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Synthesis of New Chromogenic Calix[4]crowns and Molecular Recognition of Alkylamines

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Abstract: A new type of calix[4]crown containing ester group **3** has been synthesized and selectively nitrated to give **4** or ipso-nitrated to give **6**. By nitration a novel calixcrown **5** containing a quinone segment was obtained. These nitrated calixcrowns have been used as chromogenic hosts for complexing alkylamines and the factors affecting recognition are discussed. © 1997 Elsevier Science Ltd.

INTRODUCTION

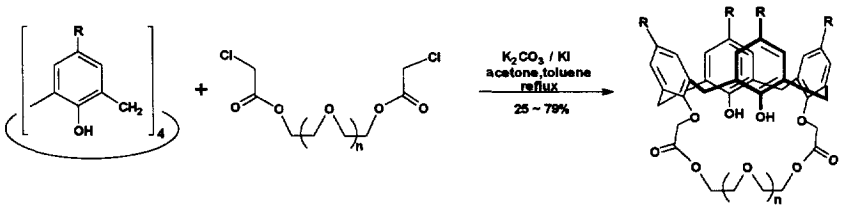
Calixarenes have aroused considerable interest as useful building blocks for the synthesis of receptor molecules for both cations and neutral molecules.[1] Since 1983, Ungaro, Reinhoudt and Shinkai etc. have synthesized a series of calixcrowns which possess a versatile calixarene moiety and a subcyclic unit of the crown ether.[1c] As an important type of ionphore, calixcrowns have high selectivity in recognition of alkali and alkaline earth metal cations. They can selectively recognize K^+ with respect to Na^+ even better than valinomycin, which is an excellent ionophore in nature.[2] Regarding crown ethers as receptor for neutral molecules, many works have been reported.[3] However, few studies have been performed concerning the recognition of neutral molecules with calixcrowns which is important for biomimetic application.[4]

We report here a facile method for synthesizing a new type of calix[4]crowns which contains an ester group in the crown ether segment. These calixcrowns were selectively nitrated or ipso-nitrated in order to investigate their recognition ability with alkylamines using UV-VIS spectroscopy. We found that nitrated calix[4]crowns can complex primary linear alkylamines better than secondary, tertiary or bulky amines in chloroform and they can be used as "naked eyes" to distinguish these amines.

RESULTS AND DISCUSSION

Synthesis of calix[4]crowns containing an ester group

Calixcrowns were synthesized from calixarene and polyethylene glycol ditosylate in the presence of ^{t}BuOK, NaH, K_2CO_3, Na_2CO_3 or Cs_2CO_3 as reported in the literature.[5] We succeeded in synthesizing calix[4]crowns containing an ester group **3a~h** by the reaction of *p-tert*-butyl-calix[4]arene **1a** or calix[4]arene **1b** with oligoethylene glycol bischloroacetate **2** in acetone/toluene (5/2 v/v) in the presence of K_2CO_3 and KI. This is a straightforward method and the yield is moderate. (see Scheme 1) Recently we found a method reported in the literature which is very similar to ours.[6]



1a R = *t*-butyl **2** (n = 0~3) **3a** R = *t*- butyl, n = 0; **3b** R = *t*-butyl, n = 1;

1b R = H **3c** R = *t*- butyl, n = 2; **3d** R = *t*-butyl, n = 3;

3e R = H, n = 0; **3f** R = H, n = 1;

3g R = H, n = 2; **3h** R = H, n = 3.

Scheme 1

The ^{1}H-NMR spectra of the products showed the characteristic AB system for the methylene bridge protons of calix[4]arene, showing these calix[4]crowns existed in cone conformation and the molecules were in high symmetry.

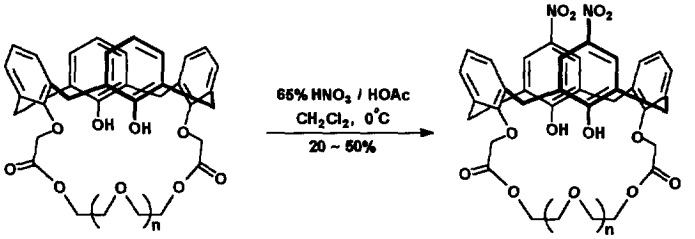
Selective nitration of calix[4]crowns

Ungaro and Reinhoudt have reported selective nitration[7] or ipso-nitration of some calixarene derivatives,[8] but until now there is no paper about nitration of calixcrowns. Because the nitro group is a good functional group or auxochrome for phenol ring, the nitration of **3** was studied.

Calix[4]crowns **3e~h** are selectively nitrated to give **4a~d** with excess of 65 % HNO_3 and acetic acid in dichloromethane at 0°C. The yield is 33 % (**4a**), 37 % (**4b**), 50 % (**4c**) and 20 % (**4d**), respectively. (see Scheme 2)

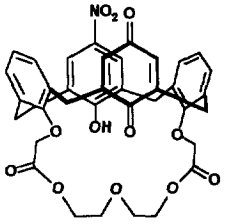
The nitrated products are characterized by ^{1}H-NMR, ^{13}C-NMR, FAB MS, IR, and elemental analysis. It has been demonstrated that the para positions of phenol rings are much more reactive than those of alkoxybenzene rings in electrophilic aromatic substitution,[9] so selective nitration may occur on the phenol rings. In the ^{1}H-NMR spectra, the OH proton signal is shifted

downfield from 7 ~ 8 ppm to about 9 ppm and the shift of the aromatic proton of nitrated phenol ring is to about 8 ppm. In the IR spectra, two very strong absorption peaks at ca. 1500 and 1320 cm^{-1} demonstrate the presence of nitro groups.



3e n = 0; **4a** n = 0;
3f n = 1; **4b** n = 1;
3g n = 2; **4c** n = 2;
3h n = 3; **4d** n = 3.

Scheme 2

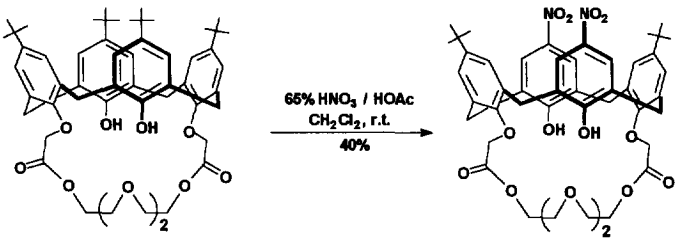


5

In the nitration of **3f**, a by-product **5** in addition to the dinitrated product is also obtained. In the ^{13}C-NMR spectrum two signals at δ 188.02 ppm and δ 185.63 ppm indicate that this product contains two carbonyl groups, and the other spectroscopic data are all consistent with this structure. The conformation of **5** is cone showed by two signals at δ 33.28 ppm and δ 30.33 ppm in the ^{13}C-NMR spectrum.[10] This kind of product derived from nitration of one phenol ring and oxidation of others is first reported.

Ipso-nitration of p-tert-butylcalix[4]crown

Ipso-nitration of calixcrowns has not been reported previously. *p-tert*-Butylcalixcrown **3c** reacts with excess of 65 % HNO_3 and acetic acid in dichloromethane at room temperature for 30 minutes to form ipso-nitrated product **6**. (see Scheme 3) The ^{1}H-NMR spectrum shows that the signals of *tert*-butyl group retain half of the protons (δ 1.19 ppm, s, 18H) and the signal of phenolic hydroxy protons is shifted downfield (9.25 ppm), which indicates that the *tert*-butyl groups in the phenol rings are directly substituted by nitro groups and *tert*-butyl groups at alkoxybenzene are retained. The conformation of **6** is cone because the signal of methylene bridge protons shows an AB system at δ 3.48 ppm and δ 4.53 ppm in the ^{1}H-NMR spectrum.



3c **6**

Scheme 3

Recognition of alkylamines by nitrated calix[4]crowns

Nitrated calix[4]crowns **4a~d** containing two phenolic moieties are strongly acidic. They can complex with amines through strong intermolecular hydrogen bonding. The nitro group is an auxochrome for the phenol ring, so we can use UV-VIS spectra to study the interaction between nitrated calixcrowns **4a~d** and alkylamines. Compound **4b** has no absorption in the visual area in chloroform, but upon addition *n*-butylamine the solution turns yellow with a large bathochromic shift of 93 nm. (see Figure 1) The existence of an isobestic point at 357 nm suggests that an equilibrium exists in the solution.

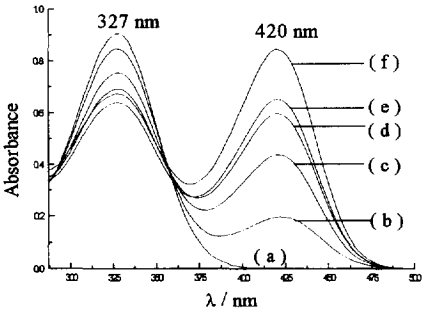


Fig. 1 Spectral changes upon the addition of (a) 0, (b) 2.5×10^{-2}, (c) 4.0×10^{-2}, (d) 5.0×10^{-2}, (e) 6.0×10^{-2}, (f) 7.5×10^{-2} mol dm^{-3} of *n*-butylamine to a chloroform solution of **4b** (5.0×10^{-5} mol dm^{-3}) at 25°C.

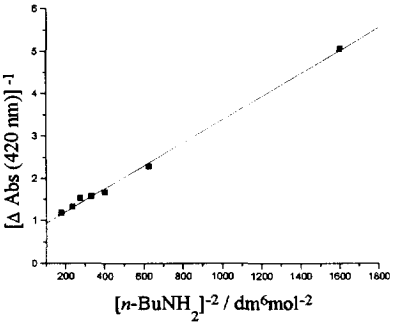


Fig. 2 Plot of 1/A vs. different concentration of *n*-butylamine with **4b** in chloroform at 25°C; [**4b**] = 5.0×10^{-5} mol dm^{-3}.

Previously, the Benesi-Hildberand equation was used to explain 1 : 1 complexation in solution.[11] We find in this system the stoichiometry of the complex is not 1 : 1, because the plot is not linear. We think that two amino groups may interact with two phenolic groups of one

calixcrown in the presence of excess of alkylamines. This conclusion is different to that previously reported.[4]

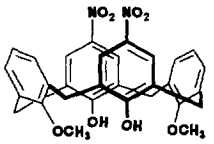
When calix[4]crown (H) forms a 1 : 2 complex with amine (G), the following equilibriums are present in the solution:

$$H + G \leftrightarrows HG_1$$

$$HG_1 + G \leftrightarrows HG_2$$

$$K_{obs} = K_1 \cdot K_2 = [HG_2]/\{[H][G]^2\}$$

The plot with 1/A versus $[G]^{-2}$ is linear (Fig 2), supporting the 1 : 2 stoichiometry of the complex. From the slope we can calculate the association constant K_{obs} = 251 $dm^6\ mol^{-2}$ and $\varepsilon_{max} = 2.93 \times 10^4\ dm^3\ mol^{-1}\ cm^{-1}$.



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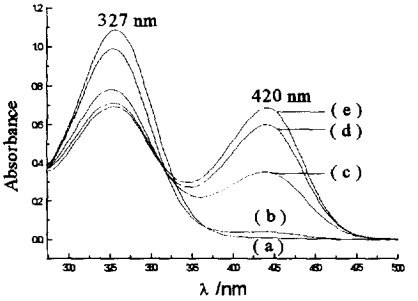

Fig. 3 Spectral changes upon the addition of 5.0×10^{-2} mol dm^{-3} *n*-butylamine to a chloroform solution of (a) **7**, (b) **4a**, (c) **4d**, (d) **4b**, (e) **4c** (5.0×10^{-5} mol dm^{-3}) at 25°C.

In order to study the effect on recognition of the different size of crown ether ring, the UV-VIS absorption spectra of the compounds **4a~d** as well as **7**[8] were measured under the same conditions (host : guest = 1 : 1000 mol/mol). Figure 3 indicates that the recognition ability of compound **7** without a crown ether ring, compound **4a** with the smallest crown ether ring and **4d** with the largest crown ring is weaker than that of compounds **4b** and **4c**. This may be caused by the hydrogen bonding between the oxygen in the crown ether with suitable ring size and the amino group. We also studied the recognition ability of compound **4b** with triethylamine and diethylamine under the same conditions (host : guest = 1 : 1000 mol/mol). The absorption of the complexes is very low, so the interaction between them is weak, and the interaction has no relation with the basicity of amines (in chloroform, the basicity: triethylamine > diethylamine > *n*-butylamine[12]).

For other butylamines (*s*-butylamine and *t*-butylamine), the recognition ability of **4b** is poorer than with *n*-butylamine. The solvent is also an important factor in recognition. If we use methanol as the solvent, the nitrated phenol moiety would transform to phenoxide and the UV-VIS spectra do not change upon the addition of alkylamines. From the above information, we conclude that the proton transfer occurs between a calix[4]crown and amines, and the resulting ammonium phenoxide may impart crown ether stabilization through solvation of the ammonium ion in the cavity and the interaction of hydrogen bonding, with the phenoxide oxygen atom acting electrostatically as the primary binding site.

EXPERIMENTAL

Mps were uncorrected. ^1H and ^{13}C NMR spectra were recorded on a Varian Unity 200 spectrometer with deuteriochloroform as solvent and tetramethylsilane as internal reference, unless otherwise indicated. IR spectra were recorded with a Perkin-Elmer 782 spectrometer. UV-VIS spectra were determined with a Uvikon 810 spectrometer. Mass spectra were recorded on a KYKY-ZHT-5 instrument. Elemental analyses were performed by the Analytical Laboratory of the Institute. *p-tert*-Butylcalix[4]arene **1a**[13] and calix[4]arene **1b**[14] were prepared according to literature procedures. The glycol or polyglycol bis (2-chloroacetate) **2** was prepared from the reaction of glycol or polyglycol with chloroacetyl chloride as described in the literature.[15]

General procedure for the preparation of calix[4]crowns containing an ester group **3a~h**:

To a solution of 2.5 mmol of glycol or polyglycol bis (2-chloroacetate) **2** and 2 mmol of *p-tert*-butylcalix[4]arene **1a** or calix[4]arene **1b** in 50 ml of acetone and 20 ml of toluene were added 2 mmol of K_2CO_3 and 4 mmol of KI. The reaction mixture was stirred under reflux for 6 ~ 23 h and the solvent was then removed under reduced pressure. The residue was dissolved in 50 ml of $CHCl_3$ and filtered to remove impurities. The $CHCl_3$ layer was concentrated and chromatographed on a silica gel column using chloroform / petroleum ether (60°C ~ 90°C) (5 : 1 v/v) as eluent to afford a white solid which was recrystallized from $CHCl_3/CH_3OH$ to give pure compound **3a~h**.

5,11,17,23- Tetra-tert-butyl-25,27- dihydroxy-26,28- (3',6'- dioxa- 2',7' - dioxooctylene)dioxycalix[4]-arene (3a): reaction time 8 h; yield 67 %; mp 275°C (dec.); UV-VIS ($CHCl_3$) λ_{max} 286 nm (log ε = 3.88); IR (KBr) ν_{max} (cm^{-1}) 3395 (OH), 1730 (OCO), 1580, 1475; ^1H-NMR δ 1.16 (s, 18H, C(CH_3)$_3$), 1.22 (s, 18H, C(CH_3)$_3$), 3.38 and 4.25 (AB, 8H, J = 13.0 Hz, ArCH_2Ar), 4.62 (s, 4H, OCH_2CH_2O), 4.67 (s, 4H, ArOCH_2CO_2), 7.01 (s, 4H, Ar*H*), 7.04 (s, 4H, Ar*H*), 8.10 (s, 2H, O*H*); ^{13}C-NMR δ 31.46 , 31.89 (C(CH_3)$_3$), 32.50 (ArCH_2Ar), 34.08, 34.53 (C(CH_3)$_3$), 62.95 (OCH_2CH_2O), 73.12 (ArOCH_2),

125.73, 126.34, 127.53, 133.48, 141.96, 148.22, 148.86, 150.83 (Ar*C*), 166.24 (O*C*O); FAB-MS: m/e 789 ([M-1]$^+$); Anal. Calcd for $C_{50}H_{62}O_8$: C, 75.92; H, 7.90. Found: C, 75.54; H, 7.59.

5,11,17,23- Tetra-tert-butyl-25,27- dihydroxy- 26,28- (2',10'- dioxo- 3',6',9'- trioxaundecylene)dioxycalix[4]arene (3b): reaction time 6 h; yield 53 %; mp 221°C (dec.); UV-VIS ($CHCl_3$) λ_{max} 282 nm (log ε = 3.89); IR (KBr) ν_{max} (cm^{-1}) 3430 (OH), 1733 (OCO), 1585, 1480; ^{1}H-NMR δ 0.97 (s, 18H, C(C*H*$_3$)$_3$), 1.26 (s, 18H, C(C*H*$_3$)$_3$), 3.31 and 4.34 (AB, 8H, *J* = 13.0 Hz, ArC*H*$_2$Ar), 3.88 (t, 4H, $CO_2CH_2CH_2O$), 4.47 (t, 4H, $CO_2CH_2CH_2O$), 4.70 (s, 4H, $ArOCH_2CO_2$), 6.79 (s, 4H, Ar*H*), 6.97 (s, 2H, O*H*), 6.99 (s, 4H, Ar*H*); ^{13}C-NMR δ 30.99, 31.62 (C(*C*H$_3$)$_3$), 31.41 (Ar*C*H$_2$Ar), 33.78, 33.89 (*C*(CH$_3$)$_3$), 65.11 ($CO_2CH_2CH_2O$), 69.11 ($CO_2CH_2CH_2O$), 72.62 ($ArOCH_2$), 124.95, 125.63, 127.52, 132.45, 141.39, 147.25, 150.20, 150.41 (Ar*C*), 169.44 (O*C*O); FAB-MS: m/e 834 (M$^+$); Anal. Calcd for $C_{52}H_{66}O_9$: C, 74.79; H, 7.97. Found: C, 74.61; H, 8.11.

5,11,17,23- Tetra-tert-butyl-25,27-dihydroxy-26,28- (2',13'-dioxo-3',6',9',12'-tetraoxatetradecylene)-dioxycalix[4]arene (3c): reaction time 23 h; yield: 38 %; mp 218°C (dec.); UV-VIS ($CHCl_3$) λ_{max} 283 nm (log ε = 3.77); IR (KBr) ν_{max} (cm^{-1}) 3425 (OH), 1735 (OCO), 1590, 1480; ^{1}H-NMR δ 1.06 (s, 18H, C(C*H*$_3$)$_3$), 1.22 (s, 18H, C(C*H*$_3$)$_3$), 3.32 and 4.44 (AB, 8H, *J* = 13.0 Hz, ArC*H*$_2$Ar), 3.73 (s, 4H, OCH_2CH_2O), 3.86 (t, 4H, $CO_2CH_2CH_2O$), 4.49 (t, 4H, $CO_2CH_2CH_2O$), 4.80 (s, 4H, $ArOCH_2CO_2$), 6.89 (s, 4H, Ar*H*), 6.96 (s, 4H, Ar*H*), 7.38 (s, 2H, O*H*); ^{13}C-NMR δ 31.09, 31.54 (C(*C*H$_3$)$_3$), 31.85 (Ar*C*H$_2$Ar), 33.75, 33.95 (*C*(CH$_3$)$_3$), 64.34 ($CO_2CH_2CH_2O$), 68.80 ($CO_2CH_2CH_2O$), 70.99 (OCH_2CH_2O), 72.41 ($ArOCH_2$), 125.05, 125.80, 127.74, 132.80, 141.48, 147.18, 149.94, 150.97 (Ar*C*), 169.56 (O*C*O); FAB-MS: m/e 878 (M$^+$); Anal. Calcd for $C_{54}H_{70}O_{10}$: C, 73.77; H, 8.03. Found: C, 73.48; H, 7.90.

5,11,17,23-Tetra-tert-butyl-25,27-dihydroxy-26,28-(2',16'-dioxo-3',6',9',12',15'-pentaoxaheptadecylene)dioxycalix[4]arene (3d): reaction time 22 h; yield 25 %; mp 181 ~ 2°C; UV-VIS ($CHCl_3$) λ_{max} 283 nm (log ε = 4.00); IR (KBr) ν_{max} (cm^{-1}) 3420 (OH), 1730 (OCO), 1590, 1475; ^{1}H-NMR δ 1.03 (s, 18H, C(C*H*$_3$)$_3$), 1.24 (s, 18H, C(C*H*$_3$)$_3$), 3.32 and 4.44 (AB, 8H, *J* = 13.0 Hz, ArC*H*$_2$Ar), 3.65 and 3.74 (A_2B_2, 8H, $CO_2CH_2CH_2OCH_2CH_2O$), 3.88 (t, 4H, $CO_2CH_2CH_2O$), 4.48 (t, 4H, $CO_2CH_2CH_2O$), 4.78 (s, 4H, $ArOCH_2$), 6.87 (s, 4H, Ar*H*), 7.00 (s, 4H, Ar*H*), 7.28 (s, 2H, O*H*); ^{13}C-NMR δ 31.01, 31.54 (C(*C*H$_3$)$_3$), 31.77 (Ar*C*H$_2$Ar), 33.73, 33.90 (*C*(CH$_3$)$_3$), 64.69 ($CO_2CH_2CH_2O$), 68.77 ($CO_2CH_2CH_2O$), 70.87 ($CO_2CH_2CH_2OCH_2CH_2O$), 70.96 ($CO_2CH_2CH_2OCH_2CH_2O$), 72.29 ($ArOCH_2$), 124.96, 125.73, 127.96, 132.83, 141.55, 147.22, 149.96, 150.48 (Ar*C*), 169.20 (O*C*O); FAB-MS m/e 921 ([M-1]$^+$); Anal. Calcd for $C_{56}H_{74}O_{11}$: C, 72.85; H, 8.08. Found: C, 72.44; H, 8.20.

25,27-Dihydroxy-26,28-(3',6'-dioxa-2',7'-dioxooctylene)dioxycalix[4]arene (3e): reaction time 10 h; yield 79 %; mp >300°C; UV-VIS ($CHCl_3$) λ_{max} 281 nm (log ε = 3.79); IR (KBr) ν_{max} (cm^{-1}) 3340 (OH), 1736 (OCO), 1585, 1465; ^{1}H-NMR δ 3.43 and 4.25 (AB, 8H, *J* = 13.0 Hz, ArC*H*$_2$Ar), 4.68 (s,

4H, OCH_2CH_2O), 4.72 (s, 4H, ArOCH_2CO_2), 6.64 (t, 2H, Ar*H*), 6.86 (t, 2H, Ar*H*), 7.02 (d, 4H, Ar*H*), 7.04 (d, 4H, Ar*H*), 8.23 (s, 2H, O*H*); ^{13}C-NMR δ 31.44 (ArCH$_2$Ar), 62.82 (OCH$_2$CH$_2$O), 72.89 (ArOCH$_2$), 119.37, 126.41, 127.83, 128.55, 129.27, 133.63, 150.15, 152.94 (Ar*C*), 167.69 (O*C*O); FAB-MS: m/e 567 ([M+1]$^+$); Anal. Calcd for $C_{34}H_{30}O_8$: C, 72.07; H, 5.34. Found: C, 71.81; H, 5.30.

25,27-Dihydroxy-26,28-(2',10'-dioxo-3',6',9'-trioxaundecylene)dioxycalix[4]arene (3f): reaction time 20 h; yield 60 %; mp 241°C (dec.); UV-VIS (CHCl$_3$) λ_{max} 278 nm (log ε = 3.86); IR (KBr) ν_{max} (cm^{-1}) 3400 (OH), 1730 (OCO), 1587, 1460; ^{1}H-NMR δ 3.38 and 4.38 (AB, 8H, *J* = 13.0 Hz, ArCH_2Ar), 3.86 (t, 4H, CO$_2$CH$_2$CH_2O), 4.51 (t, 4H, CO$_2$CH_2CH$_2$O), 4.68 (s, 4H, ArOCH_2CO_2), 6.62 ~ 6.67 (m, 4H, Ar*H*), 6.83 (d, 4H, Ar*H*), 7.04 (d, 4H, Ar*H*), 7.39 (s, 2H, O*H*); ^{13}C-NMR δ 31.20 (ArCH$_2$Ar), 65.20 (CO$_2$CH$_2$CH$_2$O), 69.08 (CO$_2$CH$_2$CH$_2$O), 72.87 (ArOCH$_2$), 118.99, 125.60, 127.79, 128.50, 129.09, 132.82, 152.42, 152.98 (Ar*C*), 168.83 (O*C*O); FAB-MS: m/e 609 ([M-1]$^+$); Anal. Calcd for $C_{36}H_{34}O_9$: C, 70.81; H, 5.61. Found: C, 70.39; H, 5.78.

25,27- Dihydroxy- 26,28- (2',13'- dioxo -3',6',9',12'- tetraoxatetradecylene)dioxycalix[4]arene (3g): reaction time 12 h; yield 29 %; mp 226°C (dec.); UV-VIS (CHCl$_3$) λ_{max} 279 nm (log ε = 3.80); IR (KBr) ν_{max} (cm^{-1}) 3390 (OH), 1730 (OCO), 1586, 1460; ^{1}H-NMR, δ 3.40 and 4.44 (AB, 8H, *J* = 13.0 Hz, ArCH_2Ar), 3.70 (s, 4H, OCH_2CH_2O), 3.87 (t, 4H, CO$_2$CH$_2$CH_2O), 4.52 (t, 4H, CO$_2$CH_2CH$_2$O), 4.78 (s, 4H, ArOCH_2CO_2), 6.63 (t, 2H, Ar*H*), 6.77 (t, 2H, Ar*H*), 6.92 (d, 4H, Ar*H*), 7.03 (d, 4H, Ar*H*), 7.78 (s, 2H, O*H*); ^{13}C-NMR δ 31.43 (ArCH$_2$Ar), 63.98 (CO$_2$CH$_2$CH$_2$O), 68.74 (CO$_2$CH$_2$CH$_2$O), 70.82 (OCH$_2$CH$_2$O), 72.43 (ArOCH$_2$), 119.16, 125.61, 128.04, 128.42, 129.12, 133.24, 152.42, 152.73 (Ar*C*), 168.88 (O*C*O); FAB-MS: m/e 654 (M$^+$); Anal. Calcd for $C_{38}H_{38}O_{10}$: C, 69.71; H, 5.85. Found: C, 69.88; H, 5.91.

25,27 - Dihydroxy - 26,28- (2',16'- dioxo - 3',6',9',12',15'- pentaoxaheptadecylene)dioxycalix[4]arene (3h): reaction time 20 h; yield 37 %; mp 215 ~ 7°C; UV-VIS (CHCl$_3$) λ_{max} 282 nm (log ε = 3.94); IR (KBr) ν_{max} (cm^{-1}) 3370 (OH), 1735 (OCO), 1578, 1453; ^{1}H-NMR δ 3.39 and 4.44 (AB, 8H, *J* = 13.0 Hz, ArCH_2Ar), 3.64 and 3.71 (A_2B_2, 8H, CO$_2$CH$_2$CH$_2$OCH_2CH_2O), 3.90 (t, 4H, CO$_2$CH$_2$CH_2O), 4.48 (t, 4H, CO$_2$CH_2CH$_2$O), 4.77 (s, 4H, ArOCH_2O), 6.65 (t, 2H, Ar*H*), 6.73 (t, 2H, Ar*H*), 6.92 (d, 4H, Ar*H*), 7.04 (d, 4H, Ar*H*), 7.72 (s, 2H, O*H*); ^{13}C-NMR δ 31.38 (ArCH$_2$Ar), 64.65 (CO$_2$CH$_2$CH$_2$O), 68.81 (CO$_2$CH$_2$CH$_2$O), 70.74 (CO$_2$CH$_2$CH$_2$OCH$_2$CH$_2$O), 71.02 (CO$_2$CH$_2$CH$_2$OCH$_2$CH$_2$O), 72.33 (ArOCH$_2$), 119.17, 125.62, 128.11, 128.41, 129.10, 133.16, 152.07, 152.74 (Ar*C*), 168.72 (O*C*O); FAB-MS: m/e 697 ([M-1]$^+$); Anal. Calcd for $C_{40}H_{42}O_{11}$: C, 68.75; H, 6.06. Found: C, 68.29; H, 6.04.

General procedure for the selective nitration of calix[4]crowns containing an ester group:

To a solution of 0.5 mmol of calix[4]crown **3e~h** in a mixture of CH_2Cl_2 (50 ml) and glacial acetic acid (36 equiv.) was added 65% HNO_3 (50 equiv.) at 0°C, the reaction mixture was stirred for 30 minutes at this temperature, then poured into water (50 ml). The organic layer was washed with water (2 × 50 ml) and brine (50 ml), dried with $MgSO_4$, then chromatographed on a silica gel column using chloroform as eluent to afford a white solid which was recrystallized from $CHCl_3/CH_3OH$ to give pure compound **4a~d**.

11,23-Dinitro-25,27-dihydroxy-26,28-(3',6'-dioxa-2',7'-dioxooctylene)dioxycalix[4]arene (4a): yield 33 %; mp >300°C; UV-VIS ($CHCl_3$) λ_{max} 327 nm (log ε = 4.30); IR (KBr) ν_{max} (cm^{-1}) 3270 (OH), 1725 (OCO), 1580, 1495 and 1320 (NO_2); ^{1}H-NMR (DMSO-d_6) δ 3.77 and 4.17 (AB, 8H, *J* = 13.0 Hz, ArC*H*$_2$Ar), 4.57 (s, 4H, OC*H*$_2$C*H*$_2$O), 4.81 (s, 4H, ArOC*H*$_2$CO$_2$), 6.92 (t, 2H, Ar*H*), 7.25 (d, 4H, Ar*H*), 8.28 (s, 4H, ArC(NO_2)C*H*), 9.44 (s, 2H, O*H*); ^{13}C-NMR (DMSO-d_6) δ 30.06 (Ar*C*H$_2$Ar), 62.61 (OCH$_2$*C*H$_2$O), 72.62 (ArO*C*H$_2$), 124.53, 126.19, 128.47, 129.65, 132.59, 139.36, 150.45, 159.19 (Ar*C*), 167.17 (O*C*O); FAB-MS: m/e 655 ([M-1]$^+$); Anal. Calcd for $C_{34}H_{28}N_2O_{12}$: C, 62.19; H, 4.30; N, 4.27. Found: C, 62.00; H, 4.59; N, 3.94.

11,23-Dinitro-25,27-dihydroxy-26,28-(2',10'-dioxo-3',6',9'-trioxaundecylene)dioxycalix[4]arene (4b): yield 37 %; mp 281°C (dec.); UV-VIS ($CHCl_3$) λ_{max} 327 nm (log ε = 4.26); IR (KBr) ν_{max} (cm^{-1}) 3340 (OH), 1720(OCO), 1580, 1500 and 1320 (NO_2); ^{1}H-NMR δ 3.52 and 4.43 (AB, 8H, *J* = 13.0 Hz, ArC*H*$_2$Ar), 3.86 (t, 4H, CO$_2$CH$_2$C*H*$_2$O), 4.57 (t, 4H, CO$_2$C*H*$_2$CH$_2$O), 4.82 (s, 4H, ArOC*H*$_2$CO$_2$), 6.89 (t, 2H, Ar*H*), 7.03 (d, 4H, Ar*H*), 8.00 (s, 4H, ArC(NO_2)C*H*), 8.80 (s, 2H, O*H*); ^{13}C-NMR δ 31.26 (ArCH$_2$Ar), 64.95 (CO$_2$*C*H$_2$CH$_2$O), 69.21 (CO$_2$CH$_2$*C*H$_2$O), 72.38 (ArO*C*H$_2$), 124.62, 126.25, 128.18, 129.83, 131.98, 139.92, 152.61, 158.74 (Ar*C*), 169.01 (O*C*O); FAB-MS: m/e 699 ([M-1]$^+$); Anal. Calcd for $C_{36}H_{32}N_2O_{13}$·0.9$CHCl_3$: C, 54.95; H, 4.10; N, 3.47; Cl, 11.85. Found: C, 54.88; H, 4.33; N, 3.57; Cl, 11.87.

11,23-Dinitro-25,27-dihydroxy-26,28- (2',13'-dioxo- 3',6',9',12'- tetraoxatetradecylene)dioxycalix[4]-arene (4c): yield 50 %; mp 259°C (dec.); UV-VIS ($CHCl_3$) λ_{max} 328 nm (log ε = 4.29); IR (KBr) ν_{max} (cm^{-1}) 3230 (OH), 1730 (OCO), 1570, 1495 and 1320 (NO_2); ^{1}H-NMR, δ 3.51 and 4.47 (AB, 8H, *J* = 13.0 Hz, ArC*H*$_2$Ar), 3.71 (s, 4H, OC*H*$_2$C*H*$_2$O), 3.86 (t, 4H, CO$_2$CH$_2$C*H*$_2$O), 4.56 (t, 4H, CO$_2$C*H*$_2$CH$_2$O), 4.83 (s, 4H, ArOC*H*$_2$CO$_2$), 6.91 (t, 2H, Ar*H*), 7.08 (d, 4H, Ar*H*), 7.98 (s, 4H, ArC(NO_2)C*H*), 9.16 (s, 2H, O*H*); ^{13}C-NMR δ 31.33 (Ar*C*H$_2$Ar), 63.72 (CO$_2$*C*H$_2$CH$_2$O), 68.85 (CO$_2$CH$_2$*C*H$_2$O), 70.60 (OCH$_2$*C*H$_2$O), 72.17 (ArO*C*H$_2$), 124.55, 126.28, 128.18, 129.80, 132.13, 139.81, 152.35, 158.93 (Ar*C*), 169.03 (O*C*O); FAB-MS: m/e 743 ([M-1]$^+$); Anal. Calcd for $C_{38}H_{36}N_2O_{14}$: C, 61.28; H, 4.87; N, 3.76. Found: C, 61.03; H, 4.95; N, 3.73.

11,23-Dinitro-25,27- dihydroxy- 26,28- (2',16'- dioxo- 3',6',9',12',15'- pentaoxaheptadecylene)dioxy-calix[4]arene (4d): yield 20 %; mp 216 ~ 7°C; UV-VIS ($CHCl_3$) λ_{max} 328 nm (log ε = 4.26); IR (KBr) ν_{max} (cm^{-1}) 3310 (OH), 1730 (OCO), 1580, 1500 and 1320 (NO_2); ^{1}H-NMR δ 3.53 and 4.45 (AB, 8H, J = 13.0 Hz, ArCH_2Ar), 3.68 and 3.70 (A_2B_2, 8H, $CO_2CH_2CH_2OCH_2CH_2O$), 3.89 (t, 4H, $CO_2CH_2CH_2O$), 4.50 (t, 4H, $CO_2CH_2CH_2O$), 4.81 (s, 4H, $ArOCH_2O$), 6.92 (t, 2H, ArH), 7.06 (d, 4H, ArH), 8.02 (s, 4H, $ArC(NO_2)CH$), 9.02 (s, 2H, OH); ^{13}C-NMR δ 31.27 (ArCH_2Ar), 64.83 (CO_2CH_2), 68.77 ($CO_2CH_2CH_2O$), 70.61 ($CO_2CH_2CH_2OCH_2CH_2O$), 71.05 ($CO_2CH_2CH_2OCH_2CH_2O$), 72.25 ($ArOCH_2$), 124.57, 126.36, 128.30, 129.83, 131.98, 139.89, 151.86, 158.99 (ArC), 168.60 (OCO); FAB-MS: m/e 787 ($[M-1]^+$); Anal. Calcd for $C_{40}H_{40}N_2O_{15}$: C, 60.91; H, 5.11; N, 3.55. Found: C, 60.92; H, 5.22; N, 3.25.

11-Nitro-27-hydroxy- 23,25-dione-26,28- (2',10'- dioxo- 3',6',9'- trioxaundecylene)dioxycalix[4]arene (5): as a by-product of **4b**, yield 11 %; mp 190°C (dec.); UV-VIS ($CHCl_3$) λ_{max} 324 nm (log ε = 4.13); IR (KBr) ν_{max} (cm^{-1}) 3270 (OH), 1720, 1700 and 1635 (CO), 1593, 1570, 1495 and 1320 (NO_2); ^{1}H-NMR δ 3.44, 3.49, 3.81 and 4.28 (two AB, 8H, J = 13.7 Hz, ArCH_2Ar), 3.83 (br, 4H, $CO_2CH_2CH_2O$), 4.46 (br, 4H, $CO_2CH_2CH_2O$), 4.40 and 4.74 (AB, 4H, J = 15.1 Hz, $ArOCH_2CO_2$), 6.65 (s, 2H, C=CHCO), 6.96 ~ 6.74 (m, 6H, ArH), 7.86 (s, 1H, OH), 8.06 (s, 2H, $ArC(NO_2)CH$); ^{13}C-NMR δ 30.33, 33.38 (ArCH_2Ar), 65.03 ($CO_2CH_2CH_2O$), 68.76 ($CO_2CH_2CH_2O$), 71.10 ($ArOCH_2$), 124.42, 125.13, 128.28, 129.56, 129.83, 130.01, 131.49, 132.82, 139.59, 146.88, 153.31, 158.96 (ArC), 168.21 (OCO), 185.64, 188.02 (C=O); FAB-MS: m/e 669 (M^+); Anal. Calcd for $C_{36}H_{31}NO_{12}$: C, 64.57; H, 4.67; N, 2.09. Found: C, 64.19; H, 4.78; N, 2.26.

5,17-Bis-tert-butyl-11,23-dinitro-25,27-dihydroxy-26,28-(2',13'-dioxo-3',6',9',12'-tetraoxatetradecyl-ene)dioxycalix[4]arene (6): To a solution of 0.5 mmol of calix[4]crown **3c** in a mixture of CH_2Cl_2 (50 ml) and glacial acetic acid (50 equiv.) was added 65 % HNO_3 (80 equiv.) at room temperature, the reaction mixture was stirred for 30 minutes at this temperature, then poured into water (50 ml). The organic layer was washed with water (2 × 50 ml) and brine (50 ml), dried with $MgSO_4$, then chromatographed on a silica gel column using chloroform as eluent to afford a white solid which was crystallized from $CHCl_3/CH_3OH$ to give pure compound **6**. Yield: 40 %; mp 282°C (dec.); UV-VIS ($CHCl_3$) λ_{max} 329 nm (log ε = 4.22); IR (KBr) ν_{max} (cm^{-1}) 3310 (OH), 1730 (OCO), 1580, 1500 and 1320 (NO_2); ^{1}H-NMR δ 1.19 (s, 18H, $C(CH_3)_3$), 3.48 and 4.53 (AB, 8H, J = 13.0 Hz, ArCH_2Ar), 3.71 (s, 4H, OCH_2CH_2O), 3.83 (t, 4H, $CO_2CH_2CH_2O$), 4.54 (t, 4H, $CO_2CH_2CH_2O$), 4.91 (s, 4H, $ArOCH_2CO_2$), 7.12 (s, 4H, ArH), 7.92 (s, 4H, $ArC(NO_2)CH$), 9.25 (s, 2H, OH); ^{13}C-NMR δ 31.16 ($C(CH_3)_3$), 31.86 (ArCH_2Ar), 34.29 ($C(CH_3)_3$), 63.93 ($CO_2CH_2CH_2O$), 68.83 ($CO_2CH_2CH_2O$), 70.74 (OCH_2CH_2O), 71.89 ($ArOCH_2$), 124.47, 126.57, 128.70, 132.05, 140.12, 149.02, 150.97,

158.49 (Ar*C*), 169.95 (O*C*O); FAB-MS: m/e 855 ($[M-1]^+$); Anal. Calcd for $C_{46}H_{52}N_2O_{14} \cdot 3/4CHCl_3$: C, 59.33; H, 5.62; N, 2.96, Cl, 8.43. Found: C, 59.31; H, 5.66; N, 3.11; Cl, 8.43.

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