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Received February 14, 1994

Introduction

Calix[4]arenes are important building blocks in supramolecular chemistry. They can be selectively functionalized both at the phenolic OH groups (lower rim) and at the para positions of the phenol rings (upper rim). The calixarene platform provides unique possibilities to organize several binding sites in an array complementary to a potential guest. Selective calixarene-based receptors for cations and neutral molecules have been synthesized in the past decade. Very recently the first representatives of calixarene-containing anion receptors have been reported.

Previously we reported that neutral metallocclefts and metallamacrocycles containing both an immobilized Lewis acidic UO₂-center and amido C(O)NH units as additional binding sites are excellent receptors for anions with a high selectivity for dihydrogen phosphate H₂PO₄⁻. In the present paper we report, in addition to the synthesis of a new representative of a UO₂-containing anion receptor based on a calix[4]arene, the first example of a neutral calix[4]arene-based bifunctional receptor which contains both anionic and cationic binding sites and is able to complex simultaneously anionic and cationic species.

Results and Discussion

The synthesis of receptors 8a,b is depicted in Scheme 1. Calix[4]arene diester 1 was prepared by alkylation of unsubstituted calix[4]arene with ethyl bromocateate in the presence of 1 equiv of potassium carbonate as a base in refluxing acetone/dilute HCl. Nitrification of 1 with 65% HNO₃ in a mixture of acetic acid and CH₂Cl₂ gave the dinitrocalix[4]arene 2 in 51% yield with the expected selectivity on the more reactive phenol unit of 1. Alkylation of 2 with ethyl bromocateate and sodium carbonate as a base in refluxing acetone/diluted HCl gave tetraester 3 in 76% yield. The ¹H NMR spectrum of 3 shows only two doublets (4.93 and 3.35 ppm, J = 13.9 Hz) for the methylene bridge protons which proves the "cone" conformation of the calix[4]arene skeleton. Subsequent reduction of 3 with SnCl₂/H₂O in refluxing ethanol gave the corresponding diaminocalix[4]arene 4b in 55% yield.

Reaction of 1,3-diaminocalix[4]arenes 4a,4b with chloroacetyl chloride in the presence of Et₃N in CH₂Cl₂ gave the corresponding 1,3-bis(chloroacetamido)calix[4]arenes 5a,b in 69 and 64% yields, respectively. Bisaldehydes 6a,b were obtained by alkylation of 2-(2-allyloxy)-3-hydroxybenzaldehyde with 5a,b in the presence of potassium carbonate in 59 and 64% yields, respectively. Subsequent palladium-catalyzed deallylation of calixarenes 6a,b afforded bisaldehydes 7a,b in quantitative yield which were used without purification for the cyclization step.

Reaction of bisaldehydes 7a,b with cis-1,2-diaminocyclohexane and UO₂(OAc)₂·H₂O in refluxing ethanol under high dilution conditions gave the receptors 8a,b which were isolated in 9% and 15% yields, respectively, after column chromatography. The moderate yields of compounds 8a,b compared with known UO₂-containing metallamacrocycles may be explained by the lack of a suitable template in the cyclization step. The absorptions in the ¹H NMR spectra at 9.34 and 9.48 ppm and in the IR spectra at 1615 and 1617 cm⁻¹ for compounds 8a and 8b, respectively, proved imino bond formation. The presence of the UO₂ moiety is in agreement with the uranium–oxygen vibrations in the IR spectra at 955–905 cm⁻¹. Because of the "cone" conformation of the calix[4]arene unit in the ¹H NMR spectra there are only two doublets (4.30 and 3.12 ppm for 8a and 4.80 and 3.19 ppm for 8b) for the methylene bridge protons.

Compounds 8a,b both contain the combination of a UO₂–Lewis acidic center and C(O)NH groups which is known to act as an anionic binding site. In addition,


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In the negative FAB mass spectra of the 1:1 complexes of 8a and 8b with BuN⁺H₂PO₄⁻, prepared by mixing of host and guest in MeCN, intense peaks corresponding to [8a + H₃PO₄⁻]⁻ and [8b + H₃PO₄⁻]⁻, respectively, were observed. Moreover, in the positive FAB mass spectrum of the 1:1 complex of 8b and NaH₂PO₄, prepared by mixing of host and guest in MeCN–H₂O, 10:1, an intense peak corresponding to [8b + Na⁺]⁺ was observed, while the corresponding negative FAB mass spectrum of the same sample yielded an intense peak for [8b + H₂PO₄⁻]⁻, which proves the complexation of both cation and anion in one bifunctional receptor molecule.

Currently we are applying calix[4]arene-based bifunctional receptors for selective separation of alkali metal phosphates by transport through supported liquid membranes.¹⁸

**Experimental Section**

Melting points are uncorrected. ¹H NMR and ¹³C NMR spectra were recorded in CDCl₃ with Me₄Si as internal standard unless stated otherwise. Fast atom bombardment (FAB) mass spectra were obtained with m-nitrobenzyl alcohol as a matrix. All solvents were purified by standard procedures. Petroleum ether refers to the fraction with bp 60–80 °C. All other chemicals were analytically pure and were used without further purification. Unsubstituted calix[4]arene is and compound 4a is prepared according to literature procedures. All reactions were carried out under an argon atmosphere.

In the workup procedures the (combined) organic layers were washed with water (2×) and dried with MgSO₄, whereupon the solvent was removed under reduced pressure. The presence of


(17) Only weak binding was obtained for the divalent HPO₄²⁻ anion.

solvent in the analytical samples was confirmed by 'H NMR spectroscopy.

25.27-Bis[ethoxy carbonyl(methoxy)-9,9,9-triethyl-9,10-dihydroxy- 9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10-dihydroxy-9,10--
5,17-[[2,2'-{1,2-Cyclohexanediyldi[benzil]}trithio-3,1-phenylene]oxy]bis(acetamido)](2-)[dioxouranium]-25,26,27,28-tetrapropoxy[4]arene (8a): yield 9%; mp 283–285 °C (acetone); $^1$H NMR (DMSO-$d_6$/CDCl$_3$, 500 MHz) $\delta$ 9.45 (br s, 2 H), 9.34 (s, 2 H), 7.31, 7.26 (d, 4 H, J = 8.0 Hz), 7.1–6.8 (m, 10 H), 6.45 (t, 2 H, J = 8.0 Hz), 4.81 (q, 4 H, J = 7.0 Hz), 4.75–4.50 (m, 2 H), 4.30, 3.12 (d, J = 13.5 Hz), 4.00, 3.61 (t, 8 H, J = 7.0 Hz), 2.3–2.0 (m, 8 H), 1.00, 0.97 (t, 12 H, J = 7.0 Hz); MS-FAB m/z 1325.7 (M$^+$, calc. 1325.3). Anal. Calcld for C$_{48}$H$_{32}$N$_2$O$_8$U-CH$_2$CN: C, 53.02; H, 5.39; N, 5.13. Found: C, 53.32; H, 5.56; N, 5.15.

5,17-[[2,2'-{1,2-Cyclohexanediyldi[benzil]}trithio-3,1-phenylene]oxy]bis(acetamido)](2-)[dioxouranium]-25,26,27,28-tetraakis[ethoxy]carbonyl]methoxy]calix[4]arene (8b): yield 15%; mp 235–238 °C (EtOH); $^1$H NMR (DMSO-$d_6$) $\delta$ 9.70 (br s, 2 H), 9.45 (s, 2 H), 7.43, 7.36 (d, 4 H, J = 8.0 Hz), 7.2–6.9 (m, 10 H), 6.65 (t, 2 H, J = 8.0 Hz), 5.24 (s, 4 H), 4.80, 3.19 (d, 8 H, J = 13.0 Hz), 4.69, 4.46 (s, 8 H), 4.7–4.6 (m, 2 H), 4.25, 4.10 (q, 8 H, J = 7.0 Hz), 2.4–2.3 (m, 2 H), 1.9–1.8 (m, 6 H), 1.30, 1.21 (t, 12 H, J = 7.0 Hz); MS-FAB m/z 1301.1 (M$^+$, calc. 1301.3). Anal. Calcld for C$_{48}$H$_{32}$N$_2$O$_8$U: C, 54.49; H, 4.70; N, 3.73. Found: C, 54.39; H, 4.86; N, 3.55.

**Determination of Association Constants.** The measurements were performed by $^1$H NMR titration experiments in DMSO-$d_6$ at 298 K using a constant host concentration of 4 mM and a varying guest concentration of 0.3–30 mM. As a probe the chemical shift of the C(O)NH signal was used. The $K_{as}$ values were calculated by nonlinear regression as described in ref 19. The estimated error is <5%.