

Molecular Recognition of Butylamines by Calixarene-Based Ester Ligands

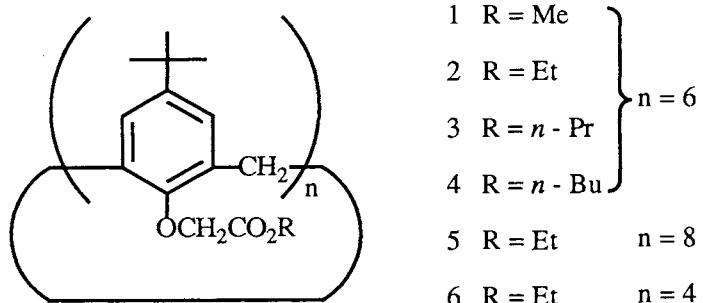
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Ester derivatives of *p*-tert-butylcalix[6]arene exhibited unique molecular recognition properties toward butylamines. Binding selectivity of hexaethyl ester, assessed by the extraction of butylammonium picrates, was found to be superior to dibenzo-18-crown-6 ether.

The selective recognition of biogenic amines is one of the fundamental interest in biomimetic chemistry.¹⁾ Numerous studies have been accomplished for the design and synthesis of a great variety of functionalized macrocycles which can recognize and/or show catalytic activities on biologically interesting ammonium guests.²⁾ Calixarenes received much attentions as useful building blocks for such new receptor molecules.³⁾ Recently we have reported the selective binding of amino acid esters to the ethyl ester derivative of *p*-tert-butylcalix[6]arene (2).⁴⁾ The observed host-guest interaction is assumed due mainly to the complexation through a tripodal arrangement of N⁺-H \cdots O=C(host) hydrogen bonds and R-NH₃⁺ \cdots O=C(host) charge-dipole interactions. Apparently, the concomitant relationship of spatial arrangement between the host and guest is subject to a fairly obvious steric constraint, which is expected to provide a valuable handle for the lateral recognition characteristics to the present host-guest system.



Compounds **1**, **3**, and **4** were prepared by transesterification of ethyl ester of *p*-*tert*-butylcalix[6]arene (**2**) following the literature procedure (about 90% yield).⁵⁾ The ¹H NMR spectra of **1-3** are simple but relatively broad and ill resolved, which suggests the fluxional behavior of the present hosts.⁶⁾ However, compound **4** with slightly bulkier *n*-butyl substituent exhibited relatively complex ¹H NMR pattern, which indicates that conformational interconversion is somewhat frozen in NMR time scale at room temperature. The temperature-dependent ¹H NMR studies revealed that coalescence temperature (T_c) of **4** is 56 °C in $CDCl_2/CDCl_2$ (500 MHz). It is known that the conformational change in related O-acyl functionalized calix[6]-arenes occurs via the "oxygen-through-annulus" rotation mechanism and the T_c is sensitive to the bulkiness of the substituent on the lower rim phenol ether oxygen.⁷⁾ In the present system, the threshold in conformational freezing in NMR time scale at room temperature is provided by *n*-butyl substituent, which would be helpful for the molecular design of more elaborate functionalized calix[6]arenes.⁸⁾

The aforementioned binding mode between ester host and alkylammonium guest was verified in part by the ¹H NMR titration experiments.⁹⁾ Upon interaction with the excess *n*-butylammonium picrate guest, among other spectral changes, the $ArCH_2Ar$ bridging methylene resonance of the ethyl ester host changed from a broad singlet to a pair of doublet at 3.42 and 4.56 ppm ($J = 14.7$ Hz) in $CDCl_3$. This is well commensurate with the adoption of cone conformation of the calix[6]arene host, which might be a process required for the recognition of alkylammonium guests.

The molecular recognition property of these ester ligands toward varying structures of butylamine was estimated by the standard solvent extraction technique of butylammonium picrates¹⁰⁾ into dichloromethane at 25 °C (Table 1). The binding stoichiometry assessed by continuous variation method in chloroform indicated a 1:1 (ligand: *n*-butylammonium picrate) stoichiometry for all the esters tested. For comparison, the extraction ability of dibenzo-18-crown-6 ether (DB18C6), which has closer structural property to the calixarenes among the crown ether family, was included.

All the hexaesters **1** - **4** exhibited unique molecular recognition properties toward butylammonium guests. In general, they interact in decreasing order for the following butylammonium salts, i.e., *n*-butyl > *iso*-butyl ≈ *sec*-butyl > *tert*-butyl, which can be explained by reasoning from steric effects. Interesting thing to note is that the extraction efficiency increased markedly on going from methyl to ethyl moiety, then levelled off with further increase in chain length up to butyl group. Especially, ethyl ester **2** showed the most pronounced discrimination behavior, and the selectivity defined by the ratio of extraction constant (K_{ex})¹¹⁾ of *n*-Bu and

Table 1. Extraction of Butylammonium Picrates^{a)}

Ligands	% Picrate extraction				Selectivity $K_{\text{ex}}(n\text{-Bu})/K_{\text{ex}}(\text{tert-Bu})$
	<i>n</i> -Bu	<i>iso</i> -Bu	<i>sec</i> -Bu	<i>tert</i> -Bu	
1	7.0	5.3	4.5	3.4	2.22
2	34.0	22.8	22.3	9.8	6.51
3	30.5	20.1	21.3	9.4	5.53
4	32.6	22.2	23.5	12.5	4.42
5	3.9	3.6	3.4	2.7	1.48
6	14.2	10.6	15.2	15.6	0.88
DB18C6	23.8	18.5	18.5	17.8	1.56

a) At 25 °C, $\text{H}_2\text{O}/\text{CH}_2\text{Cl}_2 = 5 \text{ mL}/5 \text{ mL}$: [ligand] = $3.5 \times 10^{-3} \text{ M}$, $[\text{BuNH}_3^+\text{Pic}^-] = 7.0 \times 10^{-5} \text{ M}$.

tert-Bu pair is as high as 6.51. The reason for the poor extraction efficiency of methyl ester is not yet clarified. However, the Corey-Pauling-Koltun molecular model plausibly suggests that the methyl substituent with smaller van der Waals radius should exert less lateral steric and/or hydrophobic interactions compared with ethyl and higher alkyl moiety and might result in inferior binding and recognition behavior.

On the contrary to the hexaesters, the extraction efficiency of DB18C6 is not so pronounced in spite of the well-known rigid coronand type structure. Furthermore, the discrimination behavior toward butylamines is not obvious (selectivity = 1.56), which might be originated from the two dimensional nature of coronands.¹²⁾

The well-known idea of size fit can be clearly visualized for the present host-guest system by the fact that the octameric ethyl ester **5** exhibited much inferior extraction behavior. With octaester, the proposed binding mode of previously mentioned scheme could not be fully rationalized. Another interesting but rather unexpected result is the relatively non-discriminating extraction behavior of the tetrameric ethyl ester **6**. With tetrameric ethyl ester ligand, the extraction ability is comparable to the hexaesters, which can be expected from the well-organized cone conformation of functionalized calix[4]arenes for the complexation of guests. However, the discrimination between butylammonium salts was almost disappeared. This might be, among other reasons, caused by the fact that the interannular distance of tetrameric ester is too narrow¹³⁾ for providing pseudocavity for the butylammonium guest to sit deeply into the cavity of the host to

experience a definite secondary lateral interaction.

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