A colourimetric calix[4]pyrrole–4-nitrophenolate based anion sensor†

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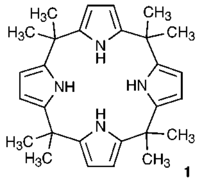
The intense yellow colour of the 4-nitrophenolate anion 2, in MeCN or CH_2Cl_2 solution, dissipates upon complex formation with *meso*-octamethylcalix[4]pyrrole 1; the complex may be used as a colourimetric sensor for halide anions, such as fluoride, that displace the phenolate anion thereby restoring the yellow colour, characteristic of free 4-nitrophenolate anion, to solutions containing 1, 2 and the anion in question.

The coordination chemistry of anions continues to attract increasing interest from the supramolecular chemistry community.[1–4] This is due, in no small part, to the crucial roles anions play in biological processes,[5,6] medicine,[7] catalysis[8] and molecular assembly.[9] Additionally various pollutant anions, such as pertechnetate, are believed to have deleterious effects on the environment.[10] Redox or photoactive sensor molecules have been developed that coordinate to anions and report their presence *via* changes in the physical properties of the host (such as redox potential, fluorescence or phosphorescence).[11,12] Another approach to anion detection, pioneered by Anslyn and co-workers, is the displacement assay (*i.e.* a host–anion complex that dissociates in the presence of other anions, triggering a change in the properties of the system).[13] Chemical systems that respond to the presence of anions by a colour change detectable *by eye* are extremely rare.[14] Colourimetric sensors do not require the use of a potentiostat or spectrometer to detect redox or optical perturbations and therefore have considerable advantages over other molecular sensors.[15] Here we report the formation of a new colourimetric displacement assay that is selective for halide anions over other putative anionic guest species and is extremely easy and inexpensive to make.

In 1996, we discovered that calix[4]pyrroles (*meso*-octalkylporphyrinogens), a class of molecule known for over a hundred years, can coordinate to anions such as fluoride, chloride and dihydrogen phosphate *via* the formation of pyrrole NH$\cdots$ anion hydrogen bonds.[16] *meso*-Octamethylcalix[4]pyrrole **1** is particularly easy to make and can be synthesised in high yield by the acid catalysed reaction of pyrrole with acetone.[17] We decided to investigate whether the formation of a calixpyrrole–anion complex with a coloured species such as 4-nitrophenolate anion **2** would perturb the electronic properties of the anion sufficiently to produce a colour change that could be used as the basis for a colourimetric displacement assay.



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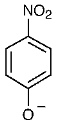

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Initial complexation studies were conducted using ^1H NMR titration techniques. Aliquots of tetrabutylammonium 4-nitrophenolate[18] (0.1 mol dm^{-3}) were added to a solution of compound **1** (0.01 mol dm^{-3}) in CD_2Cl_2 and the chemical shift of the calix[4]pyrrole NH proton noted after each addition. A significant downfield shift (from δ 7.0 to 10.6) of the pyrrole NH proton was observed upon the addition of 5 equiv. of tetrabutylammonium 4-nitrophenolate, consistent with the formation of calixpyrrole–phenolate hydrogen bonds. Analysis of the titration data using the EQNMR computer program[19] revealed that *meso*-octamethylcalix[4]pyrrole forms a 1:1 complex with 4-nitrophenolate with a stability constant of 290 (± 9.7) dm^3 mol^{-1}. Previous experiments showed that fluoride and chloride bind to compound **1** with stability constants of 17 200 and 350 dm^3 mol^{-1}, respectively, under the same conditions whilst the $\mathbf{1}\cdot H_2PO_4^-$ complex has a stability constant of 97 dm^3 mol^{-1}.[16] Competition experiments with fluoride, chloride and dihydrogenphosphate anions were then conducted. A CD_2Cl_2 solution of the complex **1·2** was prepared and aliquots of tetrabutylammonium salts of the anions added. After an initial addition of 0.2 equiv. of fluoride, the NH proton resonance broadened and could not be located in the NMR spectrum. Only after addition of 1.0 equiv. of fluoride did the NH resonance reappear, further shifted downfield by over 3 ppm as compared to **1·2**, indicating the formation of a calixpyrrole–fluoride complex. In contrast, tetrabutylammonium chloride and dihydrogenphosphate produced much smaller downfield shifts of 0.78 and 0.37 ppm, respectively, upon addition of 1.0 equiv. of the anion salt.

The colourimetric properties of this complex were then studied using UV/Vis spectroscopic techniques. Addition of calix[4]pyrrole **1** (5×10^{-2} mol dm^{-3}) to a solution of tetrabutylammonium 4-nitrophenolate **2** (3.6×10^{-5} mol dm^{-3}) in CH_2Cl_2 at 25 °C caused a significant decrease in intensity of the so-called '200 nm band' at 432 nm (Fig. 1).[20]

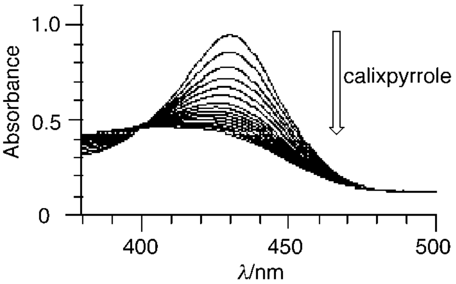

Fig. 1 Decreasing absorbance of the 4-nitrophenolate anion **2** (3.6×10^{-5} mol dm^{-3}) upon addition of calixpyrrole **1** (5×10^{-2} mol dm^{-3}) in CH_2Cl_2 at 25 °C.

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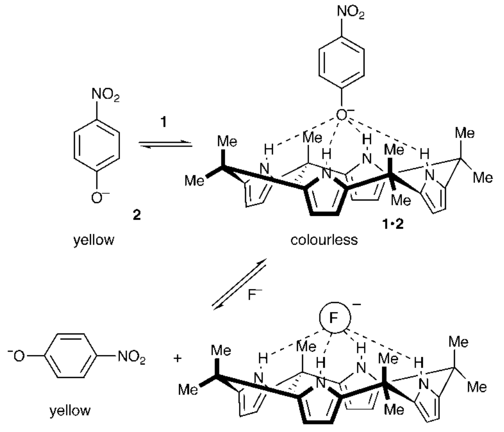
† A colour picture illustrating the dissipation and reappearance of the 4-nitrophenolate yellow colour together with NMR/UV/vis titration data are available from the RSC web site, see http://www.rsc.org/suppdata/cc/1999/1851/



Scheme 1

Table 1 Relative absorbance values for calixpyrrole–4-nitrophenolate solutions containing equimolar concentrations of various anions.[a] Since the signal being observed is due to liberated 4-nitrophenolate anion, the larger the relative absorbance, the stronger the binding (all anions were used as their tetrabutylammonium salts)

	F^-	Cl^-	$H_2PO_4^-$	Br^-	HSO_4^-
ΔAbsorbance[b]	0.282	0.193	0.162	0.092	0.015
Relative absorbance[c]	1.0	0.68	0.57	0.33	0.05

[a] *meso*-Octamethylcalix[4]pyrrole was added to a solution of tetrabutylammonium 4-nitrophenolate (6.0×10^{-6} mol dm^{-3}) in MeCN, affording a solution that was 5.0×10^{-4} mol dm^{-3} in calixpyrrole. Solutions of tetrabutylammonium fluoride, chloride, dihydrogenphosphate, hydrogensulfate and bromide were prepared using this stock solution such that the anion concentration was 1.6×10^{-2} mol dm^{-3} in all cases. UV/vis spectra were recorded immediately after the solutions were prepared. The data were averaged over three runs (errors < 15%). [b] Calculated by measuring the difference between 490 and 430 nm. All values are corrected relative to that measured for the calix[4]pyrrole stock solution (0.03 nm). [c] Calculated relative to **1**·**2** + fluoride solution, *i.e.* relative absorbance = [ΔAbsorbance (anion)/ΔAbsorbance (fluoride)].

This decrease in intensity was visible to the naked eye as a yellow-to-colourless colour change and is attributed to the formation of the calixpyrrole–phenolate complex **1**·**2**.† Control experiments showed that addition of pyrrole to solutions of **2** (2×10^{-1} mol dm^{-3}) under the same conditions caused no decrease in the intensity of this band.

Addition of anions to solutions of **1**·**2** causes the yellow colour of the 4-nitrophenolate anion to return as it is displaced from the calix[4]pyrrole anion binding site (Scheme 1). Table 1 shows the relative absorbance values for solutions of **1** (5.0×10^{-4} mol dm^{-3}) and **2** (6.0×10^{-6} mol dm^{-3}) in MeCN upon addition of various anions (solution made up to 1.6×10^{-2} mol dm^{-3}). The strongest absorbance is observed upon addition of fluoride anions followed by chloride and dihydrogenphosphate anions. This trend reflects the absolute and relative affinities of *meso*-octamethylcalix[4]pyrrole for these particular anionic guests and is illustrated in Fig. 2.

The present findings serve to illustrate that calixpyrroles, such as **1**, may be used to produce anion sensors that can report the presence of anions by means of a colour change. It may therefore be possible to incorporate analogous systems into ‘dip-sticks’ for anion detection in the field. We are presently working to covalently attach a variety of phenolate anions and dyes to calixpyrroles in order to produce discrete molecular hosts capable of reporting anion-binding events by colour changes. The results of this work will be reported in due course.

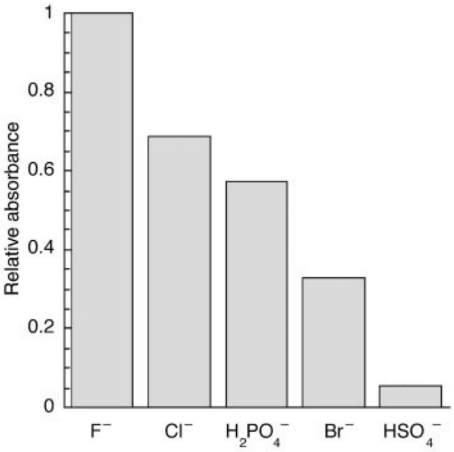


Fig. 2 Relative absorbance of solutions containing **1** (5.0×10^{-4} mol dm^{-3}), **2** (6.0×10^{-6} mol dm^{-3}) and various anions (1.6×10^{-2} mol dm^{-3}) in MeCN at 25 °C.

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