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A highly selective 'off–on' fluorescence chemosensor for Cr(III)

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Abstract—An 'off–on' fluorescence chemosensor for the selective signalling of Cr(III) has been designed exploiting the guest-induced inhibition of the photoinduced electron transfer signalling mechanism. The system shows an approximately 17-fold Cr(III)-selective chelation-enhanced fluorescence response in tetrahydrofuran and the system is highly selective against the background of environmentally and biologically relevant metal ions.

Trivalent chromium, Cr(III), is an essential component of a balanced human and animal diet. The trivalent form of chromium is an essential nutrient for humans, in amounts of 50–200 μg per day (WHO 1988) and its deficiency causes disturbances in the glucose levels and lipid metabolism. On the other hand, chromium is an environmental pollutant and its build-up due to various industrial and agricultural activities is a matter of concern.[1] Thus, there is an urgent need to develop chemical sensors[2,3] that are capable of detecting the presence of chromium ions in biological and environmental samples. While the detection of Cr(III) employing electrochemical[4] and potentiometric[5] techniques has been reported recently, selective detection of Cr(III) by fluorimetric methods,[6] which are known for their simplicity, high sensitivity and instantaneous response, has so far not been possible primarily due to two reasons. Firstly, paramagnetic Cr(III) is described as one of the most efficient fluorescence quenchers among the transition metal ions and secondly, the lack of a selective ligand system for Cr(III). In the past few years, considerable efforts have been directed towards the development of fluorescence chemosensors for the detection of paramagnetic metal ions using different design strategies,[7–18] but selective detection has been achieved only on a few occasions.[19–26] Among the first row transition metal ions, Zn(II) stands out because of its completely filled d-orbitals and thus several systems have been reported for the selective detection of Zn(II) ions.[19–21]

The selective detection of Cu(II), which occupies the highest position in the Irving–Williams series, has also been possible because of its strong complexation properties among its relatives.[22–26] It is important to note that molecular recognition can result from selective binding or selective response, but in the latter case, interfering substances will competitively inhibit the optical response to the desired analyte. Unfortunately, most of the systems are guest selective rather than guest specific because metal ions of the same family show quite similar binding properties.

In the search for efficient and selective receptor moieties, we came across the SNS (di(2-ethylsulfanylethyl)amine) ligand[27] that forms a strong complex with Cr(III).[28] We thought that the selective detection of Cr(III) might be possible by integrating the SNS ligand with a suitable fluorophore. An electron donor–acceptor system employing the SNS ligand has been developed previously.[29] However, since the central nitrogen atom of the ligand in this fluoroionophore is in conjugation with a nitro group, the electron density available at this nitrogen atom for coordination with the metal ions is significantly reduced and this leads to a change of the binding properties of the ligand.[29] Having recognized this problem, we designed **APCr** (Scheme 1)[30] in which the mixed soft and hard donor ligand, SNS, represented in the scheme as L, was employed as a guest-binding unit in such a way that the electron density of the central nitrogen atom of the ligand system was available for binding with the metal ions.

Keywords: 4-Aminophthalimide; Fluorescence chemosensor; Fluorophore-spacer-receptor system; Metal ions induced fluorescence enhancement.
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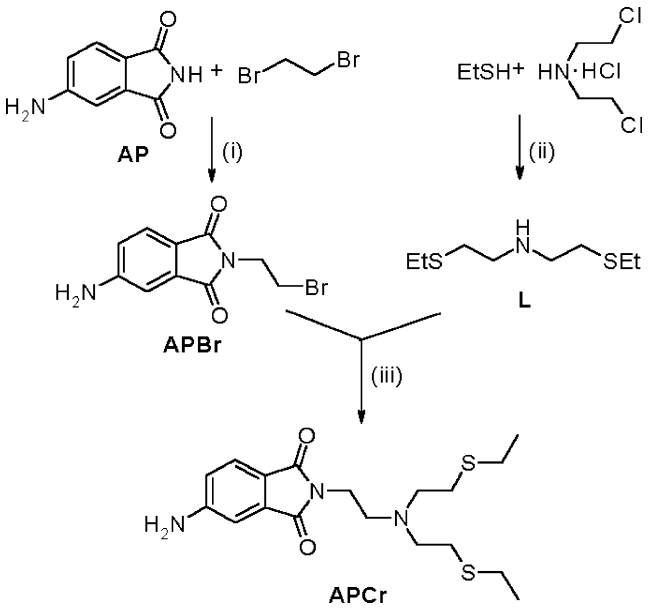

Scheme 1. Synthetic route to the fluorescence chemosensor **APCr**. Conditions: (i) NaH, DMF, room temperature, 24 h; (ii) Na, ethanol, reflux, 2 h; (iii) Na_2CO_3, KI, acetonitrile, reflux, 48 h.

APCr was synthesized in three steps (Scheme 1): the first two steps consisted of the preparation of 5-amino-2-(2-bromoethyl)-1,3-isoindolinedione (**APBr**) and SNS by following the standard procedures.[13,27] In the third step, **APBr** (0.74 mM) was added to 50 mL of dry acetonitrile in a 100-mL three-necked round-bottom flask and to this was added SNS (0.7 mM), potassium carbonate (1 mM) and a catalytic amount of KI. The mixture was allowed to reflux under a nitrogen atmosphere for 48 h with constant stirring. The removal of the solvent yielded a solid residue, which was extracted with chloroform (4×40 mL). The chloroform extract was dried over anhydrous Na_2SO_4 and evaporated to obtain a pale yellow solid that was purified by column chromatography (neutral alumina, 40:60 EtOAc/hexane).

As can be seen, in our fluoroionophore, we chose 4-aminophthalimide (**AP**) as the fluorescing moiety because of its high molar absorption coefficient, high fluorescence quantum yield and long fluorescence lifetime.[31] Another factor that influenced our choice in favour of this fluorophore was its electron-deficient nature, which is an essential criterion for 'off–on' fluorescence signalling systems for quenching metal ions.[8,13–15] The fluorophore and the guest binding units were covalently integrated to modulate the photophysical responses of the dye by introducing a possible excited-state electron transfer process between the two. This system shows selective chelation enhanced fluorescence (CHEF) in the presence of Cr(III). The Cr(III)-induced 'off–on' signalling would be observed even in a sample containing as many as 12 different metal ions including environmentally and biologically relevant alkali and alkaline earth, transition and post-transition metal ions. This study, however, was carried out in tetrahydrofuran due to the fact that complexation of the SNS ligand with Cr(III) was reported in this solvent.[28]

The optical absorption and fluorescence spectra of **APCr** were characterized by structureless bands centred at 366 nm and 455 nm, respectively, assigned to the intramolecular charge transfer (ICT) state of the fluorophore moiety. The fluorescence quantum yield of **APCr** in THF was measured to be 0.026, which is 96% lower than that of the unsubstituted fluorophore (φ_f (AP) = 0.70)[31] in the same solvent indicating photoinduced electron transfer (PET) between the fluorophore and receptor moieties. The PET in this system may appear unexpected when the influence of the internal electric (dipolar) field on the PET process, as demonstrated by de Silva and co-workers,[32] is taken into account. However, we have previously demonstrated in several aminophthalimide and aminonaphthalimide derivatives that through-space PET is not hampered by the electric dipole of the AP moiety.[8,13,33,34] A multiexponential fluorescence decay behaviour (see Supplementary data) was observed for the system yielding the following decay parameters: $\tau_1 = 0.17$ ns (64%), $\tau_2 = 0.9$ ns (23%) and $\tau_3 = 15$ ns (13%). The complex nature of the fluorescence decay behaviour is a reflection of the flexibility of the molecule, which can exist in several conformations. Two limiting situations can be considered here. One in which the spatial disposition of the fluorophore and receptor moieties is favourable for PET, which can give rise to 0.17 ns and 0.9 ns components, which are much shorter than the fluorescence lifetime of AP (12.4 ns in THF).[31] The other limiting situation in which the spatial arrangement of the receptor and fluorophore moieties is unfavourable for PET can contribute to the 15 ns component. The time-resolved data suggest that nearly 87% of the molecules are in PET communication with the receptor moiety.

We have examined the effects of various metal ion additives on the spectral features of **APCr**. It was observed that among the metal ions studied, only Cr(III) significantly modulated the absorption and fluorescence spectra of **APCr**. The progressive addition of Cr(III) to a solution of **APCr** led to a gradual bathochromic shift of the absorption maximum with a slight increase in absorption (Fig. 1). The presence of an isosbestic point

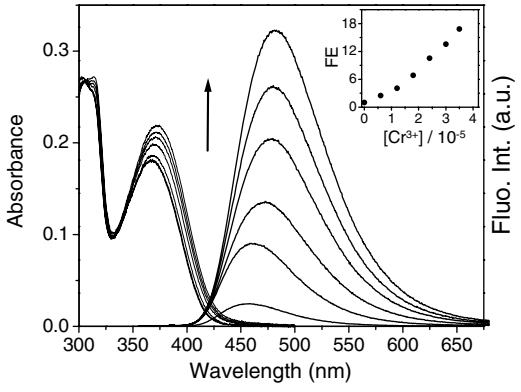

Figure 1. Absorption and fluorescence spectra of **APCr** in THF upon progressive addition of Cr(III). [**APCr**] = 1.7×10^{-5} M, [Cr^{3+}] = 0–3.5×10^{-5} M. Inset: fluorescence enhancement versus concentration of Cr(III).

in the absorption spectra at around 345 nm indicated that the optical response arises from the formation of a 1:1 complex between **APCr** and Cr(III).

The coordination of **APCr** to Cr(III) caused a 27 nm Stokes shift of the emission band and an approximately 17 fold increase in the fluorescence quantum yield (Table 1). The Stokes shift of the fluorescence maximum of **APCr** is due to an enhanced separation of charge in the electron donor–acceptor fluorophore, **AP** on complexation. The Stokes shift is indicative of the possible involvement of the carbonyl groups of the fluorophore in coordination and is consistent with the literature.[8] While Stokes shifted emission with only an approximately 4-fold increase in the quantum yield can be observed in the presence of Fe(III), all the other environmentally and biologically relevant metal ions did not show any significant response (Fig. 2). The enhancement of fluorescence is attributed to the disruption of PET communication between the receptor and the fluorophore moieties due to the introduction of metal ions into the coordination sphere of SNS. Late first-row transition metal ions such as Ni(II) and Cu(II) form strong complexes with nitrogen donor ligands and in some cases with sulfur donor ligands. However, in the present case, an effective binding occurred only with Cr(III) and Fe(III). The binding constant values (Table 1) evaluated from the absorption titration data assuming a 1:1 stoichiometry (see Supplementary data) indicate that **APCr** forms a strong complex with Cr(III) in solution. This is consistent with the literature that the SNS ligand forms a stable complex with Cr(III), which can be used as a catalyst.[28] We also studied the effect of Cr(III) on the fluorescence decay behaviour of the chemosensor. In the presence of Cr(III), the sub-nanosecond component of the decay disappears completely (see Supplementary data) confirming the inhibition of the PET quenching pathway upon Cr(III) binding. The decay profile in the presence of Cr(III) can be roughly fitted to a mono-exponential model yielding a lifetime of 10.8 ns.

Table 1. Maximum fluorescence enhancement (FE) observed and the binding constant values for selected metal ions with **APCr**[a]

Metal ion	FE	$K/10^4$ M^{-1}
None	1.0	—
Cr(III)	16.8	11.3
Mn(II)	1.3	—
Fe(III)	4.3	8.0
Co(II)	1.5	—
Ni(II)	1.2	—
Cu(II)	1.6	—
Zn(II)	1.5	—
Hg(II)	1.0	—
Pb(II)	1.4	—
H^+	5.1	—

[a] $\lambda_{exc} = 345$ nm; K values, estimated from the absorption spectral data, can be evaluated accurately only for Cr(III) and Fe(III). These values could not be estimated for the other metal ions because of the small change in the absorption behaviour.

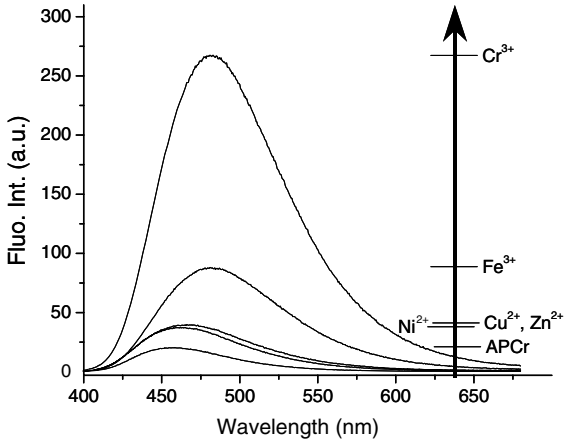

Figure 2. Fluorescence spectra of APCr (1.8×10^{-5} M) in the absence and presence of selected metal ions in THF. In the presence of other remaining metal ions, the spectrum overlaps either with that of the free sensor or with that of Ni(II), Cu(II) or Zn(II). The metal ion concentrations required for the observance of maximum fluorescence enhancement are in the range of $3.5–5 \times 10^{-5}$ M. $\lambda_{exc} = 345$ nm.

The selectivity of **APCr** for Cr(III) over alkali and alkaline earth metal ions, other transition and post-transition metal ions was further investigated and the results are depicted in Figure 3. The 'off–on' signalling of **APCr** for Cr(III) was not affected in the presence of excess alkali and alkaline earth metal ions such as Na(I), K(I), Mg(II) and Ca(II). The chemosensor was also selective for Cr(III) over the divalent first-row transition metal ions and post-transition metal Cd(II), Hg(II) and Pb(II) ions. However, for reasons not clear to us at the moment, Cr(III) could not displace Fe(III) from the coordination sphere of **APCr**. Thus, we have tested the Cr(III) selectivity by analyzing a sample containing all the metal ions except Fe(III). The introduction of

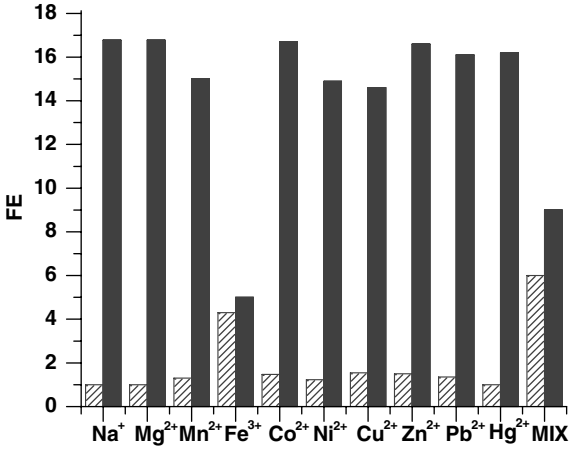

Figure 3. A bar diagram highlighting the fluorescence 'off–on' signalling response of **APCr** to Cr(III) in the presence of selected metal ions and in the presence of all the 12 metal ions (**MIX**). The patterned bars represent enhancement of fluorescence upon addition of 2 equiv of individual metal ions and the solid bars represent the fluorescence enhancement that occurs upon the introduction of 2 equiv of Cr(III) to the solutions containing **APCr** and the selected metal ion. $\lambda_{exc} = 345$ nm.

2 equiv of Cr(III) to a solution of **APCr** containing 2 equiv each of Na(I), K(I), Mg(II), Ca(II), Mn(II), Co(II), Ni(II), Cu(II), Zn(II), Cd(II), Hg(II) and Pb(II) produced a 50% increase in the fluorescence yield.

In summary, we developed an 'off–on' fluorescence chemosensor for the selective detection of Cr(III) exploiting the selective binding ability of the SNS ligand. An approximately 17-fold Cr(III)-selective chelation enhanced fluorescence response in THF was attributed to the disruption of PET communication between the receptor and the fluorophore moieties. It was demonstrated that this system in THF was highly selective over other environmentally and biologically relevant metal ions such as alkali and alkaline earth metal ions, divalent first-row transition metal ions, Group 12 metal ions and Pb(II). However, it is important to note that since the present study was carried out in THF, the findings in aqueous media could be very different from those reported here, so it may not be possible to exploit the Cr(III) selective signalling ability of the present system in practical applications except in films or organogels. Studies are in progress to explore the fluorescence signalling ability of the present system in other solvents.

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Supplementary data

The supplementary material associated with this article includes the fluorescence decay behaviour of **APCr** in the absence and presence of Cr(III), absorption and fluorescence titration plots with some other metal ions, and binding constant evaluation plots are available in the online version, at doi:10.1016/j.tetlet.2006.08.091.

References and notes

1. Zayed, M.; Norman, T. *Plant Soil* **2003**, *249*, 139.
2. *Chemosensors of Ions and Molecular Recognition*; Desvergene, J. P., Czarnik, A. W., Eds.; NATO ASI Series; Kluwer Academic: Dordrecht, 1997; p C492.
3. Spichiger-Keller, U. S. *Chemical Sensors and Biosensors for Medical and Biological Applications*; Wiley-VCH, 1998.
4. Singh, A. K.; Singh, R.; Saxena, P. *Sensors* **2004**, *4*, 187.
5. Hassan, S. S. M.; El-Shahawi, M. S.; Othman, A. M.; Mosaad, M. A. *Anal. Sci.* **2005**, *21*, 673.
6. (a) de Silva, A. P.; Gunaratne, H. Q. N.; Gunnlaugsson, T.; Huxley, A. J. M.; McCoy, C. P.; Rademacher, J. T.; Rice, T. E. *Chem. Rev.* **1997**, *97*, 1515; (b) Leyu, W.; Lun, W.; Tingtong, X.; Ling, D.; Guinorg, B.; Hongki, C. *Anal. Sci.* **2004**, *20*, 1013.
7. Ghosh, P.; Bharadwaj, P. K.; Mandal, S.; Ghosh, S. *J. Am. Chem. Soc.* **1996**, *118*, 1553.
8. Ramachandram, B.; Samanta, A. *Chem. Commun.* **1997**, 1037.
9. Rurack, K.; Kollmannsberger, M.; Resch-Genger, U.; Daub, J. *J. Am. Chem. Soc.* **2000**, *122*, 968.
10. Prodi, L.; Bolletta, F.; Montalti, M.; Zaccheroni, N. *Coord. Chem. Rev.* **2000**, *205*, 59.
11. Rurack, K. *Spectrochim. Acta, Part A.* **2001**, *57*, 2161.
12. Sankaran, N. B.; Banthia, S.; Das, A.; Samanta, A. *New J. Chem.* **2002**, *26*, 1529.
13. Banthia, S.; Samanta, A. *J. Phys. Chem. B* **2002**, *106*, 5572.
14. Sankaran, N. B.; Banthia, S.; Samanta, A. *Proc. Indian Acad. Sci.: Chem. Sci.* **2003**, *114*, 539.
15. Banthia, S.; Samanta, A. *Org. Biomol. Chem.* **2005**, *3*, 1428.
16. Banthia, S.; Sarkar, M.; Samanta, A. *Res. Chem. Intermed.* **2005**, *31*, 25.
17. Royzen, M.; Dai, Z.; Canary, W. J. *J. Am. Chem. Soc.* **2005**, *127*, 1612.
18. Banthia, S.; Samanta, A. *J. Phys. Chem. B* **2006**, *110*, 6437.
19. Hirano, T.; Kikuchi, K.; Urano, Y.; Higuchi, T.; Nagano, T. *Angew. Chem., Int. Ed.* **2000**, *39*, 1052.
20. Burdette, S. C.; Frederickson, C. J.; Bu, W.; Lippard, S. J. *J. Am. Chem. Soc.* **2003**, *125*, 1778.
21. Banthia, S.; Samanta, A. *Eur. J. Org. Chem.* **2005**, 4967.
22. Boiocchi, M.; Fabbrizzi, L.; Licchelli, M.; Sacchi, D.; Vasquez, M.; Zampa, C. *Chem. Commun.* **2003**, 1812.
23. Gunnlaugsson, T.; Leonard, J. P.; Murray, N. S. *Org. Lett.* **2004**, *6*, 1557.
24. Banthia, S.; Samanta, A. *New J. Chem.* **2005**, *29*, 1007.
25. Kaur, S.; Kumar, S. *Chem. Commun.* **2002**, 2840.
26. Wen, Z.-C.; Yang, R.; He, H.; Jiang, Y.-B. *Chem. Commun.* **2006**, 106.
27. Tanaka, M.; Nakamura, M.; Ikeda, T.; Ikeda, K.; Ando, H.; Shibutani, Y.; Yajima, S.; Kimura, K. *J. Org. Chem.* **2001**, *66*, 7008.
28. McGuinness, D. S.; Wasserscheid, P.; Keim, W.; Morgan, D.; Dixon, J. T.; Bollmann, A.; Maumela, H.; Hess, F.; Englert, U. *J. Am. Chem. Soc.* **2003**, *125*, 5272.
29. Sakamoto, H.; Ishikawa, J.; Nakao, S.; Wada, H. *Chem. Commun.* **2000**, 2395.
30. Yield 40%. CHN analysis calculated for $C_{18}H_{27}N_3O_2S_2$: C, 56.66; H, 7.13; N, 11.01. Found: C, 56.38; H, 7.46; N, 10.68. LC–MS *m*/*z* (%): 382 (100) $[M+1]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 1.20 (t, $J = 7.4$ Hz, 6H), 2.49–2.61 (m, 8H), 2.72–2.85 (m, 6H), 3.68 (t, $J = 5.3$ Hz, 2H), 4.41 (s, 2H), 6.80 (d, $J = 8.0$ Hz, 1H), 7.01 (s, 1H), 7.59 (d, $J = 8.1$ Hz, 1H).
31. Soujanya, T.; Fessenden, R. W.; Samanta, A. *J. Phys. Chem.* **1996**, *100*, 3507.
32. de Silva, A. P.; Gunaratne, H. Q. N.; Habib-Jiwan, J. L.; McCoy, C. P.; Rice, T. E.; Soumillion, J. P. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1728.
33. Sankaran, N. B.; Mandal, P. K.; Bhattacharya, B.; Samanta, A. *J. Mater. Chem.* **2005**, *15*, 2854.
34. Ramachandram, B.; Saroja, G.; Sankaran, N. B.; Samanta, A. *J. Phys. Chem. B* **2000**, *104*, 11824.