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SYNTHESIS AND PROPERTIES OF PET FLUOROIONOPHORE HAVING 1-PYRIDIN-2-YLPIPERAZINE GROUP[†]

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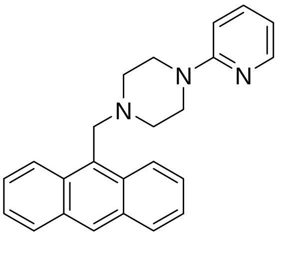
Abstract – 9-[4-(2-pyridinyl)-1-piperazinyl]methyl]anthracene (**1**) and 9,10-bis[[4-(2-pyridinyl)-1-piperazinyl]methyl]anthracene (**2**) were synthesized as a fluorescent PET sensor. The sensor functions as an off-on-off fluorescence switch for proton.

The development of photoinduced electron transfer (PET) systems of guest cations has recently gained much attention for their potential application to nanoscale devices for cation sensor and switch.[1,2] There are extensive investigations toward the characterization of PET fluoroionophores including ionophore with naphthalene, anthracene, and pyrene fluorophore.[1-3] It was found that the nitrogen atom in the azacrown and amino group acts as electron donor in a typical exciplex-forming system that involves an appropriate electron acceptor. The addition of guest cations enhanced the fluorescence emission intensity of PET fluoroionophore. Recently 9-anthrylmethylbis(2-pyridylmethyl)-amine has been reported as fluorescent PET sensor for protons and transition metal ions.[4] We have also reported the complexation and fluorescence behaviors of anthracene derivatives



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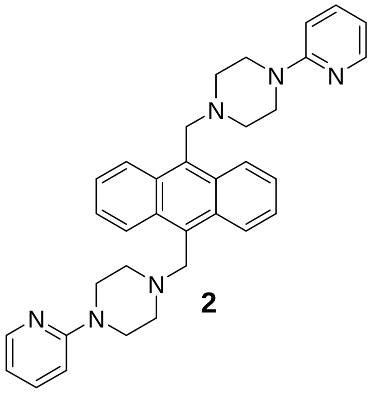

2

[†] Dedicated to Professor Ekkehard Winterfeldt on the occasion of his 75th birthday.

having diethylamine, *N*-methylpiperzine and *N,N-bis*(2-picolyl)amine unit. Most PET sensors show a spectral change in the presence of transition metal ions.[5] Measurements of intracellular pH provide valuable information on physiological states of cells. pH-Sensitive fluorescent sensors have generally been used to determine intracellular pH. As an approach to the manipulation of H^+ selective PET sensor, we now report the complexation and fluorescence behavior of 9-[4-(2-pyridinyl)-1-piperazinyl]methyl]anthracene (**1**) and 9,10-bis[[4-(2-pyridinyl)-1-piperazinyl]- methyl]anthracene (**2**). The anthracene-functionalized 1-pyridin-2-yl-piperazine derivatives (**1**, **2**) were prepared by the *N*-alkylation of 1-pyridin-2-yl-piperazine with 9-chloromethylanthracene or 9,10-bis(chloromethyl)-anthracene. The structure and purity of **1** and **2** were ascertained by ^{1}H, ^{13}C NMR spectroscopic data, and elemental analysis.[6]

Fluoroionophores (**1** and **2**: 5.00 x 10^{-6} M), when excited at 378 nm, gave weak emission bands at 406, 428 and 452 nm in methanol. The emission-band intensities of **1** and **2** were reduced to approximately one-500th and 1000th, respectively, compared with those of 9-methylanthracene (9-MA, 5.00 x 10^{-6} M) and 9,10-dimethylanthracene (9,10-DMA, 5.00 x 10^{-6} M). This indicates that the quenching of the excited-state anthracene chromophore by the 1-pyridin-2-yl-piperazine unit proceeds in a mechanism similar to that for the classical fluorescent-aliphatic amine system. The emission intensity ratio ($I_2/I_{9,10\text{-DMA}}$ = 1.0 x 10^{-3}) of **2** for 9,10-DMA is lower than that ($I_1/I_{9\text{-MA}}$ = 2.0 x 10^{-3}) for 9-MA. The larger quenching of **2** means that four intramolecular nitrogen atoms and anthracene ring participate in intramolecular electron transfer in the excited state.

Fortunately, the crystal structure of **2** could be elucidated by X-ray structural analysis as shown in Fig. 1.[7] Molecules of **2** are centrosymmetric and the two 1-pyridin-2-yl-piperazine units are *anti* with respect to one another across the anthracene ring. The anthracene ring of **2** is close to the amino nitrogen atom of piperazine unit; the distance between C3 and N1 (2.488 (2) Å) is shorter than the sum of their van der Waals radii [3.05 Å].[8] This means that an intramolecular charge transfer can take place readily between the anthracene ring and the N atom in the ground state as well as in the excited state.

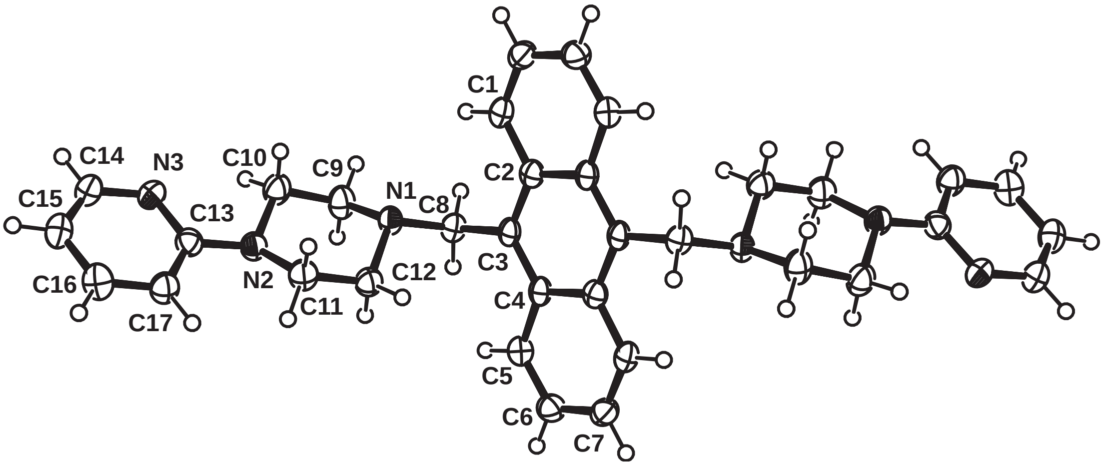

Figure 1. An ORTEP drawing of **2** showing 50% probability displacement ellipsoids.

Fig. 2 illustrates the fluorescence spectral behavior of **2** in the presence of 200 equiv. guest metal salts and hydrochloric acid in DMSO-H_2O (1:9 *v/v*) at room temperature. Dramatic changes in the emission intensity of **1** and **2** were observed upon the addition of hydrochloric acid but no appreciable spectral changes were observed upon the addition of various metal salts such as NaCl, KCl, RbCl, $MgCl_2$, $CaCl_2$, $BaCl_2$, $SrCl_2$, $NiCl_2$, $CuCl_2$, and $ZnCl_2$. This result suggests that **1** and **2** show high selectivity for H^+.

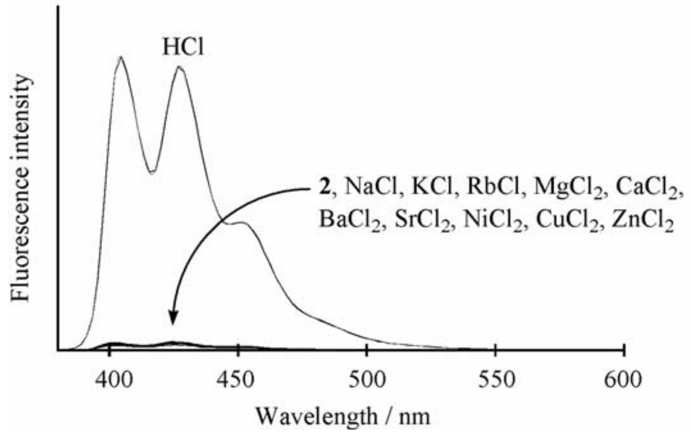

Figure 2. Fluorescence spectra of **2** (5.0×10^{-6} M) in the presence of 200 equiv. guest metal salts or hydrochloric acid in DMSO-H_2O (1:9 *v/v*).

When hydrochloric acid was added in the range of 0 to 0.1 M, the emission intensity at 405 nm enhanced (Fig. 3a). The relative emission intensity ($I_{complex}/I$), being used as a measure of the molecular recognition sensing, changed from 1 to 176 as shown in Fig. 3c.

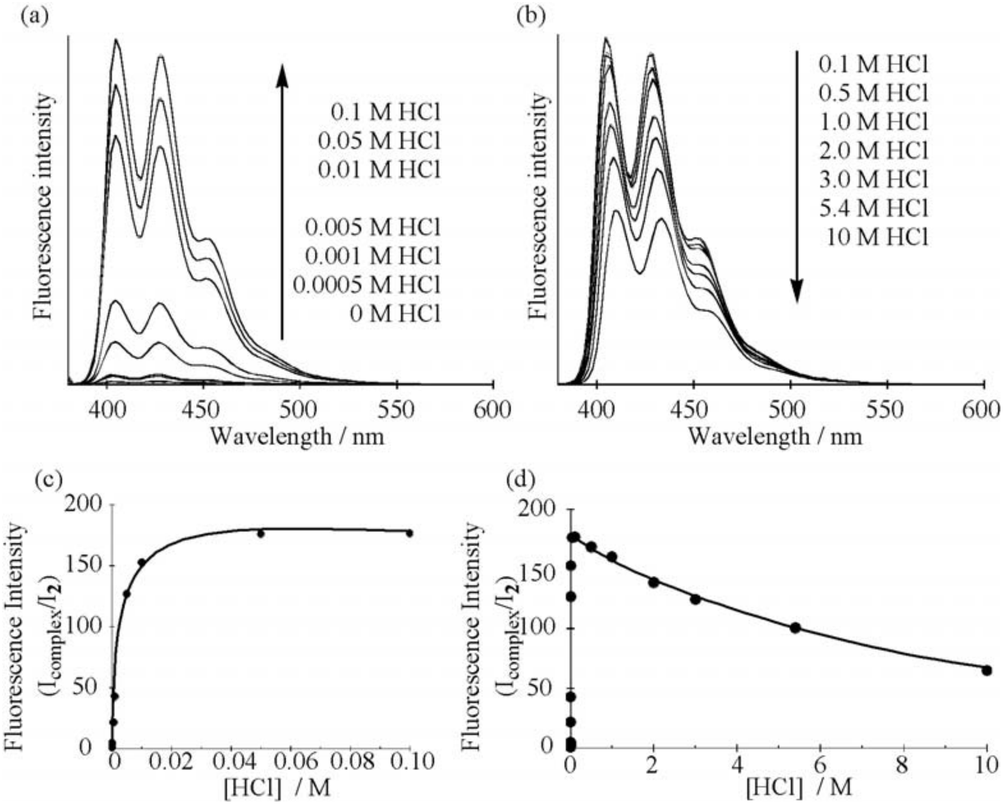

Figure 3. Fluorescence spectra of **2** (5.0×10^{-6} M) in the presence of (a) 0-0.1 M and (b) 0.1-10 M HCl and the dependence of fluorescence intensities of **2** at 405 nm on the concentration of (c) 0-0.1 M and (d) 0-10 M HCl in DMSO-H_2O (1:9 *v/v*).

This means that the protonation of alkylamine nitrogen atoms inhibit the PET from the nitrogen atom to anthracene. Further addition of hydrochloric acid caused the emission quenching (Fig. 3b). This suggest that the observed competitive quenching is due to the protonation of pyridine ring to form a pyridinium cation. The similar quenching phenomenon is observed in the off-on-off system such as 9-anthrylmethyl-*bis*(2-picolyl)amine.[4] However, 9-anthrylmethyl-*bis*(2-picolyl)amine forms the complex with Zn^{2+} as well as H^+.

In conclusion, **1** and **2** showed high H^+ selectivity and functioned as an off-on-off fluorescence switch for proton. The anthracene-functionalized 1-pyridin-2-yl-piperazine derivatives would be used as a fluorescent pH sensor of a range of pH 1-7.

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6. The synthetic details and physical properties of **1** and **2** will be reported elsewhere. **2**: ^{1}H NMR ($CDCl_3$) δ = 2.86 (8H, t, J = 4.9 Hz), 3.50 (8H, t, J = 4.9 Hz), 4.52 (4H, s), 6.57-6.60 (4H, m), 7.43 (2H, ddd, J = 9.8, 7.3, 2.0 Hz), 7.53 (4H, dd, J = 7.2, 3.2 Hz), 8.17 (2H, dd, J = 5.9, 2.0 Hz), and 8.57 (4H, dd, J = 7.2, 3.2 Hz); ^{13}C NMR ($CDCl_3$) δ = 45.4 (4C), 53.1 (4C), 54.5 (2C), 107.0 (2C), 113.0 (2C), 125.2 (4C), 125.6 (4C), 130.0 (2C), 131.2 (4C), 137.4 (2C), 147.9 (2C), and 159.5 (2C).
7. Crystal data of **2**, $C_{34}H_{30}N_6$, Mr = 522.65, Monoclinic, $P2_1/c$, a = 9.943(3) Å, b = 10.840(4) Å, c = 12.477(5) Å, β = 96.38(2)°, V = 1336.5(8) Å^3, Z = 2, D_x = 1.299 Mg m^{-3}, refinement on F^2 (*SHELXL97*),[9] $wR(F^2)$ = 0.1534, $R(F)$ = 0.0528.
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