

# Synthesis and nitration of calix[4](aza) crowns

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Calix[4](aza) crowns containing amide groups 3a—d were synthesized by the reactions of calix[4]arene (1a) or *p*-*tert*-butylcalix[4]arene (1b) with *N, N'*-ethylenebis(2-chloroacetamide) (2a) or *N, N'*-1,2-phenylenebis(2-chloroacetamide) (2b) by one step procedure in yields of 85—90%. Calix[4](aza) crowns 4a—b could be obtained by the reduction of 3a—b with LiAlH<sub>4</sub> in yields of 51 and 67%, respectively. The nitration of 3a or 3c afforded new chromogenic calix[4]arenes 5a bearing two nitrophenol moieties and 5c bearing one nitrophenol and one quinone moiety, respectively. The *ipso*-nitrations of 3b and 3d were also studied. Both gave the products containing one nitrophenol and one quinone moiety. Moreover, a very interesting calix[4]arene derivative 5d containing one cyclohexadienone moiety was also separated as the main product when 3d was *ipso*-nitrated.

**Keywords** Calix[4](aza) crown, calixarene, nitration, reduction

## Introduction

Calixarenes as a kind of important host molecules have attracted considerable interests in the field of supramolecular chemistry.<sup>1</sup> They can not only form selective inclusion complexes with cations, anions or small neutral molecules, but also be easily functionalized both at the phenolic OH groups (lower rim) and the *para* positions of the phenol rings (upper rim) to afford new host molecules.

Calixcrowns, derivatives of calixarene bridged by crown ether chain intramolecularly or intermolecularly, are one of the most important calixarene derivatives. Since the first example of calixcrowns was reported in 1983,<sup>2</sup> extensive work has been devoted to the synthesis and properties of calixcrowns for their practical applica-

tions in ionic and molecular recognition, catalysis, ion-selective electrodes preparation and supported liquid membranes.<sup>3</sup> In recent years, studies on chromogenic calixcrowns have also received considerable attention for their potential applications in optical sensors.<sup>4</sup>

The synthesis of *p*-nitrocalixarenes could be carried out by the direct nitration of unsubstituted *para* position,<sup>4c,5</sup> *ipso*-substitution of the *tert*-butyl groups,<sup>4c,6,7</sup> replacement of *p*-sulfonate moieties<sup>8</sup> or nitroso compounds.<sup>5a</sup> Otherwise, calix[4]arenes having one or two nitro groups at the upper rim have also been produced by a stepwise synthesis.<sup>9</sup> However, the nitration products of calix(aza)crowns, to our knowledge, have not been reported. In this paper, new synthetic method of calix[4](aza) crown containing amide groups was described. Their reduction, nitration and *ipso*-nitration were also reported.

## Results and discussion

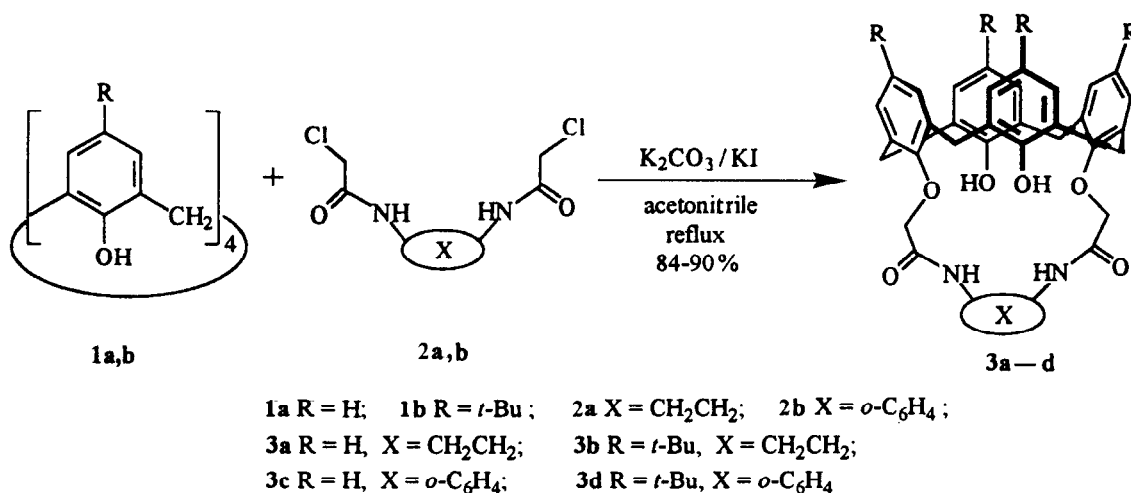
### *Synthesis of calix[4](aza) crowns containing amide groups*

The method to synthesize single bridged calix[4](aza) crowns containing amide groups at the lower rim has been reported, which utilized the condensation of *syn*-1,3-diacetic derivatives of calix[4]arene and various diamines.<sup>10</sup> Although the yield of this reaction is high, several steps are required starting from calix[4]arene. Herein, we wish to disclose a one-step reaction from calix[4]arene to 1,3-distal calix(aza)crown 3a and its similar compounds 3b—d in good yields.

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Scheme 1



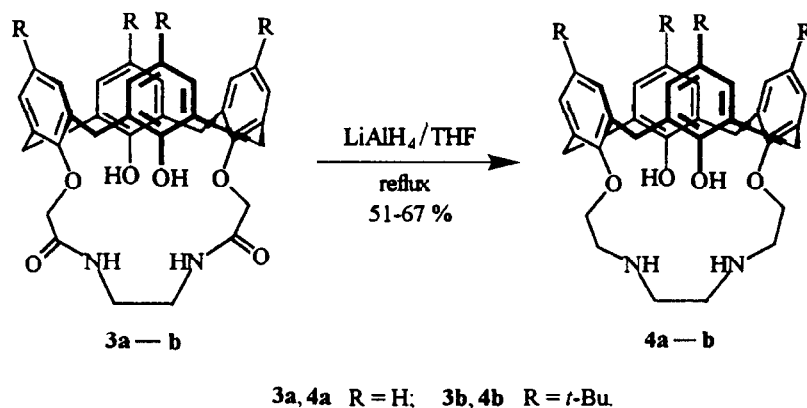
Treating calix[4]arene (**1a**) with *N,N'*-ethylenebis(2-chloroacetamide) (**2a**) in refluxing acetonitrile for 24 h under N<sub>2</sub> in the presence of anhydrous K<sub>2</sub>CO<sub>3</sub> and KI, the corresponding single bridged calix[4]-(aza)crown containing amide groups **3a** was isolated in 87% yield. According to the similar method, the compounds **3b-d** were also conveniently synthesized by the reaction of calix[4]arene (**1a**) or *p-tert*-butylcalix[4]arene (**1b**) with **2a** or *N,N'*-1,2-phenylenebis(2-chloroacetamide) (**2b**), respectively.

The <sup>1</sup>H NMR spectra of compounds **3a-d** display a pair of doublets for the methylene protons between aromatic rings, a singlet for the methylene protons linking to the α-position of carbonyl groups, which show that the **3a-d** are all 1,3-distally-bridged calix[4]arenes with cone conformation. The results were also confirmed by the <sup>13</sup>C NMR, IR, MS spectra and elemental analyses.

#### Synthesis of calix[4](aza)crowns

Ethylene diamide 1,3-distally-bridged calix[4]-(aza)crowns **3a-d** can be reduced by LiAlH<sub>4</sub> in THF to calix[4]-(aza)crowns **4a-b**, in yield of 51% and 67%, respectively. Their structures have been determined with <sup>1</sup>H NMR, <sup>13</sup>C NMR, FAB-MS, IR spectra and elemental analyses. Comparing with the compounds **3a** and **3b**, no absorption peak of carbonyl vibration was found in the IR spectra of **4a** and **4b**, and there is no signal above δ 160 for the carbonyl carbons in the <sup>13</sup>C NMR spectra. In their <sup>1</sup>H NMR, the signal of methylene protons linking to oxygen atoms shifts upwards to about δ 4.2 and changes from a singlet to a triplet. These two reduction compounds exist in cone conformation, which is indicated by a pair of doublets for the methylene protons between aromatic rings in their <sup>1</sup>H NMR.

Scheme 2



*Nitration or ipso-nitration of calix(aza)crowns containing amide groups*

The *para* positions of phenol rings have been demonstrated to be much more reactive than those of alkoxybenzene rings, as for instances illustrated in the selective nitration and *ipso*-nitration taking place exclusively at the *para* position of the phenolic units.<sup>4c,6,7</sup> Considering that compounds **3a**—**d** containing two phenolic units, they can be easily selectively nitrated or *ipso*-nitrated. Thus, when calix[4](aza)crown **3a** was treated with an excess of 65% HNO<sub>3</sub> in CH<sub>2</sub>Cl<sub>2</sub> in the presence of glacial acetic acid for 0.5 h, a dinitro-substituted product **5a** was isolated in 70% yield.

In the IR spectrum of **5a**, two very strong absorption peaks at 1510 and 1325 cm<sup>-1</sup> demonstrate the presence of nitro groups. In its <sup>1</sup>H NMR spectrum, owing to the electron withdrawing effect of nitro groups, the protons in the aromatic rings shift downward to δ 8.09, and the protons of OH groups shift downward to δ 9.26. A pair of doublets for methylene protons between aromatic rings indicates that the compound **5a** is a 1,3-distally-bridged calix[4]arene derivative with cone conformation.

Under the same condition, compound **5c** containing one nitro phenol moiety and one quinone moiety, instead of dinitro-substituted compound, was unexpectedly obtained when *o*-phenylenediamide bridged calix[4]arene **3c** was used as a substrate.

The <sup>1</sup>H NMR spectrum of **5c** shows two pairs of doublets for the methylene protons between the aromatic rings and a pair of doublets for the methylene protons linking to the α-position of carbonyl groups, which suggests that **5c** has only one plane of symmetry. The <sup>13</sup>C NMR spectrum of **5c** showed 15 signals between δ 120—160 for the aromatic carbons and two signals at δ 187.54 and δ 187.80 for the quinone carbonyl carbons. In addition, absorption at 1640 cm<sup>-1</sup> for the quinone carbonyl groups and 3320 cm<sup>-1</sup> for the phenol hydroxyl groups were observed in its IR spectrum. These data are all consistent with the structure.

Upon treating *p-tert*-butylcalix[4]arene derivative **3b** with an excess 65% HNO<sub>3</sub> in the presence of glacial acetic acid in CH<sub>2</sub>Cl<sub>2</sub> for 0.5 h, two *ipso*-nitrated products **5b** and **5b'** were isolated in 8% and 20% yields, respectively, by flash chromatography of the reaction mixture. The structure of **5b** is similar to **5a**, and the

structure of **5b'** is similar to that of **5c**.

**Table 1** Nitration or *ipso*-nitration of compounds **3**

Reactant	Product (Yield %)
<b>3a</b>	<b>5a</b> (70)
<b>3b</b>	<b>5b</b> (8), <b>5b'</b> (25)
<b>3c</b>	<b>5c</b> (68)
<b>3d</b>	<b>5d</b> (36), <b>5d'</b> (25)

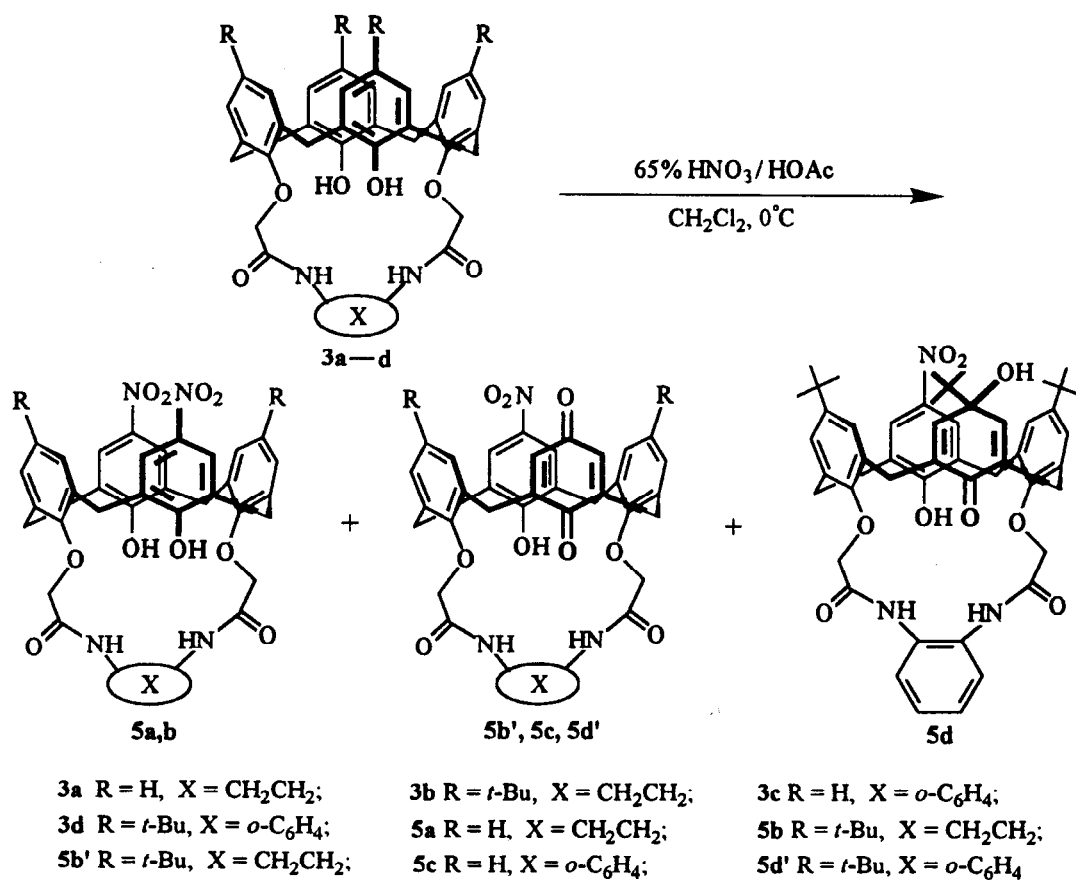
Under the same condition, the product **5d'** containing one *ipso*-nitrated phenol moiety and one quinone moiety was separated in 25% yield by the *ipso*-nitration of **3d**. In addition, a very interesting compound **5d** containing one *ipso*-nitrated phenol moiety and one cyclohexadienone moiety was also obtained in 36% yield. The mass spectrometry, elemental analysis and NMR studies of **5d** were entirely in accord with this structure. The <sup>1</sup>H NMR spectrum of **5d** shows two singlets for *tert*-butyl groups at δ 1.19 (18 H) and δ 1.02 (9 H), two singlets for hydroxyl groups (δ 8.90 and 3.00), two pairs of doublets for methylene protons (δ 4.21/3.58 and 4.16/3.02 with geminative coupling, 13.2 and 11.8 Hz), a singlet for the protons in the cyclohexadienone unit (δ 7.00), and a singlet for the protons in the nitro phenol unit (δ 8.06). The <sup>13</sup>C NMR spectrum of **5d** shows only one signal for the carbonyl (δ 184.70) except for a signal of the amide group (δ 166.37), two groups of signals for *tert*-butyl groups (δ 34.46/31.24 and 29.85/25.57).

The nitration or *ipso*-nitration of calix[4](aza)crowns **3a**—**d** is accompanied with oxidation and the mechanism may be as follows:<sup>11</sup>

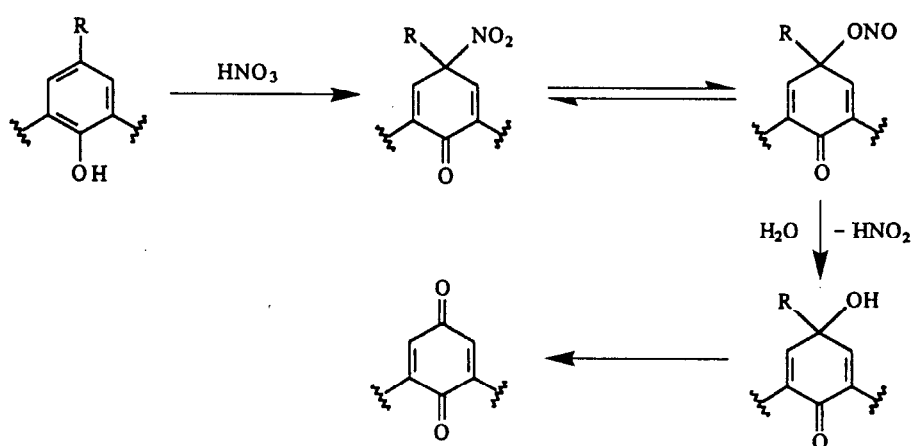
The incompletely oxidized production of **5d** confirms strongly this mechanism and to the best of our knowledge, **5d** is the first structure of calixarene containing cyclohexadienone moiety. Böhmer and co-workers have reported that the *ipso*-nitration of *tert*-butylcalix[4]arene 1,3-diethers could provide the products with two 6-nitro-cyclohexa-2,4-dienone units by attack in the *ortho* position of the phenolic hydroxy group.<sup>7</sup> However, we can not obtain this kind of products in our experiment but different kind of oxidized or nitrated product. As well known, oxidation and nitration are a pair of competitive reactions in this condition. Why do different calix[4](aza)crowns produce different kinds of nitrated or *ipso*-nitrated production? We consider that it may be due to the difference of reaction activity of phenolic rings

caused by the bridged amide groups.

Scheme 3



Scheme 4



In addition, it should be indicated that all of the nitrated or *ipso*-nitrated compounds exist mainly in cone conformation, including those containing one quinone moiety or one cyclohexadienone moiety. Ungaro and co-

workers have investigated that the conformation of calix[4]diquinones and demonstrated that quinone moiety in calix[4]arenes could invert freely in CDCl<sub>3</sub> at room temperature.<sup>12</sup> However, we have found that the nitrated or

*ipso*-nitrated calix[4](aza) crowns containing amide groups and quinone moiety or cyclohexadienone moiety are conformationally stable in CDCl<sub>3</sub> at room temperature, which can be deduced from that the AB system of methylene protons between aromatic rings in <sup>1</sup>H NMR and the chemical shifts about δ 31 for methylene carbons between aromatic rings in <sup>13</sup>C NMR.<sup>13</sup> Comparing the difference of these calix[4](aza)crowns with calix[4]-diquinones synthesized by Ungaro *etc.*, we think that the hydrogen bonding between the amide group and the quinone moiety in these calix[4](aza) crowns makes their conformation stable.

## Experimental

Melting points were uncorrected. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded in CDCl<sub>3</sub> at 200 MHz on a Varian unit-200 spectrometer. TMS was used as internal standard. UV-VIS spectra were taken on a Hitachi-340 spectrophotometer. FAB-MS spectra were obtained using a KYKY-ZHT-5 mass spectrometer. IR spectra were recorded on a Perkin-Elmer 782 spectrometer. All elemental analyses were carried out by the Analytical Laboratory of the Institute.

CH<sub>3</sub>CN was dried over molecular sieves (0.3 nm), other chemicals were of reagent grade and used without further purification. Calix[4]arene (**1a**)<sup>14</sup> and *p*-*tert*-butylcalix[4]arene (**1b**)<sup>15</sup> were prepared as described in the literature. Compounds **2a** and **2b** were prepared from ethylenediamine or *o*-phenylenediamine with chloroacetyl chloride, respectively, according to the published procedure.<sup>16</sup>

### General procedure for the synthesis of calix[4](aza)-crowns containing amide groups (**3a—d**)

A mixture of calix[4]arene (**1a**) or *p*-*tert*-butylcalix[4]arene (**1b**) (1.5 mmol), *N,N'*-ethylenedibis-(2-chloroacetamide) (**2a**) or *N,N'*-1,2-phenylenedibis-(2-chloroacetamide) (**2b**) (2 mmol), anhydrous K<sub>2</sub>CO<sub>3</sub> (1.5 mmol) and KI (3 mmol) in acetonitrile (50 mL) was refluxed for 16—24 h under N<sub>2</sub>. After the solvent was removed under reduced pressure, the residue was dissolved in chloroform (50 mL) and then filtered to remove inorganic salts. The filtrate was concentrated to give a white solid, which was recrystallized from chloroform and methanol to afford products **3a—d**.

**3a** Reaction time 24 h. Yield: 87%. mp > 310°C. ν<sub>max</sub> (KBr): 3340, 1675 (CO), 1520, 1450 cm<sup>-1</sup>. δ<sub>H</sub>: 8.51 (br, 2H, NH), 8.34 (s, 2H, OH), 7.10 (d, *J* = 7.1 Hz, 4H, ArH), 7.02 (d, *J* = 7.1 Hz, 4H, ArH), 6.87 (t, *J* = 7.1 Hz, 2H, ArH), 6.73 (t, *J* = 7.1 Hz, 2H, ArH), 4.58 (s, 4H, ArOCH<sub>2</sub>), 4.15 (d, *J* = 13.4 Hz, 4H, ArCH<sub>2</sub>Ar), 3.70 (d, *J* = 6.1 Hz, 4H, NCH<sub>2</sub>), 3.53 (d, *J* = 13.4 Hz, 4H, ArCH<sub>2</sub>Ar). δ<sub>C</sub>: 167.51 (CO), 151.90, 148.85, 132.91, 129.53, 129.13, 127.31, 126.96, 120.61 (ArC), 74.60 (ArOCH<sub>2</sub>), 39.22 (NCH<sub>2</sub>), 31.30 (ArCH<sub>2</sub>Ar). *m/z* (FAB): 563 [(M - 1)<sup>+</sup>]. Anal. C<sub>34</sub>H<sub>32</sub>N<sub>2</sub>O<sub>6</sub>. Calcd: C, 72.32; H, 5.71; N, 4.96. Found: C, 72.25; H, 5.65; N, 5.00.

**3b** Reaction time 18 h. Yield 85%. mp 270°C (dec.). ν<sub>max</sub> (KBr): 3340, 1680 (CO), 1525; 1470 cm<sup>-1</sup>. δ<sub>H</sub>: 8.58 (br, 2H, NH), 8.29 (s, 2H, OH), 7.06 (s, 8H, ArH), 4.53 (s, 4H, ArOCH<sub>2</sub>), 4.13 (d, *J* = 13.2 Hz, 4H, ArCH<sub>2</sub>Ar), 3.66 (d, *J* = 5.1 Hz, 4H, NCH<sub>2</sub>), 3.48 (d, *J* = 13.2 Hz, 4H, ArCH<sub>2</sub>Ar), 1.26 (s, 18H, C(CH<sub>3</sub>)<sub>3</sub>), 1.14 (s, 18H, C(CH<sub>3</sub>)<sub>3</sub>). δ<sub>C</sub>: 167.74 (CO), 149.51, 148.77, 147.10, 143.06, 132.55, 126.70, 126.21, 125.96 (ArC), 74.57 (ArOCH<sub>2</sub>), 39.19 (NCH<sub>2</sub>), 34.28, 33.81 (C(CH<sub>3</sub>)<sub>3</sub>), 31.96 (ArCH<sub>2</sub>Ar), 31.49 and 31.05 (C(CH<sub>3</sub>)<sub>3</sub>). *m/z* (FAB): 787 [(M - 1)<sup>+</sup>]. Anal. C<sub>50</sub>H<sub>64</sub>N<sub>2</sub>O<sub>6</sub>. Calcd: C, 76.11; H, 8.18; N, 3.55. Found: C, 75.82; H, 8.30; N, 3.65.

**3c** Reaction time 22 h. Yield: 84%. mp > 310°C. ν<sub>max</sub> (KBr): 3350, 3250, 1680 (CO), 1430 cm<sup>-1</sup>. δ<sub>H</sub>: 9.11 (s, 2H, NH), 8.28 (dd, *J* = 6.1, 3.3 Hz, 2H, ArH), 8.07 (s, 2H, OH), 7.28 (dd, *J* = 6.1, 3.3 Hz, 2H, ArH), 7.10 (d, *J* = 7.6 Hz, 4H, ArH), 7.05 (d, *J* = 7.6 Hz, 4H, ArH), 6.91 (t, *J* = 7.6 Hz, 2H, ArH), 6.73 (t, *J* = 7.6 Hz, 2H, ArH), 4.75 (s, 4H, ArOCH<sub>2</sub>), 4.17 (d, *J* = 13.3 Hz, 4H, ArCH<sub>2</sub>Ar), 3.54 (d, *J* = 13.3 Hz, 4H, ArCH<sub>2</sub>Ar). δ<sub>C</sub>: 166.24 (CO), 152.00, 149.80, 132.92, 129.91, 128.85, 127.43, 127.37, 127.03, 125.70, 124.28, 120.56 (ArC), 75.23 (ArOCH<sub>2</sub>), 31.73 (ArCH<sub>2</sub>Ar). *m/z* (FAB): 611 [(M - 1)<sup>+</sup>]. Anal. C<sub>38</sub>H<sub>32</sub>N<sub>2</sub>O<sub>6</sub>. Calcd: C, 74.49; H, 5.27; N, 4.57. Found: C, 74.25; H, 5.40; N, 4.49.

**3d** Reaction time 16 h. Yield: 90%. mp 261—263°C. ν<sub>max</sub> (KBr): 3360, 3200, 1690 (CO),

1 470  $\text{cm}^{-1}$ .  $\delta_{\text{H}}$ : 9.17(s, 2H, NH), 8.25(dd,  $J = 5.7$ , 3.4 Hz, 2H, ArH), 7.86(s, 2H, OH), 7.25(dd,  $J = 5.7$ , 3.4 Hz, 2H, ArH), 7.06(s, 4H, ArH), 7.05(s, 4H, ArH), 4.70(s, 4H, ArOCH<sub>2</sub>), 4.17(d,  $J = 13.7$  Hz, 4H, ArCH<sub>2</sub>Ar), 3.48(d,  $J = 13.7$  Hz, 4H, ArCH<sub>2</sub>Ar), 1.23(s, 18H, C(CH<sub>3</sub>)<sub>3</sub>), 1.15(s, 18H, C(CH<sub>3</sub>)<sub>3</sub>).  $\delta_{\text{C}}$ : 166.41(CO), 149.69, 148.81, 147.93, 143.16, 132.61, 127.50, 126.88, 126.58, 125.57, 125.56, 124.17(ArC), 74.99(ArOCH<sub>2</sub>), 34.28, 33.90(C(CH<sub>3</sub>)<sub>3</sub>), 32.53(ArCH<sub>2</sub>Ar), 31.55, 31.08(C(CH<sub>3</sub>)<sub>3</sub>).  $m/z$ (FAB): 835 [(M - 1)<sup>+</sup>]. Anal. C<sub>54</sub>H<sub>64</sub>N<sub>2</sub>O<sub>6</sub>. Calcd: C, 77.48; H, 7.71; N, 3.35. Found: C, 77.80; H, 7.67; N, 3.37.

*General procedure for the synthesis of calix[4](aza)-crowns (4a—b)*

To a solution of LiAlH<sub>4</sub> (20 mmol) in THF (10 mL) was added dropwise a solution of calix[4](aza)-crown containing amide groups **3a** or **3b** (1 mmol) in THF (30 mL), then this mixture was refluxed for 8 h. After the solvent was removed, the residue was slowly added to water (30 mL) in an ice-water bath (**CAUTION!**), and then extracted with chloroform (100 mL). The extract was washed with water, dried with anhydrous Na<sub>2</sub>SO<sub>4</sub>, concentrated and separated by silica gel column chromatography eluted with chloroform and methanol (20:1 *v/v*) to give the product as a white solid.

**4a** Yield 51%. mp 260°C (decomp.).  $\nu_{\text{max}}$  (KBr): 3290, 1450  $\text{cm}^{-1}$ .  $\delta_{\text{H}}$ : 8.86(s, 2H, OH), 7.05(d,  $J = 7.6$  Hz, 4H, ArH), 7.01(d,  $J = 7.6$  Hz, 4H, ArH), 6.86(t,  $J = 7.6$  Hz, 2H, ArH), 6.66(t,  $J = 7.6$  Hz, 2H, ArH), 4.32(d,  $J = 13.0$  Hz, 4H, ArCH<sub>2</sub>Ar), 4.25(t,  $J = 4.0$  Hz, 4H, ArOCH<sub>2</sub>), 3.43(d,  $J = 13.0$  Hz, 4H, ArCH<sub>2</sub>Ar), 3.29(t,  $J = 4.0$  Hz, 4H, ArOCH<sub>2</sub>CH<sub>2</sub>), 3.12(s, 4H, NCH<sub>2</sub>CH<sub>2</sub>N).  $\delta_{\text{C}}$ : 152.66, 150.62, 134.07, 129.08, 128.49, 128.12, 126.07, 119.60(ArC), 75.40(ArOCH<sub>2</sub>), 47.20(NCH<sub>2</sub>CH<sub>2</sub>O), 45.81(NCH<sub>2</sub>CH<sub>2</sub>N), 31.58(ArCH<sub>2</sub>Ar).  $m/z$ (FAB): 535 [(M - 1)<sup>+</sup>]. Anal. C<sub>34</sub>H<sub>36</sub>N<sub>2</sub>O<sub>4</sub>. Calcd: C, 76.07; H, 6.76; N, 5.22. Found: C, 75.35; H, 6.54; N, 5.29.

**4b** Yield 67%. mp 227—228°C.  $\nu_{\text{max}}$  (KBr): 3300, 1470  $\text{cm}^{-1}$ .  $\delta_{\text{H}}$ : 8.92(s, 2H, OH),

7.06(s, 4H, ArH), 7.01(s, 4H, ArH), 4.31(d,  $J = 12.0$  Hz, 4H, ArCH<sub>2</sub>Ar), 4.20(t,  $J = 4.0$  Hz, 4H, ArOCH<sub>2</sub>), 3.39(d,  $J = 12.0$  Hz, 4H, ArCH<sub>2</sub>Ar), 3.25(t,  $J = 4.0$  Hz, 4H, ArOCH<sub>2</sub>CH<sub>2</sub>), 3.09(s, 4H, NCH<sub>2</sub>CH<sub>2</sub>N), 2.80(br, 2H, NH), 1.22(s, 18H, C(CH<sub>3</sub>)<sub>3</sub>), 1.18(s, 18H, C(CH<sub>3</sub>)<sub>3</sub>).  $\delta_{\text{C}}$ : 150.31, 148.86, 147.67, 141.95, 133.55, 127.42, 125.94, 125.51(ArC), 75.40(ArOCH<sub>2</sub>), 46.83(NCH<sub>2</sub>CH<sub>2</sub>O), 45.37(NCH<sub>2</sub>CH<sub>2</sub>N), 34.22, 33.78(C(CH<sub>3</sub>)<sub>3</sub>), 32.42(ArCH<sub>2</sub>Ar), 31.57, 31.21(C(CH<sub>3</sub>)<sub>3</sub>).  $m/z$ (FAB): 759 [(M - 1)<sup>+</sup>]. Anal. C<sub>50</sub>H<sub>68</sub>N<sub>2</sub>O<sub>4</sub>. Calcd: C, 78.90; H, 9.01; N, 3.68. Found: C, 78.68; H, 8.88; N, 3.98.

*General procedure for the selective nitration or ipso-nitration of calix[4](aza) crowns containing amide groups*

To a solution of calix[4](aza) crown containing amide groups **3a—d** (1 mmol) in dichloromethane (100 mL) at an ice-water bath were added glacial acetic acid (2.9 mL, 50 mmol) and 65% HNO<sub>3</sub> (5 mL, 72 mmol) successively. After stirring for 30 min at this temperature, the mixture was washed with water (50 mL) three times, dried over anhydrous MgSO<sub>4</sub>, and concentrated under reduced pressure. The residue was separated by column chromatography on silica gel using ethyl acetate and methanol (20:1, *v/v*) as eluent to afford corresponding products, which were further purified by recrystallization from chloroform and methanol.

**5a** This compound could be obtained by nitration of **3a**. Yield 70%. mp > 300°C.  $\nu_{\text{max}}$  (KBr): 3350, 3260, 1675(CO), 1510, 1325(NO<sub>2</sub>)  $\text{cm}^{-1}$ .  $\delta_{\text{H}}$ : 9.26(s, 2H, OH), 8.18(s, 2H, NH), 8.09(s, 4H, ArH), 7.16(d,  $J = 7.5$  Hz, 4H, ArH), 7.03(t,  $J = 7.5$  Hz, 2H, ArH), 4.61(s, 4H, ArOCH<sub>2</sub>), 4.19(d,  $J = 13.0$  Hz, 4H, ArCH<sub>2</sub>Ar), 3.70(d,  $J = 5.2$  Hz, 4H, NCH<sub>2</sub>), 3.68(d,  $J = 13.0$  Hz, 4H, ArCH<sub>2</sub>Ar).  $\delta_{\text{C}}$ : 166.66(CO), 157.67, 146.88, 140.98, 131.46, 130.39, 127.90, 127.66, 125.01(ArC), 75.03(ArOCH<sub>2</sub>), 39.16(NCH<sub>2</sub>), 31.18(ArCH<sub>2</sub>Ar).  $m/z$ (FAB): 653 [(M - 1)<sup>+</sup>]. Anal. C<sub>34</sub>H<sub>30</sub>N<sub>4</sub>O<sub>10</sub>. Calcd: C, 62.38; H, 4.62; N, 8.56. Found: C, 61.55; H, 5.01; N, 8.23.

**5b** This compound could be obtained by ipso-nitration of **3b** as a minor product. Yield 8%. mp > 300°C.  $\nu_{\text{max}}$  (KBr): 3360, 1682(CO), 1510, 1330

(NO<sub>2</sub>) cm<sup>-1</sup>.  $\delta_{\text{H}}$ : 9.37(s, 2H, OH), 8.18(s, 2H, NH), 8.07(s, 4H, ArH), 7.16(s, 4H, ArH), 4.56(s, 4H, ArOCH<sub>2</sub>), 4.18(d,  $J = 13.3$  Hz, 4H, ArCH<sub>2</sub>Ar), 3.76–3.68(m, 4H, NCH<sub>2</sub>), 3.65(d,  $J = 13.3$  Hz, 4H, ArCH<sub>2</sub>Ar), 1.19(s, 18H, C(CH<sub>3</sub>)<sub>3</sub>).  $\delta_{\text{C}}$ : 166.80(CO), 157.89, 150.69, 146.99, 141.01, 130.91, 128.06, 127.09, 124.93(ArC), 75.14(ArOCH<sub>2</sub>), 39.11(NCH<sub>2</sub>), 34.59(C(CH<sub>3</sub>)<sub>3</sub>), 31.51(ArCH<sub>2</sub>Ar), 31.16(C(CH<sub>3</sub>)<sub>3</sub>).  $m/z$ (FAB): 765 [(M - 1)<sup>+</sup>]. Anal. C<sub>42</sub>H<sub>46</sub>N<sub>4</sub>O<sub>10</sub>. Calcd: C, 65.78; H, 6.05; N, 7.31. Found: C, 65.52; H, 6.15; N, 7.11.

**5b'** This compound was obtained by *ipso*-nitration of **3b**. Yield 25%. mp 275°C (decomp.).  $\nu_{\text{max}}$ (KBr): 3350, 1675(amide CO), 1645(quinone CO), 1510, 1330(NO<sub>2</sub>) cm<sup>-1</sup>.  $\delta_{\text{H}}$ : 8.86(s, 2H, NH), 8.68(s, 1H, OH), 8.07(s, 2H, ArH), 7.13(d,  $J = 2.4$  Hz, 2H, ArH), 7.04(d,  $J = 2.4$  Hz, 2H, ArH), 6.73(s, 2H, C = CHCO), 4.54(d,  $J = 14.2$  Hz, 2H, ArOCH<sub>2</sub>), 4.35(d,  $J = 14.2$  Hz, 2H, ArOCH<sub>2</sub>), 4.20(d,  $J = 12.3$  Hz, 2H, ArCH<sub>2</sub>Ar), 4.17(d,  $J = 13.4$  Hz, 2H, ArCH<sub>2</sub>Ar), 3.82–3.68(m, 4H, NCH<sub>2</sub>), 3.58(d,  $J = 13.4$  Hz, 2H, ArCH<sub>2</sub>Ar), 3.21(d, 2H,  $J = 12.3$  Hz, 2H, ArCH<sub>2</sub>Ar), 1.17(s, 18H, C(CH<sub>3</sub>)<sub>3</sub>).  $\delta_{\text{C}}$ : 187.08, 186.45(CO), 167.70(CONH), 158.39, 149.52, 148.69, 148.16, 140.54, 133.56, 131.43, 128.94, 128.03, 127.37, 126.53, 124.59(ArC), 73.91(ArCH<sub>2</sub>), 38.89(NCH<sub>2</sub>), 34.43(C(CH<sub>3</sub>)<sub>3</sub>), 31.38(ArCH<sub>2</sub>Ar), 31.12(C(CH<sub>3</sub>)<sub>3</sub>), 29.66(ArCH<sub>2</sub>Ar).  $m/z$ (FAB): 735(M<sup>+</sup>). Anal. C<sub>42</sub>H<sub>45</sub>N<sub>3</sub>O<sub>9</sub>. Calcd: C, 68.55; H, 6.16; N, 5.71. Found: C, 68.53; H, 6.14; N, 5.50.

**5c** This compound could be obtained by nitration of **3c**. Yield 68%. mp 256–258°C.  $\nu_{\text{max}}$ (KBr): 3320, 1685(amide CO), 1640(quinone CO), 1505, 1325(NO<sub>2</sub>) cm<sup>-1</sup>.  $\delta_{\text{H}}$ : 10.58(s, 2H, NH), 8.72(s, 1H, OH), 8.31(dd,  $J = 5.8, 3.4$  Hz, 2H, ArH), 8.09(s, 2H, ArH), 7.30(dd,  $J = 5.8, 3.4$  Hz, 2H, ArH), 7.20–7.10(m, 6H, ArH), 6.77(s, 2H, C = CHCO), 4.94(d,  $J = 14.7$  Hz, 2H, ArOCH<sub>2</sub>), 4.43(d,  $J = 14.7$  Hz, 2H, ArOCH<sub>2</sub>), 4.23(d,  $J = 13.9$  Hz, 2H, ArCH<sub>2</sub>Ar), 4.18(d,  $J = 12.9$  Hz, 2H, ArCH<sub>2</sub>Ar), 3.61(d,  $J = 13.9$  Hz, 2H, ArCH<sub>2</sub>Ar), 3.23(d,  $J = 12.9$  Hz, 2H, ArCH<sub>2</sub>Ar).  $\delta_{\text{C}}$ : 187.88, 187.54(CO), 166.37

(CONH), 158.85, 152.18, 148.12, 139.46, 133.55, 133.27, 130.58, 130.57, 130.04, 128.86, 127.55, 125.73, 124.75, 124.25, 123.68(ArC), 72.57(ArOCH<sub>2</sub>), 31.62, 28.85(ArCH<sub>2</sub>Ar).  $m/z$ (FAB): 672 [(M + 1)<sup>+</sup>]. Anal. C<sub>38</sub>H<sub>29</sub>N<sub>3</sub>O<sub>9</sub> · 0.07 CHCl<sub>3</sub>. Calcd: C, 67.24; H, 4.31; N, 6.18; Cl, 1.10. Found: C, 66.92; H, 4.33; N, 6.29; Cl, 1.12.

**5d** This compound could be obtained by *ipso*-nitration of **3d**. Yield 36%. mp 271–273°C.  $\nu_{\text{max}}$ (KBr): 3310, 1680(amide CO), 1635(quinone CO), 1505, 1325(NO<sub>2</sub>) cm<sup>-1</sup>.  $\delta_{\text{H}}$ : 11.00(s, 2H, NH), 8.90(s, 1H, OH), 8.23(dd,  $J = 5.8, 3.4$  Hz, 2H, ArH), 8.06(s, 2H, ArH), 7.29(dd,  $J = 5.8, 3.4$  Hz, 2H, ArH), 7.10(d,  $J = 2.4$  Hz, 2H, ArH), 7.07(d,  $J = 2.4$  Hz, 2H, ArH), 7.00(s, 2H, CH = CCO), 4.84(d,  $J = 14.8$  Hz, 2H, ArOCH<sub>2</sub>), 4.38(d,  $J = 14.8$  Hz, 2H, ArOCH<sub>2</sub>), 4.21(d,  $J = 13.2$  Hz, 2H, ArCH<sub>2</sub>Ar), 4.16(d,  $J = 11.8$  Hz, 2H, ArCH<sub>2</sub>Ar), 3.58(d,  $J = 13.2$  Hz, 2H, ArCH<sub>2</sub>Ar), 3.02(d,  $J = 11.8$  Hz, 2H, ArCH<sub>2</sub>Ar), 3.00(s, 1H, OH), 1.19(s, 18H, C(CH<sub>3</sub>)<sub>3</sub>), 1.02(s, 9H, C(CH<sub>3</sub>)<sub>3</sub>).  $\delta_{\text{C}}$ : 184.70(CO), 166.37(CONH), 159.13, 149.42, 149.25, 148.25, 140.30, 138.43, 131.84, 131.05, 128.14, 127.95, 126.97, 126.66, 125.42, 124.58, 124.42(ArC), 74.47(ArOCH<sub>2</sub>), 73.14(*t*-BuCOH), 38.90(NCH<sub>2</sub>), 34.46(C(CH<sub>3</sub>)<sub>3</sub>), 31.77(ArCH<sub>2</sub>Ar), 31.24(C(CH<sub>3</sub>)<sub>3</sub>), 31.17(ArCH<sub>2</sub>Ar), 29.85(C(CH<sub>3</sub>)<sub>3</sub>), 25.57(C(CH<sub>3</sub>)<sub>3</sub>).  $m/z$ (FAB): 840 [(M - 1)<sup>+</sup>]. Anal. C<sub>50</sub>H<sub>55</sub>N<sub>3</sub>O<sub>9</sub>. Calcd: C, 71.32; H, 6.58; N, 4.99. Found: C, 70.73; H, 6.63; N, 4.95.

**5d'** This compound was obtained by *ipso*-nitration of **3d** accompanied with **5d**. Yield 25%. mp 249–251°C.  $\nu_{\text{max}}$ (KBr): 3330, 3275, 1685(amide CO), 1640(quinone CO), 1505, 1320(NO<sub>2</sub>) cm<sup>-1</sup>.  $\delta_{\text{H}}$ : 10.59(s, 2H, NH), 8.69(s, 1H, OH), 8.23(dd,  $J = 5.8, 3.4$  Hz, 2H, ArH), 8.07(s, 2H, ArH), 7.24(dd,  $J = 5.8, 3.4$  Hz, 2H, ArH), 7.14(d,  $J = 2.4$  Hz, 2H, ArH), 7.02(d,  $J = 2.4$  Hz, 2H, ArH), 6.77(s, 2H, C = CHCO), 4.92(d,  $J = 14.8$  Hz, 2H, ArOCH<sub>2</sub>), 4.39(d,  $J = 14.8$  Hz, 2H, ArOCH<sub>2</sub>), 4.22(d,  $J = 13.2$  Hz, 2H, ArCH<sub>2</sub>Ar), 4.19(d,  $J = 12.6$  Hz, 2H, ArCH<sub>2</sub>Ar), 3.60(d,  $J = 13.2$  Hz, 2H, ArCH<sub>2</sub>Ar), 3.22(d,  $J = 12.6$  Hz, 2H, ArCH<sub>2</sub>Ar), 1.19(s, 18H, C(CH<sub>3</sub>)<sub>3</sub>).  $\delta_{\text{C}}$ : 187.89, 186.87(CO), 166.11(CONH), 158.82, 149.77, 149.50,

148.04, 140.43, 133.86, 132.15, 128.46, 127.86, 127.85, 127.61, 126.80, 125.60, 124.40, 124.25 (ArC), 74.37(ArOCH<sub>2</sub>), 34.48(C(CH<sub>3</sub>)<sub>3</sub>), 31.64 (ArCH<sub>2</sub>Ar), 31.16(C(CH<sub>3</sub>)<sub>3</sub>), 30.20(ArCH<sub>2</sub>Ar). *m/z*(FAB): 782 [(M - 1)<sup>+</sup>]. Anal. C<sub>46</sub>H<sub>45</sub>N<sub>3</sub>O<sub>9</sub>. Calcd: C, 70.48; H, 5.79; N, 5.36. Found: C, 69.60; H, 5.79; N, 5.34.

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