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New Fluorescent Photoinduced Electron Transfer Chemosensor for the Recognition of $H_2PO_4^-$

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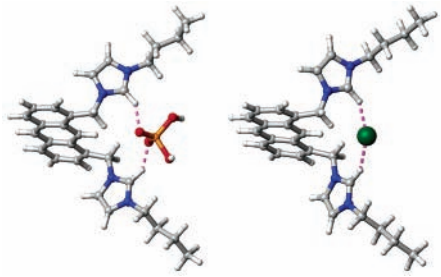
ABSTRACT



The fluorescent chemosensor 1 bearing two imidazolium groups at the 1,8-position of anthracene has been designed for the recognition of anions through the $(C–H)^+\cdots X^-$ hydrogen bond formation. As unique tweezer-like binding of 1 with anions is predicted by the ab initio calculations, strong anion-binding properties of chemosensor 1 are demonstrated by using fluorescence as well as ^1H NMR.

Selective binding of chemical species upon molecular recognition can lead to large perturbations of the host environment, especially when the guest is ionic. Since fluoroionophores can provide chemical information of ion concentrations, they have been an important subject in metal ion analysis.[1] The advent of ligand engineering has also introduced a more systematic approach to the design of receptors for the detection of anions.[2] However, the fluorescent chemosensors for anions have been extensively investigated for only a few years.[3]

In contrast to well-known types of hydrogen bonding for the anion binding such as amide, pyrrole, urea, etc., benzene-based tripodal imidazolium receptors have been utilized for halide anion recognition using the strong $(C-H)^+\cdots X^-$ hydrogen bonding between imidazolium moieties and halide anions.[4]

Utilizing these previous results, we report herein a new fluorescent photoinduced electron transfer (PET) chemosensor for the recognition of $H_2PO_4^-$. Two imidazolium moeities were immobilized on the 1,8-positions of the chemosensor, and a unique feature of the binding mode is predicted on the basis of ab initio calculations.

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(1) (a) *Fluorescent Chemosensors for Ion and Molecular Recognition*; Czarnik, A. W., Ed.; American Chemical Society: Washington, DC, 1993. (b) Czarnik, A. W. *Acc. Chem. Res.* **1994**, *27*, 302. (c) Fabbrizzi, L.; Poggi, A. *Chem. Soc. Rev.* **1994**, 197. (d) de Silva, A. P.; Gunaratne, H. Q. N.; Gunnlaugsson, T. A.; Huxley, T. M.; McCoy, C. P.; Rademacher, J. T.; Rice, T. E. *Chem. Rev.* **1997**, *97*, 1515. (e) *Chemosensors of Ion and Molecular Recognition;* Desvergne, J.-P., Czarnik, A. W., Eds.; Kluwer Academic Publishers: Dordrecht, The Netherlands, 1997.

(2) For recent reviews for anion receptors, see: (a) Beer, P. D.; Gale, P. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 486. (b) Snowden, T. S.; Anslyn, E. V. *Chem. Biol.* **1999**, *3*, 740. (c) Antonisse, M. M. G.; Reinhoudt, D. N. *Chem. Commun.* **1998**, 143. (d) Schmidtchen, F. P.; Berger, M. *Chem. Rev.* **1997**, *97*, 1609. (e) Rudkevich, D. M.; Brzozka, Z.; Palys, M.; Visser, H. C.; Verboom, W.; Reinhoudt, D. N. *Angew. Chem., Int. Ed.* **1994**, *33*, 467.

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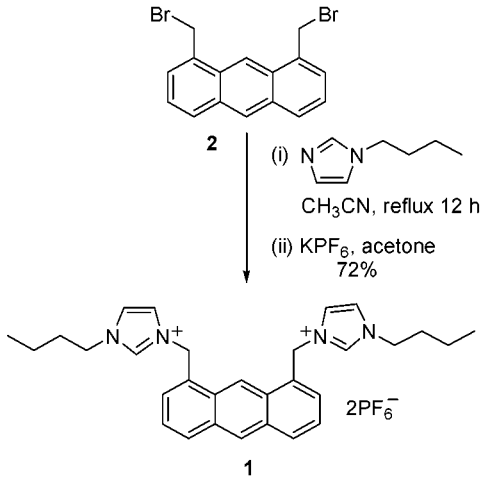
For the synthesis of chemosensor **1**, 1,8-bis(bromomethyl) anthracene was synthesized following the published procedure.[5] This intermediate was reacted with *n*-butyl imidazole followed by anion exchange with KPF_6, which gave bisimidazolium anthracene **1** in 72% yield (Scheme 1).

Scheme 1. Synthesis of 1,8-Bisimidazolium Anthracene **1**



The ab initio calculations[6] predict high binding affinity of host **1** with $H_2PO_4^-$ and F^- ions. The binding energies in the gas phase for $H_2PO_4^-$, F^-, Cl^-, and Br^- are 165.5, 181.5, 150.3, and 145.0 kcal/mol, respectively; on the other hand, these values in acetonitrile decrease dramatically to 16.1, 16.5, 8.3, and 7.0 kcal/mol, respectively (Table 1). Since ionic hydrogen bond strength is dependent on solvent polarity, the binding energies are much reduced in polar solvents.

Table 1. Calculated Interaction Energies and Experimental Free Energy Changes for the **1**−Anion Complexes in kcal/mol[a]

	$H_2PO_4^-$	F^-	Cl^-	Br^-	I^-
$-\Delta E^{gas}_{calcd}$	165.50	181.48	150.27	145.02	
$-\Delta E^{MeCN}_{calcd}$	16.14	16.54	8.30	7.06	
$-\Delta G^{scaled}$	10.50	10.75	5.40	4.59	
$-\Delta G^{NMR}_{expt}$			4.77	4.27	3.54
K_a $(M^{-1})^a$	~1 300 000		7900	4500	600
$-\Delta G^{flou}_{expt}$	~ 8.34		5.31	4.98	3.79

[a] Association constants K_a (M^{-1}) were measured using the fluorescence titrations. ΔG^{NMR}_{expt} and ΔG^{flou}_{expt} are the changes in Gibbs' free energy in acetonitrile solution measured by NMR and fluorescence titrations, respectively. ΔE^{gas}_{calcd} is the interaction energy in the gas phase calculated by the B3LYP/6-31(+)G* method. $\Delta E^{MeCN}_{calcd} = \Delta E^{MeCN}_{\mathbf{1}-anion} - \Delta E^{MeCN}_{\mathbf{2}MeCN-anion}$, where $\Delta E^{MeCN}_{\mathbf{1}-anion}$ is the interaction energy of the **1**−anion complex in acetonitrile solution based on an isodensity surface polarized continuum model (IPCM), and $\Delta E^{MeCN}_{\mathbf{2}MeCN-anion}$ is the interaction energy of the anion with two acetonitrile molecules in acetonitrile solution. We subtracted the $\Delta E^{MeCN}_{\mathbf{2}MeCN-anion}$ from the $\Delta E^{MeCN}_{\mathbf{1}-anion}$ value in order to establish the proper theoretical selectivity of the host for the anions. To compare the calculated ΔE value with the experimental ΔG value, the ΔG^{scaled} was evaluated by scaling with 65% of the ΔE^{MeCN}_{calcd}.

The calculated structures of host **1** with dihydrogen phosphate and chloride anion demonstrate a quite interesting feature of these bindings. As shown in Figure 1, unique *tweezer-like binding* modes of host **1** with dihydrogen phosphate and chloride anion are observed. Figure 2 shows the calculated interaction distances and partial atomic charges of the important sites involved in host−guest interaction of the **1**−$H_2PO_4^-$ complex. Though the $(C-H)^+$- - -O=P interaction in **1**−$H_2PO_4^-$ is dominated by H- - -O interaction at a distance of 1.85 Å, the interaction between the oxygen atom (charge, −0.66) of O=P of $H_2PO_4^-$ and the carbon atom (charge, 0.26) of imidazolium $(C-H)^+$ is also strong,

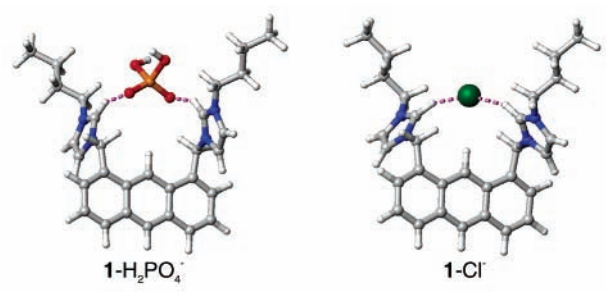


Figure 1. Calculated structures of **1** with dihydrogen phosphate and chloride anion.

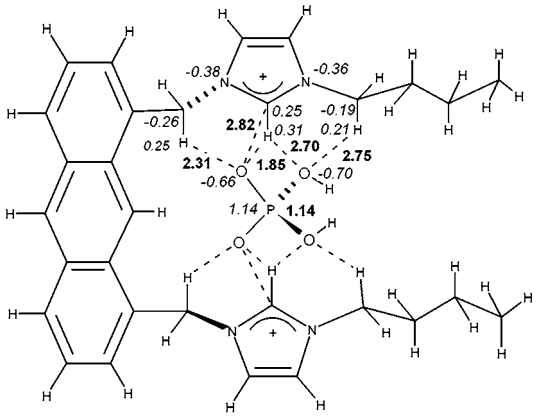


Figure 2. **1**−$H_2PO_4^-$ complex (C_2-symmetry) showing interaction distances (bold) and atomic charges (*italic*) of the important sites involved in host−guest interaction.

(3) (a) Kim, S. K.; Yoon, J. *Chem. Commun.* **2002**, 770. (b) Gunnlaugsson, T.; Davis, A. P.; O'Brien, J. E.; Glynn, M. *Org. Lett.* **2002**, *4*, 2449 and references therein. (c) Gunnlaugsson, T.; Davis, A. P.; Glynn, M. *Chem. Commun.* **2001**, 2556. (d) Nishizawa, S.; Kaneda, H.; Uchida, T.; Teramae, N. *J. Chem. Soc., Perkin Trans. 2* **1998**, 2325. (e) Fabbrizzi, L.; Faravelli, H.; Francese, G.; Licchelli, M.; Perotti, A.; Taglietti, A. *Chem. Commun.* **1998**, 971. (f) Cooper, C. R.; Spencer, N.; James, T. D *Chem. Commun.* **1998**, 1365. (g) Wu, F.-Y.; Li, Z.; Wen, Z.-C.; Zhou, N.; Zhao, Y.-F.; Jiang, Y,-B. *Org. Lett.* **2002**, *4*, 3203. (h) Causey, C. P.; Allen, W. E. *J. Org. Chem.* **2002**, *67*, 5963.

with an interaction distance of 2.82 Å. Other interactions as shown in Figure 2 (such as that between the CH_2 hydrogen atoms and the oxygen atoms for both O═P and OH of $H_2PO_4^-$) also enhance the stability of the **1**−$H_2PO_4^-$ complex.

Relatively large chemical shifts of benzylic CH_2 peaks in ^{1}H NMR support the calculated tweezer-like binding. Partial ^{1}H NMR spectra are shown in Figure 3, and each peak is

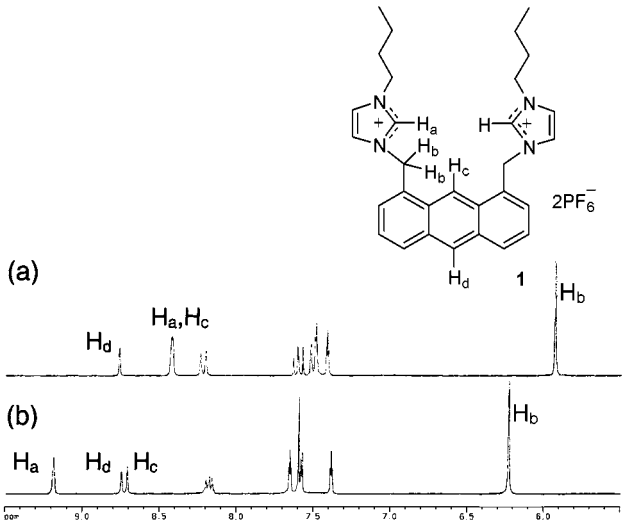


Figure 3. Partial ^{1}H NMR (250 MHz) of **1** (1 mM) in CD_3CN. (a) compound **1** only; (b) **1** + 2 equiv of tetrabutylammonium bromide.

assigned on the basis of the COSY spectrum of **1**. Upon the addition of bromide anions, large downfield shifts of the N(3) of the imidazolium ring clearly suggest the **1**−anion complexation by CH^+−anion charged hydrogen bonds. From the ^{1}H NMR titrations in CD_3CN, the association constants for Cl^-, Br^-, and I^- are calculated as 3130, 1360, and 390 M^{-1} (errors < 10%), respectively. In addition, the Job plot analysis indicates formation of 1:1 complexes.

Since host **1** is fluorescent, the binding affinity of **1** toward various anions is further investigated using fluorescence changes. The fluorescence titration experiments of **1** (0.1 μM) with I^-, Br^-, Cl^-, and $H_2PO_4^-$ are performed in acetonitrile. Figure 4 explains the fluorescence titration experiments of

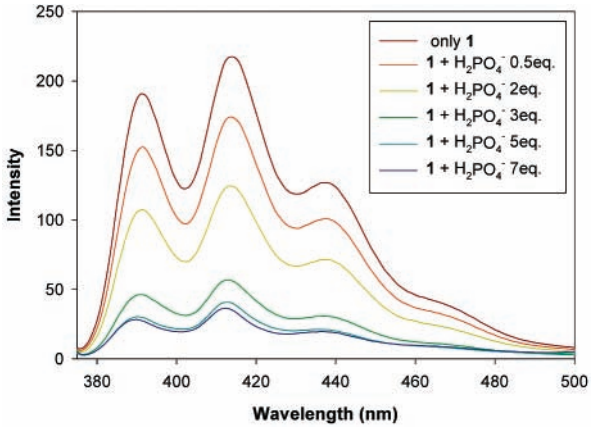


Figure 4. Fluorescent titrations of compound **1** (0.1 μM) with tetrabutylammonium dihydrogen phosphate in acetonitrile.

host **1** with $H_2PO_4^-$.[7] The association constants for $H_2PO_4^-$, Cl^-, Br^-, and I^- are found to be ~1 300 000, 7900, 4500, and 600 M^{-1} (errors < 10%), respectively.[8] The changes in Gibbs free energies for anions as determined by the fluorescence titrations were somewhat greater than those obtained from NMR titrations (Table 1). The experimental results are consistent with the calculated values. The changes in Gibbs free energy for Cl^- and Br^- as determined by NMR/fluorescence titrations are 4.77/5.31 and 4.27/4.98 kcal/mol, respectively, which is in good agreement with calculated values (5.40 and 4.59 kcal/mol, respectively). The calculations predict that the host **1** also binds tightly to F^-. Unfortunately, we were not able to obtain a consistent and reliable association constant for F^- from fluorescent titration experiments since the emission intensity did not consistently

(4) (a) Yun, S.; Ihm, H.; Kim, H. G.; Lee, C. W.; Indrajit, B.; Oh, K. S.; Gong, Y. J.; Lee, J. W.; Yoon, J.; Lee, H. C.; Kim, K. S. *J. Org. Chem.* **2003**, *68*, 2467. (b) Ihm, H.; Yun, S.; Kim, H. G.; Kim, J. K.; Kim, K. S. *Org. Lett.* **2002**, *4*, 2897. (c) Sato, K.; Arai, S.; Yamagishi, T. *Tetrahedron Lett.* **1999**, *40*, 5219.

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

(6) Density functional calculations (B3LYP/6-31(+)G*) and self-consistent reaction field (SCRF) calculations (solvent, acetonitrile; dielectric constant, 36.6) were carried out. See refs 5a,b and: Kim, K. S.; Tarakeshwar, P.; Lee, J. Y. *Chem. Rev.* **2000**, *100*, 4145.

(7) As the receptor sites are separated from the anthracene fluorophore by two −CH_2− spacers, the only interaction between the two moieties would be via electron transfer. Because of the positive center in the imidazolium ring at the binding center of the receptor, there is less quenching effect on the fluorophore. When the anion interacts with the atoms in the binding site, the formation of the (C−H)$^+$- - -X^- hydrogen bond would result in an increase in electron density at the connecting nitrogen atom between the binding site and fluorophore. This would produce the quenching effect on the fluorophore, decreasing the fluorescent intensity when the receptor is bound to the anion. This is also supported by the ab initio calculated atomic charge on the nitrogen atom in the bound form of the receptor, i.e., −0.384 for $H_2PO_4^-$, −0.377 for F^-, −0.374 for Cl^-, and −0.372 for Br^- compared to the nitrogen atomic charge (−0.355) in the free form of the receptor.

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

(9) In consideration of the atomic charges of the connecting nitrogen atoms between the bonding site and fluorophore, if PET is the only mechanism for the binding of the anion with the receptor, $H_2PO_4^-$ should be bound more than other anions. But calculated results show that F^- anion also binds to the receptor in a magnitude equal to that of $H_2PO_4^-$. This shows that PET alone cannot explain the **1**−F^- complexation with 1:1 stoichiometry. As in the case of F^- anion, the (C−H)$^+$- - -X^- hydrogen bond is very strong, and each of the binding sites in the receptor should be able to bind one F^- anion; therefore, the possibility of forming a 1:2 complex cannot be ruled out. In the case of a 1:2 complex of the **1**−F^- system, the binding affinity per fluoride anion would decrease drastically, resulting in a much lesser and different quenching effect than that of other anions. Our calculation shows that the binding energy of the **1**−2F^- is 273.67 kcal/mol (136.84 kcal/mol per F^- anion) and 16.46 kcal/mol in acetonitrile solvent (8.23 kcal/mol per F^- anion). Almost similar binding energies between the 1:1 and 1:2 complexes of the **1**−F^- in acetonitrile solvent show that there is a possibility for an equilibration between these two binding modes. This could be the reason the fluorescence emission intensity for the F^- ion is much lower than that of $H_2PO_4^-$ at an equivalent molar concentration and does not decrease consistently with the increase in F^- ion during the fluorescence titration.

decrease upon the increase of F^- ion.[9] The NMR experiment for the F^- anion was not properly observed because of precipitation during the NMR titration.

We note that, as predicted in calculations, host **1** shows a selective binding with the $H_2PO_4^-$ ion over Cl^-, Br^-, and I^- ions (Table 1). The selectivity for $H_2PO_4^-$ ion is around 200 times that for other anions such as Br^- or Cl^-.

It is worth noting that the anthracene moiety in host **1** acts not only as a fluorescent source but also as a template for introducing the binding selectivity. Host **1** can provide a preorganized and relatively rigid binding site for anions. Thus, strong $(C-H)^+ - - -X^-$ hydrogen bondings between imidazolium moieties and anions as well as the preorganized binding site in host **1** are the main reasons for high K_a values and selectivity in its binding.

In conclusion, we have shown that 1,8-bis-imidazolium anthracene **1** effectively and selectively recognizes the biologically important $H_2PO_4^-$ ion over other anions such as I^-, Br^-, or Cl^- in acetonitrile. Furthermore, these binding phenomena can be easily monitored via fluorescence quenching effects.

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Supporting Information Available: Experimental procedures and full characterization data for compound **1**. This material is available free of charge via the Internet at http://pubs.acs.org.

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