Pergamon

Tetrahedron Vol. 51, No. 46, pp. 12699-12720, 1995

0040-4020/95 $9.50+0.00

0040-4020(95)00826-8

Synthesis of Calix[6]arenes Partially Functionalized at the Upper Rim

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Abstract: Several new examples of calix[6]arenes selectively functionalized at the upper rim are reported. Starting from calix[6]arenes 1,3,5-tri-, 1,2,4,5-tetra- and 1,2,3,4,5-pentaalkylated at the lower rim, it is possible to isolate macrocycles 2,4,6-tri-, 3,6-di- and 6-mono functionalized at the upper rim (18-94% yield) with nitro, formyl, bromo, chloromethyl and 2-propenyl groups. Modifications of these moieties allow the synthesis of macrocycles bearing amino, amido, hydroxymethyl, carboxy, cyano and chloromethyl functions which can be used for further transformation and preparation of new molecular receptors, based on calix[6]arenes, which have different geometries. Examples of di- and triquinones on the hexameric macrocycle are also reported.

INTRODUCTION

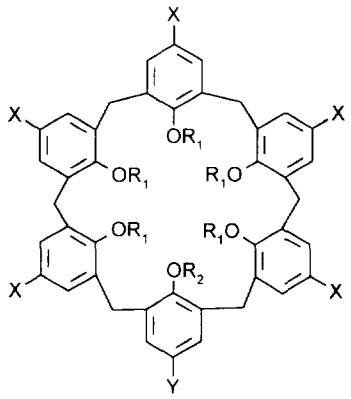
Calixarenes have been widely used in the recent years for the synthesis of receptors for ions and neutral molecules.[1,2] The increasing interest in these macrocycles is not only due to their easy synthesis through well established and simple methodologies,[3] but also to the possibility of shaping their basket through functionalization at the lower (phenolic OH groups) or at the upper rim (aromatic nuclei). Most of the studies on the *selective functionalization* of these compounds have been devoted to calix[4]arenes[4] and resulted in the synthesis of highly efficient and selective receptors for metal and ammonium ions, or neutral molecules.[2,5] However the dimensions of the conical apolar cavity of calix[4]arenes is rather small and it is only present when the macrocycle is fixed in the cone conformation, whereas their functionalization at the lower rim can also produce other stereoisomers (partial cone, 1,2-alternate, 1,3-alternate), which have no cavity. Moreover the increasing interest in complexation of larger and polyfunctional guest molecules led us to tackle the problem of selective functionalization of calix[6]arenes. These macrocycles are characterized not only by a larger cavity but also by the presence of six aromatic nuclei suitable for anchoring binding units. When they are functionalized at the proper positions calix[6]arenes may afford a wide variety of receptors with variable flexibility and shapes. However, compared with calix[4]arenes, the regiochemical control of calix[6]arene functionalization is more difficult because of the presence of a larger number of reactive centers and a higher conformational mobility. Although several papers appeared on the complete functionalization of calixarenes at the upper rim with sulfonic,[6] nitro, amino,[7] aminomethyl,[8] phosphonic,[9] acyl[10] and formyl[11] groups, and the synthesis of a large variety of partially functionalized calix[6]arenes at the lower rim are now available,[12] only

few examples of selectively substituted calix[6]arenes at the upper rim are reported. Some of them have been obtained through the stepwise synthesis route[13] while we recently published methods for the preparation of a monobromo-, a mononitro-, and a 1,4-dinitrocalix[6]arene,[14] together with a partially 1,3,5-de-butylated calix[6]arene derivative[15] which has also been obtained by others.[16]

We report in this paper the results of a more systematic work on the selective functionalization of calix[6]arenes at the upper rim.

RESULTS AND DISCUSSION

As a general strategy for the selective functionalization at the upper rim we have exploited the previously reported results on the selective alkylation of the lower rim,[12] which induces a different reactivity between the aromatic positions *para* to the free OH groups compared with those *para* to the OR groups.[17] Most of the partially alkylated compounds used as starting materials in this study are obtained from *p-tert*-butylcalix[6]arene **1**, since the corresponding derivatives of *p*-H-calix[6]arene **2** are unknown or very difficult to obtain.[12a,18] During this work we have found an excellent procedure for the preparation of monobenzylcalix[6]arene **3** in 89% yield, using a weak base (K_2CO_3) and a stoichiometric amount of benzyl bromide in dry acetone. Methylation of compound **3** with NaH/Me_2SO_4 gives the monobenzyloxy-pentamethoxycalix[6]arene **4** in quantitative yield, which is easily converted to the pentamethoxycalix[6]arene **5** by catalytic hydrogenation. No chromatographic separations are required, so compound **5** can be easily obtained in gram quantities.



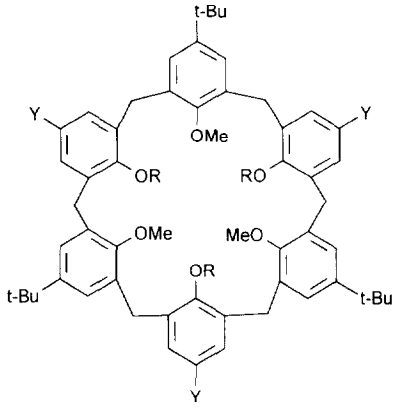
n	R_1	R_2	Y	X
1	H	H	*t*-Bu	*t*-Bu
2	H	H	H	H
3	H	$C_6H_5CH_2$	H	H
4	Me	$C_6H_5CH_2$	H	H
5	Me	H	H	H
15	Me	H	*t*-Bu	*t*-Bu
16	Me	H	NO_2	*t*-Bu
17	Me	C(O)Me	NO_2	*t*-Bu
18	Me	Me	NO_2	*t*-Bu
19	Me	H	NO_2	H
23	Me	C(O)Me	NH_2	*t*-Bu

Selective Nitration.

Ipso-nitration, i.e. substitution of *tert*-butyl with nitro groups, is a particularly useful reaction in calixarene chemistry because it uses as substrate the most readily available *p-tert*-butylcalixarenes and allows substitution of only the tert-butyl groups *para* to the free phenolic OH groups.[19]

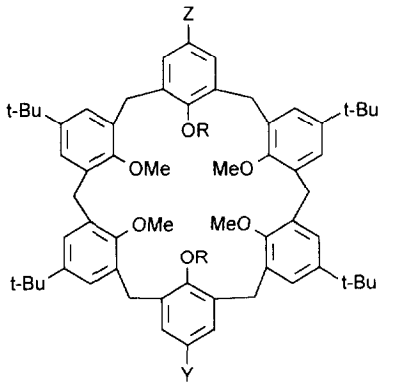
Therefore by treating several partially alkylated calix[6]arenes **6**, **10**, **13** and **15** with 1.1-1.5 equivalents of 63% HNO_3 in a 1:1 (v/v) mixture with 98% H_2SO_4, at room temperature for 40 min - 2 h in dry CH_2Cl_2 it was possible to isolate compounds **7, 11, 14, 16** nitrated in all phenolic nuclei, in 61-80% yield (Table 1). These

conditions appear to give nitrated products in better yield compared with the HNO_3 (60%)/AcOH mixture previously used.[14]

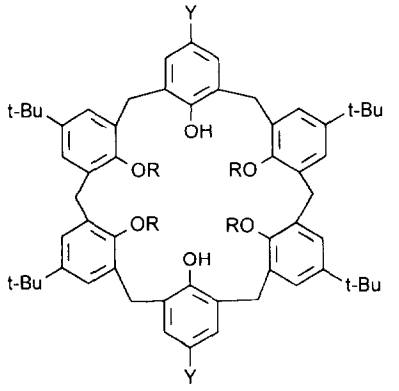


n	R	Y
6	H	*t*-Bu
7	H	NO_2
8	CH_2COOMe	NO_2
9	C(O)Me	NO_2
20	C(O)Me	NH_2
27	H	H
28	H	CHO
29	$C_6F_5CH_2$	H
30	$C_6F_5CH_2$	CHO
31	Me	H

n	R	Y
32	Me	CHO
37	$C_6F_5CH_2$	CH_2OH
38	Me	$CH(OMe)_2$
40	H	Br
41	Me	Br
42	4-Me-$C_6H_4CH_2$	Br
44	Me	CN
45	Me	CH_2Cl
46	$CH_2CH=CH_2$	H
47	H	$CH_2CH=CH_2$



n	R	Y	Z
10	H	*t*-Bu	*t*-Bu
11	H	NO_2	NO_2
12	C(O)Me	NO_2	NO_2
21	C(O)Me	NH_2	NH_2
22	C(O)Me	NO_2	NH_2
24	C(O)Me	$NHCO(CH_2)_2COOH$	$NHCO(CH_2)_2COOH$
25	C(O)Me	$NHCO(CH_2)_3COOH$	$NHCO(CH_2)_3COOH$
26	C(O)Me	$NHCOCH_2OCH_2COOH$	$NHCOCH_2OCH_2COOH$



n	R	Y
13	$C_2H_4OC_2H_4OMe$	*t*-Bu
14	$C_2H_4OC_2H_4OMe$	NO_2
35	$C_2H_4OC_2H_4OMe$	H
36	$C_2H_4OC_2H_4OMe$	CHO
39	$C_2H_4OC_2H_4OMe$	COOH
43	$C_2H_4OC_2H_4OMe$	Br
49	Bz	*t*-Bu

Acetylation and/or alkylation with $BrCH_2COOMe$ and dimethyl sulfate of compounds **7, 11, 16** gave compounds **8-9, 12, 17** and **18** completely functionalized at the lower rim and bearing three, two or one nitro groups at the upper rim. The ^1H NMR spectra (see Experimental Section) for all nitro compounds synthesized show only singlets for the methylene bridge protons, indicating a high degree of conformational mobility at room temperature.

Table 1. Nitration of Calix[6]arenes at Room Temperature in Dry CH_2Cl_2

Starting material	Product	eq HNO_3 (63%)[a]	Time (min)	Yield (%)
5	**19**	1.1	5+50[b]	28
6	**7**	1.5	50	64
10	**11**	1.5	120	61[c]
13	**14**[d]	10.0[e]	5+50[b]	66
15	**16**	1.5	50	80[f]

[a] one equivalent of HNO_3 (63%) for each phenolic nuclei to be nitrated, in 1:1 (v/v) mixture with H_2SO_4 (98%). [b] the nitrating mixture was added over 5 min to the CH_2Cl_2 solution of calixarene kept at -15°C. The reaction mixture was then stirred at room temperature for 50 min. [c] mp > 300°C (Lit.[14] mp > 300°C). [d] Compound **13** was dissolved in glacial $AcOH/CH_2Cl_2$, 1:6 (v/v). [e] HNO_3 was added neat. [f] mp > 300°C (Lit.[14] mp > 300°C).

Also the direct nitration of compound **5** derived from calix[6]arene **2** give the mononitro-pentamethoxycalix[6]arene **19** in 28% yield.

Reduction of nitrocalixarenes **9**, **12** and **17** was performed with $SnCl_2$ in dry EtOH or H_2 over PtO_2 or Pd(C) and proceeded without affecting the acetoxy groups present at the lower rim. This complete reduction of **9**, **12** and **17** afforded tri-, di- and monoaminocalix[6]arenes **20**, **21** and **23** in yields of 91%, 80% and 76% respectively. Use of H_2/PtO_2 and milder experimental conditions permitted selective reduction of dinitrocalix[6]arene **12** to its mononitro-monoamino derivative **22** in good yield (62%).

Treatment of diaminocalix[6]arene **21** with a large excess of succinic, glutaric and diglycolic anhydride in THF resulted in the isolation of the corresponding coupling products **24-26** which have two carboxylic functions at the upper rim of the macrocycle in 1,4-position. In this compounds the structure is still highly mobile thus confirming that the presence of the bulky groups such as t-Bu and $NHC(O)(CH_2)_nCOOH$ at the upper rim is not enough to freeze the conformational interconversion when relatively small groups (Me, MeCO) are present at the lower rim.

Selective formylation.

Other than *ipso*-nitration, electrophilic aromatic substitutions need to be performed on de-*tert*-butylated calix[6]arenes. Since, as mentioned before, very few examples of *p*-H-calix[6]arenes selectively *O*-alkylated at the lower rim are known, we have used compounds **27** and **35** obtained through the selective removal of *tert*-butyl groups in partially *O*-alkylated *p-tert*-butylcalix[6]arenes **6** and **13**.

Selective formylation of these macrocycles has been carried out following the methods of Gross[20] (Cl_2CHOCH_3/Lewis acid, Table 2) and Duff[21] (hexamethylene tetramine/CF_3COOH, Table 3) which have already been successfully applied to calixarenes.[22,23] However the reaction of compound **27** in the presence of $Cl_2CHOCH_3/SnCl_4$ resulted in the isolation of only small amounts of triformylated compound **28**, while parallel dealkylation reactions seem to be predominant. Better results have been obtained by treating **27** with hexamethylene tetramine (HMTA) and CF_3COOH which allows the isolation of **28** in 18% yield. Much more successful was the formylation of compound **35** which gave the diformylated derivatives **36** in 94% yield *via* the Gross method and in 44% yield under Duff's conditions.

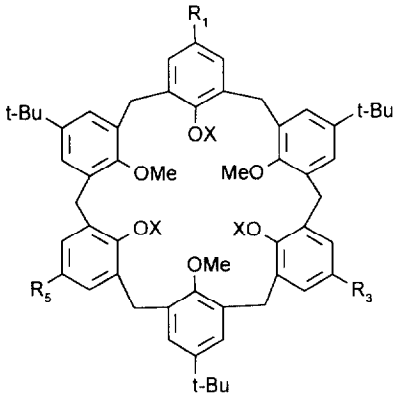
Table 2. Formylation of Calix[6]arenes **29** and **35** with Cl_2CHOCH_3 and $TiCl_4$ ($SnCl_4$) at R.T.

Starting material	Product	Molar Ratio of $TiCl_4$[a] to calix	Molar Ratio of Cl_2CHOCH_3 to calix	Time (h)	Yield (%)
29	**30**	30	30	3	18
29	**33**	15	15	1	25
29	**34**	15	15	1	23
35	**36**	10[b]	2.5	1	94

[a] freshly distilled; [b] $SnCl_4$ was used.

Table 3. Formylation of Calixarenes **27**, **31** and **35** with HMTA in CF_3COOH at Reflux.

Starting material	Product	Molar Ratio of HMTA to calix	Reaction time (h)	Yield (%)
27	**28**	27	17	18
31	**32**	42	36	74
35	**36**	18	21	44



n	X	R_1	R_3	R_5
33	$C_6F_5CH_2$	CHO	H	H
34	$C_6F_5CH_2$	CHO	CHO	H

Compound **27** has been converted to **31** by methylation with Cs_2CO_3 and MeI in DMF in higher yield (93%) than that reported by Shinkai using NaH in THF.[16] Formylation of **31** under Duff conditions gave triformylated compound **32** in 74% yield. The use of compound **29** and a large amount of $TiCl_4$ and Cl_2CHOCH_3 (30 eq.) gave compound **30** in 18% yield, while a lower amount of Lewis acid and formylating agent (15 eq.) gave a mixture of the mono- (**33**) (25%) and di- (**34**) (23%) formylated derivatives.

The formyl groups on these derivatives can be easily modified by reduction and oxidation or protected to acetals as exemplified by the synthesis of compound **37** and **39** obtained in quantitative yields and of compound **38** obtained in 81% yield using dry MeOH with a trace of CF_3COOH.

Selective halogenation.

Another interesting functionalization of calixarenes at the upper rim is halogenation (bromination or iodination)[17,24,25,26] since it allows, by subsequent reactions, the introduction of a large variety of groups such as COOR, CN, NH_2, Ph, etc. which are not easily introduced by direct electrophilic aromatic substitution. We have explored the bromination of trimethoxy-tri-*tert*-butylcalix[6]arene **27** and of tetrakis[2-(2-methoxyethoxy)ethoxy]-tetra-*tert*-butylcalix[6]arene **35** using NBS. Tribromo derivative **40** and dibromo **43**

were obtained in 48 and 34 % yield respectively when reactions were carried out in ethyl acetate as solvent, while the use of 2-butanone increased the amount of isolated **40** to 70%. Alkylation of compound **40** with Cs_2CO_3 in DMF and CH_3I or 4-methylbenzyl bromide gave compound **41** and **42**. The former was reacted under Rosenmund-von Braun conditions (anhydrous CuCN and N-methyl pyrrolidinone at 200°C) to give the tricyano compound **44** in 78% yield.

Selective chloromethylation.

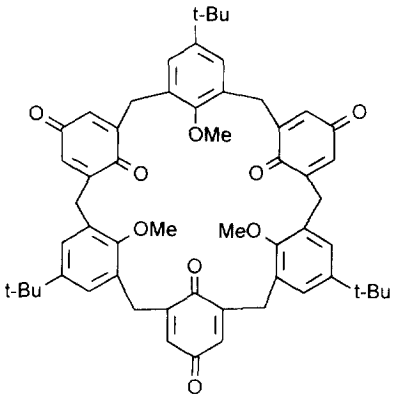
The last electrophilic aromatic substitution which we have carried out is the chloromethylation of compound **31**. As previously reported by some of us[27] for tetraalkoxycalix[4]arenes, the use of H_2CO, $SnCl_4$ and trimethylsilyl chloride is a very efficient and high yield method of chloromethylation of aromatics originally developed in polymer chemistry,[28] which avoids the use of carcinogenic $ClCH_2OCH_3$. Also for calix[6]arenes, when three positions are protected by *tert*-butyl groups it is possible to introduce three CH_2Cl groups in the 1,3,5 positions to give **45** in 80% yield. This procedure for the preparation of compound **45** is therefore comparable to that recently reported by Shinkai et al., which uses $ClCH_2OCH_3/ZnCl_2$.[16]

Claisen rearrangement.

An interesting method of functionalization of the upper rim of calixarenes is the Claisen rearrangement route.[29] The 1,3,5-trimethoxy-tri-*tert*-butylcalix[6]arene **27** could be easily alkylated with Cs_2CO_3 in DMF to tris-(2-propenyloxy) derivative **46** in 83% yield.

Subsequent reaction in refluxing N,N-dimethylaniline gave the rearrangement product **47** (42%) which is a useful intermediate for further transformations.

Calix[6]arene-quinones.



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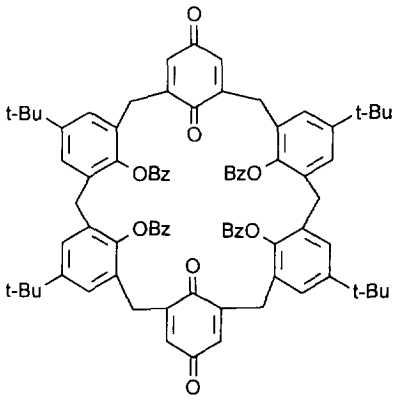

50

Oxidation of trimethoxy-tri-*p-tert*-butylcalix[6]arene **6** with $Tl(NO_3)_3 3H_2O$ gave in 24% yield the triquinone **48** while reaction of tetrabenzoyloxy-*p-tert*-butylcalix[6]arene **49** with $Tl(CF_3CO_2)_3$ in trifluoroacetic acid (TFA) afforded the diquinone **50** in 80% yield.

These calixquinones could not only show interesting redox properties,[30] but could also be useful intermediates for further modification at the upper rim[31] and for the introduction of chromophoric groups.[32]

All compounds synthesized in this work are conformationally mobile as demonstrated by their ^{1}H NMR spectra at room temperature (see Experimental Section) where singlets or broad signals for the protons of the methylene bridges are present. Only the tetraalkoxy-dibromo-tetra-*p-tert*-butylcalix[6]arene **43** shows a distinct pattern of sharp signals including the $ArCH_2Ar$ protons which remain unchanged between -50 and +70°C in $CDCl_3$ indicating a restricted mobility of the macrocycle over this range of temperature and on the 400 MHz NMR timescale.

Two-dimensional NMR experiments (XHCORR together with COSY and NOESY) allowed assignment of all signals of the NMR spectra and proposal of a preferred conformation for this compound. Two triplets at δ 39.2 and 30.7 ppm are present in the ^{13}C NMR spectrum for the methylene bridge carbons ($ArCH_2Ar$). The first correlates with a singlet of four protons at 4.06 ppm while the second one correlates with two doublets of four protons each at 4.08 and 3.76 ppm. This indicates[33] that two pairs of aromatic nuclei are each other *anti*-oriented and three sets are *syn*-oriented. The presence, in the molecule, of a symmetry element (plane or C_2 axis) as deduced from ^{1}H and ^{13}C NMR spectra suggests a 1,2,3-alternate structure (**u**,u,d,d,d,u)[34] for this compound (Figure 1).

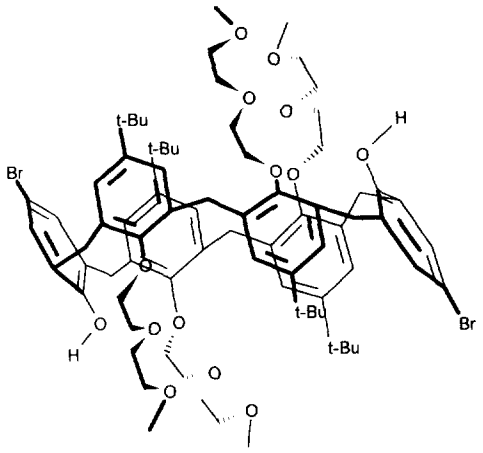

Fig.1. Proposed *1,2,3-alternate* structure for compound **43**.

EXPERIMENTAL SECTION

Melting points were determined with an Electrothermal melting point apparatus in a sealed capillary and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded with Bruker spectrometers with Me_4Si as internal standard. Mass spectra were obtained with a Finnigan MAT90, a VG Autospec spectrometer (FAB using 3-nitrobenzyl alcohol as a matrix) or with a Finnigan MAT SSQ710 spectrometer (DCI, CH_4). Analytical thin layer chromatography was performed on precoated silica gel plates (SiO_2, Merck, 60 F_{254} or Alugram Sil G/UV 254), while silica gel 60 (SiO_2, Merck, particle size 0.040-0.063 mm, 230-240 mesh) or SDS 60 (particle size 230-400 mesh) was used for preparative column chromatography.

Materials

5,11,17,23,29,35-Hexa-*tert*-butylcalix[6]arene-37,38,39,40,41,42-hexol (**1**),[35,3] calix[6]arene-37,38,39,-40,41,42-hexol (**2**),[36] 5,11,17,23,29,35-hexa-*tert*-butyl-38,40,42-trimethoxycalix[6]arene-37,39-41-triol (**6**),[37] 5,11,17,23,29,35-hexa-*tert*-butyl-38,39,41,42-tetramethoxycalix[6]arene-37,40-diol (**10**),[14] 5,11,17,23,29,35-hexa-*tert*-butyl-37,38,40,41-tetrakis[2-(2-methoxyethoxy)ethoxy]calix[6]arene-39,42-diol (**13**),[12a] 5,11,17,23,-29,35-hexa-*tert*-butyl-38,39,40,41,42-pentamethoxycalix[6]aren-37-ol (**15**),[14] and 5,17,29-tri-*tert*-butyl-38,40,-42-trimethoxycalix[6]arene-37,39,41-triol (**27**),[15] 38,39,41,42-tetrabenzoyloxy-5,11,17,23,29,35-hexa-*tert*-butylcalix[6]arene-37,40-diol (**49**)[38] were prepared as described in the literature.

37-Benzyloxycalix[6]arene-38,39,40,41,42-pentol (3)

A mixture of calix[6]arene-37,38,39,40,41,42-hexol **2** (4.0 g, 6.3 mmol) and K_2CO_3 (0.95 g, 6.9 mmol) in dry acetone (400 ml) was refluxed for 1 h. After cooling, benzyl bromide (0.82 ml, 6.9 mmol) was added, and the mixture was refluxed for 66 h. The mixture was quenched with 25% aq NH_4OH (15 ml), stirred for 20 min, acidified with 2N HCl and acetone eliminated under reduced pressure. The residue was extracted with CH_2Cl_2 (3x100 ml) and the organic layer was washed with brine and dried (Na_2SO_4). The solvent was evaporated and the residue was triturated with MeOH. The precipitate obtained was triturated with hexane and filtered to afford pure **3**. Yield 4.05 g (89%); mp 254-260°C. HRMS (FAB): *m/z* = 726.29596 (M^+, calcd for $C_{49}H_{42}O_6$ 726.29814). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 9.80 (br s, 2 H, OH), 8.90 (br s, 3 H, OH), 7.75 (d, *J* = 8.0 Hz, 2 H, ArH), 7.65 (dd, *J* = 8.0, 10.0 Hz, 2 H, ArH), 7.49 (t, *J* = 10.0 Hz, 1 H, ArH), 7.3-7.1 (m, 13 H, ArH), 6.9-6.7 (m, 5 H, ArH), 5.25 (s, 2 H, OCH_2Ar), 4.5-3.5 (br s, 12 H, $ArCH_2Ar$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.8, 151.6, 150.5, 149.1, 136.2, 133.3 (s, Ar), 129.6, 129.4, 129.2, 129.1, 129.0, 128.8, 128.7 (d, ArH), 127.82, 127.79, 127.6, 127.5, 127.4 (s, Ar), 127.3, 126.0, 122.1, 121.2, 120.7 (d, ArH), 77.8 (t, OCH_2Ar), 32.2 (t, $ArCH_2Ar$), 32.0 (t, $ArCH_2Ar$).

37-Benzyloxy-38,39,40,41,42-pentamethoxycalix[6]arene (4)

To a stirred slurry of NaH (60% oil dispersion, 0.92 mg, 23 mmol) in THF (160 ml) under argon was added a solution of calix[6]arene **3** (3.0 g, 4.1 mmol). After 30 min at r.t., Me_2SO_4 (2.35 ml, 24.6 mmol) was added. The mixture was stirred for 48 h, and quenched with 25% NH_4OH (10 ml). The resulting mixture was stirred for 15 min, acidified with 2N HCl and extracted with Et_2O (2x50 ml). The combined extracts were washed with brine (2x50 ml), dried ($MgSO_4$) and evaporated. The residue was triturated with MeOH to give pure **4**. Yield 3.14 g (95%); mp 188-190°C. An analytical sample was obtained by flash chromatography (eluent CH_2Cl_2). Anal. calcd for $C_{54}H_{52}O_6$: C, 81.37; H 6.58. Found: C, 81.60; H, 6.81. MS (FAB): *m/z* = 797.5 [$(M+H)^+$, 797.0]. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.4-7.3 (m, 5 H, ArH), 7.1-6.8 (m, 18 H, ArH), 4.75 (s, 2 H, OCH_2Ar), 3.99 (s, 4 H, $ArCH_2Ar$), 3.96 (s, 4 H, $ArCH_2Ar$), 3.93 (s, 4 H, $ArCH_2Ar$), 3.22 (s, 6 H, OCH_3), 3.12 (s, 3 H, OCH_3), 2.97 (s, 6 H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.5, 156.4, 156.1, 154.4, 137.7, 134.8, 134.6, 134.5, 134.44, 134.41, 134.3 (s, Ar), 129.7, 129.5, 129.2, 128.7, 128.6, 128.3, 128.2, 127.8, 127.7, 123.7, 123.4, 123.3 (d, ArH), 74.8 (t, OCH_2Ar), 60.2, 60.0 (q, OCH_3), 30.4, 30.3, 30.2 (t, $ArCH_2Ar$).

38,39,40,41,42-Pentamethoxycalix[6]arene-37-ol (5)

To a solution of calix[6]arene **4** (3.14 g, 3.9 mmol) in EtOAc (300 ml) was added Pd/C 10% (520 mg) and the mixture was stirred under H_2 at r.t. for 18 h. The mixture was filtered through Celite and this was washed with CH_2Cl_2, filtrates was evaporated to dryness. The residue was triturated with MeOH to afford pure **5**. Yield 2.25 g (81%); mp 275-276°C. Anal. calcd for $C_{47}H_{46}O_6$ 1/3CH_2Cl_2: C, 77.33; H, 6.40. Found: C, 77.36; H, 6.57. HRMS (FAB): *m/z* = 706.33061 (M^+, 706.32944). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.34 (s, 1 H, OH), 7.08 (dd, *J* = 2.0, 7.3 Hz, 2 H, ArH), 7.0-6.8 (m, 15 H, ArH), 6.73 (t, *J* = 7.4 Hz, 1 H, ArH), 3.97 (s, 8 H, $ArCH_2Ar$), 3.83 (s, 4 H, $ArCH_2Ar$), 3.55 (s, 3 H, OCH_3), 3.32 (s, 6 H, OCH_3), 3.22 (s, 6 H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.6, 156.3, 155.0, 153.8, 134.1, 133.95, 133.93, 133.4, (s, Ar), 129.6, 129.3, 128.7, 128.65, 128.58, 128.54, 124.1, 123.5 (d, ArH), 60.8, 60.4, 60.2 (q, OCH_3), 31.2, 30.9, 30.0 (t, $ArCH_2Ar$).

General Procedure for Nitration of Calix[6]arenes 5, 6, 10, 13 and 15

To a vigorously stirred solution of calix[6]arene (0.50 mmol) in dry CH_2Cl_2 (10 ml) the nitrating mixture (Table 1) was added under argon at room temperature. The reaction mixture was stirred for 50-120 min, quenched with H_2O (10 ml) and extracted with CH_2Cl_2 (2x25 ml). The organic layer was washed with brine (3x25 ml), dried (Na_2SO_4) and evaporated to dryness.

5,17,29-Tri-tert-butyl-38,40,42-trimethoxy-11,23,35-trinitrocalix[6]arene-37,39,41-triol (7). Purified by column chromatography (AcOEt/hexane, 1:4) and crystallized with Et_2O/hexane. Yield 64%; mp 226°C. Anal. calcd for $C_{57}H_{63}N_3O_{12}$: C, 69.71; H 6.46; N 4.28. Found: C, 69.97; H, 7.14; N, 3.61. MS (FAB): *m/z* = 1041.6 [$(M+C(NH_2)_3)^+$, 1041.5]. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.19 (s, 3 H, OH), 8.04 (s, 6 H, ArH), 7.02 (s, 6 H, ArH), 3.97 (s, 12 H, $ArCH_2Ar$), 3.57 (s, 9 H, OCH_3), 1.14 [s, 27 H, $C(CH_3)_3$]; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 158.4, 151.7, 148.5, 140.7 (s, Ar), 131.0, 127.5, 126.1, 125.0 (d, ArH), 61.7 (q, OCH_3), 34.3 [s, $C(CH_3)_3$], 31.2 [q, $C(CH_3)_3$], 30.8 (t, $ArCH_2Ar$).

5,11,23,29-Tetra-tert-butyl-38,39,41,42-tetramethoxy-17,35-dinitrocalix[6]arene-37,40-diol (11). Pure compound **11** was obtained by trituration with CH_3CN. Yield 61%; mp >300°C (Lit.[14] >300°C).

11,17,29,35-Tetra-tert-butyl-37,38,40,41-tetrakis[2-(2-methoxyethoxy)ethoxy]-5,23-dinitrocalix[6]arene-39,42-diol (14). The crude product was purified by preparative plate chromatography (silica gel, hexane/THF, 1.4:1). Yield 66%; mp 190-192°C (EtOH). Anal. calcd for $C_{78}H_{106}N_2O_{18}$: C, 68.91; H, 7.85; N, 2.06. Found: C, 68.83; H, 7.94; N, 2.13. MS (CI): *m/z* = 1359.9 [$(M+H)^+$, 1359.8]. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.80 (br s, 2 H, OH), 7.90 (br s, 4 H, ArH), 7.1-6.9 (br s, 8 H, ArH), 4.20-3.35 (br s, 44 H, OCH_2, $ArCH_2Ar$), 3.28 (s, 12 H, OCH_3), 1.07 [s, 36 H, $C(CH_3)_3$]; ^{13}C NMR (25 MHz, $CDCl_3$): δ = 159.0, 152.2, 147.1, 140.3, 133.3, 131.5 (s, Ar), 128.4, 126.8, 126.1, 124.2 (d, ArH), 72.8, 71.8, 70.3, 69.7 (t, OCH_2), 58.8 (q, OCH_3), 34.0 [s, $C(CH_3)_3$], 31.2 [q, $C(CH_3)_3$], 29.8 (t, $ArCH_2Ar$).

5,11,17,23,29-Penta-tert-butyl-38,39,40,41,42-pentamethoxy-35-nitrocalix[6]arene-37-ol (16). The residue was triturated with hexane (45 ml) and filtered; yield 80%; mp 201-202°C (Lit.[14] 201-202°C).

38,39,40,41,42-Pentamethoxy-35-nitrocalix[6]arene-37-ol (19). The residue was purified by column chromatography (AcOEt/ hexane 1:5) and then crystallized with $CHCl_3$/hexane. Yield 28%; mp 258-260°C. Anal. calcd for $C_{47}H_{45}NO_8 \cdot H_2O$: C, 73.32; H, 6.15; N, 1.82. Found: C, 73.53; H, 6.06; N, 1.86. HRMS (FAB): *m/z* = 751.31097 (M^+, 751.310495).^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.69 (s, 1 H, OH), 7.87 (s, 2 H, ArH), 7.1-6.8 (m, 15 H, ArH), 3.98 (s, 4 H, $ArCH_2Ar$), 3.96 (s, 4 H, $ArCH_2Ar$), 3.84 (s, 4 H, $ArCH_2Ar$), 3.58 (s, 3 H, OCH_3), 3.29 (s, 6 H, OCH_3), 3.27 (s, 6 H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.4, 156.7, 156.5, 154.8, 140.3, 134.7, 134.1, 134.0, 133.9, 131.6 (s, Ar), 129.7, 129.6, 129.2, 128.8, 128.7 (d, ArH), 127.9 (s, Ar), 124.7, 124.5, 123.6, 123.3 (d, ArH), 61.1, 60.5, 60.2 (q, OCH_3), 31.4, 31.1, 30.0 (t, $ArCH_2Ar$).

5,17,29-Tri-tert-butyl-38,40,42-trimethoxy-37,39,41-tris[(methoxycarbonyl)methoxy]-11,23,35-trinitro-calix[6]arene (8)

To a solution of **7** (200 mg, 0.2 mmol) in dry DMF (30 ml), Cs_2CO_3 (400 mg, 1.23 mmol) and methyl bromoacetate (120 µl, 1.14 mmol) were added, whereupon the mixture was stirred at 70°C for 18 h. After cooling the mixture was extracted with Et_2O (2x50 ml) and the organic layer was washed with HCl 5% (2x25 ml), brine (3x25 ml), dried ($MgSO_4$) and the solvent was evaporated. The residue was purified by chromatography (CH_2Cl_2) and triturated with MeOH to afford **8**. Yield 72%; mp 158-160°C. Anal. calcd for $C_{66}H_{75}N_3O_{18}$: C, 66.15; H, 6.31; N, 3.51. Found: C, 66.54; H, 6.68; N, 2.73. MS (FAB): *m/z* = 1198.7

$[(M+H)^+$, 1198.5]. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.69 (s, 6 H, ArH), 7.19 (s, 6 H, ArH), 4.32 (s, 6 H, OCH_2CO_2Me), 4.00 (bs, 12 H, $ArCH_2Ar$), 3.69 (s, 9 H, CH_3OCO), 3.02 (s, 9 H, OCH_3), 1.29 [s, 27 H, $C(CH_3)_3$]; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 168.5(s, CO), 158.9, 154.3, 147.2, 144.1, 135.8, 133.1 (s, Ar), 127.5, 123.4 (t, ArH), 69.5 (t, $OCH_2CO_2CH_3$), 60.2 (q, OCH_3), 52.1 (q, $OCH_2CO_2CH_3$), 34.3 [s, $C(CH_3)_3$], 31.4 [q, $C(CH_3)_3$], 31.3 (t, $ArCH_2Ar$).

37,39,41-Triacetoxy-5,17,29-Tri-tert-butyl-38,40,42-trimethoxy-11,23,35-trinitrocalix[6]arene (9)

Method A: To NaH (60% mineral oil, 40 mg, 1.0 mmol) was added a solution of calixarene **7** (200 mg, 0.2 mmol) in THF (10 ml). After 30 min an excess of acetyl chloride (200 μl) was dropped and the mixture stirred overnight at r.t. The solvent was eliminated and the residue was taken off with CH_2Cl_2 (75 ml), washed with 10% HCl (2x25 ml), brine (2x25 ml), dried (Na_2SO_4) and the solvent eliminated. The residue was purified by column chromatography (CH_2Cl_2) and crystallized (MeOH) to give **9.** Yield 70 mg (31%);

Method B: A solution of calixarene **7** (240 mg, 0.24 mmol), Ac_2O (10 μl) and H_2SO_4 (2 drops) was heated at 80°C under argon for 18 h. The mixture was poured into cold MeOH and the solvent was evaporated. The residue was dissolved in Et_2O (100 ml) and washed with saturated solution of Na_2CO_3, brine, dried ($MgSO_4$) and the solvent was evaporated. The residue was dissolved in THF-hexane (1:1) and filtered through silica gel to afford **9**. Yield 140 mg (63%); mp 168-172°C (dec.). Anal. calcd for $C_{63}H_{69}N_3O_{15}$: C, 68.27; H, 6.27; N, 3.79. Found: C, 68.73; H, 6.62; N, 3.43. MS (FAB): *m/z* = 1240.4 $[(M+Cs)^+$, 1240.4]. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.92 (s, 6 H, ArH), 6.90 (s, 6 H, ArH), 3.85 (br s, 12 H, $ArCH_2Ar$), 3.43 (s, 9 H, OCH_3), 1.60 (s, 9 H, $OCOCH_3$), 1.15 [s, 27 H, $C(CH_3)_3$]; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.8 (s, $OCOCH_3$), 153.6, 152.2, 147.2, 145.2, 135.5, 130.8 (s, Ar), 126.3, 123.8 (d, ArH), 60.2 (q, OCH_3), 34.2 [s, $C(CH_3)_3$], 31.3 (t, $ArCH_2Ar$), 31.2 [q, $C(CH_3)_3$], 19.9 (q, $OCOCH_3$).

37,40-Diacetoxy-5,11,23,29-tetra-tert-butyl-38,39,41,42-tetramethoxy-17,35-dinitrocalix[6]arene (12)

To a stirred slurry of NaH (60% oil dispersion, 865 mg, 19.8 mmol) in THF (50 ml) under argon was added a solution of calix[6]arene **11** (2.0 g, 1.98 mmol) in THF (50 ml), at room temperature. After 15 min, an excess of acetyl chloride (2 ml) was slowly added. The mixture was stirred at r.t. for 24 h, the solvent was evaporated, the residue was acidified with 1N HCl and extracted with CH_2Cl_2. The combined extracts were washed with H_2O, dried (Na_2SO_4) and evaporated. The residue was triturated with EtOH to give pure **12**. Yield 100%; mp > 300°C. Anal. calcd for $C_{66}H_{78}N_2O_{12}\,H_2O$: C, 71.46; H, 7.27; N, 2.52. Found: C, 71.51; H, 7.41; N, 2.40. MS (FAB): *m/z* = 1113.9 $[(M+Na)^+$, 1113.5]. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.02 (s, 4 H, ArH), 6.91 (d, *J* = 2.4 Hz, 4 H, ArH), 6.86 (d, *J* = 2.4 Hz, 4 H, ArH), 3.89 and 3.82 (br s, 12 H, $ArCH_2Ar$), 3.26 (s, 12 H, OCH_3), 1.79 (br s, 6 H, $COCH_3$), 1.15 [s, 36 H, $C(CH_3)_3$]; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.6, 146.4, 145.1, 136.3, 133.0, 130.6 (s, Ar), 127.0, 125.3, 124.1 (d, ArH), 60.4 (q, OCH_3), 34.1 [s, $C(CH_3)_3$], 31.7 (t, $ArCH_2Ar$), 31.2 [q, $C(CH_3)_3$], 30.3 (t, $ArCH_2Ar$), 20.0 (q, $ArCH_3$).

37-Acetoxy-5,11,17,23,29-penta-tert-butyl-38,39,40,41,42-pentamethoxy-35-nitrocalix[6]arene (17)

A solution of 5,11,17,23,29-penta-*tert*-butyl-38,39,40,41,42-pentamethoxy-35-nitrocalix[6]aren-37-ol (**16**) (1.0 g, 1 mmol) in acetic anhydride (25 ml) and a catalytic amount (4 drops) of conc. H_2SO_4 was stirred at room temperature for 24 h. The crude reaction was poured into methanol and the solvent was evaporated, the acetic acid was neutralized with a solution of saturated $NaHCO_3$ (200 ml) and then was extracted with $CHCl_3$

(3x75 ml). The organic layer was washed with brine, dried (Na_2SO4) and the solvent evaporated. The residue was triturated with cold MeOH and filtered to give **17**. Yield 83%; mp 185-190°C. Anal. calcd for $C_{69}H_{87}NO_9$ MeOH: C, 75.98; H, 8.29; N, 1.27. Found: C, 75.80; H, 8.28; N, 1.20. MS (FAB): *m/z* = 1073.4 (M^+, 1073.6). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.87 (s, 2 H, ArH), 7.15 (d, *J* = 2.4 Hz, 2 H, ArH), 7.10 (s, 2 H, ArH), 6.96 (d, *J* = 2.4 Hz, 2 H, ArH), 6.93 (d, *J* = 2.3 Hz, 2 H, ArH), 6.77 (d, *J* = 2.3 Hz, 2 H, ArH), 3.95 (br s, 12 H, $ArCH_2Ar$), 3.34 (s, 6 H, OCH_3), 2.97 (s, 3 H, OCH_3), 2.94 (s, 6H, OCH3), 1.71 (s, 3H, $COCH_3$), 1.23 [s, 18H, $C(CH_3)_3$], 1.22 [s, 9H, $C(CH_3)_3$], 1.05 [s, 18 H, $C(CH_3)_3$]; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.7 (s, CO), 154.2, 153.8, 153.6, 152.2, 146.4, 145.8, 145.6, 145.2, 136.2, 133.5, 133.4, 133.0, 130.6 (s, Ar), 127.8, 126.5, 125.7, 125.4, 125.1, 123.4 (d, ArH), 60.2, 60.1, 60.0 (q, OCH_3), 34.2, 34.1, 34.0 [s, $C(CH_3)_3$], 31.4, 31.3, 31.0 [q, $C(CH_3)_3$], 31.1, 31.0, 29.4, (t, $ArCH_2Ar$), 19.9 (q, $COCH_3$).

5,11,17,23,29-Penta-tert-butyl-37,38,39,40,41,42-hexamethoxy-35-nitrocalix[6]arene (18)

To a stirred slurry of NaH (60% oil dispersion, 187 mg, 4.7 mmol) in THF (80 ml) under argon was added a solution of calix[6]arene **16** (800 mg, 0.78 mmol). After 30 min at r.t., Me_2SO_4 (0.5 ml, 5.5 mmol) was added. The mixture was stirred at r.t. for 41 h, and quenched with 25% aq NH_4OH (3 ml). The resulting mixture was stirred for 15 min, acidified with 2N HCl and the solvent was evaporated. The residue was extracted with CH_2Cl_2 (2x50 ml). The combined extracts were washed with brine (2x20 ml), dried (Na_2SO_4) and evaporated. The residue was triturated with MeOH to give pure **18**: yield 72%; mp 252-254°C. Anal. calcd for $C_{68}H_{87}NO_8$ MeOH: C, 76.84; H, 8.50; N, 1.30. Found: C, 76.99; H, 8.58; N, 1.39. MS (FAB): *m/z* = 1045.6 (M^-, 1045.6). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.73 (s, 2 H, ArH), 7.14 (d, *J* = 2.5 Hz, 2 H, ArH), 7.07 (d, *J* = 2.5 Hz, 2 H, ArH), 7.06 (s, 2 H, ArH), 6.89 (d, *J* = 2.5 Hz, 2 H, ArH), 6.77 (d, *J* = 2.5 Hz, 2 H, ArH), 3.99 (br s, 4 H, $ArCH_2Ar$), 3.95 (br s, 8 H, $ArCH_2Ar$), 3.44 (s, 3 H, OCH_3), 3.32 (s, 6 H, OCH_3), 2.81 (s, 9 H, OCH_3), 1.25 [s, 18 H, $C(CH_3)_3$], 1.19 [s, 9 H, $C(CH_3)_3$], 0.99 [s, 18 H, $C(CH_3)_3$]; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.2, 154.0, 153.4, 146.4, 145.8, 145.6, 143.5, 136.5, 133.6, 133.5, 133.48, 133.2, 131.7 (s, Ar), 127.5, 126.4, 126.1, 125.2, 125.1, 123.4 (d, ArH), 60.4, 60.0, 59.9 (q, OCH_3), 34.2, 34.1, 34.0 [s, $C(CH_3)_3$], 31.4, 31.1 [q, $C(CH_3)_3$], 30.8, 30.3, 30.1 (t, $ArCH_2Ar$).

37,39,41-Triacetoxy-11,23,35-triamino-5,17,29-tri-tert-butyl-38,40,42-trimethoxycalix[6]arene (20)

Method A: A suspension of $SnCl_2 2H_2O$ (153 mg, 0.68 mmol), calix[6]arene **9** (50 mg, 0.045 mmol) in dry EtOH (3 ml) was heated at reflux for 20 h. The solvent was evaporated and the residue was treated with H_2O (15 ml) and filtered. The filtrate was treated with aqueous solution of sodium tartrate (10 ml) and filtered. The solid was dissolved in CH_2Cl_2, dried (Na_2SO_4) and the solvent eliminated to give **20**. Yield 62%.

Method B: A suspension of calix[6]arene **9** (50 mg, 0.045 mmol) and PtO_2 in THF (12 ml) was bubbled with an hydrogen stream at r.t. for 15 min. The mixture was stirred under H_2 in the dark for 20 h. Then it was filtered and the filtrate was evaporated to dryness in the dark. The residue was dried under vacuum to afford pure compound **20** that was stored under argon. Yield 91%; mp 187-189°C. MS (FAB): *m/z* = 1018.6 [$(M+H)^+$, 1018.7]. ^1H NMR (200 MHz, $CDCl_3$): δ = 7.00 (br s, 12 H, ArH), 4.20-3.20 (br s, 12 H, $ArCH_2Ar$), 3.49 (s, 9 H, OCH_3), 2.21 (br s, 9 H, $OCOCH_3$), 1.20 [s, 27 H, $C(CH_3)_3$]; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 169.8 (s, $OCOCH_3$), 154.0, 146.5, 143.9, 133.8, 132.2, 126.7 (s, Ar), 126.0, 115.3 (d, ArH), 60.3 (q, OCH_3), 34.1 [s, $C(CH_3)_3$], 31.4 [s, $C(CH_3)_3$], 29.7 (t, $ArCH_2Ar$), 20.3 (q, $OCOCH_3$).

37,40-Diacetoxy-17,35-diamino-5,11,23,29-tetra-tert-butyl-38,39,41,42-tetramethoxycalix[6]arene (21)

A suspension of calix[6]arene **12** (1.2 g, 1.0 mmol) and PtO_2 (0.48 g, 2 mmol) in THF (90 ml) was bubbled with an hydrogen stream at r.t. for 30 min. The mixture was heated at reflux under H_2 for 2 h. After cooling the mixture was filtered through a short column of Celite and the filtrate evaporated to dryness. The residue was triturated with hexane to afford pure **21**. Yield 80%; mp 243°C. Anal. calcd for $C_{66}H_{82}N_2O_8 2H_2O$: C, 74.27; H, 8.12; N, 2.62. Found: C, 74.03; H, 8.06; N, 2.41. MS (FAB): *m/z* = 1031.8 [$(M+H)^+$, 1031.6). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 6.75 (br s, 4 H, ArH), 6.6-6.5 (m, 8 H, ArH), 5.57 (br s, 4 H, NH_2), 3.66 (br s, 4 H, $ArCH_2Ar$), 3.29 (br s, 8 H, $ArCH_2Ar$), 3.17 (br s, 12 H, OCH_3), 1.87 (br s, 6 H, $COCH_3$), 0.89 [s, 36 H, $C(CH_3)_3$]; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 169.8 (s, CO), 154.6, 146.4, 145.8, 138.1, 133.7, 131.9, 126.7, 125.7, 114.5 (Ar), 60.4 (q, OCH_3), 34.1 [s, $C(CH_3)_3$], 31.6 (t, $ArCH_2Ar$), 31.3 [q, $C(CH_3)_3$], 30.7 (t, $ArCH_2Ar$), 20.5 (q, $COCH_3$).

37,40-Diacetoxy-17-amino-5,11,23,29-tetra-tert-butyl-38,39,41,42-tetramethoxy-35-nitrocalix[6]arene (22)

A suspension of calix[6]arene **12** (50 mg, 0.045 mmol) and PtO_2 (20 mg, 0.09 mmol) in THF (4 ml) was bubbled with an hydrogen stream at r.t. for 5 min. The mixture was heated over 40°C for 40 min. After cooling the mixture was filtered through a short column of Celite and the filtrate was evaporated to dryness. The residue was purified by chromatography (CH_2Cl_2:MeOH 20:1) to afford pure **22**. Yield 62%; mp 298°C (dec.). Anal. calcd for $C_{66}H_{80}N_2O_{10} H_2O$: C, 73.44; H, 7.65; N, 2.59. Found: C, 73.24; H, 7.58; N, 2.79. MS (FAB): *m/z* = 1062.0 [$(M+H)^+$, 1061.6]. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.99 (s, 2 H, ArH), 6.97 (d, *J* = 2.5 Hz, 2 H, ArH), 6.87 (br s, 2 H, ArH), 6.81 (br s, 4 H, ArH), 6.35 (s, 2 H, ArH), 3.87 and 3.82 (br s, 12 H, $ArCH_2Ar$), 3.22 (s, 12 H, OCH_3), 1.96 (s, 3 H, $COCH_3$), 1.58 (br s, 3 H, $COCH_3$) 1.15 [s, 18 H, $C(CH_3)_3$], 1.11 [s, 18 H, $C(CH_3)_3$]; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 169.9, 168.0 (s, CO), 153.8, 146.4, 145.9, 145.1, 143.7, 136.3, 134.6, 133.3, 132.9, 132.3, 130.5 (s, Ar), 127.3, 125.9, 125.5, 125.2, 124.1, 115.6 (d, ArH), 60.4, 60.3 (q, OCH_3), 34.7 [s, $C(CH_3)_3$], 31.9, 31.5 (t, $ArCH_2Ar$), 31.3 [q, $C(CH_3)_3$], 30.5 (t, $ArCH_2Ar$), 20.4, 19.9 (q, $COCH_3$).

37-Acetoxy-35-amino-5,11,17,23,29-penta-tert-butyl-38,39,40,41,42-pentamethoxycalix[6]arene (23)

A solution of calix[6]arene **17** (864 mg, 0.8 mmol) in THF (150 ml) 10% Pd(C) (1.2 g) was added and bubbled with a hydrogen stream at r.t. for 30 min. The mixture was stirred under H_2 at r.t. for 24 h. The mixture was filtered through Celite and the filtrate evaporated to dryness. The residue was triturated with hexane to afford pure **23**. Yield 76%; mp 197-201°C. Anal. calcd for $C_{69}H_{89}NO_7$: C, 79.34; H, 8.59; N, 1.34. Found: C, 79.04; H, 8.67; N, 1.27. MS (FAB): *m/z* = 1044.5 (M^+, 1043.6). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.09 (d, *J* = 2.5 Hz, 2 H, ArH), 7.08 (s, 2 H, ArH), 6.97 (t, *J* = 2.6 Hz, 4 H, ArH), 6.83 (d, *J* = 2.5 Hz, 2 H, ArH), 6.14 (s, 2 H, ArH), 3.95 (br s, 12 H, $ArCH_2Ar$), 3.30 (s, 6 H, OCH_3), 2.99 (s, 3 H, OCH_3), 2.88 (s, 6 H, OCH_3), 1.93 (s, 3 H, $COCH_3$), 1.23 [s, 18 H, $C(CH_3)_3$], 1.17 [s, 9 H, $C(CH_3)_3$], 1.09 [s, 18 H, $C(CH_3)_3$]; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.5 (s, CO), 154.1, 154.0, 153.8, 145.9, 145.7, 143.7, 139.3, 134.3, 133.6, 133.4, 133.3, 132.2 (s, Ar), 126.9, 126.4, 126.1, 125.44, 125.4, 114.6 (d, ArH), 60.1, 60.0 (q, OCH_3), 34.1, 34.07 [s, $C(CH_3)_3$], 31.42, 31.39, 31.25 [q, $C(CH_3)_3$], 31.2, 30.8, 30.5 (t, $ArCH_2Ar$), 20.3 (q, $COCH_3$).

General procedure for the synthesis of amides 24-26 from calix[6]arene 21

To a solution of calix[6]arene (**21**) (150 mg, 0.15 mmol) in THF (12ml) the corresponding anhydride (1.5 mmol) was added. After refluxing the mixture for 20 h, the solvent was removed under reduced pressure

and the residue was quenched with HCl and the resulting solid filtered and washed with H_2O.

39,42-Diacetoxy-11,17,29,35-tetra-tert-butyl-37,38,40,41-tetramethoxycalix[6]arene-5,23-disuccinamic diacid (24). Yield 77%; mp 198-200°C. Anal. calcd for $C_{74}H_{90}N_2O_{14}\cdot 3\ H_2O$: C, 69.14; H, 7.53; N, 2.18. Found: C, 69.38; H, 7.30; N, 2.06. MS (FAB): *m/z* = 1232.2 [$(M+H)^+$, 1231.7]. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.39 (s, 2 H, NH), 7.03 (br s, 4 H, ArH), 6.94 (br s, 4 H, ArH), 6.86 (br s, 4 H, ArH), 4.83 (s, 4 H, $ArCH_2Ar$), 3.65 (br s, 8 H, $ArCH_2Ar$), 3.16 (s, 12 H, OCH_3), 2.7-2.6 (m, 4 H, CH_2CO), 2.65-2.5 (m, 4 H, CH_2CO), 1.68 (br s, 6 H, $COCH_3$), 1.11 [s, 36 H, $C(CH_3)_3$]; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 174.1, 170.3, 169.7 (s, CO), 152.9, 145.0, 135.4, 133.7, 131.8, 131.2 (s, Ar), 125.6, 124.4, 120.0 (d, ArH), 59.7 (q, OCH_3), 33.4 [s, $C(CH_3)_3$], 31.3, 31.0 (t, $ArCH_2Ar$), 30.6 [q, $C(CH_3)_3$], 29.4, 28.8 (t, $COCH_2CH_2CO$), 19.2 (q, $COCH_3$).

39,42-Diacetoxy-11,17,29,35-tetra-tert-butyl-37,38,40,41-tetramethoxycalix[6]arene-5,23 diglutaramic diacid (25). Yield 88%; mp 218°C. Anal. calcd for $C_{76}H_{94}N_2O_{14}\cdot 2\ H_2O$: C, 70.45; H, 7.62; N, 2.16. Found: C, 70.13; H, 7.84; N, 1.95. MS (FAB): *m/z* = 1259.1 (M^+, 1258.7). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.18 (br s, 4 H, ArH), 6.96 (br s, 4 H, arH), 3.88 (br s, 4 H, $ArCH_2Ar$), 3.72 (br s, 10 H, $ArCH_2Ar$ and NH), 3.20 (s, 12 H, OCH_3), 2.45 (t, *J* = 2.8 Hz, 8 H, CH_2CO), 1.76 (br s, 6 H, $COCH_3$), 2.1-2.0 (m, 4 H, $COCH_2CH_2CH_2CO$), 1.17, [s, 36 H, $C(CH_3)_3$]; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 178.5, 170.8, 169.3 (s, CO), 146.0, 135.0, 134.7, 132.8, 131.7 (s, Ar), 126.4, 125.4, 125.2, 121.0 (d, ArH), 60.3 (q, OCH_3), 34.1 [s, $C(CH_3)_3$], 34.1 (t, $COCH_2$), 32.9 (t, $ArCH_2Ar$), 31.3 (t, $ArCH_2Ar$), 20.5 (t, $COCH_2CH_2CH_2CO$), 19.6 (q, $COCH_3$).

39,42-Diacetoxy-11,17,29,35-tetra-tert-butyl-37,38,40,41-tetramethoxycalix[6]arene-5,23 diglicolamic diacid (26). Yield 88%; mp 172°C. Anal. calcd for $C_{74}H_{90}N_2O_{16}\cdot 3\ H_2O$: C, 67.44; H, 7.34; N, 2.12. Found: C, 67.48; H, 7.07; N, 1.97. MS (FAB): *m/z* = 1263.8 [$(M+H)^+$, 1263.6]. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.77 (s, 2 H, NH), 7.29 (s, 4 H, ArH), 6.86 (s, 8 H, ArH), 4.17 (s, 4 H, COCH2O), 4.13 (s, 4 H, $COCH_2O$), 3.82 (s, 4 H, $ArCH_2Ar$), 3.69 (br s, 8 H, $ArCH_2Ar$), 3.15 (s, 12 H, OCH_3), 1.59 (br s, 6 H, $COCH_3$), 1.10 [s, 36 H, $C(CH_3)_3$]; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 172.4, 169.6, 168.0 (s, CO), 153.5, 146.3, 135.0, 134.2, 131.7 (s, Ar), 126.5 (d, ArH), 125.3 (s, Ar), 121.1 (d, ArH), 71.7 (t, $COCH_2O$), 68.9 (t, $COCH_2O$), 60.4 (q, OCH_3), 34.1 [s, $C(CH_3)_3$], 31.9 (t, $ArCH_2Ar$), 31.3 [q, $C(CH_3)_3$], 19.9 (q, $COCH_3$).

5,17,29-Tri-tert-butyl-37,39,41-tris(pentafluorobenzyloxy)-38,40,42-trimethoxycalix[6]arene (29)

To a suspension of **27** (500 mg, 0.59 mmol) and K_2CO_3 (330 mg, 2.4 mmol) in dry acetonitrile (50 ml) was added α-bromo-pentafluorotoluene (0.36 ml, 2.4 mmol). The mixture was refluxed for 18 h. The solvent was evaporated, and the residue was taken up in CH_2Cl_2 (100 ml), washed with 1 N HCl (2x25 ml), brine (1x25 ml) and dried over $MgSO_4$. The crude product was triturated with methanol and pure compound **29** filtered. Yield 740 mg (89%); mp 280°C. Anal. calcd for $C_{78}H_{69}O_6F_{15}\cdot 3H_2O$: C, 65.00; H, 5.24. Found: C, 65.03; H, 5.25. Karl Fischer: H_2O, 3.68. $C_{78}H_{69}O_6F_{15}\cdot 3H_2O$ requires H_2O, 3.75. MS (FAB): *m/z* = 1386.4 (M^+, 1386.5). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.17 (s, 6 H, ArH), 6.72, 6.56 (m, 9 H, ArH), 4.96 (s, 6 H, OCH_2), 3.97 (br s, 12 H, $ArCH_2Ar$) 2.50 (s, 9 H, OCH_3), 1.31 [s, 27 H, $C(CH_3)_3$]; ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 154.1, 153.1, 146.1, 134.8, 133.0 (s, Ar), 127.6, 124.2, 61.1 (t, OCH_2), 59.9 (q, OCH_3), 34.2 [s, $C(CH_3)_3$], 31.5 [q, $C(CH_3)_3$], 30.2 (t, $ArCH_2Ar$).

5,17,29-Tri-tert-butyl-37,38,39,40,41,42-hexamethoxycalix[6]arene (31)

To a stirring solution of calixarene **27** (140 mg, 0.16 mmol) in 25 ml of dry DMF, Cs_2CO_3 (320 mg, 1.0

mmol) and MeI (0.06 ml, 1.0 mmol) were added. The reaction mixture was heated at 90°C for 16 h and then quenched with 100 ml of 1N HCl and extracted with CH_2Cl_2 (2x40 ml). The combined organic extracts were washed with water (2x60 ml) and dried (Na_2SO_4). After evaporation the product was purified by column chromatography (silica gel, hexane/THF 8:2). Yield 136 mg (93%); mp 119-121°C. Anal. calcd for $C_{60}H_{72}O_6$: C, 81.05; H, 8.15. Found: C, 80.95; H, 8.22. MS (CI): *m/z* = 889.3 [$(M+H)^+$, 889.5]. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.01 (s, 6H, ArH), 6.87 (s, 9H, ArH), 3.92 (s, 12H, $ArCH_2Ar$), 3.19 (s, 9H, OCH_3), 2.99 (s, 9H, OCH_3), 1.16 [s, 27H, $C(CH_3)_3$]; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.1, 154.2, 145.9, 134.6, 133.5 (s, Ar), 128.6, 126.2, 123.3 (d, ArH), 60.1 (q, OCH_3), 34.1 [s, $C(CH_3)_3$], 31.5 [q, $C(CH_3)_3$], 30.6 (t, $ArCH_2Ar$).

11,17,29,35-Tetra-tert-butyl-37,38,40,41-tetrakis[2-(2-methoxyethoxy)ethoxy]calix[6]arene-39,42-diol (35)

To a vigorously stirred solution of **13** (2.0 g, 1.47 mmol) in dry toluene (22 ml), $AlCl_3$ (3.95 g, 29.60 mmol) was added. After 4 h the mixture was quenched with 1N HCl (20 ml) and the aqueous layer extracted with Et_2O (2x15 ml). The combined organic layers were washed with H_2O (3x20 ml) and dried ($MgSO_4$). After evaporation of the solvent the crude product was triturated with petroleum ether to afford pure **35**. Yield 1.16 g (62%); mp 134-136°C. Anal. calcd for $C_{78}H_{108}O_{14}$: C, 73.80; H, 8.57. Found: C, 73.71; H, 8.64. MS (CI): *m/z*: 1270.1 [$(M+H)^+$, 1269.8]. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 (br s, 2H, OH), 6.90 (br s, 12H, ArH), 6.65 (t, *J* = 7.2Hz, 2H, ArH), 3.80 and 3.50 (br s, 44H, $ArCH_2Ar$, OCH_2), 3.32 (s, 12H, OCH_3), 1.03 [s, 36H, $C(CH_3)_3$]; ^{13}C NMR (25 MHz, $CDCl_3$): δ = 152.8, 151.9, 146.5, 132.9, 128.3 (s, Ar), 127.5, 126.2, 125.9, 119.6 (d, ArH), 72.6, 72.0, 70.4, 70.1 (t, OCH_2), 59.0 (q, OCH_3), 34.1 [s, $C(CH_3)_3$], 31.3 [q, $C(CH_3)_3$], 30.8 (t, $ArCH_2Ar$).

General Procedure for Formylation of Calix[6]arenes via Cl_2CHOCH_3 and $TiCl_4$ ($SnCl_4$) in $CHCl_3$

To a solution of calix[6]arene (0.40 mmol) in dry $CHCl_3$ (25 ml) at -15°C, was added dropwise a mixture of Cl_2CHOCH_3 and Lewis acid (Table 2). After 1-3 h stirring at r.t., the reaction mixture was quenched with 1N HCl (20 ml) and aqueous layer extracted with CH_2Cl_2 (2x15 ml). The combined organic phases were washed with H_2O (3x30 ml), dried ($MgSO_4$) and evaporated to dryness.

5,17,29-Tri-tert-butyl-37,39,41-tris(pentafluorobenzyloxy)-11,23,35-triformyl-38,40,42-trimethoxy-calix[6]arene (30). Purified by column chromatography (CH_2Cl_2) and crystallized from $CHCl_3$/MeOH. Yield 18%; mp 252-253°C. Anal. calcd for $C_{81}H_{69}O_9F_{15}\cdot CHCl_3$: C, 61.51; H, 4.55. Found: C, 61.91; H, 4.44. MS (FAB): *m/z* = 1471.7 [$(M+H)^+$, 1471.5]. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 9.53 (s, 3 H, CHO), 7.2-7.0 (br s, 12 H, ArH), 5.01 (s, 6 H, OCH_2), 4.5-4.0, 4.0-3.5 (br s, 6 H, $ArCH_2Ar$) 2.60 (s, 9 H, OCH_3), 1.31 [s, 27 H, $C(CH_3)_3$]; ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 191.4 (d, CHO), 154.2, 146.8, 135.6, 134.5, 132.7, 132.2, 129.3, 129.0, 127.8, 127.6 (s, Ar), 59.9 (t, OCH_2), 53.4 (q, OCH_3), 34.2 [s, $C(CH_3)_3$], 31.4 [q, $C(CH_3)_3$], 30.5 (t, $ArCH_2Ar$).

5,17,29-Tri-tert-butyl--37,39,41-tris(pentafluorobenzyloxy)-11-monoformyl-38,40,42-trimethoxy-calix[6]arene (33) and 5,17,29-tri-tert-butyl-37,39,41-tris(pentafluorobenzyloxy)-11,23-diformyl-38,40,42-trimethoxycalix[6]arene (34). Purified by column chromatography (CH_2Cl_2/hexane, 1:1) and crystallized from $CHCl_3$/MeOH. **33**: Yield 25%; MS (FAB): *m/z* = 1415.7 (M^+, 1415.5). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 9.37 (s, 1 H, CHO), 7.3-7.0 (m, 8 H, ArH), 6.65-6.5 (m, 6 H, ArH), 5.02 (s, 2 H, OCH_2), 4.90 (s, 4 H, OCH_2),

4.7-4.0, 4.0-3.40 (br s, 6 H, $ArCH_2Ar$), 2.70 (s, 6 H OCH_3), 2.38 (s, 2 H, OCH_3), 1.35 [s, 27 H, $C(CH_3)_3$]; ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 190.8 (d, CHO), 158.5, 154.8, 154.7, 154.6, 153.1, 146.6, 146.1, 135.8, 134.7, 134.5 133.2, 132.9, 132.5, 131.9, 129.0, 128.1, 127.6, 127.3, 127.2, 124.4 (s, Ar), 60.8, 60.7 (t, OCH_2), 34.22, 34.21 [s, $C(CH_3)_3$], 31.54, 31.51 [q, $C(CH_3)_3$], 30.7, 30.3, 30.2 (t, $ArCH_2Ar$). **34:** Yield 23%; mp 262-263°C. Anal. calcd for $C_{80}H_{69}O_8F_{15}\cdot 2H_2O$: C, 65.23; H, 4.62. Found: C, 64.95; H, 4.97. Karl Fischer: H_2O, 2.72. $C_{80}H_{69}O_8F_{15}\cdot 2H_2O$ requires H_2O, 2.42. MS (FAB): *m/z* = 1443.4 [$(M+H)^+$, 1443.5]. ^1H NMR (250 MHz, $CDCl_3$): δ = 9.50 (s, 2 H, CHO), 7.3-7.0 (m, 10 H, ArH), 6.8-6.5 (m, 3 H, ArH), 5.02 (s, 4 H, OCH_2), 4.96 (s, 2 H, OCH_2), 4.6-3.5 (br s, 12 H, $ArCH_2Ar$), 2.81 (s, 3 H OCH_3), 2.56 (s, 6 H, OCH_3), 1.32 [s, 27 H, $C(CH_3)_3$].

11,17,29,35-Tetra-tert-butyl-5,23-diformyl-37,38,40,41-tetrakis[2-(2-methoxyethoxy)ethoxy]calix[6]arene-39,42-diol (36). The residue was purified by column chromatography (THF/hexane, 1:1.4). Yield 94%; mp 164-166°C. Anal. calcd for $C_{80}H_{108}O_{16}$: C, 72.48; H, 8.20. Found: C, 72.38; H, 8.28. MS (CI): *m/z*: 1325.6 [$(M+H)^+$, 1325.8]. ^1H NMR (400 MHz, $CDCl_3$): δ = 9.69 (s, 2 H, CHO), 8.57 (br s, 2 H, OH), 7.50 (br s, 4 H, ArH), 7.1-6.8 (br s, 8 H, ArH), 4.2-3.30 (br s, 44 H, $ArCH_2Ar$, OCH_2), 3.27 (s, 12 H, OCH_3), 1.04 [s, 36 H, $C(CH_3)_3$]; ^{13}C NMR (25 MHz, $CDCl_3$): δ = 191.3 (d, CHO), 158.9, 151.7, 147.0, 133.0, 131.9 (s, Ar), 130.9 (d, ArH), 128.8, 128.2 (s, Ar), 126.6, 125.9 (d, ArH), 72.6, 71.9, 70.4, 70.0 (t, OCH_2), 59.0 (q, OCH_3), 34.1 [s, $C(CH_3)_3$], 31.3 [q, $C(CH_3)_3$], 30.0 (t, $ArCH_2Ar$).

General Procedure for Formylation of Calix[6]arenes via HMTA in CF_3COOH

A mixture of calixarene (0.12 mmol) in 1.5 ml of CF_3COOH was added of HMTA and was refluxed for 17-36 h (Table 3). The reaction mixture was poured into 10 ml of ice-water and extracted twice with CH_2Cl_2 (2x10 ml). The organic layer was washed with H_2O (3x10 ml), dried ($MgSO_4$) and evaporated to dryness.

5,17,29-Tri-tert-butyl-11,23,35-triformyl-38,40,42-trimethoxycalix[6]arene-37,39,41-triol (28). Purified by preparative TLC (THF/hexane, 1:1.4). Yield 18%; mp 151-153°C. Anal. calcd for $C_{60}H_{66}O_9$: C, 77.40; H, 7.14. Found: C, 77.43; H, 7.21. MS (CI): *m/z*: 931.8 [$(M+H)^+$, 931.5]. ^1H NMR (100 MHz, $CDCl_3$): δ = 9.79 (s, 3 H, CHO), 8.02 (s, 3 H, OH), 7.62 (s, 6 H, ArH), 6.96 (s, 6 H, ArH), 3.94 (s, 12 H, $ArCH_2Ar$), 3.56 (s, 9 H, OCH_3), 1.08 [s, 27 H, $C(CH_3)_3$].

5,17,29-Tri-tert-butyl-11,23,35-triformyl-37,38,39,40,41,42-hexamethoxycalix[6]arene (32). The residue was crystallized from cold MeOH. Yield 74%; 168-170°C. Anal. calcd for $C_{63}H_{72}O_9$: C, 77.75; H, 7.45. Found: C, 77.67; H, 7.51. MS (CI): *m/z* = 973.3 [$(M+H)^+$, 973.5]. ^1H NMR (300 MHz, $CDCl_3$): δ = 9.74 (s, 3 H, CHO), 7.47 (s, 6 H, ArH), 6.99 (s, 6 H, ArH), 3.95 (s, 12 H, $ArCH_2Ar$), 3.30 (s, 9 H, OCH_3), 3.14 (s, 9 H, OCH_3), 1.19 [s, 27 H, $C(CH_3)_3$]; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 191.6 (d, CHO), 161.8, 154.1, 146.5, 135.7, 132.8, 131.9 (s, Ar), 130.5, 126.3 (d, ArH), 60.3, 60.1 (q, OCH_3), 34.2 [s, $C(CH_3)_3$], 31.4 [q, $C(CH_3)_3$], 30.6 (t, $ArCH_2Ar$).

11,17,29,35-Tetra-tert-butyl-5,23-diformyl-37,38,40,41-tetrakis[2-(2-methoxyethoxy)ethoxy]calix[6]arene-39,42-diol (36). The product was purified by column chromatography (THF/hexane, 1:1.4) in 44% yield, and showed the same physical and spectroscopic data as previously reported.

5,17,29-Tri-tert-butyl-37,39,41-tris(pentafluorobenzyloxy)-11,23,35-tris(hydroxymethyl)-38,40,42-trimethoxycalix[6]arene (37)

To a solution of compound **30** (41 mg, 28 μmol) in dry THF (7 ml) and MeOH (1 ml) was added $NaBH_4$

(16 mg, 0.42 mmol) and the mixture was refluxed for 2.5 h. After cooling, the reaction was quenched with a few drops of glacial acetic acid. CH_2Cl_2 was added and the organic layer was washed with 1 N NaOH (2x25 ml), brine (1x25 ml) and dried over $MgSO_4$. Yield 41 mg (100%); mp > 300°C (dec.). Anal. calcd for $C_{81}H_{75}F_{15}O_9CH_2Cl_2$: C, 63.04; H, 4.97. Found: C, 63.11; H, 4.71. MS (FAB): *m/z* = 1295.0 [$(M\text{-}CH_2C_6F_5)^+$, 1295.5]. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.14 (s, 6H, ArH), 6.5-6.2 (br s, 6H, ArH), 4.96 (s, 6H, OCH_2), 4.5-4.2 (m, 9H, $ArCH_2Ar$, OH), 4.01 (s, 6H, CH_2OH), 3.5 (d, 6H, *J* = 14 Hz, $ArCH_2Ar$), 3.0-2.8 (s, 9H, OCH_3), 1.23 [s, 27H, $C(CH_3)_3$]; ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 154.3, 154.1, 152.3, 147.1, 146.9, 137.5, 134.5, 132.7, 128.0, 127.9, 126.1, 126.0 (s, Ar), 77.2 (t, CH_2OH), 64.6 (t, OCH_2), 60.1 (q, OCH_3), 34.2 [s, $C(CH_3)_3$], 31.5 [q, $C(CH_3)_3$], 30.8 (t, $ArCH_2Ar$).

5,17,29-Tri-tert-butyl-11,23,35-tris(1,1-dimethoxymethyl)-37,38,39,40,41,42-hexamethoxycalix[6]arene (38)

To a sample of calixarene **32** (0.10 g, 0.103 mmol), dissolved in 5 ml of dry methanol was added a drop of CF_3COOH and heated at reflux for 2 h. Upon cooling product **38** precipitated as white crystals which were filtered. Yield 92 mg (81%); mp 199-201°C. Anal. calcd for $C_{69}H_{90}O_{12}$: C, 74.57; H, 8.15. Found: C, 74.46; H, 8.21. MS (CI): *m/z* = 1034.8 [$(M\text{-}CH(OCH_3)_2)^+$, 1035.6). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.17 (s, 6H, ArH), 6.87 (s, 6H, ArH), 5.30 [s, 3H, $CH(OCH_3)_2$], 3.94 (s, 12H, $ArCH_2Ar$), 3.34 (s, 9H, OCH_3), 3.26 [s, 18H, $CH(OCH_3)_2$], 2.82 (s, 9H, OCH_3), 1.04 [s, 27H, $C(CH_3)_3$]; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.5, 153.4, 145.6, 134.1, 133.3, 132.5 (s, Ar), 127.9, 125.0 (d, ArH), 102.8 [d, $CH(OCH_3)_3$], 59.9 (q, OCH_3), 52.3 [q, $CH(OCH_3)_3$], 33.9 [s, $C(CH_3)_3$], 31.1 [q, $C(CH_3)_3$], 30.3 (t, $ArCH_2Ar$).

5,23-Dicarboxy-11,17,29,35-tetra-tert-butyl-37,38,40,41-tetrakis[2-(2-methoxyethoxy)ethoxy]calix[6]arene-39,42-diol (39)

To a solution of **36** (115 mg, 0.09 mmol) in a mixture of acetone (10 ml) and $CHCl_3$ (10 ml) at 0°C were added sulfamic acid (36 mg, 0.37 mmol) and $NaClO_2$ (28 mg, 0.31 mmol) dissolved in a small quantity of H_2O. After stirring for 16 h the solvent was evaporated under reduced pressure and the residue was taken up in CH_2Cl_2 (50 ml). The organic layer was washed with 1N HCl (30 ml) and H_2O (4x30 ml). After evaporation of the solvent under reduced pressure the crude solid was triturated with acetone to give pure **39**. Yield 115 mg (97%); mp 274-276°C. Anal. calcd for $C_{80}H_{108}O_{18}$: C, 70.78; H, 8.01. Found: C, 70.67; H, 8.10. MS (CI): *m/z* = 1357.5 (M^+, 1357.8). IR (KBr): 3340 cm^{-1} (OH), 3500-2500 cm^{-1} (COOH), 1660 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.37 (br s, 2H, OH), 7.67 (s, 4H, ArH), 7.1-6.7 (br s, 8H, ArH), 4.1-3.4 (br s, 44H, $ArCH_2Ar$, OCH_2), 3.29 (s, 12H, OCH_3), 0.96 [s, 36H, $C(CH_3)_3$]; ^{13}C NMR (25 MHz, $CDCl_3/CD_3OD$ = 1/1): δ = 169.7 (s, COOH), 157.8, 152.2, 147.4, 133.6, 132.7 (s, Ar), 131.3 (d, ArH), 127.6 (s, Ar), 127.1, 126.4 (d, ArH), 121.8 (s, Ar), 73.1, 72.4, 70.7, 70.5 (t, OCH_2), 59.0 (q, OCH_3), 34.5 [s, $C(CH_3)_3$], 31.6 [q, $C(CH_3)_3$], 30.8 (t, $ArCH_2Ar$).

11,23,35-Tribromo-5,17,29-tri-tert-butyl-38,40,42-trimethoxycalix[6]arene-37,39,41-triol (40)

Method A: A suspension of calixarene **27** (200 mg, 0.24 mmol), NBS (192 mg, 1.08 mmol) in 2-butanone (5 ml) was stirred under argon at r.t. for 24 h. The mixture was extracted with CH_2Cl_2, washed with $Na_2S_2O_5$ (10 ml), brine (3 x25 ml) and dried (Na_2SO_4). The solvent was eliminated and the residue was triturated with hexane to afford **40**. Yield 188 mg (70%).

Method B: To a stirred solution of **27** (600 mg, 0.71 mmol) in ethylacetate (50 ml), NBS (770 mg, 4.33 mmol) was added. The mixture was stirred for 18 h at room temperature under nitrogen. After quenching with 10% aq $NaHSO_3$ (50 ml) the organic layer was washed with 1N HCl (1x30 ml) and H_2O until neutral pH then dried ($MgSO_4$). Evaporation of the solvent under reduced pressure afforded a crude solid that gave **40** upon trituration with CH_2Cl_2/petroleum ether. Yield 370 mg (48%); mp 219-220°C. Anal. calcd for $C_{57}H_{63}Br_3O_6$: C, 63.17; H, 5.86. Found: C, 63.07; H, 5.99. MS (FAB): *m/z* = 1084.2 [$(M+4)^+$, 1084.2)]. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.14 (s, 6H, ArH), 6.96 (s, 3H, OH), 6.94 (s, 6H, ArH), 3.85 (s, 12H, $ArCH_2Ar$), 3.50 (s, 9H, OCH_3), 1.12 [s, 27H, $C(CH_3)_3$]; ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 152.1, 151.4, 147.7, 131.6 (s, Ar), 131.3 (d, ArH), 129.3 (s, Ar), 126.0 (d, ArH), 111.7 (s, Ar), 61.5 (q, OCH_3), 34.2 [s, $C(CH_3)_3$], 31.3 [q, $C(CH_3)_3$], 30.9 (t, $ArCH_2Ar$).

11,23,35-Tribromo-5,17,29-tri-tert-butyl-37,38,39,40,41,42-hexamethoxycalix[6]arene (41)

Method A: To a stirred slurry of **40** (400 mg, 0.37 mmol) and Cs_2CO_3 (720 mg, 2.21 mmol) in dry DMF (40 ml) MeI (0.28 ml, 4.50 mmol) was added. The reaction mixture was heated at 70°C for 16 h, the solvent was distilled off under reduced pressure and the residue was taken up in CH_2Cl_2 (60 ml). The organic solution was successively washed with 1N HCl (1x30 ml), H_2O (3x30 ml) and dried ($MgSO_4$). Evaporation of the solvent afforded the product **41**. An analytical sample was recrystallized from MeOH. Yield 291 mg (70%).

Method B: To a stirred slurry of NaH (60% oil dispersion, 100 mg, 2.49 mmol) in dry THF (20 ml) was added under argon a solution of calix[6]arene **40** (300 mg, 0.28 mmol) in dry THF (20 ml). The mixture was heated at reflux for 48 h, adding MeI (0.2 ml, 3.21 mmol) as soon as the reflux began. After cooling, 10% HCl (10 ml) was added, and the reaction mixture was stirred for 1h. The solvent was removed and the residue was extracted with Et_2O (3x50 ml), dried (Na_2SO_4), and evaporated to give a solid, which was purified by trituration in hexane. Yield 260 mg (83%); mp 186-188°C. Anal. calcd for $C_{60}H_{69}Br_3O_6$: C, 64.01; H, 6.18. Found: C, 64.12; H, 6.25. MS (FAB): *m/z*: 1125.9 [$(M+4)^+$, 1126.5]. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.03 (s, 12H, ArH), 3.89 (s, 12H, $ArCH_2Ar$), 3.30 (s, 9H, OCH_3), 3.07 (s, 9H, OCH_3), 1.22 [s, 27H, $C(CH_3)_3$]; ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 155.1, 154.1, 146.3 (s, Ar), 137.0 (d, ArH), 132.9, 131.2 (s, Ar), 126.5 (d, ArH), 116.4 (s, Ar), 60.2, 60.1 (q, OCH_3), 34.2 [s, $C(CH_3)_3$], 31.5 [q, $C(CH_3)_3$], 30.5 (t, $ArCH_2Ar$).

11,23,35-Tribromo-5,17,29-tri-tert-butyl-38,40,42-trimethoxy-37,39,41-tris(4-methylbenzyloxy)calix[6]-arene (42)

A suspension of calixarene **40** (80 mg, 0.07 mmol), Cs_2CO_3 (144 mg, 0.44 mmol) and of 4-methylbenzyl bromide (82 mg, 0.44 mmol) in dry DMF (10 ml) was heated at 80°C for 18 h. The mixture was extracted with Et_2O (50 ml), washed with 10% HCl (2x20 ml), brine (25 ml), dried ($MgSO_4$) and the solvent evaporated. The residue was crystallized in $CHCl_3$/MeOH to afford **42**. Yield 90 mg (87%); mp 122°C. Anal. calcd for $C_{81}H_{87}Br_3O_6$·MeOH: C, 68.96; H, 6.42. Found: C, 68.90; H, 6.34. MS (FAB): *m/z* = 1393.04 (M^+, 1392.40). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.43 and 7.08 (AA'BB' system, 12H, $ArCH_3$), 7.03 (s, 6H, ArH), 6.69 (br s, 6H, ArH), 4.72 (br s, 6H, OCH_2ArCH_3), 4.3-3.9 (br s, 6H, $ArCH_2Ar$), 3.7-3.2 (br s, 6H, $ArCH_2Ar$), 2.68 (s, 9H, OCH_3), 2.28 (s, 9H, $ArCH_3$), 1.20 [s, 27H, $C(CH_3)_3$]; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 154.6, 153.3, 146.3, 137.7, 137.0, 134.3, 132.6 (s, Ar), 130.2, 129.1, 128.2, 127.5 (d, ArH), 116.9 (s, Ar), 74.7 (t, OCH_2ArCH_3), 60.1 (q, OCH_3), 34.2 [s, $C(CH_3)_3$], 31.5 [q, $C(CH_3)_3$], 31.0 (t, $ArCH_2Ar$), 21.3 (q, $ArCH_3$).

5,23-Dibromo-11,17,29,35-tetra-tert-butyl-37,38,40,41-tetrakis[2-(2-methoxyethoxy)ethoxy]calix[6]arene-39,42-diol (43)

To a stirred solution of **35** (190 mg, 0.15 mmol) in ethyl acetate (10 ml) was added NBS (85 mg, 0.48 mmol). The mixture was stirred for 7 h at room temperature under nitrogen. After quenching with 10% aq $NaHSO_3$ (10 ml), the separated organic layer was washed with H_2O until neutral pH and dried ($MgSO_4$). Evaporation of the solvent afforded a crude product that was triturated with MeOH to give compound **43**. Yield 73 mg (34%); mp 218-220°C. Anal. calcd for $C_{78}H_{106}Br_2O_{14}$: C, 65.63; H, 7.49. Found: C, 65.56; H, 7.54. MS (CI): *m/z* = 1428.3 [$(M+4)^+$, 1428.6]. IR (KBr): 3400 cm^{-1} (OH); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.24 (d, *J* = 2.4 Hz, 4H, ArH), 7.00 (d, *J* = 2.4 Hz, 4H, ArH), 6.63 (s, 4H, ArH), 5.48 (s, 2H, OH), 4.14 (ddd, *J* = 10.3, 4.2, 4.2 Hz, 4H, ArOC*H*HCH$_2$), 4.08 (d, *J* = 15.2 Hz, 4H, ArC*H*HAr), 4.06 (s, 4H, ArCH$_2$Ar), 3.82 (ddd, *J* = 10.3, 4.2, 7.4 Hz, 4H, ArOCH*H*CH$_2$), 3.76 (d, *J* = 15.2 Hz, 4H, ArCH*H*Ar), 3.58 (ddd, *J* = 11.8, 4.2, 4.2 Hz, 4H, OCH$_2$C*H*H), 3.38 (ddd, *J* = 11.8, 4.2, 7.4 Hz, 4H, ArOCH$_2$CH*H*), 3.35-3.25 (m, 12H, OCH$_2$), 3.25-3.20 (m, 4H, OCH$_2$), 3.21 (s, 12H, OCH$_3$), 1.27 [s, 36H, C(CH$_3$)$_3$]; ^{13}C NMR (25 MHz, $CDCl_3$): δ = 154.3, 148.3, 146.2, 133.6, 133.1, 130.3 (s, Ar), 127.4, 127.2 (d, ArH), 126.2 (s, ArBr), 124.2 (d, ArH), 71.8, 71.6, 70.4, 70.1 (t, OCH$_2$), 58.9 (q, OCH$_3$), 39.25 (t, ArCH$_2$Ar), 34.2 [s, *C*(CH$_3$)$_3$], 31.7 [q, C(*C*H$_3$)$_3$], 30.7 (t, ArCH$_2$Ar).

5,17,29-Tri-tert-butyl-11,23,35-tricyano-37,38,39,40,41,42-hexamethoxycalix[6]arene (44)

A mixture of **41** (90 mg, 0.08 mmol) and CuCN (4.5 mg, 0.50 mmol) in 3 ml of N-methylpyrrolidinone (NMP) was heated for 15 h under argon at 200°C. After cooling the reaction mixture to 100°C, a solution of 8.2 mg of $FeCl_3 H_2O$ and 4ml of 3N HCl was slowly added. Stirring was continued until the reaction mixture reached room temperature. The precipitate was filtered on a Buchner funnel, washed with H_2O and purified by column chromatography (silica gel, hexane/THF, 8:2) to give **44**. Yield 55 mg (78%); mp 256-258°C. Anal. calcd for $C_{63}H_{69}N_3O_6$: C, 78.48; H, 7.21. Found: C, 78.39; H, 7.27. MS (FAB): *m/z*: 964.6 [$(M+H)^+$, 964.5]. IR (KBr): 2220 cm^{-1} (CN); ^1H NMR (250 MHz, $CDCl_3$): δ = 7.22 (s, 6H, ArH), 7.00 (s, 6H, ArH), 3.92 (s, 12H, ArCH$_2$Ar), 3.45 (s, 9H, OCH$_3$), 3.07 (s, 9H, OCH$_3$), 1.21 [s, 27H, C(CH$_3$)$_3$]; ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 159.8, 154.1, 146.7, 136.5 (s, Ar), 132.5, 126.6 (d, ArH), 119.2 (s, CN), 107.1 (s, ArCN), 60.6, 60.1 (q, OCH$_3$), 34.2 [s, C(CH$_3$)$_3$], 31.4 [q, C(CH$_3$)$_3$], 30.9 (t, ArCH$_2$Ar).

5,17,29-Tri-tert-butyl-11,23,35-trichloromethyl-37,38,39,40,41,42-hexamethoxycalix[6]arene (45)

A mixture of calixarene **31** (0.140 g, 0.16 mmol), chlorotrimethylsilane (0.3 g, 2.4 mmol) and paraformaldeyde (73 mg, 2.4 mmol) in 10 ml of dry CH_2Cl_2 was cooled at -15°C. A solution of $SnCl_4$ (0.28 ml, 2.4 mmol) in 4 ml of CH_2Cl_2 was slowly added. After 1.5 h at -15°C the reaction mixture was stirred at room temperature for 3 h. The reaction mixture was poured into 15 ml of ice/water and extracted with 2x20 ml of CH_2Cl_2. The combined organic extracts were carefully washed with water to neutral pH and dried (Na_2SO_4). The product was crystallized from cold methanol. Yield 135 mg (81%); mp 150-152°C. Anal. calcd for $C_{63}H_{75}Cl_3O_6$: C, 73.14; H, 7.31. Found: C, 73.05; H, 7.40. MS (CI): *m/z* = 1034.8 [$(M+2)^+$, 1034.6]. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.00 (s, 6H, ArH), 6.83 (s, 6H, ArH), 4.24 (s, 6H, CH_2Cl), 3.92 (s, 12H, ArCH$_2$Ar), 3.40 (s, 9H, OCH$_3$), 3.04 (s, 9H, OCH$_3$), 1.15 [s, 27H, C(CH$_3$)$_3$]; ^{13}C NMR (75 MHz, $CDCl_3$): δ =

154.0, 146.4, 135.0, 133.0, 132.6 (s, Ar), 128.8, 126.5 (d, ArH), 60.3, 60.2 (q, OCH_3), 46.5 (t, CH_2Cl), 34.1 [s, $C(CH_3)_3$], 31.4 [q, $C(CH_3)_3$], 30.6 (t, $ArCH_2Ar$).

5,17,29-Tri-tert-butyl-38,40,42-trimethoxy-37,39,41-tris(2-propenyloxy)calix[6]arene (46)

To a stirred slurry of **27** (400 mg, 0.47 mmol) and Cs_2CO_3 (930 mg, 2.85 mmol) in dry DMF (80 ml) allyl bromide (0.25 ml, 2.85 mmol) was added at 70°C. After stirring for 18 h the solvent was evaporated under reduced pressure and the residue taken up with CH_2Cl_2 (50 ml). The organic layer was washed with 1N HCl (3x30 ml), H_2O (1x30 ml), brine (1x30 ml) and dried ($MgSO_4$). Evaporation of the solvent afforded pure product **46**. Yield 380 mg (83%); mp 96-98°C. Anal. calcd for $C_{66}H_{78}O_6$: C, 81.95; H, 8.13. Found: C, 82.07; H, 8.27. MS (FAB): *m/z*: 966.7 (M^+, 966.6). IR (KBr): 1647 cm^{-1} (C=C); ^1H NMR (250 MHz, $CDCl_3$): δ = 7.14 (s, 6H, ArH), 6.9-6.6 (m, 9H, ArH), 6.0-5.8 (m, 3H, C*H*=CH_2), 5.19 (d, *J* = 17 Hz, 3H, CH=C*H*H), 5.04 (d, *J* = 10 Hz, 3H, CH=CH*H*), 4.10 (d, *J* = 3 Hz, 6H, OCH_2CH=CH_2), 3.93 (s, 12H, $ArCH_2Ar$), 2.79 (s, 9H, OCH_3), 1.25 [s, 27H, $C(CH_3)_3$]; ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 154.6, 154.3, 145.9 (s, Ar), 134.8 (d, *C*H=CH_2), 134.0, 133.3 (s, Ar), 128.0, 126.9, 123.5 (d, ArH), 117.1 (t, CH=*C*H_2), 73.4 (t, OCH_2CH=CH_2), 60.1 (q, OCH_3), 34.2 [s, $C(CH_3)_3$], 31.5 [q, $C(CH_3)_3$], 30.7 (t, $ArCH_2Ar$).

5,17,29-Tri-tert-butyl-38,40,42-trimethoxy-11,23,35-tris(2-propenyloxy)calix[6]arene-37,39,41-triol (47)

A solution of **46** (480 mg, 0.50 mmol) in N,N-dimethylaniline (15 ml) was refluxed for 2h. The cooled reaction mixture was poured into a mixture of 12N HCl/ice (20 ml). The aqueous layer was extracted with CH_2Cl_2 (2x20 ml), washed with 1N HCl (1x20 ml), H_2O (3x30 ml), brine (1x20 ml) and dried ($MgSO_4$). After evaporation of the solvent the crude product was triturated with petroleum ether to afford pure **47**. Yield 200 mg (42%); mp 219-221°C. Anal. calcd for $C_{66}H_{78}O_6$: C, 81.95; H, 8.13. Found: C, 82.05; H, 8.21. MS (FAB): *m/z*: 966.2 (M^+, 966.6). IR (KBr): 1638 cm^{-1} (C=C); ^1H NMR (250 MHz, $CDCl_3$): δ = 6.91 (s, 6H, ArH), 6.83 (s, 6H, ArH), 6.74 (s, 3H, OH), 6.0-5.85 (m, 3H, C*H*=CH_2), 5.1-5.0 (m, 3H, CH=C*H*H), 4.95-4.90 (m, 3H, CH=CH*H*), 3.87 (s, 12H, $ArCH_2Ar$), 3.50 (s, 9H, OCH_3), 3.23 (d, *J* = 6 Hz, 6H, $ArCH_2$CH=CH_2), 1.05 [s, 27H, $C(CH_3)_3$]; ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 152.3, 150.4, 147.0 (s, Ar), 138.3 (d, *C*H=CH_2), 132.3, 131.0, 129.0 (s, Ar), 127.3, 125.8 (d, ArH), 115.0 (t, CH=*C*H_2), 61.4 (q, OCH_3), 39.4 (t, $ArCH_2$CH=CH_2), 34.1 [s, $C(CH_3)_3$], 31.2 [q, $C(CH_3)_3$], 31.0 (t, $ArCH_2Ar$).

5,17,29-Tri-tert-butyl-38,40,42-trimethoxycalix[6]arene-11,23,35,37,39,41-hexaone (48)

To a solution of **27** (230 mg, 0.27 mmol) in $CHCl_3$ (27 ml) was added $Tl(NO_3)_3 3H_2O$ (734 mg, 1.64 mmol) dissolved in a mixture of EtOH (90 ml) and MeOH (30ml) at room temperature. After stirring for 2h the reaction was quenched with 1N HCl (50ml) and the aqueous layer extracted with CH_2Cl_2 (2x60 ml). The organic phase was washed with H_2O until neutral pH and dried (Na_2SO_4). After evaporation of the solvent the crude product was purified by preparative plates (silica gel, hexane/CH_2Cl_2 1/3) followed by trituration with n-hexane. Yield 59 mg (24%); mp 200-202°C. Anal. calcd for $C_{57}H_{60}O_9$: C, 77.00; H, 6.80. Found: C, 76.89; H, 6.88. MS (CI): *m/z*: 890.0 [$(M+H)^+$, 889.4]. IR (KBr): 1670 cm^{-1}(C=O), 1620 cm^{-1}(C=C); ^1H NMR (100 MHz,

$CDCl_3$): δ = 7.07 (s, 6H, ArH), 5.98 (s, 6H, QH), 3.89 (s, 12H, $ArCH_2Ar$), 3.35 (s, 9H, OCH_3), 1.28 [s, 27H, $C(CH_3)_3$]; ^{13}C NMR (25 MHz, $CDCl_3$): δ = 187.3, 186.6 (s, C=O), 176.2, 154.1, 148.6 (s, Ar), 132.3 (d, ArH), 130.7 (s, Ar), 127.7 (d, ArH), 60.5 (q, OCH_3), 34.3 [s, $C(CH_3)_3$], 31.5 [q, $C(CH_3)_3$], 30.6 (t, $ArCH_2Ar$).

37,38,40,41-Tetrabenzoyloxy-11,17,29,35-tetra-tert-butylcalix[6]arene-5,23,39,42-tetrone (50)

To a stirred solution of 38,39,41,42-tetrabenzoyloxy-5,11,17,23,29,35-hexa-*tert*-butylcalix[6]arene-37,40-diol **49** (200 mg, 0.14 mmol) in TFA (7 ml) at room temperature, was added $Tl(CF_3CO_2)_3$ (650 mg, 1.19 mmol). After 24 h, the solvent was evaporated and the residue was partitioned in CH_2Cl_2 and H_2O. The organic layer was dried (Na_2SO_4) and the solvent was eliminated.The residue was triturated with MeOH and the resulting solid was filtered and recrystallized ($CHCl_3$/MeOH) to give **50**. Yield 150 mg (80%); mp 260°C (dec.). Anal. calcd for $C_{86}H_{80}O_{12}$·2 H_2O: C, 76.99; H, 6.31. Found: C, 76.79; H, 5.96. MS (FAB): *m/z* = 1340.6 (M^+, 1305.5). ^1H NMR (200 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 8.4 Hz, 8H, ArH), 7.50 (t, *J* = 8.4 Hz, 4H, ArH), 7.31 (t, *J* = 8.4 Hz, 8H, ArH), 7.04 (d, *J* = 2.1 Hz, 4H, ArH), 6.80 (d, *J* = 2.1 Hz, 4H, ArH), 5.79 (s, 4H, QH), 4.17 (s, 4H, $ArCH_2Ar$), 3.70 and 3.48 (AB system, 8H), 0.84 [s, 36H, $C(CH_3)_3$]; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 188.0, 186.5 (s, CO), 163.8 (s, OCOAr), 150.0, 149.5, 145.7 (s, Ar), 133.4 (d, ArH), 133.1 (s, Ar), 131.9, 130.4, 128.6 (d, ArH), 128.5, 128.2 (s, Ar), 127.1, 126.7 (d, ArH), 39.4 (t, $ArCH_2Ar$), 34.0 [s, $C(CH_3)_3$], 30.7 [q, $C(CH_3)_3$], 30.2 (t, $ArCH_2Ar$).

ACKNOWLEDGEMENTS

This work was partially supported by M.U.R.S.T. (Ministero dell'Università e della Ricerca Scientifica e Tecnologica) and by the Human Capital and Mobility Programme (Contracts n° CHRX-CT93-0145 and n° CHRX-CT94-0484).

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(*Received in UK* 4 *August* 1995; *revised* 21 *September* 1995; *accepted* 28 *September* 1995)