

Ab Initio Study of the Complexation Behavior of *p*-*tert*-Butylcalix[5]arene Derivative toward Alkyl Ammonium Cations

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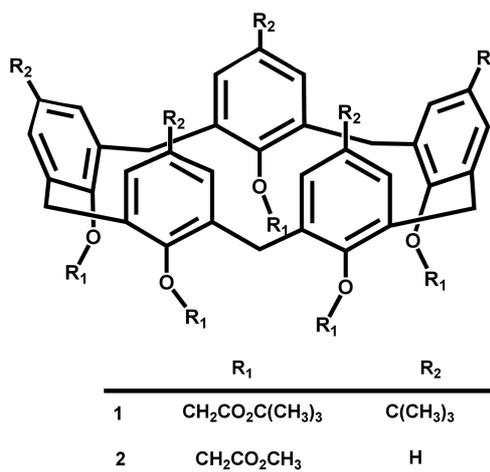
The structures and complexation energies of penta-*O*-*tert*-butyl ester **1** of *p*-*tert*-butylcalix[5]arene toward a series of alkyl ammonium guests have been optimized by *ab initio* HF/6-31G method. The calculated complexation efficiencies of **1** for alkyl ammonium guests have been found to be similar to the values of previously reported debutylated-calix[5]arene **2**. Calculation results show that both of the calix[5]aryl derivatives have much better complexation ability toward ammonium cation without alkyl group over other alkyl ammonium guests. The structural characteristics of the calculated complexes are discussed as a function of the nature of the alkyl substituents of the ammonium guests.

Key Words : *p*-*tert*-Butylcalix[5]arene, Alkyl ammonium ion, Molecular recognition, *Ab initio* HF/6-31G

Introduction

Molecular recognition of organic ammonium guests are very important in view of many functional biogenic ammonium ions, and a number of sophisticated host systems are derived from crown ethers and calixarenes.¹⁻³ Many of the molecular motifs, calixarenes are particularly attractive because of their easy functionalization toward targeted guests and vessel-like structural characteristics for the recognition of a variety of molecular guests.⁴ Selective *endo*-calix complexation of alkyl ammonium cations by functionalized (1,3)-*p*-*tert*-butylcalix[5]crown ether⁵ and by calix[5]-arene-based molecular vessels **1**⁶ 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.⁷ More recently, 1,3-bridged calix[5]crown-6-ether was investigated as a tool for the shape recognition of alkylammonium ions in focusing the *endo*- versus *exo*-cavity complexation.⁸

We previously reported the calculation results for the molecular recognition behaviors of penta-*O*-alkylated derivative and *tert*-butyl ester derivative **1** of cone-shaped *p*-*tert*-butylcalix[5]arene and their simplified structures toward a series of alkyl ammonium guests by semi-empirical AM1 method.^{10a} We also published *ab initio* HF/6-31G study of the host **2** (methyl calix[5]aryl ester having 115 atoms) which is a trimmed version of host **1** (*tert*-butyl *p*-*tert*-butylcalix[5]aryl ester constituting 220 atoms and beyond the limit of computational ability of supercomputer).^{10b} With the aid of improved speed, memory, and parallel-processing of newer supercomputer we could successfully obtain the optimized structures and energies of the bigger host **1** and its complexes toward a series of alkyl ammonium guests by *ab initio* HF/6-31G method. In this paper, we report the



Scheme 1. Chemical structure of calix[5]arene derivatives.

calculation results for the energies and structures of *tert*-butyl *p*-*tert*-butylcalix[5]aryl ester and its alkyl ammonium complexes.

Computational Methods

The initial structures of host and guest molecules were constructed by HyperChem.¹¹ In order to find optimized conformations, we executed conformational search¹² by simulated annealing method which has been described in previous publication.^{13a} *Ab initio* HF/6-31G optimization without any constraint of host **1** or its alkyl ammonium complexes by Gaussian 98 on supercomputer (NEC SX-7) with parallel processing at Okazaki National Research Institute of Japan took more than 8 days to reach an optimum conformation for each complex.

Results and Discussion

There might be a variety of conformational isomers in

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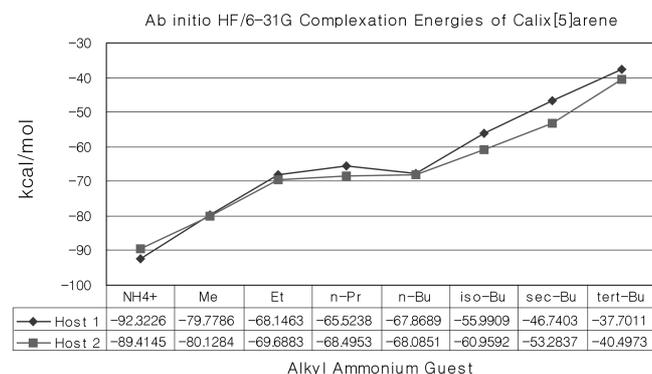
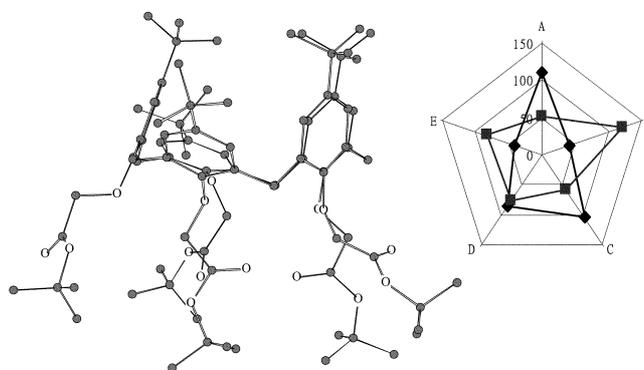
Table 1. *Ab initio* HF/6-31G Energies (A.U.)^a of Different Complexes of Calix[5]arene with Alkyl Ammonium Ions

<i>Ab initio</i>		Alkyl ammonium guest ^b								
HF/6-31G energies		NH ₄ ⁺	Me	Et	<i>n</i> -Pr	<i>n</i> -Bu	<i>iso</i> -Bu	<i>sec</i> -Bu	<i>tert</i> -Bu	
Using Gaussian 98		-56.5159	-95.5388	-134.5658	-173.5862	-212.6057	-212.6063	-212.6111	-212.6172	
Host	Guest	Complexes with host								
-4409.8495	Host 1	RNH ₃ ⁺	-4466.5125	-4505.5154	-4544.5238	-4583.5401	-4622.5633	-4622.5450	-4622.5351	-4622.5268
-3044.1610	Host 2	RNH ₃ ⁺	-3100.8194	-3139.8275	-3178.8378	-3217.8529	-3256.8751	-3256.8644	-3256.8570	-3256.8428
Host 1+Guest complexation ^c			-92.3226	-79.7786	-68.1463	-65.5238	-67.8689	-55.9909	-46.7403	-37.7011
Host 2+Guest complexation ^d			-89.4145	-80.1284	-69.6833	-68.4953	-68.0851	-60.9592	-53.2837	-40.4973

^aError limits in these calculations are about 2×10^{-5} A.U. Units for the *ab initio* total energies are in A.U., and units for complexation energies are in kcal/mol converted using conversion factor 1 A.U. = 627.50955 kcal/mol. ^bMe = methyl ammonium, Et = ethyl ammonium, *n*-Pr = *n*-propyl ammonium, *n*-Bu = *n*-butyl ammonium ion, etc. ^cComplexation energies (kcal/mol) = $E_{\text{Complex}} - E_{\text{Host}} - E_{\text{Guest}}$. ^dData for host 2 are taken from reference 10b.

ether and ester derivatives of calix[5]arene depending on the degree and nature of substitution.^{14,15} Among them, penta-O-alkylated *p-tert*-butylcalix[5]arenes, frozen in cone conformation, have received much attention as one of the most efficient and selective synthetic neutral molecular receptors for linear alkylammonium ions.⁵ As have been discussed in previous reports,¹⁰ we have focused our efforts to the elucidation of energetics and structural characteristics of most stable *endo*-cone-shaped complexes of hosts with various alkyl ammonium ions. The calculations might provide deeper insight into the selective recognition behavior of calixarene-based hosts for the recognition of a variety of important biogenic amines.

Table 1 summarizes the *ab initio* energies and the complexation efficiency of hosts 1 and 2 with various alkyl ammonium cations. For more easy comparison of the complexation efficiency of host 1 with host 2, we have converted the complexation data in Table 1 into a plot of Figure 1. When one sees the graphs in Figure 1, the trend of the complexation energies for host 1 using *ab initio* HF/6-31G method is similar to that of host 2 in the order of NH₄⁺ > MeNH₃⁺ > EtNH₃⁺ ~ *n*-PrNH₃⁺ ~ *n*-BuNH₃⁺ > *iso*-BuNH₃⁺ > *sec*-BuNH₃⁺ > *tert*-BuNH₃⁺. Therefore, it can be generalized that the complexation efficiency decreases gradually as the size and bulkiness of alkyl group increases. The complexation energy of 1 for NH₄⁺ is a little bigger in magnitude

**Figure 1.** Plot of *ab initio* complexation energies for *endo*-complexes of host 1 and 2 with alkyl ammonium guests.**Figure 2.** *Ab initio* calculated cone conformation of free host 1. Torsional angles of ϕ (♦) and χ (■) are given in sequence starting from the largest value of ϕ (See Figure 5 for ϕ and χ).

than that of host 2. However, host 1 is slightly worse than the trimmed host 2 in complexation for branched butyl ammonium ions. The calculation results for 1 and 2 suggest that the presence of *p-tert*-butyl groups in upper rim of host 1 does not affect significantly the relative stability of the host-guest complexes in the present calix[5]arene systems. However, host 1 with *tert*-butyl groups on both upper and lower rims has a little better selectivity toward the different size and shape of alkyl ammonium ions than that of host 2.

The *ab initio* optimized structure for the cone conformation of free host 1 is depicted in Figure 2. The free host 1 has somewhat irregular distorted conformation with ester carbonyl functions pointing relatively randomly with respect to the central pseudo-cavity of the host. In addition to this, the benzene rings of the calix[5]arene molecular framework also take somewhat distorted orientations although still retaining cone-type conformation.

Figures 3(a) through 3(d) show the *ab initio* calculated structures of *endo*-cone-type complex of 1 with smaller alkyl ammonium cations, in which hydrogen atoms are omitted for clarity. The structure of host 1 became more regular upon complexation with ammonium ion and ester carbonyl functions are pointing toward interior of the pseudo-cavity of the host molecule. When one sees the structure shown in Figure 3(a), the nitrogen atom in the host-guest (1+NH₄⁺)

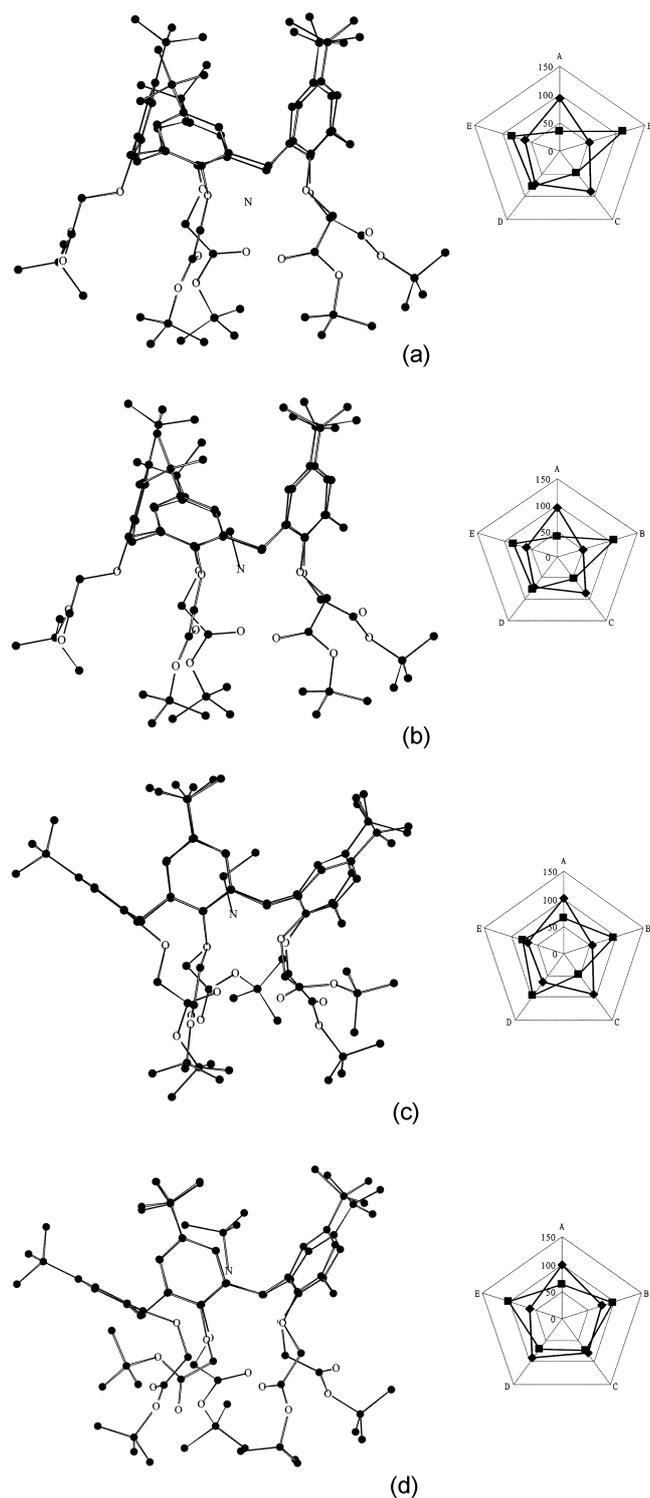


Figure 3. *Ab initio* calculated *endo-cone* conformations of **1** complexed with (a) ammonium, (b) methyl ammonium, (c) ethyl ammonium, and (d) *n*-propyl ammonium ions. Torsional angles of ϕ (♦) and χ (■) are given in sequence starting from the largest value of ϕ .

complex is located just below the mean plane comprised of five ether-oxygen atoms of host **1**. The structure implies that there exist multiple hydrogen-bonding interactions between the hydrogen atoms of NH₄⁺ and the oxygen atoms of phenol

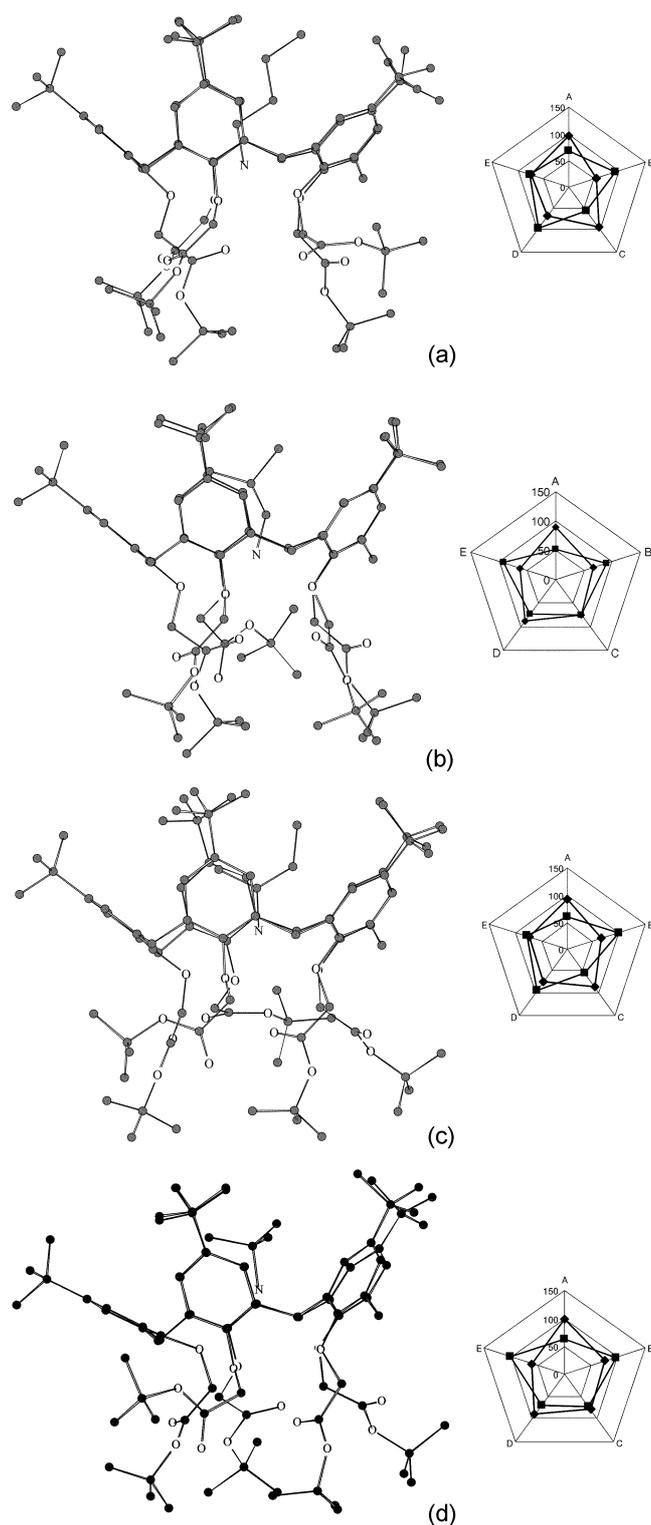


Figure 4. *Ab initio* calculated *endo-cone* conformations of **1** complexed with (a) *n*-butyl ammonium, (b) *iso*-butyl ammonium, (c) *sec*-butyl ammonium, and (d) *tert*-butyl ammonium ions. Torsional angles of ϕ (♦) and χ (■) are given in sequence starting from the largest value of ϕ .

ethers and some of carbonyl groups of ester functions. These charge-dipole and hydrogen bonding interactions resulted in the highest stability of the **1**+NH₄⁺ complex among other

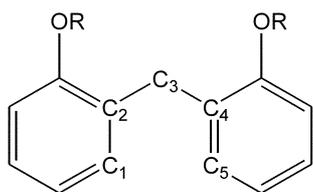


Figure 5. Conformational parameters ϕ and χ which is defined by the two torsion angles C(1)-C(2)-C(3)-C(4) and C(2)-C(3)-C(4)-C(5) between two adjacent phenolic units linked by a CH₂ group of calixarene.

complexes.

For the optimized structures shown in Figure 3(b), the nitrogen atom in the **1**+CH₃NH₃⁺ complex situated somewhat above the mean plane of five ether-oxygen atoms of host **1**. The general structural characteristics of the ligand are very similar to that of free host **1**. When one sees the optimized structures shown in Figures 3(c) and 3(d), the nitrogen atom in the **1**+RNH₃⁺ complex situated much above the mean plane of five ether-oxygen atoms of host **1**. With increasing length of alkyl chain of the ammonium ion the

steric hindrance of alkyl group increases, the ammonium group progressively located relatively away from the oxygen atoms of phenol ethers. That will weaken the interactions between alkyl ammonium guest and oxygen atoms of the host. As one sees in Figure 1, from ethyl ammonium ion and longer alkyl ammonium guests, the magnitude of the complexation energy is much smaller than methyl ammonium ion.

When we have counted the number of hydrogen bonding between the nitrogen atom of alkyl ammonium guest and the ether-oxygen atoms of host, most of RNH₃⁺ ions use all of three hydrogen atoms of ammonium moiety for hydrogen bonding, except that *sec*-BuNH₃⁺ uses two hydrogen atoms and that *tert*-BuNH₃⁺ uses only one hydrogen atom with longer H-bond distance than linear alkyl ammonium ions. As one sees in Figures 1 and 4, from *n*-butyl ammonium ion to bulkier *tert*-butyl ammonium guests, the stability of the **1**+RNH₃⁺ is drastically decreasing due to steric effects. This will give a good selectivity of host **1** toward the linear butyl over the branched butyl ammonium ions.

The molecular conformation of calixarenes can be readily understood by using conformational parameters ϕ and χ which is defined by the two torsion angles C(1)-C(2)-C(3)-C(4) and C(2)-C(3)-C(4)-C(5) between two adjacent phenolic units linked by a CH₂ group as shown in Figure 5.¹⁷ The corresponding values of conformational parameters ϕ and χ for the calculated structures are given alphabetically in decreasing values in Figure 6 (The numerical values will be provided by Supporting Tables from the correspondence author). All the structure showed conformational parameter sequence +-, +-, +-, +-, +- (taken in order: sign of ϕ sign of χ , sign of ϕ sign of χ ,...) characteristics of cone conformation. In this case, the plot showed that the free host adopts relatively distorted cone conformation having relatively wide distribution of torsional angles and the structure became more ideal cone-type conformation as the substituent of alkyl group is larger than ethyl group as evidenced by more evenly distributed torsional angles.

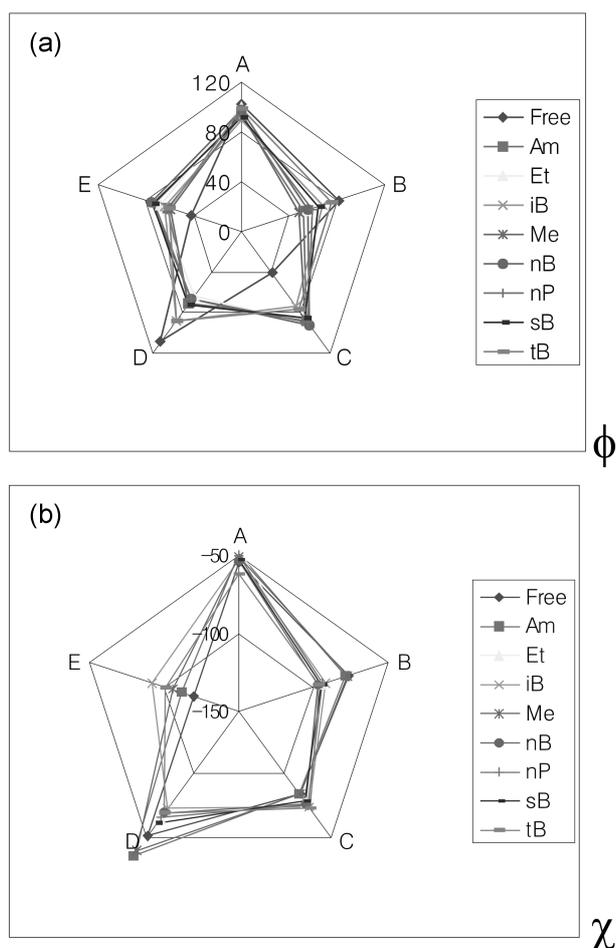


Figure 6. (a) Chart of the conformational parameter ϕ for the free and complexed *p*-*tert*-butylcalix[5]arenes. (b) Chart of the conformational parameter χ for the free and complexed *p*-*tert*-butylcalix[5]arenes.

Conclusion

Using the *ab initio* HF/6-31G level of theory, we have calculated the complexation behaviors of the derivatives of calix[5]arene toward a variety of alkyl ammonium ions. From our calculation results, ammonium cation without alkyl group has much better complexation ability over other alkyl ammonium guests in the order of NH₄⁺ > MeNH₃⁺ > EtNH₃⁺ ~ *n*-PrNH₃⁺ ~ *n*-BuNH₃⁺ > *iso*-BuNH₃⁺ > *sec*-BuNH₃⁺ > *tert*-BuNH₃⁺. The structure of the host became more symmetric cone-type conformation as the substituent of the alkyl ammonium guest is larger than ethyl group.

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Supporting Information Available: Supporting Tables 1 and 2 are available from the correspondence author.

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