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A selective colorimetric anion sensor based on an amide group containing macrocycle†

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A new colorimetric anion sensor 4 allows for selective 'naked-eye' differentiation of F^-, AcO^- and $H_2PO_4^-$ with similar basicity.

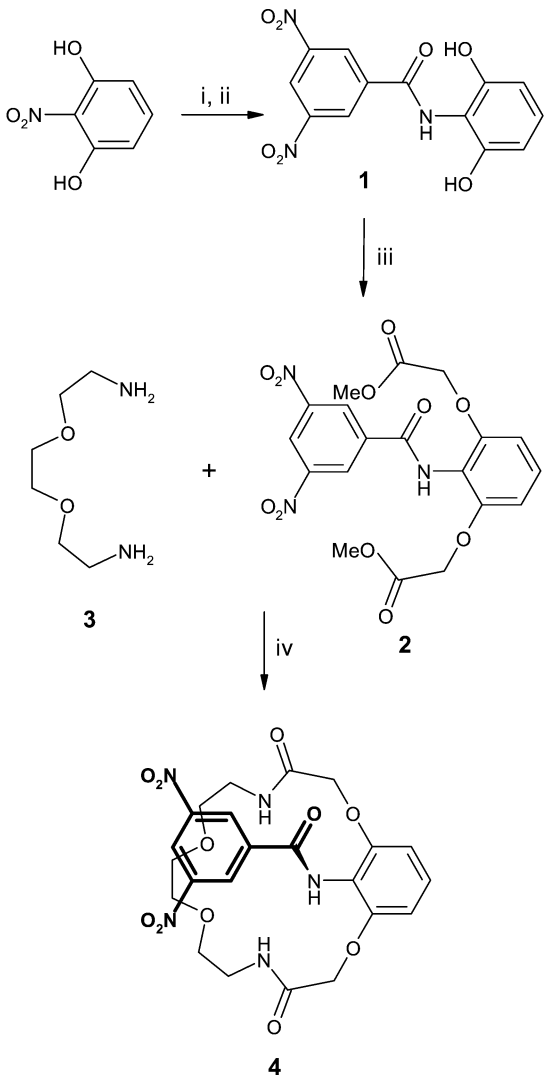
The design and synthesis of systems that are capable of sensing various biologically and/or chemically important negatively charged species is an area of current interest.[1] One of the most attractive approaches in this field involves the construction of colorimetric anion sensors.[2] Such sensors allow 'naked-eye' detection of anions without the use of any spectroscopic instrumentation. Such systems are generally composed of two parts. One is the anion binding part (receptor) which is based on various combinations of pyrrole, urea, thiourea, sulfonamide, amine or phenol moieties. The other is a chromophore which converts binding induced changes into an optical signal. These two parts are either directly linked[2] or intramoleculary associated.[3] However, few such systems exist at present, and a need for selective 'naked-eye' anion sensors remains.

Although a variety of artificial anion receptors coordinate anions by amide groups,[4] there are no colorimetric anion sensors based on such groups. In this communication, we report a new amide-based macrocyclic anion sensor **4**. This compound possesses two aromatic rings connected by an amide group. One of them is electron-rich, whereas the second has two electron withdrawing NO_2-groups. Such a system should act as an H-bond donor and an optically sensitive indicator of anion binding. The two aliphatic amide groups could serve as important additional anion binding sites.

The synthesis of receptor **4** is outlined in Scheme 1. The catalytic reduction of the nitro group of 2-nitroresorcinol and subsequent acylation of the amino function by 3,5-dinitrobenzoyl chloride gave compound **1**. Then the phenolic groups were alkylated by methyl bromoacetate in the presence of sodium carbonate and a catalytic amount of potassium iodide. Reaction of the resulting α,ω-dimethyl ester **2** with α,ω-diaminoether **3**, under non-high-dilution conditions,[5] afforded macrocyclic compound **4** in 46% yield.

The association of receptor **4** with various anionic guests, in polar solvents such as DMSO-d_6 and CD_3CN, was studied by the ^1H NMR titration method.[6] The resulting binding isoterms were analyzed by a nonlinear regression method[7] which gave the association constants listed in Table 1. All titration curves gave a satisfactory fit to a 1:1 binding model, except for fluoride anion for which a 1:2 ligand:anion complex stoichiometry was found. The selectivity trends in binding affinities of anions for receptor **4** in DMSO-d_6 were determined to be: $F^- \gg AcO^- > H_2PO_4^- > HSO_4^- > Cl^- \sim Br^-$. The observed binding order can be easily rationalized based on the guest basicity. A change of the solvent from DMSO-d_6 to CD_3CN causes crucial changes of association constants as well as the selectivity trends of the binding ability of receptor **4** for anions.

As shown in Table 1, except for the fluoride anion, an increase of all association constants were observed. The most dramatic enhancement was observed for $H_2PO_4^-$: K_a = 142 (DMSO-d_6) and K_a = 4271 (CD_3CN). In contrast to dihydrogenphosphate, the increase of association constants for more basic acetate ion was negligible. The selectivity for $H_2PO_4^-$ ion can be attributed to the additional hydrogen bonding interactions between the OH group of dihydrogenphosphate and ethereal oxygen atoms of receptor **4**. Such interactions seem to be enhanced in acetonitrile and suppressed by DMSO.



Scheme 1 The synthesis of receptor **4**. *Reagents and conditions*: (i) H_2, Pd/C, THF, rt, 10 h ; (ii) 3,4-dinitrobenzoyl chloride, Et_3N, THF, rt, 2 h, 78%; (iii) methyl bromoacetate, Na_2CO_3, KI, MeCN, 80 °C, 48 h, 58%; iv) Na, MeOH, rt, 72 h, 46%.

† Electronic supplementary information (ESI) available: experimental details for **1**, **2** and **4**; sample binding curves. See http://www.rsc.org/suppdata/cc/b2/b207335h/

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The complexation-induced chemical shifts, which are obtained during titration experiments, can be used to infer a quite detailed picture of anion binding. The aromatic amide NH signal becomes broad and disappeared when *ca.* 0.5 equivalent of F^-, $H_2PO_4^-$ or AcO^- was added. In the case of chloride and hydrogensulfate anions, this signal is easy to follow during the titration experiment, and large downfield shifts (>0.8 ppm) were observed. These findings indicated that the aromatic amide proton strongly interacts with anionic guests. Upon addition of the anions, upfield movements of all aromatic proton signals were observed. This observation was tentatively ascribed to charge transfer interactions between the amide-bound anion and the electron-deficient 3,5-dinitrobenzene moiety. Downfield shifts of the aliphatic amide NH signal, typical for hydrogen bonding interaction, were detected upon exposure to certain anions. The degree of these shifts varied considerably from 1.7 ppm for fluoride to 0.2 ppm for hydrogensulfate ion (CD_3CN).

A DMSO solution of receptor **4** (2×10^{-4} M) shows dramatic color changes upon addition of F^-, AcO^- and $H_2PO_4^-$ ions (Fig. 1). Specifically, it was found that initially colorless solutions turn dark blue (λ = 593, 708 nm), yellow (λ = 375 nm) and yellow (λ = 384 nm) when exposed to fluoride, dihydrogen phosphate and acetate ions, respectively. On the other hand, no color changes were observed upon addition of chloride, bromide or hydrogensulfate anions.

The observed color changes also took place in CH_3CN solutions. Receptor **4** forms a colorless solution, either alone or in the presence of Cl^-, Br^- or HSO_4^-. Upon addition of fluoride, acetate and dihydrogen phosphate ions, the solutions turn turquoise (λ = 408, 700 nm), yellow (λ = 378 nm) and purple (λ = 537, 393 nm), respectively. These visual changes are completely consistent with the association constants recorded for **4** in acetonitrile solutions, namely $F^- \gg H_2PO_4^- \gg AcO^- > Cl^- \sim HSO_4^- \gg Br^-$.

In conclusion, we have developed an amide-based macrocyclic sensor for anions that not only allows for the colorimetric detection of F^-, AcO^- and $H_2PO_4^-$ ions in both DMSO and acetonitrile solutions, but also shows selective coloration in acetonitrile for those anions with similar basicity.

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Table 1 Association constants ($dm^3\ mol^{-1}$) from ^1H NMR titrations for complexes of receptor **4** with anionic guests in DMSO-d_6 or CD_3CN[a]

	H:G	K_a (DMSO-d_6)	K_a (CD_3CN)	pK_a[b]
F^-	1:2	7.8×10^6	7.5×10^6	3.18
AcO^-	1:1	337	503	4.76
$H_2PO_4^-$	1:1	142	4271	2.15
HSO_4^-	1:1	32	138	−3.1
Cl^-	1:1	5	164	−6.1

[a] Anions were added as their tetrabutylammonium salts, all errors are ±10%. [b] In water at 25 C, I = 0; D. D. Perrin, *Pure Appl. Chem*., 1969, **20**,133.

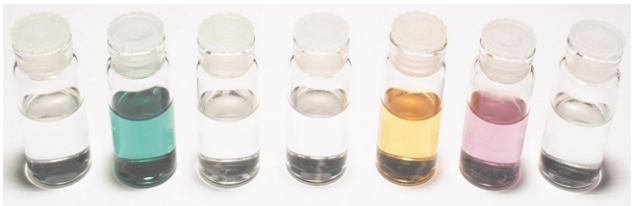

Fig. 1 Color changes (if any) induced by the addition of anions. From left to right (acetonitrile solutions): **4**; **4** + F^-; **4** + Cl^-; **4** + Br^-; **4** + AcO^-; **4** + $H_2PO_4^-$; **4** + HSO_4^-.

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