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A novel amidepyridinium-based tripodal fluorescent chemosensor for phosphate ion via binding-induced excimer formation

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ABSTRACT

A new tripodal fluorescent chemosensor **1** having amidepyridinium moiety as the key binding site and anthracene moiety as the sensing subunit was synthesized. In competitive polar organic solvent, this chemosensor **1** displayed high selectivity toward $H_2PO_4^-$ by formation of binding-induced excimer emission.

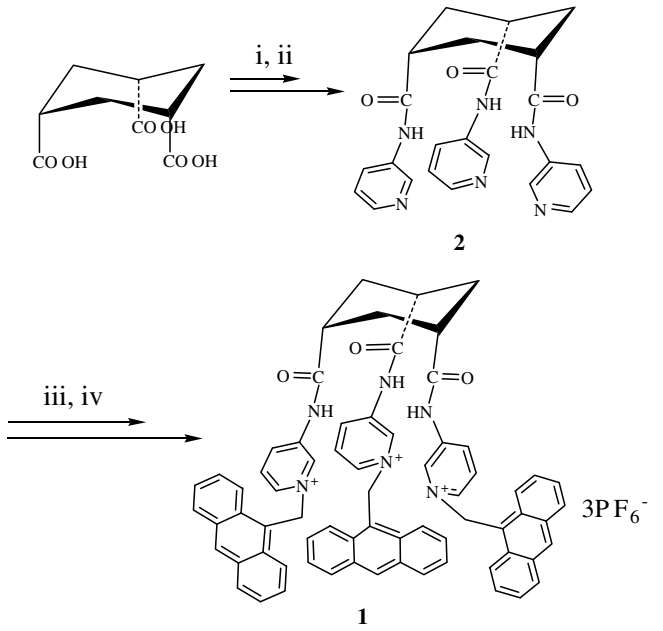
The binding and sensing of anionic species by artificial receptors is an expanding area of supramolecular chemistry.[1,2] In this sense, development and precise arrangement of cooperative binding motifs in the cavity of artificial hosts are of special importance, however extreme challenge, for efficient anion recognition. Among these binding motifs for anions, hydrogen bonds are the most widely employed due to their directional nature, which possess the capability to differentiate anionic species with different geometries.[1] During the past two decades, the hydrogen donating properties of NH groups, such as neutral amine, amide, urea, pyrrole, and indole, as well as the charged ammonium, guanidinium, and imidazolium-based anion receptors have been well established.[1g] In contrast, amidepyridinium-based anion receptors, and especially sensors which combine the hydrogen donating properties of neutral amide group and acidic C–H at the pyridinium ring, is surprisingly less investigated, although pyridinium-based anion hosts had been reported by Steed and his coworkers recently.[3]

On the other hand, the overall receptor topology has a profound effect on anion binding.[4] In comparison to those rigid cyclic structures, flexible podand receptors remain challenging and are potentially significant, since they frequently display rapid complexation/decomplexation kinetics and undergo significant conformational change on binding. Those properties form the basis of molecular switches or switchable sensing devices.[5,3b]

Intrigued by these, herein, we introduce a new tripodal fluorescent chemosensor **1,** which bears 3-amidepyridinium as the key binding motif and anthracene moiety as the sensing subunit. Under the cooperative multi-interactions of amide and acidic –CH groups, **1** displayed highly fluorescent selectivity toward $H_2PO_4^-$ than other inorganic anions, such as F^-, Cl^-, Br^-, I^-, HSO_4^- , and AcO^- by formation of unique excimer emission in competitive polar organic solvents.

The preparation of tripodal chemosensor **1** was achieved in an acceptable yield by refluxing of symmetrical amide derivative **2** with 9-chloromethylanthracene in dry CH_3CN for 48 h and then anion exchange with NH_4PF_6. The detailed synthetic route is shown in Scheme 1.[6,7]

The structure of chemosensor **1** was fully characterized with H^1 NMR, MS, and elemental analysis.[6,7] In order to provide some



Scheme 1. Synthetic route to chemosensor **1**. Reagents and condition: (i): excess $SOCl_2$, 70 °C, 8 h; (ii) 3-fold 3-aminopyridine, dry THF; (iii) 3-fold 9-chloromethylanthracene, dry CH_3CN, reflux, 48 h; (iv) mixed solvent of DMF and H_2O, excess NH_4PF_6.

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degree of preorganization into a conical conformation with all three binding sites and sensing arms co-aligned, *cis*-cyclohexane 1,3,5-tricarboxylic acid was used herein as the starting material. To the best of our knowledge, this is the first case using *cis*-cyclohexyl group as the central core of tripodal receptor for anion sensing compared to the well-estabilised podands having hexa-substituted benzene as the core.[8,3f]

It was predicted that the arrangement of multiple anthracene groups in the chemosensor **1** might report the anion binding by appearance of some unique optical phenomena. As the potential anion-dependent conformational change of host would induce the possible association between those multiple anthracene moieties to form excimer emission, giving rise to selective anion sensing.

With this in mind, the investigation on optical-response of chemosensor **1** toward various anions was first carried out by using fluorescent spectroscopy in polar organic solvent (9:1 CH_3CN–EtOH). By excitation of anthracene fluorophore at 368 nm, **1** alone displayed typical monomer emission of anthracene fluorescence consisting of three sharp bands at 387, 413, and 436 nm, as well as a shoulder at 466 nm. The relative weakly fluorescent intensity of **1** was ascribed to the quenching effect of PET process from the anthracene moieties to the charged pyridinium ring.[3f] No evidence of excimer emission was shown in fluorescence spectrum of **1**, which basically excluded the inter- or intramolecular association between anthracene moieties under the investigated conditions. This phenomenon indicated the presence of a certain favorable conformation of **1** to keep the relatively remote distance between those anthracene moieties.

Figure 1 displays the changes in fluorescence of chemosensor **1** upon addition of various inorganic anions, such as F^-, Cl^-, Br^-, I^-, HSO_4^-, AcO^-, and $H_2PO_4^-$ having tetra-*n*-butyl ammonium as the counter cation. It is worth noting from Figure 1 that only upon addition of $H_2PO_4^-$ induced a marked change of fluorescent emission of **1**, and in contrast, other anions showed negligible effect. This result demonstrated that chemosensor **1** exhibited high selectivity toward $H_2PO_4^-$ in such competitive polar organic solvent by changing its fluorescent properties. Fluorescent titration experiments pointed to 1:1 stoichiometry between **1** and $H_2PO_4^-$, which is shown in Figure 2. Furthermore, the binding constant was calculated from this titration curve to give lg*K* to be 4.28.

Just as shown in Figures 1 and 2, upon addition of $H_2PO_4^-$, a small increasing intensity of monomer fluorescence of chemosensor **1** was found due to the inhibition of the photo-induced electron transfer (PET) process from anthracene fluorophore to pyridinium moiety. More significantly, together with this PET process, a

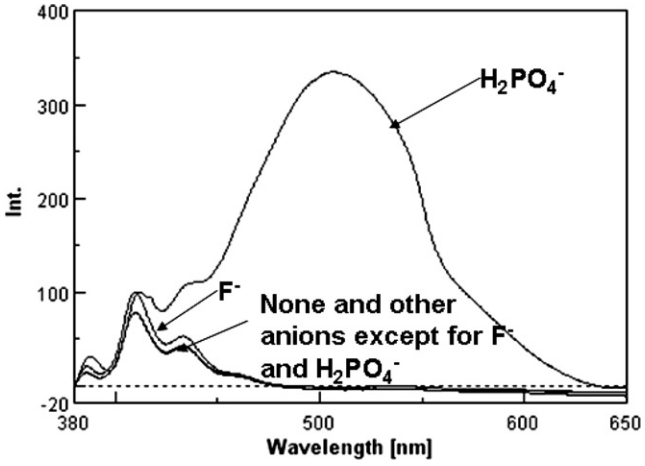

Figure 1. Changes in fluorescence spectra of **1** (50 μM) upon addition of various anions in 9:1 CH_3CN–EtOH solution with excitation at 368 nm.

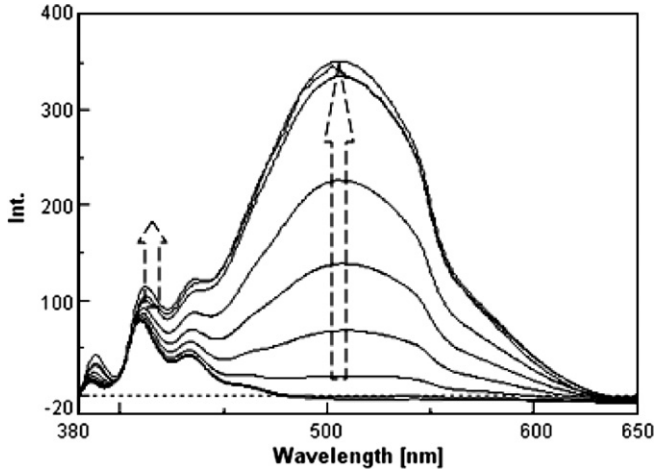

Figure 2. Changes in fluorescence spectra of **1** (50 μM) upon addition of $H_2PO_4^-$ in 9:1 CH_3CN–EtOH solution with excitation at 368 nm.

remarkably enhanced broad band (at 505 nm) corresponded to the excimer emission between anthracenes was observed simultaneously. This result demonstrated that the binding of $H_2PO_4^-$ pulled the separated anthracene moieties closer indicating the occurrence of binding-induced conformational change of tripodal chemosensor **1**.

Absorption spectra of chemosensor **1** in the presence and absence of the aforementioned anions were also measured to support those variations of fluorescence spectra. As shown in Figure 3, the absorption bands of anthracene moieties were hardly affected by F^-, Cl^-, Br^-, I^-, HSO_4^-, and AcO, which indicate the insulating role of the $-CH_2-$ group via minimizing the ground state interactions between anthracene moieties and binding sites. On the other hand, addition of $H_2PO_4^-$ induced the apparent bathochromic shift of the absorption bands of anthracene. This result implied not only the presence of strong interactions between $H_2PO_4^-$ and binding sites of chemosensor **1** but also the formation of some interaction and association between anthracenes at the ground states.[9,2c] Therefore, the appearance of the new fluorescence band at longer wavelength region in Figure 1 must be attributed to the excimer fluorescence between anthracenes.

In order to know more about the interactions between $H_2PO_4^-$ and chemosensor **1**, ^1H NMR investigation was also performed and the results are shown in Figure 4. Because the addition of more than 0.5 equiv $H_2PO_4^-$ resulted in gradually precipitation during the ^1H NMR titration and made the spectra rather unclear, just

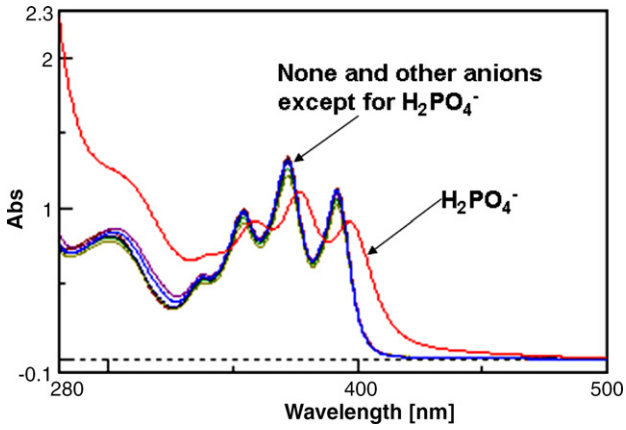

Figure 3. Changes of absorption spectra of **1** (50 μM) upon addition of various anions in 9:1 CH_3CN–EtOH solution.

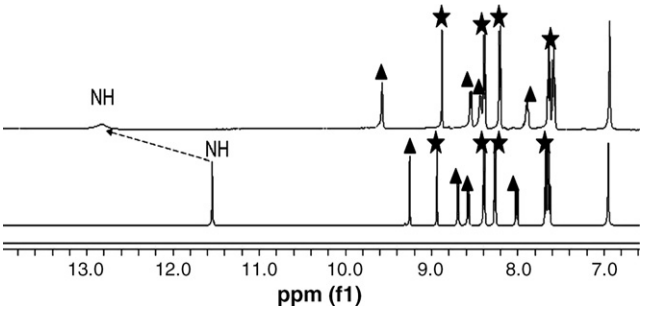

Figure 4. Partial ^{1}H NMR spectra of **1** in the absence (lower) and the presence (upper) of 0.5 equiv $H_2PO_4^-$ in DMSO-d_6. Black stars denote the all protons of anthracene moieties and black triangle show all protons of pyridinium rings.

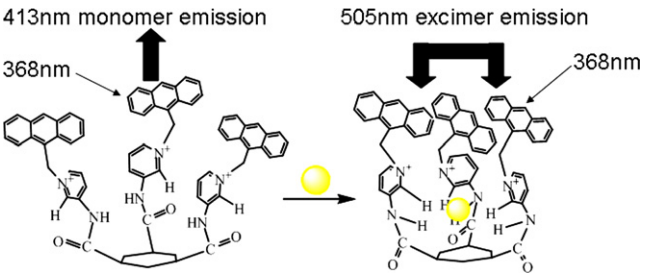

Figure 5. Fluorescent response to $H_2PO_4^-$ via formation of excimer emission.

the effect of adding 0.5 equiv $H_2PO_4^-$ was recorded. It was clear that the amide proton (from 11.55 to 12.86, 1.3 ppm shifted) and hydrogen proton at the α-position of pyridinium ring (from 9.25 to 9.60 ppm, 0.35 ppm shifted) displayed a remarkable downfield shift upon addition of 0.5 equiv $H_2PO_4^-$ in DMSO-d_6 solution, indicating the presence of hydrogen bonding interactions between NH, acidic CH and $H_2PO_4^-$ ion. On the other hand, other hydrogen protons at the pyridinium ring shifted to upfield implying the participation of electrostatic interaction of charged pyridinium ring in binding $H_2PO_4^-$. In this context, the cooperative function of multi-interactions within the binding cavity gave rise to the excellent binding and sensing properties of chemosensor **1** toward $H_2PO_4^-$ in competitive polar organic solvents. Furthermore, all protons of anthracene moieties were slightly shifted to higher magnetic field. This result suggested that the binding of $H_2PO_4^-$ via cooperation of multi-interactions induced the reduction of the distance between plural anthracene moieties and correspondingly the formation of excimer (Fig. 1).

Based on above results, the proposed binding process of receptor **1** toward $H_2PO_4^-$ is shown in Figure 5. Before complexation with $H_2PO_4^-$, anthracene moieties are separated each other remote enough to emit only monomer fluorescence. This relative remote distance between them is induced by its favorable conformation, which might be controlled by the six-membered intramolecular hydrogen bonding between carbonyl group and acidic CH at the pyridinium ring. However, when $H_2PO_4^-$ was introduced, the anion-dependent comformational change accomplished by cooperative multi-interactions induced the cavity in receptor **1** selective only for $H_2PO_4^-$ complexation. As a result, the anthracene moieties come closer and overlap some extent to form the excimer emission of them, which emitted strong green fluorescence.

In conclusion, a new tripodal fluorescent chemosensor **1** based on amidepyridinium binding motif for selective $H_2PO_4^-$ sensing was developed. The excellent $H_2PO_4^-$ binding is attributed to the cooperation of multi-interactions, such as hydrogen bonding, electrostatic interactions, as well as the dynamic conformational change via formation of unique binding-induced excimer.

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6. *Procedure for synthesis of compound* **2***:* First, *cis*-cyclohexane 1,3,5-tricarboxylic acid was reacted with thionyl chloride at 70 °C for 8 h to give the corresponding acid chloride. After drying of 1 h under reduced pressure, this acid chloride was used directly to the next reaction. Then, a solution containing 3-aminopyridine (0.282 g, 3 mmol) and Et_3N (1.01, 10 mmol) in dry THF (25 mL) was prepared and cooled by ice-water bath. The aforementioned acid chloride (1 mmol) also in dry THF (15 mL) was added dropwise into the above solution within about 20 min, and the stirring was continued for overnight under room temperature. Then, the precipitated white solid was filtered, washed several times with distilled water, and dried under reduced pressure. Without further purification, it was conformed that this white solid was the target compound **2** (74%).
For compound **2**: 1H NMR (DMSO-d_6, 500 MHz) 1.37 (m, cyclohexyl, 3H), 2.09 (m, cyclohexyl, 3H), 2.58 (m, cyclohexyl, 3H), 7.33 (dd, pyridine, 3H), 8.04 (d, J = 8.5 Hz, pyridine, 3H), 8.24 (d, J = 4 Hz, pyridine,3H), 8.73 (s, pyridine, 3H), 10.10 (br, −NH, 3H). ESI-MS (cationic mode), 445.2 (M+H); Elemental Anal. Calcd for $C_{24}H_{24}N_6O_3$: C, 64.85; H, 5.44; N, 18.91. Found: C, 64.82; H, 5.53; N, 18.76. (18.91).
7. *Procedure for synthesis of chemosensor* **1***:* A mixture of compound **2** (0.444 g, 1 mmol) with 9-chloromethylanthracene (0.68 g, 3 mmol) in dry CH_3CN was refluxed for 48 h, and gradually yellow precipitate was formed. After cooling to room temperature, the precipitate was filtered off and washed several times with cold CH_3CN. After recrystallization using EtOH, pure chemosensor **1** as chloride salt was obtained in 46% yield. Then, the chloride salt (100 mg) was dissolved in 1 ml DMF. During dropwise addition of saturated aqueous NH_4PF_6 solution (2 ml), a light yellow precipitate was formed. After washing the precipitate several times with distilled water, the desired chemosensor **1** was obtained in 88% yield.
For chemosensor **1**: 1H NMR (DMSO-d_6, 500 MHz) 1.32 (m, cyclohexyl, 3H), 1.94 (m, cyclohexyl, 3H), 2.53 (m, cyclohexyl, 3H), 6.95 (s, $-CH_2-$, 2H), 7.67 (m, anthracene, 12H), 8.02 (m, pyridinium, 3H), 8.26 (d, J = 8, anthracene, 6H), 8.39 (d, J = 8, anthracene, 6H), 8.57 (d, J = 9.5, pyridinium, 3H), 8.69 (d, J = 9.5, pyridinium, 3H), 8.94 (s, anthracene, 3H), 9.25 (s, pyridinium, 3H), 11.55 (br, −NH, 3H). ESI-MS (cationic mode), 1015.8 ($M-3PF_6^- - 2H^+$); Elemental Anal. Calcd for $C_{69}H_{57}f_{18}N_6O_3P_3$: C, 57.03; H, 3.95; N, 5.78. Found: C, 57.21; H, 3.87; N, 5.66.
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