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 \( \pi-\pi \) 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 CDC\(_3\) solution with association constants of \( K_a 2600 \) and 80 dm\(^3\) mol\(^{-1}\), respectively [Fig. 1(a)]. Since \( \pi-\pi \) 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 \( N,N',N''-\)tetra(chloromethyl)diphenylglycoluril and 1,4-dimethoxynaphthalene in refluxing 1,2-dichloroethane by a method analogous to 1 using SnCl\(_4\) 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 \(^1\)H NMR titration experiment in CDC\(_3\). 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-
tially in the plane of the benzene ring. 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)]. Molecular mechanics calculations on 1-methoxynaphthalene reveal, however, that the conformation with the methoxy group in the plane of the aromatic walls [Fig. 1(a)]. 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 benzene ring. Molecular mechanics calculations on 1-methoxynaphthalene reveal, however, that the conformation with the methoxy group in the plane of the aromatic walls [Fig. 1(a)].

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

References


† Crystal data for C$_4$H$_8$N$_4$O$_8$: M$_r$ = 728.8, T = 293 K, monoclinic, space group $P2_1/c$, $a = 17.242(2)$, $b = 11.208(2)$, $c = 19.536(2)$ Å, $\beta = 109.795(5)^{\circ}$, $V = 3552$ Å$^3$, $Z = 4$, $D_x = 1.363$ g cm$^{-3}$, Mo-K$_\alpha$ 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.