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A simple anion chemosensor based on a naphthalene–thiouronium dyad

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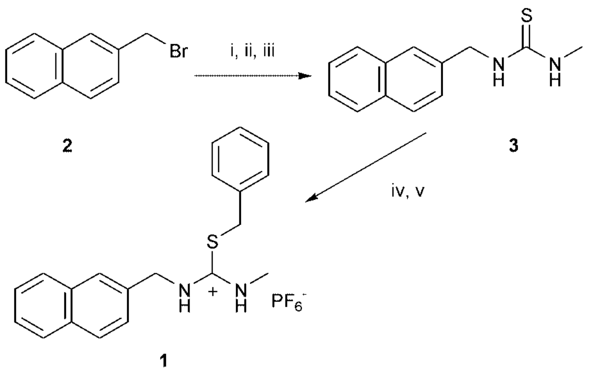
A fluorescent-active molecular dyad comprising a naphthalene moiety covalently attached, *via* a methylene spacer, to a thiouronium receptor is described where selective anion-induced fluorescence changes make it of potential use as an anion chemosensor material.

Our ongoing program aimed at the synthesis of new easy-to-make optical sensors of biologically and/or chemically important anions leads us to explore a suitable anion-binding unit capable of efficient interaction with a built-in chromophore. A family of thiouronium salts, being known not only as synthetic intermediates for the conversion of alkyl halides to the corresponding mercaptans[1] but also as classical reagents for the identification of organic acids,[2] has potential as one of key functional groups for the purpose of molecular recognition of anion species in the area of supramolecular chemistry[3] because such groups would enhance the acidity of the NH moieties compared to the corresponding thiourea.[4] Indeed, quite recently, Yeo and Hong reported new thiouronium-derived systems for a carrier of 5′-AMP[5] and oxoanion recognition.[6] It occurred to us that a sophisticated combination of the above-mentioned functional entity and a suitable chromophore such as naphthalene would, therefore, allow production of a new type of chemosensor material. The design is mainly based on our idea that anion recognition events on the electron-deficient binding site of the thiouronium moiety would be efficiently communicated to the fluorescent property of naphthalene so that an easily detectable signalling effect would occur in the system. Surprisingly, to the best of our knowledge, although a number of optical read-out chemosensors of anions have been developed[7] a thiouronium-containing system towards this end is, as yet, unknown. Here, we report the intriguing aspects on the title system **1**.

The synthesis of **1** is shown in Scheme 1: 2-(bromomethyl)naphthalene **2** was converted to the corresponding thiourea **3** *via* amination using potassium phthalimide followed by $NH_2NH_2{\cdot}H_2O$, and then condensation with methyl isothiocynate. Compound **3** was reacted with 1.1 equiv. of benzyl bromide followed by anion exchange treatment with $AgPF_6$. Purification by reversed phase column chromatography afforded the desired **1**† in excellent yield.



Scheme 1 *Reagents and conditions*: i, K$^+$ phthalamide$^-$ dry DMF; ii, $NH_2NH_2{\cdot}H_2O$, THF–EtOH; iii, MeNCS, $CHCl_3$; iv, benzyl bromide, dry EtOH; v, $AgPF_6$, dry EtOH.

System **1** showed very weak fluorescence in MeCN at 25 °C ([**1**] = 20 μM), the intensity of which was lower by a factor of 50 than that of 2-methylnaphthalene. This finding indicates that the electron-deficient thiouronium moiety acts as a quencher for the singlet state of the appended naphthalene. However, the addition of AcO^- as a putative response-induced anion was found to dramatically enhance the fluorescent intensity as illustrated in Fig. 1. Subsequently, 1 equiv. of AcO^- caused a remarkable intensity increase of up to *ca.* 350%. The acetate-induced signal effect is well explained by efficient emission retrieval upon an interaction between the anion and the thiouronium moiety of **1**. Further assessment of the receptor–anion complexation process came from a ^{1}H NMR titration; aliquots of the tetrabutylammonium salt of the anion were added to a CD_3CN solution of **1** (2 mM). Although NH resonances of the thiouronium moiety could not be detected in CD_3CN‡ because of the high acidity, significant upfield shifts (up to 0.2 ppm) of the resonances arising from two types of methylene (NaphCH_2NH– and PhCH_2S–) and methyl (–NHCH_3) protons, which are located in the periphery of the anion-binding site, were observed upon complexation with AcO^-. Judging from the titration, the strong binding of AcO^- allowed the mole ratio method[8] to be used in the determination of the binding stoichiometry, which was found to be 1 : 1 for the receptor–anion complex.

Fig. 2 shows the resulting titration curves for the fluorescent intensity when adding AcO^-, $(BuO)_2P(O)O^-$§ or Cl^- to an MeCN solution of **1** at 25 °C, supporting the formation of a 1 : 1 stoichiometry complex. The association constants (K_a)¶ could be calculated using nonlinear curve-fitting plots. As a result, interestingly, the fluorescent response of **1** was found to show a significant selectivity for the nature of anions in spite of the simple molecular system of **1** [K_a/M^{-1}: AcO^-, > 10^6; $(BuO)_2P(O)O^-$, 5.6 × 10^4; Cl^-, n.d.‖], being probably correlated with the guest basicity. Of particular note is that **1** shows not only a high susceptibility to AcO^- but also a

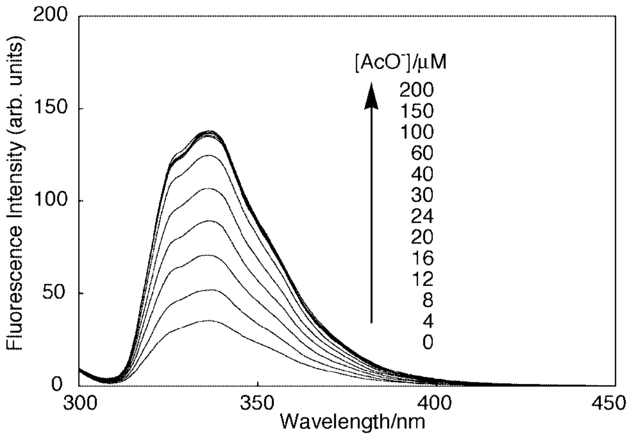


Fig. 1 Emission spectra of **1** (20 μM) in MeCN at 25 °C excited at 270 nm upon addition of AcO^- as a NBu_4 salt.

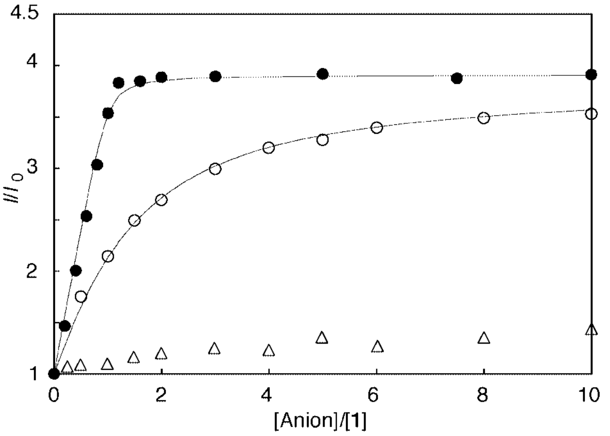


Fig. 2 Fluorescent intensity at 336 nm of **1** (20 μM) in MeCN at 25 °C excited at 270 nm as a function of anion concentration: (●) NBu_4OAc, (○) $NEt_4OP(O)(OBu)_2$, (△) NBu_4Cl.

discernible binding towards oxo-anions. Taken together, it could allow us to analyze AcO^- quantitatively[9] using an easy-to-detect fluorescent signal response. This would be most welcome to applications involving medical diagnostics.

As a control experiment, the interaction of AcO^- with 2-methylnaphthalene was investigated in the fluorescent spectra for which no change was observed. This insight supports the argument that the fluorescent enhancement of **1** induced by anions could be based on the significant change on the photoinduced charge transfer characteristics in system **1** where the anion binding event decreases the interaction between the naphthalene and thiouronium moieties.

We conclude that system **1** represents a simple, easy-to-make and hitherto unexplored class of luminescent chemosensors of anions. Owing to the unique sensing properties based on the naphthalene–thiouronium conjugate, the development of highly functional derivatives will represent an important synthetic challenge. Indeed, we are currently preparing more elaborate systems incorporating binaphthalene units.

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Notes and references

† δ_H(400 MHz, $CDCl_3$, TMS) 3.07 (s, 3H), 4.32 (s, 2H), 4.69 (s, 2H), 7.25–7.27 (m, 6H), 7.46–7.49 (m, 2H), 7.67 (br d, 1H), 7.76–7.80 (m, 3H); δ_C(100.7 MHz, $CDCl_3$) 31.07, 35.89, 48.52, 125.08, 126.63, 127.25, 127.68, 128.04, 128.96, 129.07, 129.17, 129.37, 131.80, 133.08, 133.16, 167.85; FAB-MS, *m*/*z* 321[M − PF_6]$^+$; Anal. Calc. for $C_{20}H_{21}N_2SPF_6$: C, 51.50; H, 4.54; N, 6.01. Found: C, 51.66; H, 4.53; N, 5.98%.

‡ The NH resonances were observed at δ 9.22–9.85 as a broad signal in d_6-DMSO.

§ The result of the titration by adding $H_2PO_4^-$ did not fit to curve based on a 1 : 1 host–guest stoichiometry complex, which may be due to a phosphate–phosphate dimerization.[7d,10]

¶ The K_a values were estimated by three individual fluorescent intensity titrations: λ_{max}(ex) = 270 nm, λ_{max}(em) = 336 nm in MeCN at 25 °C. The estimated error for the titration with $(BuO)_2P(O)O^-$ is < 3%.

‖ The response was too low to determine the K_a value.

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