New Fluorescent Chemosensors for Silver Ion

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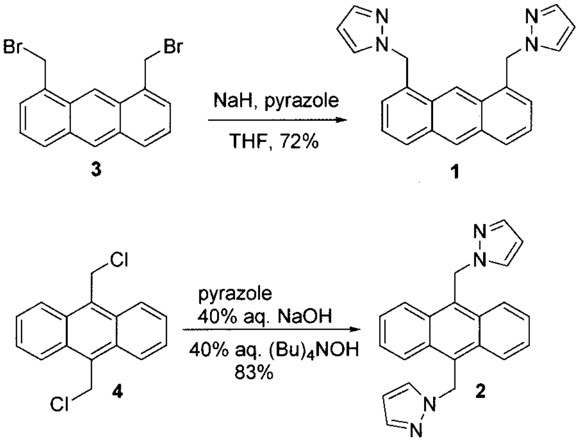
Received February 22, 2002

Abstract: New fluorescent chemosensors, 1,8-bis(pyrazolylmethyl)anthracene and 9,10-bis(pyrazolylmethyl)anthracene, were synthesized. The 1,8-isomer showed selective fluorescent quenching effects with Ag(I) and Cu(II). On the other hand, the 9,10-isomer displayed a selective fluorescent quenching effect only with Ag(I). From the association constants obtained from fluorescent titrations and by extraction, we conclude that rigid immobilization of the ligands, 1,8-isomer, plays a more important role in the binding with Ag(I) than the additional π-cation interaction offered by the 9,10-isomer.

The selective binding of chemical species upon molecular recognition can lead to large perturbations in the host environment, especially when the guest is ionic. Fluoroionophores chemically communicate ion concentrations and are the subjects of substantial investigation for metal ion analysis.[1] The advent of ligand engineering has introduced a more systematic approach to the design of chemosensors with new selectivities and signal transduction schemes. Desvergne et al. reported[2] anthracenocryptands as a new class of cation-complexing macrobicyclic fluorophores. In these reports, crystal structures, UV absorption spectra, and fluorescent emission changes illustrated an unusual interaction between the silver ion and the anthracene moiety. On the other hand, Sakamoto et al. reported a silver ion selective fluoroionophore, which was based on an anthracene-linked polythiazaalkane derivative.[3]

Here, we report upon two new fluorescent chemosensors, 1,8-bis(pyrazolylmethyl)anthracene **1** and 9,10-bis(pyrazolylmethyl)anthracene **2**, which demonstrate selective fluorescent quenching effects with silver ions. A preorganized binding site in case of **1** and an additional π-cation interaction in the case of **2** were productively compared. In our case, fluorescent titrations and extraction methods revealed that the 1,8-isomer **1** binds silver ion more tightly than the 9,10-isomer **2**.

Scheme 1. Syntheses of 1,8-Bis(pyrazolylmethyl)anthracene 1 and 9,10-Bis(pyrazolylmethyl)anthracene 2



For the synthesis of 1,8-bis(pyrazolylmethyl)anthracene **1**, 1,8-bis(bromomethyl)anthracene **3** was first synthesized following the procedures of Nakagawa.[4] Treatment of **3** with sodium hydride and pyrazole in THF led to **1** in 72% yield (Scheme 1). For the synthesis of 9,10-isomer, 9,10-bis(chloromethyl)anthracene **4** and pyrazole were reacted in the presence of 40% aqueous sodium hydroxide and 40% aqueous tetrabutylammonium hydroxide in benzene. After purification by flash chromatography, 9,10-bis(pyrazolylmethyl)anthracene **2** was obtained in 83% yield (Scheme 1).

Ag(I), Ca(II), Cd(II), Co(II), Cs(I), Cu(II), K(I), Li(I), Hg(II), Mg(II), Mn(II), Na(I), Ni(II), Pb(II), Rb(I), Sr(II), and Zn(II) ions were used to evaluate the metal ion binding properties of **1** and **2**. All titration studies were conducted in $CHCl_3$−ethanol (7:3, v/v) and using a 6 μM concentration of compound **1** or **2**. Using these metal ions (0.3 mM, 50 equiv), compound **1** displayed fluorescence quenching effects *only* with Ag(I) and Cu(II) ions. From the fluorescent titrations, the association constants for Ag(I) and Cu(II) were calculated as 125 000 and 134 000 M^{-1}, respectively.[5] Fluorescent emission changes of compound **1** upon the addition of silver ions are shown in Figure 1. On the other hand, compound **2** displayed a selective fluorescent quenching effect *only* with the Ag(I) ion. Fluorescent emission changes of compound **2** upon the addition of silver ions are shown in Figure 2. The association constant was calculated as 2440 M^{-1}, which means that the 1,8-isomer binds with Ag(I) about 100 fold more strongly than the 9,10-isomer. The overall

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(5) Dissociation constants were obtained using the computer program ENZFITTER, available from Elsevier-BIOSOFT, 68 Hills Road, Cambridge CB2 1LA, United Kingdom.

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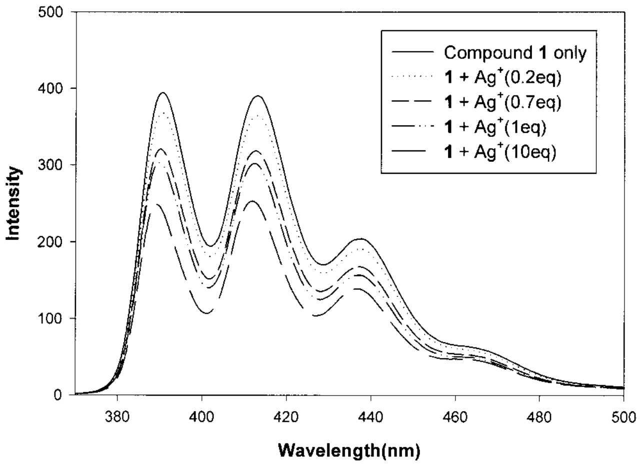

Figure 1. Changes in fluorescence emission spectra of compound **1** (6 μM) upon the addition of Ag(I) in $CHCl_3$–ethanol (7:3, v/v).

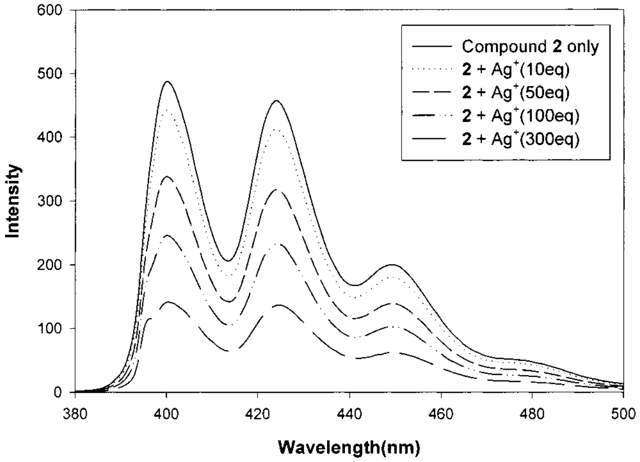

Figure 2. Changes in fluorescence emission spectra of compound **2** (6 μM) upon the addition of Ag(I) in $CHCl_3$–ethanol (7:3, v/v).

fluorescent emission change of the 9,10-isomer was ca. 20-fold and that of the 1,8-isomer 0.3-fold. These observations along with UV spectra support the fact that there is an additional π-Ag(I) interaction in the case of 9,10-isomer **2**. As the amounts of Ag(I) were increased, the UV absorptions of 9,10-isomer were consequently decreased (Figure 3). On the other hand, there was not any change in the UV absorptions of 1,8-isomer up to 150 equiv of Ag(I). A number of papers have reported such π–Ag(I) interactions.[2,6] To confirm the binding properties of the 1,8- and 9,10-isomers with the Ag(I) ion, extraction experiments were performed using silver picrate. The 1,8-isomer was found to extract the silver picrate almost twice as well as the 9,10-isomer, which is consistent with fluorescent experiments.

The binding phenomena of **1** and **2** with silver ion were further confirmed by the ^1H NMR patterns (see the Supporting Information). When 1.1 equiv of silver picrate was added to either **1** or **2** in $CDCl_3$–CD_3OD (4:1, v/v), both deshielding effects ($\Delta\delta$ = 0.02–0.18 ppm) and shielding effects ($\Delta\delta$ = −0.02 to −0.11) were observed for 1,8-isomer and 9,10-isomer. The shielding effects can be attributed to the picrate anions.

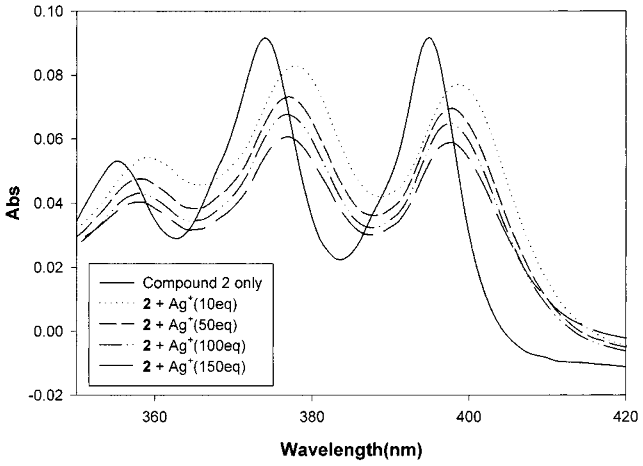

Figure 3. UV absorption spectra of compound **2** (0.3 mM) upon the addition of Ag(I) in CH_2Cl_2–acetone (8:2, v/v).

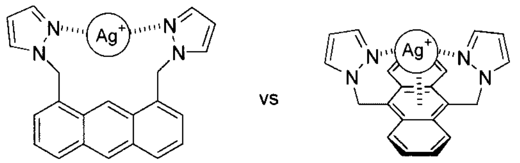

Figure 4. Proposed binding modes of **1** and **2** with Ag(I).

As illustrated in Figure 4, the 1,8-isomer contains a relatively rigid binding pocket compared to the 9,10-isomer. On the other hand, the 9,10-isomer provides an additional binding site (π-cation interaction) in addition to the two pyrazole groups. In the case of these two isomers, the preorganized receptor **1** showed a better binding with the silver ion than receptor **2**.

In conclusion, compounds **1** and **2** displayed selective fluorescent quenching effects with the silver ion. Furthermore, compound **1** and **2** present a pre-organized receptor and a receptor containing three potential binding sites, namely two pyrazole groups and an additional π-cation interaction, respectively. The pre-organized receptor **1** showed improved binding with silver ion compared to receptor **2**, which was demonstrated by fluorescent titrations and extraction experiments.

Experimental Section

General Methods. NMR spectra were recorded with a at 500 MHz (^1H NMR) and at 125 MHz (^{13}C NMR). Chemical shifts were given in ppm using TMS as internal standard. . Melting points were determined in open capillaries and are uncorrected. UV absorption spectra were obtained on double-beam UV/vis spectrometer. Fluorescence measurements were made on a spectrofluorophotometer. Flash chromatography was carried out with Merck silica gel 60 (230–400 mesh). Thin-layer chromatography was carried out with Merck 60 F_{254} plates with 0.25 mm thickness. $CHCl_3$, CH_2Cl_2, and MeOH were distilled from CaH_2, and THF was distilled from sodium-benzophenone ketyl.

1,8-Bis(pyrazolylmethyl)anthracene (1). To a reaction mixture of pyrazole (57 mg, 8.4 mmol) in THF (20 mL) was added NaH (22 mg, 9.2 mmol) at 0 °C. After the mixture was stirred for 20 min at 0 °C, 1,8-bis(bromomethyl)anthracene **3** (100 mg, 0.28 mmol) was added. After additional stirring for 1 h at room temperature, the reaction mixture was poured into 50 mL of water and extracted with $CHCl_3$. The organic layer was then separated, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. Purification by flash chro-

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matography on silica gel (1:2, hexanes−ethyl acetate) afforded **1** (145 mg, 72%) as a yellow solid: mp 162−163 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.85 (s, 4H), 6.27 (t, $J = 2.0$ Hz, 2H), 7.30 (d, $J = 6.8$ Hz, 2H), 7.44 (dd, $J = 6.8$ Hz, $J = 8.3$ Hz, 2H), 7.51 (d, $J = 2.0$ Hz, 2H), 7.61 (d, $J = 1.5$ Hz, 2H), 7.99 (d, $J = 8.8$ Hz, 2H), 8.48 (s, 1H), 8.69 (s, 1H); ^{13}C NMR 54.52, 106.10, 117.92, 125.16, 126.89, 128.11, 129.21, 129.65, 129.77, 131.76, 132.52, 139.29 ($CDCl_3$, 125 MHz); HRMS (FAB) $m/z = 361.1426$ $(M + Na + H)^+$, calcd for $C_{22}H_{19}N_4Na = 361.1429$.

9,10-Bis(pyrazolylmethyl)anthracene (2). A mixture of 9,10-bis(chloromethyl) anthracene **4** (789 mg, 0.91 mmol), pyrazole (186 mg, 2.7 mmol), benzene (15 mL), 40% aqueous sodium hydroxide (1 mL), and 40% aqueous tetrabutylammonium hydroxide (1 drop) was refluxed for 24 h. The organic layer was then separated, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. Purification by flash chromatography on silica gel (1:2, hexanes−ethyl acetate) afforded **2** (256 mg, 83%) as a yellow solid: mp 262−263 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.15 (q, $J = 2.0$ Hz, 8H), 6.38 (s, 4H), 7.03 (d, $J = 2.0$ Hz, 2H), 7.61 (d, 2H, partially hidden), 7.62 (m, 4H), 8.43 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 48.35, 105.88, 121.36, 124.53, 127.03, 127.77, 128.63, 130.89, 132.07, 138.63, 139.12; HRMS (FAB) $m/z = 339.1607$ $(M + H)^+$, calc. for $C_{22}H_{19}N_4 = 339.1610$.

Preparation of Fluorometric Metal Ion Titration Solutions. Stock solutions (1 mM) of the metal perchlorate salts (for Cd(II), chloride salt was used) were prepared using $CHCl_3$−ethanol (7:3, v/v). Stock solutions of **1** or **2** (0.6 mM) were prepared in $CHCl_3$−ethanol (7:3, v/v). Test solutions were prepared by placing 40 μL of the probe stock solution into a test tube, adding an appropriate aliquot of each metal stock, and diluting the solution to 4 mL with $CHCl_3$−ethanol (7:3, v/v).

For all measurements, excitation was at 367 nm; emission was measured at 420 nm. Both excitation and emission slit widths were 5 nm.

Acknowledgment. This work was fully supported by a Grant (No. 2001-042-D00048) from Korea Research Foundation.

Supporting Information Available: NMR spectra of compound **1** and **2** as well as the partial ^{1}H NMR spectra of these compounds upon the addition of silver picrate. This material is available free of charge via the Internet at http://pubs.acs.org.

JO020123X