

An Azophenol-Based Chromogenic Anion Sensor

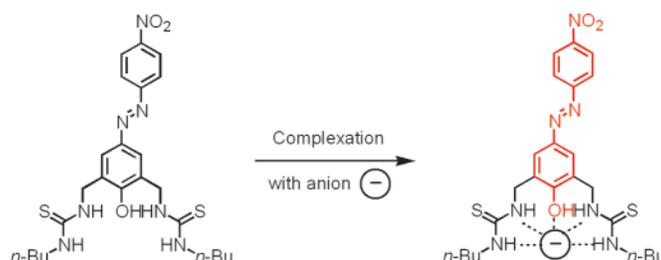
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ABSTRACT



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 attached⁴ 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 ¹H NMR spectra and by the “naked eye” (Figure 1).

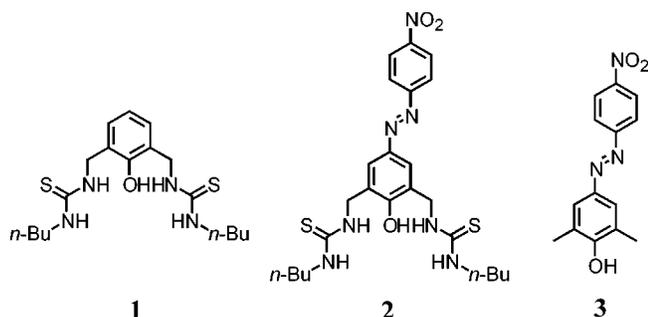
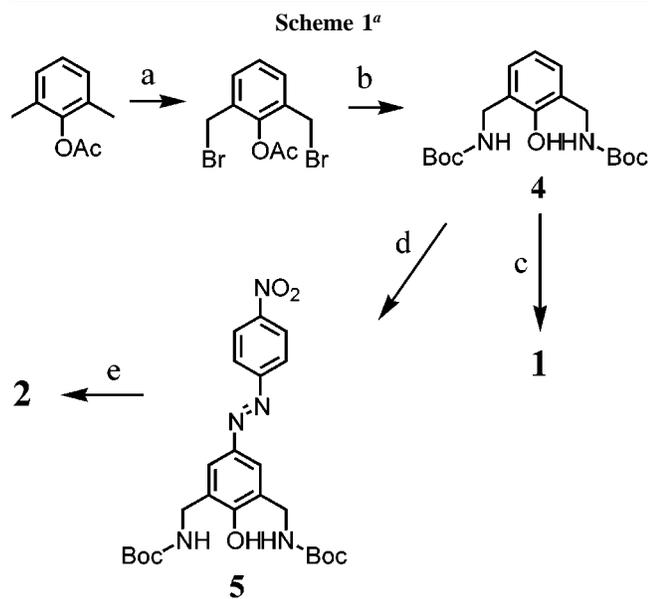


Figure 1. Anion-binding receptors.

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}



^a (a) NBS, HCO₂Me, AIBN, Δ, *hν*, 3 h, 69%; (b) i. NaN₃, DMF, rt, 3 h, ii. LAH, THF, 0 °C, iii. di-*tert*-butyl dicarbonate, THF, aq Na₂CO₃, rt, 3 h, 70%; (c) i. TFA, anisole, CH₂Cl₂, ii. *n*-BuNCS, TEA, THF, rt, 70%; (d) i. aq NaOH, MeOH, rt, ii. *p*-nitroaniline, NaNO₂, aq HCl, MeOH, 0 °C, 49%; (e) i. TFA, anisole, CH₂Cl₂, 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 ¹H NMR spectroscopy and UV-vis spectroscopy.¹⁰ Large downfield shifts of thiourea NH resonances (>2.5 ppm) were detected upon complexation with H₂PO₄⁻ 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 ¹H NMR and UV-Vis Titrations for Complexes of Host **1** with Anionic Guests in CDCl₃ at 20 °C^a

anion	H ₂ PO 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 ¹H NMR titration.

The selectivity trends of binding affinities of anions for **1** were determined to be H₂PO₄⁻ ~ AcO⁻ ≫ HSO₄⁻ > Cl⁻ > Br⁻ > I⁻. The selectivity for H₂PO₄⁻ 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} H₂PO₄⁻ and AcO⁻ give stronger complexes than other anions. Furthermore, H₂PO₄⁻ 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 H₂PO₄⁻ 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 H₂PO₄⁻, 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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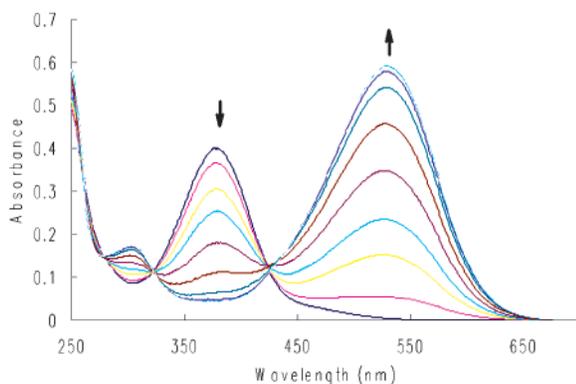


Figure 2. UV-vis titration of **2** with $\text{H}_2\text{PO}_4^-n\text{-Bu}_4\text{N}^+$ in chloroform. $[\mathbf{2}] = 1.5 \times 10^{-5}$ M, $[\text{H}_2\text{PO}_4^-] = 0\text{--}9.6$ equiv of **2**.

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).

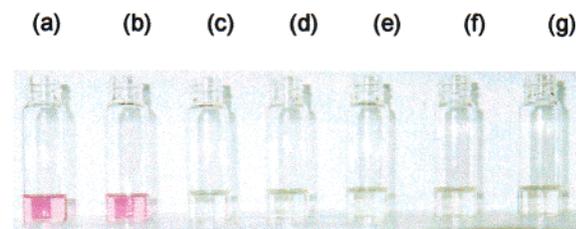


Figure 3. Color changes of **2** in CHCl_3 . $[\mathbf{2}] = 1.5 \times 10^{-5}$ M, $[\text{anion}] = 3$ equiv: (a) H_2PO_4^- , (b) AcO^- , (c) HSO_4^- , (d) Cl^- , (e) Br^- , (f) I^- , (g) only **2**.¹³

In this chromophore, electronic excitation generally occurs through a charge transfer from donor oxygen of the phenol to acceptor substituent ($-\text{NO}_2$) 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

(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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explained above are also reflected in the quantitative data in the UV-vis absorption experiment (Figure 4).

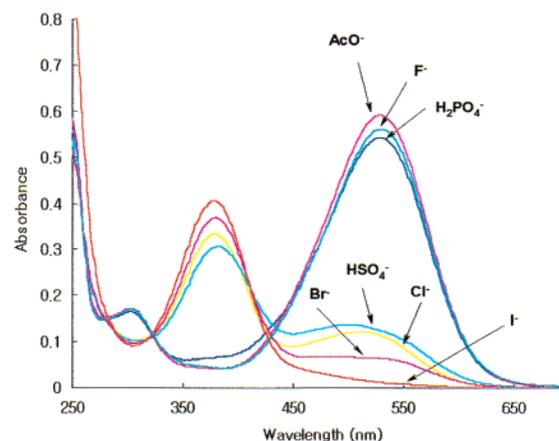


Figure 4. UV-vis changes of **2** operated in CHCl_3 (1.5×10^{-5} M) after the addition of 3 equiv of anions.

The selectivity trends of anion-induced color changes for **2** were determined to be $\text{F}^- \sim \text{H}_2\text{PO}_4^- \sim \text{AcO}^- \gg \text{HSO}_4^- \sim \text{Cl}^- > \text{Br}^- \sim \text{I}^-$. 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 $\text{AcO}^- > 10^5$ M^{-1} , K_a 's for HSO_4^- , Cl^- , $\text{Br}^- > 10^4$ 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 $\text{H}_2\text{PO}_4^-n\text{-Bu}_4\text{N}^+$ (or $\text{AcO}^-n\text{-Bu}_4\text{N}^+$) 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.

(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, ^1H 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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