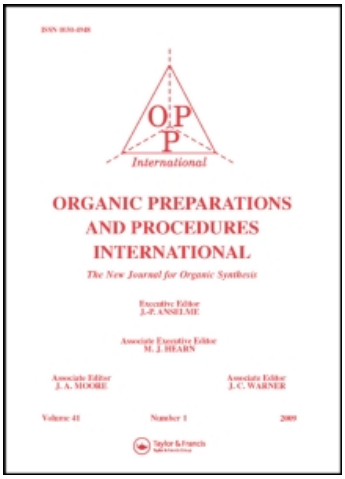

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SYNTHESIS OF CALIX[4]ARENE DIAZACROWN CONTAINING *m*-XYLYLENE PHENOL SUBUNIT

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SYNTHESIS OF CALIX[4]ARENE DIAZACROWN CONTAINING *m*-XYLYLENE PHENOL SUBUNIT

Submitted by (11/05/01)

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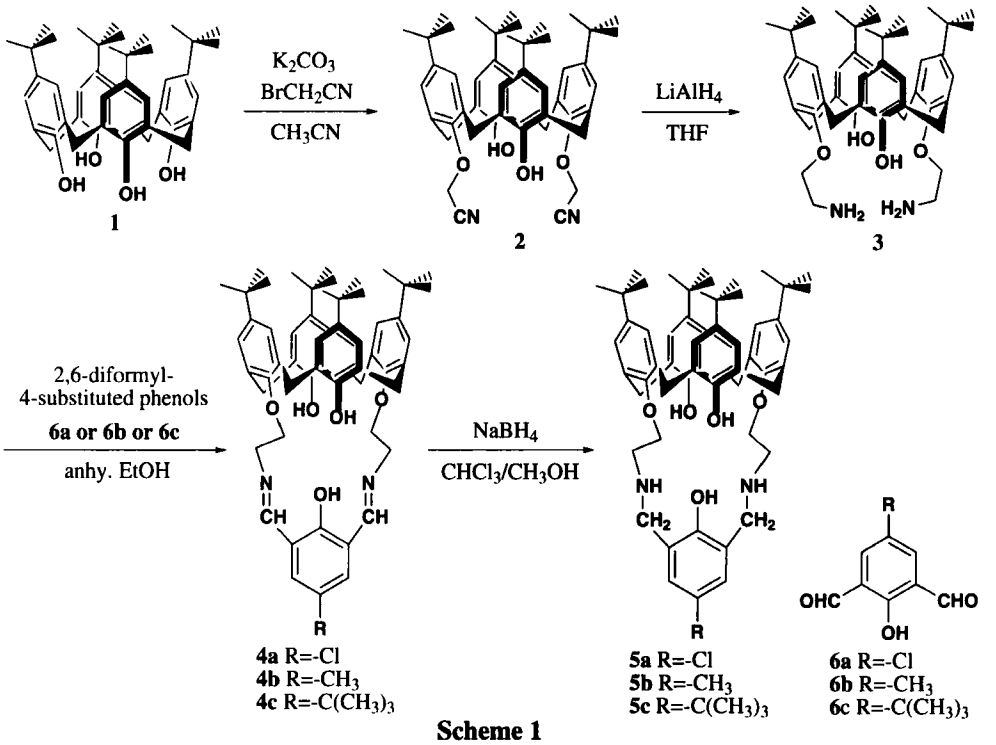
Calixcrowns, the combination of calixarene and crown ether, are a novel class of host compounds which have attracted increasing attention because of their increased ability for selective complexation of cations and neutral molecules compared with crown ethers or calixarenes.[1-3] During the past decade various calixcrowns have been synthesized[4-9] and applied as ionophores in extractive processes[8-9] or as selective ligands in ion selective electrodes.[10-12] Apart from the cavity geometry, the nature of donor sites plays an important role in determining complexation selectivity, *i.e.* azacrown ether in which nitrogen atoms are incorporated, was found to be the best liganding agent for transition metal ions.[13] In particular, the complexes of azacrowns containing *m*-xylylene phenol subunits with transition metal ions were extensively investigated as enzyme models for metalloproteins like superoxide dismutase, oxidases, and peptidases.[14-15] However, the studies of calixarene azacrowns in which the azacrown ether moiety is incorporated into the calixarene framework are relatively rare. Only a few papers report the synthesis of calixarene azacrowns, in which calix[4]arene azacrowns containing diamides were prepared by the condensation of 25, 27- dihydroxy-26, 28-*bis*[(carboxy-methyl)oxy]calix[4]arene derivatives (diester or diacid chloride) with various diamines,[16-18] and in which calix[4]arene monoazacrowns were formed by intermolecular ring closure of 25,27-dihydroxy-26,28-*bis*[(chloroethoxy)ethoxy] calix[4]arene with the appropriate amine.[19-20] We now report a novel synthetic method for calix[4]arene diazacrowns in which calix[4]arene diazacrowns **5a-c** containing *m*-xylylene phenol subunits are prepared by $NaBH_4$ reduction of the Schiff bases **4a-c**, obtained from condensation of calix[4]arene diamine **3** with 2,6-diformyl-4-substituted phenols **6a-c** under high dilution in refluxing anhydrous ethanol (*Scheme 1*). The calix[4]arene diamine **3** was easily obtained *via* a two-step synthesis in which *p*-tetra-*tert*-butyl

calix[4]arene **1** was selectively *O*-alkylated with bromoacetonitrile, and then reduced with $LiAlH_4$.[21]



Scheme 1

Table 1. Yields, mps, Elemental Analyses and MS of **4** and **5**

Compd.	Yield (%)	mp (°C)	Elemental Analyses (Found) C	H	N	MS (Found)
4a	63	264-266	76.12(76.17)	7.64(7.63)	3.17(3.03)	883.5(883.8)
4b	60	238-240	79.35(79.61)	8.12(8.04)	3.25(3.58)	863.6(863.5)
4c	70	250-252	79.60(79.80)	8.46(8.20)	3.10(2.81)	905.7(905.6)
5a	67	242-244	75.77(75.43)	8.06(7.95)	3.16(3.04)	887.5(887.6)
5b	69	260-262	78.94(78.84)	8.60(8.24)	3.23(2.95)	867.6(867.6)
5c	73	228-230	79.29(79.59)	8.87(8.63)	3.08(2.78)	909.9(909.6)

Table 2. Spectroscopic Data of **4** and **5**

Cmpd	IR (cm^{-1})	^1H NMR (δ)	^{13}C NMR (δ)
4a	3400 (br,OH) 1640.4 (C=N)	8.49 (s, 2H, 2 x CH=N), 7.53 (s, 4H, 4 x ArH),7.38 (s, 2H, 2 x ArH) 7.02 (s, 4 H4 x ArH), 4.66 (d, *J* = 12.8 Hz, 4H, 4 xendo-ArCHAr), 4.05 (t, *J* = 5.2 Hz, 4 H, 2 x OCH_2), 3.94 (t, *J* = 5.2 Hz, 4H, 2 x NC H_2) 3.52 (d, *J* = 12.8 Hz, 4H, 4 x exo-ArCH Ar), 1.28 (s, 18H, 2 x -$C(CH_3)_3$), 0.89 (s, 18H, 2 x -$C(CH_3)_3$)	166.3 (CH=N), 150.8, 149.7, 148.2, 142.3, 137.1, 133.1, 132.6, 132.1, 130.7, 127.4, 127.0, 126.5 (aromatic C), 75.46 (OCH_2), 60.7 (CH_2N), 34.4, 34.1, 33.9, 33.6, 31.4, ($C(CH_3)_3$, $ArCH_2Ar$)
4b	3400 (br,OH) 1645.2 (C=N)	8.56 (s, 2H, 2 x CH = N), 7.11(s, 2H, 2 x ArH), 7.03 (s, 4H, 4 x ArH), 6.75 (s, 4H, 4 x ArH), 4.34-3.92 (m, 12H, 4 x endo-ArCHAr, 2 x OCH_2CH_2N), 3.27 (d, *J* = 12.5 Hz, 4H, 4 x exo-ArCHAr), 1.81 (s, 3H,$ArCH_3$), 1.28 (s, 18H, 2 x $C(CH_3)_3$), 0.92 (s,18H, 2 x -$C(CH_3)_3$).	158.9 (CH = N), 151.1, 149.9,147.3, 141.5, 133.5, 132.8,131.7, 128.2, 127.9, 126.5,125.8, 125.3 (aromatic C), 75.4,(OCH_2), 60.3 (CH_2N), 35.6, 34.7, 33.6, 32.5, 31.6, 30.5($ArCH_3$, $ArCH_2Ar$, $C(CH_3)_3$)
4c	3410 (br, OH) 1642.5 (C=N)	8.69 (s, 2H, 2 x -CH = N), 7.11 (s, 2H, 2 x ArH), 7.01 (s, 4H, 4 x ArH), 6.79 (s, 4H4 x ArH) 4.31-4.10 (m, 12H, 4 x endo-ArCHAr, 2OCH_2CH_2N), 3.27 (d, *J* = 12.5 Hz, 4H, 4 exo ArCHAr), 1.28 (s, 18H, 2 x -$C(CH_3)_3$), 1.06 (s, 9H, -$C(CH_3)_3$), 1.00 (s,18H, 2 x -$C(CH_3)_3$).	158.8 (CH = N), 151.1, 149.8, 147.3, 141.8, 41.5, 132.9, 131.8, 128.6, 127.8, 125.8, 125.3, 125.1 (aromatic C), 75.3 (OCH_2), 60.5 (NCH_2), 34.3, 34.1, 32.3, 31.9, 31.7,($ArCH_2Ar$, -$C(CH_3)_3$)
5a	3355 (br, OH, NH)	7.17 (s, 2H, 2 x ArH), 7.10 (s, 4H, 2 x ArH), 6.98 (s, 4H, 2 x ArH), 4.25-4.07 (m, 12H, 2 x OCH_2CH_2NH, 4 x endo-ArCHAr), 3.41 (d, *J* = 13.0 Hz, 4H, 4 x exo-ArCHAr), 3.25 (s, 4H, -$NHCH_2Ar$), 1.28 (s, 18H, 2 x $C(CH_3)_3$), 1.07 (s, 18H, 2 x -$C(CH_3)_3$)	150.2, 149.7, 148.0, 142.8, 137.6, 133.7, 132.6, 131.5, 128.3, 126.3, 126.1, 125.8 (aromatic C),74.3 (OCH_2) 49.4, 47.8 (CH_2NHCH_2), 34.4, 34.1, 32.5, 32.0, 31.40 (-$C(CH_3)_3$, $ArCH_2Ar$)
5b	3357 (br, OH, NH)	7.06 (s, 4H, 4 x ArH), 6.97 (s, 2H, 2 x ArH), 6.93 (s, 4H, 4 x ArH), 4.25-4.17 (m, 8H, 2 x OCH_2CH_2N), 4.15 (d, *J* = 13.1Hz, 4H, 4 x endoArCHAr), 3.39 (d, *J* = 13.1Hz, 4H, 4 x exo-ArCHAr), 3.30 (s, 4H, 2 x $ArCH_2NH$), 2.06 (s, 3H, Ar-CH_3), 1.27 (s, 18H, 2 x -$C(CH_3)_3$),0.98 (s,18H, 2 x -$C(CH_3)_3$	150.3, 149.6, 148.1, 142.8, 140.8, 137.5, 136.5, 128.7 , 128.7, 128.1, 126.3, 125.8 (aromatic C),73.1(OCH_2), 49.5, 47.6 (CH_2NHCH_2), 34.5, 34.3, 32.5, 32.0, 31.4, 30.1, (-$C(CH_3)_3$,$ArCH_2Ar$)

Table 2. Continued...

Cmpd	IR (cm^{-1})	^1H NMR (δ)	^{13}C NMR (δ)
5c	3358 (br, OH, NH)	7.03 (s, 4H, 2 x ArH), 7.01 (s, 2H, ArH), 6.93 (s, 4H, 2 x ArH), 4.51-4.06 (m, 12H, 2 x OCH_2NH, 4 x endo-ArCHAr), 3.41 (d J = 11.6 Hz, 4H, 4 x exo-ArCHAr), 3.29 (s, 4H, 2 x -$NHCH_2$-Ar), 1.27 (s, 18H, 2 x $C(CH_3)_3$), 1.07 (s, 9H, -$C(CH_3)_3$), 0.98 (s, 18H, 2 x -$C(CH_3)_3$)	154.3, 150.5, 149.7, 147.9, 142.5, 133.4, 127.9, 126.3, 126.1, 125.8, 125.3, 124.8 (aromatic C), 73.8 (OCH_2), 48.4, (CH_2NHCH_2) 35.7, 34.2, 33.7, 32.8, 32.4, 32.1, 31.8 ($C(CH_3)_3$, $ArCH_2$ Ar)

Huang *et al.* [22-23] reported the synthesis of three related Schiff base calixcrowns by the condensation of **3** with terephthalic aldehyde or 1,2-*bis*(4-formylphenoxy)ethane or 1,3-*bis*(4-formylphenoxy)propane; only the corresponding 2:2 Schiff base condensation products were obtained. In our case, only the 1:1 Schiff bases were obtained in good yield (60-70%). The ^1H NMR singlet around δ 8.5 and the IR absorption peaks at 1640 cm^{-1} indicate the formation of the Schiff base. The molecular weights of **4a-c** were determined by ESIMS. The m/z values of $[M+H]^+$ were 883.8, 863.5 and 905.6. The ESIMS spectra of **4a-c** support the assigment as 1:1 Schiff bases. The reduction of the Schiff base calixcrowns was carried out with $NaBH_4$ in $CHCl_3/CH_3OH$ to give calix[4]arene diazacrowns **5a-c** in 65-70% yield. Their structures were confirmed by ^1H NMR, ^{13}C NMR, ESIMS and elemental analysis.

The experimental results indicate that the novel Schiff base and diazacrown calix[4]arenes have a strong ability to complex some transition and heavy metal cations selectively. The detail will be published elsewhere.

EXPERIMENTAL SECTION

Melting points were determined on a Yanaco micro melting point apparatus (uncorrected). Elemental analyses were carried out on Perkin Elmer 240C. ^1H NMR and ^{13}C NMR were recorded on Bruker AM 300 (Germany). MS spectra were determined by an electrospray mass spectrometer (LCQ, Finnigan) in positive mode. IR spectra were recorded on a Bruker IFS 66v (Germany). Preparative column chromatography separations were performed on G60 silica gel, while pre-coated silica gel plates (GF_{254}) were used for analytical TLC. All solvents were purified by standard procedures. Calix[4]arene diamine **3** [21] and dialdehydes **6a**, **6b**, **6c** [24] were synthesized according to literature procedures.

General Procedure for the Preparation of Schiff Base Calixcrowns. A solution of the calix[4]arene diamine **3** (200 mg, 0.27 mmol) in anhydrous EtOH (100 mL) was brought to reflux. Then an EtOH solution (100 mL) of dialdehyde **6a**, **6b** or **6c** (0.27 mmol) was added dropwise with stirring over 6 h. and the mixture was maintained at reflux for 10 h. After cooling to RT., the pale-yellow precipitate was collected and recrystallized from $CHCl_3/CH_3OH$ to give compound **4a-c**.

General Procedure for the Preparation of Calix[4]arene Diazacrowns. A mixture of compound **4a-c** (0.25 mmol) and $NaBH_4$ (60 mg, 1.62 mmol) in $CHCl_3$ (60 mL) and CH_3OH (60 mL) was stirred

for 24 h. at 25°. The color of the solution changed from pale yellow to colorless. The mixture was evaporated to dryness *in vacuo* and the residue was partitioned in water (50 mL) and $CHCl_3$ (80 mL). The organic layer was dried (Na_2SO_4), evaporated *in vacuo*, and the residue was column chromatographed (EtOAc-petroleum ether, 1:3) to give the corresponding calix[4]arene diazacrown **5a-c**.

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