DFT Study of *p-tert*-Butylcalix[5]crown-6-ether Complexed with Alkylammonium Ions

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The structures and energies of *p-tert*-butylcalix[5]crown-6-ether (**1**) and its alkylammonium complexes have been calculated by *DFT* B3LYP/6-31G(d,p) method. We have studied the binding sites of these host-guest complexes focusing on the *p-tert*-butylcalix[5]arene pocket (*endo*) or the crown-6-ether moiety (*exo*) of **1**. The smaller alkylammonium cations have the better complexation efficiency with *p-tert*-butylcalix[5]crown-6-ether than the bulkier alkylammonium ions. For the *sec-* and *tert*-butylammonium ions, the hydrogen-bond distances of the *exo*-complexes are shorter, therefore, stronger than the *endo*-cases. This *DFT* calculated result is in parallel with the trend of the experimental association constants of the branched butylammonium ions.

Key Words : Calix[5]crown-6-ether, Alkylammonium ions, *DFT* B3LYP/6-31G(d,p), Endo, Exo

Introduction

Selective binding of biologically important organic ammonium guests attracts much research interests, which results in development of many sophisticated host systems.[1-3] Calix[5]crowns are known to bind large alkali metal ions[4] and a number of organic ions;[5] similarly calix[6]crowns are quaternary alkylammonium ion[6] selective. *Endo*-calix complexation of alkylammonium cations by functionalized (1,3)-*p-tert*-butylcalix[5]crown ether[7] and by calix[5]arene-based molecular vessels[8] have been reported. Giannetto *et al.* reported a very efficient discrimination behavior between butylammonium isomers by means of calix[5]arene-based ion selective electrode technique.[9] More recently, 1,3-

bridged calix[5]crown-6-ether (**1**) was investigated as a tool for the shape recognition of alkylammonium ions in focusing the *endo*- versus *exo*-cavity complexation.[10]

Various important computational approaches in a variety of interesting supramolecular system are published.[11] We have reported computer simulations on molecular recognition of alkyl ammonium ions by ester derivatives of *p-tert*-butylcalix[6]arene (**2**).[12] In that study, *endo*-complex was reported as the most stable conformer among the different orientations of alkyl ammonium cations complexed inside the cone-shaped host. Complexes of aromatic ring with ammonium cations, which are very important in biological systems, were already studied using *ab initio* calculations.[13] The report shows that two types of NH-aromatic π and CH-aromatic π interactions in benzene ring are responsible for the binding. From analysis of the structures and energies, the π-σ^* through-space interactions are seen to be significant in both types of NH-π and CH-π interactions.[14] We have published the structures and energies of *p-tert*-butylcalix[4]-crown-6-ether (**3**) and its alkyl ammonium complexes using *ab initio* HF/6-31G method.[15] We have found that cone conformation is generally to be most stable for all the employed calculation methods. The primary binding site of host **1** for the recognition of alkyl ammonium guests was confirmed to be the central part of the crown moiety, which is in satisfactory agreement with the experimental[3e] results. *Endo*-calix complexations of alkylammonium cations by *p-tert*-calix[5]aryl ester[16] have also been calculated by using *ab initio* HF/6-31G method.

In this study we have used *DFT* B3LYP/6-31G(d,p) method for the computer simulation of the complexation behaviors of the 1,3-bridged *p-tert*-butylcalix[5]crown-6-ether toward various alkyl ammonium ions. The main emphases of this research are trying to locate the most probable binding site of the host for the recognition of alkyl ammonium guest, and to determine the selectivity of the host for different alkyl ammonium guests with varying structural characteristics. Figure 1 shows the sketchs of hosts **1**, **2**, and **3**, in which some of the hydrogen atoms are omitted for clarity.
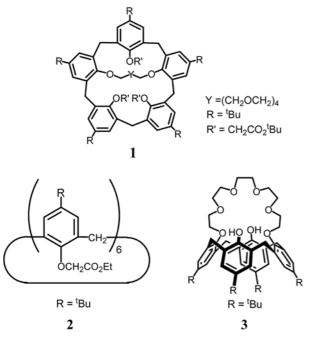

Figure 1. Chemical structures of (a) 1,3-bridged *p-tert*-butyl-calix[5]crown-6-ether **1**, (b) *p-tert*-butylcalix[6]aryl ester **2**, and (c) *p-tert*-butylcalix[4]crown-6-ether **3**.

Table 1. *DFT* B3LYP/6-31G(d,p) Calculated Complexation Energies[a] of Calix[5]crown-6 Complexes with Alkylammonium Ions

Complex(guest)[b]	NH_4^+	Me	Et	*n*-Pr	*iso*-Pr	*n*-Bu	*iso*-Bu	*sec*-Bu	*tert*-Bu
1(endo)[c]	−82.80	−73.56	−66.77	−66.56	−57.40	−65.22	−54.62	−49.11	−49.14
1(exo)[d]	−78.30	−72.90	−64.43	−59.38	−58.00	−62.03	−54.88	−54.21	−47.82

[a]Complexation energies (kcal/mol) = $E_{Complex} − E_{Host(cone)} − E_{Guest}$. Error limits in these calculations are 0.01 kcal/mol. [b]Me = methyl ammonium, Et = ethyl ammonium, *n*-Pr = *n*-propyl ammonium ion, etc. [c]Guest(endo) means that alkyl ammonium ion is contained inside of the benzene rings. [d]Guest (exo) denotes that alkyl ammonium ion is contained inside of the crown-ether ring.

Computational Methods

The initial structures of host molecule and host-guest complexes for *DFT* calculations were created by Hyper-Chem.[17] In order to find optimized conformations, we executed conformational search by simulated annealing method described in previous research.[18] B3LYP/6-31G(d,p) full re-optimization of the structure of host **1** or its alkylammonium complex was performed to get the final structure for each complex by using Gaussian 98.[19]
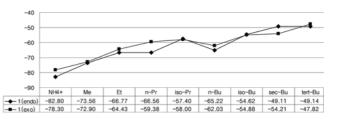
Figure 2. *DFT* B3LYP/6-31G(d,p) calculated complexation energies (kcal/mol) of *endo*- and *exo*-calix[5]crown-6-ether complexes with alkylammonium Ions.
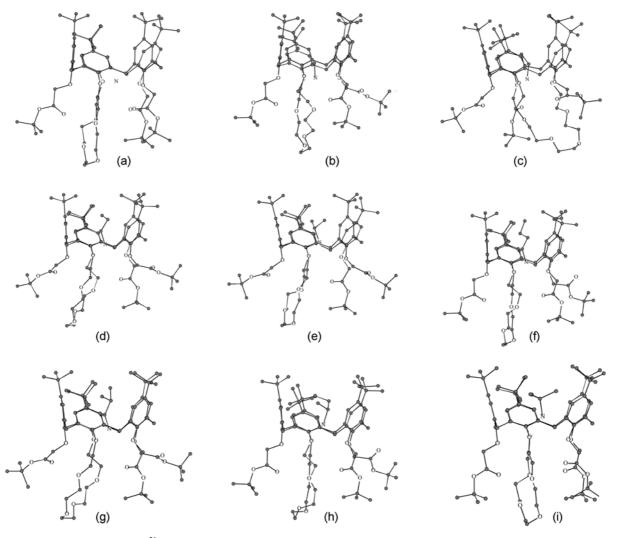
	NH4+	Me	Et	n-Pr	iso-Pr	n-Bu	iso-Bu	sec-Bu	tert-Bu
1(endo)	−82.80	−73.56	−66.77	−66.56	−57.40	−65.22	−54.62	−49.11	−49.14
1(exo)	−78.30	−72.90	−64.43	−59.38	−58.00	−62.03	−54.88	−54.21	−47.82

Figure 3. *DFT* calculated structures[21] of **1** complexed in the calix[5]arene-cavity with (a) ammonium, (b) methylammonium, (c) ethyl-ammonium, (d) *n*-propylammonium, (e) *iso*-propylammonium, (f) *n*-butylammonium, (g) *iso*-butylammonium, (h) *sec*-butylammonium, and (i) *tert*-butylammonium ions.

Results and Discussion

The B3LYP/6-31G(d,p) optimizations were carried out for two kinds of complexation mode of **1** by combining the cone conformer of host **1** with various guest cations. The results of *DFT* B3LYP/6-31G(d,p) complexation energies of the complexes of calix[5]crown-6-ether with alkyl ammonium ions are listed in Table 1 and Figure 2.

The smaller alkylammonium cations have the better complexation efficiency with *p-tert*-butylcalix[5]crown-6-ether than bulky alkylammonium ions. One should note that in the gas phase it is natural that smaller cationic species such as NH_4^+ should have higher binding energy than larger cationic species. However, in the presence of solvents, a specific size of cations (rather than a smaller cation) would more selectively bind receptors.[20]

When one compares the complexation energies, **1**+*n*-propylammonium(*endo*) complex (−66.6 kcal/mol) is found to be 7.2 kcal/mol more stable than the *exo*-complex (−59.4 kcal/mol). And the complexation energy (−65.2 kcal/mol) for **1**+*n*-butylammonium(*endo*) complex is found to be 3.2 kcal/mol more efficient than the *exo*-complex (−62.0 kcal/

mol). However, **1**+*sec*-butylammonium(*endo*) complex (−49.1 kcal/mol) is found to be 5.1 kcal/mol less stable than the *exo*-complex (−54.2 kcal/mol) due to steric hindrance of the branched butylammonium ion. These different discriminations of *n*-butyl and *sec*-butylammonium guest by the *p-tert*-butylcalix[5]crown-6-ether host are in accord with the results of the NMR titration experiments.[10] Except those cases, the complexation efficiencies for other alkylammonium ions are almost same in both of the calix[5]arene cavity (*endo*) and the crown periphery (*exo*) of *p-tert*-butyl-calix[5]crown-6-ether. Figure 3 shows the final structures[20] of cone conformation of **1** *endo*-complexed in the calix[5]-arene cavity with alkyl ammonium ions. Figure 4 shows the cone conformation of **1** *exo*-complexed in the crown-ether ring moiety.

For the complexation of alkylammonium ions by the ester derivatives of *p-tert*-butylcalix[6]arene (**2**), *endo*-calix[6]-arene complex was reported as the most stable conformer among four different orientations of alkyl ammonium cations complexed inside of the cone-shaped host.[9] For the host **2**, the most efficient binding site is a larger cavity consisted of six benzene rings which provide two types of NH-aromatic
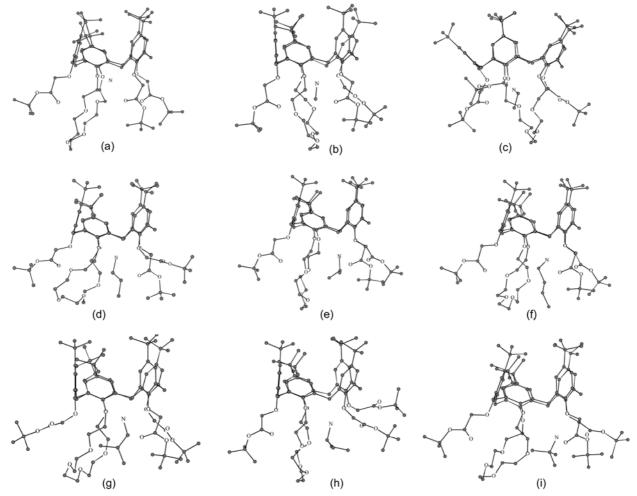

Figure 4. *DFT* calculated structures[21] of **1** complexed in crown-ether ring with (a) ammonium, (b) methyl ammonium, (c) ethyl ammonium, and (d) *n*-propyl ammonium ion, (e) *iso*-propylammonium, (f) *n*-butylammonium, (g) *iso*-butylammonium, (h) *sec*-butylammonium, and (i) *tert*-butylammonium ions.

Table 2. B3LYP/6-31G(d,p) Calculated H-Bond Distances (Å) between the Nitrogen Atom of Alkylammonium Ions and the Oxygen Atoms of Calix[5]crown-6 Complexes

Complex Mode	Guest	NH_4^+	Me	Et	*n*-Pr	*iso*-Pr	*n*-Bu	*iso*-Bu	*sec*-Bu	*tert*-Bu
	H-Bond	Complexes with Host								
1(endo)	N···O1	2.746	2.852	2.784	2.863	2.880	2.849	2.857	2.967	2.969
	N···O2	2.777	2.905	2.840	2.877	2.929	2.853	2.943	3.034	2.990
	N···O3	2.790	2.934	2.972	2.881	3.008	3.028	2.951		
	Average	2.771	2.897	2.865	2.874	2.939	2.910	2.917	3.001	2.980
1(exo)	N···O1	2.784	2.998	2.891	3.011	2.930	2.764	2.858	2.928	2.810
	N···O2	2.833	2.998	2.982	3.038	2.936	2.844	2.955	2.944	2.871
	N···O3	2.917	3.033	3.040	3.160	2.980	3.064	3.095	2.969	2.952
	Average	2.845	3.010	2.971	3.070	2.949	2.891	2.969	2.947	2.878

π and CH-aromatic π interactions.[11] However, the primary binding site of *p-tert*-butylcalix[4]crown-6-ether (**3**) for the recognition of alkyl ammonium guests was found to be the central part of the crown-6-ether moiety. But in the present case of cone-shaped *p-tert*-butylcalix[5]crown-6-ether (**1**), the cavity size of calix[5]arene of host **1** having five benzene rings is smaller than the calix[6]arene of host **2** and larger than the calix[4]arene of host **3**. Therefore, the *endo*-complexation efficiency of the host **1** has no advantage or disadvantage over *exo*-complexation in most alkylammonium guests. However, the *endo*-complexation for the hydrophobic cavity of the benzene ring might show a different efficiency in presence of solvent, depending upon aqueous or organic.

Experimentally, the steric hindrances by *p-tert*-butyl groups of **1** are severe for the entering of branched butylammonium ions into the *p-tert*-butylcalix[5]arene pocket. Therefore, bulky alkylammonium ions prefer to the crown ether moiety (*exo* mode) by experiencing both the hydrogen-bonding and electrostatic interactions. The hydrogen-bonding, electrostatic interaction, and steric hindrance of alkyl ammonium cation are the principle factors for the complexation efficiency of the *p-tert*-butylcalix[5]crown-6-ether with varying structures of the alkylammonium guests. From the calculated structures, the distances from nitrogen atom in alkylammonium guest ion to oxygen atoms in a cone-shaped host **1** are reported in Table 2 and Figure 5.

When one look at the values of smaller alkylammonium ions in Figure 5, the average hydrogen-bond distances of the *endo*-complexes is shorter, therefore, stronger than the *exo*-complexes. However, for the bulky *sec*- and *tert*-butylammonium ions, the hydrogen-bond distances of the *endo*-
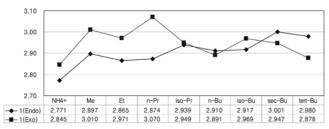
complexes are longer, therefore, weaker than the *exo*-cases. This *DFT* calculated result is again in parallel with the trend of the experimental association constants of the branched butylammonium ions,[10] although the conditions between calculation (in vacuum) and experimental environment (in solution) are different.

Conclusion

We have performed *DFT* B3LYP/6-31G(d,p) calculations for the complexation of *p-tert*-butylcalix[5]crown-6-ether with varying alkyl ammonium ions. The results show that the complexation efficiencies are almost same in both of the central part of crown periphery and the cavity of *p-tert*-butylcalix[5]arene. Complexation with the smaller alkyl-ammonium ion shows the better complexation efficiency than the bulkier alkylammonium ion. The *iso*-butylammonium cation in *endo* position of the host showed the highest complexation efficiency among the branched butylammonium ions, which is similar to the trend of the experimental association constants.

References

1. (a) *Molecular Recognition: Chemical and Biochemical Problems*; Roberts, S. M., Ed.; The Proceedings of an International Symposium, Royal Society of Chemistry: Dorset Press: Dorset, Great Britain, 1989. (b) Gutsche, C. D. *Calixarenes Revisited*; The Royal Society of Chemistry, Cambridge, 1998. (c) *Calixarenes 2001*; Asfari, Z.; Böhmer, V.; Harrowfield, J.; Vicens, J., Eds.; Kluwer: Dordrecht, 2001.
2. (a) Behr, J.-P.; Lehn, J.-M.; Vierling, P. *Helv. Chim. Acta* **1982**, *65*, 1853. (b) Fages, F.; Desvergne, J.-P.; Kampke, K.; Bouas-Laurent, H.; Lehn, J.-M.; Meyer, M.; Albrecht-Gary, A.-M. *J. Am. Chem. Soc.* **1993**, *115*, 3658. (c) Oh, K. S.; Lee, C.-W.; Choi, H. S.; Lee, S. J.; Kim, K. S. *Org. Lett.* **2000**, *2*, 2679. (d) Buhlmann, P.; Pretsch, E.; Bakker, E. *Chem. Rev.* **1998**, *98*, 1593.
3. (a) Chang, S.-K.; Hwang, H.-S.; Son, H.; Youk, J.; Kang, Y. S. *J. Chem. Soc., Chem. Commun.* **1991**, 217. (b) Chang, S.-K.; Jang,

Figure 5. *DFT* B3LYP/6-31G(d,p) calculated hydrogen-bonded distances (Å) of the alkylammonium complexes of calix[5]crown-6-ether.

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M.; Han, S. Y.; Lee, J. H.; Kang, M. H.; No, K. T. *Chem. Lett.* **1992**, 1937. (c) Song, B. M.; Chang, S.-K. *Bull. Korean Chem. Soc.* **1993**, *14*, 540. (d) Han, S. Y.; Kang, M.-H.; Jung, Y. E.; Chang, S.-K. *J. Chem. Soc., Perkin Trans. 2* **1994**, 835. (e) Jung, Y. E.; Song, B. M.; Chang, S.-K. *J. Chem. Soc., Perkin Trans. 2* **1995**, 2031.

4. (a) Arnaud-Neu, F.; Arnecke, R.; Bohmer, V.; Fanni, S.; Gordon, J. L. M.; Schwing-Weill, M.-J.; Vogt, W. *J. Chem. Soc. Perkin Trans. 2* **1996**, 1855. (b) Gordon, J. L. M.; Bohmer, V.; Vogt, W. *Tetrahedron Lett*. **1995**, *36*, 2445.

5. (a) Pappalardo, S.; Parisi, M. F. *Tetrahedron Lett.* **1996**, *37*, 1493. (b) Arnecke, R.; Bohmer, V.; Cacciapaglia, R.; Dalla Cort, A.; Mandolini, L. *Tetrahedron* **1997**, *53*, 4901. (c) Bohmer, V.; Dalla Cort, A.; Mandolini, L. *J. Org. Chem.* **2001**, *66*, 1900.

6. Casnati, A.; Iacopozzi, P.; Pochini, A.; Ugozzoli, F.; Cacciapaglia, R.; Mandolini, L.; Ungaro, R. *Tetrahedron* **1995**, *51*, 591.

7. Pappalardo, S.; Parisi, M. F. *J. Org. Chem.* **1996**, *61*, 8724.

8. Arnaud-Neu, F.; Fuangswasdi, S.; Notti, A.; Pappalardo, S.; Parisi, M. *Angew. Chem. Int. Ed.* **1998**, *37*, 112.

9. Giannetto, M.; Mori, G.; Notti, A.; Pappalardo, S.; Paris, M. F. *Anal. Chem.* **1998**, *70*, 4631.

10. Salvo, G. D.; Gattuso, G.; Notti, A.; Parisi, M.; Pappalardo, S. *J. Org. Chem.* **2002**, *67*, 684.

11. *Computational Approaches in Supramolecular Chemistry*; Wipff, G., Ed.; Kluwar Academic Publshers: Dordrecht, The Netherlands, 1994.

12. Choe, J.-I.; Kim, K.; Chang, S.-K. *Bull. Korean Chem. Soc.* **2000**, *21*, 200.

13. (a) Lee, J. Y.; Lee, S. J.; Choi, H. S.; Cho, S. J.; Kim, K. S.; Ha, T. K. *Chem. Phys. Lett.* **1995**, *232*, 67. (b) Kim, K. S.; Lee, J. Y.; Lee, S. J.; Ha, T. K.; Kim, D. H. *J. Am. Chem. Soc.* **1994**, *116*, 7399.

14. (a) Choi, H. S.; Cho, S. J.; Kim, K. S. *Proc. Natl. Acad. Sci.* **1998**, *95*, 12094. (b) Kim, K. S.; Cui, C.; Cho, S. J. *J. Phys. Chem.* **1998**, *102*, 461. (c) Cho, S. J.; Hwang, H.; Park, J.; Oh, K. S.; Kim, K. S. *J. Am. Chem. Soc.* **1996**, *118*, 485.

15. Choe, J.-I.; Chang, S.-K.; Ham, S. W.; Nanbu, S.; Aoyagi, M. *Bull. Korean Chem. Soc.* **2001**, *22*, 1248.

16. Choe, J.-I.; Lee, S. H.; Oh, D.-S.; Chang, S.-K.; Nanbu, S. *Bull. Korean Chem. Soc.* **2004**, *25*, 190.

17. *HyperChem* Release 7.5; Hypercube, Inc.: Waterloo, Ontario, Canada, 2003.

18. Choe, J.-I.; Kim, K.; Chang, S.-K. *Bull. Korean Chem. Soc.* **2000**, *21*, 465.

19. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A. Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98,* Revision A.9; Gaussian, Inc.: Pittsburgh, PA, 1998.

20. Choe, H. S.; Kim, D.; Tarakeshwar, P.; Suh, S. B.; Kim, K. S. *J. Org. Chem.* **2002**, *67*, 1848.

21. *Chem3D Molecular Modeling and Analysis*, Version 7.0; Cambridge Soft Corporation: Cambridge, 2002.