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Catalytic Ability of Flexible Octopus-Type Calix[6]arene in Ester-Forming Reactions and Its Structural Properties

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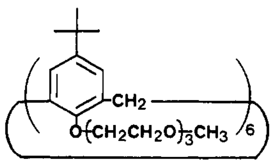
The ester-forming reaction of alkali metal carboxylates with alkyl halides was catalyzed by the octopus-type calix[6]arene 1 which bears six 3,6,9-trioxadecyl substituents at the phenolic oxygens. The catalytic ability of 1 was significantly large in CH_2Cl_2 and CH_3CN but negligible in less polar solvents such as benzene and dioxane. The catalytic ability is also affected by the amount of water present in the reaction system. A similar solvent effect was found in the alkali metal cation extraction by 1 from aqueous solutions to organic solvents. The conformation and structural mobility of 1 in organic solvents were studied by ^1H NMR spectroscopy at varying temperatures. Compound 1 had a 1,4-anti conformation (see Figure 4) both in CD_2Cl_2 and C_6D_6, but the orientation of the substituents on the aromatic rings of 1 varied with temperature. The reactivity features of 1 are discussed on the basis of its structural properties.

Calixarenes are macrocyclic oligomers that can be obtained by a base-catalyzed condensation of *para*-substituted phenols and formaldehyde. The chemistry of calixarenes has received a great deal of attention in recent years, and various types of compounds have already been synthesized.[1,2] However, research in this field has so far been focused greatly on the chemistry of calix[4]arenes in which the conformation of compounds can be readily identified, while the chemistry of calix[6]arenes remains unexplored mainly because of their conformational complexity.[3–7]



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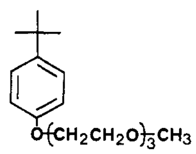

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Previously, Funada et al. reported that the calix[6]arene derivative 1, which bears six trioxadecyl groups at the phenolic oxygens, has the capability of forming complexes with alkali metal cations.[8] We have extended this chemistry and found that 1 serves as a catalyst for the ester-forming reaction from alkyl halides and alkali metal carboxyaltes.[9] We also found that the efficiency of this reaction strongly depends on the nature of solvents.[9] An important structural feature of 1 is that this molecule has an octopus-type shape and contains both a hydrophobic functionality which is composed of six aromatic groups and a hydrophilic functionality which is composed of six trioxadecyl groups. Therefore, the molecular shape of 1 appears to change significantly with the nature of solvents. Particularly, the variation in the special orientation and conformation of trioxadecyl groups may affect the chemical properties of 1 through the change in the binding ability toward metal cations. From this point of view, we have reexamined our previous work.[9] This paper deals with the following subjects: (1) the solvent effect on the catalytic ability of 1 for the ester-forming reaction of alkali metal carboxylates with alkyl halides, (2) the solvent effect on the binding ability of 1 toward alkali metal cations, and (3) the solvent effect on the conformational and structural properties of 1. The reactivity features of 1 are discussed on the basis of these results.

Results and Discussion

Ester-Forming Reactions of Alkali Metal Carboxylates with Alkyl Halides. Mixtures containing potassium acetate or sodium acetate (**3a** or **3b**, 5.6 mmol) and 4-nitrobenzyl bromide (**4**, 5.0 mmol) in a variety of organic solvents were stirred in the presence of a catalytic amount of 1 (0.13 mmol) at 40 °C for a given period of

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$$\underset{\mathbf{3a,b}}{CH_3CO_2M} + \underset{\mathbf{4}}{p\text{-}O_2NC_6H_4CH_2Br} \xrightarrow{\text{cat.}} \underset{\mathbf{5}}{p\text{-}O_2NC_6H_4CH_2OCOCH_3}$$

a: M = K
b: M = Na

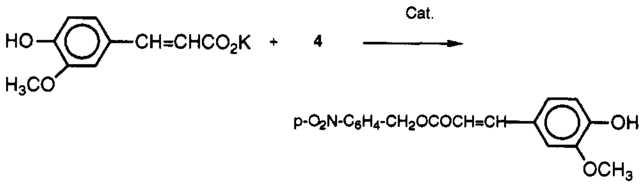
time, usually for 24 h. Workup of the resulting mixtures gave 4-nitrobenzyl acetate (**5**). In the absence of **1**, the reaction did not occur appreciably, indicating that **1** serves as a catalyst for this esterification reaction. The results are shown in Table I. It should be noted that **1** recovered from the reaction mixture exhibits essentially the same catalytic ability as does the freshly prepared material. The catalytic abilities of 1-(*p*-tert-butylphenyl)-1,4,7,10-tetraoxaundecane (**2**) (a monomer model of **1**), benzyltrimethylammonium chloride, and 18-crown-6 for the esterification reaction of **3a** with **4** were also studied under similar conditions. The results are given in Table I.

The catalytic ability of **1** strongly depended on solvents. In fact, **1** was effective as catalyst in CH_2Cl_2, but ineffective in benzene and dioxane. This is in contrast to the catalytic activity of crown ethers that serve as effective catalysts even in benzene.[10] The catalytic ability of **1** also depended on a water content in CH_2Cl_2 and alkali metal cations. In the case of **3a**, the yield of **5** reached a maximum when the water content was 0.0398% and then decreased with increasing water content. Under favorable conditions, the catalytic activity of **1** was comparable with those of benzyltrimethylammonium chloride and 18-crown-6. For **3b**, **1** showed a low catalytic activity and **2** showed no catalytic activity.

The ester-forming reactions of potassium benzoate (**6**) and potassium 3-(4-hydroxy-3-methoxyphenyl)-2-propenoate (**8**) with **4** were also catalyzed by **1** in CH_2Cl_2 and $ClCH_2CH_2Cl$, giving **7** and **9**, respectively, in high yields.

$$\underset{\mathbf{6}}{C_6H_5CO_2K\cdot 3H_2O} + 4 \xrightarrow{\text{cat.}} \underset{\mathbf{7}}{p\text{-}O_2NC_6H_4CH_2OCOC_6H_5}$$

Compound **1** was also effective as catalyst for the reaction of **6** with 1,3-dichloropropane-2-one (**10**) in acetonitrile to form the diester **11**. In these reactions, the yields of the products were appreciably improved by adding a small amount of water to the reaction systems. The results are shown in Table II.



8 **9**

$$6 + \underset{\mathbf{10}}{ClCH_2COCH_2Cl} \xrightarrow{\text{Cat.}} \underset{\mathbf{11}}{C_6H_5CO_2\text{-}CH_2COCH_2\text{-}OCOC_6H_5}$$

Binding Properties toward Alkali Metal Cations. The above results suggest that the binding ability of **1** toward alkali metal cations depends also on the nature of solvents and alkali metal cations. Hence, we studied the metal-binding properties of **1** in various organic solvents.

The binding abilities in organic solvents were estimated by measuring the equilibrium constants K_e for the extraction of alkali metal picrates (M^+Pic^-) with **1** from aqueous solution into organic solvents. Before determining the K_e values, we established the stoichiometry for the complex formation of **1** with K^+Pic^- in tetrahydrofuran (THF) by the continuous variation method.[11] The addition of **1** to a THF solution of K^+Pic^- caused a bathochromic shift of the absorption maximum λ_{max} of the picrate. The change in the λ_{max} increased with increasing the added amount of **1**. The plot of the λ_{max} vs $[K^+Pic^-]/([K^+Pic^-] + [1])$, which is shown in Figure 1, indicates that **1** forms a 1:1 complex with K^+ ion in THF. The relatively small bathochromic shift induced by **1** suggests that in the complex K^+ ion exists in a tight ion pair form with picrate anion. Unfortunately, the poor solubility of K^+Pic^- prevented determination of the stoichiometry of the complex formation in other solvents. Although no experimental evidence is available, we assume here that **1** also forms 1:1 complex with alkali metal cations in organic solvents other than THF and the ionic species in the complexes exist in the form of ion pairs.[11]

With this assumption, the alkali metal extraction equilibria with **1** from aqueous solutions to organic solvents can be expressed by

$$M^+_{aq} + Pic^-_{aq} + 1_{org} \overset{K_e}{\rightleftharpoons} \{1\cdot M^+, Pic^-\}_{org}$$

where M^+_{aq} and Pic^-_{aq} represent an alkali metal cation and the picrate anion in the aqueous phase, respectively, and $\{1\cdot M^+, Pic^-\}_{org}$ is a complex that is formed between **1** and a metal picrate in an organic solvent. The extraction equilibrium constants are taken given by

$$K_e = \frac{[\{1\cdot M^+, Pic^-\}_{org}]}{\gamma^2[M^+_{aq}][Pic^-_{aq}][1_{org}]_0 - [\{1\cdot M^+, Pic^-\}_{org}]}$$

where γ is the mean activity coefficient of the picrate anion in water. The **1**/alkali metal picrate complex concentration in organic solvents, $[\{1\cdot M^+, Pic^-\}_{org}]$, were determined spectroscopically. The results are shown in Table III. In this table, the extraction equilibrium constants for some alkali metal cations other than Na^+ and K^+ are also included for comparison.

The metal-extraction ability of **1** was markedly affected by solvents. It was sufficiently large in solvents with high E_T^N values[12] such as CH_2Cl_2 and $ClCH_2CH_2Cl$ but negligible or very small in solvents with low E_T^N values such as benzene, chlorobenzene, and $CHCl_3$. It depended also on metal cations and decreased in the order $Rb^+ > Cs^+, K^+ \gg Na^+ > Li^+$. This indicates that **1** has a higher extraction ability toward larger cations rather than toward smaller cations. Although cation radii for K^+, Rb^+, and Cs^+ increase in this order, the extraction abilities toward these cations were similar in magnitude. This may be due to the fact that **1** has flexible 3,6,9-trioxadecyl function-

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Table I. Reaction of Alkali Metal Acetate with *p*-Nitrobenzyl Bromide

CH_3COOM	catalyst	molar ratio 4/catalyst	solvent[a]	water content/wt[b] (%)	temp (°C)	reactn time (h)	yield of 5 (%)
3a	none		CH_2Cl_2[c]	0.0846	40	24	trace
3a	1	37	CH_2Cl_2[d]	0.0193	40	24	72
3a	1	37	CH_2Cl_2[e]	0.0398	40	24	100
3a	1	37	CH_2Cl_2–H_2O (100:1)[f]		40	24	38
3a	1	37	CH_2Cl_2–H_2O (20:1)[f]		40	24	27
3a	2	6	CH_2Cl_2[c]	0.0846	40	6	trace
3a	$PhCH_2(Me)_3N^+Cl^-$	2.3	CH_2Cl_2[c]	0.0846	40	24	94
3a	18-crown-6	4.4	CH_2Cl_2[c]	0.0846	40	6	99
3b	1	37	CH_2Cl_2[e]	0.0398	40	24	6.1
3b	1	37	CH_2Cl_2–H_2O (20:1)[f]		40	24	12
3b	1	37	CH_2Cl_2–H_2O (20:1)[f]		40	24	7.7
3a	none		benzene[g]		60	24	0
3a	1	37	benzene[g]		60	24	trace
3a	1	37	wet benzene[h]		60	24	7.0
3a	2	6	wet benzene[h]		60	24	trace
3b	1	37	dioxane[i]		80	6	trace

[a] Solvent: 10 mL. [b] Water contents in solvents were determined by the Karl-Fischer method before use. [c] Guaranteed reagent-grade solvent. [d] Dried over $CaCl_2$ for 1 week and then over molecular sieve 4A. [e] Dried over molecular sieve 4A. [f] Volume ratio. [g] Distilled before use. [h] Saturated with water. [i] Dried over molecular sieve 4A.

Table II. Reaction of Potassium Carboxylates with Alkyl Halides

RX	metal carboxylate	catalyst	molar ratio RX/catalyst	solvent[a]	reactn temp (°C)	reactn time (h)	product yield (%)
4	**6**	1	42	CH_2Cl_2[b]	40	20	58
4	**6**	1	42	CH_2Cl_2–H_2O (20:1)	40	20	84
4	**6**	none		CH_2Cl_2–H_2O (20:1)	40	20	trace
4	**8**[c]	1	42	$ClCH_2CH_2Cl$[d]	80	8	88
4	**8**[c]	1	42	$ClCH_2CH_2Cl$–H_2O (30:1)	80	8	66
4	**8**[c]	none		$ClCH_2CH_2Cl$[d]	80	8	trace
10	**6**	1	37	CH_3CN[e]	65	6	89
10	**6**	1	37	CH_3CN–H_2O (10:1)	65	6	97
10	**6**	none		CH_3CN[e]	65	6	16

[a] Solvent: 10 mL. [b] Guaranteed reagent-grade solvent. [c] 3-(4-Hydroxy-3-methoxyphenyl)-2-propenoic acid + KOH (1:1). [d] Guaranteed reagent-grade solvent. [e] Guaranteed reagent-grade solvent.

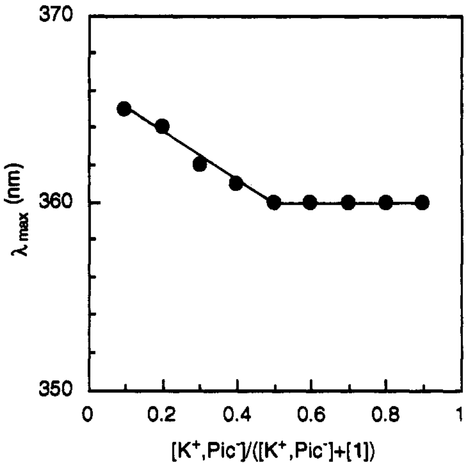

Figure 1. Plot of the absorption maxima λ_{max} of K^+Pic^- against the concentration ratios $[K^+Pic^-]/([K^+Pic^-] + [1]$, 0–4.5 × 10^{-5} mol dm^{-3}; solvent, THF.

alities that are responsible for capturing metal cations.[13] If we can assume that the K_e values are proportional to the binding ability of **1** toward alkali metal cations in metal carboxylates $RCOO^-M^+$ in organic solvents, then the above results strongly suggest that the catalytic ability of **1** for the esterification reactions is determined primarily by the binding ability toward the metal cations. The conformation of **1**, specifically a spatial arrangement of trioxadecyl groups in organic solvents, would play an important role in determining the metal-binding ability. It would also be important to note that the hexamethyl ether of *p-tert*-butylcalix[6]arene exhibits neither the complexing ability toward alkali metal cations[8] nor the catalytic ability for the esterification reaction. This result indicates that the chemical functions of **1** arise primarily from the trioxadecyl groups.

Conformation of Calixarene 1. The purity and stability of **1** used in this study was first examined as a prerequisite for elucidation of the conformational property of the compound in solution (for preparation of **1**, see the Experimental Section).

Upon recrystallization from EtOH, **1** slowly solidified as colorless, prism crystals. The thermal analysis of these crystals exhibited only one sharp endothermic peak at 131 °C where the crystals melted. The TLC analysis on silica gel with $CHCl_3$–EtOH (10:1 v/v) showed a single spot at $R_f = 0.52$. The IR and ^1H NMR spectra of these crystals remained unchanged even after heating in chlorobenzene at reflux temperature (130 °C) for 20 h. The TLC analysis of the heated sample also showed a single spot at $R_f = 0.52$. However, **1** gradually decomposed when the compound was heated in *o*-dichlorobenzene at reflux temperature (180 °C). Indeed, the TLC analysis of the sample obtained after heating at this temperature for 20 h showed many spots. These results indicate that **1** prepared in this study is stable below 130 °C.

We now discuss the conformation of **1** and its structural features in organic solvents. It is known that calix[6]arenes are, in general, conformationally more flexible than calix[4]arenes and calix[8]arenes.[14] As a result, conformations of calix[6]arenes remained unclarified in most cases.[15]

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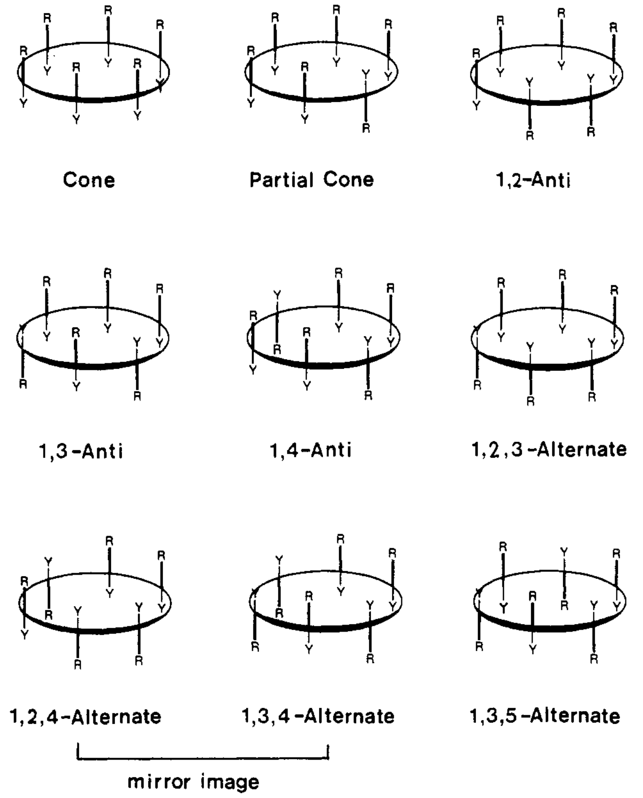
Table III. Extraction Equilibrium Constants of Alkali Metal Picrates in the Presence of 1 at 25 °C[a]

solvent	E_T^N value[b]	K_e (× 10^{-4} M^{-2}) Li$^+$ (68)	Na$^+$ (97)	K$^+$ (133)	Rb$^+$ (152)	Cs$^+$ (170)	selectivity factor $K_e(K^+)/K_e(Na^+)$
benzene	0.111	0.0031	0.021	0.036	0.034	0.029	1.71
chlorobenzene	0.188	0.0069	0.045	0.11	0.11	0.11	2.44
chloroform	0.259	0.019	0.083	0.26	0.39	0.28	3.13
dichloromethane	0.309	0.36	2.06	5.52	9.82	5.98	2.68
1,2-dichloroethane	0.327	1.79	2.75	16.8	20.9	13.9	6.11

[a] Organic phase (5 mL): [1] = 1.0 × 10^{-3} M. Aqueous phase (5 mL): [metal picrate] = (1.0–10.0) × 10^{-3} M. The two-phase mixture was shaken for 2.5 h. [b] Reichardt's polarity parameter for organic solvent (ref 12). [c] The figures in parentheses represent ionic radi in pm.



Cone

Partial Cone

1,2-Anti

1,3-Anti

1,4-Anti

1,2,3-Alternate

1,2,4-Alternate

1,3,4-Alternate

1,3,5-Alternate

mirror image

Figure 2. "Up–down" representations of conformers of calix[6]arenes.

Recently, Gutsche and his co-workers demonstrated that conformations of aroylated and arylmethylated derivatives of *p-tert*-butylcalix[6]arene can be determined by the analysis of their ^{1}H NMR signals, specifically the signals arising from the *tert*-butyl proton and also those arising from the methylene protons on the annulus of calixarenes.[16]

For 1, there are, in principle, nine possible "up–down" conformations.[17] They are illustrated in Figure 2.[18] The ^{1}H NMR spectra of 1 in CD_2Cl_2 and C_6D_6 at varying temperatures are shown in Figure 3a,b. Well-resolved signals were obtained at low temperatures in both solvents (−20 °C in CD_2Cl_2 and at −10 °C in C_6D_6). With a rise in temperature, the signals gradually broadened, especially in the region of δ 1–2 and δ 7–8. The temperature dependence of the spectral patterns was reversible, and the spectral pattern at any temperature was reproducible. This indicates that the six 3,6,9-trioxadecyl groups attached to the phenolic oxygens are not bulky enough to freeze the structural mobility of 1 at higher temperatures. However, the ^{1}H NMR spectra of 1 at low temperatures permitted determination of its conformation. The relevant spectral data are given in Table IV.

The methylene protons on the annulus of 1 showed a very complicated signal pattern in the ^{1}H NMR spectrum even at low temperature. However, the ^{1}H NMR spectrum in CD_2Cl_2 at −20 °C, especially the signal pattern of the *tert*-butyl groups, allowed us to assign the conformation of 1. The signals of the *p-tert*-butyl groups appeared at δ 1.050 and 1.402 in the intensity ratio of 4:2. This ratio suggests that 1 exists either in a 1,4-anti conformation or in a 1,2,3-alternate conformation. In the 1,4-anti conformation, two of six *p-tert*-butyl groups are placed on the "down" side of the rim and other four *p-tert*-butyl groups on the "up" side of the rim. In the 1,2,3-alternate conformation, three aryl groups are placed contiguously with each other on the "up" side of the rim and other three aryl groups on the "down" side of the rim (Figure 2). Furthermore, the aromatic ring-current effect on ^{1}H NMR signals suggests that the four *p-tert*-butyl groups, which show the higher field singlet, should lie at the position where they are faced with the plane of an aromatic ring. On the other hand, the two *p-tert*-butyl groups, which show the lower field singlet, should be located on the position where such an aromatic ring-current shielding effect is ineffective or small compared with that for the other four *p-tert*-butyl groups. The 1,4-anti conformation that is consistent with these spectral data is shown in Figure 4. A ball and stick molecular model suggests that in this conformation all the aromatic rings tend to orient perpendicularly to the average plane of the rim, thereby the molecule forms a rectangular cavity rather than a circular cavity (Figure 4).

The conformation was further supported by the ^{1}H NMR spectral data for the aromatic protons. The signals of the aromatic protons appeared as one singlet and two doublets. The singlet at δ 7.272 can be assigned to H_c, the doublet at δ 6.622 (J = 1.98 Hz) to H_a, and the doublet at δ 7.444 (J = 1.98 Hz) to H_b (see Figure 4). This assignment would be justified from the following considerations: (1) The H_a proton should appear at the highest field by the shielding effect of the aromatic rings situated at the opposite side of the rim. (2) The H_b protons are affected magnetically not only by the shielding effect of the aromatic rings situated at the opposite side of the rim but also by the deshielding effect of the neighboring aromatic rings. Since a distance between the neighboring rings is shorter than

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(14) Reference 1, Chapter 4.

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(17) (a) It is described in ref 1, p 97, that calix[6]arenes can exist in eight "up–down" conformations. (b) Taniguchi, H.; Nomura, E.; Hinomoto, T. *Chem. Express* **1992**, *7*, 853.

(18) We wish to call the conformations cone, partial cone, 1,2-anti, 1,3-anti, 1,4-anti, 1,2,3-alternate, 1,2,4-alternate, 1,3,4-alternate, and 1,3,5-alternate after naming for the four conformations of calix[4]arenes.[1] Among these conformations of calix[6]arene 1, the relationship between the 1,2,4-alternate conformation and the 1,3,4-alternate conformation is a mirror image.

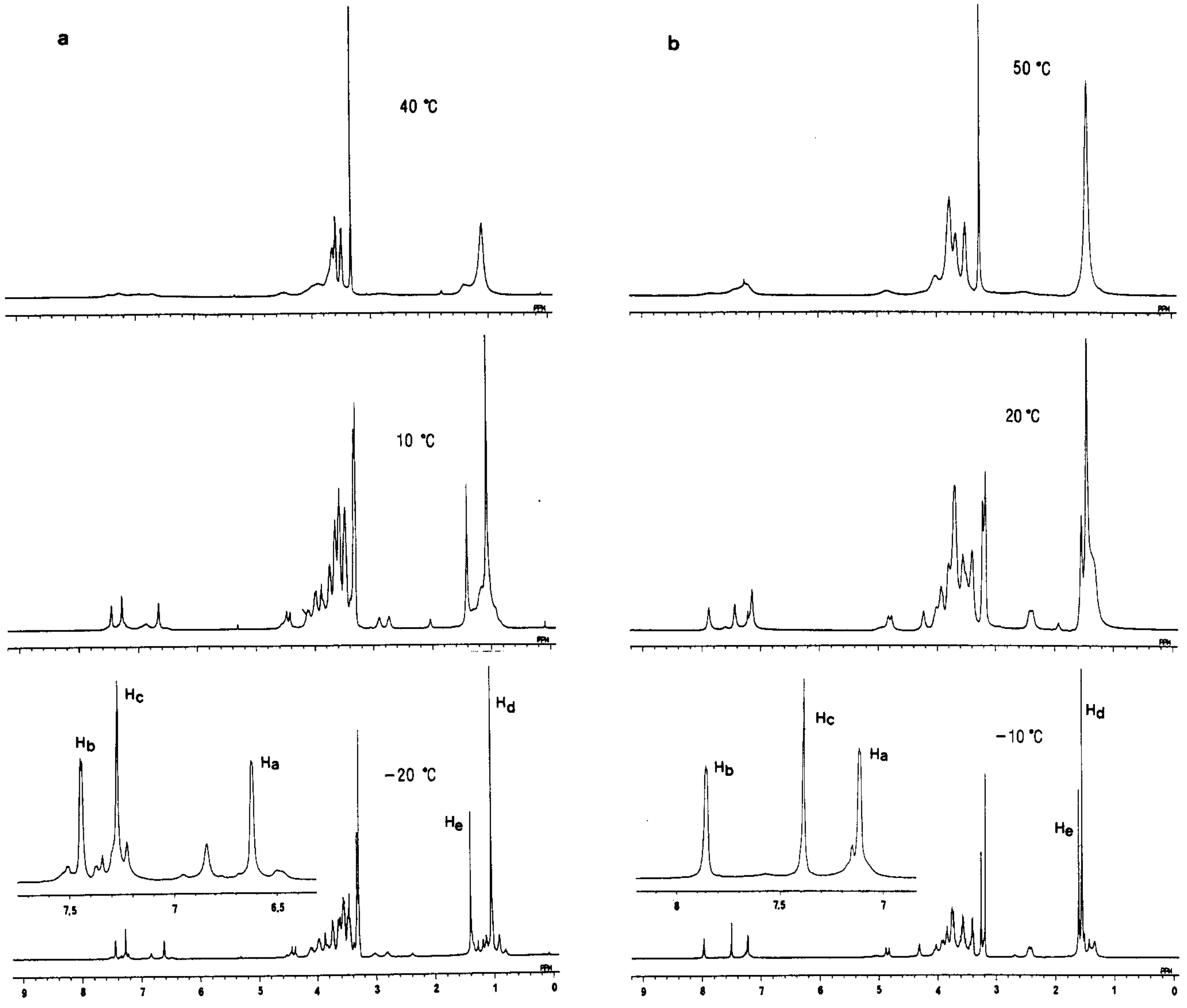


Figure 3. ^{1}H NMR spectra (270 MHz) of 1 in CD_2Cl_2 (a) and benzene-d_6 (b) at varying temperatures.

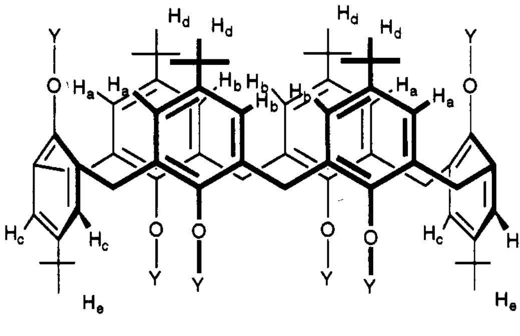
Table IV. ^{1}H NMR Spectral Data for 1

	chemical shift, δ (ppm)		
proton[a]	in CD_2Cl_2[b]	in C_6D_6[c]	$\Delta^{CD_2Cl_2}_{C_6D_6}$[d]
H_a	6.622	7.117	-0.495
H_b	7.444	7.858	-0.414
H_c	7.272	7.387	-0.115
H_d	1.050	1.468	-0.418
H_e	1.402	1.492	-0.090

[a] For assignment of protons, see Figure 4: H_a, doublet; H_b, doublet; H_c, singlet; H_d, singlet; H_e, singlet. [b] -20 °C. [c] -10 °C. [d] The difference in the chemical shifts in the two solvents: $\Delta^{CD_2Cl_2}_{C_6D_6} = \delta_{CD_2Cl_2} - \delta_{C_6D_6}$.

a distance between the aromatic rings situated at the opposite side of the rim, the deshielding effect would be larger than the shielding effect. Therefore, the H_b protons should appear at the lowest field. (3) The H_a and H_b protons should appear as a doublet because of spin-spin interaction between these two protons within the aromatic ring. (4) The H_c protons are free from the aromatic ring magnetic anisotropies. Therefore, these protons should appear at an intermediate position between the H_a and H_b protons.

The spectral assignment for the *tert*-butyl groups was also supported by the ^{1}H NMR spectral data for tetra-*O*-alkylated *p*-*tert*-butylcalix[4]arenes.[19] The proton signals for the *tert*-butyl groups of their cone conformers appear as one singlet at about δ 1.0, those of their partial



Y = $(CH_2CH_2O)_3CH_3$

Figure 4. Representative 1,4-anti conformation of 1 in which all the aromatic rings have a "vertical" orientation.

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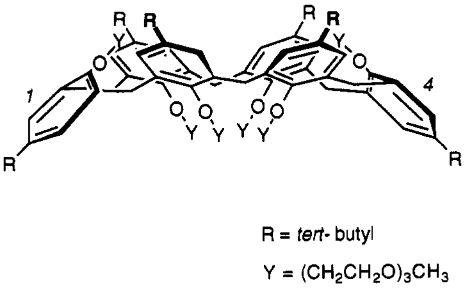

Figure 5. Representative 1,4-anti conformation of 1 in which all the aromatic rings have "out" orientation.

cone conformers as three singlets near δ 1.0 and 1.3–1.4, and those of their 1,2- or 1,3-alternate conformers as one singlet at δ about 1.3.

The ^{1}H NMR spectral pattern of 1 depended on solvents. The proton signals of the *p-tert*-butyl groups appeared at δ 1.468 and 1.492 in a 4:2 ratio in C_6D_6 at −10 °C. Although the chemical shifts of the two signals are in close proximity, the higher field signal is apparently assignable to the H_d protons and the lower field signal to the H_e protons. The signals at δ 7.117 (doublet), 7.387 (singlet), and 7.858 (doublet) are also assignable to the aromatic protons H_a, H_c and H_b, respectively. However, noteworthy are the solvent effects on the chemical shifts. The change in the chemical shifts with variation of solvents may be expressed by

$$\Delta^{CD_2Cl_2}_{C_6D_6} = \delta_{CD_2Cl_2} - \delta_{C_6D_6}$$

where $\delta_{CD_2Cl_2}$ and $\delta_{C_6D_6}$ are the δ values in CD_2Cl_2 and in C_6D_6, respectively. The results are given in Table IV. All the protons are shifted downfield by changing the solvents from CD_2Cl_2 to C_6D_6. The downfield shifts caused by this solvent change are particularly large for the H_a, H_b, and H_d protons. This result can be explained by assuming that in benzene 1 changes its molecular arrangement in such a way that the shielding effect of the aromatic rings is diminished. A molecular arrangement that meets this requirement is shown in Figure 5. In benzene, the four aromatic rings are forced to align toward an "out" orientation, rather than a "vertical" orientation, with respect to the average plane of the molecular system. A ball and stick molecular model indicates that in the out orientation the molecule would adopt a conical shape and the four 3,6,9-trioxadecyl groups may aggregate each other at the down side of the rim. It must be pointed out here that the 1,4-anti conformation of the molecule is maintained even in benzene. The temperature-dependent ^{1}H NMR spectra shown in Figure 3a,b suggest that the vertical-out orientational movement of the aromatic rings occurs in both solvents at increasingly higher rates with raising temperature.

Solvent Effect on the Catalytic Ability of 1. As mentioned earlier, the catalytic ability of 1 for the reaction of potassium acetate with 4-nitrobenzyl bromide to form the ester 5 strongly depends on solvents. This reaction is a solid–liquid two-phase reaction and proceeds efficiently in CH_2Cl_2 containing a small amount of water. In this reaction, water adsorbed on the surface of potassium acetate would facilitate formation of a partially dissociated ion pair [K^+--AcO^-] that may transfer to the organic phase where the reaction takes place. In the organic phase, potassium cation is captured by forming a complex probably with two trioxadecyl groups in a manner shown in Figure 6. The acetate anion then reacts with 4-nitrobenzyl bromide in CH_2Cl_2 in a naked, activated form. When the water content in the reaction system is large, the acetate anion would exist in a solvated form in which the reactivity of the acetate anion greatly decreases. The effect of water of this sort has also been found in crown ether- and cryptand-catalyzed nucleophilic substitution reactions in organic solvents.[10]

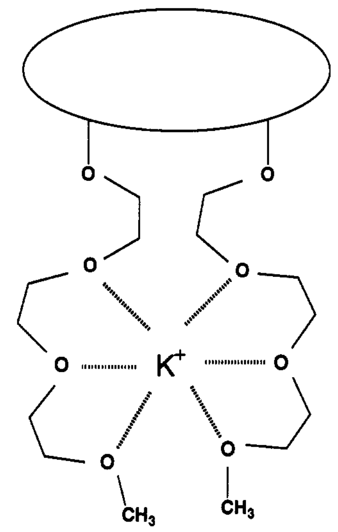

Figure 6. Complexation of potassium cation with 1.

The esterification reaction did not occur in benzene. This may be attributed to a special arrangement of the trioxadecyl groups of 1 in this solvent. As mentioned in a preceding section, the aromatic rings of 1 adopt the "out" orientation in preference to the "vertical" orientation in benzene at high temperatures. It is also supposed that the hydrophilic, long-chain trioxadecyl groups would aggregate each other on the "up" and "down" sides of the rim in a less polar solvent such as benzene. The aggregation would suppress complexation of the trioxadecyl groups with K^+ ion, so that the catalytic ability of 1 is depressed in benzene.

Experimental Section

General. Melting points are uncorrected. Column chromatography was performed with 300-mesh silica gel. Thin-layer chromatography was carried out on TLC silica gel plates. NMR spectra were recorded at 90 and 270 MHz. Chemical shifts are reported as δ values in parts per million downfield from $(CH_3)_4Si$ as an internal standard or from the residual dichloromethane signal (δ =5.32 ppm) and benzene (δ = 7.15 ppm).

5,11,17,23,29,35-Hexa-*p-tert*-butyl-37,38,39,40,41,42-hexakis(3,6,9-trioxadecyloxy)calix[6]arene (1). 3,6,9-Trioxadecyl *p*-toluenesulfonate (4.24 g, 13.3 mmol) and NaH (62.1% in oil, 0.71 g) were added to a solution of *p-tert*-butylcalix[6]arene (2.0 g, 2.1 mmol) in DMF (20 mL), and the mixture was stirred at 60 °C for 24 h. Water (200 mL) was then added gradually, and the aqueous solution was neutralized with 10% HCl. The precipitated yellowish solid was filtered and dissolved in CH_2Cl_2 (50 mL). The organic solution was dried over $MgSO_4$ and evaporated under reduced pressure. First recrystallization of the viscous oil from EtOH gave 1 as colorless prisms in 60% yield, which melted at mp 123–124 °C. Several repeated recrystallization of this material from EtOH gave pure sample also as colorless prisms: mp 131–132 °C; IR (KBr) 2950, 2920, 2850, 1600, 1580, 1480, 1460, 1110 cm^{-1}; ^{1}H NMR (C_6D_6, at −10 °C) δ 1.468 (36H, s, ArC(CH_3)), 1.492 (18H, s, ArC(CH_3)), 2.30–4.93 (102H, m, $ArCH_2Ar$ and $(CH_2CH_2O)_3CH_3$), 7.114 (4H, d, J = 1.98 Hz, ArH), 7.387 (4H, s, ArH), 7.858 (4H, d, J = 1.98 Hz, ArH). Anal. Calcd for $C_{108}H_{168}O_{24}$: C, 70.10; H, 9.15. Found: C, 69.96; H, 9.25.

Preparation of 1-(*p-tert*-Butylphenyl)-1,4,7,10-tetraoxaundecane (2). Powdered KOH (2.08 g, 31.4 mmol) was added to a solution of *p-tert*-butylphenol (4.73 g, 31.4 mmol) in CH_2Cl_2 (30 mL), and the mixture was stirred for 30 min at room temperature. 3,6,9-Trioxadecyl *p*-toluenesulfonate (10.0 g, 31.4 mmol) and benzyltrimethylammonium chloride (0.5 g, 2.7 mmol) were then added. The resulting mixture was stirred for 24 h at 40 °C, poured into ice–water (100 mL), and extracted with CH_2Cl_2 (50 mL × 4). The CH_2Cl_2 solution was washed with water, dried over $MgSO_4$, and evaporated to give **2** (9.21g, 99%) as a colorless oil: IR (neat) 2960, 2925, 2860, 1610, 1580, 1515, 1460, 1362, 1300, 1250, 1185, 1110, 1062, 945, 930, 830 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.29 (9H, s, *tert*-butyl), 3.37 (3H, s, OCH_3), 3.5-4.2 (12H, m, CH_2CH_2), 6.85 (2H, d, ArH), 7.30 (2H, d, ArH); MS *m/z* 296 (M^+), 281($M^+ - CH_3$). Anal. Calcd for $C_{17}H_{28}O_4$: C, 68.89; H, 9.52. Found: C, 68.74; H, 9.65.

General Procedure for Reaction of Alkali Metal Acetates with *p*-Nitrobenzyl Bromide. A mixture of an alkali metal acetate (5.6 mmol), *p*-nitorobenzyl bromide (**4**) (5.0 mmol) and a catalytic amount (0.135 mol) of **1** in an organic solvent was stirred at 40 °C for a given period of time. The resulting mixture was poured into a Büchner funnel paved with silica gel (10 g) and washed with the same solvent (100 mL). Evaporation of the filtrate left a mixture of *p*-nitrobenzyl acetate (**5**) and unreacted **4**. These two compounds were separated by chromatography on silica gel with hexane–benzene (1:1 v/v) to give **5** in pure form: mp 78–79 °C (lit.[20] mp 78 °C). The yield of **5** was determined by TLC analysis of the reaction mixture. The calixarene, which had been adsorbed by silica gel mass in Büchner funnel, could be recovered by extracting with EtOH.

The reaction of alkali metal acetate with **4** was also carried out in the presence of a catalytic amount of a phase-transfer catalyst such as 18-crown-6 in an organic solvent under the same conditions as above. The resulting mixture was poured onto ice–water (100 mL) and extracted with the organic solvent. The organic solution was washed with water, dried over $MgSO_4$, and concentrated to give a mixture of **4** and **5**. The yield of **5** was determiend by TLC analysis of the reaction mixture.

Reaction of Potassium Benzoate with *p*-Nitrobenzyl Bromide. The reaction was carried out in a manner similar to that described for the reaction of alkali metal acetate with **4**. This reaction gave *p*-nitrobenzyl benzoate (**7**): mp 87–89 °C (colorless prisms from benzene) (lit.[20] mp 89 °C).

Reaction of Potassium 3-(4-Hydroxy-3-methoxyphenyl)-2-propenoate with 4. A mixture of **4** (1.0 g, 4.63 mmol), 3-(4-hydroxy-3-methoxyphenyl)-2-propenoic acid (ferulic acid) (0.90 g, 4.63 mmol), powdered potassium hydroxide (0.31 g, 5.52 mmol), and **1** (0.2 g, 0.11 mmol) was stirred in $ClCH_2CH_2Cl$ (15 mL) at 80 °C for 8 h. The mixture was worked up as described above to give *p*-nitrobenzyl ferulate (**9**): mp 135–137 °C (orange needles from $ClCH_2CH_2Cl$); IR (KBr) 3480, 1700, 1650, 1600, 1510, 1455, 1435, 1350, 1280, 1250, 860, 880, 820 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.93 (s, 3H, OCH_3), 5.33 (s, 2H, CH_2), 5.95 (broad, 1H, OH), 6.36 (d, 1H, $J = 15.8$ Hz, Ar-CH=), 7.7 (d, 1H, $J = 15.8$ Hz, C=CHCO), 8.3–6.9 (m, 7H, ArH). Anal. Calcd for $C_{17}H_{15}O_6N$: C, 62.00; H, 4.59; N, 4.25. Found: C, 61.73; H, 4.56; N, 4.25.

Reaction of 6 with 1,3-Dichloropropan-2-one. The reaction was carried out in a manner similar to that described for the reaction of **3** with **4**. This reaction afforded 1,3-bis(benzoyloxy)acetone (**11**): mp 121 °C (from benzene) (lit.[21] mp 121 °C).

Alkali Metal Extraction. Extraction equilibrium constants (K_e) for the extraction of alkali metal picrates with **1** from aqueous solution to organic solvents were determined by modifying the method employed for determination of metal picrate extraction with calix[4]arene derivatives.[22] A solution of an alkali metal picrate in a deionized water and a solution of **1** in an organic solvent were made. Equal volumes (5 mL) of the organic solution of **1** (1.0×10^{-3} M) and the aqueous alkali metal picrate solution ($(1.0–10.0) \times 10^{-3}$ M) were repeatedly shaken in a stoppered flask at 25 °C for 2.5 h. After phase separation, the concentration of the complexed picrate salt in the organic layer was determined spectrophotometrically, using $\epsilon = 16\,000$ M^{-1} cm^{-1} at 363 nm for benzene, $\epsilon = 17\,000$ M^{-1} cm^{-1} at 372 nm for chlorobenzene, $\epsilon = 18\,000$ M^{-1} cm^{-1} at 374 nm for $CHCl_3$, $\epsilon = 18\,000$ M^{-1} cm^{-1} at 377 nm for CH_2Cl_2, and $\epsilon = 18\,000$ M^{-1} cm^{-1} at 378 nm for $ClCH_2CH_2Cl$. As an initial check, the decrease in concentration of the picrate salts in water (λ_{max} 354 nm, $\epsilon = 14\,500$ M^{-1} cm^{-1}) was measured, and it was found to be in agreement with those of organic layers. The activity coefficients, γ^2, that were used to calculate K_e values were 0.79 for 10^{-2} M, 0.88 for 5×10^{-3} M, and 0.95 for 10^{-3} M picrate solutions, respectively.[23]

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