



Anion sensor based on the indoaniline–thiourea system

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Abstract—A new chromogenic indoaniline–thiourea-based sensor was designed to recognize anions in an organic solvent through complementary intermolecular hydrogen bonding. Complexed anions cause significant disturbance to the intramolecular hydrogen-bonded structure of the sensor, which then induces color and UV–vis spectral changes. This sensor allows for selective colorimetric detection of tetrahedral oxoanions (HSO_4^- and H_2PO_4^-). © 2002 Elsevier Science Ltd. All rights reserved.

The development of chemosensors for biologically important anions has recently emerged as a key research area.¹ One attractive approach involves the construction of optical sensors.^{2–4} Such a system generally consists of two parts. One is the anion-binding part employing various combinations of pyrroles, guanidiniums, Lewis acids, amides and urea/thioureas.^{1–5} The other is the chromophore part which converts binding-induced changes into optical signals.^{2–4} These two parts can be either covalently attached⁴ or intermolecularly linked.^{2a,b,3} According to previous studies,⁴ F^- seems to interact with a hydrogen bond donor ($-\text{NH}_2$, $-\text{OH}$, $-\text{C}(\text{O})\text{NHR}$) of a chromophore more strongly than any other anions. This allows F^- to give rise to the most intense color change in an organic solvent among all anions. Therefore, it has been difficult for other anions to provide a more selective color change than F^- using the chemosensors with H-bond donors within a chromophoric unit. In this paper, we present a new strategy for a chemosensor to render it capable of showing more selective color and spectral changes for tetra-

hedral oxoanions (HSO_4^- and H_2PO_4^-) compared to F^- by using an indoaniline chromophore containing a quinone-type carbonyl group. This chromophore acts not only as a color-reporting group, but also as a binding affinity control group. **1** allows for selective colorimetric detection of H_2PO_4^- and HSO_4^- (Fig. 1).

Indoaniline-based sensors **1** was synthesized from a known precursor **4**.⁶ Removal of the Boc protecting group from **4** followed by treatment of the resulting ammonium salt in THF with 2 equiv. of *n*-butylisothiocyanate and TEA provided **5** in 70% yield. Condensing **5** with 4-(diethylamino)-2-methylaniline hydrochloride under alkaline conditions in the presence of $\text{K}_3[\text{Fe}(\text{CN})_6]$ as an oxidizing agent afforded the indoaniline-based anion sensor **1** (Scheme 1).^{7–9}

Compound **1** contains four thiourea NH groups as H-bond donors for anions, and one indoaniline group for monitoring anion-binding events.

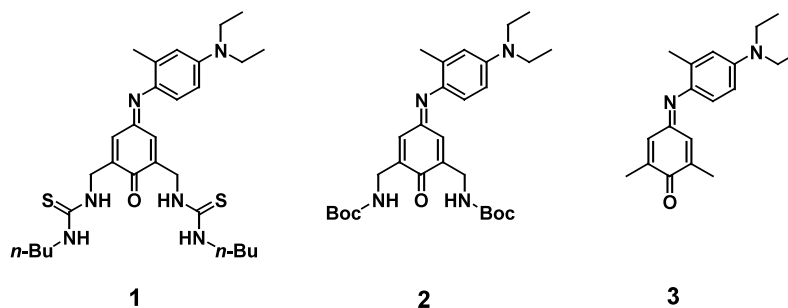
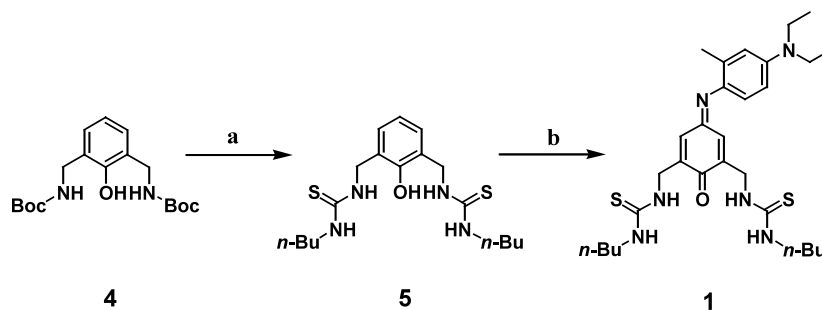


Figure 1. Indoaniline-based chromagenic sensors.

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Scheme 1. Reagents and conditions: (a) i. TFA, anisole, CH_2Cl_2 , ii. *n*-BuNCS, TEA, DMF, rt, 70%; (b) i. 4-(diethylamino)-2-methylaniline-hydrochloride, aq. NaOH, MeOH, rt, ii. $\text{K}_3[\text{Fe}(\text{CN})_6]$, 52%.

Sensor **1** showed a bathochromic shift of λ_{max} , compared to that of control **3**, which indicates that the indoaniline chromophore appears to be influenced by intramolecular hydrogen bonding between the carbonyl oxygen of indoaniline and adjacent thiourea NHs.⁷ Wavelength maxima (λ_{max}), molecular extinction coefficients, and frequencies (cm^{-1}) of C=O of **1** as well as related compounds are summarized in Table 1.

Table 1 shows an insight into the intramolecular hydrogen bonded structure of **1** and **2**. Sensors with more acidic NHs display larger bathochromic shifts and lower frequency of C=O (quinone), compared to the free indoaniline compound **3**. In the case of **1**, which has the more acidic NH group than **2**, a pronounced wavelength change (71 nm) was detected. These results, in turn, enable us to assume that an anion complexed with a bis-thiourea moiety could cause significant disturbance of an intramolecular hydrogen bonded structure of free **1** (Scheme 2). This would subsequently induce spectral absorption change in the complexes. In fact, complex of **1** and H_2PO_4^- (1:20, v/v) showed large absorption and IR spectral shifts of C=O of **1**, indicating a large degree of breakdown of the intra-molecular H-bonds in the free **1**.

Indeed, upon addition of anions, the thiourea NHs are forced to participate in the hydrogen bonding with anions, hence the contribution of NHs to the hydrogen bonding with the indoaniline C=O group decreases. This structural disturbance is reflected in the observed spectral blue shift of the complexes. In the absence of anions, the UV spectrum of **1** is characterized by the presence of an absorption band at 678 nm. Addition of H_2PO_4^- caused hypsochromic band shifts from 678 nm (λ_{max}) down to 632 nm. Complexation with a series of

Table 1. Absorption and IR spectral data of C=O of compounds **1–3** in CHCl_3

Compd	$\lambda_{\text{max}}/\text{nm}$ (ϵ_{max}^a)	ν/cm^{-1} (C=O)
1	678 (30,000)	1597
2	640 (25,000)	1601
3	607 (18,000)	1606
1-hp ^b	632 (13,000)	1603

^a The unit: $\text{dm}^3 \text{mol}^{-1} \text{cm}^{-1}$

^b Sensor **1**: $\text{H}_2\text{PO}_4^- \text{-} n\text{-Bu}_4\text{N}^+$ complex.

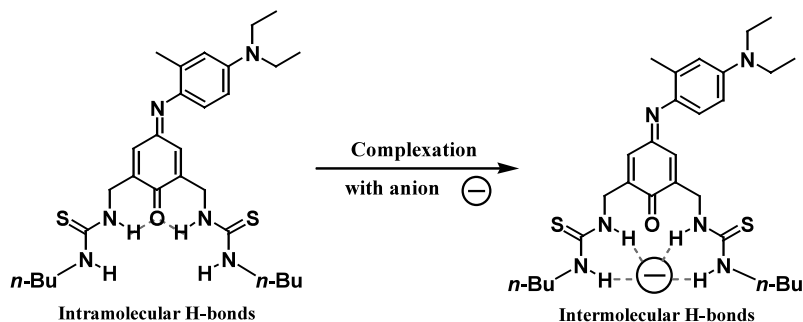
anions resulted in similar blue shift tendencies. The 1:1 binding ratio was confirmed by clear isosbestic points and Job's plots (Figs. 2 and 3). As expected from UV-vis data, a color change occurs through addition of anions to the solution of **1** (Fig. 2).

Upon the addition of H_2PO_4^- or HSO_4^- , the color of the solution changed from blue-green to deep blue. However, addition of AcO^- or F^- with higher basicity caused a less intense color change. The color change terminated after the addition of 40 equiv. of each anion. However, in the case of Cl^- , Br^- and I^- , no detectable color changes were observed upon excess addition of anions to the solution of **1** (Fig. 4). The qualitative changes described above are reflected in the quantitative data in the UV-vis absorption experiment (Table 2).^{10b} The color discrimination is explained by the difference in λ_{max} and absorbance of each complex.

The specific UV-vis absorbance for H_2PO_4^- and HSO_4^- can be rationalized on the basis of the guest structure. The structural complementarity is an important factor for effective hydrogen bonding. Thus, **1** with four NHs would preferably binds with H_2PO_4^- and HSO_4^- of a tetrahedral geometry but not with spherical (e.g. Br^-), or planar (e.g. AcO^-) ions.¹¹ Energy minimized structures for the complexes with H_2PO_4^- and HSO_4^- show multitopic hydrogen bonds between four thiourea NHs and anions as expected.¹²

In CH_3CN , the UV spectrum of **1** is characterized by the presence of an absorption band at 634 nm, indicating that intramolecular H-bonds of **1** (Scheme 2, Table 1) were weakened due to the more polar nature of CH_3CN . Although an addition of H_2PO_4^- caused hypsochromic band shift from 634 nm (λ_{max}) down to 610 nm,¹³ amount of UV absorption changes was small and color change was not detectable by 'naked eye'. However, selectivity trends for binding affinities of anions in CH_3CN was similar to those in CHCl_3 (Table 2). Thus, H_2PO_4^- and HSO_4^- of a tetrahedral geometry also showed stronger affinity to **1** with four thiourea NHs in CH_3CN . This means that the binding and sensing mode are the same in both CHCl_3 and CH_3CN .

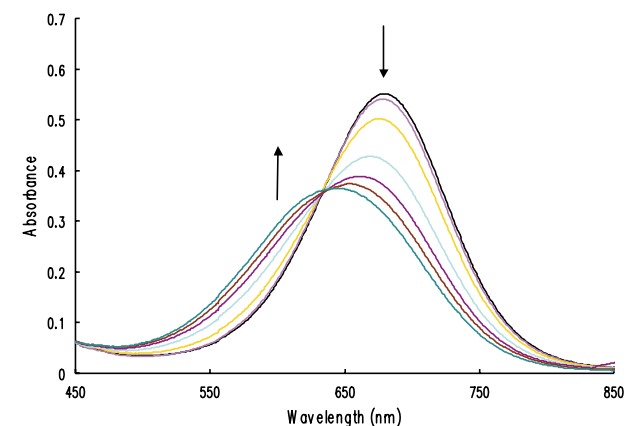
Compound **2**, which has an indoaniline and two carbamate NH groups, does not show detectable color changes upon addition of the same amounts of anions.



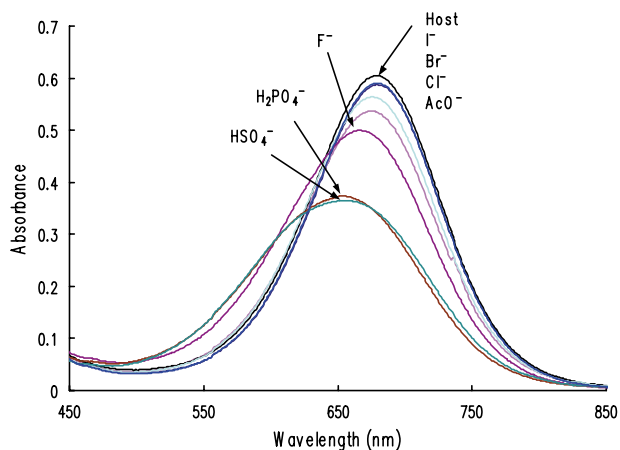
Scheme 2. Proposed mechanism for complexation of sensor **1** with anion.

This result indicates that the introduction of four thiourea NH groups as the anion-binding site increases the binding strength.

In summary, the new chromogenic indoaniline-thiourea based anion sensor **1** was designed to selectively recognize tetrahedral oxoanions (H_2PO_4^- , HSO_4^-) in an organic solvent through complementary intermolecular hydrogen bonding. Complexed anions significantly dis-



(a).



(b).

Figure 2. (a) UV-vis titration of **1** with $\text{H}_2\text{PO}_4^-n\text{-Bu}_4\text{N}^+$ in chloroform. $[\mathbf{1}] = 2.0 \times 10^{-5}$ M, $[\text{H}_2\text{PO}_4^-] = 0\text{--}40$ equiv. of **1**; (b) UV-vis changes of **1** operated in CHCl_3 (2.0×10^{-5} M) after the addition of 30 equiv. of anions.

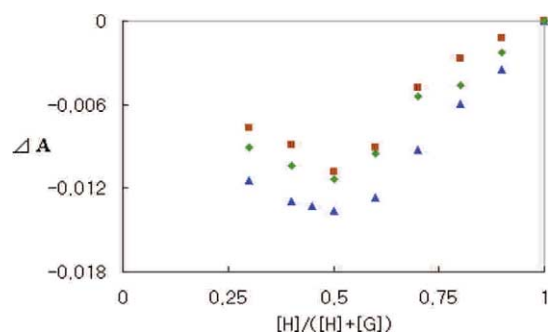


Figure 3. Job's plots between sensor **1** and anions in chloroform at 20°C . Rectangle, diamond and triangle represent $\text{AcO}^-n\text{-Bu}_4\text{N}^+$, $\text{F}^-n\text{-Bu}_4\text{N}^+$ and $\text{H}_2\text{PO}_4^-n\text{-Bu}_4\text{N}^+$, respectively. $[\text{H}] + [\text{G}] = 2.0 \times 10^{-5}$ M.



(a) (b) (c) (d)



(e) (f) (g) (h)

Figure 4. Color changes of **1** in CHCl_3 . $[\mathbf{1}] = 2.0 \times 10^{-5}$, $[\text{anion}] = 40$ equiv.: (a) **1** (b) **1**+ F^- (c) **1**+ H_2PO_4^- (d) **1**+ AcO^- (e) **1**+ HSO_4^- (f) **1**+ Br^- (g) **1**+ Cl^- (h) **1**+ I^- .

Table 2. Association constants (M^{-1}) from UV-vis titrations for complexes of **1** with anionic guests in $CHCl_3$ and MeCN at 20°C^a

	F^-	$H_2PO_4^-$	AcO^-	HSO_4^-	Cl^-
$CHCl_3$	3.0×10^3	1.1×10^4	-2.0×10^3	2.5×10^4	1.4×10^3
CH_3CN	3.3×10^3	6.3×10^3	ND ^b	1.0×10^4	ND ^b

^a The anions were added as their tetrabutylammonium salts except for Cl^- , which was used as tetraethylammonium salt.

^b ND=not determined (spectral change too small to determine).

turb the intramolecular hydrogen-bonded structure of **1**, and then induce spectral absorption change in the complexes. This system allows for selective colorimetric detection of $H_2PO_4^-$ and HSO_4^- over F^- .

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- Selected spectral data for **5**: 1H NMR (300 MHz, acetone- d_6 , ppm) δ 0.87–0.92 (t, 6H, CH_2CH_3), 1.27–1.39 (m, 4H, $CH_2CH_2CH_3$), 1.50–1.59 (m, 4H, $CH_2CH_2CH_2$), 3.46 (br, 4H, $NHCH_2CH_3$), 4.74 (br, 4H, $ArCH_2NH$), 6.74–6.79 (t, 1H, ArH), 7.15–7.18 (d, 2H, $ArHs$), 7.19 (br, 2H, $CSNHCH_2$), 7.44 (br, 2H, $ArCH_2NHCS$), 9.34 (s, 1H, $ArOH$); ^{13}C NMR (300 MHz, acetone- d_6 , ppm) δ 13.72, 20.25, 31.46, 44.37, 119.90, 125.81, 130.28, 153.57, 182.37; MS (FAB) $m/z=383.1946$ ($M+1^+$).
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