tions having $2\theta(\text{Mo K}\bar{\alpha} < 45.8°$ and $I > 3\sigma(I)$] with counter-weighted cascade block diagonal least-squares techniques and a structural model that incorporated anisotropic thermal parameters for all non-hydrogen atoms except C_{6s} and $C_{6s'}$, which were refined isotropically, and isotropic thermal parameters for all hydrogen atoms. The methyl groups were included in the refinement as idealized sp^3-hybridized rigid rotors and gave final values for the C-C-H angles that ranged from 92° to 130°. The remaining hydrogen atoms were fixed at idealized sp^2- or sp^3-hybridized positions with a C-H bond length of 0.96 Å. The methyl and I atoms bonded to the "apical" Sn atoms (Sn_1 and Sn_2) appear to be nearly statistically disordered in the solid state. The occupancy factor of an iodine atom at the positions for I_1 and I_2 refined to 0.540 (3) and 0.573 (3), respectively. A statistically disordered methyl and iodine would correspond to an occupancy factor of approximately 0.56. There also appears to be a disordered pentane molecule of crystallization in the lattice that can be specified by various combinations of atoms C_{1a}, C_{2s}, C_{3s}, C_{4s}, $C_{4s'}$, C_{5s}, C_{6s}, and $C_{6s'}$. Occupancy factors of 1.00 were used for carbon atoms at C_{2s}, C_{3s}, and C_{5s}, while occupancy factors of 0.50 were used for C_{1s}, C_{4s}, and $C_{4s'}$ and 0.25 for C_{6s} and $C_{6s'}$.

Acknowledgment. We thank Dr. Cynthia Day of Crystalytics Co. for the crystallographic analysis of **4** and the Office of Naval Research and the National Science Foundation (Grant CHE-9001462) for support of this work.

Supplementary Material Available: Detailed information concerning the spectroscopic data and crystallographic analysis of **4**, including listings of atomic coordinates and temperature factors, bond lengths, bond angles, and anisotropic temperature factors (22 pages). Ordering information is given on any current masthead page.

Synthesis and Characterization of Dimetallacalix[8]arene Complexes

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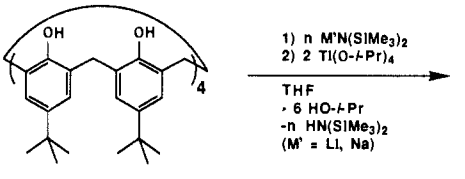
Abstract: The one-pot synthesis of a variety of [4-*tert*-butylcalix[8]arene$(MOR)_2]^-[M'$ or $R'NH_3]^+$ (M = Ti, Zr, V, Sn; M' = Li, Na, K) complexes is described. The ^1H NMR spectra of these compounds possess several interesting features, including upfield shifts (by 0.5-2.0 ppm) of α or β protons on the alkoxide ligand and a phenol hydroxyl resonance at ca. 16 ppm. The upfield shift is due to shielding of the alkoxide ligand by the aryl rings of the calixarene macrocycle. The ligands are located in cavities, made up of three aryl rings of the macrocycle. Fast atom bombardment mass spectrometry (FABMS) and tandem mass spectrometry (MS/MS and MS/MS/MS) have been used to obtain molecular ion information as well as identify fragment ions from these complexes. Two-dimensional NMR experiments have established that the solution structure is the same as in the solid state and have also allowed assignment of all of the macrocycle protons in the ^1H NMR spectrum. A difference NOE experiment has determined the location of the remaining phenol hydroxyl proton, which had not been located previously by X-ray crystallography.

Calixarenes are a class of phenol-containing macrocycles, which are easily synthesized in large quantities from commercially available starting materials (e.g. 4-*tert*-butylphenol and formaldehyde).[1] One notable property of these compounds is their ability to include small organic molecules into a cavity formed by the aryl ring framework. Furthermore, these macrocycles can be easily derivatized at the para position and/or the hydroxyl group. For example, water-soluble calixarenes have recently been synthesized by incorporating sulfate groups into the para positions of the aryl rings.[2] Further derivatization of the hydroxyl functions provided macrocyclic complexes capable of binding uranyl ions.[3]

We and others have recently reported using the hydroxyl groups in calixarenes for direct binding to metal ions.[4,5] Our interest in this area has focused on the synthesis of metallacalixarene complexes that contain metal-ligands directed into cavities composed of aryl rings. The ultimate goal of these efforts is the application of these materials in shape-selective organic synthesis. Herein, details on the synthesis and in-depth characterization of a variety of dimetalla-4-*tert*-butylcalix[8]arene complexes (dimetallacalix[8]arenes) are provided.

Results

Synthesis. The reaction of 4-*tert*-butylcalix[8]arene (**1**) with 2 equiv of $Ti(O\text{-}i\text{-}Pr)_4$ in either toluene, dichloromethane, or tetrahydrofuran (THF) (**1** is only partially soluble in any of these solvents) produced a yellow precipitate whose ^1H NMR spectrum showed that a mixture of several compounds was present. In an effort to solubilize **1**, 2 equiv of lithium or sodium bis-(trimethylsilyl)amide were added to **1** in THF. This provided a homogeneous solution to which $Ti(O\text{-}i\text{-}Pr)_4$ was added (eq 1, n = 2). These reactions yielded a product with the general molecular



1

$$\text{[calix[8]arene(TiO-}i\text{-Pr)}_2]^{n-}[M']_n^+ \quad (1)$$

(n = 2) **2a**, *b*: M' = Li, Na
(n = 1) **3a**, *b*, *c*: M' = Li, Na, K

formula [4-*tert*-butylcalix[8]arene$(TiO\text{-}i\text{-}Pr)_2]^{2-}[M']_2^+$ (**2a,b**) (established by positive ion fast atom bombardment mass spec-

(1) (a) Calixarenes. Gutsche, C. D. *Monographs in Supramolecular Chemistry*; Stoddart, J. F., Ed.; The Royal Society of Chemistry: Cambridge, 1989. (b) Gutsche, C. D. In *Progress in Macrocyclic Chemistry*; Izatt, R. M., Christenesen, J. J., Eds.; John Wiley and Sons, Inc.: New York, 1987; Vol. 3, Chapter 3. (c) Munch, J. H.; Gutsche, C. D. *Org. Synth.* **1989**, *68*, 243.

(2) Shinkai, S.; Mori, S.; Koreishi, H.; Tsubaki, T.; Manabe, O. *J. Am. Chem. Soc.* **1986**, *108*, 2409.

(3) (a) Shinkai, S.; Koreishi, H.; Ueda, K.; Manabe, O. *J. Chem. Soc., Chem. Commun.* **1986**, 233. (b) Shinkai, S. *Pure Appl. Chem.* **1986**, *11*, 1523.

(4) Hofmeister, G. E.; Hahn, F. E.; Pedersen, S. F. *J. Am. Chem. Soc.* **1989**, *111*, 2318.

(5) (a) Furphy, B. M.; Harrowfield, J. M.; Ogden, M. I.; Skelton, B. W.; White, A. H.; Wilner, F. R. *J. Chem. Soc., Dalton Trans.* **1989**, 2217. (b) Englehardt, L. M.; Furphy, B. M.; Harrowfield, J. M.; White, A. H.; Wilner, F. R. *Aust. J. Chem.* **1988**, *41*, 1465. (c) Furphy, B. M.; Harrowfield, J. M.; Kepert, D. L.; Skelton, B. W.; White, A. H.; Wilner, F. R. *Inorg. Chem.* **1987**, *26*, 4231. (d) Andreetti, G. D.; Calestani, G.; Ugozzoli, F.; Arduini, A.; Ghidini, E.; Ungaro, R. *J. Inclusion Phenom.* **1987**, *5*, 123. (e) Bott, S. G.; Coleman, A. W.; Atwood, J. L. *J. Chem. Soc., Chem. Commun.* **1986**, 610. (f) Olmstead, M. M.; Sigel, G.; Hope, H.; Xu, X.; Power, P. P. *J. Am. Chem. Soc.* **1985**, *107*, 8087.

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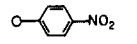
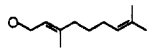
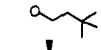
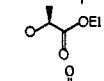
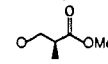
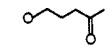
Table I. List of Compounds [4-*tert*-Butylcalix[8]arene(M-Y)$_2$]$^-$[M′ or R′NH$_3$]$^+$

Compound	M	Y	M′ or RNH$_3^+$	Method(s)
3*a*[a], *b*, *c*-*f*[a]	Ti	O-*i*-Pr	Li, Na, K, K(18-cr6), BnNH$_3$, RNH$_3$[b]	A
4*a*, *b*[a]	Ti		Li, Na	B,C
(5*a*, *b*)[a]	Ti	OEt	Li, Na	A,C
6*a*, *b*	Ti	O-*t*-Bu	K, BnNH$_3$	A
(7*a*, *b*)[a]	Ti		Na, H$_2$NMe$_2$	C
8[a]	Ti		Na	C
9	Ti		BnNH$_3$	C
(10*a*, *b*)[a]	Ti		Na, K	C
11[a]	Ti		Na	C
12	Ti		BnNH$_3$	D
13[a]	Ti		BnNH$_3$	D
14[a]	Ti		K	D
15	Zr	O-*i*-Pr	K	E
16[a]	Sn	O-*i*-Pr	K	F
17	Sn	*n*-Bu	K	F
18	V	=O	RNH$_3$[c]	G

[a] Experimental details for these compounds are available in the supplementary material. [b] Prepared from (±)-2-methyl-1-(1-naphthyl)-propylamine. [c] Prepared from (*R*)-1-(1-naphthyl)ethylamine.

trometry (+FABMS)). The ^{1}H NMR spectra indicated that these compounds possess 2-fold symmetry. The unique feature of these spectra is the position of the isopropoxide methyl groups (ca. 0.5 and −1.0 ppm) and the methine proton resonances (ca. 2.0 ppm) relative to the analogous resonances in Ti(O-*i*-Pr)$_4$ (ca. 1.5 ppm (CH_3) and 4.0 ppm (CH)).

When dissolved in chloroform or THF, **2** slowly disappears and is replaced by a new compound whose ^{1}H NMR ($CDCl_3$) spectrum is similar to its precursor but lacks the 2-fold symmetry (i.e. all of the resonances are doubled). Furthermore, there is a new resonance located between 15 and 17 ppm that accounts for one proton. These new compounds correspond to the monoprotonated analogues of **2**, namely [4-*tert*-butylcalix[8]arene (TiO-*i*-Pr)$_2$]$^-$[M′]$^+$ (**3**, Table I). The new resonance at ca. 16 ppm is attributed to a single phenol proton that is bridging between two phenoxide oxygens (vide infra). Isopropyl alcohol left over from the synthesis of **2** is the presumed source of this proton. Compound **3** can be synthesized directly by employing only 1 equiv of an appropriate base (eq 1, n = 1). These monoprotonated complexes are more stable than **2** with respect to further protonation. Furthermore, the resonance at ca. 16 ppm has proven to be a useful ^{1}H NMR handle for examining both product purity and the reaction chemistry of these compounds (vide infra). A noteworthy observation is that when 1 equiv of Ti(O-*i*-Pr)$_4$ is employed in eq 1 (n = 1), only compound **3** and unreacted calixarene are obtained.

An X-ray crystal structure of **3b** has been described elsewhere.[4] Briefly, the molecule consists of two pseudooctahedral titanium centers coordinated to all eight calix[8]arene oxygens (two of which are bridging) and two isopropoxide oxygens. The macrocyclic ligand forms a saddle-shaped surface about the titanium centers giving rise to four three-sided cavities. Two of these cavities each encompass an isopropoxide ligand (Figure 1). Binding of the macrocycle in this manner leads to the formation of enantiomeric complexes. Resolution of these stereoisomers is discussed elsewhere.[4]

Syntheses of complexes related to **3**, which differ only by the alkoxide ligand found in the cavity, were initiated by attempting

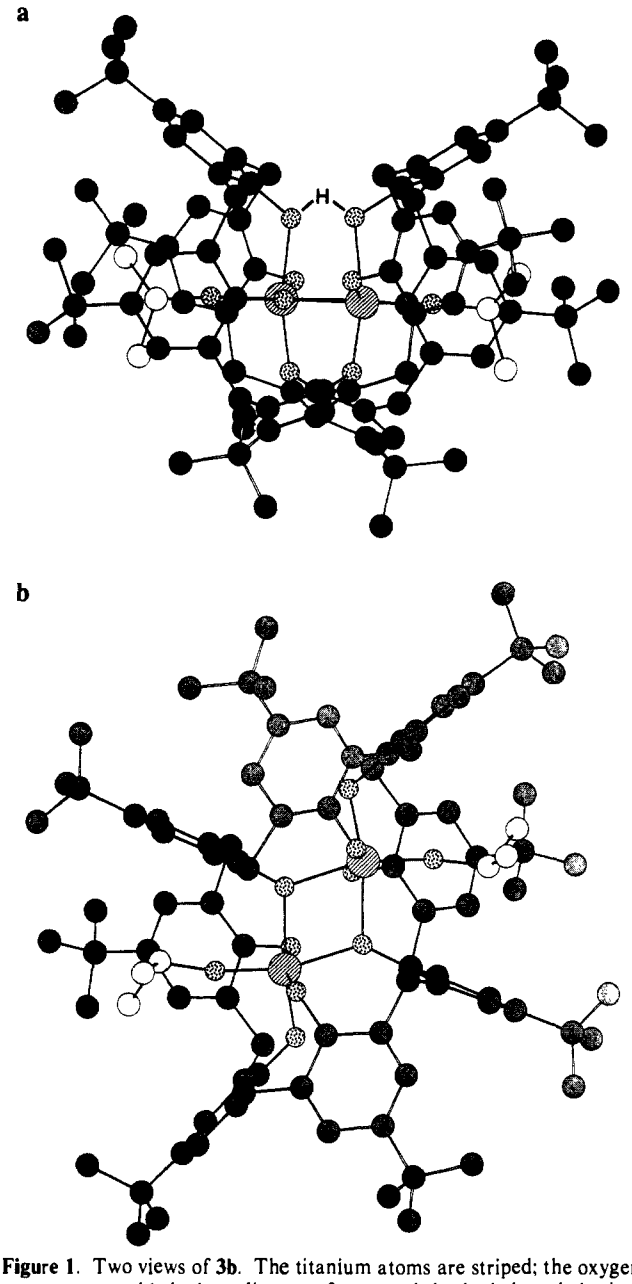


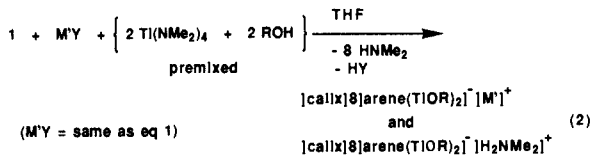
Figure 1. Two views of **3b**. The titanium atoms are striped; the oxygen atoms are speckled; the calixarene framework is shaded; and the isopropoxide ligands are white. The sodium ion is not interacting with the calixarene framework in the solid state and is therefore omitted. (a) A view from the "frontside", looking into the open side of the three-sided cavities. (b) A view from the side (90° rotation about the horizontal axis in part a). The phenolic hydroxyl proton is added in the location where it was found by NMR experiments.

alcohol exchange reactions with **3**. Addition of 2 equiv of an alcohol to either **3a** or **3b** followed by examination of the ^{1}H NMR spectrum (15–17-ppm region) clearly indicated the presence of all possible alkoxide complexes. However, reaction of **3a** or **3b** with 2 equiv of 4-nitrophenol produced good yields of a single new complex, [4-*tert*-butylcalix[8]arene(TiO-(4-NO_2Ph))$_2$]$^-$[M′]$^+$ (**4a,b**). Aryl alcohols are known to react with metal alkoxides to give metal aryloxide complexes irreversibly.[6]

Other alkoxide compounds related to **3** can be synthesized by substituting the appropriate titanium tetraalkoxide for Ti(O-*i*-Pr)$_4$ in eq 1 (n = 1). For example, the ethoxide analogue (**5**) is easily prepared in this manner from Ti(OEt)$_4$. However, this is not a versatile or practical synthesis of such compounds (i.e. few titanium

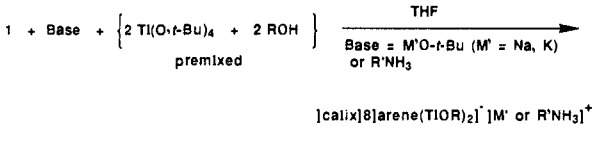
(6) Chisholm, M. H.; Rothwell, I. P. In *Comprehensive Coordination Chemistry*; Wilkinson, G., Gillard, R. D., McCleverty, J. A., Eds.; Pergamon Press: Oxford, New York, 1987; Vol. 2, pp 335–364.

tetraalkoxides are commercially available and 6 equiv of alcohol are discarded). We therefore turned to titanium amide chemistry and found that a variety of dimetallacalix[8]arene complexes can be generated by combining $Ti(NMe_2)_4$ and alcohol (2 equiv of each) in THF and then adding this mixture to the calixarene/base solution (eq 2). Although the reaction provides the desired versatility, significant amounts of byproduct, [4-*tert*-butylcalix[8]arene$(TiOR)_2]^-[H_2NMe_2]^+$ were also produced (e.g. see **7b**, Table I). Identification of these ammonium ion adducts led us to explore using an amine as the base in eq 1 (n = 1). This



particular synthesis provided us with a means of resolving the enantiomeric complexes formed in these reactions by employing chiral amines.[4]

It is apparent from the X-ray structure of **3b** that the cavities incorporating the alkoxide ligands are not capable of hosting bulky alkoxide ligands. For example, a space-filling model of the structure suggested that a *tert*-butoxy ligand would not be accommodated in the cavity. Indeed, when $Ti(O\text{-}t\text{-}Bu)_4$ is used in place of $Ti(O\text{-}i\text{-}Pr)_4$ in eq 1 (n = 1), crystalline solids are obtained whose ^1H NMR spectra are quite complicated when compared with **3** and related derivatives. However, the FAB mass spectra of these materials indicated that a compound(s) with the molecular formula [4-*tert*-butylcalix[8]arene$(TiO\text{-}t\text{-}Bu)_2]^-[M'$ or $R'NH_3]^+$ (**6a,b**) was present. Addition of isopropyl alcohol (2 equiv) to a THF solution of **6a** or **6b** provided quantitative yields of **3c** or **3e**, respectively. These observations led to the development of a one-pot synthesis of a variety of complexes with the general formula [4-*tert*-butylcalix[8]arene$(TiO\text{-}R)_2]^-[M'$ or $R'NH_3]^+$ (eq 3). In general, the crude products obtained from these reactions



are very clean (by ^1H NMR spectroscopy). Since $Ti(O\text{-}t\text{-}Bu)_4$ is easily prepared on a large scale from $Ti(O\text{-}i\text{-}Pr)_4$,[7] this reaction represents the method of choice for preparing the majority of the dititanacalix[8]arenes discussed in this paper.

When (*S*)-ethyl lactate was used in eq 3, the desired complex (**12**) was not obtained. However, **12** can be prepared by addition of 2 equiv of (*S*)-ethyl lactate to **6**. We propose that the latter reaction is successful because all of the phenoxide ligands in **6** are already bound to the two titanium centers. On the other hand, when employing the conditions outlined in eq 3, chelation of ethyl lactate may compete with the calixarene ligand for binding sites.[8] Noteworthy is the fact that even in complex **12** this ligand appears to be forming a chelate with each titanium center.[9] Other polyfunctional alkoxide complexes have also been synthesized by reacting the appropriate alcohol with **6** (**13**, **14**). However, these complexes do not appear to form stable chelate rings.

Other dimetallacalix[8]arene complexes have been prepared with use of methods analogous to those already described. For example, substitution of $Zr(O\text{-}i\text{-}Pr)_4(HO\text{-}i\text{-}Pr)$ as the metal reagent in eq 1 (n = 1) yielded the complex [4-*tert*-butylcalix[8]arene$(ZrO\text{-}i\text{-}Pr)_2]^-[K]^+$ (**15**). Tin complexes **16** and **17** (Table I) were prepared in an analogous fashion, beginning with either $Sn(O\text{-}i\text{-}Pr)_4(HO\text{-}i\text{-}Pr)$ or $Sn(O\text{-}i\text{-}Pr)_3(n\text{-}Bu)$, respectively. Finally, when 2 equiv of $V(O)(O\text{-}i\text{-}Pr)_3$ were used in eq 1 (n = 1), black crystalline complexes, [4-*tert*-butylcalix[8]arene$(V{=}O)_2]^-[M'$ or $R'NH_3]^+$ (**18**), were isolated.

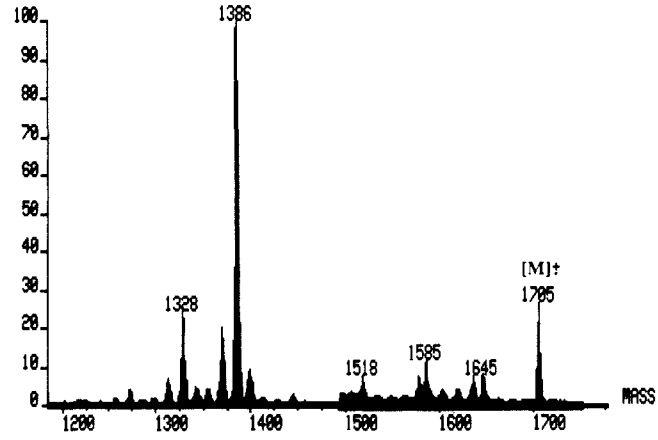


Figure 2. Partial low-resolution FAB spectrum of **3f**. The ions observed below m/z 1250 were matrix ions associated with *o*-NPOE and are therefore not shown.

Mass Spectrometry. The dimetallacalixarenes have been analyzed by mass spectrometry with fast atom bombardment (FAB) as the method of ionization.[10] This technique works extremely well for both polar compounds and salts and promotes the formation of either a protonated molecular ion $[MH]^+$ or the radical cationic species $[M]^{\cdot+}$.[11] The spectra of dimetallacalixarene compounds containing sodium or potassium counterions show both the $[MH]^+$ for the salt complex and the corresponding alkali metal cationized species ($[M + M']^+$; M' = Na, K). In all cases where the counterion is an alkali metal, the $[MH]^+$ is the most abundant ion in the molecular ion cluster. Loss of two neutral alcohol molecules is observed to arise from fragmentation of the protonated molecular ion. The ion resulting from these losses (m/z 1408 for the sodium compound and m/z 1424 for the potassium compound) is the base peak in all spectra of the alkali metal salt compounds and corresponds to $[Ti_2calix[8]arene + M']^+$ (M' = Na, K).

For compounds containing an ammonium ion, the observed molecular ion is the radical cation (Figure 2). In analogy with the sodium and potassium salt complexes, we also observe loss of two neutral alcohols, in this case from $[M]^{\cdot+}$. Presumably, the additional proton necessary for this particular fragmentation comes from the ammonium ion. In addition to the two alcohol molecules, neutral amine is lost from these compounds. The base peak in these spectra occurs at m/z 1386 and corresponds to $[Ti_2calix[8]arene]^{\cdot+}$.

Tandem mass spectrometry (MS/MS and MS/MS/MS)[12] has been used to demonstrate that the base peaks in either of the above classes of compounds arise from the molecular ions and are not due to an easily ionized impurity in our sample. An example of a MS/MS/MS spectrum of **3f** is shown in Figure 3. In this experiment the $[M]^{\cdot+}$ at m/z 1705 is passed into the MIKES collision cell and allowed to decompose unimolecularly (no collision gas). The daughter ion resulting from the first loss of isopropyl alcohol (m/z 1645) is then transmitted into the rf only quadrupole collision cell and also allowed to decompose unimolecularly. The resulting granddaughter ions are mass analyzed in the quadrupole mass analyzer. The spectrum clearly shows that both losses of

(7) Mehrotra, R. C. *J. Am. Chem. Soc.* **1954**, *76*, 2266.

(8) In a separate experiment (*S*)-ethyl lactate was combined with $Ti(O\text{-}t\text{-}Pr)_4$, and IR spectra indicated that the carbonyl was coordinated to titanium. For related examples see: (a) Williams, I. D.; Pedersen, S. F.; Sharpless, K. B.; Lippard, S. J. *J. Am. Chem. Soc.* **1984**, *106*, 6430. (b) Pedersen, S. F.; Dewan, J. C.; Eckman, R. R.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 1279.

(9) IR of **12** (Nujol mull, cm^{-1}) $\nu_{C=O}$ 1647, 1675; IR of (*S*)-ethyl lactate (thin film, cm^{-1}) $\nu_{C=O}$ 1738.

(10) (a) Barber, M.; Bordoli, R. S.; Sedgwick, R. D.; Tyler, A. N. *J. Chem. Soc., Chem. Commun.* **1981**, 325. (b) Surman, D.; Vickerman, J. C. *Ibid.* **1981**, 324. (c) Martin, S. A.; Costello, C. E.; Biemann, K. *Anal. Chem.* **1982**, *54*, 2362.

(11) Branan, D. M.; Hoffman, N. W.; McElroy, E. A.; Ramage, D. L.; Robbins, M. J.; Eyler, J. R.; Watson, C. H.; Leary, J. A. *Inorg. Chem.* **1990**, *29*, 1915.

(12) *Tandem Mass Spectrometry*; McLafferty, F. W., Ed.; John Wiley and Sons, Inc.: New York, 1983.

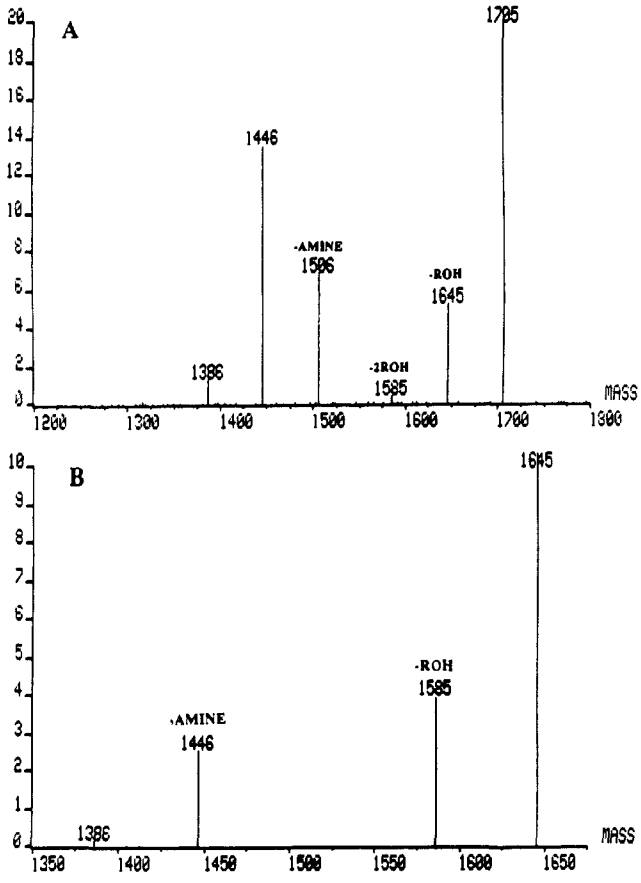


Figure 3. (A) Daughter ion spectrum of **3f**. Losses of neutrals as labeled arise from the parent ion m/z 1705. (**B**) Granddaughter ion spectrum of **3f**. Losses of neutrals as labeled arises directly from daughter ion m/z 1645 which in turn arises from parent m/z 1705.

alcohol and loss of amine (m/z 1386) are ultimately derived from the molecular ion.

NMR Spectroscopy. The ^{1}H NMR spectra of **3b** and its analogues contain a number of characteristic signals that make NMR spectroscopy a valuable tool for studying structural similarities among these various derivatives. The benzylic protons always appear as two groups of eight doublets; one group represents the protons that point toward the aryl ring protons (2.8–3.6 ppm, labeled "a" in Figure 4), and one group represents the protons pointing toward the phenol oxygen atoms (4.4–6.4 ppm, labeled "b" in Figure 4). The resonances due to α or β protons (c) on the alkoxide ligands are shifted upfield (by 0.5 to 2.0 ppm) due to their location inside the three-sided cavities. Finally, the one remaining phenol hydroxyl proton resonance (d) occurs between 15 and 17 ppm.

Several two-dimensional NMR experiments were necessary to verify that the structure in solution is the same as that in the solid state and to assign all of the signals in the ^{1}H NMR spectrum. A two-dimensional double-quantum filtered COSY spectrum[13] determines J-coupled protons, such as the geminal protons of the benzylic groups (1 & 2, 6 & 7, 11 & 12, 16 & 17 and their "primed" partners, Figure 5a,b) and the isopropoxide ligand protons (21, 22, and 23 and their "primed" partners). Furthermore, crosspeaks due to four-bond coupling between aryl protons on the same aromatic ring are observed. Therefore, the aryl protons on each separate phenol ring can be identified (3 & 5, 8 & 10, 13 & 15, 18 & 20 and their "primed" partners).

In order to determine through-space interactions, a two-dimensional rotating-frame Overhauser (ROESY) experiment was performed.[14] This experiment was necessary because in the case of medium weight molecules it provides stronger crosspeaks than the conventional NOESY experiment,[15] and it can also differentiate chemical exchange and dipolar interactions.[16] The ROESY experiment was done at −43 °C to suppress any exchange activity that may be occurring in solution (e.g. cation exchange, vide infra).[17]

A number of crosspeaks associated with the benzylic groups are observed and allow the assignment of these protons in one of two pseudo-C_2 symmetry related positions (Figure 5). The upfield benzylic proton resonances are assigned to those protons which point toward the aryl protons (2, 7, 12, 17 and their "primed" partners), due to crosspeaks observed with the aryl protons. The geminal partners of these protons point toward the phenol oxygens (1, 6, 11, 16 and their "primed" partners; Figure 5). These downfield resonances have negative crosspeaks with the aryl protons, due to a transfer NOE. Two NOE crosspeaks are observed among the downfield benzylic proton resonances, which are due to protons located on the backside of the molecule (6 and 11′, 6′ and 11; Figure 5b). The observation of crosspeaks between the remaining benzylic group protons 1, 16, and 17 (and their "primed" partners) and the methyl group 21 (and its "primed" partner) of the isopropoxide ligand confirms this assignment (Figure 5a). The benzylic protons that show the strongest NOE crosspeaks with the downfield isopropoxide methyl resonances are assigned as those closest to the cavity openings (1 and 2 and their "primed" partners). The two remaining frontside benzylic groups are those with the pseudo-C_2 symmetry related partners pointing toward one another in the center of the molecule (16 and 16′). They do not show significant cross-relaxation crosspeaks in the ROESY spectrum of **3b**; however, analogous compounds do show a through-space correlation between these protons.[18]

A one-dimensional difference NOE experiment at −40 °C has been performed, in which the hydroxyl proton at 16 ppm is irradiated. An enhancement of all four backside benzylic groups is observed. A stronger enhancement is observed between two pseudo-C_2 symmetry related groups, which are assigned as the innermost backside methylene groups (i.e. 11 and 12, 11′ and 12′; Figure 5b). This assignment is made because the most reasonable position on the backside of the molecule for the remaining hydroxyl proton is bridging the two innermost phenol oxygens (the O–O distance is 2.5 Å; see Figure 1).

The calixarene macrocycle protons can be assigned in order, by combining information from the COSY and ROESY spectra. A flow chart illustrating this methodology, along with an example, is outlined in Figure 6. Starting with a benzylic hydrogen (e.g. 17′), an aryl proton of a neighboring aryl ring is located (15′, step 1). The next aryl proton on each ring can then be located from the COSY spectrum (13′, step 2), follwed by the next benzylic group in turn (12′, step 3). The relationship of this assignment to the actual structure can be made, based on the assignments described above (e.g., 11 is an innermost backside proton, pointing toward the phenol oxygens, vide supra). In several instances, an assignment based purely on spectral information is ambiguous because some of the aryl protons overlap in the spectra. It is possible to remove these ambiguities by constraining the data with several requirements imposed by the structure. First, each pseudo-C_2 symmetry related benzylic methylene group must be four aryl rings apart. Second, the order of methylene groups must be frontside-frontside-backside-backside, etc., around the macrocycle. The result is that the entire ^{1}H NMR spectrum of **3b**

(13) (a) Marion, D.; Wuthrich, K. *Biochem. Biophys. Res. Commun.* **1983**, *113*, 967. (b) Rance, M.; Sorensen, O. W.; Bodenhausen, G.; Wagner, G.; Ernst, R. R.; Wuthrich, K. *Biochem. Biophys. Res. Commun.* **1983**, *117*, 479.

(14) The experiment was written by E. A., based on: Kessler, H.; Griesinger, C.; Kerssebaum, R.; Wagner, K.; Ernst, R. R. *J. Am. Chem. Soc.* **1987**, *109*, 607.

(15) Bax, A.; Davis, D. G. *J. Magn. Reson.* **1985**, *63*, 207.

(16) Davis, D. G.; Bax, A. *J. Magn. Reson.* **1985**, *64*, 533.

(17) In the room temperature ROESY spectrum of the complex [calix[8]arene(Ti-O-*i*-Pr)$_2$]$^-$[(±)-2-methyl-1-(1-naphthyl)propylamine]$^+$ (**3f**), counterion exchange led to exchange crosspeaks between pseudo-C_2 symmetry related pairs. However, the room temperature ROESY experiment with **3b** is essentially unchanged from the low-temperature experiment. Details of the NMR experiments performed on **3f** will be reported elsewhere.

(18) For example, **3f** (see ref 17) shows an NOE crosspeak between the two innermost frontside benzylic protons.

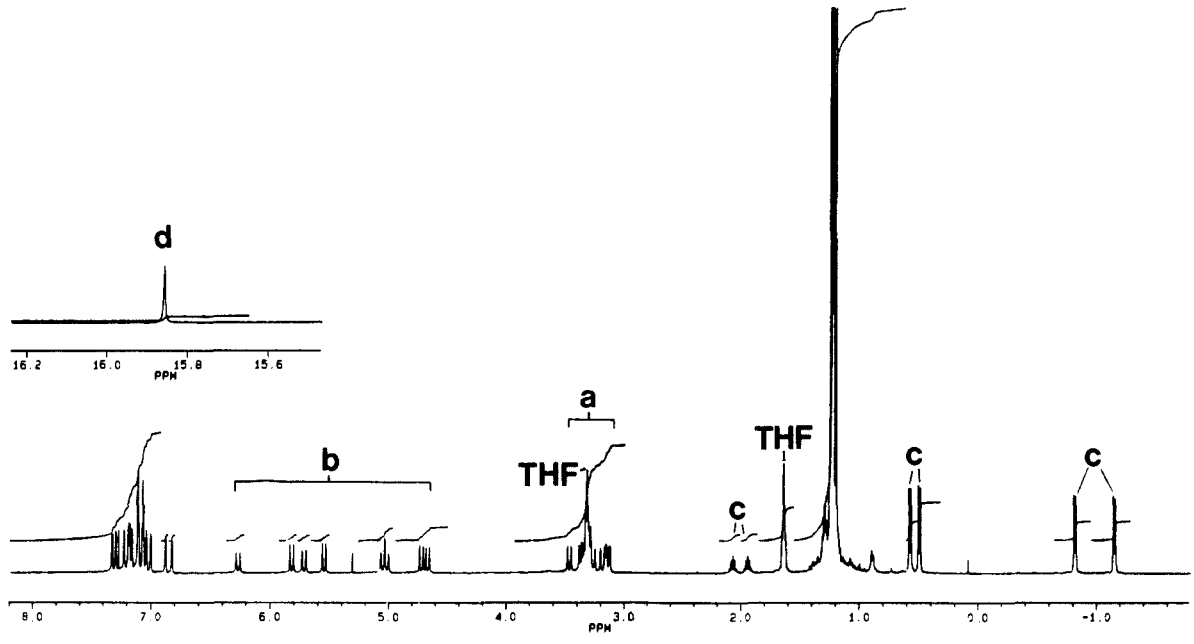


Figure 4. ^{1}H NMR ($CDCl_3$) spectrum of **3b**. The benzylic protons labeled "a" point toward the aryl ring protons. The benzylic protons labeled "b" point toward the oxygen atoms. The isopropoxide ligand resonances are labeled "c". The phenolic hydroxyl resonance is labeled "d".

has been assigned, according to the structure. Having observed the majority of NOE crosspeaks expected on the basis of the solid-state structure, the solution structure is clearly analogous.

Closer inspection of the isopropoxide ligand–macrocycle crosspeaks reveals information about the orientation of this ligand in the three-sided cavity. The isopropoxide methyl groups giving rise to the downfield resonances (21 and 21′) point out of the open side of the cavity, as indicated by crosspeaks with 1, 3, 15, 16, 17 and their "primed" partners (Figure 5). Crosspeaks between the methine proton 23 (and 23′) and aryl protons 10 and 13 (and 10′, 13′) suggest that 23 points toward the three-sided pocket corner bordered by aryl protons 10 and 13. It is clear from the X-ray crystal structure that this crevice is more narrow than that bordered by aryl protons 5 and 8, and it may not easily accommodate a methyl group. However, 23 also has a weak crosspeak with methylene proton 1. This suggests that the methine spends some time pointed toward the open side of the cavity (i.e. the ligand can rotate by ca. 40°). It is not likely that the ligand does a complete rotation, as NOE crosspeaks between the upfield methyl resonances associated with the isopropoxide ligands and the benzylic groups are not observed. Therefore, we believe that there may be some rotation of this ligand in the cavity in solution, but the ligand spends the majority of its time in the orientation indicated in the X-ray crystal structure.

Discussion

The saddle-shaped structure adopted by the majority of the complexes described within appears to represent a thermodynamic well for compounds of the formula [calix[8]arene(M-Y)$_2$]$^-$[M′]$^+$. One requirement for achieving such a structure is that the auxiliary ligands must be of a sufficient size and/or shape that they can be accommodated in the cavities defined by the macrocyclic unit. We have already noted that when this criterion is not met (e.g. when Y = O-*t*-Bu (**6**), products bearing the desired molecular formula but not the expected structure are obtained. In these cases a smaller alcohol can be added to these materials leading to ligand exchange and formation of the standard structural core.

The presence of an alkoxide ligand in the starting metal reagent appears to be crucial to the success of these reactions. We believe this is due to the fact that only such ligands provide conjugate acids (after protonation by the phenols of **1**) sufficiently acidic to allow for equilibration of the reaction mixture. It is known that phenol will react with titanium(IV) alkoxides to give tetraphenoxides, and we expect that similar events occur in the synthesis of dimetallacalixarenes from titanium alkoxides, leading to structures of the type [calix[8]areneM$_2$]. Yet in the presence of alcohol, the metal–phenoxide bonds can be reprotonated leading eventually to the thermodynamically favored products. However, when one employs other obvious starting materials such as homoleptic titanium amides and alkyls in an attempt to synthesize dimetallacalixarenes containing amido or alkyl ligands, respectively, one obtains complex reaction mixtures that may represent kinetic products. This is understandable when considering that the conjugate acids of either of these ligands will not protonate metal–phenoxide units and thus equilibration cannot take place.

If one wishes to prepare an organometallic calix[8]arene complex under these standard reaction conditions, metal reagents bearing alkoxide ligands capable of exchange and an alkyl ligand that does not undergo protonolysis in the presence of alcohols must be used. Trialkoxytin alkyls (Sn(OR)$_3$R′) fit these criteria and do in fact lead to complexes that have alkyl ligands incorporated into the calixarene cavities.

The absence of a C_2 axis of symmetry in chloroform solution (by ^{1}H NMR spectroscopy) is not clear upon first examination of the molecular structure of **3b**. However, it appears that coordination of the counterion (via phenolic oxygens) to one-half of the macrocycle and slow exchange between sides (on the NMR time scale) are the factors leading to an unsymmetric NMR spectrum. For example, when 1 equiv of 18-crown-6 was added to compound **3c**, complex **3d** was formed. The ^{1}H NMR spectrum of **3d** indicates a symmetric structure. In this case, the potassium counterion has been sequestered by the crown ether and is no longer able to bind to the macrocycle. Furthermore, the ^{1}H NMR spectrum of **3b** in THF-d_8 also indicates a symmetric structure, presumably due to the ability of THF to facilitate rapid exchange of the counterion on the NMR time scale. When an ammonium ion serves as the counterion, we propose that this ion resides (via hydrogen bonding) in one of the outside cavities of these complexes.[4] This has already been proven to occur in both solution and the solid state.[19]

Tandem mass spectrometry has determined that the base peak in the mass spectra of these complexes results from the molecular ion and not a possible impurity in the sample. Having established this result, the base peaks can be used to identify the calix[8]arene:metal ratio in unknown compounds. NMR experiments have resulted in the assignment of all the protons[20] in the ^{1}H NMR

(19) Hofmeister, G. E.; Alvarado, E.; Pedersen, S. F. Presented in part at the International Chemical Congress of Pacific Basin Societies, Honolulu, Hawaii, Dec. 17–22, 1989.

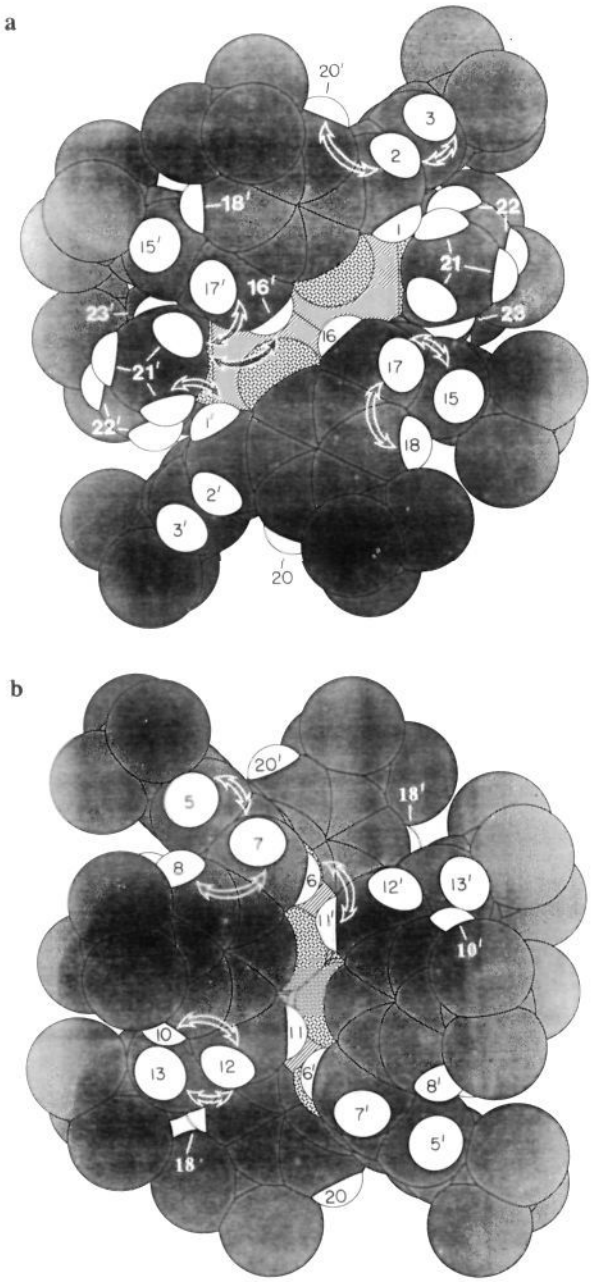


Figure 5. Space-filling diagram of **3b**; *tert*-butyl protons are removed for ease of viewing. Protons are labeled for the discussion in the text. Arrows represent observed crosspeaks between protons. (a) View from the "frontside", with the open side of the cavities facing the viewer. (b) View from the "backside" (180° rotation about the vertical axis in part a).

spectrum and confirmed the solution structure is the same as in the solid state (except for the location of the counterion). Futhermore, these experiments determined the location of the remaining phenol hydroxyl proton, which could not be located by X-ray diffraction.

In conclusion, we have identified a class of dimetallamacrocyclic complexes that incorporate two ligands into cavities defined by the macrocycle. The shape and size of these cavities are well-defined, allowing for the selective inclusion or exclusion of alkoxides. Finally, the conformation adopted by the macrocycle when bound to two metals leads to a chiral structure. The combination of these features suggests that dimetallacalixarenes might find applications in areas such as chiral recognition and separation chemistry.[21]

(20) The individual resonances associated with the *tert*-butyl groups were not assigned in the spectra of **3b**. However, NOE crosspeaks between aryl and *tert*-butyl protons were observed for compound **3f** and have allowed us to assign all of the *tert*-butyl resonances in this compound.

Experimental Section

General. All experiments (except as noted) were run under nitrogen at 25 °C in a Vacuum Atmospheres drybox. Solvents were purified and dried under N_2 by standard techniques and transferred into the drybox without exposure to air. 4-*tert*-Butylcalix[8]arene was synthesized according to the literature procedure.[1c] All alcohols were obtained from commercial sources and used as received or distilled prior to use. Titanium(IV) isopropoxide, titanium(IV) ethoxide, and vanadium(V) triisopropoxide oxide were vacuum distilled before use. Titanium(IV) *tert*-butoxide was prepared by treatment of titanium(IV) isopropoxide with an excess of *tert*-butyl acetate, followed by fractional distillation.[7] Ti(NMe$_2$)$_4$ was kindly provided by R. A. Andersen, and Zr(IV) isopropoxide isopropanolate was purchased from Alfa and used as received. Tin(IV) isopropoxide isopropanolate[22] and *n*-butyltin(IV) triisopropoxide[23] were prepared according to the literature procedures.

NMR spectra were recorded at room temperature on either a Bruker AM-500 or AM-400 spectrometer. All chemical shift data are reported in ppm relative to tetramethylsilane (TMS), based on the chemical shift of $CDCl_3$ (7.24 ppm, residual ^{1}H; 77.00 ppm, ^{13}C), C_6D_6 (7.15 ppm, *residual ^{1}H; 128.00 ppm, ^{13}C), or CD_3CN (118.20 ppm, ^{13}C).* *Infrared* spectra were obtained on a Perkin-Elmer or Nicolet 510 FT IR spectrometer. All mass spectra were obtained on either a VG ZAB2-EQ or a Kratos MS50 mass spectrometer, operated by the Mass Spectrometry facility at the University of California, Berkeley. All metallacalixarene compounds were analyzed by positive and/or negative fast atom bombardment (+ or −FAB) with 2-nitrophenyl octyl ether as a matrix solvent. Mass spectral data are reported as *m*/*z* (percent of base peak). Elemental analyses were performed by the Microanalytical Laboratory at the University of California, Berkeley. Characterization of representative compounds for each synthetic method is described below. Characterization of the remaining compounds listed in Table I is provided in the supplementary material.

Preparation of [Calix[8]arene(Ti-O-*i*-Pr)$_2$]$^{2-}$2[M′]$^+$ (2). 4-*tert*-Butylcalix[8]arene (1.56 g, 1.2 mmol) and M′N(SiMe$_3$)$_2$ (2.4 mmol, M′ = Li, Na) were combined in THF (70 mL). The mixture was stirred until the solution turned pale yellow and homogeneous (0.5 h). Ti(O-*i*-Pr)$_4$ (2.4 mmol) diluted with THF (5 mL) was added dropwise to the calix[8]arene solution. The resultant bright yellow solution was stirred for 1 h, followed by the standard workup procedure stated below.

Workup Procedure. All crude products were isolated by removal of the volatiles under reduced pressure. Purification was accomplished by crystallization unless specified otherwise. The reaction residues were usually stirred with pentane (4–5 mL for a 1-g scale), and THF was added dropwise until the compound dissolved. The solution was filtered through Celite and cooled to −40 °C. Individual crops were isolated by filtration, and pentane was added to the mother liquors in order to obtain additional crops. The final crop was usually obtained by concentrating the mother liquors to dryness, dissolving the residue in pentane, and cooling the solution to −40 °C. The reported yields are not always optimized, since obtaining more than two crops of crystals was not always pursued.

Compound 2b (M′ = Na): 71%, obtained as the bis-THF adduct; ^{1}H NMR (C_6D_6) δ 7.19, (m, 16 H), 6.42 (d, J = 11.4, 2 H), 5.60 (d, J = 13.6, 2 H), 4.96 (d, J = 11.1, 2 H), 3.55 (m, 4 H), 3.35 (m, 4 H), 2.97 (br s, 8 H, THF), 2.38 (m, 2 H), 1.64 (s, 18 H), 1.48 (s, 18 H), 1.32 (s, 18 H), 1.31 (s, 18 H), 1.17 (br s, 8 H, THF), 0.95 (d, J = 6, 6 H), −0.50 (d, J = 6, 6 H); ^{13}C{^{1}H} NMR (C_6D_6) δ 166.3, 164.2, 163.4, 158.9, 144.6, 142.1, 140.5, 140.2, 137.4, 136.4, 133.3, 133.0, 132.4, 130.8, 129.5, 129.4, 126.4, 125.3, 124.5, 124.4, 124.35, 123.8, 123.6, 123.3, 81.0, 72.8, 38.4, 37.8, 35.6, 35.1, 34.9, 34.5, 34.4, 34.3, 32.8, 32.6, 32.3, 32.1, 31.9, 25.5, 21.6; MS (+FAB) 1551 (M + H, 17), 1527 (8), 1490 (33), 1467 (50), 1408 (100), 1392 (33), 1385 (17), 1352 (17); (−FAB) 1526 (M - Na, 100), 1444 (83), 1424 (33), 1386 (17). Anal. Calcd for $C_{102}H_{134}O_{12}Na_2Ti_2$: C, 72.33; H, 7.97; Na, 2.71. Found: C, 72.44; H, 8.08; Na, 2.40.

Preparation of a Solution of [4-*tert*-Butylcalix[8]arene]$^-$[M′ or R′NH$_3$]$^+$: Procedure I. To a stirring mixture of 4-*tert*-butylcalix[8]arene (4.01 g, 3.09 mmol) and THF (200 mL) was added either (a) M′N-

(21) We are currently exploring the stability of resolved chiral dimetallacalix[8]arene complexes and alkoxide exchange dynamics with respect to these goals.

(22) Thomas, I. M. *Can. J. Chem.* **1961**, *39*, 1386.
(23) Gaur, D. P.; Srivastava, G.; Mehrotra, R. C. *J. Organomet. Chem.* **1973**, *63*, 221.

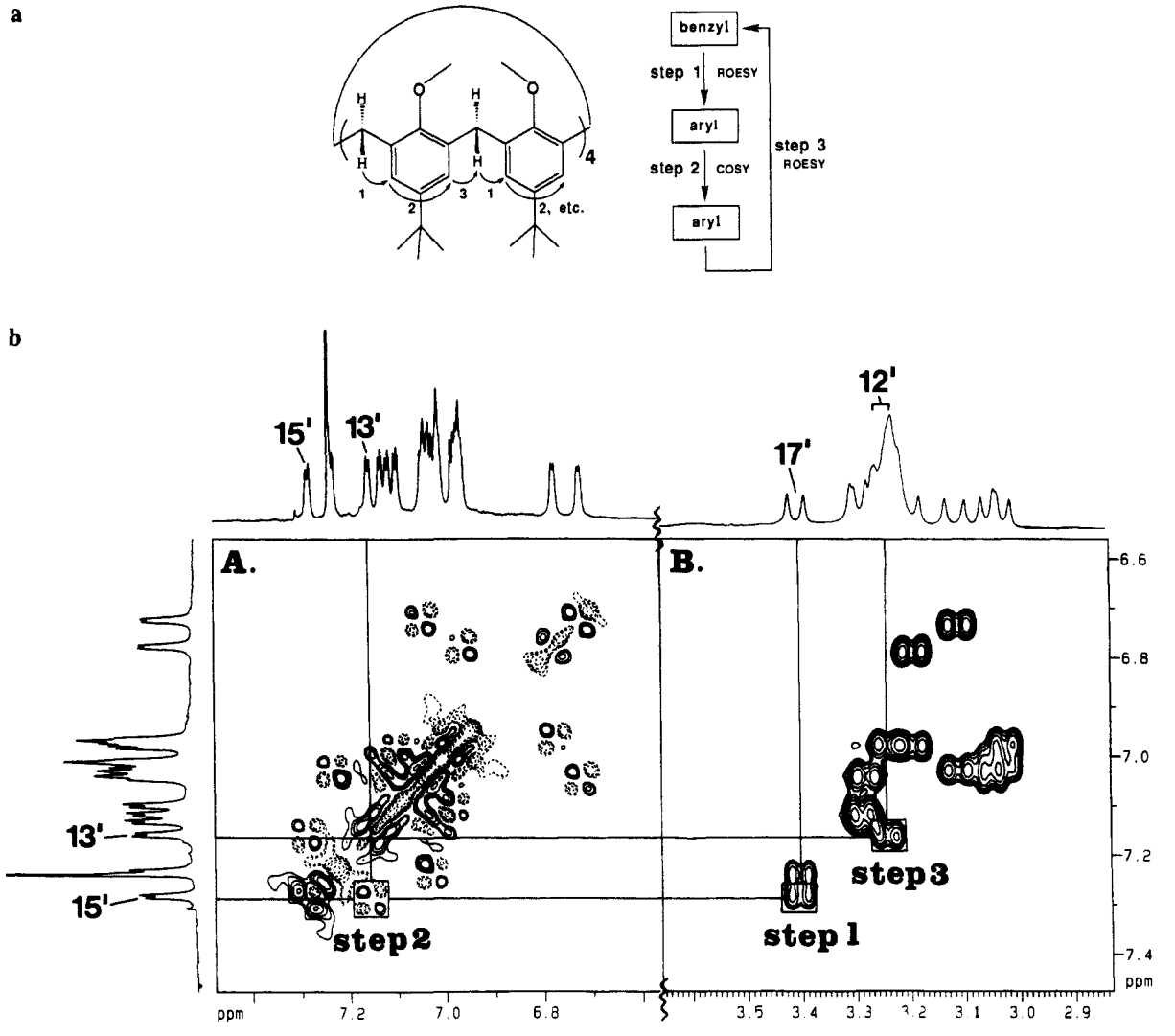


Figure 6. (a) Schematic diagram and flowchart that indicates the process used for macrocycle proton assignment. (b) Spectra section plots; positive crosspeaks are dashed, negative are solid: (A) COSY aryl–aryl cross-section; (B) ROESY aryl(Fl)–benzyl cross-section. Representative steps are shown from benzylic proton 17′ to aryl proton 15′ (step 1), to aryl proton 13′ (step 2), to benzyl proton 12′ (step 3).

$(SiMe_3)_2$ (M′ = Na, Li), (b) M′(O-*t*-Bu) (M′ = Na, K), or (c) $R'NH_2$ (3.09 mmol) in THF (5 mL). The resultant mixture was stirred for 15 minutes, and the metal reagent was added as described in Methods A–G below.

Procedure II. An alternative method for synthesizing the Na or K salts is as follows: 4-*tert*-Butylcalix[8]arene (15 g, 11.6 mmol) and 10 N M′OH (M′ = Na, K; 1.16 mL, 11.6 mmol) were combined in 250 mL of toluene. The reaction mixture was refluxed and the water was removed with use of a Dean Stark trap. The toluene was removed in vacuo leaving a white solid. A standard solution of this material was prepared by dissolving the solid (3.1 mmol, assuming the formula [4-*tert*-butylcalix[8]arene]$^-$[M′]$^+$) in THF (200 mL).

Method A: Preparation of [4-*tert*-Butylcalix[8]arene(Ti-O-R)$_2$][M′ or R′NH$_3$]$^+$ (R = *i*-Pr, Et). A THF solution (25 mL) of $Ti(OR)_4$ (R = *i*-Pr, Et; 6.18 mmol) was added dropwise to the calix[8]arene salt solution (3.09 mmol, procedure I or II). The resultant yellow solution was stirred for 4 h, followed by workup with the standard procedure.

Compound 3b (R = *i*-Pr, M′ = Na): isolated as a mono-THF adduct, 66% (one crop); IR (Nujol mull, cm^{-1}) ν 611, 749, 757, 778, 810, 824, 831, 914, 1013, 1122, 1204, 1250, 1263, 1297, 1361, 1377, 1392, 1415, 1456, 1463, 1470, 2853, 2924, 2952; ^{1}H NMR ($CDCl_3$) δ 15.89 (s, 1 H), 7.33 (s, 1 H), 7.30 (s, 1 H), 7.26 (s, 1 H), 7.24 (s, 1 H), 7.19 (s, 2 H), 7.16 (s, 1 H), 7.10, (s, 2 H), 7.07 (s, 3 H), 7.05 (s, 1 H), 7.00 (s, 1 H), 6.88 (s, 1 H), 6.82 (s, 1 H), 6.26 (d, J = 12.9, 1 H), 5.82 (d, J = 11.7, 1 H), 5.73 (d, J = 13.1, 1 H), 5.56 (d, J = 11.6, 1 H), 5.06 (d, J = 15.1, 1 H), 5.03 (d, J = 15.1, 1 H), 4.72 (d, J = 12.0, 1 H), 4.66 (d, J = 11.3, 1 H), 3.61 (t, J = 6.3, 4 H, THF), 3.47 (d, 11.5, 1 H), 3.36 (d, J = 12.6, 1 H), 3.35 (d, J = 11.7, 1 H), 3.29 (d, J = 10.9, 1 H), 3.27 (d, J = 14.0, 1 H), 3.18 (d, J = 14.0, 1 H), 3.16 (d, J = 13.8, 1 H), 3.14 (d, J = 12.6, 1 H), 2.06 (m, 1 H), 1.93 (m, 1 H), 1.78 (t, J = 6.4, 4 H, THF), 1.24 (s, 45 H), 1.22 (s, 27 H), 0.58 (d, J = 5.6, 3 H), 0.51 (d, J = 5.5, 3 H), −0.82 (d, J = 5.5, 3 H), −1.15 (d, J = 5.6, 3 H); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 165.0, 164.3, 162.8, 162.4, 159.7, 159.4, 157.0, 151.7, 145.4, 144.4, 143.6, 143.1, 142.7, 142.4, 142.3, 142.1, 137.7, 135.6, 133.3, 133.0, 131.7, 131.0, 130.9, 130.8, 130.7, 130.2, 129.1, 128.9, 128.5, 128.4, 126.0, 125.8, 125.7, 125.0, 124.9, 124.8, 124.6, 124.5, 124.4, 124.2, 123.8, 123.6, 123.2, 82.2, 79.9, 67.9 (THF), 36.7, 36.3, 36.1, 36.0, 34.0, 33.9, 33.8, 33.5, 33.4, 31.6, 31.5, 31.4, 25.5 (THF), 24.5, 21.6, 19.9; MS (+FAB) 1551 (M + Na, 10), 1527 (M + H, 7), 1490 (20), 1468 (46), 1422 (14), 1408 (100), 1392 (31); (−FAB) 1527 (M − H, 37), 1505 (20), 1444 (100), 1385 (32). Anal. Calcd for $C_{98}H_{127}NaO_{11}Ti_2$: C, 73.57; H, 8.00; Na, 1.44. Found: C, 73.64; H, 8.29; Na, 1.14.

Method B: Preparation of [4-*tert*-Butylcalix[8]arene(Ti-O-(4-NO$_2$Ph))$_2$][M′]$^+$ (4). **3a** or **3b** (0.770 mmol) was dissolved in THF (60 mL), and 4-nitrophenol (0.21 g, 1.54 mmol), in THF (5 mL), was added dropwise. The resultant dark orange solution was stirred for 2 h. Isolation of the complex was achieved with use of the standard workup procedure.

Compound 4a (M′ = Li): crystallized from diethyl ether–acetonitrile as a bis-THF, mono-acetonitrile adduct, 69%; ^{1}H NMR ($CDCl_3$) δ 16.70 (s, 1 H), 7.39 (d, J = 8.7, 4 H), 7.19 (s, 2 H), 7.16 (m, 4 H), 7.08 (s, 2 H), 6.92 (s, 2 H), 6.88 (s, 2 H), 6.85 (s, 2 H), 6.46 (s, 2 H), 5.79 (d, J = 13.7, 2 H), 5.76 (d, J = 12.1, 2 H), 5.29 (s, 4 H), 4.82 (d, J = 12.0, 2 H), 4.14 (d, J = 14.0, 2 H), 3.74 (s, 8 H, THF), 3.44 (d, J = 12.1, 2 H), 3.37 (d, 2 H), 3.19 (d, J = 12.0, 2 H), 2.89 (d, J = 14.2, 2 H), 1.87 (s, 3 H, MeCN), 1.30 (s, 18 H), 1.22 (s, 8 H, THF), 1.21 (s, 18 H), 1.15 (s, 18 H), 0.92 (s, 18 H); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 169.9, 165.4, 164.8, 158.8, 144.4, 144.1, 143.6, 143.2, 138.0, 134.3, 131.4, 131.2, 130.8, 130.7, 130.4, 129.0, 128.8, 128.7, 128.2, 126.2, 125.8, 125.3, 125.0, 124.7, 124.2, 124.1, 123.8, 123.4, 119.0, 116.9 (MeCN), 68.1 (THF), 36.4, 35.6, 34.1, 34.0, 33.9, 33.5, 31.7, 31.6, 31.6, 31.5, 31.2, 25.5 (THF), 1.30 (MeCN); MS (+FAB) 1524 (15), 1392 (43), 1385 (100), 1370 (39), 1328 (41),

1314 (19), 1272 (13); (-FAB) 1663 (100), 1647 (10), 1524 (74), 1507 (18), 1465 (10), 1400 (16), 1385 (33), 1360 (8). Anal. Calcd for $C_{110}H_{132}N_3O_{16}LiTi_2$: C, 71.23; H, 7.17; N, 2.27; Li, 0.37. Found: C, 70.80; H, 7.34; N, 2.35; Li, 0.38.

Preparation of [Calix[8]arene(Ti-O-*t*-Bu)$_2$][K or BnNH$_3$]$^+$ (6a,b). 4-*tert*-Butylcalix[8]arene (5.18 g, 3.99 mmol) and potassium *tert*-butoxide or benzylamine (3.99 mmol) were combined in THF (150 mL) providing a slurry. A THF solution (15 mL) of Ti(O-*t*-Bu)$_4$ (2.72 g, 7.98 mmol) was added dropwise, and the resultant dark orange, homogeneous solution was stirred for 4 h. The volatiles were removed under reduced pressure, and the resultant orange solid was suspended in pentane (20 mL). The volatiles were again removed in vacuo, providing a free-flowing orange solid that was then dried under vacuo (10^{-3} Torr) for ca. 12 h. Further purification of this product is not necessary for use in the syntheses described below. The NMR spectra of these compounds are complex and thus are not reported here. See the supplementary material for the ^{1}H NMR spectrum of **6a**.

Compound 6a: 99%; MS (+FAB) 1610 (M + K, 59), 1536 (100), 1521 (21), 1498 (29), 1480 (34), 1464 (34), 1424 (54), 1384 (20). Anal. Calcd for $C_{96}H_{123}O_{10}KTi_2$: C, 73.36; H, 7.89; K, 2.49. Found: C, 73.51; H, 7.72; K, 2.24.

Compound 6b: 92%; MS (+FAB) 1641 (M, 2), 1620 (2), 1604 (2), 1464 (5), 1398 (17), 1386 (100), 1370 (32), 1354 (10), 1342 (10), 1328 (31), 1314 (13), 1272 (8), 1257 (5); (-FAB) 1534 (8), 1458 (38), 1416 (13), 1402 (100), 1386 (52), 1370 (14). Anal. Calcd for $C_{103}H_{133}NO_{10}Ti_2$: C, 75.39; H, 8.17; N, 0.85. Found: C, 75.14; H, 8.28; N, 0.88.

Method C. The desired alcohol (1.54 mmol) was added to a THF solution (5 mL) of either Ti(O-*t*-Bu)$_4$ (1.54 mmol; the preferred reagent) or Ti(NMe$_2$)$_4$ (1.54 mmol) and the mixture was stirred for 5 min. This solution was added dropwise to the calix[8]arene salt mixture generated with use of procedure 1 or 11 (0.770-mmol scale). The resulting yellow solution was stirred for 4 h and then worked up with use of the standard procedure.

Compound 9 (ROH = cyclopentanol; R'NH$_2$ = BnNH$_2$): 87%; ^{1}H NMR ($CDCl_3$) δ 15.52 (s, 1 H), 7.37 (d, J = 7.5, 1 H), 7.30 (d, J = 2.3, 1 H), 7.28 (m, 2 H), 7.25 (d, J = 2.2, 1 H), 7.18 (d, J = 1.9, 1 H), 7.13 (m, 7 H), 7.07 (d, J = 2.2, 1 H), 7.05 (d, J = 2.5, 1 H), 7.02 (d, J = 2.1, 1 H), 6.98 (d, J = 2.4, 1 H), 6.87 (d, J = 1.8, 1 H), 6.85 (d, J = 1.6, 1 H), 6.40 (d, J = 7.5, 2 H), 6.02 (d, J = 13.0, 1 H), 5.78 (d, J = 11.5, 1 H), 5.75 (d, J = 12.7, 1 H), 5.49 (d, J = 11.8, 1 H), 4.98 (d, J = 13.8, 1 H), 4.93 (d, J = 13.9, 1 H), 4.70 (d, J = 12.1, 1 H), 4.38 (d, J = 11.5, 1 H), 4.22 (br s, 3 H), 3.41 (d, J = 12.0, 1 H), 3.35 (d, J = 13.1, 1 H), 3.31 (d, J = 11.8, 1 H), 3.24 (d, J = 14.0, 2 H), 3.14 (d, J = 12.1, 1 H), 3.12 (d, J = 13.0, 1 H), 2.95 (d, J = 11.7, 1 H), 2.88 (br s, 1 H), 2.76 (br s, 1 H), 2.27 (m, 1 H), 2.09 (m, 1 H), 1.28 (s, 9 H), 1.24 (s, 9 H), 1.23 (s, 27 H), 1.22 (s, 9 H), 1.21 (s, 9 H), 1.18 (s, 9 H), 1.12 (m, 3 H), 1.00 (m, 3 H), 0.80, (m, 2 H), 0.76 (m, 1 H), 0.72 (m, 1 H), 0.37 (m, 2 H), -0.36 (m, 1 H), -0.51 (m, 1 H), -1.01 (m, 1 H), -1.46 (m, 1 H); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 165.3, 164.4, 164.2, 160.9, 159.5, 159.3, 151.3, 144.7, 144.4, 143.91, 143.87, 143.0, 142.3, 142.2, 141.8, 138.4, 135.7, 133.8, 133.4, 132.5, 131.6, 131.3, 131.1, 130.82, 130.80, 130.5, 130.1, 129.8, 129.7, 129.4, 129.3, 129.0, 128.8, 128.60, 128.57, 128.54, 128.1, 126.4, 126.2, 125.8, 125.5, 125.2, 125.0, 124.9, 124.8, 124.6, 124.4, 124.3, 124.1, 123.9, 123.6, 123.4, 91.2, 89.4, 45.1, 37.0, 36.9, 36.1, 35.9, 34.12, 34.06, 34.0, 33.93, 33.90, 33.89, 33.8, 33.6, 33.4, 32.7, 31.8, 31.7, 31.68, 31.64, 31.61, 31.5, 30.2, 23.6, 23.44, 23.4, 22.3; MS (+FAB) 1665 (M, 8), 1579 (2), 1470 (3), 1400 (12), 1386 (100), 1369 (28), 1327 (26), 1313 (10), 1271 (6). Anal. Calcd for $C_{105}H_{133}O_{10}Ti_2N$: C, 75.75; H, 8.05; N, 0.84. Found: C, 75.81; H, 8.11; N, 0.91.

Method D. A THF (5 mL) solution of the desired alcohol (1.54 mmol) was added to a solution of compound **6a** or **6b** (0.77 mmol) in THF (50 mL) and stirred for 4 h. The standard workup procedure was used.

Compound 12 (ROH = (*S*)-(-)-Ethyl Lactate, R'NH$_2$ = BnNH$_2$): 81%, crystallized as a >15:1 mixture of diastereomers. Only one distinguishable resonance for the minor diastereomer was observed. IR (Nujol mull) ν (C=O) 1647, 1675; ^{1}H NMR ($CDCl_3$) δ 15.54 (s, 1 H), 7.18-7.03 (m, 15 H), 6.98 (d, J = 1.8, 1 H), 6.95 (s, 1 H), 6.92 (s, 1 H), 6.87 (s, 1 H), 6.81 (d, J = 1.6, 2 H), 6.45 (br s, 3 H), 5.97 (d, J = 13.2, 1 H), 5.75 (d, J = 13.3, 1 H), 5.74 (d, J = 12.0, 1 H), 5.46 (d, J = 11.8, 1 H), 5.17 (d, J = 13.1, 1 H), 5.14 (d, J = 13.3, 1 H), 4.79 (br s, 2 H), 4.68 (d, J = 12.1, 1 H), 4.30 (d, J = 11.6, 1 H), 4.21 (m, 1 H), 4.08 (m, 1 H), 4.02 (m, 2 H), 3.32 (d, J = 13.1, 1 H), 3.23 (d, J = 12.0, 1 H), 3.18 (d, J = 12.9, 1 H), 3.16 (d, J = 12.3, 1 H), 3.13 (d, J = 12.0, 1 H), 3.08 (d, J = 14.0, 1 H), 3.06 (d, J = 13.9, 1 H), 2.89 (d, J = 11.6, 1 H), 2.26 (q, J = 7.2, 1 H), 2.05 (q, J = 7.1, 1 H), 1.24 (s, 9 H), 1.23 (s, 18 H), 1.21 (s, 9 H), 1.20 (s, 9 H), 1.18 (s, 18 H), 1.13 (s, 9 H), -0.73 (d, J = 7.1, minor diastereomer), -0.78 (d, J = 7.1, 3 H), -1.00 (d, J = 7.1, 3 H) (the resonances due to the methyl group of the ethoxy substituents are presumably hidden under the *tert*-butyl region); MS (+FAB) 1621 (2), 1504 (7), 1397 (34), 1385 (100), 1369 (73), 1353 (20), 1341 (18), 1327 (70), 1314 (27), 1297 (9), 1271 (16), 1257 (9).

Method E: Preparation of [4-*tert*-Butylcalix[8]arene(Zr-O-*i*-Pr)$_2$][K]$^+$ (15). A solution of Zr(O-*i*-Pr)$_4$·HO-*i*-Pr (1.54 mmol) in THF (5 mL) was added dropwise to the calix[8]arene salt (0.770 mmol) solution prepared with use of procedure 11. The reaction mixture was stirred for 4 h, resulting in a clear, colorless solution. Standard workup procedures were employed: 32%; ^{1}H NMR ($CDCl_3$) δ 14.93 (s, 1 H), 7.34 (s, 1 H), 7.24 (s, 2 H), 7.18 (s, 2 H), 7.16 (s, 2 H), 7.14 (s, 1 H), 7.11 (s, 1 H), 7.10 (s, 2 H), 7.07 (s, 1 H), 7.02 (s, 1 H), 6.94 (s, 1 H), 6.90 (s, 1 H), 6.86 (s, 1 H), 6.01 (d, J = 13.3, 1 H), 5.37 (d, J = 12.1, 1 H), 5.29 (d, J = 13.6, 1 H), 5.15 (d, J = 12.1, 1 H), 4.72 (d, J = 14.3, 1 H), 4.71 (d, J = 13.9, 1 H), 4.60 (d, J = 12.3, 1 H), 4.56 (d, J = 11.9, 1 H), 3.41 (m, 2 H), 3.36 (d, J = 13.4, 1 H), 3.24 (d, J = 15.0, 1 H), 3.21 (d, J = 14.9, 1 H), 3.18 (d, J = 12.4, 1 H), 3.14 (d, J = 12.5, 1 H), 1.98 (m, 1 H), 1.83 (m, 1 H), 1.23 (s, 9 H), 1.22 (s, 9 H), 1.21 (s, 9 H), 1.20 (s, 9 H), 1.19 (s, 9 H), 1.18 (s, 9 H), 1.17 (s, 9 H), 0.35 (d, J = 6.1, 3 H), 0.22 (d, J = 6.2, 3 H), -0.70 (d, J = 6.1, 3 H), -0.96 (d, J = 6.2, 1 H); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 159.9, 158.2, 156.9, 156.7, 155.3, 154.3, 154.0, 148.0, 145.4, 145.1, 143.5, 142.3, 141.3, 141.1, 140.8, 135.9, 134.9, 133.1, 132.5, 132.1, 131.9, 131.8, 131.3, 131.17, 131.18, 130.4, 129.7, 129.6, 129.51, 129.47, 128.6, 127.2, 126.8, 125.6, 125.3, 125.1, 124.9, 124.8, 124.6, 123.8, 123.1, 71.8, 71.4, 35.8, 35.6, 35.0, 34.9, 34.6, 34.1, 34.02, 33.98, 33.88, 33.85, 33.8, 32.9, 32.7, 31.8, 31.71, 31.68, 31.6, 31.5, 31.4, 31.3, 24.1, 23.5, 22.0; MS (+FAB) 1668 (M + K, 64), 1629 (M, 22), 1608 (42), 1569 (32), 1510 (100). Anal. Calcd for $C_{94}H_{119}KO_{10}Zr_2$: C, 69.24; H, 7.36; K, 2.40. Found: C, 68.94; H, 7.67; K, 2.19.

Method F: Preparation of [4-*tert*-Butylcalix[8]arene(Sn-Y)$_2$][K]$^+$ (Y = O-*i*-Pr (16), *n*-Bu (17)). A THF solution (5 mL) of either Sn(O-*i*-Pr)$_4$·HO-*i*-Pr (0.36 mmol) or Sn(O-*i*-Pr)$_3$(*n*-Bu) (0.36 mmol) was added to the calix[8]arene salt solution (0.18 mmol) generated with use of procedure 1. The resultant pale yellow solution was stirred for 20 h, followed by workup with the standard procedure.

Compound 17 (Y = *n*-Bu): 68%; ^{1}H NMR ($CDCl_3$) δ 17.33 (s, 1 H), 7.19 (m, 12 H), 6.90 (m, 4 H), 6.44 (d, J = 13.0, 1 H), 6.04 (d, J = 11.5, 1 H), 5.82 (d, J = 13.4, 1 H), 5.77 (d, J = 11.4, 1 H), 4.99 (d, J = 12.0, 1 H), 4.85 (d, J = 11.8, 1 H), 4.23 (t, J = 15.1, 2 H), 3.57 (d, J = 11.8, 1 H), 3.53 (THF, 4 H), 3.46 (d, J = 11.8, 1 H), 3.43 (d, J = 13.5, 1 H), 3.35 (m, 2 H), 3.27 (d, J = 15.0, 1 H), 3.20 (d, J = 9.0, 1 H), 3.18 (d, J = 11.4, 1 H), 1.77 (THF, 4 H), 1.25 (m, 9 H), 1.22 (m, 54 H), 1.20 (m, 9 H), 0.88 (m, 1 H), 0.37 (m, 1 H), 0.29 (m, 1 H), 0.20 (m, 12 H), -0.10 (m, 2 H), -0.34 (m, 2 H); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 158.5, 158.2, 155.4, 154.7, 154.4, 151.8, 150.3, 150.0, 147.4, 147.2, 146.0, 145.8, 144.6, 143.1, 141.7, 141.3, 141.2, 140.9, 139.7, 137.2, 135.9, 135.3, 135.1, 134.7, 134.6, 134.3, 134.0, 133.34, 133.28, 133.2, 131.9, 130.8, 129.4, 126.6, 126.0, 125.8, 125.7, 125.50, 125.53, 125.3, 125.2, 125.04, 125.00, 124.8, 124.5, 124.1, 124.04, 124.00, 123.8, 67.7 (THF), 37.1, 36.6, 34.8, 34.5, 34.2, 34.1, 34.00, 33.98, 33.93, 33.89, 33.8, 32.4, 32.3, 31.72, 31.68, 31.63, 31.55, 31.49, 31.47, 31.46, 31.4, 28.0, 27.4, 26.4, 26.1, 25.5 (THF) 16.0, 14.0, 12.4, 12.3; MS (+FAB) 1720 ((M + K)$^+$, 100), 1682 ((M + H)$^+$, 78), 1664, (36), 1624 (23), 1606 (23).

Method G: Preparation of [4-*tert*-Butylcalix[8]arene(V=O)$_2$][(*R*)-(+)-1-(1-naphthyl)ethylamine]$^+$ (18). A THF solution (5 mL) of V(O)(O-*i*-Pr)$_3$ (1.54 mmol) was added dropwise to a calixarene salt mixture (0.770 mmole) generated with use of procedure 1. The reaction solution darkened rapidly. After the solution was stirred for 4 h, the volatiles were removed in vacuo, and the resultant black solid was crystallized from pentane–diethyl ether to give black crystals (80%). The following spectra are of a 4:1 mixture of diastereomers: IR (Nujol mull, cm^{-1}) ν(V=O) 975; ^{1}H NMR ($CDCl_3$) δ 15.02 (s, 0.75 H), 14.96 (s, 0.25 H), 7.82-7.85 (m, 1 H), 7.76 (d, J = 8.4, 0.25 H), 7.47-7.54 (m, 2.25 H), 7.35-7.40 (m, 2 H), 7.31 (s, 0.25 H), 6.92-7.31 (m, 15.25 H), 6.86 (s, 0.25 H), 6.77 (d, J = 8.4, 0.75 H), 6.69 (d, J = 2.4, 0.75 H), 6.13 (d, J = 13.1, 0.75 H), 6.07 (d, J = 7.8, 0.25 H), 5.78 (d, J = 11.6, 0.5 H), 5.77 (d, J = 13.2, 0.75 H), 5.76 (d, J = 11.8, 1.25 H), 5.69 (d, J = 13.9, 1 H), 5.62 (d, J = 14.1, 1 H), 5.37-5.42 (m, 1 H), 4.90 (d, J = 11.3, 0.75 H), 4.63 (d, J = 12.1, 0.75 H), 4.56-4.61 (m, 0.5 H), 4.10 (br s, 3 H), 3.88 (m, 1 H), 3.27-3.54 (m, 7.75 H), 3.08 (d, J = 11.4, 0.25 H), 1.27 (s, 2.25 H), 1.26 (s, 6.75 H), 1.25 (s, 9 H), 1.24 (s, 4.5 H), 1.23 (s, 13.5 H), 1.21 (s, 9 H), 1.20 (s, 6.75 H), 1.19 (s, 2.25 H), 1.18 (s, 6.75 H), 1.16 (s, 2.25 H), 1.11 (d, J = 6.9, 2.25 H), 0.78 (s, 2.25 H), 0.47 (s, 6.75 H) (the ammonium ion methyl resonance for the minor diastereomer is presumably hidden in the 1.17-1.28 ppm region). Peaks corresponding to the minor isomer were difficult to distinguish in the ^{13}C NMR spectrum of the mixture. One characteristic peak is indicated below: ^{13}C{^{1}H} NMR ($CDCl_3$) δ 174.5, 173.1, 170.1, 168.4, 168.3, 166.8, 166.4, 166.1, 165.1, 153.4, 146.6, 145.9, 145.8, 145.5, 145.41, 145.37, 145.3, 145.2, 144.7, 144.4, 136.8, 135.6, 134.0, 133.0, 132.7, 132.6, 131.7,

131.43, 131.40, 131.2, 131.0, 130.6, 129.9, 129.6, 129.55, 129.53, 129.4, 129.3, 129.2, 129.1, 129.02, 128.98, 128.7, 128.4, 128.32, 128.27, 128.21, 128.15, 127.8, 127.7, 127.5, 127.4, 126.9, 126.4, 126.1, 125.5, 125.3, 125.2, 125.1, 125.0, 124.7, 124.6, 124.4, 124.3, 124.24, 124.20, 124.04, 123.95, 123.9, 123.8, 123.6, 122.4, 121.1, 46.6, 37.1, 36.6, 36.5, 35.9, 34.9, 34.3, 34.2, 34.13, 34.11, 34.06, 34.0, 33.9, 33.8, 33.6, 32.3, 31.7, 31.67, 31.64, 31.59, 31.58, 31.5, 31.3, 31.2, 31.1, 30.6, 15.4 (minor), 15.3; MS (+FAB)1598 (M + H, 24), 1408 (100).

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Supplementary Material Available: Full characterization of compounds **2a**, **3a**,**c**-**e**, **4b**, **5**, **7**, **8**, **10**, **11**, **13**, **14**, **16** and **18**, experimental details of the mass spectrometry and two-dimensional NMR spectroscopy experiments, one-dimensional ^{1}H NMR spectrum of **3b** at −43 °C with all resonances labeled according to Figure 5, COSY spectrum of **3b** at −45 °C, ROESY spectrum of **3b** at −43 °C, and difference NOE spectrum of **3b** at −40 °C (35 pages). Ordering information is given on any current masthead page.

Nonplanar Porphyrins. X-ray Structures of (2,3,7,8,12,13,17,18-Octaethyl- and -Octamethyl-5,10,15,20-tetraphenylporphinato)zinc(II)

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Abstract: X-ray structures of the peripherally crowded porphyrins, (2,3,7,8,12,13,17,18-octaethyl-5,10,15,20-tetraphenylporphinato)Zn(II)-3MeOH solvate (ZnOETPP·3MeOH) and (2,3,7,8,12,13,17,18-octamethyl-5,10,15,20-tetraphenylporphinato)Zn(II)-pyridine-2HCCl$_3$ (ZnOMTPP·py·2HCCl$_3$) are reported. Both molecules are severely nonplanar and assume saddle shapes. ^{1}H NMR data confirm that the conformational distortions are maintained in solution. The consequences of distorting the macrocycles are significant: optical, redox, basicity, and excited-state properties are altered in agreement with previous theoretical calculations. These results form part of an expanding body of structural information that clearly demonstrates that porphinoid skeletons are flexible and that distortions of the macrocycles can be imposed by steric interactions in vitro and in vivo. Conformational variations thus provide an attractively simple mechanism for modulating a wide range of physical and chemical properties of porphyrinic chromophores and prosthetic groups in vitro and in vivo. Crystallographic data. $ZnN_4C_{60}H_{60}\cdot 3CH_3OH$: triclinic space group $P\bar{1}$, a = 14.017 (10) Å, b = 16.494 (7) Å, c = 13.073 (9) Å, α = 96.12 (5)°, β = 107.48 (6)°, γ = 105.23 (6)°, V = 2724.5 Å^3, Z = 2; R_F and R_{wF} = 0.062, based on 4281 reflections with $F_o > 2\sigma F_o$; T = 200 K. $ZnN_4C_{52}H_{44}\cdot C_5D_5N\cdot 2HCCl_3$: monoclinic space group $C2/c$, a = 22.411 (23) Å, b = 12.552 (10) Å, c = 19.287 (12) Å, β = 98.66 (10)°, V = 5363.6 Å^3, Z = 4; R_F = 0.060 and R_{wF} = 0.061, based on 1722 reflections with $F_o > 2\sigma F_o$; T = 298 K.

Introduction

Recent structural data for porphyrins, chlorins, bacteriochlorins, and isobacteriochlorins as isolated molecules and in proteins illustrate the considerable flexibility of the chromophores and the significant distortions that can be imposed upon porphinoid macrocycles by crystal packing, steric effects, or protein constraints.[2-8] Particularly intriguing are the multiple conformations reported for the bacteriochlorophylls *b* that comprise the primary donor or special pair of the reaction center of *Rhodopseudomonas viridis*,[7] and for the bacteriochlorophylls *a* that constitute a light-harvesting antenna complex of *Prosthecochloris aestuarii*.[8] Theoretical calculations[6,9] indicate that conformational variations would shift the highest occupied (HOMO) and lowest unoccupied

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