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An Azophenol-Based Chromogenic Anion Sensor

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ABSTRACT

A new chromogenic azophenol–thiourea based anion sensor, 2, has been developed. This system allows for the selective colorimetric detection of F^-, $H_2PO_4^-$, and AcO^-. Selectivity trends turned out to be dependent upon guest basicity and conformational complementarity between 2 and the guest.

Compared to the relatively well-developed cation chemosensors,[1] development of anion binding sensors is only recently emerging as a research area of significant importance.[2] One of the more attractive approaches in this field involves the construction of optical sensors.[3,4] This system generally consists of two parts. One is the anion-binding part employing various combinations of pyrroles, guanidiniums, Lewis acids, amides, and urea/thioureas.[3−5] The other is the chromophore which makes binding-induced changes into optical signals.[1,2] These two parts are either covalently attached[4] or intermolecularly associated.[2c,d,3]

However, because of the near-absence of chromophores which are responsive to anions, the number of optical sensors available for anionic species is very low.[5c,6] Only a few systems reported by several groups are known.[2−4] In this Letter we present the synthesis and binding properties of an azophenol−thiourea system.[2a,7] We show that compound **2** acts as a colorimetric sensor for selected anions by means of hydrogen-bonding interactions. Intermolecular interactions

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between **2** and anions can be easily monitored by anion complexation-induced changes in UV−vis absorption and ^{1}H NMR spectra and by the “naked eye” (Figure 1).

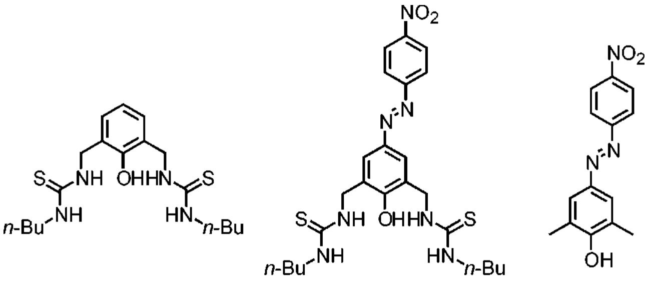
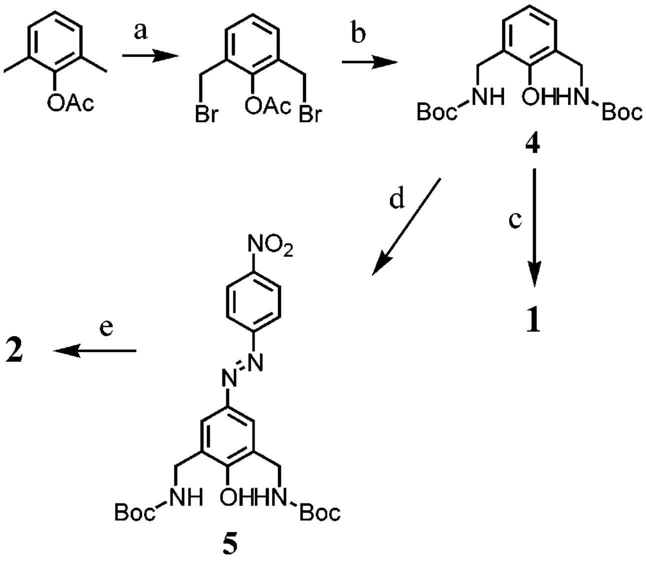


Figure 1. Anion-binding receptors.

The syntheses of **1** and **2** are outlined in Scheme 1. **4** was obtained by a literature procedure.[8] Removal of the Boc protecting group from **4** followed by treatment of the resulting ammonium salt in THF with 2 equiv of butyl isothiocyanate and TEA provided **1** in 70% yield.[9a]

Scheme 1[a]



[a] (a) NBS, HCO_2Me, AIBN, Δ, *hν*, 3 h, 69%; (b) i. NaN_3, DMF, rt, 3 h, ii. LAH, THF, 0 °C, iii. di-*tert*-butyl dicarbonate, THF, aq Na_2CO_3, rt, 3 h, 70%; (c) i. TFA, anisole, CH_2Cl_2, ii. *n*-BuNCS, TEA, THF, rt, 70%; (d) i. aq NaOH, MeOH, rt, ii. *p*-nitroaniline, $NaNO_2$, aq HCl, MeOH, 0 °C, 49%; (e) i. TFA, anisole, CH_2Cl_2, ii. *n*-BuNCS, TEA, THF, rt, 70%.

Attachment of a *p*-nitrophenylazo group on the *para* position of the phenolic OH of **4** was accomplished by a general azo-coupling method.[7] Then **2** was prepared by following the same methodology as applied in the synthesis of **1**. **1** contains four thiourea NH groups designed to be geometrically fit for anions[9b] and one phenolic OH group as both an additional binding site and a color-reporting unit.

The binding ability of **1** for anions (as tetrabutylammonium salts) was investigated by ^{1}H NMR spectroscopy and UV−vis spectroscopy.[10] Large downfield shifts of thiourea NH resonances (>2.5 ppm) were detected upon complexation with $H_2PO_4^-$ and AcO^-. Broadening of the phenolic OH resonance was also observed, indicating its participation in hydrogen-bonding interaction.

The resulting binding curves were analyzed by nonlinear regression methods which gave, as results, the association constants noted in Table 1.

Table 1. Association Constants (M^{-1}) from ^{1}H NMR and UV−Vis Titrations for Complexes of Host **1** with Anionic Guests in $CDCl_3$ at 20 °C[a]

anion	$H_2PO_4^-$	$AcO^{-\,b}$	$HSO_4^{-\,c}$	$Cl^{-\,c}$	$Br^{-\,c}$	$I^{-\,c}$
K_a	2.6×10^4	1.9×10^4	4800	3000	2000	500

[a] The anions were added as their tetrabutylammonium salts except for Cl^-, which was used as tetraethylammonium salt. [b] UV−vis titration. [c] ^{1}H NMR titration.

The selectivity trends of binding affinities of anions for **1** were determined to be $H_2PO_4^- \sim AcO^- \gg HSO_4^- > Cl^- > Br^- > I^-$. The selectivity for $H_2PO_4^-$ and AcO^- can be rationalized on the basis of the guest basicity and structure of the complex. As expected from the basicity of anions,[9b,11] $H_2PO_4^-$ and AcO^- give stronger complexes than other anions. Furthermore, $H_2PO_4^-$ with four oxygens makes the strongest complexes via multitopic hydrogen-bonding interactions with **1**. These results and broadening of the phenol OH peak lead to the idea that azophenol-based sensor **2** may cause color changes suitable for the “naked-eye” monitoring of the binding of selected anions such as $H_2PO_4^-$ and AcO^-.

The choice of azophenol as the anion-sensitive chromophoric unit comes from the fact that crowned azophenols have already been used for metal cation and amine detection.[1] Attaching anion binding sites to the azophenol dye enables azophenol derivatives to be potential colorimetric sensors for anions. It turns out that the UV−vis absorption band of **2** in chloroform undergoes a red shift as a phosphate anion is bound (Figure 2).[12]

In the absence of anions, the absorption spectrum of **2** is characterized by the presence of one absorption maximum peak at 376 nm. Upon addition of $H_2PO_4^-$, the peak at 376 nm decreases while a new peak appears at 529 nm. Complexation with a series of anions results in similar

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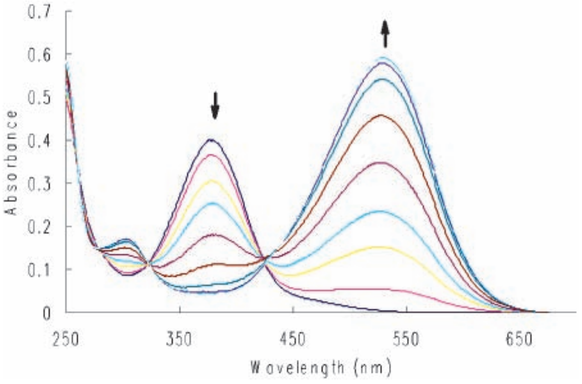

Figure 2. UV−vis titration of **2** with $H_2PO_4^-$*n*-Bu_4N^+ in chloroform. [**2**] = 1.5 × 10^{-5} M, [$H_2PO_4^-$] = 0−9.6 equiv of **2**.

tendencies of red shifts. Clear isosbestic points were observed, which shows the existence of two states of 1:1 complex. As can be expected from UV−vis data, color change occurs by addition of anions to the solution of **2**. Upon the addition of less than 1 equiv of F^-, $H_2PO_4^-$, or AcO^-, the color of the solution changes from light yellow to deep red. The degree of color changes is no longer affected by the addition of more than 3 equiv of anions (F^-, $H_2PO_4^-$, AcO^-).

However, in the case of HSO_4^- and Cl^-, the color change only occurs upon addition of more than 10 equiv of each anion, and no detectable color changes are observed upon addition of excess Br^- or I^- to the solution of **2** (Figure 3).

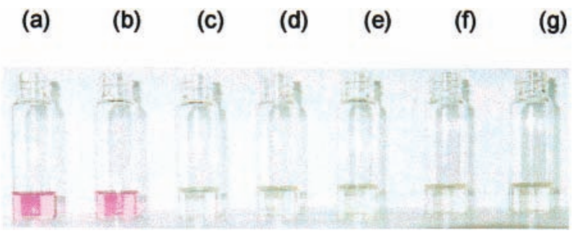

Figure 3. Color changes of **2** in $CHCl_3$. [**2**] = 1.5 × 10^{-5} M, [anion] = 3 equiv: (a) $H_2PO_4^-$, (b) AcO^-, (c) HSO_4^-, (d) Cl^-, (e) Br^-, (f) I^-, (g) only **2**.[13]

In this chromophore, electronic excitation generally occurs through a charge transfer from donor oxygen of the phenol to acceptor substituent ($-NO_2$) of the chromophore.[1c] When a complex formed between **2** and an anionic guest, the excited state would be more stabilized by anion binding, resulting in a bathochromic shift in the absorption maxima (λ_{max}) as well as a color change.[14] The color changes explained above are also reflected in the quantitative data in the UV−vis absorption experiment (Figure 4).

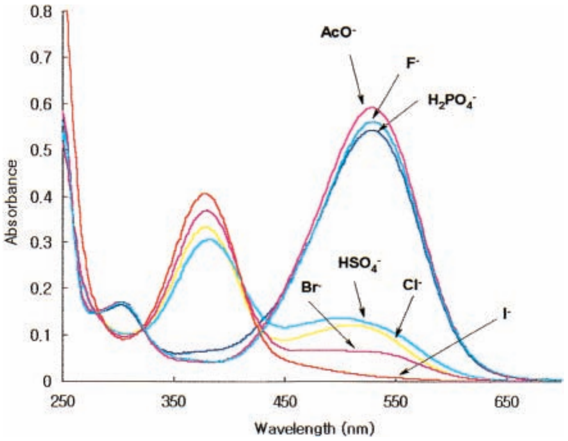

Figure 4. UV−vis changes of **2** operated in $CHCl_3$ (1.5 × 10^{-5} M) after the addition of 3 equiv of anions.

The selectivity trends of anion-induced color changes for **2** were determined to be $F^- \sim H_2PO_4^- \sim AcO^- \gg HSO_4^- \sim Cl^- > Br^- \sim I^-$. The selectivity for F^-, $H_2PO_4^-$, and AcO^- can be rationalized on the basis of the guest basicity. Because of the basicity order of anions,[11] F^-, $H_2PO_4^-$, and AcO^- give stronger complexes than other anions and show noticeable color changes compared to other anions. However, color discrimination among F^-, $H_2PO_4^-$, and AcO^- is not observed. This comes from increased binding affinity, because the azophenol OH in **2** is more acidic than the phenol OH in **1**.[1b]

The association constants of **2** for various anions in chloroform turn out to be too big to measure accurately: K_a's for $H_2PO_4^-$ and AcO^- > 10^5 M^{-1}, K_a's for HSO_4^-, Cl^-, Br^- > 10^4 M^{-1}.[15]

It is noteworthy that azophenol **3** without extra anion binding thiourea groups shows little color change upon addition of anions.[16] For instance, addition of 1 equiv of $H_2PO_4^-$*n*-Bu_4N^+ (or AcO^-*n*-Bu_4N^+) to a 1.5 × 10^{-5} M solution of **3** in $CHCl_3$ results in almost indiscernible color changes compared to the color changes in compound **2**. This result means that the introduction of thiourea for anion binding increases the number of effective collisions between the phenolic OH group of **2** and the anion.

In summary, we have developed a new colorimetric azophenol−thiourea based anion sensor which shows a selective coloration for F^-, $H_2PO_4^-$, and AcO^- ions. Selectivity trends of **1** and **2** turned out to be dependent upon the anion basicity and conformational fitness between a sensor and a guest. Color responses for selected anions (F^-, $H_2PO_4^-$, AcO^-) arise from basicity of the anions and effective binding between the azophenolic OH function of **2** and the anion.

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(13) The addition of 3 equiv of F^- to **2** causes the same color change as $H_2PO_4^-$ and AcO^- do, from light yellow to red.

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(15) Job plots show that **2** is most likely to form 1:2 complex with F^-. For details, see the Supporting Information.

(16) Azophenol **3** shows a dramatic color change from yellow to blue in the presence of fluoride anion. This result will be published elsewhere.

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Supporting Information Available: Experimental procedures and selected spectral data for compounds **1**, **2**, and **5**, ^{1}H NMR titration curves, UV−vis titration curves, and Job plots. This material is available free of charge via the Internet at http://pubs.acs.org.

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