Modified Hemispherands containing a Methoxycyclohexane Unit

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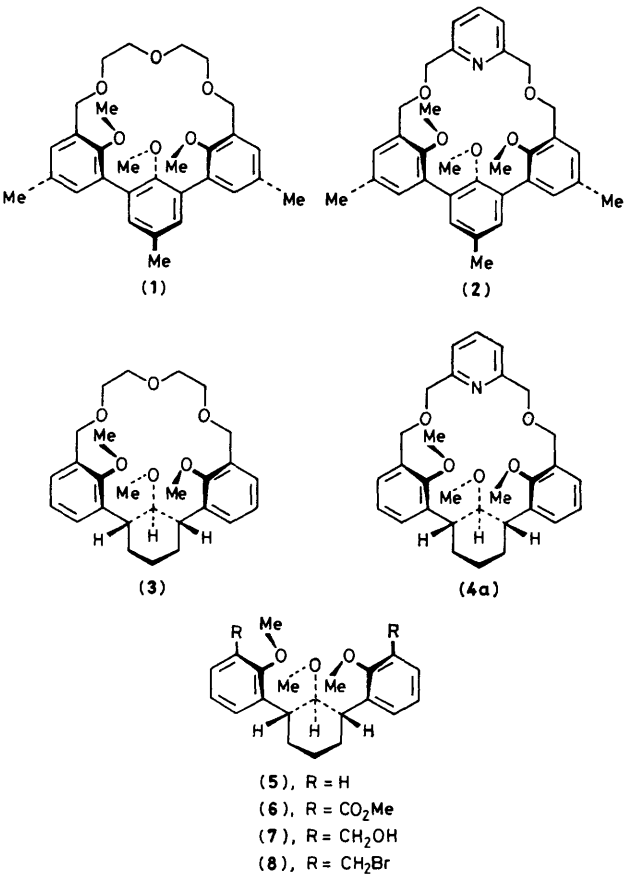
The binding properties of two new hosts are interpreted in terms of conformational reorganizations that must occur during complexation as revealed by an *X*-ray crystal structure and comparisons of their ^{1}H n.m.r. spectra.

Prior work demonstrated that the hemispherands (**1**)[1] and (**2**)[2] were superior to the chorands as complexing agents for alkali metal and alkylammonium cations.[2] This was attributed to the self-organization of the three methoxytoluene oxygens during synthesis rather than during complexation. Examination of Corey–Pauling–Koltun (CPK) molecular models of the potential hemispherands (**3**) and (**4a**) suggested that substitution of the central methoxytoluene of (**1**) and (**2**) by a methoxycyclohexane unit might also provide hosts of superior binding properties. We report here the syntheses through (**5**)—(**8**) of (**3**)† and (**4a**),† their free energies of binding, the *X*-ray crystal structure of (**4a**)‡ [see (**4b**)], and two of its complexes.

The host (**4a**) is shown in the conformation that molecular models suggested should be best for complexation. The *X*-ray crystal structures of (**4**)·$NaBPh_4$·H_2O and of (**4**)·$Bu^tNH_3ClO_4$ confirm the anticipated organizations of these complexes. The structure of (**4**)·$Bu^tNH_3ClO_4$ closely resembles that of (**1**)·$Bu^tNH_3ClO_4$.[6] In contrast, the conformation in the crystal of uncomplexed (**4**) [see (**4b**)] differs from that of uncomplexed (**1**), whose methoxytoluene units possess the same organization as complexed (**1**).[5] Although the near methoxy oxygens in crystals of (**1**)[5] and (**4**) possess mutually *anti* arrangements, and the methyl groups of the outer methoxytoluene groups in (**1**) and (**4**) both point outward, the methyl of the methoxycyclohexane unit of (**4**) points inward whereas the methyl of the central methoxytoluene unit of (**1**) points outward. The three methoxy groups of (**1**) are properly organized for complexation, but all three methoxy groups of (**4**) must undergo ring inversion before they attain the crystal structures of complexed (**4**).‡ In principle, a 180° rotation around the O–cyclohexyl bond in the crystal structure of (**4**)



† All new compounds gave C and H analyses within 0.30% of calculated values, appropriate molecular ions in their mass spectra, and expected ^{1}H n.m.r. spectra. Treatment of (**5**)[3] in sequence with BuLi–tetramethylethylenediamine, CO_2, and CH_2N_2 gave (**6**) (64%), m.p. 115—116 °C, reduction of which with $LiAlH_4$–Et_2O gave (**7**), m.p. 156—157 °C (92%). When treated with PBr_3–C_6H_6, (**7**) gave (**8**) as a gum (99%). The dibromide (**8**) in tetrahydrofuran–NaH at reflux temperature under high dilution conditions when treated with diethylene glycol gave (**3**), m.p. 109—112 °C (74%). Similarly, (**8**) with 2,6-bis(hydroxymethyl)pyridine[2] gave (**4**), m.p. 145—147 °C (71%). The free energies were determined for (**3**) and (**4**) for binding the alkali metal, ammonium, and alkylammonium picrates in $CDCl_3$ saturated with D_2O by extracting 0.05 or 0.001 M salt solutions in D_2O with solutions of hosts in $CDCl_3$ at 25 °C.[4] Table 1 records $-\Delta G°$ values for (**3**) and (**4**), for the analogues (**1**) and (**2**),[2] and for 2,3-naphtho-18-crown-6.[2] Complexes for *X*-ray crystal structure determination were prepared by mixing (**4**) in $CHCl_3$ with $NaBPh_4$ or $Bu^tNH_3ClO_4$. Suitable crystals were obtained by slow evaporation of a $CHCl_3$–C_6H_5Me solution of (**4**)·$NaBPh_4$·H_2O, by crystallization of (**4**)·$Bu^tNH_3ClO_4$ from tetrahydrofuran–$CHCl_3$, and by slow evaporation of a $CHCl_3$–C_6H_5Me solution of (**4**) itself. The *X*-ray crystal structures of (**1**)[5] and (**1**)·$Bu^tNH_3ClO_4$[6] have been reported.

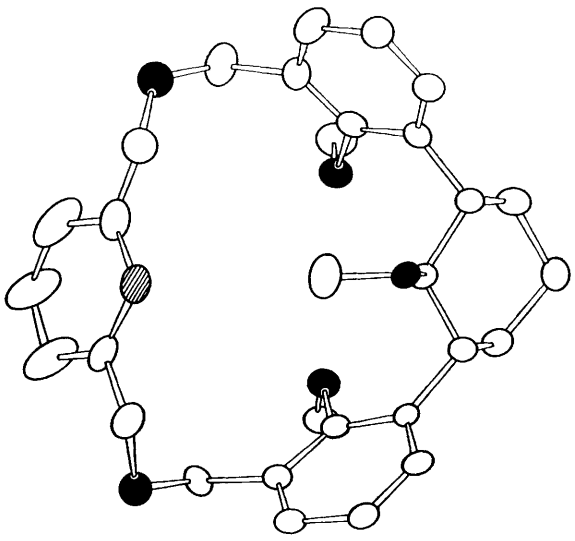
‡ *Crystal data:* (**4b**), $C_{30}H_{35}O_5N$, M = 489.6, triclinic, $P\bar{1}$, a = 7.778(3), b = 10.534(6), c = 16.429(8) Å, α = 93.90(4), β = 100.80(4), γ = 102.97(4) °, U = 1279.9 Å^3, Z = 2, μ = 0.49 cm^{-1}, λ = 0.7107 Å, crystal dimensions *ca.* (0.3 mm)^3, R = 0.081 for 3080 reflections with $F \geqslant 6\sigma(F)$; (**4**)·$NaBPh_4$·H_2O·0.5$CHCl_3$, $C_{30}H_{35}O_5N$·$C_{24}H_{20}BNa$·H_2O·0.5$CHCl_3$, M = 909.5, triclinic, $P\bar{1}$, a = 11.470(4), b = 15.189(4), c = 15.772(5) Å, α = 114.21(2), β = 104.35(3), γ = 93.60(2) °, U = 2385.5 Å^3, Z = 2, μ = 1.38 cm^{-1}, λ = 0.7107 Å, crystal dimensions *ca.* (0.3 mm)^3, R = 0.084 for 4551 reflections with $I \geqslant 3\sigma(I)$; (**4**)·$Me_3CNH_3ClO_4$·0.5-cyclohexane, $C_{30}H_{35}O_5N$·$C_4H_{12}NClO_4$·0.5C_6H_{12}, M = 705.3, orthorhombic, *Pbca*, a = 17.609(3), b = 20.446(4), c = 20.024(5) Å, U = 7209.3 Å^3, Z = 8, μ = 1.22 cm^{-1}, λ = 0.7107 Å, crystal dimensions *ca.* (0.3 mm)^3, R = 0.11 for 4666 reflections with $F \geqslant 3\sigma(F)$.

The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

Table 1. Free energies of complexation of picrate salts by various hosts in $CDCl_3$ saturated with D_2O at 25 °C.

	$-\Delta G°$ Values (kcal mol^{-1}) for hosts[b]				
Guests	(1)	(2)	(3)	(4)	(A)[a]
Li^+	7.0	7.3	<6	6.7	6
Na^+	12.3	12.0	8.8	8.7	8.3
K^+	11.8	10.9	11.2	10.0	10.8
Rb^+	10.4	9.0	9.9	8.6	9.7
Cs^+	9.0	7.8	8.7	7.7	8.2
NH_4^+	9.8	8.7	9.5	9.5	9.4
$MeNH_3^+$	8.2	7.3	7.3	7.0	7.4
$Bu^tNH_3^+$	7.7	6.3	6.6	5.7	6.8

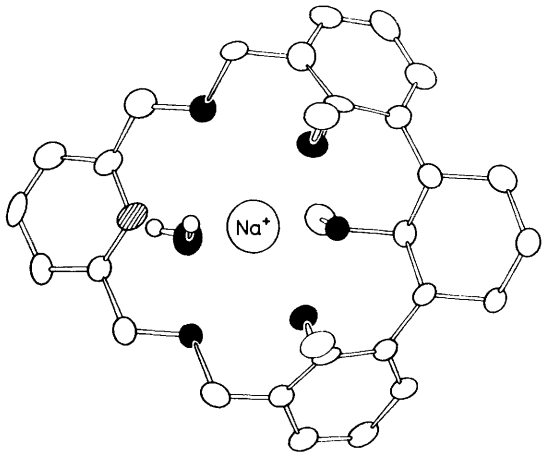
[a] (A) = 2,3-naphtho-18-crown-6. [b] 1 cal = 4.184 J.



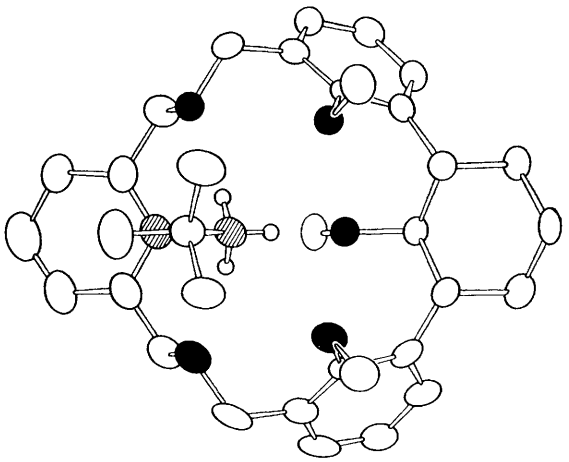
(4b)

would produce a binding conformation. In practice, this conformation is too high in energy to complex well. In CPK models the methine hydrogen of the MeOCH moiety collides with the oxygens of the two flanking methoxytoluene groups as they move to contact potential guests.

The benzyl protons in the ^{1}H n.m.r. spectrum of (3) and (4) show very broad and ill defined signals at 30 °C, which indicate the presence of several interconverting conformations. Addition of either $Bu^tNH_3ClO_4$ or $NaBPh_4$ to $CDCl_3$ solutions of (4) immediately produced a single, well resolved AB quartet. In contrast, (1) and (2) each gave a benzyl proton AB quartet, which is little changed by addition of guest.[7]



(4)·Na^+·H_2O



(4)·$Bu^tNH_3^+$

The conclusion drawn from both the crystal structure and spectral comparisons is that the methoxy oxygens and methyls of (1) and (2) are well organized for binding in the absence of guests. However, the energy cost of conformational reorganization of these groups in (3) and (4) is paid for in free energies of binding. Examination of these energies (Table 1) supports this conclusion. Thus (1) > (3) and (2) > (4) in binding almost all ions. The differences in binding patterns between chorand (A) and hemispherands (1) and (2) largely disappear in hosts (3) and (4). This fact correlates with the differences in degrees of preorganization of hemispherands on the one hand and the chorands on the other. Thus, (3) and (4) should be classed as chorands rather than as hemispherands.

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References

1 K. E. Koenig, G. M. Lein, P. Stückler, T. Kaneda, and D. J. Cram, *J. Am. Chem. Soc.*, 1979, **101**, 3553.
2 D. J. Cram, I. B. Dicker, G. M. Lein, C. B. Knobler, and K. N. Trueblood, *J. Am. Chem. Soc.*, 1982, **104**, 6827.
3 D. J. Cram, J. R. Moran, E. F. Maverick, and K. N. Trueblood, *J. Chem. Soc., Chem. Commun.*, 1983, preceding communication.
4 G. M. Lein and D. J. Cram, *J. Chem. Soc., Chem. Commun.*, 1982, 301.
5 I. Goldberg, *Cryst. Struct. Commun.*, 1980, **9**, 1201.
6 D. J. Cram and K. N. Trueblood, *Top. Curr. Chem.*, 1981, 43.
7 G. M. Lein and D. J. Cram, unpublished work.