Synthesis, *X*-Ray Crystal Structures, and Cation Transfer Properties of Alkyl Calixaryl Acetates, a New Series of Molecular Receptors

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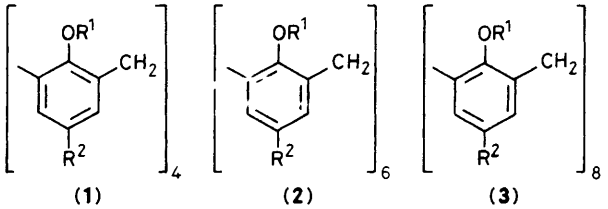
Calix[4]-, [6]-, and [8]-arenes have been converted into a series of alkyl acetates which show significant phase-transfer activity and selectivity towards alkali metal picrates; the *X*-ray crystal structures of two members of the series, (**1b**) and (**2d**), have been determined.

Calixarenes[1] are macrocyclic phenol–formaldehyde condensation oligomers whose structures are reminiscent of certain crown ethers and cavitands noted for their size-related ion–molecule binding and phase-transfer properties.[2] Although the parent *p*-t-butylcalixarenes, typically the tetramer (**1a**), hexamer (**2a**), and octamer (**3a**), form inclusion complexes with small, neutral molecules,[3] they have very little ionophoric activity for alkali metal cations as shown by their inability to transport these ions from neutral aqueous solution through a chloroform membrane.[4] Only when the source phase is the basic metal hydroxide is transport observed, phase transfer then being coupled to phenoxide ion formation. The continuing search for new synthetic receptors has recently



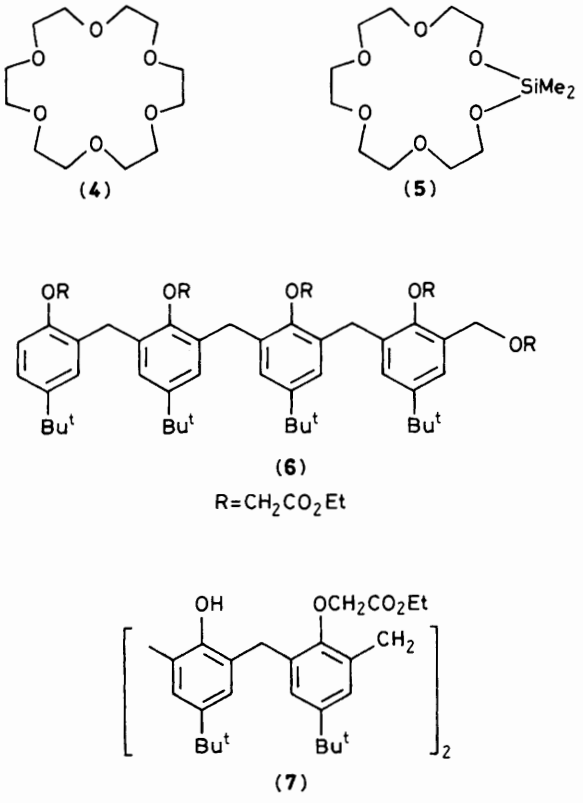
(**1**) (**2**) (**3**)

a; R^1 = H, R^2 = Bu^t
b; R^1 = CH_2CO_2Et, R^2 = Bu^t
c; R^1 = CH_2CO_2Me, R^2 = Bu^t
d; R^1 = CH_2CO_2Et, R^2 = H
e; R^1 = CH_2CO_2Me, R^2 = H

Table 1. % Extraction of alkali metal picrates in CH_2Cl_2 at 20 °C.[a]

	(1b)	(1c)	(1d)	(1e)	(2b)	(2c)	(2d)	(2e)	(3b)	(3c)	(3d)	(3e)	(4)	(5)	(6)	(7)
Li^+	15.0	6.7	1.8	1.1	11.4	1.7	4.7	2.6	1.1	0.9	0.8	0.4	8.7	0.5	2.6	0
Na^+	94.6	85.7	60.4	34.2	50.1	10.3	10.4	6.7	6.0	8.3	7.5	4.1	23.1	1.8	3.9	0
K^+	49.1	22.3	12.9	4.8	85.9	29.1	51.3	25.2	26.0	25.5	20.2	12.1	77.9	0.8	5.4	0
Rb^+	23.6	9.8	4.1	1.9	88.7	41.2	94.1	77.7	30.2	29.8	28.9	17.5	77.3	0.9	6.8	0
Cs^+	48.9	25.5	10.8	4.6	100.0	54.8	94.6	94.6	24.5	20.1	30.1	27.0	62.9	1.4	7.1	0

[a] 2.5×10^{-4} M Receptor in CH_2Cl_2; 2.5×10^{-4}M picric acid in 0.1M aqueous MOH. Receptor solution (5 ml) was shaken (3 min) with picrate solution (5 ml) and % extraction was measured from absorbance of resulting CH_2Cl_2 solution at *ca.* 378 nm; values are ± 2%. No picrate extraction in the absence of receptor.



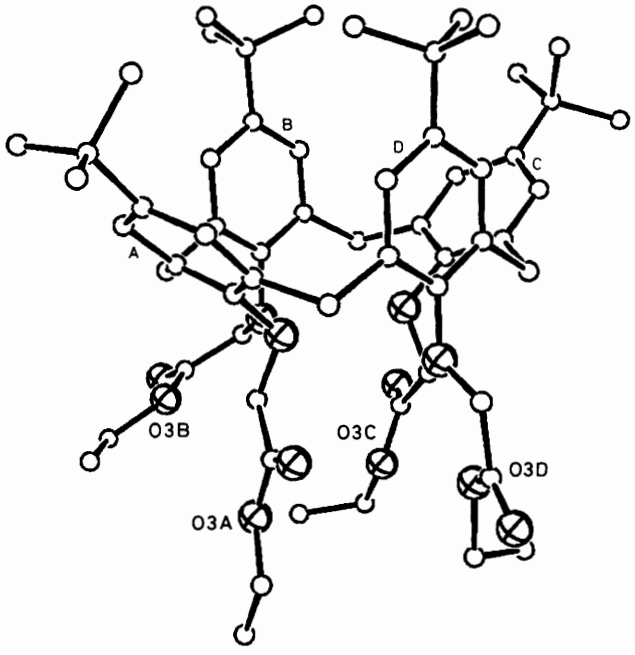


Figure 1. A view of molecule (**1b**); carbon and oxygen atoms are shown as spheres of arbitrary radius; the oxygen atoms are the larger circles and are marked with a cross. The four aromatic rings A—D are shown.

been extended to chemically modified calixarenes, but so far significant ionophoric activity has not been found in a neutral derivative.[4,5] Bearing in mind that biological receptors are rich in ester-type carbonyl groups, we have attached alkyl acetate groups to the phenolic groups in (**1a**), (**2a**), and (**3a**) and have found a high degree of phase-transfer affinity for alkali metal cations in the resulting esters.

Treatment of (**1a**) with ethyl bromoacetate (K_2CO_3, acetone) gave the ethyl ester (**1b**), m.p. 154—155 °C, which was converted (MeOH, TsOH) into the methyl ester (**1c**), m.p. 216—218 °C. Similarly, *p*-t-butylcalix[6]arene (**2a**) was transformed into esters (**2b**), m.p. 271—273 °C, and (**2c**), m.p. 245—250 °C, and *p*-t-butylcalix[8]arene (**3a**) into esters (**3b**), m.p. 228—230 °C, and (**3c**), m.p. 238—240 °C. Additionally, to probe the effect of removing the t-butyl group, (**1a**), (**2a**), and (**3a**) were dealkylated (toluene, $AlCl_3$) and converted as before into the ethyl and methyl ester series: (**1d**), m.p. 108—109 °C; (**1e**), m.p. 149—151 °C; (**2d**), m.p. 154—155 °C; (**2e**), m.p. 235—236 °C; (**3d**), m.p. 133—135 °C; (**3e**), m.p. 189—190 °C.

Results of phase-transfer measurements[6] with all twelve esters and alkali metal picrates are summarised in Table 1; included for comparison are data obtained with two commercial crown ethers, 18-crown-6 (**4**) and 'silacrown' (**5**). The results demonstrate a wide range of phase-transfer efficiency and suggest that it is a size-related phenomenon. The most significant generalisations are: (a) the smallest calixarene, the tetramer, shows peak selectivity for Na^+, regardless of whether it is the methyl or ethyl ester with or without the t-butyl group, though (**1b**) shows the highest value (94.6%); (b) phase-transfer of Li^+ is inefficient with all three series, though again the tetramer gives the highest values; (c) the larger hexamer series shows less affinity for Na^+ than for K^+ with plateau selectivity for Rb^+ and Cs^+; (d) the octamer series is the least efficient of the three, showing both low levels of transport for all five ions and low discrimination; (e) the hexamer (**2b**) is significantly better than 18-crown-6 (**4**) for Na^+ and K^+ and much better than (**4**) for Cs^+; (f) all three calixarene ester series are more efficient for ion transport than

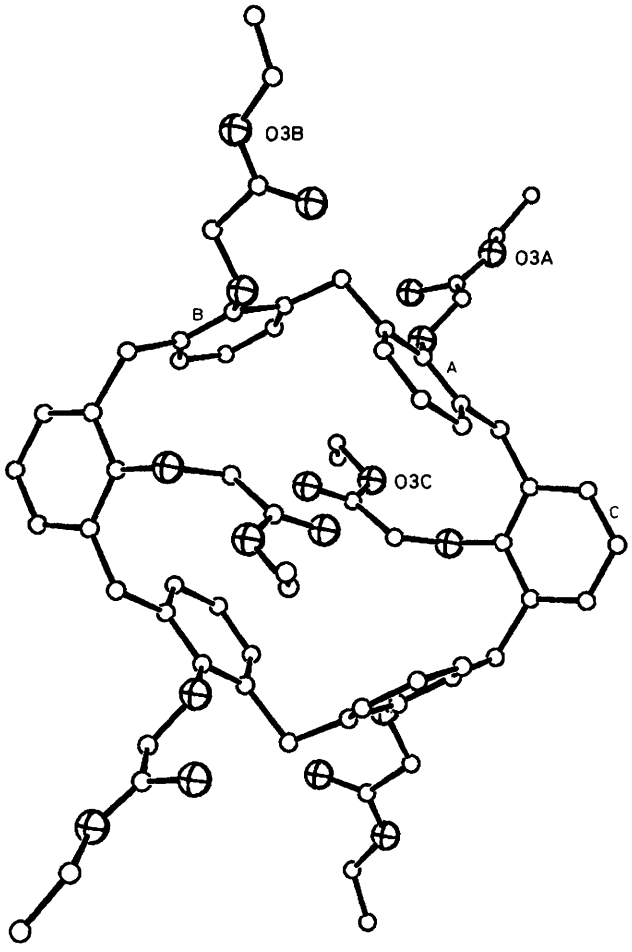


Figure 2. A view of molecule (**2d**) almost normal to the plane of the six macrocyclic CH_2 carbon atoms; oxygen and carbon atoms are indicated as in Figure 1, and three of the aromatic rings A—C are shown.

silacrown (**5**). More subtle differences are also discernible: the presence of the t-butyl group appears to have a beneficial effect on the tetramer selectivity for Na^+, though the difference between the methyl and ethyl esters is small. That there is a genuine macrocyclic effect operating is indicated by the very low level of ion transport with the acyclic pentaester analogue (**6**). Furthermore, incomplete esterification of the tetramer (**1a**), as in the diphenoldiester (**7**), drastically reduces ion transport ability.

Since ion transport with these systems appears to be a size-related phenomenon we have determined the *X*-ray crystal structures of the tetramer (**1b**) and hexamer (**2d**) in an effort to define cavity size and shape, and total receptor topology. Tetramer (**1b**)† (Figure 1) possesses a distorted cone or cup-like conformation in which the four ester groups are mutually *syn*, thus defining a central cavity with a 3.10—3.28(1) Å separation between adjacent phenolate oxygen atoms. The molecular conformation may be defined by the angles which the four aromatic rings (A—D) make with the macrocyclic ring CH_2 groups: A(41.1°), B(93.6°), C(135.8°), and D(92.2°). Rings B and D are thus essentially parallel (interplanar angle 1.9°). Rings A and C are almost normal to one another (interplanar angle 94.8°). In contrast, the centrosymmetric hexamer (**2d**)† has quite a different conformation (Figure 2). Three adjacent ester groups are *cis*, but the inversion symmetry places the other three *cis*-ester groups in the *anti* position on the opposite side of the macrocycle. A pair of symmetry-related ester groups overhang the central cavity with two inversion-related carbonyl oxygen atoms separated by 3.54 Å. Each aromatic ring is of course parallel to its centrosymmetric relation; the angles which the three unique aromatic rings A, B, and C make with the plane of the macrocyclic CH_2 groups are 60.5, 108.5, and 45.9°, respectively. Thus rings A and B are tilted so that their phenolate oxygen atoms are oriented away from the cavity centre, whereas ring C has its phenolate oxygen atom tilted towards the cavity centre. The adjacent phenolate oxygen O . . . O intramolecular contacts (4.04 and 4.70 Å) are, as a consequence, much longer than in (**1b**), in accord with the preference (Table 1) of (**2d**) for the larger cations.

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† *Crystal Data.* (**1b**) $(C_{15}H_{20}O_3)_4 \cdot 0.56\ H_2O$, M_r = 1003.1, triclinic, space group $P\bar{1}$, a = 12.434(2), b = 15.003(3), c = 17.286(4) Å, α = 103.01(2), β = 102.97(1), γ = 94.68(1)°, U = 3038 Å^3, Z = 2, D_c = 1.10 g cm^{-3}, 3884 observed reflections, R = 0.106. (**2d**) $(C_{11}H_{12}O_3)_6$, M_r = 1152.0, monoclinic, space group $C2/c$, a = 21.906(4), b = 11.805(2), c = 23.534(4) Å, β = 91.79(2)°, U = 6082.9 Å^3, Z = 4, D_c = 1.26 g cm^{-3}, 1221 observed reflections, R = 0.074. Molecules have inversion symmetry. Data collection was carried out as described previously.[7] All structures were solved using MULTAN-80[8] and refined by least squares calculations using SHELX.[9] The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.