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Quinoxaline–Imidazolium Receptors for Unique Sensing of Pyrophosphate and Acetate by Charge Transfer

N. Jiten Singh,[†] Eun Jin Jun,[‡] Kavitha Chellappan,[†] Daniel Thangadurai,[†] R. Prakash Chandran,[†] In-Chul Hwang,*[,†] Juyoung Yoon,*[,‡] and Kwang S. Kim*[,†]

Center for Superfunctional Materials, Department of Chemistry, Pohang University of Science and Technology, San 31, Hyojadong, Namgu, Pohang 790-784, Korea, and Division of Nano Science and Department of Chemistry, Ewha Womans University, 11-1 Daehyon-Dong, Sodaemun-Ku, Seoul 120-750, Korea

spfe@postech.ac.kr; jyoon@ewha.ac.kr; kim@postech.ac.kr

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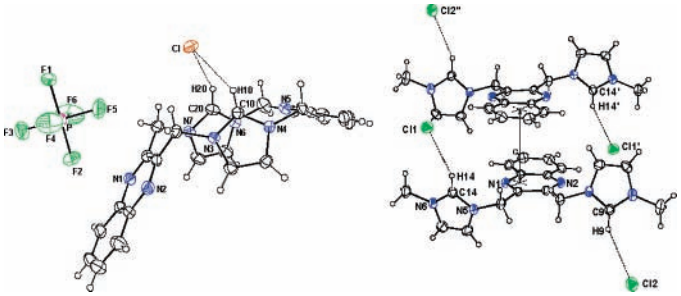
ABSTRACT



Quinoxaline derivatives (1–4) bearing two imidazolium moieties are found to strongly bind anions and show unique charge-transfer fluorescent responses to pyrophosphate and acetate, whereas they show excimer formation with other anions. Anion-binding studies are investigated with fluorescence and ^{1}H NMR analysis, single-crystal X-ray analysis, and theoretical calculations.

Anions play a fundamental role in a wide range of chemical and biological processes, and numerous efforts have been devoted to the development of abiotic receptors for anionic species.[1] Sensors based on anion-induced changes in fluorescence[2] and intramolecular/intermolecular excimer formation[3] appear to be particularly attractive. On the other hand, given that carboxylic acids (or carboxylates) are a common functional group in biological and synthetic organic molecules, the development of simple to sophisticated receptors for carboxylates has attracted immense attention.[4]

The imidazolium group can make a strong interaction with anions through the $(C-H)^+-X^-$-type ionic hydrogen bonding involving the dominating charge−charge electrostatic interaction[5] which is in contrast to well-known neutral receptors involving typical hydrogen bonding for the anion

[†] Pohang University of Science and Technology.
[‡] Ewha Womans University.

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binding such as amide, pyrrole, urea, etc.[1,2] Recently, we have reported anion-sensing capabilities of imidazolium receptors[6] by monitoring fluorescent intensity due to the photoinduced electron transfer (PET) mechanism.[6,7]

Herein, we report four new fluorescent anion receptors [**1** (open form), **2**, **3**, and **4** (closed form) (Figure 1)] bearing

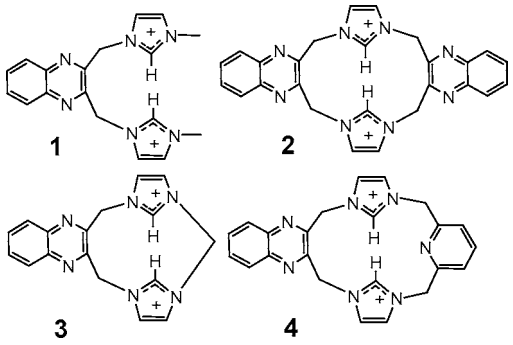

Figure 1. Host systems of the fluorescent imidazolium receptors.

two imidazolium groups at the 2,3-positions of quinoxaline. The crystal structures of **1**−Cl^-, **2**−PF_6^-−CH_3CN, and **4**−Cl^-/Br^- complexes have been isolated and characterized (Figure 2). The binding properties of these host systems toward various anions have been analyzed using fluorescence and ^{1}H NMR titration techniques. Though the quinoaxaline moiety has been explored as the fluorescent/chromogenic signaling unit[8] for the anion sensing, our receptors are the first example which shows the anion-induced excimer formation/charge-transfer phenomena among quinoxaline systems.

The synthesis of compounds **1**, **2**, **3**, and **4** started from 2,3-bis(bromomethyl)quinoxaline, which was reacted with 1-(methyl)-1*H*-imidazole, 2,3-bis(imidazolylmethyl)quinoxaline, 1-(1*H*-imidazol-1-ylmethyl)-1*H*-imidazole, and 2,6-bis-

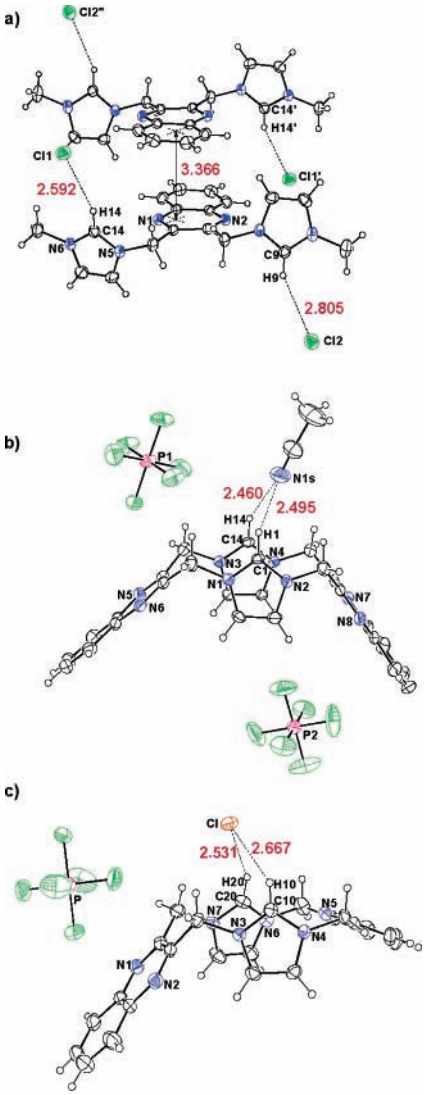

Figure 2. (a) Crystal structure of **1**·2(Cl^-)·2(H_2O), (b) **2**·2(PF_6^-)·(CH_3CN), and (c) **4**·(Cl^-)·(PF_6^-) (thermal ellipsoids set at 30% probability). H-bond distances (Å) are shown.

(imidazolylmethyl)pyridine in CH_3CN followed by anion exchange of Br^- with PF_6^-.

In the single-crystal structure of **1**·2(Cl^-)·2(H_2O) (Figure 2a) which was obtained at −30 °C, each imidazolium moiety is involved in the (C−H)$^+$···Cl^- ionic hydrogen bonding (H-bond distances: 2.592/2.805 Å). It has an intermolecular $\pi-\pi$ stack interaction[9] (distance = 3.366 Å, displaced angle 20°) between the two antiparallel quinoxaline rings.[10]

The crystal structure of **2**·2(PF_6^-)·(CH_3CN) (Figure 2b) adopts a C_{2v}-symmetry conformation with two imidazolium (C−H)$^+$ groups pointing toward the top of the macrocycle. One of the counter anions is located inside the cage, and the other is located at the side of the imidazolium ring. One acetonitrile molecule is also coordinated to the positively

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(10) See the Supporting Information for the detailed crystal data and fluorescence data.

charged imidazolium hydrogen, where the hydrogen-bonding distances and angles are (N1s−H1 = 2.460 Å, N1s−H14 = 2.495 Å, ∠(C1−H1−N1s) = 151.3°, and ∠(C14−H14−N1s) = 143.5°).

In both single crystals of **4**·(Cl^-)·(PF_6^-) and **4**·(Br^-)·(PF_6^-) (Figure 2c), the two $(C-H)^+$ imidazolium protons pointed toward the corresponding anions, where the interionic distances and angles are Cl−H10 = 2.667 Å, Cl−H20 = 2.531 Å, ∠(C10−H10···Cl) = 148.3°m and ∠(C20−H20···Cl) = 149.6° for the Cl-receptor and Br−H7 = 2.667 Å, Br−H20 = 2.531 Å, ∠(C7−H7···Br) = 151.5°, and ∠(C20−H20···Br) = 151.3° for bromide.[10]

The fluorescent study of **1**−**4** in the presence of anions (100 equiv) (Figure 3 and Figure S1, Supporting Information)[10] shows anion induced excimer formation (∼430 nm) with almost all the anions with the exceptions of $HP_2O_7^{3-}$ and $CH_3CO_2^-$ (Figure 4). However, **1** shows a distinct and intense peak at 500 nm with $HP_2O_7^{3-}$, whereas **3**, with $CH_3CO_2^-$. It seems that anions induce the formation of the excimer state due to the intermolecular $\pi-\pi$ stacking between two antiparallel quinoxaline rings, similar to what is seen in the crystal structure of **1** (ground state) complexing with Cl^- (Figure 2a). We rule out the possible formation of the intramolecular excimer in **2** as the distance (9.78 Å) between the center of mass of two quinoxaline rings is not appropriate for such formation.[11]

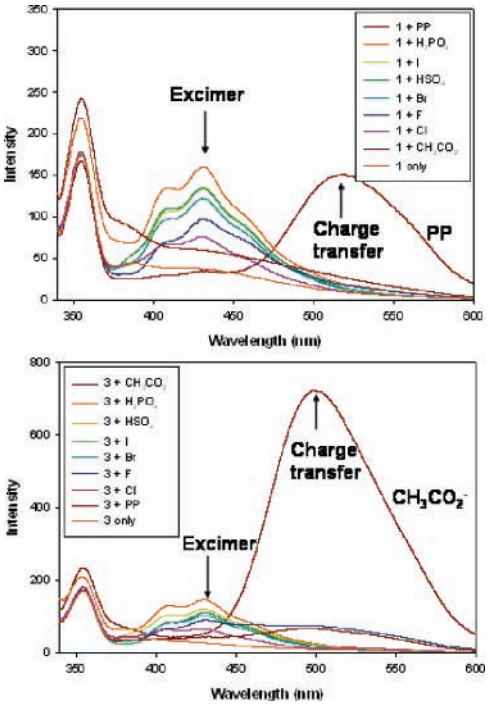

Figure 3. Fluorescent emission changes of **1** and **3** (3 μM) upon the addition of tetrabuthylammonium salt of HSO_4^-, $CH_3CO_2^-$, I^-, Br^-, Cl^-, F^-, $H_2PO_4^-$, and $HP_2O_7^{3-}$ (100 equiv) in acetonitrile (excitation at 320 nm, excitation and emission slit: 10 nm).

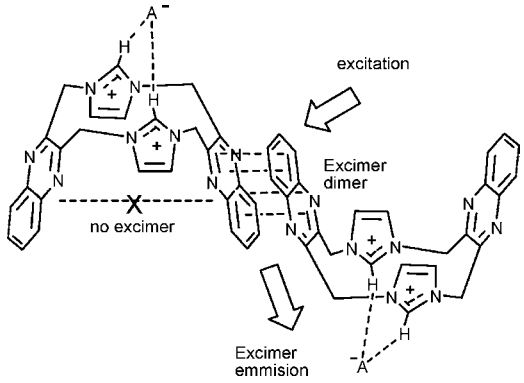

Figure 4. Proposed mechanism of the anion-induced excimer formation.

We observe the proton-transfer phenomena in **3** upon the addition of acetate in acetonitrile, where the C-2 hydrogen peak (8.7 ppm) disappears even with the low concentration of acetate. However, at higher concentration the peak appears again with downfield shift (10.0 ppm at 0.6 equiv and 10.4 ppm at 1 equiv). On the other hand, we were not able to monitor the C-2 hydrogen peak changes of **1** upon addition of $HP_2O_7^{3-}$ due to precipitation at the working concentration. Nevertheless, the deprotonation of **1**/**3** in the presence of only $HP_2O_7^{3-}$/acetate[12] could be closely related with the appearance of distinct fluorescent peak (∼500 nm) due to rapid charge-transfer phenomena from quinoxaline to deprotonated imidazolium moiety.[13] A similar kind of rapid charge transfer from quinoxaline to diketone units has been observed recently with the associated new fluorescent peak ∼500 nm.[11]

We performed the ^{1}H NMR titrations with a few selected anions to have a rough estimate of the binding constant. The binding constants of these receptors for the anions in acetonitrile are listed in Table 1. Even though the reported binding constants are larger than 10^5 (M^{-1}), we have reported them as calculated from the fitted data. The binding constants for $H_2PO_4^-$ and $HP_2O_7^{3-}$ were not determined due to precipitation during the ^{1}H NMR titration. The ^{1}H NMR competitive binding studies of F^- or acetate with $H_2PO_4^-$ or $HP_2O_7^{-3}$ for **2**−**4** show that these anions are competitive to each other, which is justified with the disappearance of the corresponding $(C-H)^+$ peak induced by acetate/F^- at 1:1 host/acetate/F^- in acetonitrile upon the addition of 1

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(12) B3LYP/6-31(+)G* calculations show that the deprotonated form of **1**−$HP_2O_7^{3-}$complex is formed during the optimization, while for **1**−CH_3COO^- the normal complex is the only stable form. On the other hand, the deprotonated forms of **3**−CH_3COO^- is ∼0.3 kcal/mol more stable than the normal complex in acetonitrile, while for **3**−$HP_2O_7^{3-}$ the normal complex is slightly more stable than that of the deprotonated complex counterparts (see the Supporting Information for details). This could lead to the shoulder (∼500 nm) in the fluorescent spectra of **3** with $HP_2O_7^{3-}$ (Figure 3). However, the intensity of this additional shoulder is not significant in comparison with the distinct charge-transfer peak associated with acetate.

(13) The charge transfer peaks of **1**/**3** with $HP_2O_7^{3-}$/$CH_3CO_2^-$ were visible (∼85% reduction in intensity) in the presence of 0.25% water and then completely disappear in the presence of 1% water. The excimer peaks of **1** and **3** with other anions however remain observable even with the presence of 10% water (Figures S2 and S3.).

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

host	anion	K_a (10^3 M^{-1})[a]	$-\Delta G_{expt}$[b]	$-\Delta E^{gas}_{calc}$	$-\Delta E^{sol}_{calc}$	$-\Delta G^{scaled}$
2	$H_2PO_4^-$			183.0	14.4	9.4
	CH_3COO^-	764	8.02	182.5	13.6	8.9
3	$H_2PO_4^-$			191.2	16.4	10.6
	CH_3COO^-	187	7.19	201.6	15.5	10.1
	F^-	162	7.10	202.6	14.2	9.2
4	$H_2PO_4^-$			174.4	12.2	7.9
	CH_3COO^-	396	7.63	180.0	11.2	7.3
	F^-	758	8.02	186.3	12.3	8.0

[a] The association constants K_a (10^3 M^{-1}) were measured using the ^1H NMR titration (25 °C). Errors estimated to be <20%. ΔE^{gas}_{calc} is the interaction energy in the gas phase at the B3LYP/6-31(+)G* level of theory. $\Delta E^{sol}_{calc} = \Delta E^{sol}_{host-anion} - \Delta E^{sol}_{sol-anion} - \Delta E^{sol}_{TBA-anion}$, where $\Delta E^{sol}_{host-anion}$ is the interaction energy of the host−anion complex in the acetonitrile solution based on the isodensity surface-polarized continuum model (IPCM) and $\Delta E^{sol}_{sol-anion}$ is the interaction energy of the anion with solvent molecules in the first solvation shell. $\Delta E^{sol}_{TBA-anion}$(sol = acetonitrile) is the interaction energy of tetrabutylammonium with the anion in solution. The countercation correction was applied only to F^-, since this correction is not significant for other anions.[6] The free energy change (ΔG^{scaled}) was approximately obtained by scaling the internal energy change.[7]

equiv of $H_2PO_4^-$/$HP_2O_7^{3-}$ and the appearance of turbidity in the solution.

Imidazolium-based receptors have strong tendency to form ionic hydrogen bonding with anions, which is explained by the ^1H NMR chemical shift of the imidazolium C-2 hydrogen. However, the precipitation of the receptors upon the addition of even a low concentration of $H_2PO_4^-$ and $HP_2O_7^{3-}$ has raised questions about the nature of the interaction between the host and guest. Therefore, theoretical investigation for the most stable conformer of the host−guest complex is crucial in order to understand the nature of the binding interaction.[7c] The optimized geometry of **2**−CH_3COO^- (Figure 5) shows a strong $(C-H)^+\cdots$anion ionic hydrogen bond. However, the interaction of **1**, **2**, and **3** with $H_2PO_4^-$ (Figure 5) is quite surprising as it forms a complex such that the orientation of the oxygen atoms in $H_2PO_4^-$ is not linear but is angled against the maximal H-bonding with the imidazolium C-2 hydrogen atoms,[9] thereby forming the ion-pair complex of host and anion (i.e., not the H-bonding complex), which is more popularly known among ammonium-containing anion receptors.[14]

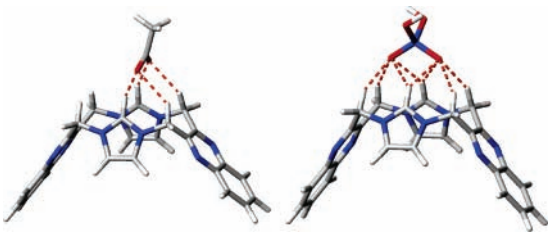

Figure 5. Optimized geometry of **2**−CH_3COO^- and **2**−$H_2PO_4^-$. Dotted lines show the distances less than 2.5 Å.

The binding energy of **3** and **4** with F^- in the gas phase is larger than other anions. However, in acetonitrile, **3** has more binding affinity toward $H_2PO_4^-$. In the meantime, the binding energy of **4** with $H_2PO_4^-$, CH_3COO^-, and F^- are competitive with each other. Since the ionic hydrogen bond strength is dependent on the solvent polarity and the interaction of the anion with the solvent molecules, the binding energies are much lower in polar solvents.[15] The calculation data show that $H_2PO_4^-$ more or less competes with $CH_3CO_2^-$ and F^- for the quinoxaline receptors. In general, the roughly calculated free energy of the host and anion complexation in acetontrile is in reasonable agreement with the experimental values (Table 1) except in the case of host **3**, where the calculated free enegry values are ∼2 kcal/mol larger than the experimental values.[9] This is quite expected as the positively charged imidazolium moieties in free **3** are too repulsive at the level of density functional theory. However, when the anion forms a complex with **3** the repulsion between the two imidazolium moieties is reduced.

From the above experimental and theoretical investigations, we conclude that both open and closed forms of the quinoxaline imidazolium receptors produce the anion-induced excimer state, while **1**/**3** shows a unique rapid charge-transfer emission response to $HP_2O_7^{3-}$/acetate. Therefore, the quinoxaline imidazolium receptors could be useful for the detection of $HP_2O_7^{3-}$ and acetate. Moreover, $H_2PO_4^-$ forms an ion-pair complex with these receptors against the conventional ionic hydrogen bonding.

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Supporting Information Available: Experimental procedures and characterization data for compounds **1**−**4** are described. This material is available free of charge via the Internet at http://pubs.acs.org.

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