

Selective anion binding and solid-state host–guest chemistry of an extended cavity calix[6]pyrrole

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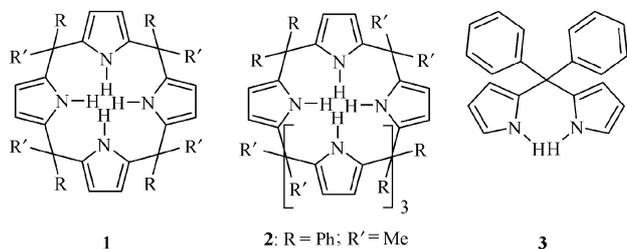
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Received (in Cambridge, UK) 26th September 2000, Accepted 7th November 2000

First published as an Advance Article on the web

Easily prepared, cone-like, extended cavity calix[6]pyrrole is shown to form strong complexes with iodine and other halide ions as well as with trihaloalkanes and electron deficient aromatic systems.

The host–guest chemistry of calixpyrroles has been the subject of intensive research aimed at gaining both understanding and control on guest recognition and binding.¹ Recently, Sessler and coworkers² reported that calix[4]pyrroles **1** are effective and



selective receptors for anions and neutral guest species. Calixpyrroles that have been tailored to the size, shape and binding modes of target guests were shown to exhibit improved binding ability.³ Here we report the selective binding of anions, haloalkanes and aromatic guests by recently reported, cone-like, extended-cavity 1,1,3,3,5,5-*meso*-hexaphenyl-2,2,4,4,6,6-*meso*-hexamethylcalix[6]pyrrole.^{2,4} Calix[6]pyrroles are a new class of molecules characterized by a six-pyrrolemethane rim. The cross section of the hexapyrrolemethane rim is significantly larger than that of calix[4]pyrroles, *ca.* 110 *cf.* 24 Å². Additionally, in the stable conformation of calix[6]pyrroles, such as **2**, three of the *meso* phenyl substituents form a trigonal cavity with a volume of *ca.* 500 Å³. Such extended-cavity receptors may allow efficient and selective binding of electron deficient aromatic guests as well as large anions such as I[−]. These substrates can not be efficiently recognized nor complexed by the smaller calix[4]pyrrole systems.^{3b,5}

Calix[6]pyrrole **2** was prepared using a modification of a previously reported method.^{4a} Benzophenone (5 g, 27.4 mmol), pyrrole (5 mL, 72.3 mmol) and BF₃·OEt (5 mL, 39.5 mmol) were dissolved in dry ethanol (250 mL) and stirred at room temperature for 5 days under an inert atmosphere. The precipitate was then filtered off and washed with cold ethanol, offering di(phenyl)di(pyrrol-2-yl)methane **3** as a colorless solid (40% yield). An additional crop of **3** could be isolated from the mother-liquor using column chromatography [silica, dichloromethane–hexane (1 : 10), 50% total yield for **3**]. Calix[6]pyrrole **2** was obtained by stirring a solution of **3** (300 mg, 1 mmol) in 60 mL of dry acetone–ethanol (1 : 1) containing CF₃CO₂H for 5 days under inert atmosphere. The product was isolated by filtration (43% yield). An additional crop of **2** could be isolated from the mother-liquor using column chromatography [silica, dichloromethane–hexane (3 : 7), 52% total yield for **2**].

Similarly to earlier studies by Sessler and coworkers on the complexation of calix[4]pyrroles with different guest species, proton NMR spectroscopy was found to be a useful tool for the

determination of binding constants between different guests and calix[6]pyrrole, **2**.⁶ Quantitative assessments of anion binding constants were made by following the induced shifts in the ¹H NMR spectra of the host as a function of the concentration of the guest in an acetonitrile–chloroform (1 : 9) solution at room temperature (298 K). Table 1 lists the association constants between **2** and the different guests. For comparison, the complexation of octamethylcalix[4]pyrrole with the same guest species was studied under the same conditions (Table 1).

In accordance with previous studies performed by Sessler and coworkers octamethylcalix[4]pyrrole displays a clear preference towards fluoride ions over larger anions, the binding order being F[−] >> Cl[−] > Br[−] > I[−]. In contrast, probably due to its extended cavity, **2** exhibits a clear preference to iodide over smaller halides. Here the binding order switches to I[−] > F[−] >> Cl[−] > Br[−]. We interpret this binding order and the high affinity towards iodide in terms of the geometrical fit between the extended cavity of **2** and the iodide ion, allowing full binding of the anion by up to six pyrrole rings. Being the smallest halide, the fluoride ion may fit and bind efficiently to only part of the pyrrolemethane ring. Similar effects have previously been reported for the binding of cations to the cavities of crown ethers.⁷

Calix[6]pyrrole **2** is found to bind also to trihalogenated species such as trichloroethanol, trifluoroethanol, tetrafluoroborate and trifluoroacetate and forms significantly stronger complexes with such guests than with their nonhalogenated analogs (Table 1). The reason for this is revealed from the crystal structure† of such a complex between 2,2,2-trichloroethanol and **2** (Fig. 1). Unlike simple calixpyrroles that bind their guests predominantly through X[−]⋯H–N bonds,^{2,3b} **2** anchors the 2,2,2-trichloroethanol guest through one (disordered) H–O⋯H–N hydrogen bond with the hydroxy group, *d*(O84b⋯H–N18) = 2.411 Å; α(O–H–N) = 169.11°; *d*(O84a⋯H–N70) = 2.412 Å; α(O–H–N) = 175.95°; *d*(O84a⋯H–N44) = 2.725 Å; α(O–H–N) = 156.97°, and three π_{phenyl}⋯Cl–C bonds between the Cl atoms of the guest and the π electron clouds of the three axial *meso*-phenyl groups forming

Table 1 Binding constants of calix[6]pyrrole **2** and 1,2,3,4-*meso*-octamethylcalix[4]pyrrole **1**, with different guest molecules

| Guest | Calix[4]pyrrole | Calix[6]pyrrole |
|--|-----------------|-----------------|
| F [−] | 23 800 | 1080 |
| Cl [−] | 6800 | 650 |
| Br [−] | 270 | 150 |
| I [−] | <10 | 6600 |
| SCN [−] | <10 | <10 |
| <i>p</i> -MeC ₆ H ₄ SO ₃ [−] | <10 | 150 |
| BF ₄ [−] | <10 | 2350 |
| MeCO ₂ [−] | 400 | <10 |
| CF ₃ CO ₂ [−] | 70 | 1150 |
| EtOH | <10 | <10 |
| CF ₃ CH ₂ OH | <10 | 80 |
| CCl ₃ CH ₂ OH | <10 | 60 |

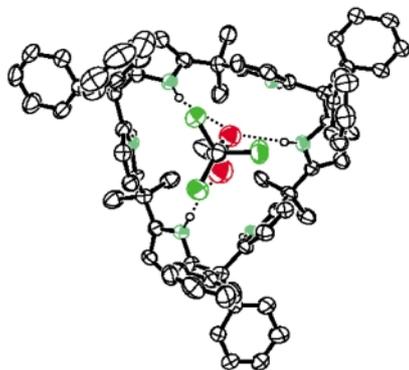


Fig. 1 The molecular structure of the complex between 2,2,2-trichloroethanol and calix[6]pyrrole **2**. Solvent and other molecules not situated in the cavity of the host have been omitted for clarity.

the pseudo-threefolded cavity of **2**: $d(\text{C179}-\pi(\text{C34}-\text{C39})) = 3.38 \text{ \AA}$; $d(\text{C180}-\pi(\text{C60}-\text{C65})) = 3.00 \text{ \AA}$; $d(\text{C181}-\pi(\text{C8}-\text{C13})) = 3.45 \text{ \AA}$.

The stable conformation of **2** brings two electron-rich pyrrole rings, situated in a 1,4 position to one another, into a parallel and cofacial orientation. These two rings are spaced *ca.* 7.1 Å apart. Being an electron rich ring system, the hexapyrrolemethane ring is suitable for hosting electron poor conjugated species in between a pair of cofacial pyrrole rings. The additional four pyrrole rings are capable of forming multiple hydrogen bonds with appropriate guests, making the system an interesting host for different nitro- and carboxy-aromatic compounds. Fig. 2 shows the crystallographic structure[†] of a complex between *p*-nitrotoluene/nitrobenzene and **2**. Interestingly, though crystallized from a solution containing nitrobenzene and *p*-nitrotoluene in a 10:1 ratio, the crystal structure clearly indicates the 1:1 inclusion of nitrobenzene and *p*-nitrotoluene within the cavity of **2**. As can be seen in Fig. 2, the nitroaromatic guest is fixed to the cavity of the host through short range π - π interactions between the nitro group of the guest and the two sandwiching pyrrole rings of the host, $d(\text{nitro}(\text{plane})\cdots\text{pyrrole}(\text{plane})) = 3.55 \text{ \AA}$. Three of the other four pyrrole rings are involved in hydrogen bonding with the nitro group of the encapsulated guest, $d(\text{NH1}\cdots\text{O80}) = 2.23 \text{ \AA}$, $d(\text{N1}\cdots\text{O80}) = 3.06 \text{ \AA}$, $\alpha(\text{O}-\text{H}-\text{N}) = 172.94^\circ$, $d(\text{NH31}\cdots\text{O80}) = 2.38 \text{ \AA}$, $d(\text{N31}\cdots\text{O80}) = 3.18 \text{ \AA}$, $\alpha(\text{O}-\text{H}-\text{N}) = 143.67^\circ$, $d(\text{NH19}\cdots\text{O81}) = 2.45 \text{ \AA}$, $d(\text{N19}\cdots\text{O81}) = 3.23 \text{ \AA}$, $\alpha(\text{O}-\text{H}-\text{N}) = 165.11^\circ$.

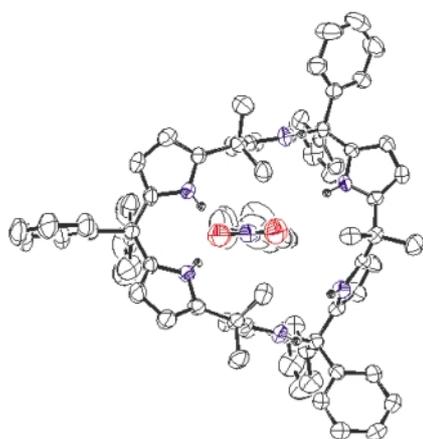


Fig. 2 The molecular structure of the complex between calix[6]pyrrole and nitrotoluene/nitrobenzene. Molecules that are not situated in the cavity of the host have been omitted for clarity.

In conclusion, calix[6]pyrrole **2** shows a wealth of binding modes to different substrates, ranging from simple anions to aromatic derivatives. The axial *meso* phenyl groups form a genuine preorganized cavity and actively participate in binding

trihalogenated compounds. The application of calix[6]pyrroles to the separation and identification of such compounds is under investigation.

This work was supported by the Israel Science Foundation, Administrated by the Israel Academy of Sciences and Humanities and by the Fund for the Promotion of Sponsored Research at the Technion.

Notes and references

[†] *Crystal data*: for 2·2.5CCl₃CH₂OH·1.5CHCl₃·3CH₂CH₂OH·5.5H₂O: grown in the dark from 2,2,2-trichloroethanol–chloroform–ethanol. A single crystal was mounted on the Nonius Kappa CCD diffractometer,⁸ and cooled to 170 K under a nitrogen stream. Data were collected with graphite-monochromated Mo-K α radiation ($\lambda = 0.71070 \text{ \AA}$) by applying ϕ and ω rotations. Data reduction was performed using DENZO-SMN software.⁹ The structure was solved using direct methods (SHELXS-97¹⁰) and refined by SHELXL-97.¹¹ All non-H atoms of the macrocycle and the trichloroethanol inside the cavity, excluding the disordered hydroxy oxygen, were refined anisotropically. Hydrogen atoms of these moieties were placed at calculated positions and refined as riding on their carbon and nitrogen atoms. Difference Fourier maps based on the macrocycle and the guest inside, revealed another moderately disordered trichloroethanol bound to the macrocycle outside the cavity, and another four sites of severely disordered molecules such as trichloroethanol, chloroform, ethanol and water. All the disordered positions of the solvent molecules were refined isotropically. 38 hydrogen atoms belonging to some of the disordered solvent molecules were not allocated. $M_r = 1804.83$, monoclinic, space group $P2_1/n$, $a = 17.773(10)$, $b = 20.2090(10)$, $c = 26.2590(10) \text{ \AA}$, $\beta = 107.730(3)^\circ$, $V = 8983.6(8) \text{ \AA}^3$, $T = 170.0(1) \text{ K}$, $Z = 4$, $\mu = 0.076 \text{ mm}^{-1}$, 14 385 reflections measured, 14 385 unique which were used in all calculations. The final $R(F^2)$ was 0.1168 [$I > 2\sigma(I)$].

For 2·2.5C₆H₅NO₂·0.5C₇H₉NO₂: grown in the dark by slow evaporation of a chloroform solution. A single crystal was mounted on the Nonius Kappa CCD diffractometer, at 293 K. Data collection and reduction as above. The structure was also solved and refined as above. All non-H atoms of the macrocycle and the guests were refined anisotropically. Hydrogen atoms were placed at calculated positions and refined as riding on their carbon and nitrogen atoms except for the N–H hydrogen atoms of the pyrrole rings which were localized on a Fourier difference map and refined isotropically. $M_r = 1392.66$, monoclinic, space group $P2_1/n$, $a = 19.455(1)$, $b = 19.762(1)$, $c = 22.027(1) \text{ \AA}$, $\beta = 115.405(2)^\circ$, $V = 7649.8(5) \text{ \AA}^3$, $T = 293 \text{ K}$, $Z = 4$, $\mu = 0.076 \text{ mm}^{-1}$, 16 018 reflections measured, 15 694 unique which were used in all calculations. The final $R(F^2)$ was 0.0740 [$I > 2\sigma(I)$].

CCDC 182/1864. See <http://www.rsc.org/org/suppdata/cc/b0/b007788g/> for crystallographic files in .cif format.

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