Lower-Rim-Substituted *tert*-Butylcalix[4]arenes; Part IX: One-Pot Synthesis of Calix[4]arene-Hydroxamates and Calix[4]arene-Amides

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Abstract: A simple method for selective acylation of protected and unprotected hydroxylamines with bis- and tetrakis-substituted *p-tert*-butylcalix[4]arene-acids through amide bond formation via mixed anhydrides is presented. The first crystal structure of calix-hydroxamate **1** is presented.

Key words: calix[4]arene-hydroxamates, calix[4]arene-amides, synthesis, mixed anhydride method

Calix[4]arenes can be treated as a scaffold for building a variety of new receptors, substituted at the lower or upper rim. There are a few reports on the synthesis and application of calix[4]arene-hydroxamates. In 1990 and 1991 Shinkai and Nagasaki presented the first example of a *p-tert*-butylcalix[n]arene (n = 6, 4) hydroxamates as ligands with remarkable extraction properties for uranyl ions (n = 6).[1a,1b] The authors acylated *O*-benzylhydroxylamine via calixarene-acid chlorides (first step), followed by the catalytic hydrogenation, which led to the tetrakis-substituted calix[4]arene-hydroxamic acids.[1b,2] The preparation of such structures in reasonable yield is not simple. McKervey et al. proposed another synthesis, the aminolysis of the calix[4]arene-tetraesters.[3,4] This reaction was also used for calix[4]arene-amides.[5] Shanzer et al. proposed an alternative method using calix[4]arene as a starting material and bromoacetate derivatives of protected hydroxylamine.[6]

Calix[4]arenes with hydroxamate moieties showed unusually high extraction properties towards Fe(III), Cu(II) and Pb(II) at pH 5.4 and at pH 2.2 high selectivity for iron(III).[7] The extraction studies were also reported by other researchers.[8] The spectacular complexing ability of calix-hydroxamates is the reason for further investigation and for improving their synthesis.

Here, we present a convenient, efficient, one-pot synthesis of known and new compounds, calix[4]arene-hydroxamates **1**–**9** and -amides **10**, **11** (see Table 1). Effective and selective acylation of the amine nitrogen was achieved via mixed anhydrides method. Compounds **1**–**11** were obtained by procedure, shown in the Scheme 1, using different calix[4]arene substrates **II**,[9,10] **V** or **VII** as acylating reagents (see experimental).

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The reaction of acylation produces tetrakis- or bis-substituted calix[4]-hydroxamates. The excess of unreacted hydroxylamine can be separated from the reaction mixture by washing the crude products dissolved in dichloromethane with water and 0.1 M hydrochloric acid. Further product purification can be achieved by recrystallization or, in the case of compounds **8** and **9**, by column chromatography.

The proposed method has many advantages: it was applied by us for the direct synthesis of calix[4]-hydroxamates with protected or unprotected hydroxylamine moieties (Figure 1). The acylation reaction of O-protected hydroxylamines and amines is rather obvious and the products are obtained in very good yield. The situation becomes more complicated in case of unprotected hydroxylamines, where O- and N-acylation are possible. We overcame the problem of mixed substitution by lowering the temperature to –10 °C. In such condition selective N-substitution takes place.

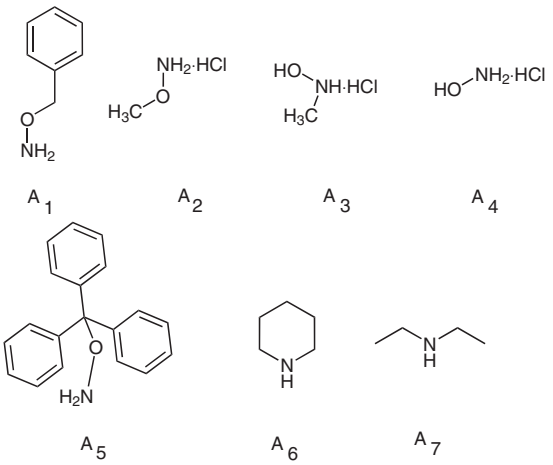
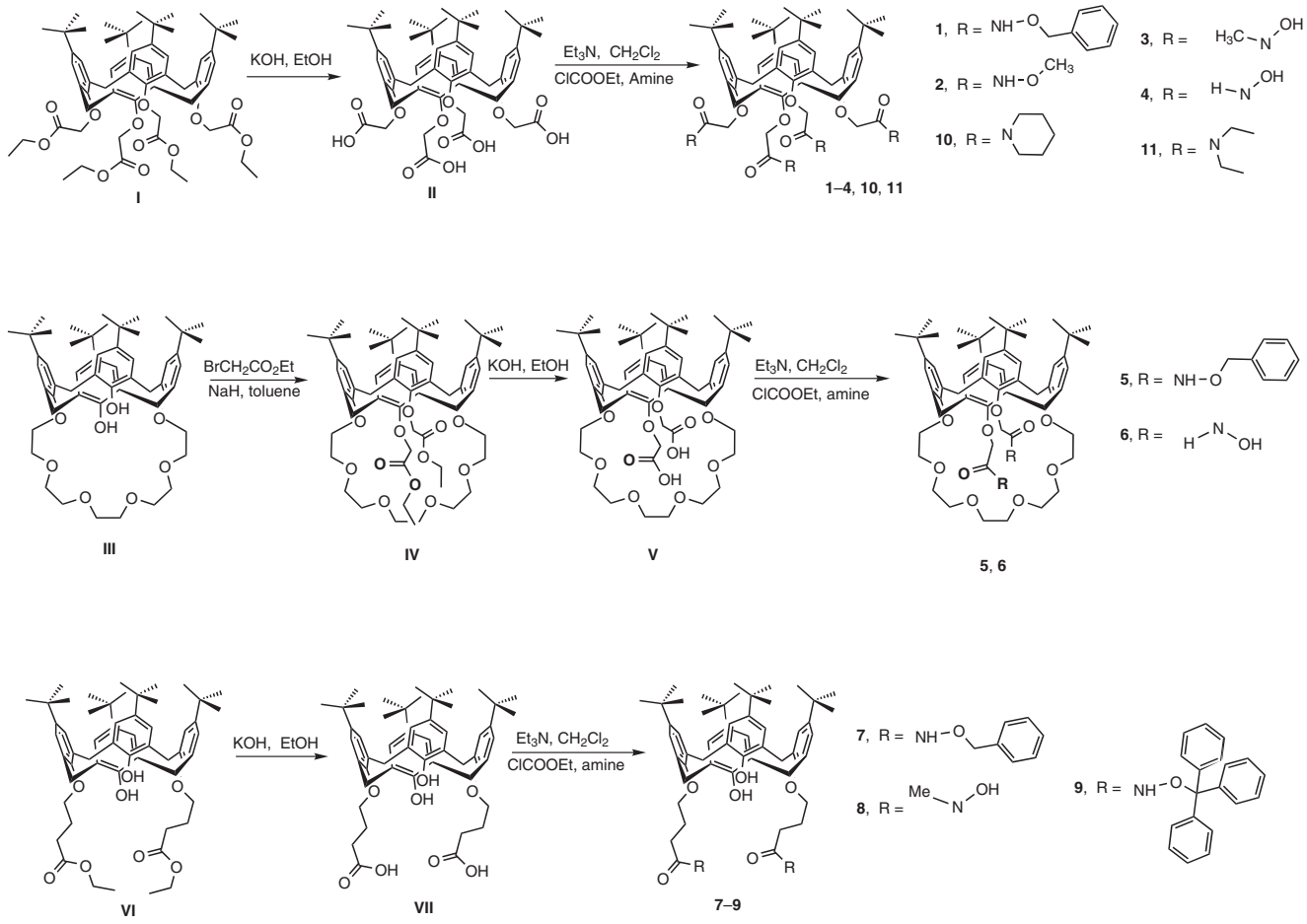


Figure 1 Hydroxylamines and amines used in the reactions

Acid chlorides are too reactive for selective acylation, giving mixture of calix[4]arene-esters and -amides (TLC). Our attempts to convert ethyl esters of calix[4]arene to calix-amides in THF/MeOH using hydroxylamine failed to give the desired product with a reasonable yield. Aminolysis is a very effective synthetic route with amines but with hydroxylamines a mixture of products is possible.[11]

Ethyl chloroformate provided almost quantitative yield and pure, crystalline products (see Table 1). The low steric barrier of ethyl formate enable the tetrasubstitution of



Scheme 1 Synthesis of compounds **1**–**11**

calix[4]arene. Other reagents like EEDQ (2-ethoxy-*N*-ethoxycarbonyl-1,2-dihydroquinoline)[12] or DCC (*N*,*N*′-dicyclohexylcarbodiimide) in our experience limited the yield of the tetra-derivatives of calix[4]arenes. The only disadvantage of the procedure described here is the fact that an excess of hydroxylamine hydrochloride used in the reactions can be complexed by the product calix[4]arene-hydroxamate. This was revealed in some cases by elemental analysis of the obtained products (**2**, **3**, **4**, **6** and **9**). Longer and careful extraction with water and HCl solution allows isolation of pure compounds.

In order to show the generality of the method we synthesized two known calix[4]arene-amides (Scheme 1, compounds **10**[13] and **11**[14]). The yield of the reactions (over 80%) was much better than published before.[13,14] The structure and purity of the amides was confirmed by ^{1}H NMR, IR, TLC and melting point comparison. All synthesized compounds **1**–**11** were obtained in the *cone* conformation.

We present here the first example of crystal structure of calix-hydroxamate **1**. X-ray analysis of the single crystals proved that compound 25,26,27,28-tetrakis(*N*-benzyloxycarbamoylmethoxy)-*p*-*tert*-butylcalix[4]arene (**1**) is in the *pinched cone* conformation (Figure 2). Two of the phenyl rings A and C are almost parallel to each other, while rings B and D are almost perpendicular giving an open cavity among the rings. Two of the calixarene units are additionally bound by two intermolecular N–H···O bonds forming a kind of dimer (Figure 3).

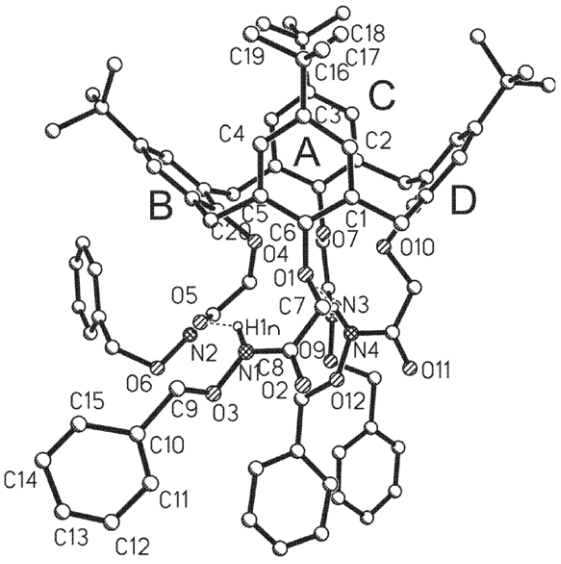


Figure 2 Molecular structure of **1**

Table 1 Protected and Unprotected Calix[4]-Hydroxyamides **1**–**9** and Amides **10**, **11**

Calix Substrate	Reaction Temp (°C)	Amine Reagent (Equiv)	Product	Mp (°C)	Yield (%)
II	–5	A_1 (20)	**1**[1b]	215.5–216	80
II	–5	A_2 (20)	**2**	195–197	98
II	–10	A_3 (20)	**3**	214–215	95
II	–10	A_4 (20)	**4**[1b,3,4]	214–217	84
V	–5	A_1 (10)	**5**	175–177	78
V	–10	A_4 (10)	**6**	185–186	65
VII	–5	A_1 (10)	**7**	176–178	80
VII	–10	A_3 (10)	**8**	106–110	67
VII	–5	A_5 (10)	**9**	130 (dec.)	61
II	–5	A_6 (20)	**10**[13]	261–265	84
II	–5	A_7 (20)	**11**[14]	220–224	86

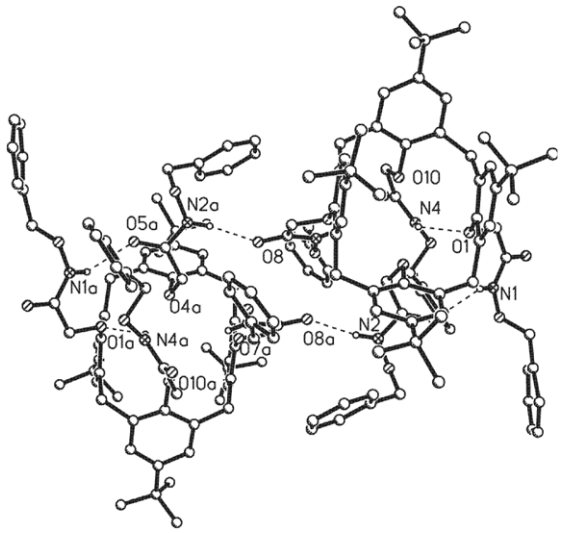


Figure 3 Dimer formed by two calix[4]arene units, linked by hydrogen bonds

In conclusion, a simple method for the synthesis of calix-hydroxamates and calix-amides is presented.[15] In a one-pot procedure, even unprotected hydroxamate compounds were obtained by lowering the reaction temperature. Inter- and intramolecular hydrogen bonds were observed in the crystal structure of **1**. The pseudo-dimer formation presented in Figure 3 is rather unusual for calixarenes and explains the possibility of interactions with other organic molecules.

Melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Varian spectrometer (200 or 500 MHz). IR spectra were recorded on a PerkinElmer 580 spectrophotometer. MS spectra were recorded on a Bruker BIFLEX 3 Mass Spectrometer. Elemental analyses were done on Carlo Erba Instruments CHNSO EA1108 Elemental Analyzer.

Ethyl chloroformate, *O*-tritylhydroxylamine (A_5), hydroxylamine hydrochloride (A_4), *N*-methylhydroxylamine hydrochloride (A_3), ethyl bromoacetete are commercially available. All solvents used were dried and distilled by standard procedure. Compounds **I**,[16] **II**,[9,10] **III**[17] were synthesized according to known procedures. Substrate **IV** was obtained by us in much better yield than published earlier.[18] Preparation of starting materials **IV**–**VII** is outlined below (Table 2).

Table 2 Substrates **I**–**VII** Prepared

Substrate	Mp (°C)	Yield (%)
I[16]	152–154	90
II[9,10]	275–278	98
III[17]	228–232	–
IV[18]	133–135.5	89
V	263	99
VI	175–176.5	62
VII	248–250.5	98

5,11,17,23-Tetrakis-*p*-*tert*-butyl-(25,27-bis(ethoxycarbonylmethoxy)calix[4]arene-crown-6 (IV)[18]

R_f 0.8 (hexane–EtOAc, 2:1).

IR (thin film): 3436, 2964, 1759, 1480, 1188, 1124 cm^{-1}.

^{1}H NMR (200 Hz, $CDCl_3$): δ (cone conformation) = 0.89 (s, 18 H, *t*-C_4H_9), 1.27 (s, 18 H, *t*-C_4H_9), 1.31 (m, 6 H, OCH_2CH_3), 3.18 and 4.55 (d, 4 H, $ArCH_2Ar$, J = 12.7 Hz), 3.72 (s, 4 H, OCH_2CH_3), 3.80 (m, 8 H, OCH_2CH_2O), 4.20 (m, 12 H, OCH_2CH_2O), 4.61 (s, 4 H, OCH_2CO), 6.55 (s, 4 H, ArH), 7.03 (s, 4 H, ArH).

MS (MALDI TOF): *m*/*z* calcd for $[M + Na]^+$ = 1045.3; found: 1045.3 $[M + Na]^+$, 1061.2 $[M + K]^+$.

25,27-Bis(ethoxycarbonylpropoxy)-*p-tert*-butylcalix[4]arene (VI)

p-tert-Butylcalix[4]arene (648 mg, 1 mmol) and K_2CO_3 (1.38 g, 10 mmol) were refluxed in acetone. Then a solution of ethyl 3-bromobutyrate (1.95 g, 10 mmol) in acetone (10 mL) was added over a period of 10 min. After 4 days, the mixture was allowed to cool to r.t. and the volatiles were removed in vacuo. The residual oil was dissolved in CH_2Cl_2 and the CH_2Cl_2 layer was washed with H_2O (20 mL), then 0.1 M HCl (20 mL) and H_2O (10 mL). The combined organic extracts were dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The product was obtained by crystallization from CH_2Cl_2–MeOH as a white solid; R_f 0.8 (hexane–EtOAc, 4:1).

IR (thin film): 3330, 2968, 1745, 1482, 1182, 1038 cm^{-1}.

^1H NMR (200 Hz, $CDCl_3$): δ (cone conformation) = 1.05 (s, 18 H, *t*-C_4H_9), 1.25 (m, 6 H, OCH_2CH_3), 1.32 (s, 18 H, *t*-C_4H_9), 2.35 (q, 4 H, $OCH_2CH_2CH_2$, J = 4.4 Hz), 2.90 (t, 4 H, $OCH_2CH_2CH_2$, J = 4.8 Hz), 3.38 and 4.30 (d, 4 H, $ArCH_2Ar$, J = 12.9 Hz), 4.10 (t, 4 H, $OCH_2CH_2CH_2$, J = 4.8 Hz), 4.20 (m, 4 H, OCH_2CH_3), 6.90 (s, 4 H, ArH), 7.12 (s, 4 H, ArH), 7.75 (s, 2 H, OH).

MS (MALDI TOF): *m*/*z* calcd for $[M + Na]^+$: 899.2; found: 899.4 $[M + Na]^+$, 915.4 $[M + K]^+$.

25,27-Bis(hydroxycarbonylmethoxy)-26,27-calix[4]arene-crown-6 (V)

This compound was synthesized in a manner similar to that described for **II**;[9,10] R_f 0.6 ($CHCl_3$–MeOH, 12:1).

IR (thin film): 3412, 2962, 1747, 1479, 1195, 1122, 760 cm^{-1}.

^1H NMR (200 Hz, DMSO-d_6): δ (cone conformation) = 0.83 (s, 18 H, *t*-C_4H_9), 1.23 (s, 18 H, *t*-C_4H_9), 3.13 and 4.42 (d, 4 H, $ArCH_2Ar$, J = 12.7 Hz), 3.62 (s, 4 H, OCH_2CH_2O), 3.68 (m, 4 H, OCH_2CH_2O), 3.72 (m, 4 H, OCH_2CH_2O), 4.10 (s, 8 H, OCH_2CH_2O), 4.41 (s, 4 H, OCH_2CO), 6.50 (s, 4 H, ArH), 7.08 (s, 4 H, ArH).

MS (MALDI TOF): *m*/*z* calcd for $[M + Na]^+$: 989.5; found: 989.5 $[M + Na]^+$, 1005.5 $[M + K]^+$.

25,27-Bis(hydroxycarbonylpropoxy)-*p-tert*-butylcalix[4]arene (VII)

Compound **VII** was synthesized in a manner similar to that described for **II**;[9,10] R_f 0.7 ($CHCl_3$–MeOH, 4:1).

IR (thin film): 3330, 2968, 1706, 1490, 1202, 1038, 764 cm^{-1}.

^1H NMR (200 Hz, $CDCl_3$): δ (cone conformation) = 0.92 (s, 18 H, *t*-C_4H_9), 1.31 (s, 18 H, *t*-C_4H_9), 2.35 (q, 4 H, $OCH_2CH_2CH_2$, J = 3.9 Hz), 2.87 (t, 4 H, $OCH_2CH_2CH_2$, J = 4.7 Hz), 3.31 and 4.29 (d, 4 H, $ArCH_2Ar$, J = 13.2 Hz), 3.92 (m, 4 H, $OCH_2CH_2CH_2$), 6.73 (s, 4 H, ArH), 7.07 (s, 4 H, ArH).

MS (MALDI TOF): *m*/*z* calcd for $[M + Na]^+$: 843.2; found: 843.3 $[M + Na]^+$, 859.3 $[M + K]^+$.

Calix[4]arene-Hydroxamates 1–9 and -Amides 10 and 11; 25,26,27,28-Tetrakis(*N*-benzyloxycarbamoylmethoxy)-*p-tert*-butylcalix[4]arene (1); Typical Procedure

Compound **II** (307 mg, 0.349 mmol) and Et_3N (141 mg, 1.4 mmol) in CH_2Cl_2 (10 mL) were cooled to –5 °C and stirred for 10 min, and then ethyl chloroformate (152 mg, 1.4 mmol) was added. The solution was stirred at –5 °C for 0.5 h and *O*-benzylhydroxylamine (1.05 g, 8.5 mmol) in CH_2Cl_2 (5 mL) was added. After 2 h, the residue was diluted with CH_2Cl_2 (15 mL), and the CH_2Cl_2 layer was washed with H_2O (10 mL), then with 0.1 M HCl (15 mL) and again with H_2O (10 mL). Additionally, the H_2O phase was extracted with CH_2Cl_2 (2 × 20 mL). The organic extracts were collected and dried ($MgSO_4$). The solution was concentrated under reduced pressure, and the residue was crystallized from CH_2Cl_2–MeOH to give **1** as white crystals; R_f 0.8 ($CHCl_3$–MeOH, 8:1).

IR (thin film): 3200, 2960, 1674, 1482, 1196, 1028, 764 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ (cone conformation) = 1.05 (s, 36 H, *t*-C_4H_9), 3.18 and 4.51 (d, 4 H, $ArCH_2Ar$, J = 12.7 Hz), 4.45 (s, 8 H, OCH_2CO), 4.82 (s, 8 H, OCH_2Ar), 6.85 (s, 8 H, ArH), 7.30 (m, 20 H, ArH_{benzyl}), 10.50 (s, 4 H, NHO).

^{13}C NMR ($CDCl_3$): δ = 167.6, 152.9, 146.1, 135.6, 133.4, 129.5, 128.8, 128.6, 125.8, 78.2, 72.7, 34.1, 31.5, 31.4, 31.3.

MS (MALDI TOF): *m*/*z* calcd for $[M + Na]^+$: 1323.6; found: 1323.7 $[M + Na]^+$, 1339.7 $[M + K]^+$.

Anal. Calcd for $C_{80}H_{92}N_4O_{12}$·0.5 MeOH: C, 73.31; H, 7.13; N, 4.25. Found: C, 73.24; H, 7.15; N, 4.28.

25,26,27,28-Tetrakis(*N*-methoxycarbamoylmethoxy)-*p-tert*-butylcalix[4]arene (2)

R_f 0.6 ($CHCl_3$–MeOH, 20:1).

IR (thin film): 3245, 2965, 1672, 1478, 1195, 1125, 1086, 1035, 872, 756 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ (cone conformation) = 1.05 (s, 36 H, *t*-C_4H_9), 3.20 (d, 4 H, $ArCH_2Ar$, J = 12.7 Hz), 3.66 (s, 12 H, OCH_3), 4.42 (m, 12 H, $ArCH_2Ar$ and OCH_2CO), 6.84 (s, 8 H, ArH), 11.37 (s, 4 H, NHO).

^{13}C NMR ($CDCl_3$): δ = 167.4, 152.8, 146.2, 133.3, 125.9, 73.0, 64.2, 62.2, 46.2, 34.1, 31.5, 31.2.

MS (MALDI TOF): *m*/*z* calcd for $[M + Na]^+$: 1019.2; found: 1019.4 $[M + Na]^+$, 1035.4 $[M + K]^+$.

Anal. Calcd for $C_{56}H_{76}N_4O_{12}$·0.5HCl·NH_2OCH_3: C, 65.38; H, 7.56; N, 6.07. Found: C, 65.43; H, 7.75; N, 5.92.

25,26,27,28-Tetrakis(*N*,*N*-methylhydroxycarbamoylmethoxy)-*p-tert*-butylcalix[4]arene (3)

R_f 0.7 ($CHCl_3$–MeOH, 4:1).

IR (thin film): 3359, 2968, 1648, 1485, 1198, 1040, 773 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ (cone conformation) = 1.16 (s, 36 H, *t*-C_4H_9), 3.15–3.20 (m, 16 H, $ArCH_2Ar$ and NCH_3), 4.78 (d, 4 H, $ArCH_2Ar$, J = 12.9 Hz), 4.88 (s, 8 H, OCH_2CO), 6.80 (s, 8 H, ArH), 9.74 (s, 4 H, NOH).

^{13}C NMR ($CDCl_3$/CH_3OH): δ = 171.2, 153.1, 145.7, 133.3, 125.7, 72.7, 36.1, 33.9, 31.4, 31.2.

MS (MALDI TOF): *m*/*z* calcd for $[M + Na]^+$: 1019.2; found: 1019.5 $[M + Na]^+$, 1035.5 $[M + K]^+$.

Anal. Calcd for $C_{56}H_{76}N_4O_{12}$·HCl·NH(OH)CH_3: C, 63.33; H, 7.68; N, 6.37. Found: C, 63.39; H, 7.59; N, 6.48.

25,26,27,28-Tetrakis(*N*-hydroxycarbamoylmethoxy)-*p-tert*-butylcalix[4]arene (4)

R_f 0.5 ($CHCl_3$–MeOH, 9:1).

IR (thin film): 3181, 2967, 1680–1635, 1475, 1196, 1117, 1048, 912, 731 cm^{-1}.

^1H NMR (500 Hz, DMSO-d_6): δ (cone conformation) = 0.78–1.3 (s, 36 H, *t*-C_4H_9), 3.11–4.50 (m, 16 H, $ArCH_2Ar$ and OCH_2CO), 6.50–7.20 (s, 8 H, ArH), 8.03 (s, 4 H, NH).

^{13}C NMR ($CDCl_3$): δ = 146.9, 144.5, 146.1, 127.9, 126.1, 46.1, 34.2, 32.8, 31.8, 31.6, 31.2.

Anal. Calcd for $C_{52}H_{68}N_4O_{12}$·0.5MeOH·0.5HCl·NH_2OH: C, 63.51; H, 7.46; N, 6.35. Found: C, 63.11; H, 7.74; N, 6.36.

25,27-Bis(*N*-benzyloxycarbamoylomethoxy)-26,28-*p-tert*-butylcalix[4]arene-crown-6 (5)

R_f 0.7 ($CHCl_3$–MeOH, 20:1).

IR (thin film): 3384, 3270, 2959, 1694, 1479, 1360, 1198, 1121, 1031, 752 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ (cone conformation) = 0.96 (s, 18 H, t-C_4H_9), 1.10 (s, 18 H, t-C_4H_9), 3.08 and 4.41 (d, 4 H, ArCH_2Ar, J = 12.2 Hz), 3.52 (s, 4 H, OCH_2CH_2O), 3.59 (s, 4 H, OCH_2CH_2O), 3.69 (s, 4 H, OCH_2CH_2O), 3.97 (s, 4 H, OCH$_2$CH_2O), 4.04 (s, 4 H, OCH_2CH_2O), 4.35 (s, 4 H, OCH_2ArH$_{benzyl}$), 4.41 (s, 4 H, OCH$_2$CO), 6.67 (s, 4 H, ArH), 6.87 (s, 4 H, ArH), 7.37 (s, 10 H, ArH$_{benzyl}$), 11.04 (s, 2 H, NHO).

^{13}C NMR ($CDCl_3$): δ = 168.6, 153.9, 152.8, 145.3, 144.9, 136.6, 135.4, 132.1, 129.4, 128.5, 126.0, 124.9, 74.7, 70.7, 70.6, 70.4, 70.1, 34.2, 33.8, 32.2, 31.9, 31.3, 31.2.

MS (MALDI TOF): m/z calcd for $[M + Na]^+$: 1199.5; found: 1199.4 $[M + Na]^+$, 1215.4 $[M + K]^+$.

Anal. Calcd for $C_{72}H_{92}N_2O_{12}$: C, 73.46; H, 7.82; N, 2.38. Found: C, 73.27; H, 7.95; N, 2.34.

25,27-Bis(*N*-hydroxycarbamoylomethoxy)-26,28-*p*-*tert*-butylcalix[4]arene-crown-6 (6)

R_f 0.7 ($CHCl_3$–MeOH, 12:1).

IR (thin film): 3302, 1960, 1681, 1480, 1198, 1119, 772 cm^{-1}.

^1H NMR (200 MHz, DMSO-d_6): δ (cone conformation) = 1.23 (s, 18 H, t-C_4H_9), 1.24 (s, 18 H, t-C_4H_9), 3.11 and 4.42 (d, 4 H, ArCH_2Ar, J = 12.7 Hz), 3.62–3.78 (m, 14 H, OCH_2CH_2O), 3.96 (m, 6 H, OCH_2CH_2O), 4.42 (s, 4 H, OCH$_2$CO), 6.82 (s, 4 H, ArH), 6.99 (s, 4 H, ArH), 8.79 (s, 2 H, OH), 10.39 (s, 2 H, N*H*OH).

^{13}C NMR ($CDCl_3$): δ = 167.3, 153.1, 151.4, 146.3, 145.4, 135.1, 132.4, 126.1, 125.9, 125.4, 125.0, 75.5, 73.0, 71.2, 71.0, 70.8, 34.3, 33.9, 32.0, 31.9, 31.5, 31.2, 31.0.

MS (MALDI TOF): m/z calcd for $[M + Na]^+$: 997.2; found: 1019.5 $[M + Na]^+$, 1035.5 $[M + K]^+$.

Anal. Calcd for $C_{58}H_{80}N_2O_{12}$·0.5MeOH·0.5NH_2OH·HCl: C, 66.93; H, 8.00; N, 3.33. Found: C, 66.37; H, 8.03; N, 3.49.

25,27-Bis(*N*-benzyloxycarbamoylpropoxy)-*p*-*tert*-butylcalix[4]arene (7)

R_f 0.4 ($CHCl_3$–MeOH, 25:1).

IR (thin film): 3300, 2960, 1675, 1486, 1200, 1028, 750 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ (cone conformation) = 1.13 (s, 18 H, t-C_4H_9), 1.18 (s, 18 H, t-C_4H_9), 2.21 (m, 4 H, OCH$_2$CH_2CH$_2$), 2.45 (m, 4 H, OCH$_2$CH$_2$CH_2), 3.42 and 4.18 (d, 4 H, ArCH_2Ar, J = 12.2 Hz), 3.9 (m, 4 H, OCH_2CH$_2$CH$_2$), 4.80 (s, 4 H, OCH_2Ar$_{benzyl}$), 4.92 (s, 8 H, OCH_2Ar), 7.15 (m, 8 H, ArH), 7.30 (m, 20 H, ArH$_{benzyl}$), 8.60 (s, 2 H, ArO*H*), 11.05 (s, 2 H, NHO).

^{13}C NMR ($CDCl_3$): δ = 170.8, 149.9, 149.3, 147.6, 142.7, 132.6, 129.1, 128.7, 128.0, 125.9, 125.5, 78.2, 74.8, 34.2, 34.1, 31.9, 31.2, 29.8, 26.0.

MS (MALDI TOF): m/z calcd for $C_{66}H_{82}N_2O_8$ $[M + Na]^+$: 1053.7; found: 1053.6 $[M + Na]^+$, 1069.5 $[M + K]^+$.

Anal. Calcd for $C_{66}H_{82}O_8N_2$·0.5MeOH: C, 76.29; H, 8.03; N, 2.67. Found: C, 76.30; H, 8.07; N, 2.76.

25,27-Bis(*N*,*N*-methylhydroxycarbamoylpropoxy)-*p*-*tert*-butylcalix[4]arene (8)

Product was purified by column chromatography using $CHCl_3$–MeOH (98:2) as eluent; R_f 0.6 ($CHCl_3$–MeOH, 8:1).

IR (thin film): 3328, 2960, 1622, 1477, 1198, 1039, 756 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ (cone conformation) = 1.12 (s, 18 H, t-C_4H_9), 1.17 (s, 18 H, t-C_4H_9), 2.22 (t, 4 H, OCH$_2$CH_2CH$_2$), 2.81 (s, 4 H, OCH_2CH$_2$CH$_2$), 3.12 (s, 6 H, NCH_3) 3.40 and 4.19 (d, 4 H, ArCH_2Ar, J = 12.7 Hz), 3.96 (s, 4 H, OCH$_2$CH$_2$CH_2), 7.15 (m, 8 H, ArH), 8.64 (s, 2 H, ArO*H*), 9.83 (s, 2 H, NOH).

MS (MALDI TOF): m/z calcd for $C_{54}H_{74}N_2O_8$ $[M + Na]^+$: 901.5; found: 901.2 $[M + Na]^+$, 917.2 $[M + K]^+$.

Anal. Calcd for $C_{54}H_{74}N_2O_8$: C, 73.70; H, 8.41; N, 3.18. Found: C, 73.52; H, 8.42; N, 3.01.

25,27-Bis(*N*-methoxytriphenylcarbamoylpropoxy)-*p*-*tert*-butylcalix[4]arene (9)

Product was purified by column chromatography using $CHCl_3$–MeOH (99:1) as eluent; R_f 0.4 ($CHCl_3$–MeOH, 25:1).

IR (thin film): 3288, 2960, 1675, 1485, 1385, 1200, 755 cm^{-1}.

^1H NMR (DMSO-d_6): δ (cone conformation) = 1.13 (s, 18 H, t-C_4H_9), 1.19 (s, 18 H, t-C_4H_9), 1.90 (m, 4 H, OCH$_2$CH_2CH$_2$), 2.22 (m, 4 H, OCH_2CH$_2$CH$_2$), 3.30 and 3.99 (d, 4 H, ArCH_2Ar, J = 12.2 Hz), 3.56 (s, 4 H, OCH$_2$CH$_2$CH_2), 7.15 (m, 8 H, ArH), 7.22 (m, 20 H, ArH$_{trityl}$), 7.38 (m, 10 H, ArH$_{trityl}$), 8.45 (s, 2 H, ArO*H*), 10.20 (s, 2 H, NHO).

^{13}C NMR ($CDCl_3$): δ = 162.7, 149.5, 147.7, 147.1, 145.4, 142.3, 141.2, 133.1,129.9, 129.4, 128.3, 128.1, 128.0, 127.9, 127.8, 128.0, 127.9, 127.8, 127.4, 125.9, 125.5, 82.2, 36.4, 34.3, 34.1, 32.4, 31.9, 31.6, 31.3.

Anal. Calcd for $C_{90}H_{98}N_2O_8$·1.5HCl·NH_2OH: C, 75.13; H, 7.51; N, 3.40. Found: C, 75.34; H, 7.66; N, 3.92.

25,26,27,28-Tetrakis(piperidylcarbamoylmethoxy)-*p*-*tert*-butylcalix[4]arene (10)

R_f 0.4 ($CHCl_3$–MeOH, 16:1).

IR (thin film): 3328, 2934, 1659, 1480, 1256, 1159, 1129, 1062, 1010, 751 cm^{-1}.

^1H NMR (200 MHz, DMSO-d_6): δ (cone conformation) = 1.09 (s, 36 H, t-C_4H_9), 1.45 [m, 24 H, $(CH_2)_3$], 3.20 and 5.02 (d, 4 H, ArCH_2Ar, J = 12.8 Hz), 3.43 (s, 8 H, NCH_2), 3.58 (s, 8 H, NCH_2), 5.08 (s, 8 H, OCH$_2$CO), 6.83 (s, 8 H, ArH).

25,26,27,28-Tetrakis(diethylcarbamoylmethoxy)-*p*-*tert*-butylcalix[4]arene (11)

R_f 0.7 ($CHCl_3$–MeOH, 8:1).

IR (thin film): 2934, 2360, 1659, 1479, 1198, 1061 cm^{-1}.

^1H NMR (200 Hz, $CDCl_3$): δ (cone conformation) = 1.08 (s, 36 H, t-C_4H_9), 1.13 [s, 12 H, $(NCH_2CH_3)_2$], 1.16 [s, 12 H, $(NCH_2CH_3)_2$], 3.26 and 5.22 (d, 4 H, ArCH_2Ar, J = 12.7 Hz), 3.36 [t, 16 H, $(NCH_2CH_3)_2$, J = 5.1 Hz], 5.03 (s, 8 H, OCH$_2$CO), 6.81 (s, 8 H, ArH).

^{13}C NMR ($CDCl_3$): δ = 169.5, 133.8, 125.5, 72.1, 41.1, 40.2, 34.05, 32.3, 31.6, 14.4, 13.3.

MS (MALDI TOF): m/z calcd for $[M + Na]^+$: 1123.5; found: 1123.5 $[M + Na]^+$, 1139.5 $[M + K]^+$.

Crystal Data of 1

Crystallization: Compound **1** was recrystallized from CH_2Cl_2–MeOH. After a few days at r.t., single crystals suitable for X-ray analysis appeared; mp 215.5–216 °C. A crystal of size 0.30 × 0.32 × 0.40 mm was used for structure investigation.

Collection of X-Ray Diffraction Data, Solution and Refinement of Crystal Structure: Experimental data were collected on KM4CCD kappa-geometry diffractometer equipped with a Sapphire2 CCD detector. Enhanced X-ray Mo Kα radiation source with a graphite monochromator was used. Determination of the elemental cell and data collection were carried out at 100 K. All preliminary calculations were done using CrysAlis v. 1.71 software package (Oxford Diffraction, 2004). The structure was solved by direct methods and

most of the non-hydrogen atoms were refined with anisotropic thermal parameters by full-matrix least squares procedure based on F^2. All hydrogen atoms were refined isotropic U values fixed to be 1.3 times U_{eq} of C atoms for CH_3 or 1.2 times U_{eq} for other cases. Calculations were carried out using the SHELX-97 program package.[19,20]

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(20) Crystallographic data for the structure of **1** reported in this paper have been deposited with Cambridge Crystallographic Data Centre as supplementary publication No. CCDC-275710 (fwd). Copies of the data can be obtained free of charge on application to CCDC, 12, Union Road, Cambridge, UK (E-mail: deposit@ccdc.cam.ac.uk).