J. Phys. Chem. A **2002,** *106,* 3008−3016

Ion-Selective Characteristics of Tetrahydrofuran-Based 16-Crown-4 Derivatives and Its Cation Complexes: Ab Initio Study

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Received: November 9, 2001; In Final Form: January 3, 2002

Structures of 1,4,6,9,11,14,16,19-tetraoxacycloeicodane (THF-based 16-crown-4 derivative, ionophore I), its derivatives, and the derivative−cation (Li^+, Na^+, K^+, and H^+) complexes have been optimized using ab initio Hartree−Fock (HF) and single point second-order Möller−Plesset (MP2) methods. The geometric structures of ionophore I, h-*tetra***Me**-ionophore, and v-*tetra***Me**-ionophore are optimized to macrocyclic cages with C_4 symmetry. Four oxygen atoms which are the binding sites of the cage are located at the bottom of the ionophore derivative. The cavity sizes of the derivatives are expanded by the symmetric substitution of the methyl groups. The symmetrically expanded derivatives can easily capture the cations to go through the cavity. In ionophore−M^+ complexes, M^+ is coordinated with four oxygen atoms of the derivatives and located at the center. Li^+ is disposed in the plane of the cyclic frame. The van der Waals radius of Li^+ fits well with the cavity size of the derivatives. While, the van der Waals radii of Na^+ and K^+ are larger than the cavity size, Na^+ and K^+ are disposed on the lower side of the mean plane of the cyclic frames. Meanwhile, in ionophore−H^+ complexes, H^+ is optimized to be bridged between two neighboring oxygen atoms. As the ionic size increases, the distances (R_{OO}) between two opposite oxygen atoms as well as the distances (R_{OM}) between a cation and the oxygen atoms also increase. The atomic charges of Li^+ are less positive than those of the other cations, and the charges of the oxygens are more negative than those of the carbon atoms. The ratio of the (atomic charge/ionic radius) of Li^+ converges to 1. The binding energies from Li^+ to K^+ decrease monotonically.

I. Introduction

Using macrocyclic ligands containing oxygen, nitrogen, and sulfur atoms, studies for the design of ion-selective liquid membranes have been extensively performed by both experimental[1−31] and theoretical[32−40] approaches. The macrocyclic ligand has a hydrophilic cavity formed from hydrophobic alkyl chains,[1−9] and it makes a complex with the metal cations to go through the lipophilic biological membranes.[10−31] The binding between a cation and a macrocyclic ligand has high selectivity. The binding of the cations depends on their ionic diameters and the site of the interactions (charge−dipole, dipole−dipole). Several metal ion-selective electrodes were developed from macrocyclic polyether materials such as noncyclic polyether diamides, phenanthroline derivatives, and crown ether molecules.[1−9] The macrocyclic ligands such as the crown ethers with 13−16 membered rings have been applied to the ion-selective electrodes for heavy metal ions.[10−31] Particularly, tetrahydrofuran-based 16-crown-4 derivatives having tetrahydrofuran (THF) as a principal chain component have been successfully applied to the ion-selective liquid membranes of the host−guest complexes.[28−31] The lipophilic compounds containing tetrahydrofuran units are formed as macrocyclic chain components containing electronegative atoms. These lipophilic compounds containing THF units also occur in natural products as in the antibiotic ionophores. Some electronegative atoms of the lipophilic cyclic ligands have potential utility because of their greater electron donor ability as well as the hydrophilic and lipophilic balance. Until now, many research efforts have been focused on the design of the macrocyclic ligand.

Recently, Kim's group[28−31] has suggested that the 16-crown-4 derivatives containing the tetrahydrofuran backbone as a lipophilic compound have high selectivity for lithium ion. Especially, 14-crown-4 ether has high selectivity for Li^+. Lipophilic tetraazacrown ether of 16-membered rings having four pyrrole units is also applied as a Ag^+-selective electrode.[31] Although Hg^+ provides some interference, the selectivity is good enough to ensure technical applications.[29] Kobuke and co-workers[12] examined the lithium coordination chemistry of a tetrameric THF-based ionophore and found remarkably strong binding. This strong binding probably arises in large measure from the conformationally "stiffened" nature of the ionophore. These ionophores containing THF units lack the conformational freedom which characterizes most of the crowns. The connectivity of these ionophores constrain the donor atoms to positions commensurate only with the coordination of lithium. X-ray diffraction of the lithium complex has revealed a square-pyramidal coordination sphere with four oxygen donor atoms disposed on one side of the mean plane of the ionophore.[17]

Although investigations for the design of ion-selective liquid membranes have been performed by many research groups,[1−40] the structures and relative stabilities of the ionophore−alkali metal cation complexes have not been studied much in detail. Due to the limited information of the ion-selective characteristics for the THF-based 16-crown-4 derivatives, further studies of their structures and hydrophilic cavity sizes seem to be worth carrying out on the basis of the following points. (i) The geometric structures of the cyclic frames of the ionophore derivatives can be modified by replacing the hydrogen atoms by methyl groups. Are the geometric structures (cavity shapes)

10.1021/jp014131d CCC: $22.00

of the cyclic frames influenced by the binding of cations? That is, is the binding between cations and the derivatives influenced by the steric hindrance of the bulky group? (ii) The cavity of 16-crown-4 derivatives is the best fit for Li^+ as the ionophore−lithium cation complexes. Are the cavity sizes of the ionophore derivatives related to the size of the cations? That is, how is the cavity size of the 16-crown-4 derivatives dependent on the kinds of cations (Li^+, Na^+, K^+, and H^+)? (iii) Is the interaction between a cation and four oxygen atoms taking place equally? (iv) Do the negative charge densities on the four oxygen atoms varies with the number of methyl groups? And is the ratio of (atomic charge/ionic radius) of the cations related to the ionic selectivity? To solve these questions, we optimized the geometric structures of the THF-based 16-crown-4 derivatives and its cation (Li^+, Na^+, K^+, and H^+) complexes.

II. Computational Methods

The geometric structures of THF-based 16-crown-4 derivative and its derivatives substituted by methyl groups were fully optimized using ab initio Hartree−Fock (HF) and single point second-order Möller−Plesset methods with the 6-31G* basis set. To obtain the optimized structures of the complexes between cation and the derivatives, calculations were performed on model systems with a cation approaching the optimized derivatives from long distances. Structures of the complexes between the optimized derivatives and the alkali metal cations (Li^+, Na^+, and K^+) as well as hydrogen cation (H^+) were also optimized. To examine the accuracy of the computational results, the geometric structures of some of the complexes have also been calculated at the Hartree−Fock/6-31+G** level. After the optimizations, the harmonic vibrational frequencies were evaluated to confirm the existence of a stable structure at the HF level. All the calculations were performed using the Gaussian 98 package.[41]

III. Results and Discussion

Optimized geometric structures of ionophore I and THF-based 16-crown-4 derivatives are shown in Figure 1. The geometric structure of ionophore I is optimized to a cyclic cage form with C_4 symmetry. The cage is formed by a chain consisting of four tetrahydrofuran units and four methylene groups. In the top view, four oxygen atoms and four hydrogen atoms of the four tetrahydrofuran units are directed inward. In the side view, four oxygen atoms of the binding site are located at the bottom of the cage, while the four hydrogen atoms of the four THF units are pointing toward the central upper side. With an increase in the number of methyl groups, the geometric structures of the derivatives are more distorted than those of the corresponding ionophore I. That is, by symmetric substitutions with two, four, and eight methyl groups, the structures of the derivatives are optimized to cages with C_2 symmetry, while, by unsymmetric substitutions, the structures are optimized to ellipsoidal cages with C_1 symmetry. The shortest distance between two opposite atoms of an ionophore derivative is denoted as *cavity size*. Ionophore derivatives substituted by four methyl groups as a horizontal and a vertical directions of the four bridged methylene backbones are denoted as h-*tetra***Me**-ionophore and v-*tetra***Me**-ionophore, respectively. The ionophore derivative simultaneously substituted horizontally and vertically by two methyl groups on a bridged methylene backbone and simultaneously substituted horizontally and vertically by two methyl groups on an opposite bridged methylene is denoted as vh-*tetra***Me**-ionophore. The ionophore derivative substituted horizontally by two methyl groups on two opposite methylene backbones and vertically by two methyl groups on the two other opposite methylenes is denoted as v,h-*tetra***Me**-ionophore.

The geometric structures of h-*tetra***Me**-ionophore and v-*tetra***Me**-ionophore are optimized to symmetric form with C_4 symmetry. Although four methyl groups are substituted horizontally and vertically, the cyclic frames of the two ionophores are similar to the structure of ionophore I. In h-*tetra***Me**-ionophore, the four hydrogen atoms on four THF units are directed toward the inner side of the cavity, while, four methyl groups are directed toward the outer side. Four oxygen atoms are located at the lower side of the cyclic frame. In v-*tetra***Me**-ionophore, the four oxygen atoms and the four hydrogen atoms are situated along the central lower and upper sides, respectively. The four methyl groups of the ionophore are pointing toward the axial side. Although the four hydrogen atoms and the four oxygen atoms of two derivatives are located at the cavity center, the cavity size of the cyclic frame is expanded symmetrically. Because of the symmetric structure and expanded size of the derivatives, it complexes with some cations to go through the cavity. Therefore, h-*tetra***Me**-ionophore and the v-*tetra***Me**-ionophore can function as molecular sieves to capture the cations.

The geometric structures of the other derivatives (h-**Me**-ionophore, h-*di***Me**-ionophore, vh-*di***Me**-ionophore, vh-*tetra***Me**-ionophore, vh-*octa***Me**-ionophore, v,h-*di***Me**-ionophore, v,h-*tetra***Me**-ionophore, v-**Me**-ionophore, and v-*di***Me**-ionophore) are optimized to distorted cages with C_1 and C_2 symmetries, respectively. Because of the flexibility of the ring frame, the structures of these derivatives are more distorted than that of ionophore I. In the derivatives, two opposite hydrogen atoms and two opposite tetrahydrofuran units on the cyclic frame are directed toward the inner side of the cavity, while the other two hydrogen atoms and two tetrahydrofuran units direct themselves to the outer side. Due to the steric hindrance, the horizontal and vertical methyl groups on the cyclic frame are directed toward the outer and lower sides of the cavity, respectively. By distortion of these derivatives, the cavity size is decreased. As a result, a cation can only approach the lower side of the cavity. Meanwhile, in the vh-*octa***Me**-ionophore, eight hydrogen atoms on four methylene groups are substituted by eight methyl groups. To reduce the repulsive force between methyl groups, the structure of vh-*octa***Me**-ionophore is optimized to distorted cages with C_2 symmetry. The optimized structure of the vh-*octa***Me**-ionophore is similar to the experimental result.[1−31]

Vogel's group[8] synthesized tetraoxaporphyrin derivatives and investigated the characteristics of the hydrophilic cavity in their center. Three kinds (D_{2d}, center of symmetry, C_1) of the geometric isomers of the derivatives were represented using X-ray structure analysis. In the derivative with D_{2d} symmetry, four furan units are located as an axial direction of the mean plane of the cyclic frame. The geometric structure cannot be a cavity as a moleculer sieve to capture a cation. In the derivatives with a center of symmetry, four oxygen atoms are directed toward the inner side of the cavity of the derivatives. The distance between two opposite oxygen atoms is shorter than that of the derivative with D_{2d} symmetry. When a cation passes through the cavity of the derivatives with a center of symmetry, the cation can easily capture the cyclic derivative. By the HPLC analysis of the ionophore derivatives,[3] the cis isomers of the derivatives bind to the silica surface through the intraannular ether oxygens. The relative binding energies depend on the number of ether oxygens of the ligand that simultaneously can

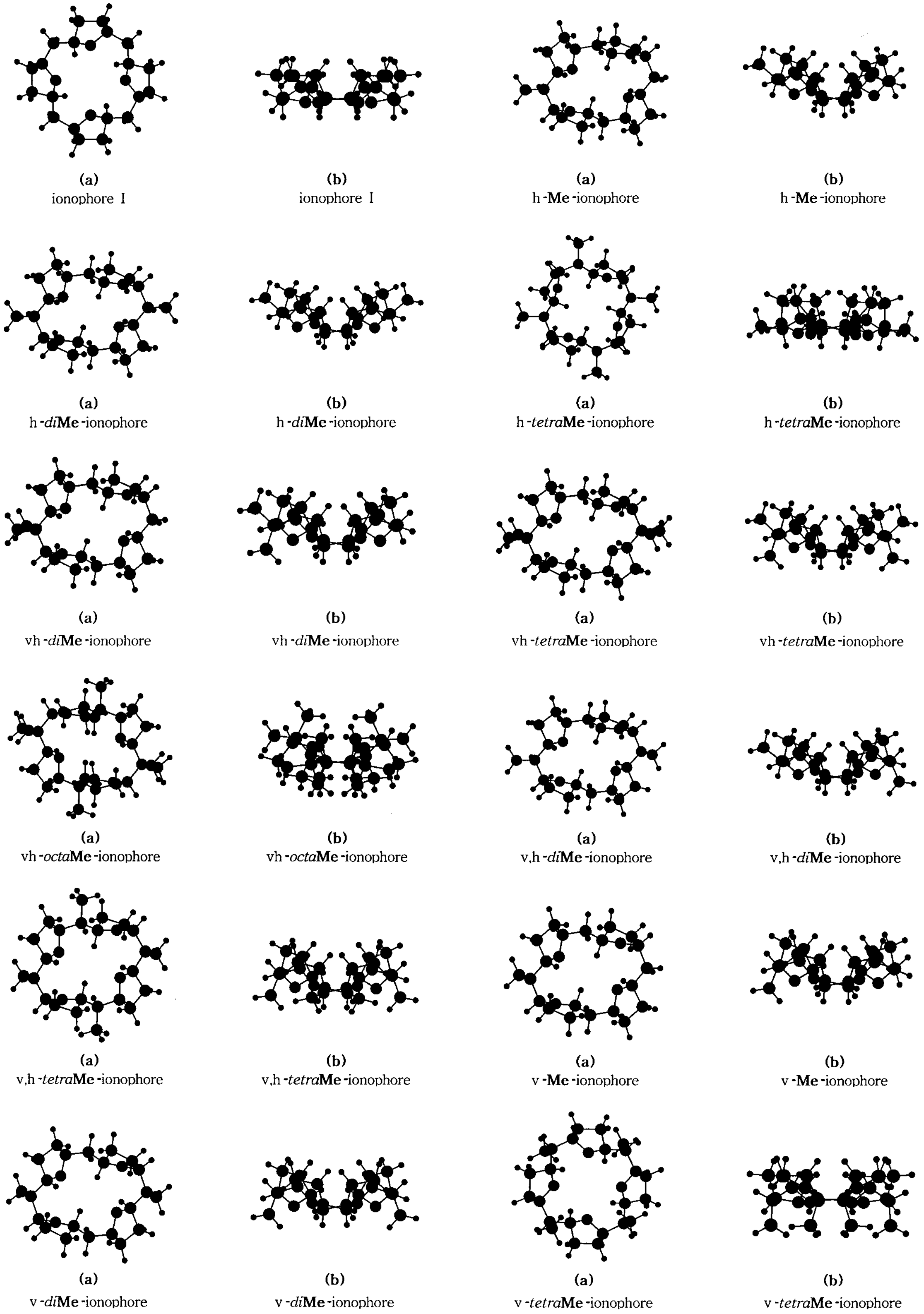
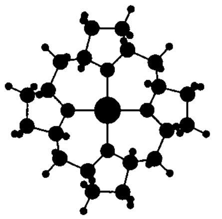


Figure 1. Geometric structures of 1,4,6,9,11,14,16,19-tetraoxacycloeicosane and its ionophore derivatives substituted by some methyl groups, optimized using the ab initio Hartree−Fock/6-31G* level. The top view is indicated as (a); the side view is indicated as (b).

be oriented into binding positions. In the cis derivatives, four oxygen atoms of the binding site are located at the bottom of the cage. Those experimental results are in line with our optimized structures.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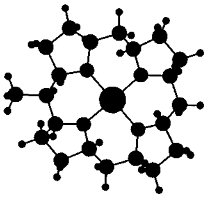
ionophore-Li$^+$


(b)
ionophore-Li$^+$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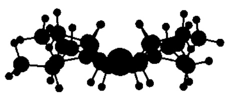
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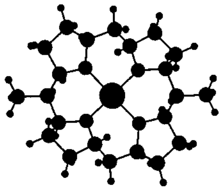
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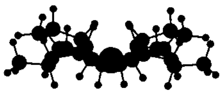
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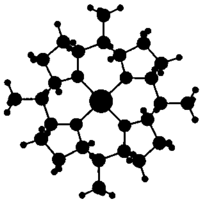
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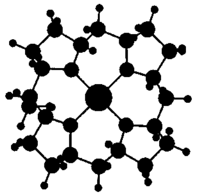
h-*tetra***Me**-ionophore-Li$^+$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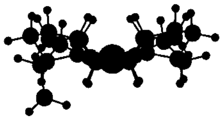
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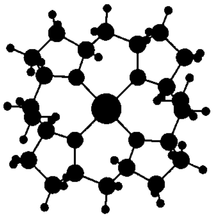
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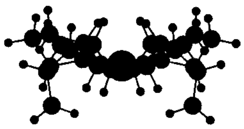
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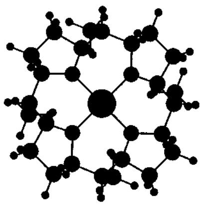
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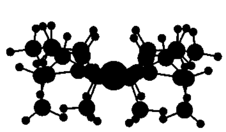
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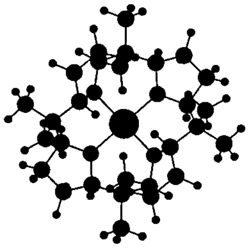
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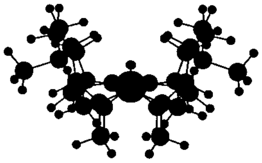
(b)
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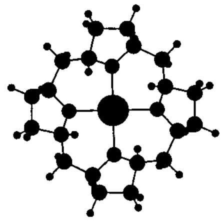
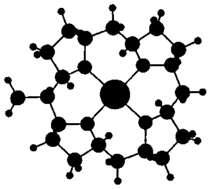

(a)
ionophore-Na$^+$


(b)
ionophore-Na$^+$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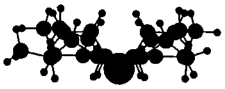
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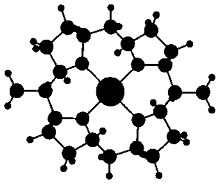
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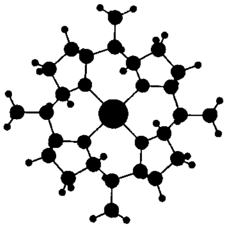
(b)
h-*di***Me**-ionophore-Na$^+$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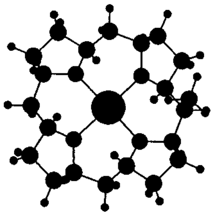
(b)
h-*tetra***Me**-ionophore-Na$^+$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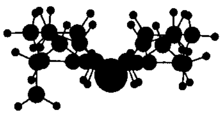
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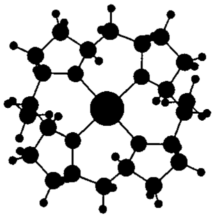
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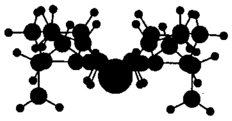
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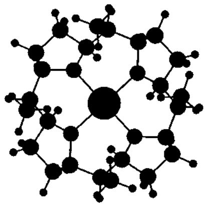
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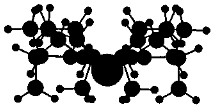
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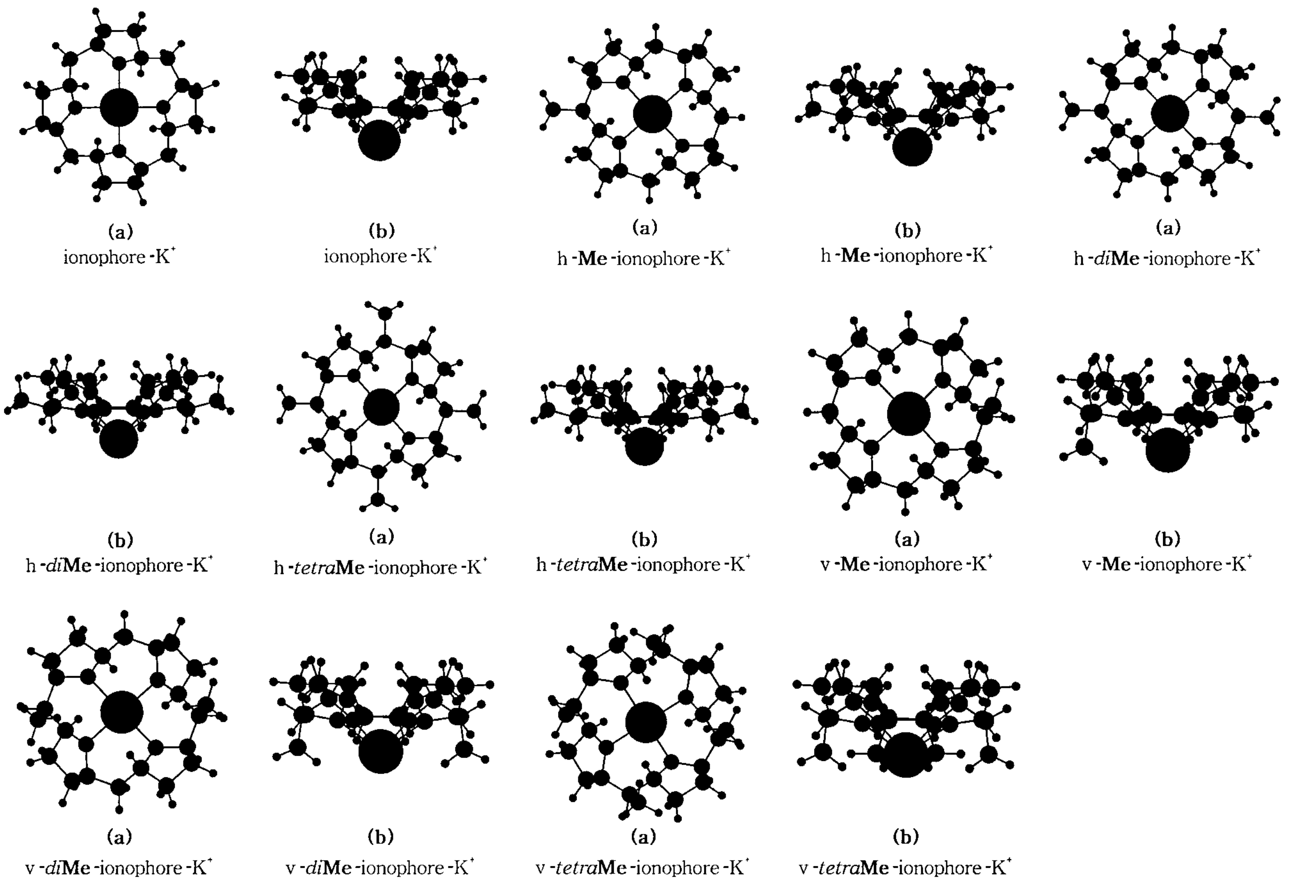

(a) ionophore-K$^+$ (b) ionophore-K$^+$ (a) h-**Me**-ionophore-K$^+$ (b) h-**Me**-ionophore-K$^+$ (a) h-*di***Me**-ionophore-K$^+$

(b) h-*di***Me**-ionophore-K$^+$ (a) h-*tetra***Me**-ionophore-K$^+$ (b) h-*tetra***Me**-ionophore-K$^+$ (a) v-**Me**-ionophore-K$^+$ (b) v-**Me**-ionophore-K$^+$

(a) v-*di***Me**-ionophore-K$^+$ (b) v-*di***Me**-ionophore-K$^+$ (a) v-*tetra***Me**-ionophore-K$^+$ (b) v-*tetra***Me**-ionophore-K$^+$

Figure 2. Geometric structures of 1,4,6,9,11,14,16,19-tetraoxacycloeicosane−alkali metal cation complexes substituted by some methyl groups, optimized using ab initio Hartree−Fock/6-31G* level. The top view is indicated as (a); the side view is indicated as (b).

As shown in Figure 2, geometric structures of the ionophore−cation (Li^+, Na^+, and K^+) complexes are optimized to a circular disk form. Cations are located at the center of the complexes. Li^+ is located in the plane of the cyclic frame, while the other cations (Na^+ and K^+) are complexed at the lower side of the mean plane of the cyclic frames. Because of the dipole−charge interaction between the cation and the derivative, the structures of the complexes are more symmetric than those of the corresponding derivatives. That is, the cyclic frames of the complexes are flatter than those of the corresponding derivatives. The notations of the ionophore−cation complexes such as h-*tetra***Me**-ionophore-M$^+$ or v-*tetra***Me**-ionophore-M$^+$ are similar to those of the corresponding derivatives. The optimized structures of vh-*di***Me**-ionophore-M$^+$, vh-*tetra***Me**-ionophore-M$^+$, v,h-*di***Me**-ionophore-M$^+$, and v,h-*tetra***Me**-ionophore-M$^+$ are not represented in Figure 2.

The structures of h-*tetra***Me**-ionophore-Li$^+$ and v-*tetra***Me**-ionophore-Li$^+$ have C_4 symmetry. Li^+ complexed with the four oxygen atoms is located at the central bottom of the cyclic frame. In these complexes, Li^+ can complex with the four oxygen atoms from both sides. The van der Waals radius of Li^+ fits well with the cavity size of the derivatives. The geometric structures of the other complexes have C_1 and C_2 symmetries. By distortion of these derivatives, the cavity sizes are reduced. The cation can complex with these derivatives on the lower side (one side) of the cavity. Particularly, because of the steric hindrance of the eight methyl groups, the geometric structure of vh-*octa***Me**-ionophore-Li$^+$ is hardly optimized with the HF/6-31+G** level. That is, vh-*octa***Me**-ionophore substituted by the eight methyl groups is hindered to be complexed with the lithium cation from long distances. The optimized structure of vh-*octa***Me**-ionophore-Li$^+$ is a distorted cage with C_2 symmetry. In the top view, four hydrogen atoms of four tetrahydrofuran units are directed inward. In the side view, Li^+ is located at the bottom of the cage, while two hydrogen atoms and two methyl groups are pointing toward an axial direction of the mean plane of the cyclic frame. The geometric structures are similar to the X-ray structure.[17] As a result, the symmetric structure (cavity size) of the cyclic frame plays an important role on the binding of Li^+.

According to the experimental results of Kim's group,[28−31] with the increase in the number of methyl or ethyl groups, the Li^+ selectivity of the electrodes based on the ionophore decreases. Bulky substitutents such as ethyl or diethyl groups on the bridged carbons have more influence on the complexation between ionophore derivatives and Li^+. Due to the steric effects, Li^+ cannot easily complex with the cyclic ligand substituted with bulky groups. Kobuke and co-workers[12] have investigated the geometric structures of the ionophore−lithium complexes. In the kinitic studies of the transport of metal cations through a liquid membrane, the best carrier for a given cation is a ligand that gives a moderately stable rather than the very stable complex in the extraction. By strong binding with the charge−dipole interaction, the ionophores containing the THF unit is conformationally "stiffened", so considerable conformational freedom is lost. In the HPLC experiment of Weber's group,[3] the relative binding energies depend on the number of ether oxygens of the ligand that simultaneously can be oriented into binding positions. The number of methyl groups that sterically interfere with binding to the surface depends on the configuration of the ligands. The maximum binding strength is attained in the all cis isomers in which all four ether oxygens can

TABLE 1: Distances (Å) and Atomic Charges (au) of Ionophore I and Its Ionophore Derivatives Substituted by Some Methyl Groups

							exptl[g]	
	R_{OO}[a]	r_{OO}[b]	O[c]	C_1[d]	C_2[e]	C_3[f]	R_{OO}	r_{OO}
ionophore I(6-31G*)	4.451	3.211	−0.655	0.001	0.365	0.037		
ionophore I(6-31+G**)	4.460	3.216	−0.659	0.003	0.368	0.039		
h-**Me**-ionophore	4.940	3.488	−0.666	0.006	0.362	0.030		
h-_di_**Me**-ionophore	4.941	3.490	−0.670	0.005	0.368	0.031		
h-_tetra_**Me**-ionophore	5.372	3.799	−0.681	0.039	0.355	0.029		
vh-_di_**Me**-ionophore	4.947	3.492	−0.668	0.008	0.364	0.029		
vh-_tetra_**Me**-ionophore	4.978	3.502	−0.673	0.037	0.372	0.029		
vh-_octa_**Me**-ionophore	5.039	3.551	−0.689	0.079	0.390	0.023		
vh-_octa_**Me**-ionophore(6-31+G**)	5.021	3.563	−0.692	0.049	0.407	0.031	5.003	3.581
v,h-_di_**Me**-ionophore	4.948	3.494	−0.668	0.008	0.363	0.030		
v,h-_tetra_**Me**-ionophore	4.983	3.523	−0.672	0.021	0.363	0.029		
v-**Me**-ionophore	4.971	3.516	−0.664	0.010	0.358	0.029		
v-_di_**Me**-ionophore	4.974	3.518	−0.669	0.013	0.358	0.029		
v-_tetra_**Me**-ionophore	5.454	3.819	−0.680	0.039	0.350	0.030		

[a] Average distance between two opposite oxygens in the ionophore derivative. [b] Average distance between two neighboring oxygens in the ionophore derivative. [c] Average charge density of four oxygen atoms in the ionophore derivative. [d] Average charge density of carbon atoms at four bridged methylene groups. [e] Charge density of the first carbon atom bonded to the oxygen atom in the tetrahydrofuran unit. [f] Charge density of the second carbon atom from the oxygen atom in the tetrahydrofuran unit. [g] Reference 17.

participate in the binding. All four methyl groups are then on the opposite side of the ligand, pointing away from the silica surface. These experimental results are in good agreement with our results.

Theoretically, Cuthbertson and Glidewell[32] determined the structures and conformations of ionophore derivatives using a semiempirical method. The optimized structure of the derivative has S_4 symmetry. Four oxygen atoms of a derivative are in an exactly planar array of D_{4h} symmetry. Four furan units of the derivative are not only tilted from the oxygen plane but skewed also. That is, the geometric structure of the derivative is a cage form. Kim's group[33−40] theoretically optimized the geometric structures of the ionophore−cation complexes. The optimized structures of the complexes have a high degree of symmetrization. A cation is located at the center of the derivatives. The cation is disposed in the plane of the cyclic frame. These theoretical results are very similar to our results.

In ionophore−Na$^+$ and −K$^+$ complexes, Na$^+$ and K$^+$ interact with four oxygen atoms at the lower side of the derivatives. The cations are located outside the cyclic frame. Since the van der Waals radii of the cations are slightly larger than the cavity size, the cations cannot pass through the cavity. Cations can only approach the lower side of the derivatives. When a cation approaches through the upper side, it hardly complexes with four oxygen atoms due to the steric hindrance of four hydrogen atoms. Meanwhile in ionophore−H$^+$ complexes, H$^+$ is bridged to two neighboring oxygen atoms of the cyclic ligand and the other two oxygen atoms are free. H$^+$ is located at a corner of the cavity. Although the bridged structure between H$^+$ and two oxygen atoms is formed, the cyclic structures of the complexes are still distorted. Because of the small ionic radius, H$^+$ can pass through the cyclic ligand. H$^+$ can be easily combined with the electronegative atoms of the derivatives. The size consistency between the van der Waals radius and the cavity size greatly influences on the binding of the cations.

Optimized distances and atomic charges of the derivatives and its complexes are listed in Tables 1 and 2. The average distances between two opposite oxygen atoms and between two neighboring oxygen atoms are denoted as R_{OO} and r_{OO}, respectively. The average distance between a cation and four oxygen atoms is denoted as R_{OM}. To examine the accuracy, some geometric structures are optimized with the HF/6-31+G** level including the diffuse basis functions. These results are similar to the results calculated with the HF/6-31G* level. In ionophore I, R_{OO} and r_{OO} are 4.460 and 3.216 Å, respectively. With increasing methyl groups, R_{OO} and r_{OO} increase monotonically. R_{OO} and r_{OO} of the derivatives are larger than those of the corresponding ionophore I. Due to reduce the intramolecular nonbonding interactions (between two methyl groups), the conformational structures of the cyclic frame consisting four methylene groups are optimized to ellipsoidal forms. R_{OO} and r_{OO} of the derivatives (v-**Me**-ionophore, v-_di_**Me**-ionophore, v-_tetra_**Me**-ionophore) vertically substituted by methyl groups are larger than those of the corresponding derivatives (h-**Me**-ionophore, h-_di_**Me**-ionophore, h-_tetra_**Me**-ionophore) substituted horizontally. Particularly, by the symmetrization of the cyclic frames, R_{OO} (5.372 and 5.454 Å) and r_{OO} (3.799 and 3.819 Å) of h-_tetra_**Me**-ionophore and v-_tetra_**Me**-ionophore are larger than those of the other derivatives. R_{OO} and r_{OO} of the derivatives depend on the number of the methyl groups substituted on the cyclic frame. R_{OO} (5.029 Å) and r_{OO} (3.550 Å) of the vh-_octa_**Me**-ionophore are in line with R_{OO} (5.003 Å) and r_{OO} (3.581 Å) of the experimental results.[17]

By dipole-positive charge interaction between a cation and four oxygen atoms, the structures of the complexes are more symmetric. That is, the form of the cavity size is more symmetric than those of the corresponding derivatives. Cation equally coordinates with four oxygen atoms of the symmetrized ionophore derivatives. R_{OO} and r_{OO} of the complexes are shorter than those of the corresponding derivatives. That is, R_{OO} (3.98 Å for ionophore−Li$^+$ and 4.44 Å for ionophore−K$^+$) of the complexes are shorter than R_{OO} (4.46 Å) of the corresponding ionophore I. R_{OO} and R_{OM} of the ionophore−Li$^+$, −Na$^+$, and −K$^+$ complexes are larger than those of the complexes horizontally and vertically substituted by methyl groups. That is, R_{OO} and R_{OM} (3.98 and 2.00 Å) of the ionophore−Li$^+$ are larger than those (3.88 and 1.95 Å) of the complexes horizontally and vertically substituted by methyl groups. As a result, by the symmetrization of the cyclic frames of the complexes, R_{OO} and R_{OM} of the ionophore−Li$^+$, −Na$^+$, and −K$^+$ complexes are larger than those of h-_tetra_**Me**-ionophore−M$^+$ and v-_tetra_**Me**-ionophore−M$^+$, respectively. To examine the accuracy of the computational results, the geometric parameters of vh-_octa_**Me**-ionophore−Li$^+$ calculated at the Hartree−Fock/6-31+G** level are compared with those of the X-ray structure.[17] R_{OO} (4.037 Å) and R_{OM} (2.044 Å) of the vh-_octa_**Me**-ionophore−Li$^+$ are in

TABLE 2: Distances (Å), Binding Energies (eV), Atomic Charges (au), and Ratio of the (Atomic Charge/Ionic Radius) for Ionophore−Cation Complexes Substituted by Some Methyl Groups

										exptl[j]	
	R_{OO}[a]	R_{OM}[b]	BE[c]	(M^+)[d]	O[e]	C_1[f]	C_2[g]	C_3[h]	(c/r)[i]	R_{OO}	R_{OM}
ionophore−H^+	4.039	1.116	−1.99	0.588	−0.568	0.023	0.371	0.011			
ionophore−Li^+(6-31G*)	3.989	2.004	−4.57	0.647	−0.771	0.029	0.385	0.019	1.08		
ionophore−Li^+(6-31+G**)	3.980	1.998	−4.57	0.612	−0.723	0.068	0.476	0.097	1.02		
h-**Me**-ionophore−Li^+	3.872	1.946	−4.95	0.651	−0.771	0.043	0.353	0.030	1.09		
h-*di***Me**-ionophore−Li^+	3.880	1.949	−4.84	0.650	−0.772	0.042	0.362	0.029	1.08		
h-*tetra***Me**-ionophore−Li^+	3.893	1.954	−4.76	0.649	−0.774	0.041	0.375	0.027	1.08		
v-**Me**-ionophore−Li^+	3.881	1.949	−5.02	0.649	−0.770	0.044	0.352	0.031	1.08		
v-*di***Me**-ionophore−Li^+	3.886	1.951	−4.87	0.648	−0.771	0.043	0.360	0.030	1.08		
v-*tetra***Me**-ionophore−Li^+	3.901	1.957	−4.80	0.648	−0.773	0.043	0.371	0.030	1.08		
vh-*octa***Me**-ionophore−Li^+	4.076	2.099	−4.91	0.657	−0.779	0.047	0.377	0.041	1.09		
vh-*octa***Me**-ionophore-Li^+(6-31+G**)	4.043	2.054	−5.03	0.661	−0.788	0.075	0.416	0.052	1.10	4.052	2.086
ionophore−Na^+(6-31G*)	4.276	2.266	−3.26	0.732	−0.760	0.020	0.387	0.014	0.77		
ionophore−Na^+(6-31+G**)	4.282	2.269	−3.25	0.724	−0.756	0.043	0.462	0.064	0.73		
h-**Me**-ionophore−Na^+	4.183	2.175	−3.60	0.737	−0.760	0.040	0.356	0.025	0.78		
h-*di***Me**-ionophore−Na^+	4.185	2.176	−3.57	0.733	−0.761	0.039	0.365	0.023	0.77		
h-*tetra***Me**-ionophore−Na^+	4.188	2.177	−3.52	0.731	−0.778	0.037	0.374	0.022	0.77		
v-**Me**-ionophore−Na^+	4.187	2.177	−3.63	0.729	−0.769	0.041	0.356	0.025	0.77		
v-*di***Me**-ionophore−Na^+	4.189	2.178	−3.58	0.727	−0.760	0.040	0.363	0.024	0.77		
v-*tetra***Me**-ionophore−Na^+	4.192	2.179	−3.55	0.726	−0.776	0.040	0.372	0.024	0.77		
ionophore−K^+(6-31G*)	4.427	2.604	−2.74	0.791	−0.678	0.037	0.343	0.019	0.60		
ionophore−K^+(6-31+G**)	4.441	2.611	−2.75	0.786	−0.672	0.045	0.423	0.052	0.66		
h-**Me**-ionophore−K^+	4.425	2.592	−2.64	0.799	−0.679	0.037	0.352	0.017	0.60		
h-*di***Me**-ionophore−K^+	4.426	2.595	−2.61	0.797	−0.681	0.036	0.360	0.017	0.60		
h-*tetra***Me**-ionophore−K^+	4.428	2.597	−2.58	0.795	−0.683	0.035	0.366	0.017	0.60		
v-**Me**-ionophore−K^+	4.429	2.601	−2.65	0.795	−0.677	0.037	0.351	0.018	0.60		
v-*di***Me**-ionophore−K^+	4.432	2.603	−2.62	0.794	−0.679	0.036	0.358	0.018	0.60		
v-*tetra***Me**-ionophore−K^+	4.436	2.604	−2.59	0.794	−0.680	0.036	0.363	0.017	0.60		

[a] Average distance between the first and third oxygens in ionophore−cation complex. [b] Average distance between cation and oxygen in ionophore−cation complex. [c] Binding energy (exothermic reaction, $\Delta H\langle 0$) between cation and derivative. [d] Cation combined with the derivative. [e] Average charge density of four oxygen atoms in ionophore−cation complex. [f] Average charge density of carbon atoms at four bridged methylene groups. [g] Charge density of the first carbon atom bonded to oxygen atom in the tetrahydrofuran unit. [h] Charge density of the second carbon atom from oxygen atom in the tetrahydrofuran unit. [i] Ratio between calculated cationic charge and cationic radius in ionophore−cation complex. Calculated cationic charge divided by cationic radius. The ionic radii of 0.60 Å for Li^+, 0.95 Å for Na^+, and 1.33 Å for K^+ cited from ref 24. [j] Reference 17.

line with R_{OO} (4.052 Å) and R_{OM} (2.086 Å) of the experimental results. Because of the steric hindrance of the eight methyl groups, the geometric parameters of vh-*octa***Me**-ionophore−Li^+ are larger than those of the other complexes.

With increasing methyl groups, R_{OO} and R_{OM} of the complexes increase. R_{OO} and R_{OM} of the v-**Me**-ionophore−M^+ (v-*di***Me**-ionophore−M^+ and v-*tetra***Me**-ionophore−M^+) are larger than those of the h-**Me**-ionophore−M^+ (h-*di***Me**-ionophore−M^+ and h-*tetra***Me**-ionophore−M^+). As the van der Waals radius of the cation increases, R_{OO} and R_{OM} also increase. That is, the cavity sizes of the complexes are increased by the longer ionic radius. R_{OO} and R_{OM} of the ionophore−Li^+ are 3.98 and 2.00 Å, respectively. R_{OO} and R_{OM} of the ionophore−K^+ are 4.44 and 2.61 Å, respectively. R_{OM} (2.00 Å) of the ionophore−Li^+ is three times the ionic radius (0.60 Å) of Li^+, while, R_{OM} (2.60 Å) of the ionophore−K^+ is two times the ionic radius (1.33 Å) of K^+. The relative value (R_{OM}/ionic radius of Li^+) of ionophore−Li^+ complexes is larger than those (R_{OM}/ionic radius of Na^+ or K^+) of ionophore−Na^+ or −K^+ complexes. Therefore, the high selectivity of the THF-based 16-crown-4 derivatives for Li^+ is in good agreement with the experimental results.[28−31]

In the ion-selective experiments,[10−31] the macrocyclic derivatives are characterized by a hydrophilic cavity in their centers in which metal cations and small molecules are selectively bound depending on their ionic diameter. The selectivity in partitioning varied with the relative fit of the ionic radius of the metal ion to the hole size of the cyclic compound. Particularly, in the experiment of Kobuke et al.,[12] metal picrate is extracted with complex formation, and the decrease in absorbance of the picrate in aqueous phase was taken to be a measure of efficiencies of macrocycles as a complexing agent for the cation. That is, ionophore I is easily complexed with the lithium cation, while it is hardly complexed with the potassium cation. With increasing bulky substituents, a measure of efficiency for the binding of the cations is decreased. A clear tendency to be noted is the close relation between the cavity size of derivatives and the ionic diameter of cations to be partitioned most favorably.

Binding energies for the complexes are listed in Table 2. The binding energies for these complexes are calculated for the first time, and there are no previously reported results for comparison. Thus the binding energies cannot be compared with previous results. Because of the positive charge−dipole interaction, the binding energies of the complexes have relatively large values. The binding energies of ionophore−Li^+ complexes (4.57 eV) are larger than those of ionophore−Na^+(3.25 eV) and −K^+(2.75 eV) complexes. The binding energies of the v-**Me**-ionophore−M^+ complexes (v-*di***Me**-ionophore−M^+ and v-*tetra***Me**-ionophore−M^+) are similar to those of the h-**Me**-ionophore−M^+ complexes (h-*di***Me**-ionophore−M^+ and h-*tetra***Me**-ionophore−M^+).

As shown in Tables 1 and 2, the average charge densities on four oxygen atoms of the derivatives and its complexes are negative, whereas those on the cations and the carbon atoms are positive. The charge densities of the cations and the oxygen atoms are relatively large values, while those of the carbon atoms are smaller. Depending on the cations, the charge densities are different from each other. The positive charge values of Li^+ are smaller than those of Na^+ and K^+. The calculated ratio (1.09)

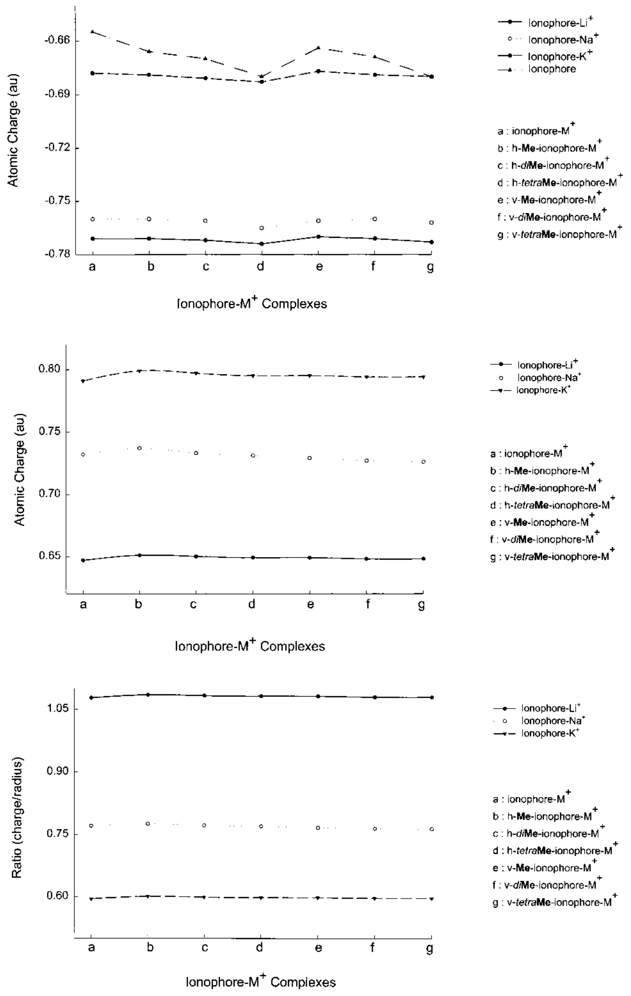

Figure 3. Plots of the atomic charges (au) and ratio of the (atomic charge/ionic radius) of ionophore−cation complexes from results of the HF/6-31G* calculations: (a) atomic charges of the oxygen atoms; (b) atomic charges of the cations; (c) ratio of the (atomic charge/ionic radius).

of the (atomic charge/ionic radius) of Li^+ is larger than that (0.77) of Na^+ and that (0.60) of K^+. Units of atomic charge and ionic radius are atomic unit and angstrom, respectively.

The charge variations of the oxygen atoms and cations and the ratio of the (atomic charge/ ionic radius) of the cations in the ionophore−M^+ complexes have been represented in Figure 3. With increasing methyl groups, the charge variations of the oxygen atoms of the derivatives are relatively large, while, in complexes, the charge variations of the oxygen atoms and cations are nearly constant. In ionophore−Li^+ complexes, the charge values of the oxygen atoms are more negative than those of the oxygen atoms of the ionophore−Na^+ and ionophore−K^+. The charge values of Li^+ are less positive than those of Na^+ and K^+. The ratio of the (atomic charge/ionic radius) of Li^+ converges to 1. That is, in ionophore−Li^+ complexes, the atomic charges of the oxygen atoms are more negative and the charges of Li^+ are less positive. The strong charge-transfer effect from the oxygen atom to the cation did not occur, and the strong binding between a cation and four oxygen atoms was not formed. If the strong charge-transfer effect from the oxygen atom to the cation occurs, the atomic charges of the oxygen atoms must be more negative and the charges of Li^+ must be more positive. It can be confirmed that there is no strong interaction between Li^+ and four oxygen atoms. Li^+ can easily complex with the derivatives and can easily dissociate from the complexes. The ratio of the (cationic charge/cationic radius) of M^+ can be considered as a measure of the binding between M^+ and four oxygen atoms.

IV. Conclusions

We optimized the geometric structures of ionophore I, ionophore derivatives substituted by methyl groups, and its derivative−cation complexes. Geometric structures of ionophore I, h-*tetra***Me**-ionophore, and v-*tetra***Me**-ionophore are optimized to stable cage forms with C_4 symmetry. Four oxygen atoms are located at the lower side of the cyclic cage. Although four methyl groups are substituted on the cyclic frame, the cavity size of the derivatives expanded symmetrically. The symmetrically expanded derivatives can capture cations to go through the cavity, while the geometric structures of the other derivatives are optimized to ellipsoidal forms with C_1 and C_2 symmetries. With increasing methyl groups, the geometric structures are unsymmetrically distorted by steric hindrance. The cation can only approach the lower side. *The symmetric derivatives can be a molecular sieve to capture the cations. The symmetric cavity size of the derivative plays an important role on the binding of the cations*.

In ionophore−M^+ complexes, Li^+ is located in the plane of the cyclic frame, while, Na^+ and K^+ are located outside the frames. In symmetric ionophore−Li^+ complexes, Li^+ can complexed with four oxygen atoms on both sides of the ionophore derivatives. The van der Waals radius of Li^+ fits well with the cavity size of the derivatives. In ionophore−Na^+ and −K^+ complexes, the van der Waals radii of the cations are slightly larger than the cavity size. In ionophore−H^+ complexes, H^+ is bridged to two neighboring oxygen atoms of the derivatives and the other two oxygen atoms are free. Due to a small ionic radius, H^+ can pass through the derivatives. *The size consistency between the van der Waals radius of the cation and the cavity largely influences the binding of the cations*.

With increasing methyl groups, R_{OO} and r_{OO} of the derivatives and its complexes increase. R_{OO} and r_{OO} of the symmetric derivatives and complexes are larger than those of the other unsymmetric compounds. Due to the interaction between cation and four oxygen atoms, R_{OO} and r_{OO} of the complexes are shorter than those of the corresponding derivatives. Along the direction of the methyl group, the variations of R_{OO} and r_{OO} are relatively small. As the van der Waals radius of the cation increases, R_{OO} and R_{OM} of the complexes increase. The symmetric derivatives (R_{OO} = 4.46 Å) can capture Li^+ (radius of 0.60 Å) to go through the cavity, while Na^+ (radius of 0.95 Å) and K^+ (radius of 1.33 Å) cannot pass through the cavity of the derivatives. *The relationship between the ionic radius and the cavity size is a decisive factor in the design of the molecular sieve*.

In the derivatives and its complexes, the average charge densities of the oxygen atoms have negative values, whereas those of the cations and the carbon atoms are positive. With increasing methyl groups, the charge variations of the oxygen atoms of the derivatives are relatively large, while the charge variations of the complexes are nearly constant. In ionophore−Li^+ complexes, the charges of Li^+ are less positive than those of the other cations, whereas the atomic charges of the oxygen atoms are more negative than those of the oxygens of the other complexes. The strong interaction between Li^+ and the four oxygen atoms does not occur. Li^+ can easily complex with the derivatives and can easily dissociate from the complexes. The ratio of the (Li^+ charge/Li^+ radius) influences the binding between Li^+ and four oxygen atoms. *The ratio of (M^+ charge/*

M^+ radius) may be considered as a measure of the ionic selectivity. On the basis of the symmetrization of the cavity shapes, the size consistency between the ionic radius and the cavity, and the ratio (atomic charge/ionic radius) of the cations, the symmetric ionophore derivatives are found to be a good molecular sieve of Li^+ and to have high lithium cation selectivity.

Acknowledgment. This work was supported by the Basic Science Research Institute program, the Ministry of Education, and the Korea Science and Engineering Foundation. The author thanks Professor Sun for the invaluable help.

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