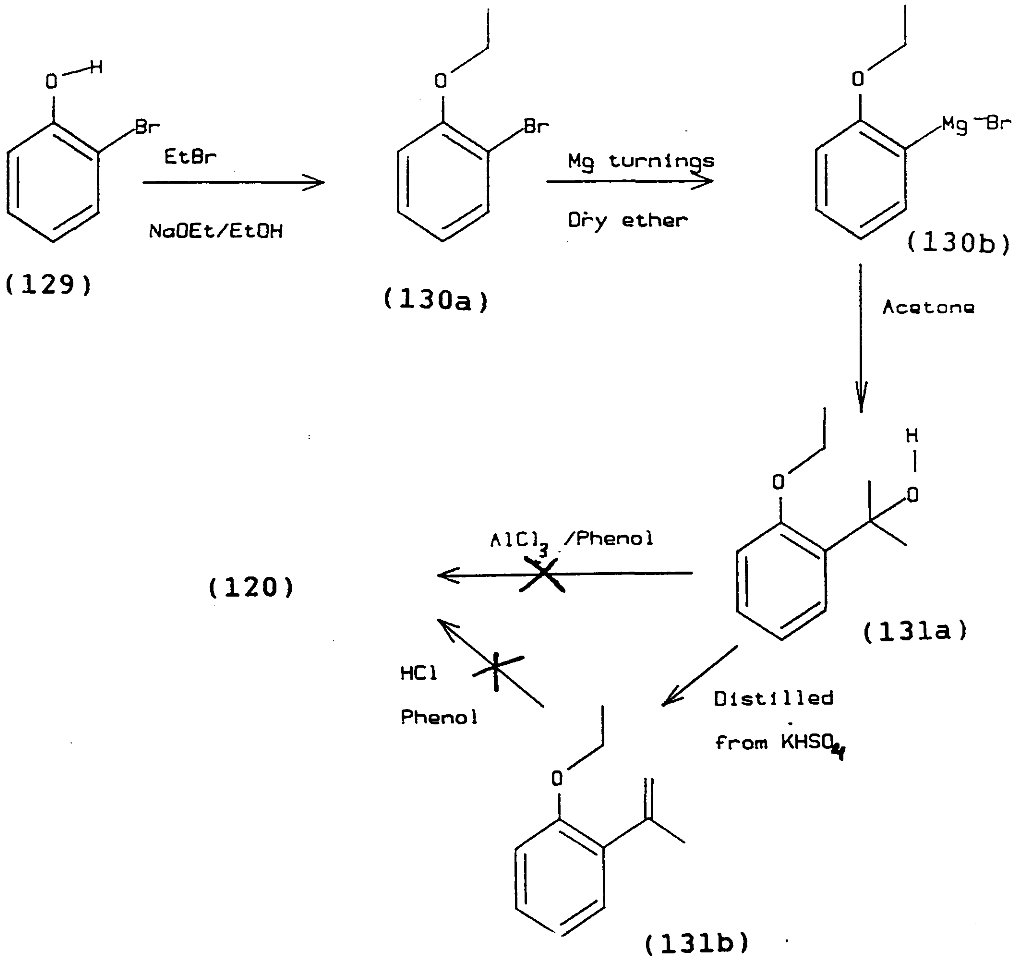


Compound (118) p-(diphenylmethyl)phenol and (119) p-(trityl)phenol were prepared from benzophenone (126). Compound (118) by treatment with sodium borohydride gave diphenylmethanol (127) which was coupled to phenol with aluminium trichloride by the method described by Drake and Walsh[75]. (119) was prepared by reacting (126) with phenylmagnesium bromide to give triphenylmethanol (128), again coupled to phenol using aluminium trichloride.

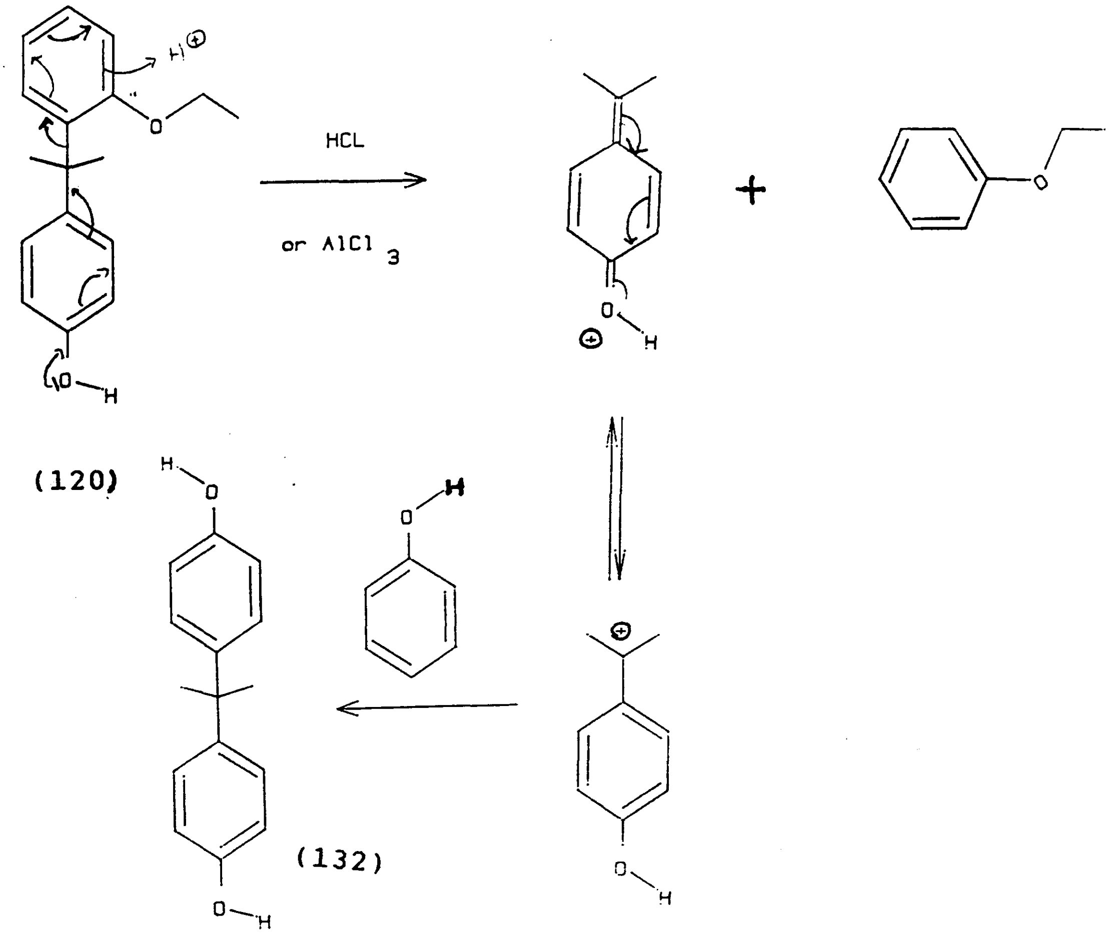


Reaction of (119) with hexaflurobenzene yielded, on two occasions, only starting materials. Similar results were obtained for compound (118). A possible explanation may lie in these materials' being too sterically hindered to give full substitution of the six fluorines in the hexaflurobenzene but it would still be expected that partially substituted species would be observed. As mixtures of this kind have in the past proved to be difficult to analyse and as NMR analysis of the materials obtained on work-up indicated mostly the presence of the starting phenols, further attempts to make hexa-host from these compounds were abandoned. Reaction between (118) and (119) and cyanuric chloride were carried out. However since this process involved the production of hydrogen chloride, the acid lability of the para substituent groups prevented the production of the corresponding triazines. Lack of time meant no solution to this problem could be found. It is felt, nonetheless that the bulk and symmetry properties of these compounds could still make them useful stepping stones to new host species.

Compounds p-(2(2-ethoxyphenyl)propyl)phenol (120) and p-(2(2-propylphenyl)propyl)lphenol (121) could not be found in the literature. The following routes were proposed for their preparation.

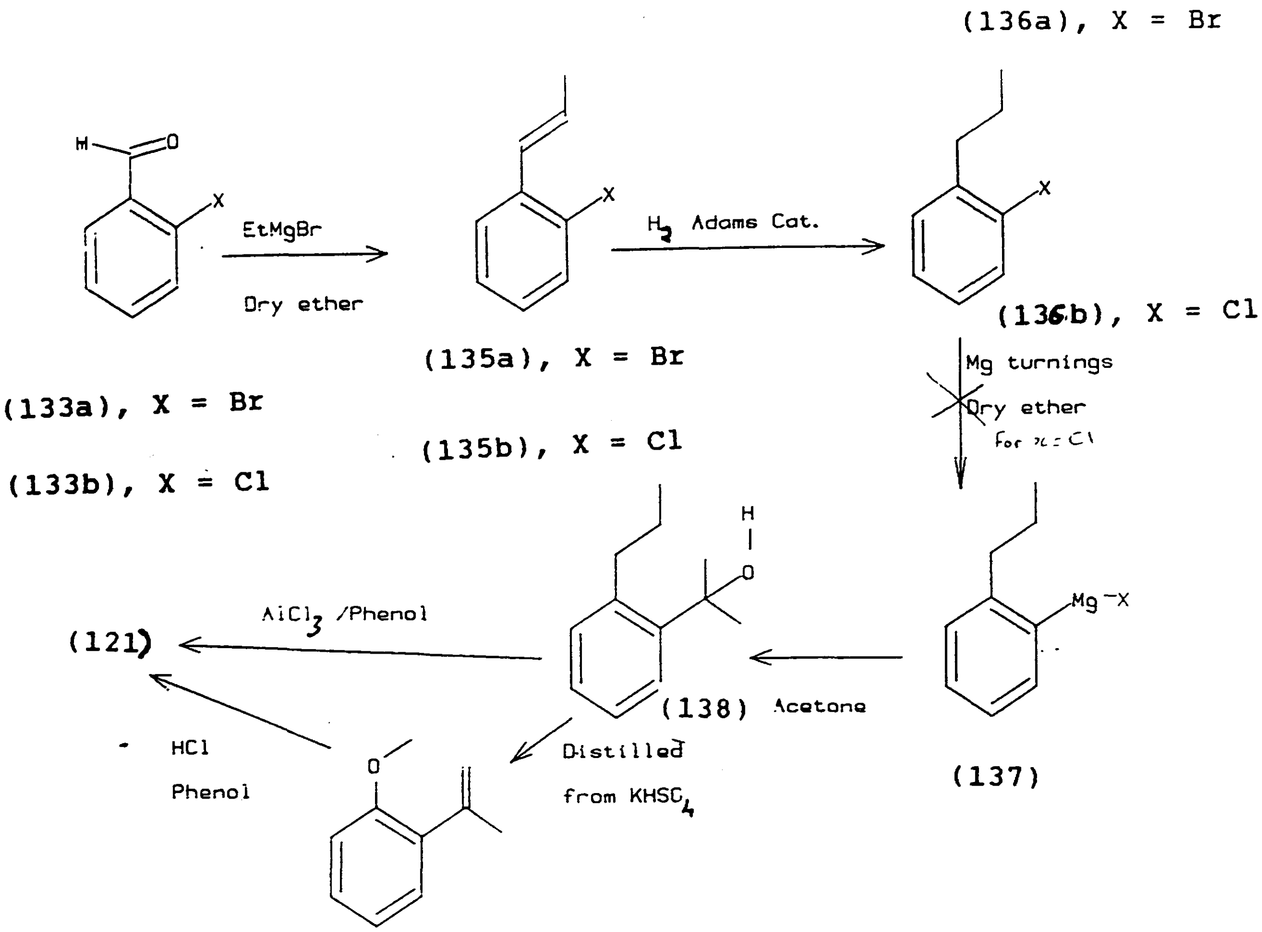


The first route involved reacting o-bromophenol (129) with ethylbromide in a concentrated ethanolic solution of sodium hydroxide[77]. Removal of the ethanol by rotary evaporation and distillation under reduced pressure gave 1-bromo-2-ethoxybenzene (130a) in good yield. The aryl Grignard (130b) was prepared from (130a), in sodium-dried diethylether, and magnesium turnings. This was reacted with acetone to give the carbinol 2-(2-ethoxyphenyl)propan-2-ol (131a). Solvent removal and distillation under reduced pressure gave a mixture of (131a) and its dehydration product 2-(2-ethoxyphenyl)propene (131b) as the distillation process appeared to induce some dehydration. Pure (131b) was obtained by heating (131a) with potassium hydrogen sulphate before a further distillation. Production of (120) from both (131a) and (131b) was attempted. Firstly (131a) was reacted with phenol in the presence of gaseous hydrogen chloride, the only crystalline product isolated from this reaction was identified, by NMR as 2,2-di(*p*-hydroxyphenyl)propane (Bisphenol A) (132). A second reaction involving the treatment of (131a) with aluminium trichloride in the presence of excess phenol again gave only (132) as an identifiable product. A mechanistic explanation for these results is shown below.



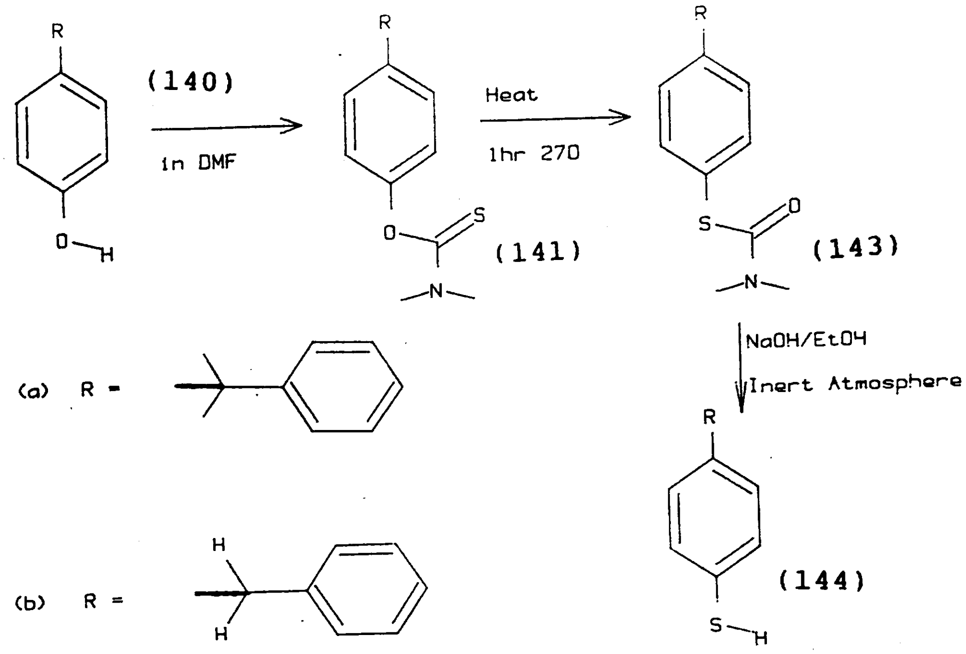
A number of small scale reactions were carried out involving different Lewis acid conditions. However since none of these indicated that (120) had been formed reluctantly this route was abandoned.

In the second route, which has the same final step as that for compound (120), no problems were anticipated as the absence of the <u>ortho</u> oxygen made a similar rearrangement unlikely.



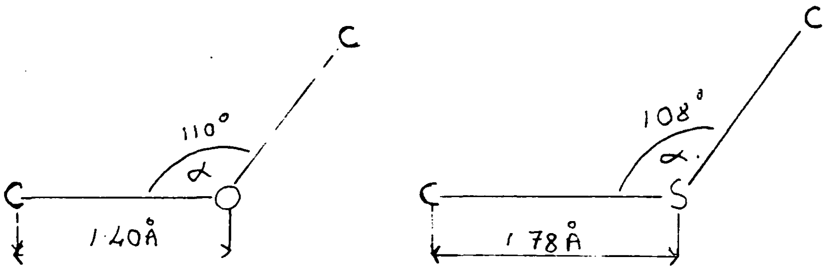
The method involved the synthesis of 1-halo-2-propylbenzenes from a 2-halobenzaldehyde as reported by Marvel and Botterton[78]. Initially 2-bromobenzaldehyde (133a) was reacted with ethylmagnesium bromide and the product distilled from potassium hydrogen sulphate giving the styrene 1-bromo-2-(prop-1-enyl)benzene (135a), via 1-(2-bromophenyl)propan-1-ol (134a), this was hydrogenated at 500psi of hydrogen gas in the presence of an Adam's catalyst. Work up led to a brown oil, purification by fractionation on a kugelrohr proved difficult and a very poor yield of 1-bromo-2-(1-propylbenzene (136a) was obtained. It was therefore decided to develop the method using the cheaper and more readily available 1-chlorobenzaldehyde (133b). A repeat of the steps described above led to 1-chloro-2-propylbenzene (136b) in good yield. In light of this and further difficulties encountered in obtaining necessary quantities of (136a) it was decided to attempt using literature methods[79,80] to produce the carbinol 2-(2-(1-propyl)phenyl)propan-2-ol (138) through the intermediate Grignard 2-(1-propyl)phenylmagnesium chloride (137). Firstly Rieke's magnesium[79] (a colloidal suspension of the metal) was prepared from potassium metal and anhydrous magnesium chloride in the presence of potassium chloride. The addition of (137) and quenching with excess acetone on work up yielded, on a number of occasions, only starting material (136b). A second attempt to generate (137) was via the formation of magnesium anthracene[80] from powdered magnesium and blue anthracene. When the orange colour of this substance was observed (136b) was again added and the product quenched with acetone; work up revealed only starting material. It is likely that steric hindrance prevented Grignard formation. In the case of the first route, above, the presence of the <u>ortho</u> oxygen may have aided in forming the Grignard at the analogous step. The problems, described above, combined with lack of time and success in other areas led to abandonment of these synthetic studies.

Another proposed route to new "leg" groups for hexa-host synthesis was the conversion of phenols to thiophenols by the method of Newman and Karnes[81].



Newman Karnes reaction

Two phenols were taken through this conversion: *p*-cumyl phenol (97) and *p*-benzylphenol (95). They were chosen as both were potenially capabable of producing trigonal crystalline materials when utilised in making hexa-substituted benzenes. A further consideration in the choice of target thiophenols was that whilst compound hexakis(*p*-cumylphenoxy)benzene (92), described earlier, gave a trigonal crystalline product, the cavity was too small to accommodate any guest. It was felt that change of the linkage atom from oxygen to sulphur might allow the new molecule to retain the ability to adopt a trigonal molecular orientation, whilst causing an increase in cavity size facilitating inclusion. Compound hexakis(*p*-benzylphenoxy)benzene (90) has the ability to form clathrates and it was felt that guest selectivity could be altered by modifying the cavity shape. One possible feature capable of inducing changes in cavity geometry is the change in distance between the central benzene ring and the inner phenyl group of the "leg" moiety. Changes in average bond length and angle associated with conversion from oxygen to sulphur are:

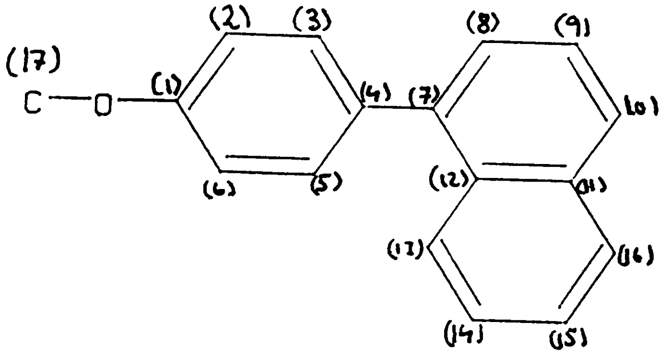


The Newman,-Karnes reaction is carried out by reacting the phenol with N,N-dimethylthiocarbamyl chloride (140) in DMF, and the resulting O-aryl thiocarbamate after purification is rearranged to the S-aryl thiocarbamate by heating sealed tube in a Wood's metal bath. The thiophenol is then generated by cleaving the S-aryl thiocarbamide in an methanolic solution of sodium hydroxide, under an inert atmosphere. The first two steps the conversion process were easily carried out for both (97) and (95), giving the compounds O-4-cumylphenyl-N,N- dimethylthiocarbamate(141a) and O-4-benzylphenyl-N,N- dimethylthiocarbamate(141b); and S-4-cumylphenyl-N,N-dimethyl- thiocarbamate; (142a) and S-4-benzylphenyl-N,N-dimetylthiocarbamate (142b). Distinguishing between the S and O-aryl thiocarbamates was achieved chiefly by ^{1}H NMR; on conversion, in both cases, two distinct peaks for the N-methyl groups of the O-aryl species collapse to give a single peak in S-aryl compound; for (141a) to (142a) δ 3.43 and 3.30 to δ 3.24 and for

(141b) to (142b) δ 3.42 and 3.29 to δ 3.22. A reduction in the melting point on going from O-aryl to S-aryl isomer is also observed. The final step to the thiophenol proved difficult to achieve in the published yields (100%). Spectroscopic analysis of these materials was largely confined to ^1H NMR measurements. A comparison of their spectra with those of the corresponding phenols showed shifts in the position of AA'BB' patterns in the aromatic region associated with the change from hydroxyl to thiol; in both cases a distinct "quartet" has collapsed to become an indistinct part of the overall aromatic region. Both p-cumylthiophenol (143a) and p-benzylthiophenol (143b) were converted to their thiophenolate salts by reaction with sodium hydride. These salts were reacted with hexaflurobenzene, in DMEU under an inert atmosphere, at ambient temperature for three days. In the case of (143a), despite exhaustive attempts no hexameric product could be identified. However (143b) gave after a long purification, by preparative T.L.C., gave a yellow powder with spectral data that was consistent with the hexameric compound hexakis(p-benzylthiophenoxy)benzene (144). At first since the ^{13}C spectrum contained only nine signals it was thought that the product was the disulphide obtained by oxidation of the thiol; however, D.E.P.T. analysis of the ^{13}C spectrum revealed the presence of four quaterniary signals at 147.77, 140.63, 138.98 and 135.16 which could only exist in the hexa-substituted product. There would have been three quaternary signals for the disulphide.

Inclusion tests showed that (144) included 1,4-dioxane and carbon tetrachloride. The host-guest ratio for dioxane was assessed by both ^{1}H NMR and themogravimetric analysis to be approximately 1:1. Multiple integration of a 90 MHz ^{1}H NMR. spectrum gave experimental ratios aromatic : benzyl methylene : dioxane methylene of 7.17:1.1:1, against theoretical values for a 1:1 clathrate of 6.75:1.5:1 The thermalgravimetrograph shown in Figure 63 shows a two- stage loss of guest; 2.5% is lost between 40°C and 94°C a second loss of 4% occurrs between 104°C and 142°C the total of 6.5% matches perfectly the theoretical % weight loss for a 1:1 adduct. A second thermalgravimetrograph for the (144).CCL_4. inclusion compound showed a 5% weight loss between 138°C and 192°C and this compares well with the theoretical value of 5.73% for a 2:1 host-to-guest ratio. A crystal of the dioxane clathrate was selected for X-ray analysis, however this had degraded, along with the rest of the sample, before data collection. This may be due in part to residual silica from the long purification which promotes oxidation of the product.

Evidence for the formation of a final hexa-substituted benzene compound hexakis(p-(1-napthylphenoxy))benzene (145) will now be presented. Compound (145) was produced, in good yield, from the sodium salt of (117) and hexaflurobenzene. The material obtained was a high melting (>320°C) off-white powder which was extremely insoluble in all solvents tried. Crystallisations from a number of solvents were achieved by experiments involving heating 10-15mg of (145) in 20ml of solvent to temperature in excess of 300°C in, sealed tube, behind safety screens (Caution). Despite repeated attempts no satisfactory microanalytical data could be obtained for compound (145). A mass spectral analysis carried out by the S.E.R.C. Mass Spectral Service in Swansea gave no peaks easily attributable to (145) it is likely that decomposition of (145) occurs before volatilisation. Identification of (145) was based exclusively on interpretation of NMR data: ^{1}H, and more importantly ^{13}C and ^{19}F NMR analysis, showed that no fluorine was present, ruling out the possibility of partial substitution products. Comparison of the proton spectra of (117) and (145) showed that one half of an AA' BB' pattern found at δ 6.88 and 6.98 in (117) (the other half being buried in the bulk of the remaining aromatic peaks between δ 7 and 8) had shifted to δ 7.02 and 7.09 in (145); any other differences were not obvious. The ^{13}C spectrum had 15 peaks. Some tentative assignments of these are, in groups, [for numbering system see below]: C(1) at 156.80ppm, C(2) and C(6) at 115.96ppm down field shift <u>ortho</u> to an ether linkage , C(3) and C(5) at 130.93ppm <u>meta</u> to an ether linkage this peak is also larger than the others in the region 125-132 this could be expected for a signal from the two symmetry related carbons, C(8),C(9) and C(10) assigned to any of the three peaks found at 127.00,127.52 and 128.21ppm, C(13),C(14),C(15) and C(16) to any of the set of peaks at 125.30,125.68,125.88 and 126.04ppm C(17) can be selected from either of the peaks at 140.42 and 139.53 by comparison with other oxygen link hexa hosts.



Numbering system for the ^{13}C n.m.r. assignment of compound (145).

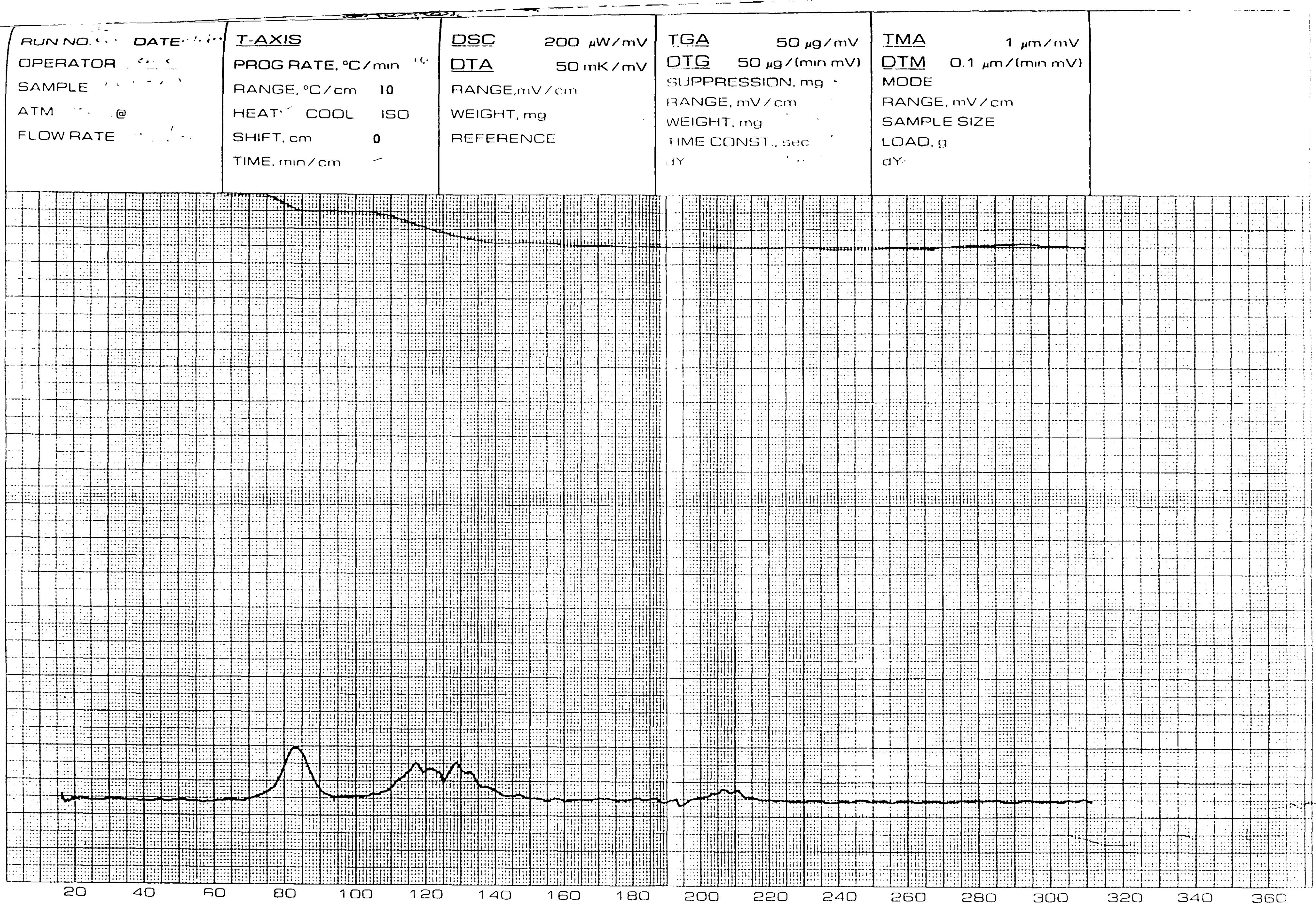


Figure 63. The thermalgravimetrograph of the 1,4-dioxane clathrate of (144).

EXPERIMENTAL.

As many of the compounds produced for the work were synthesized by variations of the same reaction route a generalised procedure is given below. Any significant deviations from these methods are explained in the compound synthesis descriptions.

GENERAL METHOD ONE (Formation of the Sodium phenolate salts)

A weighed amount of the phenol was dissolved, under an inert atmosphere, in freshly distiled THF (Tetrahydrofuran). This solution was syringed slowly into a three-necked flask fitted with a condenser, stirrer and again an inert atmosphere and containing a slight excess of sodium hydride* covered with freshly distiled THF After complete addition of the solution the reaction mixture was refluxed for 1-1.5 hours. The condenser and gas taps were replaced with rubber seals and the solvent was removed by rotary evaporation.(The vacuum being controlled with an inert gas cylinder.) The salt was then pumped to constant weight.

* Normally 60% oil dispersed sodium hydride was used. This was washed a number of times with sodium dried pentane, being syringed over the sodium hydride then removed after stirring and settling.

GENERAL METHOD TWO (Formation of hexakis(phenoxy) benzenes)

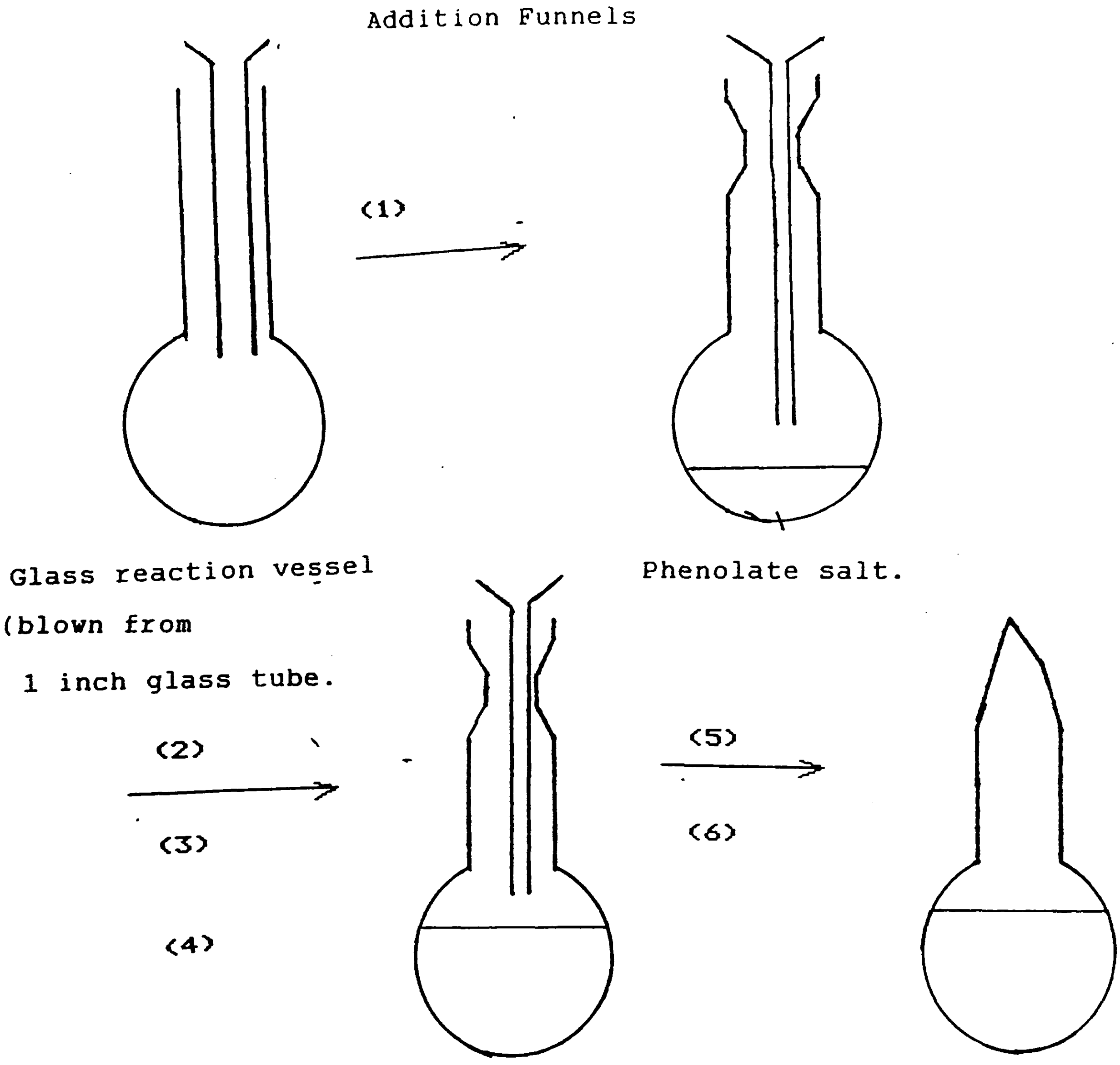
A weighed mass of the sodium phenolate was added to specially designed glass vessel, shown in Figure 66, using the equipment indicated. This was sealed with a rubber seal and evacuated. An inert atmosphere was introduced and the flask was constricted as shown; this was again sealed and evacuated. Following the introduction of an inert atmosphere dry DMEU (1,3-dimethyl-2-imidazolidinone) was syringed into the reaction vessel. The system was then pumped over night under vacuum to remove dissolved gas. The inert gas was then re-introduced and a second small volume of DMEU was added, as indicted in Figure 66, containing weighed amount of hexaflurobenzene. The molar ratio of phenolate to hexaflurobenzene was not less than 12:1. The reaction vessel was then sealed as shown in Figure 66 by a glass blower. The reaction vessel was then placed in an oven at 90° C for a minimum of four weeks.

Hexakis(p-benzylphenoxy)benzene. (90)

7.06g (0.034 mols) of sodium p-benzylphenolate, produced by General Method One from 7.00g (0.034 mols) of p-benzylphenol and 1.54g (0.038 mols) of 60% oil dispersed sodium hydride, was reacted with 0.53g (0.0028 mols) of hexaflurobenzene by General Method Two. The reaction mixture after four months at 90° C was added to ice water (500ml). The dispersion produced was extracted with toluene (two 150ml volumes) The combined extracts were washed with water, at least twelve 300ml volumes, to remove DMUE, and dried over sodium sulphate. Removal of the toluene by rotary evaporation gave brown semi-crystalline material. This on crystallisation from acetonitrile gave 2.53g of white crystals m.p. 160-164° C, yield = 75.07%.

Microanalysis: (from acetonitrile) Found: C, 85.99; H, 6.36; N, 0.52: Theory: $C_{84}H_{66}O_6$ requires (unsolvated) C, 86.13; H, 5.68 :

(from CCL_4:CH_3CN 1:1) Found C, 76.92 :H, 5.00; Cl, 10.76:



(1) Addition of phenolate salt using the long addition funnel shown.

(2) Constriction of the reaction tube.

(3) Addition of reaction solvent using addition funnel shown.

(4) De-gassing of the solvent.

(5) Addition of C_6F_6.

(6) Sealing of reaction tube.

The addition funnels were used to avoid coating the inside of the reaction vessel with reactants.

Figure 64. The equipment designed for the efficient production of hexakis(phenoxy)benzenes eg. hexakis(p-benzylphenoxy)benzene (90).

Theory $C_{84}H_{66}O_6.CCl_4$ requires for (1:1 clathrate) C, 77.03; H, 4.99; Cl, 10.77

Mass Spectral analysis *m/e* 1170 M^+ other peaks at 1171, 1080, 1004, 986(100%), 987, 896, 824, 809, 807, 724, 660, 645, 584, 569, 510, 497, 437.

^{1}H NMR $\delta(CDCl_3)$ (200MHz) Aromatic: 7.30-7.05 (30 H m), 6.94, 6.88, 6.59, 6.55 AA'BB' system centred at 6.675 (24 H), Non Aromatics: 3.84 (12 H s).

^{13}C NMR, $\delta_c(CDCl_3)$[measured with proton noise-decoupling unless otherwise stated] 155.67, 141.24, 140.12, 134.97, 129.50, 128.81, 128.36, 125.98, 115.65, 40.97.

Hexakis(p-phenoxyphenoxy)benzene. (91)

9.61g (0.046 mols) of sodium p-phenoxyphenolate, produced by General Method One from 9.30g (0.05 mols) of *p*-phenoxyphenol and 2.03g (0.05 mols) of 60% oil dispersed sodium hydride, was reacted with 0.72g (0.0039 mols) of hexaflurobenzene by General Method Two. The salt in this case was initially produced as a brown oil and only prolonged pumping under vacuum produced a material which could be used in General Method Two. The reaction mixture after six weeks at 90° C was allowed to cool to ambient temperature. This led to crystallisation of large block-like crystals from the DMEU solution. The remaining reaction mixture was treated as for compound (90). The material from this process and the block-like crystals obtained from the DMEU were crystalised from acetonitrile giving 4.15g of white crystals, m.p. 179-181° C. yield = 92.0%.

Microanalysis: (from acetonitrile) Found: C, 85.80, 85.99; H, 6.34, 6.36; N, 0.52, 0.57: Theory: (unsolvated) C, 86.13; H, 5.68 :

(from CCL_4:CH_3CN 1:1) Found C, 76.92, 77.28; H, 5.15, 5.00; Cl, 10.76: Theory (1:1 clathrate) C, 77.03; H, 4.99; Cl, 10.77

Mass Spectral analysis *m/e* 1170 M^+ other peaks at 1171, 1080, 1004, 986(100%), 987, 896, 824, 809, 807, 724, 660, 645, 584, 569, 510, 497, 437.

^{1}H NMR δ($CDCl_3$) (200MHz) Aromatic: 7.30-7.05 (30 H m), 6.94, 6.88, 6.59, 6.55 AA'BB' system centred at 6.675 (24 H), Non Aromatics: 3.84 (12 H s).

^{13}C NMR, δ_c($CDCl_3$) 155.67, 141.24, 140.12, 134.97, 129.50, 128.81, 128.36, 125.98, 115.65, 40.97.

Hexakis(p-cumylphenoxy)benzene. (92)

7.01g (0.03 mols) of sodium p-cumylphenolate, produced by General Method One from 7.52g (0.035 mols) of *p*-cumylphenol and 1.42g (0.035 mols) of 60% oil-dispersed sodium hydride, was reacted with 0.46g (0.0025 mols) of hexaflurobenzene by General Method Two. The product was worked up as described for compound (90), except, prior to crystallisation from pyridine the product was triturated with cold acetonitrile to remove any remaining parent phenol. Crystallisation gave 2.84g of white crystals, m.p. = 211-212° C. yield = 84.83.

Microanalysis: (from pyridine) Found: C, 86.06; H, 6.69; : Theory: $C_{96}H_{90}O_6$ requires (unsolvated) C, 86.10; H, 6.73 :

Mass Spectral analysis *m/e* 1338 M^+ other peaks at 1323, 1308, 1261, 1245, 1220, 1205, 1189, 1110, 1095, 1048, 1032, 1008, 993, 921.

^1H NMR $\delta(CDCl_3)$ (200MHz) Aromatic: 7.35-7.10 (30 H m), 7.03, 6.99, 6.63, 6.58 AA'BB' system centred at 6.81 (24 H), Non Aromatics: 1.64 (30 H s).

^{13}C NMR, $\delta_c(CDCl_3)$ 155.06, 150.69, 144.61, 139.73, 127.89, 127.35, 126.69, 125.52, 115.16, 42.33, 30.83.

Hexakis(p-phenylphenoxy)benzene. (93)

10.91g (0.057 mols) of sodium p-phenylphenolate, produced by General Method One from 10.04g (0.059 mols) of p-phenylphenol and 2.39g (0.059 mols) of 60% oil-dispersed sodium hydride, was reacted with 0.88g (0.0048 mols) of hexaflurobenzene by General Method Two. The product was worked up as described for compound (90) except prior to crystallisation from chloroform, the product was triturated with hot diethyl ether. Crystallisation gave 4.12g of white crystals, m.p. = 247-249° C. yield = 79.0.

Microanalysis: (from pyridine) Found: C, 86.06; H, 5.00; : Theory: $C_{78}H_{54}O_6$ (unsolvated) C, 86.19; H, 4.97 :

Mass Spectral analysis m/e 1086 M^+ other peaks at 936, 919, 784, 766, 764, 749.

^1H NMR $\delta(CDCl_3)$ (90MHz) Aromatic: 7.60-7.21 (42 H m), , 6.91, 6.83, possibly one half of an AA'BB' system

^{13}C NMR, $\delta_c(CDCl_3)$ (100MHz) 169.6, 142.8, 138.4, 130.8, 129.2, 118.2

2,4,6-Tris(p-cumylphenoxy)-1,3,5-triazine (99)

10.12g (0.047 mols) of p-cumylphenol was heated with 2.21g (0.012 mols) (a four-fold molar excess of the phenol) of cynanuric chloride at 185-220° C for 5 hours under reflux with an air condenser. The crude reaction product was triturated with boiling methanol, (twice 25ml), for 5 minutes. This left 8.17g of product as a white crystalline powder. Yield = 97.00%, M.p. = 175-180°C.

Microanalysis:Found C, 80.92; H, 6.44; N, 5.93 Theory for $C_{48}H_{45}N_3O_3$, requires C,80.95; H, 6.37; N, 5.90.

Mass Spectrum: <u>m</u>\<u>e</u> 711 M^+ other peaks at 696, 578, 500(100%), 382, 197, 166, 103, 78.

^1H NMR $\delta(CDCl_3)$ 7.32-7.01 (27 H, m, including an AA'BB' system peaks at 7.22, 7.18, 7.07, 7.03, centred at 7.125) non-aromatic 1.66 (18 H, s).

^{13}C NMR, $\delta_c(CDCl_3)$ 175.52, 150.15, 149.35, 148.36, 128.06, 127.83, 126.75, 125.76, 120.64, 42.69, 30.84.

<u>2,4,6-Tris(p-benzylphenoxy)-1,3,5-triazine</u> <u>(101)</u>

9.52g (0.052 mols) of <u>p</u>-benzylphenol was heated under reflux with 2.21g (0.013 mols) of cynanuric chloride (a four-fold excess of the phenol) at 185-220° C for 5 hours employing an air condenser. The crude reaction product was triturated with boiling methanol, (twice 25ml), for 5 minutes. This left 7.23g of the product as a white crystalline powder. Yield = 89.2%, m.p. = 175-180°C.

Microanalysis:Found C, 73.82; H, 5.55; N, 6.92: Theory for $C_{39}H_{33}N_3O_3$, requires C, 74.64; H, 5.26; N, 66.70.

Mass Spectrum: <u>m</u>\<u>e</u> 627 M^+ other peaks at 444, 418, 211, 165.5, 152, 91(100%), 71.

^1H NMR $\delta(CDCl_3)$ 7.35-7.01 (27 H, m, including an AA'BB' system peaks at 7.16, 7.12, 7.06, 7.02, centred at 7.09) non-aromatic 3.95 (18 H s).

^{13}C NMR, $\delta_c(CDCl_3)$ 173.58, 149.79, 140.53, 138.82, 129.75, 128.92, 128.49, 126.20, 121.22, 41.21.

2,4,6-Tris(*p*-phenoxyphenoxy)-1,3,5-triazine (102)

8.78g (0.047 mols) of *p*-phenoxyphenol was heated under reflux with 2.21g (0.013 mols) of cynanuric chloride (a four fold excess of the phenol) at 185-220° C for 5 hours under a reflux air condenser. The crude reaction product was triturated with boiling methanol, (twice 25ml), for 5 minutes. This left 5.21g of the product as a white crystalline powder. Yield = 70.0%, m.p. = 175-180°C.

Microanalysis:Found C, 72.63; H, 4.47; N, 6.91: Theory for $C_{39}H_{27}N_3O_6$, C, 73.93; H, 4.26, N, 6.64.

Mass Spectrum: *m\e* 633 M^+ other peaks at 448, 356, 294, 213, 186, 142, 116, 78(100%).

^1H NMR $\delta(CDCl_3)$ 7.41-6.94 (Aromatic m including an AA'BB' system peaks at 7.12, 7.08, 7.00, 6.96, centred at 7.04)

^{13}C NMR, $\delta_c(CDCl_3)$ 173.58, 149.79, 140.53, 138.82, 129.75, 128.92, 128.49, 126.20, 121.22, 41.21.

2,4,6-Tris(*p*-(1-naphthyl)phenoxy)-1,3,5-triazine (100)

4.81g (0.022 mols) of *p*-(1-naphthyl)phenol was heated under reflux with 0.92g (0.005 mols) of cynanuric chloride (a four fold excess of the phenol) at 185-220° C for 5 hours under an air condenser. The crude reaction product was triturated with boiling methanol, (twice 25ml), for 5 minutes. This left 1.79g of the product as a white crystalline powder. Yield = 48.7%, m.p. = 220-230°C.

Microanalysis:Found C, 82.57; H, 5.01; N, 5.85: Theory for $C_{51}H_{33}N_3O_3$, C, 83.26; H, 4.49, N, 5.71.

Mass Spectrum: *m\e* 735 M^+ other peaks at 516(100%), 446, 247, 120, 71.

^1H NMR $\delta(CDCl_3)$ 7.90-7.83 (18 H m) 7.53-7.28 (48 H m including an AA' BB' system peaks at 7.53, 7.49, 7.35, 7.30, centred at 7.42)

^{13}C NMR, δ_c(CDCl$_3$) 173.80, 150.84, 139.00, 138.67, 133.70, 131.39, 131.09, 128.24, 127.82, 127.08, 126.15, 125.81, 125.72, 125.29, 121.26.

Hexakis(p-cumylphenoxymethyl)benzene (104)

To 10.60g (0.05 mols) of p-cumylphenol dissolved in, dry freshly distiled diglyme (100ml) under an inert atmosphere, was added 1.15g of sodium metal. The system was maintained at 100° C until the sodium metal had dissolved completely. Following this 3.5g (0.0055 mols) of hexakis(bromomethyl)benzene was added and the reaction mixture was stirred under reflux for 24 hours. On cooling the reaction mixture was poured into ice-water (250-300ml). The very fine pink precipitate was collected by filtration, washed with water (500ml), dilute sodium hydroxide solution (500ml 0.1 molar) then again with water (twice 500ml). Drying under vacuum gave 7.78g of product as a fine white powder. Yield = 98.2% (w.r.t. hexakis(bromomethyl)benzene0). M.p. = 203-207° C (from dioxane)

Microanalysis: (unsolvated form from chlorobenzene); Found C, 84.38; H, 6.90: Theory: $C_{102}H_{102}O_6$ (unsolvated) requires C, 86.08; 7.17:

(From dioxane) Found C, 82.51; H, 7.40: Theory for $C_{102}H_{102}O_6.C_4H_8O_2$ the 1:1 clathrate requires C, 84.24; H, 7.28:

CPMAS ^{13}C (solid phase), NMR spectrum unsolvated: 157.02, 153.72, 139.85, 138.44, 129.0*, 126.93, 116.03, 109.00, 63.91, 41.57, 30.95, 28.10: (* possibly two peaks)

CPMAS^{13}C (solid phase),NMR spectrum of (104).1,4-dioxane clathrate: 156.83, 153.58, 139.79, 137.59, 129.24, 128.77, 126.97, 116.16, 109.93, 63.52, 41.50, 30.82, 28.16: (1,4-dioxane peak 66.66).

No satisfactory mass spectral or solution n.m.r spectral data could be obtained for compond (104), as discussed earlier.

<u>Hexakis(p-benzylphenoxymethyl)benzene</u> <u>(105)</u>

This was prepared analogously to (104) from 6.44g (0.035 mols) of <u>p</u>-benzylphenol, 0.805g (0.035 mols) of sodium metal and 2.47g (0.0038 mols) of hexakis(bromomethyl)benzene. An identical work up gave 4.65g of an off-white powder crystallised from methylene chloride. % Yield = 97.7% M.p. = 198-201°C.

Microanalysis (from methylenechloride) Found C, 86.10; H, 6.23: Theory for $C_{90}H_{78}O_6$ requires C, 86.12; H, 6.22.

^{1}H NMR δ(CDCl$_3$) Aromatic 7.40-7.10, 7.04, (30 H, m) 6.94, 6.81, 6.70 AA'BB' system centred at 6.875 (24 H); non-aromatic 5.31 (12 H s); 3.88 (12 H, s)

^{13}C NMR, δ_c(CDCl$_3$) 156.83, 141.39, 137.83, 133.89, 129.86, 128.76, 128.40, 125.96, 114.89, 63.57, 40.98.

No Satisfactory mass spectral data were obtained for (105).

<u>Hexakis(p-phenoxyphenoxymethyl)benzene</u> <u>(106)</u>

This was prepared analogously to (104) from 4.65g (0.025 mols) of <u>p</u>-phenoxylphenol, 0.575g (0.025 mols) of sodium metal and 1.77g (0.0027 mols) of hexakis(bromomethyl)benzene. An identical work up gave 3.18g of off-white powder crystallised twice from chlorobenzene. Yield = 90.5% m.p. = 239-243°C.

Microanalysis (from toluene) Found C, 79.65; H, 5.17: Theory for $C_{84}H_{66}O_{12}$ C, 79.62; H, 5.21.

^1H NMR $\delta(CD_2Cl_2)$ Aromatic 7.35-7.22, (12 H m); 7.10-6.98, (6 H m); 6.92-6.87 (36 H narrow m):

^{13}C NMR, $\delta_c(CD_2Cl_2)$ 158.72, 155.30, 151.49, 138.42, 130.09, 123.10, 121.04, 118.24, 116.44, 64.99.

No Satisfactory mass spectral data were obtained for (106).

Hexakis(cyclohexyloxy)benzene (108)

15.23g (0.136 mols) of cyclohexanol and 5.93g (0.146 mols) of sodium hydride were reacted by General Method One. The excess of sodium hydride was employed as cyclohexanol proved to react slowly. The salt which formed as a solid block in the reaction flask was removed and ground in a glove box before use. 14.43g (0.118 mols) of sodium cyclohexoxide was reacted with 1.10g (0.0059 mols) of hexaflurobenzene, (a 20 to 1 molar excess of the salt), by General Method Two. The initial work-up involved extraction of the reaction mixture with toluene. This caused a white precipitate to form. This precipitate was filtered, washed many times with water, and then a number of times with diethylether giving 0.453g of white semi-crystalline powder. A further 0.151g of material was obtained by treatment of the toluene solution as in the work of compound (90). The combined yield of product was 0.6048g (15.33%). Attempts to melt this material revealed that sublimation occurred between 220 and 310° C before thermal decomposition above 320°C.

Microanalysis: Found C, 75.68, 75.48; H, 10.18, 10.39:

Theory: for $C_{42}H_{66}O_6$ requires C, 75.68; H, 9.91.

Mas Spectrum m/e 666 M^+ other peaks at 584, 503, 420, 338, 256, 173(100%).

^{1}H NMR δ($CDCl_3$) 4.098-3.977 (6 H, m), 2.00-1.05 (60 H, m).

^{13}C NMR, δ_c($CDCl_3$) 141.68, 80.11, 32.71, 25.84, 24.18.

Hexakis(cyclododecyloxy)benzene (109)

17.5g (0.095 mols) of cyclododecanol was reacted 4.47g (0.11 mols) of 60% oil-dispersed sodium hydroxide by General Method One again the resultant salt was ground in a glove box prior to use. 16.89g (0.082 mols) of the resulting salt was reacted with 0.425g (0.0022 mols) of hexaflurobenzene by General Method Two. (An approximate 40:1 molar excess of salt was employed as the cyclododecanol proved to be very unreactive to the sodium hydride under the general conditions and therefore the purity of the resulting salt was very much in doubt.) Addition of water to the reaction mixture caused a white precipitate to form. This was triturated with a large excess of boiling ethanol to remove unreacted alcohol. This yielded 93mg of white powder. Yield = 3.6%, m.p. = 217-219° C.

Microanalysis: (from benzene) Found C, 80.01; H, 11.70:
Theory: for $C_{78}H_{138}O_6$ requires C, 80.00; H, 11.79.

Mas Spectrum m/e 1171 M^+ other peaks at 1005, 839, 670, 504, 338, 174(100%) 173(58.6%).

^{1}H NMR δ($CDCl_3$) 4.50-4.22 (6 H, m), 1.74-1.51 and 1.31, (132 H, broad m and broad, s).

^{13}C($CDCl_3$)(100MHz) 141.79, 79.06, 30.18, 24.56, 23.89, 23.74, 21.74.

1-(p-Methoxyphenyl)-3,4, dihydronaphthalene(124b).

This reaction was carried out many times, and a representative result is given here. A Grignard reagent was prepared by addition of 75.4g (0.40 mols) of p-bromoanisole to 9.6g (0.04 mols) of magnesium turnings in 300ml of sodium-dried diethylether. To this was added 36.2g (0.36 mols) of 1-tetralone in 300ml of sodium-dried diethylether. The reaction mixture was refluxed for a further 30 minutes. The product was worked up giving a brown oil. This was distilled under vacuum at, 0.7-0.8mm Hg, giving four fractions. The fourth fraction distilling between 180-180.5° C giving a clear oil. This oil was crystallised from methanol, to give 35.23g of product. Yield = 41.5%, m.p. = 73-75)° C.

Microanalysis: Found C, 86.28; H, 6.10: Theory: for $C_{17}H_{16}O$ requires C, 86.44: H, 6.78.

Mass Spectral: m/e 236 M^{+} other prominent peaks at 221, 214, 205, 119, 178, 171, 128, 63, 39, 27.

^{1}H NMR $\delta(CDCl_3)$ 7.31-6.85 (8 H aromatic, m), 6.20 (1 H, t, J=0.5 (olefinic)), 3.82 (3 H, s, (Me)), 2.83 (2 H, t, J=0.8 methylene at C(10)), 2.49-2.23 (2 H, m, methylene at C(9)):

1-(p-Methoxyphenyl)naphthalene. (125)

5.90g (0.025 mols) of 1-(p-methoxyphenyl)-3,4-dihydronaphthalene (124b) was heated with 0.8g (0.015 mols) of sulphur at 225° C for 4.5 hours. The mixture was cooled and the product crystallised from acetic acid, giving red-brown crystals which were dissolved in ethanol, refluxed for 2 minutes over activated charcoal, and then filtered hot giving, on crystallisation 4.98g of yellow/white crystals. M.p. = 114-115° C, yield = 81.1%.

Microanalysis: Found C, 86.95; H, 5.80: Theory: for $C_{17}H_{14}O$ requires C, 87.18, H, 5.98.

Mass Spectrum: <u>m/e</u> 234 M^+ (100%) other peaks at, 219, 191, 190, 189.

^1H NMR $\delta(CDCl_3)$ Aromatic 8.0-7.7 (3 H, m), 7.65-7.20 (6 H, m), 7.07-6.97 (one half of an AA'BB' system 2, H), non-aromatic 3.89 (3 H, s):

<u>1-(p-Hydroxyphenyl)naphthalene</u> <u>(117)</u>

10.42g (0.044 mols) of (125) was heated with 41.48g (0.36 mols) of pyridinium chloride to 205° C and held there for two hours. On cooling the product mixture was triturated with dilute sodium bicarbonate solution and then three times with water. The resulting brown oil was dissolved in toluene and dried over magnesium sulphate. The solvent was then removed by rotary evaporation giving 7.53g of crude product as a brown oil. (Crude Yield = 74.2%). This was crystallised with difficulty from cyclohexane to give 3.14g as an off-white powder. M.p. = 138-140°C.

Microanalysis: Found C, 87.45; H, 5.31: Theory: for $C_{16}H_{12}O$ requires C, 87.27; H, 5.45.

Mass Spectrum. <u>m/e</u> 220 M^+(100%), other peaks at 203, 191, 165, 163, 99 94.

^1H NMR $\delta(CDCl_3)$ aromatic 7.98-7.74 (3 H, t), 7.62-7.20 (6 H, m), 7.20-6.9 (one half of an AA'BB' system 2 H) non-aromatic 4.82 (1 H, s):

^{13}C NMR, $\delta_c(CDCl_3)$ 154.89, 139.53, 135.43, 133.91, 131.89, 131.39, 128.32, 127.44, 126.96, 126.04, 125.46, 125.17, 115.21.

p-(Diphenylmethyl)phenol (118).

The melt of 5.0g of diphenylmethanol and 1.31g (0.014 mols) of phenol was added drop-wise to a molten, vigourously stirred, mixture of 1.82g (0.014mols) of aluminium trichloride and 4.46g (0.048 mols) of phenol. The reaction mixture was maintained at approximately 100° C for 1.5 hours. On cooling the reaction mixture was treated with dilute hydrochloric acid. The resulting precipitate was filtered off and the excess phenol removed by distillation. The residue was crystallised from a 1:1 mixture of 40-60 light petrol and benzene giving 5.15g of product. M.p. = 110-117° C (literature value = 120-121° C). Yield = 92%.

Microanalysis: Found C, 87.65, 87.80; H, 6.12, 6.29: Theory: for $C^{19}H_{16}O$ requires C, 87.69, H, 6.16:

Mass Spectrum: m/e 260 M^{+} (100%), other peaks at 259, 243, 215, 183, 182, 181, 167, 154, 153, 115, 77.

^{1}H NMR δ($CDCl_3$) 7.43-7.08 (10 H aromatic, m), 7.04, 7.00, 6.78, 6.74. (4 H AA'BB' system centred at 6.89), 5.54 (1 H, s), 5.06 (1 H, s).

^{13}C NMR, δ_c($CDCl_3$) 153.64, 144.12, 136.28, 130.55, 129.32, 129.25, 126.20, 115.08, 55.68.

p-Tritylphenol (p-triphenylmethylphenol) (119).

The melt of 11.42g (0.034 mols) of triphenyl carbinol and 2.5g (0.025 mols) of phenol was added drop-wise to a molten, vigourously stirred, mixture 2.56g (0.019 mols) of aluminium trichloride and 8.02g (0.085 mols) of phenol. The reaction mixture was maintained at approximately 100° C for 1.5 hours. After cooling, the reaction mix was treated with dilute hydrochloric acid. The resulting precipitate was filtered off and the excess phenol removed by distillation. The residue was crystallised from a 1:1 mixture of 40-60 light petrol and benzene giving 13.42g of product. Yield = 90.07%, m.p. = 280-283°C. Microanalysis:Found C, 89.15; H, 6.13:Theory for $C_{26}H_{20}O$ requires C, 89.28; H, 5.93.

2-(o-Ethoxyphenyl)propan-2-ol (131a).

Step 1. A mixture of 20.23g (0.117 mols) o-bromophenol, 15.66g (0.128 mols) of ethylbromide and 6.60g (0.167 mols) of sodium hydroxide were refluxed for three hours in dry ethanol. The alcohol was removed on a rotary evaporator. Excess phenol was removed with a saturated solution of potassium hydroxide. The product was extracted into ether, washed with water (three times 100ml), dried over sodium sulphate and the ether removed. The product was distilled under vacuum 0.05 mm Hg, and the major fraction collected at 221-226° C giving 20.16g of product. (90 MHz ^{1}H NMR δ($CDCl_3$)) 7.58-7.46, 7.32-7.12, 6.95-6.68 (4 H three aromatic, m), 6.08 (2 H, q). 1.42 (3 H, t).

Step 2. 3.02g (0.015 mols) of this product, o-bromophenetol (130a), were reacted with 0.44g (0.016mols) of magnesium turnings to form the corresponding phenyl Grignard reagent (the reaction required initiation with methyl iodide). To this Grignard reagent 1.40g (0.024 mols) of acetone, dissolved in ether, was added so as to maintain steady reflux. The mixture was refluxed for a further hour. Following cooling and work up, 2.68g of brown oil resulted. On distillation three fractions were obtained: the major fraction was collected between 60-62° C at 0.05 mm Hg giving

2.01g of product. Yield = 74.4% (with respect to (130a))
Microanalysis: Found C, 72.86; H, 8.60: Theory: for $C_{11}H_{16}O_2$. requires C, 73.33; H, 8.88.
Mass Spectrum: *m/e* 180 M^+ other peaks at 165, 137, 121, 119, 91, 77, 65, 63, 51, 43(100%),29.
^1H NMR $\delta(CDCl_3)$ 7.40-7.08, 7.00-6.78 (4 H two aromatic, m), 4.14 (2 H, q), 1.60 (6 H, s), 1.39 (3 H, t).

2-(o-ethoxyphenyl)propene(131b).

A sample of (131a) was placed over fused potassium bisulphate. The mixture was heated at 150° C for 1 hour. Then the was product distilled; major fraction 40-42° C at 0.05mm Hg. This reaction was repeated a number of times a typical example being given. 4.06g (0.022 mols) of (131a) gave 3.14g (0.019 mols)of product. %Yield = 85.6%.
Microanalysis: Found C, 86.11; H, 9.04: Theory: for $C_{11}H_{16}O$ requires C, 86.84; H, 9.27.
Mass Spectrum: *m/e* 162 M^+ other peaks at 147(100%), 137, 133, 121, 105, 91, 79, 77, 43, 39, 29, 28.
^1H NMR $\delta(CDCl_3)$ 7.30-7.10, 7.04-6.68, (4 H two aromatic, m), 5.11 (2 H, broad s), 4.08 (2 H, q), 2.13 (3 H, s), 1.40 (3, H t).

o-chloropropylbenzene (136b).

Ethyl magnesium bromide was prepared from 12.5g (0.463 mols) of magnesium and 54.27, (0.444 mols) of ethylbromide. To this was added 50.02g (0.35 mols) of *o*-chlorobenzaldehyde at a rate so as to maintain mild reflux. The reaction mixture was further refluxed for 1 hour. On cooling the work up gave 38.29g of crude product, (*o*-chloro(1-(1-hydroxypropyl))benzene, identified by 90Mhz

^{1}H NMR. Aromatic 7.63-7.09 (4 H, m), non-aromatic 5.08 (1 H, t), 2.12 (1 H, s D_2O exchange), 1.96-1.63 (2 H, m), 0.98 (3 H, t).) This product was heated with 20g of fused potassium bisulphate for 5 hours at 160° C. It was then distilled under reduced pressure, major fraction collected at 50°C (0.5mm Hg), giving 27.82g of product (o-chloro) prop-1-enylbenzene 90MHz ^{1}H NMR 7.58-7.09 (4 H aromatic, m), 6.88,6.71 (1 H, d), 6.40-4.02 (1 H, m), 1.96, 1.94 and 1.88, 1.86 (3 H, double d)). This material was dissolved in ethanol, 0.1g of Adams catalyst was added and the mixture placed in a hydrogenator at approximately 3.5 atmospheres of H_2 pressure for 1.5 hours. The resulting solution was filtered through celite to remove the catalyst and the ethanol was removed by rotary evaporation. Careful distillation under vacuum ,75-78 mm Hg, yielded 20.4g of product.

Microanalysis: Found Cl, 21.85; Theory: for $C_9H_{13}Cl$ requires Cl, 22.98.* Material was too volatile to obtain carbon and hydrogen figures.

Mass Spectrum: m/e 156 M$^+$ other peaks at 155, 154, 153, 143, 140, 127, 125(100%) 115, 77.

^{1}H NMR δ($CDCl_3$) 7.43-7.16 (4 H m major peak at 7.20), 2.74 (2 H t), 1.88-1.47 (2 H m), 0.99 (3 H t).

^{13}C($CDCL_3$) 140.05, 133.99, 130.32, 129.35, 127.04, 126.52, 35.6, 22.93, 13.77.

o-(4-cumylphenyl)-N,N-dimethylthiocarbamate (141a).

13.2g (0.057 mols) of sodium p-cumylphenolate (prepared by General Method One) was added in one to a solution of 11.31g (0.105 mols) of

N,N,-dimethylthiocarbamoyl chloride in 120mls of dimethylformamide , DMF, maintained at 10° C. The temperature rose quickly and the reaction was further stirred at 40-60° C for 1.5 hours. On cooling, the product was poured into water and extracted (four times 100ml) with a 4:1 mixture of benzene and n-hexane. The combined extracts were washed with water, 5% sodium hydroxide solution, then saline solution, and finally again with water before drying over magnesium sulphate. The solvent was removed by rotary evaporation leaving a yellow oil which on crystallisation from methanol gave 12.06g of product (141a). Yield = 67.6%, m.p. = 112-113° C.

Microanalysis: Found: C, 72.16; H, 7.19; N, 4.75: Theory: for $C_{18}H_{21}NOS$ requires C, 72.24; H, 7.02, N, 4.68:

Mass Spectrum: *m/e* 299 M^{+} other prominent peaks at 227, 179, 103, 72,(100%), 42.

^{1}H NMR $\delta(CDCl_3)$ (90 MHz) 7.31-7.10 (7 H, m), 6.99 and 6.90 (one half of an AA'BB' system 2 H), 3.43 (3 H, s), 3.30 (3 H, s), 1.68 (6 H, s).

s-(4-cumylphenyl)-N,N-dimethylthiocarbamate (141b).

7.17g (0.023 mols) of *o*-4-cumyldimethylthiocarbamate (141a) was sealed into a glass tube. This was placed into a Wood's metal bath pre-heated to 200° C. The temperature was increased to 270° C and maintained for 45 minutes, removed from the bath and allowed to cool leaving a thick gum in the tube. On opening a strong fish-like smell was observed, the gum solidified giving a yellow solid. This was crystallised twice from a 1:1 mixture of ethanol and benzene giving 5.0g of product as cream coloured crystals. Yield = 69.7%, M.p.

= 101-103.5° C.

Microanalysis: Found: C, 72.33; H, 7.10; N, 4.70: Theory: for $C_{18}H_{21}NOS$ requires C, 72.24; H, 7.02, N, 4.68:

Mass Spectrum: m/e 299 M^+ other prominent peaks at 178, 165, 115, 88, 72,(100%), 51, 42.

^{1}H NMR $\delta(CDCl_3)$ (90 MHz) 7.46-7.13 (9 H, m; major peaks at 7.21, 7.27, 7.35, and 7.43), 3.21 (6 H, s), 1.63 (6 H, s).

o-(4-benzylphenyl)-N,N-dimethylthiocarbamate (142a).

Prepared analogously to the cumyl product (141a), from 16.89g (0.082 mols) of sodium p-benzylphenolate and 16.2g (0.131 mols) of N,N-dimethtylthiocarbamoyl chloride giving 15.65g of product. Yield = 72.19% M.p. = 79-81° C.

Microanalysis: Found: C, 70.95; H, 6.28; N, 5.17: Theory: for $C_{16}H_{17}NOS$ requires C, 70.84; H, 6.27, N, 5.17:

Mass Spectrum: m/e 271 M^+ other prominent peaks at 79, 73, 72,(100%).

^{1}H NMR $\delta(CDCl_3)$ (90 MHz) 7.30-7.05 (7 H, m major peaks at 7.22 and 7.13 6.99, 6.91), 3.98 (2 H, s), 3.42 (3 H, s), 3.29 (3 H, s).

s-(4-benzylphenyl)N,N-dimethylthiocarbamate (142b).

4.47g (0.0165 mols) of o-(4-benzylphenyl)-N,N-dimethylthiocarbamate was sealed into a glass tube. This was placed into a Wood's metal bath pre-heated to 200° C. The temperature was increased to 270° C and maintained for 45 minutes, removed from the bath and allowed to cool leaving a thick gum in the tube. On opening a strong fish-like smell was observed, the gum solidified giving a yellow solid. This was crystallised twice from a 9:1 mixture of ethanol:benzene giving 4.01g of product as cream

coloured crystals. Yield = 89.7%, M.p. = 46-50° C.
Microanalysis: Found: C, 70.63; H, 6.19; N, 5.24: Theory: for $C_{16}H_{17}NOS$ requires C, 70.84; H, 6.27, N, 5.16:
Mass Spectrum: m/e 271 M^+ other prominent peaks at 272, 88, 72,(100%), 42.
^1H NMR $\delta(CDCl_3)$ (90 MHz) 7.46-7.13 (9 H, m major peaks at 7.21, 7.27, 7.35, and 7.43), 3.21 (6 H, s), 1.63 (6 H, s).

Hexakis(p-benzylthiophenoxy)benzene(144).

p-Benzylthiophenol was produced from (142b) by 18 hour reflux in a sodium hydroxide solution in dry ethanol under an argon atmosphere. ^1H NMR $\delta(CDCl_3)$ 7.38-7.04 (9 H, aromatic, m), 5.94 (2 H, s), 3.38 (1 H, s removed on treatment with D_2O). 1.92g (0.0096 mols) of this thiol was reacted with 0.4g (0.01 mols) sodium hydride (60% oil-dispersion) by General Method One. The resulting material was reacted with 0.15g (0.0008 mols) of hexaflurobenzene in dry DMEU for three days at room temperature during which time a deep red colour developed in the reaction vessel. Water was added to the reaction mixture and this was extracted with benzene and many times with equivalent volumes of water. To avoid any potential loss of product on drying agent the benzene was removed by rotary evaporation and extra solvent was used to azeotrope any remaining water. The resultant material was a yellow oil, which was shown by TLC to contain a number of components. A slurry column was run in a 1:1 mixture of chloroform: 60-80 petrol from which the yellow band was collected. Evapouration of the solvent yielded 423mg of yellow powder. Yield = 41.8%, m.p. = 155-166° C.

Microanalysis: Found: C, 79.68; H, 5.36; S, 14.83: Theory: for $C_{84}H_{66}S_6$ requires C, 79.62; H, 5.21; S, 15.16.

^{1}H NMR δ($CDCl_3$) 7.23-6.58 (9 H, aromatic m, including an AA'BB' system 6.83, 6.79, 6.76, 6.72, centred at 6.775).

^{13}C NMR, δ_c($CDCl_3$) 147.77, 140.63, 138.98, 135.16, 129.47, 128.83, 128.40, 126.09, 41.253. DEPT analysis revealed the peaks from 147.77-135.16 to be quaternary in nature.

Hexakis(p-(1-naphthyl)phenoxybenzene (145)

2.74g (0.011) mols of sodium p-(1-naphthyl)phenolate produced from 2.72g (0.012 mols) of p-(1-naphthyl)phenol and 0.49g (0.012 mols) of 60% oil-dispersed sodium hydride by General Method One was reacted with 0.167g (0.0009 mols) by General Method Two. Addition of water to the cooled reaction mixture produced an off-white precipitate which was filtered and triturated with chloroform leaving 0.536g of product. Yield = 42.0%. M.p. > 320° C.

Microanalysis: Found C, 87.15; H, 4.60: Theory: for $C_{102}H_{66}O_6$, requires C, 88.31, H, 4.76.

^{1}H NMR δ($CDCl_3$) 8.18-7.65 (3 H, t), 7.65-7.20 (7 H, m), 7.20-6.9 (2 H, d):

^{13}C NMR, δ_c($CDCl_3$) 156.80, 140.42, 139.53, 135.43, 133.85, 131.73, 130.93, 128.21, 127.52, 127.00, 126.04, 125.88, 125.68, 125.30, 115.96.

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Inclusion Compound Design: the Piedfort[†] Concept

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Inclusion Compound Design: the Piedfort† Concept

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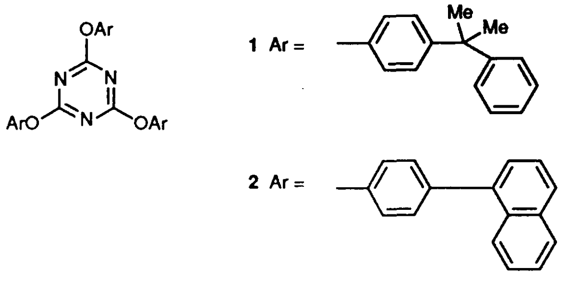
Two molecules of 2,4,6-tris[4-(2-phenylpropan-2-yl)phenoxy]-1,3,5-triazine 1 undergo self-assembly to produce a composite unit, termed Piedfort unit, which acts as a single hexa-host molecule; the structure of this new host unit, found both in the 1,4-dioxane inclusion compound of 1 and in its unsolvated crystal, has been elucidated by X-ray methods.

Rational host design greatly facilitates the discovery of new classes of host molecule capable of forming crystalline inclusion compounds.[1,2] The value of thinking by analogy is well demonstrated by the hexa-hosts,[1] the genesis of which relied on the recognition of the significance of the hydrogen-bonded hexameric unit in many phenolic hosts.[3] A typical hexa-host, a suitably hexa-substituted benzene, is shown schematically in Fig. 1(*A*), where Z represents a link atom or chain, and ○ and ● outer groups, often enantiomerically related in the crystal,[1] since the host molecule is usually located on a point of $\bar{1}$ or $\bar{3}$ symmetry. We now report the successful use of a new approach, termed the Piedfort concept, which is illustrated in Fig. 1(*B*). As can be seen the Piedfort analogue (*B*), mimicking (*A*), consists of two *tri*-substituted rings, superposed at van der Waals contact, such that the resulting (alternating) disposition of side-chain moieties and overall geometric aspects are similar; however, it should be noted that neighbouring Z atoms (or chains) on separate rings in (*B*), are somewhat further apart than the corresponding neighbouring Z moieties of (*A*). To achieve in reality the self-assembly mode implicit in (*B*), we selected target molecules 2,4,6-tris[4-(2-phenylpropan-2-yl)phenoxy]1,3,5-triazine **1** and 2,4,6-tris[4-(1-naphthyl)phenoxy]1,3,5-triazine **2**, both based on the symmetrical heteroaromatic 1,3,5-triazine ring. Compounds **1** and **2**, new materials, were prepared in good yield employing a general literature method,[4] and have spectroscopic properties (^{1}H, ^{13}C NMR, IR and mass) fully in accord with their formulated structure; **1** has m.p. 178–180 °C, for the unsolvated form (from EtOH–$CHCl_3$). Encouragingly, both **1** and **2** were found to form crystalline adducts. In order to establish whether self-assembly had occurred in the Piedfort mode sought, the triazine **1** was selected for initial X-ray crystal structure analysis. Both the 1,4-dioxane inclusion compound



of **1** and, for comparison, the unsolvated molecular crystal of **1** were studied.‡ The 1,4-dioxane adduct has a host–guest ratio 1 : 2, established by ^{1}H NMR spectroscopy (in $CDCl_3$) and by thermogravimmetric analysis.

Fig. 2(*a*) gives a general view of the host–guest packing in the 1,4-dioxane adduct of **1**, and Fig. 2(*b*) shows the packing in the molecular crystal of **1**. In the adduct, pairs of host molecules are indeed found to be self-assembled as Piedfort

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† The numismatic derivation of the name Piedfort, for this idea, comes from special coins struck at double thickness for collectors; here, two aromatic rings at van der Waals contact, which together comprise the central core of (*B*), are in combination about twice as thick as the corresponding central moiety of (*A*).

‡ *Crystal data* for $C_{48}H_{45}N_3O_3$ **1**. $M = 711.9$, triclinic, space group $P\bar{1}$, $a = 13.041(3)$, $b = 13.073(3)$, $c = 13.463(2)$ Å, $\alpha = 71.30(2)$, $\beta = 84.98(2)$, $\gamma = 64.61(2)°$, $U = 1961(1)$ Å^3, $Z = 2$, $D_c = 1.21$ g cm^{-3}, λ(Mo-Kα) = 0.7107 Å, $\mu = 0.7$ cm^{-1}, $T = 293$ K. Number of independent intensities: 8525 from colourless plate, 0.5 × 0.5 × 0.1 mm. $R = 0.041$, $R_w = 0.043$, for 3503 observed $[I/\sigma(I) > 2.0]$ reflections.

Crystal data for $C_{48}H_{45}N_3O_3$ **1**·$2C_4H_8O_2$. $M = 888.1$, triclinic, space group $P\bar{1}$, $a = 13.906(3)$, $b = 14.214(3)$, $c = 14.604(2)$ Å, $\alpha = 111.76(1)$, $\beta = 106.82(1)$, $\gamma = 96.25(2)°$, $U = 2489(1)$ Å^3, $Z = 2$, $D_c = 1.19$ g cm^{-3}, λ(Mo-Kα) = 0.7107 Å, $\mu = 0.7$ cm^{-1}, $T = 293$ K. Number of independent intensities: 10 822 from colourless hexagonal prism, 1.0 × 0.5 × 0.5 mm. $R = 0.087$, $R_w = 0.103$ for 4330 observed $[I/\sigma(I) > 2.0]$ reflections.

For both crystals, X-ray intensity measurements for all possible reflections with $\sin \theta/\lambda < 0.64$ Å^{-1} were made by 2θ–ω scans on a Nonius CAD4 diffractometer. The principal computer programs used in structure solution and refinement are listed in ref. 7. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

units; furthermore, in the unsolvated crystal these units are also present. In each case two superposed molecules of **1**, which are centrosymmetrically related, have their central rings essentially in van der Waals contact (*vide infra*). The Piedfort unit, which possesses exact C_i symmetry, has, it may be noted, the same staggered arrangement of nitrogen atoms as found by calculation[5] for the minimum energy form of the dimer of 1,3,5-triazine itself. The molecular structure of the dimer in the adduct is shown in Fig. 3. In the unsolvated crystal (atom labelling as in Fig. 3) closest intermolecular contacts N(1)···C(4*), N(3)···C(6*), N(5)···C(2*) (asterisks denote neighbouring molecules) are 3.516(3), 3.549(3), and 3.546(3) Å respectively, whilst the corresponding values for the inclusion compound are 3.458(6), 3.416(6) and 3.431(6) Å. These indicate a significantly closer approach of the central rings to exact van der Waals contact on incorporation of the guest. The triazine ring is planar to ±0.01 Å in each case, and the respective C–N–C and N–C–N ring angles have average values of 112.1 and 127.9° for the unsolvated crystal and 111.9 and 128.2° in the adduct. These angles are close to the corresponding unique values of 113.2 and 126.8° found for 1,3,5-triazine itself.[6] Interestingly, the dimeric unit in the adduct possesses approximately trigonal symmetry, a non-exact three-fold proper rotation axis running normal to the central rings. The approach to C_{3i} ($\bar{3}$) symmetry may be appreciated from Fig. 3, and sets of torsion angles for the crystallographically non-equivalent side chains: N(1)–C(2)–O(2)–C(21) (and related) −179, 172, 178°; C(2)–O(2)–C(21)–C(22) −105, −114, −77°; C(23)–C(24)–C(27)–C(30) 59, 54, 57°; C(24)–C(27)–C(30)–C(31) −160, −135, −142°. In contrast the Piedfort unit in the unsolvated crystal is much less symmetrical, although the central region retains some approximate trigonal character. The mean C–N, C–O (inner) and C–O (outer) bond lengths for **1**, unsolvated and solvated respectively, are 1.323(2), 1.338(2), 1.412(2) Å; 1.324(3), 1.338(3), 1.410(3) Å. The C–N bond length may be compared with the unique value of 1.319 Å found for the parent, 1,3,5-triazine.[6]

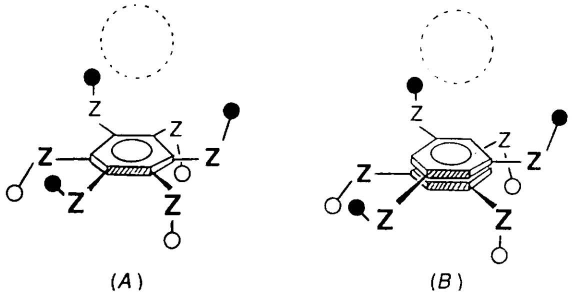

Fig. 1 A comparison of a typical hexa-host (*A*) with its Piedfort analogue (*B*), composed of two trisubstituted (6 π-electron) aromatic rings juxtaposed. The light dotted circle is symbolic of the projected guest region in each case.

The stereoview (Fig. 2*a*) illustrating the host–guest packing in the adduct reveals three crystallographically non-equivalent locations of the 1,4-dioxane guest molecule. All the dioxane guest molecules have a chair conformation; two are situated

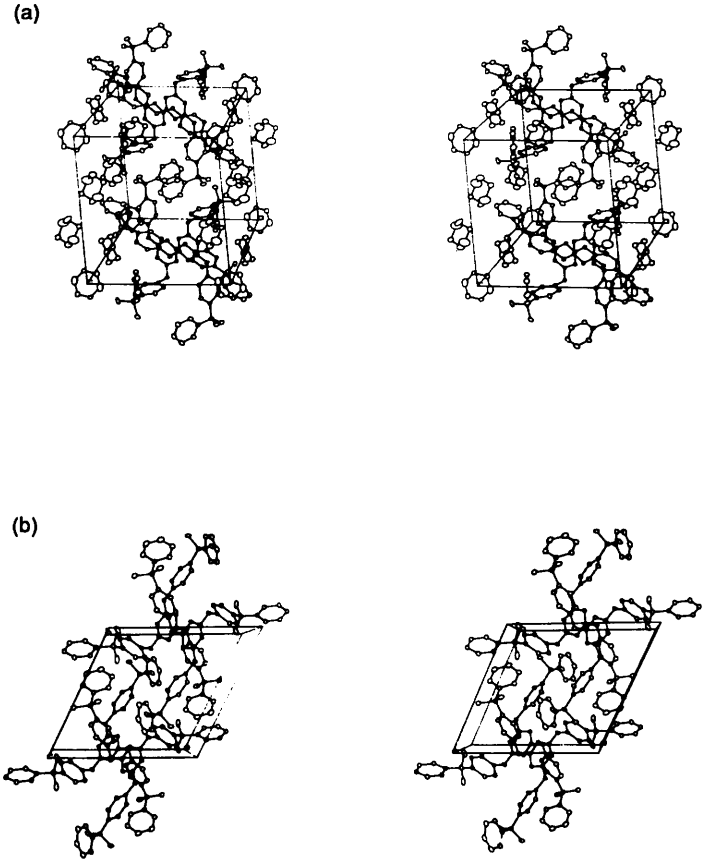

Fig. 2 Stereoviews illustrating (*a*) the host–guest packing in the 1,4-dioxane inclusion compound of 2,4,6-tris[4-(2-phenylpropan-2-yl)-phenoxy]-1,3,5-triazine **1** and (*b*) the molecular packing in unsolvated **1**

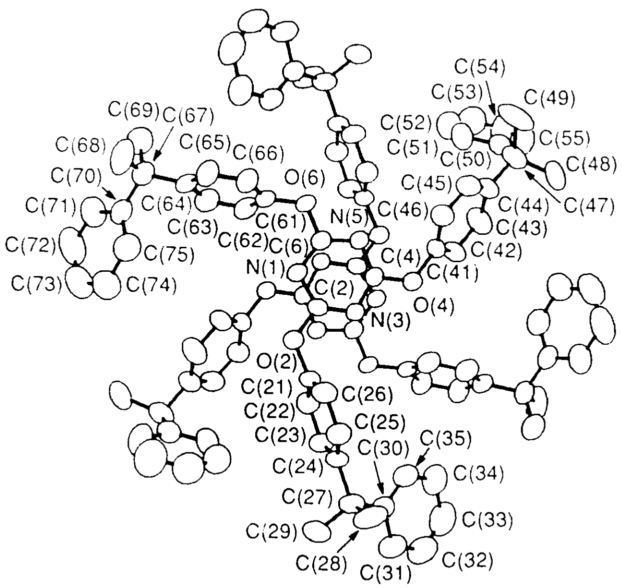

Fig. 3. A view of the Piedfort unit in the 1,4-dioxane inclusion compound of **1**, showing the atomic numbering scheme common to this and unsolvated **1**. The two central 1,3,5-triazine rings are accurately superposed but for clarity the view direction is inclined to the normal of the central ring planes.

on centres of symmetry and the third, occupying a general position, corresponds to the projected guest inclusion region (light dotted circle) in Fig. 1(*B*). The structure exhibits novel void geometry, a network consisting of intersecting channels (running along the *b* and *c* axial directions) providing accommodation for the guest species. In the *c* direction, all dioxane molecules are located on the axis, whereas a zig-zag pattern is found along *b*.

Related host **2**, which incorporates the 4-(1-naphthyl)phenoxy side chain, forms an inclusion compound with a host–guest ratio *ca.* 2 : 1 when recrystallised from propan-2-ol (at *ca.* 100 °C, sealed tube). As a consequence of the modified side-chain composition, this adduct is trigonal rather than triclinic as previously. Preliminary X-ray evidence indicates a rhombohedral lattice with parameters consistent with the presence of Piedfort units which now have attained exact three-fold symmetry.

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DESIGN AND SYNTHESIS OF RHOMBOHEDRAL CLATHRATES FOR CONTAINMENT OF SMALL, REACTIVE GUEST SPECIES

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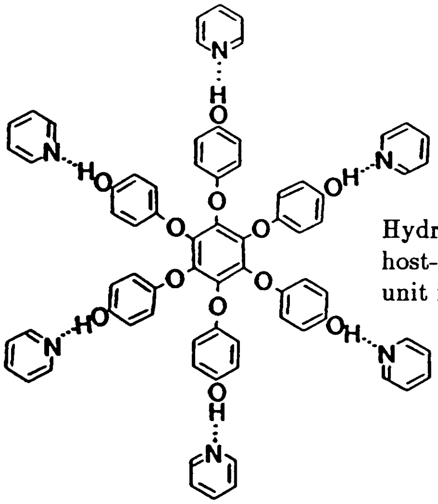
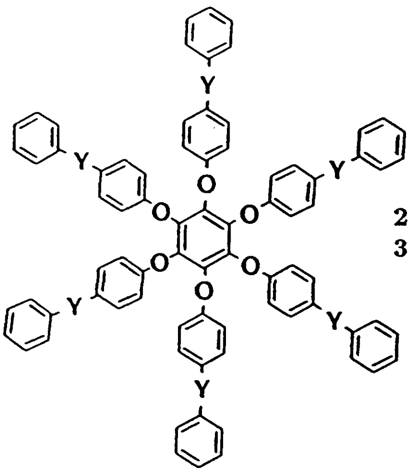
Abstract

The new hexa-hosts hexakis(*p*-phenoxyphenoxy)benzene **2** and its *p*-benzylphenoxy analogue **3**, targetted at rhombohedral clathrate packing, have been prepared. X-ray measurements have established that **2** and **3** form very similar rhombohedral closed-cage structures with common trigonal space group $R\bar{3}$. The cavities of these clathrates are potentially useful for the handling of reactive reagents, examples for **2** being phosgene, thiophosgene, thionyl chloride, and methyl iodide.

The idea of covalent fusion of several molecules previously linked only by hydrogen bonds in a molecular crystal has previously found effective application in the derivation of the hexa-host analogy [1] (new *hosts* deriving from formal combination of H-bond linked *hosts*); and in the efficient isolation [2] of *trans*-1,4-bis(hydroxymethyl)cyclohexane from a *cis,trans* mixture of isomers (new *guest* mimicking hydrogen-bonded, centrosymmetric *guest* aggregate 1,4-dioxane.$2H_2O$). The present work provides the first example of new, stable, covalently linked *hosts* which owe their existence to a pre-existing hydrogen-bonded *host-guest* assembly. Potential uses of these new hosts are also described.



Hydrogen-bonded
host-guest
unit in **1**.6py



2, X = O
3, X = CH_2

The conspicuous voids in the hydrogen-bonded adduct [3] of hexakis(*p*-hydroxyphenoxy)benzene **1** with six pyridine guest molecules, **1**.6py, suggested to us the possibility of synthesis of analogous - but highly inert - covalently linked host counterparts retaining the trigonal space group $R\bar{3}$.

Suitable molecules without reactive functionality and with potentially analogous packing characteristics were selected, namely hexakis(*p*-phenoxyphenoxy)benzene **2** and hexakis(*p*-benzylphenoxy)benzene **3**. These were prepared in high yields (*ca.* 90%) from hexafluorobenzene by dipolar aprotic solvent-promoted complete nucleophilic substitution as previously described [4]. Both **2** and **3** were fully characterised spectroscopically: ^{1}H and ^{13}C NMR, IR, mass spectrometry.

Both **2** and **3** were found to form beautifully crystalline adducts with a wide range of volatile guest species. For evaluation of their suitability as media for reagent handling, it was of prime importance to establish the nature of the voids present in these structures. The relationship to the pre-cursor host structure **1**.6py was also of interest. The methyl iodide and phosgene adducts of **2** and the CCl_3CH_3 clathrate of **3** [5] were chosen for detailed X-ray study.[1] The adducts were prepared by recrystallisation of unsolvated **2** or **3** from the appropriate pure, dry solvent, or in the case of gases, from a solution of the gas in a suitable solvent (which was not included to any significant extent). For example, the 1:1 $COCl_2$ clathrate of **2** was prepared by recrystallisation from a 12.5% (by weight) solution of $COCl_2$ in toluene, in a sealed tube. Thermogravimetric analysis (TGA) showed no guest loss below 125°C (heating rate 10°C/min, N_2 atmosphere), the main weight loss occurring in the range *ca.* 150-200°C.

Crystal Data. [6] $C_{78}H_{54}O_{12}.CH_3I$: $M = 1325.2$, rhombohedral, space group $R\bar{3}$, $a = 22.311(5)$, $c = 11.005(2)$ Å, $U = 4744(2)$ Å^3, $Z = 3$, $D_c = 1.39$ g cm^{-3}, $T = 293K$, $R = 0.085$, $R' = 0.087$ for 844 independent reflections with $F_o^2 > 2\sigma(F_o^2)$.
$C_{78}H_{54}O_{12}.COCl_2$: $M = 1282.2$, rhombohedral, space group $R\bar{3}$, $a = 22.300(7)$, $c = 10.980(3)$ Å, $U = 4729(2)$ Å^3, $Z = 3$, $D_c = 1.35$ g cm^{-3}, $T = 293K$, $R = 0.082$, $R' = 0.100$ for 874 independent reflections with $F_o^2 > 2\sigma(F_o^2)$.

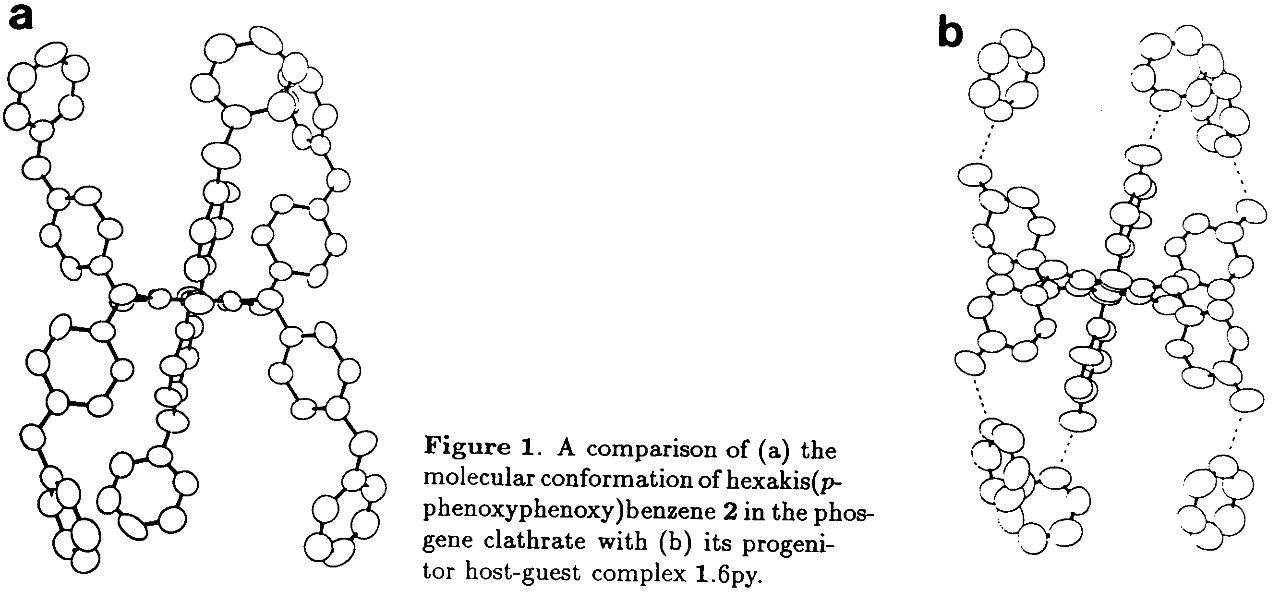


Figure 1. A comparison of (a) the molecular conformation of hexakis(*p*-phenoxyphenoxy)benzene **2** in the phosgene clathrate with (b) its progenitor host-guest complex **1**.6py.

Figure 1(a) shows the conformation of the host molecule, hexakis(*p*-phenoxyphenoxy)benzene **2**, which has exact C_{3i} ($\bar{3}$) symmetry, in its methyl iodide clathrate. This conformation is re-

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[1] The atomic coordinates for the CH_3I and $COCl_2$ adducts of **2** are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication. Supplementary data: structure factors. See Announcement to Authors, *Tetrahedron Letters,* **47**, 5154 (1983).

markably similar to the host-guest arrangement in the pre-cursor assembly **1**.6py, Figure 1(b). Whilst the central ring of **2** is effectively planar, the directly-attached oxygen atoms are alternately disposed above and below the ring plane by ±0.10(1) Å [±0.11(1) Å $COCl_2$ clathrate] in the opposite sense to that of the corresponding side chains. This may be compared with the corresponding value ±0.15(1) Å for **1**.

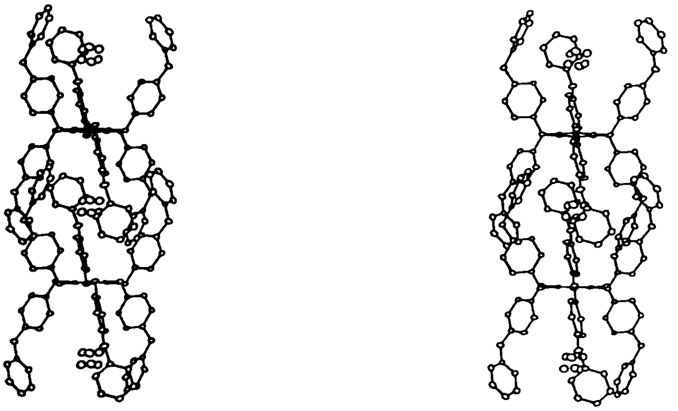

Figure 2. A stereoview normal to *c* illustrating a portion of the infinite columns along *c* in the methyl iodide clathrate of **2**. The guest's iodine atom, statistically disordered, appears in six positions close to the cage centre.

Figure 2 gives a stereoview of the infinite stacking of host molecules along the *c* axial direction, the cavities, possessing exact C_{3i} ($\bar{3}$) symmetry, being formed between adjacent host molecules. Only the iodine atom of the statistically-disordered methyl iodide could be located, and this can be seen, close to the cage centre, in Figure 2. The phosgene clathrate has a virtually identical host structure, but in this case it was not possible to locate unambiguously any guest atom. The efficient packing of columns is illustrated, for the phosgene clathrate, in Figure 3.

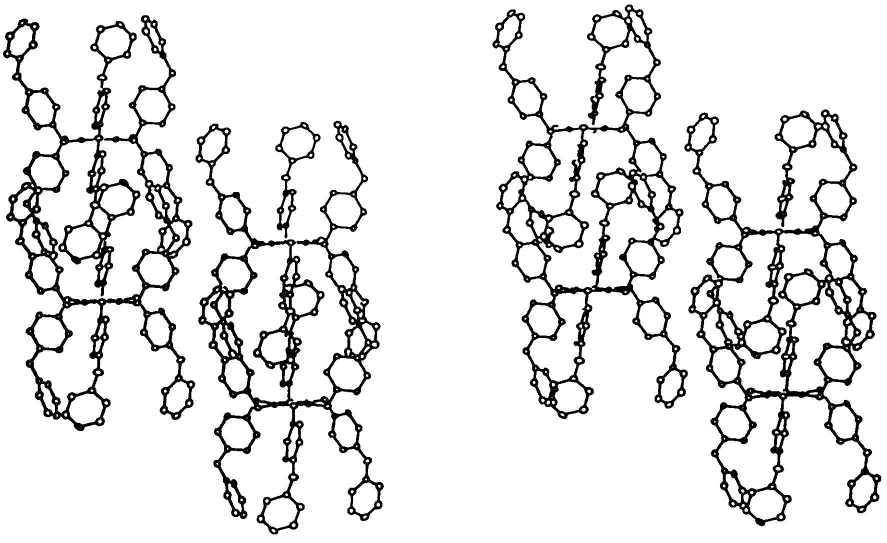

Figure 3. A stereoview illustrating the efficient packing of adjacent columns which extend infinitely along *c* in the 1:1 $COCl_2$ clathrate of **2**. The disordered phosgene molecule has been omitted for clarity.

The presence of phosgene in complexation with **2** was substantiated by microanalysis; [2] (found: C, 73.89%; H, 4.37%; Cl, 5.33%: $C_{78}H_{54}O_{12}.COCl_2$ requires: C, 74.00%; H, 4.25%; Cl, 5.53%), and confirmed by IR spectroscopy first by the presence [3] of a ν(C=O) (KBr disc) band at 1803 cm^{-1}, and then by release of the guest into a vapour phase IR cell, giving a spectrum in complete agreement with a reference vapour spectrum.

In summary, the present work represents a unique example of crystal design of highly inert crystalline host lattices [8, 9], successfully targetted at trigonal space group $R\bar{3}$, for the storage of volatile and reactive species potentially useful as synthetic reagents. The intriguing strategy of building permanent, consolidated analogues of hydrogen-bonded moieties, *cf.* ref. [1, 2] will undoubtedly lead to the synthesis of many new host lattices as well as other types of new material based on molecular crystals.

References

[1] See, for example, D.D. MacNicol in *Inclusion Compounds*, eds. J.L. Atwood, J.E.D. Davies and D.D. MacNicol, Academic Press, London, 1984, vol. 2, ch. 5.

[2] J.H. Gall, M. McCartney, D.D. MacNicol and P.R. Mallinson, *J. Incl. Phenom.* 1985, **3**, 421.

[3] D.D. MacNicol, P.R. Mallinson, A. Murphy, and C.D. Robertson, *J. Incl. Phenom.* 1987, **5**, 233.

[4] C.J. Gilmore, D.D. MacNicol, A. Murphy and M. Russell, *Tet. Lett.* 1983, **24**, 3269.

[5] The CCl_3CH_3.**3** adduct also has space group $R\bar{3}$ with closely similar lattice parameters a = 23.144, c = 11.247 Å, $Z = 3$. Current $R = 0.100$ for 851 independent reflections.

[6] X-ray intensity measurements were made by $2\theta - \omega$ scan on a Nonius CAD4 diffractometer using graphite-monochromated MoK_α radiation. Unit cell parameters were determined by least-squares refinement of diffractometer setting angles for 25 reflections. 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.

[7] Y. Ono and Y. Ueda, *Chem. Pharm. Bull.* 1970, **18**, 2013.

[8] We note the interesting use of crown complexes in the fixation, as crystalline complexes, of volatile, highly toxic molecules, for example N,N-dimethylnitrosamine, which have acidified CH_3-, $CH_2 <$ or analogous heteroatom groups (F. Vögtle and W.M. Müller, *Naturwiss.* 1980, **67**, 255).

[9] The effective storage of the volatile and extremely toxic dimethyl mercury in the clathrate cages of 4-*p*-hydroxyphenyl-2,2,4-trimethylthiacroman has previously been described (R.J. Cross, J.J. McKendrick and D.D. MacNicol, *Nature* (London) 1973, **245**, 146).

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[2] For some clathrates of **2** and **3** with halogenated guests, microanalysis for halogen consistently indicated host-guest ratios greater than 1:1, for example for the CCl_4 adduct of **2**. Since X-ray unit cell determination shows the cell (a = 22.420(10), c = 11.030(2) Å) analogous to the methyl iodide and phosgene clathrates, and CPK models show that an additional CCl_4 molecule cannot be accommodated in the cavity, it seems probable that excess guest may be situated in macroscopic defects in the crystal. For the $CSCl_2$ clathrate of **2**, obtained as golden-coloured crystals on recrystallisation of **2** from a 20% (by weight) solution of $CSCl_2$ in mesitylene, an excess over a 1:1 ratio is also obtained, and again this may be due to crystal imperfections, assuming an isostructural host lattice. Methods used to determine host-guest ratios were microanalysis, TGA, and ^{1}H NMR where appropriate.

[3] The ν(C=O) band of phosgene in the clathrate at 1803 cm^{-1} is somewhat lower than its value of 1813 cm^{-1} in CCl_4 solution. A similar effect is found for the 1:1 clathrate of CH_3COCl with **2** [7], where ν(C=O) is 1800 cm^{-1} compared to 1806 cm^{-1} in CCl_4.