Extended Structures Built on a Triphenoxymethane Platform − C_3-Symmetric, Conformational Mimics of Calix[*n*]arenes

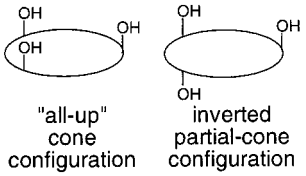
Maarten B. Dinger[a] and Michael J. Scott*[a]

Keywords: Phenoxides / Calixarenes / Molecular recognition / Extraction

A series of C_3-symmetric tris(3,5-dialkyl-2-hydroxyphenyl)-methanes (alkyl = *tert*-butyl, methyl, *tert*-pentyl) have been synthesized in high yield from their respective phenols and fully characterized, including single crystal X-ray structures for two examples. The di-*tert*-butyl-substituted compound, **1a**, has been derivatized to a tris-acid chloride, **4**, which was treated with a variety of amines (dimethylamine, benzylamine, glycine, and alanine) from which the corresponding tris-amides **5**–**8** were formed. The absolute geometry and conformation of the dimethylamine, glycine, and alanine derived systems were determined by X-ray analyses, and in all cases, the three phenolate arms point up with respect to the central methine. Alkali metal binding studies (Li, Na, K, Rb, and Cs) were carried out for the dimethylamine, benzylamine, and glycine compounds **5**–**7**, and these compounds were found to have some selectivity for potassium cations. NMR studies demonstrate that C_3 symmetry is retained in all the compounds and the stoichiometry for lithium ion complexation is 1:1, whereas two ligands are needed to complex sodium cations. Crystal structures of the dimethylamine derivative with lithium picrate and the benzylamine and glycine derivatives with sodium tetraphenylborate were also determined.

Introduction

By virtue of their predisposition to serve as host molecules, binding various neutral and ionic guest species, much attention has focused on the development of calix[*n*]arene-based macrocyclic ligands.[1−4] These macrocycles maintain reactive hydroxyl groups about their rims, and with the appropriate pendant arms, macrocycles with diverse properties can be produced. Chemical modifications with esters,[5] glycols,[3] sugars,[6] Schiff bases,[7] and peptides[8] produce compounds capable of binding a range of substrates from alkali[9] and lanthanide metals[9] to proteins.[10] Unfortunately, calixarene-like macrocycles with only three oxygen donors are often difficult to prepare. Compounds such as hexahomooxacalix[3]arenes and trihydroxy[3.3.3]metacyclophanes, require longer linkers between the phenoxide ligands.[11−13] With the increased flexibility associated with the larger cyclic structure, these macrocycles adopt multiple configurations in solution (Scheme 1), an impediment to molecular recognition. Moreover, the systematic substitution of only three of the phenolic oxygens is quite troublesome for most of the calix[*n*]arenes. Trisubstituted macrocycles can be isolated through the selective functionalization of calix[6]arene,[14−17] but, as before, the larger backbone of this compound engenders the macrocycle with immense flexibility,[18] complicating the solution structure of the larger constructs. Conformationally rigid molecules with three oxygen donor arms have been developed from *scyllo*-inositol and *cis,cis*-cyclododecane-1,5,9-triol, but these molecules are quite difficult to prepare, requiring many complex synthetic manipulations.[19] Hence, the development of simple, rigid, compact molecules with only three, oriented oxygen donor arms has been problematic.



Scheme 1

Molecules containing three appendages offer many advantages for selective recognition, especially for metal ions. Each of the three arms can be designed to provide two donor groups to a metal center allowing the metal to adopt either octahedral or trigonal prismatic stereochemistry depending on its preference. Nature has found this to be a particularly adept binding motif for metal ions. For example, the three catecholate arms of the protein Enterobactin are perfectly poised to seize an iron atom.[20]

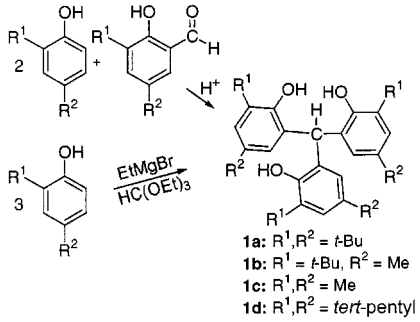
Intent on the isolation of small, uncomplicated, conformational mimics of macrocycles including calix[4]arene, we examined the literature and came across an interesting report of the preparation of a series of compounds in which three phenoxide groups are joined to a common carbon atom forming tris-phenoxidemethanes.[21] If sufficient rigidity could be built into these unique molecules, we theorized that they would serve as an ideal platform for the preparation of extended structures containing only three appendages. Herein, we report our investigations into the preparation of materials utilizing the tris(3,5-dialkyl-2-hydroxyphenyl)methane framework and an initial examination into the alkali metal binding properties of these extended structures.

[a] Department of Chemistry, University of Florida
P. O. Box 117200 Gainesville, FL 32611-7200, USA
Fax: (internat.) +1-352/392-3255
Email: mjscott@chem.ufl.edu

  1434−193X/00/0713−2467 $ 17.50+.50/0

Results and Discussion

As outlined in Scheme 2, ligands with divergent steric properties can be prepared through two different synthetic routes. Following addition of dry hydrogen chloride to a solution of a salicylaldehyde and phenol, the tris(3,5-dialkyl-2-hydroxyphenyl)methanes **1** are isolated in high yield directly from the methanol solution. Offering an added advantage, both three fold symmetric and mirror-symmetric compounds can be formed using this methodology through the judicious choice of the two starting materials. Facilitating isolation and purification of the products, the precursors are all readily soluble in methanol, yet the tris(3,5-dialkyl-2-hydroxyphenyl)methanes show only negligible solubility. Product isolation and purification is quite simple; the desired products are simply filtered off and any remaining starting materials or by-products are removed with washing of the solid. Typically, condensation reactions of this type are carried out in acetic acid,[25−27] but this solvent is unsatisfactory for the formation of **1a**−**1d**, with only very low yields collected from the acid solution, despite the insolubility of the compounds in the solvent. There is also precedence for the use of concentrated sulfuric acid as the catalyst; indeed the first triarylmethanes formed by the condensation of benzaldehyde and phenols were obtained by this route.[28] Nonetheless, when concentrated sulfuric acid was added to a methanolic solution of the aldehyde and phenol, no color change occurred and tris(3,5-dialkyl-2-hydroxyphenyl)methanes could not be detected, with NMR showing only starting materials.



Scheme 2

Although in somewhat lower yields, the ligands **1a**, **1b**, and **1d** can also be prepared directly from the phenolic precursors following a synthetic scheme originally developed by Casnati and co-workers.[21] Deprotonation of the phenol with a Grignard reagent and addition of ethyl orthoformate affords the tris-phenoxides in only moderate yield, but given the difficulties often associated with the synthesis of the salicaldehydes from the phenol, including the use of hazardous tin reagents, this procedure is normally much more convenient for the production of the threefold symmetric phenoxides. Moreover, in contrast to the acid condensation, the metal directed synthesis allows for the preparation of tris(3-alkyl-2-hydroxyphenyl)methanes lacking alkyl substitution at the *para*-position of the phenoxide arms. Finally, this reaction scheme is easier to scale up for the preparation of large quantities of **1a**, **1b**, and **1d** since it avoids the use of dry hydrogen chloride, and we routinely isolate the materials in 25 gram quantities using this procedure. Unfortunately, this synthesis is less general than the phenol/salicaldehyde condensation, and is unsatisfactory for the synthesis of **1c**, or any tris-phenoxymethane featuring a methyl substituent in the *ortho* position.[21]

As opposed to the calix[*n*]arene macrocycles where intramolecular hydrogen-bonding induces a cone-like conformation,[2] the central carbon atoms in **1a**−**d** prevent the ligand arms from aligning properly for this type of interaction. Instead, intermolecular communication between the rigid, C_3 symmetric ligands is favored. In the solid-state structure of **1a** depicted in Figure 1 (crystallographic data presented in Table 2), the two rotamers of the ligand form a dimeric structure producing six equivalent hydrogen bonds. The shortest oxygen−oxygen distance between the two convergent ligands is more than ≈2.95 Å, suggesting only a minor degree of orbital communication through this hydrogen bond. Decreasing the steric constraints at the 2- and 4-positions of the phenol engenders the ligand with a higher degree of rotational flexibility. In the solid state structure of **1c** (Figure 2, Table 2), the intermolecular oxygen−oxygen separation is reduced to ≈2.73 Å, and the ligands adopt a tetrahedral arrangement with tris-phenoxide ligands residing on the four corners with each of the three oxygen donors orientated towards a different corner. Concomitant

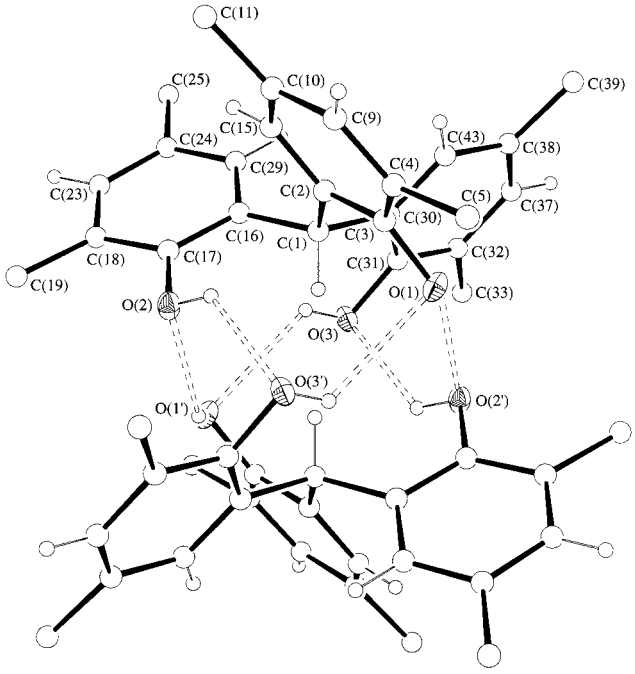


Figure 1. Diagram of **1a** · C_6H_6 hydrogen-bonded dimer, showing 30% probability ellipsoids for the oxygen atoms, and atom labeling scheme. Only one molecule of the two unique molecules in the asymmetric unit is shown. The numbering scheme for the remaining molecule is analogous. *tert*-Butyl and methyl groups and the benzene solvate are omitted, for clarity. Selected bond lengths [Å] and angles [°]: C(1)−C(2), 1.530(3); O(1)···O(2′), 3.114(5); O(2)···O(3′), 2.972(5); O(3)···O(1′), 3.009(5); O(1)H···O(2′), 2.529; O(2)H···O(3′), 2.368; O(3)H···O(1′); 2.507; O(1)−H−O(2′), 132.4(2); O(2)−H−O(3′), 127.8(2); O(3)−H−O(1′), 121.7(2)

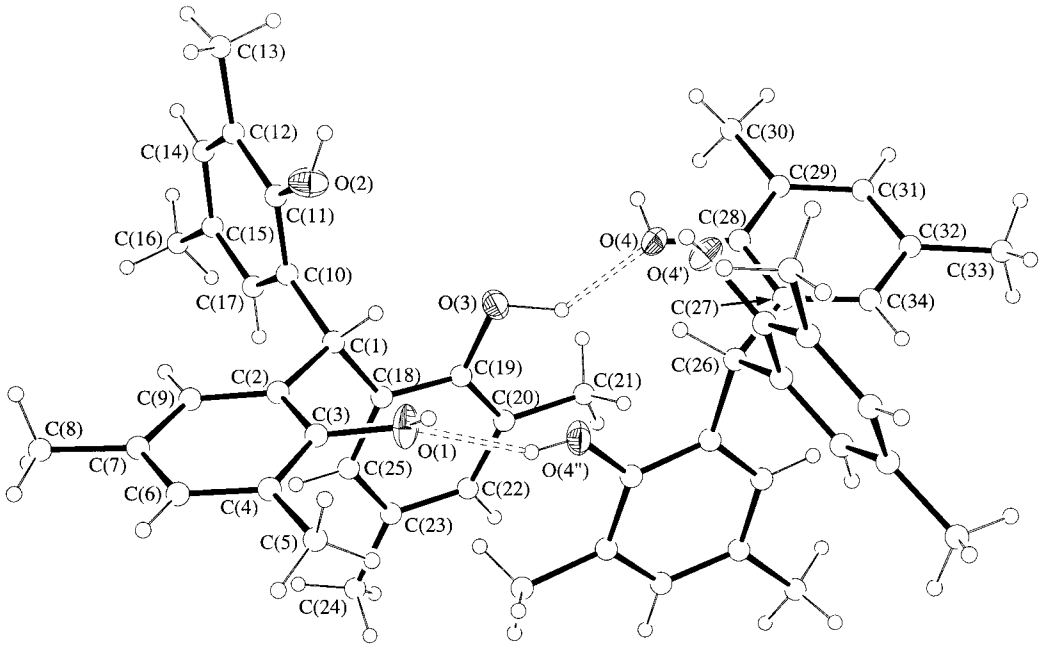
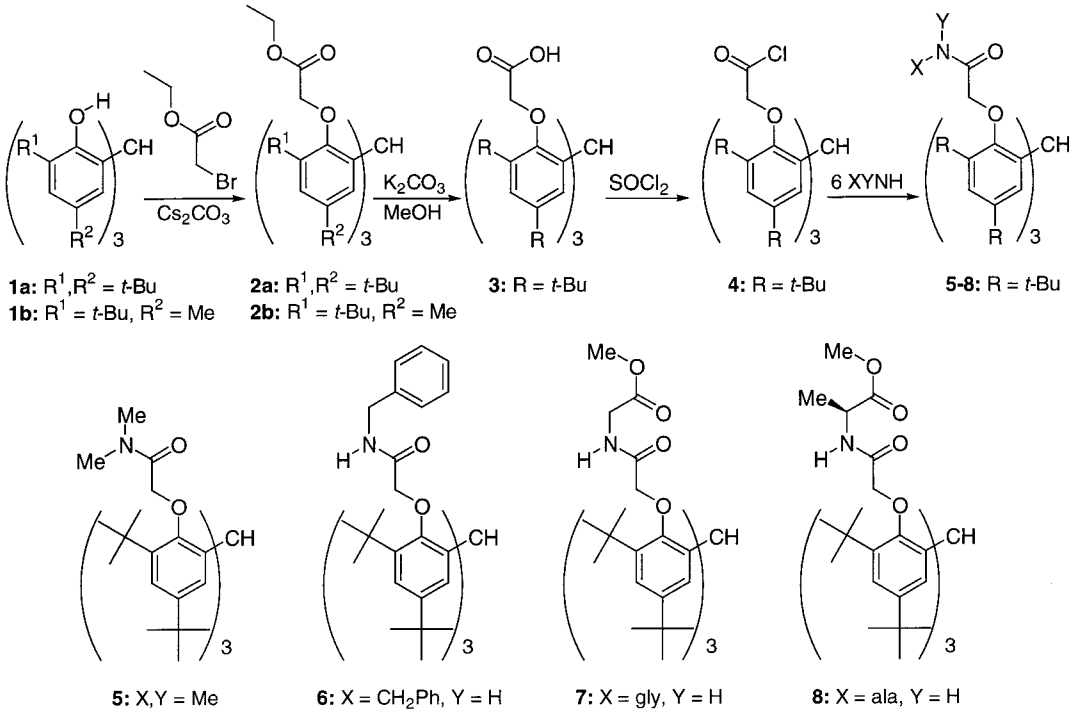


Figure 2. Crystal structure of **1c** showing half of the hydrogen-bonded tetramer, with 30% probability ellipsoids for the oxygen atoms, and atom-labeling scheme. C(26) resides on a C_3 crystallographic axis, and the unlabelled atoms of the molecule are generated by this symmetry operation. Selected bond lengths [Å] and angles [°]: C(1)−C(2), 1.518(5); O(1)O(3′), 2.732(5); O(2)O(2′), 2.746(5); O(3)O(4), 2.816(5); O(4")O(1), 2.730(5); O(1)HO(3′), 1.825; O(2)HO(2′), 1.872; O(3)HO(4); 1.948; O(4")HO(1), 2.092; O(1)−H−O(3′), 151.6(4); O(2)−H−O(2′), 161.3(4); O(3)−H−O(4), 134.2(4); O(4")−H−O(1), 139.0(4)

with the strengthening of the hydrogen-bonding interaction, the frequency of the hydroxide infrared stretch in the solid state decreases from 3503 cm^{-1} in **1a** to 3460 cm^{-1} in **1c**.

As is the case for calix[*n*]arenes,[1−3] the rigidity of the tris(3,5-dialkyl-2-hydroxyphenyl)methane platforms, notably **1a**, permits the construction of larger ligand systems with well-defined structures. A careful examination of the literature provides an overabundance of methodology for the derivatization of calix[*n*]arenes,[1−3,29,30] and many of the procedures are directly applicable to the tris-phenoxide system. Following the simple procedures outlined in Scheme 3, reactive groups can be placed on the periphery of the ligand, thus allowing a wide scope of organic fragments to be incorporated onto the platform. In the develop-



Scheme 3

ment of these procedures, the reactivity of **1a** was found to be quite comparable to calix[4]arene, although deprotonation of all three phenoxide groups requires the use of a stronger base, cesium carbonate, instead of the more typical reagent, potassium carbonate. The yields for these reactions are all excellent, and the insolubility of the products in polar solvents greatly facilitates the purification and eliminates any need for chromatography. The acid chloride **4** can be isolated in multigram quantities and it is stable indefinitely in the absence of moisture, facilitating the preparation of extended structures.

Perhaps one of the most interesting features of the complex structures derived from the calix[*n*]arene platform is their ability to selectively bind metal ions, and as depicted in Scheme 3, addition of six equivalents of an amine to the phenoxyacetyl chloride group in **4** allows for incorporation of many different groups, from simple amines to extended peptides, onto the tris-phenoxide backbone. Three different extended structures were prepared to test the ability of these compounds to extract alkali metal ions: tris(3,5-di-*tert*-butyl-2-[(dimethylamido)methoxy]phenyl)methane (**5**) which contains alkyl amido groups, normally one of the most proficient alkali metal binders in calix[4]arenes,[31] tris(3,5-di-*tert*-butyl-2-[(benzylaminocarbonyl)methoxy]phenyl)-methane (**6**), and tris{3,5-di-*tert*-butyl-2-[*N*-(methylglycyl)carbonylmethoxy]phenyl}methane (**7**) with longer amino-acid arms. The ligand tris{3,5-di-*tert*-butyl-2-[*N*-(methylalanyl)carbonylmethoxy]phenyl]methane (**8**) was also prepared to allow for a comparison of the hydrogen bonding interactions within arms with different amino acid groups.

Upon irradiation of the hydrogen on the central carbon atom in **1a**, NOE enhancements are clearly evident in the ^{1}H NMR transitions for one set of aryl rings as well as the oxo protons, intimating that the aryl rings freely rotate on the NMR timescale. Incorporation of groups onto the framework, however, appears to preclude this process as no NOE enhancements are evident between the ligand arms and the aryl rings in compounds **2**–**8** in solution at room temperature. Supporting this assignment, the solid-state structures of compounds **2b**, **3**, **4**, **5**, **7**, and **8** were all determined (Tables 2 and 3), and the arms in all of these compounds are oriented in the same direction. From a comparison of the crystal structures of **2a**[32] and **2b**, a few additional conclusions can be drawn. For the preparation of compounds with extended arms, it is essential to include sterically encumbering groups at the *para*-position of the aryl rings. With small substituents at this location, the aryl rings can rotate to reduce unfavorable steric interaction and the arms splay out away from each other. To maintain favorable binding properties, the platform must include groups such as *tert*-butyl or *tert*-pentyl at this *para*-position, which restrict the rotation of the phenoxide rings relative to each other.

Often, the arms in these extended structures exhibit extensive intramolecular hydrogen-bonding interactions, particularly between amide hydrogens and the phenolic oxygens, and these contacts may help to rigidify the arms of the ligand. An ORTEP diagram of **7**, highlighting several of these hydrogen bonds, is contained in Figure 3 and crystallographic information can be found in Table 2. In the crystal, the molecule is rigorously three fold symmetric with the amide nitrogen interacting with an intra-arm phenolic group [N···O 2.658(9) Å], in addition to an adjacent carbonyl oxygen atom [N···O 2.905(9) Å].

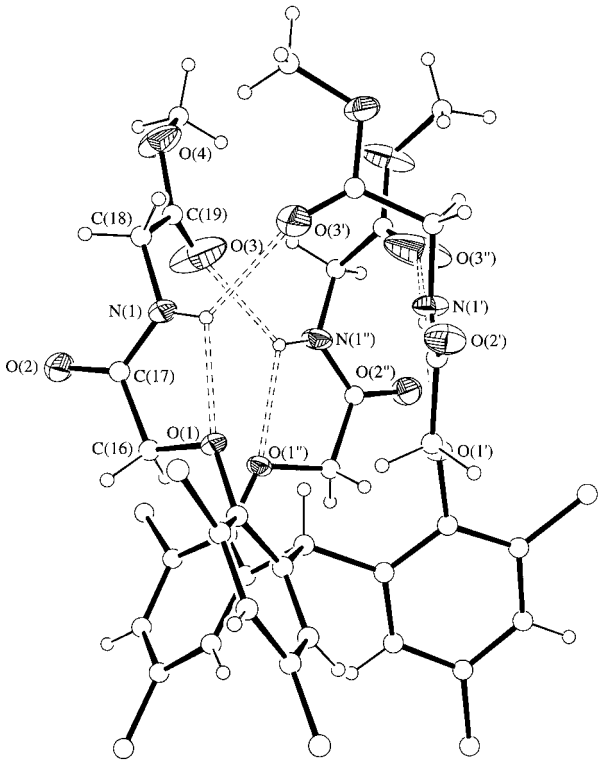


Figure 3. Diagram of $7 \cdot {}^1/_2\ C_5H_{12}$, showing 30% probability ellipsoids and atom-labeling scheme. Primed, double primed, and unprimed atoms are all related by a 3-fold symmetry operation. Only one of two unique arms in the asymmetric unit is shown. The remaining molecule follows an analogous numbering scheme. The disordered pentane solvate has been omitted for clarity. Selected bond lengths [Å] and angles [°]: N(1)−O(3′), 2.905(9); N(1)−O(1), 2.658(9); N(1)H−O(3′), 2.304; N(1)H−O(1), 2.263; N(1)−H(1)−O(3′), 127.1(8); N(1)−H(1)−O(1), 108.0(8)

Reasoning that exchange of the glycine arms with other amino acids would disrupt the hydrogen bonding interactions evident in the solid-state structure of **7**, compound **4** was treated with six equivalents of the methyl ester of L-alanine to afford tris{3,5-di-*tert*-butyl-2-[*N*-(methylalanyl)carbonylmethoxy]phenyl}methane (**8**) in high yield. The solid-state structure is depicted in Figure 4 while important metric data can be found in Table 3. As expected, placement of a methyl group on the arm disrupts the hydrogen-bonding between adjacent arms, and the amide nitrogen instead interacts with both the ester carbonyl [N···O 2.680(9) Å] and a phenolic oxygen of the same residue [N···O 2.635(9) Å]. While both **7** and **8** exhibit extensive hydrogen-bonding in the solid lattice, these interactions are only weak in solution, highlighted by the temperature dependent shifts ([D$_6$]DMSO) of the amide nitrogens from 293 to 353 K of $5.4 \cdot 10^{-3}$ ppm K^{-1} and $4.7 \cdot 10^{-3}$ ppm K^{-1}, respectively.[33,34]

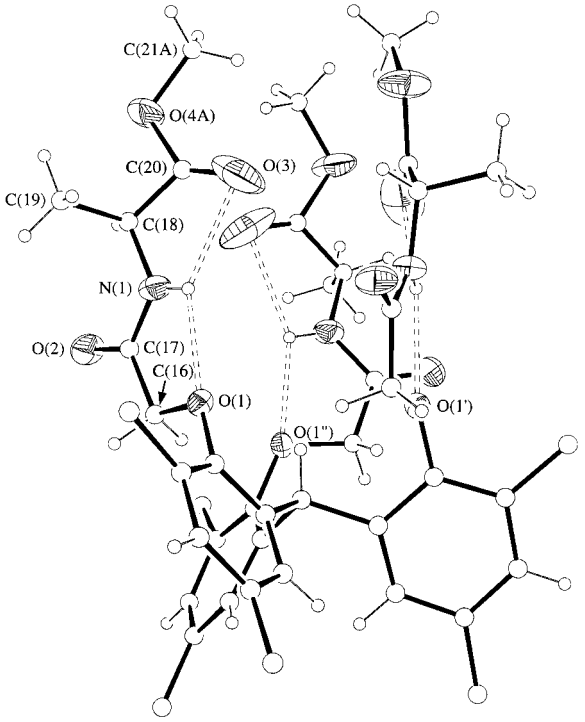


Figure 4. Diagram of **8** · $CHCl_3$, showing 30% probability ellipsoids for the oxygen and nitrogen atoms, and atom-labeling scheme. Primed, double primed, and unprimed atoms are all related by a 3-fold symmetry operation. The remaining molecule follows an analogous numbering scheme. The chloroform solvate has been omitted for clarity. Selected bond lengths [Å] and angles [°]: N(1)−O(3), 2.680(9); N(1)−O(1), 2.635(9); N(1)H−O(3), 2.352; N(1)H−O(1), 2.248; N(1)−H(1)−O(3), 103.1(8); N(1)−H(1)−O(1), 107.3(8)

Extraction of Alkali Metal Ions

Following the methodology of Cram and co-workers,[22] the association constants (K_a) for the complexation of **5**, **6**, and **7** to the alkali metals were determined in $H_2O/CDCl_3$, and the results are presented in Table 1. Although **5** does

Table 1. Comparison of R, K_a, and $-\Delta G°$ for tripodal phenoxide hosts complexing picrate salt guests in $CHCl_3$ at 25°C[22]; figures within ±10% in multiple experiments; stoichiometry, guest/host, for extractions was assumed as 1:1; NMR data may suggest a different stoichiometry for the larger cations

Compound	Picrate salt	R[a]	$K_a \times 10^{-3}$ [M^{-1}][b]	$-\Delta G°$ [kcal/mol]	% extracted
5	Li	0.1988	1210	8.3	22
	Na	0.2249	1233	8.3	25
	K	0.3231	1815	8.5	36
	Rb	0.2394	1191	8.3	30
	Cs	0.2359	977	8.2	32
6	Li	0.0655	251	7.4	9
	Na	0.0852	284	7.4	12
	K	0.1641	490	7.8	17
	Rb	0.1152	364	7.6	17
	Cs	0.1018	260	7.4	16
7	Li	0.0521	191	7.2	6
	Na	0.0513	153	7.1	6
	K	0.1538	443	7.7	18
	Rb	0.0824	234	7.3	13
	Cs	0.0848	205	7.2	10

[a] [Guest]/[host] in $CHCl_3$ layer at equilibrium. – [b] Association constant (see Equation 1).

$$H + M^+Pic^- \underset{}{\overset{K_a}{\rightleftharpoons}} M^+ \cdot H \cdot Pic^- \quad (1)$$

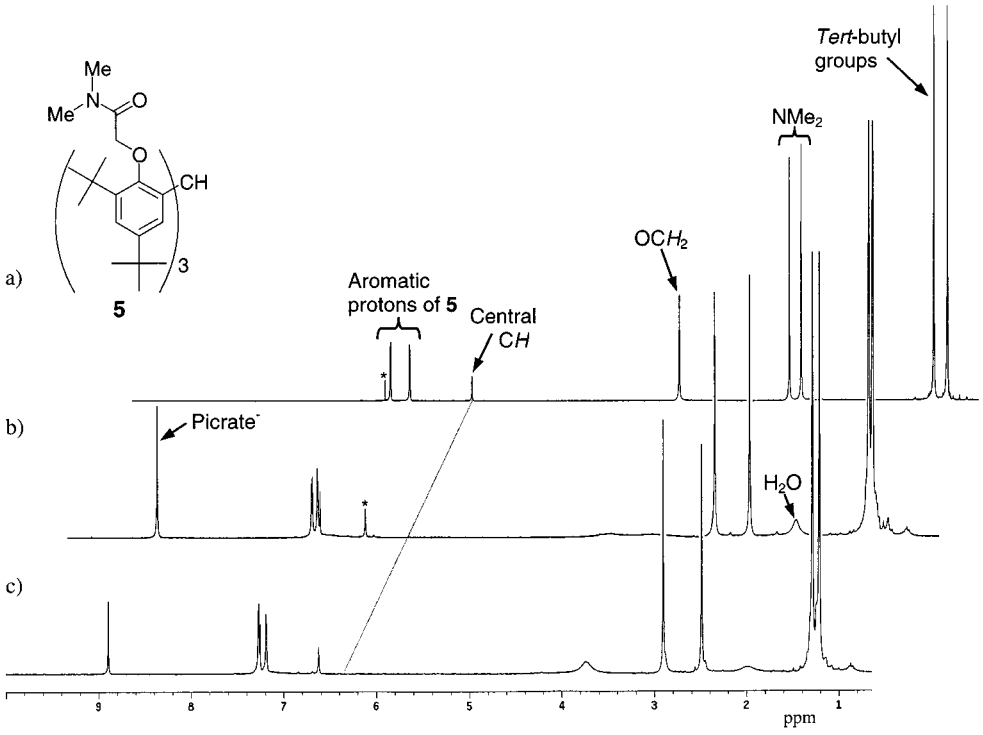


Figure 5. ^1H NMR spectra (300 MHz) of a) free **5**, b) **5** + excess lithium picrate and c) **5** + excess sodium picrate, in $CDCl_3$ after filtration. The peaks labeled * are from residual $CHCl_3$

not exhibit a particularly high degree of selectivity for the alkali metal ions, the association values do indicate that the molecule is an effective binder, on the order normally associated with calix[*n*]arenes.[5,31,35] As depicted in Figure 5, the solution structure of the lithium and sodium complexes of **5** are threefold symmetric on the time scale of the experiment, with one ligand ligating each lithium ion, while two ligands are required to bind to a sodium atom. Removing one of the alkyl substituents from the amide nitrogen decreases the electron density of the carbonyl oxygen, and **6** is a much less effective binder for all the alkali metal ions.

In order to further probe the binding properties of these ligands, the solid-state structure of the lithium picrate complex with **5** was determined, and it is depicted in Figure 6. In this complex, two water molecules bridge two metal centers, forming a dinuclear species. The water bridge is somewhat asymmetric with Li−OH_2 distances of 2.009(5) and 2.082(5) Å, and the coordination sphere of the metal contains three additional oxygen atom ligands, two carbonyl groups and one phenoxide oxygen from two different arms of **5**. The bridging molecules are further stabilized through the formation of two hydrogen bonding interactions, one to the carbonyl group on the remaining dimethylamido arm and one to a phenoxide oxygen atom. The asymmetry witnessed in these species is inconsistent with the NMR data presented in Figure 5, suggesting an alternative, symmetric species exists in solution on the time scale of the NMR experiment.

Repeated attempts to grow single crystals of the sodium complex of **5** were unsuccessful, but crystals of a complex of **6** and sodium tetraphenylborate were isolated. Although the tetraphenylborate anion was severely disordered in the crystal lattice, which prohibits a detailed discussion of the structure, the coordination environment of the metal center was unambiguously identified. As portrayed in Figure 7, the oxygen atoms from two separate threefold symmetric ligands bind to the metal in an octahedral arrangement with Na−O distances ranging from 2.366(4) to 2.375(4) Å. While the local environment about the sodium ion closely resembles the structure of potassium bound to the carbonyl groups in the cyclic dodecadepsipeptide valinomycin,[36] a

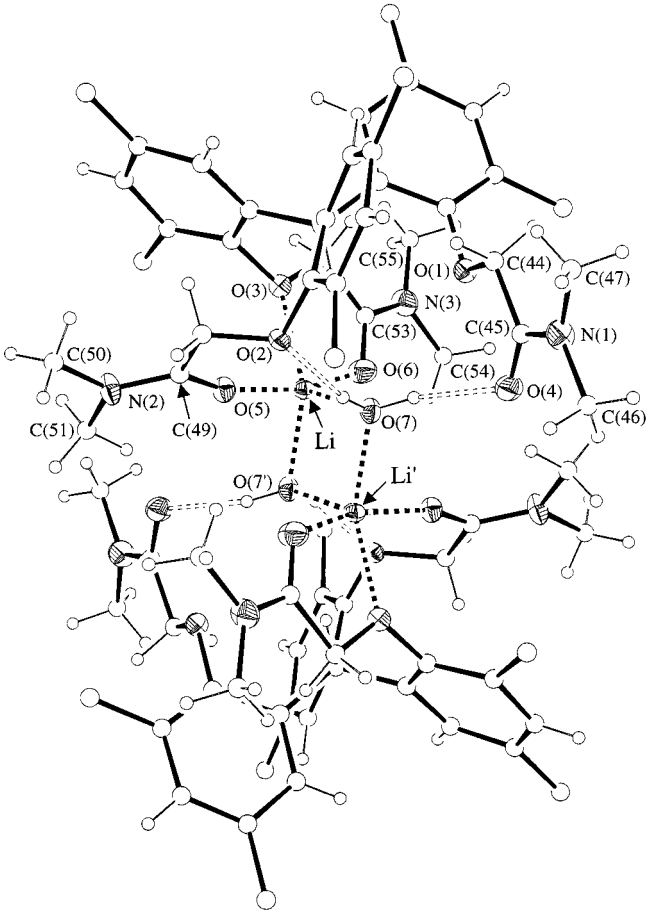


Figure 6. Crystal structure of $\mathbf{5}_2Li_2[Li_2picrate_4] \cdot 2\,C_6H_6 \cdot 2\,H_2O$, showing 30% probability ellipsoids for the oxygen, nitrogen and lithium atoms, and atom labeling scheme. The complex is centrosymmetric and only the unique atoms are labeled. The methyl carbons of *tert*-butyl groups and the $[Li_2picrate_4]^{2-}$ counter-ion have been omitted for clarity. Selected bond lengths [Å] and angles [°]: Li−O(3), 2.136(5); Li−O(5), 2.004(5); Li−O(6), 1.951(5); Li−O(7), 2.009(5); Li−O(7′), 2.082(5); O(7)H−O(2), 2.082; O(7)H−O(4), 1.982; O(3)−Li−O(7), 146.4(2); O(3)−Li−O(7′), 120.1(2); O(5)−Li−O(6), 164.3(3); Li−O(7)−Li′, 86.5(2)

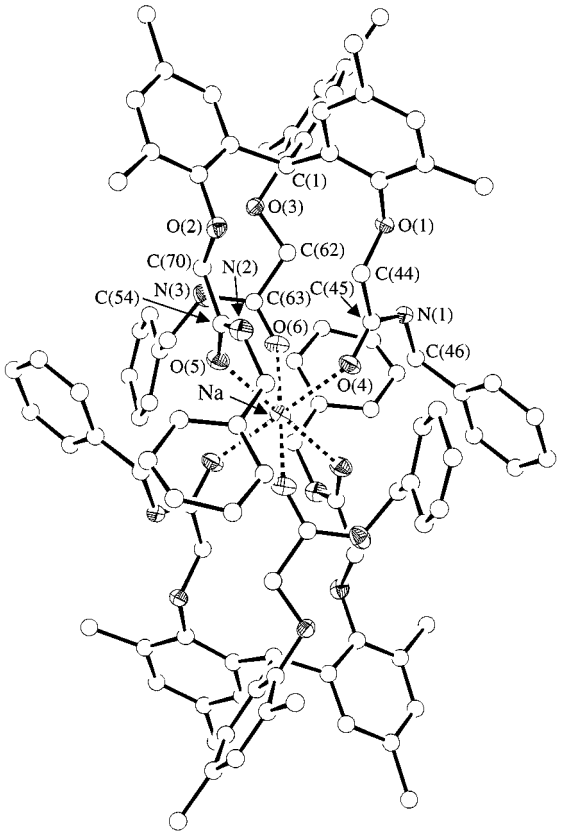


Figure 7. Crystal structure of $\mathbf{6}_2NaBPh_4 \cdot 4.5$ THF, showing 30% probability ellipsoids for the oxygen, nitrogen and sodium atoms, and atom labeling scheme. The complex resides on a crystallographic inversion center and only the symmetry unique atoms are labeled. The disordered benzyl and *tert*-butyl groups have been omitted, together with the BPh_4^-, THF solvates, and hydrogen atoms. Hydrogen bonds are evident between amide nitrogen and phenolic oxygen atoms. Selected distances [Å] and angles [°]: Na−O(5), 2.366(4); Na−O(6), 2.372(4); Na−O(4), 2.375(4); N(1)H−O(1), 2.290; N(2)H−O(2), 2.220; N(3)H−O(3), 2.214; O(5)−Na−O(6), 83.6(2); O(5)−Na−O(4), 86.6(2); O(6)−Na−O(4), 87.4(1)

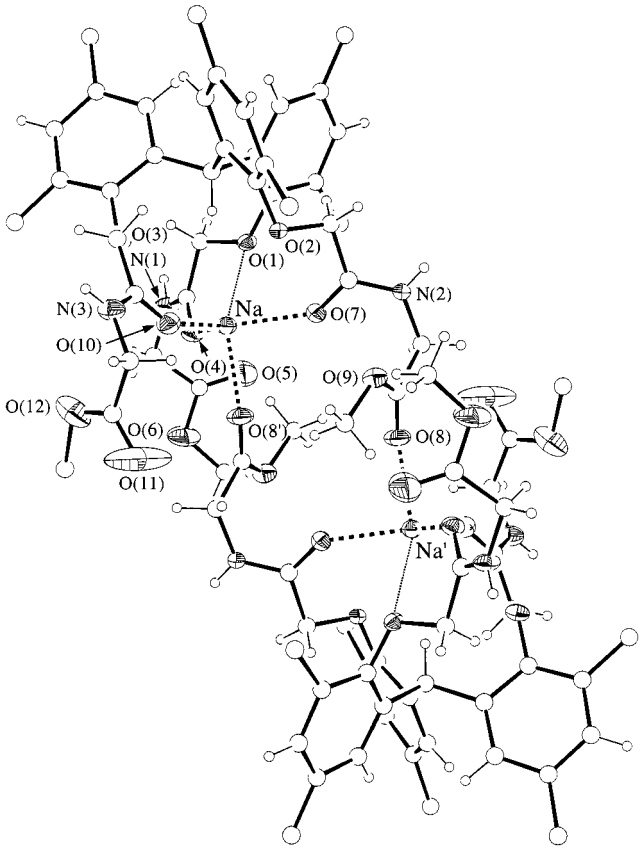


Figure 8. Crystal structure of $\mathbf{7}_2Na_2(BPh_4)_2 \cdot {}^1/_8\,C_6H_{14} \cdot {}^2/_3\,THF$, showing 30% probability ellipsoids for the oxygen, nitrogen and sodium atoms, and atom labeling scheme. The complex is centrosymmetric and prime and unprimed atoms are related by symmetry. The methyl carbons of the *tert*-butyl groups, BPh_4^- counter-ion and solvent molecules have been omitted for clarity. Selected bond lengths [Å] and angles [°]: Na−O(7), 2.264(2); Na−O(10), 2.271(3); Na−O(8′), 2.279(3); N(1)H−O(1), 2.290; Na−O(1), 2.825(2); O(7)−Na−O(10), 115.3(1); O(7)−Na−O(8′), 87.9(1); O(7)−Na−O(4), 123.98(9); O(4)−Na−O(10), 120.5(1); O(4)−Na−O(8′), 94.96(9)

direct comparison to the structure of the sodium complex of valinomycin[37] is uninformative. In the presence of picrate, the sodium ion will only coordinate to four of the carbonyl groups of valinomycin with a water molecule and the picrate ion filling the remaining coordination sphere of the metal ion. In metal complexes prepared with both **5** and **6**, there was no direct evidence of any interaction between the metal ions and the picrate anion.

Given the tendency of **6** to form this octahedral structure with two different ligands binding to the one sodium ion, the reaction of **5** and sodium picrate may form an analogous species, and this formulation would be consistent with the ^{1}H NMR data presented in Figure 5. Interestingly, in the complex presented in Figure 7, the position of each ligand arm and the orientation of the carbonyl group is stabilized for metal binding by a strong intramolecular hydrogen bond between the phenoxide oxygen and amide [avg. N···O 2.625(7) Å], but this type of interaction cannot occur in complexes of **5**.

In an attempt to improve the binding selectivity of the extended structures for the alkali metal ions, **7** was designed to present the metal ion with two different sets of donor groups, the three carbonyl oxygens from the amide linkage and the three ester carbonyl groups. Even though the glycine arms present the metals with an unfavorable seven-membered chelate ring, an enhanced preference for potassium over all the other alkali metals is evident in Table 1. As was the case for both **5** and **6**, the solution ^{1}H NMR data exhibits threefold symmetry for the metal complexes, but in contrast to **5** and **6,** integration of the NMR data indicates only one ligand is required to extract the larger metal ions. On the time scale of the NMR experiment, each of the three arms provides, on average, two donor atoms to these metal centers.

Entirely inconsistent with the C_3 symmetry witnessed in the solution NMR data, the complex of **7** and sodium tetraphenylborate adopts an asymmetric orientation in the solid-state (Figure 8, Table 3), but this structure does confirm the one to one ligand to metal stoichiometry. The difference between the solid-state and solution structure may be brought about by the unfavorable chelate rings presented to the metal by the oxygen donors of the glycine arms. The complex crystallizes as a dinuclear species with one ester carbonyl group bridging to a sodium center of an adjacent ligand. The three amide carbonyl linkages in **7** complete the coordination sphere of the metal. At 2.344(2) Å, one of the bonds to an amide carbonyl is longer than the other three Na−O distances [2.264(2) to 2.279(3) Å] presumably to allow for an extremely long interaction of 2.825(2) Å with a phenoxide oxygen atom on the same glycine residue. All attempts to crystallize **7** with potassium ions were unsuccessful.

Conclusion

With only three arms locked in alignment, the ligands constructed on the framework of **1a** are clearly distinct from the well-studied calix[*n*]arenes, and yet, this scaffold retains the simplicity of the synthetic manipulation of the calix[*n*]arene system. Having only three appendages, a variety of extended arms can be secured to the tris-phenoxide platform and this ligand has the ability to present a metal with an octahedral array of binding sites. The development of extended macromolecular complexes with these platforms may afford compounds capable of selectively binding metal ions, clusters, salts, and organic substrates. Investigations into the binding properties of this unique ligand class with different appendages including amino acid chains and carbamoylmethylphosphane oxides (CMPO),[38] designed to recognize actinide ions, are currently underway.

Experimental Section

General Remarks: ^{1}H- and ^{13}C NMR spectra were recorded in $CDCl_3$ solvent, unless otherwise stated, with a Varian VXR-300 spectrometer at 299.95 and 75.43 MHz for the proton and carbon channels, respectively. IR spectra were recorded as KBr discs, unless otherwise stated, with a Bruker Vector-22 instrument with a 4 cm^{-1} resolution.

Tris(3,5-dialkyl-2-hydroxyphenyl)methanes (1). − General Procedure: Powdered 2,4-dialkylphenol (2 equiv.) and 3,5-dialkyl-4-hydroxybenzaldehyde[39] (1 equiv.) were dissolved in methanol. The resulting solutions were immersed in ice baths and charged with dry hydrogen chloride. The reaction mixtures rapidly turned red concomitant with precipitate formation. After two hours the HCl source was replaced with a drying tube, and the reactions allowed to stir at room temperature for two days. **CAUTION:** The flask should be vented to prevent pressure buildup. The solids were filtered off and thoroughly washed with methanol to give pure **1** as white powders.

Alternatively, compounds **1a**, **1b**, and **1d** could be prepared by using a modified procedure reported by Casnati et al.[21] To a solution of phenol in anhydrous diethyl ether was added, dropwise, an equivalent of ethylmagnesium bromide. When the evolution of ethane had ceased, a third of an equivalent of triethyl orthoformate was added. The resulting solution was heated, allowing the ether to evaporate, and occasionally a small amount of toluene was added to aid mixing. The mixture was heated to 100°C for 12 hours, during which time the solution became deep blue, then gradually becoming yellow often with precipitate formation. After allowing the mixture to cool, hydrochloric acid (2 M) was added, and the product extracted into diethyl ether. Evaporation of the solvents left a viscous oil which, upon addition of methanol, precipitated out a white solid. Filtration and subsequent washing with methanol gave the corresponding tris(3,5-dialkyl-2-hydroxyphenyl)methanes as white powders in ca. 65% yield.

1a: Yield 78%. − M.p. 260°C (decomposed without melting). − IR: $\tilde{\nu}$ [cm^{-1}] 3503 (OH). − ^{1}H NMR: δ = 1.14 (s, 27 H, *t*Bu), 1.34 (s, 27 H, *t*Bu), 4.83 (s, 3 H, O*H*), 5.64 (s, 1 H, C*H*), 6.64 (d, *J* = 2.4 Hz, 3 H, Ar-H), 7.28 (d, *J* = 2.4 Hz, 3 H, Ar-H). − ^{13}C NMR: δ = 29.8, 31.4 [C(*C*H$_3$)$_3$], 34.3, 35.0 [*C*(CH$_3$)$_3$], 42.5 (*C*H), 123.5, 125.3, 137.1, 143.2, 150.8 (C_{Ar}). − MS (FAB) *m*/*z* (%) = 629 [M]$^+$ (40), 423 [M − *t*Bu$_2$C$_6$H$_3$OH]$^+$ (100), 365 [M − *t*Bu$_2$C$_6$H$_3$OH − *t*Bu]$^+$ (76). − $C_{43}H_{64}O_3$ (628.97): calcd. C 82.11, H 10.26; found C 82.17, H 10.32.

1b: Yield 75%. − M.p. 240°C (decomposed without melting). − IR: $\tilde{\nu}$ [cm^{-1}] 3507 (OH). − ^{1}H NMR: δ = 1.37 (s, 27 H, *t*Bu), 2.19 (s, 9 H, Ar−C*H*$_3$), 4.79 (s, 3 H, O*H*), 5.58 (s, 1 H, C*H*), 6.55 (s, 3 H, Ar-H), 7.08 (s, 3 H, Ar-H). − ^{13}C NMR: δ = 21.0 (*C*H$_3$) 29.7 [C(*C*H$_3$)$_3$], 34.7 [*C*(CH$_3$)$_3$], 42.4 (*C*H), 125.9, 127.2, 127.7, 130.1, 137.9, 151.1 (C_{Ar}). − MS (FAB) *m*/*z* (%) = 502 [M]$^+$ (42), 339 [M − *t*Bu − Me − C$_6$H$_3$OH]$^+$ (100), 365 [M − *t*Bu − Me − C$_6$H$_3$OH − *t*Bu]$^+$ (91). − $C_{34}H_{46}O_3$ (502.7): calcd. C 81.23, H 9.22; found C 81.15, H 9.34.

1c: Yield 60%. − M.p. 268−269°C (melts with decomposition). − IR: $\tilde{\nu}$ [cm^{-1}] 3460 (OH). − ^{1}H NMR: δ = 2.18 (s, 3 H, CH$_3$), 2.20 (s, 9 H, CH$_3$), 4.75 (s, 3 H, O*H*), 5.84 (s, 1 H, C*H*), 6.58 (s, 3 H, Ar-H), 6.89 (s, 3 H, Ar-H),. − ^{13}C NMR: δ = 16.0, 20.7 (*C*H$_3$), 40.1 (*C*H), 124.6, 126.4, 127.5, 129.8, 130.8, 149.8 (C_{Ar}). − MS (FAB) *m*/*z* (%) = 376 [M]$^+$ (100), 255 [M − Me$_2$C$_6$H$_3$OH]$^+$ (97). − $C_{25}H_{28}O_3$ (376.5): calcd. C 79.74, H 7.50; found C 79.28, H 7.80.

1d: Yield 65%. − M.p. 233−235°C. − IR: $\tilde{\nu}$ [cm^{-1}] 3500 (OH). − ^{1}H NMR: δ = 0.54 (t, *J* = 7.5 Hz, 6 H, CH$_2$C*H*$_3$), 0.60 (t, *J* = 7.5 Hz, 6 H, CH$_2$C*H*$_3$), 1.09 (s, 21 H, CMe$_2$), 1.32 (s, 21 H, CMe$_2$), 1.44 (q, *J* = 7.5 Hz, 6 H, C*H*$_2$CH$_3$), 1.77 (q, *J* = 7.5 Hz, 6 H, C*H*$_2$CH$_3$), 4.76 (s, 3 H, O*H*), 5.67 (s, 1 H, C*H*), 6.57 (d, *J* = 2.4 Hz, 3 H, Ar-H), 7.14 (d, *J* = 2.4 Hz, 3 H, Ar-H). − ^{13}C NMR: δ = 9.0, 9.7 (CH$_2$*C*H$_3$), 27.9, 28.4 [C(*C*H$_3$)$_3$], 33.2, 37.0 [*C*(CH$_3$)$_3$], 37.4, 38.6 (*C*H$_2$CH$_3$), 41.9 (*C*H), 124.3, 125.5, 123.8, 125.3, 135.3, 141.0, 150.6 (C_{Ar}). − $C_{49}H_{76}O_3$ (713.1): calcd. C 82.52, H 10.74; found C 82.42, H 11.34.

Tris(3,5-dialkyl-2-ethoxycarbonylmethoxyphenyl)methanes (2). − General Procedure: To an acetone solution of tris(3,5-dialkyl-2-hydroxyphenyl)methane (1 equiv.) was added cesium carbonate (3.5 equiv.) and ethyl bromoacetate (3.5 equiv.). The resulting mixture was refluxed under an atmosphere of dry nitrogen for about 12 h. After cooling, the acetone was removed under reduced pressure, and diethyl ether was added to the residue. The insoluble materials were filtered off, and the ether was removed under reduced pressure to leave colorless oils that slowly crystallized. The crude products **2** were essentially pure by NMR, but additional purification was readily facilitated by washing the solids with methanol.

2a: Yield 96%. − M.p. 154−155°C. − IR: $\tilde{\nu}$ [cm^{-1}] 1763, 1738 (CO). − ^{1}H NMR: δ = 1.21 (s, 27 H, *t*Bu), 1.27 (t, 9 H, *J* = 7.2 Hz, OCH$_2$C*H*$_3$), 1.33 (s, 27 H, *t*Bu), 4.21−4.28 (m, 12 H,C*H*$_2$), 6.33 (s, 1 H, C*H*), 7.19 (m, 6 H, Ar-H). − ^{13}C NMR: δ = 13.9 (OCH$_2$*C*H$_3$), 30.8, 31.3 [C(*C*H$_3$)$_3$], 34.4, 35.2 [*C*(CH$_3$)$_3$], 37.6 (*C*H), 60.5 (O*C*H$_2$CH$_3$), 69.4 (ArO*C*H$_2$), 122.4, 126.5, 136.4, 142.3, 145.1, 152.3 (C_{Ar}), 168.8 (*C*=O). − MS (FAB) *m*/*z* (%) = 926 [M + K]$^+$ (35), 910 [M + Na]$^+$ (100), 887 [M]$^+$ (18). − $C_{55}H_{82}O_9$ (887.2): calcd. C 74.46, H, 9.32; found C 74.54, H 9.44.

2b: Yield 89%. − M.p. 145−146°C. − IR: $\tilde{\nu}$ [cm^{-1}] 1766, 1732 (CO). − ^{1}H NMR: δ = 1.24 (t, *J* = 7.2 Hz, 9 H, OCH$_2$C*H*$_3$), 1.30 (s, 27 H, *t*Bu), 2.24 (s, 9 H, ArC*H*$_3$), 4.06 (s, 6 H, ArOC*H*$_2$), 4.19 (*q*, 6 H, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 6.31 (s, 1 H, C*H*), 6.94 (s, 3 H, Ar-H), 7.01 (s, 3 H, Ar-H). − ^{13}C NMR: δ = 14.0 (OCH$_2$*C*H$_3$), 21.4 (Ar*C*H$_3$), 30.8 [C(*C*H$_3$)$_3$], 35.0 [*C*(CH$_3$)$_3$], 37.1 (*C*H), 60.6 (O*C*H$_2$CH$_3$), 69.6 (ArO*C*H$_2$), 126.9, 129.9, 132.5, 137.3, 143.2, 152.6 (C_{Ar}), 168.8 (*C*=O). − MS (FAB) *m*/*z* (%) = 799 [M + K]$^+$ (100), 783 [M + Na]$^+$ (85), 761 [M]$^+$ (20). − $C_{46}H_{64}O_9$ (761.3): calcd. C 72.59, H 8.48; found C 72.46, H 8.83.

Tris(3,5-di-*tert*-butyl-2-carboxymethoxyphenyl)methane (3): Tris(3,5-di-*tert*-butyl-2-ethoxycarbonylmethoxyphenyl)methane (3.50 g, 3.95 mmol) was dissolved in a methanol/water/dichloromethane (50:10:4 mL) solvent mixture and potassium carbonate (5.50 g, 39.8 mmol) added. The mixture was refluxed for 4 hours. The resulting clear solution was poured into water (400 mL), acidified to pH 4 with dilute hydrochloric acid, and extracted with diethyl ether. The solvent was removed under reduced pressure and chloroform was added to the residue. The insoluble material was filtered and washed with additional chloroform to give **3** as white powder (2.92 g, 92%). The product can be recrystallized from diethyl ether/hexanes, although the crude workup yields very pure material, suitable for further reaction. M.p. 254−256°C. − IR: $\tilde{\nu}$ [cm^{-1}] 1740, 1713 (CO). − ^{1}H NMR (CD$_3$OD): δ = 1.21 (s, 27 H, *t*Bu), 1.36 (s, 27 H, *t*Bu), 4.04 (s, 6 H, ArOC*H*$_2$), 6.46 (s, 1 H, C*H*), 7.11 (d, *J* = 2.4 Hz, 3 H, Ar-H), 7.32 (d, *J* = 2.4 Hz, 3 H, Ar-H). − ^{13}C NMR (CD$_3$OD): δ = 31.7, 31.9 [C(*C*H$_3$)$_3$], 35.5, 36.5 [*C*(CH$_3$)$_3$], 40.0 (*C*H), 71.2 (ArO*C*H$_2$), 124.3, 128.0, 138.4, 144.0, 147.1, 154.1 (C_{Ar}), 172.3 (*C*=O). − MS (FAB) *m*/*z* (%) = 842 [M + K]$^+$ (65), 826 [M + Na]$^+$ (100), 803 [M]$^+$ (10). − $C_{49}H_{70}O_9$ (803.8): calcd. C 73.27, H 8.79; found C 73.16, H 9.17%.

Tris(3,5-di-*tert*-butyl-2-chlorocarbonylmethoxyphenyl)methane (4): Tris(3,5-di-*tert*-butyl-2-carboxymethoxyphenyl)methane was dissolved in dichloromethane and an excess of thionyl chloride added. The solution was refluxed for five hours under a nitrogen atmosphere. The solvent and excess thionyl chloride were both removed under vacuum to leave **4** as a white residue. The product was pure by NMR, and additional purification was not carried out for its use in subsequent reactions. ^{1}H NMR: δ = 1.15 (s, 27 H, *t*Bu),

1.27 (s, 27 H, *t*Bu), 4.38 (s, 6 H, ArOCH_2), 6.19 (s, 1 H, C*H*), 7.13 (d, *J* = 2.4 Hz, 3 H, Ar-H), 7.22 (d, *J* = 2.4 Hz, 3 H, Ar-H). − ^{13}C NMR: δ = 31.1, 31.2 [C(*C*H$_3$)$_3$], 34.5, 35.4 [*C*(CH$_3$)$_3$], 37.2 (*C*H), 76.1 (ArO*C*H$_2$), 126.4 127.3, 140.9, 142.7, 146.0, 146.6 (C_{Ar}), 169.1 (*C*=O).

Compounds 5−8. − General Procedure: The crude tris(3,5-di-*tert*-butyl-2-chlorocarbonylmethoxyphenyl)methane prepared above was redissolved in dichloromethane and the corresponding amine (6 equiv.) added. Immediate precipitates of the amine hydrochlorides formed. The solutions were refluxed under nitrogen for 1 hour to ensure completion. Dilute hydrochloric acid was added and the organic layers collected and dried with magnesium sulfate. Removal of the solvent gave the corresponding amides **5−8** as white solids. Although all the crude products were essentially pure by NMR, purification by recrystallization from THF/pentane was readily effected.

Tris(3,5-di-*tert*-butyl-2-dimethylamidomethoxyphenyl)methane (5): Yield 89%. − M.p. 254−257°C. − IR: ṽ [cm^{-1}] 1685, 1666, 1653 (CO). − IR ($CHCl_3$) 1673, 1639 (CO). − ^{1}H NMR: δ = 1.09 (s, 27 H, *t*Bu), 1.23 (s, 27 H, *t*Bu), 2.68 (s, 9 H, NMe), 2.81 (s, 9 H, NMe), 4.02 (s, 6 H, ArOCH_2), 6.27 (s, 1 H, C*H*), 6.94 (d, *J* = 2.4 Hz, 3 H, Ar-H tripod), 7.15 (d, *J* = 2.4 Hz, 3 H, Ar-H tripod). − ^{13}C NMR: δ = 30.8, 31.1 [C(*C*H$_3$)$_3$], 34.2 [*C*(CH$_3$)$_3$], 35.1 (NMe$_2$), 36.2 [*C*(CH$_3$)$_3$], 39.6 (*C*H), 72.0 (ArO*C*H$_2$), 122.5, 126.6, 136.7, 142.2, 145.3, 153.1 (C_{Ar}), 167.5 (*C*=O). − $C_{55}H_{85}O_6N_3$ (884.3): calcd. C 74.69, H 9.69, N 4.75; found C 74.38, H 9.93, N 4.66.

Tris(3,5-di-*tert*-butyl-2-benzylaminocarbonylmethoxyphenyl)-methane (6):Yield 93%. − M.p. 247−248°C. − IR: ṽ [cm^{-1}] 3426, 3294 v br (NH), 1679, 1656 (CO). − ^{1}H NMR: δ = 1.19 (s, 27 H, *t*Bu), 1.28 (s, 27 H, *t*Bu), 4.16 (s, 6 H, ArOCH_2), 4.34 (d, *J* = 5.4 Hz, 6 H, NHCH_2), 6.48 (s, 1 H, CH), 7.07 (s, 3 H, Ar-H tripod), 8.35 (m, 21 H, Ar-H and NH). − ^{13}C NMR: δ = 31.29, 31.31 [C(*C*H$_3$)$_3$], 34.5, 35.3 [*C*(CH$_3$)$_3$], 37.3 (*C*H), 42.6 (NH*C*H$_2$), 71.8 (ArO*C*H$_2$), 123.2, 126.5, 127.2, 127.4, 128.5, 136.4, 138.1, 141.8, 146.1, 151.3 (C_{Ar}), 168.5 (*C*=O). − $C_{70}H_{91}O_6N_3$ (1070.5): calcd. C 78.53, H 8.57, N 3.93; found C 78.24, H 8.81, N 3.90.

Tris{3,5-di-*tert*-butyl-2-[*N*-(methyl glycyl)carbonylmethoxy]-phenyl}methane (7):Yield 88%. − M.p. 191−193°C. − IR: ṽ [cm^{-1}] 3413 br, 3307 br (NH), 1759, 1689, 1667 (CO). − ^{1}H NMR (CD_2Cl_2): δ = 1.16 (s, 27 H, *t*Bu), 1.21 (s, 27 H, *t*Bu), 3.61 (s, 9 H, OMe), 3.69 (br, 6 H, NHCH_2), 4.04 (s, 6 H, ArOCH_2), 6.57 (s, 1 H, C*H* tripod), 7.19 (d, *J* = 2.4 Hz, 3 H, Ar-H), 7.22 (d, *J* = 2.4 Hz, 3 H, Ar-H), 7.64 (t, 3 H, *J* = 5.9 Hz, N*H*). − ^{13}C NMR (CD_2Cl_2): δ = 31.2, 31.4 [C(*C*H$_3$)$_3$], 34.6, 35.4 [*C*(CH$_3$)$_3$], 36.9 (*C*H tripod), 40.8 (NH*C*H$_2$), 52.3 (O*C*H$_3$), 72.2 (ArO*C*H$_2$), 123.7, 127.1, 137.1, 142.6, 146.6, 152.0 (C_{Ar}), 169.3 (NH*C*=O), 171.3 (MeO*C*=O). − $C_{58}H_{85}O_{12}N_3$ (1016.3): calcd. C 68.53, H 8.43, N 4.14; found C 68.81, H 8.76, N, 4.02.

Tris{3,5-di-*tert*-butyl-2-[*N*-(methyl alanyl)carbonylmethoxy]-phenyl}methane (8):Yield 92%. − M.p. 92−94°C. − IR: ṽ [cm^{-1}] 3411 br (NH), 1748, 1683 (CO). − ^{1}H NMR: δ =1.17 (s, 27 H, *t*Bu), 1.30 (s, 27 H, *t*Bu), 1.45 (d, *J* = 7.2 Hz, 9 H, C*H*$_3$CH), 3.91 (s, 6 H, ArOCH_2), 4.67 (quintet, 3 H, *J* = 7.2 Hz, NHC*H*), 6.41 (s, 1 H, C*H* tripod), 7.01 (d, *J* = 5.4 Hz, 3 H, Ar-H), 7.21 (d, *J* = 5.4 Hz, 3 H, Ar-H), 7.49 (s, 3 H, br, N*H*). − ^{13}C NMR: δ = 17.9 (*C*H$_3$CH), 13.1, 31.3 [C(*C*H$_3$)$_3$], 34.4, 35.2 [*C*(CH$_3$)$_3$], 38.3 (CH tripod), 42.6 (NH*C*H$_2$), 47.5 (NH*C*H), 52.3 (O*C*H$_3$), 71.8 (ArO*C*H$_2$), 123.1, 126.7, 136.6, 141.9, 146.0, 152.0 (C_{Ar}), 168.2 (NH*C*=O), 173.0 (MeO*C*=O). − $C_{61}H_{91}O_{12}N_3 \cdot {}^1/_2\ CHCl_3$ (1058.4): calcd. C 66.09, H 8.26, N 3.76; found C 66.00, H 8.47, N 3.65.

Alkali Metal Complexes. − General Procedure: To a small quantity of amide (15 mg) dissolved in $CDCl_3$ (1 mL) was added excess (10 equiv.) alkali metal salt. The resulting slurries were vigorously stirred for 24 hours. The solutions were filtered and, for the picrates, ^{1}H-, ^{13}C-NMR, and IR spectra were directly acquired. When sodium tetraphenylborate was used, the products were recrystallized by diffusion of pentane into a THF solution.

5 + Lithium Picrate: IR ($CDCl_3$): ṽ [cm^{-1}] 1652, 1619 (CO). − ^{1}H NMR: δ = 1.24 (s, 27 H, *t*Bu), 1.29 (s, 27 H, *t*Bu), 2.59 (s, 9 H, NMe), 2.97 (s, 9 H, NMe), ca. 4 (s, v br, 6 H, ArOCH_2), 6.77 (s, 1 H, C*H*), 7.28 (d, *J* = 2.4 Hz, 3 H, Ar-H tripod), 7.35 (d, *J* = 2.4 Hz, 3 H, Ar-H tripod), 9.02 (s, 2H, Ar-H picrate). − ^{13}C NMR: δ = 31.3, 31.8 [C(*C*H$_3$)$_3$], 34.6 [*C*(CH$_3$)$_3$], 35.5 (*C*H), 35.6, 35.7 (NMe$_2$), 36.0 [*C*(CH$_3$)$_3$], 70.2 (ArO*C*H$_2$), 124.3, 126.3, 128.0, 128.7, 136.0, 140.7, 142.0, 147.0, 151.3, 163.2 (C_{Ar}), 168.8 (*C*=O).

5 + Sodium Picrate: IR ($CDCl_3$): ṽ [cm^{-1}] 1664, 1635, 1616 (CO). − ^{1}H NMR: δ = 1.21 (s, 54 H, *t*Bu), 1.29 (s, 54 H, *t*Bu), 2.52 (s, 18 H, NMe), 2.91 (s, 18 H, NMe), ≈3.8 (s, v br, 12 H, ArOCH_2), 6.60 (s, 2H, C*H*), 7.17 (d, *J* = 2.4 Hz, 6 H, Ar-H tripod), 7.27 (d, *J* = 2.4 Hz, 6 H, Ar-H tripod), 8.91 (4 H, s, Ar-H picrate). − ^{13}C NMR: δ = 31.3, 31.8 [C(*C*H$_3$)$_3$], 34.5 [*C*(CH$_3$)$_3$], 35.5, 35.6 (NMe$_2$), 35.8 [*C*(CH$_3$)$_3$], 37.5 (*C*H), 70.7 (ArO*C*H$_2$), 123.9, 126.5, 127.0, 136.6, 141.8, 142.3, 146.5, 152.1 (C_{Ar}), 168.2 (*C*=O).

6 + $NaBPh_4$: IR: ṽ [cm^{-1}] 3427 br, 3366 br (NH), 1671 (CO). − ^{1}H NMR: δ = 1.08 (s, 54 H, *t*Bu), 1.35 (s, 54 H, *t*Bu), 4.34 (br, 12 H, CH_2), 5.86 (s, 2H, C*H* tripod), 6.18 (s, 6 H, N*H*), 6.87 (t, *J* = 7.1 Hz, 4 H, BPh_4), 6.96−7.01 (m, 14 H, Ar-H), 7.04 (t, *J* = 7.4 Hz, 12 H, Ar-H), 7.18−7.22 (m, 18 H, Ar-H), 7.31 (d, *J* = 2.4 Hz, 6 H, Ar-H tripod), 7.44 (br, 8 H, BPh_4). − ^{13}C NMR: δ = 31.2, 31.5 [C(*C*H$_3$)$_3$], 34.4 [*C*(CH$_3$)$_3$], 35.5, 40.0 (*C*H), 42.3 (NH*C*H$_2$), 72.6 (ArO*C*H$_2$), 121.5, 123.5, 125.5, 126.5, 126.6, 127.2, 128.4, 136.1, 136.3, 137.9, 141.7, 147.0, 151.3 (C_{Ar}), 168.4 (*C*=O). − $C_{140}H_{182}O_{12}N_6NaB(C_6H_5)_4 \cdot 4.5$ THF (2483.2): calcd. C 77.84, H 8.55, N 2.99; found C 78.03, H 8.92, N 2.94.

7 + $NaBPh_4$: IR: ṽ [cm^{-1}] 3369 br (NH), 1750, 1681 (CO). − ^{1}H NMR (CD_2Cl_2): δ = 1.15 (s, 27 H, *t*Bu), 1.21 (s, 27 H, *t*Bu), 3.67 (s, 9 H, OMe), ≈3.8 (s, v br, 6 H, CH_2), 6.24 (s, 1 H, C*H* tripod), 6.42 (br, 3 H, N*H*), 6.72 (t, 4 H, *J* = 7.2 Hz, 4 H, BPh_4), 7.08 (t, 8 H, *J* = 7.5 Hz, 4 H, BPh_4), 7.20 (br, 8 H, BPh_4), 7.27 (d, *J* = 2.4 Hz, 3 H, Ar-H tripod). − $C_{58}H_{85}O_{12}N_3NaB(C_6H_5)_4$ (1358.5): calcd. C 72.47, H 7.79, N 3.09; found C 71.91, H 7.84, N 3.01.

Determination of Binding Affinities: All extraction studies were carried out at 23 °C, with freshly distilled analytical grade solvents, using the methodology and equations described by Cram and coworkers.[22] Absorbance values were determined using a Varian Cary 50, at 380 nm. The picrate salts were prepared according to literature procedures,[23] and were thoroughly dried under vacuum prior to use. Aqueous solutions of the picrates were prepared that were 0.015 M for the Li^+, Na^+, and K^+ salts, and 0.010 M for the less soluble Ru^+ and Cs^+ salts. Aliquots of the each of the picrate solution were transferred into five glass vials using an Eppendorf micropipetter, 0.50 mL for the Li^+, Na^+, and K^+, and 0.75 mL for the Ru^+ and Cs^+ solutions. To these were added 0.5 mL of 0.015 M solutions of the host in $CHCl_3$, and capped. The vials were thoroughly shaken for 2 min, and allowed to separate. Aliquots of 0.100 mL and 0.200 mL were carefully syringed from the organic and aqueous phases, respectively, using Hamilton Gas-tight syringes, and transferred to 10 mL volumetric flasks, which were subsequently bought to the mark with CH_3CN. The absorbance of each sample was determined, and the *R*, K_a, $\Delta G°$ and percentage

extracted values calculated. The values used for the extinction coefficients (ε) of the picrate salts in CH_3CN and the distribution constants (K_d) of the picrate salts between water and $CHCl_3$, which are required for the calculations, were those previously determined by Cram and co-workers.[22]

X-ray Crystallographic Study: Unit cell dimensions and intensity data for all the structures were obtained on a Siemens CCD SMART diffractometer at −100°C, with the exception of **6**$_2$NaBPh$_4$ · 4.5 THF which was collected at −125°C, with monochromatic Mo-K_α X-rays (λ = 0.71073 Å). The data collections

Table 2. X-ray data for the crystal structures of **1a**, **1d**, **2b**, **4**, and **5**

	1a · $^1/_2$ C_6H_6	**1d**	**2b** · $1^1/_3$ CH_3OH	**4**	**5**
Total reflections	27220	24668	12140	29403	55165
Unique reflections	19934	5094	2520	10101	9238
Collection range	$1.74 < \theta < 29.37°$	$1.72 < \theta < 26.36°$	$1.31 < \theta < 23.26°$	$1.46 < \theta < 26.41°$	$1.88 < \theta < 24.71°$
$T_{max,min}$	1.00, 0.84	1.00, 0.86	1.00, 0.88	1.00, 0.47	1.00, 0.78
Empirical formula	$C_{46}H_{67}O_3$	$C_{25}H_{28}O_3$	$C_{47.33}H_{68.33}O_{10.33}$	$C_{49}H_{67}O_6Cl_3$	$C_{55}H_{85}N_3O_6$
M_r	668	376.47	812.02	858.38	884.26
Crystal system	triclinic	trigonal	trigonal	monoclinic	orthorhombic
Space group	$P\bar{1}$	$R3c$	$P\bar{3}$	$P2_1/n$	$Pbca$
a [Å]	14.0330(2)	21.9188(2)	17.9708(3)	12.2997(8)	18.928(3)
b [Å]	14.5409(1)	–	–	22.743(2)	21.703(3)
c [Å]	24.159(1)	30.2450(2)	9.3776(2)	18.203(1)	26.376(5)
α [°]	74.853(1)	–	–	–	–
β [°]	78.696(1)	–	–	104.460(1)	–
γ [°]	65.297(1)	120	120	–	–
V_c [Å^3]	4301.72(7)	12584.0(2)	2622.75(8)	4930.7(6)	10835(3)
D_c [g cm^{-3}]	1.031	1.192	1.028	1.156	1.084
Z	4	24	2	4	8
F(000)	1468	4848	1028	1840	3872
μ(Mo-$K\alpha$) [mm^{-1}]	0.062	0.077	0.08	0.23	0.069
R_1 [$I \geq 2\sigma(I)$]	0.0705 [15421]	0.0603 [3754]	0.0805 [1923]	0.0776 [5820]	0.0597 [5266]
wR_2 (all data); X, Y[a]	0.1680; 0.0367, 4.04	0.1489; 0.0633, 12.46	0.2651; 0.1675, 1.98	0.2346; 0.1057, 2.60	0.1726; 0.0867, 2.51
GoF	1.117	1.102	1.099	1.063	1.01
Largest peak, deepest trough [e Å^{-3}]	+0.75, −0.37	+0.87, −0.21	+0.84, −0.38	+0.42, −0.35	+0.64, −0.33

[a] $w = 1/[\sigma^2(F_o^2) + (XP)^2 + YP]$ where $P = (F_o^2 + 2F_c^2)/3$.

Table 3. X-ray data for the crystal structures of **7** · $^1/_2$ C_5H_{12}, **8** · $CHCl_3$, **5**$_2$Li$_4$picrate$_4$ · 2 C_6H_6 · 2 H_2O, **6**$_2$NaBPh$_4$ · $4^1/_2$ THF, and **7**$_2$Na$_2$(BPh$_4$)$_2$ · $^1/_8$ C_6H_{14} · $^2/_3$ THF

	7 · $^1/_2$ C_5H_{12}	**8** · $CHCl_3$	**5**$_2$Li$_2$[Li$_2$picrate$_4$] · 2 C_6H_6 · 2 H_2O	**6**$_2$NaBPh$_4$ · $4^1/_2$ THF	**7**$_2$Na$_2$(BPh$_4$)$_2$ · $^1/_8$ C_6H_{14} · $^2/_3$ THF
Total reflections	30003	7205	23725	19013	24616
Unique reflections	5825	3085	15772	11347	16868
Collection range	$1.80 < \theta < 22.50°$	$1.94 < \theta < 23.26°$	$1.48 < \theta < 26.37°$	$1.02 < \theta < 22.50°$	$1.03 < \theta < 26.38°$
$T_{max,min}$	1.00, 0.79	1.00, 0.55	1.00, 0.92	1.00, 0.81	1.00, 0.80
Empirical formula	$C_{60.5}H_{90.5}N_3O_{12}$	$C_{62}H_{92}N_3O_{12}Cl_3$	$C_{140}H_{188}Li_4N_{18}O_{42}$	$C_{182}H_{238}BN_6O_{16.5}Na$	$C_{167.42}H_{217.08}B_2N_6O_{24.66}Na_2$
M_r	1051.86	1177.74	2822.84	2807.58	2775.92
Crystal system	hexagonal	hexagonal	triclinic	triclinic	triclinic
Space group	$P6_3$	$R32$	$P\bar{1}$	$P\bar{1}$	$P\bar{1}$
a [Å]	12.4486(5)	12.226(4)	14.2094(6)	14.0674(6)	15.4947(7)
b [Å]	–	–	17.4119(8)	15.8351(7)	15.6292(7)
c [Å]	50.871(3)	77.63(4)	17.5694(8)	21.6376(9)	20.1703(9)
α [°]	–	–	71.068(1)	108.384(1)	78.594(1)
β [°]	–	–	83.519(1)	100.678(1)	88.268(1)
γ [°]	120	120	72.079(1)	98.822(1)	61.132(1)
V_c (Å^3)	6827.1(5)	10048(7)	3911.8(3)	4377.3(3)	4181.0(3)
D_c [g cm^{-3}]	1.023	1.102	1.198	1.065	1.102
Z	4	6	1	1	1
F(000)	2282	3792	1502	1520	1493
μ(Mo-$K\alpha$) [mm^{-1}]	0.07	0.194	0.088	0.069	0.077
R_1 [$I \geq 2\sigma(I)$]	0.0926 [4996]	0.0647 [1629]	0.0749 [10635]	0.1384 [8529]	0.0725 [8889]
wR_2 (all data); X, Y[a]	0.2599; 0.1641, 4.05	0.1693; 0.0750, 0.00	0.2438; 0.1365, 2.45	0.3916; 0.2000, 16.00	0.2503; 0.1640, 0.00
GoF	1.167	0.967	1.048	1.039	0.934
Largest peak, deepest trough (e Å^{-3})	+0.85, −0.56	+0.40, −0.39	+0.96, −0.56	+0.74, −0.67	+0.78, −0.80

[a] $w = 1/[\sigma^2(F_o^2) + (XP)^2 + YP]$ where $P = (F_o^2 + 2F_c^2)/3$.

nominally covered over a hemisphere of reciprocal space, by a combination of three sets of exposures; each set had a different φ angle for the crystal and each exposure covered 0.3° in ω. The crystal to detector distance was ca. 5.0 cm. The data sets were corrected empirically for absorption using SADABS.[24]

All the structures were solved by using the Bruker SHELXTL software package for the PC and the direct methods option of SHELXS. Space groups for all of the structures were determined from an examination of the systematic absences in the data, and the successful solution and refinement of the structure confirmed these assignments. When compounds crystallized in polar space groups, both enantiomers were refined and the final structure yielded the lower residuals. Moreover, the Flack parameter refined to the lowest value for the chosen enantiomer. Except for the hydrogens involved in hydrogen-bonding interactions, all hydrogen atoms were assigned idealized locations and were given a thermal parameter equivalent to 1.2 or 1.5 times the thermal parameter of the carbon atom to which it was attached. For the methyl groups, where the location of the hydrogen atoms is uncertain, the AFIX 137 card was used to allow the hydrogen atoms to rotate to the maximum area of residual density, while fixing their geometry. In cases of extreme disorder, the non-hydrogen atoms were refined only isotropically, and hydrogen atoms were not included in the model. Structural and refinement data for all the compounds are presented in Table 2 and Table 3 while complete experimental details are contained in the supplementary information.

Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-106701 (**1a**), CCDC-106702 (**1d**), CCDC-131462 (**2b**), CCDC-131463 (**4**), CCDC-131464 (**5**), CCDC-131465 {(**5**OH_2)$_2$[Li_4picrate$_4$]}, CCDC-131466 {(**6**$_2$Na)BPh_4}, CCDC-131467 (**7**), CCDC-131468 {(**7**Na)$_2$(BPh_4)$_2$}, CCDC-140533 (**8**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44−1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

Acknowledgments

We thank the University of Florida, the National Science Foundation (CAREER Award 9874966) and the donors of the American Chemical Society Petroleum Research Fund for funding this research. Support from the Research Corporation is also gratefully acknowledged. We also thank Dr. Khalil Abboud at the University of Florida for granting access to X-ray instrumentation.

[1] C. D. Gutsche, *Calixarenes Revisited*; Royal Society of Chemistry: Cambridge, England, **1998**.
[2] J. Vicens, V. Böhmer, *Calixarenes: a Versatile Class of Macrocyclic Compounds*; Kluwer Academic: Boston, **1991**.
[3] V. Böhmer, *Angew. Chem.* **1995**, *107*, 785−817; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 713−745.
[4] C. Wieser, C. B. Dieleman, D. Matt, *Coord. Chem. Rev.* **1997**, *165*, 93−161.
[5] G. Barrett, M. A. McKervey, J. F. Malone, A. Walker, F. Arnaud-Neu, L. Guerra, M.-J. Schwing-Weill, C. D. Gutsche, D. R. Stewart, *J. Chem. Soc., Perkin Trans. 2* **1993**, 1475−1479.
[6] A. Dondoni, A. Marra, M.-C. Scherrmann, A. Casnati, F. Sansone, R. Ungaro, *Chem. Eur. J.* **1997**, *3*, 1774−1782.
[7] R. Seangprasertkij, Z. Asfari, F. Arnaud-Neu, J. Vicens, *J. Org. Chem.* **1994**, *59*, 1741−1744.
[8] B. C. Gibb, A. R. Mezo, A. S. Causton, J. R. Fraser, F. C. S. Tsai, J. C. Sherman, *Tetrahedron* **1995**, *51*, 8719−8732.
[9] F. Arnaud-Neu, S. Cremin, S. Harris, M. A. McKervey, M.-J. Schwing-Weill, P. Schwinté, A. Walker, *J. Chem. Soc., Dalton Trans.* **1997**, 329−334.
[10] Y. Hamuro, M. C. Calama, H. S. Park, A. D. Hamilton, *Angew. Chem.* **1997**, *109*, 2797−2799; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2680−2683.
[11] K. Tsubaki, T. Otsubo, K. Tanaka, K. Fuji, T. Kinoshita, *J. Org. Chem.* **1998**, *63*, 3260−3265.
[12] T. Yamato, M. Haraguchi, J. Nishikawa, S. Ide, *J. Chem. Soc., Perkin Trans. 1* **1998**, 609−614.
[13] T. Yamato, L. K. Doamekpor, H. Tsuzuki, *Liebigs Ann./Recueil* **1997**, 1537−1544.
[14] R. G. Janssen, W. Verboom, D. N. Reinhoudt, A. Casnati, M. Freriks, A. Pochini, F. Ugozzoli, R. Ungaro, P. M. Nieto, M. Carramolino, F. Cuevas, P. Prados, J. de Mendoza, *Synthesis* **1993**, 380−386.
[15] C. Dinse, N. Baglan, C. Cossonnet, J. F. Le Du, Z. Asfari, J. Vicens, *J. Alloy Compd* **1998**, *271*, 778−781.
[16] H. Otsuka, Y. Suzuki, A. Ikeda, K. Araki, S. Shinkai, *Tetrahedron* **1998**, *54*, 423−446.
[17] S. Blanchard, L. Le Clainche, M.-N. Rager, B. Chansou, J.-P. Tuchagues, A. F. Duprat, Y. Le Mest, O. Reinaud, *Angew. Chem.* **1998**, *110*, 2861−2864; *Angew. Chem. Int. Ed.* **1998**, *37*, 2732−2735.
[18] W. P. van Hoorn, F. C. J. M. van Veggel, D. N. Reinhoudt, *J. Phys. Chem. A* **1998**, *102*, 6676−6681 and references tin.
[19] B. Tse, Y. Kishi, *J. Org. Chem.* **1994**, *59*, 7807−7814.
[20] J. R. Telford, K. N. Raymond, *Comprehensive Supramolecular Chemistry* (Ed.: J. M. Lehn; Elsevier Science Ltd.: Oxford, **1996**; Vol. 1, pp 245 and references therein.
[21] [21a] G. Casiraghi, G. Casnati, M. Cornia, V. D'Azeglio, *Tetrahedron Lett.* **1973**, 679−682. − [21b] G. Casiraghi, G. Casnati, M. Cornia, A. Pochini, *Gazz. Chim. Ital.* **1978**, *108*, 79−84.
[22] K. E. Koenig, G. M. Lein, P. Stuckler, T. Kaneda, D. J. Cram, *J. Am. Chem. Soc.* **1979**, *101*, 3553−3567.
[23] S. S. Moore, T. L. Tarnowski, M. Newcomb, D. J. Cram, *J. Am. Chem. Soc.* **1977**, *99*, 6405−6410.
[24] R. H. Blessing, *Acta Cryst.* **1995**, *A51*, 33.
[25] M. E. McGreal, V. Niederl, J. B. Niederl, *J. Am. Chem. Soc.* **1939**, *61*, 345−348.
[26] J. C. Lockhart, M. B. McDonnell, W. Clegg, M. N. S. Hill, *J. Chem. Soc., Perkin Trans. 2* **1987**, 639−649.
[27] C. Grüttner, V. Böhmer, R. Assmus, S. Scherf, *J. Chem. Soc., Perkin Trans. 1* **1995**, 93−95.
[28] Th. Zincke, *Justus Liebigs Ann. Chem.* **1939**, *363*, 268−274.
[29] F. Arnaud-Neu, E. M. Collins, M. Deasy, G. Ferguson, S. J. Harris, B. Kaitner, A. J. Lough, M. A. McKervey, E. Marques, B. L. Ruhl, M. J. Schwing-Weill, E. M. Seward, *J. Am. Chem. Soc.* **1989**, *111*, 8681−8691.
[30] F. Sansone, S. Barboso, A. Casnati, M. Fabbi, A. Pochini, F. Ugozzoli, R. Ungaro, *Eur. J. Org. Chem.* **1998**, 897−905.
[31] F. Arnaud-Neu, M.-J. Schwing-Weill, K. Ziat, S. Cremin, S. J. Harris, M. A. McKervey, *New J. Chem.* **1991**, *15*, 33−37.
[32] In all attempts to crystallize **2a**, the molecule resided on a C_3 symmetry axis and the ethoxy groups were severely disordered in the lattice, precluding an accurate determination of the structure. Nevertheless, the overall orientation of the arms with respect to the platform could be unambiguously determined, allowing for a cursory comparison to **2b**. When crystallized from methanol, the unit cell parameters for **2a** were determined to be hexagonal, space group $R\bar{3}$, a = 12.178(1) Å, c = 68.28(1) Å, V = 8770(3) Å^3, Z = 6.
[33] H. Kessler, *Angew. Chem.* **1982**, *94*, 509−520; *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 512−523.
[34] Y. A. Ovchinnikov, V. T. Ivanov, *Tetrahedron* **1975**, *31*, 2177−2209.
[35] F. Arnaud-Neu, G. Barret, S. Cremin, M. Deasy, G. Ferguson, S. J. Harris, A. J. Lough, L. Guerra, M. A. McKervey, M. J. Schwing-Weill, P. Schwinte, *J. Chem. Soc., Perkin Trans 2* **1992**, 1119−1125.
[36] J. A. Hamilton, M. N. Sabesan, L. K. Steinrauf, *J. Am. Chem. Soc.* **1981**, *103*, 5880−5885.
[37] L. K. Steinrauf, J. A. Hamilton, M. N. Sabesan, *J. Am. Chem. Soc.* **1982**, *104*, 4085−4091.

[38] F. Arnaud-Neu, V. Böhmer, J.-F. Dozol, C. Grüttner, R. A. Jakobi, D. Kraft, O. Mauprivez, H. Rouquette, M.-J. Schwing-Weill, N. Simon, W. Vogt, *J. Chem. Soc., Perkin Trans. 2* **1996**, 1175−1182.

[39] G. Casiraghi, G. Casnati, G. Puglia, G. Sartori, G. Terenghi, *J. Chem. Soc., Perkin Trans. 1* **1979**, 1862−1865.

Received February 11, 2000
[O00076]