

# Synthesis and Characterization of *Tetrakis*- Derivatives of Bisphenol-A with 4-Phenylazoaniline and 5-(4-Aminophenylazo)-25,26,27-tribenzoyloxy-28-hydroxycalix[4]arene

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**ABSTRACT:** The synthesis of *tetrakis*- derivatives of bisphenol-A containing azo groups at their 2,2',6,6'-positions is reported. Novel examples of bisphenol-A, coupled with diazonium salts and derived from 4-phenylazoaniline and 5-(4-aminophenylazo)-25,26,27-tribenzoyloxy-28-hydroxycalix [4]arene, have been synthesized. It has been observed that the coupling reaction of diazonium salt obtained from 4-phenylazoaniline with bisphenol-A gives *tetrakis*- while those derived from 5-(4-aminophenylazo)-25,26,27-tribenzoyloxy-28-hydroxycalix [4]arene give partially substituted

bisphenol-A analogues. The newly prepared *tetrakis*-azo substituted bisphenol-A compounds (**1** and **2**) are characterized by using UV-vis, FT-IR, <sup>1</sup>H-NMR spectroscopic methods as well as elemental analysis techniques. These azo compounds give rise to bathochromic shifts in the absorption spectra, which can even be detected by "naked eye." © 2011 Wiley Periodicals, Inc. *J Appl Polym Sci* 122: 76–82, 2011

**Key words:** calixarene; azocalix [4]arenes; absorption spectra; bisphenol-A

## INTRODUCTION

Bisphenol-A [BPA, 2,2'-bis(4-hydroxyphenyl)propane], abundantly present in water and sediments, has been widely used in manufacturing epoxy resins and polycarbonates. Calix[*n*]arenes are mainly cavity-shaped macrocyclic molecules formed by *n* phenol units linked via methylene groups. Since calixarenes have cavity-shaped architecture, they can be used as building blocks for host-guest type receptors with appropriate modifications. Both chemical nature and geometry of cavity seem essential for calix[4]arene complex formation.

The chemistry of calix[*n*]arenes has been well reviewed by Gutsche.<sup>1</sup> Azocalix[*n*]arenes, containing conjugated chromophore azo (-N = N-) group in *p*-positions, can be synthesized by using "one-pot" procedures in satisfactory yields.<sup>2</sup>

Anion recognition continues to be a very attractive and challenging area of research with the possible application of selective ion receptors in biological and environmental systems. Neutral receptors possessing units with hydrogen bond donor capability have drawn attention for their interaction with anionic species.<sup>3</sup>

It is well-known that calix[4]arenes can exist in cone, partial cone, 1,2-alternate cone and 1,3-alternate cone conformations.<sup>4</sup> The available sites on these macrocyclic compounds can easily be modified for many applications, such as ionophores in catalysis, heavy metal adsorption agents, and alkali metal and inclusion complexation agents.<sup>5–7</sup> Various attempts have been undertaken to incorporate calixarenes into different polymers, some of which are self-assembled systems.<sup>8–10</sup> In comparison to azocalix[*n*]arenes, *tetrakis*- azocalix[*n*] arenes are much recent innovation. Only a few examples have been reported.<sup>2</sup>

The recognition of anions using luminescent or colorimetric methods has aroused interest. In particular, charged and neutral receptors such as metal-based macrocycles,<sup>11</sup> amides,<sup>12</sup> carbamides,<sup>13</sup> and ureas<sup>14</sup> have been employed for the selective recognition of anions in relatively simple structural motifs.<sup>15</sup> Such binding sites have also been incorporated into structural frameworks such as polymeric compounds,<sup>16</sup> calixarenes<sup>1</sup> and azocalixarenes<sup>2</sup> leading to more preorganized anion recognition motifs. Moreover, such designs can give rise to larger supramolecular assemblies as demonstrated elegantly by Yilmaz et al., Gutsche et al. and our group. Anion receptors have also been employed for medical purposes as biological mimics for the transportation of anions and ion pairs across cell membranes.<sup>3</sup>

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Single or multiple calix[*n*]arenes have drawn attention of several research groups as high order supramolecular systems. Majority of these compounds include one or more calixarene units linked through the intermediacy of a proper spacer. However, first examples of bridgeless *tetra*-azo BPA **1** and *tetra*-azocalix[4]arene BPA **2**, with *tetra* units linked "head-to-head" with a direct biphenyl-like *para-para* linkage have recently been reported by our group.<sup>2</sup>

Recent works by the author have presented the syntheses of the series of twelve aromatic azocalix[4]arenes and azocalix[6]arenes and the series of seven heterocyclic azocalix[4]arenes and azocalix[6]arenes. These substances have been investigated by characterizing their absorption, chromogenic, and ionophoric properties.<sup>17-19</sup> Herein, we report the syntheses and characterization of *tetrakis*-azocalix[4]arene derivatives, investigation of ionophoric properties and their detection by "naked eye."

## EXPERIMENTAL

All reagents used were chemically pure and, were purchased from either Merck or Carlo-Erba. Melting points were determined on an Electrothermal IA9100 digital melting point apparatus and reported without correction. <sup>1</sup>H NMR spectra were referenced to tetramethylsilane (TMS) at 0.00 ppm as an internal standard and recorded on a Bruker 200 MHz spectrometer at room temperature (25 ± 1°C). <sup>13</sup>C NMR spectra were referenced to CDCl<sub>3</sub> (77.00 ppm) or TMS (0.00 ppm) and also recorded at room temperature (25 ± 1°C). IR spectra were recorded on a Mattson 1000 FTIR spectrometer by using KBr pellets. UV-vis spectra were obtained on a Shimadzu 160A UV-Visible recording spectrophotometer. The elemental analyses were performed in Laboratories of TUBITAK (Center of Science and Technology Research of Turkey).

### Preparation of the ligands

*p*-*tert*-Butylcalix[4]arene,<sup>20</sup> calix[4]arene,<sup>21</sup> and 5-(4-aminophenylazo)-25,26,27-tribenzoyloxy-28-hydroxycalix[4]arene<sup>22</sup> were synthesized by previously reported methods. Chemically pure 4-phenylazoaniline was purchased from Merck.

### Synthesis of 2,2',6,6'-tetrakis(4-phenylazophenylazo)bisphenol-a (BPA **1**)

General procedure<sup>23</sup>: A solution of 4-phenylazobenzene diazonium chloride, prepared from 4-phenylazoaniline (5.16 g, 26.2 mmol), sodium nitrite (2.50 g, 36.2 mmol) and conc. HCl (7 mL) in water (25 mL), was added slowly into a cold (5°C) solution of

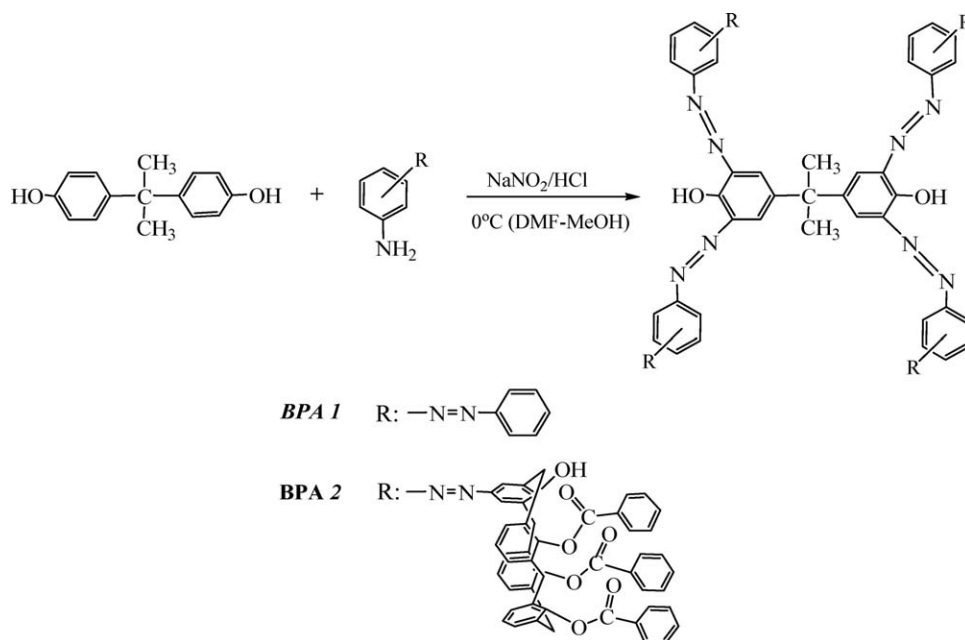
bisphenol-A (1.0 g, 4.35 mmol) and sodium acetate trihydrate (4.08 g, 30 mmol) in DMF-MeOH (26 mL, 8:5, v/v) to give a red suspension. The suspension was acidified with aqueous HCl (100 mL, 0.25%) after standing for 2 h. The mixture was heated up to 60°C and kept at that temperature for 30 min. The suspension was filtered and resulting residue was washed with water and MeOH. A sample for analysis was obtained as follows: Compound **1** was dissolved in 100 mL of a hot NaHCO<sub>3</sub> (4.2 g) solution. Activated charcoal was added to this solution (1 g). After the charcoal was filtered, the filtrate was cooled down to room temperature and acidified with conc. HCl (1 or 2 mL). The solution was heated up to 60°C again and kept at that temperature for 30 min and cooled back to room temperature. The resulting suspension was filtered and obtained residue was washed with water, and dried eventually. Final product of brown solid was prepared for analysis. Yield, 2.21 g (85%). mp. 190°C; [Found: C 75.22; H 7.07; N 10.03. C<sub>69</sub>H<sub>76</sub>N<sub>8</sub>O<sub>5</sub> requires C 75.51; H 6.98; N 10.22]. m/z: 1060. λ<sub>max</sub>(ε): 364 (5970). ν<sub>max</sub>: 3402, 3058, 1593, 1491 cm<sup>-1</sup>. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 25°C): δ<sub>H</sub>: 1.51 (6H, s, CH<sub>3</sub>), 5.43 (2H, s, -OH), 7.18 (4H, s, BPA Ar-H), 7.24-7.50 (16H, s, J = 7.5 Hz, -N = N-Ar-H), 7.70-8.04 (20H, d, Ar-H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 25°C): δ<sub>C</sub>: 145.1, 144.6, 139.8, 135.7, 135.3, 132.5, 123.6, 121.4, 25.4, 9.8.

Although, the BPA **1** can easily be dissolved in EtOH, diethyl ether, acetone, acetic acid, benzene, CHCl<sub>3</sub>, and DMSO, it is insoluble in water.

### Synthesis of 2,2',6,6'-tetrakis[5-(4-phenylazophenylazo)-25,26,27-tribenzoyloxy-28-hydroxycalix[4]arene]bisphenol-A (BPA **2**)

BPA **2** was prepared as described above, using 5-(4-aminophenylazo)-25,26,27-tribenzoyloxy-28-hydroxycalix[4]arene. The resulting suspension was filtered and acquired residue was washed with water and methanol, and dried finally. The ultimate product of dark brown solid was prepared for analysis. Yield, 2.48 g (81%). mp. 146°C; (Found: C 71.42; H 4.78; N 17.12. C<sub>211</sub>H<sub>168</sub>N<sub>16</sub>O<sub>30</sub> requires C 71.71; H 4.69; N 17.39). m/z: 3270. λ<sub>max</sub>(ε): 396 (4620). ν<sub>max</sub>: 3159, 3091, 1682, 1594, 1466 cm<sup>-1</sup>. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 25°C): δ<sub>H</sub>: 1.45 (3H, s, CH<sub>3</sub>), 1.71 (3H, s, CH<sub>3</sub>), 3.48-4.21 (32H, d, J = 7.6 Hz, Ar-CH<sub>2</sub>-Ar), 5.12 (2H, s, -OH), 6.65 (44H, t, J = 7.5 Hz, calix Ar-H), 6.95 (60H, d, J = 7.5 Hz, benzoyl Ar-H), 7.18 (4H, s, BPA Ar-H), 7.08-7.13 (20H, s, -N = N-Ar-H), 10.12 (4H, s, -OH). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 25°C): δ<sub>C</sub>: 206.8, 156.4, 154.9, 145.1, 144.2, 139.5, 135.5, 135.1, 132.3, 123.4, 120.9, 32.4, 25.9, 10.1.

Water insoluble BPA **2** is soluble in EtOH, acetone, acetic acid, benzene, CHCl<sub>3</sub>, DMSO, and slightly soluble in diethyl ether.



**Scheme 1** The synthesis reactions of BPA 1 and BPA 2.

## RESULTS AND DISCUSSIONS

### Synthesis and characterization

In recent years, various attempts have been undertaken to incorporate azocalix[*n*]arenes into different polymers including self-assembled systems. Different methods have been used to prepare diazo coupled calixarene-based polymers. The first one is the attachment of the amino calix[*n*]arene by diazotization reaction with a suitably functionalized polymer or oligomer. This approach gives well-defined products since there is no risk of incomplete substitution of the functionalized polymer. Thus, azocalix[*n*]arene monomers have widely been incorporated into dimer backbones by utilizing functional groups.

Majority of the studies on calix[4]arenes as chromogenic ionophores involves modification of the *lower rim* with metal-chelating groups such as acids, amides, esters, ketones, or any ligand containing lone pair electrons. Following, a fluorophore or chromophore is attached on the *upper rim*. Shinkai and coworkers<sup>24</sup> were the first ones to synthesize calix[4]arene with a 4-(4-nitrophenyl)azophenol unit and three ester residues on the *lower rim*. Their cation complexation experiment in the presence of imidazole revealed that the complex exhibits a new absorption maximum at 600 nm, which is "perfect" for lithium sensors. It should be noted that imidazole alone does not cause any spectral change, confirming that deprotonation and complexation are integral events in the chromogenic response. Furthermore, Reinhoudt et al.,<sup>25</sup> incorporated mono-alkylated 4-(4-nitrophenyl) azophenol on the upper rim and triamides on the lower rim of calix[4]arene,

thus formed a highly selective  $\text{Pb}^{2+}$  sensor, in which the direction of the shift totally depends on the conformation of the calix[4]arenes.

In this study, two new diazo-coupled BPA 1 and BPA 2 were synthesized by an acid-catalyzed coupling reaction of BPA with diazotized solutions of 4-phenylazoaniline and 5-(4-amino phenylazo)-25,26,27-tribenzoyloxy-28-hydroxycalix[4]arene (Scheme 1). The parent 5-(4-aminophenylazo)-25,26,27-tribenzoyloxy-28-hydroxycalix[4]arene was obtained by following literature procedures.<sup>22</sup> The coupling reaction was performed at 0–5°C in a mixed DMF/MeOH (8 : 5) solvent. Following, sodium acetate which is behaving as base added into solution before separation of the products by column chromatography to yield pure products in reasonable to good yields.

*Tetrakis*- BPA 1 and BPA 2 compounds, bearing both chromogenic *p*-phenylazophenylazo- and two free phenolic groups have been synthesized through diazo coupling reaction of corresponding diazotized amines with BPA derivatives. Both of the derivatives were afforded through *p*-phenylazophenylazo- (1) or *p*-phenylazophenylazotribenzoylcalix[4]arene- (2) of BPA derivatives.

It was interesting to note that the solvent used for the coupling reaction has a profound effect on the outcome of the reaction, i.e., the extent of substitution as well as the yield of the final product obtained. For example, when sole DMF was employed instead of DMF-MeOH in the coupling reaction, orange crystals of pure 1 in far better yields (85%) were obtained in contrast to the yields obtained from the use of DMF-MeOH mixture

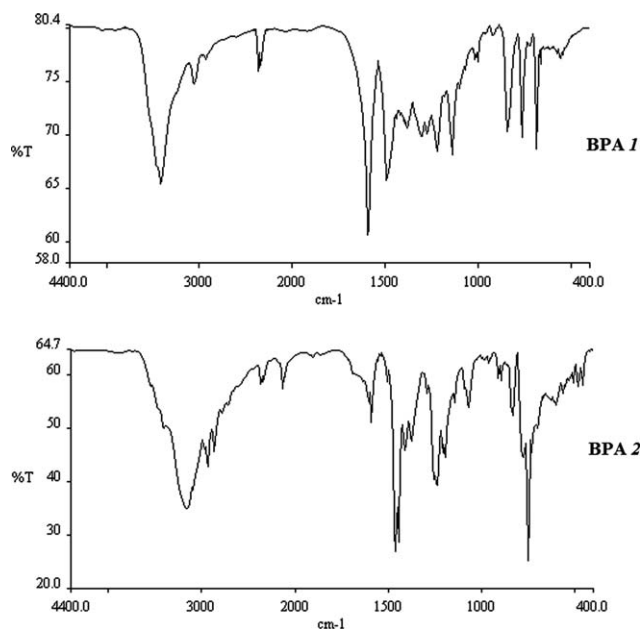


Figure 1 IR spectra of BPA 1 and BPA 2.

(81%). In addition, the latter solvent afforded a mixture of **1** and **2**.

The characteristics of IR absorptions are given in experimental section. The observed micro analytical data for C, H, and N atoms of the BPA **1** and BPA **2** demonstrates that both compounds contain water molecules, which are, identified by broad O—H absorptions around  $3159\text{--}3402\text{ cm}^{-1}$  in IR spectra. The most significant differences in the IR spectra of the BPA **1** and BPA **2** were the shifts of N = N stretching frequencies to lower frequencies due to diazocoupling reaction (Fig. 1). Furthermore, a new band has been observed around  $1466\text{--}1491\text{ cm}^{-1}$  which can be attributed to  $\nu(\text{N} = \text{N})$ . All the IR spectra information supports the suggestion of coupling of the diazo atoms of the calix[4]arene tribenzoyl moiety and the phenylazophenylazo moiety. According to the above discussion, general structures for the BPA **1** and BPA **2** are proposed as shown in Scheme 1.

The detailed  $^1\text{H}$  NMR spectral analysis of the synthesized compounds revealed that the BPA **1** and BPA **2** exhibit a singlet for the aromatic protons of the substituted bisphenol-A ring in the range  $\delta$  7.08–7.50. BPA **2** exhibits a triplet and a doublet for the aromatic and tribenzoyl protons of the azocalix[4]arene ring at  $\delta$  6.65–6.95, respectively. By analog and comparison of  $^1\text{H}$  NMR spectral data, it appears that the synthesized azocalix[4]arene (BPA **2**) has the *cone* conformation. The structural conformation of BPA **2** was determined to be cone by comparing its NMR patterns with those of similar azocalix[4]arene moieties.

### Chromogenic properties and tautomerism

The chromogenic ionophore properties of BPA **1** and BPA **2** were studied by examining the UV-vis absorption behavior of the host in DMF solution (Fig. 2). These spectra suggest that BPA **1** and BPA **2** may exist in two possible tautomeric forms at once, namely an azophenol form and quinone-hydrozone form. The visible spectral properties and tautomeric equilibrium of the bisphenol-A derivative may alter according to the substituents of azocalix[4]arene. In this case, BPA **1** and BPA **2** showed typical UV spectral behavior of phenylazo derivatives and their absorption maxima are located at 364 and 396 nm, respectively. However, BPA **1** exhibits a stronger absorption band than that of BPA **2** at 364 nm and a shoulder at 455 nm corresponding to  $\pi\text{--}\pi^*$  and  $n\text{--}\pi^*$  transitions, respectively, which are in accordance with typical diazo spectra.

A pair of characteristic bands of BPA **1** and BPA **2** in the UV-vis absorption spectra indicates that BPA **1** and BPA **2** exist as a mixture of the two tautomeric forms in DMF solution. This can be explained by the assumption that an azophenol form of BPA **1** and BPA **2** gets stabilized through a six-membered hydrogen bonded structure between nitrogen atom of azo unit and hydrogen atom of *p*-phenylazo group, or *p*-azocalixarene group represented by a quinone-hydrozone form.

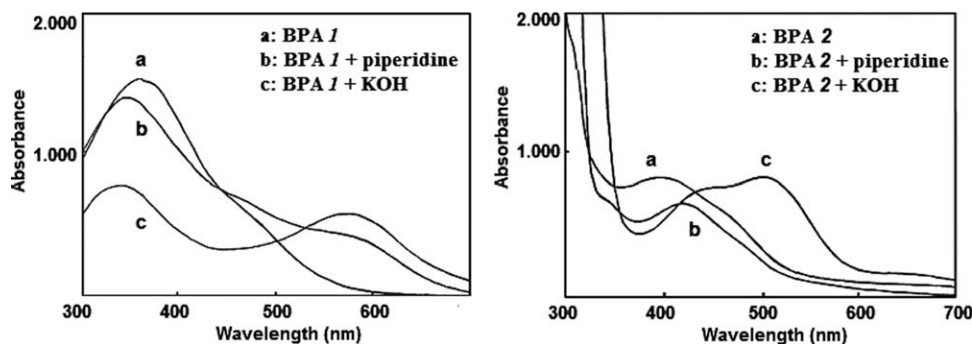
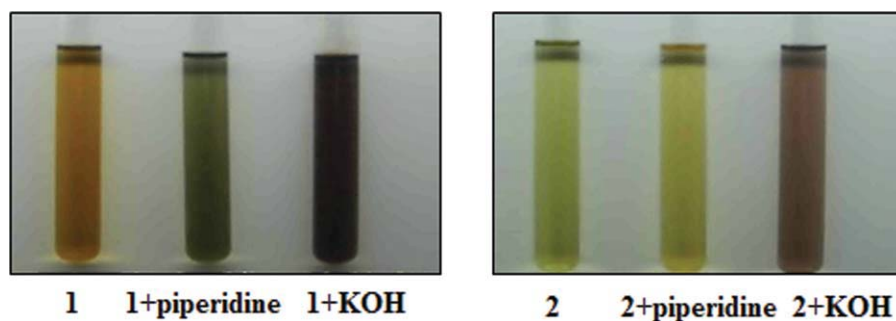


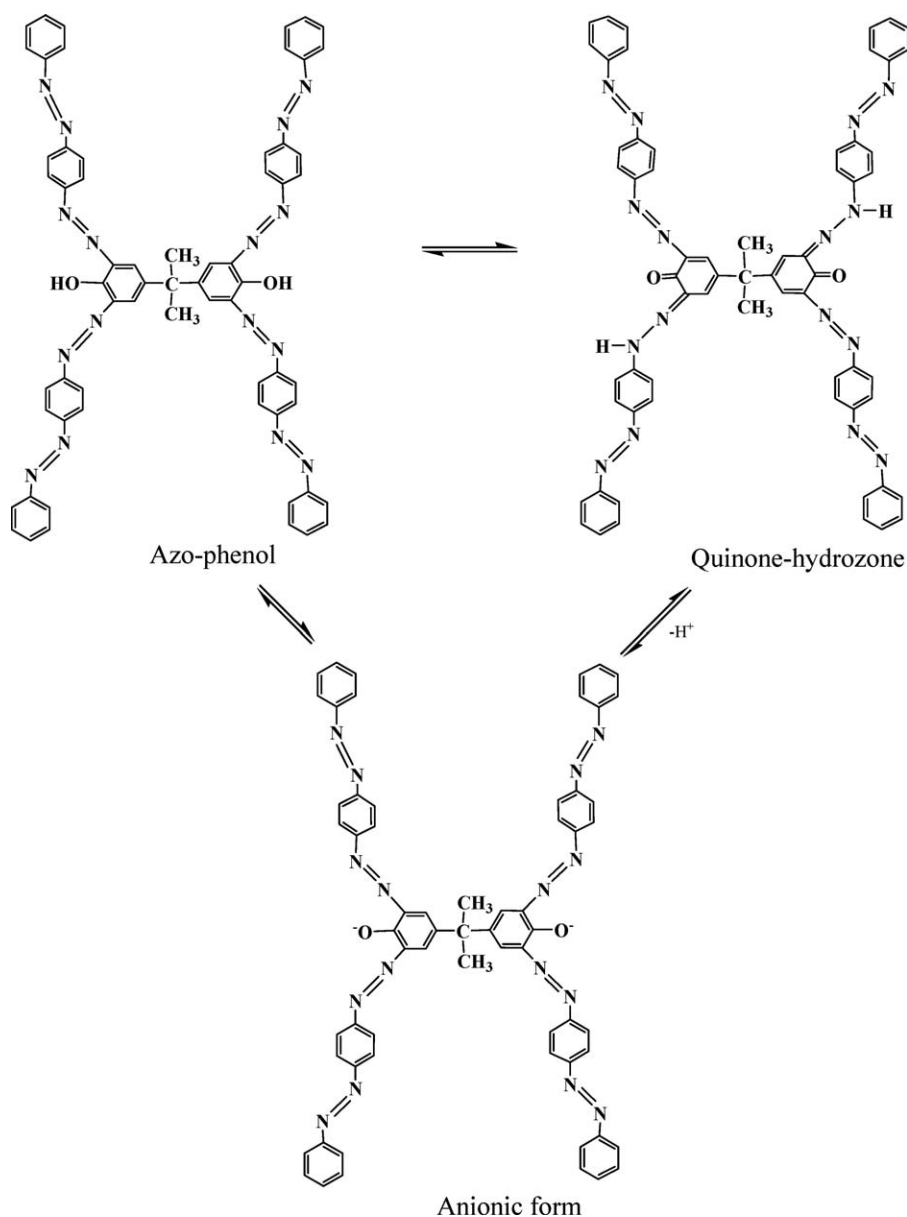
Figure 2 The absorption spectra of the BPA **1** and BPA **2** in various bases.



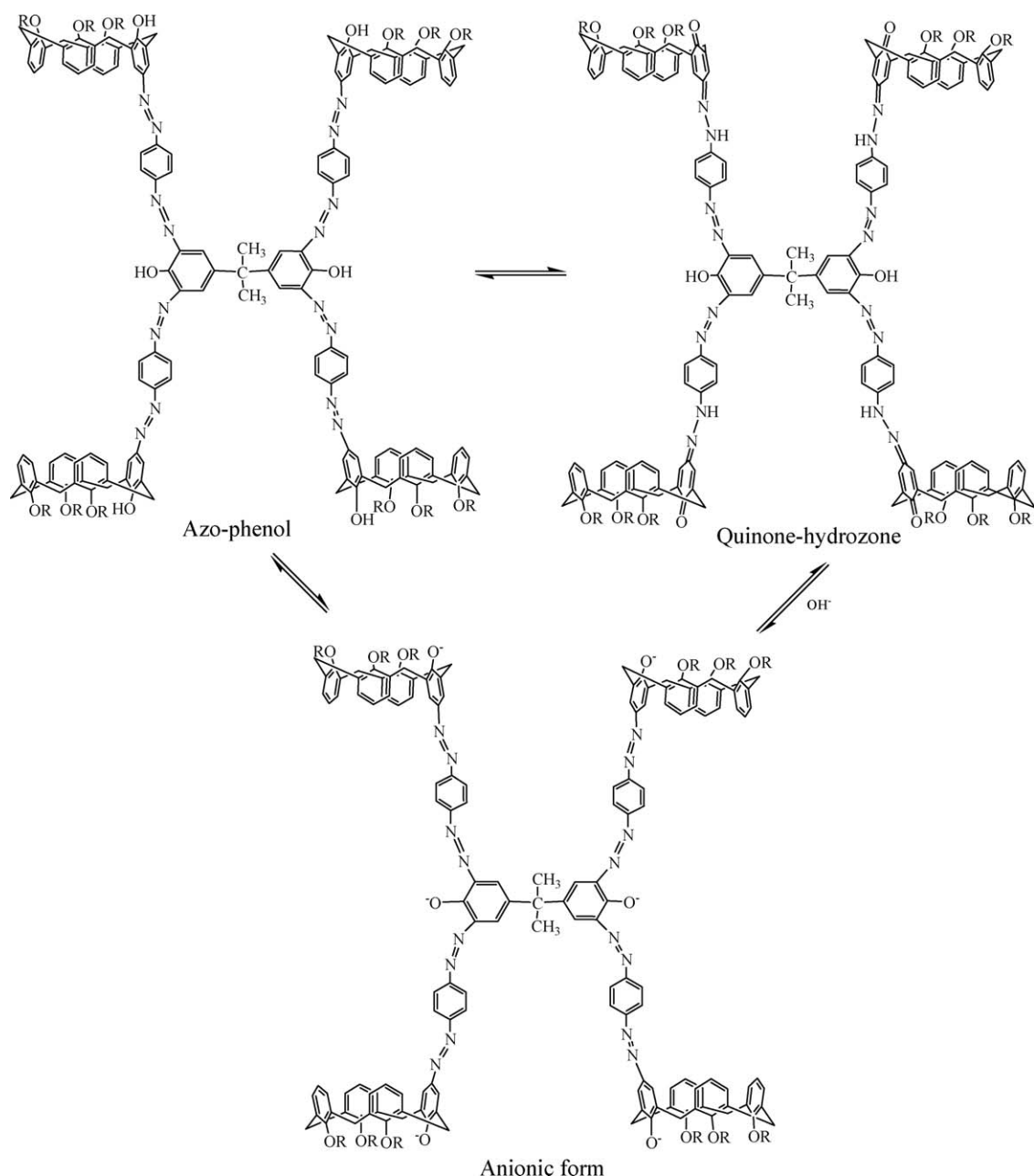
**Figure 3** The changed colors of BPA 1 and 2 in DMF at base (piperidine and MeOH+KOH). [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://wileyonlinelibrary.com).]

These azo compounds give rise to bathochromic shifts in the absorption spectra (from orange/yellow to dark red), which can even be detected by “naked

eye.” The visible color changes of BPA 1 and BPA 2 upon various bases (piperidine and MeOH+KOH) have also been observed and depicted in Figure 3.



**Scheme 2** The tautomeric and anionic forms of 2,2',6,6'-tetrakis(4-phenylazophenylazo)bisphenol-A (BPA 1).



**Scheme 3** The tautomeric and anionic forms of 2,2',6,6'-tetrakis[5-(4-phenylazophenylazo)-25,26,27-tribenzoyloxy-28-hydroxycalix[4>arene] bisphenol-A (BPA 2).

The color of DMF solutions of BPA 1 and BPA 2 turned from orange to red and yellow to deep orange in the presence of piperidine and MeOH+KOH respectively. The bases (piperidine and MeOH+KOH) have been separately added into DMF solutions of BPA 1 and BPA 2 until the color changes are observed. This unique point of view with visual color changes leads us to consideration of these compounds in the screening process of indicators.

Surprisingly, no detectable changes in absorption spectra have been observed for the phenylazo BPA 1 and BPA 2 when piperidine had been added in excess. These observations imply that there is a subtle balance

between base-induced release of protons from the azo-phenols to the quinone tautomer (Scheme 2).

Moreover, the azocalixarene substituents of the phenylazo group must have strong influence on the tautomerism of azo/hydrazone, thus showing very diverse  $\lambda_{\max}$  shifts. A picture of base-induced tautomerism of the phenylazocalix[4]arene is shown in Scheme 3.

## CONCLUSIONS

We have developed BPA 1 and BPA 2 as two novel colorimetric sensors for anions, by incorporating azo

based receptors. They are used in model compounds **1** and **2**, as *tetrakis*-substituted BPA in short and high yielding synthesis. We have demonstrated that these receptors can bind to various bases (piperidine and MeOH+KOH) in an equivalent stoichiometry with colorimetric changes. The binding occurs through hydrogen bonding and deprotonation of the receptors in either BPA **1** or **2** does not occur until high base concentrations are reached. We are currently working towards developing other analogues of BPA with the aim of achieving a more selective anion sensation and the formation of anion template self-assembly structures.

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