The First Lateral Functionalization of Calix[4]arenes by a Homologous Anionic Ortho-Fries Rearrangement

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Treatment of calix[4]arene bis-*O*-carbamates **4a**,**b**−**6a**,**b** with LDA in THF results in the regio- and stereoselective introduction of both axial and equatorial carboxamide groups at the methylene bridges via a homologous anionic ortho-Fries rearrangement to give **7**−**16**. The stereochemical outcome of the rearrangement is dependent on the reaction conditions and the conformation of the starting material. Stereochemical and structural proof has been secured by the X-ray crystal structure of calix[4]arene **10** having only one equatorial carboxamide moiety. The use of this novel class of methylene bridge-functionalized calix[4]arenes is illustrated by the formation of bis-γ-lactone **19**, while the enhanced acidity of the remaining hydroxyl groups, owing to the presence of axial carboxamide groups at the methine bridges, followed from the easy propylation of bisrearranged calix[4]arene **7**.

Introduction

Since the seminal contributions of Gutsche[1] calix[n]arenes[2] have been extensively used in supramolecular chemistry, particularly in the areas of metal,[3] anion[4] and organic molecule complexation,[5] enzyme models,[6] ion transport,[7] and nonlinear optics[8] and in sensors.[9] The selective functionalization of calix[4]arenes both at the phenolic and the para positions of the phenol rings has been elaborately studied.[2] However, only a few examples are known of bridge-functionalized calix[4]arenes,[10] and direct functionalizations of the methylene bridges other than oxidation[10e] or radical bromination[10f] have not been reported.

In this paper, we report the first method for the direct regio- and stereoselective functionalization of the methylene bridges of calix[4]arenes using a homologous anionic ortho-Fries rearrangement.[11] In this way, a novel class of cone calix[4]arenes (**7**−**16**) has been obtained. These bridge-functionalized calix[4]arenes possess carboxamide groups for further chemical manipulation and in a few cases have free phenolic hydroxyl groups with enhanced acidity for consecutive functionalizations.

Results and Discussion

Synthesis. For the homologous anionic ortho-Fries rearrangement studies, compounds **4a**,**b**−**6a**,**b** were prepared starting from calix[4]arene **1**, via dipropoxycalix[4]arene **2** and bis-*O*-carbamates **3a**,**b**, by standard alkylation/carbamoylation procedures (Scheme 1). The dipropoxycalix[4]arene diethyl *O*-carbamates were obtained exclusively in the cone (**4a**) or partial cone (**5a**)

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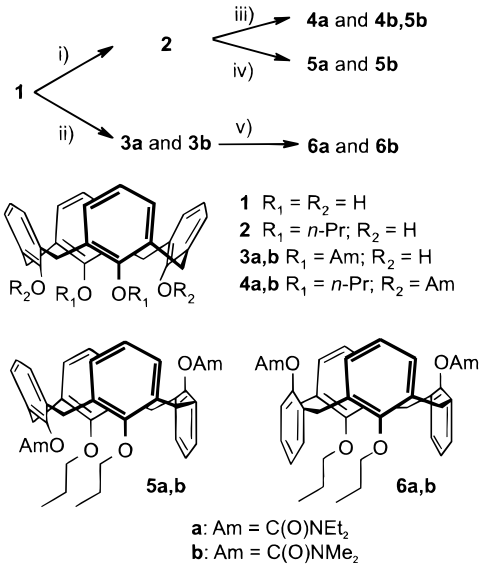
Scheme 1[a]



[a] Key: (i) K_2CO_3/*n*-PrBr/CH_3CN; (ii) K_2CO_3/AmCl/CH_3CN; (iii) NaH/AmCl/DMF; (iv) KO-*t*-Bu/AmCl/CH_3CN; (v) NaH/*n*-PrBr/DMF.

conformation when **2** was treated with NaH or KOBu-*t*, respectively, and subsequently quenched with diethylcarbamoyl chloride. The corresponding dimethyl *O*-carbamates were obtained either as a mixture of cone (**4b**) and partial cone (**5b**) conformers (NaH) or exclusively in the partial cone conformation (**5b**) (KOBu-*t*). Treatment of either diethyl **3a** or dimethyl-*O*-carbamate **3b** with NaH and subsequent propylation led exclusively to 1,3-alternate conformers **6a** and **6b**, respectively.

The ortho-Fries rearrangement of calix[4]arene bis-*O*-carbamates **4a**,**b**−**6a**,**b** was carried out with a large excess of LDA in THF; the nature (and yields) of products **7**−**16** (Scheme 2) depends strongly on the conformation of the starting material and on the reaction conditions (temperature, concentration, reaction time: Table 1). All products **7**−**16** assumed the cone conformation, even when the starting compounds had a partial cone (**5a**,**b**) or 1,3-alternate (**6a**,**b**) conformation. The reason for this is that the phenol moieties obtained after migration have the ability of rotating through the calix[4]arene ring, leading to the exclusive formation of the thermodynamically most stable cone products. If only one rearrangement takes place, the remaining *O*-carbamate is either stable (**10**, **11**) or is hydrolyzed to a hydroxyl group upon the quenching conditions (**9**, **13**). Single diastereomeric products were obtained in synthetically useful yields (63−81%), e.g., **7**, **9**, **10**, **11**, and **13** (Table 1, entries 1, 3, 4, 8, and 9, respectively).

The structures of the rearranged products were proven by ^{1}H and ^{13}C NMR spectroscopy. Conclusive structural and stereochemical proof was secured by X-ray analysis of **10** (Figure 1), which clearly shows the equatorial orientation of the migrated carboxamide moiety. In the ^{1}H NMR spectra, a large difference in chemical shift was observed for the hydrogen atoms at the bridges bearing either axial or equatorial substituents as is clearly illustrated in the case of bisrearranged calix[4]arene **8**, having both an axial and an equatorial substituent, in which the concerning hydrogen atoms resonate at δ 4.71 and 6.14, respectively. The assignment of both signals is based on the fact that in monorearranged calix[4]arene

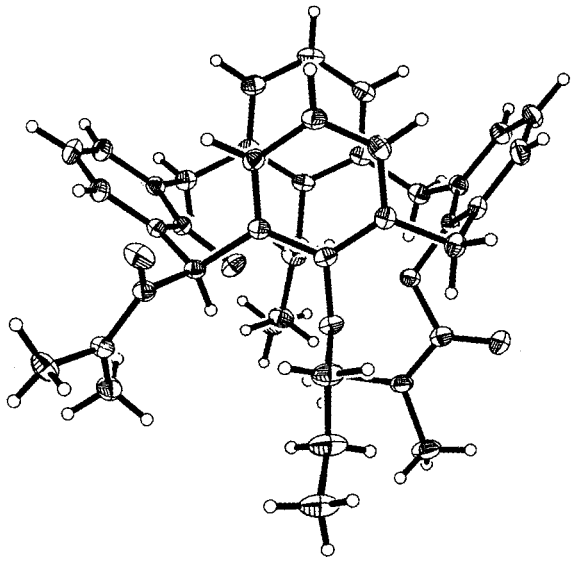


Figure 1. X-ray crystal structure of monorearranged calix[4]arene **10** showing both the *O*-carbamate and the stereochemistry at the methine carbon atom.

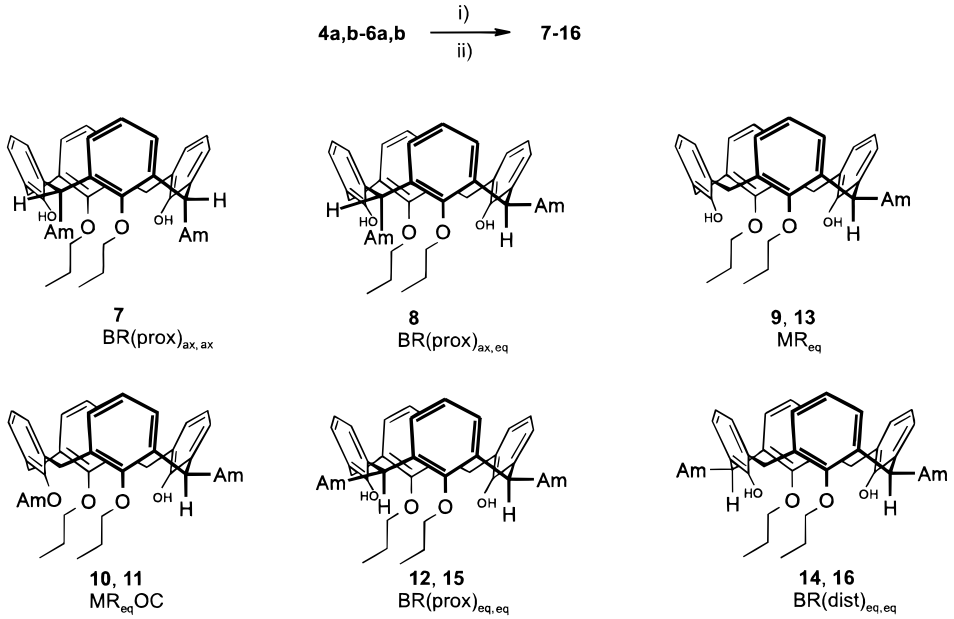
10 the hydrogen atom at the methine bridge resonates at δ 5.93. In general, it was concluded that in the ^{1}H NMR spectra of the rearranged compounds **7**−**16** the hydrogen atoms at the axially and equatorially substituted methine bridges are positioned at δ 4.71−4.99 and 5.75−6.23, respectively. These values correspond to those found for lateral alkyl- and phenyl-substituted calix[4]arenes.[10b,g] Differentiation between the distally and proximally rearranged calix[4]arenes (**7**, **12**, **14**−**16**) was easily accomplished by taking into account the symmetry elements of the molecules, which are clearly expressed in the ^{1}H and ^{13}C NMR spectra. For distally rearranged products **14** and **16**, the diametrical propoxyaryl rings are magnetically equivalent and are related by a C_2-axis of symmetry. Proximally substituted products (**7**, **12**, **15**) lack this symmetry element, and their diametrical aryl moieties are rendered magnetically inequivalent.

Three subsequent transformations illustrate the use of these calix[4]arenes as potential building blocks in supramolecular chemistry (Scheme 3). Diborane reduction of the carboxamides in **17**, prepared in 97% yield by propylation of bisrearranged calix[4]arene **14** in the presence of NaH as a base, gave the diamine **18** in 66% yield. Heating of bisrearranged calix[4]arene **7** in acetic acid afforded the bis-γ-lactone **19** in 64% yield. Obviously, the formation of a γ-lactone is only possible when axial substituents are present and clearly followed from the characteristic signal in the ^{13}C NMR spectrum for the carbonyl of the γ-lactone at δ 174.7, corroborated by the typical γ-lactone signal in the IR spectrum at 1805 cm^{-1}. In the ^{1}H NMR spectrum the original signals of the diethylamine part of the carboxamide moieties are lacking.

Compound **7**, owing to the adjacent axial carboxamides, allowed the propylation of the remaining hydroxyl groups using K_2CO_3 as a base to give tetrapropoxycalix[4]arene **20** in 92% yield. Normally this base is not strong enough to deprotonate the phenolic positions in dialkylated calix[4]arenes.[12] In the case of **14**, having two equatorial

(12) Van Loon, J.-D.; Arduini, A.; Coppi, L.; Verboom, W.; Pochini, A.; Ungaro, R.; Harkema, S.; Reinhoudt, D. N. *J. Org. Chem.* **1990**, *55*, 5639.

Scheme 2[a]



[a] Key: (i) LDA/THF; (ii) NH_4Cl. For the abbreviations, see Table 1. Am = $C(O)NEt_2$: **4a**, **5a**, **6a**, **7**, **8**, **9**, **11**, **12**, **14**. Am = $C(O)NMe_2$: **4b**, **5b**, **6b**, **10**, **13**, **15**, **16**.

Table 1. Results of Migration Studies on Carbamates 4a,b−6a,b[a,b]

entry	SM (mM)	RC	$BR(prox)_{ax,ax}$	$BR(prox)_{ax,eq}$	MR_{eq}	$MR_{eq}OC$	$BR(prox)_{eq,eq}$	$BR(dist)_{eq,eq}$
1	**4a** (36)	A	**7** (63−80)					
2	**4a** (21)	B	**7** (27)	**8** (11)	**9** (10)			
3	**4a** (36)	C			**9** (67)			
4	**4b** (36)	D				**10** (66)		
5	**5a** (36)	C		**8** (42)	**9** (23)		**12** (21)	
6	**5a** (57)	C		**8** (7)	**9** (49)			
7	**5a** (21)	C		**8** (35−42)	**9** (37)		**12** (12−19)	
8	**5a** (36)	E				**11** (73)		
9	**5b** (36)	A			**13** (67)			
10	**5b** (36)	F				**10** (81)		
11	**6a** (30)	A			**9** (11−18)		**12** (16−17)	**14** (64−65)
12	**6a** (17)	A			**9** (7−11)		**12** (19−20)	**14** (48−55)
13	**6a** (65)	C			**9** (27)		**12** (19)	**14** (34)
14	**6b** (61)	B			**13** (52)		**15** (8)	**16** (38)
15	**6b** (36)	F			**13** (7−9)		**15** (23−27)	**16** (64−65)

[a] Products **7**−**16** (yield, %) BR = bisrearranged; MR = monorearranged; OC = *O*-carbamate; prox = proximal; dist = distal; ax = axial; eq = equatorial; SM = starting material; RC = reaction conditions; A = add SM (in THF) to a solution of 12 equiv of LDA in THF at 0 °C and warm to room temperature during 4 h before quenching with $NH_4Cl_{(aq)}$; B = at −2 °C and stirred overnight; C = at −24 °C, in 6 h to room temperature and stirred overnight; D = in 3 h to room temperature; E = quenched at 0 °C after 2 h; F = quenched after 30 min at 0 °C. [b] In some cases the yields of multiple experiments are given.

substituents, propylation in the presence of K_2CO_3 as a base could not be accomplished. Apparently, the close proximity of the axial carboxamide moieties enhances the acidity of the remaining hydroxyl groups and, consequently, facilitates the propylation using K_2CO_3 as a base. The axial carboxamide substituents also strongly shield the propoxy group located between expressed in the ^1H NMR spectrum by the large upfield shift for the signals of this propoxy group [δ −0.16−0.13 (CH_2), 0.42 (CH_3) and 3.36−3.50 (OCH_2)].

Mechanism. The homologous anionic ortho-Fries rearrangement is believed to be an orbital symmetry-driven process.[13,14] Based on our results using calix[4]arene bis-*O*-carbamates in addition to the migrations described for other systems by Dankwardt[15] and Chenard,[16] we postulate that the homologous anionic ortho-Fries rearrangement proceeds via an intermediate five-membered ring (Scheme 4).[17] In Scheme 4, the formation of only one five-membered ring has been outlined either at the equatorial (**21**) or at the axial lateral position (**22**) in the cone bis-*O*-carbamates **4a**,**b**. The lateral positions of the bis-*O*-carbamates **4a**,**b**−**6a**,**b** first are deprotonated upon treatment with a large excess of LDA. The consecutive intramolecular attack[17] of lateral carbanions on the carbonyl π^* orbital of the adjacent *O*-carbamate results

(13) The migration does not take place when an anti-periplanar orientation of the carbanion and the carbonyl σ-bond cannot be attained as found in several sterically hindered (blocked) systems.

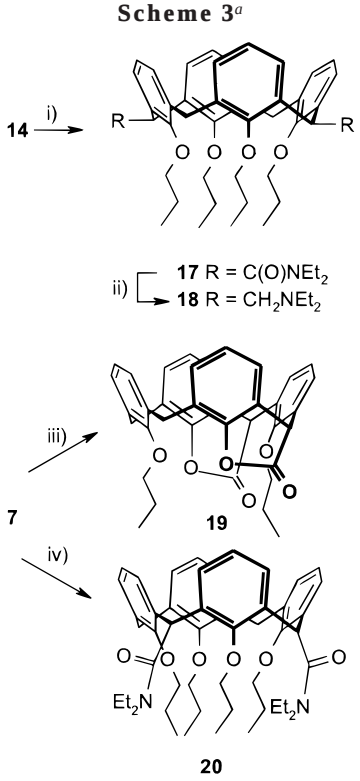
(14) This rearrangement is closely related to the documented anionic amino-Cope,[a] Claisen[b] and the [2,3]-Wittig anionic oxy-Cope[c] rearrangements. (a) Allin, S. M.; Button, M. A. C.; Baird, D. *Synlett* **1998**, 1117. (b) Copley, S. D.; Knowles, J. R. *J. Am. Chem. Soc.* **1985**, *107*, 5306. (c) Greeves, N.; Lee, W. M. *Tetrahedron Lett.* **1998**, *38*, 6445 and 6449.

(15) Tetrazole migrations via a four-membered intermediate: Dankwardt, J. W. *J. Org. Chem.* **1998**, *63*, 3753.

(16) Oxazoline migrations via a four-membered intermediate: Chenard, B. L. *J. Org. Chem.* **1983**, *48*, 2610.

(17) Corroborated by the fact that we did not observe any crossover products.

Scheme 3[a]



[a] Key: (i) NaH/*n*-PrBr/DMF (63%); (ii) B_2H_6/THF (66%); (iii) AcOH (64%); (iv) *n*-PrBr/K_2CO_3/CH_3CN (92%).

in the formation of one or two five-membered rings between the phenolic and the lateral positions. Finally, the quenching of the reaction mixture completes the migration to the corresponding lateral position, yielding **7**−**16** (Table 1).

Sterical (conformational) requirements[18] in addition to the orbital symmetry requirements[13,14] determine the nature of the intermediates, which are present in the reaction mixture. Starting from calix[4]arene bis-*O*-carbamates in the cone conformation (**4a**,**b**), both the axial and equatorial lateral positions can participate in the formation of the intermediate five-membered rings (Scheme 4). The extent of their participation is determined by the relative energies of the resulting intermediates and by a strong difference in activation energy for the formation of an intermediate five-membered ring either at the equatorial (**21**) or axial (**22**) position.[18] The reaction conditions (mainly the reaction temperature) applied determine whether only one intermediate is energetically strongly favored and either axial- (**7**) or equatorial (**9** or **10**) carboxamides will be selectively introduced (Table 1, entries 1, 3, and 4) or equilibration between multiple conformers is obtained yielding **7**−**9** (Table 1, entry 2).

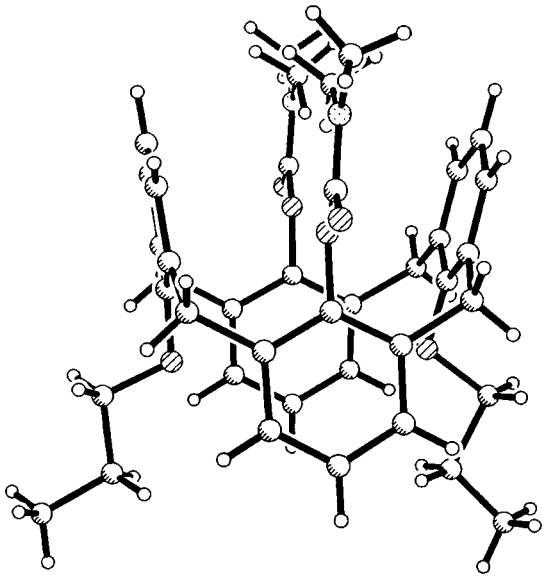
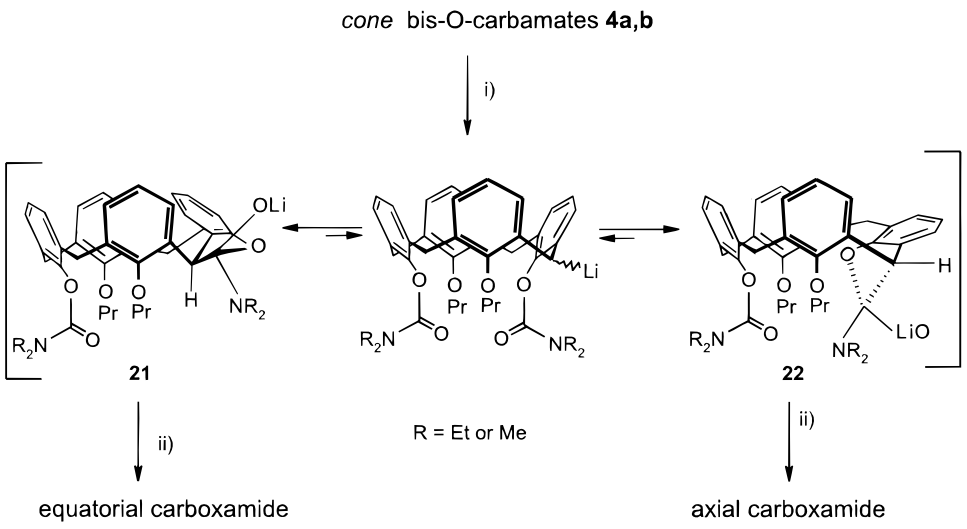


Figure 2. X-ray crystal structure of calix[4]arene **6b**.

The X-ray crystal structure of 1,3-alternate bis-*O*-carbamate **6b** (Figure 2) shows that at the appropriate lateral positions one of the hydrogen atoms points in the same direction as the *O*-carbamate. In the cases of **6a**,**b**, these lateral positions can, upon deprotonation, result in the formation of an intermediate five-membered ring nearly without altering the conformation. Hence, this intermediate will by far be lower in energy than that using the other deprotonation site at the same lateral carbon atom and is therefore highly favored. Protonation of the intermediates results in cone products **9** and **12**−

Scheme 4[a]



[a] Key: (i) LDA/THF; (ii) NH_4Cl.

16. Rotation of the phenol moieties during this isomerization of the 1,3-alternate conformation to the cone also requires the rotation of the lateral carbon atoms. The carboxamide substituents are therefore rotated into the equatorial orientation. A preference for migration to distal positions (**14** and **16**) could be observed (Table 1, entries 11−15) and regioselectivity could not be changed upon changing the reaction conditions.

The partial cone calix[4]arene bis-*O*-carbamates **5a**,**b** each have one *O*-carbamate moiety equivalent to an *O*-carbamate situated in **4a**,**b**, while the other resembles the situation of an *O*-carbamate in **6a**,**b**, as these were described above. The isolation of **10** and **11** after short reaction times (Table 1, entries 8 and 10) clearly indicates the difference in reactivity between the two different *O*-carbamate situations. The *O*-carbamate situated as in **6a**,**b** exposes a higher reactivity, and after the first migration the cone conformation is already obtained while the other *O*-carbamate is still present. The X-ray crystal structure of **10** (Figure 1) clearly shows the selective introduction of an equatorial carboxamide and the orientation of the resulting *O*-carbamate. After prolonged reaction times and applying different reaction conditions, equilibria were obtained in which the second *O*-carbamate participates (Table 1, entries 5−7).

Conclusion

In summary, the syntheses and structures of a new class of methylene bridge-functionalized calix[4]arene carboxamides, readily obtained via a homologous anionic ortho-Fries rearrangement, has been defined. Regio- and stereoselectivity for the product formation can be fully understood and is in line with the mechanistic demands we postulate. The homologous anionic Fries rearrangement proceeds via an intermediate five-membered ring. The regio- and stereochemical outcome is depending on the conformation of the starting material and on the reaction conditions. The various products obtained embody new elements of control of structural and stereochemical features in calix[4]arene chemistry and may provide new opportunities in emerging areas of biological and material sciences.[2b]

Experimental Section

General Methods. ^{1}H and ^{13}C NMR spectra were recorded on a 200 or 250 MHz spectrometer operated in Fourier transform mode using $CDCl_3$ and tetramethylsilane (TMS) as an internal standard. ^{13}C NMR spectra were proton decoupled. IR υ_{max} spectra were recorded as a KBr disk or as a liquid film. Electron impact mass spectra (EI MS) were recorded at 4kV, 35 eV, and 220 °C. Mass positive (FAB) spectra were obtained using *m*-nitrobenzyl alcohol as a matrix. Melting points are not corrected. The presence of solvents in the analytical samples was confirmed by ^{1}H NMR spectroscopy. Column chromatography was performed with silica gel 230−400 mesh, 60 Å. All reported yields are isolated yields and all solvents were purified prior to use, using standard procedures. De-*tert*-butylated calix[4]arene **1**[19] and dipropoxycalix[4]arene **2**[20] were synthesized according to literature procedures.

25,27-Bis(diethylcarbamoyloxy)-26,28-dihydroxycalix[4]arene (3a). A suspension of calix[4]arene **1** (2.00 g, 4.71 mmol) and K_2CO_3 (1.43 g, 10.37 mmol) in acetonitrile (50 mL) was refluxed for 30 min, whereupon diethylcarbamoyl chloride (2.81 g, 20.73 mmol) was added and the reaction mixture was heated at reflux for 18 h. The reaction mixture was evaporated to dryness and redissolved in water (50 mL) and $CHCl_3$ (50 mL). The aqueous layer was extracted with $CHCl_3$ (2 × 50 mL), and the combined organic layers were washed with brine, dried with $MgSO_4$, and evaporated to dryness. Recrystallization of the residue from EtOH yielded **3a** (1.75 g, 60%), as a white solid: mp 252−253 °C; ^{1}H NMR (200 MHz) δ 1.25 (t, J = 7.1 Hz, 6H), 1.36 (t, J = 7.1 Hz, 6H), 3.35−3.55 (m, 4H), 3.46 (d, J = 14.3 Hz, 4H), 3.55−3.67 (m, 4H), 4.00 (d, J = 14.1 Hz, 4H), 5.27 (s, 2H), 6.68 (s, 6H), 6.78 (t, J = 7.5 Hz, 2H), 7.14 (d, J = 7.4 Hz, 4H); ^{13}C NMR (63 MHz) δ 153.7, 152.9, 145.6, 132.4, 129.0, 128.9, 128.6, 125.9, 119.8, 31.7, 14.6, 13.3; IR υ_{max} (neat) 3540, 2975, 1720 cm^{-1}; MS (ESI 10 mM LiCl) *m*/*z* (relative intensity) 629 (100, [M + Li]$^+$). Anal. Calcd for $C_{38}H_{42}N_2O_6$: C, 73.29; H, 6.80; N, 4.50. Found: C, 73.14; H, 6.71; N, 4.33.

25,27-Bis(dimethylcarbamoyloxy)-26,28-dihydroxycalix[4]arene (3b). The same procedure as described for compound **3a** was used. Dimethylcarbamoyl chloride (2.23 g, 20.73 mmol) was used instead of diethylcarbamoyl chloride yielding **3b** (1.93 g, 72%) as a white solid: mp > 300 °C; ^{1}H NMR (200 MHz) δ 3.08 (s, 6H), 3.15 (s, 6H), 3.50 (d, J = 14.2 Hz, 4H), 3.96 (d, J = 14.2 Hz, 4H), 5.41 (s, 2H), 6.71−6.85 (m, 8H), 7.11 (d, J = 7.5 Hz, 4H); ^{13}C NMR (63 MHz) δ 154.1, 152.9, 145.7, 132.5, 129.0, 128.9, 128.3, 126.2, 119.8, 37.0, 36.2, 32.4; IR υ_{max} (neat) 3518, 2933, 1725 cm^{-1}; FAB MS (NBA) *m*/*z* 567.5 ([M + H]$^+$, calcd 567.3). Anal. Calcd for $C_{34}H_{34}N_2O_6$: C, 72.05; H, 6.05; N, 4.95. Found: C, 72.07; H, 6.07; N, 4.89.

25,27-Bis(diethylcarbamoyloxy)-26,28-dipropoxycalix[4]arene (4a) (Cone). A suspension of calix[4]arene **2** (1.02 g. 2.0 mmol), NaH (0.80 g, 20.0 mmol) in DMF (30 mL) was stirred for 20 min at room temperature, whereupon diethylcarbamoyl chloride (2.71 g, 20.0 mmol) was added. MeOH (5 mL) was added after 24 h, and the solvent was removed. Subsequently, the residue was dissolved in a mixture of 1 M HCl (25 mL) and $CHCl_3$ (20 mL). The aqueous phase was extracted with $CHCl_3$ (2 × 20 mL) and the collected organic layers were washed with brine (20 mL) and dried with $MgSO_4$. Evaporation of the solvent and recrystallization from EtOH yielded **4a** (1.08 g, 77%) as a white solid: mp 272 °C; ^{1}H NMR (200 MHz) δ 0.84 (t, J = 7.3 Hz, 6H), 1.00−1.40 (m, 12H), 1.70−1.95 (m, 4H), 3.25 (d, J = 14.1 Hz, 4H), 3.41 (brs, 4H), 3.72 (brs, 4H), 4.02 (t, J = 7.5 Hz, 4H), 4.10 (d, J = 14.1 Hz, 4H), 5.94 (d, J = 7.5 Hz, 4H), 6.27 (t, J = 7.5 Hz, 2H), 6.96 (t, J = 7.3 Hz, 2H), 7.15 (d, J = 7.3 Hz, 4H); ^{13}C NMR (50 MHz) δ 157.2, 153.4, 145.7, 137.0, 132.8, 129.6, 127.0, 124.2, 122.1, 75.2, 31.4, 22.8, 9.6; IR υ_{max} (KBr) 2969, 2876, 1711 cm^{-1}; MS (EI) *m*/*z* (relative intensity) 706 (100, M$^+$), 647 (10), 606 (6), 560 (4), 518 (7), 100 (7). Anal. Calcd for $C_{44}H_{54}N_2O_6$: C, 74.76; H, 7.70; N, 3.96. Found: C, 74.90; H, 7.96; N, 3.98.

25,27-Bis(dimethylcarbamoyloxy)-26,28-dipropoxycalix[4]arene (4b) (Cone). The same procedure as for compound **4a** was used, adding dimethylcarbamoyl chloride (2.23 g, 20.73 mmol) instead of diethylcarbamoyl chloride to yield a 1:2 mixture of **4b** and **5b**, respectively (0.82 g, 72%). The cone conformer **4b** was isolated as a white solid (228 mg, 20%) by recrystallization of the mixture from toluene: mp > 300 °C; ^{1}H NMR (200 MHz) δ 0.83 (t, J = 7.5 Hz, 6H), 1.75−1.95 (m, 4H), 3.06 (brs, 6H), 3.23 (d, J = 13.7 Hz, 4H), 3.30 (brs, 6H), 4.05 (t, J = 7.0 Hz, 4H), 4.11 (d, J = 13.7 Hz, 4H), 5.99 (d, J = 7.6 Hz, 4H), 6.29 (t, J = 7.6 Hz, 2H), 6.97 (t, J = 7.3 Hz, 2H), 7.15 (d, J = 7.3 Hz, 4H); ^{13}C NMR (50 MHz) δ 156.9, 155.4, 146.3, 136.9, 132.7, 129.5, 127.0, 124.2, 122.1, 75.3, 31.3, 22.7, 9.5; IR υ_{max} (neat) 2947, 2932, 1725 cm^{-1}; MS (EI) *m*/*z* (relative intensity) 650 (61, M$^+$), 607 (15), 577 (35), 532 (14), 504 (100), 462 (10), 72 (36); HRMS calcd for $C_{40}H_{46}N_2O_6$ 651.3434, found 651.3451. Anal. Calcd for

(18) Only equilibria starting with 1,3-alternate bis-*O*-carbamates **6a,b** are of the Curtin−Hammett type because the activation energies for the formation of five-membered rings at distal or proximal lateral positions will be equivalent. Product distribution is only being determined by the relative energies of the possible intermediates present in the reaction mixture.

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$C_{40}H_{46}N_2O_6$: C, 73.82; H, 7.12; N, 4.30. Found: C, 73.69; H, 6.95; N, 4.45.

25,27-Bis(diethylcarbamoyloxy)-26,28-dipropoxycalix[4]arene (5a) (Partial Cone). A suspension of calix[4]arene **2** (3.87 g. 7.6 mmol) and KO-*t*-Bu (3.42 g, 30.0 mmol) in acetonitrile (100 mL) was refluxed for 20 min, whereupon diethylcarbamoyl chloride (4.07 g, 30.0 mmol) was added. The reaction mixture was heated at reflux for 18 h, evaporated to dryness, and redissolved in a mixture of 1 M HCl (75 mL) and $CHCl_3$ (75 mL). The aqueous layer was extracted with $CHCl_3$ (2 × 75 mL), and the combined organic layers were washed with brine, dried with $MgSO_4$, and evaporated to dryness. Recrystallization of the residue from EtOH/H_2O yielded **5a** (3.24 g, 60%) as a white solid: mp 214−215 °C; ^{1}H NMR (200 MHz) δ 0.82−0.91 (m, 9H), 1.15−1.22 (t, J = 7.0 Hz, 9H), 1.67−1.71 (m, 4H), 2.35 (q, J = 7.3 Hz, 2H), 2.97 (q, J = 7.2 Hz, 2H), 3.22 (d, J = 12.9 Hz, 2H), 3.34 (q, J = 7.1 Hz, 4H), 3.58 (d, J = 14.7 Hz, 2H), 3.61−3.83 (m, 4H), 3.85 (d, J = 14.7 Hz, 2H), 4.08 (d, J = 12.8 Hz, 2H), 6.60 (t, J = 7.4 Hz, 2H), 6.77 (d, J = 6.0 Hz, 2H), 6.84 (d, J = 7.5 Hz, 2H), 7.03 (t, J = 7.3 Hz, 2H), 7.20−7.27 (m, 4H); ^{13}C NMR (50 MHz) δ 155.3, 155.0, 153.2, 136.2, 134.2, 134.1, 133.3, 130.1, 129.3, 129.1, 128.0, 125.0, 124.3, 122.1, 104.5, 103.5, 76.6, 40.7, 39.0, 38.9, 37.9, 23.1, 14.3, 13.8, 13.5, 13.1, 10.1; IR υ_{max} (neat) 2952, 1706 cm^{-1}; MS (ESI, 10 mM LiCl) *m*/*z* (relative intensity) 713 (100, $[M + Li]^+$), 613 (4). Anal. Calcd for $C_{44}H_{54}N_2O_6$: C, 74.76; H, 7.70; N, 3.96. Found: C, 75.00; H, 7.53; N, 4.11.

25,27-Bis(dimethylcarbamoyloxy)-26,28-dipropoxycalix[4]arene (5b) (Partial Cone). The same procedure as described for compound **5a** was used. Dimethylcarbamoyl chloride (3.34 g, 31.1 mmol) was used instead of diethylcarbamoyl chloride, yielding **5b** (3.30 g, 67%) as a white solid: mp 291−293 °C; ^{1}H NMR (250 MHz) δ 0.95 (t, J = 7.4 Hz, 6H), 1.55 (s, 3H), 1.67−1.86 (m, 4H), 2.25 (s, 3H), 2.86 (s, 3H), 2.92 (s, 3H), 3.66 (d, J = 12.8 Hz, 2H), 3.42−3.53 (m, 2H), 3.66 (d, J = 14.9 Hz, 2H), 3.68−3.76 (m, 2H), 3.87 (d, J = 15.0 Hz, 2H), 4.04 (d, J = 12.8 Hz, 2H), 6.62 (t, J = 7.4 Hz, 2H), 6.77 (d, J = 6.0 Hz, 2H), 6.87 (d, J = 7.5 Hz, 2H), 7.04 (t, J = 7.3 Hz, 2H), 7.17−7.23 (m, 4H); ^{13}C NMR (63 MHz) δ 155.3, 153.2, 147.7, 136.3, 134.8, 133.8, 133.4, 130.1, 129.1, 129.0, 128.1, 125.3, 124.5, 122.9, 76.6, 38.0, 37.5, 37.0, 36.5, 36.3, 30.2, 23.6, 10.4; IR υ_{max} (neat) 2924, 1708 cm^{-1}; MS (EI) *m*/*z* (relative intensity) 651 (100, M^+), 607 (10), 306 (8). Anal. Calcd for $C_{44}H_{54}N_2O_6$: C, 73.82; H, 7.12; N, 4.30. Found: C, 73.62; H, 7.00; N, 4.35.

25,27-Bis(diethylcarbamoyloxy)-26,28-dipropoxycalix[4]arene (6a) (1,3-Alternate). A suspension of calix[4]arene **3a** (1.75 g, 2.64 mmol) and NaH (1.06 g, 26.40 mmol) in DMF (30 mL) was stirred for 20 min at room temperature, whereupon *n*-propyl bromide (3.25 g, 26.40 mmol) was added and stirring was continued for 24 h. MeOH (5 mL) was added before the reaction mixture was evaporated to dryness, and the residue was redissolved in 1 M HCl (50 mL) and $CHCl_3$ (50 mL). The aqueous layer was extracted with $CHCl_3$ (2 × 50 mL), and the combined organic layers were washed with brine, dried with $MgSO_4$, and evaporated to dryness. Recrystallization of the residue from EtOH yielded **6a** (1.45 g, 73%) as a white solid: mp 246−248 °C; ^{1}H NMR (200 MHz) δ 0.90 (t, J = 7.5 Hz, 6H), 1.15 (t, J = 7.2 Hz, 6H), 1.26 (t, J = 7.1 Hz, 6H), 1.60−1.78 (m, 4H), 2.85 (q, J = 7.1 Hz, 4H), 3.46 (q, J = 7.1 Hz, 4H), 3.51 (d, J = 15.1 Hz, 4H), 3.60 (t, J = 7.5 Hz, 4H), 3.71 (d, J = 14.8 Hz, 4H), 6.69 (t, J = 7.5 Hz, 2H), 6.85 (t, J = 7.0 Hz, 2H), 6.90 (d, J = 7.5 Hz, 4H), 7.07 (d, J = 7.0 Hz, 4H); ^{13}C NMR (63 MHz) δ 157.3, 153.4, 148.2, 134.5, 133.1, 130.3, 130.0, 123.4, 121.2, 72.8, 39.2, 37.3, 23.1, 14.0, 12.9, 10.1; IR υ_{max} (neat) 2939, 1705 cm^{-1}; MS (ESI 10 mM LiCl) *m*/*z* (relative intensity) 713 (100, $[M + Li]^+$). Anal. Calcd for $C_{44}H_{54}N_2O_6$: C, 74.76; H, 7.70; N, 3.96. Found: C, 75.00; H, 7.52; N, 3.88.

25,27-Bis(dimethylcarbamoyloxy)-26,28-dipropoxycalix[4]arene (6b) (1,3-Alternate). The same procedure was used as described for compound **6a**, using **3b** (1.60 g, 2.64 mmol) as the starting material. The crude product was recrystallized from MeOH yielding **6b** (1.05 g, 61%) as transparent, colorless crystals: mp >300 °C; ^{1}H NMR (250 MHz) δ 0.86 (t, J = 7.5 Hz, 6H), 1.55−1.70 (m, 4H), 2.31 (s, 6H), 3.01 (s, 6H), 3.56 (d, J = 15.0 Hz, 4H), 3.73 (d, J = 15.0 Hz, 4H), 3.58 (t, J = 7.2 Hz, 4H), 6.71 (t, J = 7.4 Hz, 2H), 6.87 (t, J = 7.5 Hz, 2H), 6.90 (d, J = 7.5 Hz, 4H), 7.08 (d, J = 7.5 Hz, 4H); ^{13}C NMR (63 MHz) δ 157.4, 153.8, 134.6, 133.2, 130.0, 129.9, 123.6, 122.0, 72.5, 37.3, 36.6, 23.0, 10.0; IR υ_{max} (neat) 2922, 1714 cm^{-1}; FAB MS (NBA) *m*/*z* 651 ($[M + H]^+$, calcd 650.8). Anal. Calcd for $C_{40}H_{46}N_2O_6$: C, 73.82; H, 7.12; N, 4.30. Found: C, 73.92; H, 7.01; N, 4.32.

General Procedure for the Migration Reactions. LDA solutions used were prepared at 0 °C by adding *n*-BuLi (12 mmol), dissolved in hexane (6 mL approximately), to a solution of diisopropylamine (1.67 mL, 12 mmol) in THF (15 mL). Upon reaction with the calix[4]arene-*O*-carbamate, the reaction mixtures were quenched by the addition of 30 mL of a concentrated NH_4Cl solution in water. Workup refers to the subsequent extraction with diethyl ether (2 × 30 mL), washing the organic phase with brine (20 mL), drying the organic phase with $MgSO_4$, and evaporating the solvent. If compounds only could be synthesized as a part of a mixture and using different conditions, only the procedures giving the highest yields for these compounds have been described.

2,8-*axial*,*axial*-Bis(diethylamido)-25,27-dihydroxy-26,28-dipropoxycalix[4]arene (7). A solution of calix[4]arene **4a** (1.63 g, 2.3 mmol) in THF (5 mL) was added via a cannula to the freshly prepared LDA solution (in this case 27.6 mmol) at 0 °C. The reaction mixture was warmed to room temperature during 4 h and quenched. Workup and column chromatography (EtOAc/hexane = 4:6) exclusively yielded bismigrated compound **7** (1.31 g, 80%) as a white solid: mp 188−190 °C; ^{1}H NMR (200 MHz) δ 0.67 (t, J = 7.5 Hz, 3H), 1.00−1.20 (m, 2H), 1.03 (t, J = 7.4 Hz, 3H), 1.06 (t, J = 7.0 Hz, 6H), 1.13 (t, J = 7.0 Hz, 6H), 1.70−1.85 (m, 2H), 2.90−3.10 (m, 2H), 3.10−3.30 (m, 4H), 3.51 (d, J = 13.8 Hz, 2H), 3.67−3.86 (m, 6H), 4.27 (d, J = 13.8 Hz, 2H), 4.99 (s, 2H), 6.69−6.81 (m, 4H), 6.90−7.00 (m, 6H), 7.04 (d, J = 7.4 Hz, 2H), 7.17 (d, J = 6.6 Hz, 2H); ^{13}C NMR (50 MHz) δ 170.7, 158.0, 154.7, 153.0, 133.8, 131.9, 129.7, 128.7, 125.0, 124.7, 123.7, 118.3, 75.3, 42.0, 40.2, 23.8, 20.7, 14.1, 12.8, 10.8, 9.1; IR υ_{max} (neat) 3485, 2966, 2932 cm^{-1}; MS (EI) *m*/*z* (relative intensity) 706 (4, $[M - H]^+$), 647 (100), 574 (18); HRMS calcd for $C_{44}H_{54}N_2O_6$ 707.4060, found 707.4067. Anal. Calcd for $C_{44}H_{54}N_2O_6$: C, 74.76; H, 7.70; N, 3.96. Found: C, 74.90; H, 7.75; N, 3.97.

2,8-*axial*,*equatorial*-Bis(diethylamido)-25,27-dihydroxy-26,28-dipropoxycalix[4]arene (8). A solution of calix[4]arene **4a** (0.707 g, 1.0 mmol) in THF (5 mL) was added via a cannula to the freshly prepared LDA solution at 0 °C. The reaction mixture was warmed to room temperature during 4 h, stirred overnight and quenched. Workup and column chromatography (EtOAc/hexane = 4:6) yielded bismigrated compound **8** (300 mg, 42%), being second in order of elution of a mixture of compounds **7**, **8**, and **9**, as a white solid: mp 147−149 °C; ^{1}H NMR (200 MHz) δ 0.88 (t, J = 7.0 Hz, 3H), 1.00−1.20 (m, 12H), 1.25 (t, J = 7.4 Hz, 3H), 1.80−2.20 (m, 4H), 3.00−3.90 (m, 10H), 3.29 (d, J = 12.3 Hz, 1H), 3.45 (d, J = 13.4 Hz, 1H), 3.97 (t, J = 6.8 Hz, 2H), 4.12 (d, J = 13.4 Hz, 1H), 4.62 (d, J = 12.3 Hz, 1H), 4.71 (s, 1H), 6.14 (s, 1H), 6.55−7.40 (m, 13H), 8.70 (s, 1H); ^{13}C NMR (50 MHz) δ 171.4, 171.3, 155.0, 153.2, 152.3, 151.7, 134.5, 133.9, 133.5, 132.4, 130.3, 129.8, 129.7, 129.5, 129.2, 129.1, 128.9, 128.3, 127.8, 127.6, 126.7, 125.5, 125.1, 124.5, 119.2, 118.0, 78.2, 76.9, 56.5, 42.9, 41.4, 40.9, 40.4, 39.6, 32.5, 30.5, 23.3, 22.9, 14.5, 13.4, 12.6, 10.7, 10.3; IR υ_{max} (neat) 3306, 2972, 2935 cm^{-1}; MS (EI) *m*/*z* (relative intensity) 706 (28, $[M - H]^+$), 647 (100), 574 (7); HRMS calcd for $C_{44}H_{54}N_2O_6$ 707.4060, found 707.4062. Anal. Calcd for $C_{44}H_{54}N_2O_6$: C, 74.76; H, 7.70; N, 3.96. Found: C, 74.77; H, 7.62; N, 3.92.

2-*equatorial*-(Diethylamido)-25,27-dihydroxy-26,28-dipropoxycalix[4]arene (9). A solution of calix[4]arene **4a** (0.707 g, 1.0 mmol) in THF (5 mL) was added via a cannula to the freshly prepared LDA solution at −24 °C. The reaction mixture was warmed to room temperature during 6 h, stirred overnight, and quenched. Workup and column chromatography (EtOAc/hexane = 3:7) exclusively yielded monomigrated com-

pound **9** (410 mg, 67%) as a white solid: mp 198−200 °C; ^{1}H NMR (250 MHz) δ 1.05 (t, J = 7.0 Hz, 3H), 1.14 (t, J = 7.0 Hz, 3H), 1.26 (t, J = 7.4 Hz, 3H), 1.30 (t, J = 7.9 Hz, 3H), 1.95−2.20 (m, 4H), 3.10−3.60 (m, 4H), 3.29 (d, J = 12.5 Hz, 1H), 3.45 (d, J = 13.3 Hz, 1H), 3.46 (d, J = 13.4 Hz, 1H), 3.75−4.10 (m, 4H), 4.08 (d, J = 13.4 Hz, 1H), 4.12 (d, J = 13.3 Hz, 1H), 4.49 (d, J = 12.5 Hz, 1H), 6.17 (s, 1H), 6.62−7.13 (m, 8H), 7.15−7.33 (m, 4H), 7.89 (s, 1H), 8.48 (s, 1H); ^{13}C NMR (50 MHz) δ 171.0, 153.3, 153.2, 151.6, 151.6, 134.2, 132.5, 132.2, 132.1, 131.0, 129.1, 128.9, 128.5, 127.3, 127.2, 125.3, 125.0, 119.5, 118.9, 78.3, 41.5, 40.0, 39.0, 32.4, 32.1, 30.5, 23.4, 23.3, 13.1, 12.7, 10.7; IR υ_{max} (neat) 3309, 2930, 2874, 1645 cm^{-1}; MS (EI) m/z (relative intensity) 607 (100, M$^+$), 548 (8), 100 (16), 43 (13). Anal. Calcd for $C_{39}H_{44}NO_5$: C, 77.20; H, 7.31; N, 2.31. Found: C, 77.11; H, 7.29; N, 2.40.

2-*equatorial*-(Dimethylamido)-27-dimethylcarbamoyloxy-25-hydroxy-26,28-dipropoxycalix[4]arene (10). A solution of calix[4]arene **5b** (0.651 g, 1.0 mmol) in THF (5 mL) was added via a cannula to the freshly prepared LDA solution at 0 °C. Subsequently, the reaction mixture was stirred for 30 min at that temperature and quenched. Workup and column chromatography (EtOAc/hexane = 4:6) yielded monomigrated compound **10** (516 mg, 81%) as a white solid: mp 251−253 °C; ^{1}H NMR (250 MHz) δ 1.06 (t, J = 7.4 Hz, 6H), 1.70−2.05 (m, 4H), 2.97 (s, 3H), 3.04 (s, 3H), 3.11 (s, 3H), 3.28 (d, J = 12.9 Hz, 1H), 3.32 (d, J = 12.8 Hz, 1H), 3.43 (s, 3H), 3.48 (d, J = 13.9 Hz, 1H), 3.50−3.75 (m, 2H), 3.83 (t, J = 7.2 Hz, 2H), 4.02 (d, J = 13.9 Hz, 1H), 4.19 (d, J = 12.8 Hz, 1H), 4.23 (d, J = 12.9 Hz, 1H), 5.93 (s, 1H), 6.40−6.82 (m, 7H), 7.02−7.24 (m, 6H); ^{13}C NMR (50 MHz) δ 172.9, 155.9, 153.8, 152.1, 151.7, 147.1, 136.7, 135.5, 133.3, 131.5, 131.4, 130.9, 129.9, 129.0, 128.9, 128.6, 128.2, 127.5, 127.2, 125.9, 125.2, 124.5, 122.5, 119.1, 78.9, 42.1, 37.4, 37.4, 37.2, 35.7, 31.8, 30.0, 29.3, 23.2, 22.9, 10.7, 10.3; IR υ_{max} (neat) 3439, 2928, 2868, 1710 cm^{-1}; MS (EI) m/z (relative intensity) 650 (100, M$^+$), 591 (4). Anal. Calcd for $C_{40}H_{46}N_2O_6$: C, 73.82; H, 7.12; N, 4.30. Found: C, 74.16; H, 7.16; N, 4.56.

2-*equatorial*-(Diethylamido)-27-diethylcarbamoyloxy-25-hydroxy-26,28-dipropoxycalix[4]arene (11). A solution of calix[4]arene **5a** (0.707 g, 1.0 mmol) in THF (5 mL) was added via a cannula to the freshly prepared LDA solution at 0 °C. The reaction mixture was stirred for 2 h at that temperature and quenched. Workup and column chromatography (EtOAc/hexane = 3:7) yielded monomigrated compound **11** (516 mg, 73%) as a white solid: mp 176−177 °C; ^{1}H NMR (250 MHz) δ 0.90 (t, J = 7.4 Hz, 3H), 0.99 (t, J = 7.4 Hz, 3H), 1.16 (t, J = 7.2 Hz, 3H), 1.20 (t, J = 7.3 Hz, 3H), 1.27 (t, J = 7.0 Hz, 3H), 1.44 (t, J = 7.1 Hz, 3H), 1.60−2.00 (m, 4H), 3.10−4.20 (m, 12H), 3.28 (d, J = 13.1 Hz, 1H), 3.31 (d, J = 13.1 Hz, 1H), 3.47 (d, J = 14.0 Hz, 1H), 4.08 (d, J = 14.0 Hz, 1H), 4.23 (d, J = 13.1 Hz, 1H), 4.28 (d, J = 13.1 Hz, 1H), 5.88 (s, 1H), 6.35−6.39 (m, 4H), 6.59−6.63 (m, 2H), 6.73−6.76 (m, 2H), 7.05−7.22 (m, 2H), 7.25−7.40 (m, 2H); ^{13}C NMR (63 MHz) δ 171.2, 155.2, 154.1, 152.1, 151.9, 147.6, 137.1, 135.7, 133.4, 131.7, 131.3, 130.2, 129.0, 128.7, 128.5, 128.3, 127.4, 126.1, 125.0, 124.5, 122.5, 119.1, 78.9, 77.8, 42.2, 41.8, 40.8, 40.4, 31.4, 30.4, 29.7, 23.0, 22.9, 14.2, 14.0, 13.3, 12.9, 10.3; IR υ_{max} (neat) 3395, 2956, 2875, 1707, 1647 cm^{-1}; MS (ESI 10 mM LiCl) m/z (relative intensity) 713 (100, [M + H + Li]$^+$), 640 (60). Anal. Calcd for $C_{44}H_{54}N_2O_6$: C, 74.76; H, 7.70; N, 3.96. Found: C, 74.92; H, 7.55; N, 3.95.

2,8-*equatorial*,*equatorial*-Bis(diethylamido)-25,27-dihydroxy-26,28-dipropoxycalix[4]arene (12). A solution of calix[4]arene **5a** (0.707 g, 1.0 mmol) in THF (5 mL) was added via a cannula to the freshly prepared LDA solution at −12 °C. Subsequently, the reaction mixture was warmed to room temperature during 6 h, stirred overnight, and quenched. Workup and column chromatography (EtOAc/hexane = 4:6) yielded bismigrated compound **12** (150 mg, 21%), being the last one in order of elution of a mixture of **8**, **9**, and **12**, as a white solid: mp 239−240 °C; ^{1}H NMR (200 MHz) δ 0.95−1.25 (m, 18H), 1.80−2.20 (m, 4H), 3.10−3.55 (m, 8H), 3.44 (d, J = 13.4 Hz, 2H), 3.71 (t, J = 7.0 Hz, 2H), 3.98 (t, J = 6.9 Hz, 2H), 4.16 (d, J = 13.4 Hz, 2H), 5.75 (s, 2H), 6.60−6.76 (m, 4H), 6.86 (d, J = 7.5 Hz, 2H), 6.97 (d, J = 7.8 Hz, 2H), 7.05−7.25 (m, 4H); ^{13}C NMR (63 MHz) δ 171.0, 152.7, 132.9, 131.2, 130.4, 129.3, 128.9, 128.7, 128.2, 126.0, 125.4, 123.8, 119.4, 78.4, 42.1, 41.9, 40.2, 31.9, 23.4, 14.2, 12.8, 10.6, 10.5; IR υ_{max} (neat) 3406, 2956, 1648 cm^{-1}; MS (ESI 10 mM LiCl) m/z (relative intensity) 713 (100, [M + H + Li]$^+$), 640 (35). Anal. Calcd for $C_{44}H_{54}N_2O_6$: C, 74.76; H, 7.70; N, 3.96. Found: C, 74.80; H, 7.58; N, 3.80.

2-*equatorial*-(Dimethylamido)-25,27-dihydroxy-26,28-dipropoxycalix[4]arene (13). A solution of calix[4]arene **5b** (0.651 g, 1.0 mmol) in THF (5 mL) was added via a cannula to the freshly prepared LDA solution at 0 °C. Subsequently, the reaction mixture was warmed to room temperature during 4 h and quenched. Workup and column chromatography (EtOAc/hexane = 3:7) yielded monomigrated compound **13** (388 mg, 67%) as a white solid: mp 183−185 °C; ^{1}H NMR (250 MHz) δ 1.31 (t, J = 7.3 Hz, 3H), 1.33 (t, J = 7.1 Hz, 3H), 1.90−2.20 (m, 4H), 2.96 (s, 3H), 3.30 (d, J = 12.4 Hz, 1H), 3.45 (d, J = 13.7 Hz, 1H), 3.43 (s, 3H), 3.47 (d, J = 13.5 Hz, 1H), 3.70−4.00 (m, 4H), 4.07 (d, J = 13.7 Hz, 1H), 4.11 (d, J = 13.5 Hz, 1H), 4.50 (d, J = 12.4 Hz, 1H), 6.25 (s, 1H), 6.62−7.13 (m, 10H), 7.31−7.34 (m, 2H), 7.97 (s, 1H), 8.57 (s, 1H); ^{13}C NMR (63 MHz) δ 172.1, 153.3, 152.3, 151.7, 134.2, 132.4, 131.8, 131.1, 129.6, 128.9, 128.6, 128.4, 128.3, 127.4, 127.1, 125.3, 125.3, 125.1, 119.6, 118.9, 78.4, 39.8, 37.2, 36.0, 32.4, 32.2, 30.5, 23.4, 11.0, 10.8; IR υ_{max} (KBr) 3344, 2939, 1652 cm^{-1}; FAB MS m/z 580.6 ([M + H]$^+$, calcd 580.7). Anal. Calcd for $C_{37}H_{41}NO_5 \cdot 0.4H_2O$: C, 75.72; H, 7.18; N, 2.39. Found: C, 75.71; H, 7.14; N, 2.39.

2,14-*equatorial*,*equatorial*-Bis(diethylamido)-25,27-dihydroxy-26,28-dipropoxycalix[4]arene (14). A solution of calix[4]arene **6a** (0.707 g, 1.0 mmol) in THF (5 mL) was added via cannula to the freshly prepared LDA solution at 0 °C. Subsequently, the reaction mixture was warmed to room temperature during 4 h and quenched. Workup and column chromatography (EtOAc/hexane = 4:6) yielded bismigrated compound **14** (462 mg, 65%), being second in order of elution of a mixture of **9**, **12**, and **14**, as a white solid: mp 240−242 °C; ^{1}H NMR (200 MHz) δ 1.04 (t, J = 7.0 Hz, 6H), 1.14 (t, J = 7.0 Hz, 6H), 1.23 (t, J = 7.4 Hz, 6H), 1.95−2.10 (m, 4H), 3.10−3.60 (m, 8H), 3.47 (d, J = 13.7 Hz, 2H), 4.07 (d, J = 13.7 Hz, 2H), 3.70−4.05 (m, 4H), 6.17 (s, 2H), 6.67 (t, J = 7.6 Hz, 2H), 6.76−6.80 (m, 4H), 7.01 (d, J = 6.4 Hz, 2H), 7.11 (d, J = 6.7 Hz, 2H), 7.25−7.30 (m, 2H), 8.15 (s, 2H); ^{13}C NMR (63 MHz) δ 171.0, 152.2, 151.4, 130.7, 128.6, 127.3, 125.5, 125.1, 119.4, 78.5, 41.6, 40.0, 40.0, 32.3, 23.2, 13.8, 12.7, 10.5; IR υ_{max} (neat) 3363, 2956, 1646 cm^{-1}; MS (ESI 10 mM LiCl) m/z (relative intensity) 713 (100, [M + Li]$^+$), 640 (20), 629 (15). Anal. Calcd for $C_{44}H_{54}N_2O_6$: C, 74.76; H, 7.70; N, 3.96. Found: C, 74.66; H, 7.46; N, 3.99.

2,8-*equatorial*,*equatorial*-Bis(dimethylamido)-25,27-dihydroxy-26,28-dipropoxycalix[4]arene (15). A solution of calix[4]arene **6b** (0.651 g, 1.0 mmol) in THF (5 mL) was added via a cannula to the freshly prepared LDA solution at 0 °C. Subsequently, the reaction mixture was stirred for 30 min at this temperature and quenched. Workup and column chromatography (EtOAc/hexane = 1:1) yielded bismigrated compound **15** (152 mg, 23%), being the last one in order of elution of a mixture of **13**, **15**, and **16**, as a white solid: mp 277−279 °C; ^{1}H NMR (250 MHz) δ 1.23 (t, J = 7.4 Hz, 6H), 1.85−2.15 (m, 4H), 2.94 (s, 6H), 3.03 (s, 6H), 3.42 (d, J = 13.3 Hz, 2H), 3.75 (t, J = 6.2 Hz, 2H), 3.99 (t, J = 6.4 Hz, 2H), 4.20 (d, J = 13.3 Hz, 2H), 5.87 (s, 2H), 6.68−6.76 (m, 4H), 6.87 (d, J = 7.4 Hz, 2H), 7.04−7.20 (m, 6H); ^{13}C NMR (63 MHz) δ 171.6, 152.4, 132.8, 131.1, 130.1, 129.1, 128.7, 128.1, 125.3, 124.1, 119.6, 78.5, 77.8, 41.1, 37.4, 36.0, 31.5, 23.4, 23.3, 11.0, 10.6; IR υ_{max} (neat) 3332, 2941, 1652 cm^{-1}; FAB MS m/z 657.4 ([M + H + Li]$^+$, calcd 567.3). Anal. Calcd for $C_{40}H_{46}N_2O_6 \cdot 1.8$EtOAc: C, 70.04; H, 7.52; N, 3.46. Found: C, 70.13; H, 7.86; N, 3.42.

2,14-*equatorial*,*equatorial*-Bis(dimethylamido)-25,27-dihydroxy-26,28-dipropoxycalix[4]arene (16). A solution of calix[4]arene **6b** (0.651 g, 1.0 mmol) in THF (5 mL) was added via a cannula to the freshly prepared LDA solution at 0 °C. Subsequently, the reaction mixture was stirred for 30 min at this temperature and quenched. Workup and column

chromatography (EtOAc/hexane = 2:1) yielded bismigrated compound **16** (415 mg, 64%), being second in order of elution of a mixture of **13**, **15**, and **16**, as a white solid: mp 301−303 °C; ^{1}H NMR (250 MHz) δ 1.32 (t, J = 7.3 Hz, 6H), 1.90−2.20 (m, 4H), 2.95 (s, 6H), 3.02 (s, 6H), 3.47 (d, J = 13.7 Hz, 2H), 3.70−3.85 (m, 2H), 3.90−4.05 (m, 2H), 4.05 (d, J = 13.7 Hz, 2H), 6.23 (s, 2H), 6.67 (t, J = 7.5 Hz, 2H), 6.70−6.90 (m, 4H), 7.02 (d, J = 7.3 Hz, 2H), 7.11 (d, J = 7.5 Hz, 2H), 7.26 (d, J = 5.4 Hz, 2H), 8.31 (s, 2H); ^{13}C NMR (63 MHz) δ 172.0, 152.3, 151.3, 132.2, 130.7, 128.6, 128.5, 128.0, 127.2, 125.3, 125.2, 119.6, 78.4, 39.9, 37.2, 36.0, 32.3, 23.4, 10.9; IR υ_{max} (neat) 3332, 2940, 1650 cm^{-1}; FAB MS m/z 651.6 ([M + H]$^+$, calcd 651.8). Anal. Calcd for $C_{40}H_{46}N_2O_6$: C, 73.82; H, 7.12; N, 4.30. Found: C, 74.00; H, 6.99; N, 4.29.

2,14-*equatorial*,*equatorial*-Bis(diethylamido)-25,26,-27,28-tetrapropoxycalix[4]arene (17). A suspension of calix[4]arene **14** (356 mg, 0.5 mmol) and NaH (60% suspension in oil, 250 mg, 6.6 mmol) in DMF (10 mL) was stirred for 20 min at room temperature, whereupon *n*-propyl bromide (610 mg, 1.3 mmol) was added and stirring was continued for 24 h. MeOH (10 mL) was added, and the solvent was evaporated. The residue was dissolved in $CHCl_3$ (25 mL) and 2 N HCl (10 mL), and the organic layer was dried over Na_2SO_4 and evaporated to dryness. Column chromatography (EtOAc/hexane = 1:1) yielded **17** (338 mg, 97%) as a white solid: mp 248−250 °C; ^{1}H NMR (200 MHz) δ 0.99 (t, J = 7.4 Hz, 12H), 1.15−1.24 (m, 12H), 1.84−2.06 (m, 8H), 3.16 (d, J = 13.6 Hz, 2H), 3.43−3.53 (m, 8H), 3.75 (brs, 8H), 4.39 (d, J = 13.6 Hz, 2H), 5.79 (s, 2H), 6.08−7.07 (m, 12H); ^{13}C NMR (63 MHz) δ 171.1, 153.0, 151.4, 130.1, 128.5, 128.0, 125.6, 124.8, 122.2, 76.5, 42.9, 42.1, 40.4, 31.1, 25.5, 14.4, 12.9, 10.2; IR υ_{max} (neat) 3384, 2955, 2920, 2811, 1647 cm^{-1}; FAB MS m/z 797.0 ([M + H + Li]$^+$, calcd 797.1). Anal. Calcd for $C_{50}H_{66}N_2O_6\cdot 0.4H_2O$: C, 75.23; H, 8.43; N, 3.49. Found: C, 75.25; H, 8.52; N, 3.49.

2,14-*equatorial*,*equatorial*-Bis(diethylaminomethyl)-25,26,27,28-tetrapropoxycalix[4]arene (18). A solution of calix[4]arene **17** (316 mg, 0.4 mmol) in THF (15 mL) was treated with B_2H_6 (1.20 mL, 1.0 M in THF) at 0 °C, subsequently refluxed for 8 h, and treated again with B_2H_6 (1.20 mL, 1.0 M in THF). After 6 h of reflux, the reaction mixture was evaporated to dryness and quenched with 1 M HCl (15 mL). After the reaction mixture was stirred for 10 min, the pH was balanced to 9.0 with a 10% NaOH solution. Subsequently, the reaction mixture was extracted with $CHCl_3$ (3 × 25 mL). Further workup and column chromatography (EtOAc/hexane = 1:9) yielded **18** (201 mg, 66%) as a white solid: mp 130 °C; ^{1}H NMR (200 MHz) δ 1.02 (t, J = 7.5 Hz, 12H), 1.23 (t, J = 7.1 Hz, 12H), 2.00−2.20 (m, 8H), 2.75−3.10 (m, 8H), 3.16 (d, J = 13.1 Hz, 2H), 3.41 (d, J = 6.1 Hz, 4H), 3.75−3.90 (m, 4H), 4.00−4.15 (m, 4H), 4.40 (d, J = 13.1 Hz, 2H), 5.65 (t, J = 6.1 Hz, 2H), 6.50−6.75 (m, 12H); ^{13}C NMR (50 MHz) δ 155.6, 137.0, 134.8, 128.5, 125.2, 121.8, 61.3, 53.8, 32.5, 30.2, 23.4, 10.0, 9.1; IR υ_{max} (neat) 2955, 2936, 2881 cm^{-1}; FAB MS m/z 763.0 (M$^+$, calcd 763.1). Anal. Calcd for $C_{50}H_{70}N_2O_4$: C, 78.70; H, 9.25; N, 3.67. Found; C, 78.58; H, 8.99; N, 3.74.

26,28-Dipropoxy[2:25],[8:27]-*equatorial*,*equatorial*-calix-[4]arenebis-γ-lactone (19). A solution of calix[4]arene **7** (150 mg, 0.212 mmol) in acetic acid (3 mL) was refluxed for 24 h. Evaporation of the acid and column chromatography (EtOAc/hexane = 1:9) yielded **19** (76 mg, 64%), as a white solid: mp 270 °C; ^{1}H NMR (250 Hz) δ 0.82 (t, J = 7.4 Hz, 3H), 0.87 (t, J = 7.4 Hz, 3H), 1.70−2.00 (m, 4H), 3.24 (d, J = 13.8 Hz, 2H), 3.68−3.80 (m, 2H), 4.05−4.15 (m, 2H), 4.34 (d, J = 13.8 Hz, 2H), 4.56 (s, 2H), 6.02 (d, J = 7.1 Hz, 2H), 6.21−6.35 (m, 4H), 6.95−7.26 (m, 6H); ^{13}C NMR (50 MHz) δ 174.7, 157.9, 155.0, 150.4, 136.0, 133.2, 129.7, 129.2, 129.1, 127.8, 124.9, 124.1, 122.9, 122.7, 120.5, 82.5, 76.9, 48.3, 30.9, 22.9, 22.6, 9.4, 9.3; IR υ_{max} (neat) 3479, 2967, 2928, 2876, 1804 cm^{-1}; MS (EI) m/z (relative intensity) 560.0 (60, [M − H]$^+$, calcd 559.7), 476 (100), 430 (24), 386 (30). Anal. Calcd for $C_{36}H_{32}O_6$: C, 77.12; H, 5.75. Found: C, 76.88; H, 5.81.

2,8-*axial*,*axial*-Bis(diethylamido)-25,26,27,28-tetrapropoxycalix[4]arene (20). A suspension of calix[4]arene **7** (60 mg, 0.09 mmol), *n*-propyl bromide (141 mg, 0.3 mmol), and K_2CO_3 (136 mg, 1.0 mmol) in acetonitrile (5 mL) was refluxed overnight. The solvent was evaporated, and the residue was dissolved in $CHCl_3$ (20 mL) and 2 N HCl (10 mL), whereupon the organic layer was dried over Na_2SO_4 and evaporated to dryness. Column chromatography (EtOAc/Et_2O = 1:1) yielded **20** (67 mg, 92%) as a white solid: mp 214−217 °C; ^{1}H NMR (300 MHz) δ −0.16−0.13 (m, 2H), 0.42 (t, J = 7.3 Hz, 3H), 0.68 (t, J = 7.4 Hz, 6H), 0.91 (t, J = 7.4 Hz, 3H), 1.00−1.41 (m, 16H), 1.48−1.70 (m, 2H), 2.36−2.48 (m, 2H), 2.83−3.00 (m, 2H), 3.08−3.25 (m, 4H), 3.25−3.36 (m, 2H), 3.36−3.50 (m, 2H), 3.50−3.78 (m, 4H), 3.86 (d, J = 13.4 Hz, 2H), 3.90 (d, J = 13.4 Hz, 2H), 5.21 (s, 2H), 6.75−6.90 (m, 6H), 7.07−7.18 (m, 6H); ^{13}C NMR (50 MHz) δ 172.0, 158.8, 158.3, 156.5, 135.6, 135.3, 134.2, 132.3, 130.9, 130.5, 130.4, 126.8, 122.9, 122.8, 76.3, 73.3, 72.4, 49.6, 42.2, 40.7, 38.9, 23.7, 23.4, 20.6, 15.1, 13.2, 11.1, 10.8, 9.4; FAB MS m/z 792.0 ([M + H]$^+$, calcd 792.1). Anal. Calcd for $C_{50}H_{66}N_2O_6\cdot 0.3H_2O$: C, 75.40; H, 8.43; N, 3.52. Found: C, 75.48; H, 8.50; N, 3.50.

Crystal Data for Calix[4]arene 6b. Crystallization of **6b** from methanol containing ethanol (5%) gave single crystals suitable for X-ray diffraction. $C_{40}H_{46}N_2O_6\cdot C_2H_5OH$: M_r = 696.89, colorless tabular prism, monoclinic space group $P2_1/n$ with a = 11.550(1) Å, b = 17.761(1) Å, c = 19.339(1) Å, β = 102.591(6)°, V = 3872.0(6) Å^3, Z = 4, D_x = 1.195 g cm^{-3}, F(000) = 1496, μ(Mo Kα) = 0.81 cm^{-1}, 7169 reflections measured, 6808 independent (R_{int} = 1.57%), (4.0° < 2θ < 50.0°, ω scan, T = 180 K, Mo Kα radiation, highly oriented graphite crystal monochromator, λ = 0.71073 Å) on a Siemens P4 diffractometer using a variable scan speed of 3.00 to 30.00°/min in ω and a scan range of 1.20°. Background measurements were with a stationary crystal and stationary counter at the beginning and the end of a scan, each for 25.0% of the total scan time, and three standard reflections were measured every 100 reflections. Index ranges are: $0 \le h \le 13$, $0 \le k \le 21$, $-22 \le l \le 22$. Face-indexed numerical absorption correction was used and a min/max transmission of 0.9629/0.9760 was found. The structure was solved by automated direct methods (SHELXTL IRIS). Refinement on $\sum\omega(F_o - F_c)^2$ was carried out by full-matrix least-squares techniques for 502 parameters. For extinction correction χ = 0.00038(4), where $F^* = F[1 + 0.002\chi F^2/\sin(2\theta)]^{-1/4}$. Weighting scheme $\omega^{-1} = \sigma^2(F) + 0.00005F^2$ was used and refinement converged at a final R = 4.68% with ωR = 4.62% for 4185 observed reflections ($F > 4.0\sigma(F)$). Both *n*-propyl groups and the ethanol solvate are disordered. Hydrogen atoms were included in the refinement on calculated positions riding on their carrier atoms.

Crystal Data for Calix[4]arene 10. Crystallization of calix[4]arene **10** from methanol gave single crystals suitable for X-ray diffraction. $C_{40}H_{46}N_2O_6$: M_r = 650.82, colorless prism, monoclinic space group $P2_1/c$ with a = 19.260(2) Å, b = 14.565-(2) Å, c = 12.970(2) Å, β = 107.939(7)°, V = 3461.3 Å^3, Z = 4, D_x = 1.248 g cm^{-3}, F(000) = 1392, μ(Mo Kα) = 0.84 cm^{-1}, 6281 reflections measured, 6090 independent (R_{int} = 3.39%), (4.0° < 2θ < 50.0°, ω scan, T = 200 K, Mo Kα radiation, highly oriented graphite crystal monochromator, λ = 0.71073 Å) on a Siemens P4 diffractometer using a variable scan speed of 3.00 to 30.00°/min in ω and a scan range of 1.20°. Background measurements were with a stationary crystal and stationary counter at the beginning and the end of a scan, each for 25.0% of the total scan time, and three standard reflections were measured every 100 reflections. Index ranges are: $0 \le h \le 22$, $0 \le k \le 17$, $-15 \le l \le 14$. Face-indexed numerical absorption correction was used and a min/max transmission of 0.9528/0.9695 was found. The structure was solved by automated direct methods (SHELXTL IRIS). Refinement on $\sum\omega(F_o - F_c)^2$ was carried out by full-matrix least-squares techniques for 480 parameters. For extinction correction χ = 0.00078(3), where $F^* = F[1 + 0.002\chi F^2/\sin(2\theta)]^{-1/4}$. Weighting scheme $\omega^{-1} = \sigma^2(F)$ was used and refinement converged at a final R = 3.72% with ωR = 3.64% for 4254 observed reflections ($F > 6.0\sigma(F)$). Hydrogen atoms were included in the refinement on calculated positions riding on their carrier atoms.

Atomic coordinates, bond lengths, and thermal parameters for both calixarenes **6b** and **10** have been deposited at the Cambridge Crystallographic Data Centre.

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Supporting Information Available: X-ray data of compounds **6b** and **10**. This material is available free of charge via the Internet at http://pubs.acs.org.

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