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Colorimetric and fluorescence sensing of anions using thiourea based coumarin receptors

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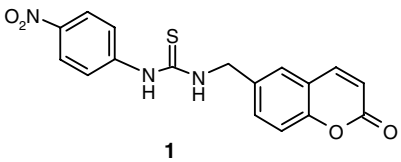
Abstract—Thiourea-containing coumarins **1**, **2** have been designed and synthesized via reaction of 6-aminomethylcoumarin and the corresponding isothiocyanates. Their anion-binding ability has been examined using UV–vis, fluorescence and ^{1}H NMR. The anion recognition takes place through charge neutral thiourea receptor sites with concomitant fluorescence quenching of the coumarin moiety with **1** showing a strong binding to $C_6H_5COO^-$ over F^- with a distinct change in color.

The design of host molecules that can recognize and sense anions selectively through visible, electrochemical and optical responses has received considerable interest in recent years because of the important roles played by the anions in biological, industrial, and environmental processes.[1] Molecules that possess functional groups such as amides,[2] ureas/thioureas,[3] guanidinium[4] and ammonium[5] derivatives have proven to be particularly effective in this regard as they are able to bind anions using directional hydrogen bonding interactions. The attachment of such functional groups with a suitable chromophoric part either covalently or intermolecularly provides a complete receptor that can intimate binding information either by a color change, fluorescence or both. Several reviews on anion binding in this regard using luminescent sensors have appeared.[1b,6] Despite the significant development in this domain, the search for new luminescent sensors with structural simplicity and easy synthesis has recently been of keen interest in molecular recognition research.

In pursuit of developing anion receptors during the course of our work on molecular recognition,[7] we present coumarin-based chemosensors **1** and **2** for the selective recognition of anions employing the criteria of PET sensing using the '*fluorophore-spacer-receptor*' model developed by de Silva for the detection of cations.[8] Although several PET sensors for anions are known,[9] no such thiourea-linked coumarin systems, employing neutral anion receptors, have been reported that exhibit an ideal PET behavior and color changes as signaling events, detectable by the naked eye, upon binding of anions.

Chemosensors **1** and **2** were easily synthesized in good yields from readily available starting materials, following Scheme 1. 6-Aminomethylcoumarin **7**, was synthesized via a series of reactions on 4-hydroxybenzaldehyde as indicated in Scheme 1, was reacted in dry THF (containing few drops of dry DMF due to insolubility) at room temperature under an inert atmosphere with an equimolar amount of isothiocyanate to afford **1** or **2** as pale



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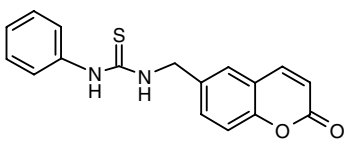

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Keywords: Anion binding; Colorimetric; Selective binding; Fluorescence quenching; Fluoride binding; Benzoate binding.
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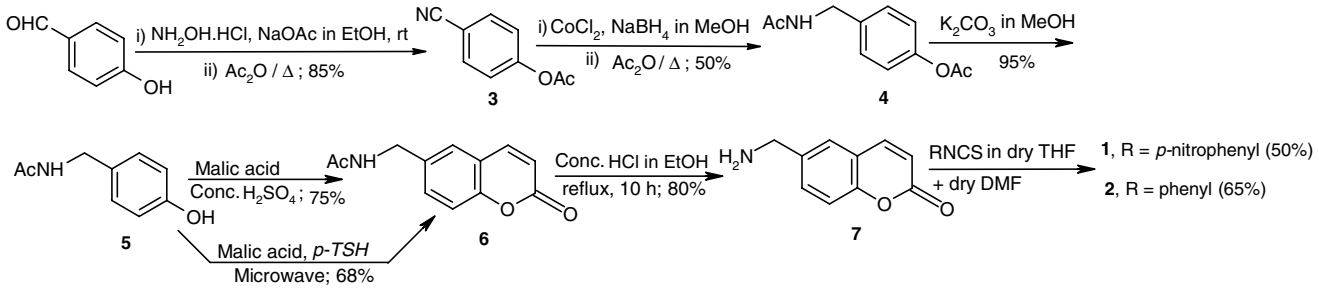

Scheme 1. Syntheses of receptors **1** and **2**.

yellow and white solids, respectively. The crude products were purified by column chromatography and were analyzed by conventional methods.[10] It is also worth noting that the amide derivative **6** was successfully synthesized in 68% yield under solvent-free conditions using microwave irradiation.

The anion-binding properties of **1** and **2** were investigated by observing the changes in their fluorescence emission, absorption spectra in CH_3CN and by ^1H NMR in $CDCl_3$. The UV–vis experiments were carried out in CH_3CN (containing 0.08% DMSO for homogeneity of the solution). The titration of **1** ($c = 5.63 \times 10^{-5}$ M), which exhibits a broad strong absorption band at 330 nm due to the coumarin moiety, was carried out with anions such as tetrabutylammonium fluoride, bromide, iodide, hydrogen sulfate and benzoate. Upon the addition of fluoride, the intensity of the absorption peak at 330 nm was remarkably reduced with a simultaneous growth of a new peak at 455 nm (Fig. 1) and the almost colorless solution turned yellow brown (Fig. 4c). In the case of benzoate, the absorption peak at 330 nm was shifted to 348 nm ($\Delta\lambda = 18$ nm) with a concomitant decrease in the intensity of the absorption (Fig. 2) and the solution turned light green in color (Fig. 4b). The presence of isobestic points during titration with both F^- and $C_6H_5COO^-$ revealed the formation of 1:1 complexes. No significant change in absorption or a noticeable color change was observed for other anions such as Br^-, I^- and HSO_4^-.

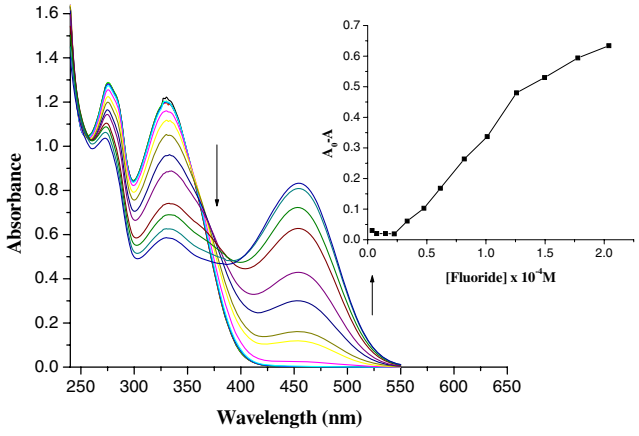

Figure 1. Changes in UV–vis spectra for **1** ($c = 5.63 \times 10^{-5}$ M) in CH_3CN upon the addition of tetrabutylammonium fluoride. Inset: differences in absorbances versus concentration of fluoride.

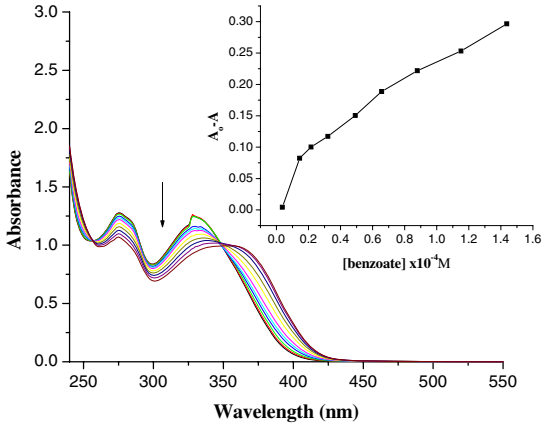

Figure 2. Changes in UV–vis spectra for **1** ($c = 5.63 \times 10^{-5}$ M) in CH_3CN upon the addition of tetrabutylammonium benzoate. Inset: differences in absorbances versus concentration of benzoate.

The study of the fluorescence of **1** also showed a similar trend. The fluorescence emission spectra of **1** ($c = 4.51 \times 10^{-4}$ M) consisted of a broad band at 420 nm when excited at 380 nm (red edge excitation). With the addition of monodentate anions such as $C_6H_5COO^-$ and F^- as $N(C_4H_9)_4^+$ salts, the emissions were ca. 88 and 99.6% '*switched off*' or quenched, due to the formation of anion-receptor hydrogen-bonded complexes (Fig. 3). During the titration there were no other observable changes in the emission spectra (Figs. 5 and 6). Upon the addition of HSO_4^-, the emission spectra were hardly affected suggesting its weak interaction with the receptor site. The addition of other spherical ions such as Br^-, I^-, etc did not cause any significant quenching of the emission, thereby ruling out quenching by the heavy atom effect. The Stern–Volmer plot (Fig. 7) illustrates the quenching process.

The analogous thiourea receptor **2** was evaluated to establish the role of the acidity of the thiourea protons in binding with the putative anions. The addition of F^-, $C_6H_5COO^-$, Br^-, I^- and HSO_4^- as tetrabutylammonium salts to a solution of **2** in CH_3CN (containing 0.08% DMSO) resulted in a minor change in the UV–vis spectrum of receptor **2** and did not result in any new peaks at higher wavelengths or color changes of the solution. The fluorescence changes of **2** upon addition of F^- and $C_6H_5COO^-$ were significant, but smaller compared to **1**. The fluorescence emissions at 369 nm ($\lambda_{ex} = 320$ nm) were ca. 12% and 19% '*switched*

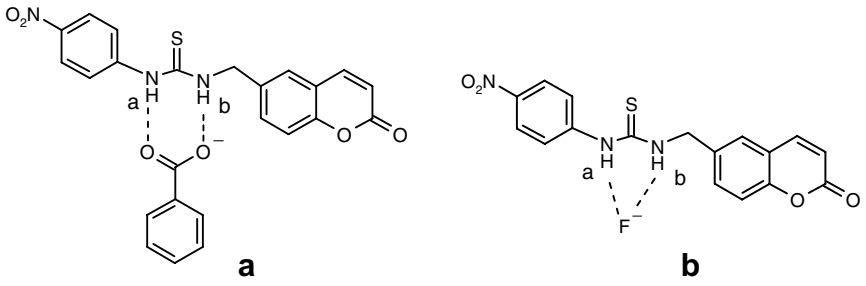

Figure 3. Hydrogen-bonded complexes of **1**: (a) with benzoate, (b) with fluoride ions.

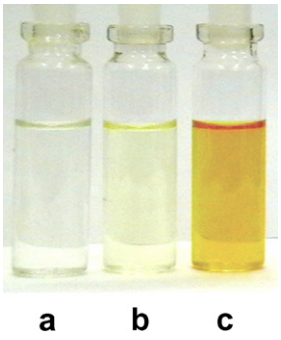

Figure 4. Color changes observed: (a) receptor **1**, (b) on addition of benzoate and (c) on addition of fluoride.

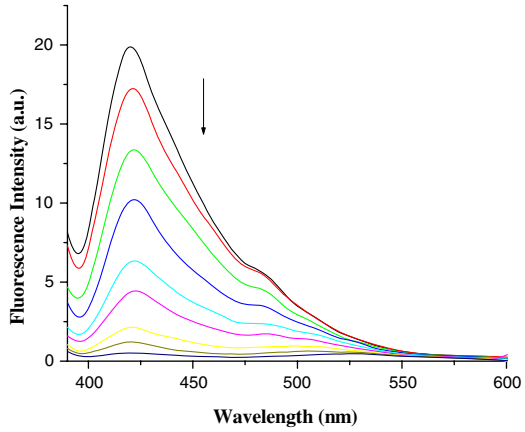

Figure 5. Changes in fluorescence spectra for **1** ($c = 4.51 \times 10^{-4}$ M) in CH_3CN upon addition of tetrabutylammonium fluoride.

off' for $C_6H_5COO^-$ and F^-, respectively. The smaller quenching of emission here was ascribed to a weak hydrogen bonding interaction between the less acidic thiourea protons and anions. This is reflected in their binding constant values (Table 1), which were measured by following the change in absorbance as a function of the concentration of the anions.[11] As shown in Table 1, it is clear that the association constants of both the receptors for benzoate is greater than for fluoride. This is solely due to strong hydrogen bonding interactions instead of deprotonation as observed in the case of fluoride.

To understand the binding events further, ^1H NMR experiments were carried out in $CDCl_3$. The large down-

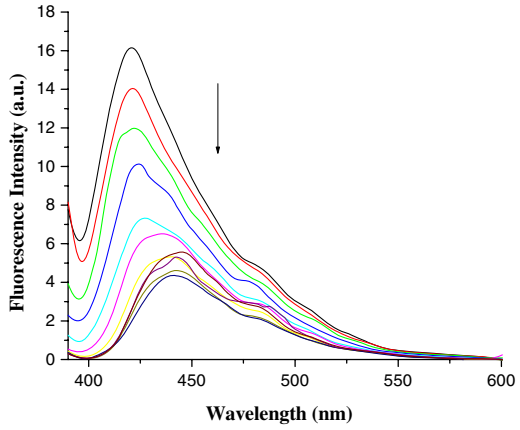

Figure 6. Changes in fluorescence spectra for **1** ($c = 4.51 \times 10^{-4}$ M) in CH_3CN upon addition of tetrabutylammonium benzoate.

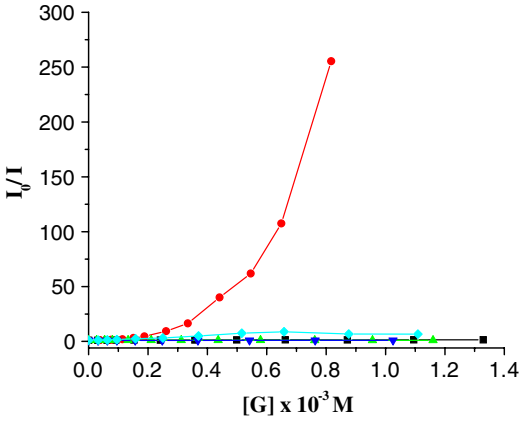

Figure 7. Stern–Volmer plot for **1** at 420 nm ((■) Br^-, (●) F^-, (▲) I^-, (▼) HSO_4^-, (◆) $C_6H_5COO^-$ ions).

Table 1. Association constants of receptors **1** and **2** with anions in CH_3CN

Anion[a]	Receptor **1** (K_a in M^{-1})	Receptor **2** (K_a in M^{-1})
F^-	5.78×10^3	2.26×10^3
$C_6H_5COO^-$	2.02×10^4	1.04×10^4
Br^-	[b]	[b]
I^-	[b]	[b]
HSO_4^-	[b]	[b]

[a] Anions were used as their tetrabutylammonium salts.
[b] The changes in the spectra were too small to calculate the association constants precisely.

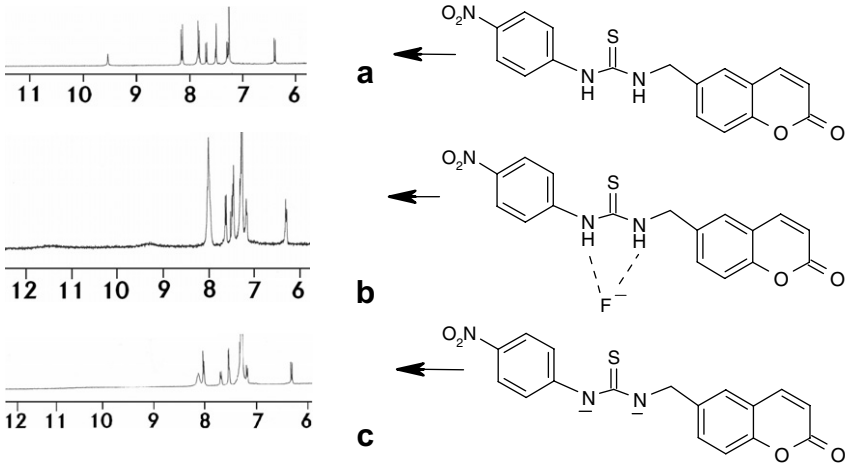

Figure 8. Partial ^{1}H NMR (400 MHz) of **1** (6 mM) in $CDCl_3$ containing 0.03% DMSO-d_6, (b) 1:1 complex with F^-, (c) in the presence of excess F^-.

field chemical shift of the thiourea protons ($\Delta\delta$ H_a 3.21, H_b 3.37 ppm) of **1** in the 1:1 complex with benzoate indicated a strong hydrogen bonding interaction. In the case of the 1:1 complex of fluoride with **1**, both the thiourea protons (H_a and H_b) underwent downfield shifts ($\Delta\delta$ H_a 1.98, H_b 1.44 ppm) and became broad and then disappeared in the presence of excess fluoride, suggesting either deprotonation or strong hydrogen bonding. The relatively smaller downfield shifting of the thiourea protons in **2** upon addition of benzoate and fluoride indicated a weaker binding. The electron donating resonance effect of the phenyl group increases the charge density on the carboxylate group allowing it to form strong hydrogen bonds with the acidic thiourea protons of **1**. Fluoride, on the other hand, due to its small size and high charge density, initially forms a hydrogen-bonded complex (see Fig. 8b) and then, in the presence of excess F^-, causes deprotonation (shown in Fig. 8c) to form the L^{2-} species (L = coumarin receptor).

However, these non-covalent interactions altogether enhance the efficiency of the PET process. The high degree of fluorescence quenching is believed to result from the increase in the reduction potential of the thiourea receptor moieties after anion recognition. This increases the rate of electron transfer from the HOMO of the thiourea-anion complex to the coumarin-excited state and encourages the PET process. It appears that the deprotonated species LH^-/L^{2-}, being more electron rich compared to the hydrogen-bonded complex with benzoate, activates the PET process more efficiently and shows a greater quenching. The origin of the color change in the host solution of **1** is ascribed to the charge-transfer interactions between the electron-rich thiourea–anion complex donor unit and the electron-deficient *p*-nitrophenyl moiety.

In conclusion, '*fluorophore-spacer-receptor*' model based thiourea linked coumarin receptors **1** and **2** have been presented. The receptor **1** shows a strong binding to benzoate over fluoride ions and can report the molecular recognition events both by changes in fluorescence and color. Further research in this direction is underway in our laboratory.

Acknowledgments

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References and notes

1. (a) *Supramolecular Chemistry of Anions*; Bianchi, E., Bowman, J. K., Garcia-Espana, E., Eds.; Wiley-VCH: New York, 1997; (b) Martinez-Manez, R.; Sancenon, F. *Chem. Rev.* **2003**, *103*, 4419; (c) Evans, L. S.; Gale, P. A.; Light, M. E.; Quesada, R. *Chem. Commun.* **2006**, 965; (d) Kirk, K. L. *Biochemistry of Halogens and Inorganic Halides*; Plenum Press: New York, 1991, p 58; (e) *Chemosensors for Ion and Molecular Recognition*; Desvergne, J.-P., Czarnik, A. W., Eds.; Kluwer: Dordrecht, 1997; Vol. 492, (f) Sohn, H.; Letant, S.; Sailor, M. J.; Trogler, W. C. *J. Am. Chem. Soc.* **2000**, *122*, 5399.
2. (a) Lee, S. H.; Kim, H. J.; Lee, Y. O.; Vicens, J.; Kim, J. S. *Tetrahedron Lett.* **2006**, *47*, 4373; (b) Causey, C. P.; Allen, W. E. *J. Org. Chem.* **2002**, *67*, 5963, and references cited therein.
3. (a) Gomez, D.; Fabbrizzi, L.; Licchelli, M. *J. Org. Chem.* **2005**, *70*, 5717; (b) Fan, E.; van Arman, S. A.; Kincaid, S.; Hamilton, A. D. *J. Am. Chem. Soc.* **1993**, *115*, 369; (c) Cho, E. J.; Ryu, B. J.; Lee, Y. J.; Nam, K. C. *Org. Lett.* **2005**, *7*, 2607, and references cited therein; (d) Kondo, S.-I.; Hiroka, Y.; Kurumatani, N.; Yano, Y. *Chem. Commun.* **2005**, 1720; (e) Lee, D. H.; Lee, H. Y.; Hong, J.-I. *Tetrahedron Lett.* **2002**, *43*, 7273.
4. Best, M. D.; Tobey, S. L.; Anslyn, E. V. *Coord. Chem. Rev.* **2003**, *240*, 3.
5. Linares, J. M.; Powell, D.; Bowman-James, K. *Coord. Chem. Rev.* **2003**, *240*, 57.
6. (a) Gale, P. A. *Coord. Chem. Rev.* **2003**, *240*, 1; (b) Sessler, J. L.; Davis, J. M. *Acc. Chem. Res.* **2001**, *34*, 989; (c) Suksai, C.; Tuntulani, T. *Chem. Soc. Rev.* **2003**, *32*, 192; (d) Yoon, J.; Kim, S. K.; Singh, J.; Kim, K. S. *Chem. Soc. Rev.* **2006**, *35*, 355.
7. (a) Ghosh, K.; Masanta, G. *Tetrahedron Lett.* **2006**, *47*, 2365; (b) Ghosh, K.; Adhikari, S. *Tetrahedron Lett.* **2006**, *47*, 3577; (c) Ghosh, K.; Masanta, G. *Chem. Lett.* **2006**, *34*, 414.
8. de Silva, A. P.; McCoy, C. P.; Rademacher, J. T.; Rice, T. E. *Chem. Rev.* **1997**, *97*, 1515.

9. (a) Gunnlaugsson, T.; Davis, A. P.; Glynn, M. *Chem. Commun.* **2001**, 2556, and references cited therein; (b) Kang, J.; Kim, H. S.; Jang, D. O. *Tetrahedron Lett.* **2005**, *46*, 6079.
10. Receptor **1**: mp 170–172 °C; yield = 50%; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 10.31 (s, 1H, urea NH), 8.77 (bt, 1H, urea NH), 8.19 (d, 2H, $J = 8$ Hz), 8.10 (d, 1H, $J = 8$ Hz), 7.84 (d, 2H, $J = 8$ Hz), 7.68 (s, 1H), 7.61 (d, 1H, $J = 8$ Hz), 7.40 (d, 1H, $J = 8$ Hz), 6.49 (d, 1H, $J = 8$ Hz), 4.80 (d, 2H, $J = 4$ Hz); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 181.4, 160.9, 153.4, 147.3, 145.1, 142.8, 135.7, 132.2, 127.9, 125.3, 121.4, 119.3, 117.1, 117.2, 47.1; FTIR (KBr pellet, cm^{-1}): 3365, 3191, 3015, 2917, 1731, 1608, 1593, 1530, 1514; HRMS (ESI, m/z) calcd for $C_{17}H_{13}N_3O_4S$: 355.0620. Found: 356.0653 (M+1).

Receptor **2**: mp 140–142 °C; yield = 65%; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 9.66 (s, 1H, urea NH), 8.22 (bt, 1H, urea NH), 8.07 (d, 1H, $J = 8$ Hz), 7.62 (s, 1H), 7.57 (dd, 1H, $J_1 = 4$ Hz, $J_2 = 8$ Hz), 7.39–7.35 (m, 3H), 7.30 (t, 2H, $J = 8$ Hz), 7.10 (t, 1H, $J = 8$ Hz), 6.46 (d, 1H, $J = 8$ Hz), 4.77 (d, 2H, $J = 4$ Hz); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 181.8, 160.8, 153.3, 143.9, 138.7, 135.5, 131.6, 129.2, 127.3, 125.6, 124.4, 118.9, 116.9, 116.8, 47.4; FTIR (KBr pellet, cm^{-1}): 3450, 3337, 3181, 2919, 1704, 1619, 1537; Mass (ESI, m/z) 311.1 $[M+H]^+$, 309.1, 292.8, 252.2 159.1.
11. Chou, P. T.; Wu, G. R.; Wei, C. Y.; Cheng, C. C.; Chang, C. P.; Hung, F. T. *J. Phys. Chem. B* **2000**, *104*, 7818.