# THE DESIGN AND SYNTHESIS OF A FAMILY OF MULTIMOLECULAR HOST-GUEST INCLUSION COMPLEXES

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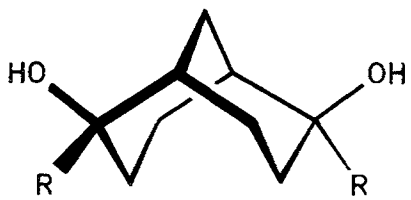
ABSTRACT. The discovery that *exo*-2,*exo*-6-dihydroxy-2,6-dimethyl-bicyclo[3.3.1]nonane (2) forms novel multimolecular canal-type inclusion complexes has led to a systematic study of related molecular structures. This synthetic programme has shown that diol (2) is the prototype of a family of host diols all with the same crystallographic space group $P3_121$, but with distinctly different canal shapes and dimensions. The structures of the first four members of this new family of hosts are described and contrasted.

## 1. INTRODUCTION

The bicyclic diol *exo*-2,*exo*-6-dihydroxy-2,6-dimethylbicyclo[3.3.1]-nonane (2) forms stable crystalline inclusion complexes when crystallised from a variety of common solvents. For example from ethyl acetate long trigonal needles of approximate composition $(diol)_3$.ethyl acetate (2E) are produced and forcing conditions ($60^{o}C$ under reduced pressure) are required to remove the guest solvent molecules from these crystals.




(1) R = H

(2) R = $CH_3$

(3) R = $CH_3$-$CH_2$

We have reported previously[1] that the crystal structure of (2E) is composed of diol molecules linked by hydrogen bonds to form helices. Two independent helices spiral along the direction of the

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needle crystal enclosing a tubular canal as shown diagrammatically in Figure 1. Consequently each crystal is composed only of one enantiomer of the diol.

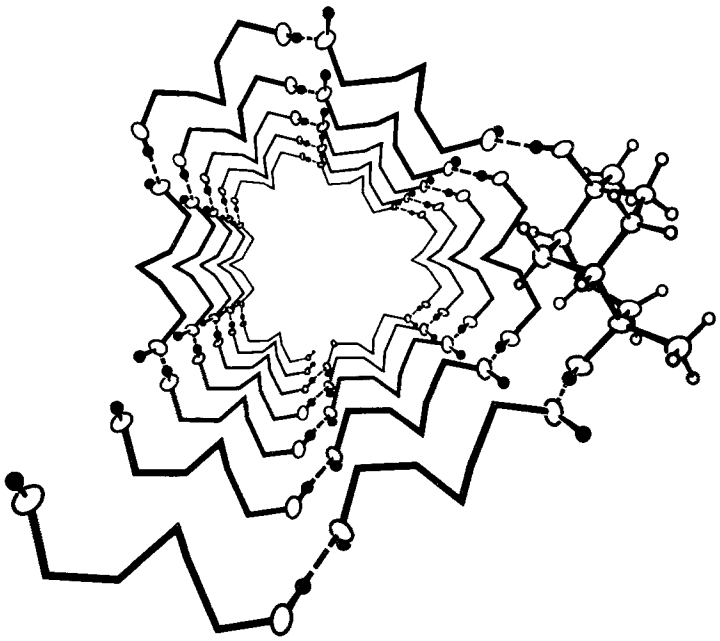


Fig. 1. Perspective view of the helical sequence of hydrogen bonded diol molecules in one canal of (2E). All except one molecule are shown diagrammatically as bridge linkages of the two OH groups. [*J. Chem. Soc., Chem. Commun.*, 992 (1979)].

Each double helix is linked to the diols of six surrounding double helices by tight spiral spines of hydrogen bonds (circled in Figure 2) and resulting in a series of parallel, tubular, chiral canals which contain the disordered ethyl acetate molecules. Both the canals and spines surround crystallographic threefold screw axes in the space group $P3_121$ (or its enantiomorph) and the canals have an approximately triangular cross section.

This type of structure is an example of an organic multimolecular inclusion complex[2], dependent on the entire packing arrangement of host molecules providing void spaces which can be occupied by guest molecules. Such materials include the familiar examples of the clathrates formed by Dianin's compound[2], and by hydroquinone[3], and the canal complexes formed by urea with n-alkanes[3].

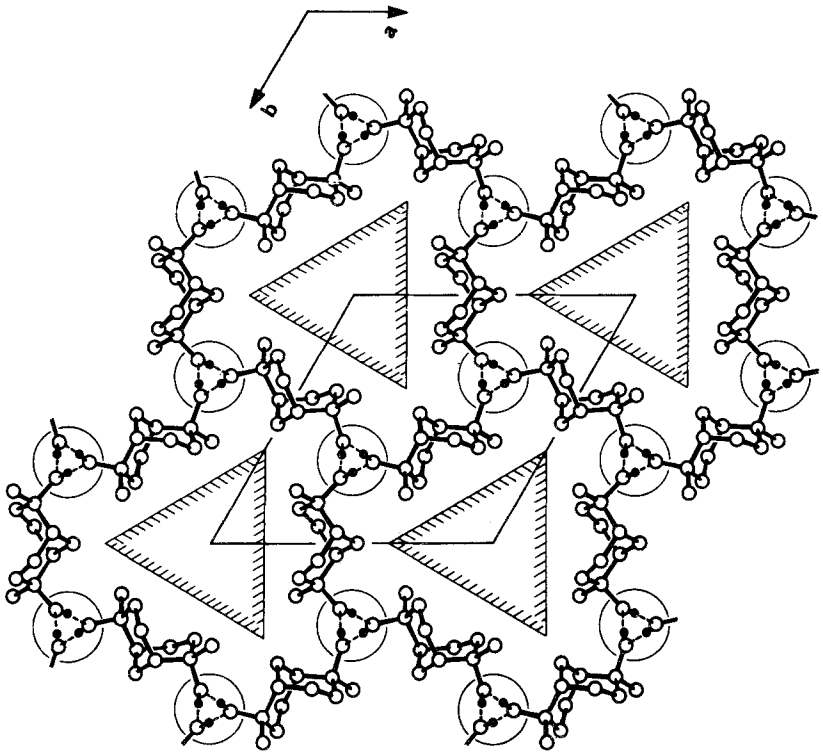


Fig. 2. Projection view, parallel to the threefold screw axes, of the diol host network of (2E). The filled circles and dotted lines represent OH hydrogen atoms and hydrogen bonds respectively. The canals are outlined as triangles, and the hydrogen bonded spines are circled. Hydrocarbon hydrogens are omitted for clarity. [*J. Chem. Soc., Perkin Trans. II*, 1159 (1982)].

## 2. CONSIDERATIONS OF STRUCTURE AND SYNTHESIS

The structure of the organic multimolecular inclusion complexes must be contrasted with that of the unimolecular complexes[2] formed from hosts such as crown ethers, cryptands and cyclodextrins, where only one host is involved in complexation with the guest species. In recent years the design and synthesis of unimolecular host molecules has reached sophisticated levels of ingenuity, as have the applications of such systems.

In contrast the development of new multimolecular complexes has proven to be less straightforward[2]. The following may be identified amongst the reasons:

(i) Most examples have been discovered by accident rather than by

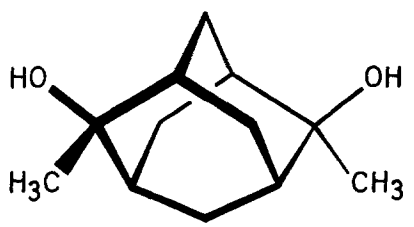
deliberate design and synthesis.
(ii) Crystal space groups generally cannot be predicted in advance for a particular molecular structure.
(iii) Modification of known hosts frequently has resulted in a new, more compact crystal packing arrangement lacking the necessary void spaces for guest molecules.
(iv) While molecular models have been invaluable in designing unimolecular hosts, they are of less use for multimolecular systems since there are too many variables in crystal structure.

Although these restraints are serious they are not insurmountable and may be viewed alternatively as presenting a novel challenge in organic synthesis which several groups have now accepted[4].

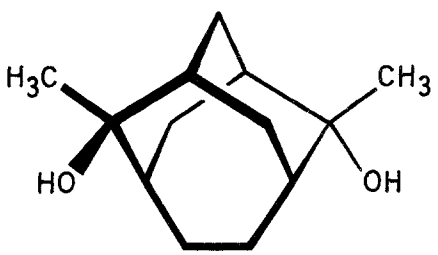
## 3. SYSTEMATIC SYNTHESIS

It appeared likely that the inclusion properties of diol (2) might also be shared by other compounds related in molecular structure. A systematic study of other alicyclic diols was therefore commenced with the intention of obtaining a family of diol hosts with a gradation of properties.

In the initial crystal structure(2E) the C2 and C6 methyl groups were apparently uninvolved in the packing arrangement and therefore the homologues (1) and (3) were the next compounds studied. Both diols adopted totally different close packed structures with no cavities[5]. Likewise the adamantane analogue (4)[6] was found to possess yet another crystal without void spaces. The disparate behaviour of these three compounds, despite their being very closely related in structure to the original diol host (2), provides a clear illustration of the structural subtleties which can be involved in this area.




(4)




(5)

In contrast to these cases, the two isomeric homoadamantane diols (5) and (6) both adopted the same crystallographic symmetry $P3_121$ as the original diol.

Tricyclo[4.3.1.1$^{3,8}$]undecane-2,7-dione[7] reacted with methyl lithium to produce *syn*-2,*syn*-7-dihydroxy-2,7-dimethyl-tricyclo[4.3.1.1$^{3,8}$]undecane (5) in 83% yield[8,9]. The projection view of the ethyl acetate complex (5E) shown in Figure 3 reveals how the differences in host diol structure and orientation have altered the canal geometry resulting in a new tri-lobed cross section.

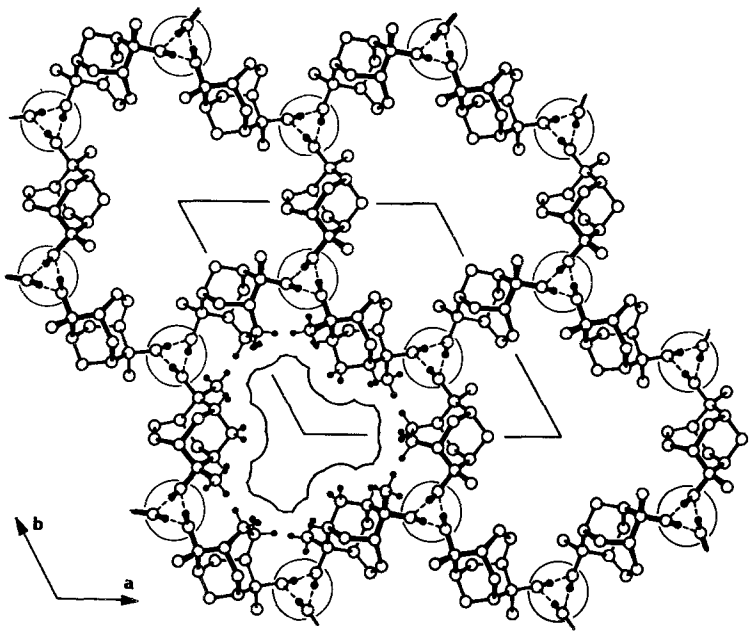
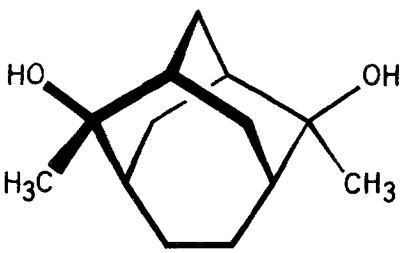
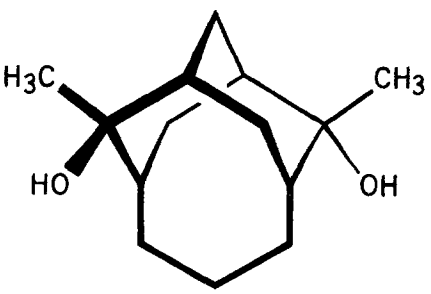



Fig. 3. Projection view of the host diol network in the crystal structure of (5E). The helical spines of hydrogen bonds are circled. Selected hydrogen atoms included with van der Waals radii define the projected cross section of one canal. [*J. Chem. Soc., Chem. Commun.*, 889 (1983)].




(6)




(7)

The same dione underwent Wittig reaction (74%), followed by hydration (55%) to yield the epimeric diol *anti*-2,*anti*-7-dihydroxy-2,7-dimethyltricyclo[4.3.1.1$^{3,8}$]undecane (6). Crystals of this substance from ethyl acetate (6E) were found not to trap this solvent but nonetheless to have the same crystallographic symmetry as (2E). The projection view shown in Figure 4 indicates how in this case the canals are now nearly completely filled by the diol molecules themselves.

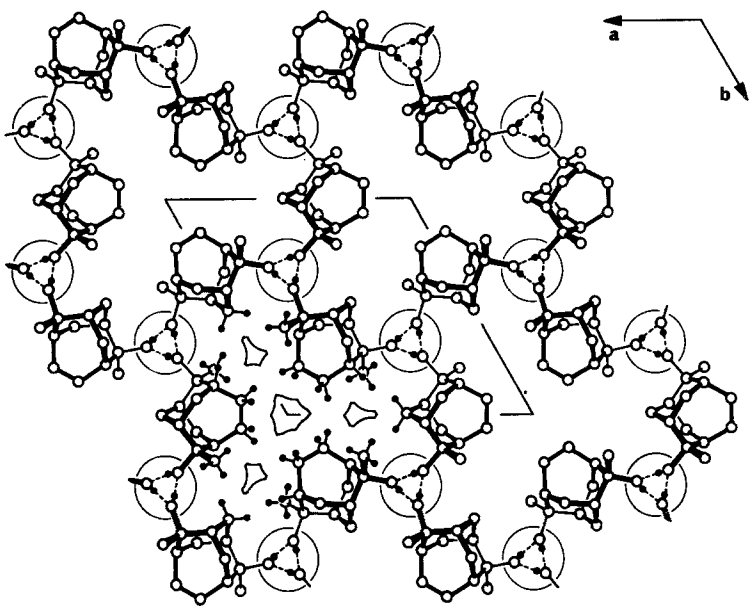



Fig. 4. Projection view of the diol network of (6E). Hydrogen atoms with their van der Waals radii are included for one canal only.

The fourth diol of this crystallographic family is *syn*-2,*syn*-8-dihydroxy-2,8-dimethyltricyclo[5.3.1.1$^{3,9}$]dodecane (7). Crystals grown from benzene (7B) have the structure shown in Figure 5 with a six-lobed canal cross section.

Although benzene is trapped in this solid it appears to be mainly occluded in pockets within the crystal rather than being present in the canals themselves. Presumably as the crystal develops the solvent cannot fit the canals properly, however, not all is excluded from the crystal in time and so it ends up in occlusion faults within the solid.

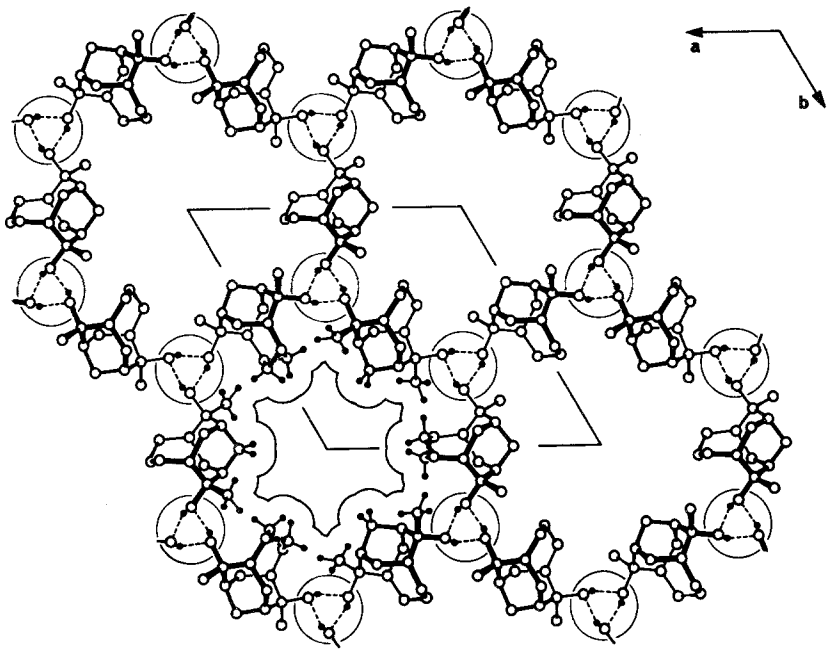



Fig. 5. Projection view of the diol network of (7B). The projected cross section of one canal is shown in detail; other hydrocarbon hydrogens are omitted for clarity. Within this canal alternative conformations of the propano bridge are indicated.

## 4. CONCLUDING REMARKS

Our first objective in commencing work in this area was to demonstrate that deliberate design and synthesis would lead to the discovery of a family of canal forming diol hosts. The results presented show that this target has been achieved and that alteration of host diol structure does cause marked change in the size and shape of the canals. Figure 6 provides a comparison of the cross section of the canals of the first four members of this family.

It should be emphasised, however, that the views shown in Figures 2 to 6 are a projection of the narrowest canal section. Since these canals are bordered by hydrogen bonded chains of diol molecules there are wider cross sections available to potential guests. We are currently working on more quantitative measurement of these cavity sizes.

Next we wish to delineate the exact structural requirements

for a molecule to belong to this family or behave otherwise. This will enable us to tackle the synthesis of more complex cases with confidence and allow the interesting potential applications of these materials to be investigated in a systematic manner.

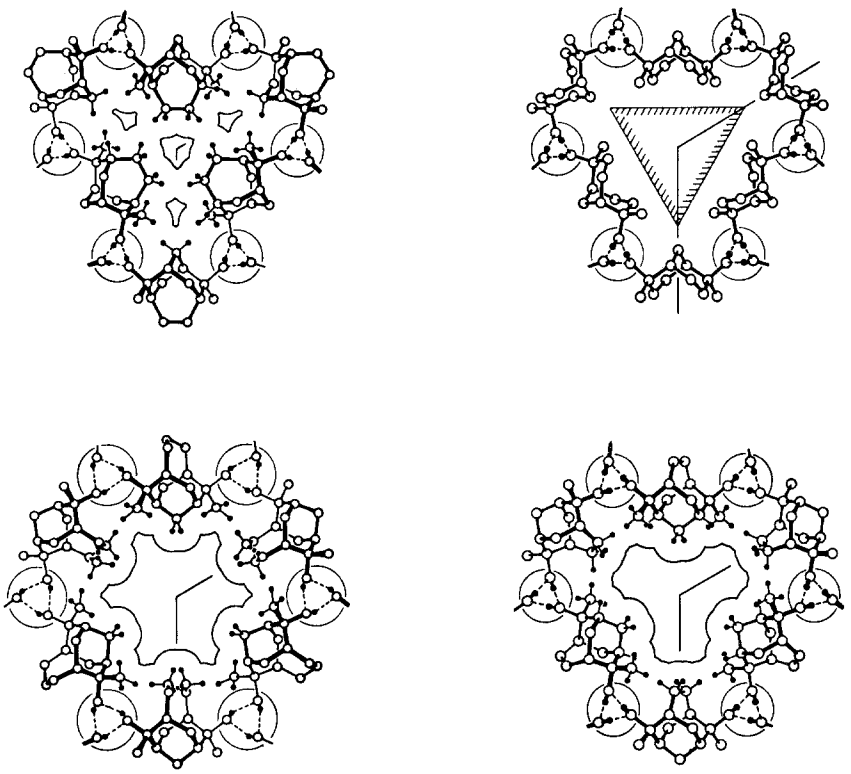


Fig. 6. Comparison of the differing canal cross sections.

## 5. REFERENCES AND NOTES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9 In this paper the terms *syn-* and *anti-* are used to define hydroxy substituents relative to the unique ethano or propano bridge present in the diol.

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