The Synthesis, Molecular Structure and Selectivity of Macrotricyclic Ammonium-ion Receptor for Bromide Ion

Naohito Ito, Mitsunori Izumi,† Kazuhiko Ichikawa,* and Motoo Shiro††
Division of Material Science, Graduate School of Environmental Earth Science, Hokkaido University, Sapporo 060
†Division of Fundamental Studies, Research Institute for Higher Education Programs, Hokkaido Tokai University, Sapporo 005
††X-Ray Research Laboratory, Rigaku Corporation, Akishima, Tokyo 196

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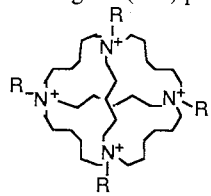
The cage receptor $[R_4N_4(C_5H_{10})_2(C_6H_{12})_4]^{4+}$ ([566]RMQA^{4+}) was designed and synthesized. X-ray crystallography, ^{1}H-NMR and molecular mechanics calculation revealed the complexibility and selectivity toward Br^-. In the presence of both Cl^- and Br^-, [566]RMQA^{4+} shows the higher selectivity toward Br^- in aqueous solution.

In most cases of halide-anion receptors the ligand species feature protonated amine groups in macrocycle: electrostatic interaction provides the binding forces owing to the molecular recognition for anionic substrates.[1] Several macrotricyclic cage receptors designed in our laboratory have characteristic feature of four positive binding sites converged to the center of the spherical intramolecular cavity: their encapsulation and selectivity for halide ions as guests show no pH-dependence in aqueous solution. Systematic variation of the cyclic methylene groups can control the complementary effect on binding power toward each halide ion of F^-, Cl^-/Br^- or I^-. Macrotricyclic quaternary ammonium ions $[R_4N_4(C_5H_{10})_6]^{4+}$ ([555]RMQA^{4+})[2] and $[R_4N_4(C_6H_{12})_6]^{4+}$ ([666]RMQA^{4+})[3] were synthesized as the F^- and I^- receptors, respectively, where [nnn] stands for all the hydrocarbon cycles consisting of the (nnn) triangular planes of n methylene-groups and R is exo-group. The receptor having a hydrophobic group for R, benzyl or naphthyl group, acts as ion carrier across phospholipid bilayer membrane.[3d]

In frequently encountered cause, the concentration of Br^- is too small to analyze and may be masked by Cl^-. In environmental water, brominated trihalomethane have been singled out as having hygienic problems similar to chloroform.[4] The receptor should be designed to detect bromide in a mixture containing much less bromide and much more chloride in amounts.

The bromide receptor was designed by critical adjustment of the size of intramolecular cavity by choosing the methylene chain length between [555] and [666]. This work synthesized $[R_4N_4(C_5H_{10})_2(C_6H_{12})_4]^{4+}$ ([566]RMQA^{4+}) which has all the triangular (566) planes.[5]



[566S]MMQA^{4+} : R=CH_3
[566S]BnMQA^{4+} : R=$CH_2C_6H_5$

The structure of amine, $[N_4(C_5H_{10})_2(C_6H_{12})_4]$ ([566]MA), shows considerable distortion of flexible framework from tetrahedral symmetry, as shown in Figure 1.[6] The molecular structure of $Br^-\subset$[566]BnMQA^{4+} modified by benzyl group as exo-group shows unambiguous encapsulation of one Br^- within the cavity, as show in Figure 2.[7] The structure after encapsulating Br^- shows tetrahedral symmetry: all the N•••N distances are lager than $Cl^-\subset$[566D]BnMQA^{4+} [8] by 0.21-0.38 Å and Br^-•••N bond distances in $Br^-\subset$[566] are longer than Cl^-•••N distances in $Cl^-\subset$[566D] by 0.01-0.20 Å, whereas [566D] consists of one (555) triangular plane and the three (566) triangular planes.

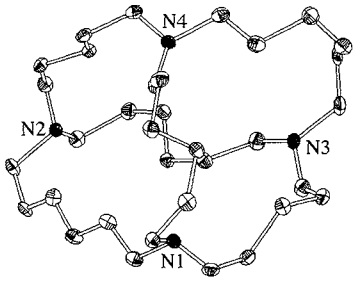


Figure 1. ORTEP representation of the structure of [566]MA with thermal ellipsoids draw at the 50% probability level. The hydrogen atoms have been omitted for clarity. Selected geometric parameters (Å): N1-N2 7.601; N1-N3 5.989; N1-N4 6.387; N2-N3 8.089; N2-N 4 6.481; N3-N4 5.670.

The complexibility and selectivity of [566]MMQA^{4+} toward halide ions in the aqueous solution have been revealed by ^{1}H-NMR measurements. The addition of Cl^- or Br^- led to downfield shift in the chemical shift of endocyclic α- and β-

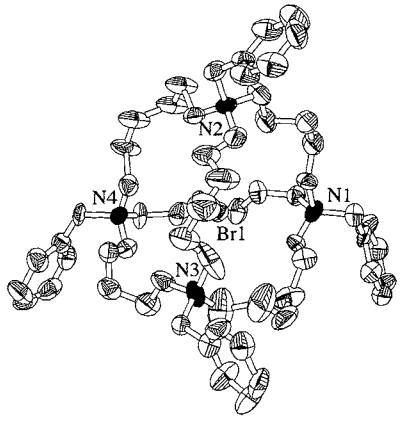


Figure 2. ORTEP representation of the structure of [566]BnMQA^{4+}•4Br^-•4H_2O with thermal ellipsoids draw at the 50% probability level. The hydrogen atoms, the other three bromide ions and the four water molecules have been omitted for clarity. Selected geometric parameters (Å):N1-N2 6.776; N1-N3 7.298; N1-N4 7.396; N2-N3 7.049; N2-N4 7.186; N3-N4 6.376; Br1-N1 4.339; Br1-N2 4.417; Br1-N3 4.026; Br1-N4 4.439.

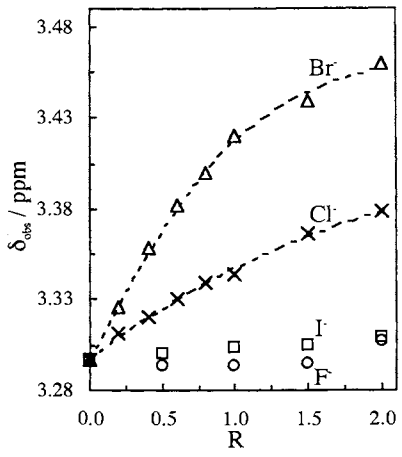


Figure 3. The R (= $[X^-]/[566]$) dependence of δ for the endocyclic in D_2O solution at $[566MMQA^{4+}]_0$ = 5 mM, ionic strength = 0.1 M KNO_3 and 30 ℃. The dashed lines were obtained by a model calculation of titration curve.

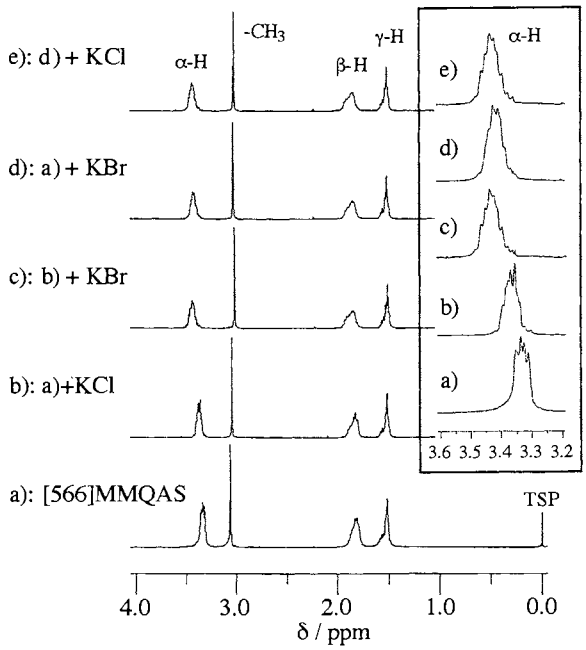


Figure 4. ^{1}H-NMR spectra of [566]MMQAS under the presence of halide ions in D_2O at 30 ℃, R (= $[X^-]_0/[566MMQA^{4+}]_0$) = 2.0, $[566MMQA^{4+}]_0$ = 5 mM and ionic strength 0.1 M KNO_3.

protons (Figure 3): F^- or I^- lead to no shift. Thus [566] shows the higher complexibility for Br^-: the stability constants are $K_{st}(Cl)$ = $110M^{-1}$ and $K_{st}(Br)$ = $990M^{-1}$. The α-H shifts of Cl^- and $Br^-\subset$ [566] are equal to δ_{Cl} = 3.37 and δ_{Br} = 3.42, respectively, whereas δ = 3.30 for [566] without any Cl^- or Br^- (Figure 4). In the presence of both chloride and bromide ions, the α-H shifts showed the magnitude similar to $Br^-\subset$[566] (δ_{Cl+Br} = 3.44, the inset of Figure 4). Thus [566] shows the higher affinity for Br^- in the presence of both Cl^- and Br^-.

The encapsulation process of $[566]MMQA^{4+}$ toward halide ions has been revealed by molecular mechanics calculations (MM2).[9] The steric energy SE of the system consisting of [566] and X^- was calculated at each distance r between X^- and N^+ at the

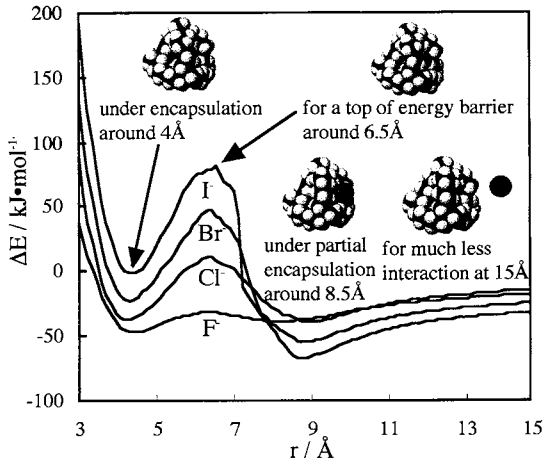


Figure 5. ΔE as a function of distance r through the center of (566) between N^+ in $[566]MMQA^{4+}$ and X^-.

other side through a center of (566).[10,11] ΔE is the difference between the SE of the encapsulated complex $X^-\subset$[566] and the sum of free [566] and free X^-. The r-dependence of ΔE showed the two minima in energy, which mean the two stable species of encapsulated X^- and partially encapsulated X^- (Figure 5).[2,3c] A maximum shows an activated state associated with energy barrier ΔE^*. The very shallow minima of ΔE and the low ΔE^* mean their unstable species for F^-: ΔE^* of I^- is too high to be encapsulated into the intramolecular cavity. The ^{1}H-NMR data demonstrate that the magnitudes of ΔE and ΔE^* for Br^- are much more reasonable for the complexibility and selectivity of [566] toward Br^-, compared with Cl^-. The stability of $Br^-\subset$[566] may be controlled by the substantial contribution of ΔE^* compared with ΔE.

References and Notes

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5 The synthetic route of [566]MMQAS and [566]BnMQAS involves the three successive cyclization for the construction of macrotricyclic amine used that we modified conventional methods. All new compounds of [566] have been identified by ^{1}H-NMR and elemental analysis.

6 The measurement was made on Rigaku RAXIS-IV imaging plate area detector (μ(MoKα) = 0.60 cm^{-1}). Crystal data of $N_4(C_5H_{10})_2(C_6H_{12})_4$, M = 532.94, Pbca, orthorhombic, a = 31.942(4), b = 17.312(3), c = 12.362(2) Å, V = 6836(1) $Å^3$, Z = 8, D_{calc} = 1.036 g/cm^3, R = 0.049.

7 The measurement was made on Rigaku RAXIS-IV imaging plate area detector (μ(MoKα) = 24.32 cm^{-1}). Crystal data of $[566]BnMQA^{4+}\cdot 4Br^-\cdot 4H_2O$: M = 1301.24, $P\bar{1}$, triclinic, a = 19.744(3), b = 24.599(4), c = 15.150(3) Å, α = 90.77(1), β = 112.36(2), γ = 83.79(1) Å, V = 6761(2) $Å^3$, Z = 4, D_{calc} = 1.278 g/cm^3, R = 0.114.

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9 Molecular mechanics calculation was accomplished with the molecular mechanics packages provided by the Tektronix CAChe System, ver. 3.7. The initial structure of $X^-\subset[566]MMQA^{4+}$ was given by X-ray structure of $Br^-\subset[566]BnMQA^{4+}$ and the exchange between the two exo-groups $-CH_3$ (M) and $-CH_2C_6H_5$ (Bn). The lowest energy structures were optimized from 3.0 Å to 15.0 Å at intervals of 0.12 Å. In this calculation the contribution from the solvent of water has never been included.

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