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A new fluorescent PET chemosensor for fluoride ions†

Sook Kyung Kim[b] and Juyoung Yoon*[ab]

[a] *Nano Applied Technology Research Center, Silla University, Pusan 617-736, Korea. E-mail: jyoon@silla.ac.kr; Fax: +82-51-309-5176; Tel: +82-51-309-5618*

[b] *Department of Chemistry, Silla University, Pusan 617-736, Korea*

Received (in Cambridge, UK) 6th November 2001, Accepted 27th February 2002
First published as an Advance Article on the web 12th March 2002

A new anthracene derivative bearing two phenylurea group at the 1,8-position of anthracene shows a selective fluorescence quenching effect with fluoride ion *via* a PET mechanism.

With the aid of supramolecular chemistry, recognizing and sensing of anionic analytes has recently emerged as a key research field.[1] Considering that NMR titrations as an anion-detecting method have been used in many cases, recent efforts by Anslyn,[2] Sessler[3] and Yamaguchi[4] in detecting anion binding by the naked eye may provide important results. On the other hand, fluorescence is another important detection method due to its simplicity and high detection limit. Even though considerable effort has been devoted to developing fluorescent chemosensors for cations and neutral guests recently,[5] there have been only a few reports regarding anion selective receptors using the fluorescent changes as the means of detection.

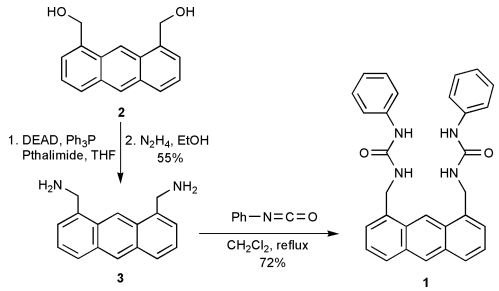
In particular, Czarnik *et al*. utilized anthrylpolyamines as PET sensors for phosphate and pyrophosphate in a 100% aqueous solution.[6] Teramae *et al*. recently reported a pyrene derivative bearing a thiourea group as a new fluorescent chemosensor for acetate anions.[7] In addition, Anslyn *et al*. reported a new chemosensor with selectivity for inositol triphosphate.[8] In this study, 5-carboxyfluorescein was used in a competitive binding assay. Recently, Fabbrizzi *et al*. utilized the dizinc(II) complex of the bistren cage to detect N_3^- *via* a fluorescent emission quenching effect.[9] On the other hand, Beer reported a new class of anion receptors utilizing tris(2,2′-bipyridyl)ruthenium(II) complexes.[10]

Fluoride ions are biologically important anions because of their important role in dental care[11] and the treatment of osteoporosis,[12] *etc*. Even though some receptor compounds for fluoride ions have been reported,[3a,b,13] there is a paucity of reports regarding a selective fluorescent PET sensor for fluoride ions. Noteworthy were papers by Sessler *et al*. reporting calixpyrrole derivatives as new fluorescent chemosensors for anions.[14] In the best case, the affinity constant for fluoride was reported as being greater than 10^6 M^{-1} in acetonitrile (0.01% v/v water). On the other hand, James *et al*. utilized boronic acids as fluorescent PET sensors, which show fluoride selective fluorescent quenching effects in aqueous solution at pH 5.5.[15]

Here, we report a new fluorescent chemosensor for fluoride ions. Since the PET process was used as a sensing mechanism, an emission change of up to 20-fold was observed. Furthermore, the selectivity for fluoride ions was almost 120 times higher when compared to chloride ions. The association constant (K_a = 71 270 M^{-1}) observed for fluoride ions must be quite high considering that a polar organic solvent such as acetonitrile–DMSO (9:1, v/v) was used.

Our synthesis began with 1,8-anthracenedimethanol **2**. Following the published procedures,[16] 1,8-anthracenedimethanamine **3** was obtained in a 53% yield. Treating this diamino anthracene **3** with phenyl isocyanate in CH_2Cl_2 gave bisurea anthracene **1**‡ in 72% yield (Scheme 1).

Because of the low solubility of this bisurea compound **1** in $CDCl_3$, the NMR data was obtained in DMSO-d_6. A partial ^1H NMR spectrum is shown in Fig. 1, and each peak was assigned based on the COSY spectrum of **1**. Upon the addition of chloride ions, downfield shifts of the NH protons were clearly observed. With bromide and iodide ions, there were no chemical shift changes for the NH peaks even when up to 6 eq. of these anions were used. Upon the addition of fluoride ions, these NH peaks disappeared. Because of the higher melting point of the solvent, low temperature experiments could not be performed. In addition, lowering the concentration of compound **1** did not solve this.



Scheme 1 Synthesis of 1,8-bisurea anthracene **1**.

In this study, a fluorescence method instead of NMR made it easily possible to follow the binding of **1** with fluoride ions. As shown in Fig. 2, and explained in Scheme 2, compound **1** (6 μM) displays a selective fluorescent quenching effect only with fluoride ions, even though compound **1** also displayed relatively small CHEQ (chelation enhanced quenching) effects with chloride and bromide ions. All of the fluorescence experiments

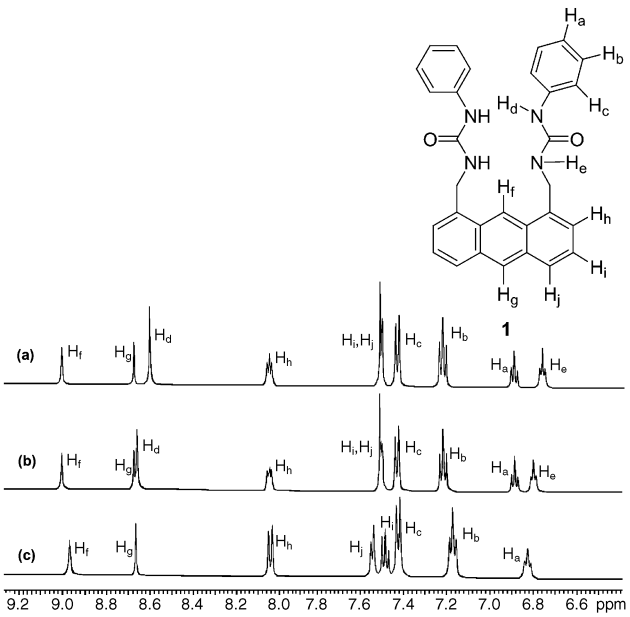


Fig. 1 Partial ^1H NMR (500 MHz) spectra of compound **1** (1 mM) in DMSO-d_6. (a) compound **1** only; (b) **1** + 2 eq. of tetraethylammonium chloride; (c) **1** + 2 eq. of tetraethylammonium fluoride.

† Dedicated to the memory of D. J. Cram.

DOI: 10.1039/b110139k

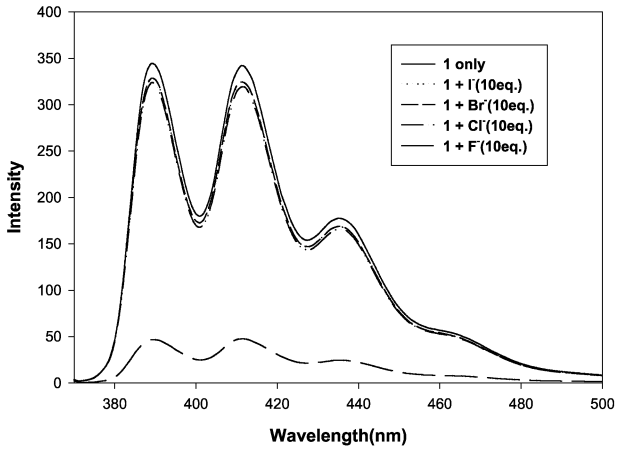
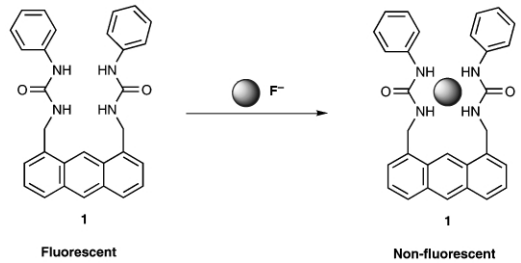


Fig. 2 Fluorescent emission changes of **1** upon the addition of tetraethylammonium fluoride, bromide, chloride and iodide in acetonitrile–DMSO (9 : 1, v/v).



Scheme 2 Proposed PET mechanism of **1** with fluoride ion.

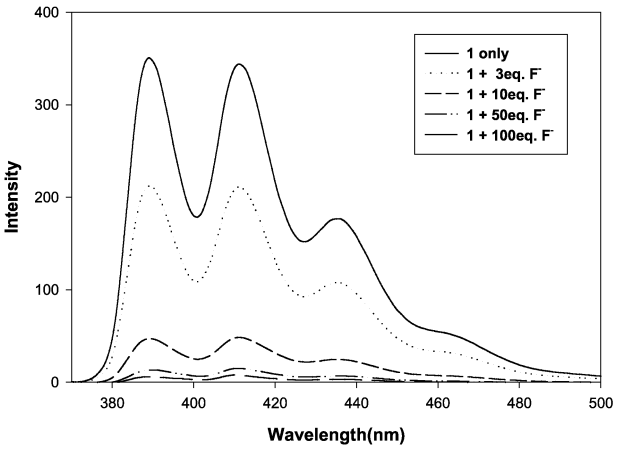


Fig. 3 Fluorescent titrations of compound **1** (6 μM) with tetraethylammonium fluoride in acetonitrile–DMSO (9 : 1, v/v).

were done in an acetonitrile–DMSO mixture (9 : 1, v/v). Fig. 3 clearly shows the fluorescence quenching effects with increasing fluoride ion concentration. From the fluorescent titrations with fluoride, chloride, bromide and iodide ions, the association constants were calculated to be 71 270, 614, 121 and 30 M^{-1} (errors < 10%), respectively.[17] The selectivity for fluoride ions was almost 120 fold compared to that of chloride ions. Since the PET mechanism from benzylic amide to anthracene was used for communicating this binding, a fluorescent emission change of up to 20 fold was observed in the case of fluoride ions.

The emission intensities of **1** with 60 μM F^- in the presence of 600 μM of Cl^-, Br^- and I^- were the same as that using 60 μM F^- alone (±5%). To confirm that this selectivity occurs through anion binding, the association constants were recalculated in the presence of 1 mM Cl^-, Br^- and I^-, with no increase in the observed association constants (±10%) noted.

In our system, bisphenylurea groups were introduced at the 1,8-position of anthracene. The anthracene moiety acts not only as a fluorescent source but also as a template for introducing the binding selectivity.

In conclusion, bisurea anthracene **1** displays a selective fluorescent quenching effect with fluoride ion in acetonitrile–DMSO (9 : 1, v/v) *via* a PET process. The binding selectivity for fluoride ions was as high as 120 times compared to that for chloride ions and the fluorescent emission increased almost 20 fold.

This work was fully supported by a Grant (R01-2000-00047) from the Korea Science & Engineering Foundation.

Notes and references

‡ Synthesis of 1,8-bis[(phenylurea)methyl]anthracene (**1**). 1,8-anthracenedimethanamine **3** was obtained in 53% yield from 1,8-anthracenedimethanol **2** following the published procedure.[13] A solution of 1,8-anthracenedimethanamine **3** (60 mg, 0.254 mmol) and phenyl isocyanate (142 mg, 1.02 mmol) in dry CH_2Cl_2 (25 mL) was refluxed for 2 h. As soon as phenyl isocyanate was added a white precipitate was formed. After cooling down to rt, the solid was filtered and washed with $CHCl_3$ followed by ethyl acetate. Analytically pure **1** was obtained in 72% yield (87 mg): mp 180–184 °C, decomp.; ^{1}H NMR (DMSO-d_6) δ 8.98 (s, 1H), 8.65 (s, 1H), 8.59 (s, 2H), 8.02 (t, 2H, J = 5.9), 7.51–7.48 (m, 4H), 7.44 (d, 4H, J = 7.8), 7.22 (t, 4H, J = 7.8), 6.90 (t, 2H, J = 7.3), 6.78 (t, 2H, J = 5.9), 4.98 (d, 4H, J = 5.9); ^{13}C NMR (DMSO-d_6) δ 155.25, 140.36, 136.08, 131.36, 129.24, 128.78, 127.64, 125.34, 124.53, 121.30, 118.13, 117.90, 117.80, 39.83; HRMS (FAB) m/z = 475.2133 $(M + H)^+$, calc. for $C_{30}H_{27}N_4O_2$ = 475.2134.

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