

Structurally Related Hosts with Remarkably Different Binding Features

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Molecular host **1** binds resorcinol and catechol in solution, whereas the structurally related host **2** does not bind these guests because its cleft is occupied by methoxy groups.

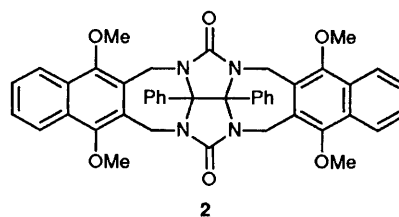
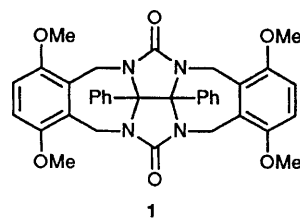
According to Cram, host and guest should have complementary surfaces for obtaining favourable binding properties.¹ In addition, the host should be preorganized to accept the guest. Recently, Hunter and Sanders have presented guidelines for the construction of organic hosts that bind aromatic guests by π - π interactions.² Following these concepts we have designed and synthesized two rigid molecular clefts, **1** and **2**, for the complexation of dihydroxybenzenes. Compounds **1** and **2** have very similar structures. Nevertheless, as is reported here, they display completely different binding properties: **1** moderately to strongly binds dihydroxybenzenes, whereas **2** has no affinity for these guests at all.

Host **1** was previously described by us.³ It has a central, concave diphenylglycoluril unit, which is flanked by two 3,6-dimethoxy-1,2-xylylene walls. These walls enclose a cleft with the right dimensions to accommodate a benzene ring. The two carbonyl groups of the diphenylglycoluril moiety are good hydrogen bond acceptors. By virtue of these properties, **1** forms 1:1 complexes with resorcinol and catechol in CDCl₃ solution with association constants of K_a 2600 and 80 dm³ mol⁻¹, respectively [Fig. 1(a)]. Since π - π interactions were shown to stabilize the complex of **1** with resorcinol,⁴ we envisioned that a host with larger aromatic surfaces, would bind resorcinol even more strongly. Compound **2** is an analogue of **1** that meets this requirement. It was synthesized from *N,N',N'',N'''*-tetra(chloromethyl)diphenylglycoluril and 1,4-dimethoxynaphthalene in refluxing 1,2-dichloroethane by a method analogous to **1** using SnCl₄ as a catalyst.⁴

The association constants of **2** with resorcinol and catechol

were evaluated from the induced shifts of the signals of the guests in a ¹H NMR titration experiment in CDCl₃. To our surprise, the induced shifts were very small. The K_a values were estimated to be lower than 1 dm³ mol⁻¹. Apparently the guest is not bound between the walls of host **2**.

From examination of Carey-Pauling-Koltun (CPK) models, it is clear that if one of the methoxy groups of **2** is pointing into the cleft, the carbonyl group on that side of the molecule will be blocked for hydrogen bonding with a dihydroxybenzene. In anisole, the methoxy group is preferen-



tially in the plane of the benzene ring.⁵ Molecular mechanics calculations as well as an X-ray structure determination show that also in host **1** the methoxy groups are more or less in the plane of the aromatic walls [Fig. 1(a)].⁶ Molecular mechanics calculations on 1-methoxynaphthalene reveal, however, that the conformation with the methoxy group in the plane of the

ring and oriented towards H-8, has a 9.15 kcal (1 cal = 4.184 J) higher energy than the conformation with the methoxy group perpendicular to the ring. The other coplanar orientation, which is the most stable one in 1-methoxynaphthalene, is inaccessible to the methoxy groups in compound **2**, because of steric interference by the diphenylglycoluril part of the molecule. Therefore, we expect that the methoxy groups in **2** either point into the cleft or are bent away from it, but are not in the plane of the walls. With this conformational preference there is a plausible cause for the low K_a of **2** with resorcinol and catechol: binding will be weak if in the minimum energy conformation of **2**, one or more of the methoxy groups are pointing into the cleft. A carbonyl group is then shielded for hydrogen bonding and a guest cannot enter the cavity of this low energy conformer. Even if the energies of conformations with one or more methoxy groups oriented inward or outward are the same, for statistical reasons only 1/16 of the molecules will be in a conformation that is able to bind a guest. In order to get information about the conformational preferences of the methoxy groups we determined the structure of **2** by X-ray diffraction. The results are shown in Fig. 1(b).[†] The most salient feature is that all four methoxy groups are pointing into the cavity. The angle between the cavity walls in **2** is larger than in **1**, viz. 53° as compared to 39.5°. There are intramolecular contacts between the methyl groups and the carbonyl oxygen atoms, (shortest methyl carbon to carbonyl oxygen distance is 3.21 Å) indicative of the presence of C-H...O bonding.⁷ Such stabilizing interactions could compensate for the additional torsional strain that will be present in the seven-membered rings of **2** due to the larger separation of the cavity walls.

The reason for the low K_a now seems to be evident: the methoxy groups have a preference for the inward orientation and consequently only a very small part or none of the molecules of **2** will be in a conformation that is able to accommodate a guest molecule. These results show that even small conformational differences, as in the present case the orientation of the methoxy groups, can completely change the complexation properties of an otherwise rigid host molecule. Similar conclusions were previously drawn by Cram for binding of alkali metal ions in anisole based spherand molecules.¹

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[†] Crystal data for C₄₂H₄₀N₄O₈: $M_r = 728.8$, T = 293 K, monoclinic, space group P2₁/c, $a = 17.242(2)$, $b = 11.208(2)$, $c = 19.536(2)$ Å, $\beta = 109.795(9)^\circ$, $V = 3552$ Å³, $Z = 4$, $D_c = 1.363$ g cm⁻³, Mo-K α radiation, $\mu = 0.89$ cm⁻¹. Final R value 0.054. R. P. Sijbesma, W. P. Bosman, P. T. Beurskens, G. Admiraal and R. J. M. Nolte, *Z. Kristallogr.*, in the press. 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.

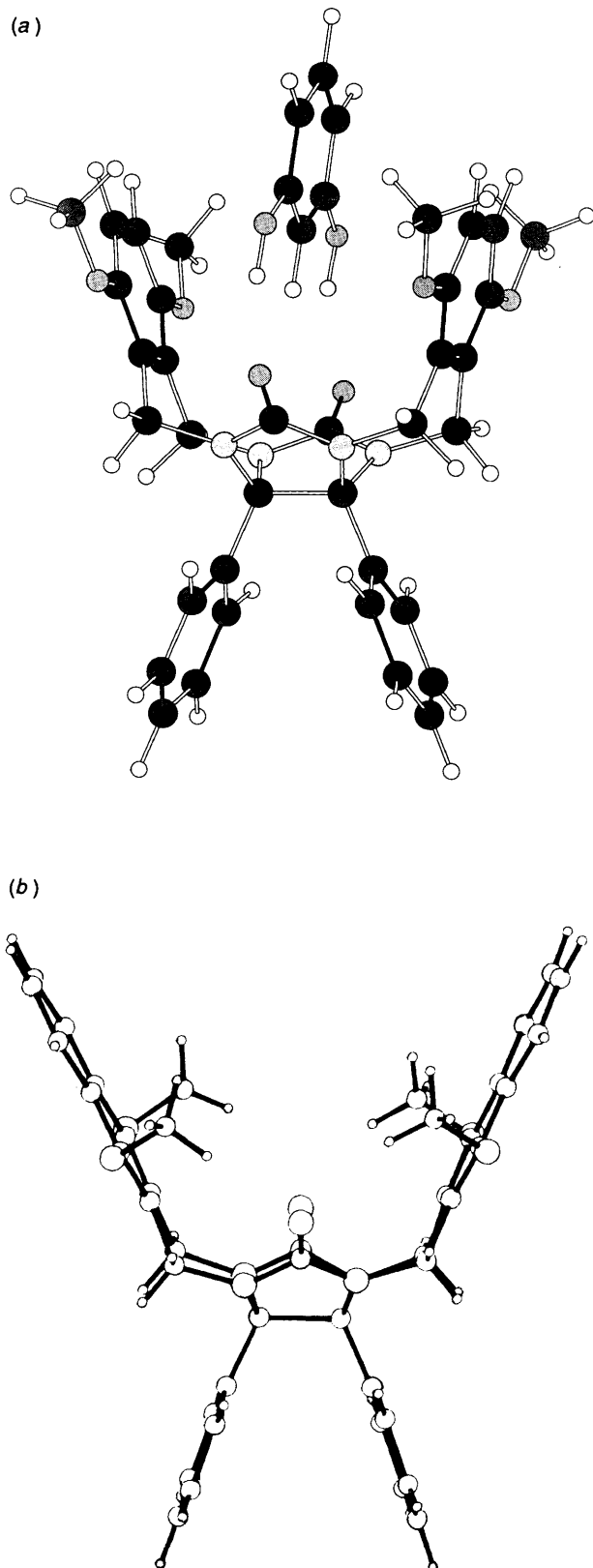


Fig 1 (a) Modelled structure of the complex of **1** with resorcinol based on ¹H NMR data and an X-ray structure determination of **1** (see ref. 4); (b) X-ray structure of **2**