A Novel Cation 'AND' Anion Recognition Host Having Pyrido[1′,2′:1,2]imidazo[4,5-*b*]pyrazine as the Fluorophore

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Novel fluorescent pyrido[1′,2′:1,2]imidazo[4,5-*b*]pyrazine derivatives having a crown ether side-arm, **1a, b**, recognise alkaline earth metal cations and thiocyanate anions coincidentally, making a function as an AND logic gate which has fluorescence quenching output.

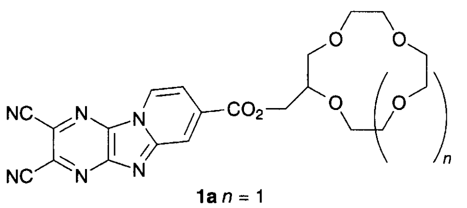
Fluorescent chemosensing is useful in biomedical research,[1–6] and it has been very recently developed into chemical logics.[7,8] In the chemical logic system, the binding of a guest molecule to a host compound corresponds to the logic input and the resulting physical property change such as absorption and/or fluorescence spectra corresponds to the logic output. Whenever the multiple chemical inputs independently produce one output, they can be regarded as OR logic gates, in other words, poorly chemoselective systems behave as OR functions. On the other hand, an AND logic gate recognises multiple chemical inputs coincidentally and produces one output where high chemoselectivity is necessary. de Silva *et al.* designed a cyanoanthracene system having both a benzocrown ring and a tertiary amino group which functions as an AND logic gate. The emission intensity of the cyanoanthracene increases in the presence of the sodium cation AND proton.[7] Two receptor sites, benzocrown ether for alkali metal ions and a tertiary amino group for protons are characteristic of the AND logic gate. Here we demonstrate a novel AND logic gate system using crown-armed pyridoimidazopyrazine (PIP) derivatives, where the crown ether receptor recognises the two input signals, alkaline earth metal cations and thiocyanate anions. Quenching of the PIP fluorescence plays a role as the output.

The PIP derivatives having a simple crown ether side-arm, 12-crown-4-methyl 7-(2,3-dicyanopyrido[1′,2′:1,2]imidazo-[4,5-*b*]pyrazine)carboxylate **1a**† and 15-crown-5 analogue **1b**† were prepared from 2-amino-3-chloro-5,6-dicyanopyrazine and the corresponding crown ether isonicotinates by previously reported methods.[9–11]

By the addition of alkali and alkaline earth metal thiocyanates or the corresponding perchlorates to the acetonitrile solution of **1a** or **b**, the emission intensity of **1** was changed. The emission and absorption wavelengths and absorption intensity were not changed. The results are summarised in Table 1. In the presence of calcium or barium thiocyanate, emission of **1** at 487 nm was dramatically quenched, whereas sodium or potassium thiocyanate brought about no significant change in the emission intensity of **1**. Such a quenching was not observed with the corresponding perchlorates.‡ These results indicate the possibility that the emission quenching takes place with the recognition of calcium or barium cation and the thiocyanate anion. When a sodium thiocyanate (source of the thiocyanate anion) solution was added to a solution of **1a** and barium perchlorate (source of the barium cation), the emission intensity at 487 nm was pronouncedly decreased, compared to that of the solution without the barium cation present (Fig. 1). These results show that the emission quenching of compound **1** needs the alkaline earth metal cation AND the thiocyanate anion.

The Benesi–Hildebrand plots of **1** with calcium or barium thiocyanate should support a 1:1 complex. The association constants (log *K*) calculated from the plots are summarized in Table 2.§[12,13] While the binding of the sodium or potassium cation to the crown ethers of **1a** and **b** is naturally anticipated, the log *K* value of compound **1** with sodium or potassium salt cannot be calculated by this method as sodium and potassium thiocyanates have only a little quenching effect.

Moreover, this quenching was not observed with a solution of methyl 7-(2,3-dicyanopyrido[1′,2′:1,2]imidazo[4,5-*b*]-



1a *n* = 1
b *n* = 2

Table 1 Fluorescence intensity change $(F_0 - F)/F_0$ by the addition of salt[a]

	Thiocyanate				Perchlorate		
	Na^+	K^+	Ca^{2+}	Ba^{2+}	Na^+	K^+	Ca^+
1a	0.08	0.10	**0.84**	**0.81**	0.02	0.03	−0.08
1b	0.17	0.18	**0.88**	**0.87**	−0.06	−0.02	−0.07
PIP–CO_2Me[b]	0.01	0.00	0.10	0.11	0.01	0.08	0.02

[a] [**1**] = 2 × 10^{-5} mol dm^{-3} in acetonitrile at 25 °C. F_0 stands for fluorescence intensity without salt, F for fluorescence intensity with salt. [Salt] = 2 × 10^{-4} mol dm^{-3}, λ_{ex} = 290 nm, λ_{em} = 487 nm. [b] Methyl 7-(2,3-dicyanopyrido[1′,2′:1,2]imidazo[4,5-*b*]pyrazine)carboxylate.

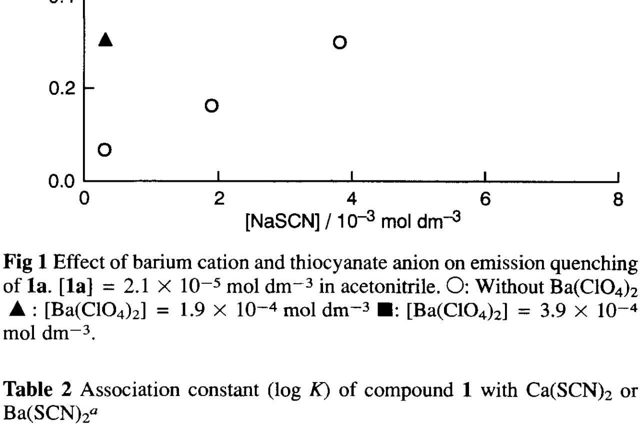


Fig 1 Effect of barium cation and thiocyanate anion on emission quenching of **1a**. [**1a**] = 2.1 × 10^{-5} mol dm^{-3} in acetonitrile. ○: Without $Ba(ClO_4)_2$ ▲: $[Ba(ClO_4)_2]$ = 1.9 × 10^{-4} mol dm^{-3} ■: $[Ba(ClO_4)_2]$ = 3.9 × 10^{-4} mol dm^{-3}.

Table 2 Association constant (log *K*) of compound **1** with $Ca(SCN)_2$ or $Ba(SCN)_2$[a]

	$Ca(SCN)_2$	$Ba(SCN)_2$
1a	4.47	3.98
1b	4.72	4.32

[a] In acetonitrile at 25 °C. Determined from a Benesi-Hildebrand equation. [**1**] = 2 × 10^{-5} mol dm^{-3}, λ_{ex} = 290 nm, λ_{em} = 487 nm.

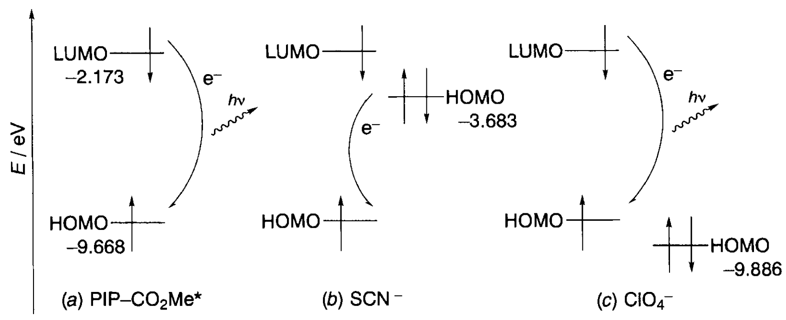


Fig. 2 PM3 calculations

pyrazine) carboxylate (PIP-CO$_2$Me) and calcium thiocyanate. This shows that crown ether receptor sites attached to PIP are required for emission quenching. According to the Benesi–Hildebrand plots, the receptor of compound **1** and calcium or barium thiocyanates form 1 : 1 complexes and the thiocyanate anion brings about the emission quenching. It should be noted that the alkaline metal cations trapped by the receptor of **1** could not control the counter anions because of their lower positive charge than the alkaline earth metal cations.

Quenching observed with the thiocyanate anion and not with the perchlorate anion is explained by the photoinduced electron transfer (PET) from the thiocyanate anion to the PIP ring.[1,3,14,15] Energy levels of the frontier orbitals of PIP–CO$_2$Me, thiocyanate anion and the perchlorate anion by PM3 calculations are illustrated in Fig. 2:[¶][16] (*a*) the photo-excited PIP–CO$_2$Me; which shows an original fluorescence, (*b*) with the thiocyanate anion an electron transfer occurs from the anion to the HOMO of the PIP ring, and (*c*) with the perchlorate anion an electron transfer cannot occur because the HOMO level of perchlorate anion is lower than the HOMO level of PIP–CO$_2$Me.

In conclusion, the crown ether-armed PIP hosts were found to function as AND logic gates having fluorescence quenching output. A distinguishing trait of these PIP hosts is the presence of only one receptor site, the armed crown ether, which is able consequently to recognise two input signals, the alkaline earth metal cations and the thiocyanate anion. It may be possible to design more sophisticated logic hosts by the selection of receptor sites.

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Footnotes

[†] Spectroscopic and physical data for **1a**: yellow powder, mp 194.0–197.0 °C (ethyl acetate); IR(KBr) ν/cm^{-1} 2220 (C≡N), 1725 (C=O) and 1140 (C–O); ^{1}H NMR (CDCl$_3$) δ 8.94 (1 H, d, *J* = 7.2 Hz, 9-H), 8.74 (1 H, s, 6-H), 7.87 (1 H, d, *J* = 7.2 Hz, 8-H), 4.60 (1 H, dd, *J* = 11.9, 5.4 Hz, CO$_2$CH$_2$), 4.46 (1 H, dd, *J* = 11.9, 5.4 Hz, CO$_2$CH$_2$), 4.22 (1 H, m, CH) and 3.65–3.90 (14 H, m, OCH$_2$); UV(acetonitrile) λ_{max}/nm 418 (ε = 7200), 352 (5200), 340 (5900), 289 (37000) and 249 (15000); emission (acetonitrile; λ_{ex} = 290 nm) λ_F = 487 nm, φ (ethanol) = 0.22, φ (acetonitrile) = 0.39 [$\phi_{standard}$ (fluorescein; ethanol) = 0.97].

For **1b**: viscous yellow oil; IR(neat) ν/cm^{-1} 2220 (C≡N), 1730 (C=O) and 1150 (C–O); ^{1}H NMR (CDCl$_3$) δ 8.95 (1 H, d, *J* = 7.1 Hz, 9-H), 8.64 (1 H, s, 6-H), 7.86 (1 H, d, *J* = 7.1 Hz, 8-H), 4.67 (1 H, dd, *J* = 12.0, 5.3 Hz, CO$_2$CH$_2$), 4.48 (1 H, dd, *J* = 12.0, 5.3 Hz, CO$_2$CH$_2$), 4.15 (1 H, m, CH) and 3.60–3.90 (18 H, m, OCH$_2$); UV(acetonitrile) λ_{max}/nm 418 (ε = 6000), 352 (5800), 338 (7200), 289 (33000) and 247 (18200) nm; emission (acetonitrile; λ_{ex} = 290 nm) λ_F = 487 nm, φ (acetonitrile) = 0.31 [$\phi_{standard}$ (fluorescein; ethanol) = 0.97]. MS(CI) *m*/*z* = 497.1 (M + 1) (calcd for $C_{23}H_{24}N_6O_7M^+$ 496.17).

[‡] No quenching was also observed with other calcium salts such as calcium nitrate, calcium iodide and calcium acetate.

[§] The determined association constants (log *K*) refer to the overall log $K_1 K_2 K_3$.

$$\mathrm{Met(SCN)_2} \xrightleftharpoons{K_1} \mathrm{Met^{2+}} + 2\mathrm{SCN^-}\ (1),\quad \mathrm{Host} + \mathrm{Met^{2+}} \xrightleftharpoons{K_2} \mathrm{Host{\cdot}Met^{2+}}\ (2),\quad \mathrm{Host{\cdot}Met^{2+}} + 2\mathrm{SCN^-} \xrightleftharpoons{K_3} \mathrm{Host{\cdot}Met(SCN)_2}\ (3).\quad (\mathrm{Met} = \mathrm{Ca\ or\ Ba}).$$

[¶] The calculation was carried out by CAChe MOPAC Ver.3.5.1.

References

1 R. A. Bissell, A. P. de Silva, H. Q. N. Gunaratne, P. L. M. Lynch, G. E. M. Maguire, C. P. McCoy and K. R. A. S. Sandanayake, *Top. Curr. Chem.*, 1993, **168**, 223.
2 A. P. de Silva, S. A. de Silva, A. S. Dissanayake and K. R. A. S. Sandanayake, *J. Chem. Soc., Chem. Commun.*, 1989, 1056.
3 T. D. James, K. R. A. S. Sandanayake and S. Shinkai, *J. Chem. Soc., Chem. Commun.*, 1994, 477.
4 M. W. Hosseini, A. J. Blacker and J.-M. Lehn, *J. Am. Chem. Soc.*, 1990, **112**, 3896.
5 M. E. Huston, E. U. Akkaya and A. W. Czarnik, *J. Am. Chem. Soc.*, 1989, **111**, 8735.
6 A. W. Czarnik, *Acc. Chem. Res.*, 1994, **27**, 302.
7 A. P. de Silva, H. Q. N. Gunaratne and C. P. N. McCoy, *Nature*, 1993, **364**, 42.
8 A. P. de Silva, H. Q. N. Gunaratne and G. E. M. Maguire, *J. Chem. Soc., Chem. Commun.*, 1994, 1213.
9 A. Katoh, S. Ueda, J. Ohkanda, M. Hirota, H. Komine and K. Mitsuhashi, *Heterocycles*, 1992, **34**, 1965.
10 K. Mitsuhashi, Y. Nagae and T. Suzuki, *J. Heterocycl. Chem.*, 1986, **23**, 1741.
11 T. Suzuki, Y. Nagae and K. Mitsuhashi, *J. Heterocycl. Chem.*, 1986, **23**, 1419.
12 H. Benesi and J. H. Hildebrand, *J. Am. Chem. Soc.*, 1949, **71**, 2703.
13 M. Takeshita and S. Shinkai, *Chem. Lett.*, 1994, 125.
14 H. Shizuka, M. Nakamura and T. Morita, *J. Phys. Chem.*, 1980, **84**, 989.
15 R. S. Sarpal and S. K. Doyra, *Indian J. Chem.*, 1994, **33A**, 111.
16 J. P. Stewart, *QCPE Bull.*, 1989, **9**, 10.