Synthesis, X-ray Crystal Structures, and Cation-Binding Properties of Alkyl Calixaryl Esters and Ketones, a New Family of Macrocyclic Molecular Receptors

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Abstract: Calix[*N*]arenes (*N* = 4, 6, 8) have been converted into polyfunctional esters and ketones in a search for new macrocycles capable of showing ionophoric activity. Treatment with alkyl bromoacetates furnished the calixaryl acetate series, whereas chloroacetone–potassium iodide, phenacyl chloride, 1-adamantyl bromomethyl ketone, and bromopinacolone were used to make the calixaryl ketones series. The crystal structures of ethyl calix[4]aryl acetate (**7**), methyl calix[4]aryl acetate (**13**), ethyl calix[6]aryl acetate (**11**), and calix[4]aryl methyl ketone (**20**) have been determined. The crystals of **7** are triclinic, space group $P\bar{1}$, with two molecules in the unit cell of dimensions a = 12.434 (2) Å, b = 15.033 (3) Å, c = 17.286 (4) Å, α = 103.01 (2)°, β = 102.97 (1)° and γ = 94.68 (1)°. The crystals of **13** are monoclinic, space group $C2/c$, with eight molecules in the unit cell of dimensions a = 27.066 (6) Å, b = 21.392 (6) Å, c = 21.348 (7) Å, and β = 119.32 (2)°. The crystals of **11** are monoclinic, space group $C2/c$, with four molecules in the unit cell of dimensions a = 21.906 (4) Å, b = 11.805 (2) Å, c = 23.534 (4) Å, and β = 91.79 (2)°. The crystals of **20** are orthorhombic, space group *Pbcn*, with four molecules in the unit cell of dimensions a = 19.644 (7) Å, b = 12.712 (3) Å, and c = 22.115 (7) Å. Both **11** and **20** have crystallographically imposed 2-fold molecular axes. The analysis establishes that all three tetramer derivatives possess the cone conformation in the solid state where the pendant-functionalized side chains are mutually syn with respect to the calixarene substructure and are thus preorganized for ion reception. NMR measurements confirm the existence of the cone conformation for these tetramers in solution at room temperature. In contrast, the centrosymmetric hexamer ester **11** has three adjacent groups syn, but the inversion symmetry places the other three ester groups in the anti position on the opposite side of the macrocycle. Extraction studies with alkali metal picrates from aqueous solution into dichloromethane, transport studies with alkali metal thiocyanates through a dichloromethane membrane, and stability constant measurements with alkali metal salts by UV absorption spectroscopy in methanol and acetonitrile were used to assess the ionophoric activity of these calixarene derivatives. The tetramer esters and ketones display peak selectivity for the sodium ion, the tetraketones being generally more efficient binders than the tetraesters. The hexaester extracts K^+ better than Na^+ and displays a plateau selectivity after K^+. The octamers are the least effective ionophores. The selectivities shown by the picrate extraction technique are broadly mirrored in the transport studies. Stability constants range from 2 to 6, with a clear maximum for Na^+ with most of the tetramers and for K^+ with the hexamer; the values are of the same order of magnitude as for dibenzo-18-crown-6. The thermodynamic results are in fairly good agreement with the extraction and transport rate data. They enable a comparison of these new calixarene receptors with respect to crowns and cryptands: they are looser binders than cryptands 221 and 222; most tetramers offer in methanol a better Na^+/K^+ selectivity than cryptand 221, and in acetonitrile, the hexamer is at least as selective for K^+ as cryptand 222.

The term "calixarene" was introduced by Gutsche[1] in 1978 to describe a homologous series of macrocyclic phenol–formaldehyde condensates whose constitution and structure had been the subject of much speculation during the preceding 30 years.[2] Gutsche, recognizing in molecular models the cuplike or chalicelike appearance of the smallest member of the series, introduced a collective term that in retrospect was a very apt description since it is the molecular receptor activity of the calixarenes that is now their most significant property. The continuing search for new synthetic molecular receptors capable of guest–host relationships with ions and neutral molecules has produced many novel structures during the past 2 decades.[3,4] The calixarenes may prove to be another milestone in receptor chemistry, though they have more in common structurally with spherands and podands than with classical crown ethers and cryptands.

The calixarenes are phenolic metacyclophanes annulated by single methylene groups.[2] There are five members of the series, ranging from the relatively rigid tetrameric calix[4]arene to the much larger (32-membered ring), and more flexible, octameric calix[8]arene (Figure 1). The calixarenes bear some resemblance to the natural cyclodextrins[5] inasmuch as each possesses a recurring structural subunit with access to conformations in which several hydroxyl groups are arranged peripherally about a central cavity. Unlike the cyclodextrins, the calixarenes are very insoluble in water. Although calix[*N*]arenes (*N* = 4, 6, 8) are receptors for small neutral molecules,[6-10] they display little or no ionophoric

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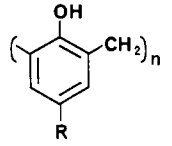


Figure 1. The calixarene family: R=H or alkyl; n = 4-8.

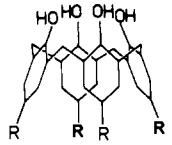


Figure 2. Calix[4]arene in the cone conformation.

activity toward metal ions in aqueous solution if the source phase is neutral. But Izatt and his co-workers[11] found that if the source phase is sufficiently basic to permit deprotonation of the phenolic groups, alkali-metal cations can be transported as neutral phenoxide complexes through a chloroform liquid membrane with a selectivity pattern, for the octamer, of $Cs^+ > Rb^+ > K^+ > Na^+ \gg Li^+$. We had demonstrated earlier this type of phenoxide-mediated ion transport with phenolic crown ethers.[12]

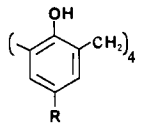
It seemed to us that the calixarenes offered several possibilities for functional group modification at the phenolic groups, and the objective of the work reported here was to use the calixarene family as molecular substructures or platforms on which to assemble groups of covalently bound ligands capable of acting as ion and molecule receptors. Some measure of preorganization of the resulting podands was clearly desirable if the ligands were to cooperate intramolecularly. Our objective is best illustrated using the tetramer in an idealized cone or calix conformation as shown in Figure 2, the preorganized podands defining the receptor volume. The idea is of course related to the lariat ether concept that Gokel[13] and others have exploited extensively with functionalized crown ethers and cryptands.[14]

Although *p-tert*-butylcalix[4]arene (**1**) is fluctional at room temperature in solution,[15] the cone conformation is preferred at low temperature and in the solid state.[6] A significant aspect of Gutsche's early work on chemical modification of the phenolic groups of **1** was the demonstration that certain functional groups made ring inversion more difficult and thus stabilized the cone conformation in solution at room temperature.[16] None of these chemically modified calixarenes was reported to have significant ionophoric activity. Ungaro and his co-workers[17] replaced the phenolic groups of **1** by linear polyethylene chains but found that this derivative adopted a partial cone conformation in which three ethereal groups were mutually syn, the fourth occupying the anti position with respect to the general plane of the macrocyclic ring; the potential ligating groups were thus not convergent, cf. Figure 2. Ungaro[18] later used a poly(ethyleneoxy) chain containing four oxygen atoms to cap two opposing phenolic groups of **1** to produce a calixaryl crown ether that did display ionophoric activity in both neutral and basic aqueous solutions. Ungaro[19] also synthesized a calixarenetetracarboxylic acid that exists in a cone conformation and whose alkali and ammonium salts are soluble in water.[20]

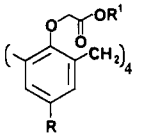
Our principal objective was to modify the *p-tert*-butylcalixarenes, **1**, **2**, and **3**, so as to impart ionophoric activity, and we turned our attention to the introduction of carbonyl groups in the expectation that ester and ketone groups might act as efficient ligating groups in much the same way that ester groups participate in ion binding with natural receptors such as valinomycin and nonactin.[21-23]

Synthesis and Structure

Literature procedures[24] were used to produce *p-tert*-butylcalix[*N*]arenes (*N* = 4, 6, and 8 for **1**, **2**, and **3**, respectively), which were dealkylated using aluminum chloride in toluene to furnish the parent calixarenes **4**, **5**, and **6**.[25] The introduction of ester and ketonic carbonyl groups was brought about by exhaustive alkylation of the phenolic groups with selected electrophiles. Use of ethyl bromoacetate in hot acetone containing anhydrous potassium carbonate furnished the ethyl *p-tert*-butylcalixaryl series **7**, **8**, and **9**, from **1**, **2**, and **3**, respectively, and in the non *tert*-butyl series **10**, **11**, and **12**, from **4**, **5**, and **6**, respectively. The methyl ester series **13–18** were obtained by exposing the ethyl esters to hot methanol containing *p*-toluenesulfonic acid.



(1) R=*t*-Bu (2) R=*t*-Bu (3) R=*t*-Bu
(4) R=H (5) R=H (6) R=H



(7) R=*t*-Bu R'=Et (8) R=*t*-Bu R'=Et (9) R=*t*-Bu R'=Et
(10) R=H R'=Et (11) R=H R'=Et (12) R=H R'=Et
(13) R=*t*-Bu R'=Me (14) R=*t* Bu R'=Me (15) R=*t*-Bu R'=Me
(16) R=H R'=Me (17) R=H R'=Me (18) R=H R'=Me
(19) R=*t*-Bu R'=*t*-Bu

Initial attempts to produce the methyl ketone series involved alkylation of the calixarenes with bromoacetone, and although the tetramer and octamer derivatives were obtained in this way, the reactions were very inefficient, and extensive purification of the products was necessary. We later found it more satisfactory to use chloroacetone as the electrophile, and have in situ halogen exchange with sodium or potassium iodide in acetone. Production

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(20) A new approach to fixing the tetramer in the cone conformation has recently been developed. It involves connecting two opposite aromatic rings through the para positions via a polymethylene chain, leaving the phenolic groups free. Variation in the chain length can then be used to distort the cone in a controlled way, especially affecting the phenolic O···O distances and thus changing the shape and volume of the cavity. See: Bohmer, V.; Goldmann, H.; Vogt, W. *J. Chem. Soc., Chem. Commun.* **1985**, 667. Goldman, H.; Vogt, W.; Paulus, E.; Bohmer, V. *J. Am. Chem. Soc.* **1988**, *110*, 6811.
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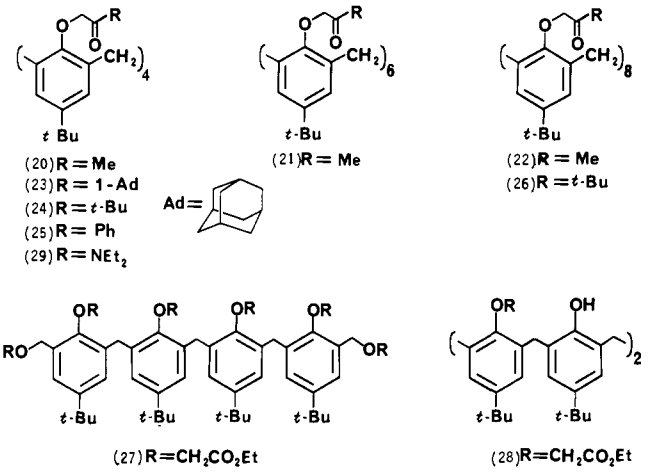

of the tetramer methyl ketone **20** in this fashion was very encouraging vis-à-vis ionophoric activity for the alkylation reaction actually produced a solid sodium/potassium iodide complex as the primary reaction product. It was necessary to heat the complex in water to release the free ketone. The sodium iodide–chloroacetone combination was also used to alkylate hexamer **2** and octamer **3**, furnishing ketones **21** and **22**, respectively in an uncomplexed state. Treatment of the *p-tert*-butylcalix[4]arene with 1-adamantyl bromomethyl ketone[26] in the presence of potassium iodide in acetone produced a potassium iodide complex that could be decomposed in hot aqueous ethanol only with some difficulty to release the tetraadamantyl derivative **23**; in the absence of potassium iodide, this reaction gave **23** directly. Bromopinacolone and tetramer **1** were combined to produce the tetra-*tert*-butyl ketone **24**, and in a similar manner phenacyl chloride and **1** furnished the tetraphenyl ketone **25**. A range of modified calixarenes with pendant ester and keto groups was thus in hand. All 19 derivatives were obtained as crystalline solids.

NMR and X-ray diffraction analysis were used to probe the conformations of these compounds in solution and in the solid state. The ^{1}H NMR data established unequivocally that the tetramer derivatives with *p-tert*-butyl substituents, namely, esters **7**, **13**, and **19** and ketones **20**, **21**, **22**, and **23**, all possess the cone conformation at ordinary temperatures. In addition to the signals unique to the ester/keto group, each spectrum consisted of a *tert*-butyl singlet, a singlet for the two equivalent aromatic protons, an OCH_2 singlet, and a single AB system for the two extremely anisotropic hydrogen atoms ($\Delta\delta \simeq 3.0$–5.0) of the four equivalent bridging methylene groups. These data discount less symmetrical conformations, such as the partial cone or alternate cone, and confirm that the four potential ligating side arms in both the ester and ketone series are preorganized to the extent that they are all mutually syn with respect to the calixarene substructure. The ^{1}H NMR data for the two tetrameric esters **10** and **16**, in which the *p-tert*-butyl group was removed, demonstrate clearly that these derivatives are also in the cone conformation. Conformational analysis by NMR of the hexamer and octamer derivatives was less straightfoward, though they were expected to be more flexible than their tetramer counterparts, and this was confirmed by the absence of an AB system for the bridging methylene groups. More detailed information concerning cavity dimensions and the mutual disposition of ester and ketone side arms was sought from X-ray diffraction analyses, which revealed that the cone conformation persists in the solid state for the tetraethyl ester **7**, the tetramethyl ester **13**, and the tetramethyl ketone **20** (Figures 3, 4, and 5) and that the four pendant groups in each, though mutually syn with respect to the calix, are asymmetrically disposed about the macrocycle. The carbonyl oxygen atoms in **7** are arranged in a propeller-like fashion, and the adjacent phenoxy oxygen atoms are separated by 3.10–3.28 Å. Thus, two types of potential binding sites are available, with the possibility of synergism between the

(26) Purchased from the Janssen Chemical Co.

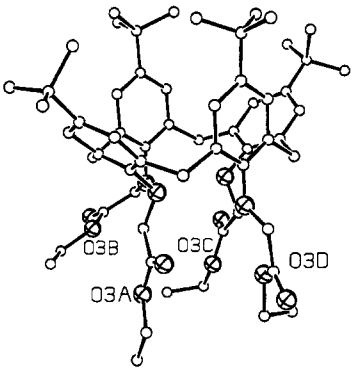

Figure 3. A view of molecule **7**; carbon and oxygen atoms are shown as spheres of arbitrary radius; the oxygen atoms are the larger circles and are marked with a cross. The four aromatic rings A–D are shown.

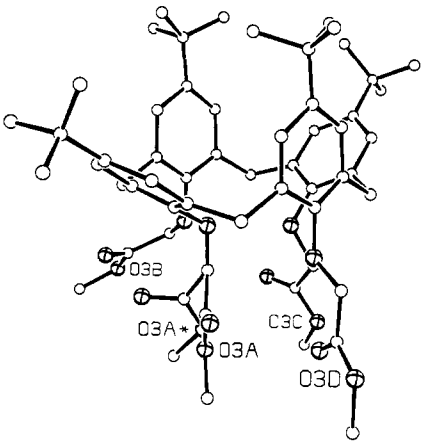

Figure 4. A view of molecule **13**; oxygen and carbon atoms are as indicated in Figure 3.

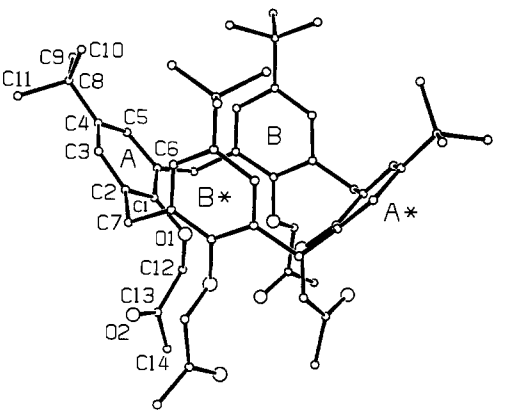

Figure 5. A view of molecule **20**; oxygen and carbon atoms are as indicated in Figure 3.

two. The molecular conformations of **7** may be defined by the angles that the four aromatic rings, A–D, make with the macrocyclic ring methylene groups: A (138°), B (94°), C (136°), and D (92°). Rings B and D are thus essentially parallel (interplanar angle 2°), while rings A and C are almost normal to one another (interplanar angle 94°). Much the same type of distorted cone conformation was found for the tetramethyl ester **13** (Figure 3). The angles that the four aromatic rings, A–D, make with the ring methylenes mean plane are A (148°), B (94°), C (130°), and D (87°); as in **7**, rings B and D are essentially parallel (interplanar angle 2°), while rings A and C are almost normal to each other (interplanar angle 98°). The orientation of the oxygenated side chain with respect to its benzene ring in both **7** and **13** is described by the C(12)–O(1)–C(1)–C(2) torsion angle which ranges from −68° to −93°. The side chain (A) in **13** is disordered equally over two sites. Most of the OCH_2COO-

Table I. Percent Extraction of Alkali Metal Picrate into CH_2Cl_2 at 20 °C[a,b]

A. Ester Series

	tetramers					hexamers				octamers			
	7	**10**	**13**	**16**	**19**	**8**	**11**	**14**	**17**	**9**	**12**	**15**	**18**
Li^+	15.0	1.8	6.7	1.1	27.6	11.4	4.7	1.7	2.6	1.1	0.8	0.9	0.4
Na^+	94.6	60.4	85.7	34.2	94.0	50.1	10.4	10.3	6.7	6.0	7.5	8.3	4.1
K^+	49.1	12.9	22.3	4.8	75.8	85.9	51.3	29.1	25.2	26.0	20.2	25.5	12.1
Rb^+	23.6	4.1	9.8	1.9	53.4	88.7	94.1	41.2	77.7	30.2	28.9	29.8	17.5
Cs^+	48.9	10.8	25.5	4.6	81.9	100.0	94.6	54.8	94.6	24.5	30.1	20.1	27.0

B. Ketone Series

	tetramers				hexamer	octamers		misc	
	20	**23**	**24**	**25**	**21**	**22**	**26**	**27**	**28**
Li^+	31.4	49.8	46.6	34.1	1.2	0.7	1.5	2.6	0
Na^+	99.2	94.0	92.8	94.3	6.2	9.9	21.6	3.9	0
K^+	84.1	72.6	81.4	47.7	12.8	25.1	7.7	5.4	0
Rb^+	53.7	23.4	43.7	27.1	11.6	20.8	1.7	6.8	0
Cs^+	83.8	17.2	31.6	50.7	13.6	15.3	4.5	7.1	0

[a] Details are in the Experimental Section. [b] Values are ±5%.

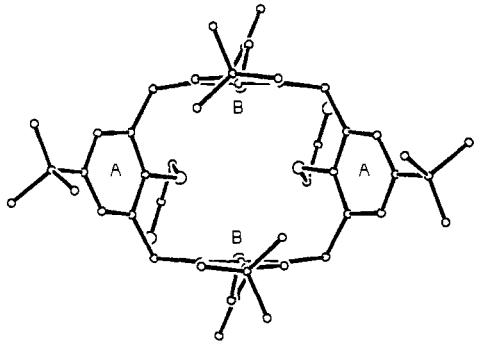

Figure 6. A view of molecule **20** almost normal to the plane of the four macrocyclic CH_2 carbon atoms; oxygen and carbon atoms are as indicated in Figure 3.

CH_2CH_3 or OCH_2COOCH_3 side chains in **7** and **13** show linear extension, with torsion angles approaching 180°. The tetramethyl ketone **20** (Figure 4) lies about a crystallographic 2-fold axis (the asymmetric unit contains half a molecule of **20**, and an acetone of crystallization (0.5 occupancy) disordered about an inversion center). As with **7** and **13**, two opposite rings are almost normal to one another (interplanar angle 85°), and two are almost parallel (interplanar angle 9°).

The mutually syn $MeCOCH_2$ moieties form the base of a cavity, with phenolate O···O intramolecular contacts O(1A)···O(1C), 3.55 (1); O(1A)···O(1B), 3.26 (1); O(1A)···O(1D), 3.03 (1); and O(1c)···O(1D), 5.16 (1) Å (Figure 5). The keto groups have a cis conformation with respect to the phenolate oxygen atoms [torsion angles O(1)–C(12)–C(13)–O(8) of 18° and 12° for A and B, respectively], such that keto oxygen O(2A) is directed away from the cavity and O(2B) points toward it. A view of the molecule almost normal to the plane of the four macrocyclic CH_2 carbon atoms is shown in Figure 6.

In contrast, the centrosymmetric hexamer **11** has a quite different conformation. Three adjacent ester groups are cis, but the inversion symmetry places the other cis ester groups in the anti position on the opposite side of the macroring (Figure 7). A pair of symmetry-related ester groups overhang the central cavity, with two inversion-related carbonyl oxygen atoms separated by 3.54 Å, and each carbonyl oxygen is directed toward the center of the calix, occupying an endo position (Figure 7). The molecular conformation is described by the angles that the three unique aromatic rings A, B, and C make with the plane of the macrocyclic ring methylene groups: A (61°), B (72°), and C (134°). Thus, rings A and B are tilted so that their phenolate oxygen atoms and contiguous side chains are oriented away from the cavity center, whereas ring C has its phenolate oxygen atom and attached side chain tilted toward the cavity center. The adjacent phenolate O···O intramolecular contacts [4.04 (O1C···O1B) and 4.70 (O1A···O1C)

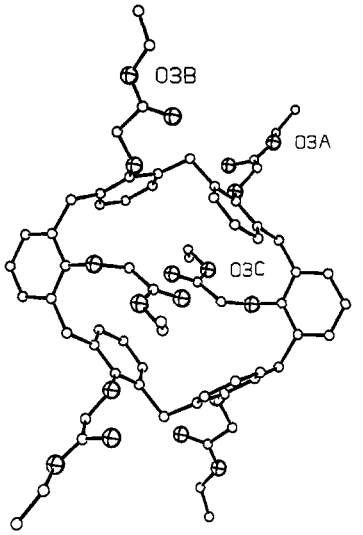

Figure 7. A view of molecule **11** almost normal to the plane of the six macrocyclic CH_2 carbon atoms; oxygen and carbon atoms are as indicated in Figure 3 and three of the aromatic rings A–C are shown.

Å] are, as a consequence, much longer than in the three tetramers. The orientation of each side chain relative to its benzene ring is described by the C(2)C(1)–O(1)C(8) torsion angle of −90° for ring A, 105° for ring B, and −99° for ring C. The side chains attached to rings A and B are not directed toward the molecular center and show linear extension, with torsion angles in the range 166–188°. By contrast, the side chain attached to ring C, and which is directed toward the molecule center, was OCH_2CO −4°, CH_2COCH_2 185°, and $COCH_2CH_3$ −133° as a consequence of the carbonyl group packing around the molecular center.

Physicochemical Studies of Alkali-Metal Cation Complexation. Results. Several aspects of the ionophoric properties of these calixarene esters and ketones toward alkali-metal cations were probed experimentally. In the first instance, we used the technique of picrate extraction devised by Pedersen as a convenient, semiquantitative assessment of ion-transport ability from aqueous solution into a nonpolar organic solvent.[27] Second, ion-transport rates were compared for passage through a liquid organic membrane. In some cases, particularly with the tetramer derivatives, complexation could be monitored by ^1H NMR spectral changes. We also obtained quantitative thermodynamic stability constants for several members of the series by UV absorption spectrophotometry, thus enabling us to make direct comparisons with existing data for cryptands and crown ethers. Finally, crystalline complexes

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Table II. Variation of Cation Flux[a] of M^+SCN^- through a Dichloromethane Membrane Containing Calixarene Ester

ionophore	Na^+	K^+	Cs^+
7	3.99	0.31	0.18
8	0.40	4.17	7.98
9	0.06	0.24	0.29
18-crown-6	0.08	6.83	1.48

[a] J_m = mol/h × 10^6. A minimum of two runs for each ion. Standard deviation: 10%.

with some alkali-metal salts were prepared.

Extraction Studies

The results of the picrate extraction studies are summarized in Table I. These data were obtained by using dichloromethane solutions of the calixarene derivative to extract metal picrate from aqueous alkaline solution, the equilibrium concentration of picrate in the organic phase then being determined spectrophotometrically. These measurements revealed a wide range of phase transfer ability for both the ester and ketone series; they also suggest that it is a size-related phenomenon. The most significant conclusions are as follows. (a) The smallest calixarenes, the tetramers, show a preference for Na^+ extraction, regardless of whether the receptor is an ester or a ketone. (b) The nature of the alkyl moiety in the ester group in the tetramer series is relatively insignificant though the *tert*-butyl ester **19** does have the highest overall phase-transfer values, showing a large response to Li^+ and K^+ in addition to Na^+. (c) The absence of the *p-tert*-butyl group in the tetramer ester series does not alter the selectivity of ion extraction, though the overall efficiency is lower than that observed with the *p-tert*-butyl series. (d) The tetrameric ketones show the broadest range of extraction ability, though the Na^+/K^+ selectivity is substantially lower than that shown by the tetramer methyl and ethyl esters. (e) In general, the tetraketones are more efficient than the tetraesters for phase transfer of Li^+. (f) The values for Rb^+ and Cs^+ with the tetraketones are generally better than those with the tetraesters. (g) The larger hexamer series shows less affinity for Na^+ than with K^+ with maximum efficiency but shows little preference, for Rb^+ and Cs^+. (h) Hexamer ketone **21** is a much poorer phase-transfer agent than any of the hexamer esters. (i) The octamer series is generally the least efficient of the three, showing both low levels of phase transfer for all five cations and poor discrimination. That there is a genuine macrocyclic effect operating with these calixarene ionophores is indicated by the very low levels of phase transfer exhibited by the acyclic analogue **28**. Furthermore, incomplete esterification of *p-tert*-butylcalix[4]arene (**1**), as in diphenol diester **28**, drastically diminished the extraction ability.

Our studies of ion-transport *rates* were much less extensive, though sufficient results were obtained to make comparisons. A liquid membrane system based on the Schulman bridge has been developed by Lamb et al.[28] to provide a simple method of measuring transport rates. We have used this system, incorporating Thoman's device of adding ferric ion to the aqueous receiving phase to monitor the rate of arrival of alkali metal thiocyanate through a dichloromethane membrane. Rate measurements of this kind are particularly system dependent; e.g., rates of stirring the phases or differences between rates of stirring can easily produce anomalous results. Nevertheless, reproducible results were obtained for the three esters studied with sodium, potassium and cesium thiocyanates; 18-crown-6 was also measured, and the data compare favorably with the published values. Quantitative monitoring of ion transport via spectrophotometry produced a linear plot of moles transferred versus time, the slope of which provides the cation flux value J_m; the results are presented in Table II. The main feature to emerge is that the three calixarene esters display the same order of ion selectivity with respect to rate of transport as they do with efficiency of phase transfer. The tetramer ester **7** produced a transport rate of 4 × 10^{-6} mol/h for Na^+, considerably faster than those for K^+ and Cs^+. The hexamer ester **8** had a cation flux of 4 × 2.10^{-5} mol/h for K^+ and an extremely high flux for Cs^+ of 8 × 10^{-6} mol/h. The octamer ester **9** displayed low rates and poor discrimination, in agreement with the picrate-transfer conclusions. These results are indicative of a situation in which the calixarene ester complexes the cation strongly enough to overcome the cation's hydration energy at the membrane source interface and yet not so strongly that it will not release the cation into the receiving phase. That the ion-transport rates mirror the phase-transfer data suggested that the stability constants for at least some members of the series should be investigated, the objective being to correlate the thermodynamic data with the structural, phase-transfer, and ionophoric properties and to position these new ligands with respect to the widely studied cryptands and crowns.

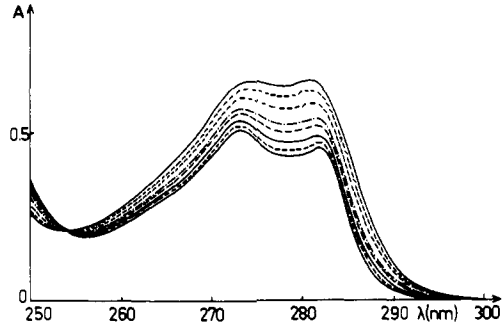

Figure 8. Change in absorption spectrum of a 2.3 × 10^{-4} M solution of the tetraethyl ester **7** in acetonitrile on increase of the Na^+ concentration ($0 \leq C_{Na^+} \leq 3.2 \times 10^{-4}$ M). Ionic strength: 0.01 M in Et_4NClO_4.

Determination of Stability Constants

We determined the stability constants, β, of the alkali-metal complexes of the following *p-tert*-butyl derivatives: the tetrameric ethyl acetate **7**, the hexameric ethyl acetate **8**, the tetrameric methyl ketone **20**, the tetrameric *tert*-butyl ketone **24**, and the tetrameric phenyl ketone **25**. Limitations in solubility prevented some derivatives from being included, notably the tetrameric adamantyl ketone **23** and the octamers. β is the concentration ratio $[ML^+]/([M^+][L])$ corresponding to the equilibrium $M^+ + L \rightleftharpoons ML^+$, with $M^+ = Li^+$, Na^+, K^+, Rb^+, or Cs^+ and L = ligand. Rigorously, the extraction equilibrium constant K_e, which can be calculated from the percentage of cation extracted, provided one neglects the ion-pair formation in the aqueous phase and the ion-pair dissociation in the organic phase, is related to both the stability constant of the 1:1 complex in *water* and to the extractability characteristics of the system. Whether the K_e sequence is governed by one or the other of these two factors depends on the system under investigation, as shown for the extraction of alkali-metal cations by crown ethers, where K_e is governed mainly by β in the case of 18-crown-6 (18C6), but not in the case of 15-crown-5 (15C5).[29] Thus, although the extraction method is widely used as a semiquantitative tool for comparing the ion-binding abilities of receptors, the affinity of a receptor for a cation is more clearly described by the stability constant of the complex in water, when available.

The calixarene derivatives in question are essentially completely insoluble in water, and the stability constants for that medium could not be determined. However, compounds **7**, **20**, and **24** are sufficiently soluble in a similar protic solvent, methanol, which is moreover a reference solvent for further discussion of the ionophoric properties. The hexamer **8** and the tetrameric phenyl ketone **25** are soluble in acetonitrile, as are **7** and **20**, which makes it possible to compare the binding abilities of the tetramer and hexamer. Both solvents are considered as totally dissociating.

The stability constants of the 1:1 complexes were determined by UV adsorption spectrophotometry, as the stepwise addition of an alkali-metal cation solution to a calixarene solution leads to a substantial change in absorbancy, sometimes accompanied

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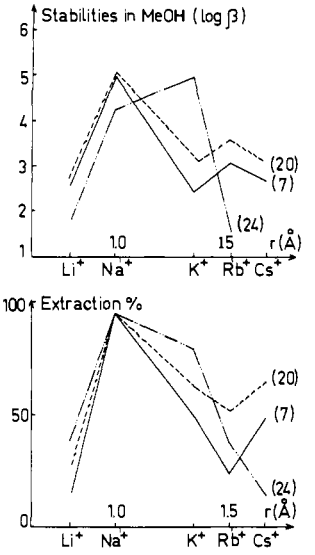

Figure 9. Logarithms of the stability constants β of the tetraester **7**, the tetramethyl ketone, and the tetra-*tert*-butyl ketone **24** in methanol vs the cation ionic radius r. For comparison, the extraction data have been added as percentage cation extracted.

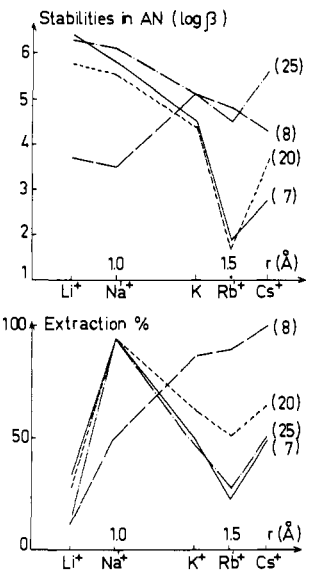

Figure 10. Logarithms of the stability constants β of the tetraester **7**, the hexaester **11**, the tetramethyl ketone **20**, and the tetraphenyl ketone **25** in acetonitrile vs the cation ionic radius r. For comparison, the extraction data have been added as percentage cation extracted.

Table III. Logarithms of the Stability Constants (β) of the Alkali-Metal Cation Complexes of Calixarene Derivatives **7**, **20**, **24**, **25**, and **8** and of Some Other Synthetic Ionophores at 25 °C[a]

solvent	cation	7	20	24	25	8	221[b]	222[b]	DB18C6[d]
MeOH	Li^+	2.6	2.7	1.8			5.4	2.6	
	Na^+	5.0[f]	5.1[f]	4.3			8.6	7.9	4.4
	K^+	2.4	3.1	5.0			8.5	10.4	5.0
	Rb^+	3.1	3.6	1.6			6.7	8.9	4.2
	Cs^+	2.7	3.1	<1			4.3	4.4	3.5
CH_3CN	Li^+	6.4	5.8		6.3	3.7	10.3	6.9	
	Na^+	5.8	5.6		6.1	3.5	>11.3	10.6[c]	4.8
	K^+	4.5	4.4		5.1	5.1	9.5	10.5[c]	4.8
	Rb^+	1.9	1.7		4.5	4.8		9.5[b]	3.7[e]
	Cs^+	2.8	3.7		5.6	4.3		4.5[b]	3.5[e]

[a] Arithmetic mean of at least two experiments. Standard deviation on the mean: σ_{n-1} = 0.2–0.3 log unit. Ionic strength = 10^{-2} M (Et_4NCl in MeOH and Et_4NClO_4 in CH_3CN). [b] Reference 31. [c] Reference 32. [d] Reference 33. [e] Reference 34. [f] Results confirmed by direct and competition potentiometry.

by small hypsochromic shifts of the positions of the maxima, leading to an isosbestic point that indicates an equilibrium involving at least two absorbing species in solution (Figure 8). Although not very spectacular, the spectral modifications were sufficient to enable a multiwavelength treatment of the data by the computer program Letagrop Spefo,[30] which provides the stability constants of the complexes as well as their calculated individual electronic spectra. Further details of the procedure are given in the Experimental Section.

Table III summarizes our results and allows a comparison with data for dibenzo-18-crown-6 (DB18C6) and cryptands 221 and 222 (221 and 222) in the same solvents. The stability constants in methanol range from about 2 to 5 log units, with a clear maximum for Na^+ with the tetramers **7** and **20**, and in acetonitrile from 2 to 6.5 log units, with a clear maximum for K^+ with the hexamer **8**. The tetramer *tert*-butyl ketone **24** complexes K^+ slightly better than Na^+. The constants are of the same order of magnitude as found for DB18C6. In methanol, for the Na^+ complexes of **7** and **20**, they are 3.5 log units lower than that of Na–221$^+$ and more than 5 log units lower than that of K–222$^+$.

Figures 9 and 10, showing the logarithms of β and the cation-extracted percentages versus the cation ionic radii in methanol and acetonitrile, respectively, enable a clearer presentation of the thermodynamic results with respect to the extraction data.

In **Methanol.** (a) The two tetramers **7** and **20** display a peak selectivity with a maximum for Na^+, just as was found in phase transfer. (b) For all cations the tetramethyl ketone **20** binds and extracts more strongly than **7**, in agreement with the more basic character of the ketonic carbonyl group in this solvent. (c) For the *tert*-butyl ketone **24**, the extraction and stability profiles show a large peak selectivity in favor of Na^+ and K^+ with, however, a slight interchange of the levels of Na^+ and K^+ since Na^+ is favored in extraction and K^+ in stability. (The order of extractability, however, was found to depend on whether the extraction is made from a neutral or from basic metal picrate solution; with neutral sodium and potassium picrate, the extraction order is the same as the stability constant order.) (d) An important point to be aware of is that the stability constants of the Na^+ complexes of **7** and **20** of about 5 log units are just about the optimal value empirically determined by Kirsch and Lehn[35] for efficient cation transport. Thus, the stability constants explain why the cation flux of Na^+ is much higher for the tetramer ester than for K^+ and Cs^+ and suggest, as far as thermodynamics are concerned, that this chemically modified calixarene may be a better transporter of Na^+ than the stronger binding cryptands.

In **Acetonitrile.** The comparison of extraction and stability data is more delicate, as this solvent is very different from water. Nevertheless, the following points emerge. (a) Of the five cations, Li^+ and the tetramers produce the highest stability constants. Furthermore, the values are higher than those found in methanol, with a maximum difference of nearly 4 log units for **7**, and are in marked contrast to the relatively low levels of extraction observed with lithium picrate (see Figure 10). This behavior, which is also exhibited by the cryptands (see Table III), may be accounted for, at least in part, by the very large transfer activity coefficient from methanol to acetonitrile of Li^+ (4.5 log units for Li^+, compared with between −1 and 1 for the other alkali-metal cations).[36] Consequently, the high stability constants for Li^+ complexes in acetonitrile are largely due to a solvent effect not encountered in extraction from aqueous medium. (b) The three tetramers **7**, **20**, and **25** have rather similar stability profiles, and the general complexation pattern mirrors the extraction pattern.

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(31) Cox, B. G.; Garcia-Rosas, J.; Scheneider, H. *J. Am. Chem. Soc.* **1981**, *103*, 1384.
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Table IV. Complexation Selectivities, S,[a] of Calixarene Derivatives **7**, **8**, **20**, and **25**

		7	**20**	**25**	**8**	221	222
	CH_3OH	400	100			1.2	
S_{Na^+}	CH_3CN	20	16	10		>63	
S_{K^+}	CH_3CN				40		0.4–50[b]

[a] S_{Na^+} is the selectivity with respect to Na^+, expressed as $\beta_{NaL^+}/\beta_{ML^+}$, and S_{K^+} is the selectivity with respect to K^+, expressed as $\beta_{KL^+}/\beta_{ML^+}$. Data for cryptands are taken from Table III and references therein. [b] Reference 32: this value becomes 2.5 if calculated from the mean values of all literature data for β_{Na^+} and β_{K^+} and ranges between 0.4 and 50 if the extreme values found in the literature are considered.

However, whereas the tetramethyl ketone **20** extracts K^+, Rb^+, and Cs^+ more than the tetraphenyl ketone 25 does, which behaves very much like the tetraester **7**, the stability constants for **25** are higher than those for **7** and **20** and even higher, in the case of Cs^+, than that of hexaester **8**. This inversion may be attributable to the higher expected lipophilicity of the phenyl ketone with respect to the methyl ketone. (c) There is also a marked difference in behavior, both in stability and extraction, between the hexaester **8** and the tetramers **7**, **20**, and **25**: with **8**, K^+, Rb^+, and Cs^+ form stronger complexes and are extracted to a greater extent than Na^+. The slightly increasing plateau from K^+ to Cs^+ observed in extraction is replaced in stability by a slightly decreasing plateau. (d) The smaller Li^+ and Na^+ cations are more efficiently extracted and are more strongly complexed by the tetramers than by hexamer **8**.

The Na^+/K^+ and K^+/Na^+ selectivities are summarized in Table IV together with those of cryptands 221 and 222, which are respectively best fitted for Na^+ and K^+ complexation. In methanol, the Na^+/K^+ selectivity, S_{Na^+}, is significantly higher for the tetramer ester **7** and ketone **20** than for 221. Tetraketone **20**, though a stronger binder, is less selective than tetraester **7**. The extent of the selectivity is, however, solvent dependent as with the cryptands, and in acetonitrile, S_{Na^+} is slightly higher for 221 than for **7**, **20**, and **25**. The K^+/Na^+ selectivity, S_{K^+}, of the hexamer **8** amounts to 40 in acetonitrile, whereas for 222 it ranges between 0.4 and 50, according to which literature data are considered. The values quoted in Table III, which are the only values originating from the same laboratory and as such could be thought to be the most reliable for estimating S_{K^+}, yield the unexpected value $S_{K^+} = 0.8$, contrasting with the usual selectivity of 222 for K^+ observed in other solvents. If one considers the mean values of all the literature data for $\log \beta_{Na^+}$ and $\log \beta_{K^+}$ in acetonitrile (respectively 10.4 and 10.8), the selectivity of 222 for K^+ with respect to Na^+ amounts to 2.5. Conclusively, in acetonitrile, the hexamer ester **8** is at least as selective for K^+ as 222.

Discussion

From the preceding discussion, it may be concluded that the thermodynamic results are in good agreement with the extraction data. These new receptors are looser binders than cryptands 221 and 222 and comparable binders to DB18C6, and most tetramers are probably better ionophores for Na^+ than 221. The tetraethyl ester and tetramethyl ketone display a better Na^+/K^+ selectivity in methanol than cryptand 221, and the hexaethyl ester displays a better K^+/Na^+ selectivity in acetonitrile than 222. The complexation of alkali-metal cations by the tetramer derivatives is consistent with predictions of the uncomplexed ligands (vide supra). These ionophores exist in the cone conformation in solution and in the solid state. The oxygenated pendant groups serve to fix the cone conformation, which thus confers a high degree of primary preorganization: the ligating groups of four ethereal (phenoxy) oxygen atoms and four ester/ketone carbonyl groups are mutually syn (and therefore convergent), defining a hydrophobic cavity as an extension of the lipophilic calix defined by the aromatic nuclei and the four *p-tert*-butyl groups. In this arrangement, only a slight rotation of the carbonyl groups toward the inside of the cavity is needed to present a total of eight binding sites toward the guest cation. Clearly, the cavity dimensions, as defined by the locations of the four ethereal oxygen atoms mutually separated by 3.10–3.28 Å in **7** and by 3.03–3.26 Å in **20**, are best adapted to accommodate the Na^+ cation. These dimensions may allow the inclusion of the smaller Li^+ cation or the larger K^+ cation by a flexing movement of the pendant ligating groups and/or a change in the tilt angle of the aromatic rings, but the resulting contraction or expansion of the cavity will be energetically expensive and will lead, in relative terms, to a destabilization of the complex. For all the cations studied, the complexes of the tetramethyl ketone **20** are stronger than those of the tetraethyl ester **7**, in agreement again with the structural data which suggest a better local preorganization of the carbonyl groups for complexation by the former coupled with the more basic character of the ketonic oxygen atoms in methanol.[37] The X-ray structure of the tetra-tert-butyl ketone **24** is not yet available. The fact that this compound does not discriminate clearly between Na^+ and K^+ in extraction and complexation may be related to an enlargement of the cavity due to steric interference between the bulk *tert*-butyl substituents. The receptor still retains the ability to discriminate between these two cations and the smaller Li^+ or larger Rb^+ and Cs^+ cations. Similar effects may operate with the tetraadamantyl ketone **23**, though at the moment we have insufficient data to make a judgement.

In contrast with these tetramer derivatives, the hexameric ethyl ester **11** does not possess the cone conformation. It is centrosymmetric and the adjacent O···O intramolecular contacts are much longer (4.04 and 4.70 Å) than in the tetramers. Although we do not have a clear picture as to how the pendant ester or ketone groups are organized in complexation, the larger cavity suggests a better binding ability for the larger cations. The flexible structure of the hexamers leads to a "plateau selectivity" after K^+, as is observed with the larger cryptands 322, 332, and 333.

Support for the interpretation of complexation by the tetramer derivatives outlined above was obtained by NMR measurements that are in excellent agreement with those recently published by Ungaro and co-workers[23] for complexation by the tetramer *tert*-butyl ester **13**. In practice, complexation of alkali-metal cations by any of the tetramer derivatives was very easily detected by either ^1H and ^{13}C measurements; only data from ^1H spectra for Li^+, Na^+, and K^+ will be included here. Two contrasting situations emerged when we examined the effect of adding incremental amounts of lithium, sodium, or potassium thiocyanate to tetramethyl ketone **20** in $CDCl_3$. A ^1H titration in which NaSCN was added showed that, with a salt/ligand ratio of less than 1, signals for both complexed and uncomplexed ligands were present in the spectrum, indicating that on the NMR time scale the exchange rate between the two species was slow at room temperature. Upon reaching a 1:1 stoichiometry, all the signals for the free ligand disappeared and an increase in the salt/ligand ratio beyond unity produced no further spectral shifts. Complexation affects all the proton chemical shifts in the ligand, the smallest change being experienced by the *tert*-butyl groups (0.05 ppm downfield) and the two largest being those of the axial proton H_A of the bridging methylene groups (cf. Figure 2) (0.51 ppm upfield) and the aromatic protons (0.29 ppm downfield). This downfield shift of the aromatic protons suggests that the phenoxy oxygen atoms are involved in complexation. By contrast, titration of the tetramethyl ketone **20** with lithium or potassium thiocyanate did produce spectral changes up to the point of 1:1 stoichiometry but did not show separate signals for complexed and uncomplexed ligand, indicating that exchange rates for K^+ and Li^+ with **20** were faster than that for Na^+. Slight differences were apparent for the K^+ and Li^+ complexation. Whereas the aromatic protons in the Li^+ complex experienced the largest shift (0.25 ppm downfield), it was the H_A protons that were most displaced in the K^+ complex (0.44 ppm upfield). This NMR treatment of Li^+, Na^+, and K^+ complexation in $CDCl_3$ was repeated with the tetraethyl ester **7**, the tetraadamantyl ketone **23**, and the tetra-*tert*-butyl ketone **24**, and although exchange rates clearly differed, comparable chemical shift differences were observed for the complexed and uncomplexed ligands.

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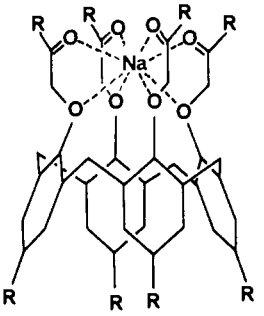

Figure 11. Encapsulation of an alkali-metal cation by a tetrameric calixarene ester or ketone.

Following these NMR studies, several stable crystalline complexes were isolated, viz. the lithium, sodium, and potassium thiocyanates of the tetramethyl ketone **20**, the tetraadamantyl ketone **23**, and the tetra-*tert*-butyl ketone **24**; the sodium and potassium iodide complexes of ketones **20** and **23**; the sodium acetate complex of ketone **23**; and the sodium thiocyanate and fluoroborate complexes of the tetraethyl ester **7**. A selection of these complexes (see Experimental Section) was prepared in methanol or acetonitrile and recrystallized from the same solvent. Unfortunately, though all of these complexes were crystalline, in no case so far have we been able to isolate crystals suitable for X-ray diffraction analysis. The difficulty appears to be the speed with which the crystal lattice collapses when the complex is isolated from its crystallization solvent. The analytical data confirmed the 1:1 stoichiometry of the complexes, though in some cases it was necessary to make the reasonable assumption that the solid complex contained solvent of crystallization.

Nevertheless, the observations described here taken together with Ungaro's[23] NMR analysis of Na^+/K^+ complexation by the tetra-*tert*-butyl ester **13** all point to the formation of a complex in which the cation is centrally located within the hydrophilic cavity defined by the four ester/ketone groups, supported electrostatically by the four ethereal oxygen atoms and the four carbonyl oxygen atoms (Figure 11). This interpretation of complexation by esters and ketones is further supported by the recently published X-ray crystal structures of the Na^+ and K^+ complexes of the calixarene tetraamide **29**,[38] which is conformationally and topologically directly related to the ester/ketone series and which reveals the cation nestling among the ethereal and amide oxygen atoms in the cone conformation.

Conclusions

In conclusion, a better understanding of alkali-metal cation complexation by functional groups preorganized in the cone conformation of the calixarene substructure has been achieved, and thermodynamical stability constants have been obtained for the first time. A direct offshoot of this study is the recent construction of a Na^+-selective electrode based on the tetramer methyl ester **14** as the ionophore.[39] The selectivity pattern of this electrode with respect to clinically common cations is better than those of some currently available sodium-selective electrodes. Other compounds in the series are also showing promise, in particular the hexamer esters in cesium electrodes.

It is now clear that the calixarenes offer many interesting possibilities in coordination and receptor chemistry. They are readily available, and the phenolic groups should be amenable to a wide range of chemical modifications for selective ion or molecular recognition and transport. While we have been concerned here with alkali-metal complexation, Chang et al.[40] have recently demonstrated the use of calixarene-based amides in alkaline-earth-metal complexation. Metallocalixarenes of transition metals are being explored with recent examples of titanium,[41,42] iron,[41] cobalt,[41] and europium[43] complexation. Bridged calixarenes are also possible in which the structural features of calixarenes and spherands are combined to make receptors fixed in a rigid binding conformation. Such a compound (calixspherand) has been prepared for Reinhoudt et al.[44] and found to exhibit very high binding power for alkali-metal cations.

Experimental Section

^1H NMR spectra were recorded in an Hitachi Perkin-Elmer Model R20A 60-MHz spectrometer or on a Jeol Model GX 400-MHz spectrometer using Me_4Si as internal standard. ^{13}C NMR spectra were recorded at 15 MHz on a Jeol Model JNM-FX60 spectrometer. Infrared spectra were recorded on a Perkin-Elmer Model 682 spectrophotometer. Melting points were recorded on a Reichert microscope and are uncorrected. Merck HF_{254} silica gel was used for analytical and preparative chromatography. Magnesium sulfate was employed as the drying agent.

Stability Constant Measurements. The spectral changes of calixarene solutions (2–5 mL) upon stepwise addition of alkali-metal salts directly in the measurement cell were recorded from 250 to 300 nm with a Shimadzu-240 spectrophotometer equipped with a thermostatted cell compartment. A large number of data selected at significant wavelengths were simultaneously treated by the computer program Letagrop-Spefo[30] on an IBM-3081 computer.

The solvents methanol (Merck, p.a. getrocknet) and acetonitrile (Merck, Uvasol) were used without further purification.

In methanol, the analytical concentrations of the tetramers were about 2×10^{-4} M, and a constant ionic strength 10^{-2} M was provided by Et_4NCl (Fluka, purum) recrystallized twice from acetone and dried under vacuum at 50 °C for 24 h. The cations were introduced as chlorides: LiCl (Fluka, purum), NaCl (Prolabo, p.a.), KCl (Merck, p.a.), RbCl (Fluka, puriss.), CsCl (Merck, p.a.). In acetonitrile, the analytical concentrations of the tetramers were about 2×10^{-4} M and, for the less soluble hexamer, they were 2×10^{-5} M. The constant ionic strength was provided by Et_4NClO_4. Due to the low solubility of the alkali metal chlorides in acetonitrile,[45,46] the cations were introduced as perchlorates ($LiClO_4$, Fluka, purum; $NaClO_4$, Merck, p.a.; $KClO_4$ Prolabo, normapur) or nitrates ($RbNO_3$ and $CsNO_3$ Fluka, purum). The absence of any spectral interference due to NO_3^- was evidenced, as well as the absence of any slow complexation kinetics.

Supracil cuves of 1-, 2-, and 5-cm path lengths were used.

Picrate Extraction Measurements. Metal picrates (2.5×10^{-4} M) were prepared in situ by dissolving the metal hydroxide (0.01 mol) in 2.5×10^{-4} M picric acid (100 mL); triply distilled water was used for all aqueous solutions. Solutions (2.5×10^{-4} M) of the calixarene derivatives were prepared in dichloromethane. Equal volumes (5 mL) of the two solutions were shaken vigorously for 1 min in a 20-mL separatory funnel. This was repeated 3 times, and the solutions were left standing until phase separation was complete. The concentration of picrate ion in the organic phase was then determined spectrophotometrically as described by Pedersen. Control experiments showed that no picrate extraction occurred in the absence of a calixarene derivative.

Ion-Transport Rate Measurements. Thoman's[47] modification of the procedure described by Lamb et al.[28] was used to measure the rates of ion transport through a dichloromethane membrane. The membrane, a 7×10^{-4} M solution of the calixarene derivative in CH_2Cl_2, was placed in a 600-mL beaker containing a 20-mm magnetic stirring bar. A 45-mm-diameter glass cylinder was inserted 15 mm into the CH_2Cl_2 solution and clamped securely in position. The source phase, 0.5 M metal thiocyanate, was very slowly run down the inner cylinder atop the CH_2Cl_2 solution. Similarly, the receving phase, 0.2 M $Fe(NO_3)_3$ in dilute nitric acid was run down the outer section (nitric acid was *essential* to suppress hydrolysis of the ferric species). The system was stirred slowly at ca. 100 rpm, which avoided the creation of a deep vortex. Reproducible stirring was *essential* to achieve reproducible results. Extremely anomalous results were obtained if concomitant stirring of the receiving phase was not maintained. This problem was overcome by using two preset stirring motors and two stirring bars and by inserting a small plastic disk con-

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taining incisions that floated on the receiving phase only and whose motion was coupled to the motion of the stirring bar. Samples were withdrawn from the receiving phase at 1–2-h intervals, and the absorbance was recorded at λ_{max} 480 nm for $Fe(SCN)^{2+}$ using the ϵ value of 4400 L mol^{-1} cm^{-1}. The experiment, when performed in the absence of calixarene, showed no transport of metal thiocyanate.

Preparation of Calixarenes (1–6). Gutsche's procedures were used to synthesize *p-tert*-butylcalix[*N*]arenes (N = 4, 6, 8). All three compounds were dealkylated with aluminum chloride in toluene to furnish the parent calixarenes.

Ethyl Calixaryl Acetates. General Procedure. The following procedure was used to transform calixarenes **1–6** into the corresponding ethyl ester series.

The calixarene was suspended in dry acetone (ca. 5% solution) containing a 50% molar excess of anhydrous potassium carbonate and a 100% molar excess of ethyl bromoacetate, and the mixture was refluxed with exclusion of moisture until TLC analysis showed the disappearance of calixarene (usually requiring 3–5 days). The cooled mixture was filtered, and the solid residue was washed several times with dichloromethane. The combined organic solutions were concentrated to an oil that contained residual ethyl bromoacetate. The latter was removed by distillation at high vacuum, leaving a residue to which sufficient ethanol was added to effect dissolution. After standing at 0 °C for ca. 12 h, the solution deposited a crystalline mass in near quantitative yield. Recrystallization from ethanol–dichloromethane gave the pure compound.

The following calixarene esters were thus prepared.

Tetraethyl *p-tert*-Butylcalix[4]arene Tetraacetate (7). *p-tert*-Butylcalix[4]arene (**1**) furnished the ester **7** in 88% yield, mp 154–155 °C; ^1H NMR ($CDCl_3$) δ (400 MHz) 1.07 (s, 36 H), 1.29 (t, 12 H), 3.19 (d, 4 H, J = 13 Hz), 4.20 (q, 8 H), 4.81 (s, 8 H), 4.85 (d, 4 H, J = 13 Hz), 6.77 (s, 8 H); ^{13}C NMR ($CDCl_3$) δ 14.23 (q), 31.38 (q), 31.90 (s), 33.85 (t), 60.30 (t), 71.34 (t), 125.33 (d), 133.52 (s), 145.15 (s), 153.01 (s), 170.49 (s); IR (KBr) 1760 cm^{-1}. Anal. Calcd for $C_{60}H_{80}O_{12}$: C, 72.58; H, 8.06. Found: C, 72.28; H, 8.03.

Hexaethyl *p-tert*-Butylcalix[6]arene Hexaacetate (8). *p-tert*-Butylcalix[6]arene (**2**) furnished the ester **8** in 88% yield, mp 271–273 °C; ^1H NMR ($CDCl_3$) δ 1.00 (s, 54 H), 1.25 (t, 18 H), 3.81–4.23 (m, 24 H), 4.50 (br s, 12 H), 6.98 (s, 12 H); ^{13}C NMR ($CDCl_3$) δ 14.23 (q), 31.25 (q), 31.34 (s), 33.98 (t), 60.75 (t), 70.69 (t), 126.44 (d), 132.81 (s), 146.53 (s), 152.88 (s), 169.45 (s); IR (KBr) 1760 and 1730 cm^{-1}. Anal. Calcd for $C_{108}H_{120}O_{18}$: C, 72.58; H, 8.06. Found: C, 72.60; H, 8.25.

Octaethyl *p-tert*-Butylcalix[8]arene Octaacetate (9). *p-tert*-Butylcalix[8]arene (**3**) furnished the ester **9** in 89% yield, mp 228–230 °C; ^1H NMR ($CDCl_3$) δ 1.10 (br s, 96 H), 3.80–4.20 (m, 48 H), 6.93 (br s, 16 H); ^{13}C NMR ($CDCl_3$) 13.90 (q), 30.15 (s), 31.32 nq), 34.18 (t), 60.95 (t), 69.98 (t), 126.05 (d), 132.61 (s), 146.71 (s), 152.88 (s), 168.74 (s); IR (KBr) 1765 cm^{-1}. Anal. Calcd for $C_{120}H_{160}O_{24}$: C, 72.58; H, 8.06. Found: C, 72.22; H, 8.24.

Tetraethyl Calix[4]arene Tetraacetate (10). Calix[4]arene (**4**) furnished the ester **1** in 68% yield, mp 108–109 °C: ^1H NMR ($CDCl_3$) δ 1.29 (t, 12 H), 3.23 (d, 4 H, J = 14 Hz), 4.21 (q, 8 H), 4.73 (s, 8 H), (4.87 d, 4 H, J = 14 Hz), 6.63 (m, 12 H); ^{13}C NMR ($CDCl_3$) δ 14.16 (q), 31.45 (t), 60.49 (t), 71.27 (t), 122.86 (d), 128.52 (d), 134.63 (s), 155.87 (s), 170.23 (s); IR (KBr) 1750 cm^{-1}. Anal. Calcd for $C_{44}H_{72}O_{12}$: C, 68.75; H, 6.25. Found: C, 68.61; H, 6.36.

Hexaethyl Calix[6]arene Hexaacetate (11). Calix[6]arene (**5**) furnished the ester **11** in 77% yield, mp 154–155 °C; ^1H NMR ($CDCl_3$) δ 1.24 (t, 18 H), 4.04 (br s, 12 H), 4.16 (q, 12 H), 4.20 (s, 12 H), 6.63 (t, 6 H), 6.77 (d, 12 H); ^{13}C NMR δ 14.23 (q), 31.58 (t), 61.08 (t), 69.98 (t), 124.75 (d), 124.49 (d), 133.59 (s), 155.03 (s), 169.19 (s); IR (KBr) 1760 cm^{-1}. Anal. Calcd for $C_{66}H_{72}O_{18}$: C, 68.75; H, 6.25. Found: C, 69.01; H, 6.30.

Transesterification of Ethyl Esters with Methanol. General Procedure. The ethyl calixaryl acetate was refluxed in methanol containing a catalytic amount of *p*-toluenesulfonic acid for 24–48 h. The solution was then concentrated under reduced pressure, and the residue was taken up in dichloromethane and washed with aqueous sodium bicarbonate and brine. The organic solution was dried and concentrated to leave the ester as a solid that was recrystallized to purity from methanol–dichloromethane.

The following methyl esters were thus obtained.

Tetramethyl *p-tert*-Butylcalix[4]arene Tetraacetate (13). Ethyl ester **7** furnished **13** (>90% yield), mp 216–218 °C; ^1H NMR ($CDCl_3$) δ 1.07 (s, 36 H), 3.20 (d, 4 H, J = 13 Hz), 3.76 (s, 12 H), 4.81 (s, 8 H), 4.83 (d, 4 H, J = 13 Hz), 6.78 (s, 8 H); ^{13}C NMR ($CDCl_3$) δ 31.38 (q), 31.71 (s), 33.85 (t), 51.33 (q), 71.15 (t), 125.40 (d), 133.39 (s), 145.28 (s), 152.88 (s), 171.01 (s). Anal. Calcd for $C_{56}H_{72}O_{12}$: C, 71.79; H, 7.69. Found: C, 71.72; H, 7.45.

Hexamethyl *p-tert*-Butylcalix[6]arene Hexaacetate (14). Ethyl ester **8** furnished **14** (>90% yield), mp 245–250 °C; ^1H NMR ($CDCl_3$) δ 1.07 (s, 54 H), 3.38 (br s, 18 H), 4.00–4.30 (m, 24 H), 7.19 (s, 12 H); ^{13}C NMR ($CDCl_3$) δ 30.86 (s), 31.38 (q), 34.24 (t), 51.46 (q), 70.30 (t), 126.70 (d), 132.61 (s), 146.58 (s), 152.88 (s), 169.58 (s). Anal. Calcd for $C_{84}H_{108}O_{18}$: C, 71.79; H, 7.69. Found: C, 71.81; H, 7.51.

Octamethyl *p-tert*-Butylcalix[8]arene Octaacetate (15). Ethyl ester **9** furnished **15** (>90% yield), mp 238–240 °C: ^1H NMR ($CDCl_3$) δ 1.10 (s, 72 H), 3.51 (s, 24 H), 4.03–4.04 (br s, 32 H), 6.95 (s, 16 H); ^{13}C NMR ($CDCl_3$) δ 30.41 (s), 31.32 (q), 34.24 (t), 51.78 (q), 69.78 (t), 126.18 (d), 132.74 (s), 146.90 (s), 152.88 (s), 169.25 (s).

Tetramethyl Calix[4]arene Tetraacetate (16). Ethyl ester **7** furnished **16** (>90% yield), mp 149–151 °C; ^1H NMR ($CDCl_3$) δ 3.25 (d, 4 H, J = 14 Hz), 3.76 (s, 12 H), 4.75 (s, 8 H), 4.85 (d, 4 H, J = 14 Hz), 6.64 (m, 12 H); ^{13}C NMR ($CDCl_3$) δ 31.38 (t), 51.46 (q), 71.15 (t), 122.93 (d), 128.58 (d), 134.56 (s), 155.81 (s), 170.62 (s). Anal. Calcd for $C_{40}H_{40}O_{12}$: C, 67.42; H, 5.62. Found: C, 67.56; H, 5.76.

Hexamethyl Calix[6]arene Hexaacetate (17). Ethyl ester **8** furnished **17** (>90% yield), mp 235–236 °C: ^1H NMR ($CDCl_3$) δ 3.55 (s, 18 H), 3.99 (s, 12 H), 4.07 (s, 12 H), 6.80 (t, 6 H), 6.97 (d, 12 H); ^{13}C NMR ($CDCl_3$) δ 31.06 (t), 51.85 (q), 69.72 (t), 124.55 (d), 129.56 (d), 133.72 (s), 154.77 (s), 169.45 (s). Anal. Calcd for $C_{60}H_{60}O_{18}$: C, 67.42; H, 5.62. Found: C, 67.29; H, 5.88.

Octamethyl Calix[8]arene Octaacetate (18). Ethyl ester **9** furnished **18** (40% yield), mp 189–190 °C: ^1H NMR ($CDCl_3$) δ 3.65 (s, 24 H), 4.15 (br s, 16 H), 4.32 (br s, 16 H), 7.00 (br s, 24 H); ^{13}C NMR ($CDCl_3$) δ 30.15 (t), 51.91 (q), 69.85 (t), 124.81 (d), 129.30 (d), 133.72 (s), 154.90 (s), 169.32 (s). Anal. Calcd for $C_{80}H_{80}O_{24}$: C, 67.42; H, 5.62. Found: C, 67.51; H, 5.83.

Tetra *tert*-Butyl *p-tert*-Butylcalix[4]arene Tetraacetate (19). This compound was prepared from **1** and *tert*-butyl bromoacetate according to the procedure of Ungaro et al.[23]

Tetramethyl *tert*-Butylcalix[4]arene Tetraketone (20). To a stirred mixture of sodium iodide (9.3 g, 0.06 mol) and chloroacetone (5 mL, 0.06 mol) in dry acetone (30 mL) was added, after 18 min, potassium carbonate (8.71 g, 0.06 mol) and *p-tert*-butylcalix[4]arene (**1**) (4.99 g, 0.008 mol) and acetone (300 mL). The reaction mixture was heated under reflux (N_2 atmosphere) with stirring for 5 h and, after cooling, was filtered through a bed of celite which was washed thoroughly with fresh acetone. Evaporation of the solvent furnished an orange solid that was suspended in water at 60 °C and stirred for 2 h. The product was extracted into dichloromethane, and the extract was washed with 0.1 N sodium thiosulfate and water and dried. Removal of the solvent left a pale-yellow solid (5.96 g), which on recrystallization from acetone furnished the tetraketone **20** (3.44 g, 51%) as white crystals, mp 204–207 °C: ν_{max} (KBr) 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.06 (s, 36 H), 2.20 (s, 12 H), 3.17 (d, 4 H, J = 13 Hz), 4.79 (d, 4 H, J = 13 Hz), 4.87 (s, 8 H), 6.79 (s, 8 H); ^1H NMR δ_c ($CDCl_3$) 26.21 (q), 31.29 (t), 31.34 (q), 33.79 (s), 79.14 (t), 125.38 (d), 133.27 (s), 145.05 (s), 152.86 (s), 205.21 (s). Anal. Calcd for $C_{56}H_{72}O_8$: C, 77.08; H, 8.25. Found: C, 77.25; H, 8.38.

Hexamethyl *tert*-Butylcalix[6]arene Hexaketone (21). *p-tert*-Butylcalix[6]arene (2.99 g, 0.003 mol) was treated with chloroacetone (2.2 mL, 0.03 mol) and sodium iodide (4.2 g, 0.03 mol) exactly as described above for the tetramethyl ketone with a reaction time of 27 h under reflux. Workup furnished the hexaketone **21** as a crystalline solid (2.4 g, 59%), mp 237–239 °C (from acetone): IR ν_{max} (KBr) 1735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.19 (s, 54 H), 1.83 (s, 18 H), 4.83 (br s, 12 H), 4.02 (s, 12 H), 7903 (s, 12 H); ^1H NMR δ_c ($CDCl_3$) 25.92 (q), 30.54 (s), 31.45 (q), 34.18 (t), 77.71 (t), 126.44 (d), 132.42 (s), 146.71 (s), 152.10 (s), 204.46 (s). Anal. Calcd for $C_{84}H_{108}O_{12}\cdot 2C_3H_6O$: C, 75.84; H, 8.42. Found: C, 75.74; H, 8.47.

Tetra-1-adamantyl *tert*-Butylcalix[4]arene Tetraketone (23). To a mixture of *p-tert*-butylcalix[4]arene (3.92 g, 0.006 mol) and potassium carbonate (4.13 g, 0.03 mol) in dry acetone (300 mL) was added with stirring a solution of 1-adamantyl bromomethyl ketone (7.62 g, 0.03 mol in dry acetone, 60 mL). The reaction mixture was then heated under reflux under nitrogen for 36 h. The cooled mixture was filtered through celite, and the filtrate and acetone washings of the celite were combined and concentrated to a residue. Trituration with cold ethanol dissolved the residual 1-adamantyl bromomethyl ketone, and the product (5.65 g) was then isolated by filtration. Crystallization from ethanol–dichloromethane yielded tetraketone **23** as white needles (4.7 g, 57.5%), mp >290 °C (dec): IR ν_{max} (KBr) 1705, 1715 cm^{-1}; ^1H NMR ($CDCl_3$) δ_H 1.04 (s, 36 H), 1.67–2.06 (m, 60 H), 3.15 (d, 4 H, J = 13 Hz), 4.86 (d, 4 H, J = 13 Hz), 5.15 (s, 8 H), 6.74 (s, 8 H); ^1H NMR δ_c ($CDCl_3$) 28.07 (d), 31.45 (q), 31.90 (t), 33.72 (s), 36.7 (t), 37.94 (t), 45.22 (t), 74.53 (t), 125.14 (d), 133.65 (s), 144.37 (s), 153.14 (s), 210.96 (s). Anal. Calcd for $C_{92}H_{120}O_8$: C, 81.67; H, 8.81. Found: C, 81.94, H, 8.82.

Tetra-*tert*-butyl *p-tert*-Butylcalix[4]arene Tetraketone (24). A mixture of *p-tert*-butylcalix[4]arene (97.2 g, 0.15 mol), 1-bromopinacolone (107.4 g, 0.60 mol), potassium iodide (99.6 g, 0.60 mol), anhydrous potassium carbonate (154 g), and dry acetone (1.2 L) was heated under

Table V. Crystal Data, Data Collection, and Refinement Details

	7	11	13	20
formula	$C_{60}H_{80}O_{12}\cdot 0.5H_2O$	$C_{66}H_{72}O_{18}$	$C_{56}H_{72}O_{12}$	$C_{56}H_{72}O_8\cdot C_3H_8O$
M_r	1002.3	1153.3	937.2	931.3
$F(000)$	1082	2448	4032	2016
space group	$P\bar{1}$	$C2/c$	$C2/c$	$Pbcn$
crystal system	triclinic	monoclinic	monoclinic	orthorhombic
Z	2	4	8	4
a, Å	12.434(2)	21.906(4)	27.066(6)	19.644(7)
b, Å	15.033(3)	11.805(2)	21.392(6)	12.712(3)
c, Å	17.286(4)	23.534(4)	21.348(7)	22.115(7)
α, deg	103.01(2)	-	-	-
β, deg	102.97(1)	91.79(2)	119.32(2)	-
γ, deg	94.68(1)	-	-	-
V, Å	3038(2)	6083(3)	10,777(1)	5522(5)
D_c, g^{-3}	1.10	1.26	1.16	1.12
μ(Mo K_α), cm^{-1}	0.71	0.85	0.75	0.70
λ, Å	0.71069	0.71069	0.71069	0.71069
θ_{max}	20°	20°	22.3°	20°
T, K	291	291	291	291
scan type	$\omega/2\theta$	$\omega/2\theta$	$\omega/2\theta$	$\omega/2\theta$
ω scan width	0.60+0.35tanθ	0.60+0.35tanθ	0.60+0.35tanθ	0.70+0.35tanθ
unique data	5636	2822	6844	2573
unique data $[I > 3\sigma I]$	3884	1221	3317	1442
final R	0.106	0.074	0.078	0.094
final wR^a	0.117	0.061	0.104	0.134

[a] Final $wR = [\sum w\Delta^2/\sum wF_o^2]^{1/2}$.

reflux with stirring under nitrogen for 17 h. The cooled reaction mixture was filtered through glass-fiber filter paper, and the filtrate was poured into cold water (5.0 L), forming a white precipitate. The mixture was extracted with dichloromethane, and the extract was washed twice with 3% sulfuric acid and twice with water. The dried organic solution was concentrated, leaving a sticky solid. The minimum amount of cold ethanol was added to give a slurry that was filtered. The solid collected was washed with cold ethanol and then was dried overnight at 55 °C to leave a white solid (85 g). This solid was boiled with methoxyethanol (170 mL) and filtered. [The filtrate deposited a solid (24 g) that has been tentatively identified as a diketone diphenol]. The undissolved solid was then boiled with ethanol to leave 42 g (27%) of product which was twice recrystallized from 1,2-dichloroethane to afford pure **24**, mp 278–281 °C; IR ν_{max} (KBr) 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ_H 1.06 (s, 36 H), 1.19 (s, 36 H), 3.13 (d, 4 H, J = 13 Hz), 3.65 (s, $ClCH_2CH_2Cl$), 4.88 (d, 4 H, J = 13 Hz), 5.19 (s, 8 H), 6.75 (s, 8 H); ^1H NMR δ_c ($CDCl_3$) 26.38 (q), 31.45 (q), 31.84 (t), 33.79 (s), 42.69 (s), 74.59 (t), 125.27 (d), 133.59 (s), 144.50 (s), 153.14 (s), 211.30 (s). Anal. Calcd for $C_{70}H_{100}O_8\cdot C_2H_4Cl$: C, 73.72; H, 8.84. Found: C, 73.87; H, 9.01.

Tetraphenyl *p-tert*-Butylcalix[4]arene Tetraketone (25). A mixture of *p-tert*-butylcalix[4]arene (8.1 g, 0.013 mol), sodium iodide (7.5 g, 0.05 mol), anhydrous potassium carbonate (7.7 g, 0.05 mol), phenacyl chloride (7.7 g, 0.05 mol), and dry acetone (150 mL) was heated under reflux under nitrogen for 48 h. The cooled reaction mixture was poured into water (1 L), and the precipitated material was taken up in dichloromethane. The extract was washed with 5% aqueous sodium metabisulfite, water, 3% sulfuric acid, and water and dried. Removal of the solvent gave a light-brown solid (14.1 g), which was boiled in methanol (2 L) and filtered. The solid product (9.2 g, ca. 81% pure) was crystallized from 2-propanol to afford tetraketone **25** (6.0 g, 43%) as colorless needles, mp 222–228 °C: IR ν_{max} 1704 cm^{-1}; ^1H NMR ($CDCl_3$) 1.11 (s, 36 H), 3.28 (d, 4 H, J = 13 Hz), 5.13 (d, 4 H, J = 13 Hz), 5.70 (s, 8 H), 6.84 (s, 8 H), 7.23–7.52 (m, 20 H). Anal. Calcd for $C_{76}H_{80}O_8$: C, 81.39; H, 7.19. Found: C, 81.68; H, 7.33.

Diester Diphenol (28). A mixture of *p-tert*-butylcalix[4]arene (**1**) (1.0 g, 1.54 mmol), potassium carbonate (1.0 g), and ethyl bromoacetate (0.34 mL, 3.09 mmol) in dry acetone (50 mL) was heated under reflux with stirring under nitrogen for 15 h. The cooled solution was filtered through celite, and the filtrate and dichloromethane washings of the celite were combined and concentrated to dryness. Recrystallization of the residue from dichloromethane–ethanol furnished the diester diphenol **28** (0.94 g, 78%), mp 182–184 °C; ^1H NMR ($CDCl_3$) δ 0.96 (s, 18 H), 1.24 (s, 18 H), 1.30 (t, 6 H), 3.2 (d, 4 H, J = 12.6 Hz), 4.23 (q, 4 H), 4.48 (d, 4 H, J = 12.6 Hz), 4.75 (s, 4 H), 6.91 (s, 4 H), 7.11 (s, 4 H), 7.12 (s, 2 H, OH); ^1H NMR δ_c 14.16 (s), 31.06 (q), 31.71 (q), 31.90 (t), 33.85 (s), 33.98 (s), 61.27 (t), 72.45 (t), 125.14 (d), 125.79 (d), 128.06 (s), 132.55 (s), 141.51 (s), 150.35 (s), 150.80 (s), 169.32 (s). Anal. Calcd for $C_{52}H_{68}O_8\cdot EtOH$: C, 74.16; H, 8.45. Found: 74.09; H, 8.46.

Preparation of Complexes. The calixarene derivative (ca. 100–300 mg) was suspended in methanol or acetonitrile (20–40 mL), and the mixture was warmed until a homogeneous solution was obtained. The metal salt (3 equiv) was added, and the mixture was heated again until homogeneous and was filtered. The solution was then allowed to cool slowly to room temperature. After several days, the crystals were collected and recrystallized from the same solvent. The resulting complexes were characterized by combustion analysis, atomic absorption, and spectroscopy.

The following complexes were thus obtained (for convenience only the ^1H NMR chemical shifts are given; the integrations and multiplicities remain the same as those quoted above for the free ligands).

Tetramethyl Ketone 20–LiSCN Complex. Mp > 173 °C (dec) (from acetonitrile); ^1H NMR ($CDCl_3$) δ 1.17, 2.28, 3.32, 4.54, 4.96, 79.07; IR (KBr) 1720, 2050 cm^{-1}. Anal. Calcd for $C_{56}H_{72}O_8\cdot LiSCN\cdot{}^3/_2CH_3CN$: C, 70.92; H, 7.66; N, 3.50; S, 3.21; Li, 0.69. Found: C, 71.00; H, 7.51; N, 3.07; S, 3.34; Li, 0.72.

Tetramethyl Ketone 20–NaSCN Complex. Mp > 210 °C (dec) (from methanol); ^1H NMR ($CDCl_3$) δ 1.14, 2.28, 3.30, 4.23, 4.70, 7.06; IR (KBr) 1730, 2050 cm^{-1}. Anal. Calcd for $C_{56}H_{72}O_8\cdot NaSCN\cdot 2CH_3OH$: C, 69.63; H, 7.86; N, 1.38; S, 3.15; Na, 2.26. Found: C, 69.71; H, 7.80; N, 1.56; S, 2.78; Na, 2.11.

Tetramethyl Ketone 20–KSCN Complex. Mp 215–218 °C (from methanol); ^1H NMR ($CDCl_3$) δ 1.13, 2.26, 3.27, 4.26, 4.67, 7.04; IR (KBr) 1725, 2045 cm^{-1}. Anal. Calcd for $C_{56}H_{72}O_8\cdot KSCN\cdot CH_3OH$: C, 69.54; H, 7.59; N, 1.40; S, 3.19; K, 3.90. Found: C, 69.06; H, 7.66; N, 1.64; S, 2.15; K, 4.29.

Tetra-*tert*-butyl Ketone 24–LiSCN Complex. Mp > 257 °C (dec) (from acetonitrile); ^1H NMR ($CDCl_3$) δ 1.13, 1.26, 3.29, 4.30, 5.03, 6.99; IR (KBr) 1715, 2050 cm^{-1}. Anal. Calcd for $C_{68}H_{96}O_8\cdot LiSCN\cdot CH_3CN$: C, 74.36; H, 8.63; N, 2.44; S, 2.80; Li, 0.61. Found: C, 75.27; H, 8.81; N, 2.10; S, 2.60; Li, 0.47.

Tetra-*tert*-butyl Ketone 24–NaSCN Complex. Mp > 247 °C (dec) (from methanol); ^1H NMR ($CDCl_3$) δ 1.13, 1.28, 3.26, 4.00, 4.72, 7.06; IR (KBr) 1710, 2040 cm^{-1}. Anal. Calcd for $C_{68}H_{96}O_8\cdot NaSCN\cdot CH_3OH$: C, 72.87; H, 8.67; N, 1.21; S, 2.78; Na, 1.99. Found: C, 73.13; H, 8.97, N, 1.43; S, 2.56; Na, 2.18.

Tetra-*tert*-butyl Ketone 24–KSCN Complex. Mp 228–230 °C (from methanol): ^1H NMR ($CDCl_3$) δ 1.14, 1.28, 3.27, 4.16, 4.74, 7.07; IR (KBr) 1770, 2050 cm^{-1}. Anal. Calcd for $C_{68}H_{96}O_8\cdot KSCN\cdot CH_3OH$: C, 71.86; H, 8.55; N, 1.20; S, 2.74; K, 3.34. Found: C, 71.57; H, 8.46; N, 1.40; S, 2.88; K, 3.68.

Tetraadamantyl Ketone 23–LiSCN Complex. Mp 266–269 °C (from acetonitrile); ^1H NMR ($CDCl_3$) δ 1.15, 1.39–2.31, 2.99–3.53, 4.06–4.56, 4.99, 7.01; IR (KBr) 1695, 1705, 2045 cm^{-1}. Anal. Calcd for $C_{92}H_{120}O_8\cdot LiSCN\cdot CH_3CN$: C, 78.20; H, 8.43; N, 1.92; S, 2.20; Li, 0.48. Found: C, 78.17; H, 8.38; N, 1.56; S, 2.11; Li, 0.50.

Tetraadamantyl Ketone 23–NaSCN Complex. Mp > 282 °C (dec) (from acetonitrile); ^1H NMR ($CDCl_3$) δ 1.19, 1.39–2.23, 3.27, 4.00, 4.67, 7.12; IR (KBr) 1705, 2045 cm^{-1}. Anal. Calcd for $C_{92}H_{120}O_8\cdot NaSCN\cdot 3CH_3CN$: C, 76.36; H, 8.28; N, 3.60, S, 2.06; Na, 1.48. Found: C, 76.19; H, 8.25; N, 3.36; S, 2.24; Na, 1.02.

Table VI. Mean Bond Lengths in **7**, **11**, **13**, and **20**

	7	11	13	20
arom C—C	1.39 (1)	1.37 (2)	1.39 (1)	1.39 (2)
C(arom)—C_{sp^3}	1.55 (1)	1.52 (2)	1.50 (1)	1.52 (2)
C_{sp^3}—C_{sp^3}	1.52 (2)	1.30 (3)	1.48 (2)	1.51 (2)
C_{sp^3}—C_{sp^2}	1.49 (1)	1.50 (2)	1.44 (1)	1.50 (2)
C(arom)—O	1.41 (1)	1.42 (1)	1.38 (1)	1.40 (1)
C_{sp^3}—O	1.46 (1)	1.45 (1)	1.42 (1)[a]	1.40 (1)
C_{sp^2}=O	1.19 (1)	1.21 (2)	1.16 (1)[a]	1.19 (1)
C_{sp^2}—O	1.31 (1)	1.30 (2)	1.29 (2)[a]	

[a] Bond lengths of disorder component A not included in the calculations.

Tetraadamantyl Ketone 23–KSCN Complex. Mp > 283 °C (dec) (from acetonitrile; ^{1}H NMR ($CDCl_3$) δ 1.19, 1.38–2.29, 3.27, 4.13, 4.69, 7.11; IR (KBr) 1695, 1705, 2045 cm^{-1}. Anal. Calcd for $C_{92}H_{120}O_8$·KSCN·CH_3CN: C, 76.52; H, 8.25; N, 1.88; S, 2.15; K, 2.62. Found: C, 76.00; H, 8.12; N, 1.67; S, 1.89; K, 3.73.

Tetraethyl Ester 7–NaSCN Complex. Mp 181–184 °C (from methanol); ^{1}H NMR ($CDCl_3$) δ 1.17, 1.38, 3.31, 3.85–4.64, 7.06; IR (KBr) 1735, 2050 cm^{-1}. Anal. Calcd for $C_{60}H_{80}O_{12}$·NaSCN: C, 68.24; H, 7.45; N, 1.30; S, 2.99; Na, 2.14. Found: 68.13; H, 7.21; N, 1.55; S, 2.94; Na, 1.94.

Tetraethyl Ester 7–NaBF$_4$ Complex. Mp 216–220 °C (from methanol); ^{1}H NMR ($CDCl_3$) δ 1.15, 1.36, 3.33, 3.89–4.54, 7.06; IR (KBr) 1740 cm^{-1}. Anal. Calcd for $C_{60}H_{80}O_{12}$·$NaBF_4$: C, 65.37; H, 7.26; B, 0.98; F, 6.89; Na, 2.09. Found: C, 65.74; H, 7.36; B, 0.98; F, 6.42; Na, 1.80.

X-ray Crystal Structure Analysis of 7, 11, 13, and 20. For the four structures, cell parameters and crystal orientation matrices were obtained by a least-squares refinement of the setting angles of 25 reflections ($6° < \theta < 15°$) measured on a Enraf-Nonius CAD4 diffractometer using graphite monochromatized Mo Kα radiation. None of the crystals diffracted well. For each compound, data were corrected for Lorentz and polarization effects; absorption corrections were not considered necessary. There was no evidence in each case for crystal decay in the X-ray beam. For **7**, the crystals are triclinic; space group $P\bar{1}$ was assumed and was confirmed by the analysis. Systematic absences for **11** and **13** allowed the space group to be $C2/c$ or Cc; in each case, the former was assumed and was confirmed by the analysis. For **20**, the orthorhombic space group $Pbcn$ is determined uniquely by the systematic absences.

The structures were solved with the aid of MULTAN 82[48] and were refined by full-matrix least-squares calculations using SHELX[49] or SDP-PLUS.[50] For **7**, one of the *tert*-butyl groups was disordered over two sites, and a partially occupied site with a water of solvation was also found. No allowance was made for hydrogen atoms. In **11** and **13**, fewer than half of the measured data had $I > 3\sigma(I)$ (because the molecules are so loosely held in the crystal lattice). One of the side chains was equally disordered over two sites. The hexamer molecule **11** lies about a crystallographic symmetry; a partially occupied acetone of solvation (disordered about an inversion center) was also found in the asymmetric unit. For **11** and **20**, hydrogen atoms were positioned on geometric ground (C–H, 0.95 Å) and included as riding atoms in the structure factor calculations. Details of the cell data, data collection, and refinement are in Table V. For the refinements, weights were derived from the counting statistics, and scattering factors were from the *International Tables for X-ray Crystallography*.[51] Difference maps computed at the conclusion of the refinements (shift/error < 0.1) were devoid of chemically sensible features. Mean dimensions are summarized in Table VI. Tables of final fractional coordinates, thermal parameters, molecular dimensions, and structure factor listings for **7**, **11**, **13**, and **20** are available as supplementary material. The drawings of the molecules (Figures 3–7) were prepared with the aid of ORTEP.[52]

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Supplementary Material Available: Tables of fractional coordinates, thermal parameters, and molecular dimensions of **7**, **11**, **13**, and **20** (58 pages); tables of calculated and observed structure factors (85 pages). Ordering information is given on any current masthead page.

Dimeric Products and Hydrogen Transfer in the Dissolving Metal Reduction of Camphor[1]

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Abstract: The hydrogen-transfer step in the dissolving metal reduction of ketones in the absence of an added proton donor has been investigated by carrying out the reduction of (+)- and (±)-3-*exo*- and -3-*endo*-deuteriocamphor (**5** and **6**). Reduction to the epimeric alcohols (**3** and **4**) proceeds principally by transfer of an *exo*-hydrogen, with negligible transfer of an *endo*-hydrogen. Enolate formation from camphor using strong, sterically hindered bases gives significant amounts of product arising by removal of an *endo*-hydrogen in contrast to results obtained using hydroxide. A detailed study of the dimeric reduction products from (+)- and (±)-camphor (**1**) indicated that not only were pinacol mixtures formed but a product (**12**) was obtained, which apparently arises from coupling of a ketyl with ketone, followed by β-cleavage of an alkoxyl radical. On the basis of these and other data, a new mechanism for the reduction of ketones by dissolving metals is suggested. The key step in this mechanism is hydrogen transfer from a ketone to a ketyl to afford an α-keto radical and an alkoxide.

The reduction of ketones by dissolving metals, in particular, alkali metals in ammonia or alcohols, is a common synthetic procedure for the conversion of ketones to secondary alcohols. In early work on conformational analysis Barton suggested that these

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