



Synthesis and Properties of Upper Rim Schiff Base Calix[4]arenes

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Abstract. The synthesis and properties of upper rim Schiff base calix[4]arenes are described in this article. Tetrakis-*p*-bromomethylcalix[4]arene (**1**) reacts with hexamethylenetetramine to give tetrakis-*p*-formylcalix[4]arene (**2**) in high yield. Then upper rim Schiff base calix[4]arenes **3** can be easily synthesized by **2** reacting with appropriate alkylamines. The complexation ability of **3** toward transition metals Pb^{2+} , Cu^{2+} and Co^{2+} was studied by UV-VIS spectrophotometry.

Key words: Schiff base, calixarene, upper rim, complexation, transition metals.

1. Introduction

Calixarenes as an important class of host molecules have been extensively studied in the last twenty years. It has been demonstrated that they are powerful building blocks for making functional receptors for cations, anions and small organic molecules [1]. Among the derivatives of calixarenes, calix[4]crowns and calix[4]podands have shown very high selectivity and strong complexation ability toward alkali and alkaline earth metals [2]. Recently, the recognition properties of chromogenic calixarenes and self-assembling calixarene capsules for organic molecules, especially for chiral organic molecules, have attracted interest [3]. Lower rim Schiff base calixarenes have been synthesized and found to complex transition metals efficiently owing to the nitrogen atoms in the imine [4]. However, there are few reports of the complexation properties of transition metals and heavy metals with the derivatives of calixarenes at the upper rim, especially the Schiff base calixarenes. Herein, we report a new method of synthesis of upper rim Schiff base calix[4]arenes and their recognition properties with transition metals such as Pb^{2+} , Cu^{2+} and Co^{2+} .

2. Experimental

2.1. MATERIALS AND METHODS

All reagents were obtained from commercial sources and used without further purification. 25,26,27,28-Tetrahydroxycalix[4]arene was synthesized according to the literature [5]. $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$ spectra were recorded on a Bruker DMX-300 instrument. Chemical shifts are reported relative to tetramethylsilane in CDCl_3 or DMSO-d_6 . IR spectra were recorded on a Perkin-Elmer 782 spectrometer. UV-VIS spectra were recorded on a HP 8452 UV-VIS spectrophotometer. Mass spectra were recorded on a KYKY-ZHT-5 instrument and the high resolution mass spectrum was recorded on a Bruker APEX II instrument. Melting points are uncorrected. Elemental analyses were carried out by the analytical laboratory of the institute.

2.2. SYNTHESIS

2.2.1. 5,11,17,23-Tetrakis(bromomethyl)-25,26,27,28-tetrahydroxycalix[4]arene (1)

To a suspension of 25,26,27,28-tetrahydroxycalix[4]arene (8.48 g, 20 mmol) and paraformaldehyde (4.8 g, 160 mmol) in glacial acetic acid (40 mL) was bubbled hydrogen bromide gas at room temperature for 30 min. The reaction mixture was stirred for another 2 h after the bubbling. The product was filtered and washed 3 times with water, then dried at mild conditions to give a pale yellow powder (14.9 g, 94%), which is pure enough to use in the following syntheses. Colorless crystals could be obtained by recrystallization from chloroform-petroleum ether (60–90 °C). m.p. 130 °C (decomp.). $^1\text{H-NMR}$ (CDCl_3) δ 10.10 (s, 4H, OH), 7.10 (s, 8H, ArH), 4.25 (s, 8H, BrCH₂), 4.21 (br, 4H, ArCH₂Ar), 3.52 (br, 4H, ArCH₂Ar). $^{13}\text{C-NMR}$ (CDCl_3) δ 148.9, 131.6, 129.9, 128.2, 33.4, 31.5. IR (KBr) ν/cm^{-1} 3160 (OH), 1600, 1486, 625. *Elemental analysis* for $\text{C}_{32}\text{H}_{28}\text{Br}_4\text{O}_4$ *calcd*: C, 48.27; H, 3.54. *Found*: C, 47.76; H, 3.53.

2.2.2. 5,11,17,23-Tetrakis(formyl)-25,26,27,28-tetrahydroxy calix[4]arene (2)

A mixture of 5,11,17,23-tetrakis(bromomethyl)-25,26,27,28-tetrahydroxycalix[4]arene (1) (8.0 g, 10.0 mmol) and hexamethylenetetramine (11.2 g, 80 mmol) was suspended in glacial acetic acid (48 mL) and stirred at ambient temperature for 20 min. After water (48 mL) was added, the suspension turned clear. This solution was stirred at room temperature for an additional 0.5 h and refluxed for 2–3 h. Then hydrochloric acid (10 mL) was added, and a yellow precipitate was formed. The mixture was refluxed for 0.5 h, cooled to room temperature, and the precipitate was filtered, washed with water several times to remove acid and then washed with methanol. After drying, 2 was obtained as a yellow solid (4.6 g). The product can be used in the following reaction without further purification. Yield 85%; m.p. 210 °C

(decomp.). $^1\text{H-NMR}$ (CDCl_3) δ 10.18 (s, 4H, OH), 9.80 (s, 4H, CHO), 7.70 (s, 8H, ArH), 4.30 (br, 4H, ArCH₂Ar), 3.80 (br, 4H, ArCH₂Ar). $^{13}\text{C-NMR}$ (DMSO-d_6) δ 190.4, 159.8, 130.5, 129.1, 128.2, 31.1. IR (KBr) ν/cm^{-1} 3160 (OH), 2840, 2720, 1675 (CO), 1590, 1450. MS-FAB (positive) m/z : 536 (M^+). *Elemental analysis* for $\text{C}_{32}\text{H}_{24}\text{O}_8$ *calcd*: C, 71.63; H, 4.51. *Found*: C, 71.05; H, 5.11.

2.2.3. Calix[4]arene Schiff bases **3**

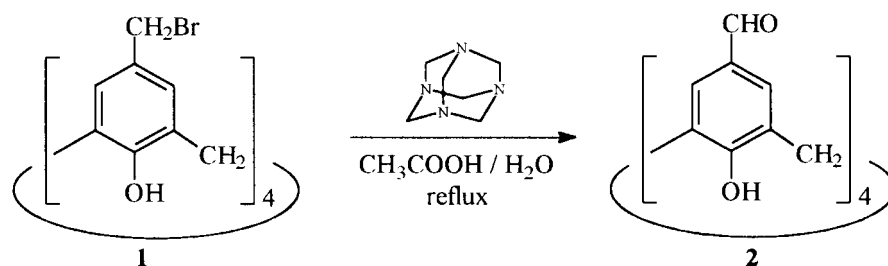
A solution of alkyl amine (4.4 mmol) in ethanol (5 mL) was added dropwise to the suspension of 5,11,17,23-tetrakis(formyl)-25,26,27,28-tetrahydroxycalix[4]arene (**2**) (0.54 g, 1 mmol) in ethanol (5 mL) at room temperature. After stirring for 20–30 min, the product precipitated, and the suspension was stirred for another 2–3 h. Calix[4]arene Schiff base **3a** or **3b** was obtained by filtration and recrystallized from ethanol as a yellow solid.

5,11,17,23-Tetrakis(butylimido)-25,26,27,28-tetrahydroxycalix[4]arene (3a): Yield 90%; m.p. 229 °C (decomp.). $^1\text{H-NMR}$ (DMSO-d_6) δ 12.00 (br, 4H, OH), 8.16 (s, 4H, CH=N), 7.53 (s, 8H, ArH), 4.30 (d, $J = 11.0$ Hz, 4H, ArCH₂Ar), 3.50 (d, $J = 11.0$ Hz, 4H, ArCH₂Ar), 3.54–3.47 (m, 8H, NCH₂), 1.64–1.54 (m, 8H, CH₂CH₂CH₃), 1.37–1.29 (m, 8H, CH₂CH₂CH₃), 0.92 (t, $J = 7.0$ Hz, 12H, CH₃). $^{13}\text{C-NMR}$ (DMSO-d_6) δ 161.3, 130.6, 130.5, 129.4, 129.0, 58.0, 32.4, 31.8, 19.7, 13.7. IR (KBr) ν/cm^{-1} 3400 (OH), 1640 (C=N), 1600. MS (high resolution, negative SIMS) m/z : 755.4540 [(M–H)[–]]; $\text{C}_{48}\text{H}_{59}\text{O}_4\text{N}_4^-$ required 755.4541. *Elemental analysis* for $\text{C}_{48}\text{H}_{60}\text{O}_4\text{N}_4$ *calcd*: C, 76.15; H, 7.99; N, 7.40. *Found*: C, 75.51; H, 7.53; N, 7.09.

5,11,17,23-Tetrakis(heptylimido)-25,26,27,28-tetrahydroxycalix[4]arene (3b): Yield 83%; m.p. 209–210 °C. $^1\text{H-NMR}$ (DMSO-d_6) δ 12.10 (br, 4H, OH), 8.12 (s, 4H, CH=N), 7.44 (s, 8H, ArH), 4.28 (d, $J = 10.0$ Hz, 4H, ArCH₂Ar), 3.44 (d, $J = 10.0$ Hz, 4H, ArCH₂Ar), 3.52–3.31 (m, 8H, NCH₂), 1.62–1.50 (m, 8H, CH₂(CH₂)₄CH₃), 1.30–1.15 (m, 32H, CH₂(CH₂)₄CH₃), 0.84 (t, $J = 7.0$ Hz, 12H, CH₃). $^{13}\text{C-NMR}$ (DMSO-d_6) δ 161.7, 130.8, 130.7, 129.7, 128.4, 58.5, 32.0, 31.6, 30.6, 28.8, 26.9, 22.4, 14.3. IR (KBr) ν/cm^{-1} 3400 (OH), 1640 (C=N), 1605. MS-FAB (positive) m/z : 924 (M^+). *Elemental analysis* for $\text{C}_{60}\text{H}_{84}\text{O}_4\text{N}_4$ *calcd*: C, 77.88; H, 9.15; N, 6.06. *Found*: C, 77.59; H, 8.99; N, 5.79.

2.3. STABILITY CONSTANT DETERMINATIONS

The stability constants in methanol were determined by UV-VIS absorption spectrophotometry at room temperature (25 °C). The procedure consisted of adding increasing amounts of a metallic salt [$\text{Pb}(\text{NO}_3)_2$, CuBr_2 , CoCl_2] solution to a solution of the ligand ($C_L = 1.75 \times 10^{-5}$ M) in methanol. The resulting spectra changes were analyzed by the program Sirko [6].



Scheme 1.

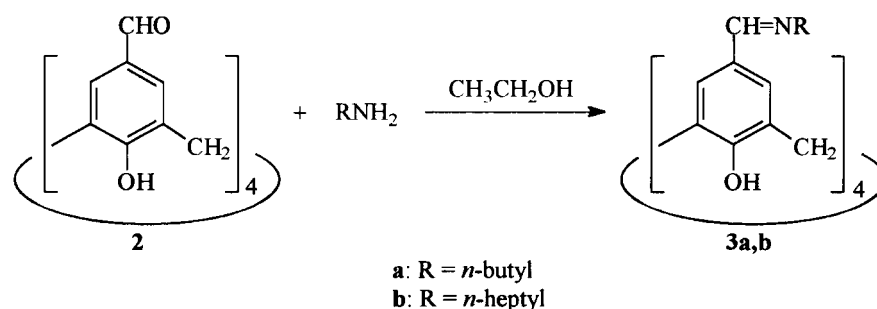
3. Results and Discussion

Two methods of introduction of the formyl group at the upper rim of calix[4]arene have been reported. One is through the ozonolysis of tetra-*p*-propenylcalix[4]arene [7], and the other is by Gross formylation of calix[4]arenes [8]. However, these methods need either several steps or a poisonous reagent such as Cl₂CHOCH₃. Now, we have synthesized tetra-*p*-formylcalix[4]arene easily by the *Sommelet reaction* [9]. 5,11,17,23-Tetrakis(bromomethyl)-25,26,27,28-tetrahydroxycalix[4]arene (**1**), which can be conveniently prepared by bromomethylation of 25,26,27,28-tetrahydroxycalix[4]arene, reacted with hexamethylenetetramine in glacial acetic acid, and the reaction mixture was treated with hydrochloric acid. (Scheme 1). Then tetra-*p*-formylcalix[4]arene (**2**) was obtained as a yellow solid pure enough to be used in the following reaction, and the yield of this reaction is greater than 85%. Compared with previously reported methods, this approach is more convenient and yields also almost no partially formylated product.

In the ¹H-NMR spectrum of **2**, the formyl protons resonated as a singlet peak at 9.80 ppm. Owing to the electron withdrawing effect of the formyl group, the protons in the aromatic ring shift downward to 7.70 ppm. Two broad peaks of methylene protons were observed at 4.30 and 3.80 ppm, indicating that this calix[4]arene mostly prefers the cone conformation, which is similar to other calix[4]arenes having four hydroxy groups at the lower rim [10].

The Schiff base calixarenes **3** can be easily obtained in excellent yields by tetra-*p*-formylcalix[4]arene (**2**) reacting with appropriate alkylamines in ethanol at ambient temperature (Scheme 2).

In the ¹H-NMR spectra of **3a** and **3b**, the AB pair of doublets pattern of the methylene bridge protons between the aromatic rings indicates that the calixarenes are all in the cone conformation. The signal at 32.4 or 32.0 ppm in the ¹³C-NMR spectra for the methylene bridge carbon between the aromatic rings of **3a** or **3b** also confirms this conclusion [11]. This conformation preference is a consequence of the hydroxyl groups which form very strong intramolecular hydrogen bonds. The chemical shift of protons in the imido group is located at about 8.1 ppm. There are two configurations, *Z* or *E*, for the Schiff base. In this experiment, the compound



Scheme 2.

Table I. Stability constants in methanol at 25 °C

Cation	Ionic radii (Å) [12]	Log <i>K</i>	
		3a	3b
Co ²⁺	0.65	5.29	5.54
Cu ²⁺	0.73	4.21	4.53
Pb ²⁺	1.19	3.53	3.74

3a or **3b** obtained is a mixture of *Z*- and *E*-configurations, as indicated by the signal for the carbon of the CH=N group in the ¹³C-NMR spectra which is broad. In the IR spectra, there is the typical absorption for CH=N at about 1640 cm⁻¹. These Schiff base calix[4]arenes **3** are not stable in the presence of acid and water, but are stable as solids.

The formation of complexes between Schiff base calix[4]arene **3a** and Pb(NO₃)₂ in DMSO was established by ¹H-NMR spectroscopy. The addition of Pb²⁺ as a solid to a DMSO-d₆ solution of **3a** resulted in significant perturbation of imido, calix methylene, aromatic and alkyl protons of the receptor, demonstrating that the binding site is the imido part.

The stability constants of complexes in methanol were determined by UV-VIS absorption spectrophotometry. The spectrum of ligand **3b** after the addition of CoCl₂ solution, illustrated in Figure 1 as an example, shows the decrease of intensity of the absorption maximum at 280 nm and the increase of the intensity at 383 nm, as well as an isosbestic point at 336 nm. The experimental data were interpreted on the assumption of a 1 : 1 complex. The values of the stability constants of the complexes were calculated with the program Sirko and are given in Table I.

The data in Table I show that the binding ability decreases with the ionic radii of the transition metals. The Schiff base calixarene containing a longer alkyl chain shows higher binding ability toward cations than that containing a shorter alkyl chain.

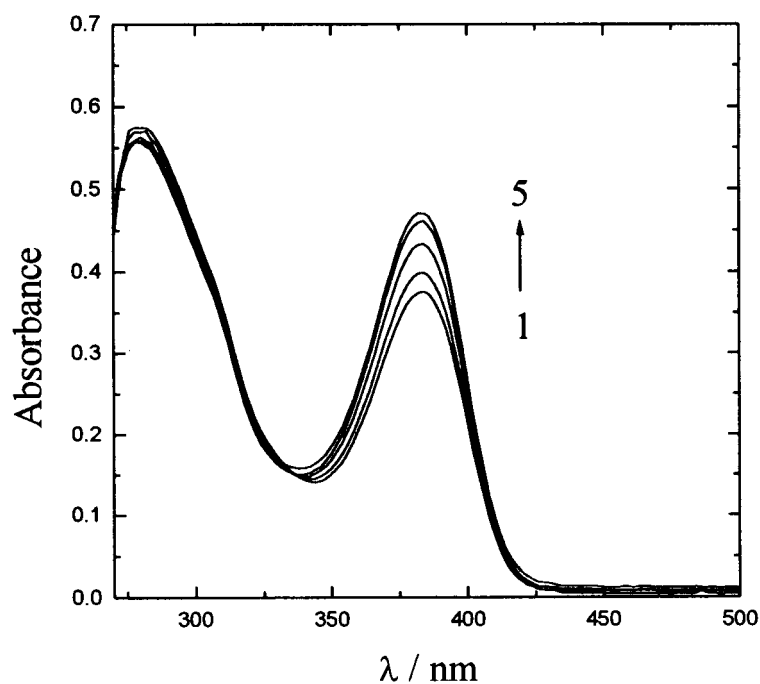


Figure 1. Change in UV absorption spectrum of (3a) (lower curve) upon addition of CoCl_2 in methanol. Concentration of (3a): 1.75×10^{-5} M. Spectra 1–5 correspond to $0 \leq C_{\text{Co}}/C_{(3a)} \leq 2$.

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