



Synthesis and Properties of a Series of Novel Calix[6]arene Diazo Derivatives

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Abstract

In this study, seven new compounds *p*-(4-butyl-phenylazo)calix[6]arene (**1**), *p*-(4-(phenylazo)phenylazo)calix[6]arene (**2**), *p*-(4-hydroxyphenylazo)calix[6]arene (**3**), *p*-{4-[*N*-(thiazol-2-yl)sulfamoyl]phenylazo}calix[6]arene (**4**), *p*-(4-acetamidophenylazo)calix[6]arene (**5**), *p*-(thiazol-2-ylazo)calix[6]arene (**6**) and *p*-(2-sulfanylphenylazo)calix[6]arene (**7**) have been synthesized from calix[6]arene by diazo coupling with the corresponding aromatic amines. UV-Vis, IR, ¹H and ¹³C NMR spectral data have been used to elucidate the structures of the compounds elemental analyses,

Introduction

Calix[*n*]arenes are macrocyclic molecules composed of *n* phenol rings linked by methylene groups. The chemistry of calix[4, 6 or 8]arenes is well represented in the literature due to the ease with which these molecules can be synthesized [1]. Various methods for functionalizing calixarenes have been developed and numerous calixarene derivatives have been synthesized in the past two decades [2]. During the past decade much research effort has been expended in embellishing calixarene frameworks, with functional groups [3]. Attention has been focused primarily on attachments to the para positions at the upper rim and the oxygens at the lower rim; relatively few attempts have been reported concerning the replacement of the hydroxy groups. Most of these studies have dealt with replacement of one to four of the hydroxy groups by hydrogen in the calix[4]arene systems [4].

The molecular design of chromogenic calix[*n*]arenes has attracted much attention in the past years. These calixarenes change their absorption (or fluorescence) spectra upon the binding of metal cations similar to chromogenic crown ethers [5]. The color formation resulting upon complexing serves as a transducer of the chemical to the physical signal. Recently a number of chromogenic calix[4]arene derivatives have been synthesized to obtain highly selective ligands which may have great potential in the development of new metal ion sensors.

In the chromogenic molecules mainly (di)nitrophenylazo groups [6] are responsible for coloration although there are also other examples such as nitrophenol [7] and iodoaniline [8]. The fluorogenic calixarenes generally contain anthracene [9], pyrene [10] and benzothiazole [11] fluorophore units. These compounds act as chromoionophores exhibiting optical responses in organic solvents on complexing with Li⁺, Na⁺ and K⁺ salts [12]. Shimizu *et al.* synthesized a chromogenic calix[4]arene containing a calix[4]arene

triester moiety as a metal binding site and an azophenol moiety as a chromophore [13]. Azo coupling reactions of calix[4]arene were studied by Morita *et al.* and Shinkai *et al.* who also described their NMR spectra [14, 15]. Nomura *et al.* described compounds containing azo groups which are of interest because of their properties of binding sites for metals or of dye chromophores. They reported the synthesis of a calix[6]arene derivative containing azo groups and its binding properties for metal ions [16].

In our recent work, we synthesized α -dioxime derivatives of calix[*n*]arenes and their complexes [17, 18], polymeric calix[*n*]arene derivatives and selective extraction of transition metal cations [19–25]. In the present paper, we report the synthesis and properties of a series of novel calix[6]arene azo derivatives. Seven new azo calix[6]arenes were synthesized from calix[6]arene and diazotized 4-butylaniline, 4-(phenylazo)aniline, 4-aminophenol, N⁴-(thiazol-2-yl)sulfanylamide, 4-aminoacetanilide, 2-aminothiazole or 2-aminobenzene-1-thiol. The structures of the synthesized compounds have been elucidated using elemental analyses, UV-vis, IR, ¹H and ¹³C NMR spectra. Physical and chemical properties such as melting points, colors and solubilities of these compounds have been examined.

Experimental

All the reagents used were purchased from Merck or Carlo-Erba Company and are chemically pure.

Melting points were determined on an Electrothermal IA9100 digital melting point apparatus and are uncorrected. ¹H and ¹³C NMR spectra were recorded on a Bruker 200 MHz spectrometer in deuterated dimethyl sulfoxide as solvent. Using TMS as internal standard all δ values are reported in ppm. IR spectra were recorded on a Mattson

1000 FTIR Spectrometer as KBr pellets. UV-Vis spectra were obtained on a Shimadzu 160A UV-Visible recording spectrophotometer. Elemental analyses were performed in TUBITAK Laboratories (Scientific and Research Council of Turkey).

Preparation of the calix[6]arenes

p-*Tert*-butylcalix[6]arene and calix[6]arene were synthesized by the method described by Gutsche [26, 27].

p-(4-Butylphenylazo)calix[6]arene (**1**). General procedure [14]

A solution of 4-butyl-benzenediazonium chloride [28], which was prepared from 3.67 g (25 mmol) of 4-*n*-butyl aniline, sodium nitrite, and conc. HCl, in 50 mL of water, was slowly added into a cold (5 °C) solution of 2.0 g (3.14 mmol) of calix[6]arene and 10.00 g (73.50 mmol) of sodium acetate trihydrate in 52 mL of MeOH-DMF (5:8, v/v) to give a magenta suspension. After standing for 2 h, the suspension was made acidic with 250 mL of aqueous (0.25%) HCl. The mixture was incubated at 60 °C for 30 min. to produce **1** as magenta pellets, which were filtered off, washed with water and MeOH. An analytical sample was obtained by the following method: 5 g of **1** was dissolved in 100 mL of a hot NaHCO₃ (6.3 g) solution. Activated charcoal (1 g) was added to this solution. After filtering off the charcoal it was cooled and acidified with 1 or 2 mL of conc. HCl. The solution was heated for 30 min and cooled again. The solid obtained was filtered off, washed with water, and dried. The yield was 4.37 g (87%), mp. 310 °C.

¹H NMR (DMSO, 25 °C) δ; 0.93 (18H, t, CH₃), 1.26 (12H, m, CH₂), 1.62 (12H, m, CH₂), 2.57 (12H, t, CH₂), 3.87–4.10 (12H, broad, ArCH₂Ar), 7.24–7.72 (36H, s, arom.-H), 9.90 (6H, s, OH). ¹³C NMR (DMSO, 25 °C): δ_C: 139.9, 135.5, 134.9, 132.6, 130.6, 128.9, 123.2, 120.2, 30.5, 20.0, 19.7, 18.0, 17.2.

The compound is soluble in DMSO, slightly soluble in acetone, benzene and CHCl₃, and insoluble in water, ethanol, diethyleter and acetic acid.

p-[4-(Phenylazo)phenylazo]calix[6]arene (**2**)

2 was prepared as described above, using 4-(phenylazo)aniline and obtained in 79% yield as a pale brown precipitate, which was filtered off, washed with water and MeOH, and dried. Yield 4.70 g (79%) of **2**, mp. 300 °C.

¹H NMR (DMSO, 25 °C), δ; 3.60–4.00 (12H, broad, ArCH₂Ar), 7.00–7.10 (66H, s, arom.-H), 10.80 (6H, s, OH). ¹³C NMR (DMSO, 25 °C): δ_C: 156.2, 145.7, 144.8, 140.2, 135.9, 135.5, 132.8, 123.9, 121.4, 32.6.

The compound is soluble in DMSO, slightly soluble in acetone and acetic acid, insoluble in water, ethanol, diethyleter, benzene, and CHCl₃.

p-(4-Hydroxyphenylazo)calix[6]arene (**3**)

3 was prepared as described above, using 4-aminophenol and obtained in 58% yield as an orange solid, which was

filtered off, washed with water and MeOH, and dried. Yield 2.47 g (58%) of **3**, mp. 218 °C.

¹H NMR (DMSO, 25 °C), δ; 3.30–4.10 (12H, broad, ArCH₂Ar), 6.73 (6H, s, OH), 7.11–7.80 (36H, s, arom.-H), 9.95 (6H, s, OH). ¹³C NMR (DMSO, 25 °C): δ_C: 148.2, 145.3, 140.7, 137.3, 136.2, 133.8, 124.5, 121.9, 33.3.

The compound is soluble in DMSO, and insoluble in water, ethanol, diethyleter, acetone, acetic acid, benzene, and CHCl₃.

p-[4-(*N*-Thiazol-2-yl)sulphamoyl]phenylazo]calix[6]arene (**4**)

4 was prepared as described above, using N⁴-(thiazol-2-yl)sulfanylamine and obtained in 67% yield as a pink solid, which was filtered off, washed with water and MeOH, and dried. Yield 4.71 g (67%) of **4**, mp. 270 °C.

¹H NMR (DMSO, 25 °C), δ; 1.20–1.25 (12H, d, =CH—), 3.80–3.90 (12H, broad, ArCH₂Ar), 6.70–7.10 (36H, s, arom.-H), 7.96 (6H, s, NH), 12.32 (6H, s, OH). ¹³C NMR (DMSO, 25 °C): δ_C: 155.7, 147.1, 145.3, 139.2, 137.6, 135.3, 133.2, 131.2, 124.8, 121.9, 120.3, 31.7.

The compound is soluble in DMSO, slightly soluble in acetone, acetic acid, and insoluble in water, ethanol, diethyleter, benzene, and CHCl₃.

p-(4-Acetamidophenylazo)calix[6]arene (**5**)

5 was prepared as described above, using 4-aminoacetanilide and obtained in 73% yield as a dark brown solid, which was filtered off, washed with water and MeOH, and dried. Yield 3.68 g (73%) of **5**, mp. 295 °C.

¹H NMR (DMSO, 25 °C), δ; 1.26 (18H, d, CH₃), 3.65–4.15 (12H, broad, ArCH₂Ar), 7.10–7.50 (36H, s, arom.-H), 10.11 (6H, s, NH), 12.34 (6H, s, OH). ¹³C NMR (DMSO, 25 °C): δ_C: 169.8, 146.5, 136.5, 135.4, 135.3, 132.9, 126.1, 123.8, 32.6, 21.4.

The compound is soluble in DMSO, slightly soluble in acetone, CHCl₃, and insoluble in water, ethanol, diethyl ether, acetic acid, and benzene.

p-(2-Thiazol-2-ylazo)calix[6]arene (**6**)

6 was prepared as described above, using 2-aminothiazol and obtained in 65% yield as a dark brown solid, which was filtered off, washed with water and MeOH, and dried. Yield 2.23 g (65%) of **6**, mp. 327 °C.

¹H NMR (DMSO, 25 °C), δ; 1.25–2.55 (12H, d, =CH—), 3.32–4.05 (12H, broad, ArCH₂Ar), 6.92–8.10 (36H, s, arom.-H), 12.68 (6H, s, OH). ¹³C NMR (DMSO, 25 °C): δ_C: 155.5, 145.1, 146.1, 137.2, 125.2, 121.6, 120.4, 31.4.

The compound is soluble in DMSO, and insoluble in water, ethanol, diethyl ether, acetic acid, acetone, benzene, and CHCl₃.

p-(2-Sulfonylphenylazo)calix[6]arene (**7**)

7 was prepared as described above, using 2-aminobenzene-1-thiol and obtained in 72% yield as a brown solid, which

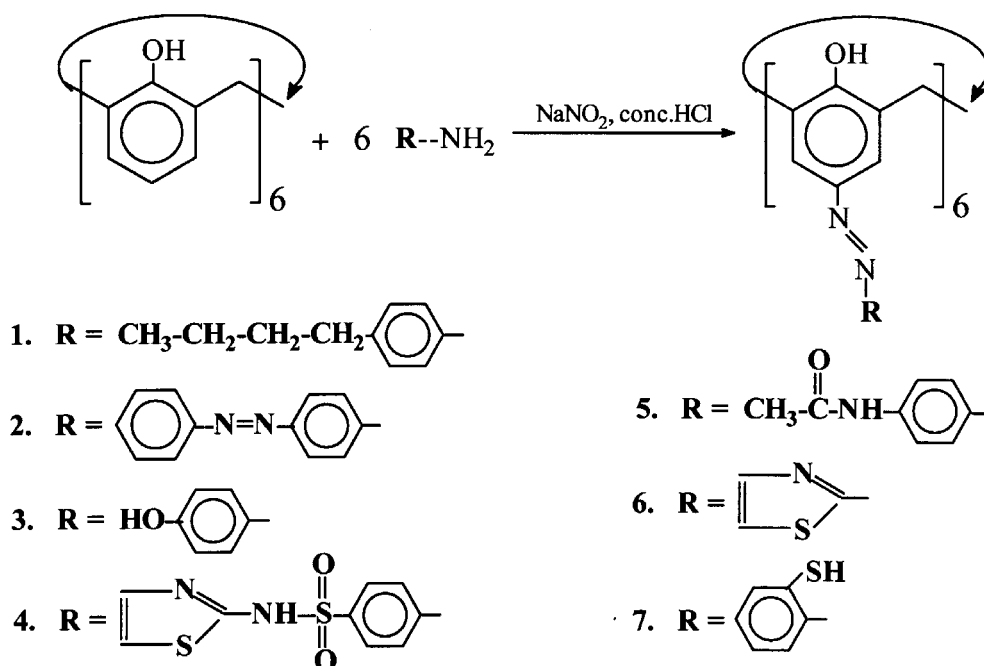


Figure 1. Azo derivatives of calix[6]arene.

was filtered off, washed with water and MeOH, and dried. Yield 2.21 g (72%) of **7**, mp. 247 °C.

^1H NMR (DMSO, 25 °C), δ : 1.25–1.30 (6H, s, SH), 2.60–3.30 (12H, broad, ArCH₂Ar), 6.80–7.80 (36H, s, arom.-H), 11.70 (6H, s, OH). ^{13}C NMR (DMSO, 25 °C): δ_{C} : 147.7, 146.4, 141.2, 138.6, 137.2, 133.8, 125.7, 121.1, 32.9

The compound is soluble in DMSO, slightly soluble in benzene, and CHCl_3 , insoluble in water, ethanol, diethyl ether, acetic acid, and acetone.

Results and discussion

In this work, the syntheses of calix[6]arenes have been performed by the method of Gutsche *et al.* [27]. Then seven new azo calix[6]arenes were synthesized from 5,11,17,23,29,35-hexahydroxycalix[6]arene and diazotized 4-butylaniline, 4-(phenylazo)aniline, 4-aminophenol, N⁴-(thiazol-2-yl)sulfanylamide, 4-aminoacetanilide, 2-aminothiazole and 2-aminobenzene-1-thiol. General formulas of these compounds are given in Figure 1.

Previously, we investigated the azo coupling reactions of calix[4]arene with 4-substituted benzenediazonium chlorides [23]. Now, we synthesized a series of seven novel azo calix[6]arene derivatives according to the method described by Morita *et al.* [14]. The reactions proceeded smoothly producing the corresponding azo compounds in good yields. All the aniline derivatives used reacted quantitatively with an equimolecular amount of calix[6]arenes.

p-(4-Butyl-phenylazo)calix[6]arene (**1**), was obtained in the following manner. First, calix[6]arene was prepared by debutylation of *p*-*tert*-butylcalix[6]arene. The azo coupling reaction of calix[6]arene with 4-

butylbenzenediazonium chloride in MeOH-DMF gave *p*-(4-butylphenylazo)calix[6]arene in 87% yield.

p-[4-(Phenylazo)phenylazo]calix[6]arene (**2**), *p*-(4-hydroxyphenylazo)calix[6]arene (**3**), *p*-[4-[*N*-(thiazol-2-yl)sulfamoyl]phenylazo]calix[6]arene (**4**), *p*-(4-acetamidophenylazo)calix[6]arene (**5**), *p*-(thiazol-2-ylazo)calix[6]arene (**6**) and *p*-(2-sulfanyl-phenylazo)calix[6]arene (**7**) were obtained in the same manner. The yields of these compounds (79%, 58%, 67%, 73%, 65% and 72%, respectively) are in good agreement with the literature [13–15]. Then the synthesized compounds were purified by crystallization in the same solvent (MeOH-DMF) and analyzed. The results are summarized in Tables 1, 2 and 3.

The obtained values for ^1H NMR chemical shifts of calix[6]arene: OH (9.60 ppm), Ar (6.90–8.50 ppm) and methylene bridge (3.50–4.50 ppm) are identical with literature values. In the ^1H NMR spectrum of compound **1**, CH₃ and CH₂ protons show a triplet (0.93 ppm) and multiplet (1.26 ppm and 1.62 ppm), respectively; the —CH₂—Ar protons resonate at 3.87–4.10 ppm.

Although the ^1H NMR signals of the aromatic protons for compound **2** and calix[6]arene are complex, the intensity and integration of the peaks showed the azo coupling of diazotized aminoazobenzene to calix[6]arene as two peaks were obtained in the ^1H NMR spectra for the OH protons of compound **3** at 9.95 ppm and of 6.73 ppm. The chemical shift for the OH protons is a characteristic value for calixarenes. In compound **4**, two symmetric =CH— protons in the thiazole ring were observed as a doublet at 1.20–1.25 ppm for compound **4**. Similar values were observed as a doublet at 1.25–2.55 ppm for compound **6**. The methyl and NH protons of compound **5** were found at 1.26 ppm and 10.11 ppm, respectively. The chemical shift values of the characteristic SH peaks for compound **7** were observed at 1.25–1.30 ppm. The secondary carbons of the character-

Table 1. Properties of azo derivatives of calix[6]arenes

Compound formulas	MW	Color	mp. (°C)	Yield %	Calcd. (Found)			
					C	H	N	S
1. 2CH ₃ OH C ₁₁₂ H ₁₀₈ N ₁₂ O ₆	1598.6	Magenta	310	87	76.66 (76.54)	6.81 (6.93)	10.52 (10.38)	–
2. CH ₃ OH C ₁₁₄ H ₈₄ N ₂₄ O ₆	1886.1	Pale brown	300	79	72.60 (72.90)	4.49 (4.38)	17.82 (17.73)	–
3. CH ₃ OH C ₇₈ H ₆₀ N ₁₂ O ₁₂	1357.4	Orange	218	58	69.02 (68.88)	4.46 (4.37)	12.38 (12.46)	–
4. 2CH ₃ OH C ₉₆ H ₇₂ N ₂₄ S ₁₂ O ₁₈	2234.5	Pink	270	67	51.60 (51.78)	3.25 (3.39)	15.04 (14.91)	17.22 (17.07)
5. 2CH ₃ OH C ₉₀ H ₇₈ N ₁₈ O ₁₂	1603.7	Dark brown	295	73	67.41 (67.22)	4.90 (5.03)	15.72 (15.67)	–
6. CH ₃ OH C ₆₀ H ₄₂ N ₁₈ S ₆ O ₆	1303.5	Dark brown	327	65	55.29 (55.54)	3.25 (3.08)	19.34 (19.12)	14.76 (14.93)
7. CH ₃ OH C ₇₈ H ₆₀ N ₁₂ S ₆ O ₆	1453.8	Brown	247	72	64.44 (64.57)	4.16 (4.02)	11.56 (11.39)	13.23 (13.04)

Table 2. Characteristic IR bands (cm⁻¹) of azo derivatives of calix[6]arenes^a

Compounds	$\nu_{\text{O-H}}$	$\nu_{\text{(CH)arom}}$	$\nu_{\text{-CH}_2\text{-}}$	$\nu_{\text{S-H(tio)}}$	$\nu_{\text{C=O}}$	$\nu_{\text{-C=C-}}$	$\nu_{\text{-N=N-}}$	$\nu_{\text{-SO}_2\text{-}}$
1. 2CH ₃ OH	3280	3150	2980	–	–	1610	1490	–
2. CH ₃ OH	3250	3100	–	–	–	1600	1480	–
3. CH ₃ OH	3400	3180	–	–	–	1610	1480	–
4. 2CH ₃ OH	3300	3190	–	–	–	1620	1490	1290
5. 2CH ₃ OH	3350	3060	–	–	1690	1600	1490	–
6. CH ₃ OH	3340	3010	–	2550	–	1620	1480	–
7. 2CH ₃ OH	3170	3120	–	–	–	1630	1490	–

^a In KBr pellets.

istic thiazole ring appear in the ¹³C NMR spectra at about 145.3–155.5 ppm for compounds (4) and (6), respectively.

Characteristic IR bands of the compounds are given in Table 2. The stretching vibrations of azo compounds 1–7 appear at 3170–3400 cm⁻¹ (OH), 3060–3190 cm⁻¹ (arom. C–H), 1600–1630 cm⁻¹ (arom. C=C) and 1480–1490 cm⁻¹ (N=N). Compounds 1, 4 and 6 exhibit characteristic strong absorption bands at 2980 cm⁻¹ (CH₂), 1290 cm⁻¹ (SO₂) and 2550 cm⁻¹ (S–H), respectively. The characteristic carbonyl peak appears at 1690 cm⁻¹ for compound 5 (Table 2). Although compounds 2, 3 and 7 do not show characteristic IR absorption peaks, the intensities of the peaks observed at around 1480–1490 cm⁻¹ were quite high.

In the electronic spectra, the absorptions at 305 and 419 nm arise from $\pi \rightarrow \pi^*$ transitions of the —N=N— bond. The synthesized diazo coupled compounds are soluble in DMSO, but dissolve difficulty with in CHCl₃.

The azo compounds synthesized have been defined in the literature [13], whose molecular design are known as chromogenic calix[4]arenes.

The calix[6]arene azo compounds act as metal ligands or as dyes. We have accomplished syntheses of these organic pigments, using cheap commercial aromatic amines. The properties of the synthesized dyes, their application to cotton

Table 3. Electronic spectra of azo derivatives of calix[6]arenes (in DMSO)

Compounds	Wavelength (nm)	ϵ
1. 2CH ₃ OH	362	6870
2. CH ₃ OH	384	7620
3. CH ₃ OH	282	5690
4. 2CH ₃ OH	305	14730
5. 2CH ₃ OH	399	2400
6. CH ₃ OH	419	6120
7. 2CH ₃ OH	305	12920

fibers and their suitability for the textile industry were investigated. Studies concerning metal binding properties of the synthesized calix[6]arene derivatives containing azo groups are in progress.

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