

Host Molecule Design *via* Lattice Considerations. Crystal Structure of the Inclusion Compound between *cis*-1,4-Bis(9-phenylfluoren-9-yloxymethyl)cyclohexane and Dioxane (2 : 1)

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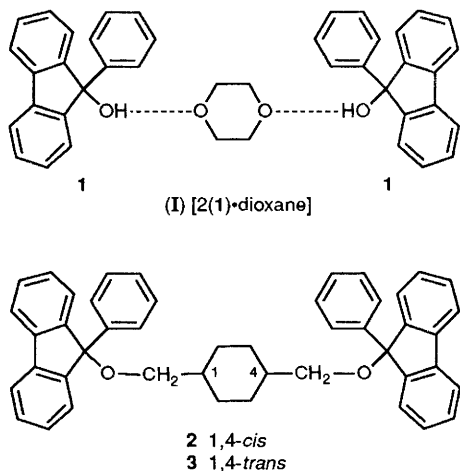
Two new host molecules, **2** and **3**, are described, representing a novel design strategy where H-bond interactions of a known inclusion compound are replaced by covalent links; the X-ray structure of the 2 : 1 (host : guest) inclusion compound of **2** with dioxane is reported.

Although crystalline inclusion compounds have been known since the early period of organic chemistry,¹ they remained accidental findings until recently, when some useful design criteria were developed.² They are based on particular features of the host molecule such as bulkiness, polarity or symmetry.³ On the other hand, lattice considerations have been used only rarely to design new inclusion structures.⁴ This is surprising, since crystalline inclusion formation is more of a lattice aggregate property than a molecular one. We report here a unique example where the framework of a known inclusion compound serves as a model for construction of new hosts.

Recent X-ray structure analysis of the dioxane inclusion compound of the 9-phenylfluoren-9-ol host **1**, with an unusual 4 : 3 host : guest stoichiometry, revealed the presence of two different types of guests in the crystal.⁵ Two of the three crystallographically independent dioxane molecules are involved in forming 2 : 1 host : guest associates *via* hydrogen bond interactions, whereas the third guest molecule is trapped in the voids between the H-bonded host-guest complexes by lattice forces only. The structure might also be regarded as an inclusion of the 'third' dioxane guest by the composite 2(1)-dioxane complex host **I**. This led us to the idea of synthesizing compounds analogous to the previous complex host **I** by substituting H-bond interactions for covalent links, and to test their clathrate forming ability. Accordingly, the novel diether type hosts **2** and **3** were prepared and investigated.

These compounds are based on a molecular model study. They were synthesized⁶ from cyclohexane-1,4-diyldimethanol (used as the normal mixture of *cis*- and *trans*-isomers) with 9-chloro-9-phenylfluorene⁷ in pyridine (100 °C, 17 h) to give a 60% total yield of **2** and **3**, which were separated by chromatography (SiO₂, eluent CHCl₃-light petroleum, b.p. 40–60 °C, 1 : 1); colourless solids, **2**: m.p. 171–174 °C, **3** m.p. 257–259 °C.

Both **2** and **3** show host properties, but of very different types, since **2** (the *cis*-compound) readily forms crystalline



inclusion compounds with a variety of apolar solvents of five- and six-membered ring type (Table 1), whereas **3** (the *trans*-compound) yields only a few inclusion complexes, and, oddly enough, exclusively with sulphur-containing solvents. The different inclusion behaviour of **2** and **3** must depend on the overall molecular shapes of the two configurational isomers, *i.e.* the more concave, less symmetric and bulkier *cis*-isomer **2** should give rise to more free space in a potential host lattice, which is in favour of inclusion formation.³ The dioxane inclusion compound of **2** shows the expected 2 : 1 host : guest stoichiometry (Table 1), thus stimulating an X-ray structural study.[†]

A perspective view of the crystallographic asymmetric unit of 2(2) dioxane, with numbering of the skeletal atoms, is shown in Fig. 1; Fig. 2 is a stereoscopic packing illustration.

The geometries of the two 9-phenylfluoren-9-yl moieties of **2** in the inclusion compound with dioxane correspond to the

Table 1 Crystalline inclusion compounds (host : guest stoichiometric ratios)^a

Guest solvent	Host compound	
	2	3
Benzene	1 : 1	—
Cyclohexane	2 : 1	—
Dioxane	2 : 1	—
Thioxane	1 : 2	1 : 2
Morpholine	1 : 1	—
Thiomorpholine	1 : 1	1 : 2
Tetrahydropyran	1 : 1	—
Tetrahydrofuran	1 : 1	—

^a Determined by NMR integration.

[†] *Crystal data:* 2·0.5 dioxane, C₄₆H₄₀O₂·0.5(C₄H₈O₂), *M* = 668.87, triclinic (*P* $\bar{1}$), *a* = 9.398(1), *b* = 13.468(1), *c* = 15.159(2) Å, α = 85.183(8), β = 84.957(8), γ = 73.977(8)°, *V* = 1833.5(4) Å³, *Z* = 2, *D_c* = 1.21 g cm⁻³ and μ = 5.40 cm⁻¹. The intensities of a total of 6643 reflections were measured (Cu-K α , θ_{\max} = 70°, room temperature) from a crystal of dimensions 0.60 × 0.45 × 0.38 mm, and corrected for background, Lorentz and polarization effects. Final *R* = 0.054 and *R_w* = 0.082 [480 variables, 4332 reflections with *I*/ σ (*I*) > 3], and *R_{w,tot}* = 0.086 (6136 unique, non-zero reflections). Weighting: *w* = 0.5638/[σ^2 (*F*) + 0.0004*F*²].⁸ The maximum and minimum values of the residual electron density in the final $\Delta\rho$ map were 0.17 and -0.20 e Å⁻³, respectively.

In the structural model (derived by MULTAN⁹ and refined by full-matrix least-squares calculations^{8,10}) the C and O atoms were allowed to vibrate anisotropically whereas isotropic displacement parameters were refined for the H atoms, assuming calculated, idealized positions with C-H = 1.00 Å. The dioxane guest is partially disordered, showing two possible major disorder sites for the O(D) atom (*cf.* Fig. 1). No constraints other than for the sum of occupancies were applied.

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.

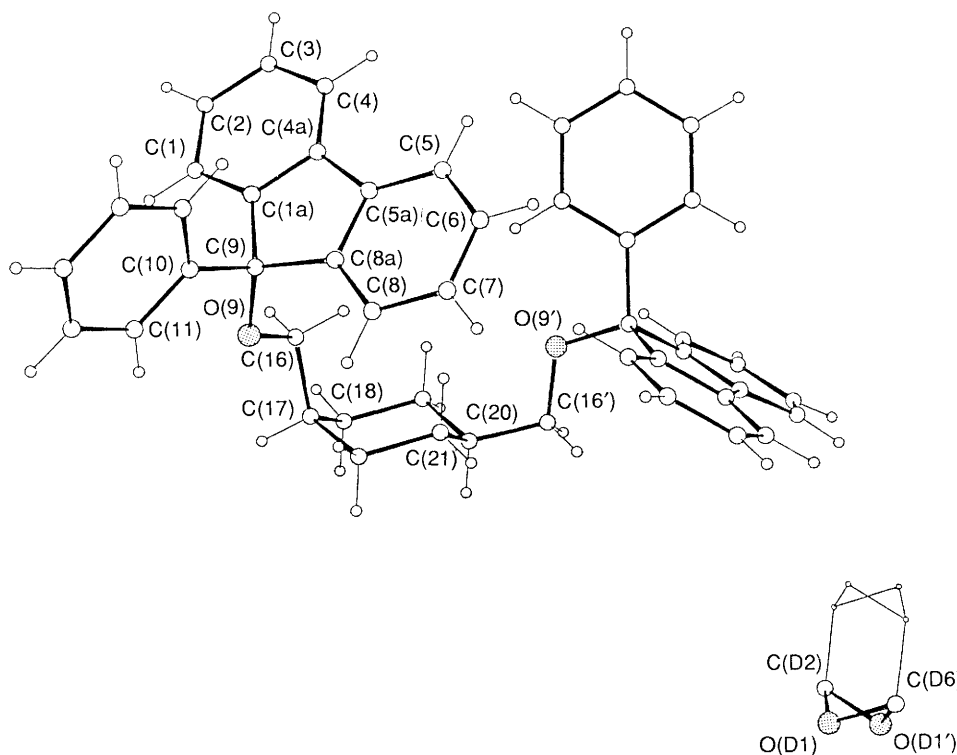


Fig. 1 Perspective view of the crystallographic asymmetric unit, containing one host **2** and one half of the dioxane guest, showing the two disorder sites of the dioxane O atom. The H atoms of the guest are omitted for clarity. The site occupancies of the disorder sites refined to values of 0.89(1) for O(D) and 0.11(1) for O(D').

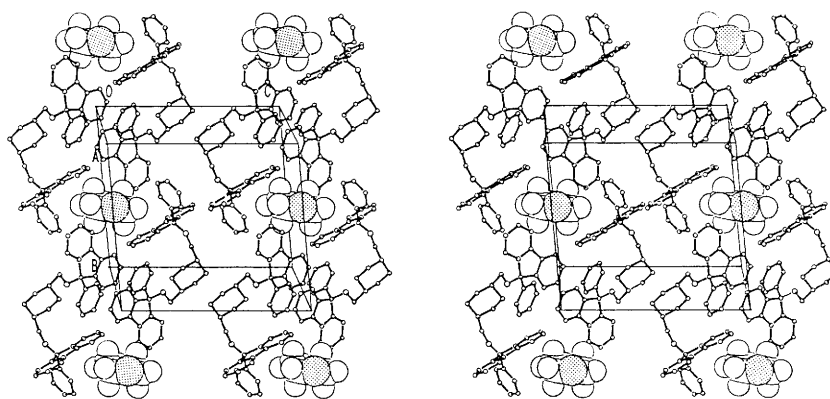


Fig. 2 Stereoscopic packing illustration. The host molecule is shown in ball-stick style and its H atoms are omitted for clarity. The guest molecule is drawn as a space-filling model with only one disorder site [O(D1)] for the oxygen atom (shaded).

previously studied 9-phenylfluoren-9-ol host molecules.⁵ The chair-shaped cyclohexane ring with a *cis*-1,4 (axial/equatorial) ether linkage of the substituents gives rise to an arched form for this host. However, in the hydrogen-bonded difluoreneol dioxane associate **I**, which served as a model for the present host, two axially positioned *trans*-directed H-bonds link the chair-shaped dioxane ring to the two fluorene molecules, resulting in a more linear form for **I**.

Despite these conformational differences, a comparison between the present (Fig. 2) and the 9-phenylfluoren-9-ol-dioxane (4:3) inclusion compound⁵ shows the two structures to be intimately related to each other. The crystallographic unit cell is triclinic with a centre of symmetry and contains two hosts (H-bonded complex or covalently bonded molecule) and one dioxane guest in both structures. The guest dioxanes are invariably located around the centre of symmetry

and are held by lattice forces only. The voids around the symmetry centres are large enough to allow lively thermal motion or disorder for these loosely bonded guest entities in both cases. Ordinary van der Waals' forces and more specific edge-to-face interactions between benzene rings hold together the host lattices. Accordingly, the model inclusion lattice of (1)-dioxane (4:3)⁵ and the present structure of (2)-dioxane (2:1) are similarly organized.

In summary, a successful example is given of host design where particular H-bond interactions between constituents of a known inclusion structure are substituted for covalent links to yield new host molecules. There are only two early references in the literature, known to the authors, showing comparable concepts. One is the development of the 'hexahosts',¹¹ whereas the other concerns a somewhat analogous guest engineering, in which *trans*-1,4-bis(hydroxymethyl)-

cyclohexane replaces the H-bonded, centrosymmetric guest aggregate 1,4-dioxane-H₂O in a preexisting adduct.¹² We suggest using this strategy to a greater extent for future construction of new host molecules and also in the engineering of organic crystalline materials.¹³

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