Colorimetric Anion Sensing

A Colorimetric Approach to Anion Sensing: A Selective Chemosensor of Fluoride Ions, in which Color is Generated by Anion-Enhanced π Delocalization**

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There is a growing interest in the design of receptors for anions, because of the important role anions play in biological systems of environmental chemistry and food science.[1] Selective recognition is important, with full discrimination from other negatively charged interferents; this is a factor addressed in the design of a receptor, whose size and shape must be complementary to those of the envisaged analyte. The energy of interaction can be provided by positively charged groups (ammonium, alkyl ammonium, guanidinium, pyridinium, transition-metal ions),[2] which should be symmetrically positioned within the receptors cavity. The primary drawback of this approach is that the positively charged receptor brings with it anions, which may be interferents. However, neutral receptors for anions exist that are based on urea and thiourea fragments, whose -NH groups are able to establish hydrogen-bonding interactions with the substrate.[3] The nature of the interaction restricts the use of such receptors to anions containing the most electronegative atoms: fluorine (F^-) and oxygen (carboxylates, phosphates). Thiourea-based systems are, however, good receptors for fluoride ions,[4] but selective recognition and subsequent signaling of their presence, with respect to oxygen-containing anions as possible interferents, are limited to a restricted number of examples.[5] Recognition is important, but its occurrence must be communicated to the outside by a visual signal, for example, a color change. The classical strategy

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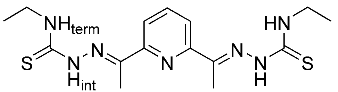
involves the covalent linking of a chromogenic fragment to the receptor. Anion binding then in some way modifies the dipole of the chromophore, thus altering the energy of the optical transition and changing the color.[6]

We describe here a simple and easy way to prepare a thiourea-based receptor, which allows naked-eye detection of fluoride ions, but which does not contain any particular chromophore. In particular, we have designed molecule **1**, which possesses two thiourea-containing unsaturated arms appended to a pyridine ring. The interaction of the thiourea hydrogen atoms with the substrate enhances π delocalization and shifts the π–π^* transition from the UV to the visible region and results in the generation of a yellow color.



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Single crystals of **1** suitable for X-ray diffraction studies[7] were grown by vapor diffusion of diethyl ether into an acetone solution of the compound (Figure 1, top). The structure reveals the formation of a symmetrical Schiff base, which adopts an open configuration in the solid state, with the two thiosemicarbazone arms disposed on either side of the pyridine ring. Multiple hydrogen-bonding interactions also exist between neighboring molecules (Figure 1, bottom). In particular, each molecule is connected to two others through hydrogen bonds between sulfur atoms and the internal -NH groups of the thiourea moieties. The final result is the assembly of discrete molecules into supramolecular 1D zig-zag chains. It must be noted that the terminal -NH groups of the thiourea units are not involved in any intra- or intermolecular hydrogen-bonding interactions.

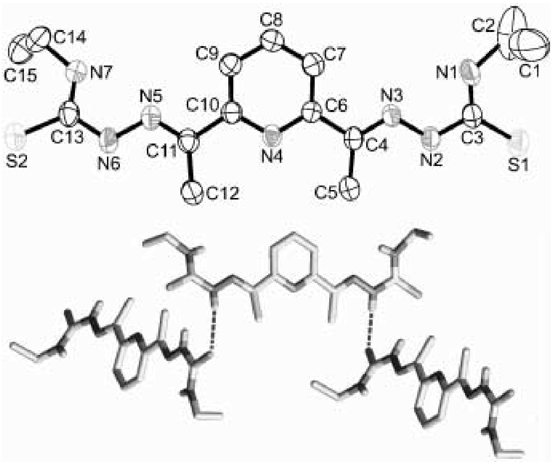


Figure 1. Top: Molecular structure of **1** showing the atomic numbering scheme. Thermal ellipsoids are drawn at the 40% probability level. Bottom: Part of the unit cell of **1** exhibiting the network of hydrogen-bonding interactions between neighboring units that give rise to the assembly of discrete molecules into infinite supramolecular zig-zag 1D chains.

The interaction of **1** with a variety of anions was investigated through spectrophotometric titrations in MeCN by addition of a standard solution of the tetraalkyl ammonium salt of the envisaged anion to a solution of **1**. Figure 2 shows the spectra obtained during the titration with fluoride ions. It is seen that addition of salt results in the intensity of the absorption band at 324 nm decreasing and the development of a new band at 412 nm. The presence of a well-defined isosbestic point indicates that only two species are present at equilibrium: **1** and a **1**·F^- adduct. Figure 2 (inset) also shows the titration profile, that is, the plot of the absorbance at 412 nm versus the number of equivalents of F^- ions, whose nonlinear least-squares processing[9] indicated the 1:1 stoichiometry of the adduct and with an association constant $\log K_{ass} = 4.14 \pm 0.02$.

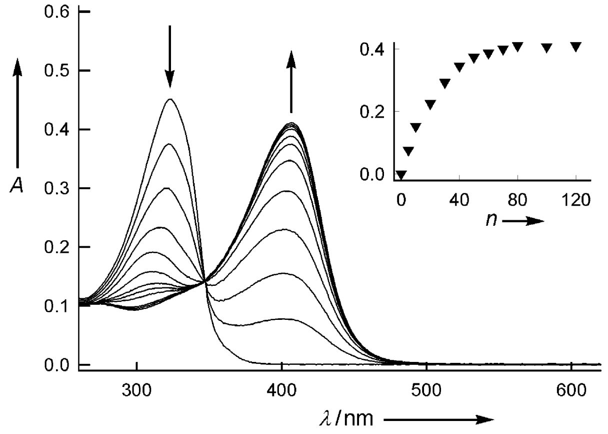


Figure 2. Titration of a 10^{-5} M solution of **1** in acetonitrile with a standard solution of tetrabutylammonium fluoride in acetonitrile. Inset: absorbance at 412 nm versus number of equivalents of F^- ions (n) added.

Moreover, the ^{1}H NMR spectrum in CD_3Cl of **1** shows dramatic changes on addition of fluoride ions: The internal -NH signal (s, 2H, $\delta = 8.94$ ppm in the free ligand) disappears rapidly and the pyridine aromatic proton signals shift upfield when F^- ions are added. On the other hand, the signal of the terminal -NH groups of the thiourea moieties (s, 2H, $\delta = 2.50$ ppm in the free ligand) does not dissappear and only shows a trivial upfield shift. This observation suggests that the fluoride ion interacts only with the internal -NH protons of the receptor.

Figure 3 shows the structure of the **1**·F^- adduct, as calculated by a semiempirical method (AM1), with the symmetrical hydrogen-bonding interactions between the anion and the two thiourea fragments. Noticeably, the fluoride ion interacts with the two internal -NH groups, whereas the two terminal -NH groups of the thiourea fragment are not involved in the bonding, which is in accordance with the ^{1}H NMR results. Conversely, a strong interaction of the F^- ion with one hydrogen atom of the thiourea unit may account for the large red-shift of the intense π–π^* absorption band. We can tentatively describe the bonding situation through the tautomeric equilibrium shown in Scheme 1. First, a hydrogen ion is released from one of the

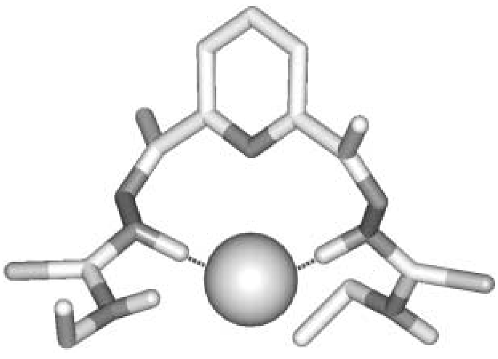
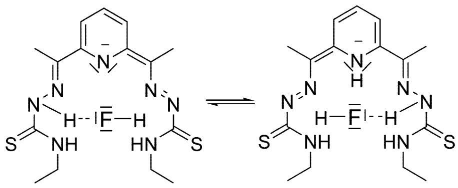


Figure 3. Optimized structure of the **1**·F^- adduct, as calculated with a semiempirical method (AM1), showing the hydrogen-bonding interactions of the fluoride ion with the two internal hydrogen atoms of the thiourea fragments.



Scheme 1. The tautomeric equilibrium illustrating the bonding situation in the **1**·F^- adduct.

two internal -NH groups to the F^- ion to give an LH^-·HF adduct ($LH_2 = \mathbf{1}$); then, a tautomeric equilibrium takes place within the LH^-·HF species, in which a hydrogen ion is transferred from an internal nitrogen atom of LH^- to the other, by bond formation/breaking with the fluoride ion. In each one of the two equivalent formulas, it is assumed that availability of a lone pair of electrons on the thiourea nitrogen atom induces extended π conjugation, which ultimately generates a negative charge on the pyridine nitrogen atom.

Enhanced π delocalization on the organic backbone is expected to reduce the energy of the π–π* transition. As a consequence, the absorption band is shifted from the UV to the visible region and a yellow color appears. The presence of anionic character, as a consequence of the interaction with a F^- ion, has been hypothesized for naphthalene-based receptors equipped with two urea-containing arms.[5b]

Moreover, π delocalization generates a dipolar situation in the **1**·F^- adduct, with a partial negative charge on the pyridine ring and a partial positive charge on the hydrogen atom interacting with the fluorine atom. The dipolar nature of the transition is demonstrated by the fact that the spectra of the **1**·F^- adduct change moderately, but significantly on varying the solvent. One would expect that solvents with higher dielectric constants would stabilize the dipole, thus causing a red-shift of the charge-transfer transition. Indeed, a roughly linear relationship exists between the λ_{max} value of the **1**·F^- adduct absorption band and the dielectric constant of the medium (Figure 4).

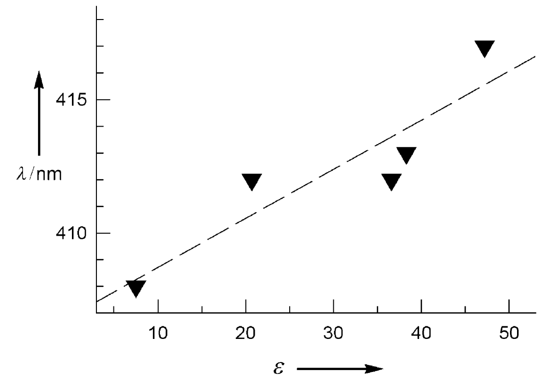


Figure 4. The relationship between the λ_{max} value of the absorption band of the **1**·F^- adduct and the dielectric constant of the medium ε (solvents used from lower to upper ε values: THF, acetone, acetonitrile, DMF, and DMSO), which demonstrates the dipolar character of the transition.

Among the other anions investigated, the highest affinity was observed with acetate. The association constant $\log K_{ass}$, calculated by processing the titration profiles, is 2.01 ± 0.01. Lower values were observed for $H_2PO_4^-$ ($\log K_{ass} = 1.70 \pm 0.03$) and Cl^- ions($\log K_{ass} = 1.27 \pm 0.08$), while Br^-, I^-, and HSO_4^- ions have $\log K_{ass} \leq 1$. It is noticeable that, among the previously investigated optical chemosensors for F^- ions, higher association constants for the 1:1 adducts were observed in the case of a triarylborane–porpyrin conjugate ($\log K_{ass} = 5.0$, in THF),[10] and a dipyrrolyl–quinoxaline conjugate ($\log K_{ass} = 5.1$ in CH_2Cl_2).[11] However, comparison with the system described here is not intrinsically correct, because of the much lower dielectric constant of THF (7.5) and CH_2Cl_2 (9.1) with respect to MeCN (36.6). Thus, $\log K_{ass}$ data are reported here only for informational purposes. No K_{ass} values were reported for other systems, and in most cases the competition by oxyanions (acetate, phosphate) was not considered.[5,11,12]

In this regard, the spectrophotometric response of **1** to the fluoride concentration does not suffer interference from any other anionic analyte even when present at millimolar concentrations. This is illustrated in Figure 5, in which the plot of the absorbance of the adduct versus anion concentration (in a logarithmic scale) emphasizes the selectivity of receptor **1** towards fluoride ions.

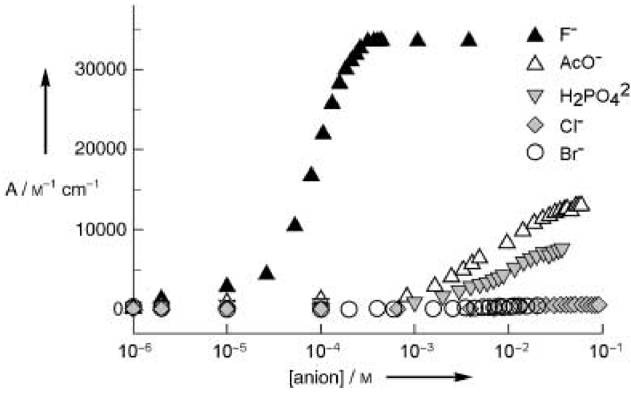


Figure 5. Titration of solutions of **1** (10^{-5} M) in acetonitrile with standard solutions of selected anions. *A* = molar absorbance at 412 nm.

Thus, system **1** appears to be a specific sensor for the fluoride ion. It is notable that in a medium such as MeCN the counterion of the investigated salt can interact with the anion. To minimize such an effect we used in all cases tetra-*n*-butylammonium salts, with the exception of chloride, for which the benzyltrimethylammonium salt was used.

Finally, Figure 6 displays the visual aspects of fluoride ion recognition and sensing. Each vial contains a 10^{-4} M solution of **1** in MeCN. The addition of one equivalent of F^- ions induces the appearance of a bright yellow color (vial b) while the addition of ten equivalents of the other anions (vials c–h) does not induce any color development.

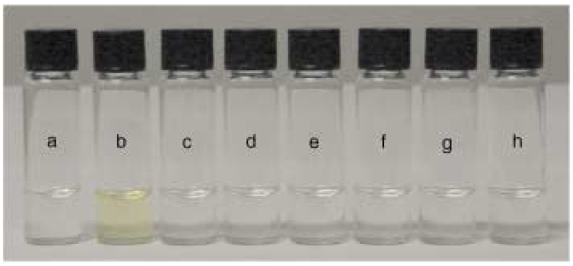


Figure 6. Visual features of the interactions of anions with sensor **1** in acetonitrile solution (a: **1** (1×10^{-4} M); b: **1** + F^- (1 equiv); c: **1** + Cl^- (10 equiv); d: **1** + Br^- (10 equiv); e: **1** + I^- (10 equiv); f: **1** + AcO^- (10 equiv); g: **1** + $H_2PO_4^-$ (10 equiv); h: **1** + HSO_4^- (10 equiv)).

Thus, it is demonstrated that a chromogenic sensor for fluoride ions can be designed even in the absence of any defined chromophore. It is the very strong interaction between the F^- ion and the internal -NH fragment of the thiourea group that enhances π delocalization over the receptor's framework, thus causing the π–π* transition to shift from the UV to the visible region. The presence of two equivalent unsaturated arms extends the π delocalization and increases the red-shift as well as enhancing the affinity and selectivity for F^- ions.

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[7] Crystal structure analysis of **1**. X-ray diffraction data were collected from a colorless prismatic crystal (~$0.26\times0.15\times0.12$ mm) by means of a Smart CCD-1000 BRUKER diffractometer using graphite-monochromatized $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å*)* from a fine focus sealed tube source. Crystal data for $C_{15}H_{23}N_7S_2$: $M_r = 365.52$, $T = 293(2)$ K, orthorhombic, space group *Pna*2(1) (no. 33), $a = 9.378$ (6), $b = 12.366$ (9), $c = 16.306$ (22) Å, $\alpha = \beta = \gamma = 90.00°$, $V = 1891(2)$ Å°, $Z = 4$, $\rho_{calc} = 1.284$ g cm^{-3}, $\mu = 0.294$ mm^{-1}, 16155 measured reflections, 2240 independent reflections ($R_{int} = 0.0660$), 2240 independent reflections with $I_O > 2\sigma(I_O)$, 219 parameters refined, GOF 1.003, $R_1 = 0.0518$ ($I_O > 2\sigma(I_O)$) and 0.1209 (for all data), $R_{2w} = 0.1039$ ($I_O > 2\sigma(I_O)$) and 0.1391 (for all data), min/max residual electron density 0.353/–0.343 e Å^{-3}. The crystal structure was solved by direct methods and refined by full-matrix least-square procedures on F^2 using SHELX-97 software.[8] All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were included in the model at calculated positions. CCDC-221833 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

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