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Syntheses of All Possible Calix[6]arene Derivatives with MeO- and ROCOCH2O- Substituents and Their Metal Binding Properties

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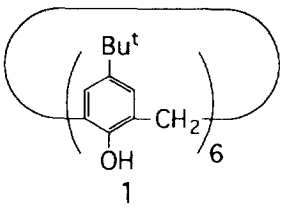
Abstract: It has become possible to synthesize all possible calix[6]arene derivatives with MeO- and $ROCOCH_2O$- substituents from corresponding O-methylated calix[6]arenes(**2-7**). The yields of these reactions were relatively high and the products could be easily purified because of the absence of other regioisomers. They are one mono-, three di-, three tri-, three tetra-, one penta-, and one hexa-$EtOCOCH_2O$-substituted products. It was proved that O-methylation products act as useful basic skeletons to design functionalized calix[6]arenes with the desired number of $ROCOCH_2O$ substituents and the regioselectively-positioned $ROCOCH_2O$ groups.

INTRODUCTION

Calix[n]arenes are cyclic oligomers which belong to the class of $[1_n]$-metacyclophanes. As calix[n]arenes have a cavity-shaped architecture, they are useful as building blocks for host-guest-type receptors and catalysts through appropriate modification of the edges.[1] Functional groups can be introduced either to the upper rim by means of electrophilic substitution reactions[1-5] or to the lower rim by means of Williamson-type OH-modifications,[1,6-12] but there is no doubt that the latter method is much more convenient than the former. Functionalization of OH groups in calix[4]arenes has been thoroughly investigated.[1,6-14] By the skillful use of solvents, bases, molar ratio of reactants, protecting groups, *etc.*, it is now possible to selectively synthesize all possible O-alkylation products (including conformational isomers) derivable from calix[4]arenes.[1,6-14] In contrast, the selective syntheses of O-alkylation products derivable from calix[6]arenes have still been investigated only partially.[5a,6c,7c,15] The difficulty of this investigation arises from complicated isolation and identification of starting 5,11,17,23,29,35-hexa-*tert*-butylcalix[6]arene-37,38,39,40,41,42-hexol (**1**) and 12 O-alkylation products from mono- to hexa-O-alkylated calix[6]arenes (**2-7**: see Scheme I). Gutsche *et al.*[6c] carried out arylmethylations to determine the effect of para substituents on the structural and/or conformational outcome of the reactions. Casnati *et al.*[7c] reported that refluxing of **1** with K_2CO_3 and MeI in dry acetone gives symmetrically tri-substituted 5,11,17,23,29,35-hexa-*tert*-butyl-37,39,41-trimethoxy-38,40,42-trihydroxy-calix[6]arene ($\mathbf{4}_{1,3,5}$) in 30% yield, but the reason for the formation of $\mathbf{4}_{1,3,5}$ as the major product was not explained. More recently, Janssen *et al.*[15] carefully analyzed O-methylation

products obtained from the reaction of **1** and MeI and isolated several new products. Very recently, we completed the systematic synthesis of all possible O-methylation products derivable from **1** (Scheme 1).[16] The strategies used for this purpose are (i) direct O-methylation at the different $1/K_2CO_3$ ratio, (ii) selective mono-O-methylation of O-alkylation products, (iii) demethylation with $TiCl_4$ or LiI, and (iv) protection-deprotection with a benzyl group or an *o*- or *m*-xylenyl group.[16] From these compounds one can now synthesize regioselectively $EtOCOCH_2O$-substituted calix[6]arenes(**7**-**13**): they have the different number of $EtOCOCH_2O$ groups and **9**, **10**, and **11** consists of three different regioisomers These compounds are useful to examine whether the ionophoricity is effected not only by the number of ionophoric $EtOCOCH_2O$ groups but also by the arrangement of $EtOCOCH_2O$ groups: for example, $\mathbf{10}_{1,2,3}$ would cover only one side of a bound metal cation whereas $\mathbf{10}_{1,3,5}$ would provide a C_3-symmetrical ionophoric cavity for the metal- and the guest-binding. It is of great significance to estimate whether such differences are reflected by the metal and the guest affinity and selectivity.



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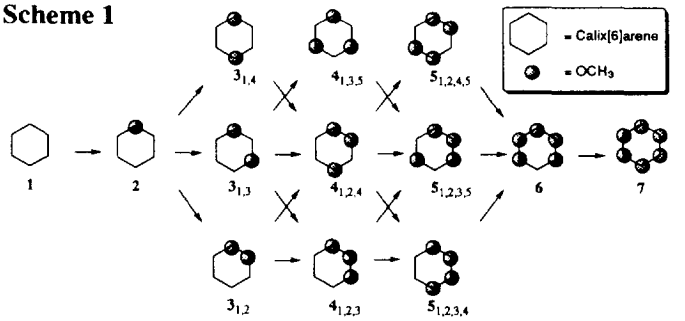
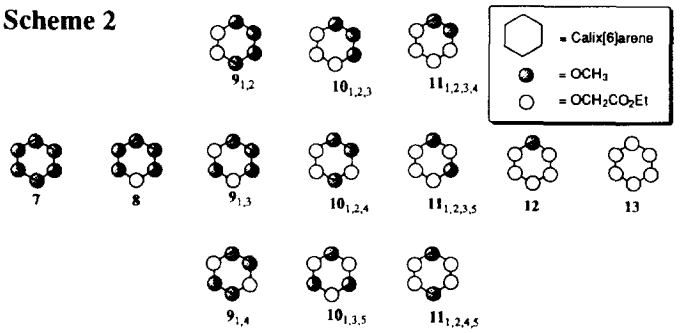
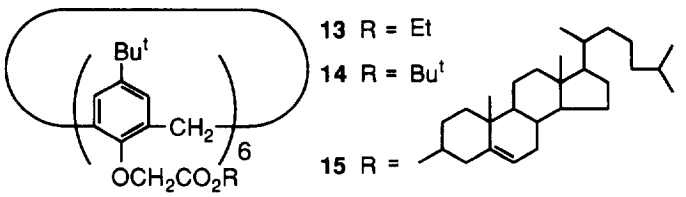
Scheme 1



Scheme 2





RESULTS AND DISCUSSION

Syntheses. As shown in Scheme 2, there are 12 different $EtOCOCH_2O$-substituted calix[6]arene derivatives(**8-13**): only one product exists in mono-substituted **8**, penta-substituted **12**, and hexa-substituted **13** whereas three regioisomers can exist in di-substituted **9**, tri-substituted **10**, and tetra-substituted **11**. They were synthesized by the reaction of corresponding **1-6** with ethyl bromoacetate in the presence of appropriate base. In general, the molecule having the high symmetry showed the high melting point (in **11**, for example, **11** $_{1,2,4,5}$, mp (decomp.) > 280 °C) and can be easily purified by recrystallization. In contrast, the isolation of the molecule without the high symmetry was relatively difficult and the melting point was relatively low (in **11**, for example, **11**$_{1,2,3,4}$, mp 100-102 °C; **11**$_{1,2,3,5}$, mp 105-107 °C). We applied column chromatography for these compounds.

The ^1H NMR spectra of most compounds afforded broad peaks, indicating that the rate of the phenyl group rotation exists in a range comparable with the NMR time-scale. At 130 °C in 1,1,2,2-tetrachloroethane-d_2 these compounds gave splitting patterns consistent with those expected from their molecular symmetries. The theoretical and observed splitting patterns are summarized in Table 1. The sole exception is **10** $_{1,3,5}$. Casnati *et al.* [7c] reported that the conformation of a tri-*tert*-butyl ester analog of **10** $_{1,3,5}$ (**16**) is "frozen" in a cone conformation because the ^1H NMR spectrum gives a pair of doublets at the wide temperature range. It was later corroborated, however, that this is rather due to the slow ring inversion rate.[17-19] In **16**, three MeO groups are flattened and point inside the calix[6]arene cavity while three Bu^tOCOCH_2O groups stand up.[7c] This conformation is very advantageous for reducing both the electrostatic repulsion among phenolic-oxygen lone-pair electrons and the steric crowding among bulky Bu^tOCOCH_2O groups. The exceptional stabilization of the initial state makes the ring inversion rate exceptionally slow. Although the ^1H NMR peaks for **10**$_{1,3,5}$ are somewhat broader than those for **16**, one can assign the conformation to a cone with δ 3.49 and 4.55 ppm (broad doublet each) for the $ArCH_2Ar$ protons. The peak broadening indicates that a change from Bu^t to Et affects the ring inversion rate: that is, the para-subsitituent-through-the-annulus rotation is involved in ring inversion of calix[6]arenes.[17-19]

Table 1 The theoretical and observed splitting patterns of calix[6]arene derivatives with MeO- and $EtOCOCH_2O$- substituents.

Derivative [a]	Observed pattern (theoretical pattern)[b]		
	Bu^t	$ArCH_2Ar$	OCH_2CH_3
 **7**	6	12	-
 **8**	1:2:2:1	4:4:4	3
 $\mathbf{9}_{1,2}$	2:2:2	2:4:4:2	6
 $\mathbf{9}_{1,3}$	1:2:2:1	4:4:4	6
 $\mathbf{9}_{1,4}$	2:4	4:8	6
 $\mathbf{10}_{1,2,3}$	1:2:2:1	4:4:4	3:6
 $\mathbf{10}_{1,2,4}$	1:1:1:1:1:1	2:2:2:2:2:2	3:3:3
 $\mathbf{10}_{1,3,5}$	3:3	6:6[double doublet] (12)	9
 $\mathbf{11}_{1,2,3,4}$	2:2:2	2:4:4:2	6:6
 $\mathbf{11}_{1,2,3,5}$	1:2:2:1	4:4:4	3:6:3
 $\mathbf{11}_{1,2,4,5}$	2:4	4:8	12
 **12**	1:2:2:1	4:4:4	3:6:6
 **13**	6	12	18

a) Hexagonal denotes calix[6]arene skeleton, shadowed circle denotes MeO- group and open circle denotes $EtOCOCH_2$- group. b) Signals for Bu^t and $ArCH_2Ar$ groups are all singlets except $\mathbf{10}_{1,3,5}$ and signals for OCH_2CH_3 groups are all triplets.

Alkali Metal Extraction with 13, 14, and 15 and Their Complex Structures. It is known that calix[6]aryl ester derivatives do not show high metal selectivity toward alkali metal cations as calix[4]aryl ester derivatives show toward Na^+.[1] The broad selectivity is attributed to the flexibility and the rotational freedom remaining in the calix[6]arene skeleton. For example, it has been shown that phenyl units in calix[6]aryl esters such as $\mathbf{10}_{1,3,5}$, **13**, and **15** still enjoy the rotation in the ^1H NMR time-scale. The immobilization is achieved only by bridging plural phenyl units by a cap.[20-23] As shown in Figure 1, extraction of alkali metal picrates with **13**, **14**, and **15** showed selectivity toward K^+ and Cs^+ but they also extracted Na^+ with 65-90% extractability(Ex%).

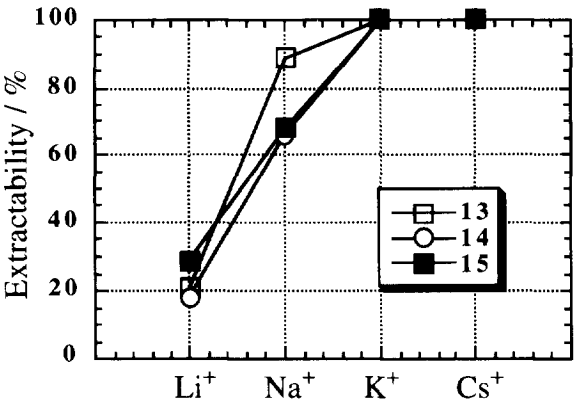


Figure 1 Extraction of alkali metal picrates, organic phase: [calix] = 2.5×10^{-3} M CH_2Cl_2, aqueous phase : [MPic] = 2.5×10^{-4} M, [MOH] = 1.0×10^{-1} M, [MCl] = 5.0×10^{-1} M

The Ex% values were scarcely affected by the alkyl group in the ester moiety. The ^1H NMR spectroscopic examination revealed, however, that the structure of the metal complexes are considerably different. It is known that **14** tends to adopt a 1,2,3-alternate conformation in the absence of metal cations whereas it changes to a regular cone conformation with C_6 symmetry upon K^+ complexation.[17,18] This is evidenced by ^1H NMR spectra affording a pair of doublets for the $ArCH_2Ar$ protons. The similar splitting pattern was also observed for the **14**·Cs^+ complex, indicating that the calix[6]arene skeleton in this complex also retains C_6 symmetry. On the other hand, when K^+ is bound to **13**, the ^1H NMR spectrum becomes very complicated (Figure 2): the ArH protons split into three peaks and both the $ArCH_2Ar$ protons and the $ArOCH_2$ protons give three pairs of doublets. In addition, the Et protons split into a 2 : 4 ratio, the 2H at higher magnetic field and the 4H at lower magnetic field. The splitting pattern suggests that the **13**·K^+ complex adopts a distorted cone with the lozenge-shaped ring in which two distal phenyl units are equivalent but inclined to one direction (Figure 3). The 2 : 4 splitting of the Et protons suggests that 1,2,4,5-phenyl units are more flattened and strongly interact with K^+ while remaining 3,6-phenyl units relatively stand up and only weakly interact with K^+. When Cs^+ is bound to **13**, the ^1H NMR spectrum at 30 °C is consistent with a regular cone conformation (a pair of

doublets for the $ArCH_2Ar$ protons at 3.51 and 4.38 ppm), but it becomes more complicated at low temperature (Figure 4). At -30 °C peaks are split into two sets in a 1 : 1 ratio. The finding suggests that the **13**·Cs^+ complex adopts C_{3v} symmetry and 1,3,5-phenyl units and 2,4,6-phenyl units are interconverting in the NMR time-scale (Figure 5). This situation is similar to calix[4]arenes which seem apparently C_4-symmetrical from the ^1H NMR spectra at room temperature but actually are subjected to C_{2v}-C_{2v} interconversion.[24] Hence, it seems reasonable to consider that "flattened" three alternate phenyl units interact with Cs^+ strongly while "stand-up" three alternate phenyl units interact with Cs^+ weakly.

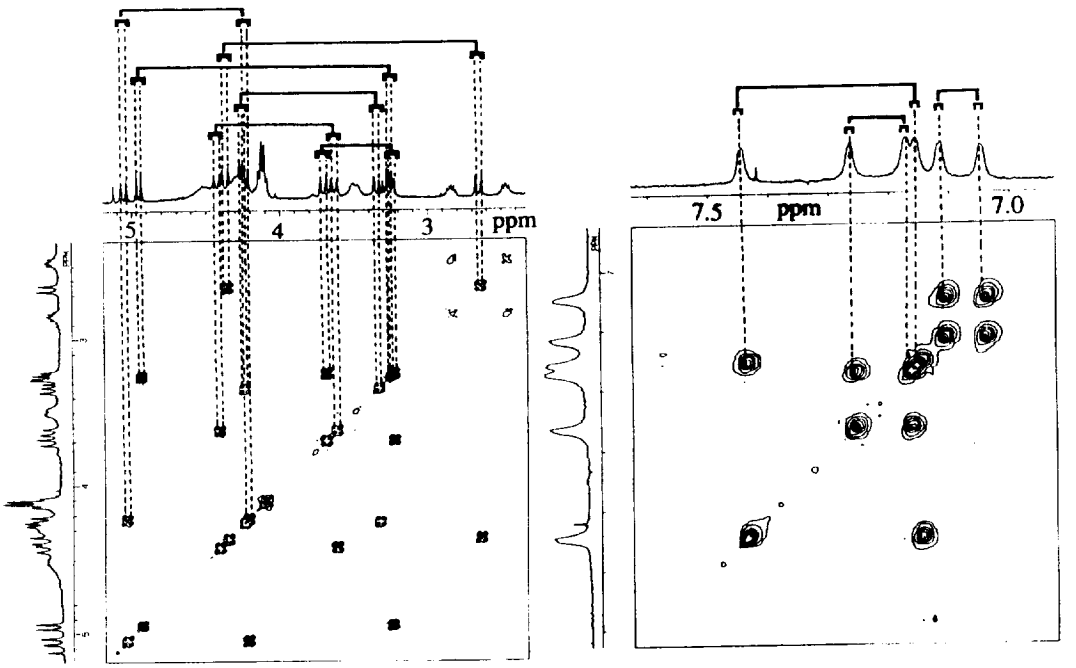


Figure 2 Partial ^1H-^1H COSY spectrum of the **13**·K^+ complex (400 MHz, CD_2Cl_2:CD_3CN = 4:1 v/v, 30°C)

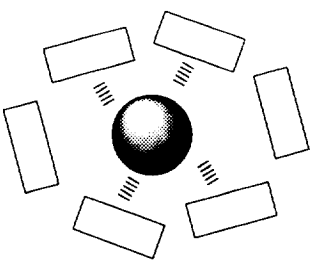


Figure 3 Proposed structure for the **13**·K^+ complex

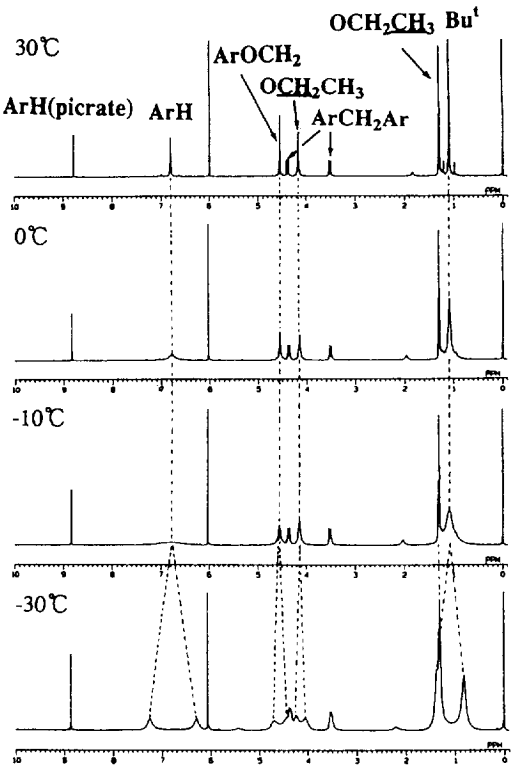


Figure 4 Temperature dependence of ^1H NMR spectra for the **13**·Cs^+ complex (400 MHz, $CDCl_3$)

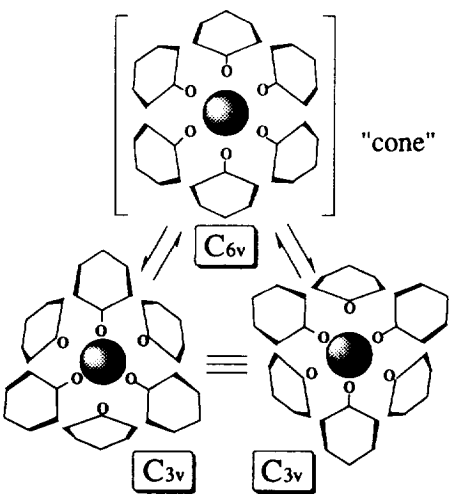


Figure 5 Proposed structure for the **13**·Cs^+ complex (C_{3v}-C_{3v} interconversion)

Alkali Metal Extraction with 7-13. The metal affinity (for K^+ and Cs^+) of **7-13** was estimated by two-phase solvent extraction of alkali picrates. The results are illustrated in Figure 6. Basically, the Ex % increased with increasing $EtOCOCH_2O$ group number, indicating the high metal cation affinity of the EtOCOCH2O group relative to the MeO group. However, we can raise several interesting metal-binding spectra for these regio-isomers. Firstly, we predicted that judging from the structure of the **13**·K^+ complex (Figure 3), $\mathbf{11}_{1,2,4,5}$ would show the K^+ affinity comparable with **13** because the ester groups on the 3,6-phenyl units only weakly interact with K^+. Contrary to our prediction, however, it showed the lowest affinity with K^+ among three **11** regio-isomers. The result implies that the more reasonable explanation is the following: $\mathbf{11}_{1,2,4,5}$ can take the **13**·K^+-like structure only when two 3,6-MeO groups stand up. This chance is rather limited in probability and the less bulky MeO groups rather tend to be flattened. Secondly, the similar unexpected result is seen for $\mathbf{10}_{1,3,5}$. Since the **13**·Cs^+ complex preferably adopts C_3 symmetry (Figure 5), we first expected that $\mathbf{10}_{1,3,5}$ would show the highest affinity with Cs^+. Contrary to our expectation again, $\mathbf{10}_{1,3,5}$ showed the lowest affinity with Cs^+ among three **10** regio-isomers. This may be explained on the same basis as that for $\mathbf{11}_{1,2,4,5}$. Thirdly, $\mathbf{10}_{1,3,5}$ showed the highest affinity with K^+ among three **10** regio-isomers. It is known that the ion size of K^+ is comparable with RNH_3^+. The result seems a little strange to us because K^+ is efficiently bound to $\mathbf{10}_{1,3,5}$ whereas RNH_3^+ is scarcely bound to $\mathbf{10}_{1,3,5}$.[7c,25] In $\mathbf{10}_{1,3,5}$ three MeO groups are flattered and three $EtOCOCH_2O$ groups stand up.[7c,17-19] Hence, the discrepancy is probably adjustable by the explanation that K^+ is bound in a sandwich manner between three MeO oxygens sinking in the cavity and three ester carbonyl oxygens standing on the lower rim.

Conclusions. The present paper demonstrates that all possible MeO and $EtOCOCH_2O$ substituted calix[6]arenes can be synthesized by the reaction of ethyl bromoacetate and the corresponding partially MeO substituted calix[6]arenes. It was found that their metal-binding properties are unique because of the action of regioselectively-introduced $EtOCOCH_2O$ groups. We are now applying these novel calix[6]arenes to recognition of guest molecules with the different shape and the different size.

EXPERIMENTAL SECTION

Materials

Compounds **8-13** were synthesized by the reaction of corresponding **1-6** with ethyl bromoacetate. We here describe only the syntheses of new compounds.

5,11,17,23,29,35-Hexa-*tert*-butyl-37-[(ethoxycarbonyl)methoxy]-38,39,40,41,42-penta-methoxy calix[6]arene (8). A DMF solution (30 ml) containing **6** (300 mg, 0.29 mmol), ethyl bromoacetate (0.16 ml, 1.44 mmol), and Cs_2CO_3 (468 mg, 1.44 mmol) was heated at 70°C for 5h under a nitrogen atmosphere. The solution was concentrated to dryness. The residue was mixed with aqueous 0.01 M HCl solution (10 ml) and extracted with chloroform. The chloroform layer was washed with water and dried over $MgSO_4$. The solution was concentrated to dryness, the residue being recrystallized

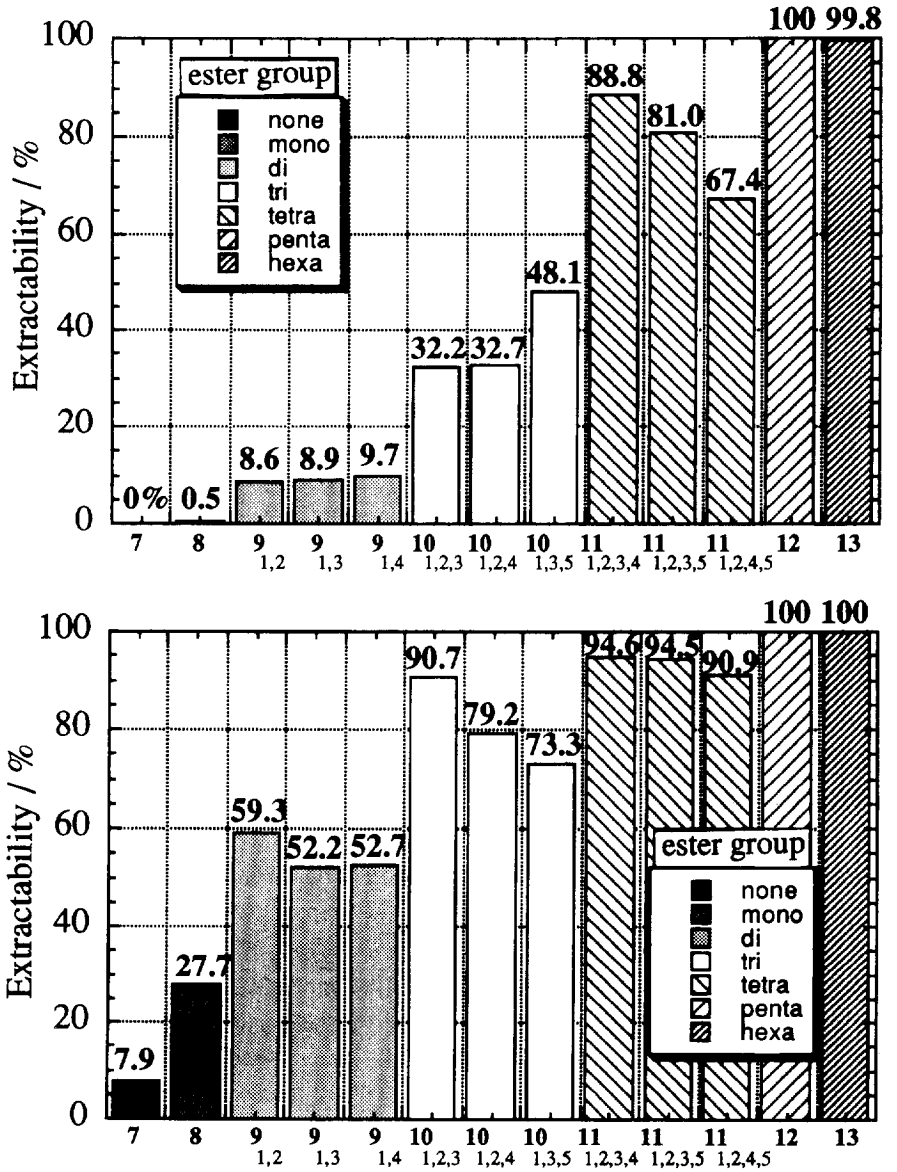


Figure 6 Extraction of alkali metal picrate [KPic(upper),CsPic(lower)], organic phase: [calix] = 2.5x 10^{-3} M CH_2Cl_2, aqueous phase : [MPic] = 2.5x10^{-4} M, [MOH] = 1.0x10^{-1} M, [MCl] = 5.0x10^{-1} M

from ethanol: mp 231-233°C, yield 86%; IR(nujol) no ν_{OH}, $\nu_{C=O}$ 1760cm^{-1} ; ^{1}H-NMR (400MHz, $(CDCl_2)_2$, 130°C, TMS, δ/ppm) 0.97, 1.06, 1.21, and 1.26 (9H, 18H, 9H, and 18H respectively, s each, t-Bu), 1.29 (3H, t (J=7.0Hz), OCH_2CH_3), 2.72, 2.91, and 3.20(6H, 3H, and 6H respectively, s each, OCH_3), 3.8-4.0 (4H each, s each, $ArCH_2Ar$), 4.25(2H, q(J=7.0Hz), OCH_2CH_3), 4.38(2H, s, $ArOCH_2$), 6.84, 6.86, 6.92, 7.05, 7.06, and 7.19(2H each, s, d (J=2.1Hz), d (J=2.1Hz), d (J=2.2Hz), s, and d(J=2.2Hz) respectively, ArH). Anal. Calcd for $C_{75}H_{100}O_8$+ 1.15$CHCl_3$: C, 72.16; H, 8.17%. Found: C, 72.20; H, 8.05%.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38-bis[(ethoxycarbonyl)methoxy]-39,40,41,42-tetramethoxycalix[6]arene($9_{1,2}$), 5,11,17,23,29,35-hexa-*tert*-butyl-37,39-bis[(ethoxycarbonyl) methoxy]-38,40,41,42-tetramethoxycalix[6]arene($9_{1,3}$), and 5,11,17,23,29,35-hexa-*tert*-butyl-37,40-bis-[(ethoxycarbonyl)methoxy]-38,39,41,42-tetramethoxycalix[6]arene($9_{1,4}$). Compounds $9_{1,2}$, $9_{1,3}$, and $9_{1,4}$ were synthesized from $5_{1,,2,3,4}$, $5_{1,,2,3,5}$, and $5_{1,,2,4,5}$, respectively. Compound $5_{1,2,3,4}$, (600 mg, 0.58 mmol) was dissolved in a THF (60 ml)-DMF (6 ml) mixed solvent and treated with oil-dispersed NaH (140 mg, 3.5 mmol). The mixture was stirred at the reflux temperature for 30 min and then ethyl bromoacetate was added. The reaction mixture was stirred at the reflux temperature for 24 H under a nitrogen atmosphere. The subsequent work-up is similar to that described for **8**. The final residue was recrystallized from dichloromethane-ethanol: mp 243-245 °C, yield 71%; IR(nujol) no ν_{OH}, $\nu_{C=O}$ 1770cm^{-1} ; ^{1}H-NMR (400MHz, $(CDCl_2)_2$, 130°C, TMS, δ/ppm) 1.06, 1.13, and 1.24 (18H each, s each, t-Bu), 1.29 (6H, t (J=7.1Hz), OCH_2CH_3), 2.54 and 3.10 (6H each, s each, OCH_3), 3.8-4.1(12H, m, $ArCH_2Ar$), 4.24(4H, q(J=7.1Hz), OCH_2CH_3), 4.30(4H, s, $ArOCH_2$), 6.80, 6.90, 7.00, 7.02, 7.08, and 7.23 (2H each, d(J=3.0Hz) each, ArH). Anal. Calcd for $C_{78}H_{104}O_{10}$ + 0.4CH_2Cl_2: C, 76.32; H, 8.52%. Found: C, 76.49; H, 8.44%.

The synthesis of $9_{1,3}$ and $9_{1,4}$ is basically the same as that of $9_{1,2}$, so that we here record only the analytical data. $9_{1,3}$ (recrystallized from ethanol): mp 240-242 °C, yield 85%; IR(nujol) no ν_{OH}, $\nu_{C=O}$ 1740, 1760cm^{-1} ; ^{1}H-NMR (400MHz, $(CDCl_2)_2$, 130°C, TMS, δ/ppm) 0.90, 1.01, 1.29, and 1.36 (18H, 9H, 18H, and 9H respectively, s each, t-Bu), 1.29 (6H, t (J=7.1Hz), OCH_2CH_3), 2.34, 2.69, and 3.29 (3H, 6H, and 3H respectively, s each, OCH_3), 3.91(12H, m, $ArCH_2Ar$), 4.25 (4H, q(J=7.1Hz), OCH_2CH_3), 4.47 (4H, s, $ArOCH_2$), 6.70, 6.80, 6.83, 7.09, 7.21, and 7.24(2H each, d(J=3.2Hz), d(J=3.2Hz), s, d(J=3.1Hz), s, and d(J=3.1Hz) respectively, ArH). Anal. Calcd for $C_{78}H_{104}O_{10}$: C, 77.96; H, 8.72%. Found: C, 77.93; H, 8.72%. $9_{1,4}$ (recrystallized from ethanol): mp 314-316 °C, yield 81%; IR(nujol) no ν_{OH}, $\nu_{C=O}$ 1760cm^{-1} ; ^{1}H-NMR (250MHz, $CDCl_3$, 25°C, TMS, δ/ppm) 1.06 and 1.20 (18H and 36H respectively, s each, t-Bu), 1.30 (6H, t (J=7.2Hz), OCH_2CH_3), 2.79 (12H, s, OCH_3), 3.91(12H, m, $ArCH_2Ar$), 3.9-4.2(4H, m, $ArOCH_2$), 4.25 (4H, q(J=7.2Hz), OCH_2CH_3), 6.96 and 7.21(8H and 4H respectively, m and s respectively, ArH). Anal. Calcd for $C_{78}H_{104}O_{10}$: C, 77.96; H, 8.72%. Found: C, 77.83; H, 8.76%.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,39-tris[(ethoxycarbonyl)methoxy]-40,41,42-trimethoxycalix[6]arene($10_{1,2,3}$), 5,11,17,23,29,35-hexa-*tert*-butyl-37,38,41-tris[(ethoxycarbonyl)methoxy}-39,40,42-trimethoxycalix[6]arene($10_{1,2,4}$) and 5,11,17,23,29,35-hexa-*tert*-butyl(-37,39,41-tri[(ethoxy carbonyl)methoxy]-38,41,42-trimethoxycalix[6]arene ($10_{1,3,5}$). Compounds $\mathbf{10}_{1,2,3}$, $\mathbf{10}_{1,2,4}$, and $\mathbf{10}_{1,3,5}$ were synthesized from $\mathbf{4}_{1,2,3}$, $\mathbf{4}_{1,2,4}$, and $\mathbf{4}_{1,3,5}$, respectively. Compound $\mathbf{4}_{1,2,3}$ (500 mg, 0.49 mmol) was dissolved in a THF (80 ml)-DMF (8 ml) mixed solvent and treated with oil-dispersed NaH (178 mg, 4.44 mmol). The subsequent operation with ethyl boromoacetate (0.99 ml, 8.82 mmol) is similar to that described for $\mathbf{9}_{1,2}$. The final residue was recrystallized from chloroform-ethanol: mp 172-174 °C, yield 89%; IR(nujol) no ν_{OH}, $\nu_{C=O}$ 1730, 1750cm^{-1} ; ^{1}H-NMR (400MHz, $(CDCl_2)_2$, 130°C, TMS, δ/ppm) 0.93, 0.98, 1.25, and 1.34 (18H, 9H, 9H, and 18H, respectively, s each, t-Bu), 1.27 and 1.29 (6H and 3H, respectively, t(J=7.2Hz) each, $OCH_2\mathit{CH_3}$), 2.25 and 3.50 (6H and 3H, respectively, s each, OCH_3), 3.85-4.05(12H, m, $ArCH_2Ar$), 4.04 and 4.42(2H, 4H respectively, s each, $ArOCH_2$), 4.22 and 4.24 (4H and 2H respectively, q(J=7.2Hz) each, $O\mathit{CH_2}CH_3$), 6.70, 6.79, 6.89, 7.16, 7.17, and 7.24(2H each, s, s, s, d(J=2.4Hz), d(J=2.4Hz), and s respectively, ArH). Anal. Calcd for $C_{81}H_{108}O_{12}$+ 0.35$CHCl_3$: C, 74.27; H, 8.30%. Found: C, 74.14; H, 8.36%. $\mathbf{10}_{1,2,4}$ (recrystallized from chloroform-ethanol): mp 266-268 °C, yield 75%; IR(nujol) no ν_{OH}, $\nu_{C=O}$ 1760cm^{-1}; ^{1}H-NMR (400MHz, $(CDCl_2)_2$, 130°C, TMS, δ/ppm) 0.99, 0.99, 1.13, 1.19, 1.22, and 1.36 (9H each, s each, t-Bu), 1.28, 1.29, and 1.30 (3H each, t each (J=7.1Hz), $OCH_2\mathit{CH_3}$) 2.05, 2.66, and 2.93 (3H each, s each, OCH_3), 3.80-4.00 (12H, m, $ArCH_2Ar$), 4.15, 4.15, and 4.15(2H each, q(J=7.0Hz) each, $O\mathit{CH_2}CH_3$), 4.15, 4.41, and 4.46 (2H each, s each, $ArOCH_2$), 6.64, 6.74, 6.87, 6.91, 6.92, 6.94, 7.05, 7.16, 7.20, 7.20, 7.27, and 7.36 (2H each, d(J=2.4Hz) each, ArH). Anal. Calcd for $C_{81}H_{108}O_{12}$: C, 76.38; H, 8.55%. Found: C, 75.99; H, 8.47%. $\mathbf{10}_{1,3,5}$ (recrystallized from chloroform-ethanol); mp 196-198°C. This compound was previously reported in the literature[25], so that we did not indicate the further analytical data.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,39,40-tetrakis[(ethoxycarbonyl)methoxy}-41,42-dimethoxycalix[4]arene($11_{1,2,3,4}$), 5,11,17,23,29,35-hexa-*tert*-butyl-37,38,39,41-tetrakis[(ethoxycarbonyl)methoxy]-40,42-dimethoxycalix[6]arene($11_{1,2,3,5}$), and 5,11,17,23,29,35-hexa-*tert*-butyl-37,38, 40,41-tetrakis[(ethoxycarbonyl)methoxy]-39,42-dimethoxycalix[6]arene($11_{1,2,4,5}$). Compounds $\mathbf{11}_{1,2,3,4}$, $\mathbf{11}_{1,2,3,5}$, and $\mathbf{11}_{1,2,4,5}$ were synthesized from $\mathbf{3}_{1,2}$, $\mathbf{3}_{1,3}$, and $\mathbf{3}_{1,4}$, respectively. Compound $\mathbf{3}_{1,2}$,(500 mg, 0.50 mmol) was dissolved in a THF (80 ml)-DMF (8 ml) mixed solvent and treated with oil-dispersed NaH (240 mg, 6.0 mmol). The subsequent treatment with ethyl bromoacetate (0.69 ml, 8.0 mmol) is similar to that described for $\mathbf{9}_{1,2}$. It was difficult to grow crystals of $\mathbf{11}_{1,2,3,4}$ from recrystallization solvent so that we used purification with column chromatography. The final residue was purified with column chromatography (silica gel, acetone: hexane = 1:4 v/v): mp 100-102 °C, yield 58%; IR(nujol) no ν_{OH}, $\nu_{C=O}$ 1740, 1760cm^{-1} ; ^{1}H-NMR (400MHz, $(CDCl_2)_2$, 130°C, TMS, δ/ppm) 1.06, 1.09, and 1.21 (18H each, s each, t-Bu), 1.22 and 1.25 (6H each, t (J=7.1Hz) each, $OCH_2\mathit{CH_3}$), 2.83 (6H, s, OCH_3), 3.81, 3.90, 3.99, and 4.00(2H, 4H, 2H, and 4H respectively, s each, $ArCH_2Ar$), 4.15 and 4.19(4H each,q(J=7.1Hz) each, $O\mathit{CH_2}CH_3$), 4.20 and 4.28(4H each, s each, $ArOCH_2$), 6.87, 6.90, 6.97, 6.98, 7.03, and 7.11(2H each, d(J=2.0Hz) each, ArH). Anal. Calcd for $C_{84}H_{112}O_{14}$ + 0.75C_6H_{14}:

C, 75.36; H, 8.75%. Found: C, 75.50; H, 8.70%. **11**$_{1,2,3,5}$ [purified with column chromatography (silica gel, ethyl acetate : hexane = 1:3 v/v)] : mp 105-107 °C, yield 62%; IR(nujol) no ν_{OH}, $\nu_{C=O}$ 1720, 1750cm^{-1}; ^{1}H-NMR (400MHz, $(CDCl_2)_2$, 130°C, TMS, δ/ppm) 0.91, 0.92, 1.28, and 1.37(18H, 9H, 9H, and 18H respectively, s each, t-Bu), 1.28, 1.32 (9H and 3H respectively, t(J=7.1Hz) each, OCH_2CH_3) 2.16 (6H, s, OCH_3), 3.92, 4.00 and 4.07(4H each, s each, $ArCH_2Ar$), 4.23, 4.24 and 4.28(2H, 4H and 2H respectively, q(J=7.0Hz) each, OCH_2CH_3), 4.44 and 4.47(2H and 6H respectively, s each, $ArOCH_2$), 6.65, 6.74, 6.87, 7.19, 7.22, and 7.29(2H each, d(J=2.0Hz), s, d(J=2.0Hz), d(J=2.4Hz), d(J=2.4Hz), and s respectively, ArH). Anal. Calcd for $C_{84}H_{112}O_{14}$: C, 74.97; H, 8.39%. Found: C, 74.69; H, 8.34%. **11**$_{1,2,4,5}$ (recrystallized from dichloromethane-ethanol): mp (decomp.) > 280°C, yield 83%; IR(nujol) no ν_{OH}, $\nu_{C=O}$ 1750cm^{-1} ; ^{1}H-NMR (400MHz, $(CDCl_2)_2$, 130°C, TMS, δ/ppm) 1.06 and 1.36 (36H and 18H respectively, s each, t-Bu), 1.29(12H, t(J=7.1Hz), OCH_2CH_3), 1.83(6H, s, OCH_3), 3.84 and 3.99(8H and 4H, respectively, s each, $ArCH_2Ar$), 4.25(8H, q(J=7.1Hz), OCH_2CH_3), 4.44(8H, s, $ArOCH_2$), 6.64, 7.15, and 7.44(4H each, d(J=2.0Hz), s, and d(J=2.0Hz), respectively, ArH). Anal. Calcd for $C_{84}H_{112}O_{14} + 0.75CH_2Cl_2$: C, 72.40; H, 8.06%. Found: C, 72.31; H, 8.19%.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,39,40,41-pentakis[(ethoxycarbonyl)methoxy]-42-methoxycalix[6]arene (12). A THF solution (80 ml) containing **2** (540 mg, 0.55 ml), ethyl bromoacetate (0.60 ml, 5.48 mmol), and *t*-BuOK (615 mg, 5.48 mmol) was refluxed for 24 h under a nitrogen atmosphere. The subsequent work-up is similar to that described for **9**$_{1,2}$. The final residue was recrystallized from chloroform-ethanol: mp 191-193 °C, yield 64%; IR(nujol) no ν_{OH}, $\nu_{C=O}$ 1750cm^{-1} ; ^{1}H-NMR (400MHz, $(CDCl_2)_2$, 130°C, TMS, δ/ppm) 1.00, 1.01, 1.14, and 1.35(18H, 9H, 18H, and 9H respectively, s each, t-Bu), 1.25 (15H, m, OCH_2CH_3), 2.18(3H, s, OCH_3), 3.88, 3.97, and 4.02(4H each, s each, $ArCH_2Ar$), 4.18(12H, m, OCH_2CH_3), 4.18, 4.19, and 4.43(2H, 4H, and 4H respectively, s each, $ArOCH_2$), 6.72, 6.80, 6.92, 7.01, 7.17, and 7.19(2H each, d (J=2.2Hz), s, d (J=2.2Hz), d (J=2.2Hz), s, and d (J=2.2Hz) respectively, ArH). Anal. Calcd for $C_{87}H_{116}O_{16} + 0.45CHCl_3$): C, 71.38; H, 7.98%. Found: C, 71.32; H, 8.11%.

Miscellaneous

^{1}H NMR, IR, and UV-vis spectral measurements were carried out with a Bruker AC 250P spectrophotometer and a JEOL GSX 400 spectrophotometer, a JASCO A-100 infrared spectrometer, and a Shimadzu UV-160 UV visible recording spectrophotometer, respectively.

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