Functionalization of *p-tert*-Butylcalix[5]arene by Alkylation with 2-(Chloromethyl)pyridine Hydrochloride

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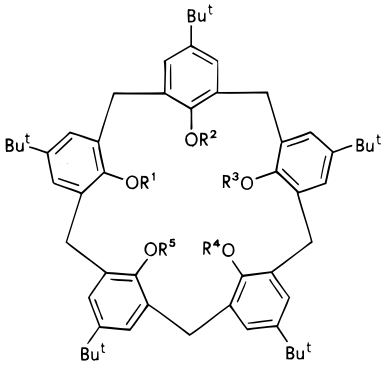
A study of the base-catalyzed alkylation of *p-tert*-butylcalix[5]arene (**1**) with 2-(chloromethyl)pyridine hydrochloride (PicCl·HCl) in DMF has led to the isolation and identification of the 7 possible pyridinyl homologues of **1** in the cone conformation. Reactions of **1** with limiting amounts of alkylating agent (2 to 4 equiv) and base (CsF, $KHCO_3$, BaO/$Ba(OH)_2$, K_2CO_3, NaH) produced invariably complex mixtures, which were separated into the pure components by chromatographic means. Regioselective 1,2,4- or 1,2,3-tri-O-alkylation has been achieved in moderate yield (21−22%) by an appropriate choice of molar ratios, solvent, and base. Pentaethers **8**−**10**, endowed with 2-pyridinyl, 3-pyridinyl, and 2-quinolylmethyl pendant groups at the lower rim, respectively, have been also prepared in good yield. The cone conformation in solution for all new compounds has been established by NMR spectroscopy and confirmed for 1,2,3-tri-O-alkylated **5** by a single-crystal X-ray analysis. In the solid state the cone conformation of **5** is mainly determined by the presence of intramolecular hydrogen bonds between adjacent phenolic oxygens, and between the phenolic oxygen and the proximal pyridinyl nitrogen.

Introduction

The chemistry of readily accessible even-membered calix[*n*]arenes ($n = 4, 6, 8$) has been extensively studied,[1] while that of odd-membered calix[*n*]arenes ($n = 5, 7$) has lagged behind, mainly due to the very low yield of existing synthetic procedures.[2] The calix[5]arenes are especially attractive members of the calixarene family, because they possess a larger cavity than the calix[4]arenes while retaining the capability of assuming a true cone conformation. Improved synthetic procedures[3] now allow the easy accumulation of workable amounts of *p-tert*-butylcalix[5]arene (**1**), opening new prospects for the design and synthesis of novel classes of molecular hosts and ligands. The state of the art of the preparation, conformational behavior, chemical transformations at either the upper and lower rim, and complexation properties of calix[5]arenes has been recently reviewed by Vicens.[4]

Following earlier studies concerning the synthesis, structure, and conformation of even membered calix[*n*]arenes ($n = 4, 6$) bearing pyridinyl pendant groups at the lower rim,[5] we have now investigated the base-catalyzed alkylation of **1** with 2-(chloromethyl)pyridine hydrochloride (PicCl·HCl). We have found that by tuning the reaction conditions (amount of electrophile, base, solvent) it is possible to isolate in variable yield the seven possible pyridino homologues **2**−**8** derivable from **1** (Chart 1). Besides, exhaustive alkylation of **1** with the appropriate *N*-heterocyclic electrophiles has produced pentaethers **9** and **10**, endowed with 3-pyridinyl and 2-quinolylmethyl pendant groups at the lower rim. In this paper we report the synthesis, structural characterization and conformation of these compounds. A result

Chart 1



Compd	R^1	R^2	R^3	R^4	R^5
1	H	H	H	H	H
2	2-Pic	H	H	H	H
3	2-Pic	2-Pic	H	H	H
4	2-Pic	H	2-Pic	H	H
5	2-Pic	2-Pic	2-Pic	H	H
6	2-Pic	2-Pic	H	2-Pic	H
7	2-Pic	2-Pic	2-Pic	2-Pic	H
8	2-Pic	2-Pic	2-Pic	2-Pic	2-Pic
9	3-Pic	3-Pic	3-Pic	3-Pic	3-Pic
10	2-Quin	2-Quin	2-Quin	2-Quin	2-Quin

[⊗] Abstract published in *Advance ACS Abstracts,* March 1, 1996.

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(2) Ninagawa, A.; Matsuda, H. *Makromol. Chem., Rapid Commun.* **1982**, *3*, 65. Markowitz, M. A.; Janout, V.; Castner, D. G.; Regen, S. L. *J. Am. Chem. Soc.* **1989**, *111*, 8192.

(3) Stewart, D. R.; Gutsche, C. D. *Org. Prep. Proc. Int.* **1993**, *25*, 137. Iwamoto, K.; Araki, K.; Shinkai, S. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 1499.

(4) Asfari, Z.; Vicens, J. *Acros Org. Acta* **1995**, *1*, 18.

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Table 1. Product Composition in the Base-Catalyzed Lower-Rim Alkylation of *p-tert*-butylcalix[5]arene 1 (0.5 mmol) in dry DMF at 60 °C for 20 h

entry	electrophile (equiv)	base (equiv)	product distribution (%)[a]
1	2-PicCl·HCl (2)	$KHCO_3$ (4)	**2** (66), **3** (<2), **4** (trace), **6** (7)
2	2-PicCl (2)[b]	CsF (4)	**2** (63), **3** (2), **4** (4), **6** (9)
3	2-PicCl (4)[c]	CsF (4)	**2** (54), **3** (8), **4** (3), **6** (22)
4	2-PicCl·HCl (2)	$BaO/Ba(OH)_2$ (4)	**2** (43), **3** (2), **4** (trace), **5** (18), **6** (trace)
5	2-PicCl·HCl (2)	K_2CO_3 (2)	**2** (trace), **3** (6), **4** (trace), **5** (21)
6	2-PicCl·HCl (4)	K_2CO_3 (4)	**3** (18), **4** (trace), **5** (6), **6** (2), **7** (17)
7	2-PicCl·HCl (2)	NaH (4)	**2** (<2), **3** (<2), **4**(<2), **5** (10), **6** (<2), **7** (<2)
8	2-PicCl·HCl (20)	K_2CO_3 (40)	**8** (80)
9	3-PicCl (30)[d]	NaH (30)	**9** (42)
10	2-QuinCl·HCl (20)	K_2CO_3 (40)	**10** (77)

[a] Isolated yield. [b] In dry MeCN at reflux for 24 h. [c] In dry MeCN−acetone (2:1, v/v) at reflux for 24 h. [d] In THF at reflux for 8 h.

of particular interest is that (1,2,3)- or (1,2,4)-tri-O-alkylation can be realized with elevated regioselectivity by a proper choice of the molar ratios between the reactants, the solvent, and the strength of the base applied.

Results and Discussion

Alkylation of *p-tert*-butylcalix[5]arene (**1**) with PicCl·HCl (2−20 equiv) was carried in anhydrous *N*,*N*-dimethylformamide (DMF) at 60 °C for 20 h in the presence of base (CsF, $KHCO_3$, $BaO/Ba(OH)_2$, K_2CO_3, or NaH). Table 1 summarizes the product composition as a function of the molar ratios between the reactants and the identity of the base applied. Reactions with limiting amounts of electrophile led to complex mixtures of products of partial alkylation, which could be eventually separated into the pure components by careful chromatography (SiO_2, a gradient of AcOEt in cyclohexane as the eluent), followed by crystallization. Conversely, exhaustive alkylation reactions were clean, leading to the desired pentaethers in moderate to good yields. The molecular weights of the pure components were deduced by microanalytical data and FAB (+) MS, their structures being firmly established by ^{1}H NMR/^{13}C NMR spectroscopy.

Syntheses. Treatment of *p-tert*-butylcalix[5]arene with limiting amounts of PicCl·HCl and base gave complex mixtures of products representing various stages of alkylation. When **1** was reacted with PicCl·HCl (2 equiv) and very weak bases ($KHCO_3$ or CsF, Table 1, entries 1 and 2), monoether **2** was isolated as the main compound (63−66% yield), along with minute amounts of (1,2)- and (1,3)-diethers **3** and **4**, and (1,2,4)-triether **6** (7−9% yield). The yield of **6** could be reasonably improved (22%) by using the free PicCl and CsF (4 equiv each) in refluxing MeCN−acetone (Table 1, entry 3).

The use of a little stronger base, such as $BaO/Ba(OH)_2$, and 2 equiv of electrophile decreased the yield of monoether **2** to 43%, while sizable amounts of (1,2,3)-triether **5** (18%) could be isolated (Table 1, entry 4). By replacing K_2CO_3 (2 equiv) for $BaO/Ba(OH)_2$ (Table 1, entry 5), almost complete disappearance of compound **2** was observed, and the product mainly consisted of (1,2,3)-triether **5** (21%), accompanied by minor amounts of (1,2)-diether **3** (6%) and unreacted **1** (ca. 60%).

When alkylation of **1** was conducted with PicCl·HCl and K_2CO_3 (4 equiv each, Table 1, entry 6), tetraether **7** was isolated in 17% yield, in addition to (1,2)-diether **3** (18%) and small amounts of regioisomeric triethers **5** and **6**.

No selectivity at all was observed when **1** was subjected to 2 equiv of electrophile in the presence of the very strong base NaH (4 equiv, Table 1, entry 7), the product consisting of a mixture of all possible partially alkylated calix[5]arenes **2**−**7**, along with massive amounts of unreacted **1**.

Exhaustive alkylation of **1** with a large excess of *N*-heterocyclic electrophile (20−30 equiv) and base (K_2CO_3 or NaH) in anhydrous DMF or THF afforded penta-O-alkylated compounds **8**−**10** in 42−80% yield (Table 1, entries 8−10).

On the basis of product composition as a function of the molar ratios between the reagents (Table 1), two main reaction pathways can be envisaged for the partial alkylation of **1** with PicCl·HCl, depending on the identity and strength of the base applied (Figure 1). By using very weak bases (CsF) and 4 equiv of electrophile, the alkylation process can be driven with elevated regioselectivity to the (1,2,4)-trisubstitution, while with stronger bases ($BaO/Ba(OH)_2$ or K_2CO_3) accumulation of the alternative (1,2,3) tri-O-alkylated product is achieved.

The proposed reaction pathways are corroborated by the results of alkylation reactions of isolated samples of either of the diethers (kee intermediates). Alkylation of 1,3-diether **4** with PicCl (free base, 1 equiv) and CsF (1 equiv) in dry DMF at 70 °C produced (1,2,4)-triether **6** in 30% yield, a trace amount of regioisomer **5**, and tetraether **7** (13%), along with unreacted **4** (42%). On the other hand, alkylation of diether **3** with PicCl·HCl (1 equiv) and K_2CO_3 (2 equiv) under analogous conditions was less selective, affording both tri-O-alkylated derivatives **5** and **6** (ratio ca. 3:2 from ^{1}H NMR analysis), along with sizable amounts of tetraether **7**.

The origin of regioselective (1,2,4)-tri-O-alkylation of **1** with CsF can be explained by the discriminating ability of our electrophile toward phenoxide intermediates of different stability. By assuming that the reaction proceeds through stepwise substitution of the OH groups, the first obvious step is the conversion of **1** to **2**. By analogy with the alkylation mechanism proposed for calixarenes having an even number of phenol residues,[6] further alkylation of **2** is likely to occur *via* a sequence of alternating deprotonation and alkylation steps involving *preferentially* the phenoxide anion(s) stabilized by two flanking hydrogen bonds (leading to intermediate **4**) and then by a single hydrogen bond (leading to compound **6**).

The results of the partial alkylation of **1** and **3** in the presence of little stronger bases [$BaO/Ba(OH)_2$, K_2CO_3] jar a bit with the above rationale based simply on the stability of monophenoxide anion intermediates, and it seems that additional factors may affect the reaction

(6) van Loon, J. D.; Verboom, W.; Reinhoudt, D. N. *Org. Prep. Proc. Int.* **1992**, *24*, 437. Neri, P.; Consoli, G. M. L.; Cunsolo, F.; Piattelli, M. *Tetrahedron Lett.* **1994**, *35*, 2795. Neri, P.; Battocolo, E.; Cunsolo, F.; Geraci, C.; Piattelli, M. *J. Org. Chem.* **1994**, *59*, 3880.

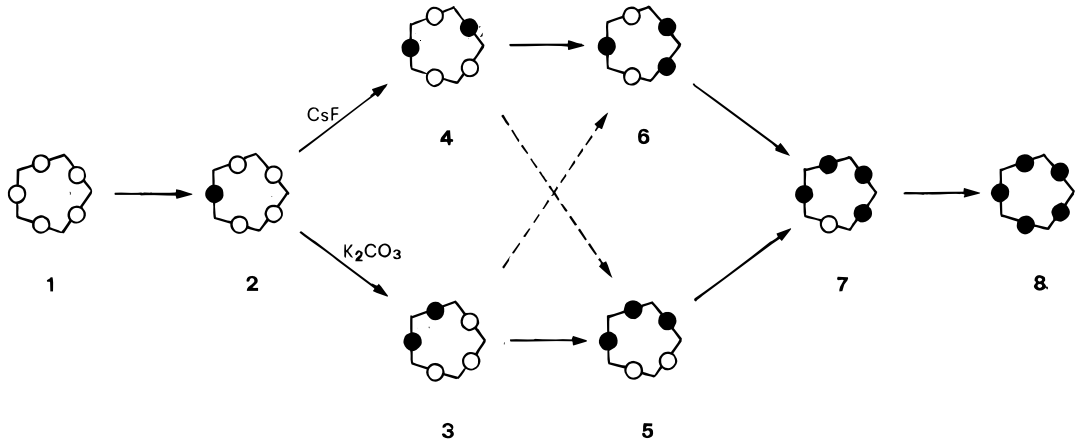

Figure 1. Schematic representation of the seven pyridino homologues **2**−**8** derivable from *p-tert*-butylcalix[5]arene (**1**), and possible reaction pathways for their formation, depending on the base applied. Dashed arrows refer to less plausible reaction courses. Filled and empty spheres represent alkylated and unalkylated phenol rings, respectively.

course: among these, one may take into account a possible role of the coordinating ability of the α-picolyl substituent on the stabilization of K^+ or Ba^{2+} phenolates, generated by deprotonation of the adjacent OH group, to explain the formation of 1,2-diether **3**.

In agreement with the conclusions drawn by Gutsche for the partial alkylation of **1** with MeI and $KHCO_3$,[7] di-O-alkylated regioisomers **3** and **4** are isolated in low yield in our experiments, since they appear to be much more reactive than monoether **2**.

NMR Spectral Features and Conformation. NMR spectroscopy has been shown to provide a powerful tool for determining the conformation and conformational mobility of calixarenes in solution. In the case of the four extreme conformers of pyridinocalix[4]arenes, the methylene and oxymethylene protons and carbons displayed distinctive NMR spectral patterns arising from each conformation.[5f] Similarly to calix[4]arenes, the calix[5]arenes present conformational isomerism and can exist in four basic up/down conformations which can be designated as cone, partial cone, 1,2-alternate, and 1,3-alternate. NMR measurements are also useful for making the conformational assignments of calix[5]arene derivatives, and Gutsche has described the symmetry characteristics and expected resonance patterns associated with ArH, $ArCH_2Ar$, and *tert*-butyl hydrogens for the various conformers of **1**.[7]

The ^1H NMR spectra of partially alkylated calix[5]arenes **2**-**7** show spectral patterns fully compatible with a C_s symmetry point group of the molecules, i.e. three sets of resonances for the *tert*-butyl groups, the bridging methylenes, and aromatic protons in a 2:2:1 ratio, which allow us to rule out the presence of asymmetric structures in solution at ordinary temperatures.

The three sets of doublets in a 2:2:1 ratio for $ArCH_2Ar$ groups in the usual region (δ 3.32−3.59 and 4.05−4.76), and the presence of $ArCH_2Ar$ methylene carbon resonances[8,9] in the range 28.20−31.33 ppm are commensurate with a cone conformation for **2**-**7**.

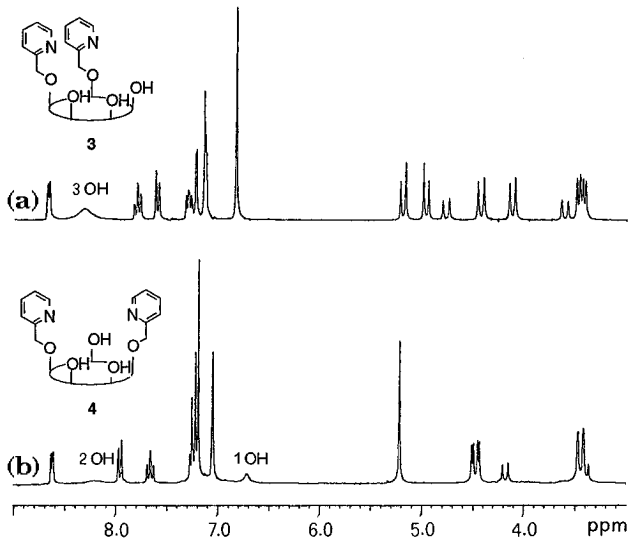

Figure 2. The 3.0−9.0 ppm region of the ^1H NMR spectra ($CDCl_3$, 250 MHz, 295 K) of (1,2)- and (1,3)-di-O-alkylated regioisomers **3** and **4**, respectively.

Apart from differences associated with the split pattern of heteroaromatic residues attached to phenoxy groups, pentaethers **8**-**10** display very similar ^1H NMR spectra. The *tert*-butyl, oxymethylene, and aromatic protons appear as singlets with an AX system ($\Delta\delta > 1$) for the bridging methylene protons (C_{5v} symmetry), a pattern reminiscent of a calix[4]arene in a stable cone conformation. These data along with a single methylene carbon resonance at ca. 29.5 ppm suggest that pentaethers **8**-**10** also possess a fixed conelike conformation.

As far as the structural assignments are concerned, regioisomeric diethers **3** and **4,** and triethers **5** and **6** can be easily distinguished by ^1H NMR spectroscopy. Compound **3** displays (Figure 2a) a twelve-line pattern arising from the three well-resolved AB systems for $ArCH_2Ar$ groups, a diagnostically important AB system for the diastereotopic oxymethylenes, and a very broad downfield resonance (integrating for three protons exchangeable with D_2O), suggestive of a continuous row of intramolecular hydrogen bonded OH groups. In sharp contrast, calix[5]arene **4** exhibits (Figure 2b) a sharp singlet for oxymethylenes, and more importantly two broad resonances at δ 8.20 and 6.70 ppm in the ratio 2:1 for the OH groups. The downfield signal is assigned to the two

(7) Stewart, D. R.; Krawiec, M.; Kashyap, R. P.; Watson, W. H., Gutsche, C. D. *J. Am. Chem. Soc.* **1995**, *117*, 586.

(8) We have observed that the single rule proposed by de Mendoza for the determination of calix[4]arene conformations (i.e., $ArCH_2Ar$ resonances at δ 30−33 or 36−38 ppm indicative of *syn* or *anti* orientation of adjacent aryl rings, respectively),[9] can be *reliably* extended to the larger calixarenes only when interconversion between conformers is inhibited.

(9) Jaime, C.; de Mendoza, J.; Prados, P.; Nieto, P. M.; Sánchez, C. *J. Org. Chem.* **1991**, *56*, 3372.

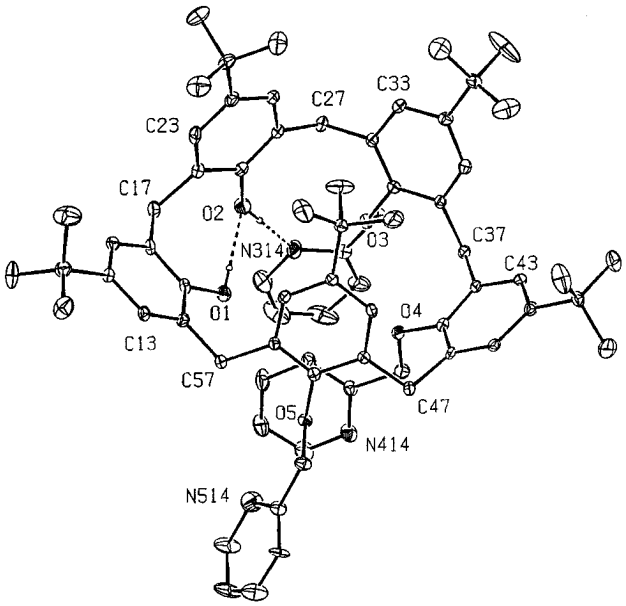

Figure 3. A view of **5**, with an indication of the crystallographic numbering scheme. For clarity, thermal ellipsoids are drawn at the 20% probability level, and only the two hydroxyl H atoms are shown.

adjacent OH groups involved in a strong intramolecular hydrogen bonding, while the upfield resonance is obviously attributed to the "isolated" OH group sandwitched between adjoining OCH_2Py groups.[10]

The structures of regioisomers **5** and **6** were tentatively assigned by using similar arguments on the positions of the OH resonances (a broad downfield resonance at δ 8.21 ppm in **5** and a sharp upfield singlet at δ 7.18 ppm in **6**).

The assignments made are completely substantiated by a single-crystal X-ray analysis of triether **5**. A view of **5** showing the conformation in the solid state is reported in Figure 3. Molecular dimensions are in accord with accepted values. This calix[5]arene adopts a distorted cone conformation, with four of the *tert*-butyl substituted phenyl rings being tilted away from the center of the calix cup, while the remaining ring is tilted so that its *tert*-butyl group is directed toward the cup. Dihedral angles (deg) which the aromatic ring planes make with the mean plane of the five CH_2 moieties are as follows: ring 1, +30.1(1); ring 2, + 76.3(1); ring 3, +67.7(1); ring 4, + 41.7(3); ring 5, −58.4(1) (positive values indicate that the ring is tilted so that its *tert*-butyl group is directed away from the ring center). The conformation in the solid state is partially determined by intramolecular O−H···O hydrogen bonding between O1 and O2 (O···O 3.025(6) Å, Figure 3). The N atom of one of the pendant $OCH_2C_5H_4N$ groups is the acceptor in a O−H···N hydrogen bond involving the hydroxyl group at O2 (O2···N314 2.772(7) Å). This conformation effectively precludes any solvent molecule from being enclathrated in the calix cone; a dichloromethane molecule of solvation was found in the lattice lying between calix[5] molecules (with 0.5 occupancy).

The parent *p-tert*-butylcalix[5]arene (**1**) is a conformationally flexible molecule, as deduced from the broad singlet for the $ArCH_2Ar$ protons at room temperature, and dynamic ^{1}H NMR measurements have demonstrated

(10) The structure of isomeric (1,2)- and (1,3)-bridged calix[5]crown ethers has been assigned similarly: Kraft, D.; Arnecke, R.; Böhmer, V.; Vogt, W. *Tetrahedron* **1993**, *49*, 6019.

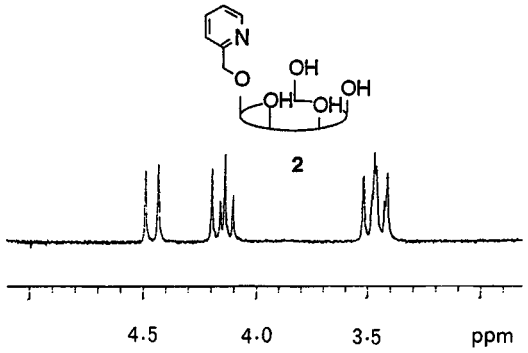

Figure 4. The methylene region in the ^{1}H NMR spectrum (DMSO-d_6, 250 MHz, 385 K) of monoether **2**.

a facile interconversion among various conformers with a coalescence temperature of 271 K and an inversion barrier of 13.2 kcal mol^{-1} in $CDCl_3$.[11] Due to the presence of the large *p-tert*-butyl groups, conformational interconversion of **1** likely occurs via the "lower rim through the annulus" pathway. However, upon conversion to ethers or esters the conformation mobility changes, generally in the direction of diminished mobility.[7,12] Conversion of **1** to the monoether **2** reduces drastically the conformational mobility, as inferred from a set of three pairs of doublets at room temperature for the bridging methylene protons in $CDCl_3$ which show no hint for coalescence up to 385 K in DMSO-d_6 (Figure 4), with an estimated ΔG > 20 kcal mol^{-1}. The strong intramolecular hydrogen bonding between OH groups and the steric hindrance effect of the 2-pyridinyl substituent are believed to act cooperatively in reducing the conformational mobility of **2**. Compound **2** is assumed to be in the cone-in conformation, with the shielded *tert*-butyl group of the alkylated phenol ring canted inward in the calix cavity and the pyridinyloxy group attached to it oriented outward.

Preliminary extraction experiments (metal picrates, water/CH_2Cl_2) with pentaethers **8** and **10** show a preference for the complexation of the larger alkali cations. In addition, the 1:1 Rb^+ picrate complex with **8** has been prepared in high yield by treating the ligand with a fourfold excess of salt in $CHCl_3$. The ^{1}H NMR spectrum of the Rb^+ complex with **8** in $CDCl_3$ shows that oxymethylene and H4, H5, and H6 pyridyl protons are shifted downfield ($\Delta\delta$ = 0.09−0.22 ppm), as compared to the free ligand, while H3 pyridyl protons and axial methylenes move upfield with a shielding of 0.31 and 0.39 ppm, respectively. This trend parallels the one already observed in the complexation of alkali metal cations by the smaller cone *p-tert*-butyltetrakis[(2-pyridylmethyl)oxy]-calix[4]arene,[14] suggesting that also in the present case both oxygen and nitrogen donor atoms act cooperatively in the complexation of alkali metal ions.

Conclusions

The alkylation of *p-tert*-butylcalix[5]arene (**1**) with PicCl·HCl in DMF under different reaction conditions (molar ratios of the reactants, base, solvent) has led to

(11) Gutsche, C. D.; Bauer, L. J. *J. Am. Chem. Soc.* **1985**, *107*, 6052.
(12) Souley, B.; Asfari, Z.; Vicens, J. *Polish J. Chem.* **1993**, *67*, 763.
(13) Pappalardo, S.; Ferguson, G.; Neri, P.; Rocco, C. *J. Org. Chem.* **1995**, *60*, 4756.
(14) Ferguson, G.; Gallagher, J. F.; Giunta, L.; Neri, P.; Pappalardo, S.; Parisi, M. *J. Org. Chem.* **1994**, *59*, 42.

the isolation and identification of the seven possible pyridinocalix[5]arene homologues in a cone conformation. Regioselective (1,2,3)- or (1,2,4)-tri-O-alkylation has been realized in reasonable yield by using K_2CO_3 or CsF, respectively. Mono- to tri-O-alkylated calix[5]arenes **2-6** are very useful intermediates to generate inherently chiral derivatives,[14,15] since they present only a plane of symmetry, which can be lost by appropriate functionalization at the lower rim. Taking advantage of the basic knowledge achieved by the present study on the partial alkylation of **1**, future work will be directed toward the exploration of chemical modifications leading to molecular asymmetry in calix[5]arenes.

Experimental Section[16]

Partial Alkylation of 1 with 2-PicCl·HCl. A stirred mixture of **1** (405 mg, 0.5 mmol), 2-PicCl·HCl and base (see Table 1 for molar ratios) in dry DMF (10 mL) was kept at 60 °C for 1 d under N_2. The solvent was evaporated in vacuo, and the residue was partitioned between water and $CHCl_3$. The organic layer was dried over $MgSO_4$ and evaporated. The crude product was subjected to column chromatography (SiO_2, eluent CH_2Cl_2 to remove unreacted **1**, followed by a gradient of AcOEt in cyclohexane) to afford the pure components. The product distribution and isolated yields are shown in Table 1.

5,11,17,23,29-Penta-*tert*-butyl-31-[(2-pyridylmethyl)oxy]-32,33,34,35-tetrahydroxycalix[5]arene (2): mp 193−195 °C (EtOH); R_f = 0.78 (cyclohexane−AcOEt 3:1); ^{1}H NMR δ 1.08, 1.24, 1.28 [s, ratio 1:2:2, 45 H], 3.45, 3.46 (d, J = 14.0 Hz, 5 H), 4.08, 4.15, 4.48 (d, J = 14.0 Hz, ratio 1:2:2, 5 H), 5.33 (s, 2 H), 7.13, 7.18, 7.20 (s, ratio 1:2:2, 10 H), 7.36 (m, 1 H), 7.90−7.96 (m, 2 H), 8.00, 8.16 (bs, 2 H each), and 8.68 (dt, J = 4.9, 1.3 Hz, 1 H); ^{13}C NMR δ 30.68 (t), 31.15, 31.41, 31.54 (q), 33.86, 34.11 (s), 77.18 (t), 122.32, 123.26, 125.45, 125.70, 125.93, 126.12 (d), 126.44, 126.78, 126.97, 132.30 (s), 137.51 (d), 142.80, 143.72, 147.40, 147.73 (s), 149.06 (d), 150.68, and 156.53 (s); FAB (+) MS m/z 902 (100, MH^+). Anal. Calcd for $C_{61}H_{75}NO_5$: C, 81.20; H, 8.38; N, 1.55. Found: C, 81.44; H, 8.15; N, 1.43.

5,11,17,23,29-Penta-*tert*-butyl-31,32-bis[(2-pyridylmethyl)oxy]-33,34,35-trihydroxycalix[5]arene (3): mp 161−163 °C (EtOH); R_f = 0.41 (cyclohexane−AcOEt 3:1); ^{1}H NMR δ 0.84, 1.21, 1.26 [s, ratio 2:1:2, 45 H], 3.38, 4.07 (ABq, J = 14.0 Hz, 4 H), 3.41, 4.38 (ABq, J = 14.5 Hz, 4 H), 3.56, 4.72 (ABq, J = 15.3 Hz, 2 H), 4.92, 5.14 (ABq, J = 12.5 Hz, 4 H), 6.78 (s, 4 H), 7.08, 7.18 (ABq, J = 2.3 Hz, 4 H), 7.10 (s, 2 H), 7.24 (m, 2 H), 7.55 (d, J = 7.7 Hz, 2 H), 7.75 (td, J = 7.6, 1.3 Hz, 2 H), 8.27 (bs, 3 H), and 8.62 (d, J = 4.8 Hz, 2 H); ^{13}C NMR δ 30.99, 31.41, 31.53 (q), 31.25 (t), 33.82 (s), 75.37 (t), 122.15, 122.82, 124.94, 125.32, 125.46, 125.61, 126.06 (d, ArH), 126.17, 126.41, 127.19, 132.87, 133.48 (s), 137.28 (d), 142.45, 142.88 (s), 146.61, 147.83, 148.90 (s), 148.78 (d), 151.75, and 157.19 (s); FAB (+) MS m/z 993 (100, MH^+). Anal. Calcd for $C_{67}H_{80}N_2O_5$: C, 81.01; H, 8.12; N, 2.82. Found: C, 80.82; H, 8.36; N, 2.72.

5,11,17,23,29-Penta-*tert*-butyl-31,33-bis[(2-pyridylmethyl)oxy]-32,34,35-trihydroxycalix[5]arene (4): mp 135−139 °C (MeOH); R_f = 0.28 (cyclohexane−AcOEt 3:1); ^{1}H NMR δ 1.00, 1.28, 1.33 (s, ratio 2:2:1, 45 H), 3.35−3.46 (m, 5 H), 4.17, 4.45, 4.47 (d, J = 13.9, 14.0, and 14.1 Hz, respectively, ratio 1:2:2, 5 H), 5.20 (s, 4 H), 6.70 (bs, 1 H), 7.04, 7.18, 7.21 (s, ratio 2:2:1, 10 H), 7.23 (m, 2 H), 7.65 (td, J = 7.7, 1.6 Hz, 2 H), 7.95 (d, J = 7.8 Hz, 2 H), 8.20 (bs, 2 H), and 8.61 (d, J = 4.5 Hz, 2 H); ^{13}C NMR δ 30.34, 30.41, 31.33 (t) 31.10, 31.57, 31.69 (q), 33.85, 34.10 (s), 76.91 (t), 121.83, 122.84, 125.22, 125.63, 125.77, 126.13, 126.19 (d), 126.62, 127.07, 132.12, 132.49 (s), 137.25 (d), 141.74, 142.47, 147.23 (s), 149.03 (d), 149.15, 150.34, 150.45, and 156.84 (s); FAB (+) MS m/z 993 (100, MH^+). Anal. Calcd for $C_{67}H_{80}N_2O_5$: C, 81.01; H, 8.12; N, 2.82. Found: C, 81.44; H, 8.22; N, 2.68.

5,11,17,23,29-Penta-*tert*-butyl-31,32,33-tris[(2-pyridylmethyl)oxy]-34,35-dihydroxycalix[5]arene (5): mp 257−262 °C (CH_3CN); R_f = 0.29 (cyclohexane−AcOEt 1:1); ^{1}H NMR δ 0.71, 1.29, 1.42 (s, ratio 2:2:1, 45 H), 3.35, 4.44 (ABq, J = 13.9 Hz, 4 H), 3.39, 4.34 (ABq, J = 14.8 Hz, 4 H), 3.45, 4.35 (ABq, J = 13.9 Hz, 2 H), 4.79, 4.88 (ABq, J = 13.8 Hz, 4 H), 4.82 (s, 2 H), 6.63, 6.69 (ABq, J = 2.2 Hz, 4 H), 6.86 (d, J = 7.8 Hz, 2 H), 7.00 (dd, J = 7.0, 5.1 Hz, 1 H), 7.08 (m, 2 H), 7.11, 7.23 (ABq, J = 2.4 Hz, 4 H), 7.32 (td, J = 7.7, 1.8 Hz, 2 H), 7.36 (s, 2 H), 7.60 (d, J = 7.9 Hz, 1 H), 7.82 (td, J = 7.7, 1.7 Hz, 1 H), 8.21 (bs, 2 H), 8.40 (d, J = 4.0 Hz, 1 H), and 8.46 (d, J = 4.8 Hz, 2 H); ^{13}C NMR δ 29.48, 31.13 (t), 30.87, 31.59, 31.69 (q), 33.86, 34.30 (s), 74.90, 75.82 (t), 120.97, 121.60, 122.38, 124.41, 125.62, 126.24, 127.04, 126.01, 132.37, 133.01, 134.75 (s), 136.68, 137.90 (d), 142.40, 146.21 (s), 147.15, 148.73 (d), 149.33, 150.95, 152.86, 157.03, and 158.42 (s); FAB (+) MS m/z 1084 (100, MH^+). Anal. Calcd for $C_{73}H_{85}N_3O_5$: C, 80.85; H, 7.90; N, 3.87. Found: C, 80.58; H, 7.71; N, 3.96.

5,11,17,23,29-Penta-*tert*-butyl-31,32,34-tris[(2-pyridylmethyl)oxy]-33,35-dihydroxycalix[5]arene: mp 250−255 °C (EtOH); R_f = 0.37 (cyclohexane−AcOEt 1:1); ^{1}H NMR δ 0.83, 1.12, 1.31 (s, ratio 2:1:2, 45 H), 3.38, 3.41, 3.43 (d, J = 14.8, 14.6 and 13.9 Hz, respectively, ratio 1:2:2, 5 H), 4.35, 4.42 (d, J = 14.7 and 14.1 Hz, respectively, 5 H), 4.90, 5.10 (ABq, J = 14.0 Hz, 4 H), 5.09 (s, 2 H), 6.68, 6.75 (ABq, J = 2.2 Hz, 4 H), 7.02−7.26 (m, 14 H), 7.64 (m, 3 H), and 8.48 (m, 3 H); ^{13}C NMR δ 29.67, 29.95, 30.43 (t), 31.01, 31.22, 31.63 (q), 33.87, 34.18 (s) 75.22, 77.63 (t), 120.97, 121.92, 122.08, 122.68, 124.65, 125.31, 125.86, 125.92, 126.01 (d), 126.79, 126.91, 132.40, 133.51, 133.59 (s), 136.83, 137.54 (d), 142.07, 146.84, 147.21 (s), 148.19, 148.83 (d), 150.00, 150.15, 151.34, 156.24, and 157.68 (s); FAB (+) MS m/z 1084 (100, MH^+). Anal. Calcd for $C_{73}H_{85}N_3O_5$: C, 80.85; H, 7.90; N,3.87. Found: C, 80.67; H, 8.04; N, 3.72.

5,11,17,23,29-Penta-*tert*-butyl-31,32,33,34-tetrakis[(2-pyridylmethyl)oxy]-35-hydroxycalix[5]arene: mp 275−280 °C (CH_3CN); R_f = 0.10 (cyclohexane−AcOEt 1:1); ^{1}H NMR δ 0.69, 1.32, 1.33 (s, ratio 2:2:1, 45 H), 3.21 (d, J = 13.2 Hz, 1 H), 3.38 (t, J = 15.3 Hz, 4 H), 4.40, 4.42, 4.45 (d, J = 14.9, 13.8 and 13.2 Hz, respectively, ratio 2:2:1, 5 H), 4.68, 4.77 (ABq, J = 14.0 Hz, 4 H), 4.79, 4.92 (ABq, J = 13.3 Hz, 4 H), 6.48, 6.68 (ABq, J = 2.3 Hz, 4 H), 6.94 (d, J = 7.8 Hz, 2 H), 6.99 (ddd, J = 6.6, 4.8, 1.9 Hz, 2 H), 7.08 (ddd, J = 7.4, 4.9, 0.9 Hz, 2 H), 7.17 (s, 2 H), 7.26−7.37 (m, 10 H), 7.40 (s, 1 H), and 8.43 (m, 4 H); ^{13}C NMR δ 28.22, 29.16 (t), 30.98, 31.59, 31.69 (q), 33.81, 33.91, 34.23 (s), 75.89, 76.10 (t), 120.99, 121.65, 121.87, 122.12, 124.42, 124.54, 126.00, 126.46 (d), 126.70, 132.27, 133.17, 133.71, 134.03 (s), 136.55, 137.25 (d), 142.12, 145.86, 146.18 (s), 147.81, 148.67 (d), 151.00, 151.19, 152.42, 157.54, and 158.33 (s); FAB (+) MS, m/z 1175 (100, MH^+). Anal. Calcd for $C_{79}H_{90}N_4O_5$: C, 80.71; H,7.72; N, 4.77. Found: C, 80.63; H, 7.96; N, 4.89.

5,11,17,23,29-Penta-*p-tert*-butyl-31,32,33,34,35-pentakis[(2-pyridylmethyl)oxy]calix[5]arene (8). A stirred mixture of **1** (405 mg, 0.5 mmol), PicCl·HCl (1.64 g, 10 mmol) and anhydrous K_2CO_3 (2.76 g, 20 mmol) in dry DMF (20 mL) was heated at 60 °C for 20 h under N_2. After cooling, the mixture was poured into water (50 mL) to give the crude derivative (0.53 g, 80%) as an off-white powder. Recrystallization from aqueous MeOH, and then from MeCN afforded white crystals, mp 237−239 °C; ^{1}H NMR δ 1.04 (s, 45 H), 3.19, 4.48 (AXq, J = 14.1 Hz, 10 H), 4.76 (s, 10 H), 6.92 (s, 10 H), 7.00 (m, 5 H), 7.38 (m, 10 H), and 8.41 (dt, J = 4.7, 1.5 Hz, 5 H); ^{13}C NMR δ 29.51 (t), 31.22 (q), 33.82 (s), 76.28 (t), 121.88, 122.76, 125.59 (d), 133.31 (s), 136.24 (d), 145.21 (s), 148.18 (d), 152.05, and 157.81 (s); FAB (+) MS m/z 1266 (100, MH^+). Anal. Calcd for $C_{85}H_{95}N_5O_5$: C, 80.60; H, 7.56; N, 5.53. Found: C, 80.88; H, 7.75; N, 5.44.

(15) Böhmer, V.; Kraft, D.; Tabatabai, M. *J. Incl. Phenom.* **1994**, *19*, 17.

(16) Melting points were determined on a Kofler or Electrothermal melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded in $CDCl_3$ at 200 or 250 MHz. ^{13}C NMR spectra were recorded at 62.5 MHz. Chemical shifts (δ) are expressed in ppm relative to the internal tetramethylsilane (TMS). FAB (+) MS were obtained using 3-nitrobenzyl alcohol as a matrix. All chemicals were reagent grade and were used without further purification. Anhydrous DMF and MeCN were purchased from Fluka. *p-tert*-Butylcalix[5]arene was synthesized according to a reported procedure.[3a]

Table 2. Summary of Crystal Data, Data Collection, Structure Solution, and Refinement Details for 5

Crystal Data	
empirical formula	$C_{73}H_{82}N_3O_5,0.5CH_2Cl_2$
molar mass	1123.88
color, habit	colorless, block
crystal size, mm	0.40 × 0.30 × 0.20
crystal system	monoclinic
a, Å	13.6017(13)
b, Å	24.344(2)
c, Å	20.655(4)
α, deg	90
β, deg	97.358(10)
γ, deg	90
V, Å^3	6782.7(14)
space group	*Cc*
Z	4
F(000)	2408
d_{calc}, g cm^{-3}	1.101
μ, mm^{-1}	0.106
Data Acquisition[a]	
temp, K	294(1)
unit-cell reflcns (*θ*-range deg)	8.1 12.0
max. *θ* (deg) for reflcns	24.9
hkl range of reflcns	−16 16; 0 28; 0 24
variation in 3 standard reflcns	2.0
reflcns measured	6123
unique reflcns	6123
reflcns with $I > 2\sigma(I)$	3102
absorption correction type	none
Structure Solution and Refinement[b]	
refinement on	F^2
solution method	Shelx86
H-atom treatment	riding
no. of variables in L.S.	730
weights: either	
k in $w = 1/(\sigma^2F_o^2 + k)$	$(0.0769P)^2$
$[P = (F_o^2 + 2F_c^2)/3]$	
R, R_w, *gof*	0.051, 0.132, 0.83
density range in final Δ-map, e Å^{-3}	−0.166, 0.147
final shift/error ratio	−0.007

[a] Data collection on an Enraf Nonius CAD4 diffractometer with graphite monochromatized Mo Kα radiation (*λ* 0.71067 Å). [b] All calculations were done on a Silicon Graphics 4D-35TG computer system with the NRCVAX system of programs (E. J. Gabe, Y. Le Page, J.-P. Charland, F. L. Lee, and P. S. White. *J. Appl. Cryst.* **1989**, *22*, 384−389) for refinement with observed data on *F*, or with SHELXL-93 (G. M. Sheldrick, 1993) for refinement with all data on F^2.

5,11,17,23,29-Penta-*tert*-butyl-31,32,33,34,35-pentakis-[(3-pyridylmethyl)oxy]calix[5]arene (9). A solution of 3-PicCl·HCl (2.5 g, 15.2 mmol) in water was basified by addition of solid K_2CO_3 and extracted with Et_2O. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was dissolved in dry THF (10 mL) and added dropwise to a stirred mixture of **1** (405 mg, 0.5 mmol) and NaH (0.36 g, 15 mmol) in dry THF (20 mL). The mixture was refluxed for 8 h. The reaction was quenched by addition of MeOH and the solvent evaporated. The residue was partitioned between water and $CHCl_3$. The organic extract was dried ($MgSO_4$) and concentrated. The resulting residue was triturated with hot MeOH (20 mL) and filtered. The filtrate was dilute with an equal volume of water and refluxed for 30 min. After cooling, the precipitate obtained was collected by filtration and dried. Recrystallization from hexane−acetone gave colorless crystals, (0.26 g, 42%); mp 205−208 °C; ^{1}H NMR *δ* 1.01 (s, 45 H), 2.98, 4.11 (AXq, J = 13.9 Hz, 10 H), 4.31 (s, 10 H), 6.86 (s, 10 H), 7.19 (dd, J = 7.7, 4.9 Hz, 5 H), 7.63 (dt, J = 7.8, 1.8 Hz, 5 H), 8.36 (d, J = 1.6 Hz, 5 H), and 8.56 (dd, J = 4.8, 1.6 Hz, 5 H); ^{13}C NMR *δ* 29.50 (t), 31.29 (q), 33.99 (s), 73.09 (t), 123.12, 125.74 (d), 133.27, 133.77 (s), 136.73 (d), 145.97 (s), 148.97 (d), 150.35 (d), and 151.05 (s); FAB (+) MS *m*/*z* 1266 (100, MH$^+$). Anal. Calcd for $C_{85}H_{95}N_5O_5$: C, 80.60; H, 7.56; N, 5.53. Found: C, 80.32; H, 7.59; N, 5.47.

5,11,17,23,29-Penta-*tert*-butyl-31,32,33,34,35-pentakis-[(2-quinolylmethyl)oxy]calix[5]arene (10). The procedure described above for **8** was repeated with 2-(chloromethyl)-quinoline hydrochloride as the electrophile and the same molar proportions to afford the pentaquinolyl ether, which was crystallized from MeCN-CH_2Cl_2 to give the pure compound (77% yield); mp 278−280 °C; ^{1}H NMR *δ* 1.07 (s, 45 H), 3.31, 4.70 (AXq, J = 14.1 Hz, 10 H), 4.96 (s, 10 H), 6.98 (s, 10 H), 7.21−7.50 (m, 25 H), and 7.82 (d, J = 8.5 Hz, 5 H); ^{13}C NMR *δ* 29.71 (t), 31.30 (q), 33.95 (s), 77.07 (t), 120.46, 125.64, 127.25, 128.63, 128.84, 125.93 (d), 127.04 (s), 133.27 (s), 136.06 (d), 145.53, 146.89, 152.28, and 158.31 (s); FAB (+) MS *m*/*z* 1516 (100, MH$^+$). Anal. Calcd for $C_{105}H_{105}N_5O_5$: C, 83.13; H, 6.98; N, 4.62. Found, C, 83.50; H, 7.11; N, 4.45.

8·Rb$^+$ Picrate Complex. To a solution of pentaether **8** (0.05 mmol) in dry $CHCl_3$ (10 mL) was added solid rubidium picrate (4 equiv). The mixture was stirred at rt for 1 d. After filtration, the solvent was evaporated to give the corresponding 1:1 complex in almost quantitative yield. It was triturated with Et_2O, collected by filtration, and dried; ^{1}H NMR (200 MHz) *δ* 1.01 (s, 45 H), 3.16, 4.09 (ABq, J = 14.2 Hz, 10 H), 4.85 (s, 10 H), 6.91 (s, 10 H), 7.07 (d, J = 7.7 Hz, 5 H), 7.18 (dd, J = 7.0, 5.3 Hz, 5 H), 7.60 (td, J = 7.6, 1.5 Hz, 5 H), 8.54 (d, J = 4.3 Hz, 5 H), and 8.77 (s, 2 H); FAB (+) MS *m*/*z* 1350 (46, M$^+$).

X-ray Experimental. Details of the X-ray experimental conditions, cell data, data collection, solution and refinement of **5** are summarized in Table 2. Atomic coordinates and full details of molecular dimensions have been deposited with the Cambridge Crystallographic Data Centre. The coordinates can be obtained on request from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK. Copies of the complete Crystallographic Information File (CIF) for **5** are also available from the authors.

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Supporting Information Available: ^{1}H and ^{13}C NMR assignments for all new compounds (4 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current musthead page for information.

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