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Calix[4]arene-porphyrin Conjugates as Versatile Molecular Receptors for Anions

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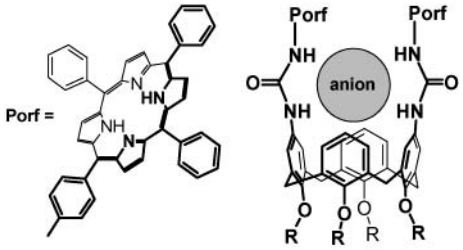
ABSTRACT



Appending tetraphenylporphyrin units to the calix[4]arene skeleton via the ureido function leads to novel anion receptors designed for anion and/or cation detection by UV–vis spectroscopy. Calixarenes in the cone or 1,3-alternate conformations bearing two ureido moieties on the upper rim represent well-preorganized cavities where the anion can be held by synchronous hydrogen bonding interaction with the NH groups.

Calix[4]arenes are macrocyclic molecules with unique three-dimensional structures. Because of their custom chemical derivatization and good complexation ability,[1] these compounds have been widely used in supramolecular chemistry as building blocks or molecular scaffolds for the construction of various receptors. While the selective complexation of cations by functionalized calixarenes has been studied broadly for almost two decades,[2] the development of calixarene-based receptors for anion recognition is a relatively new research topic.[3] It is well-known[4] that activated amides or urea derivatives can interact with anions using hydrogen bonding interactions of NH groups. Hence, ureido functions added to calixarene can form a suitably preorganized cavity with potential anion recognition capability.[5] Previously, we have reported[6] on the cone and 1,3-alternate calixarene conformers bearing two urea functions on the

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(1) For books on calixarenes, see: (a) *Calixarenes 2001*; Asfari, Z., Böhmer, V., Harrowfield, J., Vicens, J., Eds.; Kluwer Academic Publishers: Dordrecht, 2001. (b) *Calixarenes in Action*; Mandolini, L.; Ungaro, R., Ed.; Imperial College Press: London, 2000. (c) Gutsche, C. D. *Calixarenes Revisited: Monographs in Supramolecular Chemistry*; Stoddart, J. F., Ed.; The Royal Society of Chemistry: Cambridge, 1998: Vol. 6. (d) *Calixarenes 50th Anniversary: Commemorative Issue*; Vicens, J., Asfari, Z., Harrowfield, J. M., Eds.; Kluwer Academic Publishers: Dordrecht, 1994. (e) C*alixarenes: A Versatile Class of Macrocyclic Compounds*; Vicens, J., Böhmer, V., Eds.; Kluwer Academic Publishers: Dordrecht, 1991.

(2) See, for instance: Pochini, A.; Ungaro, R. In *Comprehensive Supramolecular Chemistry;* Vögtle, F., Ed.; Pergamon Press: Oxford, 1996; Vol. 2, pp 103−142. McKervey, M. A.; Schwing-Weill, M. J.; Arnaud-Neu, F. In *Comprehensive Supramolecular Chemistry*; Gokel, G., Ed.; Pergamon Press: Oxford, 1996; Vol.1, pp 537−603.

(3) See, for instance: Beer, P. D. *Chem. Commun.* **1996**, 689−696.

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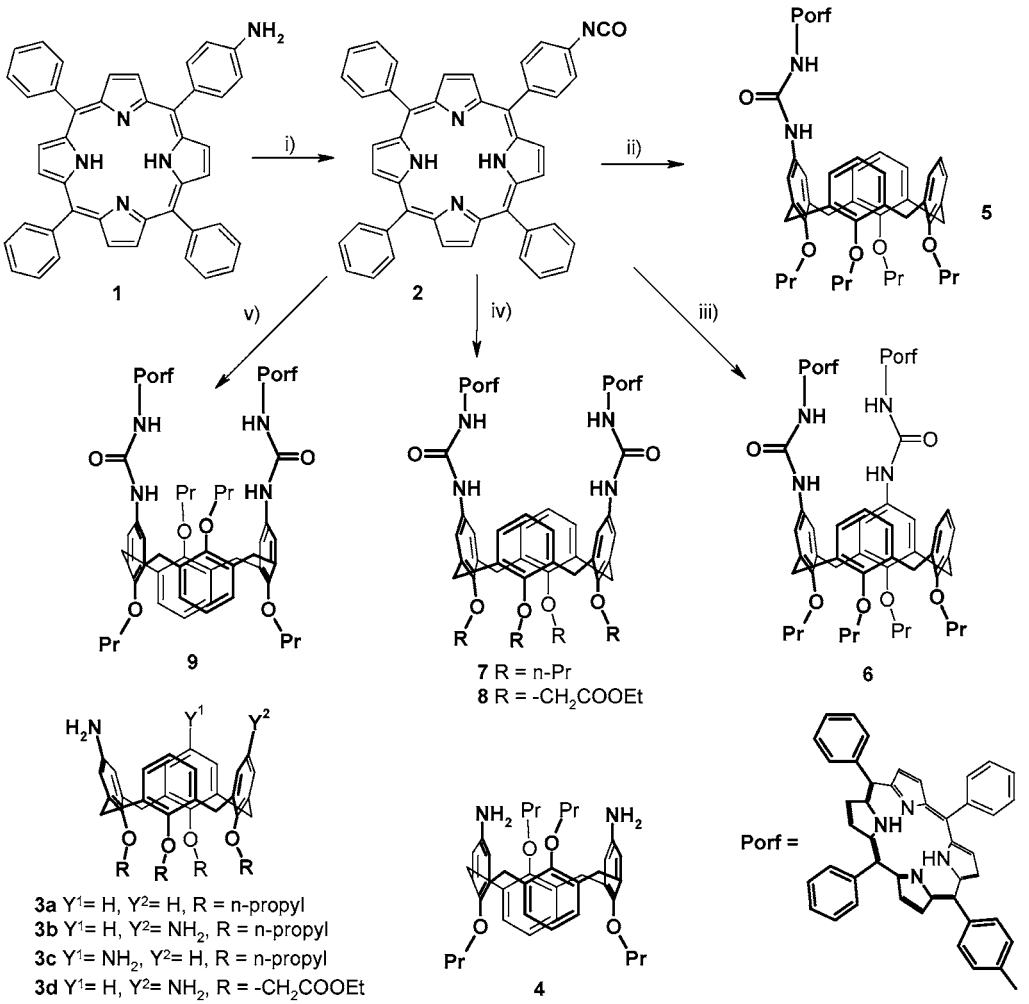
Scheme 1. Synthesis of Calixarene-porphyrin Conjugates[a]



[a] Conditions: (i) triphosgene/Et_3N, 1,2-dichloroethane, reflux; (ii) +**3a**, reflux, 68%; (iii) +**3c**, 55%; (iv) +**3b**, 54%, +**3d**, 42%; (v) +**4**, 33%.

upper rim that can bind anions such as halogenides and carboxylates. By contrast, the cone derivatives bearing four urea units tend to assemble into dimeric structures via intermolecular hydrogen bonding.[7] We now report the first synthesis of novel calix[4]arene-porphyrin conjugates connected via ureido functions. As the binding of anions is accompanied by changes in the UV−vis spectra of appended porphyrin moieties, these compounds can serve as anion receptors. Adding the acetate groups at the lower rim creates the additional binding site for cations.

The synthesis of conjugates **5**−**9** is depicted in Scheme 1. Starting amino-substituted porphyrin **1** or calix[4]arenes **3a**−**d** and **4**, immobilized in the cone or 1,3-alternate conformations, were prepared by the reduction of the corresponding nitro derivatives.[8] Aminoporphyrin[8c] **1** was transformed into appropriate isocyanate **2** by refluxing with triphosgene[9] in 1,2-dichloroethane in the presence of Et_3N. Due to its alleged instability, the solution of **2** thus obtained was used in the next step without further purification and characterization. The addition of aminocalixarenes **3** or **4** and the stirring of the reaction mixture for several hours led smoothly to the ureido conjugates **5**−**9** in fairly good yields of 33−68% after the column chromatography. In the case of diureido derivative **7**, we have also applied a different synthetic procedure where the isocyanate derived from calix[4]arene **3b** was condensed with porphyrin **1**. This inverted approach gave a much lower yield of **7** (<10%). The structures of the conjugates were confirmed by ^1H and ^{13}C NMR, IR, and MS spectroscopy and elemental analysis.

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The complexation of selected anions (Cl^-, Br^-, I^-, and NO_3^-) by the porphyrin conjugates was studied by UV−vis titrations in CH_2Cl_2. The addition of anions (Bu_4N^+ salts) resulted in a tiny red shift (0.5 nm), a hypochromicity of the Soret maximum, a small broadening at about 440 nm, and well-defined isosbestic points (Figure 1). Changes in the

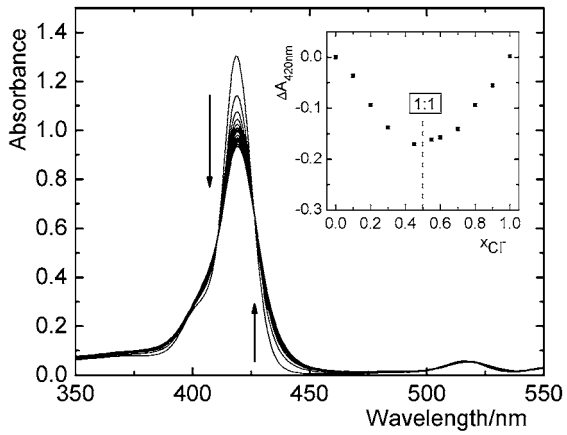

Figure 1. UV−vis titration of 1.6 μM **7** with $Bu_4N^+Cl^-$ in CH_2Cl_2. Arrows show changes due to increasing concentration of Cl^-. Inset: Job plot recorded at 420 nm. Sum of concentrations was fixed at 4.0 μM.

Soret region of **6** upon the addition of anions are not as substantial as those observed for other receptors. All titrations were performed with an approximately 1 μM concentration of receptor, giving binding isotherms (Figure 2) reproducible

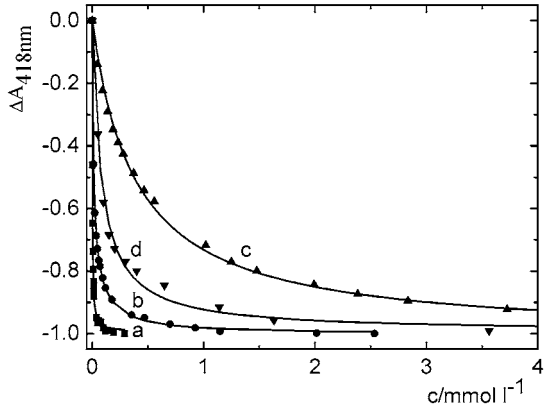

Figure 2. Absorbance changes of **7** at 418 nm upon the addition of Cl^- (a), Br^- (b), I^- (c), and NO_3^- (d) in CH_2Cl_2 normalized to ΔA_∞ equal to unity (1.2 μM **7**, $\Delta A_\infty = -0.243, -0.259, -0.230, -0.167$ from Cl^- to NO_3^-). Solid lines are the theoretical isotherms obtained by the least-squares fit to the experimental data.

and suitable for fitting analysis.[10] Further indications of anion complexation were obtained from ^{1}H NMR titrations. While the NH groups became invisible upon addition of anions, the signals of aromatic protons located next to the ureido groups are visibly shifted upfield (e.g., ca. 0.25 ppm for **7** + Cl^-).

To determine the stoichiometry of the anion complexation, the Job plots were constructed from both UV−vis and ^{1}H NMR titration data. In all cases, the formation of the 1:1 complexes was clearly confirmed (Figure 1, inset). The complexation-induced NMR shifts indicate that the ureido groups form a binding site and that hydrogen bonding is responsible for anion binding. From a structural point of view, an anion is inserted within the closed cavity composed of the upper rim of calix[4]arene and two porphyrin units are attached by the urea linkers.

The deliberate modification of the structural motif provides further insight into the relation between the structure of the binding site and complexation ability (Table 1). Receptors

Table 1. Binding Constants K [M^{-1}] of Calix[4]arene-porphyrin Conjugate toward Selected Anions in CH_2Cl_2 at 24 °C (UV−vis)[c]

	5	**6**	**7**	**8**	**9**
Cl^-	6.3×10^3	5.8×10^5	6.9×10^5	1.4×10^6	6.6×10^5
Br^-	1.2×10^3	7.8×10^4	6.9×10^4	2.2×10^5	6.5×10^4
I^-	240	8×10^3 [b]	2.4×10^3	2.9×10^4	4.8×10^3
NO_3^-	820	3×10^4 [b]	1.3×10^4	a	4.5×10^3

[a] Very low absorption changes. [b] Values of K were estimated because of low absorption changes. [c] Most titrations were not studied by ^{1}H NMR spectroscopy because the K values were too large. For less effectively bound anions, the ^{1}H NMR titrations give fully comparable results: e.g., 3.0×10^3 M^{-1} for **7** and I^- (25 °C, CD_2Cl_2).

6, **7**, and **9** exhibit affinity similar to those of small spherical anions such as Cl^- and Br^-. This fact implies that the linkers connecting calix[4]arene and the porphyrin moiety are sufficiently flexible to accommodate Cl^- and Br^- regardless of their mutual position (proximal **6** versus diametrical **7**). Moreover, as documented by the behavior of 1,3-alternate **9**, the propoxy groups oriented between the porphyrin arms do not hinder the formation of the complex with anion. On the other hand, significant differences in binding constants are observed for larger anions I^- and NO_3^-, probably because of steric hindrance imposed on the binding site. As follows from the data in Table 1, the binding constants of halides decrease with the anion diameter, which reflects the size recognition ability of the novel receptors[11] [e.g., **7**: K_{Cl} (6.9×10^5 M^{-1}) > K_{Br} (6.9×10^4 M^{-1}) > K_I (2.4×10^3 M^{-1})].

The effect of the number of NH bonds on the anion complexation is seen by comparing the binding affinity of **7**

(10) Binding isotherms were analyzed using the hyperbolic relationship between the observed absorbance change ($\Delta A = A - A_o$) and the equilibrium free molar concentration of anion [L], $\Delta A = \Delta A_\infty K_b[L]/(1 + K_b[L])$, where K_b is the binding constant, A_o is the absorbance in the absence of anion, and $\Delta A_\infty = A_\infty - A_o$. The free molar concentration was expressed as a function of the added total anion concentration using $L_t = [L] + P_t K_b[L]/(1 + K_b[L])$, where P_t is the total molar concentration of the porphyrin receptor (Connors, K. A. *Binding Constants, The Measurement of Molecular Complex Stability*; Wiley & Sons: New York, 1987). All titration experiments were performed in CH_2Cl_2 at 24 °C. Measurements were repeated several times and found to be reproducible to within 15%.

($K_{Cl} = 6.9 \times 10^5$ M^{-1}) with that of derivative **5** ($K_{Cl} = 6.3 \times 10^3$ M^{-1}) possessing only one urea unit. The difference of 2 orders of magnitude demonstrates the importance of a hydrogen bonding array for effective anion binding. Accordingly, the complexation ability of receptors in methanol, being highly competitive toward hydrogen bonding, disappears.

Conjugate **8** represents a special case of the anion receptor because it has a second binding site at the calix[4]arene lower rim created by four ethyl acetate groups capable of concerted binding of alkaline metal cations. Conjugate **8** shows a high affinity toward Cl^- with the binding constants of 1.4×10^6 M^{-1} and 1.5×10^5 M^{-1} in CH_2Cl_2 and acetonitrile, respectively.[12] The complexation occurs within the ureido binding site and is accompanied by the same spectral features described above. On the other hand, **8** displays a sharpening of the Soret band concomitant with a considerable hyperchromicity upon the addition of $LiClO_4$ or $NaClO_4$ in acetonitrile (Figure 3). This sharpening indicates that the

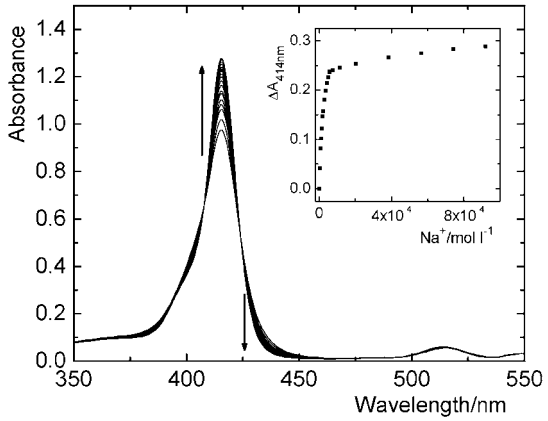

Figure 3. UV−vis titration of 1.9 μM **8** with Na^+ in acetonitrile. Arrows show changes due to increasing concentration of Na^+. Inset: Binding isotherm measured at the Soret maxima at 414 nm.

absorbance changes are due to cation complexation. The complexation by the ethyl acetate groups was confirmed and the stoichiometry verified unambiguously by ^{1}H NMR. Two sets of signals for complexed and uncomplexed species of an **8**/Na^+ system reveal the 1:1 stoichiometry under slow-exchange conditions (4:1 v/v $CDCl_3/CD_3CN$, room temperature). However, the binding isotherms could not be satisfactorily fitted under the assumption of a 1:1 complex (Figure 3, inset). The reason is not clear. It is possible that the counteranion modifies the overall absorption envelope, thus affecting the features of the binding isotherms. This assumption is supported by the independent finding that receptor **7** binds ClO_4^- under comparable conditions ($Bu_4N^+ClO_4^-$, ^{1}H NMR, 4:1 v/v $CDCl_3/CD_3CN$) with a low binding constant ($K_{ClO4} \cong 200$ M^{-1}). The estimated binding constants for Na^+ and Li^+ complexation were obtained from the beginning of the isotherms and are on the order of 10^4 M^{-1}.

It is obvious that cation complexation at the lower rim of **8** results in the solidification of the whole calixarene skeleton. Hence, the absorbance band sharpening can be explained by the changes in exciton coupling between closely separated porphyrin units. Upon the addition of cations, the porphyrin units are more distant, and consequently the Soret band sharpens due to the less effective exciton coupling. Cation-controlled anion sensing is currently under investigation.

In conclusion, the calix[4]arene-porphyrin conjugates **5**−**9** connected via ureido functions represent novel anion receptors with a distinctive size selectivity toward halides. As we have demonstrated, the binding of anions is caused by synchronous hydrogen bonding interactions and is accompanied by changes in UV−vis spectra.

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Supporting Information Available: General procedure for the preparation of receptors, characterization, spectral properties, Job plots, and binding isotherms. This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) Receptor **7** exhibits better complexation ability towards Cl^- ($K_{Cl} = 1.9 \times 10^4$ M^{-1} and 1.5×10^4 M^{-1} by ^{1}H NMR and UV−vis, respectively) than the previously reported[6a] receptor bearing phenyls instead of porphyrin units ($K_{Cl} = 4.6 \times 10^3$ M^{-1}) (^{1}H NMR, 300 MHz) in 4:1 v/v $CDCl_3/CD_3CN$ (rt).

(12) A similar receptor bearing two octyl groups[5c] does not complex halide anions in the absence of Na^+ or K^+ cations.