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ORIGINAL ARTICLE

Synthesis and metal extraction studies of a novel chromogenic 5,17-bisazocalix[4]arenes

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Abstract Three novel chromogenic *cone* azocalix[4]arenes **5a**–**c**, which have cavity and the azo groups as metal-binding sites and as coloration sites were synthesized. They were studied by the liquid–liquid extraction of selected metal cations (Sr^{2+}, Ag^{+}, Hg^{+}, Hg^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cr^{3+}, Al^{3+}). Through examination of the extraction, a novel selectivity of these compounds toward Hg^{2+} cations has been determined. Besides, it has been also found that azocalix[4]arene **5c** is highly sensitive to acid–base titration, which can be detected by the *naked eye*.

Keywords Calixarene · Bisazocalix[4]arenes · Picrate extraction · pH effect · *Naked eye*

Introduction

Calix[4]arenes have been shown to be useful molecular scaffold in the development of chromoionophores, especially for metal ion recognition [1–3]. Azocalix[*n*]arenes, generated by the insertion of nitrogen atoms into the *p*-position unit of the calix[*n*]arene structure, have several isomers based on the positions of the nitrogen atoms and its ring cavity. The first reported calixarene diazo coupling has involved the reaction of *p*-nitrobenzenediazonium tetrafluoroborate with calix[4]arene [4, 5].

The synthesis of new chemosensors for metal ions plays an important role in the field of supramolecular chemistry due to their fundamental agent in biological, environmental, and chemical processes. Chromogenic ionophores have been intensively investigated as a specific metal ion indicator for the use of 4-(4-nitrophenyl)azo-coupled crowns and azacrowns as chromoionophores. They showed large UV–Vis band shifts when cations were added [6–8].

Over the last few decades, as a major activity in supramolecular chemistry, chemists have synthesized many types of receptors for complexing cations, anions and neutral molecules both in solution and in the solid state [9]. Ungaro et al. [10] have first reported the binding of potassium by calix[4]crown-5 ligands. The use of crown ethers covalently bound to calix[4]arenes has been studied extensively for selective extraction of cations. Their studies have expanded to include calix[4]arene in modified crown structures. Among them, the family of calix[4]azacrowns refers to molecules combining calix[4]arene elements, which may also serve as linking functions and chelating groups [11]. The linkage of the azacrown unit on the calix[4]arene is often conducted by coupling diacylchloride or diethylester calix derivatives with polyamino alkylene diamino compounds to give bridged calix(aza)crowns [12].

Much of our earlier work in this area has concentrated on calix[*n*]arene with *lower rim* and *upper rim* in the form of mono oxime, *vic*-dioxime, polymeric, Schiff base, azo groups and telomeric structure [13, 14]. Extraction, transport, thermal behavior and stability constant which have been investigated by spectrophotometric studies have provided evidences that many of these *lower rim* derivatives have very significant ionophoric properties for cations, several with good selectivity within groups of metals [15–17].

Electronic supplementary material The online version of this article (doi:10.1007/s10847-014-0408-4) contains supplementary material, which is available to authorized users.

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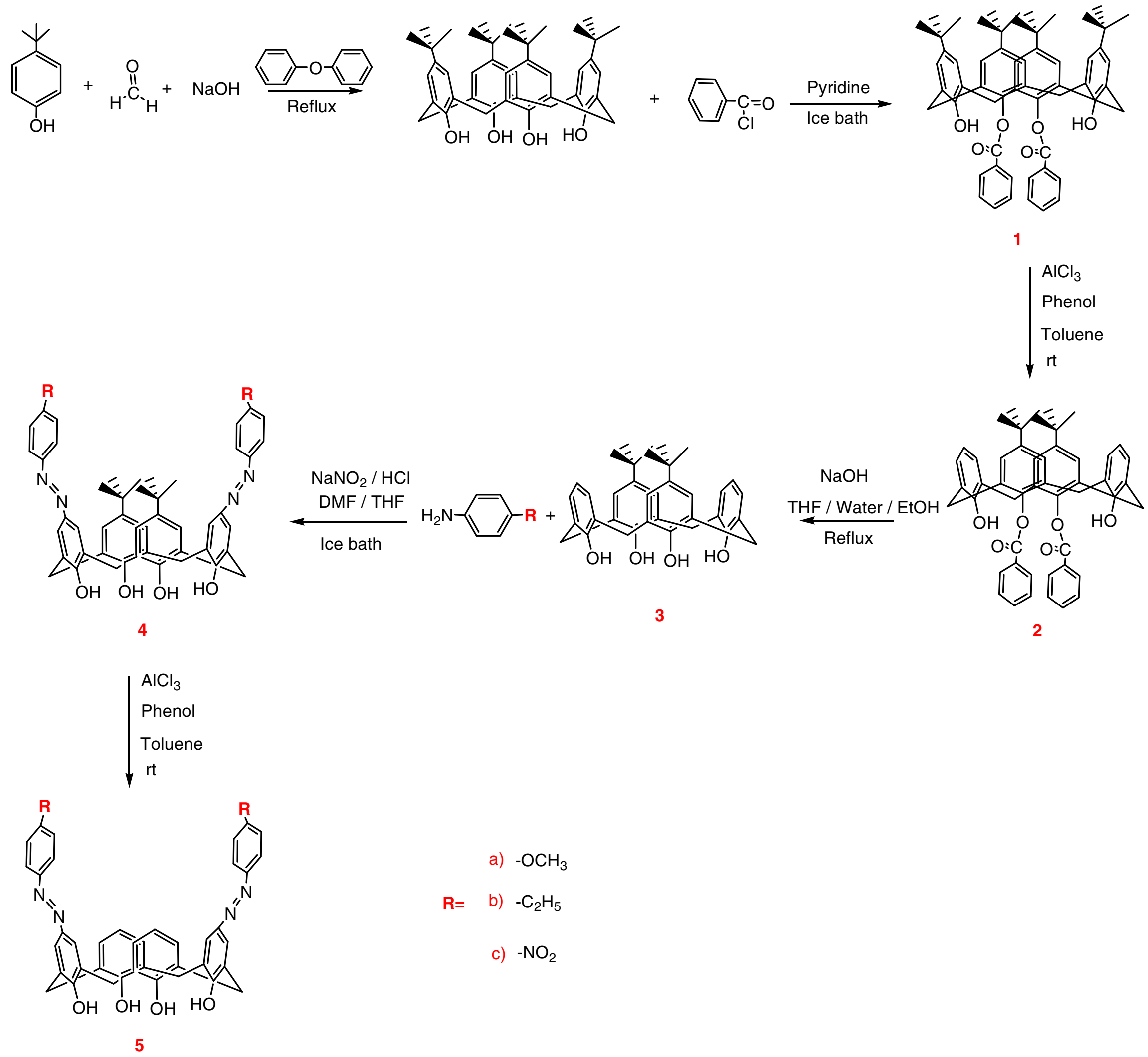


Scheme 1 Diazo-coupled bisazocalix[4]arene derivatives **5a–c**

In the crystal state, some calix[4]azacrowns have been shown to form tubular architectures, in which the channels are filled by methanol [18].

In the examples given in the literature, the calix core of the azocalix[4]arenes is bridged either by one or two bridge. In this Letter, we report here the synthesis of a novel chromogenic 5,17-bisazocalix[4]arenes using the click chemistry [19] of a calix ester and an aniline derivatives to form a diazo cationic binding site. Three azocalix[4]arenes **5a–c** are connected via diazo coupling reaction in *cone* conformation and compared with the extraction properties of both compounds.

In continuation of our work, our research group has been also interested in the designing selective coloring chemosensor towards specific metal cations. In the end, we found an outstanding result that combinational use of the compounds **5a–c** are able to selectively discriminate metal ions.

Experimental

Chemicals

All of the chemical reagents and solvents used were of analytical grade purity and used without further purification. All aqueous solutions were prepared with deionized water purified by human power plus I + UV water purification system.

Instrumentation

Melting points were measured using an Electrothermal IA9100 digital melting point apparatus in capillaries sealed under nitrogen and were uncorrected. ^{1}H NMR spectra were referenced to tetramethylsilane (TMS) at 0.00 ppm as internal standard solution and recorded on a Bruker 400 MHz spectrometer at room temperature (25 ± 1 °C).

IR spectra were recorded by a Mattson 1000 FTIR spectrometer as KBr pellets. UV–Vis spectra were recorded by a Shimadzu 1601 UV–Visible spectrophotometer. The elemental analyses were performed in the The Scientific and Technological Research Council of Turkey (TUBITAK) Laboratories.

Synthesis

The synthesis of bisazocalix[4]arene derivatives **5a–c** were depicted in Scheme 1. Our synthesis began *p-tert*-butylcalix[4]arene and their dibenzoyl ester **1** were obtained in literature [20, 21]. First, 11,23-di(*p-tert*-butyl)calix[4]arene dibenzoyl ester **2** was prepared by debutylation of calix 4arene **1**. Secondly, the synthesized calix 4arene **2** was hydrolized by NaOH in THF/Water/EtOH [22].

After then, the synthesis of azocalix[4]arenes **4a–c** were coupled with 11,23-di(*tert*-butyl)calix[4]arene **3** followed by diazo coupling reaction using 4-methoxy, 4-ethyl and 4-nitro aniline in HCl and NaNO$_2$ in DMF and THF gave the desired product **4** [23]. AlCl$_3$-catalyzed debutylation reaction of azocalixarenes **4a–c** with toluene/phenol in the Click condition afforded the 5,17-bis(*p*-substituephenyl)azocalix[4]arenes **5a–c** in 68–83 % yield [22]. Azocalixarene **5a** was synthesized in 79 % yield from azocalixarene **4a**. Compound 5c was purified by column chromatography from calix[4]aren [24].

*25,26,27,28-Tetrahydroxy-5,17-(4-methoxyphenylazo)calix[4]arene (**5a**)*

A mixture of compound **4a** (1 g, 1.24 mmol), phenol (1.17 g, 12.42 mmol) and AlCl$_3$ (2.15 g, 16.15 mmol) in 100 mL of toluene was stirred at room temperature for 24 h. HCl (50 mL, 0.2 M) was added dropwise into the toluene solution. The toluene phase was separated and washed with water (3 × 50 mL), and the combined organic phases evaporated to dryness. The residue was precipitated with MeOH (100 mL). After removal of solvents, the crude mixture was crystallized with CHCl$_3$/CH$_3$OH (50 mL, 2:3 v/v)) to give 0.68 g of compound **5a** (79 %), brown precipitate, m.p. (318 °C (dec.)). Found: C: 72.96 %; H: 5.17 % N: 7.98 %; C$_{42}$H$_{36}$N$_4$O$_6$ requires C: 72.82 %; H: 5.24 % N: 8.09 %. IR (KBr) υ: 1,458 cm^{-1} (–N=N). ^{1}H-NMR (CDCl$_3$, 25 °C) δ$_H$: 3.67 (s, 4H, Ar**CH**$_2$Ar), 3.85 (s, 6H, –**OCH$_3$**), 4.31 (s, 4H, Ar**CH**$_2$Ar), 6.79 (t, $J = 7.56$ Hz, 2H, Ar**H**), 6.95 (d, $J = 9.05$ Hz, 4H, Ar**H**), 7.18 (d, $J = 7.60$ Hz, 4H, Ar**H**), 7.65 (s, 4H, Ar**H**), 7.80 (d, $J = 9.07$ Hz, 4H, Ar**H**), 10.21 (s, 4H, Ar**OH**).

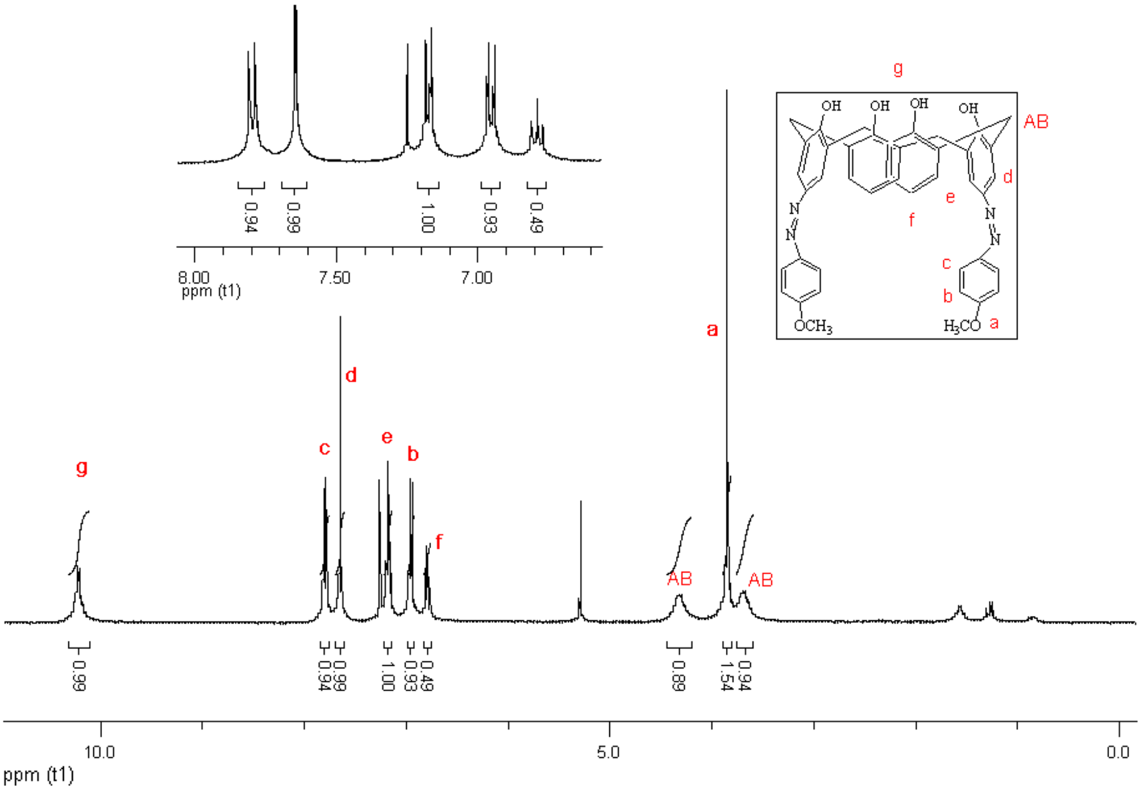


Fig. 1 ^{1}H-NMR Spectrum of 5,17-bis(4-methoxyphenyl)azocalix[4]arene **5a**

*25,26,27,28-Tetrahydroxy-5,17-(4-ethylphenylazo)calix[4]arene (**5b**)*

Azocalix[4]arene **5b** was prepared as described for **5a** using phenol, $AlCl_3$ and toluene and obtained which was filtered, washed with water, precipitated with MeOH, crystallized with $CHCl_3/CH_3OH$ (50 mL, 2:3 v/v). The resulting solid was a dark orange product (yield, 0.71 g (83 %), m.p. (295 °C (dec.)). Found: C: 76.85 %; H: 5.79 % N: 8.07 %; $C_{44}H_{40}N_4O_4$ requires C: 76.72 %; H: 5.85 % N: 8.13 %. IR (KBr) υ: 1,458 cm^{-1} (–N=N). ^1H-NMR ($CDCl_3$, 25 °C) δ_H: 1.26 (t, $J = 7.53$ Hz, 6H, CH_2-**CH_3**), 2.70 (q, $J = 7.45$ Hz, 4H, **CH_2**CH_3), 3.69 (s, 4H, Ar**CH_2**Ar), 4.31 (s, 4H, Ar**CH_2**Ar), 6.80 (t, $J = 7.54$ Hz, 2H, Ar**H**), 7.19 (d, $J = 7.57$ Hz, 4H, Ar**H**), 7.28 (d, $J = 8.22$ Hz, 4H, Ar**H**), 7.69 (s, 4H, Ar**H**), 7.74 (d, $J = 8.27$ Hz, 4H, Ar**H**), 10.23 (s, 4H, Ar**OH**).

*25,26,27,28-Tetrahydroxy-5,17-(4-nitrophenylazo)calix[4]arene (**5c**)*

Azocalix 4arene **5c** was prepared as described for **5a** using phenol, $AlCl_3$ and toluene and obtained which was filtered, washed with water, precipitated with MeOH, crystallized with $CHCl_3/CH_3OH$ (50 mL, 2:3 v/v). The resulting solid was a dark brown product (yield, 0.59 g (68 %), m.p. (312 °C (dec.)). Found: C: 66.55 %; H: 4.09 % N: 11.52 %; $C_{40}H_{30}N_6O_8$ requires C: 66.48 %; H: 4.18 % N: 11.63 %. IR (KBr) υ: 1,458 cm^{-1} (–N=N). ^1H-NMR ($CDCl_3$, 25 °C) δ_H: 3.75 (s, 4H, Ar**CH_2**Ar), 4.37 (s, 4H, Ar**CH_2**Ar), 6.86 (t, $J = 7.59$ Hz, 2H, Ar**H**), 7.23 (d, $J = 7.61$ Hz, 4H, Ar**H**), 7.78 (s, 4H, Ar**H**), 7.94 (d, $J = 9.08$ Hz, 4H, Ar**H**), 8.36 (d, $J = 9.08$ Hz, 4H, Ar**H**), 10.23 (s, 4H, Ar**OH**).

Result and discussion

The molecular structure of bisazocalix[4]arenes **5a–c** given in Scheme 1 were in agreement with the data obtained from micro analysis. Besides the structures of all these azocalix[4]arenes **5a–c** were also certified by traditional organic spectroscopic identification (^1H-NMR and FTIR spectra). They confirmed the structures to be in *cone* conformations.

The ^1H NMR spectrum of the azocalix[4]arene **5a** exists in a *cone* conformation was deduced from the presence of two set of characteristic AB systems at 3.67 and 4.31 ppm respectively. On the basis of spectroscopic evidence, molecular structure of compounds **5a** is within *cone* conformation (Fig. 1).

^1H NMR data all of the bisazocalix[4]arenes **5a–c** showed that a peak due to the presence of aromatic protons (phenylazo) were observable at the chemical shift

Table 1 Extraction of metal picrates with bisazocalix[4]arene derivatives **5a–c**

	Picrate salt extracted (%)									
Ligand	Sr^{2+}	Ag^+	Hg^+	Hg^{2+}	Co^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}	Cr^{3+}	Al^{3+}
5a	<3.0	9.7	30.7	39.8	<3.0	<3.0	<3.0	<3.0	9.6	6.6
5b	<3.0	12.8	35.8	40.3	<3.0	<3.0	<3.0	<3.0	17.5	12.1
5c	<3.0	10.1	29.6	38.1	<3.0	<3.0	<3.0	<3.0	10.6	8.1

$H_2O/CHCl_3 = 10/10$ mL (v/v): picric acid = 2×10^{-5} *M*, ligand = 1×10^{-3} *M*, metal nitrate = 1×10^{-2} *M*; 298 K, 1 h contact time. Experimental error was ±2 %

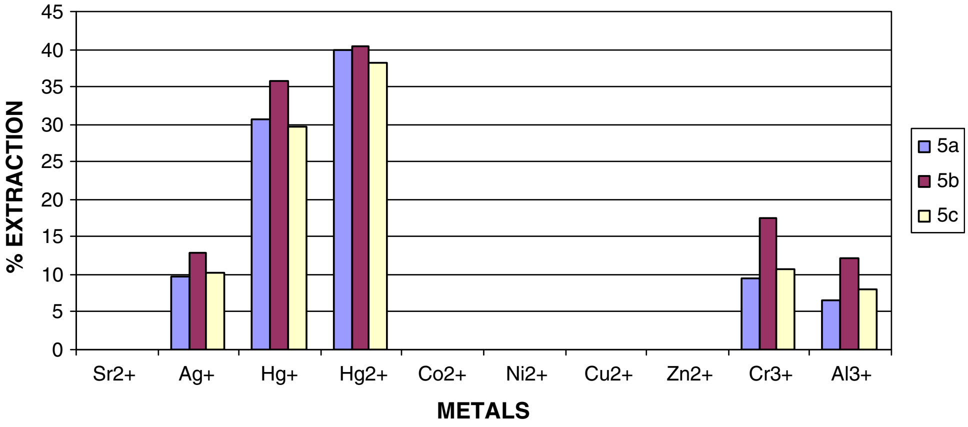


Fig. 2 Extraction percentages of azocalix[4]arene derivatives **5a–c**

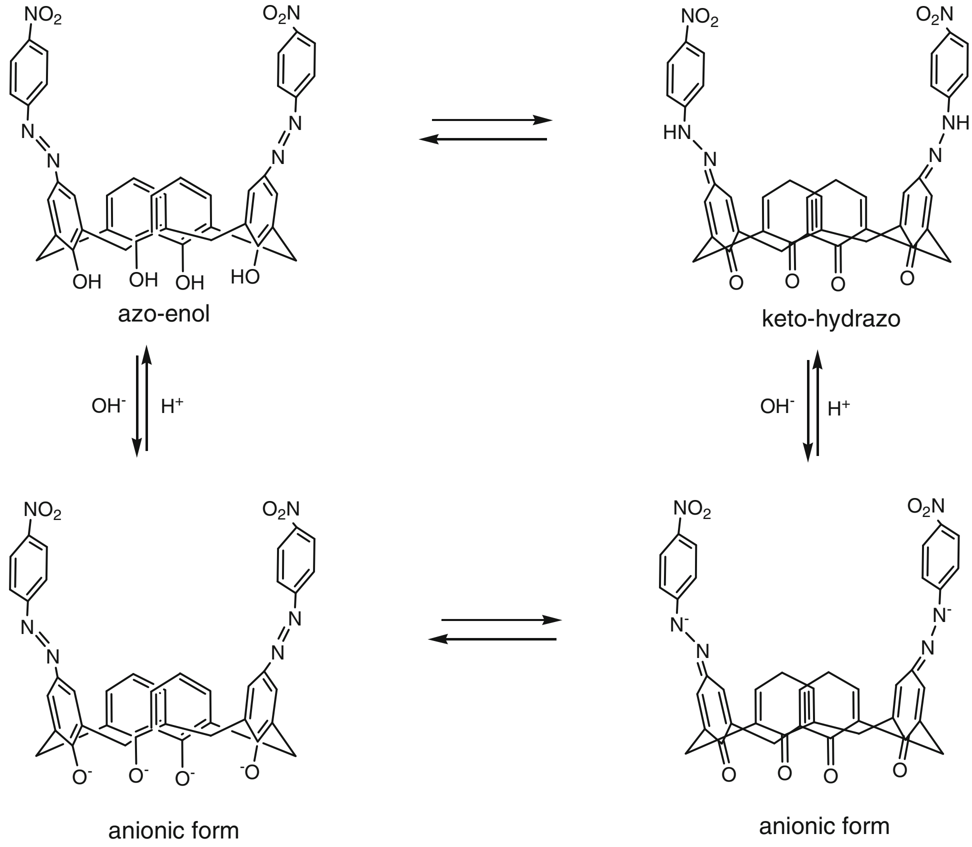
$\delta = 6.95$–7.80 ppm for methoxy-, 7.28–7.74 ppm for ethyl- and 7.94–8.36 ppm for nitro-, respectively. However, the appearance of a peak within the range of $\delta = 6.79$, 7.18 and 7.65 ppm were due to the presence of proton of core calixarene aromatic group for azocalix[4]arene **5a**.

In the ^{1}H NMR spectra of the bisazocalix[4]arenes **5a–c**, the singlets in the 10.21 and 10.23 ppm area can be attributed to the proton of the –OH groups. In addition, the 4-ethyl moiety of azocalix[4]arene **5b** are shown at 1.26 ppm methyl and 2.70 ppm methylene protons as a triplet and quarted, respectively. The methoxy (–OCH_3) groups of **5a** is shown at 3.85 ppm as a singlet too (Fig. 1). The OH peaks disappear together with addition of the D_2O.

The ionophoric properties of the bisazocalix[4]arenes **5a–c** towards the metal cations were investigated by the picrate extraction method [15–17]. The results expressed as a percentage of cation extracted (E%) are collected in Table 1 and shown graphically in Fig. 2.

The extractions of these cations (Sr^{2+}, Ag^+, Hg^+, Hg^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cr^{3+} and Al^{3+}) with bisazocalix[4]arenes **5a–c** have been performed using previously reported method in same experimental conditions. Unlike the calix[4]arene used in the previously studies contained –N=N– functional groups, in this study the bisazocalix[4]arene derivatives containing electron-donating and withdrawing groups such as methoxy-, ethyl- and nitro-groups have been selected. The reason why these

Fig. 3 Color changes corresponding to different pH values [0.01 g of **5c** in $CHCl_3$–CH_3OH–H_2O (200 mL, 1:1:8 v/v)]



Scheme 2 The azo-enol and keto-hydrazo tautomer form of bisazocalix[4]arene **5c**

bisazocalix[4]arenes are selected. Because, these functional groups are containing the electron-donating and electron-withdrawing groups. This situation increases or decrease the efficiency of extraction. This is mainly due to the positive or negative effect of these functional groups on electron density leading higher efficiencies of extraction. Besides a comparison with our data is corrected, some remarks can be made. While the extraction levels [35.8 % Hg^+ and 40.3 % Hg^{2+}] for **5b** are very superior to the extraction levels [30.7 % Hg^+ and 39.8 % Hg^{2+}] and [29.6 % Hg^+ and 38.1 % Hg^{2+}] for **5a** and **5c** respectively. Compound **5b** contain electron-donating group which preferres superior to soft metal (Hg^{2+}) cation than compounds **5a** and **5c**. It can be explained by the (hard–soft) acid–base (HSAB) principle.

On the other hand, the complexation ability of azocalix[4]arens toward transition metal cations has been reported in the literature [25]. We titrated 0.01 g of bisazocalix[4]arene **5c** in $CHCl_3$–CH_3OH–H_2O (200 mL, 1:1:8 v/v)] with dilute aqueous HCl/NaOH (1.25×10^{-4} M) at room temperature. The observed color change may be ascribed to the protonation or deprotonation of the phenol, –N=N–, $-NO_2$ moiety (Fig. 3).

The visible color changes of bisazocalix[4]arene **5c** upon different pH values were also observed and depicted. The color of **5c** solution turned orange to dark red in the presence of acid–base solution. In this unique point of view with visual color changes, it is surprising that only we can consequently demonstrate the screening process of the unknown pH (about 2 and 12) with following two steps and simple screening of its color change with '*naked eye*' is given in Fig. 3.

The color change of the solution has been observed for the very popular phenylazo bisazocalix[4]arene **5c** when dilute aqueous HCl/NaOH had separately been added in excess. These observations imply that there is a subtle balance between in base-induced release of protons from the azophenols to the quinone tautomer. Moreover, the nitro-substituents of the phenylazo groups must have strong influence on the tautomerism of azo/hydrazo, thus showing very diverse λ_{max} shifts. A base-induced tautomerism of the bisazocalix[4]arene **5c** is shown in Scheme 2.

Conclusion

In summary, we have successfully synthesized and investigated compounds **5a–c** as mercury-ion selective sensor based on metal picrate extraction, pH change, ^1H NMR and FTIR spectra. The present paper demonstrated that we have developed a new bisazo calix[4]arene sensor with bisazo and core cavity as the metal ion binding sites as the signal transduction unit, which showed selective of Hg^{2+} cation. The bisazocalix[4]arene **5c** gives rise to a large bathochromic shift in the absorption spectrum with different pH values (from yellow to dark red), which is clearly visible to the *naked eye*. NMR spectral analysis also verifies the formation of intended synthesis.

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References

1. Halouani, H., Dumazet-Bonnamour, I., Lamartine, R.: Synthesis of novel chromogenic bi- and tri-functionalized calix[4]arenes. Tetrahedron Lett. **43**, 3785–3788 (2002)
2. Kim, J.Y., Kim, G., Kim, C.R., Lee, S.H., Lee, J.H., Kim, J.S.: UV band splitting of chromogenic azo-coupled calix[4]crown upon cation complexation. J. Org. Chem. **68**, 1933–1937 (2003)
3. Chawla, H.M., Singh, S.P., Upreti, S.: Synthesis of calix[4]arene(amido)monocrowns and their photoresponsive derivatives. Tetrahedron **62**, 9758–9768 (2006)
4. Shinkai, S., Araki, K., Shibata, J., Manabe, O.: Autoaccelerative diazo coupling with calix[4]arene—unusual co-operativty of the calixarene hydroxy-groups. J. Chem. Soc. Perkin Trans. **1**, 195–196 (1989)
5. Deligöz, H.: Azocalixarenes: synthesis, characterization, complexation, extraction, absorption properties and thermal behaviours. J. Incl. Phenom. Macrocycl. Chem. **55**, 197–218 (2006)
6. Buhlmann, P., Pretsch, E., Bakker, E.: Carrier-based ion-selective electrodes and bulk optodes. 2. Ionophores for potentiometric and optical sensors. Chem. Rev. **98**, 1593–1687 (1998)
7. Gunnlaugsson, T., Leonard, J.P., Murray, N.S.: Highly selective colorimetric naked-eye Cu(II) detection using an azobenzene chemosensor. Org. Lett. **6**, 1557–1560 (2004)
8. Jiang, P., Guo, Z.: Fluorescent detection of zinc in biological systems: recent development on the design of chemosensors and biosensors. Coord. Chem. Rev. **248**, 205–229 (2004)
9. Lehn, J.-M.: Toward self-organization and complex matter. Science **295**, 2400–2403 (2002)
10. Alfieri, C., Dradi, E., Pochini, A., Ungaro, R., Andreetti, G.D.: Synthesis, and X-ray crystal and molecular-structure of a novel macrobi-cyclic ligand—crowned para-tert-butyl-calix[4]arene. J. Chem. Soc. Chem. Commun. **19**, 1075–1077 (1983)
11. Casnati, A., Ungaro, R., Asfari, Z., Vicens, J.: In Calixarenes 2001, Asfari, Z., Böhmer, V., Harrowfield, J., Vicens, J (eds.), pp. 365–384. Kluwer Academic Publishers, Dordrecht (2001)
12. Oueslati, I.: Calix(aza)crowns: synthesis, recognition, and coordination. A mini review. Tetrahedron **63**, 10840–10851 (2007)
13. Deligöz, H., Yılmaz, M.: Selective complexation of Na^+ by polymeric calix[4]arene tetraesters. J. Polym. Sci. Part A: Polym. Chem. **33**, 2851–2853 (1995)
14. Deligöz, H., Yılmaz, M.: Synthesis of polymer-supported calix[4]arenes and selective extraction of Fe^{3+}. React. Funct. Polym. **31**, 81–88 (1996)
15. Yılmaz, M., Deligöz, H.: Selective extraction of Fe^{3+} cation by callxarene-based cyclic ligands. Sep. Sci. Technol. **31**, 2395–2402 (1996)
16. Deligoz, H., Yilmaz, M.: Liquid–liquid-extraction of transition-metal cations by calixarene based cyclic ligands. Solvent Extr. Ion Exch. **13**, 19–26 (1995)
17. Qazia, M.A., Ocak, Ü., Ocak, M., Memon, S.: An excellent copper selective chemosensor based on calix[4]arene framework. Anal. Chim. Acta **761**, 157–168 (2013)

18. Oueslati, I., Thuéry, P., Shkurenko, O., Suwinska, K., Harrowfield, J.M., Abidi, R., Vicens, J.: Calix[4]azacrowns: self-assembly and effect of chain length and *O*-alkylation on their metal ion-binding properties. Tetrahedron **63**, 62–70 (2007)
19. Rostovtsev, V.V., Green, L.G., Fokin, V.V., Sharpless, K.B.: A stepwise huisgen cycloaddition process: copper(I)-catalyzed regioselective “ligation” of azides and terminal alkynes. Angew. Chem. Int. Ed. **41**, 2596–2599 (2002)
20. Gutsche, C.D., Iqbal, M.: Para-tert-butylcalix[4]arene. Org. Synth. **68**, 234–238 (1990)
21. Dalbavie, J.-O., Regnouf-de-Vains, J.-B., Lamartine, R., Lecocq, S., Perrin, M.: Complexation of cobalt(II) at the upper rim of two new calix[4]arene/bipyridine-based podands. Eur. J. Inorg. Chem. **4**, 683–691 (2000)
22. Gutsche, C.D., Iqbal, M., Stewart, D.: Calixarenes. 18. Synthesis procedures for *p*-tert-butylcalix[4]arene. J. Org. Chem. **51**, 742–745 (1986)
23. Elçin, S., Deligöz, H.: Di-substituted azocalix[4]arenes containing chromogenic groups: synthesis, characterization, extraction, and thermal behavior. Tetrahedron **69**, 6832–6838 (2013)
24. Jin, C.M., Lu, G.Y., Liu, Y., You, X.Z., Wang, Z.H., Wu, H.M.: Synthesis of (*p*-substituted phenyl)azocalix[4]arenes. Chin. J. Chem. **22**, 1080–1087 (2002)
25. Leilei, L., Zhigang, R., Hongxi, L., Hai, S., Jianping, L.: 5,11,17,23-Tetrakis[(*p*-carboxyphenyl)azo]-25,26,27,28-tetrahydroxy calix[4]arene: crystal structure and pH sensing properties. Chin. J. Chem. **28**, 1829–1834 (2010)