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Notes

Discrimination of Primary Alkyl and Arylamines by a New Binaphthyl-Azacrown-Anthracene Fluorophore

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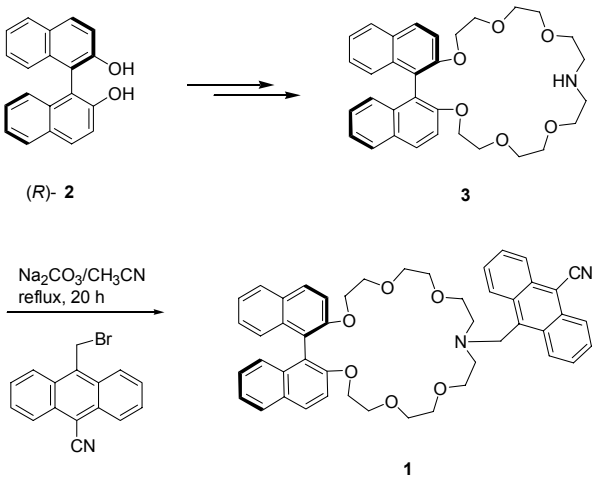
The development of highly sensitive and selective detection techniques for the discrimination of biologically toxic materials is of considerable importance in the fields of chemical, biological, and environmental sciences.[1] Primary arylamines originated from occupational sources and/or tobacco smoking are known to be carcinogenic.[2] For example, 4-aminobiphenyl, 2-naphthylamine and benzidine have been known to induce bladder cancer.[3] In this instance, the methods for the detection of primary arylamines are quite important.

Fluorescence chemosensors are quite attractive because of their high sensitivity and simplicity. Actually, fluorescence chemosensors have been successfully utilized for the selective detection of cations,[4] anions[5] or chiral molecules.[6] In this field, we have demonstrated that fluorescent receptors based on binaphthyl-azacrown-anthracene derivatives exhibit large fluorescent changes with aqueous Hg^{2+}, Cu^{2+} and Zn^{2+} and moderate selectivity for the hydrogenperchlorate salt of (*R*)-2-phenylglycinol over the (*S*)-isomer.[7] During the study for the further utilization of binaphthyl-azacrown-anthracene derivatives, we found that they can also be used to discriminate between primary alkylamines and arylamines. In this study, we report the synthesis of a new binaphthyl-azacrown-anthracene fluorophore (**1**) and its binding properties as a selective fluorescence chemosensor for primary arylamines.

A new binaphthyl-azacrown-anthracene fluorophore (**1**) was prepared starting from (*R*)-(+)-1,1'-bi-2-naphthol (**2**) as shown in Scheme 1. (*R*)-**2** was converted to binaphthyl-azacrown compound **3** *via* the known procedure.[8] And then compound **3** was treated with 9-bromomethyl-10-cyanoanthracene[9] to afford a new binaphthyl-azacrown-anthracene fluorophore (**1**).

Binding properties of compound **1** for primary alkylamines and arylamines were investigated by monitoring fluorescence changes upon the addition of primary alkylamines and arylamines as their HCl salt in ethanol. As primary alkylamine HCl salts, propylamine HCl, butylamine HCl and octylamine HCl were used. In addition, benzylamine HCl and 1-naphthylmethylamine HCl were used as primary alkylamines even though they contain aromatic groups. As primary arylamine HCl salts, aniline HCl, 1-naphthylamine HCl, 2-naphthylamine HCl and 4-biphenylamine HCl were used. The fluorescence emi-



Scheme 1. Synthesis of binaphthyl-azacrown-anthracene fluorophore (**1**).

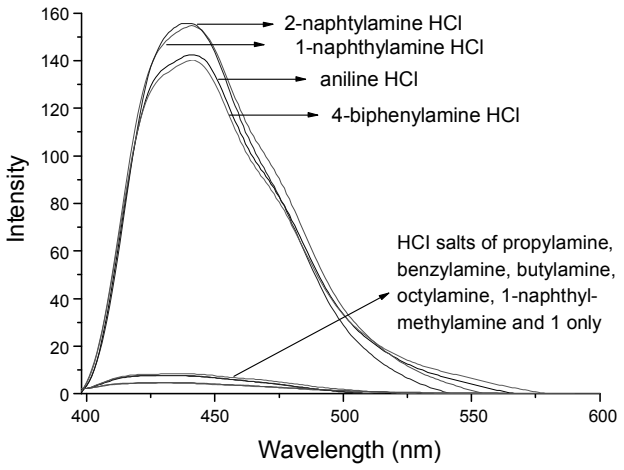


Figure 1. Fluorescent emission changes of **1** (60 μM) upon addition of various primary alkylamines and arylamines as their HCl salts (50 equiv) in ethanol (excitation at 390 nm).

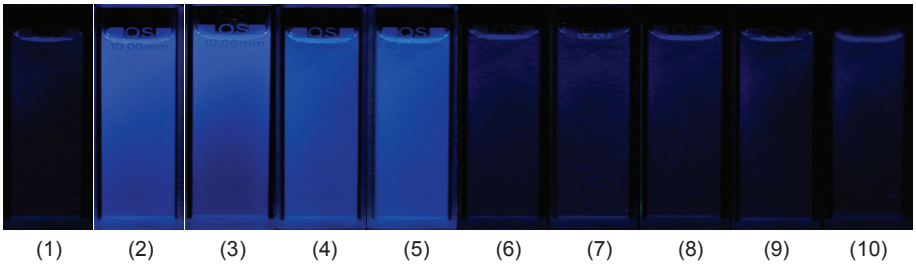


Figure 2. Visualized fluorescent emission changes of **1** (20 μM) upon addition of various primary alkylamines and arylamines as their HCl salts (100 equiv) in ethanol. (1) **1** only, (2) **1** + 2-naphthylamine HCl, (3) **1** + 1-naphthylamine HCl, (4) **1** + aniline HCl, (5) 4-biphenylamine HCl, (6) **1** + propylamine HCl, (7) **1** + benzylamine HCl, (8) **1** + butylamine HCl, (9) **1** + octylamine HCl and (10) **1** + 1-naphthylmethylamine HCl.

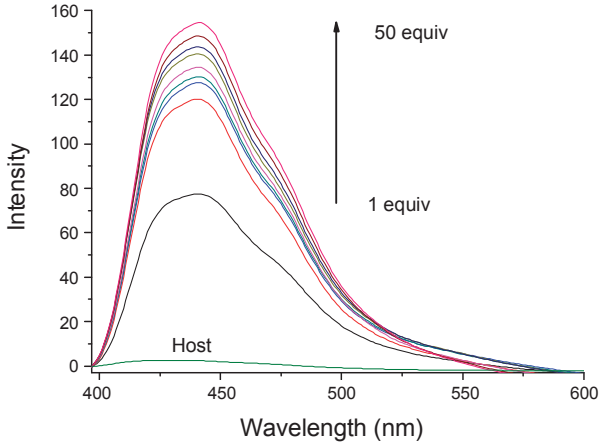


Figure 3. Fluorescent titration of **1** (60 μM) with 1-naphthylamine HCl (1 equiv ~ 50 equiv) in ethanol (excitation at 390 nm).

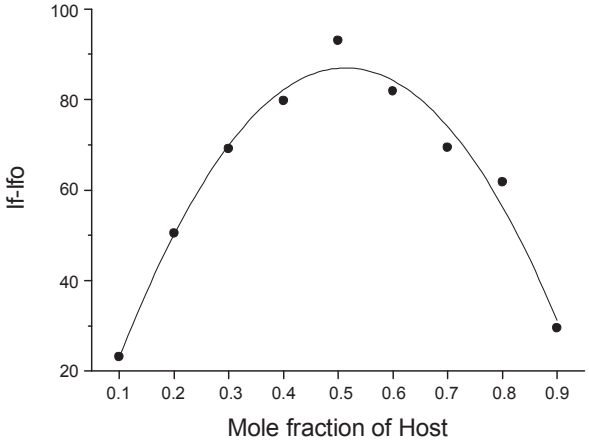


Figure 4. Job plot of a 1 : 1 complex of **1** and 1-naphthylamine HCl.

ssion changes of compound **1** upon the addition of various primary alkylamine HCl salts and arylamine HCl salts are presented in Figure 1. Compound **1** shows a pronounced fluorescence enhancement for primary arylamine HCl salts while it does not show any fluorescence enhancement for primary alkylamine HCl salts. The distinct fluorescence enhancement of compound **1** upon the addition of primary arylamine HCl salts are shown visually in Figure 2.

From the fluorescent titrations of compound **1** upon the addition of each of arylamine HCl salts (for example, see Figure 3

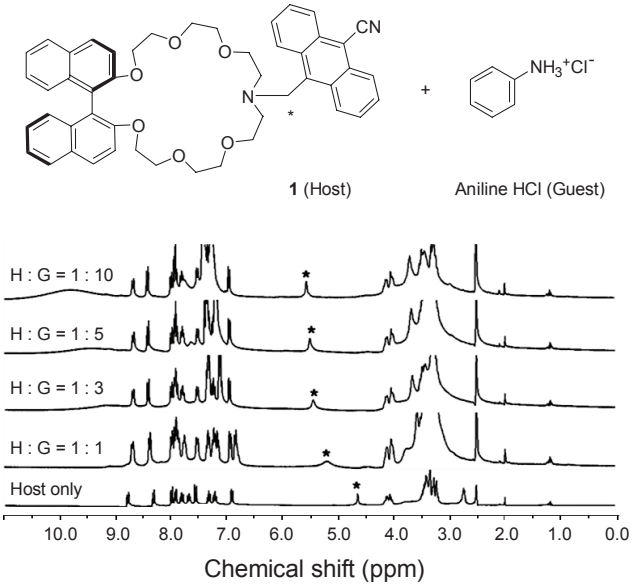


Figure 5. ^{1}H NMR (300 MHz) titration of **1** (20 mM) upon addition of aniline HCl (0 ~ 200 mM) in DMSO-d_6.

for 1-naphthylamine HCl), the association constants for aniline HCl, 1-naphthylamine HCl, 2-naphthylamine HCl and 4-biphenylamine HCl were calculated to be 1.09×10^4, 1.17×10^4 1.54×10^4 and 2.73×10^4 M^{-1}, respectively, according to the Benesi-Hildebrand expressin.[10]

Job's plot experiment was also carried out by varying the concentration of both compound **1** and 1-naphthylamine HCl as shown in Figure 4. The maximum point at the mole fraction of 0.5 indicates the formation of typical 1 : 1 (host : guest) complexes.

Complexation of compound **1** with the arylammonium ions is expected to inhibit the photo-induced electron transfer (PET) from the non-bonded electrons of the intramolecular azacrown nitrogen atom to the anthracene π-system, which effectively quenches fluorescence,[11] and as results chelation-enhanced fluorescence (CHEF) is observed. The reason why primary alkylamine HCl salts including benzylamine HCl and 1-naphthylmethylamine HCl are not involved in the complexation with compound **1** and do not show the CHEF effect is not clear yet. The greater acidity of arylamine HCl salts compared to that of alkylamine HCl salts might be responsible for the effective complexation with compound **1**. ^{1}H NMR titration study for

the complexation of compound **1** with aniline HCl shown in Figure 5 shows that the chemical shift corresponding to the methylene proton (indicated by the asterisk in Figure 5) of compound **1** moves down field upon addition of aniline HCl. The complexation of the ammonium ion of aniline HCl inside the cavity of the azacrown ether ring through the hydrogen bonding between the N-H hydrogen of the ammonium ion of aniline HCl and the azacrown nitrogen atom of compound **1** is expected to diminish the electron density at the methylene group of compound **1** and consequently the chemical shift of the methylene proton of compound **1** should move to down field. In contrast, ^{1}H NMR titration study for the complexation of compound **1** with primary alkylamine HCl salts including benzylamine HCl and 1-naphthylmethylamine HCl did not show any difference in the chemical shifts of compound **1**.

In conclusion, a new binaphthyl-azacrown-anthracene fluorophore (**1**) was prepared and utilized as a selective fluorescent chemosensor for the discrimination of primary alkyl and arylamine HCl salts in ethanol. Primary arylamine HCl salts were found to induce large CHEF effects with the excitation wavelength of 390 nm. On the other hand, primary alkylamine HCl salts were found not to induce any CHEF effect with the excitation wavelength of 390 nm. From the ^{1}H NMR titration study, we found that primary arylamine HCl salts form complex effectively with compound **1** while primary alkylamine HCl salts do not.

Experimental Section

Preparation of 1. Compound **3** (317 mg, 0.6 mmole), which was prepared from **2** by the adaption of reported procedure,[8] and 9-bromomethyl-10-cyanoanthracene (177 mg, 0.6 mmole) were dissolved in 20 mL of acetonitrile. To the solution was added sodiumcarbonate (127 mg, 1.2 mmole) and the resulting whole solution was heated to reflux for 20 h under argon atmosphere. Upon completion of the reaction, the mixture was cooled to room temperature and the organic solvent was removed under reduced pressure. The residue was dissolved in methylene chloride and the organic solution was washed with water. The organic solution was dried over anhydrous $MgSO_4$. Organic solvent was removed under reduced pressure. Column chromatography of the residue on silica gel with ethyl acetate-hexane (1:1) as eluent afforded 0.35 g of compound **1** (yield: 77%). mp 70 ~ 71 ^{o}C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.70-2.75 (m, 4H), 3.18-3.50 (m, 16H), 4.01-4.15 (m, 4H), 4.66 (s, 2 H), 6.90 (d, J = 8.0 Hz, 2H), 7.22 (t, J = 7.1 Hz, 2H), 7.33 (t, J = 6.9 Hz, 2H), 7.57 (d, J = 9.1 Hz, 2H), 7.69 (t, J = 7.0 Hz, 2H), 7.83 (t, J = 6.6 Hz, 2H), 7.93 (d, J = 8.0 Hz, 2H), 8.00 (d, J = 9.1 Hz, 2H), 8.33 (d, J = 8.0 Hz, 2H), 8.80 (d, J = 8.8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 52.1, 54.0, 69.90, 70.1, 70.3, 70.5, 70.8, 106.4, 116.3, 117.8, 120.8, 123.9, 125.7, 126.1, 126.5, 126.6, 128.1, 128.6, 129.5, 129.7, 130.8, 133.1, 134.3, 138.5, 154.7; IR (KBr pellet) cm^{-1} 3053, 2864, 2360, 2341, 2212, 1508, 1269; MS(FAB) m/z (M + H$^+$) calcd. for $C_{48}H_{46}N_2O_6$ 747.33. Found: 747.23.

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