

DFT study of a series of crown-4 ethers and their selectivity trend for alkali metal cations: Li^+ and Na^+

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Abstract The molecular and electronic structures for 12- to 16-crown-4 (named 12C4, 13C4, 14C4, 15C4, 16C4, respectively) and 2,3,5,6,8,9-hexahydrobenzo[b][1,4,7,10]tetraoxacyclododecine (B12C4) 3,5,6,7,9,10-hexahydro-2H-benzo[e][1,4,7,10]tetraoxacyclotridecine (B13C4) and their complexes with alkali metal cations Li^+ and Na^+ have been explored using the density functional theory (DFT) with B3LYP/6-31G* method. The nucleophilicity of crown-4 ethers has been investigated by the Fukui function. Their selectivity trend shows that of all the crown-4 ethers, 14C4 shows the highest cation selectivity for Li^+ over Na^+ , has been achieved on the basis of thermodynamic analysis. In addition, Li^+ /crown-4 series are more stable than Na^+ /crown-4 series in the gas phase. The calculated results are in good agreement with the experimental observation.

Keywords Cation selectivity · Crown-4 ethers complexes · Density functional theory (DFT) · Thermodynamic analysis

Introduction

Crown ethers have been of great interest since their first synthesis by Pedersen in 1967 [1]. And it is of great significance to investigate a highly selective crown for Li^+ and Na^+ in life science, for people show violent or dementia if their is an abnormal content of Li^+ in the body [2].

Introduction of additional methylene to rigid crown to change the molecule symmetry is a new way to design and synthesize highly selective host compounds. Generally, four ether oxygen crown ethers are used to selectively complex small cations: Li^+ and Na^+ [3, 4].

The purpose of this research is to investigate the electronic and molecular structures for a series of four ether oxygen crowns and their complexes with alkali metal cations Li^+ and Na^+ [5, 6] by quantum chemistry calculations with Gaussian 03 W. Thermodynamic properties were calculated as well to shed light on the selectivity trend of crown-4 series for Li^+ and Na^+ .

Theory and methods

All calculations for the system was conducted using the density functional theory (DFT) and B3LYP method with 6-31G* basis set. DFT is capable of providing adequately accurate conformational analysis [7–10], and the calculated electronic binding energies (ΔE^b s) are also in excellent agreement with the experimental binding enthalpies [11]. B3LYP method involves the use of Beck's three-parameter function and the LYP correlation function [12, 13]. It has fewer convergence problems than those commonly found for pure DFT methods. The "6" in 6-31G* indicates that, when using a Slater-type orbital containing a single exponent ζ (single- ζ) to represent an atomic orbital field, the Slater field is composed of six CGTOs. The "31" indicates that, among the valence atomic orbital field, each atomic orbit is split into two STOs, i.e., having two orbital exponents (double- ζ). One of the two STOs is composed of "three" CGTOs and the other is represented by "one" CGTO, resulting in the "31" term. The "G" in "6-31G*" represents GTO and the "*" indicates that six polarized d functions ($d_x^2, d_y^2, d_z^2, d_{xy}$,

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d_{yz}, d_{xz}) were added to the non-hydrogen atoms such as carbon, nitrogen, and oxygen to increase the accuracy of calculations. It is found that 6–31G* basis set reproduce the experimental data even better than more complete basis sets, probably due to a fortuitous cancellation of errors when coupled with limited chemical methods [14–16].

Full geometry optimization were performed to generate the unique minimum energy conformation for each crown-4 ether, and some electronic and structural characteristics, such as charge distribution, HOMO energies (ϵ_{HOMO}), LUMO energies (ϵ_{LUMO}), energy gap ($\Delta\epsilon_{\text{LUMO-HOMO}}$), ionization potentials (I_p), electron affinity (E_a), bond length were obtained. Frequency calculations were carried out in order to obtain thermal properties and shown that conformation is located at a stable, minimal point of the potential energy surface.

The energy gap ($\Delta\epsilon_{\text{LUMO-HOMO}}$) is equal to the energy difference between the lowest unoccupied molecular orbital and the highest occupied molecular orbital ($\Delta\epsilon_{\text{LUMO-HOMO}} = \epsilon_{\text{LUMO}} - \epsilon_{\text{HOMO}}$). It is an important parameter for determining the molecule stability.

The ionization potential (I_p) and electron affinity (E_a) for these compounds were evaluated using equations:

$$I_p = E(C) - E_t \quad (1)$$

$$E_a = E_t - E(A) \quad (2)$$

where E_t , $E(C)$, $E(A)$ are the calculated total energies for the neutral, the cationic, and the anionic states, respectively. I_p and E_a are used to understand the molecular nucleophilic and electrophilic properties.

The Fukui function $f^{\pm}(r)$ as proposed by Parr and Yang [17], is defined as the partial derivative of the electron density $\rho(r)$ with respect to the total number of electrons N of the system at the constant external potential $v(r)$: $f^{\pm}(r) = \left(\frac{\partial\rho(r)}{\partial N}\right)_{v(r)}^{\pm}$. The condensed Fukui function calculations are based on the finite difference approximation and partitioning of the electron density $\rho(r)$ between atoms in a molecular system. Yang and Mortier proposed f_k calculations from atomic charges as follows:

$$\text{for nucleophilic attack } f_k^+ = q_{N+1} - q_N \quad (3)$$

$$\text{for electrophilic attack } f_k^- = q_N - q_{N+1} \quad (4)$$

where q_N , q_{N+1} and q_{N-1} are the atomic charges of the systems with N , $N+1$ and $N-1$ electrons, respectively. The condensed Fukui function is a local reactivity descriptor only to compare reactive atomic centers within the same molecule.

The binding energies and enthalpies in gas phase were calculated for the reactions:

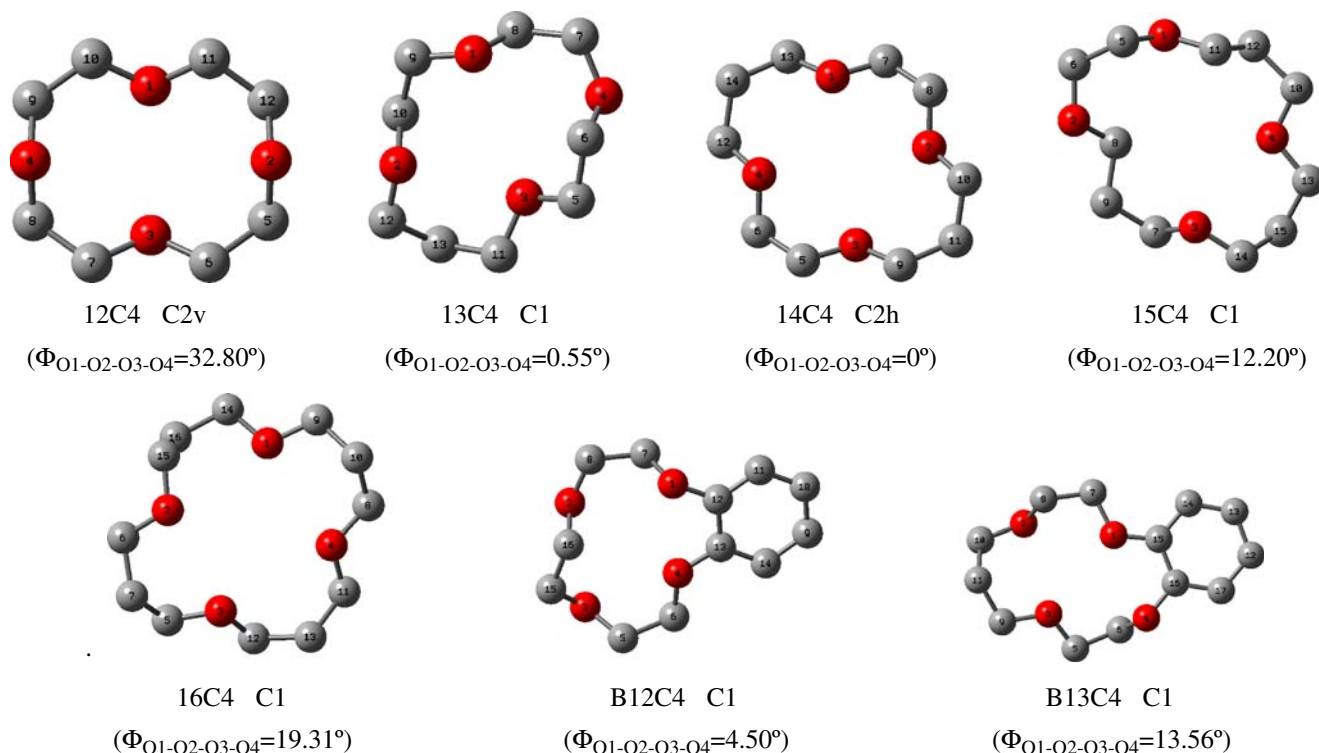
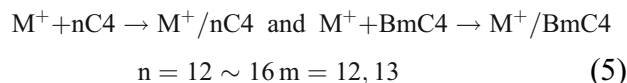
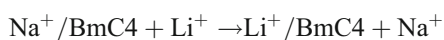
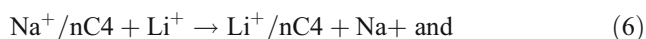


Fig. 1 Optimized structures of crown-4 ethers calculated by the B3LYP/6–31G* method

Table 1 Fukui functions values for a nucleophilic for the crown-4 ethers

Atom	12C4					13C4		14C4		15C4		16C4		B12C4		B13C4	
	f_k^+	f_k^+	f_k^+	f_k^+	f_k^+	f_k^+	f_k^+	f_k^+	f_k^+	f_k^+	f_k^+	Atom	f_k^+	Atom	f_k^+		
O1	0.066	0.071	0.059	0.071	0.079	O1	0.084	O1	0.038			O1	0.084	O1	0.038		
O2	0.067	0.017	0.059	0.114	0.075	O2	-0.008	O2	-0.002			O2	-0.008	O2	-0.002		
O3	0.066	0.081	0.059	0.068	0.016	O3	-0.015	O3	-0.037			O3	-0.015	O3	-0.037		
O4	0.067	0.123	0.059	0.026	0.041	O4	0.058	O4	0.085			O4	0.058	O4	0.085		
						C5	0.010	C12	0.036			C5	0.010	C12	0.036		
						C8	0.014	C13	0.025			C8	0.014	C13	0.025		
						C9	0.019	C14	0.025			C9	0.019	C14	0.025		
						C10	0.032	C15	0.063			C10	0.032	C15	0.063		
						C11	0.016	C16	0.088			C11	0.016	C16	0.088		
						C12	0.101	C17	0.018			C12	0.101	C17	0.018		
						C13	0.052					C13	0.052				
						C14	0.061					C14	0.061				

The enthalpies of crown ether exchange reaction between Li^+ and Na^+ in gas phase were calculated for the reactions:



$$n = 12 \sim 16 \quad m = 12, 13$$

Results and discussion

Crown-4 ether systems

A. Structure The optimized structures for crown-4 ethers in their ground states are shown in Fig. 1. Through analyzing the planarity of the four ether oxygens in each crown-4, 14C4 has the best planarity for oxygens ($\Phi_{\text{O1-O2-O3-O4}}=0^\circ$), while 12C4 shows the most distorted ($\Phi_{\text{O1-O2-O3-O4}}=32.80^\circ$). Overall all of the crowns show relatively good planarity for four oxygens. On the other hand, calculated vibration frequencies of all the crown-4 ethers are positive, indicating that the molecules are located at a stable.

B. Nucleophilic attack sites The condensed Fukui function was used to analyze the local reactivity which contains the information regarding electrophilic/nucleophilic power of a given atomic site in a molecule. Thus, the site for nucleophilic attack will be the place where the value of f_k^+ is a maximum. In turn, the site for electrophilic attack is controlled by the value of f_k^- . Only the site for nucleophilic attack was discussed, for the crown ethers are nucleophilic ligands in the reaction with Li^+ and Na^+ . The

values of the Fukui functions for a nucleophilic attack are given for the crown-4 ethers in Table 1 (only for the oxygen atom and positive f_k^+ for carbon atoms.). The result of the condensed Fukui function shows that, for nucleophilic attack, the most reactive sites are on the oxygen atoms for 12 to 16-crown-4 in the gas phase. As for B12C4 and B13C4, only the O1 and O4 are nucleophilic attack sites, besides the phenyl rings at B12C4 and B13C4 are both nucleophilic. Furthermore, the C5 and C8 at B12C4 are also nucleophilic. The addition of phenyl rings at B12C4 and B13C4 hardly

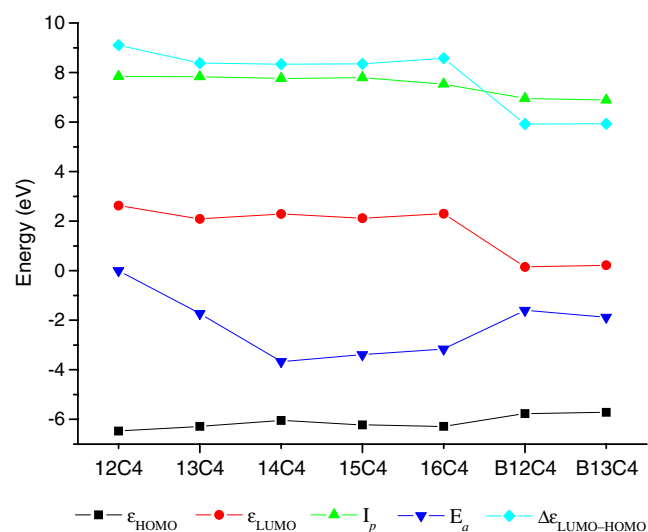


Fig. 2 HOMO and LUMO energies (ϵ_{HOMO} and ϵ_{LUMO}), energy gap ($\Delta\epsilon_{\text{LUMO-HOMO}}$), ionization potential (I_p), and electron affinity (E_a) for the crown-4 ethers by B3LYP/6-31G* method (in eV)

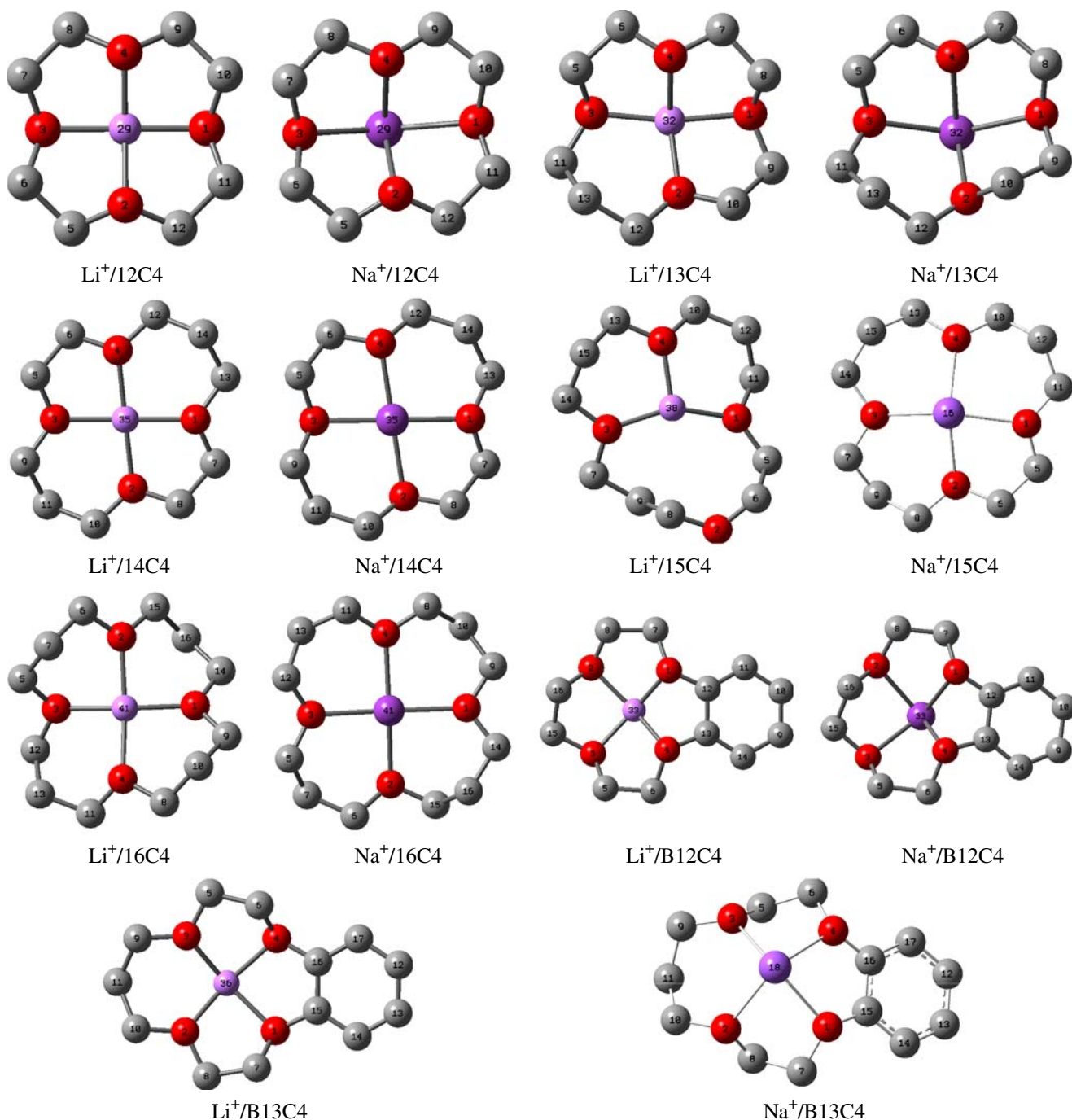


Fig. 3 Optimized structures of the crown-4 ethers complexing with Li^+ and Na^+ by B3LYP/6-31G* method

strengthens the nucleophilicity of the oxygen atoms in crown-4 ethers.

C. Electronic properties Figure 2 shows the calculated values of the HOMO and LUMO energies, energy gaps and I_p and E_a for the series of crown-4 ethers at B3LYP/6-31G* level. On the whole, HOMO and LUMO energies and I_p

change mildly as the crown-4 ethers size increases from 12 to 16. The E_a of 12C4 is equal to zero, and it has the largest energy gaps, both indicating that it has the best stability and most rigid structure. The introduction of the phenyl rings to 12 and 13 crown-4 evidently decreased the energy gap and LUMO energies for B12C4 and B13C4, indicating increased reactivity.

Table 2 Geometrical parameters of crown-4 ethers complexing with Li⁺ and Na⁺ by B3LYP/6–31G* method

Metal cations	parameters	12C4	13C4	14C4	15C4	16C4	B12C4	B13C4
Li ⁺	$r_{\text{Li-O1}}$ (Å)	1.8869	1.9831	1.9468	1.9166	1.9784	1.9492	1.9810
	$r_{\text{Li-O2}}$	1.8784	1.8777	1.9457	3.6141	2.0030	1.9101	1.9044
	$r_{\text{Li-O3}}$	1.8881	1.9291	1.9456	1.8973	1.9696	1.8952	1.9045
	$r_{\text{Li-O4}}$	1.8768	1.9475	1.9474	1.8813	2.0454	1.9532	1.9809
	$\Phi_{\text{O1-O2-O3-O4}}$ (°)	32.40	34.42	0.03	11.01	19.89	6.00	0.14
Na ⁺	$r_{\text{Na-O1}}$ (Å)	2.2999	2.3503	2.1466	2.2624	2.2527	2.5699	2.3116
	$r_{\text{Na-O2}}$	2.2926	2.2500	2.1454	2.2445	2.2537	2.2763	2.3248
	$r_{\text{Na-O3}}$	2.2993	2.3063	2.1459	2.2402	2.2623	2.2705	2.3251
	$r_{\text{Na-O4}}$	2.2923	2.3248	2.1468	2.2104	2.2417	2.4393	2.3121
	$\Phi_{\text{O1-O2-O3-O4}}$ (°)	30.13	21.98	0.10	6.40	10.84	4.40	0.03

M⁺/crown-4 series

A. Geometrical structure The optimized structures for crown-4 ethers complexes with Li⁺ and Na⁺ are shown in Fig. 3, and their bond lengths data of alkali metal cations with coordinated O atoms are given in Table 2. It can be observed from Table 2 that the sites of the coordination of Li⁺ and Na⁺ with the crown-4 ethers are all on the O atoms and Li⁺ binds more closely with the donor atoms than the Na⁺ in the complexes, indicating that Li⁺ matches crown-4 ethers better than Na⁺. However, 15C4 binds the Li⁺ not very well, leaving a Li-O bond length of 3.6141 Å. The most asymmetrical structure of 15C4 and the smaller volume of Li⁺ both contribute to it. In addition, the geometry of 14C4 with and without the metallic cations hardly makes conformational changes ($\Phi_{\text{O1-O2-O3-O4}} \approx 0^\circ$), indicating that they match well.

B. Binding energies The calculated binding energies, enthalpies and Gibbs free energies of M⁺/crown-4 series,

based on the reaction (5), at the B3LYP levels of theory using the 6–31G* basis set are listed in Table 3, and the evolution of the energies are displayed in Fig. 4. The binding energies were corrected for the undesirable effects of basis set superposition error (BSSE) using the counterpoise (CP) method [18] with relaxed fragment geometries.

The key findings revealed in our calculations are as follows: (1) the gas phase binding energies, enthalpies, and Gibbs free energies increase monotonically for Li⁺ and Na⁺/nC4 series, except for Li⁺/15C4 and Na⁺/14C4, indicating that introduction of additional methylene increases the selectivity of rigid crown. (2) On the whole, the gas phase crown-4 ethers bind Li⁺ more strongly than Na⁺ for simple electrostatic reasons. However, in aqueous solution, the binding preference of the 12C4 is shifted away from Li⁺ and toward Na⁺. The most plausible reason for this is that the calculations lack solvent effect and Li⁺ is even more strongly solvated [19]. (3) The introduction of phenyl ring decreases the stability of B12C4 and B13C4

Table 3 Calculated binding energies ΔE^b (Kcal/mol), binding enthalpies ΔH^b (Kcal/mol), and Gibbs free energies ΔG^b (Kcal/mol) in gas phase for the complexes at 298 K

Ligand	Metal cation	$-\Delta E^b$	BSSE	$-\Delta H^b_{\text{BSSE}}$	$-\Delta H^b$	$-\Delta G^b$
12C4	Li ⁺	93.8462	7.8723	85.9739	91.9201	81.3478
	Na ⁺	58.2628	6.4828	51.7799	57.3054	46.9327
13C4	Li ⁺	99.1580	6.8654	92.2926	97.2847	87.5759
	Na ⁺	68.1435	6.2634	61.8800	67.0412	57.4083
14C4	Li ⁺	110.6890	6.5934	104.0960	108.1590	98.0779
	Na ⁺	67.8044	8.2671	59.5373	67.1190	55.8408
15C4	Li ⁺	95.6214	5.2528	90.3686	93.7204	84.8744
	Na ⁺	78.8901	6.7581	72.1319	77.648	68.5466
16C4	Li ⁺	117.6440	6.1648	111.479	115.305	105.108
	Na ⁺	85.0246	7.2842	77.7403	83.8993	73.0917
B12C4	Li ⁺	84.1604	6.5451	77.6153	82.9204	73.3753
	Na ⁺	53.8958	5.7844	48.1114	53.2630	44.2928
B13C4	Li ⁺	99.3055	5.7566	93.5489	97.4711	89.0392
	Na ⁺	69.1231	5.4868	63.6363	67.9461	58.7173

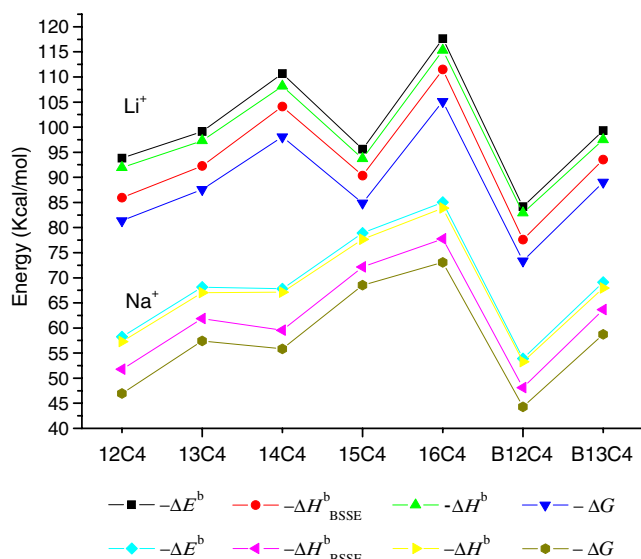


Fig. 4 Calculated binding energies ΔE^b (Kcal/mol), binding enthalpies ΔH^b (Kcal/mol), and Gibbs free energies ΔG^b (Kcal/mol) in gas phase for crown-4 ethers complexing with Li^+ and Na^+ at 298 K

complexes, and makes no obvious contribution to complex with cations, compared to 12C4 and 13C4, in accordance with above electronic property data.

C. Cation exchange reaction enthalpies and Gibbs free energies The enthalpies ΔH and Gibbs free energies ΔG of cation exchange reaction (6) can approximately evaluate the stabilities of Li^+ /crown-4 and Na^+ /crown-4 in gas phase, respectively. The ΔH and ΔG values of reaction (6) are shown in Table 4.

The reaction enthalpies ΔH : Generally, the assumption of significant reaction efficiency for exothermic reactions and low efficiency for endothermic reactions is still reasonable for these metal transfer reactions [20]. In Table 4, the metal exchange reactions for the series of crown-4 ethers are all endothermic, which indicates that Li^+ /crown-4 series are more stable than Na^+ /crown-4 series in the gas phase.

The reaction Gibbs free energies ΔG : The negative values of ΔG confirm the feasibility of the exchange reaction. And ΔG for the series of crown-4 ethers are: $14\text{C4} > 12\text{C4} > 16\text{C4} > \text{B13C4} > 13\text{C4} > \text{B12C4} > 15\text{C4}$. 14-Crown-4 gave the highest ΔG among the crown-4 series, eventually showing the highest cation selectivity for Li^+

over Na^+ , which is in agreement with the studies in aqueous solution [5, 6]. The highly selective binding of Li^+ by 14-crown-4 originates from cooperative entropic and enthalpic contributions at this ring size, both of which may be attributable to the least conformational changes and the most extensive desolvation caused by the size-fitted combination of cation and cavity diams.

Conclusions

With quantum chemistry calculations, theoretical data of a series of crown-4 ethers complexing with Li^+ and Na^+ were successfully established. The following conclusions can be drawn from this research:

The computation models for the series of crown-4 ethers are stable according to the positive vibration frequencies. With the calculation of the Fukui functions, it is found that the reactive sites of the gas phase crown-4 ethers are mainly located at oxygen atoms, as well as in the phenyl rings. The electronic data confirm that 12C4 has the most rigid structure, and the introduction of the phenyl rings to crown-4 ethers evidently decreased the energy gap and LUMO energies.

Analyzing the geometry of crown-4 ether complexes, Li^+ matches crown-4 ethers better than Na^+ . The calculated binding energies indicate that the gas phase crown-4 ethers bind Li^+ more strongly than Na^+ for simple electrostatic reasons. However in aqueous solution, the binding preference of the 12C4 is shifted away from Li^+ and toward Na^+ , because the calculations lack solvent effect and Li^+ is even more strongly solvated. The introduction of phenyl ring makes no contribution for B12C4 and B13C4 to binding cations, compared to 12C4 and 13C4, in accordance with electronic property data.

The cation exchange reaction enthalpies show that Li^+ /crown-4 series are more stable than Na^+ /crown-4 series in the gas phase, and 14C4 gave the highest reaction Gibbs free energies among the crown-4 series, showing the highest cation selectivity for Li^+ over Na^+ , which is in agreement with the studies in aqueous solution.

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Table 4 Calculated reaction enthalpies ΔH (Kcal/mol) and Gibbs free energies ΔG (Kcal/mol) for the cation exchange reaction in gas phase at 298 K

Li^+ vs Na^+	12C4	13C4	14C4	15C4	16C4	B12C4	B13C4
$-\Delta H$	34.6147	31.0146	42.8850	16.0724	31.4062	29.6574	29.5250
$-\Delta G$	34.4151	30.1675	42.2370	16.3278	32.0162	29.0826	30.3219

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