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2,6-Bis(2-benzimidazolyl)pyridine as a chemosensor for fluoride ions

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Abstract—2,6-Bis(2-benzimidazolyl)pyridine, a neutral tridentate ligand, is employed as a chemosensor for the detection of fluoride ions. The binding of anionic guest species with this ligand is studied using UV–vis spectroscopy, fluorescence spectroscopy, and ^{1}H NMR techniques. The results indicate that 2,6-bis(2-benzimidazolyl)pyridine can be used as a chemical shift and optical modification based sensor for the detection of fluoride ions.

The development of synthetic receptors capable of selectively recognizing anions continues to attract a great deal of interest due to their significance in a plethora of biological, chemical, and environmental processes.[1] Despite their popularity, the design of 'substrate specific' synthetic receptors still remains a great challenge for supramolecular scientists due to (1) the large size of anions compared to the cations (2) the chemical environment that determines the strength of interaction and (3) the pH of the medium. Efforts to overcome the above challenges, foremost by Sessler,[2] Jeong,[3] Gale, and Beer[4] have led to considerable advancement of several classes of anion receptors and provided insight into newer host molecules. We recently illustrated that structurally simple molecules such as 2,6-bis(2-benzimidazolyl) pyridine, **1**, (Fig. 1) form excellent host–guest complexes with neutral guests like urea and toxic benzene metabolites at extremely low concentrations.[5] In the present work, we have examined the utility of **1**, as a sensor for anions. Numerous neutral receptors exist for anions; most of them containing –NH fragments, which act as hydrogen bond donors for the anions.[6,7]

Ligand **1** has two –NH fragments that can form hydrogen-bonded adducts with anions. It is structurally very simple, stable to heat/light and can be synthesized readily in one step from commercially cheap starting materials. Due to its well-defined internal cavity consisting of two NH hydrogen atoms, **1** can function as an ideal host for the recognition of anions by hydrogen bonding interactions.

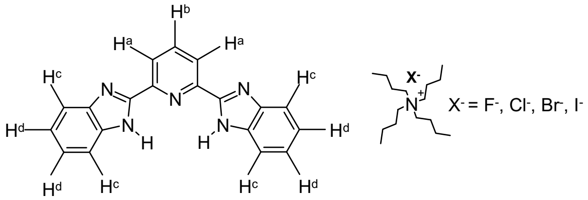

Figure 1. 2,6-Bis(2-benzimidazolyl)pyridine, **1** and various anions.

Initial binding studies were carried out by adding the tetrabutylammonium salts (TBAX) ($[Bu_4N]^+X^-$; $X^- = F^-, Cl^-, Br^-, I^-$) to a CD_3CN solution of **1**. The changes in the chemical shifts of **1** were examined by recording ^{1}H NMR spectra at room temperature (Fig. 2). The largest chemical shift for the aromatic protons of **1** was observed on adding the $[Bu_4N]^+$-fluoride salt, which indicated a strong interaction of **1** with F^-. Significant chemical shift changes (upon addition of the fluoride salt of $[Bu_4N]^+X^-$ to **1**), were observed for the H^c and H^d proton signals which were shifted upfield to 7.5 and 7.05 ppm, respectively, from 7.7 and 7.3 ppm. On the other hand, addition of the Cl^-, Br^-, and I^- salts of $[Bu_4N]^+$ led to negligible changes in the chemical shifts of protons H^c and H^d (Fig. 2). Thus larger the anions, the more difficult it is to accommodate them within the cavity of **1**. The reason for the large chemical shift changes in **1**, on the addition of $[Bu_4N]^+F^-$ arises from the fact that F^- has a higher negative charge and better hydrogen bond acceptor properties compared to

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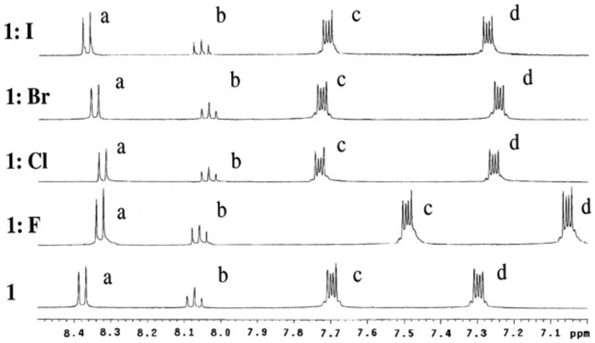

Figure 2. ^{1}H NMR, 400 MHz spectra taken over the course of the titration of a CD_3CN solution of **1** with 1 equiv of $[Bu_4N]F$, $[Bu_4N]Cl$, $[Bu_4N]Br$, and $[Bu_4N]I$.

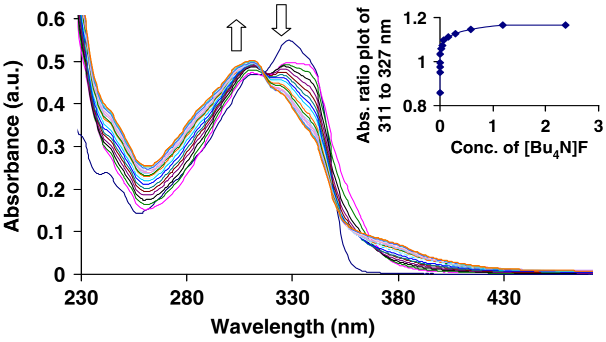

Figure 3. UV–visible spectra of **1** (6.35×10^{-6} M in dry CH_3CN) during titration with $[Bu_4N]F$ from 0 to 2 equiv (v/v). Inset—absorbance ratio plot of 311 nm to 327 nm as a function of fluoride ion concentration.

the other anions. When the fluoride and **1** form a complex adduct (with the –NH protons of the benzimidazole rings) a reasonably large conformational twist occurs to accommodate the fluoride in the cavity of **1**. This may be a further reason for the observed chemical shifts of the H^c and H^d protons. No chemical shift for the H^b protons present on the pyridine ring and only a negligible change in the position of the H^a proton occurred after formation of a complex of **1** with fluoride, which rules out the possibility of the direct participation of the pyridine ring nitrogen in hydrogen bonding with the anions. Thus it could be easily predicted that fluoride ions form a hydrogen-bonded complex with the two –NHs present at the inner cavity of **1**, and to accommodate fluoride into its cavity, **1** undergoes a moderate twist. The smaller size of fluoride compared to chloride, bromide, and iodide allows it to be accommodated in the cavity of **1**. Though, in all possibilities other anions form hydrogen-bonded complexes with **1**, the larger diameter of these anions compared to fluoride may not allow them to enter the cavity of **1** due to steric reasons. These studies thus indicate that **1** can be used as a chemical sensor for the detection of fluoride anions and ^{1}H NMR could be employed as a chemical shift based probe.

The interactions of **1** with the $[Bu_4N]^+X^-$ salts of fluoride, chloride, bromide, and iodide were further investigated by spectrophotometric titration experiments in acetonitrile solution. The optical changes were evaluated by titrating 0.1 equiv of anion aliquots into a solution of **1** at regular intervals and recording the changes in the UV–visible and fluorescence spectra. In particular, a standard solution of $[Bu_4N]F$ was added in fixed aliquots to a standard solution of **1** (9.64×10^{-6} M) and the spectra are reported below (Fig. 3). Upon addition of fluoride, the band at 327 nm progressively decreased in intensity with broadening and a new peak at 311 nm appeared. Along with the above observation, a clear isosbestic point at 315 nm was observed. The formation of this isosbestic point indicates that at least one stable species is present at equilibrium and that a stable complex forms between **1** and fluoride.

The inset in Figure 3 shows the changes in the titration profile of the band at 327 nm corresponding to the **1**:$[Bu_4N]^+F^-$, hydrogen-bonded complex. On addition of 1 equiv of fluoride, the band at 327 nm is totally quenched and a new peak corresponding to the **1**:fluoride complex appears at 311 nm. The association constant (*K*a) calculated[8] was found to be 439.49 M^{-1}, suggesting strong hydrogen bonding between **1** and fluoride.

Fluorescence spectroscopy studies were also carried out in order to evaluate the ability of **1** to operate as a fluorescent anion sensor (Fig. 4). Remarkable quenching of the fluorescence was observed on addition of anions. The changes observed in the fluorescence spectra of a solution of **1** in acetonitrile on adding up to 2.0 equiv of $[Bu_4N]F$ are depicted in Figure 4. A large quenching (>85%) in intensity of the 375 nm band was observed on the addition of 1.0 equiv of $[Bu_4N]F$ indicating that on formation of the hydrogen-bonded complex between $[Bu_4N]F$ and **1**, the excited state was modified considerably leading to the quenching of fluorescence. On continuous addition of $[Bu_4N]F$ to a solution of **1** the peak was slowly red shifted to 434 nm. The changes observed in the fluorescence spectra on adding more than 1 equiv of $[Bu_4N]F$ aliquots to **1** were insignificant, which is in good agreement with the results of the UV–visible titration. Figure 4 inset shows the changes in the titration profile of the band at 373 nm corresponding to the **1**:$[Bu_4N]F$, hydrogen-bonded complex.

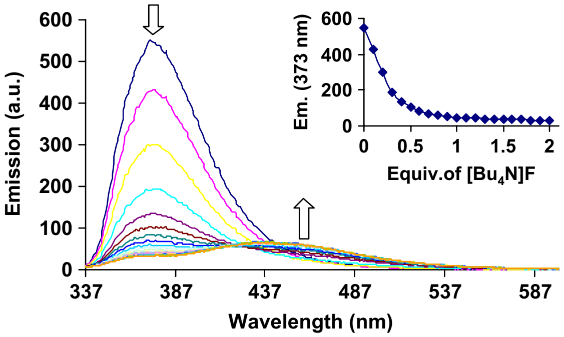

Figure 4. Emission spectra of **1** (7.05×10^{-7} M in dry CH_3CN) during the titration with $[Bu_4N]F$ from 0 to 2 equiv (v/v). Inset—plot of the emission intensity (373 nm) of **1** as a function of equiv of $[Bu_4N]F$.

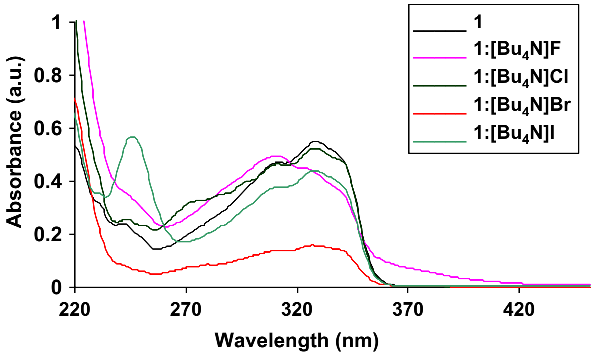

Figure 5. UV–visible spectra of **1** with $[Bu_4N]F$, $[Bu_4N]Cl$, $[Bu_4N]Br$, and $[Bu_4N]I$ in 1:1 ratio.

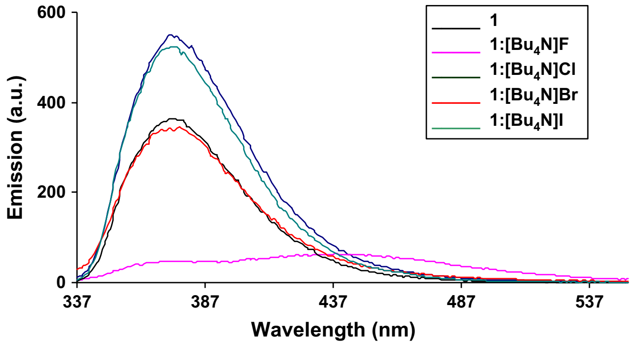

Figure 6. Emission spectra of **1** with $[Bu_4N]F$, $[Bu_4N]Cl$, $[Bu_4N]Br$, and $[Bu_4N]I$ in 1:1 ratio.

Analogous investigations were carried out with Cl^-, Br^-, and I^- and the titration experiments were monitored by UV–visible (Fig. 5) and fluorescence (Fig. 6) spectroscopy. A acetonitrile solution of **1** was titrated with a standard solution of the tetrabutylammonium salt of the chosen anions (Supplementary data). In all cases, a new absorption band developed on titration and sharp isosbestic points were observed in the recorded spectra. The spectral variations observed for **1** on titrating with the anions mentioned above are represented as a 1:1 ratio plot, where unique spectral features were observed for each anionic guest hydrogen bonded with **1**, thereby demonstrating the selective nature of **1** as a sensitive chemical sensor for recognizing different anionic guest molecules.

The association constants (K_a) calculated from the UV–visible plot at 327 nm show very strong binding of **1** with fluoride ions compared with the other anions studied here (Table 1). The UV–visible and fluorescence data are clear indications that **1** can be used as a chemical sensor to detect fluoride anions.

Table 1. Association constants (K_a) of **1** with anions in CH_3CN

Anion	K_a (M^{-1})
F^-	439.49
Cl^-	41.18
Br^-	21.96
I^-	24.46

In summary, we have reported that 2,6-bis(2-benzimidazolyl)pyridine, **1**, shows high selectivity for fluoride over other halide anions at concentrations as low as 10^{-7} M. The binding of the above tridentate ligand with a series of anions was monitored by changes in ^1H NMR chemical shifts, as well as by UV–visible and fluorescence spectroscopy. To the best of our knowledge, ligand **1** is the simplest tridentate molecule used for anion recognition that shows high binding constants. Results of this ligand as a chemical sensor for other anionic species will be reported in due course.

Acknowledgments

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Supplementary data

The supplementary data includes the UV–visible and fluorescence titration profiles of **1** with tetrabutylammonium salts of chloride, bromide, and iodide. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.11.011.

References and notes

1. (a) Martinez-Máñez, R.; Sancenón, F. *Chem. Rev.* **2003**, *103*, 4419–4476; (b) Beer, P. D.; Gale, P. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 486–516; (c) Lehn, J.-M. *Supramolecular Chemistry, Concepts and Perspectives*; VCH: Weinheim, Germany, 1995; pp. 139–160.
2. (a) Sessler, J. L.; Gross, D. E.; Cho, W.-S.; Lynch, V. M.; Schmidtchen, F. P.; Bates, G. W.; Light, M. E.; Gale, P. A. *J. Am. Chem. Soc.* **2006**, *128*, 12281–12288; (b) Miyaji, H.; Kim, H.-K.; Sim, E.-K.; Lee, C.-K.; Cho, W.-S.; Sessler, J. L.; Lee, C.-H. *J. Am. Chem. Soc.* **2005**, *127*, 12510–12512; (c) Sessler, J. L.; An, D.; Cho, W.-S.; Lynch, V.; Marquez, M. *Chem. Commun.* **2005**, *4*, 540–542; (d) Shevchuk, S. V.; Lynch, V. M.; Sessler, J. L. *Tetrahedron* **2004**, *60*, 11283–11291; (e) Miyaji, H.; Sessler, J. L. *Angew. Chem., Int. Ed.* **2001**, *40*, 154–157; (f) Anzenbacher, P., Jr.; Try, A. C.; Miyaji, H.; Jursikova, K.; Lynch, V. M.; Marquez, M.; Sessler, J. L. *J. Am. Chem. Soc.* **2000**, *122*, 10268–10272; (g) Anzenbacher, P., Jr.; Jursikova, K.; Sessler, J. L. *J. Am. Chem. Soc.* **2000**, *122*, 9350–9351; (h) Black, C. B.; Andrioletti, B.; Try, A. C.; Ruiperez, C.; Sessler, J. L. *J. Am. Chem. Soc.* **1999**, *121*, 10438–10439; (i) Shionoya, M.; Furuta, H.; Lynch, V.; Harriman, A.; Sessler, J. L. *J. Am. Chem. Soc.* **1992**, *114*, 5714–5722.
3. (a) Kim, N.-K.; Chang, K.-J.; Moon, D.; Lah, M. S.; Jeong, K.-S. *Chem. Commun.* **2007**, 3401–3403; (b) Lee, J.-Y.; Lee, M.-H.; Jeong, K.-S. *Supramol. Chem.* **2007**, *19*, 257–263; (c) Chang, K.-J.; Kang, B.-N.; Lee, M.-H.; Jeong, K.-S. *J. Am. Chem. Soc.* **2005**, *127*, 12214–12215; (d) Chang, K.-J.; Moon, D.; Lah, M. S.; Jeong, K.-S. *Angew. Chem., Int. Ed.* **2005**, *44*, 7926–7929.
4. (a) Bates, G. W.; Gale, P. A.; Light, M. E. *Chem. Commun.* **2007**, 2121–2123; (b) Garcia-Garrido, S. E.; Caltagirone, C.; Light, M. E.; Gale, P. A. *Chem. Commun.* **2007**, 1450–1452; (c) Gale, P. A.; Quesada, R. *Coord. Chem. Rev.* **2006**,

3219–3244; (d) Vickers, M.; Martindale, K. S.; Beer, P. D. *J. Mater. Chem.* **2005**, *15*, 2784–2790; (e) Wong, W. W. H.; Vickers, M. S.; Cowley, A. R.; Paul, R. L.; Beer, P. D. *Org. Biomol. Chem.* **2005**, *3*, 4201–4208; (f) Curiel, D.; Cowley, A.; Beer, P. D. *Chem. Commun.* **2005**, 236–238; (g) Beer, P. D.; Gale, P. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 486–516; (h) Beer, P. D.; Drew, M. G. B.; Gradwell, K. *J. Chem. Soc., Perkin Trans. 2* **2000**, 511–519; (i) Beer, P. D.; Szemes, F.; Balzani, V.; Sala, C. M.; Drew, M. G. B.; Dent, S. W.; Maestri, M. *J. Am. Chem. Soc.* **1997**, *119*, 11864–11875.

5. (a) Chetia, B.; Iyer, P. K. *Tetrahedron Lett.* **2007**, *48*, 47–50; (b) Chetia, B.; Iyer, P. K. *Tetrahedron Lett.* **2006**, *47*, 8115–8117.
6. Bianchi, A.; Bowman, J. K.; Garcia-Espana, E. *Supramolecular Chemistry of Anions*; New York: Wiley-VCH, 1997.
7. Boiocchi, M.; Del Boca, L.; Gomez, D. E.; Fabbrizzi, L.; Licchelli, M.; Monzani, E. *J. Am. Chem. Soc.* **2004**, *126*, 16507–16514.
8. Chou, P. T.; Wu, G. R.; Wei, C. Y.; Cheng, C. C.; Chang, C. P.; Hung, F. T. *J. Phys. Chem. B* **2000**, *104*, 7818–7829.