The complexation of halide ions by a calix[6]pyrrole

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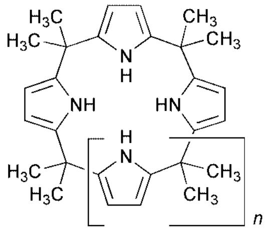
Received (in Cambridge) 20th March 2000, Accepted 23rd May 2000

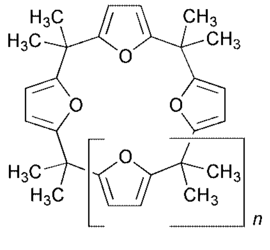
The X-ray crystal structures of the 1 : 1 complexes formed by calix[6]pyrrole 1b with Bu^n_4NCl and Bu^n_4NBr show the macrocycle to adopt D_{3d} symmetry and to encapsulate the halide ions within the macroring cavity *via* six N–H···X$^-$ hydrogen bonds; the macrocycle subtly adjusts its conformation to accommodate the differently sized anions; preliminary extraction experiments indicate that 1b is a dramatically stronger chloride ion complexing agent than its smaller analogue calix[4]pyrrole 1a.

Molecular receptors for cations and neutral guests have been extensively studied for many years.[1] In contrast, macrocycles capable of binding anions have attracted considerably less attention. However, because of the key role of anions in fundamental aspects of chemistry and biology, the search for novel and selective hosts for anions is a rapidly developing area of supramolecular chemistry.[2]

Significant progress in this field has been made by the discovery that, for example, pyrrole-based analogues of the calix[4]arenes such as **1a** are capable of binding fluoride and chloride ions.[3–5] However, complexation occurs by means of a facial arrangement involving hydrogen bonding interactions between the four pyrrole N–H and the anions and not by inclusion within the macrocyclic cavity, which is too small for either the fluoride or the chloride ions.



n = 1 **1a** *n* = 3 **1b**



n = 3 **2**

These observations led us to synthesise[6] the larger calix[6]pyrrole **1b** from the known furan-based analogue **2**. This new synthesis provided a novel route to **1b** which, unlike its smaller analogue **1a**, is not readily isolated from the mixture of compounds obtained by the previously employed condensation reaction of pyrrole and acetone.[3b] We were thus able to investigate, for the first time, the behaviour of **1b** as a molecular receptor for halide ions. We expected **1b** to be an appreciably better complexing agent for the halide ions than **1a** both in terms of strength (it has the potential to form an additional two N–H···X$^-$ hydrogen bonds) and selectivity (owing to the possible inclusion of the ion within the larger macroring cavity—and hence achieve size-discrimination).

In order to estimate the improved binding of **1b** towards chloride and bromide with respect to that of **1a**, we compared the ability of the two macrocycles to complex and transfer these ions from a water phase to a lipophilic dichloromethane phase. The tests were extended to include also fluoride and iodide. In a series of extraction experiments, solutions of Bu^n_4NF, Bu^n_4NCl, Bu^n_4NBr and Bu^n_4NI in D_2O (10^{-2} M) were extracted with equal volumes of solutions containing **1a** or **1b** (10^{-2} M) in CD_2Cl_2 under identical conditions and temperature (16 °C). After separation of the two phases, the amount of anion transferred in each case was calculated from the ^1H NMR spectra of the CD_2Cl_2 solutions using the ratios between the integration values for the resonances of the protons of the macrocycles and those of the ammonium ion (which has to follow the halogen ion into the organic phase).† The values obtained were also confirmed by the corresponding decrease of the amount of salt in the D_2O phase which was measured by integration of ^1H NMR peak profiles with respect to a known amount of dioxane added as an internal standard.

In order to single out the contributions of the macrocycles to the phase transfer of the anions from other factors (halogen lipophilicity and phase transfer due to the $Bu^n_4N^+$ cation) the partition of these salts between the two phases was also determined in the absence of **1a** or **1b**. Macrocycles **1a** and **1b** are insoluble in water.

The results obtained (Table 1) indicate that the contribution of **1a** to the phase transfer of fluoride, chloride, bromide and iodide (if it exists) is marginal and its magnitude is at most within the experimental error. On the other hand, **1b** can effectively bind and transfer both chloride and bromide ions into a DCM phase and shows a *ca.* six-fold selectivity factor for chloride with respect to bromide.

The ^1H NMR spectra of **1b** in the presence of chloride and bromide (at the percentage concentration extracted) also show significant shifts of the pyrrole N–H resonances from its uncomplexed value of δ 7.67 towards higher values (up to δ 10.93 for chloride and δ 8.40 for bromide) which are certainly due to the involvement of the N–H protons in hydrogen bonding interactions with the halogen ions. A line broadening of the C–H resonances is also observed especially for the chloride complex.

Encouraged by these results, and to test the potential for inclusion as a function of the anion size, as well as to gain information on the mode of binding, we subjected 1 : 1 solutions of **1b** with Bu^n_4NCl and with Bu^n_4NBr in DCM to slow evaporation of the solvent to give, in each case, single crystals of 1 : 1 complexes suitable for X-ray analysis (mp 232–234 and 189–191 °C, respectively).

Table 1 Transfer of Bu^n_4NF, Bu^n_4NCl, Bu^n_4NBr and Bu^n_4NI (%) between D_2O and CD_2Cl_2 at 16 °C with and without **1a** and **1b**. The figures indicate the percentage variation in the concentration of salt in each phase after equilibration and were reproducible within a ±2% error

	Macrocycle					
	None		**1a**		**1b**	
	D_2O	CD_2Cl_2	D_2O	CD_2Cl_2	D_2O	CD_2Cl_2
Bu^n_4NF	[a]	[b]	[a]	[a]	[a]	[a]
Bu^n_4NCl	−4	[b]	−4	+4	−65	+65
Bu^n_4NBr	−20	[b]	−22	+22	−31	+31
Bu^n_4NI	−86	[b]	−86	+86	−86	+86

[a] Value within experimental error (< 2%). [b] The percentage variation was not measured.

DOI: 10.1039/b002239j

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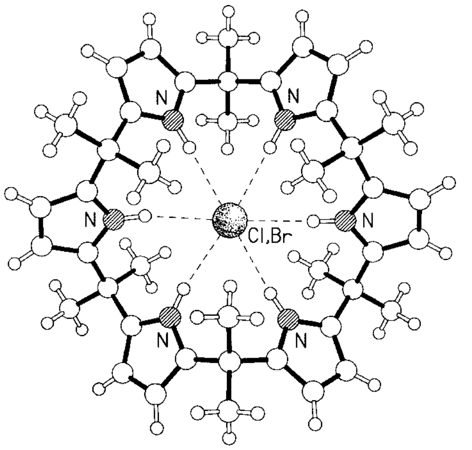

Fig. 1 Plan view of the X-ray structure of the 1 : 1 complexes formed between calix[6]pyrrole **1b** and Cl$^-$ and Br$^-$. The hydrogen bonding geometries: N··X, H··X distances (Å), and N–H··X angles (°) are in the ranges 3.265(5)–3.305(5), 2.39–2.42 and 166–177 in the chloride and 3.344(5)–3.404(5), 2.46–2.51 and 170–178 in the bromide.

The X-ray analysis of the 1 : 1 complex‡ formed between the calix[6]pyrrole **1b** and chloride shows (Fig. 1), that to achieve binding, the host macrocycle undergoes a substantial conformational change from that observed for the 1 : 1 complex with water.[6] In the water complex the macrocycle adopts a tennis-ball-seam (D_{2d}) conformation whereas here with chloride the symmetry approximates closely to D_{3d}. The chloride anion is positioned centrally with respect to the six pyrrole nitrogen atoms (which are coplanar to within 0.02 Å) and displaced out of this plane by 0.37 Å along the molecular C_3 axis. Binding is *via* six N–H··Cl hydrogen bonds for which the N··Cl and H··Cl distances (Å) range between 3.265(5) and 3.305(5) [*cf.* a range of 3.264(7)–3.331(7) in the tetrapyrrole structure[7]], and 2.39 and 2.42 respectively; the N–H··Cl angles are in the range 166–177°. The small displacement of the chloride ion out of the plane of the six pyrrole nitrogens is accompanied by a slight 'flowering' of the macrocycle, the mean C··C separations between the inwardly directed methyl groups of the 'upper' and 'lower' set of isopropylidene groups being 5.25 and 4.40 Å, respectively.

The expectation that this 'flowering' in the case of the bromide complex would be more pronounced than in the chloride, owing to the larger anion size, was confirmed by X-ray analysis‡ (Fig. 2). Surprisingly, despite the inclusion in both structures of substantial amounts of disordered solvent, the structures are isomorphous. In the bromide complex the anion is again centrally positioned within the macrocycle which adopts a more distorted conformation but one which still approximates to D_{3d}. The bromide ion is bound by six N–H··Br hydrogen bonds with N··Br and H··Br distances ranging between 3.344(5) and 3.404(5), and 2.46 and 2.51 Å respectively; the N–H··Br angles are in the range 160–178°. Accompanying the increase in anion size (and lengthening of the hydrogen bonds) is an increase in the displacement of the anion (Br$^-$) from the plane of the six pyrrole nitrogen atoms (0.69 Å) and 'flowering' of the macrocycle, the Br$^-$ adopting a 'perching' geometry analogous to that of, for example, ammonium ions with 18-crown-6. Here, the mean C··C separations (**a**–**f** in Fig. 2) between the inwardly directed methyl groups of the 'upper' and 'lower' set of isopropylidene groups are 5.62 and 4.31 Å, respectively. The anions, cations and solvent are, in both structures, well separated and there are no significant intermolecular interactions. The differences in the two solid state structures are consistent with the ability of **1b** to discriminate by size between the two halogen anions chloride and bromide.

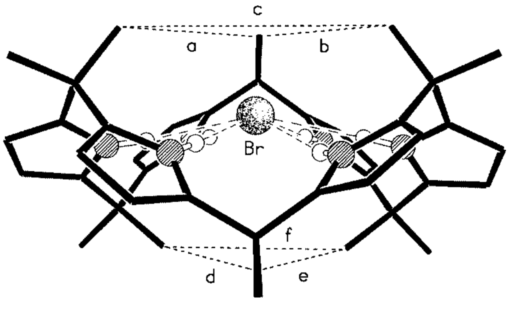

Fig. 2 Elevation of the X-ray structure of the 1 : 1 complex between calix[6]pyrrole **1b** and Br$^-$ showing the 'perching' geometry of the hydrogen bonded Br$^-$ ion within the 'flowered' macrocyclic conformation. The distances **a**–**c** and **d**–**f** between the inwardly directed isopropylidene methyl carbon atoms are in the ranges 5.46–5.72 and 4.26–4.38 Å respectively (*cf.* 5.11–5.37 and 4.34–4.48 Å respectively, in the chloride complex).

Work is in progress in our laboratory to determine the values of the association constants of **1b** with the halogen ions. Selectivity tests will include competitive binding experiments and transport across liquid membranes.

Notes and references

† The equilibrium of transfer between the two phases was always achieved within 10 min of vigorous stirring. The amount of $\mathrm{Bu^n_4N^+}$ transferred between the two phases was not affected by the addition of NaOH to the water phase.

‡ *Crystal data for* [**1b**–Cl$^-$][$\mathrm{Bu^n_4N^+}$]: $[\mathrm{C_{42}H_{54}N_6{\cdot}Cl}][\mathrm{C_{16}H_{36}N}]{\cdot}4\mathrm{CH_2Cl_2}$, M = 1260.5, monoclinic, Pn (no. 7), a = 17.592(1), b = 9.970(1), c = 20.050(1) Å, β = 90.55(1)°, V = 3516.4(4) Å^3, Z = 2, D_c = 1.191 g cm^{-3}, μ(Cu-Kα) = 35.8 cm^{-1}, $F(000)$ = 1344, T = 293 K; Siemens P4/RA diffractometer, ω-scans, 4370 independent reflections refined on F^2 to give R_1 = 0.053, wR_2 = 0.147 for 3700 independent observed absorption corrected reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta \le 124°$] and 704 parameters. The polarity of the structure could not be unambiguously determined from either an R-factor test (R_1^+ = 0.0544, R_1^- = 0.0545) or by use of the Flack parameter [x^+ = +0.49(5), x^- = +0.51(5)]; evidence suggested a degree of racemic twinning. For [**1b**·Br$^-$][$\mathrm{Bu^n_4N^+}$]: $[\mathrm{C_{42}H_{54}N_6{\cdot}Br}][\mathrm{C_{16}H_{36}N}]{\cdot}4\mathrm{CH_2Cl_2}$, M = 1298.9, monoclinic, Pn (no. 7), a = 17.472(2), b = 9.801(1), c = 20.037(1) Å, β = 90.00(1)°, V = 3431.1(5) Å^3, Z = 2, D_c = 1.257 g cm^{-3}, μ(Cu-Kα) = 40.0 cm^{-1}, $F(000)$ = 1368, T = 183 K; Siemens P4/RA diffractometer, ω-scans, 5380 independent reflections refined on F^2 to give R_1 = 0.054, wR_2 = 0.142 for 5253 independent observed absorption corrected reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta \le 128°$] and 704 parameters. The polarity of the structure was determined by a combination of an R-factor test (R_1^+ = 0.0540, R_1^- = 0.0568) and by use of the Flack parameter [x^+ = +0.15(4), x^- = +0.85(4)]. CCDC 182/1654. See http://www.rsc.org/suppdata/cc/b0/b002239j/ for crystallographic files in .cif format.

1 B. Dietrich, in *Comprehensive Supramolecular Chemistry*, ed. G. W. Gokel, Elsevier, Exeter, 1996, vol. 1, p. 153.

2 For recent examples and reviews, see: P. D. Beer, *Chem. Commun.*, 1996, 689; J. L. Atwood, K. T. Holman and J. W. Steed, *Chem. Commun.*, 1996, 1401; D. M. Rudkevich, W. Verboom, Z. Brzozka, M. J. Palys, W. P. R. V. Stauthamer, G. J. van Hummel, S. M. Franken, S. Harkema, J. F. J. Engbersen and D. N. Reinhoudt, *J. Am. Chem. Soc.*, 1994, **116**, 4341; W. Xu, J. J. Vittal and R. J. Puddephatt, *J. Am. Chem. Soc.*, 1995, **117**, 8362; *Supramolecular Chemistry of Anions*, ed. A. Bianchi, E. García-España and K. Bowman-James, Wiley–VCH, Weinheim, 1997; J. Scheerder, J. F. J. Engbersen and D. N. Reinhoudt, *Recl. Trav. Chim. Pays-Bas*, 1996, **115**, 307; R. Vilar, D. M. P. Mingos, A. J. P. White and D. J. Williams, *Chem. Commun.*, 1999, 229.

3 (*a*) P. A. Gale, J. L. Sessler and V. Král, *Chem. Commun.*, 1998, 1 and references therein; (*b*) P. A. Gale, J. L. Sessler, J. W. Genge, V. Kral, A. Andrievsky, V. Lynch, P. I. Samsom, W. E. Allen, C. T. Brown and A. Gebauer, *World Pat.*, WO97/37995 (*Chem. Abstr.*, 1997, **127**, 346236).

4 For recent examples of calix[4]pyrrole derivatives as anion sensors see: H. Miyaji, P. Anzenbacher, Jr., J. L. Sessler, E. R. Bleasdale and P. A. Gale, *Chem. Commun.*, 1999, 1723; P. A. Gale, L. J. Twyman, C. I. Handlin and J. L. Sessler, *Chem. Commun.*, 1999, 1851.

5 For a recent example of chloride binding by means of C–H··Cl hydrogen bonding, see: E. Alcade, C. Alvarez-Rúa, S. Garcia-Granada, E. Garcia-Rodriguez, N. Mesquida and L. Pérez-García, *Chem. Commun.*, 1999, 295.

6 G. Cafeo, F. H. Kohnke, G. L. La Torre, A. J. P. White and D. J. Williams, *Angew. Chem., Int. Ed.*, 2000, **39**, 1496.

7 P. A. Gale, J. L. Sessler, V. Král and V. Lynch, *J. Am. Chem. Soc.*, 1996, **118**, 5140.