

Theoretical Study of Chemical Interactions in Crown Ether-Cation Complexes

Itaru Hataue, Yasuo Oishi, Masaaki Kubota and Hiroshi Fujimoto*

Division of Molecular Engineering, Kyoto University

Kyoto 606, Japan

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Abstract: The stable structures of complexes of crown ether, (8-crown-4), and its nitrogen and sulfur homologues, (8-N-4) and (8-S-4), with a guest cation Li^+ have been obtained by the minimal basis set ab initio MO calculations. By applying the interacting-orbital-pair scheme, a feature of chemical interactions in these species has been elucidated. An important factor which should control the stability of these complexes and the size of cavity is suggested. The binding ability of spherand compounds for lithium cation is studied by setting a simple model system.

Introduction The host-guest chemistry is one of the most exciting topics in modern science and has drawn growing attention of organic chemists.¹ Since Moore and Pressman found that the physiological processes of the antibiotic substance should depend strongly on the existence of the complex-forming alkali cations in the medium,² clathrate compounds of those metal ions have been studied vitally in the up-to-date applied synthetic chemistry. The idea that these clathrate compounds should play an important part as the specific ion carriers was confirmed and their functions were studied in detail.^{3,4}

Clathrate compounds are classified into two groups. One is obtained naturally like cyclodextrins and the other is artificially synthesized, e.g., crown ethers and cyclophanes. Among the compounds in the latter group, macrocyclic polyethers (crown ethers), originally prepared by Pedersen⁵ in 1967, have been studied most extensively as a typical artificial host-ligand. Because crown ethers bind strongly cations of alkali metals, alkali

earth metals, ammonium cation⁶ and so on, they make soluble inorganic reagents that are primarily insoluble in organic solvents. Thus, crown ethers are getting to be increasingly important in industrial applications, e.g., reagents for solvent extraction in analytical chemistry, packing agent for separation of *d,l*-amino acid by column chromatography.¹ In the presence of these host–ligands, anions are freed from their counter–cations and show enhanced reactivity. For instance, bimolecular nucleophilic elimination reactions of 2–phenylethylchlorides and bromides by *t*-BuOK were shown to be accelerated by adding crown ethers.⁷

The stabilization in forming a crown ether–cation complex is supposed to be due mainly to the electrostatic interactions. However, steric hindrance within the crown ring and the binding ability of a host–ligand by means of the exchange and charge–transfer interactions with a cation cannot be disregarded as the distance between the host–ligand and a cation becomes shorter. In this paper, we study orbital interactions between a lithium cation and 8–crown–4 (1,3,5,7–tetraoxacyclooctane), **1**, as a model host–ligand and also those between the cation and 8–N–4 (1,3,5,7–tetraazacyclooctane), **2**, and 8–S–4 (1,3,5,7–tetrathiacyclooctane), **3**, in which the oxygen atoms in **1** are replaced by >NH groups and sulfur atoms, respectively. These model crown compounds cannot form stable clathrate complexes with lithium cation, but form nesting complexes. Therefore, it may be difficult to have relevance of these models to actual cases. However, reasons why we selected these models are as follows;

- (1)The alternate conformer, which forms the clathrate complex, is not adequate to investigate the contribution of orbital interactions and electrostatic one to the complex formation, because the dependence of crown ether–Li⁺ distance on the stability in the complexation is not clear in the alternate conformer.⁸
- (2)Eight-membered ring compounds adopted here are regarded as the sufficient models in clarifying differences of orbital interactions among **1**, **2**, and **3** from the viewpoint of the local nature of the interaction.
- (3)The geometry optimization of larger systems becomes more difficult.

We try first to calculate the stable structures of these complexes and then to analyze chemical interactions in these species by applying paired orbital transformations.⁹ The results of MO calculations for these systems are translated into an intuitively understandable form. We discuss also a possible effect of solvents. Spherands are the host–ligands that have been designed by Cram so as to take Li⁺ ion most strongly into its cavity.¹⁰ Cram proposed an interesting concept of "convergent binding sites".¹¹ A host–ligand has multiple binding sites. Those sites tend to orient round a point when a host–ligand gets in the interaction with a guest molecule. The convergent binding sites seem somehow to be connected with orbital interactions oriented specifically between the lone–pairs of a crown ligand and the trapped cation. We study an interaction of a model of spherand systems and compare it with that of a 18–crown–6 (1,4,7,10,13,16–hexaoxacyclooctadecane) molecule.

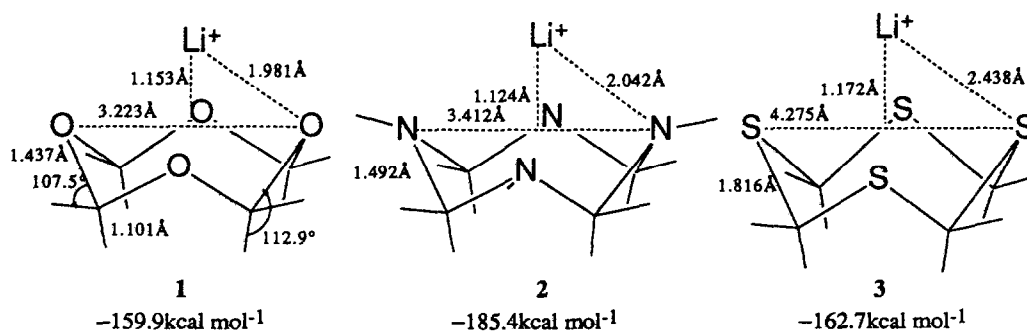
Results and Discussion All the calculations have been performed by using the GAUSSIAN 82 program.¹² Since the systems treated are pretty large, we have adopted the STO–3G minimal basis set. Our primary purpose is to see some aspects of interactions in the title species. The validity of the small basis set calculations is examined for a CH₃OH–Li⁺ complex.

Stable Structures of Crown Ether–Li⁺ Complexes.--- The optimized structures of the complexes of **1**, **2** and **3** are shown in Figure 1. The separation between the cation and a sulfur atom is shown to be considerably longer than the O–Li and N–Li distances. The O–Li distance is shown to be longer by 0.2–0.3Å than those calculated for the Li⁺ complexes of smaller organic molecules having an oxygen atom, as shown in Table I.^{13–15}

Table I. Calculated O-Li Bond Lengths.

Molecule	Basis Set	O-Li Distance ^a	ΔE ^b	Reference
8-crown-4	STO-3G	1.981	-159.9	
methanol	3-21G	1.76	-41.2	(13)
acetaldehyde	3-21G	1.71	-45.4	(13)
oxirane	6-31G*	1.80	-43.5	(14)
dimethyl ether	3-21G	1.75	-41.4	(13)

^a In Å.
^b In kcal mol⁻¹.

Figure 1. Structures of Li⁺ complexes of (8-crown-4), (8-N-4) and (8-S-4).

We presented in Figure 1 the energy of interaction, ΔE_{int} , that was defined as the difference in energy between a complex and its fragment species. The negative value indicates a stabilization upon complex formation. The geometry of crowns was frozen in calculating ΔE_{int} . Though the energy values are likely to be overestimated, the stabilization in the three systems studied here is seen to be similar in magnitude. When the O-Li bonds were shortened to 1.687 Å from their calculated equilibrium bond lengths, the complex of 1 was destabilized to give $\Delta E_{\text{int}} = -114.7$ kcal mol⁻¹. On the other hand, the electrostatic interaction in the complex of 1 that was estimated from the net Mulliken atomic population of the constituent atoms by applying a point-charge approximation was shown to be strengthened from -51.4 kcal mol⁻¹ in the equilibrium geometry to -61.6 kcal mol⁻¹. This indicates that orbital interactions play significant roles in determining the stable structures of these complexes.

Interactions in Crown Ether-Li⁺ Complexes.--- Figure 2 illustrates the orbital interactions in the Li⁺ complex of 1 by means of paired interacting orbitals. We have selected the interfragment part of the bond-order matrix of the composite complex, e.g., (8-crown-4)-Li⁺, as a measure of interactions between the two fragment species, Li⁺ and 1. Then, the MOs of two fragment species have been transformed simultaneously within each fragment so that the mode and strength of interaction in the complex are characterized by several pairs of orbitals, ϕ_i of the cation and ϕ_j of 1.⁹ Since the lithium cation has no electron in the valence-shell orbitals in the

beginning, the orbital interactions $((\phi_1, \phi_1) \sim (\phi_4, \phi_4))$ indicate primarily electron delocalization from the crown ether to the cation. If the two species came too close to each other, the inner-shell 1s AO of the cation was shown to overlap with the lone-pair orbitals of ethers to yield overlap repulsion. This repulsive interaction is involved in the fifth orbital pair, (ϕ_5, ϕ_5) .

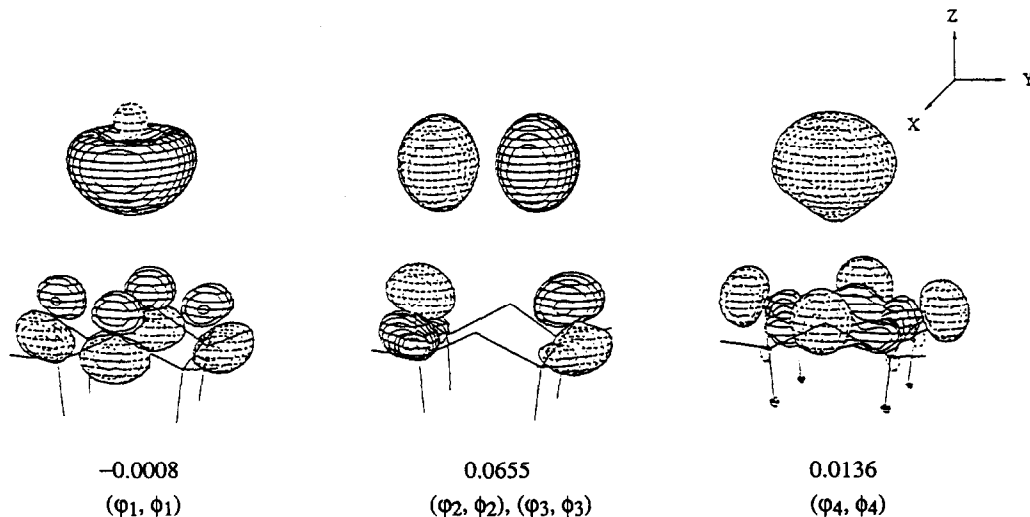


Figure 2. Four major orbital pairs of a (8-crown-4)-Li⁺ complex participating in electron delocalization. Note that (ϕ_2, ϕ_2) and (ϕ_3, ϕ_3) are degenerate by symmetry.

The first pair of orbitals (ϕ_1, ϕ_1) represents electron delocalization from the lone-pair orbitals of oxygens in **1** to the 2s and 2p_z orbitals of Li⁺. The orbital (ϕ_1) of **1** also has contributions of the carbon and oxygen 2s AOs which overlap out-of-phase with the 2s AO of the cation. The total overlap population in this orbital pair is very small and negative, ~ -0.001 . The π -type degenerate orbitals ϕ_2 and ϕ_3 consist also mainly of the lone-pair orbitals of **1** and interact in a bonding manner with the 2p_x and 2p_y AOs of Li⁺. The fourth orbital pair is bonding between the oxygen 2p_x and 2p_y AOs and the lithium 2s and 2p_z AOs. These orbitals of the crown ether, ϕ_1, ϕ_4 and also ϕ_2 and ϕ_3 in combination, are multi-centered and oriented toward the attached Li⁺. When the cation is pulled closer, the antibonding interaction between the carbon and oxygen 2s AOs and the lithium 2s AO in (ϕ_1, ϕ_1) is strengthened. In the case that the O-Li distance was 1.687 Å, the overlap population was shown to get larger and negative (-0.034). It is very likely therefore that a balance between the bonding and antibonding interactions involved in the orbital pair (ϕ_1, ϕ_1) plays a crucial role in determining the position of the cation and, hence, the size of cavity.

Figure 3 shows the paired interacting orbitals, (ϕ_1, ϕ_1) and (ϕ_4, ϕ_4) , of the complexes of **2** and **3**. The lithium 2s AO overlaps more strongly with the nitrogen 2p_z AOs in **2** than with the oxygen 2p_z AOs in **1**. On the other hand, the overlap populations of (ϕ_4, ϕ_4) is much smaller in **2** than in **1**. This result is attributed obviously to the fact that the 2p_x and 2p_y AOs of nitrogen atoms in **2** have already been used to make the N-H bonds. The difference between **1** and **2** found in the interactions with Li⁺ is smaller than that found for smaller molecules.¹⁶ In the complex of **3**, the sulfur 3p AOs are diffuse and overlap strongly with the lithium 2s AO at

a longer distance. The ϕ_1 orbital of 3 is seen to be oriented more effectively toward the attached cation than that of 1 and of 2. The antibonding interaction between the carbon 2s AOs and the lithium 2s AO is weaker in 3 than in 1 and in 2 at the calculated equilibrium geometry and, as a result, the orbital pair (ϕ_1, ϕ_1) gives a positive and larger overlap population in 3.

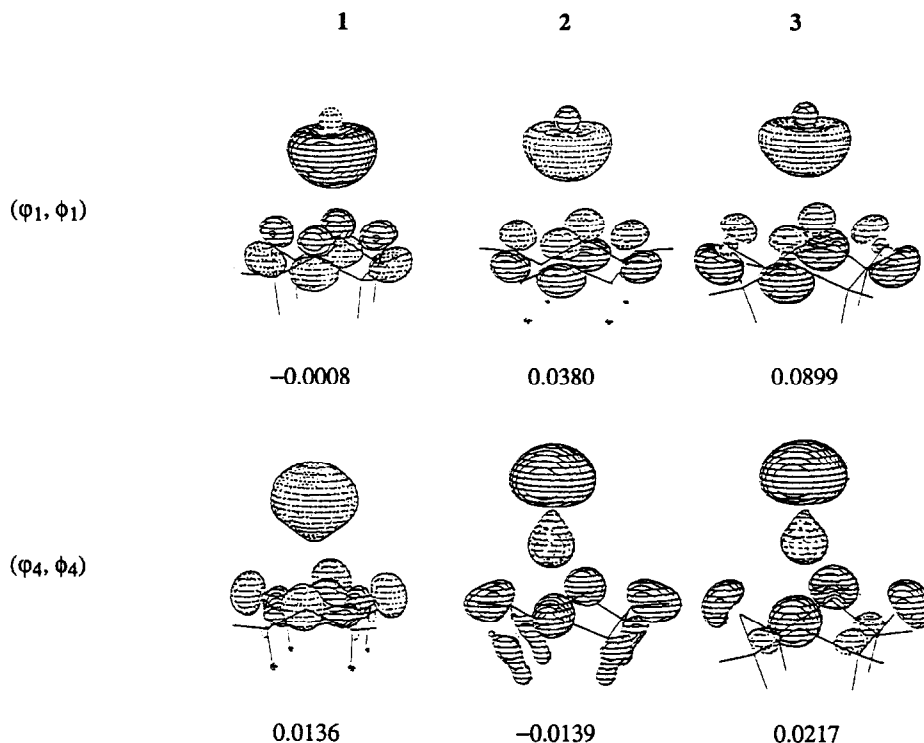


Figure 3. Comparison of orbital pairs for the Li^+ complex of (8-crown-4), (8-N-4) and (8-S-4).

Here we may refer briefly to the basis set. We have analyzed the interaction between a methanol molecule and Li^+ by using the STO-3G and 6-31G** basis functions as presented in Figure 4. The geometry of the combined system was fixed to the one that had been optimized by an STO-3G calculation. By taking the x - z plane as the symmetrical plane σ , the oxygen atom and the lithium cation were placed on the z -axis. In case of the 6-31G** extended basis calculation, the interaction is represented by fifteen pairs of interacting orbitals. Of these, we present in Figure 4 four orbital pairs that participate dominantly in the interaction. Other orbitals show their amplitude mainly on the inner-shell or diffuse and polarization functions. It is seen that they bear a close resemblance to the orbitals obtained with the minimal basis set calculations. The polarization functions are seen to distort slightly the interacting orbitals of Li^+ . For example, the polarization function d_{yz} of the cation participates in the interaction with the oxygen p_y orbital of the alcohol molecule to give a stronger π -type interaction in the orbital pair, (ϕ_2, ϕ_2) . The effect of polarization function is not so obvious in the orbitals of

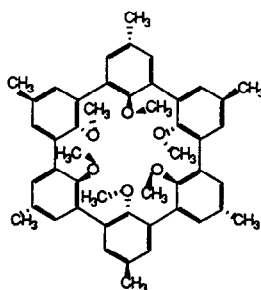
Cations may be solvated by other solvent molecules in actual systems. We calculated a model system in which a dimethyl ether molecule solvates Li^+ from the backside of the Li -(8-crown-4) interaction. The oxygen atom of dimethyl ether was placed at a distance of 1.5 Å and of 2.0 Å from the cation on the four-fold rotational symmetry axis. Table II compares overlap populations of the orbital pairs. The $2p_y$ AO of Li^+ is partially populated by an electronic charge transferred from the ether molecule and electron delocalization from the crown lone pairs is suppressed. The overlap population of the orbital pair (ϕ_3, ϕ_3) is reduced significantly in the presence of the ether molecule. On the other hand, the electron population of the other π -type orbital pair (ϕ_2, ϕ_2) that is orthogonal to the lone-pair orbitals of the ether molecule remains almost unchanged. This result indicates that electron delocalization between the cation and the solvent molecule and that between the cation and the crown ether take place specifically by means of orbital overlap.

Table II. Effect of a Dimethyl ether Molecule on the Overlap Population of Orbital Pairs of (8-crown-4)- Li^+ Complex.

orbital pair	none	$r = 2.0 \text{ \AA}$	$r = 1.5 \text{ \AA}^a$
(ϕ_1, ϕ_1)	-0.0008	-0.0011	-0.0007
(ϕ_2, ϕ_2)	0.0655	0.0630	0.0622
(ϕ_3, ϕ_3)	0.0655	0.0567	0.0461
(ϕ_4, ϕ_4)	0.0136	0.0092	0.0106

^a Distance between Li^+ and the oxygen of dimethyl ether.

A Spherand Model. --- Spherands,^{10,17-19} a typical compound of which is shown below, are the host-molecules that have an extraordinarily strong binding ability for a lithium cation. Common crown ethers do not necessarily have cavities in an uncomplexed state, but cavities are created upon complexation with guest-cations. Spherands are designed to have cavities in their uncomplexed state. In 4, the six oxygen atoms, being arranged hexagonally, form a large cavity. The equilibrium constant (K_s) of complexation with Li^+ is greater than 10^6 M^{-1} ,¹⁸ while other alkaline and alkali earth metal ions, K^+ , Mg^+ and Ca^{2+} , are not accepted. With a



view of investigating this property of spherands, a model host-system has been set up in the following manner; six dimethylether molecules are arranged in such a manner as to bring their oxygen atoms in the positions of oxygens of **4** that have been determined experimentally.²⁰ The O-C bonds are directed to make the carbons occupy the positions that are closest to those of the adjacent carbons in **4**. The cation was placed in the center of $((\text{CH}_3)_2\text{O})_6$. Here we mention the dependency of the character of the oxygen atom upon the orbital interaction with lithium cation before discussing the interaction of model $((\text{CH}_3)_2\text{O})_6$ system. Though the character of oxygen atoms in our model system is aliphatic alcohol type, that in spherands is phenol type. We have analyzed the orbital interaction between a phenol molecule and lithium cation and compared the results with the methanol case (Figure 4). Figure 5 shows the interacting orbital pairs (ϕ_1, ϕ_1) and (ϕ_2, ϕ_2) in phenol-Li⁺ system. There is only a minor difference of the orbital interaction pattern around the reactive domain between Figure 4 and 5. The calculated 2s:2p AO coefficient ratio of the oxygen atom in ϕ_1 is 0.093 in methanol and 0.082 in phenol. This shows that both of lone-pair orbitals of oxygen atoms which are related to the electron delocalization have a high p nature and are not affected by the character of their molecules.

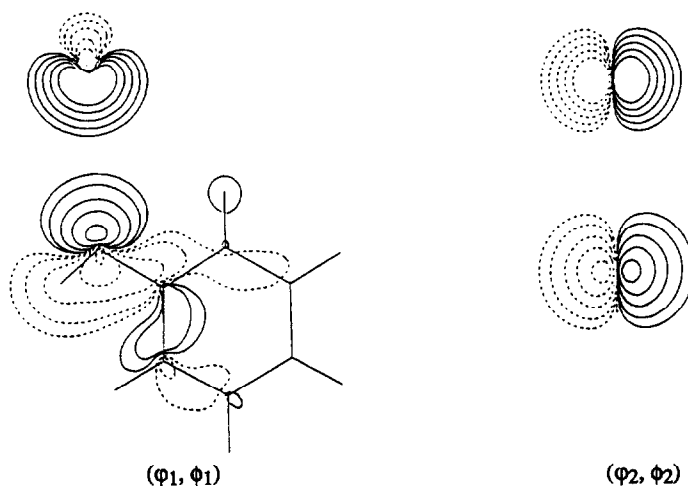


Figure 5. Orbital pairs that represent the interaction in a Li⁺-phenol.

The guest cation is located considerably above the plane of crown ethers in the Li⁺ complexes of **1**, **2** and **3**, as studied above. The bonding interaction has been shown to be weakened and become repulsive when Li⁺ comes closer to **1**. We examine here if strong electron delocalization could take place to retain the cation in the cavity in this large host-ligand. Figure 6 illustrates the interacting orbitals for the model host system with a lithium cation. Electron delocalization is represented approximately by four pairs of fragment orbitals, (ϕ_i, ϕ_i) ($i=1\sim 4$). All of these four orbitals overlap in-phase to give positive and large overlap populations. Thus, the model system is shown to have a strong binding ability for Li⁺. Each oxygen atom extends a binding lobe toward the cation in the cavity in each orbital pair. In the system composed of $((\text{CH}_3)_2\text{O})_6$ and a lithium cation, there exists an antibonding interaction between the lithium 2s AO and the 2s AO of carbons as shown by (ϕ_5, ϕ_5) . This antibonding interaction is similar to that shown in the Li⁺ complex of **1** and will be stronger when spherands try to capture larger cations. We also calculated the (18-crown-6)-Li⁺ complex by using the structure determined experimentally.²¹ The cation was placed in the center. Figure 7 presents the interacting

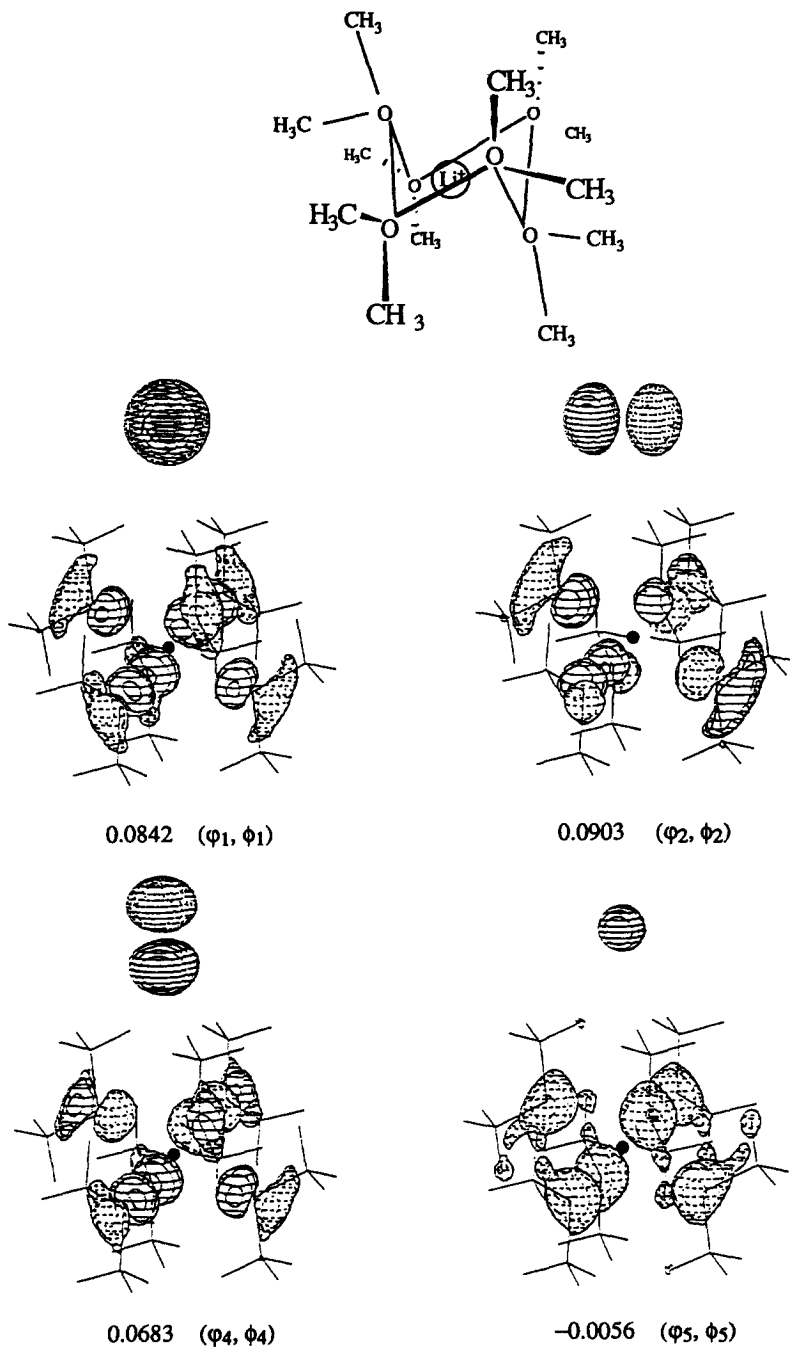


Figure 6. Orbital pairs that represent the interaction in a $\text{Li}^+ - ((\text{CH}_3)_2\text{O})_6$ complex. The cation was placed in the center of six oxygen atoms as denoted by a dot. Note that (ϕ_3, ϕ_3) is degenerate with (ϕ_2, ϕ_2) by symmetry.

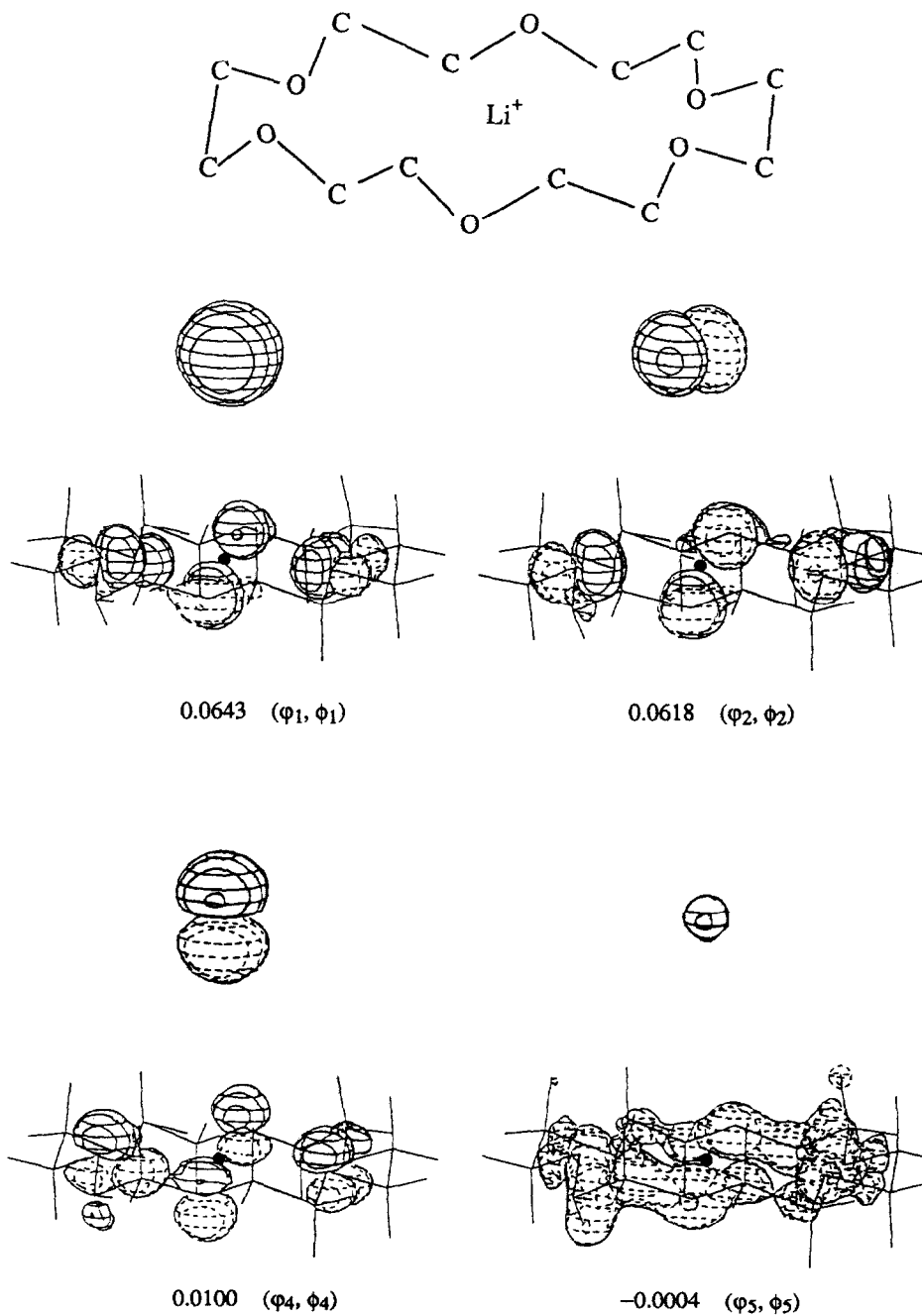


Figure 7. Orbital pairs taking part in the interactions between a Li^+ and a (18-crown-6) molecule. The cation is located in the plane determined by the six oxygen atoms as denoted by a dot. The orbital pairs (ϕ_3, ϕ_3) and (ϕ_2, ϕ_2) are degenerate.

orbitals. Because the size of cavity is much larger than the ionic radius of Li^+ , orbital interactions in this complex are weaker than those in the model shown in Figure 6. The interaction manner of a model of spherand (Figure 6) is more three-dimensional and stronger than that of 18-crown-6 system (Figure 7). In fact, crystal structure analyses showed that the crown was distorted in the complex by the actions of encapsulated water molecules which had the double roles of serving as coordinating agents against Li^+ and as hydrogen-bond donors to the ether oxygens.²¹

Conclusion We have studied above some models of crown ether–lithium cation complexes. Our calculations showed that the crown ether homologue of sulfur, **3**, should form a more stable complex than the crown ether, **1**. By representing the interactions between the two fragment species in terms of paired interacting orbitals, we could look at a basic aspect of interactions in these complexes. It is suggested that cognition of cations is made by a combination of bonding interactions between the cation and the binding sites and antibonding interactions between the cation and the groups adjacent to the binding sites in the host molecule. Orbital interactions are multi-centered and specifically oriented. It may be possible to calculate the electronic structure of small clathrate compounds by applying more sophisticated ab initio MO methods to study their energetics. However, it should be more practical to see the basic aspects of interactions for the design and syntheses of useful host ligands. Our scheme of orbital interactions can be used for that purpose.

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