Isothiouronium-derived simple fluorescent chemosensors of anions

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Received (in Cambridge, UK) 25th March 2002, Accepted 5th June 2002
First published as an Advance Article on the web 25th June 2002

Fluorescence-active chemosensors comprising a naphthalene moiety covalently attached, *via* a methylene spacer, to a isothiouronium anion-binding subunit have been proposed and characterized. The corresponding 2-[(*S*-benzyl-*N*′-methyl-*N*-isothiouronio)methyl]naphthalene hexafluorophosphate **1** and dissymmetric 3,3′-bis[(*S*-benzyl-*N*′-methyl-*N*-isothiouronio)methyl]-2,2′-dimethoxy-1,1′-binaphthalene bis(hexafluorophosphate) **2**, prepared in multi-synthetic paths *via* the corresponding thiourea derivatives as key synthons, respectively, showed almost no fluorescence spectra in MeCN based on a photoinduced electron transfer (PET) quenching process ("switch off" state). However, the binding of anionic guests to the isothiouronium unit could regulate the efficiency of the PET process to induce selective anion-induced fluorescence emission ("switch on" state), due to the fluorescent enhancement of the PET quenched fluorophore (retrieval) of the naphthalene unit. Notably, in the case of **2**, the maximum enhancement (*ca.* 1600%) in the emission was reached upon addition of 3 equiv. of AcO^-, compared to that with no anion bound. In this way, the PET sensors exhibited favorable affinity for oxoanions, which are functional groups of important biological relevance, emitting fluorescence in the presence of the anions. The findings suggest that use of the isothiouronium group would be extremely advantageous for designing new "switch on"-type chemosensors of oxoanions.

Introduction

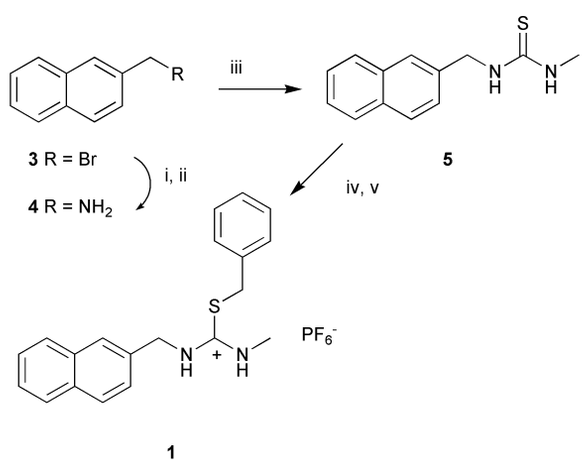
Much attention has been focused on chemosensors for the detection of chemically and/or biologically important anions.[1] In this context, the design of easy-to-make and "switch on"-type fluorescent sensors based on host–guest interaction is still a synthetic challenge and it would be desirable not only in the field of analytical chemistry but also in biomedical and environmental research because highly sensitive assay systems might then be feasible. In particular, the demand for detection of oxoanions involving carboxylates and phosphates leads us to search for a suitable anion-binding unit capable of efficient interaction with a built-in chromo(fluoro)phore, based on the fact that oxoanions play critical roles in biological systems.[2] A family of isothiouronium salts, which are known not only as synthetic intermediates for the conversion of alkyl halides to the corresponding thiols,[3] but also as classical reagents for the identification of organic acids,[4] has potential as one of key functional groups for the purpose of molecular recognition of anions in supramolecular chemistry.[5] This may be attributable to the fact that such groups would enhance the acidity of the NH moieties compared to that of the corresponding thiourea.[6] Indeed, recently, functional isothiouronium-derived systems have been reported for a carrier of 5′-AMP[7] and oxoanion recognition.[8] It therefore occurred to us that a sophisticated combination of the aforementioned functional entity and a suitable fluorophore could allow production of a new type of chemosensor material. The design is mainly based on our idea that anion recognition events at the electron-deficient binding site of the isothiouronium moiety would be efficiently communicated to the fluorescent fragment so that an easily detectable signalling effect would occur in such a system. Although numerous fluorescent chemosensors have been proposed so far in supramolecular chemistry,[6l,6m,9] the development of the related simple systems possessing isothiouronium moieties is quite new. Thus, we have utilized the attractive features of the isothiouronium group to prepare fluorescent agents for the detection of oxoanions in solution.[10] Here, we report intriguing aspects of the title systems.

Results and discussion

Synthesis

In order to exploit the prototypical features of the isothiouronium-derived fluorescent chemosensors, we employed naphthalene and 1,1′-binaphthalene units as suitable fluorophores to set up the targets **1** and **2**, respectively. The latter unit is well known as one of the key parts often used in catalytic reagents and chiral receptors.[11]

In the initial step of this research, the synthesis of the naphthalene–isothiouronium dyad **1** was carried out as outlined in Scheme 1; 2-bromomethylnaphthalene **3** was converted to



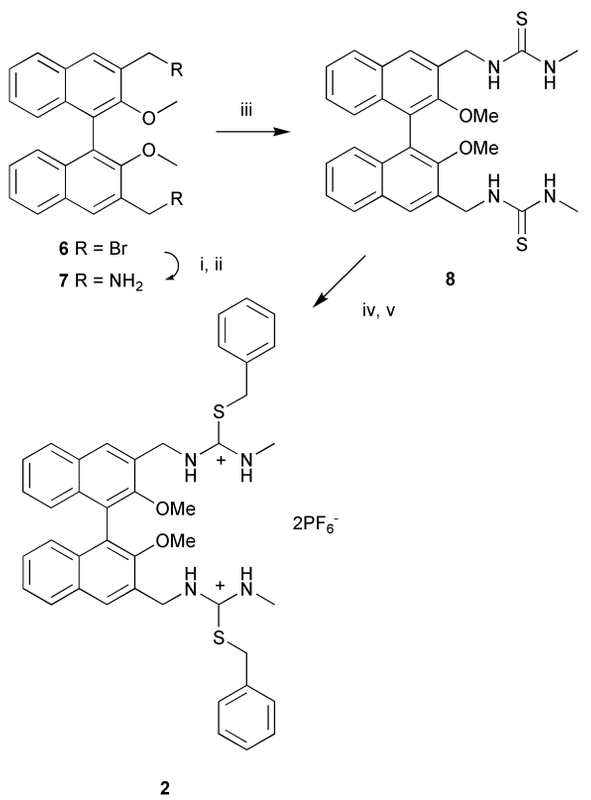
Scheme 1 *Reagents and conditions*: i, K^+ phthalimide$^-$, dry DMF; ii, $NH_2NH_2{\cdot}H_2O$, THF–EtOH; iii, MeNCS, $CHCl_3$; iv, benzyl bromide, dry EtOH; v, $AgPF_6$, dry EtOH.

the 2-aminomethyl derivative **4**[12] *via* Gabriel synthesis,[13] during which **3** was allowed to react with potassium phthalimide, followed by treatment with $NH_2NH_2{\cdot}H_2O$. The condensation of **4** with MeNCS in $CHCl_3$ gave the corresponding thiourea derivative **5** in 68% yield, which was amenable to reaction with

DOI: 10.1039/b202953g

1.1 equiv. of benzyl bromide. This was finally followed by anion exchange treatment with $AgPF_6$. Purification by reversed phase column chromatography afforded the desired **1** in an excellent yield.

The synthesis of dissymmetric **2** could be achieved in a similar manner from 3,3′-bis(bromomethyl)-1,1′-binaphthalene **6**[14] (Scheme 2): after amination of **6** to give **7** (76% yield),



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Scheme 2 *Reagents and conditions*: i, K^+ phthalimide$^-$, 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.

compound **6** was also allowed to react with MeNCS to give **7** in 75% yield, followed by conversion to the desired compound **2** in 91% yield. The assignments of both structures were deduced from various analytical data.

Optical sensing studies of naphthalene–isothiouronium dyad 1

The absorption spectrum of **1** displays a maximum at 225 nm (ε 80500 cm^{-1} M^{-1}) as well as a shoulder at 270 nm (ε 5730 cm^{-1} M^{-1}) in MeCN. Also, when AcO^- as a potential anion was added to the solution, almost no change was observed in the absorption spectrum. However, **1** showed very weak fluorescence in MeCN at 25 °C ([**1**] = 2×10^{-5} M) at an excitation wavelength of 270 nm, the intensity of which was lower by a factor of 50 than that of 2-methylnaphthalene. The finding could be explained on the basis of efficient quenching by the isothiouronium moiety (*vide infra*). However, the addition of AcO^- was found to significantly enhance the fluorescent intensity as illustrated in Fig. 1. As a result, addition of 1.2 equiv. of AcO^- caused a remarkable intensity increase up to *ca.* 380%. The acetate-induced signal effect would be well-accounted for by efficient retrieval upon interaction between the anion and the isothiouronium moiety of **1**. This interpretation was also supported by a control experiment in which almost no change in the emission intensity of 2-methylnaphthalene was obtained as the concentration of AcO^- was increased, indicating that the emission is not caused directly by an interaction between the naphthalene and AcO^-. Further assessment of the host–

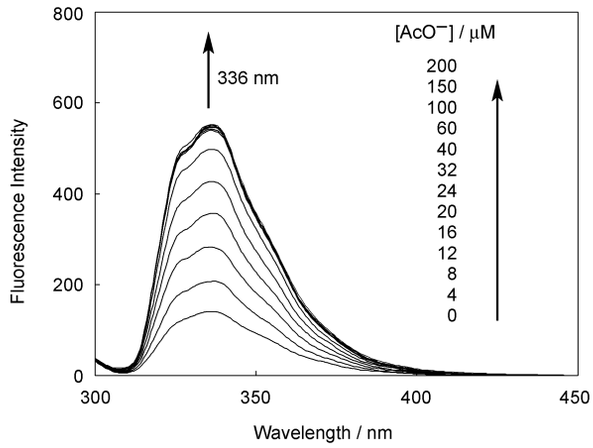


Fig. 1 Emission spectra of **1** (2×10^{-5} M) in MeCN at 25 °C excited at 270 nm upon addition of AcO^- as the Bu^n_4N salt.

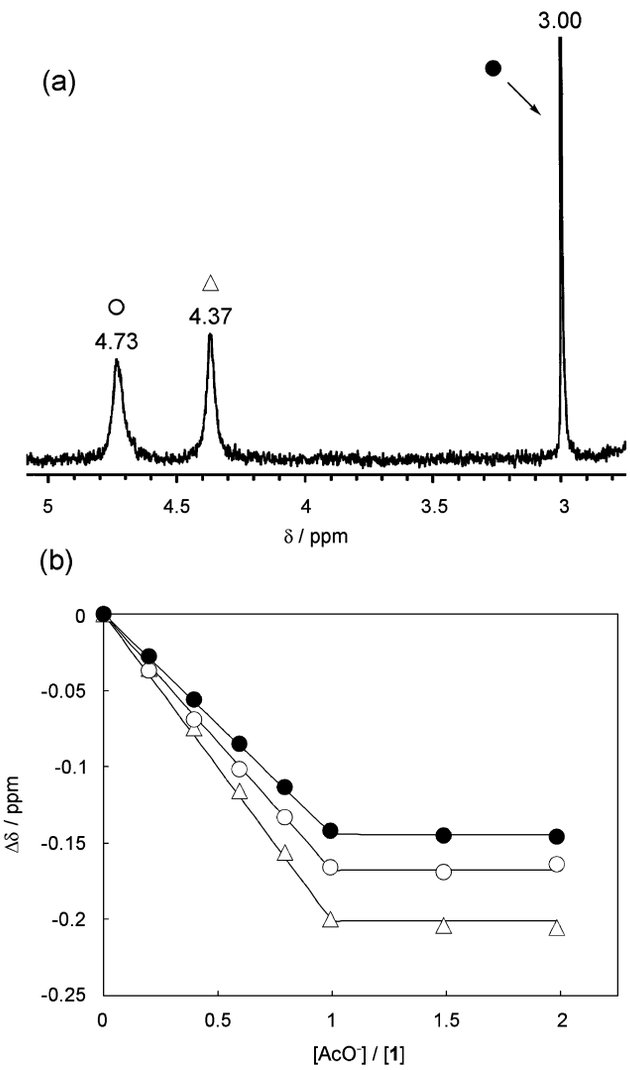


Fig. 2 (a) ^1H NMR spectrum (400 MHz, CD_3CN) at 25 °C of **1**. (b) ^1H NMR spectral changes for **1** (2×10^{-3} M) in CD_3CN at 25 °C upon addition of AcO^- as the Bu^n_4N salt: (●) Me–; (△) $PhCH_2S$–, (○) $NaphCH_2NH$–.

anion complexation process came from ^1H NMR titrations (Fig. 2); aliquots of the tetra-*n*-butylammonium salt of the anion were added to a CD_3CN solution of **1** (2×10^{-3} M) at 25 °C. Although the NH resonances of the isothiouronium moiety could not be detected in the solution because of the high acidity, the singlets 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

sites, could be located at 4.73, 4.37 and 3.00 ppm, respectively (Fig. 2a). Upon complexation with AcO^-, significant upfield shifts (up to 0.2 ppm) of the resonances were observed, indicating that the isothiouronium unit and the anion form a complex *via* hydrogen bonding and electrostatic interactions (Fig. 2b). Judging from the titrations, the strong binding of AcO^- allowed the mole ratio method[15] to be used in the determination of the binding stoichiometry, which was found to be a 1 : 1 host-to-anion complexation.

The response of the fluorescent spectra toward several anions of physiological importance was examined; Fig. 3 shows the

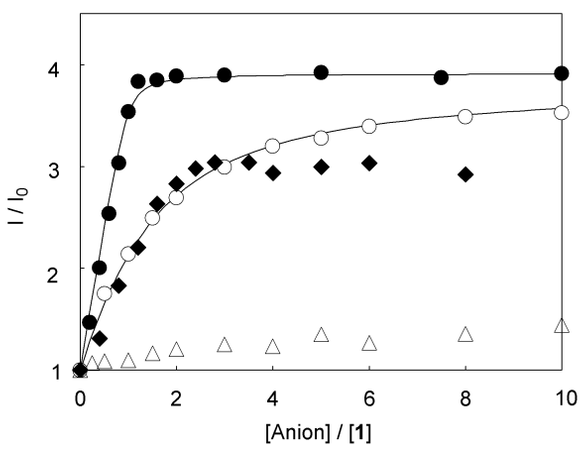


Fig. 3 Fluorescence intensity at 336 nm of **1** (2×10^{-5} M) in MeCN at 25 °C excited at 270 nm as a function of anion concentration: (●) Bu^n_4NOAc, (◆) $Bu^n_4NH_2PO_4$, (○) $(Bu^nO)_2P(O)ONEt_4$, (△) Bu^n_4NCl.

resulting titration curves for the fluorescence intensity upon addition of several anions to a solution of **1** in MeCN at 25 °C. The addition of $H_2PO_4^-$ as an oxoanion other than AcO^- shows moderate enhancement, reaching a plateau at a $[H_2PO_4^-]$: [**1**] ratio of 3 : 1, which is indicative of a lower response ability compared to the case of AcO^-. However, the result of the titration did not fit to the curve based on a 1 : 1 host-to-guest stoichiometry complex. This unexpected result motivated us to employ a Job plot[15] to estimate the stoichiometry. Such an approach revealed that the relative concentration of the dihydrogen phosphate–**1** complex approaches a maximum when the molar fraction of [**1**]/[**1**] + $[H_2PO_4^-]$ is approximately 0.3 (Fig. 4a), which is expected for the formation of a 1 : 2 complex between **1** and $H_2PO_4^-$. This finding, although initially surprising, could be interpreted in terms of a phosphate–phosphate dimerization.[16] We consider that an interaction between the isothiouronium unit and $H_2PO_4^-$ caused an increase in the acidity of the uncomplexed OH groups of the phosphate, and then a second $H_2PO_4^-$ participated in a hydrogen bonding interaction. Subsequently, a termolecular complex became the dominant species upon addition of $H_2PO_4^-$. To avoid this process, $(Bu^nO)_2P(O)O^-$, which does not possess any OH groups, was employed in the titration experiment, which then resulted in the formation of a complex of 1 : 1 stoichiometry, as inferred from the Job plot (Fig. 4b). Also, in the presence of Cl^- the fluorescent intensity hardly changed (Fig. 3); the response was too small to permit determination of the association constant (K_a). On the basis of the titration results discussed above, we calculated K_a values for AcO^- and $(Bu^nO)_2P(O)O^-$ using a nonlinear curve fitting plot. Subsequently, the fluorescent response of **1** was found to show significant selectivity for the nature of the anion [K_a/M^{-1}: AcO^-, $>10^6$; $(Bu^nO)_2P(O)O^-$, 5.6×10^4], which is probably corrected for the guest's basicity.[17] Of particular note is that **1** shows not only a high susceptibility to AcO^- but also a discernible affinity towards oxoanions. Taken together, this could allow us to determine AcO^- quantitatively using a fluorescent signal response.

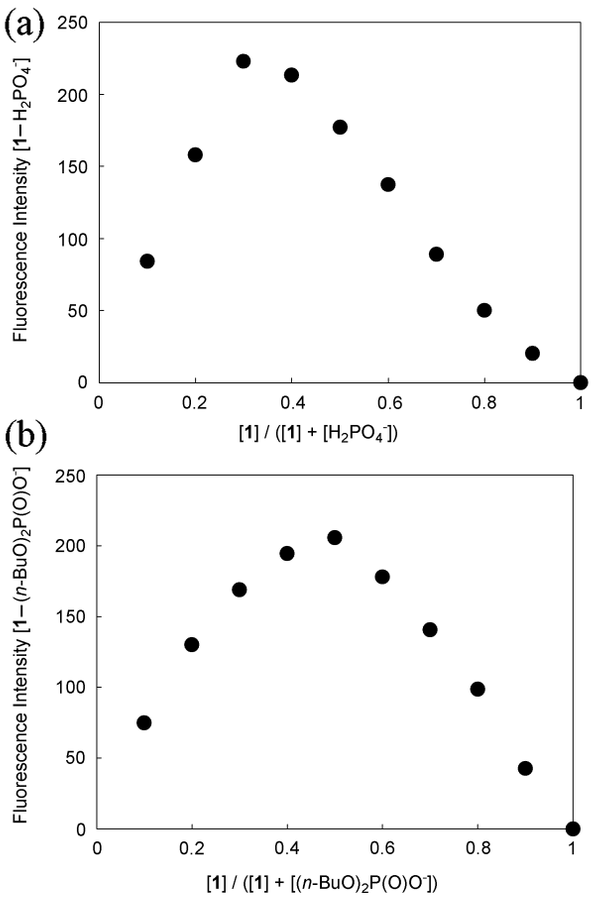
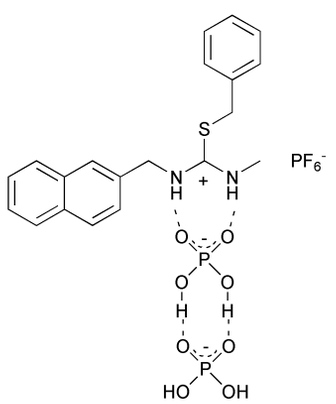


Fig. 4 Job plots for (a) **1**–$H_2PO_4^-$ and (b) **1**–$(Bu^nO)_2P(O)O^-$ complexes in MeCN; [**1**] + $[H_2PO_4^-]$ = [**1**] + $[(Bu^nO)_2P(O)O^-]$ = 2×10^{-5} M.



Mechanism of the anion-induced fluorescent change

System **1** showed very weak fluorescence in MeCN at 25 °C (*vide supra*), indicating that the electron-deficient isothiouronium moiety acts as a quencher for the singlet state of the appended naphthalene. The feasibility of the PET process could be estimated according to the Rehm–Weller equation:[18] the thermodynamic driving force (ΔG_{PET}) is calculated as follows:

$$\Delta G_{PET} = 23.06[E(D^+/D) - E(A/A^-)] - w_p - E_{00}(D) \quad (1)$$

where $E(D^+/D)$, $E(A/A^-)$, w_p and $E_{00}(D)$ are the oxidation potential of the donor, the reduction potential of the acceptor, the radical ion pair energy and the singlet excitation energy of the donor, respectively.[19] The values of $E(D^+/D)$ and $E_{00}(D)$ of naphthalene are known to be 1.54 V and 3.99 eV, respectively.[20] Cyclic voltammetry measurements were performed using a

1×10^{-3} M solution of **1** in MeCN using 0.1 M $Bu^n_4NClO_4$. The cyclic voltammograms for the reduction of **1** showed an irreversible wave and two cathodic peaks at −1.23 and −1.61 V *vs.* Fc/Fc^+ when a carbon electrode was used as the working electrode (Fig. 5). Although an accurate ΔG_{PET} value could not

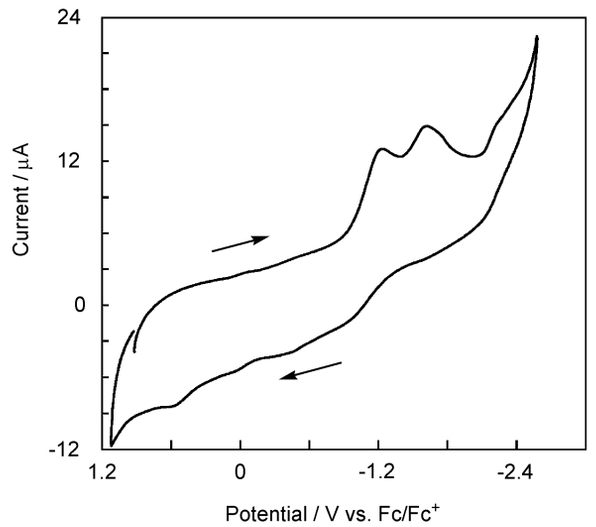
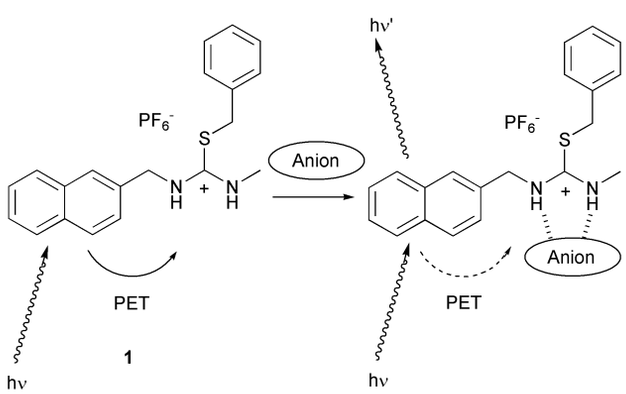


Fig. 5 Cyclic voltammogram of **1** (1×10^{-3} M) in MeCN solution containing 0.1 M $Bu^n_4NClO_4$, Ag/Ag^+ reference electrode, referenced *vs.* ferrocene, scan rate = 0.1 V s^{-1}.

be calculated because of the irreversible profile, we could assume that the ΔG_{PET} value is negative from these parameters. Furthermore, when **1** was studied in the presence of 1.3 equiv. of AcO^- in MeCN, a cathodic shift of 78 mV due to the isothiouronium reduction wave was obtained, suggesting that the electron-deficiency of the isothiouronium unit was decreased by the binding of AcO^-. Taken together, the interaction of the anion with the isothiouronium unit could diminish the efficiency of the PET process to induce the "switch on" action based on the fluorescent retrieval of the naphthalene unit; a plausible mechanism is depicted in Scheme 3.



Scheme 3 Plausible mechanism for the "switch on" anion chemosensor **1**.

Dissymmetric 1,1′-binaphthalene-derived bis(isothiouronium) system 2

Since synthetic variations in binaphthyl subunits could provide an entry into a potentially wide and varied array of new systematic materials,[11] investigation of system **2** might be useful for developing advanced anion sensor materials. System **2** not only contains a 1,1′-binaphthalene unit with methoxy groups that serve as electron-donating groups, but also includes two isothiouronium units that would allow a more efficient PET process and regulation of anion binding at the isothiouronium units compared to the case of **1**, so that an enhanced response upon complexation with suitable anions would be possible. Fig. 6 illustrates the fluorescence spectra of the complex formed by the interaction of AcO^- with **2**.

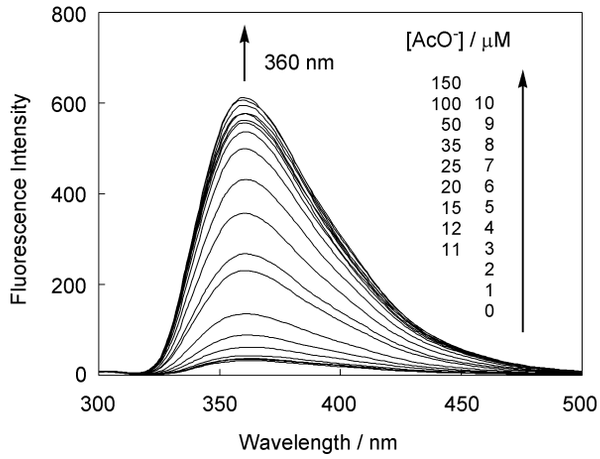


Fig. 6 Emission spectra of **2** (5×10^{-5} M) in MeCN at 25 °C excited at 278 nm upon addition of AcO^- as the Bu^n_4N salt.

It is noteworthy that addition of the anion induced a dramatic enhancement of the fluorescence intensity, the high response presumably being due to an efficient anion-induced reduction of the PET interaction between 2,2′-dimethoxy-1,1′-binaphthalene and the two isothiouronium units. Indeed, determination of the stoichiometry using the Job plot indicated the formation of a 1 : 2 host-to-anion complex. This finding also suggests that the 2,2′-dimethoxy groups of the binaphthalene ring sterically prevent formation of a 1 : 1 complex in which AcO^- could be bound to the two isothiouronium units in a concave fashion. The titration curve, as well as those of $(n\text{-BuO})_2P(O)O^-$ and Cl^-, is shown in Fig. 7: at this stage, we

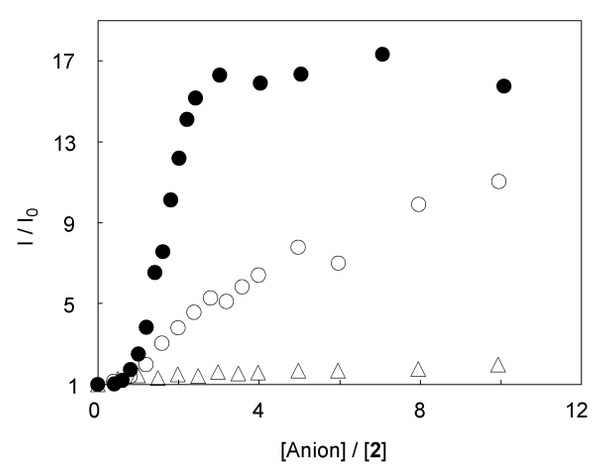


Fig. 7 Fluorescence intensity at 360 nm of **2** (5×10^{-6} M) in MeCN at 25 °C excited at 278 nm as a function of anion concentration: (●) Bu^n_4NOAc, (○) $(Bu^nO)_2P(O)ONEt_4$, (△) Bu^n_4NCl.

performed a titration with $H_2PO_4^-$ under similar conditions. However, enhanced scattering light was obtained, meaning that some precipitation may have occurred. From Fig. 7, it appears that a sharp endpoint for AcO^- was obtained at a $[AcO^-]$: [**2**] ratio of 3 : 1, at which an almost maximum enhancement of *ca.* 1600% was achieved. In an effort to estimate the association constant of compound **2** with anionic guests, the sigmoidal curves obtained as a result of the titrations were analysed. On the basis of the assumption that a 1 : 2 host-to-anion complex would be formed *via* the corresponding 1 : 1 complex, we tried to fit the results using a global spectral fitting program (Specfit). A fit of the AcO^- data implied that there were eight species in solution, a result clearly not consistent with the Job plot. It is

possible that a drastic change in the ionic strength of the solution during titration would induce a sigmoidal curve; similar phenomena have been reported.[21] However, the selectivity for the anions seems to run in the following order: $AcO^- > (Bu^nO)_2P(O)O^- > Cl^-$. The higher response of **2** compared with **1** may be potentially advantageous in biologically important oxoanion-sensing applications where a high concentration of interfering Cl^- is present (Fig. 7).

Conclusion

Systems **1** and **2** emit weakly as a result of PET processes from the singlet excited state of the naphthalene-type fluorophore to the electron-deficient isothiouronium unit. Upon selective anion complexation, the isothiouronium unit becomes involved in the complexation process, and then can no longer fully participate in the PET process, causing the emission to increase. Utilizing this property, we have presented new, simple and easy-to-make fluorescent chemosensors of anions. Taken together, we believe that the use of the isothiouronium group would be extremely advantageous for designing new chemosensors because of its electron-deficient and oxoanion-binding properties, and also the synthetic versatility of the isothiouronium unit. A "preorganized approach" based on the isothiouronium group could lead us to develop various kinds of fluorescent receptors for chemically and/or biologically important guest species.

Experimental

NMR spectra were taken on a Bruker ARX 400 (400 MHz) spectrometer. Chemical shifts (δ) are reported downfield from the initial standard Me_4Si. For routine ^1H NMR spectroscopy, Bruker AC 300 (300 MHz) or Gemini 2000 (200 MHz) instruments were used. Absorption spectra were measured using a Shimadzu UV-3100PC spectrophotometer and fluorescence spectra were measured with a JASCO FP-750 spectrophotometer. In the latter case, the slits of the excitation and emission monochromators were 10 and 5 nm (for the titrations with **1**), and 5 and 5 nm (for the titrations with **2**), respectively. Fast atom bombardment (FAB) mass spectra were obtained on a JEOL JMS-DX 303 double focusing spectrometer. *m*-Nitrobenzyl alcohol was used as a matrix. Elemental analyses were obtained using an EISON EA1108. Cyclic voltammetry was performed by means of an ALS600 system. A three-electrode system containing a glassy carbon working electrode, a platinum wire counter electrode and a Ag/Ag^+ electrode as reference was adopted. The electrolytic solvent was MeCN containing 0.1 M $Bu^n_4NClO_4$ as the supporting electrolyte. The solutions were degassed with N_2 before measurements were made.

Materials

Unless specified otherwise, reagent-grade reactants and solvents were used as received from chemical suppliers. *N*,*N*-Dimethylformamide (DMF) was predried over anhydrous $CuSO_4$, and then distilled from CaH_2. Tetrahydrofuran (THF) was predried over NaH. After Na and benzophenone were added to the solution, the resulting solution was distilled. EtOH was distilled from Na. Acetone was distilled from Drierite. 2-Bromomethylnaphthalene was synthesized from 2-methylnaphthalene (78%). Dissymmetric 3,3′-bis(bromomethyl)-2,2′-dimethoxy-1,1′-binaphthalene was prepared according to the literature procedure.[22] Tetraalkylammonium salts were prepared by known methods.[23]

2-[(*N*-Methylthioureido)methyl]naphthalene (5)

Compound **4**[12] (300 mg, 1.91 mmol) was dissolved in $CHCl_3$ (7 mL). After a $CHCl_3$ solution (3 mL) containing MeNCS (419 mg, 5.73 mmol) had been added to the solution, the resulting mixture was stirred at room temperature overnight. The resulting solution was partitioned between $CHCl_3$ (100 mL) and water (40 mL). The $CHCl_3$ layer was washed with water (40 mL × 3), dried with anhydrous $MgSO_4$ and evaporated. The residue was recrystallized from $CHCl_3$–Et_2O to afford the desired **5** (299 mg, 68%), δ_H(300 MHz, $CDCl_3$) 2.97 (3H, d, *J* 4.8, Me), 4.81 (2H, d, *J* 4.1, CH_2), 5.96 (1H, br, NH), 6.12 (1H, br, NH), 7.43 (1H, dd, *J* 1.8 and 8.4, Ar-H), 7.46–7.52 (2H, m, Ar-H), 7.75 (1H, d, *J* 0.7, Ar-H) and 7.85–7.80 (3H, m, Ar-H).

2-[(*S*-Benzyl-*N*′-methyl-*N*-isothiouronio)methyl]naphthalene hexafluorophosphate (1)

Compound **5** (338 mg, 1.47 mmol) was dissolved in dry EtOH (25 mL) under an Ar atmosphere. After a dry EtOH solution (5 mL) of benzyl bromide (281 mg, 1.64 mmol) had been added to the solution, the resulting mixture was stirred at 40 °C for 4 h. After evaporation, the residue was recrystallized from MeOH–Et_2O to afford the desired bromo salt (544 mg, 92%). It was then dissolved in dry EtOH (11 mL) and a dry EtOH solution (1.5 mL) of $AgPF_6$ (127 mg, 0.5 mmol) was added to the solution. The resulting solution was subjected to reversed silica gel chromatography (Merck Silica gel 60 Silanized) with EtOH as eluent in order to remove AgBr, and then evaporated. In this way, 232 mg of **1** were obtained quantitatively, δ_H(400 MHz, $CDCl_3$) 3.07 (3H, s, Me), 4.32 (2H, s, SCH_2Ph), 4.69 (2H, s, Naph-C*H*$_2$-NH), 7.25–7.27 (6H, m, Ar-H), 7.46–7.49 (2H, m, Ar-H), 7.67 (1H, s, Ar-H) and 7.76–7.80 (3H, m, Ar-H); δ_C(100.7 MHz, $CDCl_3$) 31.07 (Me), 35.89 (SCH_2Ph), 48.52 (Naph-CH_2-NH), 125.08, 126.63, 127.25, 127.68, 128.04, 128.96, 129.07, 129.17, 131.80, 133.08 and 133.16 (Ar-C) and 167.85 (isothiouronium-C); FAB-MS (*m*/*z*) 321 $[M - PF_6]^+$ (Found: C, 51.66; H, 4.53; N, 5.98. $C_{20}H_{21}N_2SPF_6$ requires C, 51.50; H, 4.54; N, 6.01%).

3,3′-Bis(aminomethyl)-2,2′-dimethoxy-1,1′-binaphthalene (7)

Dissymmetric 3,3′-bis(bromomethyl)-2,2′-dimethoxy-1,1′-binaphthalene **6** (351 mg, 0.70 mol) was dissolved in dry DMF (9 mL) under an Ar atmosphere. After addition of potassium phthalimide (455 mg, 2.46 mmol), the resulting solution was stirred at 90 °C for 5 h. The solution was partitioned between $CHCl_3$ (150 mL) and water (150 mL). The $CHCl_3$ layer was washed with water (100 mL × 3), dried with anhydrous $MgSO_4$, and recrystallized from $CHCl_3$–*n*-hexane. In this way, 397 mg of 3,3′-bis(phthalimidomethyl)-2,2′-dimethoxy-1,1′-binaphthalene were obtained (95 %), δ_H(200 MHz, $CDCl_3$) 3.37 (6H, s, OMe), 5.19 (4H, s, CH_2), 7.11–7.37 (6H, m, Ar-H), 7.74–7.80 (8H, m, Ar-H) and 7.91–7.96 (4H, m, Ar-H).

The above compound (700 mg, 1.11 mmol) was dissolved in 30 mL of THF–EtOH (1 : 2 v/v). After addition of $NH_2NH_2 \cdot H_2O$ (0.6 mL, 12.4 mmol), the resulting solution was stirred at 60 °C for 1.5 h. After the solvent had been removed *in vacuo*, the residue was partitioned between $CHCl_3$ (200 mL) and water (150 mL). The $CHCl_3$ layer was dried with anhydrous $MgSO_4$. The removal of the solvent afforded **7** (350 mg, 80%), δ_H(200 MHz, $CDCl_3$) 1.76 (4H, s, NH_2), 3.31 (6H, s, OMe), 4.08 (2H, d, *J* 14.8, CH_2), 7.11–7.22 (4H, m, Ar-H), 7.39 (2H, dt, *J* 1.4 and 6.8, Ar-H), 7.88 (2H, d, *J* 8.0, Ar-H), 7.94 (2H, s, Ar-H).

3,3′-Bis[(*N*′-methylthioureido)methyl]-2,2′-dimethoxy-1,1′-binaphthalene (8)

Compound **7** (417 mg, 1.12 mmol) was dissolved in $CHCl_3$ (9 mL). After 500 mg of MeNCS (6.84 mmol) had been added to the solution, the mixture was stirred at room temperature for *ca.* 15 h. The resulting solution was partitioned between $CHCl_3$ (100 mL) and water (50 mL). The $CHCl_3$ layer was washed with water (50 mL × 3), dried over anhydrous $MgSO_4$,

and evaporated. The residue was chromatographed on silica gel (Wacogel C-300) using 3% (v/v) MeOH in $CHCl_3$ as eluent, and then recrystallized from $CHCl_3$–*n*-hexane to afford the desired **8** (435 mg, 75%), δ_H(300 MHz, $CDCl_3$) 3.00 (6H, d, *J* 4.8, NH-C*H*$_3$), 3.27 (6H, s, OMe), 4.76–5.12 (4H, m, CH_2), 6.30–6.34 (2H, m, NH), 6.57 (2H, br, NH), 7.12 (2H, d, *J* 8.5, Ar-H), 7.23–7.28 (2H, m, Ar-H), 7.41 (2H, dt, *J* 1.1 and 7.0, Ar-H), 7.88 (2H, d, *J* 8.1, Ar-H) and 8.00 (2H, s, Ar-H); FAB-MS (*m*/*z*) 518 [M^+].

3,3′-Bis[(*S*-benzyl-*N*′-methyl-*N*-isothiouronio)methyl]-2,2′-dimethoxy-1,1′-binaphthalene bis(hexafluorophosphate) (2)

Compound **8** (251 mg, 0.48 mmol) was dissolved in dry EtOH (20 mL) under an Ar atmosphere. After a dry EtOH solution (3 mL) of benzyl bromide (256 mg, 1.49 mmol) had been added to the solution, the resulting mixture was stirred at 50 °C for 2 h. The solvent was evaporated, and then the residue was chromatographed on reversible silica gel (Merck Silica gel 60 Silanized) using 60% (v/v) EtOH in water as eluent to afford the desired dibromo salt (372 mg, 89%). This salt (73.5 mg, 0.085 mmol) was then dissolved in dry EtOH (3 mL). After a dry EtOH solution (1.5 mL) of $AgPF_6$ (43.2 mg, 0.17 mmol) had been added to the solution, the resulting solution was subjected to reversed silica gel chromatography (Merck Silica gel 60 Silanized) with EtOH as eluent in order to remove AgBr, and then evaporated. In this way, 80 mg of **2** were obtained (95%), δ_H[400 MHz, CD_3OD–CD_3CN (1 : 4 v/v), 60 °C] 3.07 (6H, s, NH-C*H*$_3$), 4.40 (4H, s, SCH_2Ph), 4.83 (4H, s, Naph-C*H*$_2$-NH), 7.06 (2H, d, *J* 8.4, Ar-H), 7.27–7.34 (12H, m, Ar-H), 7.47 (2H, t, *J* 7.5, Ar-H), 7.92 (2H, s, Ar-H) and 7.96 (2H, d, *J* 8.2, Ar-H); FAB MS (*m*/*z*) 845 [$M - PF_6$]$^+$, 699 [$M - 2PF_6 - H$]$^+$ (Found: C, 50.71; H, 4.41; N, 5.52. $C_{42}H_{44}N_4SO_2F_{12}P_2S_2$ requires C, 50.91; H, 4.48; N, 5.65%).

Binding studies

Association constants (K_a) derived from fluorescence titrations were calculated from a plot of the observed change in the fluorescence intensity at 336 nm for **1** (λ_{ex} = 270 nm) as a function of the concentration of added AcO^- or $(Bu^nO)_2P(O)O^-$. These date were fitted with a nonlinear curve fitting procedure (Microsoft Excel), assuming a host-to-analyte complexation of 1 : 1. The K_a values in this study were estimated by three separate titrations. The estimated error for the titration with $(Bu^nO)_2P(O)O^-$ is <3%.

Note added in proof

After the submission of this manuscript, related sensors were reported, see Ref. 24

Acknowledgements

Y. K. acknowledges PRESTO (Precursory Research for Embryonic Science and Technology) of Japan Science and Technology (JST) for financial support. This research has been supported in part by a TORAY Award in Synthetic Organic Chemistry in Japan, Saneyoshi Scholarship Foundation, The Nishida Research Fund for Fundamental Organic Chemistry and a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sport and Culture of Japan (No. 13650911). The authors thank Professor M. Sato of Saitama University, Japan, for recording the cyclic voltammograms. Y. K. also thanks Dr P. A. Gale (University of Southampton, UK) for helpful discussions.

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