



Deep cavitands for anion recognition

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Abstract

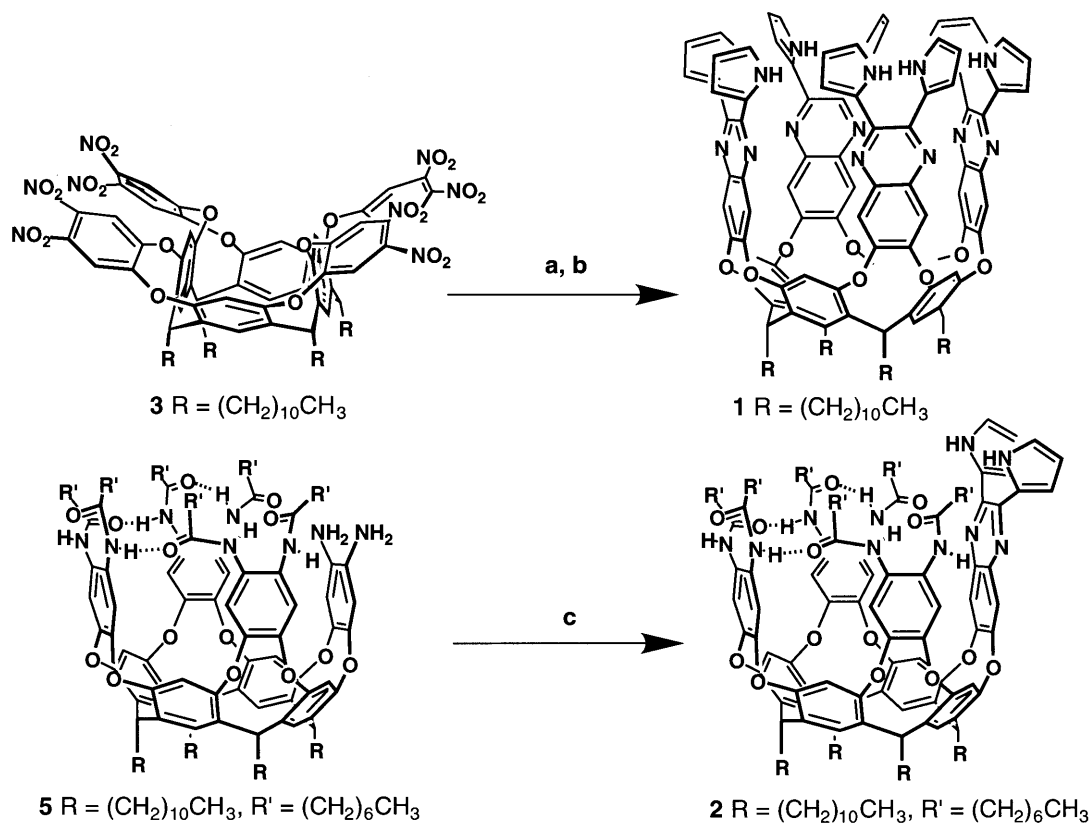
The synthesis of deep cavitands **1** and **2** bearing dipyrrolylquinoxaline walls is presented. Spectroscopy showed that **1** and **2** complex inorganic anions such as F^- and $CH_3C(O)O^-$ in aprotic organic solvents. In addition, the cavity in **2** is capable of hosting neutral guest species—adamantane and cyclohexane derivatives, as well as *N*-Me quinuclidinium cations—with high kinetic stability of the complexes. © 2000 Elsevier Science Ltd. All rights reserved.

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Cavitands are open-ended molecular vessels capable of binding smaller organic compounds within their interiors.¹ We recently prepared deeper cavitands featuring high kinetic and thermodynamic stabilities of their complexes. In these, intramolecular hydrogen bonding and solvent effects control the inner cavity's conformational dynamics and therefore its complexing ability.^{2,3} These cavitands have been further functionalized with peripheral porphyrin and Kemp's triacid groups^{4,5} and elaborated into much larger, nanoscale semi-capsular structures.⁶ Here we describe modifications leading to cavitands capable of anion recognition. The results show promise for the synergetic use of the inner cavity and anion binding sites.⁷

The rationale is based on the dipyrrolylquinoxaline anion binding motif⁸ recently discovered by Sessler and coworkers. Earlier we had developed methods for deepening cavitands through heterocycle formation between 1,2-arylene diamines and 1,2-diketones.³ For the case at hand, octanitro derivative² **3** was reduced (Ra/Ni, toluene) and subsequently condensed with 2,3-dipyrrol-2'-ylethanedione⁹ **4** to give cavitand **1** featuring four anion detecting walls (12% overall yield). Hexa-amide cavitand **2** was prepared similarly (42% yield) from **4** and diamine cavitand **5** described previously (Scheme 1).¹⁰

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Scheme 1. (a) Raney Ni, H_2 , toluene/EtOH (10/1), 16 h; (b) 2,3-dipyrrol-2'-ylethanedione **4** (5 equiv.), AcOH, reflux, 16 h, 12% (a+b); (c) 2,3-dipyrrol-2'-ylethanedione **4** (2 equiv.), AcOH, reflux, 3 h, 42%

Cavitands **1** and **2** exist in solution as vase-like structures (Fig. 1A,B), a conclusion supported by their ^1H NMR spectra. For molecule **1**, only one set of sharp signals was found for all groups of protons in acetone- d_6 . In chlorinated and aromatic deuterated solvents, broadening of these signals occurred at ambient temperatures, indicating conformational dynamics in a process that is intermediate in rate on the NMR timescale. Three C(O)–NH resonances of cavitand **2** are observed as far downfield as 8 ppm (in CDCl_3 , benzene- d_6 , toluene- d_8 , etc.). As in previously described cavitands,² the secondary amides form a seam of intramolecular C=O \cdots H–N hydrogen bonds (Fig. 1B,C) which hold the molecule in its vase-like conformation. The interconversion between the two cycloenantiomeric structures in **2** is fast on the NMR timescale (600 MHz, 295 K) since the spectrum indicates a plane of symmetry (Fig. 1B). The internal cavity dimensions in **1** and **2** are estimated at $\sim 9 \times 10 \text{ \AA}$ and the distance between the cavity's bottom and the pyrrol fragments is $\sim 10\text{--}11 \text{ \AA}$ (Fig. 1C).

Cavitands **1** and **2** can be used as visual detectors of fluoride and acetate anions (as tetrabutyl ammonium salts) in aprotic solvents such as acetone and CH_2Cl_2 . A dramatic color change from yellow to dark red accompanies binding. For example, upon addition of a ~ 50 -fold excess $n\text{-Bu}_4\text{N}^+\text{F}^-$ or $n\text{-Bu}_4\text{N}^+\text{OAc}^-$ to the acetone solution of **1**, the band at $\lambda_{\text{max}} = 420 \text{ nm}$ disappeared and two new bands at $\lambda_{\text{max}} = 350$ and 490 nm emerged (Fig. 2A). Similar behavior was observed for cavitand **2** in acetone and CH_2Cl_2 . No Cl^- and very weak H_2PO_4^- complexation was

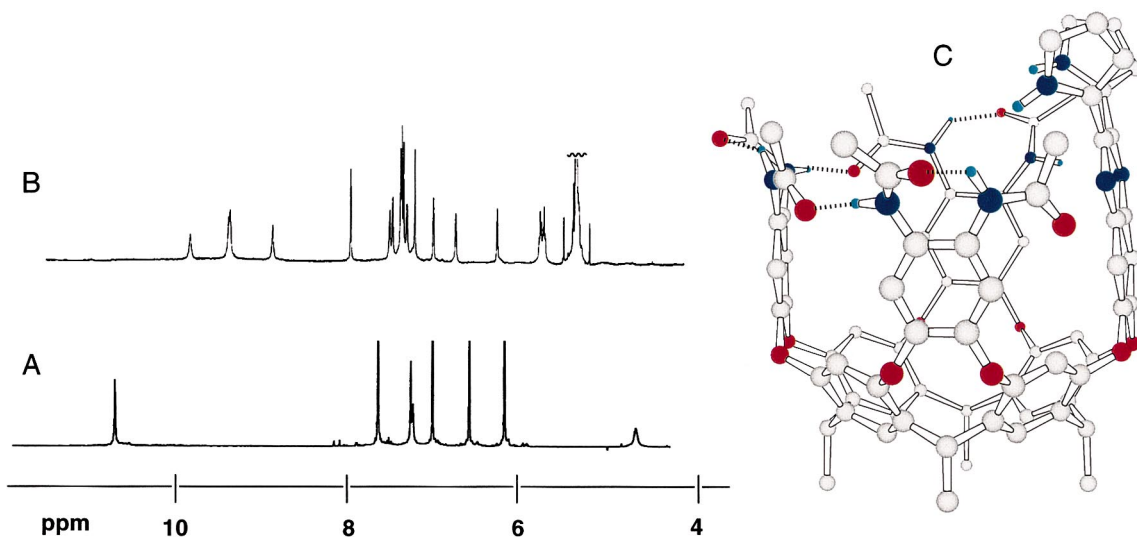


Figure 1. (A) Portion of the ^1H NMR spectra (600 MHz, 295 K) of **1** in acetone- d_6 . In the downfield region, the pyrrole NH singlet is situated; the methine CH triplet is at 4.65 ppm. (B) Portion of the ^1H NMR spectra (600 MHz, 295 K) of **2** in CD_2Cl_2 . In the downfield region, the pyrrole NH and three amide C(O)NH singlets are situated; the methine CH triplets are at ~ 5.7 ppm. (C) Energy-minimized structure of **2** (Amber* force field, MacroModel). Long alkyl chains and CH bonds have been omitted for viewing clarity

detected. The ^1H NMR spectra of the F^- and OAc^- anion complexes with **1** and **2** showed significant broadening of all groups of protons, especially the pyrrolyl CH and NH signals. The latter were also shifted ~ 2 ppm downfield. No anion binding was detected in deuterated aromatic solvents.

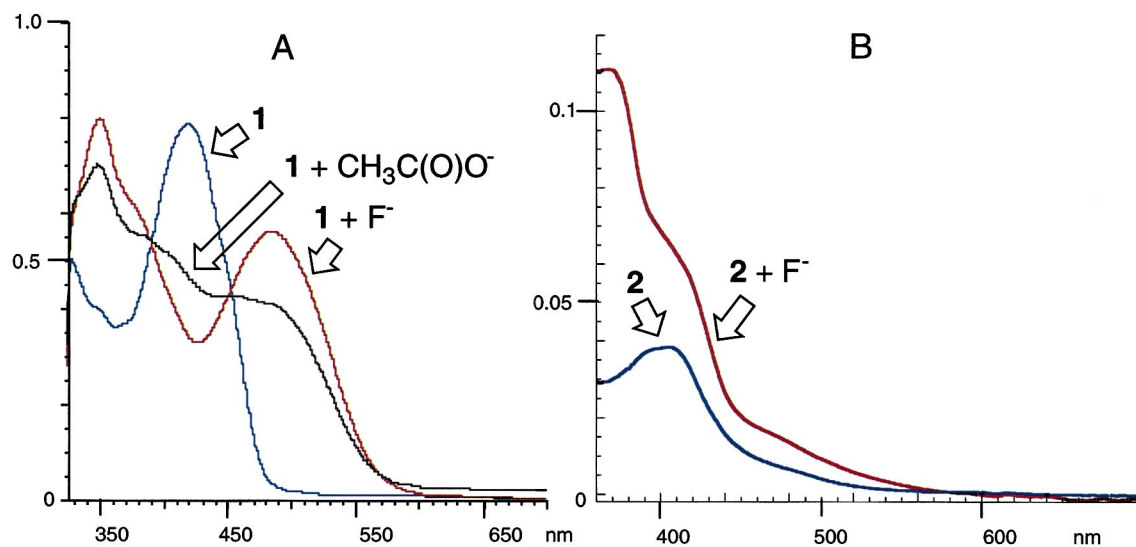


Figure 2. UV-vis measurements of anion binding. (A) **1** in acetone; (B) **2** in toluene-acetone, 4:1 v/v

Cavitand **1** in deuterated toluene, acetone or chlorinated solvents binds neither tetrabutylammonium and quinuclidinium salts, nor adamantane derivatives. The cavity is apparently conformationally labile³ and the guest exchange is fast on the NMR timescale, if it occurs at all. In contrast, conformationally fixed cavitand **2** gives kinetically stable complexes with adamantane and cyclohexane amides. The bound guest signals were clearly seen upfield at 0 ppm in toluene-*d*₈. On the other hand, no cavitplexes with *n*-Bu₄N⁺ groups, adamantane- and cyclohexane amides were detected in acetone-*d*₆ and CD₂Cl₂. Apparently, in these solvents the inner cavity is well solvated and the solvent molecule replacement is not an energetically favorable process.

The use of binary solvent mixtures allowed both encapsulation and anion recognition processes to take place. In toluene–acetone (4:1 v/v) cavitand **2** was found to bind F⁻ anion: the band at $\lambda_{\text{max}}=420$ nm decreased in intensity and a new intense band at $\lambda_{\text{max}}=370$ nm emerged (Fig. 2B). In addition, in the toluene–acetone or toluene–CH₂Cl₂ (1:1 v/v) solvent mixtures cavitand **2** forms kinetically stable complexes with some adamantane derivatives and also with *N*-Me quinuclidinium cation.

In principle, two different guest species—a neutral organic molecule and inorganic anion—can be simultaneously bound by the new, deep cavity-containing structures. If the two guests are in close proximity it may be possible to arrange bimolecular reactions between them. We are currently pursuing this goal.

Acknowledgements

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- All new compounds were purified first by column chromatography and then by preparative TLC (silica gel) and characterized by high-resolution NMR spectroscopy and MALDI-TOF mass spectrometry. The experimental details will be published in a full paper. Selected spectral data. Cavitand **1**: ¹H NMR (acetone-*d*₆, 295 K) δ 10.85

(s, 8 H, NH), 7.71 (s, 8 H, CH_{ar}), 7.32 (s, 4 H, CH_{ar}), 7.30 (s, 4 H, CH_{ar}), 7.06 (s, 8 H, CH_{pyr}), 6.62 (s, 8 H, CH_{pyr}), 6.20 (s, 8 H, CH_{pyr}), 4.65 (s, 4 H, CH), 2.02 (br, 8 H, CHCH₂), 1.5–0.9 (m, 72 H, CH₂), 0.87 (t, $J=7.0$, 12 H, CH₃); MALDI-TOF MS: m/z 2130, calcd for C₁₃₆H₁₄₄N₁₆O₈: 2130. Cavitand **2**: ¹H NMR (CD₂Cl₂, 295 K) δ 9.76 (s, 2 H, NH), 9.34 (s, 2 H, NH), 9.32 (s, 2 H), 8.84 (s, 2 H, NH), 7.93 (s, 2 H), 7.48 (s, 2 H), 7.45 (s, 2 H), 7.35 (s, 2 H), 7.34 (s, 2 H), 7.32 (s, 2 H), 7.28 (s, 2 H), 7.19 (s, 2 H), 6.97 (s, 2 H), 6.71 (s, 2 H), 6.24 (s, 2 H), 5.85–5.65 (m, 4 H), 2.70–0.50 (m, 182 H); MALDI-TOF MS: m/z 2431, calcd for C₁₅₄H₂₁₆N₁₀O₁₄H: 2432.