ORGANIC LETTERS

2009
Vol. 11, No. 3
669−672

Imidazolium-Functionalized BINOL as a Multifunctional Receptor for Chromogenic and Chiral Anion Recognition

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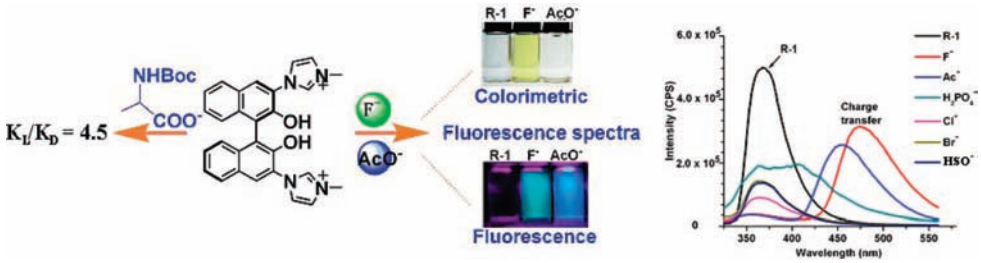
Received November 25, 2008

ABSTRACT



A novel imidazolium-functionalized BINOL fluorescent receptor R-1 was developed as a multifunctional receptor for both chromogenic and chiral anion recognition. The different fluorescent responses and color changes of R-1 could be applied to the detection of fluoride and acetate ions by the naked eye. Furthermore, the chiral recognition of the two enantiomers of α-amino carboxylates was also studied, and R-1 displayed a remarkable binding ability for the *t*-Boc alanine anion with an interesting enantioselectivity (K_L/K_D = 4.5).

In recent years, the development of molecule-based sensors for the recognition or sensing of physiologically important anions has attracted considerable attention.[1] Most anion receptors have amide, pyrrole, or urea groups as binding sites to form N−H···anion hydrogen bonds or the positively charged ammonium groups (or guanidinium groups) that involve N^+−H···X^--type hydrogen bonds.[2,3] More recently, 1,3-disubstituted imidazolium groups have been introduced to bind anions by forming $(C-H)^+\cdots X^-$ ionic hydrogen bonds between C(2)-H of imidazolium rings and the anion.[4] Fluorescent imidazolium receptors were preferred due to the advantages of the technique such as practical convenience, high sensitivity, and low cost. A series of fluorescent receptors bearing imidazolium groups as binding sites have been recently studied by Yoon, Kim, and co-workers.[5] These fluorescent imidazolium receptors have been synthesized and can recognize small biologically important molecules such as $H_2PO_4^-$ and pyrophosphate through the PET (photoinduced electron transfer) mechanism. Although a great development of fluorescent imidazolium receptors has been

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10.1021/ol8027303 CCC: $40.75
Published on Web 01/14/2009

achieved, multifunctional imidazolium receptors are quite rare and still highly desirable.[6]

Herein, a multifunctional anion fluorescent receptor, in which the imidazolium groups are directly attached to the 3,3′-positions of BINOL, has been developed (Figure 1). The

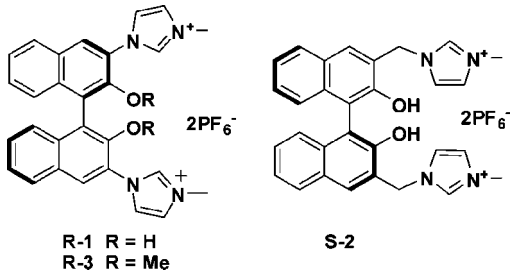

Figure 1. Imidazolium-functionalized anion-binding receptors.

choice of **R-1** as the fluorescent sensor was mainly based on the fact that (i) **R-1** contains both OH groups and imidazolium rings that have been extensively employed in the development of anion receptors and sensors; (ii) the imidazolium groups are directly attached to the BINOL, which might show synergistic coordination with the phenolic OH at the ortho position; (iii) the binaphthyl backbone for the construction of the unique chiral and aromatic structure can provide both excellent chiral recognition capability and interesting fluorescence signals.[7] The ligand **R-1** has been applied as a colorimetric sensor for recognition of anions by charge transfer and chiral recognition of the two enantiomers of α-amino carboxylates. The binding properties of these host systems toward various anions have been analyzed using color changes, fluorescence, ^{1}H NMR spectroscopy, and theoretical calculations.

The synthesis of **R-1**, **R-3**, and **S-2** was achieved by a straightforward process as shown in Schemes S1−S3 (Supporting Information). The detailed synthesis and characterization of these receptors are explained in the Supporting Information.[8,9]

First, **R-1** was evaluated as a chemosensor for various anionic species in acetonitrile. A solution of **R-1** (3 μM) was treated with representative anions such as F^-, $CH_3CO_2^-$, $H_2PO_4^-$, Br^-, Cl^-, and HSO_4^- (100 equiv, as tetrabutylammonium salts). The fluorescence spectra show a distinct and intense peak at 454 nm with $CH_3CO_2^-$ and 474 nm with F^- together with the quenching of original peaks, whereas $H_2PO_4^-$, a slightly intense peak, appears at 405 nm. However, no bathochromic shift caused by other anions was observed as shown in Figure 2A. The fluorescent titration data for **R-1**

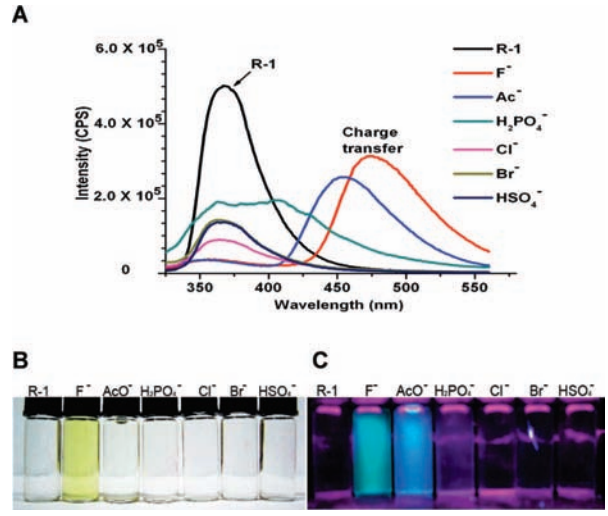

Figure 2. (A) Fluorescent emission changes of **R-1** (3 μM) upon addition of tetrabutylammonium salts of F^-, $CH_3CO_2^-$, $H_2PO_4^-$, Br^-, Cl^-, and HSO_4^- (100 equiv) in CH_3CN (λ_{ex} = 290 nm, excitation and emission slit: 1.5 nm). (B) color changes of **R-1** (50 μM) on the additions of tetrabutylammonium salts of F^-, $CH_3CO_2^-$, $H_2PO_4^-$, HSO_4^-, Cl^-, and Br^- (2.5×10^{-3} M) in 9:1 (v/v) of CH_3CN/DMSO. (C) Relative fluorescent responses.

with F^- and $CH_3CO_2^-$ and the relative association constants (M^{-1}) are shown in the Supporting Information (Figure S1 and Table S1). We note that, as shown in Table S1, **R-1** shows a selective binding with the F^- ion over Cl^- and Br^-. Around 140-fold and 585-fold selectivities for F^- over Cl^- and Br^- were observed, respectively.

As can be expected from the results of fluorescent experiments, noticeable color changes were observed after the addition of various anions to a solution of **R-1** in 9:1 (v/v) of CH_3CN/DMSO, as shown in Figure 2B. In particular, the colorless **R-1** solution became markedly yellow after the addition of F^-, while a pale yellow color was induced by $CH_3CO_2^-$. No color changes were observed by the additions of other anions. When **R-1** was excited at 365 nm in the presence of various anions, a bright green fluorescent response and a bright blue response were selectively observed in the presence of F^- and $CH_3CO_2^-$, respectively (Figure 2C). A slight fluorescent response was also observed in the presence of $H_2PO_4^-$. According to previous reports, the receptors containing both hydroxy and amide groups displayed the F^- and $CH_3CO_2^-$ recognition selectivity due to the excited-state intermolecular proton transfer in the sensor−anion complexes, but most of those receptors could not distinguish these two anions.[10] By using **R-1** as a

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fluorecent chemosensor, much different fluorescent responses and distinct color changes could be applied to the detection of F^- and $CH_3CO_2^-$, respectively, by the naked eye.

^1H NMR experiments in DMSO-d_6 were conducted to look into the effects of the anions on **R-1**. A series of anions such as Cl^-, $CH_3CO_2^-$, and F^- (as tetrabutylammonium salts) were treated with **R-1**, as shown in the Supporting Information (Figure S2). Concomitant downfield shifts of the imidazolium C(2)-H (δ 9.66−9.78) and part of the aromatic hydrogen signals were observed by the titration with up to 15 equiv of Cl^- to the solution of **R-1** (2 mM). In contrast to Cl^-, the imidazolium C(2)-H displayed a similar downfield shift (δ 9.66−9.82) with the treatment of 2 equiv of $CH_3CO_2^-$. The most obvious spectral changes were observed by the treatment of F^-: the imidazolium C(2)-H displayed a large downfield shift (δ 9.66−11.41) upon the addition of 2 equiv of F^-, while several aromatic peaks between δ 7.0 and 8.5 ppm split to multiplets at δ 6.6 and 7.5 ppm. Moreover, an obvious triplet peak at δ 16.1 was found, indicating the formation of FHF.[11] For the ^1H NMR spectra, two effects were responsible for the signal changes upon the addition of anions: (1) the expected strong $(C-H)^+ \cdots X^-$ ionic hydrogen bonds between C(2)-H of imidazolium rings and the anion (this interaction led to the downfield shift of the C(2)-H of imidazolium rings); (2) an overall change of electronic distributions in the chromophore[11] was induced by F^-, and as a result, the strong high-field shifts of all the naphthyl and imidazolium ring proton signals were observed, giving evidence for the deprotonation of imidazolium moieties. Unfortunately, phenolic OH chemical shifts of **R-1** could not be observed in the ^1H NMR spectra under this condition.

To further understand the nature of the binding interactions, the most stable conformers of host−guest complexes were theoretically investigated.[12] The optimized geometry of **R-1**$-CH_3COO^-$ (Figure 3A) showed a strong $(C-H)^+ \cdots$ anion ionic hydrogen between C(2)-H of imidazolium rings and CH_3COO^-. Meanwhile, strong O−H $\cdots$ anion hydrogen bonds could also form between phenolic hydroxyls and oxygen atoms of CH_3COO^-. The synergistic coordinations, which may enhance the charge transfer from the donor oxygen of naphthol to the acceptor substituent (imidazolium),[13] play a critical role in the binding process. In the case of **R-1**$-F^-$ (Figure 3B), gas phase geometry optimization of the normal form of **R-1**$-F^-$ led to the formation of a deprotonated complex because both the imidazolium hydrogen atoms were transferred to F^-, which agrees well with the ^1H NMR experiments observation. The deprotonation induced by F^- conduces to a unique rapid charge-transfer emission response. Therefore, different fluorescence responses are observed between F^- and CH_3COO^-.

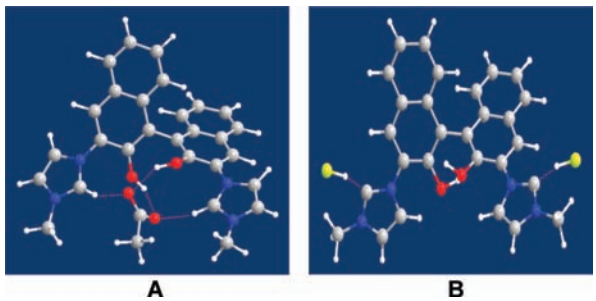

Figure 3. Calculations carried out at the B3LYP/6-31G* level. Optimized geometry of **R-1**$-CH_3COO^-$ (A) and. **R-1**$-F^-$ (B). Red dotted lines show the distances less than 2.5 Å.

Besides **R-1**, similar experiments employing receptor **S-2** containing a flexible methylene linker and the Me-protected ligand **R-3** were also conducted. As expected, only fluorescent quenching effects with no bathochromic shift were observed (Supporting Information, Figures S3−S4).

Hosts **R-1** and **S-2** were then examined for chiral recognition with various amino acid derivatives (Supporting Information, Figures S6−S13). Tetrabutylammonium salts of *t*-Boc-amino acids, such as alanine (Ala), serine (Ser), leucine (Leu), and phenylalanine (Phe), were used for the binding study. Figure 4 explained the fluorescent titrations of hosts

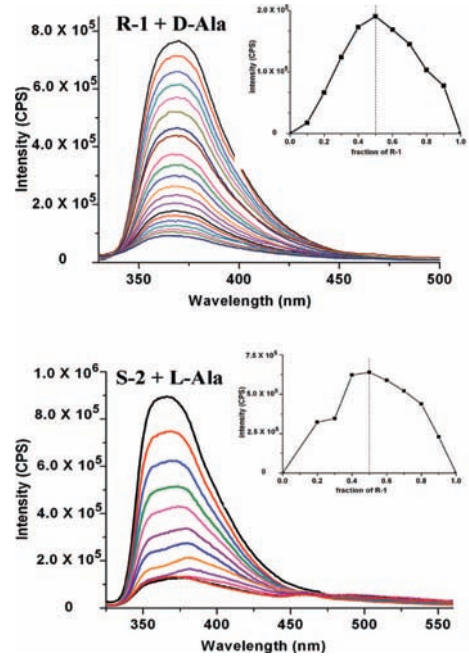

Figure 4. Fluorescent titrations of **R-1** (3 μM) with D-Boc-alanine (up) and **S-2** (3 μM) with L-Boc-alanine (down) in acetonitrile. Inset: job plot for the host with an amino acid derivative.

R-1 (3 μM) with D-Boc-alanine and **S-2** (3 μM) with L-Boc-alanine in acetonitrile. Hosts **R-1** and **S-2** showed chelation enhanced quenching (CHEQ) effects with amino acid deriva-

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Table 1. Association Constants (M^{-1}) of **R-1** and **S-2** with *t*-Boc-Amino Acids Derivatives in CH_3CN

	R-1			S-2		
guest	K_L (M^{-1})	K_I/K_D	K_D (M^{-1})	K_L (M^{-1})	K_D/K_L	K_D (M^{-1})
Ala	$4.55 \cdot 10^5$	4.5	$1.02 \cdot 10^5$	$2.13 \cdot 10^5$	2.9	$6.26 \cdot 10^5$
Ser	$7.31 \cdot 10^5$	2.1	$3.45 \cdot 10^5$	$8.03 \cdot 10^5$	1.8	$14.2 \cdot 10^5$
Leu	$2.12 \cdot 10^5$	3.9	$0.55 \cdot 10^5$	$3.96 \cdot 10^5$	1.5	$5.94 \cdot 10^5$
Phe	$3.23 \cdot 10^5$	1.7	$1.93 \cdot 10^5$	$3.50 \cdot 10^5$	1.5	$5.26 \cdot 10^5$

tives. These CHEQ effects for **S-2** could be attributed to photoinduced electron transfer (PET). A similar fluorescent quenching process due to the PET had been previously reported.[14] On the other hand, fluorescent quenching effects of **R-1** could be attributed to the photoinduced charge transfer (PCT). The PCT-induced quenching effects of quinoxaline−imidazolium receptors with anions have also been reported.[15]

The fluorescent quenching effects (%) of **R-1** with D- and L-Boc-alanine were 88.2 and 89.6, respectively, while the values (%) of **S-2** with D- and L-Boc-alanine were 86.4 and 85.6, respectively. According to the nonlinear curve fitting,[16] the measured emission [F/F_0] at 370 nm varied as a function of amino acids in a linear relationship ($R > 0.99$), indicating that **R-1** and D-Ala anion formed a 1:1 complex. The 1:1 stoichiometry was further confirmed by a Job plot (inset of Figure 4, Supporting Information, Figure S5).[17] As shown in Table 1, the association constants of **R-1** with L- and D-Boc alanine were calculated as 4.55×10^5 and 1.02×10^5 M^{-1}, respectively, and K_L/K_D was found to be 4.5. **S-2**, bearing imidazolium rings attached to a flexible methylene linker, displayed a higher association constant with both L- and D-Boc alanine but gave only moderate enantioselectivity ($K_D/K_L = 2.9$). We speculated that the poor enantioselectivity of **S-2** was most likely a consequence of the reduction of steric factors between the BINOL unit and imidazolium caused by the flexible methylene linker.

From the ^1H NMR experiments of **R-1** (2 mM) with L/D-*t*-Boc-alanine (0.5 equiv) in DMSO-d_6, the imidazolium C(2)-H peak displayed downfield shifts (δ 9.66−9.80 for D-alanine, δ 9.66−9.82 for L-alanine), which supported the fluorescent data. Addition of 5 equiv of L-*t*-Boc-alanine to **R-1** in DMSO-d_6 led to broadening and an upfield shift of aromatic protons (Supporting Information, Figure S14). The strong $(C-H)^+\cdots X^-$ ionic hydrogen bonds between C(2)-H of imidazolium rings and the anion are also confirmed due to the downfield shift of the C(2)-H of imidazolium rings. On the contrary, when **S-2** was treated with L/D-*t*-Boc-alanine (0.5 equiv) in DMSO-d_6, the signals of imidazolium C(2)-H and the benzyl hydrogens showed no obvious changes, and the phenolic OH at δ 8.9 ppm disappeared (Supporting Information, Figure S15). We deduced that the OH···anion hydrogen bond formed first beween amino acid anions and phenolic OH, and the imidazolium group had to undergo a rotation to achieve effective coordination. As a result, the interaction between the imidazolium C(2)-H and the benzyl hydrogens was greatly impaired. Further explorations toward the recognition mechanisms are currently underway.

In conclusion, we have designed and synthesized a novel imidazolium-functionalized BINOL **R-1** and some relative ligands as multifunctional fluorescent receptors. Their chromogenic and chiral recognition properties toward various kinds of anions were studied. Unlike most fluorescent sensors for fluoride ions that cannot tell F^- from $CH_3CO_2^-$, **R-1** shows excellent selectivity for F^- over $CH_3CO_2^-$. This specialty may be attributed to the unique rapid charge-transfer emission response induced by F^-, leading to the discernment of the subtle difference in the affinity of F^- and $CH_3CO_2^-$. On the other hand, **R-1** displayed a remarkable binding ability for the *t*-Boc alanine anion with an interesting enantioselectivity ($K_L/K_D = 4.5$).

Acknowledgment. This work was financially supported by the National Natural Science Foundation of China (Nos. 20725206 and 20732004), Specialized Research Fund for the Doctoral Program of Higher Education, and Scientific Fund of Sichuan Province for Outstanding Young Scientist.

Supporting Information Available: Experimental procedures, synthetic and spectroscopic data for various compounds, and supplementary spectral data. This material is available free of charge via the Internet at http://pubs.acs.org.

OL8027303

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