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A highly selective fluorescent chemosensor for dihydrogen phosphate via unique excimer formation and PET mechanism

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Abstract—A new fluorescent chemosensor bearing two imidazolium groups as well as two anthracene groups has been synthesized. This chemosensor displayed a highly selective fluorescence quenching effect and a unique excimer peak only with $H_2PO_4^-$. The association constant of **1** with $H_2PO_4^-$ was calculated as $>10^6\ M^{-1}$.

Anions play an important role in a wide range of chemical and biological processes, and the development of anion selective receptors has received considerable attention.[1] Accordingly, sensors based on the anion-induced changes in fluorescence appear to be particularly attractive due to the simplicity and high detection limit of the fluorescence.[1,2] Phosphate ions and their derivatives play important roles in signal transduction and energy storage in biological systems.[3] In particular, the detection and discrimination of $H_2PO_4^-$ has been the main focus of many research groups. The most common approach has been the utilization of urea or thiourea groups[4] in PET (photo-induced electron transfer) type fluorescent chemosensors. This is despite the fact that there has been considerable research into metal ion-induced binding[5] and other types of hydrogen bonding receptors.[6,7] However, as reported in previous examples of urea or thiourea type receptors,[4] similar fluorescence quenching effects of F^- or $CH_3CO_2^-$ have always been obstacles to the design of selective fluorescent chemosensors for $H_2PO_4^-$.

We report the synthesis and binding properties of a new imidazolium receptor (**1**) bearing two anthracene moieties, which shows effective selectivity for $H_2PO_4^-$ over other anions, such as $CH_3CO_2^-$, HSO_4^-, F^-, Cl^-, Br^-, and I^-. Upon the addition of $H_2PO_4^-$, compound **1** has a selective fluorescence quenching effect and a unique excimer peak.

1-(9-Anthracenylmethyl)imidazole **2** was prepared from 9-bromomethylanthracene[8] by a modification of the procedure reported elsewhere.[9] Compound **3** was also synthesized using a published procedure.[10] Compounds **2** and **3** were refluxed in acetonitrile for 24 h. After washing the precipitate several times with cold CH_2Cl_2, aqueous KPF_6 was added to the bromide salt of compound **1** in DMF to give compound **1**[11] as a light yellow solid in a yield of 75% (Scheme 1). Compound **1** was fully characterized by ^1H NMR, ^{13}C NMR (see Supplementry data) and high resolution FAB mass spectroscopy.

Figure 1 shows the fluorescence emission changes in compound **1** (6 μM) upon the addition of $H_2PO_4^-$, HSO_4^-, $CH_3CO_2^-$, I^-, Br^-, Cl^-, and F^- (10 equiv, tetrabutylammonium salts). The fluorescence spectra were obtained by the excitation of the anthracene fluorophore at 368 nm. As shown in Figure 1, there was a unique change in the emission spectrum only with $H_2PO_4^-$. A large fluorescence quenching effect and a unique excimer peak (at 485 nm) were observed. As mentioned above, compound **1** showed highly selective fluorescent changes with $H_2PO_4^-$ compared with those of other anions, particularly F^- or $CH_3CO_2^-$. The job plot for the binding between compound **1** with $H_2PO_4^-$ showed a 1:1 stoichiometry. Figure 2 shows the fluorescent titration data for compound **1** with $H_2PO_4^-$. From the fluorescence

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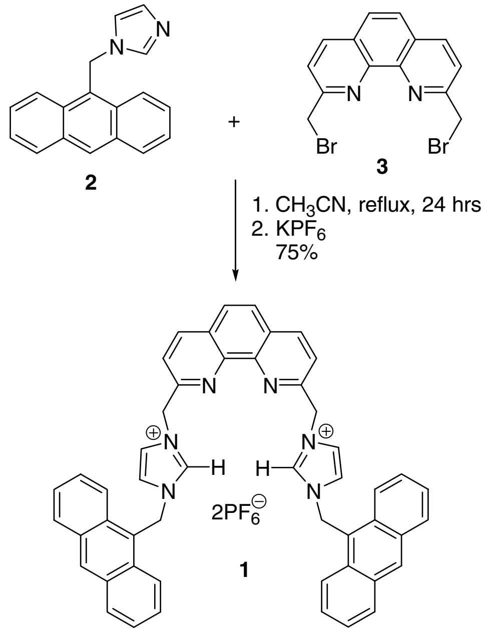

Scheme 1. Synthesis of compound **1**.

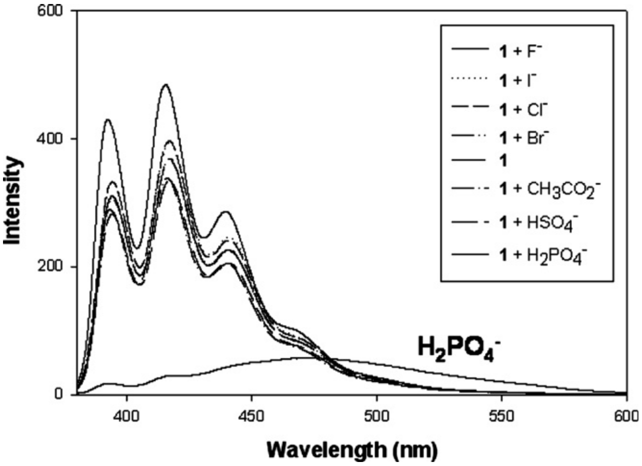

Figure 1. Fluorescent emission changes of **1** (6 μM) upon the addition of various anions (10 equiv) in CH_3CN (excitation at 368 nm).

titration, the association constant of complex **1** with $H_2PO_4^-$ was observed to be $2.2 \times 10^5\ M^{-1}$ (errors < 10%).[12]

The expected strong $(C–H)^+–X^-$ hydrogen bonding between the imidazolium moieties and $H_2PO_4^-$ was further confirmed by ^1H NMR (Fig. 3). As shown in Figure 3, the imidazolium C–H displayed a large downfield shift (δ 9.19–9.45) upon the addition of $H_2PO_4^-$ (0.5 equiv) in DMSO-d_6. On the other hand, the aromatic protons in the phenanthroline moiety as well as benzylic CH_2 peaks did not show any significant change in the ^1H NMR spectrum, which can exclude the possibility of a hydrogen bonding interaction between the O–H of $H_2PO_4^-$ and the nitrogen on the phenanthroline moiety or between O^- of $H_2PO_4^-$ and benzylic CH_2 groups. The addition of more than 0.5 equiv of $H_2PO_4^-$ resulted in precipitation during the NMR titration. The fluorescent quenching effect can be due to a photo-induced electron transfer (PET) mechanism as explained in the precedent reports.[6] On the other hand, the new peak at 485 nm corresponds to the excimer peak of anthracenes. This suggests that the two anthracene groups are located closer due to the hydrogen binding between $H_2PO_4^-$ and the two imidazolium moieties, which can induce excimer formation. The phenanthroline moiety in compound **1** may act as a template for introducing the binding selectivity.

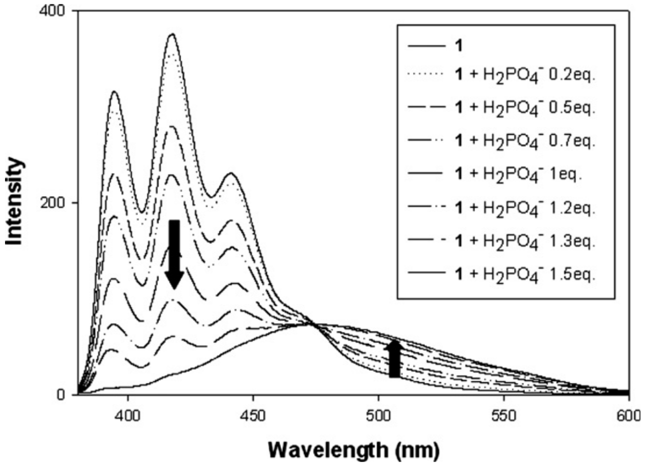

Figure 2. Fluorescent titrations of **1** (6 μM) with $H_2PO_4^-$ in CH_3CN (excitation at 368 nm).

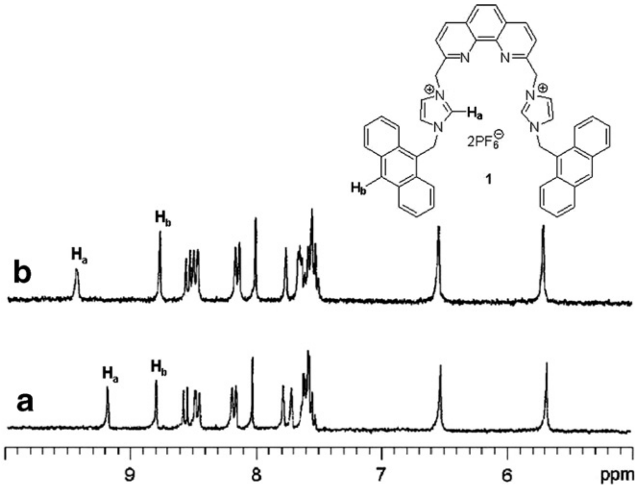

Figure 3. Partial ^1H NMR (250 MHz) spectra of **1** (2 mM) in DMSO-d_6: (a) **1** only, (b) **1** + 0.5 equiv of $H_2PO_4^-$.

Figure 4 shows the competition experiments of compound **1** between $H_2PO_4^-$ and other anions. The presence of other anions (10 equiv) did not cause any significant changes to the emission of compound **1** (6 μM) with $H_2PO_4^-$ (2 equiv) (Fig. 5).

In conclusion, a new imidazolium receptor (**1**) containing two anthracene moieties was synthesized as a fluorescent chemosensor for $H_2PO_4^-$. The title compound displays effective selectivity for $H_2PO_4^-$ over other anions, particularly over $CH_3CO_2^-$ and F^-. Upon the

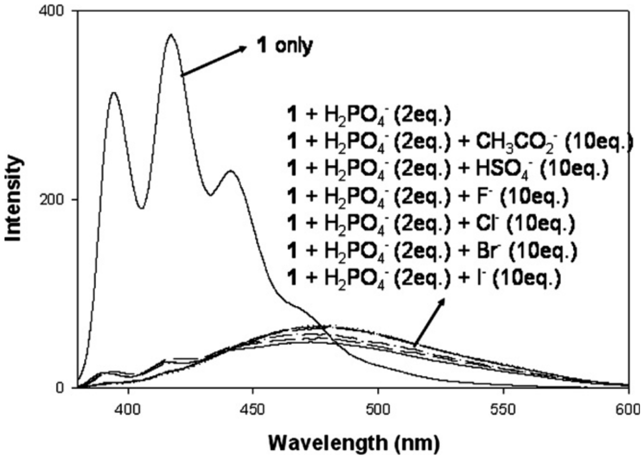

Figure 4. Fluorescent changes of **1** (10 μM) with $H_2PO_4^-$ (2 equiv) in the presence of 10 equiv of various anions in CH_3CN (excitation at 368 nm).

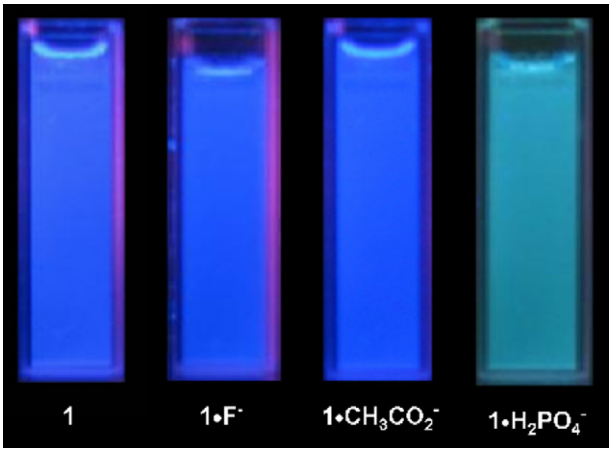

Figure 5. Colorimetric changes of **1** (10 μM) with 2 equiv of F^-, $CH_3CO_2^-$ and $H_2PO_4^-$ in acetonitrile.

addition of $H_2PO_4^-$, compound **1** displayed a selective PET quenching effect and a unique excimer peak at 485 nm. The association constant of complex **1** with $H_2PO_4^-$ was found to be 2.2×10^5 M^{-1}. This interaction was attributed to the strong $(C–H)^+–X^-$ hydrogen bonding between the imidazolium moieties and $H_2PO_4^-$.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.03.159.

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11. Compound **1**: A mixture of **2** (300 mg, 1.16 mmol) and **3** (150 mg, 0.41 mmol) in acetonitrile (40 mL) was refluxed for 24 h under N_2. After cooling to the room temperature, the precipitate was filtered and washed with cold CH_2Cl_2. The bromide salt (310 mg, 86%) was dissolved in 3.5 mL

DMF. During the dropwise addition of saturated aqueous KPF_6 solution (1.5 mL), a light yellow precipitate was formed. After washing the precipitate several times with water, desired product was obtained as a light yellow solid (266 mg, 75%). Mp: 166–173 °C; ^1H NMR (DMSO, 250 MHz) δ 9.18 (s, 2H), 8.79 (s, 2H), 8.55 (d, $J = 8.4$ Hz, 2H), 8.46 (d, $J = 8.4$ Hz, 4H), 8.17 (d, $J = 8.0$ Hz, 4H), 8.02 (s, 2H), 7.93 (s, 2H), 7.85 (s, 2H), 7.56 (m, 10H), 6.43 (s, 4H), 5.66 (s, 4H); ^{13}C NMR (CD_3CN, 125 MHz) δ 153.34, 145.17, 138.22, 136.26, 131.72, 131.18, 130.96, 129.80, 128.96, 128.23, 127.29, 125.90, 123.76, 122.99, 122.47, 122.31, 54.63, 46.05; HRMS (FAB) calcd for $C_{50}H_{38}F_6N_2P$ $[M-PF_6]^+$ 867.2800. Found: 867.2801.

12. (a) Association constants were obtained using the computer program ENZFITTER, available from Elsevier-BIOSOFT, 68 Hills Road, Cambridge CB2 1LA, United Kingdom; (b) Conners, K. A. *Binding Constants, The Measurement of Molecular Complex Stability*; Wiley: New York, 1987.