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SIZE SELECTIVE RECOGNITION OF ANIONS BY A TETRACATIONIC IMIDAZOLIOPHANE

Kiyoshi Sato*, Tomomi Onitake, Sadao Arai, and Takamichi Yamagishi

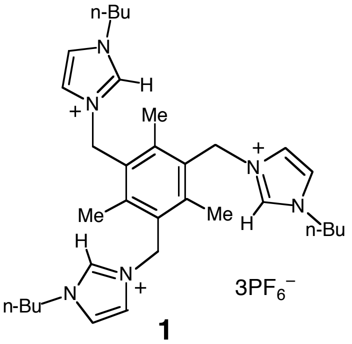
Department of Applied Chemistry, Graduate School of Engineering, Tokyo Metropolitan University, 1-1 Minami-ohsawa, Hachioji, Tokyo 192-0397, Japan
E-mail: sato-kiyoshi@c.metro-u.ac.jp

Abstract – The reaction of 1:1 mixture of 1,3-bis(1-imidazolyl)propane and 1,4-bis(chloromethyl)durene gives a new tetracationic heterophane (**2**), which forms a 1:1 inclusion complex with halides and oxoanions in DMSO-d_6 in the order of $HSO_4^- > Br^- > H_2PO_4^- > Cl^- > I^- > ClO_4^-$ depending on the size of anions.

As the importance of negatively charged species in biological as well as in chemical processes is increasingly recognized, the design of receptors for selective anion recognition has become a vigorously active research area in recent years.[1] However, the design and synthesis of anion binding hosts have been relatively slow to develop, in contrast to the analogous chemistry of cation receptors.[2]

In the previous paper, we demonstrated that the imidazolium group is an effective anion binding unit, and the tripodal receptor (**1**) shows a high binding affinity for halide anions in acetonitrile by electrostatic force, together with [C-H･･･X^-] type hydrogen bonds.[3] The anion selectivity feature of this acyclic receptor (**1**) depends on hydrogen bonding abilities and surface charge density of the anions ($Cl^- > Br^- > I^-$). No size discrimination was observed due to its conformational flexibility. This inherent binding preference, however, could be tuned by changing the receptor structure. It has been reported that convergence of anion binding units in a macrocyclic framework result in increased complex stability and enhanced selectivity for a suitable guest. For example, macrocyclic polyammoniums[4] and polyguanidiniums,[5] expanded porphyrins (sapphyrins),[6] calixpyrroles,[7] and cyclic thioureas[8] and polylactams[9] act as size-selective anion receptors for a variety of anions.

Although a number of macrocyclic compounds incorporated with imidzolium ring systems have been synthesized in the last few years,[10-14] anion binding study of the heterophanes with two imidazolium units has been only reported by Alcade[10e] and Xie.[11g] However, from the X-Ray crystal structure analysis, complexation occurs at the outer side of the dicationic imidazoliophanes and not by inclusion within their cavity because it is too small for halide anions.



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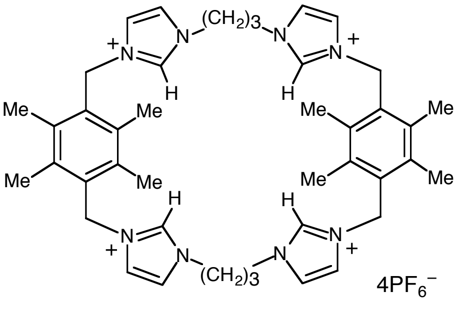

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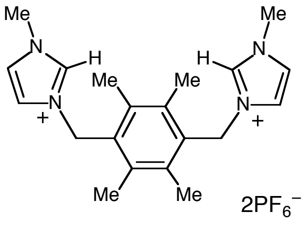

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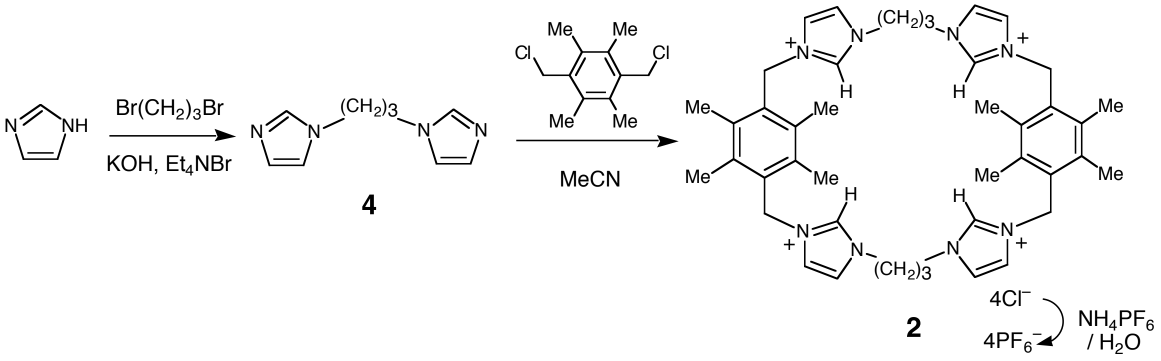
Presently, we report the first synthesis of a novel macrocyclic imidazoliophane (**2**) with four imidazolium groups[14] and a suitable size cavity (approximately 4 x 4.5 Å) for the inclusion of small inorganic anions. Additionally we are describing the anion binding feature of **2** toward various anions in a polar solvent.

The synthetic route of the cyclophane (**2**) is shown in Scheme 1. 1,3-Bis(1-imidazolyl)propane (**4**) was obtained in good yield (72%) by the reaction of imidazole with 1,3-dibromopropane in the presence of tetraethylammonium bromide as a phase-transfer catalyst.[11a] Treatment of **4** with 3,5-bis(chloromethyl)durene in boiling acetonitrile overnight provided a single [2+2] coupling product (**2**) in moderate yield (53% yield) without high-dilution conditions.[15,16] After counter ion exchange, the ESI-MS of the product showed peaks at m/z 1107 $[\mathrm{M}-\mathrm{PF}_6^{-}]^+$, 481 $[(\mathrm{M}-2\mathrm{PF}_6^{-})/2]^+$, and 272 $[(\mathrm{M}-3\mathrm{PF}_6^{-})/3]^+$, strongly supporting the structure of **2**.[17]



Scheme 1

The anion binding properties of **2**·$4PF_6^-$ for various univalent inorganic anions have been investigated in ^{1}H NMR titration experiments.[18] As shown in Figure 1 (left), the addition of halide anions (Et_4N^+ salts) to a DMSO-d_6 solution of the heterophane (**2**) induced downfield shifts of the C(2)-H resonance of the imidazolium rings. These downfield shifts can be ascribed to a formation of [C-H···X^-] hydrogen bonds[3] between the imidazolium units and the added anion. Cl^- induces a larger downfield shift than Br^- and I^-. For instance, addition of the 3 equiv. of $Et_4N^+Cl^-$ to **2** caused a downfield shift of 0.4 ppm for the C(2)-H hydrogen of imidazolium units, whereas addition of the same amount of $Et_4N^+Br^-$ and $Et_4N^+I^-$ gave downfield shifts of 0.2 and 0.03 ppm, respectively. However, the sharp turning of the titration curve towards Br^- at [anion]/[**2**] = 1 indicates a higher affinity for Br^-.

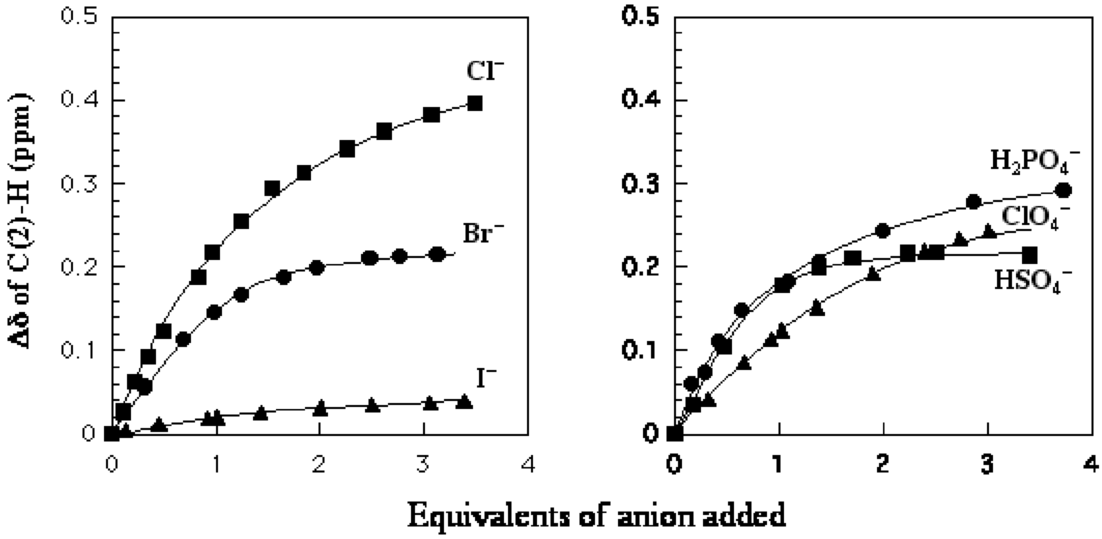


Figure 1. ^{1}H NMR titration curves of the receptor (**2**)·$4PF_6^-$ (2.0 mM in DMSO-d_6) with halides (left) and oxoanions (right), respectively.

Analysis of the titration curves gave binding constants K_a, listed in Table 1. The heterophane (**2**) shows a three-fold larger binding affinity for Br^- than Cl^- and five-fold larger than I^- in DMSO-d_6. The preference for Br^- over Cl^- and I^- suggests that the cavity of the macrocycle (**2**) should be more complementary to the size of Br^- than to that of Cl^- and I^-. In contrast, the acyclic analogues, **1** and 1,4-bis[1-(3-methylimidazolio)methyl]durene (**3**), showed a smaller shift of the C(2)-H signal of the imidazolium moieties in the same concentration range and no size-dependent selectivity observed in **2** was obtained.

Further titration studies of **2** with tetrahedral oxoanions (HSO_4^-, $H_2PO_4^-$, and ClO_4^-; as n-Bu_4N^+ salts) in DMSO-d_6 also afforded titration curves suggesting 1:1 stoichiometry (Figure 1 (right)). The binding constants collected in Table 1 indicate that the cyclic receptor (**2**) has a similar size-dependent selectivity toward the oxoanions ($HSO_4^- > H_2PO_4^- > ClO_4^-$).

Table 1. Binding constants K_a of the receptors (**1**, **2**, and **3**) with anions in DMSO-d_6.

		K_a[a] / M^{-1}					
Receptor	Anion[b]	Cl^-	Br^-	I^-	HSO_4^-	$H_2PO_4^-$	ClO_4^-
	r[c] / Å	1.81	1.96	2.20	1.90	2.00	2.40
1		760	200	94	200	$>10^3$ [e]	-[d]
2		720	2230	460	8500	1350	290
3		140	59	-[d]	-[d]	-[d]	-[d]

[a] Determined in DMSO-d_6 at 298 K, errors are estimated to be <10%.

[b] Et_4N^+ and n-Bu_4N^+ salts were used for halides and oxoanions, respectively.

[c] Ion radius are taken from ref. 19. (PF_6^-: 2.45 Å)

[d] K_a values could not be determined due to too small shifts.

[e] Accurate K_a values could not be determined because precipitation occurred during the titration.

In summary, we have shown that the new tetracationic imidazolium heterophane (**2**) has a high affinity and size selectivity for spherically shaped inorganic anions ($HSO_4^- > Br^- > H_2PO_4^- > Cl^- > I^- > ClO_4^-$) by the formation of 1:1 inclusion complexes in a polar solvent. Further investigation on this and related systems are ongoing in order to obtain better and more selective receptors for a variety of anionic guests.

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This paper is dedicated to Emeritus Professor Soichi Misumi on the occasion of his 77th birthday

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