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Pyridinium amide-based simple synthetic receptor for selective recognition of dihydrogenphosphate

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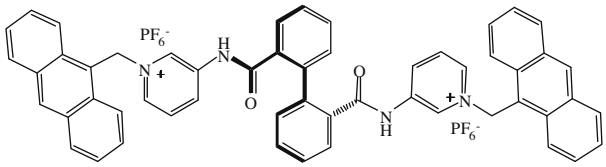
ABSTRACT

A new fluorescent receptor **1** built on biphenyl motif has been designed and synthesized. Pyridinium amide moiety in **1** acts as binding site and shows selective complexation of isophthalate and $H_2PO_4^-$ under the mastery of biphenyl spacer. Binding-induced increase in emission was used to determine the selectivity and sensitivity of **1** toward a series of anions such as different dicarboxylates, HSO_4^-, ClO_4^-, and $H_2PO_4^-$. The binding characteristics were established by ^1H NMR, UV–vis, and fluorescence spectroscopic methods.

Design and synthesis of hydrogen-bonding fluororeceptor for selective sensing of anions are the focus of interest for chemists in the past decade due to the important roles of anions in many biological and chemical systems.[1–6] In developing such receptors searching of new binding sites and their placement onto the different rigid and semi rigid spacers are challenging tasks. Among the different binding motifs for anions, the hydrogen-bonding properties of NH groups in neutral amines,[7] amide,[8] urea/thiourea,[9,10] indole,[11] pyrrole,[12] guanidinium,[13] and imidazolium[14] groups are well established. In this connection, pyridinium amide motif for anions is less explored. To investigate the significance of unconventional C–H···O hydrogen bonds in highly polar solvents for carboxylate ion recognition, Jeong and Cho reported the use of a pyridinium salt.[15] This pyridinium motif was further used by Steed and co-workers[16] in the synthesis of tripodal-shaped receptor for selective sensing of Cl^- ion. During the course of our work on anion binding we placed these pyridinium motifs onto the different scaffolds for fluorometric assessment of specific anion.[17,18] Later, this idea was extended by Gong and Hiratani for the synthesis of tripodal receptor for dihydrogenphosphate.[19] Selective recognition of dihydrogenphosphate is an important topic and various receptors of different topologies are known in the literature.[20–22] In the present study we report a new fluororeceptor **1** which elegantly shows selective binding of $H_2PO_4^-$, HSO_4^-, and isophthalate in $CHCl_3$ containing 2% CH_3CN. Binding-induced significant change in emission intensity of **1** at 513 nm clearly distinguishes $H_2PO_4^-$, HSO_4^-, and isophthalate from other anions studied.



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The receptor **1** was synthesized according to Scheme 1. Initially, 2,2′-diphenic acid was converted to the corresponding diacid chloride **2** which was subsequently coupled with 3-aminopyridine in dry CH_2Cl_2 in the presence of Et_3N to afford the diamide **3**. Diamide **3** was isolated in low yield due to poor reactivity of 3-aminopyridine. After work-up, unreacted 3-aminopyridine was recovered. On refluxing diamide **3** in the presence of 9-chloromethylanthracene in dry CH_3CN and DMF solvent mixture for 36 h, the chloride salt **4** was obtained in 22% yield. Due to poor solubility of diamide **3** in CH_3CN the chloride salt **4** was isolated in low yield. The anion exchange using NH_4PF_6 gave the receptor **1** as light yellow solid. Compound **1** was fully characterized by ^1H NMR, ^{13}C NMR, and mass spectroscopy.[23]

Prior to study the complexation, gas phase optimization of **1** was performed at AM1 level.[24] The conformational behavior of

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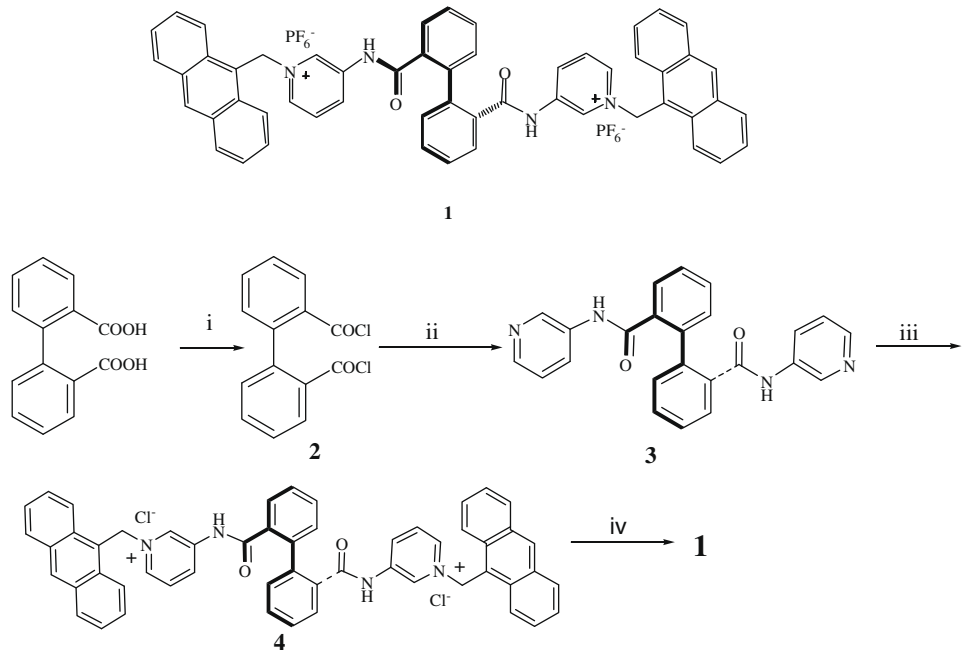

Scheme 1. Reagents and conditions: (i) PCl_5, dry C_6H_6; (ii) 3-aminopyridine, Et_3N, in dry CH_2Cl_2 (isolated yield: 39%); (iii) 9-chloromethylanthracene in dry CH_3CN and DMF mixture, reflux for 36 h (isolated yield: 22%); and (iv) NH_4PF_6, aq CH_3OH (yield: 57%).

biphenyl system provides a well-defined cleft for complexation (Fig. 1). In the energetically favorable conformation anthracenes are aligned in the same face showing a distance of 4.48 Å.

The ability of the receptor **1** toward anion recognition was evaluated by ^1H NMR, fluorescence, and UV–vis spectroscopic methods. The fluorescence spectrum of **1** in $CHCl_3$ containing 2% CH_3CN solution showed a strong emission band at 413 nm attributing to the anthryl group (excitation at 370 nm) along with a weak emission at 513 nm. The emission at 513 nm is aroused due to the formation of excimer between the closely spaced anthracene.[25] Upon addition of $H_2PO_4^-$, HSO_4^-, ClO_4^-, and different dicarboxylates in the form of their tetrabutylammonium (TBA) salts, the emission intensity at 413 nm was increased marginally. In comparison, the emission at 513 nm was enhanced and it varied with the nature of the guest. Figure 2 represents the change in emission of **1** in the presence of 10 equiv amounts of different guests. As can be seen from Figure 2, only upon addition of $H_2PO_4^-$ a marked change in emission at 513 nm is observed. Other anions such as acetate and different dicarboxylates exhibit weak effect. Among the isomeric aromatic dicarboxylates, iso-

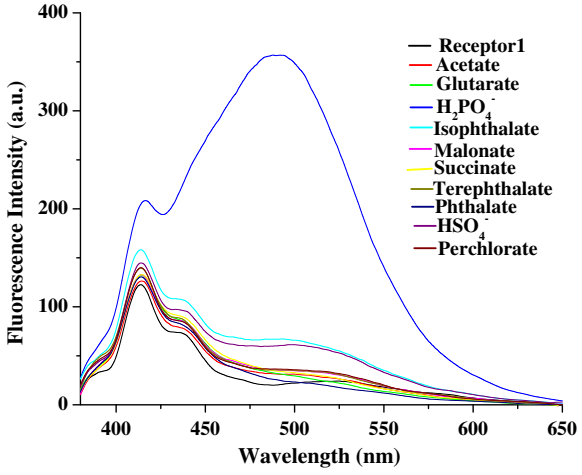

Figure 2. Change in fluorescence emission of **1** ($c = 6.617 \times 10^{-5}$ M) in the presence of 10 equiv amounts of tetrabutylammonium salt of different guests.

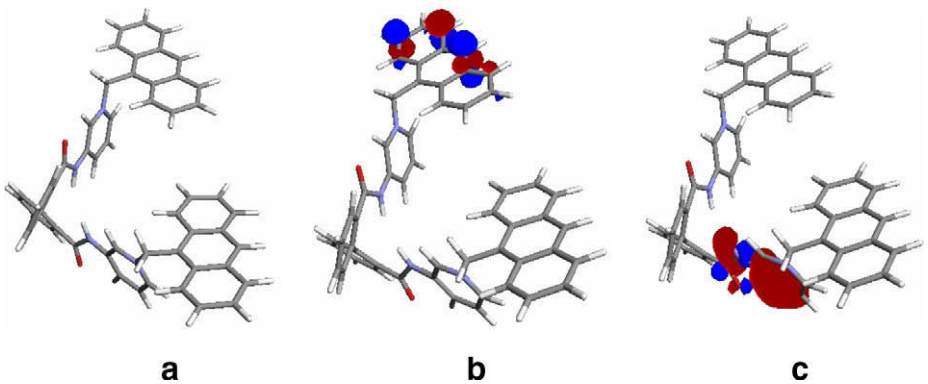

Figure 1. (a) AM1-optimized geometry ($E = -327.542$ au), (b) positions of HOMO, and (c) LUMO in **1**.

phthalate shows stronger interaction. A similar effect is observed in the presence of HSO_4^-. Perchlorate anion did not show any measurable interaction. Figure 3 shows the comparison of change in emission of **1** at 513 nm in the presence of 10 equiv amounts of a particular guest in $CHCl_3$ containing 2% CH_3CN. It is evident from Figure 3 that the receptor **1** has a clear-cut selectivity for $H_2PO_4^-$. Figures 4 and 5 display the change in emission of **1** upon gradual addition of $H_2PO_4^-$ and isophthalate into the solution of **1** in $CHCl_3$ containing 2% CH_3CN, respectively.

The observed increase in emission upon complexation is attributed to the inhibition of PET process occurring in-between the excited state of anthracene and pyridinium amide-binding site. The assignment of HOMO and LUMOs in the optimized geometry of **1** (see Fig. 1) clearly demonstrates the direction of PET process in the uncomplexed state. The strong enhancement of emission at 513 nm in the presence of tetrahedral-shaped $H_2PO_4^-$ is corroborated by its strong hydrogen bonding and charge–charge interactions into the binding cleft according to the mode A (host/guest = 1:1) shown in Figure 6. At the higher concentration of $H_2PO_4^-$ the binding may take place via mode B involving either 1:1 (guest/host) or 2:1 (guest/host) binding stoichiometry and this may remain in equilibrium with mode A in solution (Fig. 6). However, binding of $H_2PO_4^-$ in mode A results in a subtle conformational change of **1** for which anthracene moieties are pulled more closely for the formation of stable and stronger excimer.

This is indeed found less effective in the presence of dicarboxylates although isophthalate exhibited a weak change in emission of the excimer. This has presumably happened due to bulkier nature of the dicarboxylate guest that weakens the binding in the mode A as shown in Figure 6. This was supported by the titration experiment of **1** with AcO^-. Upon increasing the addition of AcO^- to the solution of **1** the excimer emission at 513 nm was almost unperturbed (see Supplementary data). This underlines the fact that simultaneous coordination of the two arms of **1** via hydrogen bonding and charge–charge interactions are necessary for a change in emission intensity at 513 nm.

To realize the ground state interaction, simultaneous UV–vis titration experiments of **1** with the guests were carried out under controlled conditions. The change in absorbance of **1** was appreciable in the presence of $H_2PO_4^-$ anion. Other anions, that is, the different dicarboxylates (both aliphatic and aromatic) interacted weakly thereby resulting in minor changes in UV–vis spectra of **1** (see Supplementary data). Figure 7 shows the UV–vis titration spectra of **1** upon gradual addition of $H_2PO_4^-$. Inset of Figure 5 indicates the change in absorbance of **1** in the presence of isophthalate.

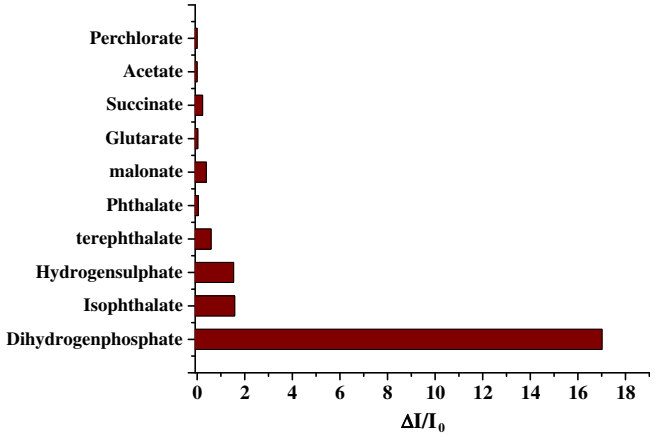

Figure 3. Fluorescence ratio ($\Delta I/I_0$) of receptor **1** ($c = 6.617 \times 10^{-5}$ M) at 513 nm upon addition of 10 equiv tetrabutylammonium salt of a particular anion.

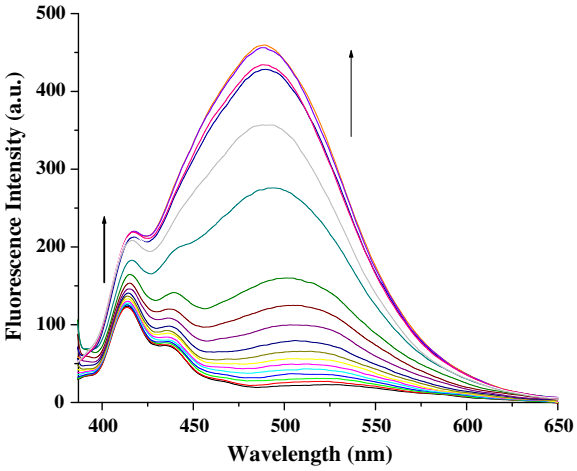

Figure 4. Change in emission of **1** ($c = 6.617 \times 10^{-5}$ M) in the presence of increasing amounts of $H_2PO_4^-$ (10 equiv) in $CHCl_3$ containing 2% CH_3CN.

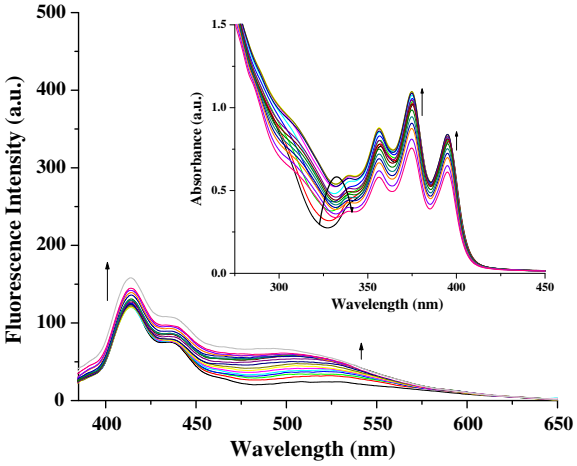

Figure 5. Change in emission of **1** ($c = 6.617 \times 10^{-5}$ M) in the presence of increasing amounts of isophthalate; inset: UV–vis titration spectra of **1** ($c = 6.617 \times 10^{-5}$ M) upon gradual addition of isophthalate (10 equiv) in $CHCl_3$ containing 2% CH_3CN.

In order to understand the binding potencies and selectivities of **1** for the anions studied, fluorescence and UV–vis titration data were used to calculate the binding constant values (Table 1).[26] It is evident from Table 1 that the receptor **1** exhibits a selectivity for $H_2PO_4^-$ accompanying with a higher binding constant value. The binding constant for $H_2PO_4^-$ is particularly found to be higher in the excited state and it is presumably due to more polar character of the receptor in the excited state. On the other hand, isophthalate was bound strongly compared to its isomers and other aliphatic dicarboxylates. It is suggested that when receptor **1** binds with isophthalate, the two binding arms in the non-planar cavity are cooperatively involved for compact chelation for which the appended anthracenes form excimer with significant intensity. This is in contrast to phthalate where the excimer intensity is less compared to the case of isophthalate and the excimer is disrupted at high concentration of phthalate (see Supplementary data). Thus the non-planar arrangement of the binding groups around the biphenyl spacer of **1** has an influence in discriminating the isomeric dicarboxylates. The stoichiometries of the complexes were ascertained from the break of the fluorescence titration curves (Fig. 8). From the broadening nature of the curve for $H_2PO_4^-$ shown in Figure 8, it was difficult to determine the exact stoichiometry of the complex of **1** with $H_2PO_4^-$. For other anions, curvature at [G]/

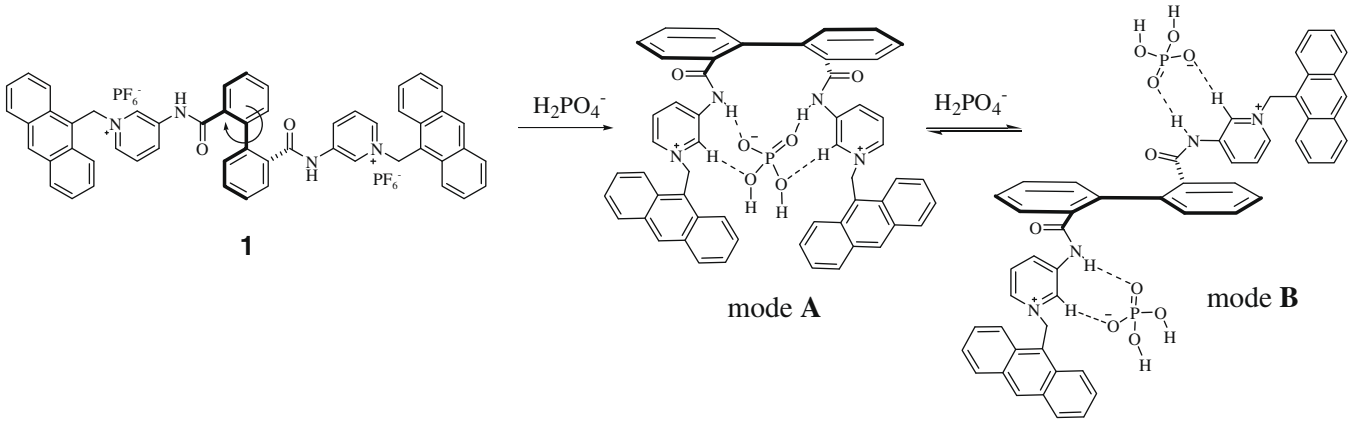

Figure 6. Possible hydrogen bonding modes of complexation of **1** with $H_2PO_4^-$.

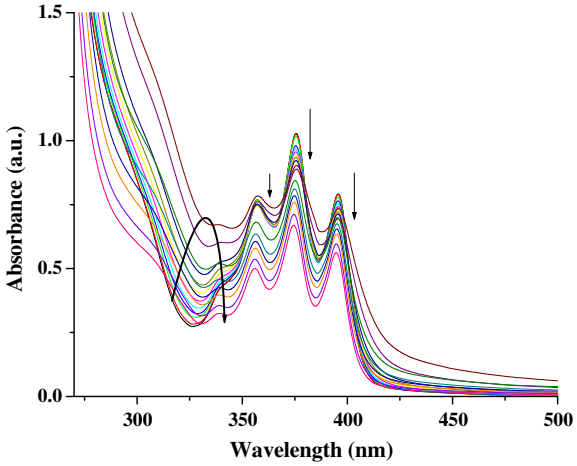

Figure 7. Change in UV–vis spectra of **1** ($c = 6.617 \times 10^{-5}$ M) in the presence of increasing amounts of $H_2PO_4^-$ (10 equiv) in $CHCl_3$ containing 2% CH_3CN.

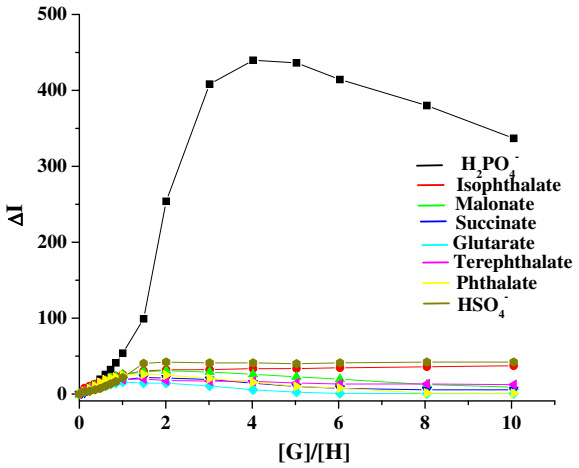

Figure 8. Plot of change in emission of **1** at 513 nm versus the ratio of guest to host concentration.

Table 1
Binding constant values for **1** with the guests in $CHCl_3$ containing 2% CH_3CN

Guests	K_a[a,e] (M^{-1})	K_a[b,e] (M^{-1})
Acetate[d]	6.61×10^2	[c]
Dihydrogenphosphate[d]	8.35×10^3	1.22×10^4
Hydrogen sulfate[d]	1.39×10^3	2.36×10^3
Perchlorate	6.04×10^2	[c]
Isophthalate	2.98×10^3	2.73×10^3
Phthalate	3.40×10^2	8.37×10^2
Terephthalate	9.65×10^2	5.03×10^2
Glutarate	2.45×10^2	1.71×10^2
Malonate	5.29×10^2	3.52×10^2
Succinate	8.31×10^2	6.95×10^2

[a] Determined by UV method at 375 nm.
[b] Determined by fluorescence at 513 nm.
[c] Not determined due to irregular and minor changes.
[d] Based on K_{11}.
[e] Error <10%.

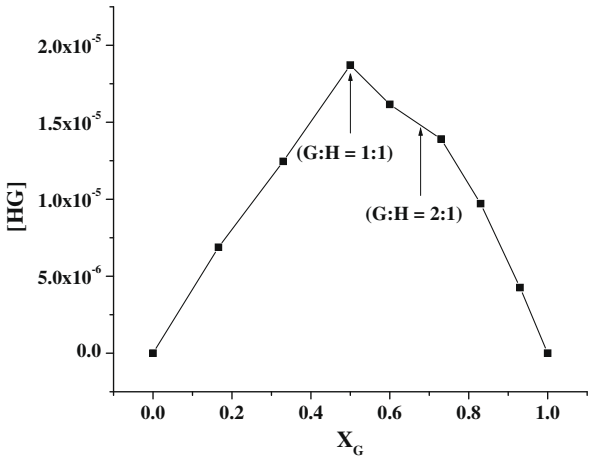

Figure 9. UV–vis Job plot of **1** with $H_2PO_4^-$.

[H] = 1 stated 1:1 binding mode. The 1:1 stoichiometry of the complexes was further proved by Job plots (see Supplementary data). Figure 9 represents the UV Job plot for **1** with $H_2PO_4^-$. In the plot, a maximum at 0.5 mol fraction was observed along with a small inflection at 0.66 mol fraction of the guest. This, indeed, underlines the fact that the receptor **1** initially forms 1:1 complex with $H_2PO_4^-$ ion and then equilibrates to a 2:1 stoichiometry in the presence of excess $H_2PO_4^-$ ion. A similar situation in fluorescence job (Supplementary data) was noticed. Like $H_2PO_4^-$, HSO_4^- exhibited an equilibrium between 1:1 and 2:1 stoichiometries of the complexes (see Supplementary data).

In quest of application of this simple receptor in aqueous system we performed the complexation study of **1** in aq CH_3CN (CH_3CN/H_2O = 4:1 v/v) with different phosphate salts. Surprisingly,

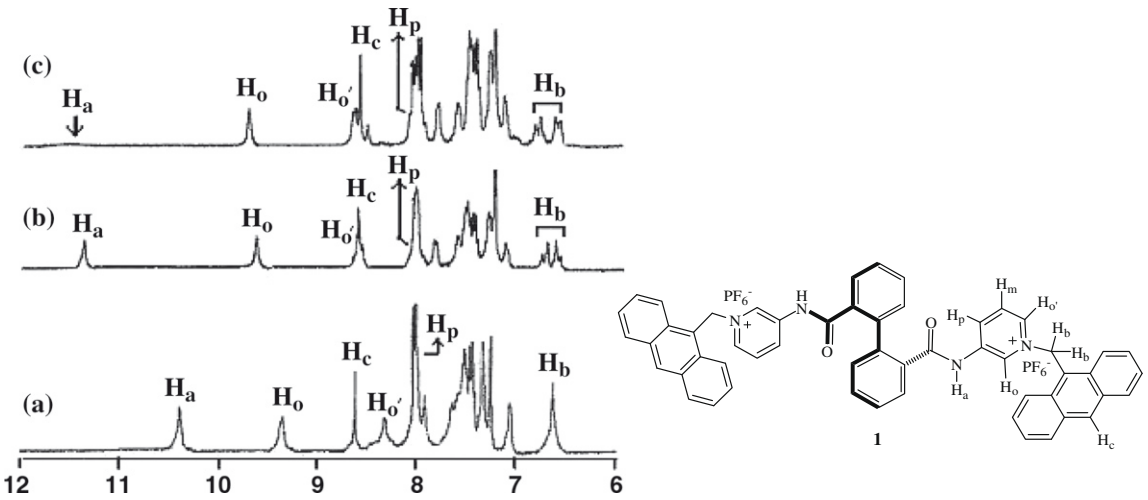

Figure 10. Partial ^{1}H NMR (300 MHz, $CDCl_3$ containing 2% CD_3CN) spectra of (a) **1** and its 1:1 complexes with (b) $H_2PO_4^-$ and (c) isophthalate.

the excimer emission of **1** at longer wavelength was completely destroyed in aq CH_3CN and no measurable change in monomer emission was observed during titration with the phosphate salts (see Supplementary data). This suggested weak or no interactions of **1** in aq CH_3CN.

However, the expected strong interaction between **1** and $H_2PO_4^-$ in $CDCl_3$ containing 2% CD_3CN was further confirmed by ^{1}H NMR (Fig. 10). As shown in Figure 10, the amide proton H_a, pyridinium proton H_o of **1** underwent downfield chemical shifts of 0.97 and 0.28 ppm, respectively, in the presence of equivalent amount of $H_2PO_4^-$. During interaction the pyridinium proton $H_{o'}$ moved to the downfield direction ($\Delta\delta = 0.26$). Similarly, the pyridinium proton H_p, which appeared at 7.92 ppm underwent a downfield chemical shift of 0.13 ppm upon complexation suggesting its involvement in the binding process. This is evident from the molecular modeling (Fig. 1) where one of the binding arms of **1** provides H_p toward the cavity for complexation. A similar findings in ^{1}H NMR were observed when equivalent amount of isophthalate was added to the solution of **1** $\Delta\delta_{H_a} = 0.24$, $\Delta\delta_{H_o} = 0.36$, $\Delta\delta_{H_{o'}} = 0.36$, and $\Delta\delta_{H_p} = 0.09$; Fig. 10c). During the interaction of **1** with the guests, the signal for H_b protons of **1** was split into two doublets suggesting a conformational change for which they become chemically non-equivalent.

In conclusion, we have designed a new type of dihydrogenphosphate receptor with unique recognition and sensing properties. It provides well-defined structure for efficient and selective complexation of $H_2PO_4^-$ with 1:1 binding stoichiometry. Although the sensing and binding of **1** with isophthalate are not extremely strong in the present study, the binding selectivity is high in comparison with isomeric and other dicarboxylate anions. Addition of $H_2PO_4^-$, HSO_4^-, and isophthalate to the solution of **1** in $CHCl_3$ containing 2% CH_3CN causes change in monomer emission of anthracene followed by appearance of excimer. This excimer emission is diagnostic to recognize $H_2PO_4^-$ from other anions in the present study. The high affinity and selectivity of this simple fluororeceptor are due to the combined effects of semi-rigid structures, charge–charge interactions, and the involvement of both N–H···O and C–H···O hydrogen bonds.

Acknowledgments

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Supplementary data

Supplementary data (Figures showing the change in absorption and fluorescence spectra and the Job plots of receptor **1** in presence of the guests, Binding constant curves, Change in emission of **1** in presence of different phosphate salts in aq CH_3CN are available) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.09.043.

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23. Mp 225 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 11.07 (s, NH, 2H), 8.80 (s, 4H), 8.70 (s, 2H), 8.38 (br s, 2H), 8.34 (d, 4H, J = 6.4 Hz), 8.20 (d, 4H, J = 7 Hz), 7.95 (br s, 2H), 7.64–7.58 (m, 10H), 7.45–7.39 (m, 4H), 7.11 (br s, 2H), 6.91 (s, 4H); ^{13}C NMR (DMSO-d_6, 100 MHz): 174.0, 144.7, 143.5, 143.0, 139.3, 138.8, 138.5, 136.5, 136.4, 136.0, 135.6, 134.8, 134.5, 133.4, 133.1, 132.7, 132.5, 130.5, 127.3, 125.3, 61.7; FTIR: ν cm^{-1} (KBr): 3375, 3062, 1665, 1627, 1591, 1556, 1499; m/z (ES$^+$): 921.6 [M−PF_6^-]$^+$, 775.7 [M−1−2PF_6^-]$^+$.
24. AM1 calculation was performed using minimal valance basis as STO 3G in ArgusLab 4.0.1, copyright (c) 1997–2004 Mark Thompson and Planaria Software LLC, http://www.arguslab.com.
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