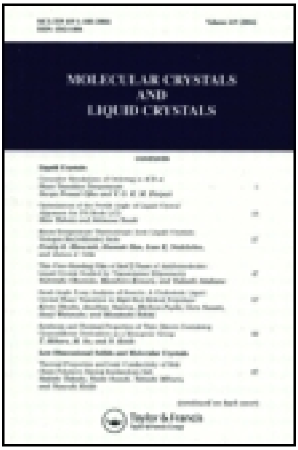

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Role of the $(O\text{-}H)_6$ Synthon in the Construction of Organic Inclusion Compounds

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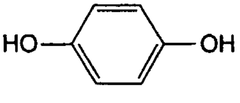
The racemic diol **5** crystallises from ethanol in the orthorhombic space group *Cmca* (*a* 19.05, *b* 14.93, *c* 10.12 Å) as the cocrystalline solid $5{\bullet}C_2H_5OH$. In contrast, the racemic diol **6** crystallises from benzene in the cubic space group *Ia3* (*a* 19.85 Å) as a clathrate compound. The principal supramolecular synthon involved in both cases is a cyclic hexamer of hydrogen bonded hydroxy groups, $(O\text{-}H)_6$. While the former cycle is almost planar, rather uncommonly the latter is cyclohexane-like in geometry. A major function of the $(O\text{-}H)_6$ cycle is to allow efficient packing between opposite enantiomers within the crystal lattice.

Keywords: hydrogen bonding; inclusion compounds; host-guest compounds; supramolecular synthons; hydroxy groups; enantiomeric packing

INTRODUCTION

The ability of hydroxy groups to associate via ···H-O···H-O···H-O··· hydrogen bonding into cyclic hexamers $(O\text{-}H)_6$ has been known for many years. This supramolecular synthon[1] is of historical significance since it helps create the host lattices of two classic groups of clathrate compounds, namely those formed by hydroquinone **1**[2] and those formed by Dianin's compound **2**.[3]



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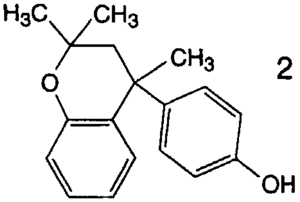

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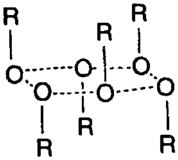
In these structures six phenolic host molecules each contribute one hydroxy group to the hexamer. In each $(O\text{-}H)_6$ cycle the adjacent contributing host molecules are alternately subtended up-down-up (etc.) relative to the ring. This stereochemical preference was later exploited by MacNicol in the design of his entirely new hexahost family of compounds.[4]



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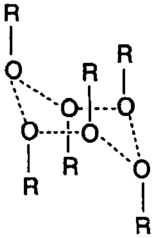

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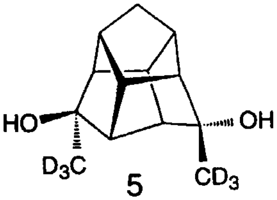
Omitting the light hydrogen atoms and considering only the six oxygen atoms, these $(O\text{-}H)_6$ cycles are often nearly planar (as in **3**). A three-dimensional cyclohexane-like structure (as in **4**) is, however, also possible. In this paper we present some preliminary data on the prevalence of these two ring types, on two new hosts **5** and **6** which use the $(O\text{-}H)_6$ cycle in their inclusion compounds, and on the crystal-packing role of this synthon.



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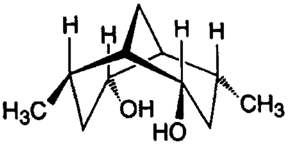

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RESULTS AND DISCUSSION

A Cambridge Structural Database[5] search (CSD; April 1999 version 5.17) for $(O-H)_6$ cycles present in crystal structures belonging to the rhombohedral, hexagonal, and cubic crystal systems (where threefold symmetry was especially likely) produced 57 hits. No exclusions were made on the basis of the residual values. All these cycles had the groups R alternately above, then below, the hydrogen bonded ring. Both phenol and alcohol hydroxy groups were noted forming $(O-H)_6$ cycles.

Considering the O···O···O angles, and completely ignoring the hydrogen atoms, a tetrahedral arrangement at oxygen would have an angle of 109.5^o while a planar structure would have a 120^o angle. The values recorded (Figure 1) ranged from 82.8^o to 126.9^o, but the mean value was 117.6^o. Hence there is a clear preference for a nearly planar $(O-H)_6$ cycle in these structures.

The corresponding O···O distances present in these structures (Figure 2) ranged from 2.61 to 2.98 Å, with a mean value of 2.75 Å. These values lie within the normal range of values encountered in hydroxy hydrogen bonding.

The cage diol 4,7-dimethylpentacyclo[$6.3.0.0^{2,6}.0^{3,10}.0^{5,9}$]-undecane-*anti*-4,*anti*-7-diol has been reported by us to form helical tubulate inclusion compounds if crystallised from solvents like acetone.[6] When crystallised, however, from ethanol it was observed to form a different type of inclusion product. The X-ray structure of its d_6-derivative **5** revealed that this involved $(O-H)_6$ cycles.

Racemic diol **5** crystallises from ethanol in the orthorhombic space group *Cmca* as the 1:1 compound $\mathbf{5}\cdot C_2H_5OH$. This material is a cocrystalline solid with its two components intimately hydrogen bonded together to form layers.

Molecules in the *ab* plane are linked along *a* as infinite chains in the sequence ···(-)-**5**···ethanol···(+)-**5**···ethanol···(-)-**5**···. Pairs of these chains link through hydroxy group hydrogen bonding involving $(O-H)_6$ cycles to produce double-stranded chains running along *a* (Figure 3).

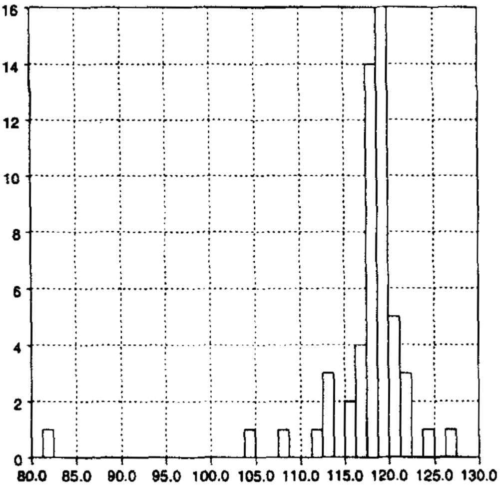

FIGURE 1 Plot of the number against value (in degrees) for the O···O···O angles found in the CSD survey of $(O\text{-}H)_6$ cycles.

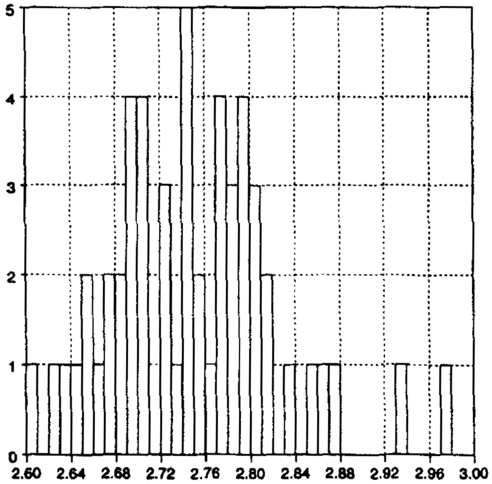

FIGURE 2 Plot of the number against value (in Å) for the O···O distances found in the CSD survey of $(O\text{-}H)_6$ cycles.

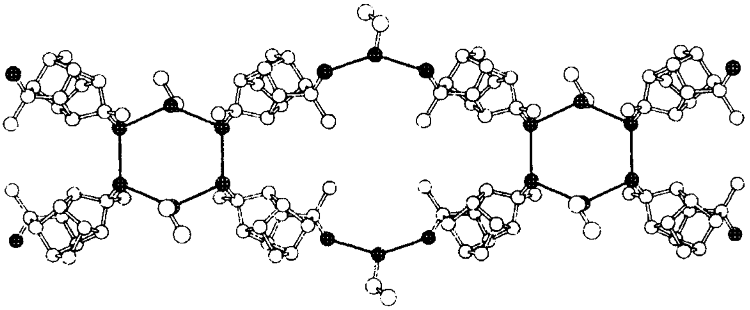

FIGURE 3 Formation of a double stranded chain of diol 5 and ethanol molecules along the *a* direction. Two complete $(O\text{-}H)_6$ cycles are shown in the plane of the page. The incomplete cycles continue up or downwards to create a layer structure. Oxygen atoms are indicated by cross-hatching, hydrogen atoms are omitted, and hydrogen bonds indicated as solid lines

Identical $(O\text{-}H)_6$ cycles are subtended above and below each double strand resulting in layers in the *ac* plane (Figure 4).

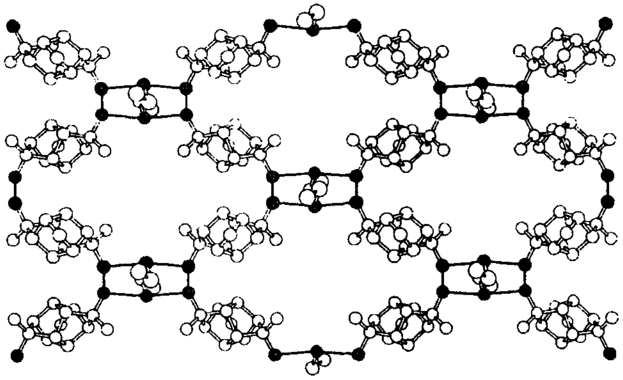

FIGURE 4 Part of a layer in the *ac* plane of the diol 5 and ethanol cocrystalline solid showing five complete, and several incomplete, $(O\text{-}H)_6$ cycles. All the $(O\text{-}H)_6$ cycles holding the lattice structure together are identical but occupy two different orientations.

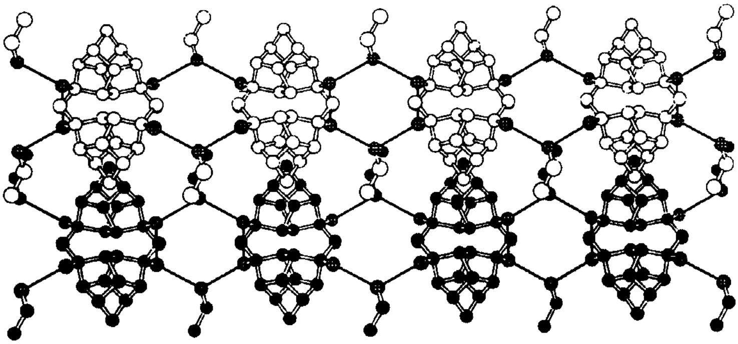

FIGURE 5 Parts of two neighbouring layers in the *ab* plane showing how these interleave and produce stacks of ethanol molecules along *c*. The carbon atoms of the two layers are white and black respectively.

The hydrophobic parts of adjacent layers interleave in the *b* direction, as shown in Figure 5, to complete the structure. Although stacks of ethanol molecules are present along *c* in this lattice they are not linked by hydrogen bonding.

The bicyclic dialcohol *endo*-4,*endo*-8-dimethylbicyclo[3.3.1]-nonane-*endo*-2,*endo*-6-diol **6** also forms inclusion compounds involving $(O\text{-}H)_6$ cycles. For example, racemic **6** crystallises from benzene in the cubic space group *Ia*3 as $(\mathbf{6})_3{\cdot}C_6H_6$. This material is a clathrate compound. There is one guest, represented here as a black sphere, on each side of a $(O\text{-}H)_6$ cycle at a distance of 8.6 Å from it (Figure 6). The two halves of each diol are related by twofold symmetry, and the $(O\text{-}H)_6$ cycle is generated by $\bar{3}$ symmetry at its centre. Each guest molecule is also located on a $\bar{3}$ symmetry site and is therefore disordered.

Comparison of the $(O\text{-}H)_6$ cycles involving diols 5 and 6

The $(O\text{-}H)_6$ cycle present in $\mathbf{5}{\cdot}C_2H_5OH$ contains two different O···O···O angles. That centred around the ethanol hydroxy group is

121.6°, while that centred around a diol hydroxy group is 116.3°. By coincidence all the O···O distances have the same value of 2.70 Å. Hence the hydrogen bonded cycle in this cocrystalline compound is roughly planar (Figure 7), in common with the majority of structures located in our CSD survey.

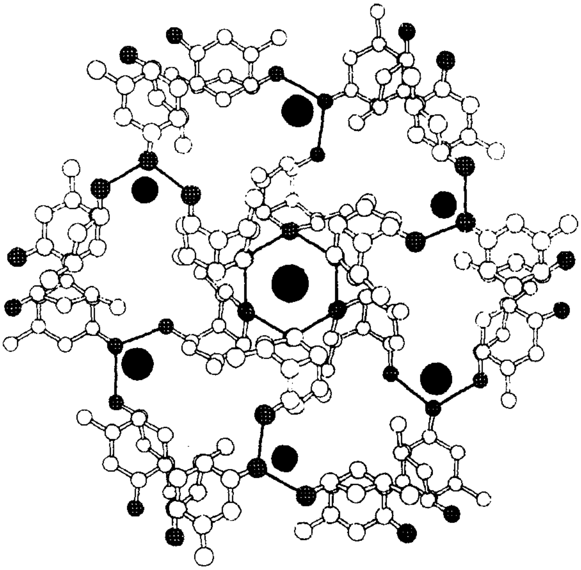

FIGURE 6 The lattice structure of (**6**)$_3$•C_6H_6 showing one complete, and several partial, (O-H)$_6$ cycles. Oxygen atoms are indicated by cross-hatching, all hydrogen atoms are omitted, and the hydrogen bonds are indicated by solid lines. The disordered benzene guest molecules are represented as black spheres.

In contrast, the (O-H)$_6$ cycle present in (**6**)$_3$•C_6H_6 is much more cyclohexane-like with all of its O···O···O angles equal to 104.3° (Figure 7). This is a rather uncommon outcome based on the findings of our CSD structural survey.[7] The O···O distance in this compound is also 2.70 Å.

Diol **6** is proving to be a versatile host for the inclusion of small organic guest molecules. For example it forms isostructural cubic compounds with diethyl ether and benzene. These, and other host-guest combinations, are currently under detailed investigation by us.

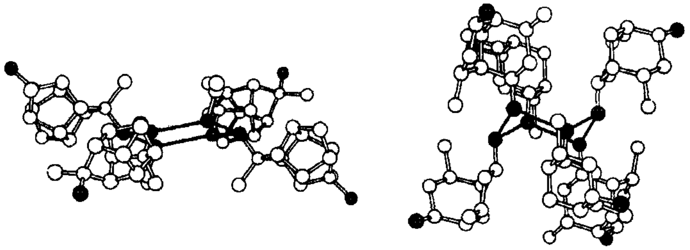

FIGURE 7 Comparison of the $(O\text{-}H)_6$ cycles present in the two inclusion compounds. Left: **5**$\cdot C_2H_5OH$, right: (**6**)$_3\cdot C_6H_6$. Oxygen atoms are designated by cross-hatching, hydrogen atoms are omitted, and hydrogen bonding is indicated by solid lines between the oxygen atoms.

Structural role of the $(O\text{-}H)_6$ synthon

In both cases described in this paper the racemic diol compounds were used and the resulting $(O\text{-}H)_6$ cycles were centrosymmetric. This was also true for all the cycles located during our CSD survey. In all these structures the hydroxy compounds involved were either achiral or racemic materials. We are unaware of any chirally pure hydroxy compounds which form an $(O\text{-}H)_6$ cycle, although this is structurally feasible. As part of our investigation we intend resolving the enantiomers of diol **6** to see how the enantiomerically pure compound behaves.

The role of the $(O\text{-}H)_6$ cycle in crystal packing is to provide a centrosymmetric site. In this way it provides a facile and convenient method for the two different enantiomers of a racemic hydroxy compound to associate efficiently within the lattice.

Acknowledgement

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[7] Figure 1 includes an outlier value of only 82.8° which is present in the guayacanin•acetone solvate structure, refcode GUAYAC: R.Y. Wong, K.J. Palmer, G.D. Manners and L. Jurd, *Acta Crystallogr., Sect. B,* **32,** 2396 (1976). This anomalous outcome appears to be caused by the influence of aryl edge-face attractions between the neighbouring host molecules.