Pergamon

Tetrahedron Letters 40 (1999) 5219–5222

TETRAHEDRON LETTERS

A New Tripodal Anion Receptor with C-H···X⁻ Hydrogen Bonding

Kiyoshi Sato*, Sadao Arai[†], and Takamichi Yamagishi

Department of Applied Chemistry, Graduate School of Engineering, Tokyo Metropolitan University, 1-1 Minami-ohsawa, Hachioji, Tokyo 192-0397, Japan

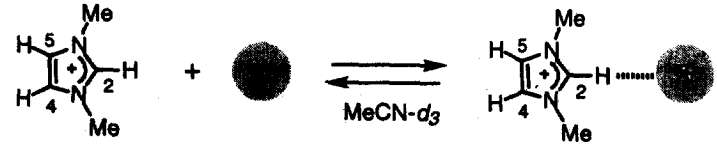
Received 8 April 1999; revised 6 May 1999; accepted 7 May 1999

Abstract: 1,3,5-{Tris(3-*n*-butylimidazolio)methyl}-2,4,6-trimethybenzene **1**, which has three imidazolium groups connected through a 1,3,5-trimethylbenzene spacer, has been synthesized as a novel receptor for halide anions. This tripodal receptor is shown to bind strongly Cl^-, Br^-, and I^- anions in CD_3CN through electrostatic interactions and C-H···X^- hydrogen bonds.

Numerous artificial receptors for neutral and cationic species have been explored, whereas the coordination chemistry and recognition of anions, in spite of their very important roles in chemistry and in biology, have not received much attention until recently.[1,2] The majority of positively charged anion receptors are equipped with ammonium or guanidinium groups as binding sites which form stable host-guest complexes to anions using electrostatic force, sometimes together with N^+-H ··· X^- hydrogen bonds.[2]

As a novel binding subunit for anions, we noticed the 1,3-disubstituted imidazolium group since this cationic heterocycle is expected to interact strongly with anions through not only electrostatic force but also C-H ··· X^- type hydrogen bond between the hydrogen on the electron-deficient C(2) carbon atom of the imidazolium ring and the guest anion. Such unique hydrogen bonding properties of the imidazolium cation have been found in 1-ethyl-3-methylimidazolium (EMI^+) salts of halides and tetrachlorometalate in solid state[3] and in solution.[4] Here we report the first example of a halide anion receptor based on an imidazolium subunit.

Initial binding experiments were performed using a model compound, 1,3-dimethylimidazolium (DMI^+) hexafluorophosphate, followed by ^1H NMR spectroscopy. Addition of tetraethylammonium halides ($Et_4N^+X^-$) to a deuterated acetonitrile solution of $DMI^+ \cdot PF_6^-$ produced characteristic downfield shifts ($\Delta\delta$ = 0.2–0.9 ppm) of the C(2)-H proton. ^1H NMR titrations gave the association constants of K = 78 (Cl^-), 59 (Br^-), and 28 (I^-) $dm^3\ mol^{-1}$ (± 10%), respectively.



These findings led us to design a new acyclic tripodal anion receptor[5], 1,3,5-[tris(3-*n*-butylimidazolio)methyl]-2,4,6-trimethylbenzene (**1**) which posesses three imidazolium groups connected through a 1,3,5-trimethylbenzene spacer.[6] From a molecular modeling study, it was found **1** has an appropriate cavity size for halide ions. Receptor **1** was synthesized by the reaction of 1,3,5-tris(bromomethyl)-2,4,6-trimethylbenzene[7] with 3 equivs. of 1-*n*-butylimidazole in acetonitrile (96% yield). The bromide salt was converted into a hexafluorophosphate salt by counter ion exchange. Recrystallization of the PF_6^- salt from acetonitrile-ethanol (1:4) gave **1**·3PF_6^- as colorless needles in 58% yield.[8]

0040-4039/99/$ - see front matter
PII: S0040-4039(99)00942-9

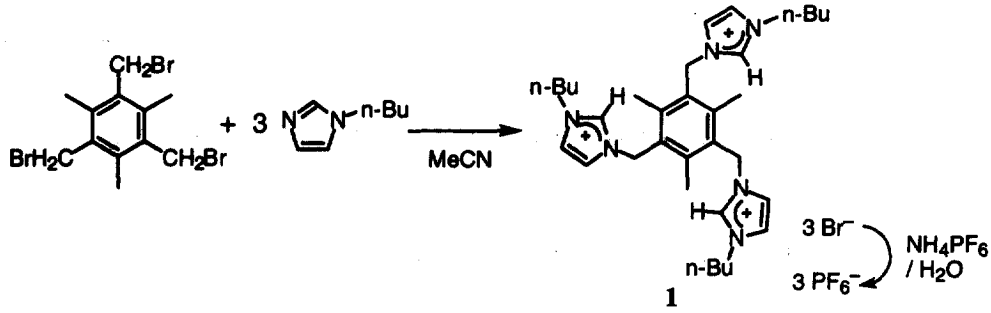


Figure 1 shows the ^{1}H NMR spectral change caused by addition of $Et_4N^+Cl^-$ to a deuterated acetonitrile solution of $\mathbf{1}\cdot 3PF_6^-$, which revealed significant large downfield shifts ($\Delta\delta > 1.3$ ppm) with concomitant broadening in the signal of the C(2)-H of imidazolium moieties until 1 equiv. of Cl^- was added. Further addition of Cl^- resulted in saturation of the chemical shift changes. These observations upon ^{1}H NMR titration experiments clearly suggest that the receptor **1** formed stable 1:1 stoichiometric complexes with Cl^- and the formation of C(2)-H ··· Cl^- hydrogen bonds[4a] in acetonitrile solution.

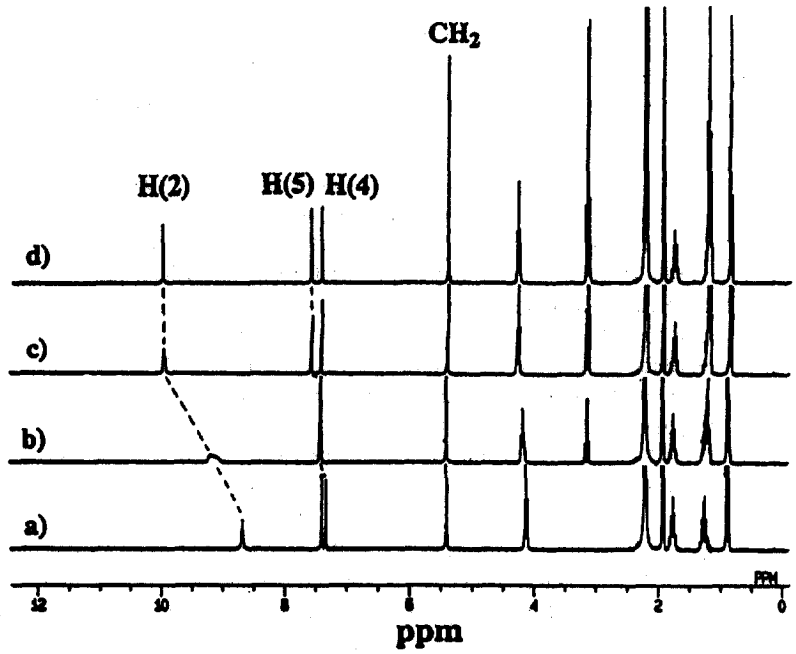


Figure 1. ^{1}H NMR spectra of the receptor $\mathbf{1}\cdot 3PF_6^-$ (2.6 mM in CD_3CN) in the presence of a) 0, b) 0.5, c) 1.0, and d) 1.5 equiv. of tetraethylammonium chloride.

Subsequent ^{1}H NMR titration studies of **1** with Br^- and I^- in CD_3CN also produced titration curves suggesting 1:1 stoichiometry (Fig. 2). The association constants and binding free energies were determined from their titration curves by using a nonlinear least-squares curve-fitting program[9] and are collected in Table 1. The association constants are fairly large (75000–7200 $dm^3\ mol^{-1}$). The magnitude of the chemical shift changes and association constants decrease in the order $Cl^- > Br^- > I^-$, consistent with their relative hydrogen-bonding abilities and surface charge density.[4a]

Complex formation was also confirmed by mass spectrometry. The ESI mass spectra of 1:1 mixture of $\mathbf{1}\cdot 3PF_6$ with tetraethylammonium salts of halides showed signals 712 [$\mathbf{1}\cdot PF_6^- + Cl^-]^+$, 755 and 757 [$\mathbf{1}\cdot PF_6^- + Br^-]^+$, and 804 [$\mathbf{1}\cdot PF_6^- + I^-]^+$, respectively. Further evidence for the complexation of the halide anion *via*

hydrogen bonding was obtained from FT-IR spectroscopy. On the complexation with Cl^-, in addition to the general broadening and shifting of peaks assigned to aromatic C-H stretch bands (3170-3100 cm^{-1}), a shoulder peak emerges at the 2980 cm^{-1} side of alphatic C-H stretch bands (3000-2870 cm^{-1}). Furthermore, the C(2)-D stretch band of the deuterated host **1**[12] at 2350 cm^{-1} is clearly shifted to 2260 cm^{-1} in the presence of Cl^-. These band-shifts to lower wavenumbers could be attributed to the formation of C(2)-H/D ··· Cl^- hydrogen bonds.[4b]

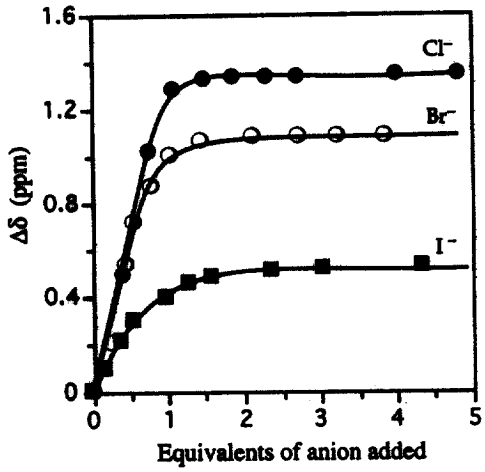


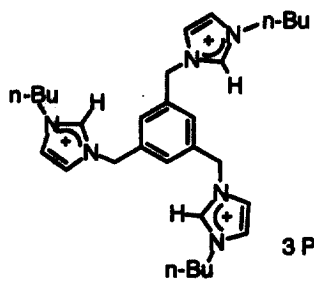
Figure 2. ^1H NMR titration curves of the receptor **1**•3PF_6^- (2.6 mM in CD_3CN) with halide anions. Δδ is the shift difference in ppm of the 2-H proton.

Table 1. Association constants K and binding free energies ΔG° for 1:1 complexes of receptors **1-3** with halide anions in CD_3CN at 298 K

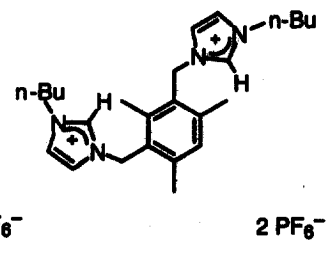
Receptor	Anion	K[a] / $dm^3\,mol^{-1}$	ΔG°_{298} / kcal mol^{-1}
1	Cl^-	75000	−6.65
1	Br^-	46000	−6.35
1	I^-	7200	−5.26
2	Cl^-	1500	−4.32
3	Cl^-	1300	−4.25
DMI	Cl^-	78	−2.58

[a] Errors are estimated to be <10%.

For comparison purpose, further titration experiments of compounds **2** and **3** were carried out. These receptors also form 1:1 stoichiometric complexes with the Cl^- anion. However, those association constants are relatively small compared to that of **1** (see Table 1). In **2**, the absence of the methyl groups at the ortho positions resulted in a 50-times smaller association constant than the value of **1** for chloride, presumably because of conformational flexibility by free rotation about the $C_{benzene}$–CH_2 bonds.[5a,5b,10] A similar tendency was observed in bidentate receptor **3**, in which one of the imidazoliomethyl units was removed. Therefore, both the three imidazoliomethyl groups at the 1,3,5-positions and the 2,4,6-substituents are believed to provide a favorable environment for the formation of a stable complex with halide anions. We propose that a possible structure in the complexes between **1** and the halide ion is all syn conformation (Fig. 3).



2



3

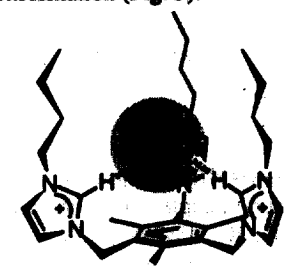


Figure 3. A possible structure of **1** with halide ions.

In summary, we have demonstrated that the imidazolium-based tripodal receptor **1** has considerable affinity for halide anions in polar solvent through electrostatic interactions and C-H ··· X^- hydrogen bonds. Recently, C-H ··· O hydrogen bonding in solution has been reported.[11] However, to the best of our knowledge,

this is the first example of C-H ··· X^- hydrogen bond interaction of imidazolium in host-guest chemistry. We are currently investigating various receptors incorporated with imidazolium rings as anion binding subunits.

Acknowledgment This work was financially supported by Grant-in-Aid for 1997 Promoted Research by Young Researchers (T.M.U.). The authors are indebted to Dr. T. Suzuki for his help in elemental analyses.

References and Notes

[†] *Present address*: Tokyo Medical College, 6-1-1 Shinjuku, Shinjuku-ku, Tokyo 160, Japan.

1. Lehn, J.-M. *Supramolecular Chemistry*; VCH: Weinheim, 1995; pp. 31-35.
2. For recent reviews of anion recognition: a) Schmidtchen, F. P.; Berger, M. *Chem. Rev.* **1997**, *97*, 1609-1646. b) Scheerder, J.; Engbersen, J. F. J.; Reinhoudt, D. N. *Recl. Trav. Chim. Pays-Bas* **1996**, *115*, 307-320.
3. X-ray studies of 1-ethyl-3-methylimidazolium (EMI^+) salts; a) Elaiwi, A.; Hitchcock, P. B.; Seddon, K. R.; Srinivasan, N.; Tan, Y.-M.; Welton, T.; Zola, J. A. *J. Chem. Soc., Dalton Trans.* **1995**, 3467-3472. b) Hitchcock, P. B.; Seddon, K. R.; Welton, T. *J. Chem. Soc., Dalton Trans.* **1993**, 2639-2643. c) Wilkes, J. S.; Zaworotko, M. J. *J. Chem. Soc., Chem. Commun.* **1992**, 965-967. d) Dymek Jr., C. J.; Grossie, D. A.; Fratini, A. V.; Adams, W. W. *J. Mol. Structure* **1989**, *213*, 25-34. e) Abdul-Sada, A. K.; Greenway, A. M.; Hithchcock. P. B.; Mohammed, T. J.; Seddon, K. R.; Zora, J. A. *J. Chem. Soc., Chem. Commun.* **1986**, 1753-1754. f) Fuller, F.; Carlin, R. T.; De Long, H. C.; Haworth, D. *J. Chem. Soc., Chem. Commun.* **1994**, 299-300.
4. a) Avent, A. G.; Chaloner, P. A.; Day, M. P.; Seddon, K. R.; Welton, T. *J. Chem. Soc., Dalton Trans.* **1994**, 3405-3413. b) Dieter, K. M.; Dymek, Jr., C. J.; Heimer, N. E.; Rovang, J. W.; Wilkes, J. S. *J. Am. Chem. Soc.*, **1986**, *110*, 2722-2726. and references therein.
5. Examples of tripodal anion receptors: a) Metzger, A.; Lynch, V. M.; Anslyn E. V. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 862-865. b) Beer, P. D.; Fletcher, N. C.; Grieve, A.; Wheeler, J. W.; Moore, C. P.; Wear, T. *J. Chem. Soc., Perkin Trans. 2* **1996**, 1545-1551. c) Raposo, C.; Almaraz, M.; Martin, M.; Weinrich, V.; Mussons, M. L.; Alcazar, V.; Caballero, M. C.; Moran, J. R. *Chem. Lett.* **1995**, 759-760. d) Raposo, C.; Perez, N.; Almaraz, M.; Mussons, M. L.; Caballero, M. C.; Moran, J. R. *Tetrahedron Lett.* **1995**, *36*, 3255-3258. e) Valiyaveettil, S.; Engbersen, J. F. J.; Verboom, W.; Reinhoudt, D. N. *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 900-901. f) Beer, P. D.; Chen, Z.; Goulden, A. J.; Graydon, A.; Stokes, S. E.; Wear, T. *J. Chem. Soc., Chem. Commun.* **1993**, 1834-1836. g) Beer, P. D.; Hazlewood, C.; Hesek, D.; Hodacova, J.; Stokes, S. E. *J. Chem. Soc., Dalton Trans.* **1993**, 1327-1332. h) Garratt, P. J.; Ibbett, A. J.; Ladbury, J. E.; O'Brien, R.; Hursthouse, M. B.; Abdul Malik, K. M. *Tetrahedron*, **1998**, *54*, 949-968.
6. *N-tert*-Butyl derivative of **1** was synthesized as a precursor of a tridentate carbene ligand: Dias, H. V. R.; Jin, W. *Tetrahedron Lett.* **1994**, *35*, 1365-1366.
7. a) Zavada, J.; Pankova, M.; Holy, P.; Tichy, M. *Synthesis* **1994**, 1132. b) van der Made, A. W.; van der Made, R. H. *J. Org. Chem.* **1993**, *58*, 1262-1263.
8. Some analytical data for **1**·3PF_6^-; mp. 167-168 °C; ^{1}H NMR (270 MHz, CD_3CN): δ 0.87 (t, J = 7.3 Hz, $C\underline{H}_3C_3H_6$, 9H), 1.25 (m, $CH_3C\underline{H}_2C_2H_4$, 6H), 1.75 (m, $C_2H_5C\underline{H}_2CH_2$, 6H), 2.20 (s, Ar-$C\underline{H}_3$, 9H), 4.11 (t, J = 7.2 Hz, $C_3H_7C\underline{H}_2$, 6H), 5.39 (s, $C\underline{H}_2$, 6H), 7.32 (s, C(5)$\underline{H}$, 3H), 7.39 (s, C(4)$\underline{H}$, 3H), 8.68 (s, C(2)$\underline{H}$, 3H); ^{13}C NMR (67.8 MHz, CD_3CN): δ 13.5, 16.7, 19.8, 32.4, 49.1, 50.4, 123.1, 123.6, 130.0, 135.6, 142.7; elemental analysis: calcd. for $C_{33}H_{51}N_6P_3F_{18}$: C, 41.00; H, 5.32; N, 8.70 %. Found: C, 40.76; H, 5.42; N, 8.59 %.
9. "AGRNMRL" programmed by Professor Emeritus M. Hida (T.M.U.).
10. Other examples of preorganization for acyclic receptors, see: Rebek, Jr, J. *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 245-255. and *Acc. Chem. Res.* **1990**, *23*, 399-404.
11. Recent examples of C-H ··· O hydrogen bonding in solution: a) Shinoda, S.; Tadokoro, M.; Tsukube, H.; Arakawa, R. *J. Chem. Soc., Chem. Commun.* **1998**, 181-182. b) Jeong, K.-S.; Cho, Y. L. *Tetrahedron Lett.* **1997**, *38*, 3279-3282. c) Musah, R. A.; Jensen, G. M.; Rosenfeld, R. J.; McRee, D. E.; Goodin, D. B. *J. Am. Chem. Soc.* **1997**, *119*, 9083-9084 and references therein.
12. The hydrogens of the C(2) position of imidazolium selectively deuterated by D_2O. See also ref. 4b.