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. 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. 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. It has a central, concave diphenylglycoluril unit, which is flanked by two 3,6-dimethoxy-1,2-xylene 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 dm⁻³ mol⁻¹, respectively [Fig. 1(a)]. Since π-π interactions were shown to stabilize the complex of 1 with resorcinol, 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 $N,N',N''$-tetra(chloromethyl)diphenylglycoluril and 1,4-dimethoxynaphthalene in refluxing 1,2-dichloroethane by a method analogous to 1 using SnCl₄ as a catalyst. The association constants of 2 with resorcinol and catechol were evaluated from the induced shifts of the signals of the guests in a $^1$H 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 dm⁻³ 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-
Molecular mechanics calculations as well as an X-ray structure determination show
that in host 1 the methoxy groups are more or less in the plane of the aromatic walls [Fig. 1(a)]. Molecular mechanics calculations on 1-methoxynaphthalene reveal, however, that the conformation with the methoxy group in the plane of the benzene ring. Molecular mechanics the conformation with the methoxy group in the plane of the aromatic walls [Fig. 1(a)]. Molecular mechanics calculations 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°. 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. 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 Kₐ 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 Crum for binding of alkali metal ions in anisole based spherand molecules.

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References

* Crystal data for Cₛ₂H₆N₆O₄: Mᵣ = 728.8, T = 293 K, monoclinic, space group P₂₁/c, a = 17.242(2), b = 11.208(2), c = 19.536(2) Å, β = 109.75(9)°, V = 3552 Å³. Z = 4, Dᵣ = 1.363 g cm⁻³, Mo-Kα radiation, μ = 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.