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Helical tubulate inclusion compounds

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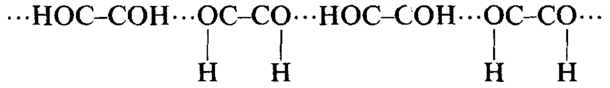
The inclusion properties of the first helical tubuland diol hosts 1–5 have been surveyed and are reported. Bicyclic diol 1 forms helical tubulate inclusion compounds with most small solvent molecules, but with certain phenols hydrogen bonded co-crystalline materials are produced instead. Diol 2 yields helical tubulates with larger guest molecules, but if smaller solvents are used then an alternative host system is obtained. This has the guests trapped in ellipsoidal cavities located along constricted canals and is termed the ellipsoidal clathrate type. In some cases both inclusion types can be produced from 2 by varying the experimental conditions. The free volume present in the helical tubuland lattices of 3 and 5 is insufficient for guest inclusion. Diol 4 has the largest void space and can form inclusion compounds with large molecules such as ferrocene and squalene. X-ray crystal structures of representative examples of these compounds are discussed.

INTRODUCTION

The alicyclic diols **1–5** are the first members of the helical tubuland diol family.[1] These tubuland[2] compounds crystallize from ethyl acetate as conglomerates[3] in space group $P3_121$ (or enantiomorph $P3_221$) as long trigonal needles containing parallel helical canals which may contain trapped guest molecules.

The structural core of each crystal is a series of tight spiral spines of hydrogen bonds with the sequence: $\cdots$O–H$\cdots$O–H$\cdots$O–H$\cdots$O–H$\cdots$. Diol molecules radiate from and interconnect these spines such that a hexagonal arrangement of six spines encloses each canal. The resulting canals are lined only with hydrocarbon hydrogens. As illustrated below, variation of the diol molecular structure results in considerable modification of the canal topology and dimensions. Unobstructed cross-sectional areas are shown in Figure 1 for one canal only of crystalline **1–5**. It should be noted that these representations show a slice across the canal and therefore they appear as flat projections with loss of the three-dimensional canal characteristics.

The canal walls involve a double helical array of diol molecules hydrogen-bonded in the sequence:



$$\cdots\mathrm{HOC{-}COH}\cdots\underset{\substack{|\\\mathrm{H}}}{\mathrm{O}}\mathrm{C{-}C}\underset{\substack{|\\\mathrm{H}}}{\mathrm{O}}\cdots\mathrm{HOC{-}COH}\cdots\underset{\substack{|\\\mathrm{H}}}{\mathrm{O}}\mathrm{C{-}C}\underset{\substack{|\\\mathrm{H}}}{\mathrm{O}}\cdots$$

This arrangement is shown in Figure 2 diagrammatically and in exaggerated perspective for the example of one canal of **1**.

Appropriate guests can occupy these canals resulting in helical tubulate lattice inclusion compounds. The formation of such materials may be monitored in several ways. One of the most useful techniques is infrared spectroscopy (paraffin mull) where the guest absorptions are superimposed on those expected for the host alone. Combustion analysis also is valuable in detecting the presence of guest inclusion and furthermore indicates the composition of the material. Solution ^{1}H- and ^{13}C-NMR spectroscopy has also been used.

The structures of specific examples of the inclusion compounds formed have been determined by single crystal X-ray diffraction methods. However for general screening purposes we have used X-ray powder diffraction methods. The type of crystal lattice present results in characteristic peak patterns which indicate the presence of the helical tubulate type or alternative structures.

RESULTS AND DISCUSSION

Diol 1 helical tubulates

In the case of **1** the canals are of triangular cross-section (side *ca.* 6.3 Å) with an unobstructed cross-sectional area of approximately 22.4 Å^2 as shown in Figure 3. Inclusion compounds are produced when **1** is crystallized from small solvent molecules comprising a wide variety of functional group classes.[4] These include alkenes, amines, aromatic hydrocarbons, aryl halides, ethers, esters, ketones, nitriles and

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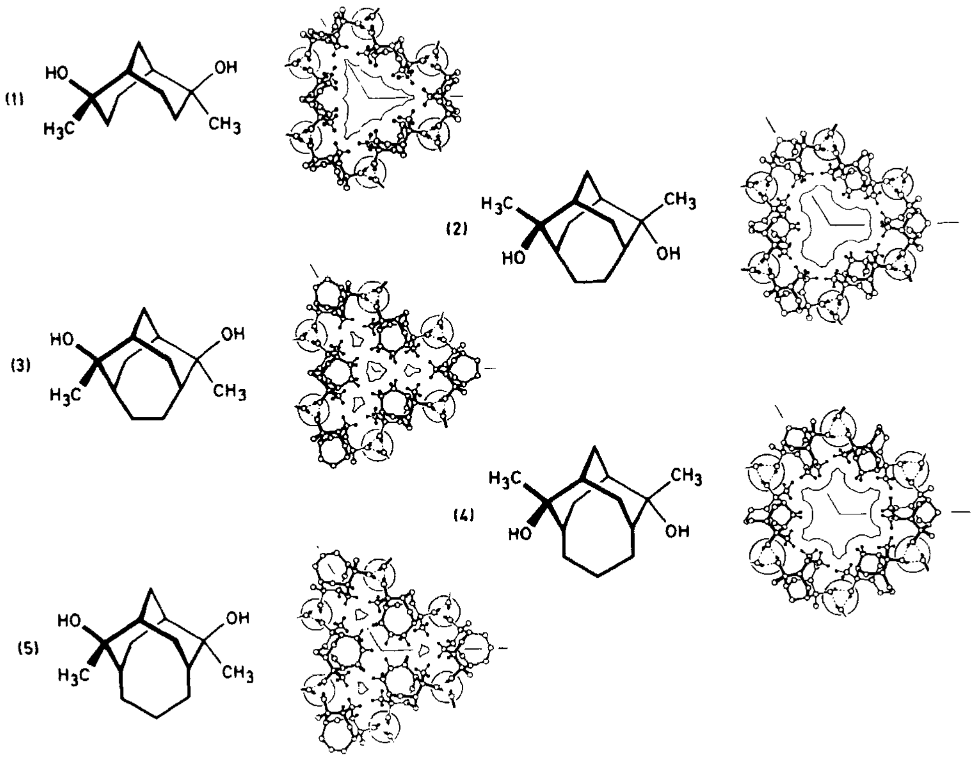

Figure 1 Structures of alicyclic diols **1**–**5** showing for each a slice through one canal only of the helical tubuland lattice as a flat projection in the *ab* plane. Key hydrogen atoms are shown as filled circles to define the van der Waals inner surface of the canals. Hydrogen bonds are indicated as broken lines and the resulting helical spines are circled.

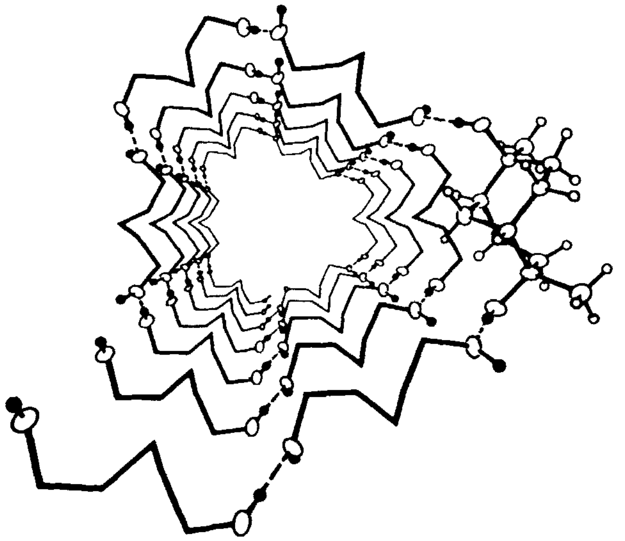

Figure 2 The sequence of hydrogen-bonded diol **1** molecules around one canal of its helical tubuland structure shown diagrammatically with all except one molecule being represented as solid lines between the –OH groups.[5]

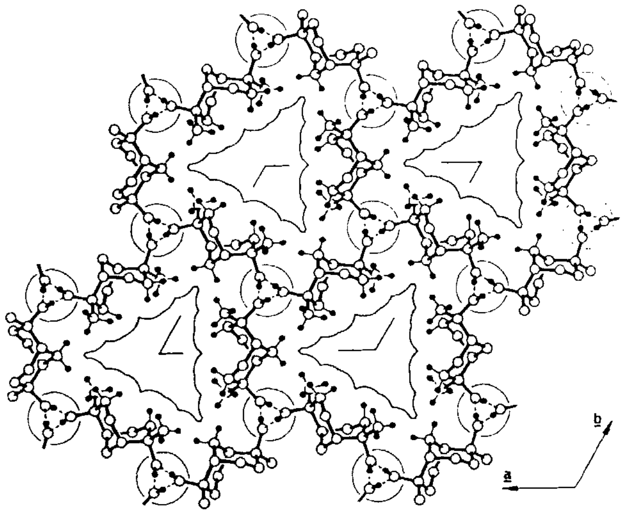

Figure 3 Projection view of the diol host network in crystalline $(\mathbf{1})_3\cdot$(ethyl acetate). Selected hydrogen atoms, shown as filled circles, mark the edges of the canals. These have a triangular unobstructed cross-sectional area, with sides *ca.* 6.3 Å.[1]

sulphides. Esters are particularly favoured as guest species. A major exception to this list of functionalities is the behaviour of phenols which will be discussed later.

A major problem in studying the detailed interaction of host and guest in these compounds using single crystal X-ray crystallography is the incongruent symmetry of the two components. This difficulty is compounded by disorder of the guest within the highly ordered host lattice. Thus the structure of $(\mathbf{1})_3\cdot$(ethyl acetate) was refined to give a structure factor residual of 0.049 without consideration of the guest molecules within the canals.[5] Low-angle scattering and difference map data supported the presence of disordered guest molecules in the structure. In the structures presented here these difficulties have been tackled by employing guests with their own symmetry and in some cases containing heavy atoms.

These considerations are well illustrated by the helical tubulate compound $(\mathbf{1})_3\cdot$(thiophene). The planar guest is placed along one face of the triangular canal. However, there are three such equivalent canal faces and since the thiophene molecule has pseudo 5-fold symmetry it may adopt five rotational positions and still remain aligned with the canal wall. The space-filling representation shown in Figure 4 therefore shows a typical guest arrangement within one canal of the inclusion compound. Similarly, other Figures in this paper show typical orientations of guests.

Figures 5 and 6 illustrate the helical tubulate inclusion compound $(\mathbf{1})_3\cdot(\text{monoglyme})_{0.75}$. The first shows a slice across one canal with the guest fitting neatly into the central region, while the other presents a side view with one of the six surrounding diol molecules removed to show the guest orientation along the canal direction.

Di-iodine can also be trapped within crystalline diol **1**. Crystalline material from a solution of the diol and di-iodine in ethanol had the composition $(\mathbf{1})_3\cdot(\mathrm{I}_2)_{0.5}\cdot(\text{ethanol})_{0.5}$. The crystal structure (Fig 7) showed that the di-iodine guests were located centrally within the canal with an I···I separation of 11.4 Å, but failed to reveal the ethanol. However, the latter was clearly indicated by solution ^{1}H-NMR measurements. It is presumed that O···I interactions, similar to those noted in cyclodextrin inclusion compounds of di-iodine,[6-8] stabilize the combination since only CH···I van der Waals attractions are possible between the di-iodine and the host walls. This inclusion compound is believed to be the first where di-iodine molecules, as opposed to polyiodide species, are included in a parallel tubular lattice.

These crystal structures reveal that the host lattice of **1** can alter its dimensions to accommodate guests. The values of *a*, *b* for these three materials are 12.4083(5), 12.0416(3), and 12.068(2) Å respectively, showing that the canal cross-section can alter significantly to include the thiophene guest. In contrast, the

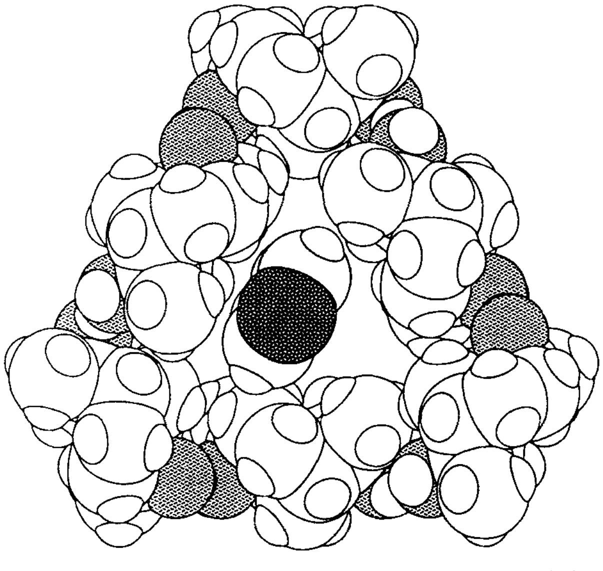

Figure 4 A section through one canal only of the helical tubulate $(\mathbf{1})_3\cdot$(thiophene) showing one typical orientation of the guest along one edge of the canal. In this, and subsequent Figures, the oxygen atoms of the host are stippled and the atoms of the guest are shaded or otherwise marked for clarity.[4]

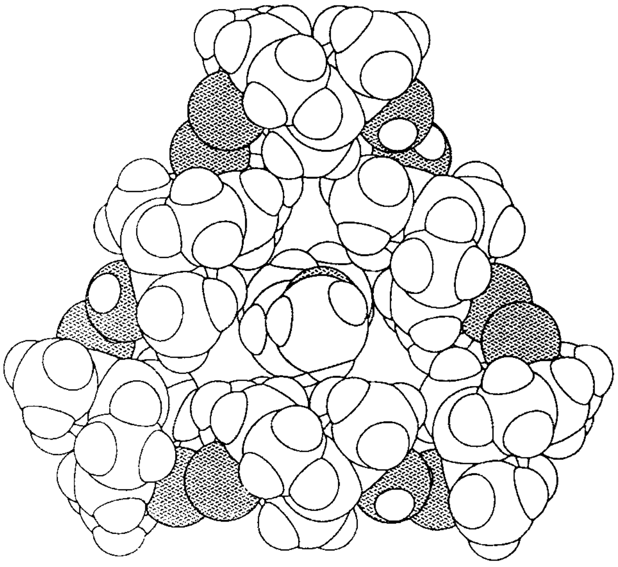

Figure 5 Projection view in the *ab* plane of one canal only of $(\mathbf{1})_3\cdot(\text{monoglyme})_{0.75}$ indicating the centrally situated guest molecule. Comparison with Figure 4 reveals the decrease in canal cross-section caused by the shorter *a,b* lengths.[4]

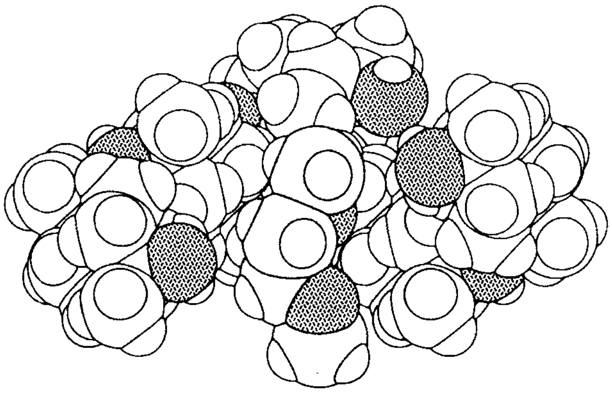

Figure 6 Side view of Figure 5 with the canal axis vertical and one of the six diol molecules removed to reveal the position of the monoglyme guest along the canal.[4]

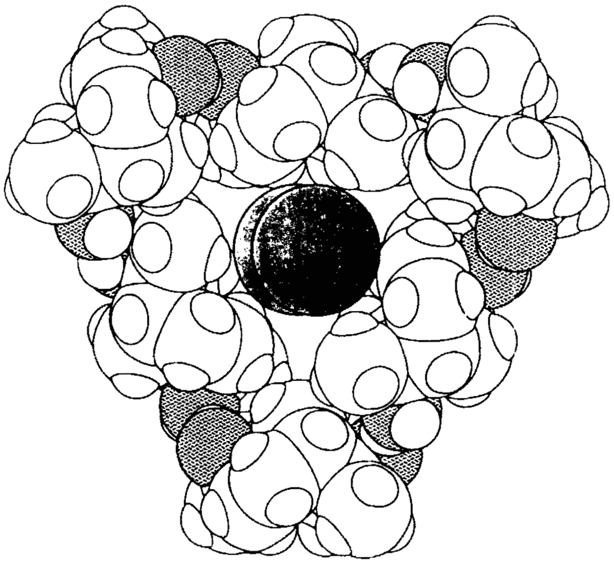

Figure 7 Projection view of one canal only of the helical tubulate $(\mathbf{1})_3 \cdot (I_2)_{0.5} \cdot (\text{ethanol})_{0.5}$. The di-iodine guest is shown centrally located within the canal, but the ethanol co-guest is not revealed by the crystallographic determination.[4]

values of *c* (the canal axis direction) are almost constant at 6.9702(4), 7.0110(2), and 6.984(3) Å respectively. This pattern of behaviour is also shown by the other diol hosts. Consequently there is a size limitation for guests in each of these host lattices and the likelihood of a particular guest being included or excluded can be predicted with good accuracy.

Diol 2 helical tubulates

The helical tubuland lattice formed by diol **2** has a trefoil-shaped cross-section (see Fig 1). The canals are now larger and have an unobstructed cross-sectional area of approximately 30.2 Å^2. As a consequence, bulkier guests can fit into the crystal lattice.[9] Guests resulting in helical tubulates include ethyl acetate, carbon tetrachloride, carbon tetrabromide, 1,1,1-trichloroethane, ethyl benzene, 1,2-dibromoethane, 1,3-dibromopropane, *n*-butyl benzene, 1,4-dibromobutane; chlorocyclohexane, *o*-xylene, *m*-xylene, *p*-xylene and di-*n*-butyl ether.

Examples shown here are the helical tubulates $(\mathbf{2})_3 \cdot (CCl_4)_{1.2}$, $(\mathbf{2})_3 \cdot$(1,3-dibromopropane), and $(\mathbf{2})_3 \cdot$(*o*-xylene)$_{1.2}$. In each case (Figs 8–10) it is noteworthy how the typical guest orientations are arranged to maximize van der Waals contacts with the canal walls.

Other guests result in an alternative type of inclusion system, the ellipsoidal clathrate type, which is discussed later in this paper.

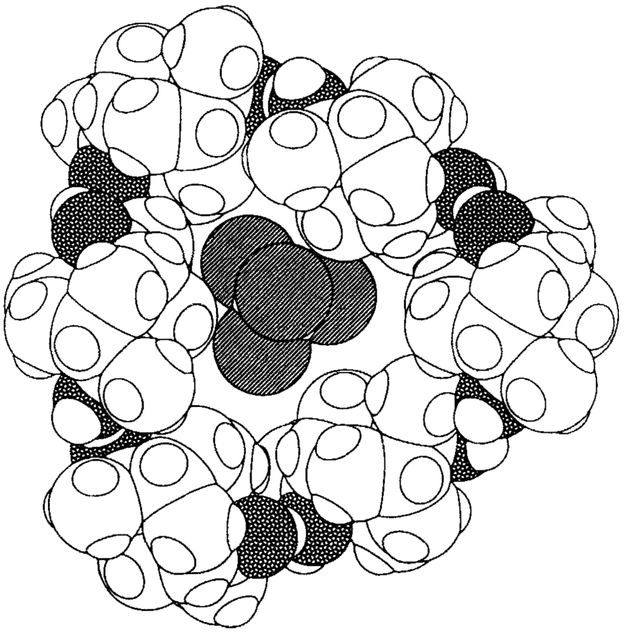

Figure 8 Typical orientation of carbon tetrachloride in one canal of the helical tubulate $(\mathbf{2})_3 \cdot (CCl_4)_{1.2}$ showing how the guest maximizes van der Waals contact with the canal walls.[9]

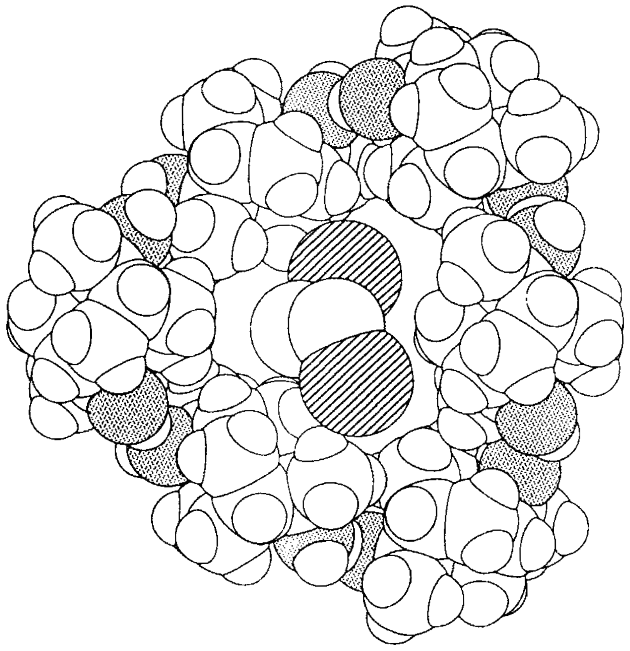

Figure 9 One canal only of the inclusion compound $(\mathbf{2})_3 \cdot$(1,3-dibromopropane) with the larger guest now occupying most of the available void space.[9]

Diols 3 and 5

The crystal structures of these solvent-free diols were found to retain the helical tubuland lattice.[10,11] However their canals are already largely occupied by parts of their own structures as indicated in Figure 1. As a result, despite having very small volumes of space available, they are unable to form inclusion compounds.

Diol 4 helical tubulates

The unobstructed cross-sectional area of the canals of crystalline **4** is *ca.* 34.7 Å^2, with a 6-pointed star shape

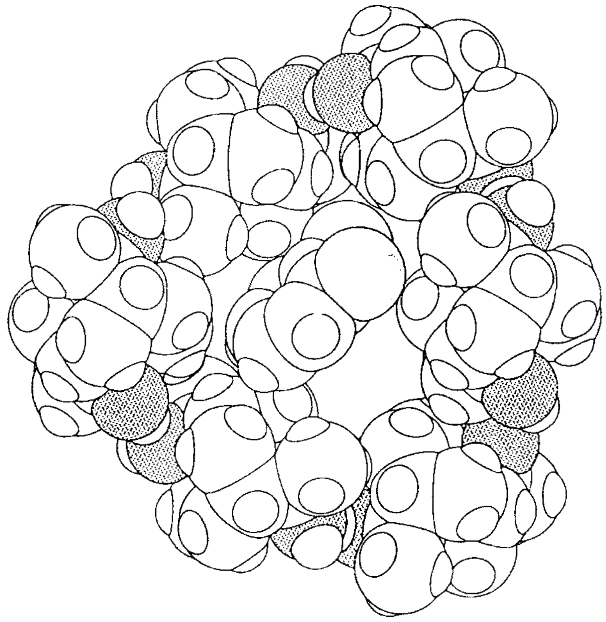

Figure 10 Projection view of one canal of $(\mathbf{2})_3\cdot(o\text{-xylene})_{1.2}$ showing how the planar guest typically orientates itself along one edge of the trefoil-shaped canal. Hydrogen atoms of the methyl groups of the guest are omitted.[9]

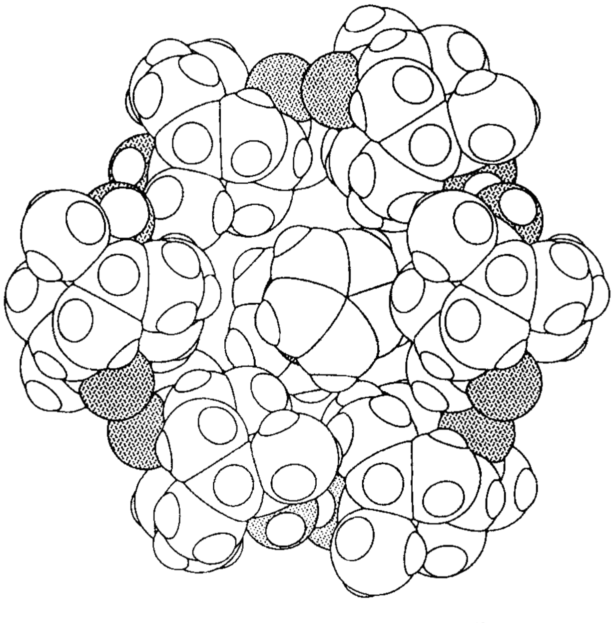

Figure 11 Structure of the helical tubulate $(\mathbf{4})_3\cdot(\text{ferrocene})_{0.75}$ showing the tilted orientation of the ferrocene guest in the host canal.

(see Fig 1). This area is the largest of the five original helical tubuland diols and relatively large guest molecules can be accommodated.[12] The illustration in Figure 11 shows how ferrocene is arranged in one such canal of $(\mathbf{4})_3\cdot(\text{ferrocene})_{0.75}$. Ferrocene has previously been included in the thiourea canal host lattice.[13]

So far the longest guest molecule trapped is squalene. The crystal structure of the inclusion compound $(\mathbf{4})_3\cdot(\text{squalene})_{0.23}$ shows how the guest can fit tightly within the canal (Fig 12), and how the squalene molecule is arranged within the helices of the host (Fig 13). The molecules of diol **4** at the front of this view have been removed to reveal the worm-like

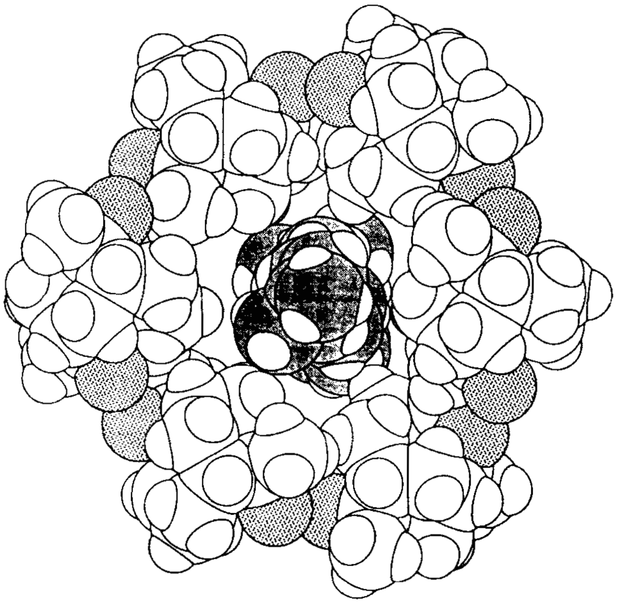

Figure 12 View along one canal of $(\mathbf{4})_3\cdot(\text{squalene})_{0.23}$ showing how the guest fits neatly within the available canal cross-sectional area.

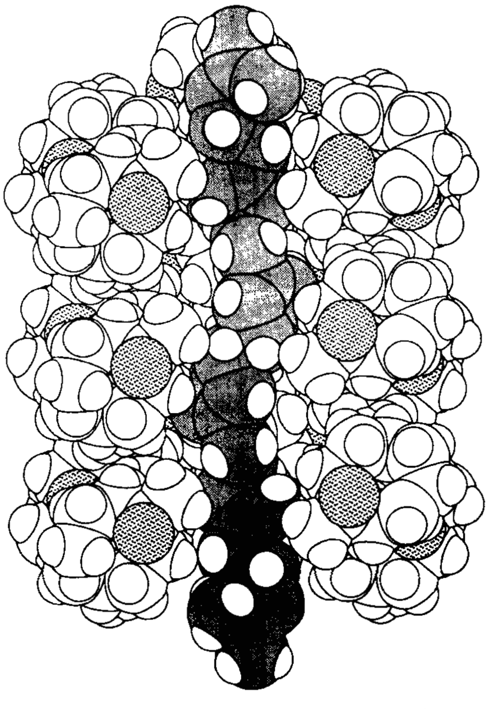

Figure 13 Side view of one canal of the helical tubulate $(\mathbf{4})_3\cdot(\text{squalene})_{0.23}$ with one vertical column of diol host molecules removed to show the squalene guest.

guest molecule. These results should be compared with the earlier hexa-host inclusion compound of squalene and hexakis(*p*-t-butylphenylthiomethyl)benzene.[14]

Diol 2 ellipsoidal clathrates

Diol **2** is also capable of forming an alternative type of inclusion system, the ellipsoidal clathrate type, with space group $I4_1/acd$. This is produced when the guest molecules are small in size, with most monosubstituted benzenes, and most disubstituted benzenes except the xylenes. Guests resulting in ellipsoidal clathrates include acetone, acetonitrile, dichloromethane, benzene, toluene, nitrobenzene, benzyl cyanide, chlorobenzene, *p*-dichlorobenzene, *p*-dibromobenzene, *p*-bromotoluene and *p*-nitrotoluene.[9]

The host lattice of the ellipsoidal clathrate structure is shown in Figure 14, with hydrogen atoms omitted for clarity. In this type of lattice both diol enantiomers are present. One enantiomer forms a double spiralling hydrogen-bonded chain around a 4_1 screw axis and the other a similar arrangement around a 4_3 screw axis. Four parallel canals are produced surrounding each screw axis. However these are constricted rather than being open tubes as for the helical tubuland structure. The resulting ellipsoidal-shaped cavities enclose the guest molecules as a clathrate. Successive cavities down a canal are orthogonal as illustrated in Figure 15 for the compound $(\mathbf{2})_4\cdot$(benzene).[15]

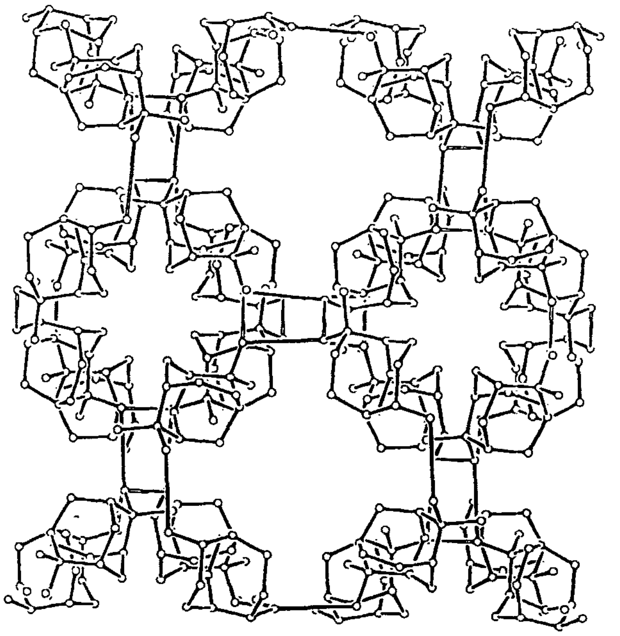

Figure 14 Representation of the host lattice in crystalline $(\mathbf{2})_4\cdot$(benzene) with all hydrogen atoms omitted and hydrogen bonds shown as hollow bonds. The star-shaped motifs result from the hydrogen-bonded doubly spiralling chains of diol molecules (one enantiomer clockwise, the other anticlockwise). Between these, the cross-shaped sites are the positions of the vertical constricted canals which contain the guest molecules.

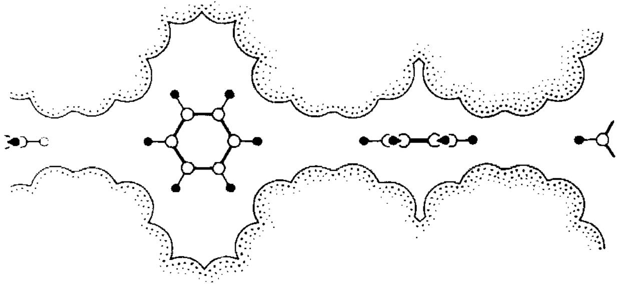

Figure 15 Representation of the constricted canals and the ellipsoidal cavities containing benzene guests in the ellipsoidal clathrate structure $(\mathbf{2})_4\cdot$(benzene). Successive cavities are orthogonal along each canal as shown.[15]

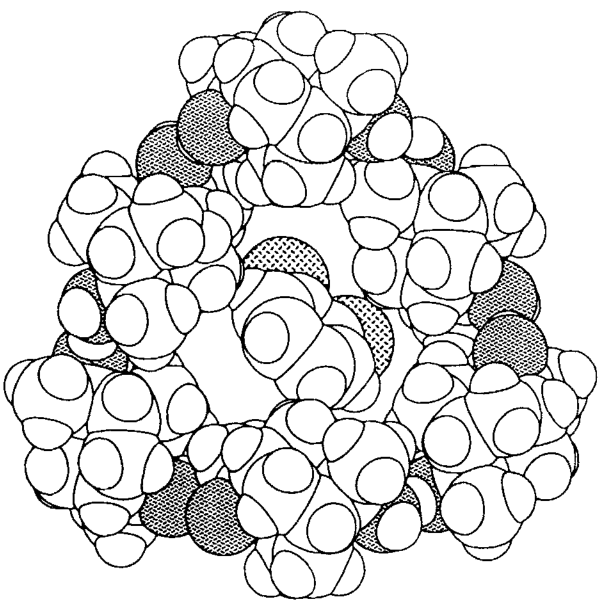

Figure 16 View of the *o*-dichlorobenzene guest within the helical tubulate compound $(\mathbf{2})_3\cdot$(*o*-dichlorobenzene).[16]

Since both the helical tubulate and ellipsoidal clathrate inclusion structures are produced using diol **2**, both arrangements must have almost identical free energies. The choice of guest molecule is sufficient to change from one type to the other. Consideration of patterns of behaviour and molecular modelling experiments led us to suspect that certain guests might be able to yield crystals of both inclusion types under appropriate conditions. This has now been demonstrated for several guests including chloroform, bromobenzene, and *o*-dichlorobenzene.[16]

For example, if **2** is allowed to crystallize from *o*-dichlorobenzene solution at 0°C then the crystal polymorph which dominates is the helical tubulate type. Figure 16 shows the crystal structure of one canal only of the helical tubulate inclusion compound $(\mathbf{2})_3 \cdot$(*o*-dichlorobenzene).

In contrast, if **2** is allowed to crystallize from *o*-dichlorobenzene at room temperature then the ellipsoidal clathrate type is the polymorph which dominates. Two views of the crystal structure of the ellipsoidal clathrate inclusion compound $(\mathbf{2})_4 \cdot$(*o*-dichlorobenzene) are shown. Figure 17 shows one turn of four diol molecules with the guest nesting on top. Addition of a further four molecules of diol **2** encloses the *o*-dichlorobenzene guest in its ellipsoidal cavity. This is now only just visible through the constriction of the canal in Figure 18. If warmed in a sealed capillary this structure is unchanged, but the helical tubulate form is transformed into its ellipsoidal clathrate polymorph. These findings indicate that the latter is the more stable crystal type and the one which will be favoured if the guest has a size and shape that is compatible with the dimensions possible for the ellipsoidal cavities. Consequently, the helical tubulate type is produced with aliphatic or elongated guests and with alkylbenzenes more alkylated than toluene. This dimorphic behaviour is not shown by diols **1** (smaller canal cross-section) or **4** (larger canal cross-section).

Helical tubuland diol:phenol co-crystalline compounds

Diols **1**, **2** and **4** form stoichiometric co-crystalline compounds with certain phenols. The diol and phenol molecules are intimately hydrogen-bonded together, with molecules of the phenol replacing one of the three eclipsed arms of the original helical tubuland spine. A major structural consequence is that the resulting lattice changes from a three- to a two-dimensional hydrogen-bonded network involving layers.[17]

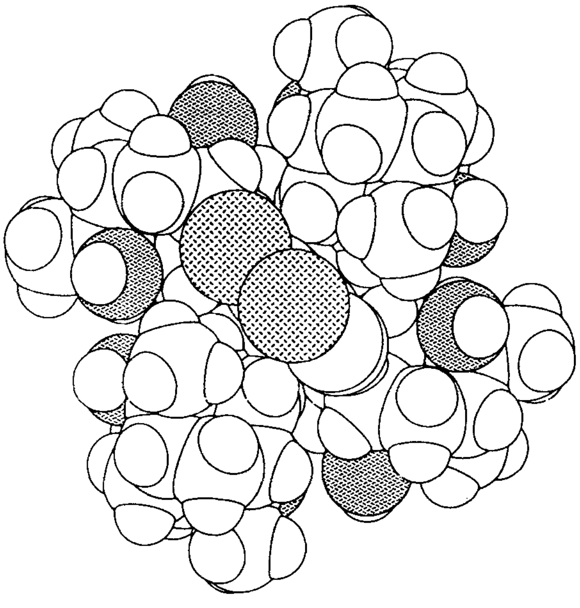

Figure 17 The bottom half of one ellipsoidal cavity in the ellipsoidal clathrate compound $(\mathbf{2})_4 \cdot$(*o*-dichlorobenzene) showing the guest molecule nesting in the hollow produced by four diol molecules.[16]

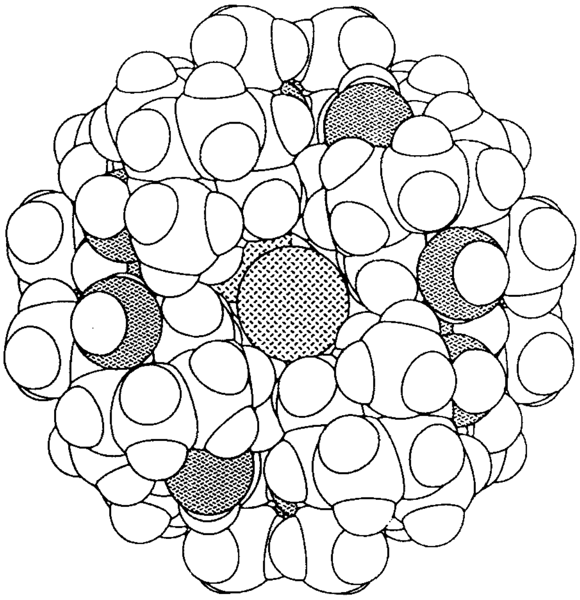

Figure 18 Addition of a further four molecules of **2** to Figure 17 sealing the *o*-dichlorobenzene guest within its ellipsoidal cavity. Only one of the chlorine atoms now remains visible through the constriction in the canal.[16]

These features are illustrated here for the case of diol **1** and *p*-chlorophenol. Figure 19 shows a section of one hydrogen-bonded spine in the helical tubuland lattice of pure **1**. In the co-crystalline compound $(\mathbf{1})\cdot$(*p*-chlorophenol) the new arrangement is altered to that shown in Figure 20. A structural feature frequently encountered in crystal structures of chloro compounds is association of the halogen atoms. Thus the crystal structure of this material (Fig 21) can be understood in terms of two previously recognized types of intermolecular attraction: the hydrogen-bonded trigonal spine,[1] and the Cl···Cl···Cl··· interaction.[18] Only one diol enantiomer can be accommodated in the hydrogen-bonded spine, making this part of the structure chiral. However the resulting layers alternate with those of the opposite chirality, thus producing an overall achiral structure in space group $P2_1/c$. The co-crystalline compound $(\mathbf{2})\cdot$(*p*-chlorophenol) is isostructural. However, only some phenols and some helical tubuland diols exhibit this novel behaviour. Although studies of this phenomenon are still in progress, it looks as if the diol and the phenol components[19] must both belong to those which have inclusion chemistry in their own right.

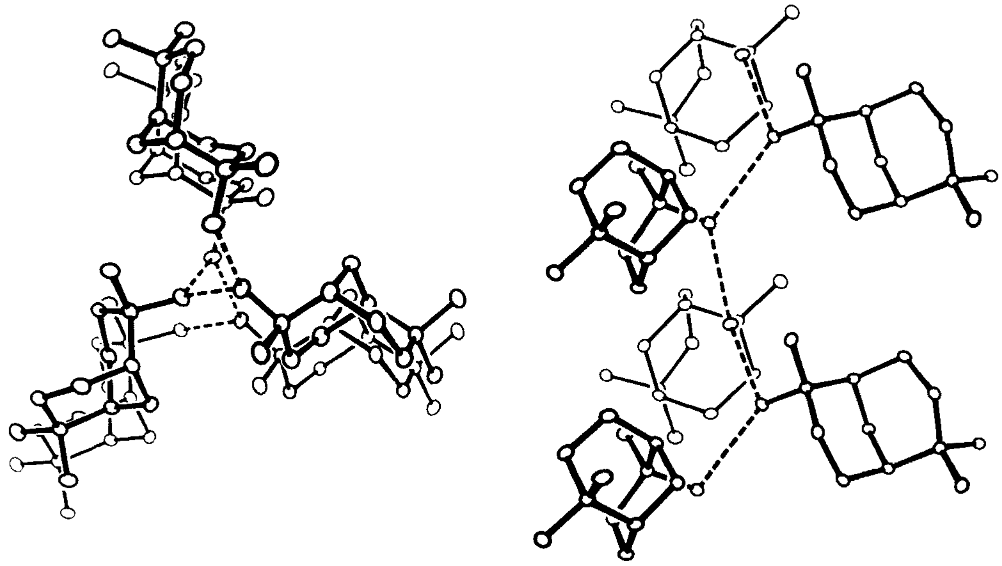

Figure 19 Part of a typical tight spiral spine of diol **1** molecules which constitute the structural core of the helical tubuland lattice. Left: projection in the *ab* plane. Right: the canal axis *c* is vertical.[17]

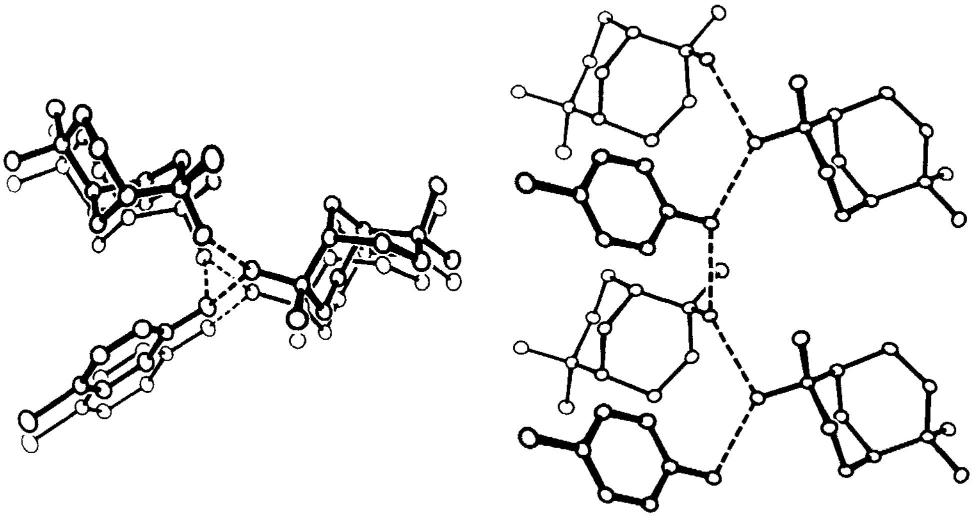

Figure 20 Part of a typical hydrogen-bonded spiral spine in the co-crystalline compound (**1**)·(*p*-chlorophenol). The phenol molecules have replaced the diol molecules in one arm of the sub-structure.[17]

CONCLUSIONS AND COMMENTS

Preliminary investigation of the potential inclusion chemistry of the helical tubuland diols **1**–**5** has been carried out. Diols **1**, **2** and **4** are potent inclusion hosts for a wide range of small guest molecules, and X-ray single crystal structural determinations of typical examples have been presented. The relationship between the helical tubulate and ellipsoidal clathrate inclusion structures formed by diol **2** has been explored in some detail. Early results on the co-crystalline behaviour of **1** and phenols are discussed.

A central theme behind our helical tubuland diol chemistry has been to explore the structural requirements for formation of this type of lattice. Such rules have been established and new host diols with particular canal sizes can be predicted in advance of synthesis.[20,21] Very recent work has led to further members of this family which also have inclusion properties. The intention has therefore been to develop a range of hosts with varied inclusion properties.

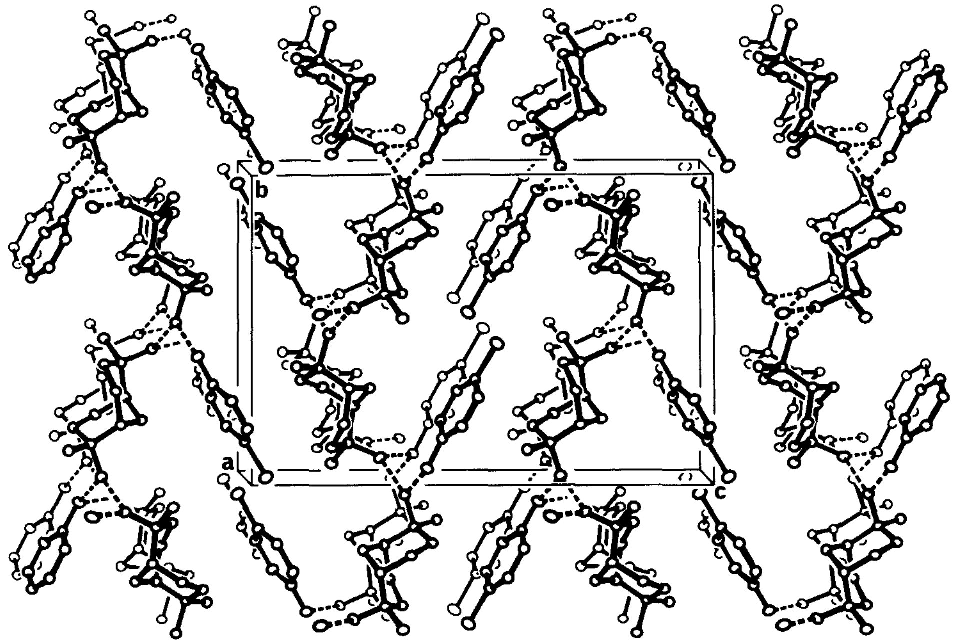

Figure 21 The unit cell of the co-crystalline material (1)·(*p*-chlorophenol). Eclipsed stacks of diol **1** molecules, *p*-chlorophenol molecules, and chlorine atoms are clearly visible.[17]

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