Molecular Recognition of Alkylamines: Conformational and Binding Properties of Calix[6]arene-based Ester Ligands†

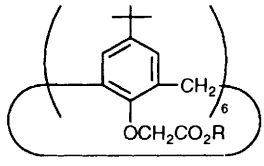
Sang-Yoon Han, Myong-Hee Kang, YeonEui Jung and Suk-Kyu Chang*
Department of Chemistry, Chung-Ang University, Seoul 156-756, Korea

A series of alkyl $1^5,3^5,5^5,7^5,9^5,11^5$-hexa-*tert*-butyl-1,3,5,7,9,11-hexa[1,3]benzenacyclododecaphane esters have been prepared that selectively bind to alkylammonium cations. Ester ligands showed extraction efficiency toward alkylamines in the sequence of ammonium < Me ≃ Et > Pr > Pr^i > Bu > Bu^i ≃ Bu^s > *tert*-butylammonium guests. Single and competitive transport experiments of butylamines also confirmed the binding properties obtained with extraction experiments and the transport selectivity for Bu/Bu^t pair exceeds 25. Conformational properties, such as T_c and $\Delta G_c^{\ddagger}$, of ester ligands were investigated by means of temperature-dependent ^{1}H NMR spectroscopy. Conformational freedom was generally found to decrease as the size of substituent of ester side chain increased. ^{1}H NMR complexation studies of ethyl ester **2** with caesium tetraphenylborate and butylammonium picrate guests suggest that the conformational reorganization into a cone conformation has provoked complex formation.

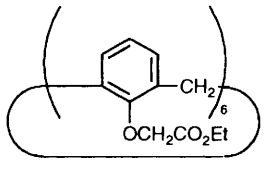
Numerous attempts have been made to design new host systems which can selectively interact and perform intriguing molecular recognitions, mimicking closely related fundamental biological processes.[1,2] Particularly, selective binding of organic ammonium guests attracts much research interest, which results in the development of many sophisticated host systems.[3–5]

Calixarenes received much interest as a building block for the construction of a versatile biomimetic system.[6] Much attention in this area has focused principally on the functionalization of calix[4]arenes among the calixarene family.[6–9] However, calix[6]arenes have a higher degree of functionality and attractive structural properties that originate from their molecular flexibility and the possibility of making them rigid. In this regard, there are strong demands for the introduction of more elaborate functional groups onto the rigid framework of calix[6]arenes for the development of novel biomimetic systems.[10–14]

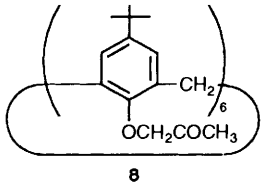
We have focused our attention on the construction of a novel device for the molecular recognition of alkylammonium guests which is based upon the calixarene framework.[15,16] Even though some progress has been made on the design of suitably functionalized calixarene derivatives for the molecular recognition of amine and related compounds,[17] a lot remains to be done. In this paper, we report the conformational and the molecular recognition behaviour toward alkylammonium guests of calix[6]arene-based ester derivatives, aiming for the design of a more elaborate host for biogenic amines as well as many related biologically interesting guests.



1 R = Me
2 R = Et
3 R = Pr
4 R = Pr^i
5 R = Bu
6 R = Bu^t



7



8

Experimental

General.—All reagents were used as received without further purification: solvents were purified according to standard procedures. ^{1}H NMR spectra were obtained on a Varian Gemini-300 spectrometer (300 MHz) or Bruker AMX-500 spectrometer (500 MHz) using Me_4Si as an internal standard. UV spectra were recorded on a Shimadzu UV-240 spectrophotometer. Melting points were measured with a Gallenkamp melting point apparatus and are not corrected. Elemental analyses were carried out by a Perkin-Elmer CHN 2400 instrument at Korea Basic Science Center in Seoul, Korea. Analytical TLC was performed on precoated silica gel 60F-254 plates.

Preparation of Ligands.—The methyl and ethyl esters of $1^5,3^5,5^5,7^5,9^5,11^5$-hexa-*tert*-butyl-1,3,5,7,9,11-hexa[1,3]benzenacyclododecaphane, **1** and **2**, were prepared according to the reported standard procedure.[14] The debutylated ethyl ester **7** and the methyl ketone **8** were also prepared according to the reported procedure.[14]

The propyl ester **3** and butyl ester **5** were prepared in the same manner as **1** by transesterification reactions with propyl and butyl alcohols, respectively, in the presence of toluene-*p*-sulfonic acid. After standard work-up, the product was purified by recrystallization from CH_2Cl_2–methanol mixture.

$1^5,3^5,5^5,7^5,9^5,11^5$-*Hexa*-tert-*butyl*-$1^2,3^2,5^2,7^2,9^2,11^2$-*hexa*-(*propoxycarbonylmethoxy*)-1,3,5,7,9,11-*hexa*[1,3]*benzenacyclododecaphane* (**3**). Yield 88%, m.p. 223–224 °C; δ_H(300 MHz; $CDCl_3$) 0.99 (54 H, s), 1.01 (18 H, t), 1.63 (12 H, m), 4.13

† Calix[6]arene ≡ 1,3,5,7,9,11-hexa[1,3]benzenacyclododecaphane.

(12 H, t), 3.97 (12 H, s), 4.5–4.7 (12 H, br s) and 6.92 (12 H, s) (Found: C, 73.3; H, 8.4. $C_{96}H_{132}O_{18}$ requires C, 73.25; H, 8.45%).

The butyl ester **5**. Yield 78.5%, m.p. 201–203 °C; δ_H[500 MHz; $(Cl_2DC)_2$; 80 °C] 0.96 (72 H, br s), 1.43 (12 H, m), 1.68 (12 H, t), 4.0–4.2 (12 H, br s), 4.21 (12 H, t), 4.60 (12 H, s) and 6.96 (12 H, s) (Found: C, 74.1; H, 9.1. $C_{102}H_{144}O_{18}$ requires C, 73.88; H, 8.75%).

The isopropyl ester **4** was prepared by direct alkylation with isopropyl bromoacetate following the same procedure to that employed for the preparation of **2**.

The isopropyl ester **4**. Yield 76%, m.p. 297 °C; δ_H[500 MHz; $(Cl_2DC)_2$; 100 °C] 0.99 (54 H, s), 1.32 (36 H, s), 4.11 (12 H, s), 4.59 (12 H, s), 5.14 (6 H, s) and 6.94 (12 H, s) (Found: C, 73.5; H, 8.4. $C_{96}H_{132}O_{18}$ requires C, 73.25; H, 8.45%).

The tert-*butyl ester* **6**. To a mixture of $1^5,3^5,5^5,7^5,9^5,11^5$-hexa-*tert*-butyl-1,3,5,7,9,11-hexa[1,3]benzenacyclododecaphane (1.96 g, 2.0 mmol), K_2CO_3 (2.48 g, 18 mmol) and KI (40 mg) in methyl isobutyl ketone (MIBK) (160 cm^3) was added *tert*-butyl bromoacetate (2.92 cm^3, 18 mmol) under N_2. After 24 h of refluxing the reaction mixture was concentrated under reduced pressure and the residue was partitioned between water and CH_2Cl_2. The separated organic layer was washed successively with saturated aqueous $NaHCO_3$ and water, then dried ($MgSO_4$). The evaporated residue was recrystallized from methanol to give colourless crystals of **6** (72%): m.p. 290 °C (decomp.); δ_H[500 MHz; $(Cl_2DC)_2$; 100 °C] 0.97 (54 H, s), 1.54 (54 H, s), 3.95–4.15 (12 H, br s), 4.56 (12 H, s) and 6.97 (12 H, s) (Found: C, 72.9; H, 8.9. $C_{102}H_{144}O_{18}$ requires C, 73.88; H, 8.75%).

Extraction Experiments.—Alkylammonium picrates were prepared by the neutralization of appropriate alkylamines with picric acid in methanol or ethanol.[18] The picrate stock solution was prepared (7.0×10^{-5} mol dm^{-3}) using deionized water. The ligand was 3.5×10^{-3} mol dm^{-3} in CH_2Cl_2. Each solution (5 cm^3) was placed in a centrifuge tube stoppered with a Teflon-lined screw cap and the mixture was placed in a temperature-regulated circulating thermostat (25 ± 0.1 °C) for 1 h to ensure the thermal equilibrium. The mixture was then mixed thoroughly for 1 min with a Vortex-Genie and centrifuged to hasten the phase separation. Concentration of the picrate salt in aqueous and organic phases were determined by UV spectrophotometry: $\lambda_{max}(H_2O)$/nm 356 (ε/dm^3 mol^{-1} cm^{-1} 1.45×10^4); $\lambda_{max}(CH_2Cl_2)$/nm 378 (ε/dm^3 mol^{-1} cm^{-1} 1.8×10^4).[19] For each ligand and guest cation, at least three separate measurements were performed to ensure the values.

Transport Experiments.—Transport experiments across the liquid membrane were performed at 25 °C using a U-tube (1.8 cm, i.d.) apparatus.[20] A chloroform solution (15 cm^3) containing carrier (3.3 mmol dm^{-3}) was placed at the bottom of the apparatus. On the source phase was carefully added aqueous alkylammonium perchlorate solution (0.05 mol dm^{-3}; 10 cm^3) and on the receiving phase was placed deionized water (10 cm^3). The membrane phase was magnetically stirred at constant speed of 200 rpm. The transport rates were obtained by measuring co-transported ClO_4^- ion in the receiving aqueous phase by the ion selective electrode method (Orion Microprocessor Ionalyzer 901, Orion 93-81 perchlorate electrode).

Competitive transport of butylammonium guests was performed using identical U-tube apparatus except employing deuteriated solvents for the sake of detectability. The source phase was a mixture of four butylammonium guests (each 0.50 mmol) in 5.0 cm^3 of D_2O and the receiving phase was 5.0 cm^3 of D_2O. The membrane phase was a 3.0 mmol dm^{-3} solution of carrier in 15 cm^3 of $CDCl_3$. The total transport rate was determined by measuring co-transported perchlorate concentration in the receiving aqueous phase and the individual transport rates of constituent guests were determined by ^1H NMR spectroscopy (500 MHz).

Results and Discussion

Synthesis and Conformational Properties of Ligands.—The hexa-*tert*-butylhexabenzenacyclododecaphane-based ester hosts were prepared by alkylation with the appropriate alkyl bromoacetate or by a transesterification reaction of the ethyl ester derivative **2** with the appropriate alcohol in the presence of toluene-*p*-sulfonic acid.[14] The *tert*-butyl ester was obtained by the direct alkylation with *tert*-butyl bromoacetate in the presence of K_2CO_3 under refluxing MIBK. This is a rather strenuous reaction condition, using high boiling MIBK, in order to realize exhaustive alkylation.

Temperature-dependent ^1H NMR (500 MHz) properties of the ester derivatives were investigated using $CDCl_3$ or $(Cl_2DC)_2$ as solvent. From these experiments, the coalescence temperature (T_c) and free energy of activation ($\Delta G_c^{\ddagger}$) were estimated[21] and the results are summarized in Table 1.

The methyl and ethyl esters **1** and **2** exhibited relatively broad resonance lines for all the protons at room temperature. Their spectra transformed into a sharp resonance pattern upon cooling down to 243 K as shown in Fig. 1 for the methyl ester **1**. Of particular interest is that the resonances of the bridging

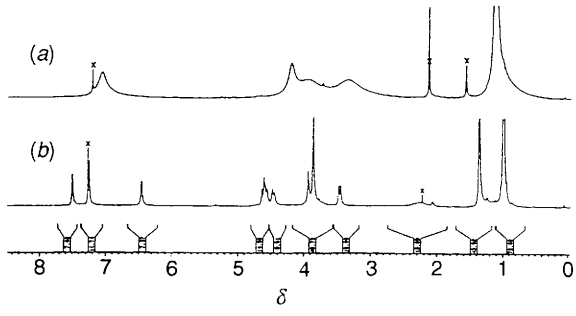


Fig. 1 ^1H NMR spectra of methyl ester **1** in $CDCl_3$: (*a*) 33, (*b*) at −30 °C. Signals marked with x are from residual solvents.

Table 1 T_c and $\Delta G_c^{\ddagger}$ for ester derivatives **1**–**6**[a]

Ester	Solvent	T_c °C	Methylene shift Hz H(A)	H(B)	k_c/s^{-1}	$\Delta G_c^{\ddagger}$/kcal mol^{-1}
1	$CDCl_3$	15	2229.9	1732.1	1109	12.9
2	$CDCl_3$	−2	2252.6	1793.3	1023	12.2
3	$CDCl_3$	32	2262.6	1796.2	1038	13.7
4	$(Cl_2DC)_2$	56	2244.7	1786.2	1021	14.8
5	$(Cl_2DC)_2$	59	2372.9	1784.0	1311	14.7
6	$(Cl_2DC)_2$	86	2407.1	1776.5	1403	15.9

[a] At 500 MHz.

methylene protons are resolved from a broad singlet into a pair of doublets, with a singlet intervening at low temperature. That may be due to the adoption of the 1,2,3-alternate conformation at low temperature.[11,22] The free energy of conformational interconversion of **1** and **2** is estimated to be 12.9 and 12.2 kcal mol^{-1}, respectively. That is smaller than the value of 13.3 kcal mol^{-1} of the unmodified hexa-*tert*-butylhexabenzenacyclododecaphane,[21] which suggests that the conformational properties of the ester derivatives **1** and **2** are rather flexible, compared with that of the unsubstituted parent compound. One thing to be noted is that methyl ester **1** is found to have a slightly larger activation energy for conformational interconversion than the ethyl ester **2**, which is contrary to the expectation from simple bulkiness of the substituent.

For the propyl ester **3**, T_c was found to be 305 K, and for **5** with the more bulky butyl substituent, T_c increases again to 329 K with a concomitant increase in $\Delta G_c^{\ddagger}$. The trend is well explained by simply invoking the oxygen-through annulus rotation,[23] and that T_c is sensitive to the bulkiness of the substituent on the lower rim phenol ether oxygen.[24] Meanwhile, for the isopropyl ester **4**, T_c increases up to 332 K; which is even higher than that of the butyl derivative. This observation indicates that the introduction of an extra α-methyl group on the alkyl side chain of the ester function has a significant effect on the conformational freedom of the present host system.

Of particular interest is that the *tert*-butyl ester **6** showed a relatively simple ^1H NMR spectral pattern at room temperature suggesting that **6** has a high degree of symmetry in solution ($CDCl_3$). All the peaks are relatively sharp, compared with the NMR spectrum of lower homologue esters, which means that the conformational interconversion through oxygen-through annulus is somewhat frozen. There are two singlets and two pairs of doublets in the region of 3.0–5.5 ppm. Two cross peaks appeared in the COSY spectrum that may be ascribed to the bridging methylene and O–CH_2–CO_2 protons, respectively (Fig. 2). The familiar pattern of one singlet and a pair of doublets arising from the bridging methylene protons is diagnostic and well commensurate with the 'up-out-up-down-out-down' 1,2,3-alternate conformation.[11]

The same pattern consisting of a doublet intervening with a singlet was also observed for the O–CH_2–CO_2 protons. That may be due to the restricted rotation of the methylene protons adjacent to the carbonyl function of side chains. Examination of Corey–Pauling–Koltun molecular model of **6** suggests that the periphery of the hexa-*tert*-butylhexabenzenacyclododecaphane cavity is too crowded, with 12 *tert*-butyl groups, to allow free rotation of the substituents. Even with these circumstances, the outward and central part of the 1,2,3-alternate region might still possess a symmetry plane that yields a singlet peak. However, the lateral up or down part of the ligands lacks any symmetry elements, that makes the O–CH_2–CO_2 portion diastereotopic and results in splitting into a pair of doublets.

To investigate the conformational behaviour of the present host system more deeply, we performed a ^1H NMR titration ($CDCl_3$) with Cs^+ cation that is known to form a very strong complex with ester derivatives of calix[6]arene.[25] Upon interaction with caesium tetraphenylborate, the bridging methylene resonance of **2** started to change from a broad singlet into a well defined pattern of a pair of doublets (Fig. 3). That is a characteristic pattern of the cone conformation of calixarenes.[26] With 0.5 equivalent of guest, there exists both signals for free and complexed host indicating that the complexation rate is relatively slow on the NMR time scale.[27] Propyl and butyl esters also showed the above mentioned characteristic spectral changes. The strong interaction with Cs^+ ion seems to overcome the activation barrier for the conformational reorganization of host into its cone conformation. To be noted is that the methyl ester **1** exhibits an almost featureless and broad

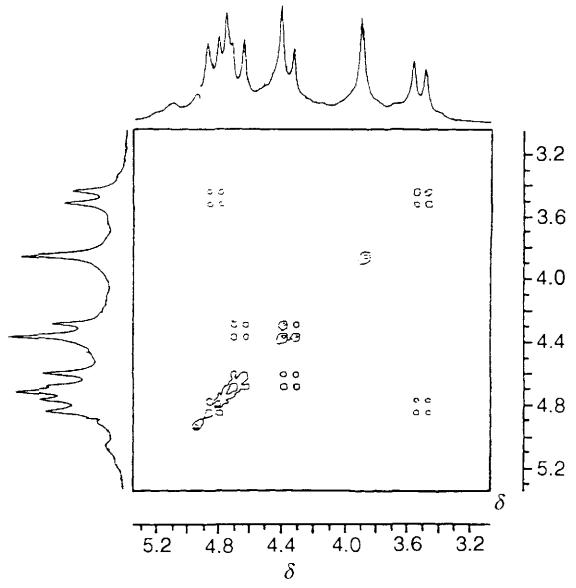


Fig. 2 Methylene region of a COSY spectrum of **6** in $CDCl_3$

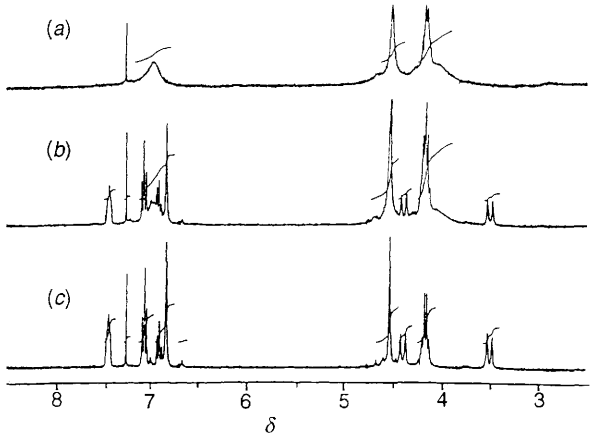


Fig. 3 Partial ^1H NMR spectra of **2** (5.0×10^{-3} mol dm^{-3}): (*a*) in the absence of guest, (*b*) in the presence of 0.5 equiv. $CsBPh_4$ and (*c*) in the presence of 1.0 equiv. $CsBPh_4$ ($CDCl_3$, 300 MHz)

^1H NMR spectrum upon titration with caesium salt. The intermolecular association–dissociation rate of complexation of Cs^+ for **1** seems to be somewhat faster than the ethyl ester **2** and higher homologues.

Titration of the ethyl ester **2** with butylammonium picrate also was performed. Upon interaction with excess butylammonium picrate guest, the $ArCH_2Ar$ bridging methylene resonance of the host **2** changed from a broad singlet into a pair of doublets at 3.42 and 4.56 ppm (J = 14.7 Hz) in $CDCl_3$. This is again commensurate with the adoption of a cone conformation of the calix[6]arene host, which is requisite for the binding of alkylammonium guests.[15]

Extraction of Alkylammonium Picrates.—The molecular recognition properties of ester derivatives were determined by the standard solvent extraction technique of picrate salts at 25 °C and the results are summarized in Table 2. The employed ligands are of varying structures ranging from methyl to butyl esters. To verify the detailed structural features of the guests on the binding, common isomers of primary alkylamines up to butylamines were systematically tested as guests.

The binding affinity is markedly dependent upon the structural features of both hosts and guests. Generally, for a given ester derivative, the extraction efficiency increases on going from ammonium to ethylammonium guest, then

Table 2 Extraction of alkylammonium picrates[a]

Ligand	Picrate extraction (%)								
	R = H	Me	Et	Pr	Pr^i	Bu	Bu^i	Bu^s	Bu^t
1	1.3	18.3	24.4	8.6	7.2	7.0	4.5	5.3	3.4
2	11.4	71.2	76.4	51.3	44.5	34.0	22.3	22.8	9.8
3	10.5	71.2	74.1	48.3	43.9	30.5	21.3	20.1	9.4
4	10.6	64.7	74.1	56.6	49.6	40.9	27.6	28.3	11.5
5	11.5	59.0	73.9	49.0	45.5	32.6	23.5	22.2	12.5
6	3.7	34.9	73.3	67.7	61.9	45.1	48.8	38.5	16.7
7	6.9	26.9	13.9	13.3	5.6	15.9	1.3	3.0	1.7
8	1.3	3.3	6.5	4.0	3.9	6.3	5.9	5.6	4.8
DB18C6	2.0	3.6	5.7	12.4	11.8	23.8	18.5	17.9	17.8

[a] At 25 °C; organic phase (5 cm^3): [ligand] = 3.5×10^{-3} mol dm^{-3}; aqueous phase (5 cm^3): [alkylammonium picrate] = 7.0×10^{-5} mol dm^{-3}.

gradually decreases down to butylammonium guests. That is, the sequence is: ammonium < Me ≃ Et > Pr > Pr^i > Bu > Bu^i ≃ Bu^s > *tert*-butylammonium salt. This observation suggests that, in addition to the electrostatic and hydrogen bonding interaction between the ester carbonyl binding sites and the ammonium moiety, the secondary interaction between the alkyl side chain of the ester function of the hexa-*tert*-butylhexabenzenacyclododecaphane derivative and alkyl moiety of the guest ammonium salt is operating. Within the butylammonium guests the general trend in extraction efficiency decreased in the sequence Bu > Bu^i ≃ Bu^s > Bu^t.[15]

As regards to the effect of substituent of the hosts, an interesting fact to be noted is that the binding efficiency markedly increases from methyl to ethyl ester. A similar observation of less efficient binding of the methyl ester **1** toward metal ions was reported earlier by McKervey *et al.*[14] It is noteworthy that higher homologues **2**–**5** exhibit quite similar binding behaviour toward all the tested guests.

The presence of the *tert*-butyl substituent on the upper rim of calixarene is found to have a pronounced effect on the binding properties. That is, the debutylated ethyl ester **7** exhibited much inferior extraction behaviour compared with **2**, which might be due to the decreased lipophilicity and/or increased conformational freedom as judged from its temperature dependent ^1H NMR behaviour.

Also to be noted is that the methyl ketone derivative **8** exhibits much reduced binding efficiency compared with that of ester derivatives.[14] This result shows the relatively optimized structure of ester derivatives for the molecular recognition of amines.

The binding properties of the present ester functions were compared with that of dibenzo-18-crown-6* (DB18C6), which has a somewhat related structural property with the present ester ligands among the crown ether family. DB18C6 exhibited gradually increasing extraction behaviour toward ammonium guests of increasing alkyl substituents from ammonium picrate to butylammonium salt. However, the extraction ability was less pronounced than that of calix[6]arene-based ester ligands in spite of the well known rigid coronand type structure. Furthermore, the discrimination behaviour toward alkylamines is not obvious. That might be due to the two dimensional coronand nature of the crown ethers.[4]

Liquid Membrane Transport.—To understand the molecular recognition properties better, ester ligands were examined as carriers for the transport of butylammonium perchlorates through a chloroform liquid membrane using a U-tube apparatus.[20] Butylamines were chosen as guests because they possess the representatively varying alkyl substituent suitable for the elucidation of the effect of subtle structural variations for the molecular recognition of biogenic amines.[28] The transport experiment was performed until less than 1% of employed guest was transported. In single transport, the rate was determined by means of a perchlorate selective electrode from the appearance of co-transported perchlorate salt in the receiving aqueous phase and the results are summarized in Table 3.

Table 3 Single transport of butylammonium perchlorates by esters **1**–**5**[a]

Carrier	Transport rate/10^{-6} mol dm^{-3} h^{-1}				
	Bu	Bu^i	Bu^s	Bu^t	Bu/Bu^t[b]
Control	0.20	0.20	0.20	0.14	1.5
1	1.6	0.65	0.39	0.43	3.7
2	11.3	4.2	2.8	0.80	14.2
3	9.8	3.7	3.6	0.70	14.1
4	11.4	5.0	3.9	0.97	11.8
5	12.4	3.8	3.4	0.85	14.6

[a] Source phase: aqueous solution contains 0.5 mmol of butylammonium perchlorates (10 cm^3). Membrane: 0.05 mmol carrier in $CHCl_3$ (15 cm^3). [b] Selectivity factor.

All the tested ester carriers exhibited significant transport efficiency and selectivity toward butylammonium guests. The transport properties of calix[6]arene-based ester carriers are found to be strongly dependent upon the alkyl substituent of the ester side chains duplicating the trend obtained with extraction experiments. That is the transport efficiency of ester derivative changes in the following sequence; **1** < **2** ≃ **3** ≃ **4** ≃ **5**. The transport behaviour was unique in the methyl ester again, among the tested carriers. The methyl ester **1** showed much inferior transport behaviour; inferior both in transport rate and selectivity. Of particular interest is the discrimination behaviour toward the Bu/Bu^t pair, which is described as the selectivity factor of the transport rate of corresponding guests. They ranged from 3.70 to 14.6 for **1** and **5**, respectively.

To obtain more insight into the selective transport behaviour of the present carriers toward butylammonium salts, we performed competition transport from aqueous solution containing mixtures of four butylammonium perchlorate salts. Esters **2** and **4** were chosen as carriers because they showed somewhat different single transport behaviour. The transport system was the same as for single transport, except for employing deuteriated solvents in order to avoid interference from the large residual solvent peaks in ^1H NMR spectra. The transported amounts were measured after 24 h of stirring from the integrals of characteristic peaks for each constituent butylammonium guest in the receiving aqueous phase by ^1H NMR spectroscopy (500 MHz). For comparison the result for DB18C6 is included.

As can be seen from Table 4, the general trend in single transport behaviour is retained in competitive transport.

* Dibenzo-18-crown-6 ≡ 1,9-di[1,2]benzena-2,5,8,10,13,16-hexaoxacyclohexadecaphane.

Table 4 Competitive transport of butylammonium perchlorates[a]

Carrier	Transport rate/10^{-6} mol dm^{-3} h^{-1}			
	Bu	Bu^{i}	Bu^{s}	Bu^{t}
2	5.1	2.1	1.7	0.21
4	4.6	2.1	1.9	0.11
DB18C6	4.3	2.6	2.3	1.6

[a] Source phase: aqueous solution contains 0.5 mmol each of butylammonium perchlorates in D_2O (5 cm^3). Membrane: 0.05 mmol carrier in $CDCl_3$ (15 cm^3).

However, the selectivity between the Bu/Bu^{t} pair increased around two-fold as compared with single transport experiment. The selectivity factor of *ca.* 25 for ester derivatives is much larger than that of 2.7 for DB18C6. In fact, the selectivity might be much better than this estimate, because the reported values could not be corrected from the control experiment with reasonable accuracy.*

Acknowledgements

This work was supported by the Korea Science and Engineering Foundation (1991) and is gratefully acknowledged.

* The individual transport rates of the control experiment could not be measured, because the transport rate was so low for the observing signal in the receiving phase even with a 500 MHz NMR instrument.

References

1 J. L. Atwood, ed., *Inclusion Phenomena and Molecular Recognition*, Plenum, New York, 1990; V. Balzani and L. De Cola, ed., *Supramolecular Chemistry*, Kluwer, Dordrecht, 1992.
2 J.-M. Lehn, *Angew. Chem., Int. Ed. Engl.*, 1988, **27**, 89; D. J. Cram, *Angew. Chem., Int. Ed. Engl.*, 1988, **27**, 1009; J.-M. Lehn, *Angew. Chem., Int. Ed. Engl.*, 1990, **29**, 1304.
3 G. W. Gokel, *Crown Ethers and Cryptands*, Royal Society of Chemistry, Cambridge, 1991.
4 I. O. Sutherland, *Chem. Soc. Rev.*, 1986, **15**, 63.
5 F. Fages, J.-P. Desvergne, K. Kampke, H. Bouas-Laurent, J.-M. Lehn, M. Meyer and A.-M. Albrecht-Gary, *J. Am. Chem. Soc.*, 1993, **115**, 3658.
6 C. D. Gutsche, *Calixarenes*, Royal Society of Chemistry, Cambridge, 1989; J. Vicens and V. Böhmer, eds., *Calixarenes: A Versatile Class of Macrocyclic Compounds*, Kluwer, Dordrecht, 1991.
7 A. Arduini, G. Manfredi, A. Pochini, A. R. Sicuri and R. Ungaro, *J. Chem. Soc., Chem. Commun.*, 1991, 936.
8 K. Iwamoto and S. Shinkai, *J. Org. Chem.*, 1992, **57**, 7066.
9 E. van Dienst, W. I. I. Bakker, J. F. J. Engbersen, W. Verboom and D. N. Reinhoudt, *Pure Appl. Chem.*, 1993, **65**, 387.
10 A. Casnati, P. Minari, A. Pochini and R. Ungaro, *J. Chem. Soc., Chem. Commun.*, 1991, 1413.
11 J. S. Rogers and C. D. Gutsche, *J. Org. Chem.*, 1992, **57**, 3152; S. Kanamathareddy and C. D. Gutsche, *J. Org. Chem.*, 1992, **57**, 3160.
12 P. Neri, M. Foti, G. Ferguson, J. F. Gallagher, B. Kaitner, M. Pons, M. A. Molins, L. Giunta and S. Pappalardo, *J. Am. Chem. Soc.*, 1992, **114**, 7814.
13 S. Shinkai, Y. Shirahama, T. Tsubaki and O. Manabe, *J. Am. Chem. Soc.*, 1989, **111**, 5477.
14 F. Arnaud-Neu, E. M. Collins, M. Deasy, G. Ferguson, S. J. Harris, B. Kaitner, A. J. Lough, M. A. McKervey, E. Marques, B. L. Ruhl, M. J. Schwing-Weill and E. M. Seward, *J. Am. Chem. Soc.*, 1989, **111**, 8681.
15 S.-K. Chang, M. Jang, S. Y. Han, J. H. Lee, M. H. Kang and K. T. No, *Chem. Lett.*, 1992, 1937.
16 B. M. Song and S.-K. Chang, *Bull. Korean Chem. Soc.*, 1993, **14**, 540.
17 L. J. Bauer and C. D. Gutsche, *J. Am. Chem. Soc.*, 1985, **107**, 6063; S.-K. Chang, H.-S. Hwang, H. Son, J. Youk and Y. S. Kang, *J. Chem. Soc., Chem. Commun.*, 1991, 217; C. D. Gutsche and K. A. See, *J. Org. Chem.*, 1992, **57**, 4527; A. F. Danil de Namor, P. M. Blackett, M. T. Garrido Pardo, D. A. Pacheco Tanaka, F. J. Sueros Velarde and M. C. Cabaleiro, *Pure Appl. Chem.*, 1993, **65**, 415.
18 C. Almansa, A. Moyano and F. Serratosa, *Tetrahedron*, 1992, **48**, 1497.
19 H. K. Frensdorff, *J. Am. Chem. Soc.*, 1971, **93**, 4684.
20 H. Tsukube, K. Takagi, T. Higashiyama, T. Iwachido and N. Hayama, *J. Chem. Soc., Perkin Trans. 2*, 1985, 1541.
21 C. D. Gutsche and L. J. Bauer, *J. Am. Chem. Soc.*, 1985, **107**, 6052.
22 M. A. Molins, P. M. Nieto, C. Sánchez, P. Prados, J. de Mendoza and M. Pons, *J. Org. Chem.*, 1992, **57**, 6924.
23 T. Arimura, S. Shinkai, T. Matsuda, Y. Hirata, H. Satoh and O. Manabe, *Bull. Chem. Soc. Jpn.*, 1988, **61**, 3733.
24 C. D. Gutsche and L. J. Bauer, *J. Am. Chem. Soc.*, 1985, **107**, 6059.
25 S.-K. Chang and I. Cho, *J. Chem. Soc., Perkin Trans. 1*, 1986, 211; A. Cadogan, D. Diamond, M. R. Smyth, G. Svehla, M. A. McKervey, E. M. Seward and S. J. Harris, *Analyst*, 1990, **115**, 1207.
26 A. Arduini, A. Pochini, S. Reverberi, R. Ungaro, G. D. Andreetti and F. Ugozzoli, *Tetrahedron*, 1986, **42**, 2089.
27 F. Ohseto, T. Sakaki, K. Araki and S. Shinkai, *Tetrahedron Lett.*, 1993, **34**, 2149.
28 E. Bacon, L. Jung and J.-M. Lehn, *J. Chem. Res. (S)*, 1980, 136; J.-P. Behr, J.-M. Lehn and P. Vierling, *Helv. Chim. Acta*, 1982, **65**, 1853.

Paper 3/06398D
Received 26*th October* 1993
Accepted 3*rd December* 1993